The Hong Kong Polytechnic University

Department of Applied Biology and Chemical Technology

Design of Highly Efficient Catalyst for Transition-Metal Catalyzed Cross-Coupling Processes

By

Chau-Ming SO

A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Doctor of Philosophy

August, 2010

Declaration

I hereby declare that this thesis is my own work and that, to the best of my knowledge and belief, it reproduces no material previously published or written, nor material that has been accepted for the award of any other degree or diploma, except where due acknowledgement has been made in the text.

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Chau-Ming SO

August, 2010

Abstract of thesis entitled “Design of Highly Efficient Catalyst for Transition-Metal Catalyzed Cross-Coupling Processes”

Submitted by Chau-Ming SO

for the Degree of Doctor of Philosophy

at The Hong Kong Polytechnic University

in August, 2010

Abstract

A new family of monodentate phosphine ligands based on the use of indole as the ligand template were designed and synthesized. These ligand templates are inexpensive, readily available and highly diversified. This family of ligand scaffold could be easily prepared and diversified from inexpensive arylhydrazines and substituted acetophenones by straightforward Fischer-Indolization. Two classes of ligands, N-P bound amino-phosphine ligands and C-P bound phosphine ligands, were synthesized and derivatized by using a modular approach.

The amino-phosphine ligands had exhibited exceedingly high activity in the Suzuki-Miyaura coupling of aryl chlorides. The sterically hindered and deactivated aryl chlorides with arylboronic acid could cross-coupling to afford the biaryl products in excellent yields. The catalyst bearing the amino-phosphine ligand could achieve very low catalyst loading in the Suzuki coupling reaction.

The Pd-C-P type indolyl phosphine complexes in which the phosphine group (-PPh_2 or -PCy_2) was attached at the C-3 position were also highly active towards the Suzuki-Miyaura coupling of aryl chlorides. The Pd/CPPh o-Andole-phos and Pd/CPPh α -Nadole-phos could catalyze the tetra-*ortho*-substituted biaryl coupling reaction.

The Pd-C-P type indolyl phosphine complexes in which the phosphine group was attached at the ortho position of the bottom ring were highly active towards coupling reactions of aryl tosylates and previously unexplored aryl mesylates. This Pd/CM-Phos catalytic systems showed good to excellent catalytic activity in the Suzuki coupling reaction, amination reaction, and Hiyama coupling reaction of the aryl tosylates and/or aryl mesylates.

Publications

So, C. M.; Lau, C. P.; Kwong, F. Y., Easily Accessible and Highly Tunable Indolyl Phosphine Ligands for Suzuki-Miyaura Coupling of Aryl Chlorides, *Organic Letters* **2007**, *9*, 2795-2798.

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So, C. M.; Lau, C. P.; Kwong, F. Y., Palladium-Catalyzed Direct Arylations of Heteroarenes with Aryl Mesylates, *Chemistry – A European Journal* **2010**, *in press.*

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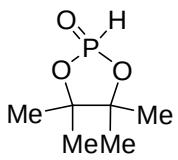
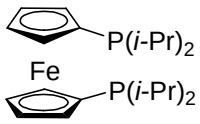
Abbreviations

δ	Chemical shift (NMR)
η	Descriptor for hapticity
υ	Frequency
m/z	Mass-to-charge ratio
s	Singlet
d	Doublet
t	Triplet
q	Quartet
m	Multiplet
GC	Gas chromatography
HRMS	High resolution mass spectroscopy
MS	Mass spectrometry
IR	Infra-red
NMR	Nuclear magnetic resonance spectroscopy
equvi.	Equivalent
h	Hour
rt	Room temperature
L	Generalized ligand, in particular a $2e^-$ ligand
L_nM	Generalized metal fragment with n ligands
THF	Tetrahydrofuran
MeOH	Methanol
EtOH	Ethanol
Et_2O	Diethyl ether
EA	Ethyl acetate
DMF	Dimethyl formamide
DCE	1,2-Dichloroethane
DCM	Dichloromethane
$ClPPh_2$	Chlorodiphenylphosphine
$ClPCy_2$	Chlorodicyclohexylphosphine
Cl*P*t-Bu_2	Di-*tert*-butylchorophosphine

n-BuLi	*n*-Butyllithium
t-BuLi	*tert*-Butyllithium
R	Generalized alkyl group
Me	Methyl
Et	Ethyl
n-Bu	*n*-butyl
i-Pr	Isopropyl
t-Bu	*t*-butyl
Ar	Aryl
Ph	Phenyl
Bn	Benzyl
Cy	Cyclohexyl
Cp	Cyclopentadienyl
TBAF	Tetrabutylammonium fluoride
OTf	Trifluoromethanesulfonate
OTs	*p*-Toluenesulfonate
OMs	Methanesulfonate
ONf	Nonafluorobutanesulfonate
NHC	N-Heterocyclic Carbene
PPh_3	Triphenylphosphine
P(*o*-tol)	Tri-*ortho*-tolylphosphine
PCy_3	Tricyclohexylphosphine
P(*t*-Bu)$_3$	Tri-*tert*-butylphosphine
Dppm	Bis(diphenylphosphino)methane
Dppe	1,1'-Bis-(diphenylphosphino)ethane
Dppp	1,1'-Bis-(diphenylphosphino)propane
Dppb	1,1'-Bis-(diphenylphosphino)butane
Dppf	1,1'-Bis-(diphenylphosphino)ferrocene
BINAP	2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl
PinP(O)H	

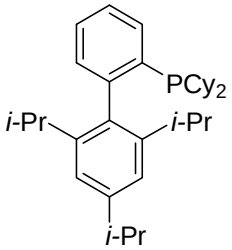
4,4,5,5-Tetramethyl-1,3,2-dioxaphospholane 2-oxide

dipf



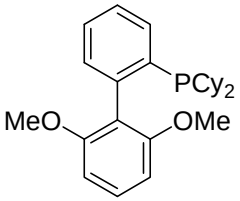
1,1'-bis(diisopropylphosphino)ferrocene

X-Phos



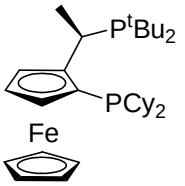
2-Dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl

S-Phos



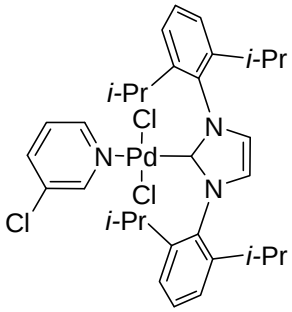
2-Dicyclohexylphosphino-2',6'-dimethoxybiphenyl

CyPF-*t*-Bu



(*R*)-(–)-1-[(*S*)-2-(diphenylphosphino)ferrocenyl]ethyldi-*t*-butyl phosphine

PEPPSI-IPr Complex

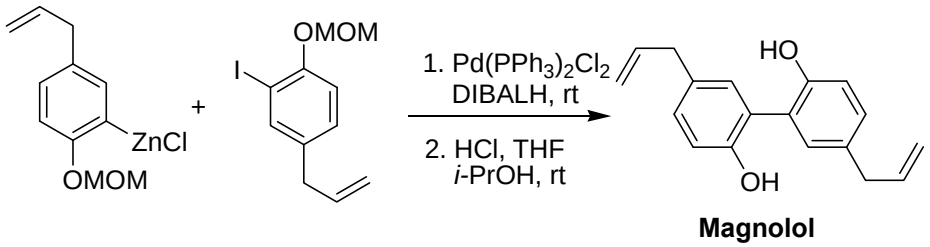


[1,3-Bis(2,6-Diisopropylphenyl)imidazol-2-ylidene](3-chloropyridyl)palladium(II) dichloride

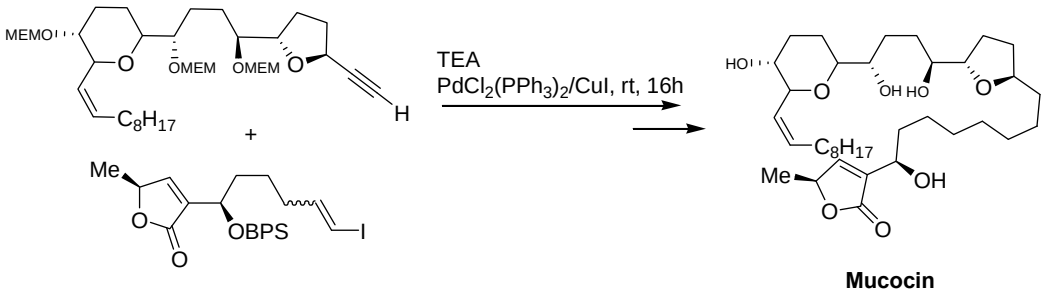
Chapter 1 Introduction

1.1 Background

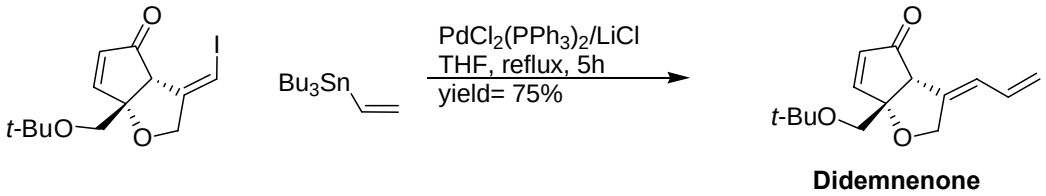
Aryl-aryl bond formation is one of the most important tools in modern organic synthesis. These bonds are very often found in natural products such as alkaloids, as well as in numerous biologically active parts of pharmaceutical, medicinal and agrochemical specialties. Also, many commercial dyes and organic conductors/semiconductors consist of several aromatic rings to polyaromatics. The exploration and development of both new and general catalytic methods for organic synthesis as well as biosynthesis remain at the center of modern day organic chemistry. In order to form carbon-carbon or/and carbon-heteroatom bond between unsaturated groups, several transition metal-catalyzed cross-coupling reactions such as Kharash coupling, Ullmann coupling, Negishi coupling, Stille coupling, Kumada coupling, Suzuki-Miyaura coupling, Hiyama coupling, Liebeskind–Srogl coupling and Buchwald–Hartwig amination were developed.[1-3] The applications of C-C bond cross-coupling to the synthesis of diversified natural products are well demonstrated, for examples, Magnolol (from Negishi-coupling),[4] Didemnenone (from Stille-coupling)[5], and Mucocin (from Sonogashira-coupling).[6]



Scheme 1.1 Magnolol synthesized by Negishi coupling



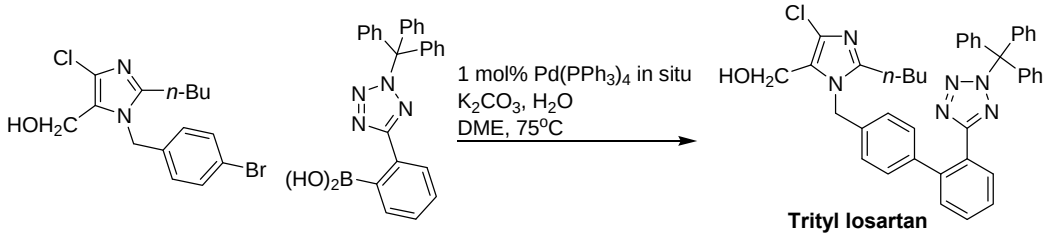
Scheme 1.2 Mucocin synthesized by Sonogashira coupling



Scheme 1.3 Didemnenone synthesized by Stille coupling

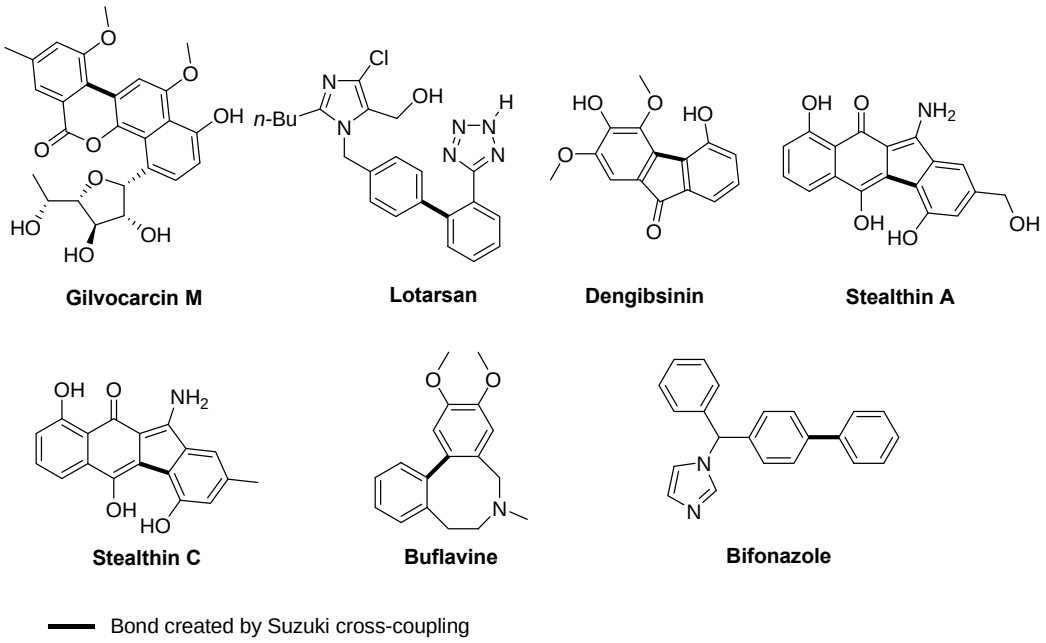
1.1.1 Applications of Suzuki-Miyaura Coupling

Among these methods, Suzuki coupling reaction is one of the most successful methods which have been applied to the synthesis of many important products. For examples, Smith *et al.* in 1994 studied the use of Suzuki coupling reaction to synthesize trityl losartan (Scheme 1.4), which belongs to a new class of drugs (angiotensin II receptor antagonists) and was developed to treat high blood pressure and heart failure.[7]

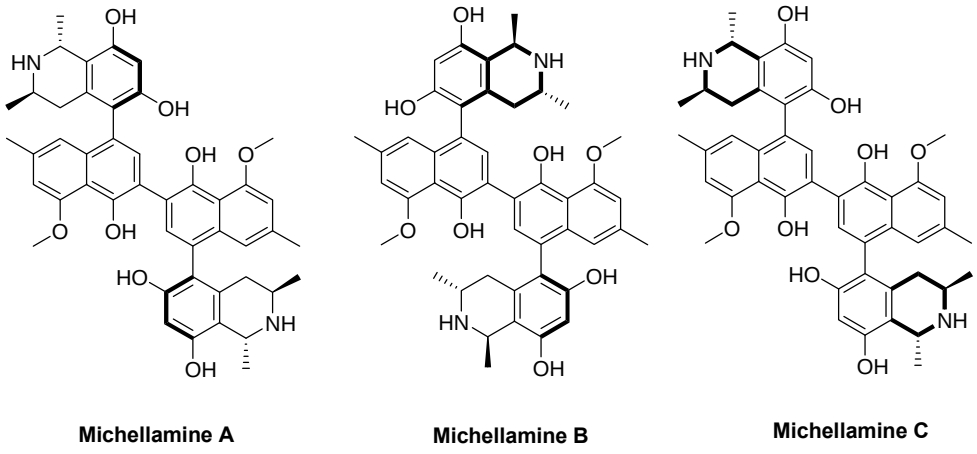


Scheme 1.4 Suzuki coupling reaction to synthesize the trityl losartan

Suzuki cross couplings were also applied in the syntheses of many natural products and biologically active compounds[8-17] since biaryls are often included in those compounds such as the synthesis of gilvocarcin M,[8,9] lotarsan,[10-13] dengibsinin,[14] stealthins A, stealthins C,[15] buflavine,[16] and bifonazole[17] (Scheme 1.5).



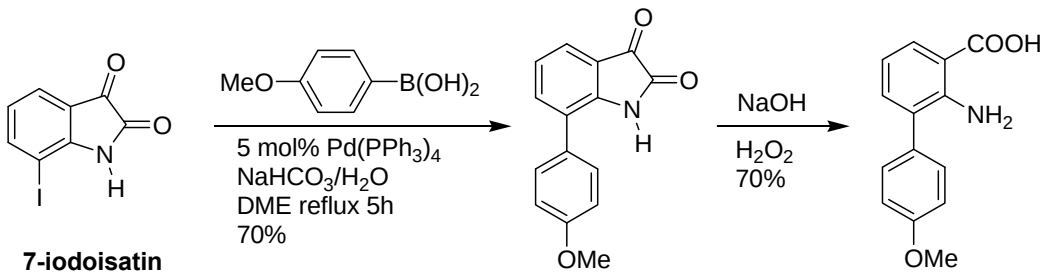
Scheme 1.5 Natural compounds synthesized by Suzuki coupling reaction



Scheme 1.6 Michellamines synthesized by Suzuki coupling reaction

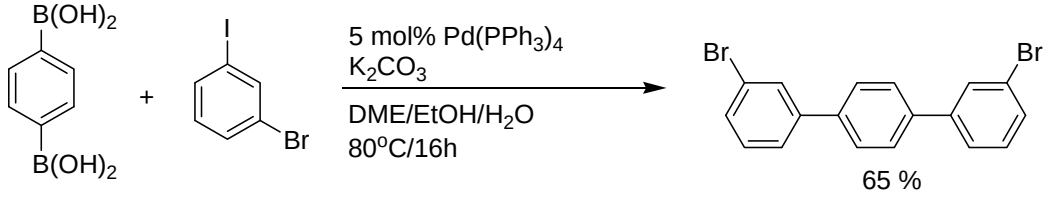
The synthesis of michellamines A, B, and C that showed activity against HIV (Scheme 1.6) can be quoted as a particular example.[18-22] Recently, the application of Suzuki cross coupling to 7-iodoisatin prepared from iodoaniline

enabled the synthesis of biarylamino acids (Scheme 1.7).[23]



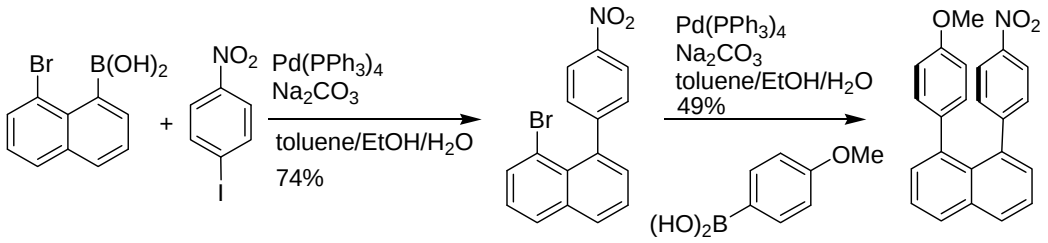
Scheme 1.7 7-Iodoisatin synthesized by Suzuki coupling

Apart from the synthesis of drugs, natural products and biologically active compounds, Suzuki cross coupling can also be applied to synthesize advanced materials. For example, the physical and electronic properties of fused polycyclic aromatics such as liquid crystal are interesting for electronic applications. In 1995, Hird *et al.* developed an efficient synthetic route to unsymmetrical triphenylene mesogens.[24] In 1997, Abell *et al.* synthesized terphenyls (Scheme 1.8) from aromatic diboronic acids. This method has been applied to the synthesis of reactive liquid crystals.[25-26]



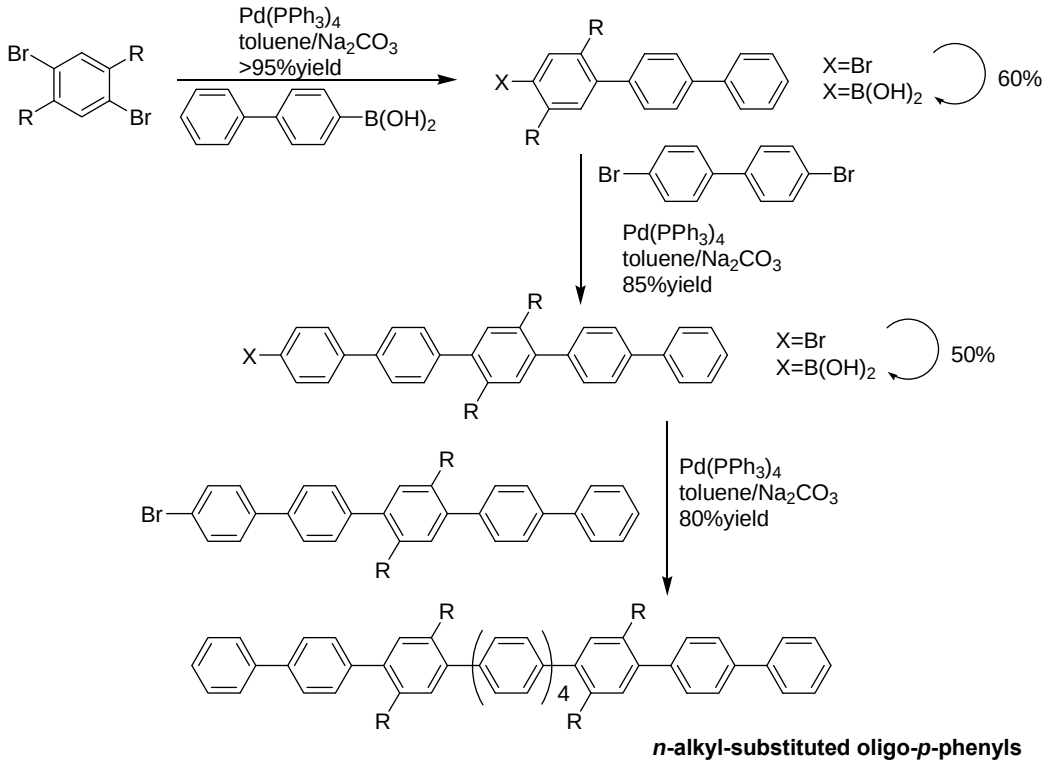
Scheme 1.8 Terphenyls synthesized by Suzuki coupling

Moreover, novel blue-transparent frequency doublers were prepared by the Suzuki cross coupling of naphthylboronic acids with aryl halides (Scheme 1.9).[27]



Scheme 1.9 Synthesis of 1-(4-methoxyphenyl)-8-(4-nitrophenyl)naphthalene

Polymer, one of the most useful materials, can also be synthesized by the Suzuki coupling reaction. Suzuki polycondensation, unlike other common synthetic method, focuses on the preparation of regiospecific aryl polymers with high molecular weights and various functional groups. For example, the Suzuki procedure has been applied to the preparation of oligo-*p*-phenyls as well as functionalized oligo-*p*-phenyls, which are model compounds for studying the spectroscopic and redox properties of polyaromatic systems. Galda and Rehahn[28] use 2,5-dialkyl-1,4-dibromobenzene derivatives and biphenylboronic acid in the heterogeneous system of toluene/Na_2CO_3 with catalytic amounts of $Pd(PPh_3)_4$ for the preparation of constitutionally homogeneous *n*-alkyl-substituted oligo-*p*-phenyls in excellent yields (Scheme 1.10).



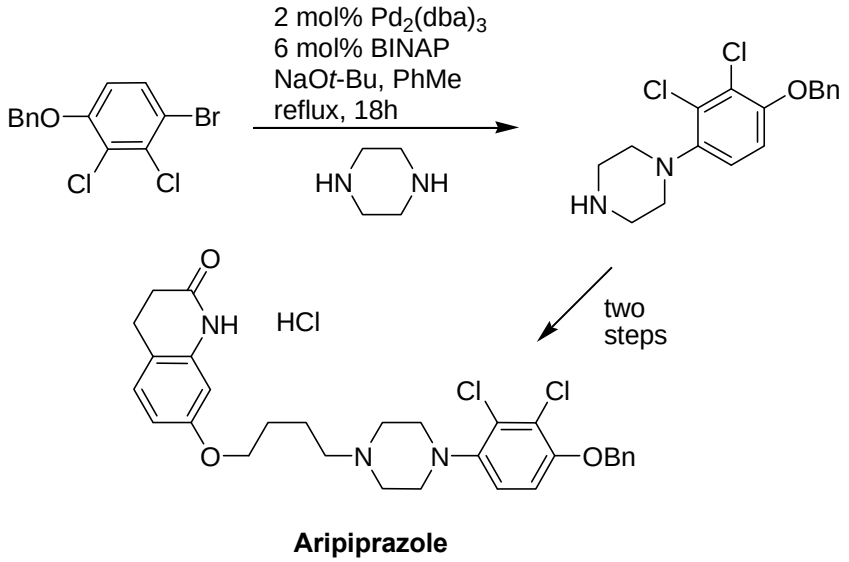
Scheme 1.10 *n*-Alkyl-substituted oligo-*p*-phenyls synthesized by Suzuki coupling

1.1.2 Applications of Buchwald-Hartwig Amination

Apart from biaryl-containing compounds, aromatic amines and heterocycles are also important in the application of pharmaceutical, medicinal, and material science. For example, N-arylpiperazines are common substructures of molecules that influence various biological processes.

Various research groups have studied the arylation of monoprotected and the single arylation of unprotected piperazines to synthesize N-arylpiperazines for further study. For example, Morita *et al.* used the catalytic carbon-nitrogen bond construction protocol in the synthesis of arylpiperazine metabolites of the

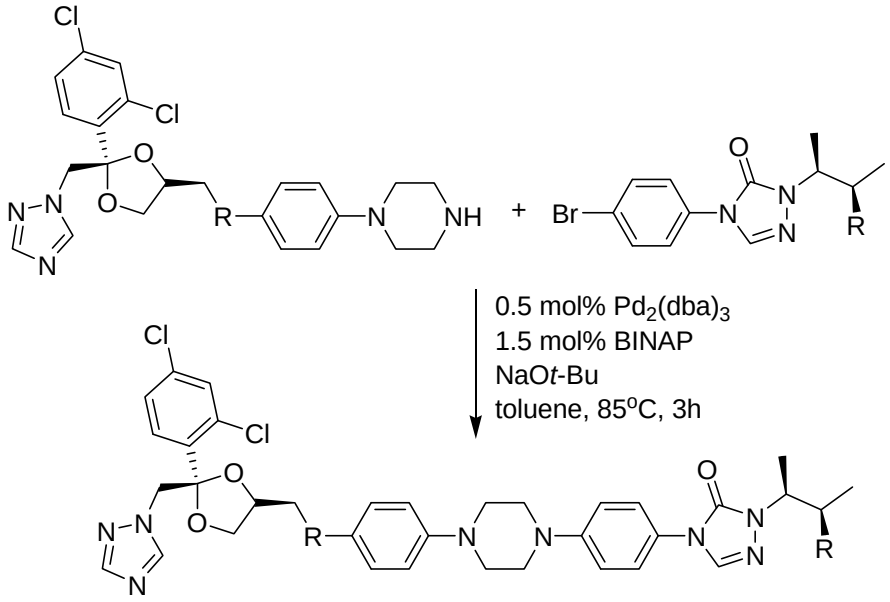
antipsychotic aripiprazole (Scheme 1.11). [29]



Aripiprazole

Scheme 1.11 Aripiprazole synthesized by amination reaction

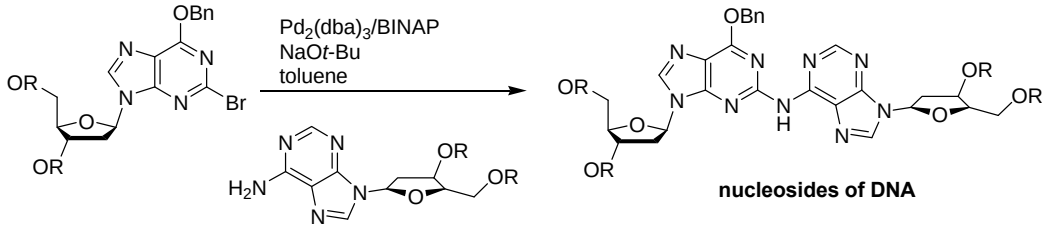
Scientists at Sepracor also used this catalyst for the key bond construction in the preparation of the antifungal hydroxyitraconazole (Scheme 1.12).[30]



Hydroxyitraconazole

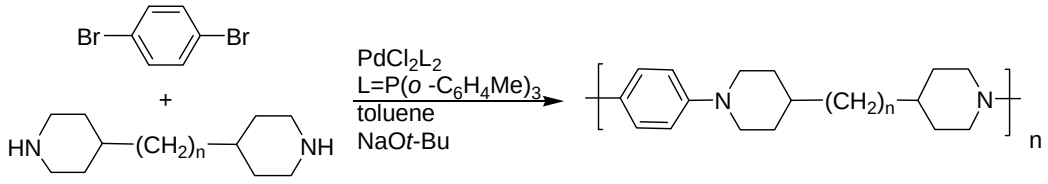
Scheme 1.12 Hydroxyitraconazole synthesized by amination reaction

Sigurdsson, Hopkins *et al.* used the palladium-catalyzed formation of diaryl amines to prepare nucleosides of damaged DNA(Scheme 1.13). [31]



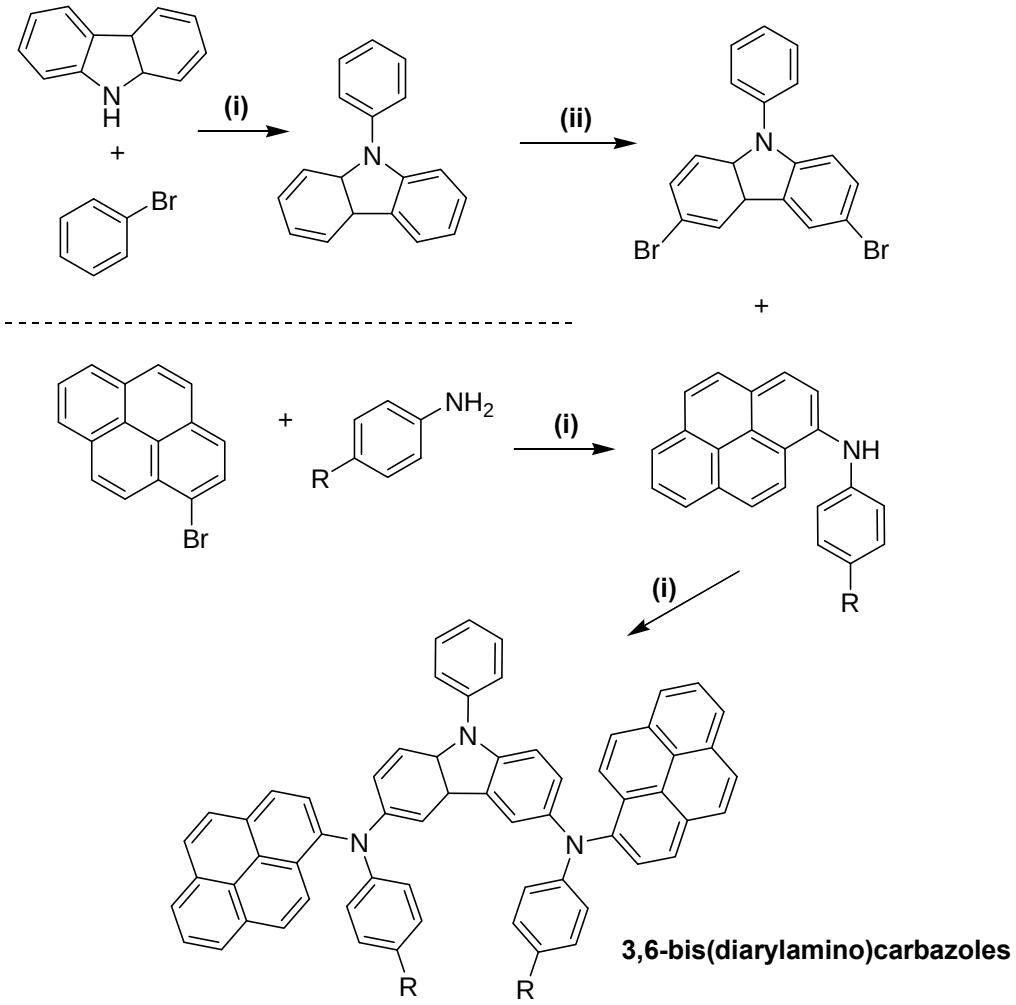
Scheme 1.13 Nucleosides synthesized by amination reaction

Arylamines are also favorable for materials science due to their electronic properties. They are readily oxidized to the aminium form, and this oxidation leads to conductivity in polyanilines, hole-transport properties in triarylamines, stable polyradicals with low-energy or ground-state high-spin states, and the potential to conduct electrochemical sensing. Therefore, the palladium-catalyzed formation of di- and triarylamines can be widely applied to access both small molecules and discrete oligomeric or polymeric macromolecules. For example, Hasegawa *et al.* used the initial amination of aryl halides with dialkylamines to prepare arylamine polymers by coupling a bifunctional diamine and a dihaloarene as shown in Scheme 1.14.[32] The highest molecular weights achieved were in the range of 5000-6000.



Scheme 1.14 Arylamine polymers synthesized by amination reaction

Palladium-catalyzed amination has also been used to prepare small arylamines that can function as sensors, nonlinear optical materials, magnetic materials, electrode modifiers, hole-transport materials, and dyestuffs. For example, Lin, Tao and co-workers used the palladium-catalyzed amination to synthesize the generated green light-emitting carbazole derivatives.[33] The synthesis pathway is shown in scheme 1.15.



(i) 2 mol% $Pd(dba)_2$, 2-3 mol% P(*t*-Bu)$_3$, 1.5 equiv. NaO*t*-Bu, toluene, 6h at 80^oC
(ii) NBS, DMF, 0^oC

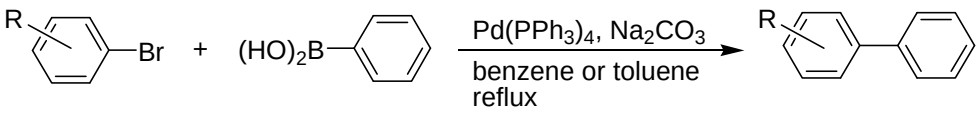
Scheme 1.15 Green light-emitting carbazole synthesized by amination reaction

1.2 Development of the Coupling Reactions and the Use of Aryl Triflates as Coupling Partner

These examples demonstrated the importance of the cross-coupling method in the synthetic organic, material, pharmaceutical, and medicinal chemistry. Cross-coupling reaction can be commonly referred as the use of a wide range of organometallic reagents and electrophiles to provide a common class of synthetic transformations, but our discussion will be mainly on the palladium-catalyzed Suzuki-Miyaura coupling (C-C bond formation) and Buchwald–Hartwig amination (C-N bond formation). Moreover, it will focus on the use and development of the aryl sulfonates (aryl triflates, aryl nonaflates, aryl tosylates and aryl mesylates) as the electrophiles in the coupling reaction.

1.2.1 Development of Suzuki-Miyaura Coupling Reaction

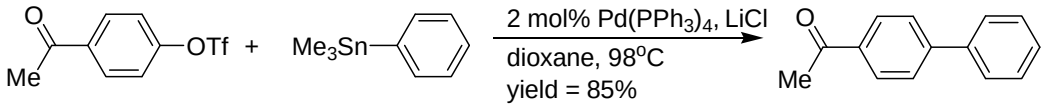
The first observation on the preparation of biaryls was reported in 1981 when Suzuki *et al.* reported the coupling of aryl iodides/bromides with phenylboronic acid in toluene or benzene by using $Pd(PPh_3)_4$ as catalyst and sodium carbonate as base (Scheme 1.16).



Scheme 1.16 The first Suzuki reaction reported in 1981

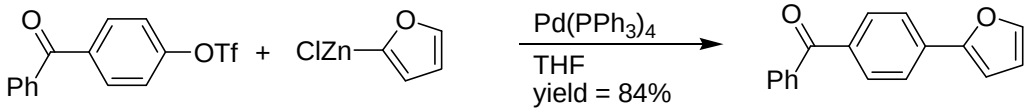
Various modifications were made to the reaction conditions after this discovery. A combination of $Pd(PPh_3)_4$ or $PdCl_2(PPh_3)_2$ and different kinds of base such as Et_3N,[34] $Na_2CO_{3(aq)}$,[35] $NaHCO_3$,[36] Cs_2CO_3,[37] Tl_2CO_3,[38] and K_3PO_4 was reported to work successfully for aryl iodides, and bromides. The palladium-catalyzed cross-coupling reaction of alkyl,[39] 1-alkenyl,[40] and arylboron[41,42] derivatives with organic halides such as alkyl,[43] 1-alkenyl, aryl, 1-alkynyl, allylic, and benzylic halides was reported afterwards.

Aryl triflates were found to be possible electrophiles for the aryl-aryl coupling reaction. In 1987, Stille *et al.* firstly reported the palladium-catalyzed aryl-aryl cross-coupling reaction of aryl triflates with organostannanes (Scheme 1.17).[44]



Scheme 1.17 The first palladium-catalyzed Stille coupling reaction of aryl triflates

Apart from coupling with organostannane, aryl triflates also undergo clean couplings with aluminum[45] and zinc (Scheme 1.18)[46].



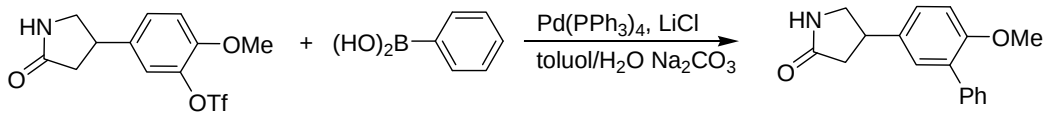
Scheme 1.18 Palladium-catalyzed Negishi coupling of aryl triflates

In fact, triflates are especially valuable as partners for the cross-coupling reaction, in part due to the easy access from phenols or carbonyl enolates that allows the regioselective formation of aryl and 1-alkenyl electrophiles.[47]

In particular, the easy preparation of cycloalkenyl triflates from cyclic ketones has a greater advantage over the synthesis of corresponding halides.

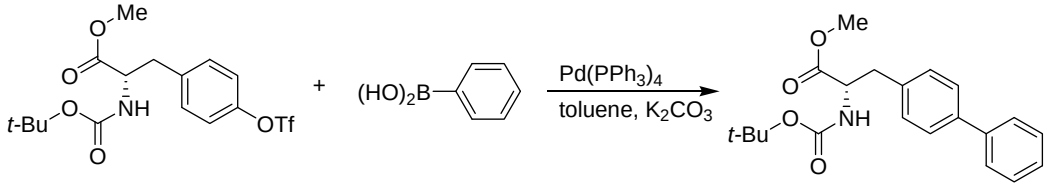
The successful examples of the coupling reaction of aryl triflates with nucleophiles (eg. $ArSnR_3$ and ArZnCl) and the usefulness of the aryl triflates in the coupling reaction prompted scientists to study the uses of the aryl triflates in the Suzuki coupling.

In 1989, Schumann *et al.* reported the use of aryl triflates and boronic acids to synthesize the biarylic compounds (Scheme 1.19).[48]



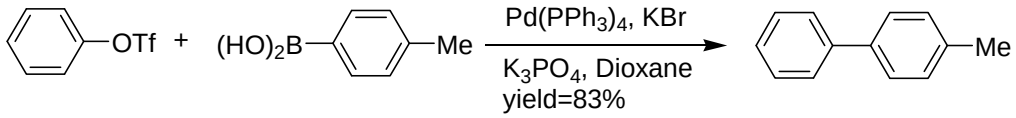
Scheme 1.19 Biarylic compounds synthesized from aryl triflate precursors

At the same time, Carlson *et al.* reported the use of aryl triflates and boronic acids to synthesize the 4-arylphenylalanines (Scheme 1.20).[49]



Scheme 1.20 4-Arylphenylalanines synthesized from aryl triflates precursor

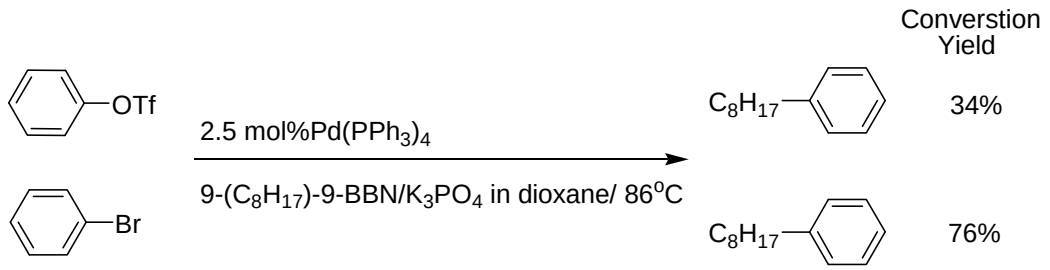
The general Suzuki coupling with triflates was reported by Suzuki *et al.* in 1993 (Scheme 1.21). The scope and limitation of the palladium-catalyzed Suzuki coupling reaction with triflates and their synthetic application, as well as the effects of varying the reaction conditions were studied.[50] In this report, aryl boronic acid, 9-alkyl-9-borabicyclo[3.3.1]nonane, and l-alkenyl -1,3,2-benzodioxaborole were coupled with 1-alkenyl or aryl triflates in high yields. $Pd(PPh_3)_4$ or $Pd(dppf)Cl_2$ were used as catalyst and K_3PO_4 was used as base. The reaction conditions were sufficiently mild so that a variety of functionalized arenes alkenes, and alkadienes were tolerated.



Scheme 1.21 The general Suzuki coupling with triflates by Suzuki *et al.* in 1993

Not only the substrates scopes but also reactivity of triflates over halides was compared in this report. In the palladium-catalyzed cross-coupling with organic halides, the I > Br » Cl order of reactivity is commonly observed. In the competition experiment, an equimolar mixture of bromobenzene and phenyl triflate were allowed to react with an equivalent of 9-octyl-9-BBN in dioxane at 86 °C in the presence of K_3PO_4 (1.5 equiv) and 2.5 mol% $Pd(PPh_3)_4$. Analysis of

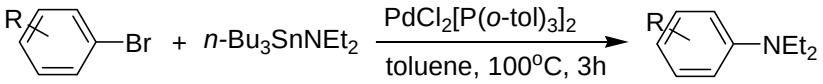
the reaction mixture indicates that 24% and 66% of unreacted bromobenzene and phenyltriflate are recovered (Scheme 1.22). Under similar conditions, iodobenzene is consumed exclusively in the presence of phenyl triflate. Thus, the order of reactivity is I > Br > OTf.



Scheme 1.22 Competition experiment to examine the reactivity order between aryl triflates and aryl bromides

1.2.2 Development of Hartwig-Buchwald Reaction

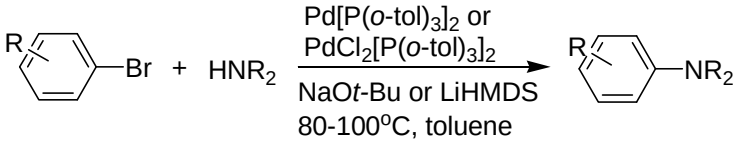
Compared with carbon-carbon coupling reaction, only limited examples of carbon-nitrogen coupling reaction had been reported until the mid-1990s. In 1983, Kosugi *et al.* reported the coupling of aryl halides with aminostannanes in the presence of a catalytic amount of $Cl_2Pd[P(o\text{-tol})_3]_2$ (Scheme 1.23).[51]



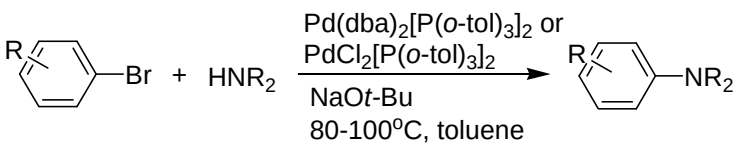
Scheme 1.23 The first palladium-catalyzed coupling of aryl halides with aminostannanes

There were many limitations reported in Kosugi *et al.*'s findings. For example, only moderate yield could be obtained in the combination of dialkylaminostannanes and electron-neutral aryl halides. Moreover, only electron-neutral aryl halides could give reaction products in the coupling reaction. Functionalized aryl halides such as nitro-, acyl-, methoxy-, and dimethylamino-substituted aryl halides only gave poor yields.

After Kosugi *et al.*'s report, there was no further improvement of this reaction until the mid-1990s. In 1995, Hartwig (Scheme 1.24) and Buchwald (Scheme 1.25) concurrently published their group's results on tin-free amination of aryl halides.[52,53] They used similar palladium catalysts in the presence of tri-*o*-tolylphosphine. This tin free amination reaction significantly improved the source of amido group which can be less toxic, more thermally stable, and less air-sensitive.

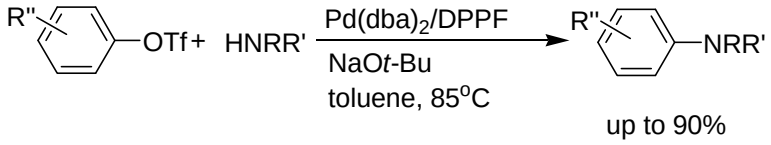


Scheme 1.24 The first tin free amination reaction reported by Hartwig *et al.*

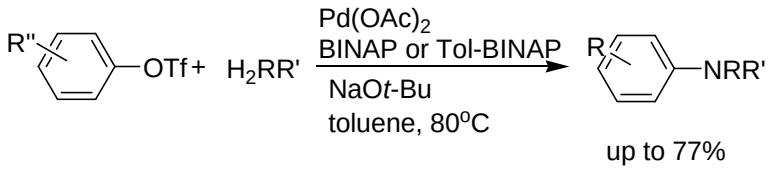


Scheme 1.25 The first tin free amination reaction reported by Buchwald *et al.*

However, the combination of palladium (0) complexes with P(*o*-tol)$_3$ as a ligand showed low reactivity toward the amination of aryl triflates.[54] To solve this problem, Hartwig *et al.* (Scheme 1.26) and Buchwald *et al.* (Scheme 1.27) concurrently reported the use of aryl triflates in the amination reaction in 1997.[55,56] The palladium complexes with the chelating phosphines DPPF and BINAP were effective in the amination of aryl triflates.



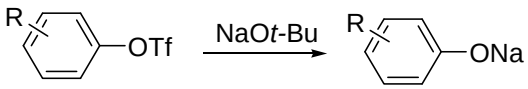
Scheme 1.26 The first amination of aryl triflates reported by Hartwig *et al.*



Scheme 1.27 The first amination of aryl triflates reported by Buchwald *et al.*

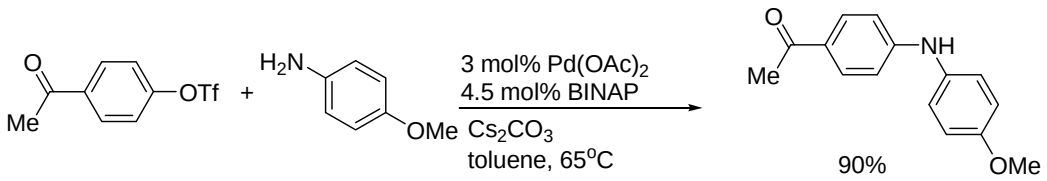
In these two reports, by using DPPF as ligand, neutral aryl triflates with alkylamines gave yields in the range of 42-75 % whereas BINAP or tol-BINAP gave yields in the range of 54-77 %. For some substrates such as *p*-OMe-substituted aryl triflate, Pd/BINAP catalyst showed higher yields in reactions than Pd/DPPF catalyst. However, the low product yields induced by the easy hydrolyses of aryl triflates properties was observed. The lower yields of

electron-poor substrates were attributed to the rapid cleavage of the triflates by the attack of NaO*t*-Bu on sulfur that led to the corresponding sodium phenoxide (Scheme 1.28).



Scheme 1.28 Hydrolyses of aryl triflates by NaO*t*-Bu

To increase the product yields, several methods such as slow addition of the aryl triflates,[56] using Cs_2CO_3 as base[57,58] and non-polar toluene as solvent were employed in the amination reaction. Under these conditions, primary and secondary amines reacted in high yields with both electron-poor and electron-rich aryl triflates in the presence of BINAP-ligated palladium as the catalyst (Scheme 1.29).



Scheme 1.29 Amination of electron-poor aryl triflates in the presence of weak base

1.2.3 Limitation of the Aryl Triflates as Electrophiles in the Coupling Reaction

Although aryl triflates proceed well in many carbon-carbon and carbon-nitrogen coupling reactions, there are many shortages. For example, the rapid base-promoted nucleophilic cleavage of the triflate moiety often lowers the yields of desired products. Although the use of weaker bases (e.g., Cs_2CO_3, K_3PO_4) and the slow addition of the aryl triflates gave significant improvement of the product yields, such protocol is not always successful or practical. Since aryl triflates are usually in the form of colorless oil, they cannot be purified by simple recrystallization. Moreover, they hydrolyze easily and degrade gradually at room temperature and thus are required to be kept dry and stored at refrigerator. Furthermore, they are considerably expensive.

1.3 Development of other Aryl Fluorine Sulfonates to Replace Aryl Triflates

1.3.1 Development of Aryl Fluorosulfonates and Aryl *p*-Florobenzenesulfonates

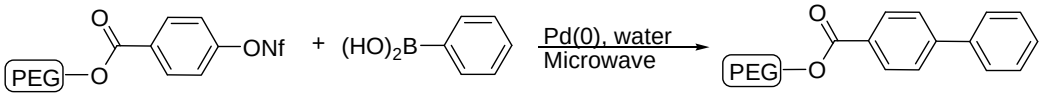
The use of aryl fluorosulfonates as a cheaper alternative to triflates has been attempted.[59] In fact, fluorosulfonates and aryl triflates have similar reactivities. However, the fluorosulfonic anhydride is highly volatile (boiling point = 50^{o}C) and has a comparable toxicity to phosgene (lethal to rats at 10ppm constant level for 4-hour exposure).[60] Moreover, it is not broadly commercialized. The high toxicity and difficult handling of the fluorosulfonic anhydride retarded the further development of the use of aryl fluorosulfonates in the coupling reactions.

In 1992, Badone *et al.* reported the palladium-catalyzed coupling of aryl *p*-fluorobenzenesulfonates with organostannanes.[61] The toxicity of the *p*-fluorobenzenesulfonyl chloride is much lower than the fluorosulfonic anhydride and the aryl *p*-fluorobenzenesulfonates are crystalline solids instead of oily liquid. However, only electron-deficient aryl *p*-fluorobenzenesulfonates give moderate to good yields, while electron-rich aryl *p*-fluorobenzenesulfonates give very poor yields and/or undesired products. The cost of aryl *p*-fluorobenzenesulfonates is similar to the corresponding aryl triflates because the sulfonating agent (*p*-fluorobenzenesulfonates) is also very expensive.

1.3.2 Development of Aryl Nonaflates

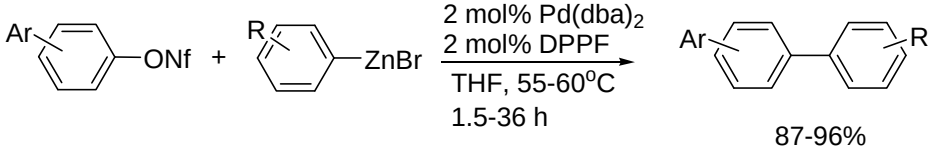
Aryl nonaflates (ArONf) ($ArOSO_2$-$(CF_2)_3$-CF_3) has been proposed as an attractive alternative to triflates. They can be readily prepared from the corresponding phenol using commercially available fluoroalkanesulfonic anhydrides or halides.[47] They are stable toward chromatography, more stable toward hydrolysis than the corresponding aryl triflates[62] and can be stored at room temperature.[63]

Aryl nonaflates have been used in many coupling reactions, for example, microwave-assisted Suzuki coupling of poly(ethylene glycol) ester of nonafluorosulfonyloxy-*para*-substituted benzoates with arylboronic acids.(Scheme 1.30)



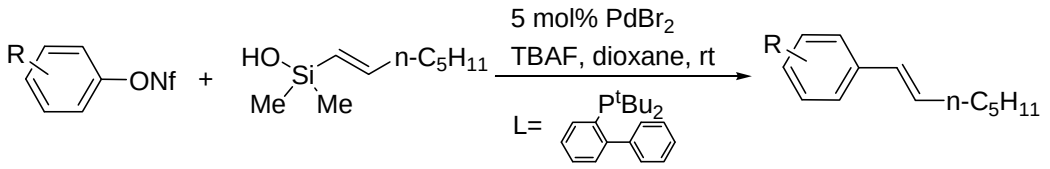
Scheme 1.30 Microwave-assisted Suzuki coupling of aryl nonaflates

The palladium-catalyzed Negishi coupling of aryl nonaflates with organozincs has also been reported.[64] (Scheme 1.31)



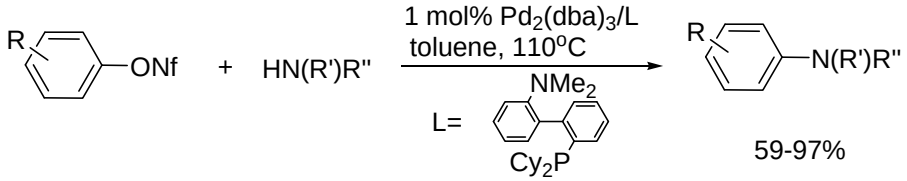
Scheme 1.31 Palladium-catalyzed Negishi coupling of aryl nonaflates with organozincs

In 2002, Denmark *et al.* reported the design and development of an effective protocol for the palladium-catalyzed cross-coupling of (*E*)- and (*Z*)-heptenyldimethylsilanols with nonaflates. (Scheme 1.32) [65]



Scheme 1.32 The palladium-catalyzed cross-coupling of (*E*)- and (*Z*)-heptenyldimethylsilanols with nonaflates

For the amination reaction, the use of aryl nonaflates was first mentioned by Rudolph *et al.*[66] and Hartwig *et al.*[67] In 2003, Buchwald *et al.* reported the first detailed study on the palladium-catalyzed amination of aryl nonaflates.[68] In this report, electron-rich and -poor aryl nonaflates were effectively coupled with both primary and secondary amines. (Scheme 1.33)



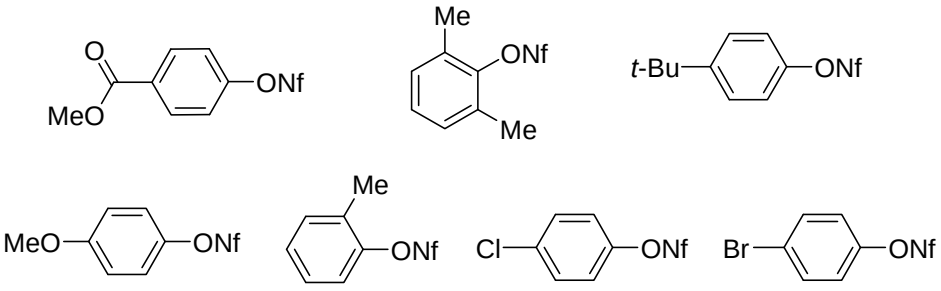
Scheme 1.33 The first detailed study of the palladium-catalyzed amination of aryl nonaflates

Aryl nonaflates, which have been shown to have reactivity similar to aryl triflates, are an effective alternative to triflates in coupling reaction due to their increased stability.

1.3.3 Limitation of Aryl Nonaflates

Although aryl nonaflates have reactivity similar to that of aryl triflates in various coupling reactions and are more stable toward hydrolysis, they still have some disadvantages. For example, the cost of the preparation of aryl nonaflates is as high as that of the corresponding aryl triflates. The cost of the perfluoro-1-butanesulfonyl fluoride is $210US/100g while trifluoromethanesulfonic anhydride costs $195US/100g only. The cost of using nonafluorobutanesulfonic anhydride ($1540US/100g) as the nonaflating agent is even higher than using the trifluoromethanesulfonic anhydride.

On the other hand, many aryl nonaflates, similar to the aryl triflates, are in the form of colorless oil that limits the use of simple recrystallization for purification(Scheme 1.34).[68] Therefore, column chromatography or vacuum distillation, both a difficult process for large scale preparation, is needed for the purification of aryl nonaflates.



Scheme 1.34 Examples of aryl nonaflates in form of colorless oil

1.4 Advantages and Difficulties of the Use of Aryl Tosylates and Mesylates in the Coupling Reactions

Since there are many problems and difficulties for the aryl sulfonates that mentioned in Section 1.3, investigations looking for alternatives go on. Aryl benzenesulfonates, tosylates and mesylates are some of the more attractive alternatives. They are easily prepared from the corresponding phenols (Scheme 1.35), more thermally stable and more persistent to the hydrolysis than aryl nonaflates.

Scheme 1.35 Easy synthesis of aryl benzenesulfonates, tosylates and mesylates

On the other hand, the costs of preparing aryl benzenesulfonates, tosylates and mesylates are just a small fraction of the preparation of corresponding aryl triflates. The cost of the trifluoromethanesulfonic anhydride is $ 1450 US/kg, while benzenesulfonyl chloride is $75.9US/kg, *p*-toluenesulfonyl chloride is $65.7US/kg and methanesulfonyl chloride is $136.5US/liter. These sulfonating agents are 10-20 times less expensive than the triflating agent.

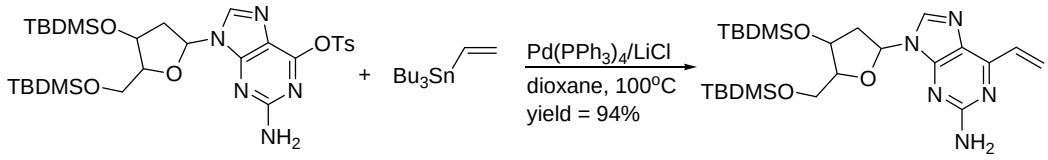
Unlike aryl nonaflates and aryl triflates, most of the aryl tosylates and mesylates have high crystallinity so these aryl sulfonates are usually in the solid

form. Therefore, the use of simple recrystallization for purification is possible. This facilitates large scale preparation.

Although the use of the aryl tosylates and mesylates as the coupling reagent has many advantages, the high stability of the sulfonates groups also induce difficulties in the activation of C-O bond in the coupling reaction. In order to keep the advantages of the aryl tosylates and mesylates, several groups have attempted to utilize them as the coupling partner.

1.5 From Nickel to Palladium: Development of Nickel-Catalyzed Coupling of Aryl Tosylates and Mesylates

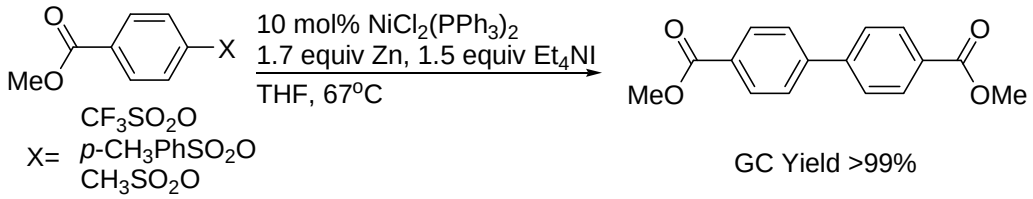
As early as 1995, Sasaki *et al.* reported an example of Stille coupling that used guanosine-based tosylates and vinyltributylstannane in the presence of $Pd(PPh_3)_4$ as the catalyst (Scheme 1.36).



Scheme 1.36 The Stille coupling of guanosine-based tosylates with vinyltributyltin

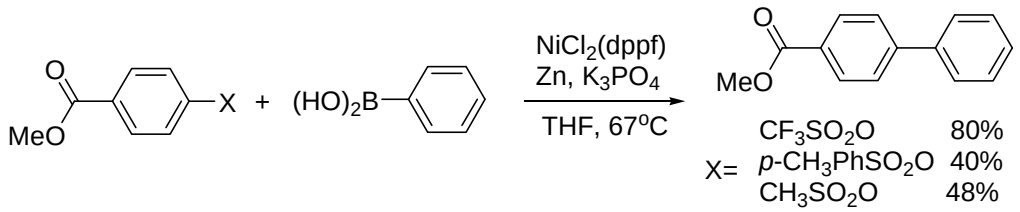
Meanwhile, Percec *et al.* reported the first detailed study on the feasibility of using aryl tosylates and mesylates in the nickel/palladium catalyzed homo-

and cross-coupling reactions. In the nickel-catalyzed homo-coupling reaction, aryl sulfonates were mediated by a nickel catalyst generated from $NiCl_2(PPh_3)_2$ (0.10 equiv) in the presence of excess Zn (1.7 equiv) and Et_4NI (1.5 equiv) in THF (Scheme 1.37).



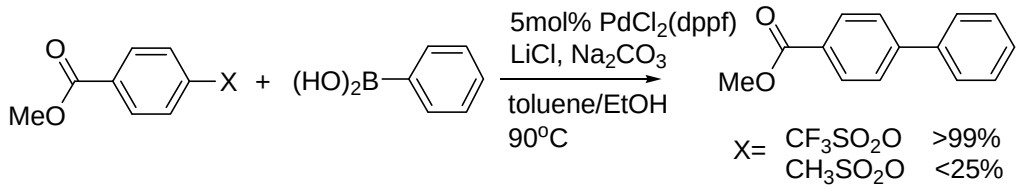
Scheme 1.37 The first nickel-catalyzed homo-coupling of aryl tosylates.

Although the catalyst loading was as high as 10 mol% nickel complex, the homo-coupling of different sulfonates, *p*-toluenesulfonate and methanesulfonate resulted in high yields that equaled to those obtained with the triflates. The highest yields were obtained when the aryl group had electron-withdrawing substituents in para position. Good yields were also obtained in the homo-coupling of neutral aryl sulfonates. However, the same catalytic system demonstrated no reactivity in the cross-coupling reaction. $NiCl_2$(dppf)-catalyzed cross-coupling of methyl 4-(methanesulfonate)-benzoate with phenylboronic acid gave only poor yield (Scheme 1.38). The highest yield (67%) was obtained in those activated substrates that used dioxane as solvent and with the temperature increased to 95°C.



Scheme 1.38 Nickel-catalyzed Suzuki coupling of aryl tosylates, mesylates and triflates.

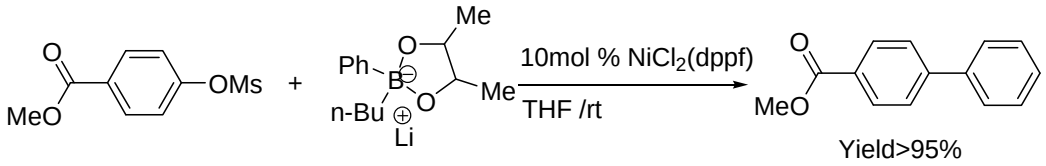
On the other hand, the palladium-catalyzed cross-coupling reactions were not successful. Only poor product yield could be obtained in the cross-coupling of activated methyl 4-(methanesulfonate)-benzoate with phenylboronic acid after various attempts (Scheme1.39).



Scheme 1.39 Lower reactivity of aryl tosylates toward palladium-catalyzed Suzuki coupling reaction

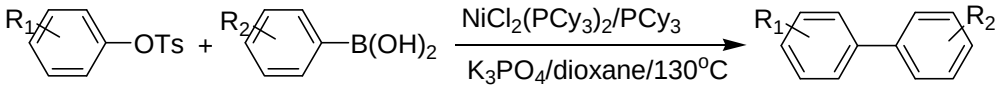
Indeed, Percec *et al.* successfully demonstrated the feasibility of using aryl tosylates and mesylates as coupling partner in the nickel- and palladium-catalyzed cross-coupling reactions even though the substrates scoops were narrow. Especially, the detail study on the nickel-catalyzed aryl sulfonates coupling reactions provided a foundation for the further development of the general nickel-catalyzed coupling reactions of aryl tosylates and mesylates.

By following Percec *et al.*'s reports, Kobayashi *et al.* used the $NiCl(dppf)_2$ to catalyze the coupling reaction of methyl 4-(methanesulfonate)-benzoate with lithium phenylborates at room temperature and obtained the products up to 95% yield (Scheme 1.40). However, only activated aryl mesylates can be used as substrates and the catalyst loading was still as high as 10 mol%.



Scheme 1.40 Nickel-catalyzed Suzuki coupling of aryl mesylates with lithium phenylborates

In year 2001, Monteiro *et al.* reported the first general nickel-catalyzed Suzuki cross-coupling of aryl tosylates. In the nickel-catalyzed Suzuki cross-coupling, aryl tosylates were mediated by a $NiCl_2(PCy_3)_2$ associated with PCy_3 in the presence of K_3PO_4 as base and dioxane as solvent (Scheme 1.41).[69]

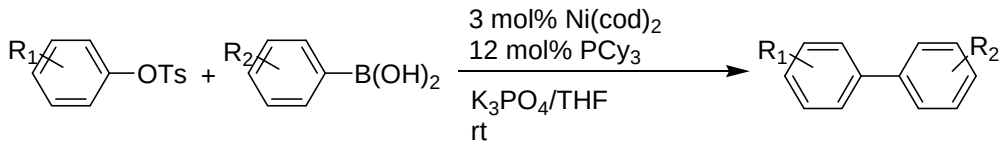


Scheme 1.41 The first general nickel-catalyzed Suzuki coupling of aryl tosylates

Monteiro *et al.*'s report made some breakthroughs. In this catalytic system, the electron-rich and bulky tricyclohexylphosphine was used as ligand. It was

firstly pre-catalyzed with $Ni(COD)_2$ to form $NiCl_2(PCy_3)_2$, a stable complex which was easy to prepare and manipulate. Moreover, the catalyst loading was relatively low so the reaction could be carried out with 1.5-3 mol% of $NiCl_2(PCy_3)_2$ only. Also, reducing agents such as Zn were not necessary in the coupling reaction. Last but not least, this system catalyzed the cross-coupling of neutral and activated aryl tosylates with arylboronic acids under relatively mild reaction conditions, and a variety of functional groups such as keto, ester and cyano were tolerated.

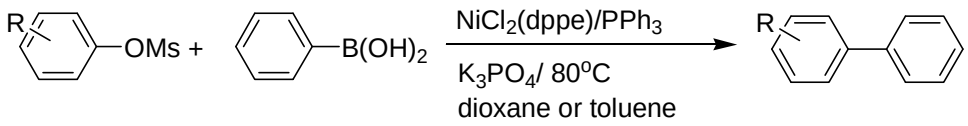
In 2004, according to the Monteiro *et al.*'s report, Hu *et al.* focused on using $Ni(COD)_2$ as the catalyst precursor for the room-temperature Suzuki-Miyaura couplings of aryl arenesulfonates (Scheme 1.42).[70]



Scheme 1.42 The first room temperature nickel-catalyzed Suzuki coupling of aryl tosylates

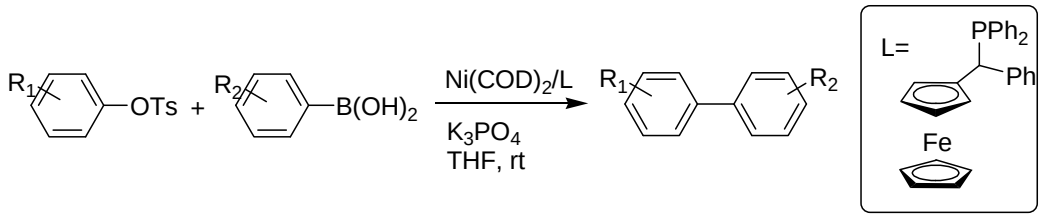
In 2004, ten years after the first report of the nickel-catalyzed coupling of aryl mesylates, Percec *et al.* reported the reactivity of different nickel catalysts such as $NiCl_2$(dppe)-, $NiCl_2$(dppb)-, $NiCl_2$(dppf)-, $NiCl_2$- $(PCy_3)_2$-, and $NiCl_2(PPh_3)_2$ in the Suzuki coupling of aryl mesylates and tosylates.[71] They

discovered that the inexpensive $NiCl_2$(dppe) in the presence of excess dppe was the most general nickel catalyst for the cross-coupling of aryl mesylates and tosylates that contained electron-withdrawing substituents, while for the $NiCl_2$(dppe) that contained excess PPh_3, $NiCl_2$(dppe)/PPh_3 was a general catalyst for the cross-coupling of aryl mesylates that contained both electron-donating and electron-withdrawing substituents (Scheme 1.43).



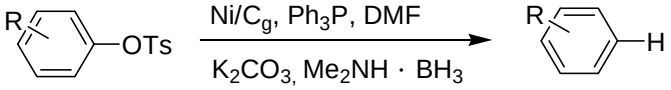
Scheme 1.43 $NiCl_2$(dppe)/PPh_3 catalyzed Suzuki coupling of aryl mesylates

After Monteiro *et al.* reported the first general nickel-catalyzed Suzuki cross-coupling of aryl tosylates, other research groups established many successful examples. For example, according to the Monteiro *et al.*'s report, Hu *et al.* reported the Suzuki coupling of activated alkenyl tosylates at room temperature.[72] Later, Hu *et al.* reported the use of ferrocenylmethylphosphines as ligands in the nickel-catalyzed Suzuki coupling reactions of aryl tosylates in good yield and aryl mesylates at moderate yield at room temperature (Scheme 1.44).[73]

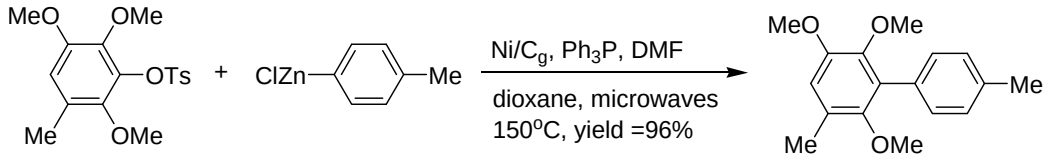


Scheme 1.44 Room temperature nickel-catalyzed Suzuki coupling of activated alkenyl tosylates

Various kinds of nickel-catalyzed coupling reactions of aryl tosylates and mesylates were also reported. Park *et al.* reported the nickel-catalyzed Kumada coupling of aryl arenesulfonates by using NiCl(dppf) as catalyst.[74] Lipshutz *et al.* reported the reduction (Scheme 1.45), Negishi coupling (Scheme 1.46) and Suzuki coupling of aryl tosylates and mesylates with heterogeneous catalysis (Ni/C_g).[75-77]



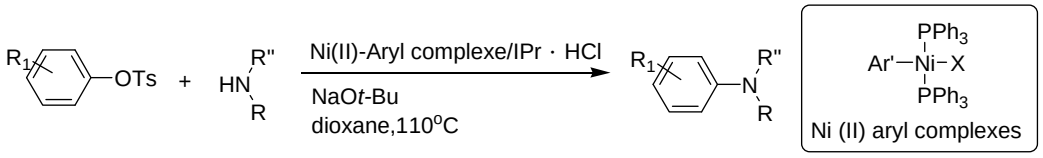
Scheme 1.45 Reduction of aryl tosylates by Ni/C_g



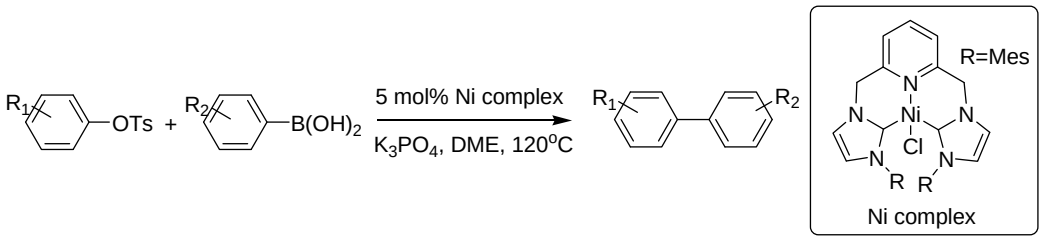
Scheme 1.46 Negishi coupling of aryl tosylates by Ni/C_g

Up to recently, the use of N-heterocyclic carbene ligands has been applied to the coupling reaction of aryl tosylates and mesylates in 2008. For example,

Yang *et al.* reported the nickel-catalyzed amination of aryl tosylates (Scheme 1.47).[78] Doi *et al.* reported the use of N-heterocyclic carbene derived nickel-pincer to catalyze the Suzuki coupling reaction of aryl/alkenyl tosylates and mesylates (Scheme 1.48).[79]



Scheme 1.47 Ni/NHCs catalyzed amination of aryl tosylates

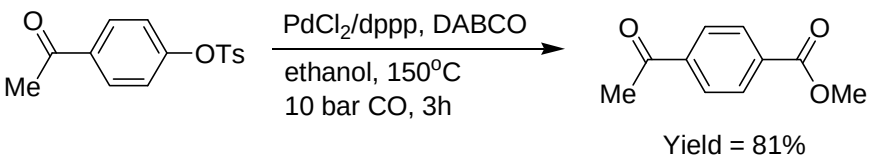


Scheme 1.48 Ni/NHCs catalyzed Suzuki coupling of aryl tosylates

1.6 From Nickel to Palladium: Development of Palladium-Catalyzed Coupling of Aryl Tosylates

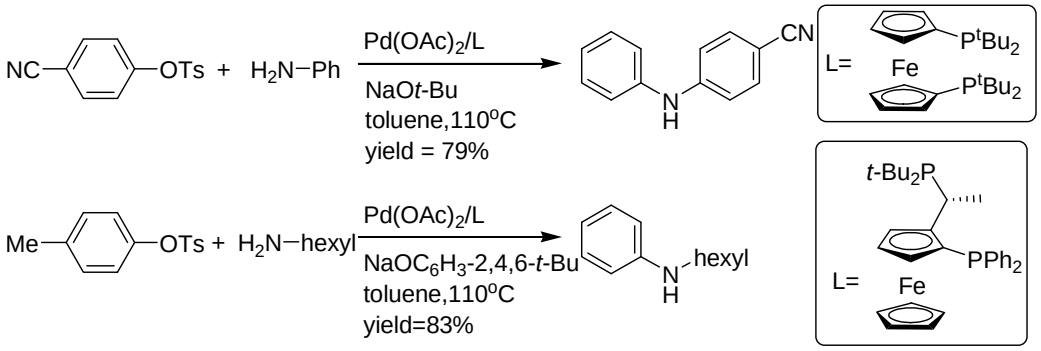
Although the nickel-catalyzed coupling reaction of aryl tosylates/mesylates gained its breakthrough in the mid-1990s and generalized after year 2000, the palladium-catalyzed coupling reaction of aryl tosylates/mesylates still have not been reported until 2003. Although further success with nickel-based catalysts has been observed, there are certain drawbacks associated with the use of nickel complexes compared with palladium complexes, such as lower functional group tolerance,[80] lower selectivity[81] and greater toxicity[82].

Before 2003, there are only several fragmentary reports on the palladium-catalyzed coupling reaction of aryl tosylates. For example, Sugi *et al.* reported the palladium-catalyzed alkoxycarbonylation of aryl tosylates. However, only 4-acetophenyl tosylate could give good yield in the carbonylation reaction (Scheme 1.49). Other kinds of aryl tosylates such as bearing cyano, chloro, phenyl and methyl group only gave poor yield.



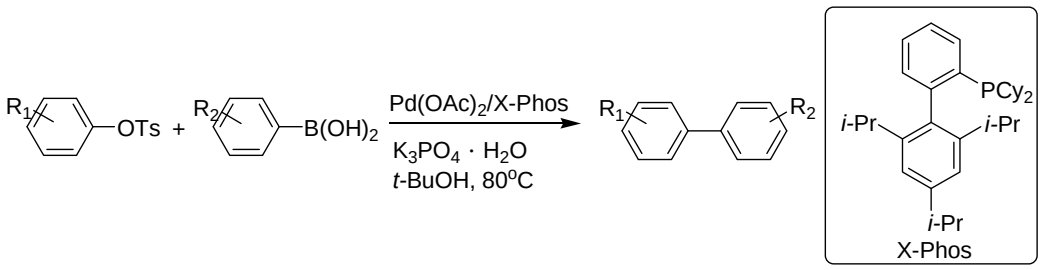
Scheme 1.49 Palladium-catalyzed alkoxycarbonylation of aryl tosylates

Hartwig *et al.* reported the first amination of aryl tosylates, but there were only two examples of coupling of aryl tosylates with primary amines (Scheme 1.50).[83]



Scheme 1.50 Two examples of the amination of aryl tosylates by Hartwig *et al.*

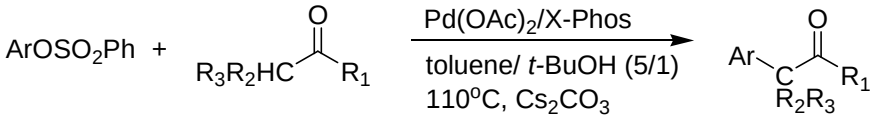
Until 2003, Buchwald *et al.* reported the first general method for the palladium-catalyzed Suzuki coupling of aryl tosylates with aryl benzenesulfonates using $Pd(OAc)_2$ as palladium source and X-Phos as the ligand (Scheme 1.51).[84]



Scheme 1.51 The first general palladium-catalyzed Suzuki coupling of aryl tosylates and aryl benzenesulfonates

Polar solvents such as THF and *t*-BuOH that increase the solubility of the aryl tosylates and arylboronic acids were found to facilitate the coupling reaction.

The reactions were generally completed in 3 hour at 80 ^{o}C and the catalyst loading was around 2 mol% Pd. Common functional groups such as cyano, aldehyde, nitro and ketones were tolerated. Enolate arylation of aryl benzenesulfonates was also demonstrated in this report (Scheme 1.52).

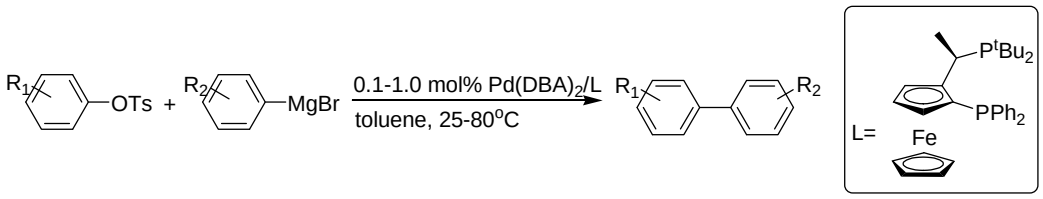


Scheme 1.52 Palladium-catalyzed enolate arylation of aryl benzenesulfonates

The successful demonstration of a general method for the palladium-catalyzed coupling of aryl tosylates and aryl benzenesulfonates drew the research group's attention to the exploration and expansion of the scope of the palladium-catalyzed coupling reaction of aryl tosylates and mesylates. Since 2005, various kinds of palladium-catalyzed coupling reaction such as Kumada coupling, Negishi coupling, Hiyama coupling, Buchwald-Hartwig amination, Sonogashira reaction, Heck reaction, thiolation, phosphination and C-H direct arylation using the aryl / alkenyl benzenesulfonates and tosylates as electrophiles were gradually reported by different research groups. Examples are listed as follows:

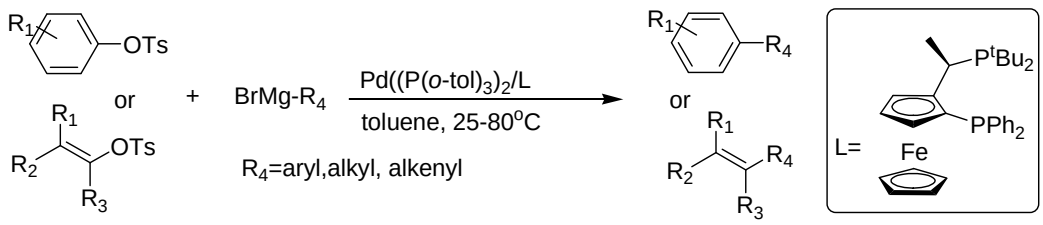
1.6.1 Palladium-Catalyzed Kumada Coupling of Aryl Tosylates

In 2003, Hartwig *et al.* reported the first detailed study on the palladium-catalyzed Kumada coupling of aryl tosylates.[85] The use of Pd(0) precursor and sterically hindered versions of the Josiphos ligands system successfully catalyzed the Kumada coupling of the aryl tosylates with aryl Grignard reagents (Scheme 1.53). This report demonstrated the feasibility of the room temperature palladium-catalyzed Kumada coupling reaction.



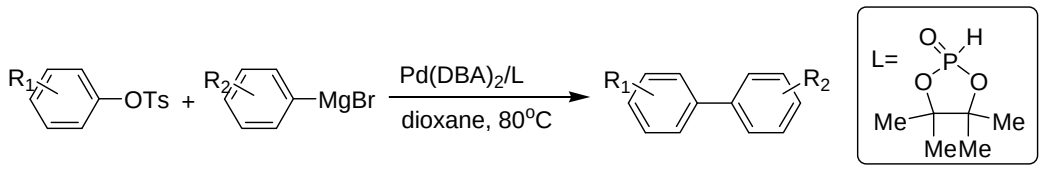
Scheme 1.53 Pd/Josiphos catalyzed Kumada coupling of aryl tosylates

In 2005, Hartwig *et al.* reported a follow-up investigation of the palladium-catalyzed Kumada coupling of aryl and alkenyl tosylates with aryl, alkenyl, and alkyl Grignard reagents.[86] This catalytic system catalyzed the Kumada couplings of activated, deactivated, and certain sterically hindered aryl tosylates with Grignard reagents generating biaryl and styrenyl compounds in good to excellent yields, often at room temperature (Scheme 1.54).



Scheme 1.54 Palladium-catalyzed Kumada coupling of aryl and alkenyl tosylates with aryl, alkenyl, and alkyl Grignard reagents

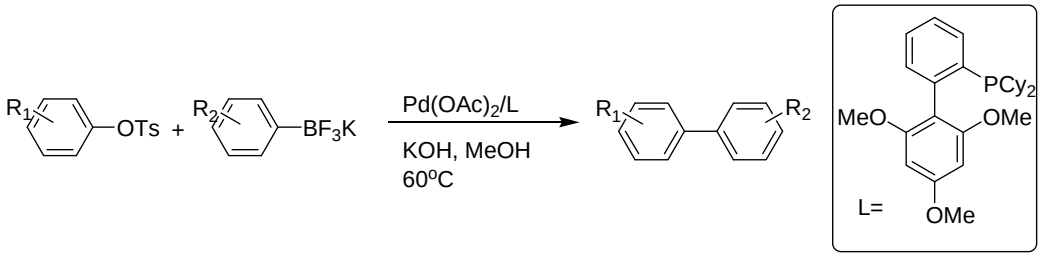
In 2006, Ackermann *et al.* reported an alternative ligand system that used a secondary phosphine oxide as preligand for cross coupling reactions between aryl tosylates and Grignard reagents (Scheme1.55).[87] The palladium catalyst derived from PinP(O)H proved to be applicable to the Kumada coupling reactions of electron-rich as well as electron-poor aryl tosylates, including heteroaromatic electrophiles.



Scheme 1.55 Pd/PinP(O)H catalyzed Kumada coupling of aryl tosylates

1.6.2 Palladium-Catalyzed Suzuki Coupling of Alkyl and Alkenyl Tosylates

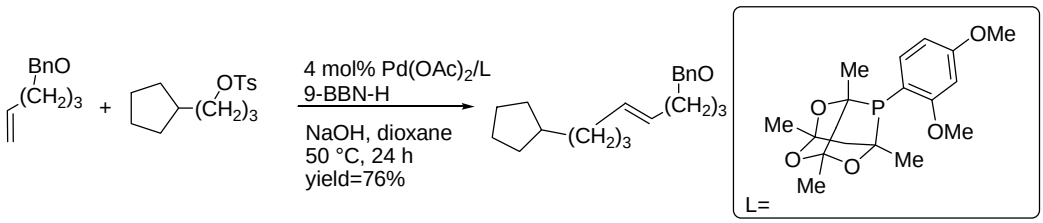
After Buchwald *et al.* had reported the first general method for the palladium-catalyzed Suzuki coupling of aryl tosylates and aryl benzenesulfonates, several papers related to the Suzuki coupling were reported. For example, aryl trifluoroborate salts, regarded as alternative to aryl boronic acids, were used as the coupling partner. Wu *et al.* reported the use of $Pd(OAc)_2$ / Buchwald type ligand to the Suzuki coupling of aryl tosylates with potassium aryl trifluoroborates by using ethanol as solvent (Scheme 1.53).[88]



Scheme 1.56 Suzuki coupling of aryl tosylates with potassium aryl trifluoroborates

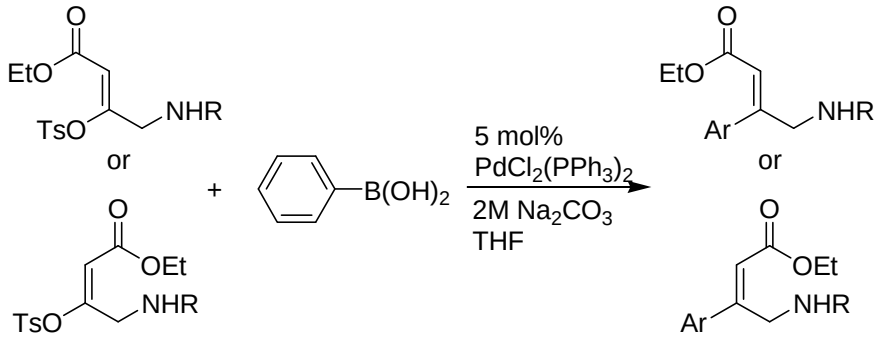
In fact, only a few reports of further investigation of the palladium-catalyzed Suzuki coupling of aryl tosylates were published. Studies have been concentrating on the palladium-catalyzed Suzuki coupling of alkyl and alkenyl tosylates which are easier to be activated than the aryl tosylates. For example, in 2004, Capretta *et al.* reported the use of phosphaadamantanes type

phosphine as ligands for palladium-catalyzed Suzuki coupling of alkyl tosylates (Scheme 1.57).[89] Although the reaction conditions were mild to tolerate ketone and ester functional groups, the product yields were moderate. Moreover, only four examples were demonstrated in this report.



Scheme 1.57 Palladium-catalyzed Suzuki coupling of alkyl tosylates

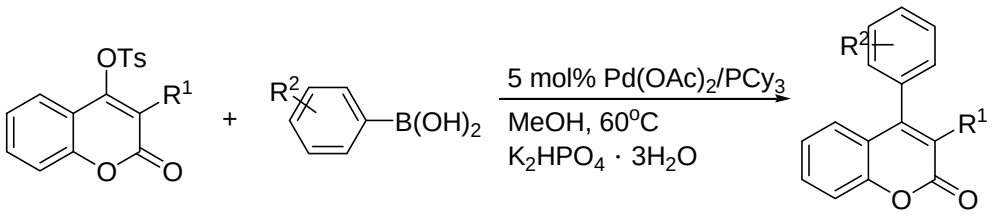
In 2005, Baxter *et al.* reported the (*E*)- and (*Z*)- stereoretentive Suzuki coupling of geometric enol tosylate with arylboronic acids (Scheme 1.58).[90]



Scheme 1.58 Stereoretentive Suzuki coupling of geometric enol tosylate

In 2007, Wu *et al.* reported the palladium-catalyzed site-selective cross-coupling reactions of 3-bromo-4-tosyloxycoumarin to synthesis the

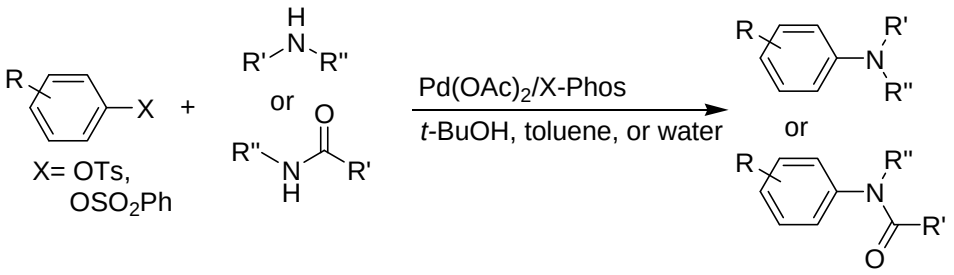
3,4-disubstituted coumarins (Scheme 1.59).[91]



Scheme 1.59 Synthesis of 3,4-disubstituted coumarins by selective Suzuki coupling

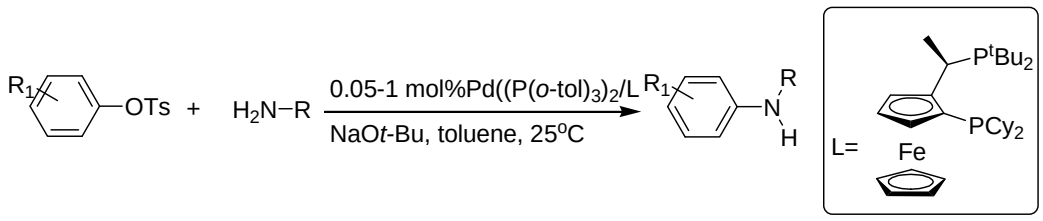
1.6.3 Palladium-Catalyzed Buchwald-Hartwig Amination of Aryl Tosylates

After Hartwig *et al.* reported two examples that aryl tosylates couple with primary amines in 1998,[83] no further investigation was reported. In 2003, Buchwald *et al.* reported the palladium-catalyzed amination and amidation of aryl benzenesulfonates and tosylates by using the combination of $Pd(OAc)_2$ and X-Phos as catalyst (Scheme 1.60).[92] The improvement made in this system is that both primary and secondary (both cyclic and acyclic) aliphatic amines, anilines, diarylamines, indole, benzophenone imine (an ammonia equivalent), and benzophenone hydrazone can couple with aryl benzenesulfonates and tosylates in good yield. Also, amidation of aryl benzenesulfonates can also be successfully catalyzed in this system.



Scheme 1.60 Palladium-catalyzed amination and amidation of aryl benzene sulfonates and tosylates

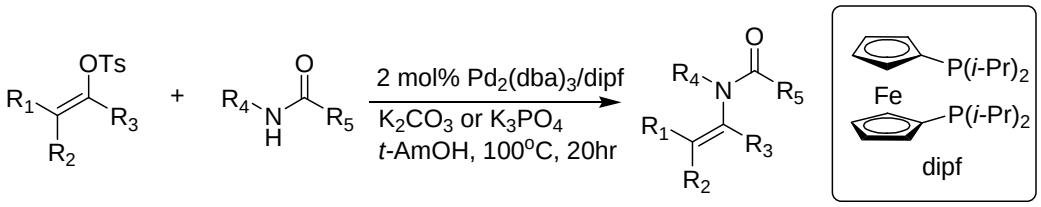
In 2008, Hartwig *et al.* continued the palladium-catalyzed amination of aryl tosylates and then reported the amination of aryl tosylates at room temperature.[93] The combination of the hindered Josiphos ligand CyPF-*t*-Bu with the unconventional Pd(0) precursor Pd[P(*o*-tol)$_3$]$_2$ was used to catalyze aryl tosylates with primary alkylamines, arylamines, and N-H imines with fast rates and high turnover numbers under mild conditions. However, this system can only be applied to the primary amines.



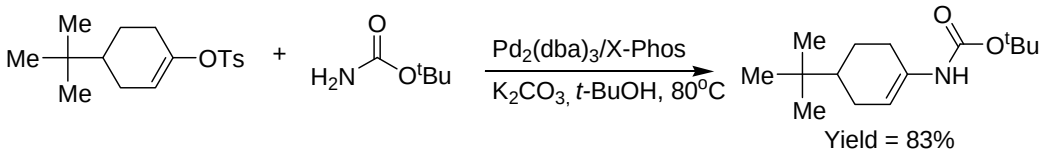
Scheme 1.61 Palladium-catalyzed amination of aryl tosylates

Apart from the amination of aryl tosylates, amidation of alkenyl tosylates have also been reported. In 2005 Klapars *et al.* reported the palladium-catalyzed amidation of enol tosylates by using the combination of ferrocene based ligand

and $Pd_2(dba)_3$ as catalyst (Scheme 1.62).[94] At the same year, Holmes *et al.* also reported the palladium-catalyzed amidation of enol tosylates by using a combination of X-phos and $Pd_2(dba)_3$ as catalyst. Although good yield could be obtained in the catalytic system, only two examples were reported (Scheme 1.63).[95]



Scheme 1.62 Pd/dipf catalyzed amidation of enol tosylates



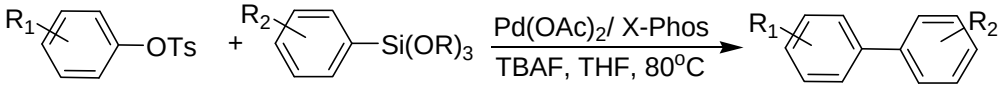
Scheme 1.63 Pd/X-Phos catalyzed amidation of enol tosylates

1.6.4 Miscellaneous

There are some other kinds of coupling of aryl tosylates reported. However, only few papers or entries were reported for the each kind of coupling reactions. The reactions are summarized as follows:

1.6.4.1 Palladium-Catalyzed Hiyama Coupling of Aryl Tosylates

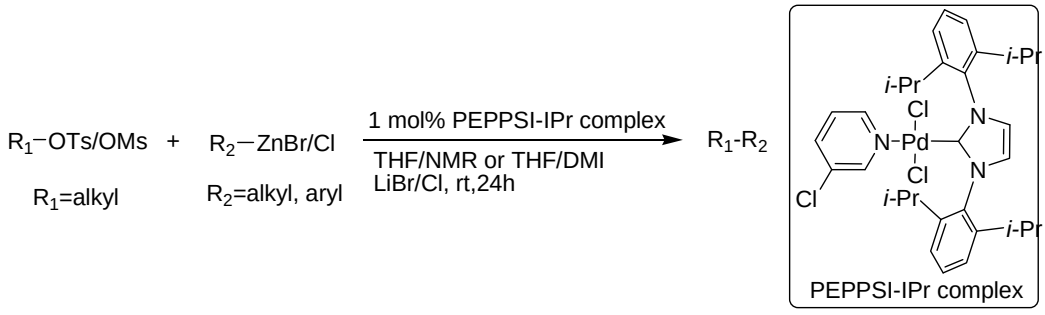
By following the catalytic system ($Pd(OAc)_2$/X-Phos) developed by Buchwald *et al.*, Wu *et al.* reported the palladium-catalyzed Hiyama coupling of aryl tosylates with arylsilanes (Scheme 1.64).[96]



Scheme 1.64 Palladium-catalyzed Hiyama coupling of aryl tosylates

1.6.4.2 Palladium-Catalyzed Negishi Coupling of Alkyl Tosylates and Mesylates

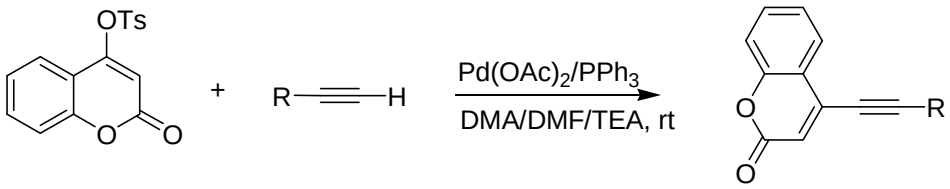
In 2006, Organ *et al.* reported the palladium-catalyzed Negishi coupling of alkyl tosylates and mesylates by using the precatalyst of $PdCl_2$ and N-Heterocyclic Carbene to generate PEPPSI-IPr complex as catalyst (Scheme 1.65).[97] However, only three examples were reported and no yield could be obtained in the case of using aryl tosylates and mesylates as coupling partners.



Scheme 1.65 Palladium-catalyzed Negishi coupling of alkyl tosylates and mesylates

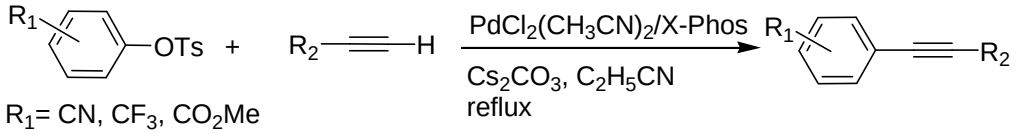
1.6.4.3 Palladium-Catalyzed Sonogashira Reaction of Alkenyl and Aryl Tosylates

In fact, only limited achievements that are related to Sonogashira reaction have been reported. In 2002, Fu *et al.* reported the copper-free palladium-catalyzed cross coupling reaction of vinyl tosylates with terminal acetylenes. However, only coumarin tosylate was demonstrated as a successful example (Scheme 1.66).[98]



Scheme 1.66 Copper-free palladium-catalyzed cross coupling reaction of coumarin tosylate

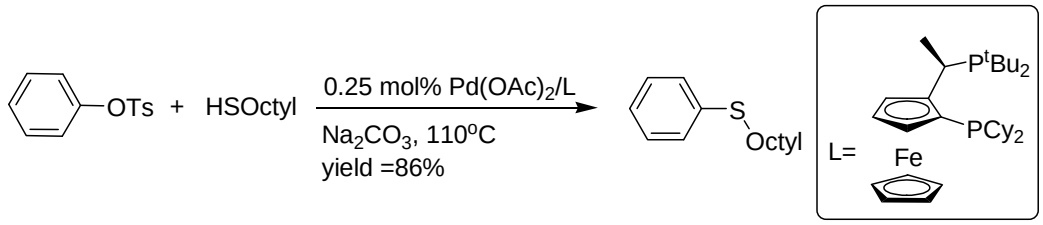
In 2003, Buchwald *et al.* reported the palladium-catalyzed Sonogashira reaction of aryl tosylates with terminal alkynes by using the combination of $PdCl_2(CH_3CN)_2$ and XPhos as catalyst (Scheme 1.67).[99] However, only three examples that used activated aryl tosylates as coupling partners were reported and only moderate yield could be obtained.



Scheme 1.67 Palladium-catalyzed Sonogashira reaction of activated aryl tosylates

1.6.4.4 Palladium-Catalyzed Thiolation of Aryl Tosylates

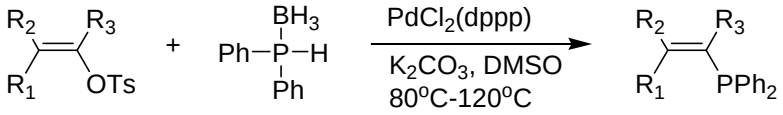
For the palladium-catalyzed coupling of aryl tosylates with thiols, only one entry was reported by Hartwig *et al.* in 2006 (Scheme 1.68).[100]



Scheme 1.68 Palladium-catalyzed thiolation of aryl tosylates

1.6.4.5 Palladium-Catalyzed Phosphination of Alkenyl Tosylates

In 2009, Gaumont *et al.* reported two examples of the C-P coupling reaction of vinyl tosylates with diphenylphosphine derivative (Scheme 1.69). [101]

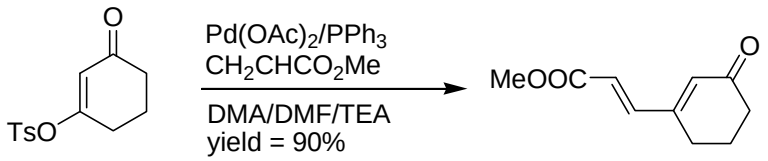


Scheme 1.69 Palladium-catalyzed phosphination of alkenyl tosylate

1.6.4.6 Palladium-Catalyzed Heck Reaction of Alkenyl Tosylates

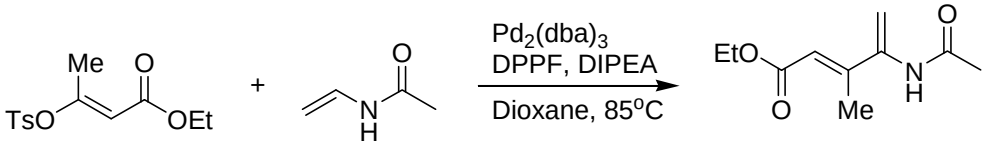
There are several reports related to the palladium-catalyzed Heck coupling reaction of alkenyl tosylates. In 2002, Fu *et al.* first reported the use of $Pd(OAc)_2/PPh_3$ system to the Heck coupling of 3-oxocyclohex-1-enyl tosylate

and 5,5-dimethyl-3-oxocyclohex-1-enyl tosylate with methyl acrylate in good yield (Scheme 1.70).[102]



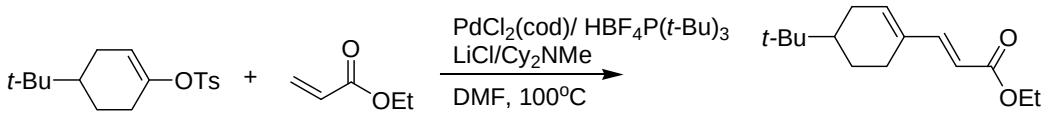
Scheme 1.70 Palladium-catalyzed Heck coupling reaction of alkenyl tosylates

In 2005, Skrydstrup *et al.* reported the regioselective Heck couplings of reported the regioselective Heck couplings of activated alkenyl tosylates and mesylates with electron rich olefins (Scheme 1.71).[103]



Scheme 1.71 Palladium-catalyzed regioselective Heck couplings of activated alkenyl tosylates

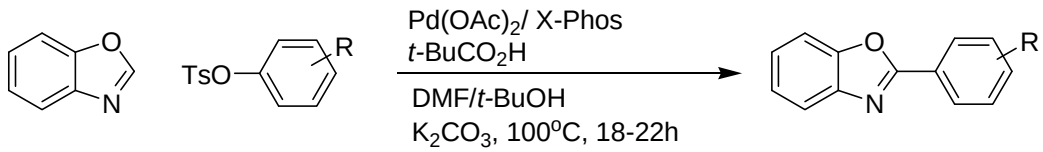
By following up the above experiments, Skrydstrup *et al.* reported the Heck coupling of non-activated alkenyl tosylates with olefins in 2006 (Scheme 1.72).[104]



Scheme 1.72 Palladium-catalyzed Heck coupling of non-activated alkenyl tosylates

1.6.4.7 Palladium-Catalyzed C-H Direct Arylation

For the palladium-catalyzed C-H direct arylation reaction, there is only one example related to the use of aryl tosylates. In 2009, Ackermann *et al.* reported the first direct arylation of heteroarenes with aryl tosylates and mesylates by using the combination of $Pd(OAc)_2$ and X-Phos as catalyst and by the aid with the addition of trimethyl acetic acid as additive (Scheme 1.73).[105]



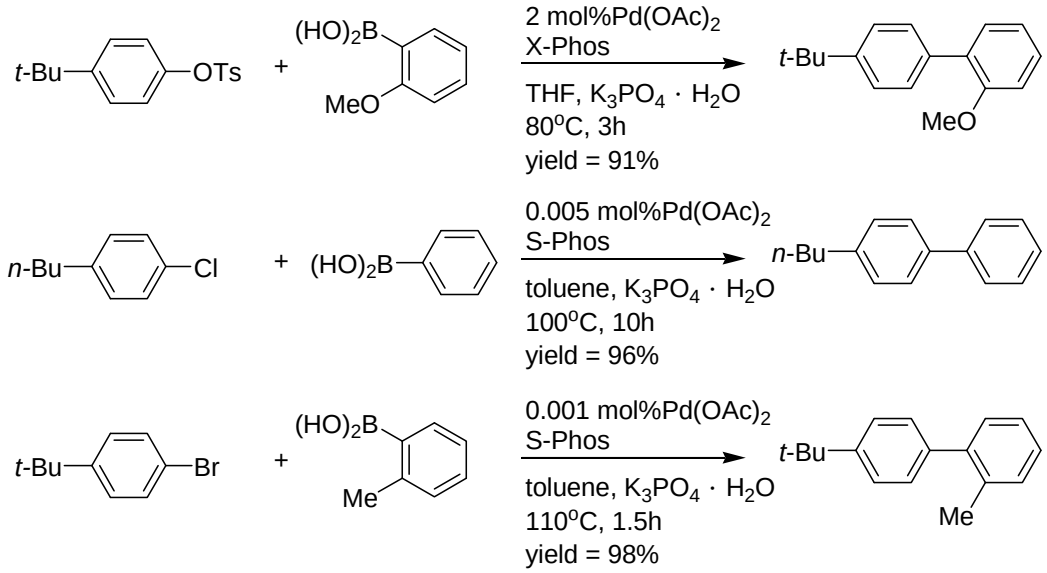
Scheme 1.73 Palladium-catalyzed C-H direct arylation reaction

1.7 Potential for the Further Study of the Use of Aryl Sulfonates in the Coupling Reaction

From Section 1.6, we can observe that there are wide applications of the sulfonates to different kinds of coupling reactions. For the palladium-catalyzed coupling reaction, the use of aryl/alkenyl/alkyl benzenesulfonates, tosylates and mesylates as electrophiles for the Kumada coupling, Negishi coupling, Hiyama coupling, Buchwald-Hartwig amination, Sonogashira reaction, thiolation, phosphination, Heck reaction and C-H direct arylation were attempted by different research groups in the last five years. However, as we can see also, there are only a limited number of published papers related to the use of the

sulfonates as the coupling partner. SciFinder gives a simple comparison between the use of aryl sulfonates and aryl halides in the coupling reaction. There are 3057 published papers related to the concepts of aryl halide couplings but only 69 published ones reporting the aryl sulfonate couplings since 2000. The use of aryl halides as coupling partner is 40 times more than that of aryl sulfonates in the last ten years. If we focus on the palladium-catalyzed coupling reaction, the difference increases to more than 54 times as there are 1302 published papers related to aryl halides but only 24 for aryl sulfonates.

On the other hand, by comparing the reports for the aryl halide and the aryl sulfonates, significant differences can be observed in their catalyst loading and reaction conditions. For example, in the Suzuki coupling, catalyst loading as low as 0.005mol%Pd has already been achieved even for non-activated aryl chloride.[106] However, for the Suzuki coupling of aryl tosylates, the catalyst loading for the similar entry requires 2 mol%Pd, which is 100 times higher than that in the case of aryl chloride and 1000 times higher than in the case of aryl bromide (Scheme 1.74).[84]



Scheme 1.74 Comparison of the reactivity between aryl tosylates, chlorides and bromides in the Suzuki coupling reaction.

Besides, only a few catalytic systems were reported for the coupling of aryl sulfonates. In fact, several kinds of catalytic systems have been developed for the coupling of alkyl/alkenyl/aryl tosylates. However, by comparing the variety of catalytic systems developed for the coupling of aryl chlorides with aryl sulfonates, effective catalytic systems for the general palladium-catalyzed coupling of aryl tosylates are still mainly limited to the combination of $Pd(OAc)_2$/X-Phos and $Pd(P(o\text{-}tol)_3)_2$/Josiphos as the catalysts.

Moreover, there are still many limitations in the $Pd(OAc)_2$/X-Phos and $Pd(P(o\text{-}tol)_3)_2$/Josiphos catalytic systems for the coupling of aryl sulfonates. For example, instead of aryl tosylates which are more difficult to be activated, mainly aryl benzenesulfonates are used for the $Pd(OAc)_2$/X-Phos-catalyzed amination and amidation reactions.[92] $Pd(OAc)_2$/X-Phos catalyzed Sonogashira reaction is

limited to activated aryl tosylates only and a syringe pump is required to perform the addition of the alkynes slowly.[99] $Pd(P(o\text{-tol})_3)_2$/Josiphos-catalyzed amination is limited to aryl tosylates with primary amines only. And no yield can be obtained if aryl mesylates are used as substrates.[93] On the other hand, further development of Suzuki coupling is mainly concentrated at alkenyl tosylate/mesylates but not aryl tosylates/mesylates. Moreover, until 2006, only one entry was reported for thiolation of aryl tosylate which can be quoted as an example to demonstrate the limitation of aryl sulfonates coupling reaction.[100]

Last but not least, there is no successful example for the palladium-catalyzed coupling reaction for the aryl mesylates. The use of aryl mesylates in the coupling reactions is more attractive than that of the corresponding aryl tosylates This is because aryl mesylates, like the corresponding aryl tosylates, are cheap, readily available, easy to handle and stable crystalline solids, and with the advantage of being more atom economical over the corresponding aryl tosylates due to their significantly lower molecular weight. The latter advantage is of increasing importance as greener processes are sought out of environmental concerns. One of the limitations of the use of aryl mesylates in coupling reaction is that the relative acidity of the methyl group renders them incompatible with procedures that require a strong base. Most

importantly, the aryl mesylates are lot more inactive than the aryl tosylates because the C-O bond strength of aryl mesylates is higher than that of the corresponding aryl tosylates. Usually, the lower the pKa of the conjugate acid, the better the leaving group is (Figure 1.1).[107]

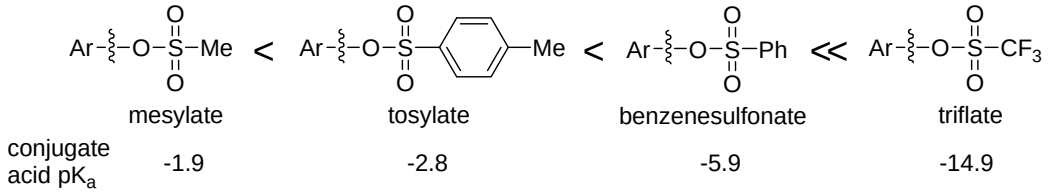


Figure 1.1 A comparison on the leaving-group-activity of commonly used sulfonate groups based on the pKa value of their conjugate acids.

At the beginning of our study, there was only one paper reporting an example of the palladium-catalyzed Suzuki coupling of the aryl mesylate in 1995 (Scheme 1.39).[108] However, in this report, only poor product yield could be obtained even using activated aryl mesylate as substrate.[108] No successful example of palladium catalyzed coupling of aryl mesylates had been reported before 2006.

Although there are still many limitations in the existing coupling methods for aryl sulfonates, the above examples demonstrate the possibility to apply aryl sulfonates in various coupling reactions. Our discussion shows that there are great potential to develop the use of aryl sulfonates as coupling partner due to

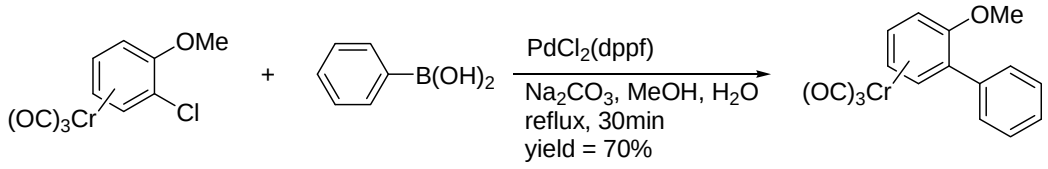
their extremely wide applications. There is large room for further development of the aryl sulfonates coupling reactions such as expanding the substrate scopes and lowering the catalyst loading. Therefore, we would like to put our effort in the development of a new catalytic system for the coupling reaction of aryl sulfonates, especially aryl tosylates and aryl mesylates.

1.8 Ligand Development: Historically proven to be the Key to Success

Until the late 1990s, one major limitation of all palladium-catalyzed coupling reactions had been the poor reactivity of aryl chlorides, aryl tosylates and mesylates compared to the more traditionally employed and more reactive aryl bromides, iodides and triflates. The aryl chlorides, aryl tosylates and mesylates are highly attractive to the large-scale pharmaceutical and industrial coupling processes due to their lower cost and more readily available as compared to their more reactive counterparts. Although further success has been observed with nickel-based catalysts, there are certain drawbacks associated with the use of nickel versus palladium complexes, such as lower functional group tolerance, lower selectivity and higher toxicity.

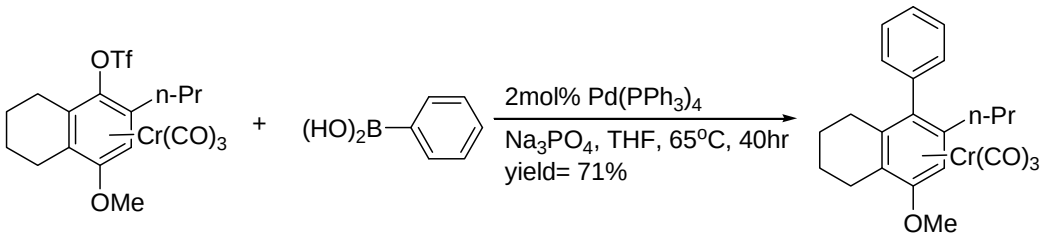
1.8.1 Various Kinds of Attempts for the Coupling of Aryl Chlorides

Several approaches have been attempted in order to utilize aryl chlorides as coupling partner in the palladium-catalyzed coupling reaction. It is believed that the reluctance resistance of these compounds to undergo oxidative addition by palladium (0) causes low reactivity of the electron-rich aryl triflates and aryl chlorides in the coupling reactions. One of the solutions is to coordinate the aryl chlorides to the chromium tricarbonyl complex whose strong electron group can intensively reduce the electron density from the arene ring so as to facilitate the oxidative addition step. In 1994, Uemura *et al.* reported the palladium-catalyzed cross coupling of (η^6-chlorobenzene) chromium tricarbonyl complexes with arylboronic acid in good yield (Scheme 1.76).[109]



Scheme 1.75 Palladium-catalyzed Suzuki coupling of (η^6-chlorobenzene) chromium tricarbonyl complexes

At that time, electron-rich and sterically hindered aryl triflates were also difficult substrates for the coupling reaction. By using a similar approach, Wulff *et al.* reported the palladium-catalyzed cross coupling of (η^6- arene) chromium tricarbonyl triflate complexes (Scheme 1.77).[110]

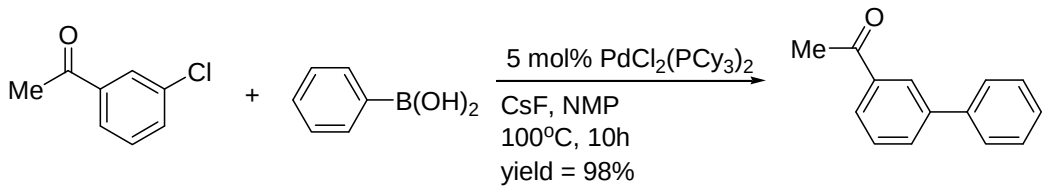


Scheme 1.76 Palladium-catalyzed Suzuki coupling of (η^6- arene) chromium tricarbonyl triflate complexes

Another approach is to convert the difficult aryl chlorides to easy aryl iodides for the coupling reaction. In 1997, Joule *et al.* tried to synthesize and examine the potentially electroactive molecules 1,8-bis(thianthrenyl)anthracenes.[111] 1,8-Dichloroanthra-9,10-quinone is commercially available and easily converts to 1,8- dichloroanthracene in 74% yield through a single step reaction.[112] However, meanwhile, there was no effective coupling method for the coupling of aryl chlorides. Therefore, Joule *et al.* tried to convert the 1,8-dichloroanthra-9,10-quinone to 1,8- diiodoanthracene through a multi-step reaction but only 30% product yield was obtained. After that the 1,8-diiodoanthracene was coupled with thianthrene 1- and 2- boronic acids to give 1,8-bis(thianthrenyl)anthracenes. However, these compromising methods only partially solve the problems of high cost in terms of the atom economy and environmental friendliness.

1.8.2 Ligand Development Leads to Successful Coupling of Aryl Chlorides

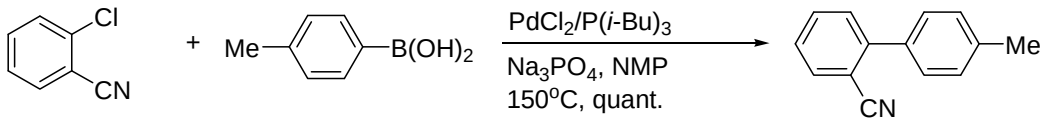
In 1997, Shen *et al.* reported an important observation regarding Suzuki coupling of aryl chlorides.[113] They established a palladium complex that includes a bulky, electron-rich trialkylphosphine (PCy_3) which catalyzes cross-coupling reaction (Scheme 1.78). Although only electron-deficient aryl chlorides were examined in their report, the authors proposed an important concept that more electron donating nature of PCy_3 might enhance the oxidative addition of palladium into the Ar-Cl bond so that tricyclohexylphosphine is a more effective ligand than the common triarylphosphine in the Suzuki coupling reaction.



Scheme 1.77 Pd/PCy_3 catalyzed Suzuki coupling of aryl chlorides

After Shen *et al.*'s report, the high catalytic activity of palladium complexes of the bulky, electron-rich trialkylphosphines in the Suzuki coupling of activated aryl chlorides was observed by Monteith *et al.* during the development of a

manufacturing route to 2-cyano-4'-methylbiphenyl (Scheme 1.79).[114] It was observed that P(*i*-Pr)$_3$ and P(*i*-Bu)$_3$ were also effective ligands in the coupling reaction.



Scheme 1.78 Pd/P(*i*-Bu)$_3$ catalyzed Suzuki coupling of aryl chlorides

Those significant observations caught many research groups' attention that the coordinating ligands have significant impact on the outcome of the coupling reactions. To date, the common view regarding efficient phosphine ligands for coupling reactions is that they are electron-rich and bulky. These electron-rich ligands are suggested to increase the electron density around a metal center (such as palladium center), thereby facilitating the oxidative addition step of unreactive substrates. Bulky ligands will probably shift the equilibrium between LPd and L_2Pd in favor of LPd, which is believed to be the active species in the catalytic cycle.[115]

Since 1998, Beller, Buchwald, Fu, Hartwig and Verkade groups have contributed a huge amount of work in the phosphine ligand design and synthesis (Figure 1).[116-119] In particular, the P*t*-Bu$_3$ by Fu[120-123]and Koie,[124] the

ferrocenyl-based dialkylphosphine by Hartwig,[125,126] the elegantly designed biphenyl-based dialkylphosphine by Buchwald[84,106,127-131] and the heteroaromatic dialkylphosphine by Beller[132-134] are highly versatile (Figure 1.2). Moreover, phosphine ligands with hemilabile coordinating ability have been reported to be effective in coupling reactions with low catalyst loading.[135] These novel ligand designs have been found to be important for substantial improvements in transition metal-catalyzed cross coupling reactions.[132]

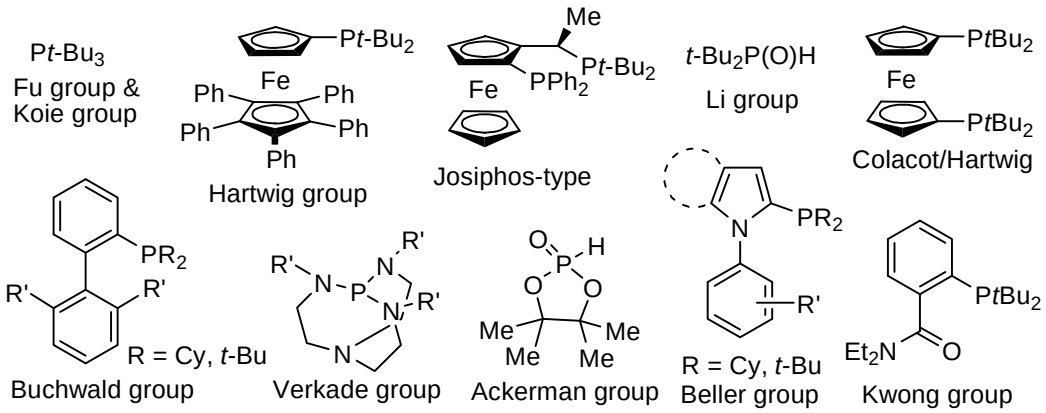


Figure 1.2 Selected examples of effective phosphine ligands

1.8.3 Recent Ligand Designs and Difficulties for the Coupling of Aryl Sulfonates

After yearly improvements to the supporting ligands are made, palladium-catalyzed coupling reaction of aryl chlorides can be performed under mild reaction conditions and very low catalyst loading as mentioned before.

However, aryl tosylates and mesylates remain problematic substrates in the palladium-catalyzed cross-coupling reactions. It is believed that a strategic design of ligand with appropriate steric/electronic natures and great diversity is crucial in dealing with the challenging and problematic aryl tosylates and mesylates in the coupling reaction. However, it has been shown that the common efficient ligands for the aryl halides coupling reactions are not effective in the sulfonates coupling reactions.

Different kinds of ligands have been examined by research groups in order to develop a general and effective palladium-catalyzed coupling reaction. It is found that traditional ligands for the coupling of aryl bromides, iodides and triflates, such as PPh_3,[108] dppf,[108] dppp,[96] and P(*o*-toyl)$_3$[96], are not effective in the aryl tosylates coupling reaction. Also, the common bulky and electron-rich trialkylphosphine ligands such as PCy_3[88] and P*t*-Bu_3[84] are also ineffective in the aryl tosylates coupling reaction. In fact, when the palladium-catalyzed aryl tosylate coupling reaction was performed with these ligands, only trace yield was obtained in the most of the cases.

Interestingly, some of the most efficient ligands developed recently that are known to be effective ligands for the palladium aryl chlorides coupling are not effective in the sulfonates coupling reaction (Figure 1.3).[84,92]

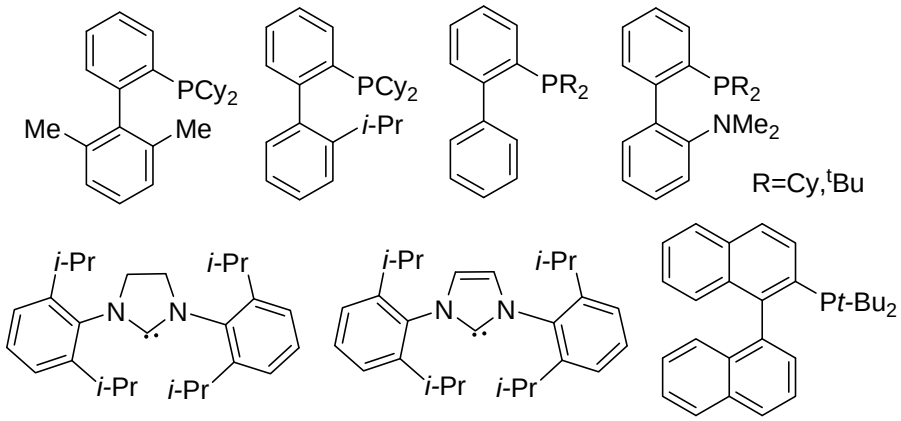


Figure 1.3 Ineffective supporting ligands in the palladium-catalyzed coupling of aryl tosylates

Until recently, the effective ligands for the palladium-catalyzed coupling of aryl tosylates have been mainly X-Phos developed by Buchwald and hindered Josiphos ligand CyPF-*t*-Bu developed by Hartwig. We can find some limitations and interesting phenomenan from the reported papers regarding the use of these supporting ligands (Figure 1.4). For example, hindered Josiphos ligand CyPF-*t*-Bu is an effective supporting ligand for the palladium-catalyzed amination reaction[93] and Kumada coupling[86] of the aryl tosylates under room temperature while Josiphos ligand CyPF-*t*-Bu shows no reactivity for the Suzuki coupling of aryl tosylates[84] and no reactivity for the amination of aryl mesylates.[93] On the other hand, X-Phos is an effective supporting ligand for the palladium-catalyzed Suzuki coupling reaction and generally shows reactivity towards various kinds of coupling reactions. However, Josiphos ligand CyPF-*t*-Bu demonstrates superior reactivity in the amination reaction to the X-Phos in terms of catalyst loading and reaction conditions. Moreover, for the

Pd/X-Phos catalyzed-Sonogashira reaction, it is not general as only activated aryl tosylates can be used as coupling partner.

S-Phos shows very low catalytic activity in the Hiyama coupling reaction of aryl tosylates[96] while moderate yield can be obtained in the Suzuki coupling of aryl tosylates with potassium phenyltrifluoroborate. After substituting a methoxy group to the *para*-position of S-Phos, good yield can be obtained even in the Suzuki coupling of aryl tosylates with potassium phenyltrifluoroborate.[88] Moreover, if the PCy_2 group of the X-Phos is changed to the more electron-rich and bulky P*t*-Bu_2 group, the yield of the Suzuki coupling of aryl tosylates drops nearly half.[84]

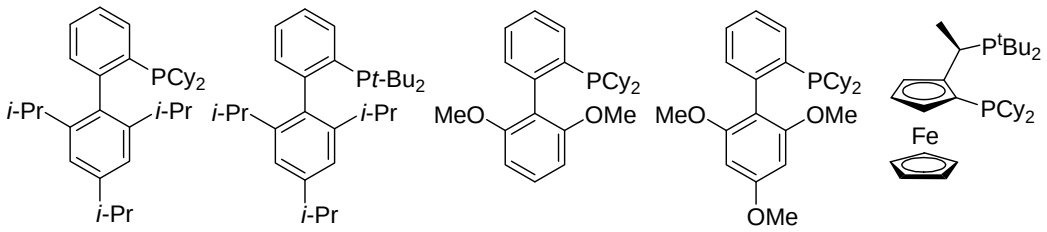
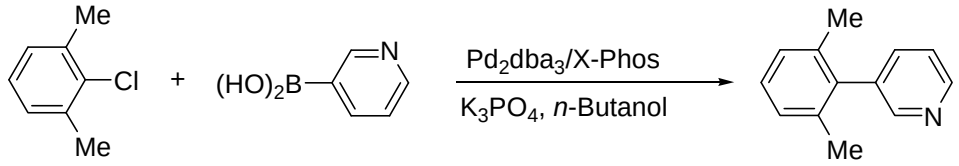


Figure 1.4 Effective ligands in the palladium-catalyzed coupling of aryl tosylates

As mentioned before, many effective supporting ligands for the coupling reaction of aryl halides are not effective in the sulfonates coupling reaction. Interestingly, the effective supporting ligands for the palladium-catalyzed coupling reaction of aryl tosylates are also effective for the coupling reaction of

aryl halides. For example, Pd/X-Phos can effectively catalyze the sterically hindered 2-chloro-*m*-xylene with pyridylboronic acids in good yield (Scheme 1.79).[131]



Scheme 1.79 Pd/X-Phos catalyzed Suzuki coupling of aryl chlorides

These examples show that the common view of efficient phosphine ligands for coupling reactions of aryl halides that are electron-rich and bulky may not be directly applicable to the coupling for the aryl tosylates and aryl mesylates. In fact, up to now, there is no detailed explanation why X-Phos and Josiphos CyPF-*t*-Bu are effective ligands in the palladium-catalyzed coupling reaction. Moreover, the relationship between the ligand structure and the catalyst reactivity in the coupling reaction of aryl tosylates and mesylates is still unclear. What has been recognized is that the supporting ligand employed in the coupling reaction has significant impact on the outcome of the reactions.

1.9 Entire New Classes of Ligands: Strategy to Explore the Palladium-Catalyzed Coupling of Aryl Sulfonates

In order to explore the palladium-catalyzed coupling of aryl sulfonates, we plan to

1. Strategically design entirely new classes of monodentate phosphine ligands with great diversity that can provide the possibility to fulfill the appropriate steric/electronic natures for the coupling reaction.
2. Explore the catalytic activity of entire new classes of monodentate phosphine ligands beginning from the Suzuki coupling of aryl halides.
3. Apply the new classes of monodentate phosphine ligands towards the palladium-catalyzed coupling of aryl tosylates. If good results can be obtained, we will attempt to apply this new ligand to the unexplored coupling reaction of aryl mesylates.

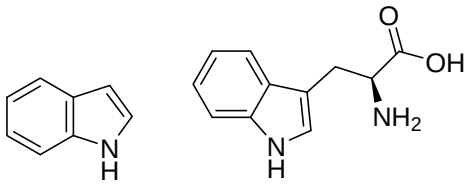
Chapter 2 Designs and Syntheses of New Classes of Monodentate Indolyl Phosphine Ligands

2.1 Introduction

It is well known that ligand design and synthesis are very important for the metal-catalyzed coupling reactions. After recognizing the preliminary relationship between the ligand structure and the outcome of the coupling reaction, various research groups have designed and synthesized countless supporting ligands for the coupling reactions. From simple ligands such as P*t*-Bu_3[120-123] to the highly versatile Buchwald ligand kit[84,106,127-131] and Josiphos kit[125,126] have been designed and synthesized. Although a variety of ligands have been introduced, rapid assembly of structurally diverse ligand systems *via* simple synthetic methods is still important for the development of versatile catalysts for more widespread applications of coupling reactions.

2.1.1 Strategic Design of New Classes of Ligands

The pervious discussion provides us a clues that the design of ligand is possibly a key to success to the palladium catalyst coupling of aryl sulfonates. We have the following strategic considerations for the design of easily synthesized and effective ligands for the coupling reactions: (1) the starting materials should be inexpensive and readily available; (2) the ligand synthesis should be simple and straightforward (an elimination of metal/halogen exchange (from ArBr or ArI) would be even more advantageous); (3) the ligand diversity should be easily accessible, and should conveniently provide high level of steric and electronic fine-tunings. Based on these three points, we chose indole as the template to design and explore a new class of monodentate indolyl phosphine ligands. Indole is an aromatic heterocyclic organic compound. It has a bicyclic structure that consists of a six-membered benzene ring fused to a five-membered nitrogen-containing pyrrole ring. Indoles widely exist in many natural compounds, such as amino acid tryptophan, a precursor of neurotransmitter serotonin (Figure 2.1). Many indolyl alkaloids possess useful biological activities and are precursor to many pharmaceuticals.



indole **tryptophan**

Figure 2.1 Structure of indole and tryptophan

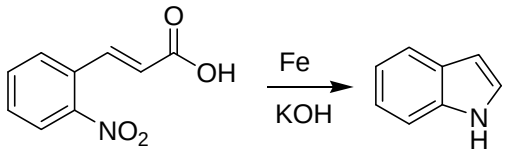
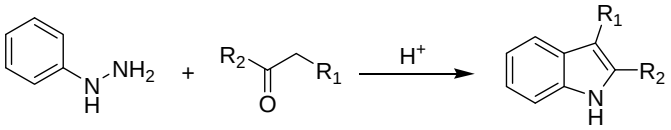
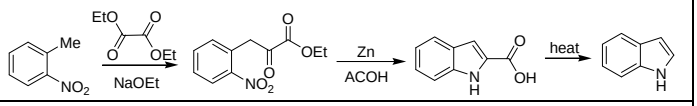
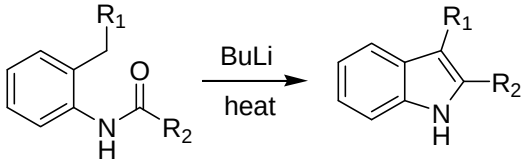
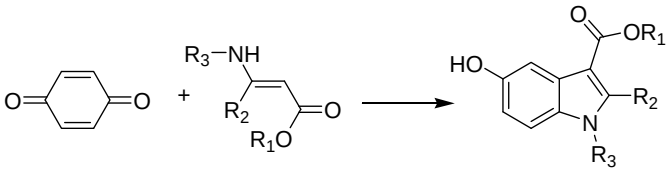
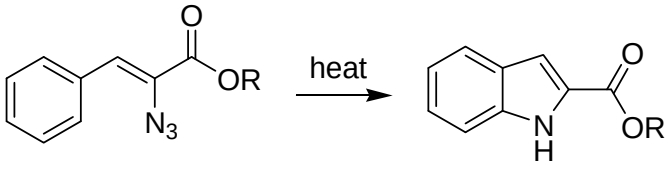
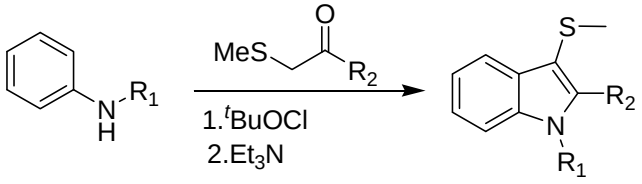
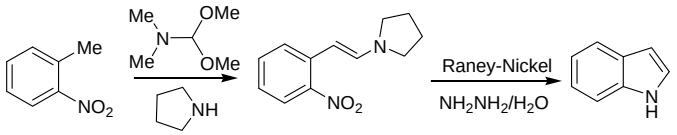
2.1.2 Considerations of Indole as a New Ligand Scaffold

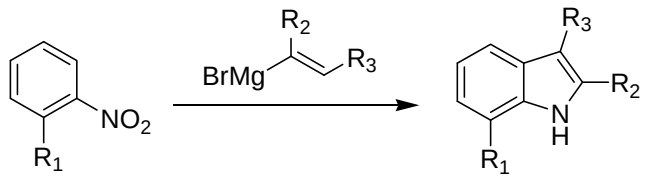
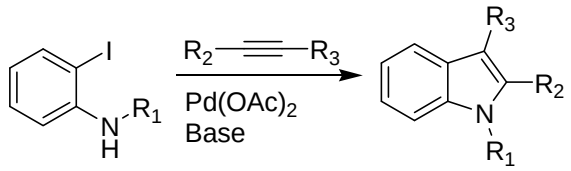
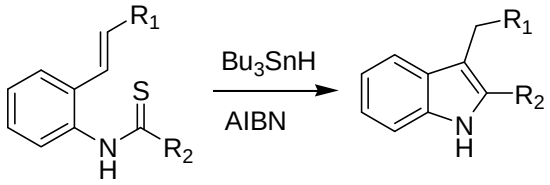
We herein selected the indole as template to design and explore a new class of phosphine ligands. There were several reasons for the choice of indole. First of all, indole is generally an inexpensive chemical that only costs USD 123/kg only. The cost for some indole derivatives, such as the USD 98/100g 2-phenylindole, is still reasonable. Moreover, the starting materials to synthesize indole derivatives such as phenylhydrazine (50 USD/500g) and acetophenone (12 USD/kg) are also inexpensive.

Generally, indole and its derivatives are readily available. In fact, many indole derivatives are commercially available too. Since indole derivatives are kinds of important compounds, many synthetic methods of indoles have been reported for over hundreds of years. More than ten different kinds of indole synthesis methods, from the most well known and general Fischer indole synthesis to most recent metal catalyzed indole synthesis, have been reported. These well-developed indole synthesis methods provide us a foundation to

synthesize desired indoles. The common indole synthesis methods are briefly summarized in the following table:

Table 2.1 The History of Indole Synthesis Methods Developed (Year 1869-1999)

Name / Discovery Year	Simplified Synthetic Scheme
Baeyer-Emmerling indole synthesis[136] **Year 1869**	
Fischer indole synthesis[137] **Year 1883**	
Reissert indole synthesis[138] **Year 1897**	
Madelung synthesis[139] **Year 1912**	
Nenitzescu indole synthesis[140] **Year 1929**	
Hemetsberger-Knittel synthesis[141] **Year 1972**	
Gassman indole synthesis[142] **Year 1973**	
Leimgruber-Batcho indole synthesis[143] **Year 1985**	

Bartoli indole synthesis[144] **Year 1989**	
Larock indole synthesis[145] **Year 1998**	
Fukuyama indole synthesis[146] **Year 1999**	

Last but not least, the chemical properties of indole scaffold can provide potential for diversification of the new ligands. One of the modern concepts for the phosphine ligand design is the rapid assembly of the two major compartments. One compartment is the phosphorus atom that attaches two of the simple equivalent groups that can be an aryl or alkyl group such as diphenyl or dicyclohexyl group. Another compartment is the ligand template that provides steric and electronic fine tuning for the phosphine ligand. In our blueprint, the indole scaffold provides at least four possible positions that can readily attach to the phosphino group (Figure 2.2).

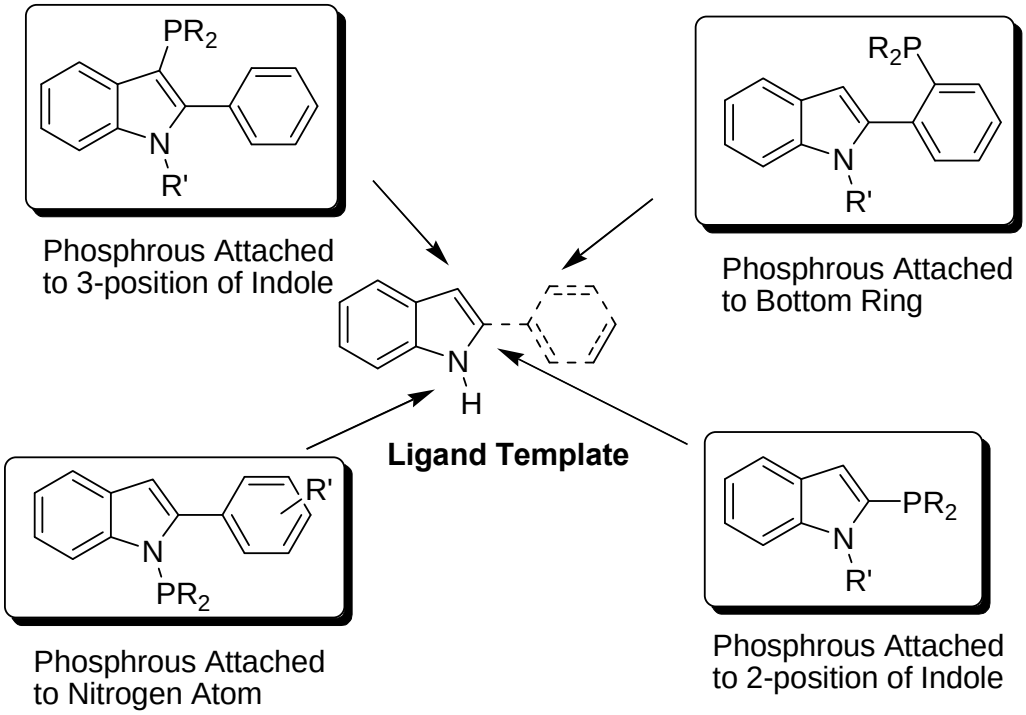


Figure 2.2 Four possible positions for attaching the phosphino group

Ligand template flexibility is also an important consideration for the ligand design, because tunability of the ligand is important and sometimes even crucial to deal with difficult substrates that may need specific steric and electronic geometry of the ligand. The ligands that derived from our indole ligand template were highly tunable in both steric and electronic effects. No matter which part of the ligand template the phosphorus group attached to, the remaining part of the ligand template could always provide room for further fine-tuning. The effective fine-tuning position of each ligand is illustrated in the following:

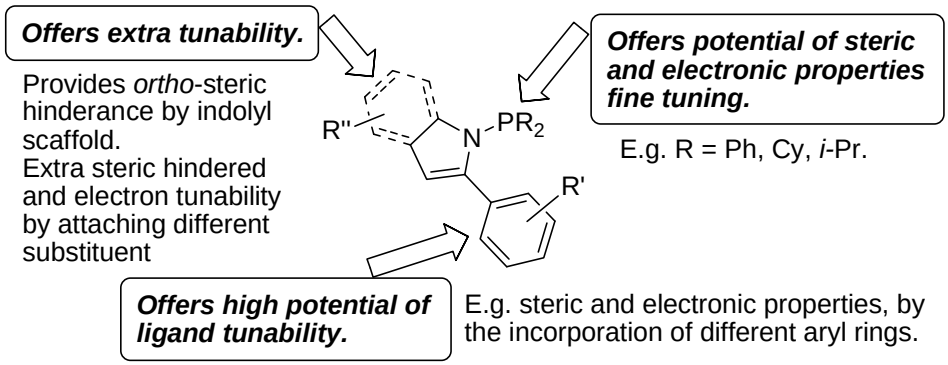


Figure 2.3 Tunable position for the phosphorus atom attached to the nitrogen atom

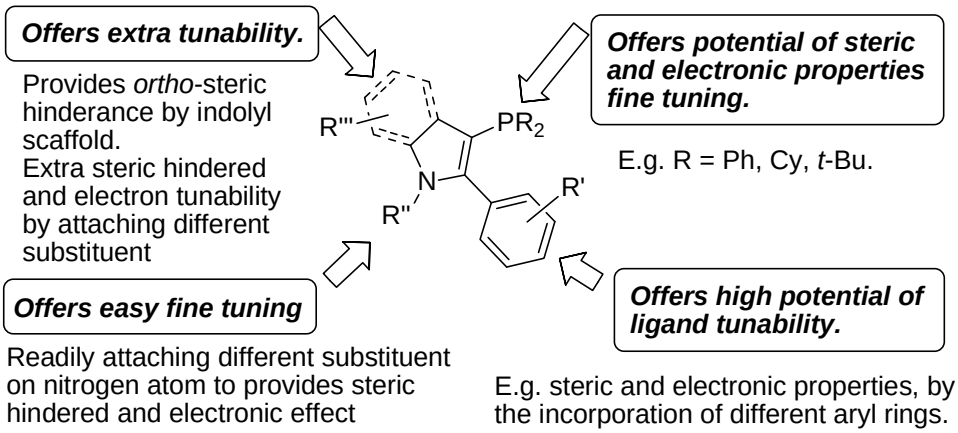


Figure 2.4 Tunable position for the phosphorus atom attached to the 3-position of indole

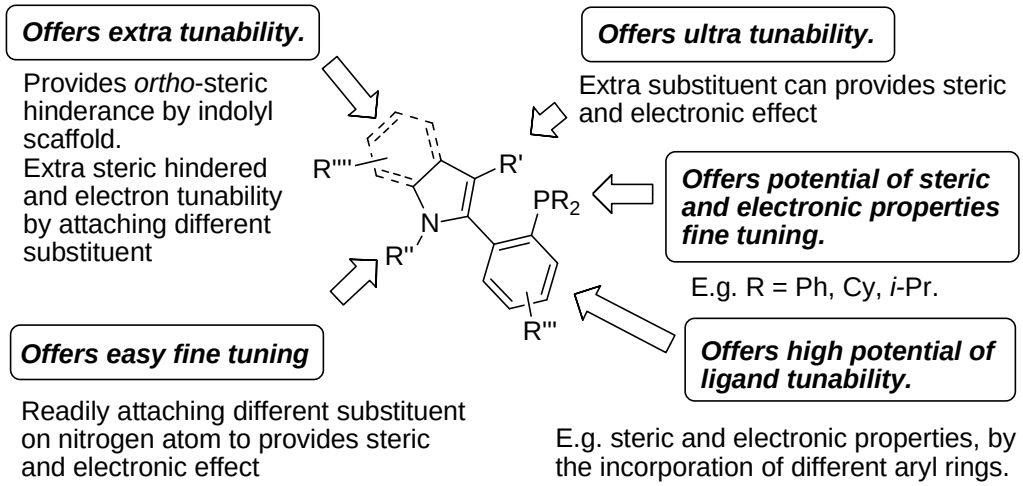


Figure 2.5 Tunable position for the phosphorus atom attached to the bottom ring

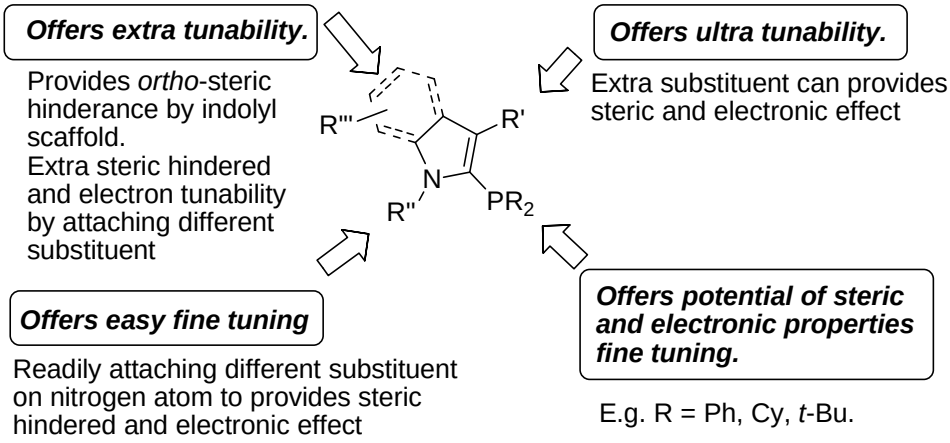


Figure 2.6 Tunable position for the phosphorus atom attached to the 2-position of indole

To sum up, the indole ligand template 1) is inexpensive; 2) can be readily available from commercially accessible starting materials; 3) can be synthesized from well developed synthesis methods; and 4) has high potential for diversification and easy steric and electronic fine-tuning. We therefore selected indole as template to design and explore a new class of phosphine ligands.

2.1.3 A Modular Approach to Synthesize and Classify New Classes of Indolyl Phosphines

The indole template that possesses all those convenient properties opens up the possibilities for us to use a modular approach to synthesize the highly diversified phosphine ligand in a rapid and simple manner. By using Fischer indole synthesis, we can simply cross matching the commercially available and inexpensive phenylhydrazine and acetophenones to synthesize a series of 2-arylindole scaffolds. Most importantly, the steric and electronic effects on the ligand framework can be simply modified by a random matching of arylhydrazines and substituted acetophenones. By using this modular approach, several kinds of ligands can be synthesized. Base on the phosphine group attached to nitrogen atom or carbon atom, we classify the new indolyl phosphine ligand into two major classes: N-P bound amino-phosphine ligand and C-P bound phosphine ligand.

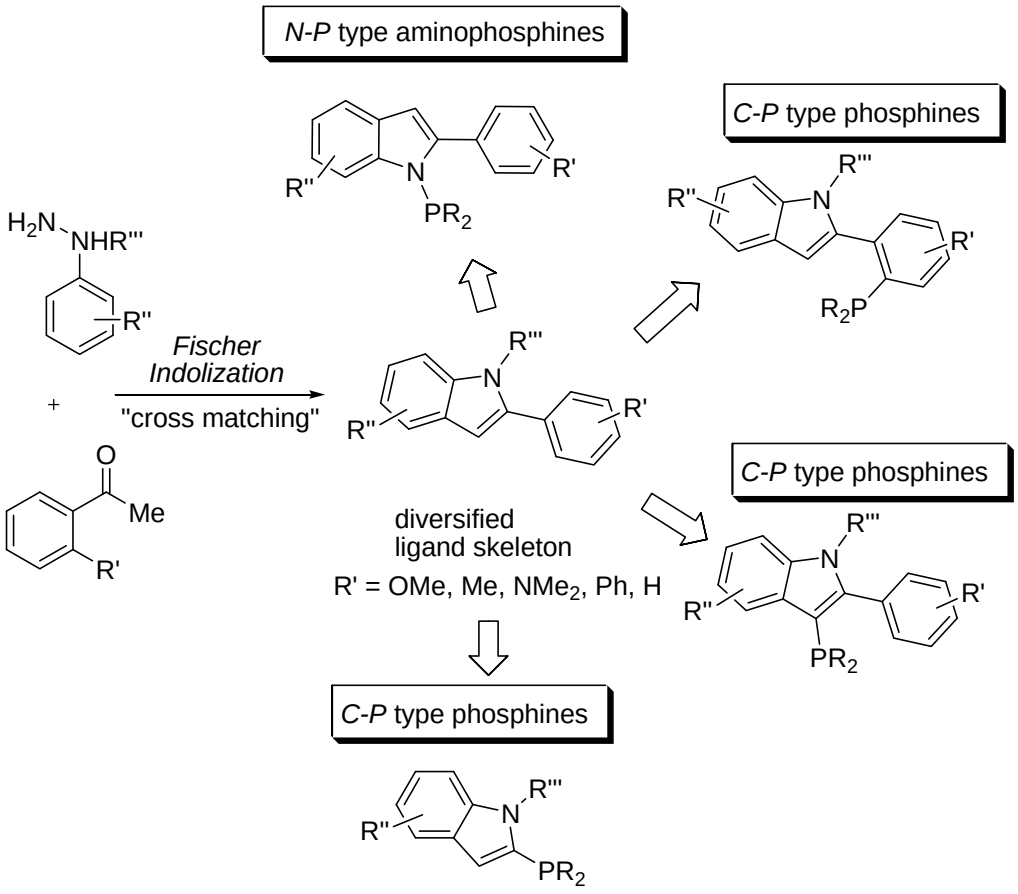


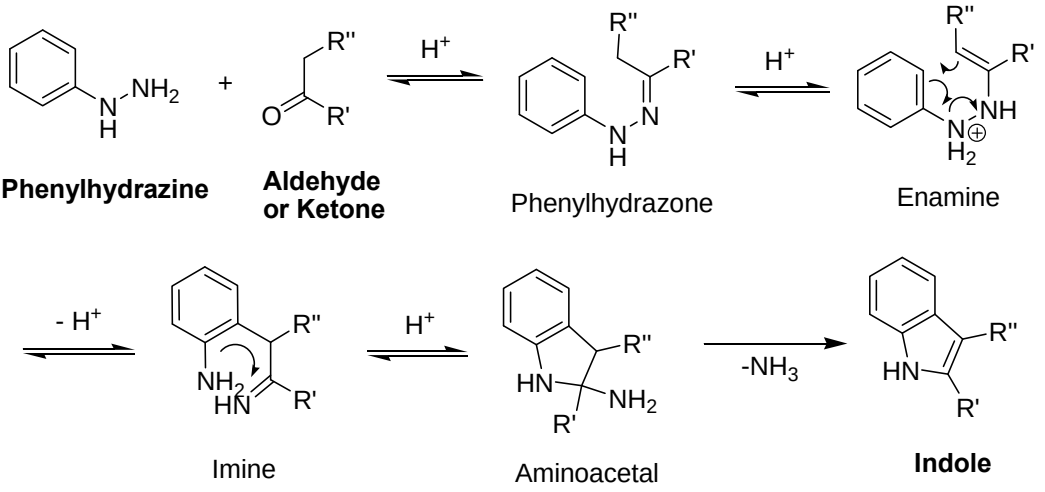
Figure 2.7. Ligand diversification from 2-arylindole template

2.2 Results and Discussion

2.2.1 Fischer Indole Synthesis of the Ligand Template

Among those indole synthesis methods introduced in Section 2.1.2, we selected the Fischer indole synthesis as our primary tool to synthesize the indole templates. The Fischer indole synthesis, developed by E. Fischer *et al.* in 1883,[137] is the most versatile method that can make use of the commercially available and inexpensive arylhydrazines and acetophenones as precursors for the preparation of indole derivatives. Under acidic conditions, phenylhydrazine and an aldehyde or ketone can react to form indole. The reaction mechanism is briefly described as follows:

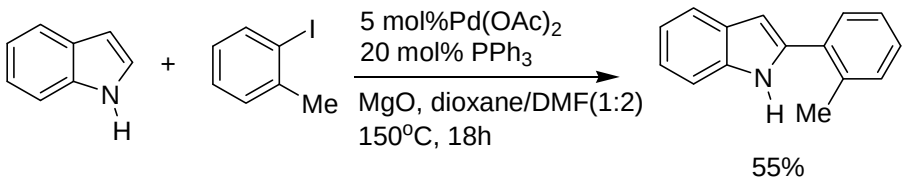
The reaction of a (substituted) phenylhydrazine with an aldehyde or ketone initially forms a phenylhydrazone which isomerizes to the respective enamine (or 'ene-hydrazine'). After protonation, a cyclic [3,3]-sigmatropic rearrangement occurs producing an imine. The resulting imine forms a cyclic aminoacetal (or aminal), which under acid catalysis that eliminates NH_3, results in the energetically favorable aromatic indole.[147]



Scheme 2.1 Mechanism of the Fischer indole synthesis

2.2.1.1 Synthesis of the Ligand Template for N-P Type Indolyl Phosphine

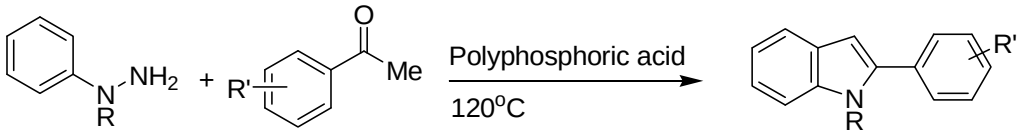
2-Arylindole scaffolds were efficiently synthesized by the Fischer indole synthesis in good yields (Table 2.2). One of the challenges in using the Fischer indole synthesis to prepare the ligand templates is the lack of available literature on the direct Fischer indolization to synthesize 2'-substituted 2-arylindoles. According to the literature reports, these sterically hindered indole templates were prepared by transition metal-catalyzed coupling method. (Scheme 2.2).[148]

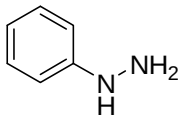
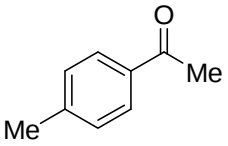
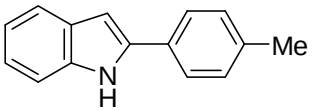
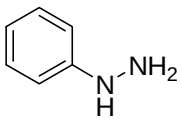
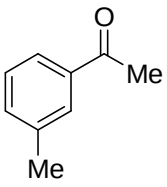
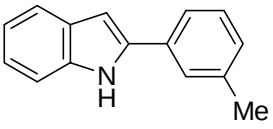
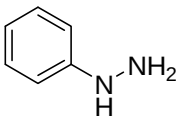
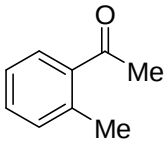
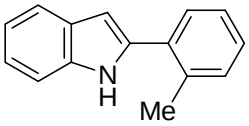
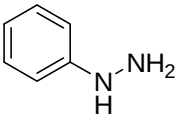
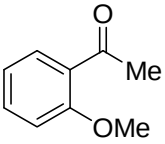
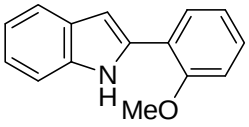


Scheme 2.2 Synthesis of 2'-substituted 2-arylindoles through direct arylation

The modified Fischer indolization in our study was successful in synthesizing sterically hindered 2'-substituted 2-arylindoles. The product yield did not diminish significantly, and it was as good as the non-hindered product (Table 2.2).

Table 2.2 The Fischer Indole Synthesis of 2-Aryl-*1H*-indoles[a]

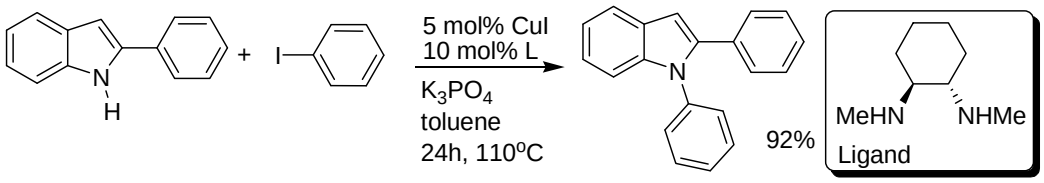


entry	Arylhydrazine	Acetophenone	product	%yield[b]
1				79
2				71
3				71
4				71

[a]Reaction conditions: Phenylhydrazine: Acetophenones = 1:1, reaction time =2h, Temperature = 120°C; [b]Isolated yield.

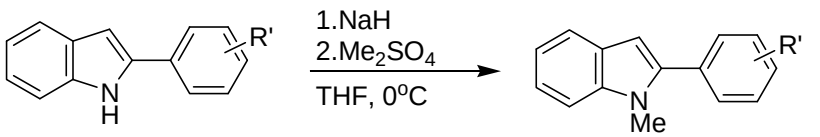
2.2.1.2 Synthesis of the Ligand Template for C-P Type Indolyl Phosphine

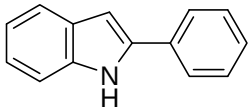
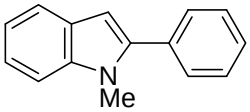
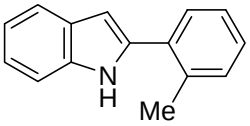
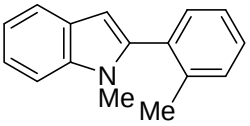
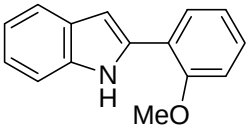
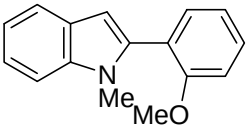
For the synthesis of C-P type indolyl phosphine ligand, the acidic proton on the nitrogen atom will first react in the basic condition instead of our target carbon position. Therefore, we need to protect the nitrogen atom with a protecting group to prevent retardation of C-P bond formation. The selection of the protecting group is a part of our ligand design because the substitute group attached to the nitrogen atom can also offer steric and electronic fine-tuning of our ligand. In general, there are two methods for introducing a protecting group to the nitrogen atom. For example, we can effectively introduce an alkyl group, such as a methyl group and an ethyl group, by a simple substitution reaction. It is also possible to introduce an aryl group by a relatively inexpensive copper-catalyzed amination reaction (Scheme 2.3).[149] Among those choices, we strategically chose the simplest methyl group as the substituent in order to rapidly synthesize and examine the catalytic activity of the whole classes of ligands in our preliminary study.



Scheme 2.3 N-arylindole synthesis by copper-catalyzed amination reaction

Table 2.3 Methylation of 2-Arylindoles[a]



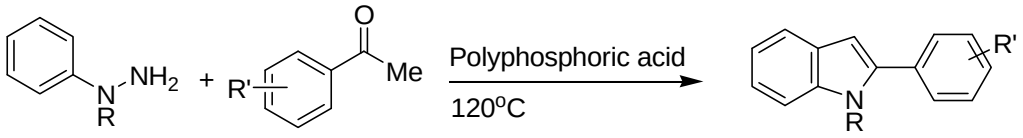
entry	2-arylindole	product	%yield[b]
1			90
2			86
3			92

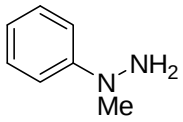
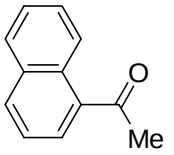
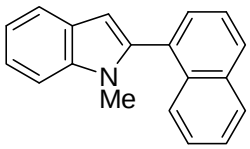
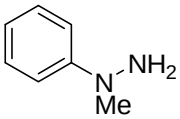
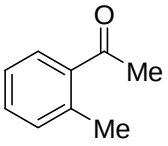
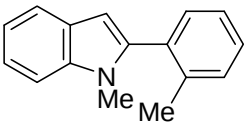
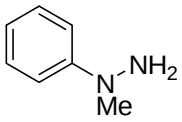
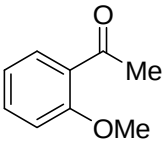
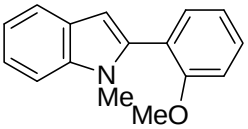
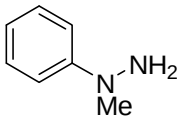
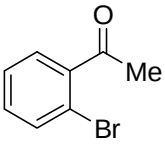
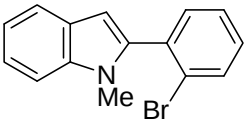
[a]Reaction conditions: 2-arylindole: Dimethylsulfate = 1:1.1, THF, Temperature = 0°C; [b]Isolated yield.

As expected, N-methylated 2-arylindoles could be obtained in excellent yield by using sodium hydride to abstract the acidic proton from the 2-arylindoles and then quenching with dimethylsulfate (Table 2.3). Although the reagents are inexpensive and the procedure is relatively simple, dimethylsulfate is a very toxic reagent. In order to reduce the number of synthetic steps and prevent the use of very toxic reagents, we attempted to use N-methylphenylhydrazine to replace phenylhydrazine in the initial Fischer indole synthesis. However, the lack of literature report on the direct Fischer indolization in synthesizing N-methylated 2'-substituted 2-arylindoles presented another

challenge. As expected the steric effect introduced by an extra methyl group might retard the Fischer indolization.

Table 2.4 Synthesis of N-Methylated 2-Arylindoles by the Fischer Indole Synthesis[a]



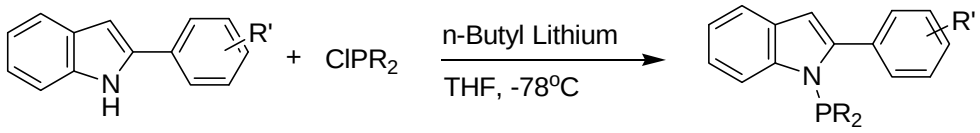
entry	arylhydrazine	acetophenone	product	%yield[b]
1				54
2				63
3				68
4				75

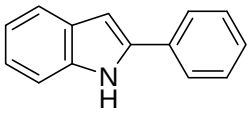
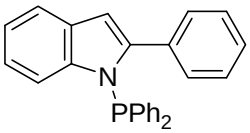
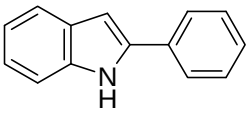
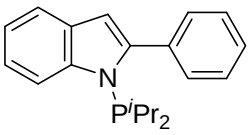
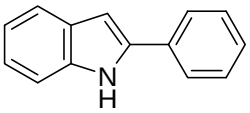
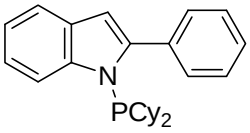
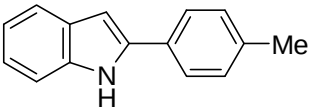
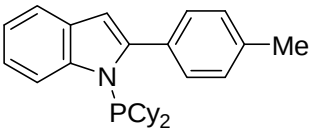
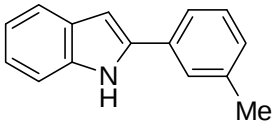
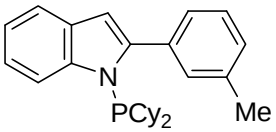
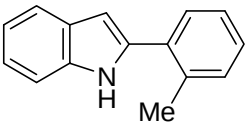
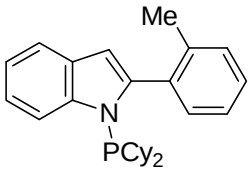
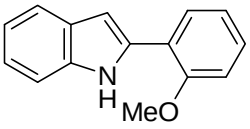
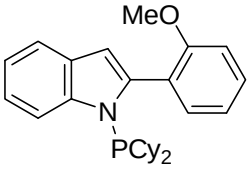
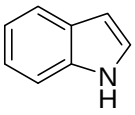
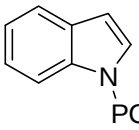
[a]Reaction conditions: Phenylhydrazine: Acetophenones = 1:1.2, reaction time =2hr, Temperature = 120°C; [b]Isolated yield.

Fortunately, the modified Fischer indolization was successful in synthesizing sterically hindered N-methylated 2'-substituted 2-arylindoles in good yield (Table 2.4).

2.2.2 Synthesis of N-P Type Indolyl Phosphine

Table 2.5 Synthesis of N-P Type Indolyl Phosphine Ligands[a]



entry	ligand precursor	$ClPR_2$	product	%yield[b]
1		$ClPPh_2$		78
2		$ClPi\text{-}Pr_2$		71
3		$ClPCy_2$		85
4		$ClPCy_2$		77
5		$ClPCy_2$		79
6		$ClPCy_2$		74
7		$ClPCy_2$		80
8		$ClPCy_2$		73

[a]Reaction conditions: 2-arylindole: $ClPR_2$: $^{n}BuLi$ = 1:1.1:1.1, THF, Temperature = -78°C; [b]Isolated yield.

The straightforward deprotonation of 2-arylindole by *n*-BuLi and the trapping of the lithiated intermediate by $ClPR_2$ afforded the corresponding indolyl phosphines in excellent yields (Table 2.5). Essentially complete conversion was observed that highlighted the ease of purification process by single crystallization. Particularly noteworthy is that this class of ligand exhibits high air stability in both solid and solution states. There was no detectable phosphine oxide signal from ^{31}P NMR when the solid-form ligand was placed under air atmosphere for 5 days or in solution form for at least 3 days. In contrast, P*t*-Bu_3 has been shown to be destroyed in air within 2 hours.[127]

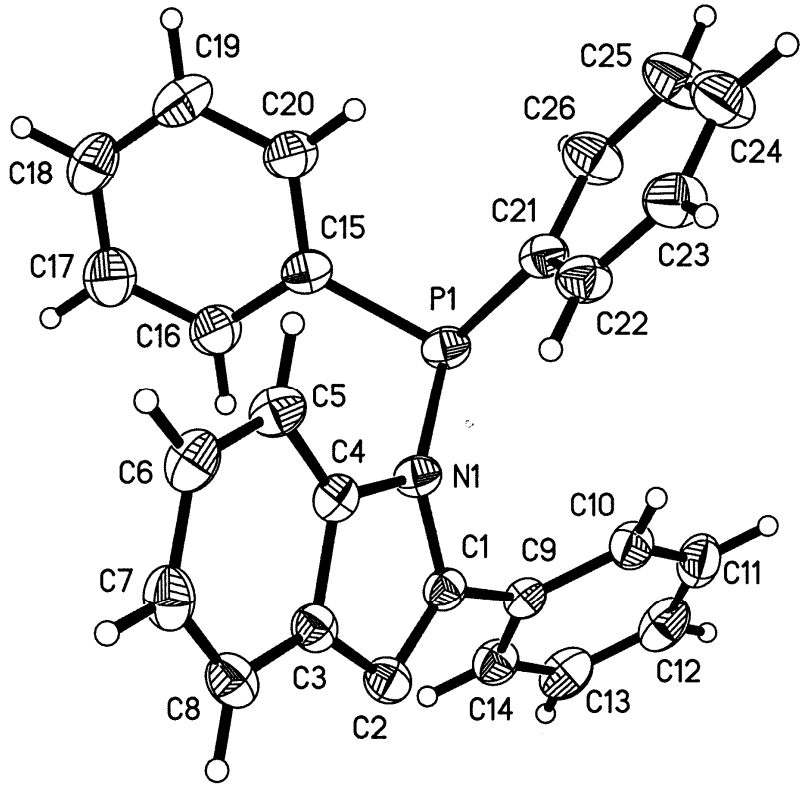


Figure 2.8 ORTEP representation of the NPPh Phendole-phos (30% probability ellipsoids)

Table 2.6 Crystal Data and Structure Refinement of NPPh Phendole-phos

Empirical formula	$C_{26}H_{19}NP$	
Formula weight	376.39	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2/c	
Unit cell dimensions	a = 28.347(5) Å	$\alpha = 90°$.
	b = 9.9905(17) Å	$\beta = 128.409(6)°$.
	c = 18.612(4) Å	$\gamma = 90°$.
Volume	4130.2(13) $Å^3$	
Z	8	
Density (calculated)	1.211 Mg/m^3	
Absorption coefficient	0.143 mm^{-1}	
F(000)	1576	
Crystal size	0.50 x 0.50 x 0.48 mm^3	
Theta range for data collection	1.83 to 27.56°.	
Index ranges	-36<=h<=36, -12<=k<=12, -24<=l<=24	
Reflections collected	18818	
Independent reflections	4767 [R(int) = 0.0462]	
Completeness to theta = 27.56°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.000 and 0.770	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4767 / 0 / 253	
Goodness-of-fit on F^2	1.020	
Final R indices [I>2sigma(I)]	R1 = 0.0493, wR2 = 0.1268	
R indices (all data)	R1 = 0.0876, wR2 = 0.1481	
Largest diff. peak and hole	0.605 and -0.213 $e.Å^{-3}$	

Table 2.7 Selected Bond Distances (Å) and Angles (˚) for NPPh Phendole-phos

Bond distances (Å)			
P(1)-N(1)	1.7383(17)	P(1)-C(21)	1.816(2)
P(1)-C(15)	1.827(2)	N(1)-C(1)	1.402(2)
N(1)-C(4)	1.414(2)		

Bond angles (˚)			
C(15)-P(1)-C(21)	103.65(9)	C(21)-P(1)-N(1)	104.15(9)
C(15)-P(1)-N(1)	101.44(9)	C(1)-N(1)-P(1)	121.02(13)
C(4)-N(1)-P(1)	130.03(16)	C(4)-N(1)-C(1)	106.54(16)

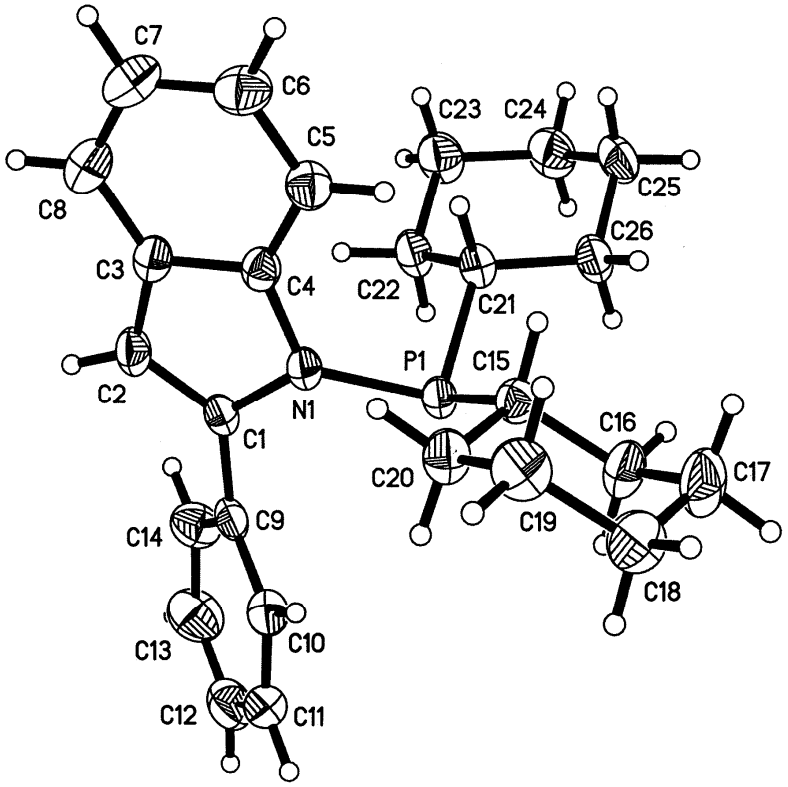


Figure 2.9 ORTEP representation of the NPCy Phendole-phos (30% probability ellipsoids)

Table 2.8 Crystal Data and Structure Refinement of NPCy Phendole-phos

Empirical formula	$C_{26}H_{32}NP$	
Formula weight	389.50	
Temperature	294(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	Pbca	
Unit cell dimensions	a = 8.1156(10) Å	$\alpha = 90°$.
	b = 16.098(2) Å	$\beta = 90°$.
	c = 34.528(4) Å	$\gamma = 90°$.
Volume	4510.8(10) $Å^3$	
Z	8	
Density (calculated)	1.147 Mg/m^3	
Absorption coefficient	0.133 mm^{-1}	
F(000)	1680	
Crystal size	0.50 x 0.50 x 0.18 mm^3	
Theta range for data collection	2.36 to 27.55°.	
Index ranges	-10<=h<=10, -20<=k<=20, -44<=l<=34	
Reflections collected	28917	
Independent reflections	5190 [R(int) = 0.1008]	
Completeness to theta = 27.55°	99.5 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.000 and 0.628	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5190 / 0 / 253	
Goodness-of-fit on F^2	0.991	
Final R indices [I>2sigma(I)]	R1 = 0.0515, wR2 = 0.1127	
R indices (all data)	R1 = 0.1298, wR2 = 0.1442	
Largest diff. peak and hole	0.228 and -0.223 $e.Å^{-3}$	

Table 2.9 Selected Bond Distances (Å) and Angles (˚) for NPCy Phendole-phos

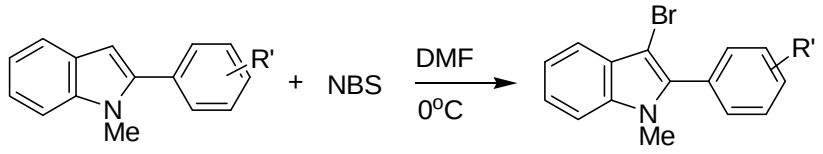
Bond distances (Å)			
P(1)-N(1)	1.7519(18)	P(1)-C(21)	1.859(2)
P(1)-C(15)	1.860(2)	N(1)-C(1)	1.417(3)
N(1)-C(4)	1.402(3)		

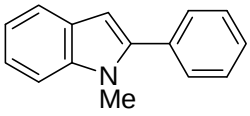
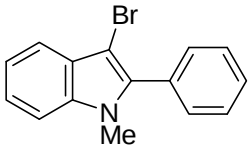
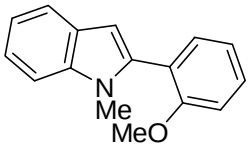
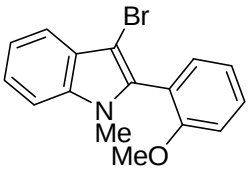
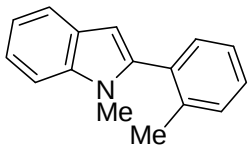
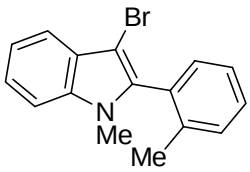
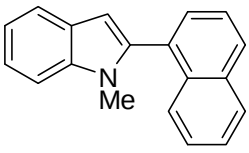
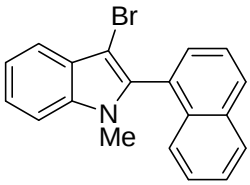
Bond angles (˚)			
C(15)-P(1)-C(21)	103.62(11)	C(21)-P(1)-N(1)	99.35(9)
C(15)-P(1)-N(1)	103.88(10)	C(1)-N(1)-P(1)	120.21(16)
C(4)-N(1)-P(1)	127.69(15)	C(4)-N(1)-C(1)	106.48(17)

2.2.3 Synthesis of C-P Type Indolyl Phosphine

2.2.3.1 Phosphine Group Attached to Indole 3-Position

Table 2.10 Bromination of 3-Position of 2-Arylindoles[a]



entry	ligand precursor	product	%yield[b]
1			86
2			81
3			87
4			62

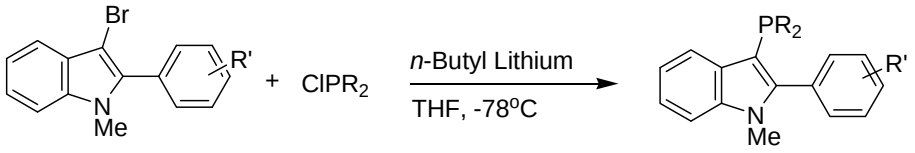
[a]Reaction conditions: 2-arylindole: NBS = 1:1.1, DMF, Temperature = 0°C; [b]Isolated yield.

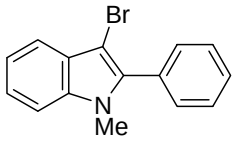
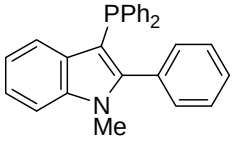
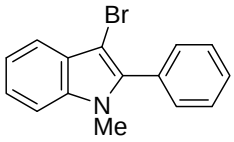
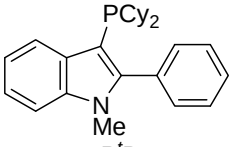
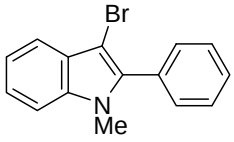
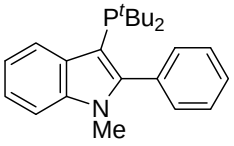
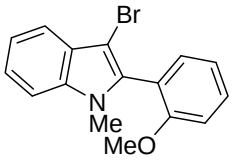
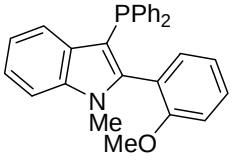
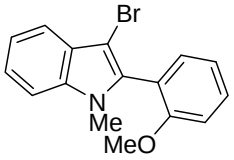
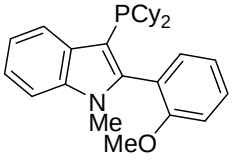
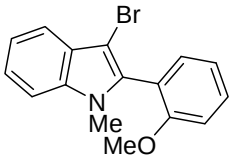
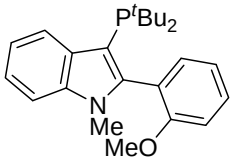
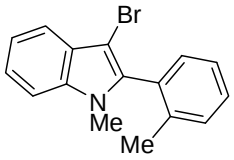
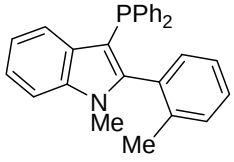
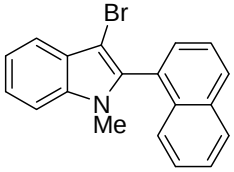
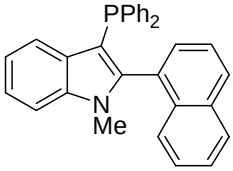
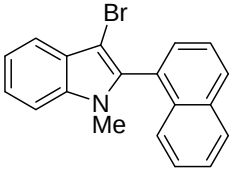
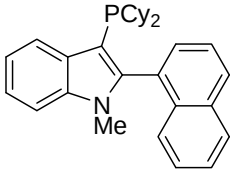
We successfully synthesized N-methylated 2-arylindole by the Fischer indole synthesis. However, the proton at the 3-postion of the indole ring could not be directly deprotonated even by *tert*-butyllithium. Therefore, we had to

replace the proton with a bromine group through selective bromination of the indole. As indole can readily undergo electrophilic substitution predominately at the 3-prosition of indole ring, we successfully selectively brominated the indole 3-position in excellent yield by using N-bromosuccinimide as brominating reagent and DMF as solvent (Table 2.10).

Lithium/bromide exchange of 3-bromo-2-arylindole by *n*-BuLi and trapping the lithiated intermediate by $ClPR_2$ afforded the corresponding indolyl phosphines in good yields (Table 2.11). Essentially complete conversion was observed in most of the cases. The products can be simply purified by successively washing with methanol. The low yield of the ligands (Table 2.11, entries 3, 6), bearing di-*tert*-butyl phosphine moiety, might be explained by the difficulties in linking the highly congested indole and the di-*tert*-butyl phosphine group. Similar to the N-P type indolyl phosphine ligand, C-P type indolyl phosphine ligand also exhibits high air stability in both solid and solution form. There was no detectable phosphine oxide signal from ^{31}P NMR when the solid-form ligand was either under air atmosphere for 5 days or in solution form for at least 3 days.

Table 2.11 Synthesis of C-P Type Indolyl Phosphine Ligands[a]



entry	ligand precursor	$ClPR_2$	product	%yield[b]
1		$ClPPh_2$		51
2		$ClPCy_2$		71
3		ClP^tBu_2		33
4		$ClPPh_2$		80
5		$ClPCy_2$		71
6		ClP^tBu_2		47
7		$ClPPh_2$		80
8		$ClPPh_2$		63
9		$ClPCy_2$		75

[a]Reaction conditions: 3-bromo-2-arylindole : *n*-BuLi : $ClPR_2$ = 1: 1.2 :1.2, THF, Temperature = -78°C; [b]Isolated yield.

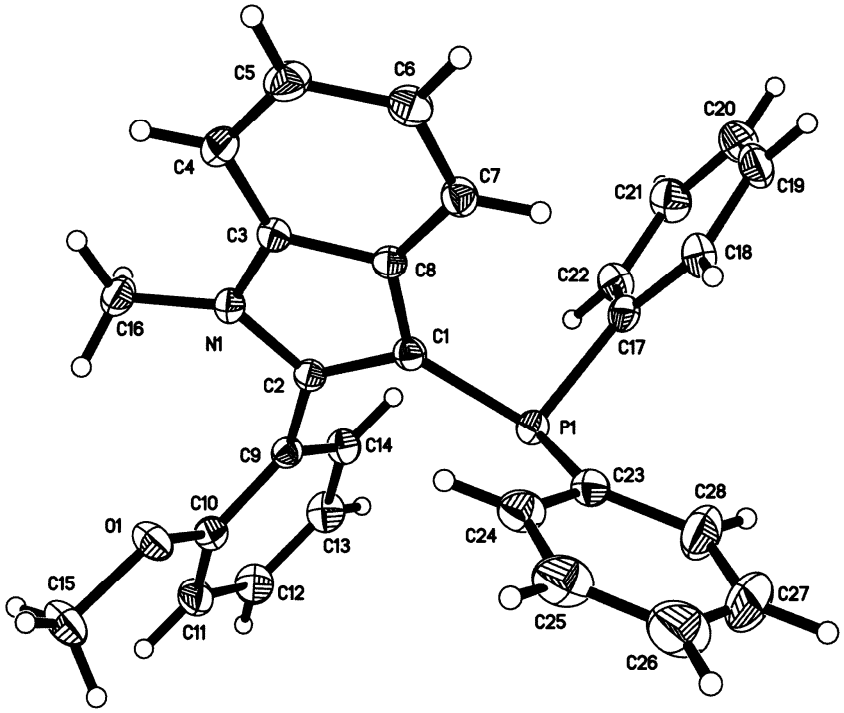


Figure 2.10 ORTEP representation of the CPPh o-Andole-phos (30% probability ellipsoids)

Table 2.12 Selected Bond Distances (Å) and Angles (˚) for CPPh o-Andole-phos

Bond distances (Å)			
P(1)-C(1)	1.798(3)	P(1)-C(23)	1.830(3)
P(1)-C(17)	1.833(3)	C(1)-C(8)	1.445(3)
C(1)-C(2)	1.387(3)		

Bond angles (˚)			
C(1)-P(1)-C(23)	104.39(13)	C(1)-P(1)-C(17)	101.54(12)
C(23)-P(1)-C(17)	104.56(13)	C(2)-C(1)-P(1)	123.53(19)
C(8)-C(1)-P(1)	130.8(2)	C(2)-C(1)-C(8)	105.7(2)

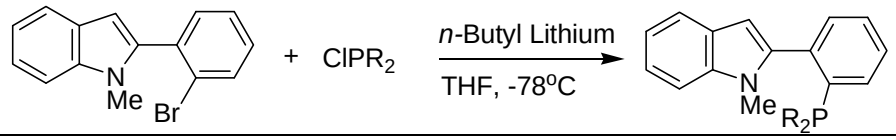
Table 2.13 Crystal Data and Structure Refinement of CPPh o-Andole-phos

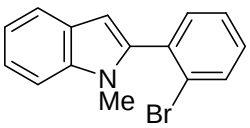
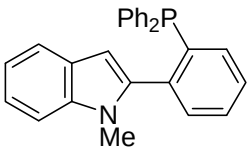
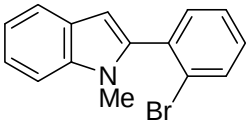
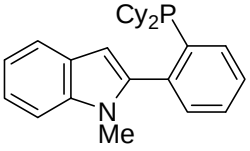
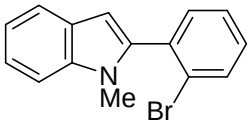
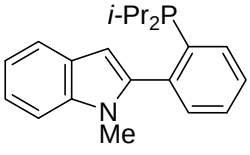
Empirical formula	$C_{28}H_{24}NOP$	
Formula weight	421.45	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 11.3813(2) Å	α = 90°.
	b = 8.8300(2) Å	β = 101.4480(10)°.
	c = 23.4724(5) Å	γ = 90°.
Volume	2311.97(8) $Å^3$	
Z	4	
Density (calculated)	1.211 Mg/m^3	
Absorption coefficient	0.138 mm^{-1}	
F(000)	888	
Crystal size	0.44 x 0.38 x 0.22 mm^3	
Theta range for data collection	1.77 to 27.39°.	
Index ranges	-14<=h<=14, -11<=k<=11, -30<=l<=30	
Reflections collected	18637	
Independent reflections	5250 [R(int) = 0.0688]	
Completeness to theta = 27.39°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.000 and 0.502	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5250 / 0 / 280	
Goodness-of-fit on F^2	1.002	
Final R indices [I>2sigma(I)]	R1 = 0.0606, wR2 = 0.1489	
R indices (all data)	R1 = 0.1219, wR2 = 0.1813	
Largest diff. peak and hole	0.284 and -0.295 $e.Å^{-3}$	

2.2.3.2 Phosphine Group Attached to Non-Indolyl Ring

The ligand skeleton was conveniently obtained in good yield from commercially available N-methylphenylhydrazine and bromoacetophenone by the straightforward Fischer-Indole synthesis (Table 2.4, entry4). Since the bromo group was already attached on the bottom, lithium /bromide exchange could be performed by *n*-BuLi and trapping the lithiated intermediate by $ClPR_2$ afforded the corresponding indolyl phosphines in good to excellence yields (Table 2.14). Essentially complete conversion was observed in most of the cases. The products can be simply purified by successively washing with methanol. This class of ligand also exhibits high air stability in both solid and solution forms.

Table 2.14 Synthesis of C-P Type Indolyl Phosphine Ligands[a]



entry	ligand precursor	$ClPR_2$	product	%yield[b]
1		$ClPPh_2$		64
2		$ClPCy_2$		88
3		ClP^iPr_2		75

[a]Reaction conditions: 1-Methyl 2-(2'-Bromophenyl)indole : *n*-BuLi : $ClPR_2$ = 1: 1.2 :1.2, THF, Temperature = -78°C; [b]Isolated yield.

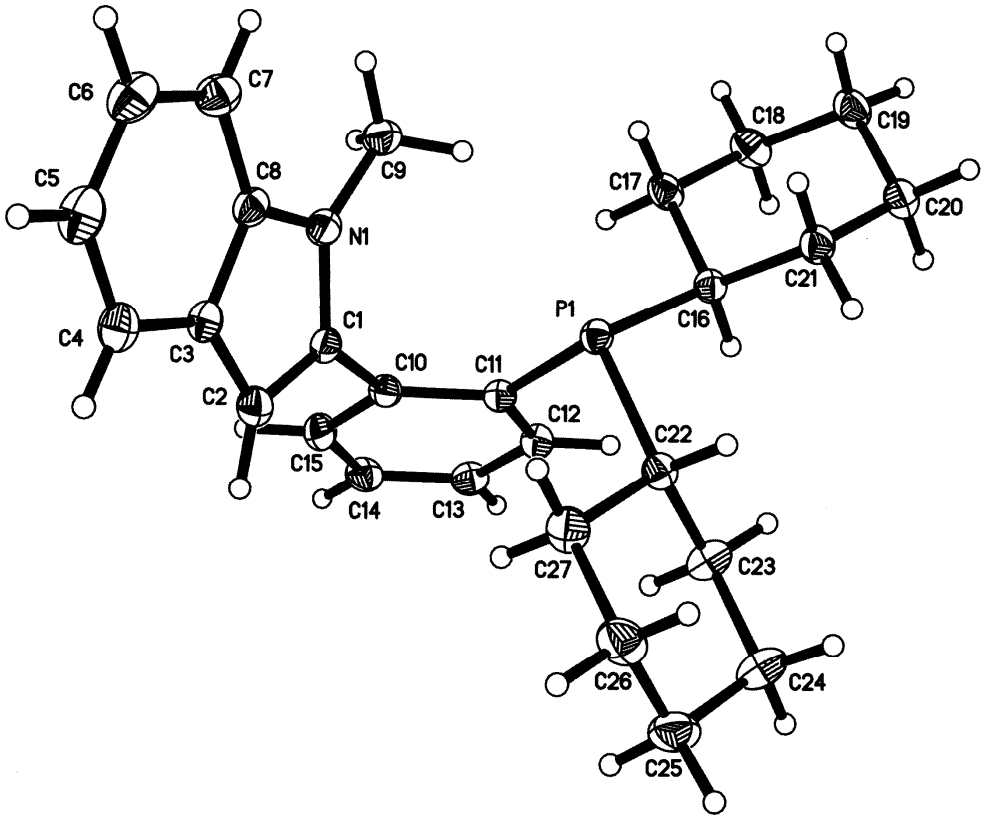


Figure 2.11 ORTEP representation of CM-phos (30% probability ellipsoids)

Table 2.15 Selected Bond Distances (Å) and Angles (˚) for CM-phos

Bond distances (Å)			
P(1)-C(11)	1.851(2)	P(1)-C(16)	1.851(2)
P(1)-C(22)	1.857(2)		

Bond angles (˚)			
C(11)-P(1)-C(16)	100.98(9)	C(11)-P(1)-C(22)	102.96(10)
C(16)-P(1)-C(22)	103.66(10)		

Table 2.16 Crystal Data and Structure Refinement of CM-phos

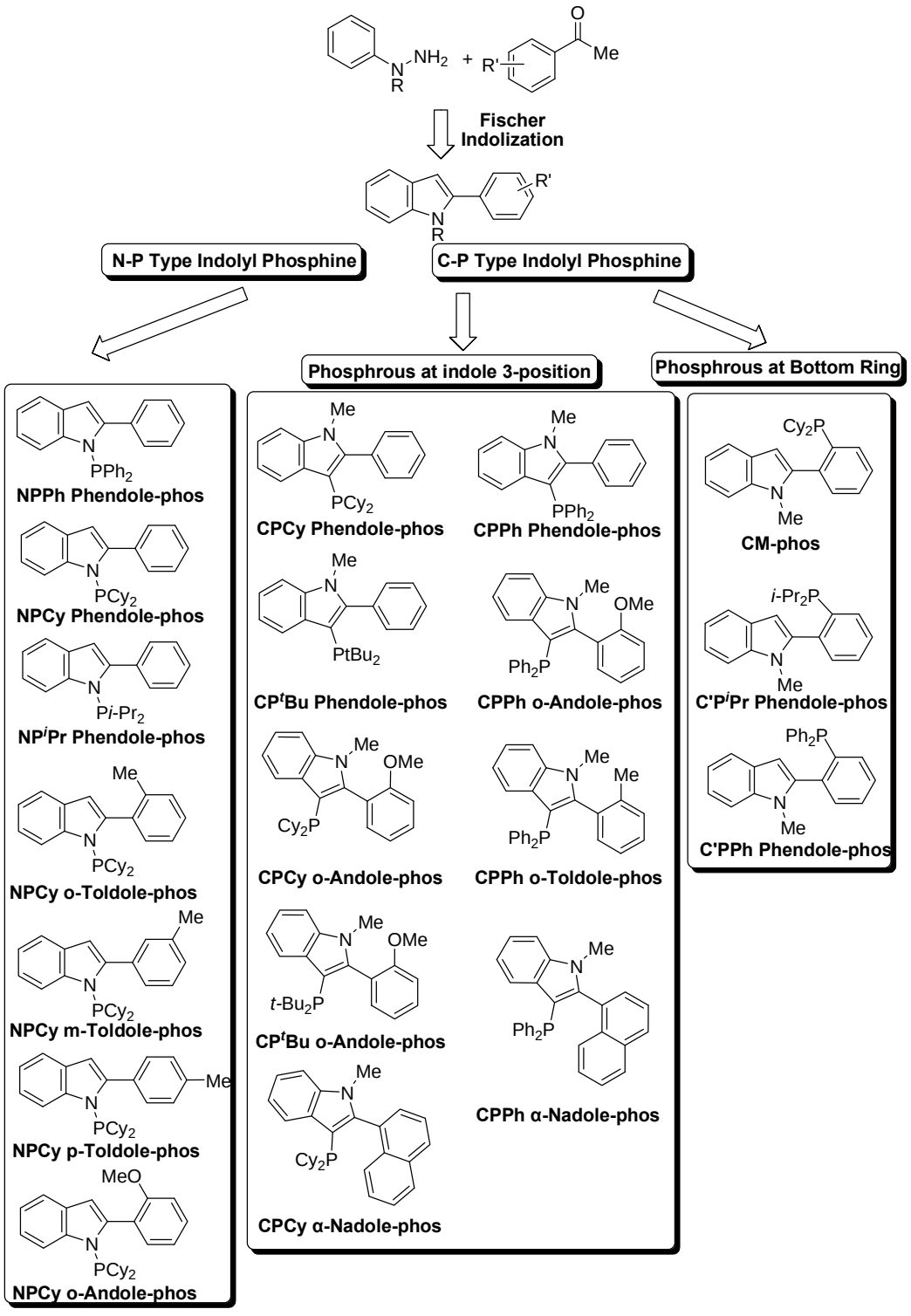
Empirical formula	$C_{27}H_{34}NP$	
Formula weight	403.52	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 11.9114(3) Å	α = 90°.
	b = 13.9864(4) Å	β = 90.156(2)°.
	c = 13.7411(4) Å	γ = 90°.
Volume	2289.23(11) $Å^3$	
Z	4	
Density (calculated)	1.171 Mg/m^3	
Absorption coefficient	0.133 mm^{-1}	
F(000)	872	
Crystal size	0.36 x 0.20 x 0.20 mm^3	
Theta range for data collection	2.08 to 27.62°.	
Index ranges	-15<=h<=15, -18<=k<=18, -16<=l<=17	
Reflections collected	27811	
Independent reflections	5257 [R(int) = 0.0929]	
Completeness to theta = 27.62°	99.1 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.000 and 0.657	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5257 / 0 / 262	
Goodness-of-fit on F^2	1.004	
Final R indices [I>2sigma(I)]	R1 = 0.0591, wR2 = 0.1468	
R indices (all data)	R1 = 0.1406, wR2 = 0.1811	
Largest diff. peak and hole	0.257 and -0.228 $e.Å^{-3}$	

2.3 Conclusion

In conclusion, we have designed and used a modular approach to synthesize new classes of phosphine ligands that use the indole as ligand template. The indole ligand template 1) is inexpensive; 2) is readily available from commercially accessible starting materials; 3) can be synthesized from well developed synthesis methods; and 4) has high potential for diversification and easy steric and electronic fine-tuning. Therefore, we chose indole as the template to design and explore a new class of phosphine ligands.

The Fischer indole synthesis is an effective method for the synthesis of 2-arylindole. The 2'-substituted 2-arylindoles and N-methylated 2'-substituted 2-arylindoles were synthesized at the first time. Both N-P type and C-P type indolyl phosphines were obtained in good to excellent yield. Moreover, these ligands can be easily purified by single crystallization or washing with alcoholic solvent.

All classes of indolyl phosphines exhibited high air stability in both solid and solution forms and no detectable phosphine oxide signal was detected in the ^{31}P NMR spectrum for at least 3 days at ambient conditions.



Scheme 2.4 A summary of the new indolyl phosphine ligands

2.4 Experimental Section

2.4.1 General Considerations

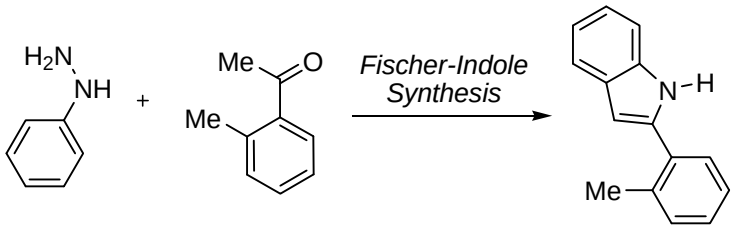
Unless otherwise noted, all reagents were purchased from commercial suppliers and used without further purification. Toluene and tetrahydrofuran (THF) were distilled from sodium and sodium benzophenone ketyl under nitrogen, respectively.[150] Chlorodiphenylphosphine (Tech grade from Aldrich) was distilled under vacuum prior to use.[150] A new bottle of *n*-butyllithium was used. Thin layer chromatography was performed on Merck pre-coated silica gel 60 F_{254} plates. Silica gel (Merck, 70-230 and 230-400 mesh) was used for gel filter. Melting points were recorded on an uncorrected Büchi Melting Point B-545 instrument. ^{1}H NMR spectra were recorded on a Bruker (400 MHz) or Varian (500 MHz) spectrometer. Spectra were referenced internally to the residual proton resonance in $CDCl_3$ (δ 7.26 ppm), or with tetramethylsilane (TMS, δ 0.00 ppm) as the internal standard. Chemical shifts (δ) were reported as part per million (ppm) in δ scale downfield from TMS. ^{13}C NMR spectra were referenced to $CDCl_3$ (δ 77.0 ppm, the middle peak). ^{31}P NMR spectra were referenced to 85% H_3PO_4 externally. Coupling constants (*J*) were reported in Hertz (Hz). Mass spectra (EI-MS and ES-MS) were recorded on a HP 5989B Mass Spectrometer. High-resolution mass spectra (HRMS) were

obtained on a Brüker APEX 47e FT-ICR mass spectrometer (ESIMS). GC-MS analysis was conducted on a HP 5973 GCD system using a HP5MS column (30 m × 0.25 mm).

2.4.2 Fischer Indole Synthesis of Indole Ligand Templates

2.4.2.1 Synthesis of 2-Aryl-1*H*-indoles

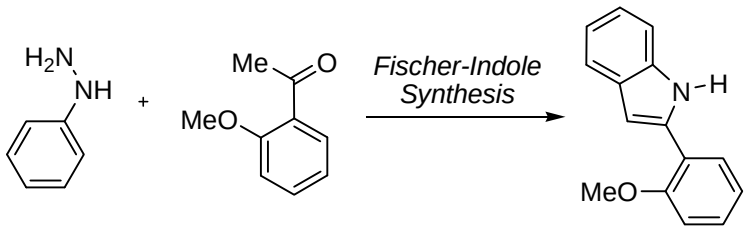
2-(2'-Tolyl)-1*H*-indole[151]



General procedure for the Fischer indole synthesis of 2-aryl-1H-indoles: 2'-Methylacetophenone (1.31 mL, 10 mmol) was mixed with phenylhydrazine (0.99 mL, 10 mmol) in ethanol (5 mL) with a few drops of glacial acetic acid. The reaction was heated to 80 °C and stirred for 1 hour. The solvent was evaporated to yield the phenylhydrazone intermediate, which was then added to polyphosphoric acid (20 g). Exothermic reaction was observed and the reaction mixture was slowly heated to 120 °C (kept for 1 hour). The mixtures were poured into crushed ice cubes and then neutralized with 2 M NaOH to give the desired 2-(2'-tolyl)-1*H*-indole (1.48 g, 71%) as an off-white solid, which was then dried under reduced pressure. Melting point. 93.0-94.3 ^{o}C, lit. 92-93 ^{o}C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.55 (s, 3H), 6.67 (d, *J* = 1.9 Hz, 1H), 7.19-7.51 (m, 7H), 7.72 (d, *J* = 7.7 Hz, 1H), 8.10 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.03, 102.86, 110.73, 119.87, 120.45, 121.96, 126.00, 127.88, 128.75, 128.90, 130.99, 132.51, 135.97, 136.08, 137.34; IR (cm^{-1}) 3395.73, 3052.63, 3016.79, 2960.46, 1603.41, 1485.63, 1454.91, 1398.58, 1347.37, 1301.28, 1224.47, 1116.93, 1040.11, 799.43, 743.10, 712.38, 671.41, 533.14; MS (EI): *m/z* (relative intensity) 207 (M^+, 100), 191 (5), 178 (20), 165 (5), 152 (5).

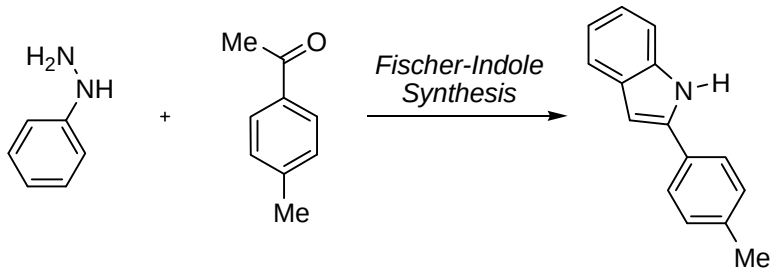
2-(2'-Methoxyphenyl)-1*H*-indole[152]



General procedures for the synthesis of 2-arylindole **2-(2'-tolyl)-1*H*-indole** were used. 2'-Methoxylacetophenone (1.38 mL, 10 mmol), phenylhydrazine (0.99 mL, 10 mmol), ethanol (5 mL), glacial acetic acid (a few drops) and PPA (20 g) were used to afford 2-(2'-methoxyphenyl)-1*H*-indole (1.58 g, 71%) as an off-white solid. Melting point. 78.5-81.0 °C, lit. 75-77 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.00 (s, 3H), 7.00 (d, *J* = 1.5 Hz), 7.05 (d, *J* = 8.2 Hz), 7.10-7.34 (m, 4H), 7.50 (d, *J* = 8.0 Hz), 7.74 (d, *J* = 7.7 Hz), 7.91 (dd, *J* = 1.6 Hz and 7.7 Hz), 9.72 (bs, NH, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.68, 99.76, 110.87, 111.83,

119.70, 120.18, 120.50, 121.41, 121.73, 128.03, 128.17, 128.46, 135.89, 136.03, 155.66; IR (cm^{-1}) 3446.94, 3042.93, 3001.42, 2939.97, 2837.55, 1598.29, 1577.81, 1541.96, 1460.03, 1434.42, 1311.52, 1234.71, 1173.26, 1122.05, 1019.63, 922.33, 789.19, 732.86, 661.17, 558.75; MS (EI): *m/z* (relative intensity) 223 (M^+, 100), 208 (35), 193 (20), 180 (35), 165 (20), 152 (25).

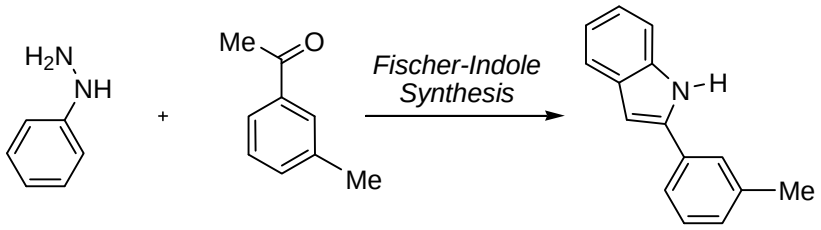
2-(4'-Tolyl)-1*H*-indole[153]



General procedures for the synthesis of 2-arylindole **2-(2'-tolyl)-1*H*-indole** were used. 4'-Methylacetophenone (1.34 mL, 10 mmol), phenylhydrazine (0.99 mL, 10 mmol), ethanol (5 mL), glacial acetic acid (a few drops) and PPA (20 g) were used to afford 2-(4'-tolyl)-1*H*-indole (1.64 g, 79%) as an off-white solid. Melting point. 218.0-219.9 °C, lit. 220 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3H), 6.81 (s, 1H), 7.13-7.27 (m, 4H), 7.39 (d, *J* = 7.7 Hz, 1H), 7.56 (d, *J* = 7.7 Hz, 2H), 7.65 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.19, 99.35, 110.79, 120.15, 120.48, 122.07, 125.02, 129.29, 129.51, 129.66, 136.65, 137.60, 138.02; IR (cm^{-1}) 3431.58, 3047.51, 3021.91, 2909.25, 1501.00, 1454.91,

1424.18, 1347.37, 1296.16, 1229.59, 1122.05, 825.04, 789.19, 732.86, 656.05, 512.66; MS (EI): *m/z* (relative intensity) 207 (M^+, 100), 191 (4), 178 (7), 165 (4), 152 (2).

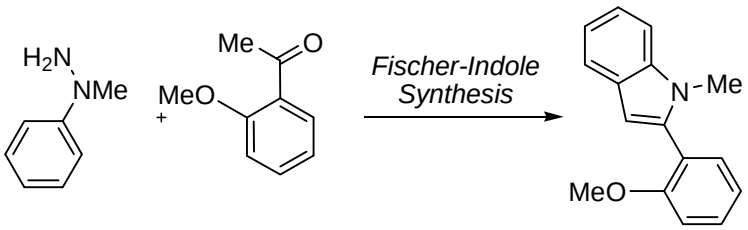
2-(3'-Tolyl)-1*H*-indole[154]



General procedures for the synthesis of 2-arylindole **2-(3'-tolyl)-1*H*-indole** were used. 3'-Methylacetophenone (1.36 mL, 10 mmol), phenylhydrazine (0.99 mL, 10 mmol), ethanol (5 mL), glacial acetic acid (a few drops) and PPA (20 g) were used to afford 2-(3'-tolyl)-1*H*-indole (1.47 g, 71%) as an off-white solid. Melting point. 149.2-152.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.46 (s, 3H), 6.86 (m, 1H), 7.16-7.26 (m, 3H), 7.34-7.42 (m, 2H), 7.47-7.51 (m, 2H), 7.68 (d, *J* = 7.7 Hz, 1H), 8.32 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 99.7, 100.8, 120.1, 120.5, 122.1, 122.2, 125.8, 128.4, 128.8, 129.2, 132.2, 136.7, 137.9, 138.5; IR (cm^{-1}) 3390.61, 3052.63, 3027.03, 2909.25, 1603.41, 1449.79, 1347.37, 1301.28, 1224.47, 1173.26, 1086.20, 778.95, 753.34, 691.89, 671.41; MS (EI): *m/z* (relative intensity) 207 (M^+, 100), 191 (4), 178 (7), 165 (4).

2.4.2.2 Synthesis of N-Methylated Indole Templates

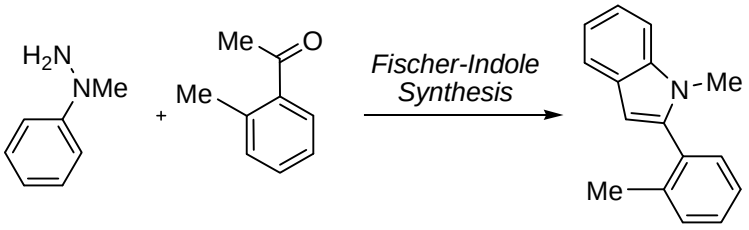
2-(2-Methoxyphenyl)-1-methyl-*1H*-indole[155]



General procedure for the Fischer-indole synthesis of N-methylated Indole Templates: 2'-Methoxyacetophenone (6.9 ml, 50 mmol) was mixed with N-methylphenylhydrazine (7.1 ml, 60 mmol) in 10 ml phosphoric acid and stirred at room temperature for 30 min. About 50 g of PPA was added to the mixture and an exothermic reaction ensure whereupon the mixture was slowly heated to 120 ^{o}C and kept at this temperature for 1 h. The mixture was poured into ice water and then extracted with Et_2O. The organic phase was combined and dried over Na_2SO_4. The concentrated organic phase was filtered over a pad of silica (5 × 2 inch) and washed with hexane then EA/hexane (2:8). The solution was evaporated to yield a light yellow solid product. Little amount of cooled hexane was used to further purify of the product. The final product N-methyl-2-(2'-methoxyphenyl)indole was dried under vacuum (8.0 g, 68%) to form a light yellow solid. Melting point 106.9-111.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.72 (s, 3H), 3.92 (s, 3H), 6.62 (bs, 1H), 7.13 (d, *J* = 8.2 Hz, 1H), 7.20 (t, *J* = 7.4 Hz, 1H), 7.28 (t, *J* = 8.2 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 1H), 7.50-7.58

(m, 3H), 7.81 (d, J = 7.8, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.6, 55.3, 109.3, 110.7, 119.3, 120.3, 120.5, 121.2, 121.8, 127.8, 130.0, 132.4, 137.5, 157.3; IR (cm^{-1}) 3446.5, 3040.9, 2998.1, 2939.0, 1838.1, 1886.6, 1771.7, 1600.2, 1577.1, 1540.9, 1467.0, 1436.1, 1384.5, 1366.3, 1338.4, 1312.5, 1278.4, 1249.2, 1178.4, 1165.2, 1130.1, 1115.7, 1096.7, 1049.9, 1021.5, 1002.8, 860.1, 845.4, 816.8, 794.4, 780.6, 762.8, 750.5, 669.5, 564.4 ;MS (EI): *m/z* (relative intensity) 237 (M^+, 100), 222 (25), 206 (12), 194 (8); HRMS: calcd. for $C_{16}H_{16}NOH^+$: 238.1232, found 238.1238.

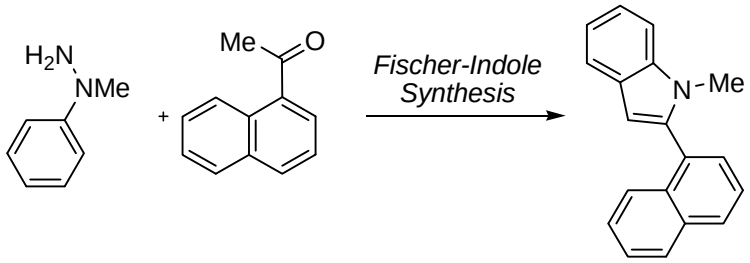
1-Methyl-2-*o*-tolyl-1*H*-indole[156]



The general Fischer indole synthesis of N-methylated Indole **2-(2-Methoxyphenyl)-1-methyl-*1H*-indole** procedure was followed. 2'-Methylacetophenone (2.68 g, 20 mmol), N-methylphenylhydrazine (22 mmol) and PPA (30 g) were used to yield the desired product (2.8 g, 63%) as a light brown solid. Melting point 89.0-90.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.46 (s, 3H), 3.72 (s, 3H), 6.71 (s, 1H), 7.42 (t, , J = 7.2 Hz, 1H), 7.49-7.60 (m, 6H), 7.91 (d, J = 7.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9, 30.1, 101.4, 109.3,

119.5, 120.3, 121.2, 125.4, 127.9, 128.5, 129.9, 131.0, 132.4, 137.2, 137.9, 140.3; IR (cm^{-1}) 3419.8, 3053.7, 2954.6, 1603.3, 1573.1, 1465.5, 1431.4, 1375.8, 1360.2, 1336.7, 1313.45, 1274.2, 1235.0, 1209.4, 1193.8, 1168.0, 1145.9, 1128.5, 1116.6, 1100.3, 1049.1, 1030.2, 1004.7, 983.2, 949.6, 921.7, 839.0, 793.8, 768.3, 749.6, 735.0, 670.2, 590.6, 581.3, 549.0, 529.5; MS (EI): *m/z* (relative intensity) 221 (M^+, 100), 206 (23), 178 (15); HRMS: calcd. for $C_{16}H_{15}NH^+$: 222.1283, found 222.1285.

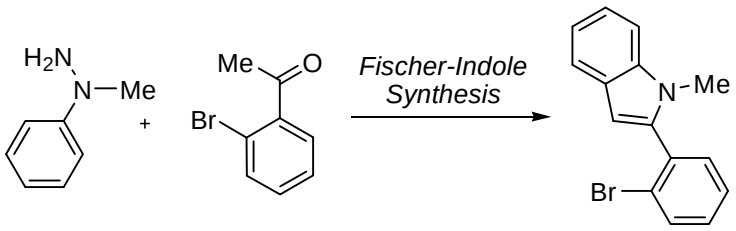
1-Methyl-2-(naphthalen-1-yl)-1H-indole[155]



The general procedure for the Fischer indole synthesis of N-methylated Indole **2-(2-Methoxyphenyl)-1-methyl-*1H*-indole** was followed. 1-Acetonaphthone (7.55 ml, 50 mmol) and N-methylphenylhydrazine (7.1 ml, 60 mmol) were used to yield the product 1-methyl-2-(naphthalen-1-yl)-1*H*-indole (7.0 g, 54%) as a light yellow solid. Melting point 94.2-96.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.55 (s, 3H), 6.72 (s, 1H), 7.28 (t, *J* = 7.5 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.47-7.52 (m, 2H), 7.55-7.63 (m, 3H), 7.78 (d, *J* = 8.0 Hz, 2H),

7.98-8.02 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.7, 103.0, 109.4, 119.7, 120.4, 121.5, 125.1, 126.0, 126.6, 128.0, 128.2, 128.9, 130.5, 132.9, 133.4, 137.6, 139.3; IR (cm^{-1}) 3421.7, 3050.2, 2935.0, 1594.1, 1544.2, 1500.4, 1464.1, 1427.8, 1392.6, 1358.7, 1337.2, 1309.7, 1261.0, 1236.1, 1225.5, 1213.0, 1164.5, 1145.9, 1126.9, 1095.4, 1011.4, 968.4, 808.2, 786.0, 769.5, 748.2, 732.1, 677.1, 657.7, 644.6, 579.2, 544.2, 517.2; MS (EI): *m/z* (relative intensity) 257 (M^+, 100), 241 (25); HRMS: calcd. for $C_{19}H_{16}NH^+$: 258.1283, found 258.1278.

2-(2-Bromophenyl)indole

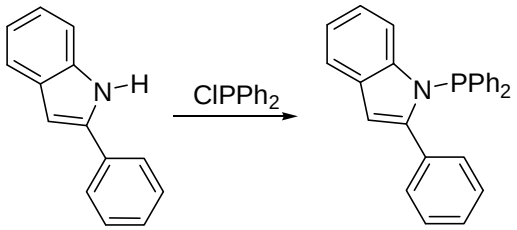


The general procedure for the Fischer indole synthesis of N-methylated Indole **2-(2-Methoxyphenyl)-1-methyl-*1H*-indole** was followed. 2'-Bromoacetophenone (1.31 mL, 10 mmol), N-methylphenylhydrazine (1.3 mL, 11 mmol) and PPA (30 g) were used to yield the N-methyl-2-(2'-bromophenyl)indole ((2.35 g, 75%) as a light yellow solid. Melting point. 85.5-87.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.61 (s, 3H), 6.56 (s, 1H), 7.20-7.45 (m, 6H), 7.70-7.75 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.5, 102.0, 109.4, 119.7, 120.6, 121.6, 125.0, 127.1, 127.5 130.0, 132.6 132.7,

134.1, 137.1, 139.5; IR (cm^{-1}) 3049.43, 2933.63, 1536.35, 1457.76, 1431.08, 1382.94, 1337.55, 1309.58, 1164.78, 1061.55, 1023.56, 791.60, 749.44, 662.83, 578.63, 536.74, 454.92; MS (EI): *m/z* (relative intensity) 285 (M^+, 100), 204 (75), 190 (10), 178 (20); HRMS: calcd. for $C_{15}H_{12}BrNH^+$: 286.0231, found 286.0280.

2.4.3 Preparation of N-P Type Indolyl Phosphine

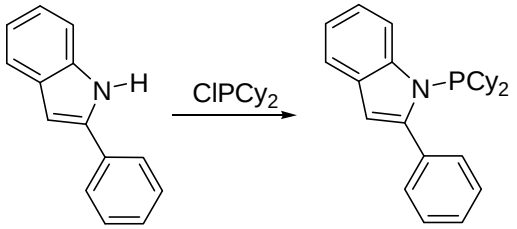
N-(Diphenylphosphino)-2-phenylindole (NPPh Phendole-phos)



General procedure for direct ligand synthesis: Commercially available 2-phenylindole (1.93 g, 10.0 mmol) was dissolved in freshly distilled THF (50 mL) at room temperature under nitrogen atmosphere. The solution was cooled to -78 °C in a dry ice/acetone bath. Titrated *n*-BuLi (11.0 mmol) was added dropwise with a syringe. After the reaction mixture was stirred for 15 min at -78 °C, distilled chlorodiphenylphosphine (1.97 mL, 11.0 mmol) in THF (20 mL) was added. The reaction was allowed to warm to room temperature and stirred overnight. The solvent was removed under reduced pressure. Toluene (10 mL × 4) was added and the solution was filtered over Celite. The combined solvent

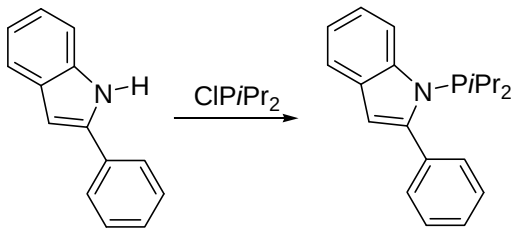
was removed in *vacuo*. The crude product was recrystallized in hot ethanol under nitrogen. White crystals of N-(diphenylphosphino)-2-phenylindole (2.95 g, 78%) were obtained after standing overnight at room temperature. Melting point. 160.3-162.3 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.93 (d, J = 2.9 Hz, 1H), 6.97-7.05 (m, 2H), 7.21-7.25 (m, 1H), 7.44-7.46 (m, 6H), 7.51-7.57 (m, 7H), 7.69-7.72 (m, 2H), 7.76 (d, J = 7.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 106.55, 106.58, 115.33, 120.60, 121.11, 121.59, 127.90, 127.98, 128.42, 128.48, 128.92, 130.11, 130.16, 130.83, 131.03, 131.47, 133.63, 133.69, 134.78, 134.95, 139.92, 140.01, 146.92, 147.41; ^{31}P NMR (202 MHz, $CDCl_3$) δ 38.09; IR (cm^{-1}) 3052.63, 3006.54, 1603.41, 1480.51, 1444.67, 1429.30, 1321.76, 1265.43, 1122.05, 1075.96, 994.03, 768.71, 743.10, 691.89, 589.47, 512.66, 461.45; MS (EI): *m/z* (relative intensity) 376 (M^+-1, 80), 300 (5), 222 (10), 193 (10), 183 (100), 165 (15), 152 (10) ; HRMS: calcd. for $C_{26}H_{20}NPH^+$: 378.1412, found 378.1410.

N-(Dicyclohexylphosphino)-2-phenylindole (NPCy Phendole-phos)



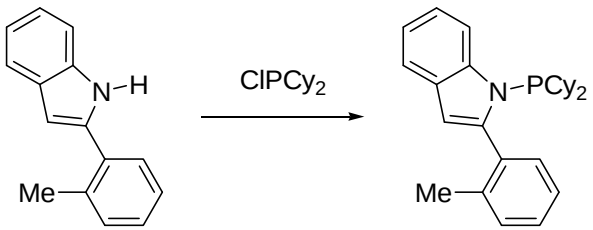
General procedures for the synthesis of ligand **NPPh Phendole-phos** were followed. 2-phenylindole (386 mg, 2.0 mmol), *n*-BuLi (2.4 mmol), chlorodicyclohexylphosphine (486 μL, 2.2 mmol) were used to afford N-(dicyclohexylphosphino)-2-phenylindole (660 mg, 85%) as white crystal. Melting point. 143.8-145.2 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.1-1.8 (m, 20H), 2.72 (m, 2H), 6.57(d, *J* = 1.9 Hz, 1H), 7.19-7.27 (m, 2H), 7.4-7.5 (m, 5H), 7.65-7.69 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.82, 26.02, 26.27, 26.41, 26.46, 26.54, 28.73, 28.82, 30.35, 30.62, 36.67, 36.84, 105.18, 113.67, 120.70, 120.81, 121.53, 127.49, 130.88, 130.92, 131.06, 134.36, 134.41, 140.44, 140.55, 148.02, 148.25; ^{31}P NMR (162 MHz, $CDCl_3$) δ 58.04; IR (cm^{-1}) 3078.24, 3057.75, 2929.73, 2909.25, 2842.67, 1485.63, 1444.67, 1321.76, 1260.31, 1070.84, 994.03, 850.64, 825.04, 758.46, 732.86, 691.89; MS (EI): *m/z* (relative intensity) 388 (M^+-1, 100), 334 (2), 307 (15), 224 (90), 193 (60), 165 (10), 145 (5); HRMS: calcd. for $C_{26}H_{32}NPH^+$: 390.2351, found 390.2361.

N-(Diisopropylphosphino)-2-phenylindole (NP^{i}Pr Phendole-phos)



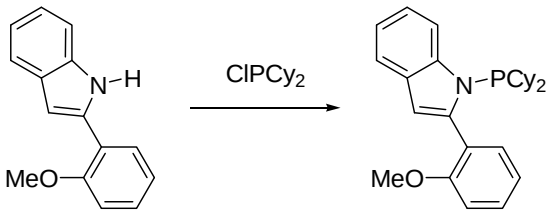
General procedures for the synthesis of ligand **NPPh Phendole-phos** were followed. 2-phenylindole (772 mg, 4.0 mmol), *n*-BuLi (4.8 mmol), chlorodiisopropylphosphine (710 μL, 4.4 mmol) were used to afford N-(dicyclohexylphosphino)-2-phenylindole (880 mg, 71%) as white crystal. Melting point. 74.9-76.2 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.02 (dd, J = 6.9 Hz and 12.8 Hz, 6H) 1.33 (dd, J = 6.8 Hz and J = 18.2 Hz, 6H), 3.09 (m, 2H), 6.76 (d, J = 1.9 Hz, 1H), 7.37-7.40 (m, 2H), 7.54-7.83 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.66, 19.82, 19.93, 19.99, 20.30, 20.48, 26.59, 26.75, 105.47, 113.78, 113.79 (overlapped), 120.88, 120.98 (overlapped), 121.59, 127.63, 130.97; ^{31}P NMR (162 MHz, $CDCl_3$) δ 68.35; IR (cm^{-1}) 3042.39, 2970.70, 2939.97, 2909.25, 2852.92, 1444.67, 1321.76, 1265.43, 1224.47, 1173.26, 1122.05, 1075.96, 983.78, 922.33, 753.34, 691.89, 650.92, 579.23, 492.18; MS (EI): *m/z* (relative intensity) 308 (M^+-1, 95), 266 (20), 224 (100), 193 (30), 165 (20), 146 (15); HRMS: calcd. for $C_{20}H_{24}NPH^+$:310.1725, found 310.1736

N-(Dicyclohexylphosphino)-2-(2'-tolyl)indole (NPCy o-Toldole-phos)



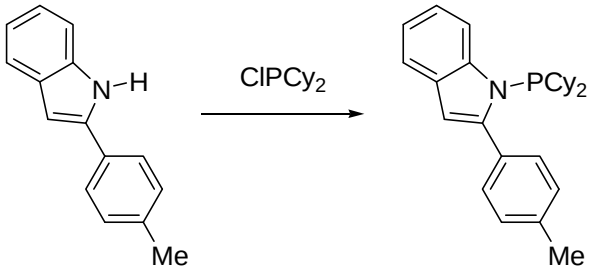
General procedures for the synthesis of ligand **NPPh Phendole-phos** were followed. 2-(2'-Tolyl)-1*H*-indole (414 mg, 2.0 mmol), *n*-BuLi (2.4 mmol), chlorodicyclohexylphosphine (486 μL, 2.2 mmol) were used to afford N-(dicyclohexylphosphino)-2-(2'-tolyl)indole (600 mg, 74%) as white crystal. Melting point. 147.4-148.6 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.09-1.77 (m, 20H), 2.25 (s, 3H), 2.63 (m, 2H), 6.45 (d, *J* = 2.3 Hz, 1H), 7.16-7.36 (m, 6H), 7.61-7.66 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.67, 26.06, 26.25, 26.45, 26.59, 26.64, 26.72, 29.09, 29.16, 30.54, 30.81, 37.08, 37.13, 105.41, 113.56, 120.51, 120.64, 121.34, 121.53, 124.56, 128.22, 129.52, 131.13, 132.43, 132.59, 134.24, 134.30, 137.60, 139.85, 139.96, 146.49, 146.75; ^{31}P NMR (162 MHz, $CDCl_3$) δ 57.79; IR (cm^{-1})3073.12, 3057.75, 3011.66, 2924.61, 2837.55, 1444.67, 1311.52, 1255.19, 1122.05, 1065.72, 994.03, 804.55, 758.46, 737.98, 589.47; MS (EI): *m/z* (relative intensity) 402 (M^+-1, 100), 388 (100), 320 (15), 306 (15), 238 (95), 222 (50), 207 (80), 191 (5), 178 (10); HRMS: calcd. for $C_{27}H_{34}NPH^+$: 404.2507, found 404.2515.

N-(Dicyclohexylphosphino)-2-(2'-methoxyphenyl)indole
(NPCy o-Andole-phos)



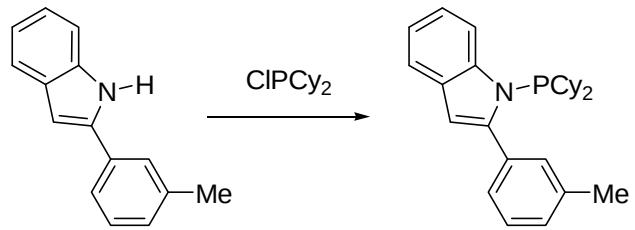
General procedures for the synthesis of ligand **NPPh Phendole-phos** were followed. 2-(2'-Methoxyphenyl)-1*H*-indole (446 mg, 2.0 mmol), *n*-BuLi (2.4 mmol), chlorodicyclohexylphosphine (486 μL, 2.2 mmol) were used to afford N-(dicyclohexylphosphino)-2-(2'-methoxyphenyl)indole (670 mg, 80%) as white crystal. Melting point. 131.1-132.5ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12-1.81 (m, 20H), 2.65 (m, 2H), 6.52 (d, *J* = 1.6 Hz, 1H), 6.99 (d, *J* = 8.2 Hz, 1H), 7.05 (t, *J* = 7.3 Hz, 1H), 7.16-7.30 (m, 3H), 7.44-7.48 (m, 1H), 7.63-7.67 (m, 2H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.03, 26.18, 26.43, 26.58, 26.63, 28.45, 28.53, 30.39, 30.59, 30.87, 36.72, 36.88, 54.87, 104.91, 110.04, 113.43, 119.83, 120.17, 120.78, 121.25, 123.83, 123.88, 129.83, 131.22, 132.84, 140.02, 140.13, 144.87, 145.14, 157.27; ^{31}P NMR (162 MHz, $CDCl_3$) δ 59.90; IR (cm^{-1}) 3078.24, 3006.54, 2919.49, 2842.67, 1582.93, 1541.96, 1490.75, 1444.67, 1326.88, 1244.95, 1122.05, 1024.75, 999.15, 778.95, 743.10, 661.17, 471.69; MS (EI): *m/z* (relative intensity) 418 (M^+-1, 2), 388 (100), 306 (4), 254 (10), 239 (13), 222 (10), 209 (3), 192 (2); HRMS: calcd. for $C_{27}H_{34}NOPH^+$: 420.2456, found 420.2469.

N-(Dicyclohexylphosphino)-2-(4'-tolyl)indole (NPCy p-Toldole-phos)



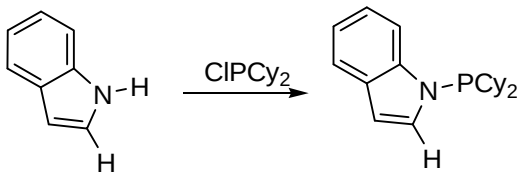
General procedures for the synthesis of ligand **NPPh Phendole-phos** were followed. 2-(4'-Tolyl)-1*H*-indole (414 mg, 2.0 mmol), *n*-BuLi (2.4 mmol), chlorodicyclohexylphosphine (486 μL, 2.2 mmol) were used to afford N-(dicyclohexylphosphino)-2-(4'-tolyl)indole (620 mg, 77%) as white crystal. Melting point. 168.8-169.2 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.14-1.83 (m, 20H), 2.46 (s, 3H), 2.73 (m, 2H), 7.56 (d, *J* = 1.0 Hz, 1H), 7.20-7.29 (m, 4H), 7.40 (d, *J* = 7.5 Hz, 2H), 7.65-7.69 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.32, 26.02, 26.29, 26.44, 26.47, 26.56, 28.73, 28.82, 30.35, 30.63, 36.67, 36.84, 104.4, 113.63, 120.63, 120.70, 121.37, 128.33, 130.70, 130.74, 131.12, 131.45, 131.50, 137.25, 140.38, 140.49, 148.10, 148.34; ^{31}P NMR (162 MHz, $CDCl_3$) δ 57.71; IR (cm^{-1}) 3083.36, 3042.39, 3016.79, 2914.37, 2842.67, 1495.87, 1439.54, 1321.76, 1260.31, 1183.50, 1116.93, 1070.84, 994.03, 819.91, 784.07, 748.22, 727.74, 686.77, 574.11; MS (EI): *m/z* (relative intensity) 403 (M^+, 100), 321 (20), 238 (95), 222 (30), 207 (70), 191 (3), 178 (5), 165 (2); HRMS: calcd. for $C_{27}H_{34}NPH^+$: 404.2507, found 404.2513.

N-(Dicyclohexylphosphino)-2-(3'-tolyl)indole (NPCy m-Toldole-phos)



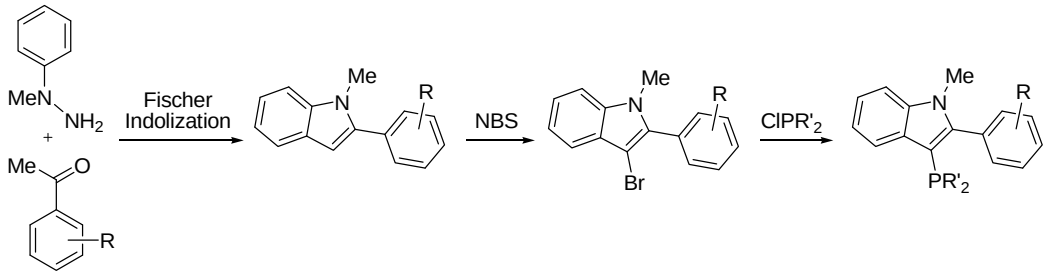
General procedures for the synthesis of ligand **NPPh Phendole-phos** were followed. 2-(3'-Tolyl)-1*H*-indole (414 mg, 2.0 mmol), *n*-BuLi (2.4 mmol), chlorodicyclohexylphosphine (486 μL, 2.2 mmol) were used to afford N-(dicyclohexylphosphino)-2-(3'-tolyl)indole (635 mg, 79%) as white crystal. Melting point. 149.2-152.8 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.15-1.37 (m, 12H), 1.65-1.85 (m, 9H), 2.49 (s, 3H), 2.75 (m, 2H), 6.59-6.60 (m, 1H), 7.22-7.40 (m, 6H), 7.69 (t, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 21.5, 26.0, 26.3, 26.4, 26.5, 28.8, 28.8, 30.4, 30.6, 36.7, 36.9, 105.0, 113.7, 120.6, 120.7, 121.4, 127.3, 128.0, 128.3, 131.1, 131.5, 131.5, 137.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ 57.99; IR (cm^{-1}) 3441.82, 3057.75, 3016.79, 2909.25, 2837.55, 1603.41, 1444.67, 1444.67, 1316.64, 1270.55, 1122.05, 1075.96, 1009.39, 773.83, 732.86, 702.13, 466.57; MS (EI): *m/z* (relative intensity) 402 (M^+, 98), 321 (17), 238 (100), 222 (30), 207 (80); HRMS: calcd. for $C_{27}H_{34}NPH^+$: 404.2507, found 404.2503.

N-(Dicyclohexylphosphino)indole (NPCy Indole-phos)



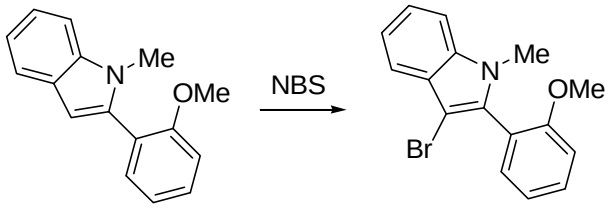
General procedures for the synthesis of ligand **NPPh Phendole-phos** were followed. Indole (469 mg, 4.0 mmol), *n*-BuLi (4.4 mmol), and chlorodicyclohexylphosphine (972 μL, 4.4 mmol) were used to afford N-(dicyclohexylphosphino)indole (921 mg, 73%) as white crystal. Melting point. 65.0-66.9 ºC; ^{1}H NMR (400 MHz, C_6D_6) δ 1.05-1.22 (m, 11H), 1.47-1.82 (m, 11H), 1.99 (s, 2H), 6.74 (d, *J* = 2.6 Hz, 1H), 7.10 (s, 1H), 7.24-7.39 (m, 2H), 7.77 (d, *J* = 7.7 Hz, 1H), 8.14 (d, *J* = 6.0 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 26.88, 27.03, 27.36, 27.42, 27.44, 27.55, 28.82, 28.89, 30.07, 30.28, 37.12, 37.27, 106.77, 113.42, 113.58, 121.36, 121.63, 123.06, 130.98; ^{31}P NMR (162 MHz, C_6D_6) δ 47.82; IR (cm^{-1}) 3042.93, 2914.37, 2847.80, 1444.67, 1291.04, 1270.55, 1132.29, 1004.27, 881.37, 763.58, 737.98, 640.68, 492.18; MS (EI): *m/z* (relative intensity) 313 (M^+, 40), 258 (3), 231 (40), 197 (4), 148 (100), 117 (30); HRMS: calcd. for $C_{20}H_{28}NPH^+$: 314.2038, found 314.2043.

2.4.4 Preparation of C-P Type Indolyl Phosphine (Phosphorus attached to indole 3-position)



2.4.4.1 Bromination of N-Methylated Indole Templates

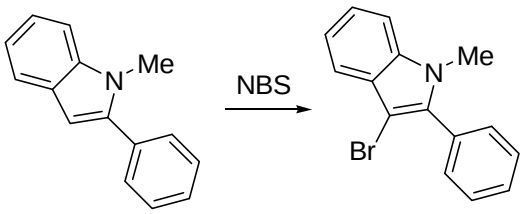
3-Bromo-2-(2-methoxyphenyl)-1-methyl-*1H*-indole



General procedure for the bromination of the indole at 3-position: The synthesis of N-methyl-2-(2-methoxyphenyl)-3-bromoindole from the literature method was slightly modified.[157] To a solution of N-methyl-2-(2-methoxyphenyl)indole (1.35 g, 5.7 mmol) in anhydrous DMF (15 mL), a solution of N-bromosuccinimide (1.05 g, 6.0 mmol) in anhydrous DMF (10 mL) was added at room temperature. After stirring for 2 hours, the reaction mixture was poured onto crushed ice and DCM was added to the flask followed by water. The organic phase was washed with a large amount of water, and then

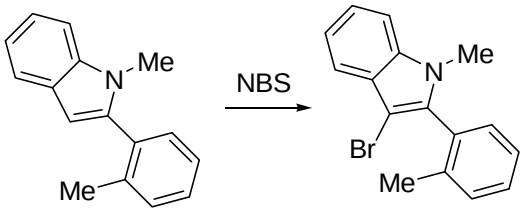
concentrated. The concentrated solution was filtered over a pad of silica (6 × 2 inch) and washed with hexane then EA/hexane (1:15). The solution was evaporated to give a white solid product. Little amount of cooled hexane was used to further purify of the product (if necessary). The final product N-methyl-2-(2-methoxyphenyl)-3-bromoindole was dried under vacuum (1.46g, 81%) to give a white solid as the desired compound. Melting point 82.9-83.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.61 (s, 3H), 3.82 (s, 3H), 7.08 (d, *J* = 8.3 Hz, 1H), 7.15 (dt, *J* = 8.2 Hz, *J* = 0.8 Hz, 1H), 7.25-7.28 (m, 1H), 7.34 (dt, *J* = 8.2 Hz, *J* = 1.0 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.44 (dd, *J* = 7.5 Hz, *J* = 1.7 Hz, 3H), 7.52 (m, 1H), 7.67 (d, *J* = 7.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.1, 55.4, 90.1, 109.4, 111.1, 119.1, 119.3, 120.0, 120.5, 122.3, 127.0, 130.7, 133.2, 135.4, 136.4, 157.7; IR (cm^{-1}) 3414.9, 3054.2, 3026.3, 2998.2, 2958.5, 2934.6, 2877.5, 2831.4, 1936.6, 1899.5, 1603.2, 1578.7, 1544.6, 1463.9, 1432.9, 1381.2, 1361.3, 1339.1, 1320.9, 1279.5, 1249.3, 1232.2, 1209.4, 1178.7, 1155.7, 1117.6, 1103.5, 1056.9, 1014.0, 945.1, 853.3, 790.6, 779.2, 755.1, 733.5, 667.9, 617.5, 592.7, 564.5, 545.6 ;MS (EI): *m/z* (relative intensity) 315 (M^+, 100), 236 (80), 220 (83), 204 (30), 193 (25); HRMS: calcd. for $C_{16}H_{15}NOBrH^+$: 316.0337, found 316.0338.

3-Bromo-1-methyl-2-phenyl-1*H*-indole[158]



The general synthetic procedures for the bromination of the indole at 3-position were followed. Commercially available N-methyl-2-phenylindole (10.4 g, 50 mmol) and N-bromosuccinimide (10.6 g, 60 mmol) were used to yield the desired product (12.3 g, 86%) as a white solid. Melting point 60.5-61.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.76 (s, 3H), 7.50-7.56 (m, 3H), 7.65-7.72 (m, 5H), 7.96 (d, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.3, 89.8, 109.6, 119.0, 120.3, 122.6, 127.0, 128.2, 128.4, 130.1, 130.4, 136.6, 137.7; MS (EI): *m/z* (relative intensity) 285 (M^+, 100), 204 (45), 191 (15), 178 (14).

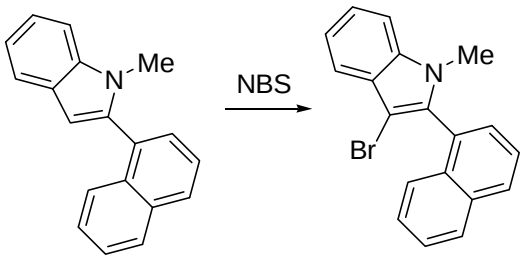
3-Bromo-1-methyl-2-*o*-tolyl-1*H*-indole



The general synthetic procedure for bromination of the indole at 3-position was followed. N-Methyl-2-(2-methylphenyl)indole (2.2 g, 10 mmol) and N-bromosuccinimide (1.77 g, 11 mmol) were used to yield the product (2.61 g,

87%) as a grey gel. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.20 (s, 3H), 3.53 (s, 3H), 7.26-7.41 (m, 7H), 7.65 (d, *J* = 7.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.6, 30.9, 90.3, 109.5, 119.1, 120.3, 122.4, 125.7, 127.0, 129.4, 130.1, 131.2, 136.3, 137.9, 138.6; IR (cm^{-1}) 3056.5, 2938.3, 1609.8, 1573.5, 1550.1, 1463.0, 1428.0, 1377.8, 1359.1, 1338.9, 1320.8, 1235.7, 1219.9, 1195.6, 1155.5, 1128.4, 1116.9, 1103.5, 1031.3, 1010.6, 946.7, 839.8, 795.4, 781.8, 741.2, 723.1, 617.1, 592.0, 551.6; MS (EI): *m/z* (relative intensity) 299 (M^+, 70), 220 (100), 204 (80), 179(20); HRMS: calcd. for $C_{16}H_{14}BrNH^+$: 300.0388, found 300.0392.

3-Bromo-1-methyl-2-(naphthalen-1-yl)-1*H*-indole

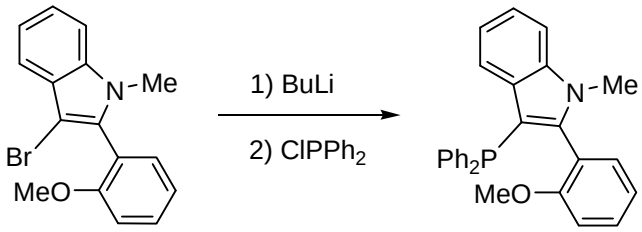


The general synthetic procedure for bromination of indole at 3-position was followed. 1-Methyl-2-(naphthalen-1-yl)-1H-indole (6.0 g, 23 mmol) and N-bromosuccinimide (4.5 g, 26 mmol) were used to yield the product (4.8 g, 62%) as a white solid. Melting point 149.7-151.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.53 (s, 3H), 7.38-7.53 (m, 4H), 7.58-7.70 (m, 4H), 7.81 (d, *J* = 7.6 Hz, 1H), 8.02 (d, *J* = 8.2 Hz, 1H), 8.07 (d, *J* = 7.9 Hz, 1H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ 31.2, 91.55, 109.6, 119.2, 120.4, 122.7, 125.1, 125.6, 126.2, 126.8, 127.1, 128.1, 128.4, 129.6, 129.8, 132.5, 133.5, 136.6; IR (cm^{-1}) 3415.5, 3050.3, 2931.7, 1675.5, 1500.5, 1463.9, 1392.7, 1356.6, 1334.9, 1322.7, 1258.4, 1228.5, 1202.8, 1176.7, 1156.5, 1128.5, 1100.2, 1051.9, 1007.5, 983.3, 946.4, 808.0, 791.3, 768.3, 740.7, 680.9, 655.3, 588.7, 549.3, 525.4; MS (EI): *m/z* (relative intensity) 335 (M^+, 60), 256 (70), 241 (100); HRMS: calcd. for $C_{19}H_{15}NBrH^+$: 336.0388, found 336.0394.

2.4.4.2 Phosphination of N-Methylated Indole

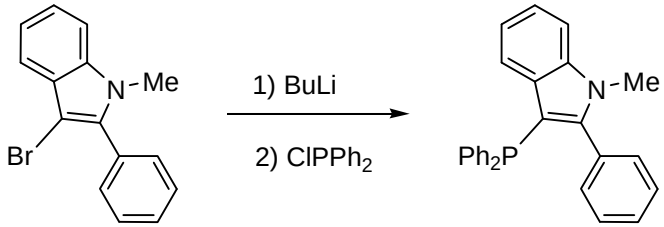
2-(2-Methoxyphenyl)-1-methyl-3-(diphenylphosphino)-1*H*-indole



General procedure for the synthesis of the indolyl diphenylphosphine: N-Methyl-2-(2-methoxyphenyl)-3-bromoindole (4.0 g, 12.6 mmol) was dissolved in freshly distilled THF (50 mL) at room temperature under nitrogen atmosphere. The solution was cooled to -78 °C in a dry ice/acetone bath. Titrated *n*-BuLi (13.8 mmol) was added dropwise with a syringe. After the reaction mixture was stirred for 30 min at -78°C, chlorodiphenylphosphine (2.5

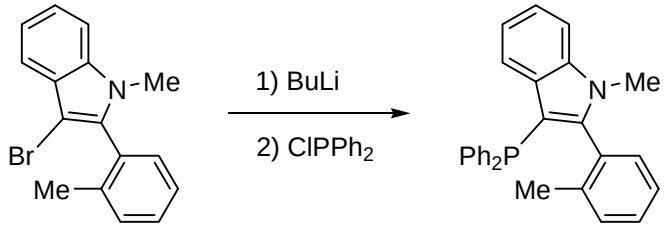
ml, 13.8 mmol) in THF (5 mL) was added. The reaction was allowed to warm to room temperature and stirred overnight. The solvent was removed under reduced pressure. After the solvent was removed under vacuum, the product was successively washed with cold MeOH. The product was then dried under vacuum. 2-(2-Methoxyphenyl)-1-methyl-3-(diphenylphosphino)-1*H*-indole was obtained as a white solid (4.25 g, 80%). Melting point 149.3-150.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.72 (s, 3H), 3.75 (s, 3H), 6.97-7.12 (m, 4H), 7.34-7.43 (m, 8H), 7.45-7.60 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.7, 55.1, 103.7, 109.5, 110.8, 119.7, 120.0, 121.5, 121.6, 127.0, 127.5, 127.7, 127.8, 127.9, 128.0, 130.5, 131.9, 132.0, 132.4, 132.6, 133.1, 133.1, 138.3, 138.4, 146.4, 146.8, 157.8 (unresolved C-P couplings were observed); ^{31}P NMR (162 MHz, $CDCl_3$) δ -27.53; IR (cm^{-1}) 3417.6, 3050.7, 3066.5, 3009.8, 2964.2, 2930.7, 2832.5, 1877.0, 1601.9, 1578.4, 1518.8, 1459.8, 1434.5, 1376.1, 1296.0, 1277.3, 1177.8, 1163.0, 1130.6, 1121.0, 1107.4, 1091.9, 1034.2, 1022.7, 999.8, 967.9, 934.6, 917.9, 833.7, 792.2, 780.7, 754.2, 738.9, 695.7, 671.6, 624.9, 595.7 580.3, 567.8, 546.9, 511.6 ; MS (EI): *m/z* (relative intensity) 421 (M^+, 11), 390 (100), 298 (5), 252 (11); HRMS: calcd. for $C_{28}H_{25}NOPH^+$: 422.1674, found 422.1675.

1-Methyl-2-phenyl-3-(diphenylphosphino)-1*H*-indole[159]



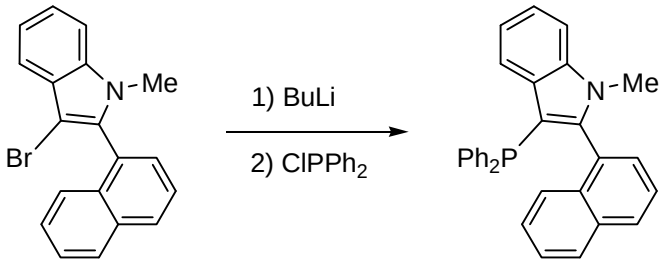
The general synthetic procedure for the synthesis of the indolyl diphenylphosphine was followed. N-Methyl-2-phenyl-3-bromoindole (1.43 g, 5.0 mmol), *n*-BuLi (5.5 mmol) and chlorodiphenylphosphine (0.99 ml, 5.5 mmol) were used to yield the desired product (1.0 g, 51%) as a white solid. Melting point 156.3-158.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.70 (s, 3H), 6.96 (t, J = 7.5 Hz, 1H), 7.03 (d, J = 7.9 Hz, 1H), 7.24-7.30 (m, 7H), 7.42-7.49 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.2, 103.9, 109.7, 120.1, 121.9, 127.5, 127.9, 128.0, 128.1, 128.6, 129.5, 129.6, 131.1, 131.2, 131.5, 132.3, 132.5, 138.2, 138.3, 138.5, 149.4, 149.9 (unresolved C-P couplings were observed); ^{31}P NMR (162 MHz, $CDCl_3$) δ -27.73; IR (cm^{-1}) 3428.4, 3053.3, 3010.2, 2939.0, 1601.4, 1582.4, 1464.3, 1431.7, 1374.9, 1332.8, 1303.2, 1271.3, 1232.5, 1210.4, 1178.6, 1154.1, 1133.4, 1068.3, 1094.6, 1023.5, 1049.6, 963.2, 923.1, 913.8, 850.0, 820.8, 796.7, 747.2, 738.7, 697.2, 624.8, 576.4, 550.8; MS (EI): *m/z* (relative intensity) 391 (M^+, 100), 314 (8), 298 (8), 283 (32), 267 (8), 236 (50); HRMS: calcd. for $C_{27}H_{22}NPH^+$: 392.1568, found 392.1575.

1-Methyl-3-(diphenylphosphino)-2-*o*-tolyl-1*H*-indole



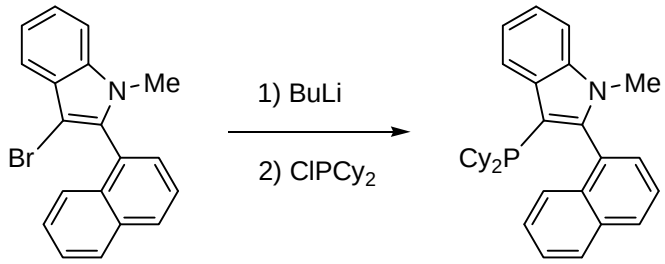
The general synthetic procedure for the synthesis of the indolyl diphenylphosphine was followed. N-Methyl-2-phenyl-3-bromoindole (2.99 g, 10 mmol), *n*-BuLi (11 mmol) and chlorodiphenylphosphine (1.98 ml, 11 mmol) were used to yield the product (1.7 g, 40%) as a white solid. Melting point 157.4-160.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.15 (s, 3H), 3.55 (s, 3H), 6.98 (t, J = 7.6 Hz, 1H), 7.10 (d, J = 7.9 Hz, 1H), 7.27-7.49 (m, 16H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 30.5, 103.8, 109.6, 120.0, 121.7, 121.8, 125.4, 127.3, 127.5, 127.9, 128.0, 128.1, 129.2, 129.5, 129.8, 131.5, 132.1, 132.3, 132.4, 132.6, 138.1, 138.3, 149.0, 149.5 (unresolved C-P couplings were observed); ^{31}P NMR (162 MHz, $CDCl_3$) δ -28.27; IR (cm^{-1}) 3430.3, 3067.3, 3050.9, 2919.2, 1582.9, 1526.7, 1478.7, 1463.6, 1430.9, 1376.4, 1334.8, 1305.8, 1282.1, 1236.2, 1219.1, 1193.0, 1156.9, 1132.1, 1118.7, 1094.3, 1068.2, 1050.9, 1026.0, 1015.4, 998.8, 971.8, 782.5, 799.7, 759.4, 746.4, 736.3, 723.6, 702.4, 693.1, 625.4, 537.0; MS (EI): *m/z* (relative intensity) 405 (M^+, 50), 390 (100), 314 (19), 296 (10); HRMS: calcd. for $C_{28}H_{24}NPH^+$: 406.1725, found 406.1721.

1-Methyl-2-(naphthalen-1-yl)-3-(diphenylphosphino)-1*H*-indole



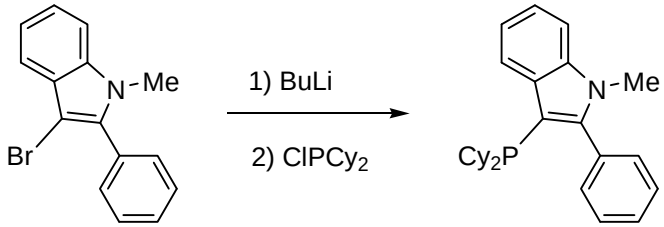
The general synthetic procedure for the synthesis of the indolyl diphenylphosphine was followed. 3-Bromo-1-methyl-2-(naphthalen-1-yl)-1*H*-indole (1.1 g, 3.3 mmol), *n*-BuLi (3.6 mmol) and chlorodiphenylphosphine (0.65 ml, 3.6 mmol) were used to yield the desired product (0.9 g, 63%) as a white solid. Melting point 172.5-175.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.50 (s, 3H), 7.05 (m, 1H), 7.20-7.60 (m, 18H), 7.97-8.03 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.9, 105.5, 109.7, 121.9, 122.0, 125.7, 126.0, 126.6, 127.2, 127.5, 127.8, 127.9, 128.0, 128.0, 128.3, 129.5, 132.0, 132.2, 132.5 ,132.7, 138.5, 147.6, 148.1 (unresolved C-P couplings were observed); ^{31}P NMR (162 MHz, $CDCl_3$) δ -28.17; IR (cm^{-1}); 3424.1, 3048.7, 2934.6, 1538.6, 1518.0, 1495.7, 1477.7, 1463.6, 1431.7, 1389.9, 1370.5, 1333.38, 1303.6, 1257.0, 1238.7, 1218.4, 1153.5, 1133.3, 1091.9, 1067.5, 1051.5, 1025.8, 1016.1, 984.9, 969.4, 811.1, 789.9, 775.8, 740.4, 694.7, 605.5; MS (EI): *m/z* (relative intensity) 440 (M^+, 100), 333 (6), 286 (20), 271 (9); HRMS: calcd. for $C_{31}H_{25}NPH^+$: 442.1725, found 442.1715.

1-Methyl-2-(naphthalen-1-yl)-3-(dicyclohexylphosphino)-1H-indole



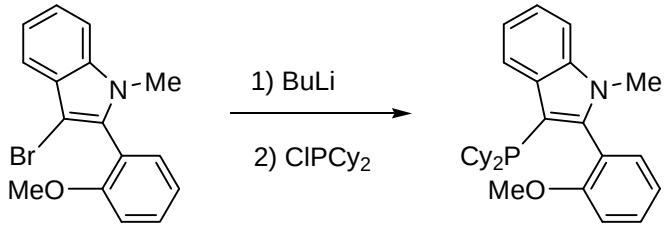
The general synthetic procedure for the synthesis of the indolyl diphenylphosphine was followed. 3-Bromo-1-methyl-2-(naphthalen-1-yl)-1*H*-indole (1.68 g, 5 mmol), *n*-BuLi (6 mmol) and chlorodicyclohexylphosphine (1.32 ml, 6 mmol) were used to yield the product (1.7g, 75%) as a pale yellow solid. Melting point 209.5-211.5 °C; ^{1}H NMR (400 MHz, CD_2Cl_2) δ 1.14-1.29 (m, 10H), 1.55-1.76 (m, 10H), 2.17-2.18 (m, 1H), 2.39-2.40 (m, 1H), 3.34 (s, 3H), 7.18-7.22 (m, 1H), 7.28-7.35 (m, 2H), 7.38-7.54 (m, 4H), 7.59-7.63 (m, 1H), 7.91-8.01(m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.3, 26.3, 26.9, 27.1, 27.2, 27.2, 27.3, 30.2, 30.3, 30.7, 31.8, 33.2, 33.3, 34.4, 34.5, 105.4, 105.5, 109.5, 119.7, 121.5, 121.9, 124.8, 125.8, 126.0, 126.2, 128.2, 128.9, 129.1, 130.1, 130.4, 130.6, 130.6, 133.2, 138.1, 147.7, 148.1(unresolved C-P couplings were observed); ^{31}P NMR (162 MHz, C_6D_6) δ -18.12; IR (cm^{-1}); 3429.9, 3045.6, 2919.7, 2845.6, 1498.6, 1444.6, 1389.5, 1366.6, 1333.9, 1264.2, 1232.7, 1128.4, 1009.9, 853.1, 808.7, 773.7, 738.9, 527.2, 418.1; MS (EI): *m/z* (relative intensity) 453 (M^+, 20), 371 (30), 288 (100), 272 (20).

N-Methyl-2-phenyl-3-(dicyclohexylphosphino)indole (C'PCy Phendole-phos)



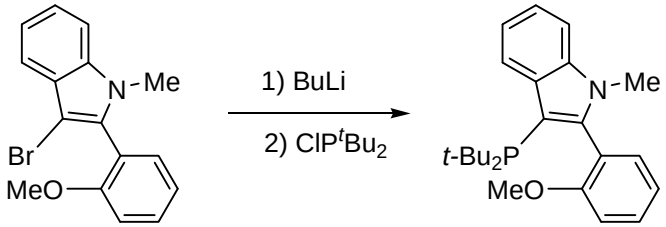
The general synthetic procedure for the synthesis of the indolyl diphenylphosphine was followed. N-Methyl-2-phenyl-3-bromoindole (0.855 g, 3.0 mmol), *n*-BuLi (3.3 mmol) and chlorodicyclohexylphosphine (0.66 mL, 3.3 mmol) were used to yield N-methyl-2-phenyl-3-(dicyclohexylphosphino)indole (0.85 g, 71%) as a white solid. Melting point. 122.0-123.2 °C; ^{1}H NMR (400 MHz, C_6D_6) δ 1.19-2.55 (m, 22H), 3.08 (s, 3H), 7.19-7.39 (m, 6H), 7.51 (d, *J*=7.3 Hz, 2H), 8.16-8.18 (m, 1H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 26.8, 27.3, 27.5 (overlapped), 27.6, 30.7 (overlapped), 31.0, 31.1, 32.5, 32.8, 34.8, 34.9, 105.1, 105.3, 110.3, 120.5, 122.1 (overlapped), 127.8, 127.9, 131.3 (overlapped), 132.1 (overlapped), 133.3 (overlapped), 138.8 (overlapped), 149.8, 150.2 (unresolved complex C-P splittings were observed); ^{31}P NMR (162 MHz, C_6D_6) δ -18.36; IR (cm^{-1}) 3049.36, 2921.78, 2845.98, 1465.12, 1443.10, 1372.54, 1336.47, 1264.83, 1106.31, 1021.29, 887.02, 849.63, 795.91, 737.94, 698.91, 619.86, 550.50; MS (EI): *m/z* (relative intensity) 403(M^+, 25), 348 (5), 321 (30), 238 (100), 222 (25), 207 (10); HRMS: calcd. for $C_{27}H_{34}NPH^+$: 404.2507, found 404.2511.

2-(2-Methoxyphenyl)-1-methyl-3-(dicyclohexylphosphino)-1*H*-indole



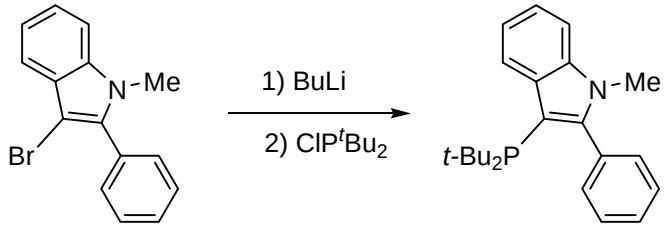
The general synthetic procedure for the synthesis of the indolyl diphenylphosphine was followed. N-Methyl-2-(2-methoxyphenyl)-3-bromoindole (1.3 g, 3 mmol), *n*-BuLi (3.3 mmol) and chlorodicyclohexylphosphine (1.98 ml, 3.3 mmol) were used to yield the product (0.93 g, 71%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.04-1.37 (m, 11H), 1.62-1.95 (m, 11H), 2.21-2.26 (m, 1H), 2.42 (m, 1H), 7.04 (d, *J* = 8.2 Hz, 1H), 7.12 (d, *J* = 7.3 Hz, 1H), 7.21 (d, *J* = 7.3 Hz, 1H), 7.30 (m, 2H), 7.42 (d, *J* = 7.9 Hz, 1H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.94 (d, *J* = 7.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.7, 25.8, 26.3, 26.3, 27.1, 27.1, 27.2 29.9, 30.0, 30.3, 30.4, 30.5, 31.2, 31.4, 31.7, 31.9, 33.3, 33.4, 34.1, 34.2, 55.0, 103.6, 103.8, 109.3, 110.4, 119.2, 119.9, 121.0, 121.5, 121.6, 130.2, 130.6, 130.7, 133.5, 133.5, 137.9, 137.9, 146.4, 146.8, 157.9 (unresolved C-P couplings were observed); ^{31}P NMR (162 MHz, C_6D_6) δ -17.65; IR (cm^{-1}); MS (EI): *m/z* (relative intensity) 402 (M^+, 100), 320 (15), 268 (50), 252 (40), 234 (20); HRMS: calcd. for $C_{28}H_{37}NPH^+$: 434.2613, found 434.2625.

2-(2-Methoxyphenyl)-1-methyl-3-(di-*tert*-butylphosphino)-1*H*-indole



The general synthetic procedure for the synthesis of the indolyl diphenylphosphine was followed. N-Methyl-2-(2-methoxyphenyl)-3-bromoindole (1.1 g, 2.5 mmol), *n*-BuLi (2.75 mmol) and di-*tert*-butylchlorophosphine (0.52 ml, 2.75 mmol) were used to yield the product (0.63 g, 47%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40 (d, J = 11.7 Hz, 9H), 1.50 (d, J = 11.7 Hz, 9H), 3.18 (s, 3H), 3.32 (s, 3H), 6.68 (d, J = 8.1Hz, 1H), 7.02 (t, J = 7.1Hz, 1H), 7.20-7.46 (m, 6H), 8.32 (d, J = 7.5Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 30.9, 32.2, 32.4, 32.7, 32.9, 33.5, 33.5, 33.7, 33.8, 55.2, 107.1, 107.4, 110.6, 111.1, 120.5, 120.7, 122.1, 123.7, 123.7, 125.1, 130.7, 131.0, 131.1, 134.7, 134.8, 139.5, 149.0, 149.6, 158.9 (unresolved C-P couplings were observed); ^{31}P NMR (162 MHz, C_6D_6) δ 17.87; IR (cm^{-1}); MS (EI): *m/z* (relative intensity) 381 (M^+, 10), 350 (35), 268 (100), 252 (35), 234 (20); HRMS: calcd. for $C_{24}H_{33}NPH^+$: 382.2300, found 382.2310.

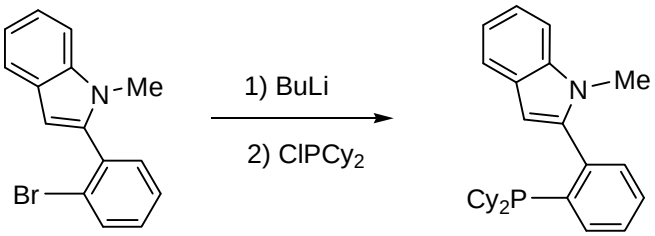
N-Methyl-2-phenyl-3-(di-*tert*-butylphosphino)indole



The general synthetic procedure for the synthesis of the indolyl diphenylphosphine was followed. N-Methyl-2-(2-methoxyphenyl)-3-bromoindole (1.43 g, 5 mmol), *n*-BuLi (5.5 mmol) and di-*tert*-butylchlorophosphine (1.04 ml, 5.5 mmol) were used to yield the product (0.59 g, 33%) as a white solid. ^{1}H NMR (400 MHz, C_6D_6) δ 1.42 (d, J = 11.7 Hz, 18H), 3.04 (s, 3H), 7.18-7.24 (m, 2H), 7.25-7.32 (m, 2H), 7.36-7.41 (m, 4H), 8.31-8.33 (m, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 32.9, 32.9, 34.1, 34.2, 35.3, 35.5, 112.3, 122.4, 124.1, 127.0, 132.5, 132.5, 134.1, 134.1, 141.1, 141.1, 153.6, 154.1 (unresolved C-P couplings were observed); ^{31}P NMR (162 MHz, C_6D_6) δ 16.84; IR (cm^{-1}); MS (EI): *m/z* (relative intensity) 351 (M^+, 15), 294 (15), 238 (100), 222 (20), 207 (8); HRMS: calcd. for $C_{23}H_{21}NPH^+$: 352.2194, found 352.2195.

2.4.5 Preparation of C-P Type Indolyl Phosphine (Phosphorus attached to bottom ring)

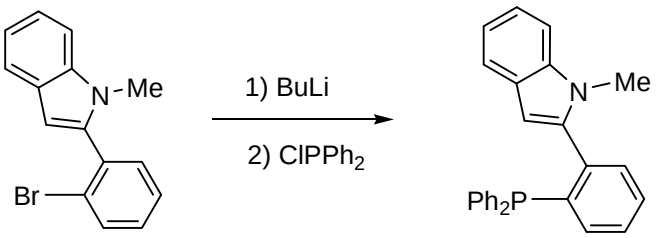
N-Methyl-2-(2'- Dicyclohexylphosphinophenyl)indole (CM-phos)



General procedure for ligand synthesis: N-Methyl-2-(2'-bromophenyl)indole (2.2 g, 7.7 mmol) was dissolved in freshly distilled THF (25 mL) at room temperature under a nitrogen atmosphere. The solution was cooled to -78 °C in adry ice/acetone bath. Titrated *n*-BuLi (8.47 mmol) was added dropwise with a syringe. After the reaction mixture was stirred at -78 °C for 30 min, chlorodicyclohexylphosphine (1.87 mL, 8.47 mmol) in THF (5 mL) was added. The reaction was allowed to warm to room temperature and stirred overnight. The solvent was removed under reduced pressure, after which the product was successively washed with a cold MeOH/EtOH mixture. The product was then dried under vacuum. A white solid of N-methyl-2-(2'-dicyclohexylphosphinophenyl)indole (2.75g, 88%) was obtained. Melting point. 171.9-174.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20-1.80 (m, 22H), 3.53 (s, 3H), 6.44 (s, 1H), 7.15(t, *J*=7.4 Hz, 1H), 7.24-7.27 (m, 1H),

7.36-7.50 (m, 4H), 7.66 (d, *J*=7.7 Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$) δ 25.5, 26.2, 27.1, 28.9, 29.3, 29.5, 30.1, 30.7, 103.2, 109.3, 119.3, 120.2 121.0, 127.6, 127.8, 128.0, 128.2, 128.4, 131.8, 131.9, 132.7, 136.6 (unresolved complex C-P splittings were observed); ^{31}P NMR (162 MHz, C_6D_6) δ -9.87; IR (cm^{-1}) 2422.67, 3050.84, 2924.05, 2846.58, 1445.74, 1384.98, 1338.55, 1309.68, 1264.17, 1123.17, 1001.01, 886.58, 848.87, 769.86, 746.53, 523.77; MS (EI): *m/z* (relative intensity) 403(M^+, 25), 348 (5), 321 (30), 238 (100), 222 (30), 207 (20); HRMS: calcd. for $C_{27}H_{34}NP$: 403.2423, found 403.2414.

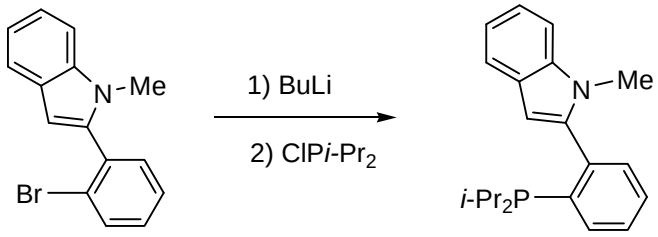
N-Methyl-2-(2'-Diphenylphosphinophenyl)indole (C'PPh Phendole-phos)



General procedures for the synthesis of ligand **L2** were followed. N-Methyl-2-(2'-bromophenyl)indole (1.89 g, 6.6 mmol), *n*-BuLi (6.9 mmol), and chlorodiphenylphosphine (1.25 mL, 7.0 mmol) were used to afford N-methyl-2-(2'-diphenylphosphinophenyl)indole (1.65 g, 64%) as a white crystal. Melting point. 122.0-125.5 ºC; ^{1}H NMR (400 MHz, C_6D_6) δ 3.18 (s, 3H), 6.55 (s,1H), 7.08-7.66 (m, 18H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 30.5, 103.7, 103.8, 109.5, 119.5, 120.4, 121.5, 127.6, 128.5 (overlapped), 128.6, 128.7, 128.8, 131.6

(overlapped), 133.7, 133.8, 133.9, 137.2, 137.4, 137.5, 139.6 (overlapped) (unresolved complex C-P splittings were observed); ^{31}P NMR (162 MHz, C_6D_6) δ -12.02; IR (cm^{-1}) 3446.06, 3048.19, 2931.48, 1582.52, 1461.53, 1429.92, 1377.43, 1359.35, 1336.25, 1308.54, 1235.94, 1176.72, 1123.94, 1093.80, 1025.26, 999.97, 924.13, 943.98 ,769.18, 745.33, 695.27, 539.41, 495.26; MS (EI): *m/z* (relative intensity) 391 (M^+, 100), 376 (50), 314 (30), 298 (27), 281 (5), 261 (5), 236 (50), 222 (40), 204 (25); HRMS: calcd. for $C_{27}H_{22}NPH^+$: 392.1568, found 392.1579.

N-Methyl-2-(2'-Diisopropylphosphinophenyl)indole(C'P^{i}Pr Phendole-phos)



General procedures for the synthesis of ligand were followed. N-Methyl-2-(2'-bromophenyl)indole (1.66 g, 5.8 mmol), *n*-BuLi (6.38 mmol), and chlorodiisopropylphosphine (1.03 mL, 6.4 mmol) were used to afford N-methyl-2-(2'-diisopropylphosphinophenyl)indole (1.41 g, 75%) as a white crystal. Melting point. 146.1-147.8 ºC; ^{1}H NMR (400 MHz, CD_2Cl_2) δ 1.06-1.15 (m, 12H), 1.80-2.80 (m, 2H), 3.61 (s, 3H), 6.52 (s, 1H), 7.23-7.77 (m,

8H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 20.0, 20.2, 23.3, 25.7 (overlapped), 30.8 (overlapped), 103.3 (overlapped), 109.4, 119.4, 120.1, 121.1, 127.8, 128.2, 128.4, 131.7, 131.8, 132.5, 132.6, 136.7, 137.9, 138.1, 140.6, 140.9, 141.5, 141.5 (overlapped) (unresolved complex C-P splitting was observed); ^{31}P NMR (162 MHz, CD_2Cl_2) δ -1.29; IR (cm^{-1}) 3445.89, 3050.50, 2941.77, 2860.55, 1542.40, 1454.90, 1420.35, 1380.67, 1336.26, 1309.58, 1237.42, 1119.75, 1005.64, 880.09, 778.80, 747.64, 676.90, 653.14, 606.16, 583.14, 531.39, 459.25; MS (EI): *m/z* (relative intensity) 323 (M^+, 20), 280 (100), 236 (40), 222 (30), 204 (5); HRMS: calcd. for $C_{21}H_{26}NP$: 323.1797, found 323.1803

Chapter 3 Easily Accessible and Highly Tunable Indolyl Phosphine Ligands for Suzuki-Miyaura Coupling of Aryl Chlorides

3.1 Introduction

Hundreds of supporting ligands for palladium-catalyzed coupling reactions have been designed and synthesized since 1998. Among them, the P*t*-Bu_3 by Fu[120-123]and Koie,[124] the ferrocenyl-based dialkylphosphine by Hartwig,[125,126] the elegantly designed biphenyl-based dialkylphosphine by Buchwald[84,106,127-131] and the heteroaromatic dialkylphosphine by Beller[132-134] are highly versatile and effective for the palladium-catalyzed coupling reaction (Figure 1.2). Among the various reported supporting ligands, phosphorus donor ligands that possess the N-P bond in the ligand scaffold have remained sporadically studied.[160-163]The unique electron-donating capability of these ligands reported by Woollins and co-workers[163] showed that phosphine containing N-P bound amino group could provide unusual electron-rich donor character on the phosphorus atom. In fact, amino-phosphine can be conveniently prepared by the deprotonation of amine followed by quenching with chlorophosphine. Avoiding the metal/halogen exchange pathway from ArBr or ArI can make the ligand synthesis more atom-economic. Therefore, this convenient synthesis is a very attractive method

for the preparation of amino-phosphine for large scale industrial synthesis. Moreover, these conceptually interesting ligands are effective in cross-coupling reactions.[164] Recently, Verkade has reported the palladium-catalyzed Suzuki coupling reaction with triaminophosphine (pro-azaphosphatranes) as supporting ligand.[165,166]

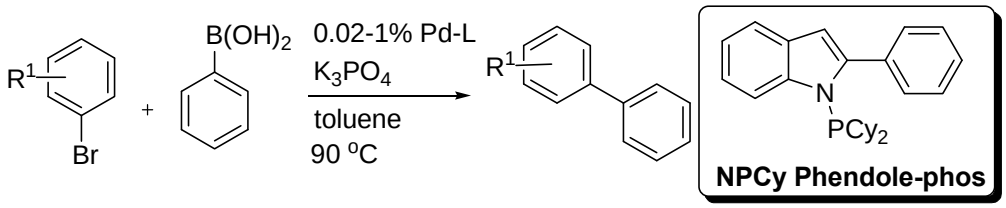
Although a variety of ligands have been introduced, rapid assembly of structurally diverse ligand system via simple synthetic methods is still important for the development of versatile catalysts for widespread applications of coupling reactions of aryl halides. Apart from coupling reaction of aryl sulfonates, we also attempted to develop an effective system for the coupling reaction of aryl halides in the course of our studies. In this chapter, the effectiveness of both N-P and C-P type indolyl phosphine ligands in the palladium-catalyzed Suzuki coupling of aryl halides would be evaluated.

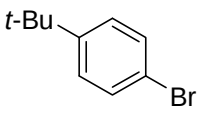
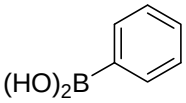
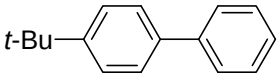
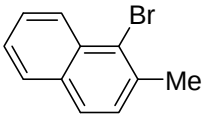
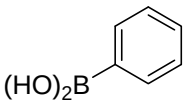
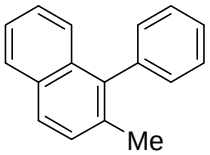
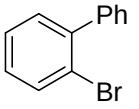
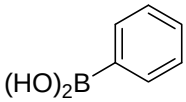
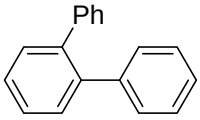
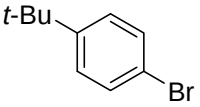
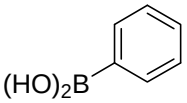
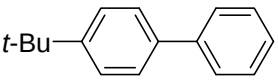
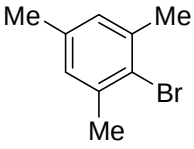
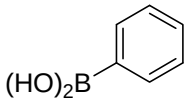
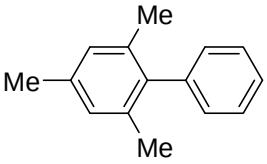
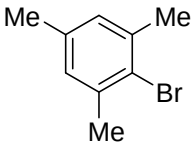
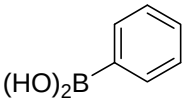
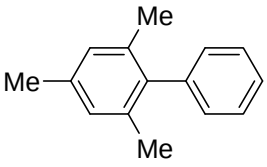
3.2 Results and Discussion

3.2.1 Study the Catalytic Activity of N-P Type Indolyl Phosphine

3.2.1.1 Preliminary Evaluation of New Indolyl Phosphine (Aryl Bromides)

Table 3.1 Pd-Catalyzed Suzuki-Miyaura Coupling of ArBr[a]



entry	ArCl	Ar'B(OH)$_2$	product	mol% Pd	%yield[b]
1				1% 16 h	>99
2				1% 16 h	97
3				1% 16 h	97
4				0.2% 16 h	>99
5				0.02% 16 h	>99
6				0.1% 10min	>99

[a]Reaction conditions: ArBr : ArB(OH)$_2$: K_3PO_4 = 1: 1.5 : 3; Pd : L = 1: 2; toluene (2 mL) under N_2; Temperature=90^{o}C; mol% of Pd (from Pd(OAc)$_2$) with respect to ArBr. [b]Yield by GC(FID).

To evaluate the effectiveness of the new indolyl phosphine, aryl bromides were firstly employed in the palladium-catalyzed Suzuki coupling reaction. Under 1 mol% Pd catalyst loading, both non-hindered 4-*tert*-butylbromobenzene and bulky 2-phenylbromobenzene were smoothly converted to biaryl products. Highly bulky 2,4,6-trimethylbromobenzene was also successfully turned into biaryl products in excellent yield. Finally, it was observed that a turn-over frequency as high as 6000 cycle/h could be achieved in the coupling reaction of the bulky 2,4,6-trimethylbromobenzene. These results showed that the newly developed NPCy Phendole-phos is an effective supporting ligand for the Suzuki coupling of aryl bromides.

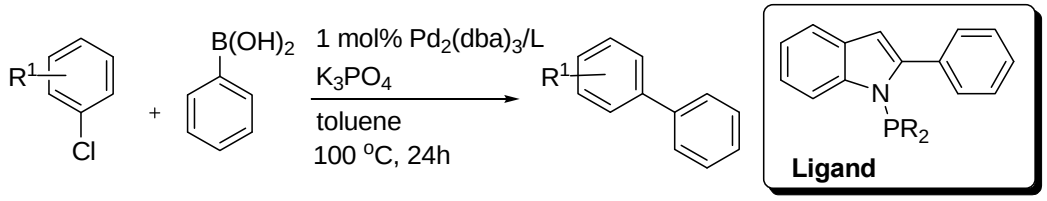
3.2.1.2 Preliminary Evaluation of New Indolyl Phosphine (Aryl Chlorides)

In order to fully understand the catalytic reactivity of the new indolyl phosphine ligands, more inert aryl chlorides were used to explore the catalytic reactivity of the new indolyl phosphine ligands.

The reaction condition was directly applied to catalyze the Suzuki coupling of aryl chlorides. However, the biaryl product yield was only less than 30%. Since aryl chlorides are more reluctant towards oxidative addition, active Pd(0) catalysts may decompose before the effective collision occur. Increasing the

ligand concentration may prevent the rapid decomposition of active Pd(0) catalysts to form inactive palladium black. Therefore, we changed the ligand ratio increasing from 1:2 to 1:4. The biaryl product yields were successfully improved from less than 30% to more than 70%.

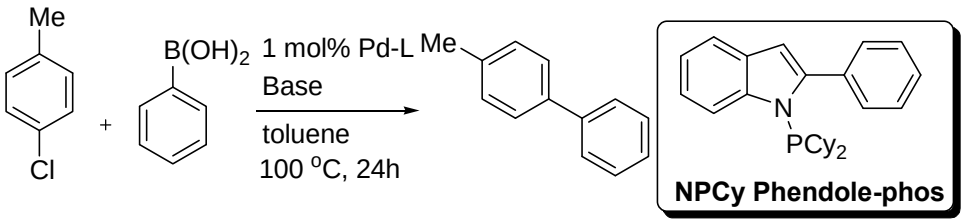
Table 3.2 The Ligand to Metal Ratio Effect on the Suzuki-Miyaura Coupling Reaction[a]



entry	M:L	ligand	ArCl, R^1	%yield[b]
1	1:2	NPCy Phendole-phos	4-Me	<30%
2	1:2	NP^{i}Pr Phendole-phos	4-Me	<30%
3	1:4	NPCy Phendole-phos	4-Me	93
4	1:4	NPCy Phendole-phos	2-Me	91
5	1:4	NP^{i}Pr Phendole-phos	4-Me	73

[a]Reaction conditions: ArCl : $ArB(OH)_2$: K_3PO_4 = 1: 1.5 : 3; toluene (2 mL) under N_2; mol% of Pd (from $Pd_2(dba)_3$) with respect to ArCl. [b]GC(FID) yields.

Table 3.3 Base Screening for the Suzuki Coupling Reaction [a]



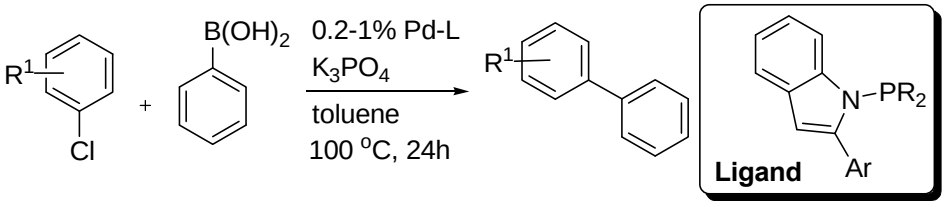
entry	base	GC yield (%)
1	K_3PO_4	93
2	Cs_2CO_3	58
3	CsF	41
4	Na_2CO_3	14
5	KO*t*-Bu	5

[a]Reaction conditions: ArCl : $ArB(OH)_2$: Base = 1: 1.5 : 3; toluene (2 mL) under N_2; mol% of Pd (from $Pd_2(dba)_3$) with respect to ArCl.

The preliminary results showed that the new indolyl phosphine is an effective supporting ligand for the palladium-catalyzed Suzuki coupling of aryl halides. Before further detail study of the reactivity of the new indolyl phosphine, the reaction conditions were optimized. Several bases such as K_3PO_4, Cs_2CO_3, CsF and KO*t*-Bu were examined in the presence of NPCy Phendole-phos. K_3PO_4 was found to be the base of choice for this catalytic system.

3.2.1.3 Investigation of the Relationship Between Ligand Structure and the Reactivity in the Coupling Reaction

Table 3.4 The Relationship Between Ligand Structure and the Reactivity in the Coupling Reaction[a]



entry	%Pd	M:L	Ligand	ArCl	%yield[b]
1	1	1:4	NPCy Phendole-phos	4-Me	93
2	1	1:4	NPCy Indole-phos	4-Me	55
3	1	1:4	NPCy o-Toldole-phos	4-Me	>99
4	1	1:4	NPCy p-Toldole-phos	4-Me	87
5	1	1:4	NPCy m-Toldole-phos	4-Me	85
6	1	1:4	NPCy o-Andole-phos	4-Me	>99
7	1	1:2	NPCy o-Andole-phos	2-Me	>99
8	1	1:2	NPCy o-Andole-phos	4-Me	>99
9	1	1:2	NPCy o-Toldole-phos	2-Me	>99
10	1	1:2	NPCy o-Toldole-phos	4-Me	>99
11	0.2	1:2	NPCy o-Toldole-phos	4-Me	84
12	0.2	1:2	NPCy o-Andole-phos	4-Me	91
13	0.2	1:2	NPCy o-Toldole-phos	2-Me	96
14	0.2	1:2	NPCy o-Andole-phos	2-Me	88

[a]Reaction conditions: ArCl : $ArB(OH)_2$: K_3PO_4 = 1: 1.5 : 3; toluene (2 mL) under N_2; mol% of Pd (from $Pd_2(dba)_3$) with respect to ArCl. [b]GC(FID) yields.

In order to understand the relationship between the structure of the new indolyl phosphine and its reactivity, various kinds of indolyl phosphines bearing substitute groups at different positions were synthesized and screened.

To study the importance of the bottom ring of the indolyl phosphine ligand, we prepared NPCy Indole-phos. As we can see NPCy Indole-phos without the the bottom Ar-ring showed significant lower conversion (Table3.4, entry 2) compared with the NPCy Phendole-phos (Table3.4, entry 1). This comparative results demonstrated the crucial role of the aryl ring which was directly attached to the 2-position of the indole scaffold.

To further investigate the substitute group/catalytic activity effect of the bottom ring, indolyl phosphine ligand bearing the methoxy group and methyl group on the bottom ring was synthesized. The results showed that the substitute group attached to the *ortho*-position of the bottom ring had exceedingly high catalytic activity toward the coupling reaction.

In fact, there are two effects introduced by the ortho substituted groups. The methoxy group and methyl group are electron donating groups that can increase the electron density of the indolyl phosphine ligand while as substituted group at the ortho position of the bottom ring can increase the bulkiness of the ligand.

To understand the effect of the substitute group on the bottom ring, NPCy

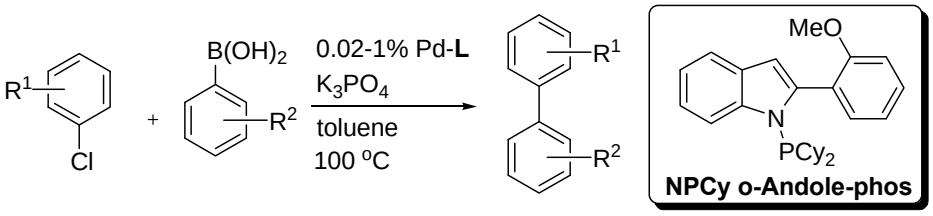
m-Toldole-phos and NPCy p-Toldole-phos were synthesized. The methyl group at the meta and para position of the bottom ring could also increase the electron density of the ligands but not the bulkiness around the metal center. However, NPCy m-Toldole-phos and NPCy p-Toldole-phos (Table3.4, entries 4, 5) showed catalytic activity similar to that of the NPCy Phendole-phos (Table3.4, entry 1). Therefore, the substitute groups attached to the ortho position of the bottom ring played an important role in the catalytic reactivity of the ligands. The ortho substituted group on the bottom ring could increase the congested environment around the metal center which might create unsaturation of the palladium center that facilitated the oxidative addition of aryl chlorides.

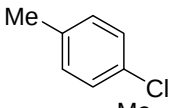
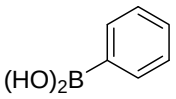
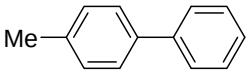
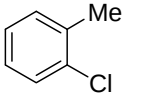
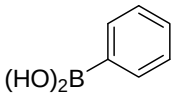
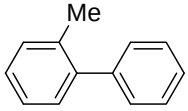
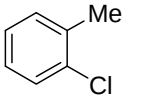
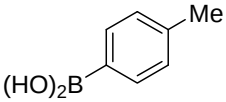
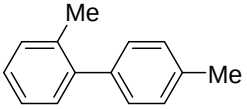
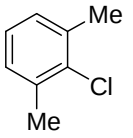
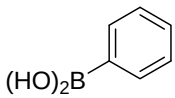
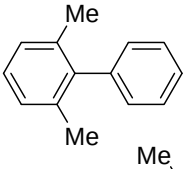
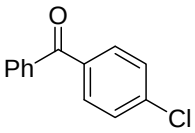
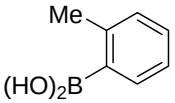
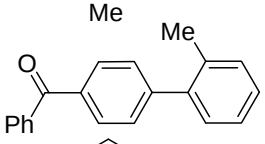
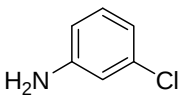
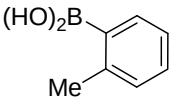
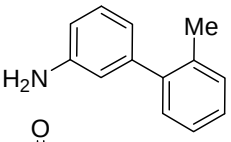
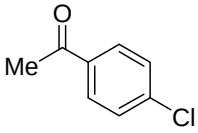
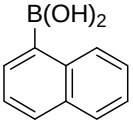
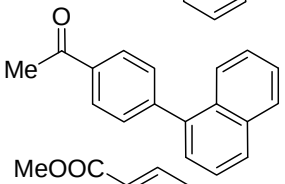
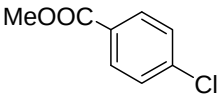
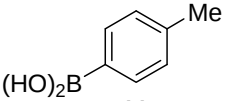
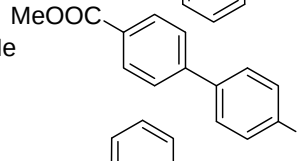
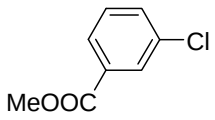
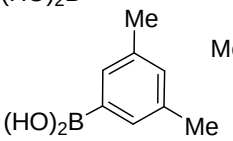
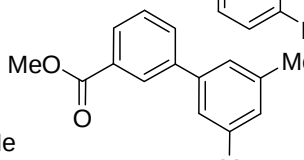
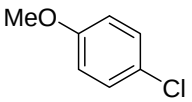
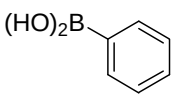
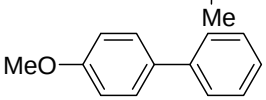
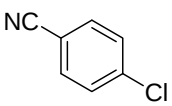
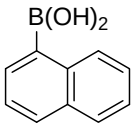
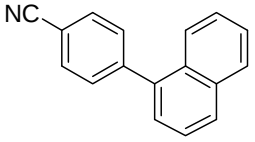
We investigated the catalytic activity of the NPCy o-Toldole-phos and NPCy o-Andole-phos in the coupling reaction. Excellent yield could still be obtained even when the catalyst loading was lowered to 0.2 mol% Pd (Table3.4, entries 11-14). On the other hand, different substitute groups of the indole aryl ring showed different reactivities towards different substrates. As we can see NPCy o-Toldole-phos is more active ligand towards 2-chlorotoluene while NPCy o-Andole-phos is more active ligand towards 4-chlorotoluene. This phenomenon demonstrated that the high diversity of the ligand template provides the flexibility for the synthesizing certain kinds of drugs that have special structure.

3.2.1.4 Exploration of the Catalytic Activity of New Indolyl Phosphine Ligands: The Use of Aryl Chlorides Bearing Different Functional Groups as Substrates

A good catalytic system should be highly active towards the desired functional group (Ar-X, X=Cl, Br in this case) and should be inert towards other functional groups. To examine the functional group compatibility of our catalytic system, we used different kinds of aryl chlorides bearing functional groups as substrates in the coupling reaction.

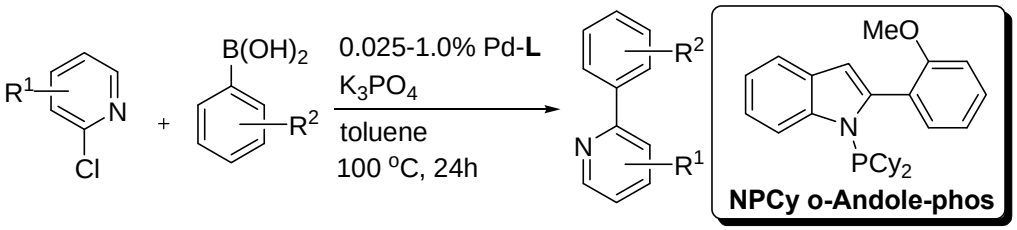
Table 3.5 Pd-Catalyzed Suzuki-Miyaura Coupling of ArCl [a]

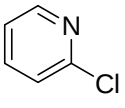
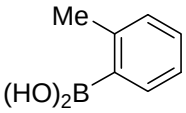
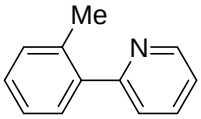
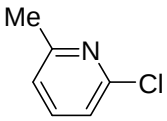
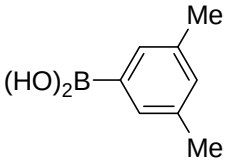
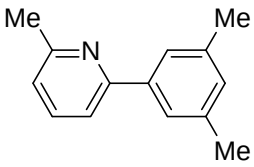
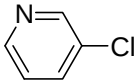
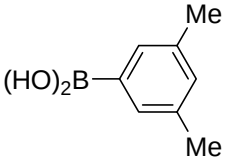
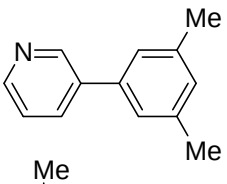
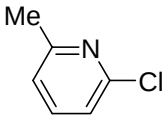
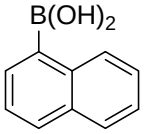
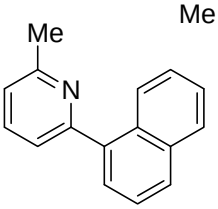
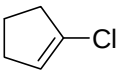
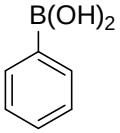
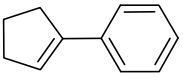
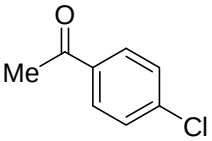
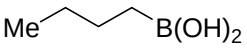
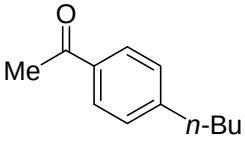


entry	ArCl	$Ar'B(OH)_2$	product	mol% Pd	%yield[b]
1				0.2% 24 h	92
2				0.2% 24 h	95
3				1% 24 h	91
4				1% 24 h	94
5				0.05% 16 h	98
6				0.05% 24 h	85
7				0.1% 16 h	93
8				0.02% 24 h	96
9				0.1% 16 h	97
10				0.5% 24 h	95
11				0.05% 16 h	96

[a]Reaction conditions: ArCl : $ArB(OH)_2$: K_3PO_4 = 1: 1.5 : 3; Pd : L = 1: 4; toluene (2 mL) under N_2; mol% of Pd (from $Pd_2(dba)_3$) with respect to ArCl. [b]Isolated yields.

Table 3.6 Pd-Catalyzed Suzuki-Miyaura Coupling of Heteroaryl and Alkenyl Chloride with Aryl or Alkylboronic Acid[a]



entry	Het-ArCl	$Ar'B(OH)_2$	product	mol% Pd	%yield[b]
1				0.025% 16 h	99
2				0.05% 16 h	99
3				0.1% 16 h	90
4				0.05% 16 h	95
5				1.0% 24 h	54
6				0.5% 24h	96

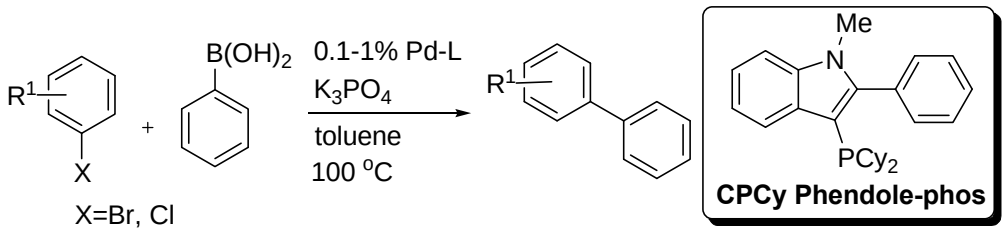
[a]Reaction conditions: ArCl : $ArB(OH)_2$: K_3PO_4 = 1: 1.5 : 3; Pd:L = 1:4; toluene (2 mL) under N_2; mol% of Pd (from $Pd_2(dba)_3$) with respect to ArCl. [b]Isolated yields.

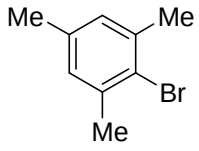
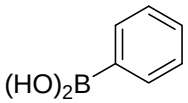
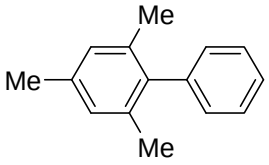
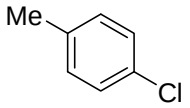
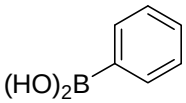
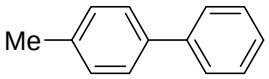
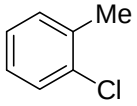
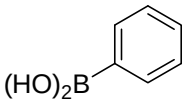
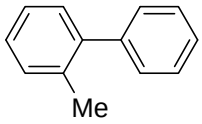
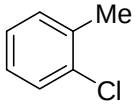
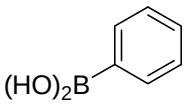
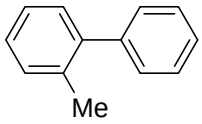
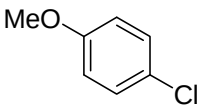
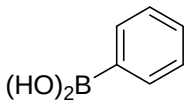
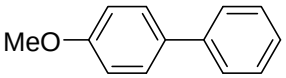
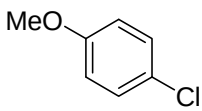
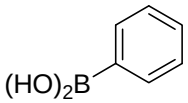
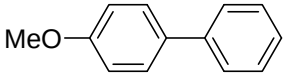
A range of aryl chlorides were examined using the preliminary optimized reaction conditions with impressive results. Sterically hindered aryl chlorides were coupled with arylboronic acids in excellent yields (Table 3.5, entries 2-4). Functional groups such as keto, amino, ester and nitriles were compatible in these reaction conditions, and the catalyst loading ranging from 0.02-0.1 mol% of Pd were achieved (Table 3.5, entries 5-9 and 11,). Deactivated aryl chloride was coupled with boronic acid in excellent yield (Table 3.5, entry 10). Apart from functionalized aryl chlorides, heteroaryl and alkenyl chlorides were effective substrates for Suzuki-Miyaura coupling (Table 3.6). In addition, preliminary studies on the coupling of alkylboronic acid with aryl chlorides were successful (Table 3.6, entry 6).

3.2.2 Study of the Catalytic Activity of C-P Type Indolyl Phosphine

3.2.2.1 Preliminary Evaluation of New Indolyl Phosphine (Aryl Chlorides)

Table 3.7 Pd-Catalyzed Suzuki-Miyaura Coupling of ArX[a]



entry	ArX	Ar'B(OH)$_2$	product	mol% Pd	%yield[b]
1				0.1% 10min	>99
2				1% 24 h	>99
3				1% 24 h	>99
4				0.1% 24 h	>99
5				1% 4 h	>99
6				0.1% 24 h	86

[a]Reaction conditions: ArX : ArB(OH)$_2$: K_3PO_4 = 1: 1.5 : 3; Pd : L = 1: 2; toluene (2 mL) under N_2; Temperature=100°C; mol% of Pd ((from $Pd_2(dba)_3$) with respect to ArX. [b]Yield by GC(FID).

The Pd/N-P type indolyl phosphine system showed high catalytic activity towards the Suzuki coupling of the aryl chlorides. We investigated the catalytic activity of C-P type indolyl phosphine as supporting ligand in the palladium-catalyzed Suzuki coupling reaction. At the very beginning, the coupling of very bulky 2,4,6-trimethylbromobenzene with phenyl boronic acid was used as the benchmark (Table3.7, entry 1). The result showed that the Pd/CPCy Phendole-phos system was also highly active towards the Suzuki coupling of the aryl bromides like the Pd/NPCy Phendole-phos system. Aryl chlorides were then used as substrates to probe the catalytic activity of the system. Under 1 mol%Pd loading, relatively bulky 2-chlorotoluene and deactivated 4-chloroanisole were smoothly coupled with phenylboronic acid to from biaryl product in excellent yield. Even if the catalyst loading was decreased to 0.1 mol%Pd, excellent biaryl product yield could still be obtained. Comparing the results of Table 3.5, entry 10 and Table 3.7, entry 6, Pd/NPCy o-Andole-phos system required catalyst loading as high as 0.5 mol% Pd to achieve complete consumption of the 4-chloroanisole. These primary screenings told us that the catalytic activity of Pd/CPCy Phendole-phos system was even higher than that of the Pd/NPCy o-Andole-phos system in the Suzuki coupling reaction.

The extra catalytic activity of Pd/CPCy Phendole-phos system can be

accounted by the differences in electron density between the NPCy Phendole-phos and CPCy Phendole-phos. Since both the N-P type phosphine and the C-P type one bear the same phenyl bottom ring, the steric factor of both types of phosphine can be regarded as the same. The electron density on the phosphorus atom can account for the differences in catalytic activity since electron-rich ligands will increase the electron density around a metal center (such as palladium center) so as to facilitate the oxidative addition of aryl chlorides. Therefore, the C-P type phosphorus atom is electron-richer than the corresponding N-P type phosphorus atom.

Although it is proposed that the lone pair on the nitrogen atom may donate extra electron density to the phosphorus atom, the higher electronegativity of the nitrogen atom may also draw electron density away from the phosphorus atom. In our case, it seemed that the nitrogen atom electronegativity effect was over the nitrogen atom lone pair electron donating effect. Therefore, the C-P type phosphine ligand was electron-richer than the corresponding N-P type phosphine.

However, it is difficult to measure or account for this compensatory effect of the ligand on the phosphorus atom. In our C-P type indolyl phosphine ligand, there is another factor, the resonance effect, which influenced the electron density on the phosphorus atom. Indole is a ten-π electron aromatic system

whose delocalization of the lone pair of electons from the nitrogen atom is necessary for aromaticity (Figure 3.1). It is well known that electron-rich heterocycle indole can readily undergo aromatic electrophilic substitution reaction selectively at the C3 position.

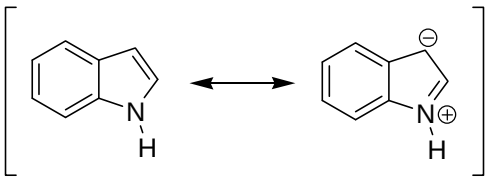


Figure 3.1 Delocalization of the nitrogen lone pair

Therefore, the resonance effect introduced by the indole scaffold may increase the electron density on the phosphorus atom (Figure 3.2).

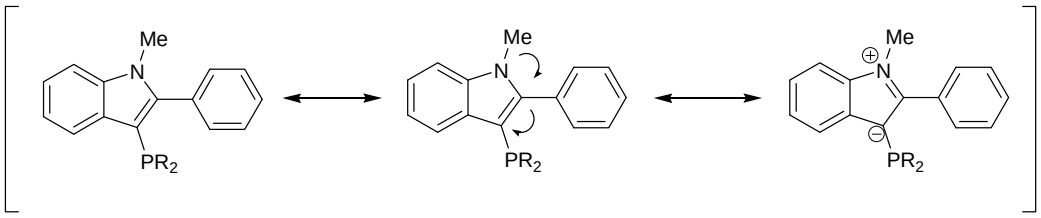


Figure 3.2 Extra electron density introduced by resonance effect

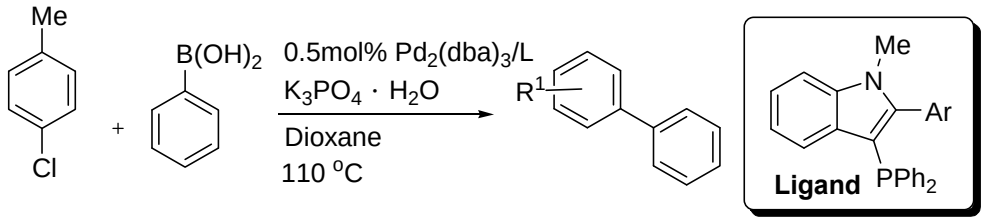
The very high catalytic activity of the Pd/C-P type dialkyl phosphine in the Suzuki coupling of aryl chlorides inspired us to attempt the Pd/C-P type diphenyl phosphine system. As discussed in Introduction, in order to utilize the relatively inert electrophiles as coupling partners, scientists have been made extensive efforts on phosphine ligand improvements. Those effective ligands often have a

bulky and electron-rich dialkylphosphino group such as dicyclohexylphosphino (–PCy_2) and di-*tert*-butylphosphino (–P*t*Bu_2) groups to enhance the oxidative addition of aryl halides. However, chlorodicyclohexylphosphine and di-*tert*-butylchlorophosphine, the precursor to synthesize the supporting ligand, are much more expensive than the chlorodiphenylphosphine. According to the 2009 Aldrich Catalogue, 5 g of Cy_2PCl and $^tBu_2PCl$ cost USD 232.5 and USD 80.8 respectively while 500g of Ph_2PCl cost only USD 395.0. Therefore, ligand featuring a –PPh_2 group would be very attractive in terms of air-stability and cost if high catalytic activity could be achieved. Furthermore, it would be a considerable development in coupling technology if researchers can utilize triarylphosphines in tackling difficult cross-couplings, especially in the synthesis of sterically congested biaryls. As our new C-P type phosphine showed high cataltic activity towards the coupling reaction and the speicality of the indolyl lignad template might potentially complement the insufficient diphenylphosphine moiety, we then investagated the cataltic activity of the C-P Type diphenyl indolyl phosphine ligand in the Suzuki coupling reaction.

3.2.2.2 Study of the Reactivity and Ligand Structure of C-P Type Diphenyl Indolyl Phosphine

To probe the effectiveness of the Pd/C-P Type diphenyl indolyl phosphine and the relationship between reactivity and structure of the ligand, we synthesized a series of ligand as shown in **Table 3.8**.

Table 3.8 Preliminary Screening of C-P Type Diphenyl Indolyl Phosphine[a]



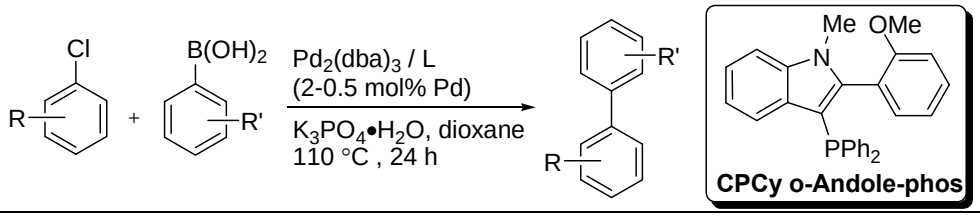
entry	Ligand	%yield[b]
1	CPPh Phendole-phos	34
2	CPPh o-Toldole-phos	87
3	CPPh o-Andole-phos	90
4	CPPh α-Nadole-phos	71

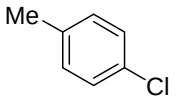
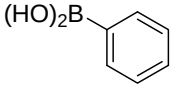
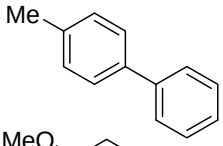
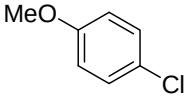
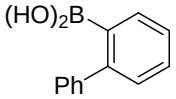
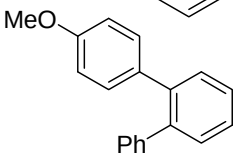
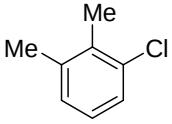
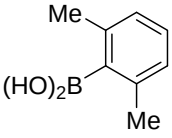
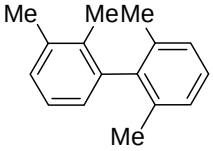
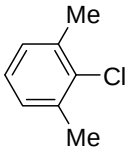
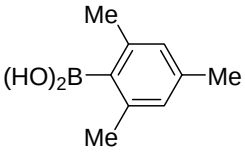
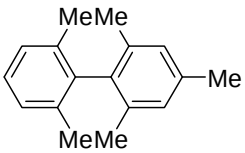
[a]Reaction conditions: ArCl (1.0 mmol), Ar'B(OH)$_2$ (1.5 mmol), base (3.0 mmol), Pd/L = 1:2, solvent (3.0 mL) was stirred for 24 h at 110 °C under nitrogen. [b]Calibrated GC yields were reported using dodecane as the internal standard.

The CPPh o-Toldole-phos and CPPh o-Andole-phos were effective ligands for the Suzuki coupling reaction of aryl chlorides. In general, the steric effect introduced by the substitute groups on the bottom ring was similar to the corresponding N-P type ligand.

3.2.2.3 Preliminary Study of Pd/C-P Type Diphenyl Indolyl Phosphine Catalyzed Aryl Chlorides and Tetra-*Ortho*-Substituted Biaryl Syntheses

Table 3.9 Palladium-$ArPPh_2$-Catalyzed Suzuki-Miyaura Coupling of Aryl Chlorides[a]



entry	ArCl	Ar'B(OH)$_2$	product	mol% Pd	%yield[b]
1				0.5	97
2				0.5	80
3				0.67	87
4[c]				2.0	82
5[c,d]				1.0	82

[a]Reaction conditions: ArCl (1.0 mmol), Ar'B(OH)$_2$ (1.5 mmol), $Pd_2(dba)_3$ (mol% as indicated), ligand (Pd:L = 1:4), K_3PO_4•H_2O (3.0 mmol) and dioxane (3.0 mL), under N_2 at 110 °C for 24 h (reaction time for each substrate was not optimized). [b]Isolated yields were reported. [c]Cs_2CO_3 was used as base. [d]CPPh α-Nadole-phos was used as ligand.

To test the effectiveness of the Pd/**CPPh o-Andole-phos** catalytic system, a set of aryl chlorides was examined. Non-activated 4-chlorotoluene coupled with phenylboronic acid gave biaryl product in excellence yield. Deactivated

4-chloroanisole, a ligand electron density demanding substrate, also coupled with hindered 2-biphenylboronic acid in good yield. Surprisingly, the couplings of sterically hindered substrates (both electrophilic and nucleophilic partners) in generating tri-*ortho*-substituted and tetra-*ortho*-substituted biaryls were also successfully accomplished (Table 3.9, entries 3-5). In fact, there are limited catalytic systems that are able to catalyze the coupling of both di-*ortho*-substituted aryl chlorides and arylboronic acids to synthesize tetra-*ortho*-substituted biaryls. Moreover, the phosphine ligands used in those catalytic systems often consist of dialkylphosphino groups, such as $-PCy_2$ or $-PtBu_2$ groups.[106,167-173]

Interestingly, CPPh α-Nadole-phos showed higher catalytic activity than the CPPh o-Andole-phos for the tetra-*ortho*-substituted biaryls synthesis (Table 3.9, entries 4-5). This result was contradictory to the preliminary ligand structure study (Table 3.8, entries 2-5). This might be because of the less bulky CPPh α-Nadole-phos that possibly fulfilled the steric requirement for the extremely congested tetra-*ortho*-substituted coupling such as facilitate the transmetallation during the course of the coupling reaction. Moreover, this result also reflected the importance of high diversity of ligand design to satisfy various kinds of substrates in the cross-coupling reaction.

3.3 Conclusion

In summary, we have developed a new series of monophosphine ligands (N-P type and C-P type) bearing a diversified indolyl scaffold. Palladium complexes derived from these ligands provide highly active catalysts for the Suzuki-Miyaura coupling of aryl chlorides.

The *N*-*P*-type phosphines have exceedingly high activity in carbon-carbon bond-forming process. The sterically hindered and deactivated aryl chlorides with arylboronic acids are able to afford the product in excellent yields. The catalyst loading can be as low as 0.02 mol% of Pd. In fact, it is the lowest catalyst loading for amino-phosphine-type ligand in the Suzuki coupling reaction achieved so far.

In the prelimiary study, the Pd/*C*-*P*-type phosphine system has shown high activity in the Suzuki coupling reaction. Remarkably, the Pd/*C*-*P*-type diphenyl indolyl phosphine system can effectively catalyze the coupling of aryl chlorides. Notably, we have succeeded in showing the possibility of Pd-catalyzed tetra-*ortho*-substituted biaryl synthesis by simply using arylphosphine.

3.4 Experimental Section

3.4.1 General Considerations

Unless otherwise noted, all reagents were purchased from commercial suppliers and used without further purification. All Suzuki-Miyaura reactions were performed in Rotaflo® (England) resealable screw-cap Schlenk flasks (approx. 20 mL volume) in the presence of Teflon coated magnetic stirrer bars. Toluene, tetrahydrofuran (THF) and dioxane were distilled from sodium and sodium benzophenone ketyl under nitrogen, respectively.[150] Commercially available aryl chlorides (liquid form only) were purified by passing through a short plug (0.5 cm width × 4 cm height) of neutral alumina. Most commercially available arylboronic acids were used as received. Some arylboronic acids might require further recrystallization depending on the received conditions. $Pd(OAc)_2$ and $Pd_2(dba)_3$ were purchased from Strem Chemical. K_3PO_4 was purchased from Fluka. Thin layer chromatography was performed on Merck pre-coated silica gel 60 F_{254} plates. Silica gel (Merck, 70-230 and 230-400 mesh) was used for column chromatography. Melting points were recorded on an uncorrected Büchi Melting Point B-545 instrument. ^1H NMR spectra were recorded on a Bruker (400 MHz) or Varian (400 MHz or 500 MHz) spectrometer.

Spectra were referenced internally to the residual proton resonance in $CDCl_3$ (δ 7.26 ppm), or with tetramethylsilane (TMS, δ 0.00 ppm) as the internal standard. Chemical shifts (δ) were reported as part per million (ppm) in δ scale downfield from TMS. ^{13}C NMR spectra were referenced to $CDCl_3$ (δ 77.0 ppm, the middle peak). ^{31}P NMR spectra were referenced to 85% H_3PO_4 externally. Coupling constants (*J*) were reported in Hertz (Hz). Mass spectra (EI-MS and ES-MS) were recorded on a HP 5989B Mass Spectrometer. High-resolution mass spectra (HRMS) were obtained on a Brüker APEX 47e FT-ICR mass spectrometer (ESIMS). GC-MS analysis was conducted on a HP 5973 GCD system using a HP5MS column (30 m × 0.25 mm). The products described in GC yield were according to the authentic samples/dodecane calibration standard from HP 6890 GC-FID system. All yields reported refer to the isolated yield of compounds. Compounds described in the literature were characterized by comparison of their ^{1}H, and/or ^{13}C NMR spectra to the previously reported data. The procedures in this section are representative, and thus the yields may differ from those reported in tables.

3.4.2 General Procedures for N-P Type Ligand and Reaction Conditions Screening

General procedure for screening: A stock solution of $Pd_2(dba)_3$ (15 mg) with ligand in freshly distilled toluene (10 mL) was initially prepared with continuously stirring at room temperature. 4-Chlorotoluene (82.9 mg), phenylboronic acid (120 mg), base (3.0 equiv.) and magnetic stirrer bar (2 mm × 7 mm) were charged to an array of Schlenk tubes. Each tube was carefully evacuated and backfilled with nitrogen (3 cycles). A Stock solution of palladium complex (2 mL, 1 mol% Pd) was added by syringe. This batch of Schlenk tube was resealed and magnetically stirred in a preheated oil bath. The reactions were allowed to reach room temperature. Diethylether (~5 mL), dodecane (149 μL, internal standard) and water (~5 mL) were added. The organic layer was subjected to GC analysis. The GC yield was previously calibrated by authentic sample/dodecane calibration curve.

3.4.3 General Procedures for Pd/N-P Type Ligand Catalyzed Suzuki-Miyaura Couplings of Aryl Chlorides

General procedure for Suzuki-Miyaura coupling of aryl chlorides: A stock solution of $Pd_2(dba)_3$ (3 mg) with ligand (Pd:L = 1:4) in freshly distilled toluene (2 mL, 1.0 mol% Pd) was initially prepared with continuously stirring at room temperature. Aryl chloride (0.65 mmol), arylboronic acid (1.5 equiv.), K_3PO_4 (3.0 equiv.) and magnetic stirrer bar (2 mm × 7 mm) were charged to an array of Schlenk tubes. Each tube was carefully evacuated and backfilled with nitrogen (3 cycles). The stock solution was further diluted to give different concentrations of palladium complex (final solution volume: 2 mL). The diluted solutions were then transferred to Schlenk tubes *via* syringes. This batch of Schlenk tubes was resealed and magnetically stirred in a preheated oil bath. After the completion of reaction as judged by GC or TLC analysis, the reactions were allowed to reach room temperature. Water (~3 mL) and diethylether (~10 mL × 3) were added. The organic layers were combined and concentrated. The crude products were purified by column chromatography on silica gel (230-400 mesh).

3.4.4 General Procedures for C-P Type Ligand Screening

General procedure for Suzuki-Miyaura coupling of aryl chlorides (Pd catalysts loading ranging from 0.5-4 mol %): $Pd_2(dba)_3$ and ligand were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar (4 mm × 10 mm). The tube was evacuated and flushed with nitrogen for three times. Precomplexation was applied by adding freshly distilled solvent (1.0 mL) into the tube. The palladium complex stock solution was continuously stirred at room temperature for about 10 mins. 4-Chlorotoluene (1.0 mmol), phenylboronic acid (1.5 equiv.), and base (3.0 equiv.) were then added to the Schlenk tubes. A further 2.0 mL of solvent was added (to rinse the tube wall) with stirring at room temperature for several minutes. The tubes were then placed into a preheated oil bath (110 °C) and stirred for the duration as indicated. The reactions were allowed to reach room temperature. Diethylether (~15 mL), dodecane (227 μL, internal standard), and water were added. The organic layer was subjected to GC analysis. The GC yield was previously calibrated by authentic sample/dodecane calibration curve.

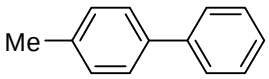
General procedure for Suzuki-Miyaura coupling of aryl chlorides (Pd catalysts loading lower than 0.25 mol %): A stock solution of $Pd_2(dba)_3$ (4.6 mg) with ligand in freshly distilled solvent was initially prepared with continuous stirring at room temperature. Phenylboronic acid (1.5 equiv.), base (3.0 equiv.) and magnetic stirrer bar (4 mm × 10 mm) were charged to Schlenk tube. Each tube was carefully evacuated and backfilled with nitrogen (3 cycles). 4-Chlorotoluene (1.0 mmol) and stock solution of palladium complex were added by syringe. Further solvent was added to up to a final volume of 3.0 mL. This batch of Schlenk tubes was resealed and then placed into a preheated oil bath (110 °C) and stirred for the time indicated. The reactions were allowed to reach room temperature. Diethylether (~15 mL), dodecane (227 μL, internal standard), and water were added. The organic layer was subjected to GC analysis. The GC yield was previously calibrated by authentic sample/dodecane calibration curve.

3.4.5 General Procedures for Pd/C-P Type Ligand Catalyzed Suzuki-Miyaura Couplings of Aryl Chlorides

General procedure for Suzuki-Miyaura coupling of aryl chlorides: $Pd_2(dba)_3$ and ligand were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar (4 mm × 10 mm). The tube was evacuated and flushed with nitrogen for three times. Precomplexation was applied by adding freshly distilled dioxane (1.0 mL) into the tube. The palladium complex stock solution was continuously stirred at room temperature for about 10 mins. Aryl chloride (1.0 mmol), arylboronic acid (1.5 equiv.), and base (3.0 equiv.) were then added to the Schlenk tubes. A further 2.0 mL of dioxane was added (to rinse the tube wall) with stirring at room temperature for 1-2 minutes. The tube was then placed into a preheated oil bath (110 °C) and stirred for the time as indicated. The reactions were allowed to reach room temperature. After the completion of reaction as judged by GC or TLC analysis, the reactions were allowed to reach room temperature and quenched with water and diluted with diethylether. The filtrate was concentrated under reduced pressure. The crude products were purified by flash column chromatography on silica gel (230-400 mesh) to afford the desired products.

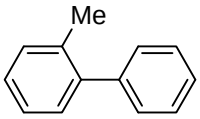
3.4.6 Characterization Data for Coupling Products

4-Methylbiphenyl (Table 3.5, entry 1; Table 3.9, entry 1).[174]



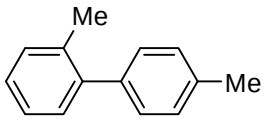
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.55 (s, 3H), 7.40 (d, *J* = 7.9 Hz, 2H), 7.45-7.50 (m, 1H), 7.36 (t, *J* = 7.4 Hz, 2H), 7.66 (d, *J* = 8.12, 2H), 7.74-7.76 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.02, 126.89, 126.92, 128.65, 129.42, 136.89, 138.28, 141.08; MS (EI): *m/z* (relative intensity) 168 (M^+, 100), 152 (30), 128 (10).

2-Methylbiphenyl (Table 3.5, entry 2).[174]



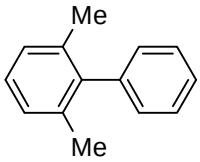
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 3H), 7.39-7.42 (m, 4H), 7.47-7.49 (m, 3H), 7.53-7.57 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.41, 125.71, 126.70, 127.19, 128.00, 129.13, 129.74, 130.25, 135.24, 141.88, 141.91; MS (EI): *m/z* (relative intensity) 168 (M^+, 100), 153 (40), 128 (10).

2-Methyl-4'-methylbiphenyl (Table 3.5, entry 3).[174]



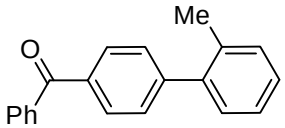
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.45 (s, 3H), 2.56 (s, 3H), 7.38-7.41 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.44, 21.09, 125.69, 127.01, 128.72, 129.01, 129.79, 130.22, 135.28, 136.25, 139.00, 141.83; MS (EI): *m/z* (relative intensity) 182 (M^+, 95), 167 (100), 152 (25), 141 (10), 128 (10).

2,6-Dimethylbiphenyl (Table 3.5, entry 4).[175]



^{1}H NMR (400 MHz, $CDCl_3$) δ 2.22 (s, 6H), 7.2-7.6 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.77, 126.54, 126.97, 127.23, 128.35, 128.94, 135.92, 141.05, 141.80; MS (EI): *m/z* (relative intensity) 182 (M^+, 95), 167 (100), 152 (30), 139 (10), 128 (10).

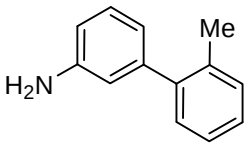
4-(2'-Tolyl)benzophenone (Table 3.5, entry 5).[126]



^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (s, 3H,), 7.33-7.28 (m, 4H), 7.62-7.5 (m, 5H),

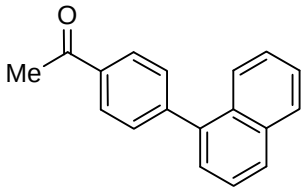
7.89 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.34, 125.84, 127.77, 128.18, 129.05, 129.45, 129.90, 130.43, 132.25, 135.06, 135.83, 137.59, 140.67, 146.21, 196.25; MS (EI): *m/z* (relative intensity) 272 (M^+, 70), 195 (100), 164 (40), 152 (40), 105 (40).

3-(2'-Tolyl)aniline (Table 3.5, entry 6).[176]



^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (s, 3H), 3.72 (bs, 2H, NH), 6.67-6.71 (m, 2H), 6.76-6.78 (m, 1H), 7.2-7.32 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.34, 113.46, 115.88, 119.56, 125.52, 127.01, 128.83, 129.47, 130.10, 135.21, 142.04, 143.01, 146.02; MS (EI): *m/z* (relative intensity) 183 (M^+, 100), 165(45), 152(20).

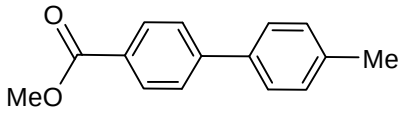
4-(1-Naphthyl)acetophenone (Table 3.5, entry 7).[177]



^{1}H NMR (400 MHz, $CDCl_3$) δ 2.68 (s, 3H), 7.42-7.56 (m, 4H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.88-7.95 (m, 3H), 8.10 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz,

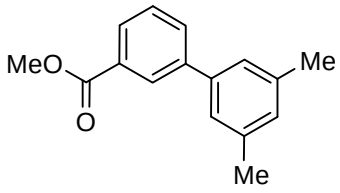
$CDCl_3$) δ 26.47, 125.15, 125.35, 125.81, 126.20, 126.75, 128.17, 128.25, 130.08, 130.98, 133.61, 135.76, 138.78 ,145.51, 197.55; MS (EI): *m/z* (relative intensity) 246 (M^+, 90), 231 (100), 202 (95), 176 (10).

Methyl 4-(4'-tolyl)benzoate (Table 3.5, entry 8).[174]



^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3H), 3.95 (s, 3H), 7.27 (d, *J* = 8.0Hz, 2H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.65 (d, *J* = 8.3 Hz), 8.11 (d, *J* = 8.3 Hz, 2H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.00, 51.89, 126.60, 126.93, 128.44, 129.51, 129.94, 136.89, 137.92, 145.38, 166.85; MS (EI): *m/z* (relative intensity) 226 (M^+, 85), 195 (100), 165 (40), 152 (50), 139 (10).

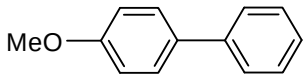
Methyl 3-(3',5'-dimethylphenyl)benzoate (Table 3.5, entry 9).[178]



^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 3H), 3.98 (s, 3H), 7.05 (s, 1H), 7.28 (s, 1H), 7.50 (t, *J* = 7.76 Hz, 1H), 7.78-7.80 (m, 1H), 8.03-8.06 (m, 1H), 8.33 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.17, 51.90, 124.86, 127.98, 128.04, 128.53, 129.20, 130.39, 131.33, 138.18, 139.85, 141.50, 166.89; MS (EI): *m/z*

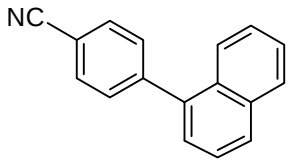
(relative intensity) 240 (M^+, 100), 209 (80), 181 (25), 165 (60), 152 (10).

4-Phenylanisole (Table 3.5, entry 10).[87]



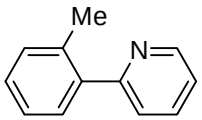
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.92 (s, 3H), 7.09 (dt, 2H, J = 8.72 Hz and J = 2.45 Hz), 7.42 (m, 1H), 7.53 (m, 2H), 7.64-7.68 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.15, 114.13, 126.56, 126.62, 128.039, 128.649, 133.63, 140.71, 159.08; MS (EI): *m/z* (relative intensity) 184 (M^+, 100), 169 (55), 152 (10), 141 (50), 115 (40).

4-(1-Naphthyl)benzonitrile (Table 3.5, entry 11).[179]



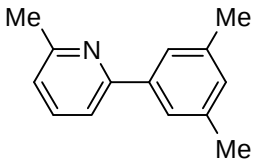
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.96 (m, 11H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 110.88, 118.72, 124.95, 125.15, 125.98, 126.45, 126.84, 128.35, 128.57, 130.54, 130.69, 131.88, 133.57, 137.95, 145.33; MS (EI): *m/z* (relative intensity) 229 (M^+, 100), 201 (15), 189 (5).

2-(2'-Tolyl)pyridine (Table 3.6, entry 1).[87]



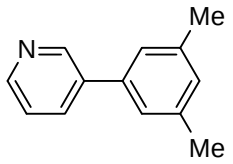
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 3H), 7.18-7.45 (m, 6H), 7.72 (dt, *J* = 7.7 Hz and 1.8 Hz, 1H), 8.69-8.71 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.12, 121.45, 123.91, 125.70, 128.10, 129.45, 130.57, 135.57, 135.93, 140.28, 149.02, 159.88; MS (EI): *m/z* (relative intensity) 168 (M^+, 100), 141 (5), 128 (2), 115 (5).

2-(3',5'-Dimethylphenyl)-6-methylpyridine (Table 3.6, entry 2).



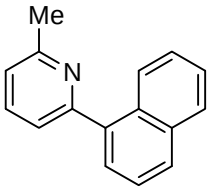
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.40 (s, 6H), 2.64 (s, 3H), 7.05-7.08 (m, 2H), 7.49 (d, *J* = 7.8 Hz, 1H); 7.58-7.62 (m, 3H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.35, 24.67, 117.72, 121.37, 1247.83, 130.33, 136.72, 138.07, 139.65, 157.28, 158.12; MS (EI): *m/z* (relative intensity) 197 (M^+, 100), 181 (25), 167 (10), 152 (5), 139 (3); HRMS: calcd. for $C_{14}H_{15}N$: 198.1283, found 198.1282

3-(3',5'-Dimethylphenyl)pyridine (Table 3.6, entry 3).



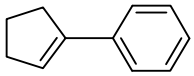
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.39 (s, 6H), 7.04 (m, 1H), 7.19 (s, 2H), 7.32 (dd, *J* = 7.8 Hz and *J* = 4.8 Hz, 1H), 7.84 (dt, *J* = 7.9 Hz and 1.9 Hz), 8.57 (m, 1H), 8.84 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.23, 123.40, 124.90, 129.64, 134.39, 136.84, 137.88, 138.53, 147.89, 147.98; MS (EI): *m/z* (relative intensity) 183 (M^+, 100), 168 (60), 152 (7), 139 (8), 128 (5); HRMS: calcd. for $C_{13}H_{13}N$: 184.1126, found 184.1121

2-(1-Naphthyl)-6-methylpyridine (Table 3.6, entry 4).



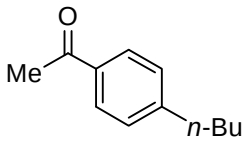
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.71 (s, 3H), 7.18 (d, *J* = 7.67 Hz, 1H), 7.36 (d, *J* = 7.64 Hz, 1H), 7.42-7.70 (m, 5H), 7.91-7.93 (m, 2H), 8.11-8.14 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.56, 121.32, 121.81, 125.12, 125.55, 125.58, 126.11, 127.12, 128.07, 128.46, 131.08, 133.76, 136.32, 138.59, 157.95, 158.38; MS (EI): *m/z* (relative intnsity) 218 (M^+-1, 100), 204 (10), 189 (5), 176 (5), 163 (2), 151 (4); HRMS: calcd. for $C_{16}H_{13}N$: 220.1126, found 220.1133

1-Phenylcyclopentene (Table 3.6, entry 5).[180]



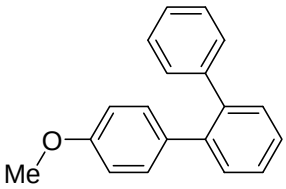
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.04-2.12 (m, 2H), 2.57-2.62 (m, 2H), 2.75-2.80 (m, 2H), 6.24-6.26 (m, 1H), 7.25-7.39 (m, 3H), 7.51 (d, *J* = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.31, 33.12, 33.31, 125.49, 126.01, 126.03, 126.76, 128.20, 136.75, 142.38; MS (EI): *m/z* (relative intensity) 144 (M^+, 100), 129 (15), 115 (40), 102 (10), 91 (12), 77 (10).

4-(*n*-Butyl)acetophenone (Table 3.6, entry 6).[44]



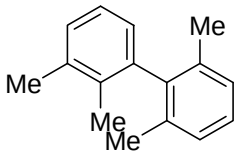
^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, *J* = 7.3 Hz, 3H), 1.35 (m, 2H), 1.59 (m, 2H), 2.55 (s 3H), 2.64 (t, *J* = 7.7 Hz, 2 H), 7.24 (d, *J* = 8.2 Hz, 2H), 7.86 (d, *J* = 8.2 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ13.78, 22.20, 26.40, 33.13, 35.56, 128.34, 128.49, 134.80, 148.66, 197.69; MS (EI): *m/z* (relative intensity) 176 (M^+, 20), 161 (100), 133 (10), 118 (5), 105 (15).

4-Methoxy-1, 1': 2', 1"terphenyl (Table 3.9, entry 2)[181]



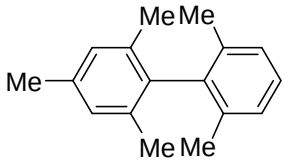
DCM:Hexane = 1:4, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.88 (s, 3H), 6.92 (d, *J* = 8.6 Hz, 2H), 7.26 (d, *J* = 8.5Hz, 2H), 7.35-7.39 (m, 5H), 7.54-7.60 (m, 4H), ^{13}C NMR (100 MHz, $CDCl_3$) δ54.9, 113.2, 126.2, 127.0 127.3, 127.8, 129.7, 130.4, 130.5, 130.8, 133.7, 140.0, 140.3, 141.6, 158.1; MS (EI): *m/z* (relative intensity) 260 (M^+, 100), 245 (10), 229 (30).

2, 2', 3, 6'-Tetramethylbiphenyl (Table 3.9, entry 3)[167]



Pure Hexane, R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ2.11 (s, 3H), 2.16 (s, 6H), 2.53 (s, 3H), 7.07-7.09 (m, 1H), 7.30-7.38 (m, 5H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.6, 20.3, 20.5, 125.6 126.5, 126.7, 127.1, 128.4, 134.0, 135.8, 136.7, 140.4, 141.6; MS (EI): *m/z* (relative intensity) 210 (M^+, 50), 195 (100), 181 (35).

2,2',4,6,6'-Pentamethylbiphenyl (Table 3.9, entry 4, 5)[182]



Hexane, R_f=0.7; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.90 (s, 6H), 1.94 (s, 6H), 2.37 (s, 3H), 6.99 (s, 2H), 7.14-7.20 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ19.6, 19.7, 19.8, 21.0, 126.6, 127.3, 128.2, 135.1, 135.4, 135.6, 135.9, 136.1, 136.9, 139.9; MS (EI): *m/z* (relative intensity) 224 (M^+, 70), 209 (100), 194 (40), 179 (38).

Chapter 4 Suzuki-Miyaura Coupling and Amination of Aryl Tosylates

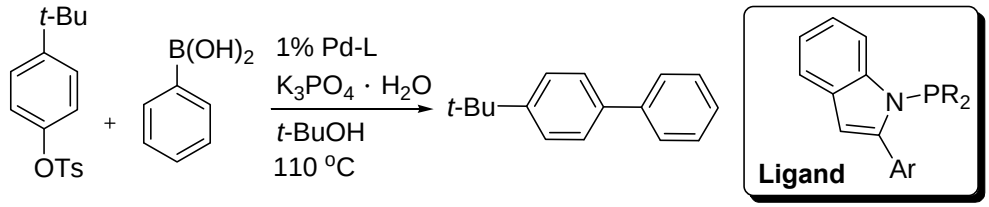
4.1 Introduction

In chapter 3, both new classes of N-P and C-P type indolyl phosphine ligands demonstrated excellent catalytic activity in the coupling reaction. The N-P type indolyl phosphine ligand showed the highest activity for the Suzuki-Miyaura coupling of aryl chlorides employing amino-phosphine ligands achieved so far while the C-P type indolyl phosphine ligand showed the possibility of palladium-catalyzed tetra-*ortho*-substituted biaryl synthesis by using triarylphosphine. Those promising results gave us confidence to apply the new indolyl phosphine of ligands to the more problematic substrates aryl sulfonates. In this chapter, the efficacy of both N-P bound and C-P bound indolyl phosphine ligands on Suzuki-Miyaura coupling of tosylate substrate would be investigated.

4.2 Results and Discussion

4.2.1 Investigation of the Efficacy of N-P Type Indolyl Phosphine Ligand on Suzuki-Miyaura Coupling of Aryl Tosylates

Table 4.1 Investigations on the Effectiveness of the N-P Type Indolyl Phosphine Ligands in Suzuki-Miyaura Coupling of Non-Activated ArOTs[a]



entry	Ligand	%yield[b]
1	no ligand	0
2	NPPh Phendole-phos	<1
3	NPCy Phendole-phos	<1
4	NP^{i}Pr Phendole-phos	<1
5	NPCy o-Toldole-phos	<1
6	NPCy o-Andole-phos	2
7[c]	NPCy o-Andole-phos	2

[a]Reaction conditions: ArOTs (1.0 mmol), $PhB(OH)_2$ (2.0 mmol), $K_3PO_4 \bullet H_2O$ (3.0 mmol), 1.0 mol%$Pd(OAc)_2$, Pd:L=1:4, *t*-BuOH (3.0 mL), at 110 °C under N_2 for 24 h. [b]Calibrated GC yields were reported using dodecane as the internal standard. [c]Toluene solvent was used.

The effectiveness of the N-P type indolyl phosphine ligands for Suzuki coupling of aryl tosylates was investigated. The non-activated 4-*tert*-butylphenyl tosylate and phenylboronic acid were used as the model substrates for our trial runs (Table 4.1). 1 mol% of $Pd(OAc)_2$ with 4 equivalents of ligands was initially applied for the prototypical reactions. According to the study from Buchwald and coworkers,[84] polar solvents such as THF and *t*-BuOH can facilitate the coupling reaction of aryl tosylates. It is believed that polar solvents may increase the solubility of the polar aryl tosylates and arylboronic acids, allowing them to proceed at rates much faster than protodeboronation. It has been reported that *t*-BuOH is even a better solvent then THF for difficult substrates.[84] Therefore, *t*-BuOH was selected as solvent for the preliminary screening of the aryl tosylates coupling reaction.

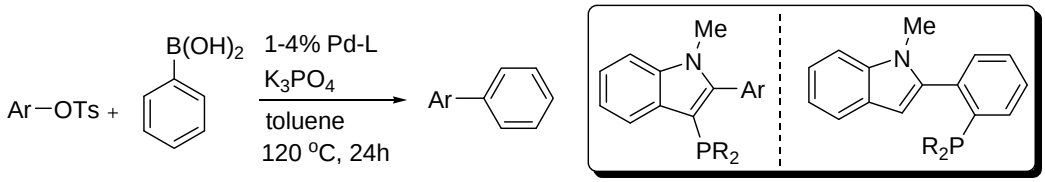
The results were disappointing. In general, amino-phosphines were not effective ligands towards the aryl tosylates coupling reaction (Table 4.1). From the relatively electron-poor NPPh Phendole-phos to the efficient NPCy o-Andole-phos, all ligands for the aryl chlorides coupling failed to give any coupling products. We observed ligand decomposition (from hydrolysis of N-P bond) during the course of the reactions. We thought that amino-phosphines were not effective under these alcoholic reaction conditions. In order to solve the

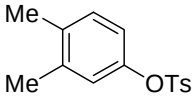
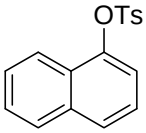
hydrolytic cleavage problem of amino-phosphines, we further investigated the applicability of these ligands using toluene as the reaction medium (Table 4.1, entry 7). Neither ligand decomposition nor any significant conversion of the substrate was observed. Thus, the N-P bound amino-phosphines were generally inferior in tosylate coupling reactions.

4.2.2 Investigation of the Efficacy of C-P Type Indolyl Phosphine Ligand on Suzuki-Miyaura Coupling of Aryl Tosylates

We then focused our attention to the C-P type indolyl phosphine ligands after the failure of the N-P type indolyl phosphine ligands in the aryl tosylates coupling reaction. The efficacy of two kinds of C-P bound indolyl phosphine ligands on the Suzuki-Miyaura coupling of tosylate substrate was investigated. The first kind of the C-P type indolyl phosphine ligand is the phosphorus atom attached to indole ring and the second kind is the phosphorus atom attached to the bottom ring. Three kinds of non-activated tosylates, 3,4-dimethylphenyl tosylate, 1-naphthyl tosylate and 4-*tert*-butylphenyl tosylate, were used in our trial runs (**Table 4.2**). 1 mol% of palladium sources with 4 equivalents of ligands were used as catalyst while K_3PO_4 as base and toluene as solvent were used for the prototypical reactions.

Table 4.2 Investigations on the Effectiveness of the C-P Type Indolyl Phosphine Ligands in Suzuki-Miyaura Coupling of Non-Activated ArOTs[a]



entry	Ar-OTs	metal	ligand	%yield[b]
1		1mol% $Pd(OAc)_2$	CPCy Phendole-phos	<1
2		1mol% $Pd(OAc)_2$	CP^{t}Bu Phendole-phos	10
3		0.5mol% $Pd_2(dba)_3$	CP^{t}Bu Phendole-phos	<1
4		1.5mol% $Pd_2(dba)_3$	CP^{t}Bu Phendole-phos	6
5		0.5mol% $Pd_2(dba)_3$	CP^{t}Bu o-Andole-phos	10
6		1mol% $Pd(OAc)_2$	CPCy o-Andole-phos	<1
7		0.5mol% $Pd_2(dba)_3$	CPCy α -Nadole-phos	<1
8[c]		3mol% $Pd(OAc)_2$	CP^{t}Bu o-Andole-phos	6
9[d]		3mol% $Pd(OAc)_2$	CM-phos	59
10[d]		4mol% $Pd(OAc)_2$	CM-phos	90
11[d]		4mol% $Pd(OAc)_2$	CM-phos	40
12[e]		4mol% $Pd(OAc)_2$	CM-phos	67

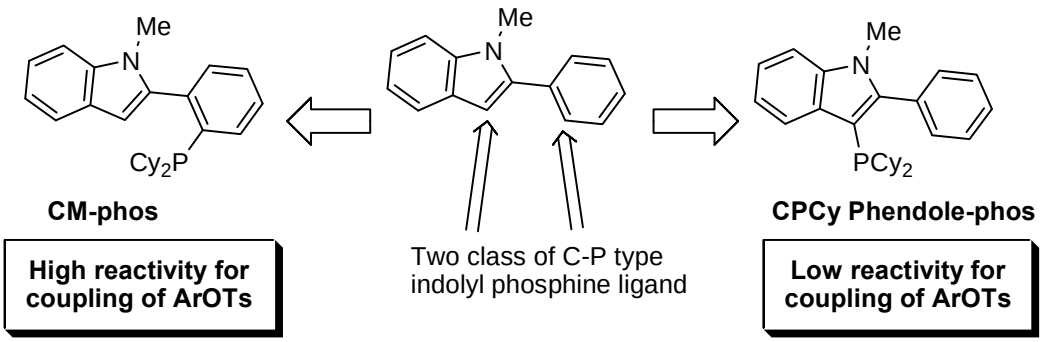
[a]Reaction conditions: ArOTs (1.0 mmol), $PhB(OH)_2$ (2.0 mmol), K_3PO_4 (3.0 mmol), Pd:L=1:4, toluene (3.0 mL), at 120 °C under N_2 for 24 h. [b]Calibrated GC yields were reported using dodecane as the internal standard. [C]*t*-BuOH was used as solvent. [d]reaction time=3h. [e]reaction time =12h.

In general, the C-P bound indolyl phosphine ligands where the phosphorus atom is attached to indole ring are inferior in tosylate coupling reactions. From electron-rich CPCy Phendole-phos to very bulky and electron-rich CP^{t}Bu o-Andole-phos, the catalytic activity of the ligands in the aryl tosylate coupling reaction were examined. No significant amounts of coupling products were observed in the coupling reaction. Two kinds of palladium sources were also examined. Although $Pd(OAc)_2$ as palladium source was slightly more effective than $Pd_2(dba)_3$, there was still no significant conversion of aryl tosylate observed (Table 4.2, entries 2, 3). Moreover, increasing the catalyst loading from 1mol%Pd to 3mol%Pd and using polar alcoholic solvent were ineffectual to improve the product yield (Table 4.2, entry 8).

Surprisingly, considerable conversion was observed when the C-P bound indolyl phosphine ligands where the phosphorus atom is attached to the bottom ring was used as supporing ligand. Moreover, the product yield was now sensitive to the catalyst loading and reaction time. Slightly activated 1-naphthyl tosylate was coupled with phenylboronic acid to give 59% yield under 3 mol%Pd. Increasing the catalyst loading to 4 mol%Pd gave about 90% yield of the biaryl product within 3 hours. For non-activated 4-*tert*-butylphenyl tosylate, 40% product yield was obtained within 3 hours while 67% yield was obtained after 12

hours. This preliminary results showed that the C-P bound indolyl phosphine ligands whose the phosphorus atom is attached to the bottom ring are potential ligand in tosylate coupling reactions.

In fact, we were surprised that the dramatic difference on reactivity was obtained when the position of the phosphino group was interchanged (Scheme 4.1). It might be that tosylate couplings are very sensitive to the structure of the ligand. Presumably the phosphino group on the aryl ring (instead of the heterocyclic ring) provided better geometry of chelation to the palladium center and facilitated the oxidative addition of the Ar-OTs bond.



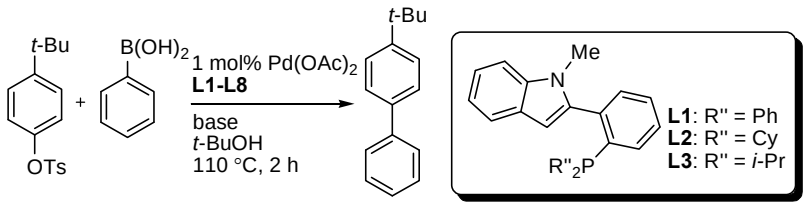
Scheme 4.1 Interchanging phosphino group position at the same ligand scaffold

4.2.3 Reaction Condition Optimization for Suzuki-Miyaura Coupling of Aryl Tosylates

The preliminary results in **Section 4.2.2** showed that the C-P bound indolyl phosphine ligands whose phosphorus atom was attached to the bottom ring were potential ligand in tosylate coupling reactions. In this section, we would focus our attention on this class of ligands in order to investagate its catalytic activity on the aryl tosylate coupling reaction so as to screening the optimum reaction conditions.

The solvent effect on the coupling reaction was firstly investigated. The use of *t*-BuOH and DMF as the reaction solvent gave comparable results (Table 4.3, entries 2 and 4), while dioxane and THF provided moderate product yields. Comparing the results between entry 11 in Table 4.2 and entry 2 in Table 4.3, when *t*-BuOH instead of toluene was used as solvent, the yield was significantly improved from 40% to 93% while the catalyst could be down to 1 mol%Pd. Therefore, it seems that the coupling reaction of aryl tosylates were sensitive to the solvent polarity and the results consistent with the results from Buchwald and coworkers, who showed that high polar solvent could facilitate the coupling reaction of aryl tosylates. Although DMF provided a slightly better product yield, *t*-BuOH was chosen for further study due to its relatively less toxicity.

Table 4.3 Investigations on the Effectiveness of the Indolyl Phosphine Ligands in Suzuki-Miyaura Coupling of Non-Activated ArOTs[a]



entry	Ligand	base	Solvent	[b]GC yield (%)
1	C'PPh Phendole-phos	$K_3PO_4 \bullet H_2O$	*t*-BuOH	<1
2	CM-phos	$K_3PO_4 \bullet H_2O$	*t*-BuOH	93
3	C'P^{i}Pr Phendole-phos	$K_3PO_4 \bullet H_2O$	*t*-BuOH	86
4	CM-phos	$K_3PO_4 \bullet H_2O$	DMF	99
5	CM-phos	$K_3PO_4 \bullet H_2O$	Dioxane	45
6	CM-phos	$K_3PO_4 \bullet H_2O$	THF	46
7[c]	CM-phos	$K_3PO_4 \bullet H_2O$	Toluene	40
8	CM-phos	Na_2CO_3	*t*-BuOH	1
9	CM-phos	CsF	*t*-BuOH	95
10	CM-phos	Cs_2CO_3	*t*-BuOH	85
11	CM-phos	KO*t*-Bu	*t*-BuOH	14

[a]Reaction conditions: ArOTs (1.0 mmol), $PhB(OH)_2$ (2.0 mmol), base (3.0 mmol), $Pd(OAc)_2$ (0.01 mmol, 1.0 mol%), Ligand (0.04 mmol), *t*-BuOH (3.0 mL), at 110 °C under N_2 for 2 h. [b]Calibrated GC yields were reported using dodecane as the internal standard. [c]3 mol%Pd was used.

The C-P type ligands with different phosphine moiety were then examined. Ligand C'PPh Phendole-phos with a diphenylphosphino moiety that may not provide sufficient electron density gave no substrate conversion in the aryl tosylates coupling reaction. In contrast, the more electron-rich dicyclohexylphosphino CM-phos and diisopropylphosphino C'P*i*Pr Phendole-phos analogues showed good to excellent catalytic activity (Table 4.3, entries 1-3).

Upon screening some commonly used inorganic bases, we found that K_3PO_4 monohydrate, Cs_2CO_3 and CsF were suitable bases for this aryl tosylate coupling reaction (entries 9-11).

In the combination of 1 mol%$Pd(OAc)_2$/CM-phos as catalyst, $K_3PO_4 \bullet H_2O$ as base and *t*-BuOH as solvent, 4-*tert*-butylphenyl tosylate and phenylboronic acid could be converted into the corresponding coupling product in 93% yield. Those screening results confirmed that the C-P bound indolyl phosphine ligands whose the phosphorus atom was attached to the bottom ring were effective ligands for the palladium catalysted Suzuki coupling of aryl tosylates.

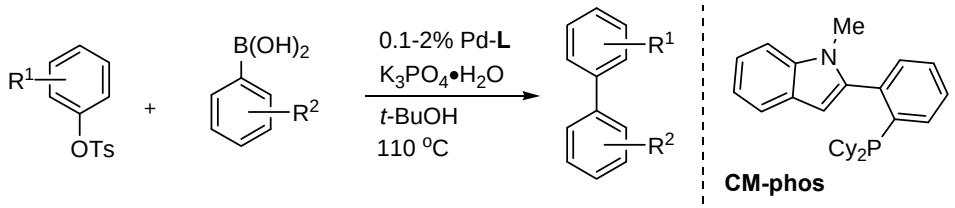
4.2.4 Suzuki-Miyaura Coupling of Non-Activated and Functionalized Aryl Tosylates

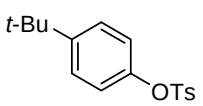
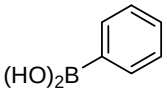
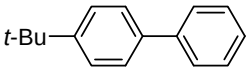
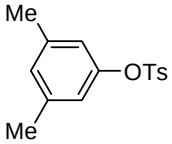
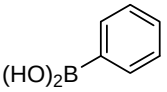
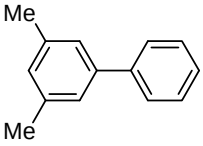
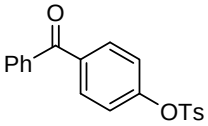
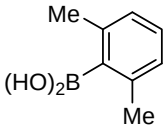
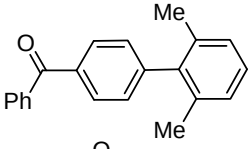
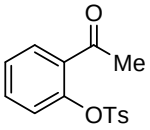
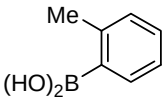
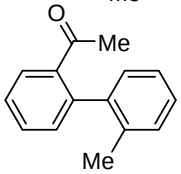
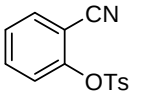
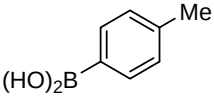
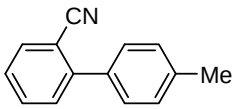
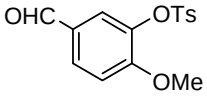
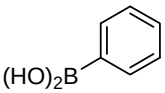
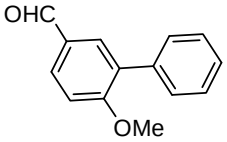
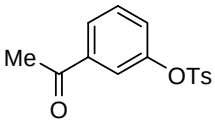
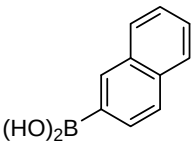
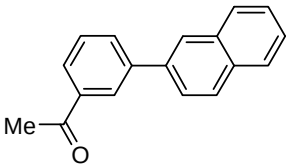
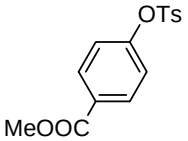
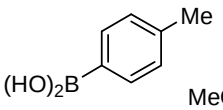
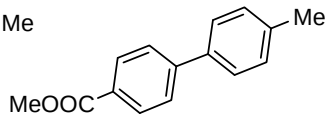
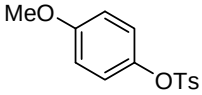
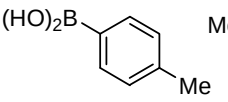
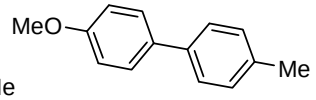
The preliminary results confirmed that $Pd(OAc)_2$/CM-phos was an effective catalytic system towards the coupling reaction of aryl tosylates. To further examine the scope of this catalytic system, a series of aryl tosylates were examined using the optimized reaction conditions (Table 4.4).

In general, essentially complete conversions were observed within 2-4 hours when 0.5-1 mol% of Pd was used. Homocoupled and reduction side-products were not observed from GC-MS analyses. Notably, the catalyst loading for the coupling of non-activated aryl tosylate could be down to 0.2 mol% of Pd for the first time (Table 4.4, entry 2).

A variety of functional groups, namely keto, nitrile, aldehyde and ester (Table 4.4, entries 4-9), were compatible under these mild reaction conditions. Aryl tosylates (Table 4.4, entry 5-7) bearing ortho substitued groups were also effective substrates towards the coupling reaction. For the first time, the electron-rich (deactivated) *p*-anisyl tosylate was demonstrated to be a feasible coupling partner (Table 4.4, entry 10).

Table 4.4 Pd-Catalyzed Suzuki-Miyaura Coupling of Aryl Tosylates with Arylboronic Acids[a]



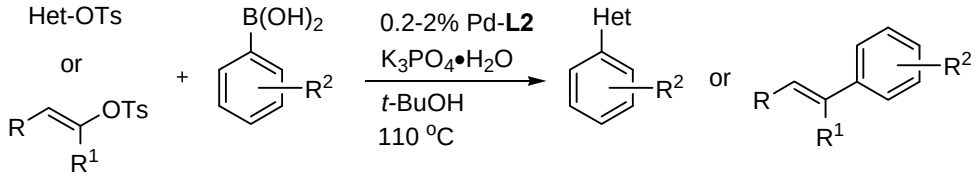
entry	ArOTs	$Ar'B(OH)_2$	product	mol% Pd	% yield[b]
1				1%, 2 h	92
2				0.2%, 12.5 h	85
3				1%, 2 h	94
4				0.5%, 2 h	90
5				1%, 3.5 h	86
6				0.5%, 2 h	83
7				2%, 2 h	87
8				0.5%, 3 h	89
9				0.2%, 2 h	80
10				3%, 4 h	90

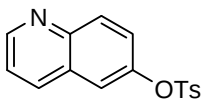
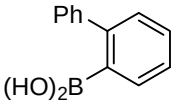
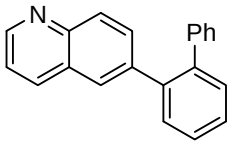
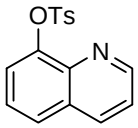
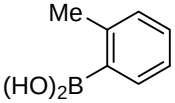
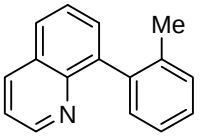
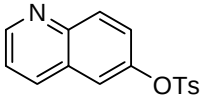
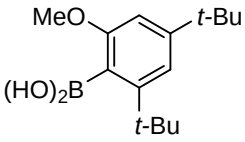
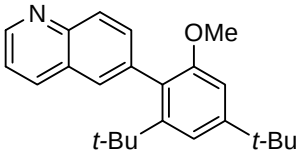
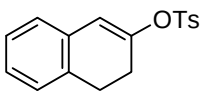
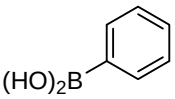
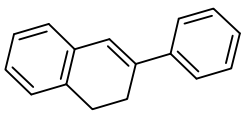
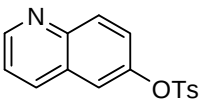
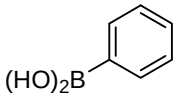
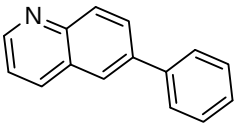
[a]Reaction conditions: ArOTs (1.0 mmol), $Ar'B(OH)_2$ (2.0 mmol), $K_3PO_4•H_2O$ (3.0 mmol), $Pd(OAc)_2$ (mol% as indicated), Pd:L = 1:4, *t*-BuOH (3.0 mL), at 110 °C under N_2 for indicated period of time. [b]Isolated yields.

4.2.5 Suzuki-Miyaura Coupling of Heterocyclic Aryl Tosylates

Apart from functionalized aryl tosylates, heteroaryl and vinyl tosylates were also effective substrates in the Pd/**CM-phos** catalytic system (Table 4.5).

Table 4.5 Pd-Catalyzed Suzuki-Miyaura Coupling of Heteroaryl or Vinyl Tosylates with Arylboronic Acids[a]

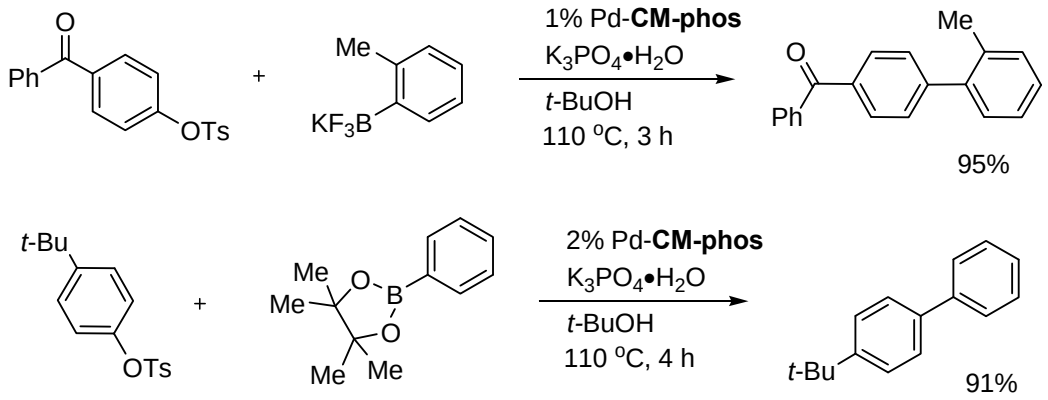


entry	Het-OTs or VinylOTs	$Ar'B(OH)_2$	product	mol% Pd	% yield[b]
1				0.2%, 2 h	99
2				2%, 4.5 h	99
3				1%, 3 h	91
4				0.5%, 2 h	98
5[c]				4%, 78 h ***room temp.***	94

[a]Reaction conditions: Het-OTs or VinylOTs (1.0 mmol), Ar'$B(OH)_2$ (2.0 mmol), $K_3PO_4•H_2O$ (3.0 mmol), $Pd(OAc)_2$ (mol% as indicated), Pd:L = 1:4, *t*-BuOH (3.0 mL), at 110 °C under N_2.
[b]Isolated yields. [c]DMF solvent was used.

Sterically congested arylboronic acids were efficiently coupled with quinolyl tosylates in excellent yields (Table 4.5, entries 1-2). It is noteworthy that the extremely hindered 2,4-di-*tert*-butyl-6-methoxyphenylboronic acid was found to be a capable coupling partner in this reaction (Table 4.5, entry 3). The scope of tosylate coupling reactions could also be extended to vinyl tosylate (Table 4.5, entry 4). Remarkably, an example of aryl tosylate coupling at room temperature reaction was realized (Table 4.5, entry 5). These results indicated the palladium catalyst derived from **CM-phos** was highly active for tosylate coupling reactions.

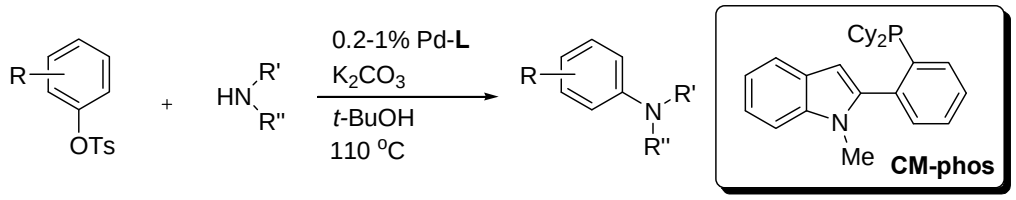
Although boronic acids are widely used as coupling nucleophiles, the exploration of other boronic acid surrogates in this catalytic system is still needed.[183] An aryl trifluoroborate salt and a pinacol boronate ester were successfully coupled with aryl tosylates under our catalytic system (Scheme 4.2).

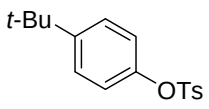
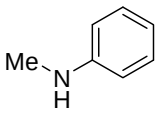
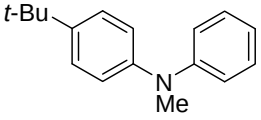
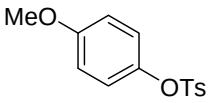
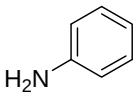
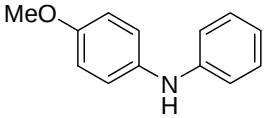
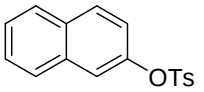
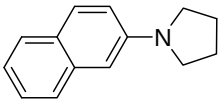
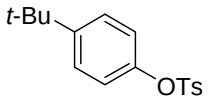
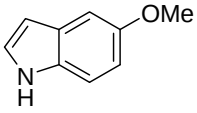
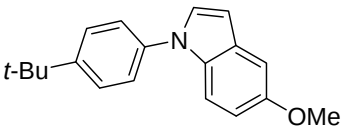
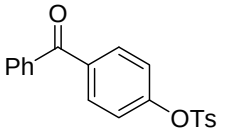
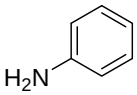
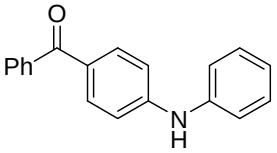
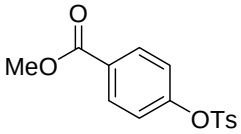
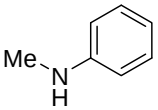
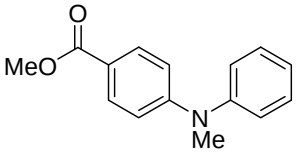
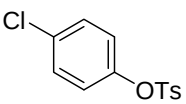
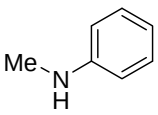
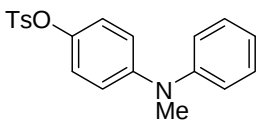


Scheme 4.2 Suzuki-Miyaura coupling of aryl tosylates with other organoboron nucleophiles

4.2.6 Preliminary Study of Buchwald-Hartwig Amination of Aryl Tosylates

Table 4.6 Palladium-Catalyzed Amination of Aryl Tosylates[a]



entry	ArOMs	amine	product	mol% Pd	% yield[b]
1[c]				0.2%	90
2				1%	77
3[c]				1%	91
4				0.5%	91
5				0.5%	92
6				0.5%	90
7[c,d]				1%	93

[a]Reaction conditions: ArOTs (1.0 mmol), amine (1.5 mmol), K_2CO_3 (2.5 mmol), $Pd(OAc)_2$/L (mol% as indicated) (Pd/L atom = 1:4), $PhB(OH)_2$ (0.04 mmol), ^tBuOH (3 mL), at 110℃ under N_2 for 24 h. [b]Isolated yields. [c]K_3PO_4 as base. [d]ArOTs (1.5 mmol), amine (1.0 mmol).

The success of the Suzuki coupling of aryl tosylates led us to further explore the Pd/CM-phos system to one of the most important reactions in the field of

coupling reactions, the amination reaction. For preliminary rapid reaction scope screening, we selected some of the representative combinations to examine the effectiveness of the Pd/CM-phos system in the amination of aryl tosylates (Table 4.6). The reaction condition applied for the Suzuki coupling of aryl tosylates was directly applied for the amination reaction. The coupling of unactivated aryl tosylates with N-methylaniline could be performed with 0.2 mol% of Pd (Table 4.6, entry 1). Moreover, the deactivated *p*-anisyl tosylates were found to be a feasible substrate (Table 4.6, entry 2). We should highlight the fact that secondary cyclic or acyclic amines were also effective coupling partners (Table 4.6, entries 1-3). One of the breakthroughs was that the Pd/CM-phos system was effective for different kinds of amine, regardless whether they were primary or secondary amines, compared with the Pd/Josiphos system in which only the primary amines were effective substrates.[93] Keto and ester group were compatible under these reaction conditions (Table 4.6, entry 5, 6). To further explore the effectiveness of the Pd/CM-phos catalytic system, a range of nitrogen heterocycles were investigated. Substituted indoles were N-arylated smoothly in good yields (Table 4.6, entry 4). A highly selective aryl chloride coupling was observed when p-chlorophenyl tosylates substrate was applied (Table 4.6, entry 7).

4.3 Conclusion

In conclusion, a series of simple indolyl phosphines were developed to the Suzuki-type coupling and amination of aryl tosylates.

For Suzuki coupling, a variety of aryl, heteroaryl and vinyl tosylates were efficiently coupled with different organoboron nucleophiles. These easily accessible indolyl-type phosphine ligands in combination with Pd-complex precursor showed good activity (0.2 to 3.0 mol% Pd) in non-activated tosylate coupling reactions. Particularly noteworthy was that the first example of room-temperature Pd-catalyzed Suzuki-Miyaura cross-coupling of aryl tosylates was also successfully realized.

For amination reaction, primary, secondary cyclic, and acyclic amines and indoles were all effectively coupled with unactivated and deactivated aryl tosylates. Keto and ester groups were compatible under the mild reaction conditions.

Pd/CM-phos catalyst which constitute effective Suzuki-Miyaura coupling and amination of aryl tosylates provided a useful alternative system to the Buchwald-type biaryl phosphines and Pd/Josiphos systems.

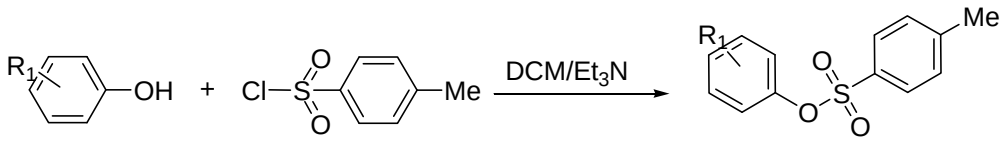
4.4 Experimental Section

4.4.1 General Considerations

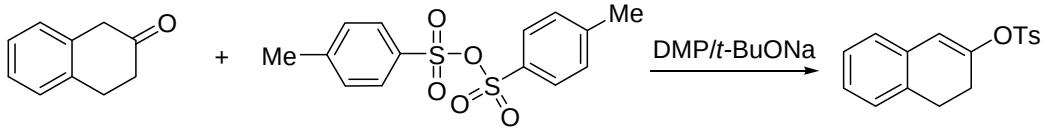
Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. All Suzuki-Miyaura reactions were performed in a resealable screw cap Schlenk flask (approx. 20 mL volume) in the presence of a Teflon coated magnetic stirrer bar (3 mm × 8 mm). Toluene and tetrahydrofuran (THF) were distilled from sodium and sodium benzophenone ketyl under nitrogen.[150] *tert*-Butanol was distilled from sodium under nitrogen.[150] Most commercially available arylboronic acids were used as received. Some arylboronic acids might require further recrystallization, depending on the received conditions. $K_3PO_4 \bullet H_2O$ was purchased directly from a commercial supplier and used without grinding. Thin layer chromatography was performed on precoated silica gel 60 F_{254} plates. Silica gel (70-230 and 230-400 mesh) was used for column chromatography. Melting points were recorded on an uncorrected instrument. ^{1}H NMR spectra were recorded on a 400 MHz spectrometer. Spectra were referenced internally to the residual proton resonance in $CDCl_3$ (δ 7.26 ppm), or with tetramethylsilane (TMS, δ 0.00 ppm) as the internal standard. Chemical shifts (δ) were reported as part per

million (ppm) in δ scale downfield from TMS. ^{13}C NMR spectra were referenced to $CDCl_3$ (δ 77.0 ppm, the middle peak). ^{31}P NMR spectra were referenced to 85% H_3PO_4 externally. Coupling constants (*J*) were reported in Hertz (Hz). Mass spectra (EI-MS and ES-MS) were recorded on a Mass Spectrometer. High-resolution mass spectra (HRMS) were obtained on an ESIMS mass spectrometer. GC-MS analysis was conducted on a GCD system using a column with a dimension of 30 m × 0.25 mm. The products described in GC yield were according to the authentic samples/dodecane calibration standard from GC-FID system. All yields reported refer to isolated yield of compounds estimated to be greater than 95% purity as determined by capillary gas chromatography (GC) or ^{1}H NMR. Compounds described in the literature were characterized by comparison of their ^{1}H, and/or ^{13}C NMR spectra to the previously reported data. The procedures in this section were representative, and thus the yields might differ from those reported in tables.

4.4.2 Synthesis of Tosylates



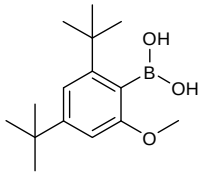
4-*tert*-Butylphenyl tosylate[69], 4-anisole tosylates[70], 2-naphyl tosylate[70], 4-benzophenone tosylate[184], 4-(methoxycarbonyl)phenyl tosylate[108], 4-chlorophenyl tosylate[84], 3,4-dimethylphenyl tosylate[185], 2-acetophenyl tosylate[186], 2-cyanophenyl tosylate[187], 5-formyl-2-methoxyphenyl tosylate[186], 3-acetophenyl tosylates[75], 6-quinolinyl tosylate[188], and 8-quinolinyl tosylate[189] were prepared from their corresponding phenols with TsCl in the presence of triethylamine in CH_2Cl_2 according to the literature method.[190]



1,2-dihydronaphthalen-3-yl tosylate was prepared according to a literature method.[94]

4.4.3 Synthesis of Arylboronic Acid

2,4-Di-*tert*-butyl-6-methoxyphenylboronic acid[191]



n-Butyllithium (1.6 M in hexane, 25 mL, 40 mmol) was added to a solution of 2-bromo-3,5-di-*tert*-butylanisole (12 g, 40 mmol) in THF (20 mL) at -78 °C under nitrogen. The mixture was stirred for 1 h and then transferred to a solution of distilled $B(OMe)_3$ (9.1 mL, 80 mmol) in THF (10 mL) at -78 °C under nitrogen. It was allowed to warm to room temperature and added with water. The organic layer was separated, and the aqueous phase was extracted with ether (3 × ~100 mL). The combined organic phases were washed with brine. After removing the solvent, the residue was re-dissolved in ethanol (60 mL). A solution of NaOH (2 M) was added and the mixture was stirred for 2 h. The solvent was rotary-evaporated, and the remaining aqueous layer was extracted with ether (3 × ~100 mL). The organic layer was then washed with brine and dried over $MgSO_4$. The solvent was removed, and the residue was recrystallized from ether/hexane to give 2,4-di-*tert*-butyl-6-methoxyphenylboronic acid as colorless crystals (7.8 g, 74%). The product was used without further characterization.

4.4.4 General Procedures for Initial Ligand and Reaction Conditions Screening

General procedure for screening: $Pd(OAc)_2$ (2.3 mg, 0.010 mmol) and ligand (Pd:L = 1:4) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The tube was evacuated and flushed with nitrogen for three times. Precomplexation was applied by adding freshly distilled dichloromethane and Et_3N into the tube. The palladium complex stock solution was stirred and warmed using a hair drier for about 1 to 2 minutes until the solvent started to boil. The solvent was then evaporated under high vacuum. 4-*tert*-Butylphenyl tosylate (1.0 mmol), phenylboronic acid (2.0 mmol) and base (3.0 mmol) were loaded into the tube, and the system was further evacuated and flushed with nitrogen for three times. The solvent (3.0 mL) was added with stirring at room temperature for several minutes. The tube was then placed into a preheated oil bath (110 °C) and stirred for the time as indicated. After completion of reaction, the reaction tube was allowed to cool to room temperature. Ethyl acetate (~10 mL), dodecane (227 μL, internal standard) and water were added. The organic layer was subjected to GC analysis. The GC yield obtained was previously calibrated by authentic sample/dodecane calibration curve.

4.4.5 General Procedures for Suzuki-Miyaura Couplings of Aryl Tosylates

General procedure for Suzuki-Miyaura coupling of aryl tosylates: $Pd(OAc)_2$ (2.3 mg, 0.010 mmol) and ligand (Pd:L = 1:4) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The tube was evacuated and flushed with nitrogen for several times. Precomplexation was applied by adding freshly distilled dichloromethane and Et_3N into the tube. The solution was stirred and warmed using hair drier for about 1 to 2 minutes until the solvent started boiling. The solvent was then evaporated under high vacuum. Aryl tosylate (1.0 mmol), aryl boronic acid (2.0 mmol) and $K_3PO_4 \bullet H_2O$ (3.0 mmol) were loaded into the tube, and the system was further evacuated and flushed with nitrogen for several times. The solvent *tert*-butanol (3.0 mL) was then added. The tube was stirred at room temperature for several minutes and then placed into a preheated oil bath (110 ^oC) for the time as indicated. After completion of reaction as judged by GC analysis, the reaction tube was allowed to cool to room temperature and quenched with water and diluted with EtOAc. The organic layer was separated and the aqueous layer was washed with EtOAc. The filtrate was concentrated under reduced pressure. The crude products were purified by flash column chromatography on silica gel (230-400 mesh) to afford the desired product.

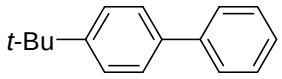
4.4.6 General Procedures for Buchwald-Hartwig Amination of Aryl Tosylates

General procedure for amination of aryl tosylate: $Pd(OAc)_2$ (2.3 mg, 0.010 mmol) and ligand **L** (Pd:L = 1:4) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The tube was evacuated and flushed with nitrogen for several times. Precomplexation was applied by adding freshly distilled dichloromethane and Et_3N into the tube. The solution was stirred and warmed using a hair drier for about 1 to 2 minutes until the solvent started to boil. The solvent was then evaporated under high vacuum. Aryl tosylate (1.0 mmol), K_2CO_3 (2.5 mmol), solid amines (1.5 mmol) and phenyl boronic acid (0.04 mmol) were loaded into the tube, and the system was further evacuated and flushed with nitrogen for several times. Liquid amines (1.5 mmol) were also loaded into the tube. The solvent *tert*-butanol (3-5 mL) was then added. The tube was stirred at room temperature for several minutes and then placed into a preheated oil bath (110 ^oC) for the time as indicated. After completion of reaction as judged by GC analysis, the reaction tube was allowed to cool to room temperature and quenched with water and diluted with EtOAc. The organic layer was separated and the aqueous layer was washed with EtOAc. The filtrate was concentrated under reduced pressure. The crude products were purified by flash column

chromatography on silica gel (230-400 mesh) to afford the desired product.

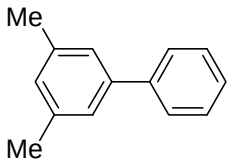
4.4.7 Characterization Data for Coupling Products

4-*tert*-Butylbiphenyl (Table 4.4, entries 1 and 2).[175]



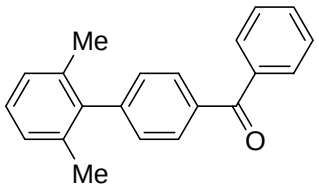
Hexane, R_f=0.55; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.72 (s, 9H), 7.64 (t, *J*=7.4 Hz, 1H), 7.72-7.82 (m, 4H), 7.89-7.96 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.3, 34.4, 125.6, 126.7, 126.9, 128.6, 138.2, 140.9, 150.0; MS (EI): *m/z* (relative intensity) 210 (M^+, 35), 195 (100), 178 (20), 167 (30).

3,5-Dimethylbiphenyl (Table 4.4, entry 3).[192]



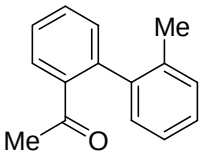
Hexane, R_f=0.55; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.76 (s, 6H), 7.37(s, 1H), 7.63(s, 2H), 7.67-7.71 (m,1H), 7.77-7.80 (m, 2H), 7.95-7.99 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 125.0, 126.9, 127.0, 128.5, 128.8, 138.0, 141.1, 141.3, MS (EI): *m/z* (relative intensity) 182 (M^+, 100), 167 (70), 152 (25).

4-(2,6-Dimethylphenyl)benzophenone (Table 4.4, entry 4).



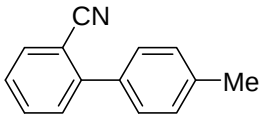
EA:Hexane = 1:20, R_f=0.4; white solid, m.p. = 76.5-78.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.13 (s, 6H), 7.17-7.32 (m, 5H), 7.51-7.63 (m, 3H), 7.92-7.97 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 127.1, 127.2, 127.9, 128.7, 129.6, 130.0, 131.9, 135.1, 135.5, 137.3, 140.3, 145.4, 195.8; MS (EI): *m/z* (relative intensity) 286 (M^+, 80), 209 (100), 181 (25), 165 (50), 105 (45). HRMS: calcd. for $C_{21}H_{18}O$: 287.1436, found 287.1442.

2-Acetyl-2'-methylbiphenyl (Table 4.4, entry 5).[193]



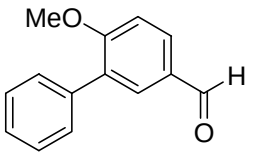
DCM:Hexane = 2:8, R_f=0.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.98 (s, 3H), 2.14 (s, 3H), 7.13 (d, *J*=7.4 Hz, 1H), 7.21-7.30 (m, 4H), 7.40-7.52 (m, 2H), 7.69-7.71(m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9, 29.5, 125.6, 127.2, 127.8, 128.0, 129.3, 130.0, 130.4, 130.7, 135.3, 139.9, 140.3, 140.5, 202.7; MS (EI): *m/z* (relative intensity) 210 (M^+, 10), 195 (100), 177 (15), 165 (45), 152 (30).

2-Cyano-4'-methylbiphenyl (Table 4.4, entry 6).[194]



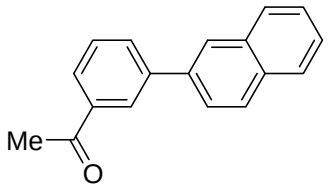
DCM:Hexane = 2:8, R_f=0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 3H,), 7.32 (d, *J*=7.9 Hz, 2H), 7.40 (dt, *J*=1.1, 7.6 Hz, 1H), 7.49-7.51 (m, 3H), 7.61 (dt, *J*= 1.2, 7.7 Hz, 1H), 7.74 (dd, *J*=0.8, 7.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 110.6, 118.5, 126.9, 128.2, 129.0, 129.6, 132.4, 133.3, 134.9, 138.2, 145.0; MS (EI): *m/z* (relative intensity) 193 (M^+, 100), 177 (10), 165 (35)

3-Phenyl-4-methoxybenzaldehyde (Table 4.4, entry 7).[195]



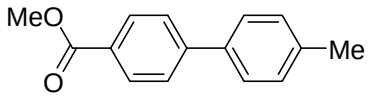
EA:Hexane = 1:9, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.82 (s, 3H), 7.04 (d, *J*=8.3 Hz, 1H), 7.37-7.84 (m, 7H), 9.89 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.3, 110.7, 127.1, 127.7, 129.0, 129.4, 130.8, 131.0, 131.6, 136.7, 161.0, 190.3; MS (EI): *m/z* (relative intensity) 212 (M^+, 100), 197(3), 183(5), 168(25).

3-(2-Naphthyl)acetophenone (Table 4.4, entry 8).



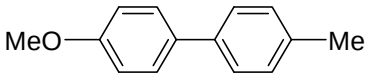
EA:Hexane = 1:9, R_f=0.35; White solid, m.p. = 69.5-71.8 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.60 (s, 3H), 7.45-7.50 (m, 3H), 7.68 (dd, *J*=1.6, 8.5 Hz, 1H), 7.78-7.89 (m, 5H), 8.00 (bs, 1H), 8.30 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.2, 124.7, 125.5, 125.8, 126.0, 126.5, 126.8, 127.2, 127.8, 128.2, 128.6, 131.3, 132.4, 133.2, 136.8, 137.2, 140.9, 197.5; MS (EI): *m/z* (relative intensity) 246 (M^+, 100), 231 (90), 202 (95). HRMS: calcd. for $C_{18}H_{14}O$: 247.1123, found 247.1106.

Methyl 4-(4'-tolyl)benzoate (Table 4.4, entry 9).[196]



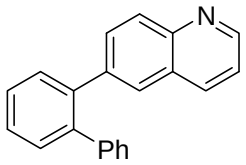
EA:Hexane = 1:9, R_f=0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3H), 3.95 (s, 3H), 7.27 (d, *J* = 8.0 Hz, 2H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.65 (d, *J* = 8.3 Hz), 8.12 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 51.8, 126.5, 126.9, 128.4, 129.4, 129.9, 136.8, 137.9, 145.3, 166.8; MS (EI): *m/z* (relative intensity) 226 (M^+, 85), 195 (100), 165 (40), 152 (50), 139 (10).

4-(4'-Tolyl)anisole (Table 4.4, entry 10).[197]



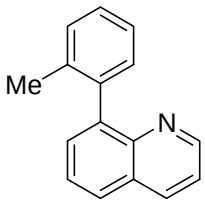
Hexane, R_f=0.1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.53 (s, 3H), 3.94 (s, 3H), 7.10 (d, *J*=8.7 Hz, 2H), 7.37 (d, *J*=7.9 Hz, 2H), 7.61 (d, *J*=8.0 Hz, 2H), 7.66 (d, *J*=8.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 55.0, 114.0, 126.4, 127.8, 129.3, 133.5, 136.1, 137.8, 158.8; MS (EI): *m/z* (relative intensity) 198 (M^+, 100), 183 (60), 165 (10), 155 (35).

5-(2-Biphenyl)quinoline (Table 4.5, entry 1).



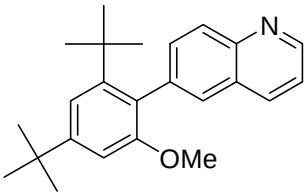
EA:Hexane = 1:9, R_f=0.15; light yellow viscous liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (bs, 5H), 7.25-7.54 (m, 6H), 7.69 (s, 1H), 7.94-7.98 (m, 2H), 8.85 (d, *J*= 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 120.8, 126.4, 127.4, 127.7, 127.8, 127.9, 128.3, 129.6, 130.4, 130.5, 131.7, 135.6, 139.2, 139.7, 140.4, 140.8, 146.8, 149.9; MS (EI): *m/z* (relative intensity) 281 (M^+, 100), 266 (30), 252 (20); HRMS: calcd. for $C_{21}H_{15}N$: 281.1199, found 281.1203.

7-(2'-Tolyl)quinoline (Table 4.5, entry 2).[198]



EA:Hexane = 1:9, R_f=0.25; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.28 (s, 3H), 7.42-7.53 (m, 5H), 7.67-7.76 (m, 2H), 7.92-8.25 (m, 2H), 9.07-9.09 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.1, 120.4, 125.0, 125.7, 127.1, 127.2, 127.9, 129.3, 129.8, 129.9, 135.6, 136.4, 139.5, 141.0, 146.1, 149.8; MS (EI): *m/z* (relative intensity) 218 (M^+, 85), 204 (100), 188 (5), 176 (3).

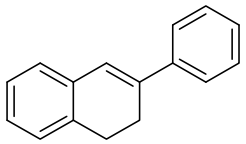
6-(2,4-Di-*tert*-butyl-6-methoxyphenyl)quinoline (Table 4.5, entry 3).



EA:Hexane = 1:9, R_f=0.15; white solid, m.p. = 136.4-138.1 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.19 (s, 9H), 1.42 (s, 9H), 3.56 (s, 3H), 6.92 (s, 1H); 7.24-7.31 (m, 4H), 8.02 (d, *J*=7.9 Hz, 1H), 8.14 (d, *J*=8.5 Hz, 1H), 8.87 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.1, 32.5, 34.8, 36.6, 55.5, 105.7, 116.0, 120.5, 127.0, 127.2, 127.5, 129.2, 133.9, 135.5, 138.3, 147.0, 148.4, 149.6, 150.6, 157.3; MS (EI): *m/z* (relative intensity) 347 (M^+, 100), 332 (75), 317 (5), 302 (3), 290 (5),

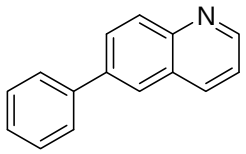
276(75), 261(30); HRMS: calcd. for $C_{24}H_{29}NO$: 347.2244, found 347.2253.

1,2-Dihydro-3-phenylnaphthalene (Table 4.5, entry 4) [199]



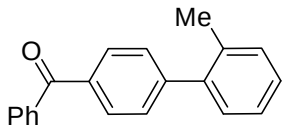
Hexane, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.00-3.04 (m, 2H), 3.21-3.25 (m, 2H), 7.19 (s, 1H), 7.44-7.69 (m, 7H), 7.84-7.85 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 27.9, 124.2, 124.9, 126.4, 126.5, 126.8, 127.0, 127.1, 128.2, 134.5, 138.3, 140.8; MS (EI): *m/z* (relative intensity) 206 (M^+, 100), 191 (20), 178 (5), 165 (5), 128 (30), 91(55);

6-Phenylquinoline (Table 4.5, entry 5) [174]



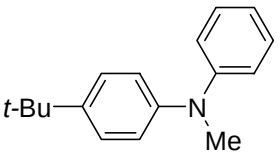
EA:Hexane = 2:8, R_f=0.25; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21-7.33 (m, 2H), 7.37-7.71 (m, 2H), 7.58-7.60 (m, 2H), 7.82-7.87 (m, 2H), 7.96-8.15 (m, 2H), 8.83 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 121.0, 125.0, 127.0, 127.3, 128.0, 128.5, 128.7, 129.4, 135.7, 138.7, 139.7, 147.2, 149.9; MS (EI): *m/z* (relative intnsity) 205 (M^+, 100), 176 (10).

4-(2'-Tolyl)benzophenone (Scheme 4.2) [126]



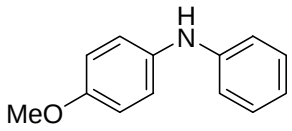
EA:Hexane = 1:20, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (s, 3H,), 7.30-7.33 (m, 4H), 7.46-7.61 (m, 5H), 7.90-7.93 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.2, 125.7, 127.6, 128.0, 128.9, 129.3, 129.7, 130.3, 132.0, 135.6, 137.4, 140.4, 146.0, 195.9; MS (EI): *m/z* (relative intensity) 272 (M^+, 70), 195 (100), 164 (40), 152 (40), 105 (40).

N-Methyl-N-(4-*tert*-butylphenyl)aniline (Table 4.6, entry 1)[200]



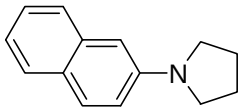
DCM:Hexane = 1:20, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.55 (s, 9H), 3.49 (s, 3H), 7.10 (t, *J*=7.3 Hz, 1H), 7.18-7.25 (m, 4H), 7.43-7.47 (m, 2H), 7.52-7.54 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.4, 34.1, 40.1, 118.9, 120.2, 121.2, 126.0, 129.0, 144.6, 146.3, 149.1;MS (EI): *m/z* (relative intensity) 239 (M^+, 45), 224(100), 209 (13), 194 (6).

N-(4-Methoxyphenyl)aniline (Table 4.6, entry 2) [201]



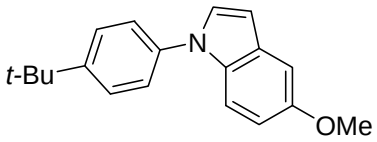
EA:Hexane = 1:9, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.87 (s, 3H), 5.56 (bs, 1H), 6.91-7.00 (m, 5H), 7.15 (d, *J*=8.8 Hz, 2H), 7.29-7.33 (m, 2H),; ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.4, 114.5, 115.5, 119.4, 122.0, 129.2, 135.6, 145.0, 155.1; MS (EI): *m/z* (relative intensity) 199 (M^+, 69), 184 (100), 154 (8), 128 (8).

N-(2-Naphthyl)pyrrolidine (Table 4.6, entry 3) [202]



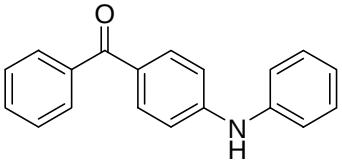
DCM:Hexane = 1:4, R_f=0.6; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.08-2.11 (m, 4H), 3.44-3.47 (m, 4H), 6.83 (m, 1H), 7.04-7.07 (m, 1H), 7.22-7.26 (m, 1H), 7.41-7.45 (m, 1H), 7.71-7.78 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.4, 47.7, 104.6, 115.6, 120.1, 125.7, 126.1, 126.2, 127.5, 128.7, 135.2, 145.8; MS (EI): *m/z* (relative intensity) 197 (M^+, 100), 141 (38), 127 (31), 115 (9).

1-(4-*tert*-butylphenyl)-5-methoxy-1*H*-indole (Table 4.6, entry 4)



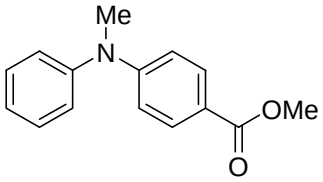
EA:Hexane = 1:9, R_f=0.6; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.57 (s, 9H), 4.03 (s, 3H), 6.79 (d, *J*=3.1 Hz, 1H), 7.10 (q, *J*=6.5 Hz, 1H), 7.36 (d, *J*=2.4 Hz, 1H), 7.45 (d, *J*=3.2 Hz, 1H), 7.54-7.56 (m, 2H), 7.64-7.68 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.3, 34.4, 55.6, 102.5, 102.9, 111.3, 112.3, 123.4, 126.3, 128.2, 129.7, 131.0, 137.2, 149.0, 154.4; MS (EI): *m/z* (relative intensity) 279 (M^+, 100), 264 (100), 249 (13), 118 (19).

Phenyl[4-(phenylamino)phenyl]methanone (Table 4.6, entry 5)[203]



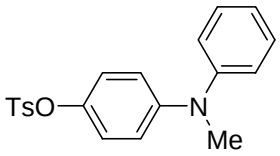
EA:Hexane = 2:8, R_f=0.33; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.55 (bs, 1H), 7.02-7.10 (m, 3H), 7.21 (d, *J*=7.7 Hz, 2H), 7.34 (t, *J*=7.7 Hz, 2H), 7.47 (t, *J*=7.5 Hz, 1H), 7.54-7.56 (m, 1H), 7.78 (t, *J*=7.6 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 114.2, 120.6, 123.1, 128.0, 128.2, 129.4, 129.5, 131.5, 132.6, 138.6, 140.6, 148.3, 195.2; MS (EI): *m/z* (relative intensity) 273 (M^+, 95), 196 (100), 167 (47), 77 (21).

Methyl 4-[methyl(phenyl)amino]benzoate (Table 4.6, entry 6)[126]



EA:Hexane = 1:9, Assist with high vacuum, R_f=0.33; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.34 (s, 3H), 3.86 (s, 3H), 6.78 (d, *J*=8.9 Hz, 2H), 7.19-7.22 (m, 2H), 7.37-7.41 (m, 2H), 7.90 (d, *J*=8.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 39.9, 51.3, 113.5, 118.8, 125.1, 125.6, 129.5, 130.7, 147.2, 152.2, 166.9; MS (EI): *m/z* (relative intensity) 241 (M^+, 100), 210 (73), 181 (11), 167 (23).

4-[Methyl(phenyl)amino]phenyl 4-methylbenzenesulfonate (Table 4.6, entry 7)



EA:Hexane = 7:3, R_f=0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44 (s, 3H), 3.26 (s, 3H), 6.80-6.87 (m, 4H), 7.03-7.07 (m, 3H), 7.29-7.32 (m, 4H), 7.75 (d, *J*=8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 40.0, 118.3, 122.2, 122.6, 128.2, 129.2, 129.5, 132.2, 142.3, 145.0, 147.5, 148.1; MS (EI): *m/z* (relative intensity) 353.1 (M^+, 6), 198.1 (100), 182 (4), 154 (6).

Chapter 5 General Palladium-Catalyzed Suzuki-Miyaura Coupling of Aryl Mesylates

5.1 Introduction

Aryl mesylates are more attractive than the corresponding aryl tosylates as the coupling substrates. Aryl mesylates are not only cheap, readily available and convenient, but also more atom economical than corresponding aryl tosylates due to their significantly lower molecular weights. However, the coupling reaction of aryl mesylates remains highly challenging since the aryl mesylate electrophiles are proposed to be more inert and reluctant to oxidative addition than the corresponding aryl arenesulfonates (e.g. benzenesulfonate or *p*-tolylsulfonate) in coupling reactions.

Although Ni-catalyzed mesylate couplings have been reported by Percec and coworkers in as early as 1995, a general palladium system capable of handling aryl mesylates remains no report. During our study, palladium-catalyzed Suzuki-Miyaura coupling on unactivated aryl mesylates had not yet been reported. In fact, there was only one publication at that time on palladium-catalyzed mesylate couplings, namely carbonylation in the presence of

$Cy_2P(CH_2)_3PCy_2 \bullet HBF_4$/Pd complex reported by Buchwald's group.[204] The ligand structure seems to be crucial to successfully achieve specific catalysis. Thus, there is room to apply a versatile family of ligands to solve the present coupling problems, as well as to tackle challenging electrophile, the aryl mesylate. With a series of indolylphosphine ligands which is successful in the Suzuki coupling and amination of aryl tosylates, the feasibility on Suzuki-type coupling of the unexplored aryl mesylates was then investigated.

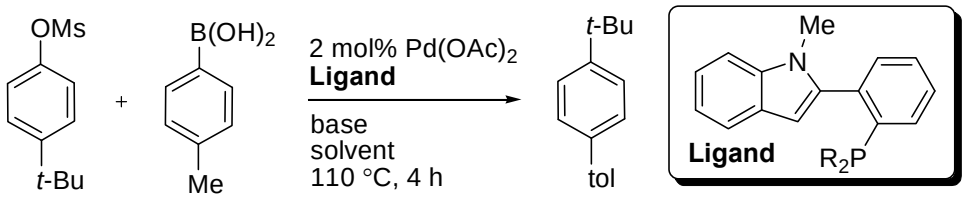
5.2 Results and Discussion

5.2.1 Investigation of the Efficacy of C-P Type Indolyl Phosphine Ligand on Suzuki-Miyaura Coupling of Aryl Mesylates and Reaction Condition Optimization

In the preliminary study, the same reaction conditions used in the Suzuki coupling of aryl tosylates was directly employed to Suzuki coupling of aryl mesylates. Electronically neutral 4-*tert*-butylphenyl mesylate and 4-tolylboronic acid were used as the prototypical substrates in our benchmark reaction (Table 5.1).

Fortunately, in the combination of 2 mol% $Pd(OAc)_2$/CM-phos as catalyst, $K_3PO_4 \bullet H_2O$ as base and *t*-BuOH as solvent, 4-*tert*-butylphenyl mesylate and 4-tolylboronic boronic acid were converted into the corresponding coupling product in 89% yield. In general, the catalytic activity of $Pd(OAc)_2$/CM-phos system towards coupling reaction of aryl mesylates was similar to the corresponding aryl tosylates. The major different between the coupling reaction of aryl mesylates and that of aryl tosylates was that the former required higher catalyst loading. These results showed that aryl mesylates were more inert than the corresponding aryl tosylates.

Table 5.1 Initial Screening of Suzuki-Miyaura Coupling of Unactivated ArOMs[a]



entry	Ligand	base	Solvent	GC yield (%)
1	C'PPh Phendole-phos	$K_3PO_4 \cdot H_2O$	*t*-BuOH	<1%
2	C'P^{i}Pr Phendole-phos	$K_3PO_4 \cdot H_2O$	*t*-BuOH	84%
3	CM-phos	$K_3PO_4 \cdot H_2O$	*t*-BuOH	89%
4	CM-phos	$K_3PO_4 \cdot H_2O$	Toluene	42%
5	CM-phos	$K_3PO_4 \cdot H_2O$	DMF	50%
6	CM-phos	$K_3PO_4 \cdot H_2O$	*t*-BuOH	89%
7	CM-phos	$K_3PO_4 \cdot H_2O$	THF	33%
8	CM-phos	Cs_2CO_3	*t*-BuOH	83%
9	CM-phos	CsF	*t*-BuOH	93%
10	CM-phos	K_2CO_3	*t*-BuOH	79%
11	CM-phos	*t*-BuOK	*t*-BuOH	<1%
12	CM-phos	K_3PO_4	*t*-BuOH	97%
13	CM-phos	K_3PO_4	DMF	81%

[a]Reaction conditions: ArOMs (1.0 mmol), Ar'$B(OH)_2$ (2.0 mmol), base (3.0 mmol), $Pd(OAc)_2$ (2 mol%), Ligand (0.04 mmol), solvent (3.0 mL), at 110 °C under N_2 for 4 h. [b]Calibrated GC yields were reported using dodecane as the internal standard.

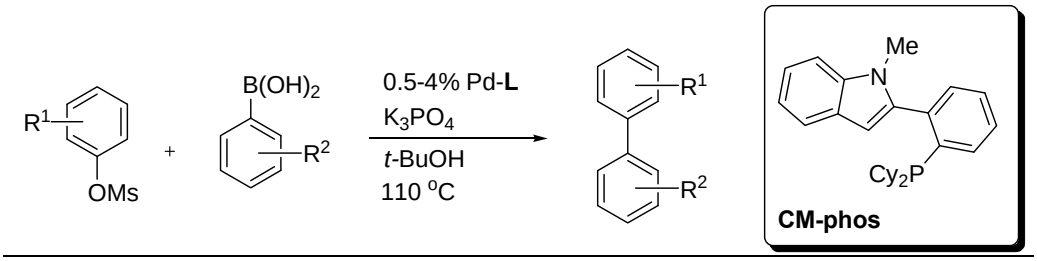
In general, the screening results are similar to the Suzuki coupling of aryl tosylates. Ligand C'PPh Phendole-phos with a diphenylphosphino moiety apparently provided no conversion while the dicyclohexylphosphino CM-phos and diisopropylphosphino C'P^{i}Pr Phendole-phos analogues showed good to excellent catalytic activity in the coupling of aryl mesylates (Table 5.1, entries 1-3). Polar solvent such as *t*-BuOH and DMF provided the best product yield among *t*-BuOH, toluene, DMF and THF (entries 2 and 5-7).

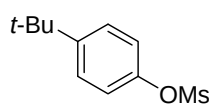
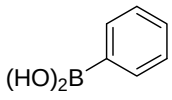
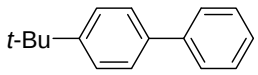
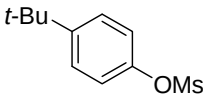
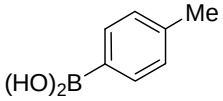
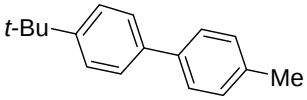
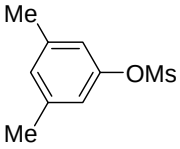
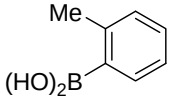
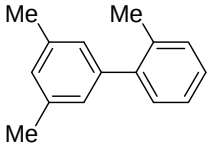
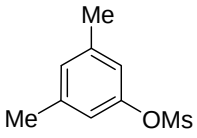
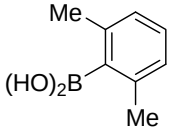
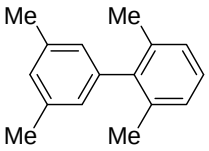
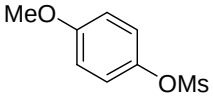
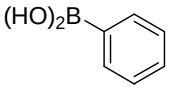
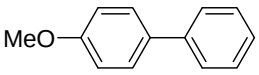
It was observed that $K_3PO_4 \cdot H_2O$ as base gave a some phenolic side product in the course of the reaction which slightly lowered the product yield. The relative acidity of the methyl group made the aryl mesylates relatively more sensitive to the hydrolysis than with the corresponding aryl tosylates. When *t*-BuOK base was applied in this reaction, a significant amount of phenolic side products (from hydrolysis of sulfonate) was observed (entry 11). Upon the screening of some commonly used inorganic bases, CsF and K_3PO_4 were found to be suitable bases for this aryl mesylate coupling reaction (entries 11-12).

The combination of 2 mol% $Pd(OAc)_2$/CM-phos as catalyst, K_3PO_4 as base and *t*-BuOH as solvent was then selected for the optimized reaction conditions.

5.2.2 Suzuki-Miyaura Coupling of Non-Activated and Functionalized Aryl Mesylates

Table 5.2 Palladium-Catalyzed Suzuki-Miyaura Coupling of ArOMs with $Ar'B(OH)_2$[a]



entry	ArOMs	Ar'B(OH)$_2$	product	mol% Pd	% yield[b]
1				1%, 19 h	91
2				0.5%, 24 h	88
3				1%, 19 h	90
4				3%, 8 h	97
5				4%, 8 h	70
6				4%, 8 h	89

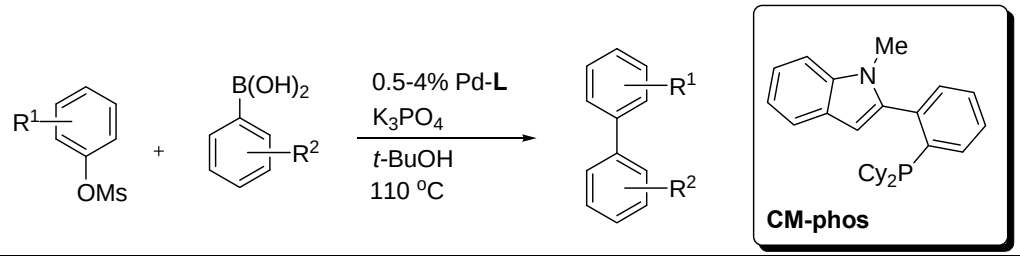
[a]Reaction conditions: ArOMs (1.0 mmol), $Ar'B(OH)_2$ (2.0 mmol), K_3PO_4 (3.0 mmol), $Pd(OAc)_2$/CM-phos (mol% as indicated), *t*-BuOH (3.0 mL), at 110 °C under N_2 for indicated period of time. [b]Isolated yields.

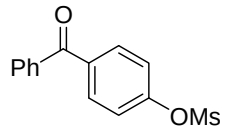
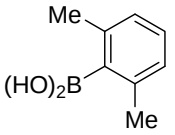
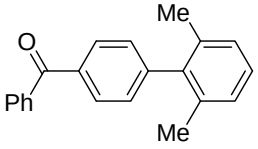
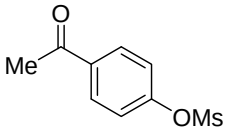
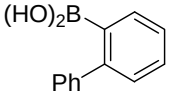
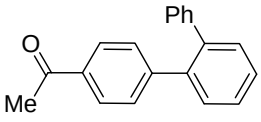
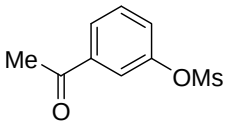
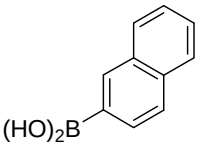
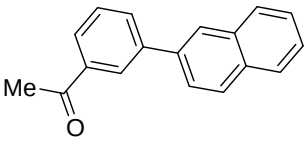
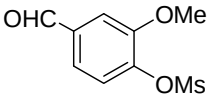
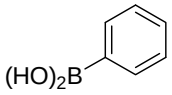
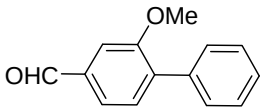
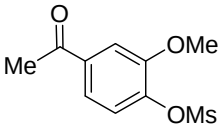
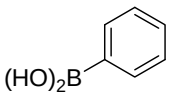
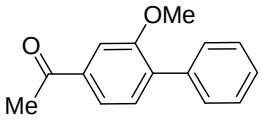
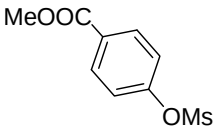
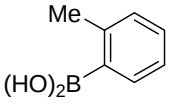
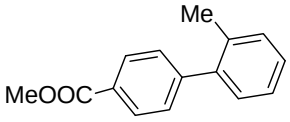
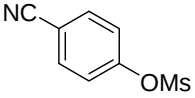
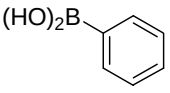
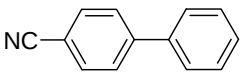
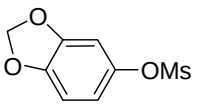
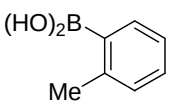
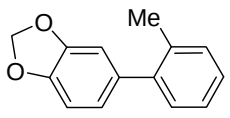
To test the effectiveness of the Pd/CM-phos catalytic system, a range of aryl mesylates were examined using the preliminary optimized reaction conditions (Table 5.2).

In general, complete conversions were observed within 3 hours when 2 mol% of Pd was used. Sterically bulky *ortho*- and di-*ortho*- substituted arylboronic acids were effectively coupled with aryl mesylates in good to excellent yield (Table 5.2, entries 4, 5). Homocoupled side-products were not observed in GC-MS analyses. Notably, the coupling of non-activated aryl mesylate could be performed with 0.5 mol% of Pd (Table 5.2, entry 2). Moreover, deactivated *p*-methoxyphenyl mesylate was demonstrated to be a feasible coupling partner (Table 5.2, entry 6).

A variety of common functional groups were compatible under these mild reaction conditions, for example, keto, aldehyde, ester and nitrile (Table 5.3). Aryl mesylates (Table5.3, entries 4-5) and arylboronic acids (Table5.3, entries 1, 2, 6, 8) that bear ortho substituent were also effective substrates towards the coupling reaction.

Table 5.3 Palladium-Catalyzed Suzuki-Miyaura Coupling of Functionalized ArOMs with Ar'$B(OH)_2$[a]

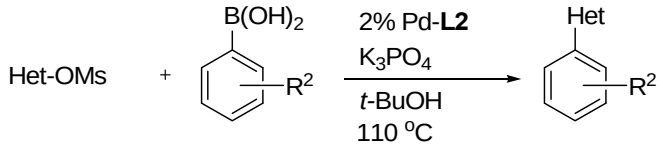


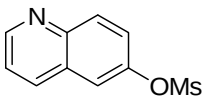
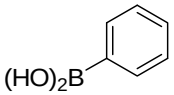
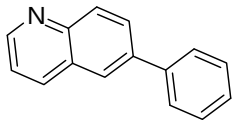
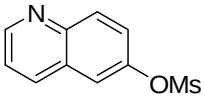
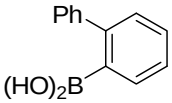
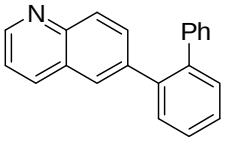
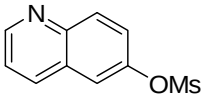
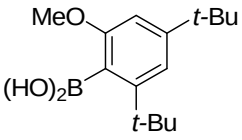
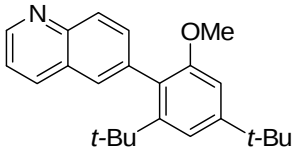
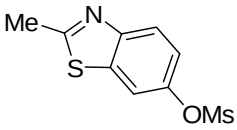
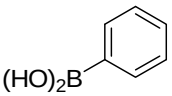
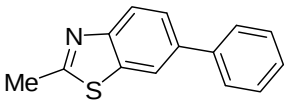
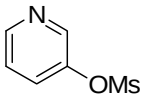
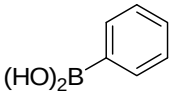
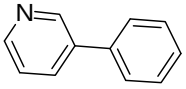
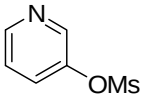
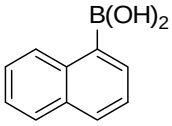
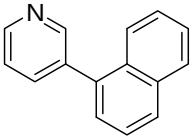
entry	ArOMs	Ar'$B(OH)_2$	product	mol% Pd	% yield[b]
1				2%, 3 h	93
2				2%, 3 h	92
3				2%, 3 h	94
4				2%, 3 h	81
5				2%, 3 h	95
6				2%, 3 h	97
7				2%, 3 h	95
8				2%, 3 h	89

[a]Reaction conditions: ArOMs (1.0 mmol), Ar'$B(OH)_2$ (2.0 mmol), K_3PO_4 (3.0 mmol), $Pd(OAc)_2/L_2$ (mol% as indicated), *t*-BuOH (3.0 mL), at 110 °C under N_2 for indicated period of time. [b]Isolated yields.

5.2.3 Suzuki-Miyaura Coupling of Heterocyclic Aryl Mesylates

Table 5.4 Palladium-Catalyzed Suzuki-Miyaura Coupling of Heterocyclic ArOMs with Ar'B(OH)$_2$[a]



entry	Het-OMs	Ar'B(OH)$_2$	product	mol% Pd	% yield[b]
1				2%, 3 h	97
2				2%, 3 h	91
3				2%, 3 h	77
4				2%, 3 h	91
5				2%, 3 h	84
6				2%, 3 h	85

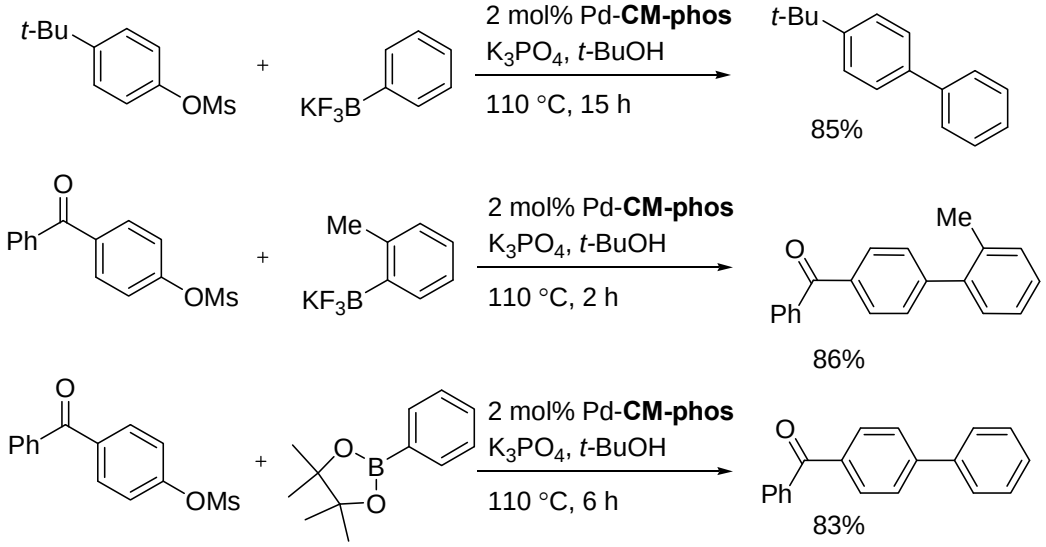
[a]Reaction conditions: Het-OMs (1.0 mmol), Ar'B(OH)$_2$ (2.0 mmol), K_3PO_4 (3.0 mmol), Pd(OAc)$_2$/L$_2$ (mol% as indicated), *t*-BuOH (3.0 mL), at 110 °C under N_2. [b]Isolated yields.

Apart from functionalized aryl mesylates, the scope of Pd/**CM-phos** catalytic system can be extended to heteroaryl mesylates (Table 5.4). Sterically congested arylboronic acids were efficiently coupled with quinolyl mesylate in excellent yields (Table 5.4, entries 1-3). Particularly noteworthy was that the

extremely hindered 2,4-di-*tert*-butyl-6-methoxyphenylboronic acid was found to be a capable coupling partner in this reaction (Table 5.4, entry 3). Benzothiazolyl and pyridyl mesylates could be coupled with arylboronic acids to furnish the corresponding desired product in good yields (Table 5.4, entries 4-6).

5.2.4 Suzuki-Miyaura Coupling of Aryl Mesylates with Aryl Trifluoroborate Salts and Pinacol Boronate Esters

In addition to arylboronic acids that are widely used as coupling partners, using boronic acid surrogates are also highly attractive to the coupling reaction.[183] Other organoboron nucleophiles such as aryl trifluoroborate salts and a pinacol boronate ester were successfully coupled with aryl mesylates in our Pd/**CM-phos** catalytic system (Scheme 5.1).



Scheme 5.1 Palladium-catalyzed Suzuki-type coupling of ArOMs with Ar'BF_3K and Ar'BPin

5.2.5 Structural Insight of New Palladium Catalyst System

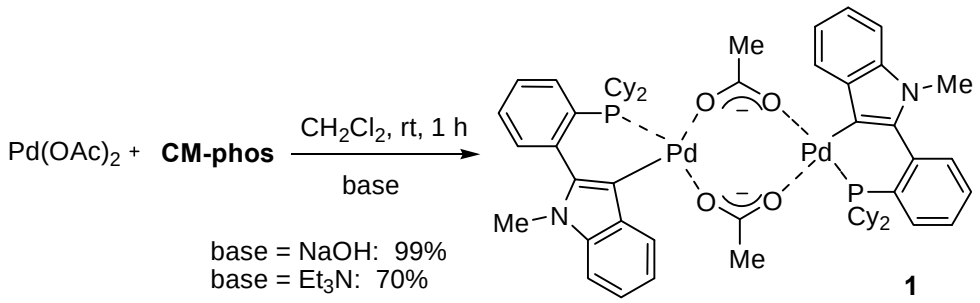


Figure 5.1 Independent synthesis of palladium complex

In order to have a better structural insight of our new palladium catalyst system, we attempted to prepare the palladium complex from our newly developed indolyl phosphine ligand **CM-phos**. Palladium complex **1** was synthesized from $Pd(OAc)_2$ with **CM-phos** under basic medium at room temperature (Figure 5.1). The single crystals of **1** were grown from CH_2Cl_2/ethereal layers at room temperature. The X-ray crystallographic data revealed that **1** was a dimeric complex with two acetate bridging groups and the palladacycle formation was through the 3-C-H position from the indolyl scaffold (Figure 5.2). The six-membered cyclometallated ring was puckered and the bite angle was 82.01(10)° [C(10)-Pd(1)-P(1)]. The bond length on the palladacyclic Pd-C bond [Pd(1)-C(10), 1.986(3) Å, (Figure 5.2)] is similar to those of other palladacycles[205] but significantly shorter than that of Pd-C_{ipso} coordination [c.f. 2.191(3) Å].[106,206-208]

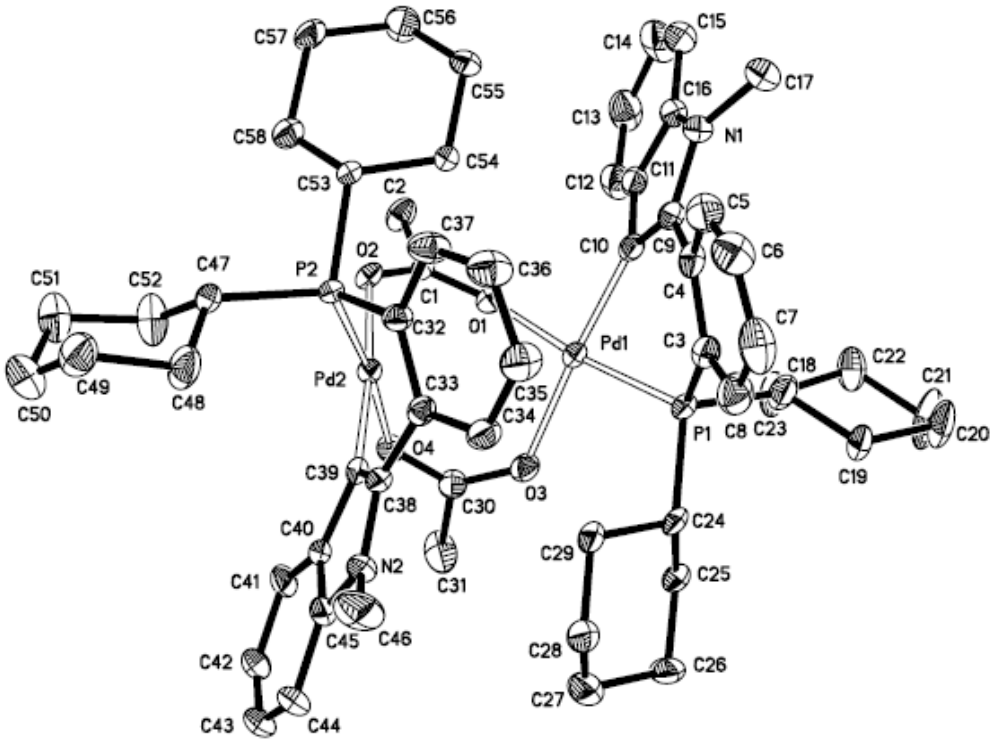


Figure 5.2 ORTEP representation of dimeric complex **1** (30% probability ellipsoids). Hydrogen atoms have been omitted for clarity purpose.

Table 5.5 Selected Bond Distances (Å) and Angles (˚) for Dimeric Complex **1**

Bond distances (Å)			
Pd(1)-C(10)	1.986(3)	Pd(1)-O(3)	2.123(3)
Pd(1)-O(1)	2.138(2)	Pd(1)-P(1)	2.2108(10)
Pd(2)-C(39)	2.005(3)	Pd(2)-O(4)	2.117(2)
Pd(2)-O(2)	2.124(2)	Pd(2)-P(2)	2.2036(7)

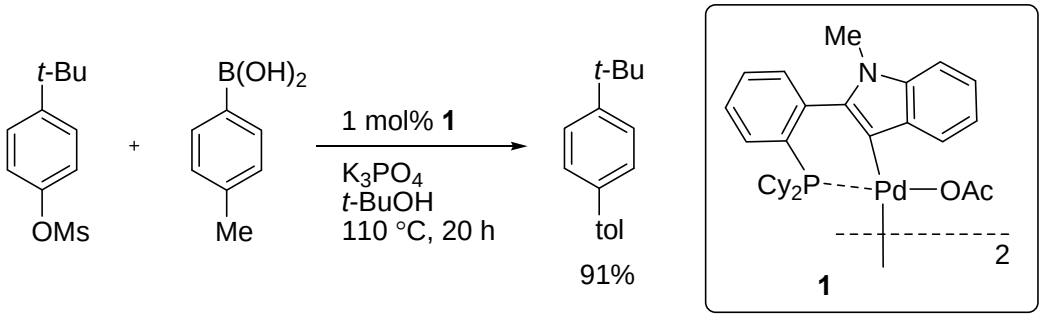
Bond angles (˚)			
C(10)-Pd(1)-O(3)	173.07(11)	C(10)-Pd(1)-O(1)	92.92(12)
O(3)-Pd(1)-O(1)	86.43(10)	C(10)-Pd(1)-P(1)	82.01(10)

Table 5.6 Crystal Data and Structure Refinement of Dimeric Complex **1**

Empirical formula	$[Pd(CH_3COO)(PC_{27}H_{33}N)]_2$	
Formula weight	1220.84	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	Cc	
Unit cell dimensions	a = 14.4891(4) Å	$\alpha = 90°$.
	b = 24.1281(7) Å	$\beta = 105.194(2)°$.
	c = 18.4037(5) Å	$\gamma = 90°$.
Volume	6208.9(3) $Å^3$	
Z	4	
Density (calculated)	1.306 Mg/m^3	
Absorption coefficient	0.760 mm^{-1}	
F(000)	2520	
Crystal size	0.50 x 0.50 x 0.42 mm^3	
Theta range for data collection	1.68 to 27.58°.	
Index ranges	-18<=h<=13, -22<=k<=31, -23<=l<=21	
Reflections collected	24656	
Independent reflections	10715 [R(int) = 0.0346]	
Completeness to theta = 27.62°	99.3 %	
Absorption correction	Multi scan	
Max. and min. transmission	0.7409 and 0.7026	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	10715 / 38 / 659	
Goodness-of-fit on F^2	1.002	
Final R indices [I>2sigma(I)]	R1 = 0.0550, wR2 = 0.1435	
R indices (all data)	R1 = 0.0775, wR2 = 0.1693	
Absolute structure parameter	-0.01(4)	
Largest diff. peak and hole	0.935 and -0.647 $e.Å^{-3}$	

5.2.6 Preliminary Study of the Catalytic Reactivity of the Palladacyclic Complex 1

Single-component palladium pre-catalysts have recently received increasing attention.[205,209-212] In addition to their handling convenience, they display comparative (or sometimes even more reactive) activity with respect to *in situ*-generated catalysts in cross-coupling reactions. With regard to their significance, we applied the isolated palladacyclic complex **1** to the Suzuki-Miyaura coupling of aryl mesylates (Scheme 5.2). This air-stable palladium complex **1** with additional three-fold of CM-Phos displayed essentially the same reactivity as that of the *in-situ* generated catalyst (Scheme 5.2 *vs*. Table 5.2, entry 1).



Scheme 5.2 Application of palladacyclic complex **1** in Suzuki-Miyaura coupling of ArOMs

5.3 Conclusion

We have succeeded in the first Suzuki-Miyaura coupling of unactivated aryl mesylates. The Pd/**CM-phos** catalyst system displays excellent reactivity in the coupling of aryl and heteroaryl mesylates with various organoboron-nucleophiles, namely arylboronic acids, pinacol esters and trifluoroborate salts. These easily accessible indolyl-type phosphine ligands in combination with Pd-complex precursors showed good activity (0.5 to 4.0 mol% Pd) in non-activated mesylate coupling reactions. A variety of aryl, heteroaryl and vinyl mesylates were efficiently coupled with different organoboron nucleophiles.

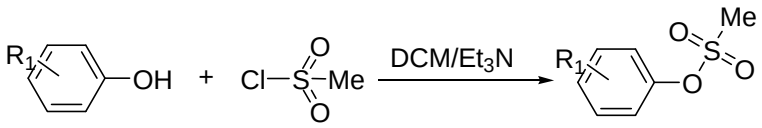
5.4 Experimental Section

5.4.1 General Considerations

Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. All Suzuki-Miyaura reactions were performed in Rotaflo® (England) resealable screw cap Schlenk flasks (approx. 20 mL volume) in the presence of Teflon coated magnetic stirrer bar (3 mm × 10 mm). Toluene and tetrahydrofuran (THF) were distilled from sodium and sodium benzophenone ketyl under nitrogen.[150] *tert*-Butanol was distilled from sodium under nitrogen.[150] Most commercially available arylboronic acids were used as received. Some arylboronic acids might require further recrystallization depending on the received conditions. 2,4-di-*tert*-butyl-6-methoxyphenylboronic acid was synthesized according to literature methods. $K_3PO_4 \bullet H_2O$ and K_3PO_4 were purchased from Fluka. Thin layer chromatography was performed on Merck precoated silica gel 60 F_{254} plates. Silica gel (Merck, 70-230 and 230-400 mesh) was used for column chromatography. Melting points were recorded on an uncorrected Büchi Melting Point B-545 instrument. ^{1}H NMR spectra were recorded on a Bruker (400 MHz) spectrometer. Spectra were referenced internally to the residual proton resonance

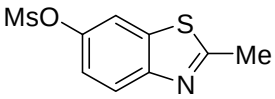
in $CDCl_3$ (δ 7.26 ppm), or with tetramethylsilane (TMS, δ 0.00 ppm) as the internal standard. Chemical shifts (δ) were reported as part per million (ppm) in δ scale downfield from TMS. ^{13}C NMR spectra were referenced to $CDCl_3$ (δ 77.0 ppm, the middle peak). ^{31}P NMR spectra were referenced to 85% H_3PO_4 externally. Coupling constants (*J*) were reported in Hertz (Hz). Mass spectra (EI-MS and ES-MS) were recorded on a HP 5989B Mass Spectrometer. High-resolution mass spectra (HRMS) were obtained on a Brüker APEX 47e FT-ICR mass spectrometer (ESIMS). GC-MS analysis was conducted on a HP 5973 GCD system using a HP5MS column (30 m × 0.25 mm). The products described in GC yield were according to the authentic samples/dodecane calibration standard from HP 6890 GC-FID system. All yields reported refer to isolated yield of compounds estimated to be greater than 95% purity as determined by capillary gas chromatography (GC) or ^1H NMR. Compounds described in the literature were characterized by comparison of their ^1H, and/or ^{13}C NMR spectra to the previously reported data. The procedures in this section are representative, and thus the yields may differ from those reported in tables.

5.4.2 Preparation of Aryl Mesylates



4-*tert*-Butylphenyl mesylate[213], 4-methoxyphenyl mesylate[108], 4-acetylphenyl mesylate[108], 4-benzoylphenyl mesylate[214], 4-acetyl-2-methoxyphenyl mesylate[215], 1,3-Benzodioxol-5-ol mesylate[216], 4-formyl-2-methoxyphenyl mesylate[217], 3-pyridyl mesylate[218], 4-cyanophenyl mesylate[108], and 4-(methoxycarbonyl)phenyl mesylate[108] were prepared from their corresponding phenols with MsCl in the presence of triethylamine in CH_2Cl_2 according to the literature method.[190] New aryl mesylates were prepared by literature procedures.[190] Characterizations data of new aryl mesylates are shown below.

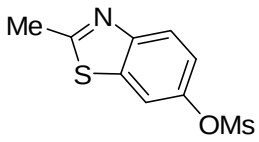
2-Methyl-5-benzothiazolyl mesylate



General procedures for preparation of aryl mesylate: To a stirred solution of 5-hydroxy-2methylbenzothiazole (3.30 g, 20 mmol) in anhydrous dichloromethane (20 mL) cooled to 0 °C was added distilled triethylamine (4.17 mL, 30 mmol). Mesyl chloride (1.94 mL, 25 mmol) was added dropwise *via* a

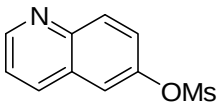
syringe over 15 min to this solution. The reaction was stirred at 0 °C for 2 hour, and then quenched with water. The aqueous layer was extracted with dichloromethane (3 × 100 mL) and the combined organics were dried over $MgSO_4$ and concentrated in *vacuo*. The crude products were purified by column chromatography on silica gel using DCM/hexane solvent mixtures as the eluent to obtain the titled compound in 38% yield,

2-Methyl-5-benzothiazol mesylate



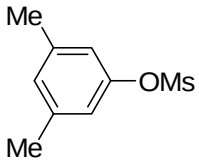
Obtained in 38% yield as white crystals: mp 119.5-120.8 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.76 (s, 3H), 3.12 (s, 3H), 7.24 (dd, *J*=2.3Hz, 8.7Hz, 1H), 7.74-7.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 37.1, 115.4, 118.9, 122.1, 134.4, 147.4, 153.7, 169.6; MS (EI): *m/z* (relative intensity) 243 (M^+, 35), 164 (100), 136 (28), 122 (15), 95 (18). HRMS: calcd. for $C_9H_9N_1O_3S_2$: 243.0018, found 243.0023.

6-(Mesyloxy)quinoline



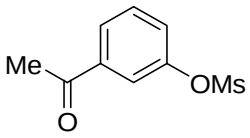
Obtained in 58% yield as deep purple crystals: mp 84.6-86.2 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.15 (s, 3H), 7.32-7.35 (m, 1H), 7.52-7.55 (m, 1H), 7.67 (d, *J*=2.6Hz, 1H), 8.04-8.07 (m, 2H), 8.83-8.85 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 37.4, 119.2, 121.8, 124.0,128.1, 131.6, 135.7, 146.4, 146.4, 150.7; MS (EI): *m/z* (relative intensity) 223 (M^+, 63), 145 (60), 116 (100), 89 (30), 63 (10). HRMS: calcd. for $C_{10}H_9N_1O_3S_1$: 223.0298, found 223.0292.

3,5-Dimethylphenyl mesylate.



Obtained in 95% yield as white crystals: mp 41.7-43.4 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.30 (s, 3H), 3.07 (s, 3H), 6.88 (s, 2H), 6.93 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 36.8, 119.1, 128.7, 139.7, 149.0; MS (EI): *m/z* (relative intensity) 200 (M^+, 65), 122 (100), 107 (20), 91 (30), 77 (30). HRMS: calcd. for $C_9H_{12}O_3S_1$: 200.0502, found 200.0507.

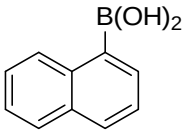
3-Acetylphenyl mesylate



Obtained in 83% yield as white crystals: mp 50.1-52.4 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.56 (s, 3H), 3.14 (s, 3H), 7.44-7.48 (m, 2H), 7.78 (s, 1H), 7.86 (d, *J*=7.1Hz, 1H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.5, 37.4, 121.4, 126.5, 127.0, 130.2, 138.7, 149.2, 196.3; MS (EI): *m/z* (relative intensity) 214 (M^+, 28), 199 (100), 171 (5), 121 (35), 92 (10). HRMS: calcd. for $C_9H_{10}O_4S_1$: 214.2940, found 214.0304.

5.3.3 Synthesis of Arylboronic Acid

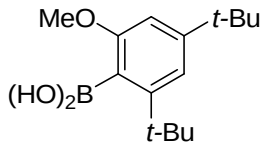
1-Naphthylboronic acid[219]



Anhydrous THF (20 mL) was added to 1-bromonaphthalene (5.56 mL, 40 mmol) under nitrogen at room temperature. *n*-Butylithium (44 mmol) was added dropwise to the solution at -78 ^{o}C and stirred for 30min. The reaction mixture was transferred to a solution of B(O*i*-Pr)$_3$ (18.6 mL, 80 mmol) in THF (10 mL) at -78 °C *via* cannular under nitrogen. The solution was warmed to room

temperature and stirred overnight. Diluted HCl (10%, 20 mL) was added to the mixture and stirred for 30 min. The organic layer was separated and the aqueous phase was extracted by diethyl ether (50 mL × 3). The combined organic extracts were washed with brine and dried over $MgSO_4$. The solvent was removed and the residue was crystallized under ether/hexane to give colorless crystals (5.0 g, 72%). The product was used without further characterization.

2,4-Di-*tert*-butyl-6-methoxyphenylboronic acid[191]



n-Butyllithium (1.6 M in hexane, 25 mL, 40 mmol) was added to a solution of 2-bromo-3,5-di-*tert*-butylanisole (12 g, 40 mmol) in THF (20 mL) at -78 °C under nitrogen. The mixture was stirred for 1 h and then transferred to a solution of distilled $B(OMe)_3$ (9.1 mL, 80 mmol) in THF (10 mL) at -78 °C under nitrogen. It was allowed to warm to room temperature and water was added. The organic layer was separated, and the aqueous phase was extracted with ether (3 × ~100 mL). The combined organic phases were washed with

brine. After removing the solvent, the residue was redissolved in ethanol (60 mL). A solution of NaOH (2 M) was added and the mixture was stirred for 2 h. The solvent was rotary-evaporated, and the remaining aqueous layer was extracted with ether (3 × ~100 mL). The etheral layer was then washed with brine and dried over $MgSO_4$. The solvent was removed, and the residue was recrystallized from ether/hexane to give 2,4-di-*tert*-butyl-6-methoxyphenylboronic acid as colorless crystals (7.8 g, 74%). The product was used without further characterization.

5.4.4 General Procedures for Initial Ligand and Reaction Condition Screenings

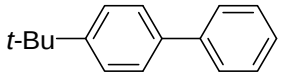
General procedure for screening: $Pd(OAc)_2$ (6.8 mg, 0.030 mmol) and ligand (Pd:L = 1:4) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The tube was evacuated and flushed with nitrogen for three times. Precomplexation was applied by adding freshly distilled dichloromethane (0.5 mL) and Et_3N (50 μL) into the tube. The palladium complex stock solution was stirred and warmed using a hair drier for about 1 to 2 minutes until the solvent started to boil. The solvent was then evaporated under high vacuum. 4-*tert*-Butylphenyl mesylate (1.0 mmol), 4-methylphenylboronic acid (2.0 mmol) and base (3.0 mmol) were loaded into the tube, and the system was further evacuated and flushed with nitrogen for three times. The solvent (3.0 mL) was added with stirring at room temperature for several minutes. The tube was then placed into a preheated oil bath (110 ^oC) and stirred for the time as indicated. After completion of reaction, the reaction tube was allowed to cool to room temperature. Ethyl acetate (~10 mL), dodecane (227 μL, internal standard) and water were added. The organic layer was subjected to GC analysis. The GC yield obtained was previously calibrated by authentic sample/dodecane calibration curve.

5.4.5 General Procedures for Suzuki-Miyaura Couplings of Aryl Mesylates

General procedure for Suzuki-Miyaura coupling of aryl mesylates: $Pd(OAc)_2$ (2.3 mg, 0.010 mmol) and ligand (Pd:L = 1:4) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The tube was evacuated and flushed with nitrogen for several times. Precomplexation was applied by adding freshly distilled dichloromethane (0.5 mL) and Et_3N (50 μL) into the tube. The solution was stirred and warmed using a hair drier for about 1 to 2 minutes until the solvent started to boil. The solvent was then evaporated under high vacuum. Aryl mesylate (1.0 mmol), arylboronic acid (2.0 mmol) and K_3PO_4 (3.0 mmol) were loaded into the tube, and the system was further evacuated and flushed with nitrogen for several times. The solvent *tert*-butanol (3.0 mL) was then added. The tube was stirred at room temperature for several minutes and then placed into a preheated oil bath (110 ^oC) for the time period as indicated in Tables. After completion of reaction as judged by GC analysis, the reaction tube was allowed to cool to room temperature, quenched with water, and diluted with EtOAc. The organic layer was separated and the aqueous layer was washed with EtOAc. The filtrate was concentrated under reduced pressure. The crude products were purified by flash column chromatography on silica gel (230-400 mesh) to afford the desired product.

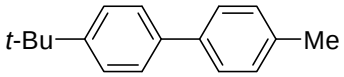
5.4.6 Characterization Data for Coupling Products

4-*tert*-Butylbiphenyl (Table 5.2, entries 1 and 2, Scheme 5.1).[175]



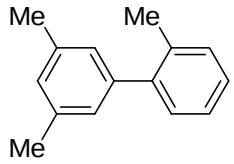
Hexane, R_f=0.55; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.72 (s, 9H), 7.64 (t, *J*=7.4 Hz, 1H), 7.72-7.82 (m, 4H), 7.89-7.96 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.3, 34.4, 125.6, 126.7, 126.9, 128.6, 138.2, 140.9, 150.0; MS (EI): *m/z* (relative intensity) 210 (M^+, 35), 195 (100), 178 (20), 167 (30).

4-Methyl-4'-*tert*-butylbiphenyl (Table 5.2, entry 3).[220]



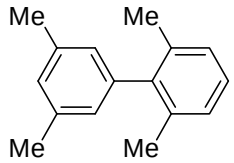
Hexane, R_f=0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.65 (s, 9H), 2.65 (s, 3H), 7.49 (d, *J*=8.0 Hz, 2H), 7.73 (*J*=8.4 Hz, 2H), 7.78 (*J*=8.0 Hz, 2H), 7.82 (*J*=8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 31.3, 34.4, 125.6, 126.5, 126.7, 129.4, 136.5, 138.1, 138.2, 149.7; MS (EI): *m/z* (relative intensity) 224 (M^+, 33), 209 (100), 193 (5), 181 (14), 165 (10).

3, 5-Dimethyl-2'-methylbiphenyl (Table 5.2, entry 4).[221]



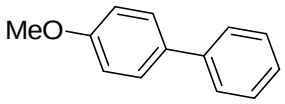
Hexane, R_f=0.55; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.59 (s, 3H), 2.65 (s, 6H), 7.27 (m, 3H), 7.50-7.54 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.4, 21.2, 125.6, 126.9, 128.3, 129.6, 130.1, 135.1, 137.3, 141.9, 142.1; MS (EI): *m/z* (relative intensity) 196 (M^+, 70), 181 (100), 165 (45), 152 (10).

3, 5-Dimethyl-2',6'-dimethylbiphenyl (Table 5.2, entry 5).[222]



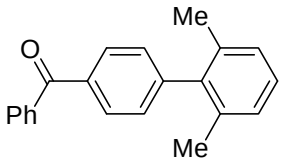
Hexane, R_f=0.55; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.29 (s, 6H), 2.57 (s, 6H), 7.01 (s, 2H), 7.20 (s, 1H), 7.30-7.40 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 21.3, 126.6, 127.1, 128.1, 135.8, 137.6, 11.0, 142.0; MS (EI): *m/z* (relative intensity) 210 (M^+, 65), 195 (100), 180 (30), 152 (25).

4-Phenylanisole (Table 5.2, entry 6).[71]



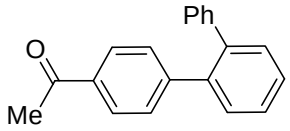
EA:Hexane = 1:20, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.97 (s, 3H), 7.17 (d, *J*=8.7 Hz, 2H), 7.51-7.54 (m, 1H), 7.62 (t, *J*=7.8 Hz, 2H), 7.73-7.79 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.0, 114.1, 126.5, 127.9, 128.3, 128.6, 133.5, 140.6, 159.0; MS (EI): *m/z* (relative intensity) 184 (M^+, 100), 169 (50), 141 (50), 115 (40).

4-(2,6-Dimethylphenyl)benzophenone (Table 5.3, entry 1).



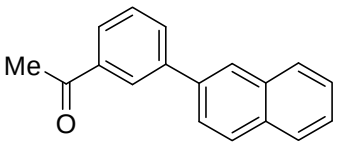
EA:Hexane = 1:20, R_f=0.4; white solid, m.p. = 76.5-78.9 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.13 (s, 6H), 7.18-7.25 (m, 3H), 7.33 (d, *J*=8.2 Hz, 2H), 7.54 (t, *J*=7.7Hz, 2H), 7.62-7.63 (m, 1H), 7.93-7.98 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 127.1, 127.2, 127.9, 128.7, 129.6, 130.0, 131.9, 135.1, 135.5, 137.3, 140.3, 145.4, 195.8; MS (EI): *m/z* (relative intensity) 286 (M^+, 80), 209 (100), 181 (25), 165 (50), 105 (45). HRMS: calcd. for $C_{21}H_{18}O$: 287.1436, found 287.1442.

4-(2-Biphenyl)acetophenone (Table 5.3, entry 2).[181]



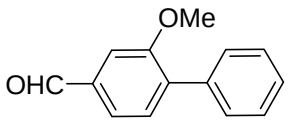
EA:Hexane = 1:20, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.56 (s, 3H), 7.20-7.31 (m, 7H), 7.46-7.49 (m, 4H), 7.86 (d, *J*=8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.2, 126.5, 127.4, 127.7, 127.8, 127.9, 129.0, 129.8, 130.1, 130.5, 134.8, 139.0, 140.3, 140.7, 146.3; MS (EI): *m/z* (relative intensity) 272 (M^+, 70), 257 (100), 228 (50), 202 (20).

3-(2-Naphthyl)acetophenone (Table 5.3, entry 3).



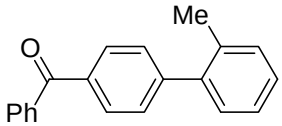
EA:Hexane = 1:9, R_f=0.35; White solid, m.p. = 69.5-71.8 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.60 (s, 3H), 7.45-7.50 (m, 3H), 7.68 (dd, *J*=1.6, 8.5 Hz, 1H), 7.78-7.89 (m, 5H), 8.00 (bs, 1H), 8.30 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.2, 124.7, 125.5, 125.8, 126.0, 126.5, 126.8, 127.2, 127.8, 128.2, 128.6, 131.3, 132.4, 133.2, 136.8, 137.2, 140.9, 197.5; MS (EI): *m/z* (relative intensity) 246 (M^+, 100), 231 (90), 202 (95). HRMS: calcd. for $C_{18}H_{14}O$: 247.1123, found 247.1106.

3'-Methoxy-4'-phenylbenzaldehyde (Table 5.3, entry 4).[84]



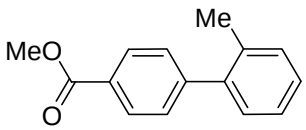
EA:Hexane = 1:9, R_f=0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.86 (s, 3H), 7.39-7.59 (m, 8H), 10.00 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.3, 109.4, 124.0, 127.6, 127.8, 129.1, 130.9, 136.4, 136.8, 136.9, 156.7, 191.5; MS (EI): *m/z* (relative intensity) 212 (M^+, 100), 169 (20), 152 (10), 139 (20), 115(15).

3'-Methoxy-4'-phenylacetophenone (Table 5.3, entry 5).[223]



EA:Hexane = 1:9, R_f=0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.61 (s, 3H), 3.82 (s, 3H), 7.37-7.46 (m, 4H), 7.57-7.62 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 55.1, 109.5, 121.3, 127.2, 129.0, 130.3, 135.1, 136.8, 137.0, 156.2, 197.0; MS (EI): *m/z* (relative intensity) 226 (M^+, 80), 211 (100), 183 (10), 168 (30).

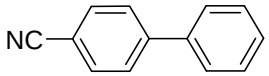
Methyl 4-(2'-tolyl)benzoate (Table 5.3, entry 6).



EA:Hexane = 1:9, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.3 (s, 3H), 3.96 (s,

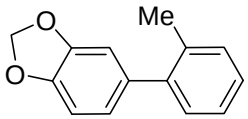
3H), 7.24-7.32 (m, 4H), 7.42(d, *J* = 8.0 Hz, 2H), 8.14 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.1, 125.6, 127.5, 128.3, 129.0, 129.1, 129.2, 130.2, 134.8, 140.5, 146.4, 166.6; MS (EI): *m/z* (relative intensity) 226 (M^+, 100), 195 (98), 168 (60), 152 (50), 139 (7).

4-Cyanobiphenyl (Table 5.3, entry 7).[224]



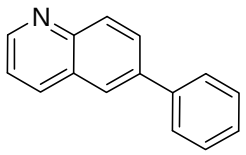
DCM:Hexane = 1:20, R_f=0.35; ^1H NMR (400 MHz, $CDCl_3$) δ 7.43-7.50 (m, 3H), 7.57-7.59 (m, 2H), 7.64-7.70 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 110.6, 118.6, 126.9, 127.4, 128.4, 128.8, 132.3, 138.8, 145.2; MS (EI): *m/z* (relative intnsity) 179 (M^+, 100), 151 (20).

2'-Methyl- 3,4-methylenedioxy biphenyl (Table 5.3, entry 8).[126]



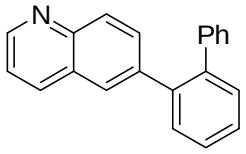
EA:Hexane = 1:4, R_f=0.7; ^1H NMR (400 MHz, $CDCl_3$) δ 2.44 (s, 3H), 6.07 (s, 2H), 6.91-7.01 (m, 3H), 7.37-7.39 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.3, 100.8, 107.8, 109.6, 122.3, 125.6, 127.0, 129.6, 130.1, 135.2, 135.7, 141.4, 146.3, 147.1; MS (EI): *m/z* (relative intnsity) 212 (M^+, 100), 181 (20), 153 (30).

6-Phenylquinoline (Table 5.4, entry 1).[196]



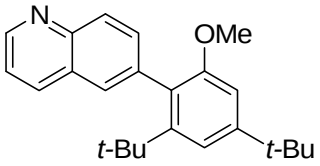
EA:Hexane = 1:4, R_f=0.25; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21-7.33 (m, 2H), 7.37-7.71 (m, 2H), 7.58-7.60 (m, 2H), 7.82-7.87 (m, 2H), 7.96-8.15 (m, 2H), 8.83 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 121.0, 125.0, 127.0, 127.3, 128.0, 128.5, 128.7, 129.4, 135.7, 138.7, 139.7, 147.2, 149.9; MS (EI): *m/z* (relative intnsity) 205 (M^+, 100), 176 (10).

5-(2-Biphenyl)quinoline (Table 5.4, entry 2).



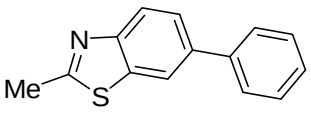
DCM, R_f=0.2; light yellow viscous liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (bs, 5H), 7.25-7.54 (m, 6H), 7.69 (s, 1H), 7.94-7.98 (m, 2H), 8.85 (d, *J*= 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 120.8, 126.4, 127.4, 127.7, 127.8, 127.9, 128.3, 129.6, 130.4, 130.5, 131.7, 135.6, 139.2, 139.7, 140.4, 140.8, 146.8, 149.9; MS (EI): *m/z* (relative intensity) 281 (M^+, 100), 266 (30), 252 (20); HRMS: calcd. for $C_{21}H_{15}N$: 281.1199, found 281.1203.

6-(2,4-Di-*tert*-butyl-6-methoxyphenyl)quinoline (Table 5.4, entry 3).



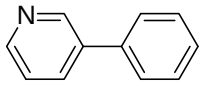
EA:Hexane = 1:9, R_f=0.15; white solid, m.p. = 136.4-138.1 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.19 (s, 9H), 1.42 (s, 9H), 3.56 (s, 3H), 6.92 (s, 1H); 7.24-7.31 (m, 4H), 8.02 (d, *J*=7.9 Hz, 1H), 8.14 (d, *J*=8.5 Hz, 1H), 8.87 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.1, 32.5, 34.8, 36.6, 55.5, 105.7, 116.0, 120.5, 127.0, 127.2, 127.5, 129.2, 133.9, 135.5, 138.3, 147.0, 148.4, 149.6, 150.6, 157.3; MS (EI): *m/z* (relative intensity) 347 (M^+, 100), 332 (75), 317 (5), 302 (3), 290 (5), 276(75), 261(30); HRMS: calcd. for $C_{24}H_{29}NO$: 347.2244, found 347.2253.

2-Methyl-5-phenylbenzothiazole (Table 5.4, entry 4).[225]



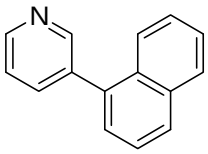
EA:Hexane = 1:4, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.73 (s, 3H), 7.22-7.24 (m, 1H), 7.40 (t, *J*=8.3Hz, 2H), 7.62 (d, *J*=7.3Hz, 1H), 7.69 (d, *J*=8.3Hz, 2H), 8.21 (d, *J*=1.1Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5, 120.1, 121.0, 123.5, 126.8, 126.9, 128.4, 134.1, 138.9, 140.2, 153.6, 167.0; MS (EI): *m/z* (relative intensity) 225 (M^+, 100), 184 (10), 152 (10).

3-Phenyl pyridine (Table 5.4, entry 5). [226]



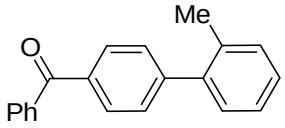
EA:Hexane = 3:7, R_f=0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.83 (m, 7H), 8.5-8.58 (m, 1H), 8.85 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 123.3, 126.8, 127.9, 128.8, 134.2, 136.4, 137.4, 147.8, 147.9; MS (EI): *m/z* (relative intensity) 155 (M^+, 100), 127 (10), 102 (7).

3-(1-Naphthalenyl) pyridine (Table 5.4, entry 6).[227]



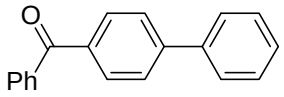
EA:Hexane = 1:4, R_f=0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.48 (m, 5H), 7.50-7.86 (m, 4H), (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 122.7, 124.8, 125.0, 125.7, 126.1, 127.0, 128.1, 131.0, 133.4, 135.8, 135.9, 136.9, 148.1, 150.1; MS (EI): *m/z* (relative intensity) 205 (M^+, 90), 204 (100), 176 (18), 151 (10).

4-(2'-Tolyl)benzophenone (Scheme 5.1).[126]



EA:Hexane = 1:20, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (s, 3H,), 7.30-7.33 (m, 4H), 7.46-7.61 (m, 5H), 7.90-7.93 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.2, 125.7, 127.6, 128.0, 128.9, 129.3, 129.7, 130.3, 132.0, 135.6, 137.4, 140.4, 146.0, 195.9; MS (EI): *m/z* (relative intensity) 272 (M^+, 70), 195 (100), 164 (40), 152 (40), 105 (40).

4-Phenylbenzophenone (Scheme 5.1).[228]



EA:Hexane = 1:20, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.42 (m, 1H,), 7.46-7.51 (m, 4H), 7.57-7.61 (m, 1H), 7.65-7.71 (m, 4H), 7.82-7.92 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 126.6, 126.9, 127.9, 128.0,128.6, 129.6, 130.4, 132.0, 135.8, 137.4, 139.5, 144.7, 195.7; MS (EI): *m/z* (relative intensity) 258 (M^+, 75), 181 (100), 152 (40), 105 (20), 77 (19).

Chapter 6 Palladium-Catalyzed Room Temperature Suzuki Coupling of Aryl Mesylates

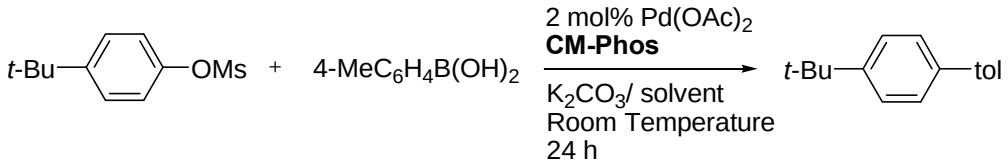
6.1 Introduction

The Suzuki-Miyaura coupling reactions are among the most powerful transformations in organic synthesis, and scientists have dedicated much efforts to expand the coupling scopes as well as to seek gentle the reaction conditions in the past several decades. Remarkable progress has been made in expanding the substrate scopes such as the employing of very inert, widely available aryl chlorides as coupling partners in Suzuki-Miyaura coupling reactions. For the mild reaction conditions, there are many examples of room temperature Suzuki-Miyaura coupling of aryl chlorides and sometimes the reaction can be performed under air atmosphere.[229] Room temperature nickel-catalyzed Suzuki coupling of aryl tosylates was reported by Hu and co-workers.[70] Hartwig et al. reported room temperature palladium-catalyzed Kumada coupling of aryl tosylates.[86] However, palladium-catalyzed Suzuki coupling of aryl tosylates and mesylates has not been established. The first example of palladium-catalyzed coupling reaction of aryl tosylates (Table 4.5, entry 5), shown in Chapter 4, inspired us to investigate the possibility of the room temperature Suzuki coupling of aryl mesylates.

6.2 Results and Discussion

6.2.1 Investigation of the Catalytic Activity of Pd/CM-phos System towards Room Temperature Suzuki Coupling of Aryl Mesylates.

Table 6.1 Initial Screening of Room Temperature Suzuki Coupling of Aryl Mesylates[a]



entry	Atmosphere	Solvent	GC yield (%)
1	Air	MeOH	93%
2	Air	EtOH	41%
3	Air	*i*-PrOH	43%
4	Air	*t*-amyl alcohol	38%
5	Air	DMF	16%
6	Air	THF	3%
7	Air	Dioxane	8%
8	Air	*t*-BuOH	7%
9	Air	MeOH	90%
10	N_2	MeOH	91%
11	O_2	MeOH	2%

[a]Reaction conditions: ArOMs (1.0 mmol), Ar'B$(OH)_2$ (2.0 mmol), K_2CO_3 (3.0 mmol), $Pd(OAc)_2$ (2 mol%), CM-phos (0.04 mmol), solvent (3.0 mL), at room temperature under air for 24 h

[b]Calibrated GC yields were reported using dodecane as the internal standard.

In the preliminary study, electronically neutral 4-*tert*-butylphenyl mesylate and 4-tolylboronic acid were used as prototypical substrates in our benchmark reaction (Table 6.1). A series of solvents was then examined. Surprisingly, fair to excellent yields of the coupling product could be obtained under air atmosphere condtion when solvents such as methanol, ethanol, isopropanol, and *tert*-amylalcohol were used in the coupling reaction of aryl mesylates (Table 6.1, entries1-4). However, DMF, an effective solvent in the room temperature Suzuki coupling of aryl tosylates, was now a poor solvent for the Suzuki coupling of aryl mesylates (Table 6.1, entry 5). Moreover, ^{t}BuOH, an effective solvent in the high temperature Suzuki coupling of aryl tosylates and mesylates, was also a poor solvent for the room temperature Suzuki coupling of aryl mesylates. It gave almost no coupling product (Table 6.1, entry 8).

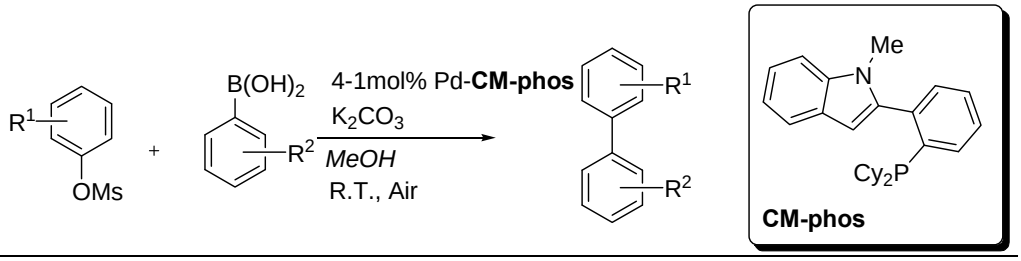
To investgate the effect of atmosphere on coupling reaction, nitrogen, air, and oxygen were used in the parallel experiment (Table 6.1, entries 9-11). The experiment showed that the yield of coupling product given by the coupling reaction that performed under nitrogen and that under air atmosphere were essentially the same. The only difference was that about 5-10% of the 4-tolylboronic acid homo-coupling product was observed under air atmosphere while only about 1-2% 4-tolylboronic acid homo-coupling product was observed

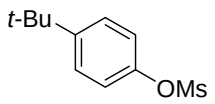
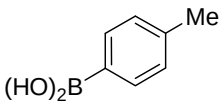
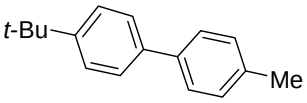
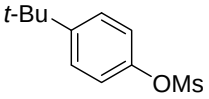
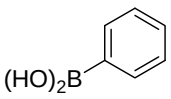
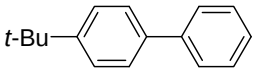
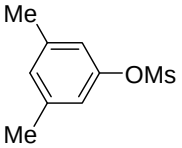
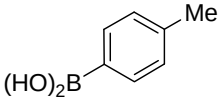
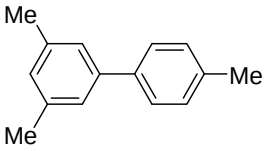
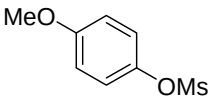
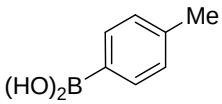
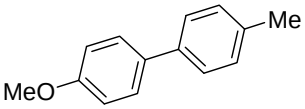
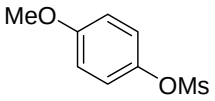
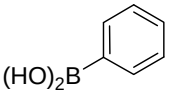
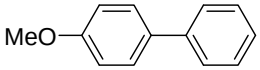
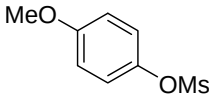
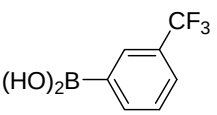
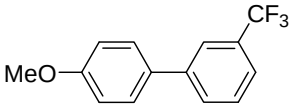
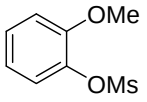
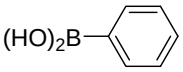
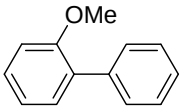
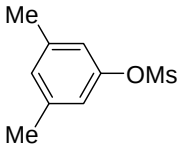
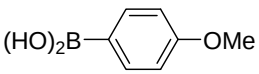
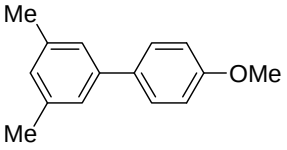
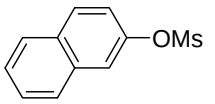
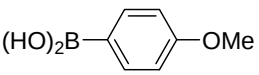
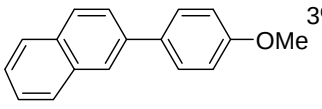
under nitrogen atmosphere. However, if the coupling reaction was under oxygen atmosphere, the yield of the coupling product was close to zero and a large amount of homo-coupling product was observed in GC analysis. These results implied that the $Pd(OAc)_2$/CM-phos catalytic system was relatively tolerated in the oxidation reaction. Under a low concentration of oxygen such as in the air atmosphere, the oxidation of Pd(0) to the Pd(II) was far slower than the oxidative addition of aryl mesylates to the active Pd(0) species. Under a high concentration of oxygen such as in a pure oxygen atmosphere, the oxidation of Pd(0) to the Pd(II) is dominant. These results also imply that the coupling reaction in this study underwent common Pd(0)/(II) mechanism instead of the Pd(II)/(IV). Therefore, reduction of Pd(II) to Pd(0) through the homo-coupling of the arylboronic acid was essential.

6.2.2 Room Temperature Suzuki-Miyaura Coupling of Non-Activated Aryl Mesylates

To test the effectiveness of the Pd/**CM-phos** catalytic system, a range of aryl mesylates were examined using the preliminary optimized reaction conditions (Table 6.2). Complete conversions were observed within 24 hours when 4 mol% of Pd were used. In general, non-activated and deactivated aryl mesylates were all effective substrates for room temperature Suzuki coupling reaction. Higher catalyst loading was required for the deactivated aryl mesylates entries (Table 6.2, entries 6-9). For the room temperature Suzuki coupling reaction, there was almost a linear relation between the catalyst loading and the reaction time (Table 6.2, entries 5-6). Doubling the catalyst loading could reduce the reaction time by half while the product yield remained almost the same. This result is different from high temperature Suzuki coupling reaction which usually does not have such a relationship. Notably, electron-deficient 3-trifluoromethanephenylboronic acid was coupled with deactivated 4-anisyl mesylate in good yield (Table 6.2, entry 8). Bulky *ortho*-substituted 2-anisylmesylates were effectively coupled with phenylboronic acid in good yield too (Table 6.2, entry 9).

Table 6.2 Palladium-catalyzed Room Temperature Suzuki Coupling of Non-Activated Aryl Mesylates[a]



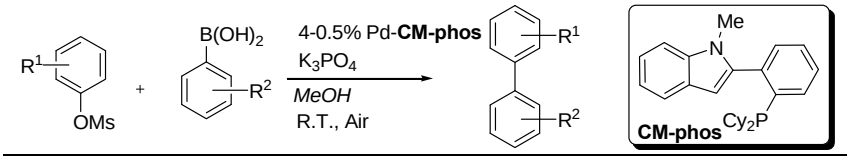
entry	ArOMs	$Ar'B(OH)_2$	product	mol% Pd	% yield[b]
1				4%, 15 h	90
2				1%, 24 h	95
3				1%, 24 h	90
4				1%, 24 h	95
5				4%, 24 h	92
6				2%, 48 h	87
7				4%, 24 h	91
8				4%, 24 h	86
9				4%, 24 h	74
10				3%, 24 h	94
11				3%, 24 h	85

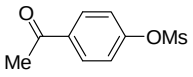
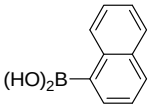
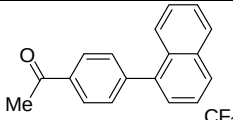
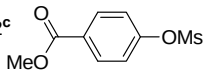
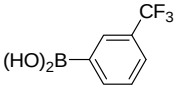
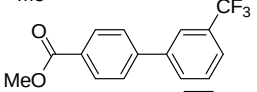
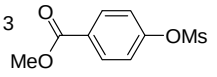
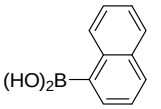
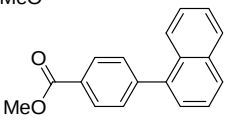
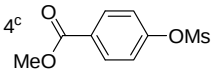
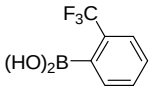
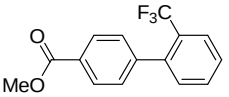
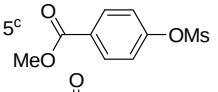
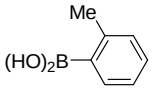
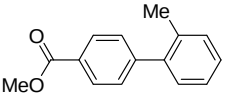
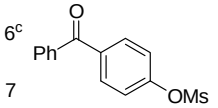
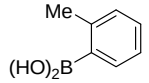
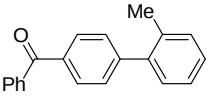
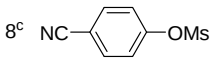
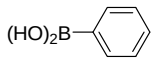
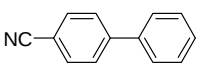
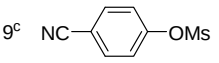
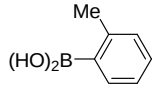
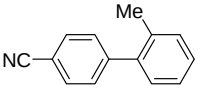
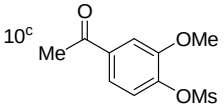
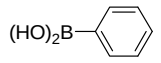
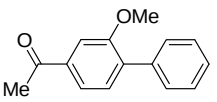
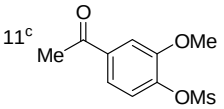
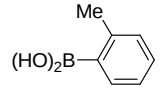
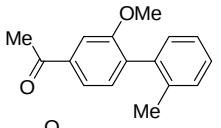
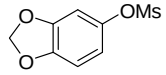
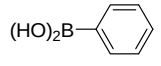
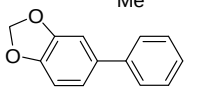
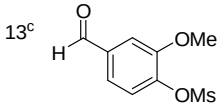
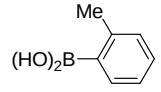
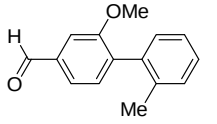
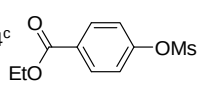
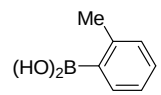
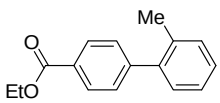
[a]Reaction conditions: ArOMs (1.0 mmol), $Ar'B(OH)_2$ (2.0 mmol), K_2CO_3 (3.0 mmol), $Pd(OAc)_2$/CM-phos (mol% as indicated), MeOH (3.0 mL), at Room Temperature under Air for indicated period of time. [b]Isolated yields.

6.2.3 Room Temperature Suzuki-Miyaura Coupling of Functionalized Aryl Mesylates

The compatibility of the functional groups was not a problem under this extremely mild reaction conditions. Aryl mesylates bearing the common functional groups such as keto, aldehyde, ester and nitrile were all effective substrates for the coupling reaction (Table 6.3). In general, the coupling product yields of the functionalized aryl mesylates were over 90%, and for specific entries as high as 99% can be achieved. Similar to the high temperature Suzuki coupling reaction, aryl mesylates and/or arylboronic acid that bearing ortho substitute groups were effective substrates towards the coupling reaction (Table 6.3, entry 11). Electron-deficient and steric hindered 2-(trifluoromethane)phenyl boronic was coupled with aryl mesylates in excellent yield (Table 6.3, entry 4). Although K_2CO_3 was a more efficient base for the Suzuki coupling reaction, extremely mild base Na_2CO_3 was used instead in the noted entries. It was observed that in the presence of K_2CO_3 as base, about 5-10% functionalized aryl mesylates could couple with the methanol to form the corresponding phenyl methyl ether instead of the biaryl coupling product. Replacing K_2CO_3 with Na_2CO_3, the phenyl methyl ethers were not observed. This might be due to the basicity of the Na_2CO_3 being too insufficient to deprotonate the acidic methanol.

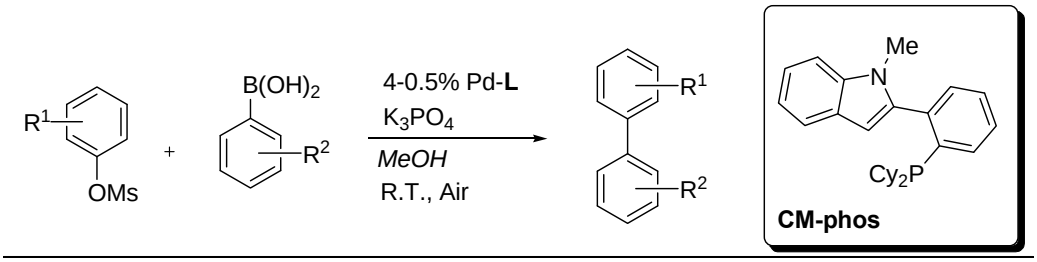
Table 6.3 Palladium-Catalyzed Room Temperature Suzuki Coupling of Functionalized Aryl Mesylates[a]

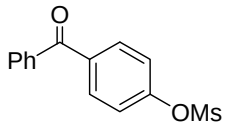
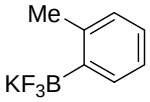
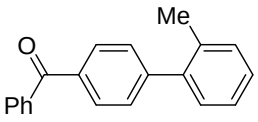
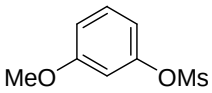
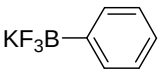
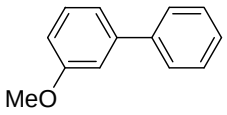
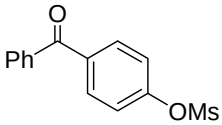
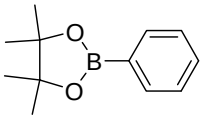
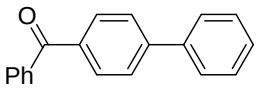
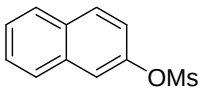
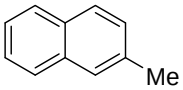
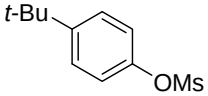
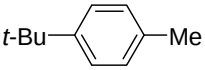


entry	ArOMs	$Ar'B(OH)_2$	product	mol% Pd	% yield[b]
1				1%, 18 h	97
2[c]				1%, 24 h	91
3				0.5%, 17 h	97
4[c]				1%, 24 h	98
5[c]				1%, 18 h	96
6[c]				1%, 15 h	99
7				0.5%, 19 h	93
8[c]				2%, 18 h	93
9[c]				2%, 18 h	95
10[c]				2%, 20 h	97
11[c]				2%, 18 h	98
12				4%, 24 h	93
13[c]				2%, 24 h	81
14[c]				2%, 18 h	99

[a]Reaction conditions: ArOMs (1.0 mmol), $Ar'B(OH)_2$ (2.0 mmol), K_2CO_3 (3.0 mmol), $Pd(OAc)_2$/CM-phos (mol% as indicated), MeOH (3.0 mL), at Room Temperature under Air for indicated period of time. [b]Isolated yields. [c]Na_2CO_3 as Base.

Table 6.4 Palladium-Catalyzed Room Temperature Suzuki Coupling of Aryl Mesylates with Aryltrifluoroborate Salts, Pinacol Boronate Esters and Alkyl Boronic Acid[a]



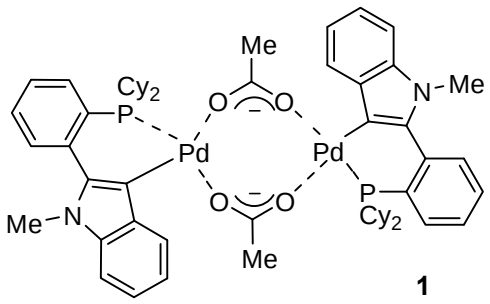
entry	ArOMs	Ar'B(OH)$_2$	product	mol% Pd	% yield[b]
1				1%, 24 h	81
2				4%, 40 h	77
3[c]				2%, 19 h	92
4		MeB(OH)$_2$		2%, 18 h	93
5		MeB(OH)$_2$		2%, 24 h	77

[a]Reaction conditions: ArOMs (1.0 mmol), Ar'B(OH)$_2$ (2.0 mmol), K_2CO_3 (3.0 mmol), Pd(OAc)$_2$/CM-phos (mol% as indicated), MeOH (3.0 mL), at Room Temperature under Air for indicated period of time. [b]Isolated yields. [c]Na_2CO_3 as Base.

Alkylboronic acid, potassium aryltrifluoroborate salt, and pinacol boronate ester were coupled with non-activated and functionalized aryl mesylates in good to excellent yields under room temperature. (Table 6.4)

6.2.4 Preliminary Study of the Reactivity/Structure of Pd/CM-phos

In chapter 4, the comparative experiment shows that the phosphine ligands that the phosphine group attached to the 3-position of indole ring are inferior to the aryl tosylates coupling reaction. In chapter 5, we have followed the pre-complex procedure used in the coupling reaction, in which $Pd(OAc)_2$ is complexed with CM-phos in the present of Et_3N. We have isolated the palladium dimeric complex and confirmed with X-ray crystallography. Form the X-ray crystallographic data, the palladacycle formation is through the 3-C-H position from the indolyl scaffold (Figure 6.1).



1

Figure 6.1 Palladium complex isolated from the reaction mixture

To investigate the catalytic reactivity of the palladium complex **1**, we applied palladium complex 1 with additional three-fold of ligand in the coupling reaction. The result showed that palladium complex **1** displayed essentially the same reactivity as in the *in-situ* generated catalyst. Moreover, if we substitute the

proton on the indole 3-position to a methyl group, the catalytic activity of this ligand drops significantly to the coupling of aryl tosylates. By combining these observations, we found that the indole 3-position may play an important role in the aryl sulfonates coupling reaction. Also, the potential provided from the proton at the indole 3-position for the formation of palladacycle may also crucial for the activation of aryl sulfonates.

However, these observations are different from the Buchwald and coworkers' reports. In fact, Pd/X-Phos system also catalyst the Suzuki coupling of aryl tosylates. However, there is no palladacycle formed between the palladium and X-Phos while only Pd-C(ipso) was observed from the palladium complex (Figure 6.2).[230] The prevention of the formation of palladacycle by substituting the isopropyl groups at the *ortho*-position may account for the catalytic reactivity of the X-Phos.

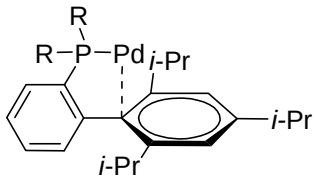


Figure 6.2 Pd-$C_{(ipso)}$ interaction form with the palladium and X-Phos

During investigation of the room temperature Suzuki coupling of aryl mesylates, we found that the pre-complex procedure performed with the

methanol form a sharp peak in ^{31}P NMR spectrum while other solvents did not give such a sharp signal. After deducing form the 2D-NMR (HSQC and HMBC), we found that the sharp peak is induced from a phosphonium salt that phosphorus atom is attached to the 3-position of the indole ring. The exact structure was then confirmed by X-ray crystallography (Figure 6.3).

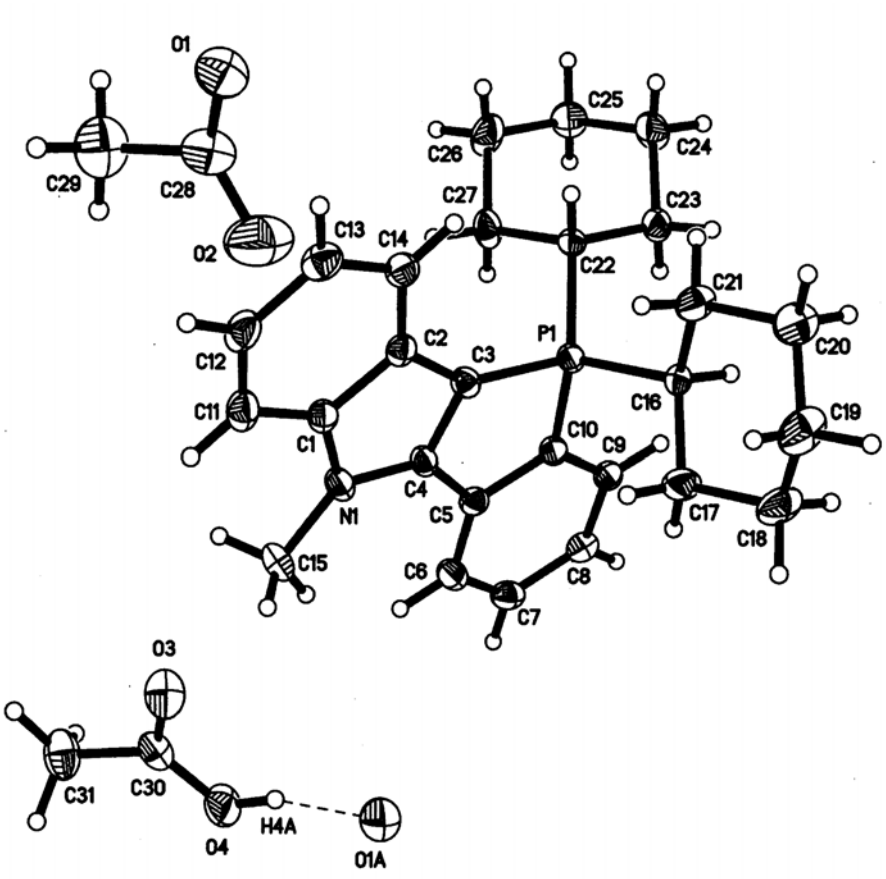


Figure 6.3 ORTEP representation of the isolated phosphonium salt (30% probability ellipsoids)

Table 6.5 Crystal Data and Structure Refinement of Phosphonium Salt

Empirical formula	$P(C_6H_{11})_2(C_{15}H_{11}N)\cdot CH_3COO\cdot CH_3COOH$	
Formula weight	521.61	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 10.9129(7) Å	$\alpha = 90°$.
	b = 14.7871(10) Å	$\beta = 104.412(2)°$.
	c = 18.5181(11) Å	$\gamma = 90°$.
Volume	2894.2(3) $Å^3$	
Z	4	
Density (calculated)	1.197 Mg/m^3	
Absorption coefficient	0.130 mm^{-1}	
F(000)	1120	
Crystal size	0.50 x 0.50 x 0.40 mm^3	
Theta range for data collection	1.78 to 27.30°.	
Index ranges	-14<=h<=13, -18<=k<=15, -22<=l<=23	
Reflections collected	21373	
Independent reflections	6326 [R(int) = 0.0755]	
Completeness to theta = 27.59°	97.1 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9498 and 0.9378	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6326 / 0 / 325	
Goodness-of-fit on F^2	1.004	
Final R indices [I>2sigma(I)]	R1 = 0.0754, wR2 = 0.2160	
R indices (all data)	R1 = 0.1713, wR2 = 0.2631	
Largest diff. peak and hole	0.586 and -0.438 $e.Å^{-3}$	

Table 6.6 Selected Bond Distances (Å) and Angles (˚) for Phosphonium Salt

Bond distances (Å)			
P(1)-C(3)	1.735(2)	P(1)-C(10)	1.807(2)
P(1)-C(16)	1.8011(18)	P(1)-C(22)	1.8175(17)

Bond angles (˚)			
C(3)-P(1)-C(16)	114.44(9)	C(3)-P(1)-C(22)	112.45(2)
C(3)-P(1)-C(10)	93.14(10)	C(16)-P(1)-C(22)	111.35(3)
C(16)-P(1)-C(10)	110.36(9)	C(10)-P(1)-C(22)	113.99(7)

Recently, some research groups reported the palladacycle precursor in which the palladium is complexing with the phenylethylamine is a highly useful palladium source for catalysis (Figure 6.4).[231,232] The reductive elimination of the palladacycle to form indoline can effectively reduce Pd(II) to Pd(0) which is active center for the oxidative addition of the substrates.

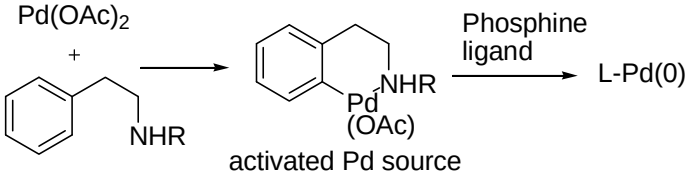


Figure 6.4 Palladacycle precursor for the coupling reactions

In our system, the pre-complex of $Pd(OAc)_2$/CM-Phos to form palladacycle and than formation of phosphonium salt may support that the indolyl phosphine ligand scaffold assist the pre-activation of the palladium catalyst and generating the L-Pd(0). The pre-activation of the palladium catalyst can smoothly be preformed in the methanol under room temperature and generating the active L-Pd(0). It may be accounted for the reason that methanol is an effective solvent for the room temperature Suzuki coupling of aryl mesylates. However, the exact reasons to account for the catalytic activity of CM-phos are still unclear and under investigation.

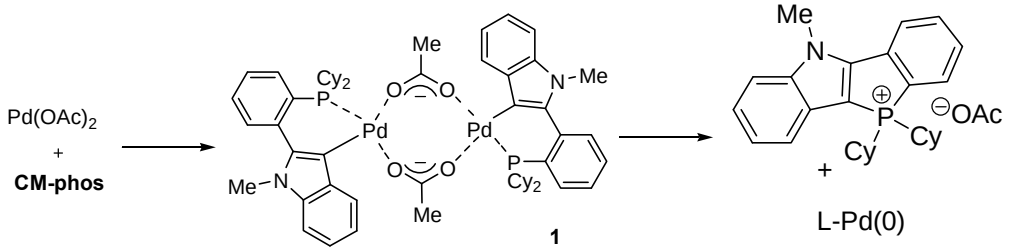


Figure 6.5 Pre-activation of the palladium catalyst

6.3 Conclusion

In conclusion, we have succeeded in showing the first room temperature Suzuki-Miyaura coupling of unactivated aryl mesylates under atmospheric condition. The Pd/**CM-phos** catalyst system has displayed excellent reactivity in the coupling of aryl and heteroaryl mesylates with various organoboron-nucleophiles including arylboronic acids, alkylboronic acids, pinacol esters and trifluoroborate salts in room temperature. Moreover, these reactions can be performed in air atmosphere without any need of special experimental precautions, thus rendering this method highly attractive for small- and large-scale synthesis.

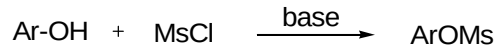
6.4 Experimental Section

6.4.1 General Considerations

Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. All Suzuki-Miyaura reactions were performed in screw cap vials (approx. 8 mL volume) in the presence of a Teflon coated magnetic stirrer bar (4.5 mm × 12 mm). Tetrahydrofuran (THF) was distilled from sodium and sodium benzophenone ketyl under nitrogen.[150] *tert*-Butanol was distilled from sodium under nitrogen.[150] Water was distilled from 0.25% of solid NaOH and 0.05% of $KMnO_4$. Methanol of high moisture content was distilled from calcium hydride. Most commercially available arylboronic acids were used as received. Some arylboronic acids might require further recrystallization depending on the received conditions. K_2CO_3 and Na_2CO_3 were purchased from Fluka. Thin layer chromatography was performed on Merck precoated silica gel 60 F_{254} plates. Silica gel (Merck, 70-230 and 230-400 mesh) was used for column chromatography. Melting points were recorded on an uncorrected Büchi Melting Point B-545 instrument. ^{1}H NMR spectra were recorded on a Bruker (400 MHz) spectrometer or Varian (500 MHz) spectrometer. Spectra were referenced internally to the residual proton resonance

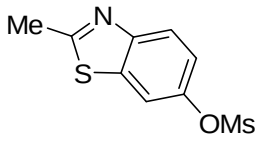
in $CDCl_3$ (δ 7.26 ppm), or with tetramethylsilane (TMS, δ 0.00 ppm) as the internal standard. Chemical shifts (δ) were reported as part per million (ppm) in δ scale downfield from TMS. ^{13}C NMR spectra were referenced to $CDCl_3$ (δ 77.0 ppm, the middle peak). ^{31}P NMR spectra were referenced to 85% H_3PO_4 externally. Coupling constants (*J*) were reported in Hertz (Hz). Mass spectra (EI-MS and ES-MS) were recorded on a HP 5989B Mass Spectrometer. High-resolution mass spectra (HRMS) were obtained on a Brüker APEX 47e FT-ICR mass spectrometer (ESIMS). GC-MS analysis was conducted on a HP 5973 GCD system using a HP5MS column (30 m × 0.25 mm). The products described in GC yield were accorded to the authentic samples/dodecane calibration standard from HP 6890 GC-FID system. Compounds described in the literature were characterized by comparison of their ^{1}H, and/or ^{13}C NMR spectra to the previously reported data. The procedures in this section are representative, and thus the yields may differ from those reported in the tables.

6.4.2 Preparation of Aryl Mesylates



4-*tert*-Butylphenyl mesylate[213], 4-methoxyphenyl mesylate[108], 4-acetylphenyl mesylate[108], 4-benzoylphenyl mesylate[214], 4-acetyl-2-methoxyphenyl mesylate[215], 1,3-Benzodioxol-5-ol mesylate[216], 4-formyl-2-methoxyphenyl mesylate[217], 3-pyridyl mesylate[218], 4-cyanophenyl mesylate[108], 4-(methoxycarbonyl)phenyl mesylate[108], 2-methoxyphenyl mesylate[233], 2-naphthyl mesylate[234], and 4-(ethoxycarbonyl)phenyl mesylate[235] were prepared from their corresponding phenols with MsCl in the presence of triethylamine in CH_2Cl_2 according to the literature method.[190]

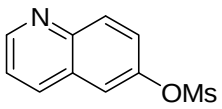
2-Methyl-5-benzothiazol mesylate



General procedures for preparation of aryl mesylate: To a stirred solution of 5-hydroxy-2-methylbenzothiazole (3.30 g, 20 mmol) in anhydrous dichloromethane (20 mL) cooled to 0 °C was added distilled triethylamine (4.17 mL, 30 mmol). To this was added mesyl chloride (1.94mL, 25 mmol) dropwise *via* syringe over 15 min. The reaction was stirred at 0 °C for 1 hour then quenched with water and the phases separated. The aqueous layer was extracted

with dichloromethane (3 × 100 mL) and the combined organics were dried over MgSO4 and concentrated in *vacuo*. The crude products were purified by column chromatography on silica gel using DCM/hexane solvent mixtures as the eluent to obtain the titled compound in 38% yield, 1.85 g, as a white solid. mp 119.5-120.8 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) 2.76 (s, 3H), 3.12 (s, 3H), 7.24 (dd, *J*=2.3Hz, 8.7Hz, 1H), 7.74-7.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) 20.0, 37.1, 115.4, 118.9, 122.1, 134.4, 147.4, 153.7, 169.6; MS (EI): *m/z* (relative intensity) 243 (M^+, 35), 164 (100), 136 (28), 122 (15), 95 (18). HRMS: calcd. for $C_9H_9N_1O_3S_2$: 243.0018, found 243.0023.

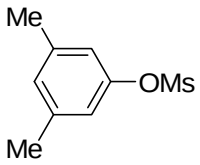
6-(Mesyloxy)quinoline



General procedures for the preparation of aryl mesylate were as follows. 6-Hydroxyquinoline (2.9 g, 20 mmol) was used to afford the titled compound in 58% yield, 2.59 g, as a deep purple solid. M.p. 84.6-86.2 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.15 (s, 3H), 7.32-7.35 (m, 1H), 7.52-7.55 (m, 1H), 7.67 (d, *J*=2.6Hz, 1H), 8.04-8.07 (m, 2H), 8.83-8.85 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 37.4, 119.2, 121.8, 124.0,128.1, 131.6, 135.7, 146.4, 146.4, 150.7; MS (EI): *m/z* (relative intensity) 223 (M^+, 63), 145 (60), 116 (100), 89 (30), 63

(10). HRMS: calcd. for $C_{10}H_9N_1O_3S_1$: 223.0298, found 223.0292.

3,5-Dimethylphenyl mesylate.



General procedures for the preparation of aryl mesylate were as follows. 3,5-Dimethylphenol (2.44 g, 20 mmol) was used to afford the titled compound in 95% yield, 3.80 g, as white crystals. M.p. 41.7-43.4 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.30 (s, 3H), 3.07 (s, 3H), 6.88 (s, 2H), 6.93 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 36.8, 119.1, 128.7, 139.7, 149.0; MS (EI): *m/z* (relative intensity) 200 (M^+, 65), 122 (100), 107 (20), 91 (30), 77 (30). HRMS: calcd. for $C_9H_{12}O_3S_1$: 200.0502, found 200.0507.

6.4.3. General Procedures for Initial Ligand and Reaction Condition Screenings

General procedure for screening: $Pd(OAc)_2$ (4.5 mg, 0.020 mmol) and ligand (Pd:L = 1:2) were loaded into 8 mL screw-capped vials equipped with a Teflon-coated magnetic stirring bar. 1 mL solvent was then added, and the vials were closed. The mixture was stirred vigorously for 60 seconds. The substrates and base were then loaded into the vials in the following order: *1*. K_2CO_3 (3.0 mmol), *2*. 4-*tert*-Butylphenyl mesylate (1.0 mmol) and *3*. 4-methylphenylboronic acid (2.0 mmol). 2.0 mL of solvent was finally added. The vials were closed and the mixture was stirred at room temperature (28-32^{o}C) for the time indicated. After completion of reaction, water (~2 ml), ethyl acetate (~3 mL), and dodecane (227 μL, internal standard) were added to the vials. The organic layer was subject to GC analysis. The GC yield obtained was previously calibrated by authentic sample/dodecane calibration curve.

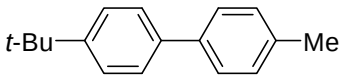
6.4.4. General Procedures for Suzuki-Miyaura Couplings of Aryl Mesylates

General procedure for Suzuki-Miyaura coupling of aryl mesylates: $Pd(OAc)_2$ (2.3 mg, 0.010 mmol) and ligand (Pd:L = 1:2) were loaded into 8 mL screw-capped vials equipped with a Teflon-coated magnetic stirring bar. 1 mL methanol was then added, and the vials were closed. The mixture was stirred vigorously for 60 seconds. The mixture turned reddish-purple. The substrates and base were then loaded into the vials in the following order: *1*. Base (3.0 mmol), *2*. Aryl mesylate (1.0 mmol) and *3*. Arylboronic acid (2.0 mmol). 2.0 mL of solvent was finally added. The vials were closed and the mixture was stirred at room temperature (~28-32^{o}C) for the time indicated. After completion of reaction, water (~2 ml) and ethyl acetate (~3 mL) were added to the vials. The completion of reaction was judged by GC analysis. The organic layer was separated and the aqueous layer was washed with EtOAc. The filtrate was concentrated under reduced pressure. The crude products were purified by flash column chromatography on silica gel (230-400 mesh) to afford the desired product.

General procedure for Suzuki-Miyaura coupling of aryl mesylates by using water as solvent: $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) and ligand (Pd:L = 1:4) were loaded into 8 mL screw-capped vials equipped with a Teflon-coated magnetic stirring bar. 1 mL methanol was then added, and the vials were closed. The mixture was stirred vigorously for 60 seconds. The mixture turned reddish-purple. The methanol was then evaporated under high vacuum. Aryl mesylate (1.0 mmol), arylboronic acid (2.0 mmol) and base (3.0 mmol) were loaded into the tube. The solvent water (3.0 mL) was then added. The tube was stirred at room temperature for 1 minute and then placed into a preheated oil bath (110 ^{o}C) for the time period as indicated. After completion of reaction, ethyl acetate (~5 mL), was added to the vials. The completion of reaction was judged by GC analysis. The organic layer was separated and the aqueous layer was washed with EtOAc. The filtrate was concentrated under reduced pressure. The crude products were purified by flash column chromatography on silica gel (230-400 mesh) to afford the desired product.

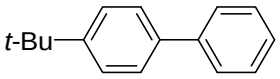
6.4.5. Characterization Data of the Coupling Products

4-Methyl-4'-*tert*-butylbiphenyl (Table 6.2, entry 1,2).[220]



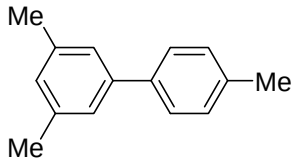
Hexane, R_f=0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.66 (s, 9H), 2.66 (s, 3H), 7.72-7.83 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 31.3, 34.4, 125.6, 126.5, 126.7, 129.4, 136.5, 138.1, 138.2, 149.7; MS (EI): *m/z* (relative intensity) 224 (M^+, 33), 209 (100), 193 (5), 181 (14), 165 (10).

4-*tert*-Butylbiphenyl (Table 6.2, entries 3).[175]



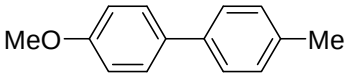
Hexane, R_f=0.55; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.72 (s, 9H), 7.59-7.64 (m, 1H), 7.72-7.82 (m, 4H), 7.85-7.92 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.3, 34.4, 125.6, 126.7, 126.9, 128.6, 138.2, 140.9, 150.0; MS (EI): *m/z* (relative intensity) 210 (M^+, 35), 195 (100), 178 (20), 167 (30).

1-(4-Methylphenyl)-3,5-dimethylbenzene (Table 6.2, entry 4)[236]



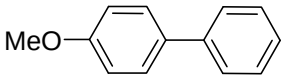
Pure Hexane, R_f=0.55; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.7 (s, 9H), 7.29 (s, 1H), 7.52-7.54 (m, 4H), 7.81 (d, *J*= 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 21.3, 124.8, 126.6, 126.9, 128.5, 129.2, 129.3, 136.5, 138.0, 138.5, 141.1; MS (EI): *m/z* (relative intensity) 196 (M^+, 100), 181 (45), 165(35).

4-Methoxy-4'-methylbiphenyl (Table 6.2, entry 5, 6) [87]



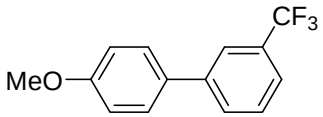
EA:Hexane = 1:20, R_f=0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.52 (s, 3H), 3.93 (s, 3H), 7.10 (d, *J*= 8.6 Hz, 2H), 7.36 (d, *J*= 8.0 Hz, 2H), 7.60 (d, *J*= 8.0 Hz, 2H), 7.65 (d, *J*= 8.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 55.1, 114.0, 126.4, 127.8, 129.3, 133.5, 136.1, 137.8, 158.8; MS (EI): *m/z* (relative intensity) 198 (M^+, 100), 183 (65), 155 (35).

4-Phenylanisole (Table 6.2, entry 7).[71]



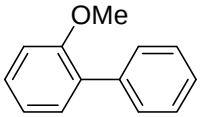
EA:Hexane = 1:20, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.85 (s, 3H), 6.98 (d, *J*=8.7 Hz, 2H), 7.28-7.32 (m, 1H), 7.42 (t, *J*=7.8 Hz, 2H), 7.52-7.56 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.0, 114.1, 126.5, 127.9, 128.3, 128.6, 133.5, 140.6, 159.0; MS (EI): *m/z* (relative intensity) 184 (M^+, 100), 169 (50), 141 (50), 115 (40).

4-Methoxy-3'-(triflоromethyl)biphenyl (Table 6.2, entries 8)[87]



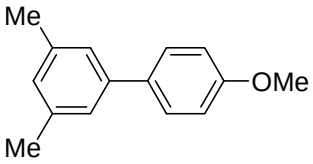
EA:Hexane = 1:20, R_f=0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.90 (s, 3H), 7.05-7.08 (m, 2H), 7.53-7.65 (m, 4H), 7.76 (d, *J*= 7.6 Hz, 1H), 7.91 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.0, 114.3, 122.9, 123.2, 123.2, 125.6, 128.1, 128.3, 129.1, 129.2, 129.8, 130.5, 130.8, 131.1, 131.4, 132.0, 141.5, 159.7; MS (EI): *m/z* (relative intensity) 252 (M^+, 100), 237 (35), 209 (40), 183 (10).

2-Phenylanisole (Table 6.2, entry 9) [237]



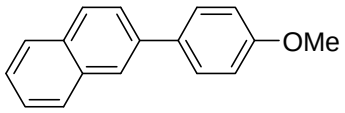
EA:Hexane = 1:20, R_f=0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.99 (s, 3H), 7.20 (d, *J*= 8.2 Hz, 1H), 7.28 (t, *J*= 7.4 Hz, 1H), 7.53-7.61 (m, 3H), 7.67 (t, *J*= 7.7 Hz, 2H), 7.83 (d, *J*= 7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.2, 111.0, 120.6, 126.7, 127.8, 128.4, 129.4, 130.5, 130.7, 138.4, 156.3; MS (EI): *m/z* (relative intensity) 184 (M^+, 100), 169 (60), 152 (13), 141 (35), 151 (37).

4-(3,5-Dimethylphenyl)anisole (Table 6.2, entry 10) [238]



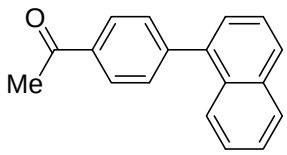
EA:Hexane = 1:20, R_f=0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.62 (s, 3H), 4.00(s, 3H), 7.19 (d, *J*= 8.6 Hz, 3H), 7.45 (s, 2H), 7.77 (d, *J*= 8.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 54.9, 113.9, 124.5, 127.9, 128.1, 133.7, 137.9, 140.6, 158.8; MS (EI): *m/z* (relative intensity) 212 (M^+, 100), 197 (55), 169 (22), 153 (17).

2-(4-Methoxyphenyl)naphthalene (Table 6.2, entries 11) [190]



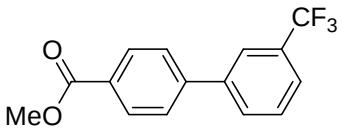
EA:Hexane = 1:20, R_f=0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.90 (s, 3H), 7.07 (d, *J*= 8.6 Hz, 2H), 7.50-7.57 (m, 2H), 7.72 (d, *J*= 8.5 Hz, 2H), 7.77 (m, 1H), 7.90-7.95 (m, 3H), 8.05 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.2, 114.1, 124.9, 125.3, 125.5, 126.1, 127.5, 128.0, 128.3, 128.3, 132.2, 133.5, 133.7, 138.0, 159.1; MS (EI): *m/z* (relative intensity) 234 (M^+, 100), 219 (55), 189 (30), 165 (13).

4'-(1-Naphthyl)acetophenone(Table 6.3, entry 1) [239]



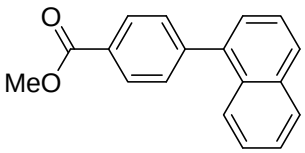
EA:Hexane = 1:9, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.67 (s, 3H), 7.41-7.59 (m, 6H), 7.89-7.94 (m, 3H), 8.08 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.3, 125.0, 125.2, 125.7, 126.1, 126.6, 128.0, 128.1, 129.9, 130.8, 133.5, 135.6, 138.6, 145.3, 197.4; MS (EI): *m/z* (relative intensity) 246 (M^+, 88), 231 (100), 202 (90).

Methyl 4-(3-trifluoromethylphenyl)benzoate(Table 6.3, entries 2) [240]



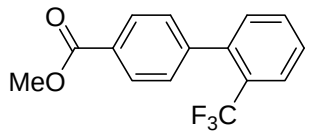
EA:Hexane = 1:20, R_f=0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.90 (s, 3H), 7.05-7.08 (m, 2H), 7.53-7.65 (m, 4H), 7.76 (d, *J*= 7.6 Hz, 1H), 7.91 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.0, 114.3, 122.9, 123.2, 123.2, 125.6, 128.1, 128.3, 129.1, 129.2, 129.8, 130.5, 130.8, 131.1, 131.4, 132.0, 141.5, 159.7; MS (EI): *m/z* (relative intensity) 252 (M^+, 100), 237 (35), 209 (40), 183 (10).

Methyl 4-(1-naphthalenyl)Benzoate (Table 6.3, entry 3) [241]



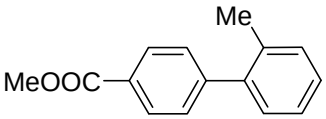
EA:Hexane = 1:20, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.02 (s, 3H), 7.43-7.47 (m, 2H), 7.49-7.56 (m, 2H), 7.60 (d, *J*= 8.2 Hz, 2H), 7.90-7.95 (m, 3H), 8.25 (d, *J*= 8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 51.8, 125.0, 125.2, 125.6, 126.0, 126.6, 128.0, 128.1, 128.7, 129.3, 129.8, 130.9, 133.5, 138.7, 145.2, 166.6; MS (EI): *m/z* (relative intensity) 262 (M^+, 100), 231 (50), 202 (80).

Methyl 4-(2-trifloromethyl)benzoate (Table 6.3, entry 4) [242]



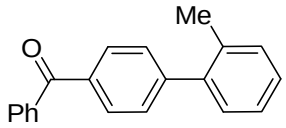
EA:Hexane = 1:20, R_f=0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.89 (s, 3H), 7.27 (d, *J*= 7.5 Hz, 1H), 7.38 (d, *J*= 8.0 Hz, 2H), 7.43 (t, *J*= 7.6 Hz, 1H), 7.52 (t, *J*= 7.5 Hz, 1H), 7.72 (d, *J*= 7.8 Hz, 1H), 8.07 (d, *J*= 8.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 51.8, 119.8, 122.5, 125.2, 125.9, 125.9, 127.7, 127.9, 127.9, 128.2, 128.5, 128.8, 129.3, 129.5, 131.2, 131.3, 140.0, 144.3, 166.5; MS (EI): *m/z* (relative intensity) 280 (M^+, 45), 249 (100), 201 (65).

Methyl 4-(2-methylphenyl)benzoate (Table 6.3, entry 5). [243]



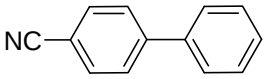
EA:Hexane = 1:20, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.30 (s, 3H), 3.97 (s, 3H), 7.26-7.33 (m, 4H), 7.43 (d, *J* = 8.0 Hz, 2H), 8.15 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 51.7, 125.6, 127.5, 128.3, 128.9, 129.1, 129.2, 130.2, 134.8, 140.5, 146.4, 166.6; MS (EI): *m/z* (relative intensity) 226 (M^+, 100), 195 (98), 168 (60), 152 (50), 139 (7).

4-(2'-Tolyl)benzophenone (Table 6.3, entry 6,7; Table 6.4, entry 1).[126]



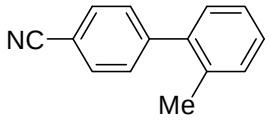
EA:Hexane = 1:20, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.35 (s, 3H,), 7.31-7.33 (m, 4H), 7.47-7.55 (m, 4H), 7.60-7.64 (m, 1H), 7.90-7.93 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.2, 125.7, 127.6, 128.0, 128.9, 129.3, 129.7, 130.3, 132.1, 134.9, 135.6, 137.4, 140.5, 146.0, 196.0; MS (EI): *m/z* (relative intensity) 272 (M^+, 70), 195 (100), 164 (40), 152 (40), 105 (40).

4-Cyanobiphenyl (Table 6.3, entry 8).[224]



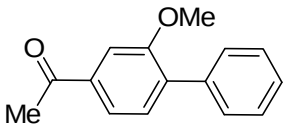
DCM:Hexane = 1:9, R_f=0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.50 (m, 3H), 7.56-7.58 (m, 2H), 7.61-7.67 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 110.4, 118.5, 126.8, 127.2, 128.3, 128.7, 132.1, 138.6, 145.1; MS (EI): *m/z* (relative intensity) 179 (M^+, 100), 151 (15).

4-Cyanobiphenyl (Table 6.3, entry 9).[224]



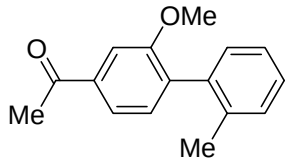
DCM:Hexane = 1:9, R_f=0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.30 (s, 3H), 7.22 (d, *J*= 7.1 Hz, 1H), 7.30 (m, 3H), 7.42 (d, *J*= 8.1 Hz, 2H), 7.67 (d, *J*= 8.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.8, 110.1, 118.4, 125.6, 127.8, 128.9, 129.4, 130.2, 131.4, 134.4, 139.4, 146.1; MS (EI): *m/z* (relative intensity) 193 (M^+, 100), 178 (15), 165 (40).

3'-Methoxy-4'-phenylacetophenone (Table 6.3, entry 10).[223]



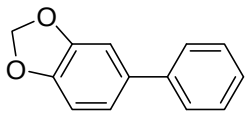
EA:Hexane = 1:9, R_f=0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.62 (s, 3H), 3.84 (s, 3H), 7.37-7.46 (m, 4H), 7.56-7.62 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.2, 55.2, 109.5, 121.4, 127.3, 127.7, 129.1, 130.4, 135.2, 136., 137.0, 156.3, 197.2; MS (EI): *m/z* (relative intensity) 226 (M^+, 80), 211 (100), 183 (10), 168 (30).

4-Acetyl-2-methoxy-2'-methylbiphenyl (Table 6.3, entry 11) [84]



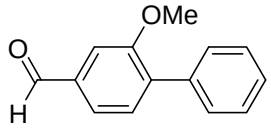
EA:Hexane = 1:9, R_f=0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.19 (s, 3H), 2.68 (s, 3H), 3.84 (s, 3H), 7.21 (d, *J*= 7.1 Hz, 1H), 7.27-7.33 (m, 4H), 7.64-7.66 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5, 26.3, 55.2, 109.1, 121.2, 125.2, 127.5, 129.3, 129.4, 130.7, 135.9, 136.1, 137.3, 156.6, 197.4; MS (EI): *m/z* (relative intensity) 240 (M^+, 75), 225 (100), 182 (20), 165 (20), 152 (20).

3,4-Methylenedioxybiphenyl (Table 6.3, entry 12) [244]



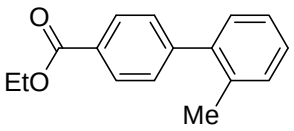
EA:Hexane = 1:4, R_f=0.7; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.05 (s, 2H), 7.01 (d, *J*= 8.0 Hz, 1H), 7.19-7.24 (m, 2H), 7.45 (t, *J*= 7.5 Hz, 1H), 7.54 (t, *J*= 7.5 Hz, 2H), 7.67 (d, *J*= 7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 100.94, 107.4, 108.3, 120.4, 126.7, 126.7, 128.5, 135.3, 140.7, 146.9, 147.9; MS (EI): *m/z* (relative intensity) 198 (M^+, 100), 139 (50).

2-Methoxy-4-formylbiphenyl (Table 6.3, entry 13) [245]



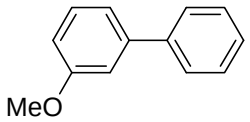
EA:Hexane = 1:9, R_f=0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.85 (s, 3H), 7.38-7.52 (m, 6H), 7.59 (d, *J*= 7.9 Hz, 2H), 10.00 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.3, 109.3, 123.9, 127.5, 127.8, 129.1, 130.9, 136.4, 136.7, 136.9, 156.7, 191.4; MS (EI): *m/z* (relative intensity) 212 (M^+, 100), 169 (25), 152 (13), 139 (26), 115 (18).

Ethyl 2'-methylbiphenyl-4-carboxylate (Table 6.3, entry 14) [246]



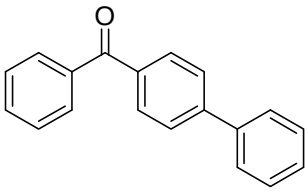
EA:Hexane = 1:9, R_f=0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (t, *J*= 7.1 Hz, 3H), 2.31 (s, 3H), 4.46 (q, *J*= 7.1 Hz, 2H), 7.25-7.32 (m, 4H), 7.43 (d, *J*= 8.2 Hz, 2H), 8.17 (d, *J*= 8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 20.1, 60.6, 125.6, 127.5, 128.7, 128.9, 129.1, 129.2, 130.2, 134.85, 140.6, 146.3, 166.1; MS (EI): *m/z* (relative intensity) 240 (M^+, 75), 212 (18), 195 (100), 165 (55), 152 (45).

3-Methoxybiphenyl (Table 6.4, entry 2)[247]



EA:Hexane = 1:20, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.97 (s, 9H), 7.05-7.07 (m, 1H), 7.33-7.37 (m, 2H), 7.49-7.57 (m, 2H), 7.59 (t, *J*= 7.3 Hz, 2H), 7.77 (d, *J*= 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.0, 112.5, 112.7, 119.5, 127.0, 127.2, 128.6, 129.6, 140.9, 142.6, 159.8; MS (EI): *m/z* (relative intensity) 184 (M^+, 100), 154 (30), 141 (32), 115 (32).

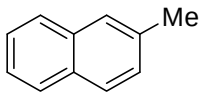
4'-Phenylbenzophenone (Table 6.4, entry 3)[245]



EA:Hexane = 1:9, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (t, *J*= 7.2 Hz, 1H), 7.47-7.52 (m, 4H), 7.60 (d, *J*= 7.3 Hz, 1H), 7.66 (d, *J*= 7.4 Hz, 2H), 7.71 (d, *J*= 8.2 Hz, 2H), 7.87 (d, *J*= 7.2 Hz, 2H), 7.92 (d, *J*= 8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 126.7, 127.0, 127.9, 128.1, 128.7, 129.7, 130.5, 132.1, 135.9, 137.5, 139.6, 144.9, 195.9; MS (EI): *m/z* (relative intensity) 258 (M^+, 70),

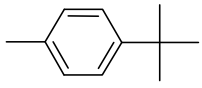
181 (100), 152 (50).

2-Methylnaphthalene (Table 6.4, entry 4) [248]



Pure Pentane, R_f=0.55; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.68 (s, 3H), 7.48 (d, *J*= 8.3 Hz, 1H), 7.56-7.64 (m, 2H), 7.77 (s, 1H), 7.90-7.98 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 124.8, 125.8, 126.8, 127.1, 127.5, 127.6, 128.0, 131.6, 133.6, 135.3; MS (EI): *m/z* (relative intensity) 142 (M^+, 100), 115 (30).

1-*tert*-Butyl-4-methylbenzene (Table 6.4, entry 5) [249]



Pure Pentane, R_f=0.55; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (s, 9H), 2.47 (s, 3H), 7.27 (d, *J*= 8.0 Hz, 2H), 7.44 (d, *J*= 8.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 31.4, 34.2, 125.1, 128.7, 134.7, 148.1; MS (EI): *m/z* (relative intensity) 148 (M^+, 25), 133 (100), 115 (10), 105 (50).

Chapter 7 Palladium-Catalyzed Amination of Aryl Mesylates

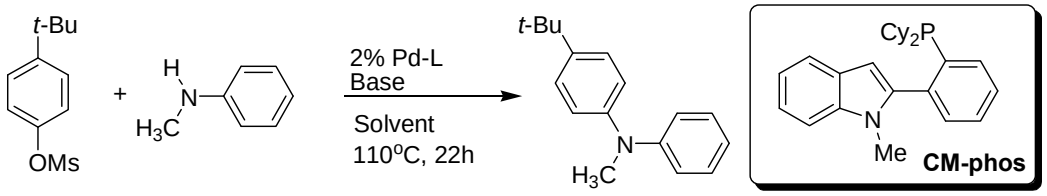
7.1 Introduction

Palladium-catalyzed amination of aryl halides occurs under mild conditions with many catalysts, but there are only a few examples that demonstrate the more challenging amination of aryl sulfonates such as aryl tosylates and benzenesulfonates. As the literature study in the Introduction shows, inert aryl mesylates have limited use in cross-coupling processes. There is only limited precedent for palladium-catalyzed cross-coupling of aryl mesylates, with only one publication related to carbonylation reaction in 2008.[204] To the best of our knowledge, aryl mesylates have never been applied in amination reactions. This area remains highly challenging as mesylates are regarded as the least active sulfonate leaving group. In the previous chapters, our palladium-indolyl phosphine catalyst system has been successfully applied for the amination of aryl tosylates as well as the Suzuki coupling of aryl tosylates and aryl mesylates. With a series of effective C-P type indolyl phosphines in hand, we attempted to investigate the palladium-catalyzed amination of aryl mesylates.

7.2 Results and Discussion

7.2.1 Screening for Optimizing Amination Reaction Condition

Table 7.1 Screening Table for Amination of Aryl Mesylates[a]



entry	base	Solvent	GC yield (%)[b]
1	K_3PO_4	*t*-BuOH	93%
2	K_3PO_4	Toluene	57%
3	K_3PO_4	*t*-BuOH/Toluene 1:1	22%
4	K_3PO_4	DMF	74%
5	K_3PO_4	THF	19%
6	*t*-BuOK	Toluene	0%
7	*t*-BuOK	*t*-BuOH	0%
8	$K_3PO_4 \cdot H_2O$	*t*-BuOH	42%
9	CsF	*t*-BuOH	84%
10	Cs_2CO_3	*t*-BuOH	9%
11	K_2CO_3	*t*-BuOH	94%
12	Na_2CO_3	*t*-BuOH	17%

[a]Reaction conditions: ArOMs (1.0 mmol), Amine (1.5 mmol), Base (2.5 mmol), $Pd(OAc)_2$/CM-phos (mol% as indicated), $PhB(OH)_2$ (0.04 mmol) *t*-BuOH (3.0 mL), at 110 °C under N_2 [b]Calibrated GC yields were reported using dodecane as the internal standard.

In the preliminary study, the same reaction conditions in the amination of aryl tosylates was directly employed in the amination of aryl mesylates. Electronically neutral 4-*tert*-butylphenyl mesylate and N-methylaniline were used as the model substrate for the screening (Table 7.1).

The reaction parameters such as base and solvent effects were investigated. We found that K_2CO_3, K_3PO_4 and CsF were effective base for the coupling of 4-*tert*-butylphenyl mesylate with N-methylaniline to give the desired product. However, Cs_2CO_3, Na_2CO_3 and NaO*t*-Bu were ineffective base for the amination of aryl mesylates. Among those ineffective bases, a large amount of unreactive 4-*tert*-butylphenyl mesylates remained if Na_2CO_3 was used as base. On the other hand, in the presence of Cs_2CO_3 and NaO*t*-Bu as base in the amination reaction, a significant amount of phenolic side products were observed as indicated by GC-MS analysis. These results implied that the ineffectiveness of the Na_2CO_3 as base in the amination reaction might be caused by the weak basicity of Na_2CO_3 being too insufficient to take up the proton from the amine during the course of reaction. On the contrary, the basicity of Cs_2CO_3 and NaO*t*-Bu was too strong that caused ineffectiveness in the amination of aryl mesylate. Aryl mesylates can be regarded as a protecting group that can easily undergo alkaline hydrolysis with a strong base to form phenoxide in the presence of polar solvent.[250]

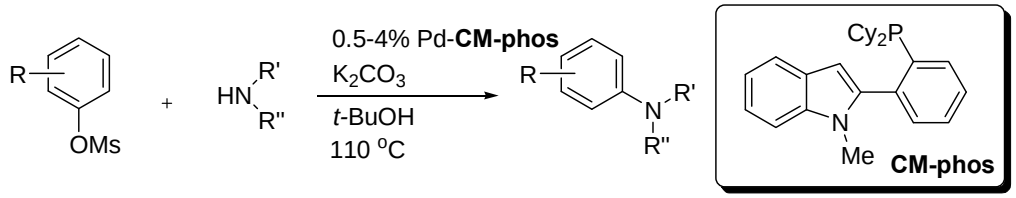
Therefore, choosing a suitable base sufficient to take up the proton from the amine but not hydrolysis the mesylates is a more difficult process for the coupling reaction of aryl sulfonates than the corresponding aryl halides. In fact, in some of the aryl sulfonates coupling reactions, only few bases are effective. This problem will be further discussed in the next chapter.

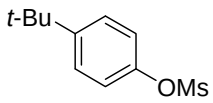
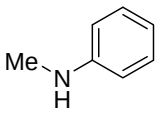
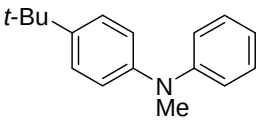
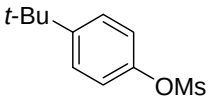
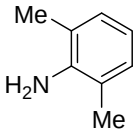
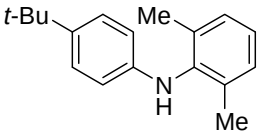
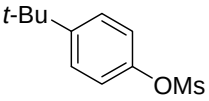
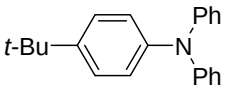
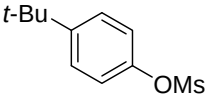
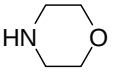
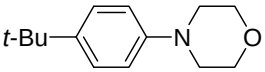
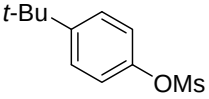
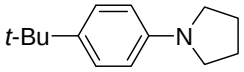
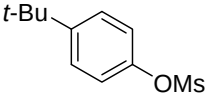
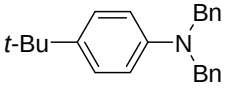
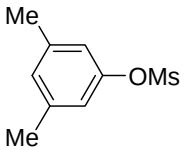
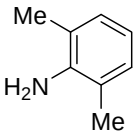
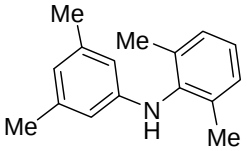
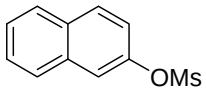
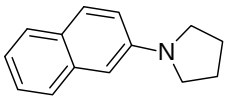
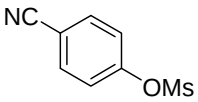
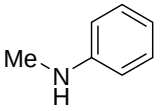
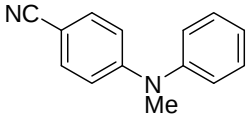
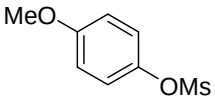
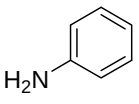
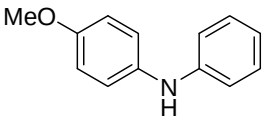
In the solvent screening, *t*-BuOH was found to be the best solvent of choice while DMF and toluene gave only moderate yield of the product. Therefore, *t*-BuOH was selected as solvent and K_3PO_4 or K_2CO_3 was selected as base conditionally.

7.2.2 Pd-Catalyzed Amination of Aryl Mesylates with Primary and Secondary Amines.

The scope of the amination reaction with regard to the aryl mesylates and amines was next examined (Table 7.2). The coupling of unactivated aryl mesylate with N-methylaniline could be performed with 0.5 mol% of Pd (Table 7.2, entry 2). Sterically hindered aniline and diphenylamine were transformed to their corresponding product in good yields (Table 7.2, entries 3-4). Secondary cyclic and acyclic amines were effective coupling partners (Table 7.2, entries 6-7). Cyano group was compatible under these reaction conditions (Table 7.2, entry 10). Moreover, the deactivated *p*-anisole mesylate was found to be a feasible substrate (Table 7.2, entry 11).

Table 7.2 Pd-Catalyzed Amination of Aryl Mesylates[a]



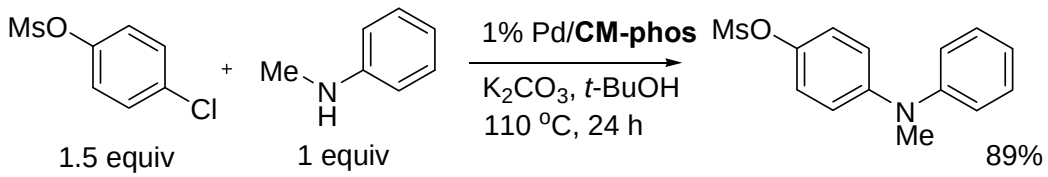
entry	ArOMs	amine	product	mol% Pd	% yield[b]
1				2%, 24 h	93
2				0.5%, 24 h	96
3				1%, 24 h	90
4				4%, 24 h	80
5				1%, 18 h	90
6[c]				2%, 24 h	93
7[c]				4%, 24 h	81
8				1%, 24 h	87
9				2%, 24 h	85
10				1%, 24 h	82
11				2%, 24 h	78

[a]Reaction conditions: ArOMs (1.0 mmol), Amine (1.5 mmol), K_2CO_3 (2.5 mmol), $Pd(OAc)_2$/CM-phos (mol% as indicated), $PhB(OH)_2$ (0.04 mmol) *t*-BuOH (4.0 mL), at 110 °C under N_2 for indicated period of time [b]Isolated yields. [c]K_3PO_4 was used.

7.7.3 Pd-Catalyzed Amination of Aryl Mesylates with Nitrogen Heterocycles

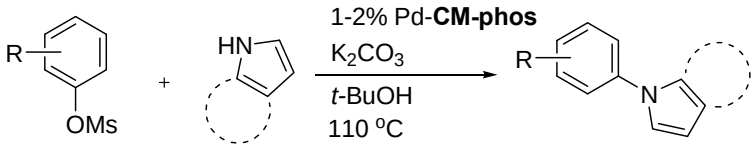
To further explore the effectiveness of the Pd/**CM-phos** catalytic system, a range of nitrogen heterocycles were investigated (Table 7.3). Indole and substituted indoles were N-arylated smoothly in good yields (Table 7.3, entries 1-4). Pyrrole and carbazole were effective substrates (Table 7.3, entries 5-6). Keto and methyl ester groups were compatible under these reaction conditions (Table 7.3, entries 7-8).

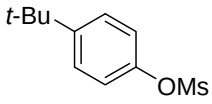
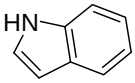
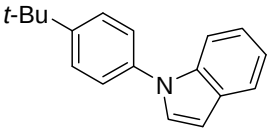
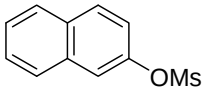
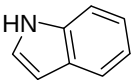
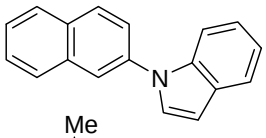
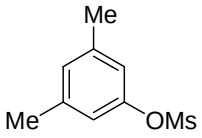
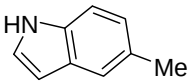
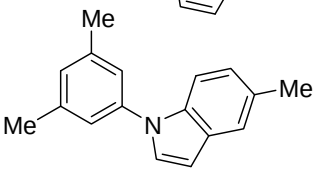
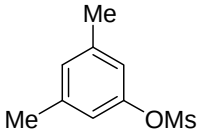
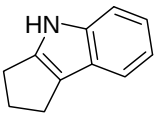
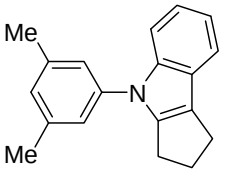
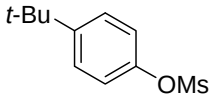
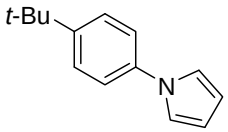
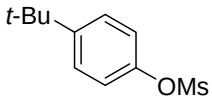
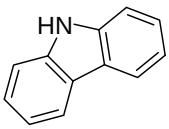
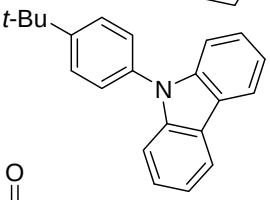
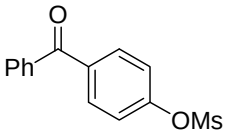
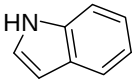
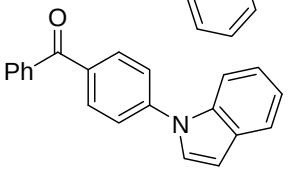
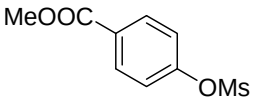
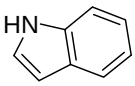
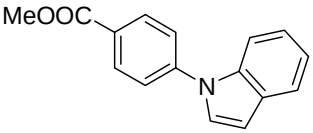
4-Chlorophenyl mesylate coupled with N-methylaniline was used to examine the selectivity of the Pd/**CM-phos** catalytic system. A highly selective aryl chloride coupling was observed.



Scheme 7.1 Selectivity experiment for the chloride and mesylate group

Table 7.3 Pd-Catalyzed N-Arylation of Nitrogen-Heterocycles[a]



entry	ArOMs	*N*-heterocycle	product	mol% Pd	% yield[b]
1				1%, 24 h	93
2				1%, 20 h	89
3				1%, 24 h	96
4				2%, 24 h	84
5				1%, 24 h	80
6[c]				2%, 24 h	98
7				1%, 24 h	88
8				1%, 24 h	79

[a]Reaction conditions: ArOMs (1.0 mmol), N-heterocycle (1.5 mmol), K_2CO_3 (2.5 mmol), $Pd(OAc)_2$/CM-phos (mol% as indicated), $PhB(OH)_2$ (0.04 mmol) *t*-BuOH (4.0 mL), at 110 °C under N_2 for indicated period of time. [b]Isolated yields. [c]ArOMs (1.5 mmol), carbazole (1.0 mmol) were used.

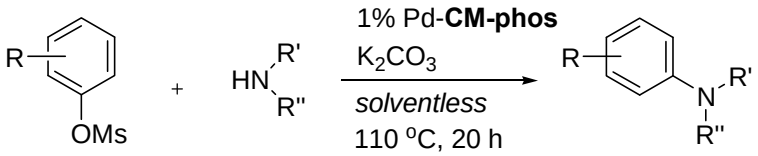
7.2.4 Solventless Pd-Catalyzed Amination of Aryl Mesylates

Removing organic solvents in chemical synthesis is important in the drive towards benign chemical technologies. Organic solvents are high on the list of toxic or otherwise damaging compounds because of the large volumes used in industry, and the difficulties in containing volatile compounds. One of the alternatives is the so-called solventless reactions that do not use any reaction medium. Advantages of solventless reactions, particularly those described herein, over organic or other reaction media include: (i) there is no reaction medium to collect, purify or recycle; (ii) the compounds formed are often sufficiently pure to circumvent extensive purification using chromatography, and in some cases the need for recrystallization: (iii) sequential solventless reactions are possible in high yielding systems; (iv) the reactions can be rapid, often reaching substantial completion in a few minutes compared to hours in organic solvents; (v) specialized equipment is usually not needed; (vi) energy usage can be much lower; (vii) the need for pre-formed salts and metal–metalloid complexes may often be dispensed with; (viii) functional group protection–deprotection can be avoided; (ix) lower capital outlay for equipment to set up industrial processes, and (x) considerable batch size reduction and processing cost savings are

achievable so that such solvent-free protocols are not only more environmentally friendly but also more economically feasible. [251,252]

Owing to those attractive advantages of a solvent free catalytic system, we take a step forward to attempt the solventless condition for the amination of aryl mesylates.

Table 7.4 Pd-Catalyzed Solventless Amination of Aryl Mesylates[a]



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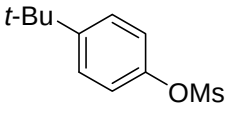
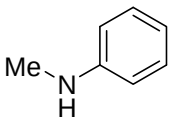
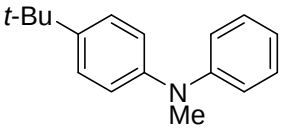
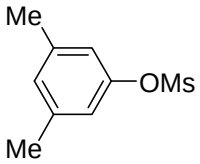
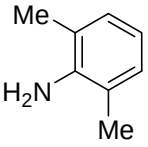
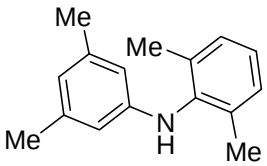
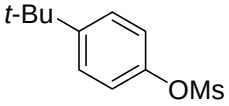
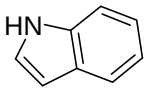
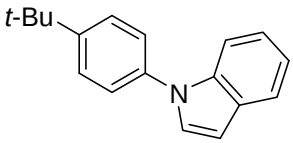
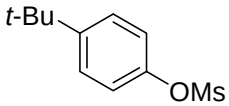
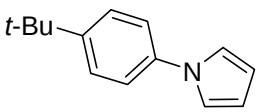
1				93
2				97
3				91
4				83

[a]Reaction conditions: ArOMs (1.0 mmol), amine (5.0 mmol), K_2CO_3 (2.5 mmol), $Pd(OAc)_2$/CM-phos (1 mol%), $PhB(OH)_2$ (0.04 mmol) in solventless conditions at 110 °C under N_2 (reaction times are unoptimized). [b]Isolated yields.

Solvent-free reactions are commonly defined as those employing less than 5 equiv of one reactant with respect to the substrate.[253] Therefore, 5 equiv of amines were employed in the amination reaction.

In general, the amination of aryl mesylate can be successfully performed under solvent-free reaction conditions without deleterious effect (Table 7.4). Moreover, kinetic study showed that the rate of reaction in the solvent-free condition was slightly higher than the rate of reaction in the present of organic solvent, which might be due to the higher concentration of the reactants. Anilines, indole and pyrrole were successfully coupled with aryl mesylates to generate the corresponding products in good to excellent yields.

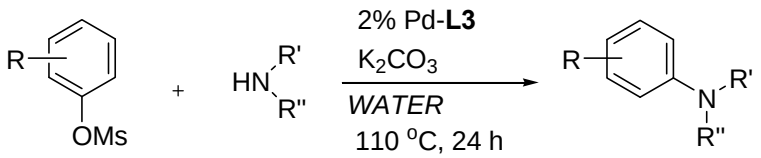
7.2.5 Aqueous Pd-Catalyzed Amination of Aryl Mesylates

Although solventless reaction has many merits, there are some disadvantages in practical industrial synthesis. For examples, the use of solventless reaction may lead to formation of hot spots and the possibility of runaway reactions especially for the highly exothermic reactions. Also, it is difficult to handle solid or highly viscous material. Solventless reactions may be more appropriate for small volume commodity chemicals than high throughput.[251] These problems are solvable using developments in engineering reactor technology. However, the use of solvents is sometimes necessary.

If solvents are required in a reaction, water would be a possible alternative. There are many potential advantages of replacing those unnatural solvents with water. Firstly, water is much cheaper than those organic solvents. Secondly, water much safer than those flammables, explosives, and carcinogenics organic solvents. Last but not least, water is a unhazardous and environmental friendly alternative to the common organic solvents used in the chemical industry.[252] Aqueous transition metal-catalyzed reactions have attracted much attentions recently.[254,255] Aryl halides have been reported to be applicable in cross-coupling under aqueous medium. However, it is challenging to catalyze the aryl sulfonates couplings under aqueous conditions as they are known to decompose

easily via alkaline hydrolysis to form the phenolic side products.

Table 7.5 Pd-Catalyzed Amination of Aryl Mesylates in Aqueous Medium[a]



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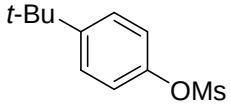
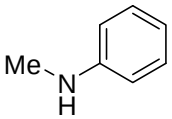
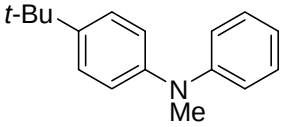
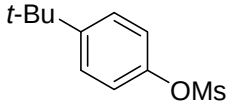
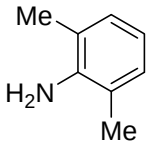
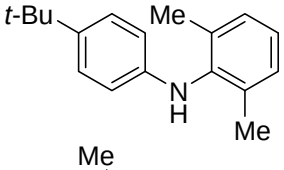
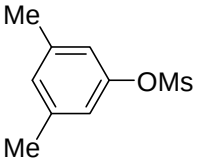
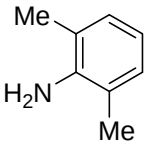
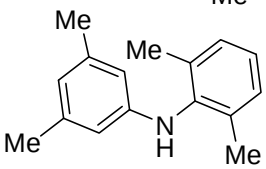
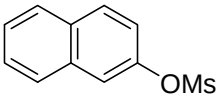
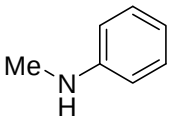
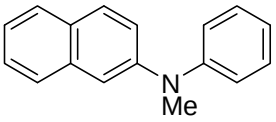
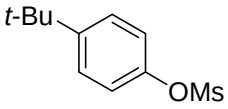
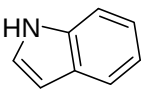
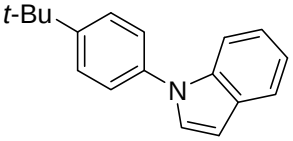
1				90
2				77
3				89
4				86
5				75

[a]Reaction conditions: ArOMs (1.0 mmol), amine (2.0 mmol), K_2CO_3 (2.5 mmol), $Pd(OAc)_2$/CM-phos (2 mol%, unoptimized), $PhB(OH)_2$ (0.04 mmol), water (3.0 mL) at 110 °C under N_2 (Note: reaction parameters are unoptimized). [b]Isolated yields.

To our delight, the Pd/**CM-Phos** catalyst system can affect the amination of aryl mesylate even in water medium (Table 7.5). Under the unoptimized reaction conditions for this aqueous catalysis, anilines and indole were still successfully coupled with aryl mesylates to furnish the corresponding products in good yields.

7.3 Conclusion

In summary, we have succeeded in showing the first amination of aryl mesylates. CM-phos in combination with $Pd(OAc)_2$ precatalyst can handle a range of aryl mesylates as well as the amine nucleophiles, including anilines, aliphatic amines, indole, pyrrole and carbazole. We have also shown the first examples of aryl mesylate coupling that can be performed under aqueous basic medium without any deleterious effect.

7.4 Experimental Section

7.4.1 General Considerations

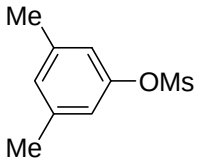
Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. All Suzuki-Miyaura reactions were performed in Rotaflo® (England) resealable screw-capped Schlenk flasks (approx. 20 mL volume) in the presence of a Teflon coated magnetic stirrer bar (3 mm × 8 mm). Toluene and tetrahydrofuran (THF) were distilled from sodium and sodium benzophenone ketyl under nitrogen, respectively.[150] *tert*-Butanol was distilled from sodium under nitrogen.[150] Most commercially available amines were used as received. Some amines might require distillation depending on the conditions. K_2CO_3 and K_3PO_4 were purchased from Fluka. Thin layer chromatography was performed on Merck precoated silica gel 60 F_{254} plates. Silica gel (Merck, 70-230 and 230-400 mesh) was used for column chromatography. Melting points were recorded on an uncorrected Büchi Melting Point B-545 instrument. ^{1}H NMR spectra were recorded on a Bruker (400 MHz) spectrometer. Spectra were referenced internally to the residual proton resonance in $CDCl_3$ (δ 7.26 ppm), or with tetramethylsilane (TMS, δ 0.00 ppm) as the internal standard. Chemical shifts (δ) were reported as part per

million (ppm) in δ scale downfield from TMS. ^{13}C NMR spectra were referenced to $CDCl_3$ (δ 77.0 ppm, the middle peak). ^{31}P NMR spectra were referenced to 85% H_3PO_4 externally. Coupling constants (*J*) were reported in Hertz (Hz). Mass spectra (EI-MS and ES-MS) were recorded on a HP 5989B Mass Spectrometer. High-resolution mass spectra (HRMS) were obtained on a Brüker APEX 47e FT-ICR mass spectrometer (ESIMS). GC-MS analysis was conducted on a HP 5973 GCD system using a HP5MS column (30 m × 0.25 mm). The products described in GC yield were accorded to the authentic samples/dodecane calibration standard from HP 6890 GC-FID system. All yields reported refer to isolated yield of compounds estimated to be greater than 95% purity as determined by capillary gas chromatography (GC) or ^{1}H NMR. Compounds described in the literature were characterized by comparison of their ^{1}H, and/or ^{13}C NMR spectra to the previously reported data. The procedures in this section are representative, and thus the yields may differ from those reported in tables.

7.4.2. Preparation of Aryl Mesylates

4-*tert*-Butylphenyl mesylate[213], 4-methoxyphenyl mesylate[108], 2-naphyl mesylate[256], 4-benzoylphenyl mesylate[214], 4-cyanophenyl mesylate[108], and 4-(methoxycarbonyl)phenyl mesylate[108] were prepared from their corresponding phenols with MsCl in the presence of triethylamine in CH_2Cl_2 according to the literature method.[190]. Physical characterizations of new aryl mesylate that were prepared according to literature procedure are shown below.[190]

3,5-dimethylphenyl mesylate



Obtained in 95% yield as white crystals: mp 41.7-43.4 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.30 (s, 3H), 3.07 (s, 3H), 6.88 (s, 2H), 6.93 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 36.8, 119.1, 128.7, 139.7, 149.0; MS (EI): *m/z* (relative intensity) 200 (M^+, 65), 122 (100), 107 (20), 91 (30), 77 (30). HRMS: calcd. for $C_9H_{12}O_3S_1$: 200.0502, found 200.0507.

7.4.3 General Procedures for Initial Ligand and Reaction Conditions Screening

General procedure for screening: $Pd(OAc)_2$ (4.5 mg, 0.020 mmol) and ligand (Pd:L = 1:4) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The tube was evacuated and flushed with nitrogen for three times. Precomplexation was applied by adding freshly distilled dichloromethane and Et_3N into the tube. The palladium complex stock solution was stirred and warmed using a hair drier for about 1 to 2 minutes until the solvent started to boil. The solvent was then evaporated under high vacuum. 4-*tert*-Butylphenyl mesylate (1.0 mmol), base (2.5 mmol) and phenylboronic acid (0.04mmol) were loaded into the tube, and the system was further evacuated and flushed with nitrogen for three times. N-methylaniline (1.5 mmol) was also loaded into the tube. The solvent (3.0 mL) was added with stirring at room temperature for several minutes. The tube was then placed into a preheated oil bath (110 ^{o}C) and stirred for 22hr. After completion of reaction, the reaction tube was allowed to cool to room temperature. Ethyl acetate (~10 mL), dodecane (227 μL, internal standard) and water were added. The organic layer was subject to GC analysis. The GC yield obtained was previously calibrated by authentic sample/dodecane calibration curve.

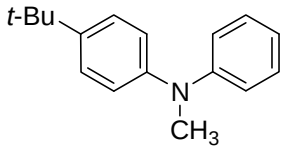
7.4.4 General Procedures for Palladium-Catalyzed Amination of Aryl Mesylates

General procedure for amination of aryl mesylates: $Pd(OAc)_2$ (2.3 mg, 0.010 mmol) and ligand (Pd:L = 1:4) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The tube was evacuated and flushed with nitrogen for several times. Precomplexation was applied by adding freshly distilled dichloromethane and Et_3N into the tube. The solution was stirred and warmed using a hair drier for about 1 to 2 minutes until the solvent started to boil. The solvent was then evaporated under high vacuum. Aryl mesylate (1.0 mmol), K_2CO_3 (2.5 mmol), solid amines and phenyl boronic acid (0.04 mmol) were loaded into the tube, and the system was further evacuated and flushed with nitrogen for several times. Liquid amines (1.5 mmol) were also loaded into the tube. The solvent *tert*-butanol (3-5 mL) was then added. The tube was stirred at room temperature for several minutes and then placed into a preheated oil bath (110 ^{o}C) for the time period as indicated in Tables. After completion of reaction as judged by GC analysis, the reaction tube was allowed to cool to room temperature and quenched with water and diluted with EtOAc. The organic layer was separated and the aqueous layer was washed with EtOAc. The filtrate

was concentrated under reduced pressure. The crude products were purified by flash column chromatography on silica gel (230-400 mesh) to afford the desired product.

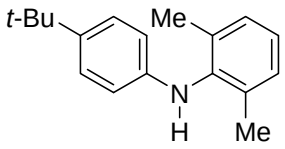
7.4.5 Characterization Data for Coupling Products

N-Methyl-N-(4-*tert*-butylphenyl)aniline (Table 7.2, entry 1, 2; Table 7.4, entry 1; Table 7.5, entry 1).[200]



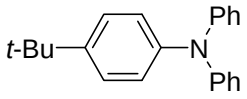
DCM:Hexane = 1:20, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.60 (s, 9H), 3.53 (s, 3H), 7.14 (t, *J*=7.2 Hz, 2H), 7.23-7.29 (m, 4H), 7.51 (t, *J*=7.4 Hz, 2H), 7.58 (d, *J*=1.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.4, 34.0, 40.1, 118.8, 120.1, 121.2, 125.9, 128.9, 144.5, 146.3, 149.0; MS (EI): *m/z* (relative intensity) 239 (M^+, 36), 224(100), 209 (9), 194 (3).

N-(4-*tert*-Butylphenyl)-2,6-dimethylbenzenamine (Table 7.2, entry 3; Table 7.5, entry 2).[257]



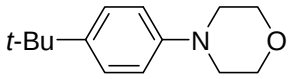
DCM:Hexane = 1:4, R_f=0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.62 (s, 9H), 2.52 (s, 6H), 5.31 (s,1H), 6.77 (d, *J*=8.5 Hz, 1H), 7.38-7.42 (m, 3H), 7.49 (d, *J*=8.54 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.2, 31.4, 33.7, 113.2, 125.3, 125.7, 128.4, 135.3, 138.6, 140.7, 143.6; MS (EI): *m/z* (relative intensity) 253 (M^+, 37), 238 (100), 223 (3), 194 (8).

N-(4-*tert*-Butylphenyl)-N-phenylbenzenamine (Table 7.2, entry 4).[125]



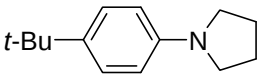
DCM:Hexane = 1:9, R_f=0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.51 (s, 9H), 7.12 (t, *J*=7.2 Hz, 2H), 7.20-7.27 (m, 6H), 7.38 (t, *J*=7.3 Hz, 4H), 7.44 (d, *J*=1.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.4, 34.2, 122.2, 123.8, 124.0, 126.0, 129.0, 145.0, 145.5, 147.9; MS (EI): *m/z* (relative intensity) 301 (M^+, 53), 286 (100), 271 (10), 244 (8), 167 (18).

4-(4-*tert*-Butylphenyl)morpholine (Table 7.2, entry 5).[258]



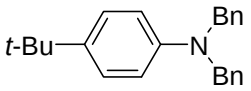
EA:Hexane = 1:20, R_f=0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 (s, 9H), 3.22 (t, *J*=4.8 Hz, 4H), 3.94 (t, *J*=4.9 Hz, 4H), 6.98 (d, *J*=8.7 Hz, 2H), 7.43 (d, *J*=8.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.2, 33.7, 49.3, 66.7, 115.2, 125.6, 142.4, 148.7; MS (EI): *m/z* (relative intensity) 219 (M^+, 27), 204 (100), 146 (30), 131 (9).

1-(4-*tert*-Butylphenyl)pyrrolidine (Table 7.2, entry 6).[55]



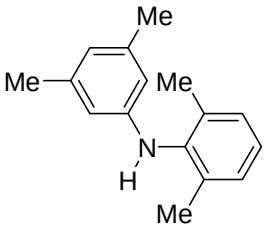
EA:Hexane = 1:4, R_f=0.6; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.52 (s, 9H), 2.14-2.18 (m, 4H), 3.44-3.48 (m, 1H), 6.74 (d, *J*=8.7 Hz, 2H), 7.47 (t, *J*=8.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.3, 31.5, 33.6, 47.5, 111.25, 125.7, 137.7, 145.7; MS (EI): *m/z* (relative intensity) 203 (M^+, 21), 188 (100), 173 (5).

4-*tert*-Butyl-N,N-dibenzylbenzenamine (Table 7.2, entry 7).[259]



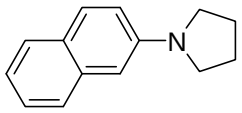
EA:Hexane = 1:4, R_f=0.6; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.64 (s, 9H), 4.95 (s, 4H), 7.06 (d, *J*=8.7 Hz, 2H), 7.53-7.64(m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.5, 33.6, 54.1, 112.0, 125.8, 126.6, 126.7, 128.5, 138.8, 139.0, 146.8; MS (EI): *m/z* (relative intensity) 329 (M^+, 55), 314 (100), 222 (13), 91 (37).

2,6-Dimethyl-N-(3,5-dimethylphenyl)benzenamine (Table 7.2, entry 8; Table 7.4, entry 2; Table 7.5, entry 3).



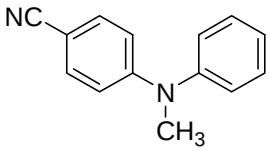
DCM:Hexane = 1:4, R_f=0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.48 (s, 6H), 2.49 (s, 2.49), 5.2 (s, 1H), 6.69 (s, 1H), 7.34-7.40 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.2, 21.3, 111.2, 120.1, 125.4, 128.3, 135.7, 138.3, 138.6, 146.1; MS (EI): *m/z* (relative intensity) 225 (M^+, 100), 210 (60), 195 (32), 180 (6). HRMS: calcd. for $C_{16}H_{19}NH^+$: 226.1596, found 226.1597.

N-(2-Naphthyl)pyrrolidine (Table 7.2, entry 9). [260]



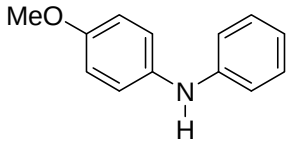
DCM:Hexane = 1:4, R_f=0.6; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.15-2.20 (m, 4H), 3.53-3.56 (m, 4H), 7.02 (m, 1H), 7.19-7.22 (m, 1H), 7.49 (t, *J*=7.7Hz, 1H), 7.68 (t, *J*=8.0Hz, 1H), 7.95-8.00 (m, 3H), 7.93-7.98 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.1, 47.4, 104.4, 115.5, 120.9, 125.6, 125.9, 126.1, 127.4, 128.5, 135.1, 145.6; MS (EI): *m/z* (relative intensity) 197 (M^+, 100), 180 (3), 167 (8), 154 (10), 141 (40), 127 (33), 115 (10).

4-(N-Methyl-N-phenylamino)benzonitrile (Table 7.2, entry 10).[261]



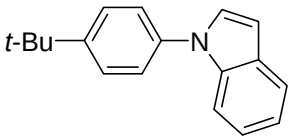
DCM:Hexane = 1:4, R_f=0.25; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.32 (s, 3H), 6.71 (d, *J*=8.9Hz, 2H), 7.17-7.26 (m, 3H), 7.35-7.43 (m, 4H), 8.00 (bs, 1H), 8.30 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 39.7, 98.7, 113.4, 119.9, 125.8, 126.0, 129.6, 132.7, 146.3, 151.5; MS (EI): *m/z* (relative intensity) 208 (M^+, 100), 192 (22), 167 (7), 129 (7).

N-(4-Methoxyphenyl)benzenamine (Table 7.2, entry 11).[201]



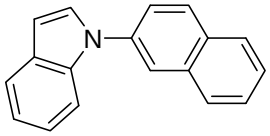
DCM:Hexane = 1:4, R_f=0.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.87 (s, 3H), 5.5 (bs, 1H), 6.93-7.00 (m, 5H), 7.15 (d, *J*=8.7Hz, 2H), 7.31 (t, *J*=7.7Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.3, 114.5, 115.5, 119.3, 121.9, 129.1, 135.6, 145.0, 155.0; MS (EI): *m/z* (relative intensity) 199 (M^+, 66), 184 (100), 167 (5), 154 (10), 128 (10).

1-(4-*tert*-Butylphenyl)-1H-indole (Table 7.3, entry 1; Table 7.4, entry 3, Table 7.5, entry 5)[262]



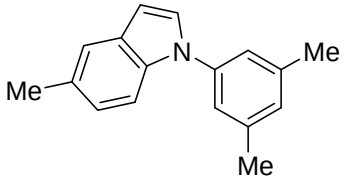
DCM:Hexane = 1:20, R_f=0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.69 (s, 9H), 6.98 (d, *J*=3.2Hz, 1H), 7.48-7.52 (m, 2H), 7.59 (d, *J*=3.2Hz, 1H), 7.68-7.71(m, 2H), 7.77-7.79 (m, 2H), 7.88-7.90 (m, 1H), 8.00-8.03 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.3, 34.5, 103.2, 110.5, 120.1, 121.0, 122.1, 123.8, 126.3, 127.9, 129.1, 135.8, 137.1, 149.2; MS (EI): *m/z* (relative intensity) 249 (M^+, 56), 234 (100), 219 (10), 206 (10).

1-(Naphthalen-2-yl)-1H-indole (Table 7.3, entry 2).[263]



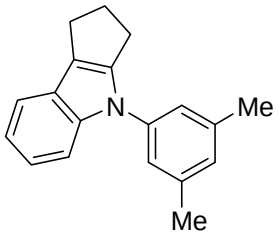
DCM:Hexane = 1:20, R_f=0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 (d, *J*=3.2Hz, 1H), 7.52-7.55 (m, 2H), 7.63 (d, *J*=3.2Hz, 1H), 7.71-7.75 (m, 3H), 7.81-7.84 (m, 1H), 7.92-7.94 (m, 1H), 8.01-8.11 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 103.7, 110.4, 120.4, 121.1, 121.6, 122.3, 122.9, 125.8, 126.7, 127.5, 127.6, 127.9, 127.9, 129.3, 131.5, 133.6, 15.8, 137.0; MS (EI): *m/z* (relative intensity) 243 (M^+, 100), 215 (20), 120 (17).

5-Methyl-1-(3,5-dimethylphenyl)-1H-indole (Table 7.3, entry 3)[264]



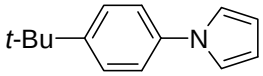
DCM:Hexane = 1:20, R_f=0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.53 (s, 6H), 2.63 (s, 3H), 6.72 (m, 1H), 7.11 (s, 1H), 7.20 (d, *J*=7.8Hz, 1H), 7.26 (m, 2H), 7.41 (m, 1H), 7.62-7.64 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 102.7, 110.3, 120.6, 121.7, 123.7, 127.8, 127.9, 129.3, 129.5, 134.1, 139.2, 139.8; MS (EI): *m/z* (relative intensity) 235 (M^+, 100), 218 (8), 204(7), 191(2).

1,2,3,4-Tetrahydro-4-(3,5-dimethylphenyl)cyclopenta[b]indole (Table 7.3, entry 4)



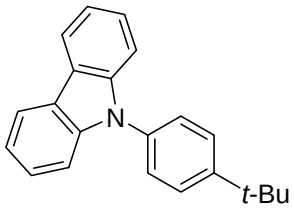
DCM:Hexane = 1:9, R_f=0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.58 (s, 6H), 2.70-2.77 (m, 2H), 3.07-3.14 (m, 4H), 7.16 (s, 1H), 7.27 (s, 2H), 7.33-7.35 (m, 2H), 7.66-7.72 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 24.5, 26.1, 28.2, 110.8, 118.5, 119.8, 119.9, 120.6, 122.4, 124.8, 127.7, 138.7, 139.0, 140.9, 145.5; MS (EI): *m/z* (relative intensity) 261 (M^+, 100), 246 (23), 231 (11), 218 (5). HRMS: calcd. for $C_{19}H_{19}NH^+$: 262.1596, found 262.1599.

1-(4-*tert*-Butylphenyl)-1H-pyrrole (Table 7.3, entry 5).[265]



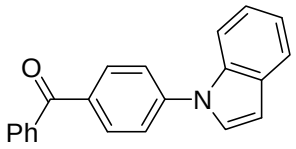
DCM : Hexane = 1:9, R_f=0.6; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.63 (s, 9H), 6.64 (t, *J*=2.1Hz, 2H), 7.35 (t, *J*=2.1Hz, 2H), 7.58 (d, *J*=8.6Hz, 2H), 7.69 (d, *J*=8.6Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.2, 34.3, 110.0, 119.1, 120.0, 126.2, 138.2, 148.3; MS (EI): *m/z* (relative intensity) 199 (M^+, 40), 184 (100), 169 (14), 156 (16), 143 (7).

9-(4-*tert*-butylphenyl)-9H-carbazole (Table 7.3 entry 6)[266]



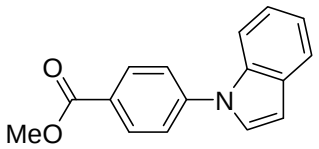
DCM:Hexane = 1:9, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.56 (s, 9H), 7.41 (m, 2H), 7.50-7.60 (m, 6H), 7.70 (d, *J*=8.5Hz, 2H), 8.28 (d, *J*=7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.3, 34.7, 109.8, 119.6, 120.1, 123.2, 125.7, 126.5, 126.6, 134.8, 140.9, 150.2; MS (EI): *m/z* (relative intensity) 299 (M^+, 100), 284 (98), 269 (11), 256 (8), 241 (10), 166 (17), 128 (23).

(4-(1H-indol-1-yl)phenyl)(phenyl)methanone (Table 7.3, entry 7).[267]



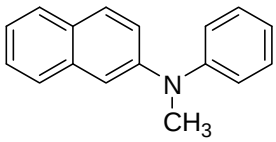
DCM:Hexane = 3:7, R_f=0.15; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (d, *J*=3.2Hz, 1H), 7.25-7.37 (m, 2H), 7.42 (d, *J*=3.3Hz, 1H), 7.54-7.68 (m, 5H), 7.74-7.79 (m, 2H), 7.93 (d, *J*=7.1Hz, 2H), 8.01 (d, *J*=8.5Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 104.7, 110.3, 120.7, 121.1, 122.6, 127.1, 128.1, 129.5, 129.6, 131.5, 132.2, 134.4, 135.0, 137.2, 142.9, 195.0; MS (EI): *m/z* (relative intensity) 297 (M^+, 100), 220 (23), 191 (23).

Methyl 4-(1H-indol-1-yl)benzoate (Table 7.3, entry 8) [262]



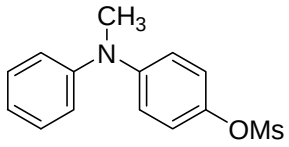
DCM:Hexane = 3:7, R_f=0.15; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.00 (s, 4H), 6.77-6.78 (m, 1H), 7.25-7.33 (m, 2H), 7.37 (d, *J*=3.3Hz, 1H), 7.56-7.60 (m, 2H), 7.67-7.77 (m, 2H), 8.20-8.24 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.0, 104.7, 110.4, 120.8, 121.2, 122.6, 122.9, 127.1, 127.2, 129.6, 131.0, 135.1, 143.4, 166.1; MS (EI): *m/z* (relative intensity) 251 (M^+, 100), 220 (27), 191 (27), 165 (5).

N-methyl-N-phenylnaphthalen-2-amine (Table 7.5, entry 4).[268]



DCM:Hexane = 1:9, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.62 (s, 3H,), 7.28 (t, *J*=7.2Hz, 1H), 7.37 (d, *J*=8.2Hz, 2H), 7.48-7.51 (m, 1H), 7.54-7.60 (m, 4H), 7.67 (t, *J*=7.7Hz, 1H), 7.90-7.99 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.3, 114.3, 121.2, 121.6, 121.8, 123.5, 126.1, 126.6, 127.4, 128.4, 128.9, 129.1, 134.5, 146.4, 148.8; MS (EI): *m/z* (relative intensity) 233 (M^+, 100), 217 (35), 204 (5), 192 (10).

4-(N-Methyl-N-phenylamino)phenyl methanesulfonate (Scheme 7.1)



EA:Hexane = 1:4, R_f=0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.11 (s, 3H), 3.32 (s, 3H), 6.95 (d, *J*=9.0Hz, 2H), 7.08-7.16 (m, 3H), 7.17 (d, *J*=9.0Hz, 2H), 7.34 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 36.5, 40.0, 118.6, 122.2, 122.3, 122.7, 129.2, 141.9, 147.8, 148.0; MS (EI): *m/z* (relative intensity) 277 (M^+, 16), 198 (100), 183 (8), 168 (4). HRMS: calcd. for $C_{14}H_{15}NO_3SH^+$: 278.0851, found 278.0864.

Chapter 8 Palladium-Indolyl Phosphine-Catalyzed Hiyama Cross-Coupling of Aryl Mesylates

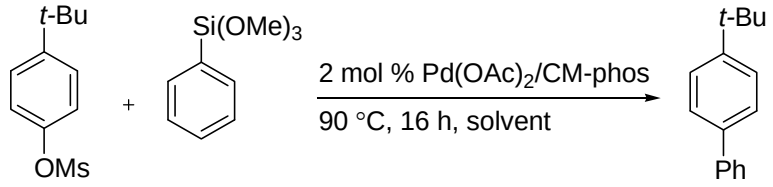
8.1 Introduction

Pd-catalyzed Hiyama coupling of organosilicon compounds with organic electrophiles is an important method for C-C bond formation.[269] Although some arylsiloxanes are not commercially available and are hard to prepare, this reaction has advantages over traditional cross-coupling protocols[269], such as the Suzuki–Miyaura (organoboron) and Stille (organostannane) coupling reactions, because the siloxane method eliminates the purification difficulties associated with organoboron reagents[270], and the toxic byproducts associated with the use of organotin compounds[271,272]. Moreover, silicon compounds are more stable toward air/moisture than organomagnesium and organozinc reagents. Although couplings of arylhalides with organosilicon compounds have been well developed, during our investigation period, aryl mesylates have never been applied in the Hiyama coupling reactions. With a series of indolyl phosphines which demonstrated exceedingly catalytic reactivity towards palladium-catalyzed Suzuki coupling and amination reaction of aryl sulfonates in hand, we were prompted to investigate the Hiyama couplings of aryl mesylates.

8.2 Results and Discussion

8.2.1 Screening for Optimization Reaction Condition

Table 8.1 Initial Screening on the Feasibility of Hiyama Cross-Coupling of Aryl Mesylate[a]



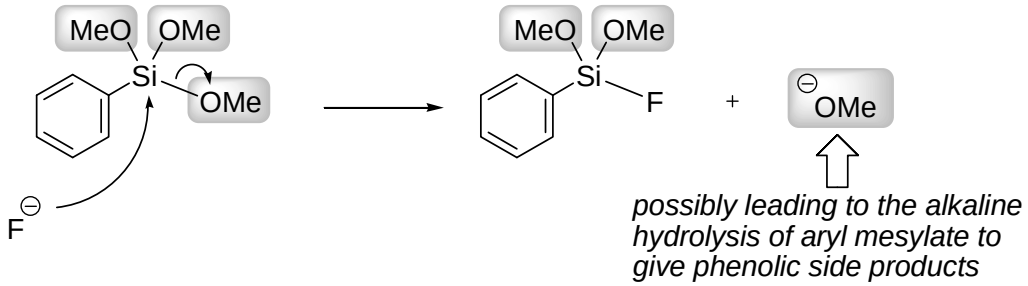
entry	promotor/base	solvent	% yield[b]
1	TBAF	toluene	23
2	TBAF	THF	14
3	TBAF	DMF	4
4	TBAF	THF/*t*-BuOH (1:1)	58
5	TBAF	*t*-BuOH	81
6	TBAF	toluene/*t*-BuOH (1:1)	83
7	CsF	*t*-BuOH	0
8	KF	*t*-BuOH	trace
9	K_2CO_3	*t*-BuOH	0
10	K_3PO_4	*t*-BuOH	0
11	Cs_2CO_3	*t*-BuOH	0
12[c]	TBAF	*t*-BuOH	8

[a]Reaction conditions: ArOMs (0.5 mmol), ArOMs:$PhSi(OMe)_3$:TBAF = 1:2:2; $Pd(OAc)_2$:CM-phos = 1:4; 90 °C for 16 h in the specified solvent (1.0 mL, total solvent volume) under N_2. [b]Calibrated GC yields were reported using tetra-decane as the internal standard. [c]4 mol % $Pd(OAc)_2$ was used at 60 °C.

In order to probe the feasibility of a Hiyama cross-coupling of an aryl mesylate, a series of screening experiments were carried out (Table 8.1). 4-*tert*-Butylphenyl mesylate and $PhSi(OMe)_3$ were used as the model substrates and 2 mol % of $Pd(OAc)_2$ with CM-phos ligand were used as the initial catalytic system for our prototypical reaction. Since the transmetallation of organosilanes proceeds smoothly after the activation by fluoride anion,[273] we initially applied TBAF as the promoter. Among the commonly used organic solvents we examined, *t*-BuOH and toluene/*t*-BuOH mixtures gave the best results (Table 8.1, entries 1-6). We next tested other fluoride salts. However neither CsF nor KF provided the desired product (Entries 7-8). In fact, similar results were also reported in the palladium-catalyzed Hiyama cross-coupling reaction of aryl halides.[272] One of the possible reasons proposed by Hiyama and coworkers for the low activity of these inorganic salts was the insolubility in the reaction media.[273] General inorganic bases such as K_2CO_3, K_3PO_4 and Cs_2CO_3 that cannot provide fluoride ion were found to be inferior in the reaction (Table 8.1, entries 9-11). Lowering the reaction temperature to 60°C significantly retarded the rate of reaction (Table 8.1, entry 12).

8.2.2 Additive Effect on the Hiyama Coupling Reaction

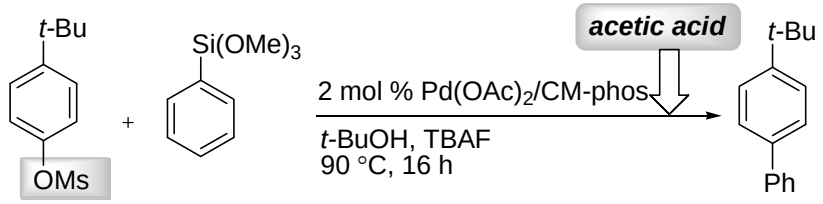
We routinely observed ~10-15% of problematical phenolic side products being formed during the course of the initial screenings as judged by GC-MS analyses. We wondered whether the formation of these phenolic side products was triggered by the alkaline hydrolysis of the aryl mesylate in the presence of the methoxide, which was generated by the nucleophilic cleavage of silyl ether using TBAF (Scheme 8.1).[274] In order to reduce side product formation, as well as to further increase the desired product yield, we introduced an acid additive to the reaction mixture (Table 8.2).



Scheme 8.1 Silyl Ether Cleavage by TBAF

Our rationale purpose for adding acetic acid to the reaction mixtures was to neutralize the methoxide anion, and thus to reduce the possibility of alkaline hydrolysis of the aryl mesylate. Gratifyingly, the desired product yield was enhanced when 0.25 equivalent of acetic acid was introduced (Table 8.2, Entry 1 *vs* 2). In general, the addition of 0.25-0.50 equivalent of acetic acid was sufficient to suppress the phenolic side product formation (Table 8.2, Entries 2-3). However, the addition of excess acetic acid could reduce the rate of reaction (Table 8.2, Entries 4-5).

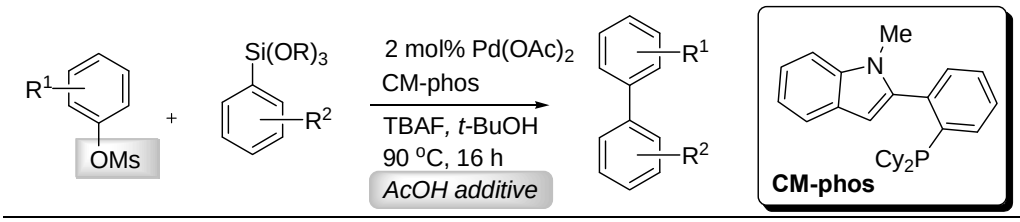
Table 8.2 Acid Additive Effect in Hiyama Coupling of ArOMs[a]

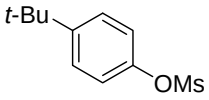
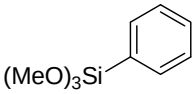
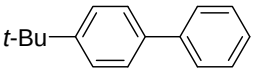
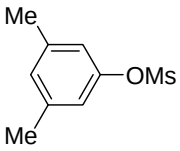
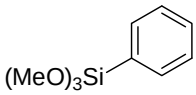
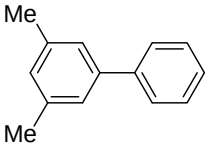
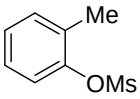
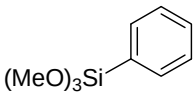
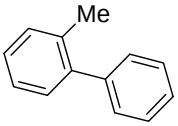


entry	acid additive[b]	% yield[c]
1	no AcOH added	75
2	0.25 equiv AcOH	88 (94)[d]
3	0.50 equiv AcOH	85
4[e]	1.00 equiv AcOH	(65)[d]
5[e]	2.00 equiv AcOH	(27)[d]

[a]Reaction conditions: ArOMs (0.5 mmol), ArOMs:$PhSi(OMe)_3$:TBAF = 1:2:2; $Pd(OAc)_2$:CM-phos = 1:4; 90 °C for 16 h in the specified solvent (1.0 mL, total solvent volume) under N_2 [b]Equivalence with respected to TBAF. [c]Isolated yields. [d]Calibrated GC yield in parentheses. [e]4 mol % of $Pd(OAc)_2$ was used, at 90 °C for 8 h.

Table 8.3 General Beneficial Effects of Acetic Acid



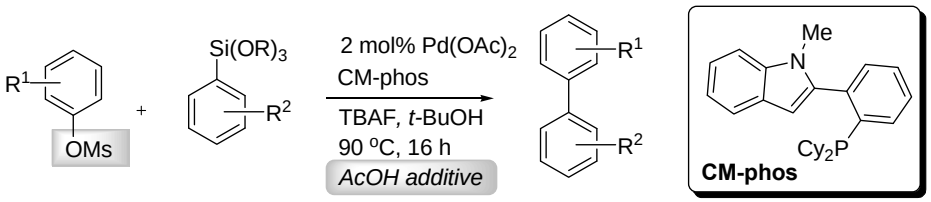
entry	ArOMs	Ar'Si(OR)$_3$	product	AcOH	% yield[b]
1				0.25 equiv	88
2				without AcOH	75
3				0.25 equiv	92
4				without AcOH	84
5				0.25 equiv	61
6				without AcOH	40

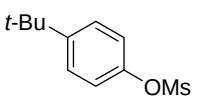
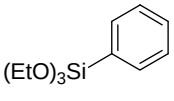
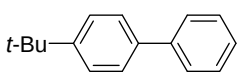
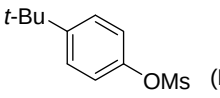
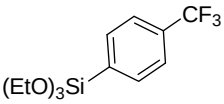
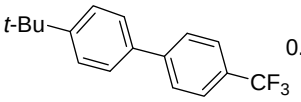
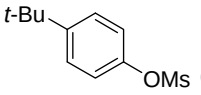
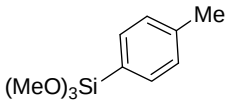
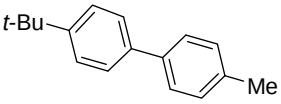
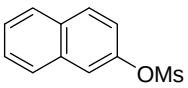
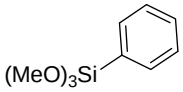
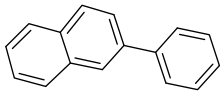
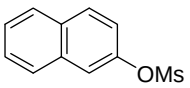
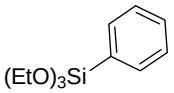
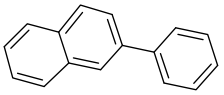
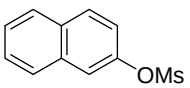
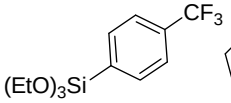
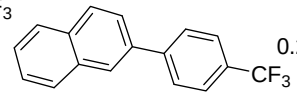
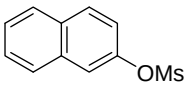
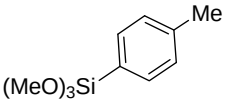
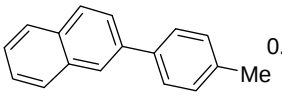
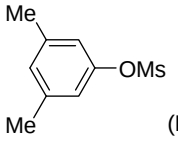
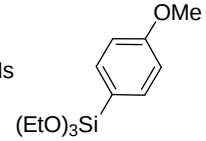
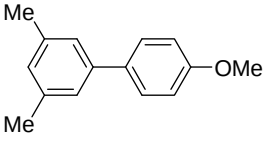
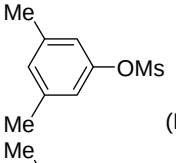
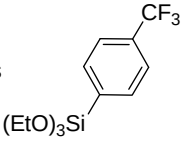
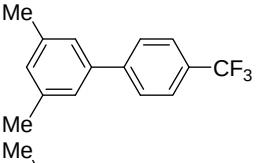
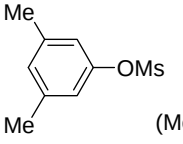
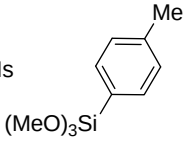
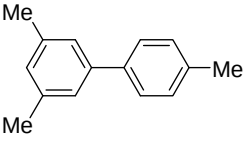
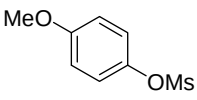
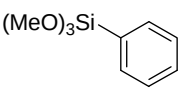
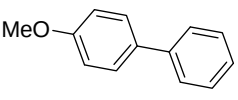
[a]Reaction conditions: ArOMs (0.5 mmol), ArOMs:PhSi(OMe)$_3$:TBAF = 1:2:2; Pd(OAc)$_2$:CM-phos = 1:4; 90 °C for 16 h in the specified solvent (1.0 mL, total solvent volume) under N_2. [b] Isolated yields.

Beneficial effects of the acid additive were generally found (Table 8.3, e.g. entries 1 *vs* 2, 3 *vs* 4 and 5 *vs* 6).

8.2.3 Palladium-Catalyzed Hiyama Coupling of Aryl Mesylates

Table 8.4 Pd-Catalyzed Hiyama Cross-Coupling of Neutral ArOMs[a]

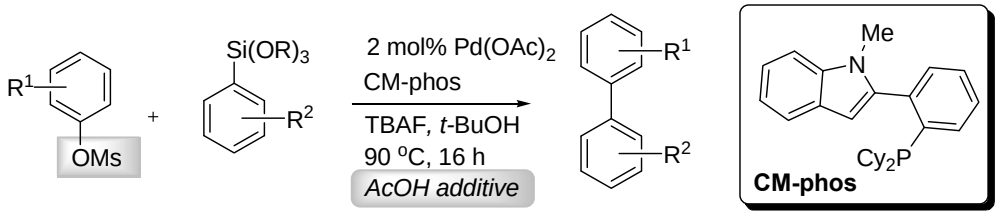


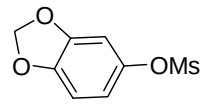
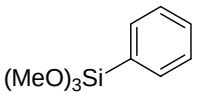
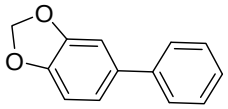
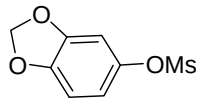
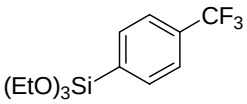
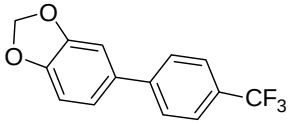
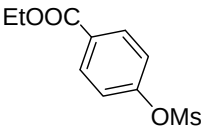
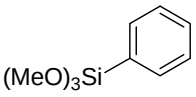
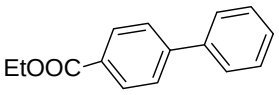
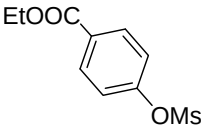
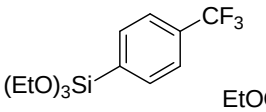
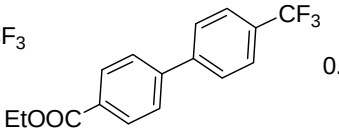
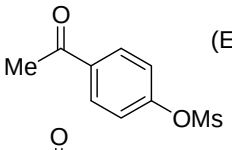
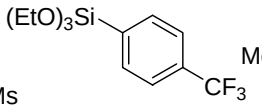
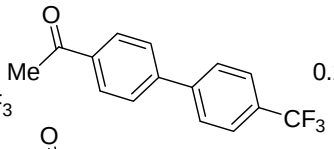
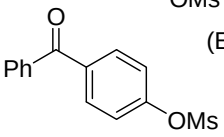
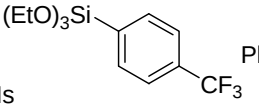
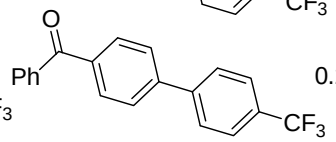
entry	ArOMs	Ar'Si(OR)$_3$	product	AcOH	% yield[b]
1				0.25 equiv	80
2				0.25 equiv	83
3				0.25 equiv	76
4				0.25 equiv	80
5				0.25 equiv	85
6				0.25 equiv	92
7				0.25 equiv	71
8				0.25 equiv	78
9				0.25 equiv	77
10				0.25 equiv	84
11				0.25 equiv	79

[a]Reaction conditions: see Table 8.1 and 8.2. [b]Isolated yields.

To evaluate the effectiveness of our new catalytic system, a range of aryl mesylates was examined using the preliminary optimized reaction conditions (Table 8.4). Complete conversions of aryl mesylates were normally observed between 6-16 hours at 90 °C. Both $PhSi(OMe)_3$ and $PhSi(OEt)_3$ provided similar yields of the desired product (Table 8.3, entry 1; Table 8.4, entry 1). Electron-deficient nucleophiles furnished the coupling product in good yield (Table 8.4, entry 2). Essentially no electronic effect on either electrophilic or nucleophilic partners was observed in this coupling process, which was contrary to Wu's report.[275] Sterically hindered substrates also coupled smoothly to give the desired product (Table 8.3, entry 6). Deactivated 4-methoxyphenyl mesylate was found to be a feasible substrate in this reaction (Table 8.4, entry 11).

Table 8.5 Pd-Catalyzed Hiyama Cross-Coupling of Functionalized ArOMs[a]

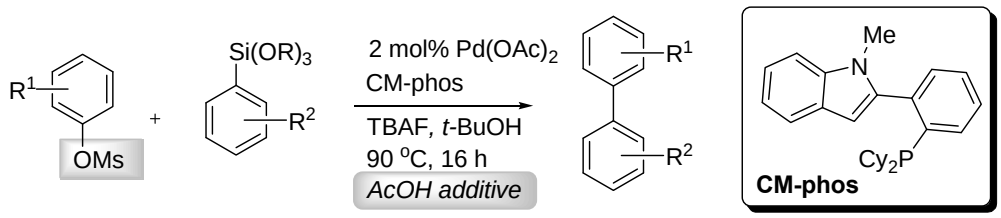


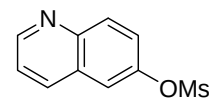
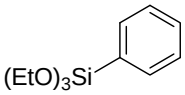
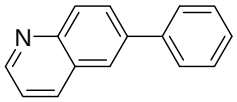
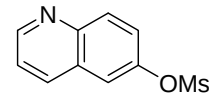
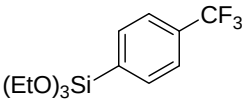
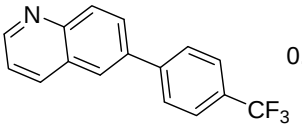
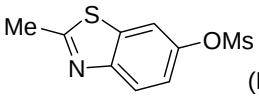
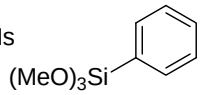
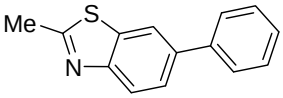
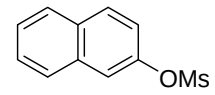
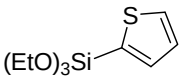
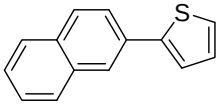
entry	ArOMs	Ar'Si(OR)$_3$	product	AcOH	% yield[b]
1				0.25 equiv	78
2				0.25 equiv	91
3				0.25 equiv	50
4				0.25 equiv	66
5				0.25 equiv	59
6				0.25 equiv	58

[a]Reaction conditions: see Table 8.1 and 8.2. [b]Isolated yields.

Functional groups such as ester and ketone were compatible under these reaction conditions (Table 8.5). For instance, we also examined the relative activity between the chloro and mesylate group (data not shown). 4-Chloro-phenyl mesylate was used as the model substrate in this investigation. Almost complete selectivity (>99%) on the coupling of the chloro group was observed (i.e. no 4-chlorobiphenyl was formed as monitored by GC-MS analysis).

Table 8.6 Pd-Catalyzed Hiyama Coupling of Heteroaryl Mesylates[a]



entry	ArOMs	Ar'Si(OR)$_3$	product	AcOH	% yield[b]
1				0.25 equiv	62
2				0.25 equiv	76
3				0.25 equiv	68
4				0.25 equiv	29

[a]Reaction conditions: see Table 1 and 2. [b]Isolated yields.

Apart from a variety of aryl mesylates, heteroaryl mesylates were effective substrates for Hiyama coupling (Table 8.6). Quinolyl and benzothiazolyl substrates provided moderate to good yields of the corresponding coupling products (Table 8.6, entries 1-3). However, when the heterocyclic substrate was used as the nucleophilic partner, only 29% of the desired product was obtained (Table 8.6, entry 4).

8.3 Conclusion

In summary, we have succeeded in devising an effective system to perform Hiyama cross-couplings on aryl and heteroaryl mesylates. In the presence of CM-phos ligand, 2 mol % of Pd is generally sufficient to catalyze this coupling process. Particularly noteworthy is that we have also demonstrated the beneficial effect of acid additives which is effective to suppress the phenolic side product formation. These findings may improve Si-based cross-couplings of aryl sulfonates (e.g. mesylate/tosylate/triflate) and open up the possibility of expanding the scope to other related types of catalysis.

8.4 Experimental Section

8.4.1 General Considerations

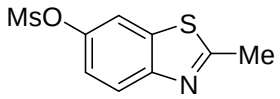
Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. All Hiyama-type reactions were performed in Rotaflo® (England) resealable screw-capped Schlenk flasks (approx. 20 mL volume) in the presence of Teflon coated magnetic stirrer bar (3 mm × 10 mm). Toluene and tetrahydrofuran (THF) were distilled from sodium and sodium benzophenone ketyl under nitrogen, respectively.[150] *tert*-Butanol was distilled from sodium under nitrogen.[150] New bottles of tetrabutylammonium fluoride (TBAF) solution (1M in THF) were used. K_3PO_4 and K_2CO_3 were purchased from Fluka. Thin layer chromatography was performed on Merck precoated silica gel 60 F_{254} plates. Silica gel (Merck, 70-230 and 230-400 mesh) was used for column chromatography. Melting points were recorded on an uncorrected Büchi Melting Point B-545 instrument. ^{1}H NMR spectra were recorded on a Bruker (400 MHz) spectrometer. Deuteriated chloroform was treated with anhydrous K_2CO_3 and furnace dried 4Å molecular sieves. Spectra were referenced internally to the residual proton resonance in $CDCl_3$ (δ 7.26 ppm), or with tetramethylsilane (TMS, δ 0.00 ppm) as the internal standard. Chemical shifts (δ) were reported as part per million (ppm) in δ scale downfield from TMS.

^{13}C NMR spectra were referenced to $CDCl_3$ (δ 77.0 ppm, the middle peak). Coupling constants (J) were reported in Hertz (Hz). Mass spectra (EI-MS and ES-MS) were recorded on a HP 5989B Mass Spectrometer. High-resolution mass spectra (HRMS) were obtained on a Brüker APEX 47e FTICR mass spectrometer (ESIMS). GC-MS analysis was conducted on a HP 5973 GCD system using a HP5MS column (30 m × 0.25 mm). The products described in GC yield were accorded to the authentic samples/tetradecane calibration standard from HP 6890 GC-FID system. Compounds described in the literature were characterized by comparison of their ^{1}H, and/or ^{13}C NMR spectra to the previously reported data.

8.4.2. Preparation of Aryl Mesylates

4-*tert*-Butylphenyl mesylate[276], 4-methoxyphenyl mesylate[277], 4-acetylphenyl mesylate[277], 4benzoylphenyl mesylate[214], 1,3-Benzodioxol-5-ol mesylate, 5 were prepared from their corresponding phenols with MsCl in the presence of triethylamine in CH_2Cl_2 according to the literature method.[70] New aryl mesylates were prepared by following the literature procedures.[190] Characterizations data of new aryl mesylates are shown below.

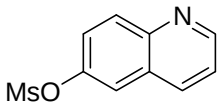
2-Methyl-5-benzothiazolyl mesylate



General procedures for preparation of aryl mesylate: To a stirred solution of 5-hydroxy-2methylbenzothiazole (3.30 g, 20 mmol) in anhydrous dichloromethane (20 mL) cooled to 0 °C was added distilled triethylamine (4.17 mL, 30 mmol). To this was added mesyl chloride (1.94 mL, 25 mmol) dropwise *via* syringe over 15 min. The reaction was stirred at 0 °C for 1 hour, then quenched with water and the phases separated. The aqueous layer was extracted with dichloromethane (3 × 100 mL) and the combined organics were dried over $MgSO_4$ and concentrated in *vacuo*. The crude products were purified

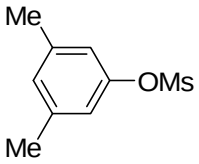
by column chromatography on silica gel using DCM/hexane solvent mixtures as the eluent to obtain the entitled compound in 38% yield, 1.85 g, as a white solid. M.p. 119.5-120.8 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.76 (s, 3H), 3.12 (s, 3H), 7.24 (dd, *J*=2.3Hz, 8.7Hz, 1H), 7.74-7.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 37.1, 115.4, 118.9, 122.1, 134.4, 147.4, 153.7, 169.6; MS (EI): *m/z* (relative intensity) 243 (M^+, 35), 164 (100), 136 (28), 122 (15), 95 (18). HRMS: calcd. for $C_9H_9N_1O_3S_2$: 243.0018, found 243.0023.

6-(Mesyloxy)quinoline



General procedures for the preparation of aryl mesylate were as follows. 6-Hydroxyquinoline (2.9 g, 20 mmol) was used to afford the title compound in 58% yield, 2.59 g, as a deep purple solid. M.p. 84.6-86.2 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.15 (s, 3H), 7.32-7.35 (m, 1H), 7.52-7.55 (m, 1H), 7.67 (d, *J*=2.6Hz, 1H), 8.04-8.07 (m, 2H), 8.83-8.85 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 37.4, 119.2, 121.8, 124.0,128.1, 131.6, 135.7, 146.4, 146.4, 150.7; MS (EI): *m/z* (relative intensity) 223 (M^+, 63), 145 (60), 116 (100), 89 (30), 63 (10). HRMS: calcd. for $C_{10}H_9N_1O_3S_1$: 223.0298, found 223.0292.

3,5-Dimethylphenyl mesylate.



Obtained in 95% yield as white crystals: mp 41.7-43.4 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.30 (s, 3H), 3.07 (s, 3H), 6.88 (s, 2H), 6.93 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 36.8, 119.1, 128.7, 139.7, 149.0; MS (EI): *m/z* (relative intensity) 200 (M^+, 65), 122 (100), 107 (20), 91 (30), 77 (30). HRMS: calcd. for $C_9H_{12}O_3S_1$: 200.0502, found 200.0507.

8.4.3 General Procedures for Initial Reaction Condition Screenings

General procedure for screening experiments (in the case of solid base): $Pd(OAc)_2$ (2.3 mg) and CM-phos ligand (Pd:L = 1:4) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The tube was evacuated and flushed with nitrogen for three times. Precomplexation was applied by adding freshly distilled dichloromethane (~1 mL) and Et_3N (0.1 mL) into the tube. The solution was stirred and warmed using a hair drier for about 1 to 2 minutes until the solvent started to boil. The solvent was then evaporated under high vacuum. 4-*tert*-Butylphenyl mesylate (0.5 mmol), phenyltrimethoxysilane (1.0 mmol) and base (1.0 mmol) were loaded into the tube. The solvent (1.0 mL) was added with continuous stirring at room temperature for another several minutes. The tube was then placed into a preheated oil bath (90 ^{o}C) and stirred for the time as indicated in the Tables. After completion of reaction, the reaction tube was allowed to cool to room temperature. Ethyl acetate (~10 mL), and tetradecane (130 μL, internal standard) were added. The organic layer was subject to GC analysis. The GC yield obtained was previously calibrated by authentic sample/tetradecane calibration curve.

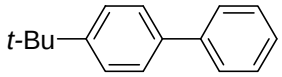
General procedure for screening using TBAF: $Pd(OAc)_2$ (2.3 mg) and ligand (Pd:L = 1:4) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The tube was evacuated and flushed with nitrogen for three times. Precomplexation was accomplished by adding 1.0 mL of 1M TBAF in THF into the Schlenk tube and the solution was stirred and warmed using a hair drier for about 1 minute. The solvent was then evaporated under high vacuum. Phenyltrimethoxysilane (1.0 mmol) was then added via autopipette, followed by the addition of 1.0 mL of solvent as indicated. The entire solution was then stirred for 1-2 minutes. Acetic acid was then added. 4-*tert*-Butylphenyl mesylate (0.5 mmol), was loaded into the tube. The tube was then placed into a preheated oil bath (90 ^{o}C) and stirred for the time as indicated in Tables. After completion of reaction, the reaction tube was allowed to cool to room temperature. Ethyl acetate (~10 mL), and tetradecane (130 μL, internal standard) were added. The organic layer was subject to GC analysis. The GC yield obtained was previously calibrated by authentic sample/tetradecane calibration curve.

8.4.4 General Procedures for Hiyama Cross-Couplings of Aryl Mesylates

General procedures for Hiyama cross-coupling of aryl mesylates: $Pd(OAc)_2$ (2.3 mg) and ligand (Pd:L = 1:4) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The tube was evacuated and flushed with nitrogen for three times. Precomplexation was accomplished by adding 1.0 mL of 1.0M TBAF in THF into the Schlenk tube and the solution was stirred and warmed using a hair drier for about 1 minute. The solvent was then evaporated under high vacuum. Aryltrialkoxysilane (1.0 mmol) was then added via autopipette, followed by 1.0 mL of *tert*-butanol solvent. The entire solution was then stirred for 1-2 minutes. Acetic acid was then added via autopipette (if needed, as indicated in Table 3). Aryl mesylate (0.5 mmol) was loaded into the tube. The tube was stirred at room temperature for several minutes and then placed into a preheated oil bath (90 ^{o}C) for the time as indicated in Tables. After completion of reaction as determined by GC analysis, the reaction tube was allowed to cool to room temperature and the reaction mixture was diluted with EtOAc. The filtrate was concentrated under reduced pressure. The crude products were purified by flash column chromatography on silica gel (230-400 mesh) to afford the desired product.

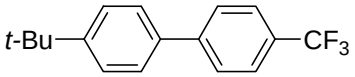
8.4.5 Characterization Data for Coupling Products

4-*tert*-Butylbiphenyl (Table 8.3, entry 1, 2; Table 8.4, entry 1) [175]



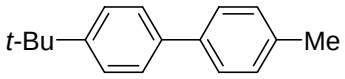
Hexane, R_f=0.55; 1H NMR (400 MHz, $CDCl_3$) δ 1.54 (s, 9H), 7.48 (t, J = 7.1 Hz, 1H), 7.58 (t, J = 7.5 Hz, 2H), 7.63 (d, J = 8.2 Hz, 2H), 7.71-7.77 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.3, 34.5, 125.7, 126.8, 126.9, 127.1, 128.7, 138.3, 141.0, 150.2; MS (EI): m/z (relative intensity) 210 (M^+, 40), 195 (100), 178 (15), 167 (30).

4-Trifluoromethyl-4'-*tert*-butylbiphenyl (Table 8.4, entry 2) [278]



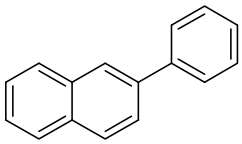
Hexane, R_f=0.55; ^{1}H NMR (400 MHz, $CDCl_3$) δ1.48 (s, 9H), 7.59-7.65 (m, 4H), 7.77-7.79 (m, 4H); ^{13}C NMR (100 MHz, CDCl3) δ 31.2, 34.6, 123.0, 125.6, 125.7, 125.9, 126.9-127.6 (overlapped with C-F couplings), 129.0 (q, J_{CF} = 32.3 Hz), 136.8, 144.5, 151.4. MS (EI): m/z (relative intensity) 278 (M^+, 35), 263 (100), 235 (40).

4-Methyl-4'-*tert*-butylbiphenyl (Table 8.4, entry 3)[74]



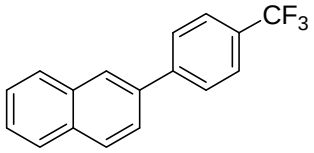
Hexane, R_f=0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.50 (s, 9H), 2.52 (s, 3H), 7.37 (d, *J*=7.9 Hz, 2H), 7.58-7.68 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 31.3, 34.4, 125.6, 126.5, 126.8, 129.4, 136.6, 138.1, 138.2, 149.9; MS (EI): m/z (relative intensity) 224 (M^+, 50), 209 (100), 193 (5), 181 (20), 165 (15).

2-Phenylnaphthlene (Table 8.4, entry 4, 5)[279]



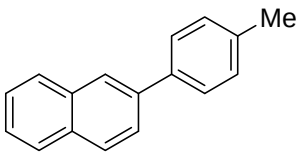
Hexane, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-7.53 (m, 1H), 7.60-7.64 (m, 4H), 7.86-7.90 (m, 3H), 8.02-8.05 (m, 3H), 8.20 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 125.5, 125.7, 125.9, 126.2, 127.3, 127.4, 127.6, 128.1, 128.4, 128.8, 132.6, 133.6, 138.4, 141.0; MS (EI): m/z (relative intensity) 204 (M^+, 100), 101 (20).

2-(4-Trifluoromethylphenyl)naphthalene (Table 8.4, entry 6)[280]



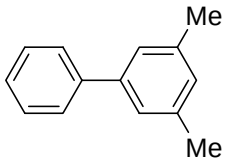
Hexane, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55-7.57 (m, 2H), 7.73-7.77 (m, 3H), 7.81-7.83 (m, 2H), 7.90-7.97 (m, 3H), 8.08 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ123.0, 125.1, 125.7, 126.3, 126.4-126.5 (overlapped with C-F couplings), 127.6, 128.2, 128.7, 129.3 (q, J_{CF} = 32.2 Hz), 132.9, 133.5, 136.9, 144.6; MS (EI): m/z (relative intensity) 272 (M^+, 100), 251 (10), 202 (50).

2-(4-Methylphenyl)naphthalene (Table 8.4, entry 7)[96]



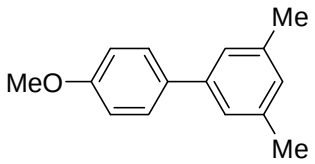
Hexane, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.55 (s, 3H), 7.41 (d, J = 7.9 Hz, 2H), 7.59-7.62 (m, 2H), 7.76 (d, J = 8.0 Hz, 2H), 7.88 (d, J = 8.0 Hz, 1H), 7.96-8.02 (m, 3H), 8.16 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 125.3, 125.5, 125.7, 126.1, 126.7, 127.2, 127.6, 128.1, 128.3, 129.4, 129.5, 132.5, 133.7, 137.1, 138.1, 138.4; MS (EI): m/z (relative intensity) 218 (M^+, 100), 202 (40), 189 (10).

3,5-Dimethylbiphenyl (Table 8.3, entry 3, 4) [281]



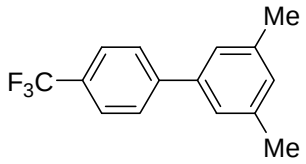
Hexane, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.57 (s, 6H), 7.18 (s, 1H), 7.41 (s, 2H), 7.51 (d, *J* = 7.3 Hz, 1H), 7.60 (t, *J* = 7.7 Hz, 2H), 7.77 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 125.1, 127.0, 127.1, 128.6, 128.7, 128.8, 138.1, 141.2, 141.4; MS (EI): m/z (relative intensity) 182 (M^+, 100), 167 (70), 152 (20).

4-(3,5-Dimethylphenyl)anisole (Table 8.4, entry 8) [282]



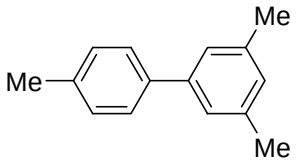
Hexane, R_f=0.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.48 (s, 6H), 3.92 (s, 3H), 7.05-7.07 (m, 3H), 7.29 (s, 2H), 7.62 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 55.2, 114.0, 124.6, 128.1, 128.3, 133.9, 138.1, 158.9; MS (EI): m/z (relative intensity) 212 (M^+, 100), 197, 70), 169, (30), 153 (20).

1-Trifluoromethyl-4-(3,5-dimethylphenyl)benzene (Table 8.4, entry 9)[282]



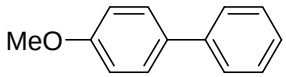
Hexane, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.50 (s, 6H), 7.16 (s, 1H), 7.31 (s, 2H), 7.76-7.78 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 125.1, 125.5, 125.5-127.5 (overlapped with C-F couplings), 129.8, 139.5, 139.7, 144.9; MS (EI): m/z (relative intensity) 250 (M^+, 100), 235 (50), 215 (10), 181 (20), 165 (40).

1-(4-Methylphenyl)-3,5-dimethylbenzene (Table 8.4, entry 10)[283]



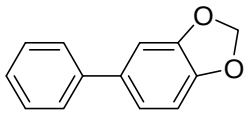
Hexane, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.54 (s, 9H), 7.13 (s, 1H), 7.37-7.40 (m, 4H), 7.65 (d, *J* = 7.9 Hz, 2H); 13C NMR (100 MHz, $CDCl_3$) δ 21.0, 21.4, 124.9, 126.7, 126.9, 128.6, 129.3, 136.7, 138.1, 138.5, 141.1; MS (EI): m/z (relative intensity) 196 (M^+, 100), 181, (50), 165 (40).

4-Phenylanisole (Table 8.4, entry 11) [71]



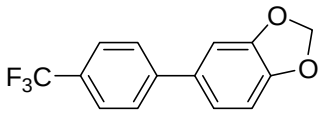
EA:Hexane = 1:20, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.91 (s, 3H), 7.06 (d, *J* = 8.7 Hz, 2H), 7.37-7.41 (m, 1H), 7.50 (t, *J* = 7.8 Hz, 2H), 7.61-7.66 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.2, 114.1, 126.5, 126.6, 128.1, 128.7, 133.6, 140.7, 159.1; MS (EI): m/z (relative intensity) 184 (M^+, 100), 169 (50), 141 (50), 115 (40).

3,4-Methylenedioxyphenylbenzene (Table 8.5, entry 1)[244]



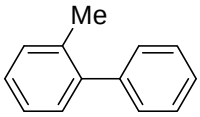
EA:Hexane = 1:10, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.03, (s, 2H), 6.95 (d, *J* = 8.0 Hz, 1H), 7.13-7.17 (m, 2H), 7.38-7.40 (m, 1H), 7.48 (t, *J* = 7.4 Hz, 2H), 7.59 (d, *J* = 7.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 101.0, 107.6, 108.4, 120.5, 126.7, 126.8, 128.6, 135.5, 140.8, 146.9, 148.0; MS (EI): m/z (relative intensity) 198 (M^+, 100), 139, (55).

4-Trifluoromethyl-1-(3,4-methylenedioxyphenyl)benzene (Table 8.5, entry 2)[244]



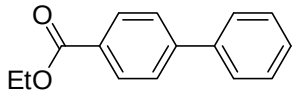
EA:Hexane = 1:10, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.02, (s, 2H), 6.91 (d, *J* = 8.6 Hz, 1H), 7.08-7.10 (m, 2H), 7.61 (d, *J* = 8.2 Hz, 2H), 7.67 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (100 MHz, CDCl3) δ 101.3, 107.6, 108.7, 120.9, 122.9, 125.6-127.5 (overlapped with C-F couplings), 128.7 (q, J_{CF} = 31.0 Hz), 144.3, 147.8, 148.3; MS (EI): m/z (relative intensity) 266 (M^+, 100), 247 (10), 207 (10), 188 (10), 139 (30).

2-Methylbiphenyl (Table 8.3, entry 5, 6) [238]



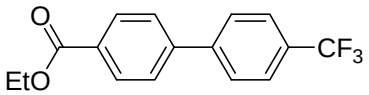
Hexane, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34, (s, 3H), 7.30-7.33 (m, 4H), 7.37-7.41 (m, 3H), 7.45-7.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.4, 125.7, 126.7, 127.1, 128.0, 128.7, 129.1, 129.7, 130.3, 135.3, 141.9; MS (EI): m/z (relative intensity) 168 (M+, 100), 153 (50), 115 (10).

Ethyl 4-phenylbenzoate (Table 8.5, entry 3) [284]



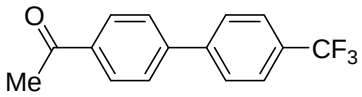
EA:Hexane = 1:10, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 (t, *J* = 7.1 Hz, 3H), 4.42 (q, *J* = 7.1 Hz, 2H), 7.42-7.46 (m, 1H), 7.47-7.49 (m, 2H), 7.62-7.68 (m, 4H), 8.14 (d, J = 8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 60.9, 126.9, 127.1, 128.0, 128.8, 129.1, 129.9, 139.9, 145.4, 166.4; MS (EI): m/z (relative intensity) 226 (M^+, 70), 198 (30), 181 (100), 152 (60).

Ethyl 4-(trifluoromethylphenyl)benzoate (Table 8.5, entry 4) [285]



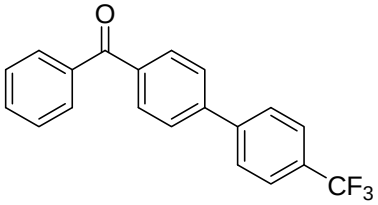
EA:Hexane = 1:10, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 (t, *J* = 7.1 Hz, 3H), 4.41 (q, *J* = 7.1 Hz, 2H), 7.63 (d, *J* = 8.2 Hz, 2H), 7.69-7.70 (overlapped multiplet, 4H), 8.14 (d, *J* = 8.3 Hz 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 61.0, 125.7, 125.8, 127.1, 127.5 129.8-130.1 (overlapped C-F couplings), 143.4, 143.8, 166.1; MS (EI): m/z (relative intensity) 294 (M^+, 40), 266 (50), 249 (100), 221 (10), 201 (30), 152 (30).

4-(4-Trifluoromethylphenyl)acetophenone (Table 8.5, entry 5) [286]



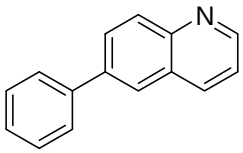
EA:Hexane = 1:10, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.62 (s, 3H), 7.65-7.69 (m, 6H), 8.04 (d, J = 8.3 Hz 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.5, 122.7, 125.4, 125.7, 125.8, 127.3-128.9 (overlapped with C-F couplings), 130.1 (q, *J* = 32.2 Hz), 136.5, 143.2, 143.9, 197.4; MS (EI): m/z (relative intensity) 264 (M^+, 40), 249 (100), 221 (20), 201 (30), 152 (30).

4-(4-Trifluoromethylphenyl)benzophenone (Table 8.5, entry 6) [287]



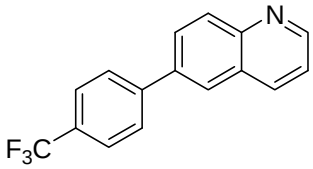
EA:Hexane = 1:10, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49-7.53 (m, 2H), 7.59-7.61 (m, 1H), 7.70-7.77 (m, 6H), 7.85 (d, *J* = 8.0 Hz, 2H), 7.92 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 125.4, 125.8, 125.9, 127.5-130.7 (overlapped with C-F couplings), 132.5, 137.0, 137.4, 143.4, 143.8, 196.1; MS (EI): m/z (relative intensity) 326 (M^+, 70), 249 (100), 201 (30), 152 (30).

6-Phenylquinoline (Table 8.6, entry 1) [288]



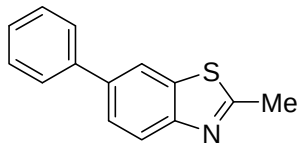
EA:Hexane = 1:4, R_f=0.25; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.44 (m, 2H), 7.48-7.52 (m, 2H), 7.71 (d, *J* = 7.7 Hz, 2H), 7.97-7.99 (m, 2H), 8.17-8.21 (m, 2H), 8.92 (d, *J* = 3.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 121.3, 125.3, 127.3, 127.6, 128.3, 128.8, 129.0, 129.7, 136.1, 139.1, 140.1, 147.5, 150.2; MS (EI): m/z (relative intnsity) 205 (M^+, 100), 176 (15).

6-(Trifluoromethylphenyl)quinoline (Table 8.6, entry 2) [287]



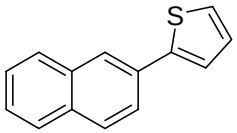
EA:Hexane = 1:4, R_f=0.25; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.36 (m, 1H), 7.65-7.71 (m, 4H), 7.85-7.90 (m, 2H), 8.09-8.17 (m, 2H), 8.88-8.89 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 121.5, 122.7, 125.4, 125.6-130.0 (overlapped with C-F couplings), 136.1, 137.5, 143.5, 147.7, 150.7; MS (EI): m/z (relative intnsity) 273 (M^+, 100), 254 (5), 204 (10).

2-Methyl-5-phenylbenzothiazole (Table 8.6, entry 3) [225]



EA:Hexane = 1:4, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.84 (s, 3H), 7.35-7.39 (m, 1H), 7.47 (t, *J* = 8.3Hz, 2H), 7.58 (d, *J* = 7.3Hz, 1H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.83 (d, *J* = 8.3 Hz, 1H), 8.20 (d, *J* = 1.2 Hz, 1H); ^{13}C NMR (100 MHz, CDCl3) δ 20.0, 120.5, 121.4, 124.0, 127.2, 127.3, 128.8, 134.5, 139.3, 140.6, 153.9, 167.5; MS (EI): m/z (relative intensity) 225 (M^+, 100), 184 (10), 139 (10).

2-(2-Naphthyl)thiophene (Table 8.6, entry 4) [289]



EA:Hexane = 1:4, R_f=0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16-7.17 (m, 1H), 7.34-7.36 (d, *J* = 5.0 Hz, 1H), 7.47-7.53 (m, 4H), 7.80-7.89 (m, 5H), 8.10 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 123.4, 124.1, 124.4, 125.0, 125.8, 125.9, 126.4, 127.7, 127.8, 127.9, 128.1, 128.5, 131.7, 132.7, 133.6, 144.4; MS (EI): m/z (relative intensity) 210 (M^+, 100), 165 (20).

Chapter 9

Conclusion

We have successfully designed and explored new classes of monodentate indolyl phosphine ligands that use indole scaffold. The indole templates are inexpensive, readily available and highly diversified. They could be easily synthesized from inexpensive arylhydrazines and substituted acetophenones by Fisher-Indole synthesis. Two classes of ligands, N-P bound amino-phosphine ligands and C-P bound phosphine ligands, have been synthesized.

Indolyl phosphine ligands are effective supporting ligands for various kinds of coupling reactions.

The *N*-*P*-type phosphines have exceedingly high activity in Suzuki-Miyaura coupling reaction of aryl chlorides. Both sterically hindered and deactivated aryl chlorides could couple with arylboronic acid to form the biaryl products in excellent yields. The catalyst loading can be as low as 0.02 mol% of Pd, which is the lowest catalyst loading ever achieved for amino-phosphine-type ligand in the Suzuki coupling reaction.

The *C*-*P*-type phosphine that the phosphine group attached to the C-3 position of indole has shown high activity in the Suzuki coupling reaction. Remarkably, the Pd/*C*-*P*-type diphenyl indolyl phosphine system can effectively

catalyze the coupling of aryl chlorides. Notably, we have succeeded in showing the possibility of Pd-catalyzed tetra-*ortho*-substituted biaryl synthesis by using arylphosphines as ligands.

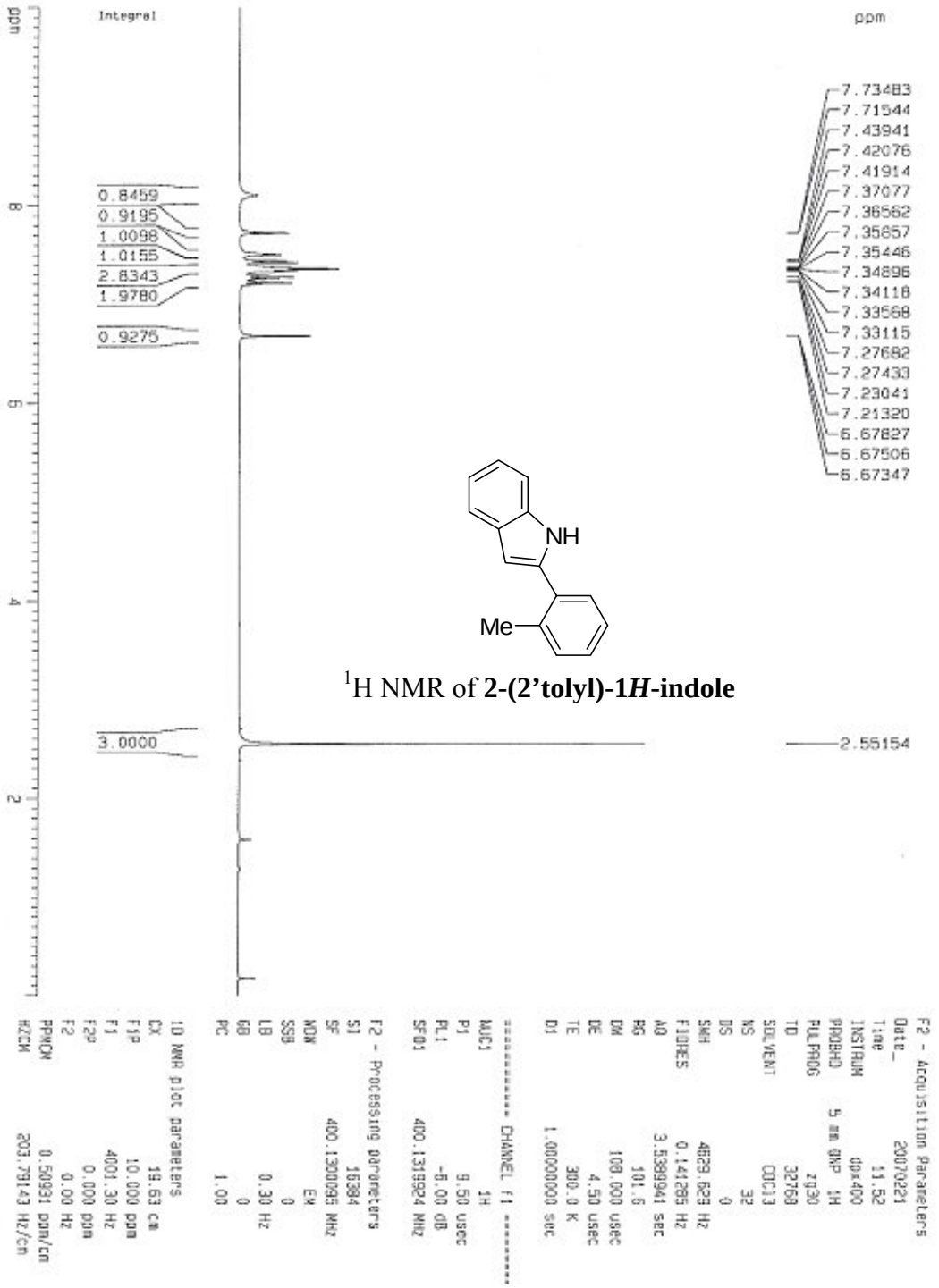
The *C-P*-type phosphine that the phosphine group attached to the bottom ring has shown high activity in the aryl tosylates/mesylates coupling reactions. For Suzuki coupling, a variety of aryl, heteroaryl and vinyl tosylates/mesylates have been efficiently coupled with different organoboron nucleophiles. CM-Phos in combination with Pd-complex precursor have shown good activity (0.2 to 4.0 mol% Pd) in non-activated tosylate/mesylates coupling reactions. For amination reaction, primary, secondary cyclic, acyclic amines and indoles have all been effectively coupled with unactivated and deactivated aryl tosylates/mesylates. Keto and ester groups are compatible under the mild reaction conditions. Moreover, the amination reaction could proceed without solvent or with water as solvent. It is noteworthy that we have successfully demonstrated the first successful examples of the Suzuki coupling and amination of aryl mesylates. Particularly noteworthy is that the first examples of room-temperature Pd-catalyzed Suzuki-Miyaura cross-coupling of aryl tosylates/mesylates have also been successfully realized. Pd/CM-phos catalyst which effectively catalyzed Suzuki-Miyaura coupling and amination of aryl tosylates has provided a useful

alternative system to the Buchwald-type biaryl phosphines and Pd/Josiphos systems.

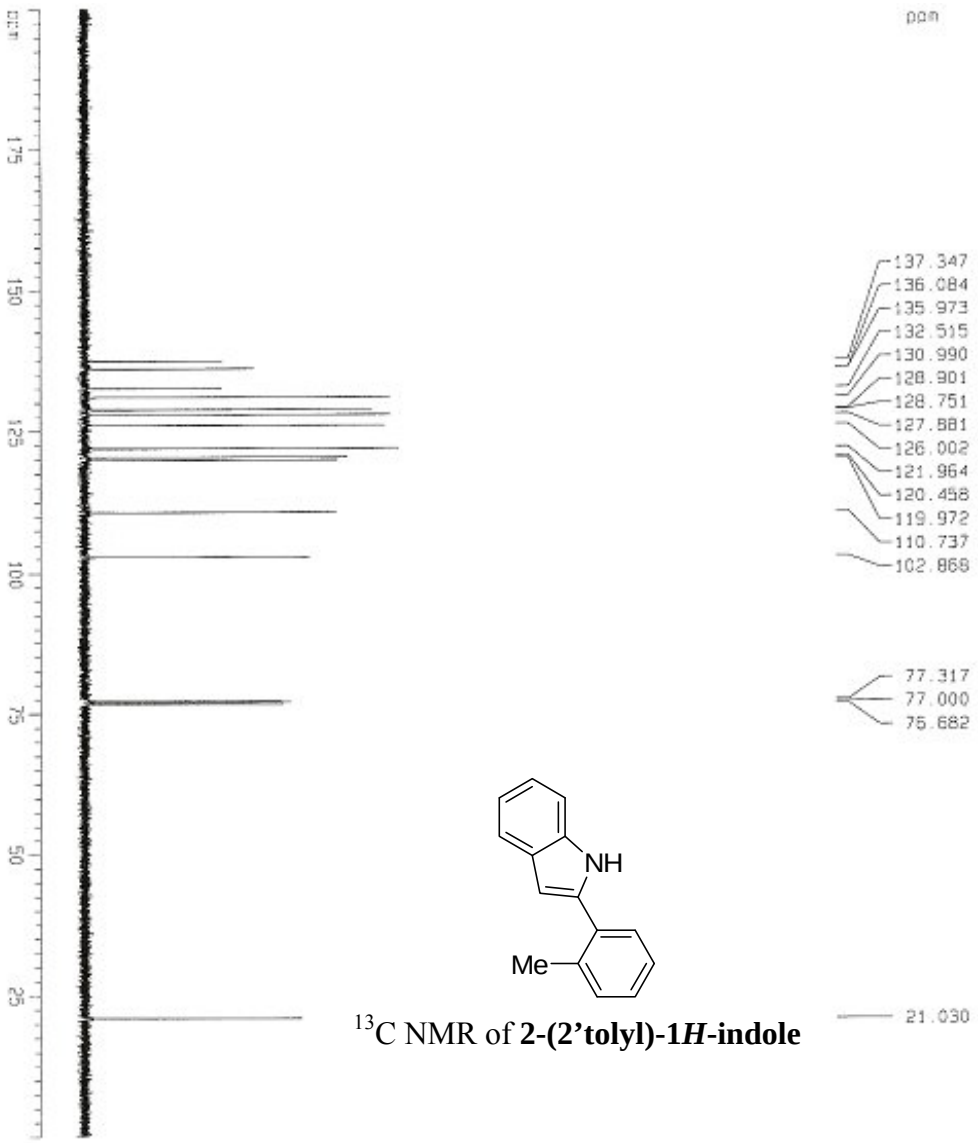
We have succeeded in devising an effective system for performing Hiyama cross-couplings of aryl and heteroaryl mesylates. In the presence of CM-phos ligand, 2 mol % of Pd is generally sufficient to catalyze this coupling process. Particularly noteworthy is that we have also demonstrated the beneficial effect of acid additives which are very effectively in suppressing phenolic side product formation. These findings may prove to be relevant for improving Si-based cross-couplings of aryl sulfonates (e.g. mesylate/tosylate/triflate) and open up the possibility of expanding the scope to other related types of catalysis.

Appendix

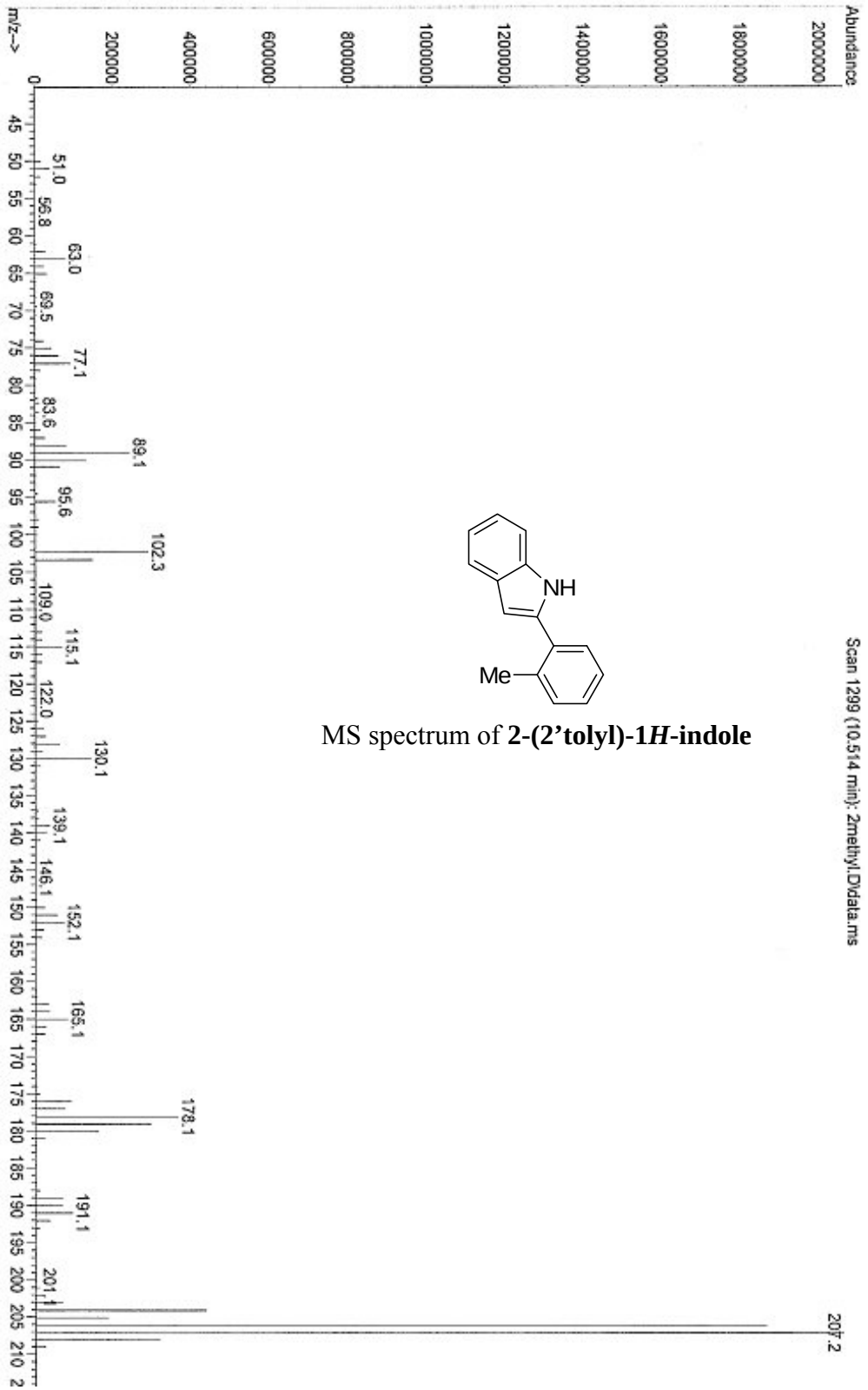
N-P Ligand Indole Templates



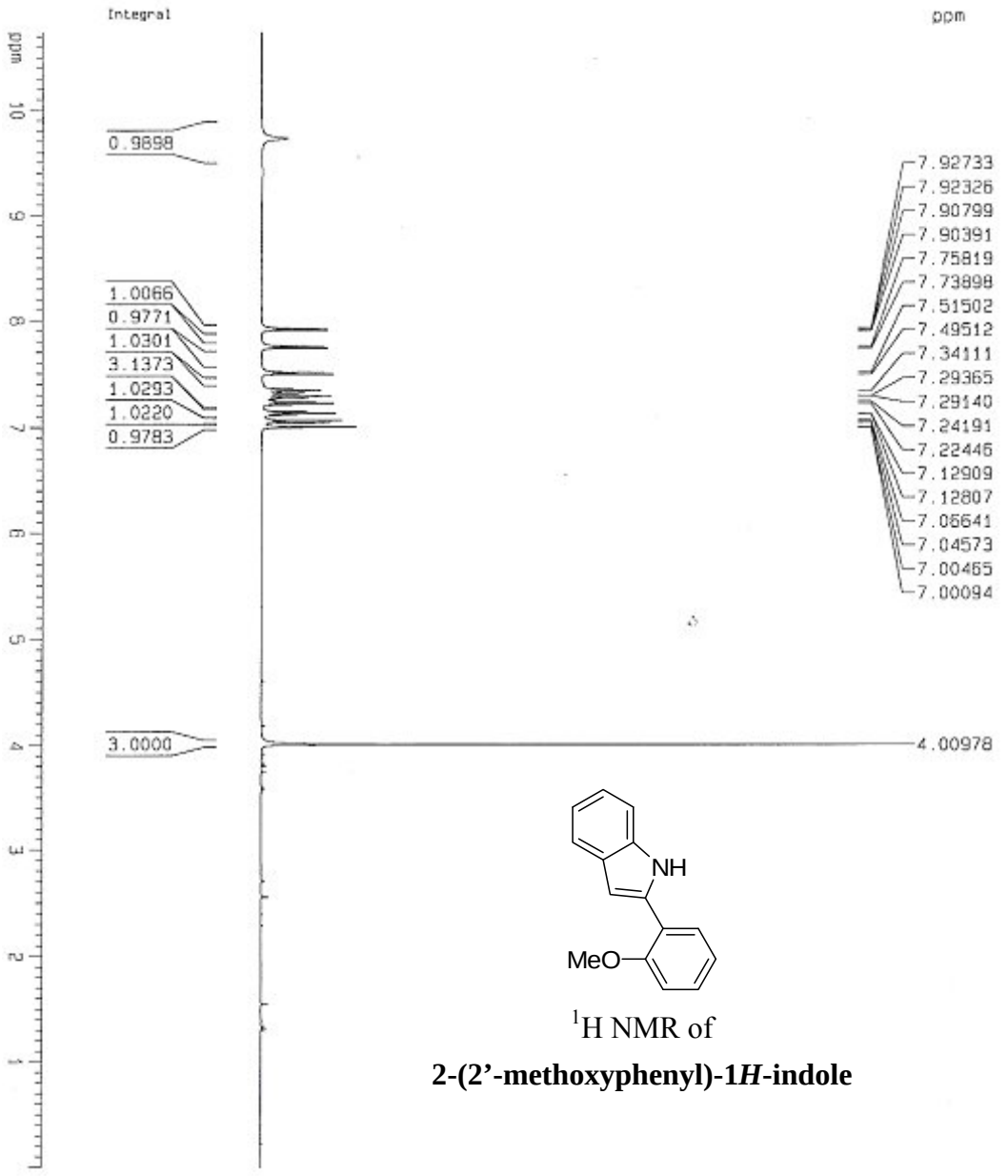
^{1}H NMR of **2-(2'tolyl)-1*H*-indole**



^{13}C NMR of **2-(2'tolyl)-1*H*-indole**

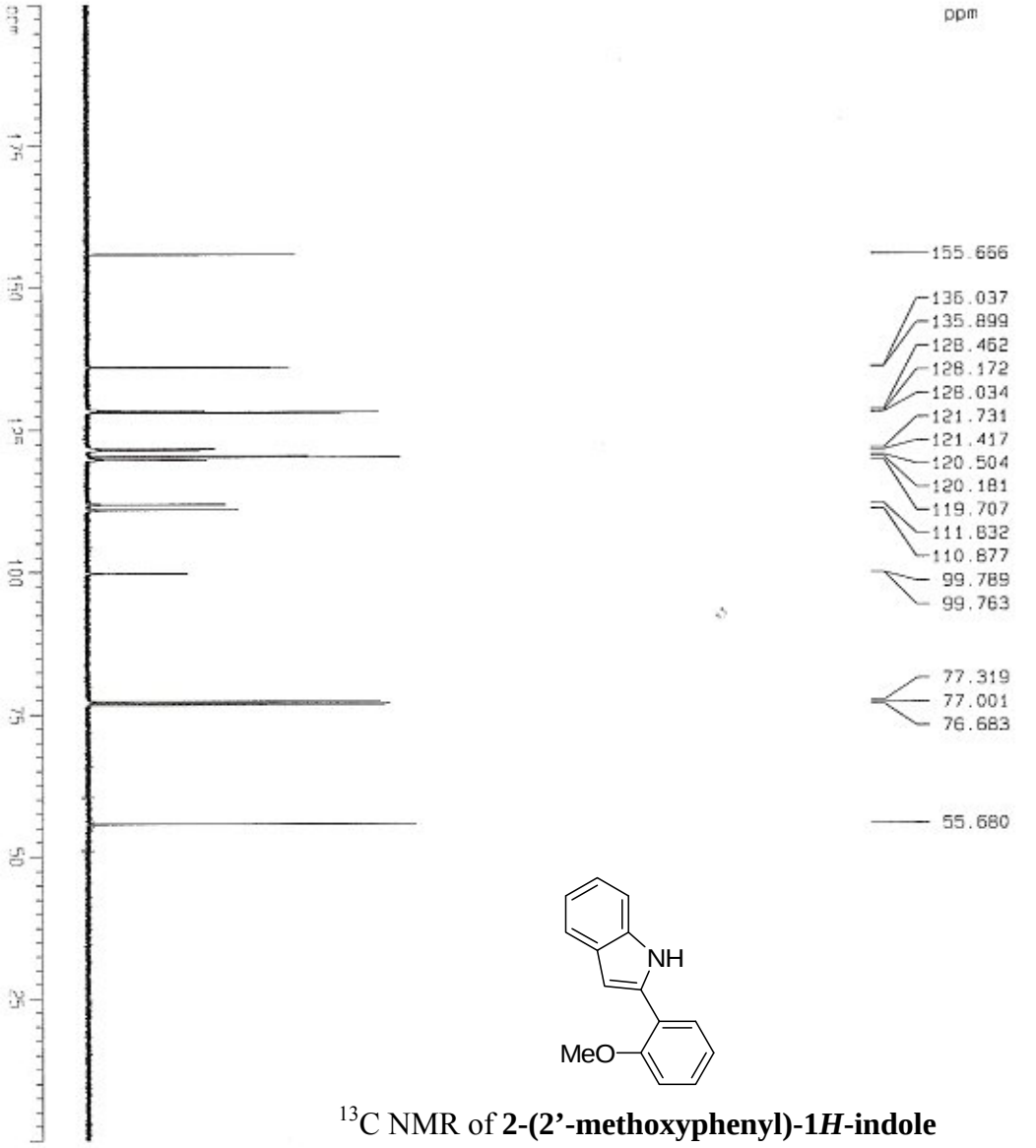


MS spectrum of **2-(2'tolyl)-1*H*-indole**



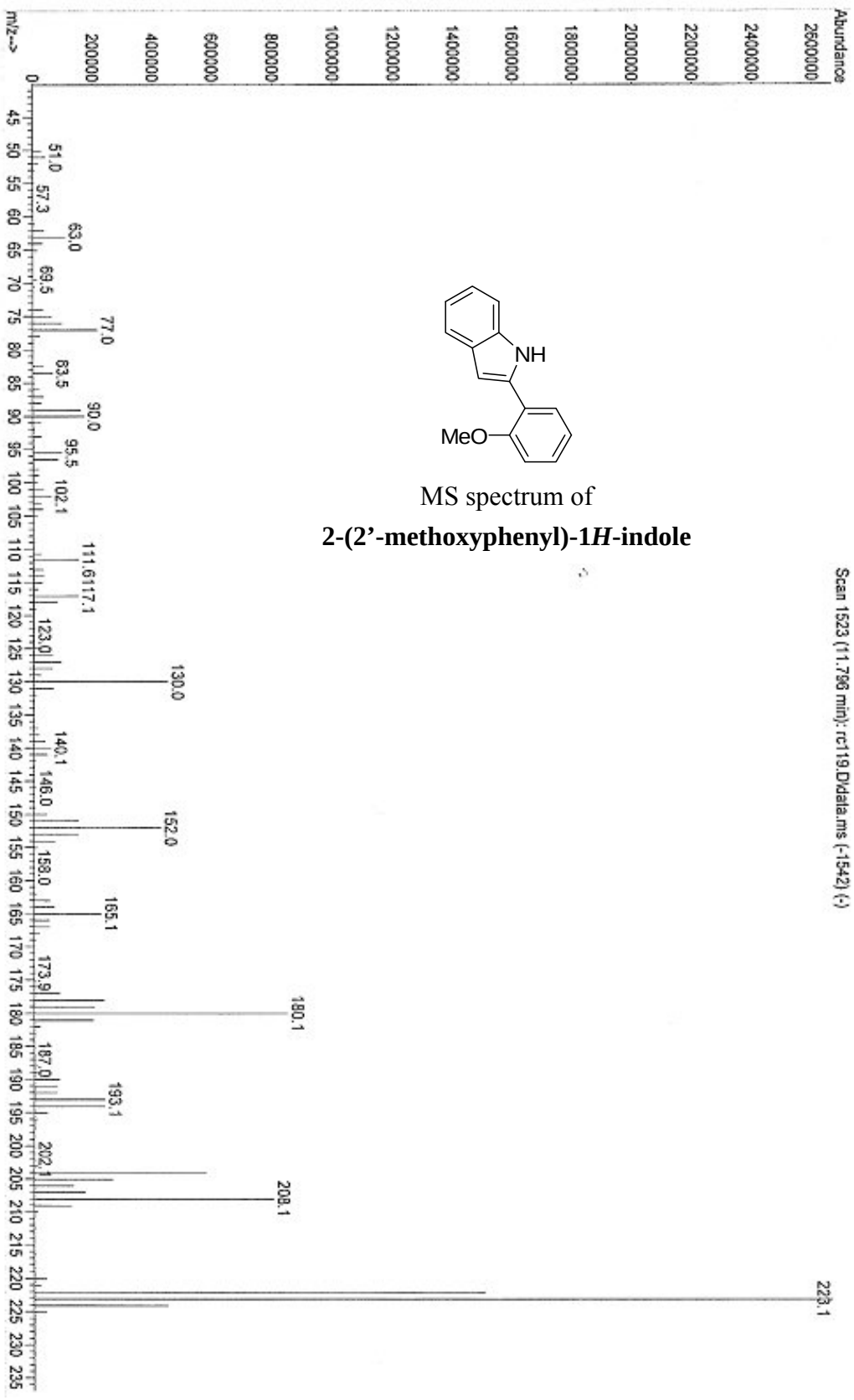
^{1}H NMR of

2-(2'-methoxyphenyl)-1*H*-indole



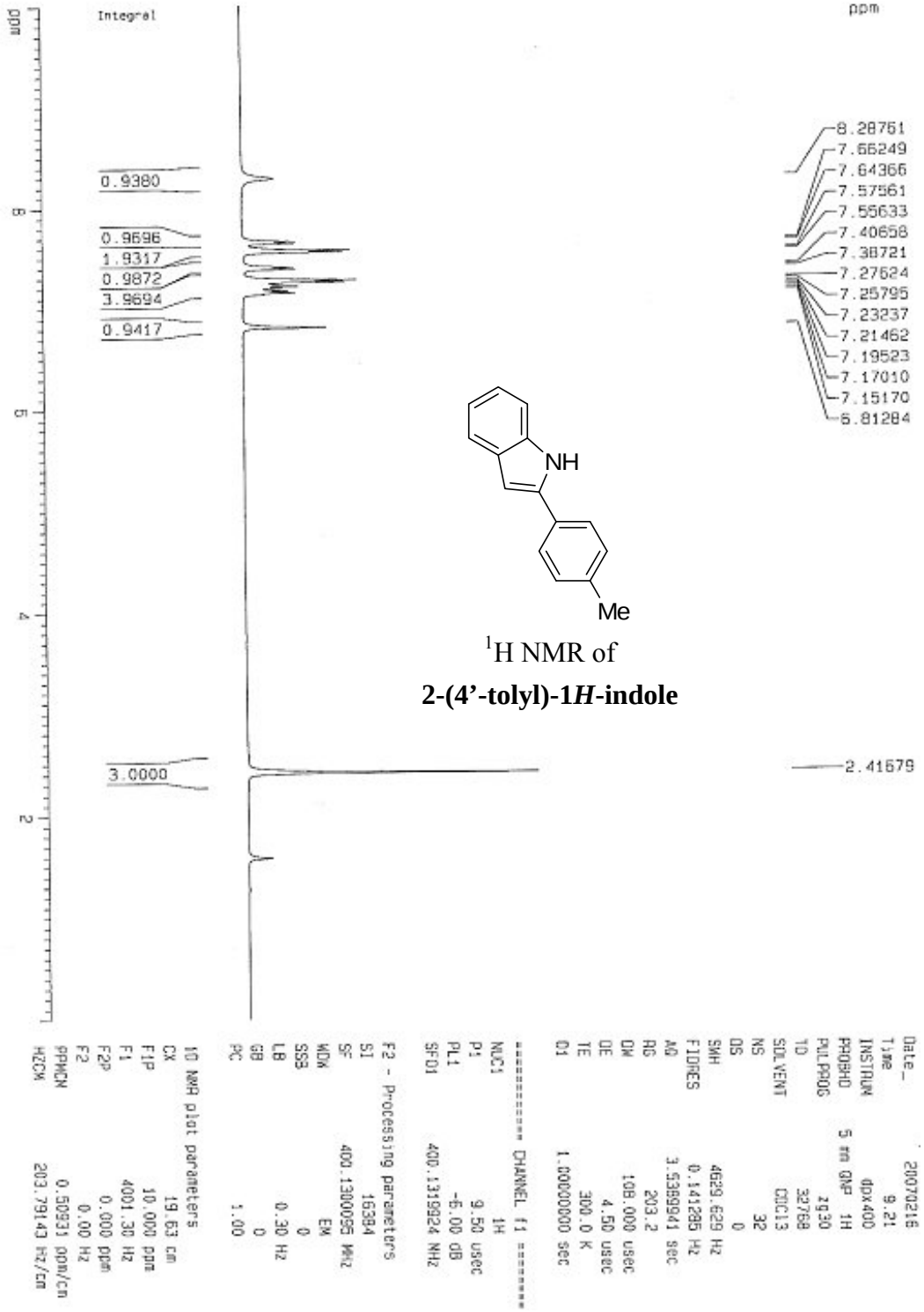
^{13}C NMR of **2-(2'-methoxyphenyl)-1*H*-indole**

PROBHD 5 mm DNP 1H
PULPROG zgdc30
TD 131072
SOLVENT CDCl3
NS 512
DS 0
SWH 25125.629 Hz
FIDRES 0.191693 Hz
AQ 2.6083827 sec
RG 9195.2
DW 19.900 usec
DE 4.50 usec
TE 300.0 K
D1 3.00000000 sec
d11 0.03000000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 5.80 usec
PL1 -6.00 dB
SFO1 100.6231263 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 71.00 usec
PL2 120.00 dB
PL12 17.00 dB
SFO2 400.1308230 MHz
F2 - Processing parameters
SI 65536
SF 100.6127698 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 19.50 cm
F1P 200.000 ppm
F1 20122.56 Hz
F2P -0.000 ppm
F2 -0.00 Hz
PPMCM 10.25641 ppm/cm
HZCM 1031.92615 Hz/cm



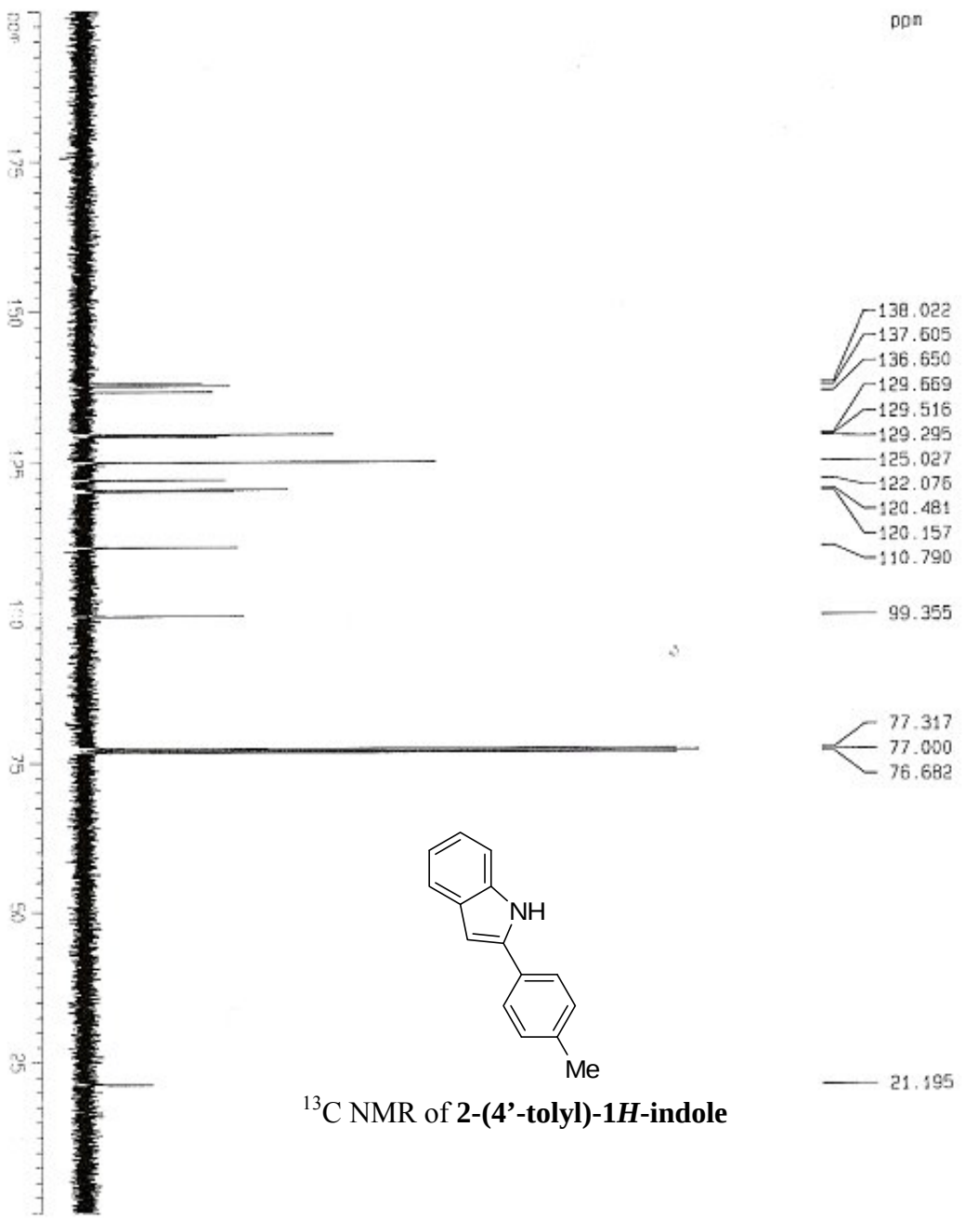
MS spectrum of

2-(2'-methoxyphenyl)-1*H*-indole



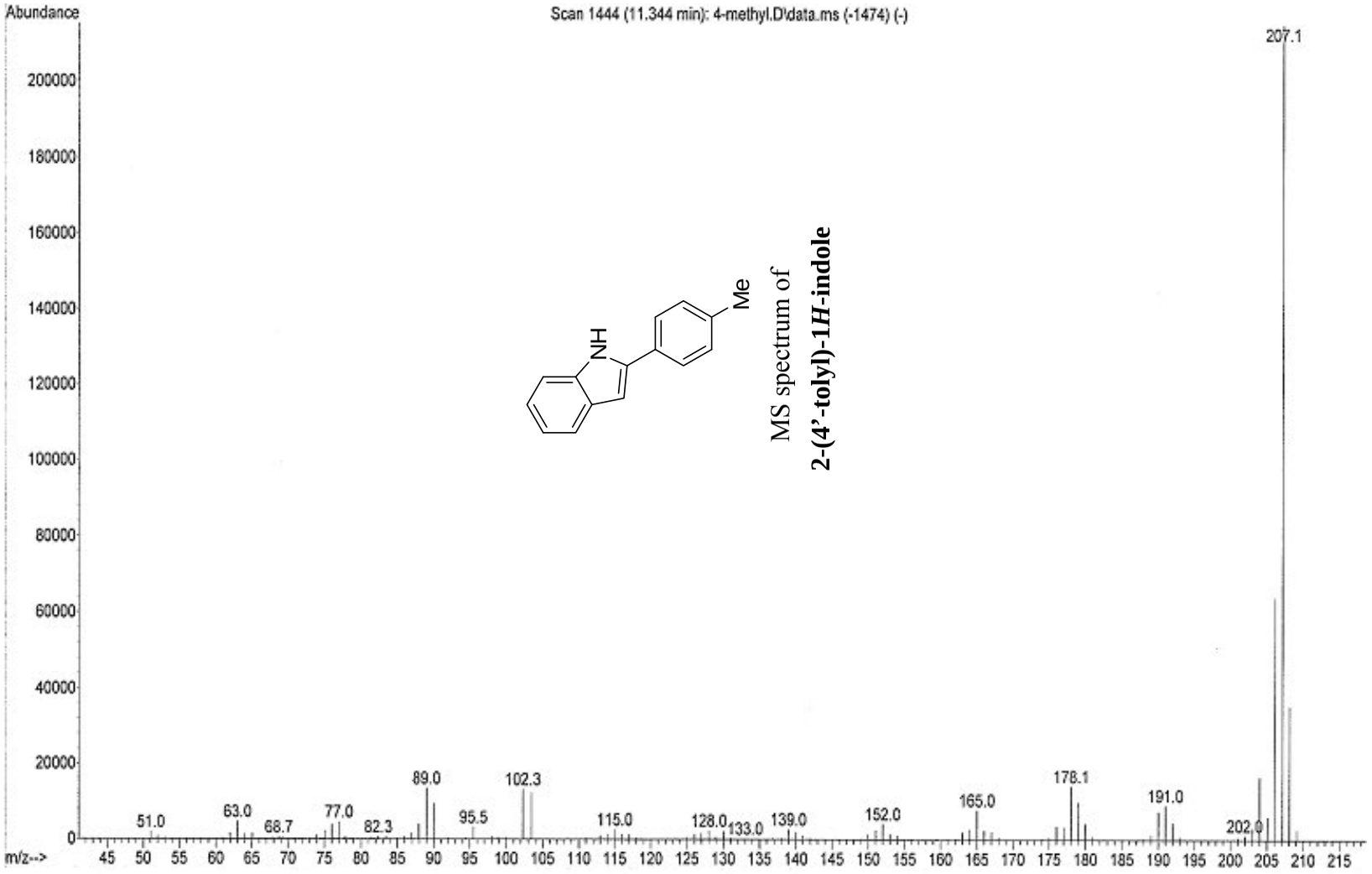
^{1}H NMR of

2-(4'-tolyl)-1*H*-indole



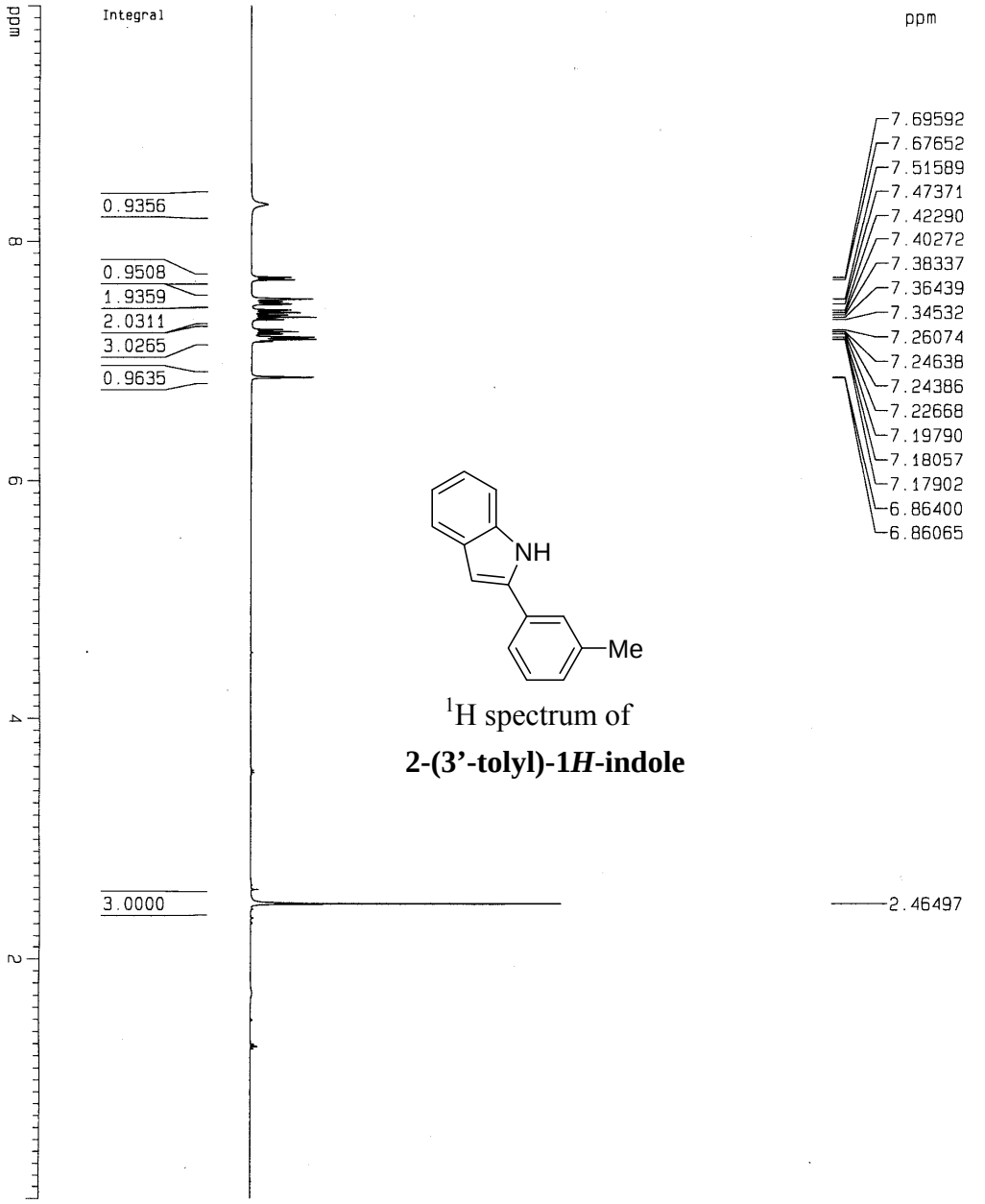
^{13}C NMR of **2-(4'-tolyl)-1*H*-indole**

PROBHD 5 mm QNP 1H
PULPROG zgdc30
TD 131072
SOLVENT CDCl3
NS 256
DS 0
SWH 25125.628 Hz
FIDRES 0.191693 Hz
AQ 2.6083827 sec
RG 9195.2
DW 19.900 usec
DE 4.50 usec
TE 300.0 K
D1 3.00000000 sec
d11 0.03000000 sec
---------- CHANNEL f1 ----------
NUC1 13C
P1 5.80 usec
PL1 -5.00 dB
SF01 100.6232693 MHz
---------- CHANNEL f2 ----------
CPDPRG2 waltz16
NUC2 1H
PCPD2 71.00 usec
PL2 120.00 dB
PL12 17.00 dB
SFO2 400.1308230 MHz
F2 - Processing parameters
SI 65536
SF 100.6127767 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 19.50 cm
F1P 200.000 ppm
F1 20122.55 Hz
F2P -0.000 ppm
F2 -0.00 Hz
PPMCM 10.25641 ppm/cm
HZCM 1031.92680 Hz/cm



MS spectrum of

2-(4'-tolyl)-1*H*-indole



^{1}H spectrum of

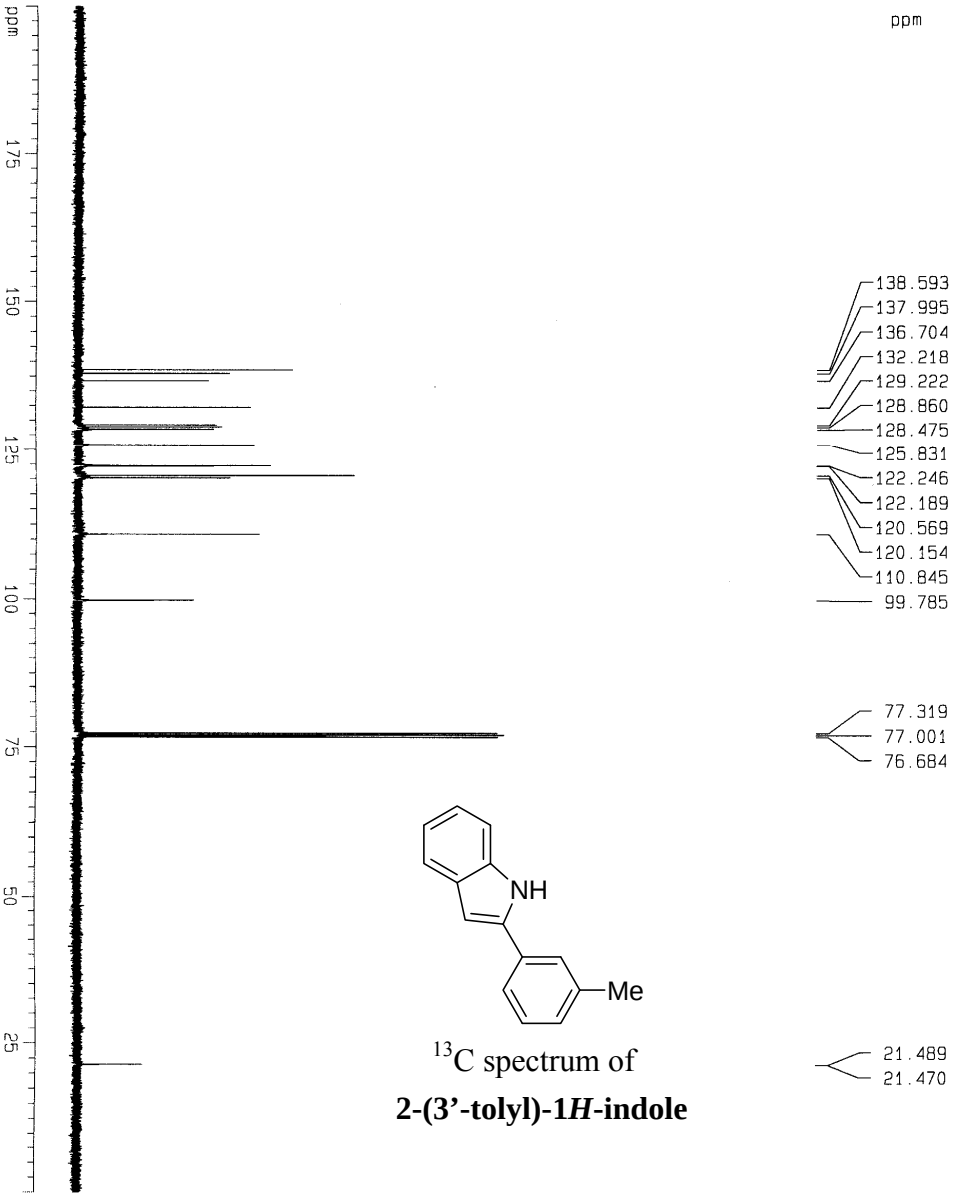
2-(3'-tolyl)-1*H*-indole

```
F2 - Acquisition Parameters
Date_              20070216
Time               15.28
INSTRUM              dpx400
PROBHD     5 mm GNP 1H
PULPROG              zg30
TD                 32768
SOLVENT            CDCl3
NS                    32
DS                     0
SWH             4629.629 Hz
FIDRES             0.141285 Hz
AQ              3.5389941 sec
RG                   181
DW                 108.000 usec
DE                   4.50 usec
TE                 300.0 K
D1              1.00000000 sec

========== CHANNEL f1 ==========
NUC1                 1H
P1                 9.50 usec
PL1                -6.00 dB
SFO1          400.1319924 MHz

F2 - Processing parameters
SI                 16384
SF          400.1300095 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00

1D NMR plot parameters
CX                19.63 cm
F1P               10.000 ppm
F1               4001.30 Hz
F2P               0.000 ppm
F2                0.00 Hz
PPMCM             0.50931 ppm/cm
HZCM            203.79143 Hz/cm
```



^{13}C spectrum of

2-(3'-tolyl)-1*H*-indole

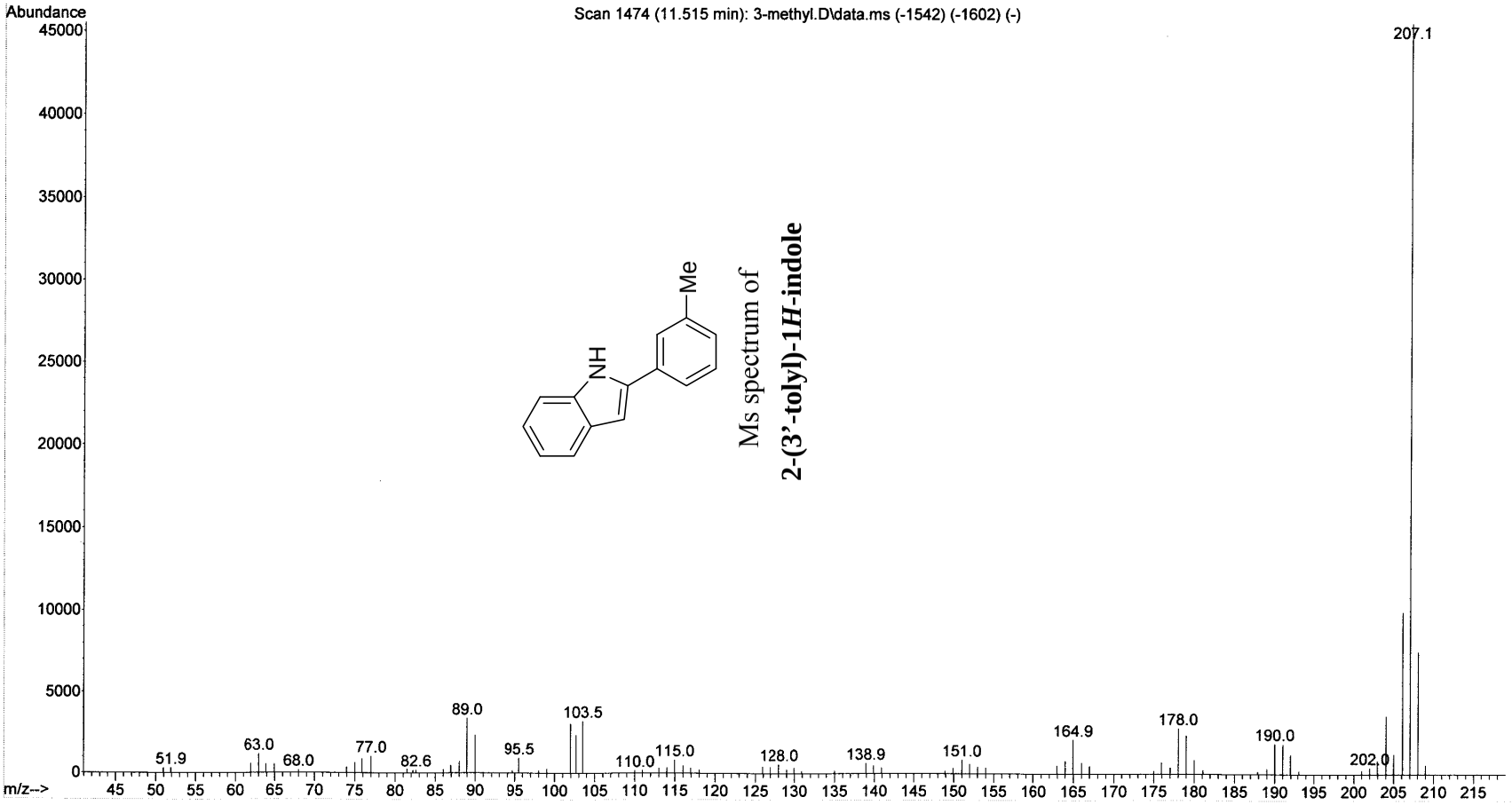
```
F2 - Acquisition Parameters
Date_              20070216
Time               15.31
INSTRUM            dpx400
PROBHD     5 mm QNP  1H
PULPROG            zgdc30
TD                 131072
SOLVENT            CDCD
NS                 256
DS                 0
SWH                25125.629 Hz
FIDRES             0.191693 Hz
AQ                 2.6083827 sec
RG                 9195.2
DW                 19.900 usec
DE                 4.50 usec
TE                 300.0 K
D1                 3.00000000 sec
D11                0.03000000 sec

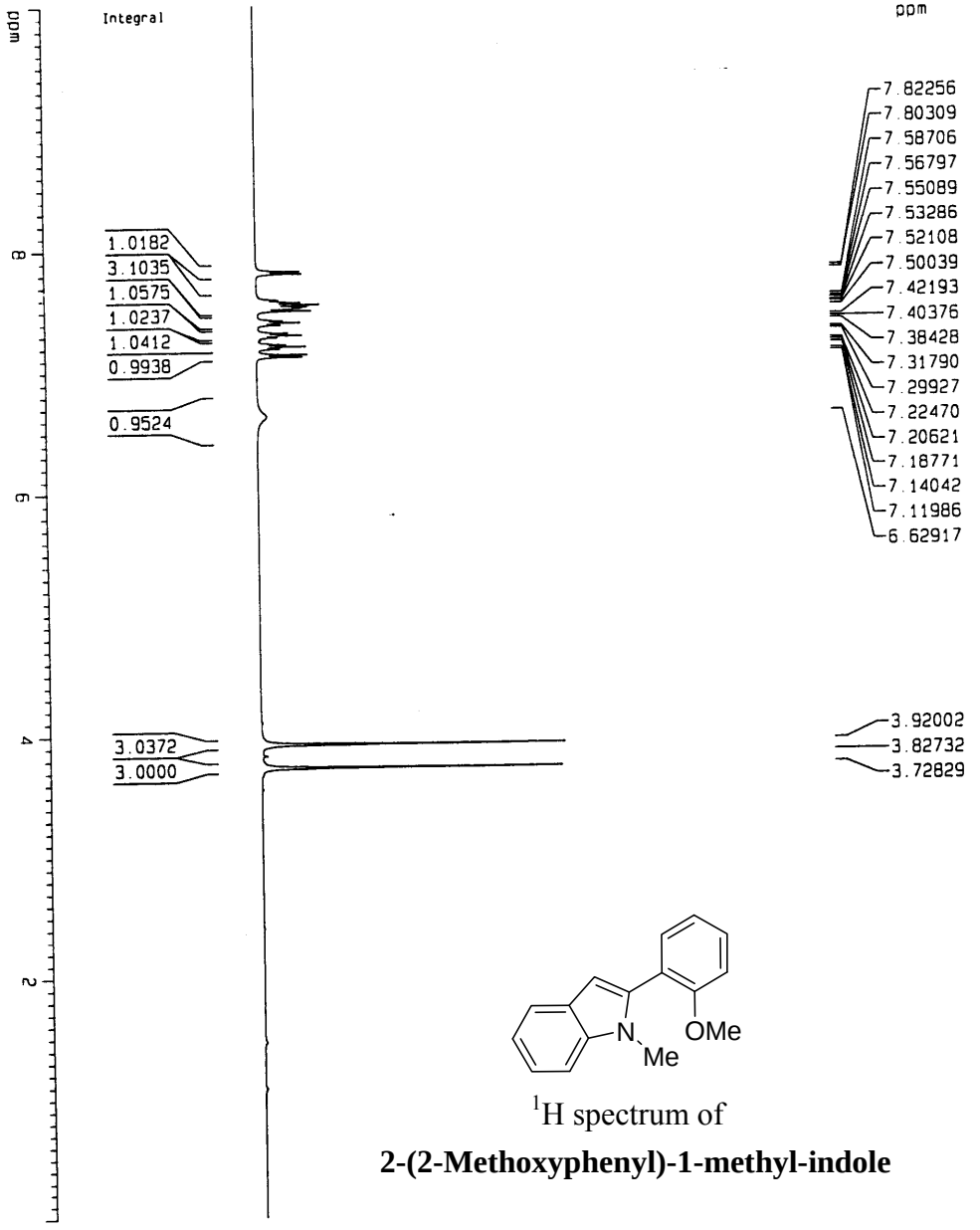
============== CHANNEL f1 ==============
NUC1               13C
P1                 5.80 usec
PL1                -6.00 dB
SFO1               100.6231263 MHz

============== CHANNEL f2 ==============
CPDPRG2            waltz16
NUC2               1H
PCPD2              71.00 usec
PL2                120.00 dB
PL12               17.00 dB
SFO2               400.1308230 MHz

F2 - Processing parameters
SI                 65536
SF                 100.6127809 MHz
WDW                EM
SSB                0
LB                 0.30 Hz
GB                 0
PC                 1.00

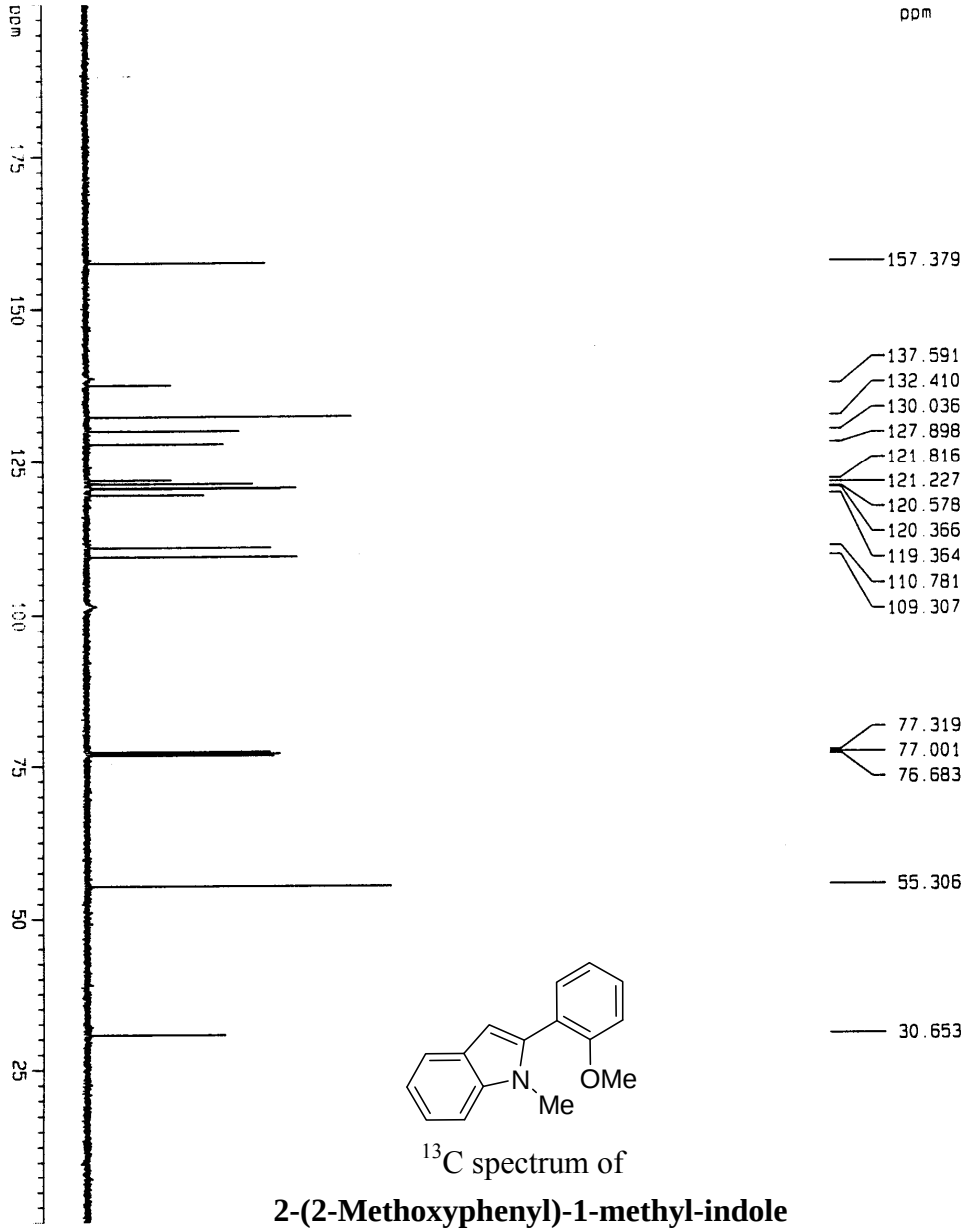
1D NMR plot parameters
CX                 19.50 cm
F1P                200.000 ppm
F1                 20122.55 Hz
F2P                -0.000 ppm
F2                 -0.00 Hz
PPMCM              10.25641 ppm/cm
HZCM               1031.92590 Hz/cm
```


Abundance
Scan 1474 (11.515 min): 3-methyl.D\data.ms (-1542) (-1602) (-)
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
m/z-->
207.1
89.0
103.5
63.0
77.0
51.9
68.0
82.6
95.5
110.0
115.0
128.0
138.9
151.0
164.9
178.0
190.0
202.0
NH
Me
Ms spectrum of
2-(3'-tolyl)-1H-indole



^{1}H spectrum of

2-(2-Methoxyphenyl)-1-methyl-indole



^{13}C spectrum of

2-(2-Methoxyphenyl)-1-methyl-indole

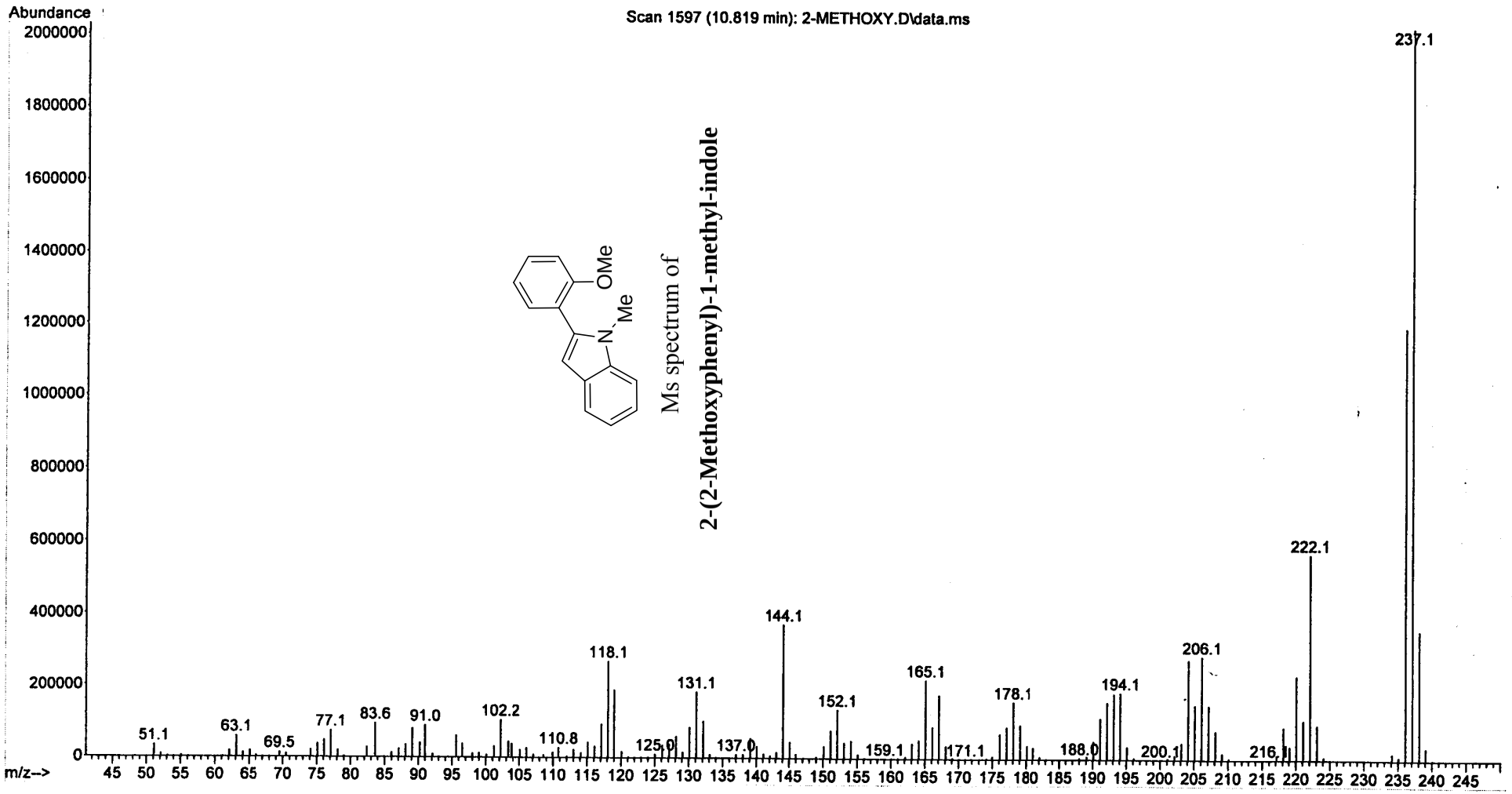
```
Date_                20070316
Time                     20.14
INSTRUM                dpx400
PROBHD      5 mm QNP  1H
PULPROG                zgdc30
TD                     131072
SOLVENT                CDCl3
NS                        128
DS                          0
SWH                 25125.629 Hz
FIDRES              0.191693 Hz
AQ                  2.6083827 sec
RG                     9195.2
DW                  19.900 usec
DE                   4.50 usec
TE                     300.0 K
D1                  3.00000000 sec
d11                 0.03000000 sec

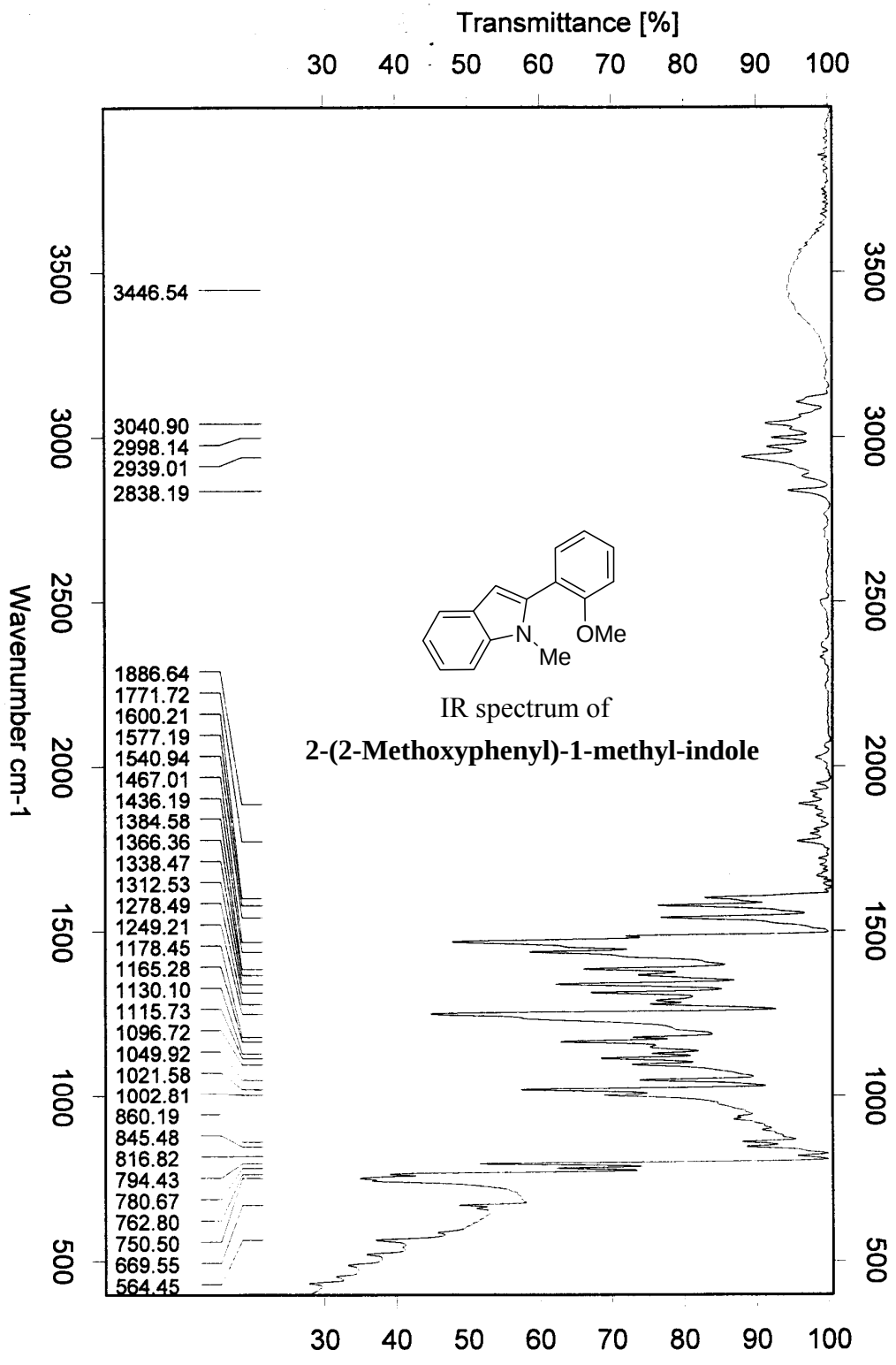
============== CHANNEL f1 ==============
NUC1                      13C
P1                       5.80 usec
PL1                      -6.00 dB
SFO1             100.6231263 MHz

============== CHANNEL f2 ==============
CPDPRG2                waltz16
NUC2                       1H
PCPD2                71.00 usec
PL2                  120.00 dB
PL12                  17.00 dB
SFO2             400.1324008 MHz

F2 - Processing parameters
SI                        65536
SF               100.6127978 MHz
WDW                          EM
SSB                           0
LB                         0.30 Hz
GB                            0
PC                         1.00

1D NMR plot parameters
CX                        19.50 cm
F1P                     200.000 ppm
F1                    20122.56 Hz
F2P                    -0.000 ppm
F2                     -0.00 Hz
PPMCM                 10.25641 ppm/cm
HZCM                1031.92615 Hz/cm
```

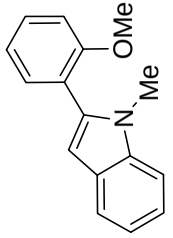

Abundance
Scan 1597 (10.819 min): 2-METHOXY.D\data.ms
2000000
1800000
1600000
1400000
1200000
1000000
800000
600000
400000
200000
0
m/z-->
45 50 55 60 65 70 75 80 85 90 95 100 105 110 115 120 125 130 135 140 145 150 155 160 165 170 175 180 185 190 195 200 205 210 215 220 225 230 235 240 245
237.1
222.1
144.1
118.1
206.1
165.1
131.1
194.1
178.1
152.1
102.2
91.0
83.6
77.1
63.1
51.1
69.5
110.8
125.0
137.0
159.1
171.1
188.0
200.1
216.1
OMe
Me
N
Ms spectrum of
2-(2-Methoxyphenyl)-1-methyl-indole



IR spectrum of

2-(2-Methoxyphenyl)-1-methyl-indole

HRMS spectrum of **2-(2-Methoxyphenyl)-1-methyl-indole**



Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 60.0

Selected filters: None

Monoisotopic Mass, Even Electron Ions

44 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

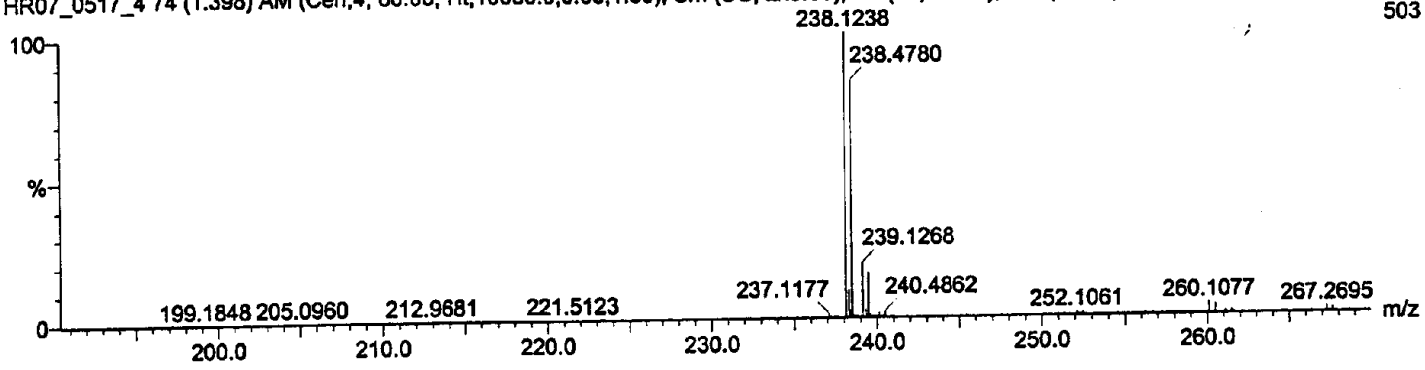
C: 0-27 H: 0-1000 N: 0-2 O: 0-1 P: 0-1

So Chau Ming, N-methyl 2-(2-methoxyphenyl)indole

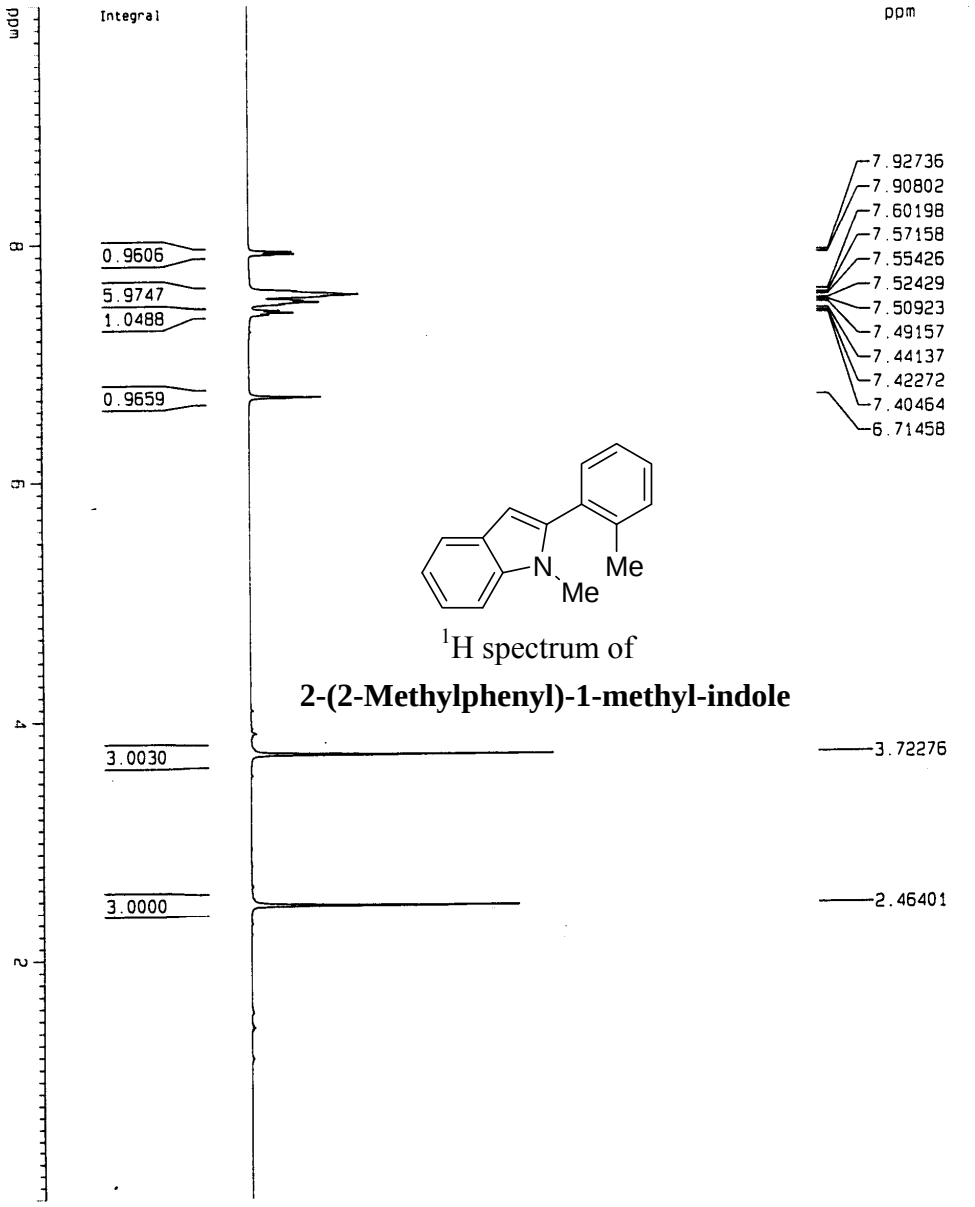
HR07_0517_4 74 (1.398) AM (Cen,4, 80.00, Ht,10000.0,0.00,1.00); Sm (SG, 2x3.00); Sb (15,10.00); Cm (69:81)

TOF MS ES+

503



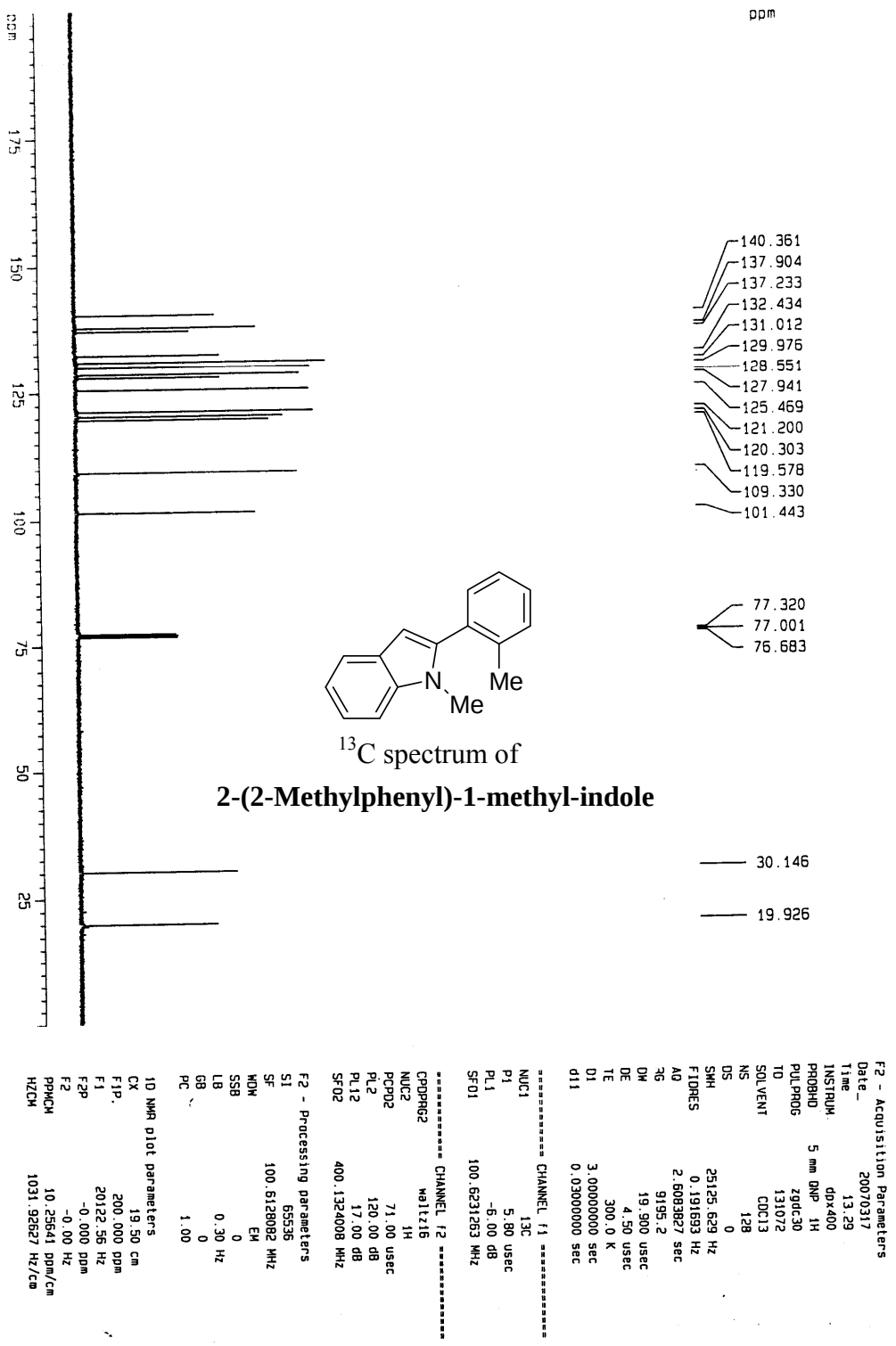
Minimum:				-1.5		
Maximum:		5.0	5.0	60.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
238.1238	238.1232	0.6	2.5	9.5	0.1	C16 H16 N O



^{1}H spectrum of

2-(2-Methylphenyl)-1-methyl-indole


```
F2 - Acquisition Parameters
Date_              20070317
Time                  13.26
INSTRUM             dpx400
PROBHD   5 mm QNP  1H
PULPROG             zg30
TD                  32768
SOLVENT             CDCl3
NS                  32
DS                  0
SWH                 4629.629 Hz
FIDRES              0.141285 Hz
AQ                  3.5389941 sec
RG                  32
DW                  108.000 usec
DE                  4.50 usec
TE                  300.0 K
D1                  1.00000000 sec
============== CHANNEL f1 ==============
NUC1                1H
P1                  9.50 usec
PL1                 -6.00 dB
SFO1                400.1319924 MHz
F2 - Processing parameters
SI                  16384
SF                  400.1300086 MHz
WDW                 EM
SSB                 0
LB                  0.30 Hz
GB                  0
PC                  1.00
1D NMR plot parameters
CX                  19.63 cm
F1P                 10.000 ppm
F1                  4001.30 Hz
F2P                 0.000 ppm
F2                  0.00 Hz
PPMCM               0.50931 ppm/cm
HZCM                203.79143 Hz/cm
```



^{13}C spectrum of

2-(2-Methylphenyl)-1-methyl-indole

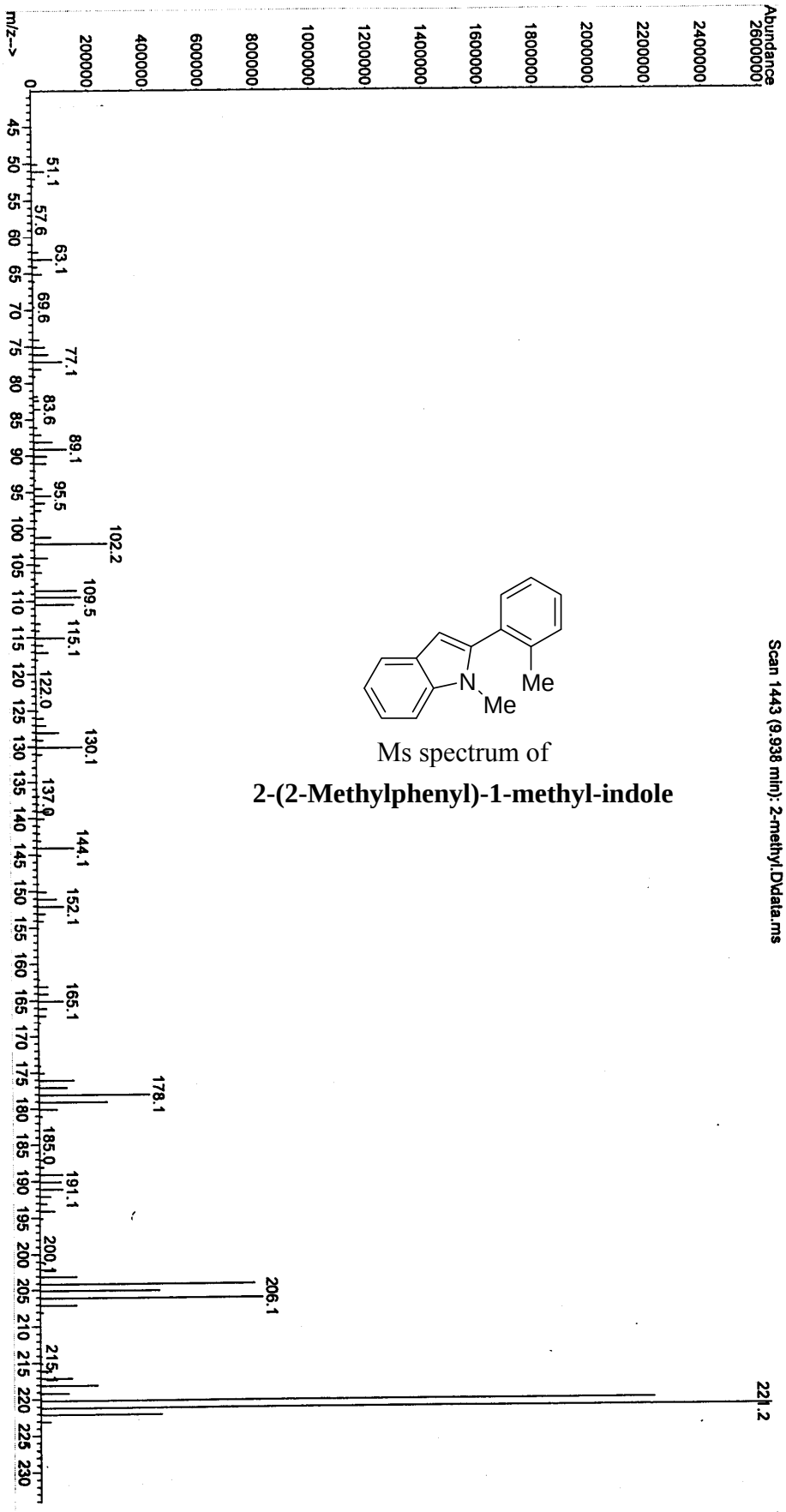
F2 - Acquisition Parameters
Date_ 20070317
Time 13.29
INSTRUM dpx400
PROBHD 5 mm DNP 1H
PULPROG zgdc30
TD 131072
SOLVENT CDCl3
NS 128
DS 0
SWH 25125.629 Hz
FIDRES 0.191693 Hz
AQ 2.6083827 sec
RG 9195.2
DW 19.900 usec
DE 4.50 usec
TE 300.0 K
D1 3.00000000 sec
d11 0.03000000 sec

======== CHANNEL f1 ========
NUC1 13C
P1 5.80 usec
PL1 -6.00 dB
SFO1 100.6231263 MHz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 71.00 usec
PL2 17.00 dB
PL12 17.00 dB
SFO2 400.1324008 MHz

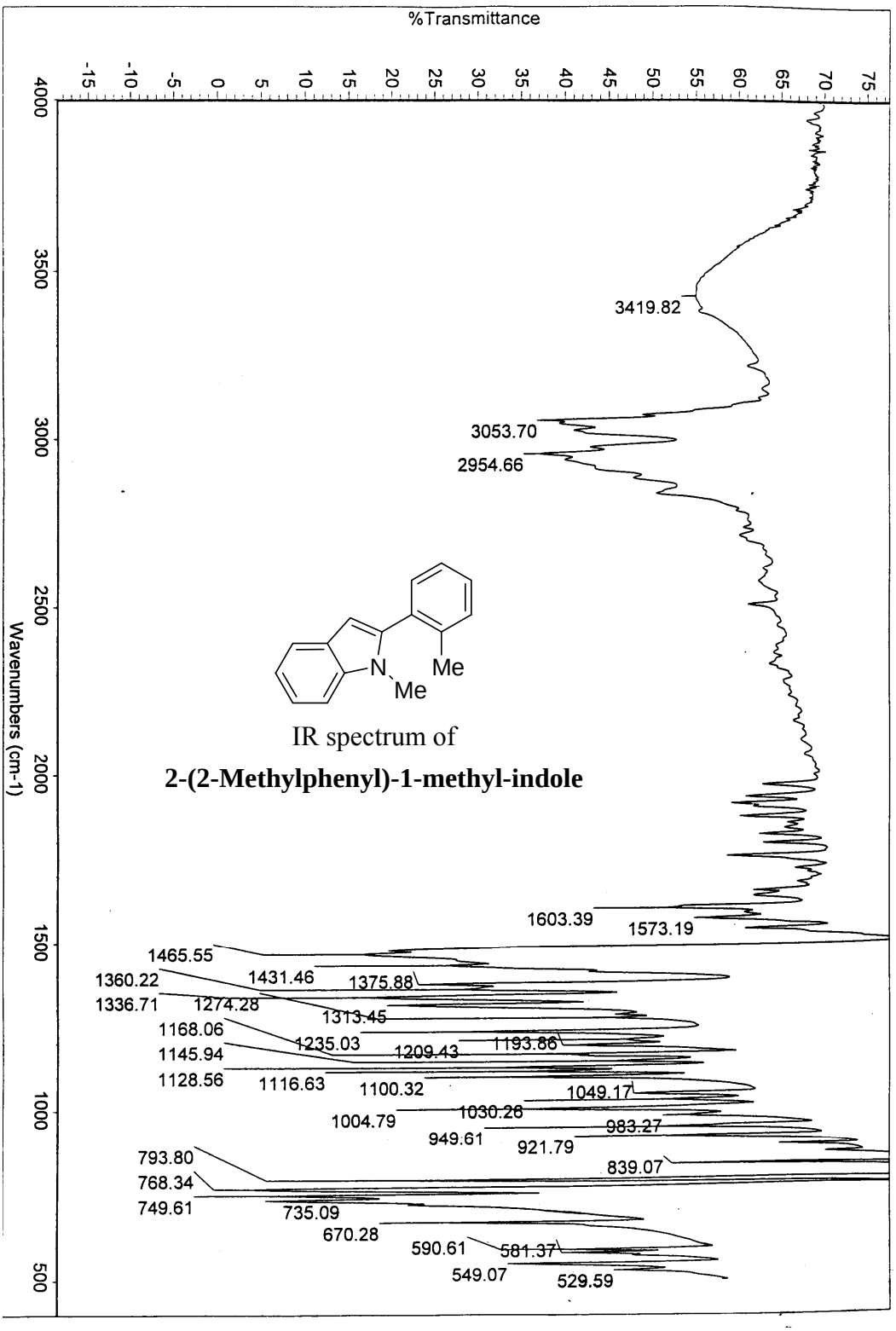
F2 - Processing parameters
SI 65536
SF 100.6128082 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 19.50 cm
F1P 200.000 ppm
F1 20122.56 Hz
F2P -0.000 ppm
F2 -0.00 Hz
PPMCM 10.25641 ppm/cm
HZCM 1031.92627 Hz/cm



Ms spectrum of

2-(2-Methylphenyl)-1-methyl-indole

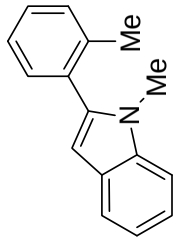


IR spectrum of

2-(2-Methylphenyl)-1-methyl-indole

HRMs spectrum of

2-(2-Methylphenyl)-1-methyl-indole



Elemental Composition Report

Single Mass Analysis

Tolerance = 10.0 PPM / DBE: min = -1.5, max = 60.0

Selected filters: None

Monoisotopic Mass, Even Electron Ions

5 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

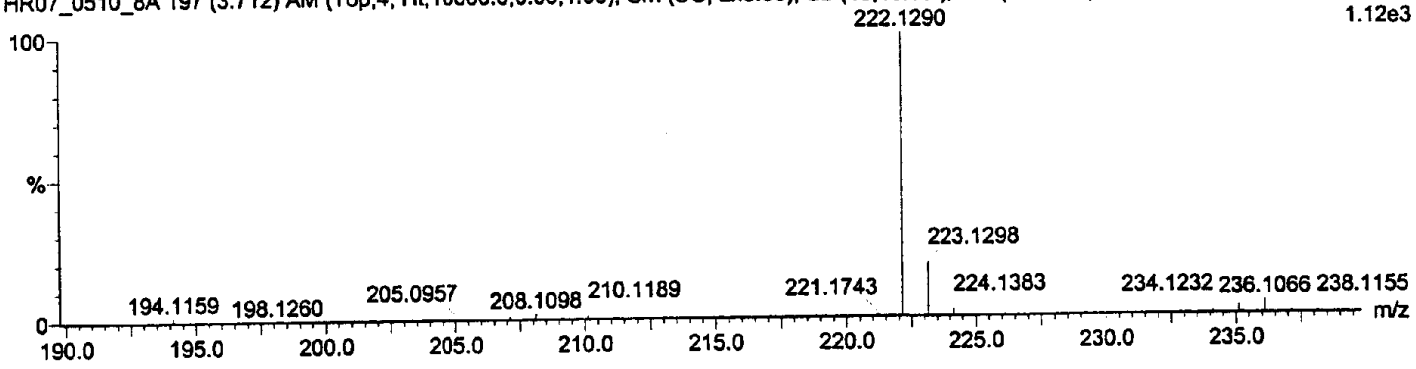
C: 0-16 H: 0-1000 N: 0-1

So Chau Ming, N-methyl 2(2-methylphenyl)indole

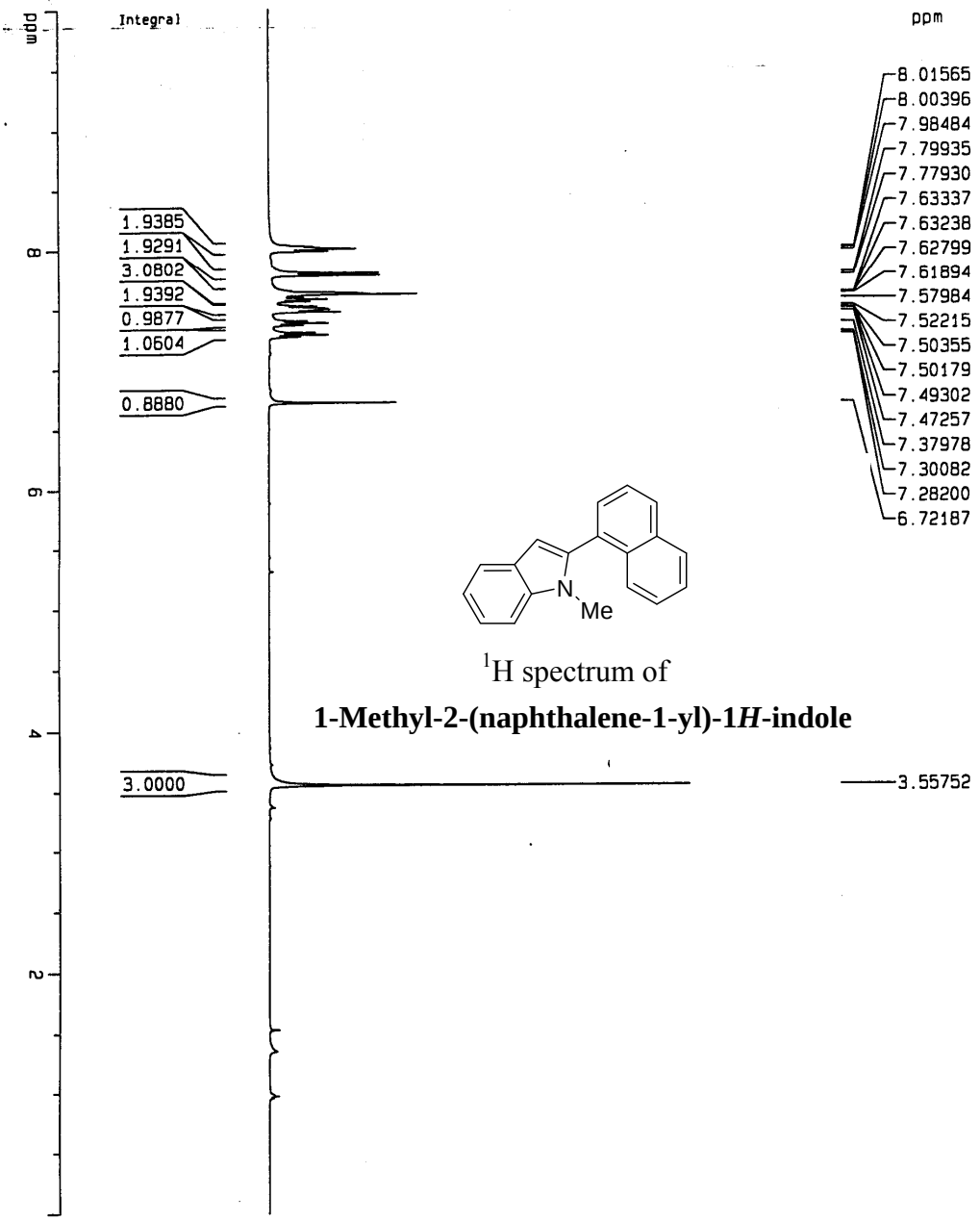
HR07_0510_8A 197 (3.712) AM (Top,4, Ht,10000.0,0.00,1.00); Sm (SG, 2x3.00); Sb (15,10.00); Cm (195:274)

TOF MS ES+

1.12e3



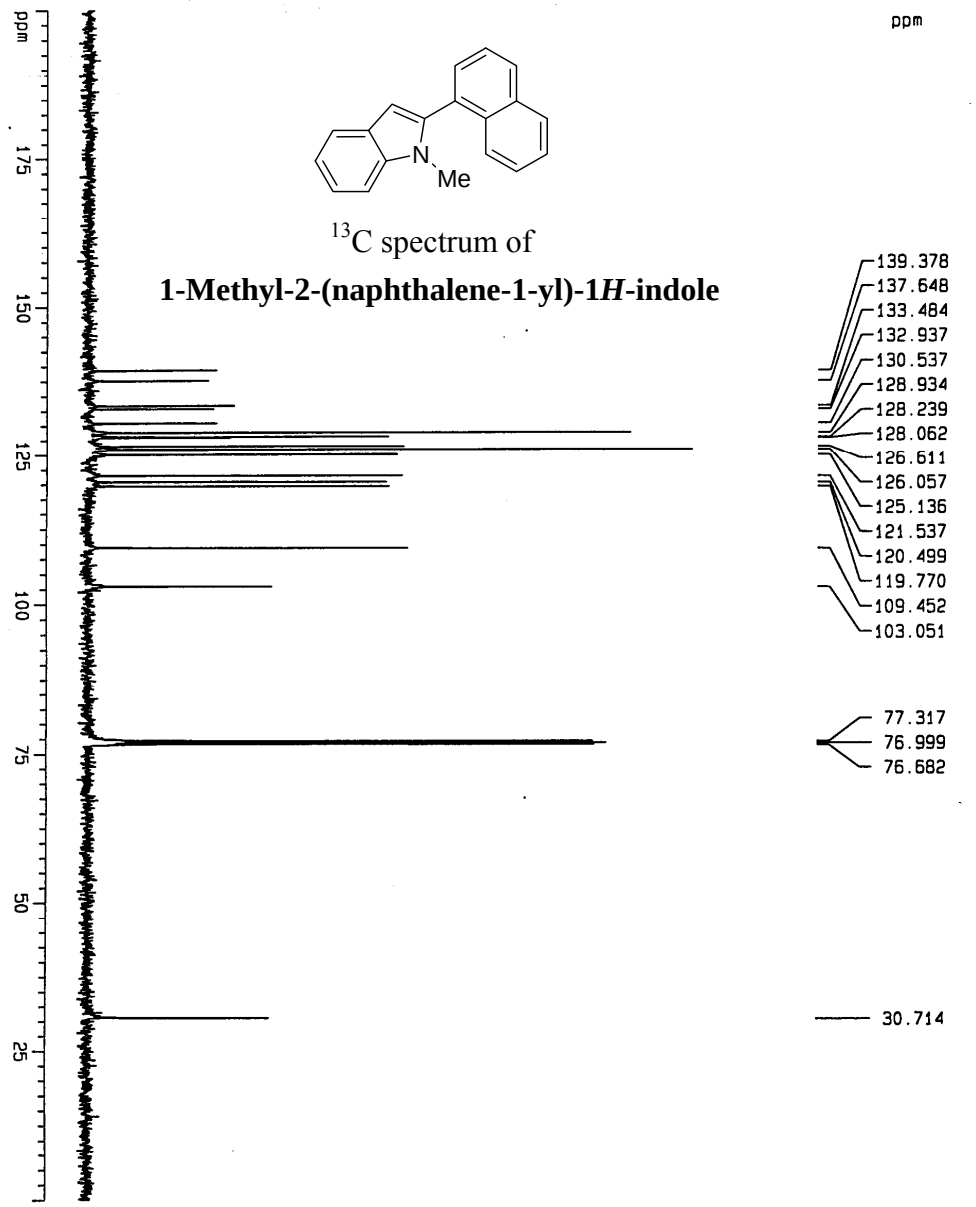
Minimum:				-1.5		
Maximum:		5.0	10.0	60.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
222.1290	222.1283	0.7	3.2	9.5	0.7	C16 H16 N



^{1}H spectrum of

1-Methyl-2-(naphthalene-1-yl)-1*H*-indole

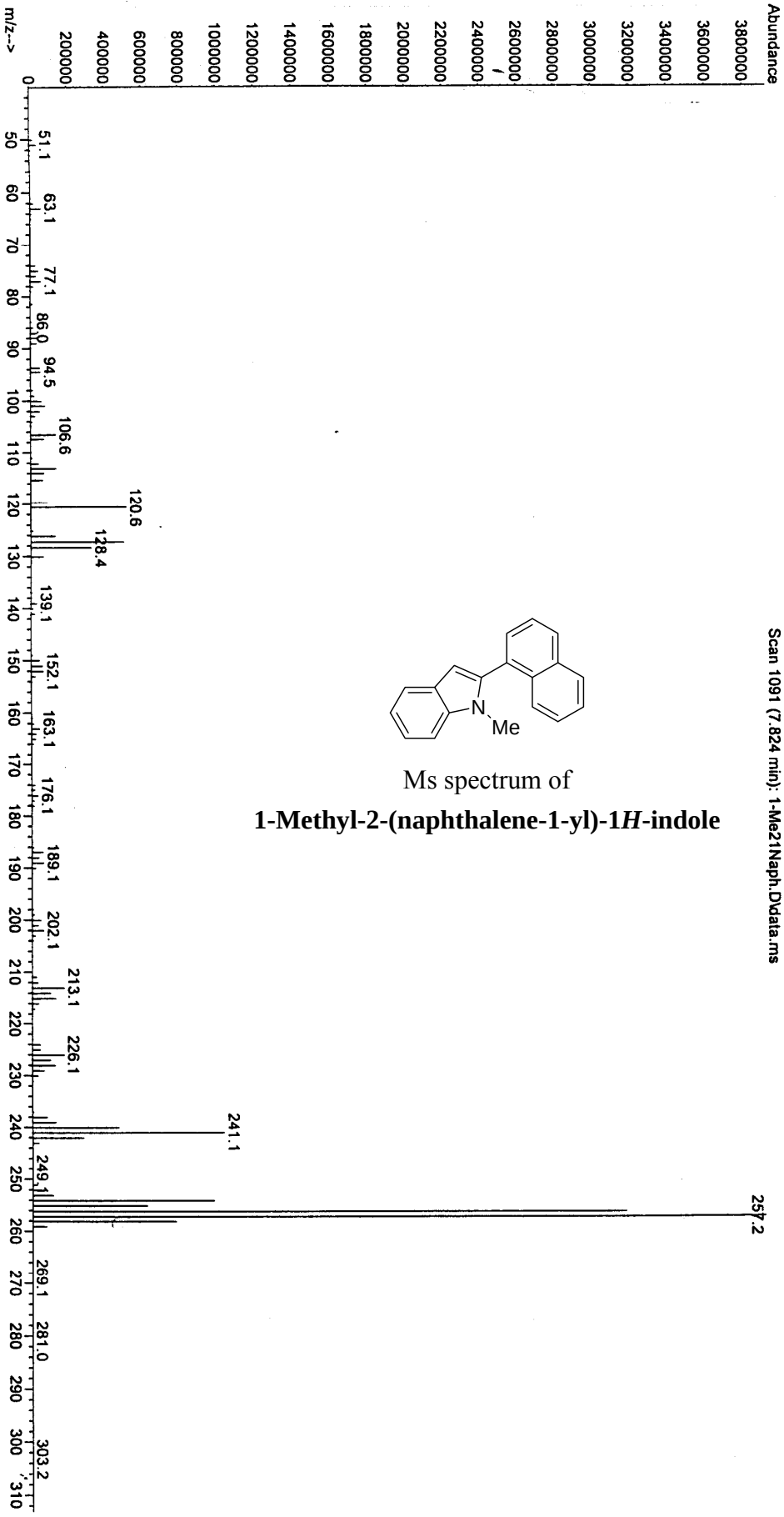
F2 - Acquisition Parameters
Date_ 20080913
Time 17.01
INSTRUM dpx400
PROBHD 5 mm QNP 1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 0
SWH 5995.204 Hz
FIDRES 0.182959 Hz
AQ 2.7329011 sec
RG 90.5
DW 83.400 usec
DE 4.50 usec
TE 300.0 K
D1 1.00000000 sec
========== CHANNEL f1 ==========
NUC1 1H
P1 9.50 usec
PL1 -6.00 dB
SFO1 400.1320098 MHz
F2 - Processing parameters
SI 16384
SF 400.1300092 MHz
WDW EM
SSB 0
LB 0.40 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 19.63 cm
F1P 10.000 ppm
F1 4001.30 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.50931 ppm/cm
HZCM 203.79143 Hz/cm



^{13}C spectrum of

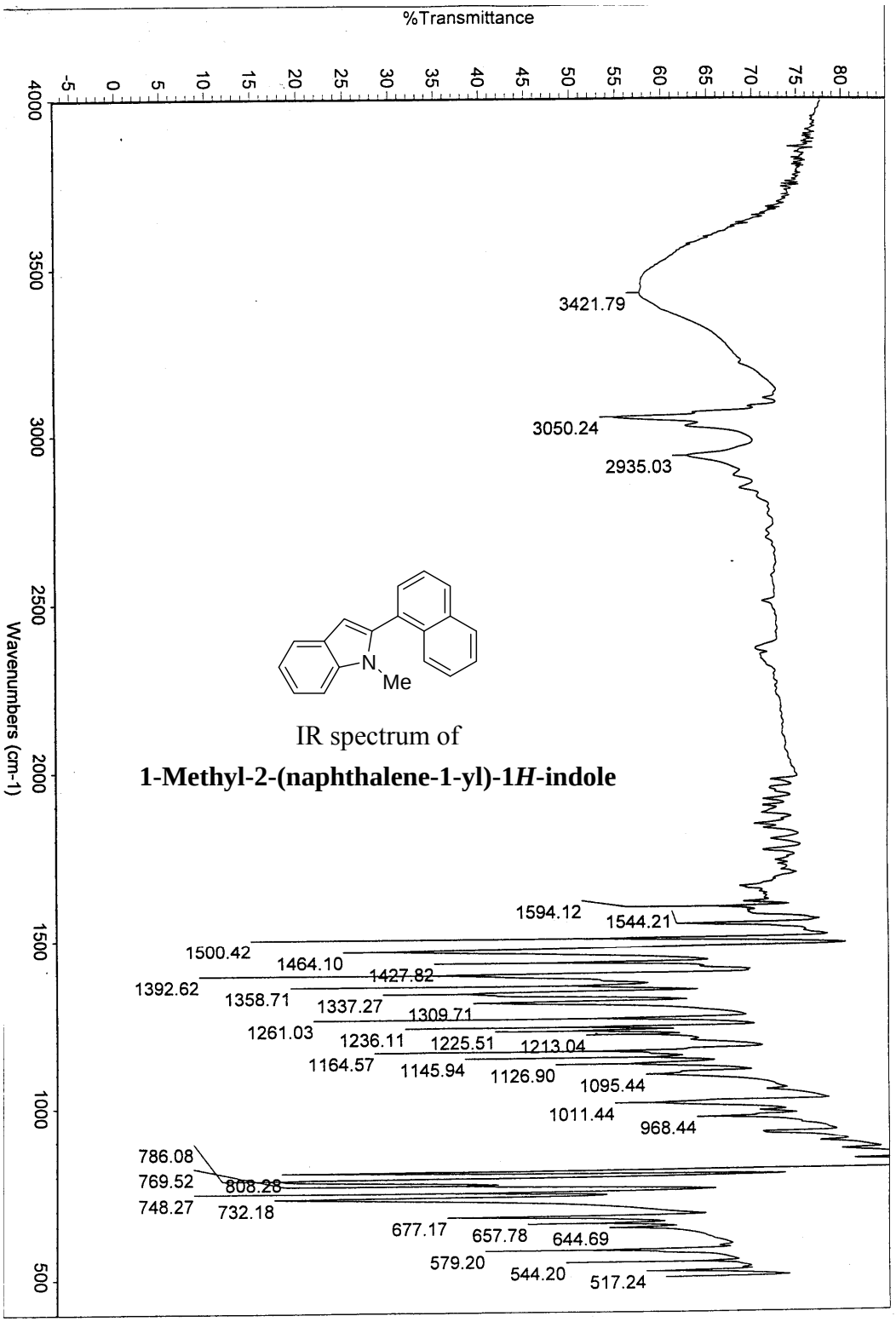
1-Methyl-2-(naphthalene-1-yl)-1*H*-indole

F2 - Acquisition Parameters
Date_ 20080913
Time 17.04
INSTRUM dpx400
PROBHD 5 mm QNP 1H
PULPROG zgdc30
TD 131072
SOLVENT CDCl3
NS 170
DS 0
SWH 27624.309 Hz
FIDRES 0.210757 Hz
AQ 2.3724532 sec
RG 7298.2
DW 18.100 usec
DE 4.50 usec
TE 300.0 K
D1 3.00000000 sec
d11 0.03000000 sec
---------- CHANNEL f1 ----------
NUC1 13C
P1 5.80 usec
PL1 -6.00 dB
SF01 100.6231263 MHz
---------- CHANNEL f2 ----------
CPDPRG2 waltz16
NUC2 1H
PCPD2 71.00 usec
PL2 120.00 dB
PL12 17.00 dB
SF02 400.1326008 MHz
F2 - Processing parameters
SI 65536
SF 100.6127818 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 19.50 cm
F1P 200.000 ppm
F1 20122.56 Hz
F2P -0.000 ppm
F2 -0.00 Hz
PPMCM 10.25641 ppm/cm
HZCM 1031.92603 Hz/cm



Ms spectrum of

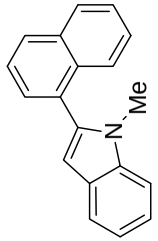
1-Methyl-2-(naphthalene-1-yl)-1*H*-indole



IR spectrum of

1-Methyl-2-(naphthalene-1-yl)-1*H*-indole

HRMs spectrum of **1-Methyl-2-(naphthalene-1-yl)-1*H*-indole**



Elemental Composition Report

Single Mass Analysis

Tolerance = 10.0 PPM / DBE: min = -1.5, max = 60.0

Selected filters: None

Monoisotopic Mass, Even Electron Ions

5 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

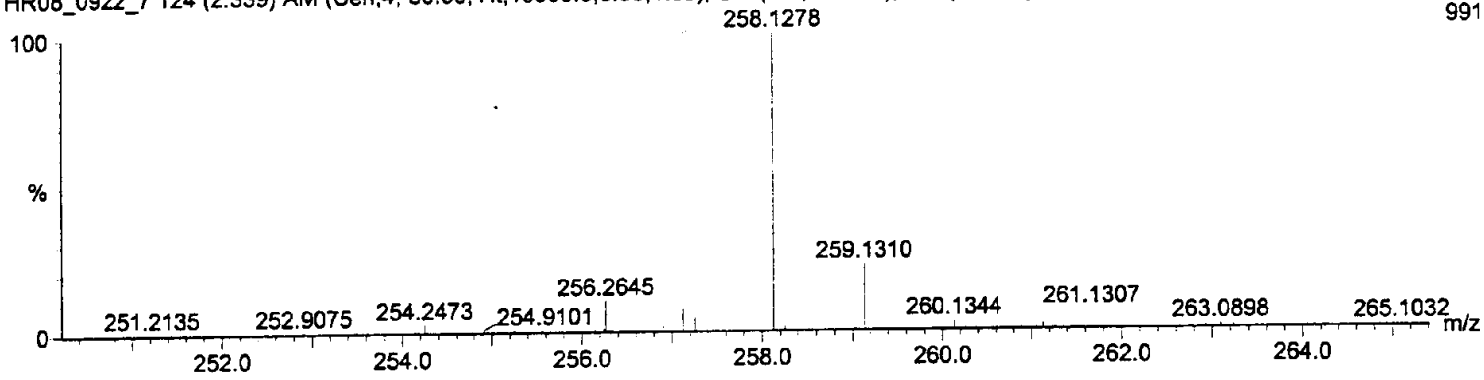
C: 0-19 H: 0-1000 N: 0-1

So Chau Ming, C19H15N

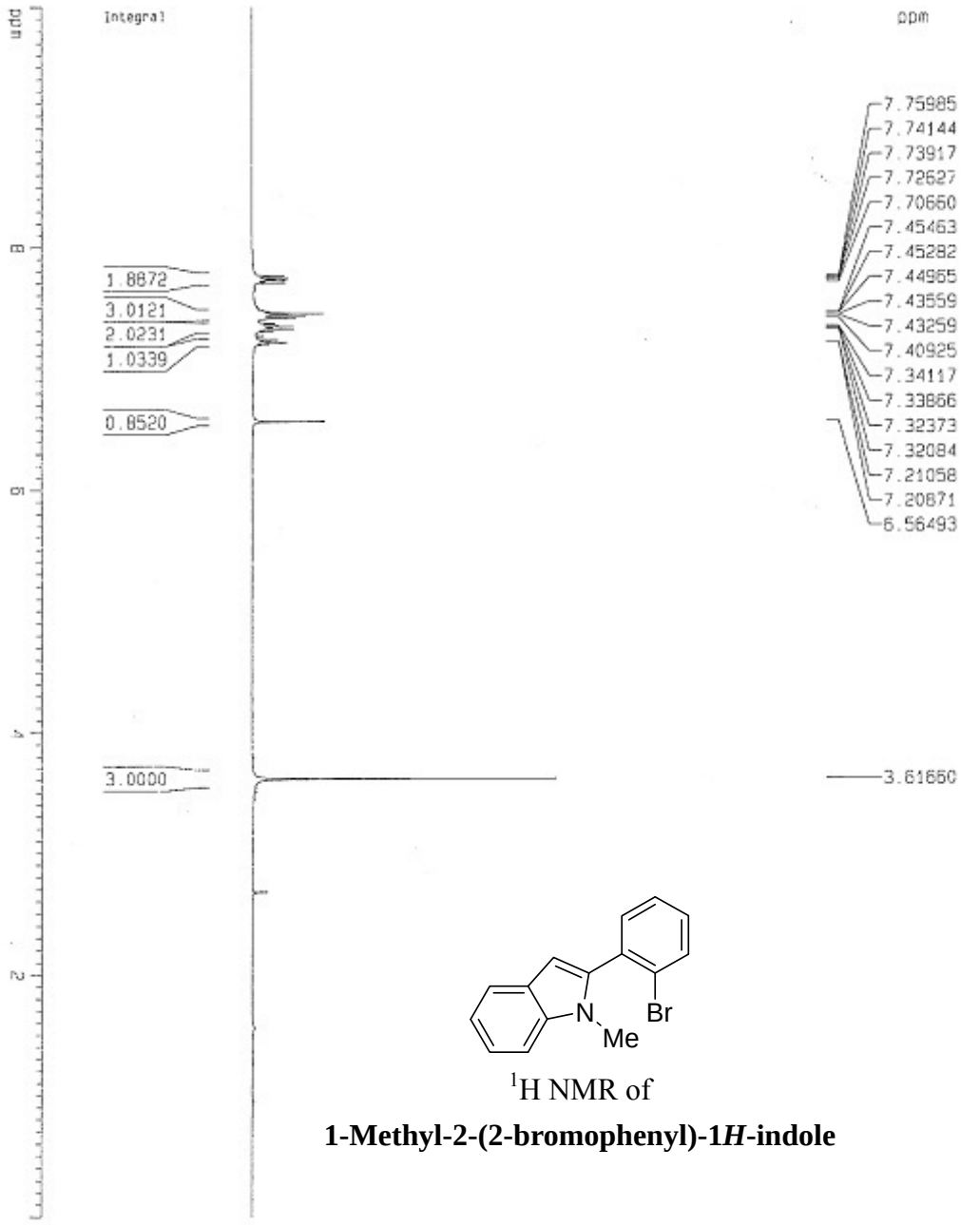
HR08_0922_7 124 (2.339) AM (Cen,4, 80.00, Ht,10000.0,0.00,1.00); Sm (SG, 2x3.00); Cm (82:124)

TOF MS ES+

991



Minimum:				-1.5		
Maximum:		100.0	10.0	60.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
258.1278	258.1283	-0.5	-1.9	12.5	0.6	C19 H16 N



^{1}H NMR of

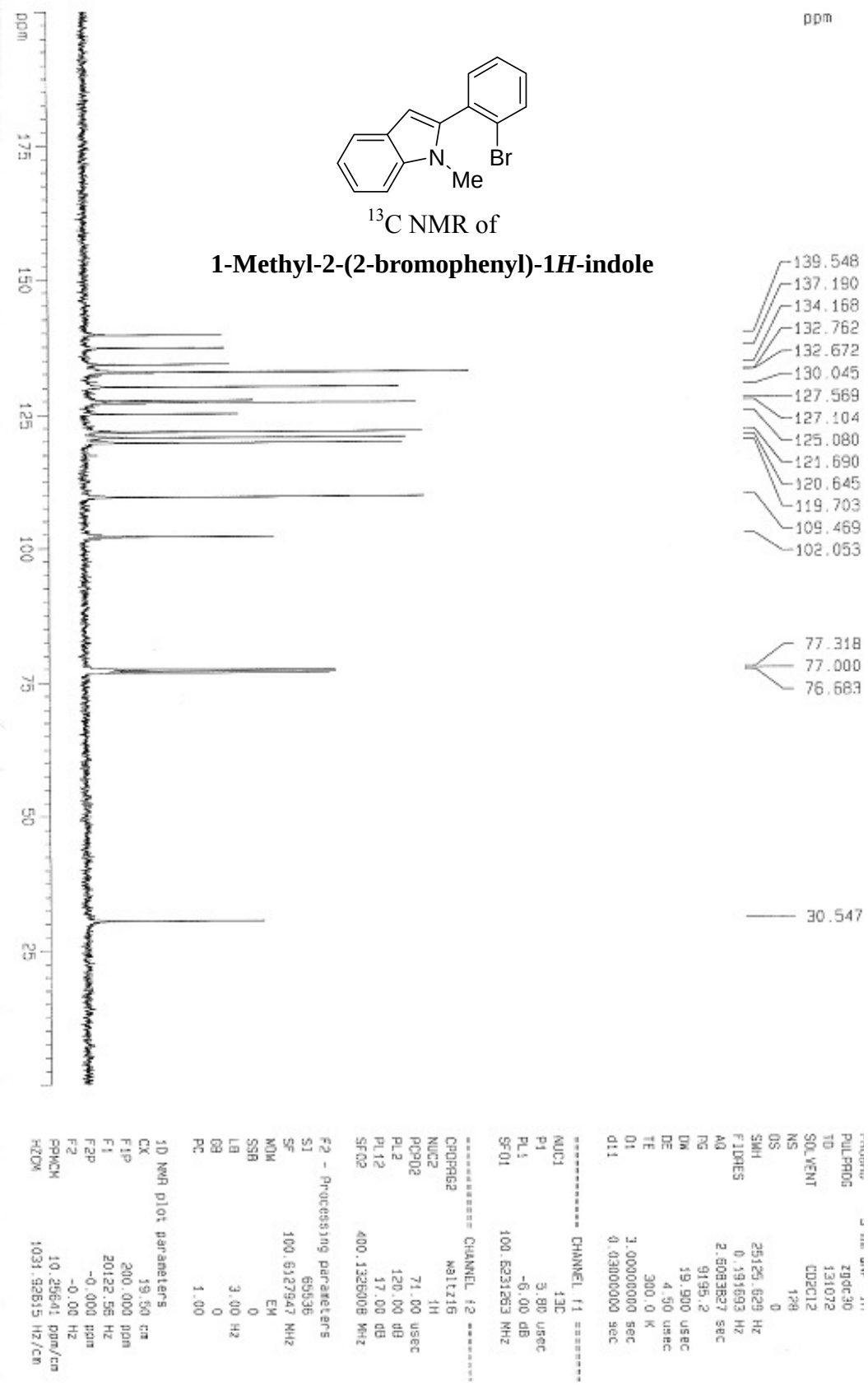
1-Methyl-2-(2-bromophenyl)-1*H*-indole


```
F2 - Acquisition Parameters
Date_              20070529
Time                   8.37
INSTRUM              dpx400
PROBHD     5 mm QNP 1H
PULPROG              zg30
TD                  32768
SOLVENT             CDCl3
NS                     32
DS                      0
SWH              4629.629 Hz
FIDRES           0.141285 Hz
AQ               3.5389941 sec
RG                     128
DW               108.000 usec
DE                 4.50 usec
TE                 300.0 K
D1               1.00000000 sec

======== CHANNEL f1 ======
NUC1                   1H
P1                 9.50 usec
PL1                -6.00 dB
SFO1         400.1319924 MHz

F2 - Processing parameters
SI                    16384
SF           400.1300092 MHz
WDW                      EM
SSB                       0
LB                 0.30 Hz
GB                        0
PC                 1.00

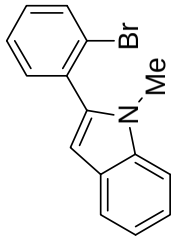
1D NMR plot parameters
CX                19.63 cm
F1P           10.000 ppm
F1              4001.30 Hz
F2P            0.000 ppm
F2               0.00 Hz
PPMCM          0.50931 ppm/cm
HZCM         203.79143 Hz/cm
```

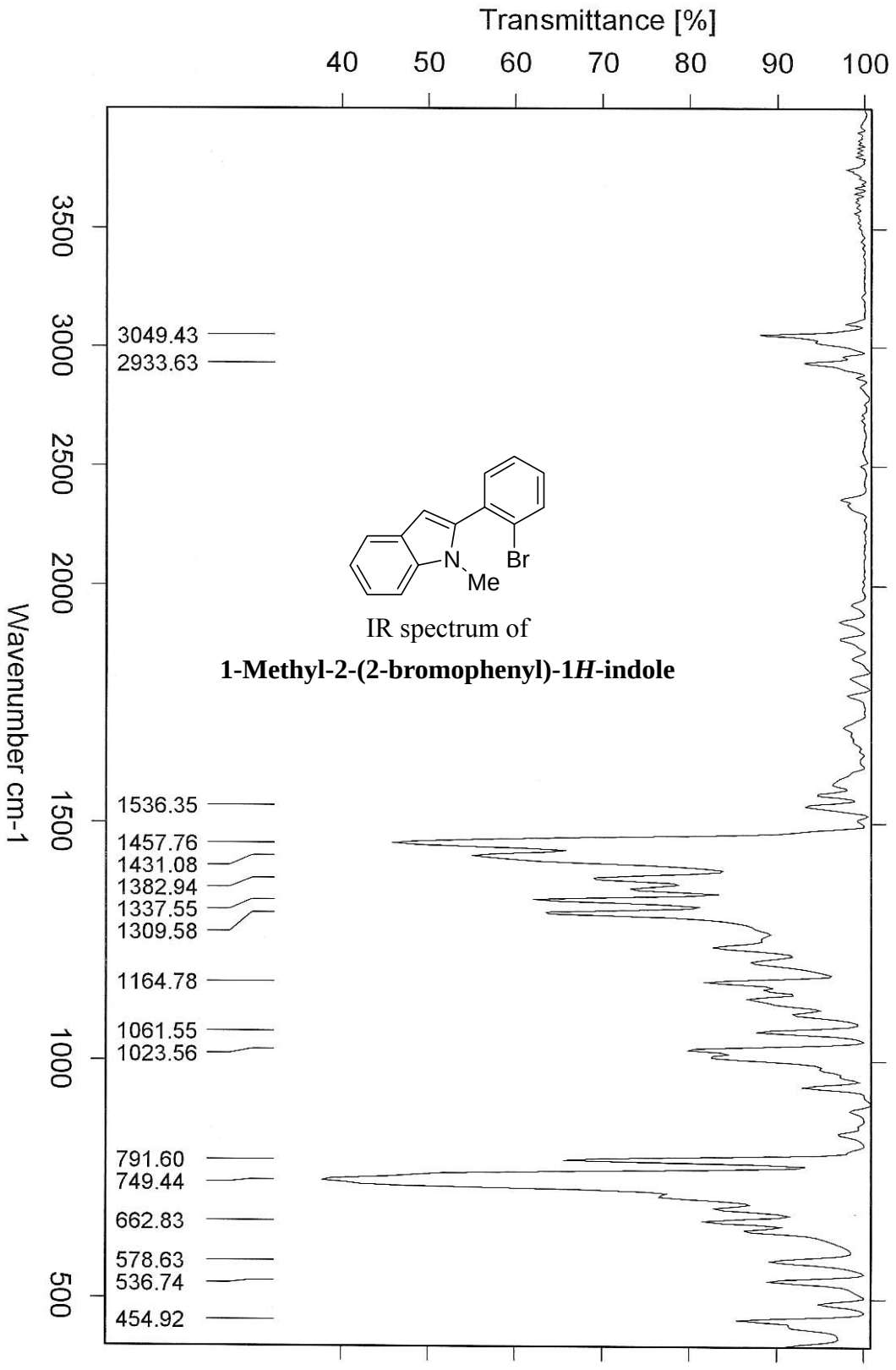


^{13}C NMR of

1-Methyl-2-(2-bromophenyl)-1*H*-indole

MS spectrum of **1-Methyl-2-(2-bromophenyl)-1*H*-indole**



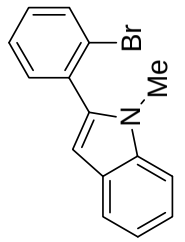


IR spectrum of

1-Methyl-2-(2-bromophenyl)-1*H*-indole

HRMs spectrum of

1-Methyl-2-(2-bromophenyl)-1*H*-indole



Elemental Composition Report

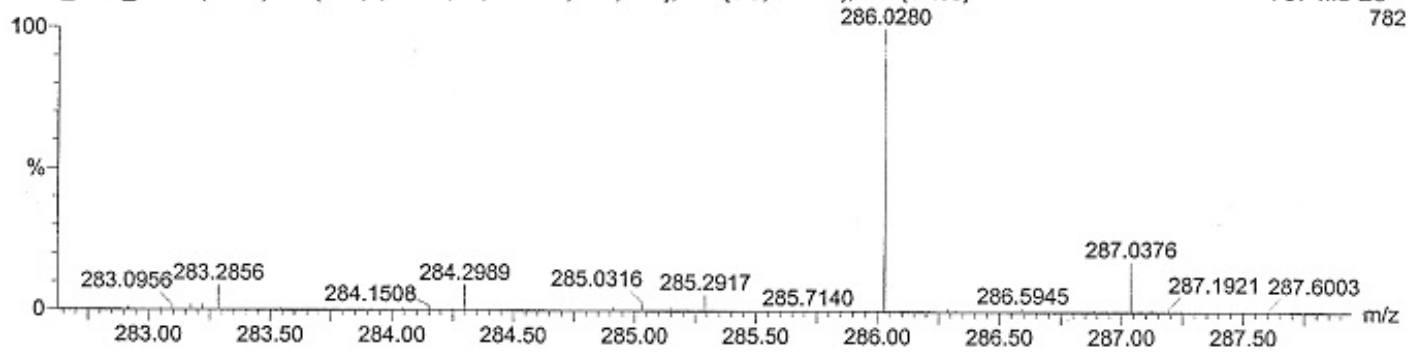
Single Mass Analysis

Tolerance = 100.0 PPM / DBE: min = -1.5, max = 60.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
7 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-15 H: 0-1000 N: 0-1 Br: 0-1

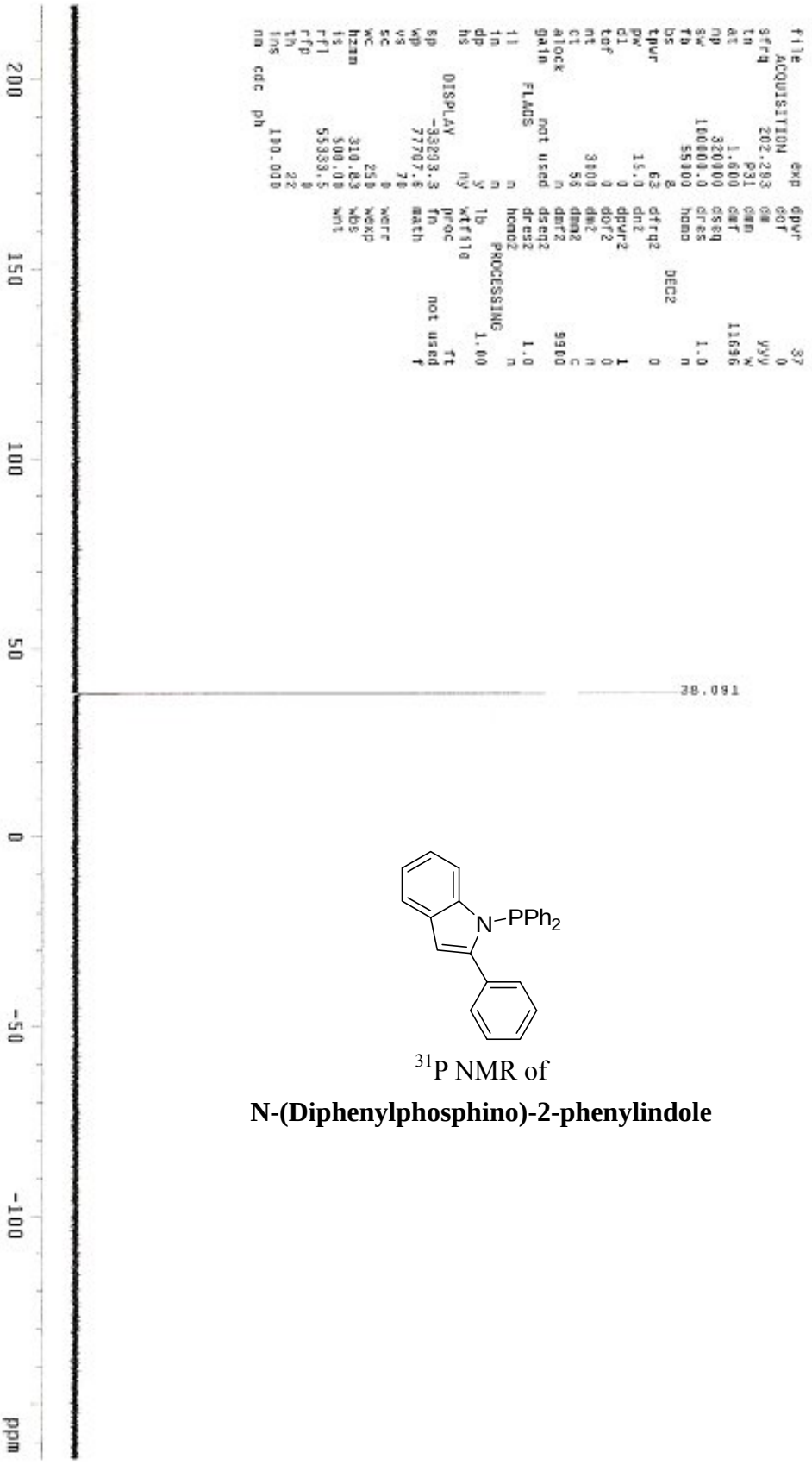
So Chau Ming, N-methyl 2(2Bromophenyl)indole
HR07_0615_4B 41 (0.778) AM (Cen,5, 80.00, Ht,10000.0,0.00,0.70); Sm (SG, 3x2.00); Cm (41:59)

15-Jun-2007
TOF MS ES+
782



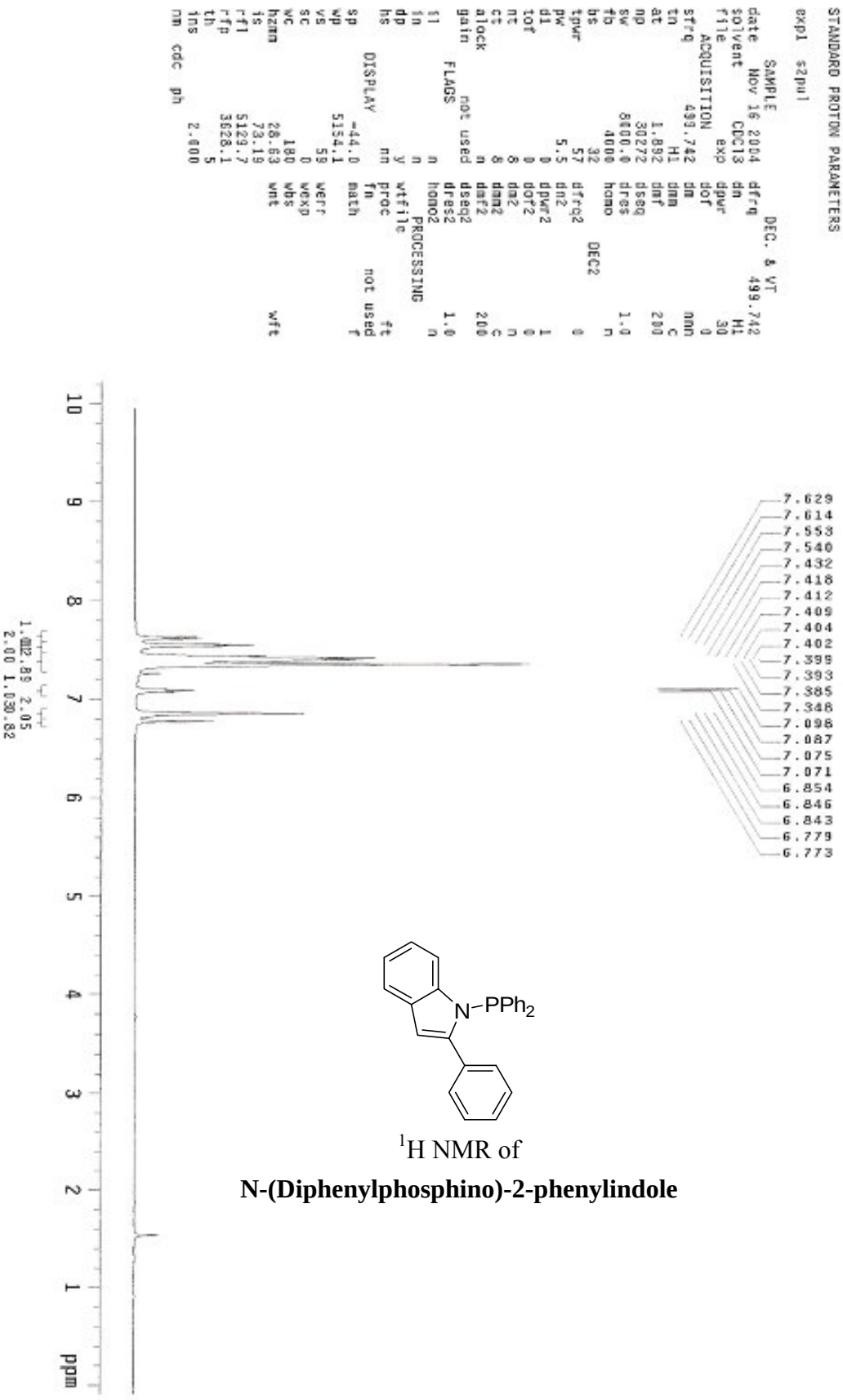
Minimum:				-1.5		
Maximum:		5.0	100.0	60.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
286.0280	286.0231	4.9	17.1	9.5	463.5	C15 H13 N Br

N-P Type Indolyl Phosphine



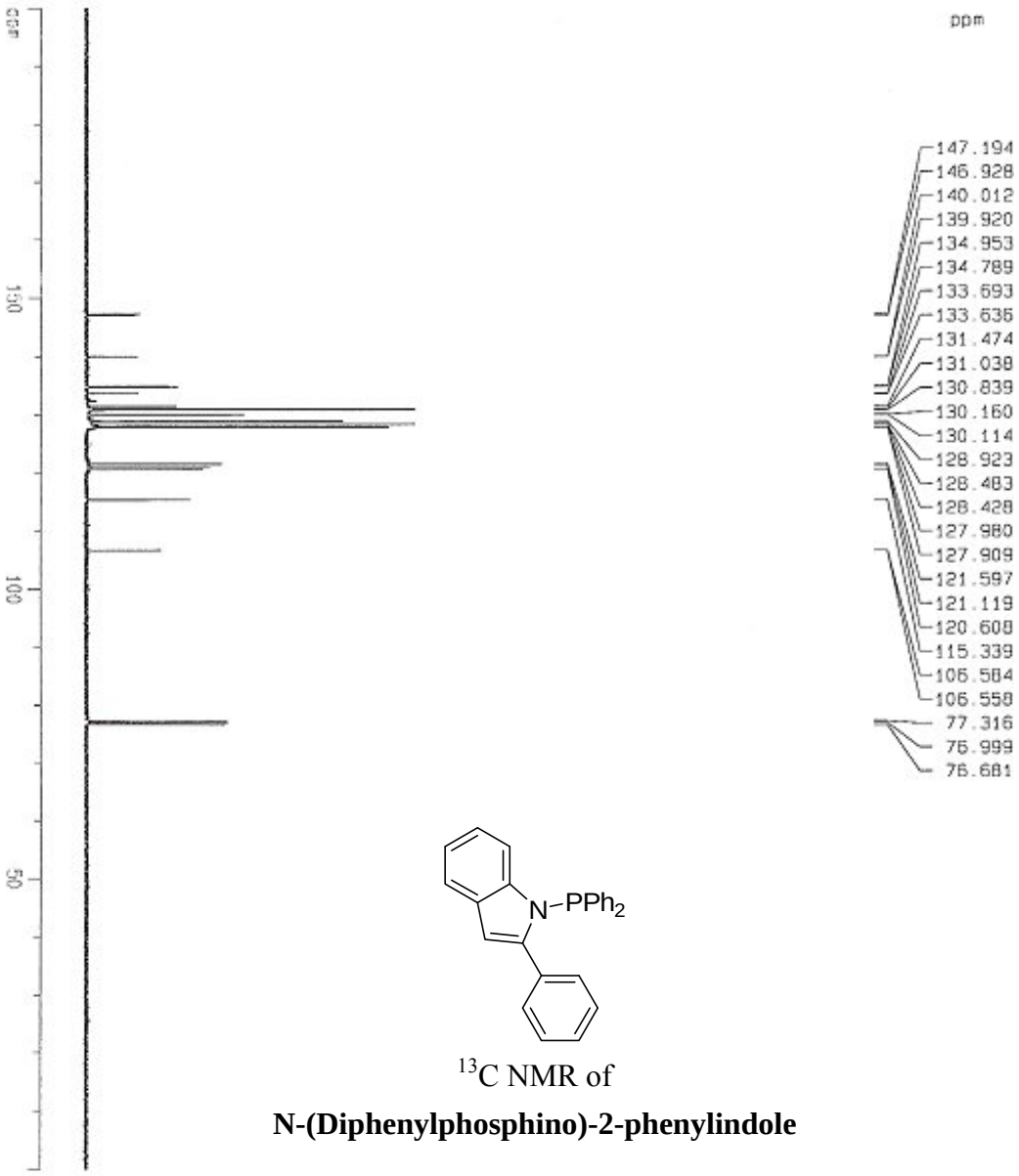
^{31}P NMR of

N-(Diphenylphosphino)-2-phenylindole



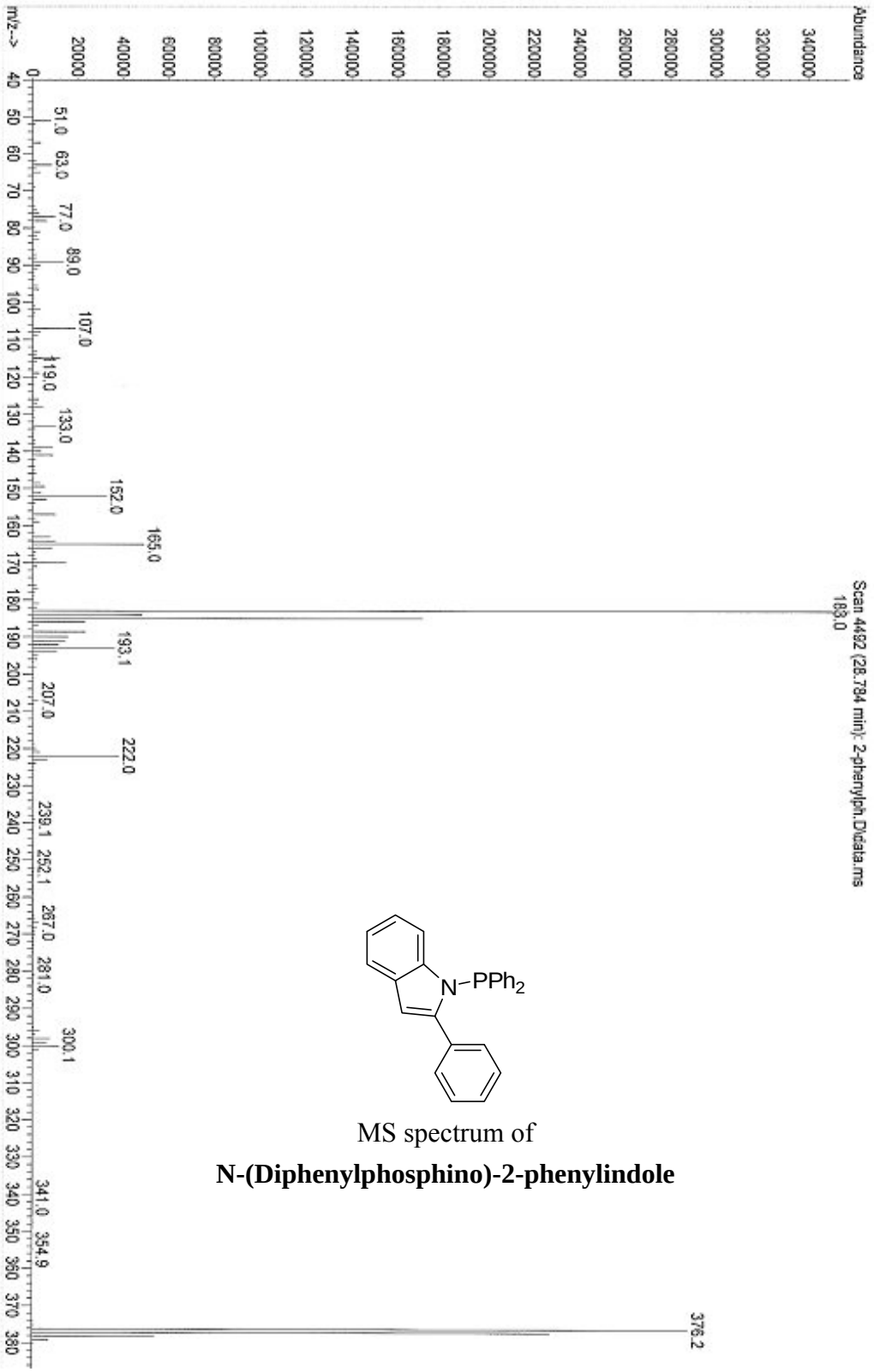
^{1}H NMR of

N-(Diphenylphosphino)-2-phenylindole



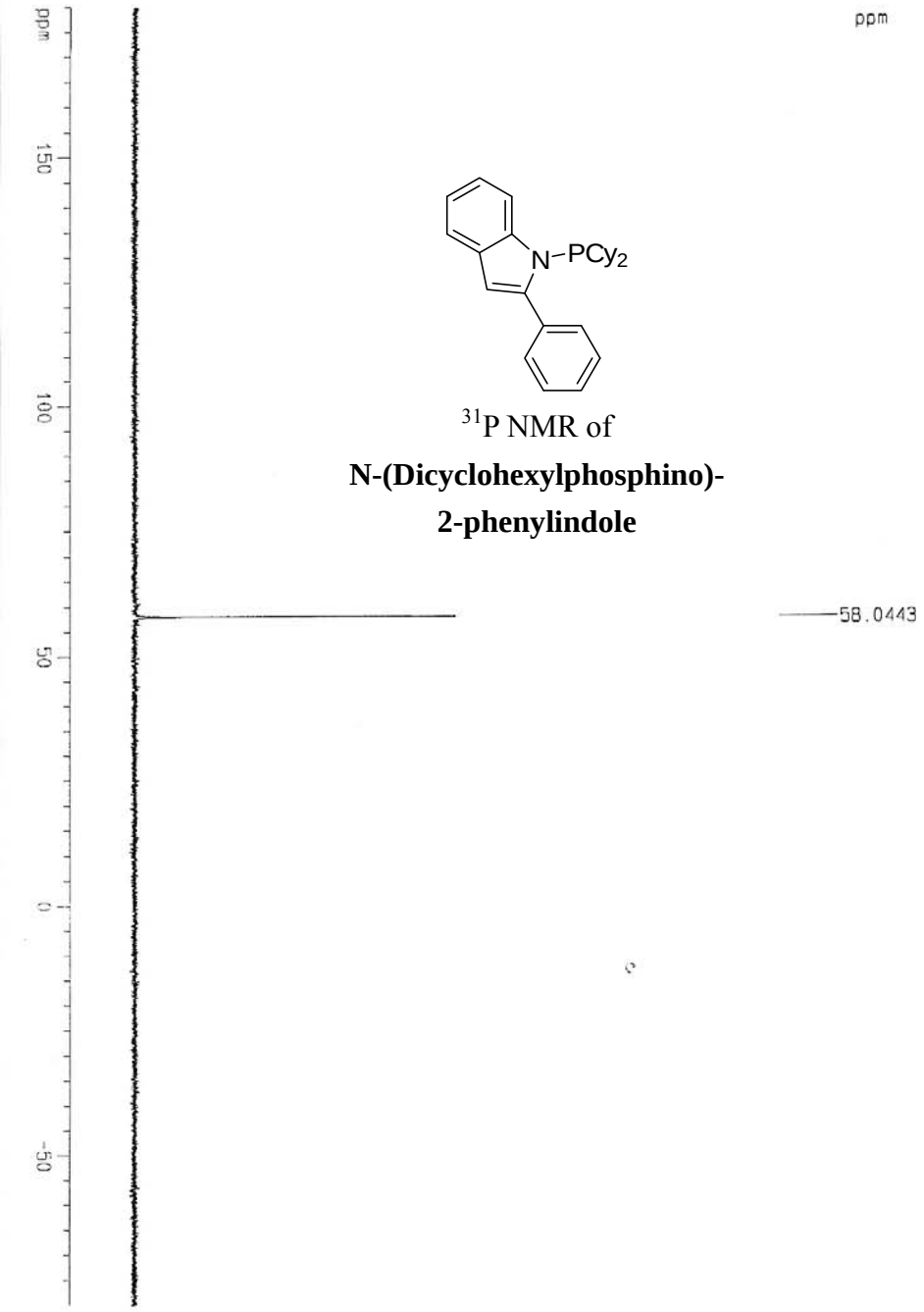
^{13}C NMR of

N-(Diphenylphosphino)-2-phenylindole



MS spectrum of

N-(Diphenylphosphino)-2-phenylindole



^{31}P NMR of

N-(Dicyclohexylphosphino)-2-phenylindole

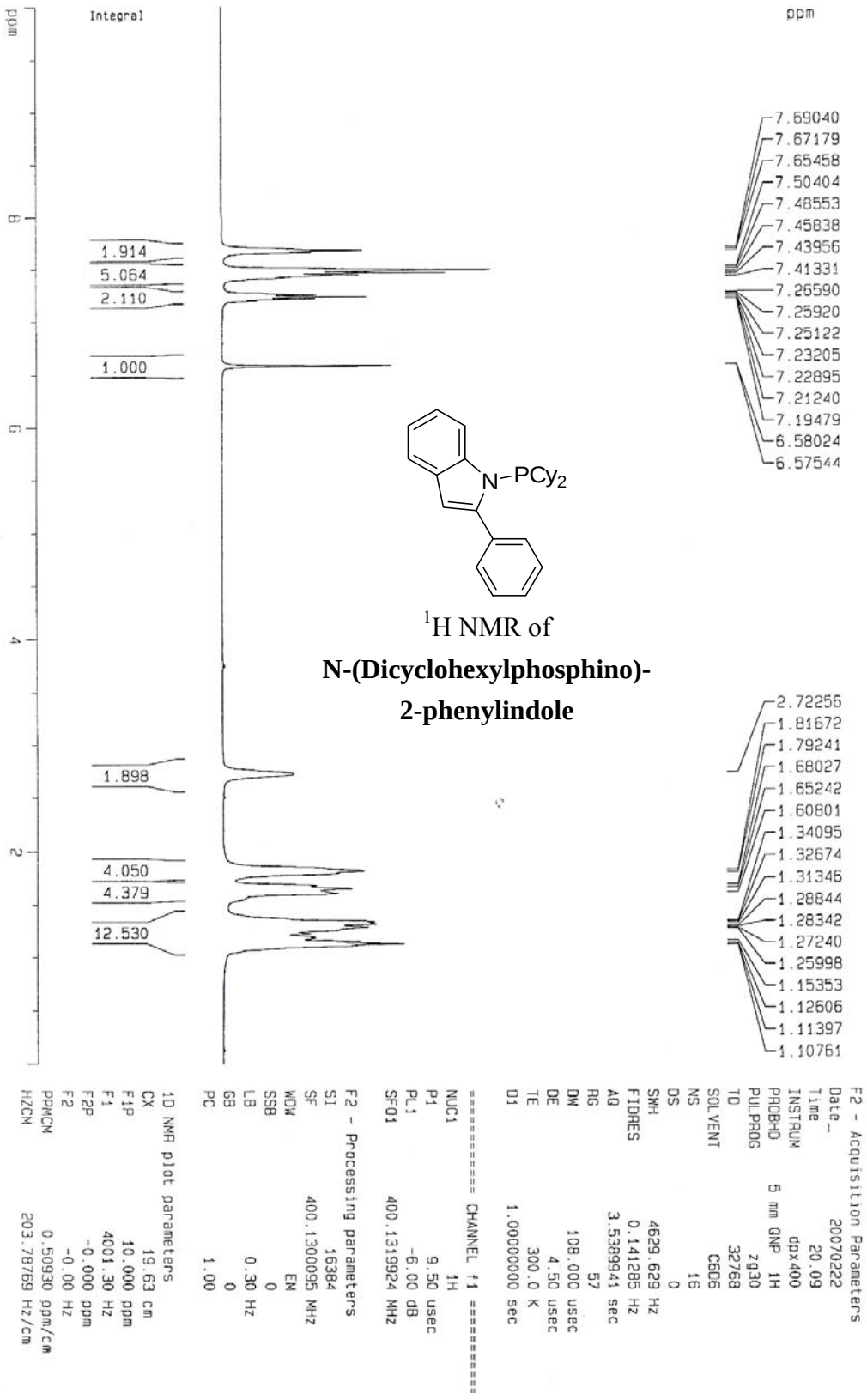

```
F2 - Acquisition Parameters
Date_              20070222
Time               13.48
INSTRUM              dpx400
PROBHD     5 mm QNP 1H
PULPROG              zgpc30
TD                   65536
SOLVENT              CDCl3
NS                   27
DS                   0
SWH              48661.801 Hz
FIDRES           0.742620 Hz
AQ               0.6734324 sec
RG               11586.2
DW               10.275 usec
DE               4.50 usec
TE                   300.0 K
D1               1.00000000 sec
d11              0.03000000 sec

======== CHANNEL f1 ========
NUC1                 31P
P1                   7.20 usec
PL1                  -6.00 dB
SFO1             161.9851115 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                 1H
PCPD2                71.00 usec
PL2                  120.00 dB
PL12                 17.00 dB
SFO2             400.1319910 MHz

F2 - Processing parameters
SI                   32768
SF               161.9755831 MHz
WDW                  EM
SSB                  0
LB                   3.00 Hz
GB                   0
PC                   1.40

1D NMR plot parameters
CX                   20.00 cm
F1P                  180.000 ppm
F1               29155.61 Hz
F2P                  -80.000 ppm
F2               -12958.05 Hz
PPMCM                13.00000 ppm/cm
HZCM             2105.62252 Hz/cm
```



^{1}H NMR of

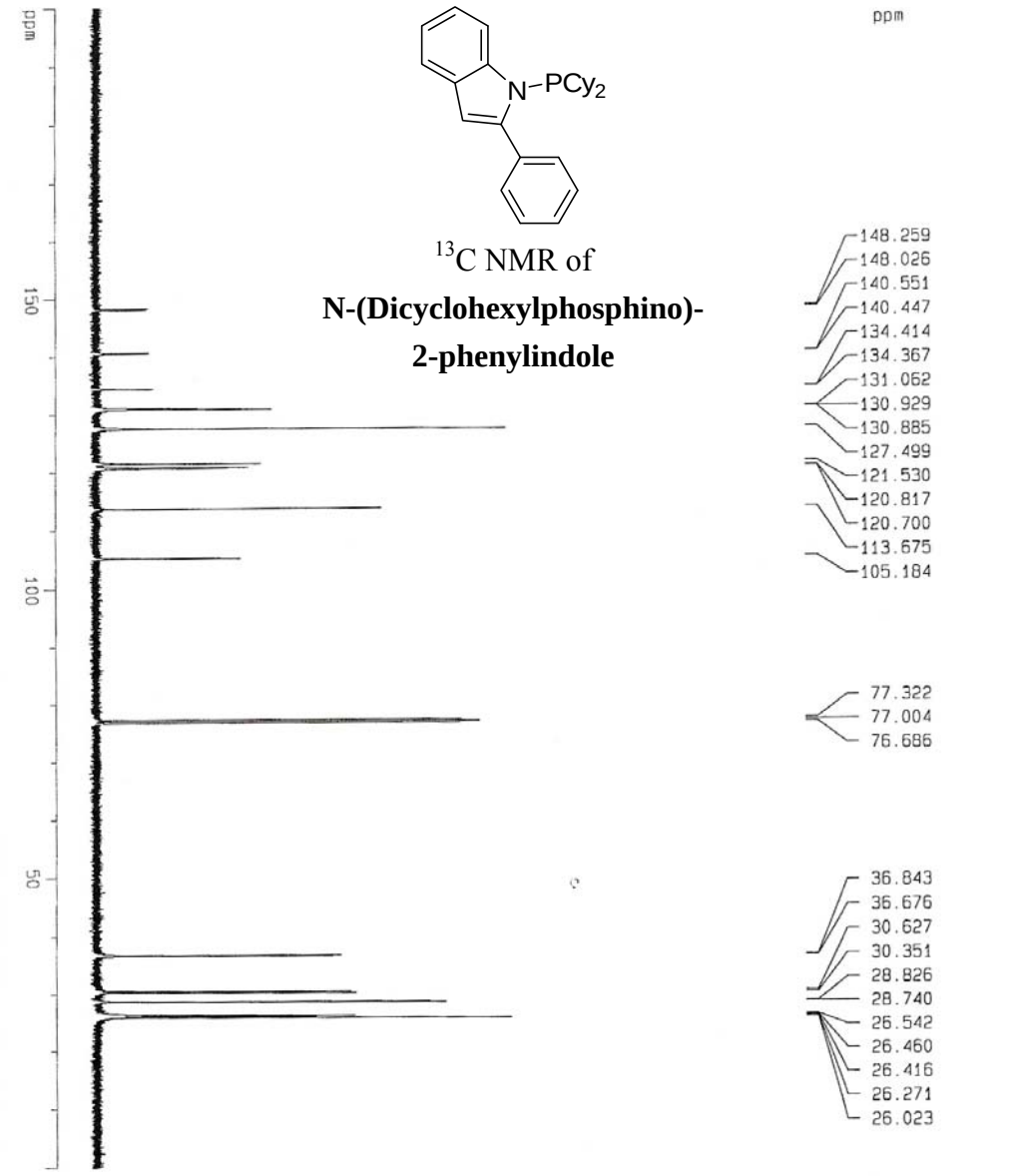
N-(Dicyclohexylphosphino)-2-phenylindole

F2 - Acquisition Parameters
Date_ 20070222
Time 20.09
INSTRUM dpx400
PROBHD 5 mm QNP 1H
PULPROG zg30
TD 32768
SOLVENT C6D6
NS 16
DS 0
SWH 4629.629 Hz
FIDRES 0.141285 Hz
AQ 3.5389941 sec
RG 57
DW 108.000 usec
DE 4.50 usec
TE 300.0 K
D1 1.00000000 sec

========== CHANNEL f1 ==========
NUC1 1H
P1 9.50 usec
PL1 -6.00 dB
SFO1 400.1319924 MHz

F2 - Processing parameters
SI 16384
SF 400.1300095 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

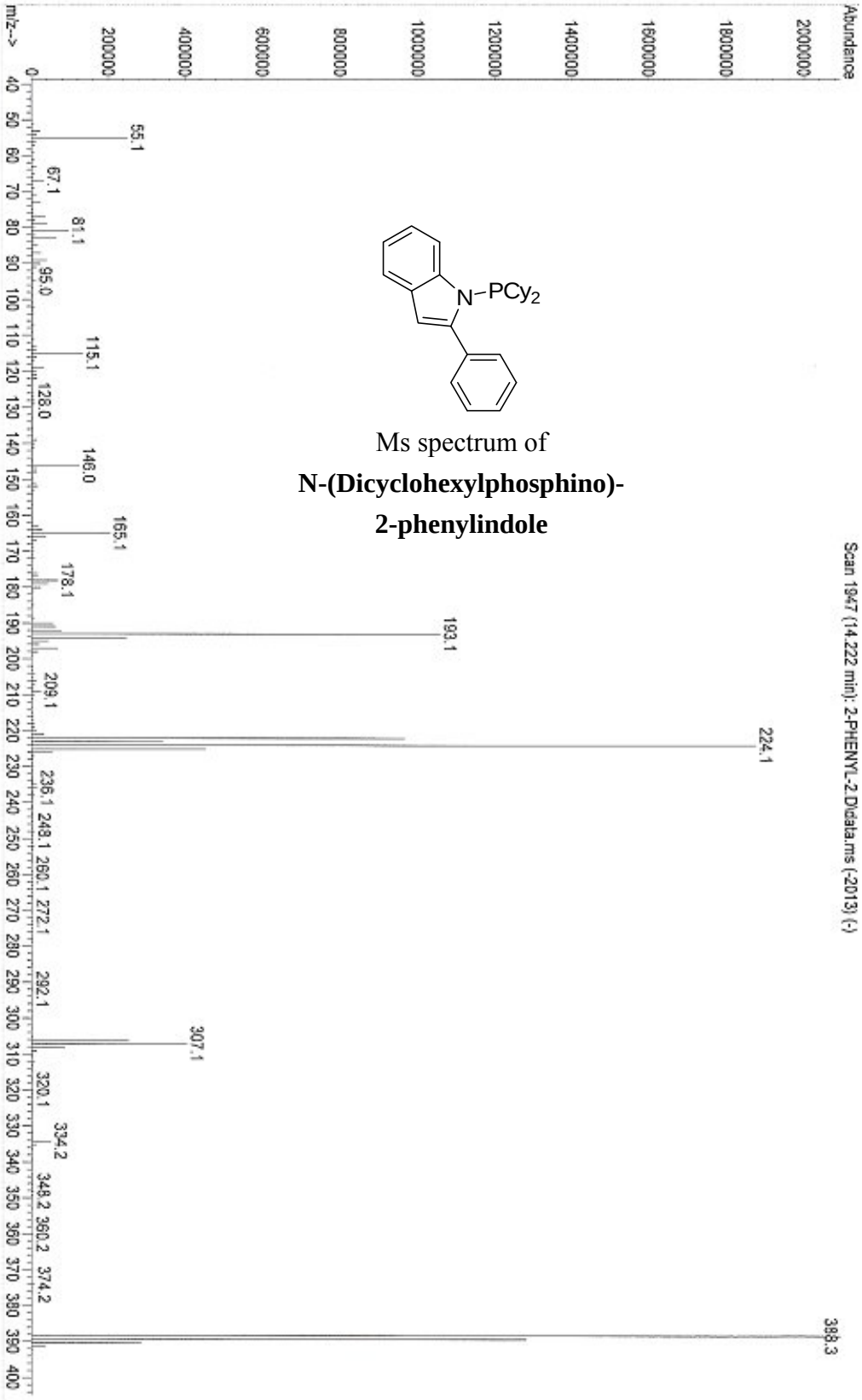
1D NMR plot parameters
CX 19.63 cm
F1P 10.000 ppm
F1 4001.30 Hz
F2P -0.000 ppm
F2 -0.00 Hz
PPMCM 0.50930 ppm/cm
HZCM 203.78769 Hz/cm



^{13}C NMR of

N-(Dicyclohexylphosphino)-2-phenylindole

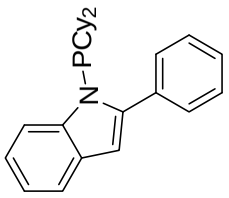
```
F2 - Acquisition Parameters
Date_              20070222
Time                   20.33
INSTRUM                dpx400
PROBHD  5 mm QNP 1H
PULPROG                zgdc30
TD                     131072
SOLVENT                CDCl3
NS                       256
DS                         0
SWH                25125.629 Hz
FIDRES                 0.191693 Hz
AQ                 2.6083827 sec
RG                      8192
DW                    19.900 usec
DE                     4.50 usec
TE                    300.0 K
D1                 3.00000000 sec
d11                0.03000000 sec
========== CHANNEL f1 ==========
NUC1                      13C
P1                       5.80 usec
PL1                     -6.00 dB
SF01           100.6231263 MHz
========== CHANNEL f2 ==========
CPDPRG2                 waltz16
NUC2                        1H
PCPD2                  71.00 usec
PL2                    120.00 dB
PL12                    17.00 dB
SFO2           400.1308230 MHz
F2 - Processing parameters
SI                         65536
SF             100.6127947 MHz
WDW                        EM
SSB                         0
LB                       0.30 Hz
GB                          0
PC                       1.00
1D NMR plot parameters
CX                       19.50 cm
F1P                    200.000 ppm
F1             20122.56 Hz
F2P                   -0.000 ppm
F2                     -0.00 Hz
PPMCM                 10.25640 ppm/cm
HZCM           1031.92505 Hz/cm
```



Ms spectrum of

N-(Dicyclohexylphosphino)-2-phenylindole

HRMs spectrum of **N-(Dicyclohexylphosphino)-2-phenylindole**



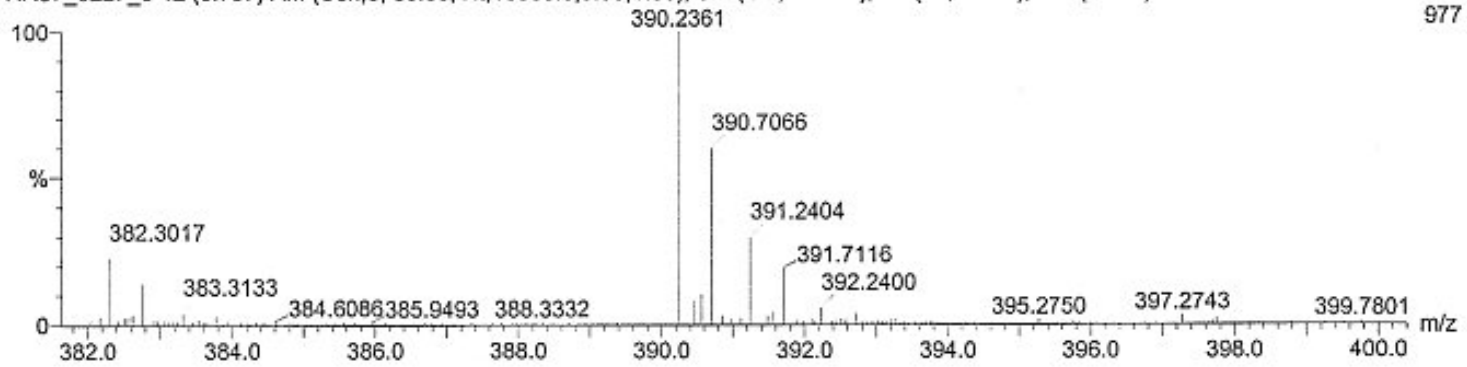
Elemental Composition Report

Single Mass Analysis

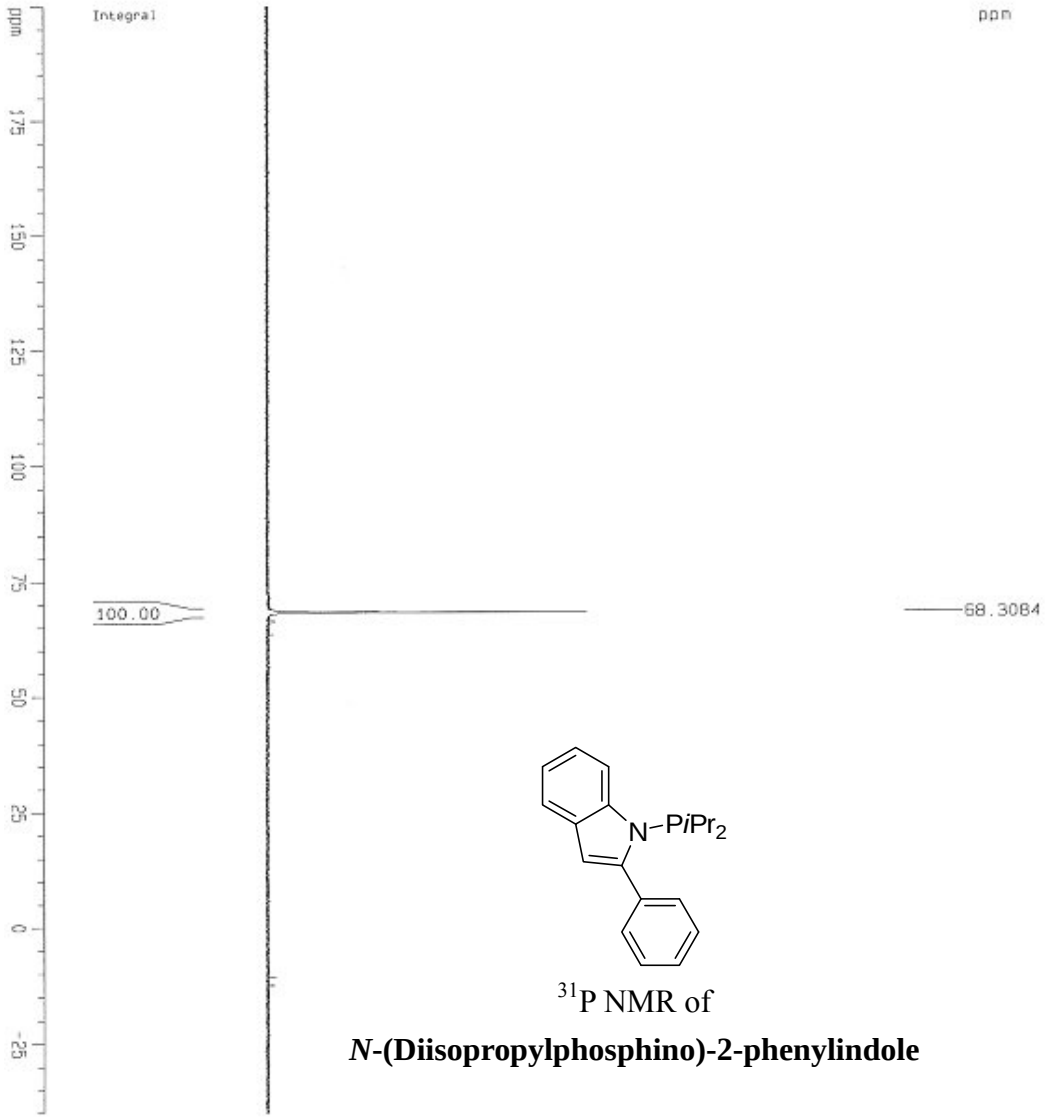
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 60.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
7 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-26 H: 0-1000 N: 0-1 P: 0-1

So Chau Ming, 2-phenylindole cy2 phosphine
HR07_0227_6 42 (0.797) AM (Cen,5, 80.00, Ht,10000.0,0.00,1.00); Sm (SG, 3x3.00); Sb (15,20.00); Cm (25:47) TOF MS ES+ 977



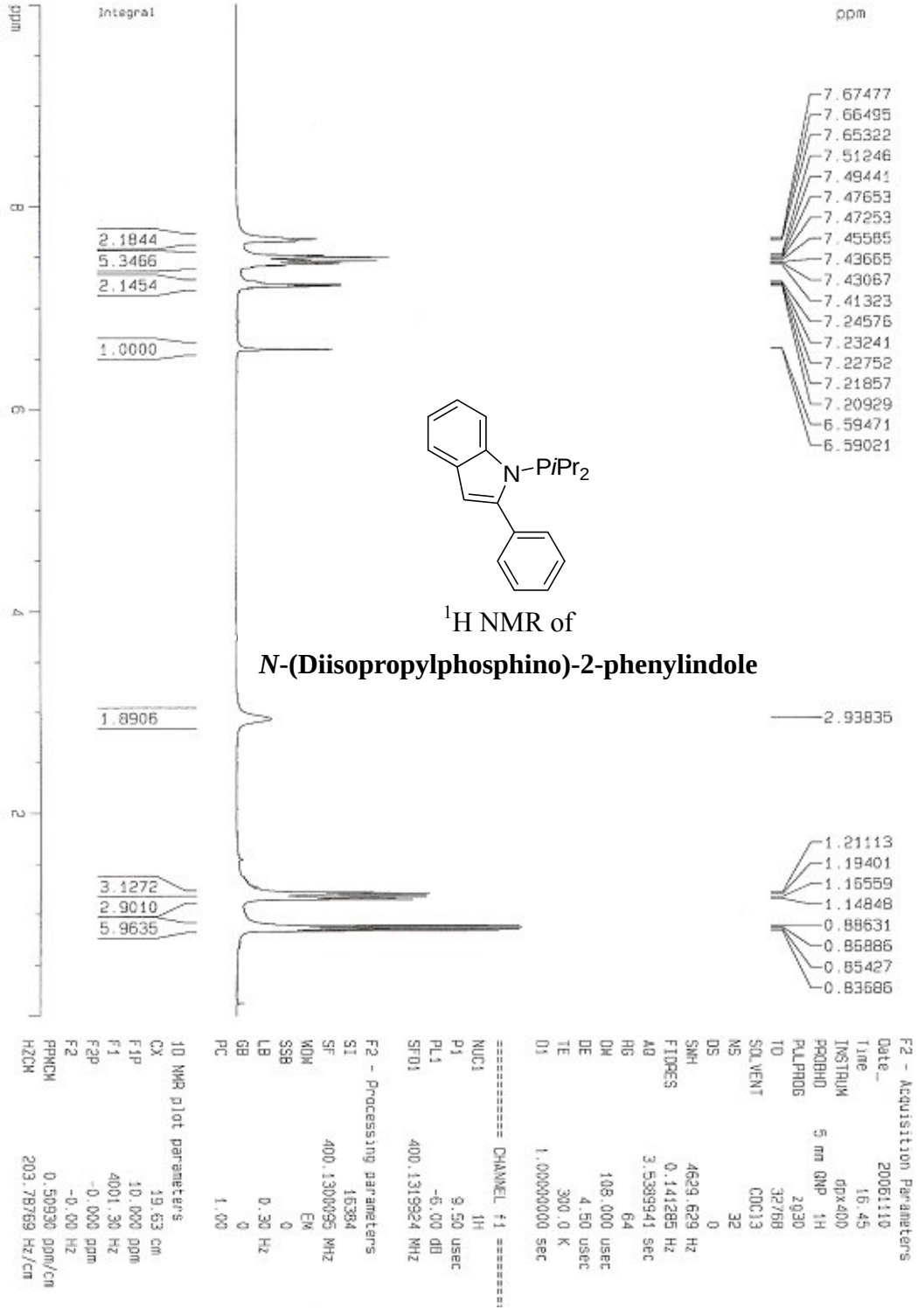
Minimum:				-1.5		
Maximum:		100.0	5.0	60.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
390.2361	390.2351	1.0	2.6	11.5	1.4	C26 H33 N P



^{31}P NMR of

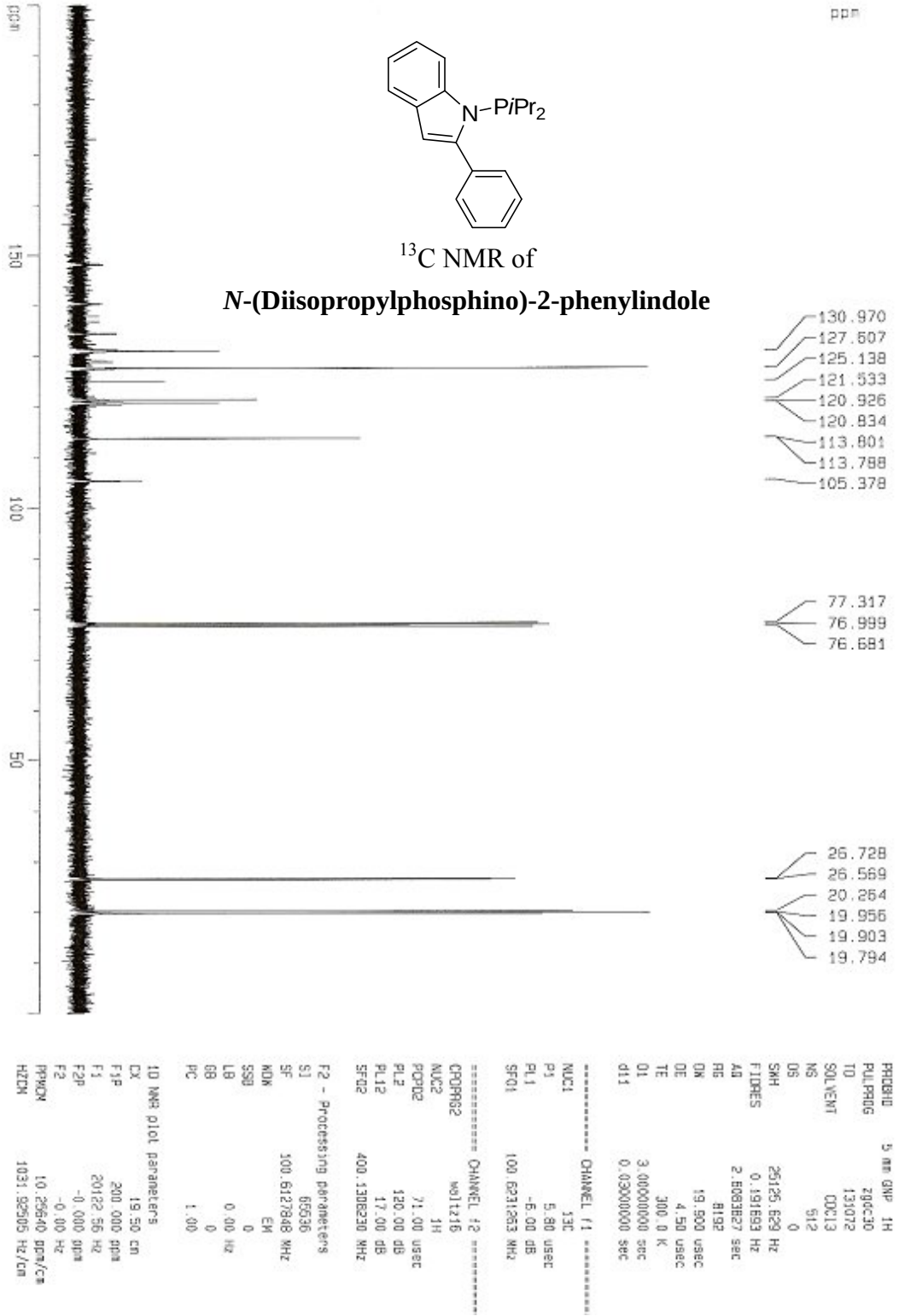
***N*-(Diisopropylphosphino)-2-phenylindole**

F2 - Acquisition Parameters
Date_ 20070224
EXPNO 126
PROCNO 1
TIME 9.57
INSTRUM qdx400
PRHEAD 5 mm QNP 1H
PULPROG zgdc30
TD 65536
SOLVENT CDCl3
NS 16
DS 0
SWH 48661.691 Hz
FIDRES 0.742580 Hz
AQ 0.6734324 sec
RG 11585.2
DW 10.275 usec
DE 4.50 usec
TE 300.0 K
D1 1.00000000 sec
d11 0.03000000 sec
========== CHANNEL f1 ==========
NUC1 31P
P1 7.20 usec
PL1 -6.00 dB
SFO1 161.9851195 MHz
========== CHANNEL f2 ==========
CPDPRG2 waltz16
NUC2 1H
PCPD2 71.00 usec
PL2 120.00 dB
PL12 17.00 dB
SFO2 400.1319010 MHz
F2 - Processing parameters
SI 32768
SF 161.9755031 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
1D NMR plot parameters
CX 20.00 cm
F1P 200.000 ppm
F1 32395.12 Hz
F2P -40.000 ppm
F2 -6479.02 Hz
PPMCM 12.00000 ppm/cm
HZCM 1943.70691 Hz/cm



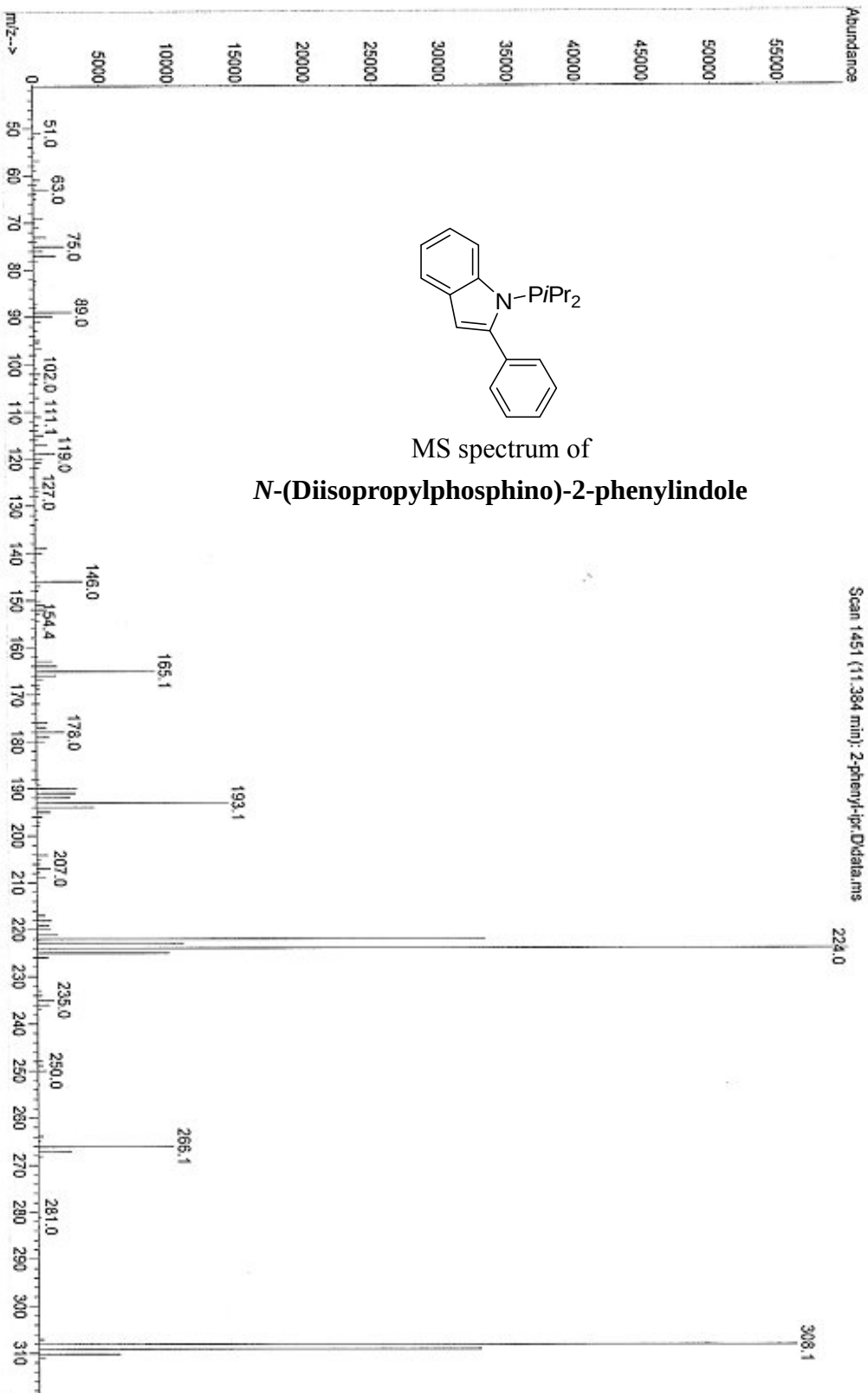
^{1}H NMR of

***N*-(Diisopropylphosphino)-2-phenylindole**



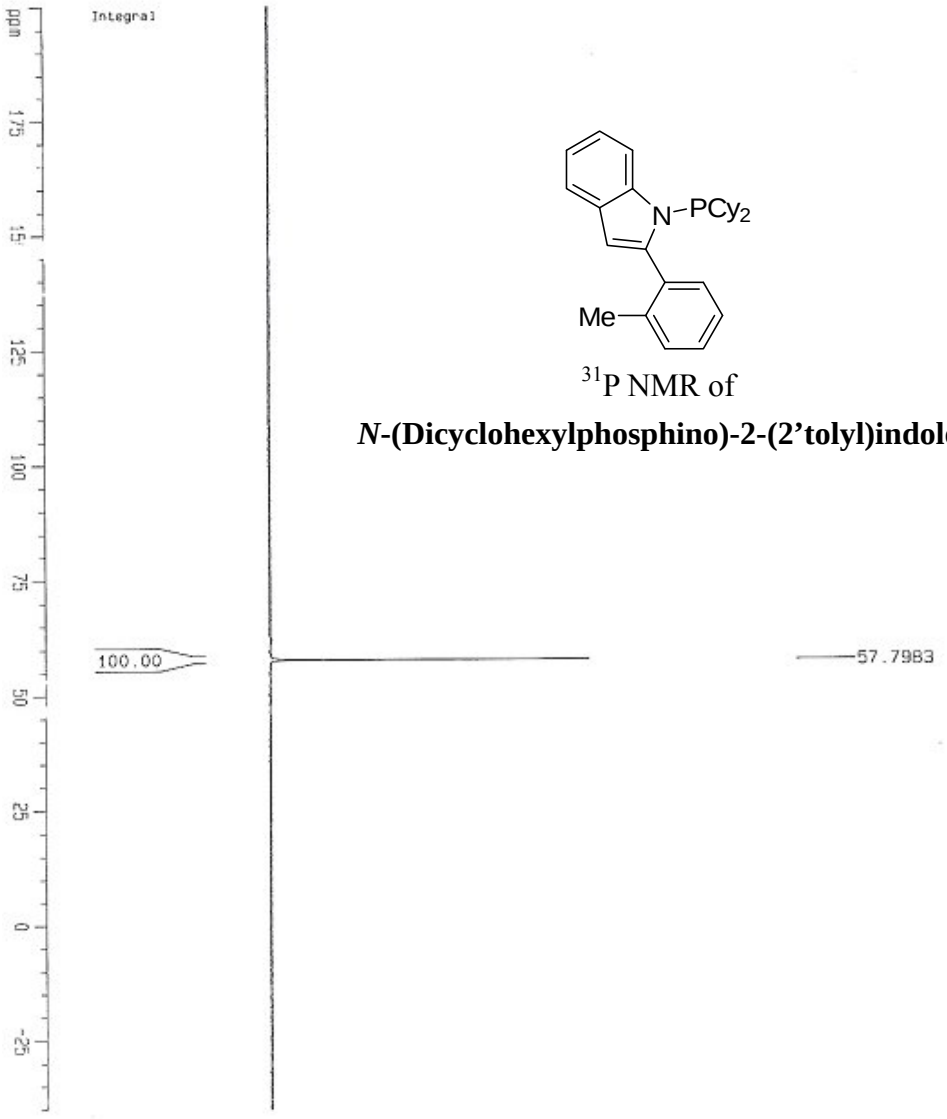
^{13}C NMR of

_N_-(Diisopropylphosphino)-2-phenylindole



MS spectrum of

***N*-(Diisopropylphosphino)-2-phenylindole**



^{31}P NMR of

***N*-(Dicyclohexylphosphino)-2-(2'tolyl)indole**

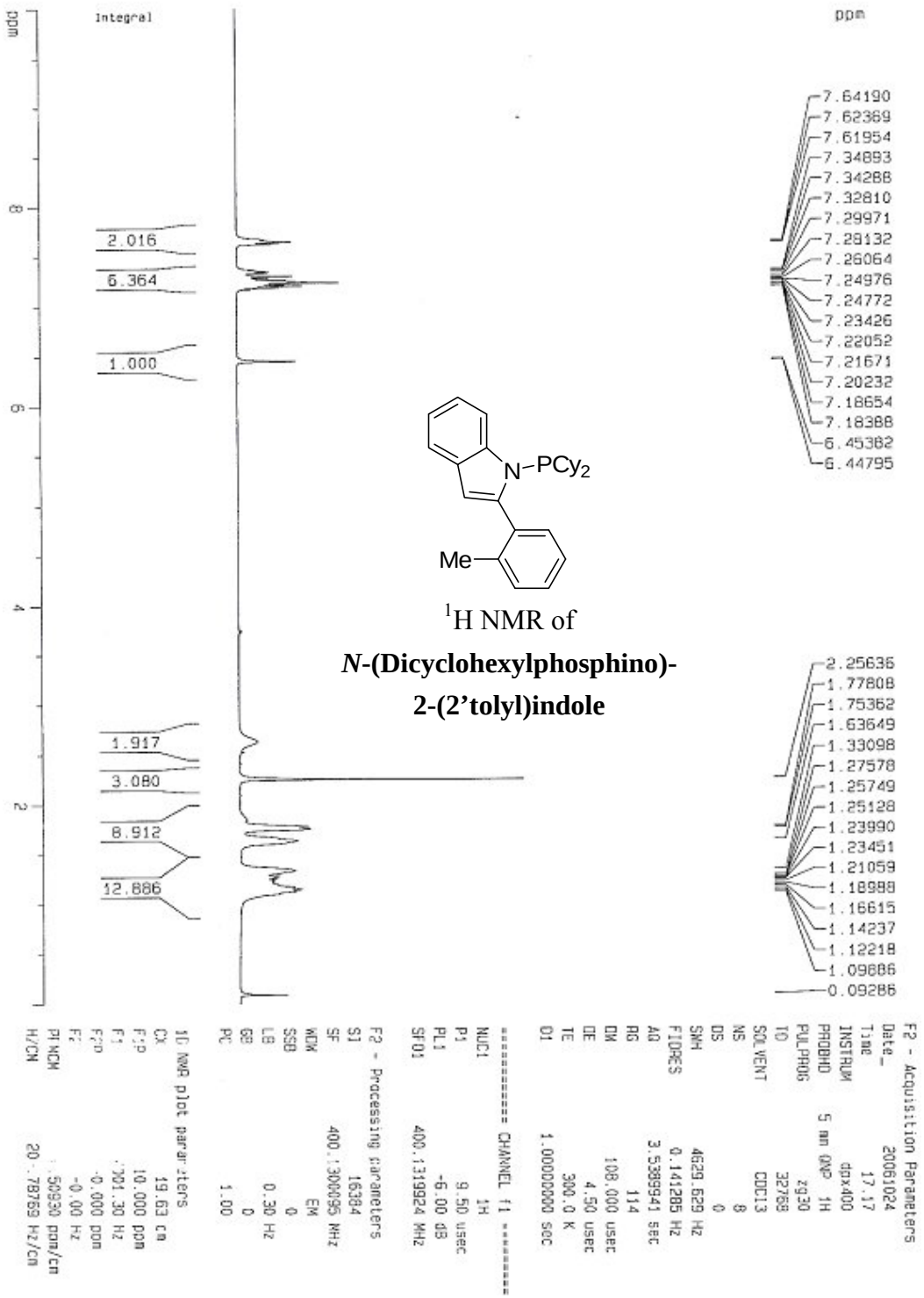

```
Date_                 20070223
Time                     10.24
INSTRUM                 qnx400
PROBHD     5 mm QNP  1H
PULPROG                 zgdc30
TD                       65536
SOLVENT                  CDCl3
NS                          16
DS                           0
SWH                  48661.801 Hz
FIDRES                0.742520 Hz
AQ                    0.6734324 sec
RG                      11585.2
DW                       10.275 usec
DE                         4.50 usec
TE                        300.0 K
D1                    1.00000000 sec
d11                   0.03000000 sec

========== CHANNEL f1 ==========
NUC1                        31P
P1                         7.20 usec
PL1                      -6.00 dB
SFO1                 161.9861115 MHz

========== CHANNEL f2 ==========
CPDPRG2                 waltz16
NUC2                         1H
PCPD2                     71.00 usec
PL2                      120.00 dB
PL12                      17.00 dB
SFO2                 400.1319010 MHz

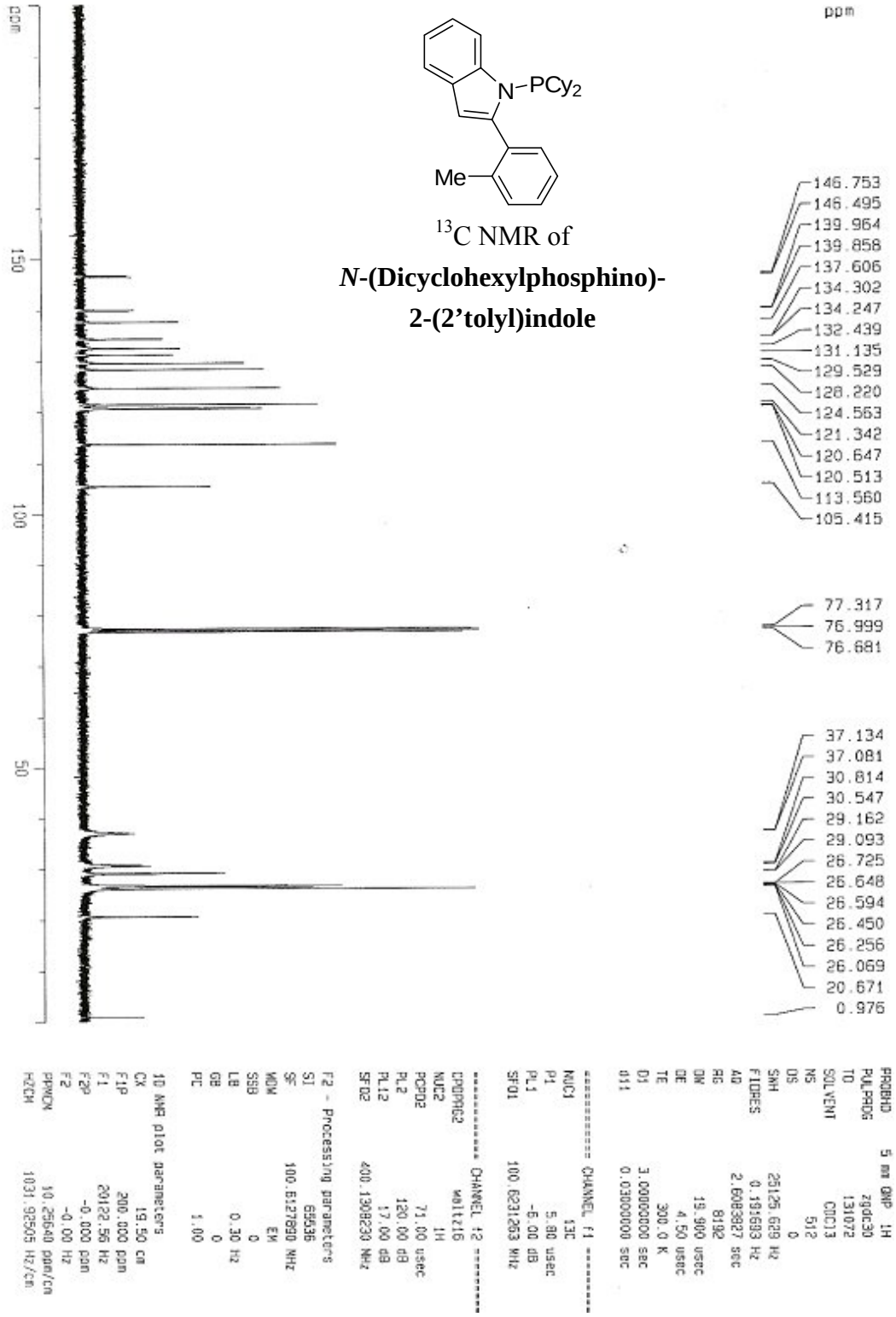
F2 - Processing parameters
SI                        32768
SF                   161.9765831 MHz
NDM                          EM
SSB                           0
LB                         3.00 Hz
GB                            0
PC                         1.40

1D NMR plot parameters
CX                       20.00 cm
F1P                     200.000 ppm
F1                    32395.12 Hz
F2P                    -40.000 ppm
F2                    -6479.02 Hz
PPMCM                 12.00000 ppm/cm
HZCM                  1943.70691 Hz/cm
```



^{1}H NMR of

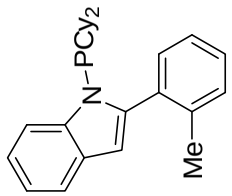
***N*-(Dicyclohexylphosphino)-2-(2'tolyl)indole**



^{13}C NMR of

***N*-(Dicyclohexylphosphino)-2-(2'tolyl)indole**

HRMS spectrum of ***N*-(Dicyclohexylphosphino)-2-(2'tolyl)indole**



Elemental Composition Report

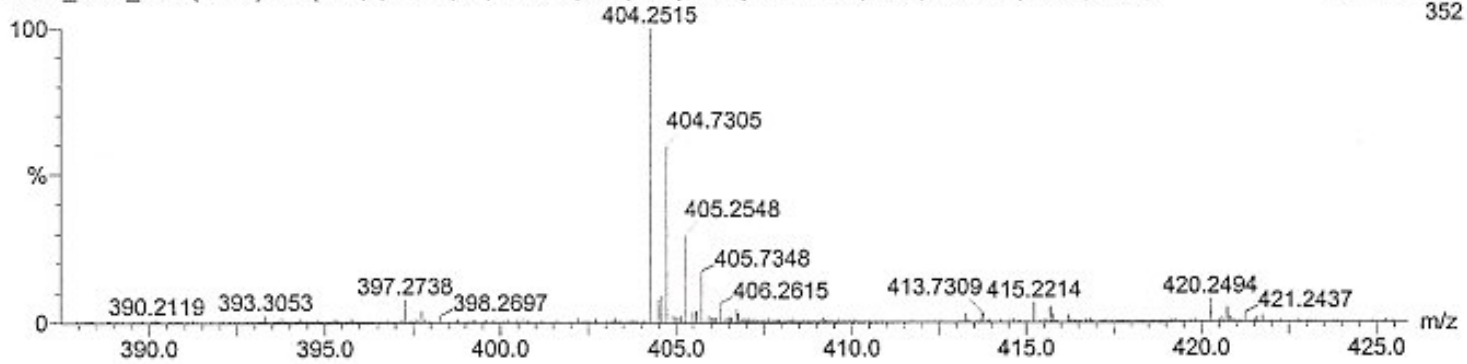
Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 60.0
Selected filters: None

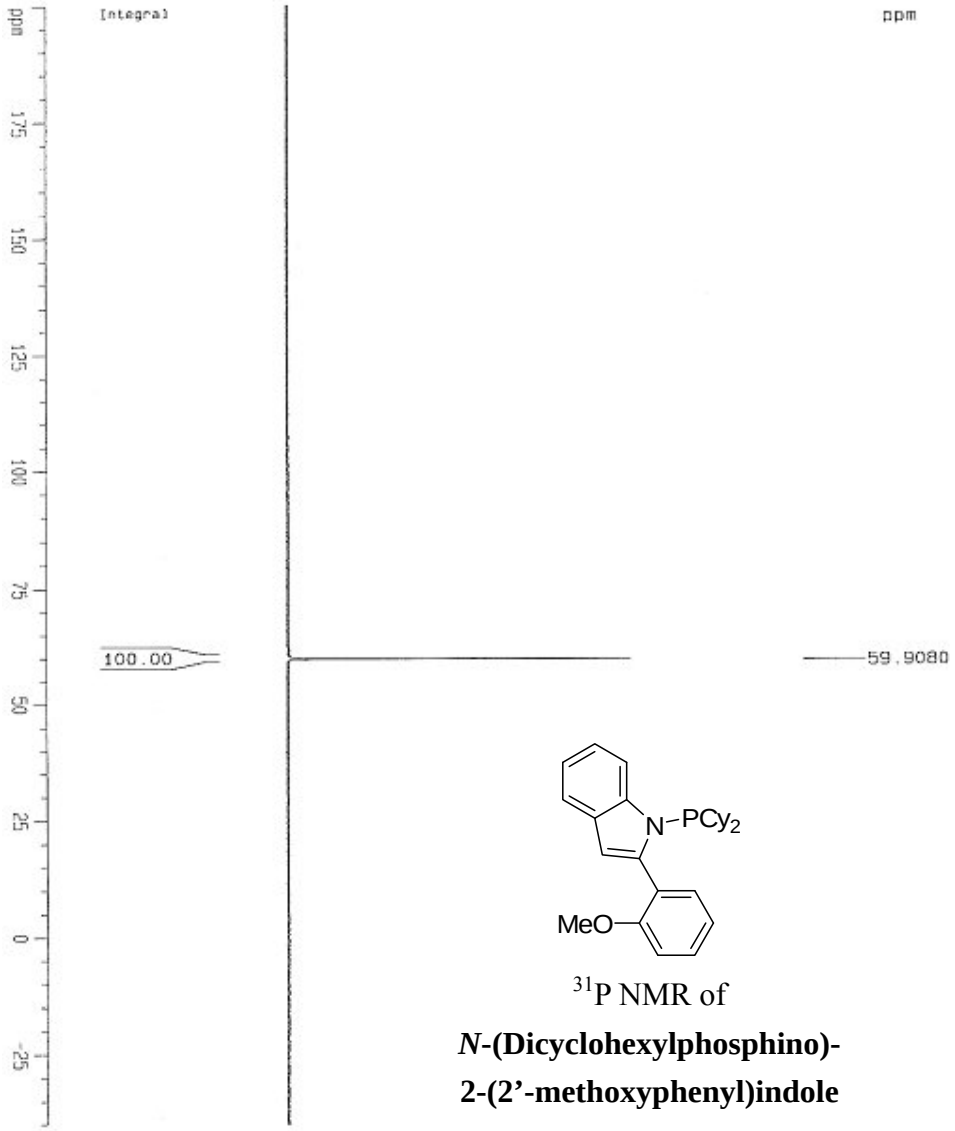
Monoisotopic Mass, Even Electron Ions
17 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-27 H: 0-1000 N: 0-1 O: 0-1 P: 0-1

So Chau Ming, 2(2-methylphenyl)indole cy2 phosphine
HR07_0227_2 66 (1.249) AM (Cen,5, 80.00, Ht,10000.0,0.00,1.00); Sm (SG, 3x3.00); Sb (15,20.00); Cm (60:66)

TOF MS ES+
352

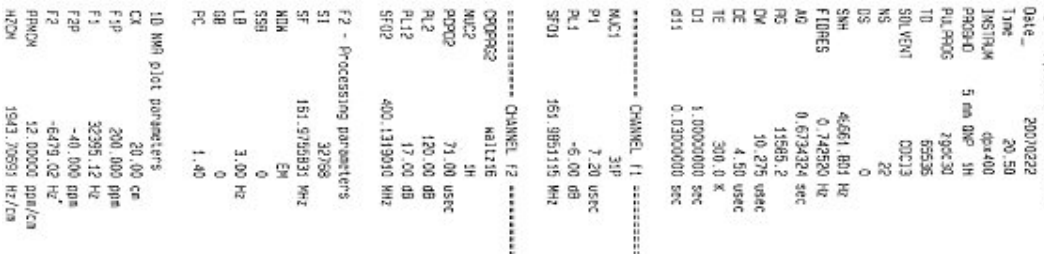


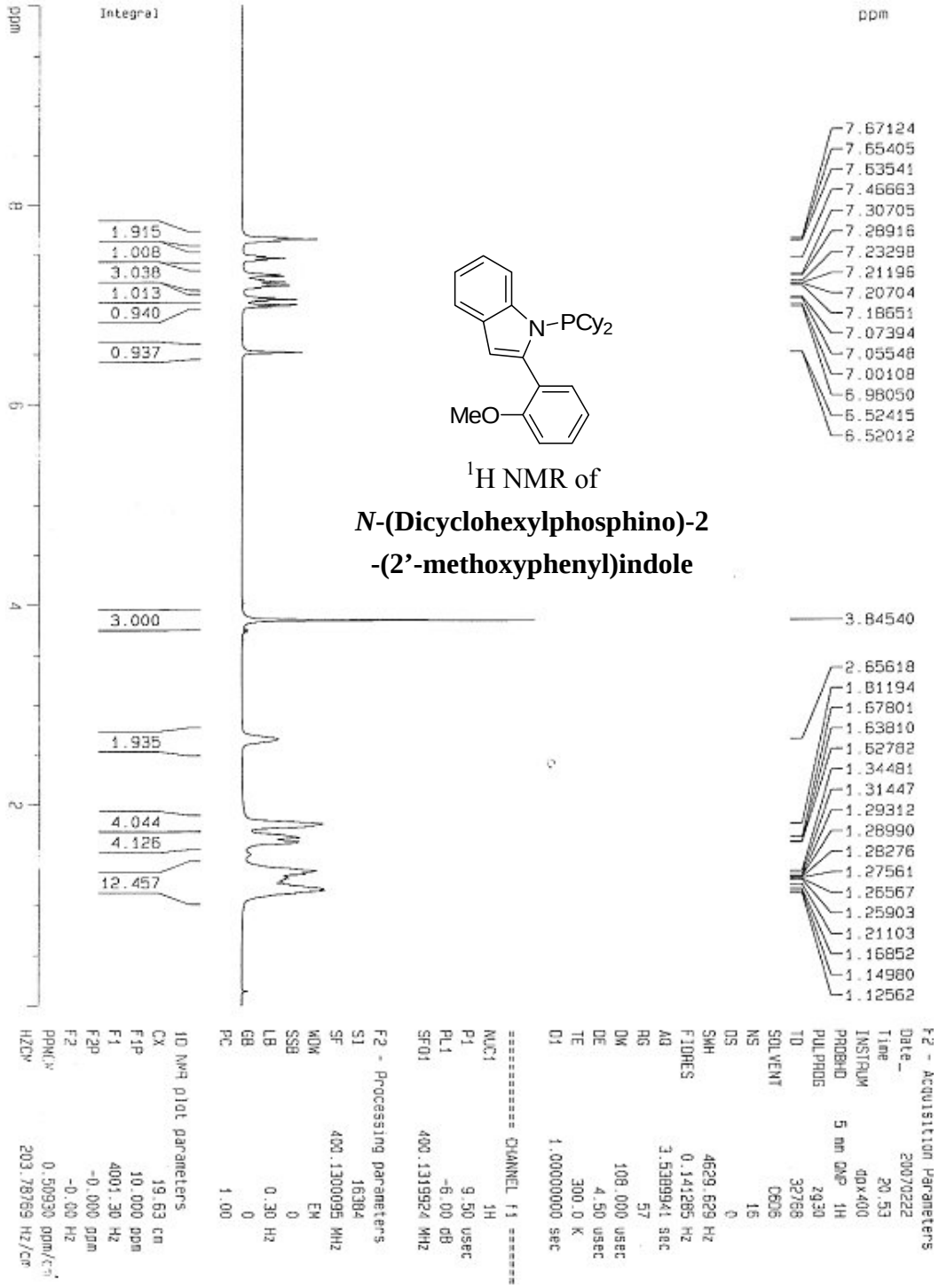
Minimum:				-1.5		
Maximum:		100.0	5.0	60.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
404.2515	404.2507	0.8	2.0	11.5	0.8	C27 H35 N P



^{31}P NMR of

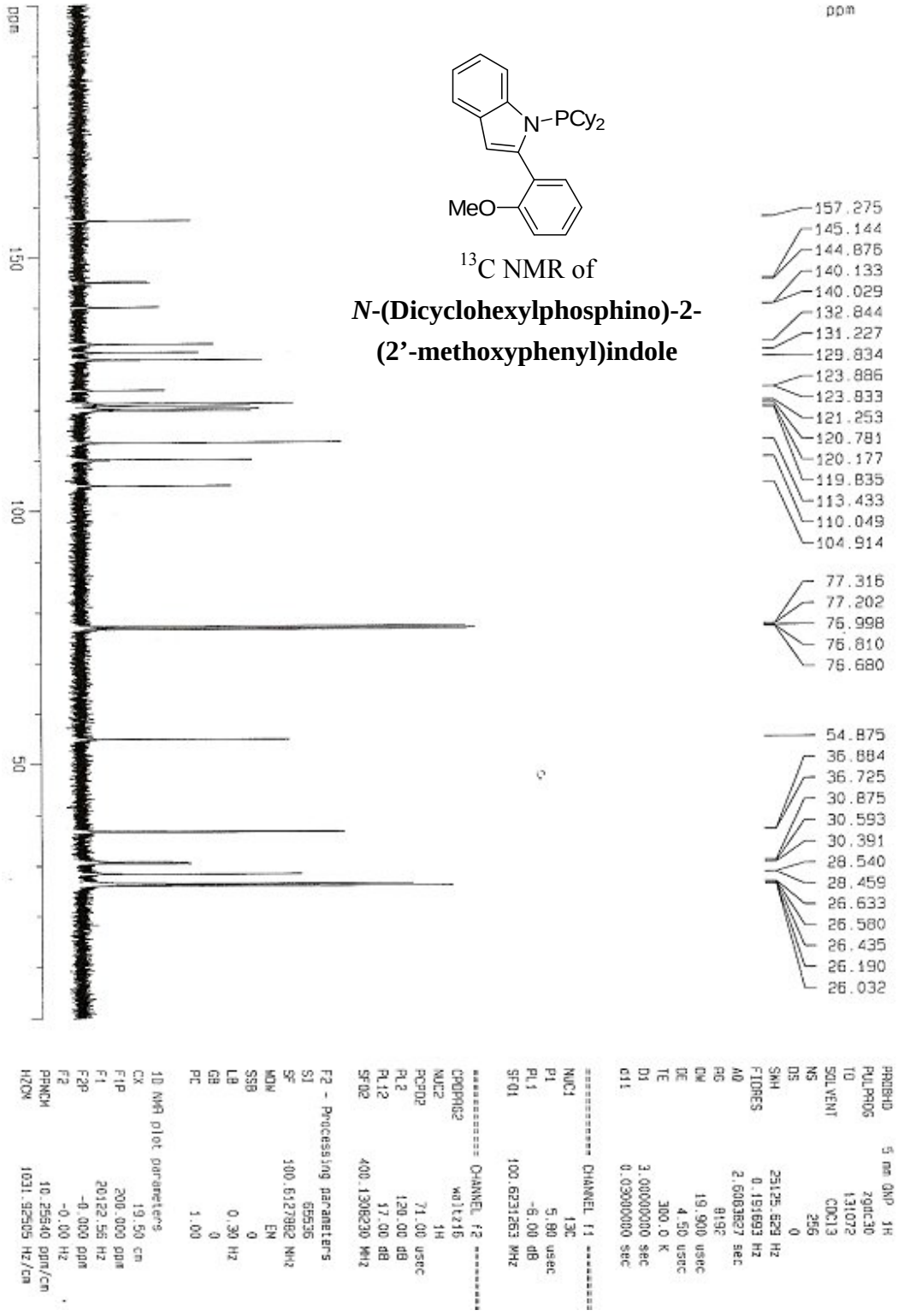
***N*-(Dicyclohexylphosphino)-2-(2'-methoxyphenyl)indole**





^{1}H NMR of

***N*-(Dicyclohexylphosphino)-2-(2'-methoxyphenyl)indole**



^{13}C NMR of

_N_-(Dicyclohexylphosphino)-2-(2'-methoxyphenyl)indole

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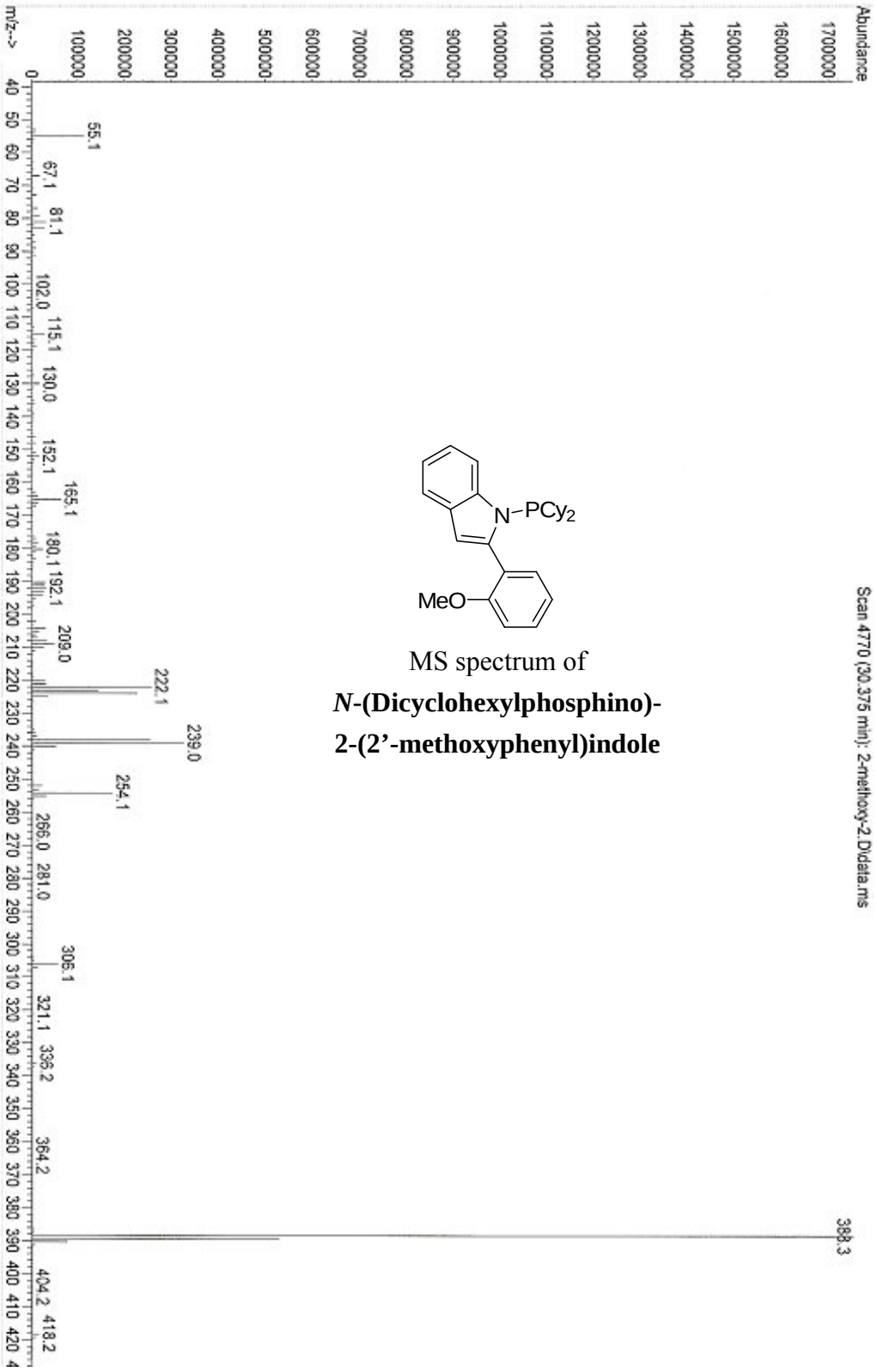
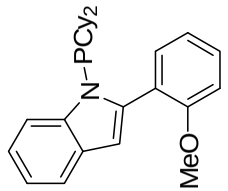
PULPROG zgdc30
TD 131072
SOLVENT CDCl3
NS 256
DS 0
SWH 25125.629 Hz
FIDRES 0.191693 Hz
AQ 2.6083827 sec
RG 8192
DW 19.900 usec
DE 4.50 usec
TE 300.0 K
D1 3.00000000 sec
d11 0.03000000 sec
========== CHANNEL f1 ==========
NUC1 13C
P1 5.80 usec
PL1 -6.00 dB
SF01 100.6231263 MHz
========== CHANNEL f2 ==========
CPDPRG2 waltz16
NUC2 1H
PCPD2 71.00 usec
PL2 120.00 dB
PL12 17.00 dB
SF02 400.1308230 MHz
F2 - Processing parameters
SI 65536
SF 100.6127882 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 19.50 cm
F1P 200.000 ppm
F1 20122.56 Hz
F2P -0.000 ppm
F2 -0.00 Hz
PPMCM 10.25540 ppm/cm
HZCM 1031.92505 Hz/cm



MS spectrum of

***N*-(Dicyclohexylphosphino)-2-(2'-methoxyphenyl)indole**

HRMS spectrum of **_N_-(Dicyclohexylphosphino)-2-(2'-methoxyphenyl)indole**



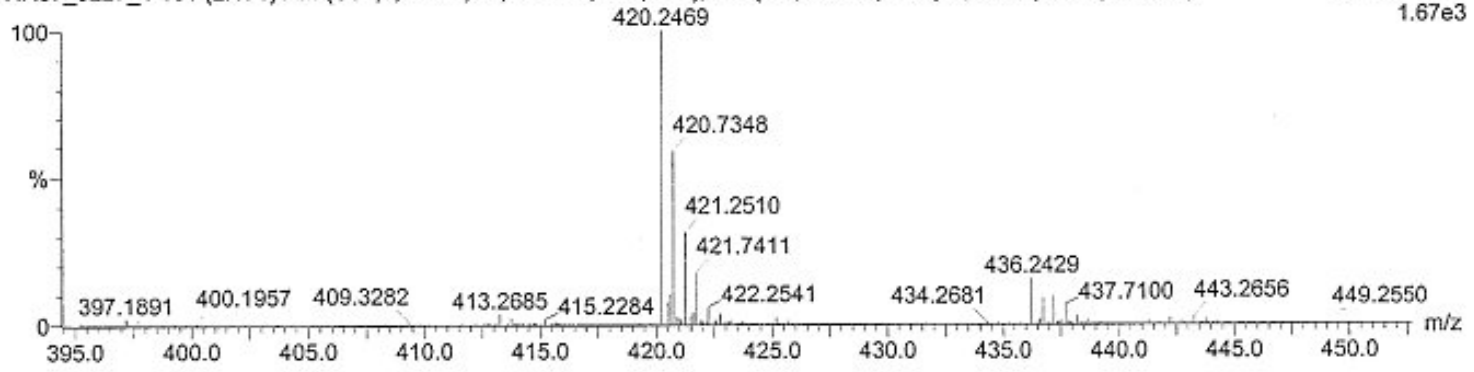
Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 60.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
12 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-27 H: 0-1000 N: 0-1 O: 0-1 P: 0-1

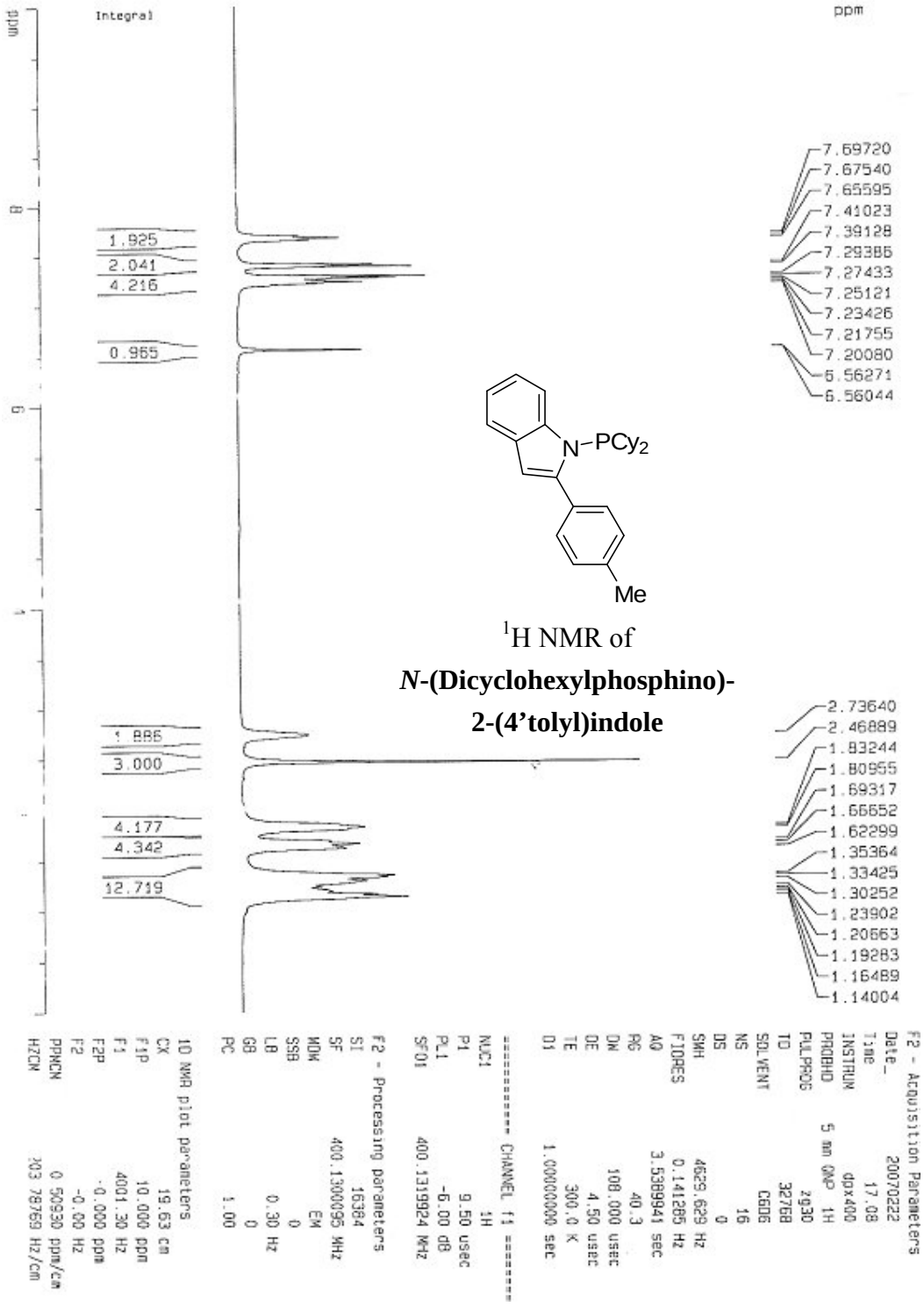
So Chau Ming, 2(2-methoxyphenyl)indole cy2 phosphine
HR07_0227_1 131 (2.471) AM (Cen,5, 80.00, Ht,10000.0,0.00,1.00); Sm (SG, 3x3.00); Sb (15,20.00); Cm (119:136) TOF MS ES+ 1.67e3



Minimum:				-1.5		
Maximum:		100.0	5.0	60.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
420.2469	420.2456	1.3	3.1	11.5	1.7	C27 H35 N O P

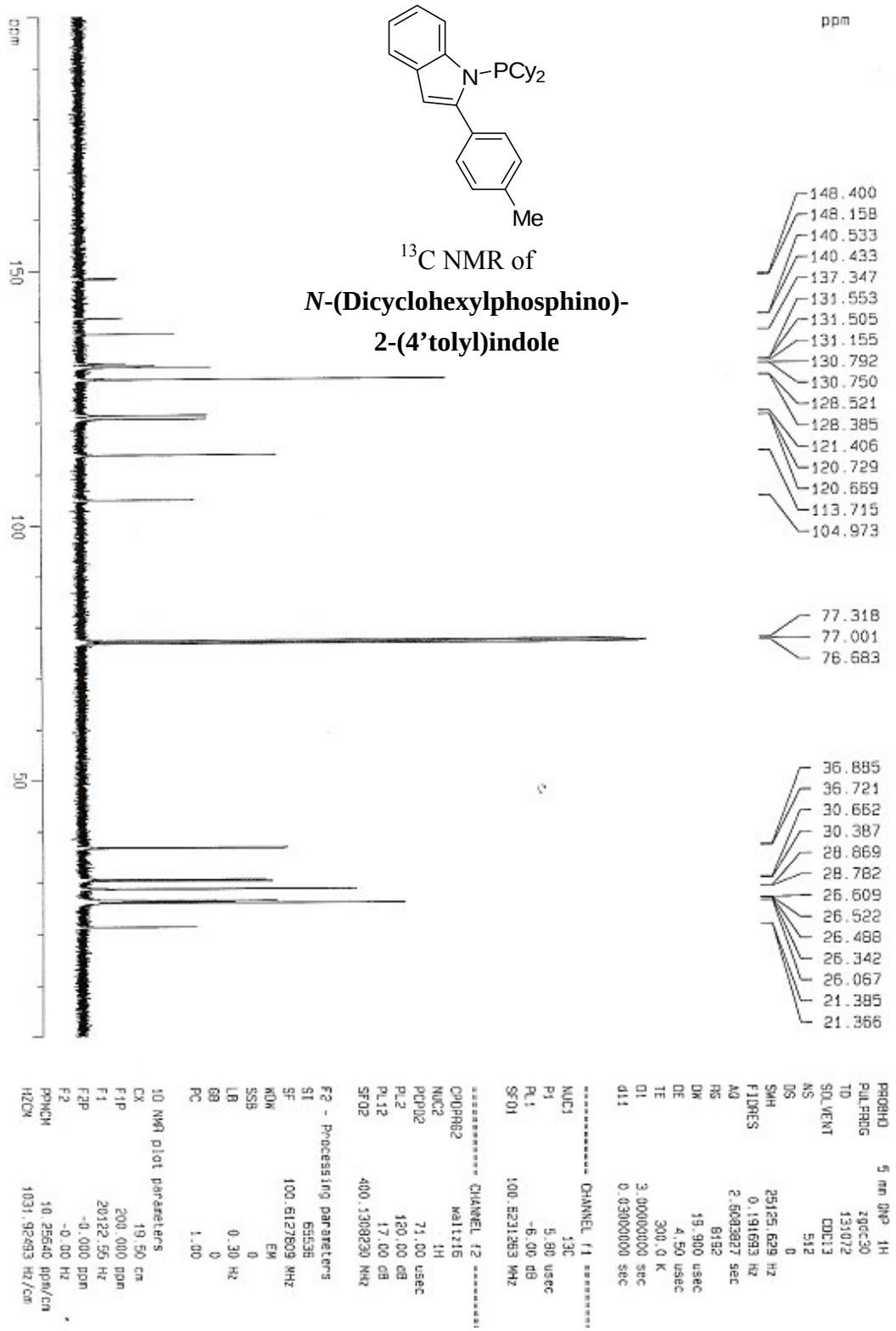
^{31}P NMR of

***N*-(Dicyclohexylphosphino)-2-(4'tolyl)indole**



^{1}H NMR of

***N*-(Dicyclohexylphosphino)-2-(4'tolyl)indole**



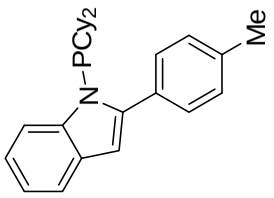
^{13}C NMR of

***N*-(Dicyclohexylphosphino)-2-(4'tolyl)indole**

MS spectrum of

***N*-(Dicyclohexylphosphino)-2-(4'tolyl)indole**

HRMS spectrum of ***N*-(Dicyclohexylphosphino)-2-(2'tolyl)indole**



Elemental Composition Report

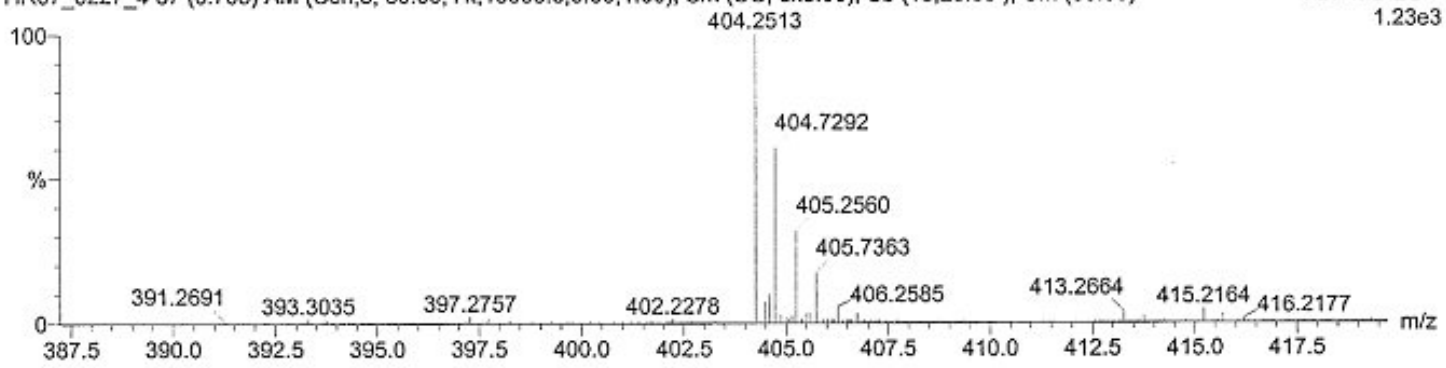
Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 60.0
Selected filters: None

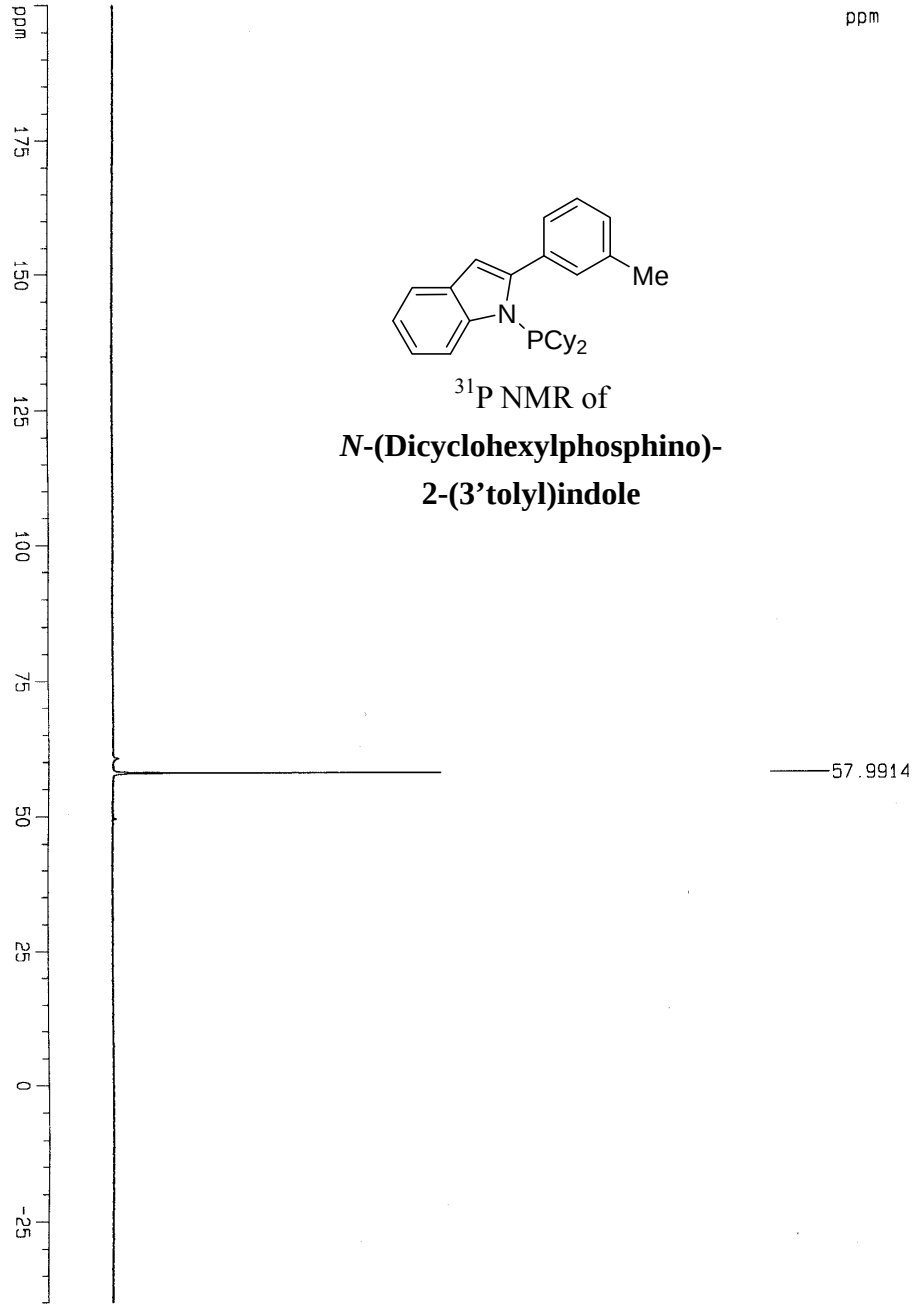
Monoisotopic Mass, Even Electron Ions
17 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-27 H: 0-1000 N: 0-1 O: 0-1 P: 0-1

So Chau Ming, 2(4-methylphenyl)indole cy2 phosphine
HR07_0227_4 37 (0.703) AM (Cen,5, 80.00, Ht,10000.0,0.00,1.00); Sm (SG, 3x3.00); Sb (15,20.00); Cm (30:39)

TOF MS ES+
1.23e3



Minimum:				-1.5		
Maximum:		100.0	5.0	60.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
404.2513	404.2507	0.6	1.5	11.5	0.6	C27 H35 N P



^{31}P NMR of

_N_-(Dicyclohexylphosphino)-2-(3'tolyl)indole

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Time                  20.52
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PULPROG             zgdc30
TD                   65536
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NS                      32
DS                       0
SWH              48661.801 Hz
FIDRES               0.742520 Hz
AQ                   0.6734324 sec
RG                      13004
DW                   10.275 usec
DE                    4.50 usec
TE                   300.0 K
D1                   1.00000000 sec
d11                  0.03000000 sec

============== CHANNEL f1 ==============
NUC1                   31P
P1                    7.20 usec
PL1                  -5.00 dB
SFO1             161.9851115 MHz

============== CHANNEL f2 ==============
CPDPRG2             waltz16
NUC2                   1H
PCPD2                71.00 usec
PL2                 120.00 dB
PL12                 17.00 dB
SFO2             400.1319010 MHz

F2 - Processing parameters
SI                     32768
SF               161.9755831 MHz
WDW                    EM
SSB                     0
LB                   3.00 Hz
GB                      0
PC                    1.40

1D NMR plot parameters
CX                   20.00 cm
F1P                 200.000 ppm
F1                32395.12 Hz
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F2                -6479.02 Hz
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HZCM              1943.70691 Hz/cm
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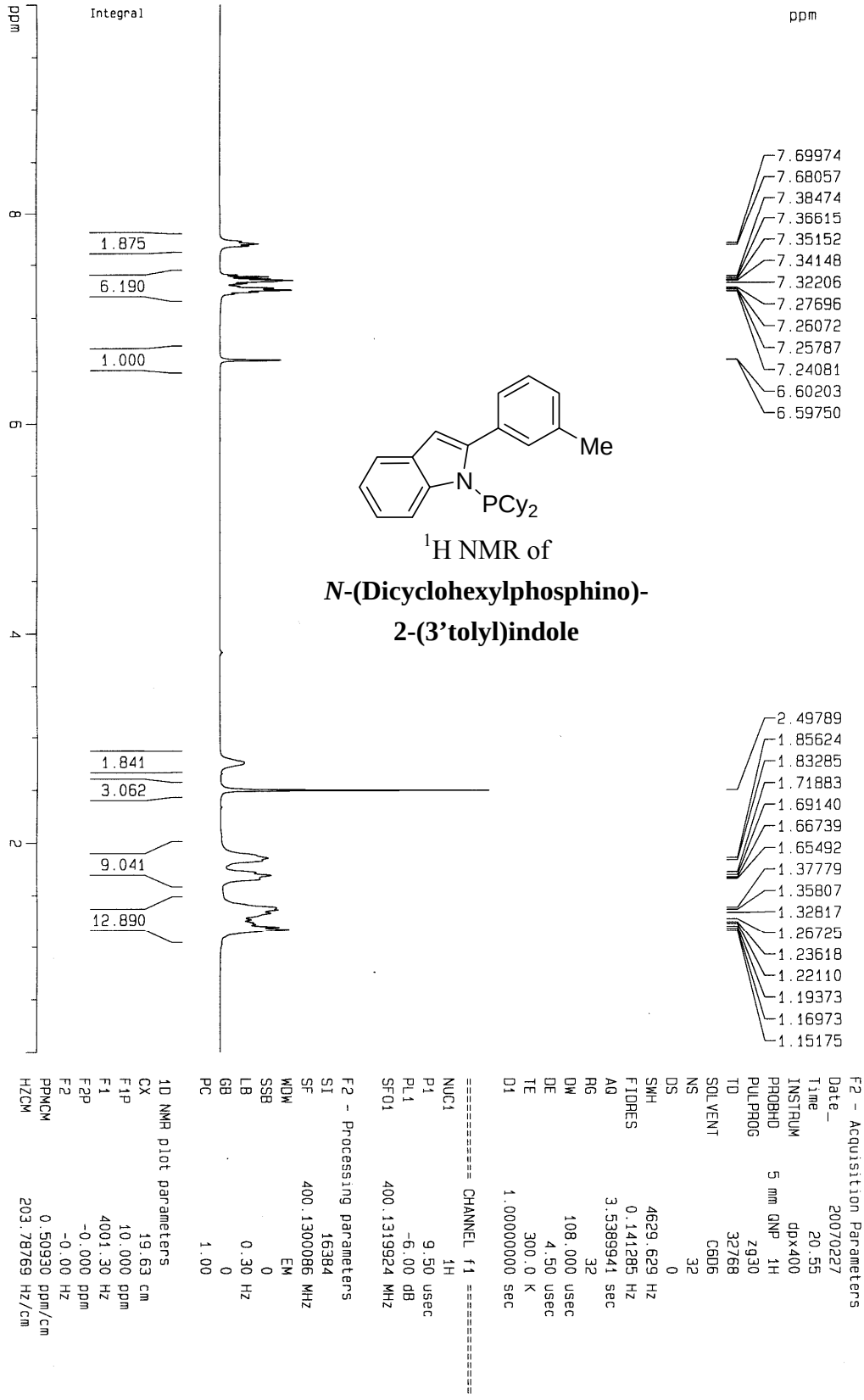
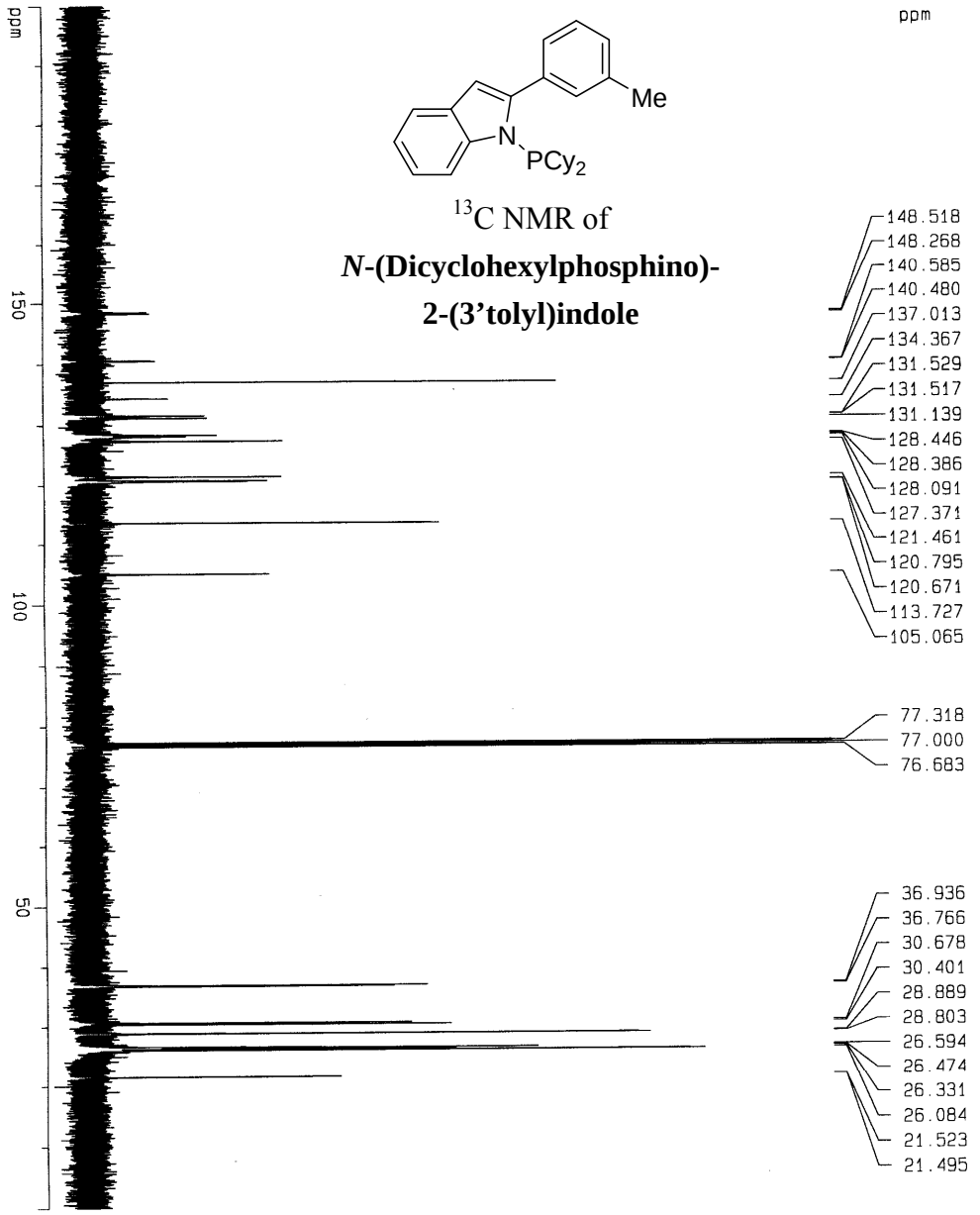


^{1}H NMR of

_N_-(Dicyclohexylphosphino)-2-(3'tolyl)indole



^{13}C NMR of

_N_-(Dicyclohexylphosphino)-2-(3'tolyl)indole

```
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Time                    20.58
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PROBHD       5 mm QNP  1H
PULPROG                 zgdc30
TD                      131072
SOLVENT                 CDCl3
NS                         512
DS                           0
SWH                  25125.629 Hz
FIDRES                0.191693 Hz
AQ                    2.6083827 sec
RG                         8192
DW                     19.900 usec
DE                      4.50 usec
TE                     300.0 K
D1                   3.00000000 sec
D11                  0.03000000 sec

======== CHANNEL f1 ========
NUC1                       13C
P1                        5.80 usec
PL1                      -6.00 dB
SFO1            100.6231263 MHz

======== CHANNEL f2 ========
CPDPRG2                 waltz16
NUC2                       1H
PCPD2                   71.00 usec
PL2                     120.00 dB
PL12                     17.00 dB
SFO2            400.1308230 MHz

F2 - Processing parameters
SI                        65536
SF              100.6127832 MHz
WDW                          EM
SSB                           0
LB                       0.00 Hz
GB                            0
PC                         1.00

1D NMR plot parameters
CX                       19.50 cm
F1P                     200.000 ppm
F1                    20122.56 Hz
F2P                    -0.000 ppm
F2                      -0.00 Hz
PPMCM                 10.25640 ppm/cm
HZCM                1031.92505 Hz/cm
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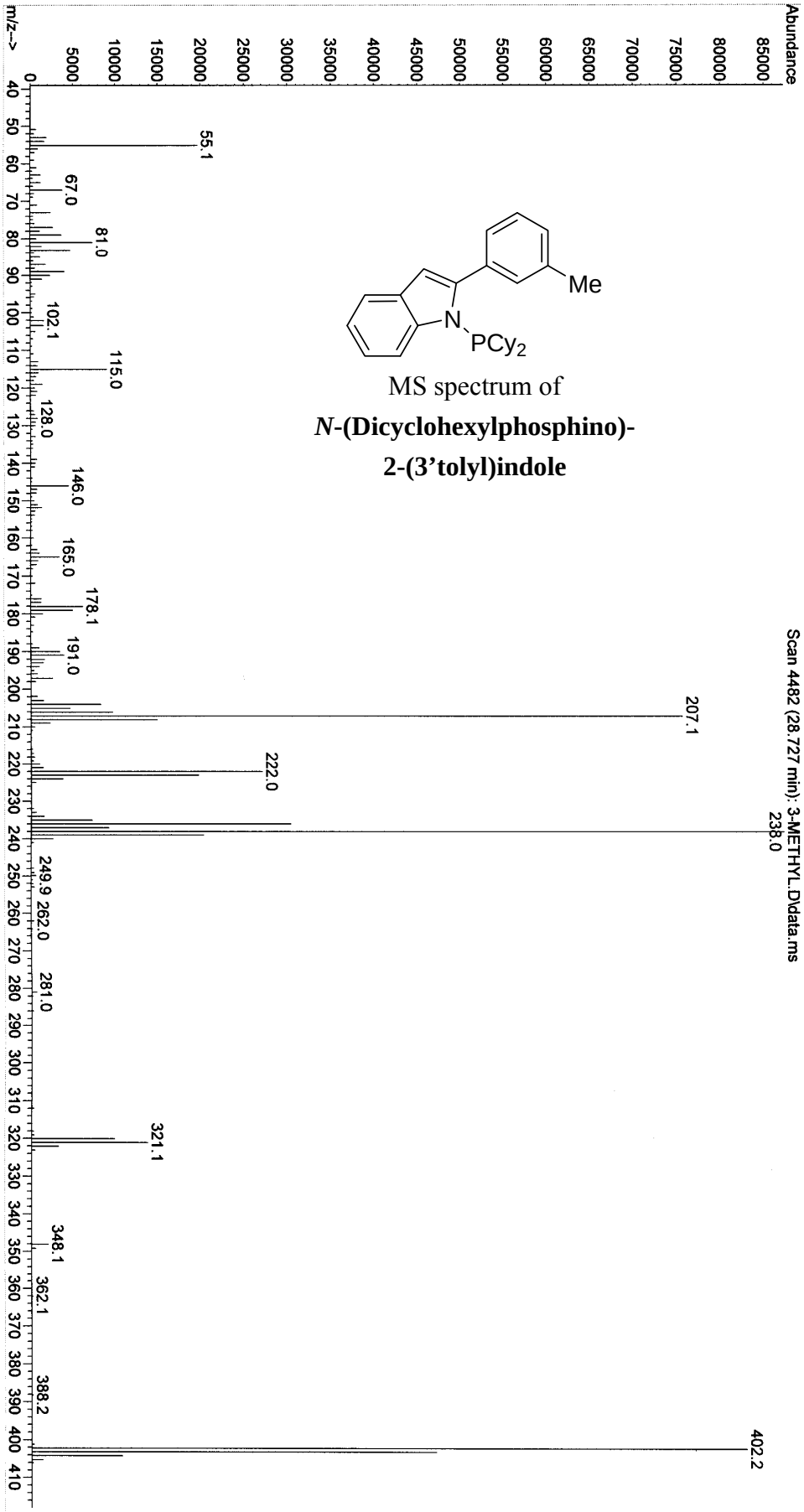
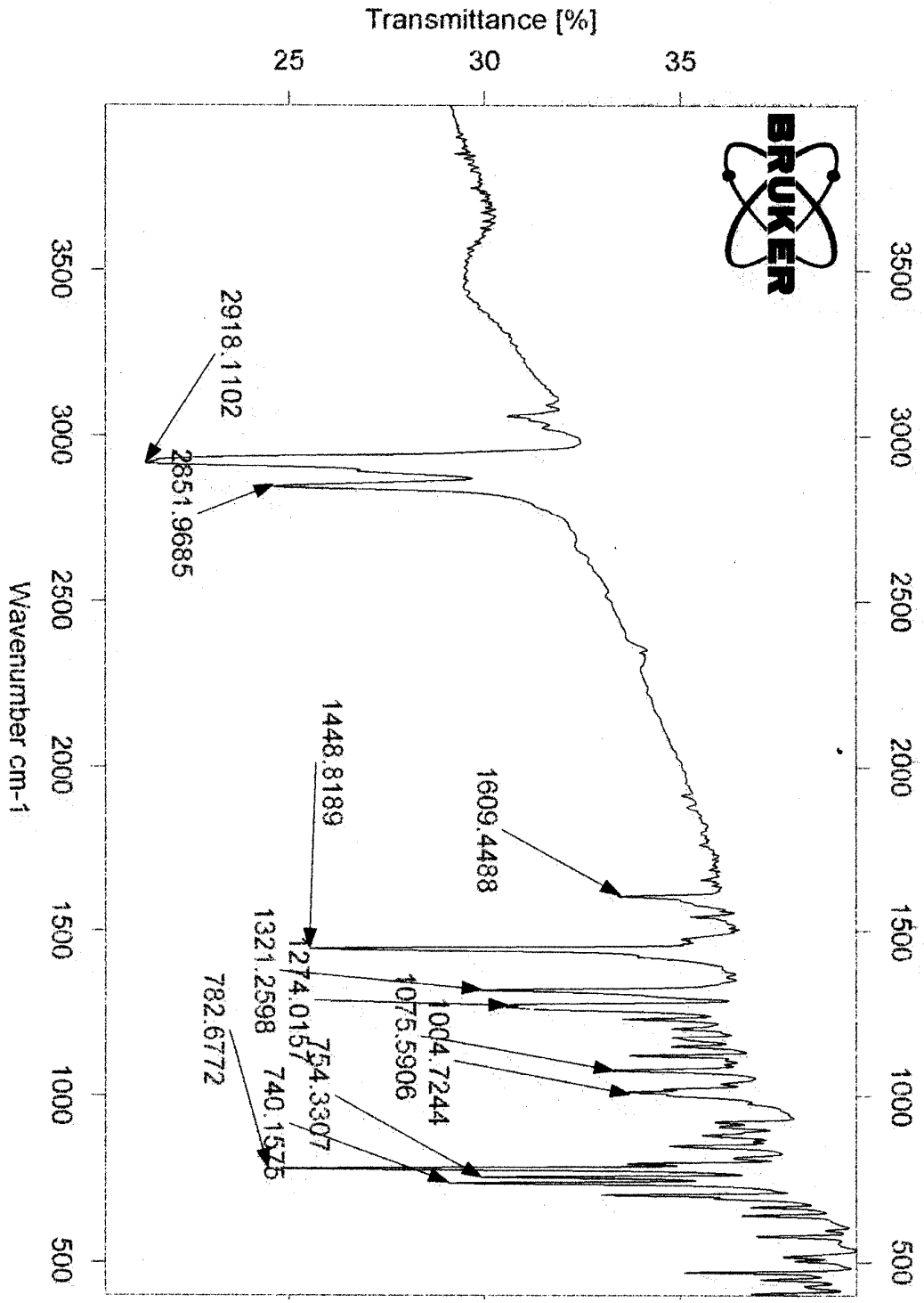
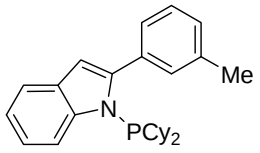


MS spectrum of

***N*-(Dicyclohexylphosphino)-2-(3'tolyl)indole**



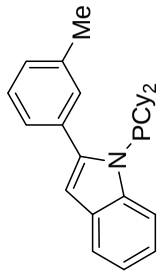


IR spectrum of

***N*-(Dicyclohexylphosphino)-**

2-(3'tolyl)indole

HRMs spectrum of ***N*-(Dicyclohexylphosphino)-2-(3'tolyl)indole**



Elemental Composition Report

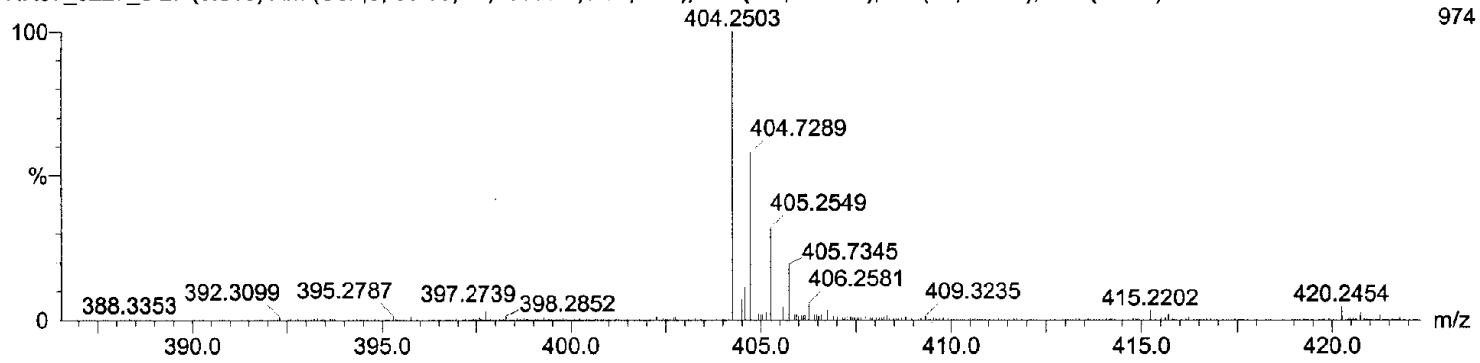
Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 60.0
Selected filters: None

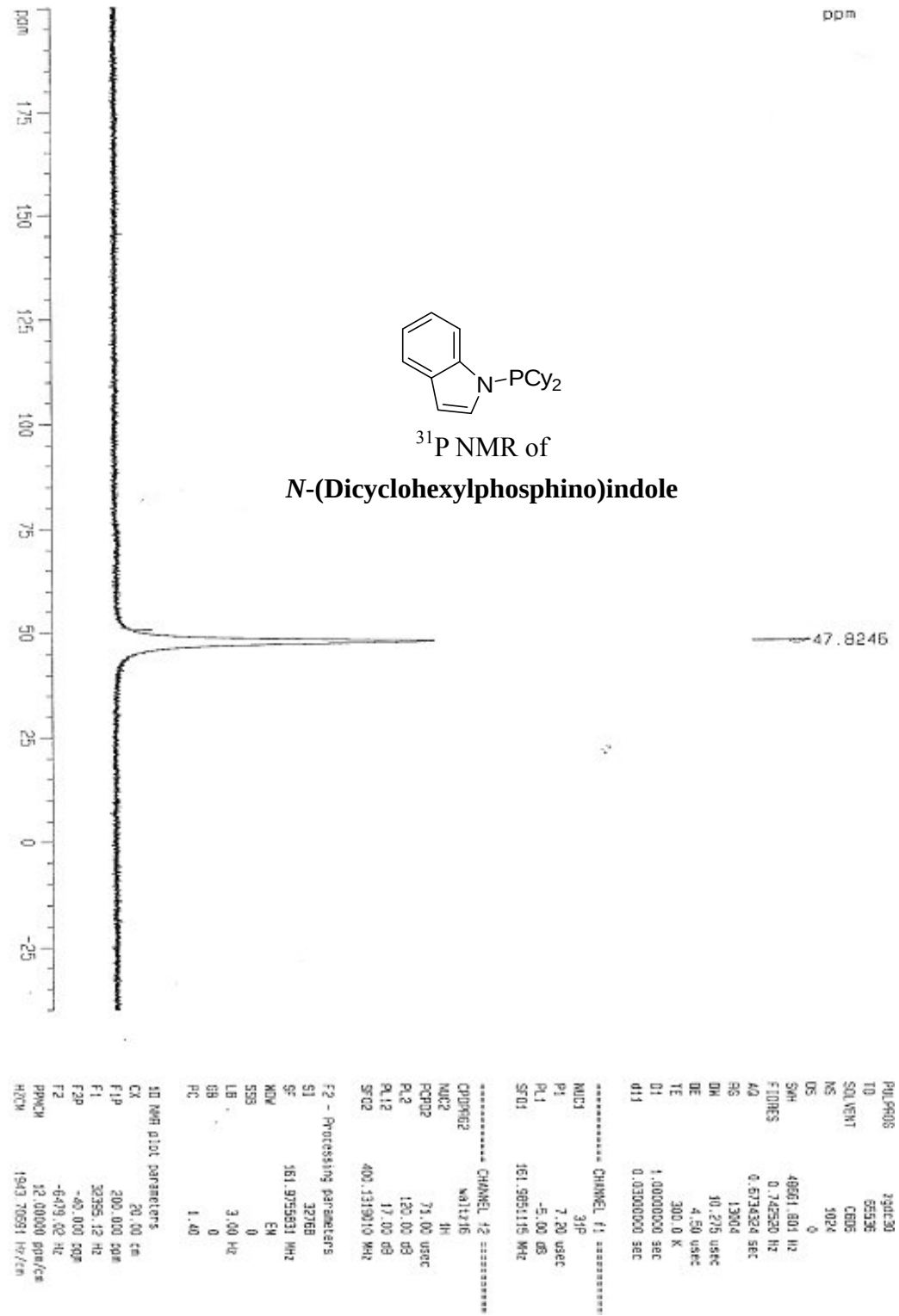
Monoisotopic Mass, Even Electron Ions
17 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-27 H: 0-1000 N: 0-1 O: 0-1 P: 0-1

So Chau Ming, 2(3-methylphenyl)indole cy2 phosphine
HR07_0227_3 27 (0.515) AM (Cen,5, 80.00, Ht,10000.0,0.00,1.00); Sm (SG, 3x3.00); Sb (15,20.00); Cm (27:33)

TOF MS ES+
974

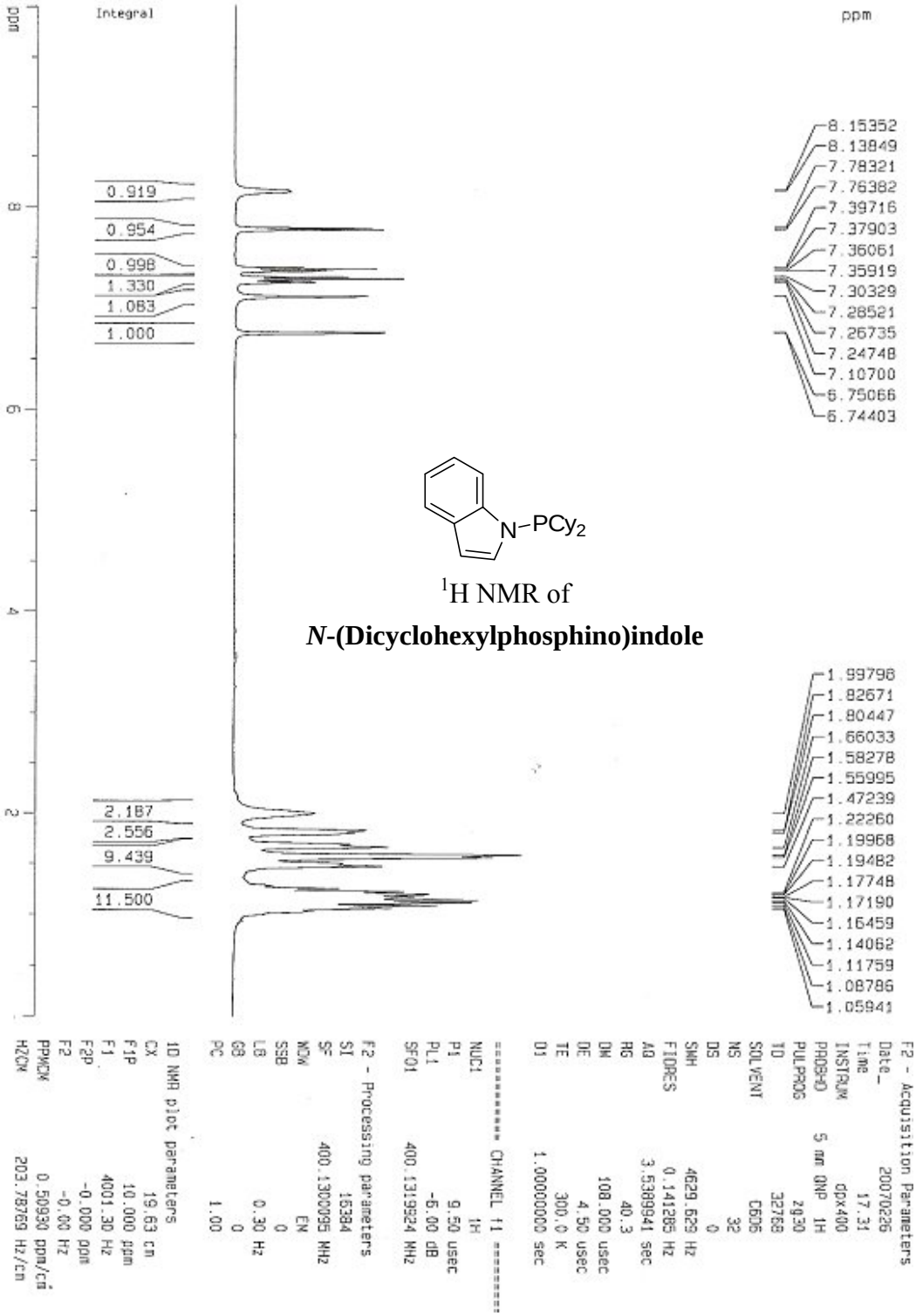


Minimum:				-1.5		
Maximum:		100.0	5.0	60.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
404.2503	404.2507	-0.4	-1.0	11.5	0.7	C27 H35 N P



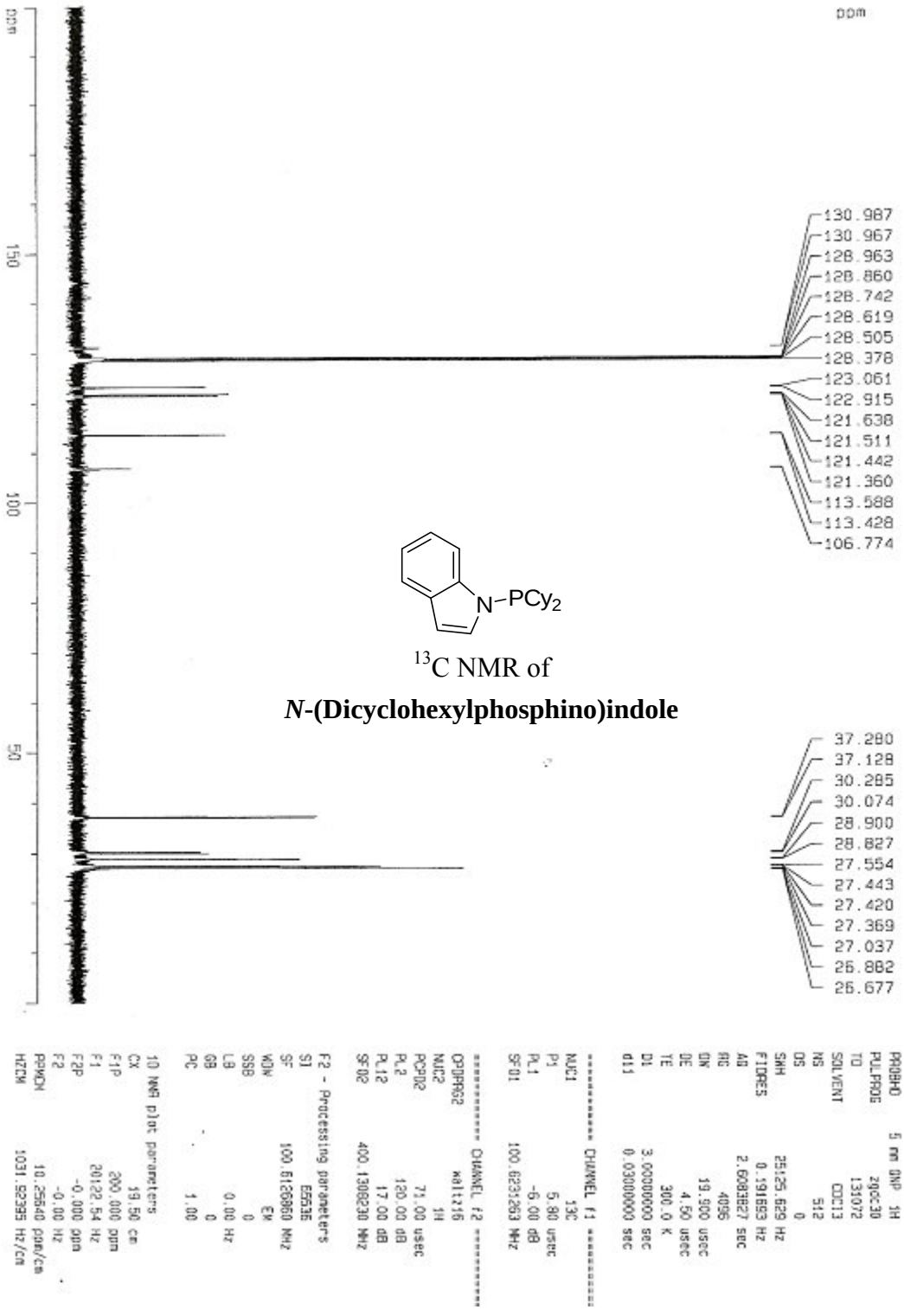
^{31}P NMR of

***N*-(Dicyclohexylphosphino)indole**



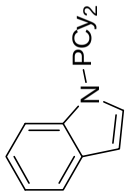
^{1}H NMR of

***N*-(Dicyclohexylphosphino)indole**



^{13}C NMR of

***N*-(Dicyclohexylphosphino)indole**

HRMS of 

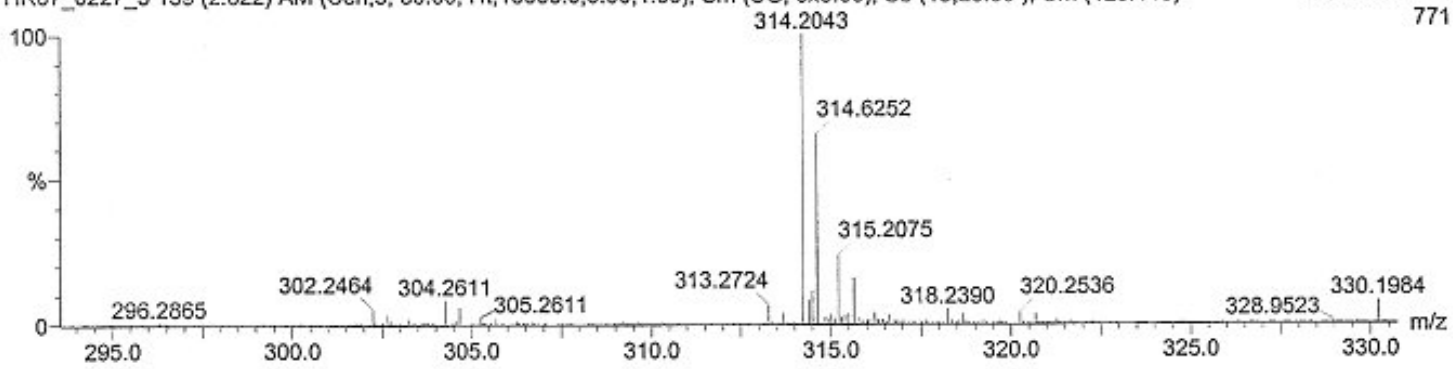
***N*-(Dicyclohexylphosphino)indole**

Elemental Composition Report **Page 1**

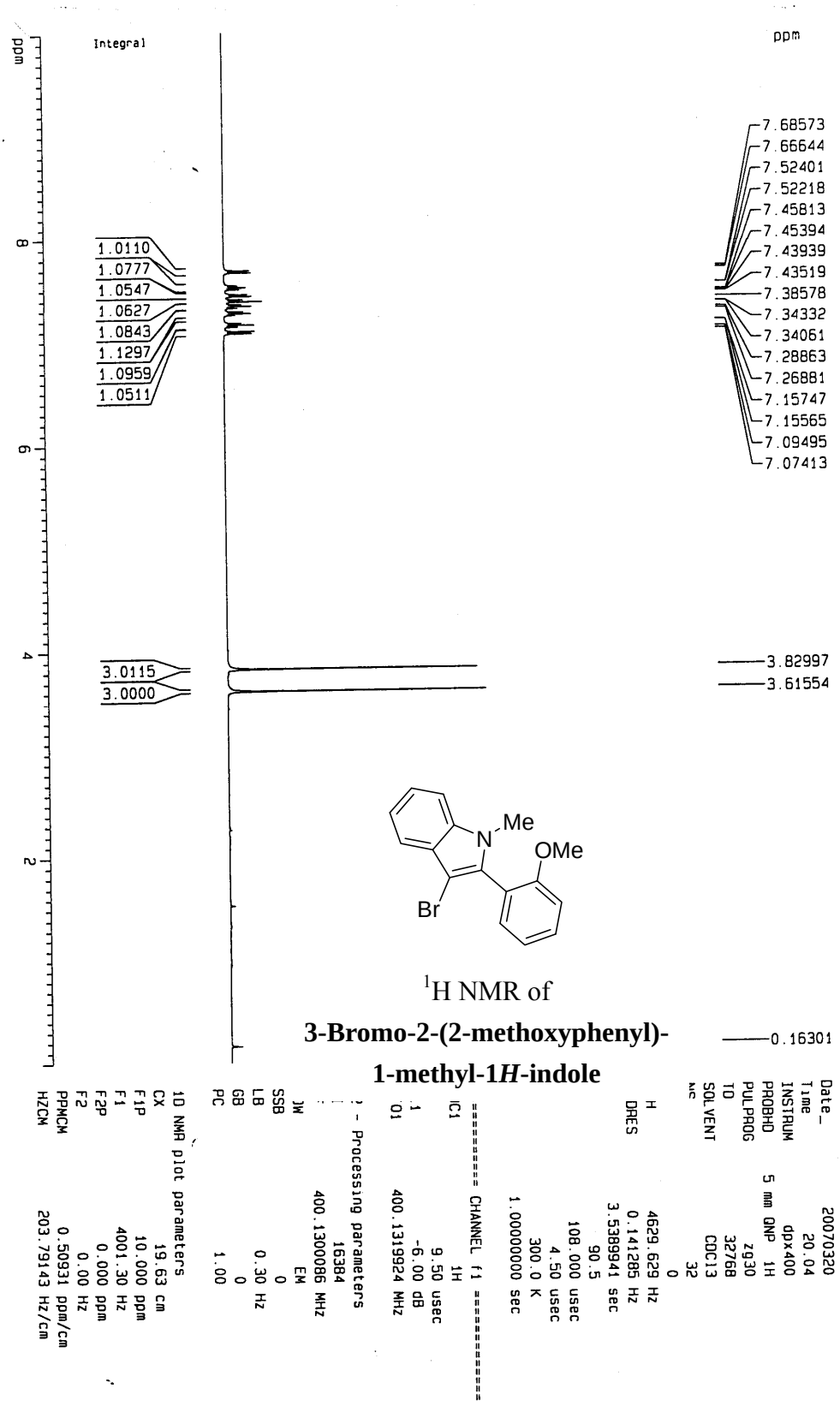
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 60.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
5 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-20 H: 0-1000 N: 0-1 P: 0-1

So Chau Ming, Indole cy2 phosphine
HR07_0227_5 139 (2.622) AM (Cen,5, 80.00, Ht,10000.0,0.00,1.00); Sm (SG, 3x3.00); Sb (15,20.00); Cm (123:143) TOF MS ES+
771

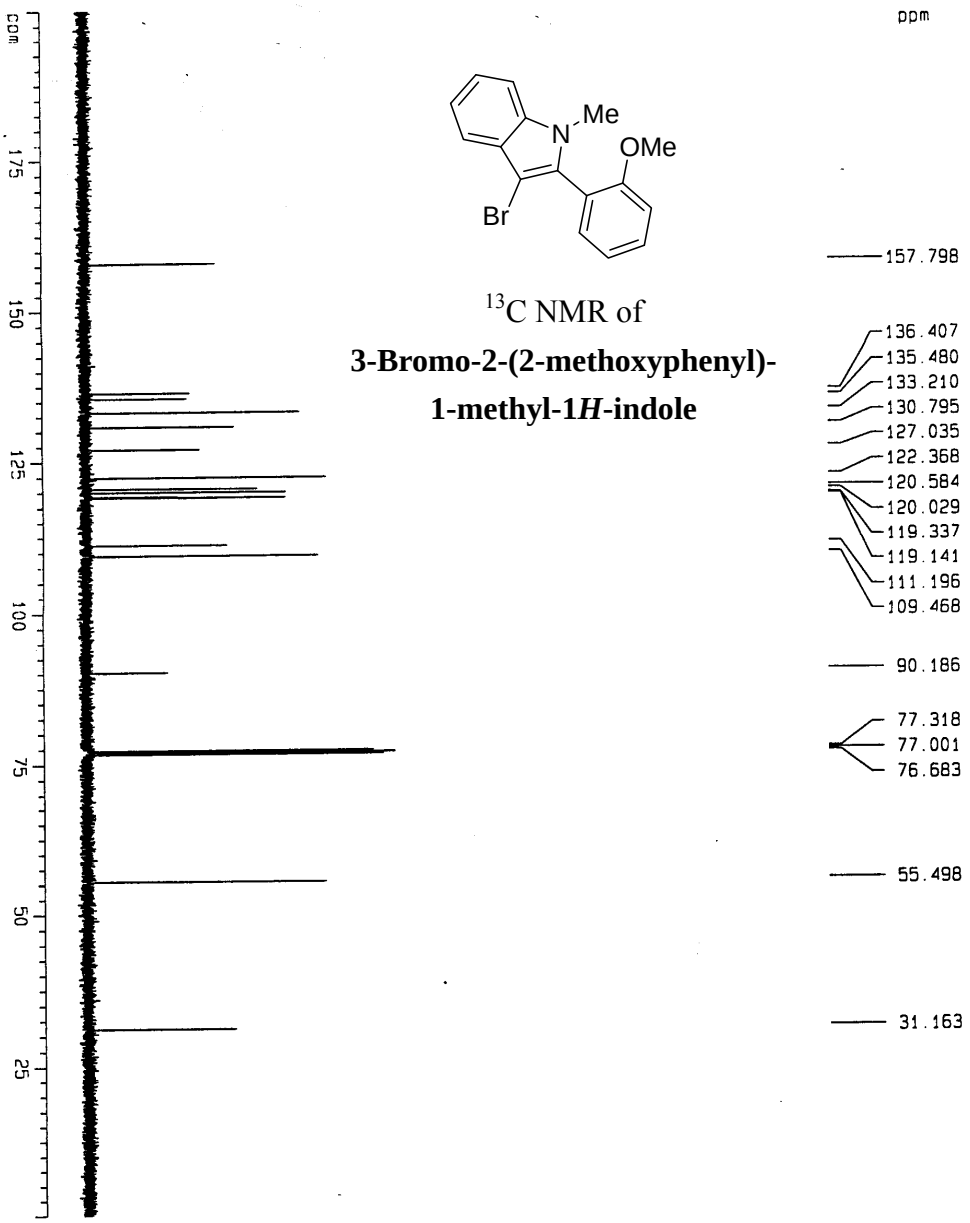


Minimum:				-1.5		
Maximum:		100.0	5.0	60.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
314.2043	314.2038	0.5	1.6	7.5	2.4	C20 H29 N P



^{1}H NMR of

3-Bromo-2-(2-methoxyphenyl)-1-methyl-1*H*-indole



^{13}C NMR of

3-Bromo-2-(2-methoxyphenyl)-1-methyl-1*H*-indole

Date_ 20070320
Time 20.08
INSTRUM dpx400
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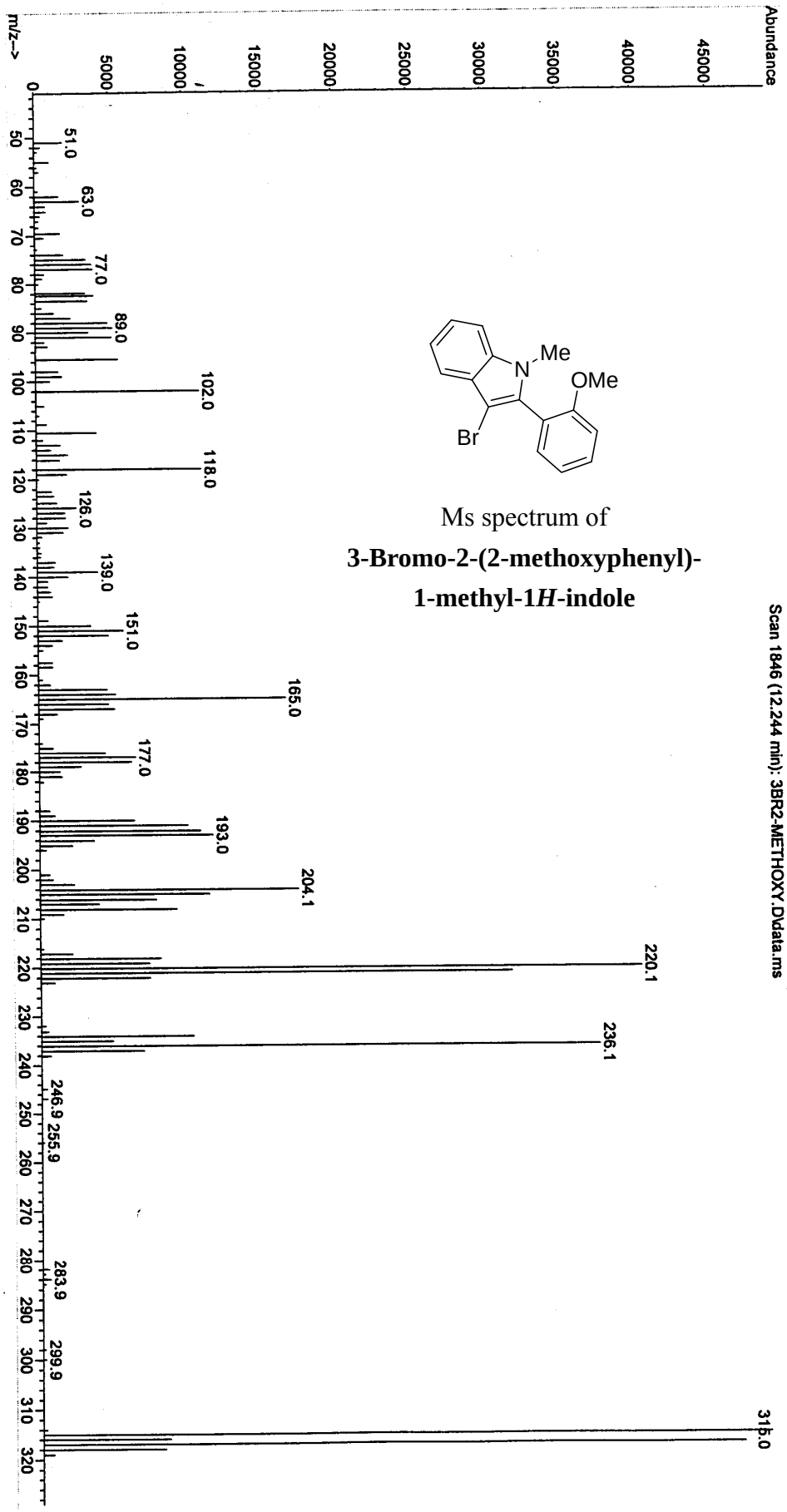
PULPROG zgdc30
TD 131072
SOLVENT CDCl3
NS 128
DS 0
SWH 25125.629 Hz
FIDRES 0.191693 Hz
AQ 2.6083827 sec
RG 9195.2
DW 19.900 usec
DE 4.50 usec
TE 300.0 K
D1 3.00000000 sec
d11 0.03000000 sec

======== CHANNEL f1 ========
NUC1 13C
P1 5.80 usec
PL1 -6.00 dB
SFO1 100.6231263 MHz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 71.00 usec
PL2 120.00 dB
PL12 17.00 dB
SFO2 400.1324008 MHz

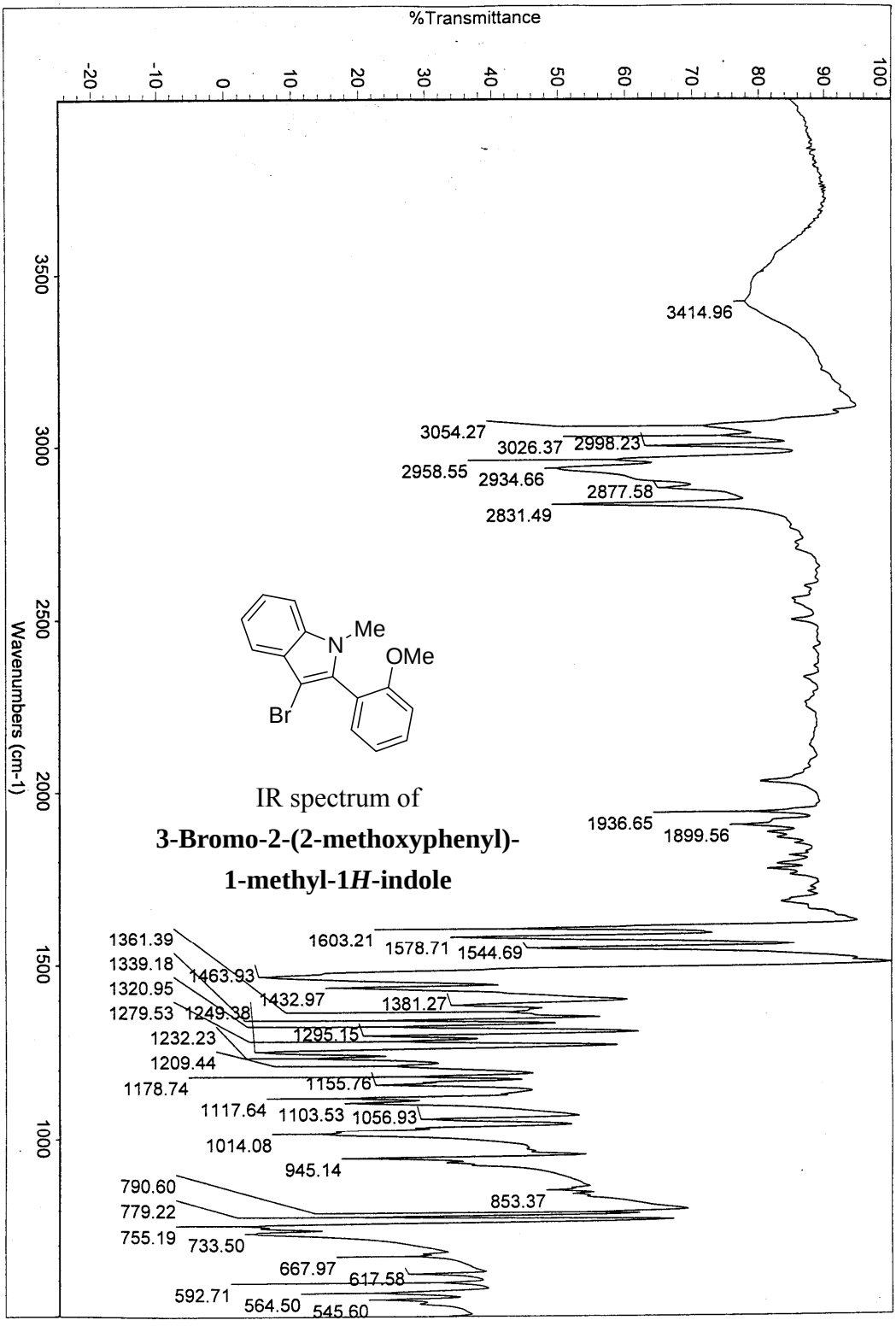
F2 - Processing parameters
SI 65536
SF 100.6127817 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 19.50 cm
F1P 200.000 ppm
F1 20122.56 Hz
F2P -0.000 ppm
F2 -0.00 Hz
PPMCM 10.25641 ppm/cm
HZCM 1031.92603 Hz/cm



Ms spectrum of

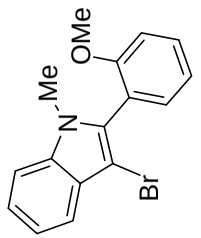
3-Bromo-2-(2-methoxyphenyl)-1-methyl-1*H*-indole



IR spectrum of

3-Bromo-2-(2-methoxyphenyl)-1-methyl-1*H*-indole

HRMS spectrum of **3-Bromo-2-(2-methoxyphenyl)-1-methyl-1*H*-indole**



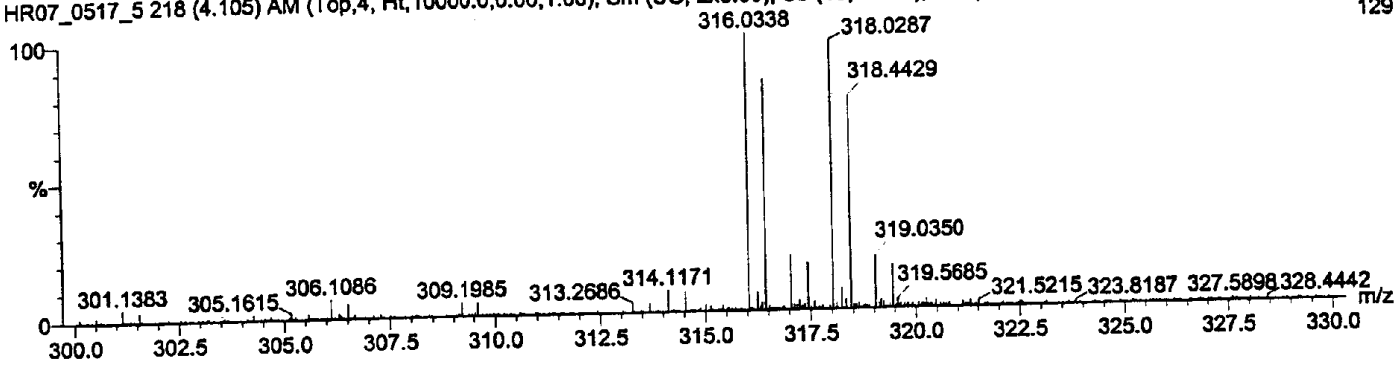
Elemental Composition Report

Single Mass Analysis
Tolerance = 100.0 PPM / DBE: min = -1.5, max = 60.0
Selected filters: None

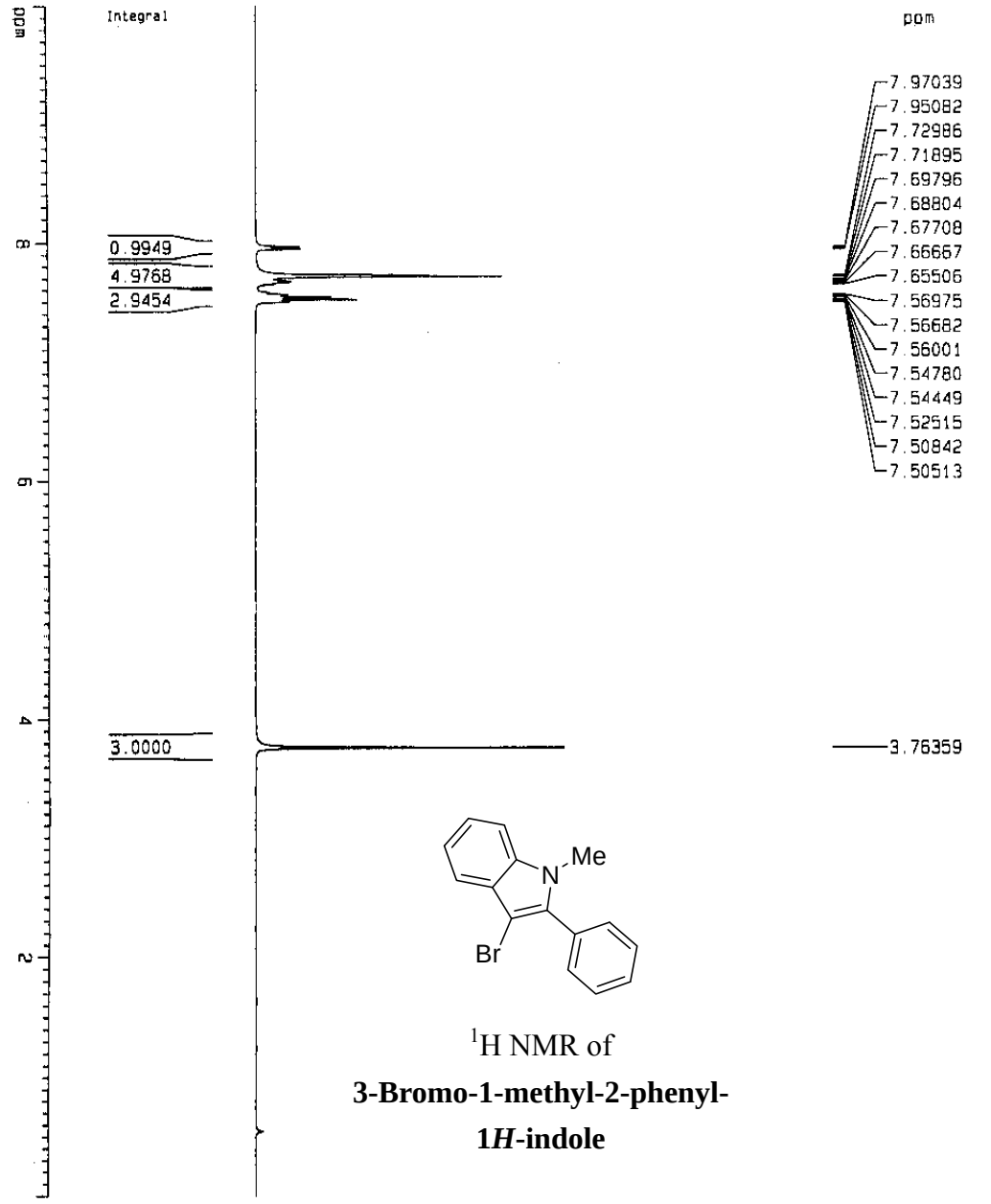
Monoisotopic Mass, Even Electron Ions
11 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-16 H: 0-1000 N: 0-1 O: 0-1 Br: 0-1

So Chau Ming, N-methyl 2-(2-methoxyphenyl)indole 3-Br
HR07_0517_5 218 (4.105) AM (Top,4, Ht,10000.0,0.00,1.00); Sm (SG, 2x3.00); Sb (15,10.00); Cm (159:223)

TOF MS ES+
129



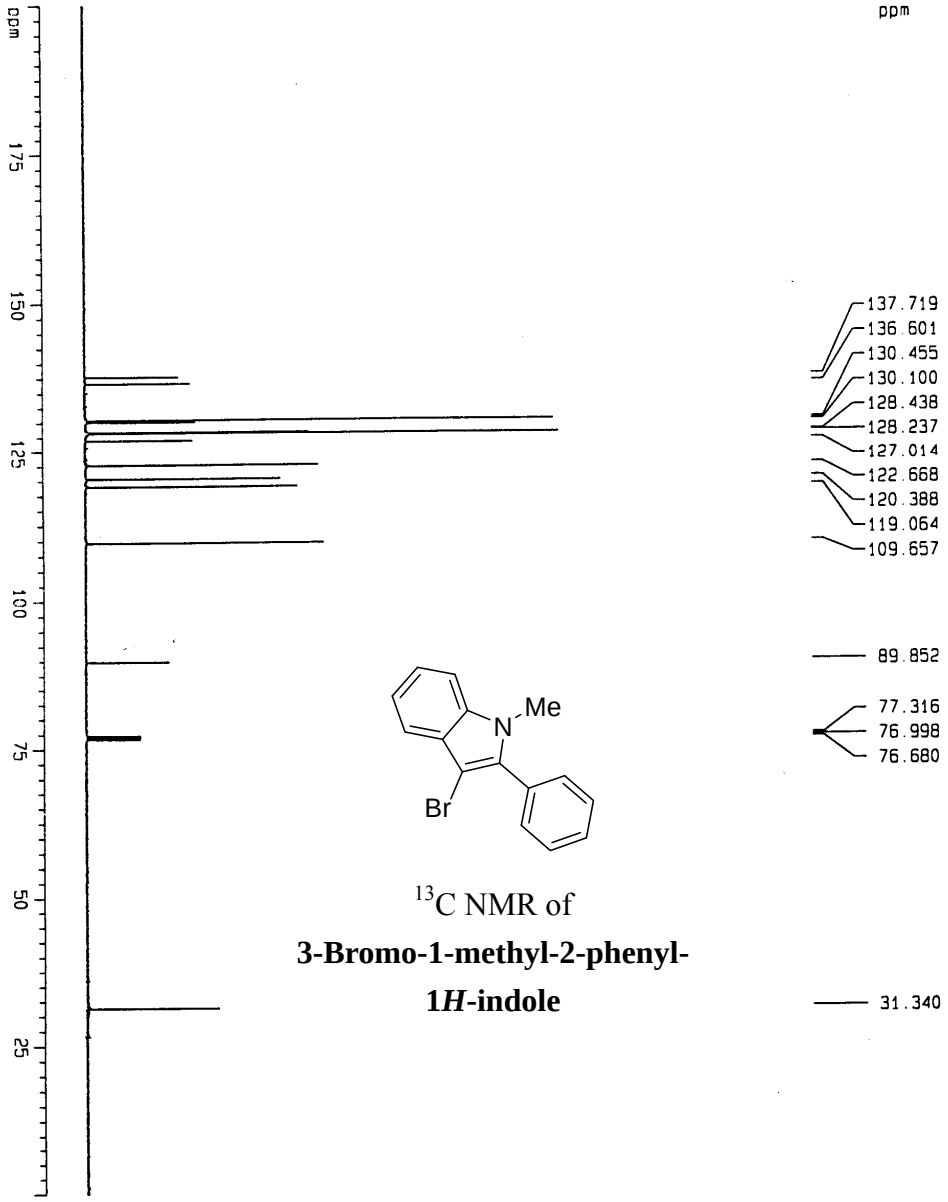
Minimum:		5.0	100.0	-1.5		
Maximum:				60.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
316.0338	316.0337	0.1	0.3	9.5	0.1	C16 H15 N O Br



^{1}H NMR of

3-Bromo-1-methyl-2-phenyl-1*H*-indole

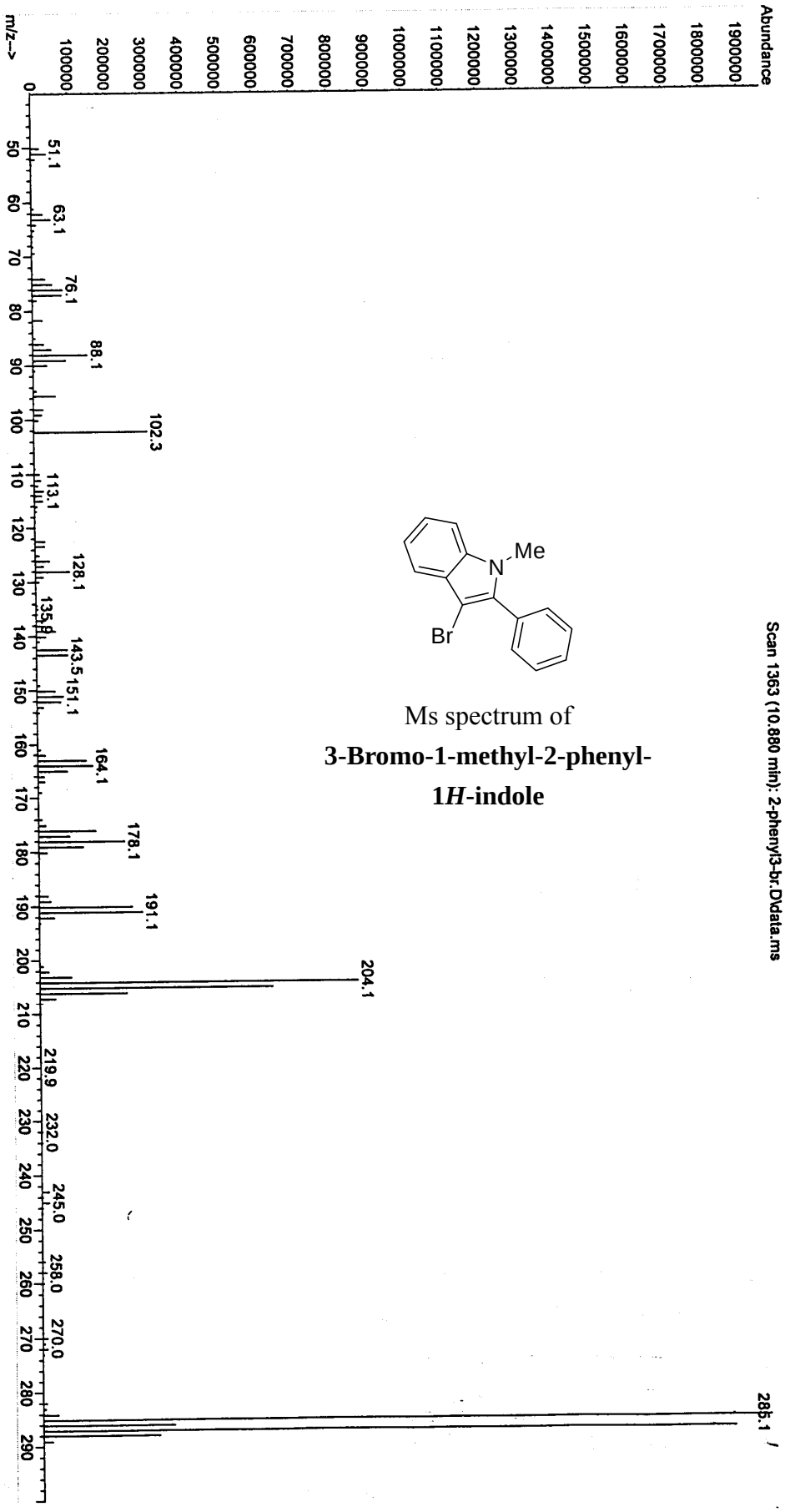
```
F2 - Acquisition Parameters
Date_           20070327
Time                8.44
INSTRUM           dpx400
PROBHD  5 mm QNP  1H
PULPROG             zg30
TD                 32768
SOLVENT             CDCl3
NS                     32
DS                      0
SWH              4629.629 Hz
FIDRES           0.141285 Hz
AQ               3.5389941 sec
RG                     18
DW                108.000 usec
DE                  4.50 usec
TE                 300.0 K
D1               1.00000000 sec
======== CHANNEL f1 ========
NUC1                   1H
P1                   9.50 usec
PL1                 -6.00 dB
SFO1          400.1319924 MHz
F2 - Processing parameters
SI                    16384
SF          400.1300092 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
1D NMR plot parameters
CX                  19.63 cm
F1P                 10.000 ppm
F1                4001.30 Hz
F2P                 0.000 ppm
F2                  0.00 Hz
PPMCM             0.50931 ppm/cm
HZCM            203.79143 Hz/cm
```



^{13}C NMR of

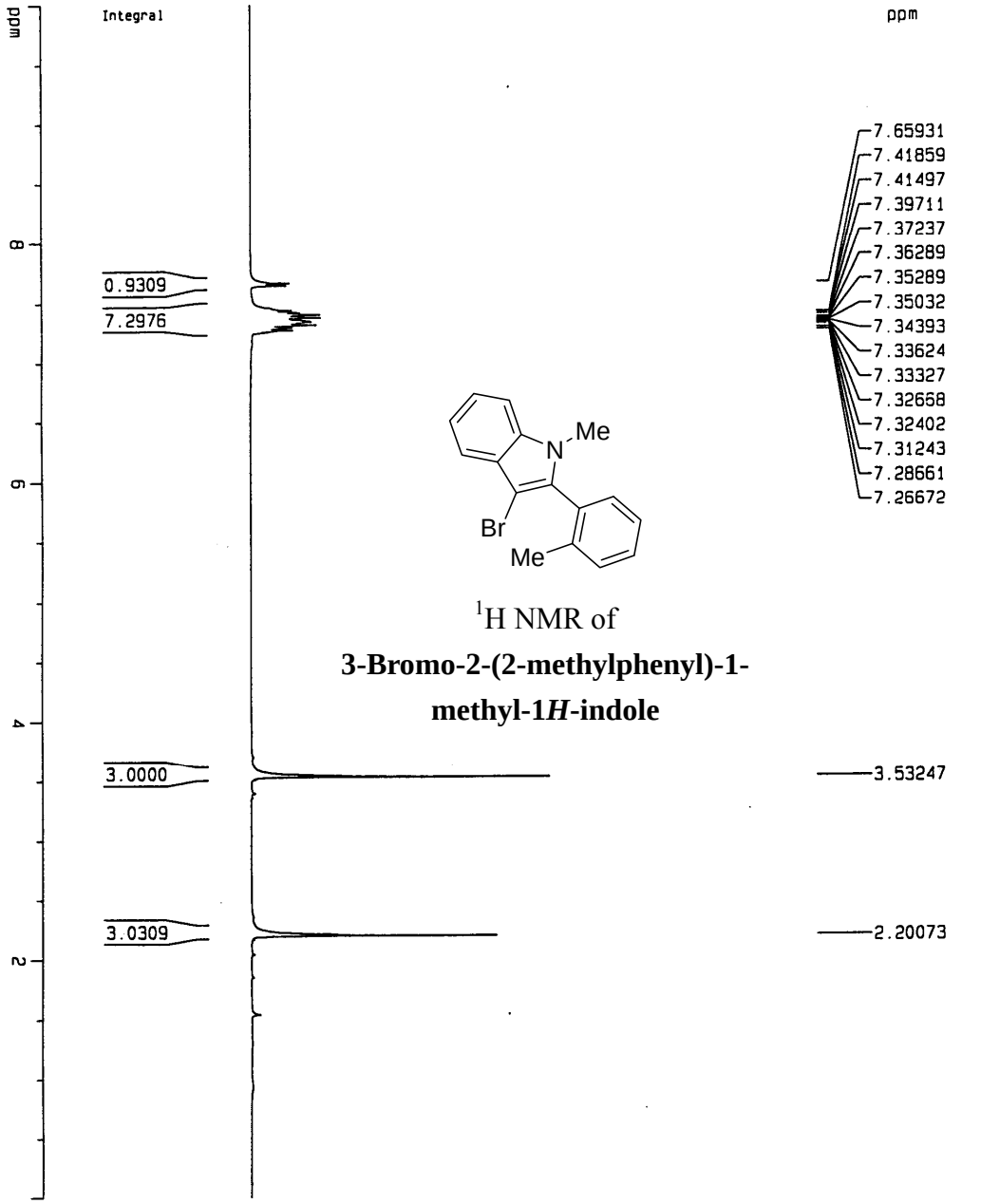
3-Bromo-1-methyl-2-phenyl-1*H*-indole

```
F2 - Acquisition Parameters
Date_              20070327
Time                   8.48
INSTRUM              dpx400
PROBHD     5 mm QNP 1H
PULPROG            zgdc30
TD                 131072
SOLVENT            CDCl3
NS                     128
DS                       0
SWH              25125.629 Hz
FIDRES               0.191693 Hz
AQ                 2.6083827 sec
RG                    6502
DW                  19.900 usec
DE                   4.50 usec
TE                  300.0 K
D1                 3.00000000 sec
D11                0.03000000 sec
======== CHANNEL f1 ========
NUC1                    13C
P1                   5.80 usec
PL1                  -6.00 dB
SFO1           100.6231263 MHz
======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                    1H
PCPD2               71.00 usec
PL2                 120.00 dB
PL12                17.00 dB
SFO2           400.1322007 MHz
F2 - Processing parameters
SI                     65536
SF             100.6128250 MHz
WDW                      EM
SSB                       0
LB                   0.70 Hz
GB                        0
PC                     1.00
1D NMR plot parameters
CX                    19.50 cm
F1P                 200.000 ppm
F1                20122.56 Hz
F2P                -0.000 ppm
F2                   -0.00 Hz
PPMCM              10.25641 ppm/cm
HZCM             1031.92639 Hz/cm
```



Ms spectrum of

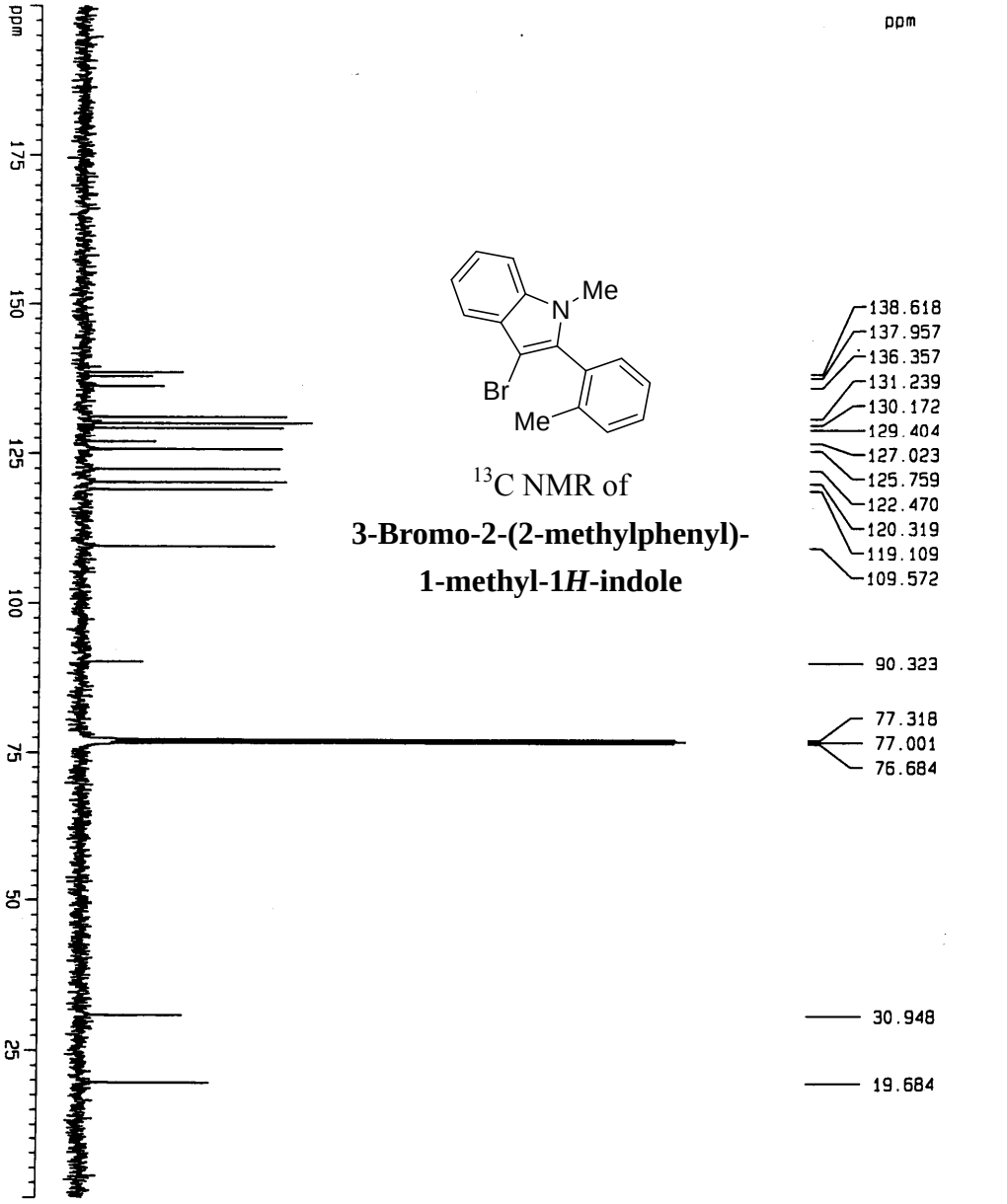
3-Bromo-1-methyl-2-phenyl-1*H*-indole



^{1}H NMR of

3-Bromo-2-(2-methylphenyl)-1-methyl-1*H*-indole

F2 - Acquisition Parameters
Date_ 20080916
Time 19.45
INSTRUM dpx400
PROBHD 5 mm QNP 1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 0
SWH 5995.204 Hz
FIDRES 0.182959 Hz
AQ 2.7329011 sec
RG 161.3
DW 83.400 usec
DE 4.50 usec
TE 300.0 K
D1 1.00000000 sec
========== CHANNEL f1 ==========
NUC1 1H
P1 9.50 usec
PL1 -6.00 dB
SFO1 400.1320098 MHz
F2 - Processing parameters
SI 16384
SF 400.1300092 MHz
WDW EM
SSB 0
LB 0.40 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 19.63 cm
F1P 10.000 ppm
F1 4001.30 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.50931 ppm/cm
HZCM 203.79143 Hz/cm



^{13}C NMR of

3-Bromo-2-(2-methylphenyl)-1-methyl-1*H*-indole

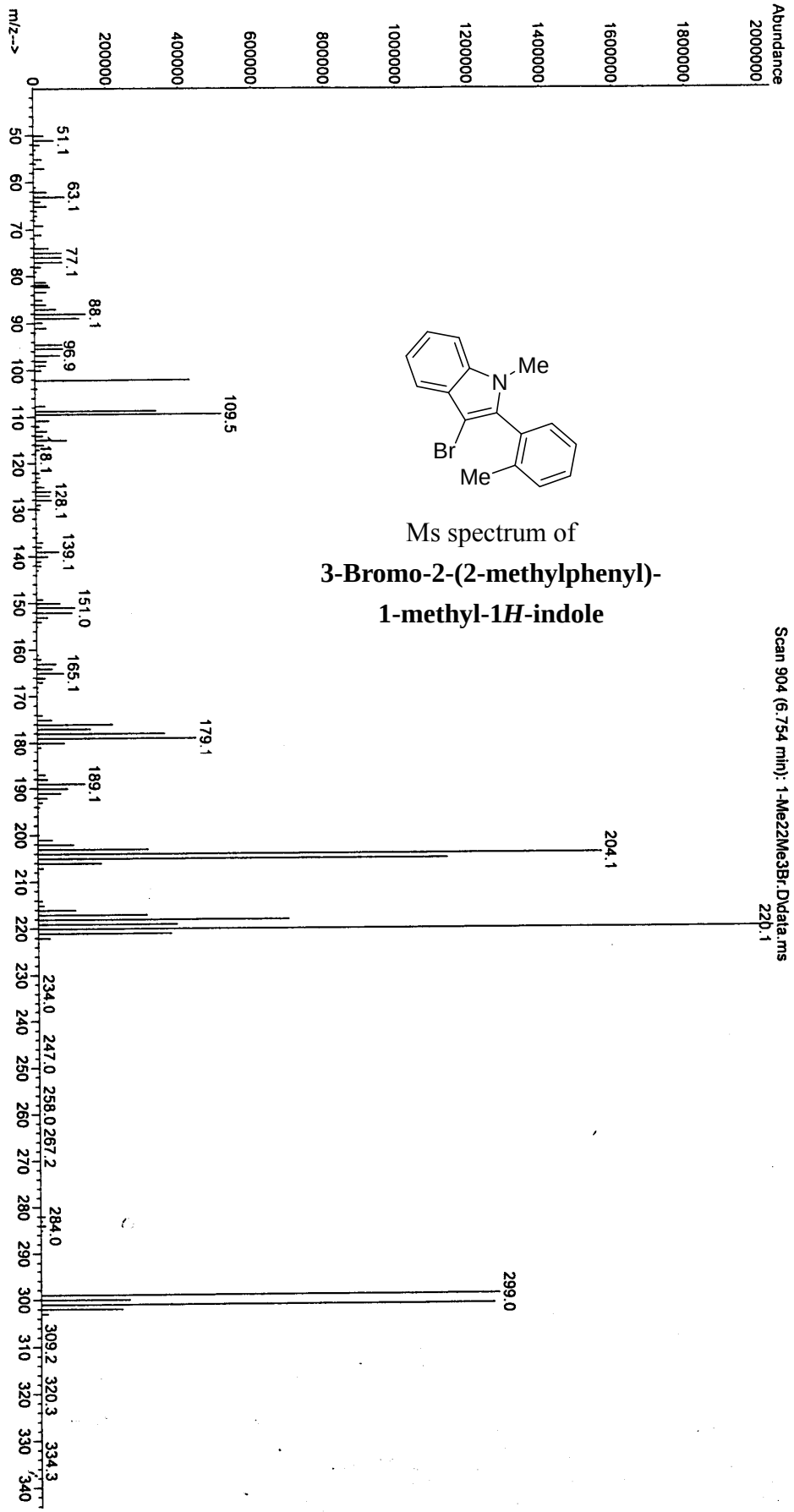

```
Date_                20080916
Time                    19.48
INSTRUM                 dpx400
PROBHD     5 mm QNP  1H
PULPROG                 zgdc30
TD                      131072
SOLVENT                 CDCl3
NS                         100
DS                           0
SWH                  27624.309 Hz
FIDRES                0.210757 Hz
AQ                    2.3724532 sec
RG                       7298.2
DW                     18.100 usec
DE                      4.50 usec
TE                       300.0 K
D1                    3.00000000 sec
d11                   0.03000000 sec

---------- CHANNEL f1 ----------
NUC1                       13C
P1                        5.80 usec
PL1                      -6.00 dB
SFO1                100.6231263 MHz

---------- CHANNEL f2 ----------
CPDPRG2                 waltz16
NUC2                        1H
PCPD2                     71.00 usec
PL2                      120.00 dB
PL12                      17.00 dB
SFO2                400.1326008 MHz

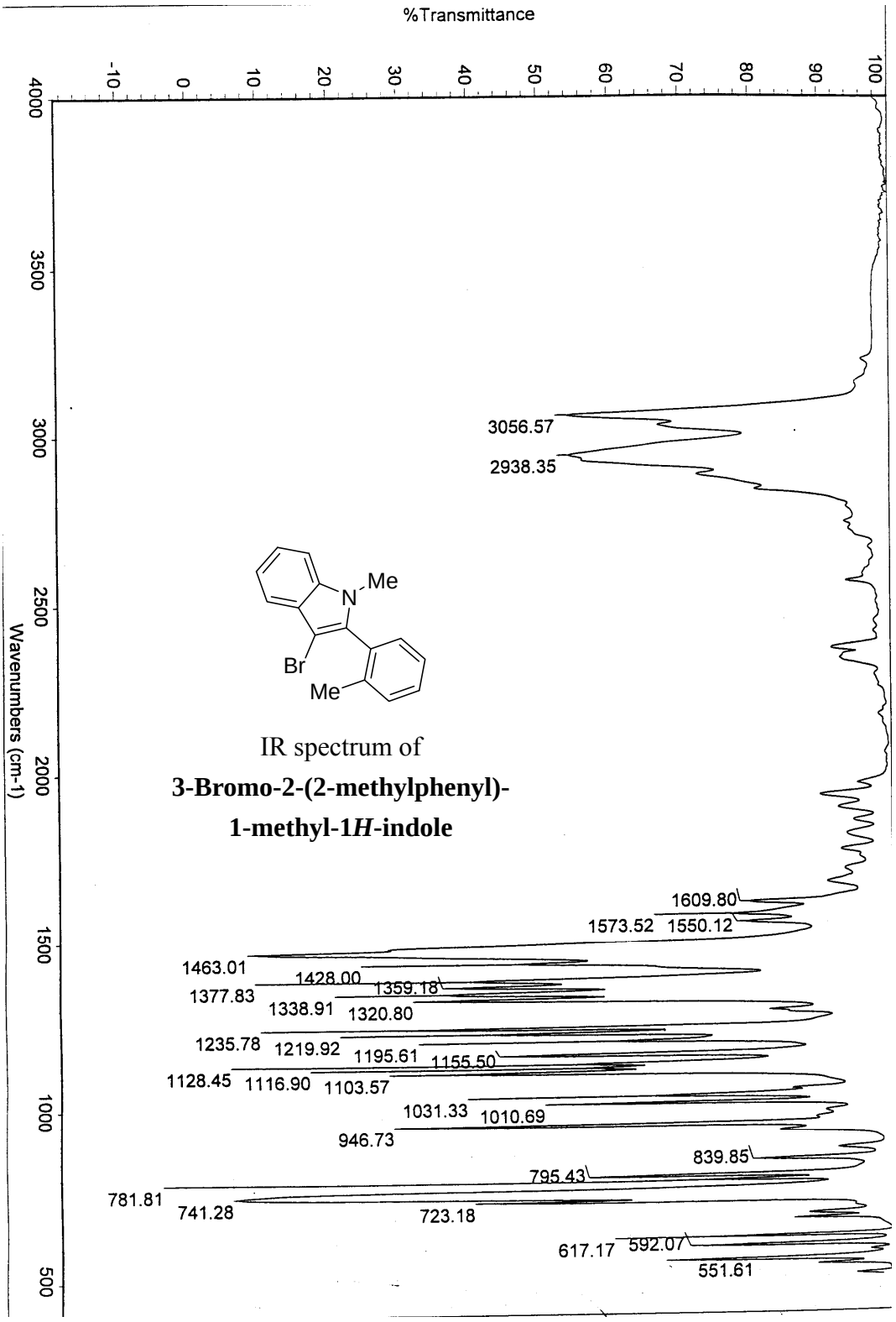
F2 - Processing parameters
SI                         65536
SF                  100.6127755 MHz
WDW                           EM
SSB                            0
LB                      3.00 Hz
GB                             0
PC                          1.00

1D NMR plot parameters
CX                         19.50 cm
F1P                      200.000 ppm
F1                     20122.55 Hz
F2P                      -0.000 ppm
F2                        -0.00 Hz
PPMCM                   10.25641 ppm/cm
HZCM                 1031.92590 Hz/cm
```



Ms spectrum of

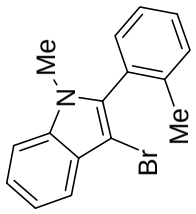
3-Bromo-2-(2-methylphenyl)-1-methyl-1*H*-indole



IR spectrum of

3-Bromo-2-(2-methylphenyl)-1-methyl-1*H*-indole

HRMS spectrum of **3-Bromo-2-(2-methylphenyl)-1-methyl-1*H*-indole**



Elemental Composition Report

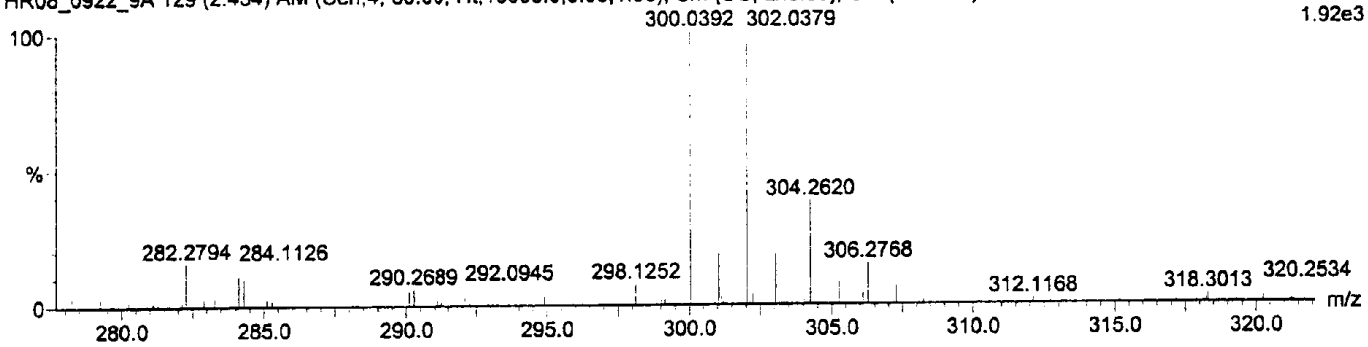
Single Mass Analysis

Tolerance = 100.0 PPM / DBE: min = -1.5, max = 60.0
Selected filters: None

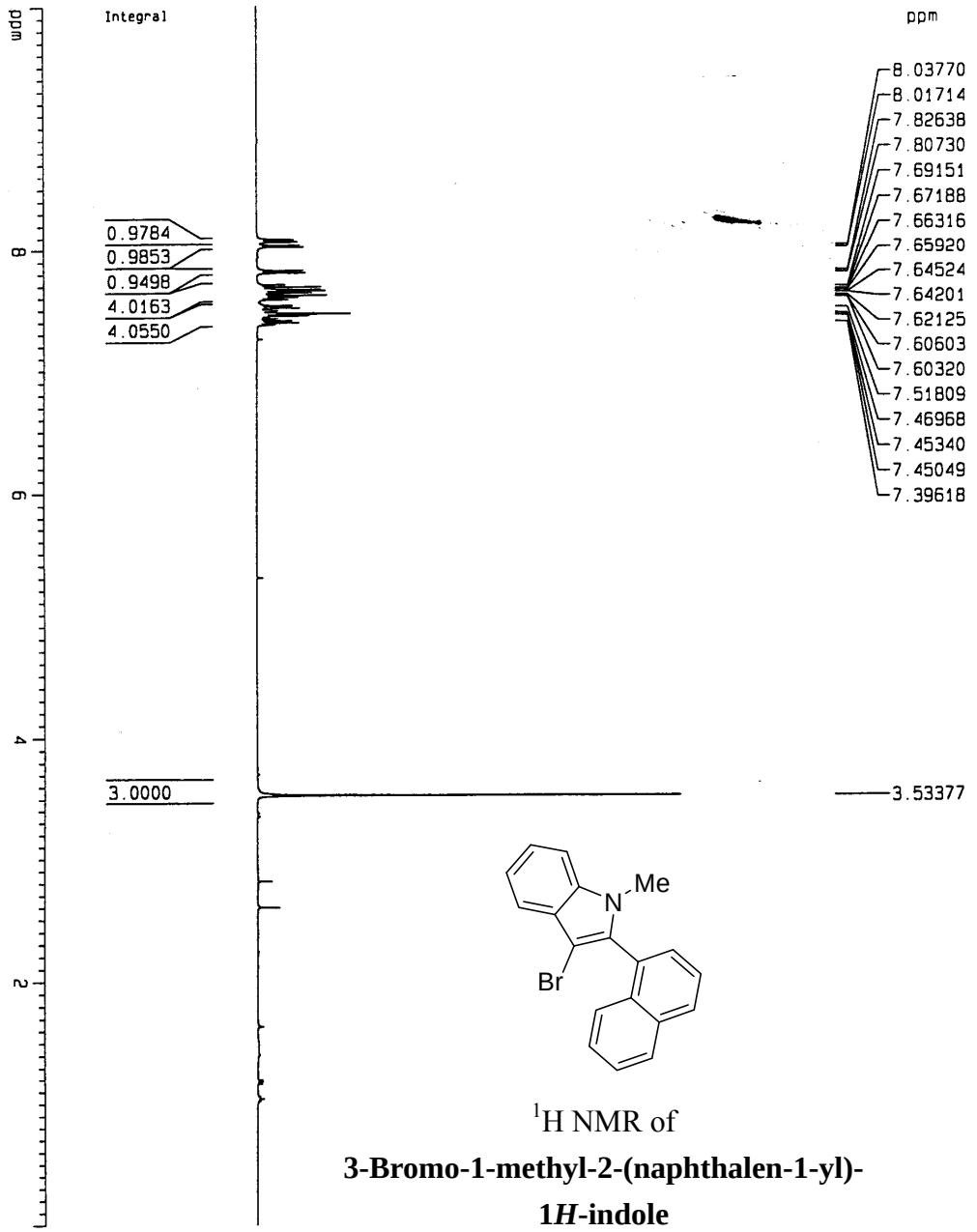
Monoisotopic Mass, Even Electron Ions
10 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-19 H: 0-1000 N: 0-1 Br: 0-1

So Chau Ming, C16H14BrN
HR08_0922_9A 129 (2.434) AM (Cen,4, 80.00, Ht,10000.0,0.00,1.00); Sm (SG, 2x3.00); Cm (112:138)

TOF MS ES+
1.92e3



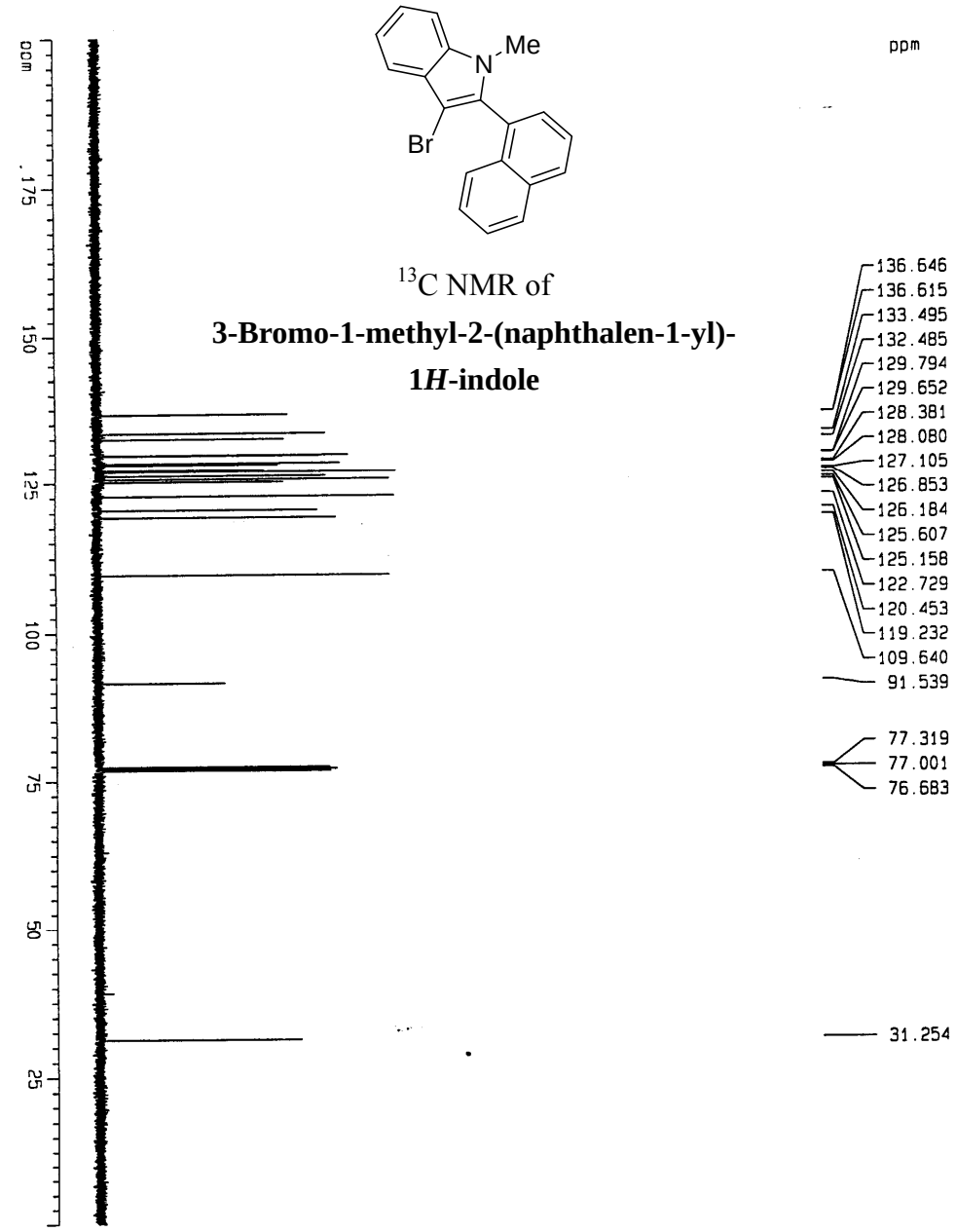
Minimum:				-1.5		
Maximum:		100.0	100.0	60.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
300.0392	300.0388	0.4	1.3	9.5	0.7	C16 H15 N Br



^{1}H NMR of

3-Bromo-1-methyl-2-(naphthalen-1-yl)-1*H*-indole

```
F2 - Acquisition Parameters
Date_              20070515
Time                   16.10
INSTRUM              dpx400
PROBHD     5 mm QNP 1H
PULPROG              zg30
TD                  32768
SOLVENT             CDCl3
NS                     16
DS                      0
SWH              4629.629 Hz
FIDRES           0.141285 Hz
AQ               3.5389941 sec
RG                     57
DW                108.000 usec
DE                 4.50 usec
TE                 300.0 K
D1               1.00000000 sec
======== CHANNEL f1 ========
NUC1                   1H
P1                  9.50 usec
PL1                 -6.00 dB
SFO1           400.1319924 MHz
F2 - Processing parameters
SI                     16384
SF           400.1300095 MHz
WDW                    EM
SSB                     0
LB                 0.30 Hz
GB                      0
PC                   1.00
1D NMR plot parameters
CX                  19.63 cm
F1P                10.000 ppm
F1               4001.30 Hz
F2P                 0.000 ppm
F2                  0.00 Hz
PPMCM            0.50931 ppm/cm
HZCM           203.79143 Hz/cm
```



^{13}C NMR of

3-Bromo-1-methyl-2-(naphthalen-1-yl)-1*H*-indole

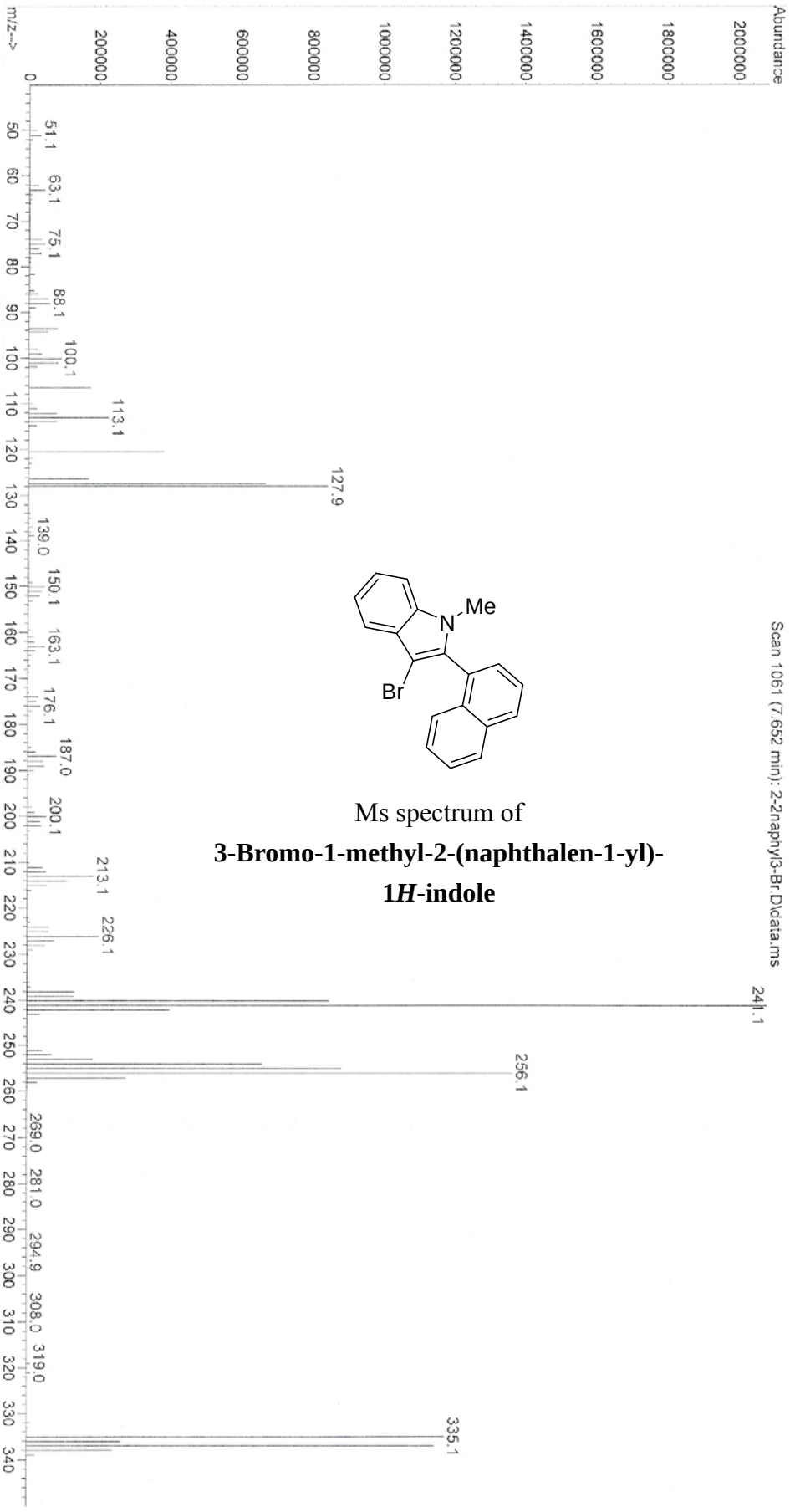
```
Date_                20070515
Time                    16.12
INSTRUM                 dpx400
PROBHD          5 mm QNP  1H
PULPROG                 zgdc30
TD                      131072
SOLVENT                 CDCl3
NS                      80
DS                      0
SWH                     25125.629 Hz
FIDRES                  0.191693 Hz
AQ                      2.6083827 sec
RG                      9195.2
DW                      19.900 usec
DE                      4.50 usec
TE                      300.0 K
D1                      3.00000000 sec
d11                     0.03000000 sec

======== CHANNEL f1 ========
NUC1                    13C
P1                      5.80 usec
PL1                     -6.00 dB
SF01                    100.6231263 MHz

======== CHANNEL f2 ========
CPDPRG2                 waltz16
NUC2                    1H
PCPD2                   71.00 usec
PL2                     120.00 dB
PL12                    17.00 dB
SF02                    400.1324008 MHz

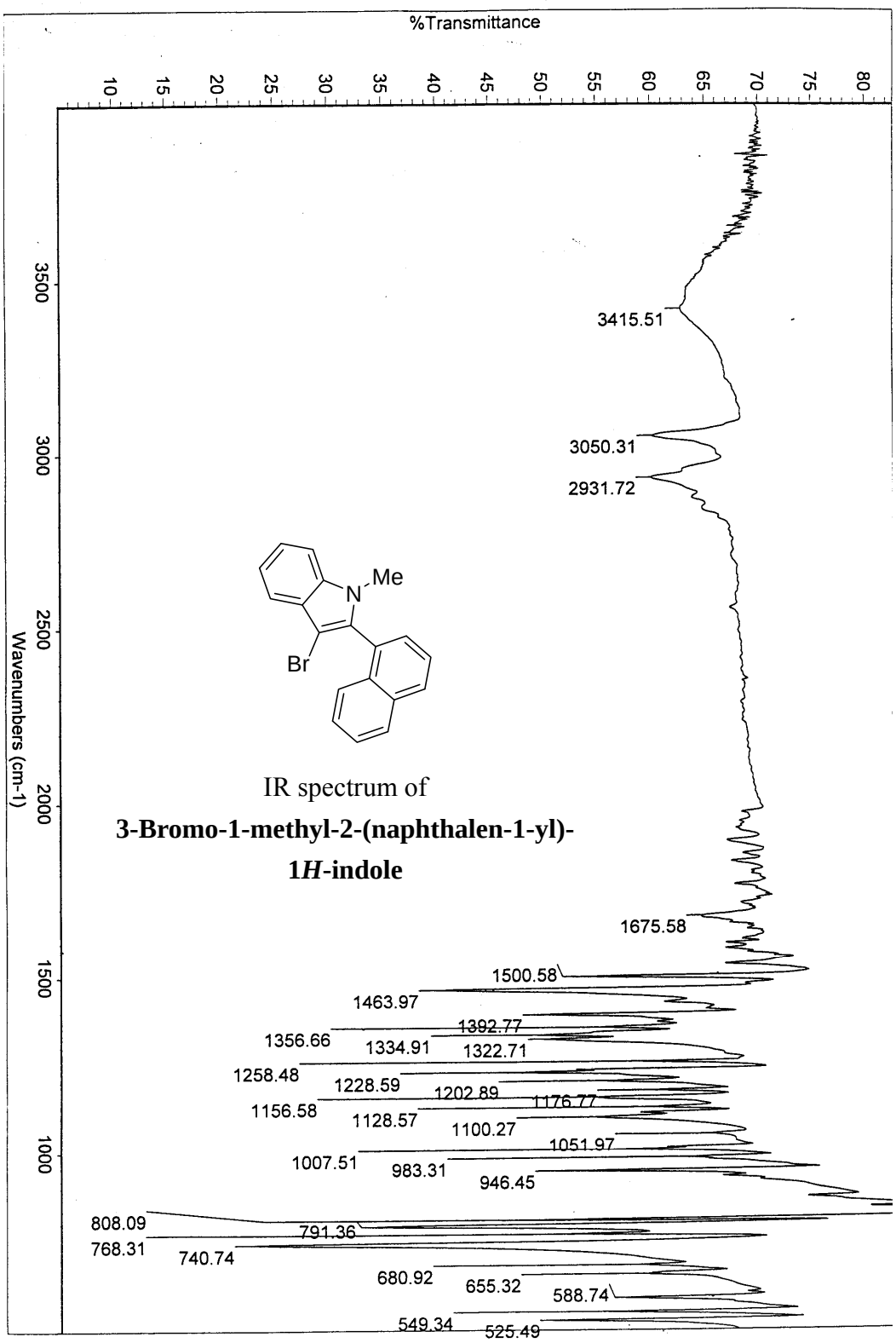
F2 - Processing parameters
SI                      65536
SF                      100.6127917 MHz
WDW                     EM
SSB                     0
LB                      0.30 Hz
GB                      0
PC                      1.00

1D NMR plot parameters
CX                      19.50 cm
F1P                     200.000 ppm
F1                      20122.56 Hz
F2P                     -0.000 ppm
F2                      -0.00 Hz
PPMCM                   10.25641 ppm/cm
HZCM                    1031.92615 Hz/cm
```



Ms spectrum of

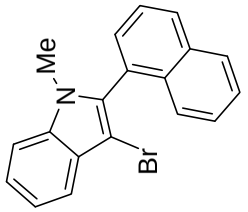
3-Bromo-1-methyl-2-(naphthalen-1-yl)-1*H*-indole



IR spectrum of

3-Bromo-1-methyl-2-(naphthalen-1-yl)-1*H*-indole

HRMs spectrum of **3-Bromo-1-methyl-2-(naphthalen-1-yl)-1*H*-indole**



Elemental Composition Report

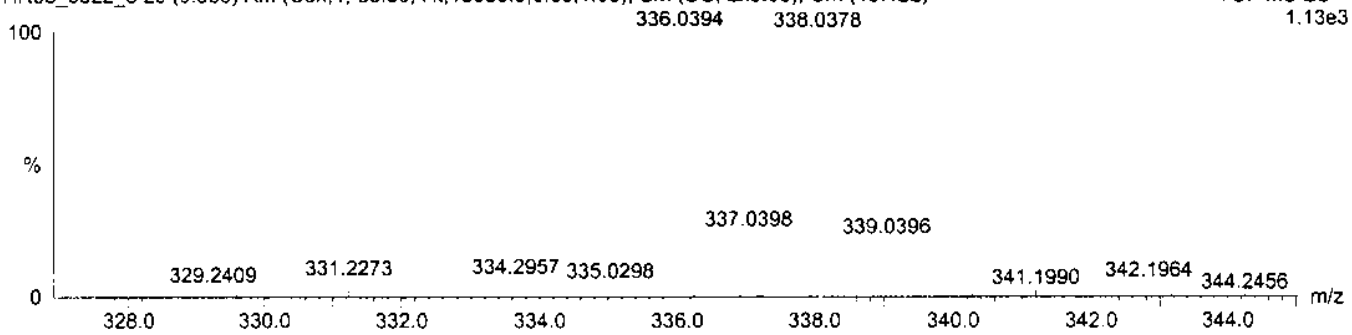
Single Mass Analysis

Tolerance = 10.0 PPM / DBE: min = -1.5, max = 60.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
7 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-19 H: 0-1000 N: 0-1 Br: 0-1

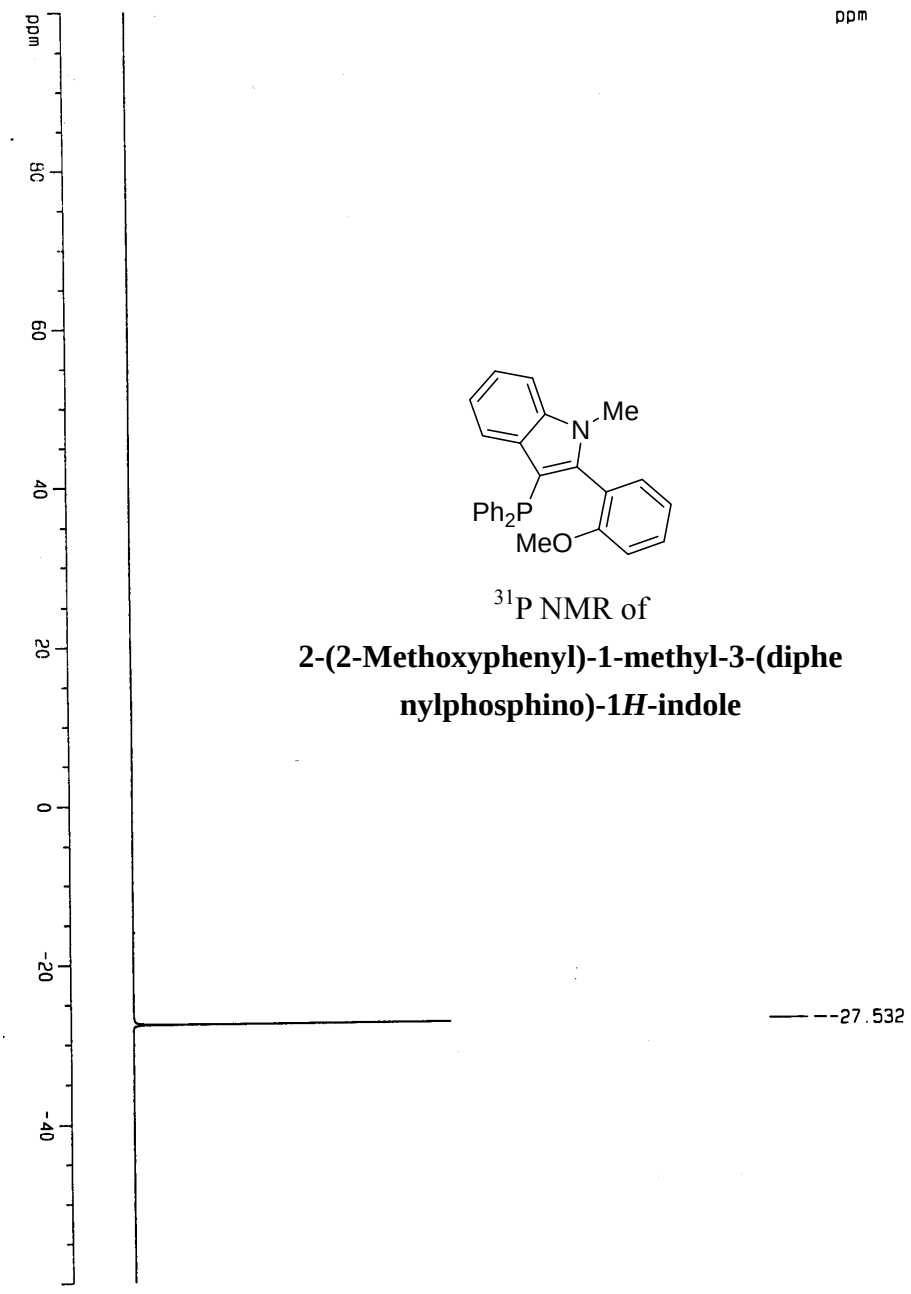
So Chau Ming, C19H14BrN
HR08_0922_8 20 (0.383) AM (Cen,4, 80.00, Ht,10000.0,0.00,1.00); Sm (SG, 2x3.00); Cm (19:122)

TOF MS ES+
1.13e3



Minimum:				-1.5		
Maximum:		100.0	10.0	60.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
336.0394	336.0388	0.6	1.8	12.5	1.9	C19 H15 N Br

C-P Type Indolyl Phosphine Ligand (Phosphine Group Attached to 3-Position of Indole Ring)



^{31}P NMR of

2-(2-Methoxyphenyl)-1-methyl-3-(diphenylphosphino)-1*H*-indole

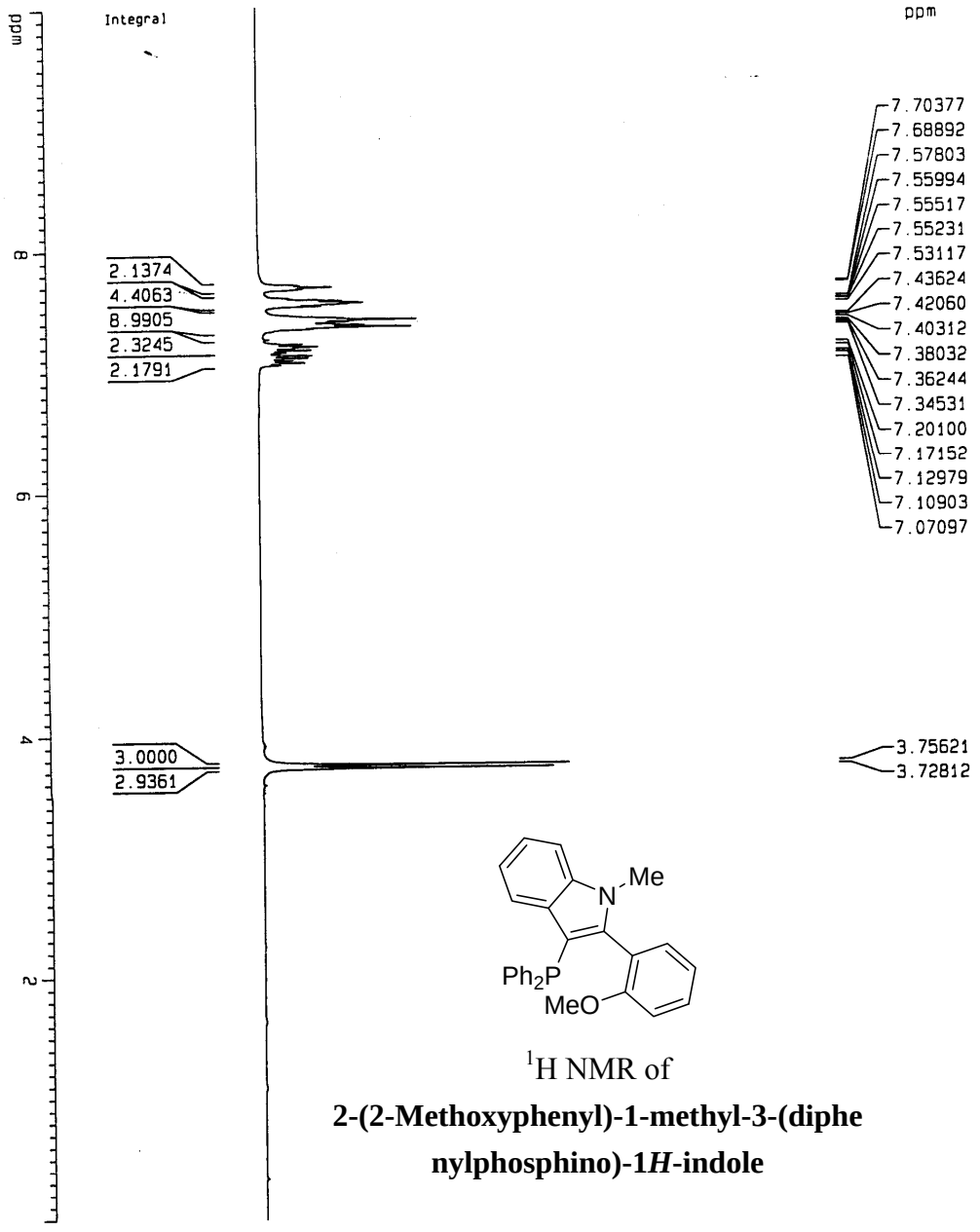
```
F2 - Acquisition Parameters
Date_            20070321
Time                19.39
INSTRUM           dpx400
PROBHD  5 mm QNP  1H
PULPROG          zgqc30
TD                65536
SOLVENT           CDCl3
NS                   64
DS                    0
SWH           8861.801 Hz
FIDRES        0.742520 Hz
AQ            0.6734324 sec
RG                 6502
DW               10.275 usec
DE                4.50 usec
TE                300.0 K
D1             1.00000000 sec
d11            0.03000000 sec

========== CHANNEL f1 ==========
NUC1               31P
P1                7.20 usec
PL1              -5.00 dB
SFO1       161.9851115 MHz

========== CHANNEL f2 ==========
CPDPRG2          waltz16
NUC2                1H
PCPD2            71.00 usec
PL2              120.00 dB
PL12              17.00 dB
SFO2       400.1324008 MHz

F2 - Processing parameters
SI                 32768
SF         161.9755831 MHz
WDW                   EM
SSB                    0
LB                3.00 Hz
GB                     0
PC                  1.40

1D NMR plot parameters
CX                20.00 cm
F1P              100.000 ppm
F1              16197.56 Hz
F2P             -60.000 ppm
F2              -9718.54 Hz
PPMCM           8.00000 ppm/cm
HZCM          1295.80469 Hz/cm
```



^{1}H NMR of

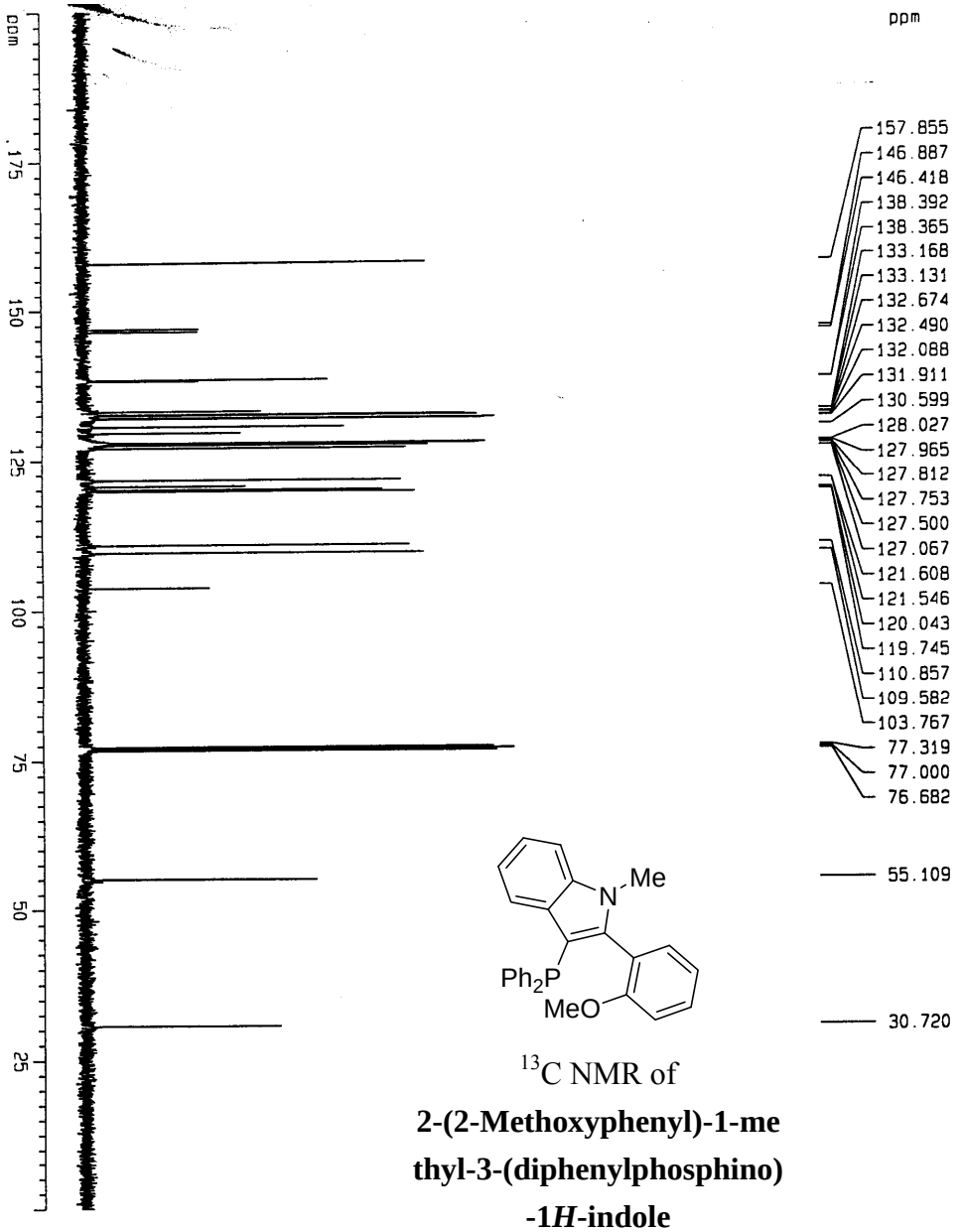
2-(2-Methoxyphenyl)-1-methyl-3-(diphenylphosphino)-1*H*-indole

```
F2 - Acquisition Parameters
Date_              20070321
Time                  20.02
INSTRUM             dpx400
PROBHD   5 mm QNP 1H
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    32
DS                     0
SWH              4629.629 Hz
FIDRES           0.141285 Hz
AQ               3.5389941 sec
RG                    35.9
DW                108.000 usec
DE                  4.50 usec
TE                 300.0 K
D1               1.00000000 sec

============== CHANNEL f1 ==============
NUC1                  1H
P1                 9.50 usec
PL1               -6.00 dB
SFO1         400.1319924 MHz

F2 - Processing parameters
SI                 16384
SF           400.1300086 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                 1.00

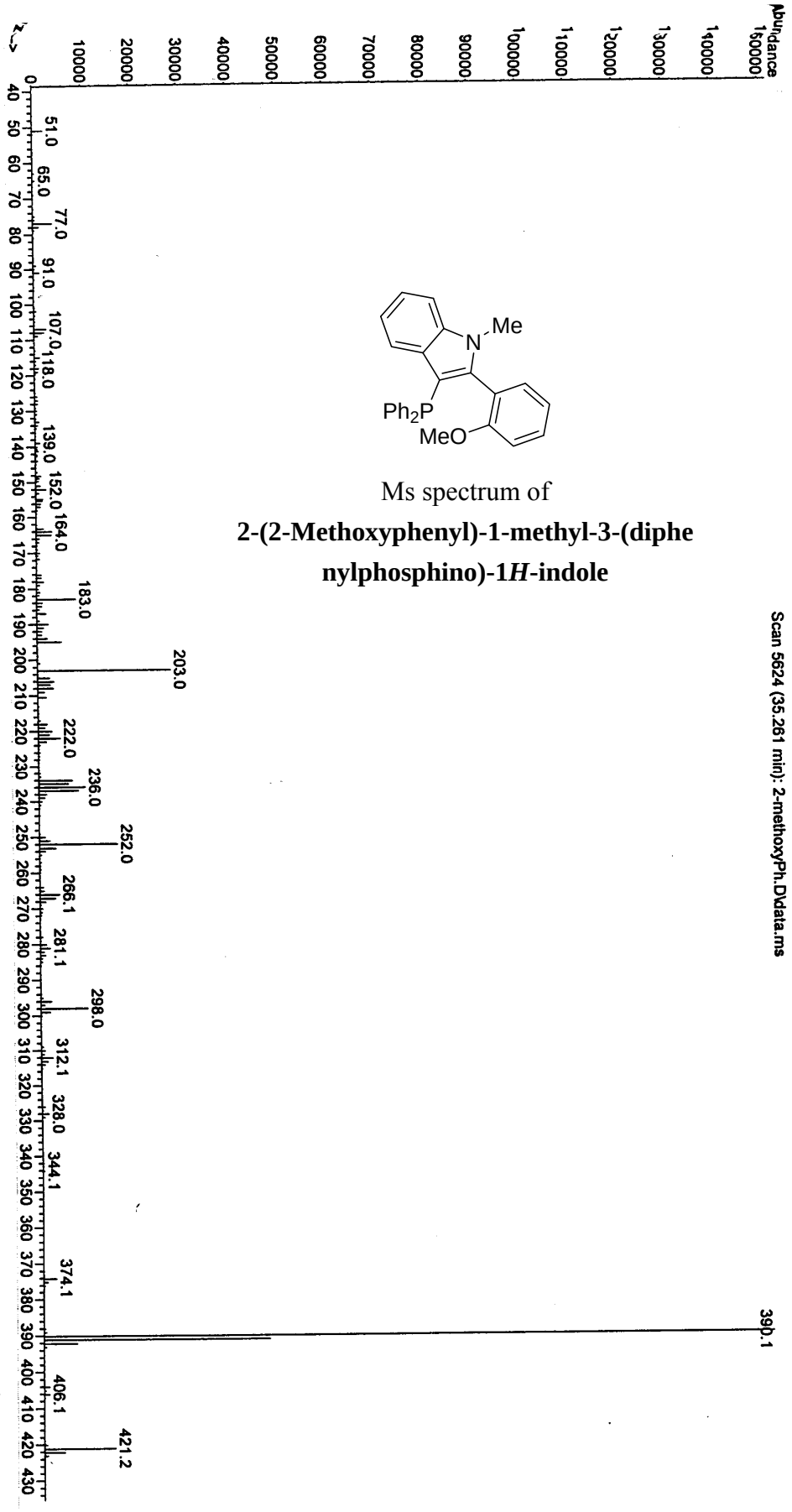
1D NMR plot parameters
CX                19.63 cm
F1P              10.000 ppm
F1             4001.30 Hz
F2P               0.000 ppm
F2                0.00 Hz
PPMCM          0.50931 ppm/cm
HZCM          203.79143 Hz/cm
```



^{13}C NMR of

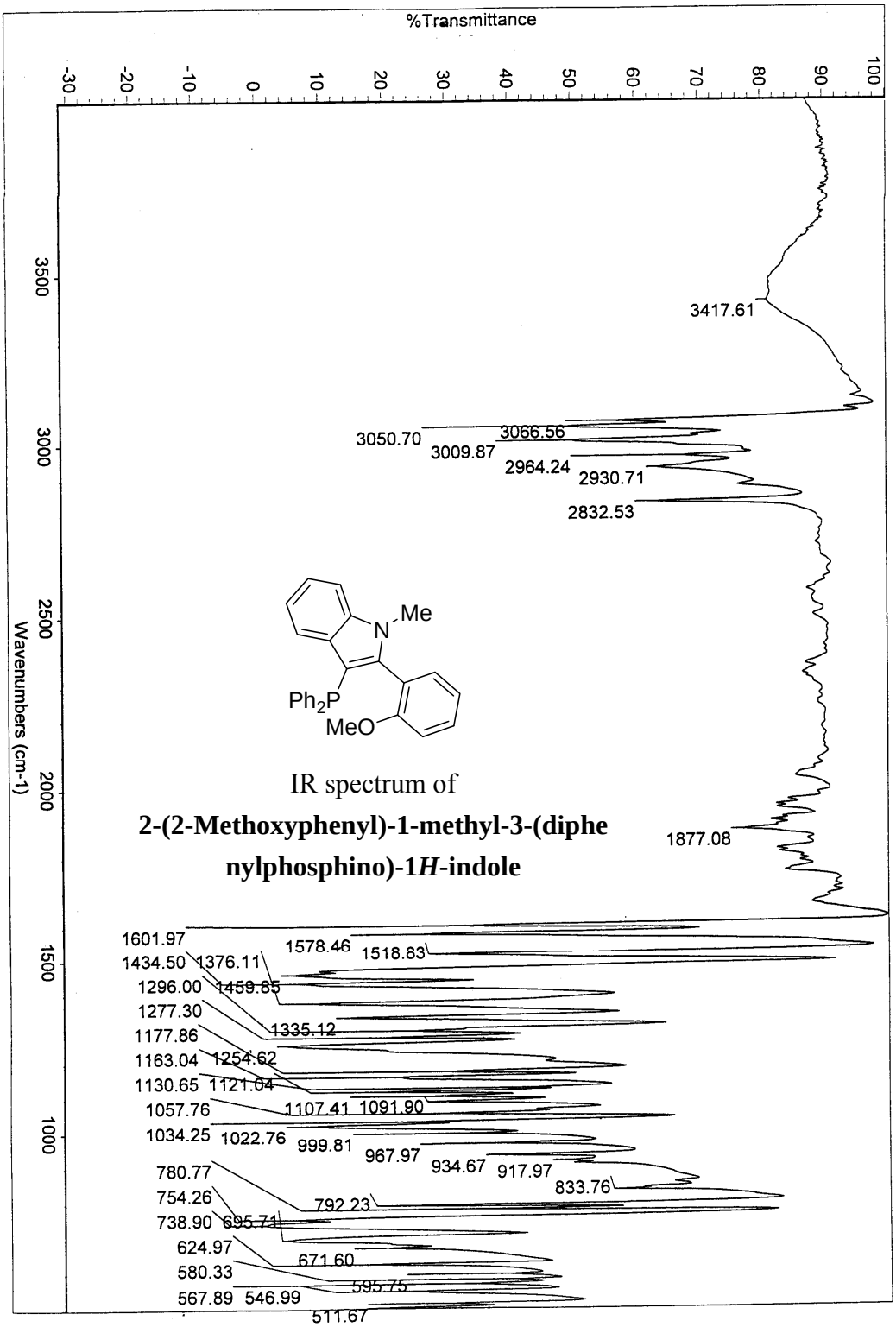
2-(2-Methoxyphenyl)-1-methyl-3-(diphenylphosphino)-1*H*-indole

```
Date_                20070321
Time                    20.25
INSTRUM                 dpx400
PROBHD          5 mm QNP 1H
PULPROG                 zgdc30
TD                      131072
SOLVENT                 CDCl3
NS                         121
DS                           0
SWH                  25125.629 Hz
FIDRES               0.191693 Hz
AQ                   2.6083827 sec
RG                      9195.2
DW                   19.900 usec
DE                    4.50 usec
TE                      300.0 K
D1                   3.00000000 sec
d11                  0.03000000 sec
================ CHANNEL f1 ================
NUC1                       13C
P1                        5.80 usec
PL1                      -6.00 dB
SF01                 100.6231263 MHz
================ CHANNEL f2 ================
CPDPRG2                 waltz16
NUC2                         1H
PCPD2                    71.00 usec
PL2                      120.00 dB
PL12                      17.00 dB
SF02                 400.1322007 MHz
F2 - Processing parameters
SI                          65536
SF                   100.6128051 MHz
WDW                            EM
SSB                             0
LB                       0.70 Hz
GB                              0
PC                           1.00
1D NMR plot parameters
CX                       19.50 cm
F1P                     160.000 ppm
F1                     16098.05 Hz
F2P                     100.000 ppm
F2                     10061.28 Hz
PPMCM                  3.07692 ppm/cm
HZCM                 309.57788 Hz/cm
```



Ms spectrum of

2-(2-Methoxyphenyl)-1-methyl-3-(diphenylphosphino)-1*H*-indole

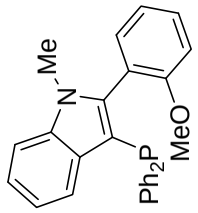


IR spectrum of

2-(2-Methoxyphenyl)-1-methyl-3-(diphenylphosphino)-1*H*-indole

HRMs spectrum of

2-(2-Methoxyphenyl)-1-methyl-3-(diphenylphosphino)-1*H*-indole



Elemental Composition Report

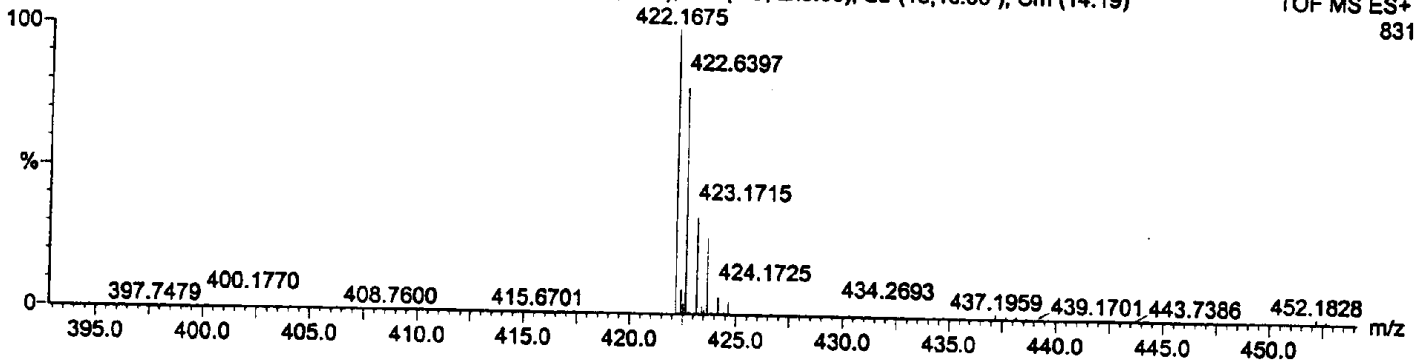
Single Mass Analysis

Tolerance = 100.0 PPM / DBE: min = -1.5, max = 60.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
16 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-28 H: 0-1000 N: 0-1 O: 0-1 P: 0-1

So Chau Ming, N-methyl2(2-methoxyphenyl)indole 3-ph2phosphine
HR07_0516_13 14 (0.271) AM (Cen,4, 80.00, Ht,10000.0,0.00,1.00); Sm (SG, 2x3.00); Sb (15,10.00); Cm (14:19)

TOF MS ES+
831



Minimum:				-1.5		
Maximum:		5.0	100.0	60.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
422.1675	422.1674	0.1	0.2	17.5	0.9	C28 H25 N O P

^{31}P NMR of

1-Methyl-2-phenyl-3-(diphenyl phosphino)-1*H*-indole

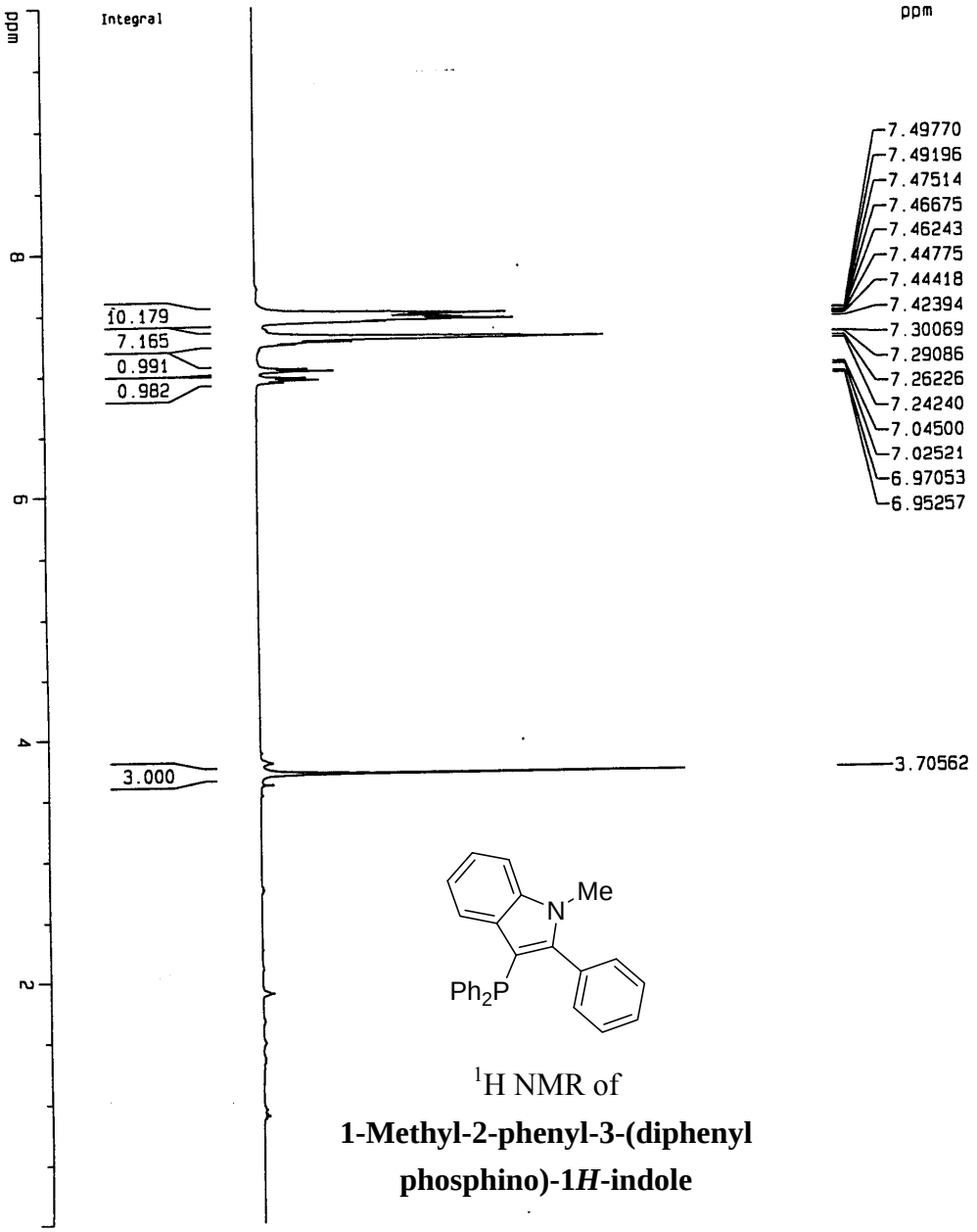
```
F2 - Acquisition Parameters
Date_              20080910
Time                  15.32
INSTRUM             dpx400
PROBHD   5 mm BNP 1H
PULPROG            zgdc30
TD                  65536
SOLVENT             CDCl3
NS                     13
DS                      0
SWH              48661.801 Hz
FIDRES               0.742520 Hz
AQ                0.6734324 sec
RG                   11585.2
DW                  10.275 usec
DE                   4.50 usec
TE                  300.0 K
D1                1.00000000 sec
d11               0.03000000 sec

========== CHANNEL f1 ==========
NUC1                    31P
P1                    7.20 usec
PL1                  -5.00 dB
SF01           161.9851115 MHz

========== CHANNEL f2 ==========
CPDPRG2             waltz16
NUC2                    1H
PCPD2                71.00 usec
PL2                  120.00 dB
PL12                 17.00 dB
SF02           400.1324008 MHz

F2 - Processing parameters
SI                     32768
SF             161.9755831 MHz
WDW                    EM
SSB                     0
LB                   3.00 Hz
GB                      0
PC                    1.40

1D NMR plot parameters
CX                   20.00 cm
F1P                200.000 ppm
F1               32395.12 Hz
F2P                -80.000 ppm
F2               -12958.05 Hz
PPMCM              14.00000 ppm/cm
HZCM           2267.65796 Hz/cm
```



^{1}H NMR of

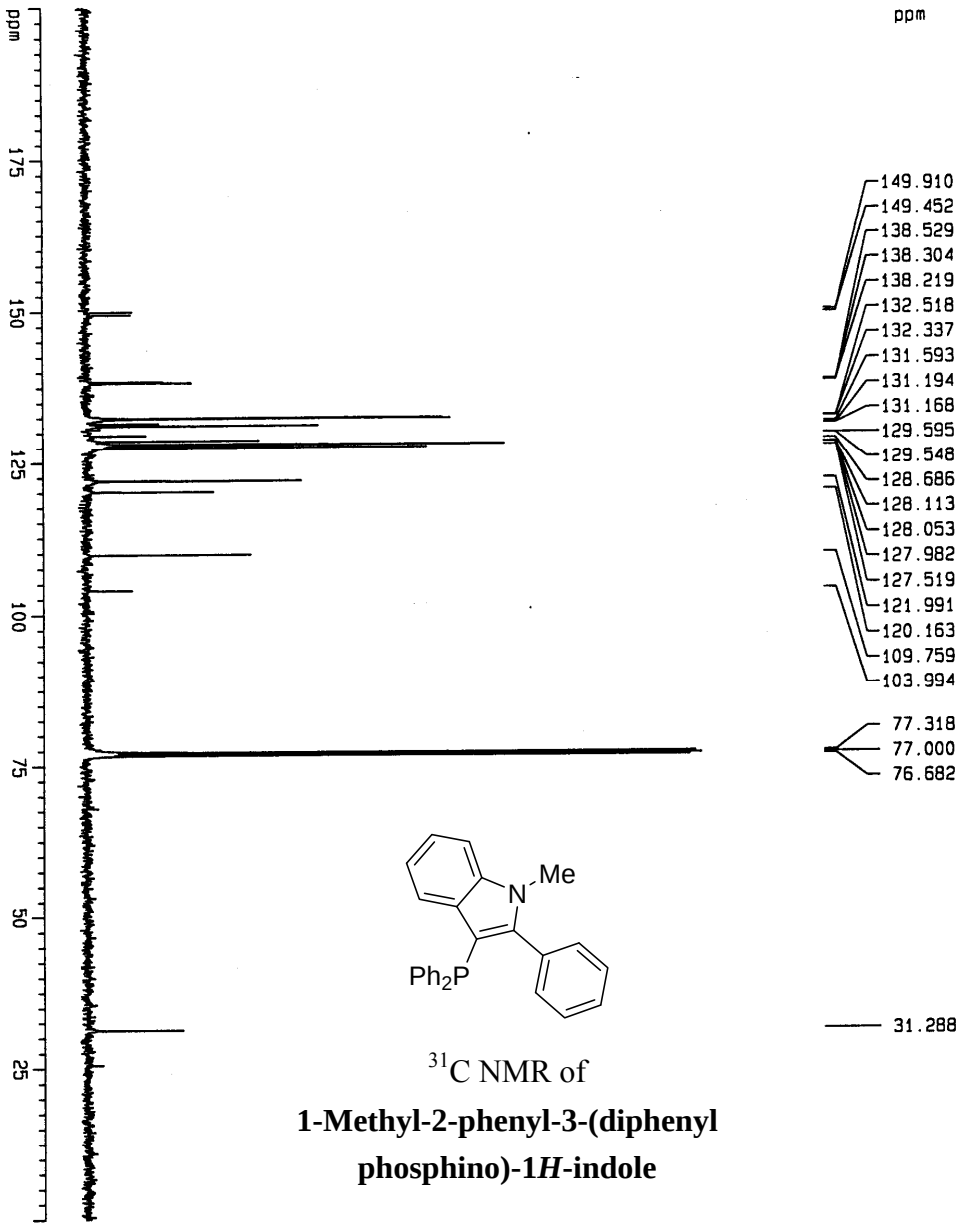
1-Methyl-2-phenyl-3-(diphenyl phosphino)-1*H*-indole

```
F2 - Acquisition Parameters
Date_              20080910
Time                  15.34
INSTRUM             dpx400
PROBHD   5 mm QNP  1H
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     0
SWH              5995.204 Hz
FIDRES           0.182959 Hz
AQ               2.7329011 sec
RG                   128
DW                83.400 usec
DE                 4.50 usec
TE                300.0 K
D1               1.00000000 sec

======== CHANNEL f1 ========
NUC1                1H
P1                9.50 usec
PL1               -6.00 dB
SFO1         400.1320098 MHz

F2 - Processing parameters
SI                 16384
SF           400.1300092 MHz
WDW                   EM
SSB                    0
LB                0.40 Hz
GB                     0
PC                  1.00

1D NMR plot parameters
CX                 19.63 cm
F1P               10.000 ppm
F1              4001.30 Hz
F2P               0.000 ppm
F2                 0.00 Hz
PPMCM          0.50931 ppm/cm
HZCM         203.79143 Hz/cm
```



^{31}C NMR of

1-Methyl-2-phenyl-3-(diphenyl phosphino)-1*H*-indole

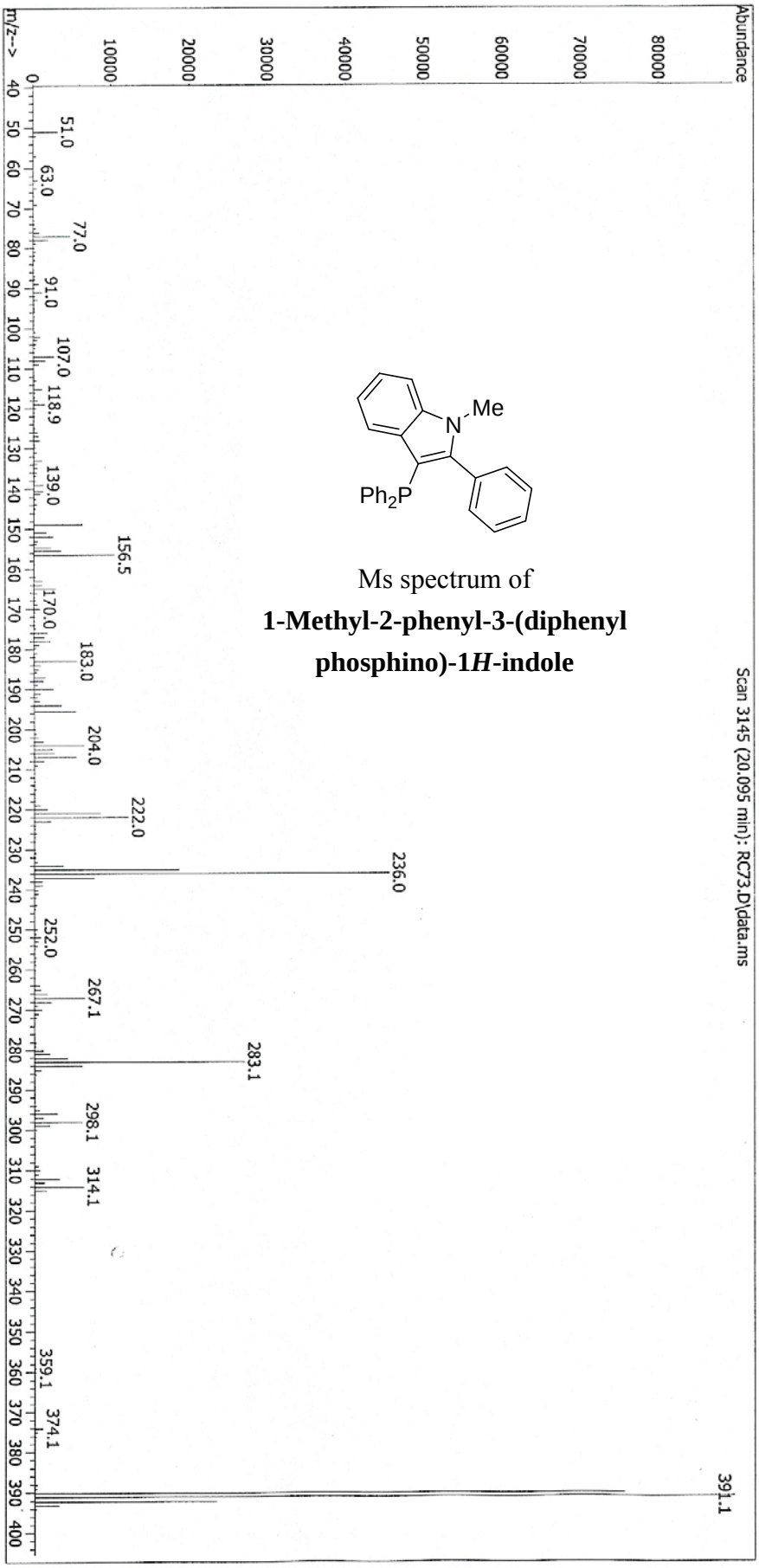
```
Date_                20080910
Time                     15.38
INSTRUM                dpx400
PROBHD      5 mm QNP  1H
PULPROG                zgdc30
TD                     131072
SOLVENT                CDCl3
NS                        248
DS                          0
SWH                27624.309 Hz
FIDRES             0.210757 Hz
AQ                 2.3724532 sec
RG                      7298.2
DW                  18.100 usec
DE                   4.50 usec
TE                     300.0 K
D1                 3.00000000 sec
d11                0.03000000 sec

======== CHANNEL f1 ========
NUC1                       13C
P1                        5.80 usec
PL1                      -6.00 dB
SFO1              100.6231263 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                   71.00 usec
PL2                    120.00 dB
PL12                    17.00 dB
SFO2              400.1326008 MHz

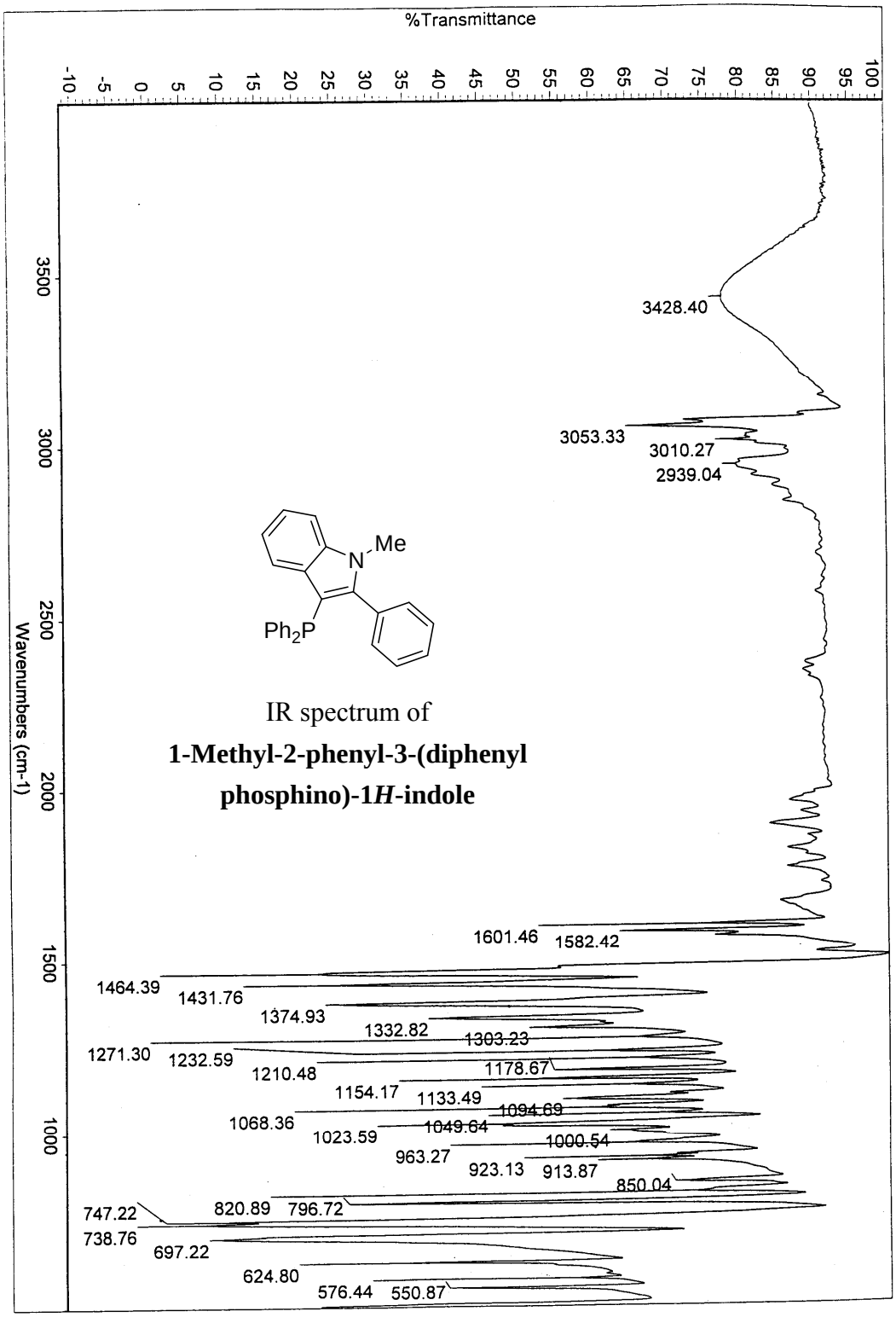
F2 - Processing parameters
SI                        65536
SF                100.6127792 MHz
WDW                          EM
SSB                           0
LB                         3.00 Hz
GB                            0
PC                         1.00

1D NMR plot parameters
CX                        19.50 cm
F1P                     200.000 ppm
F1                    20122.55 Hz
F2P                    -0.000 ppm
F2                     -0.00 Hz
PPMCM                 10.25641 ppm/cm
HZCM                1031.92590 Hz/cm
```



Ms spectrum of

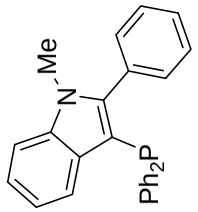
1-Methyl-2-phenyl-3-(diphenyl phosphino)-1*H*-indole



IR spectrum of

1-Methyl-2-phenyl-3-(diphenyl phosphino)-1*H*-indole

HRMs spectrum of **1-Methyl-2-phenyl-3-(diphenylphosphino)-1*H*-indole**



Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 60.0

Selected filters: None

Monoisotopic Mass, Even Electron Ions

29 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

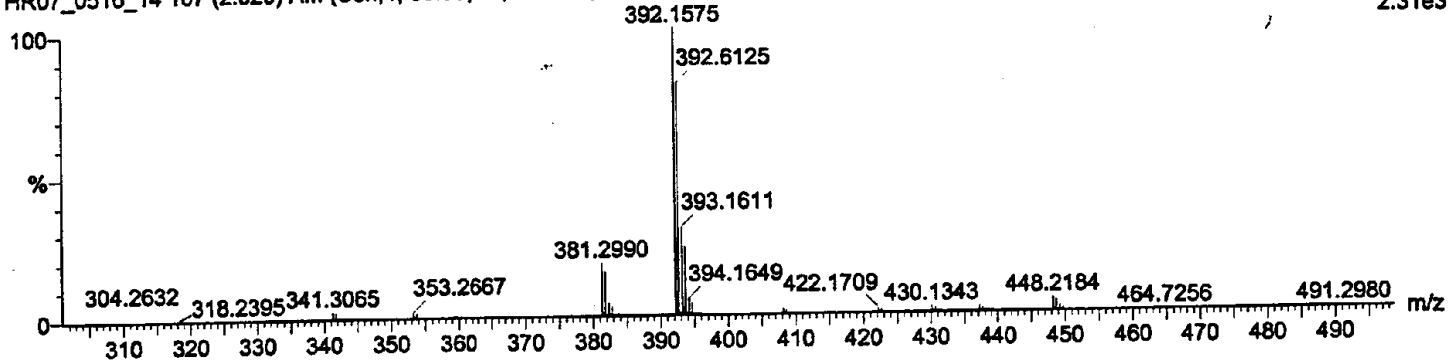
C: 0-28 H: 0-1000 N: 0-1 O: 0-1 P: 0-1

So Chau Ming, N-methyl 2-phenlindole 3-ph2phosphine

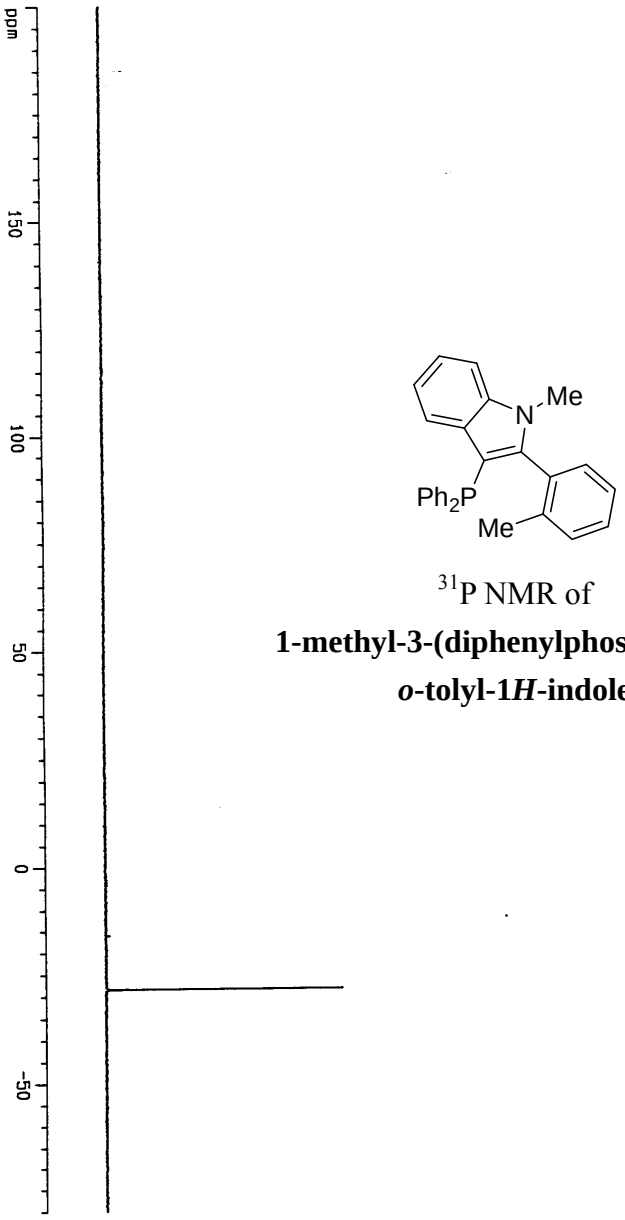
HR07_0516_14 107 (2.020) AM (Cen,4, 80.00, Ht,10000.0,0.00,1.00); Sm (SG, 2x3.00); Sb (15,10.00); Cm (103:135)

TOF MS ES+

2.31e3



Minimum:				-1.5		
Maximum:		5.0	5.0	60.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
392.1575	392.1568	0.7	1.8	17.5	1.4	C27 H23 N P



^{31}P NMR of

1-methyl-3-(diphenylphosphino)-2-*o*-tolyl-1*H*-indole


```
Current Data Parameters
NAME                  PCPindole
EXPNO                       114
PROCNO                        1

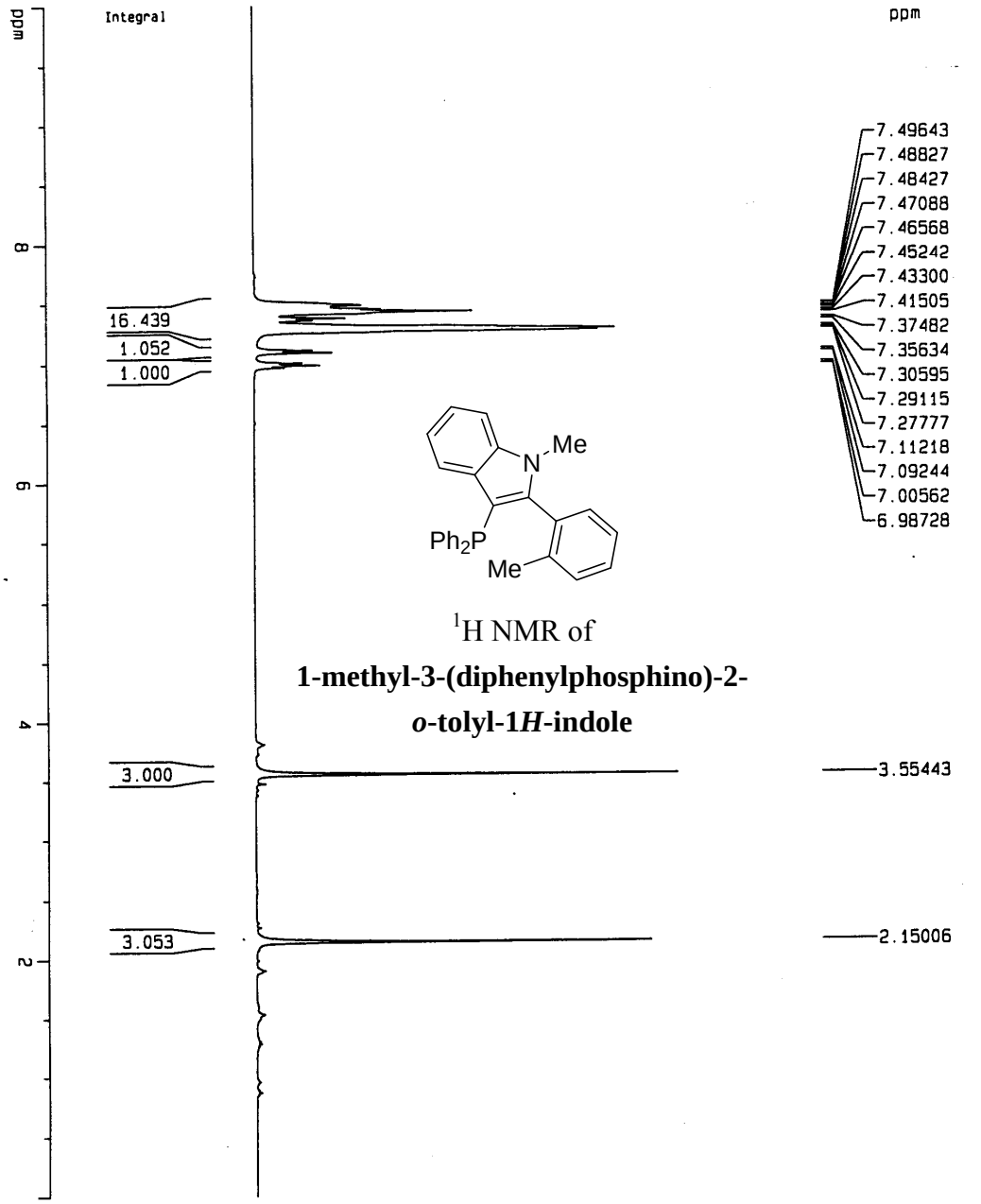
F2 - Acquisition Parameters
Date_              20080916
Time                   11.07
INSTRUM                dpx400
PROBHD     5 mm QNP 1H
PULPROG                zgdc30
TD                     65536
SOLVENT                CDCl3
NS                         7
DS                         0
SWH                48661.801 Hz
FIDRES             0.742520 Hz
AQ                 0.6734324 sec
RG                     11585.2
DW                    10.275 usec
DE                     4.50 usec
TE                    300.0 K
D1                 1.00000000 sec
d11                0.03000000 sec

========== CHANNEL f1 ==========
NUC1                      31P
P1                       7.20 usec
PL1                     -5.00 dB
SFO1           161.9851115 MHz

========== CHANNEL f2 ==========
CPDPRG2                waltz16
NUC2                        1H
PCPD2                  71.00 usec
PL2                    120.00 dB
PL12                    17.00 dB
SFO2           400.1324008 MHz

F2 - Processing parameters
SI                         32768
SF             161.9755831 MHz
WDW                           EM
SSB                            0
LB                      3.00 Hz
GB                             0
PC                          1.40

1D NMR plot parameters
CX                      20.00 cm
F1P                   200.000 ppm
F1                  32395.12 Hz
F2P                   -80.000 ppm
F2                  -12958.05 Hz
PPMCM                 14.00000 ppm/cm
HZCM                2267.65796 Hz/cm
```



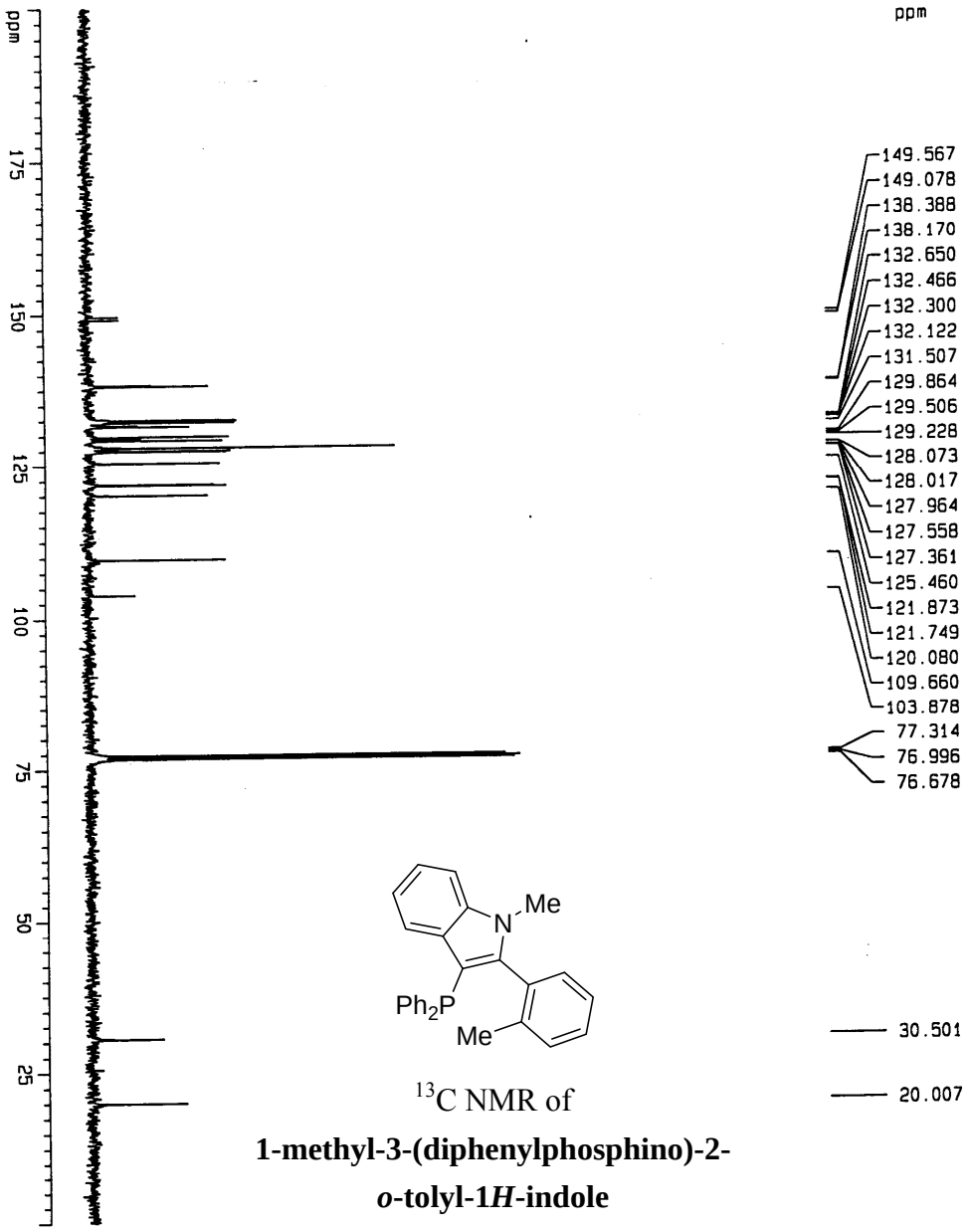
^{1}H NMR of

1-methyl-3-(diphenylphosphino)-2-*o*-tolyl-1*H*-indole

```
F2 - Acquisition Parameters
Date_              20080916
Time                   11.05
INSTRUM              dpx400
PROBHD     5 mm QNP 1H
PULPROG              zg30
TD                  32768
SOLVENT             CDCl3
NS                     16
DS                      0
SWH              5995.204 Hz
FIDRES           0.182959 Hz
AQ               2.7329011 sec
RG                   90.5
DW                 83.400 usec
DE                  4.50 usec
TE                 300.0 K
D1               1.00000000 sec
======== CHANNEL f1 ========
NUC1                   1H
P1                  9.50 usec
PL1                 -6.00 dB
SFO1         400.1320098 MHz

F2 - Processing parameters
SI                    16384
SF           400.1300092 MHz
WDW                    EM
SSB                     0
LB                   0.40 Hz
GB                      0
PC                   1.00

1D NMR plot parameters
CX                   19.63 cm
F1P                 10.000 ppm
F1                4001.30 Hz
F2P                0.000 ppm
F2                   0.00 Hz
PPMCM             0.50931 ppm/cm
HZCM            203.79143 Hz/cm
```



^{13}C NMR of

1-methyl-3-(diphenylphosphino)-2-*o*-tolyl-1*H*-indole

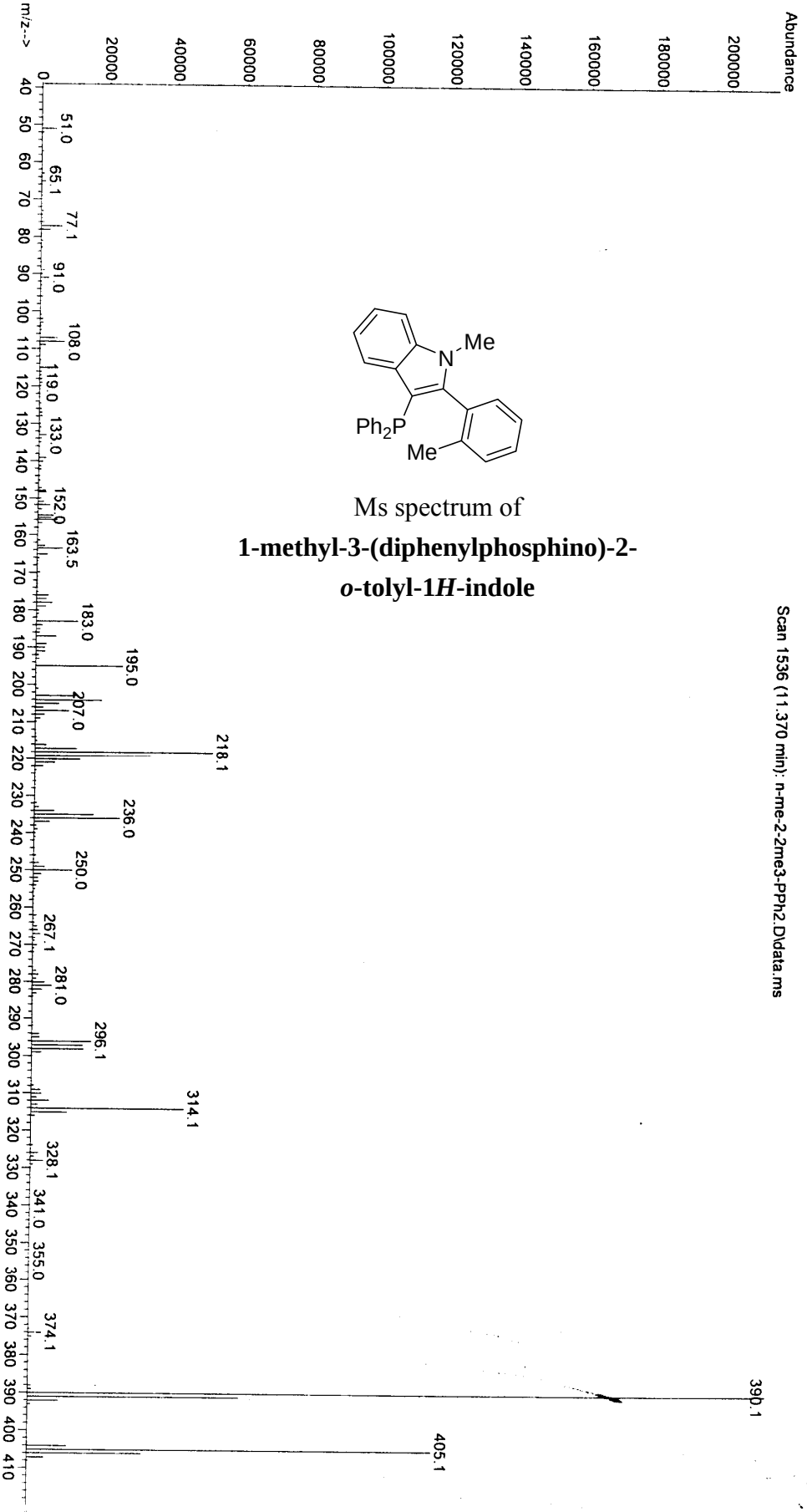
```
Date_                20080916
Time                     11.22
INSTRUM                 dpx400
PROBHD        5 mm QNP 1H
PULPROG                 zgdc30
TD                      131072
SOLVENT                 CDCl3
NS                          99
DS                           0
SWH                  27624.309 Hz
FIDRES                0.210757 Hz
AQ                    2.3724532 sec
RG                       7298.2
DW                       18.100 usec
DE                        4.50 usec
TE                       300.0 K
D1                    3.00000000 sec
d11                   0.03000000 sec

======== CHANNEL f1 ========
NUC1                        13C
P1                         5.80 usec
PL1                       -6.00 dB
SFO1                100.6231263 MHz

======== CHANNEL f2 ========
CPDPRG2                  waltz16
NUC2                          1H
PCPD2                     71.00 usec
PL2                       120.00 dB
PL12                       17.00 dB
SFO2                400.1326008 MHz

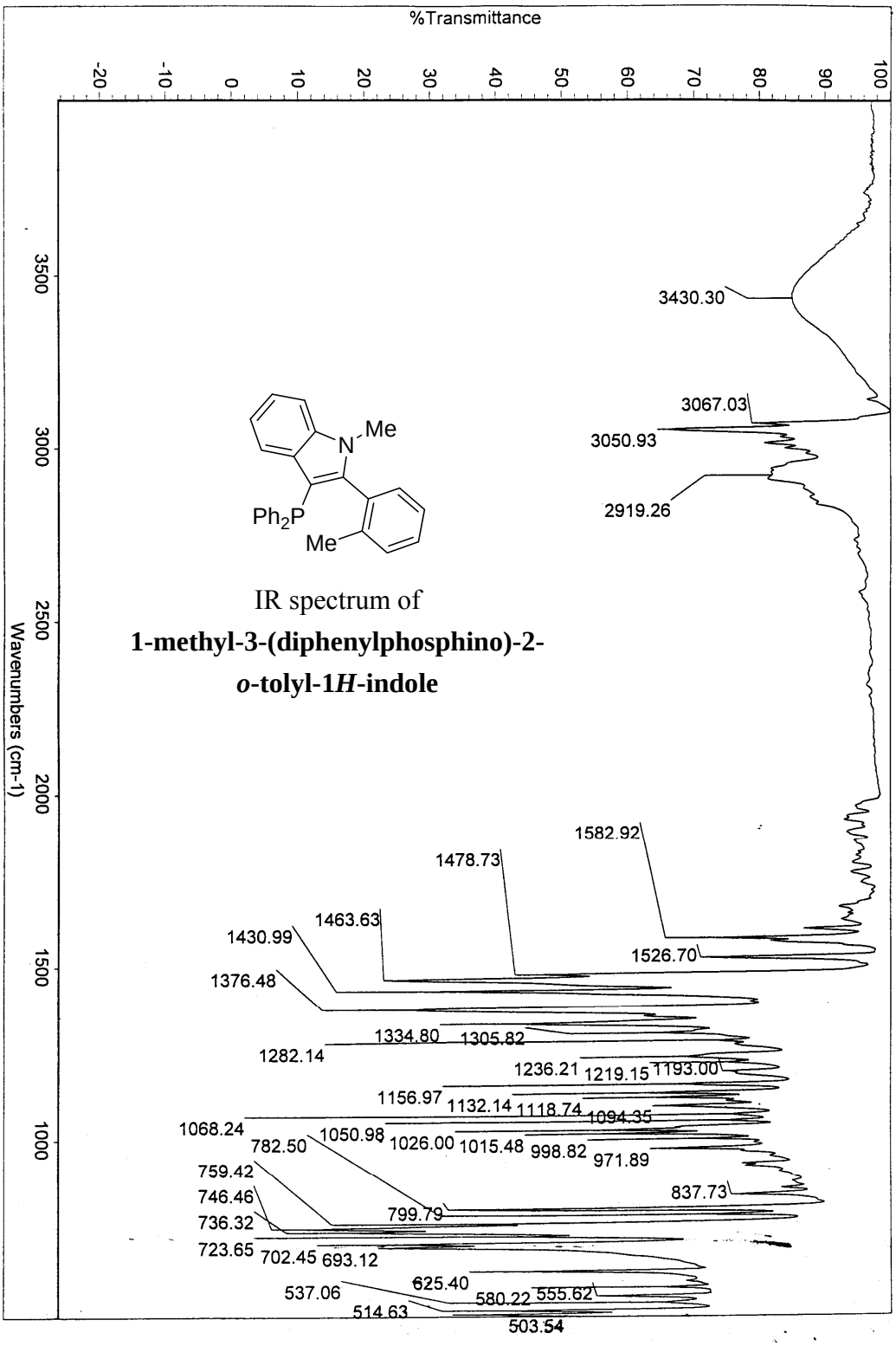
F2 - Processing parameters
SI                         65536
SF                  100.6127814 MHz
MDM                           EM
SSB                            0
LB                          3.00 Hz
GB                             0
PC                          1.00

1D NMR plot parameters
CX                         19.50 cm
F1P                      200.000 ppm
F1                     20122.55 Hz
F2P                      -0.000 ppm
F2                       -0.00 Hz
PPMCM                  10.25641 ppm/cm
HZCM                1031.92590 Hz/cm
```



Ms spectrum of

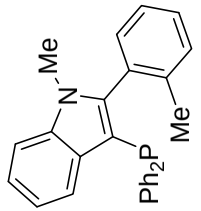
1-methyl-3-(diphenylphosphino)-2-*o*-tolyl-1*H*-indole



IR spectrum of

1-methyl-3-(diphenylphosphino)-2-*o*-tolyl-1*H*-indole

HRMs spectrum of **1-methyl-3-(diphenylphosphino)-2-*o*-tolyl-1*H*-indole**



Elemental Composition Report

Single Mass Analysis

Tolerance = 100.0 PPM / DBE: min = -1.5, max = 60.0

Selected filters: None

Monoisotopic Mass, Even Electron Ions

9 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

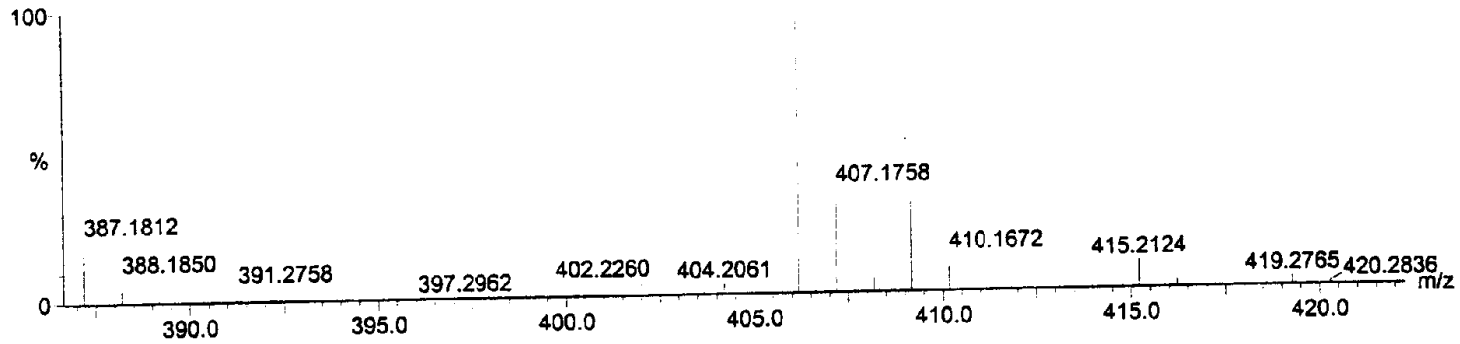
C: 0-28 H: 0-1000 N: 0-1 P: 0-1

So Chau Ming, C28H24NP

HR08_0922_10 28 (0.534) AM (Cen,4, 80.00, Ht,10000.0,0.00,1.00); Sm (SG, 2x3.00); Cm (25:87)

TOF MS ES+

2.99e3



Minimum:				-1.5		
Maximum:		100.0	100.0	60.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
406.1721	406.1725	-0.4	-1.0	17.5	0.0	C28 H25 N P

^{31}P NMR of

1-methyl-2-(naphthalene-1-yl)-3-(diphenylphosphino)-1*H*-indole

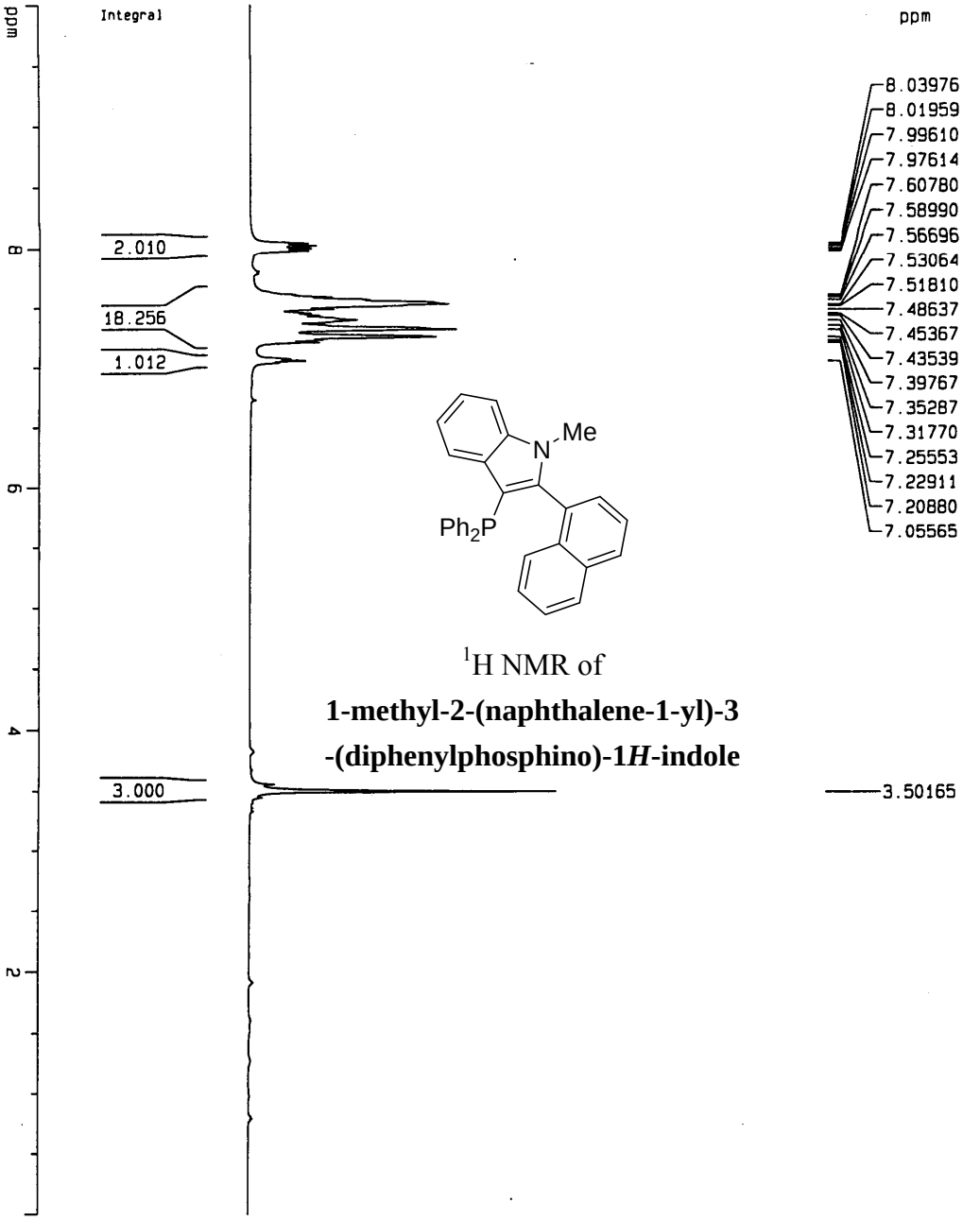
```
F2 - Acquisition Parameters
Date_              20080916
Time                  14.53
INSTRUM             dpx400
PROBHD   5 mm QNP 1H
PULPROG             zgdc30
TD                   65536
SOLVENT              CDCl3
NS                       7
DS                       0
SWH              48661.801 Hz
FIDRES           0.742520 Hz
AQ               0.6734324 sec
RG                  11585.2
DW                 10.275 usec
DE                  4.50 usec
TE                 300.0 K
D1                 1.00000000 sec
d11                0.03000000 sec

============== CHANNEL f1 ==============
NUC1                   31P
P1                  7.20 usec
PL1                -5.00 dB
SFO1         161.9851115 MHz

============== CHANNEL f2 ==============
CPDPRG2             waltz16
NUC2                   1H
PCPD2              71.00 usec
PL2                120.00 dB
PL12                17.00 dB
SFO2         400.1324008 MHz

F2 - Processing parameters
SI                    32768
SF           161.9755831 MHz
WDW                      EM
SSB                       0
LB                 3.00 Hz
GB                        0
PC                 1.40

1D NMR plot parameters
CX                 20.00 cm
F1P              200.000 ppm
F1               32395.12 Hz
F2P              -80.000 ppm
F2               -12958.05 Hz
PPMCM             14.00000 ppm/cm
HZCM         2267.65796 Hz/cm
```



^{1}H NMR of

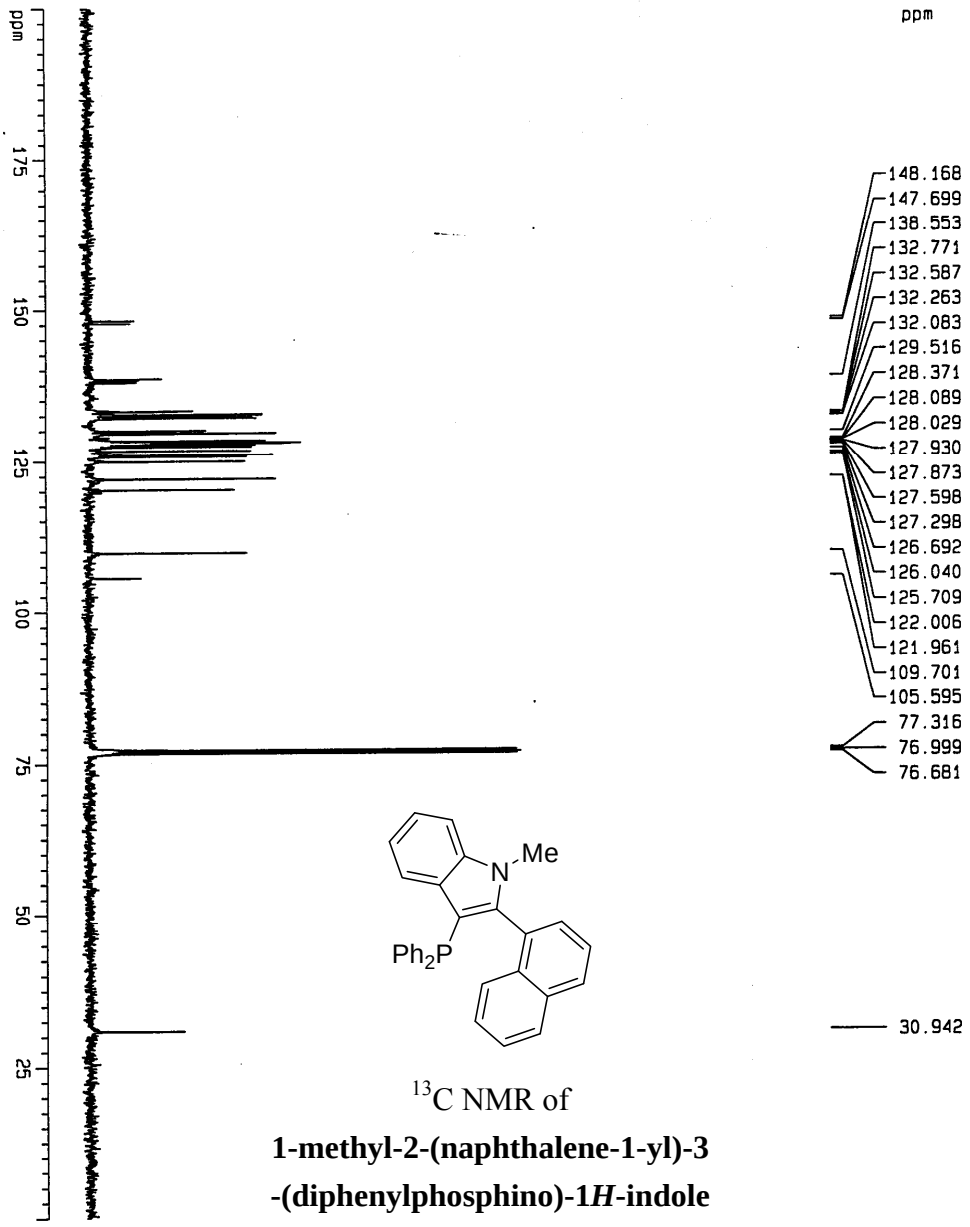
1-methyl-2-(naphthalene-1-yl)-3-(diphenylphosphino)-1*H*-indole

F2 - Acquisition Parameters
Date_ 20080916
Time 18.44
INSTRUM dpx400
PROBHD 5 mm QNP 1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 0
SWH 5995.204 Hz
FIDRES 0.182959 Hz
AQ 2.7329011 sec
RG 71.8
DW 83.400 usec
DE 4.50 usec
TE 300.0 K
D1 1.00000000 sec

========== CHANNEL f1 ==========
NUC1 1H
P1 9.50 usec
PL1 -6.00 dB
SF01 400.1320098 MHz

F2 - Processing parameters
SI 16384
SF 400.1300092 MHz
WDW EM
SSB 0
LB 0.40 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 19.63 cm
F1P 10.000 ppm
F1 4001.30 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.50931 ppm/cm
HZCM 203.79143 Hz/cm

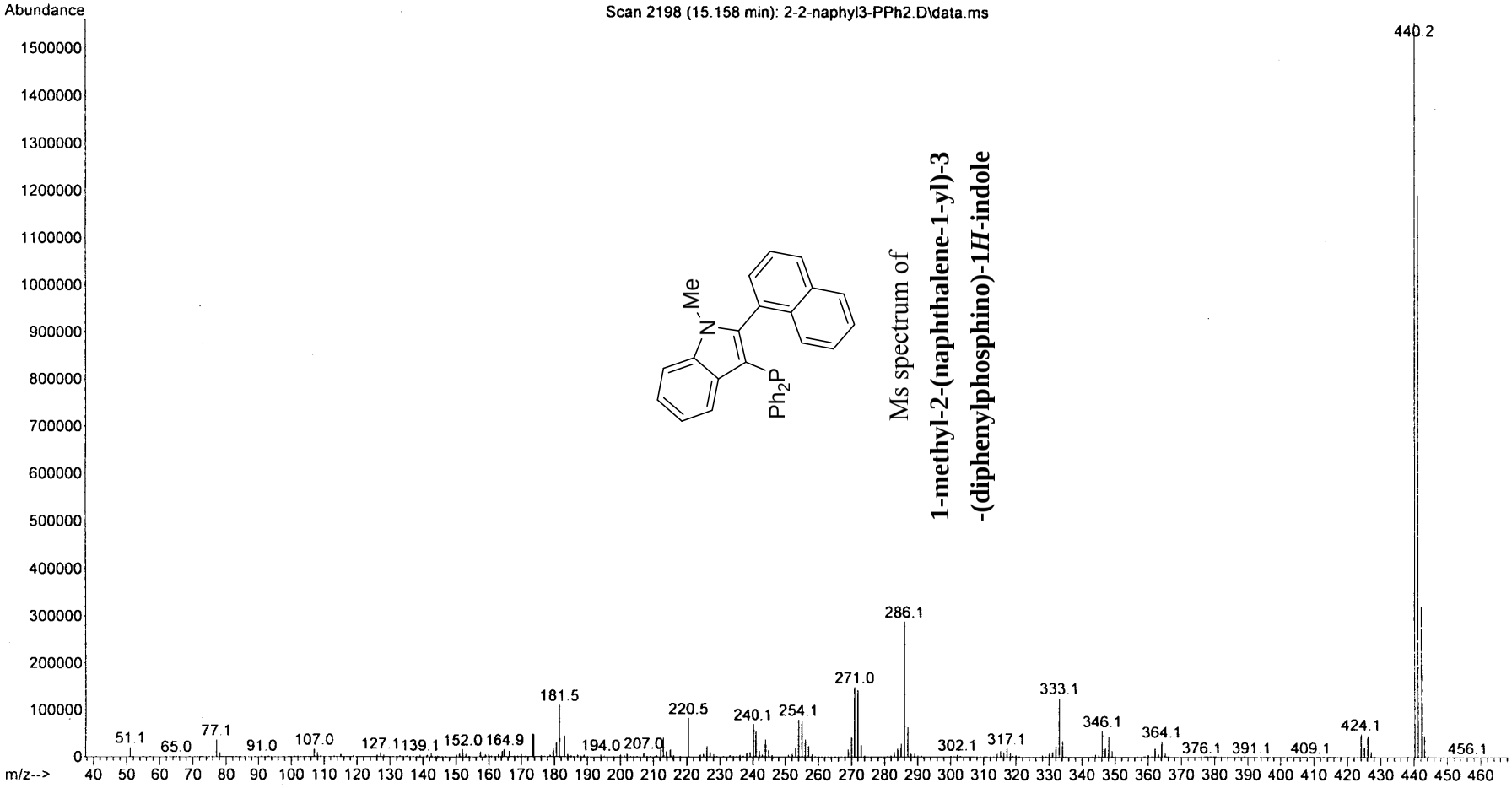


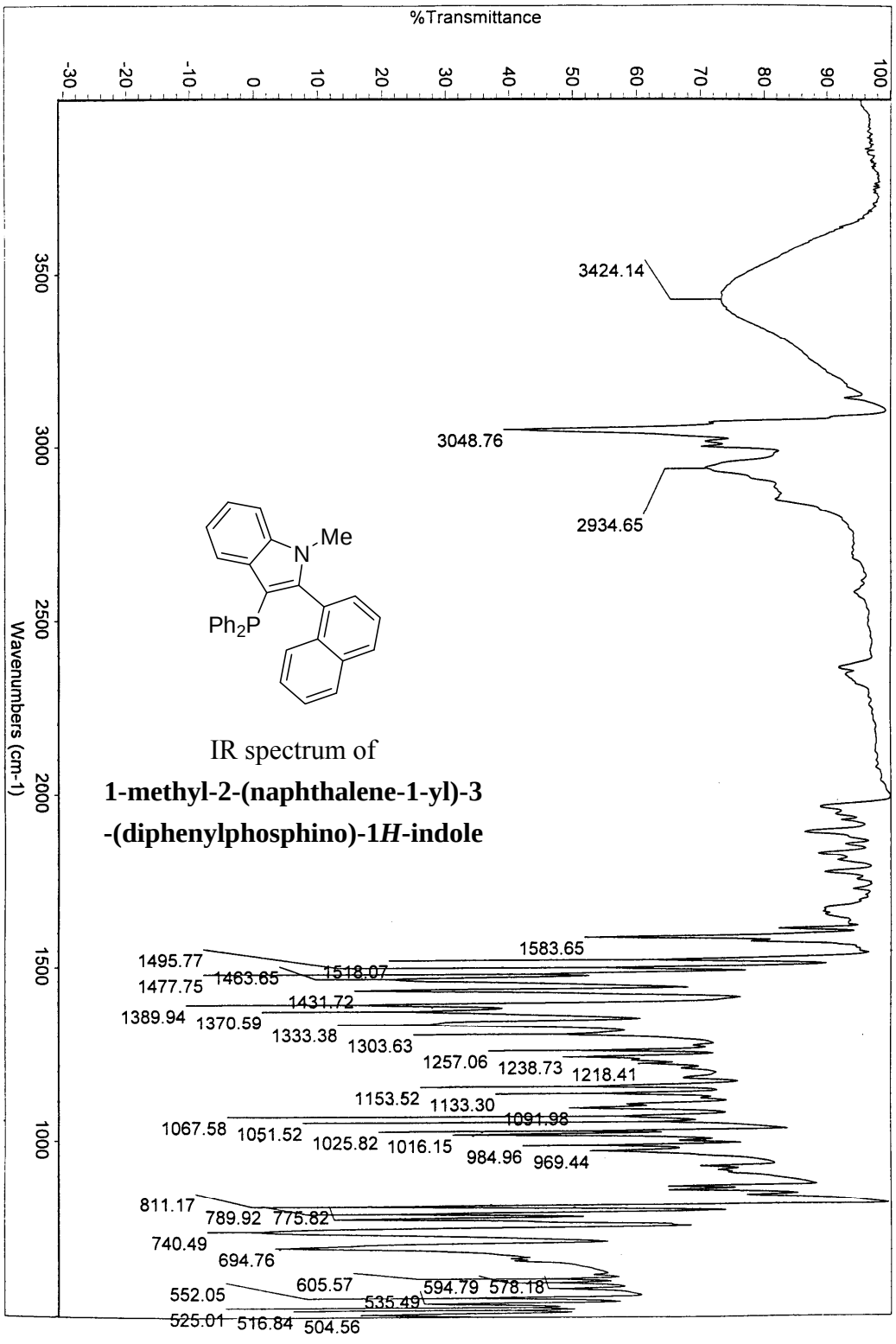
^{13}C NMR of

1-methyl-2-(naphthalene-1-yl)-3-(diphenylphosphino)-1*H*-indole

```
Date_                20080916
Time                    18.48
INSTRUM                 dpx400
PROBHD       5 mm QNP 1H
PULPROG                 zgdc30
TD                      131072
SOLVENT                 CDCl3
NS                         157
DS                           0
SWH                  27624.309 Hz
FIDRES                0.210757 Hz
AQ                    2.3724532 sec
RG                       7298.2
DW                      18.100 usec
DE                       4.50 usec
TE                      300.0 K
D1                    3.00000000 sec
d11                   0.03000000 sec
---------- CHANNEL f1 ----------
NUC1                        13C
P1                         5.80 usec
PL1                       -6.00 dB
SF01           100.6231263 MHz
---------- CHANNEL f2 ----------
CPDPRG2                 waltz16
NUC2                        1H
PCPD2                    71.00 usec
PL2                      120.00 dB
PL12                      17.00 dB
SFO2           400.1326008 MHz
F2 - Processing parameters
SI                         65536
SF             100.6127843 MHz
WDW                           EM
SSB                            0
LB                          3.00 Hz
GB                             0
PC                          1.00
1D NMR plot parameters
CX                         19.50 cm
F1P                      200.000 ppm
F1                     20122.56 Hz
F2P                     -0.000 ppm
F2                      -0.00 Hz
PPMCM                  10.25641 ppm/cm
HZCM           1031.92603 Hz/cm
```

Ms spectrum of **1-methyl-2-(naphthalene-1-yl)-3-(diphenylphosphino)-1*H*-indole**

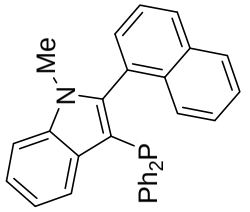




IR spectrum of

1-methyl-2-(naphthalene-1-yl)-3-(diphenylphosphino)-1*H*-indole

HRMs spectrum of **1-methyl-2-(naphthalene-1-yl)-3-(diphenylphosphino)-1*H*-indole**



Elemental Composition Report

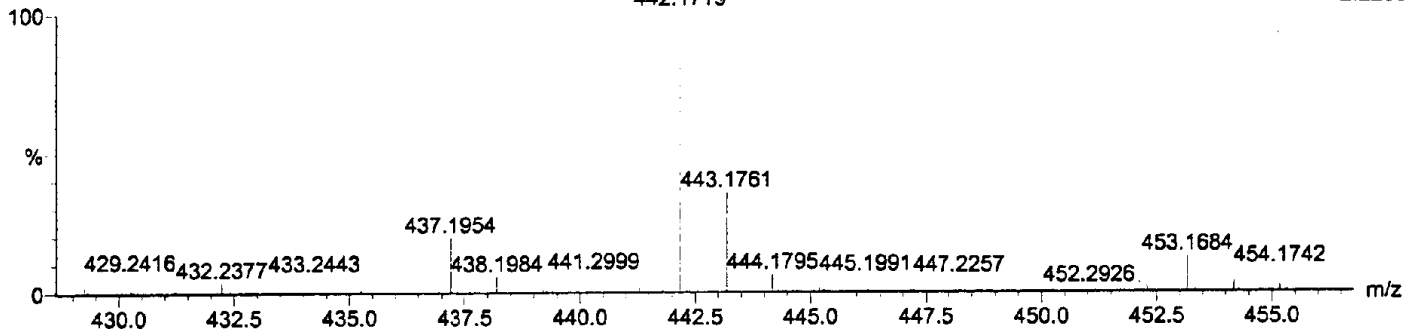
Single Mass Analysis

Tolerance = 10.0 PPM / DBE: min = -1.5, max = 60.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
10 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-31 H: 0-1000 N: 0-1 P: 0-1

So Chau Ming, C31H24NP
HR08_0922_6 19 (0.364) AM (Cen,4, 80.00, Ht,10000.0,0.00,1.00); Sm (SG, 2x3.00); Cm (17:37)

TOF MS ES+
2.22e3



Minimum:				-1.5		
Maximum:		100.0	10.0	60.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
442.1715	442.1725	-1.0	-2.3	20.5	0.1	C31 H25 N P

^{31}P NMR of

1-methyl-2-(naphthalene-1-yl)-3-(dicyclohexylphosphino)-1*H*-indole

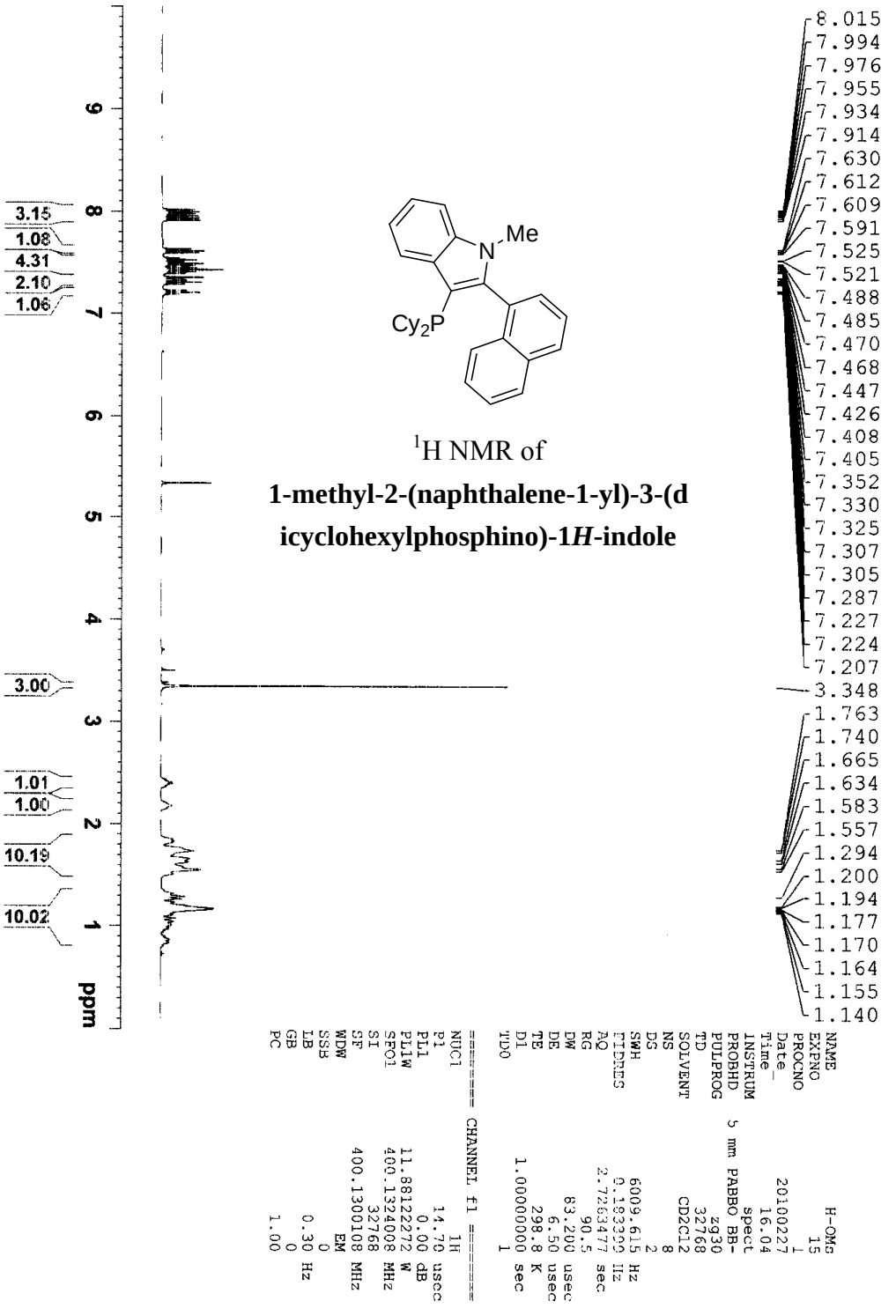
F2 - Acquisition Parameters
Date_ 20070515
Time 20.05
INSTRUM dpx400
PROBHD 5 mm QNP 1H
PULPROG zgdc30
TD 65536
SOLVENT CDCl3
NS 64
DS 0
SWH 49651.801 Hz
FIDRES 0.742520 Hz
AQ 0.6734324 sec
RG 13004
DW 10.275 usec
DE 4.50 usec
TE 300.0 K
D1 1.00000000 sec
d11 0.03000000 sec

========== CHANNEL f1 ==========
NUC1 31P
P1 7.20 usec
PL1 -5.00 dB
SFO1 161.9861115 MHz

========== CHANNEL f2 ==========
CPDPRG2 waltz16
NUC2 1H
PCPD2 71.00 usec
PL2 120.00 dB
PL12 17.00 dB
SFO2 400.1324008 MHz

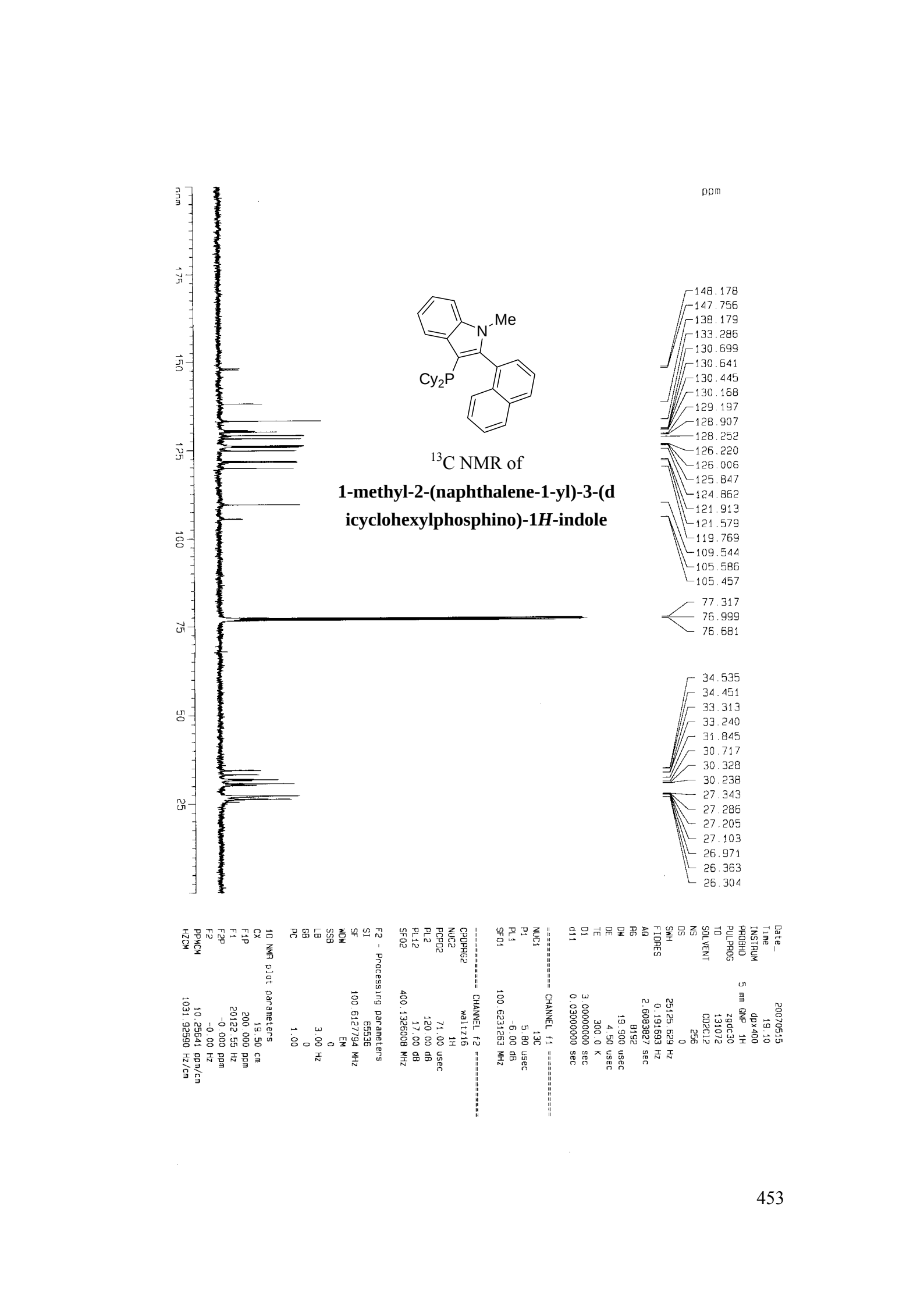
F2 - Processing parameters
SI 32768
SF 161.9755831 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40

1D NMR plot parameters
CX 20.00 cm
F1P 120.000 ppm
F1 19437.07 Hz
F2P -60.000 ppm
F2 -9718.54 Hz
PPMCM 9.00000 ppm/cm
HZCM 1457.78027 Hz/cm



^{1}H NMR of

1-methyl-2-(naphthalene-1-yl)-3-(dicyclohexylphosphino)-1*H*-indole



^{13}C NMR of

1-methyl-2-(naphthalene-1-yl)-3-(dicyclohexylphosphino)-1*H*-indole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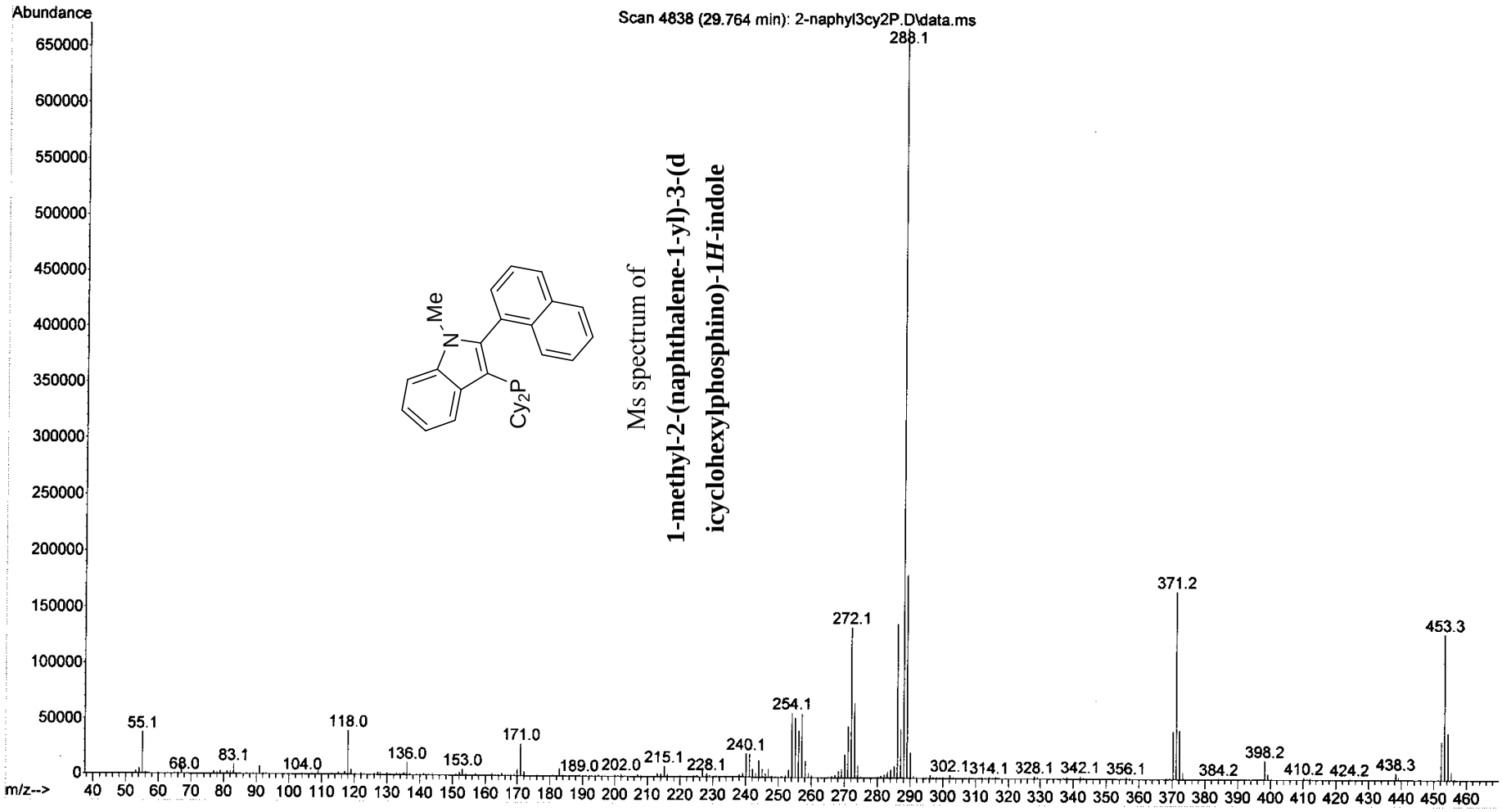
Date_                20070515
Time                    19.10
INSTRUM                 dpx400
PROBHD       5 mm QNP  1H
PULPROG                 zgqc30
TD                      131072
SOLVENT                 CDCl2
NS                      256
DS                      0
SWH                     25125.629 Hz
FIDRES                  0.191693 Hz
AQ                      2.6083827 sec
RG                      8192
DW                      19.900 usec
DE                      4.50 usec
TE                      300.0 K
D1                      3.00000000 sec
d11                     0.03000000 sec

================ CHANNEL f1 ================
NUC1                    13C
P1                      5.80 usec
PL1                     -6.00 dB
SFO1                    100.6231263 MHz

================ CHANNEL f2 ================
CPDPRG2                 waltz16
NUC2                    1H
PCPD2                   71.00 usec
PL2                     120.00 dB
PL12                    17.00 dB
SFO2                    400.1326008 MHz

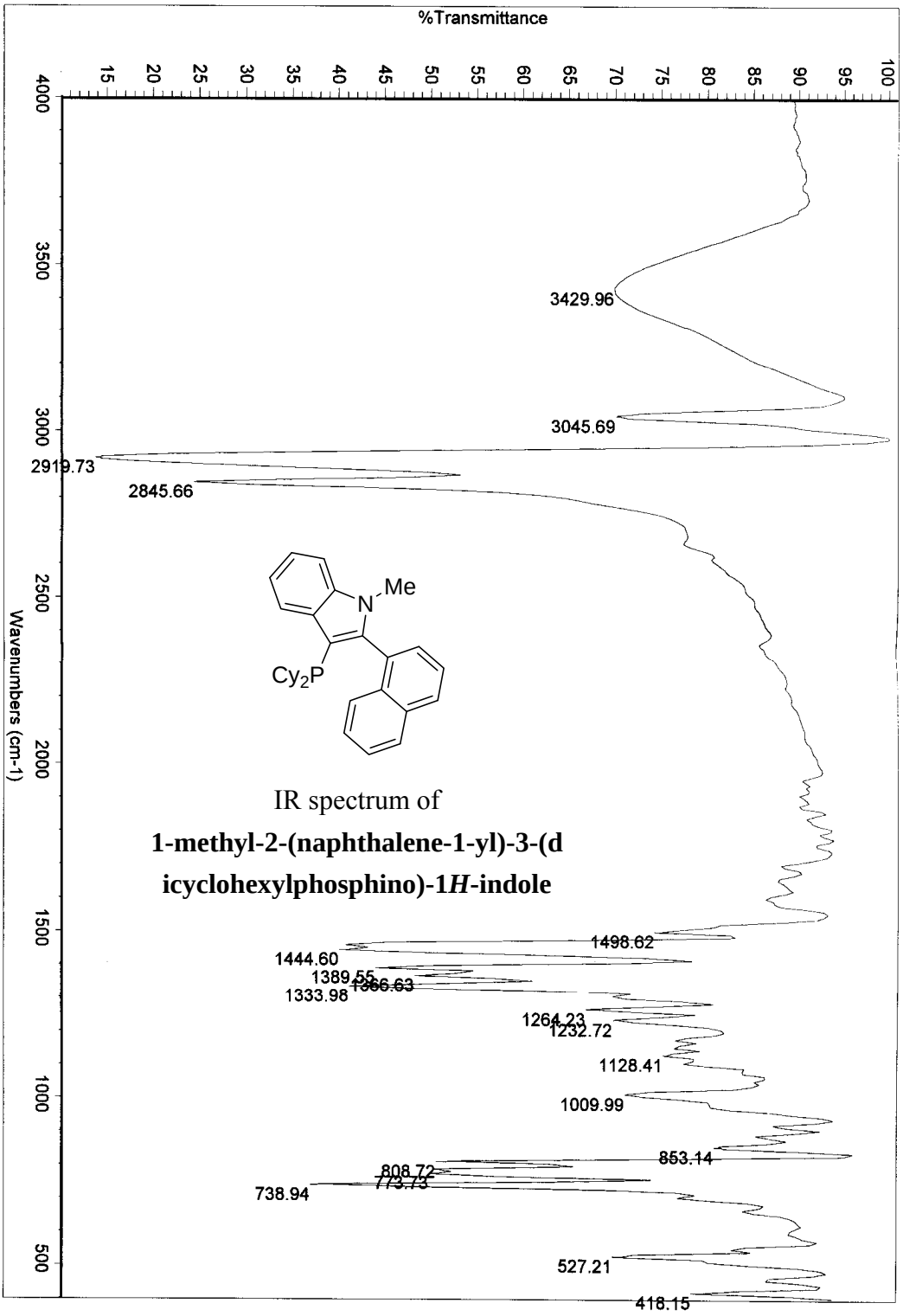
F2 - Processing parameters
SI                      65536
SF                      100.6127794 MHz
WDW                     EM
SSB                     0
LB                      3.00 Hz
GB                      0
PC                      1.00

1D NMR plot parameters
CX                      19.50 cm
F1P                     200.000 ppm
F1                      20122.55 Hz
F2P                     -0.000 ppm
F2                      -0.00 Hz
PPMCM                   10.25641 ppm/cm
HZCM                    1031.92590 Hz/cm
```



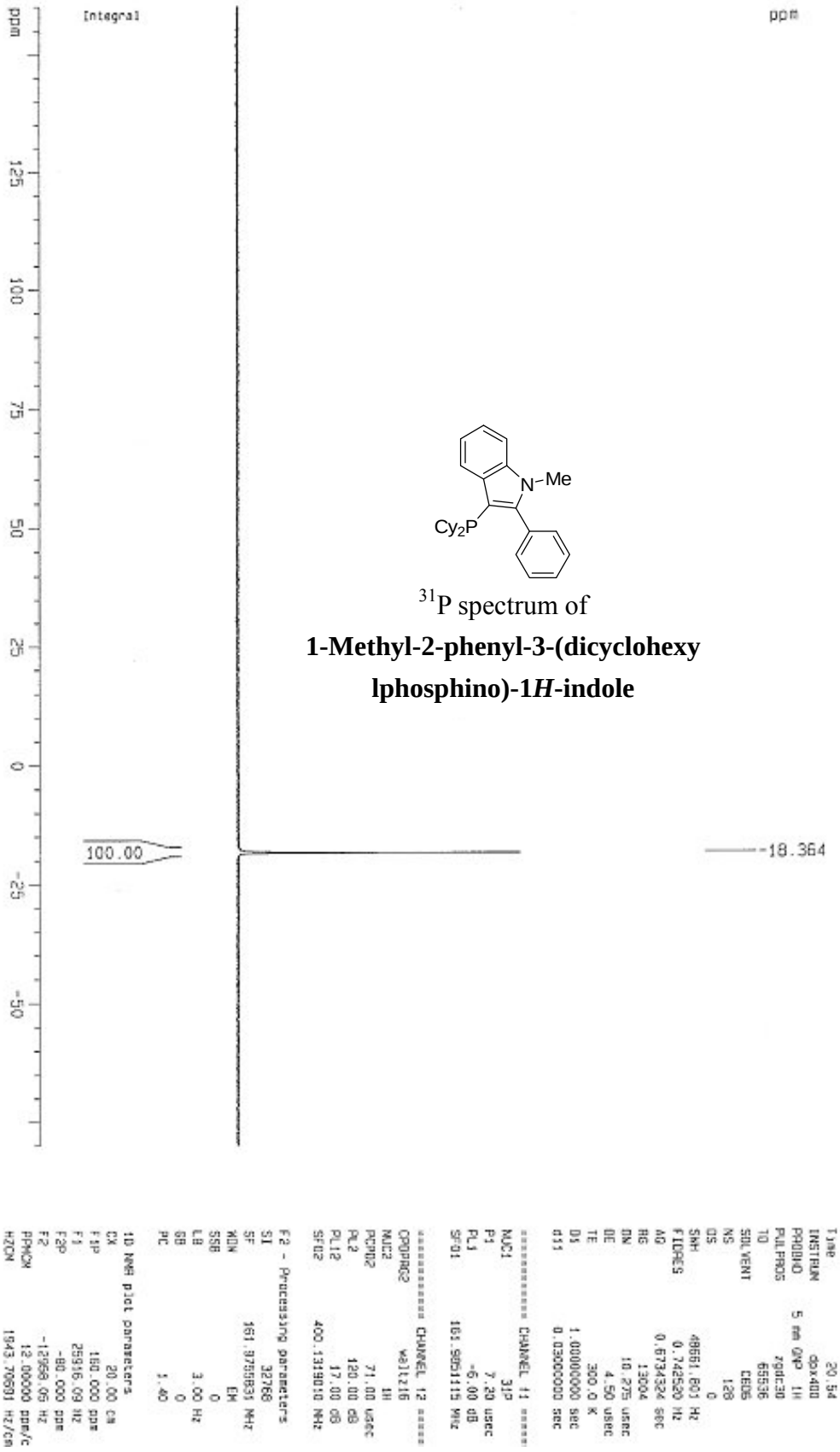
Ms spectrum of

1-methyl-2-(naphthalene-1-yl)-3-(dicyclohexylphosphino)-1*H*-indole



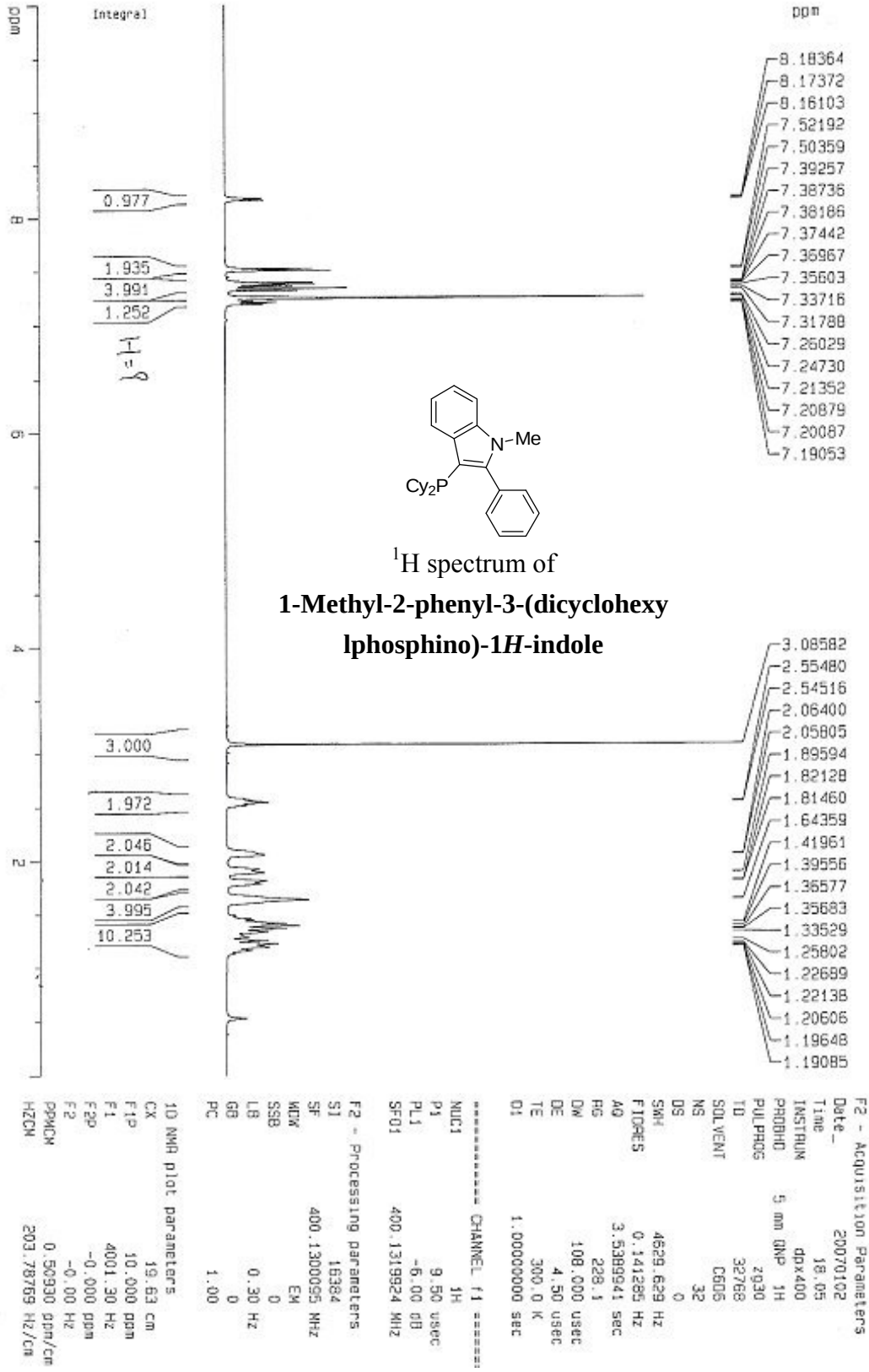
IR spectrum of

1-methyl-2-(naphthalene-1-yl)-3-(dicyclohexylphosphino)-1*H*-indole



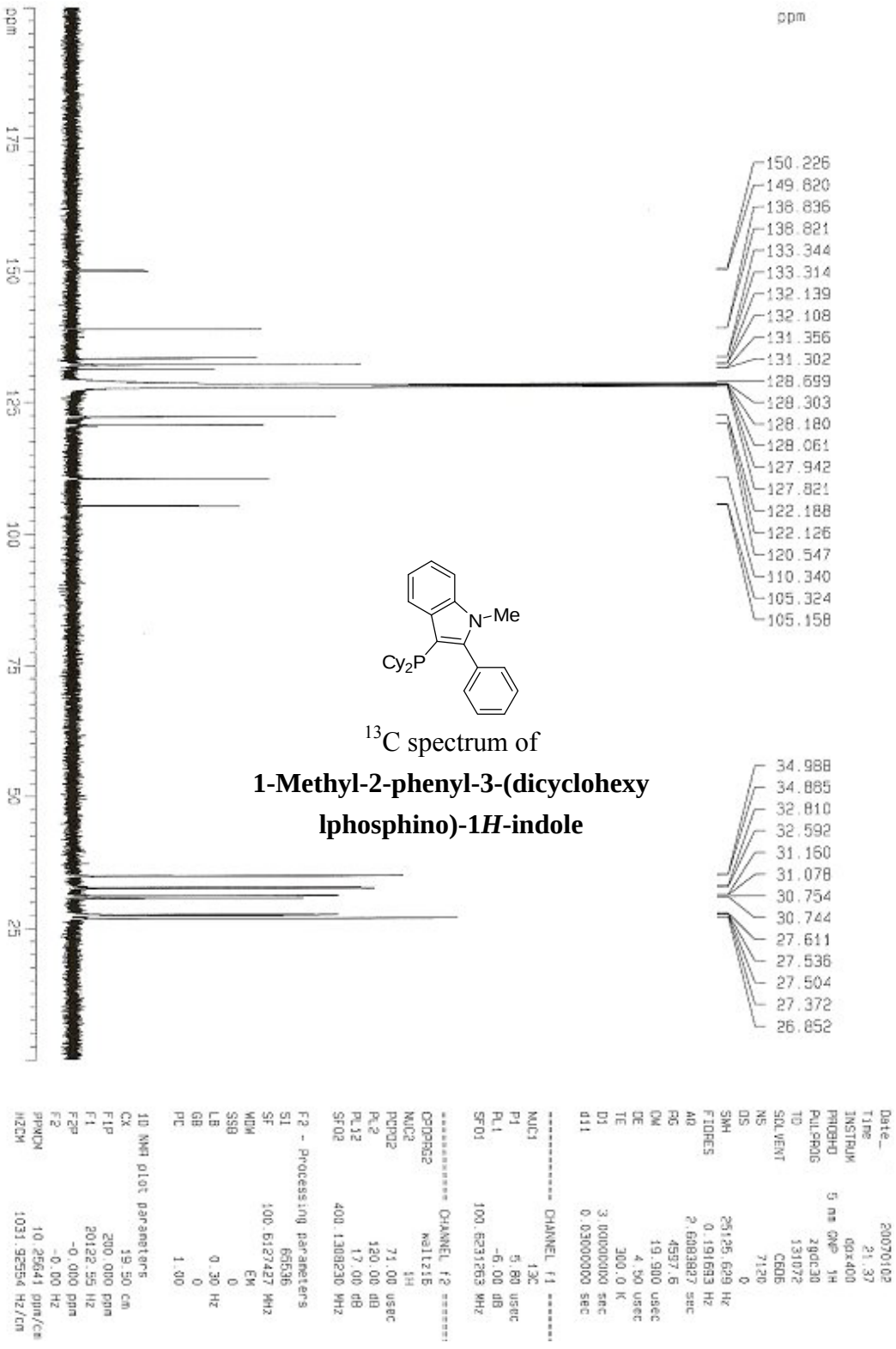
^{31}P spectrum of

1-Methyl-2-phenyl-3-(dicyclohexylphosphino)-1*H*-indole



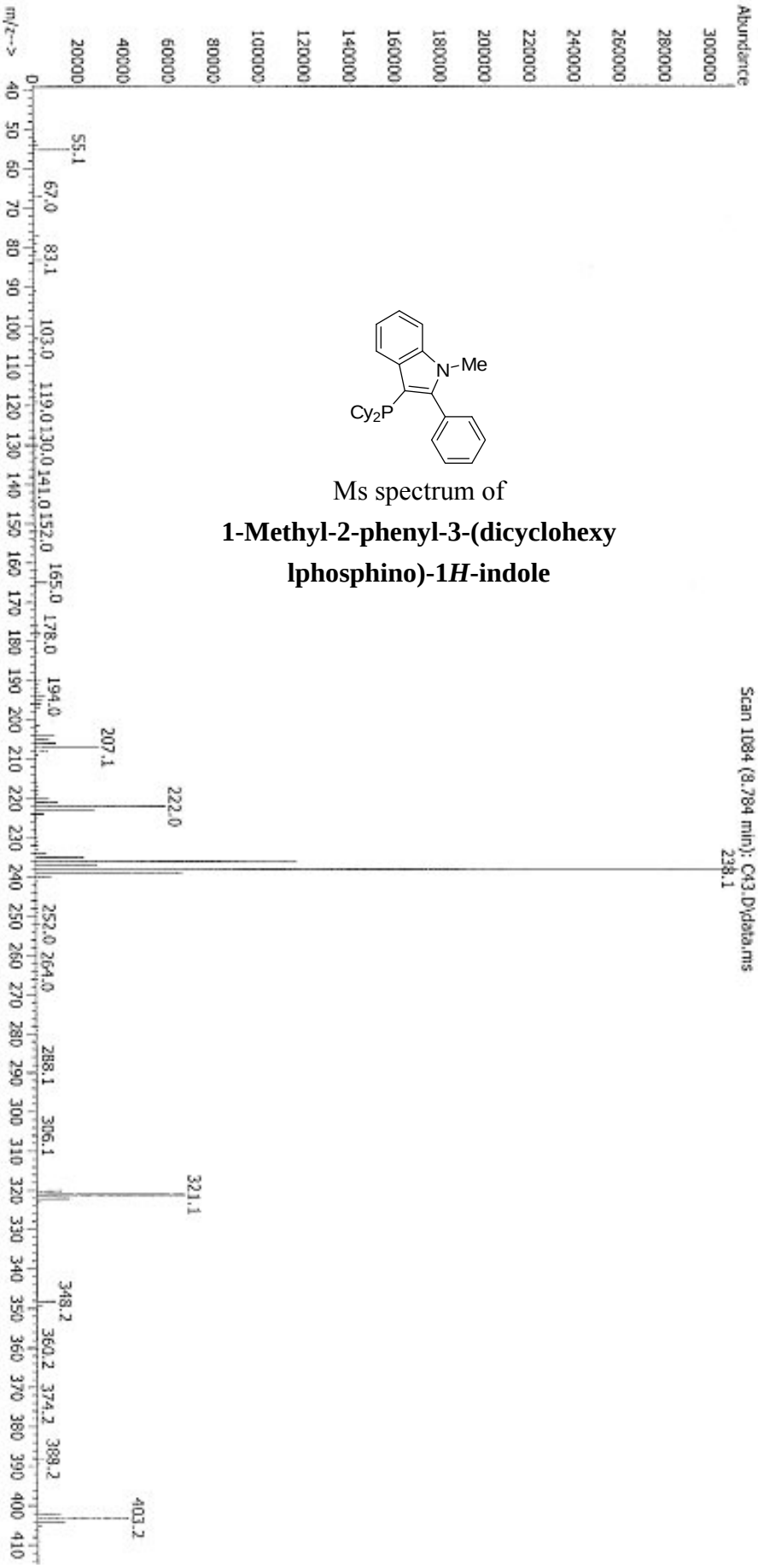
^{1}H spectrum of

1-Methyl-2-phenyl-3-(dicyclohexylphosphino)-1*H*-indole



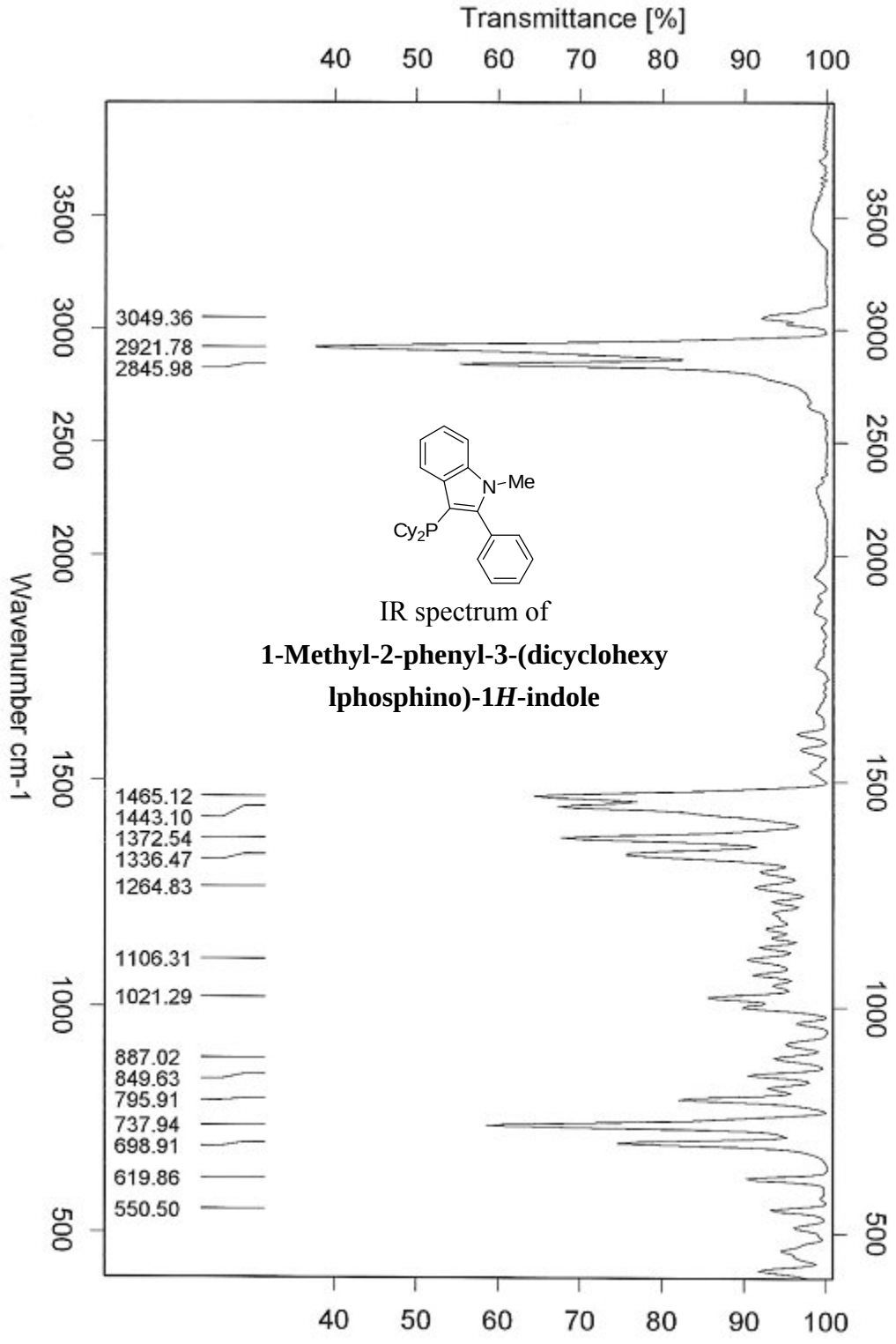
^{13}C spectrum of

1-Methyl-2-phenyl-3-(dicyclohexylphosphino)-1*H*-indole



Ms spectrum of

1-Methyl-2-phenyl-3-(dicyclohexylphosphino)-1*H*-indole



IR spectrum of

1-Methyl-2-phenyl-3-(dicyclohexylphosphino)-1*H*-indole

Elemental Composition Report

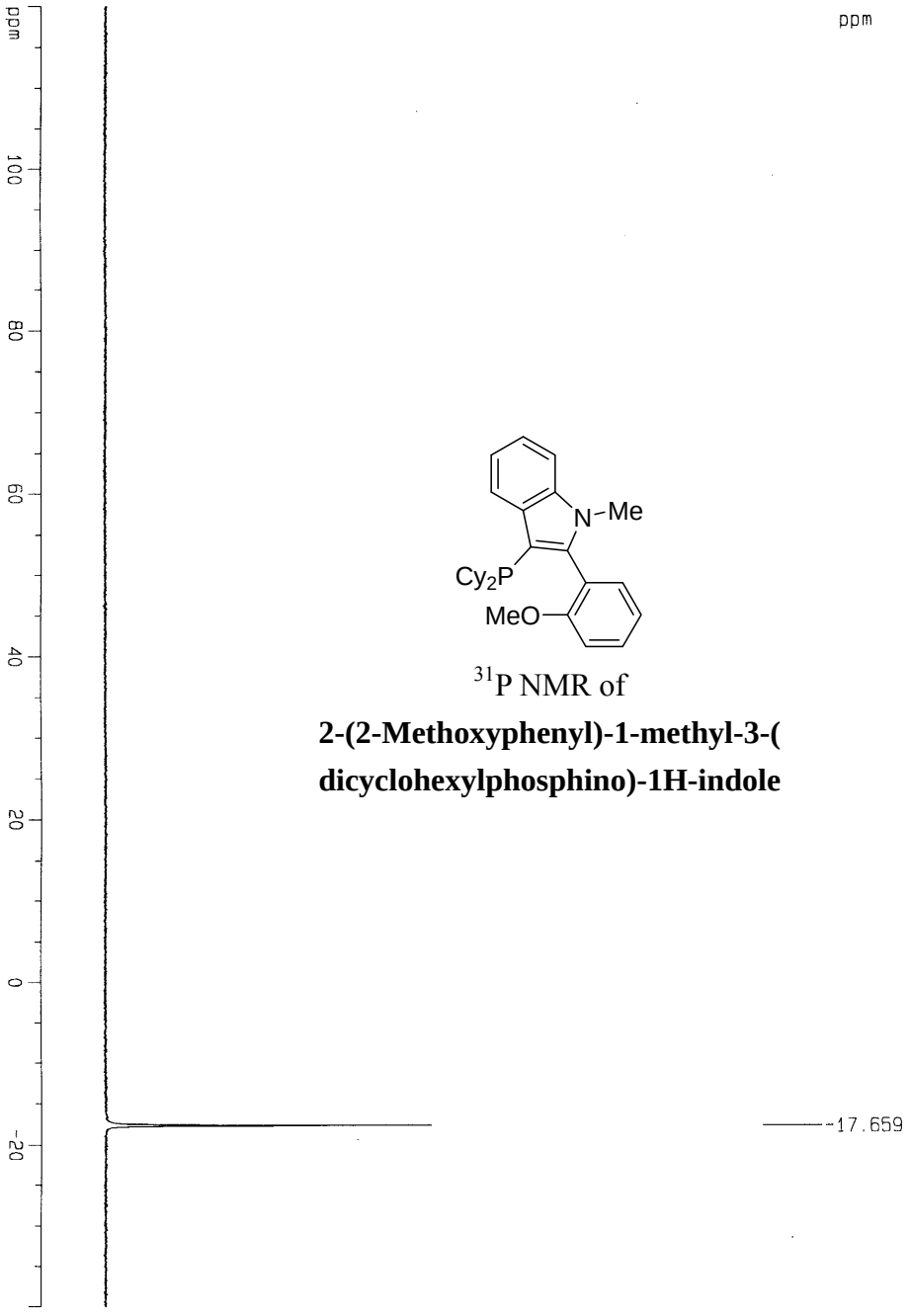
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 60.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
24 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-28 H: 0-1000 N: 0-1 O: 0-1 P: 0-1
So Chau Ming, N-methyl 2-phenylindole 3-cy2Phosphine
HR07_0517_1 14 (0.271) AM (Cen,4, 80.00, Ht,10000.0,0.00,1.00); Sm (SG, 2x3.00); Sb (15,10.00); Cm (13:19)
TOF MS ES+
193

Minimum:			-1.5		
Maximum:		5.0	5.0	60.0	
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
404.2511	404.2507	0.4	1.0	11.5	1.1	C27 H35 N P

HRMs spectrum of
1-Methyl-2-phenyl-3-(dicyclohexylphosphino)-1*H*-indole

Catalyst



^{31}P NMR of

2-(2-Methoxyphenyl)-1-methyl-3-(dicyclohexylphosphino)-1H-indole

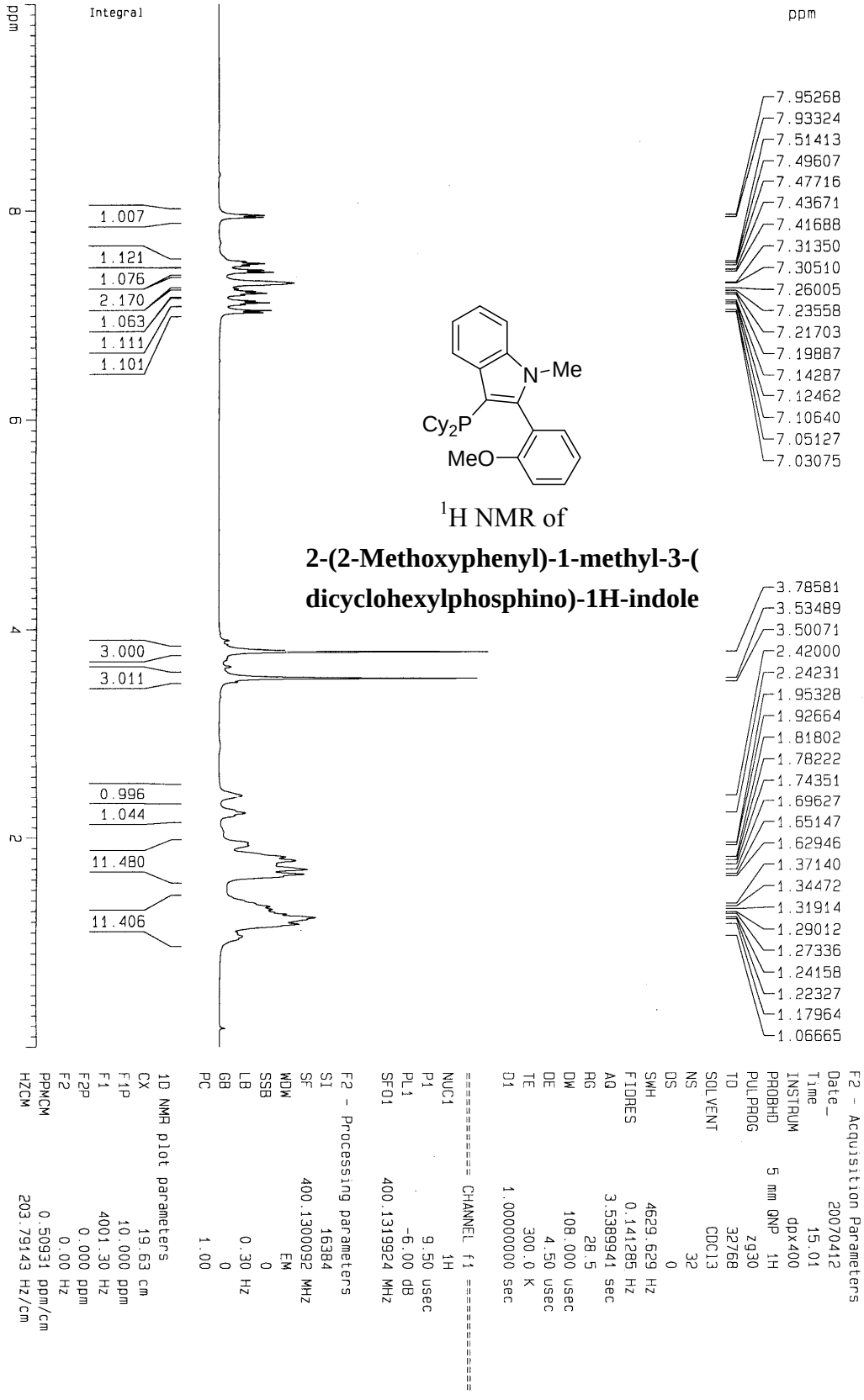
```
F2 - Acquisition Parameters
Date_              20070412
Time               15.51
INSTRLM              dpx400
PROBHC     5 mm QNP 1H
PULPRG               zgdc30
TD                   65536
SOLVENT              C6D6
NS                   64
DS                   0
SWH              48661.801 Hz
FIDRES               0.742520 Hz
AQ               0.6734324 sec
RG                   14596.5
DW                   10.275 usec
DE                   4.50 usec
TE                   300.0 K
D1               1.00000000 sec
d11              0.03000000 sec

============== CHANNEL f1 ==============
NUC1                 31P
P1                   7.20 usec
PL1                  -5.00 dB
SFO1             161.9851115 MHz

============== CHANNEL f2 ==============
CPDPRG2              waltz16
NUC2                 1H
PCPD2                71.00 usec
PL2                  120.00 dB
PL12                 17.00 dB
SFO2             400.1324008 MHz

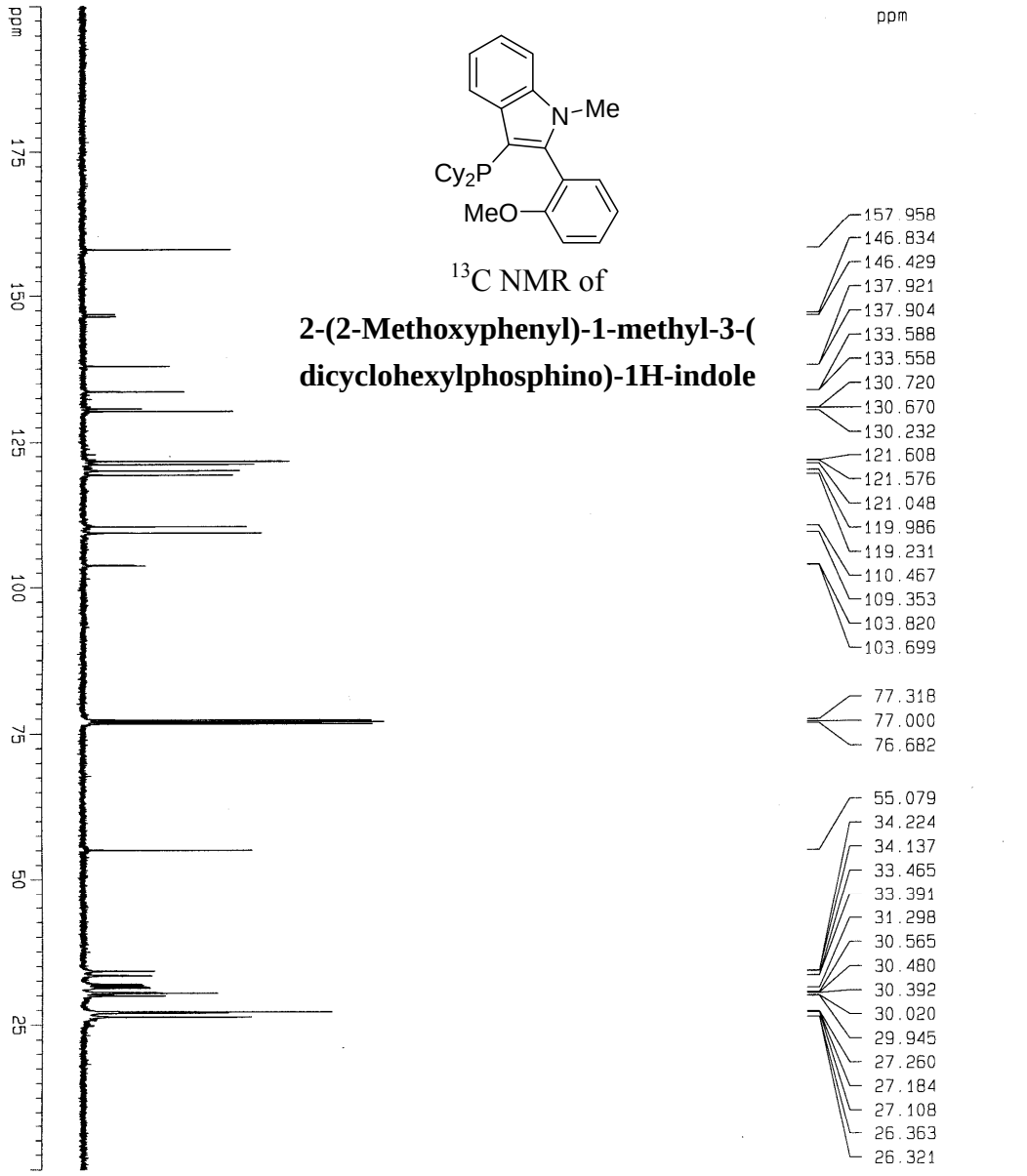
F2 - Processing parameters
SI                   32768
SF               161.9755831 MHz
WDW                  EM
SSB                  0
LB                   3.00 Hz
GB                   0
PC                   1.40

1D NMR plot parameters
CX                   20.00 cm
F1P                  120.000 ppm
F1                   19437.07 Hz
F2P                  -40.000 ppm
F2                   -6479.03 Hz
PPMCM                8.00000 ppm/cm
HZCM             1295.80481 Hz/cm
```



^{1}H NMR of

2-(2-Methoxyphenyl)-1-methyl-3-(dicyclohexylphosphino)-1H-indole



^{13}C NMR of

2-(2-Methoxyphenyl)-1-methyl-3-(dicyclohexylphosphino)-1H-indole

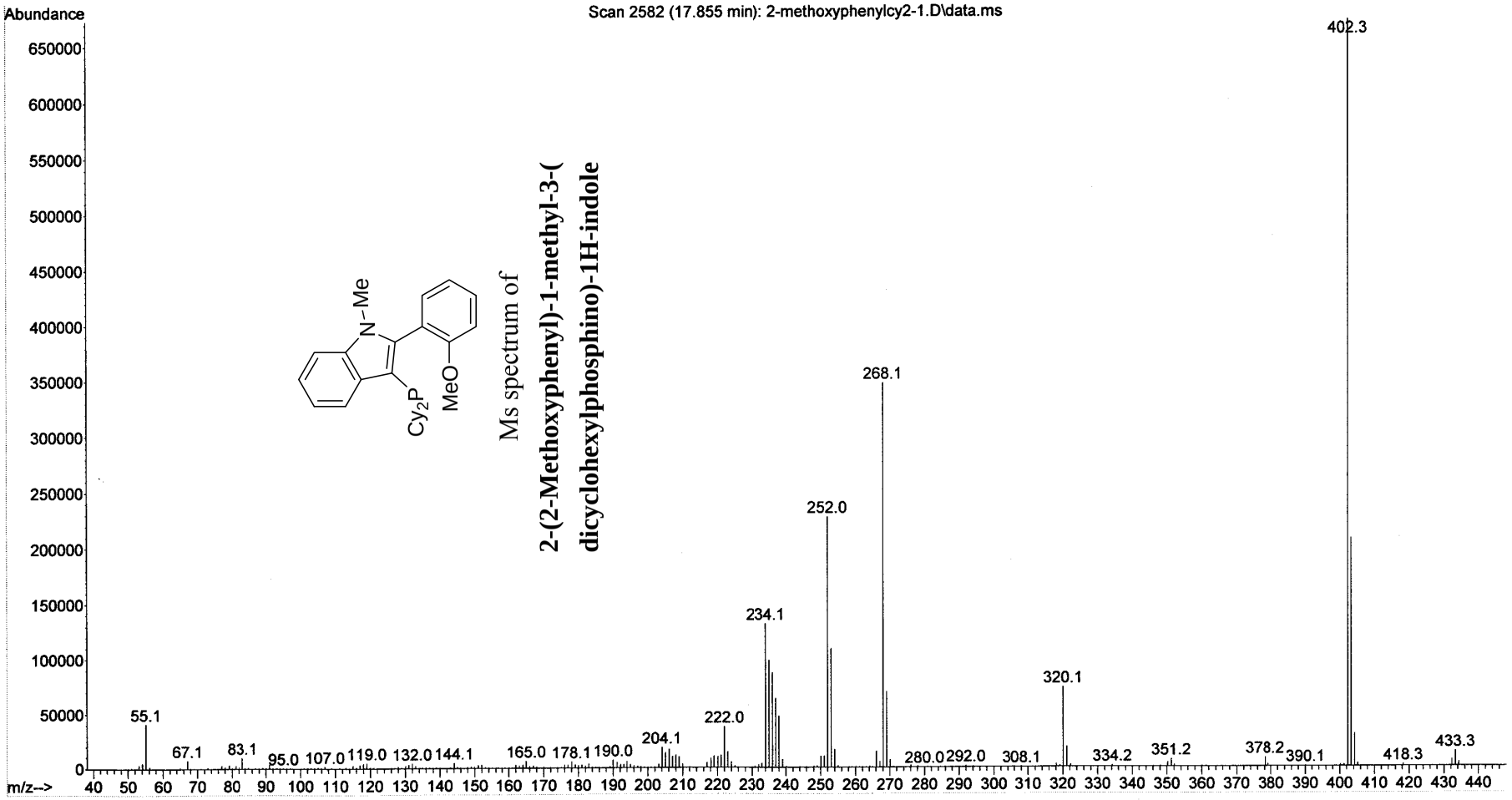

```
F2 - Acquisition parameters
Date_              20070412
Time                  15.25
INSTRUM             dpx400
PROBHD   5 mm QNP  1H
PULPROG             zgdc30
TD                  131072
SOLVENT             CDCl3
NS                     256
DS                       0
SWH               25125.629 Hz
FIDRES                0.191693 Hz
AQ                2.6083827 sec
RG                      8192
DW                19.900 usec
DE                 4.50 usec
TE                   300.0 K
D1                3.00000000 sec
d11               0.03000000 sec

======== CHANNEL f1 ========
NUC1                     13C
P1                    5.80 usec
PL1                  -6.00 dB
SFO1          100.6231263 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                     1H
PCPD2                71.00 usec
PL2                  120.00 dB
PL12                  17.00 dB
SFO2          400.1324008 MHz

F2 - Processing parameters
SI                      65536
SF            100.6127928 MHz
WDW                        EM
SSB                         0
LB                       1.00 Hz
GB                          0
PC                       1.00

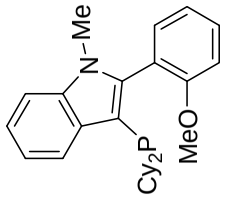
1D NMR plot parameters
CX                      19.50 cm
F1P                   200.000 ppm
F1                  20122.56 Hz
F2P                   -0.000 ppm
F2                     -0.00 Hz
PPMCM                 10.25641 ppm/cm
HZCM                1031.92615 Hz/cm
```



Ms spectrum of

2-(2-Methoxyphenyl)-1-methyl-3-(dicyclohexylphosphino)-1H-indole

HRMs spectrum of **2-(2-Methoxyphenyl)-1-methyl-3-(dicyclohexylphosphino)-1H-indole**



Elemental Composition Report

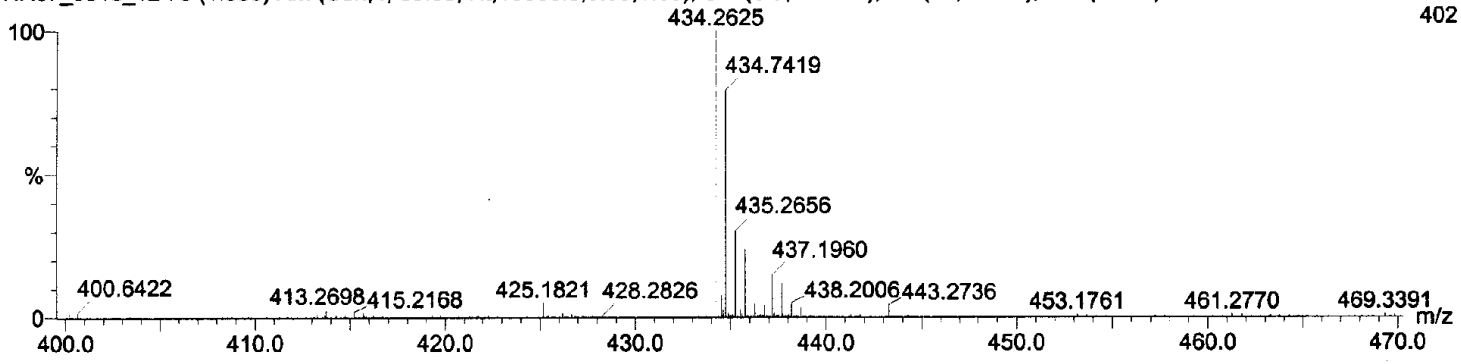
Single Mass Analysis

Tolerance = 100.0 PPM / DBE: min = -1.5, max = 60.0
Selected filters: None

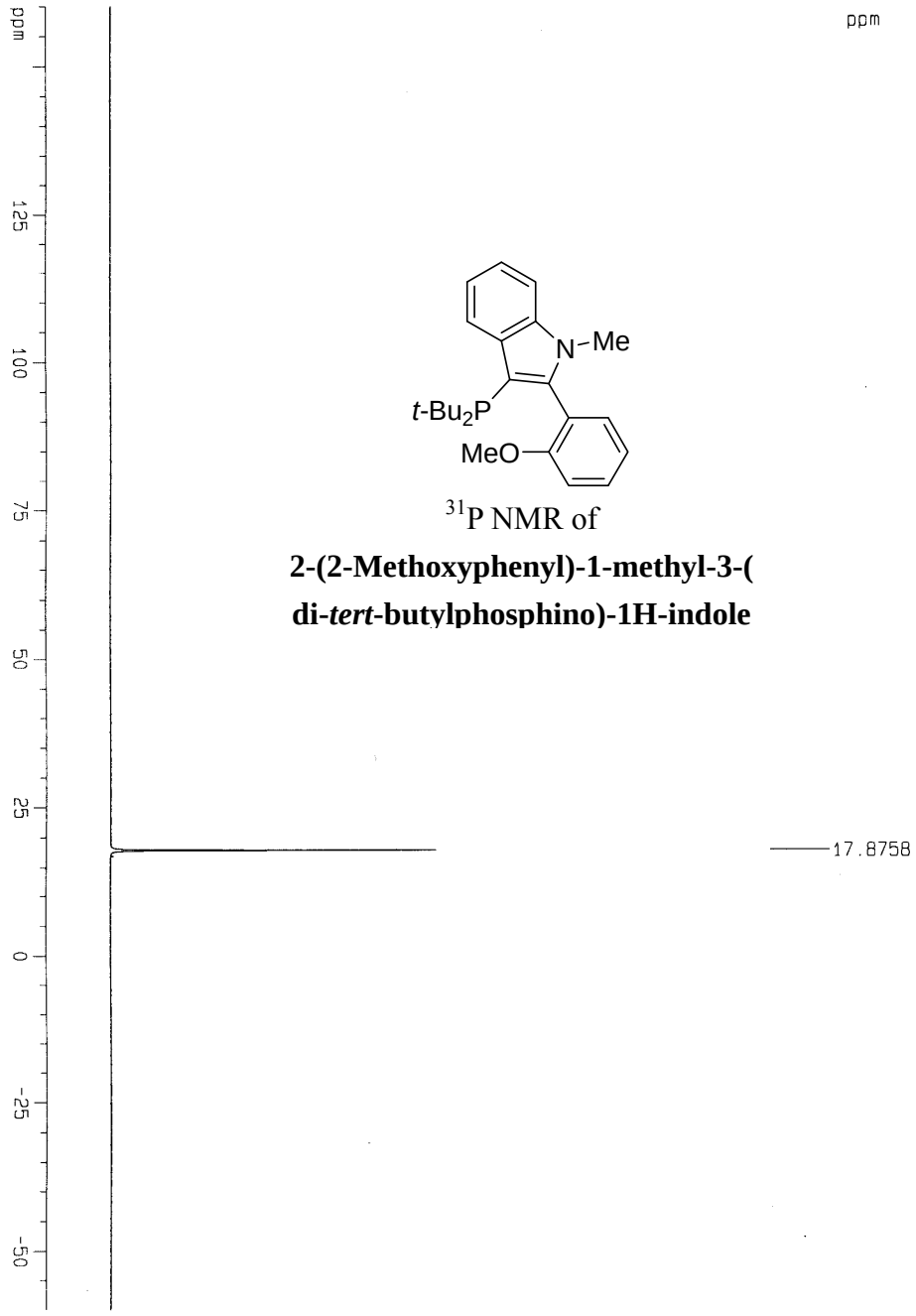
Monoisotopic Mass, Even Electron Ions
12 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-28 H: 0-1000 N: 0-1 O: 0-1 P: 0-1

So Chau Ming, N-methyl2(2-methoxyphenyl)indole 3-cy2phosphine
HR07_0516_12 73 (1.380) AM (Cen,4, 80.00, Ht,10000.0,0.00,1.00); Sm (SG, 2x3.00); Sb (15,10.00); Cm (73:86)

TOF MS ES+
402



Minimum:				-1.5		
Maximum:		5.0	100.0	60.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
434.2625	434.2613	1.2	2.8	11.5	0.2	C28 H37 N O P



^{31}P NMR of

2-(2-Methoxyphenyl)-1-methyl-3-(di-*tert*-butylphosphino)-1H-indole

```
F2 - Acquisition Parameters
Date_              20070331
Time                  11.43
INSTRUM             dpx400
PROBHD     5 mm QNP 1H
PULPROG             zgdc30
TD                   65536
SOLVENT              CDCl3
NS                      64
DS                       0
SWH               4866.801 Hz
FIDRES               0.742520 Hz
AQ                0.6734324 sec
RG                   10321.3
DW                  10.275 usec
DE                   4.50 usec
TE                   300.0 K
D1                1.00000000 sec
D11               0.03000000 sec

======== CHANNEL f1 ========
NUC1                    31P
P1                   7.20 usec
PL1                  -5.00 dB
SF01          161.9851115 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                    1H
PCPD2               71.00 usec
PL2                 120.00 dB
PL12                 17.00 dB
SFO2          400.1324008 MHz

F2 - Processing parameters
SI                     32768
SF            161.9755831 MHz
WDW                    EM
SSB                     0
LB                   3.00 Hz
GB                      0
PC                   1.40

1D NMR plot parameters
CX                   20.00 cm
F1P                 160.000 ppm
F1                25916.09 Hz
F2P                -60.000 ppm
F2                -9718.53 Hz
PPMCM             11.00000 ppm/cm
HZCM              1781.73132 Hz/cm
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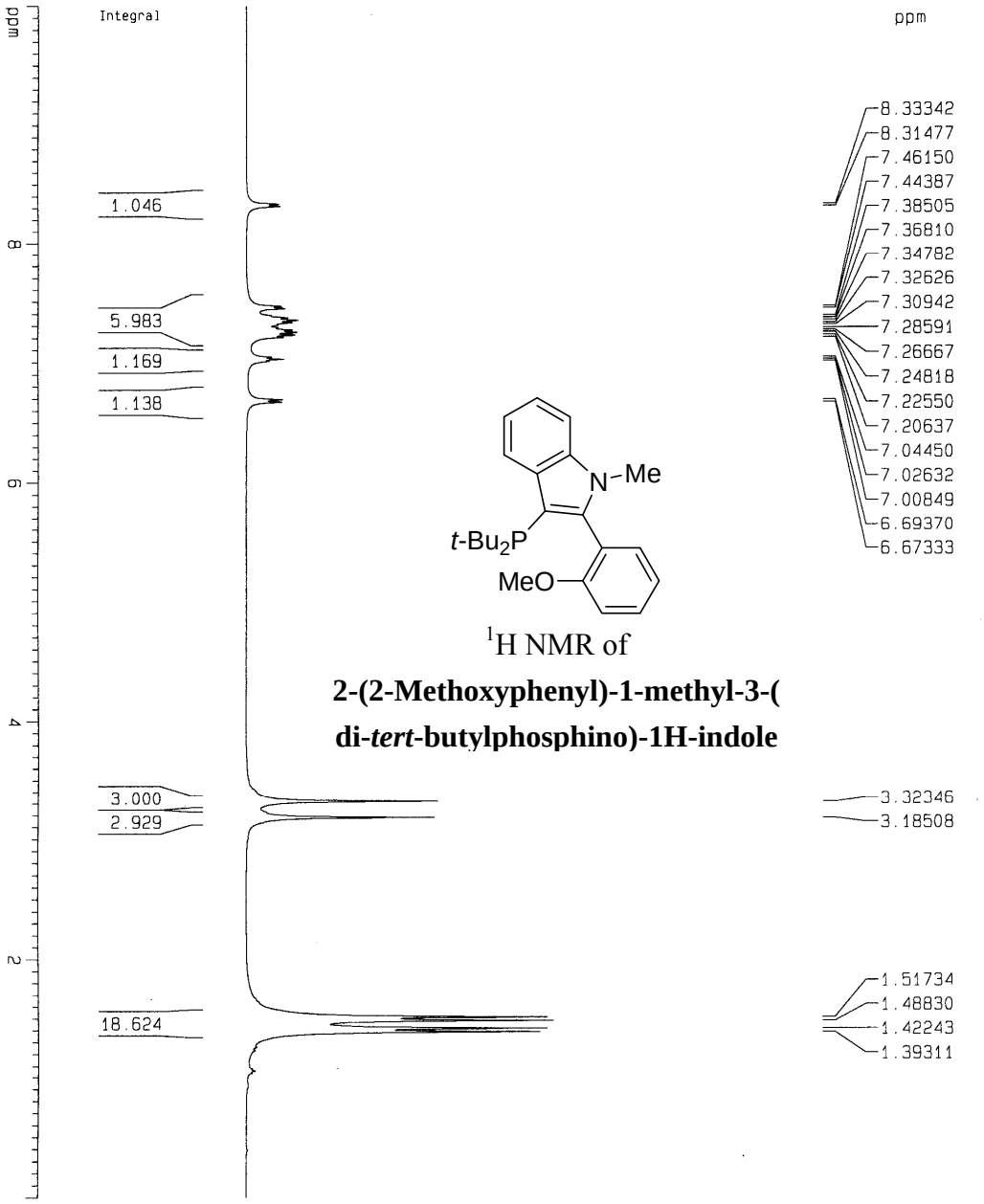
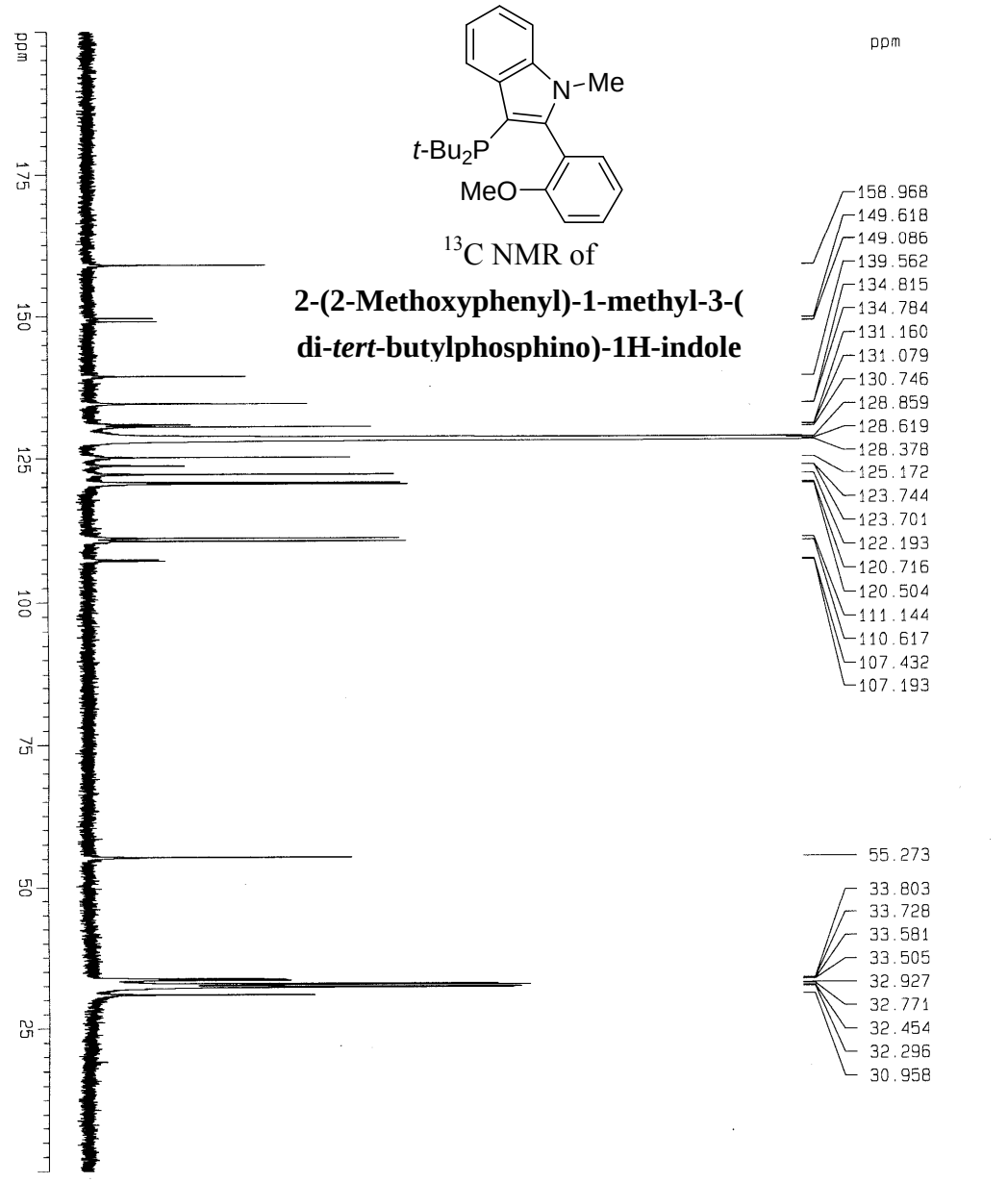


^{1}H NMR of

2-(2-Methoxyphenyl)-1-methyl-3-(di-*tert*-butylphosphino)-1H-indole

F2 - Acquisition Parameters
Date_ 20070331
Time 11.39
INSTRUM dpx400
PROBHD 5 mm QNP 1H
PULPROG zg30
TD 32768
SOLVENT C6D6
NS 32
DS 0
SWH 4629.629 Hz
FIDRES 0.141285 Hz
AQ 3.5389941 sec
RG 25.4
DW 108.000 usec
DE 4.50 usec
TE 300.0 K
D1 1.00000000 sec
========== CHANNEL f1 ==========
NUC1 1H
P1 9.50 usec
PL1 -6.00 dB
SFO1 400.1319924 MHz
F2 - Processing parameters
SI 16384
SF 400.1300092 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 19.63 cm
F1P 10.000 ppm
F1 4001.30 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.50931 ppm/cm
HZCM 203.79143 Hz/cm



^{13}C NMR of

2-(2-Methoxyphenyl)-1-methyl-3-(di-*tert*-butylphosphino)-1H-indole

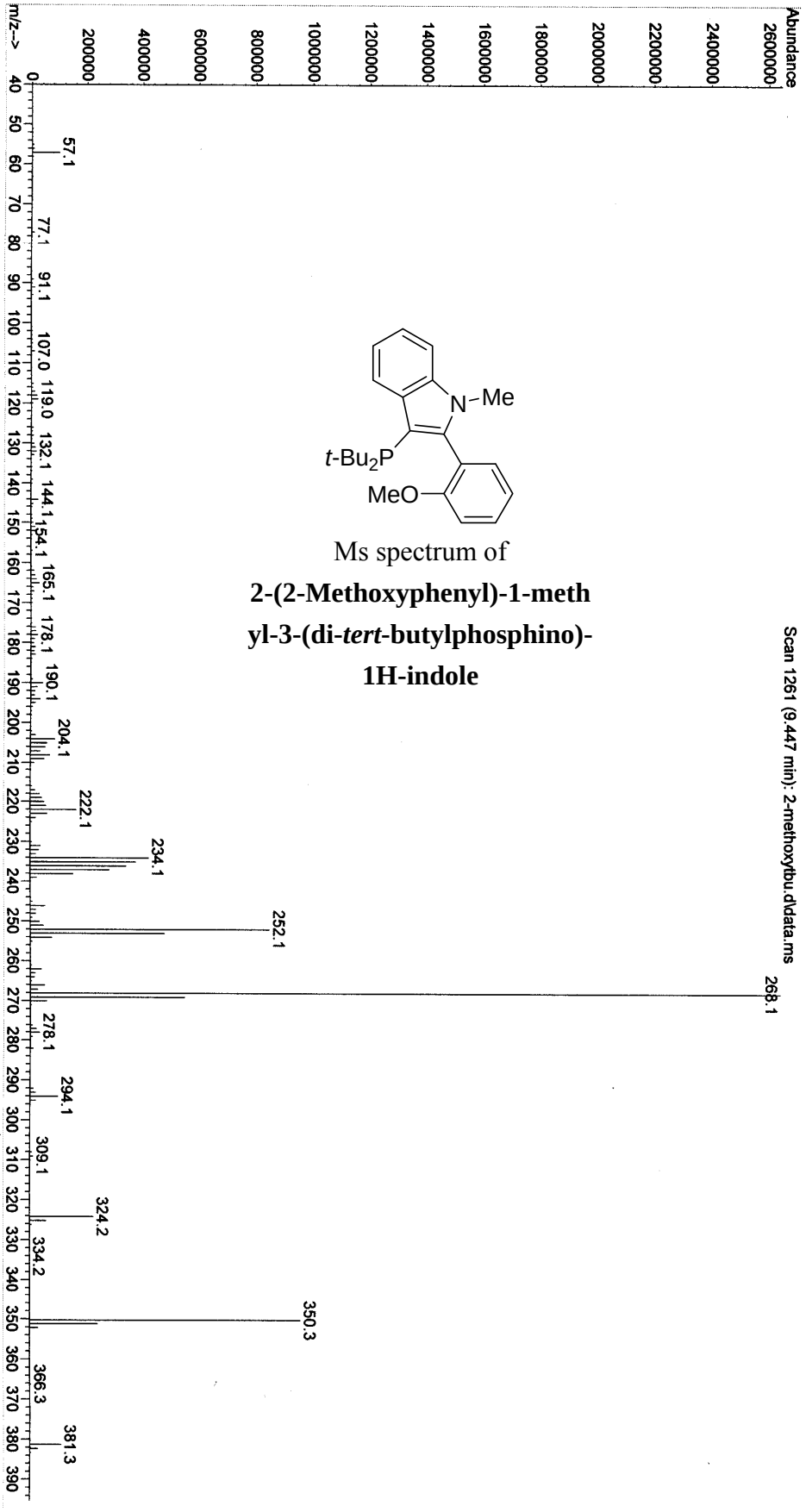
```
Date_                20070331
Time                     11.51
INSTRUM                  dpx400
PROBHD     5 mm QNP 1H
PULPROG                  zgdc30
TD                       131072
SOLVENT                  CDCl3
NS                          768
DS                            0
SWH                  25125.629 Hz
FIDRES                0.191693 Hz
AQ                    2.6083827 sec
RG                         6502
DW                       19.900 usec
DE                        4.50 usec
TE                       300.0 K
D1                    3.00000000 sec
d11                   0.03000000 sec

======== CHANNEL f1 ========
NUC1                        13C
P1                         5.80 usec
PL1                       -6.00 dB
SFO1                100.6231263 MHz

======== CHANNEL f2 ========
CPDPRG2                 waltz16
NUC2                         1H
PCPD2                     71.00 usec
PL2                      120.00 dB
PL12                      17.00 dB
SFO2                400.1320007 MHz

F2 - Processing parameters
SI                         65536
SF                100.6126887 MHz
WDW                           EM
SSB                            0
LB                         1.00 Hz
GB                             0
PC                         1.00

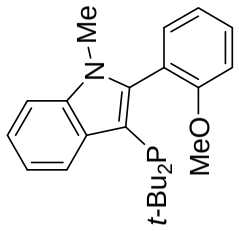
1u NMR plot parameters
CX                        19.50 cm
F1P                     200.000 ppm
F1                    20122.54 Hz
F2P                    -0.000 ppm
F2                     -0.00 Hz
PPMCM                 10.25641 ppm/cm
HZCM                1031.92505 Hz/cm
```



Ms spectrum of

2-(2-Methoxyphenyl)-1-methyl-3-(di-*tert*-butylphosphino)-1H-indole

HRMs spectrum of **2-(2-Methoxyphenyl)-1-methyl-3-(di-*tert*-butylphosphino)-1H-indole**



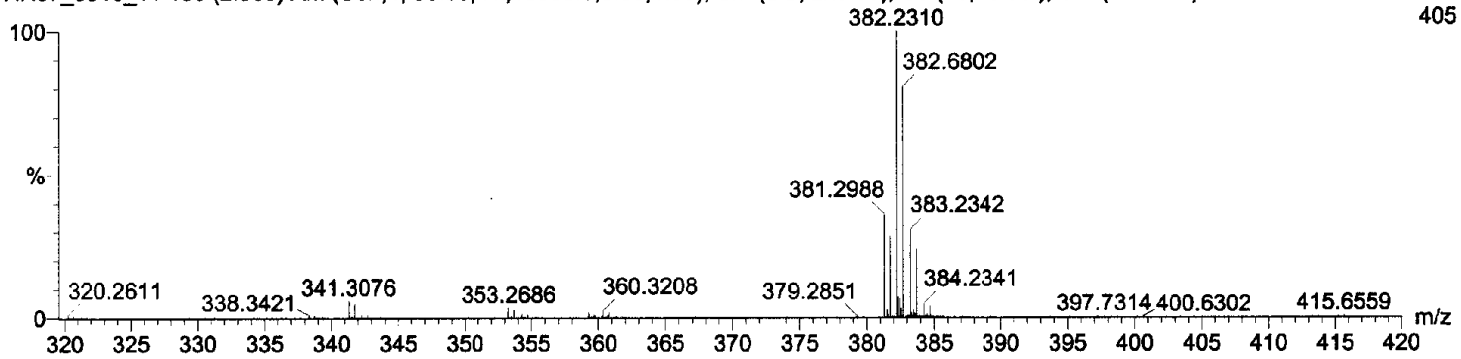
Elemental Composition Report

Single Mass Analysis

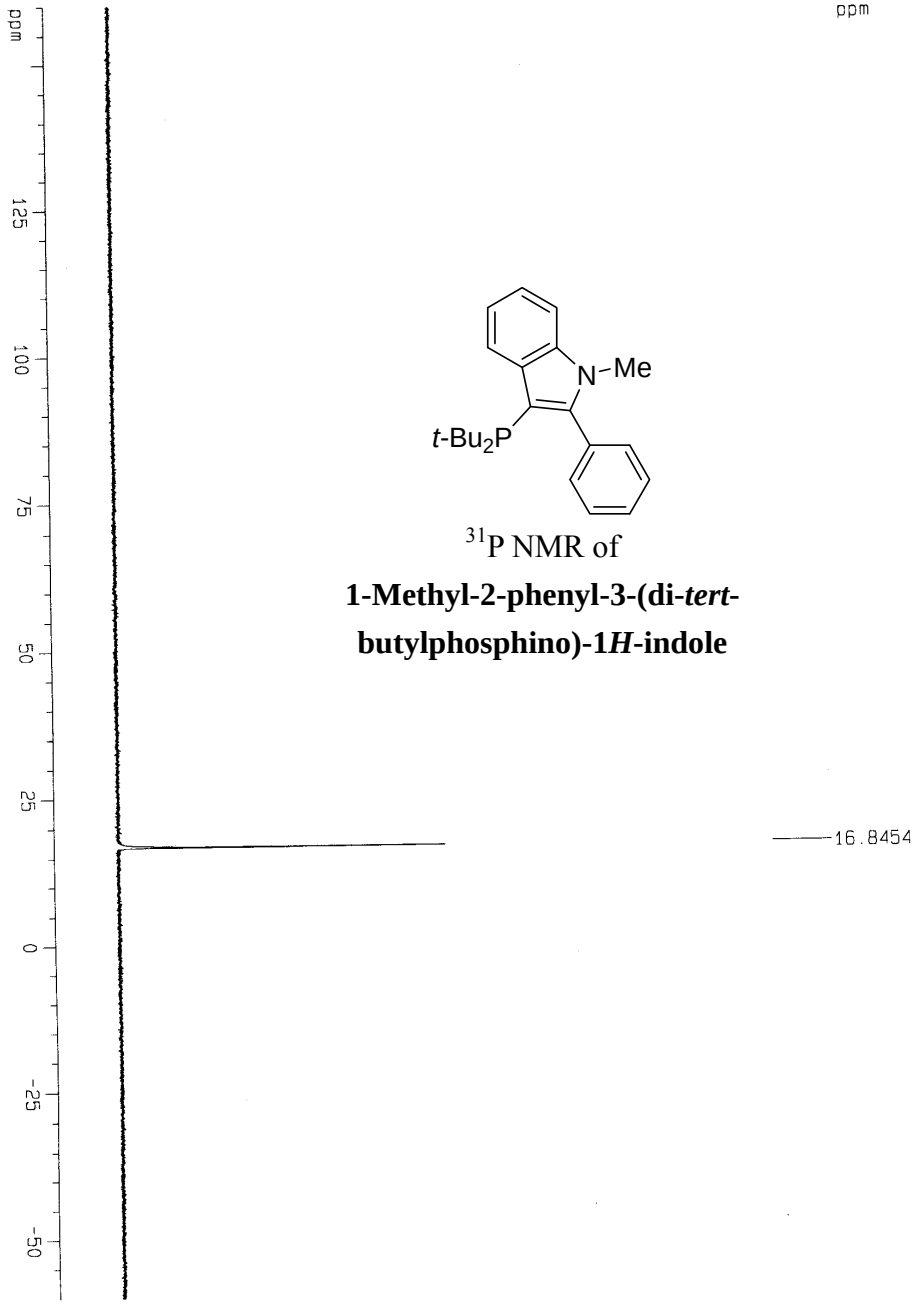
Tolerance = 100.0 PPM / DBE: min = -1.5, max = 60.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
11 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-24 H: 0-1000 N: 0-1 O: 0-1 P: 0-1

So Chau Ming, N-methyl2(2methoxyphenyl)indole 3-tBu2phosphine
HR07_0516_11 136 (2.565) AM (Cen,4, 80.00, Ht,10000.0,0.00,1.00); Sm (SG, 2x3.00); Sb (15,10.00); Cm (127:153) TOF MS ES+ 405



Minimum:				-1.5		
Maximum:		5.0	100.0	60.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
382.2310	382.2300	1.0	2.6	9.5	0.8	C24 H33 N O P



^{31}P NMR of

1-Methyl-2-phenyl-3-(di-*tert*-butylphosphino)-1*H*-indole

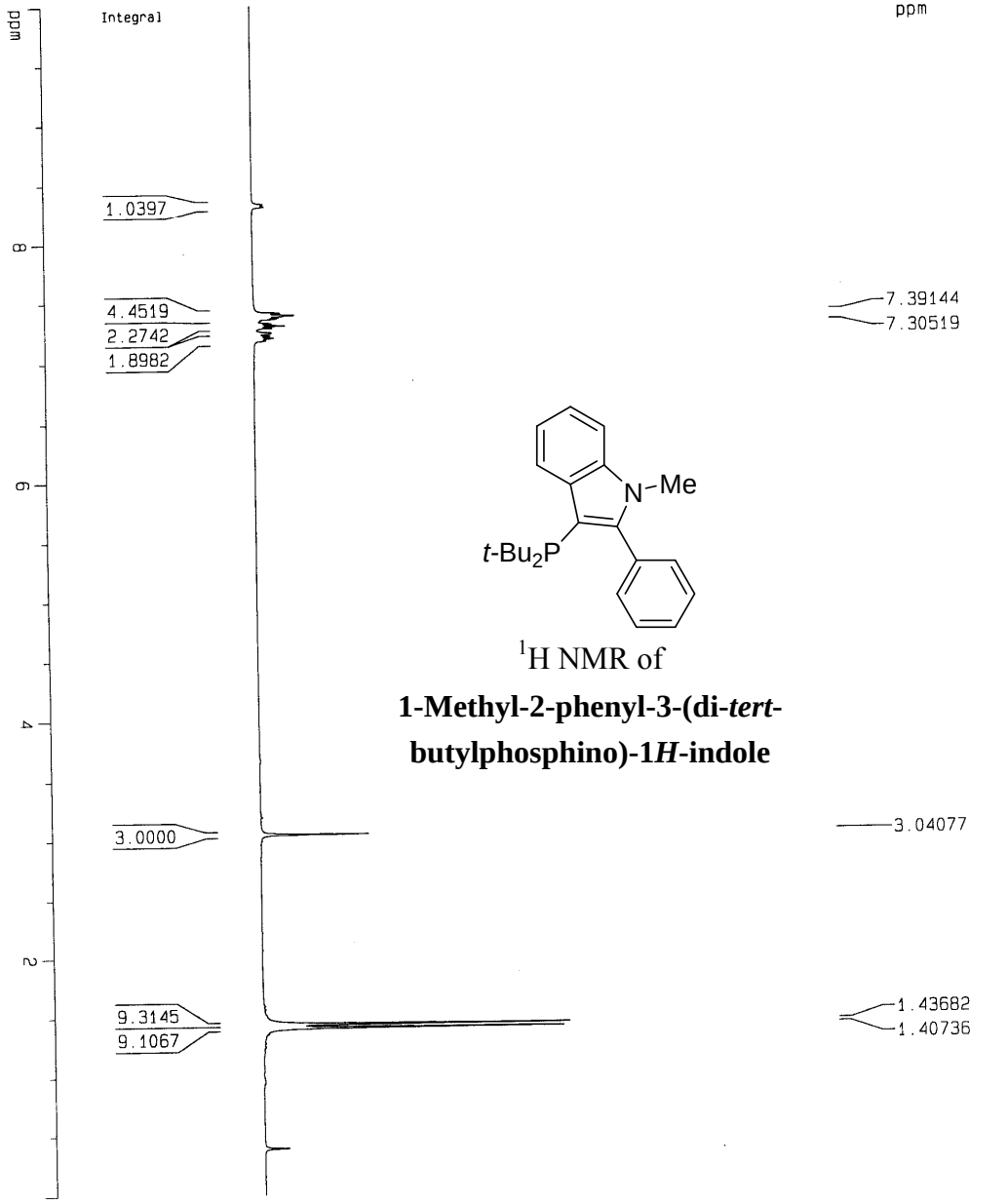
```
F2 - Acquisition Parameters
Date_              20070331
Time                  14.58
INSTRUM             dpx400
PROBHD   5 mm QNP 1H
PULPROG             zgdc30
TD                   65536
SOLVENT               C6D6
NS                      64
DS                       0
SWH              46661.801 Hz
FIDRES           0.742520 Hz
AQ               0.6734324 sec
RG                  14596.5
DW                 10.275 usec
DE                  4.50 usec
TE                   300.0 K
D1              1.00000000 sec
d11             0.03000000 sec

============== CHANNEL f1 ==============
NUC1                   31P
P1                  7.20 usec
PL1                -5.00 dB
SFO1          161.9851115 MHz

============== CHANNEL f2 ==============
CPDPRG2             waltz16
NUC2                   1H
PCPD2               71.00 usec
PL2                120.00 dB
PL12               17.00 dB
SFO2          400.1324008 MHz

F2 - Processing parameters
SI                     32768
SF            161.9755831 MHz
WDW                       EM
SSB                        0
LB                  3.00 Hz
GB                         0
PC                      1.40

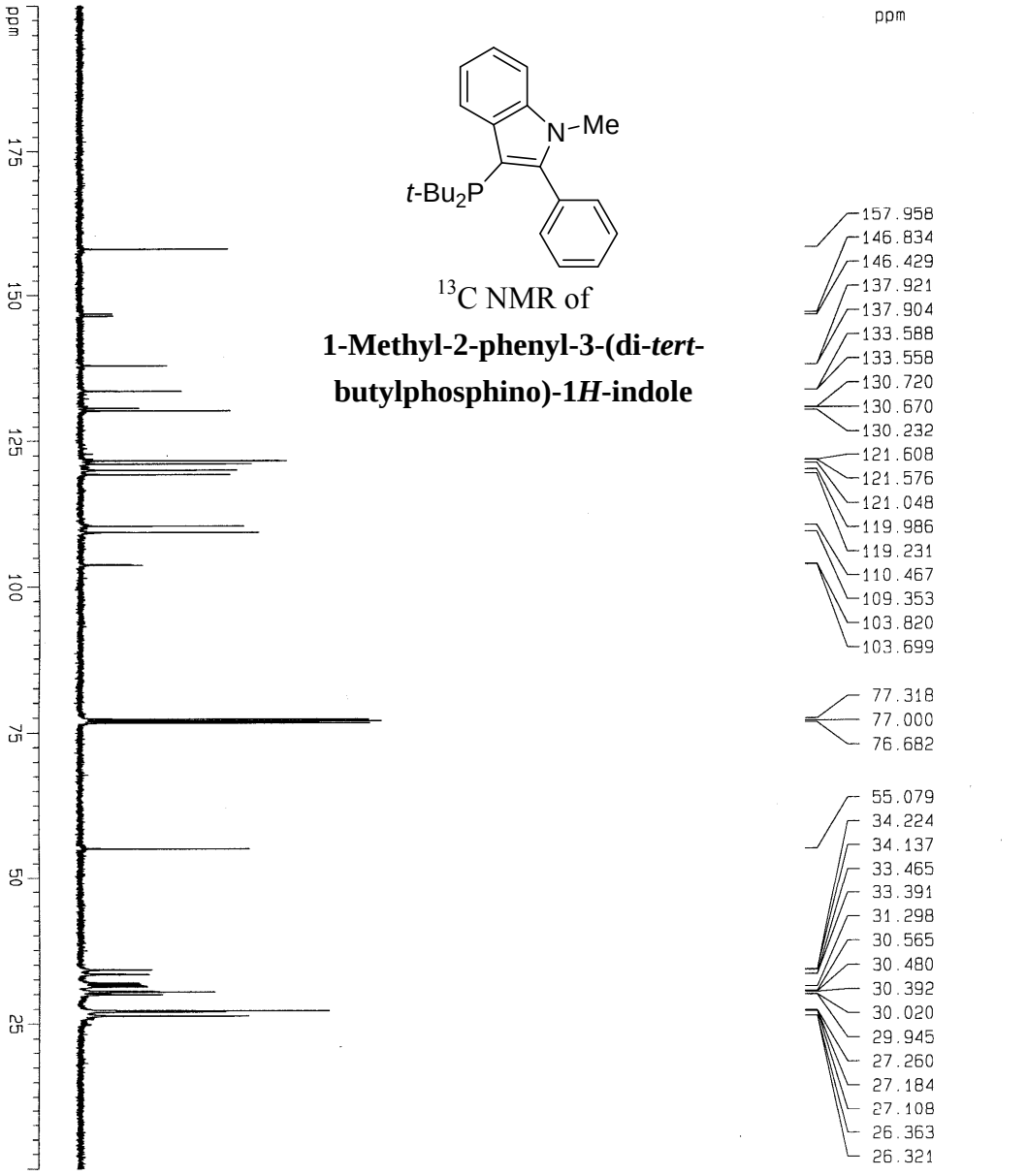
1D NMR plot parameters
CX                  20.00 cm
F1P                160.000 ppm
F1                25916.09 Hz
F2P                -60.000 ppm
F2                -9718.53 Hz
PPMCM             11.00000 ppm/cm
HZCM          1781.73132 Hz/cm
```



^{1}H NMR of

1-Methyl-2-phenyl-3-(di-*tert*-butylphosphino)-1*H*-indole

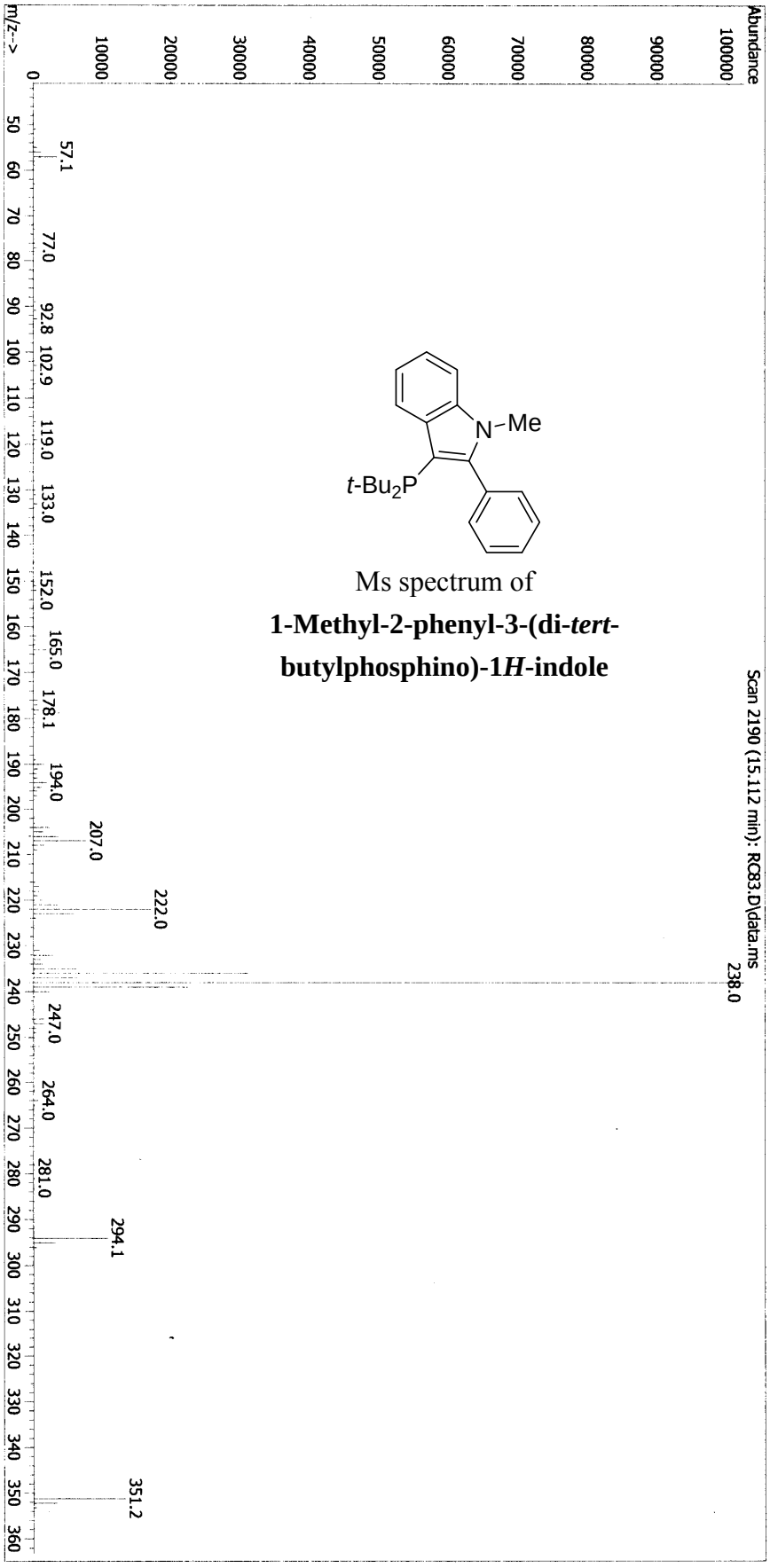
F2 - Acquisition Parameters
Date_ 20070111
Time 21.28
INSTRUM dpx400
PROBHD 5 mm GNP 1H
PULPROG zg30
TD 32768
SOLVENT C6D6
NS 16
DS 0
SWH 4629.629 Hz
FIDRES 0.141285 Hz
AQ 3.5389941 sec
RG 90.5
DW 108.000 usec
DE 4.50 usec
TE 300.0 K
D1 1.00000000 sec
========== CHANNEL f1 ==========
NUC1 1H
P1 9.50 usec
PL1 -6.00 dB
SFO1 400.1319924 MHz
F2 - Processing parameters
SI 16384
SF 400.1300095 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 19.63 cm
F1P 10.000 ppm
F1 4001.30 Hz
F2P -0.000 ppm
F2 -0.00 Hz
PPMCM 0.50930 ppm/cm
HZCM 203.78769 Hz/cm



^{13}C NMR of

1-Methyl-2-phenyl-3-(di-*tert*-butylphosphino)-1*H*-indole

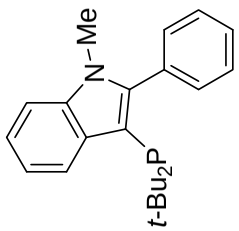

```
F2 - Acquisition parameters
Date_              20070412
Time               15.25
INSTRUM            dpx400
PROBHD      5 mm QNP 1H
PULPROG            zgdc30
TD                 131072
SOLVENT            CDCl3
NS                 256
DS                 0
SWH                25125.629 Hz
FIDRES             0.191693 Hz
AQ                 2.6083827 sec
RG                 8192
DW                 19.900 usec
DE                 4.50 usec
TE                 300.0 K
D1                 3.00000000 sec
d11                0.03000000 sec
============== CHANNEL f1 ==============
NUC1               13C
P1                 5.80 usec
PL1                -6.00 dB
SFO1               100.6231263 MHz
============== CHANNEL f2 ==============
CPDPRG2            waltz16
NUC2               1H
PCPD2              71.00 usec
PL2                120.00 dB
PL12               17.00 dB
SFO2               400.1324008 MHz
F2 - Processing parameters
SI                 65536
SF                 100.6127928 MHz
WDW                EM
SSB                0
LB                 1.00 Hz
GB                 0
PC                 1.00
1D NMR plot parameters
CX                 19.50 cm
F1P                200.000 ppm
F1                 20122.56 Hz
F2P                -0.000 ppm
F2                 -0.00 Hz
PPMCM              10.25641 ppm/cm
HZCM               1031.92615 Hz/cm
```



Ms spectrum of

1-Methyl-2-phenyl-3-(di-*tert*-butylphosphino)-1*H*-indole

HRMs spectrum of **1-Methyl-2-phenyl-3-(di-*tert*-butylphosphino)-1*H*-indole**



Elemental Composition Report

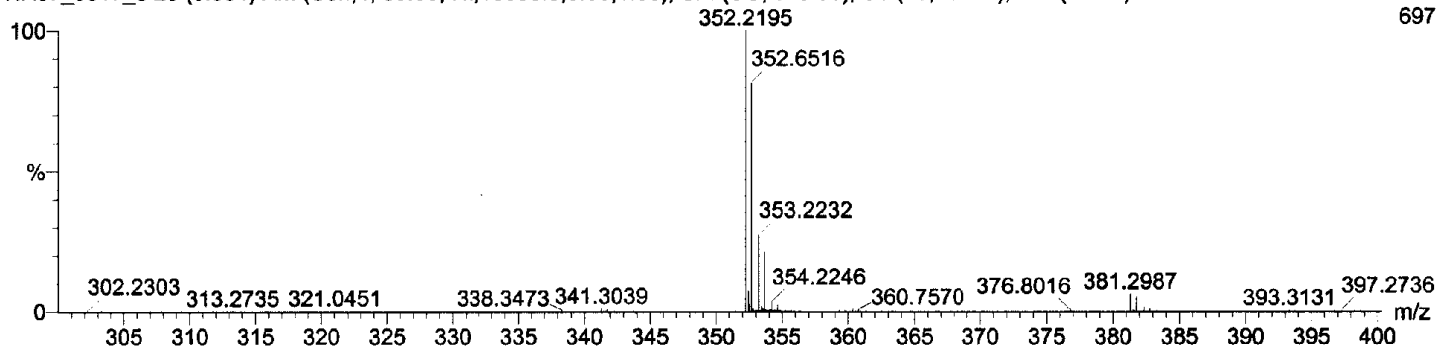
Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 60.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
55 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-27 H: 0-1000 N: 0-2 O: 0-1 P: 0-1

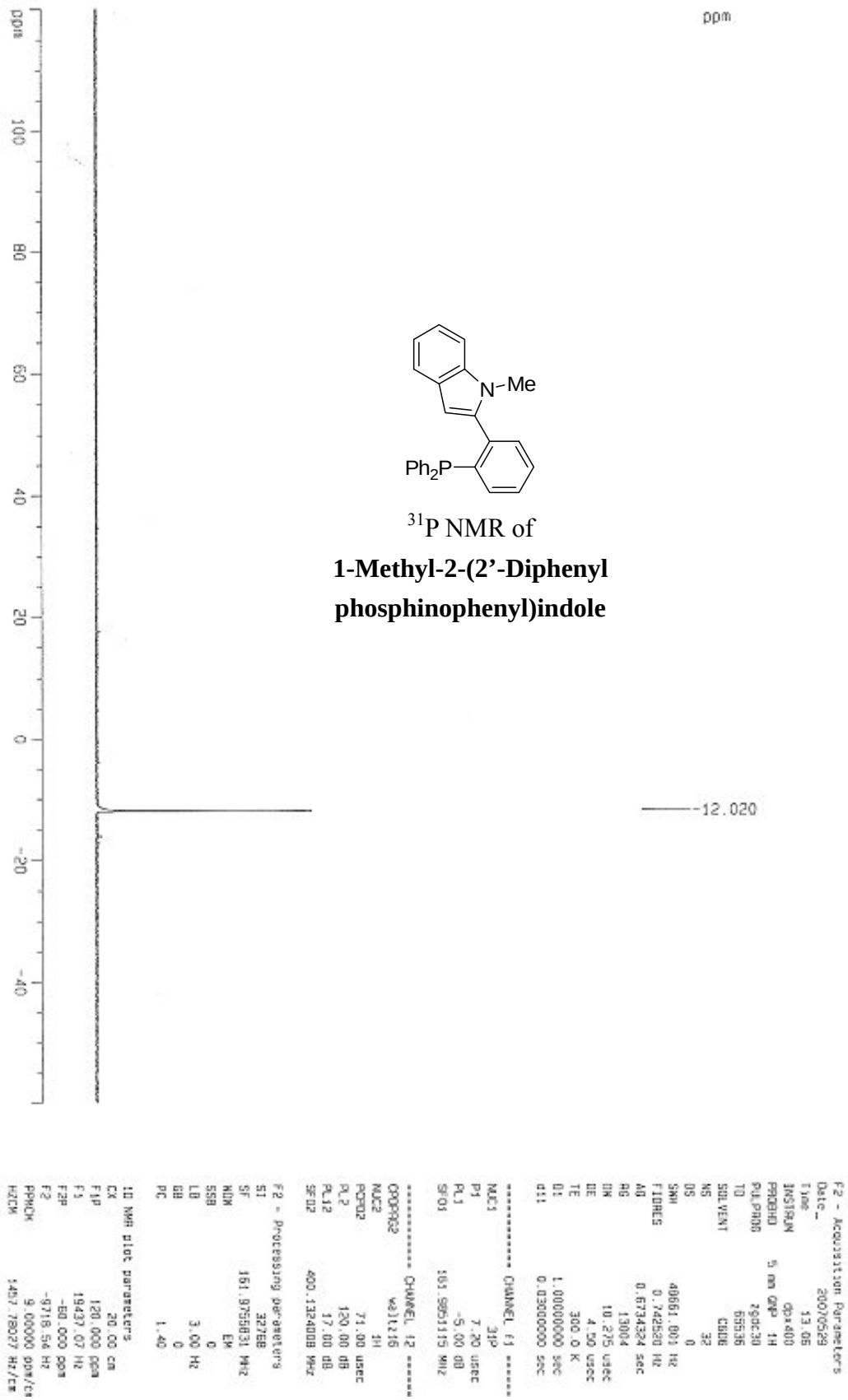
So Chau Ming, N-methyl 2-phenylindole 3-tBu2phosphine
HR07_0517_3 28 (0.534) AM (Cen,4, 80.00, Ht,10000.0,0.00,1.00); Sm (SG, 2x3.00); Sb (15,10.00); Cm (28:31)

TOF MS ES+
697



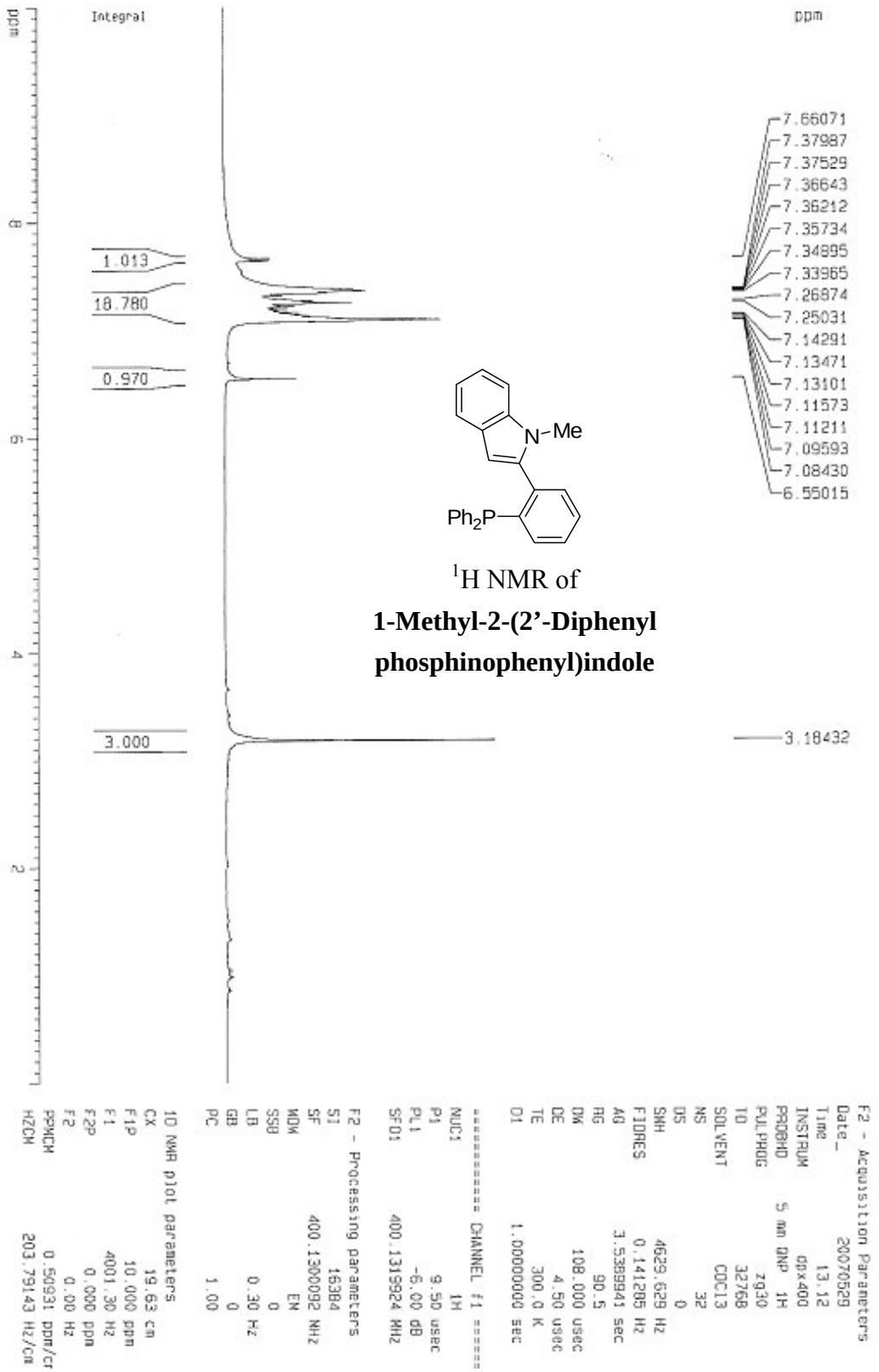
Minimum:				-1.5		
Maximum:		5.0	5.0	60.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
352.2195	352.2194	0.1	0.3	9.5	0.1	C23 H31 N P

C-P Type Indolyl Phosphine Ligand (Phosphine Group Attached to Bottom Ring)



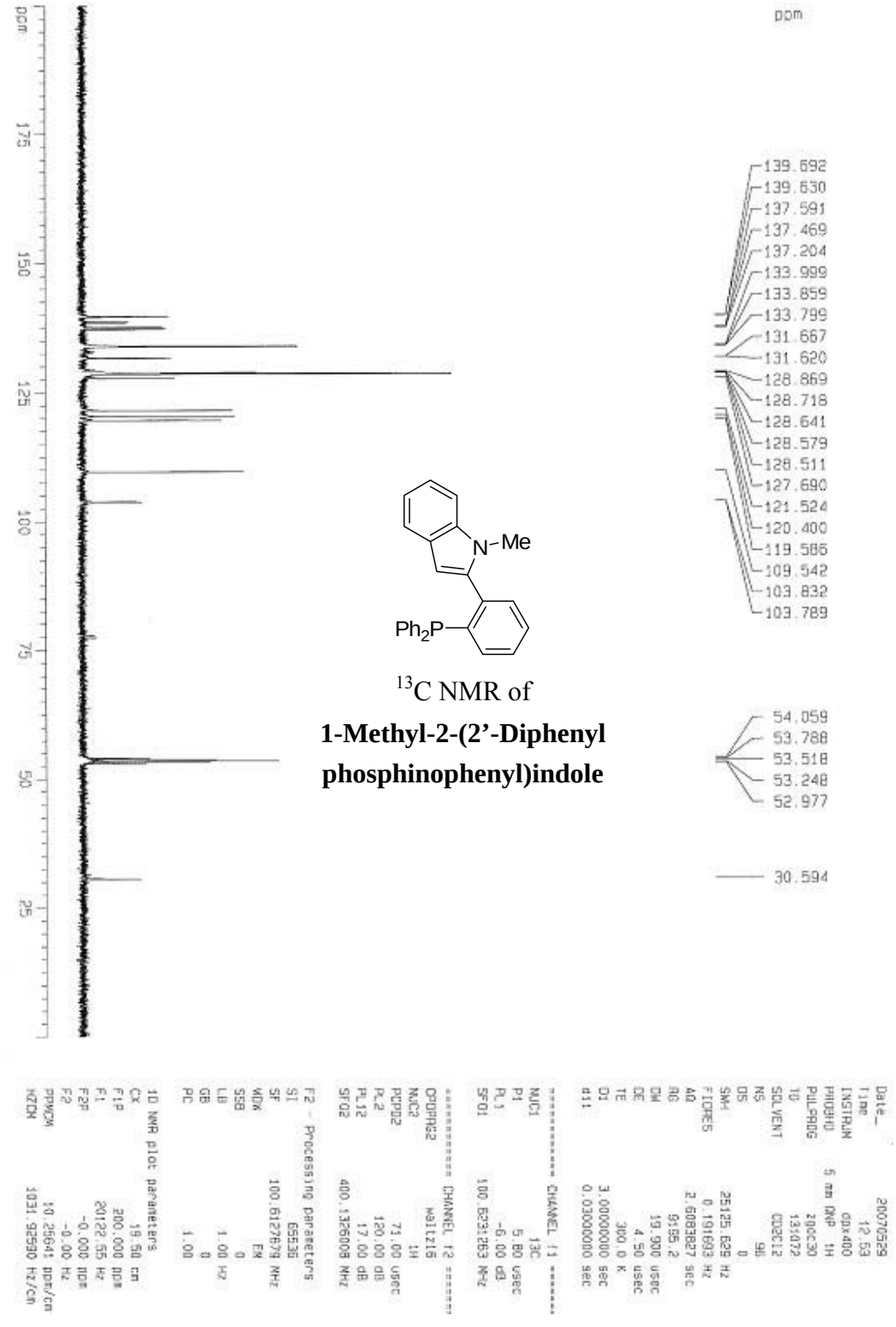
^{31}P NMR of

1-Methyl-2-(2’-Diphenyl phosphinophenyl)indole



^{1}H NMR of

1-Methyl-2-(2'-Diphenyl phosphinophenyl)indole



^{13}C NMR of

1-Methyl-2-(2'-Diphenyl phosphinophenyl)indole

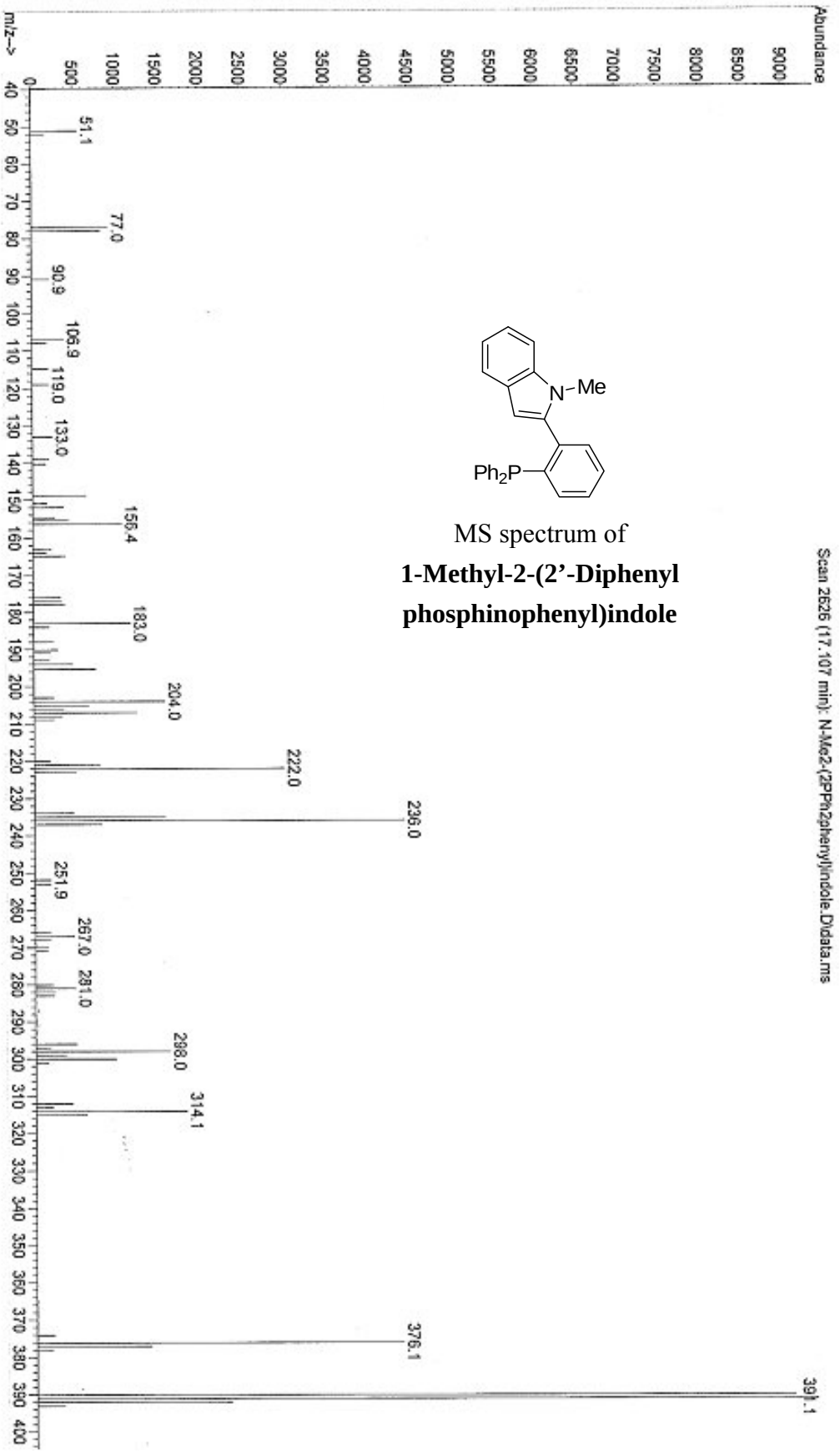

```
Date_                 20070529
Time                      12.53
INSTRUM                spect 400
PROBHD     5 mm QNP 1H/13C/31P
PULPROG                zgpg30
TD                        13072
SOLVENT                CDCl3
NS                           96
DS                            0
SWH                  25125.628 Hz
FIDRES                0.191693 Hz
AQ                    2.6083827 sec
RG                         9195.2
DW                        19.900 usec
DE                         4.50 usec
TE                        300.0 K
D1                    3.00000000 sec
d11                   0.03000000 sec

======== CHANNEL f1 ========
NUC1                         13C
P1                         5.80 usec
PL1                       -6.00 dB
SFO1                 100.6232263 MHz

======== CHANNEL f2 ========
CPDPRG2                  waltz16
NUC2                         1H
PCPD2                     71.00 usec
PL2                      120.00 dB
PL12                      17.00 dB
SFO2                 400.1326008 MHz

F2 - Processing parameters
SI                         65536
SF                 100.6127679 MHz
WDW                           EM
SSB                            0
LB                          1.00 Hz
GB                             0
PC                          1.00

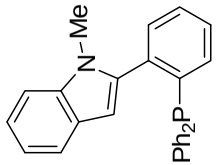
1D NMR plot parameters
CX                        19.50 cm
CY                       200.000 ppm
F1P                      201.55 Hz
F1                     20122.55 Hz
F2P                       -0.000 ppm
F2                        -0.00 Hz
PPMCM                   10.25641 ppm/cm
HZCM                 1031.92530 Hz/cm
```



MS spectrum of

1-Methyl-2-(2'-Diphenyl phosphinophenyl)indole

HRMS spectrum of **1-Methyl-2-(2'-Diphenyl phosphinophenyl)indole**



Elemental Composition Report

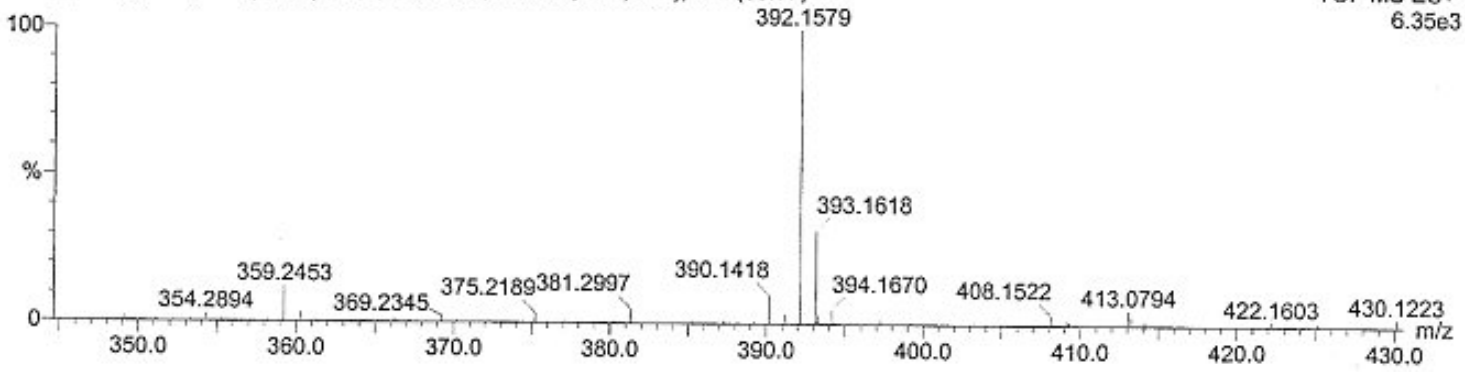
Single Mass Analysis

Tolerance = 100.0 PPM / DBE: min = -1.5, max = 60.0
Selected filters: None

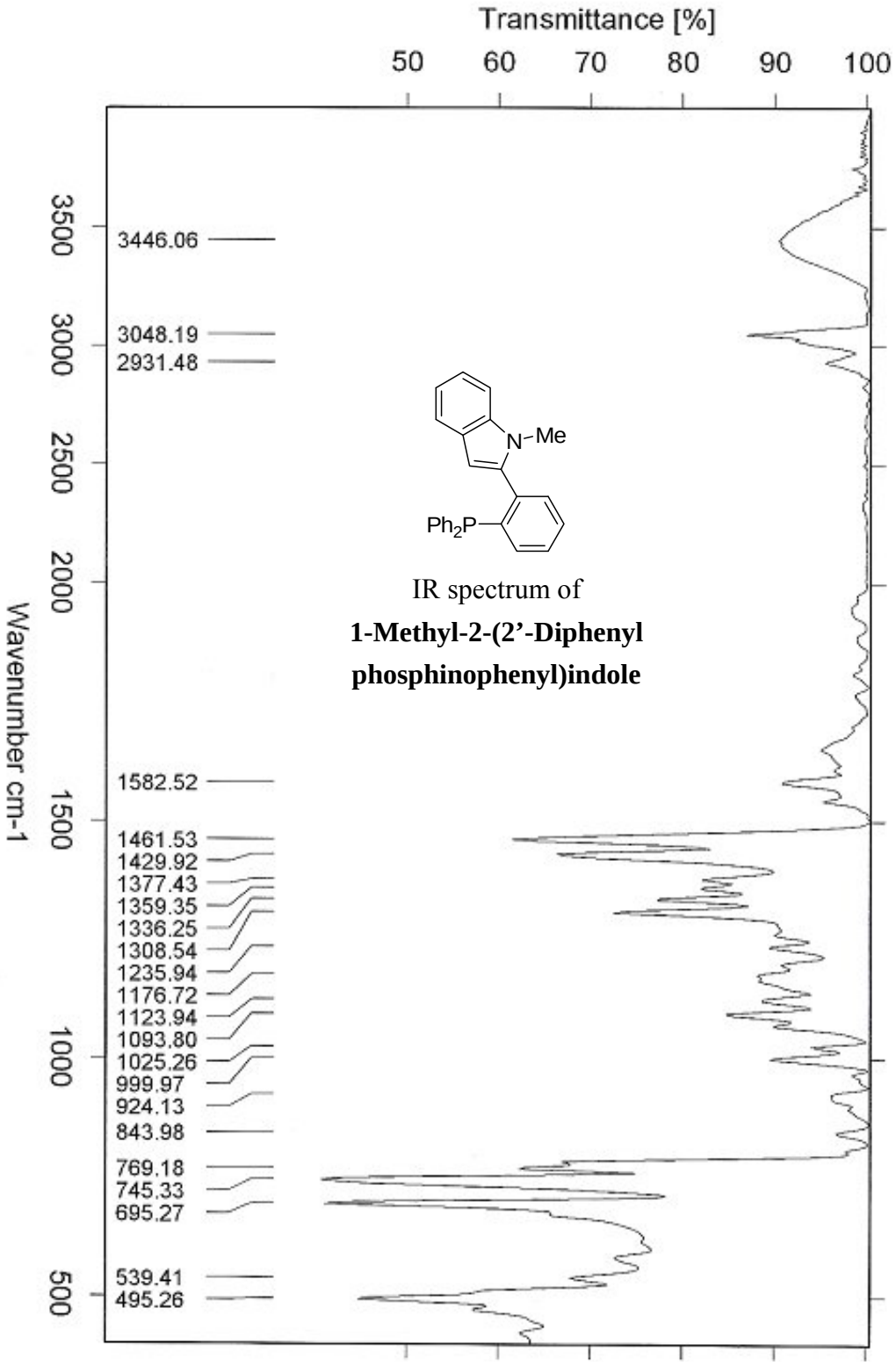
Monoisotopic Mass, Even Electron Ions
9 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-27 H: 0-1000 N: 0-1 P: 0-1

So Chau Ming, 2-(N-methylindolylphenylPh2phosphine
HR07_0615_7 66 (1.249) AM (Cen,5, 80.00, Ar,10000.0,0.00,0.70); Cm (66:77)

15-Jun-2007
TOF MS ES+
6.35e3

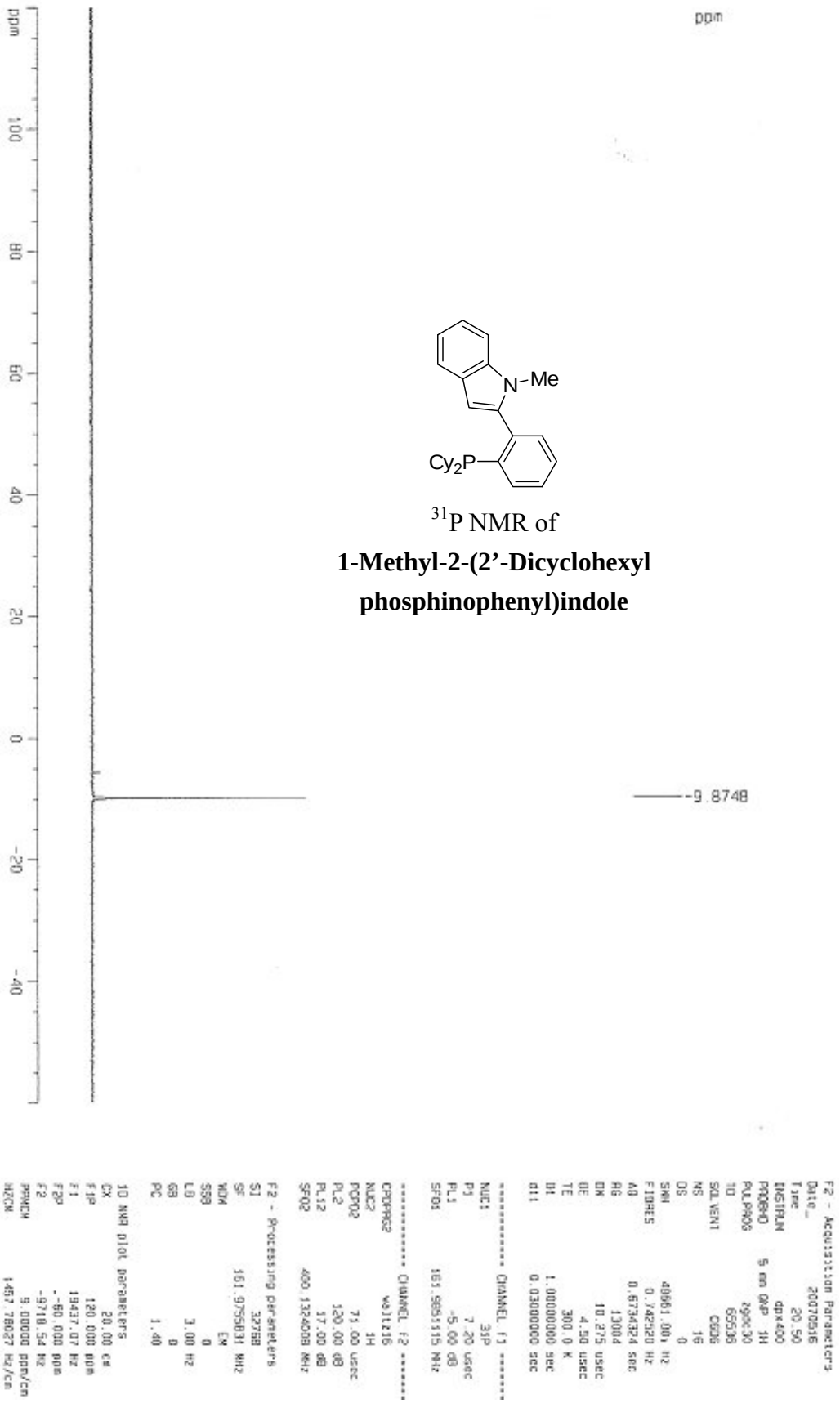


Minimum:				-1.5		
Maximum:		5.0	100.0	60.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
392.1579	392.1568	1.1	2.8	17.5	1.2	C27 H23 N P



IR spectrum of

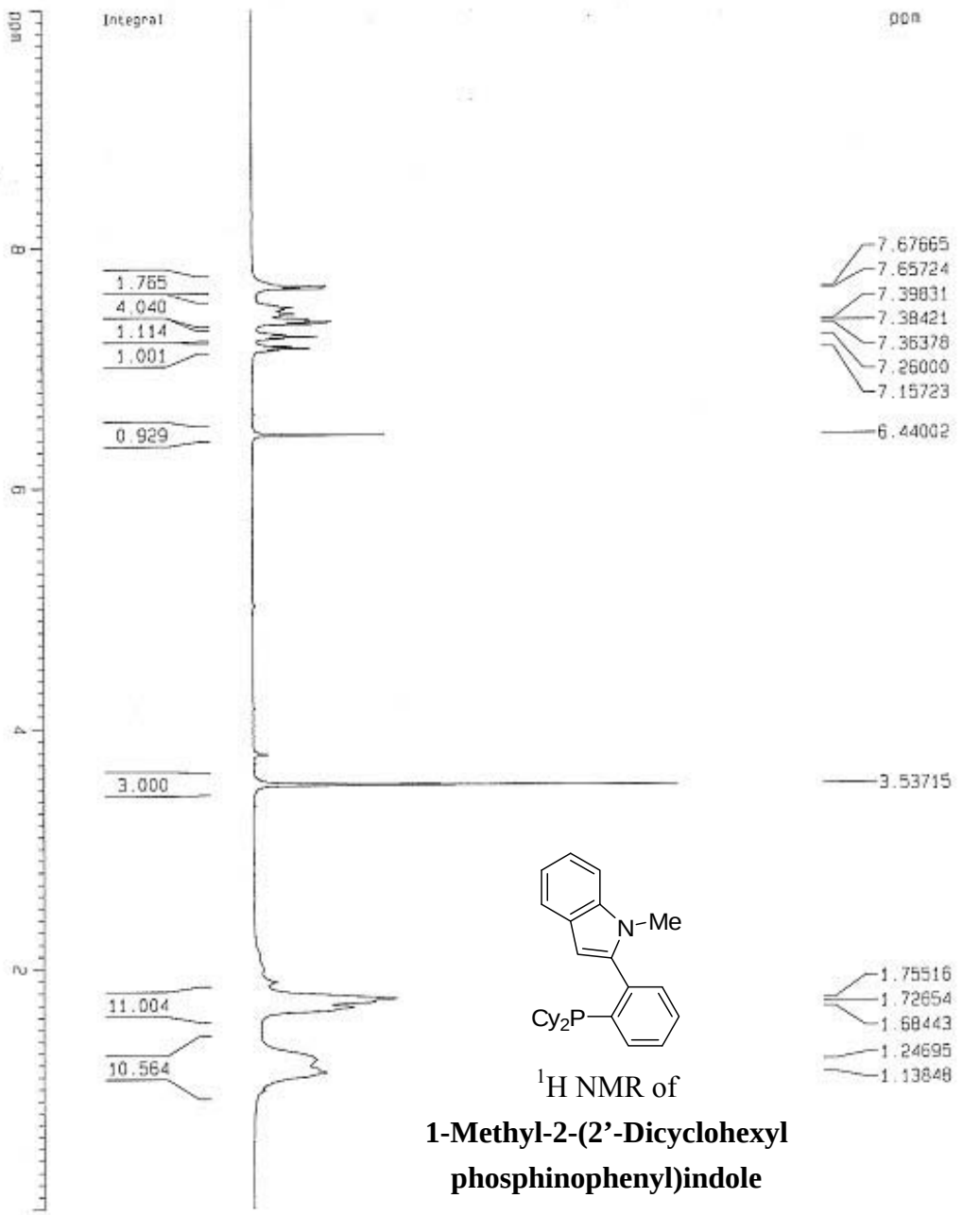
1-Methyl-2-(2'-Diphenyl phosphinophenyl)indole



^{31}P NMR of

1-Methyl-2-(2'-Dicyclohexyl phosphinophenyl)indole

F2 - Acquisition Parameters
Date_ 20070516
Time 20.50
INSTRUM dpx400
PROBHD 5 mm QNP 1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 16
DS 0
SWH 40661.001 Hz
FIDRES 0.742520 Hz
AQ 0.6734324 sec
RG 13004
DW 10.275 usec
DE 4.50 usec
TE 300.0 K
D1 1.00000000 sec
d11 0.03000000 sec
======== CHANNEL f1 ========
NUC1 31P
P1 7.20 usec
PL1 -5.00 dB
SFO1 161.9853115 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 71.00 usec
PL2 120.00 dB
PL12 17.00 dB
SFO2 400.1324009 MHz
F2 - Processing parameters
SI 32768
SF 161.9756031 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
1D NMR plot parameters
CX 20.00 cm
F1P 120.000 ppm
F1 19437.07 Hz
F2P -60.000 ppm
F2 -9710.54 Hz
PPMCM 5.00000 ppm/cm
HZCM 1457.78027 Hz/cm



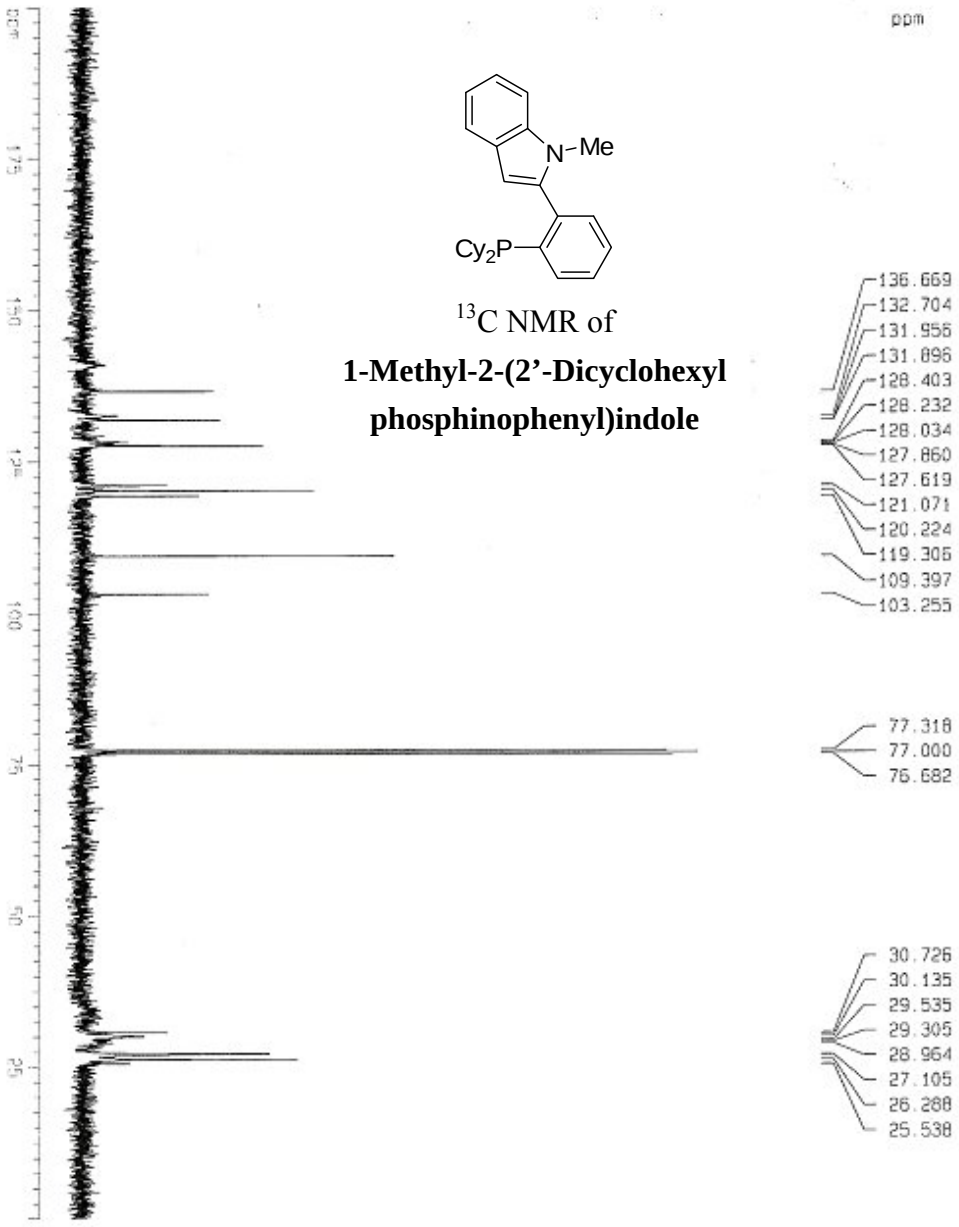
^{1}H NMR of

1-Methyl-2-(2'-Dicyclohexyl phosphinophenyl)indole

```
F2 - Acquisition Parameters
Date_              20070516
Time                  20.10
INSTRUM             dpx400
PROBHD       5 mm DUP 1H
PULPROG              zg30
TD                  32768
SOLVENT           CDCl3
NS                    32
DS                     0
SWH              4629.629 Hz
FIDRES           0.141285 Hz
AQ               3.5389941 sec
RG                    35.9
DW                108.000 usec
DE                  4.50 usec
TE                300.0 K
D1               1.00000000 sec
============== CHANNEL f1 ======
NUC1                  1H
P1                 9.50 usec
PL1                -6.00 dB
SFO1         400.1319924 MHz

F2 - Processing parameters
SI                   16384
SF           400.1300092 MHz
WDW                     EM
SSB                      0
LB                  0.30 Hz
GB                       0
PC                   1.00

1D NMR plot parameters
CX                  19.63 cm
F1P               10.000 ppm
F1              4001.30 Hz
F2P               0.000 ppm
F2                 0.00 Hz
PPMCM          0.50931 ppm/cm
HZCM         203.79143 Hz/cm
```



^{13}C NMR of

1-Methyl-2-(2'-Dicyclohexyl phosphinophenyl)indole

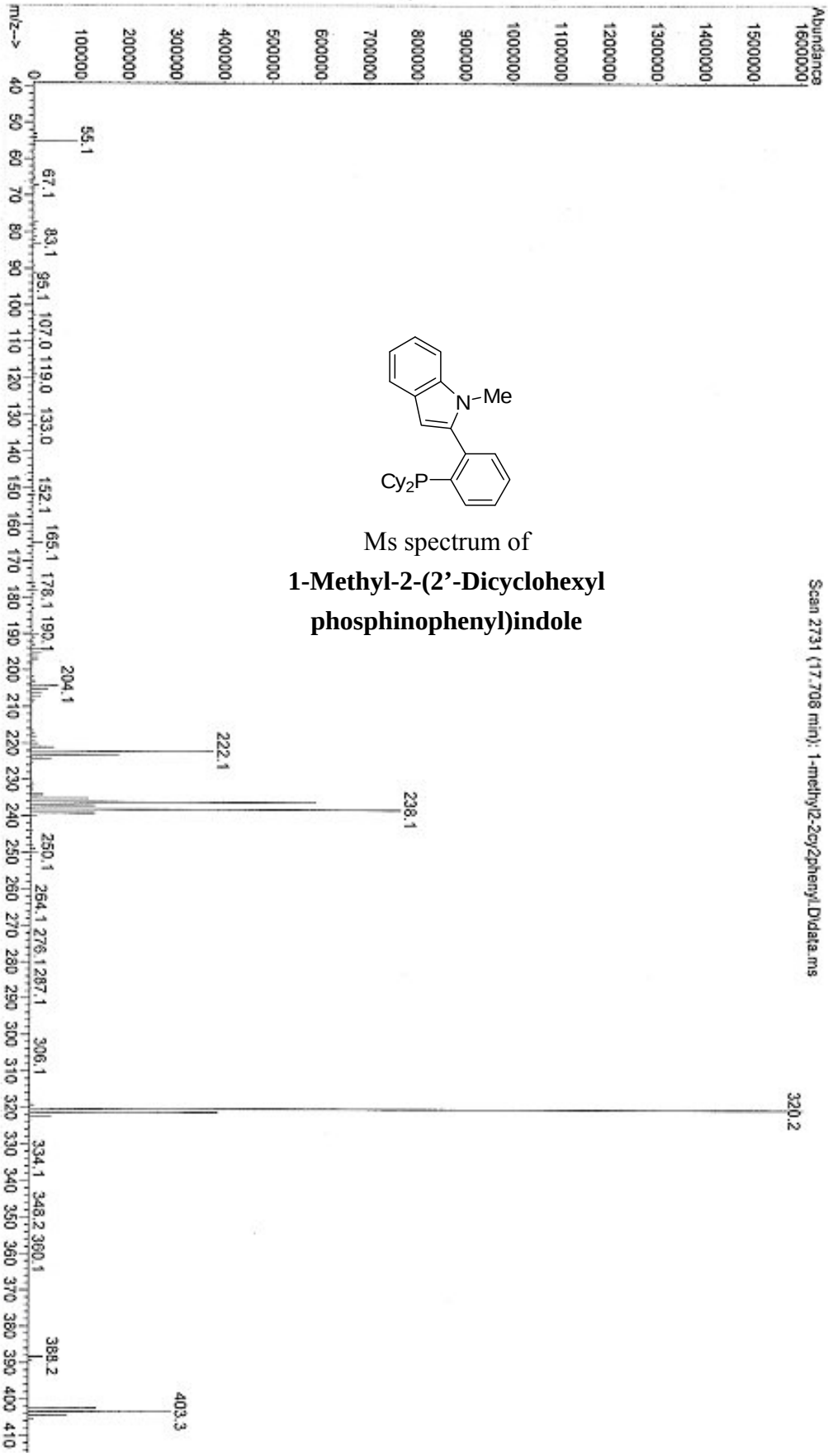

```
F2 - Acquisition Parameters
Date_           20070516
Time              20.14
INSTRUM           dpx400
PROBHD     5 mm QNP 1H
PULPROG           zgdc30
TD                131072
SOLVENT           CD2Cl2
NS                  128
DS                    0
SWH           25125.629 Hz
FIDRES        0.191693 Hz
AQ            2.6083827 sec
RG                9195.2
DW               19.900 usec
DE                4.50 usec
TE              300.0 K
D1            3.00000000 sec
d11           0.03000000 sec

============== CHANNEL f1 ========
NUC1                13C
P1                 5.80 usec
PL1               -5.00 dB
SF01        100.6231263 MHz

============== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                1H
PCPD2             71.00 usec
PL2              120.00 dB
PL12              17.00 dB
SF02        400.1320008 MHz

F2 - Processing parameters
SI                 65536
SF          100.6127838 MHz
WDW                   EM
SSB                    0
LB                1.00 Hz
GB                     0
PC                1.00

1D NMR plot parameters
CX                19.50 cm
FIP           200.000 ppm
F1p           20122.96 Hz
F2P            -0.000 ppm
F2             -0.00 Hz
PPMCM         10.26641 ppm/cm
HZCM          1031.96603 Hz/cm
```



Ms spectrum of

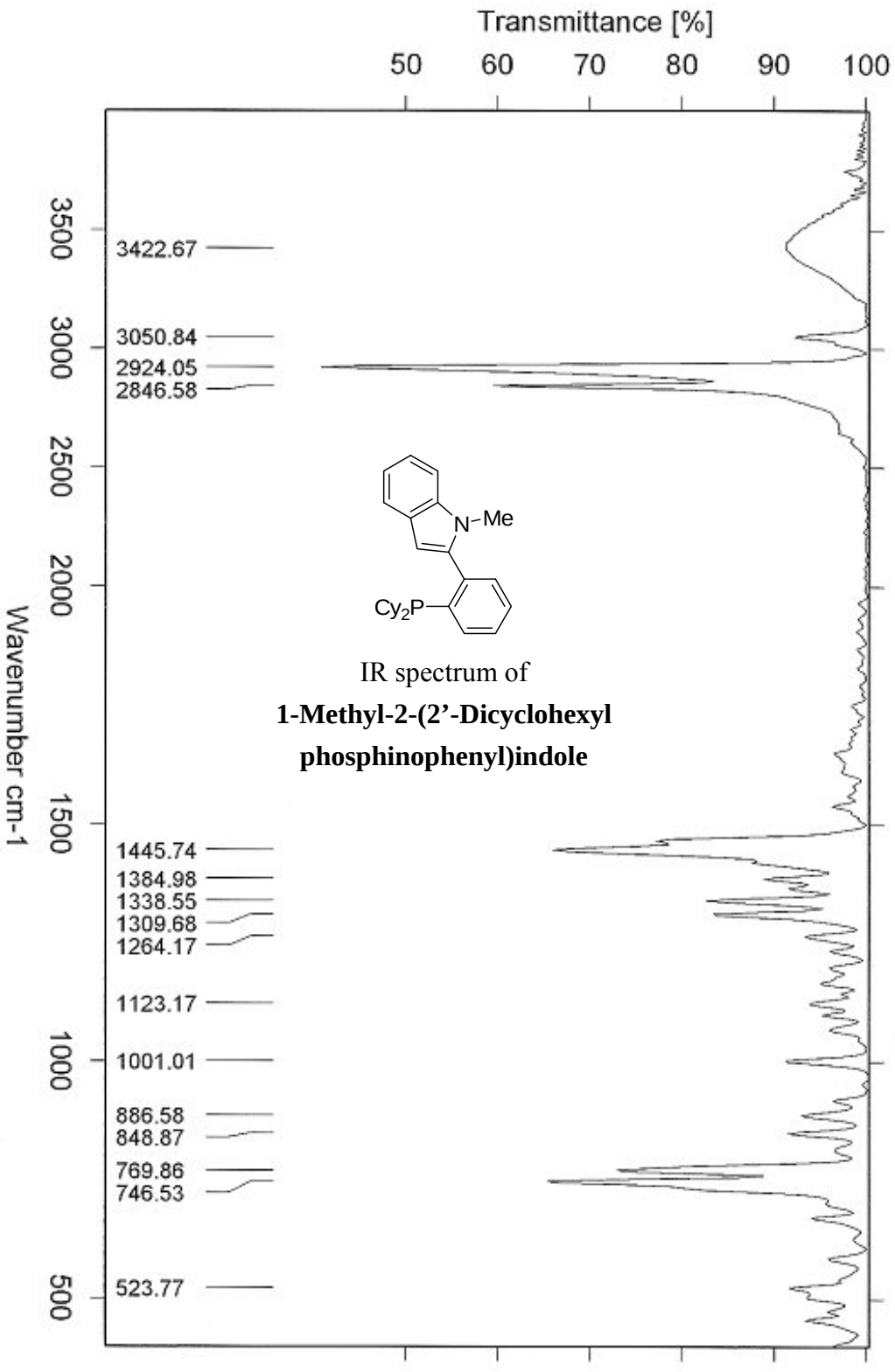
1-Methyl-2-(2'-Dicyclohexyl phosphinophenyl)indole

Accurate Mass Measurement:

Molecular formula:
$C_{27}H_{34}N_1P_1$
$[M]^+$ (theoretical)
= 403.2423

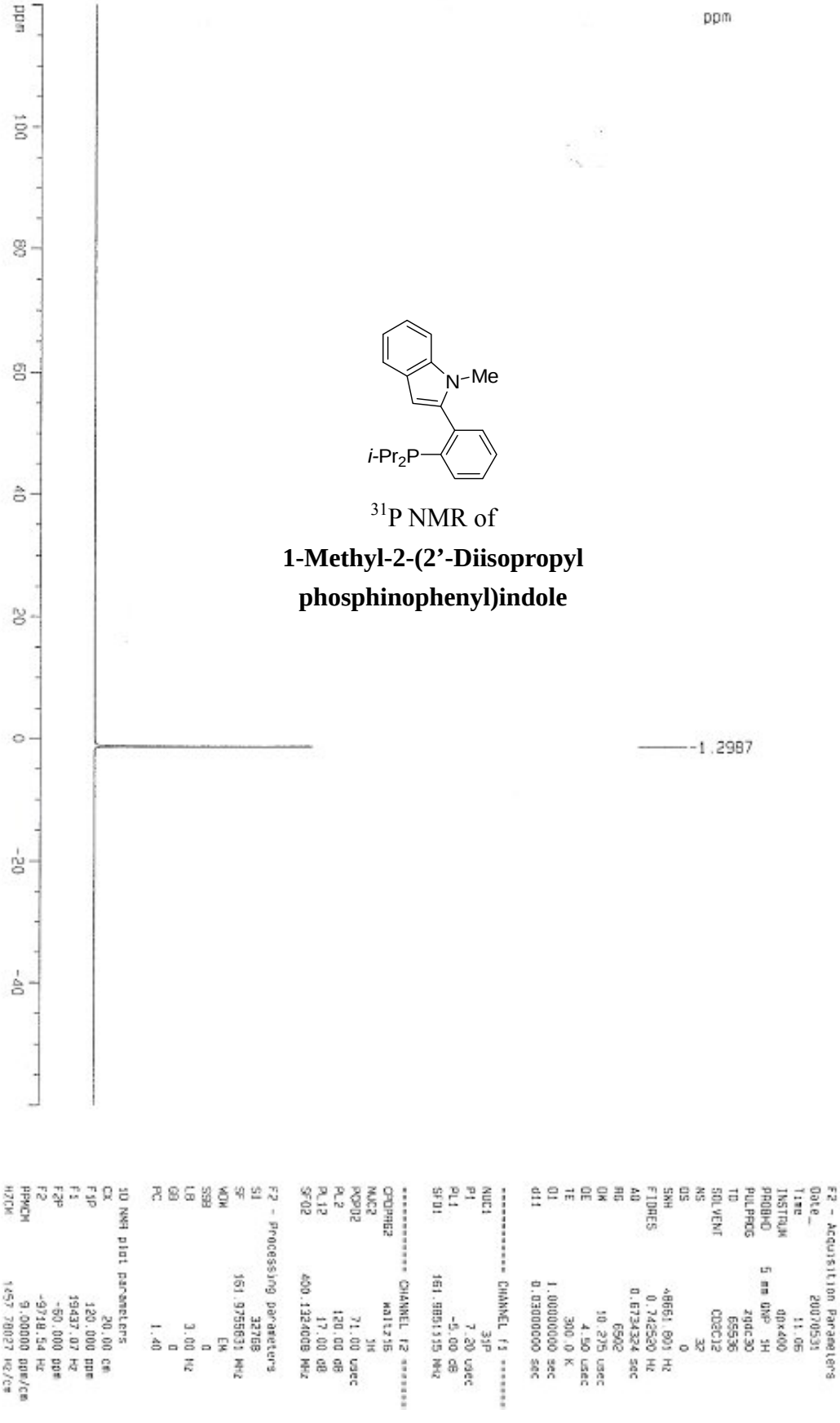
HRMs spectrum of

1-Methyl-2-(2'-Dicyclohexyl phosphinophenyl)indole



IR spectrum of

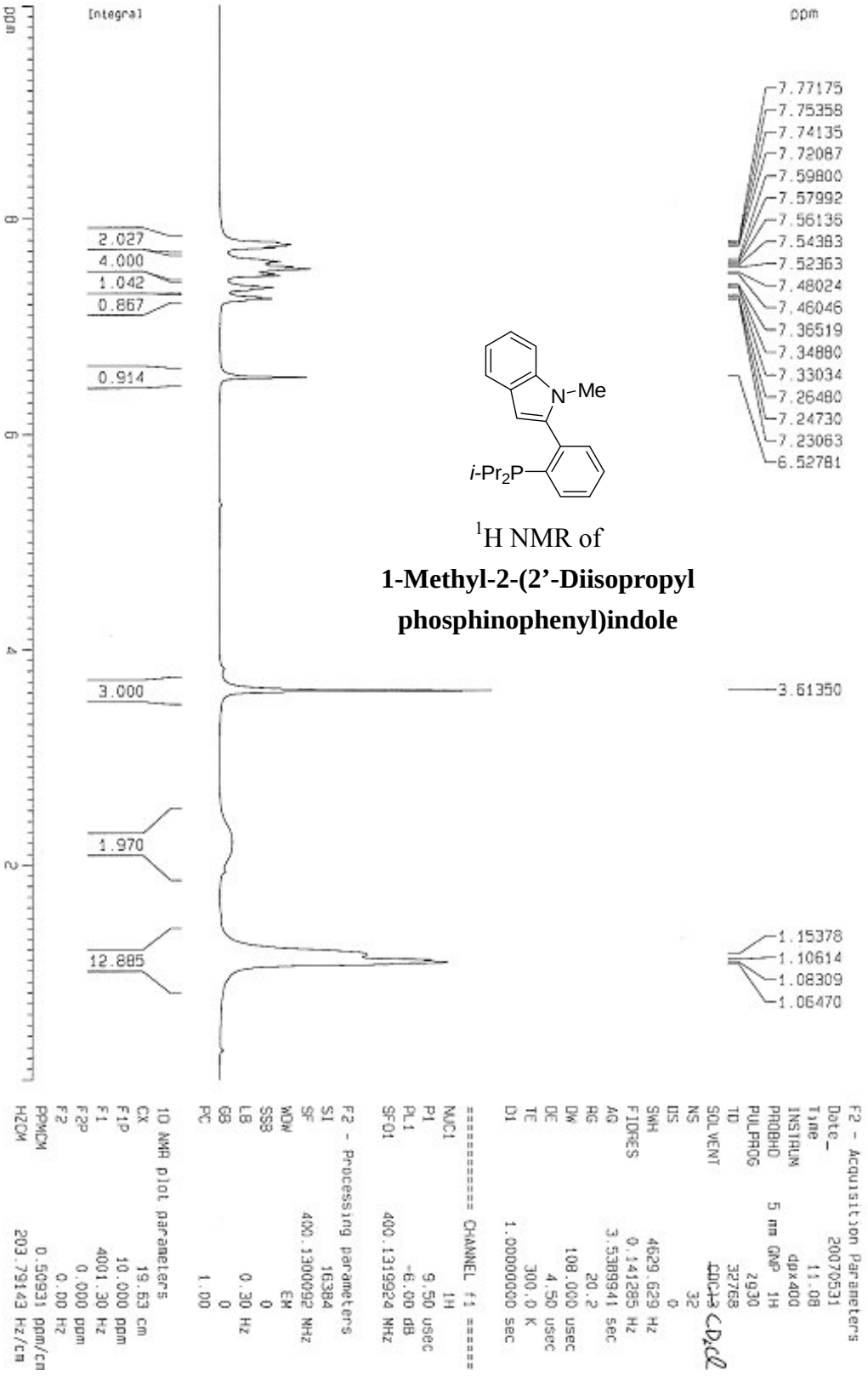
1-Methyl-2-(2'-Dicyclohexyl phosphinophenyl)indole



^{31}P NMR of

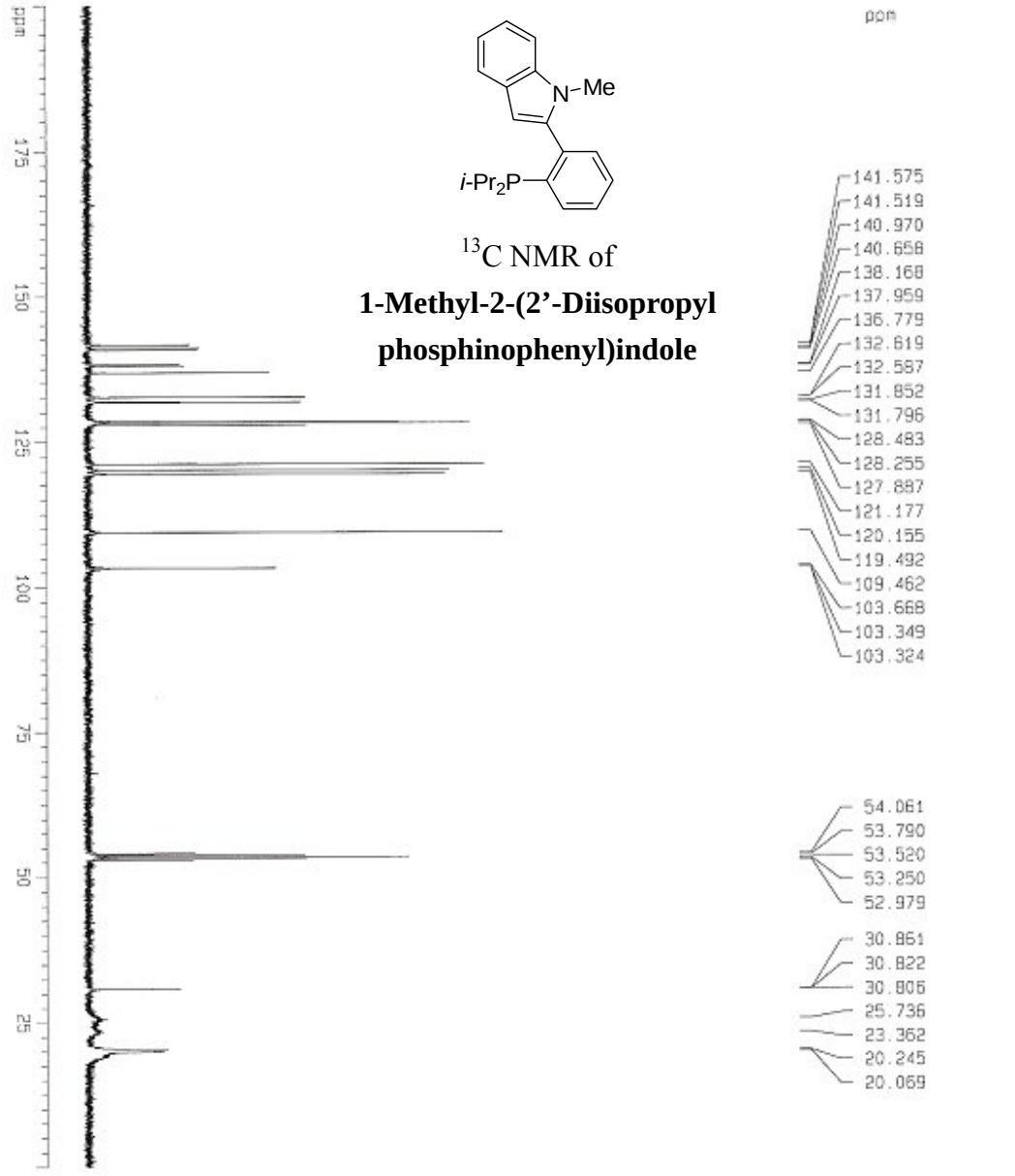
1-Methyl-2-(2'-Diisopropyl phosphinophenyl)indole

F2 - Acquisition Parameters
Date_ 20070531
Time 11.05
INSTRUM dpx400
PROBHD 5 mm DNP 1H
PULPROG zgdc30
TD 65536
SOLVENT CDCl3
NS 32
DS 0
SWH 48661.601 Hz
FIDRES 0.742520 Hz
AQ 0.6734324 sec
RG 6502
DW 10.275 usec
DE 4.50 usec
TE 300.0 K
D1 1.00000000 sec
d11 0.03000000 sec
========== CHANNEL f1 =======
NUC1 31P
P1 7.20 usec
PL1 -5.00 dB
SF01 161.9851315 MHz
========== CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 71.00 usec
PL2 120.00 dB
PL12 17.00 dB
SFO2 400.1324008 MHz
F2 - Processing parameters
SI 32768
SF 161.9756831 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
1D NMR plot parameters
CX 20.00 cm
F1P 120.000 ppm
F1 19437.07 Hz
F2P -60.000 ppm
F2 -9718.54 Hz
PPMCM 9.00000 ppm/cm
HZCM 1457.70027 Hz/cm



^{1}H NMR of

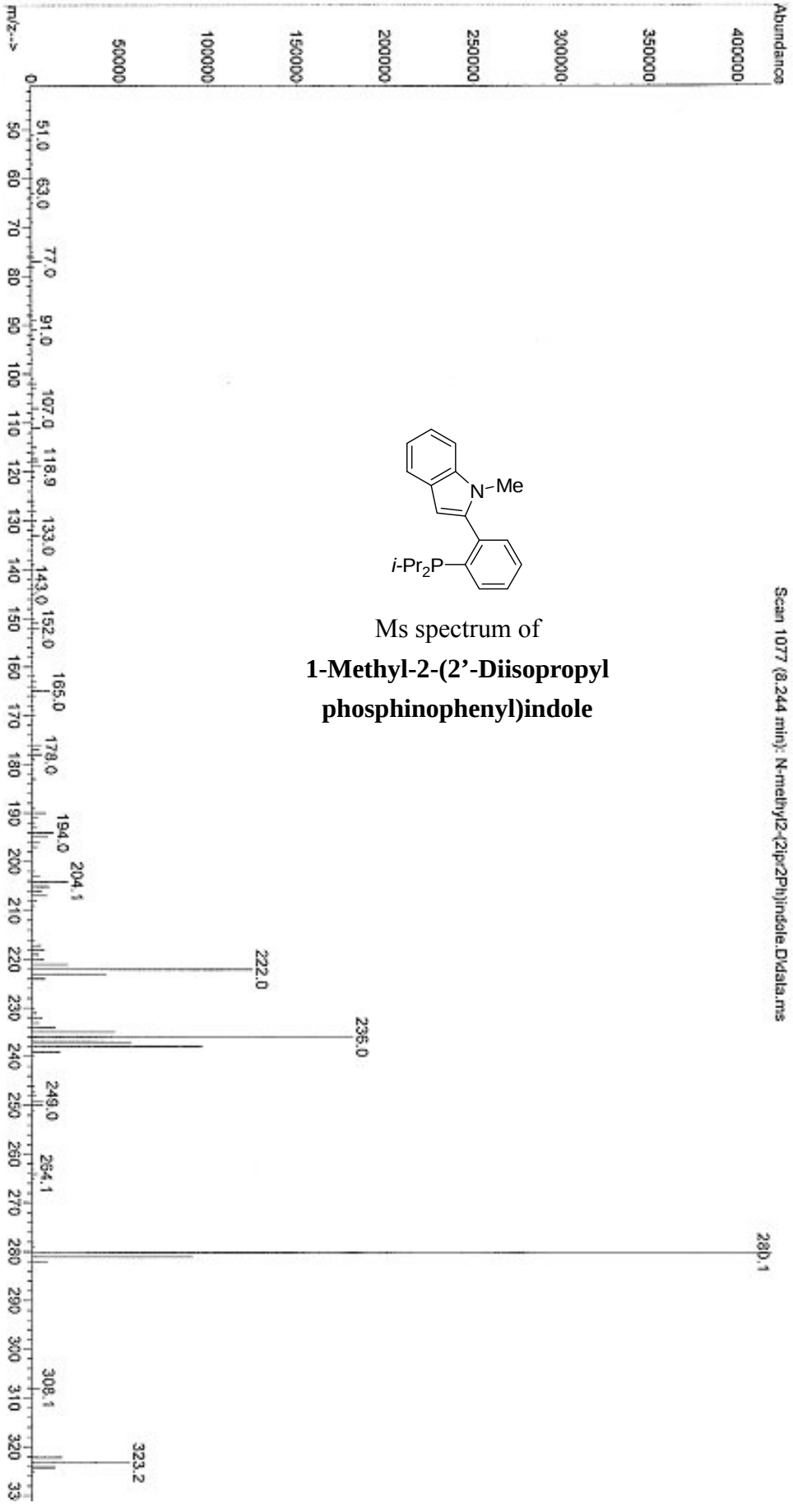
1-Methyl-2-(2'-Diisopropyl phosphinophenyl)indole



^{13}C NMR of

1-Methyl-2-(2'-Diisopropyl phosphinophenyl)indole

F2 - Acquisition Parameters
Date_ 20070531
Time 11.20
INSTRUM dpx400
PROBHD 5 mm BNP 1H
PULPROG zgdc30
TD 131072
SOLVENT CDCl3
NS 128
DS 0
SWH 25125.629 Hz
FIDRES 0.191693 Hz
AQ 2.6083827 sec
RG 9195.2
DW 19.900 usec
DE 4.50 usec
TE 300.0 K
D1 3.00000000 sec
d11 0.03000000 sec
========== CHANNEL f1 ========
NUC1 13C
P1 6.80 usec
PL1 -6.00 dB
SF01 100.6231263 MHz
========== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 71.00 usec
PL2 120.00 dB
PL12 17.00 dB
SF02 400.1320008 MHz
F2 - Processing parameters
SI 65536
SF 100.6137679 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 19.50 cm
F1P 200.000 ppm
F1 20122.55 Hz
F2P -0.000 ppm
F2 -0.00 Hz
PPMCM 10.25641 ppm/cm
HZCM 1031.92590 Hz/cm



Ms spectrum of

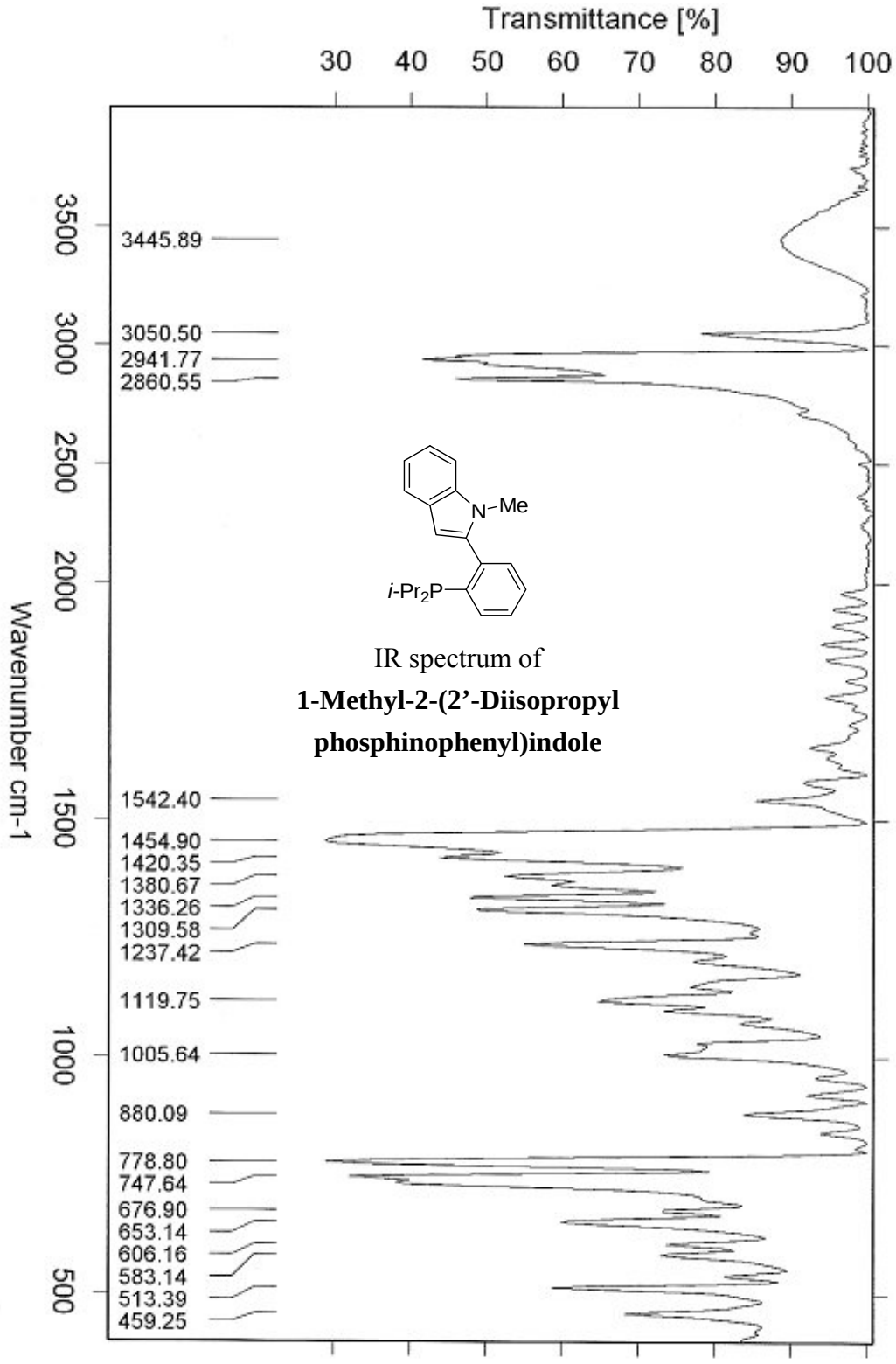
1-Methyl-2-(2'-Diisopropyl phosphinophenyl)indole

Accurate Mass Measurement:

Molecular formula: $C_{21}H_{26}N_1P_1$
$[M]^+$ (theoretical) = 323.1797

HRMs spectrum of

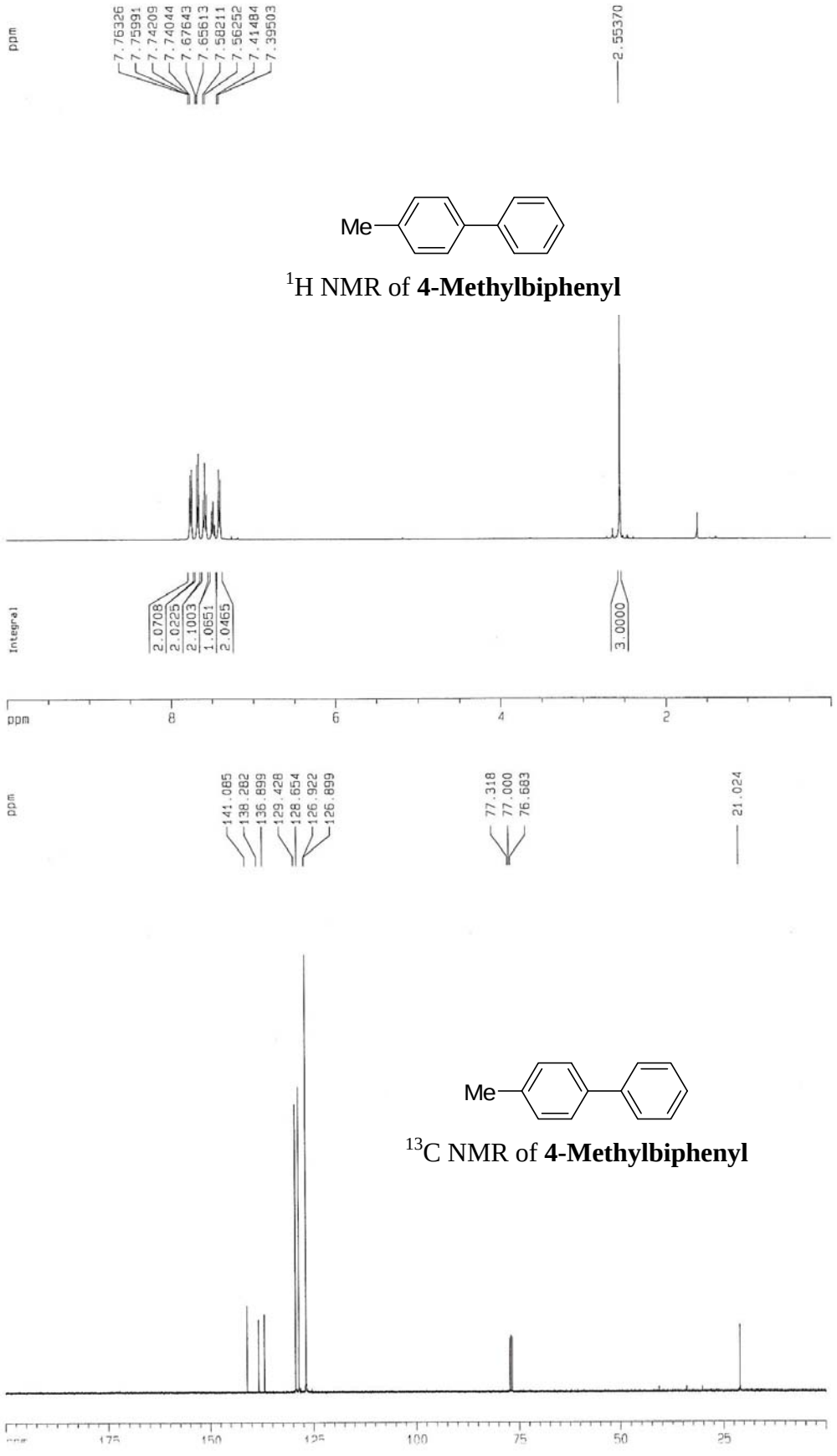
1-Methyl-2-(2'-Diisopropyl phosphinophenyl)indole



IR spectrum of

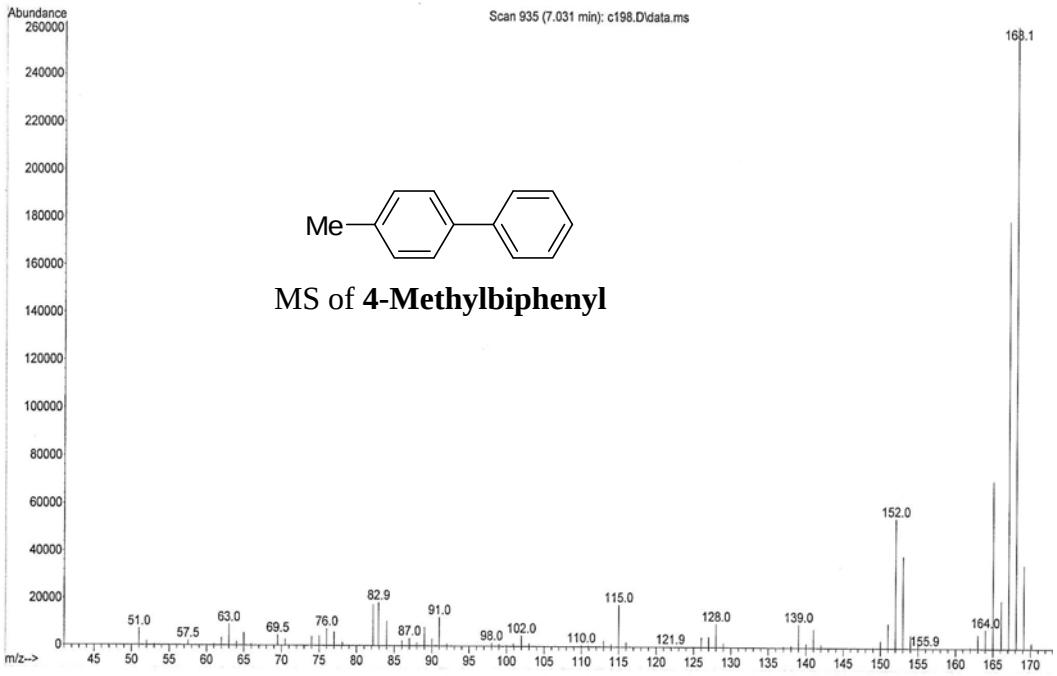
1-Methyl-2-(2'-Diisopropyl phosphinophenyl)indole

Product Spectrum

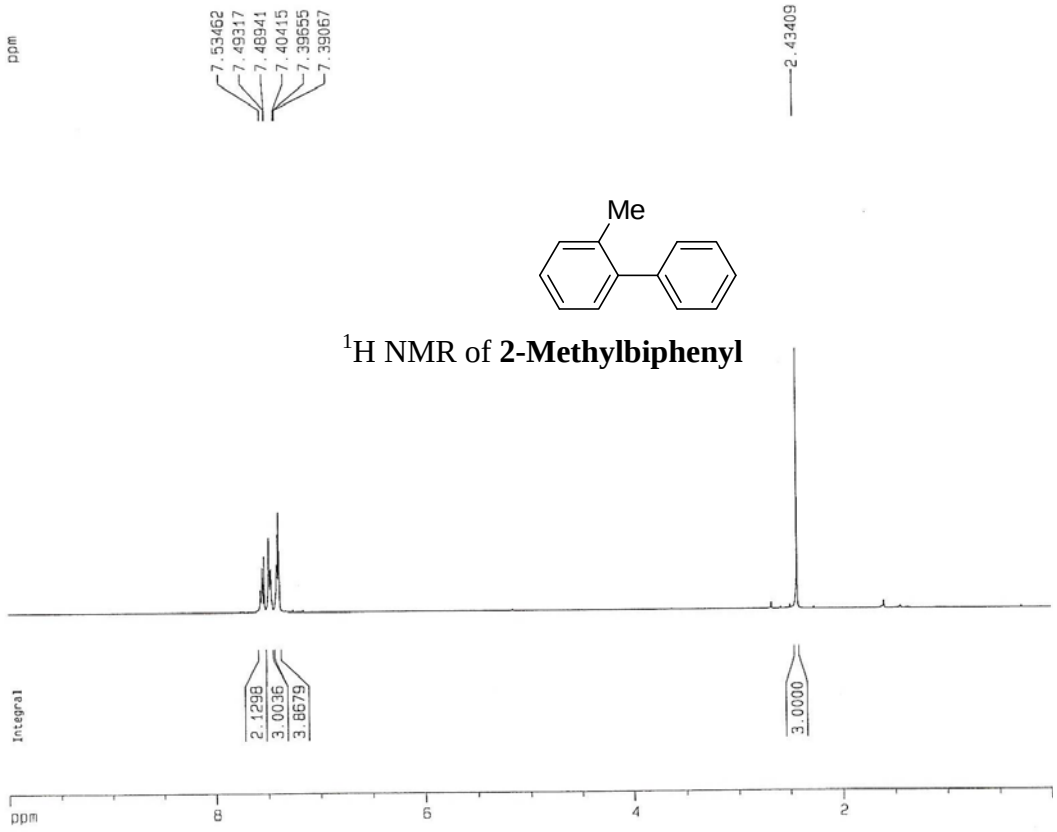


^{1}H NMR of **4-Methylbiphenyl**

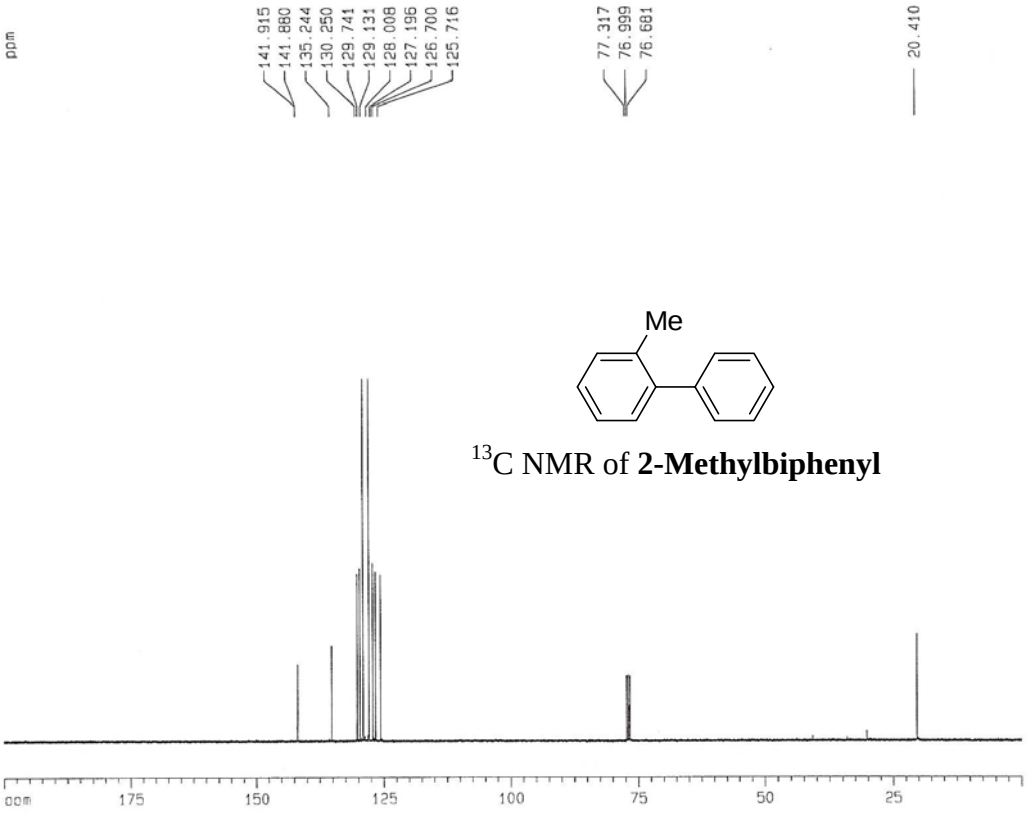
^{13}C NMR of **4-Methylbiphenyl**



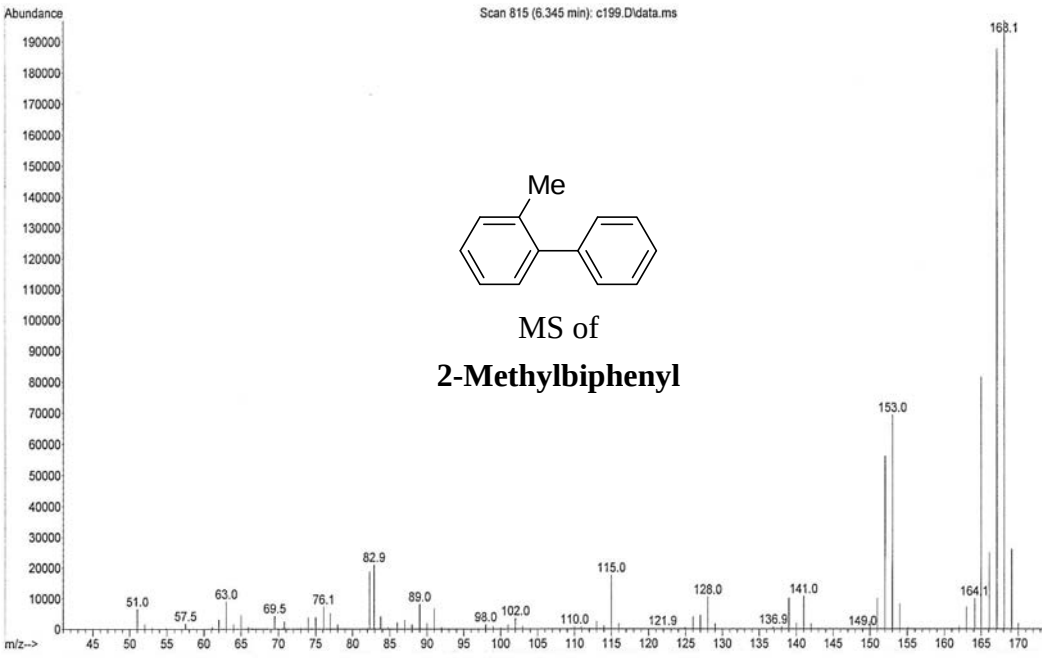
MS of **4-Methylbiphenyl**



^{1}H NMR of **2-Methylbiphenyl**

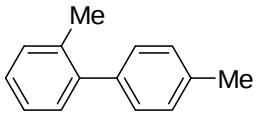


^{13}C NMR of **2-Methylbiphenyl**



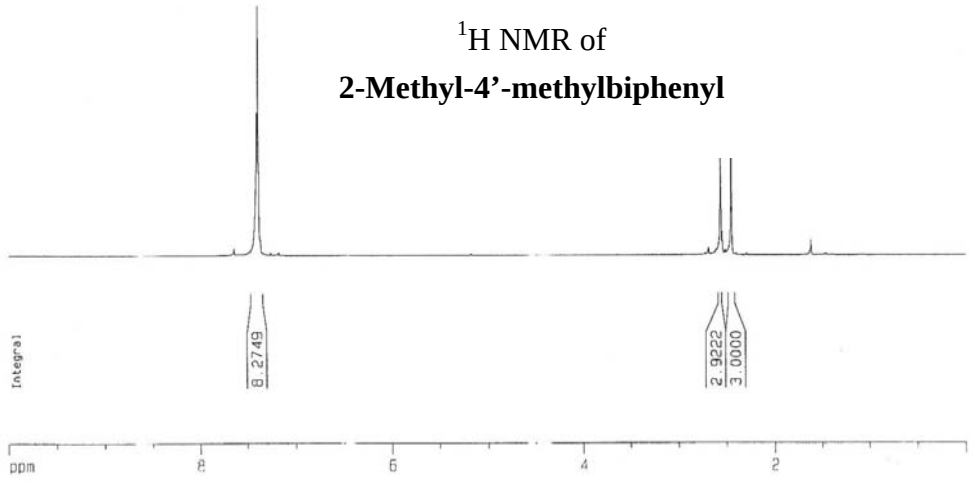
MS of

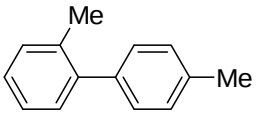
2-Methylbiphenyl



^{1}H NMR of

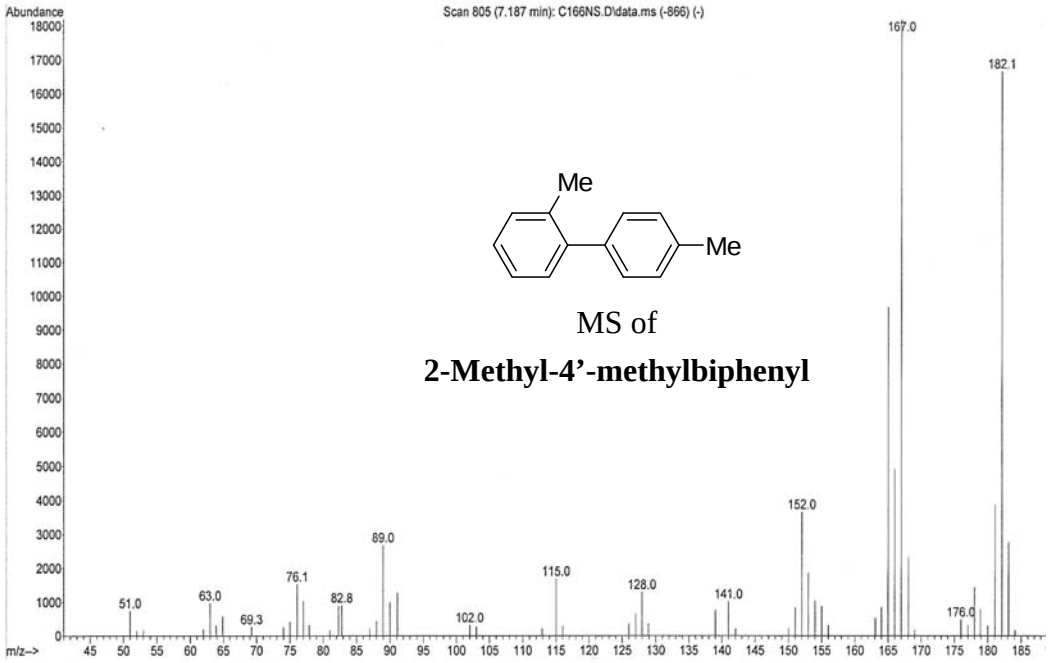
2-Methyl-4’-methylbiphenyl





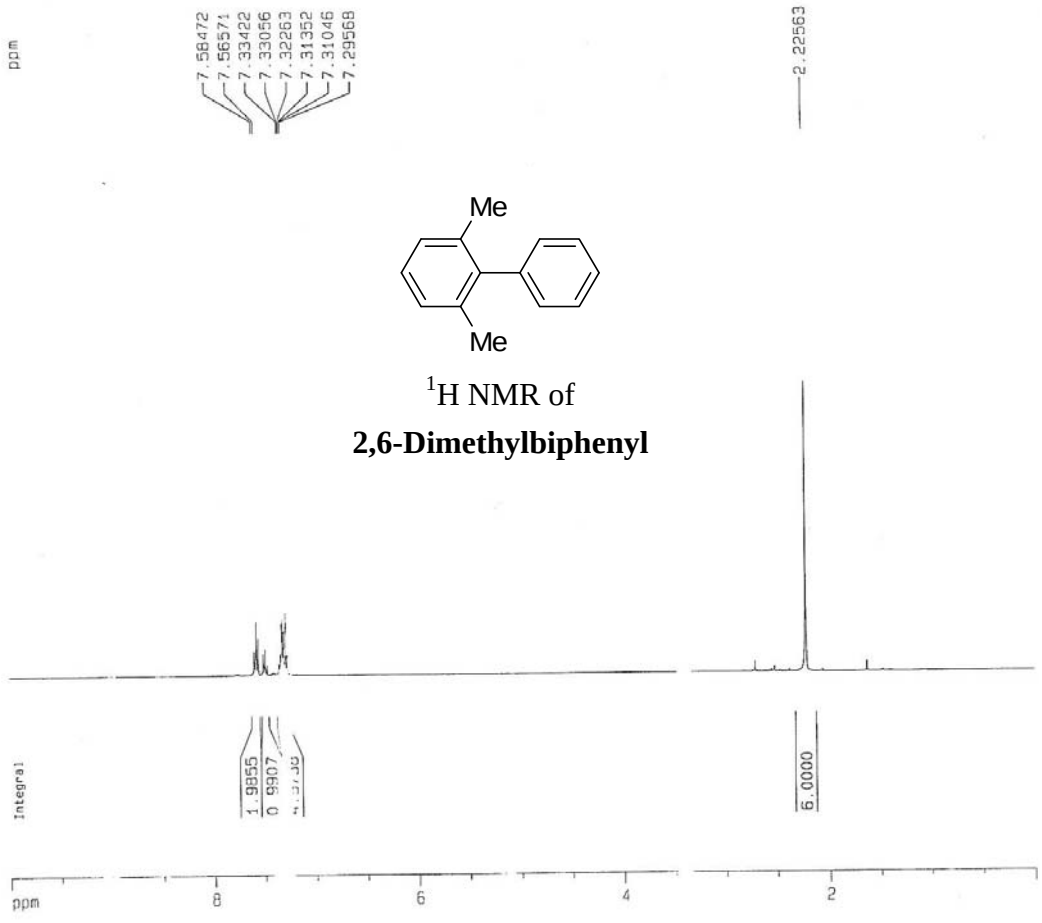
^{13}C NMR of

2-Methyl-4’-methylbiphenyl



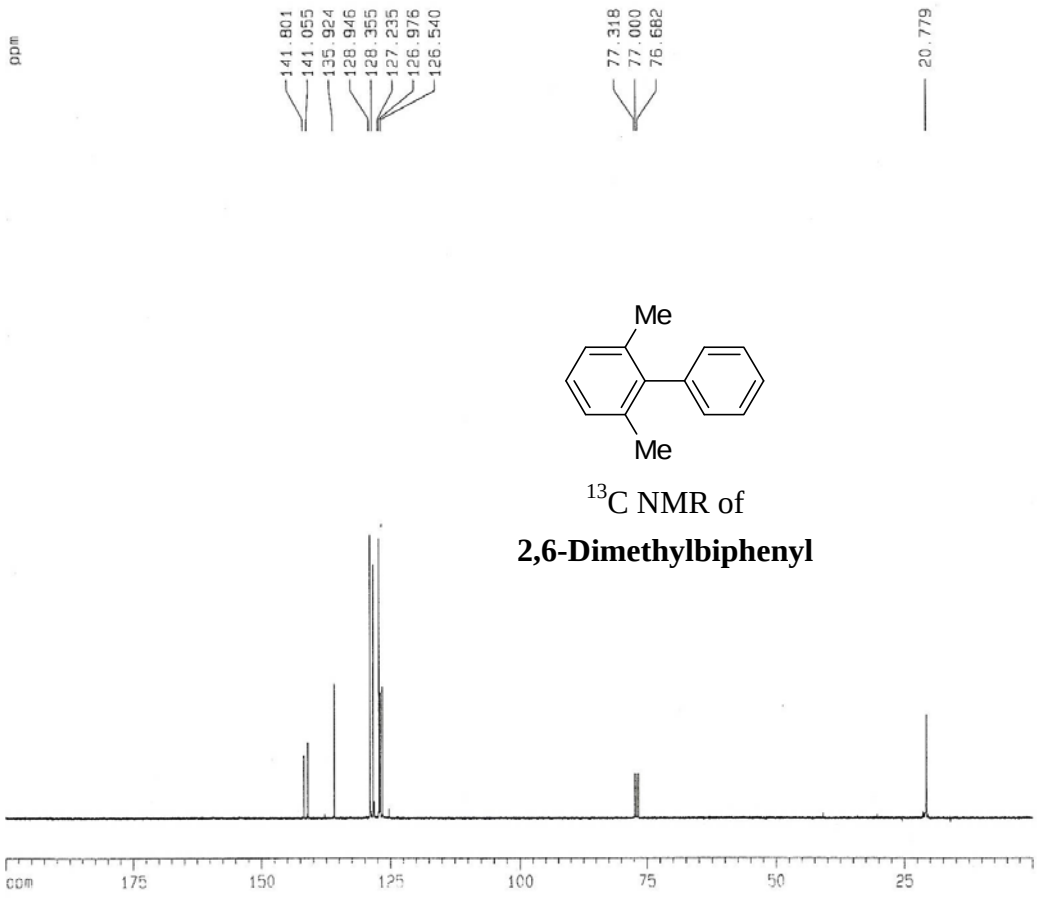
MS of

2-Methyl-4'-methylbiphenyl



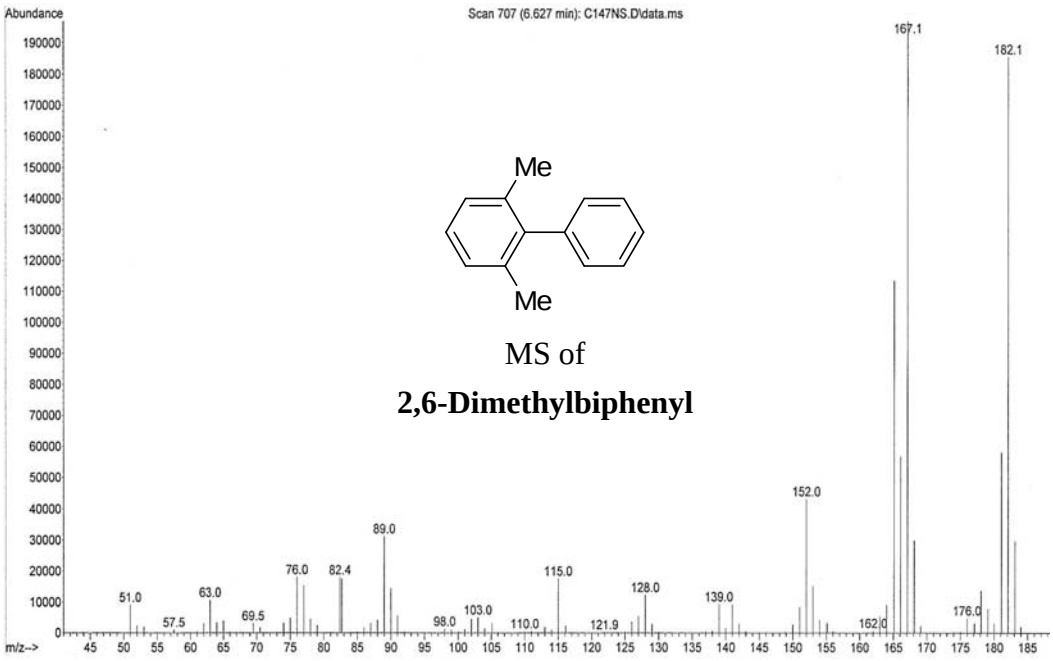
^{1}H NMR of

2,6-Dimethylbiphenyl



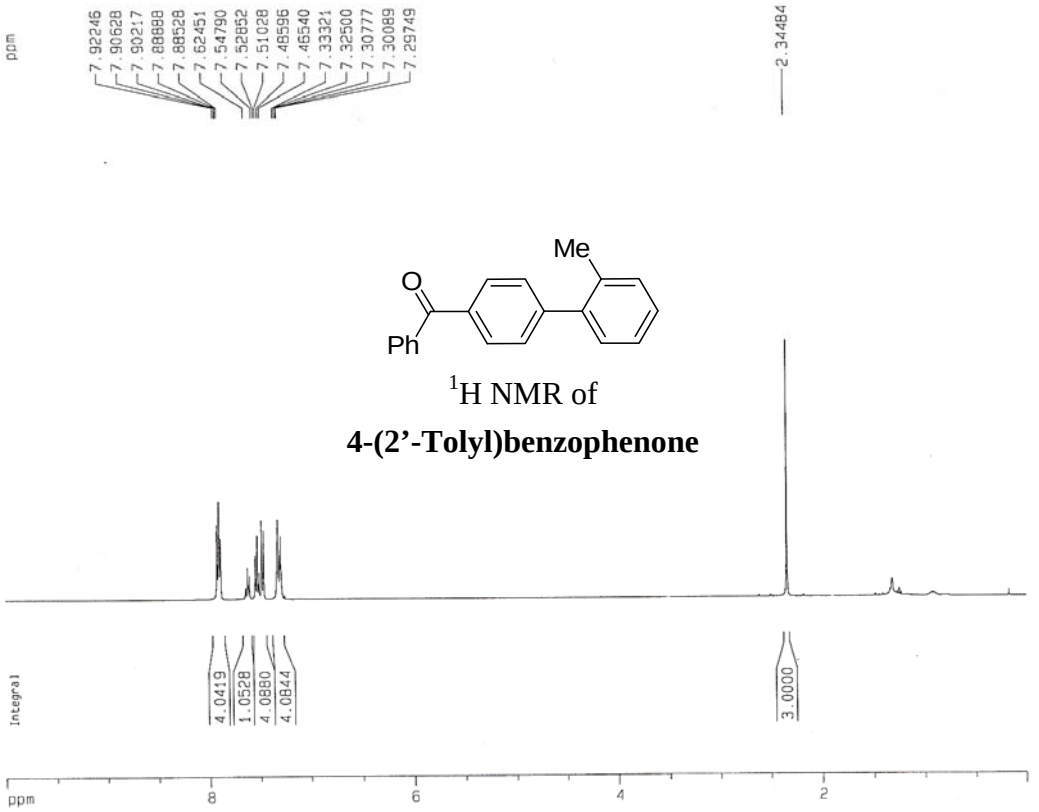
^{13}C NMR of

2,6-Dimethylbiphenyl



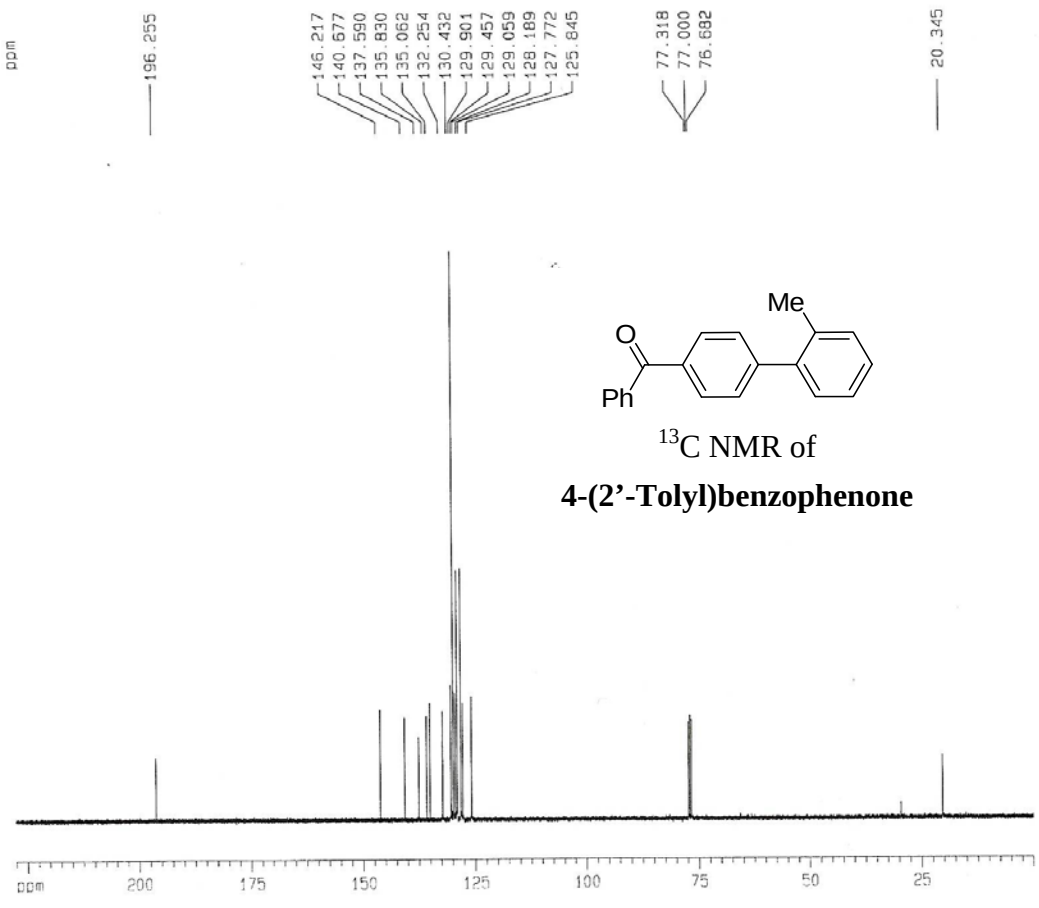
MS of

2,6-Dimethylbiphenyl



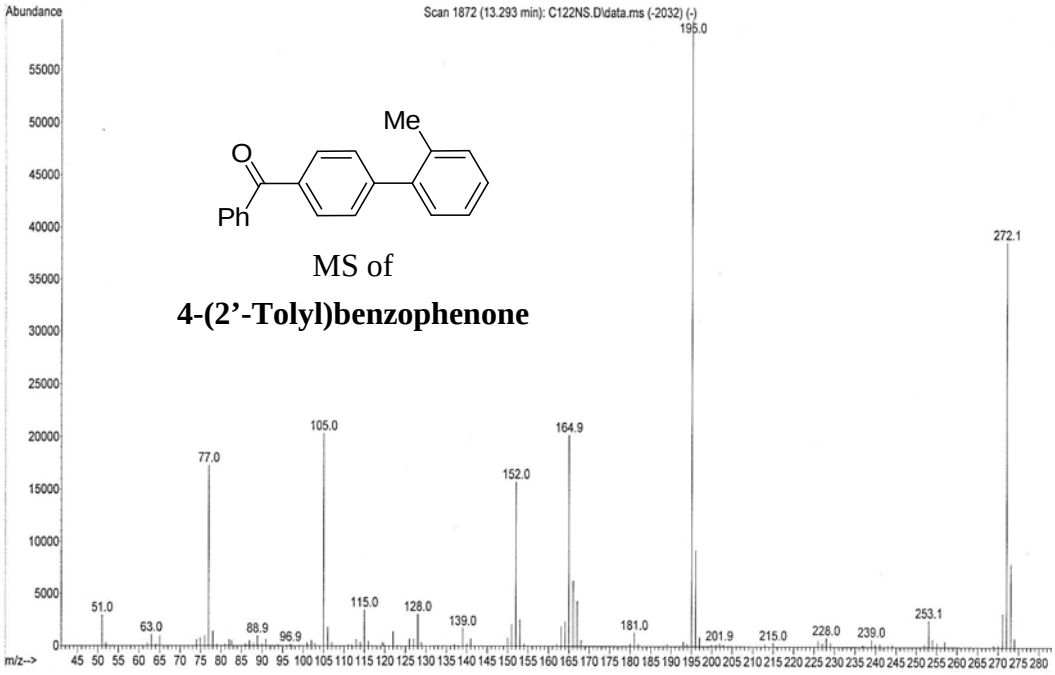
^{1}H NMR of

4-(2'-Tolyl)benzophenone



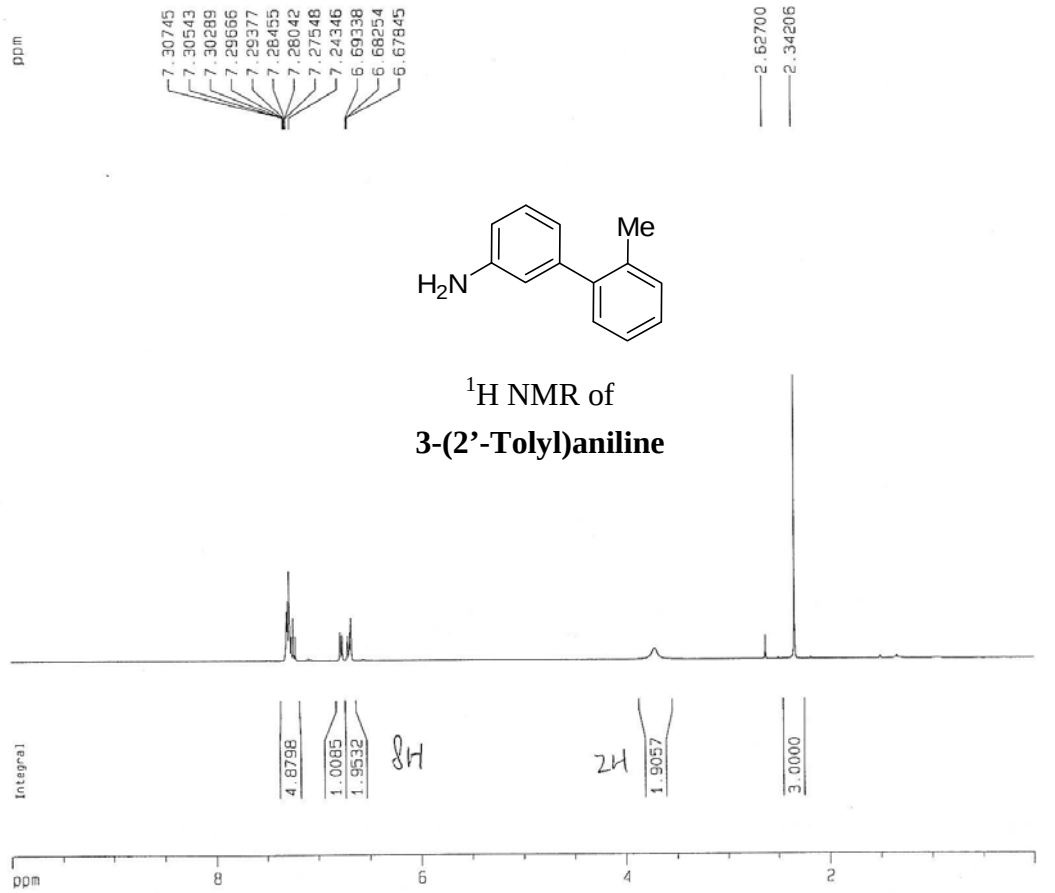
^{13}C NMR of

4-(2'-Tolyl)benzophenone



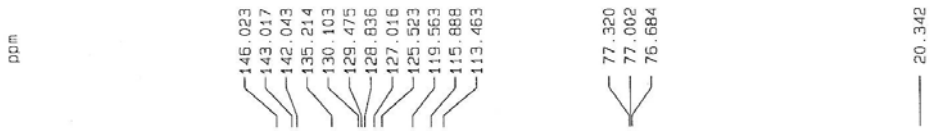
MS of

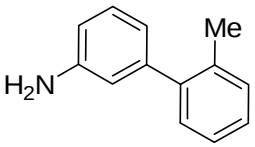
4-(2'-Tolyl)benzophenone



^{1}H NMR of

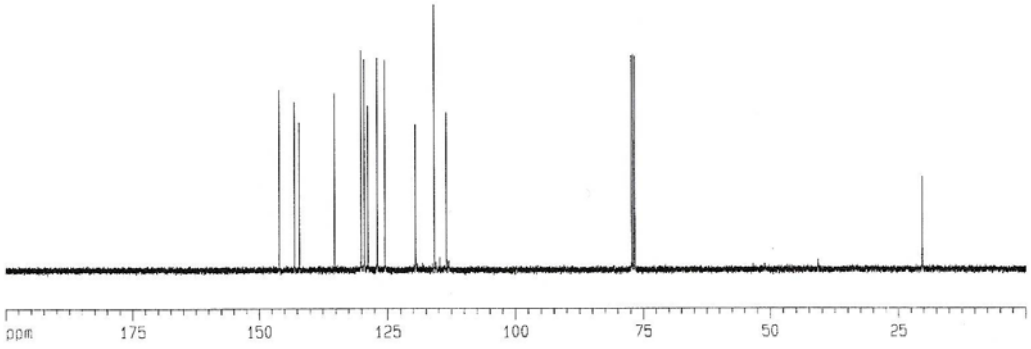
3-(2'-Tolyl)aniline

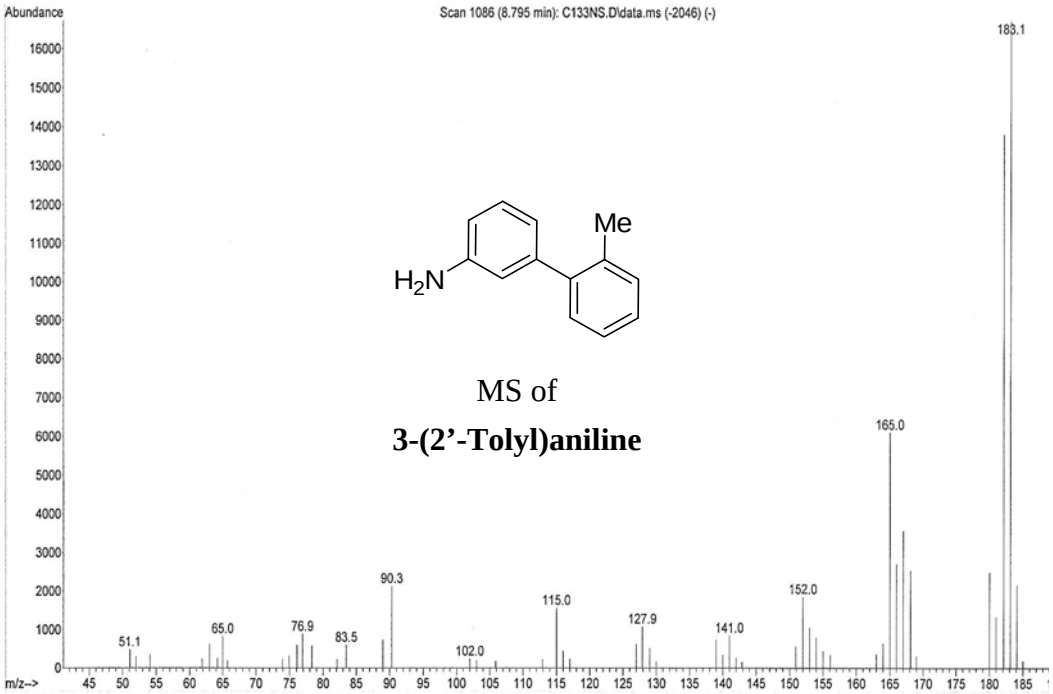




^{13}C NMR of

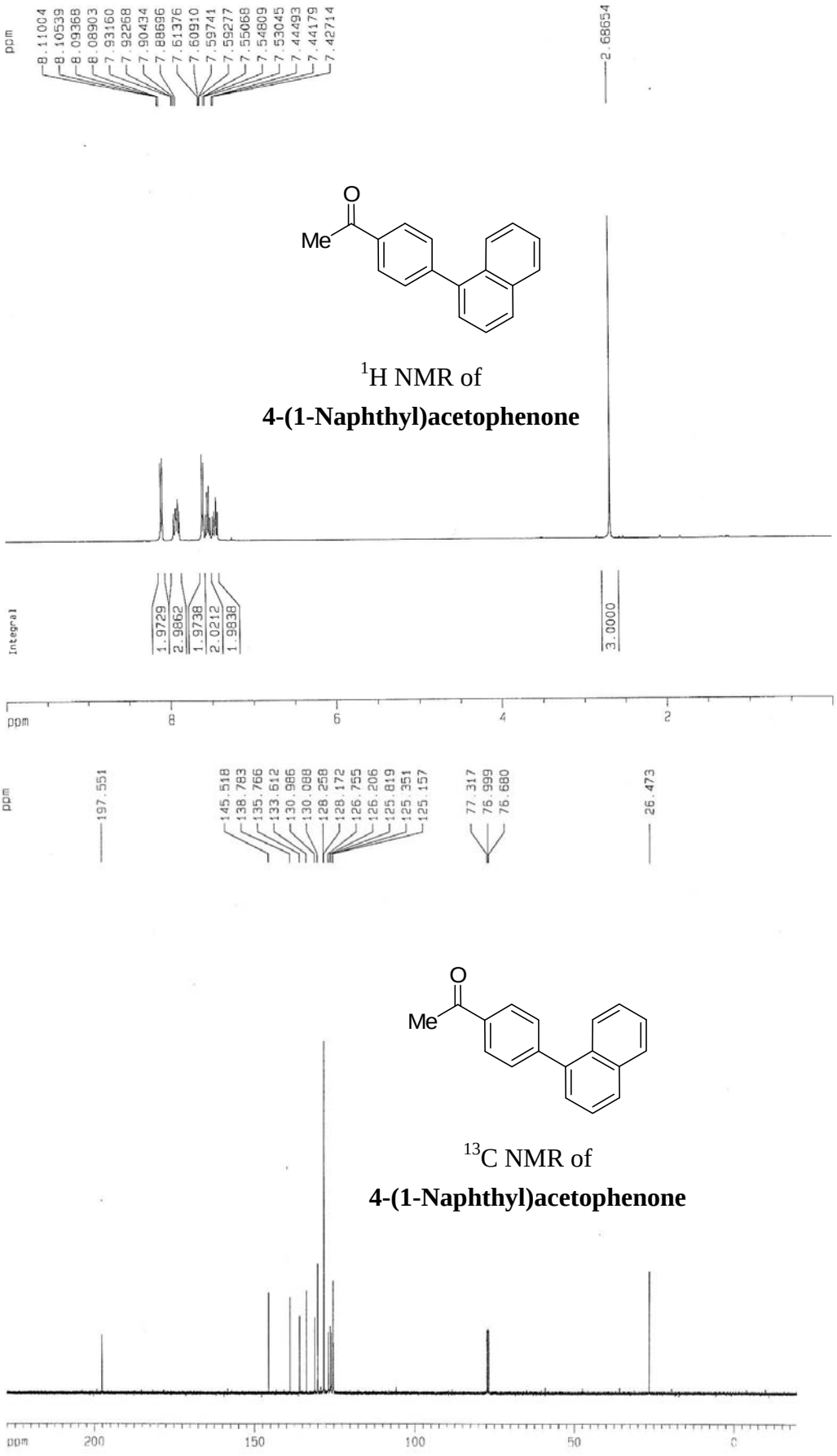
3-(2'-Tolyl)aniline





MS of

3-(2'-Tolyl)aniline

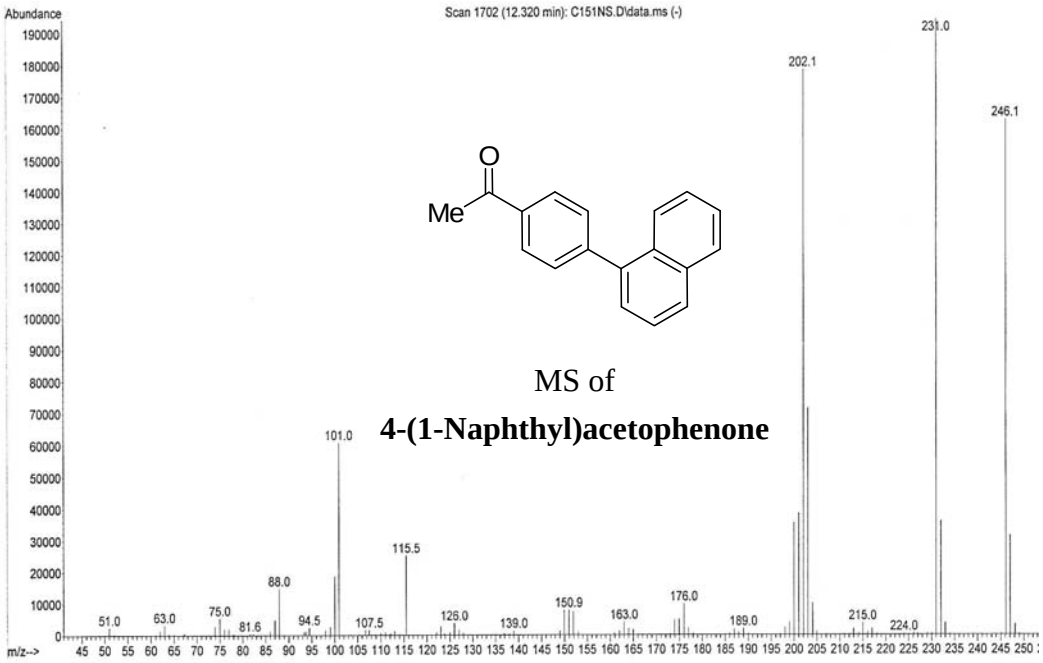


^{1}H NMR of

4-(1-Naphthyl)acetophenone

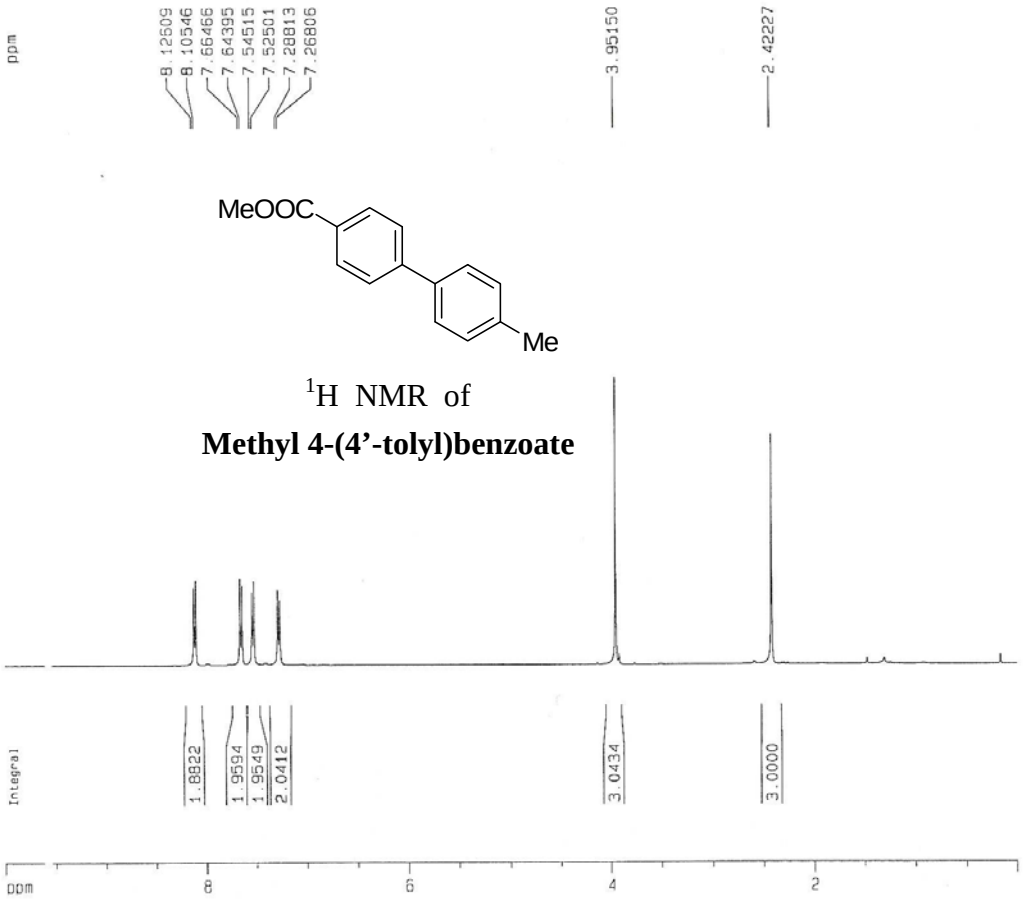
^{13}C NMR of

4-(1-Naphthyl)acetophenone



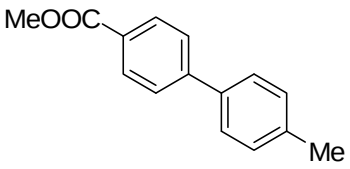
MS of

4-(1-Naphthyl)acetophenone



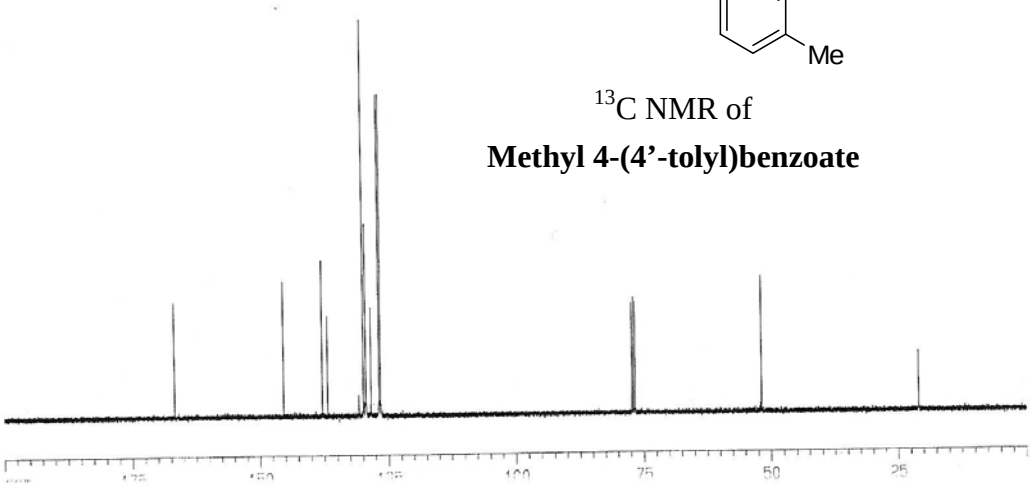
^{1}H NMR of

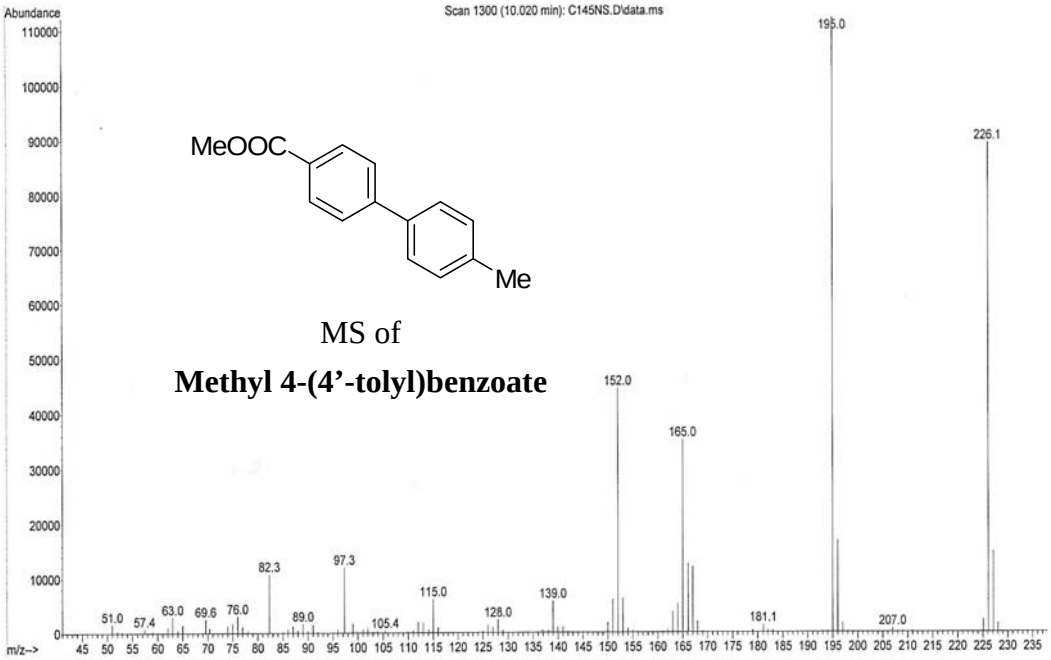
Methyl 4-(4'-tolyl)benzoate



^{13}C NMR of

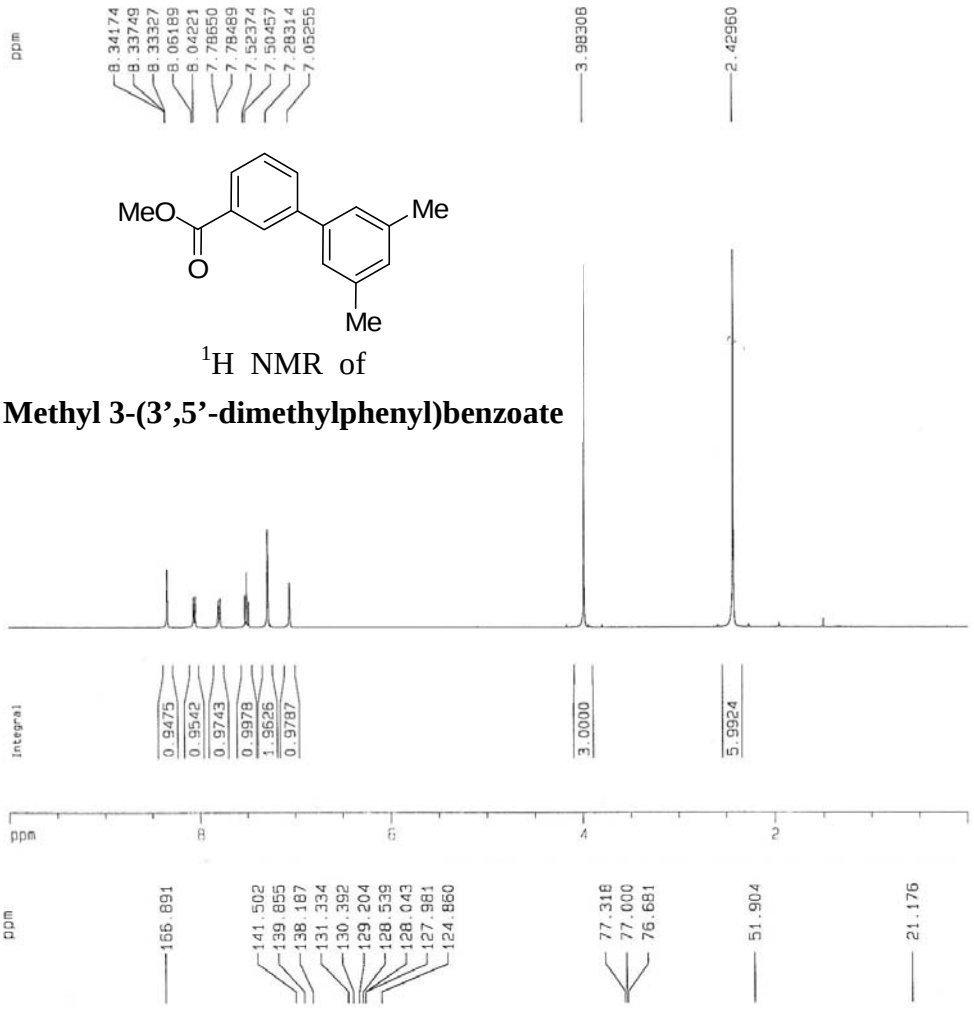
Methyl 4-(4'-tolyl)benzoate





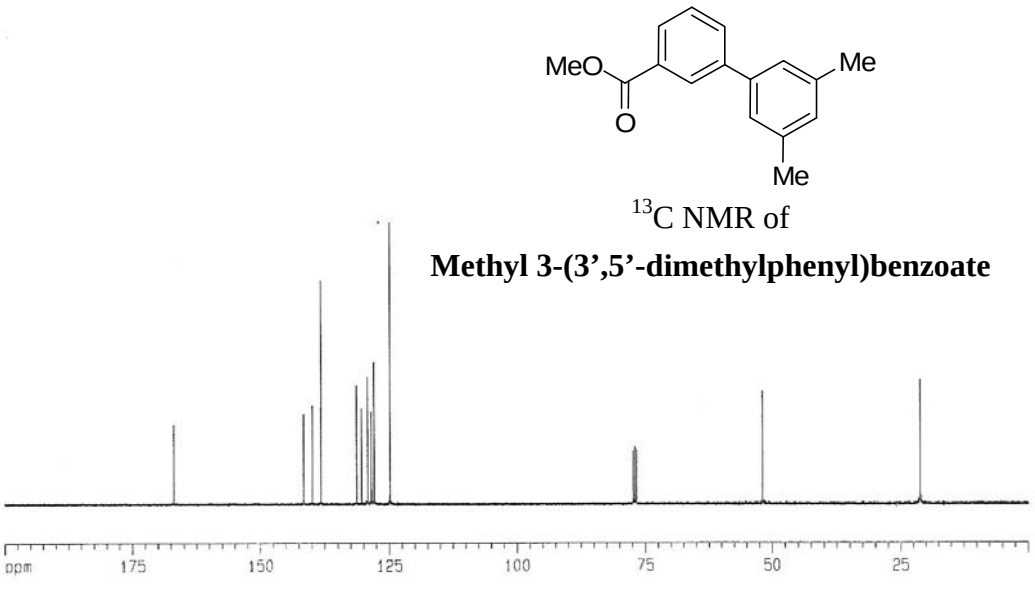
MS of

Methyl 4-(4'-tolyl)benzoate



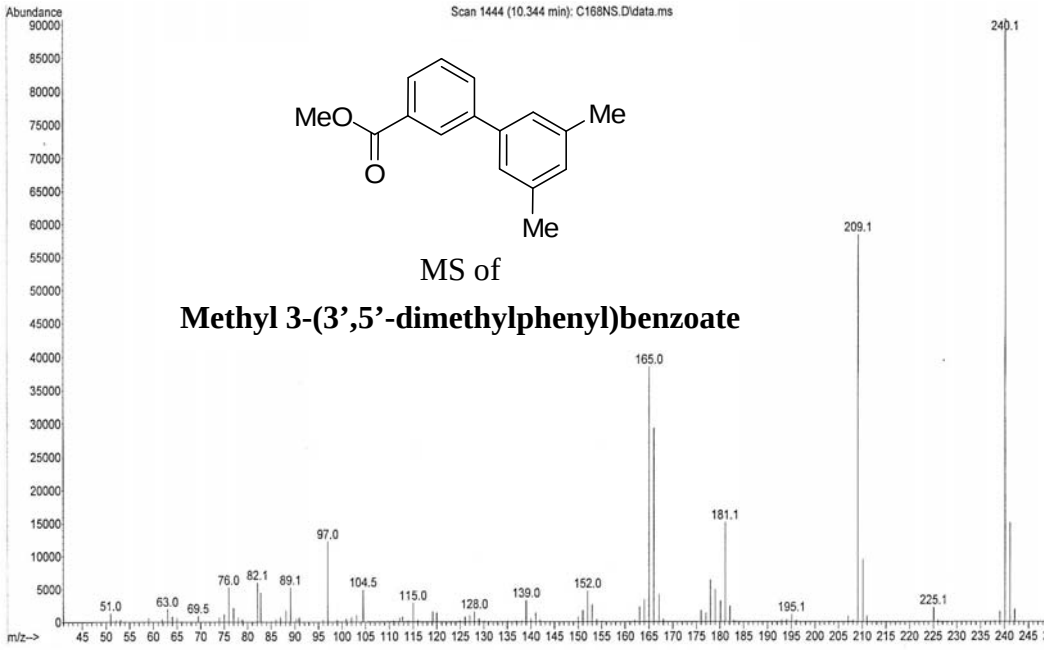
^{1}H NMR of

Methyl 3-(3',5'-dimethylphenyl)benzoate



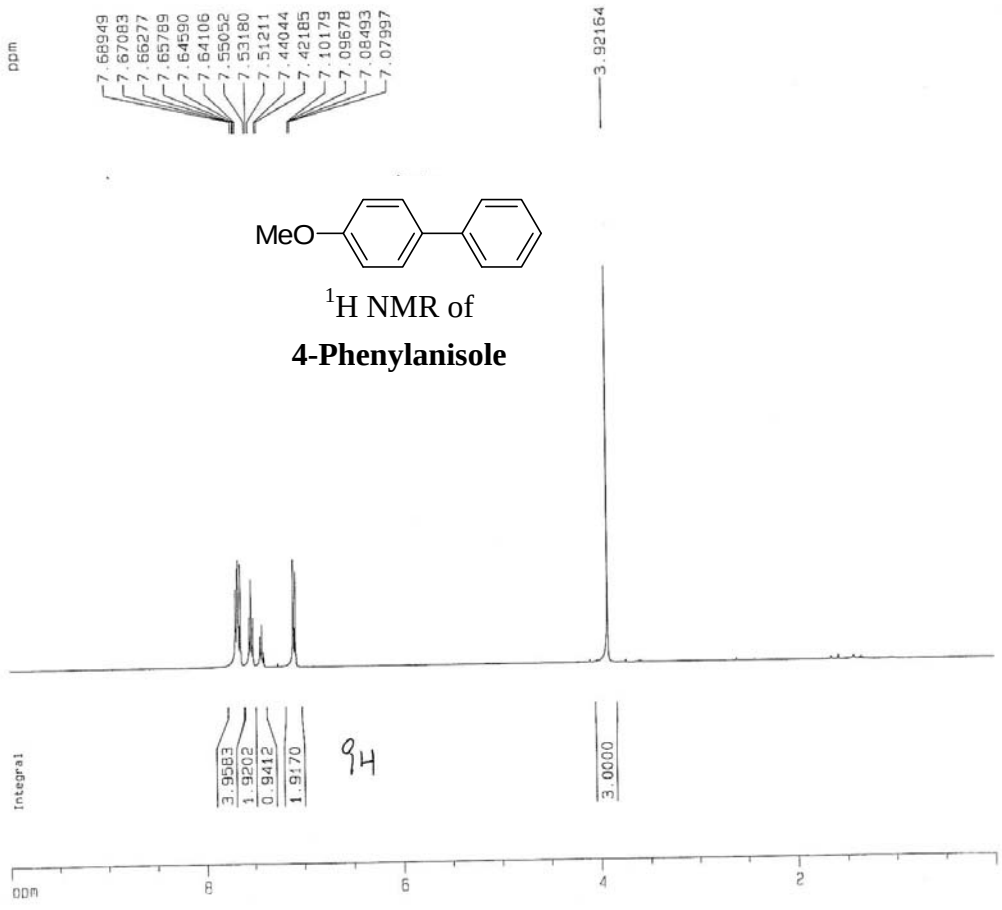
^{13}C NMR of

Methyl 3-(3',5'-dimethylphenyl)benzoate



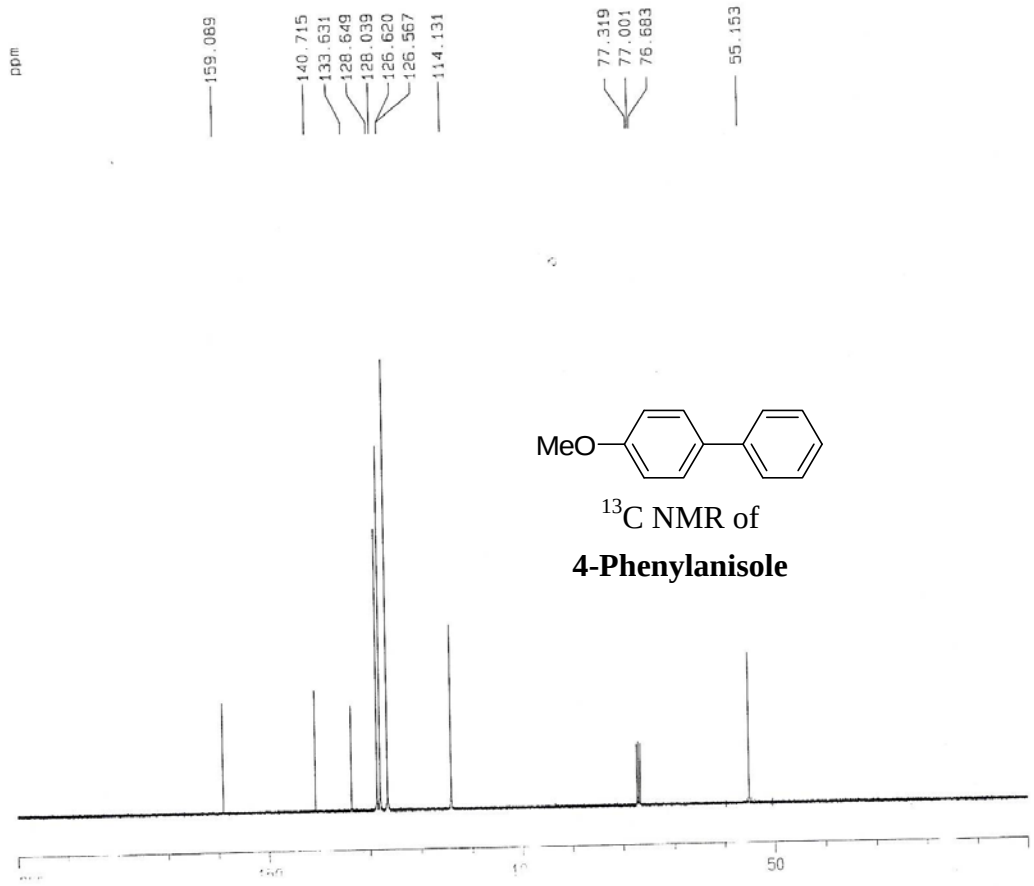
MS of

Methyl 3-(3',5'-dimethylphenyl)benzoate

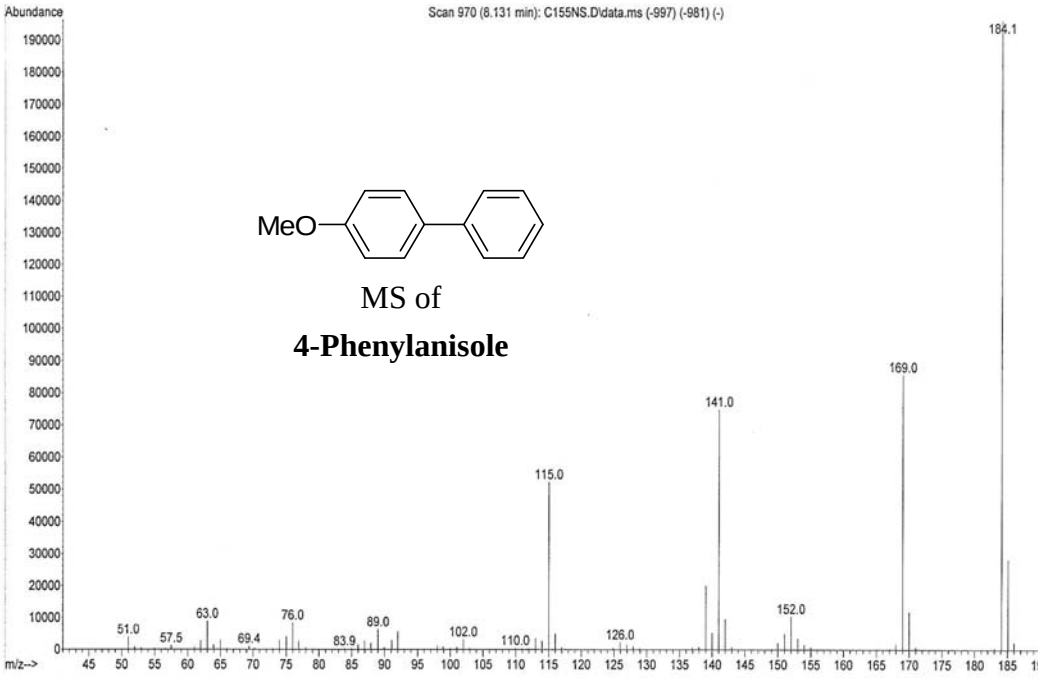


^{1}H NMR of

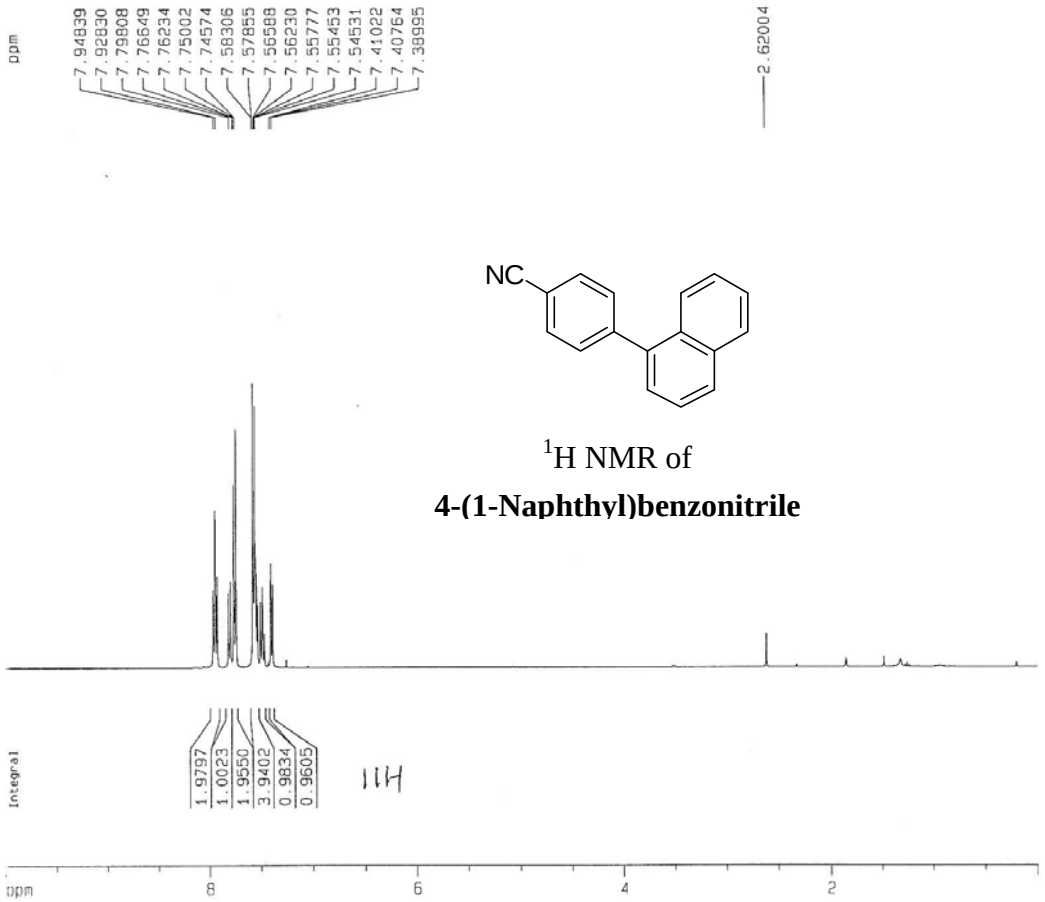
4-Phenylanisole



^{13}C NMR of
4-Phenylanisole

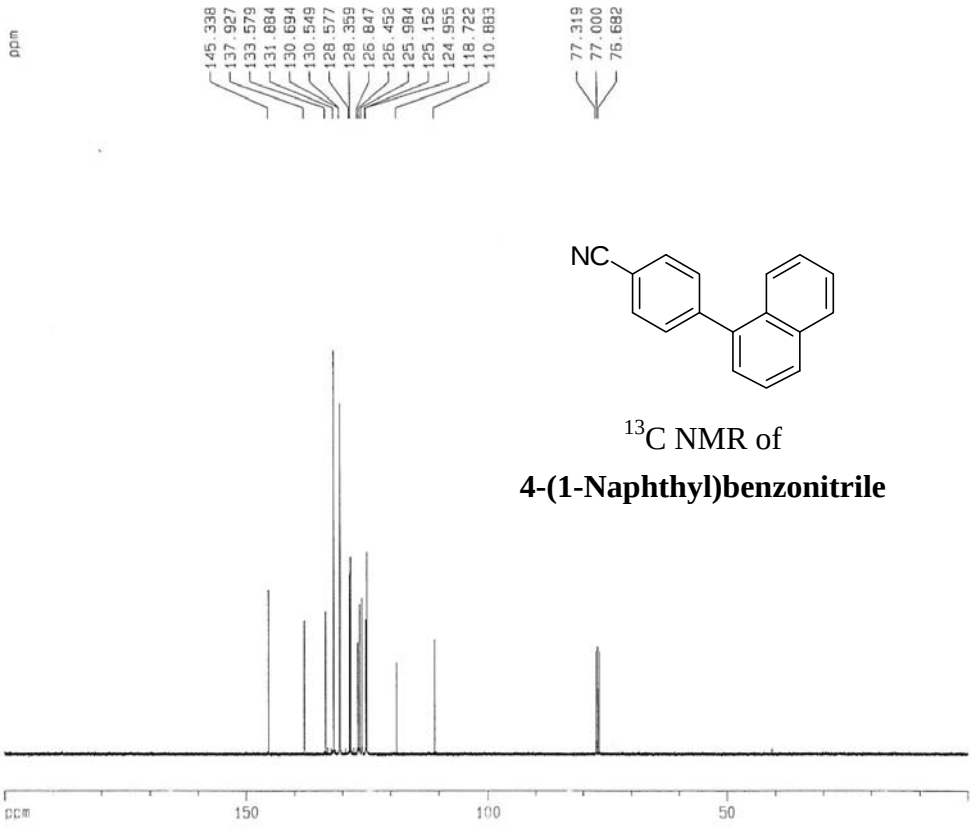


MS of
4-Phenylanisole



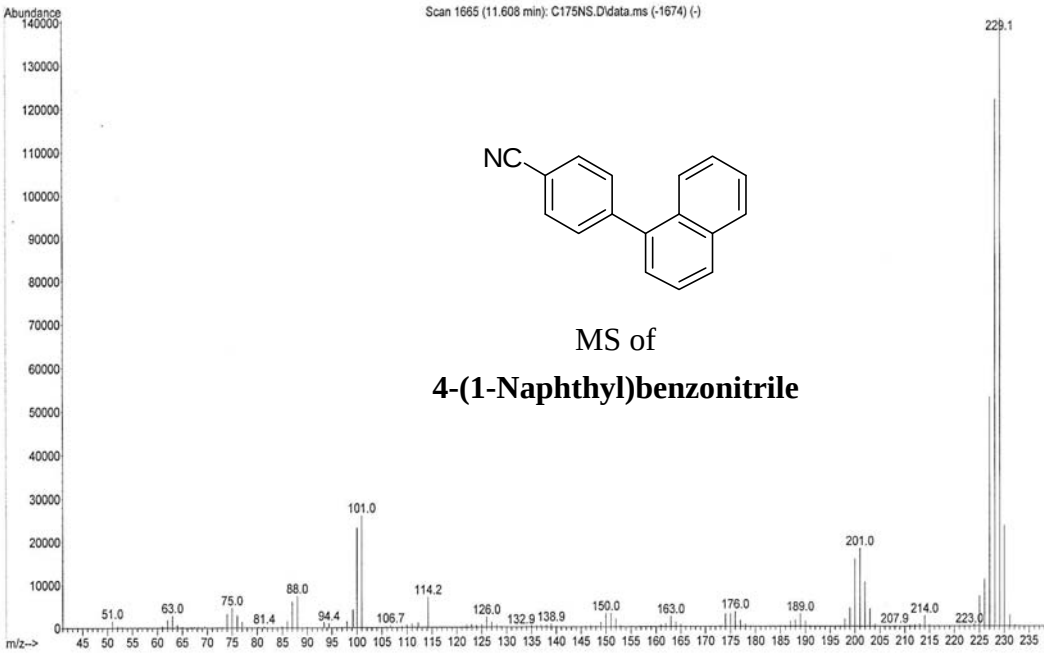
^{1}H NMR of

4-(1-Naphthyl)benzonitrile



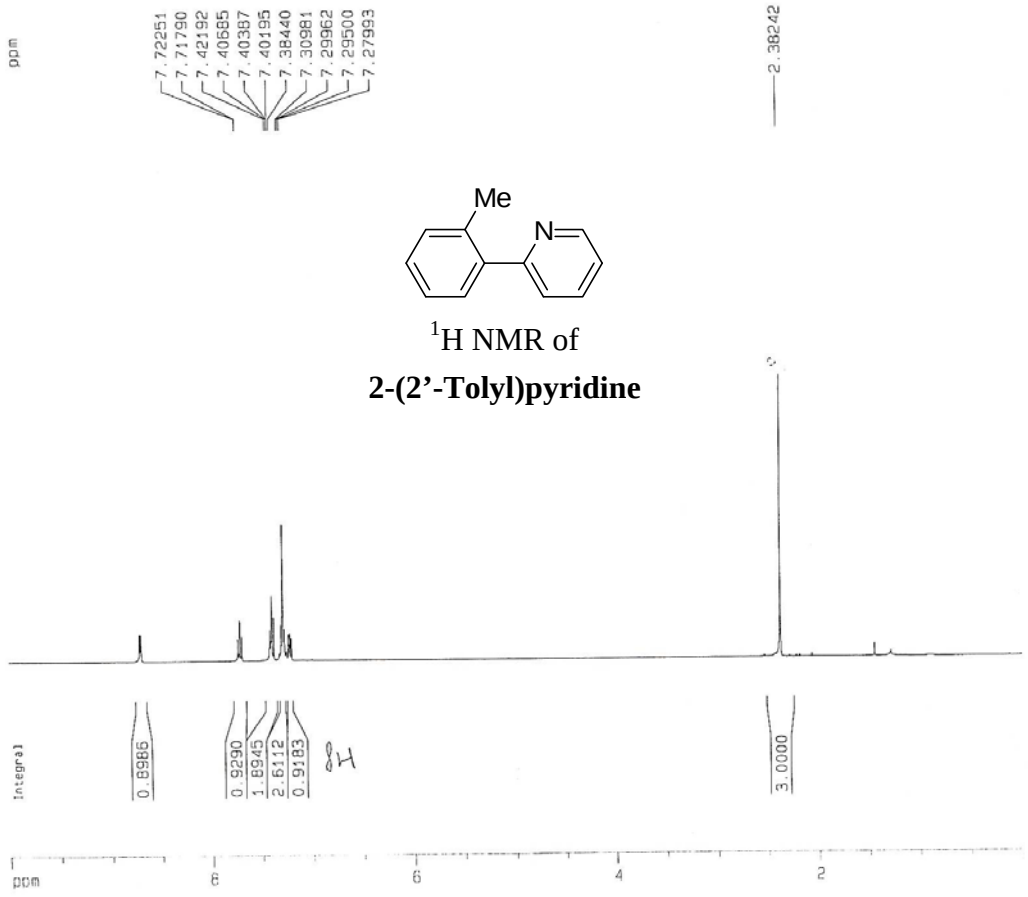
^{13}C NMR of

4-(1-Naphthyl)benzonitrile



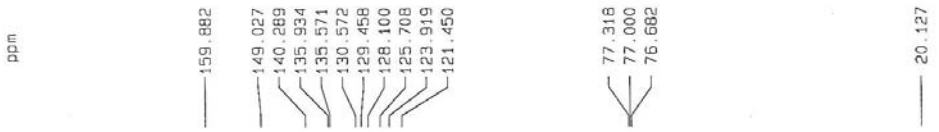
MS of

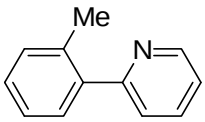
4-(1-Naphthyl)benzonitrile



^{1}H NMR of

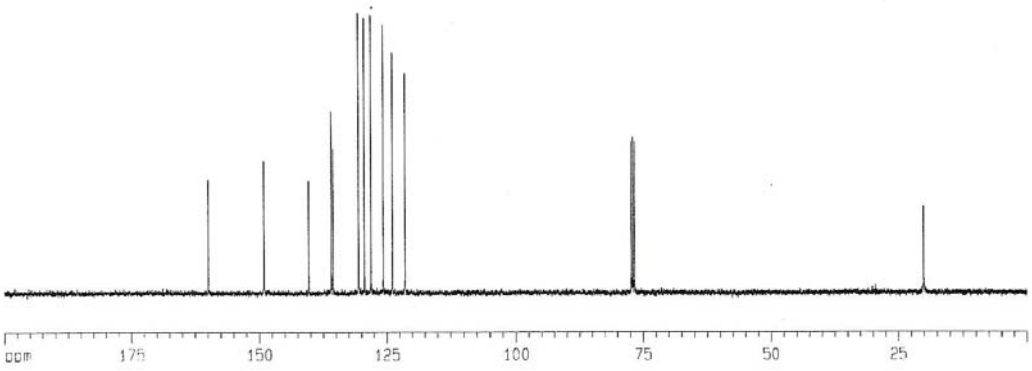
2-(2'-Tolyl)pyridine

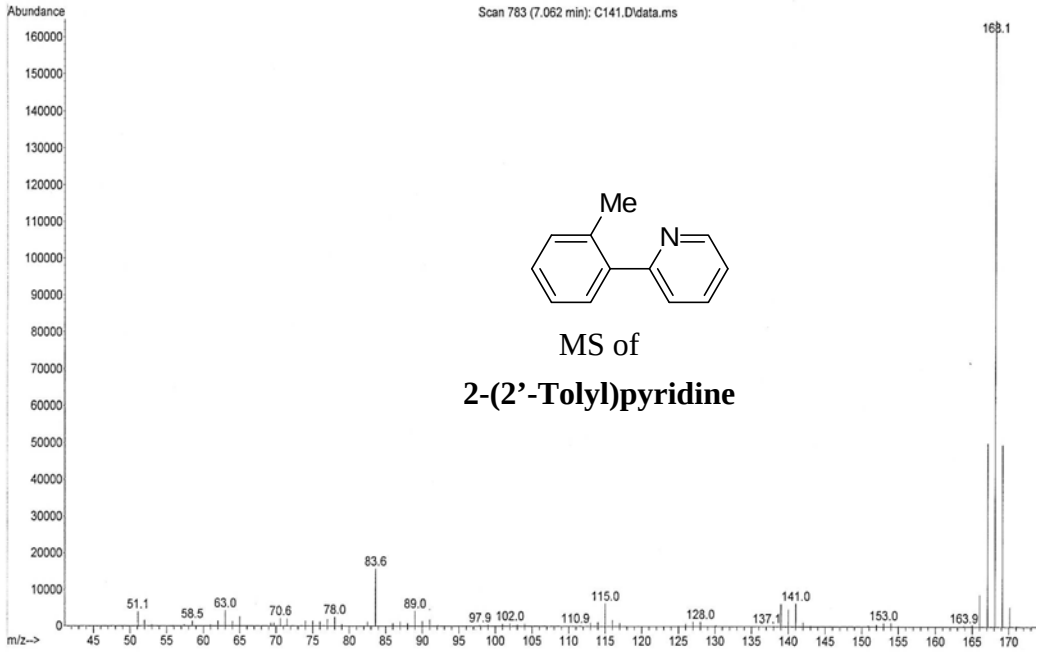




^{13}C NMR of

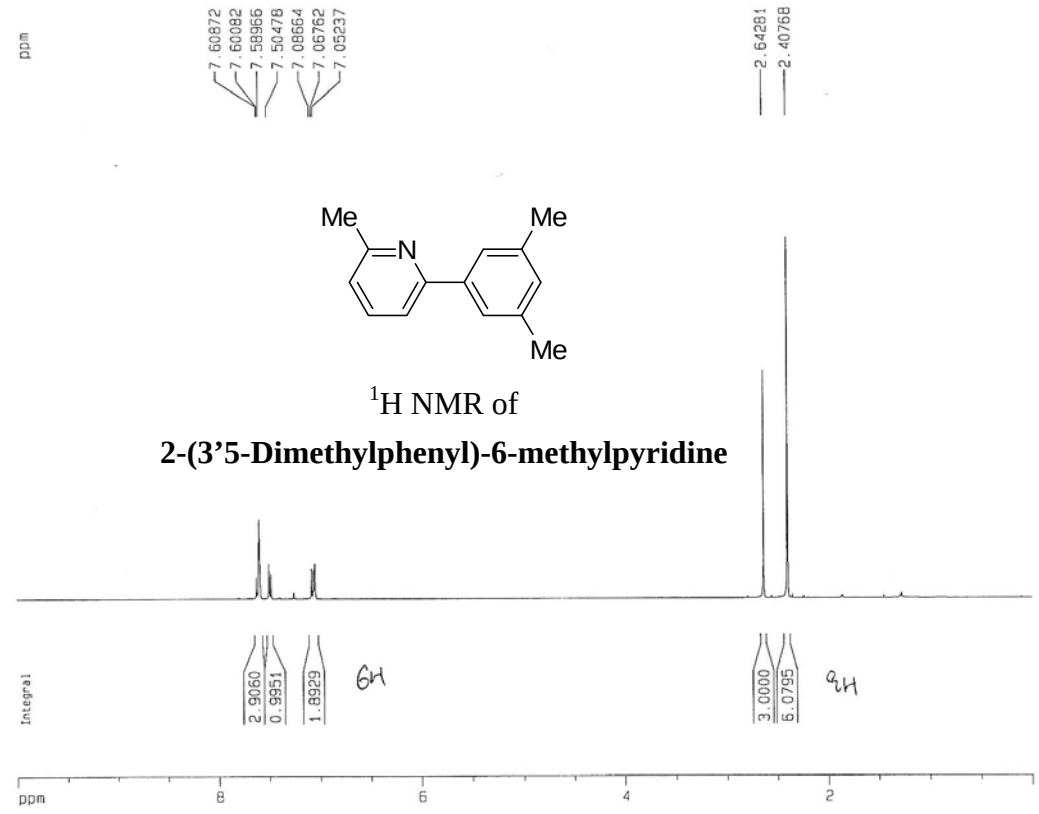
2-(2'-Tolyl)pyridine





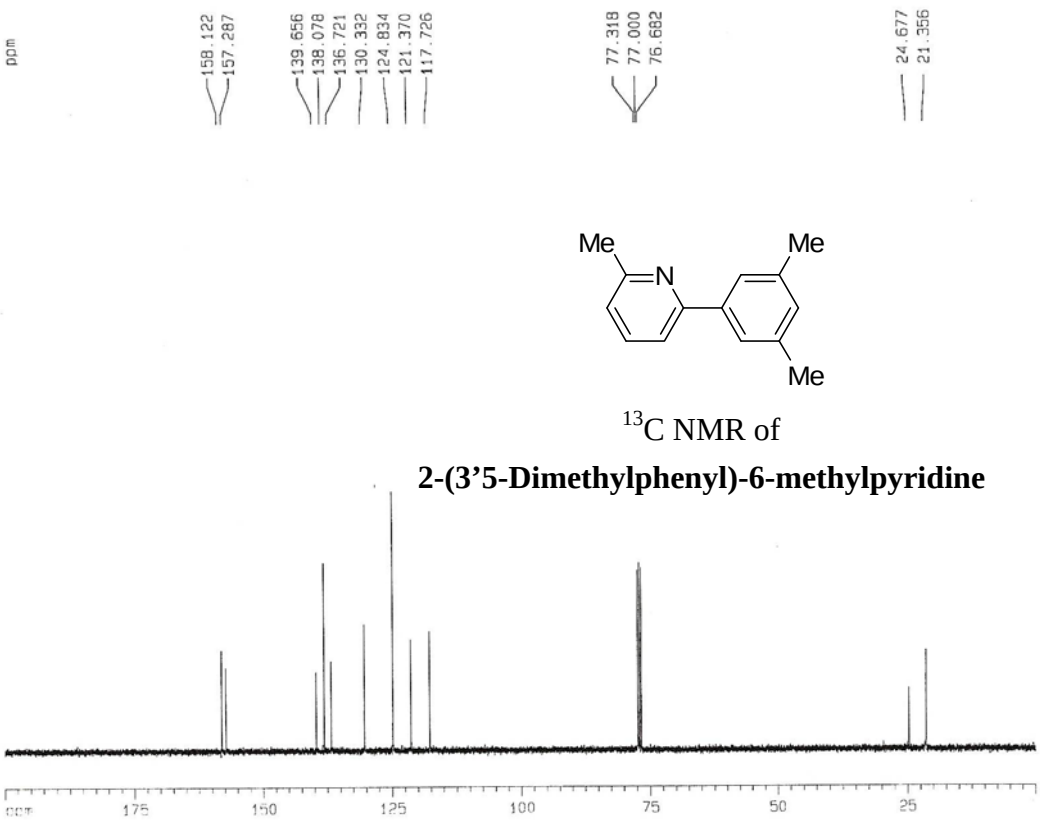
MS of

2-(2'-Tolyl)pyridine



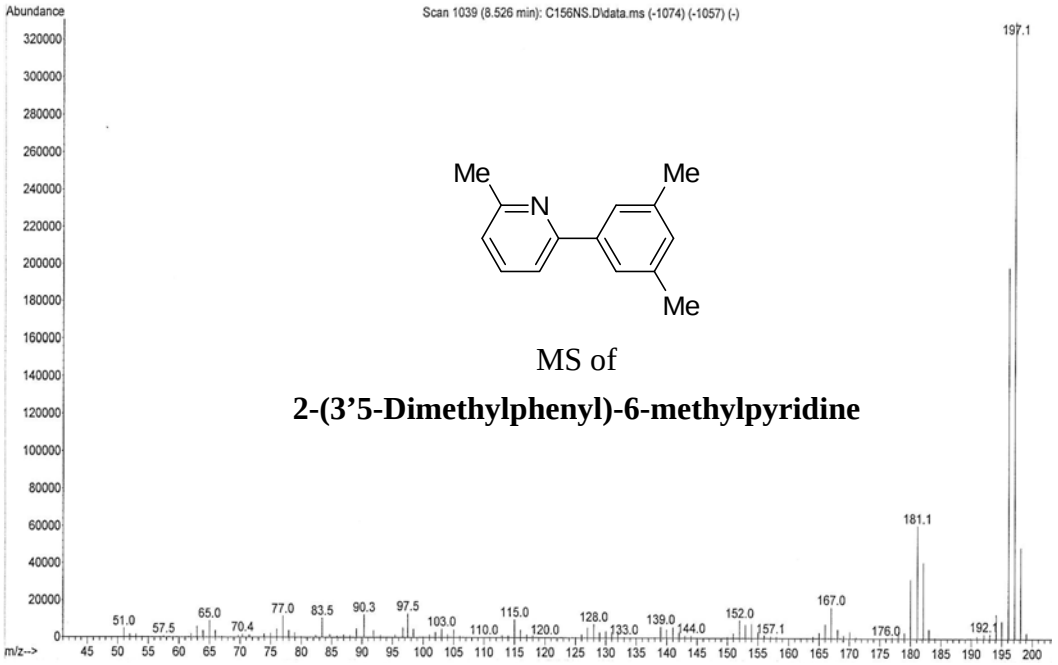
^{1}H NMR of

2-(3'5-Dimethylphenyl)-6-methylpyridine



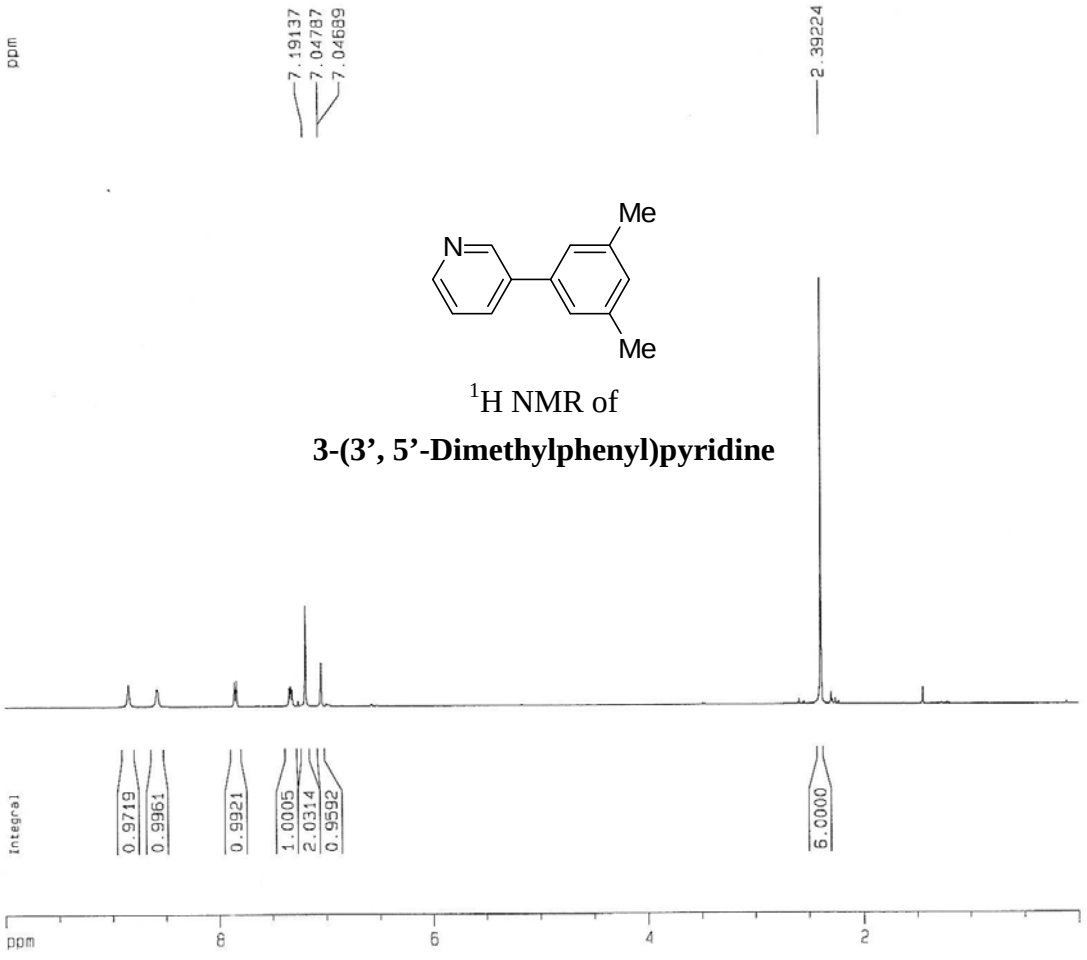
^{13}C NMR of

2-(3'5-Dimethylphenyl)-6-methylpyridine



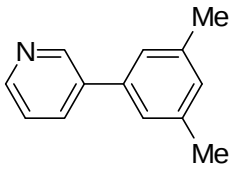
MS of

2-(3'5-Dimethylphenyl)-6-methylpyridine



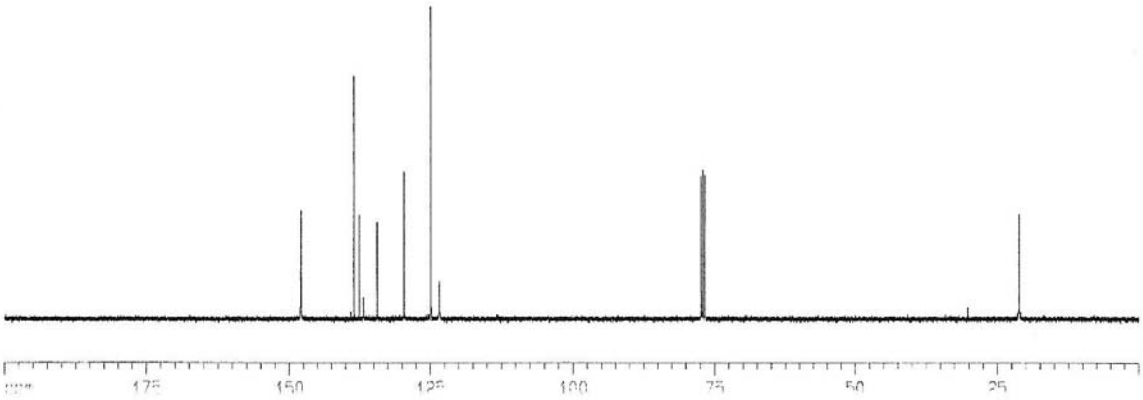
^{1}H NMR of

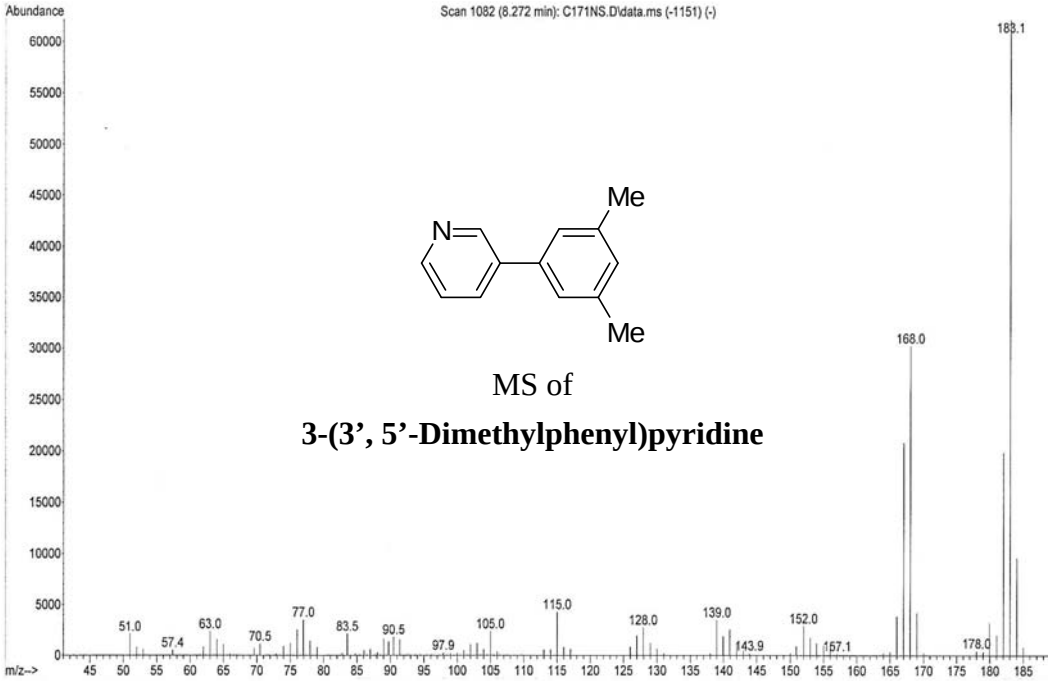
3-(3', 5'-Dimethylphenyl)pyridine



^{13}C NMR of

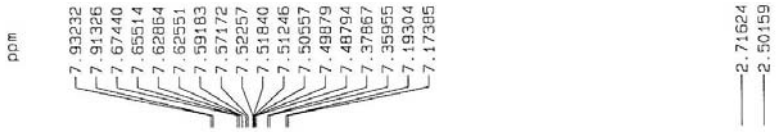
3-(3', 5'-Dimethylphenyl)pyridine

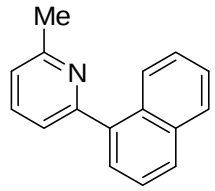




MS of

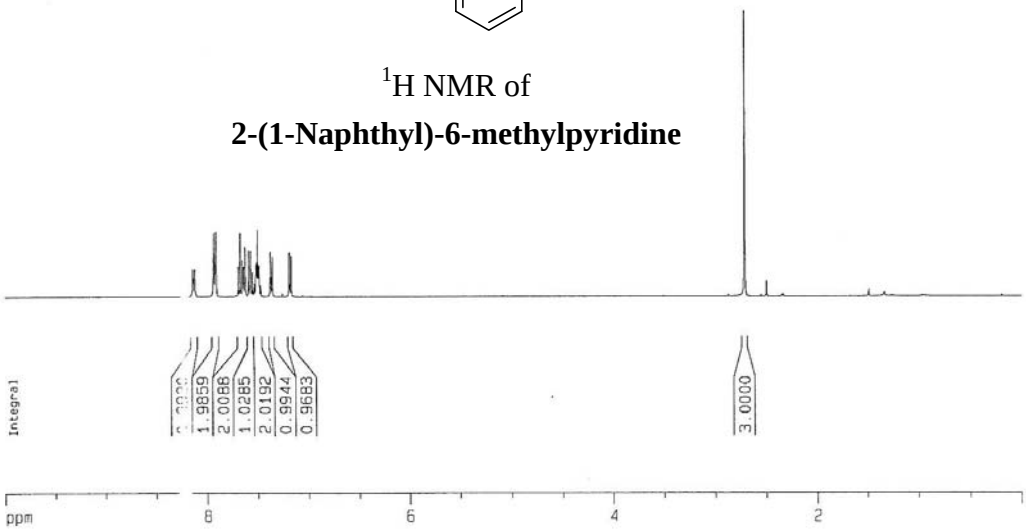
3-(3', 5'-Dimethylphenyl)pyridine

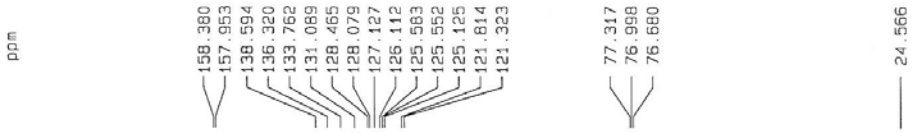


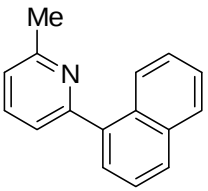


^{1}H NMR of

2-(1-Naphthyl)-6-methylpyridine

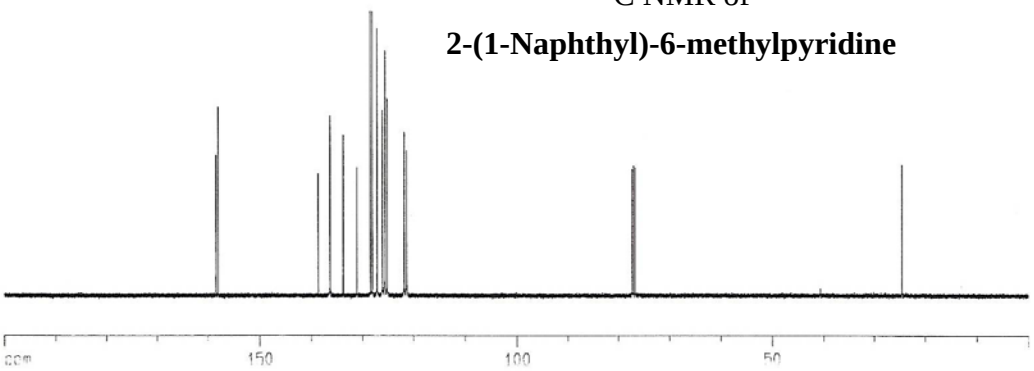


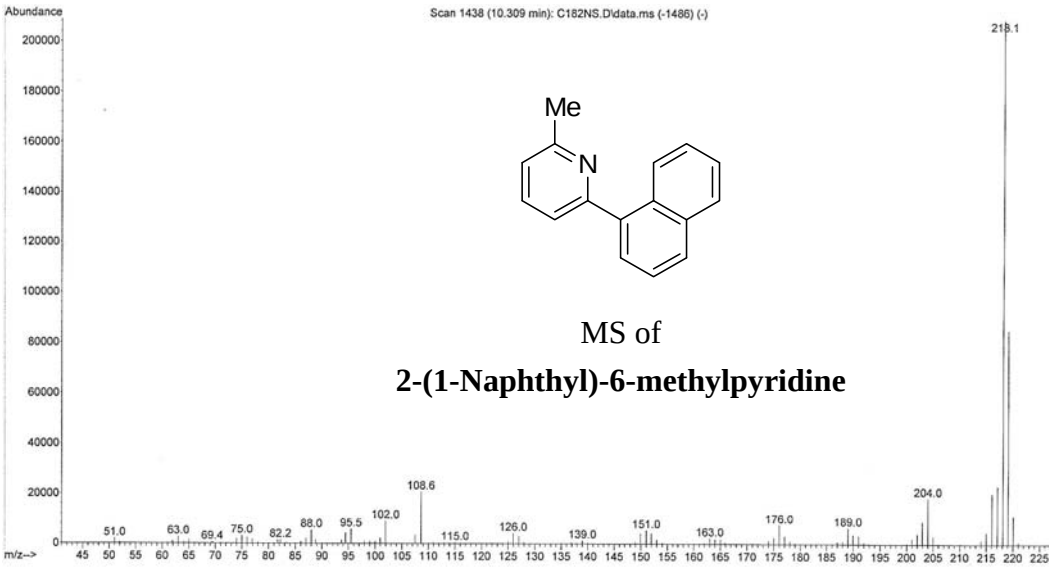




^{13}C NMR of

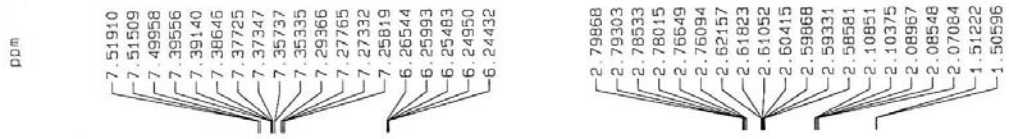
2-(1-Naphthyl)-6-methylpyridine

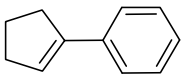




MS of

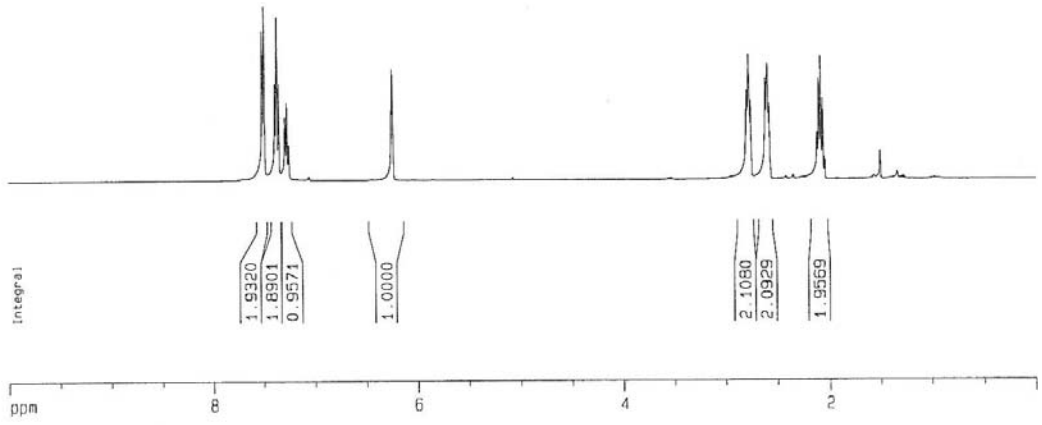
2-(1-Naphthyl)-6-methylpyridine

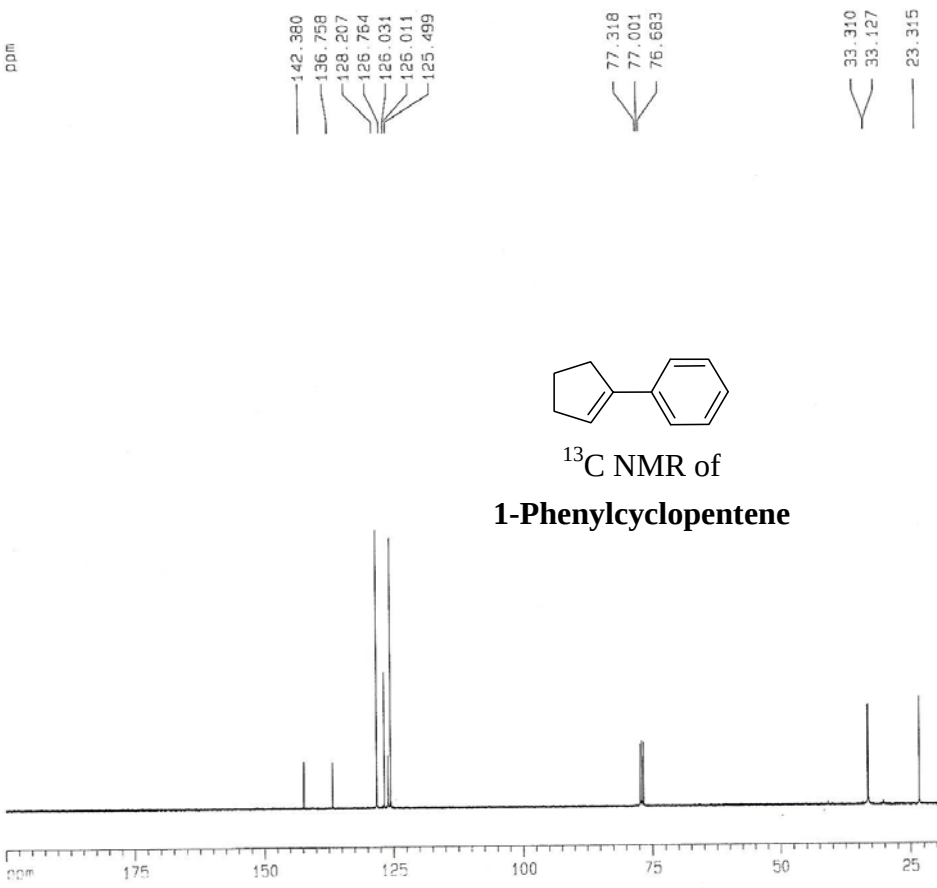




^{1}H NMR of

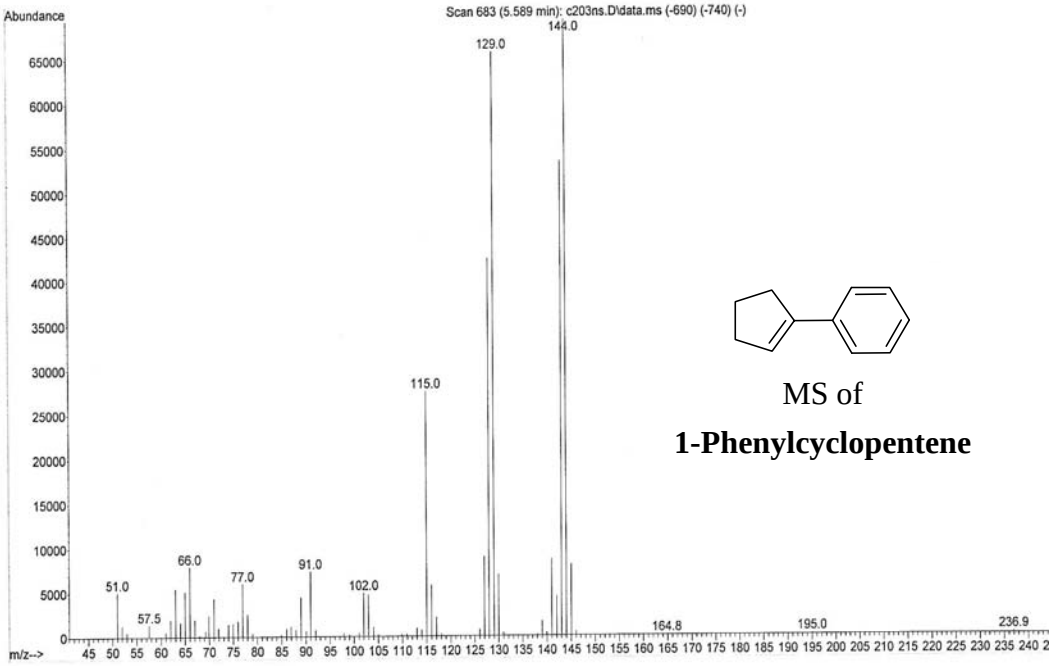
1-Phenylcyclopentene





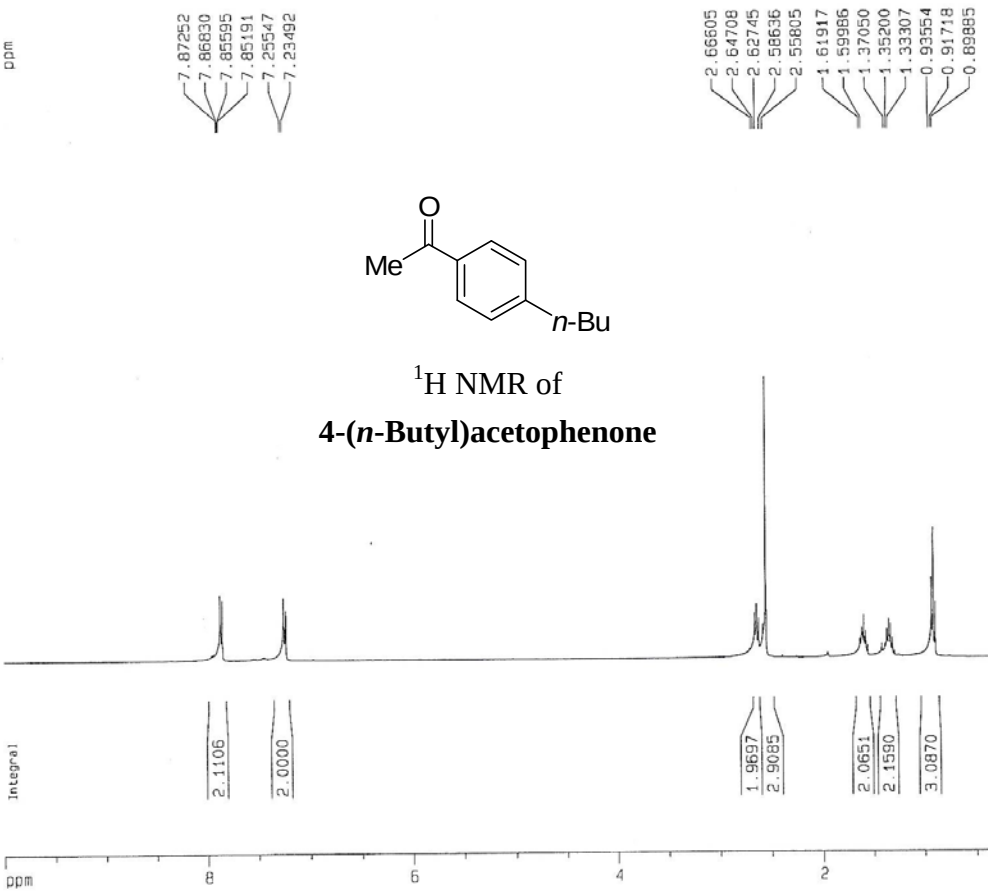
^{13}C NMR of

1-Phenylcyclopentene



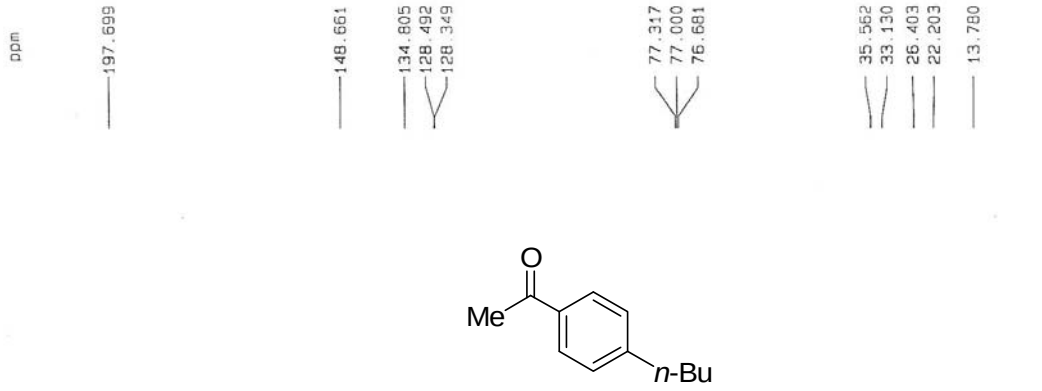
MS of

1-Phenylcyclopentene



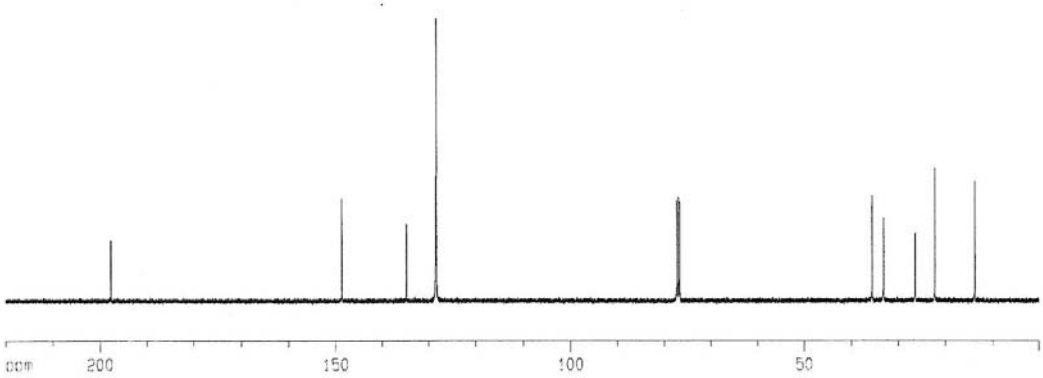
^{1}H NMR of

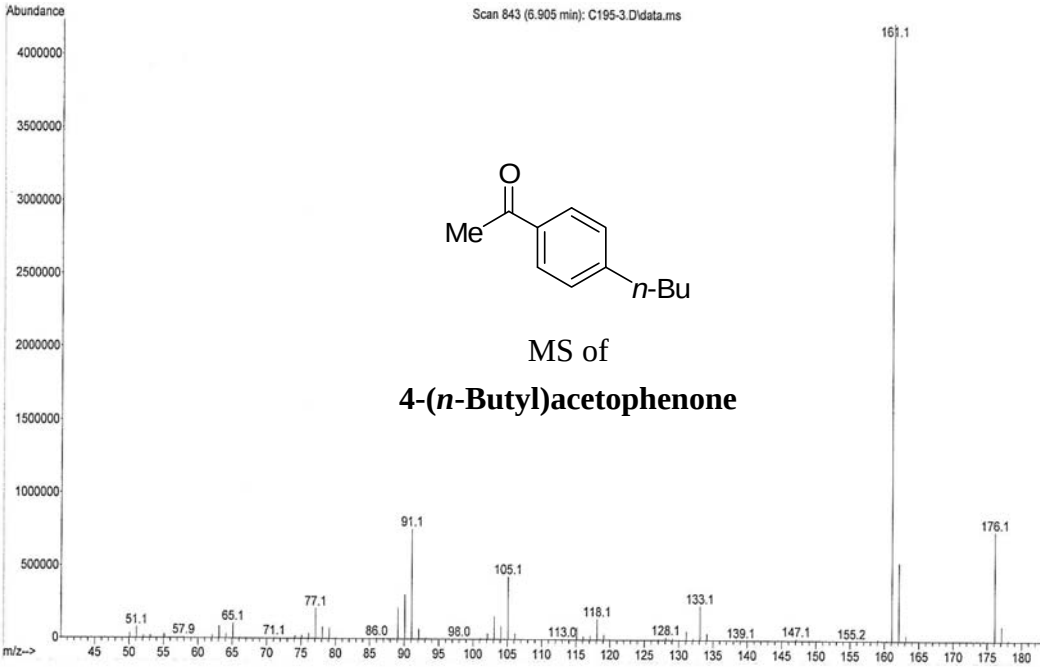
4-(*n*-Butyl)acetophenone



^{13}C NMR of

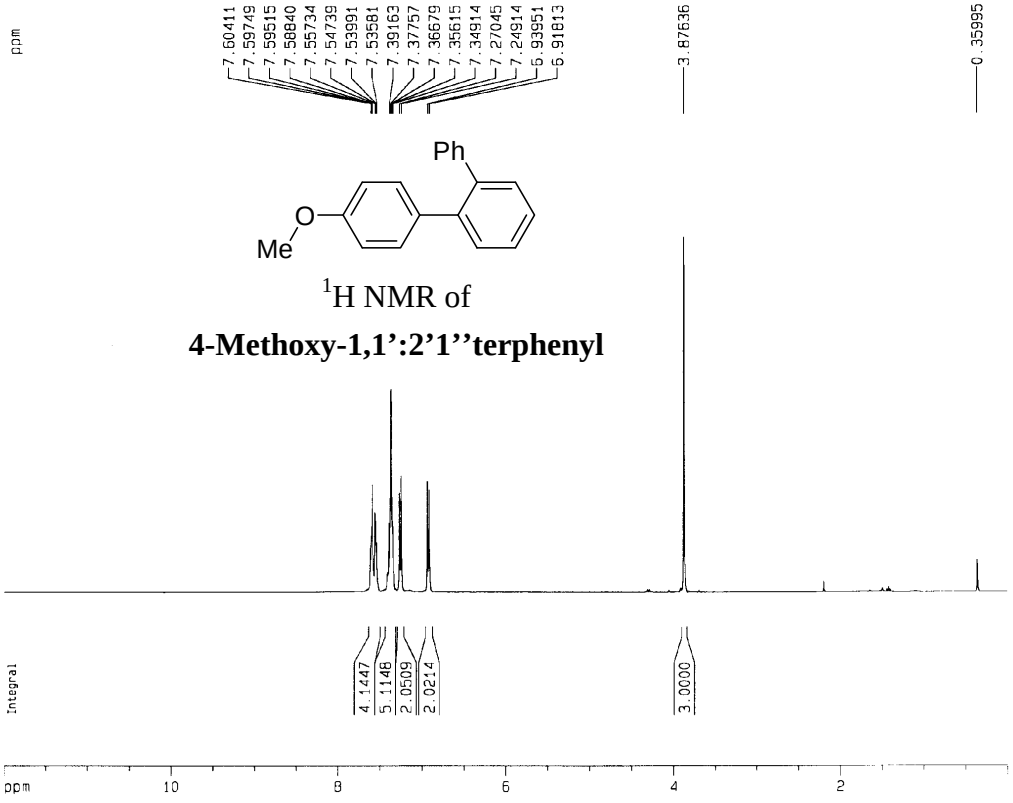
4-(*n*-Butyl)acetophenone





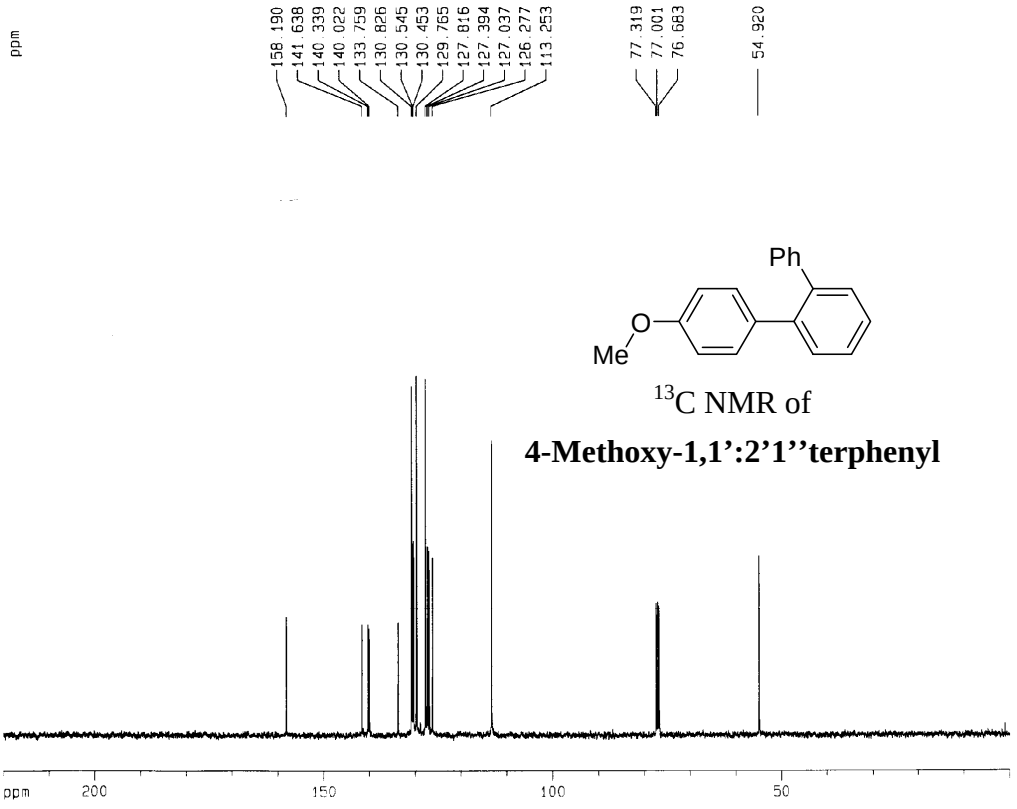
MS of

4-(*n*-Butyl)acetophenone



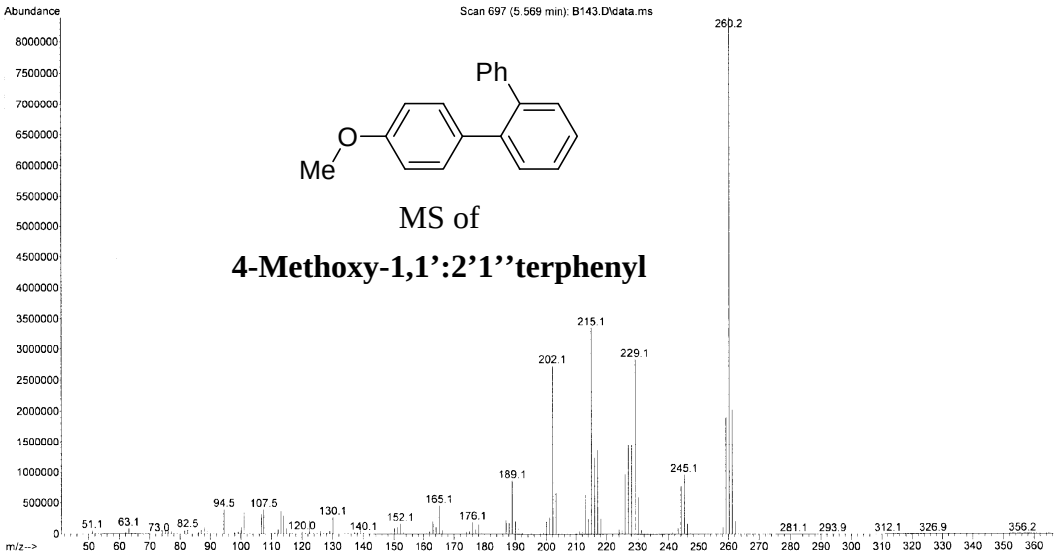
^{1}H NMR of

4-Methoxy-1,1’:2’1’’terphenyl



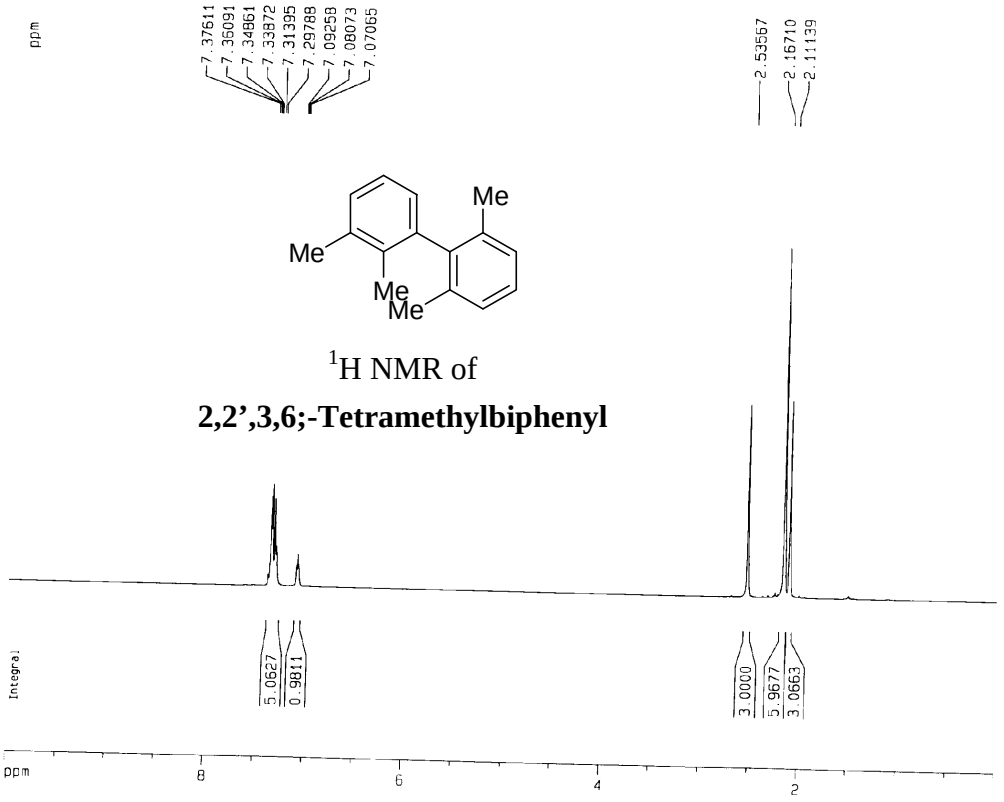
^{13}C NMR of

4-Methoxy-1,1’:2’1’’terphenyl



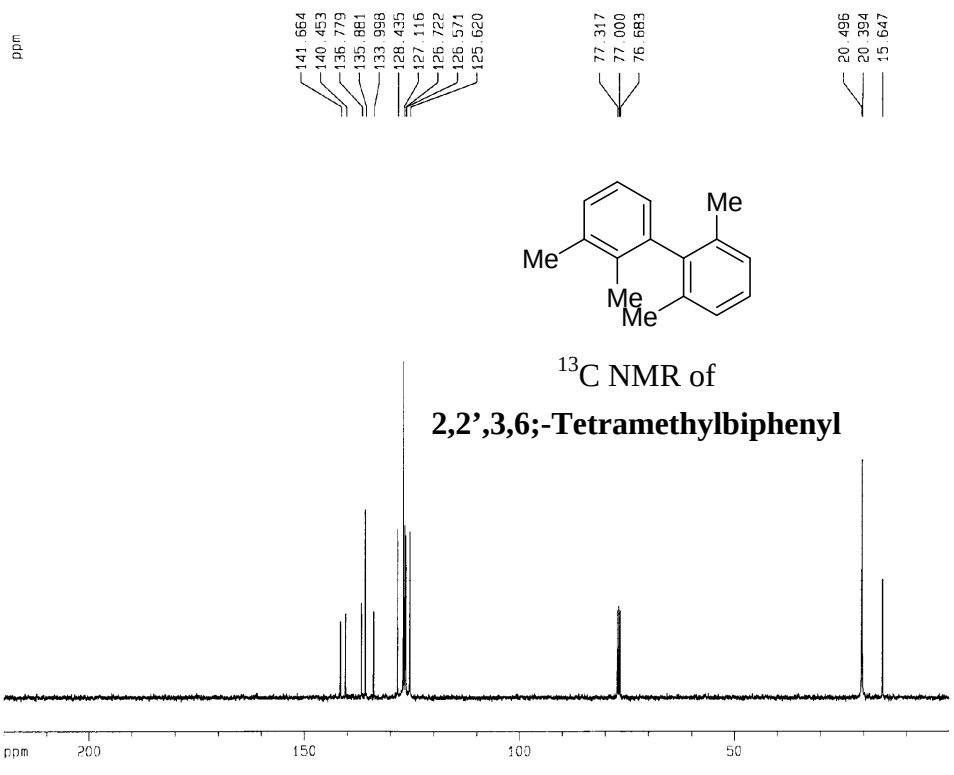
MS of

4-Methoxy-1,1’:2’1’’terphenyl



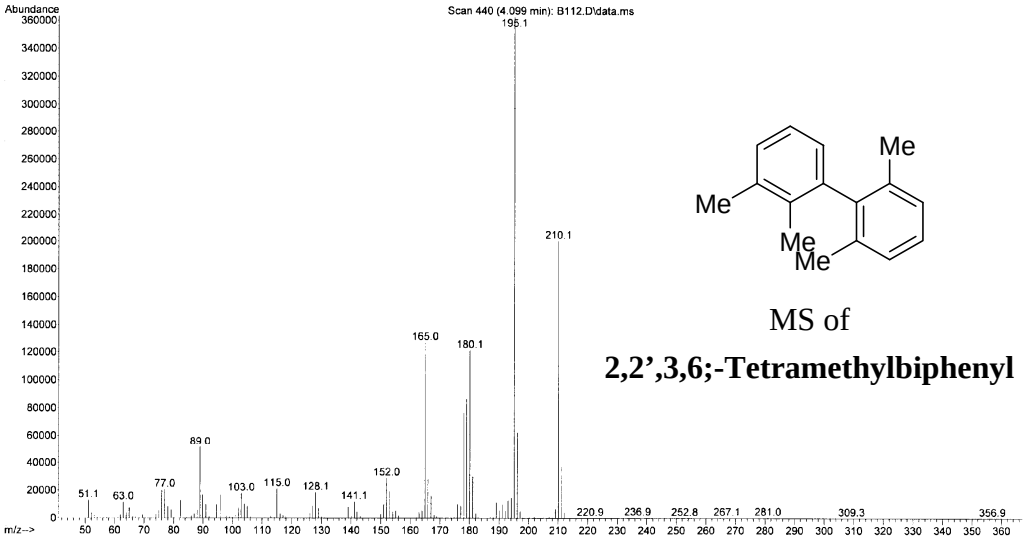
^{1}H NMR of

2,2',3,6;-Tetramethylbiphenyl



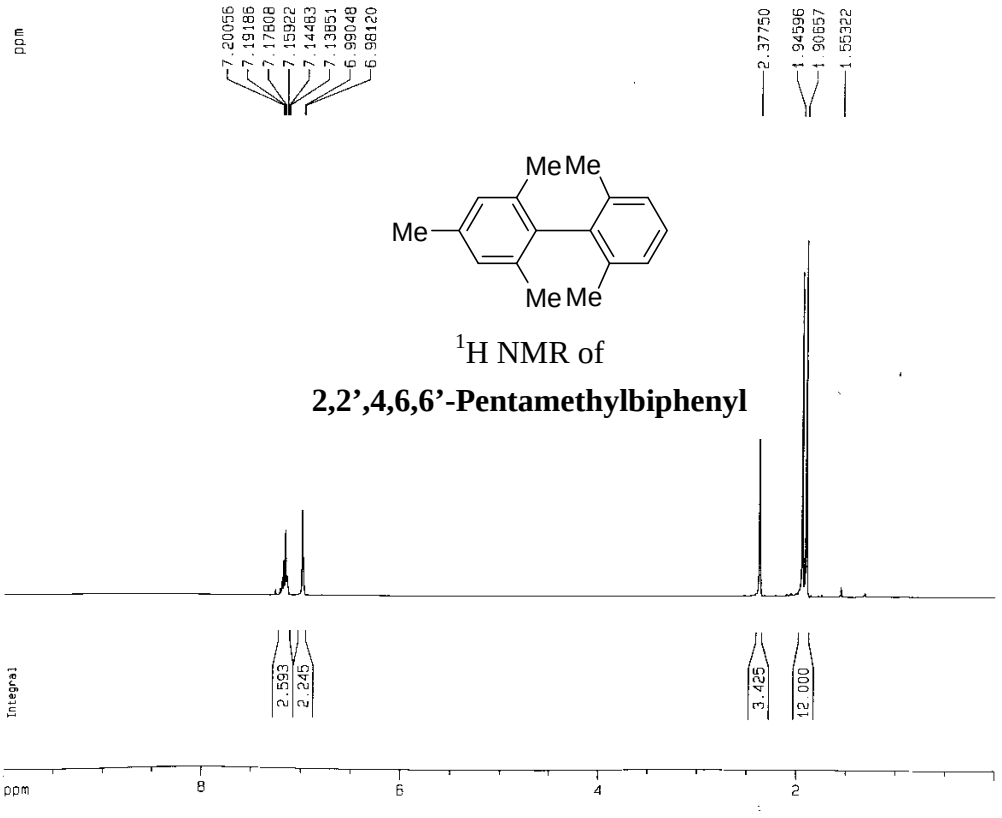
^{13}C NMR of

2,2',3,6;-Tetramethylbiphenyl



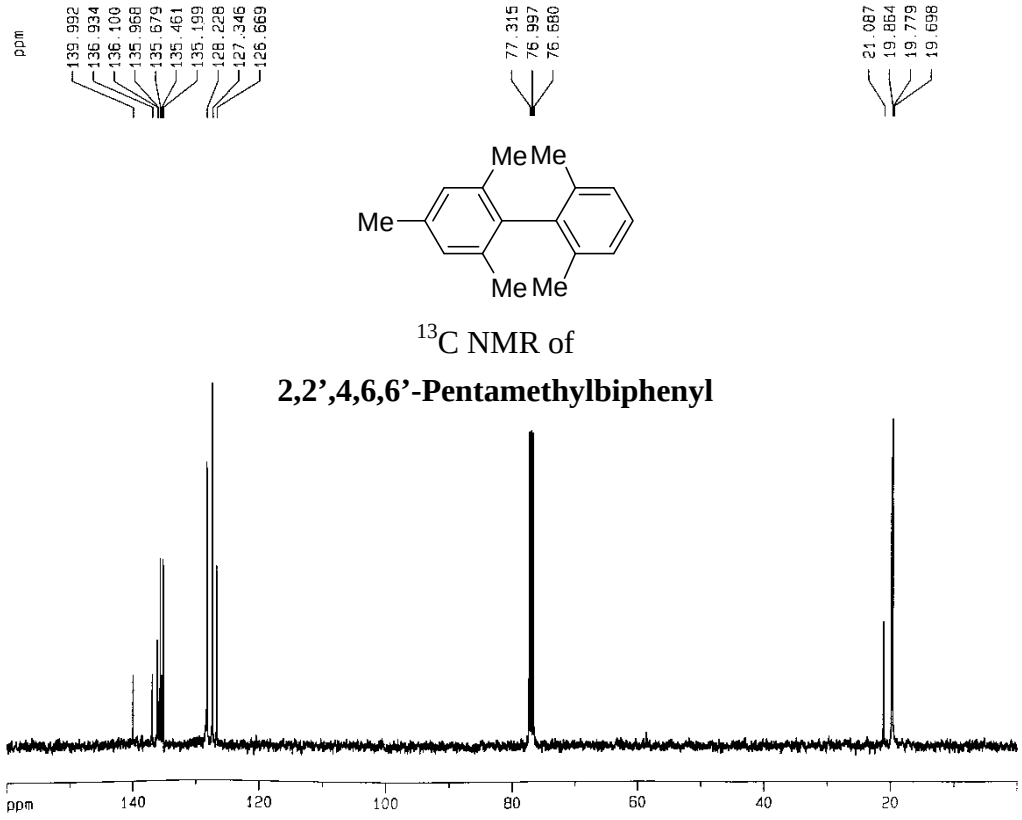
MS of

2,2',3,6;-Tetramethylbiphenyl



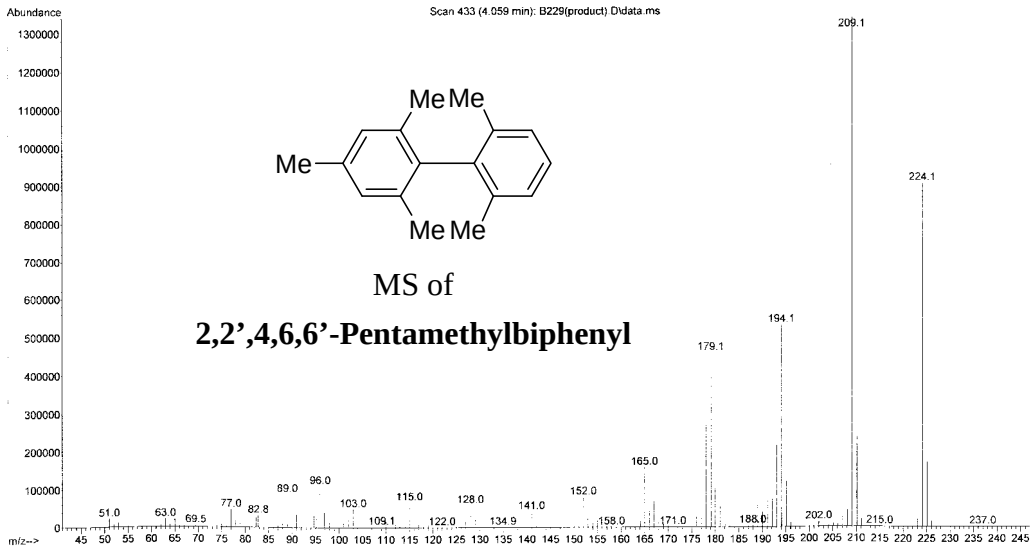
^{1}H NMR of

2,2',4,6,6'-Pentamethylbiphenyl



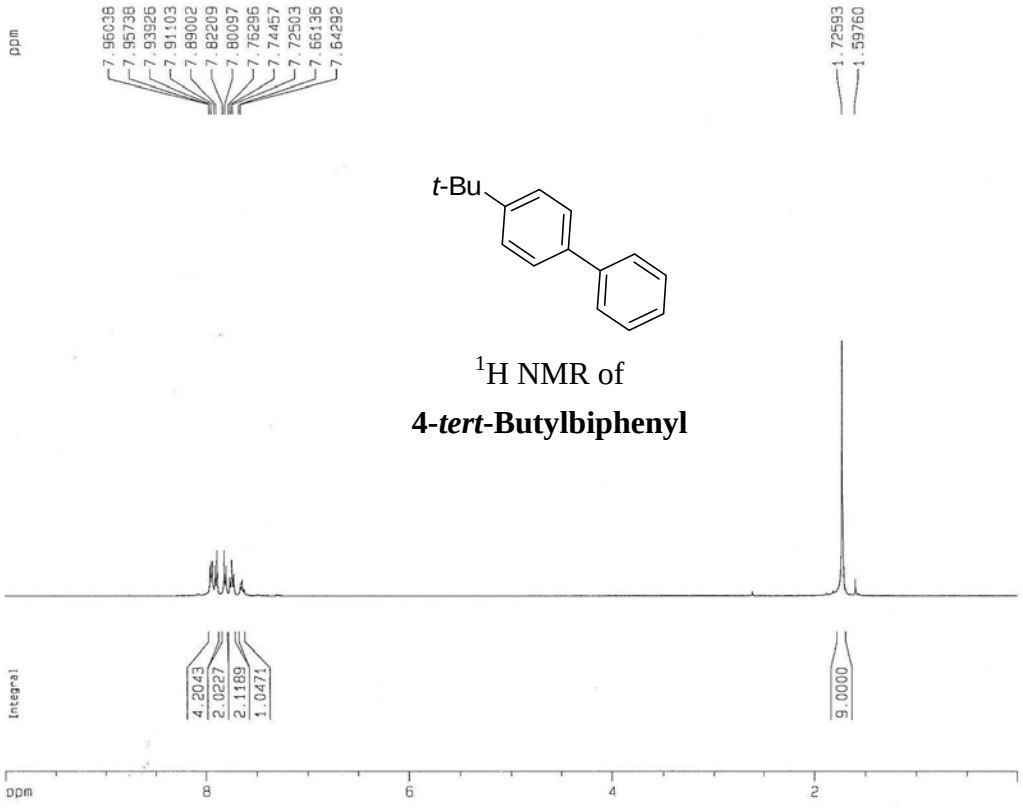
^{13}C NMR of

2,2',4,6,6'-Pentamethylbiphenyl



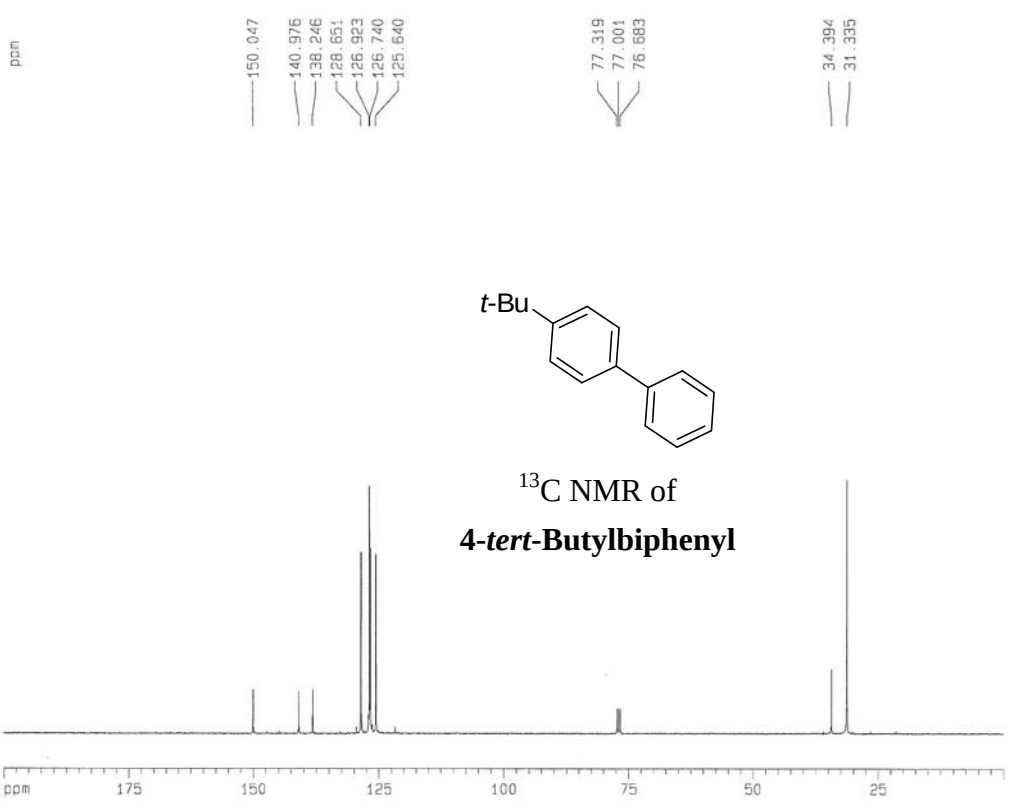
MS of

2,2',4,6,6'-Pentamethylbiphenyl



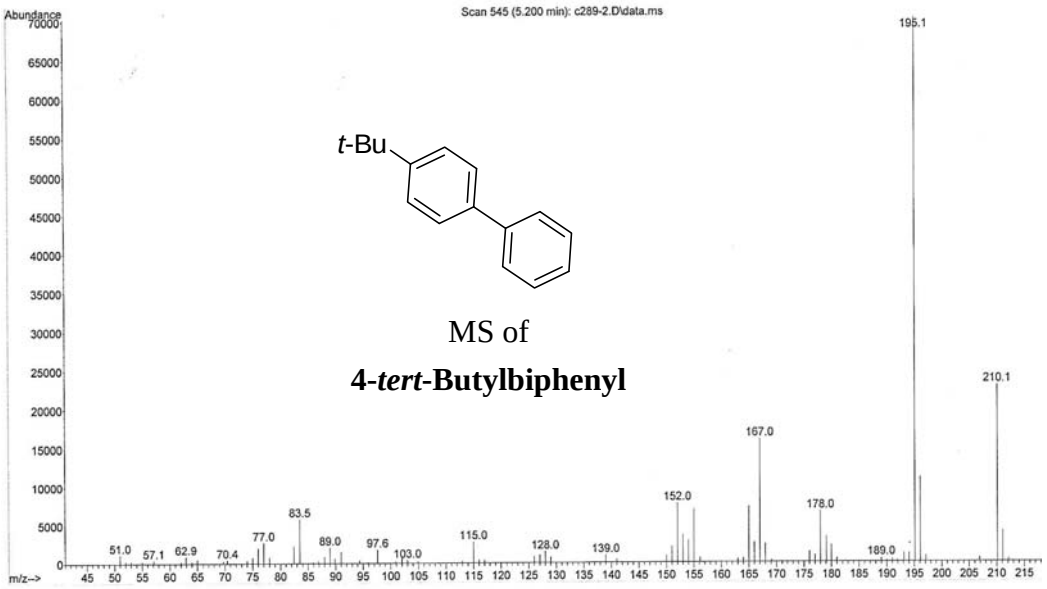
^{1}H NMR of

4-*tert*-Butylbiphenyl



^{13}C NMR of

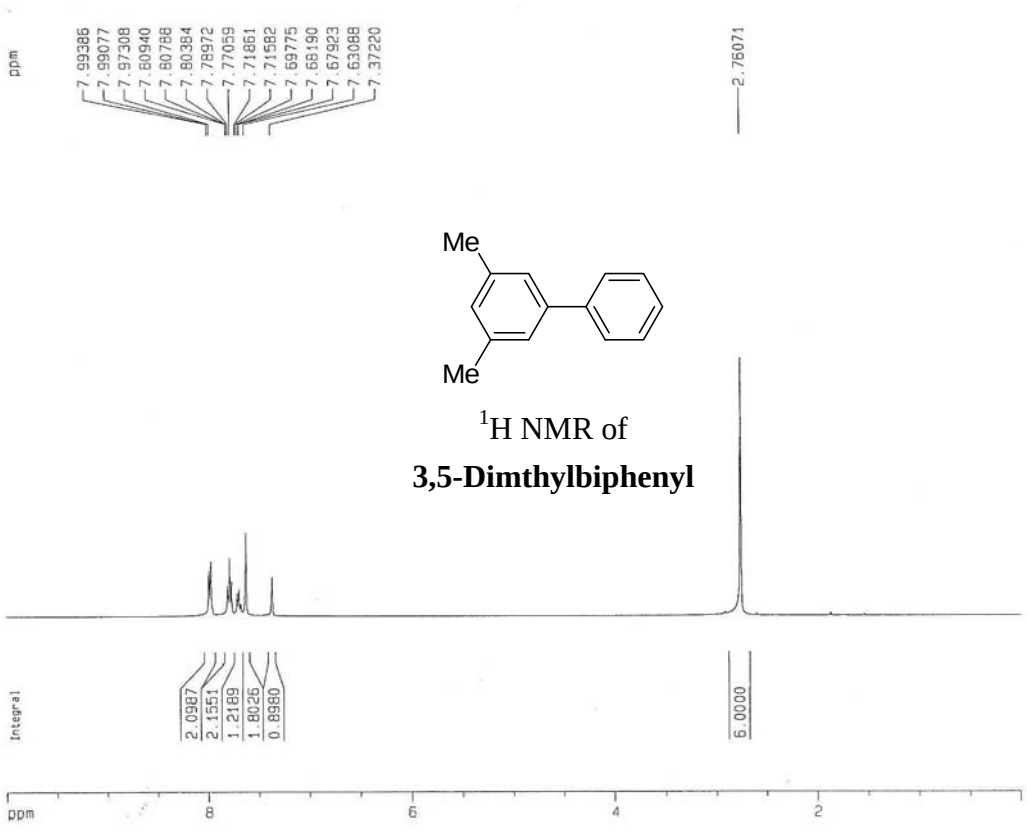
4-*tert*-Butylbiphenyl



t-Bu

MS of

4-*tert*-Butylbiphenyl

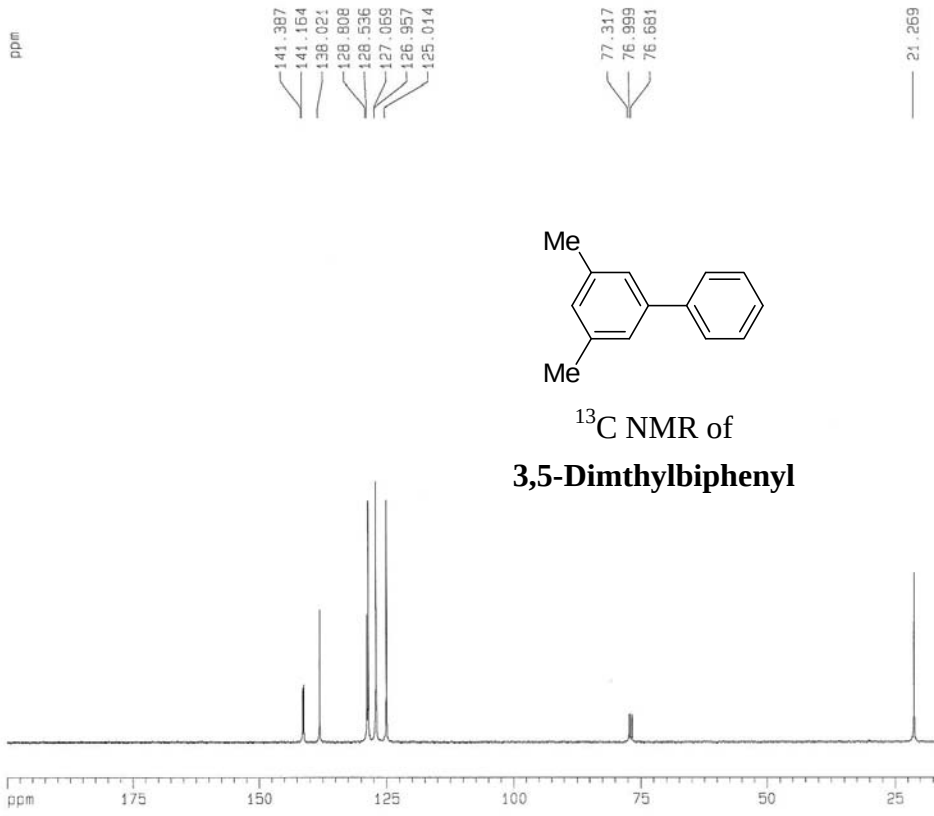


Me

Me

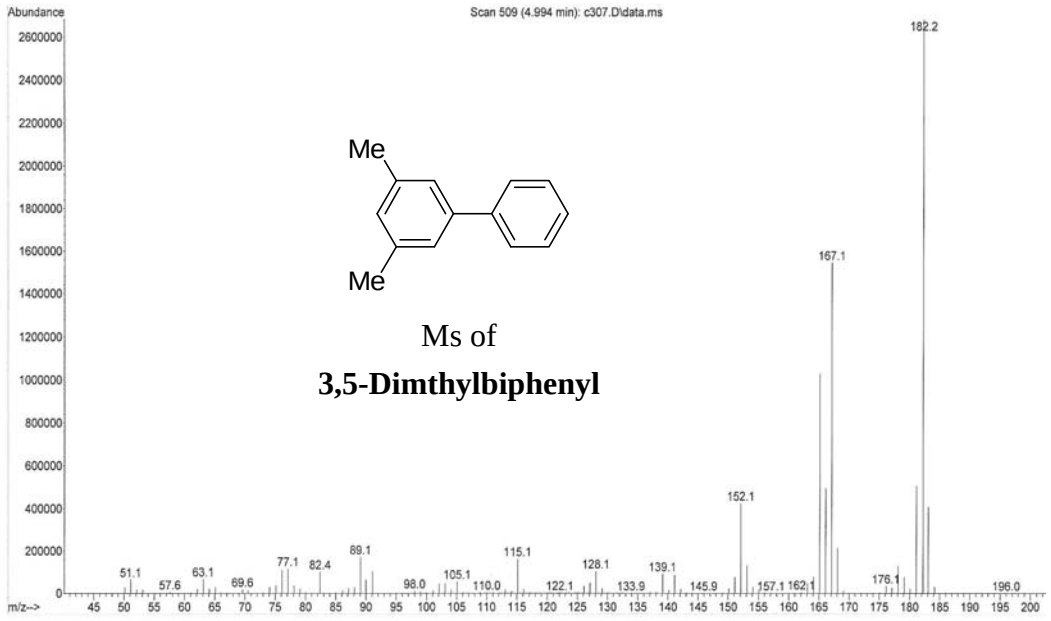
^{1}H NMR of

3,5-Dimthylbiphenyl



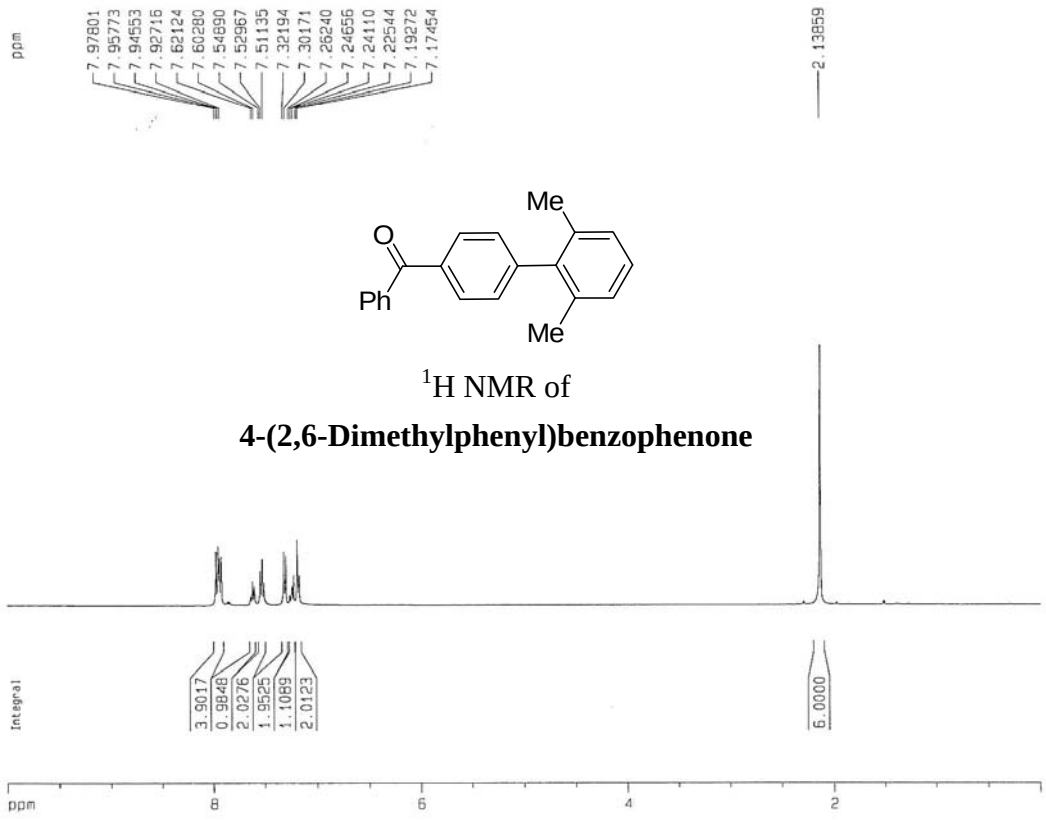
^{13}C NMR of

3,5-Dimthylbiphenyl



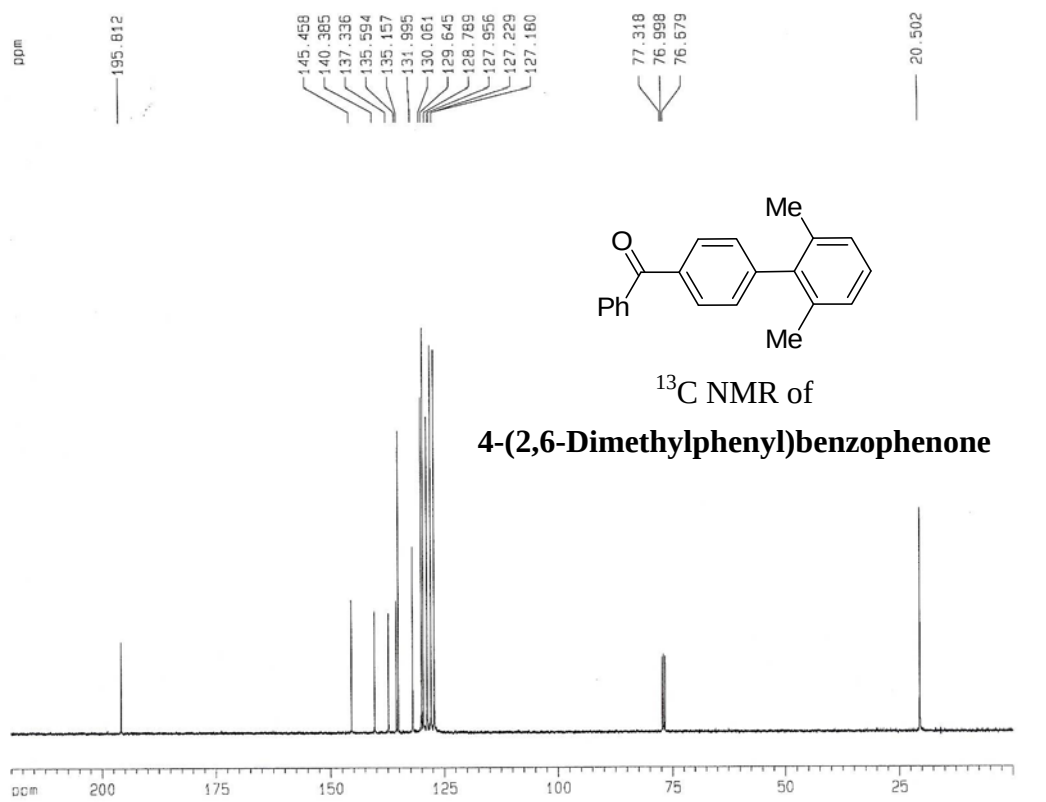
Ms of

3,5-Dimthylbiphenyl



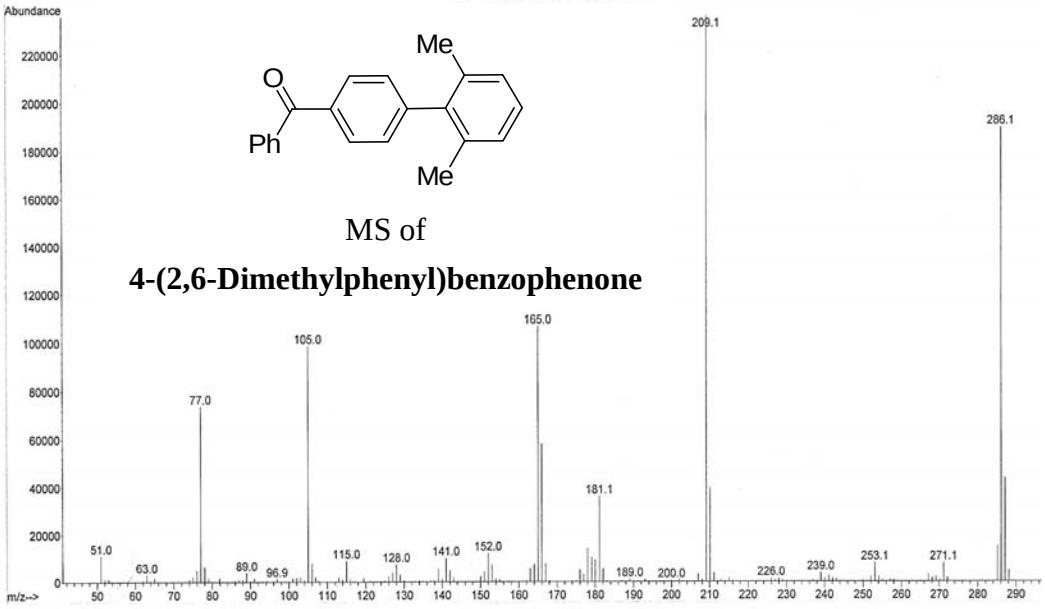
^{1}H NMR of

4-(2,6-Dimethylphenyl)benzophenone



^{13}C NMR of

4-(2,6-Dimethylphenyl)benzophenone



MS of

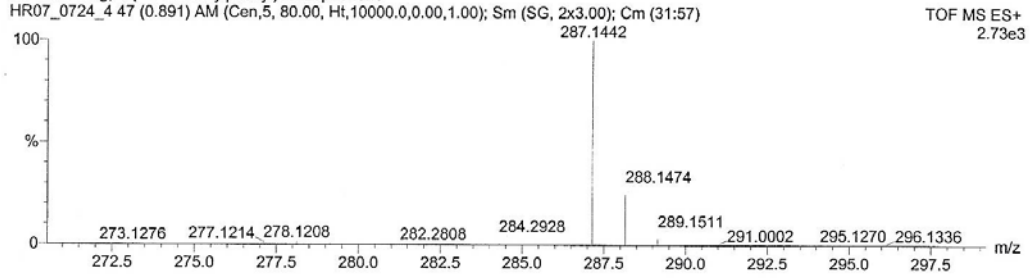
4-(2,6-Dimethylphenyl)benzophenone

Elemental Composition Report Page 1

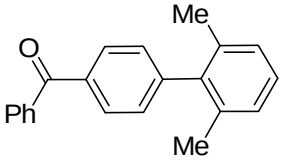
Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
5 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-21 H: 0-1000 O: 0-1

So chau Ming, 4-(2'6'-dimethylphenyl)benzophenone
HR07_0724_4 47 (0.891) AM (Cen,5, 80.00, Ht,10000.0,0.00,1.00); Sm (SG, 2x3.00); Cm (31:57) TOF MS ES+
2.73e3

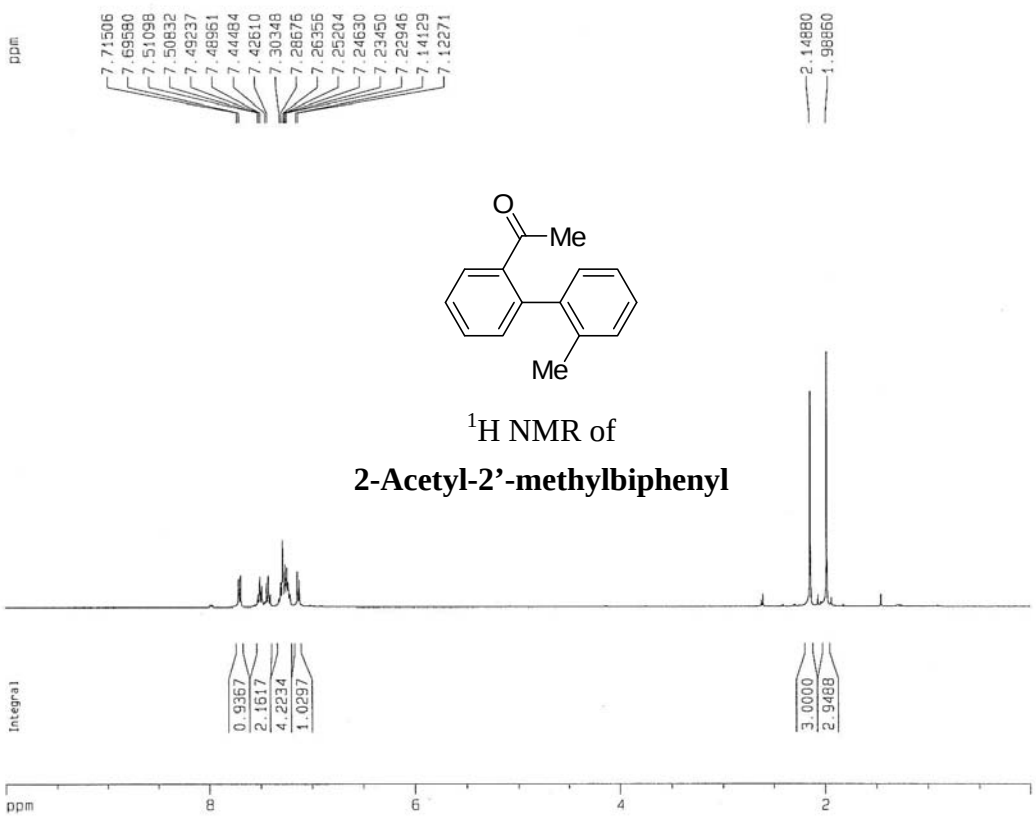


Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
287.1442	287.1436	0.6	2.1	12.5	0.7	C21 H19 O



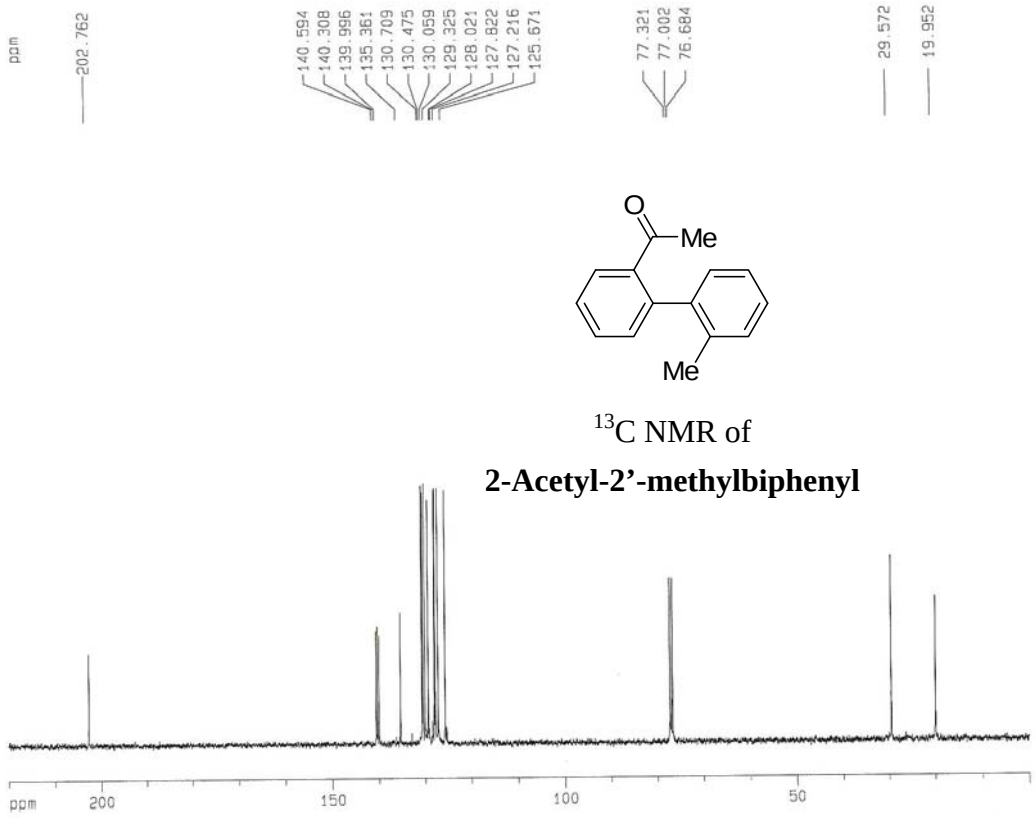
HRMS of

4-(2,6-Dimethylphenyl)benzophenone



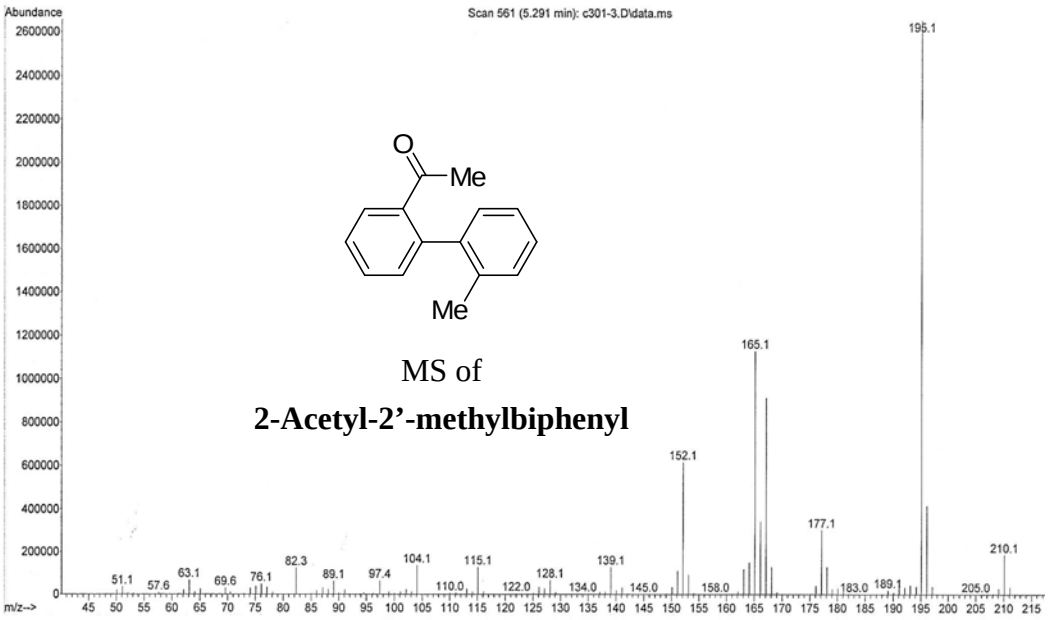
^{1}H NMR of

2-Acetyl-2'-methylbiphenyl



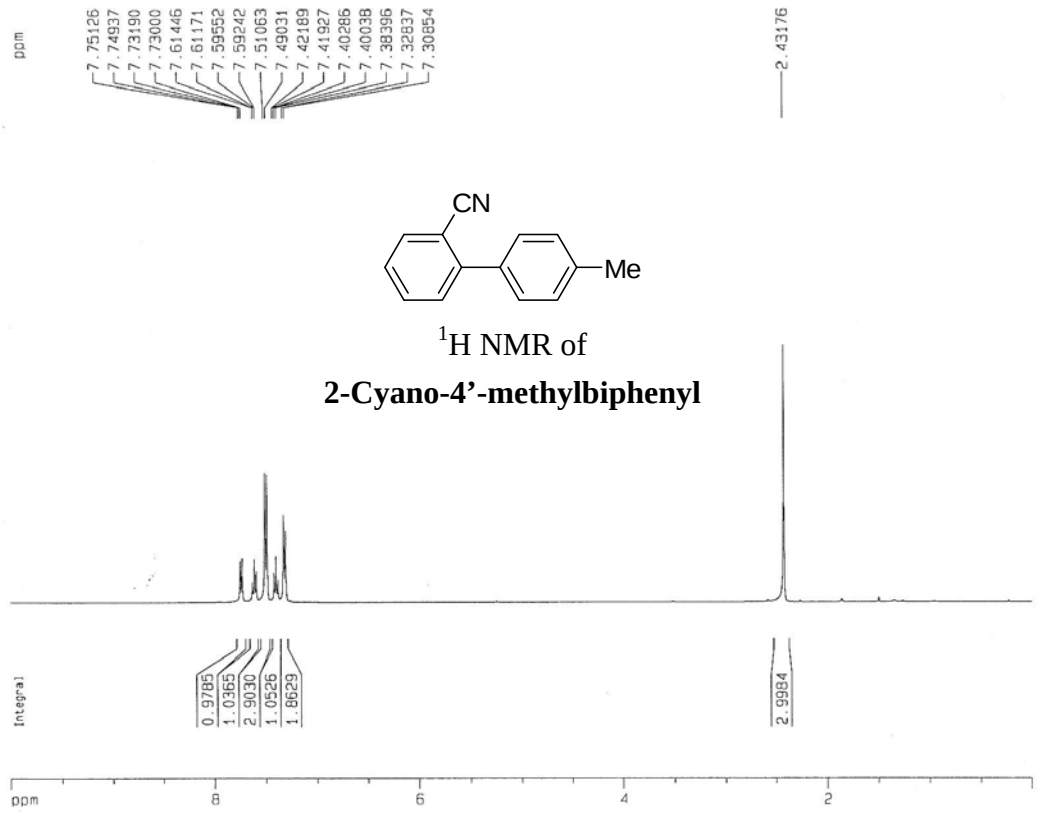
^{13}C NMR of

2-Acetyl-2'-methylbiphenyl



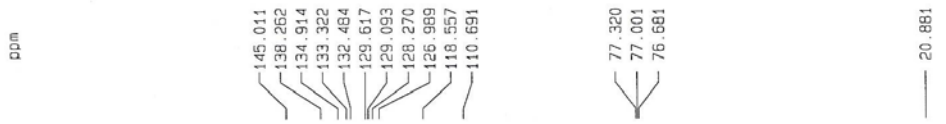
MS of

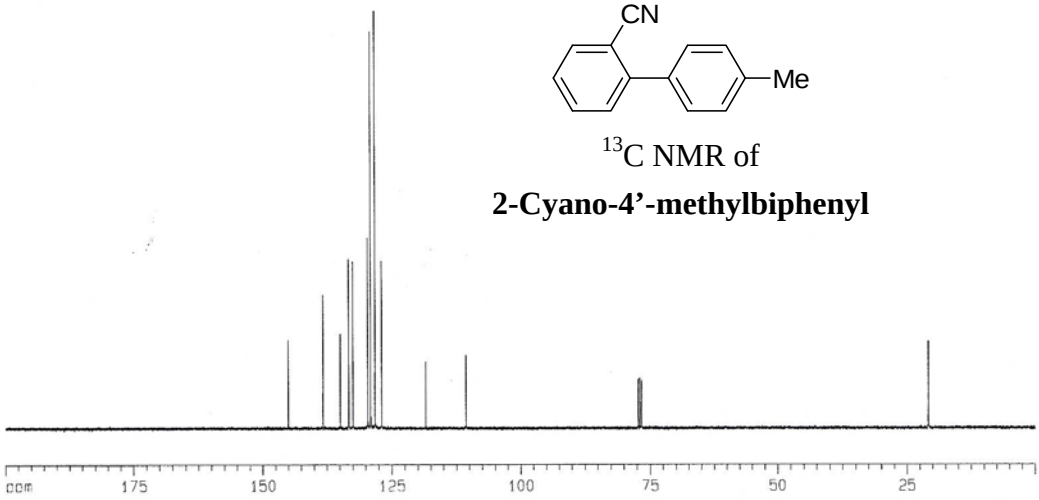
2-Acetyl-2’-methylbiphenyl



^{1}H NMR of

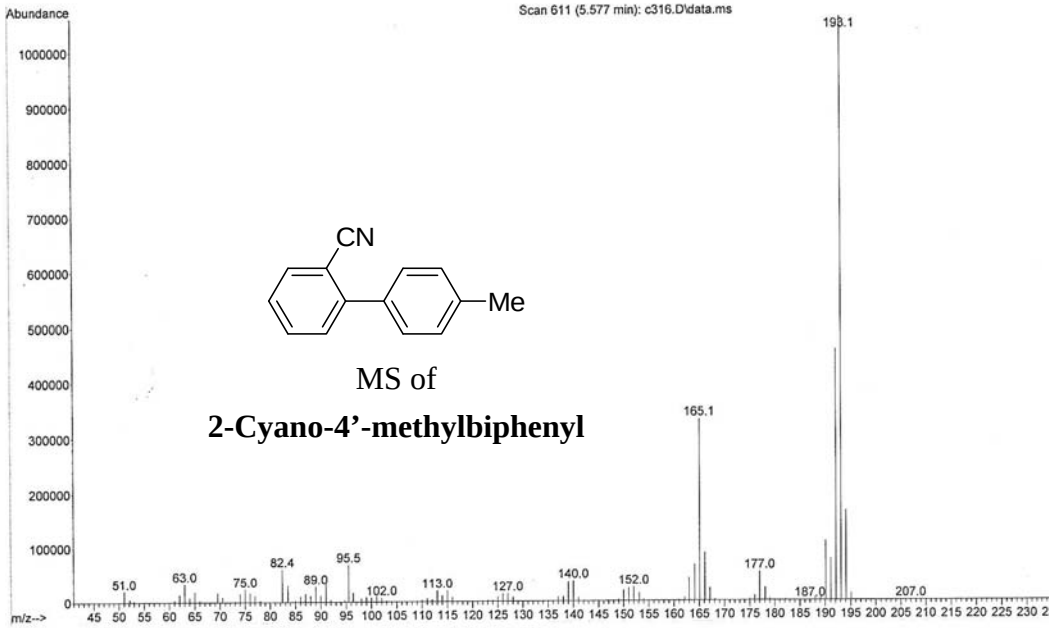
2-Cyano-4’-methylbiphenyl





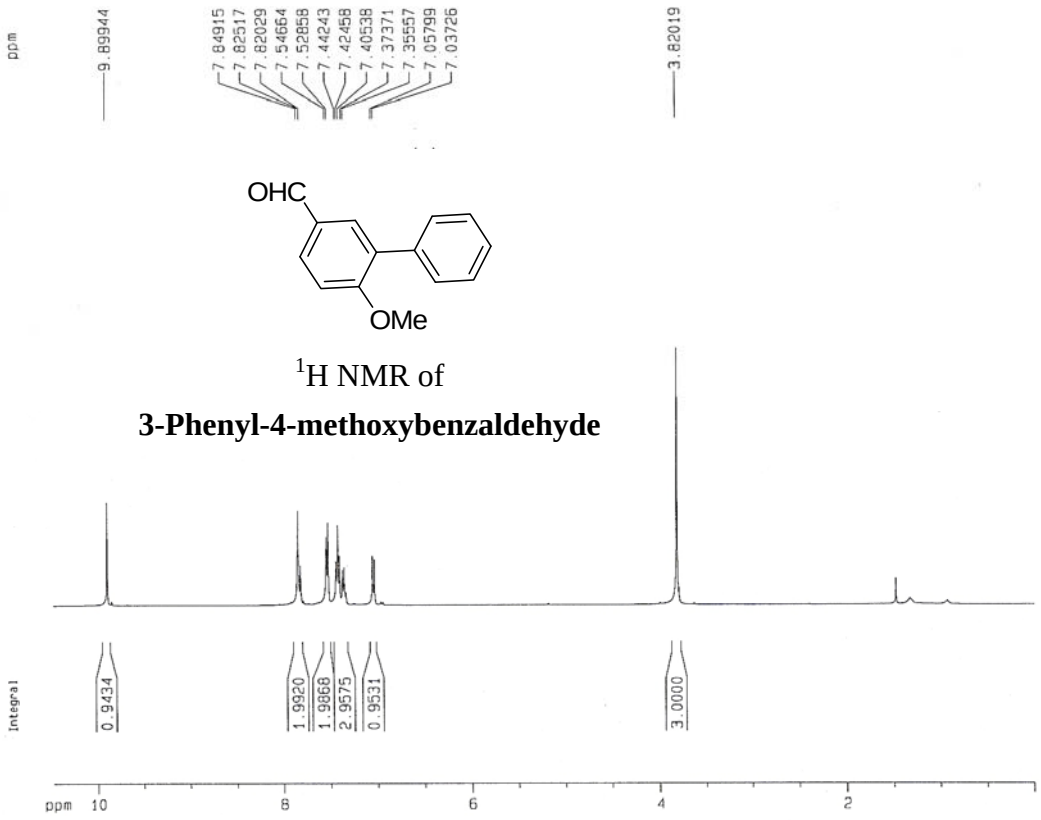
^{13}C NMR of

2-Cyano-4'-methylbiphenyl



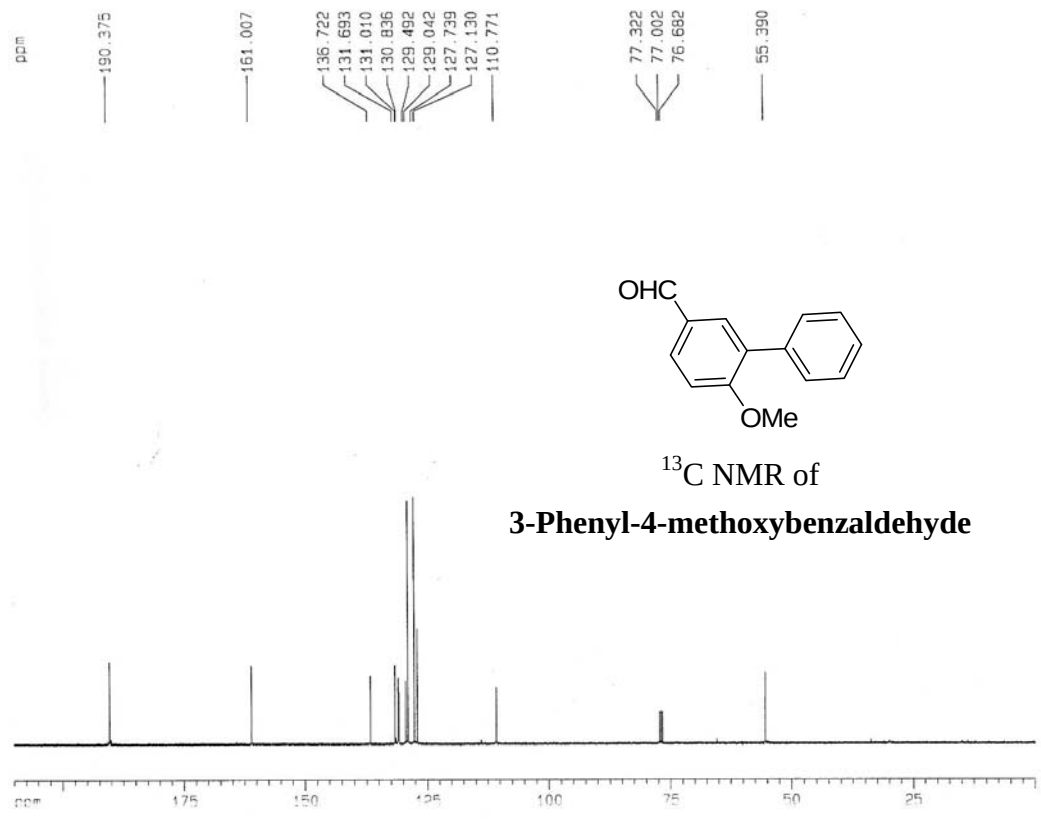
MS of

2-Cyano-4'-methylbiphenyl



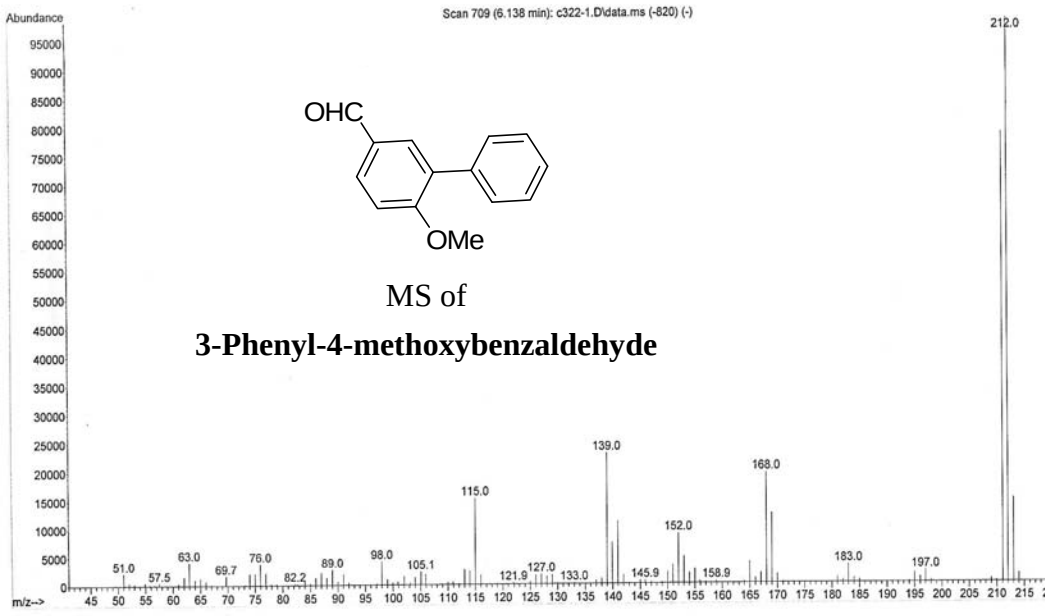
^{1}H NMR of

3-Phenyl-4-methoxybenzaldehyde



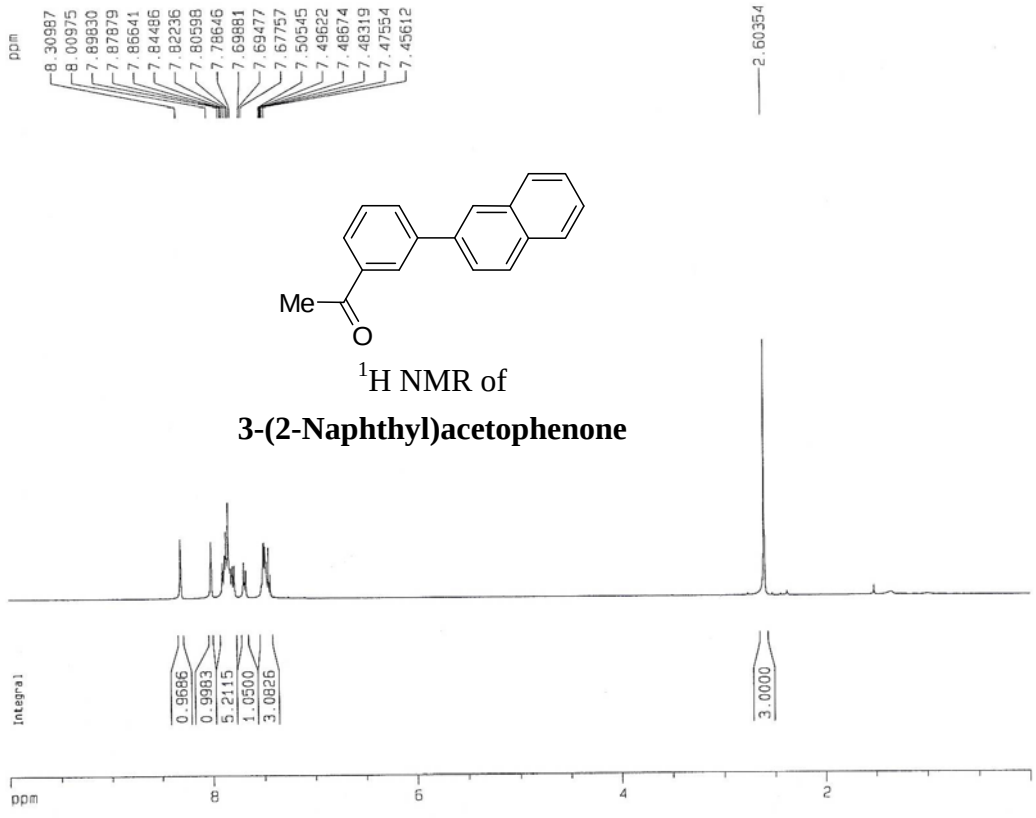
^{13}C NMR of

3-Phenyl-4-methoxybenzaldehyde



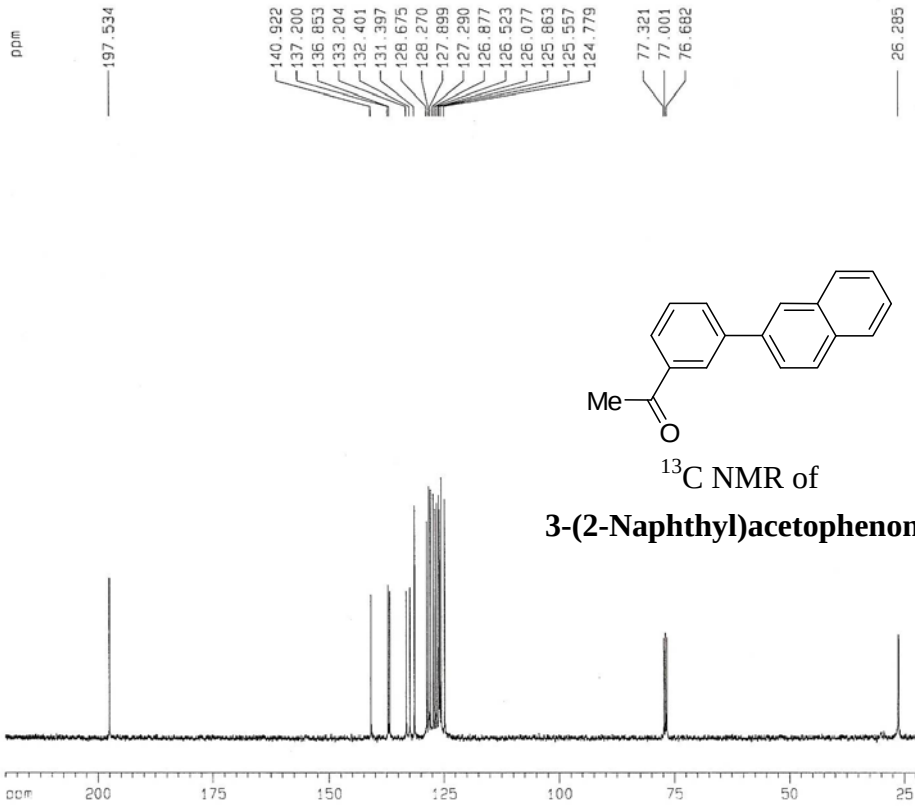
MS of

3-Phenyl-4-methoxybenzaldehyde



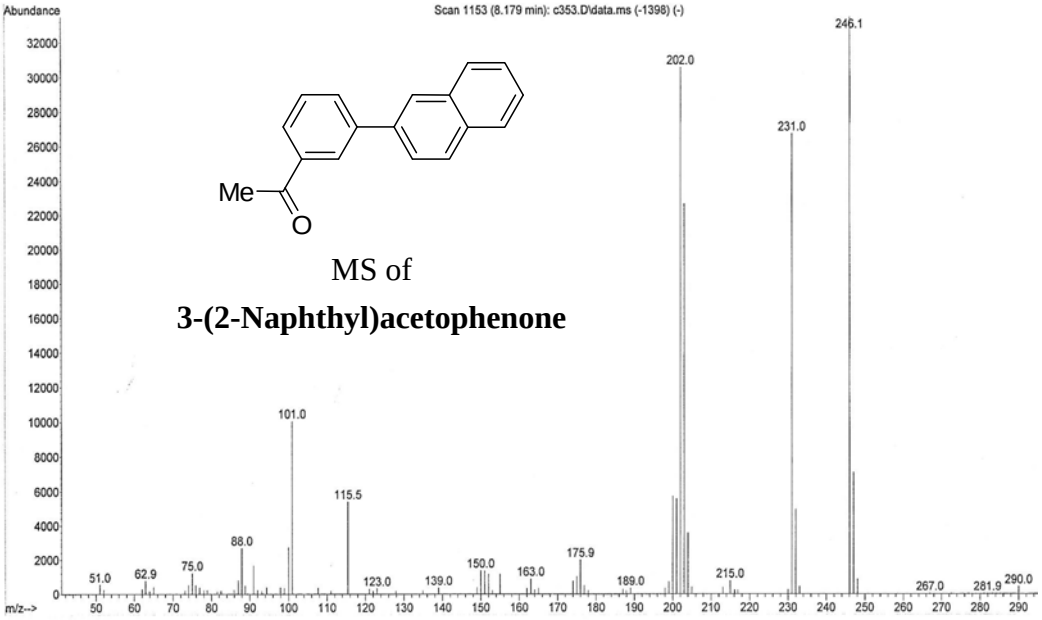
^{1}H NMR of

3-(2-Naphthyl)acetophenone



^{13}C NMR of

3-(2-Naphthyl)acetophenone



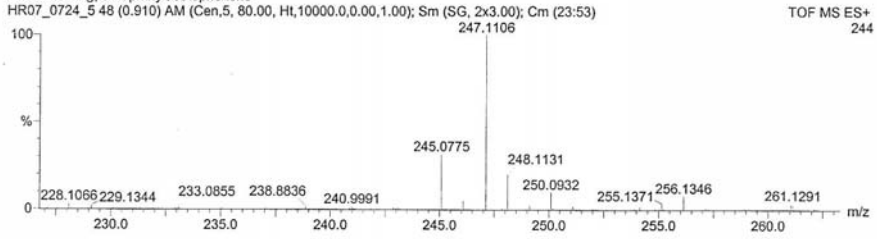
MS of

3-(2-Naphthyl)acetophenone

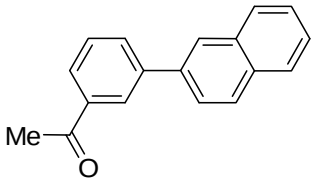
Elemental Composition Report Page 1

Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
8 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-21 H: 0-1000 O: 0-1
So Chau Ming, 3-naphthylacetophenone
HR07_0724_5 48 (0.910) AM (Cen,5, 80.00, Ht,10000.0,0.00,1.00); Sm (SG, 2x3.00); Cm (23:53) TOF MS ES+ 244

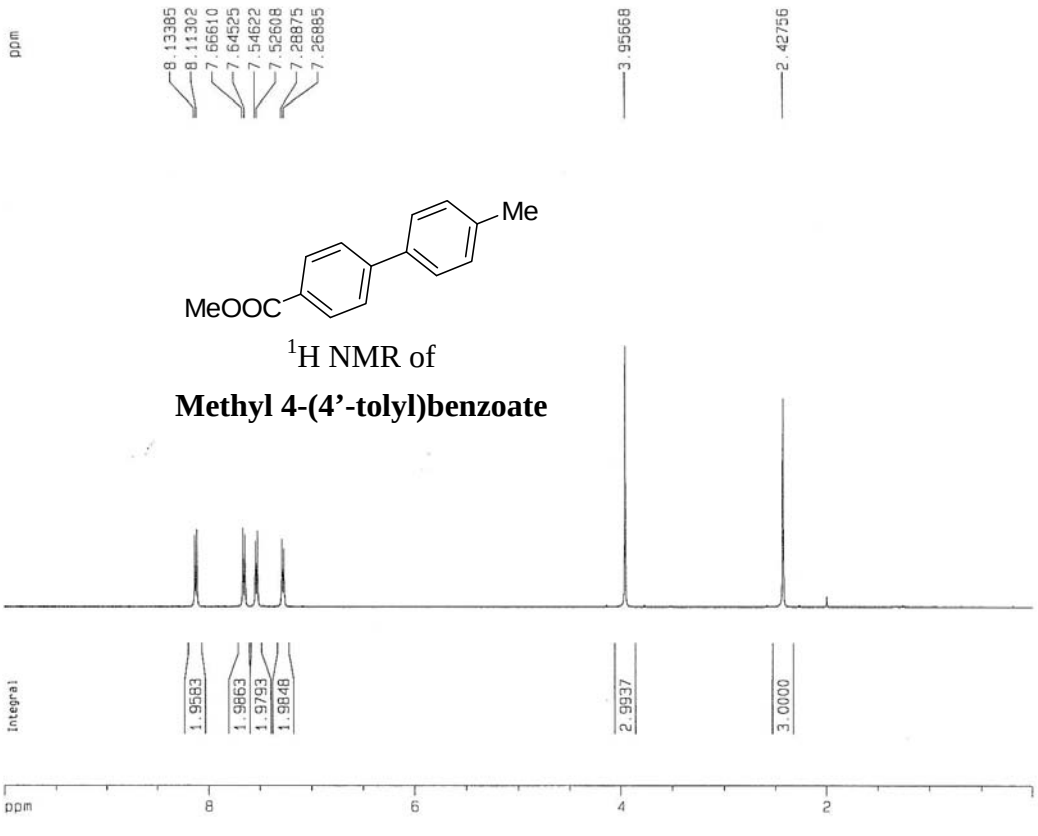


Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
247.1106	247.1123	-1.7	-6.9	11.5	0.1	C18 H15 O



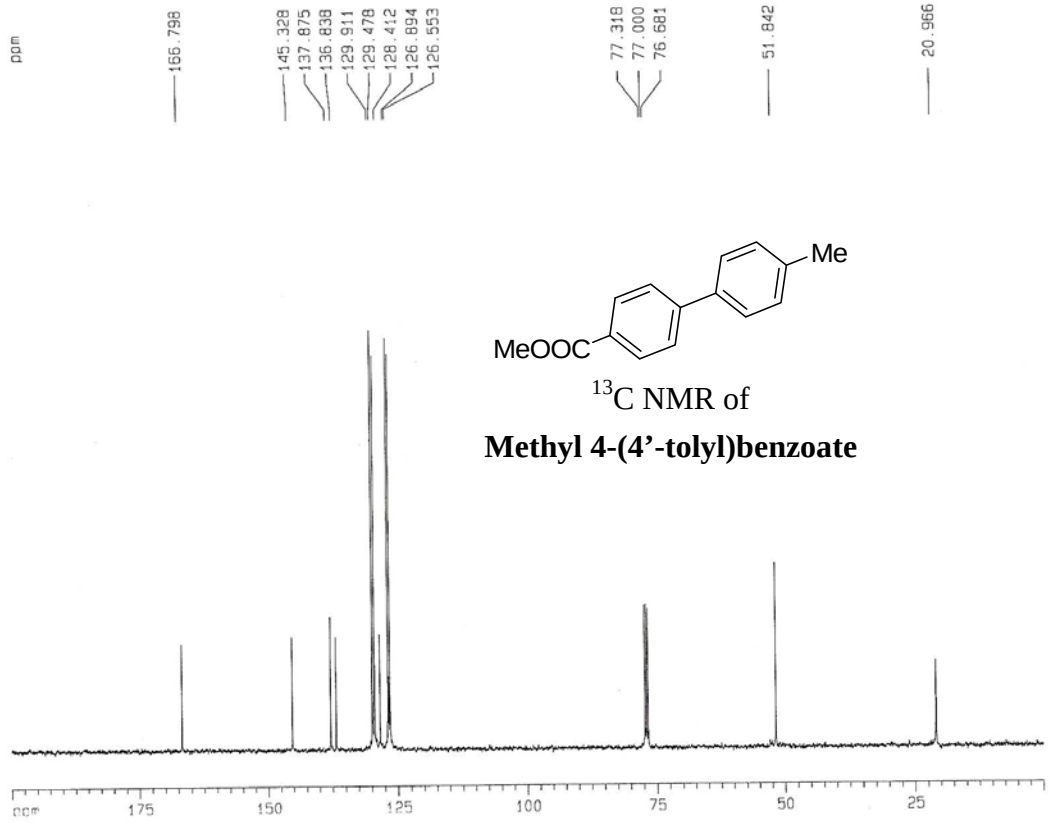
HRMS of

3-(2-Naphthyl)acetophenone



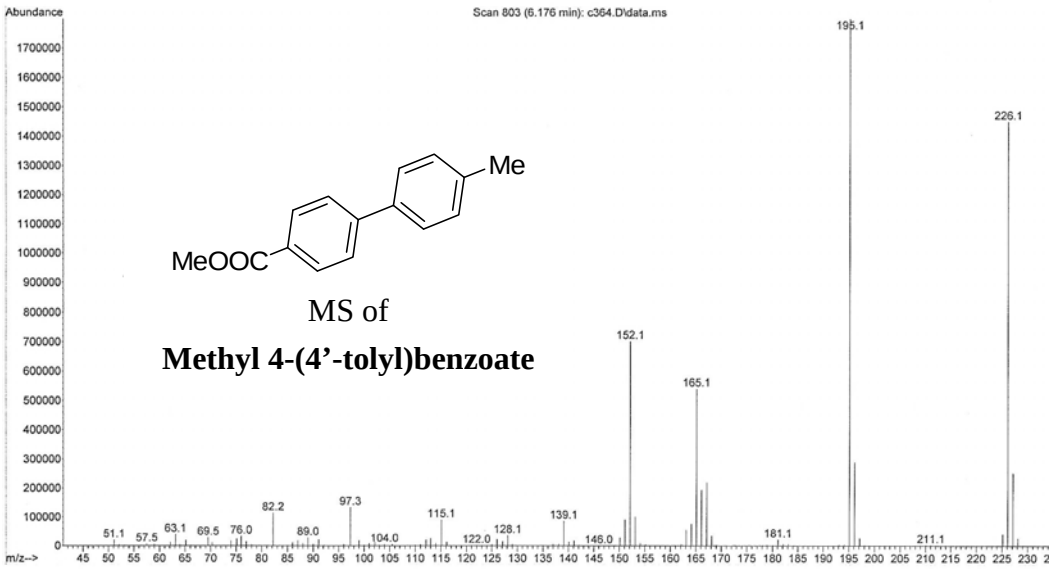
^{1}H NMR of

Methyl 4-(4'-tolyl)benzoate



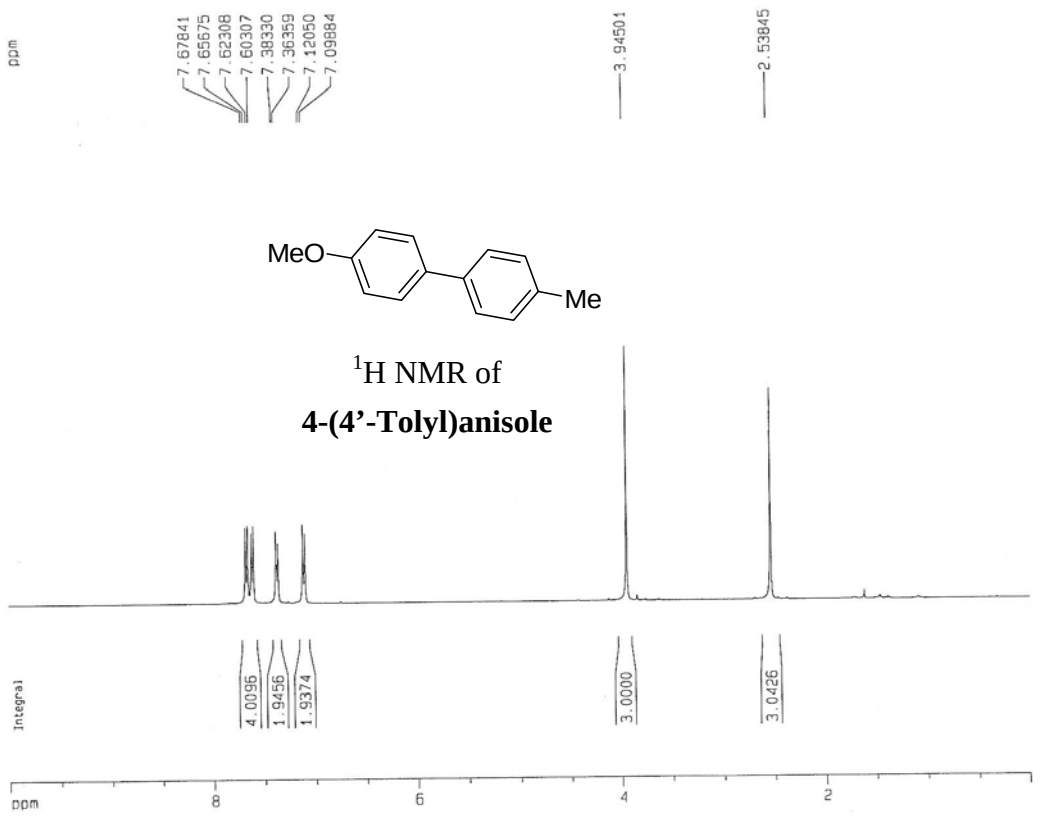
^{13}C NMR of

Methyl 4-(4’-tolyl)benzoate



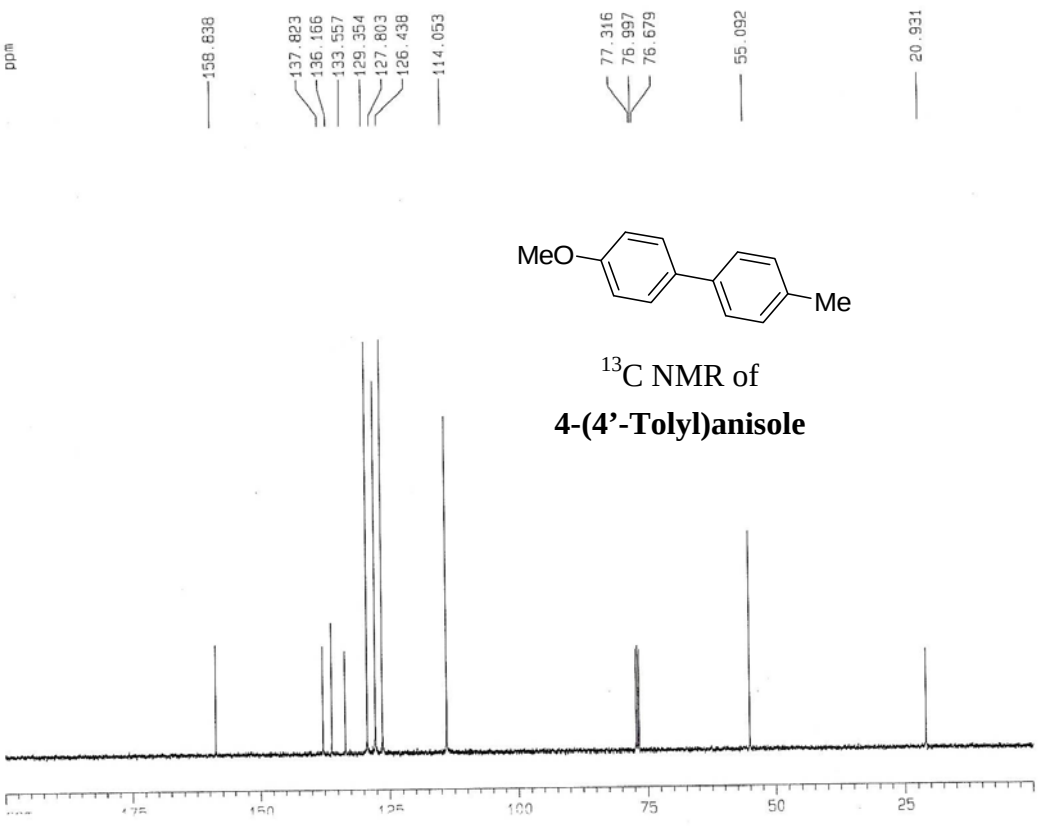
MS of

Methyl 4-(4’-tolyl)benzoate



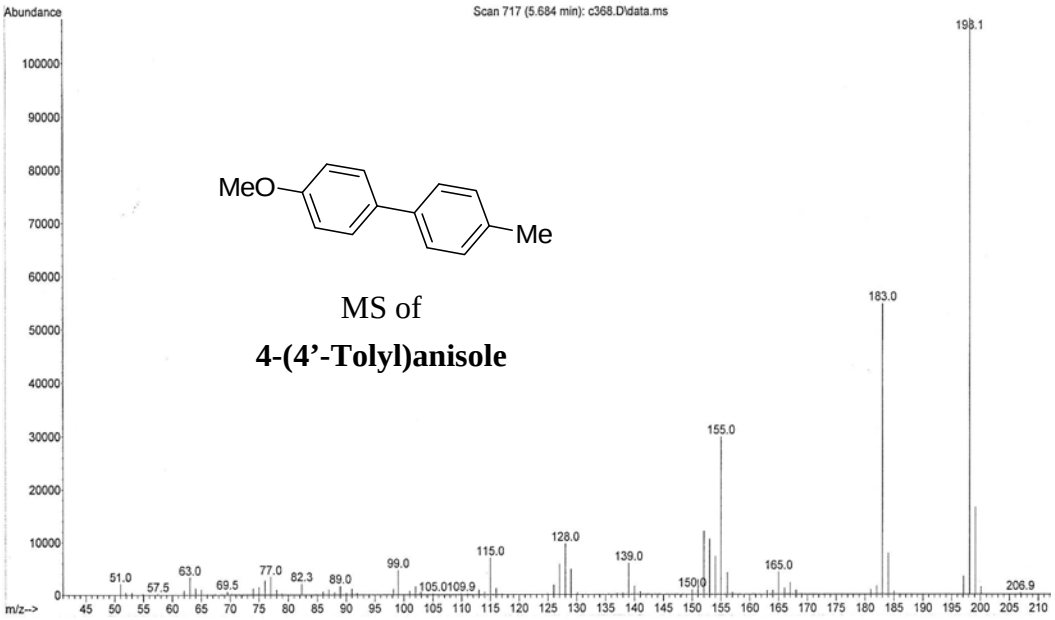
^{1}H NMR of

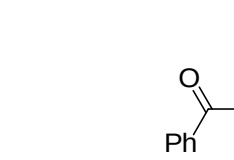
4-(4’-Tolyl)anisole



^{13}C NMR of

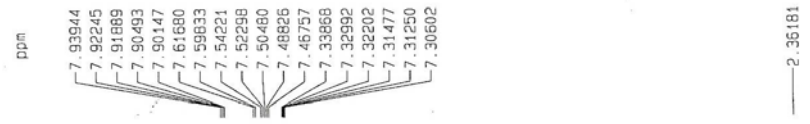
4-(4’-Tolyl)anisole

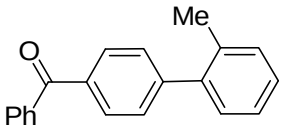




MS of

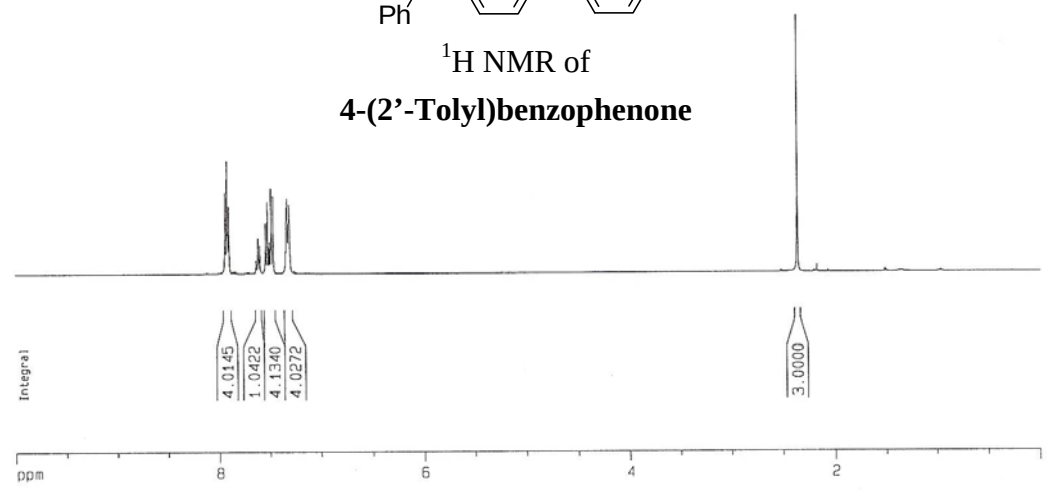
4-(4'-Tolyl)anisole

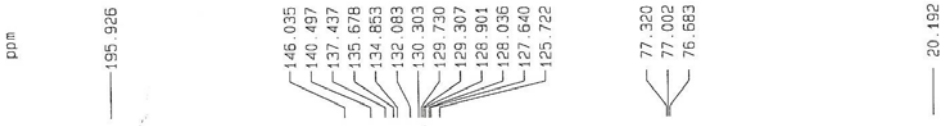


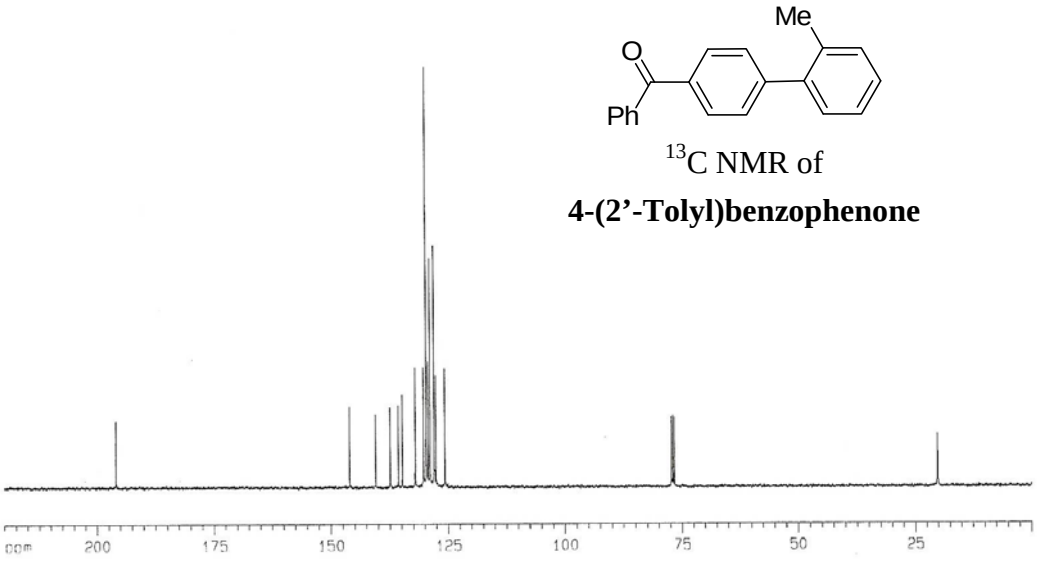


^{1}H NMR of

4-(2'-Tolyl)benzophenone

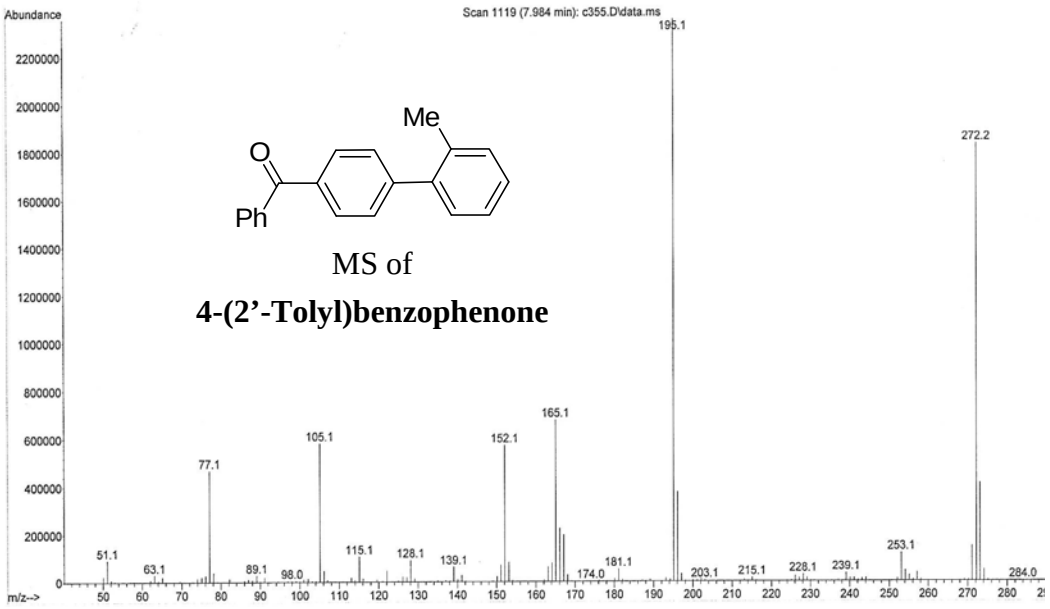






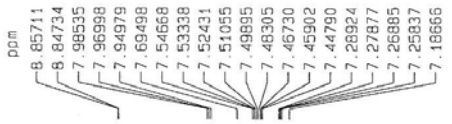
^{13}C NMR of

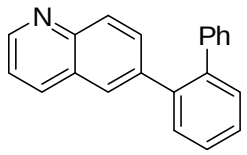
4-(2'-Tolyl)benzophenone



MS of

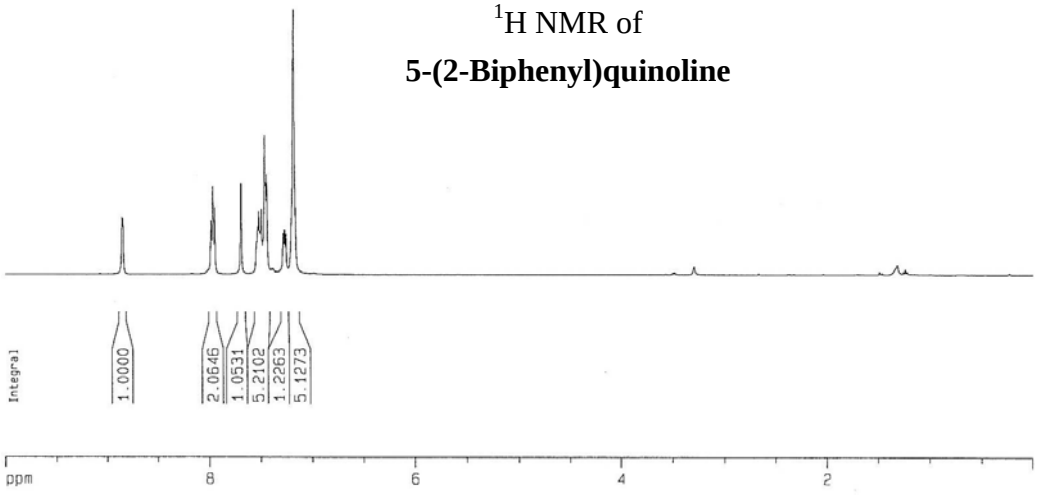
4-(2'-Tolyl)benzophenone

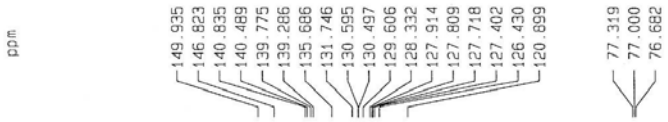


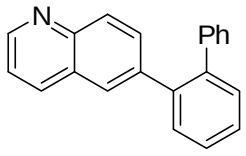


^{1}H NMR of

5-(2-Biphenyl)quinoline

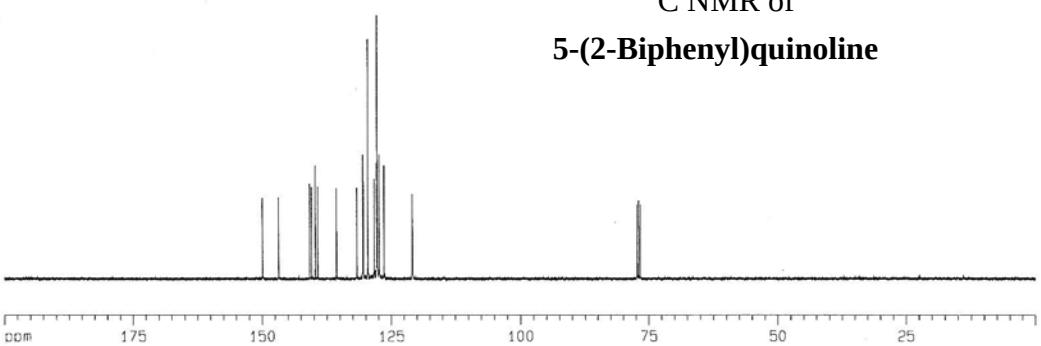


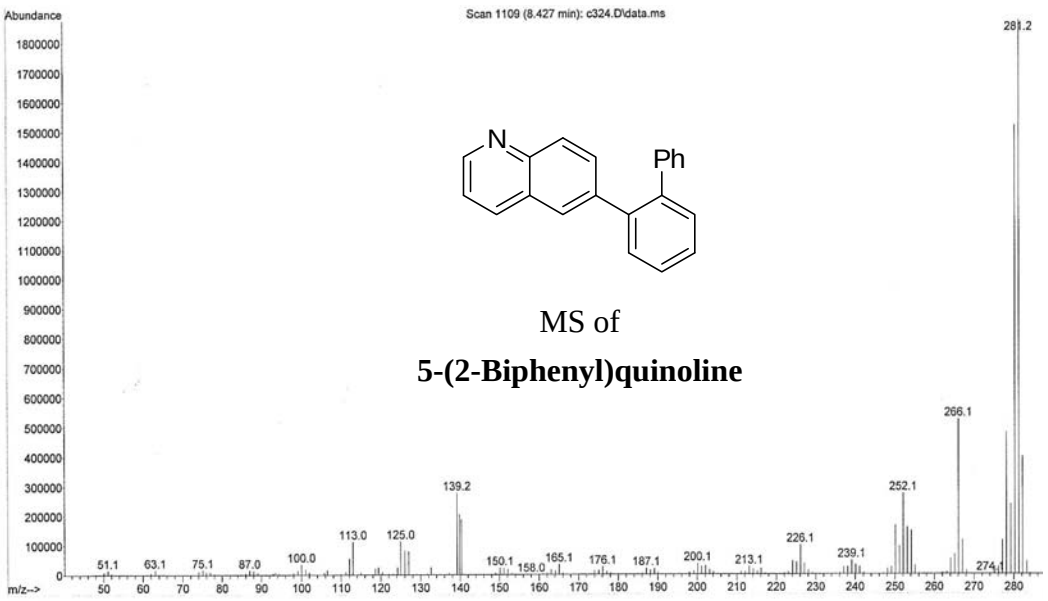




^{13}C NMR of

5-(2-Biphenyl)quinoline

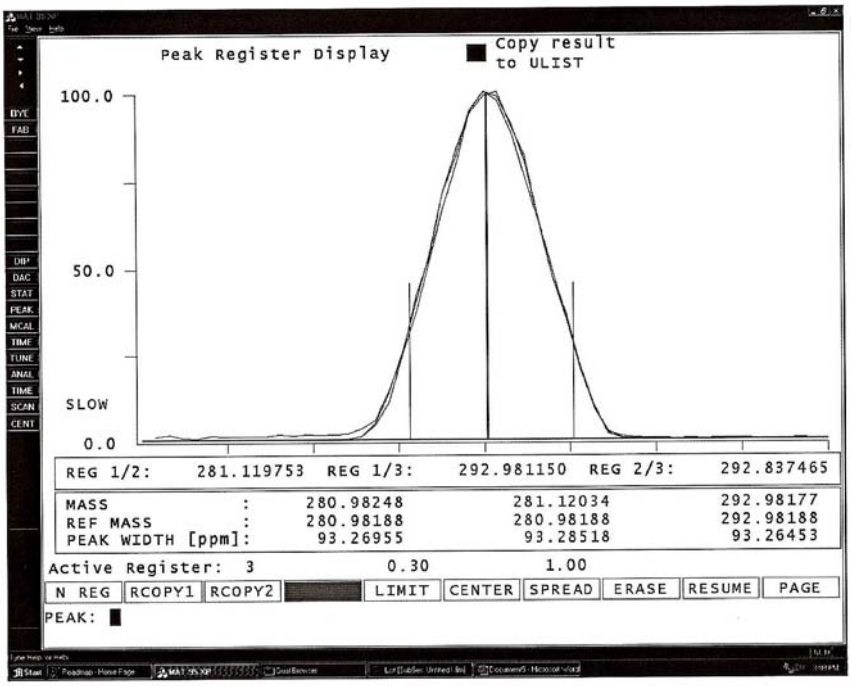




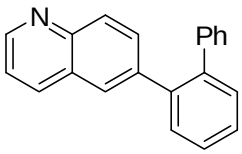
MS of

5-(2-Biphenyl)quinoline

Accurate Mass Measurement:

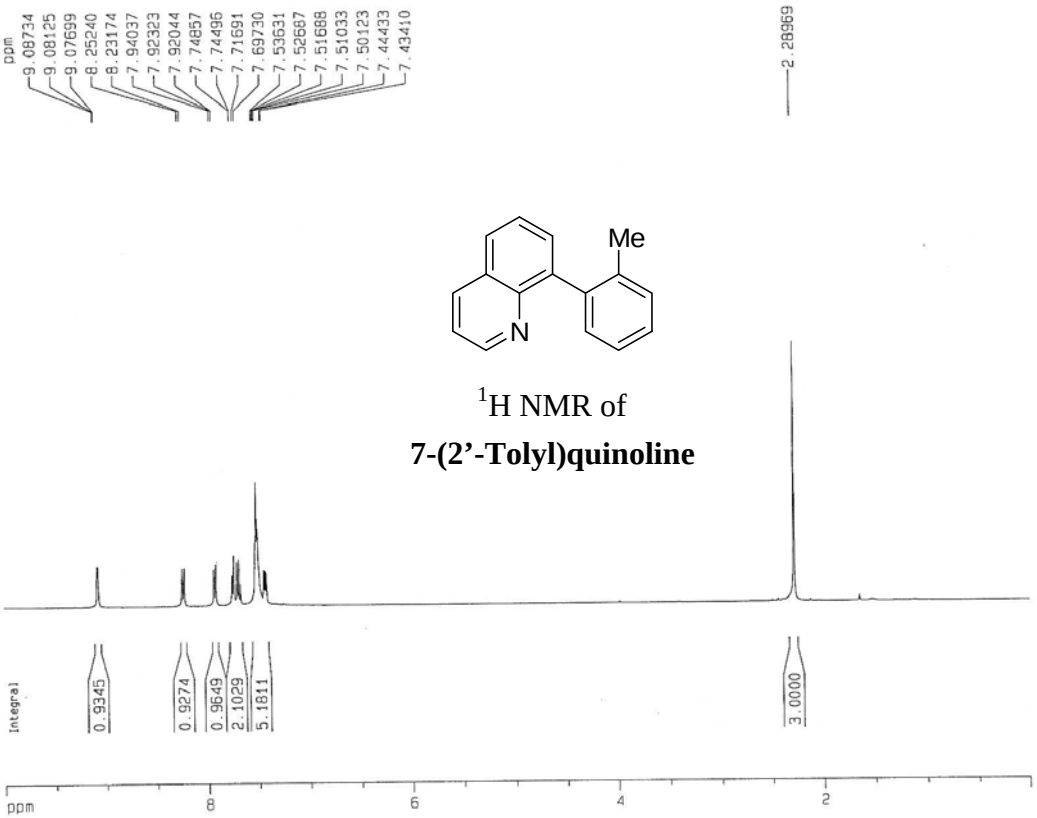


Molecular formula: $C_{21}H_{15}N_1$
$[M]^+$ (theoretical) = 281.1199



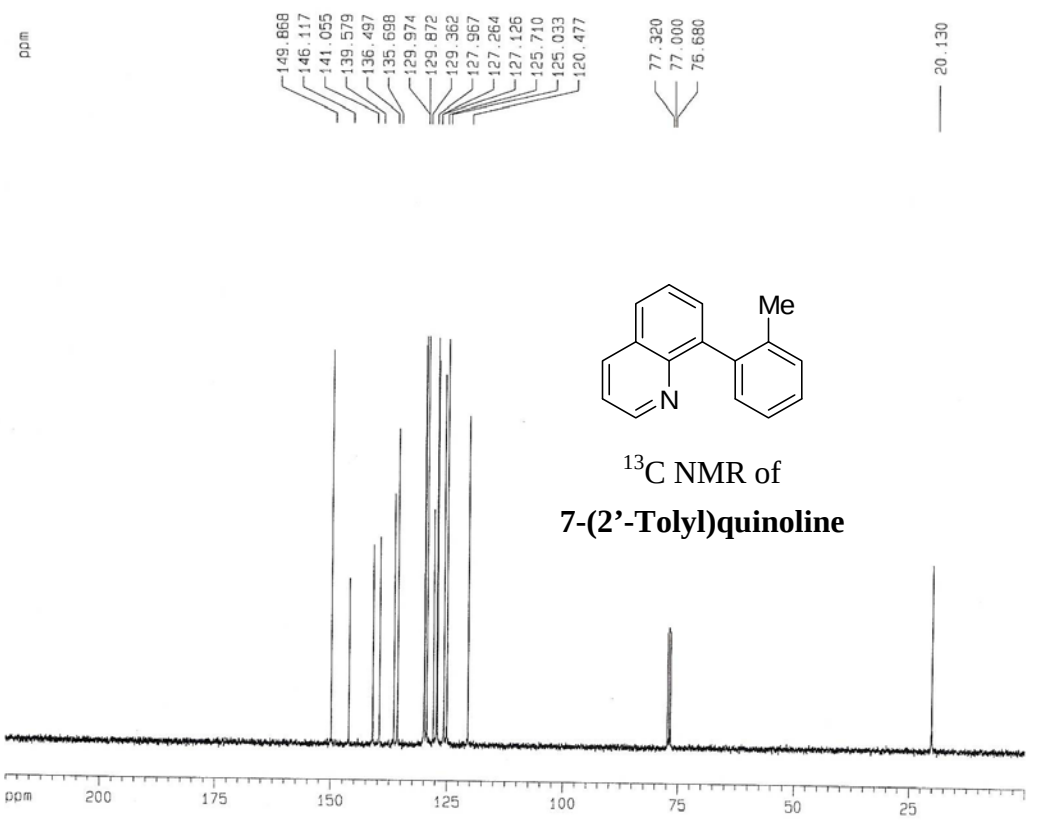
HRMS of

5-(2-Biphenyl)quinoline



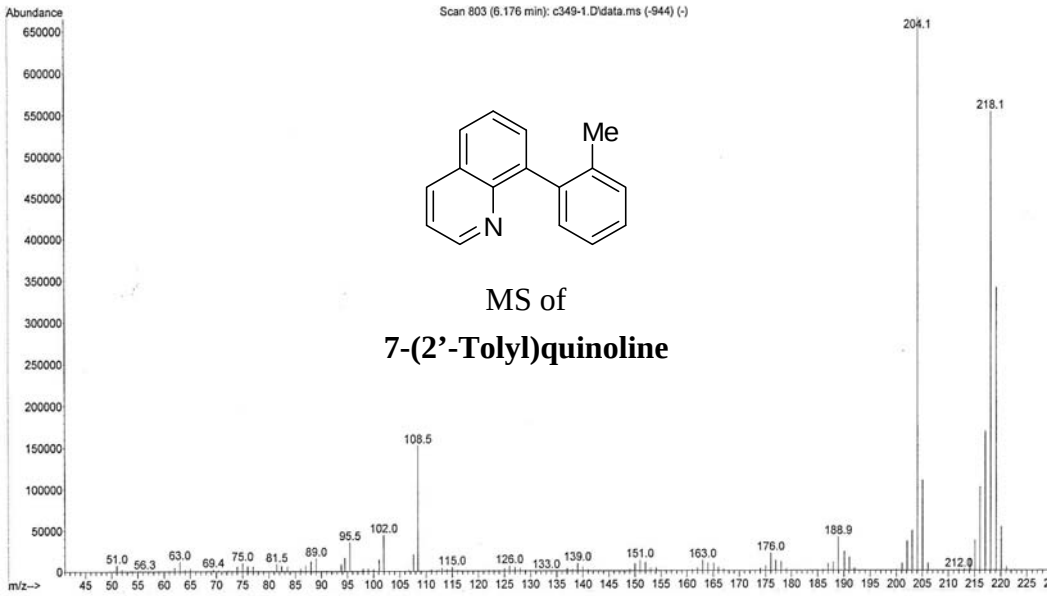
^{1}H NMR of

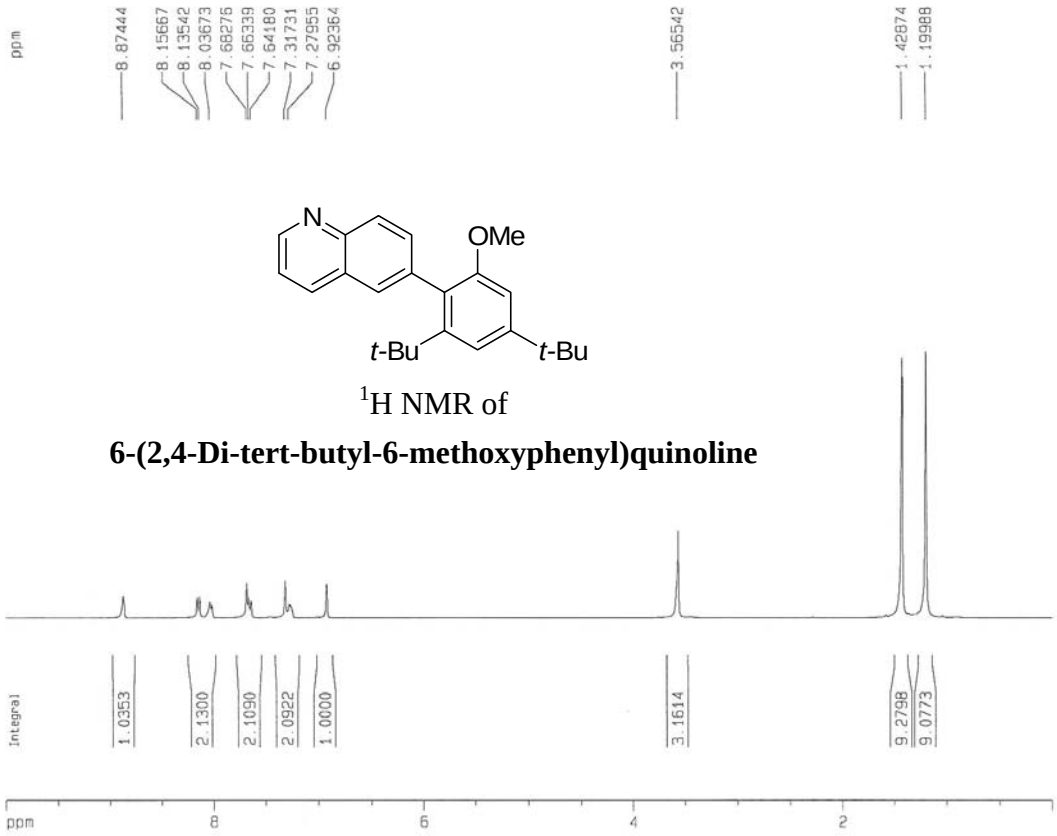
7-(2'-Tolyl)quinoline



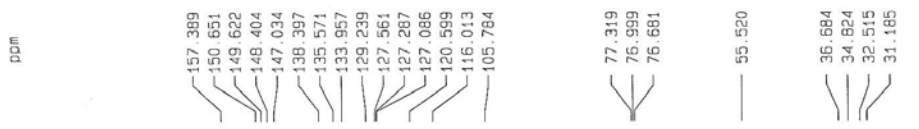
^{13}C NMR of

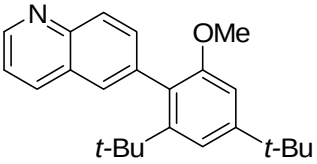
7-(2'-Tolyl)quinoline





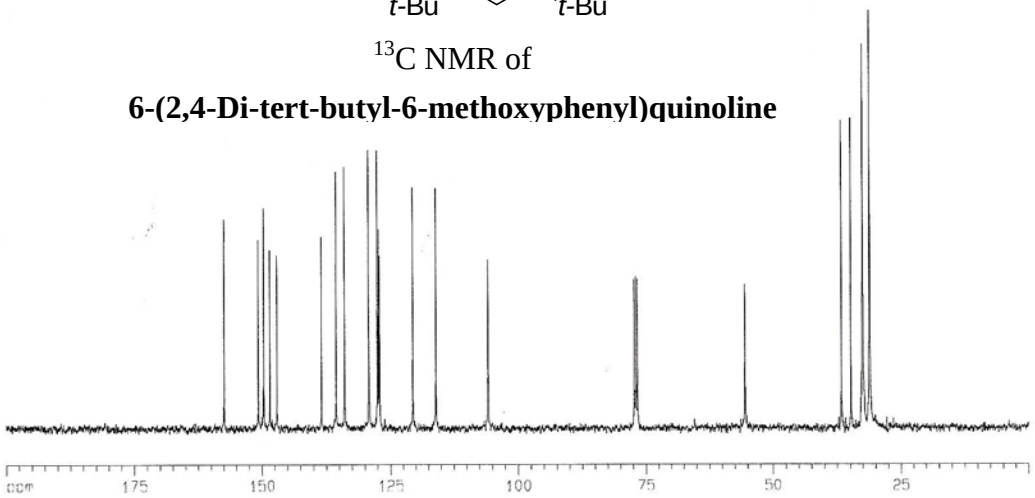
^{1}H NMR of
6-(2,4-Di-tert-butyl-6-methoxyphenyl)quinoline

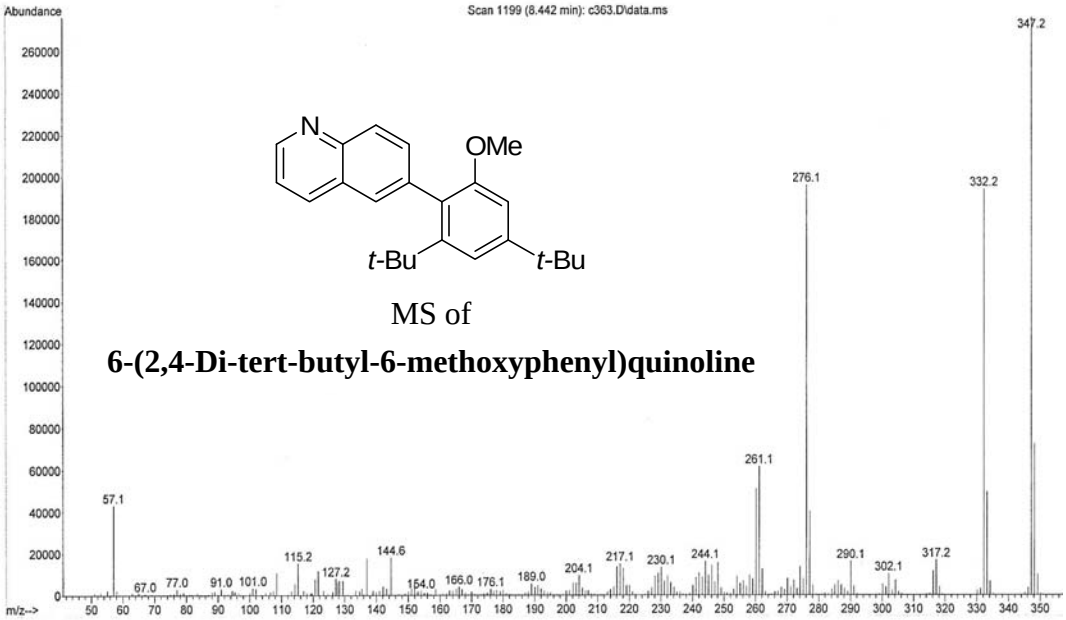




^{13}C NMR of

6-(2,4-Di-tert-butyl-6-methoxyphenyl)quinoline

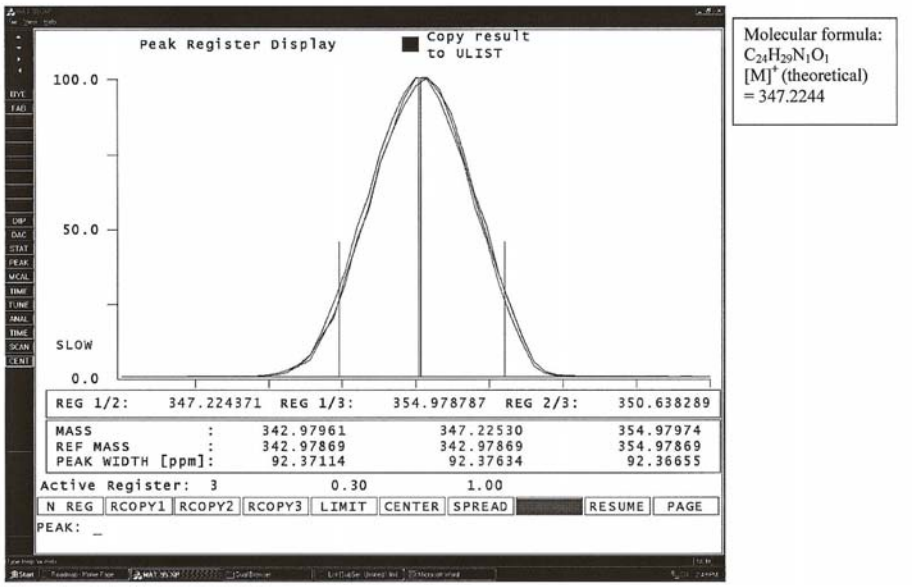


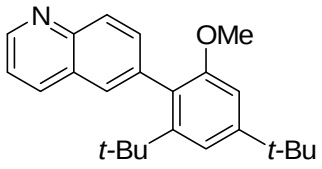


MS of

6-(2,4-Di-tert-butyl-6-methoxyphenyl)quinoline

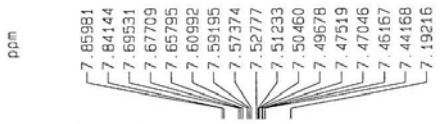
Accurate Mass Measurement:

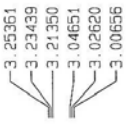


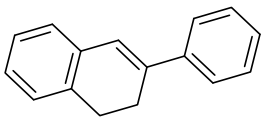


HRMS of

6-(2,4-Di-tert-butyl-6-methoxyphenyl)quinoline

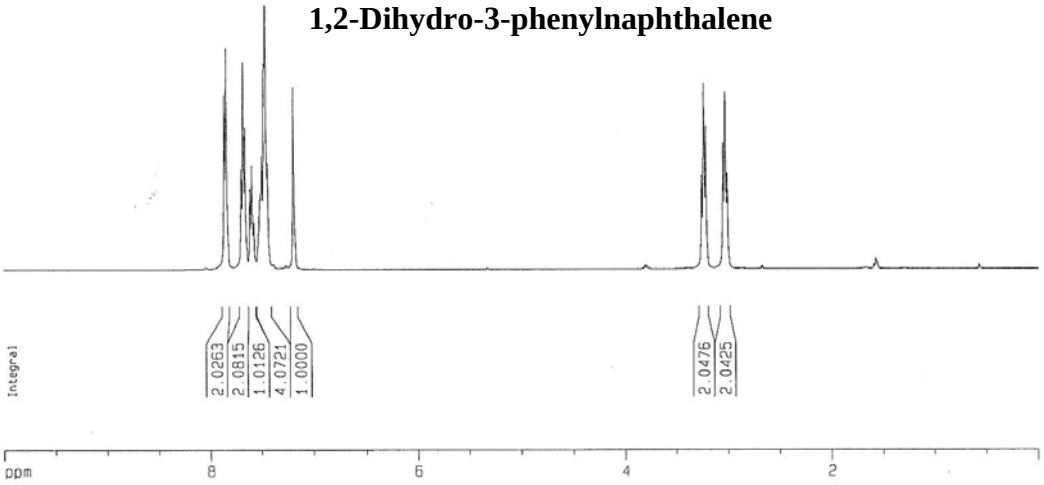


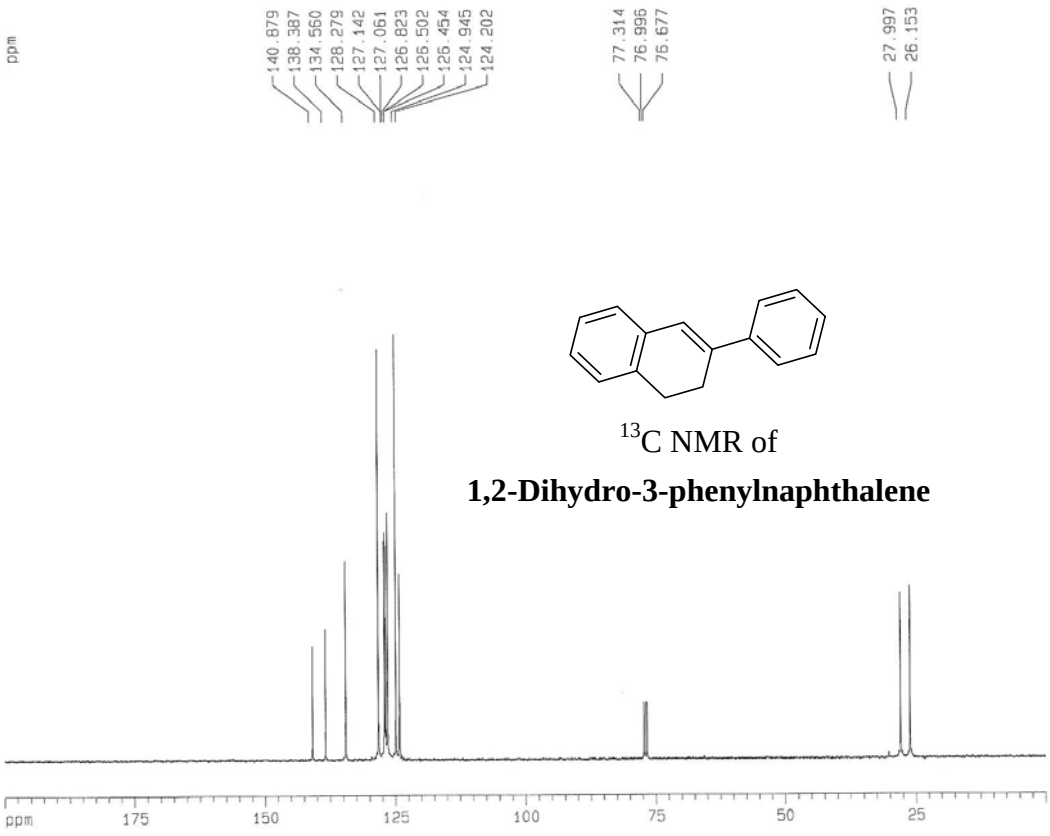




^{1}H NMR of

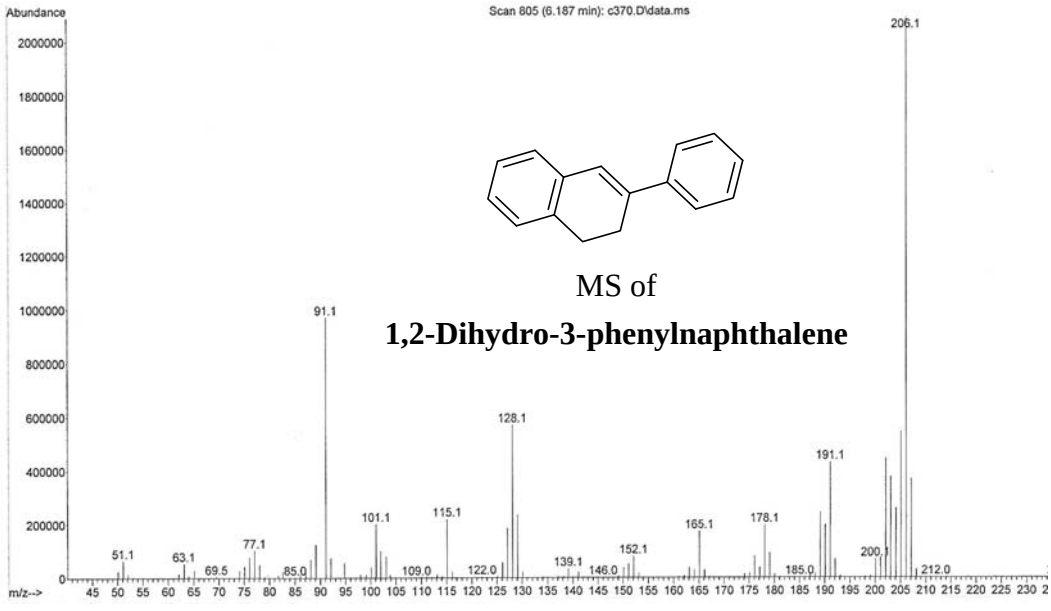
1,2-Dihydro-3-phenylnaphthalene





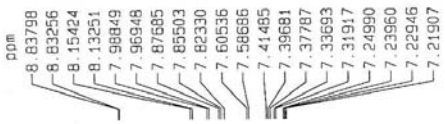
^{13}C NMR of

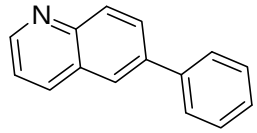
1,2-Dihydro-3-phenylnaphthalene



MS of

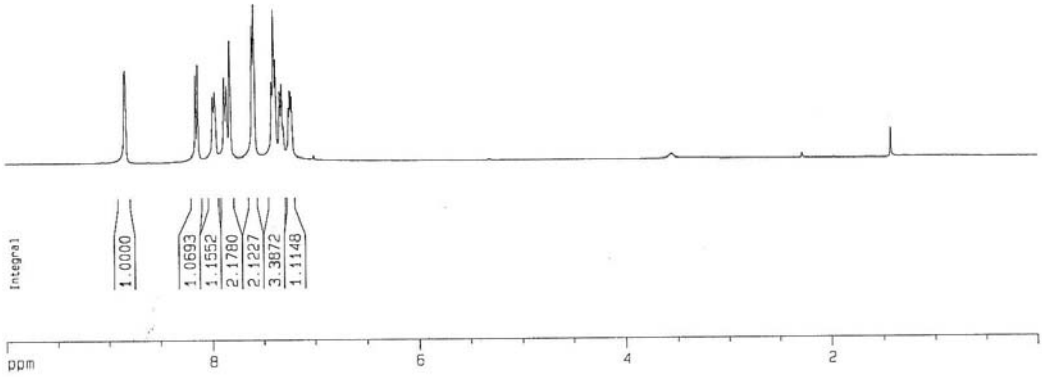
1,2-Dihydro-3-phenylnaphthalene

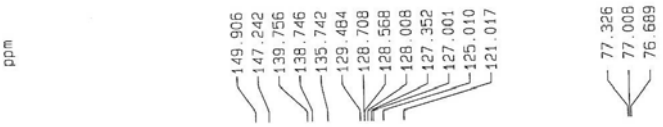


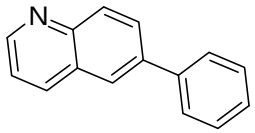


^{1}H NMR of

6-Phenylquinoline

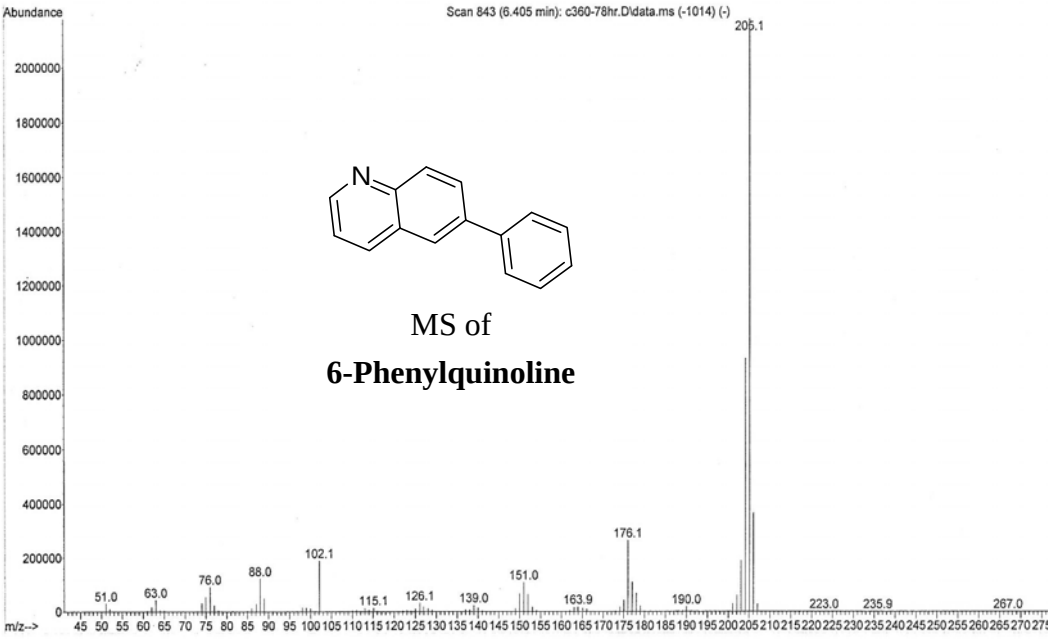






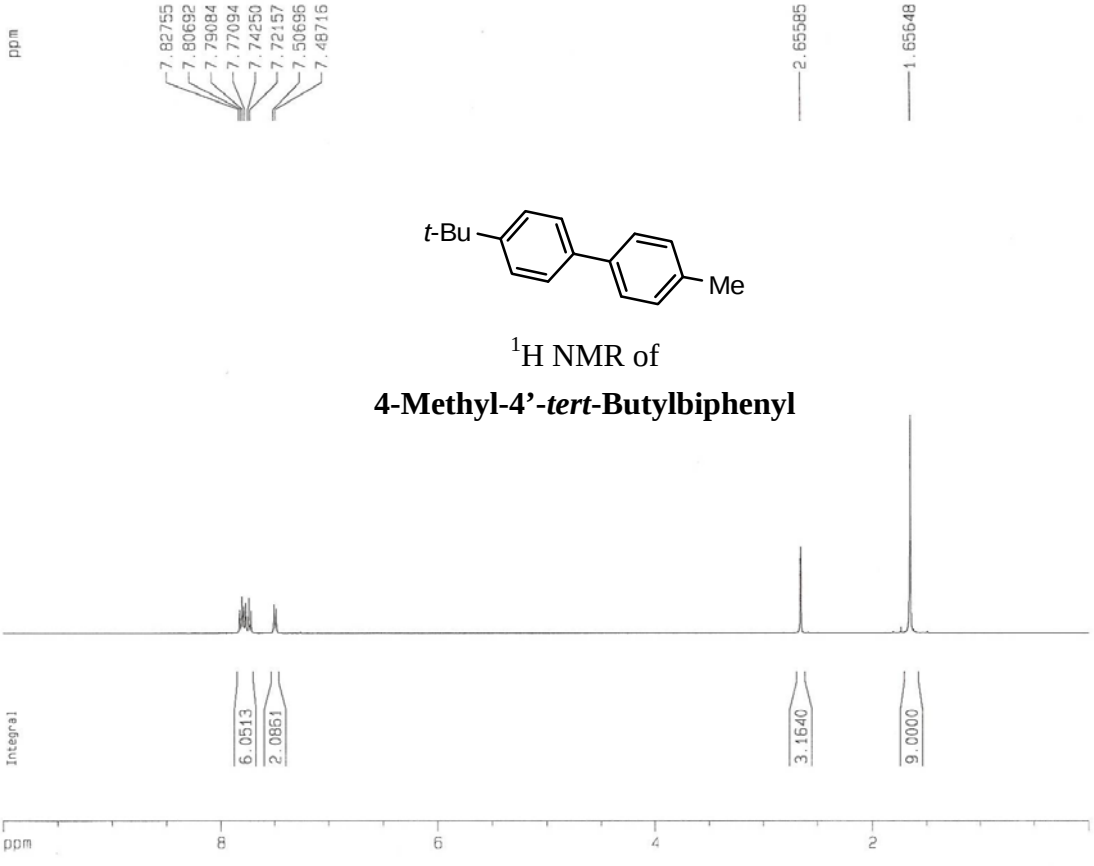
^{13}C NMR of

6-Phenylquinoline



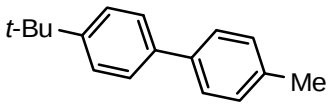
MS of

6-Phenylquinoline



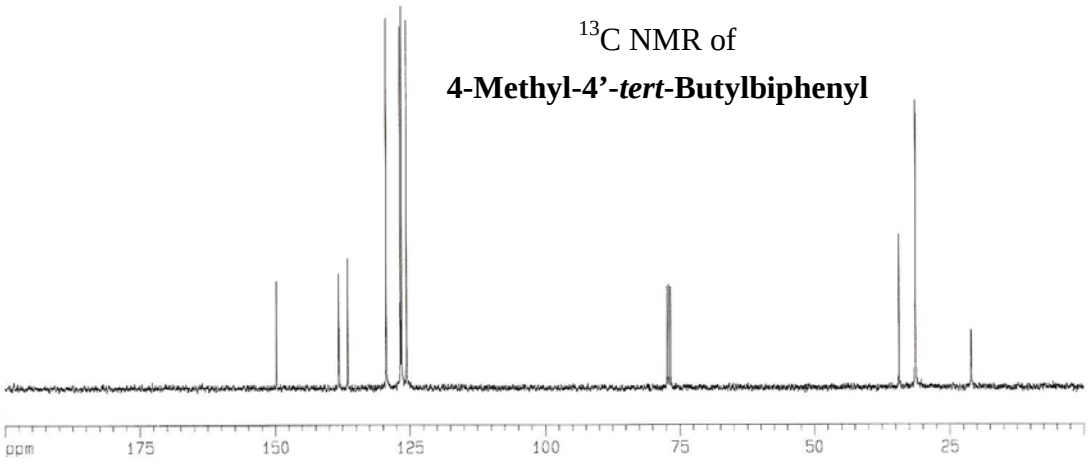
^{1}H NMR of

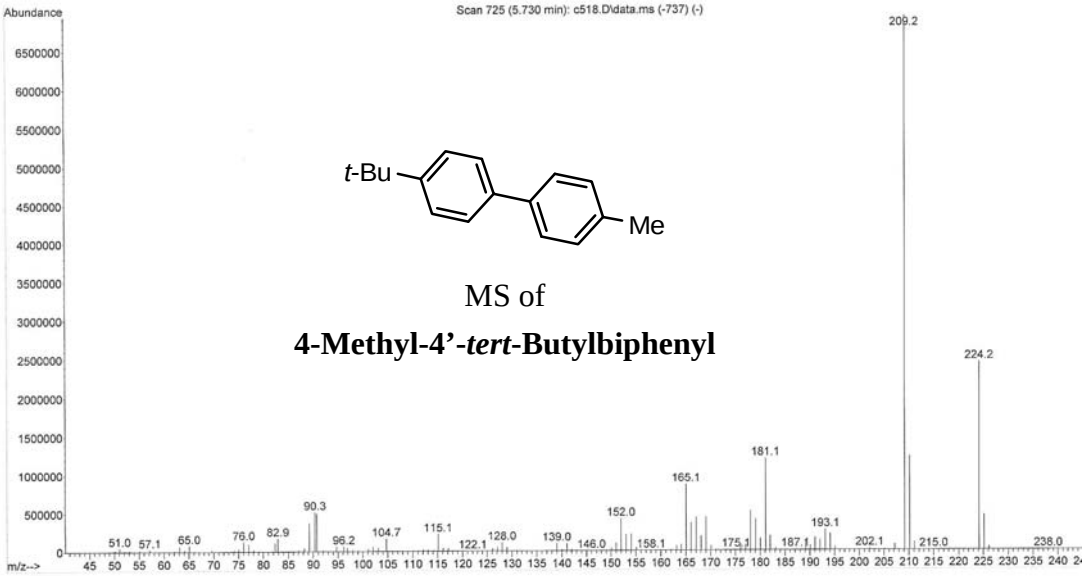
4-Methyl-4'-*tert*-Butylbiphenyl



^{13}C NMR of

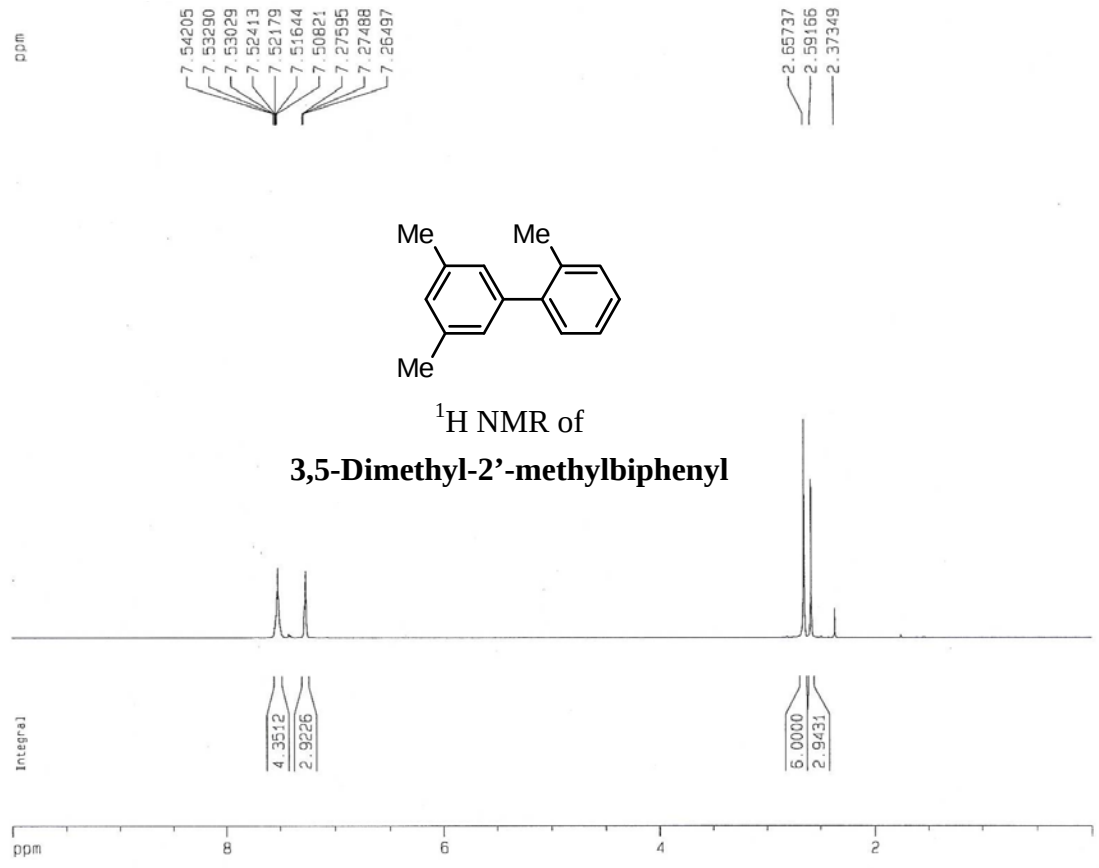
4-Methyl-4'-*tert*-Butylbiphenyl





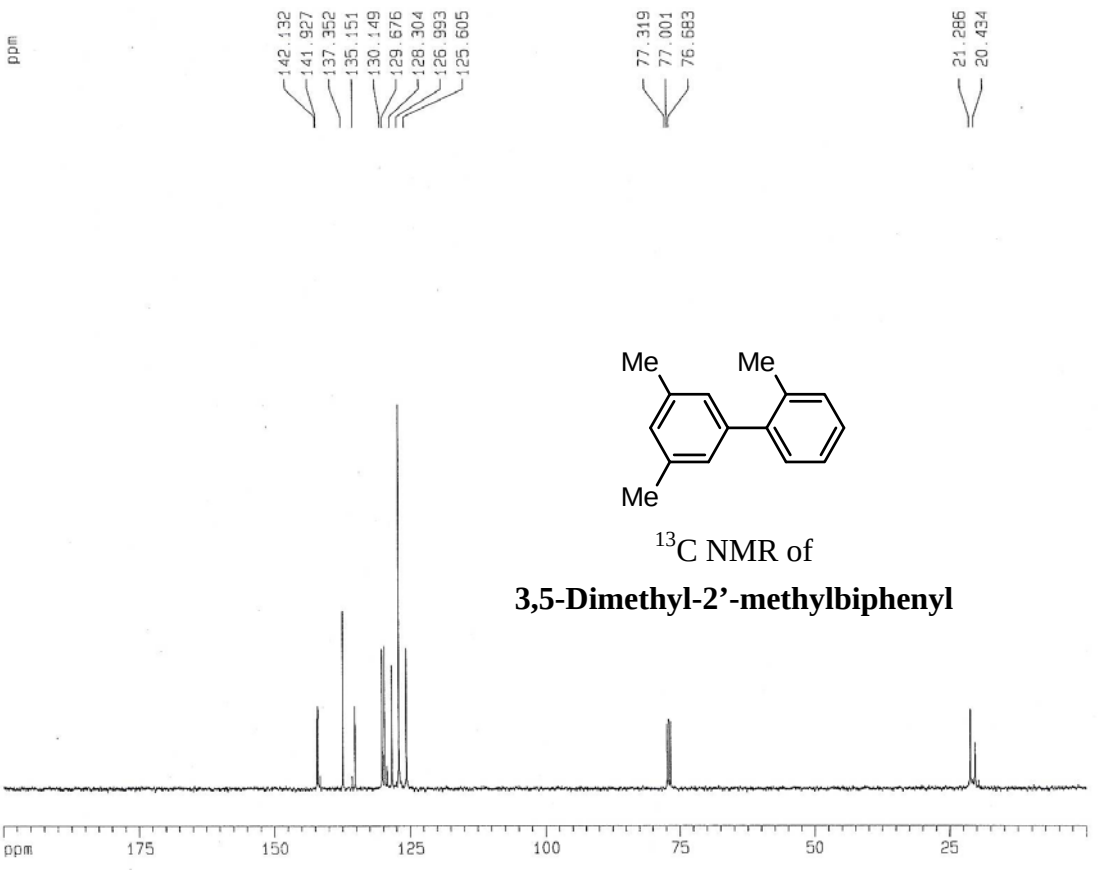
MS of

4-Methyl-4'-*tert*-Butylbiphenyl



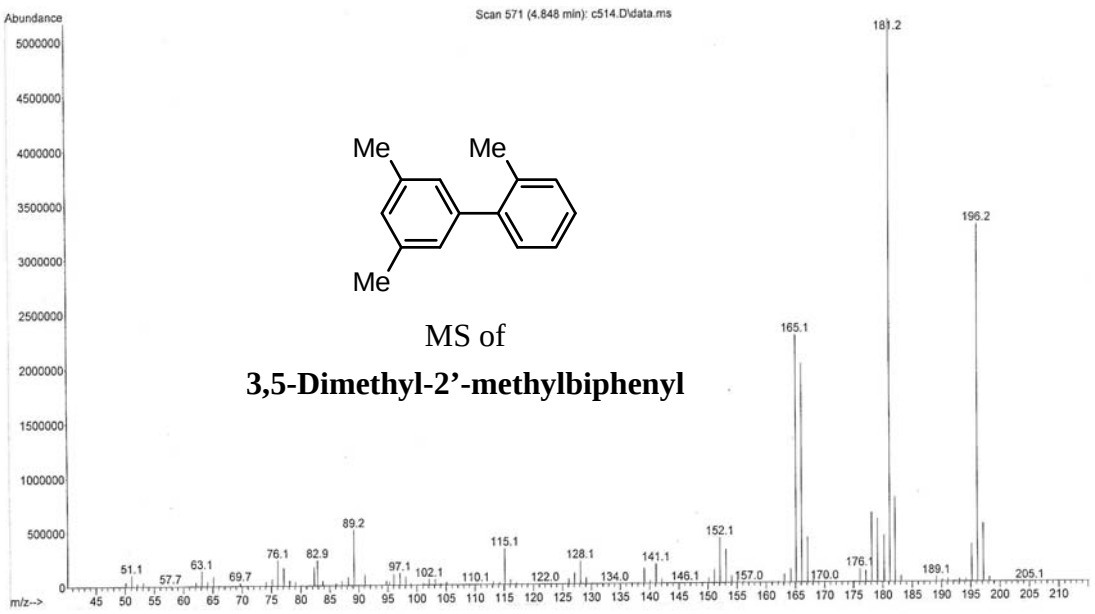
^{1}H NMR of

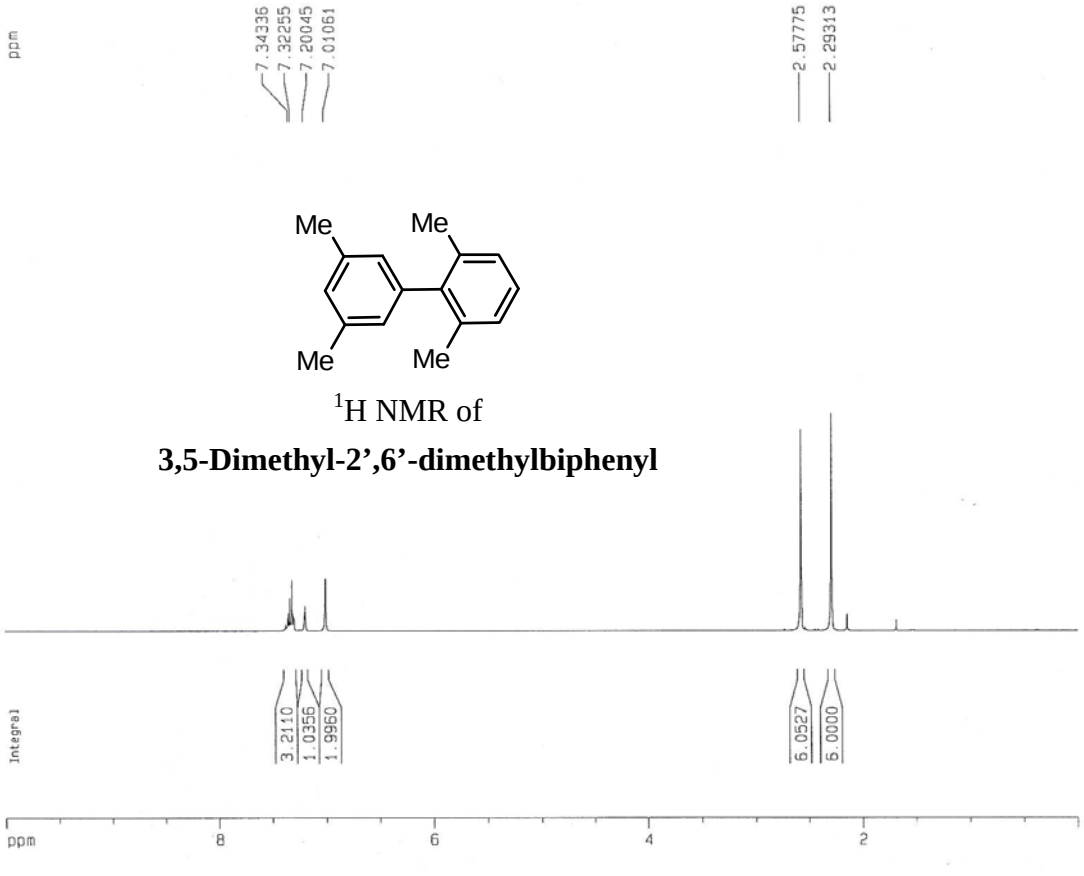
3,5-Dimethyl-2'-methylbiphenyl

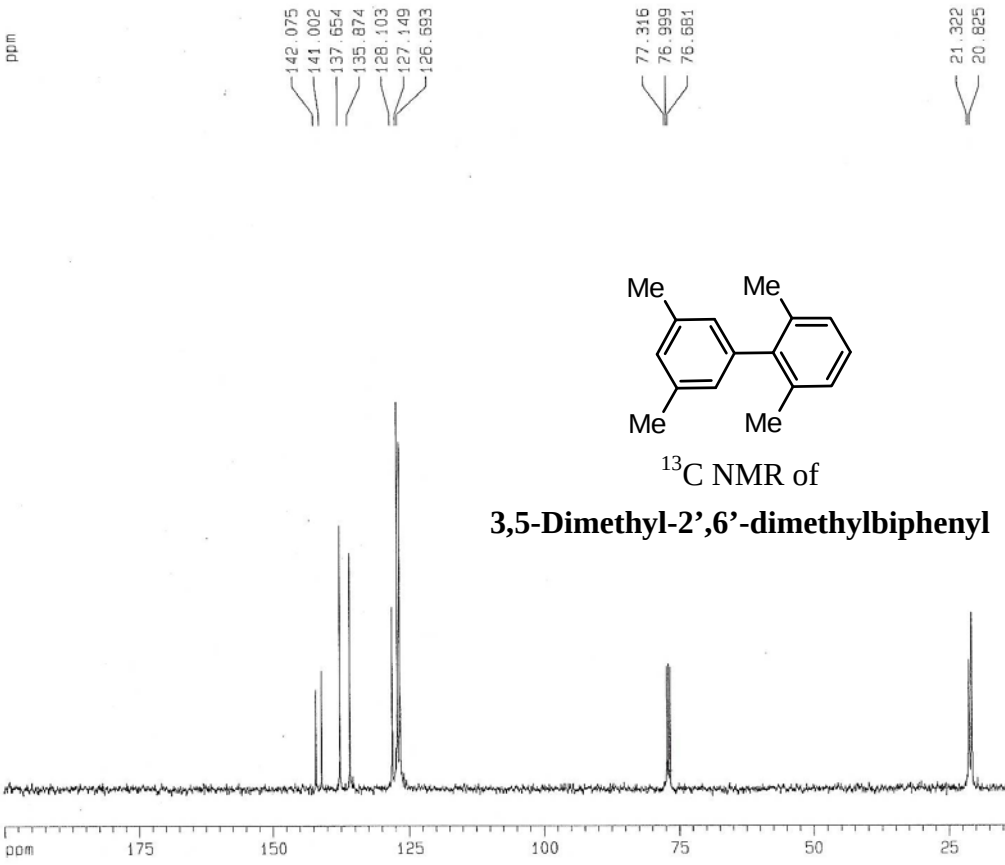


^{13}C NMR of

3,5-Dimethyl-2'-methylbiphenyl

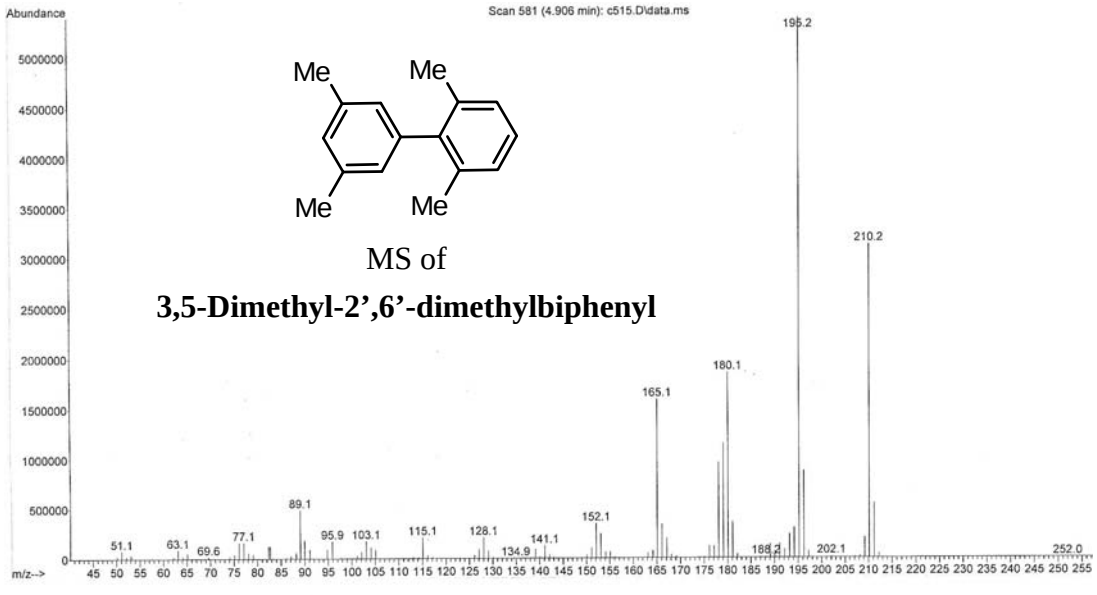

Abundance
Scan 571 (4.848 min): c514.D\data.ms
Me
Me
Me
MS of
3,5-Dimethyl-2'-methylbiphenyl
m/z-->


ppm
7.34336
7.32255
7.20045
7.01061
2.57775
2.29313
Me
Me
Me
Me
^{1}H NMR of
3,5-Dimethyl-2',6'-dimethylbiphenyl
Integral
3.2110
1.0356
1.9960
6.0527
6.0000
ppm



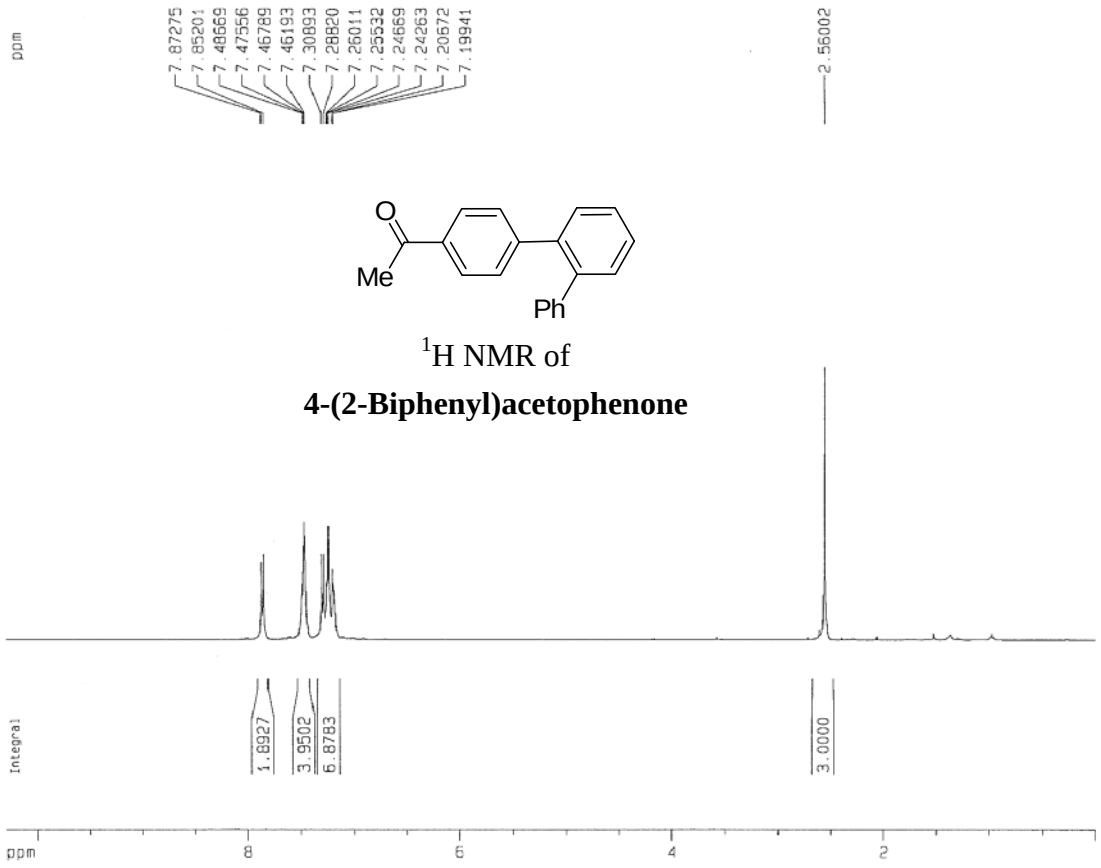
^{13}C NMR of

3,5-Dimethyl-2’,6’-dimethylbiphenyl



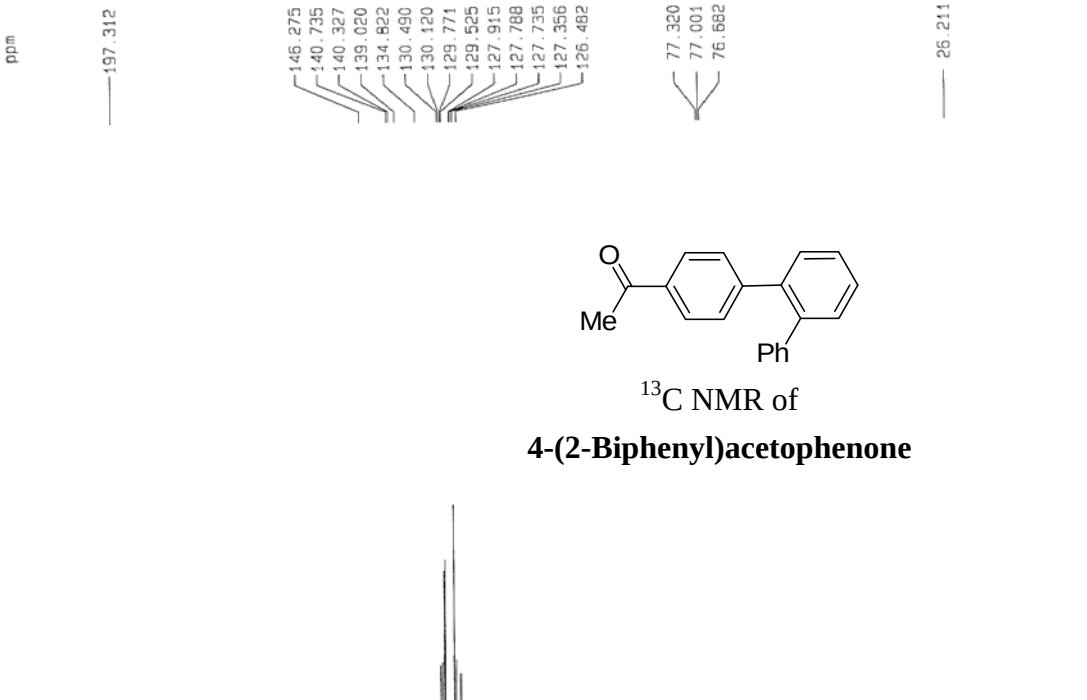
MS of

3,5-Dimethyl-2’,6’-dimethylbiphenyl



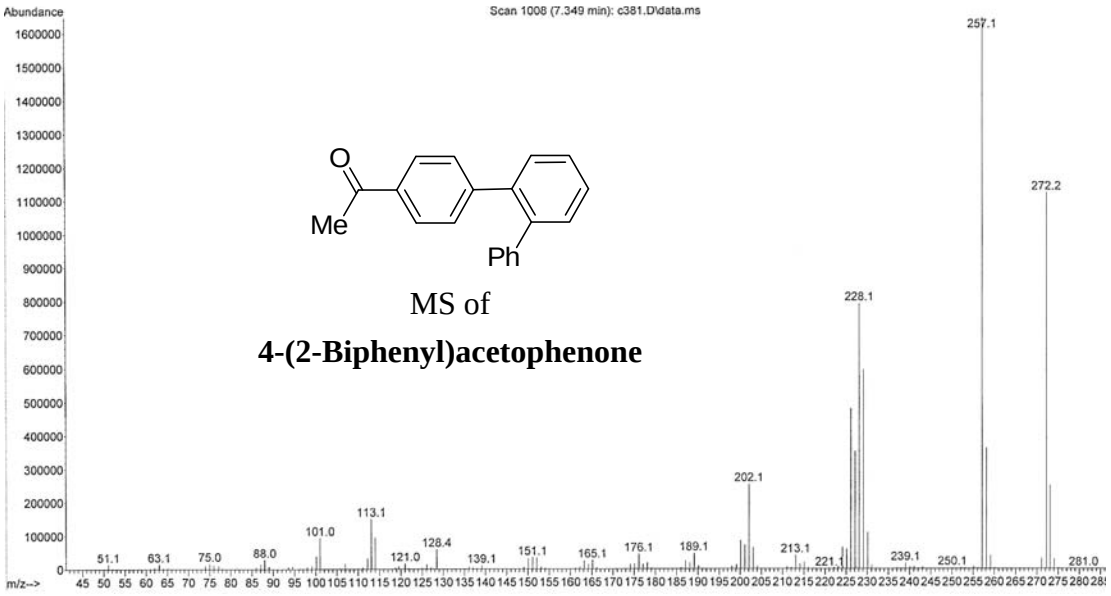
^{1}H NMR of

4-(2-Biphenyl)acetophenone



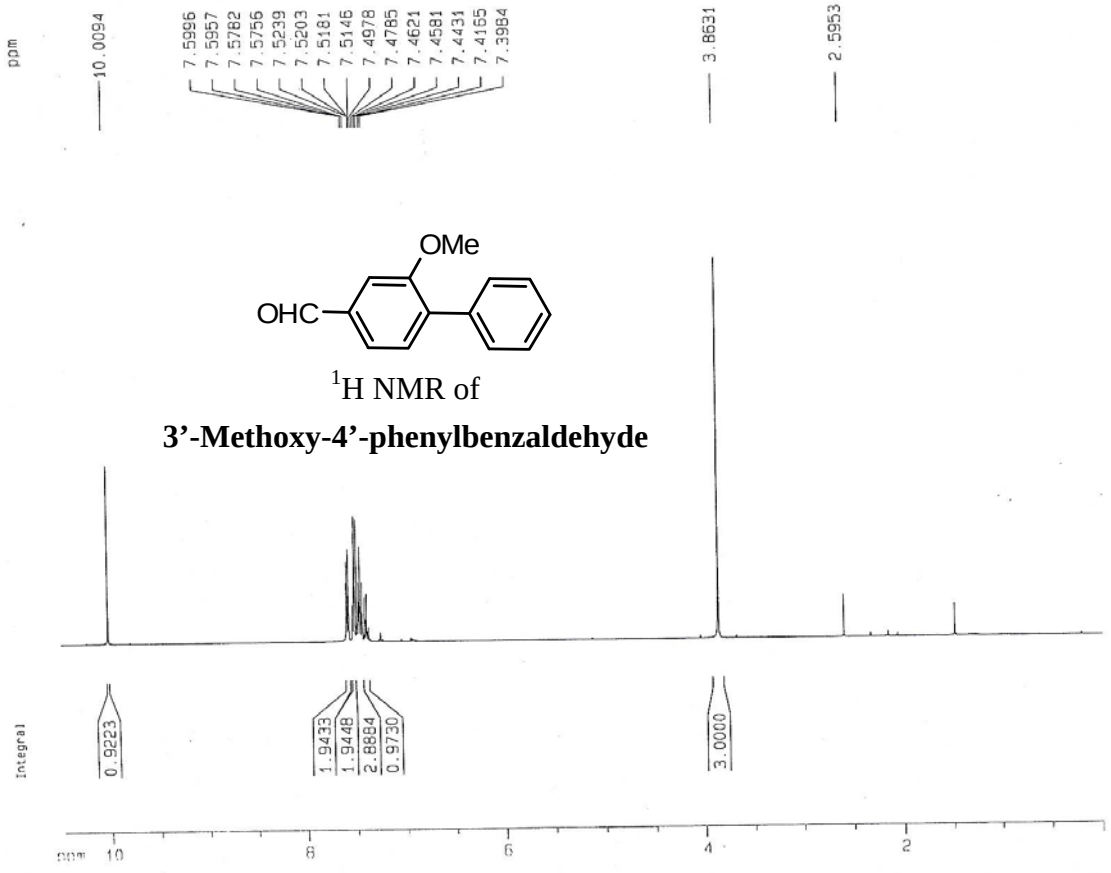
^{13}C NMR of

4-(2-Biphenyl)acetophenone



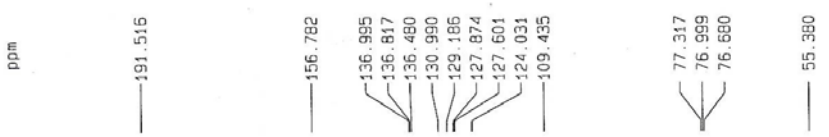
MS of

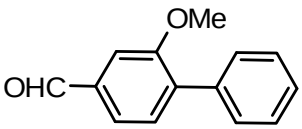
4-(2-Biphenyl)acetophenone



^{1}H NMR of

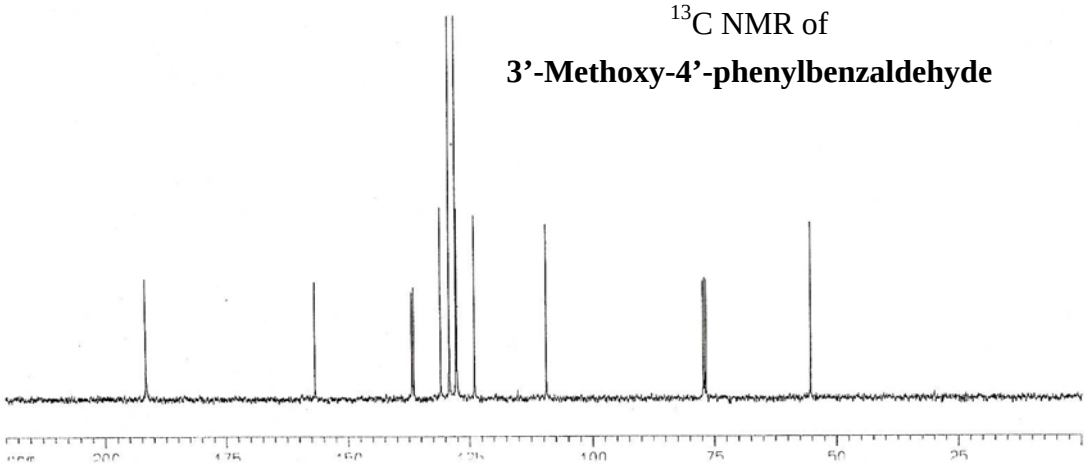
3’-Methoxy-4’-phenylbenzaldehyde

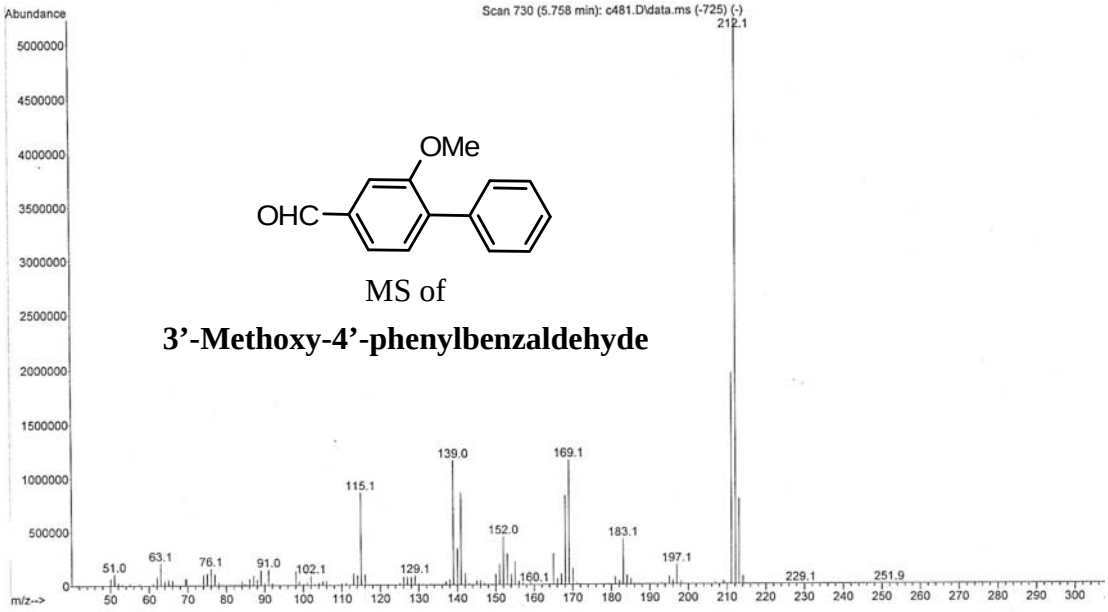




^{13}C NMR of

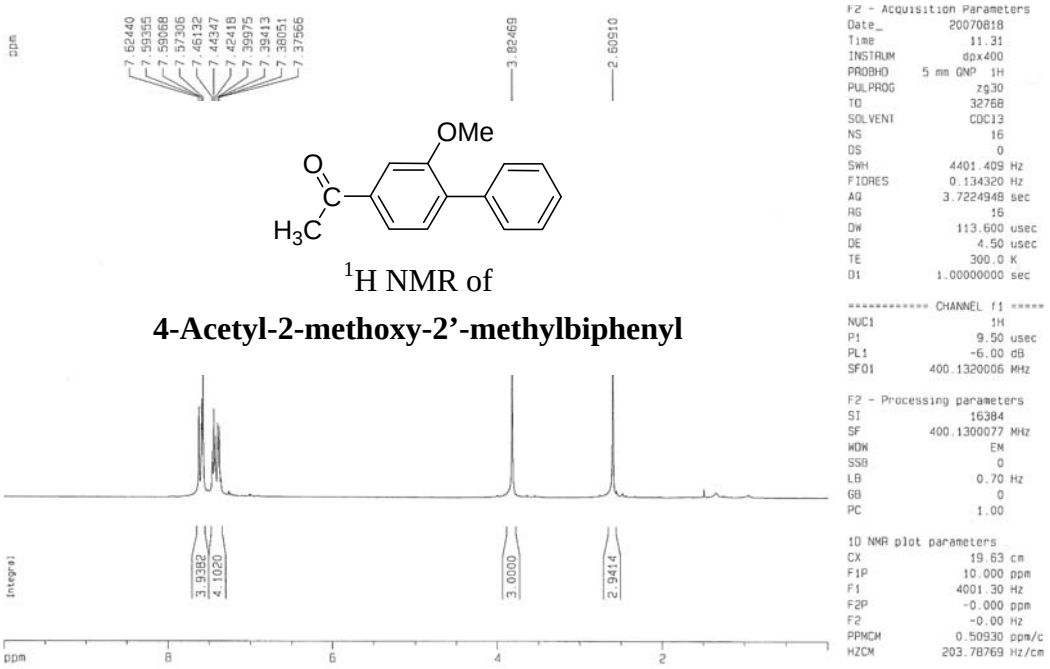
3’-Methoxy-4’-phenylbenzaldehyde





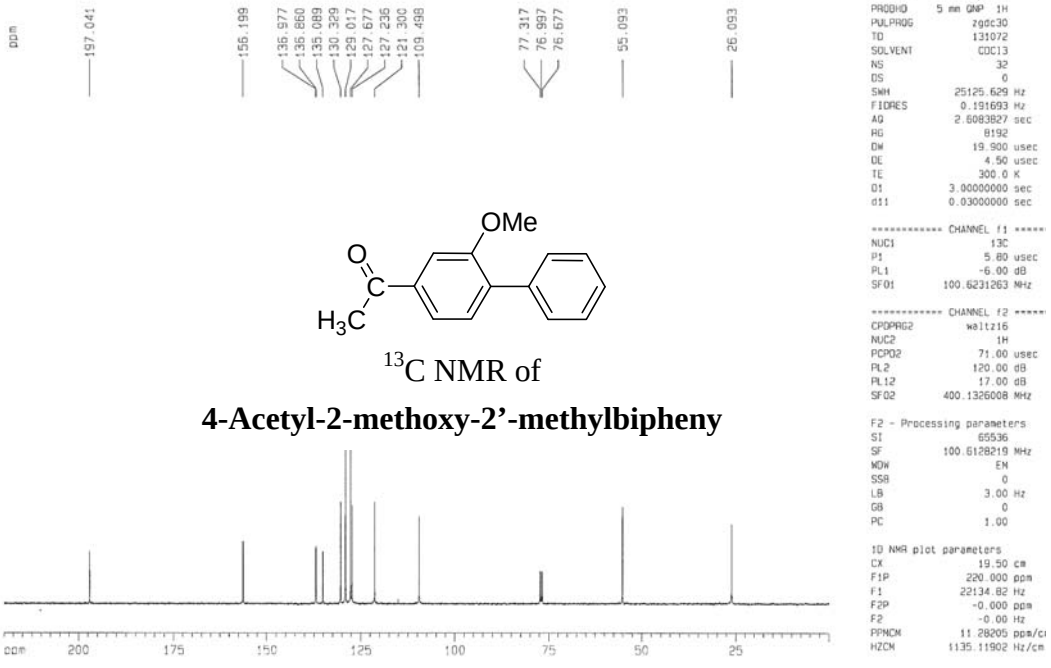
MS of

3’-Methoxy-4’-phenylbenzaldehyde



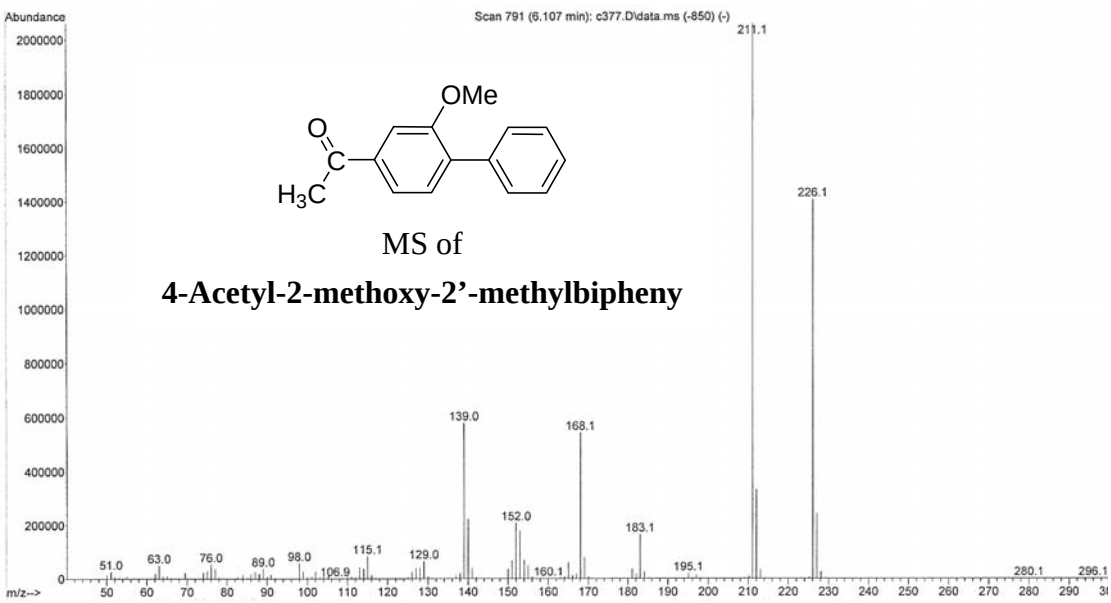
^{1}H NMR of

4-Acetyl-2-methoxy-2’-methylbiphenyl



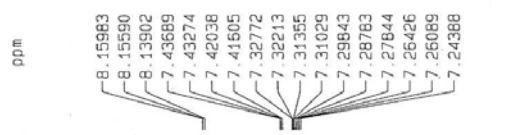
^{13}C NMR of

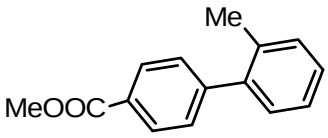
4-Acetyl-2-methoxy-2’-methylbipheny



MS of

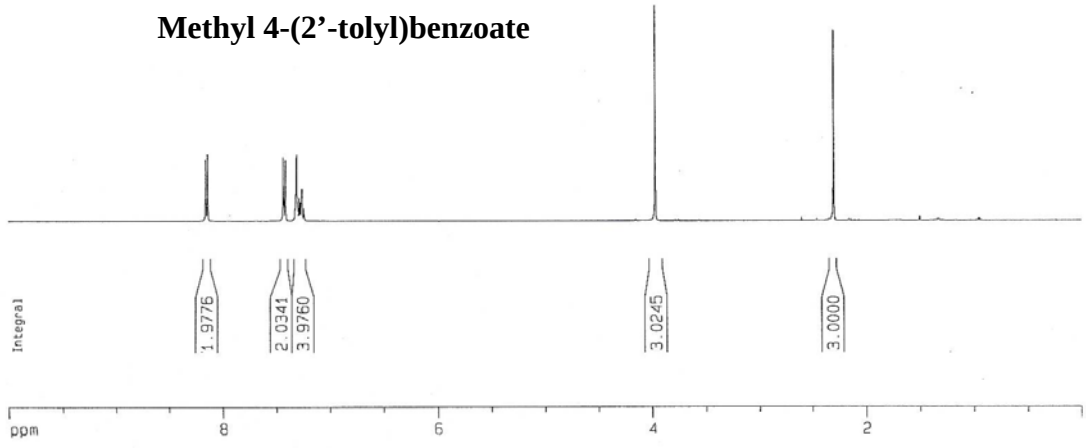
4-Acetyl-2-methoxy-2'-methylbipheny

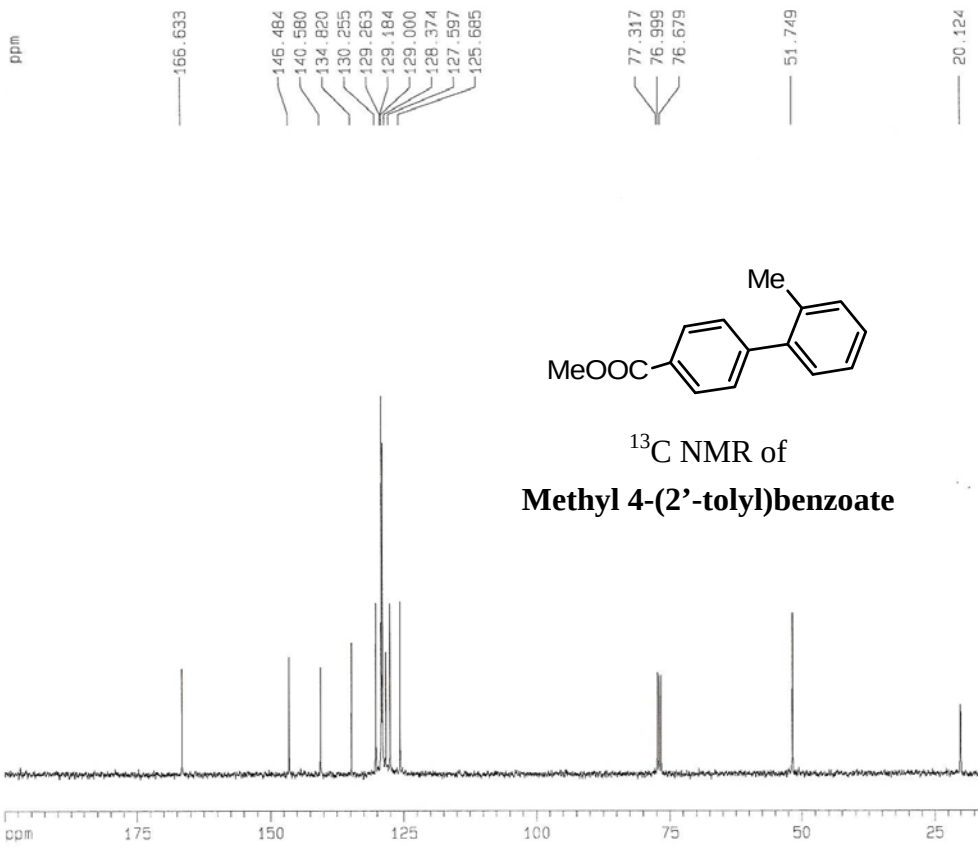




^{1}H NMR of

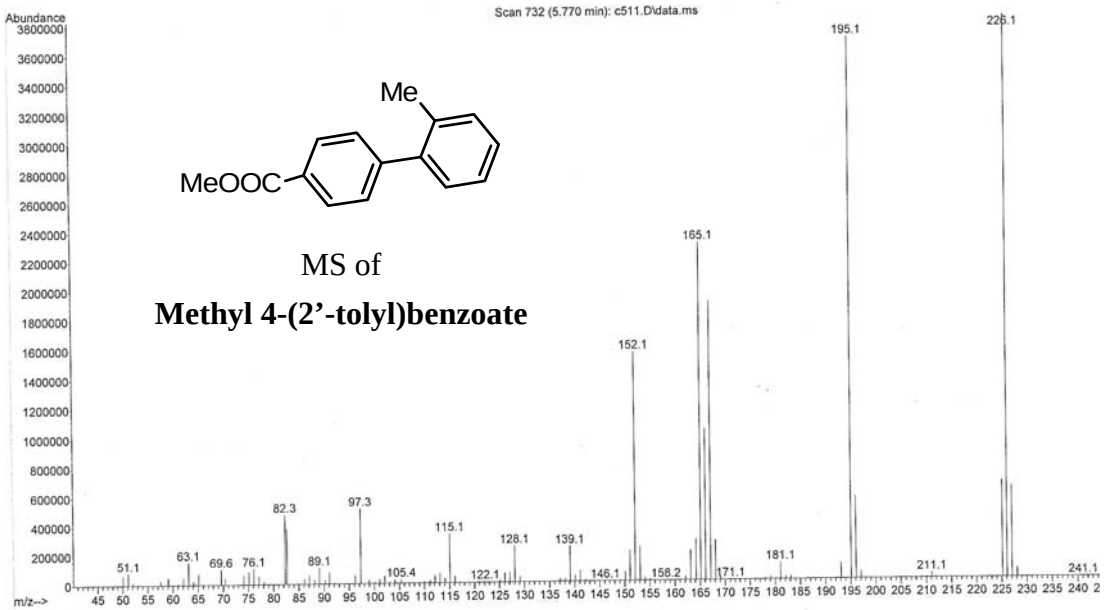
Methyl 4-(2'-tolyl)benzoate





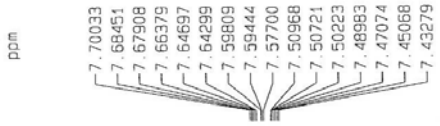
^{13}C NMR of

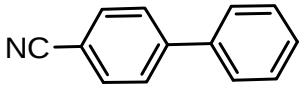
Methyl 4-(2'-tolyl)benzoate



MS of

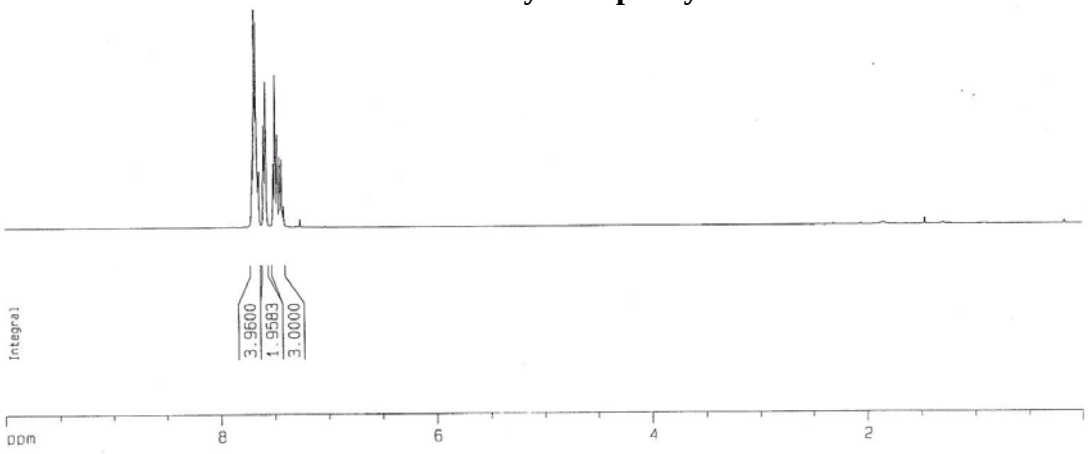
Methyl 4-(2'-tolyl)benzoate

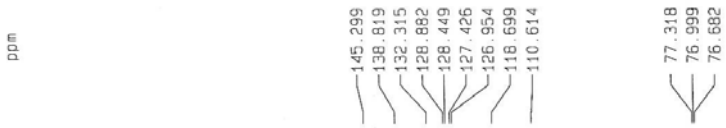


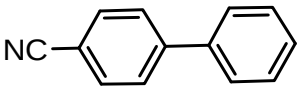


^{1}H NMR of

4-Cyanobiphenyl

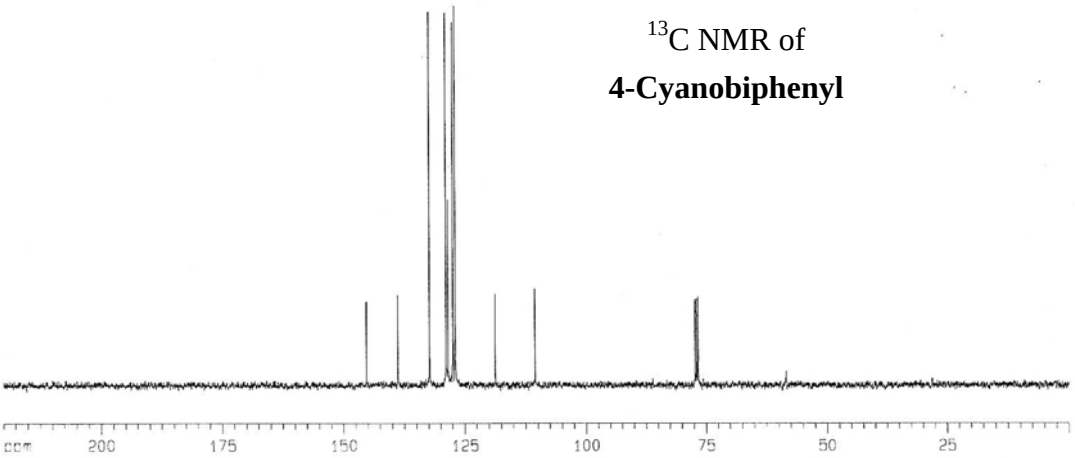


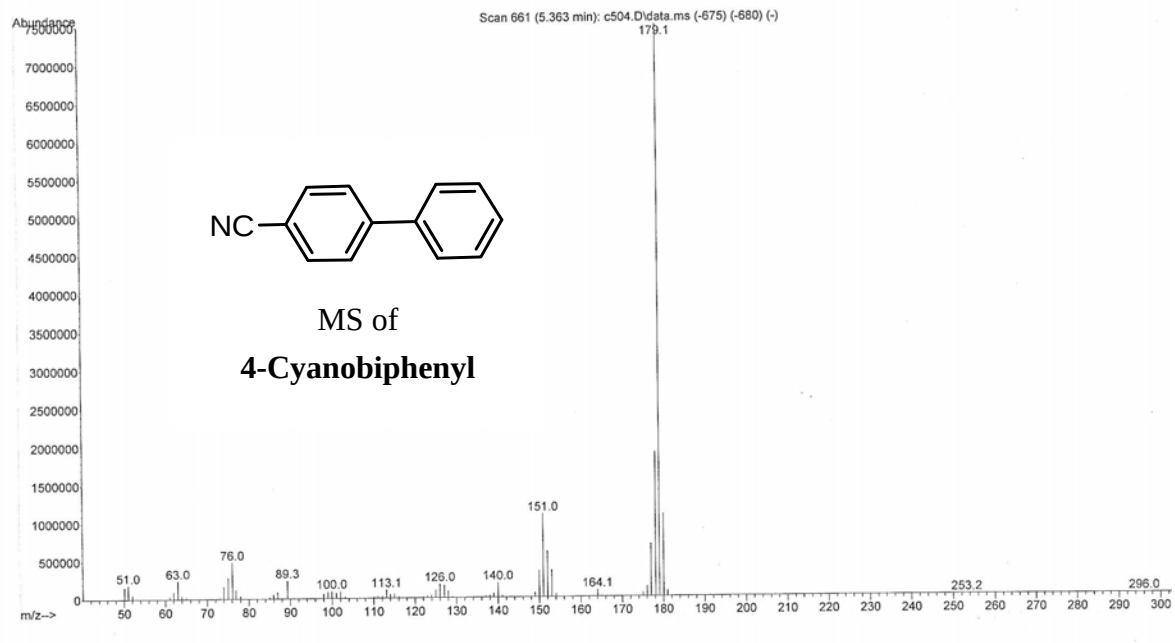




^{13}C NMR of

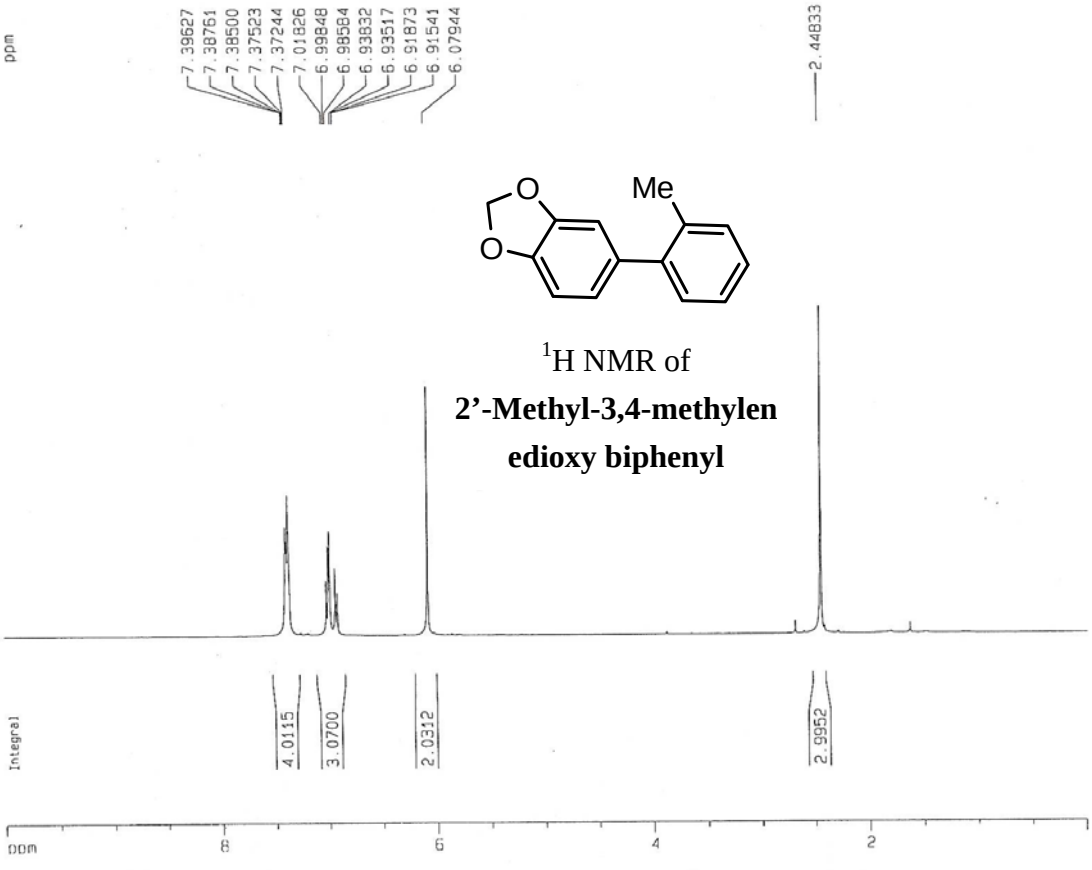
4-Cyanobiphenyl





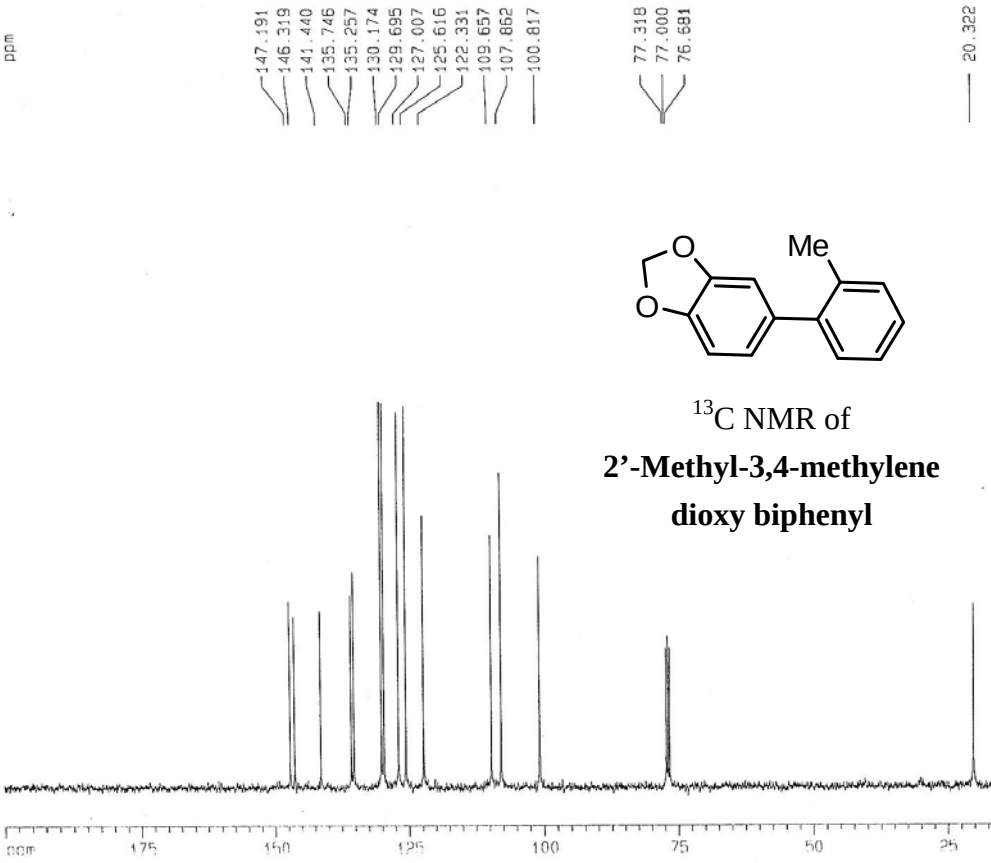
MS of

4-Cyanobiphenyl



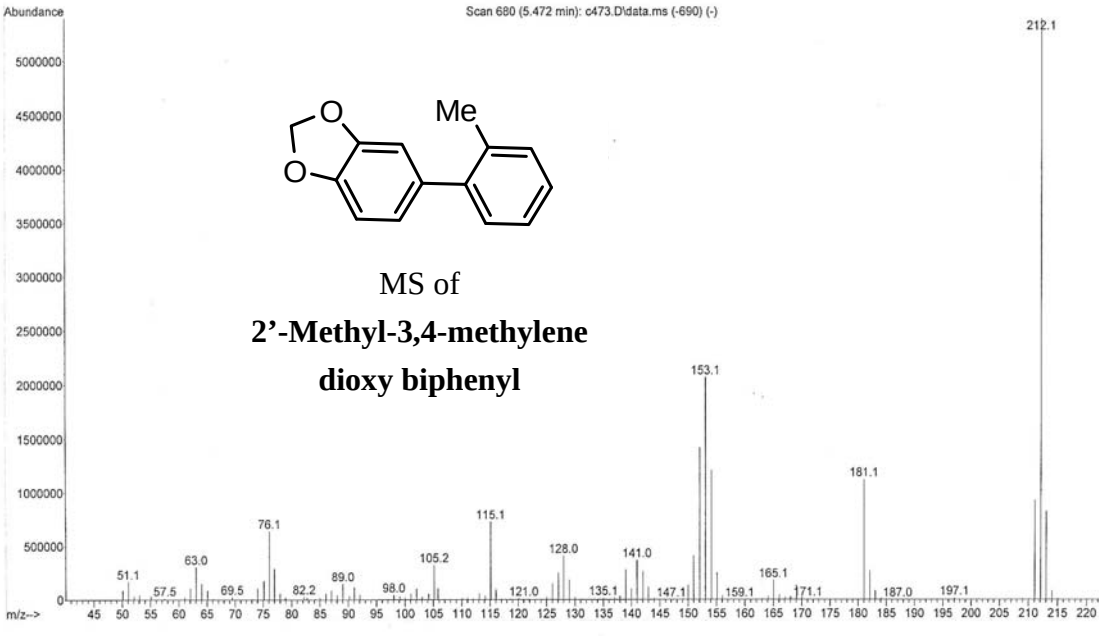
^{1}H NMR of

2'-Methyl-3,4-methylen edioxy biphenyl



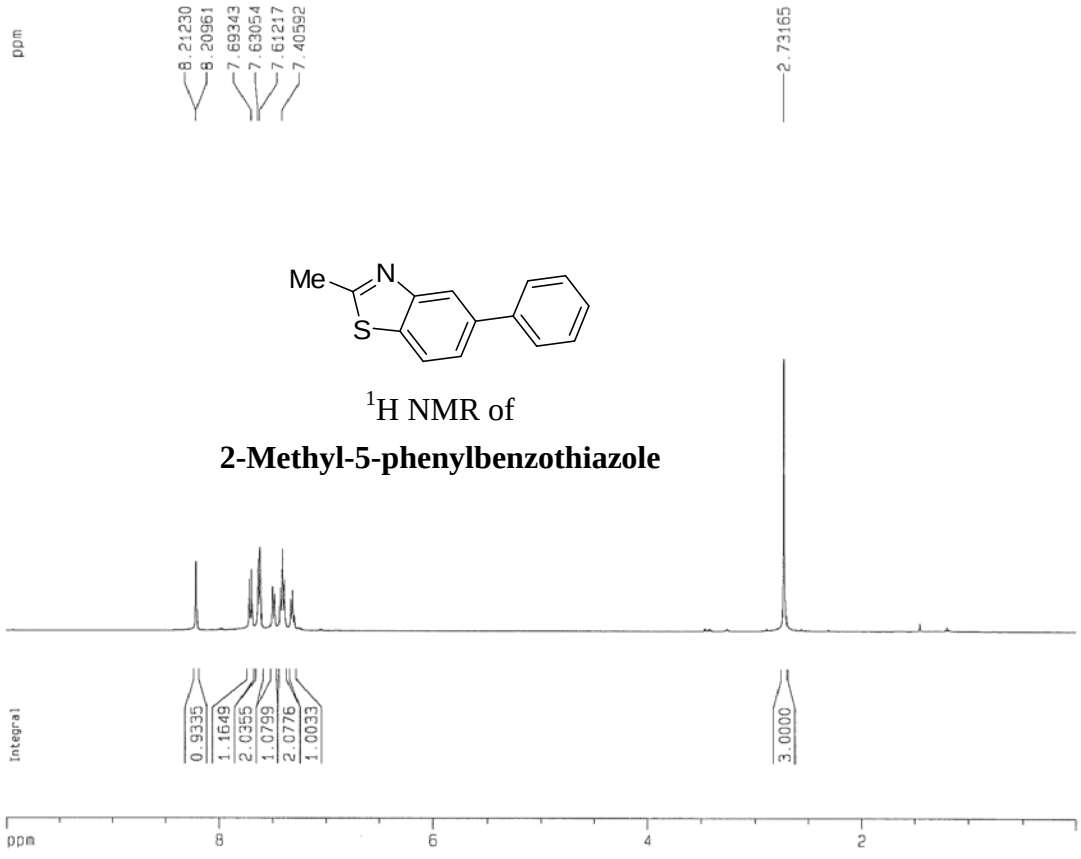
^{13}C NMR of

2’-Methyl-3,4-methylene dioxy biphenyl



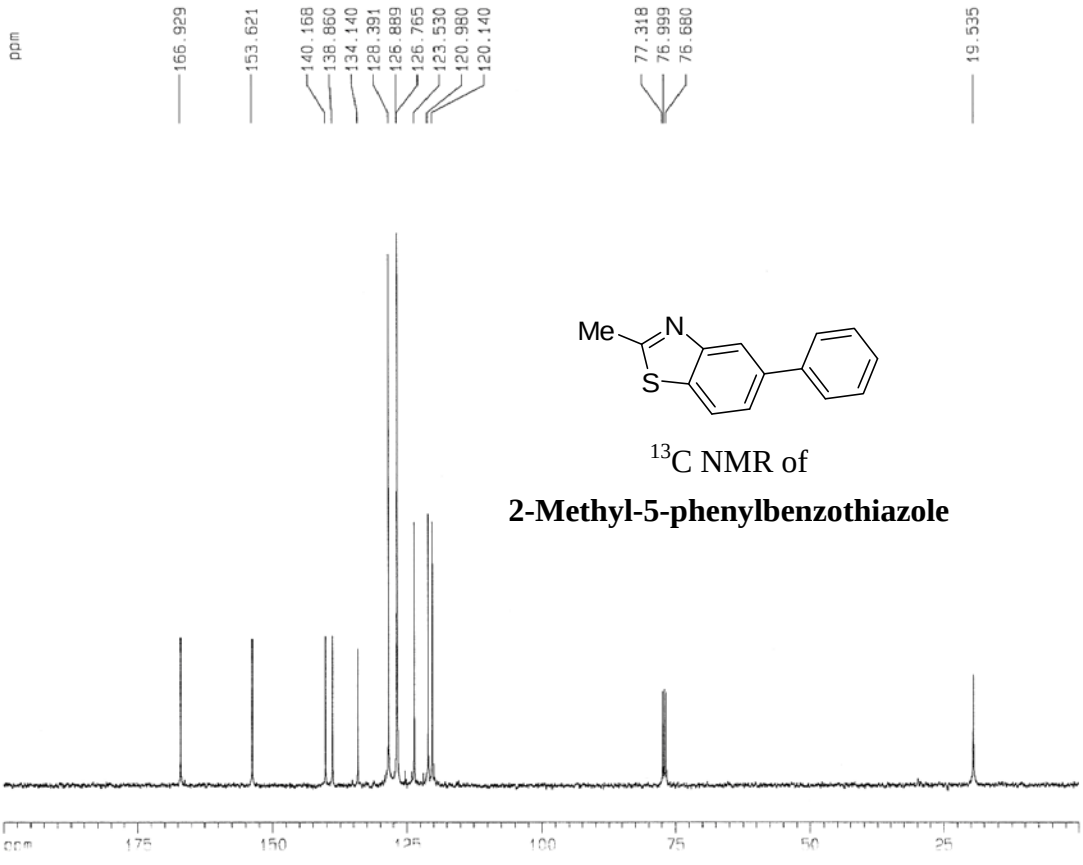
MS of

2’-Methyl-3,4-methylene dioxy biphenyl



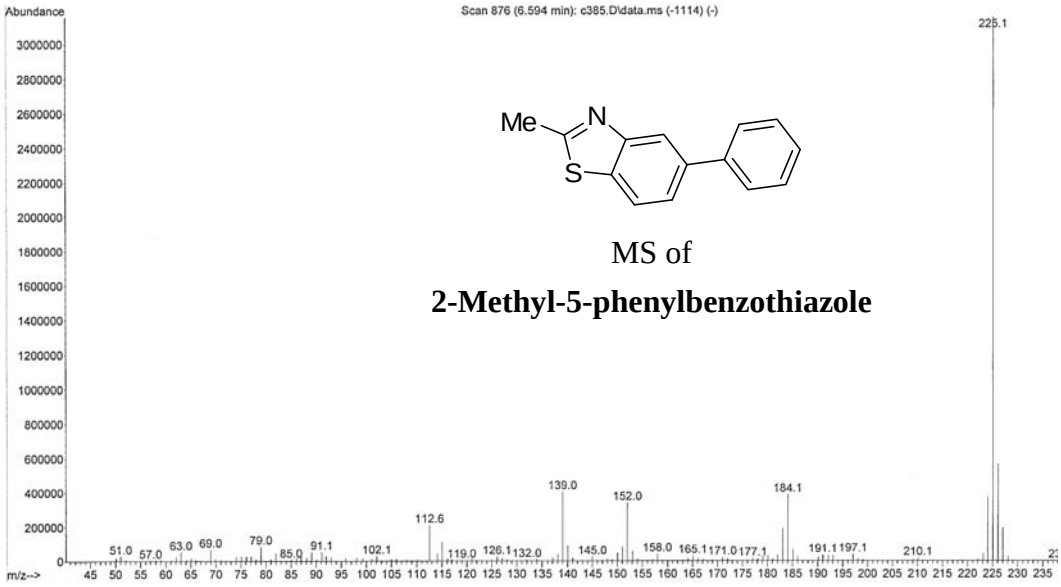
^{1}H NMR of

2-Methyl-5-phenylbenzothiazole



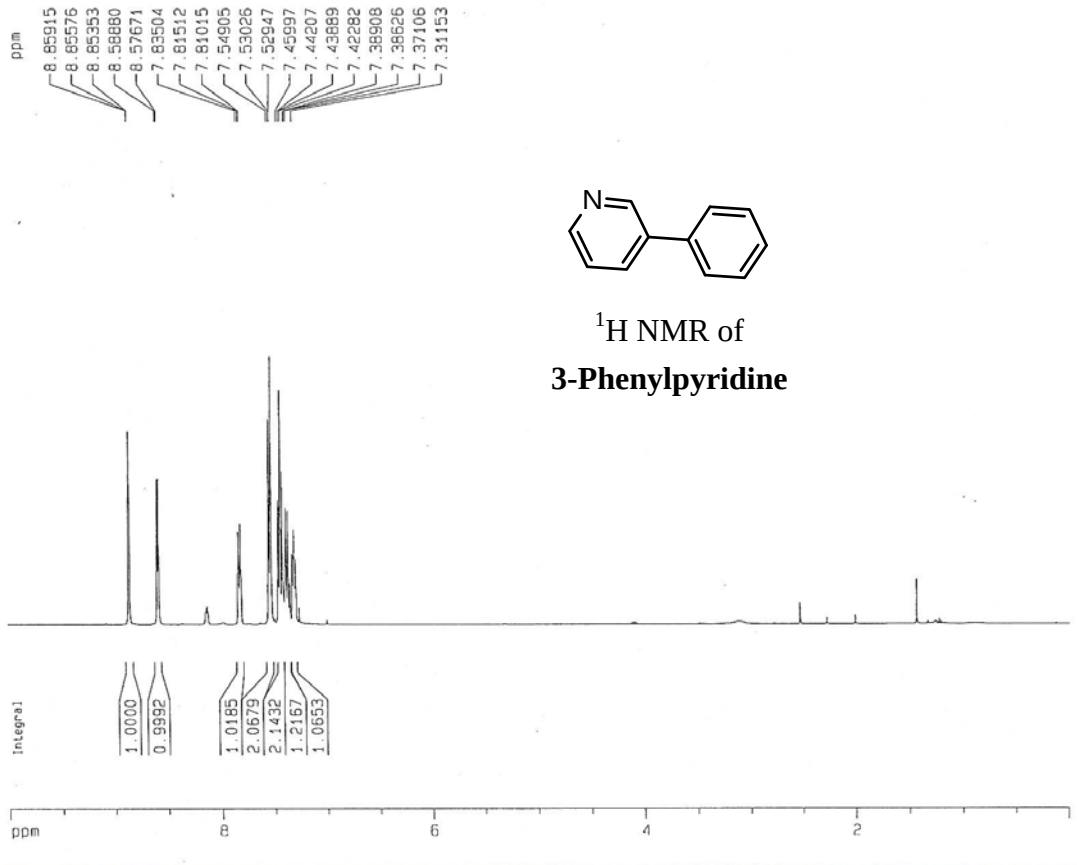
^{13}C NMR of

2-Methyl-5-phenylbenzothiazole



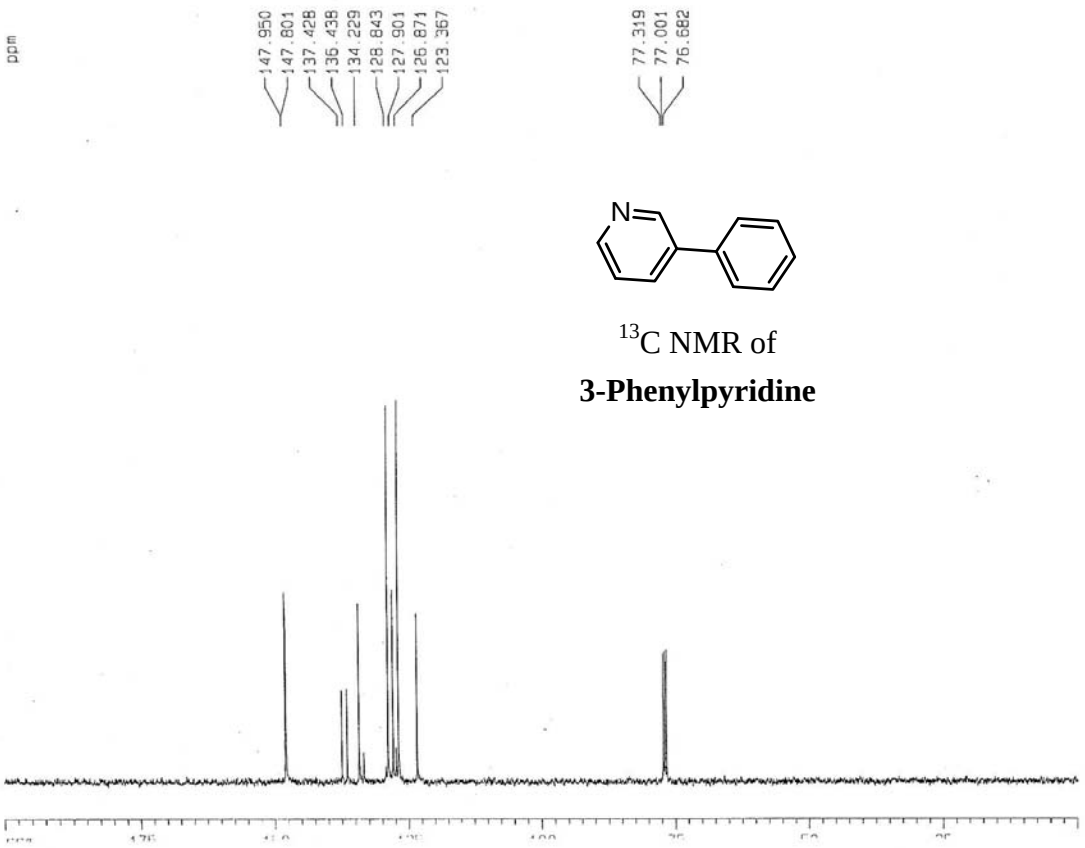
MS of

2-Methyl-5-phenylbenzothiazole



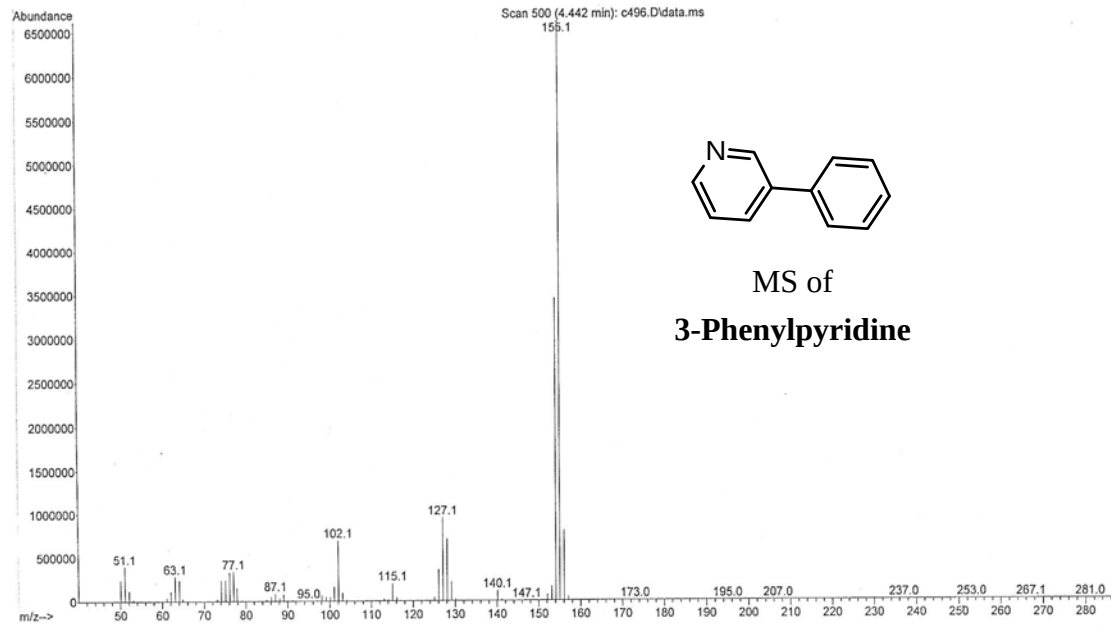
^{1}H NMR of

3-Phenylpyridine



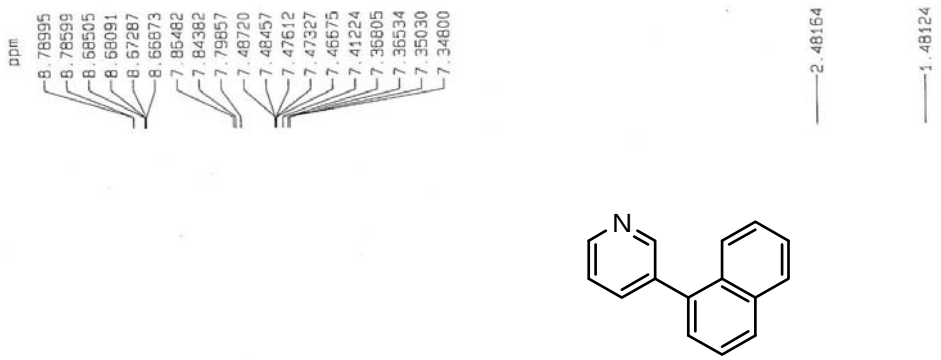
^{13}C NMR of

3-Phenylpyridine



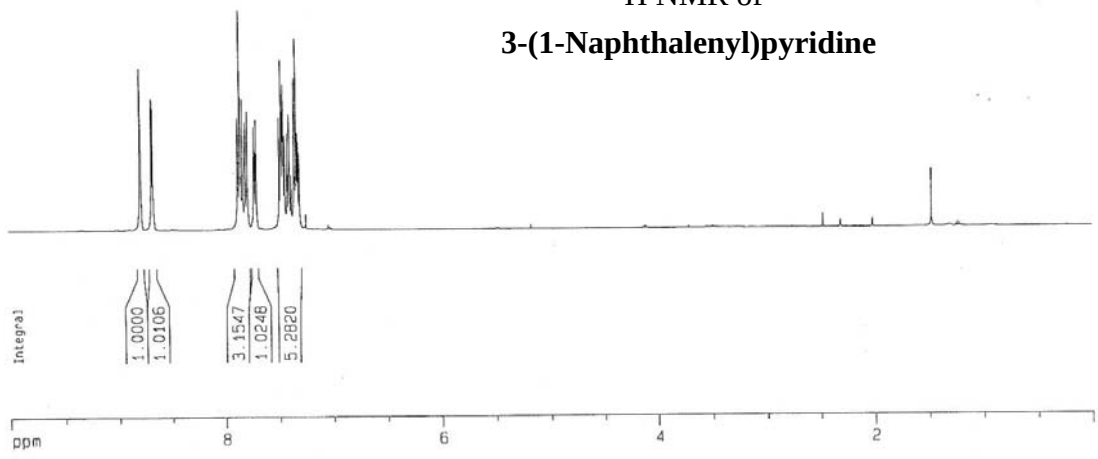
MS of

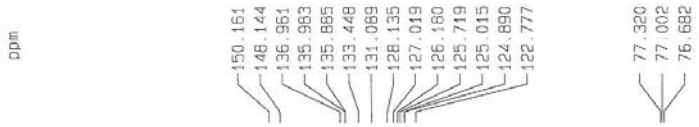
3-Phenylpyridine

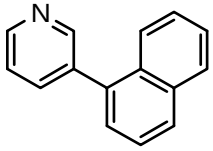


^{1}H NMR of

3-(1-Naphthalenyl)pyridine

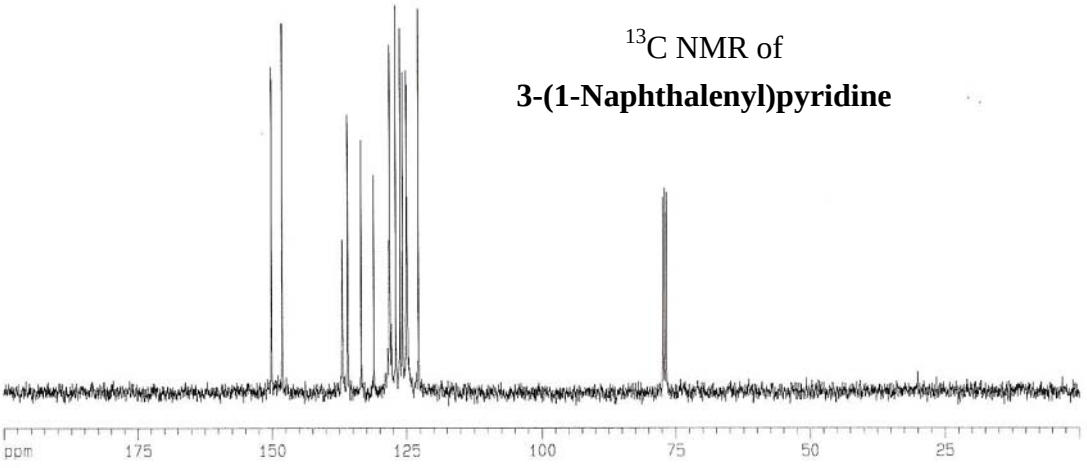


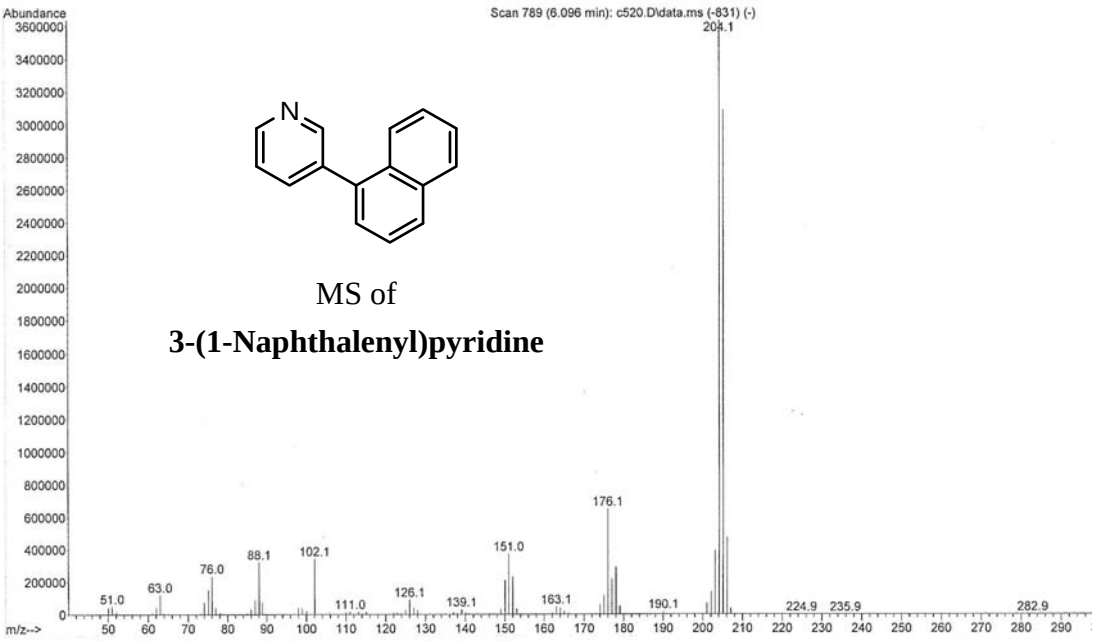




^{13}C NMR of

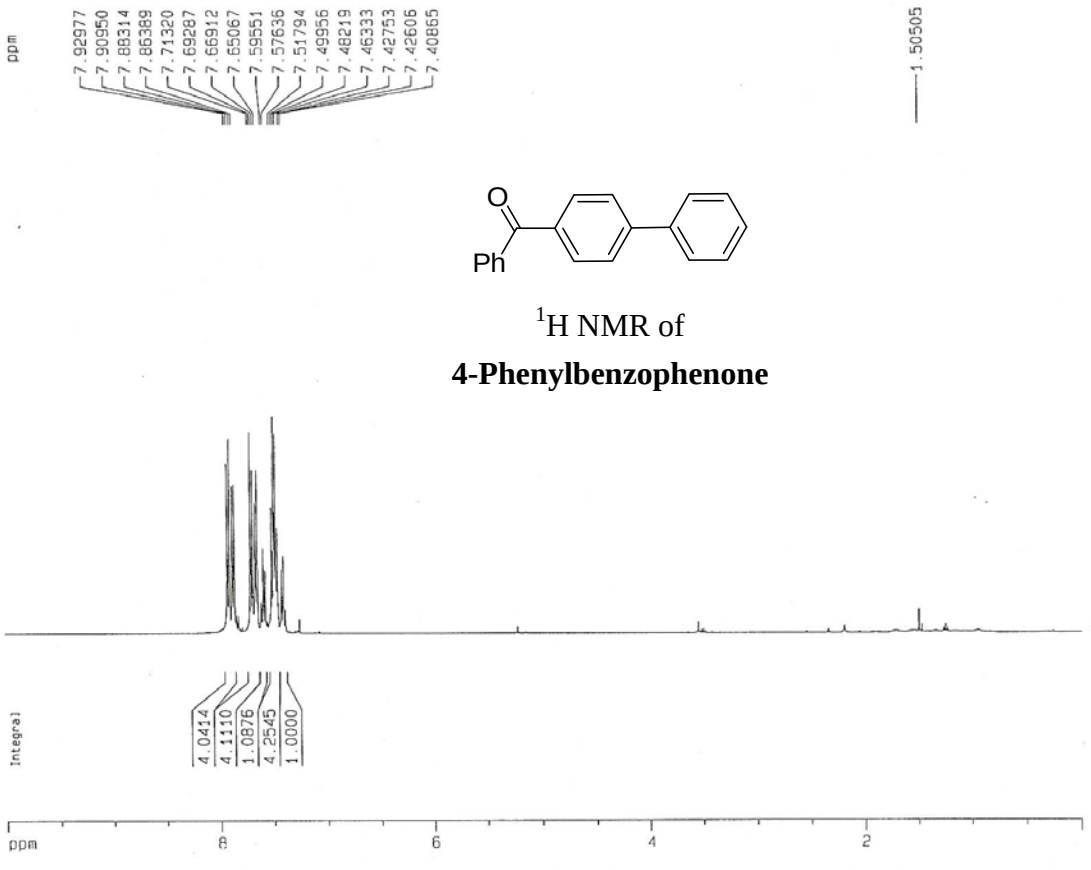
3-(1-Naphthalenyl)pyridine





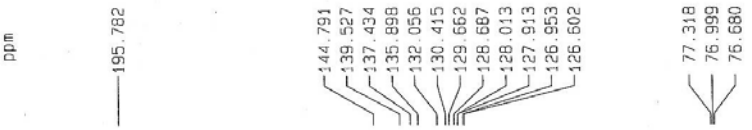
MS of

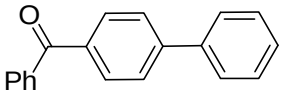
3-(1-Naphthalenyl)pyridine



^{1}H NMR of

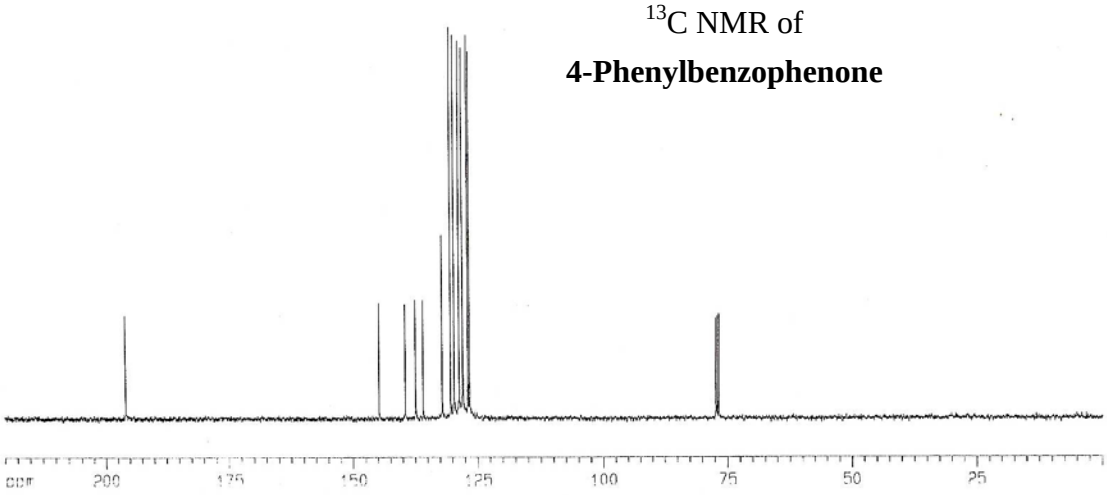
4-Phenylbenzophenone

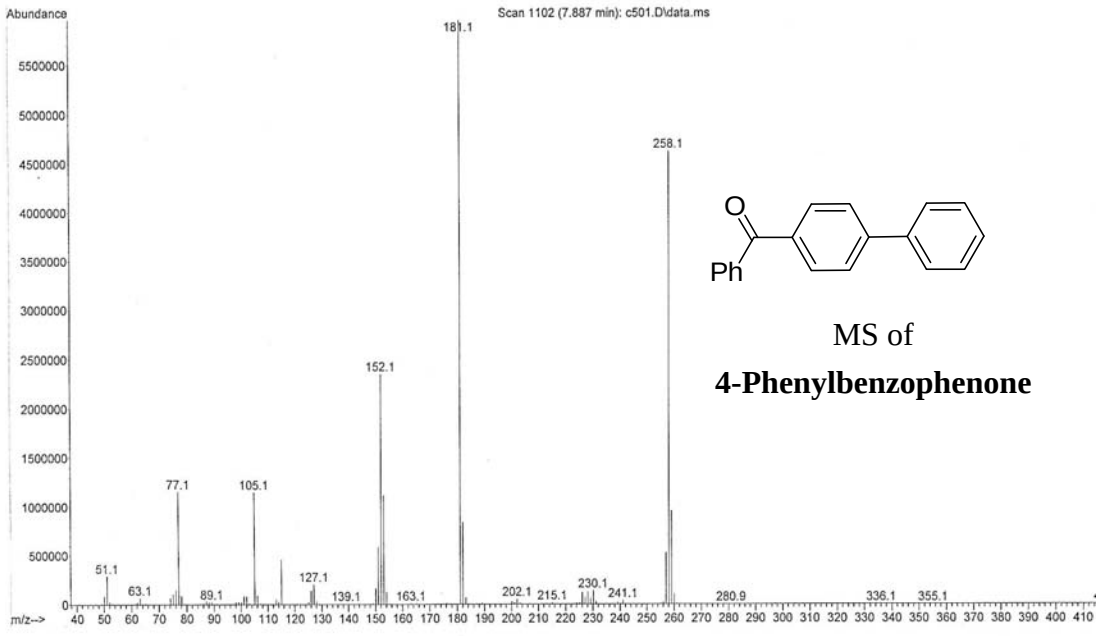




^{13}C NMR of

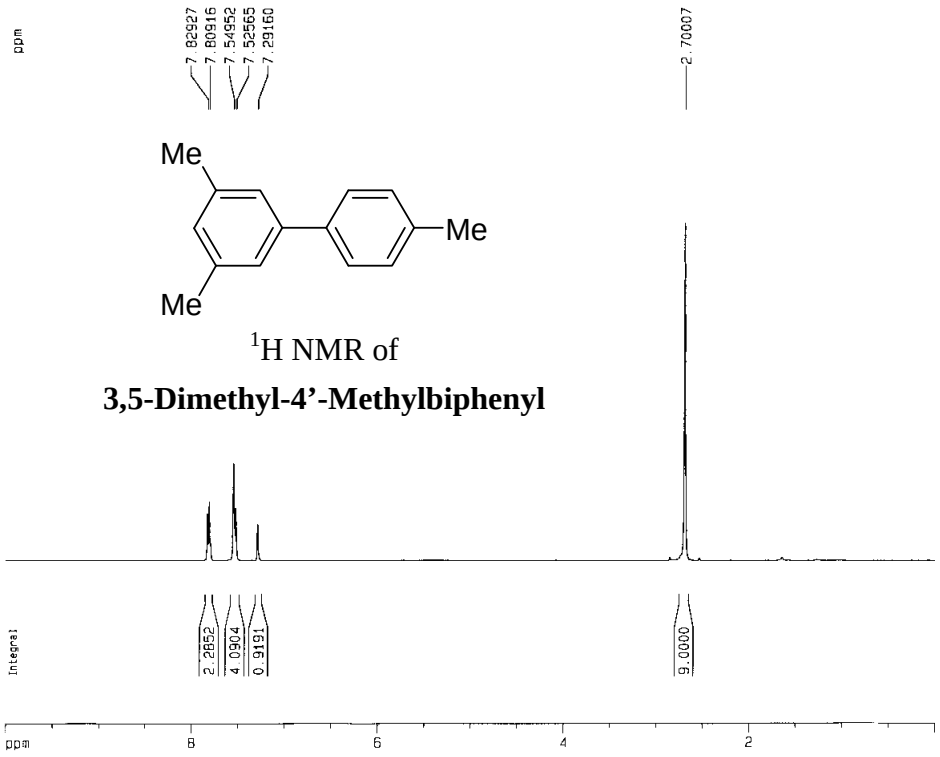
4-Phenylbenzophenone





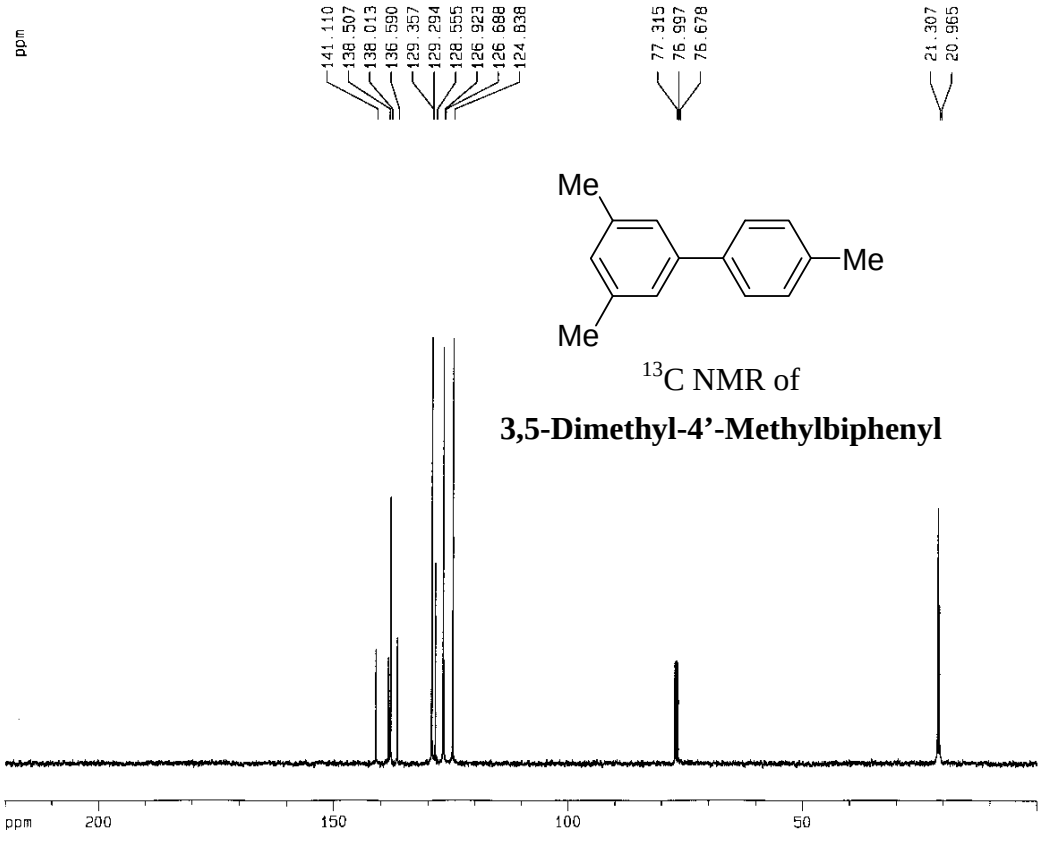
MS of

4-Phenylbenzophenone



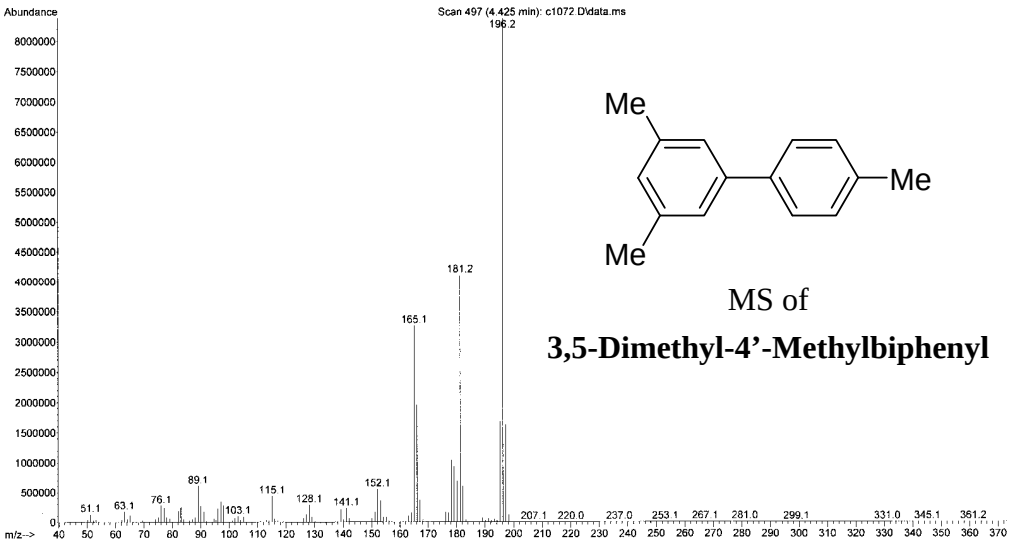
^{1}H NMR of

3,5-Dimethyl-4’-Methylbiphenyl



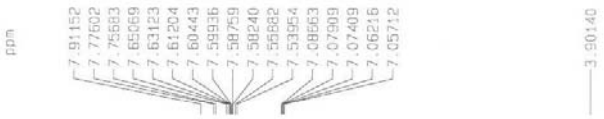
^{13}C NMR of

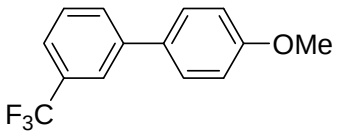
3,5-Dimethyl-4’-Methylbiphenyl



MS of

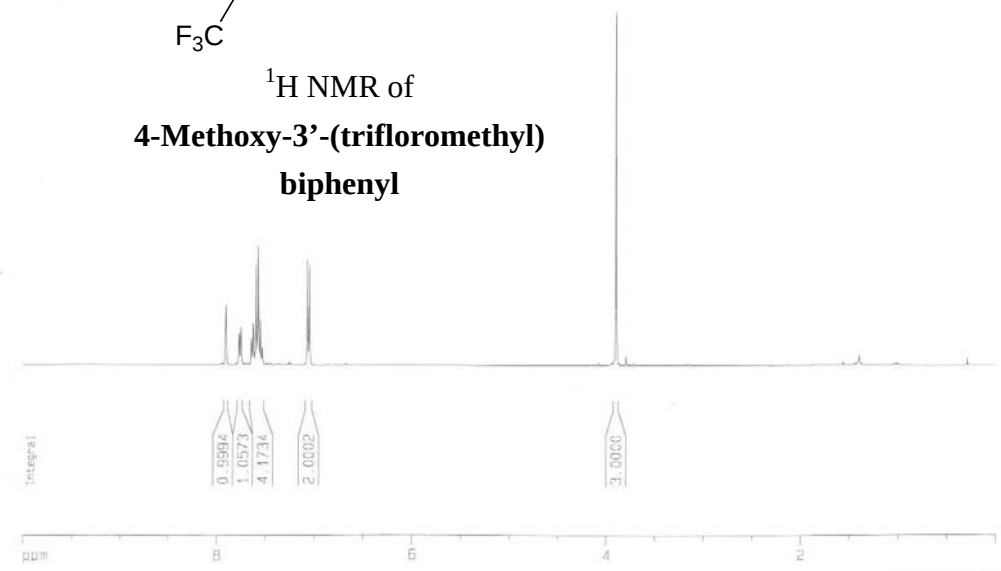
3,5-Dimethyl-4’-Methylbiphenyl

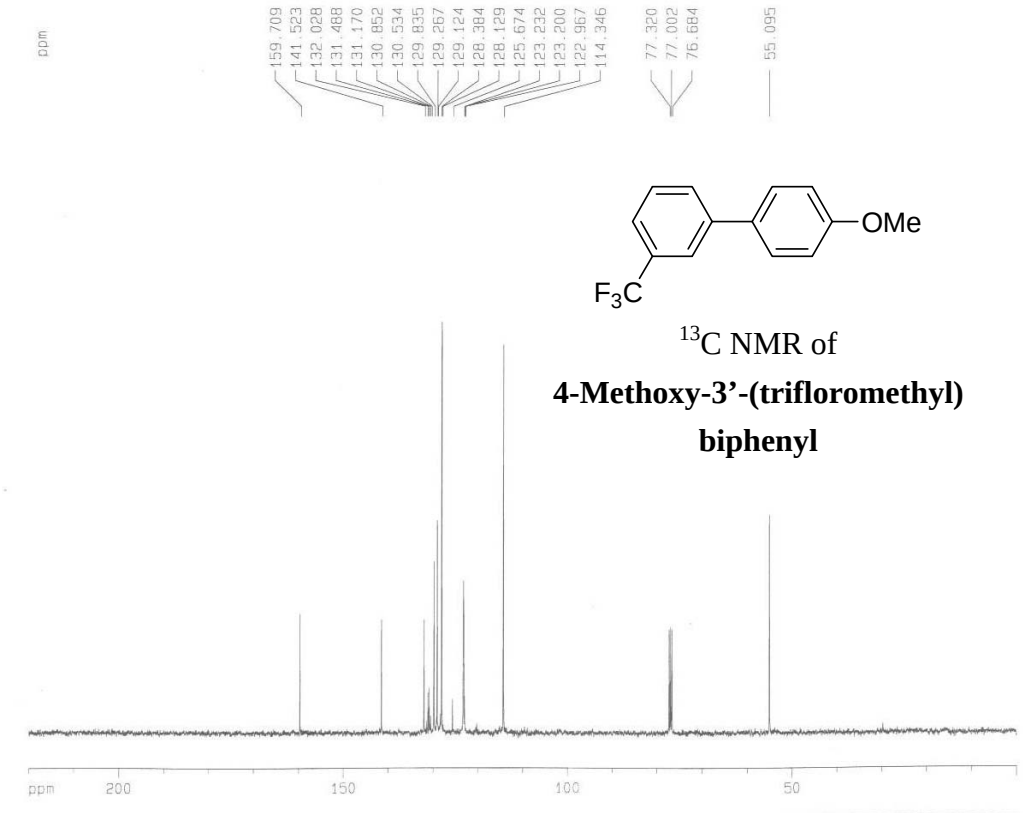




^{1}H NMR of

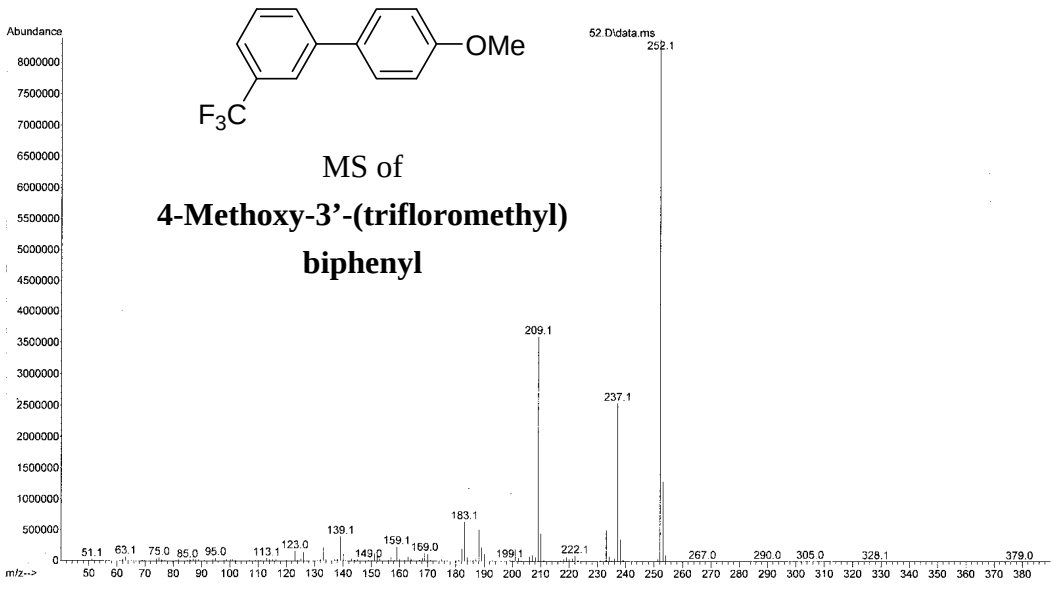
4-Methoxy-3’-(trifloromethyl) biphenyl





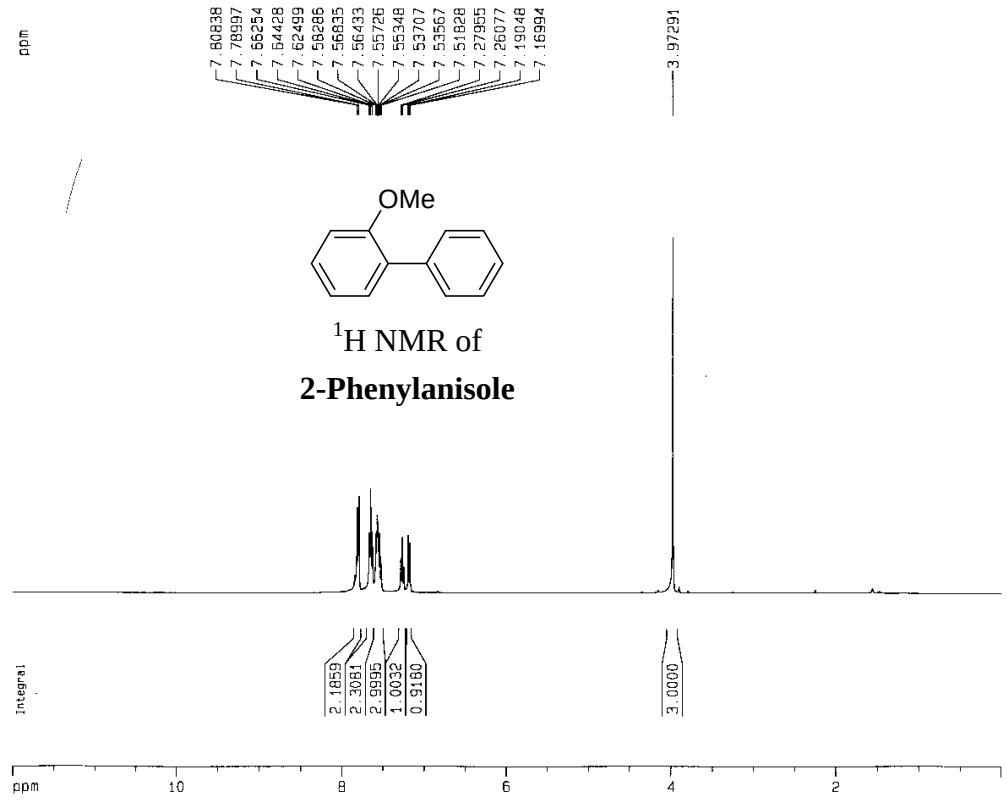
^{13}C NMR of

4-Methoxy-3'-(trifloromethyl) biphenyl



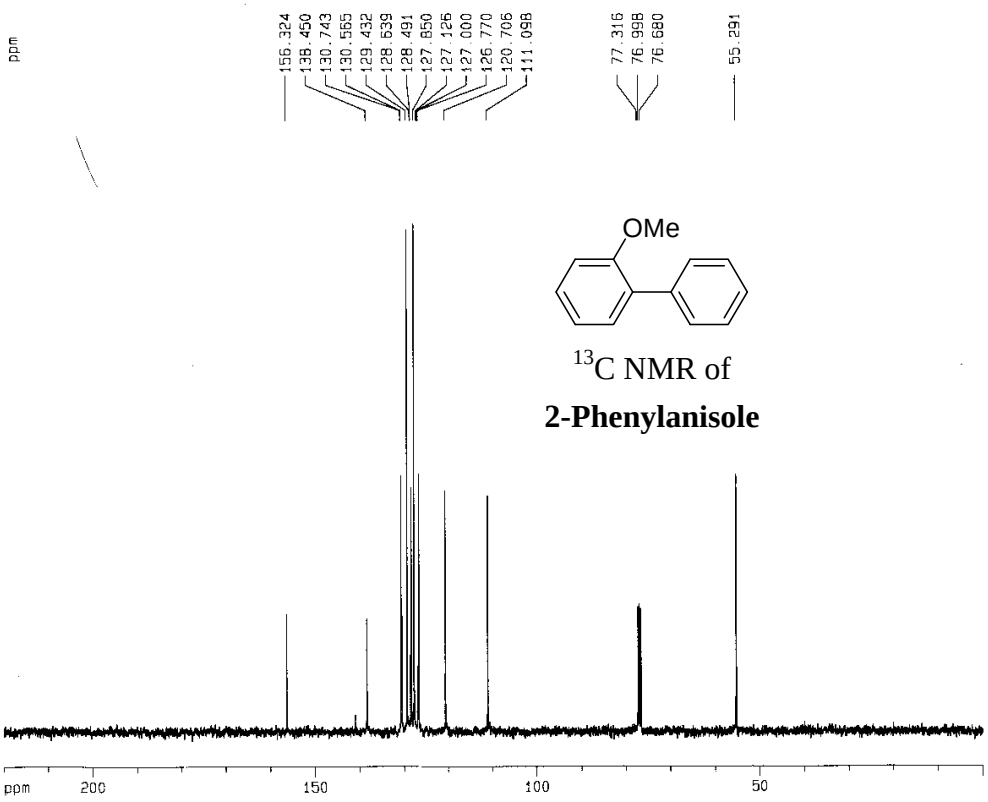
MS of

4-Methoxy-3'-(trifloromethyl) biphenyl



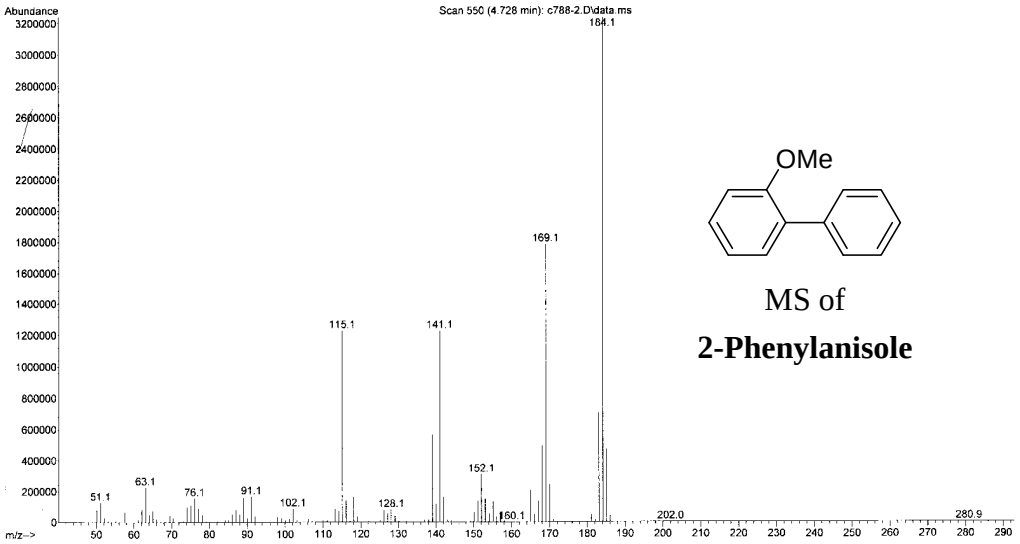
^{1}H NMR of

2-Phenylanisole



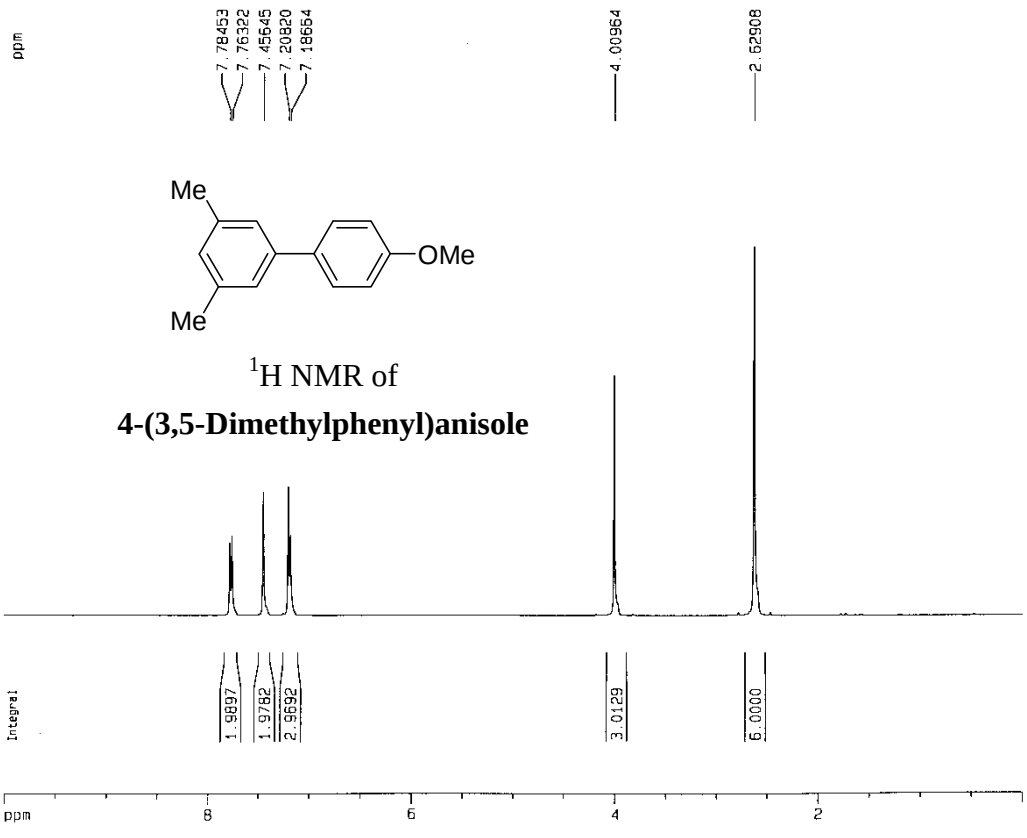
^{13}C NMR of

2-Phenylanisole



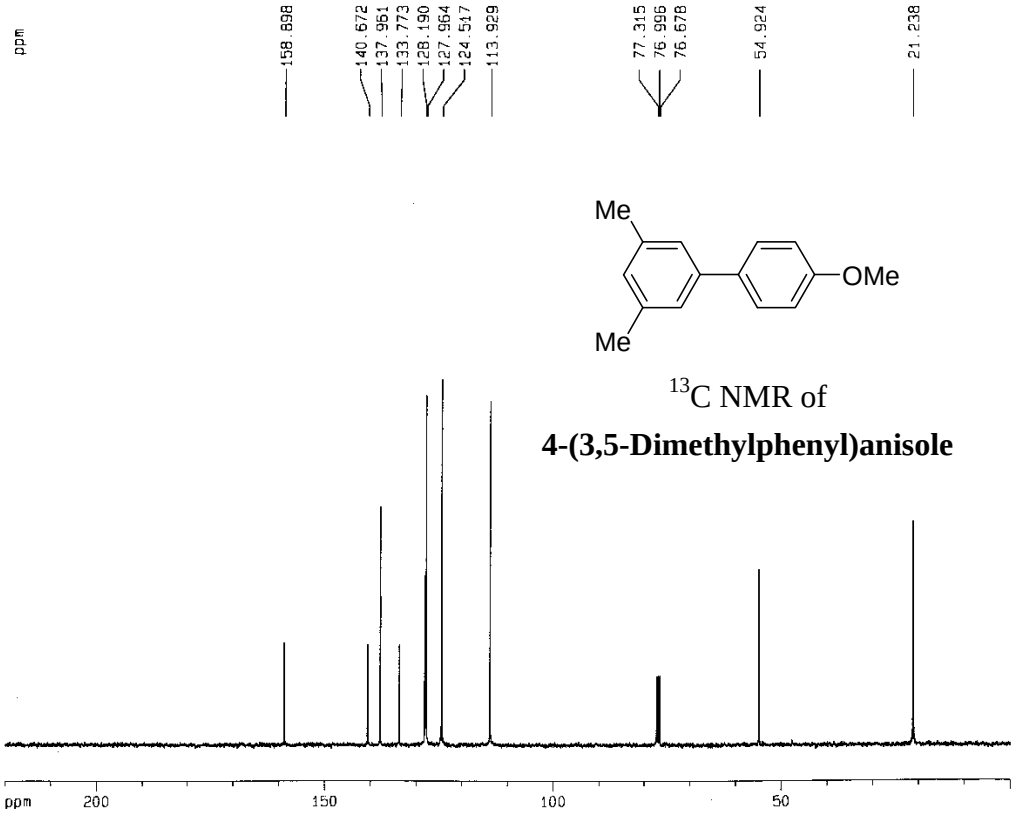
MS of

2-Phenylanisole



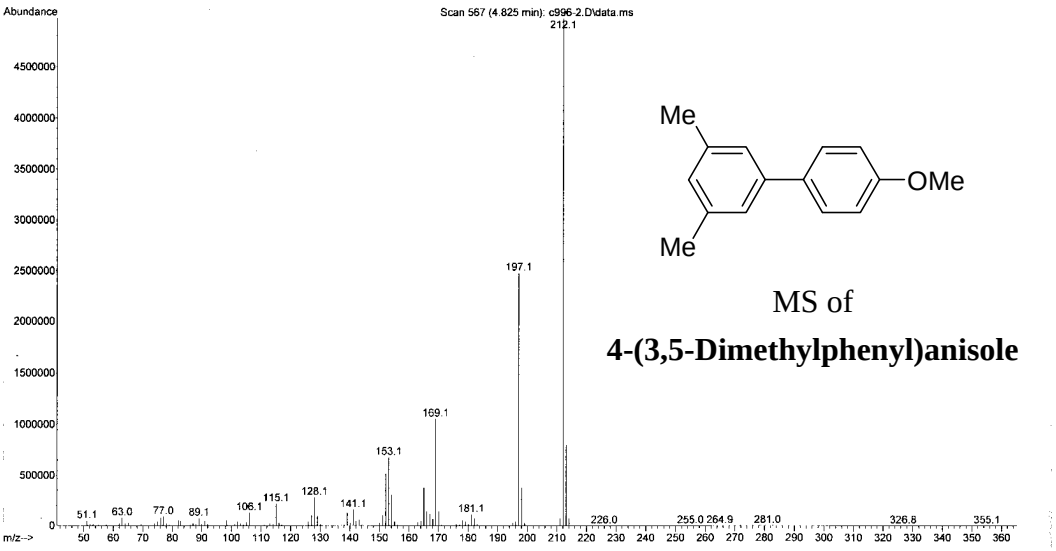
^{1}H NMR of

4-(3,5-Dimethylphenyl)anisole



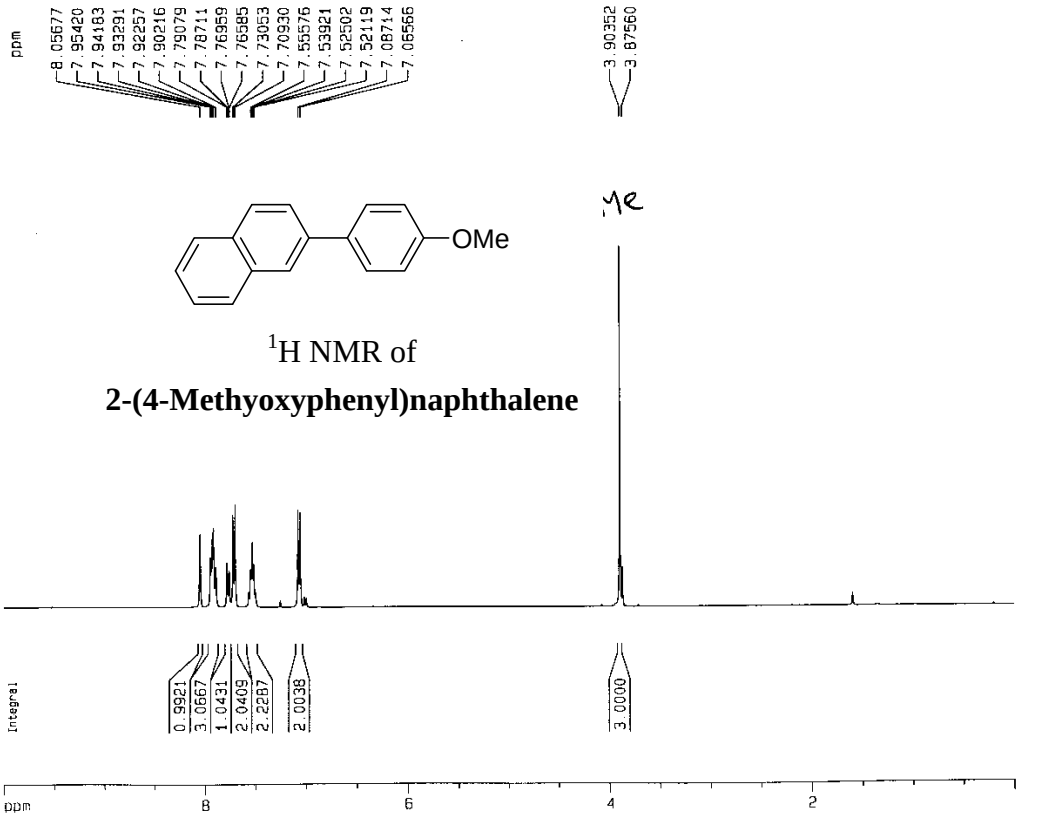
^{13}C NMR of

4-(3,5-Dimethylphenyl)anisole



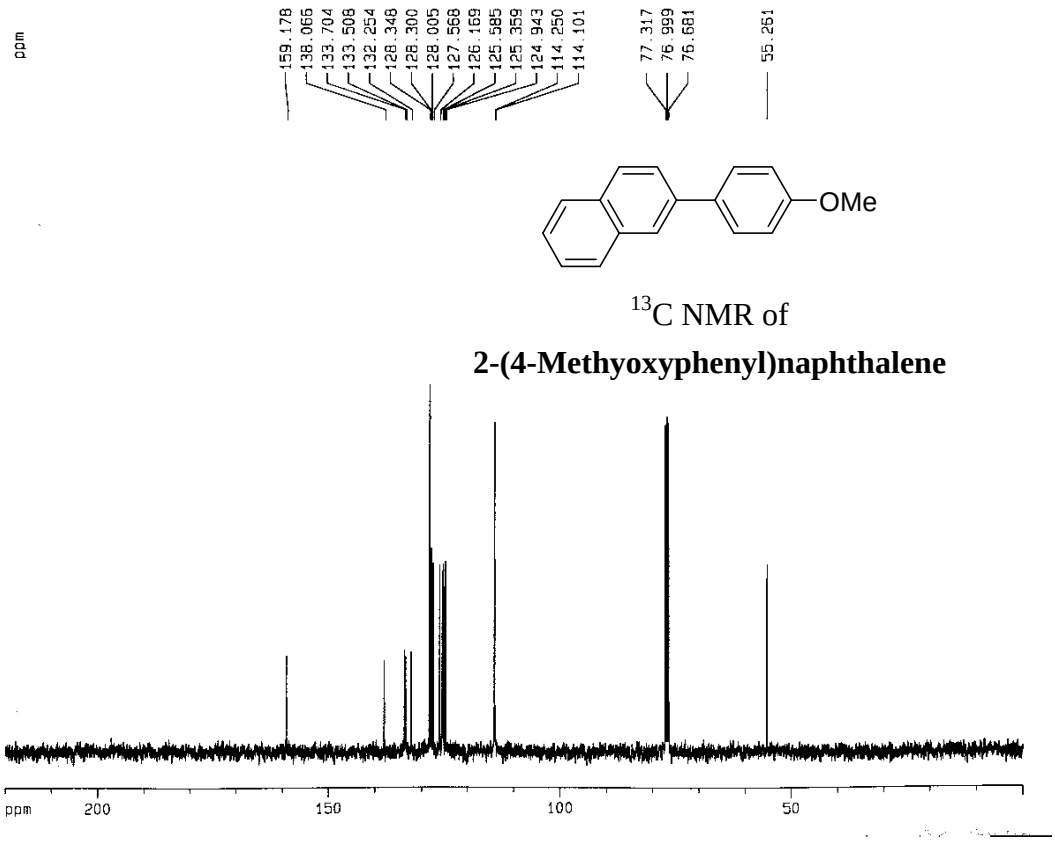
MS of

4-(3,5-Dimethylphenyl)anisole



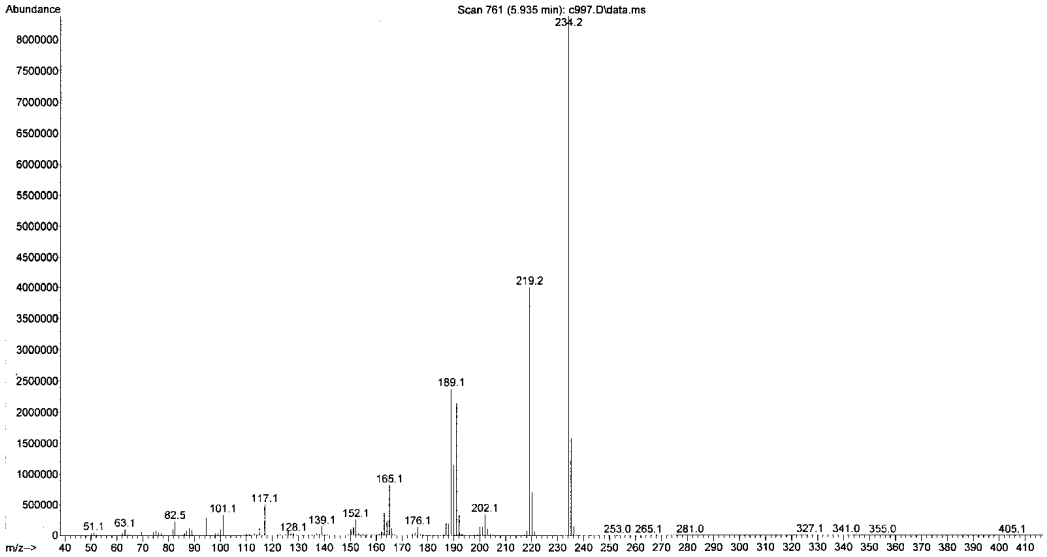
^{1}H NMR of

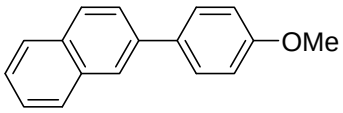
2-(4-Methyoxyphenyl)naphthalene



^{13}C NMR of

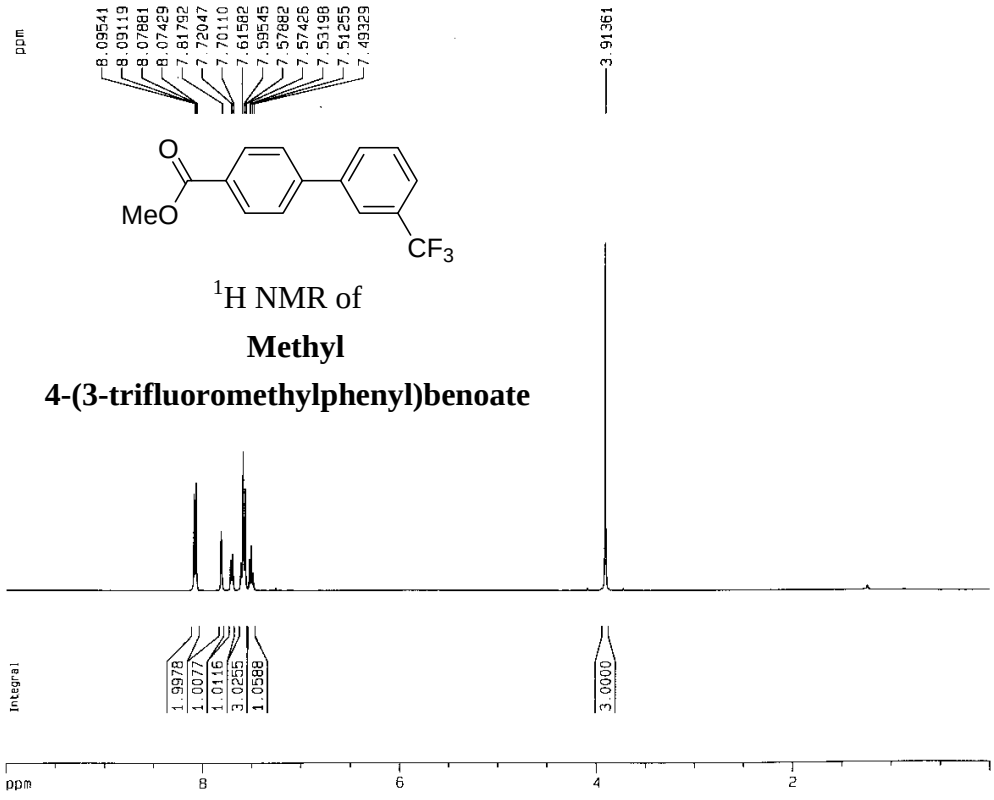
2-(4-Methyoxyphenyl)naphthalene





MS of

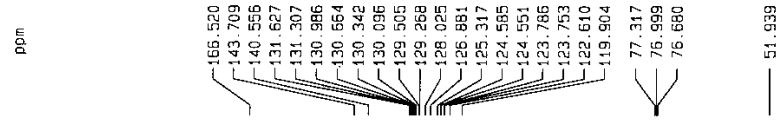
2-(4-Methyoxyphenyl)naphthalene

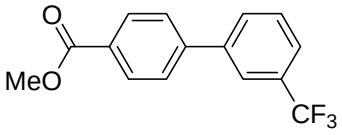


^{1}H NMR of

Methyl

4-(3-trifluoromethylphenyl)benoate

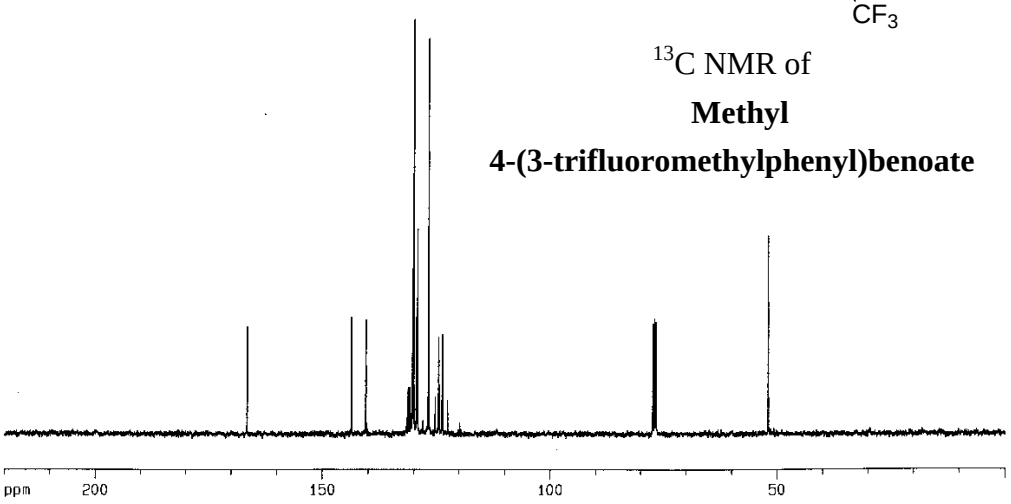


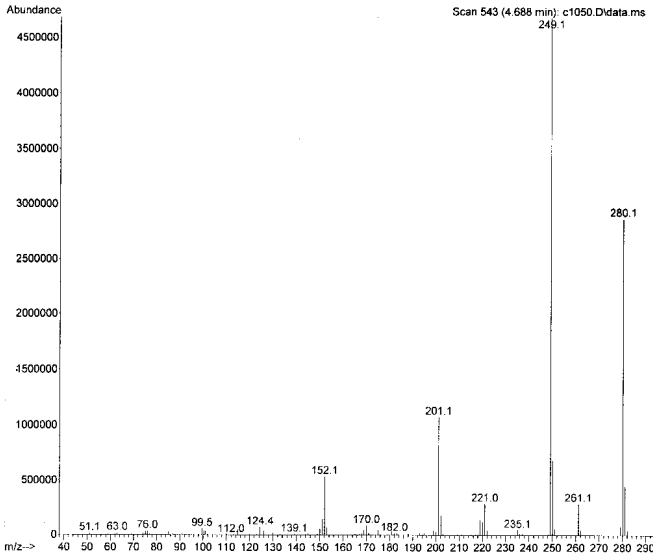


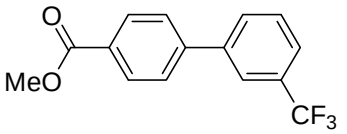
^{13}C NMR of

Methyl

4-(3-trifluoromethylphenyl)benoate



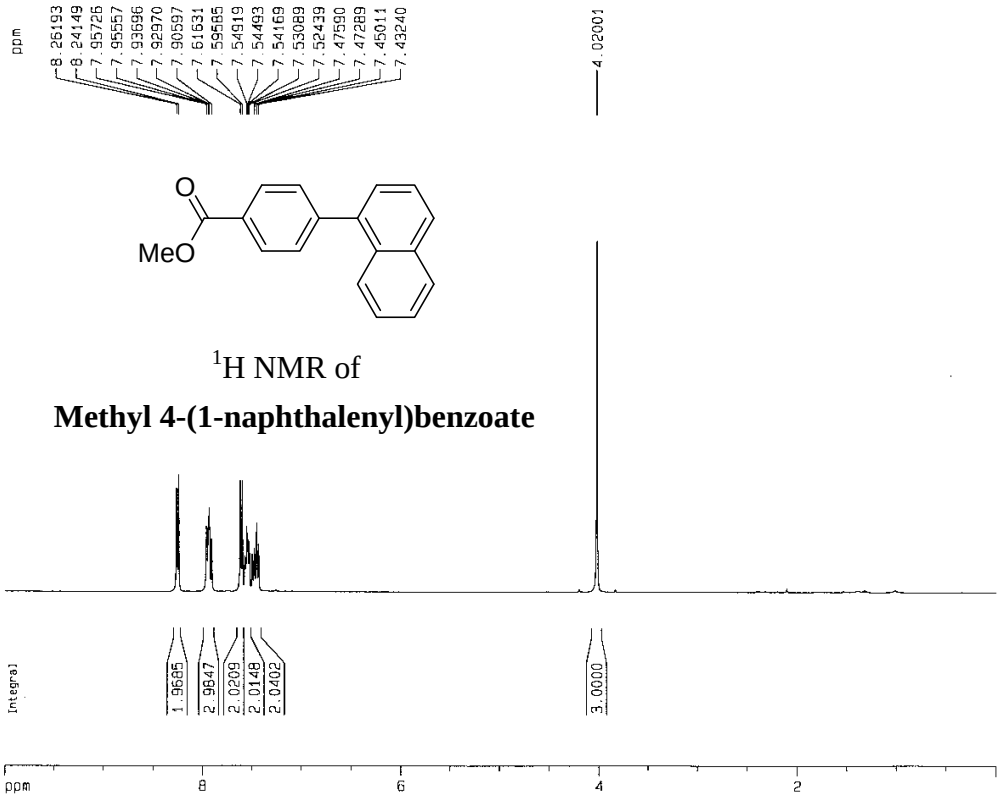




^{13}C NMR of

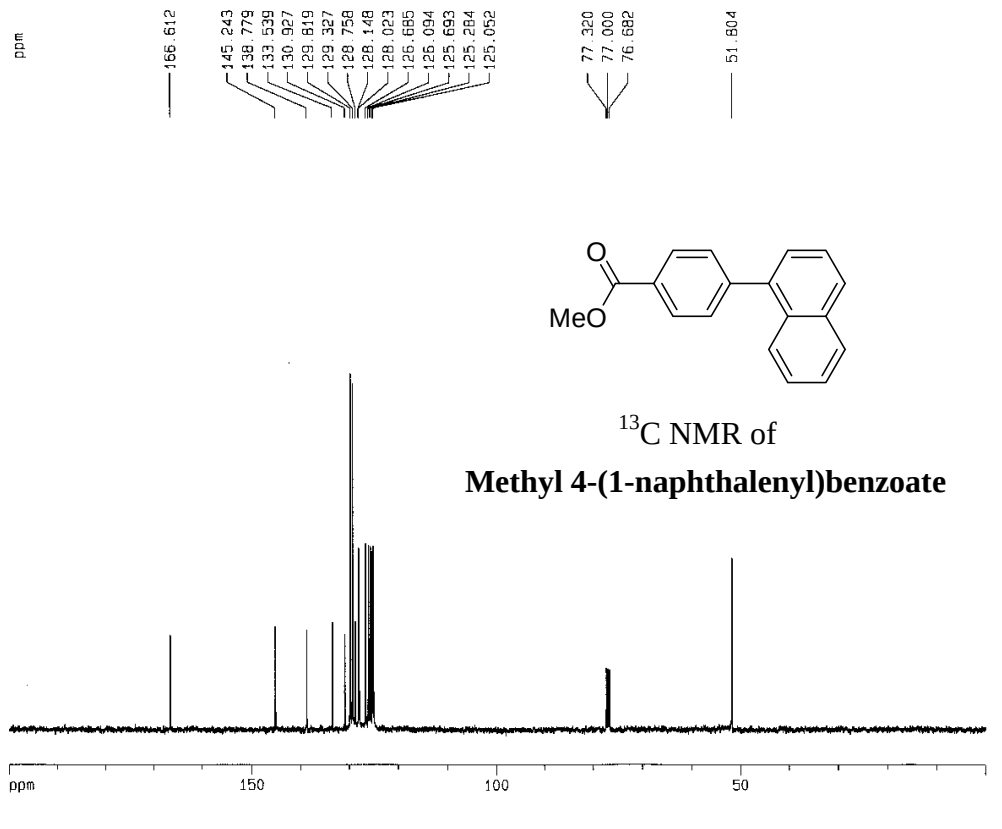
Methyl

4-(3-trifluoromethylphenyl) benoate



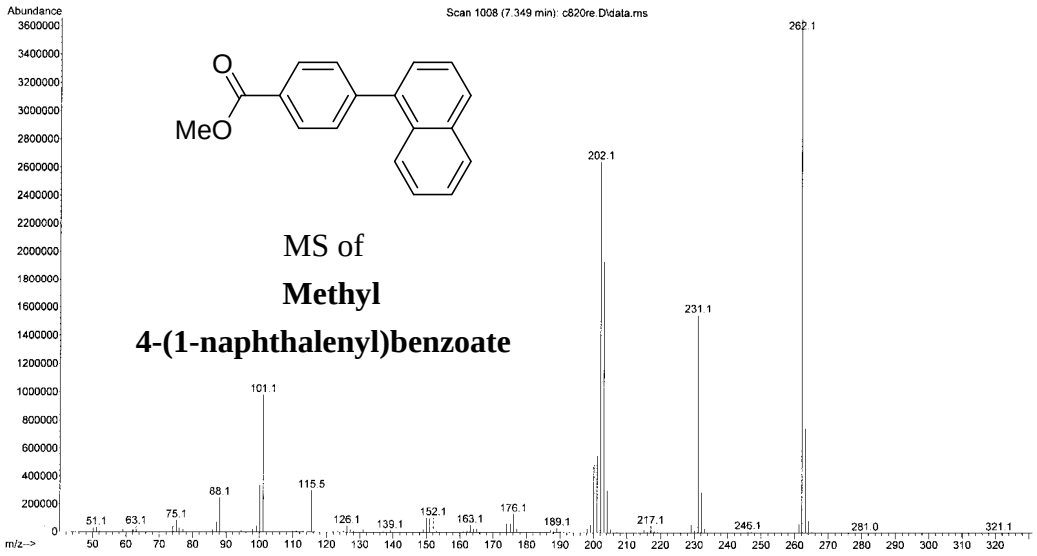
^{1}H NMR of

Methyl 4-(1-naphthalenyl)benzoate



^{13}C NMR of

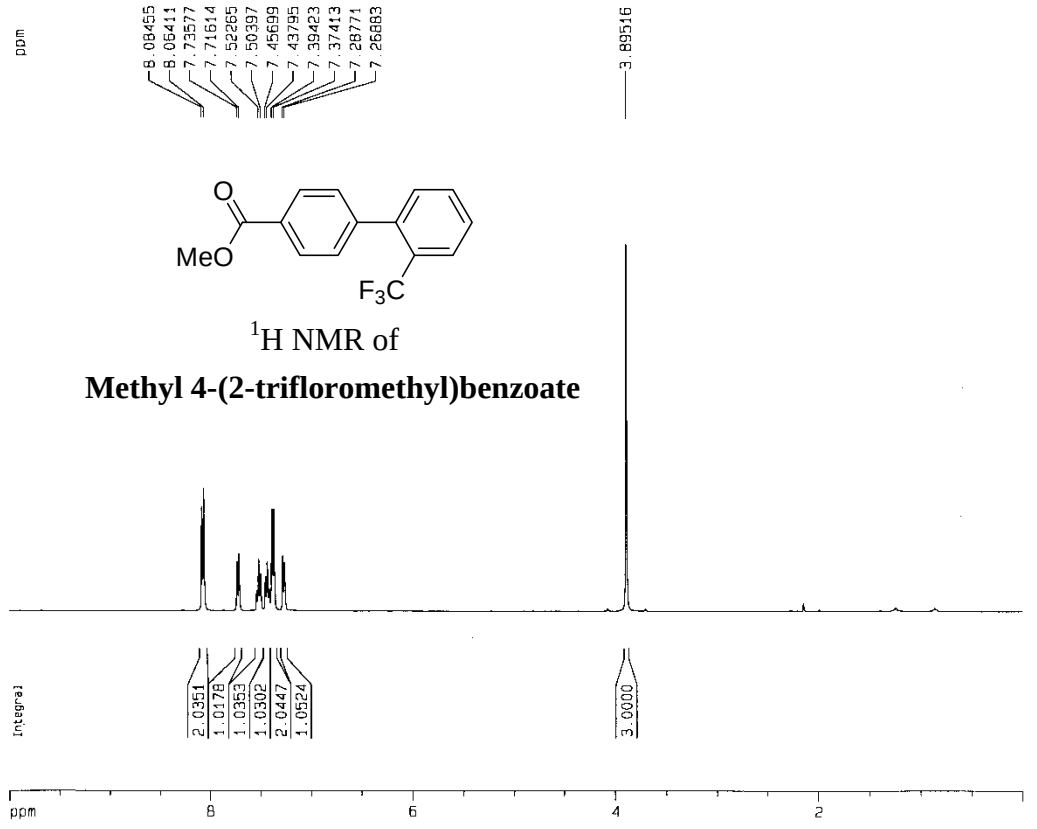
Methyl 4-(1-naphthalenyl)benzoate



MS of

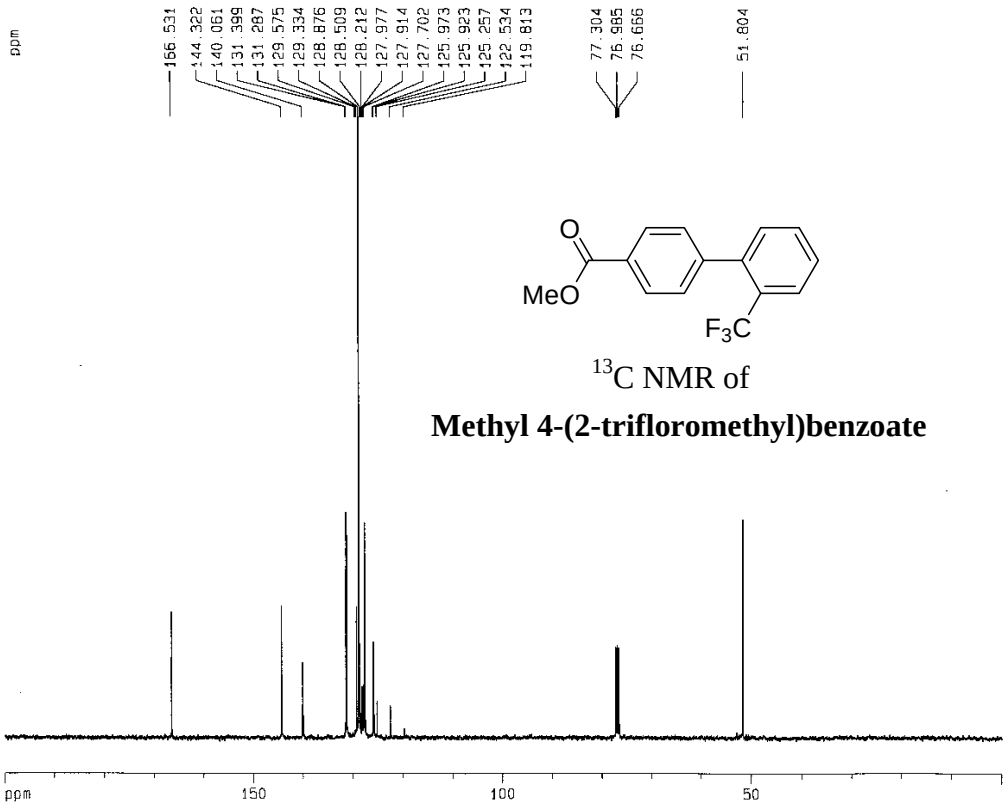
Methyl

4-(1-naphthalenyl)benzoate



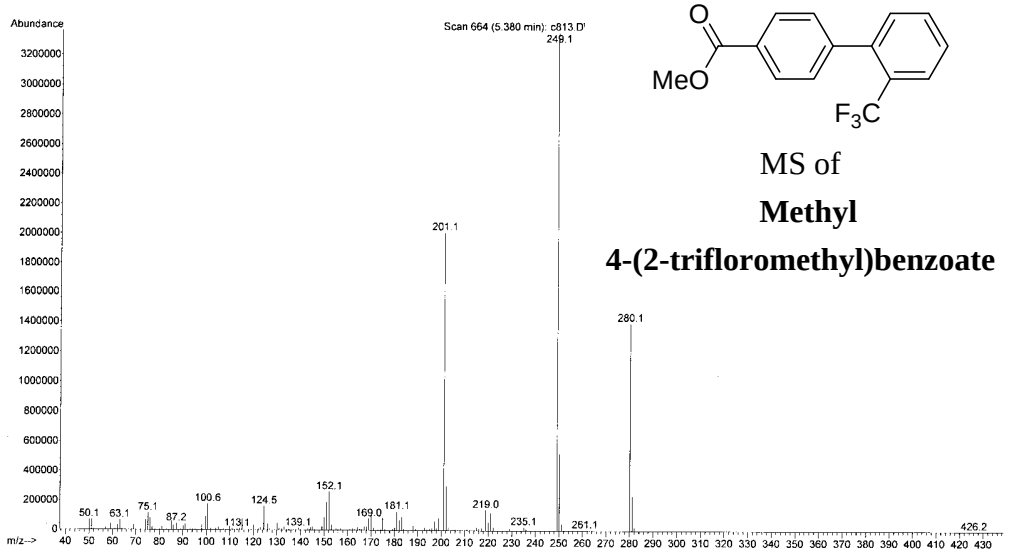
^{1}H NMR of

Methyl 4-(2-trifloromethyl)benzoate



^{13}C NMR of

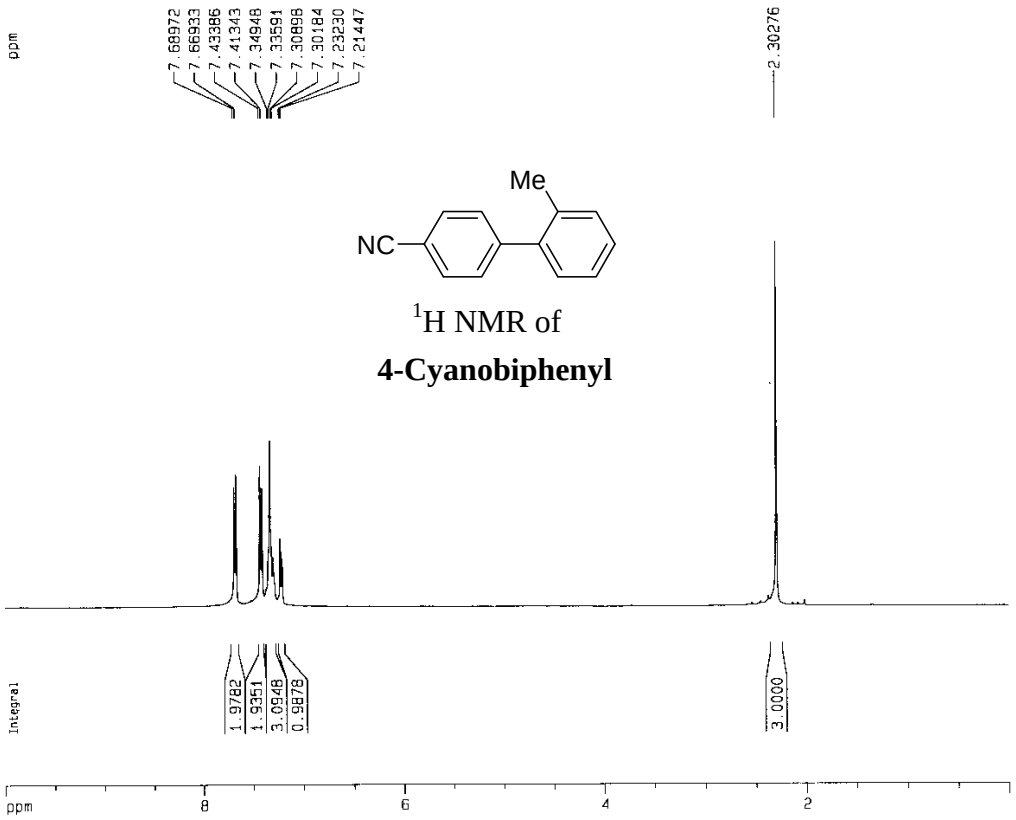
Methyl 4-(2-trifloromethyl)benzoate



MS of

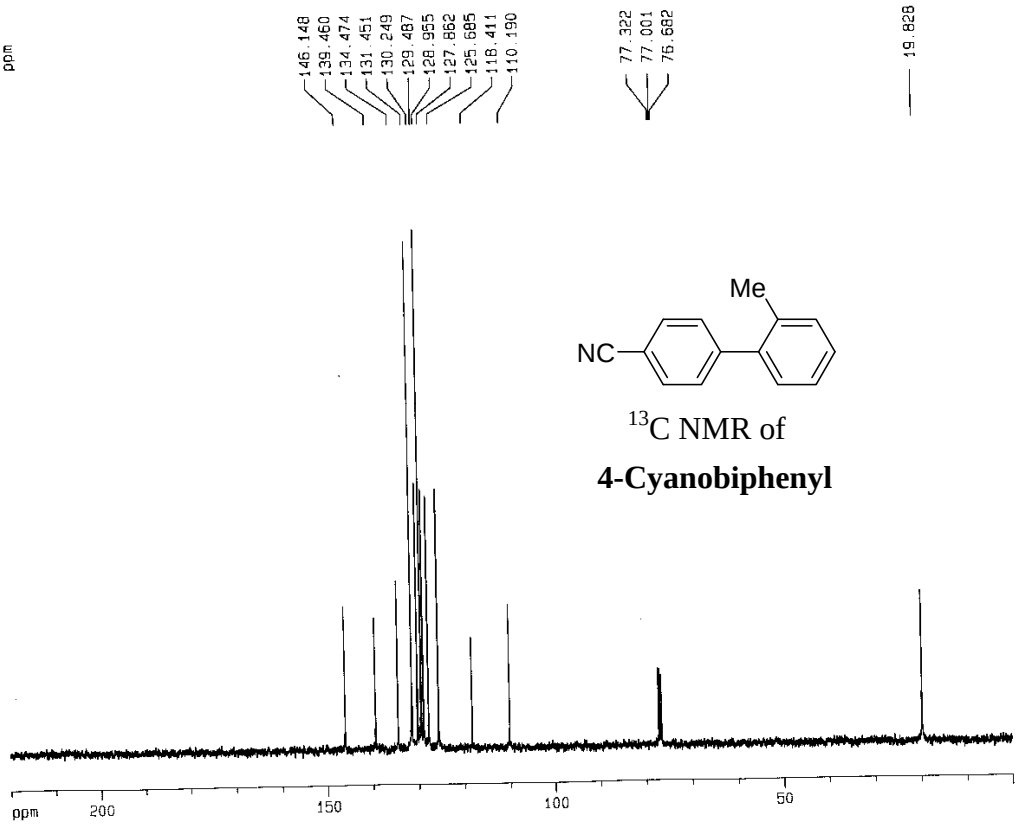
Methyl

4-(2-trifloromethyl)benzoate



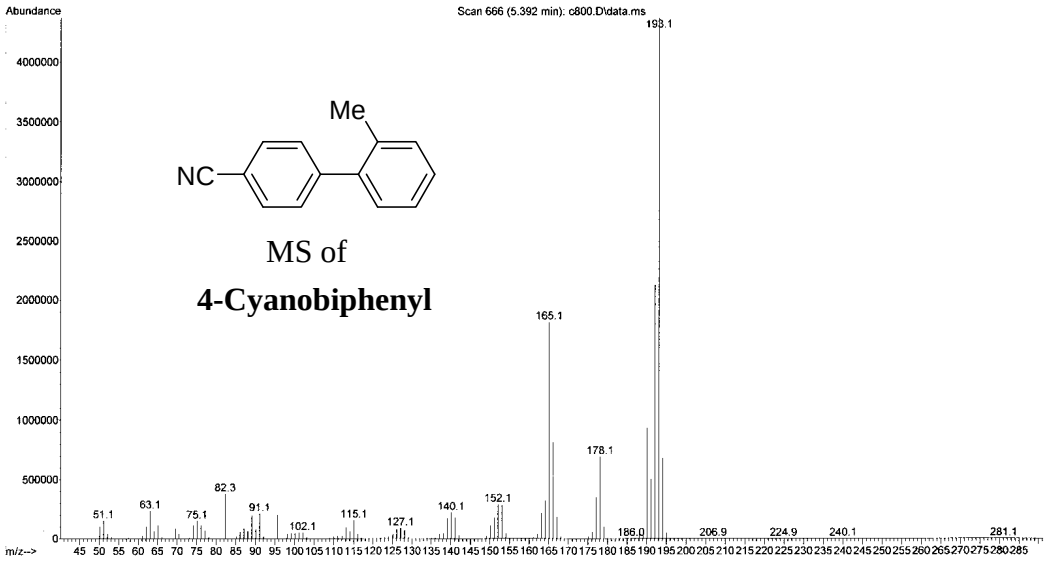
^{1}H NMR of

4-Cyanobiphenyl



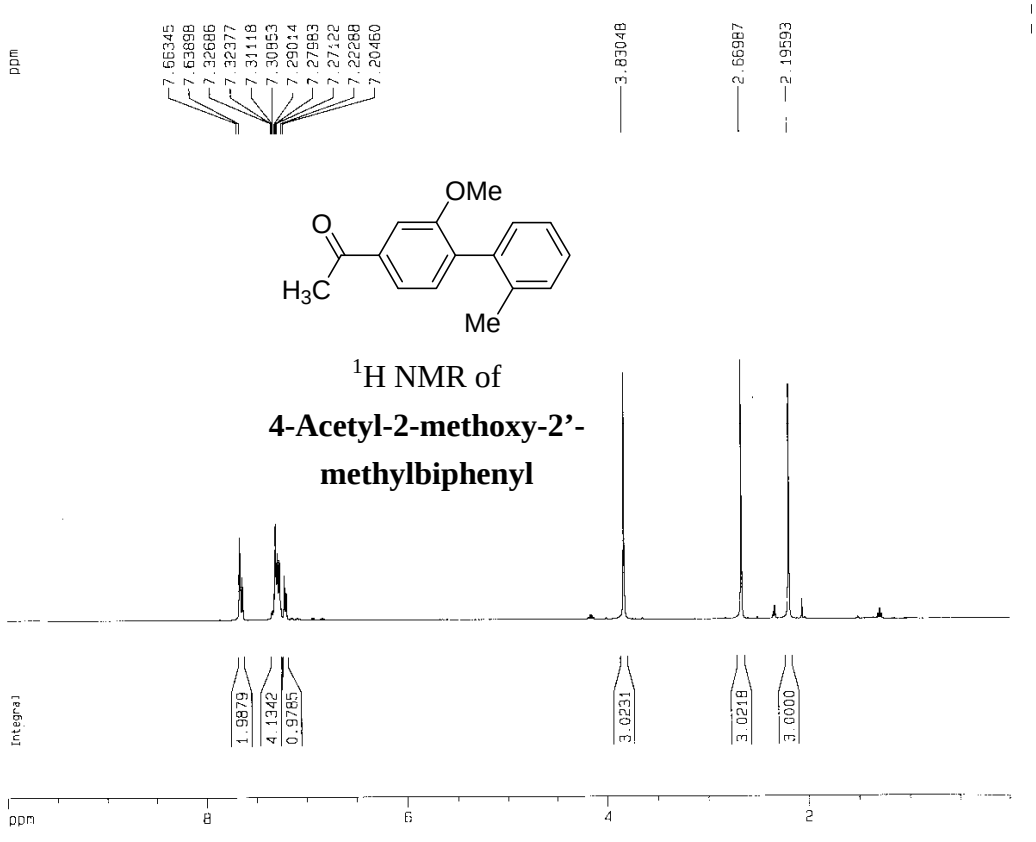
^{13}C NMR of

4-Cyanobiphenyl



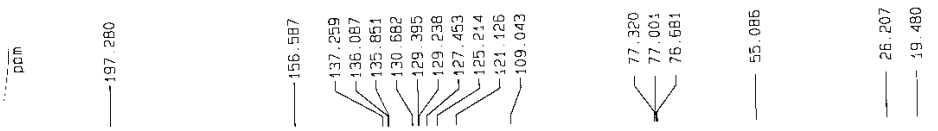
MS of

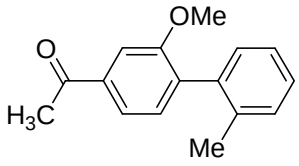
4-Cyanobiphenyl



^{1}H NMR of

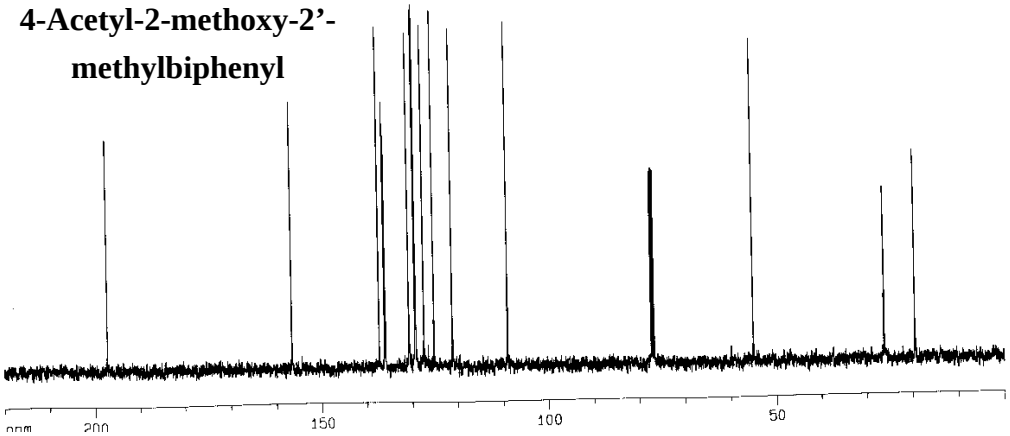
4-Acetyl-2-methoxy-2'-methylbiphenyl

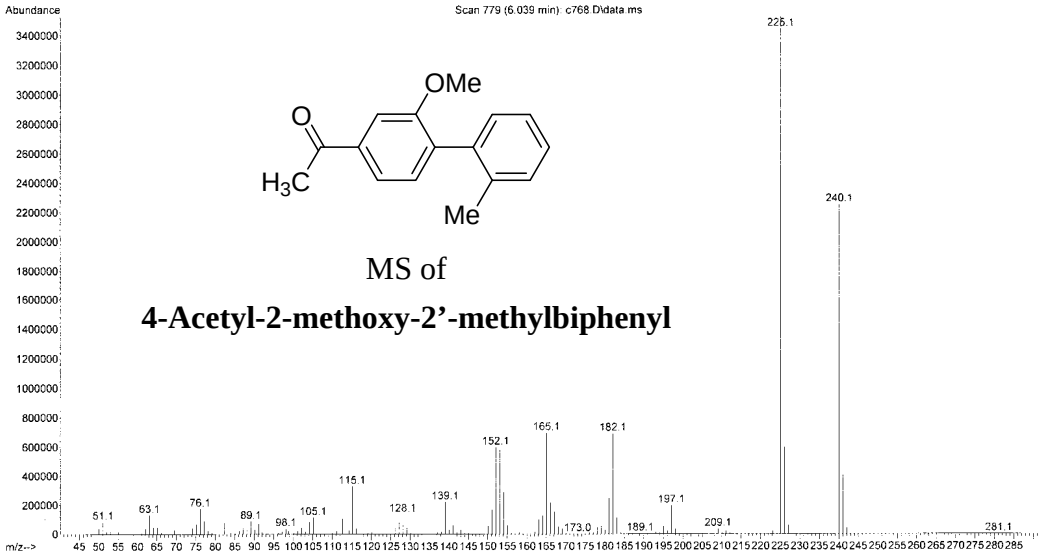




^{13}C NMR of

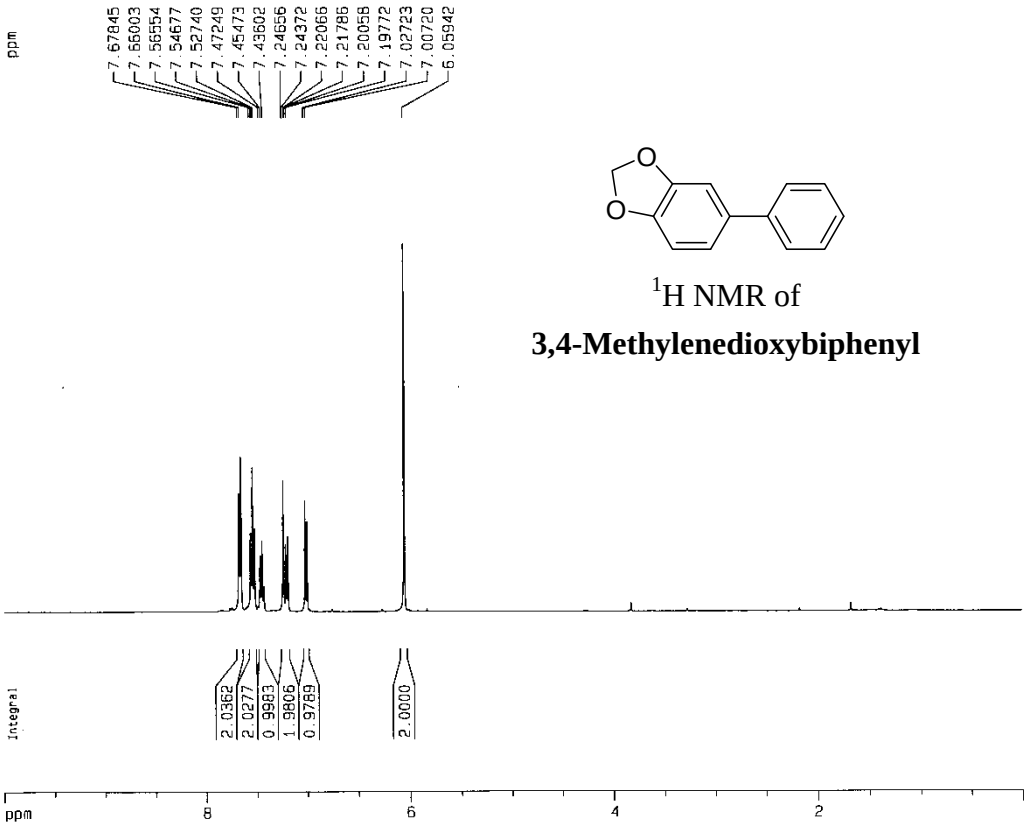
4-Acetyl-2-methoxy-2'-methylbiphenyl





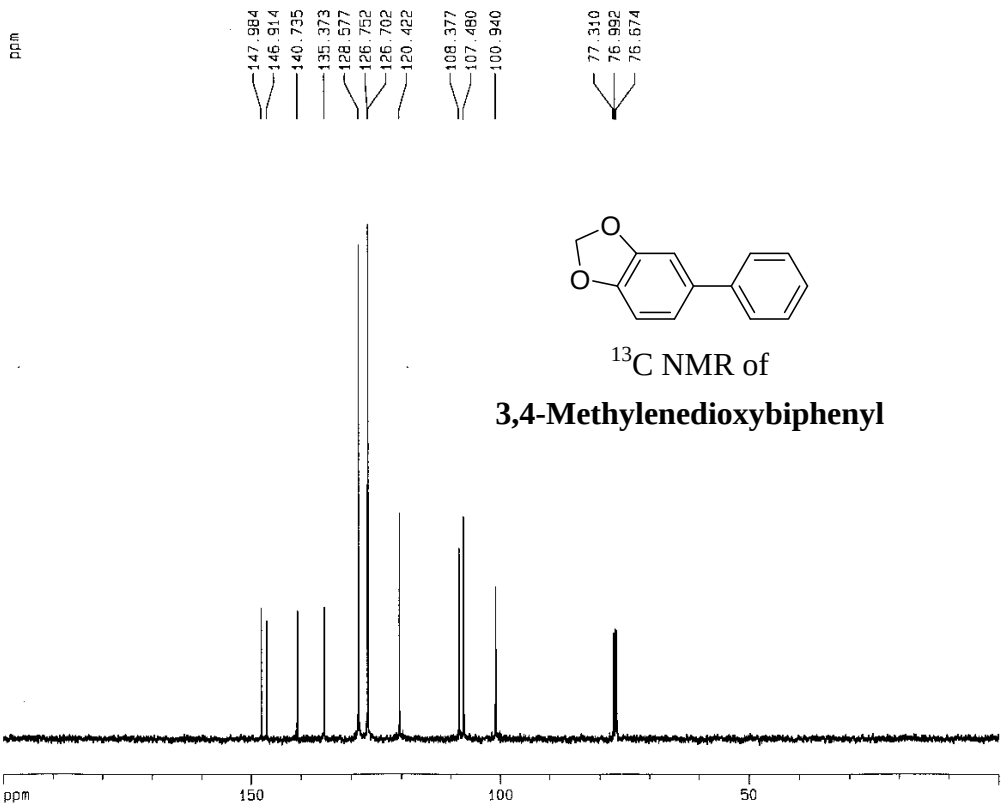
MS of

4-Acetyl-2-methoxy-2'-methylbiphenyl



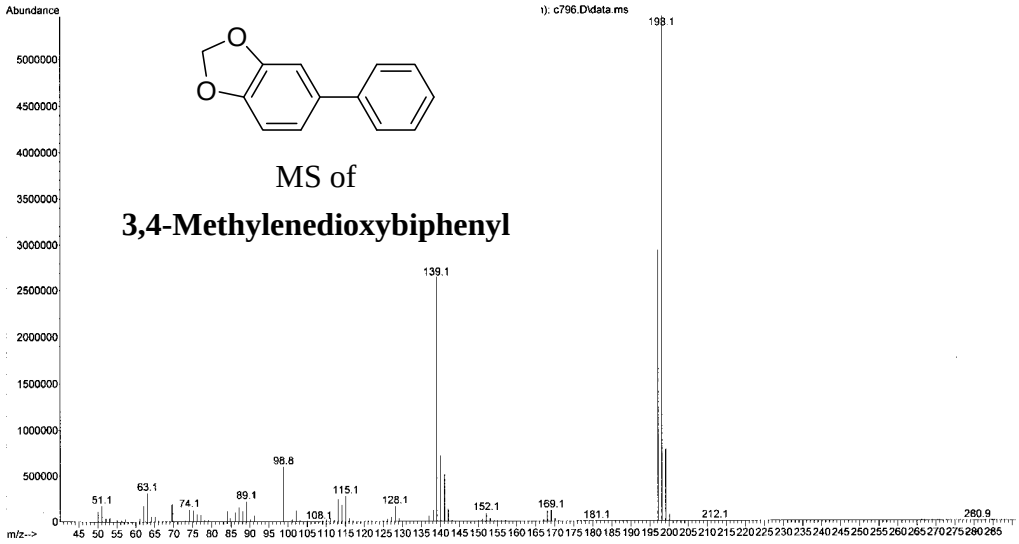
^{1}H NMR of

3,4-Methylenedioxybiphenyl



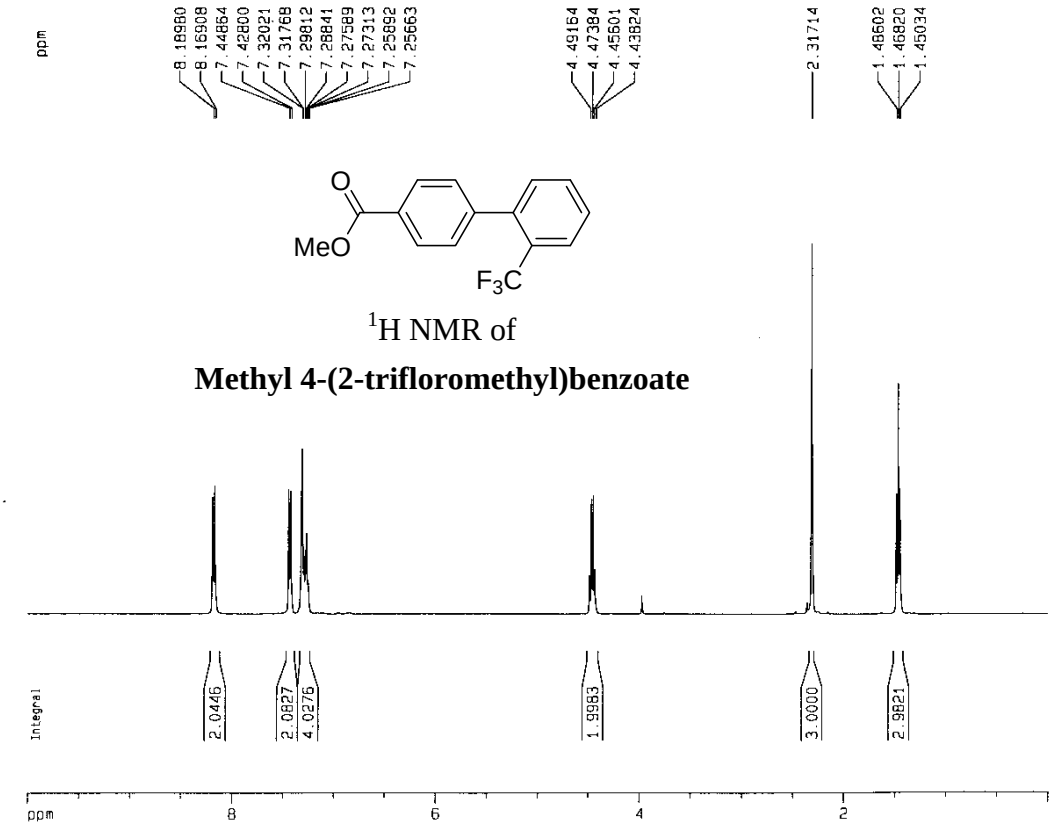
^{13}C NMR of

3,4-Methylenedioxybiphenyl



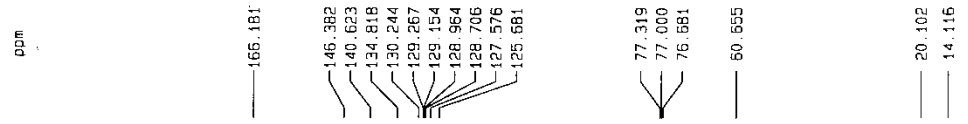
MS of

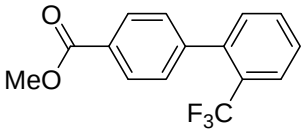
3,4-Methylenedioxybiphenyl



^{1}H NMR of

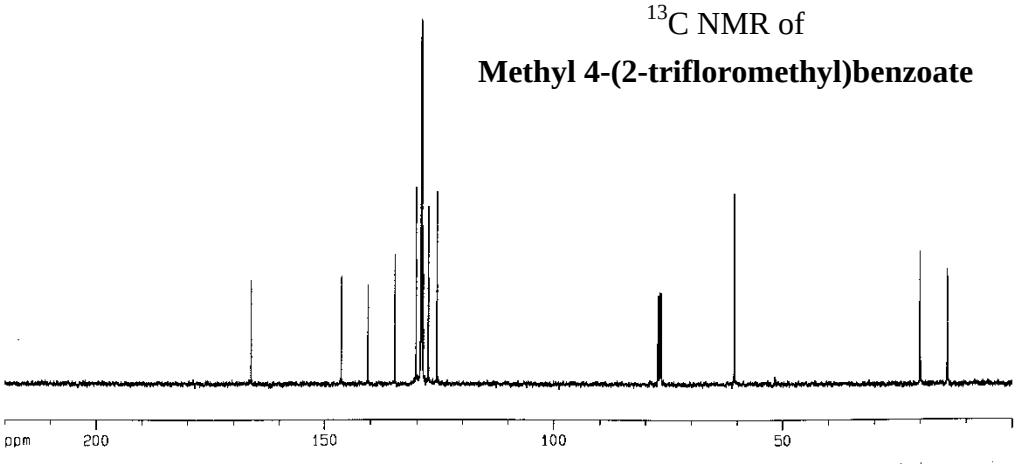
Methyl 4-(2-trifloromethyl)benzoate

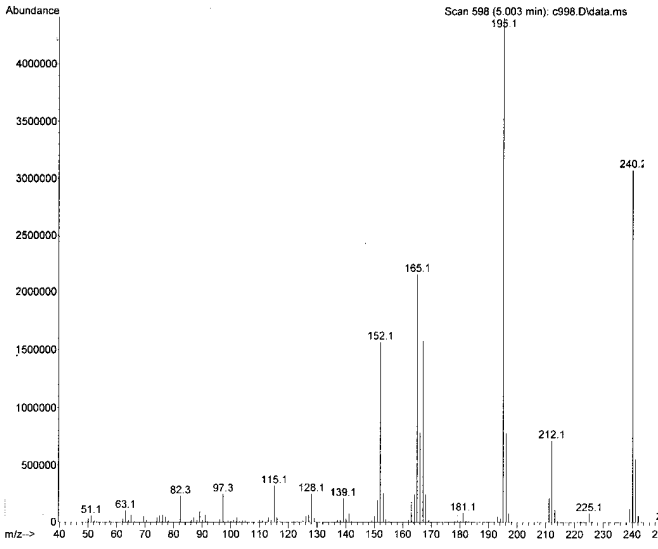


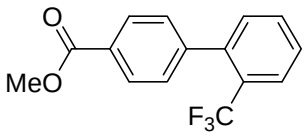


^{13}C NMR of

Methyl 4-(2-triflоromethyl)benzoate



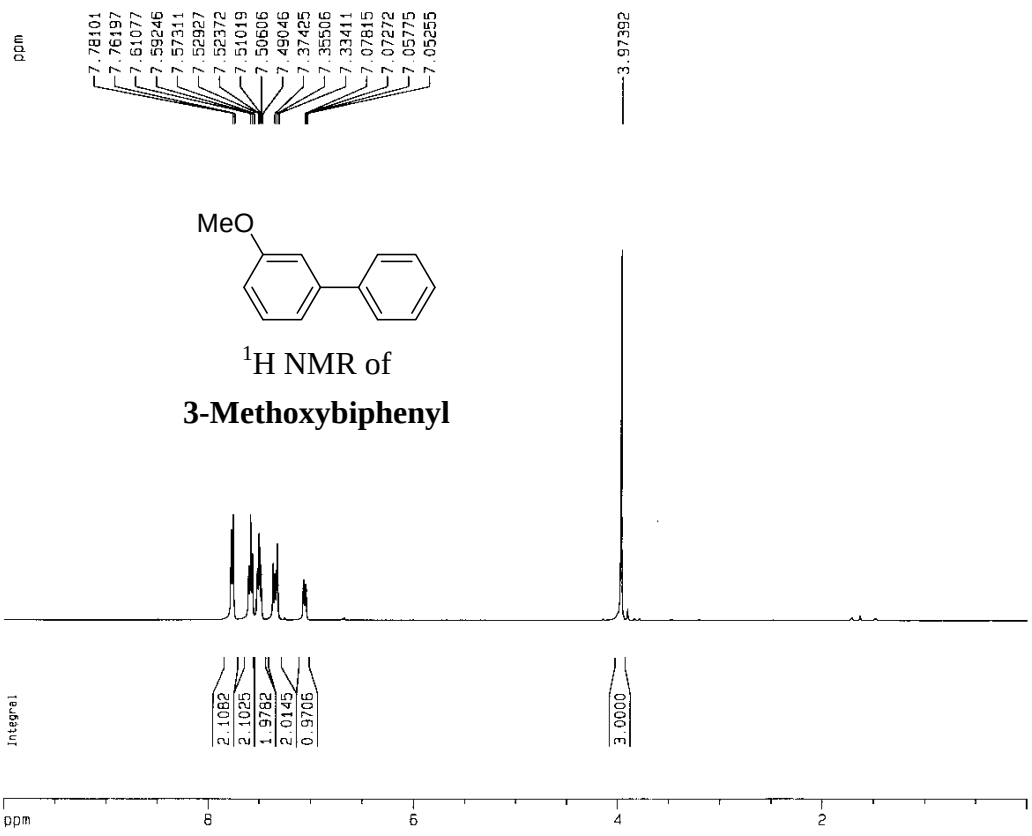




MS of

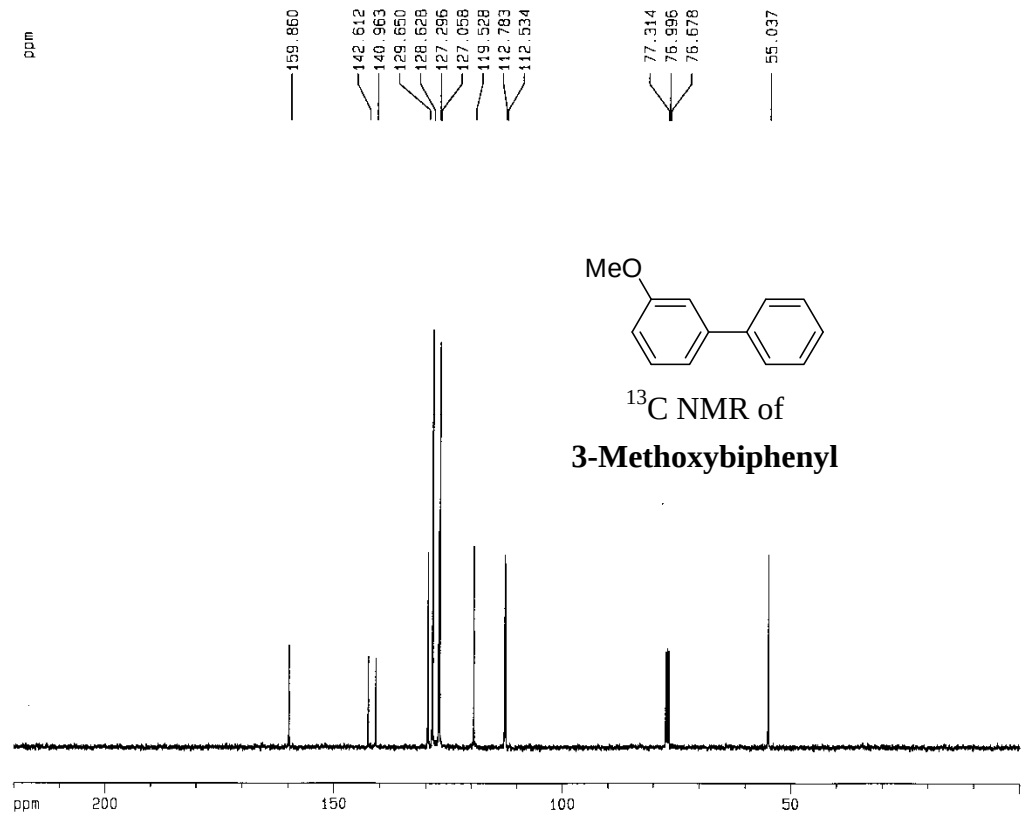
Methyl

4-(2-triflоromethyl)benzoate



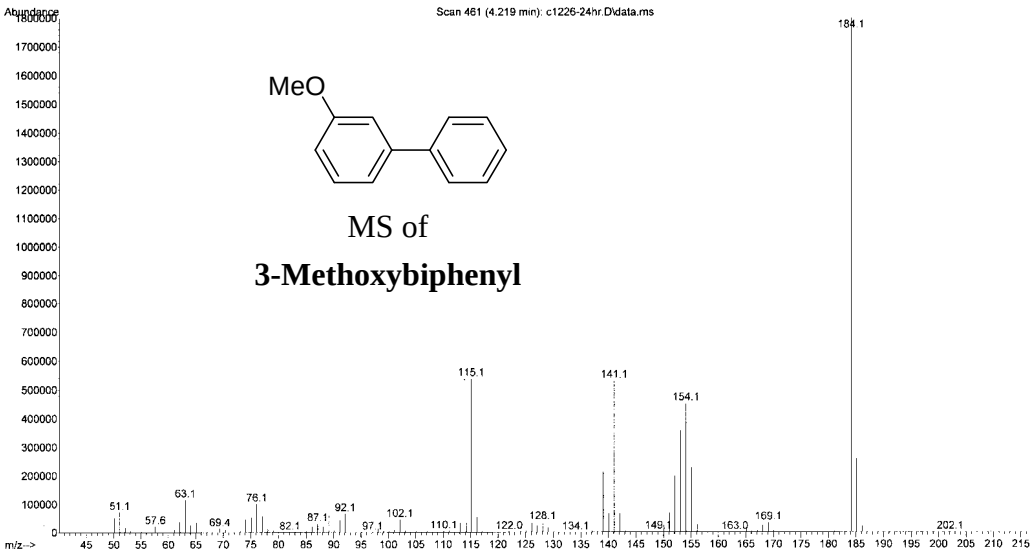
^{1}H NMR of

3-Methoxybiphenyl



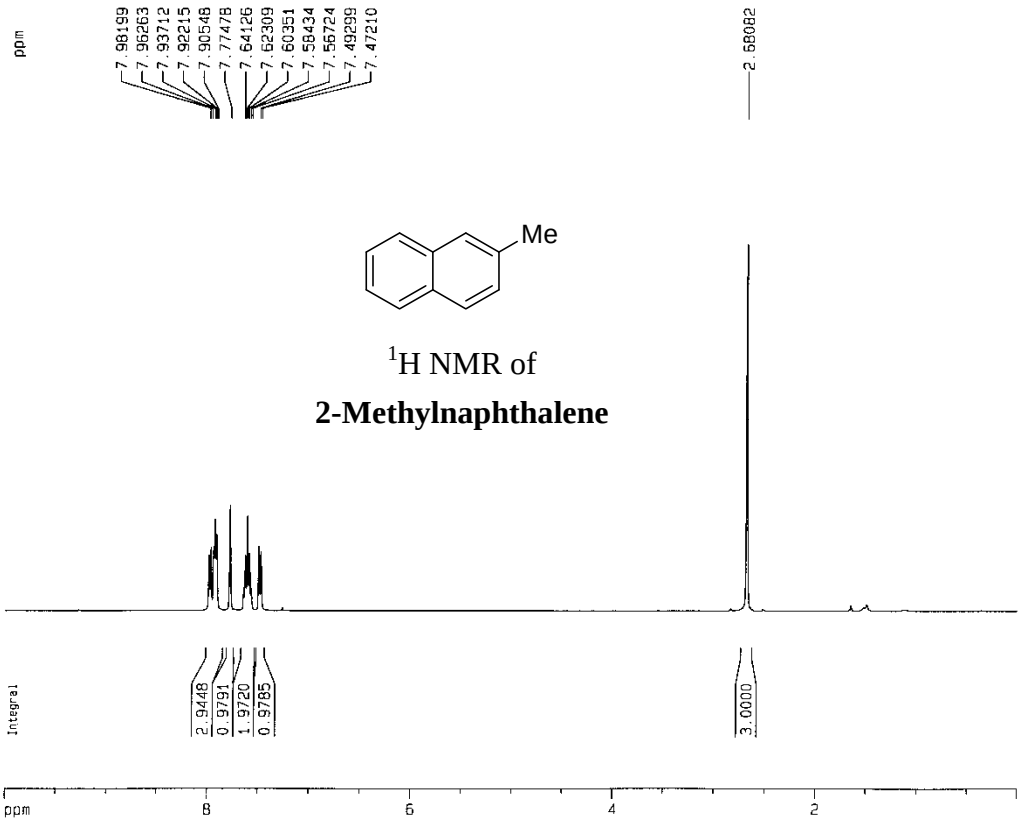
^{13}C NMR of

3-Methoxybiphenyl



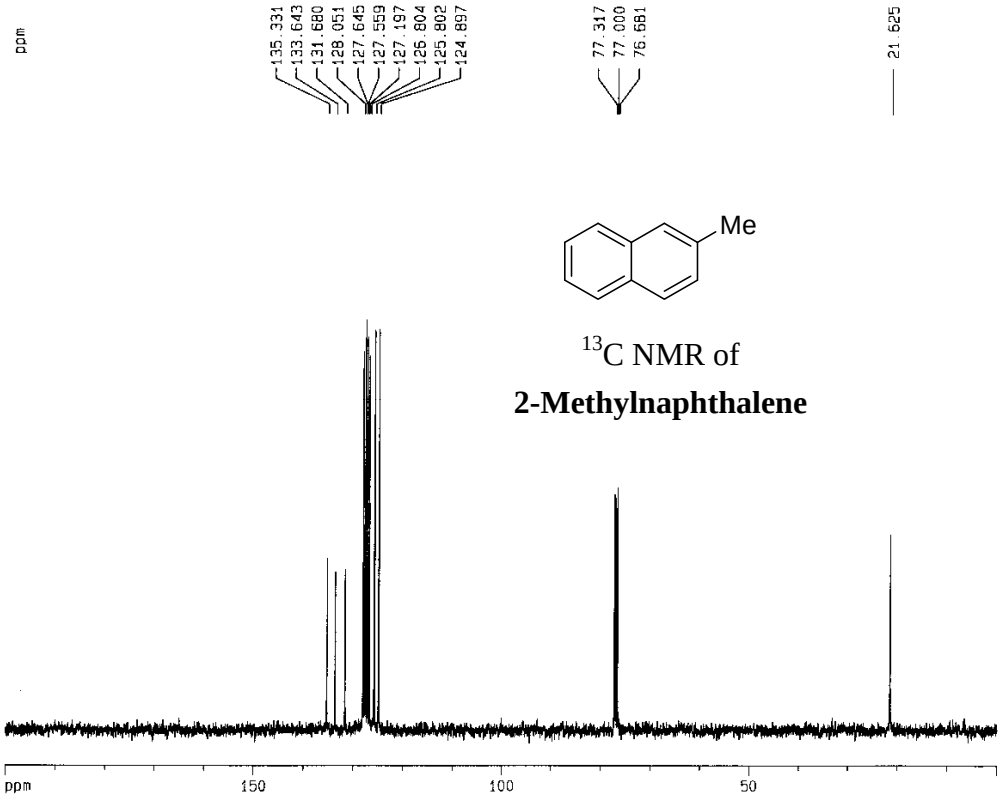
MS of

3-Methoxybiphenyl



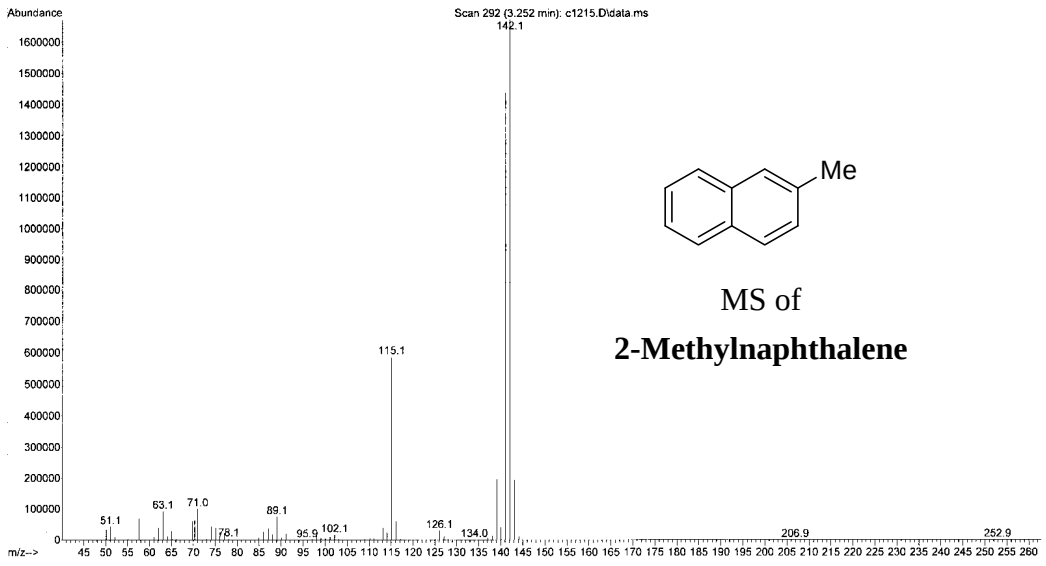
^{1}H NMR of

2-Methylnaphthalene



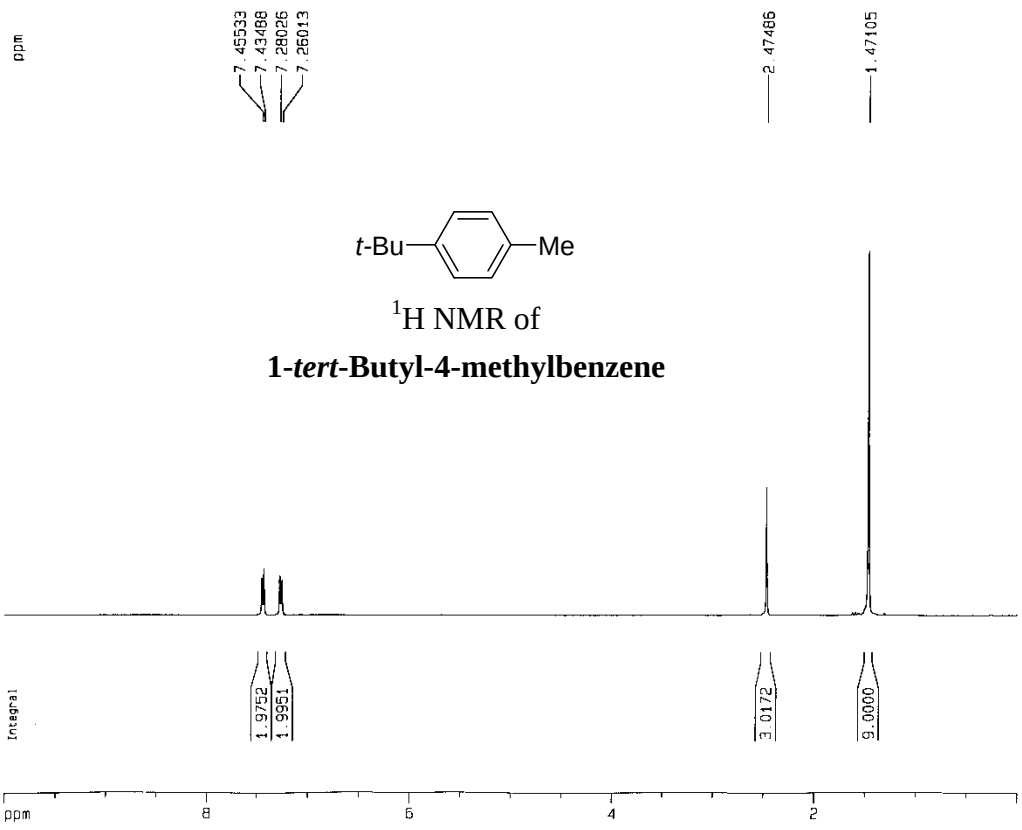
^{13}C NMR of

2-Methylnaphthalene



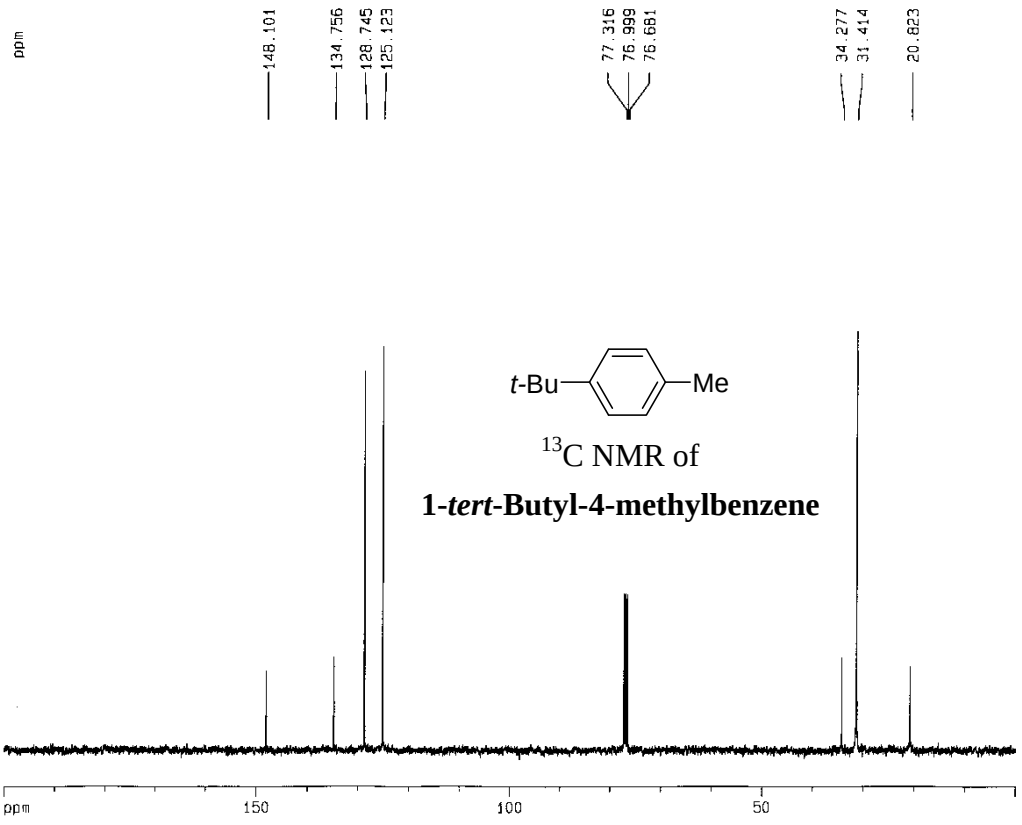
MS of

2-Methylnaphthalene



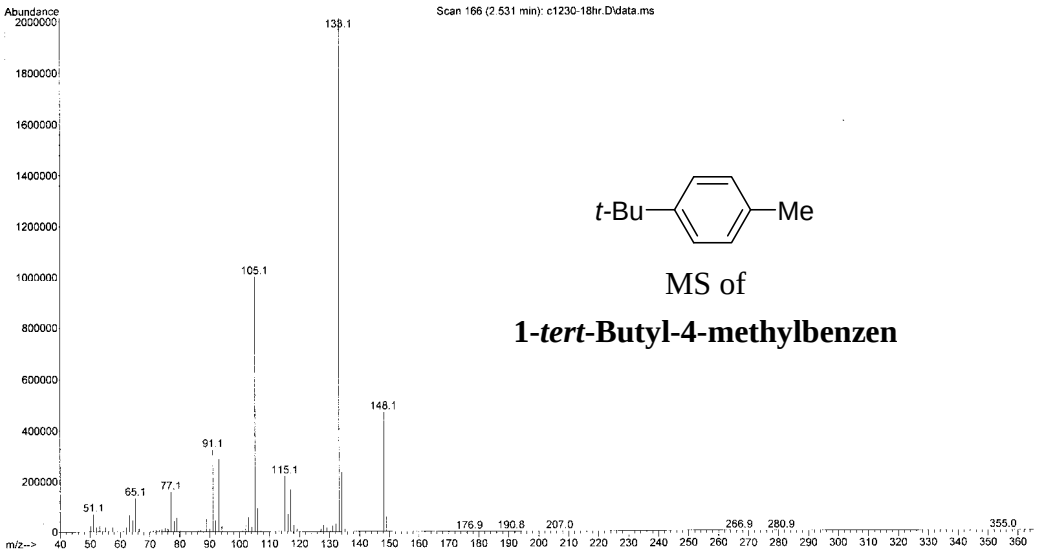
^{1}H NMR of

1-*tert*-Butyl-4-methylbenzene



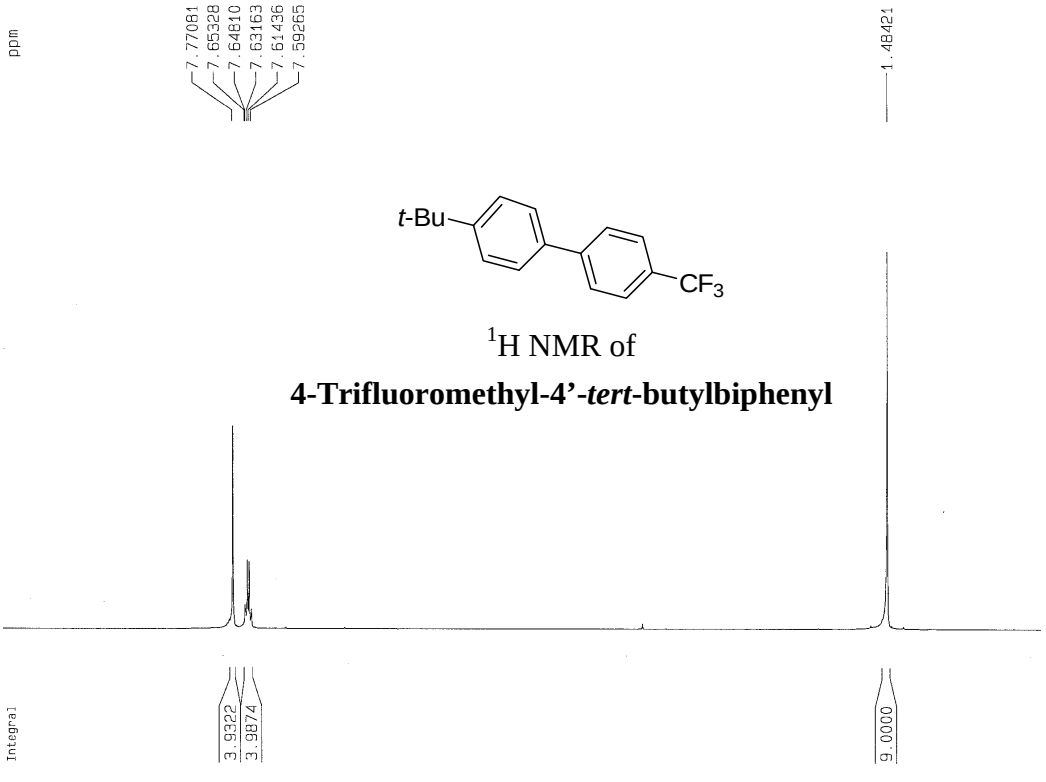
^{13}C NMR of

1-*tert*-Butyl-4-methylbenzene



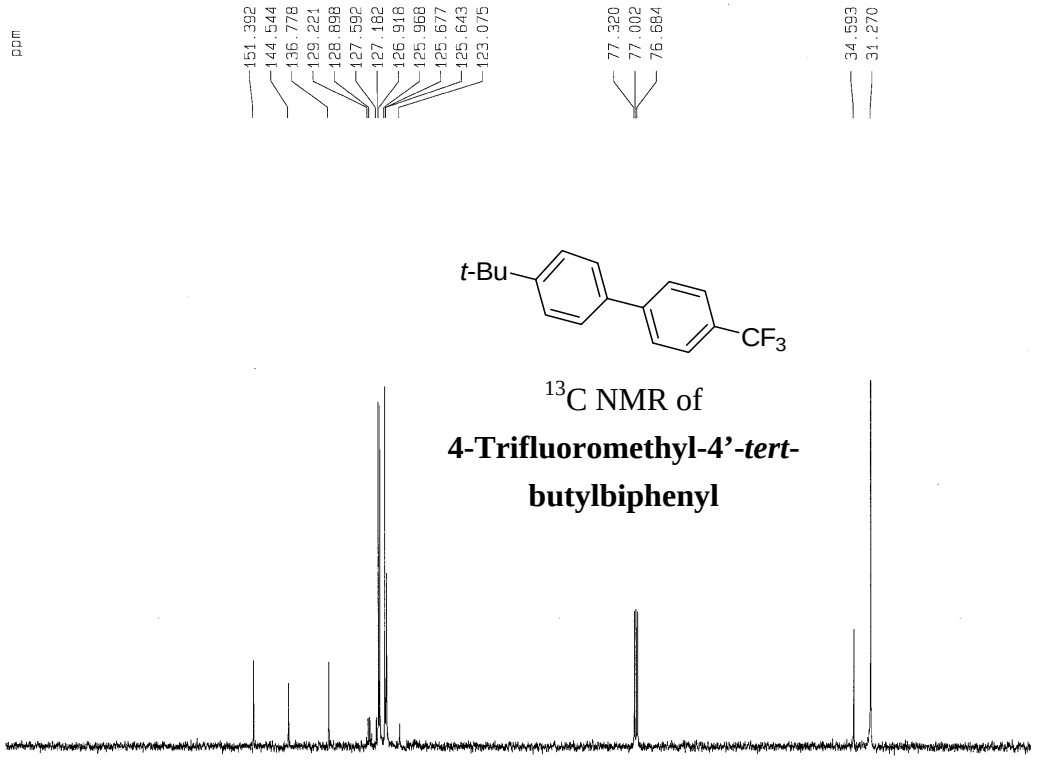
MS of

1-*tert*-Butyl-4-methylbenzen

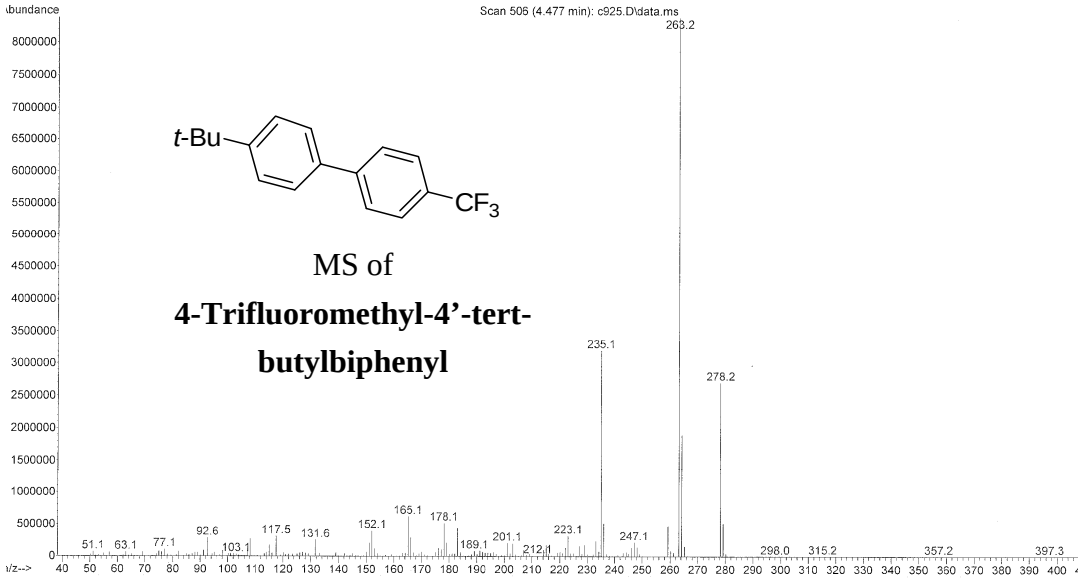


^{1}H NMR of

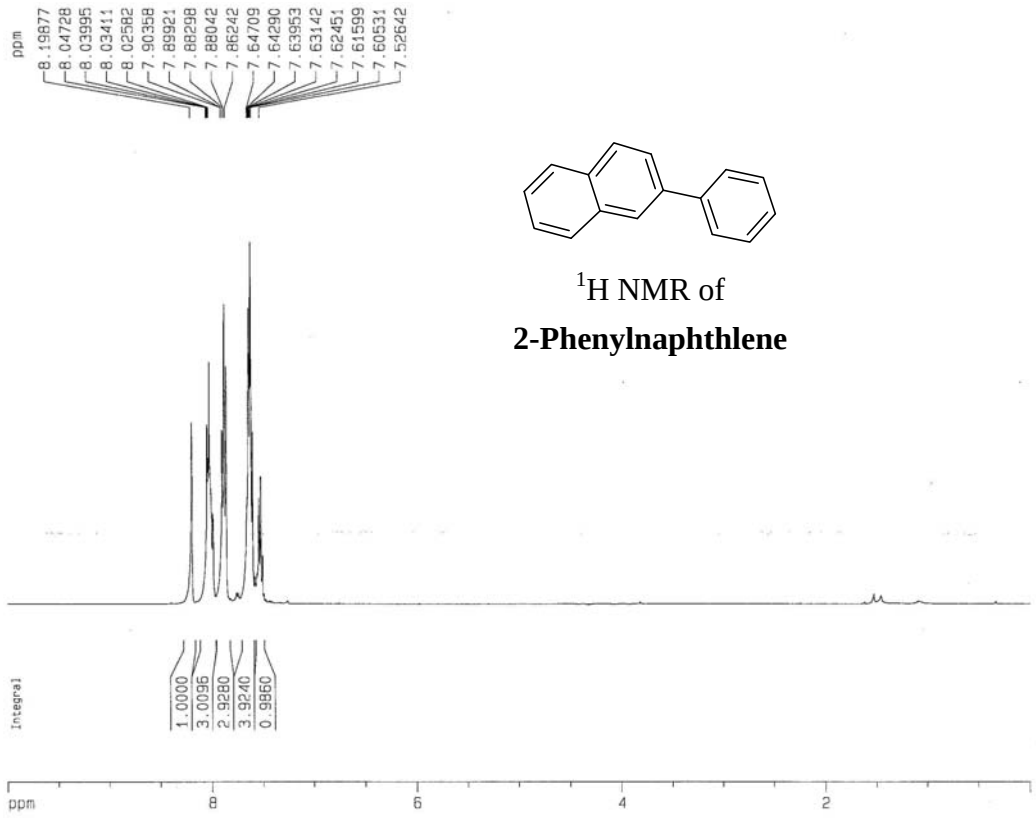
4-Trifluoromethyl-4'-*tert*-butylbiphenyl



^{13}C NMR of
4-Trifluoromethyl-4'-*tert*-butylbiphenyl

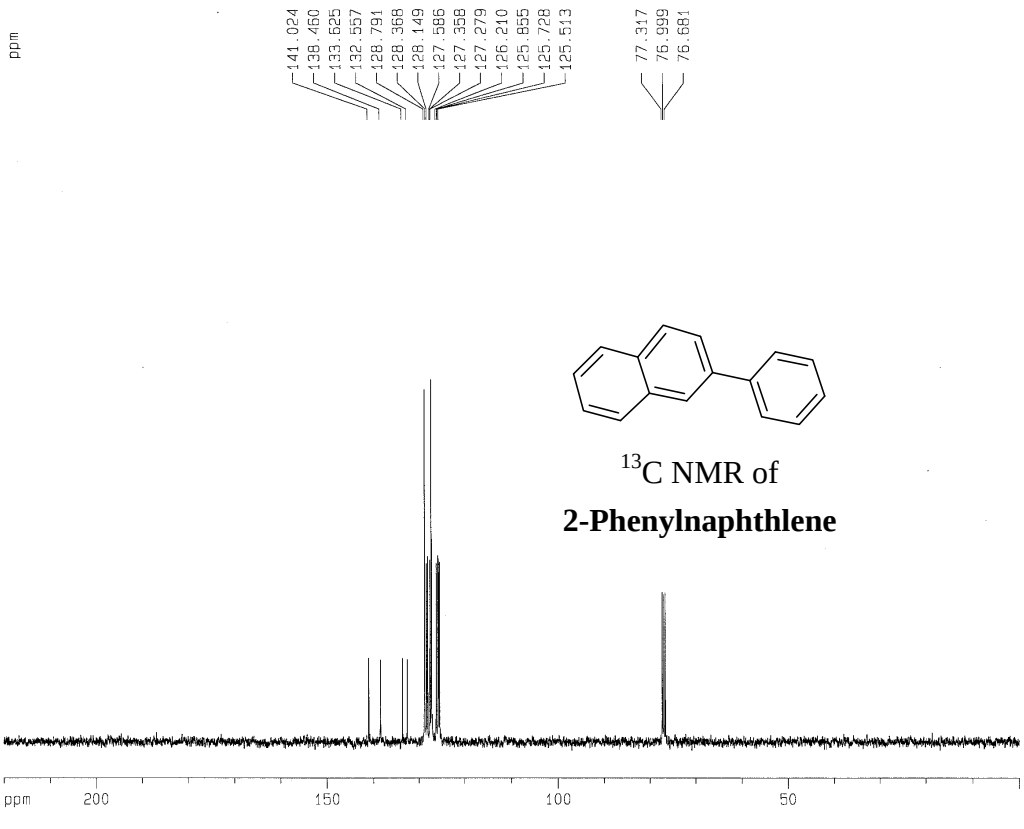


MS of
4-Trifluoromethyl-4'-tert-butylbiphenyl



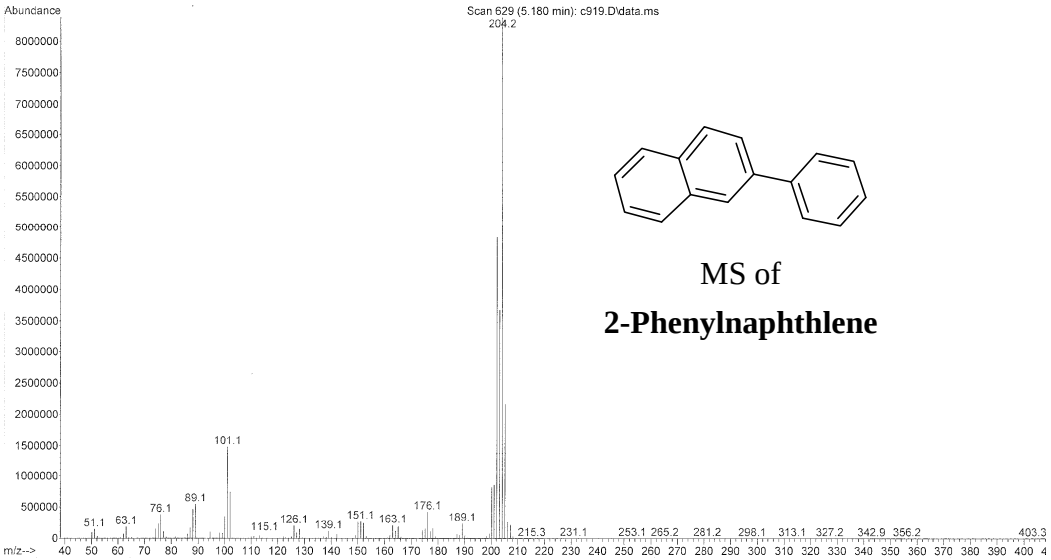
^{1}H NMR of

2-Phenylnaphthlene



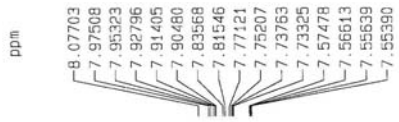
^{13}C NMR of

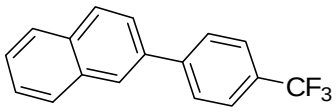
2-Phenylnaphthlene



MS of

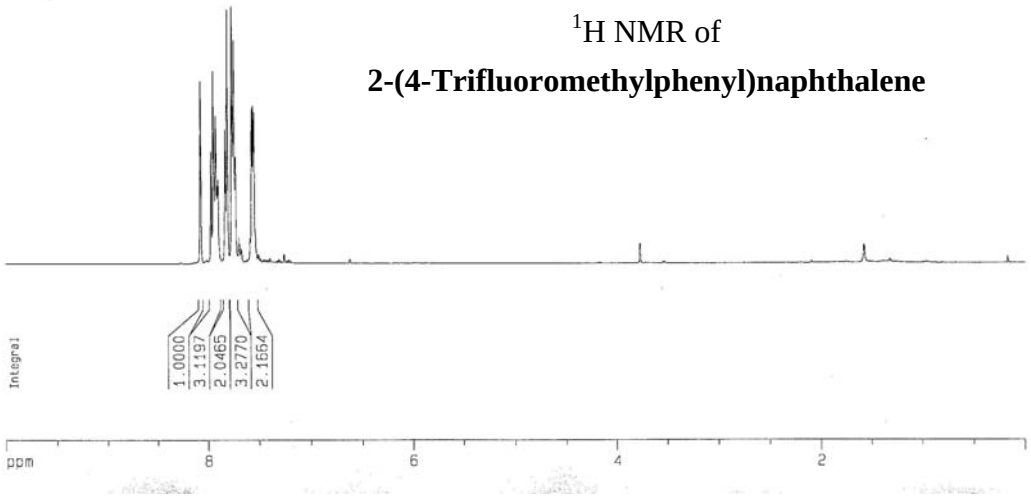
2-Phenylnaphthlene

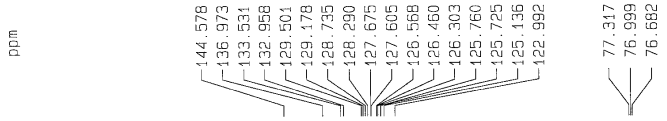


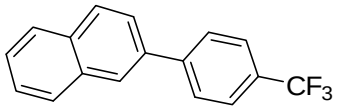


^{1}H NMR of

2-(4-Trifluoromethylphenyl)naphthalene

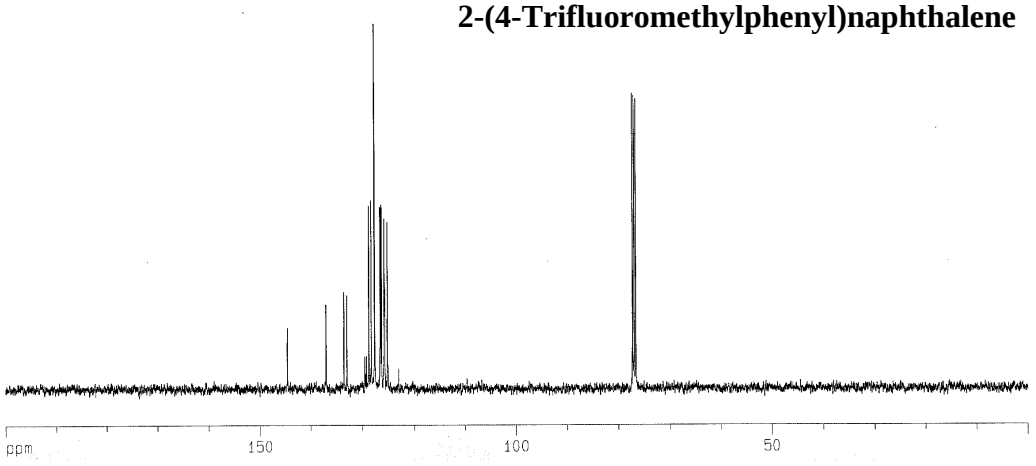


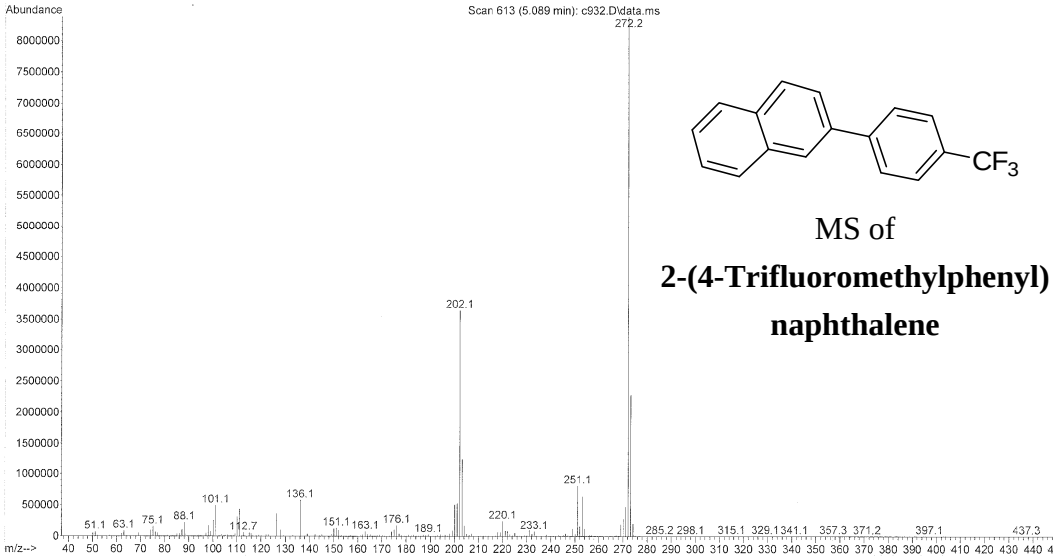




^{13}C NMR of

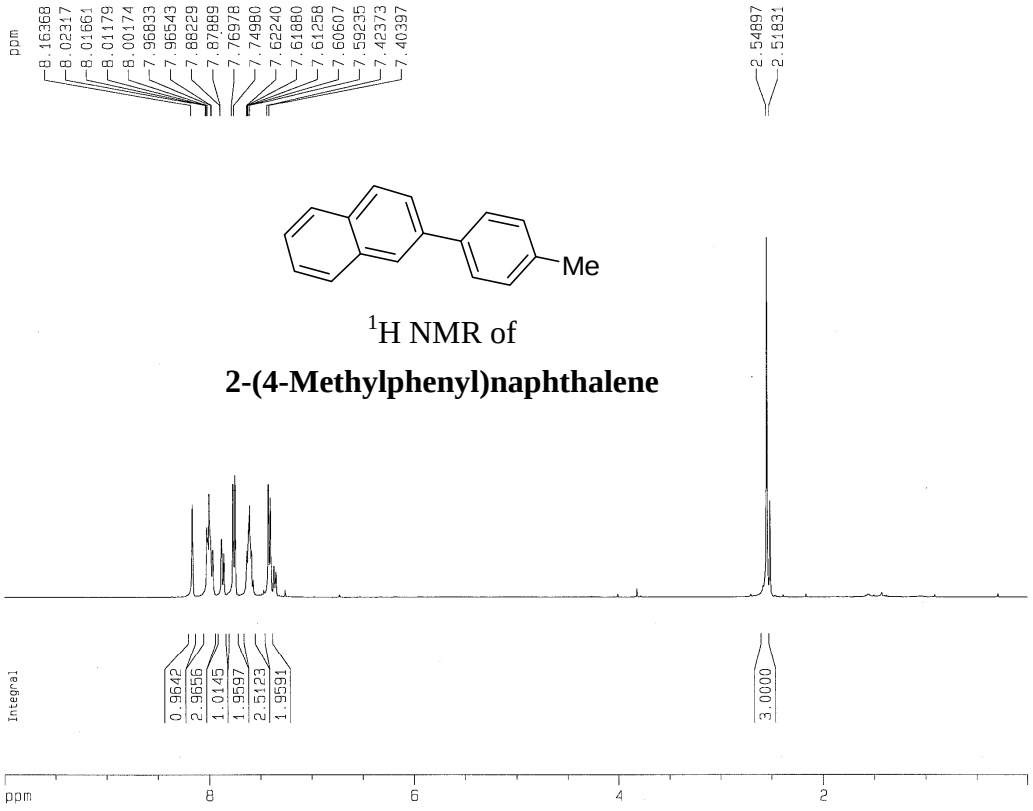
2-(4-Trifluoromethylphenyl)naphthalene





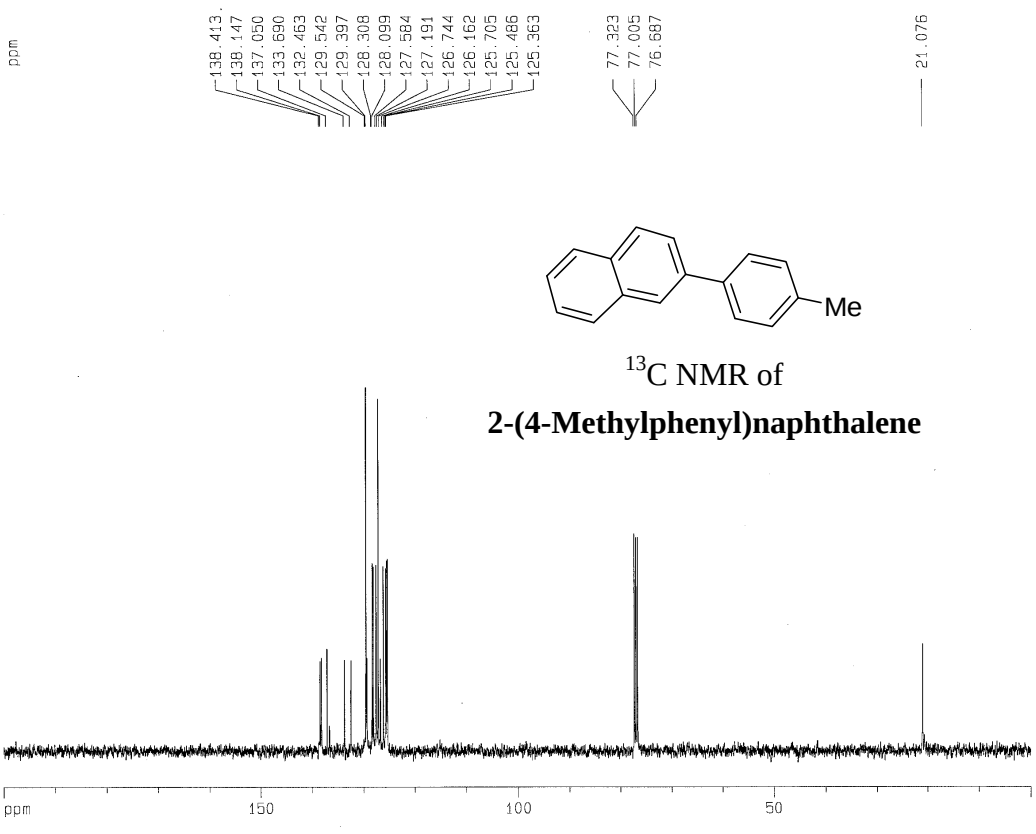
MS of

2-(4-Trifluoromethylphenyl) naphthalene



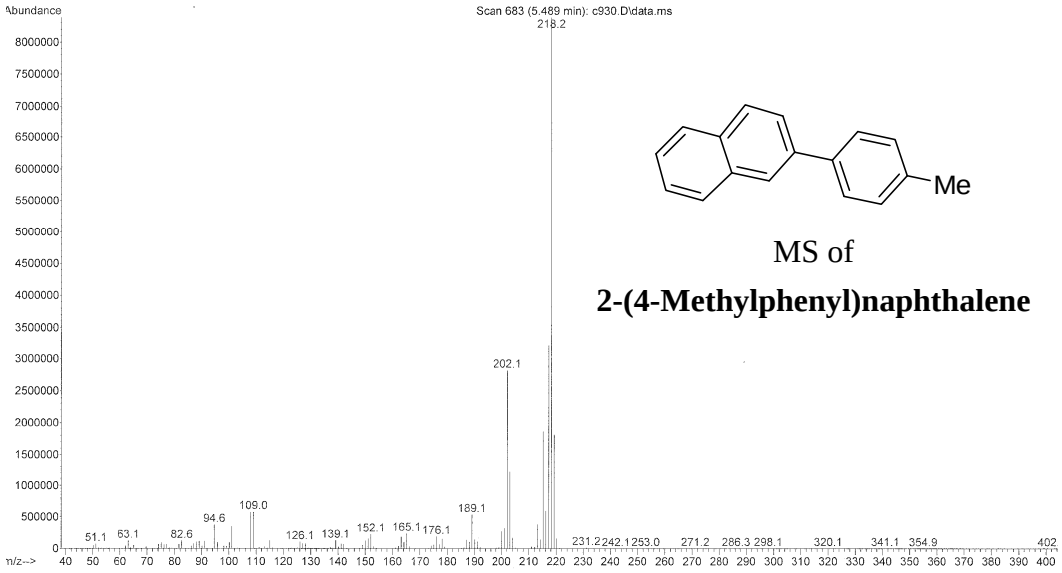
^{1}H NMR of

2-(4-Methylphenyl)naphthalene



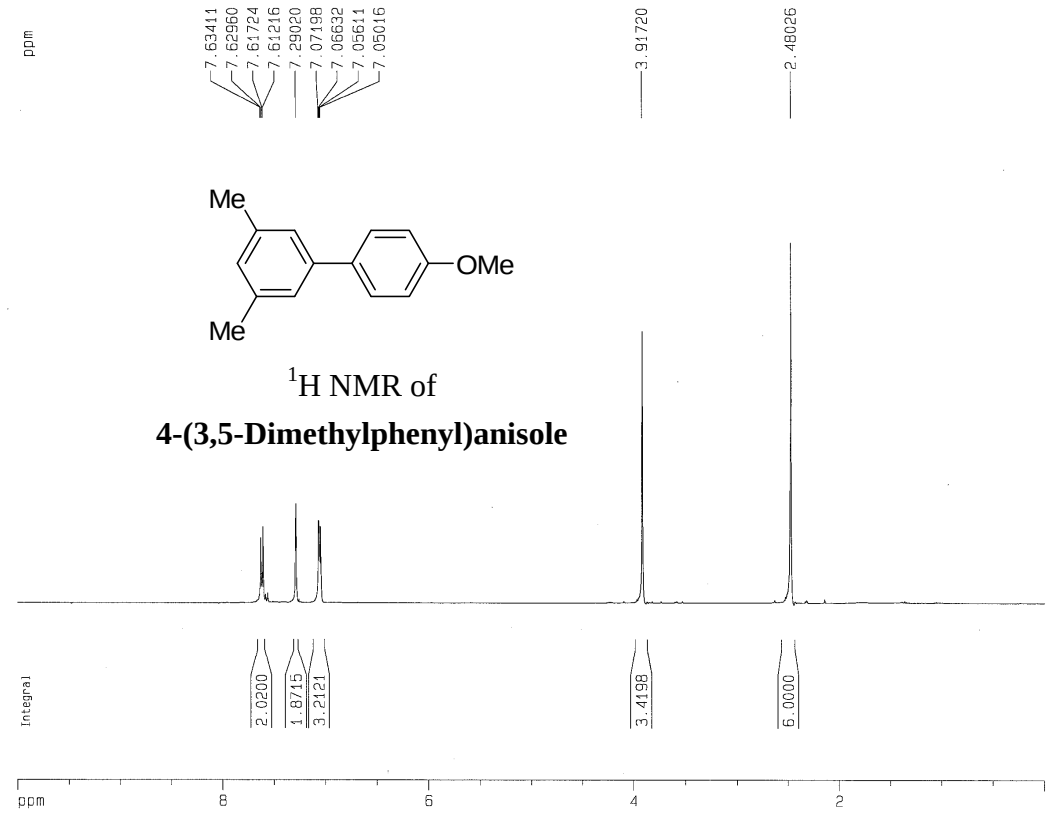
^{13}C NMR of

2-(4-Methylphenyl)naphthalene



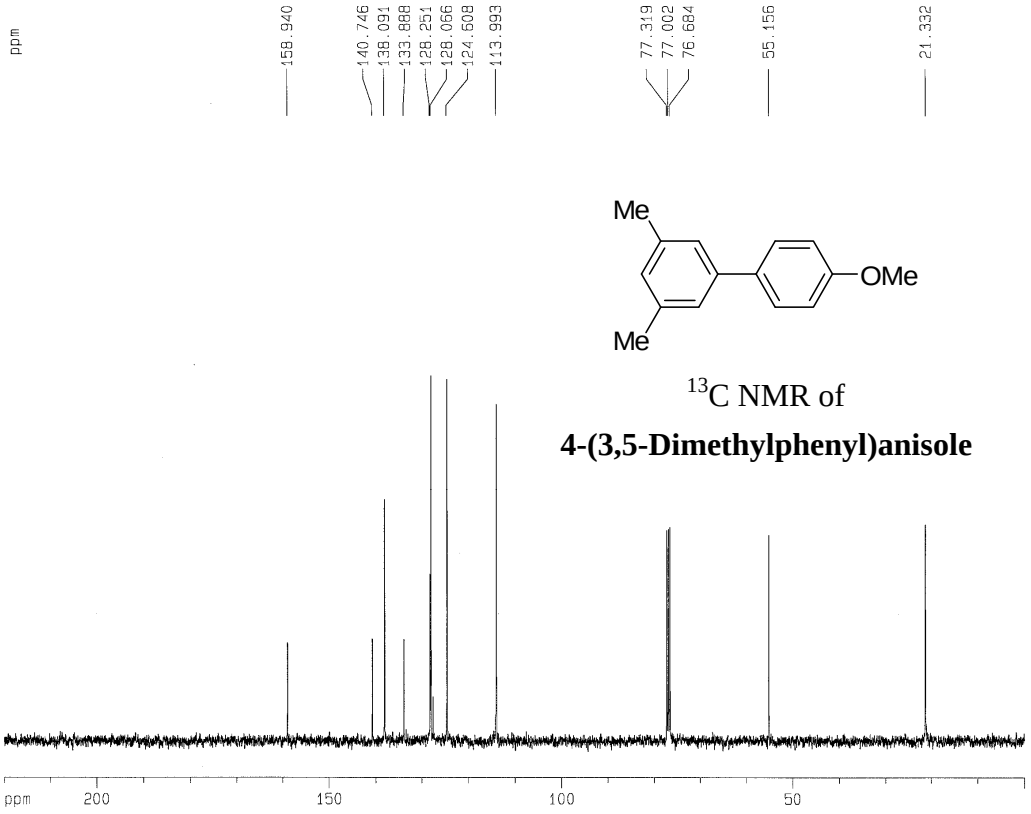
MS of

2-(4-Methylphenyl)naphthalene



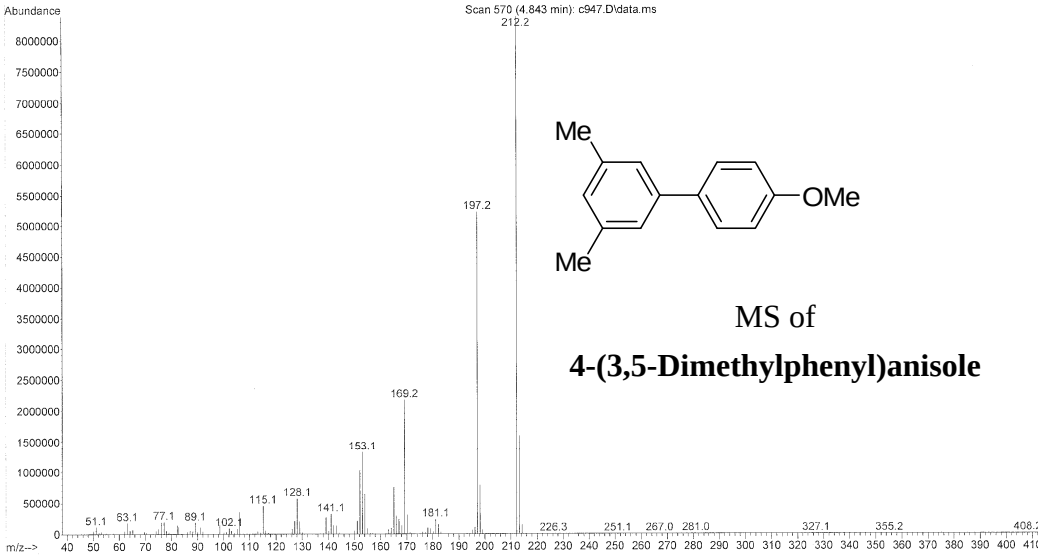
^{1}H NMR of

4-(3,5-Dimethylphenyl)anisole



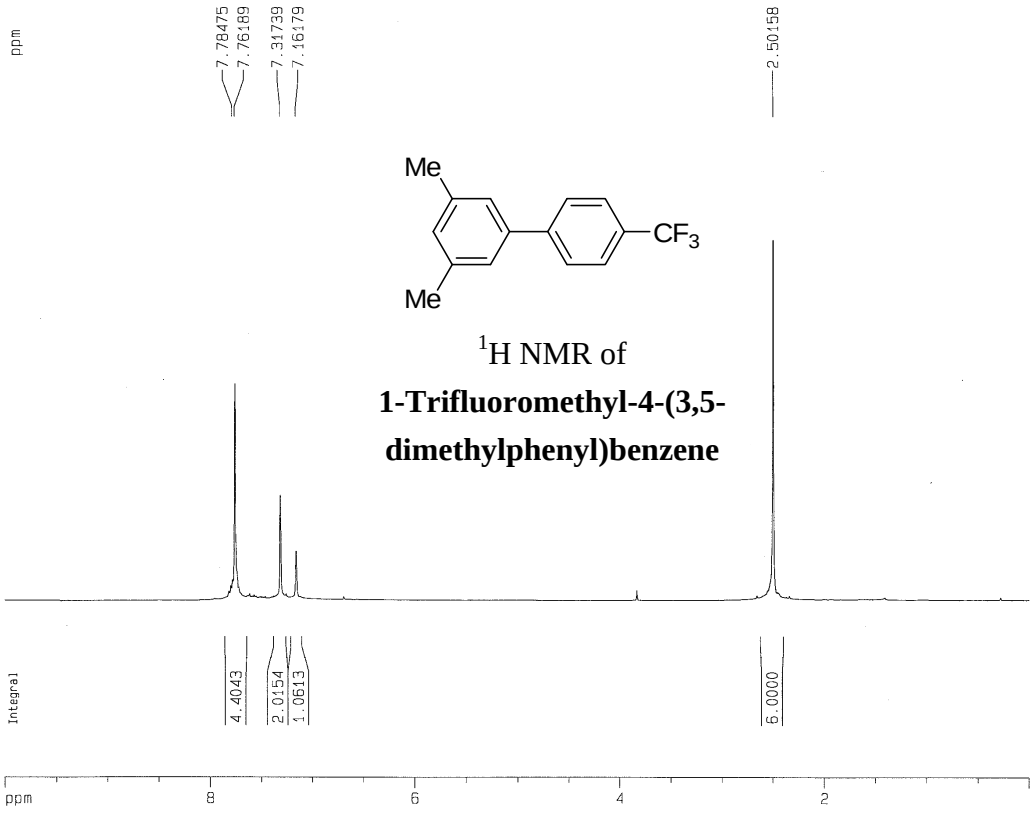
^{13}C NMR of

4-(3,5-Dimethylphenyl)anisole

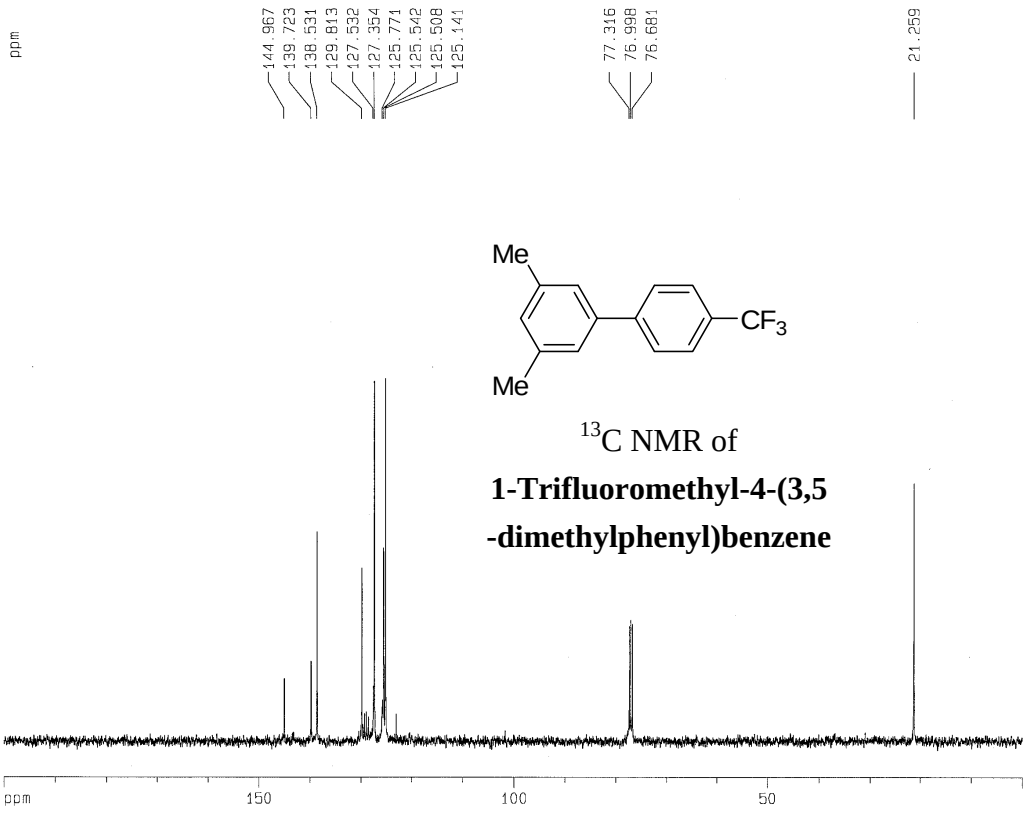


MS of

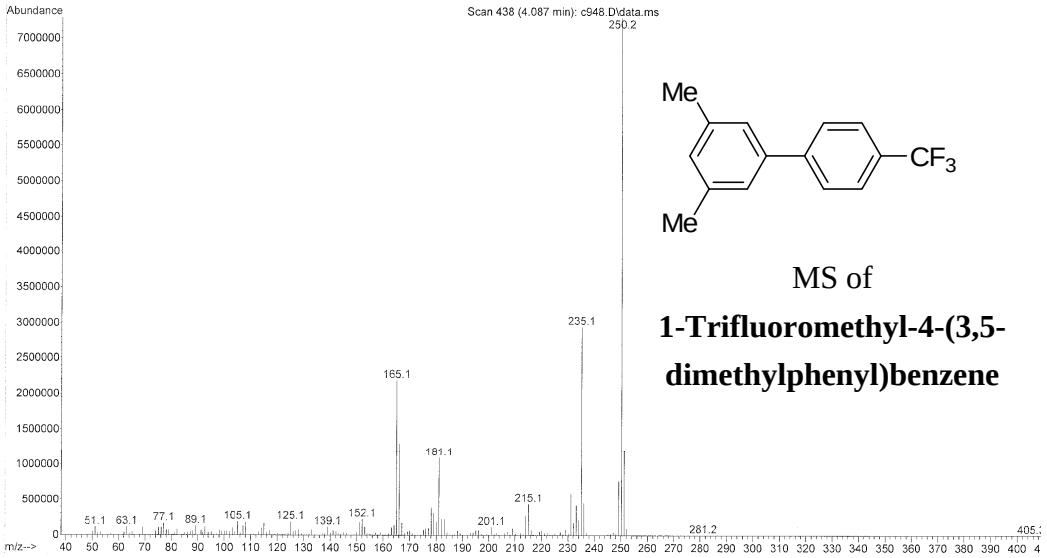
4-(3,5-Dimethylphenyl)anisole



^{1}H NMR of
1-Trifluoromethyl-4-(3,5-dimethylphenyl)benzene

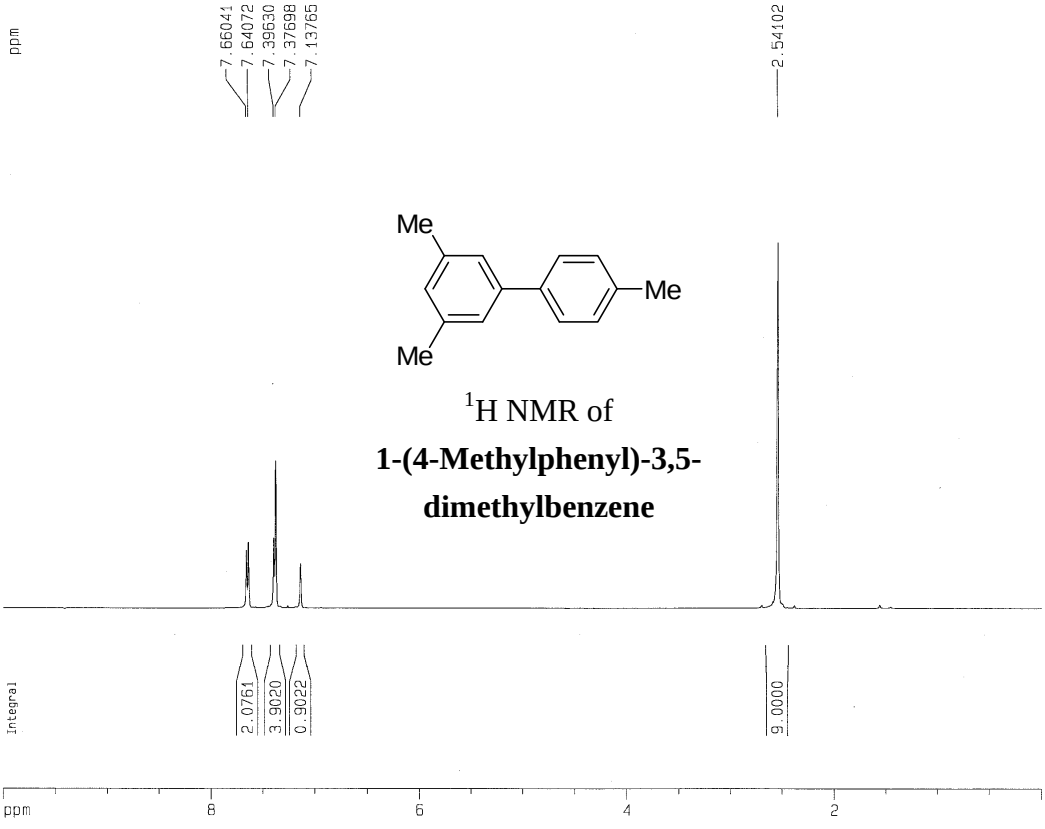


^{13}C NMR of
1-Trifluoromethyl-4-(3,5-dimethylphenyl)benzene



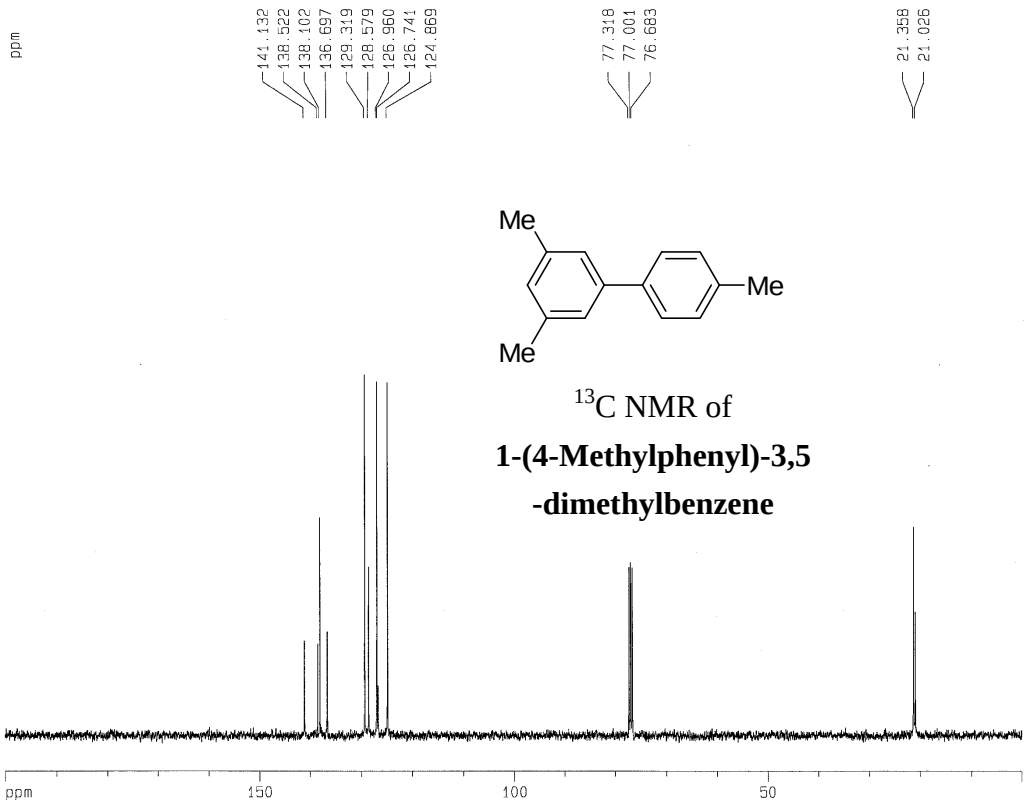
MS of

1-Trifluoromethyl-4-(3,5-dimethylphenyl)benzene



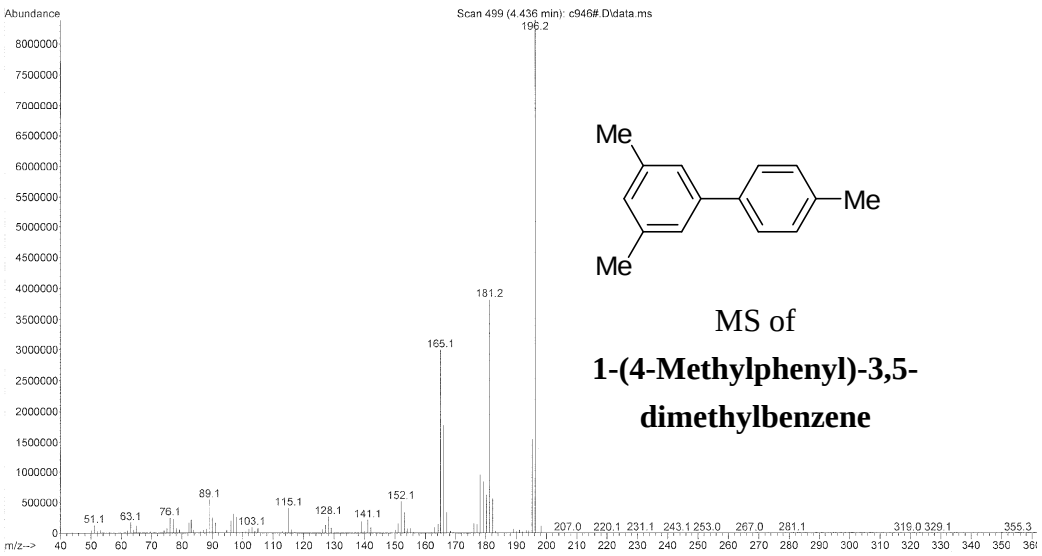
^{1}H NMR of

1-(4-Methylphenyl)-3,5-dimethylbenzene



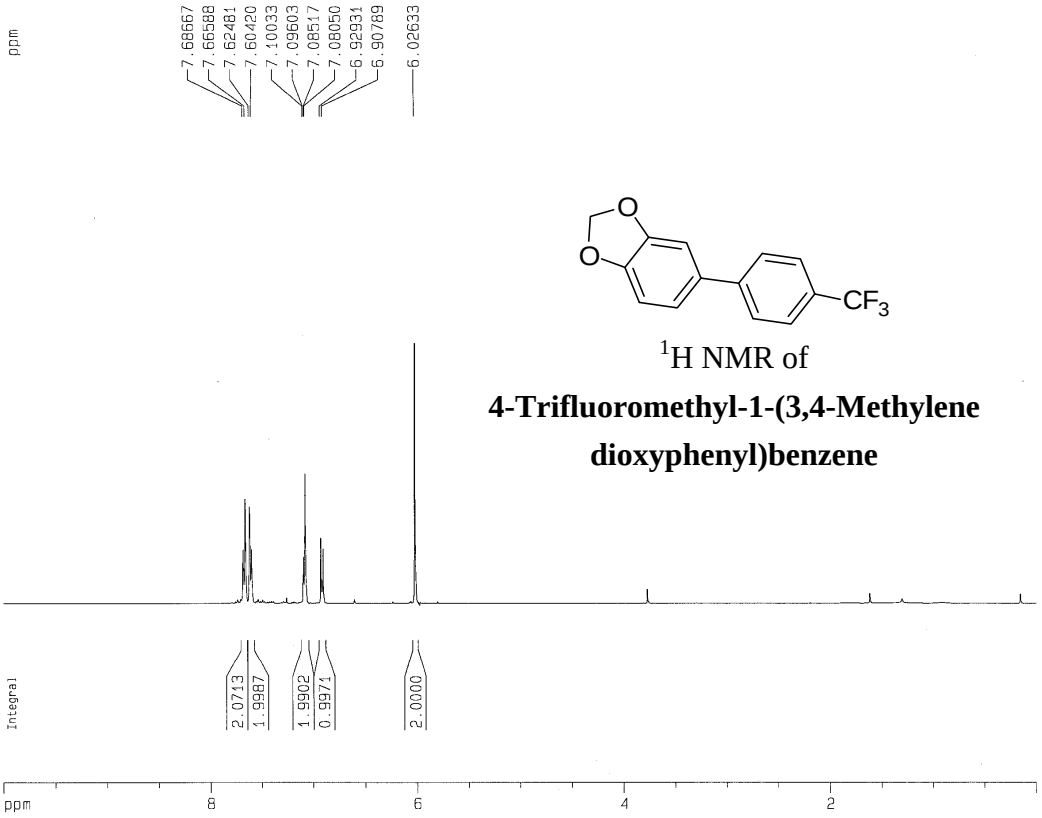
^{13}C NMR of

1-(4-Methylphenyl)-3,5 -dimethylbenzene



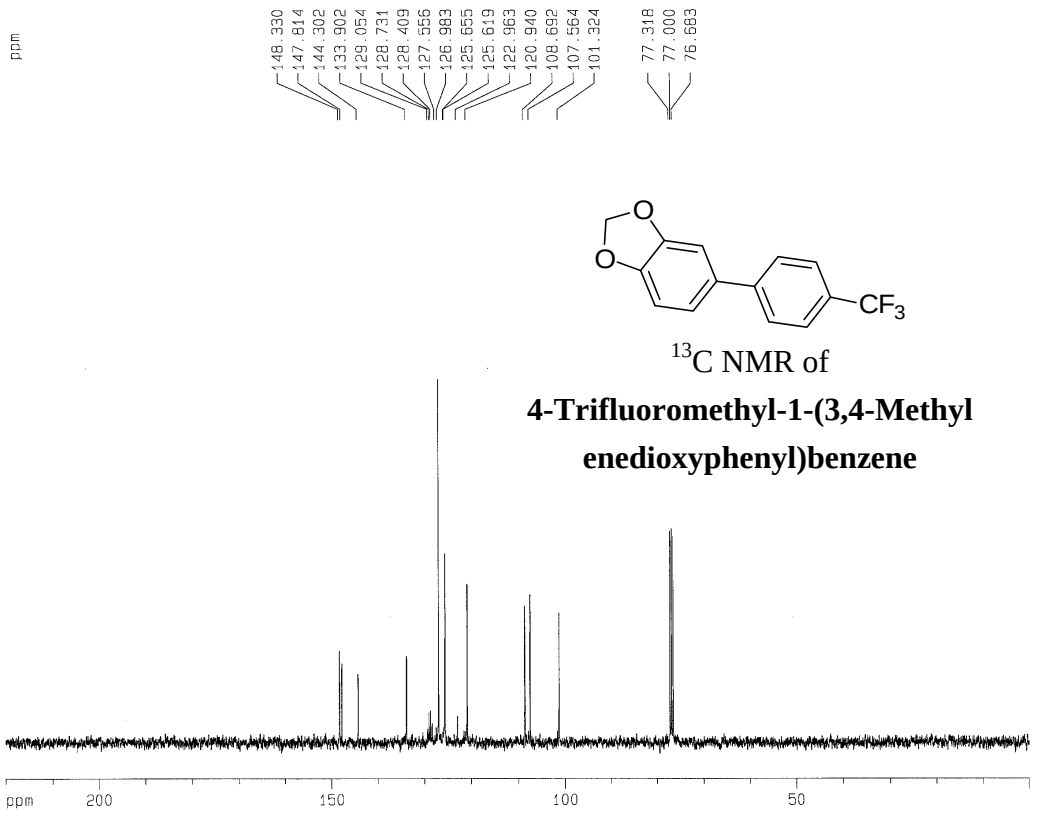
MS of

1-(4-Methylphenyl)-3,5-dimethylbenzene



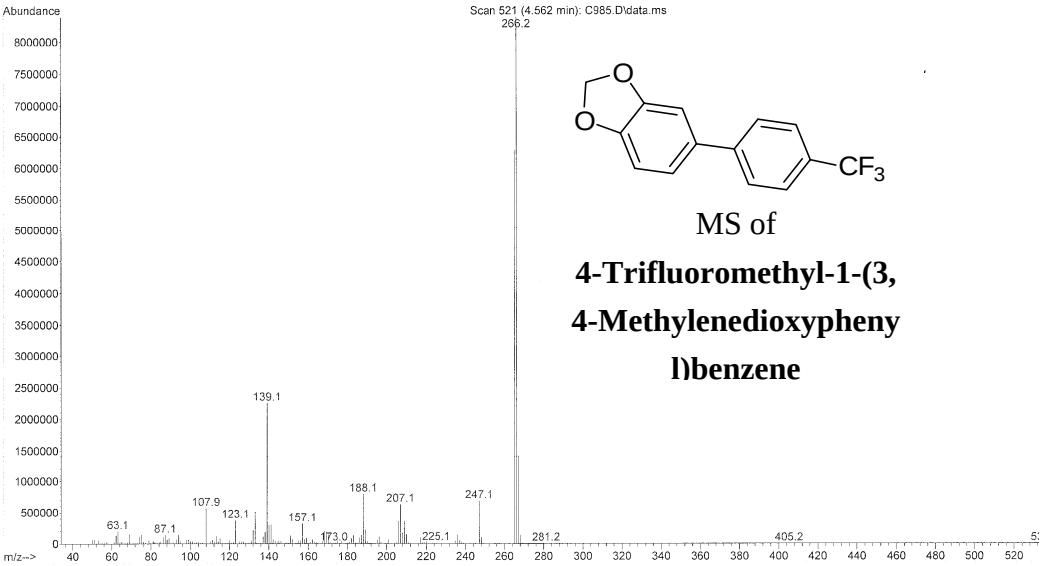
^{1}H NMR of

4-Trifluoromethyl-1-(3,4-Methylene dioxyphenyl)benzene



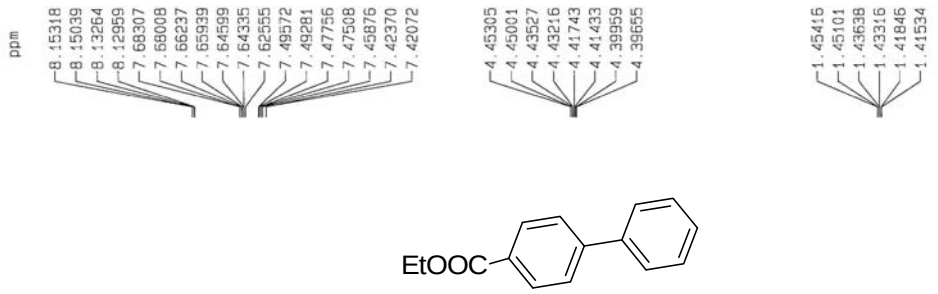
^{13}C NMR of

4-Trifluoromethyl-1-(3,4-Methyl enedioxyphenyl)benzene



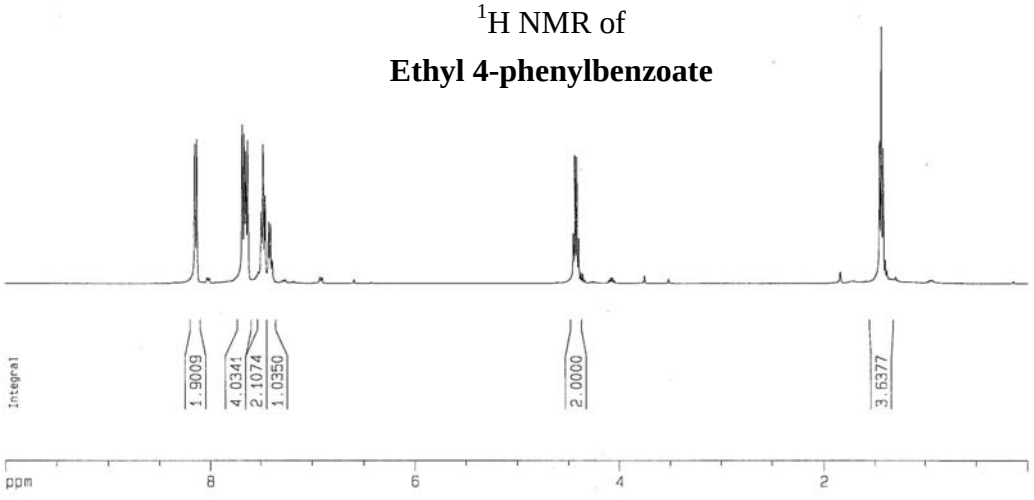
MS of

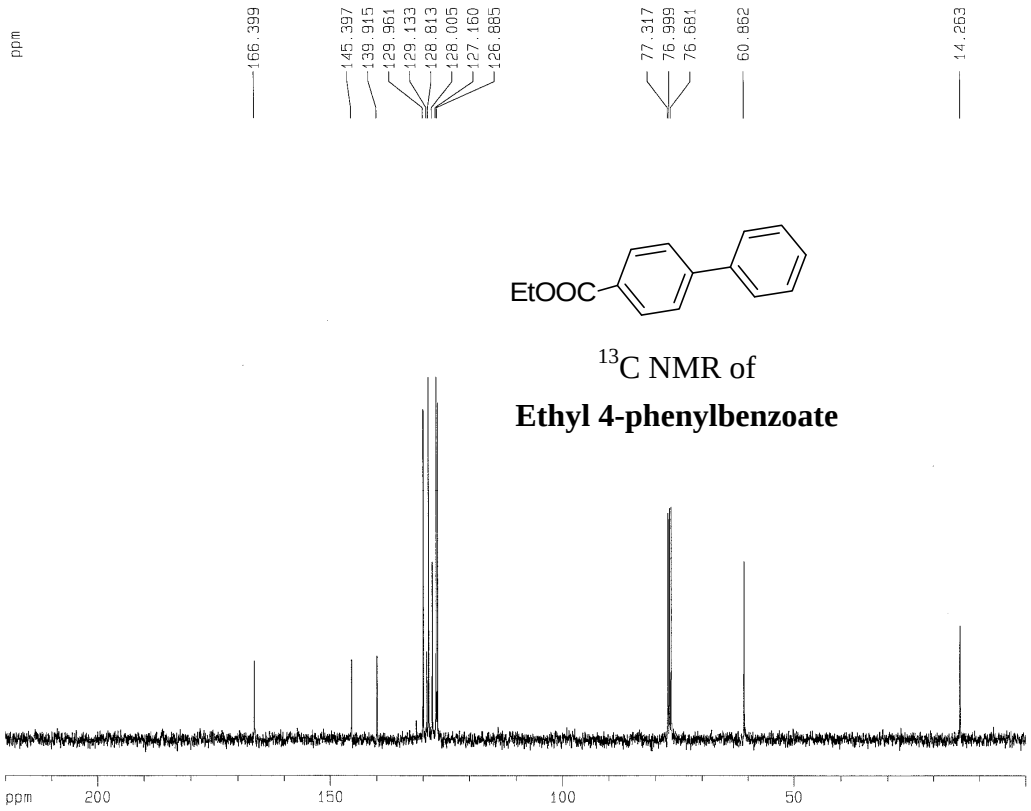
4-Trifluoromethyl-1-(3, 4-Methylenedioxypheny l)benzene



^{1}H NMR of

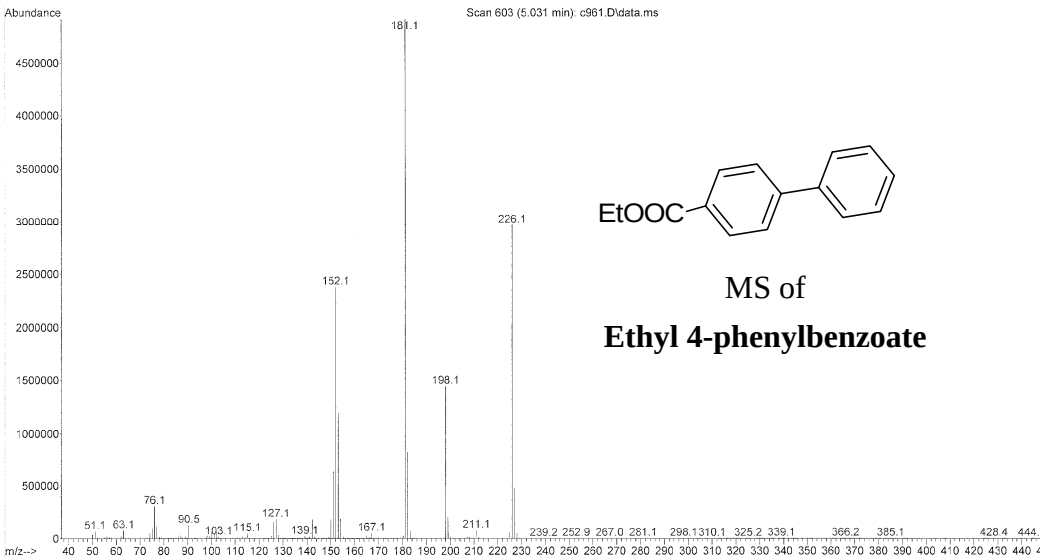
Ethyl 4-phenylbenzoate





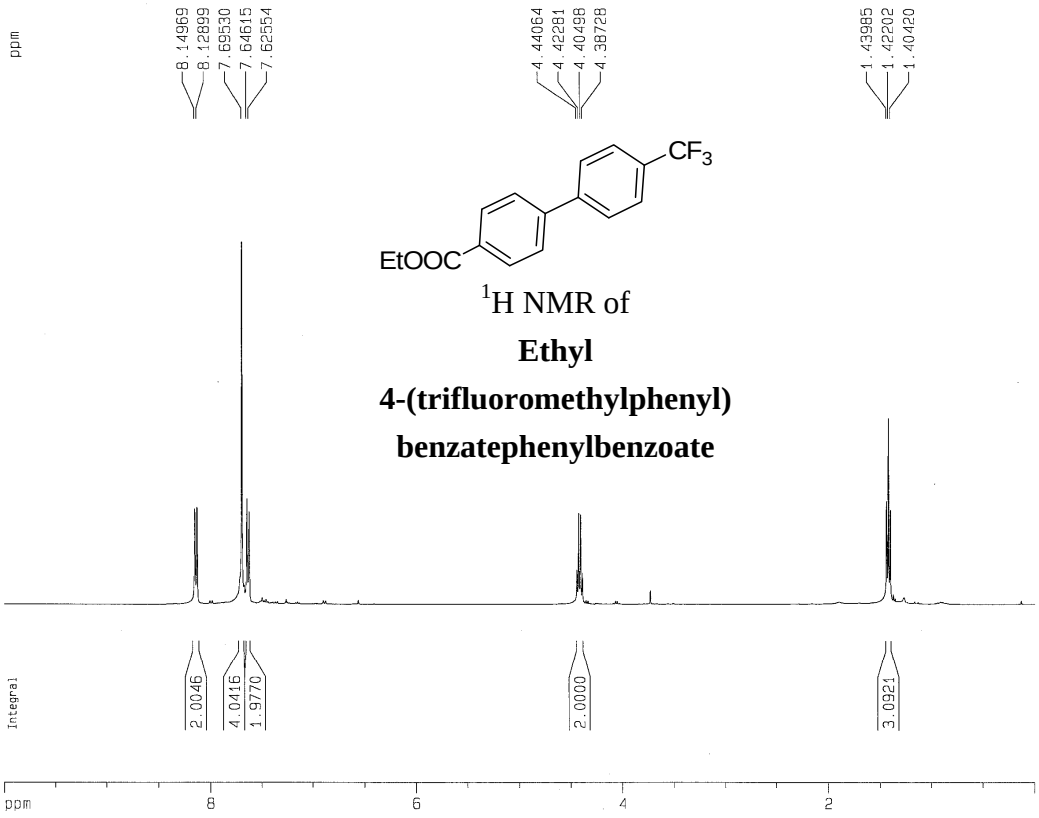
^{13}C NMR of

Ethyl 4-phenylbenzoate



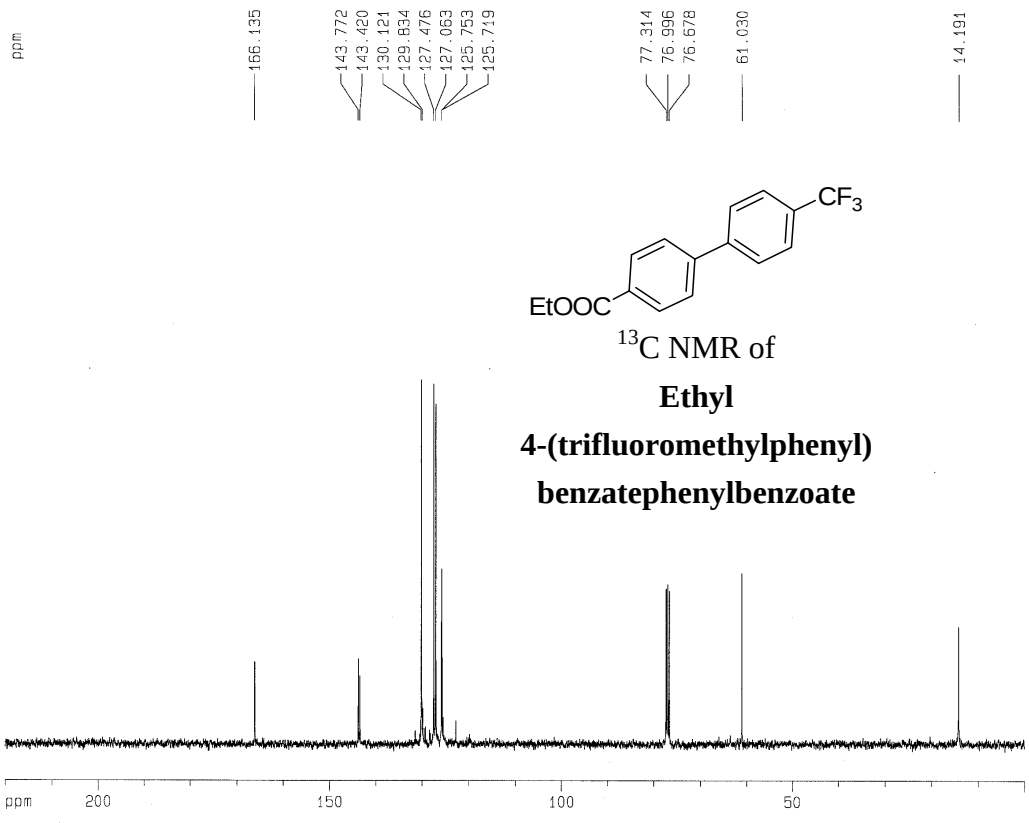
MS of

Ethyl 4-phenylbenzoate



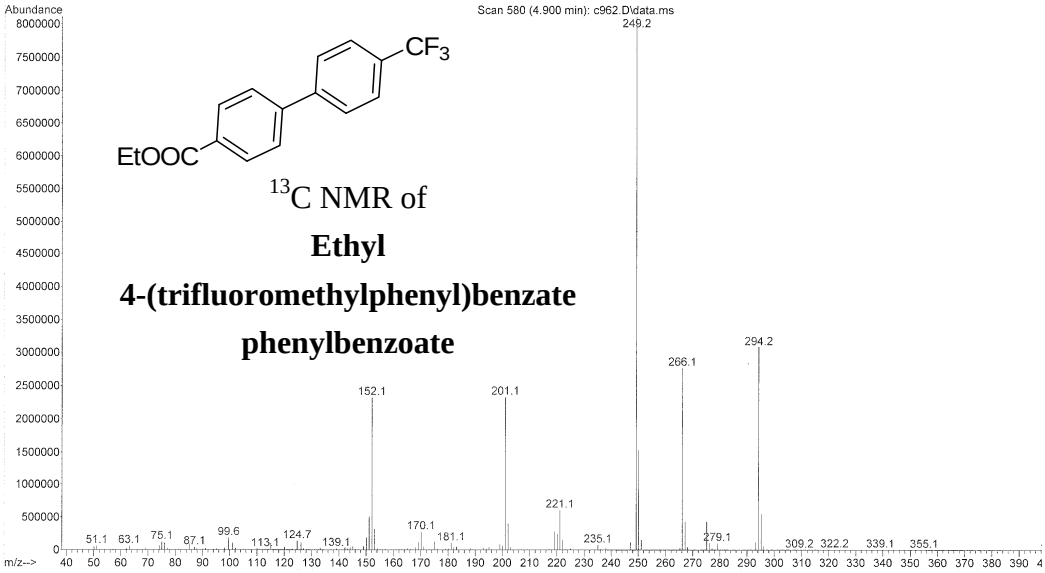
^{1}H NMR of

Ethyl
4-(trifluoromethylphenyl)
benzatephenylbenzoate



^{13}C NMR of

Ethyl
4-(trifluoromethylphenyl)
benzatephenylbenzoate

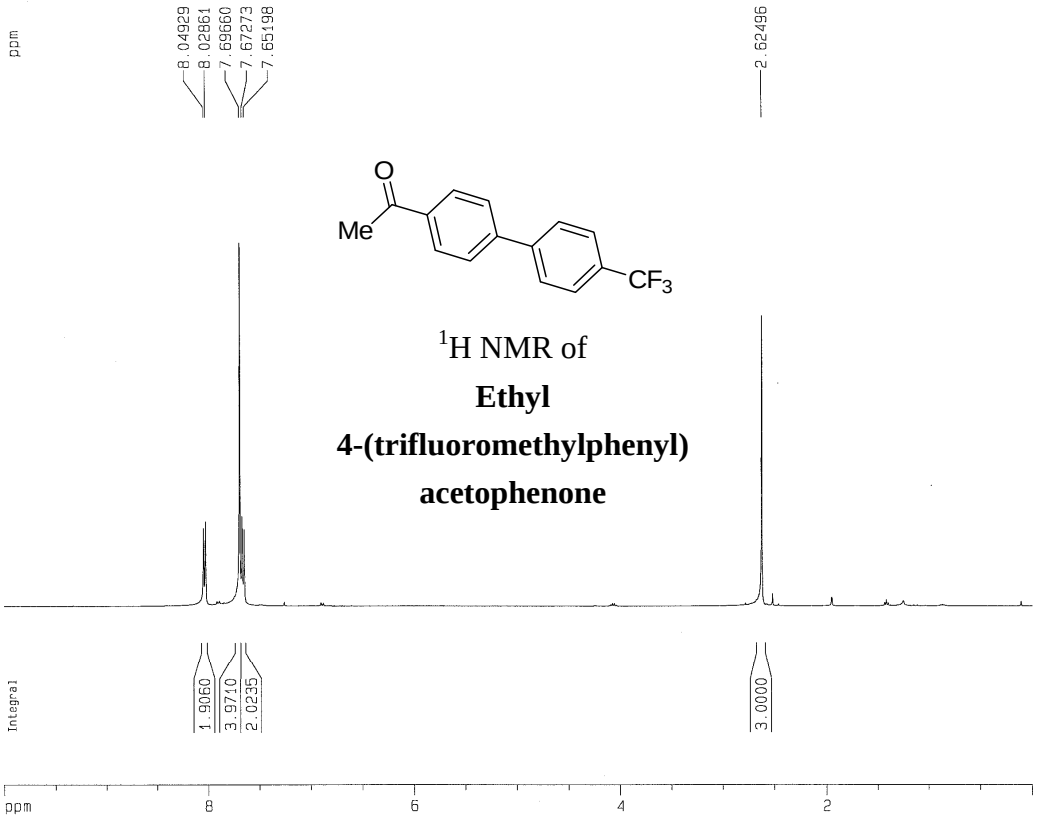


^{13}C NMR of

Ethyl

4-(trifluoromethylphenyl)benzate

phenylbenzoate

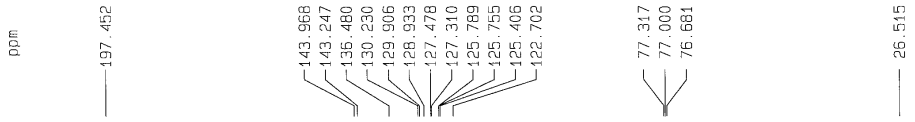


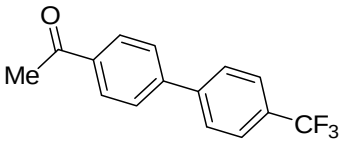
^{1}H NMR of

Ethyl

4-(trifluoromethylphenyl)

acetophenone

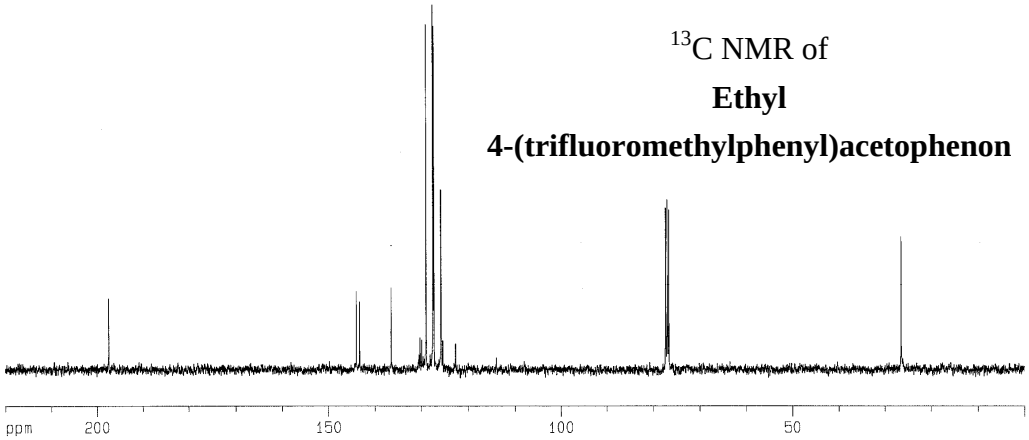


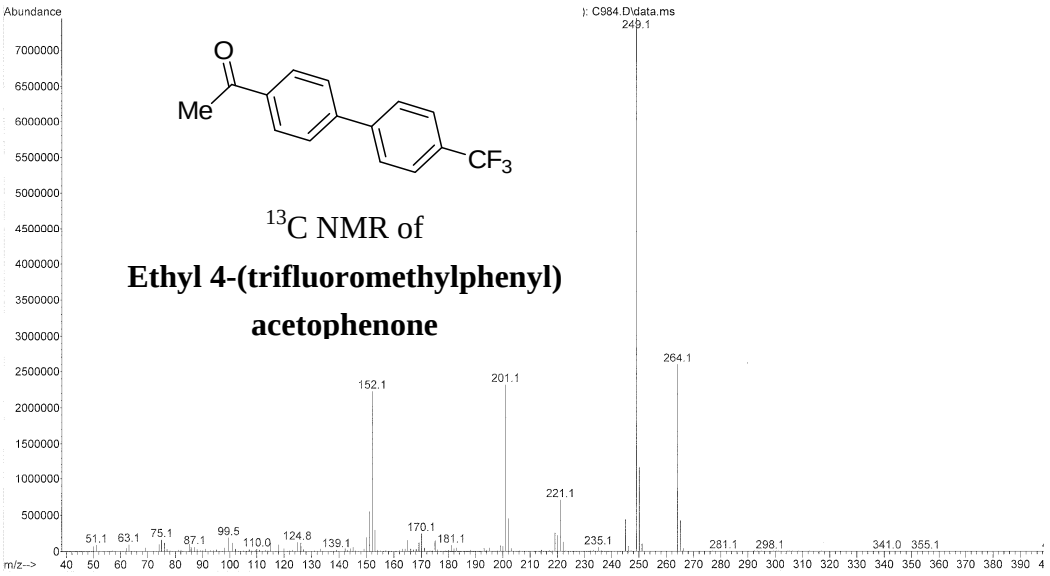


^{13}C NMR of

Ethyl

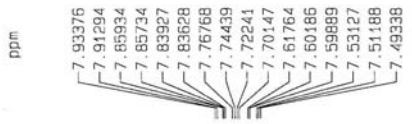
4-(trifluoromethylphenyl)acetophenon

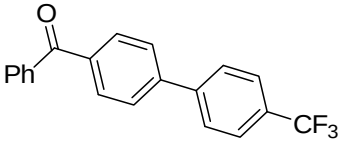




^{13}C NMR of

Ethyl 4-(trifluoromethylphenyl) acetophenone

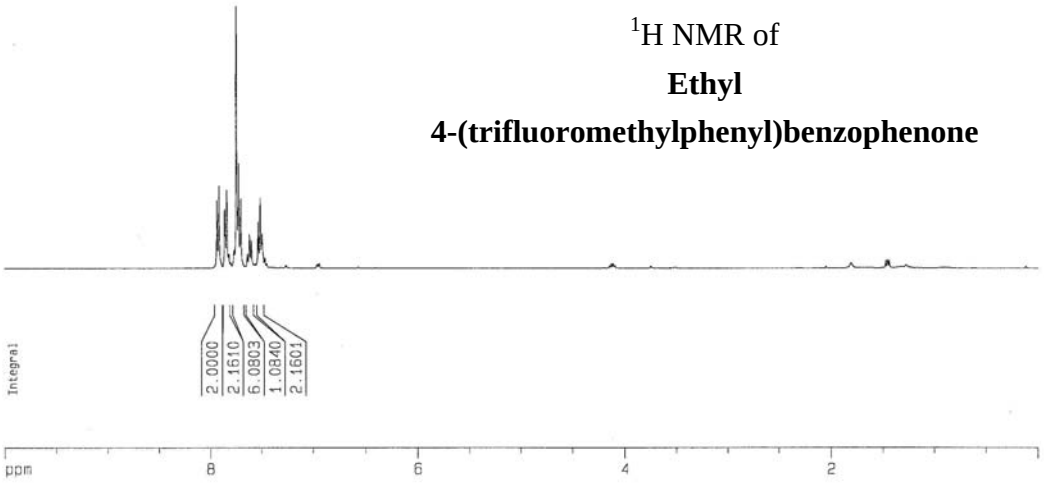


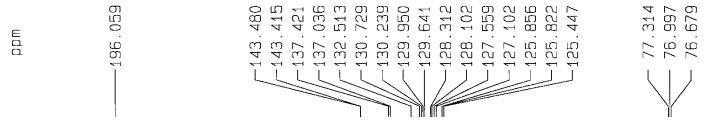


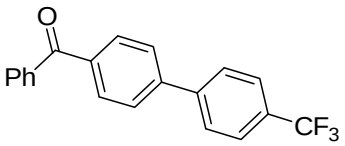
^{1}H NMR of

Ethyl

4-(trifluoromethylphenyl)benzophenone



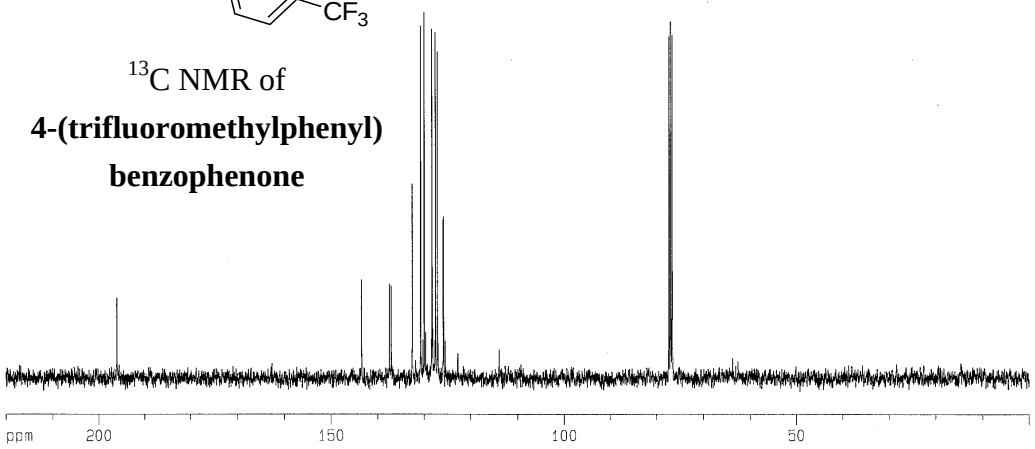


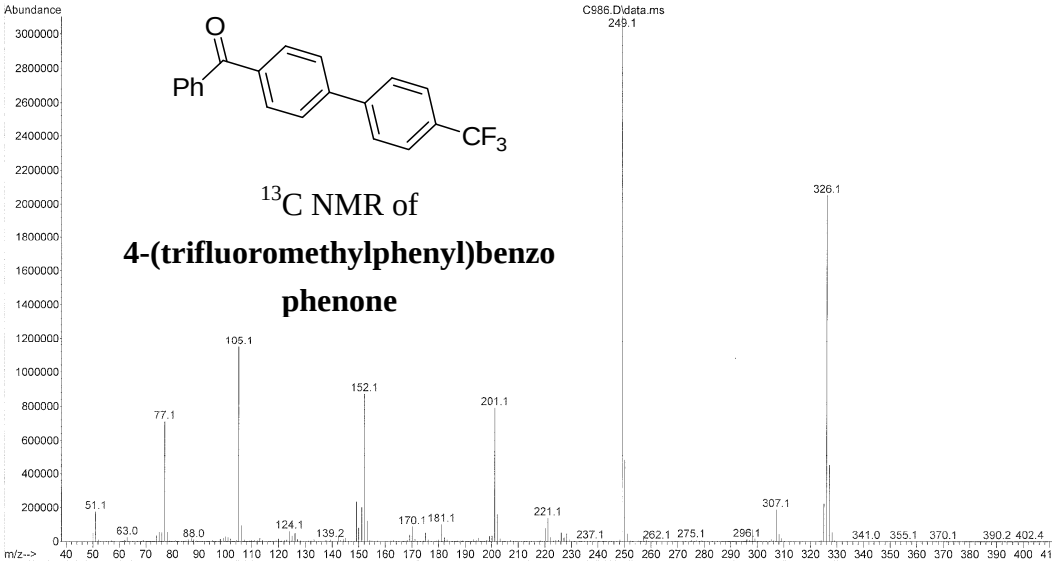


^{13}C NMR of

4-(trifluoromethylphenyl)

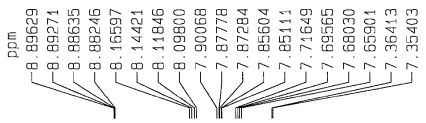
benzophenone

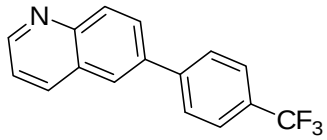




^{13}C NMR of

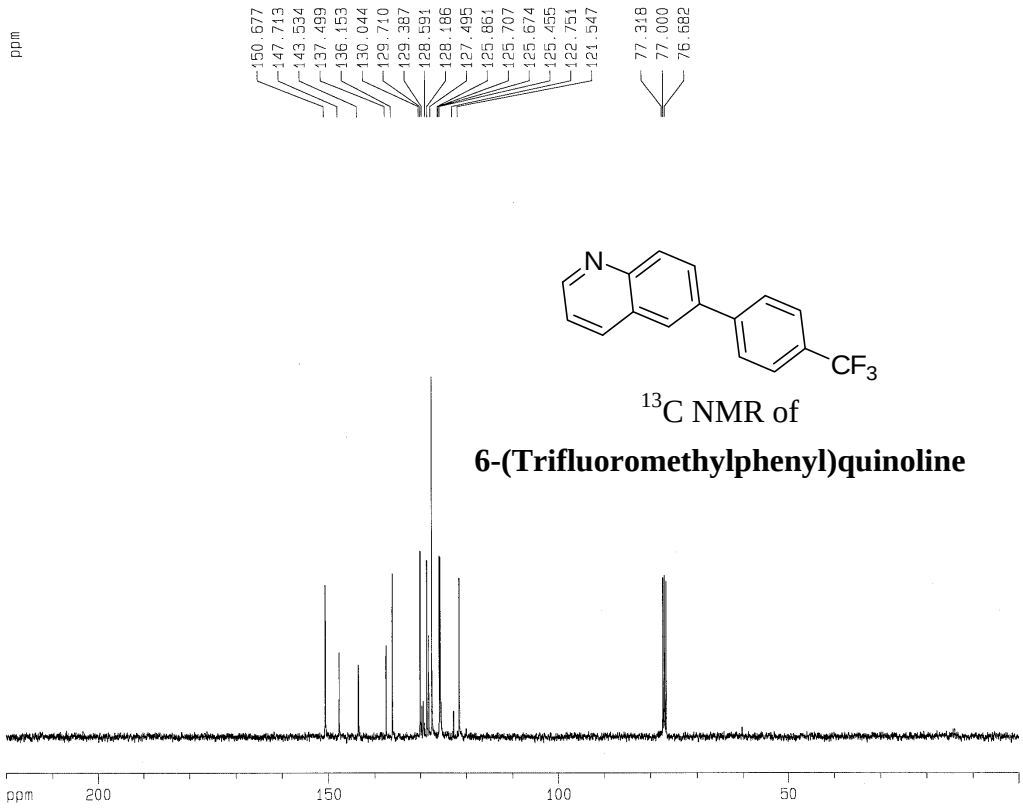
4-(trifluoromethylphenyl)benzophenone





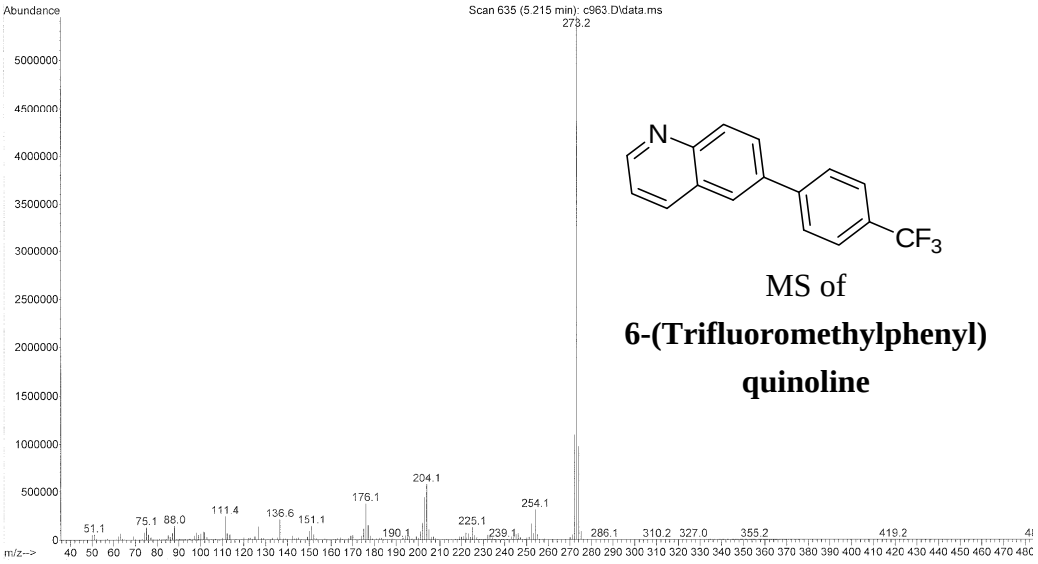
^{1}H NMR of

6-(Trifluoromethylphenyl)quinoline



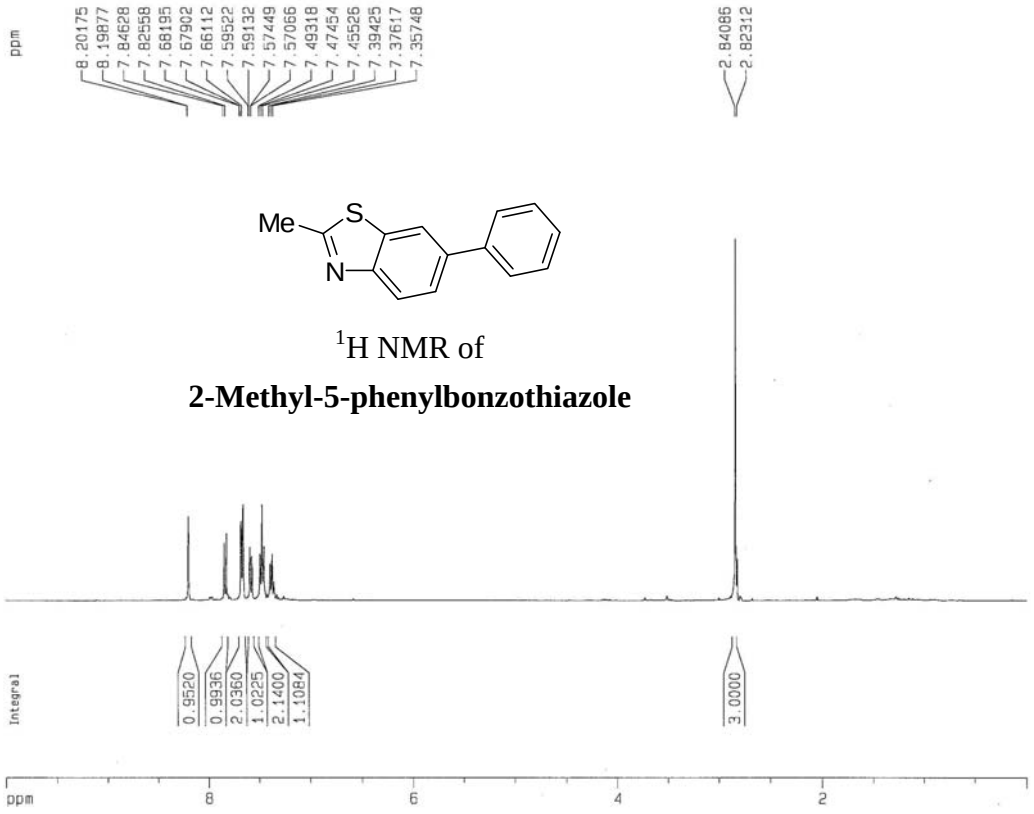
^{13}C NMR of

6-(Trifluoromethylphenyl)quinoline



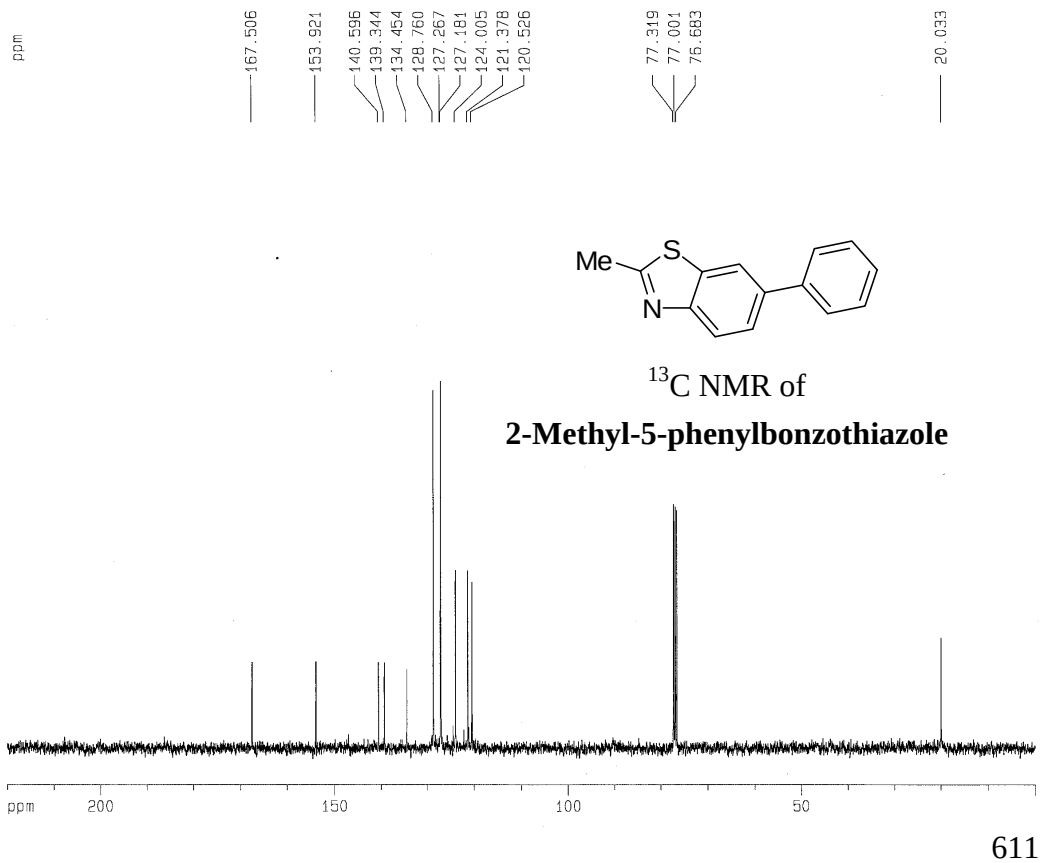
MS of

6-(Trifluoromethylphenyl) quinoline



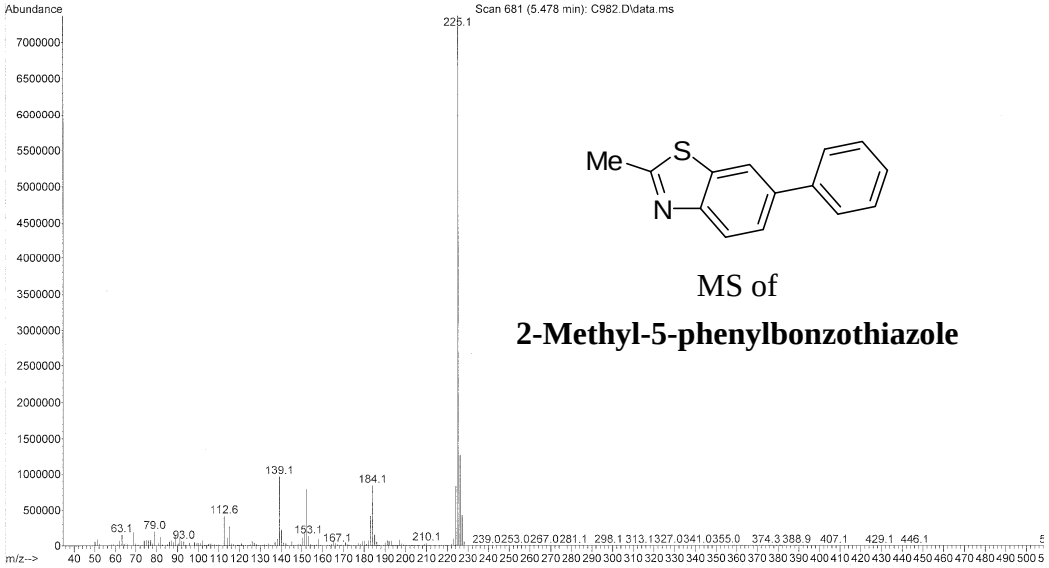
^{1}H NMR of

2-Methyl-5-phenylbonzothiazole



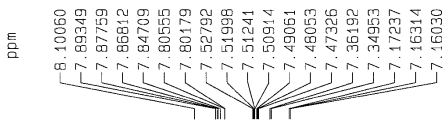
^{13}C NMR of

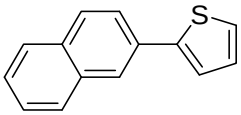
2-Methyl-5-phenylbonzothiazole



MS of

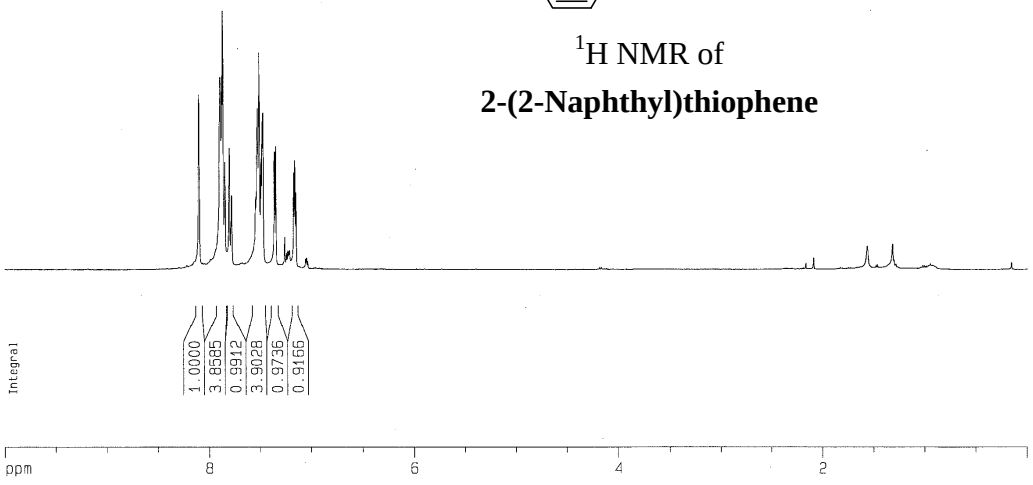
2-Methyl-5-phenylbonzothiazole

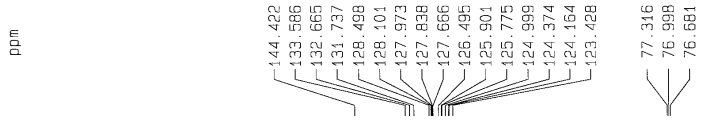


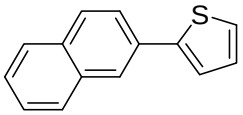


^{1}H NMR of

2-(2-Naphthyl)thiophene

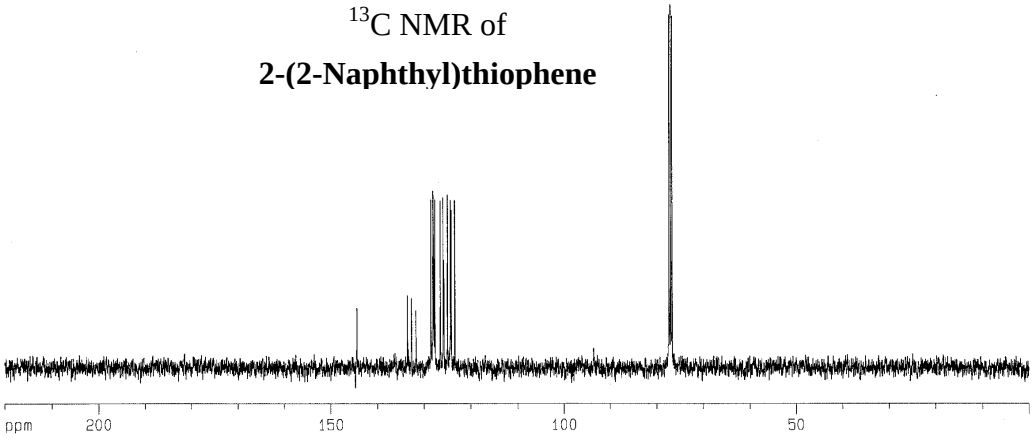


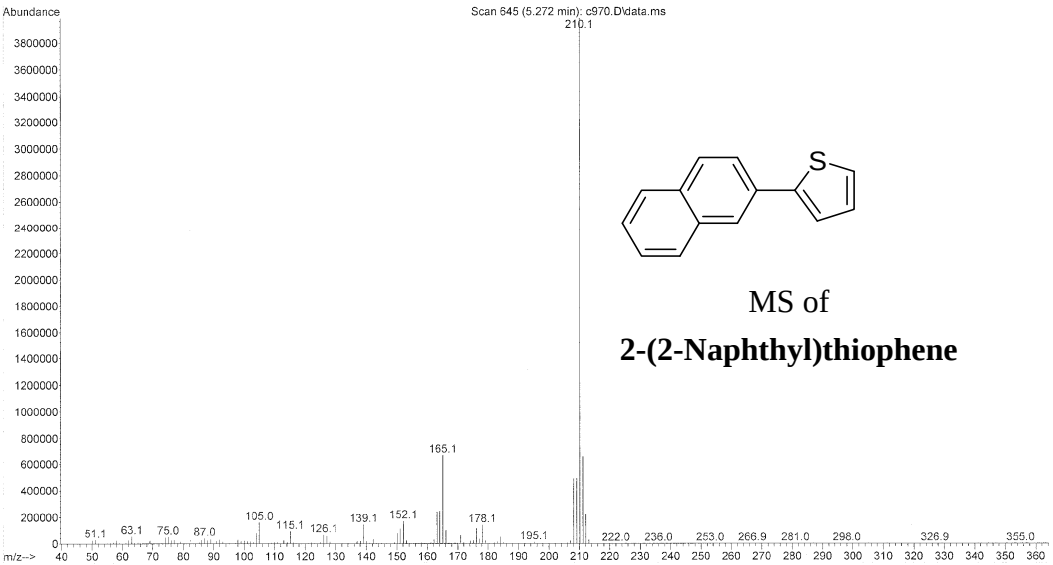




^{13}C NMR of

2-(2-Naphthyl)thiophene

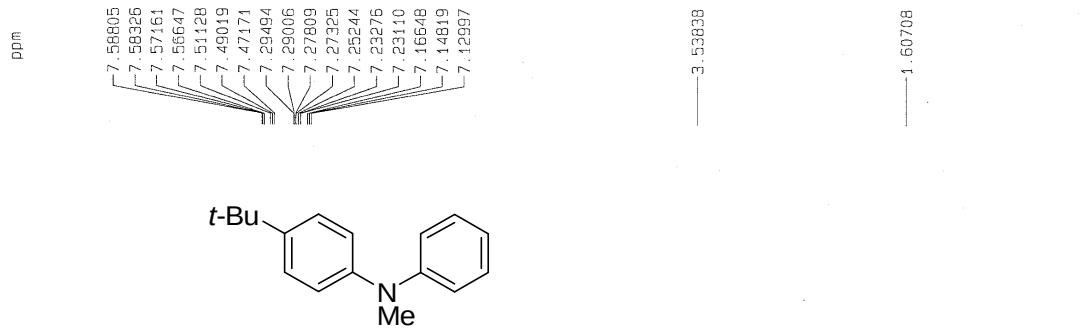




MS of

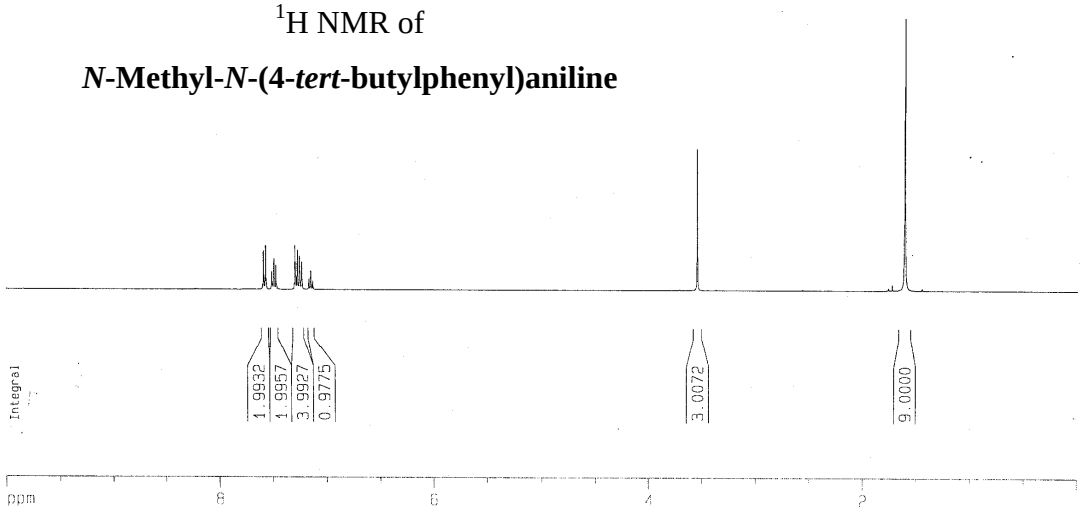
2-(2-Naphthyl)thiophene

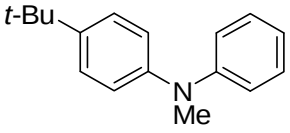
Amination Products



^{1}H NMR of

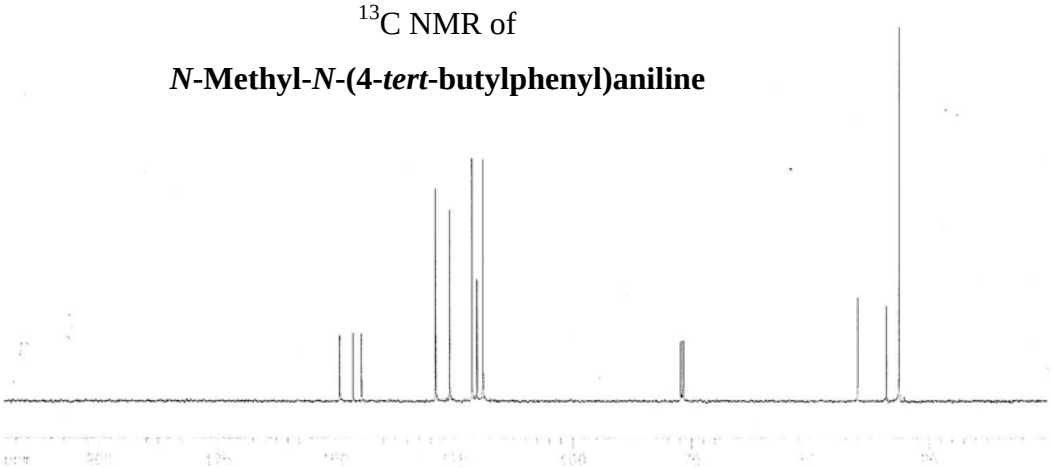
***N*-Methyl-*N*-(4-*tert*-butylphenyl)aniline**

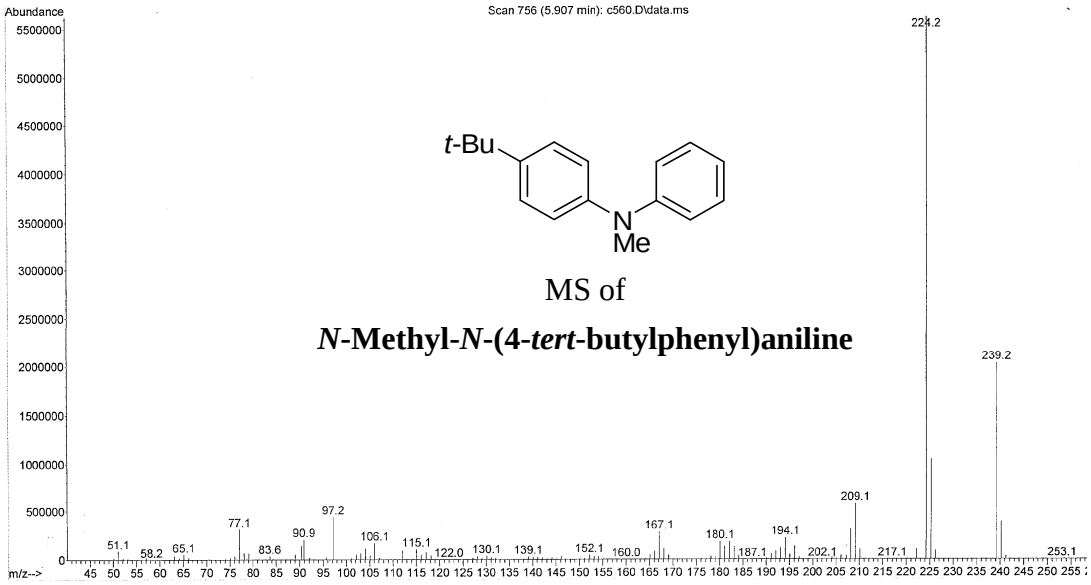




^{13}C NMR of

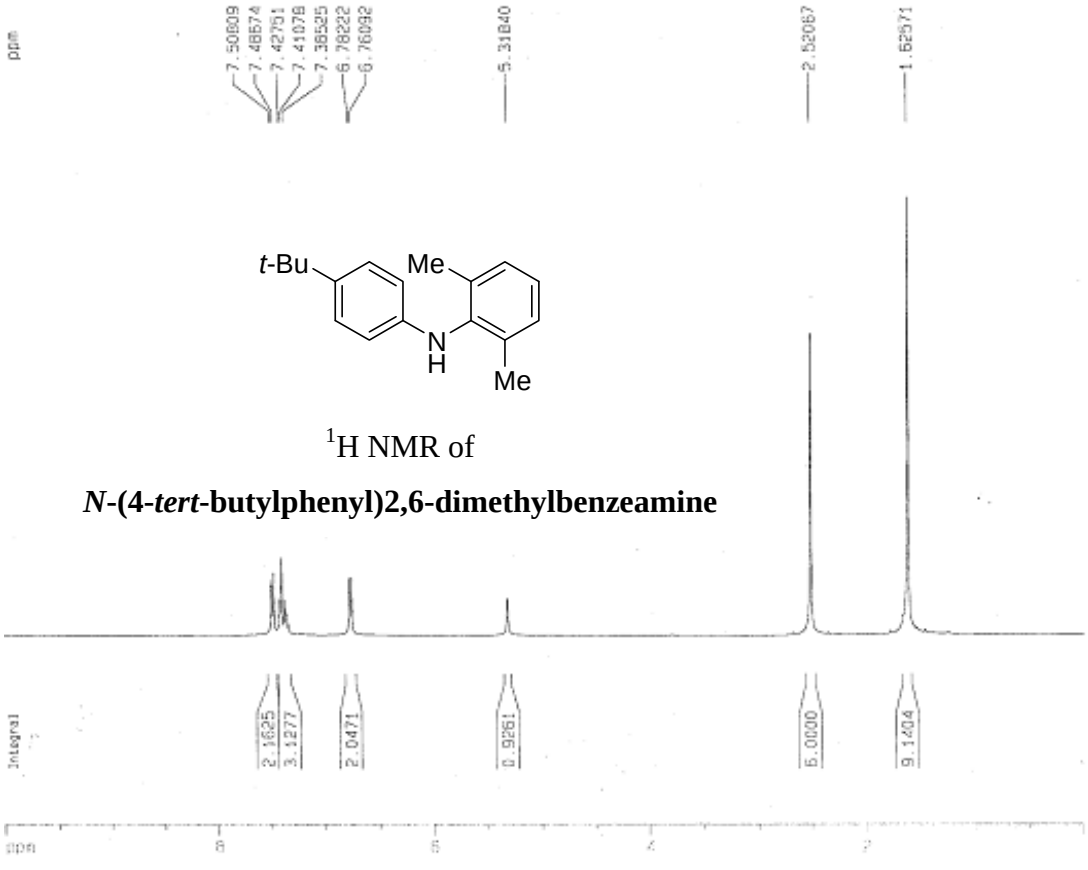
***N*-Methyl-*N*-(4-*tert*-butylphenyl)aniline**





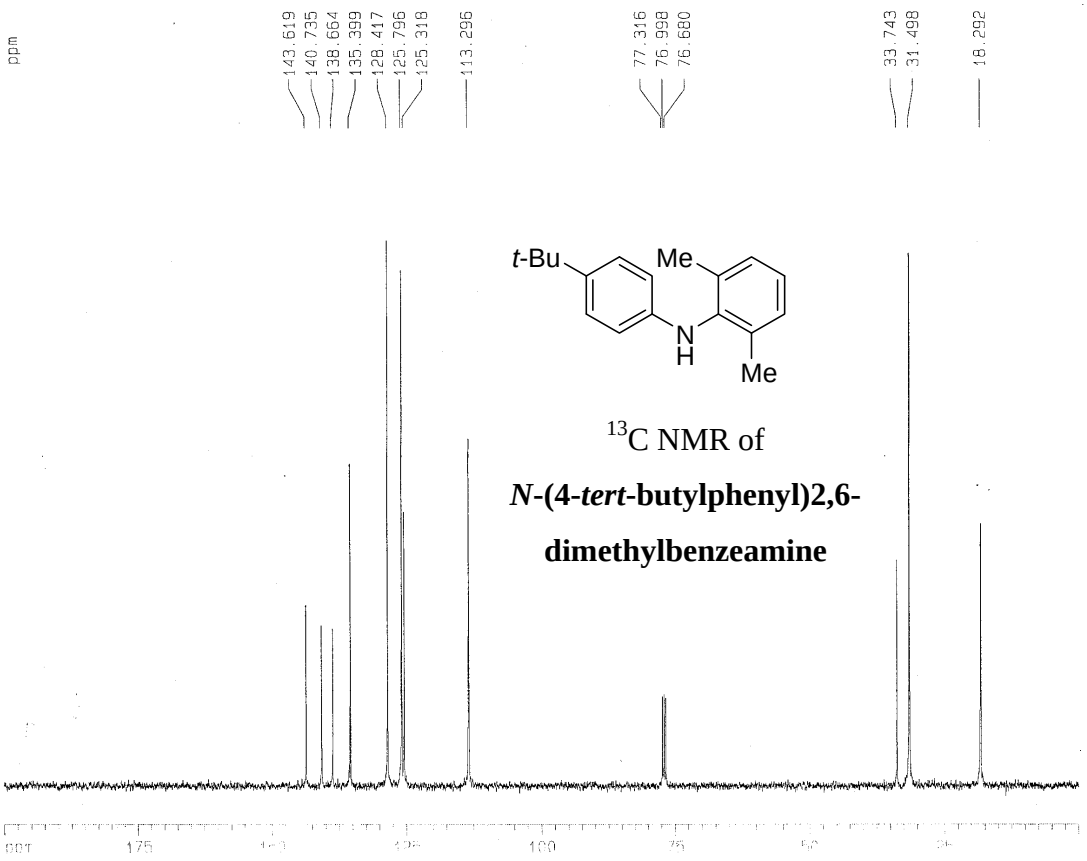
MS of

_N_-Methyl-_N_-(4-_tert_-butylphenyl)aniline



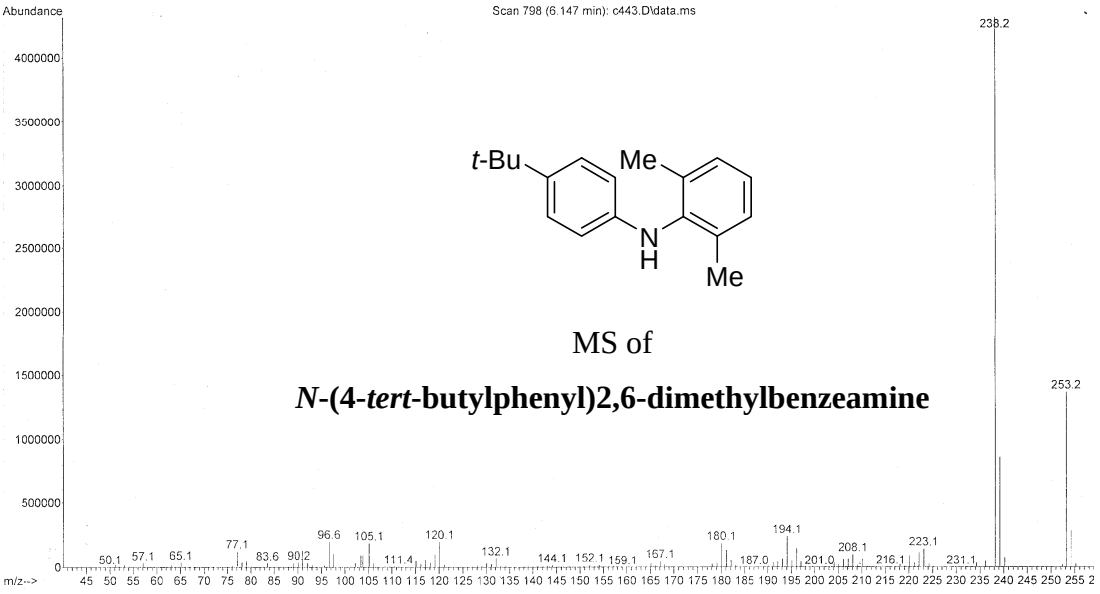
^{1}H NMR of

_N_-(4-_tert_-butylphenyl)2,6-dimethylbenzeamine



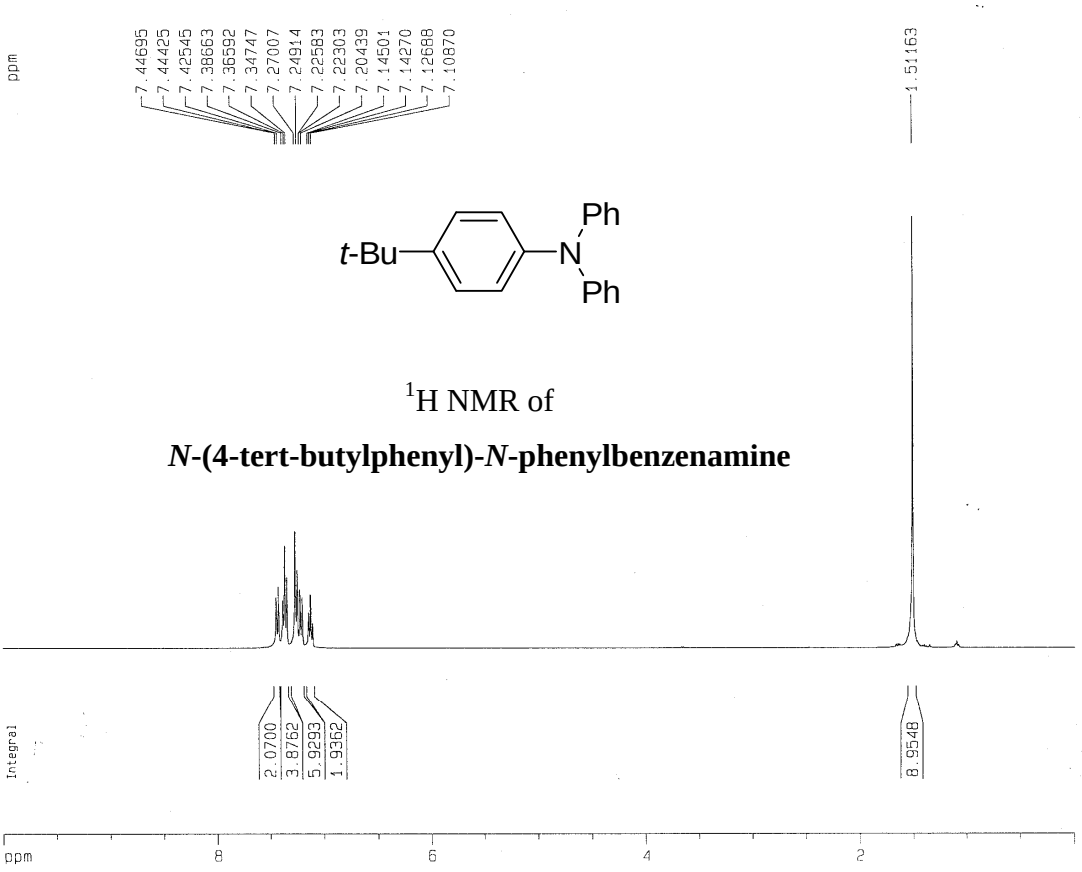
^{13}C NMR of

***N*-(4-*tert*-butylphenyl)2,6-dimethylbenzeamine**



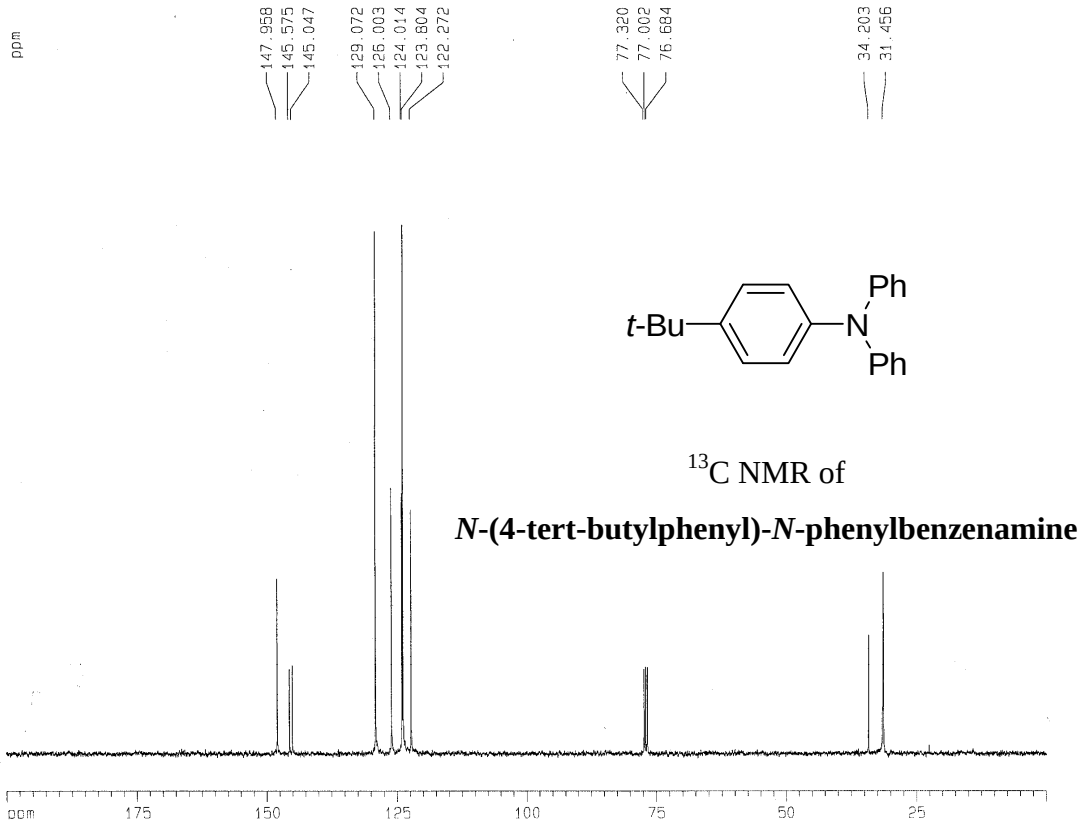
MS of

***N*-(4-*tert*-butylphenyl)2,6-dimethylbenzeamine**



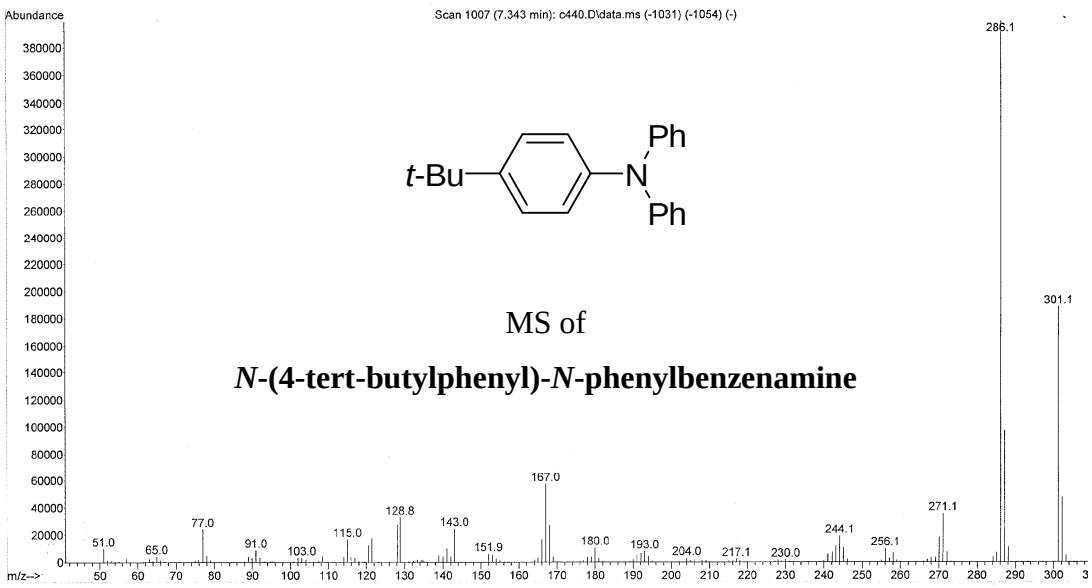
^{1}H NMR of

_N_-(4-tert-butylphenyl)-_N_-phenylbenzenamine



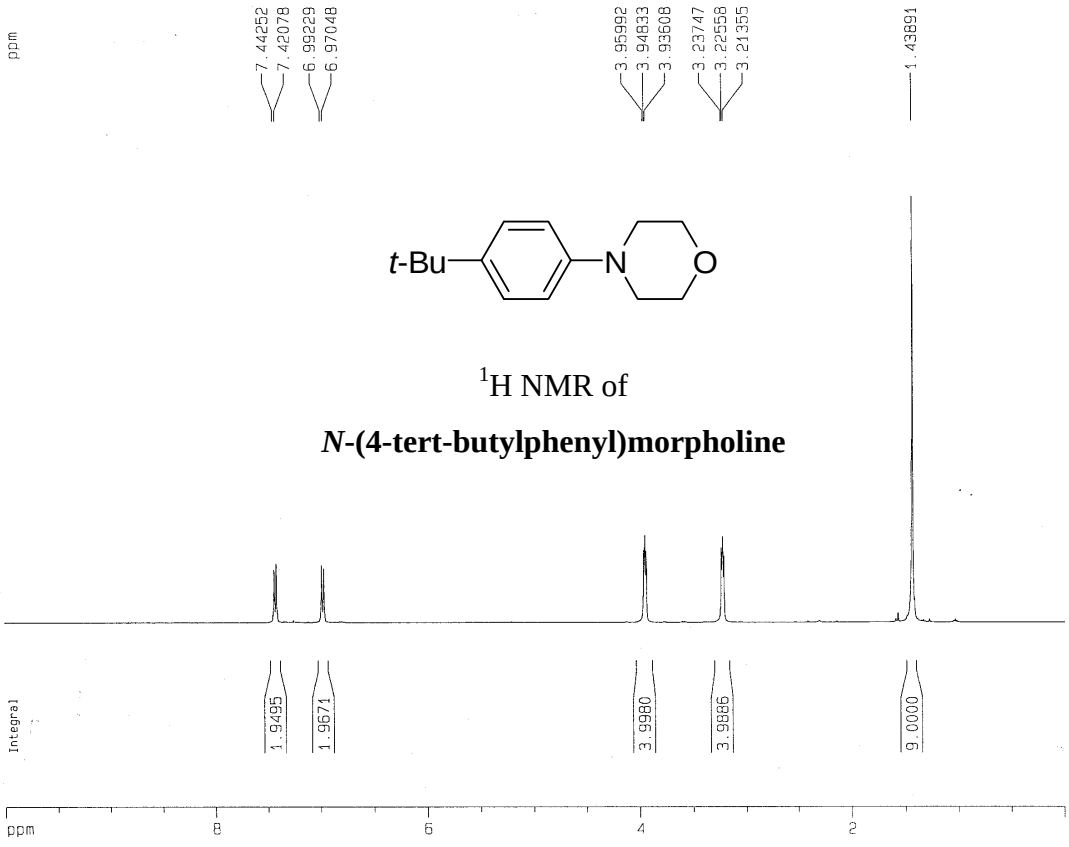
^{13}C NMR of

_N_-(4-tert-butylphenyl)-_N_-phenylbenzenamine



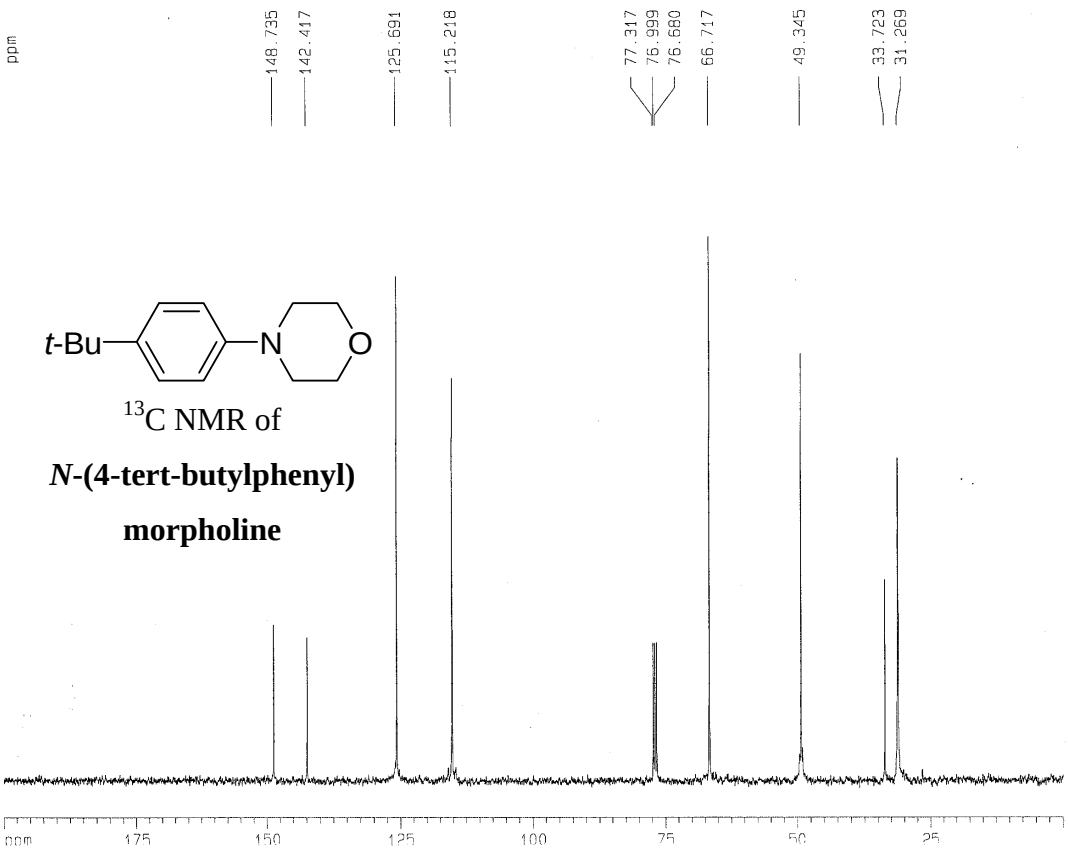
MS of

_N_-(4-tert-butylphenyl)-_N_-phenylbenzenamine



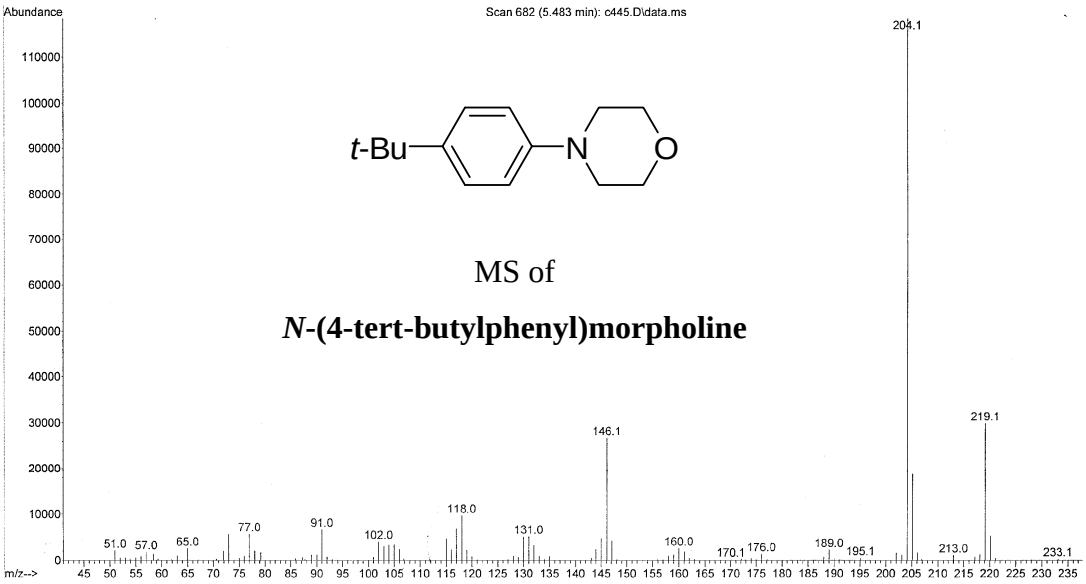
^{1}H NMR of

_N_-(4-tert-butylphenyl)morpholine



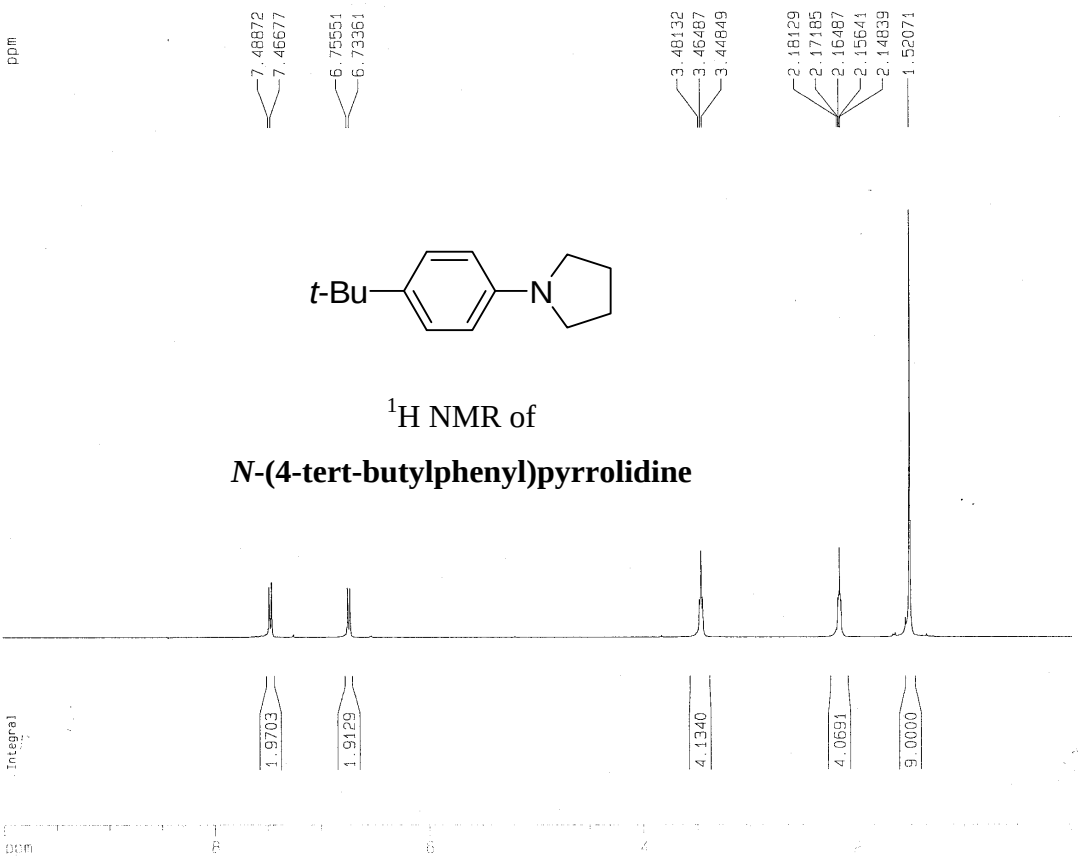
^{13}C NMR of

***N*-(4-tert-butylphenyl) morpholine**



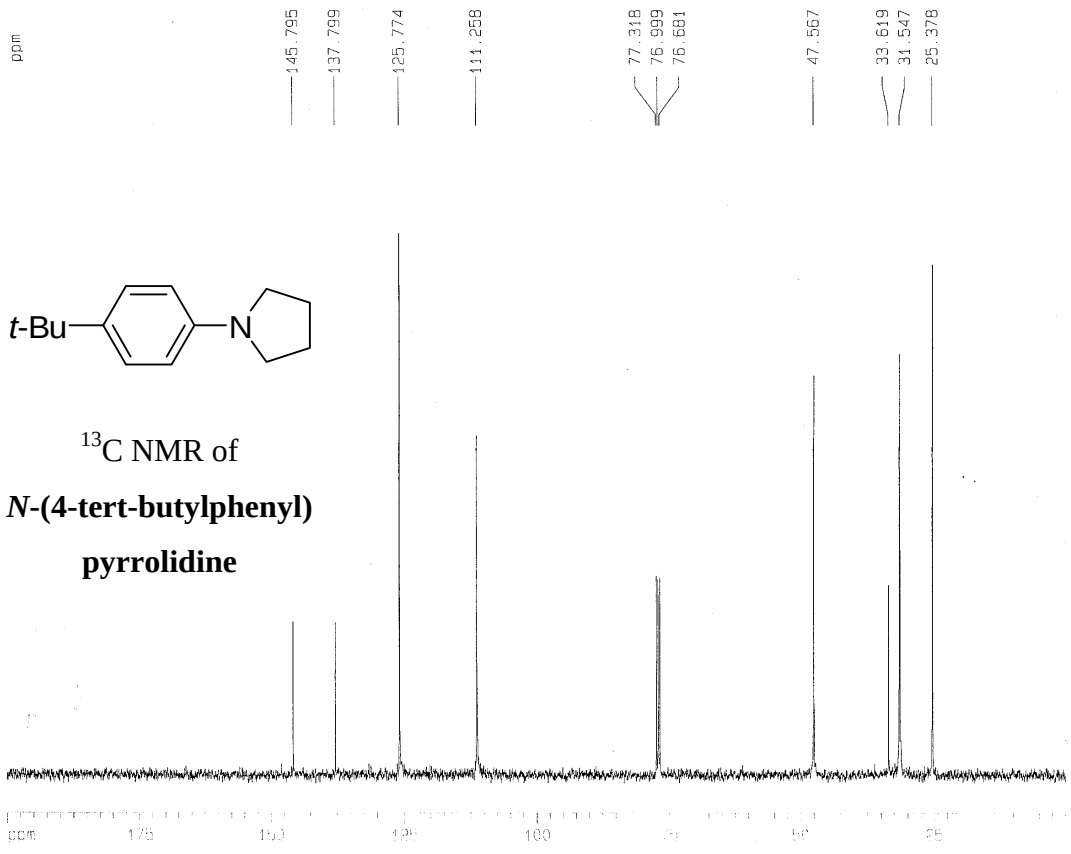
MS of

***N*-(4-tert-butylphenyl)morpholine**



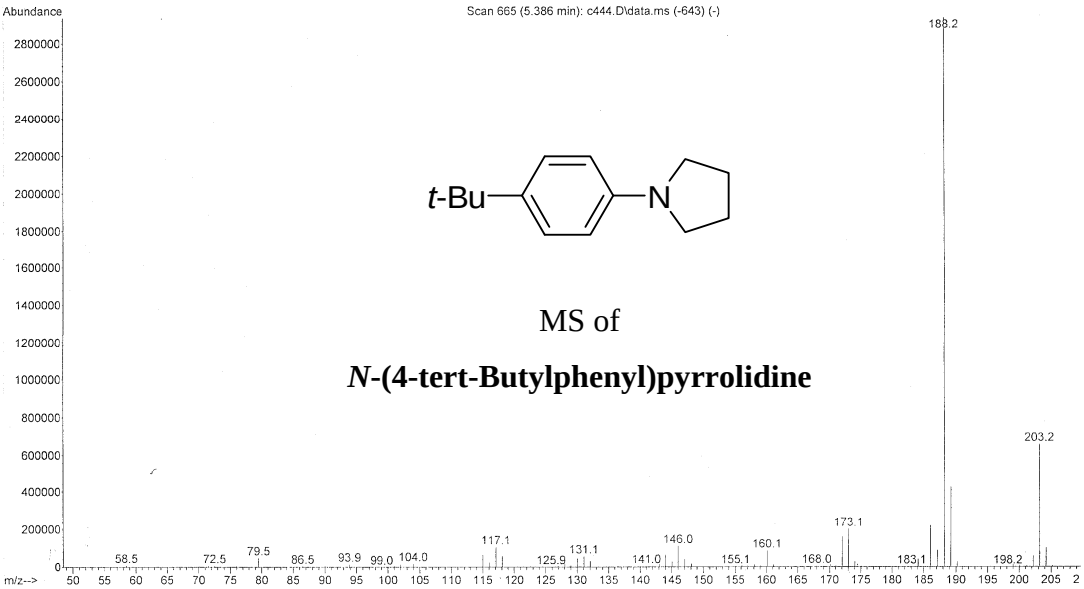
^{1}H NMR of

***N*-(4-tert-butylphenyl)pyrrolidine**



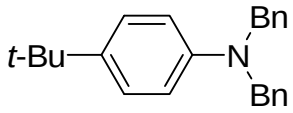
^{13}C NMR of

***N*-(4-tert-butylphenyl) pyrrolidine**



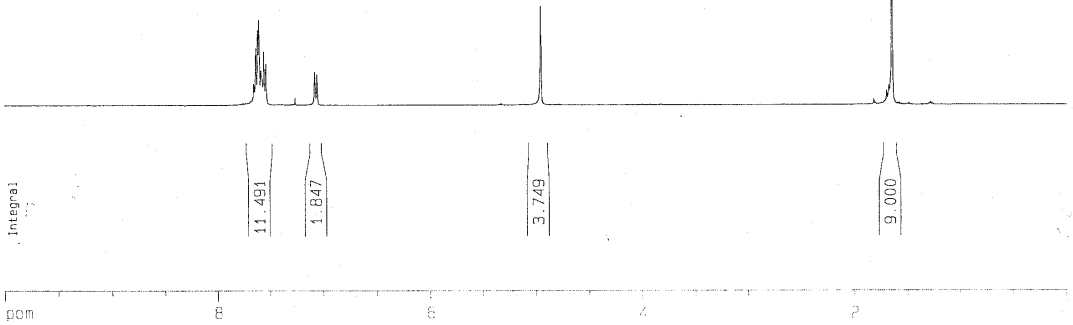
MS of

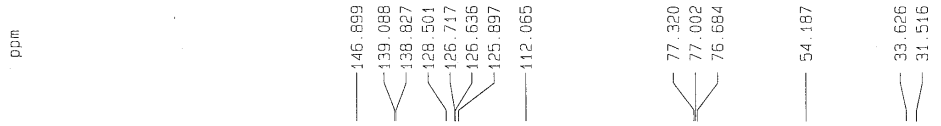
_N_-(4-tert-Butylphenyl)pyrrolidine

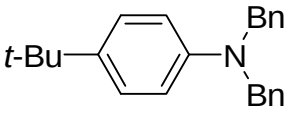


^{1}H NMR of

4-tert-Butyl-_N_,_N_-dibenzylbenzenamine

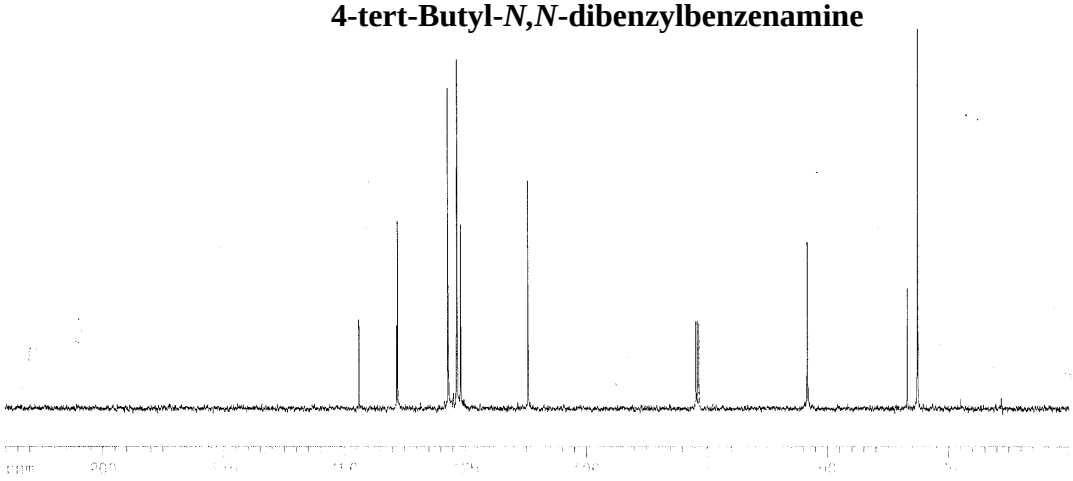


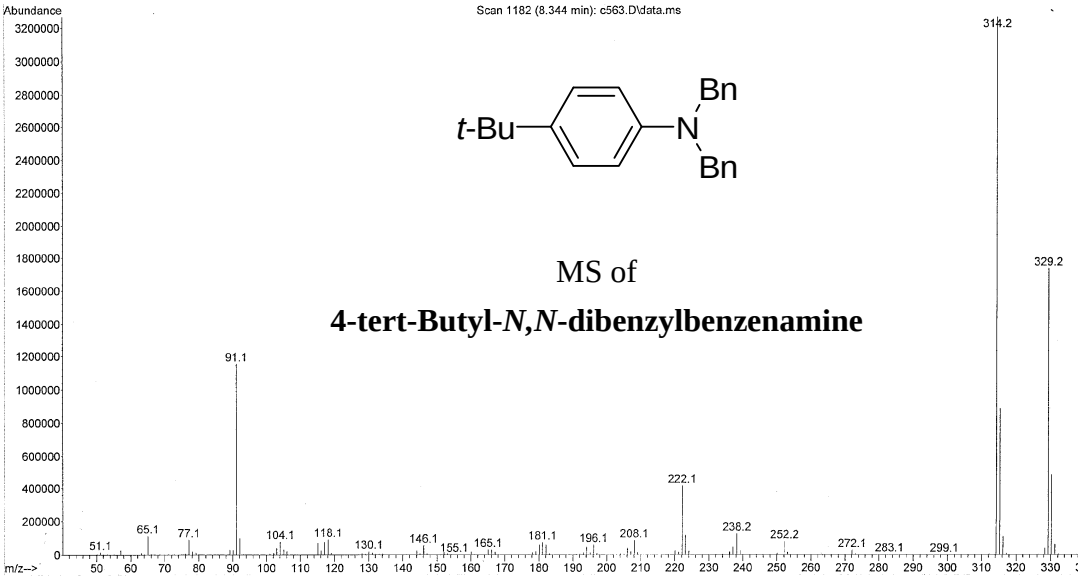




^{13}C NMR of

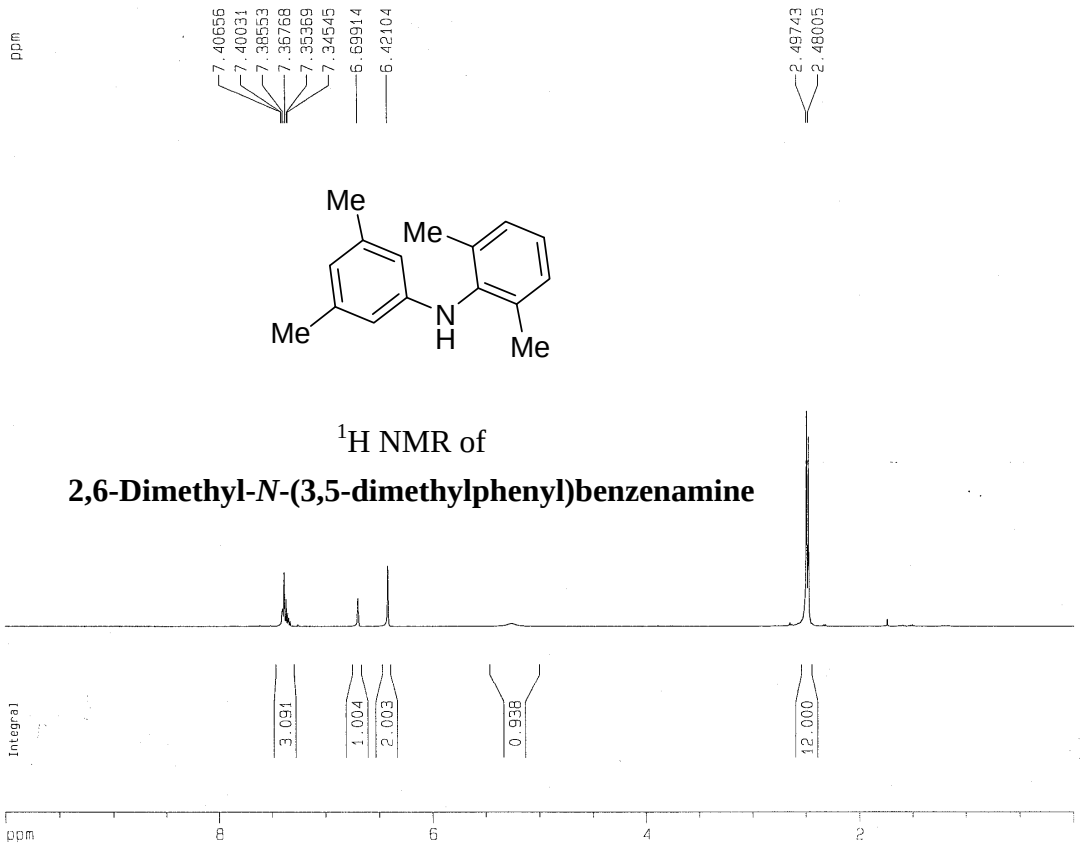
4-tert-Butyl-*N*,*N*-dibenzylbenzenamine





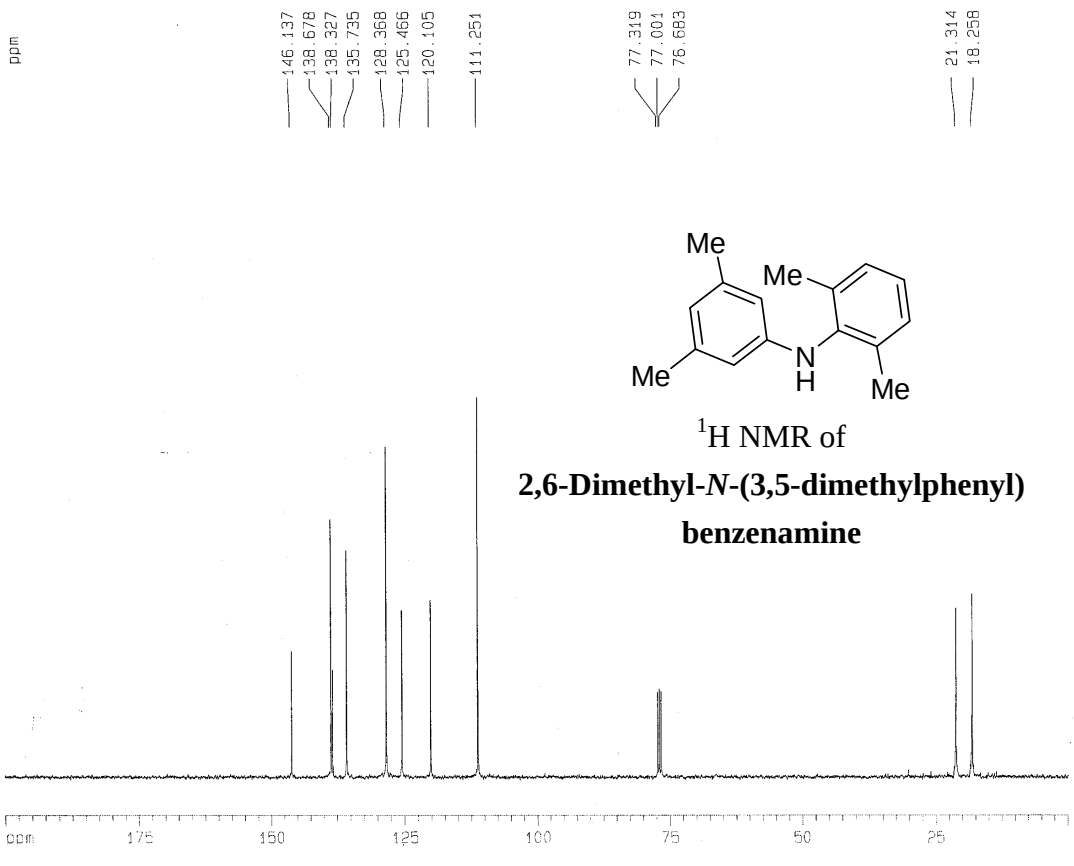
MS of

4-tert-Butyl-*N*,*N*-dibenzylbenzenamine



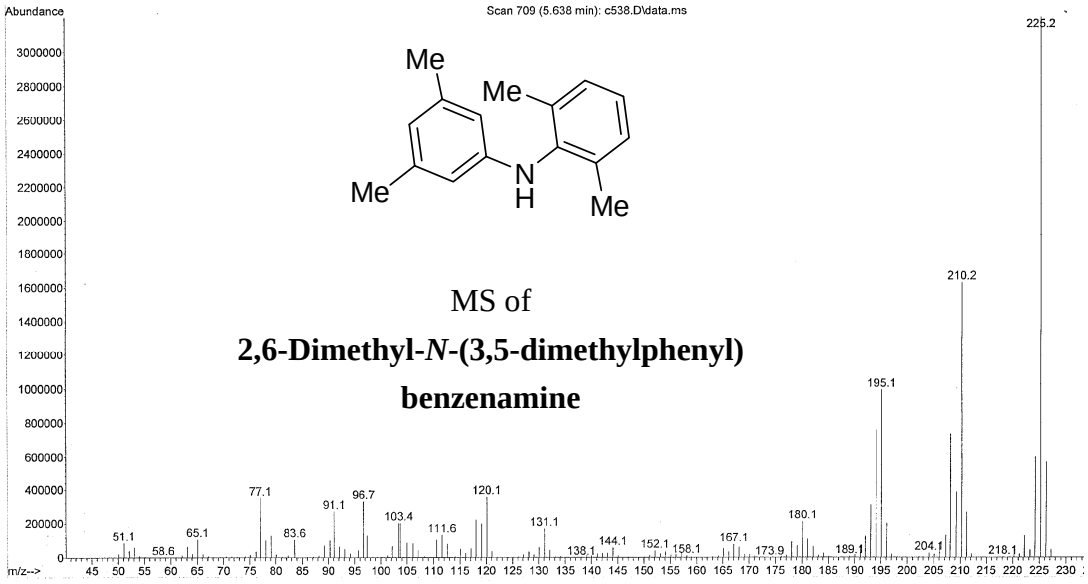
^{1}H NMR of

2,6-Dimethyl-*N*-(3,5-dimethylphenyl)benzenamine



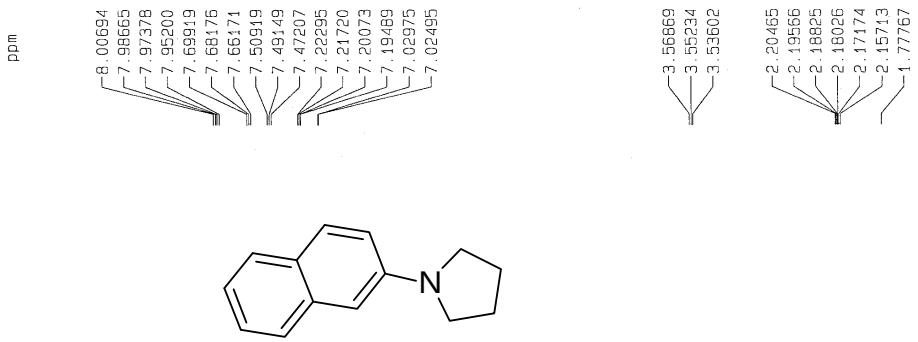
^{1}H NMR of

2,6-Dimethyl-*N*-(3,5-dimethylphenyl) benzenamine



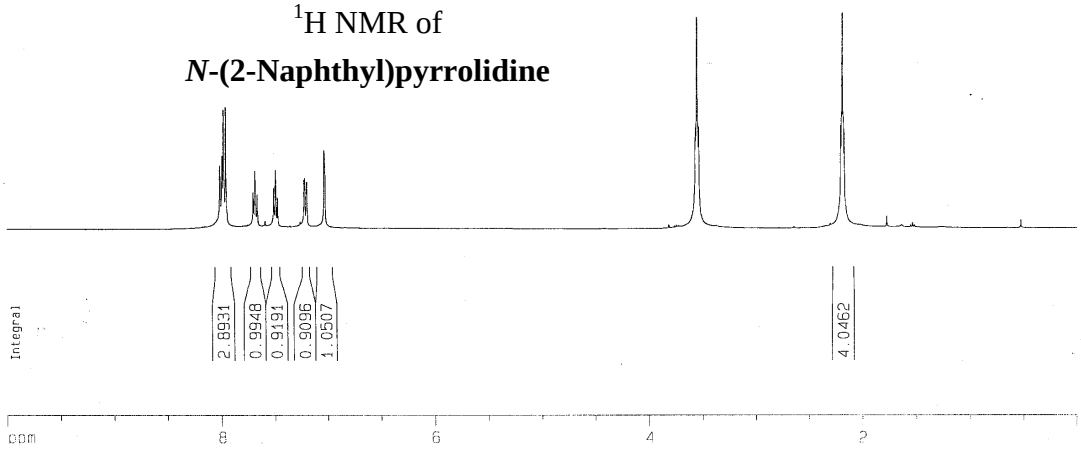
MS of

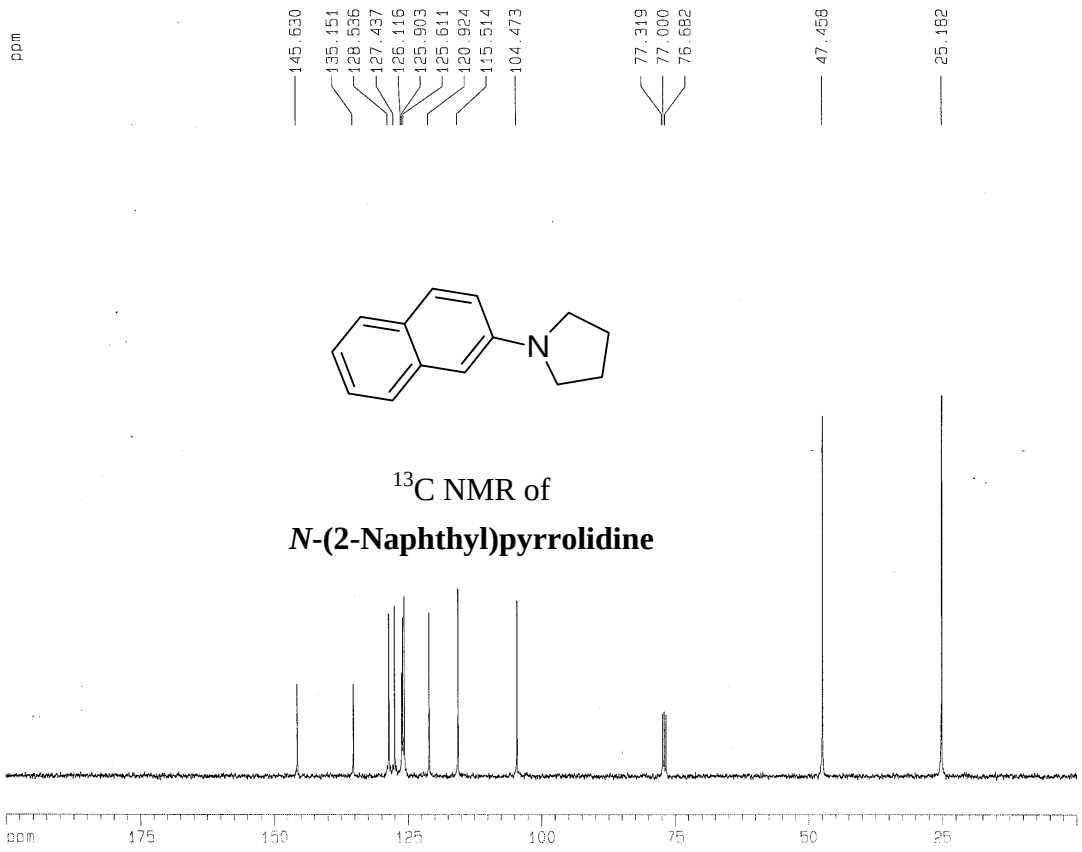
2,6-Dimethyl-*N*-(3,5-dimethylphenyl) benzenamine



^{1}H NMR of

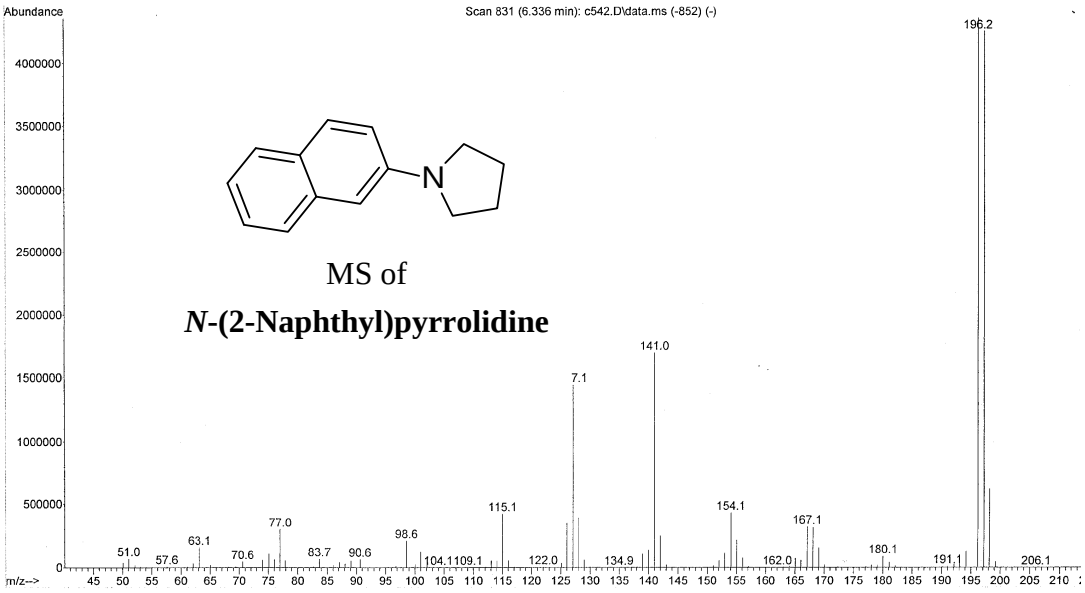
***N*-(2-Naphthyl)pyrrolidine**





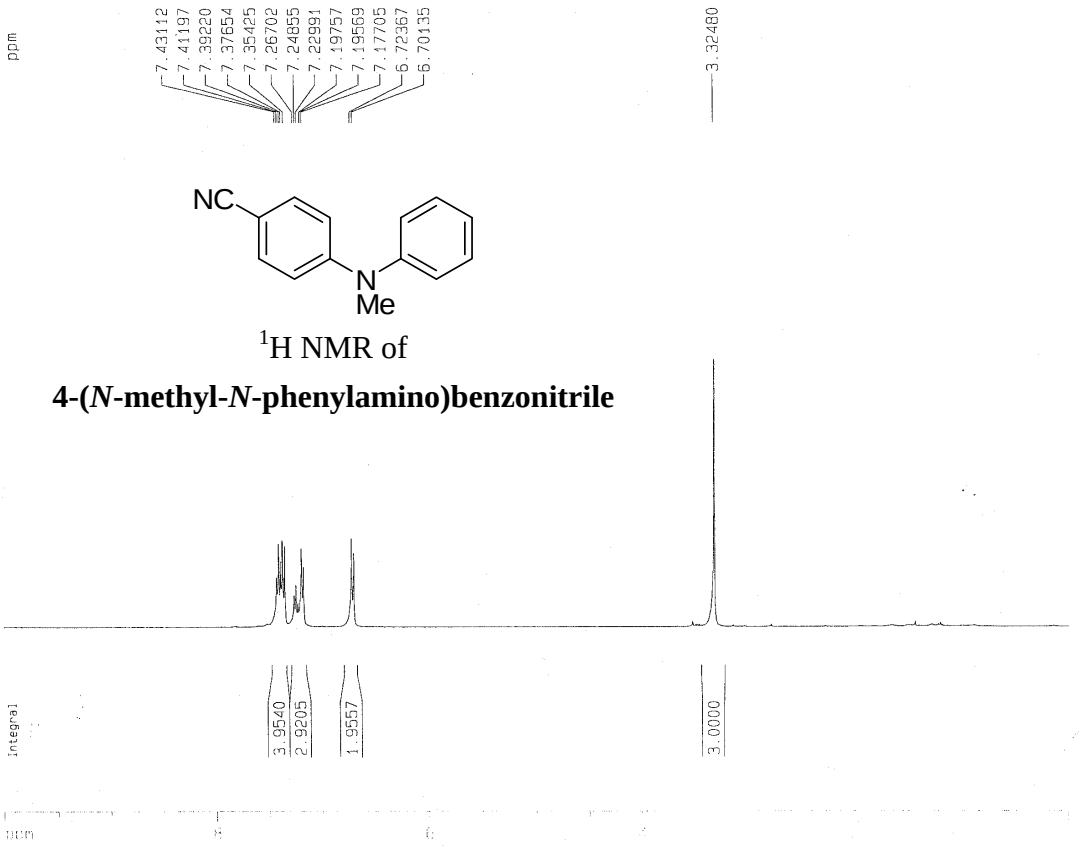
^{13}C NMR of

***N*-(2-Naphthyl)pyrrolidine**



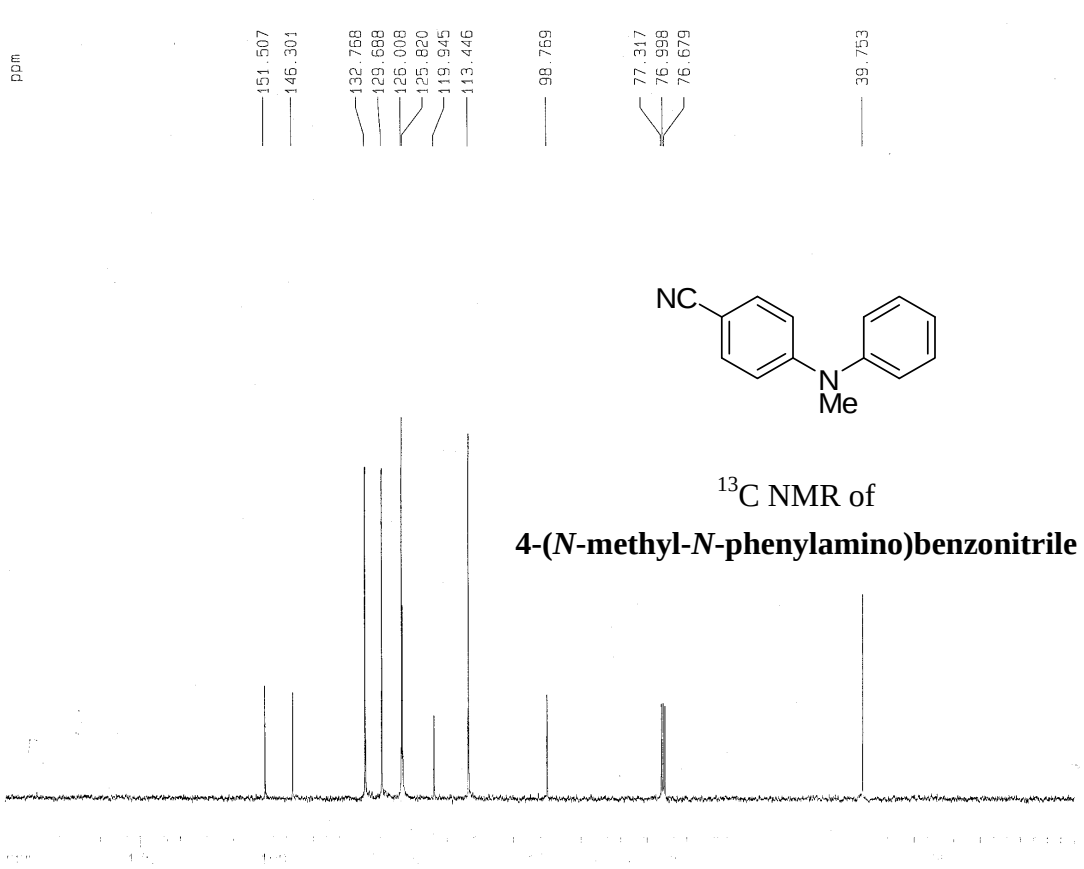
MS of

***N*-(2-Naphthyl)pyrrolidine**



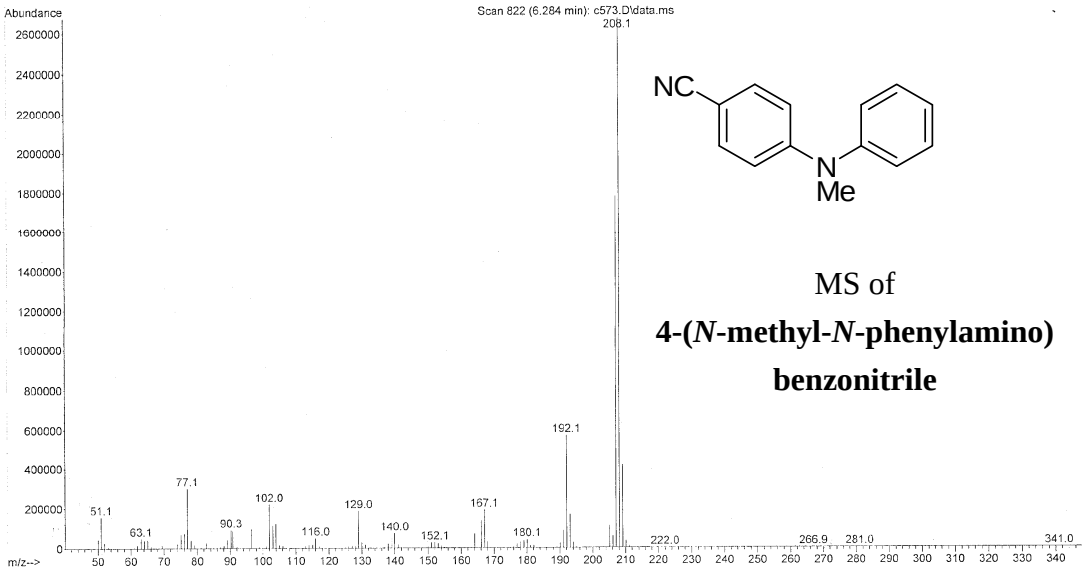
^{1}H NMR of

4-(*N*-methyl-*N*-phenylamino)benzonitrile



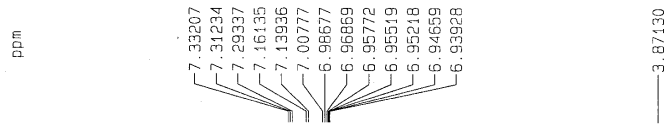
^{13}C NMR of

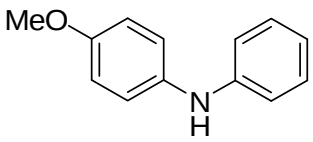
4-(*N*-methyl-*N*-phenylamino)benzonitrile



MS of

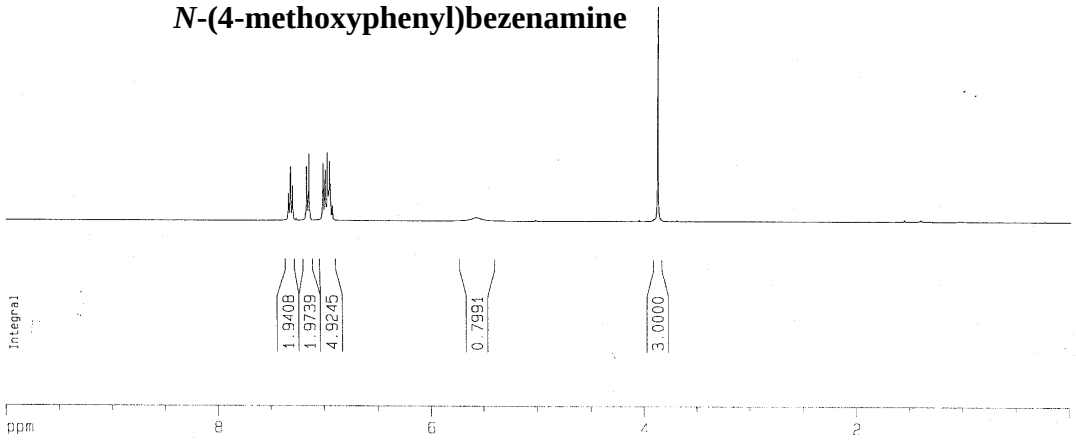
4-(*N*-methyl-*N*-phenylamino) benzonitrile

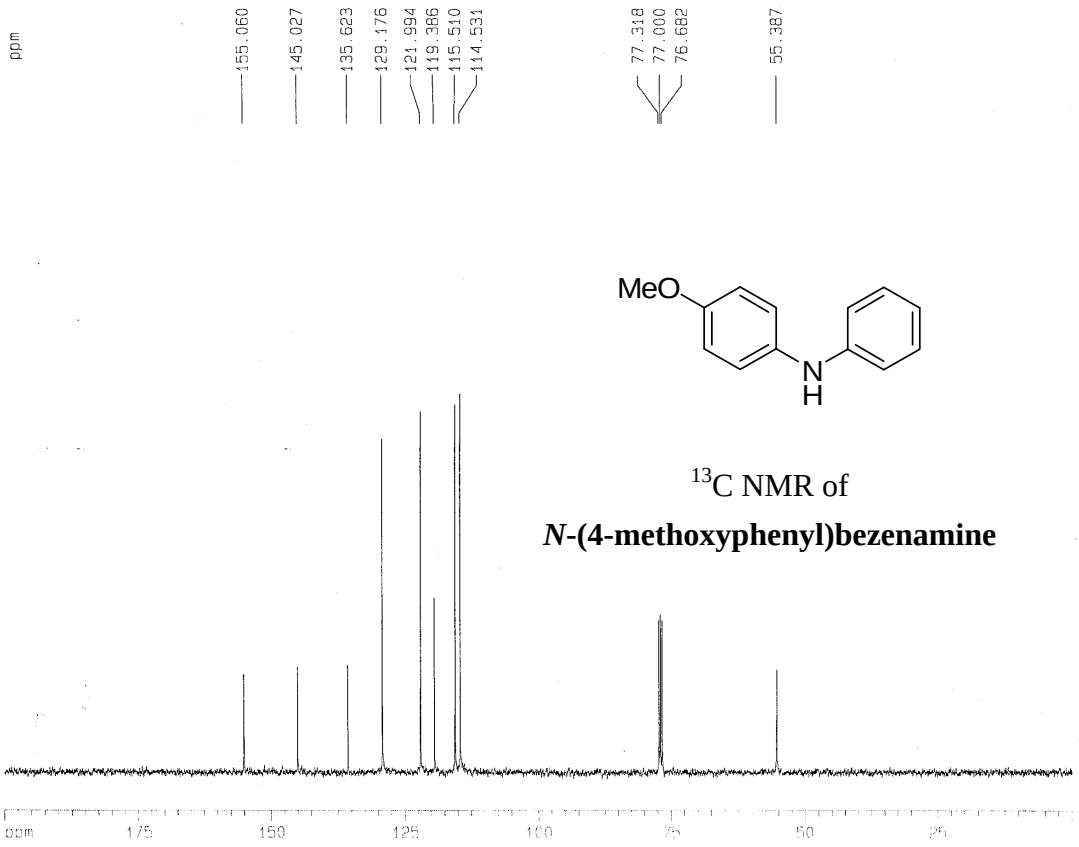




^{1}H NMR of

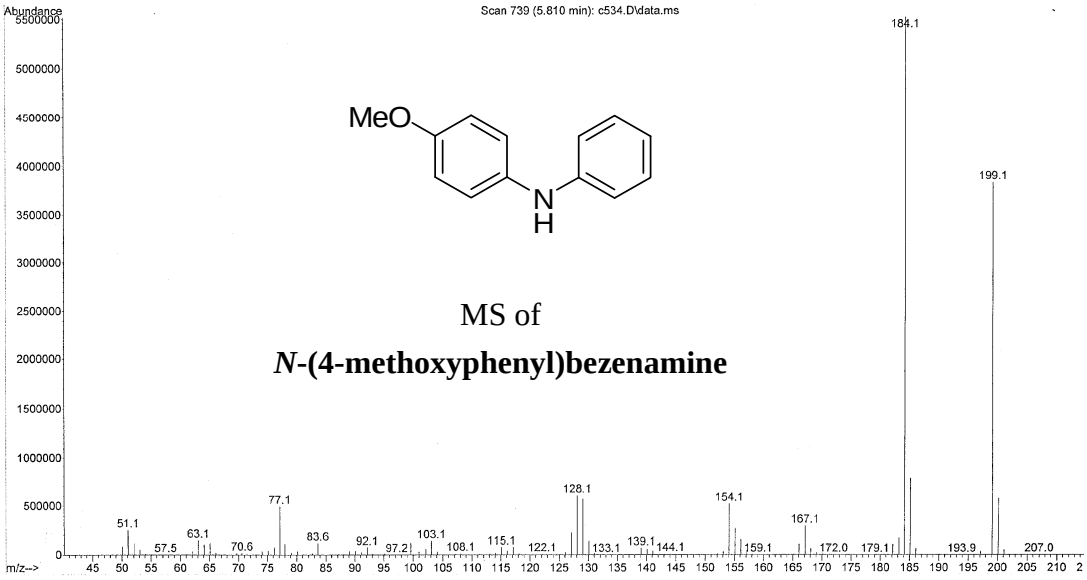
***N*-(4-methoxyphenyl)bezenamine**





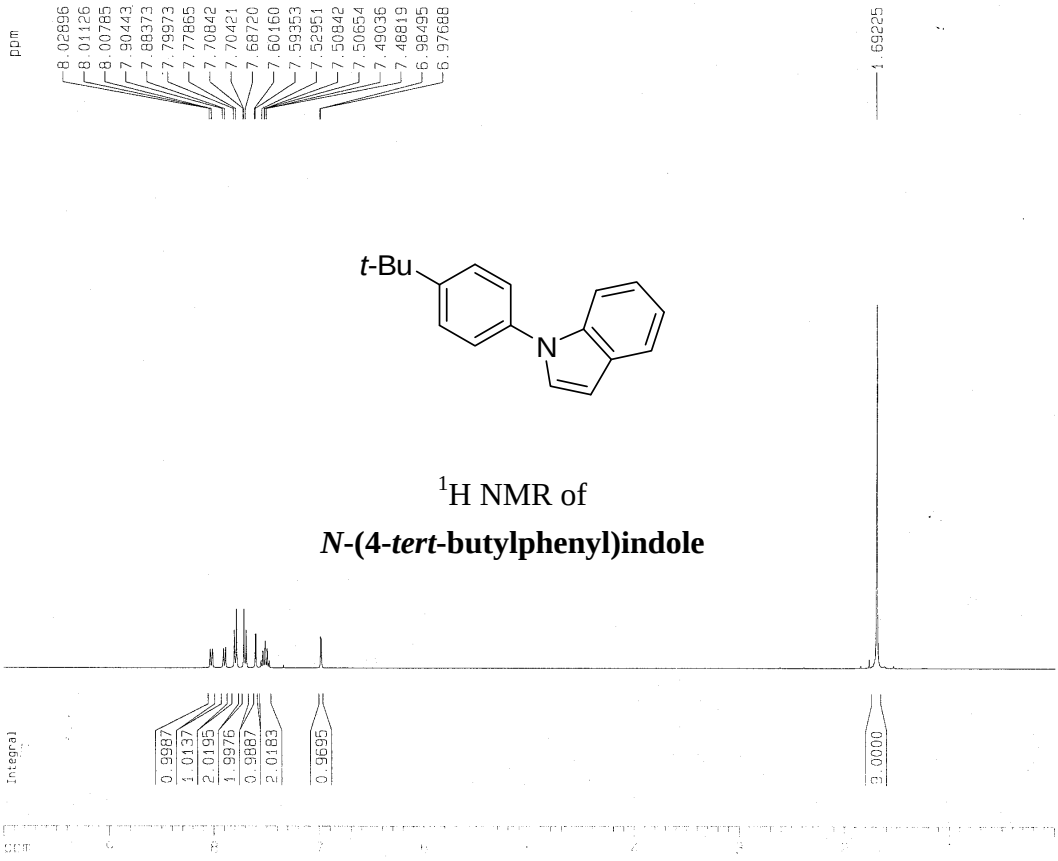
^{13}C NMR of

***N*-(4-methoxyphenyl)bezenamine**



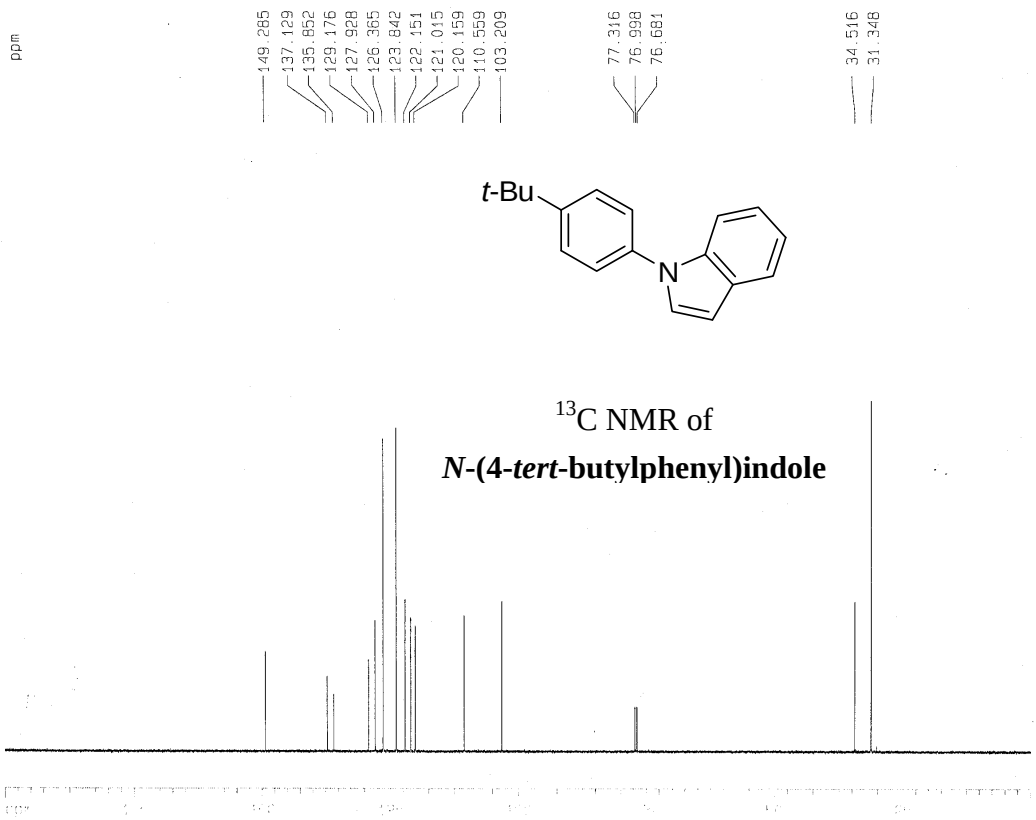
MS of

***N*-(4-methoxyphenyl)bezenamine**



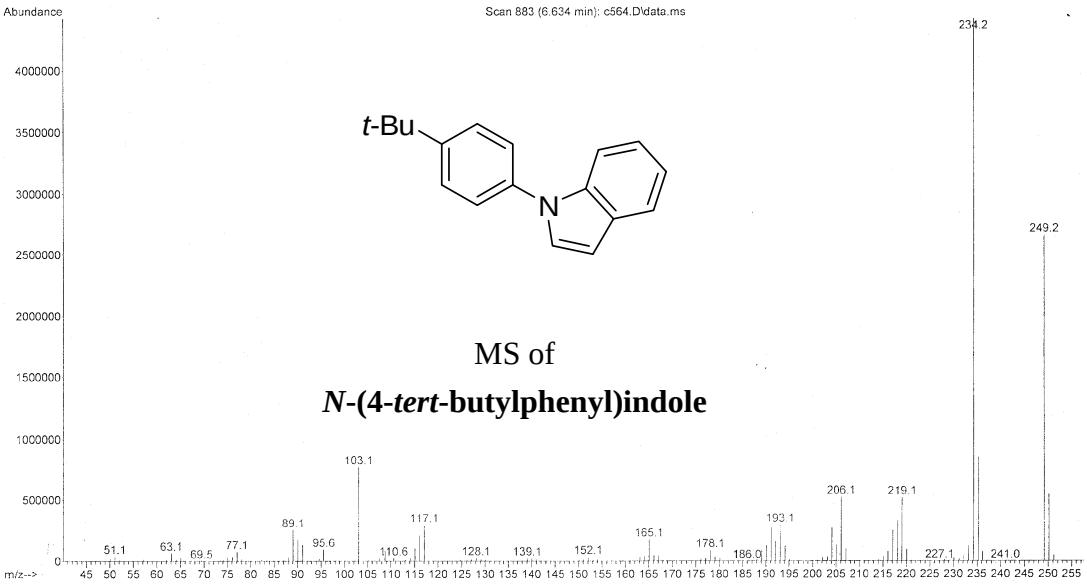
^{1}H NMR of

***N*-(4-*tert*-butylphenyl)indole**



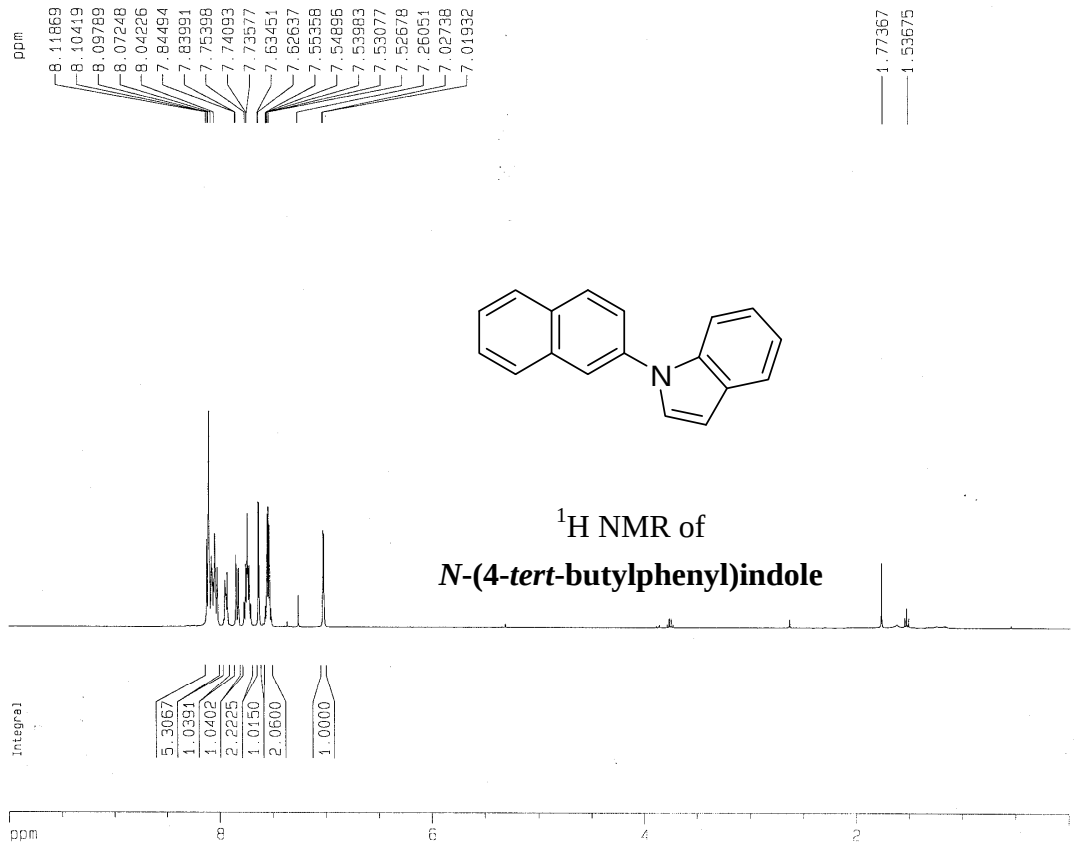
^{13}C NMR of

***N*-(4-*tert*-butylphenyl)indole**



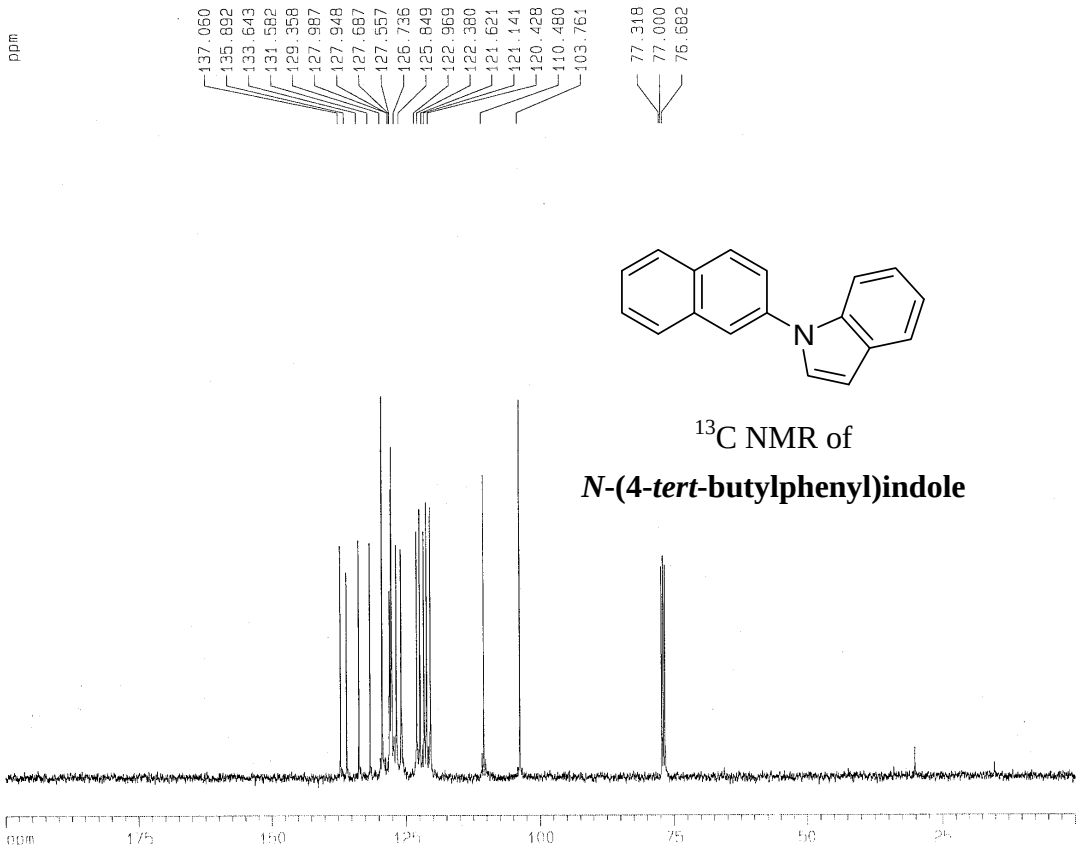
MS of

***N*-(4-*tert*-butylphenyl)indole**



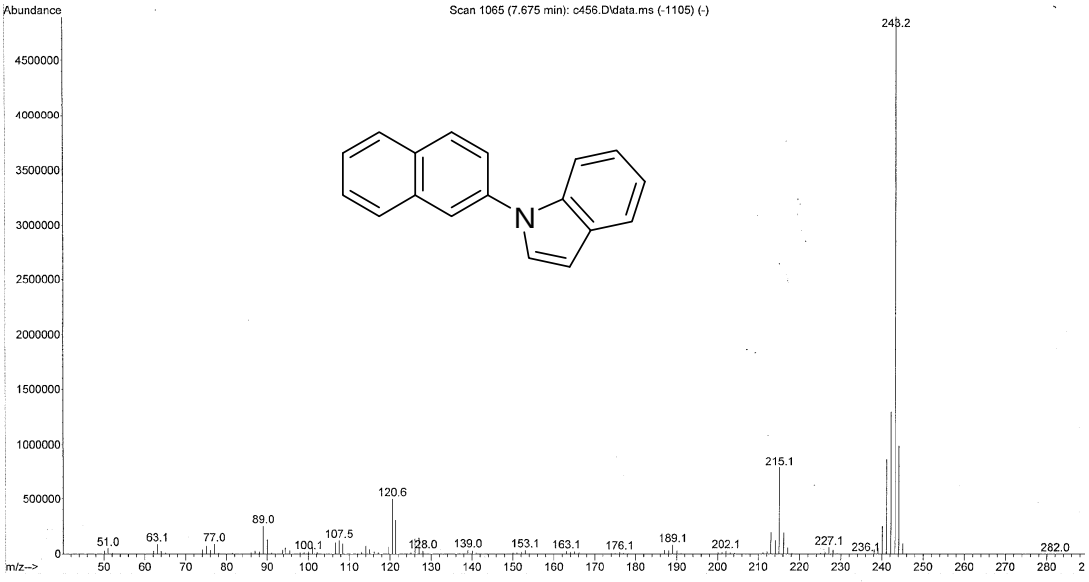
^{1}H NMR of

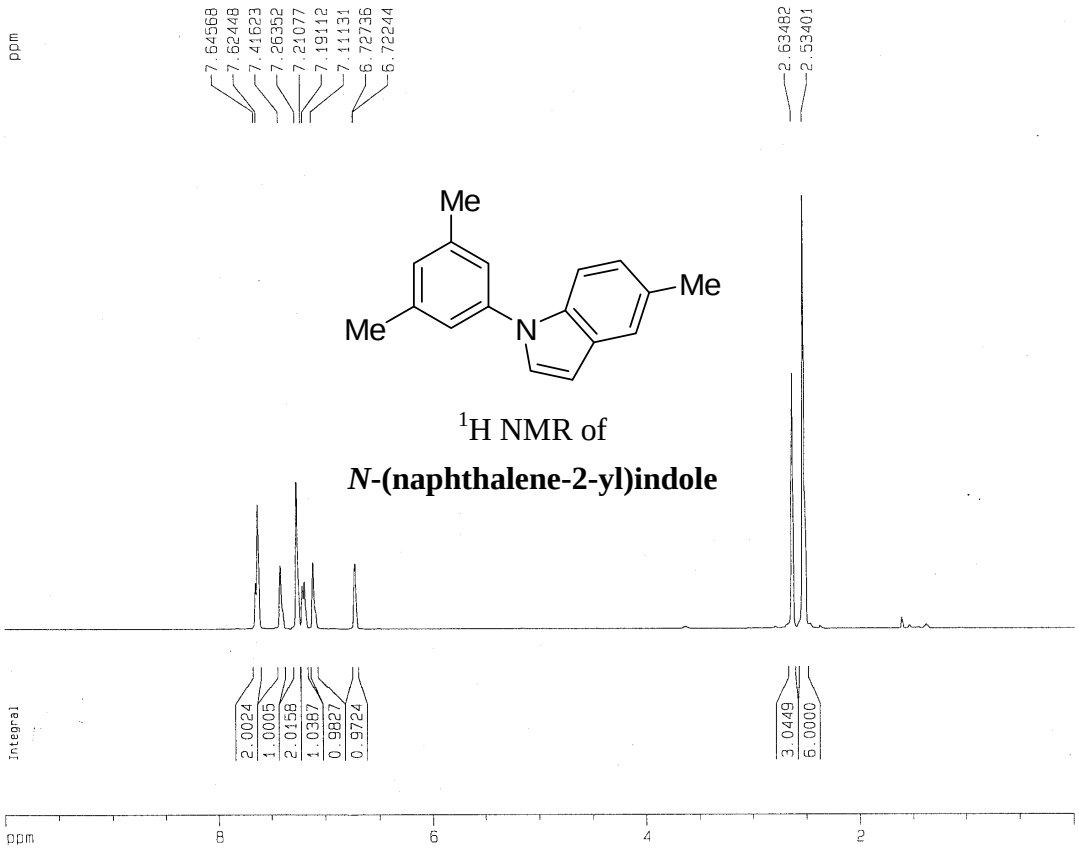
***N*-(4-*tert*-butylphenyl)indole**



^{13}C NMR of

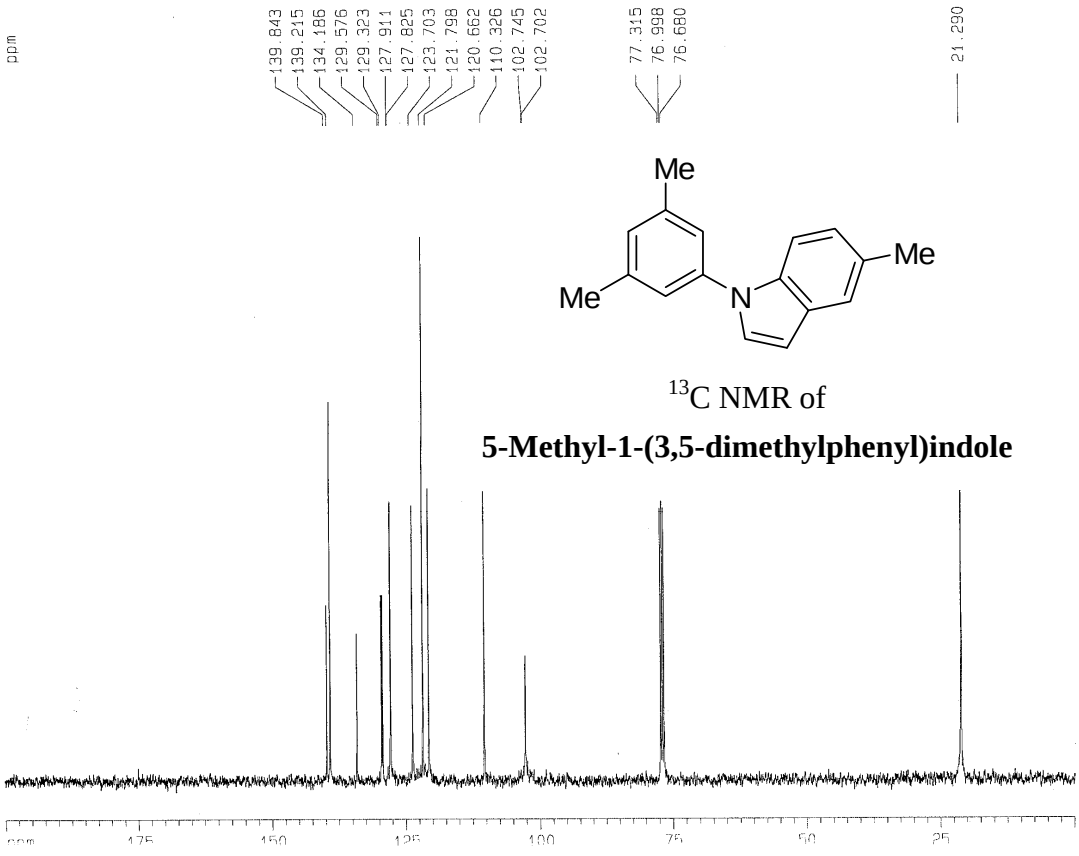
***N*-(4-*tert*-butylphenyl)indole**





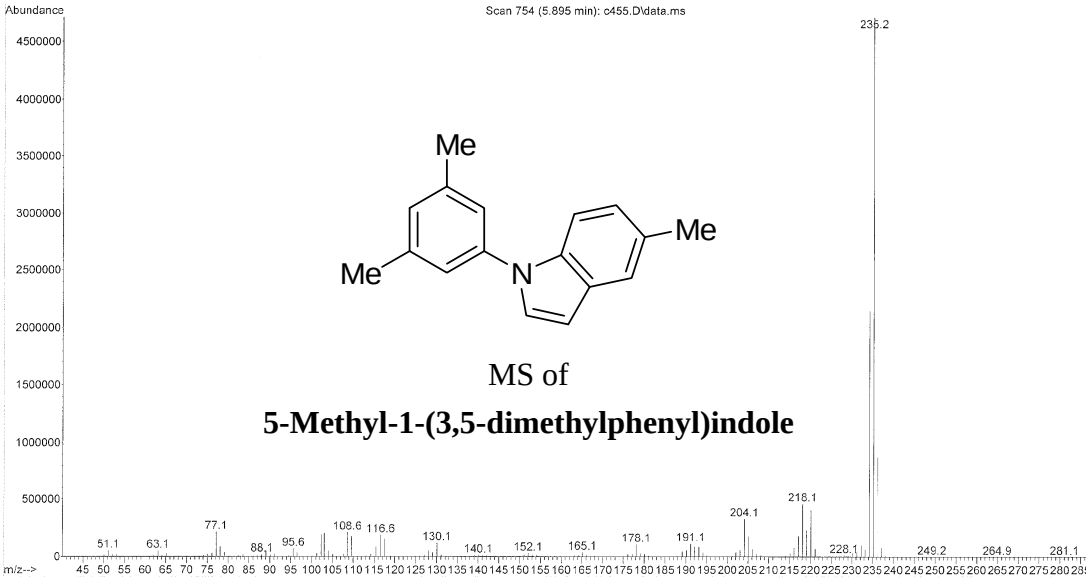
^{1}H NMR of

***N*-(naphthalene-2-yl)indole**



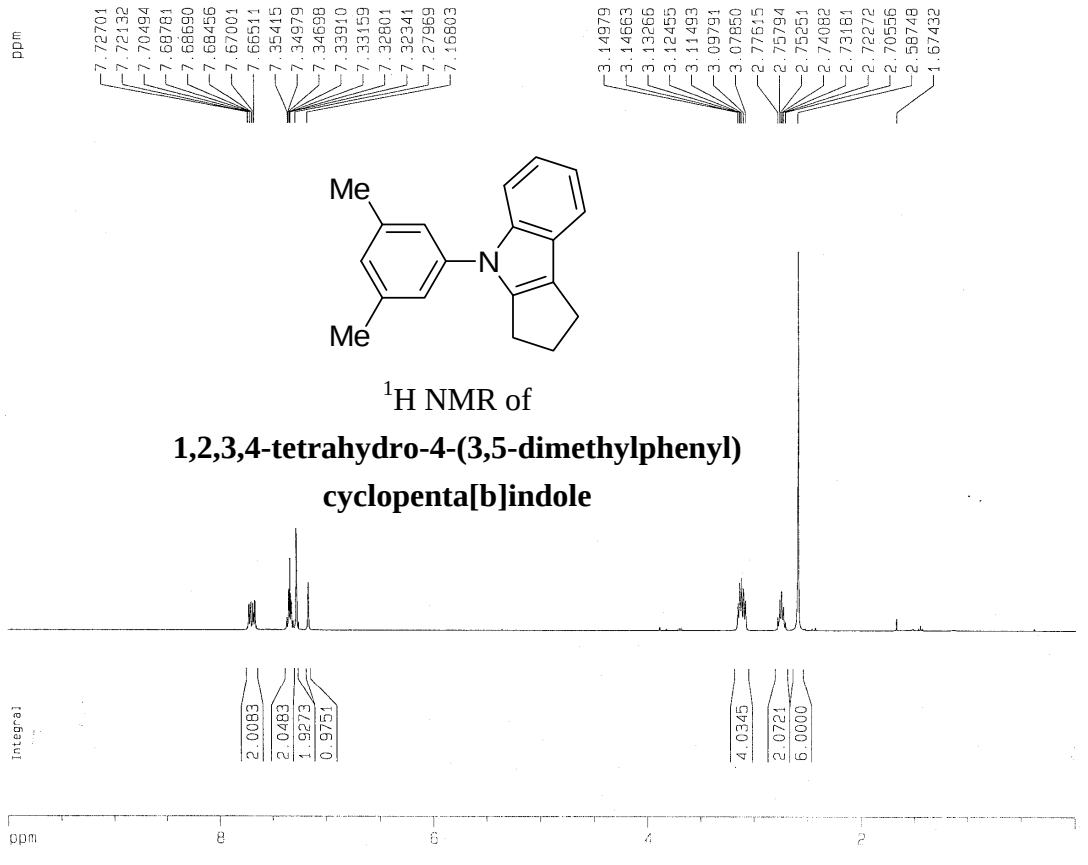
^{13}C NMR of

5-Methyl-1-(3,5-dimethylphenyl)indole



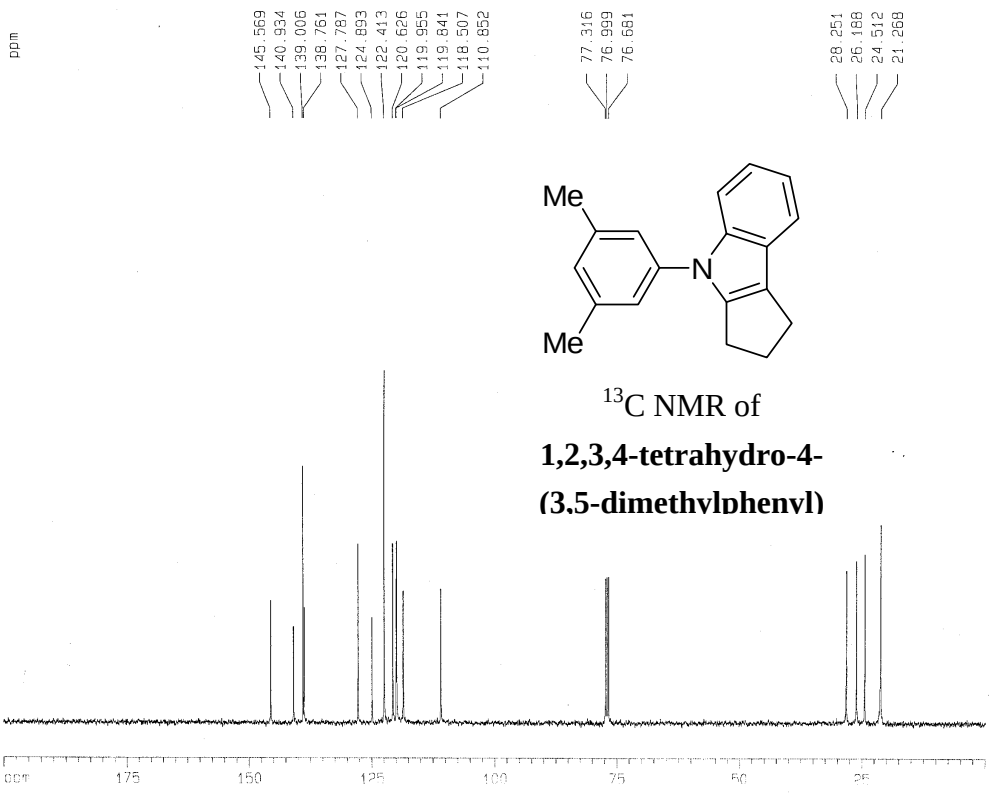
MS of

5-Methyl-1-(3,5-dimethylphenyl)indole

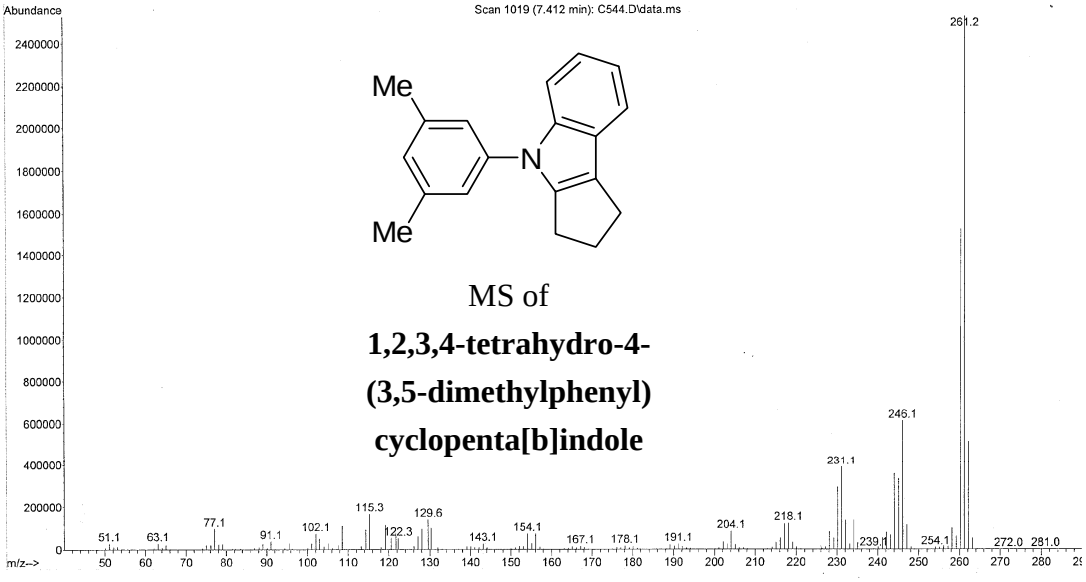


^{1}H NMR of

1,2,3,4-tetrahydro-4-(3,5-dimethylphenyl) cyclopenta[b]indole



^{13}C NMR of **1,2,3,4-tetrahydro-4-(3,5-dimethylphenyl)**



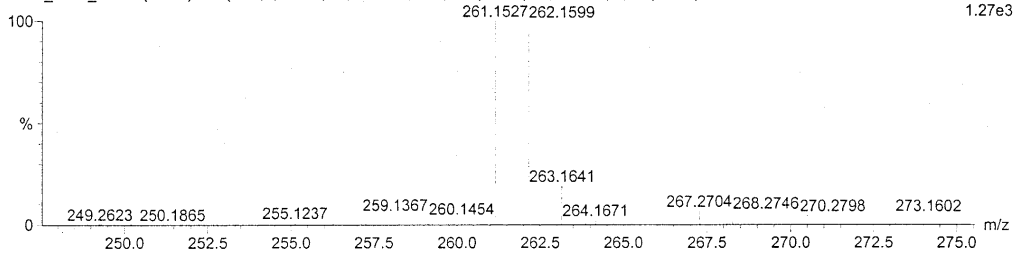
MS of **1,2,3,4-tetrahydro-4-(3,5-dimethylphenyl) cyclopenta[b]indole**

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
11 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-19 H: 0-1000 N: 0-1 Na: 0-1

So Chau Ming
HR08_0423_2A 58 (1.084) AM (Cen,5, 80.00, Ht,10000.0,0.00,1.00); Sm (SG, 2x3.00); Cm (47:61) TOF MS ES+
1.27e3



Minimum:				-1.5		
Maximum:		100.0	5.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
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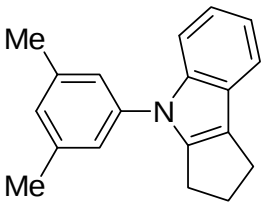
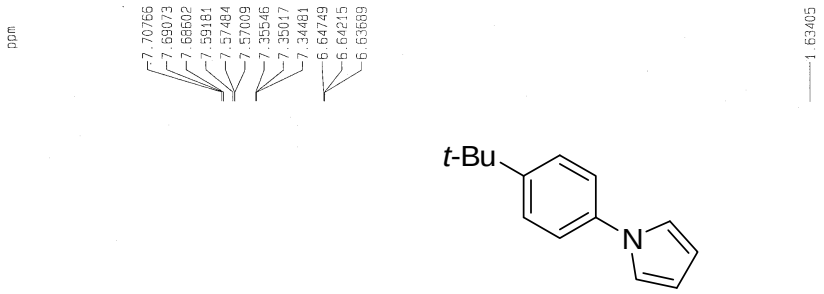


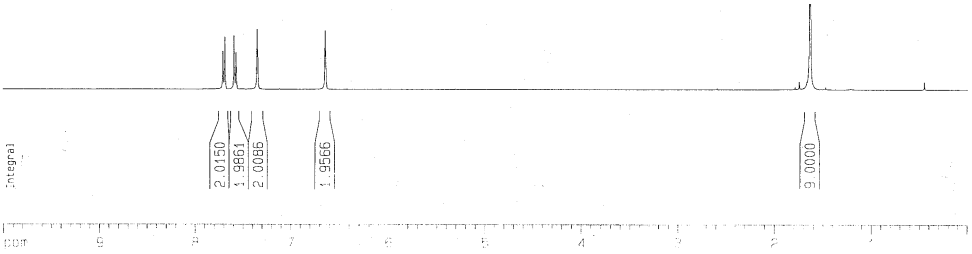
HRMS of

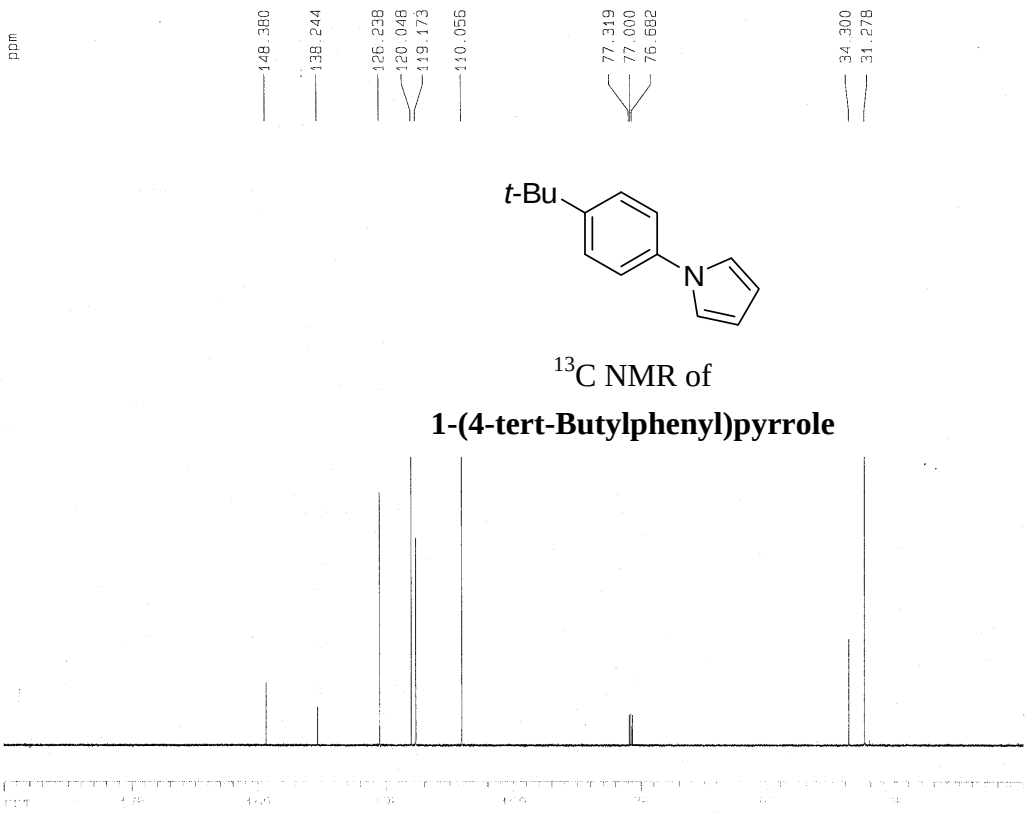
1,2,3,4-tetrahydro-4-(3,5-dimethylphenyl)cyclopenta[b]indole



^{1}H NMR of

1-(4-tert-Butylphenyl)pyrrole





^{13}C NMR of

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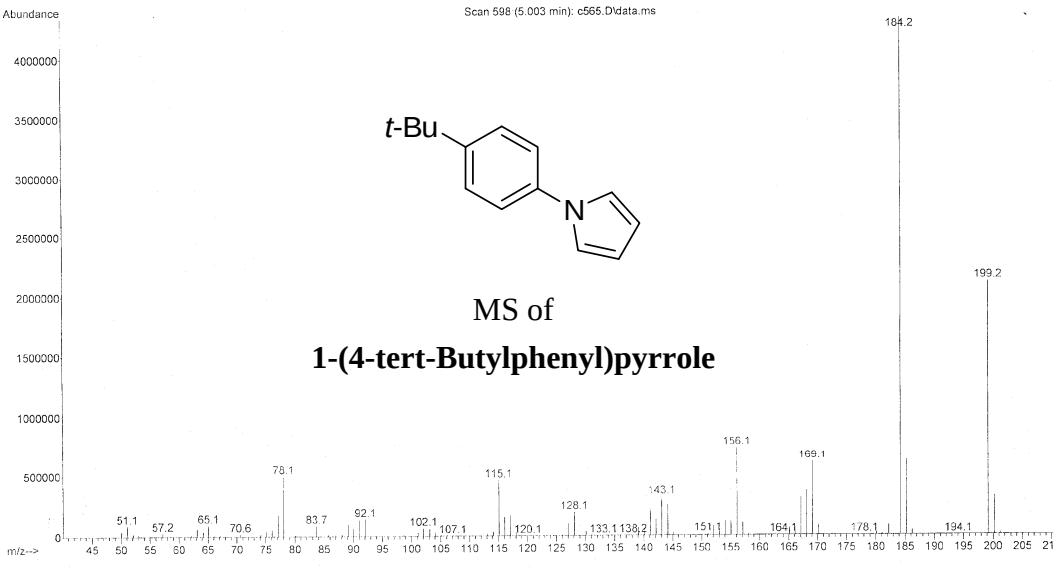

MS of

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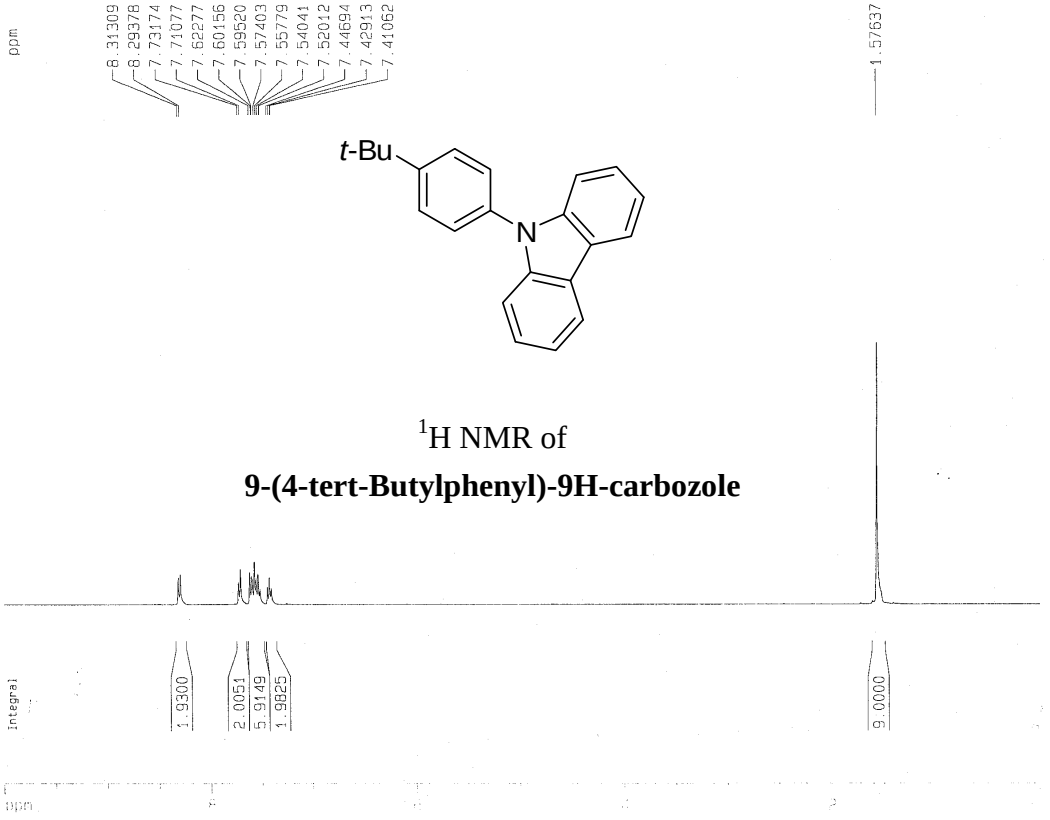
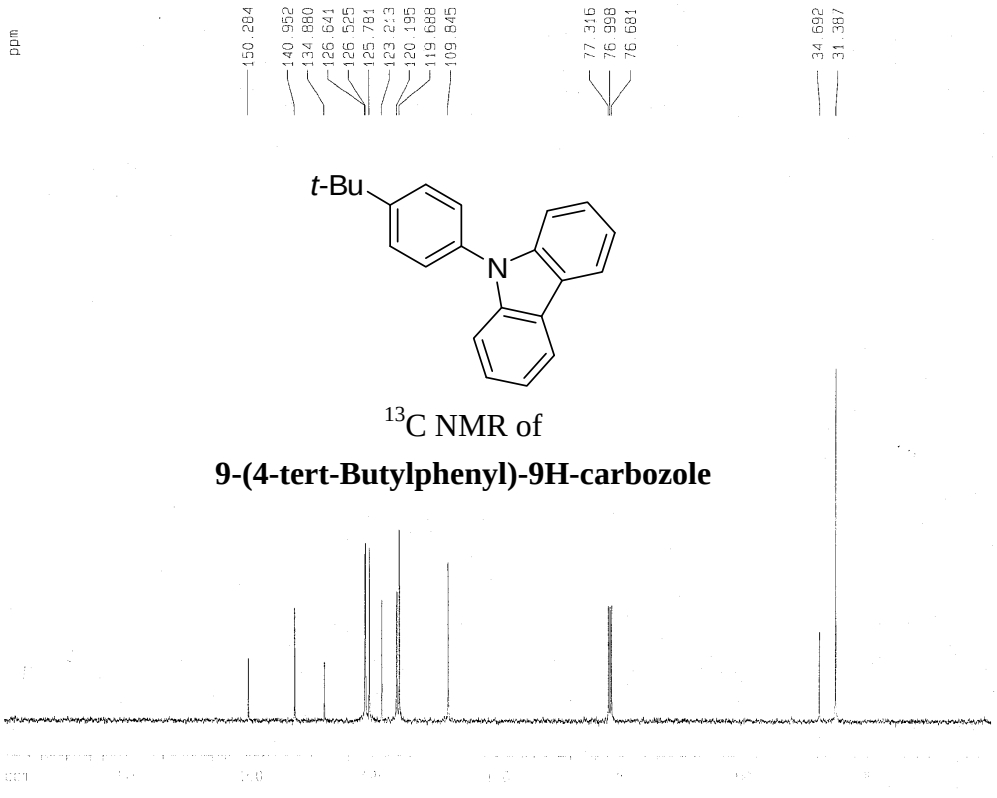


^{1}H NMR of

9-(4-tert-Butylphenyl)-9H-carbozole



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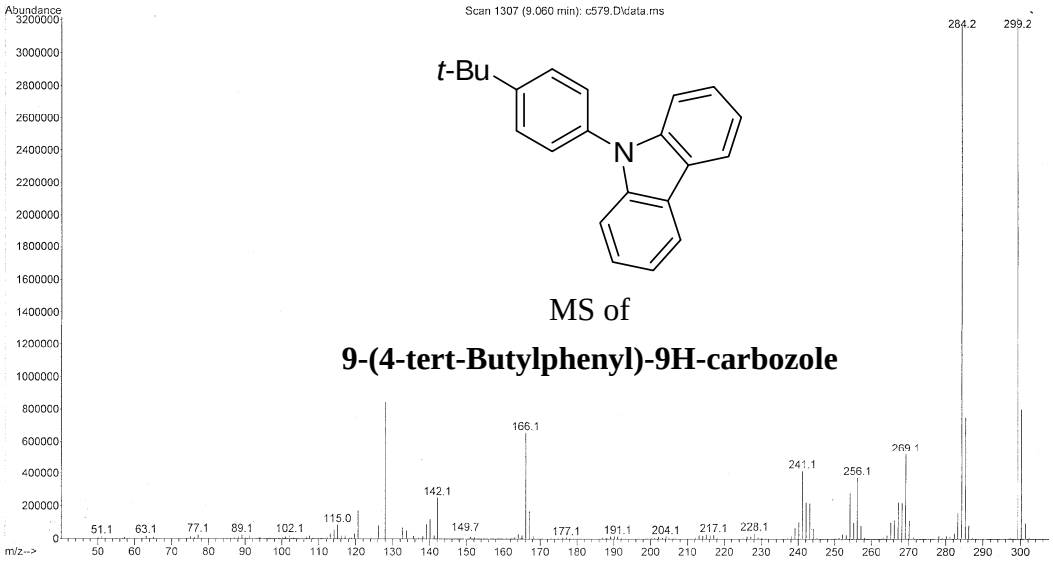

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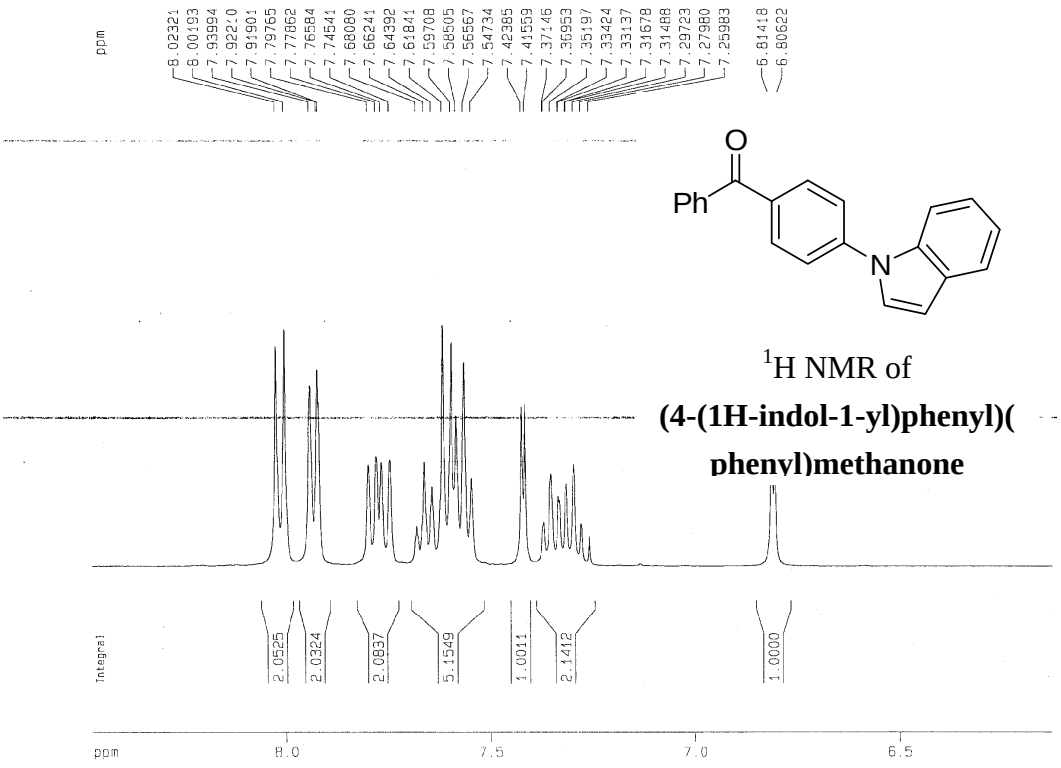

^{1}H NMR of

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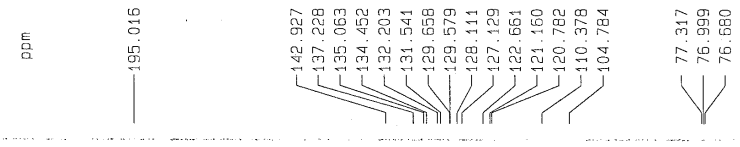
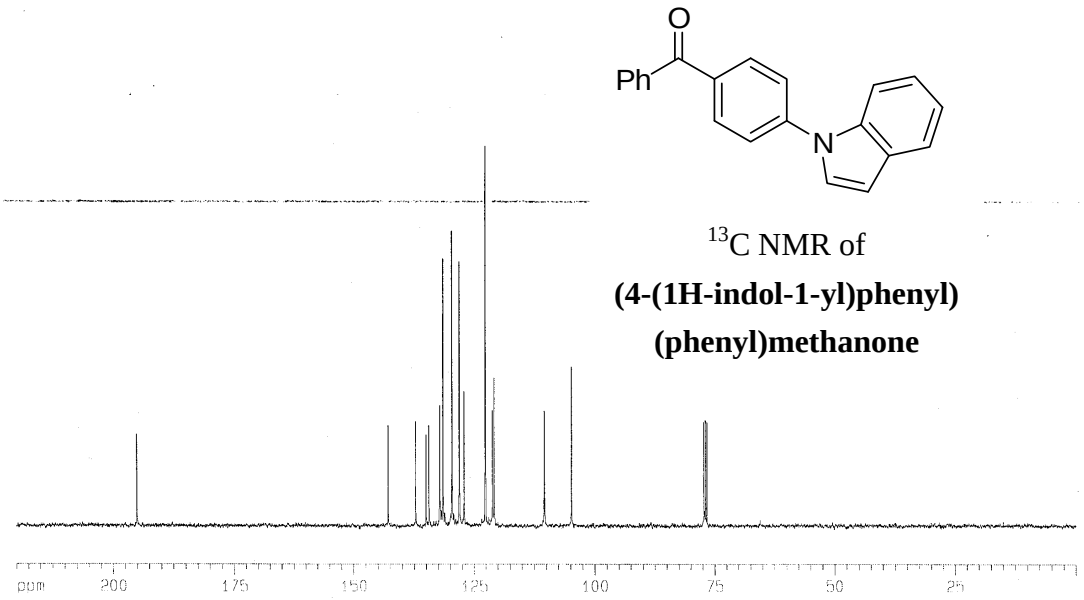
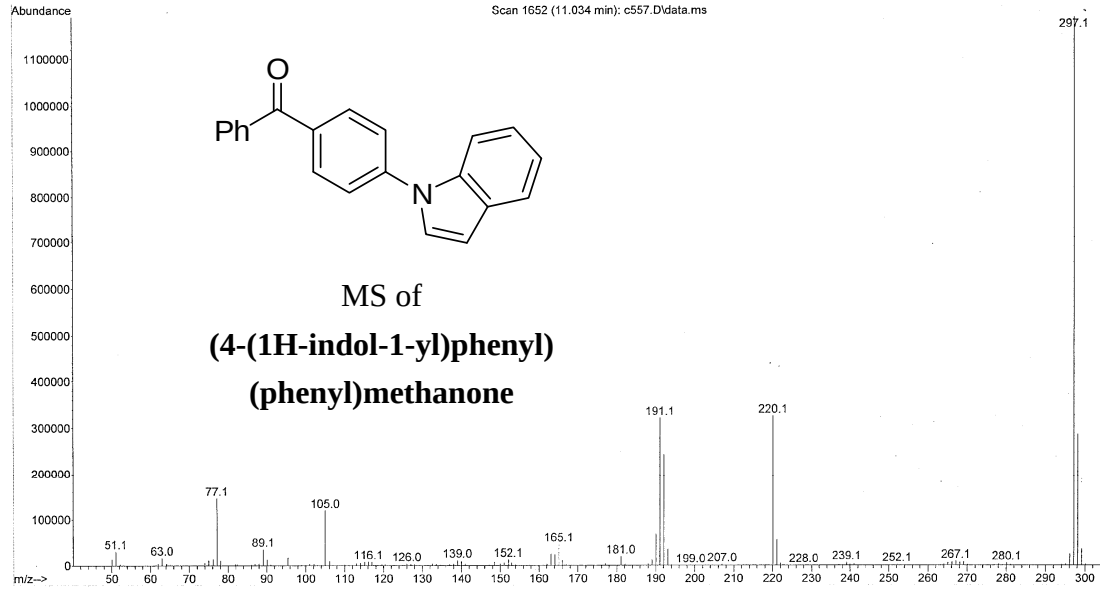




^{13}C NMR of

(4-(1H-indol-1-yl)phenyl)

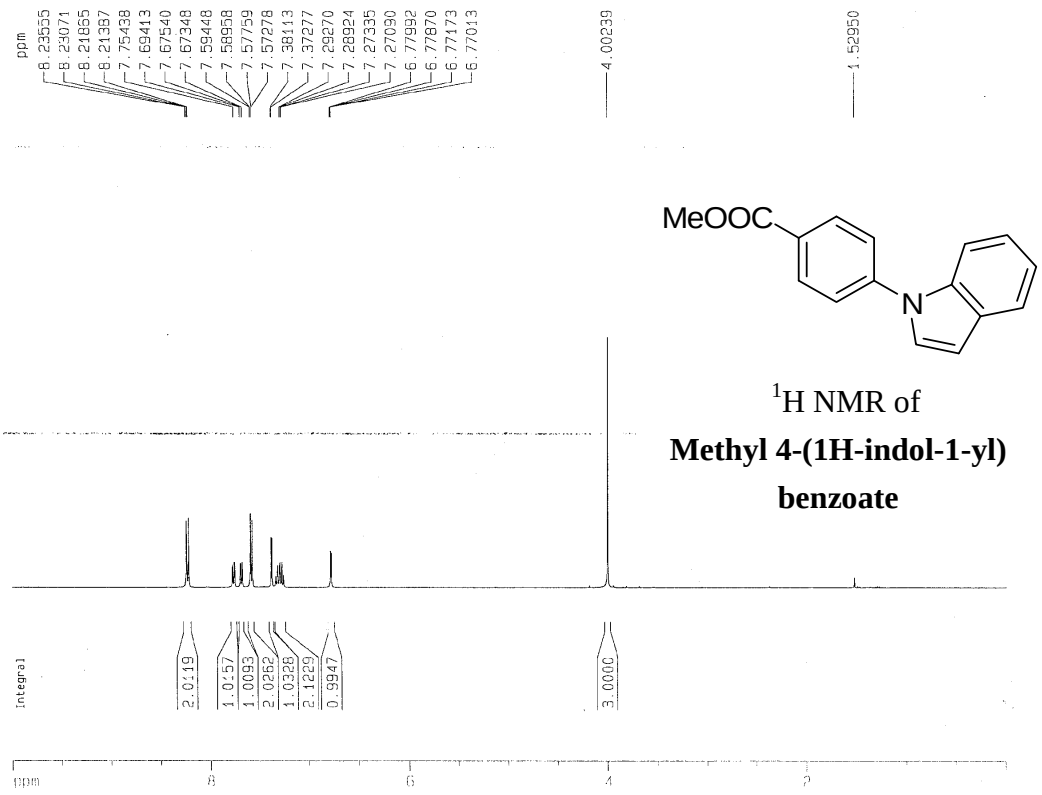
(phenyl)methanone



MS of

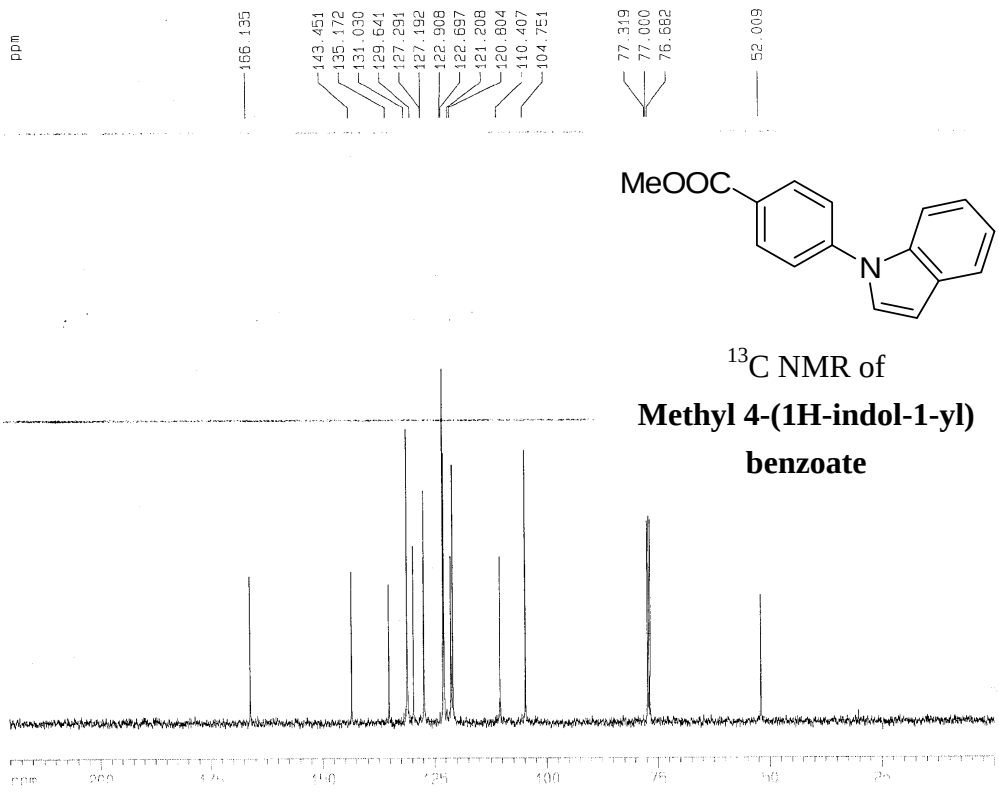
(4-(1H-indol-1-yl)phenyl)

(phenyl)methanone



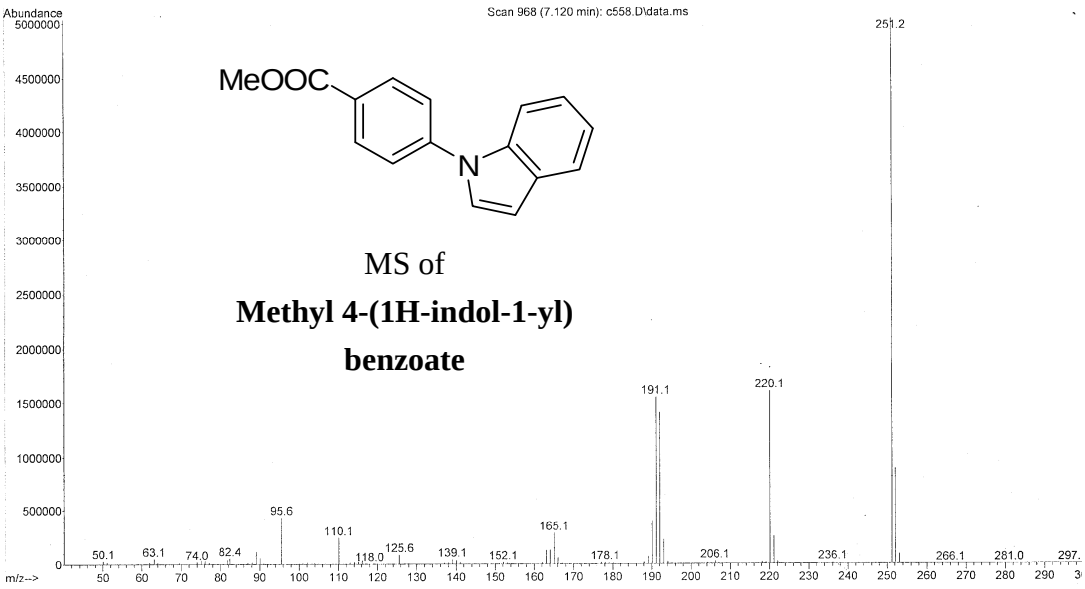
^{1}H NMR of

Methyl 4-(1H-indol-1-yl) benzoate



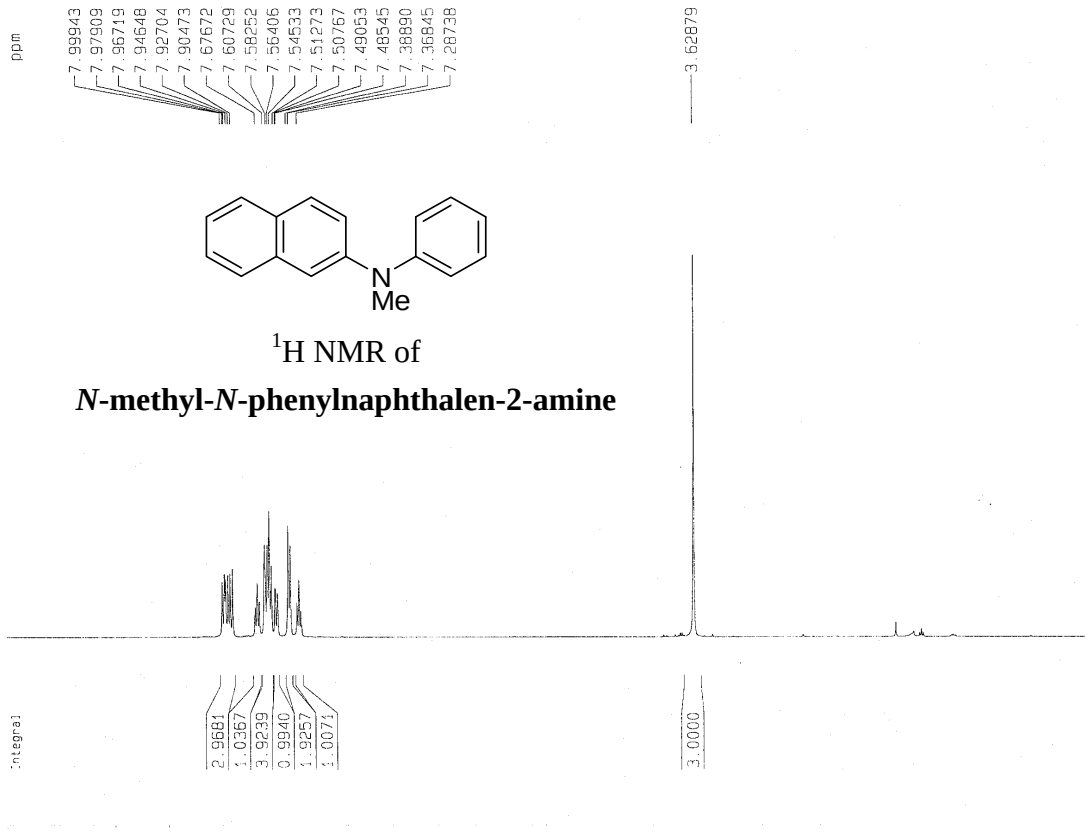
^{13}C NMR of

Methyl 4-(1H-indol-1-yl) benzoate



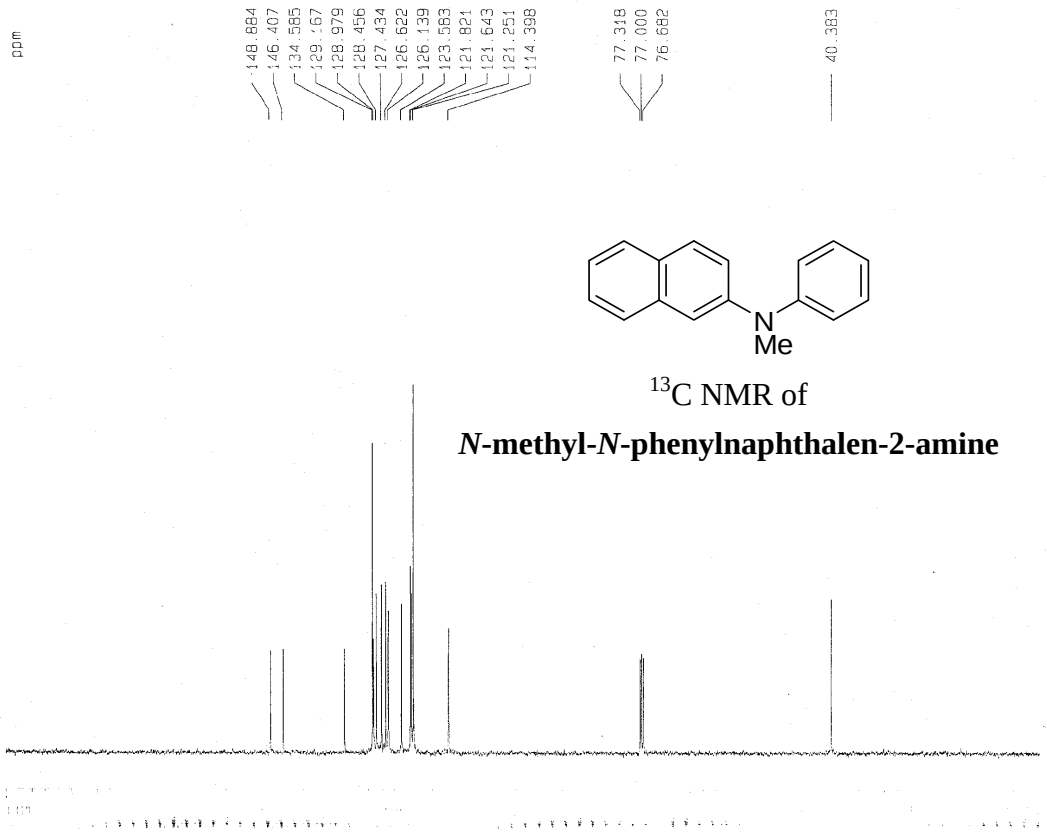
MS of

Methyl 4-(1H-indol-1-yl) benzoate



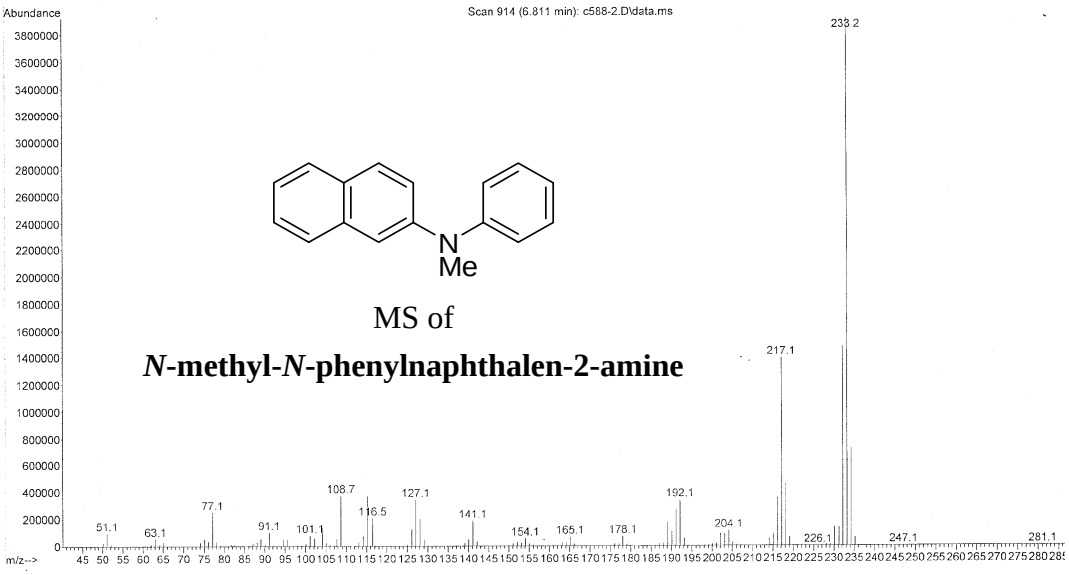
^{1}H NMR of

***N*-methyl-*N*-phenylnaphthalen-2-amine**



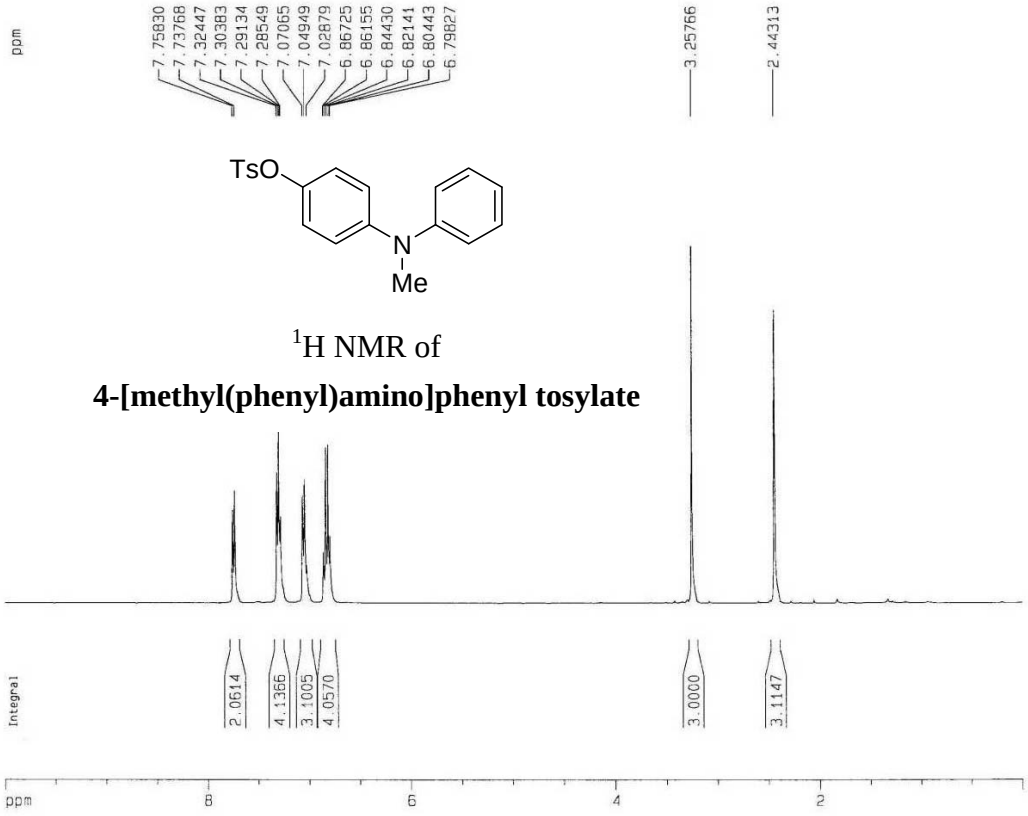
^{13}C NMR of

***N*-methyl-*N*-phenylnaphthalen-2-amine**



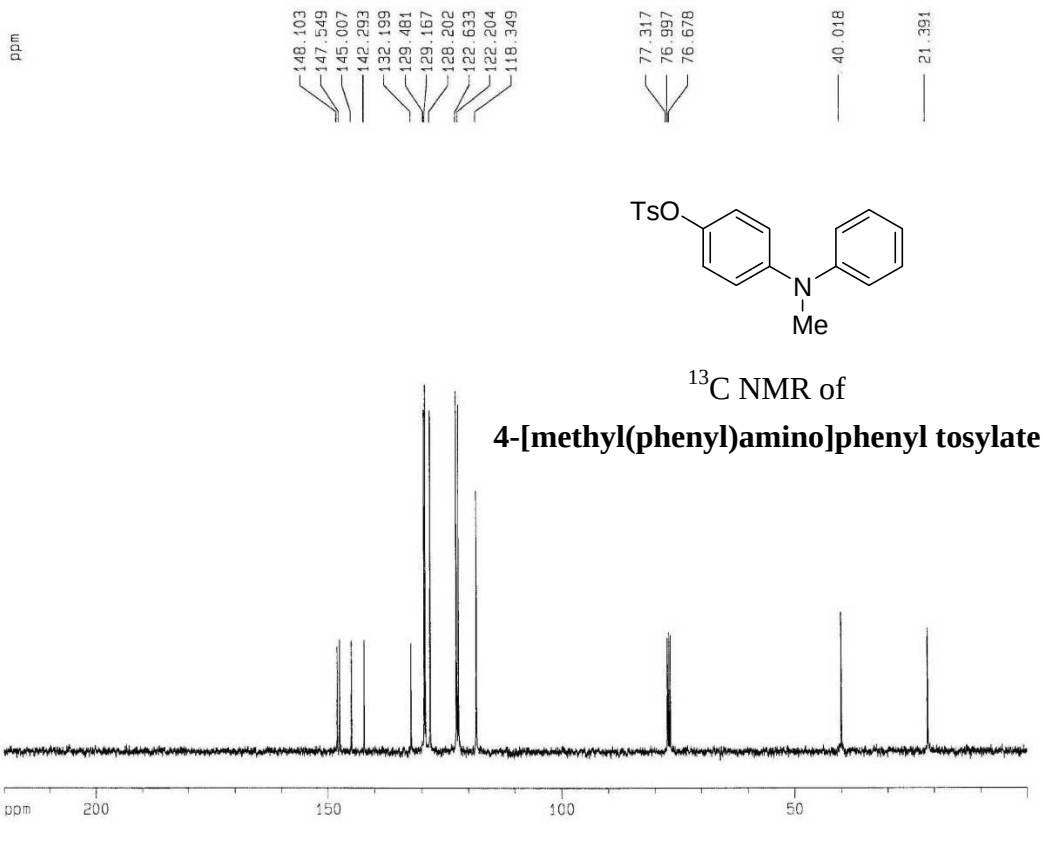
MS of

***N*-methyl-*N*-phenylnaphthalen-2-amine**



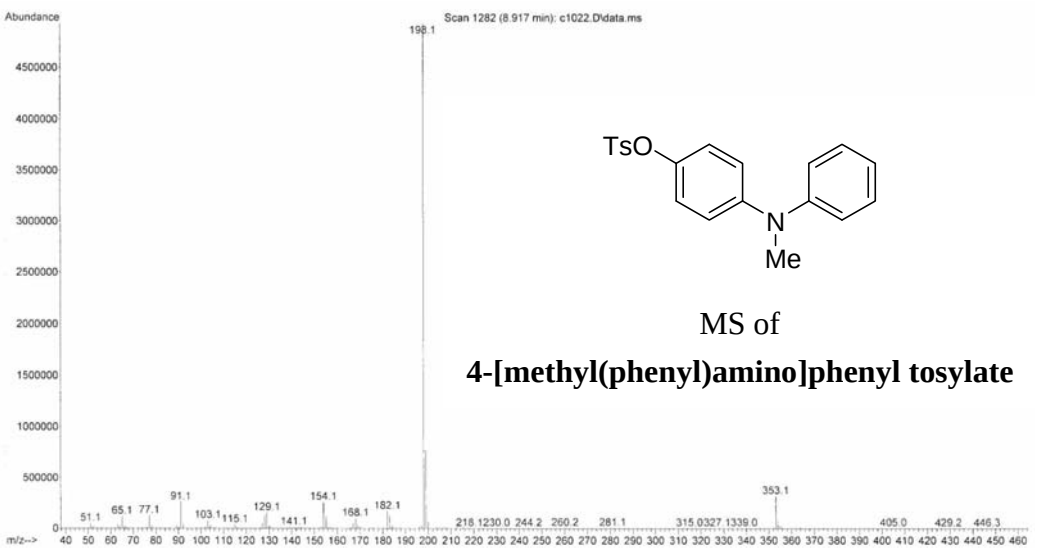
^{1}H NMR of

4-[methyl(phenyl)amino]phenyl tosylate



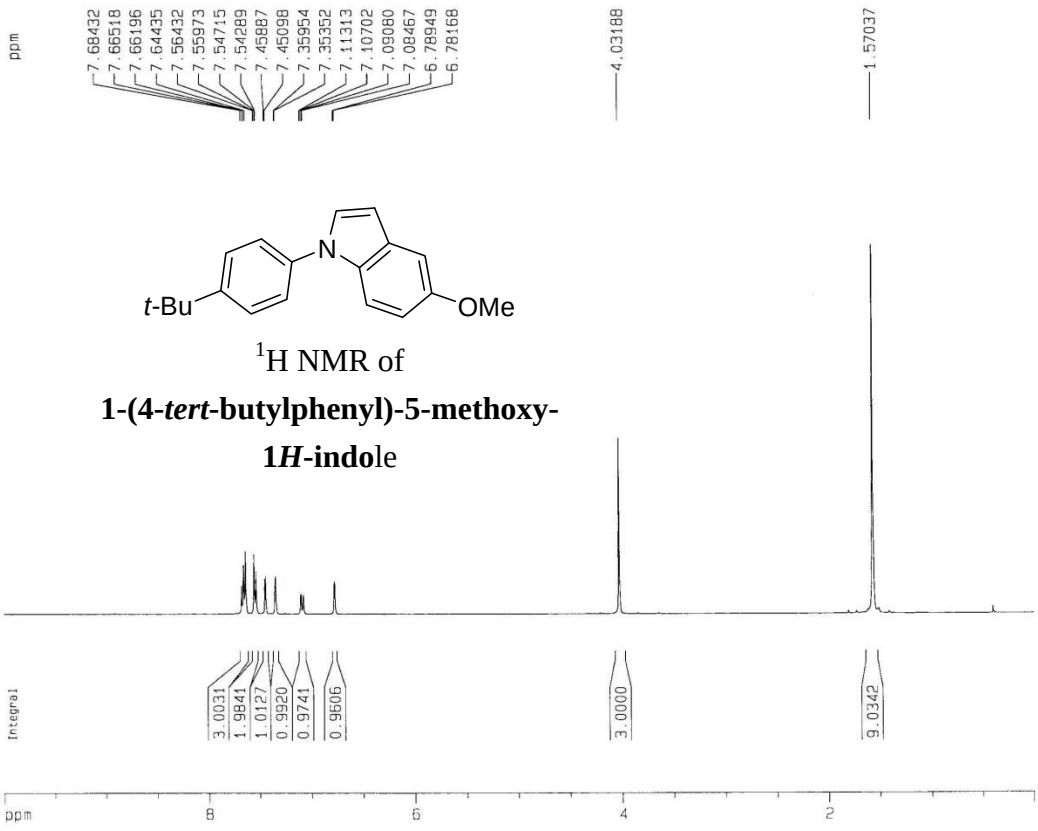
^{13}C NMR of

4-[methyl(phenyl)amino]phenyl tosylate



MS of

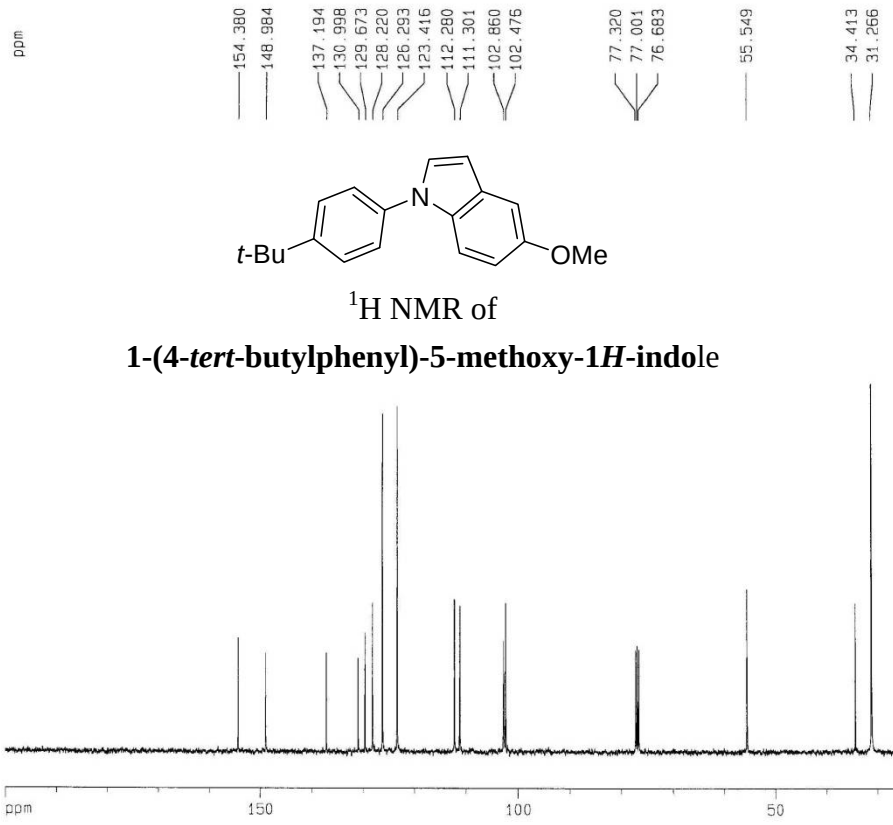
4-[methyl(phenyl)amino]phenyl tosylate



^{1}H NMR of

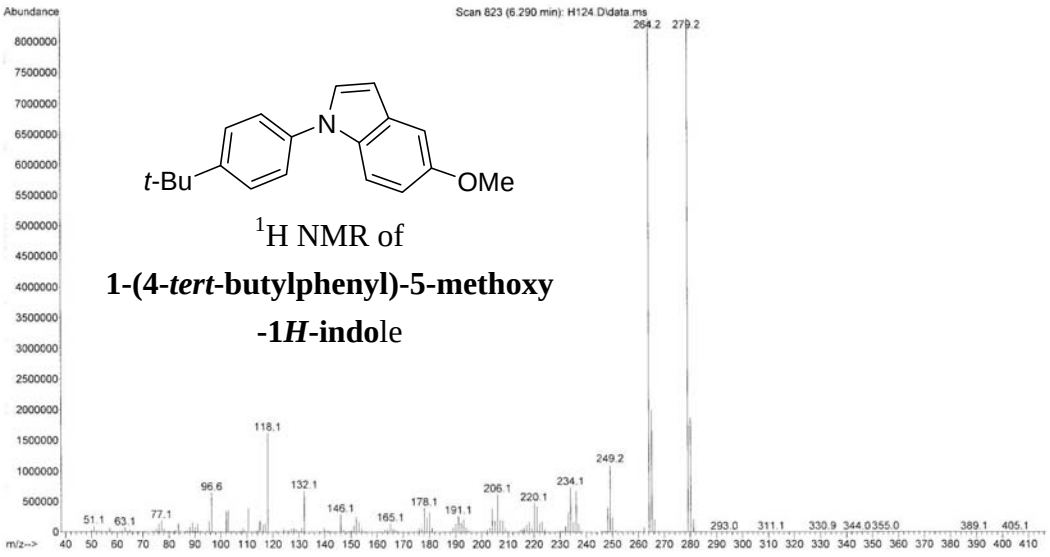
1-(4-*tert*-butylphenyl)-5-methoxy-

1*H*-indole



^{1}H NMR of

1-(4-*tert*-butylphenyl)-5-methoxy-1*H*-indole



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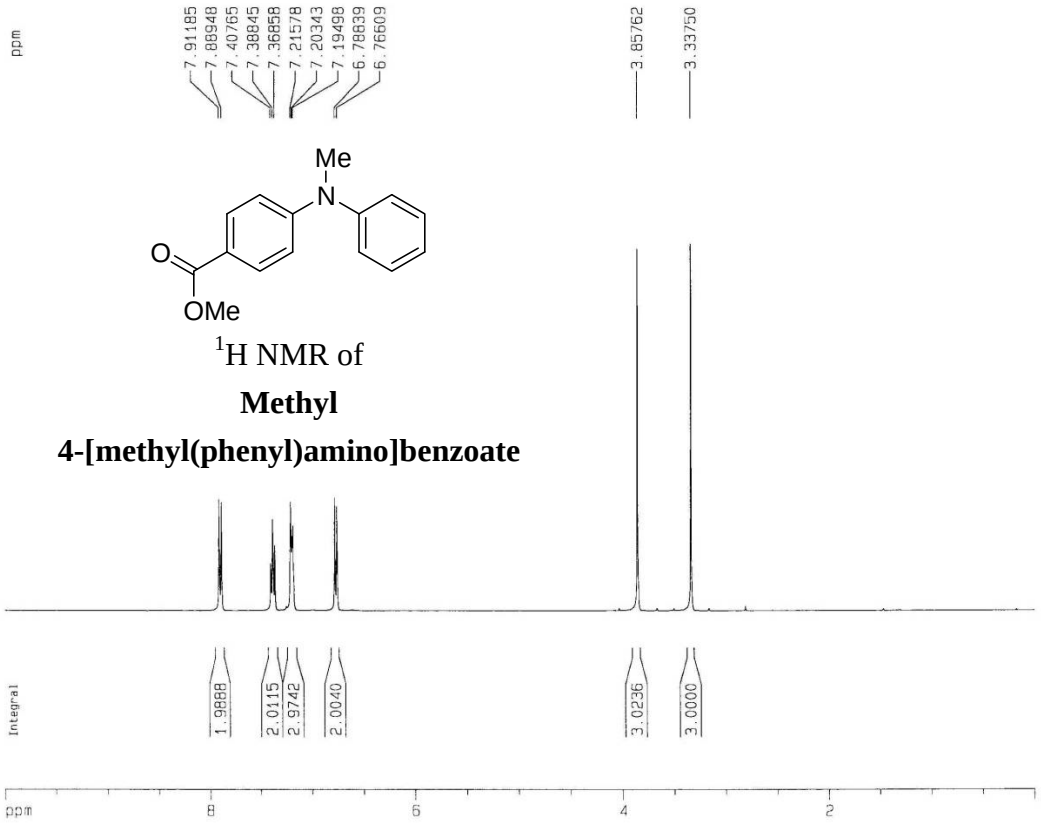
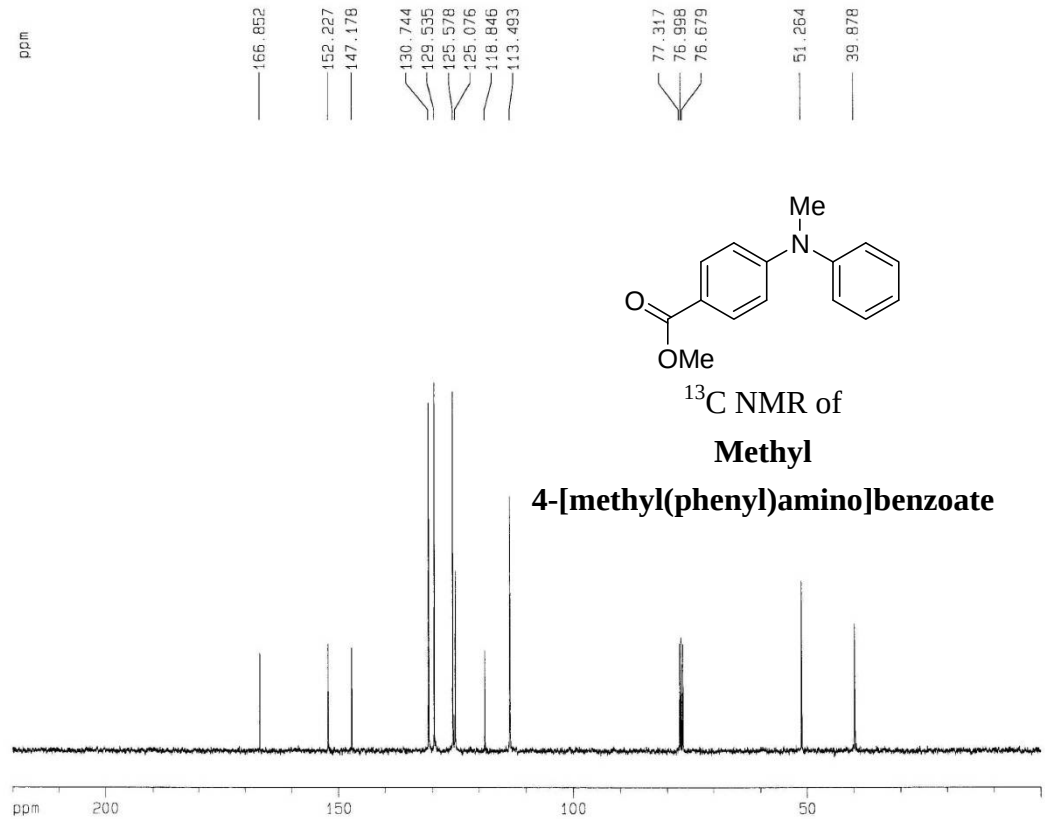
1-(4-*tert*-butylphenyl)-5-methoxy-1*H*-indole



^{1}H NMR of

Methyl

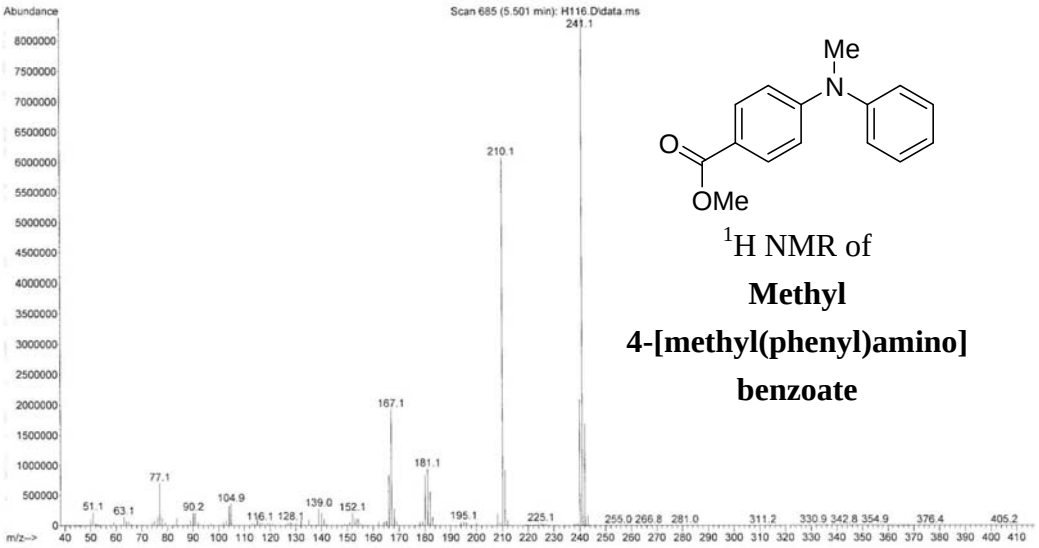
4-[methyl(phenyl)amino]benzoate



^{13}C NMR of

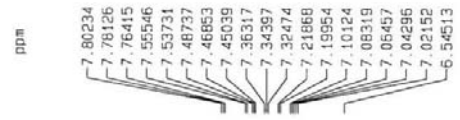
Methyl

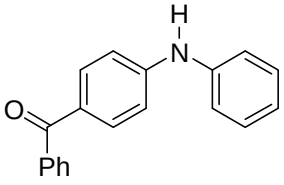
4-[methyl(phenyl)amino]benzoate



^{1}H NMR of

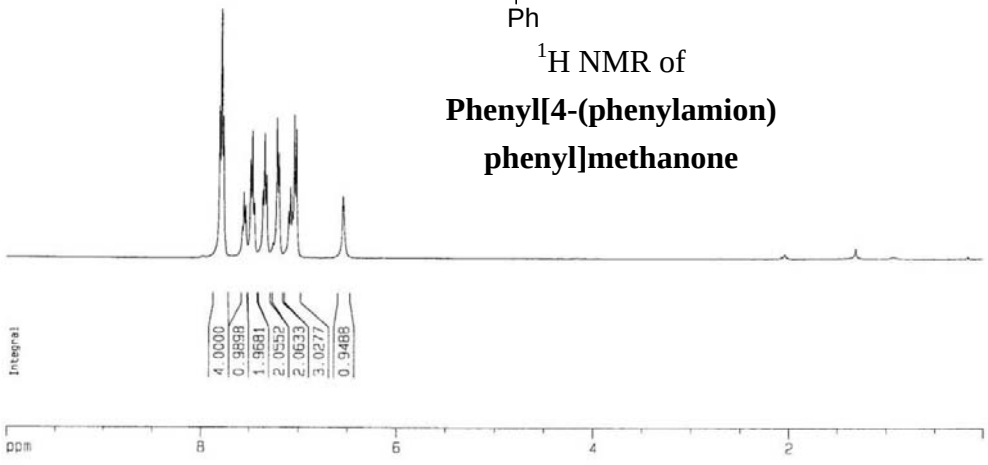
Methyl 4-[methyl(phenyl)amino] benzoate

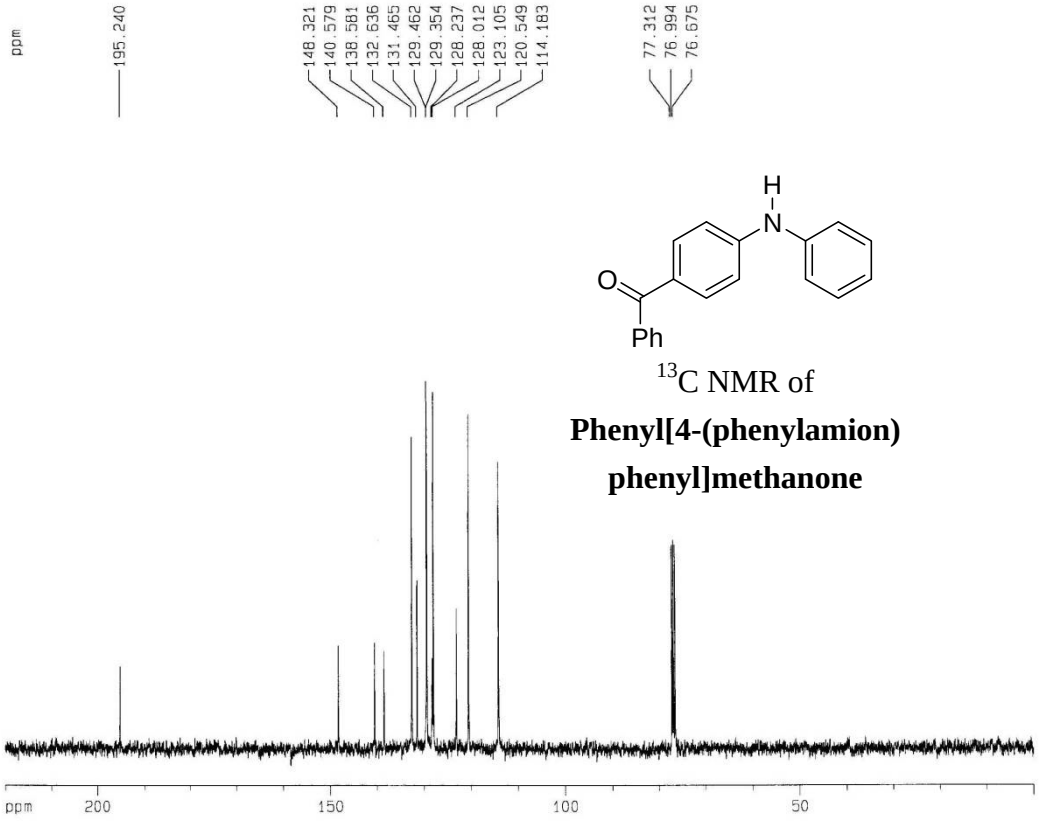




^{1}H NMR of

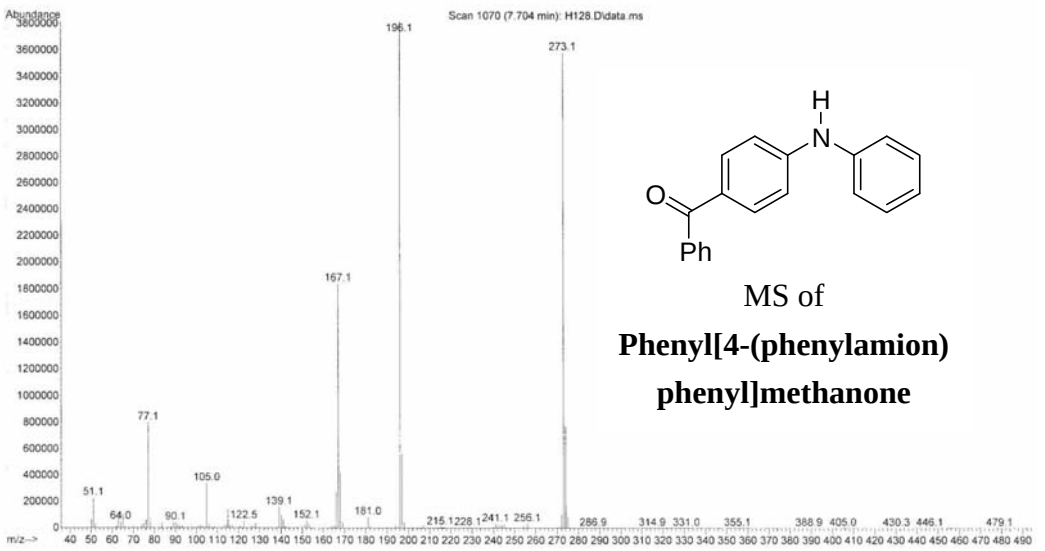
Phenyl[4-(phenylamion) phenyl]methanone





^{13}C NMR of

Phenyl[4-(phenylamion) phenyl]methanone



MS of

Phenyl[4-(phenylamion) phenyl]methanone

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