TRANSITION METAL-CATALYZED OXIDATIVE C-H BOND FUNCTIONALIZATION REACTIONS

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Transition Metal-Catalyzed Oxidative C-H Bond Functionalization Reactions

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A thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy

August, 2015

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.

Yuen On Ying

August, 2015

Abstract

Abstract of thesis entitled “Transition Metal-Catalyzed Oxidative C-H Bond Functionalization Reactions”

Submitted by On-Ying YUEN

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in August 2015

Transition metal-catalyzed C-H bond functionalization for the construction of carbon-carbon and carbon-heteroatom bonds that has numerous applications in pharmaceutical, material, and agricultural chemistry has received much attention in the past decade. It is more straightforward and attractive alternative to traditional cross-coupling reactions with organometallic reagents because of better atom economy, environmental friendliness and more streamlined chemical synthesis. Although significant advances to this field have been reported during the past decade, several challenges remains such as difficulty in activation of inert C-H bond and control of site selectivity. This thesis is to explore transition metal-catalyzed cross-coupling reactions through C-H bond functionalization.

In the first half of this dissertation, four studies on palladium-catalyzed functionalization of C-H bonds are explored. Three studies are concerning oxidative reactions between two nucleophiles while another study is regarding traditional protocol utilizing electrophiles and nucleophiles. Firstly, a palladium-catalyzed oxidative Mizoroki-Heck reaction of arylsulfonyl hydrazides with alkenes is developed under atmospheric air as the sole oxidant in an open manner. Using

$Pd(OAc)_2$ (OAc= acetate) and inexpensive, air-stable and moisture-stable phenyl isonicotinate (Chapter 2, **L9**) as a catalytic system, the efficiency of the reaction can be significantly enhanced. A wide range of arylsulfonyl hydrazides undergo oxidative Mizoroki-Heck reaction with alkenes smoothly. Good to excellent product yields and excellent regio- and steroselectivity are achieved. Functional groups such as halo and ester are well tolerated under this optimized reaction condition. Importantly, this reaction is conducted under atmospheric air in open manner that can reduce heavy metal wastes and lessen the complication of setting reactions' procedures. Secondly, a direct oxidative C-2-arylation of benzoxazoles using arylsulfonyl hydrazides as the aryl sources is described. A simple catalyst system comprising of $Pd(OAc)_2$ and PPh_3 allows the reactions to proceed smoothly under oxidative reaction conditions. A broad range of arylsulfonyl hydrazides is coupled successfully. Other heteroarenes such as caffeine and benzothiazole are also applicable substrates. Notably, this catalytic system tolerates halogen substituents that offer complement to current cross-coupling reactions which use aryl halides. Thirdly, a general and simple method of copper-mediated direct and regioselective oxidative C3-cyanation of 2,3-unsubstituted indoles using benzyl cyanide as the cyanide anion source is developed. A wide range of indoles undergo cyanation smoothly by employing an inexpensive reaction system of copper(I) iodide under open-to-air vessels. Lastly, the first general examples of direct coupling of heteroaryl chlorides, especially substituted 2-pyridyl chlorides as electrophile in which they were previously found to be problematic, with electron deficient polyfluoroarenes as nucleophiles are reported. $Pd(OAc)_2$ associated with PCy_2-Phendolephos (Chapter 5, **L1**) serves as the effective catalyst which allows the challenging direct coupling of heteroaryl chlorides and polyfluoroarenes to be succeeded. In addition to heterocycles, a wide range of non-activated and activated aryl chlorides and alkenyl chloride are

also applicable under this catalyst system. A variety of functional groups such as aldehyde, keto, ester, nitile and amide is well tolerated. The catalyst loading down to 1 mol% Pd can be achieved.

In the second half of dissertation, two studies with regard to traditional cross-coupling reactions of aryl chlorides with organometallic reagents are carried out. Firstly, palladium-catalyzed Hiyama cross-coupling reaction of aryl and heteroaryl chlorides with aryl and heteroaryltrialkoxysilanes under solvent-free reaction condition is presented. The catalyst system comprising of $Pd(OAc)_2$ and PCy_2-Andolephos (Chapter 6, **L2**) is a highly effective for this coupling reaction with low catalyst loading (down to 0.05 mol% Pd) and short reaction time (3 h). A broad substrate scope containing electron-rich, -neutral, and –deficient and sterically hindered aryl chlorides is achieved. Notably, the first general examples of Hiyama cross-coupling reaction using heteroaryltrialkoxysilanes are demonstrated. The presence of acetic acid or water suppresses the decomposition of aryl chlorides and promotes the product yields. A large scale experiment without degasification and purification of reactants is also conducted smoothly. Last but not least, a general palladium-catalyzed borylation of aryl chlorides with pinacol borane is reported. A newly modified indolylphosphine ligand (Chapter 7, **L18**) is prepared via an efficient protocol involving Fischer indolization from readily available phenylhydrazine and 2'-hydroxyacetophenone. The combination of $Pd(dba)_2$ and newly modified indolylphosphine ligand (Chapter 7, **L18**) are shown to be an effective catalyst for the borylation of non-activated and activated aryl chlorides with pinacol borane. Addition of tetra-*n*-butylammoniumiodide (TBAI) is highly effective for coupling of aryl chlorides bearing function groups such as keto, nitile and ester. 1 mol% Pd catalyst loading can be achieved using this catalytic system.

Publications

1. Chow, W. K.; Yuen, O. Y.; So, C. M.; Wong, W. T.; Kwong, F. Y. Carbon-Boron Bond Cross-Coupling Reaction Catalyzed by -PPh_2 Containing Palladium-Indolylphosphine Complexes, *J. Org. Chem.* **2012**, *77*, 3543-3548.

2. Yuen, O. Y.; So, C. M.; Wong, W. T.; Kwong, F. Y. Direct Oxidative C-H Arylation of Benzoxazoles with Arylsulfonyl Hydrazides Promoted by Palladium Complexes, *Synlett* **2012**, *23*, 2714-2718.

3. Yuen, O. Y.; Choy, P. Y.; Wong, W. T.; Kwong, F. Y. Synthesis of 3-Cyanoindole Derivatives Mediated by Copper(I) Iodide using Benzyl Cyanide, *J. Org. Chem.* **2013**, *78*, 3374-3378.

4. Chow, W. K.; Yuen, O. Y.; Choy, P. Y.; So, C. M.; Lau, C. P.; Wong, W. T.; Kwong, F. Y. A Decade Advancement of Transition Metal-Catalyzed Borylation of Aryl Halides and Sulfonates, *RSC Adv.* **2013**, *3*, 12518-12539.

5. Yuen, O. Y.; Wong, S. M.; Chan, K. F.; So, C. M.; Kwong, F. Y. A General Suzuki-Miyaura Coupling of Aryl Chlorides with Potassium Aryltrifluoroborates in Water Catalyzed by An Efficient CPCy Phendole-phos-palladium Complex, *Synthesis* **2014**, *46*, 2826-2832.

6. Yuen, O. Y.; Charoensak, M.; So, C. M.; Kwong, F. Y. A General Direct Arylation of Polyfluoroarenes with Heteroaryl and Aryl Chlorides Catalyzed by Palladium Indolylphosphine Complexes, *Chem. Asian J.* **2015,** *10*, 857-861.

7. Wong, S. M.; Yuen, O. Y.; Choy, P. Y.; Kwong, F. Y. When Cross-Coupling Partners Meet Indolylphosphines, *Coord. Chem. Rev.* **2015**, *293-294*, 158-186.

8. Wong, S. M.; Choy, P. Y.; Yuen, O. Y.; So, C. M.; Kwong, F. Y. Palladium-catalyzeed Buchwald-Hartwig Amination and Suzuki-Miyaura Cross-coupling Reaction of Aryl Mesylates, *Org. Synth.* **2015**, *92*, 195-212.

9. Wong, S. M.; Yuen, O. Y.; Choy, P. Y.; So, C. M.; Kwong, F. Y. Preparation of 2-(2-(dicyclohexylphosphino)phenyl)-1-methyl-1*H*-indole (CM-phos), *Org. Synth.* **2016**, *93*, 14-28.

10. Yuen, O. Y.; So, C. M.; Man, H. W.; Kwong, F. Y. A General Palladium-Catalyzed Hiyama Cross-Coupling Reaction of Aryl and Heteroaryl Chlorides, *Chem. Eur. J.* **2016**, *accepted*.

11. Yuen, O. Y.; So, C. M.; Kwong, F. Y. Open-Air Oxidative Mizoroki-Heck Reaction of Arylsulfonyl Hydrazides with Alkenes, *RSC Adv.* **2016**, *manuscript under revision*.

12. Yuen, O. Y.; So, C, M.; Kwong, F. Y. Palladium-Catalyzed Borylation of Aryl Chlorides with Pinacol Borane, to be submitted to *J. Org. Chem. manuscript in preparation*.

13. Yuen, O. Y.; So, C. M.; Kwong, F. Y. Palladium-Catalyzed Direct Arylation of Isophorones with Aryl Chlorides, to be submitted to *Chem. Commun. manuscript in*

preparation.

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Abbreviations

δ	Chemical shift (NMR)
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
equiv.	Equivalent
h	Hour
min	minute
rt	Room temperature
L	Generalized ligand
THF	Tetrahydrofuran
MeOH	Methanol
EtOH	Ethanol
Et_2O	Diethyl ether
EA	Ethyl acetate
DMF	*N*, *N*-dimethyl formamide
DCM	Dichloromethane

DME	1,2-Dimethoxyethane
t-BuOH	*tert*-Butanol
t-AmOH	*tert*-Amyl alcohol
$ClPPh_2$	Chlorodiphenylphosphine
$ClPCy_2$	Chlorodicyclohexylphosphine
dba	dibenzylideneacetone
n-BuLi	*n*-Butyllithium
R	Generalized alkyl group
Me	Methyl
Et	Ethyl
n-Bu	*n*-butyl
i-Pr	*iso*-propyl
t-Bu	*tert*-butyl
Ar	Aryl
Ph	Phenyl
Bn	Benzyl
Cy	Cyclohexyl
Ac	Acetyl
Ad	Adamantyl
Tol	Toluene
OTf	Trifluoromethanesulfonate
OTs	*p*-Toluenesulfonate
OMs	Methanesulfonate
NHC	*N*-Heterocyclic Carbene

Chapter 1 Introduction

1.1 Introduction to transition metal-catalyzed C-H functionalization

1.1.1 Background and challenges of C-H functionalization

Functionalizing traditionally inert C-H bonds represents a powerful tool in organic synthesis. C-H bonds embedded in complex molecules are transformed into a wide range of other functional groups such as C-O, C-S, C-X, C-N and C-C bonds which have widespread applications in the synthesis of pharmaceuticals, natural products, polymers and agrochemicals.[1]

Although transition metal-catalyzed cross-coupling reactions between organic (pseudo) halides and stoichiometric amounts of organometallic reagents are widely studied for the construction of C-C bonds and C-X bonds, direct C-H bonds functionalization reactions are more attractive. The organometallic reagents are often not readily available or are relatively high cost. They usually prepared from the corresponding arenes through a series of synthetic operations. Undesired byproducts are generated in the course of the preparation of organometallic reagents. Therefore, direct reactions through cleavage of C-H bonds represent an environmentally and economically more attractive protocols which can minimize the formation of side products and allow for streamlining organic synthesis.[2]

Direct C-H bond functionalization reactions still remain two major challenges: (1) the inert nature of most C-H bonds that have the inherently high bond dissociation energies and (2) the control of site selectivity in complex molecules that contain diverse C-H groups.[1,3] The harsh reaction conditions such as very high temperature and the presence of strong oxidants and acidic or basic additives are frequently necessitated for functionalizing C-H bonds. Poor compatibility with most functional groups would be exhibited.[4]

Different approaches have been introduced over the past decade in order to address the main challenges in direct C-H functionalization reactions: (1) substrate-based control over selectivity through the use of directing groups, (2) substrate control through the use of electronically activated substrates and (3) catalyst-based control. For approach 1, functionalizations tend to occur at the C-H bonds *ortho* to a directing group. For instance, a strongly coordinating nitrogen-containing directing group is typically required to promote facile cyclometallation. For approach 2, the substrates have a significant electronic or steric bias for metalation at a specific site. Electron rich heterocycles are common targets for this approach. For approach 3, metal complexes are specifically applied in direct C-H bond functionalization and they can be tailor-made through the unique ligand design. The site selectivity can be tuned by modifying the structure of the supporting ligands on the metal catalyst.[5]

In this thesis, our aim was to develop the transition metal-catalyzed mild, regio-, and chemoselective method to functionalize C-H bonds and the corresponding products are essential building blocks in natural products, bioactive molecules, functional materials and pharmaceuticals.

1.2 Oxidative cross-coupling reactions

1.2.1 Palladium-catalyzed oxidative Mizoroki-Heck Reactions

Mizoroki-Heck reaction is one of the powerful protocols to form carbon-carbon bonds. The vinylic C-H bonds in terminal alkenes is directly transformed to synthesize 1,2-disubstituted alkenes in high steroselectivity. Stereodefined alkenes are commonly structural motifs in many biologically relevant molecules, for example, chalcone derivatives have biological activities (antiparasitic, antibacterial, anticancer)

and diketo acids and their amino acid/ dipeptidic analogues are for the development of bacterial methionine aminopeptidase inhibitors (Figure 1.1).[6]

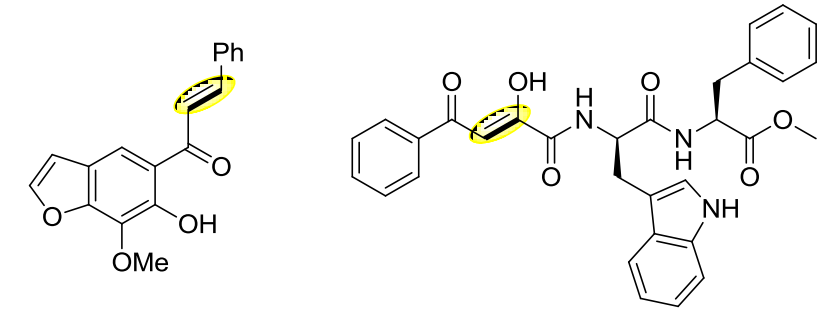


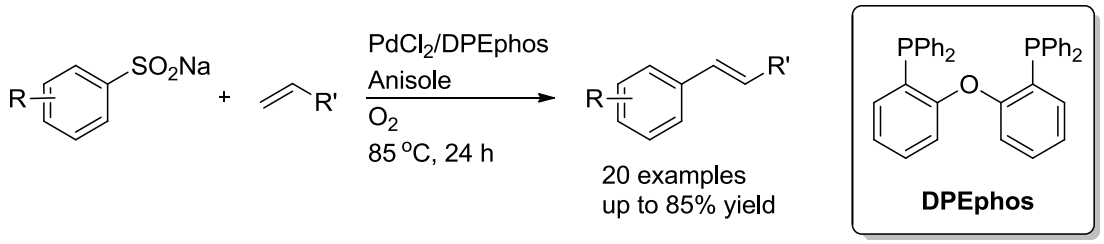
Figure 1.1 Examples of biological molecules containing alkene motifs

Since Mizoroki[7] and Heck[8] discovered the first palladium-catalyzed arylation or vinylation of alkenes with organic halides, numerous modifications of the Mizoroki-Heck reaction have been carried out. For the traditional Mizoroki-Heck reaction, different types of aryl sources including aryl halides,[9] aryl sulfonates,[10] aryldiazonium salts[11] and arylsulfonyl chlorides[12] are utilized. For oxidative Mizoroki-Heck reaction,[13] the scope of aryl sources has been significantly expanded to aromatics,[14] arylcarboxylic acids,[15] arylboronic acids or esters,[16] arylphosphonic acids,[17] aryl sulfinic acids or their sodium salts,[18] aryl hydrazines,[19] arylsulfonyl hydrazides,[20] aroyl hydrazides[21] and carbazates.[22]

1.2.1.1 Development of palladium-catalyzed oxidative Mizoroki-Heck Reactions through cleavage of carbon-nitrogen and/or carbon-sulfur bonds

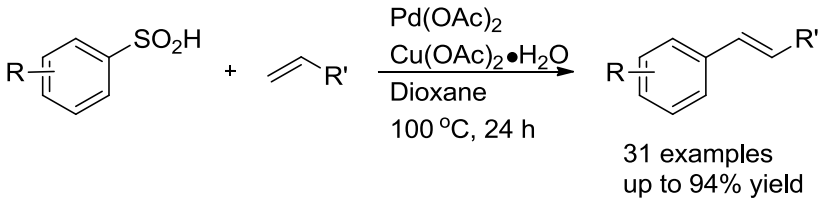
The cross-coupling reactions through cleavage of the unreactive carbon-nitrogen and/or carbon-sulfur bonds are rarely reported among oxidative Mizoroki-Heck reactions.

In 2011, Deng and coworkers reported palladium-catalyzed desulfitative Heck-type reaction of aryl sulfinic acid sodium salts with alkenes using oxygen as the oxidant (Scheme 1.1).[18a] The reaction conditions were milder than those using aryl carboxylic acids as cross-coupling partners. The loss of SO_2 occurred at 85 ^oC which was much lower than the loss of CO_2. They found that in the combination of $PdCl_2$ and DPEphos as a catalyst system in anisole, a variety of aryl sulfinic acid sodium salts with alkenes gave the desired products in high yield and selectivity.



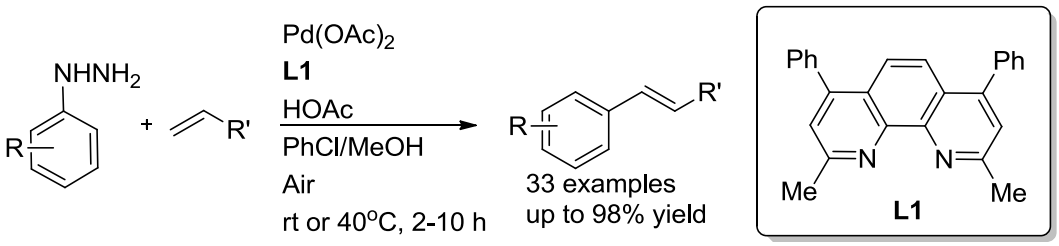
Scheme 1.1 Palladium-catalyzed Heck reaction of aryl sulfinic acid sodium salts with alkenes

Later on, Miao and coworkers have developed an efficient protocol for palladium-catalyzed desulfitative Heck-type reaction of aryl sulfinic acids with alkenes (Scheme 1.2).[18b] In the presence of the catalytic amount of $Pd(OAc)_2$ and $Cu(OAc)_2{\cdot}H_2O$ as oxidant, a wide range of aryl sulfinic acids coupled with alkenes afforded good to excellent product yields.



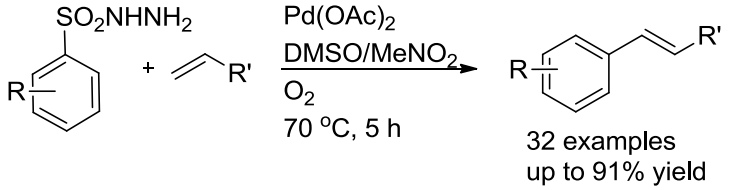
Scheme 1.2 Palladium-catalyzed Heck reaction of aryl sulfinic acids

After that, Loh and coworkers demonstrated palladium-catalyzed Heck reaction of arylhydrazines with alkenes through the cleavage of carbon-nitrogen bond (Scheme 1.3).[19] In the presence of $Pd(OAc)_2$ and bipyridine ligand **L1**, various arylhydrazines reacted with olefins under very mild reaction conditions.



Scheme 1.3 Palladium-catalyzed Heck reaction of arylhydrazines

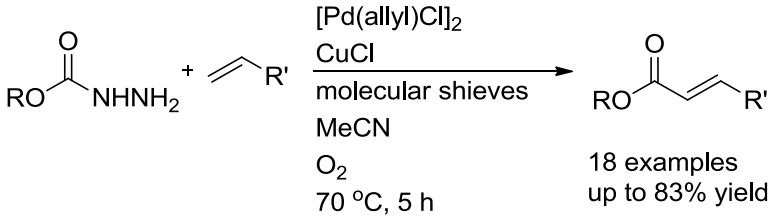
It is difficult to occur for the cleavage of unreactive carbon-nitrogen and carbon-sulfur bonds at the same time. In 2012, Tian and coworkers have developed an unprecedented oxidative Heck reaction of arylsulfonyl hydrazides (Scheme 1.4).[20] In the presence of $Pd(OAc)_2$ and oxygen, a broad range of arylsulfonyl hydrazides underwent oxidative Heck reaction smoothly and afforded desired products in good to excellent yields and with excellent regio- and steroselectivity.



Scheme 1.4 Palladium-catalyzed Heck reaction of arylsulfonyl hydrazides

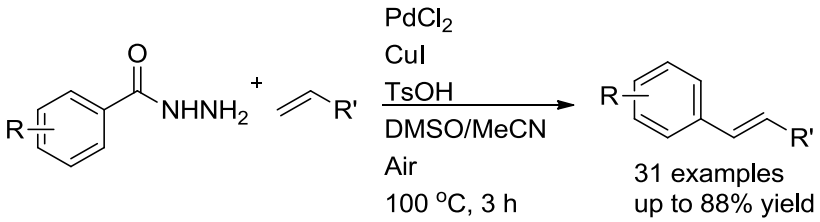
In 2013, they reported palladium-catalyzed oxidative alkoxycarbonylation of alkenes with carbazates (Scheme 1.5).[21] A wide range of alkenes coupled with carbazates smoothly under oxygen atmosphere to generate derivatives of

α,β-unsaturated esters in moderate to good yields with excellent regio- and steroselectivity.



Scheme 1.5 Palladium-catalyzed alkoxycarbonylation of alkenes with carbazates

Afterwards, they have developed palladium and copper-catalyzed oxidative Heck reaction of aroyl hydrazides with alkenes (Scheme 1.6).[22] 1,2-disubstituted alkenes were prepared from aroyl hydrazides open to air in a 1:1 mixture of dimethyl sulfoxide and acetonitrile. They found that oxygen in air and dimethyl sulfoxide were terminal oxidants.



Scheme 1.6 Palladium and copper-catalyzed oxidative Heck reaction of aroyl hydrazides

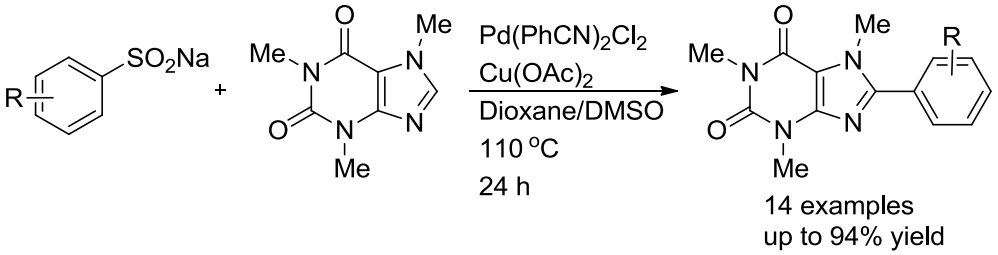
1.2.2 Palladium-catalyzed oxidative direct arylation of heteroarenes

Aryl and heteroaryl compounds are ubiquitous in natural products, bioactive molecules, functional materials and pharmaceuticals.[23] Due to some intrinsic limitations of organometallic reagents, direct C-H functionalization of heteroarenes is another attractive alternative. This cross-coupling protocol has better atom economy, environmental friendliness and more streamlined chemical synthesis.[24,25] In the past decades, great achievements were achieved in transition metal-catalyzed direct C-H

arylation of heteroarenes with aryl halides for construction of aryl and heteroaryl motifs. Apart from aryl halides,[26] the scope has been extended to other arylating agents such as arylsulfonates,[27] aryl silanes,[28] aryl carboxylic acids,[29] aryl sodium sulfonates,[30] and aryl sulfonyl hydrazides.[31]

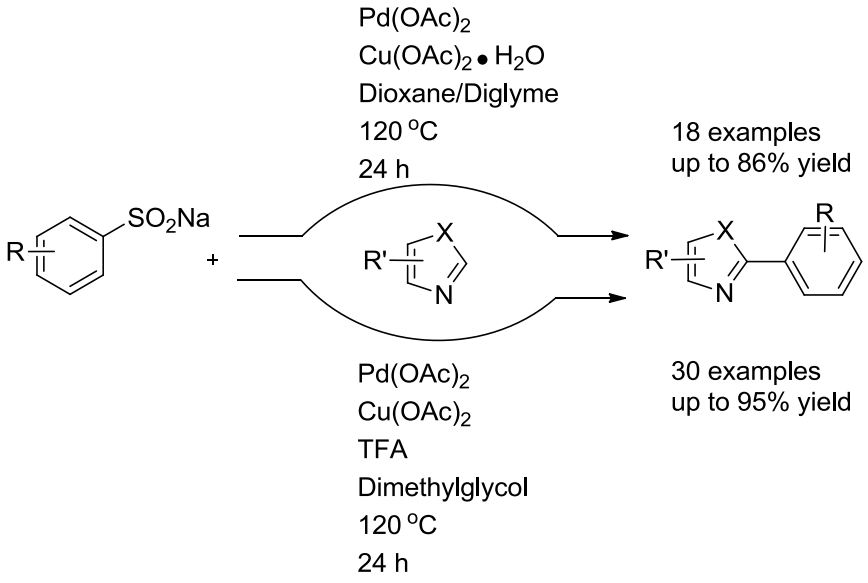
1.2.2.1 Development of palladium-catalyzed oxidative direct arylation of heteroarenes through cleavage of carbon-nitrogen and/or carbon-sulfur bonds

In 2011, You and co-workers reported palladium-catalyzed desulfitative C-H arylation of heteroarenes with sodium sulfonates for the first time (Scheme 1.7).[30a] A wide range of *N*-heteroarenes such as xanthines and azoles was found to be good cross-coupling partners for building aryl-heteroaryl compounds.



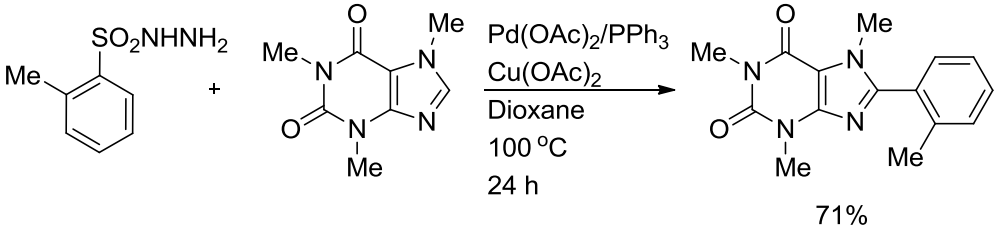
Scheme 1.7 Palladium-catalyzed direct C-H arylation of caffeine with aryl sulfinic acid sodium salt

Deng and Wang demonstrated the same reaction using similar reaction conditions individually (Scheme 1.8).[30b, 30c] A series of aryl-substituted azoles have been synthesized in moderate to good yields.



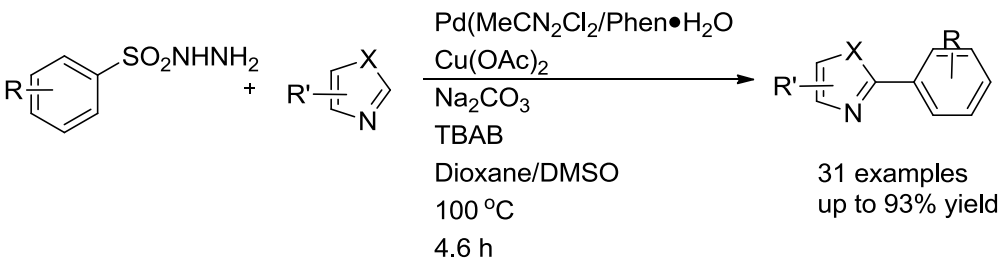
Scheme 1.8 Palladium-catalyzed direct C-H arylation of azoles with aryl sulfinic acid sodium salt

Later on, You and Wan performed palladium-catalyzed direct C-H arylation of *N*-heteroarenes with arylsulfonyl hydrazides individually. You and coworkers carried out the reaction utilizing the combination of $Pd(OAc)_2$ and PPh_3 as a catalyst system and $Cu(OAc)_2$ as an oxidant.[31a] This protocol offers convenient means for constructing aryl-heteroaryl motifs in good to excellent product yields (Scheme 1.9).



Scheme 1.9 Palladium-catalyzed direct C-H arylation of *N*-heteroarenes with aryl sulfonyl hydrazides

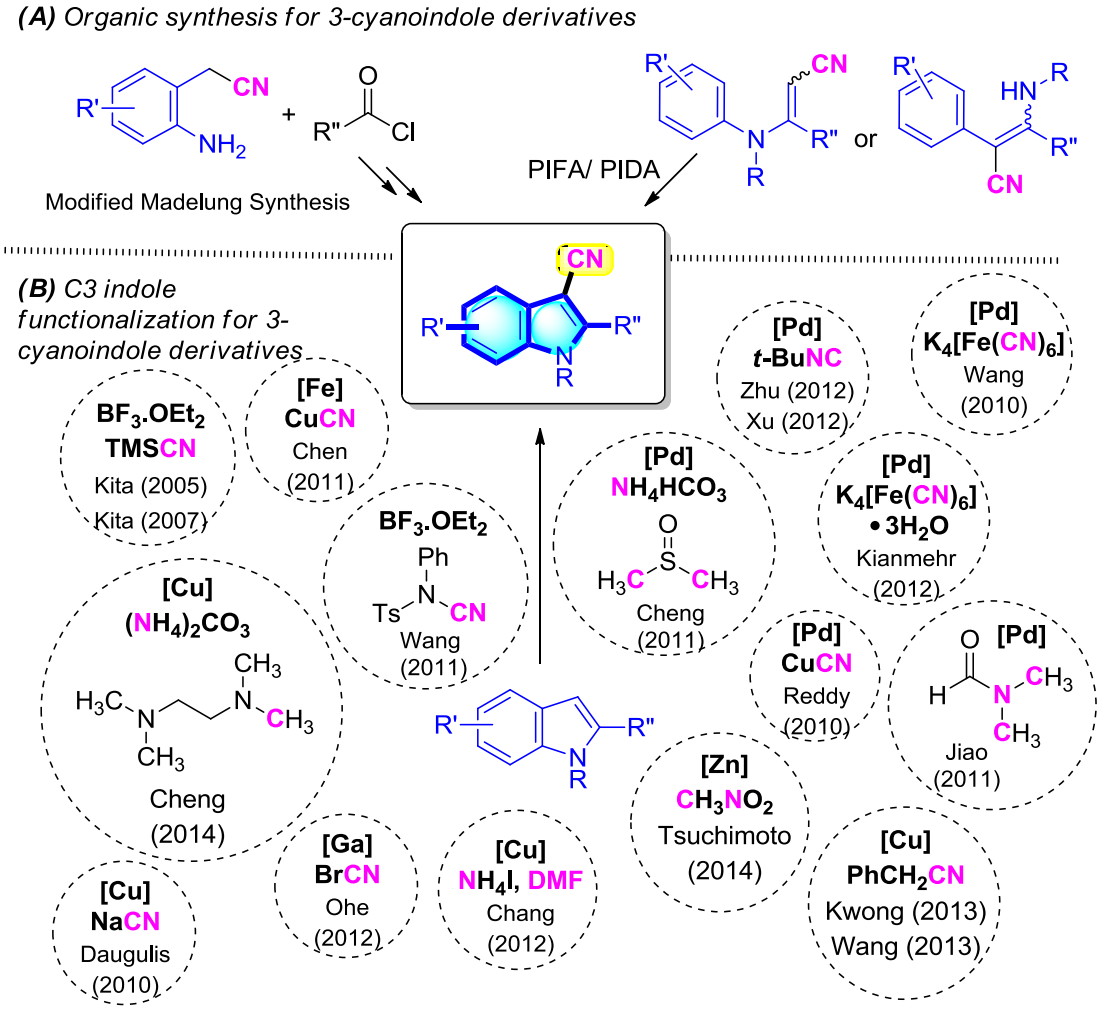
Wan and coworkers employed different catalyst system and reaction condition for this reaction (Scheme 1.10).[31b] A broad range of azoles and arylsulfonyl hydrazides has been coupled to product arylated azoles in high yields.



Scheme 1.10 Palladium-catalyzed direct C-H arylation of azoles with aryl sulfonyl hydrazides

1.2.3 Transition metal-catalyzed cyanation of indole derivatives

Indoles are common structural motifs that are frequently found in natural products, biologically active molecules and pharmaceutical compounds. [32] 3-cyanoindoles are important precursors of antiviral, antibacterial and cytotoxic natural products.[33] In addition, the nitrile moiety can further transform to a wide range of function groups such as amines, aldehydes, acids, ketones, amides and heterocycles. [34] Palladium- and copper-catalyzed cyanation of aryl halides and sulfonates are common protocols to produce aryl nitriles.[35] However, there are few reports regarding cyanation of 3-iodoindole and 3-bromoindole and no reports concerning 3-chloroindole and 3-sulfonylindole. The reaction conditions of cyanation of 3-iodoindolee and 3-bromoindole were harsh and the product yields were unsatisfied. [36] Organic transformations from modified Madelung reaction [37] and metal-free oxidative synthesis from *N*-aryl enamines[38] are alternative approaches to afford 3-cyanoindoles (Scheme 1.11A). Direct C-H functionalization of indole derivatives are attractive protocols to produce 3-cyanoindoles.[39] Lewis acid, Fe, Cu and Pd salts are usually employed as the catalyst for accessing 3-cyanoindole using different cyanide sources (Scheme 1.11B).



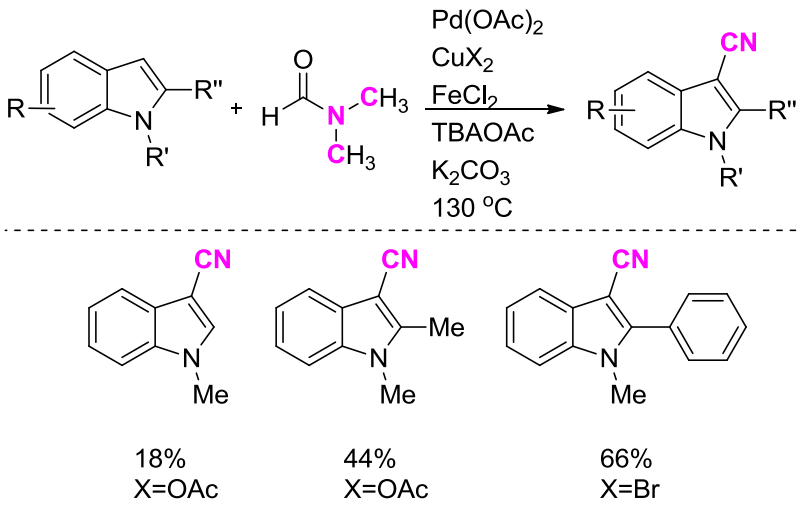
Scheme 1.11 Selected synthetic methods for 3-cyanoindoles using different cyanide sources

1.2.3.1 Development of transition metal-catalyzed cyanation of indole derivatives using organic cyanide sources

Metal cyanide sources have several drawbacks: (1) the metal cyanides employed are generally toxic and careful handling is required to prevent the generation of hazardous HCN gas. (2) environmental issue is raised because metal waste is generated in stoichiometric amounts. (3) a careful control of the cyanide concentration is often required to maintain the catalyst activity.[40] Although $K_4[Fe(CN)_6]$ is exceptionally non-toxic, its low solubility in organic solvent limited its applicability.

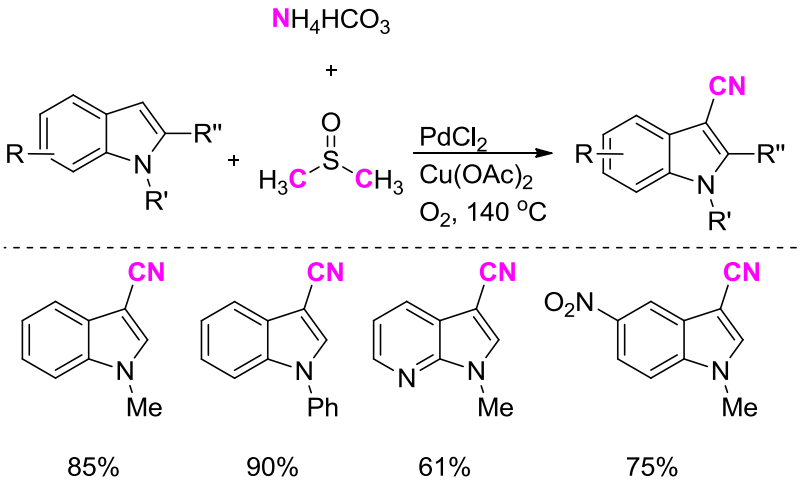
As a result, organic cyanide sources for direct C-3 cyanation of indole derivatives are highly recommended.

In 2011, Jiao and coworker reported palladium-catalyzed cyanation of indoles employing DMF for direct transformation to CN source (Scheme 1.12).[39f] Isotopic labeling experiments indicated that both the nitrogen and the carbon incorporated into the cyano group are derivated from DMF. Apart from indoles, the scope could be extended to benzofuran.



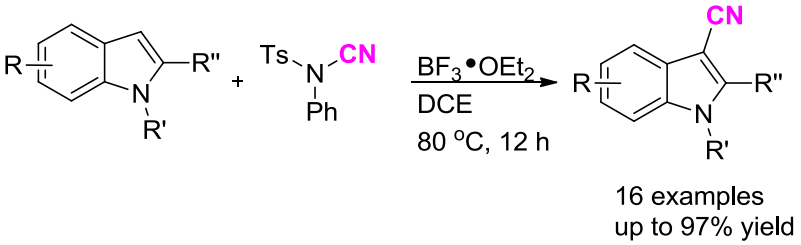
Scheme 1.12 Palladium-catalyzed cyanation of indole employing DMF

Later on, Cheng and coworkers demonstrated palladium-catalyzed cyanation of indoles using the combination of NH_4HCO_3 and DMSO as a CN source (Scheme 1.13).[39g] 3-cyanoindole derivatives were obtained in moderate to good yields with excellent regioselectivity.



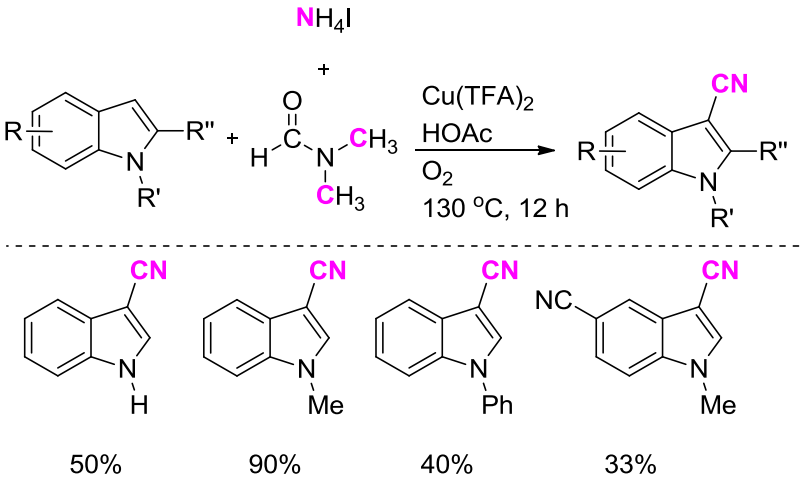
Scheme 1.13 Palladium-catalyzed cyanation of indole using NH_4HCO_3 and DMSO

Lewis acid-catalyzed cyanation of indoles with *N*-cyano-*N*-phenyl-p-toluenesulfonamide (NCTS) was reported by Wang and coworkers (Scheme 1.14).[39h] The reaction was broad in scope with respect to indoles and pyrroles.



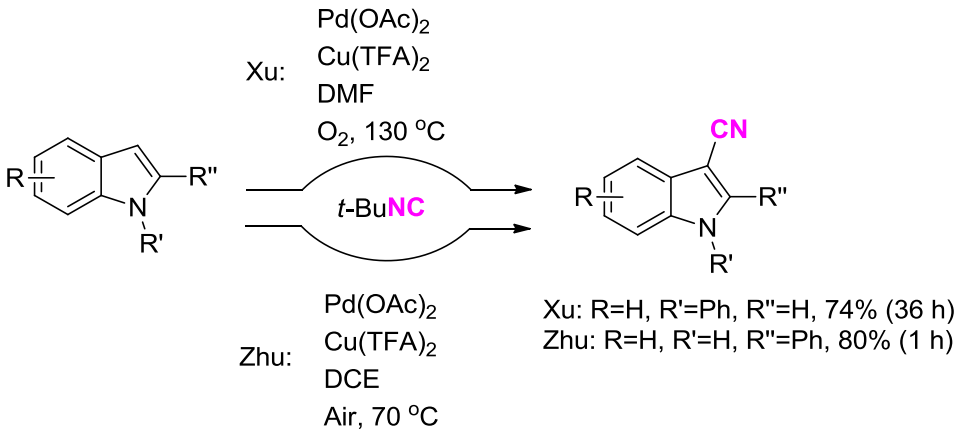
Scheme 1.14 $BF_3{\cdot}OEt_2$-catalyzed cyanation of indoles using NCTS

Copper-mediated cyanation of indoles using ammonium iodide and DMF as a combined CN source was developed by Chang and coworkers (Scheme 1.15).[39j] The reaction proceeded through two sequential steps: initial iodination followed by cyanation. The substrate scope was broad and functional groups were well tolerated.



Scheme 1.15 Copper-mediated cyanation of indoles using ammonium iodide and DMF

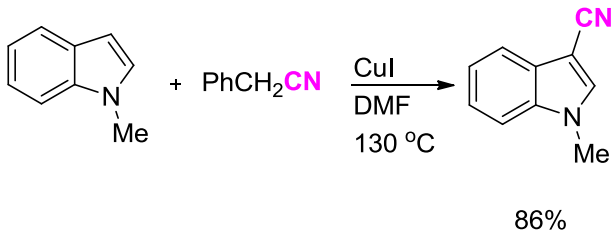
Xu and Zhu reported palladium-catalyzed cyanation of indoles using *t*-butyl isocyanide as a CN source individually (Scheme 1.16).[39k, 39l] Zhu and coworkers found that a key electrophilic imidoyl palladium(II) intermediate is followed by the C-N bond breakage to give cyanated product and a tertiary carbon cation-based fragment.



Scheme 1.16 Palladium-catalyzed cyanation of indoles with *t*-butyl isocyanide

In 2013, Wang and coworkers demonstrated copper-mediated cyanation of indoles with benzyl cyanide using copper iodide as a metal source (Scheme 1.17).[39m]

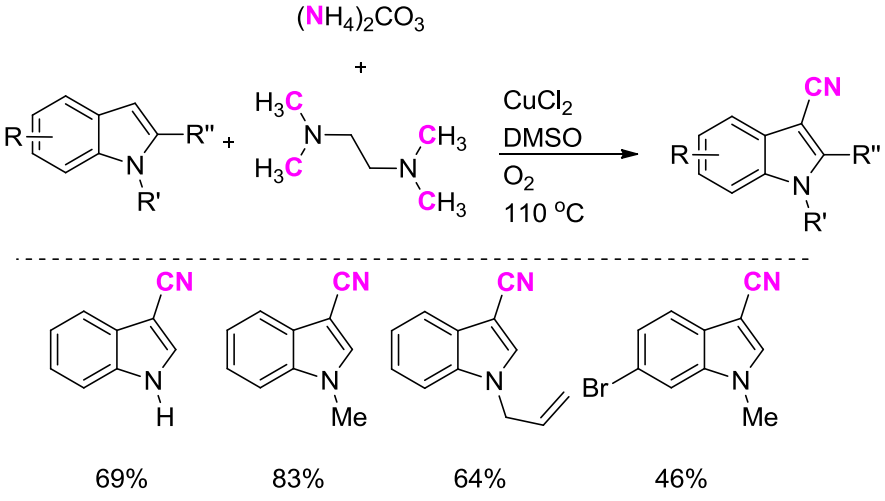
The reaction involved a copper-catalyzed aerobic C-H oxidation, a C-CN bond cleavage and a copper-catalyzed aerobic oxidative C-H functionalization of indoles without directing groups.



86%

Scheme 1.17 Copper-mediated cyanation of indoles using benzyl cyanide

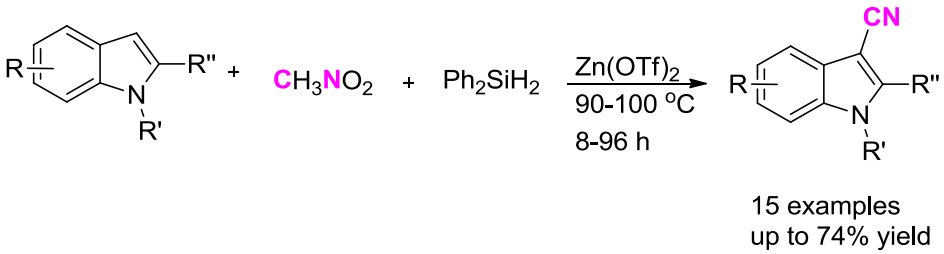
In 2014, Cheng and coworkers demonstrated copper-mediated cyanation of indoles employing *N*, *N*, *N*', *N*'-tetramethyl-ethane-1,2-diamine and $(NH_4)_2CO_3$ as a combined CN source (Scheme 1.18).[39o] *N*, *N*, *N*', *N*'-tetramethyl-ethane-1,2-diamine generated the iminium ion as the intermediate under oxidative condition. The iminium is sequentially electrophilically attacked by indole and water followed by hydrolyzation to form the aldehyde. The reaction between the aldehyde and ammonium afforded 3-cyanoindoles in good to excellent yield.



69% 83% 64% 46%

Scheme 1.18 Copper-mediated cyantion of indoles using amine and ammonium

Tsuchimoto and coworkers reported zinc-catalyzed cyanation of indoles using nitromethane as a CN source (Scheme 1.19).[39q] $Zn(OTf)_2$ acted as lewis acid which promoted the reaction efficiently.



Scheme 1.19 Zinc-catalyzed cyanation of indoles with nitromethane

1.3 Traditional cross-coupling reactions

1.3.1 Transition metal-catalyzed direct arylation of polyfluoroarenes

Polyfluorobiaryl motifs are commonly found in pharmaceutical and material molecules.[41] Fluorine introduced into small molecules has historis merits in drug discovery such as increasing their binding affinity and selectivity to the target proteins,[42] fine tuning lipophilicity[43] and averting metabolism.[44] In material chemistry, polyfluorobiaryl compounds have applications as high mobility *n*-type semiconductors, liquid crystals and optoelectronics.[45] Most importantly, the fluorinated compounds play an important role as active materials in electronic devices, such as organic light-emitting diodes and field-effect transistors. The polyfluorinated aryl group can enhance the photoluminescene efficiency, minimize the self-quenching behavior and lower the HOMO and LUMO energy levels.[45]

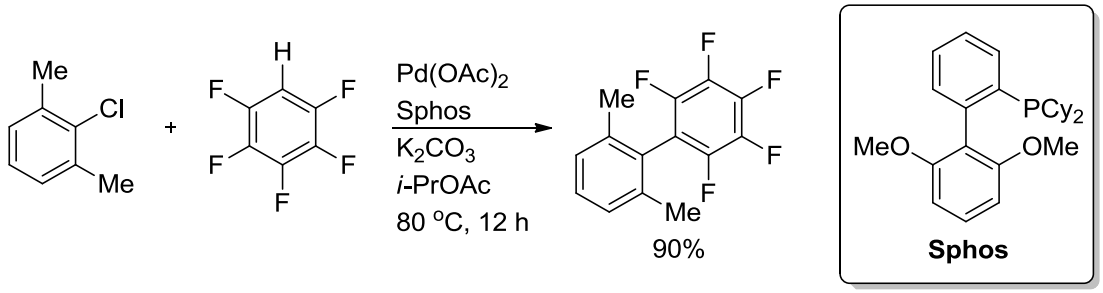
Traditional cross-coupling reactions such as Suzuki,[46] Hiyama,[47] Negishi[48] and Kumada[49] are successful tools for synthesizing biaryl compounds. However, they suffer from some drawbacks. For example, highly electron-deficient nucleophiles ($C_6F_5B(OH)_2$) have the difficulty in preparation. The application of electron-poor

nucleophilic cross-coupling parnters remains problematic due to the transmetallation step may proceed with difficulty.[50] Therefore, the direct arylation of electron-deficient polyfluoroarenes has emerged.[51] These protocols are attractive when compared with conventional coupling methods due to high atom economy and reduction of the metal wastes.

1.3.1.1 Development of direct arylation of polyfluoroarenes with aryl chlorides

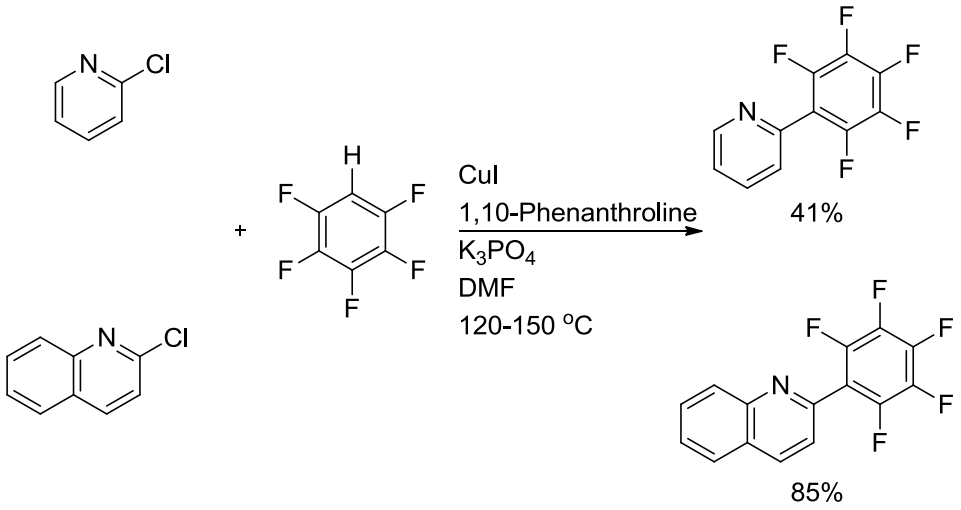
In 2006, Fagnou and coworkers reported the first direct arylation of polyfluoroarenes with aryl halides.[52] In the combination of $Pd(OAc)_2$ and P*t*-$Bu_2Me{\cdot}HBF_4$ as a catalytic system, a wide range of aryl bromides coupled with polyfluoroarenes in good to excellent yields. However, only one examples of aryl chloride was demonstrated and the corresponding product was obtained in moderate yield. Aryl chlorides are generally more desirable than aryl iodides and bromides because of relatively low cost and broad availability.

Later on, they developed mild and general conditions for direct arylation of polyfluoroarenes with sterically hindered aryl bromides and aryl chlorides (Scheme 1.20).[53] The reaction performed at 80 ^{o}C in isopropyl acetate with a catalyst system including $Pd(OAc)_2$ and Sphos. A wide range of aryl and heteroaryl halides were feasible cross-coupling partners under 5 mol% Pd catalyst loading.



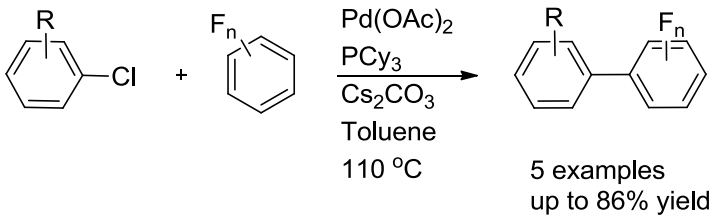
Scheme 1.20 Palladium-catalyzed direct arylation of pentafluorobenzene with sterically hindered aryl chloride

In 2008, they demonstrated copper-catalyzed direct arylation of sp^2 C-H bonds with pKa value below 35 such as azoles, caffeine, thiophenes, benzofuran, pyridine oxides, pyradazine, pyrimidine, and polyfluorobenzenes with aryl halides.[54] However, there are only two examples of aryl chlorides coupled with pentafluorobenzenes (Scheme 1.21).



Scheme 1.21 Copper-catalyzed direct arylation of pentafluorobenzenes with heteroaryl chlorides

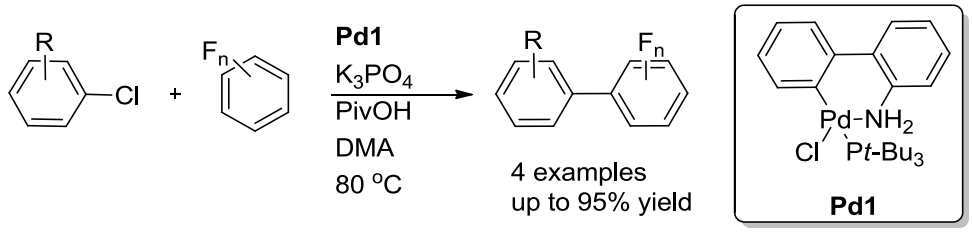
Notable findings showed a great achievement in direct arylation of polyfluorobenzenes with aryl iodides, bromides and sulfonates.[55] However, using aryl chlorides as electrophiles were still keep silent until 2014. Liu and coworkers reported direct arylation of polyfluoroarenes with aryl bromides and chlorides in the combination of $Pd(OAc)_2$ and PCy_3 as a catalyst system (Scheme 1.22).[56] However, 10 mol% Pd catalyst loading was necessitated.



Scheme 1.22 Palladium-catalyzed direct arylation of polyfluoroarenes with aryl

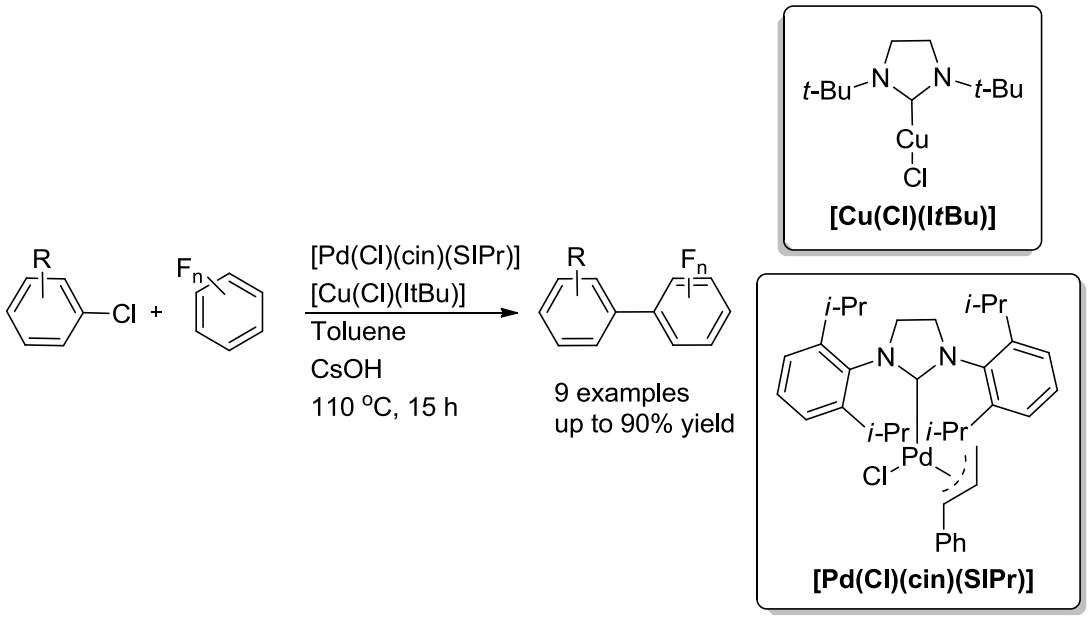
chlorides

A *t*-Bu_3P-coordinated 2-phenylaniline-based palladacycle complex (**Pd1**) was found to be effective precatalyst for direct arylation of polyfluoroarenes with aryl bromides and chlorides (Scheme 1.23).[57] Good to excellent product yields were obtained, yet high catalyst loading (10 mol% Pd) was required for aryl chlorides.



Scheme 1.23 Palladium-catalyzed direct arylation of polyfluoroarenes with aryl chlorides

Cazin and coworkers employed a dual metal system involving [Cu(Cl)(NHC)] and [Pd(Cl)(cin)(NHC)] which was effective for the direct arylation of polyfluoroarenes (Scheme 1.24).[58] However, the substrate scope only limited to non-activated aryl chlorides without any functional groups.



Scheme 1.24 Direct C-H arylation of polyfluorobenzenes using Pd-Cu system

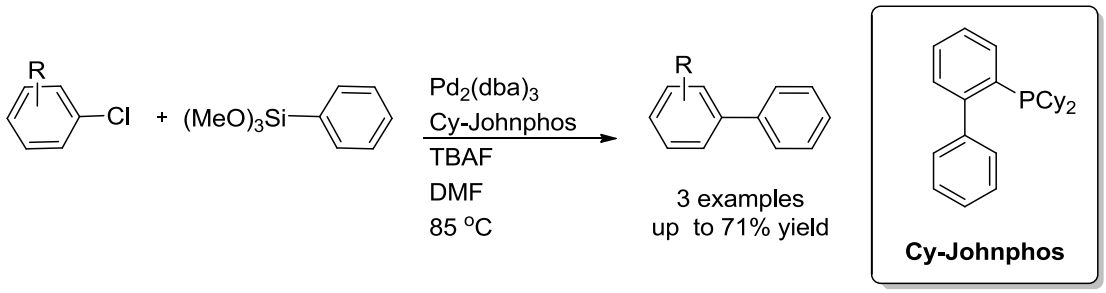
1.3.2 Palladium-catalyzed Hiyama cross-coupling reactions

Palladium-catalyzed cross-coupling reactions constitute an extremely versatile protocol in organic synthesis for the connection of two different fragments via the formation of either carbon-carbon and/or carbon-heteroatom bonds.[59] Hiyama,[47] Kumada,[49] Stille[60] and Suzuki[46] reactions are common methods for the construction of diversified biaryl motifs, which are important in pharmaceutical, material and agricultural applications.[23] Hiyama cross-coupling reaction is one of the potentially most attractive methods because organosilanes are commercially available, low cost, non-toxic, stable and can be easily prepared. However, it constitutes a challenge due to unreactive C-Si bond which has a difficulty in the transmetallation step.

1.3.2.1 Development of palladium-catalyzed Hiyama cross-coupling reaction of aryl chlorides

Although Hiyama cross-coupling reactions are widely studied in the recent years, aryl iodides and bromides as the coupling partners of organosilanes are mainly utilized.[61] Aryl chlorides are highly desirable as they are relatively low cost and readily available.

In 1999, DeShong and coworkers reported the first example of Hiyama cross-coupling of aryl chlorides with aryltrimethoxysilanes (Scheme 1.25).[62] However, only three examples in moderate product yields were demonstrated even through 10 mol% Pd_2dba_3 and Cy-Johnphos were used.



Scheme 1.25 The first palladium-catalyzed Hiyama cross-coupling reaction of aryl chlorides

After that, noticeable findings regarding Hiyama cross-coupling reaction of aryl chlorides and aryltrimethoxysilanes were reported. The catalyst systems such as $Pd(OAc)_2$/Imidazolium chloride (**L2**),[63] palladium-phosphinous acid (POPd1),[64] $Pd(OAc)_2$/DABCO,[65] palladium-*β*-diimine complex (**Pd2**),[66] oxime-derived palladacycles (**Pd3** and **Pd4**),[67] $PdCl_2(MeCN)_2$/P(*o*-Toly)$_3$,[68] $Pd(acac)_2$/phosphite (**L3**),[69] $Pd(dba)_2$/ *i*-Pr-DPEphos,[70] $Pd(dba)_2$/ *H*-phosphonatee (**L4**),[71] $PdCl_2$,[72] $Pd(OAc)_2$/cyclic thiourea (**L5**),[73] palladium on carbon with or without phosphine ligands,[74] $PdCl_2$/ *N*-methyliminodiacetic acid ligand (**L6**)[75] and functionalized SBA-15-supported Pd nanoparticles[76] were effective for Hiyama cross-coupling reaction of aryl halides (Figure 1.2). However, they suffered from several drawbacks. For example, high catalyst loadings (3-7 mol% Pd) were nessciated. The substrate scopes were narrow. Only activated aryl chlorides were found to be feasible cross-coupling partners. Cross-coupling reaction of aryl chlorides with aryltrimethoxysilanes kept silent until 2011.

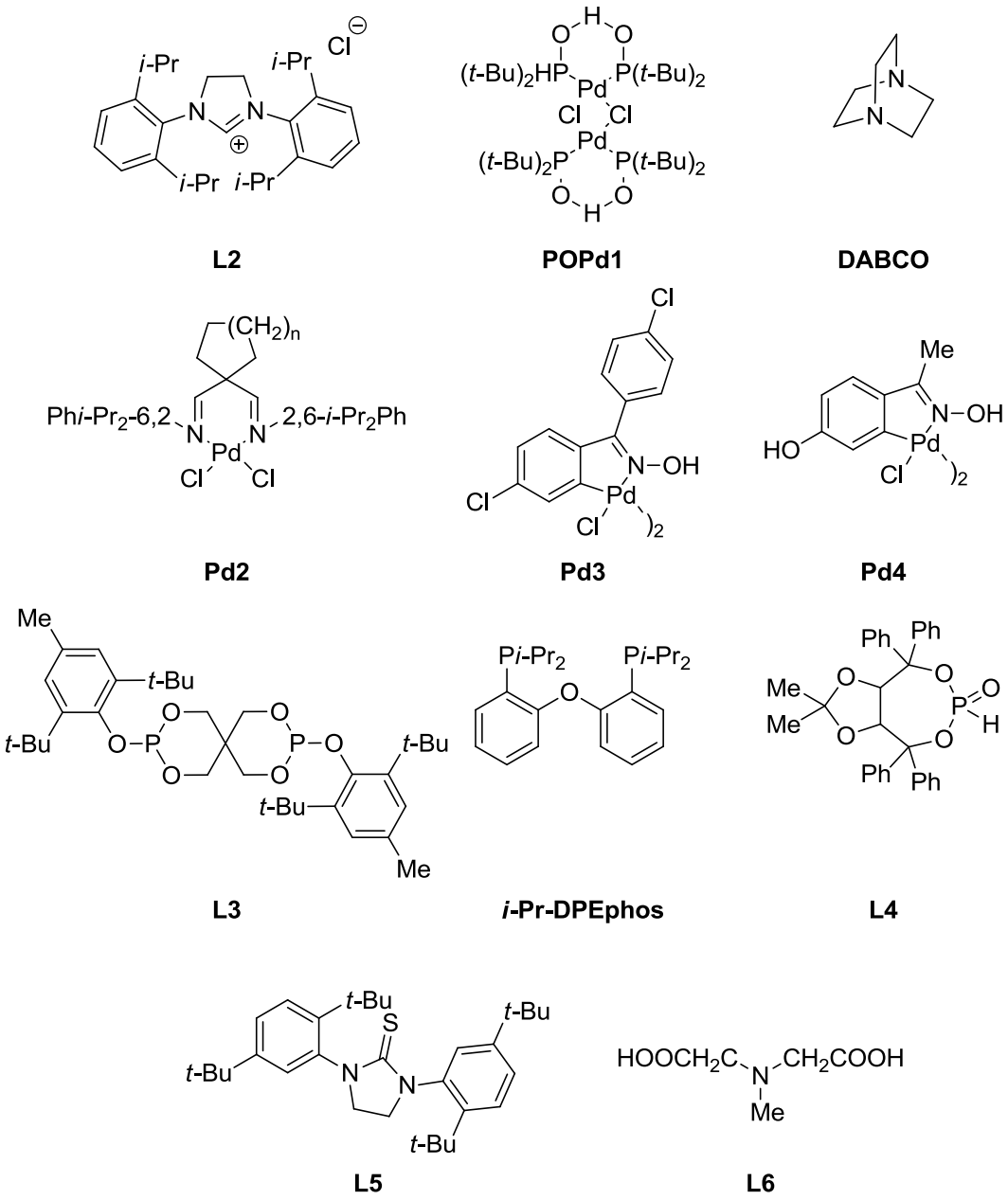
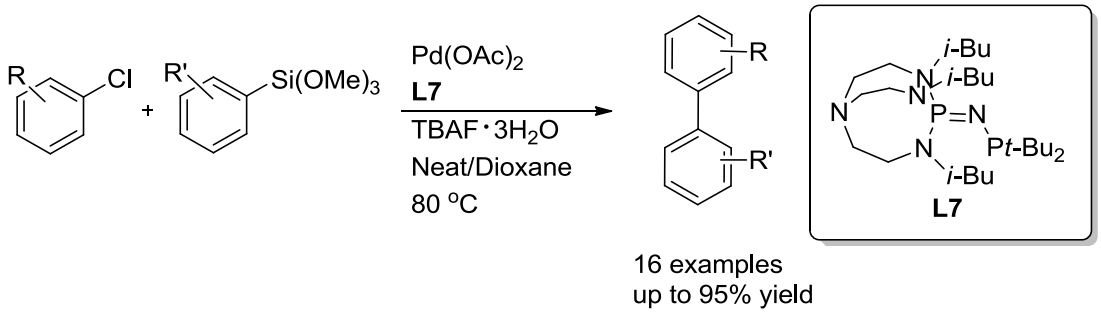


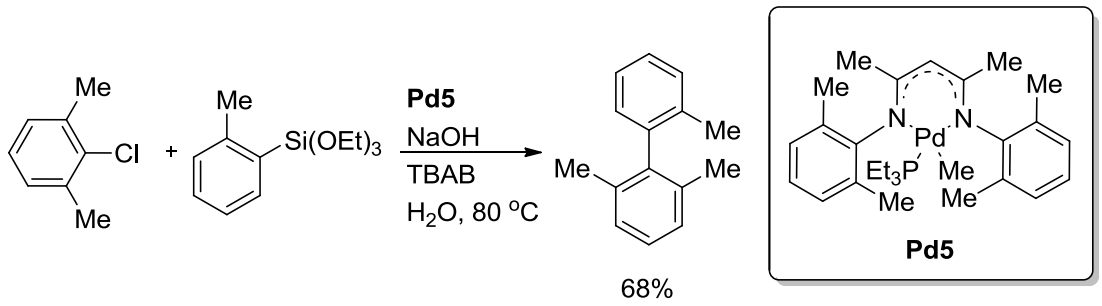
Figure 1.2 Ligands and palladium complexes in Hiyama cross-coupling reactions

In 2011, Verkade and coworkers demonstrated Hiyama cross-coupling reaction of aryl bromides and chlorides employing $Pd(OAc)_2$ and *t*-Bu_2P-N=P(*i*-BuN$CH_2CH_2)_3$N (**L7**) as a catalyst system (Scheme 1.26). [77] Electron-rich, -neutral and -deficient aryl chlorides and heteroaryl chlorides were compatible under their reaction condition. The catalyst loading was ranged from 0.5 mol% to 1 mol% Pd and the reaction was completed within 3 h.



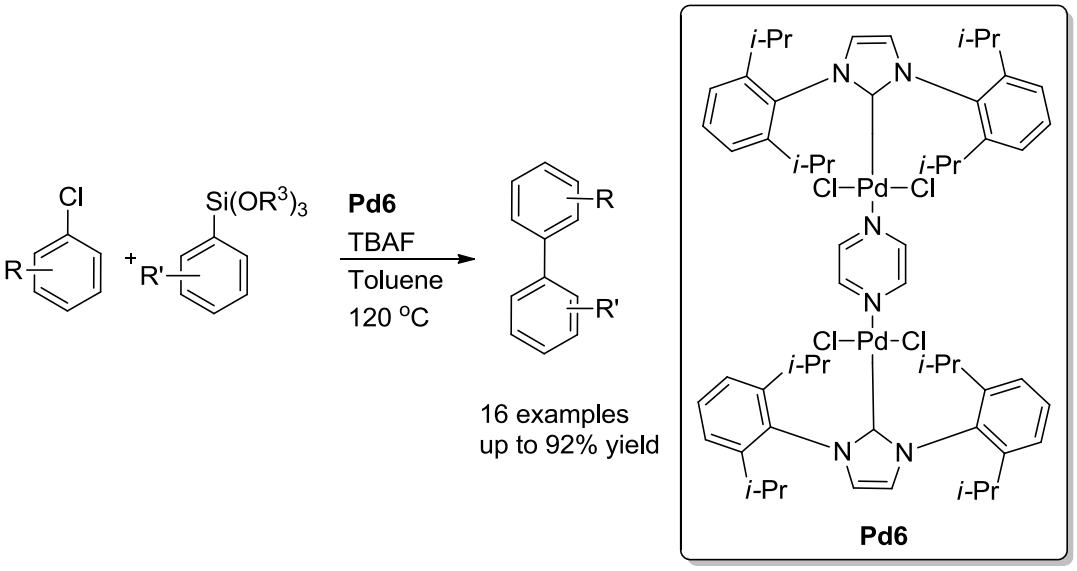
Scheme 1.26 Hiyama cross-coupling reaction of aryl chlorides

Jin and coworkers found that the β-diketiminatophosphane Pd complex was an effective catalyst for Hiyama cross-coupling reaction of a wide range of aryl chlorides and aryltriethoxysilanes in water. Tri-*ortho*-substituted biary synthesis was achieved successfully (Scheme 1.27).[78] The efficient one-pot double Hiyama cross-coupling reaction of aryl dichlorides was realized for the first time.



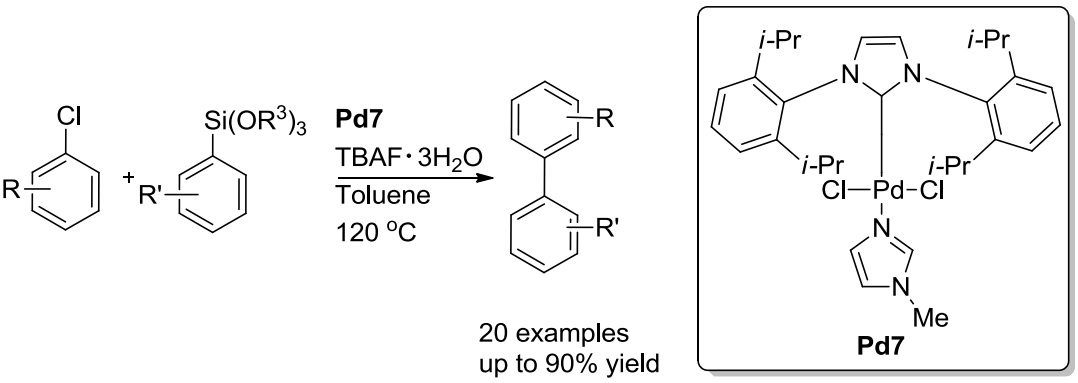
Scheme 1.27 Tri-*othro*-substituted biaryl synthesis through Hiyama cross-coupling reaction

In 2012, Wang and coworkers reported Hiyama cross-coupling reaction of aryltrialkoxysilanes with aryl chlorides using *N*-heterocyclic carbene (NHC)-palladium complexes (Scheme 1.28).[79] A wide range of aryl and heteroaryl chlorides was coupled with phenyltrialkoxysilanes successfully under 0.5 mol% Pd catalyst loading.



Scheme 1.28 Hiyama cross-coupling reaction of aryl chlorides using dinuclear NHC-palladium complex

Later on, Lu and coworkers proved that NHC-Pd(II)-Im complex was an efficient catalyst for the Hiyama cross-coupling of a variety of aryl chlorides with aryltrimethoxysilanes (Scheme 1.29).[80] The reaction performed smoothly and gave the corresponding coupling products in moderate to high yield under 1 mol% Pd catalyst loading. However, the reaction of electron-rich aryl chlorides was still a problem.



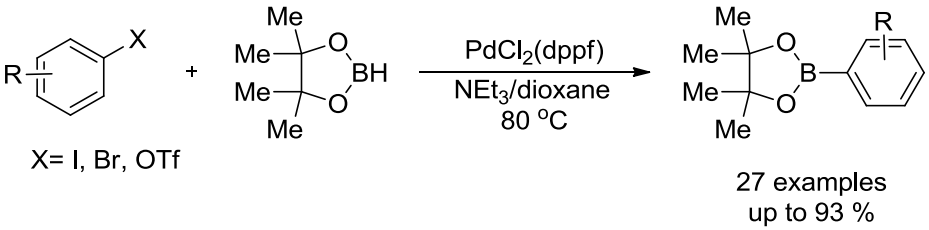
Scheme 1.29 NHC-Pd(II)-Im complex catalyzed Hiyama cross-coupling reaction

1.3.3 Palladium-catalyzed borylation of aryl halides

Aryl boronic acids, boronate esters and potassium trifluoroborate salts are versatile chemical building blocks and intermediates in organic synthesis. They are important nucleophilic partners in the preparation of diversified biaryl compounds through Suzuki-Miyaura cross-coupling reactions.[81] They are usually prepared through the metal-halogen exchange (e.g. Mg or Li) from aryl bromides or iodides and subsequent trapping with trialkylborates. However, this conventional protocol is not compatible with relatively cheaper and commercially available aryl chlorides and aryl halides bearing base-sensitive functional groups (e.g. aldehyde, ketone, nitrile etc.). The additional protection and deprotection steps are required.[81b] As a result, transition metal-catalyzed borylation of aryl halides with alkoxyboroanes has emerged.

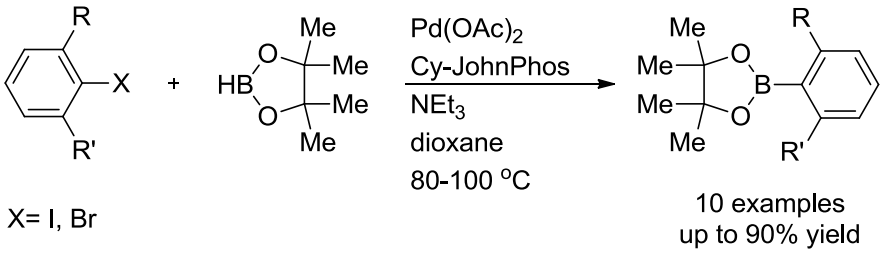
1.3.3.1 Development of palladium-catalyzed borylation of aryl halides with pinacol borane

In 1995, Miyaura and co-workers pioneered a palladium-catalyzed borylation of aryl halides with bis(pinacolato)diboron.[82] Since then, considerable attentions have been focused on palladium-catalyzed borylation of aryl bromides and iodides to construct the corresponding aryl boronate esters.[83] Apart from tetraalkoxydiboranes, dialkoxyboranes are more attractive, readily available, and more atom-economical than diboron reagents. In 1997 and 2000, Masuda found that dialkoxyhydroboranes could serve as effective boron sources for coupling with aryl halides and triflates (Scheme 1.30).[84] Aryl boronate esters bearing a variey of functional groups such as –COMe, -CN and -NO_2 were readily prepared.



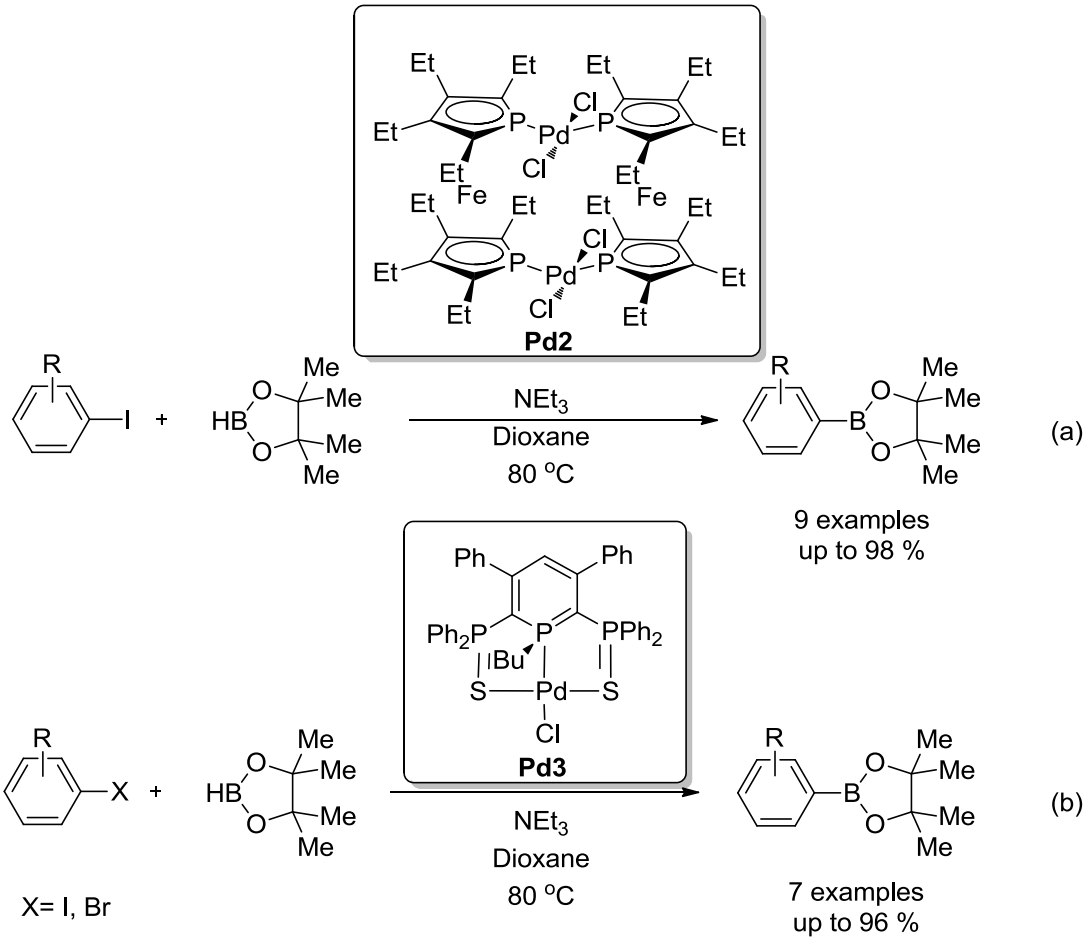
Scheme 1.30 Palladium-catalyzed borylation of aryl halides and triflates with pinacolborane

Baudoin and coworkers demonstrated that a catalyst system combining $Pd(OAc)_2$ with Cy-JohnPhos was effective for the borylation of *ortho*-substituted aryl bromides and iodides (Scheme 1.31). [85] These findings were extended to unprecedented one-pot-two-steps reaction with *ortho*-substituted aryl iodides to synthesize sterically hindered 2,2'-biphenyls.



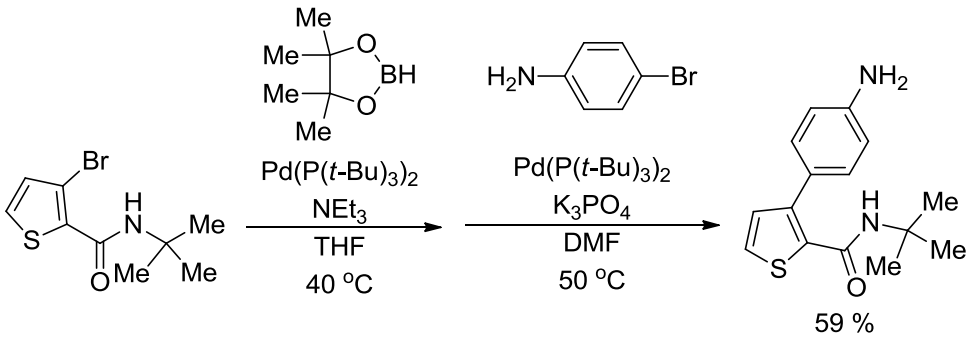
Scheme 1.31 Palladium-catalyzed borylation of *ortho*-substituted aryl halides with pinacolborane

In 2001, Floch and co-workers illustrated borylation of aryl iodides with pinacol borane catalyzed by bis(diphosphaferrocenes)$PdCl_2$ dimers (Scheme 1.32a). [86] Non-activated aryl and heteroaryl iodides coupled with pinacol borane in excellent product yields. Subsquently, they designed a palladium(II) complex of a S-P-S pincer ligand which was applied in borylation of aryl iodides successfully (Scheme 1.32b).[87]



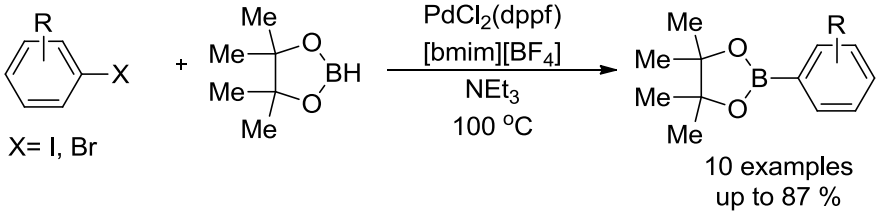
Scheme 1.32 (a) Borylation of aryl iodides with pinacol borane utilizing bis(diphosphaferrocene)$PdCl_2$ dimer. (b) Synthesis of arylboronate esters using a palladium(II) complex of a S-P-S pincer ligand.

In 2003, Christophersen and coworkers developed a protocol for the synthesis of 2-substituted 3-thienylboronic acids and esters as well as 3-substituted 2-thienylboronic acids.[88] A range of 2-substituted 3-bromothiophenes together with 3-substituted 2-bromothiophenes were borylated with pinacol borane by Pd_2dba_3 and P(*t*-Bu)$_3$ as a catalyst system under mild reaction condition. Borylation and subsequent Suzuki-Miyaura cross-couping reaction were demonstrated to afford heteroaryl-aryl compounds without isolation of borate esters (Scheme 1.33).



Scheme 1.33 One-pot-two-step synthesis of 2,3-disubstituted thiophene

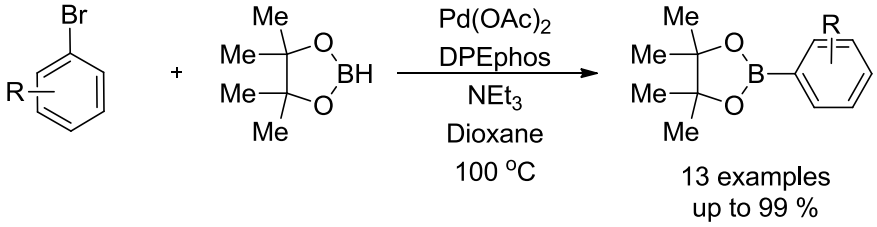
Zaidlewicz and coworkers described palladium-catalyzed borylation of aryl bromides and iodides with pinacolborane in ionic liquids (Scheme 1.34).[89] Their results showed that the reaction time was shorter compared with that using conventional solvents. The benefits of using ionic liquids include that the products could be directly obtained from the reaction mixtures in good purity by simple extraction and the solution of catalyst in ionic liquid could be recycled.



Scheme 1.34 Palladium-catalyzed borylation of aryl halides in ionic liquids

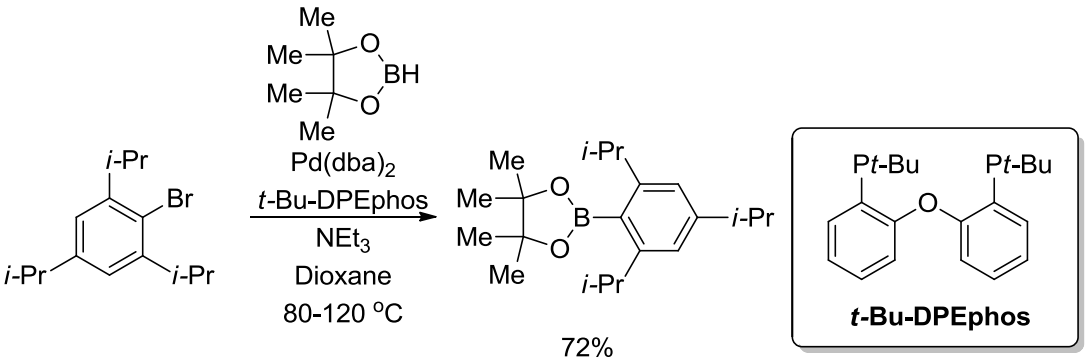
In 2004, Colobert and coworkers described palladium-catalyzed borylation of non-activated and sterically hindered aryl bromides with pinacol boranes in the presence of a catalytic amount of $Pd(OAc)_2$ and DPEphos (Scheme 1.35).[90] Compared with the phosphine ligands in the previous reports for synthesizing *ortho*-substituted aryl boronate esters, the advantage of DPEphos toward dppf is its cheaper availabity and its higher air stability compared to Cy-JohnPhos. These findings were extended to one-pot-two-step Suzuki-Miyaura reaction with different

substituted aryl bromides to synthesize unsymmetrical biaryl compounds.



Scheme 1.35 Palladium-catalyzed borylation of aryl bromides using $Pd(OAc)_2$ and DPEphos catalyst system

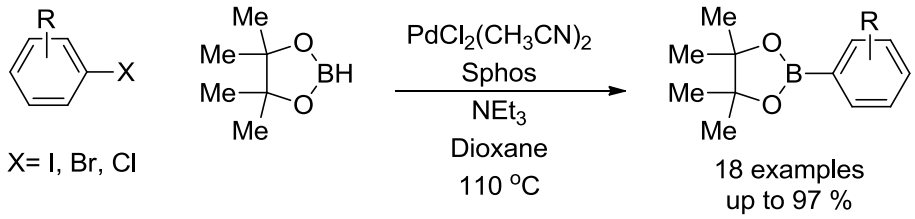
In 2006, Murate and coworkers developed a general method for the borylation of aryl halides with pinacolboranee using $Pd(dba)_2$ and *t*-Bu-DPEPhos as a catalytic system.[91] Electron-rich and deficient aryl bromides were coupled with pinacol borane in good to excellent yields. Extremely sterically hindered aryl bromides also were feasible cross-coupling partners (Scheme 1.36). Particularly, borylation of electron-rich aryl chlorides was reported for the first time although only two examples were demonstrated successfully under 5 mol% Pd catalyst loadings.



Scheme 1.36 Palladium-catalyzed borylation of 2-bromo-1,3,5-triisopropylbenzene

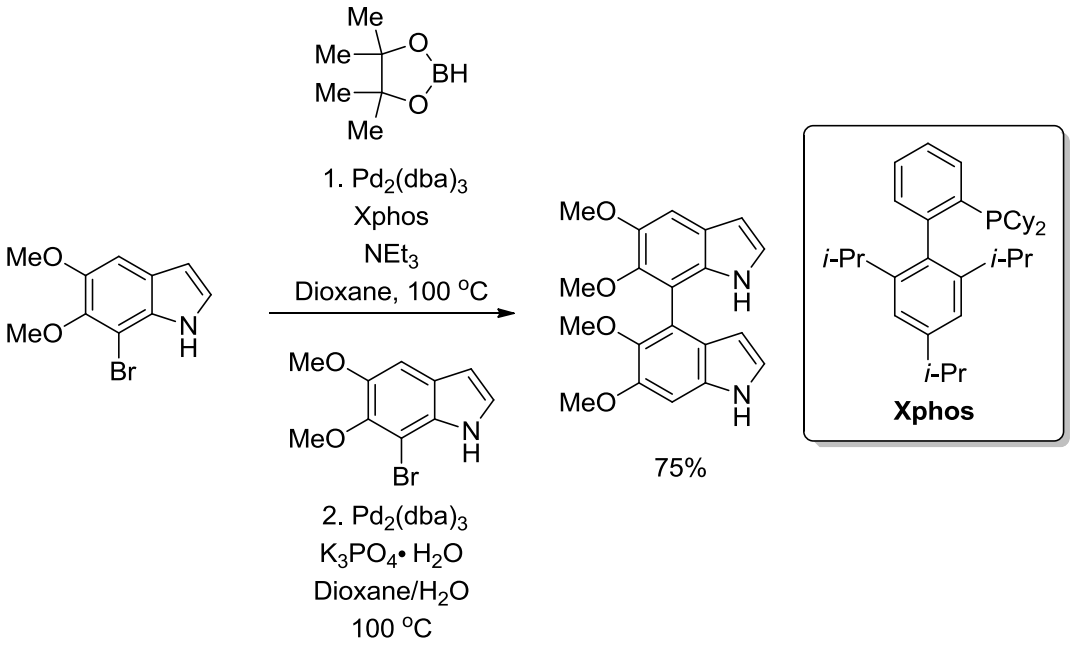
Notably, Buchwald and coworkers found that a $PdCl_2(CH_3CN)_2$ and Sphos catalyst system was efficient for the borylation of aryl halides with pinacolborane (Scheme 1.37).[92] The reaction of aryl iodides and bromides conducted with relative low Pd catalyst loadings and short reaction times. Moreover, this protocol represented

the first general method for the borylation of aryl and heteroaryl chlorides. However, this method was only applicable to non-activated aryl chlorides under 3 mol% Pd catalyst loadings.



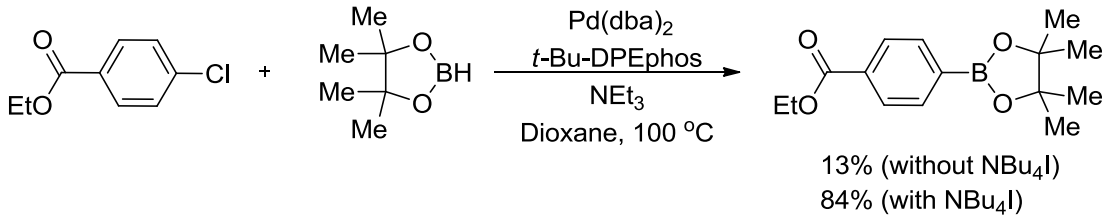
Scheme 1.37 Palladium-catalyzed borylation of aryl halides using $PdCl_2(CH_3CN)_2$ and Sphos catalyst system

Chai and coworkers demonstrated an unprecedented synthesis of a range of high value homo and heterobiindolyls.[93] The borylation of piancolborane and subsequent Suzuki-Miyaura reaction allowed for the construction of biindolyl compounds (Scheme 1.38).



Scheme 1.38 Synthesis of homo and heterobiindolyls through borylation and subsequent Suzuki-Miyaura reaction

The borylation of aryl chlorides bearing electron-withdrawing groups with pinacolborane is still a challenge. The product yields were low because of the formation of reduced arenes competiting with products. In 2010, Murata and coworkers reported the first general palladium-catalyzed borylation of electron-deficient aryl chlorides with pinacolborane using $Pd(dba)_2$ and *t*-Bu-DPEphos as a catalyst system (Scheme 1.39).[94] They found that addition of *n*-Bu_4I could improve the product yields of the corresponding electron-deficient aryl chlorides efficiently. The role of iodide ion may be attributed to the halide ligand exchange of the arylpalladium(II) chloride intermediate.



Scheme 1.39 Palladium-catalyzed borylation of electron-deficient aryl chlorides using tetrabutylammonium iodide

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Chapter 2 Palladium-Catalyzed Oxidative Mizoroki-Heck Reaction of Arylsulfonyl Hydrazides with Alkenes under air

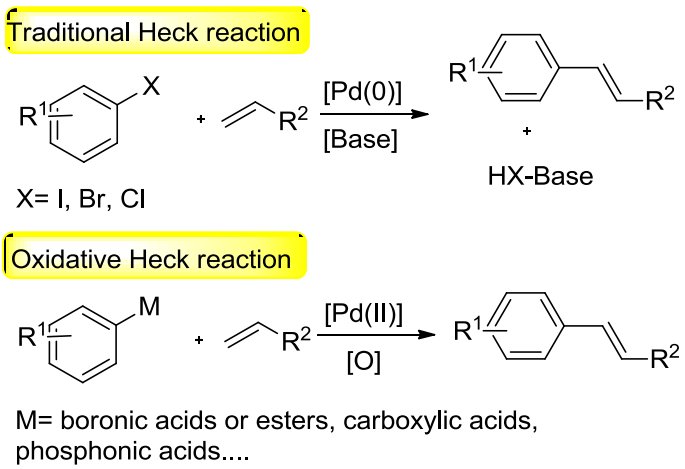
2.1 Introduction

The palladium-catalyzed Mizoroki-Heck reaction is one of the most powerful tools for the formation C-C double bond in organic synthesis[1] and plays an important role in both preparative laboratories and industrial applications.[2] In traditional Heck reaction, aryl halides act as electrophiles and couple with alkenes in the presence of palladium catalysts and bases to produce higher substituted alkenes.[3] Other than aryl halides, aryl sulfonates,[4] aryl diazonium salts,[5] arylsulfonyl halides,[6] and arylcarboxylic acid derivatives[7] are also effective aryl sources in the Mizoroki-Heck type reactions.

Oxidatve Heck reaction is also an excellent pathway to access the substituted alkene products.[8] The most striking difference between traditional Heck reaction and oxidative Heck reaction is the reaction mechanism. The former is that electrophiles act as self-oxidant carrying out oxidative addition to palladium(0) species to form arylpalladium(II) species. The latter is that extra oxidants such as oxygen or copper(II) salts are required to re-oxidize palladium(0) species to palladium(II) species. Aromatics,[9] arylcarboxylic acids,[10] arylboronic acid derivatives,[11] arylphosphonic acids,[12] arylsulfinic acids[13] and its sodium salts,[14] arylhydrazines,[15] carbazates[16] and aroyl hydrazides[17] are effectively couple with alkenes in the oxidative reactions (Scheme 2.1).

Arylsulfonyl hydrazides are recently a rising electrophile which are readily accessible solids, stable in air and moisture and can be easily prepared in one step from arylsulfonyl chlorides and hydrazine hydrates.[18] Particular noteworthy is that they can serve as arylating agents, which are subjected to denitrogenation and

desulfitation to generate the aryl source for the oxidative palladium-catalyzed coupling reactions.[19] Oxidative Heck reaction [19a], oxidative direct arylation of heteroarenes [19b-d], oxidative conjugate addition reaction [19e], oxidative homo-coupling reaction [19f], oxidative Suzuki reaction [19g] and oxidative Hiyama reaction [19h] are reported. However, most of these reactions require excess amount of $Cu(OAc)_2$ or pure oxygen to act as oxidant. The use of $Cu(OAc)_2$ would generate stoichiometric amount of heavy metal waste which is not environmentally benign and reduce the atom economy. Regardless of the use of pure oxygen which may associate with hazardous and dangerous handling (gas tube), the extra gas pressure generates from denitrogenation (N_2) and desulfitation (SO_2) of arylsulfonyl hydrazides under high temperature and the control of the composition of oxygen atmosphere may limit the utility of the technology for industrial applications. Therefore, if the atmospheric air can act as the re-oxidant allowing the open-air manner, the value of the transformation enhances significantly. However, in general, only inferior yield can be obtained in use of air as reaction atmosphere especially for the heck-type reactions.[19a,e]



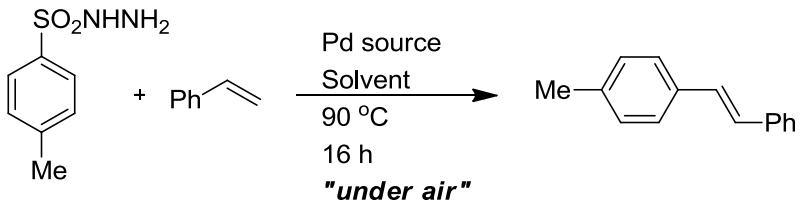
Scheme 2.1 Traditional Heck reaction of aryl halides and oxidative Heck reaction of other aryl sources with alkenes

2.2 Results and discussion

2.2.1 Preliminary evaluation of palladium-catalyzed oxidative Mizoroki-Heck reaction of arylsulfonyl hydrazides with alkenes

In order to test the feasibility of palladium-catalyzed oxidative Mizoroki-Heck reaction of arylsulfonyl hydrazides with alkenes, a series of initial screenings was conducted (Table 2.1). 4-methylbenzenesulfonyl hydrazide and styrene were used as the benchmark substrate. In the survey of common solvents, the solvent DMF gave the best result (Table 2.1, entry 2 and entries 1-11). The initial screening of palladium sources (Table 2.1, entries 12-18) indicated that $Pd(OAc)_2$ was the suitable Pd source for this coupling reaction.

Table 2.1 Initial screening of palladium-catalyzed oxidative Mizoroki-Heck reaction of arylsulfonyl hydrazides[a]



Entry	Catalyst (mol%)	Solvent	%Yield[b]
1	$Pd(OAc)_2$ (10)	Dioxane	40
2	$Pd(OAc)_2$ (10)	DMF	55
3	$Pd(OAc)_2$ (10)	DMA	47
4	$Pd(OAc)_2$ (10)	NMP	40
5	$Pd(OAc)_2$ (10)	DMSO	14
6	$Pd(OAc)_2$ (10)	THF	7
7	$Pd(OAc)_2$ (10)	*t*-BuOH	20
8	$Pd(OAc)_2$ (10)	Toluene	5

9	$Pd(OAc)_2$ (10)	MeCN	13
10	$Pd(OAc)_2$ (10)	PhCN	26
11	$Pd(OAc)_2$ (10)	AcOH	17
12	$Pd_2(dba)_3$ (10)	DMF	15
13	$Pd(TFA)_2$ (10)	DMF	41
14	$Pd(acac)_2$ (10)	DMF	23
15	$PdCl_2(CH_3CN)_2$ (10)	DMF	51
16	$PdCl_2(PPh_3)_2$ (10)	DMF	32
17	$PdCl_2(COD)_2$ (10)	DMF	Trace
18	$PdCl_2$ (10)	DMF	40

[a] Reaction condition: 4-methylbenzenesulfonyl hydrazide (0.45 mmol), styrene (0.3 mmol), Pd source (10 mol%), solvent (3.0 mL) were stirred at 90 ^{o}C for 16 h under air. [b] Calibrated GC yields were reported using dodecane as internal standard.

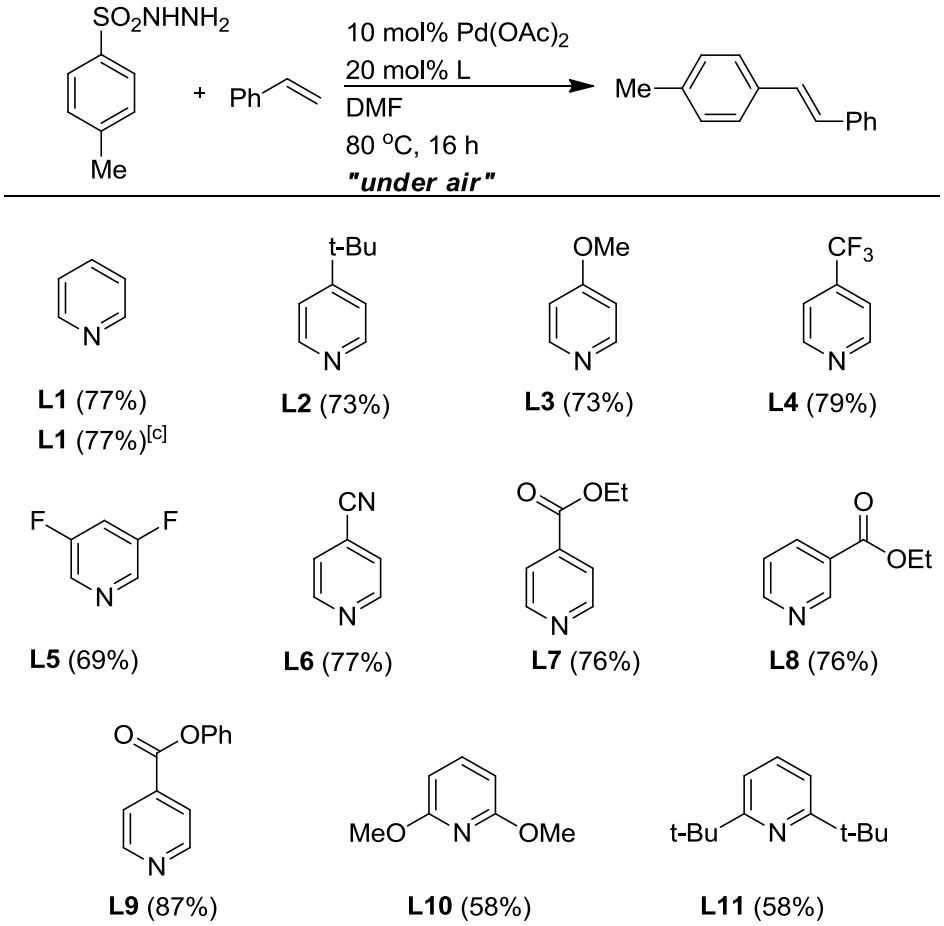
After the detailed screening of solvents and Pd sources, we still found that the product yield was unsatisfied. Inspired by the poor result of $Pd(OAc)_2$/DMSO system which is one of the well-known catalyst system for the palladium-catalyzed oxidative reactions and also analogy to the aerobic alcohol oxidation reaction and oxidative amination of olefins reaction,[20] we suspect that the inferior yield may result from the slow aerobic oxidation of Pd(0) species to Pd(II) especially under air atmosphere which is low oxygen concentration. Pd(0) species easily aggregate and agglomerate to unreactive palladium black and retard the coupling reaction in the ligand-free heck reactions. Oxidatively stable ligands have been identified to enhance the rate of Pd(0) oxidation particularly with respect to competing Pd(0) aggregation so as to promote catalytic turnover, improve catalyst stability and increases regio- and stereoselectivity

of the reaction.[20]

Uemura's $Pd(OAc)_2$/pyridine catalyst system were found to be able to promote the oxidation of Pd(0) to Pd(II) in the aerobic alcohol oxidation reaction.[20] Herein, we adopt the $Pd(OAc)_2$/pyridine catalyst system for the oxidative Heck reaction of arylsulfonyl hydrazides with alkenes for the first time.

We found that when pyridine was added, the product yield improved dramatically from 55 % to 77 % (Table 2.2, **L1**). When the reaction temperature was lowered from 90 ^{o}C to 80 ^{o}C, the product yield was the same. Investigation of different substituted pyridine ligands **L2**-**L11** indicated that phenyl isonicotinate gave the best yield of product (**L9**). Although the electronic inference of the pyridine-type ligands in this oxidative heck reaction is still unclear, sterically hindered pyridine type ligands (**L10**-**L11**) which hinder the facial coordination to Pd center show minor enhancing effect of the product yield imply the importance of the ligand coordination effect.

Table 2.2 Ligand screening for palladium-catalyzed oxidative Mizoroki-Heck reaction of arylsulfonyl hydrazides[a,b]

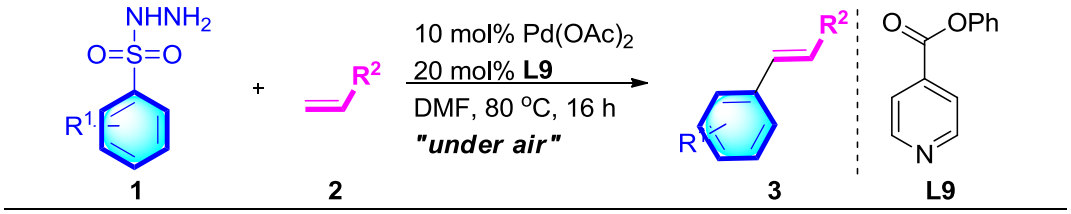


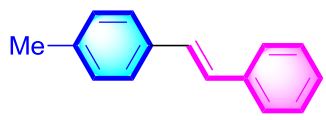
[a] Reaction conditions: 4-methylbenzenesulfonyl hydrazide (0.45 mmol), styrene (0.3 mmol), $Pd(OAc)_2$ (10 mol%), L (20 mol%) and DMF(3.0 mL) were stirred at indicated temperature for 16 h under air. [b] Calibrated GC yields were reported using dodecane as internal standard. [c] The reaction was conducted at 90 °C.

2.2.2 Scope of palladium-catalyzed oxidative Mizoroki-Heck reaction of arylsulfonyl hydrazides with alkenes

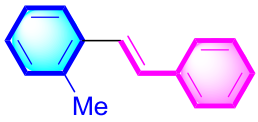
With the $Pd(OAc)_2$/ **L9** system in hand, we next investigated the scope of Mizoroki-Heck reaction of arylsulfonyl hydrazides with alkenes. The results were summarized in Table 2.3. In the presence of 10 mol% $Pd(OAc)_2$, 20 mol% **L9**, a wide range of arylsulfonylhydrazides carried out oxidative Mizoroki-Heck reaction with styrene smoothly to give 1,2-disubstituted alkenes in moderate to excellent yields under air. *Ortho*-substituted arylsulfonyl hydrazides were good combinations for this reaction (Table 2.3, compound 3bk and 3gk). Electron rich arylsulfonyl hydrazide afforded moderate yield (Table 2.3, compound 3hk). The highly sterically hindered arylsulfonyl hydrazide could couple with styrene in moderate yield (Table 2.3, compound 3ik). Apart from styrene, a variety of substituted styrenes and acrylates was examined and provided good to excellent product yields. To our delight, the highly sterically hindered arylsulfonyl hydrazide coupled with butyl acrylate in good yield (Table 2.3, compound 3in). Both of electron-deficient and electron-rich substituents on styrenes were feasible cross-coupling partners that provided good to excellent product yields (Table 2.3, compound 3ao, 3ap, 3aq, 3as, 3at and 3au). The highly sterically crowded 2,4,6-trimethylstyrenes was proceeded with 4-chlorobenzenesulfonyl hydrazide smoothly (Table 2.3, compound 3fv). Notably, bromo and chloro groups were compatible under this optimized reaction condition, which are useful components for potential chemical transformations using coupling technology (Table 2.3, compound 3fk, 3aq, 3au and 3fv). A few of arylsulfonyl hydrazides and alkenes were applied in this optimized reaction condition but no desired products could be obtained (Scheme 2.2).

Table 2.3 Palladium-catalyzed oxidative Mizoroki-Heck reaction of arylsulfonylhydrazides and olefins[a]

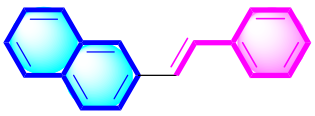




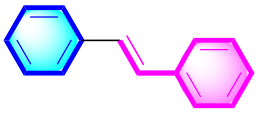
3ak 87%



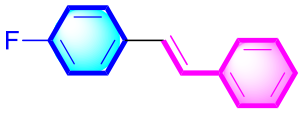
3bk 90%



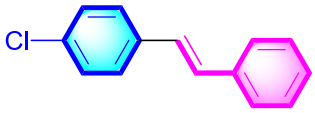
3ck 83%



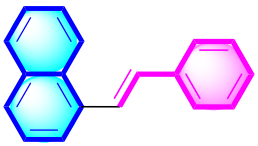
3dk 84%



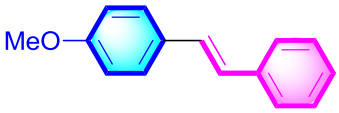
3ek 82%



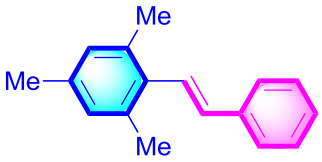
3fk 81%



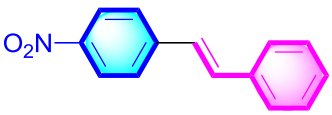
3gk 75%



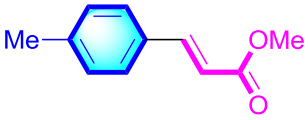
3hk 59%



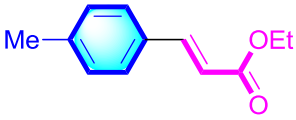
3ik 50%[c]



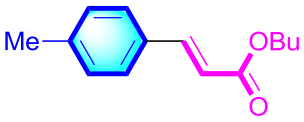
3jk 41%[d]



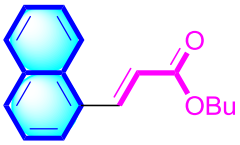
3al 64%[e]



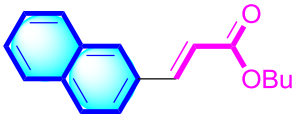
3am 75%



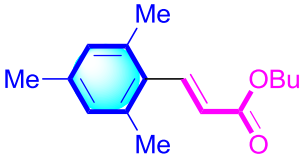
3an 84%



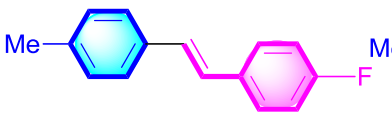
3gn 95%



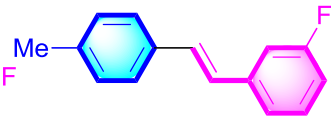
3cn 99%



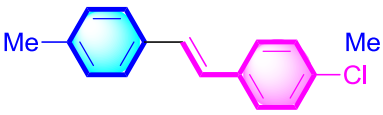
3in 81%[c]



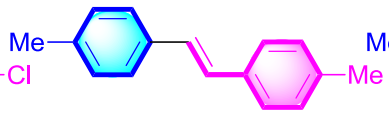
3ao 72%



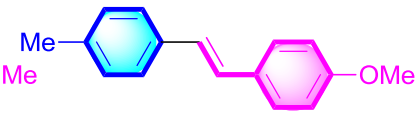
3ap 77%



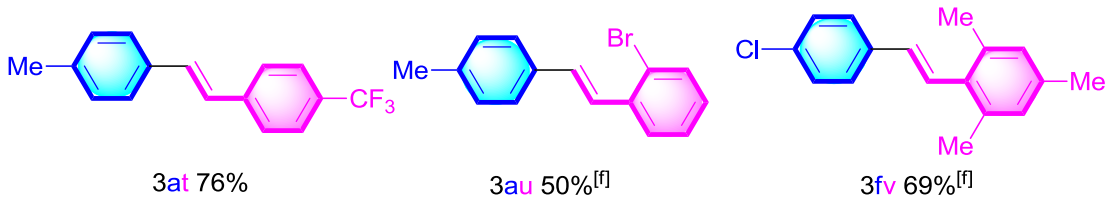
3aq 79%



3ar 83%



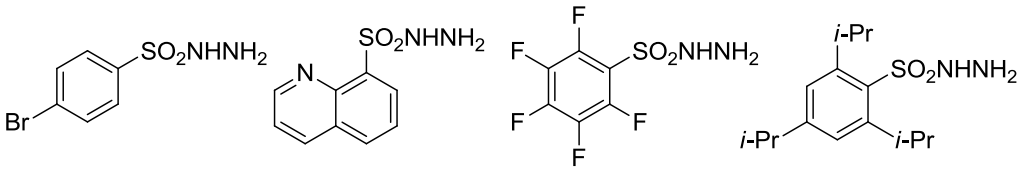
3as 68%



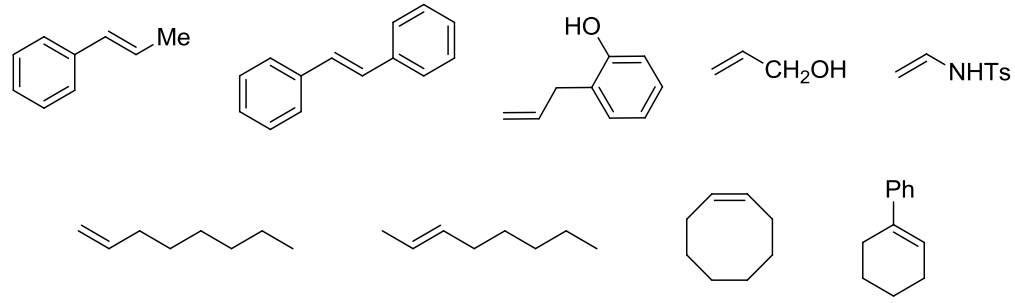
3at 76% 3au 50%[f] 3fv 69%[f]

[a] Reaction condition: aryl sulfonylhydrazide (0.45 mmol), alkene (0.3 mmol), $Pd(OAc)_2$ (10 mol%), L9 (20 mol%) and DMF (3 mL) were stirred at 80 ^oC for 16 h under air. [b] Isolated yield. [c] The reaction was conducted at 70 ^oC. [d] The reaction was conducted at 100 ^oC. [e] Close system was used. [f] The reaction was conducted for 24 h.

Arylsulfonyl Hydrazides:

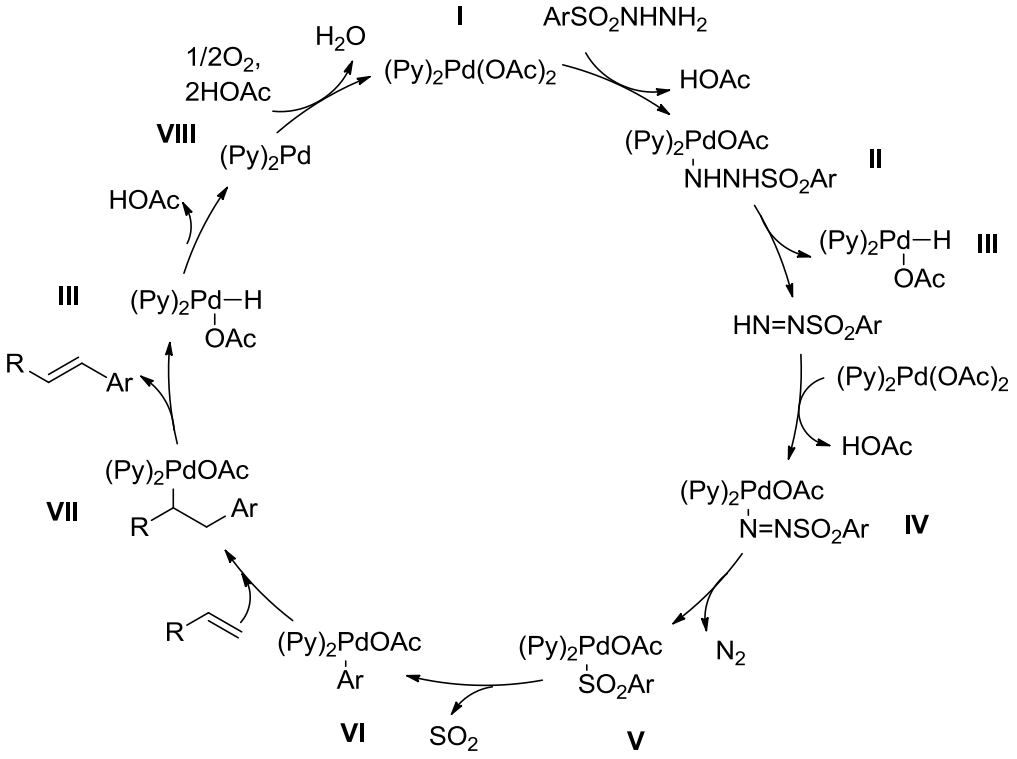


Alkenes:



Scheme 2.2 Unsuccessful examples of arylsulfonyl hydrazides and alkenes in oxidative Mizoroki-Heck reaction (Reaction conditions were same as Table 2.3, compound 3ak)

A proposed catalytic cycle, as adapted from the mechanistic studies performed on the Pd-catalyzed coupling reactions of arylsulfonyl hydrazides and $Pd(OAc)_2$/pyridine oxidation reaction mechanism, is shown in Scheme 2.3.[19,20] The coordination of the pyridine ligand to $Pd(OAc)_2$ generate complex **I** which is converted to complex **II** and HOAc by deprotonation with arylsulfonyl hydrazide. Complex **II** undergoes β-hydride elimination to give complex **III** and sulfonyl diazene. Displacement of complex **I** with sulfonyl diazene gives complex **IV**. Liberation of N_2 with complex **IV** generates the complex **V** which is then successive extrusion of SO_2 to form complex **VI**. The coordination of alkene to complex **VI** which followed by alkene insertion generates complex **VII**. Complex **VII** undergoes β-hydride elimination to generate complex **III**. Reductive elimination of complex **III** generates complex **VIII** which is followed by oxidation with oxygen regenerates complex **I**.



Scheme 2.3 Proposed catalytic cycle

2.3 Conclusion

In summary, we have reported that the oxidative Mizoroki-Heck reaction of arylsulfonyl hydrazides with alkenes in open-air manner using the stable and inexpensive pyridine ligand **L9**. The $Pd(OAc)_2$/ **L9** catalyst system is effective for the coupling of a wide range of arylsulfonyl hydrazides and alkenes. It is noteworthy that the reaction was conducted under atmospheric air, instead of using Cu(II) salts or pure oxygen. It can reduce heavy metal wastes, risks of explosion and minimized complication of reaction procedures.

2.4 Experimental section

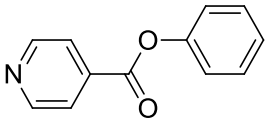
2.4.1 General considerations

Unless otherwise noted, all reagents were purchased from commercial suppliers and used without purification. All oxidative heck reactions were performed in an open vessel. A vial (approx. 40 mL volume) fitted with an air condenser as cooler was in the presence of Telfon coated magnetic stirrer bar (4 mm x 10 mm). All arylsulfonyl hydrazides except trimethylbenzenesulfonohydrazide were synthesized according to the literatutre report.[21] Phenyl isonicotinate was produced by the following procedures. 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. NMR spectra were recorded on a Brüker spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C and 376 MHz for ^{19}F). 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). ^{19}F NMR chemical shifts were determined relative to $CFCl_3$ as the external standard and low field is positive. 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 (ESI-MS). 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 ^1H NMR. Compounds described in the literature were characterized by comparison of their ^1H, ^{13}C and/or ^{19}F 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.

2.4.2 General procedure for the preparation of phenyl isonicotinate L9

Phenyl isonicotinate L9[22]



Thionyl chloride (5.95 g, 50 mmol) was added dropwise to isonicotinic acid (6.15 g, 50 mmol) and triethylamine (5.05 g, 50 mmol) in chloroform (200 mL). The mixture was refluxed for 2 h and cooled down to room temperature. Phenol (8.78 mL, 100 mmol) was added dropwise to the THF solution containing sodium hydride (4.80 g, 60% in mineral oil, 120 mmol, 2.4 equiv.) suspended in THF (100 mL) under nitrogen and cooled to 0^oC in an ice bath and stirred for 1 h to generate a THF

solution of sodium phenoxide. Then a THF solution of sodium phenoxide was added dropwise to the resulting isonicotinyl chloride solution, cooled by salt and ice water. The solution was further refluxed for 2 h, and then water (100 mL) and Ethyl acetate (200 mL) was added. The organic layer was successively washed with 1M sodium hydroxide solution and then washed with saturated brine solution. The organic layer was concentrated under vacuum and pass through a calica pad (5x3 cm) (Eluents = EtOAc: Hexane = 1: 9). The organic layer was concentrated. A white solid was obtained and then further washed with small amount of cool hexane and dry under vacuum. 4.2g (42% yield) product yield of phenyl isonicotinate was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 – 7.23 (m, 2H), 7.26 – 7.32 (m, 1H), 7.42-7.47 (m, 2H), 7.99 - 8.00 (m, 2H), 8.84 - 8.86 (m, 2H) ; ^{13}C NMR (100 MHz,$CDCl_3$) δ 121.3, 123.1, 126.3, 129.6, 136.8, 150.4, 150.8, 163.4; MS (EI): *m/z* (relative intensity) 199.0 (M^+, 37), 106.0 (100), 78.0 (50), 65.0 (7), 51.0 (24).

2.4.3 General procedure for the reaction condition screening without pyridine ligand

All reagents were weighted in air and the reactions were performed in an open vessel. Palladium source (0.03 mmol), 4-methylbenzenesulfonyl hydrazide (0.0838 g, 0.45 mmol) and styrene (34.4 μL, 0.3 mmol) were loaded into a 40 mL vial equipped with a Teflon-coated magnetic stir bar. The solvent (3 mL) was added at room temperature. The vial was fitted with an air condenser as cooler and then placed into a preheated oil bath (90 ^{o}C) and vigorously stirred for 16 h. After the completion of reaction, the reaction vial was allowed to cool at room temperature. Ethyl acetate(~10 mL) and dodecane (68.4μL, internal standard) were added. The organic layer was subjected to GC analysis. The GC yield obtained was previously calibrated by

anthentic sample/dodecane calibration curve.

2.4.4 General procedure for the reaction condition screening with pyridine ligand

All reagents were weighted in air and the reactions were performed in an open vessel. $Pd(OAc)_2$ (0.0068 g, 0.03 mmol) and pyridine ligand (Pd:L = 1:2) were loaded into a 40 mL vial equipped with a Teflon-coated magnetic stir bar. Precomplexation was applied by adding DMF (1 mL) in to the vial. The palladium complex stock solution was stirred for 10 minutes. 4-methylbenzenesulfonyl hydrazide (0.0838 g, 0.45 mmol) and styrene (34.4 μL, 0.3 mmol) were loaded into the vial. DMF (2 mL) was added with continuous stirring at room temperature. The vial was fitted with an air condenser as cooler and then placed into a preheated oil bath which the temperature was indicated in the table and vigorously stirred for 16 h. After the completion of reaction, the reaction vial was allowed to cool at room temperature. Ethyl acetate(~10 mL) and dodecane (68.4 μL, internal standard) were added. The organic layer was subjected to GC analysis. The GC yield obtained was previously calibrated by anthentic sample/dodecane calibration curve.

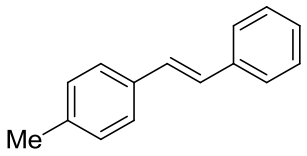
2.4.5 General procedure for the oxidative heck reaction of arylsulfonyl hydrazides with alkenes

All reagents were weighted in air and the reactions were performed in an open vessel. $Pd(OAc)_2$ (0.0068 g, 0.03 mmol) and L9 (Pd:L = 1:2) were loaded into a 40 mL vial equipped with a Teflon-coated magnetic stir bar. Precomplexation was applied by adding DMF (1 mL) in to the vial. The palladium complex stock solution was stirred for 10 minutes. Arylsulfonyl hydrazide (0.45 mmol) and alkenes (0.3 mmol) were loaded into the vial. DMF (2 mL) was added with continuous stirring at

room temperature. The vial was fitted with an air condenser as cooler and then placed into a preheated oil bath which the temperature was indicated in the table and vigorously stirred for 16 h. After the completion of reaction, the reaction vial was allowed to cool at room temperature. Ethyl acetate (~10 mL) was added. The organic layer was subjected to GC analysis. After analyzing GC spectra, the crude product in the organic layer was extracted and the vial washed with ethyl acetate. The filtrate was concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (230 -400 mesh) to afford the desired product.

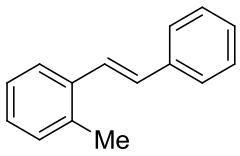
2.4.6 Characterization data of coupling products

Benzene, 1-methyl-4-[(1*E*)-2-phenylethenyl]- (Table 2.3, compound 3ak)[19a]



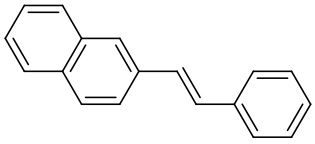
Eluents (Hexane, R_f= 0.56) was used for flash column chromatography. White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2,45 (s, 3H), 7.12-7.21 (m, 2H), 7.26 (d, *J*= 8.0 Hz, 2H), 7.31-7.36 (m, 1H), 7.44 (t, *J*= 6.8 Hz, 2H), 7.51 (d, *J*= 8.0 Hz, 2H), 7.59 (d, *J*= 7.6 Hz, 2H) ; ^{13}C NMR (100 MHz,$CDCl_3$) δ 21.2, 126.4, 127.4, 127.7, 128.6, 129.4, 134.5, 137.5; MS (EI): *m/z* (relative intensity) 194.1 (M^+, 96), 179.0 (100), 165.0 (12), 152.0 (9), 115.0 (11).

Benzene, 1-methyl-2-[(1*E*)-2-phenylethenyl]- (Table 2.3, compound 3bk)[17]



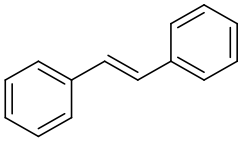
Eluents (Hexane, R_f= 0.56) was used for flash column chromatography. White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.52 (s, 3H), 7.07-7.11 (d, *J*= 16 Hz, 1H), 7.26-7.38 (m, 4H), 7.41-7.47 (m, 3H), 7.61 (d, *J*= 8.0 Hz, 2H), 7.69 (d, *J*= 6.8 Hz, 1H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 19.9, 125.3, 126.2, 126.5, 127.5, 128.6, 130.0, 130.4, 135.8, 136.4, 137.6; MS (EI): *m/z* (relative intensity) 194.1 (M^+, 79), 179.0 (100), 165.0 (13), 152.0 (8), 115.0 (22).

Naphthalene, 2-[(1*E*)-2-phenylethenyl]- (Table 2.3, compound 3ck)[19a]



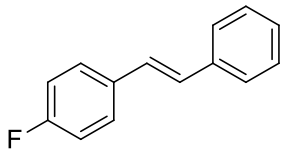
Eluents (Hexane, R_f= .38) was used for flash column chromatography. White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25-7.35 (m, 3H), 7.41-7.45 (m, 2H), 7.47-7.56 (m, 2H), 7.60-7.62 (m, 2H), 7.77-7.80 (m, 1H), 7.85-7.89 (m, 4H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 14.2, 21.0, 29.7, 60.4, 123.5, 125.9, 126.3, 126.6, 127.7, 128.0, 128.3, 128.7, 129.0, 171.1; MS (EI): *m/z* (relative intensity) 230.1 (M^+, 100), 215.0 (23), 202.0 (11), 114.1 (3), 101.0 (9)

Benzene, 1,1'-(1*E*)-1,2-ethenediylbis- (Table 2.3, compound 3dk)[19a]



Eluents (Hexane, R_f= 0.50) was used for flash column chromatography. White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (s, 2H), 7.30-7.34 (m, 2H), 7.40-7.44 (m, 4H), 7.57-7.59 (m, 4H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 126.4, 127.5, 128.6, 137.3; MS (EI): *m/z* (relative intensity) 180.0 (M^+, 100), 165.0 (49), 152.0 (13), 89.0 (27), 76.0 (20), 51.0 (19).

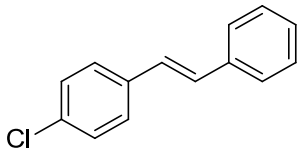
Benzene, 1-fluoro-4-[(1*E*)-2-phenylethenyl]- (Table 2.3, compound 3ek)[19a]



Eluents (Hexane, R_f= 0.44) was used for flash column chromatography. White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04-7.14 (m, 4H), 7.28-7.33 (m, 1H), 7.39-7.43 (m,

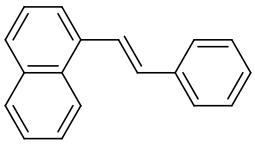
2H), 7.49-7.55 (m, 4H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 115.5, 115.7, 126.4, 127.4, 127.6, 127.9, 128.4, 133.5, 137.1, 161.1, 163.5; ^{19}F NMR (400 MHz,$CDCl_3$) δ -114.2; MS (EI): *m/z* (relative intensity) 198.0 (M^+, 100), 183.0 (38), 170.0 (8), 120.0 (5), 98.0 (10).

Benzene, 1-chloro-4-[(1*E*)-2-phenylethenyl]- (Table 2.3, compound 3fk)[19a]



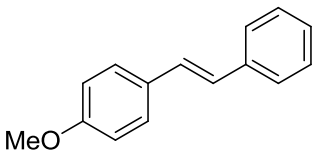
Eluents (Hexane, R_f=0.49) was used for flash column chromatography. White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06-7.15 (m, 2H), 7.28-7.43 (m, 5H), 7.46-7.49 (m, 2H), 7.53-7.55 (m, 2H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 126.5, 127.3, 127.6, 127.8, 128.7, 128.8, 129.3, 133.1, 135.8, 136.9; MS (EI): *m/z* (relative intensity) 214.0 (M^+, 78), 178.0 (100), 152.0 (14), 115.0 (2), 76.0 (18).

Naphthalene, 1-[(1*E*)-2-phenylethenyl]- (Table 2.3, compound 3gk)[19a]



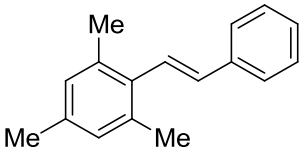
Eluents (Hexane, R_f= 0.54) was used for flash column chromatography. Yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J*= 16.0 Hz, 1H), 7.36-7.38 (m, 1H), 7.45-7.48 (m, 2H), 7.53-7.62 (m, 3H), 7.66-7.68 (m, 2H), 7.81 (d, *J*= 7.2 Hz, 1H), 7.86 (d, *J*= 8.4 Hz, 1H), 7.92-7.97 (m, 2H), 8.28 (d, *J*= 8.6 Hz, 1H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 123.6, 123.7, 125.7, 125.8, 126.1, 126.7, 127.7, 128.0, 128.6, 128.7, 131.4, 131.7, 133.7, 135.0, 137.6; MS (EI): *m/z* (relative intensity) 229.1 (M^+, 100), 215.0 (18), 202.0 (13), 152.0 (21), 128.0 (5).

Benzene, 1-methoxy-4-[(1*E*)-2-phenylethenyl]- (Table 2.3, compound 3hk)[19a]



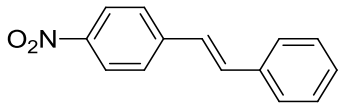
Eluents (EtOAc: Hexane = 1: 20, R_f= 0.40) was used for flash column chromatography. White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.87 (s, 3H), 6.93-6.97 (m, 2H), 7.01-7.14 (m, 2H), 7.26-7.31 (m, 1H), 7.38-7.41 (m, 2H), 7.49-7.55 (m, 4H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 55.29, 114.13, 126.2, 126.6, 127.2, 127.7, 128.2, 128.6, 130.1, 137.6, 159.3; MS (EI): *m/z* (relative intensity) 210.1 (M^+, 100), 195.0 (18), 179.0 (15), 165.0 (38), 152.0 (23).

Benzene, 1,3,5-trimethyl-2-[(1*E*)-2-phenylethenyl]- (Table 2.3, compound 3ik)[19a]



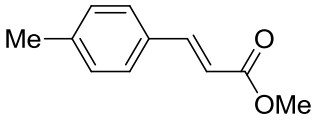
Eluents (Hexane, R_f= 0.50) was used for flash column chromatography. White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (s, 3H), 2.41 (s, 6H), 7.66 (d, *J*= 16.8 Hz, 1H), 6.97 (s, 2H), 7.17 (d, *J*= 16.8 Hz, 1H), 7.33-7.36 (m, 1H), 7.42-7.45 (m, 2H), 7.57 (d, *J*= 7.2 Hz, 2H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 20.9, 126.2, 126.8, 127.4, 128.6, 133.6, 133.9, 136.1, 136.2, 137.7; MS (EI): *m/z* (relative intensity) 222.1 (M^+, 91), 207.1 (100), 192.0 (78), 178.0 (9), 144.0 (9).

Benzene, 1-nitro-4-[(1*E*)-2-phenylethenyl]- (Table 2.3, compound jk)[19a]



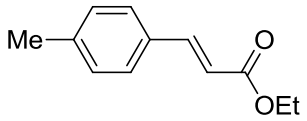
Eluents (EtOAc: Hexane = 1: 9, R_f= 0.70) was used for flash column chromatography. Yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, *J*= 16.4 Hz, 1H), 7.27-7.45 (m, 4H), 7.56-7.59 (m, 2H), 7.64-7.67 (m, 2H), 8.22-8.26 (m, 2H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 124.1, 126.3, 126.8, 127.0, 128.9, 133.3, 136.2, 143.8, 146.8; MS (EI): *m/z* (relative intensity) 225.0 (M^+, 83), 207.0 (9), 178.0 (100), 165.0 (13), 152.0 (25).

2-Propenoic acid, 3-(4-methylphenyl)-, methyl ester, (2*E*)- (Table 2.3, compound 3al)[13b]



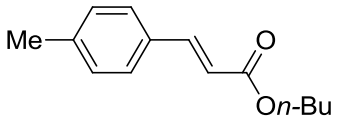
Eluents (EtOAc: Hexane = 1: 9, R_f= 0.53) was used for flash column chromatography. White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.40 (s, 3H), 3.82 (s, 3H), 6.42 (d, *J*= 16.0 Hz, 1H), 7.21 (d, *J*= 8.0 Hz, 2H), 7.44 (d, *J*= 8.0 Hz, 2H), 7.70 (d, *J*= 16.0 Hz, 1H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 21.4, 51.6, 116.7 128.0, 129.6, 131.6, 140.7, 144.8, 167.6; MS (EI): *m/z* (relative intensity) 176.0 (M^+, 63), 161.0 (6), 145.0 (100), 115.0 (50), 91.0 (20).

2-Propenoic acid, 3-(4-methylphenyl)-, ethyl ester, (2*E*)- (Table 2.3, compound 3am)[16]



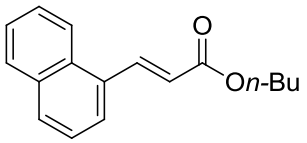
Eluents (EtOAc: Hexane = 1: 20, R_f= 0.52) was used for flash column chromatography. Yellow liquid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (t, *J*= 7.2 Hz, 3H), 2.39 (s, 3H), 4.26 – 4.31 (m, 2H), 6.42 (d, *J*= 16.0 Hz, 1H), 7.21 (d, *J*= 8.0 Hz, 2H), 7.44 (d, *J*= 8.0 Hz, 2H), 7.69 (d, *J*= 15.6 Hz, 1H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 14.3, 21.4, 60.4 117.1, 128.0, 129.6, 131.7, 140.6, 144.5, 167.1; MS (EI): *m/z* (relative intensity) 190.0 (M^+, 48), 175.0 (3), 162.0 (13), 145.0 (100), 115.0 (46).

2-Propenoic acid, 3-(4-methylphenyl)-, butyl ester, (2*E*)- (Table 2.3, compound 3an)[19a]



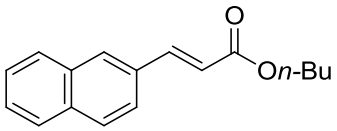
Eluents (EtOAc: Hexane = 1: 20, R_f= 0.52) was used for flash column chromatography. Colorless liquid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99 (t, *J*= 7.6 Hz, 3H), 1.44-1.49 (m, 2H), 1.69 – 1.73 (m, 2H), 2.39 (s, 3H), 4.23 (t, *J*= 6.4 Hz, 2H), 6.42 (d, *J*= 16.0 Hz, 1H), 7.21 (d, *J*= 8.0 Hz, 2H), 7.45 (d, *J*= 8.0 Hz, 2H), 7.68 (d, *J*=16.0 Hz, 1H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 13.7, 19.1, 21.4 30.7, 64.2, 117.1, 128.0, 129.5, 131.7, 140.5, 144.5, 167.2; MS (EI): *m/z* (relative intensity) 218.1 (M^+, 26), 162.0 (95), 145.0 (100), 115.0 (51), 91.0 (25).

2-Propenoic acid, 3-(1-naphthalenyl)-, butyl ester, (2*E*)- (Table 2.3, compound 3gn)[23]



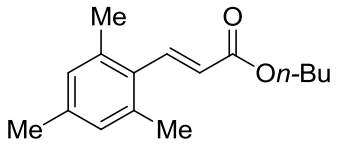
Eluents (EtOAc: Hexane = 1: 20, R_f= 0.64) was used for flash column chromatography. Yellow liquid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.04 (t, *J*= 7.2 Hz, 3H), 1.49-1.54 (m, 2H), 1.74-1.79 (m, 2H), 4.31 (t, *J*= 6.4 Hz, 2H), 6.58 (d, *J*= 15.6 Hz, 1H), 7.49-7.63 (m, 3H), 7.78 (d, *J*= 6.8 Hz, 1H), 7.91 (t, *J*= 7.2 Hz, 2H), 8.23 (d, *J*= 8.4 Hz, 1H), 8.57 (d, *J*= 15.6 Hz, 1H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 13.7, 19.2, 30.8, 64.5, 120.9, 123.3, 124.9, 125.4, 126.1, 126.8, 128.7, 130.4, 131.4, 131.8, 133.6, 141.5, 166.9; MS (EI): *m/z* (relative intensity) 254.1 (M^+, 27), 198.0 (7), 181.0 (25), 153.0 (100), 76.1 (5).

2-Propenoic acid, 3-(2-naphthalenyl)-, butyl ester, (2*E*)- (Table 2.3, compound 3cn)[13b]



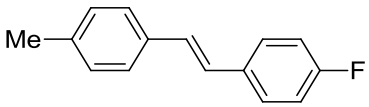
Eluents (EtOAc: Hexane = 1: 20, R_f= 0.60) was used for flash column chromatography. Colorless liquid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.02 (t, *J*= 7.2 Hz, 3H), 1.47-1.53 (m, 2H), 1.71-1.77 (m, 2H), 4.28 (t, *J*= 6.8 Hz, 2H), 6.59 (d, *J*= 16.0 Hz, 1H), 7.52-7.54 (m, 2H), 7.68 (d, *J*= 8.4 Hz, 1H), 7.83-7.94 (m, 5H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 1.0, 13.7, 19.2, 30.8, 64.4, 118.4, 123.4, 126.6, 127.1, 127.7, 128.5, 128.6, 129.8, 131.9, 133.2, 134.1, 144.5, 167.1; MS (EI): *m/z* (relative intensity) 254.1 (M^+, 52), 198.0 (100), 181.0 (70), 152.0 (65), 127.0 (11).

2-Propenoic acid, 3-(2,4,6-trimethylphenyl)-, butyl ester, (2*E*)- (Table 2.3, compound 3in)[13b]



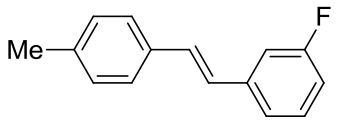
Eluents (EtOAc: Hexane = 1: 20, R_f= 0.49) was used for flash column chromatography. White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (t, *J*= 7.6 Hz, 3H), 1.45-1.51 (m, 2H), 1.70-1.75 (m, 2H), 2.32 (s, 3H), 2.36 (s, 6H), 4.25 (t, *J*= 6.8 Hz, 2H), 6.09 (d, *J*= 16.4Hz, 1H), 6.92 (s, 2H), 7.87 (d, *J*= 16.4Hz, 1H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 13.7, 19.2, 20.9, 21.0, 30.7, 64.3, 123.1, 129.1, 130.9, 136.7, 138.2, 143.1, 167.0; MS (EI): *m/z* (relative intensity) 246.1 (M^+, 27), 231.1 (5), 173.0 (100), 144.1 (52), 129.0 (39).

Benzene, 1-fluoro-4-[(1*E*)-2-(4-methylphenyl)ethenyl]- (Table 2.3, compound 3ao)[24]



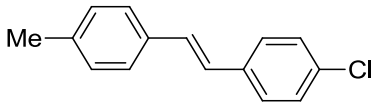
Eluents (Hexane, R_f= 0.56) was used for flash column chromatography. White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3H), 7.05-7.11 (m, 4H), 7.22 (d, *J*= 8.0 Hz, 2H), 7.45 (d, *J*= 8.0 Hz, 2H), 7.49-7.52 (m, 2H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 21.2, 115.4, 115.6, 126.3, 126.4, 127.7, 127.8, 128.4, 129.4, 133.6, 134.3, 137.5, 160.9, 163.4; ^{19}F NMR (400 MHz,$CDCl_3$) δ -114.6; MS (EI): *m/z* (relative intensity) 212.1 (M^+, 100), 197.0 (67), 177.0 (18), 115.0 (8), 91.1 (10).

Benzene, 1-fluoro-3-[2-(4-methylphenyl)ethenyl]-, (*E*)- (Table 2.3, compound 3ap)[25]



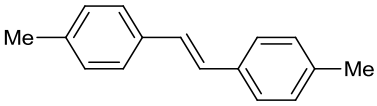
Eluents (Hexane, R_f= 0.56) was used for flash column chromatography. White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3H), 6.96-7.01 (m, 1H), 7.04-7.15 (m, 2H), 7.22-7.38 (m, 5H), 7.46 (d, *J*= 8.0 Hz, 2H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 21.3, 112.5, 112.7, 114.0, 114.2, 122.3, 126.5, 126.8, 129.4, 130.0, 134.0, 138.0, 139.9, 162.0, 164.4; ^{19}F NMR (400 MHz,$CDCl_3$) δ -113.5; MS (EI): *m/z* (relative intensity) 212.1 (M^+, 100), 197.0 (88), 177.0 (24), 115.0 (8), 91.1 (10).

Benzene, 1-chloro-4-[(1*E*)-2-(4-methylphenyl)ethenyl]- (Table 2.3, compound 3aq)[19a]



Eluents (Hexane, R_f= 0.56) was used for flash column chromatography. White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.39 (s, 3H), 7.00-7.11 (m, 2H), 7.20 (d, *J*= 7.6 Hz, 2H), 7.33-7.36 (m, 2H), 7.42-7.47 (m, 4H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 21.3, 126.4, 126.5, 127.5, 128.8, 129.3, 129.4, 132.9, 134.2, 136.1, 137.8; MS (EI): *m/z* (relative intensity) 228.0 (M^+, 100), 213.0 (16), 192.0 (26), 178.0 (95), 94.7 (12).

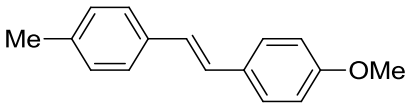
Benzene, 1,1'-(1*E*)-1,2-ethenediylbis[4-methyl- (Table 2.3, compound 3ar)[19a]



Eluents (Hexane, R_f= 0.56) was used for flash column chromatography. White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 6H), 7.10 (s, 2H), 7.22 (d, *J*= 8.0 Hz, 4H), 7.46

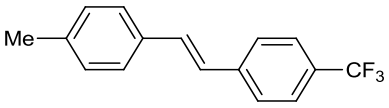
(d, *J*= 8.0 Hz, 4H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 21.2, 126.3, 127.6, 129.3, 134.7, 137.2; MS (EI): *m/z* (relative intensity) 208.1 (M^+, 100), 193.0 (57), 178.0 (59), 152.0 (5), 115.0 (13).

Benzene, 1-methoxy-4-[(1*E*)-2-(4-methylphenyl)ethenyl]- (Table 2.3, compound 3as)[19a]



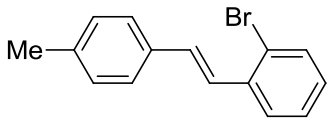
Eluents (EtOAc: Hexane = 1: 20, R_f= 0.48) was used for flash column chromatography. White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.40 (s, 3H), 3.86 (s, 3H), 6.92-6.96 (m, 2H), 6.97-7.09 (m, 2H), 7.20 (d, *J*= 7.6 Hz, 2H), 7.42-7.50 (m, 4H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 21.2, 55.3, 114.1, 126.1, 126.5, 127.2, 127.6, 129.3, 130.3, 134.8, 137.0, 159.1; MS (EI): *m/z* (relative intensity) 224.1 (M^+, 100), 209.0 (25), 194.0 (5), 178.0 (9), 165.0 (33).

Benzene, 1-[(1*E*)-2-(4-methylphenyl)ethenyl]-4-(trifluoromethyl)- (Table 2.3, compound 3at)[25]



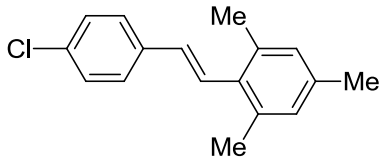
Eluents (Hexane, R_f= 0.56) was used for flash column chromatography. White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3H), 7.10 (d, *J*= 16.4 Hz, 1H), 7.18-7.23 (m, 3H), 7.46 (d, *J*= 8.4 Hz, 2H), 7.59-7.64 (m, 4H); ^{13}C NMR (100 MHz,$CDCl_3$) δ , 21.3, 125.6, 126.1, 126.4, 126.7, 128.8, 129.5, 131.1, 133.8, 138.3, 141.0; ^{19}F NMR (400 MHz,$CDCl_3$) δ -62.4; MS (EI): *m/z* (relative intensity) 262.1 (M^+, 100), 247.0 (41), 227.0 (18), 115.0 (7), 91.0 (8).

Benzene, 1-bromo-2-[(1*E*)-2-(4-methylphenyl)ethenyl]- (Table 2.3, compound 3au)[26]



Eluents (Hexane, R_f= 0.56) was used for flash column chromatography. Colorless liquid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3H), 7.06 (d, *J*= 16.0 Hz, 1H), 7.12-7.16 (m, 1H), 7.20-7.23 (m, 2H), 7.32-7.36 (m, 1H), 7.44-7.50 (m, 3H), 7.60-7.63 (m, 1H), 7.69-7.71 (m, 1H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 21.3, 124.0, 126.5, 127.5, 128.5, 128.9, 129.4, 131.4, 132.9, 133.0, 134.2, 137.3, 138.0; MS (EI): *m/z* (relative intensity) 272.0 (M^+, 38), 193.0 (23), 178.0 (100), 165.0 (12), 115.0 (7).

Benzene, 1-chloro-4-[(1*E*)-2-(1,3,5-trimethylphenyl)ethenyl]- (Table 2.3, compound 3av)



Eluents (Hexane, R_f= 0.55) was used for flash column chromatography. White solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.35 (s, 3H), 2.40 (s, 6H), 6.60 (d, *J*= 16.8 Hz, 1H), 6.97 (s, 2H), 7.13 (d, *J*= 16.4 Hz, 1H), 7.37-7.40 (m, 2H), 7.45-7.48 (m, 2H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 21.0, 127.4, 127.6, 132.3, 133.0, 133.6, 136.1, 136.2, 136.5; MS (EI): *m/z* (relative intensity) 256.0 (M^+, 63), 241.0 (23), 221.1 (27), 206.0 (100), 191.0 (15); HRMS (ESI) calcd. for $C_{17}H_{17}Cl$ [M + H^+]: 256.1019, found 256.1018.

2.5 References

(1) (a) Heck, R. F. *Acc. Chem. Res.* **1979**, *12*, 146; (b) Daves, G. D.; Jr.; Hallberg, A. *Chem. Rev.* **1989**, *89*, 1433; (c) Cabri, W.; Candiani, I. *Acc. Chem. Res.* **1995**, *28*, 2; (d) Crisp, G. T. *Chem. Soc. Rev.* **1998**, *27*, 427; (e) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009; (f) Littke, A. F.; Fu, G. C. *Angew. Chem. Int. Ed.* **2002**, *41*, 4176.

(2) Lawrence, N. J. *In Preparation of Alkenes: a Practical Approach*; J. M. J. Williams, Ed.; Oxford University Press: Oxford, UK, 1995.

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Chapter 3 Palladium-Catalyzed Direct Oxidative C-H Arylation of Benzoxazoles with Arylsulfonyl Hydrazides under air

3.1 Introduction

Cross-coupling protocol has been successful in modern modular organic syntheses for the connection of two different fragments together via the formation of carbon-carbon and/or carbon-heteroatom bonds.[1] To prepare useful biaryl motifs,[2] coupling methods such as Hiyama, Kumada, Negishi, Stille and Suzuki-Miyaura coupling have been found versatile in the past few decades.[1] Even though these reactions are effective, some intrinsic drawbacks are still exist in which the corresponding organometallic nucleophiles are necessary to be prepared in-situ (e.g. Ar-MgBr, Ar-ZnCl) or require isolation, in general, prior to the catalysis (e.g. Ar-$B(OH)_2$). Thus, the assembling and subsequent disposal of stoichiometric organometallic agents are relatively not desirable. In fact, direct C-H functionalization of heteroarenes is actually more straightforward. This protocol serves as an attractive alternative to conventional coupling protocols in terms of better atom economy, environmental friendliness and more streamlined chemical synthesis.[3,4]

In continuing our research focus of applying arylsulfonyl compounds as effective aryl sources,[5] we envisioned that arylsulfonyl hydrazides could be employed as versatile arylating agents. Indeed, arylsulfonyl hydrazides are readily accessible solids, stable in air and moisture and can be simply prepared in one step from commonly available arylsulfonyl chlorides and hydrazine hydrates. In 2012, Tian and co-workers reported the first palladium-catalyzed Mizoroki-Heck reaction of alkenes with arylsulfonyl hydrazides.[6] To the best of our knowledge, the direct C-H arylation of benzoxazoles using arylsulfonyl hydrazides remain sporadically studied.[7]

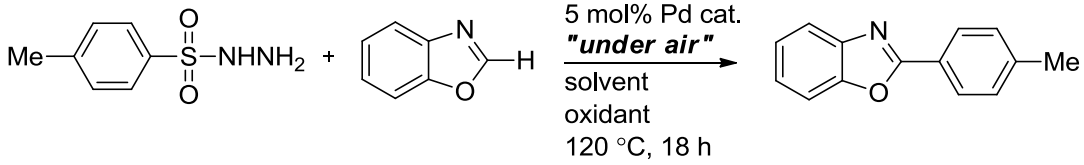
In fact, with respect to the reaction of olefins, the arylation of heteroarenes is known to be even more challenging because of the undesirable homocoupling outcome and decomposition of heteroarenes are often observed under oxidative conditions. In continuing our research program on C-2 functionalization of benzoxazoles,[8] we herein report our efforts in the palladium-catalyzed direct C-H arylation of benzoxazoles using arylsulfonyl hydrazides under oxidative reaction conditions.

3.2 Results and discussion

3.2.1 Preliminary evaulation of palladium-catalyzed oxidative C-H arylation of benzoxaxoles with arylsulfonyl hydrazides

In order to investigate the efficacy of arylsulfonyl hydrazide as the aryl source in the direct C-H arylation of heteroarenes, a series of initial screenings was conducted (Table 3.1). Benzoxazole and 4-tolylsulfonyl hydrazide were used as benchmark substrates. Among commonly used solvents screened, dioxane provided the best results (Table 3.1, entries 1-7). There were little differences in product yield observed in the model reaction when other palladium precursors were investigated (Table 3.1, entries 1 and 8-13). The palladium complex associated with triphenylphosphine gave slightly higher yield (Table 3.1, entry 9 and 13). Common inorganic/organic oxidants were also surveyed (Table 3.1, entries 1 and 14-21). Copper(II) acetate gave the best results while BQ and O_2 provided inferior product yields.

Table 3.1 Initial screening of oxidative arylation of 4-methylbenzenesulfonyl hydrazide and benzoxazole[a]

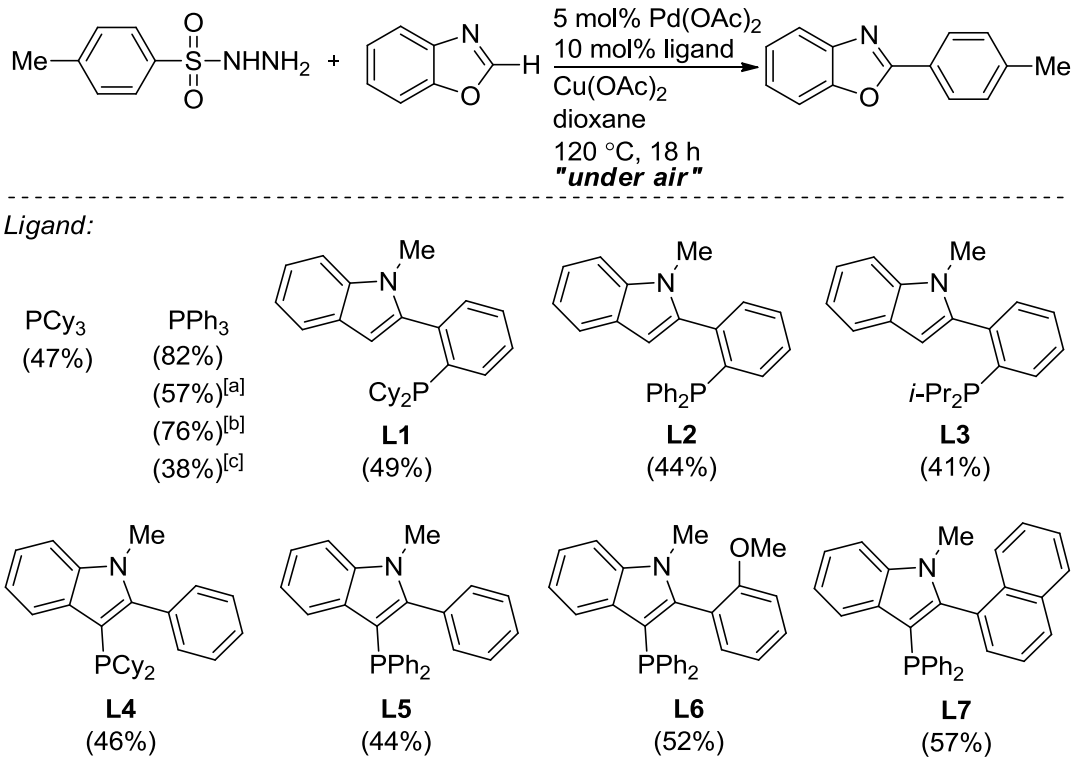


entry	Pd source	solvent	oxidant	yield%[b]
1	$Pd(OAc)_2$	dioxane	$Cu(OAc)_2$	51
2	$Pd(OAc)_2$	DMF	$Cu(OAc)_2$	6
3	$Pd(OAc)_2$	DMA	$Cu(OAc)_2$	39
4	$Pd(OAc)_2$	NMP	$Cu(OAc)_2$	10
5	$Pd(OAc)_2$	DMSO	$Cu(OAc)_2$	34
6	$Pd(OAc)_2$	toluene	$Cu(OAc)_2$	16
7	$Pd(OAc)_2$	water	$Cu(OAc)_2$	0
8	$Pd(TFA)_2$	dioxane	$Cu(OAc)_2$	48
9	$PdCl_2$	dioxane	$Cu(OAc)_2$	52
10	$Pd(acac)_2$	dioxane	$Cu(OAc)_2$	47
11	$PdCl_2(MeCN)_2$	dioxane	$Cu(OAc)_2$	57
12	$PdCl_2(PCy_3)_2$	dioxane	$Cu(OAc)_2$	46
13	$PdCl_2(PPh_3)_2$	dioxane	$Cu(OAc)_2$	54
14	$Pd(OAc)_2$	dioxane	$Cu(OAc)_2 \cdot H_2O$	36
15	$Pd(OAc)_2$	dioxane	$Cu(acac)_2$	28
16	$Pd(OAc)_2$	dioxane	$CuCl_2$	0
17	$Pd(OAc)_2$	dioxane	$CuBr_2$	0
18	$Pd(OAc)_2$	dioxane	AgOAc	0
19	$Pd(OAc)_2$	dioxane	BQ	0
20	$Pd(OAc)_2$	dioxane	$K_2S_2O_8$	0

21 $Pd(OAc)_2$ dioxane O_2 0

[a] Reaction conditions: 4-Tolylsulfonyl hydrazide (0.45 mmol), benzoxazole (0.3 mmol), Pd catalyst (5 mol%), solvent (3 mL) and oxidant (0.6 mmol) were stirred at 120 ^oC for 18 h under air. [b] Calibrated GC yields were reported using dodecane as internal standard.

In light of the successful initial results achieved, we next examined the effect of phosphine ligands in this reaction (Scheme 3.1). Palladium(II) acetate with triphenylphosphine promoted the reaction and gave the highest product yield. Yet, catalytic system employing our previously developed tunable indolylphosphine ligands (**L1**-**L7**) showed moderate efficiency.[9]



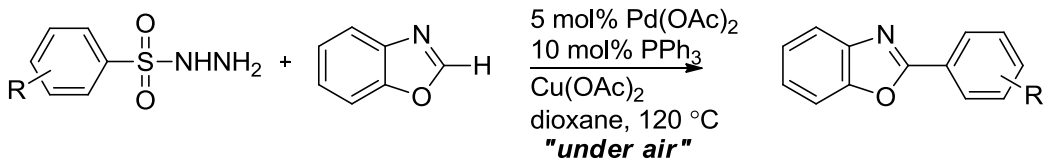
Scheme 3.1 A survey of ligand effect in oxidative arylation of benzoxazole (Reaction conditions: 4-methylbenzenesulfonyl hydrazide (0.45 mmol), benzoxazole (0.3 mmol), $Pd(OAc)_2$ (5 mol%), Ligand (10 mol%) , Dioxane (3 mL), $Cu(OAc)_2$ (0.6 mmol) were

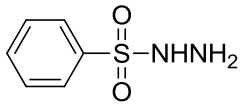
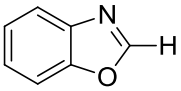
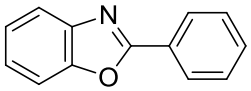
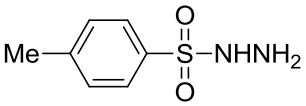
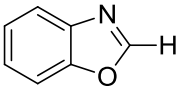
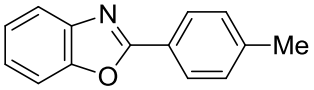
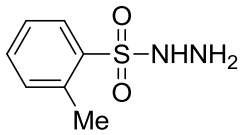
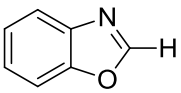
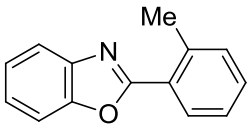
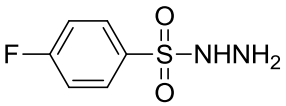
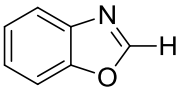
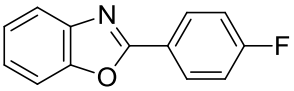
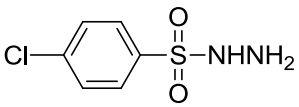
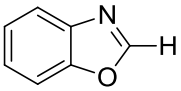
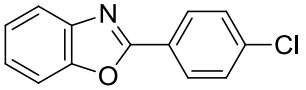
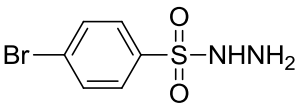
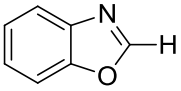
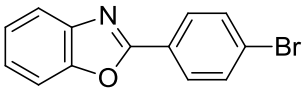
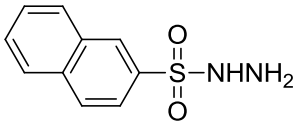
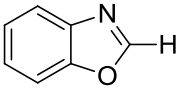
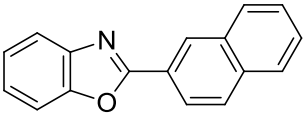
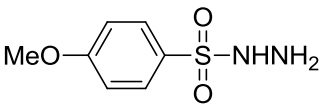
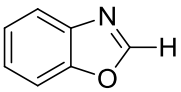
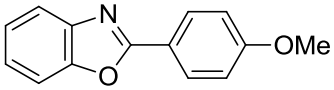
stirred at indicated temperature for 18 h under air. Calibrated GC yields were reported using dodecane as internal standard. [a] 100 ^{o}C was conducted. [b] 110 ^{o}C was conducted. [c] 130 ^{o}C was conducted.

3.2.2 Scope of palladium-catalyzed oxidative C-H arylation of benzoxaxoles with arylsulfonyl hydrazides

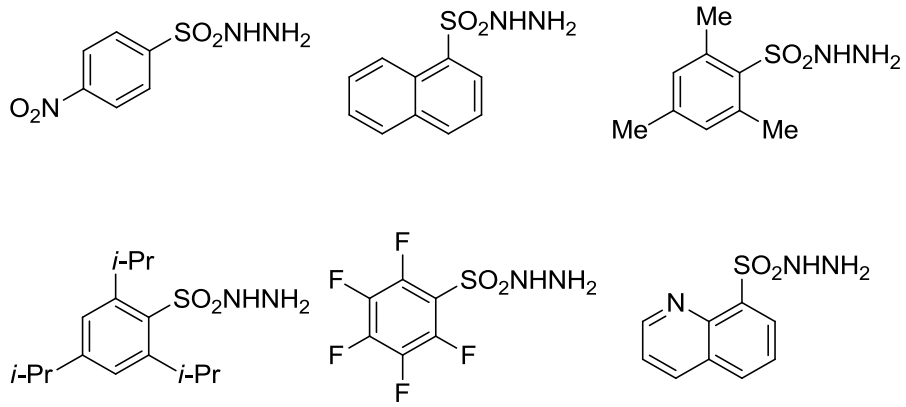
With our optimized reaction conditions in hand, we next tested the scope of arylsulfonyl hydrazides (Table 3.2). The coupling reaction of sterically hindered 2-tolylsulfonyl hydrazide proceeded smoothly (Table 3.2, entry 3). Halogen substitutents (-F, -Cl, -Br) on arylsulfonyl hydrazide were found to be compatible under these reaction conditions (Table 3.2, entries 4-6). Particularly noteworthy is that the tolerance of chloro and bromo groups can offer an avenue for further versatile functionalization using traditional cross-coupling protocols.[1] A few of arylsulfonyl hydrazides was examined but no desired products could be obtained (Scheme 3.2).

Table 3.2 Palladium-catalyzed oxidative arylation of benzoxazole using arylsulfonyl hydrazides[a]



entry	Ar-SO_2-$NHNH_2$	benzoxazole	product	yield[b]
1[c]				76
2				78
3[d]				72
4				66
5[c]				60
6[d]				59
7				67
8				52

[a] Reaction conditions: Arylsulfonyl hydrazide (0.45 mmol), benzoxazole (0.3 mmol), $Pd(OAc)_2$ (5 mol%), PPh_3 (10 mol%), dioxane (3 mL), $Cu(OAc)_2$ (0.6 mmol) were stirred at 120 ^oC for 18 h under air. [b] Isolated yields. [c] The reaction was conducted at 110 ^oC. [d] The reaction was conducted at 100 ^oC.

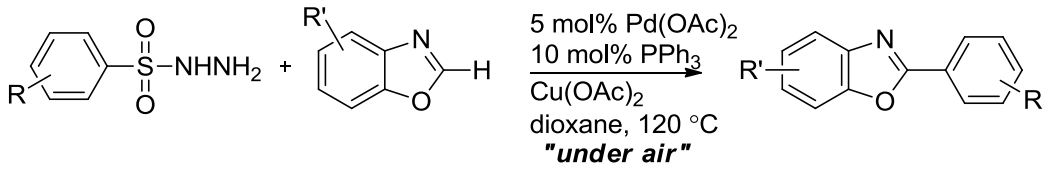


Scheme 3.2 Unsuccessful arylsulfonyl hydrazides in direct C-2 arylation of benzoxazole (Reaction condtions were same as Table 3.2, entry 2)

3.2.3 Scope of palladium-catalyzed oxidative C-H arylation of substituted benzoxaxoles and other heteroarenes with arylsulfonyl hydrazides

In addition to a variety of arylsulfonyl hydrazides examined, the substituted benzoxazoles were found feasible substrates (Table 3.3). Fluoro and chloro groups remained intact during the course of the reaction (Table 3.3, entries 5-6). However, 5-acetylbenzoxazole was incompatible under this optimized reaction condition.

Table 3.3 Palladium-catalyzed oxidative arylation of substituted benzoxazoles with arylsulfonyl hydrazides[a]



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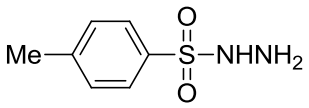
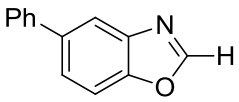
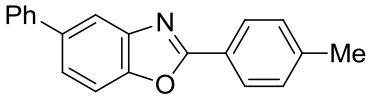
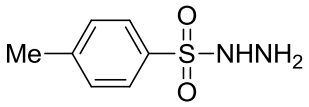
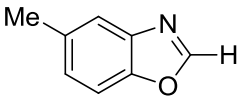
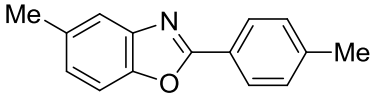
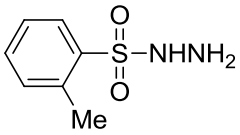
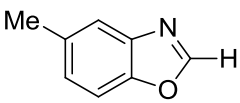
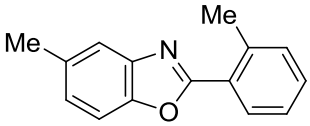
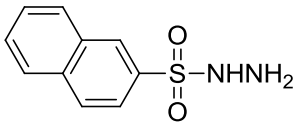
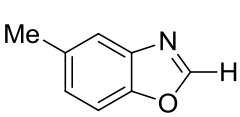
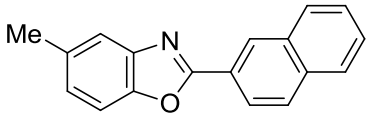
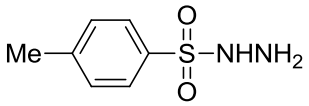
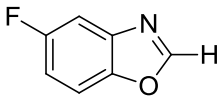
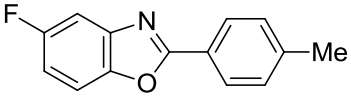
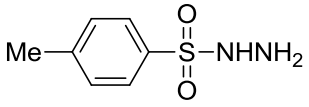
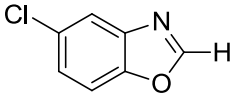
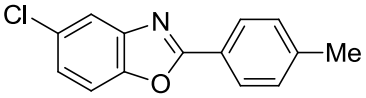
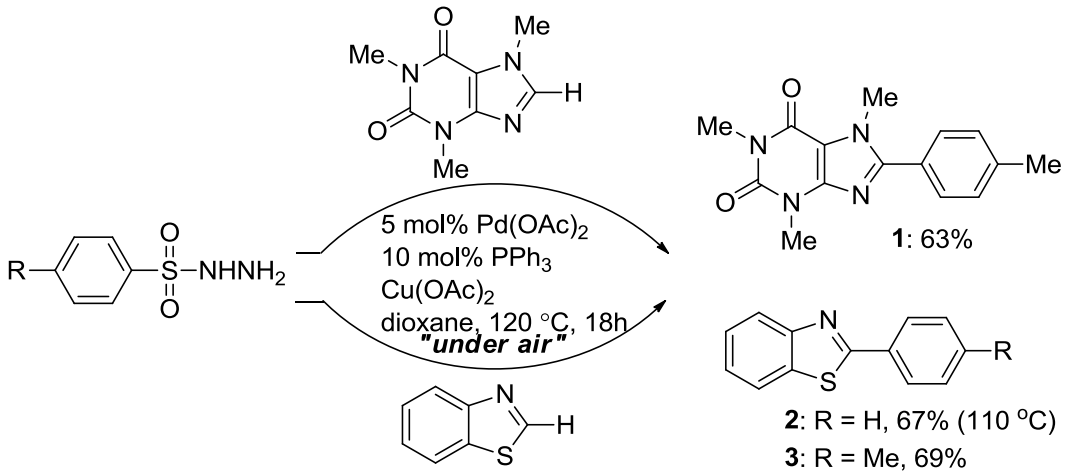
1				70
2				75
3[c]				72
4				67
5				71
6				72

[a] Reaction conditions: Arylsulfonyl hydrazide (0.45 mmol), substituted benzoxazole (0.3 mmol), $Pd(OAc)_2$ (5 mol%), PPh_3 (10 mol%), dioxane (3 mL), $Cu(OAc)_2$ (0.6 mmol) were stirred at 120 ^oC for 18 h under air. [b] Isolated yields. [c] The reaction was conducted at 100 ^oC.

Apart from benzoxazole, other heteroarenes were applicable. Caffeine and benzothiazole could be applied in this catalytic system (Scheme 3.3). Moderate-to-good product yields were observed. In particular, the product 1 is a

useful fluorescent molecule for cell imaging.[10] Yet, when benzimidazole and 1-methylbenzimidazole were applied as substrates in this optimized reaction condition, no desired products could be obtained.



Scheme 3.3 Palladium-catalyzed direct C-H arylation of caffeine and benzothiazole with arylsulfonyl hydrazides (Reaction conditions: Arylsulfonyl hydrazide (0.45 mmol), heteroarene (0.3 mmol), $Pd(OAc)_2$ (5 mol%), PPh_3 (10 mol%), dioxane (3 mL), $Cu(OAc)_2$ (0.6 mmol) were stirred at 120 ^oC for 18 h under air and product yields were isolated yields.)

3.3 Conclusion

In summary, we have reported an oxidative protocol for C-2 arylation of benzoxazoles using readily available and easy-to-handle arylsulfonyl hydrazides as the aryl sources. Particularly noteworthy is that only a simple catalyst system ($Pd(OAc)_2$ and PPh_3) is required for this coupling reaction. This methodology is a useful complement to current cross-coupling protocols as it tolerates halogen substitutents on both arylsulfonyl hydrazide and heteroarene coupling partners. Detail mechanistic study is currently underway.

3.4 Experimental section

3.4.1 General considerations

Unless otherwise noted, all reagents were purchased from commercial suppliers and used without purification. All oxidative arylations were performed in an open vessel. A vial (approx. 60 mL volume) fitted with an air condenser as cooler was in the presence of Telfon coated magnetic stirrer bar (4 mm x 10 mm). The indolylphosphine ligands (**L1**-**L7**) were developed and prepared by our group.[9, 11] All arylsulfonyl hydrazides were synthesized by the following procedure. [12] 5-methylbenzoxazole, 5-phenylbenzoxazole, 5-chlorobenzoxazole and 5-fluorobenzoxazole were synthesized according to the literature method.[8, 13] 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. NMR spectra were recorded on a Brüker spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C and 376 MHz for ^{19}F). 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). ^{19}F NMR chemical shifts were determined relative to $CFCl_3$ as the external standard and low field is positive. 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 (ESI-MS). 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, ^{13}C and/or ^{19}F 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 procedure for the reaction condition screening without phosphine ligand

All reagents were weighted in air and the reactions were performed in an open vessel. Palladium source (0.015 mmol), 4-methylbenzenesulfonyl hydrazide (0.0838 g, 0.45 mmol), benzoxazole (0.0358 g, 0.30 mmol) and oxidant (0.60 mmol) were loaded into a 60 mL vial equipped with a Teflon-coated magnetic stir bar. The solvent (3.0 mL) was added at room temperature. The vial was fitted with an air condenser as cooler and then placed into a preheated oil bath (120 ^{o}C) and vigorously stirred for 18 h. After the completion of reaction, the reaction vial was allowed to cool at room temperature. Ethyl acetate (~20 mL), water (~10 mL) and dodecane (68.4 μL, internal standard) were added. The organic layer was subjected to GC analysis. The GC yield obtained was previously calibrated by anthentic sample/dodecane calibration curve.

3.4.3 General procedure for the reaction condition screening with phosphine ligand

All reagents were weighted in air and the reactions were performed in an open vessel. $Pd(OAc)_2$ (0.0034 g, 0.015 mmol), phosphine ligand (Pd:L = 1:2), 4-methylbenzenesulfonyl hydrazide (0.0838 g, 0.45 mmol) , benzoxazole (0.0358 g,

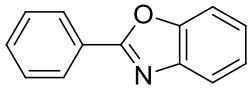
0.30 mmol) and $Cu(OAc)_2$ (0.60 mmol) were loaded into a 60 mL vial equipped with a Teflon-coated magnetic stir bar. Dioxane (3.0 mL) was added at room temperature. The vial was fitted with an air condenser as cooler and then placed into a preheated oil bath which the temperature was indicated in the table and vigorously stirred for 18 h. After the completion of reaction, the reaction vial was allowed to cool at room temperature. Ethyl acetate (~20 mL), water (~10 mL) and dodecane (68.4 μL, internal standard) were added. The organic layer was subjected to GC analysis. The GC yield obtained was previously calibrated by anthentic sample/dodecane calibration curve.

3.4.3 General procedure for the oxidative arylation of arylsulfonyl hydrazides with heteroarenes

All reagents were weighted in air and the reactions were performed in an open vessel. $Pd(OAc)_2$ (0.0034g, 0.015 mmol), PPh_3 (Pd:L = 1:2), arylsulfonyl hydrazides (0.45 mmol) , heteroarenes (0.30 mmol) and $Cu(OAc)_2$ (0.60 mmol) were loaded into a 60 mL vial equipped with a Teflon-coated magnetic stir bar. Dioxane (3.0 mL) was added at room temperature. The vial was fitted with an air condenser as cooler and then placed into a preheated oil bath which the temperature was indicated in the table and vigorously stirred for 18 h. After the completion of reaction, the reaction vial was allowed to cool at room temperature. Ethyl acetate (~20 mL), water (~10 mL) was added. The organic layer was subjected to GC analysis. After analyzing GC spectra, the crude product in the organic layer was extracted and the vial washed with ethyl acetate. The filtrate was concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (230 -400 mesh) to afford the desired product.

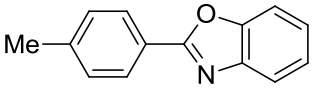
3.4.4 Characterization data of coupling products

2-Phenylbenzoxazole (Table 3.2, entry 1)[8]



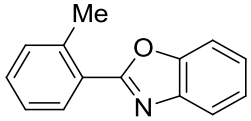
Eluents (EtOAc: Hexane = 1: 20, R_f= 0.62) was used for flash column chromatography. 44.5 mg, 76 % yield, white solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.40 (m, 2H), 7.52-7.57 (m, 3H), 7.58-7.63 (m, 1H), 7.79-7.83 (m, 1H), 8.28 -8.31 (m, 2H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 110.5, 120.0, 124.5, 125.1, 127.1, 127.6, 128.8, 131.5, 142.0, 150.7, 163.0; MS (EI): *m/z* (relative intensity) 195.0 (M^+, 100), 167.0 (18), 139.0 (3), 92.0 (5), 63.0 (14).

2-(4-Methylphenyl)benzoxazole (Table 3.2, entry 2)[14]



Eluents (EtOAc: Hexane = 1: 20, R_f= 0.61) was used for flash column chromatography. 48.9 mg, 78 % yield, white solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.45 (s, 3H), 7.34-7.39 (m, 4H), 7.58-7.60 (m, 1H), 7.78-7.80 (m, 1H), 8.17 (d, *J*= 8.5 Hz, 2H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 21.6, 110.4, 119.8, 124.3, 124.4, 124.8, 127.5, 129.6, 142.0, 142.1, 150.6, 163.2; MS (EI): *m/z* (relative intensity) 209.0 (M^+, 100), 180.0 (8), 116.0 (4), 91.0 (9), 77.0 (2).

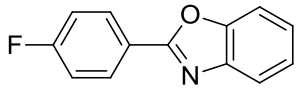
2-(2-Methylphenyl)benzoxazole (Table 3.2, entry 3)[15]



Eluents (EtOAc: Hexane = 1: 20, R_f= 0.64) was used for flash column chromatography. 45.1 mg, 72 % yield, white solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.85 (s, 3H), 7.36-7.46 (m, 5H), 7.60-7.64 (m, 1H), 7.82-7.85 (m, 1H), 8.21 (d, *J*= 7.6

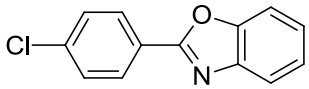
Hz, 1H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 22.2, 110.5, 120.1, 124.3, 125.0, 126.0, 126.2, 129.9, 130.9, 131.8, 138.8, 142.1, 150.3, 163.4; MS (EI): *m/z* (relative intensity) 209.0 (M^+, 100), 180.0 (30), 116.0 (6), 91.0 (13), 77.0 (5).

2-(4-Fluorophenyl)benzoxazole, (Table 3.2, entry 4)[15]



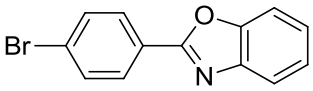
Eluents (EtOAc: Hexane = 1: 20, R_f= 0.54) was used for flash column chromatography. 42.2 mg, 66 % yield, white solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19-7.25 (m, 2H), 7.28-7.39 (m, 2H), 7.56-7.60 (m, 1H), 7.77-7.79 (m, 1H), 8.24-8.29 (m, 2H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 110.5, 116.0, 116.2, 119.9, 123.4, 124.6, 125.1, 129.7, 129.8, 142.0, 150.7, 162.1, 163.5, 166.0; ^{19}F NMR (400 MHz,$CDCl_3$) δ -107.5; MS (EI): *m/z* (relative intensity) 213.0 (M^+, 100), 185.0 (19), 92.2 (6), 75.0 (4), 63.0 (17).

2-(4-Chlorophenyl)benzoxazole (Table 3.2, entry 5)[15]



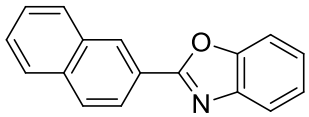
Eluents (EtOAc: Hexane = 1: 20, R_f= 0.66) was used for flash column chromatography. 41.3 mg, 60 % yield, white solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.40 (m, 2H), 7.51 (d, *J*= 8.0 Hz, 2H), 7.55-7.61 (m, 1H), 7.76-7.81 (m, 1H), 8.20 (d, *J*= 8.8 Hz, 2H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 110.6, 120.0, 124.7, 125.3, 125.6, 128.8, 129.2, 137.7, 142.0, 150.7, 162.0; MS (EI): *m/z* (relative intensity) 229.0 (M^+, 100), 201.0 (11), 166.0 (7), 139.0 (3), 111.0 (3).

2-(4-Bromophenyl)benzoxazole (Table 3.2, entry 6)[15]



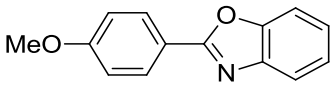
Eluents (EtOAc: Hexane = 1: 20, R_f= 0.63) was used for flash column chromatography. 48.3 mg, 59 % yield, white solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.41 (m, 2H), 7.55-7.61 (m, 1H), 7.68 (d, *J*= 8.4 Hz, 2H), 7.77-7.80 (m, 1H), 8.13 (d, *J*= 6.8 Hz, 2H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 110.6, 120.1, 124.7, 125.3, 126.1, 126.2, 129.0, 132.2, 142.0, 150.7, 162.1; MS (EI): *m/z* (relative intensity) 272.9 (M^+, 100), 246.9 (8), 194.0 (9), 166.0 (7), 140.0 (7).

2-(2-Naphthalenyl)benzoxazole (Table 3.2, entry 7)[8]



Eluents (EtOAc: Hexane = 1: 20, R_f= 0.50) was used for flash column chromatography. 49.2 mg, 67 % yield, white solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.40 (m, 2H), 7.55-7.64 (m, 3H), 7.99 (t, *J*= 7.8 Hz, 2H), 8.33 (d, *J*= 8.8 Hz, 1H), 8.78 (s, 1H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 110.6, 120.0, 123.9, 124.4, 124.6, 125.1, 126.9, 127.7, 127.9, 128.1, 128.7, 128.9, 132.9, 134.7, 142.2, 150.8, 163.2; MS (EI): *m/z* (relative intensity) 245.0 (M^+, 100), 216.0 (6), 153.0 (9), 127.0 (12), 92.0 (3).

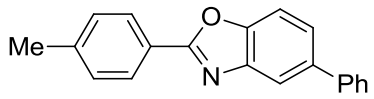
2-(4-Methoxyphenyl)benzoxazole (Table 3.2, entry 8)[8]



Eluents (EtOAc: Hexane = 1: 20, R_f= 0.39) was used for flash column chromatography. 35.1 mg, 52 % yield, white solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.90 (s, 3H), 7.04 (d, *J*= 8.8 Hz, 2H), 7.31-7.37 (m, 2H), 7.57 (d, *J*= 6.2 Hz, 1H), 7.76 (d, *J*= 6.0 Hz, 1H), 8.22 (d, *J*= 8.8 Hz, 2H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 55.4, 110.3,

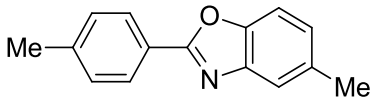
114.3, 119.6, 119.7, 124.4, 124.6, 129.3, 142.2, 150.6, 162.3, 163.1; MS (EI): *m/z* (relative intensity) 225.0 (M^+, 100), 206 (34), 182.0 (36), 127.0 (9), 90.0 (1).

2-(4-Methylphenyl)-5-phenylbenzoxazole (Table 3.3, entry 1)[16]



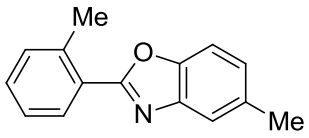
Eluents (EtOAc: Hexane = 1: 20, R_f= 0.47) was used for flash column chromatography. 59.9 mg, 70 % yield, white solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.47 (s, 3H), 7.35-7.68 (m, 9H), 7.99 (s, 1H), 8.19 (d, *J*= 7.6 Hz, 2H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 21.6, 110.4, 118.2, 124.3, 124.4, 127.1, 127.4, 127.6, 128.8, 129.6, 138.3, 141.1, 142.1, 142.8, 150.2, 163.8; MS (EI): *m/z* (relative intensity) 285.1 (M^+, 100), 207.0 (6), 139.0 (30), 114.0 (2), 89.0 (3).

5-Methyl-2-(4-methylphenyl)benzoxazole (Table 3.3, entry 2)[14]



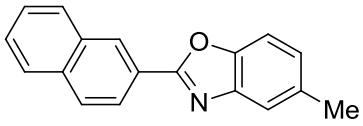
Eluents (EtOAc: Hexane = 1: 20, R_f= 0.50) was used for flash column chromatography. 50.2 mg, 75 % yield, white solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.45 (s, 3H), 2.50 (s, 3H), 7.15 (d, *J*= 8.2 Hz, 1H), 7.33 (d, *J*= 8.0 Hz, 2H), 7.45 (d, *J*= 8.0 Hz, 1H), 7.56 (s, 1H), 8.15 (d, *J*= 8.0 Hz, 2H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 21.5, 21.6, 109.8, 119.7, 124.5, 125.9, 127.5, 129.6, 134.2, 141.8, 142.4, 148.9, 163.4; MS (EI): *m/z* (relative intensity) 223.0 (M^+, 100), 194.0 (5), 111.5 (4), 78.0 (16), 51.0 (8).

5-Methyl-2-(2-methylphenyl)benzoxazole (Table 3.3, entry 3)



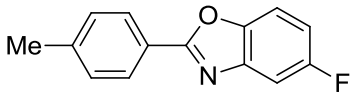
Eluents (EtOAc: Hexane = 1: 20, R_f= 0.66) was used for flash column chromatography. 48.2 mg, 72 % yield, white solid, m.p. 92-95 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.52 (s, 3H), 2.84 (s, 3H), 7.19 (d, *J*= 8.2 Hz, 1H), 7.35-7.49 (m, 4H), 7.63 (s, 1H), 8.19 (d, *J*= 6.4 Hz, 1H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 21.4, 22.1, 109.7, 120.0, 125.9, 126.0, 126.3, 129.8, 130.7, 131.7, 134.1, 138.7, 142.3, 148.5 163.5; MS (EI): *m/z* (relative intensity) 223.1 (M^+, 100), 194.0 (14), 180.0 (9), 91.0 (5), 77.0 (12); HRMS (ESI) calcd. for $C_{15}H_{14}NO$ [M + H^+]: 224.1075, found 224.1072.

5-Methyl-2-(2-naphthalenyl)benzoxazole (Table 3.3, entry 4)[17]



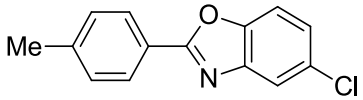
Eluents (EtOAc: Hexane = 1: 20, R_f= 0.49) was used for flash column chromatography. 52.1 mg, 67 % yield, white solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.52 (s, 3H), 7.19 (d, *J*= 8.0 Hz, 1H), 7.50 (d, *J*= 8.4 Hz, 1H), 7.55-7.61 (m, 3H), 7.90 (d, *J*= 7.6 Hz, 1H), 7.99 (t, *J*= 8.0 Hz, 2H), 8.32 (d, *J*= 8.6 Hz, 1H), 8.77 (s, 1H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 21.5, 109.9, 119.9, 123.9, 124.5, 126.2, 126.8, 127.7, 127.8, 127.9, 128.7, 128.9, 132.9, 134.4, 134.6, 142.4, 149.1, 163.2; MS (EI): *m/z* (relative intensity) 259.0 (M^+, 100), 230.0 (5), 153.0 (16), 127.0 (9), 77.0 (11).

5-Fluoro-2-(4-methylphenyl)benzoxazole (Table 3.3, entry 5)[18]



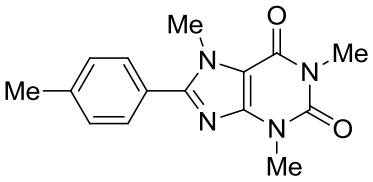
Eluents (EtOAc: Hexane = 1: 20, R_f= 0.51) was used for flash column chromatography. 48.4 mg, 71 % yield, white solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.45 (s, 3H), 7.04-7.09 (m, 1H), 7.33 (d, *J*= 8.0 Hz, 2H), 7.43-7.50 (m, 2H), 8.12 (d, *J*= 8.4 Hz, 2H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 21.6, 106.1, 106.4, 110.6, 110.7, 112.2, 112.5, 124.1, 127.6, 129.7, 142.4, 142.9, 143.1, 147.0, 158.9, 161.3, 165.0; ^{19}F NMR (400 MHz,$CDCl_3$) δ -117.9; MS (EI): *m/z* (relative intensity) 227.0 (M^+, 100), 198.0 (5), 116.0 (4), 91.0 (15), 63.0 (7).

5-Chloro-2-(4-methylphenyl)benzoxazole (Table 3.3, entry 6)[14]



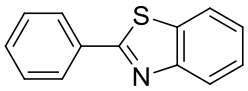
Eluents (EtOAc: Hexane = 1: 20, R_f= 0.53) was used for flash column chromatography. 52.6 mg, 72 % yield, white solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.45 (s, 3H), 7.29-7.34 (m, 3H), 7.47 (d, *J*= 8.4 Hz, 1H), 7.73 (s, 1H), 8.12 (d, *J*= 8.0 Hz, 2H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 21.7, 111.1, 119.8, 123.9, 125.1, 127.7, 129.7, 129.9, 142.5, 143.3, 149.2, 164.6; ^{19}F NMR (400 MHz,$CDCl_3$) δ -117.9; MS (EI): *m/z* (relative intensity) 243.0 (M^+, 100), 215.0 (3), 116.0 (4), 91.0 (17), 63.0 (23).

1,3,7-Trimethyl-8-(4-tolyl)-xanthine (Scheme 3.3, compound 1)[14]



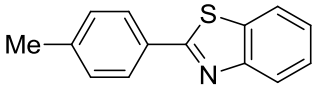
Eluents (EtOAc: Hexane = 1: 20, R_f= 0.44) was used for flash column chromatography. 53.7 mg, 63 % yield, white solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44 (s, 3H), 3.43 (s, 3H), 3.62 (s, 3H), 4.05 (s, 3H), 7.33 (d, *J*= 7.6 Hz, 2H), 7.58 (d, *J*= 8.4 Hz, 2H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 21.4, 27.8, 29.7, 33.8, 108.3, 125.4, 128.9, 129.5, 140.6, 148.2, 151.6, 152.2, 155.4; MS (EI): *m/z* (relative intensity) 284.1 (M^+, 100), 255.0 (4), 226.0 (5), 184.0 (5), 82.0 (30).

2-Phenylbenzothiazole (Scheme 3.3, compound 2)[14]



Eluents (EtOAc: Hexane = 1: 20, R_f= 0.64) was used for flash column chromatography. 42.4 mg, 67 % yield, white solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (t, *J*= 7.0 Hz, 1H), 7.50-7.55 (m, 4H), 7.93 (d, *J*= 8.0 Hz, 1H), 8.11-8.15 (m, 3H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 121.6, 123.2, 125.2, 126.3, 127.5, 129.0, 130.9, 133.6, 135.0, 154.1, 168.0; MS (EI): *m/z* (relative intensity) 211.0 (M^+, 100), 184.0 (4), 167.0 (5), 108.0 (20), 69.0 (13).

2-(4-Methylphenyl)benzothiazole (Scheme 3.3, compound 3)[14]



Eluents (EtOAc: Hexane = 1: 20, R_f= 0.59) was used for flash column chromatography. 46.6 mg, 69 % yield, white solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.45 (s, 3H), 7.32 (d, *J*= 8.0 Hz, 2H), 7.39 (t, *J*= 7.0 Hz, 1H), 7.51 (t, *J*= 7.2 Hz, 1H), 7.91 (d, *J*= 7.8 Hz, 1H), 8.01 (d, *J*= 8.0 Hz, 2H), 8.10 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR

(100 MHz,$CDCl_3$) δ 21.5, 121.6, 123.1, 125.0, 126.2, 127.5, 129.7, 131.0, 135.0, 141.4, 154.2, 168.2; MS (EI): *m/z* (relative intensity) 225.0 (M^+, 100), 108.0 (7), 91.0 (4), 68.9 (8), 51.0 (2).

3.5 References

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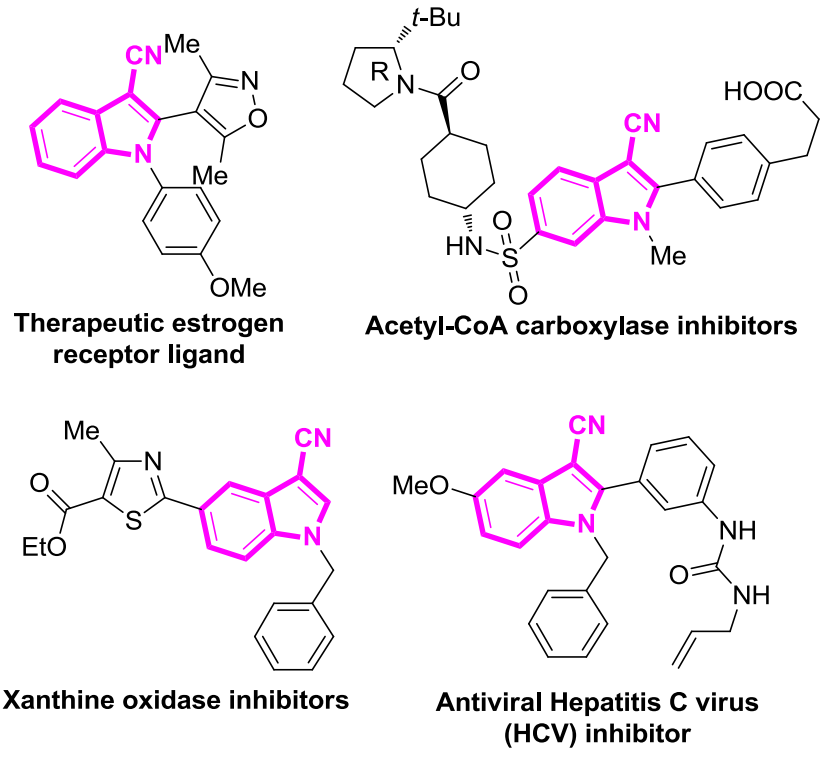
Chapter 4 Copper-Mediated C-3 Cyanation of Indole Derivatives using Benzyl Cyanide as cyanating agent

4.1 Introduction

Indole scaffold is exemplified as an important subunit not only in pharmaceutical and agrochemical products, but also basic constituents of dyes and herbicides.[1] In particular, 3-cyanoindole is a key building block in pharmaceutical syntheses that can be applied in medicinal chemistry and drug discovery. With the nitrile moiety, further transformations of this group into a broad range of functional groups, such as amines, aldehydes, acids, amides, ketones and heterocycles, can be made.[2] In fact, 3-cyanoindole scaffold containing structures have been well-known for their uses as therapeutic estrogen receptor ligand,[3] acetyl-CoA carboxylase inhibitors for type 2 diabetes,[4] xanthine-oxidase inhibitors,[5] antiviral hepatitis C virus inhibitors,[6] aldosterone synthase modulator for cardiovascular diseases,[7] anticancer agents,[8] and antithrombotics factor Xa inhibitors (Figure 4.1).[9]



Therapeutic estrogen receptor ligand

Acetyl-CoA carboxylase inhibitors

Xanthine oxidase inhibitors

Antiviral Hepatitis C virus (HCV) inhibitor

Figure 4.1 Examples of useful substituted 3-cyanoindole containing molecules

Aryl nitriles are generally prepared from classical organic transformations, such as Sandmeyer[10] and Rosenmund-von Braun reaction,[11] in which pre-functionalized starting materials are often required. Palladium- and copper-catalyzed cyanation of aryl halides and sulfonates are also well documented methods.[12] Yet, there has been no example reported for the conversion of 3-bromoindole to 3-cyanoindole. In fact, organic transformations from modified Madelung reaction,[13] metal-free oxidative synthesis from *N*-aryl enamines[14], palladium-catalyzed *N*-heterocyclization[15] and propylphosphonic anhydride-promoted conversion of aldehydes[16] are alternative approaches to afford 3-cyanoindoles. Indeed, emerging methods for facile synthesis of 3-cyanoindoles using direct C-H functionalization protocol are highly desirable. Lewis acid, Fe, Cu and Pd salts are usually employed as the catalyst for accessing 3-cyanoindole using various metal cyanides and other cyanide anion (CN^-) surrogates .[17]

Nevertheless, most commonly available metal cyanides are extremely toxic. Although $K_4[Fe(CN)_6]$ is exceptionally non-toxic, its low solubility in organic solvent limited its applicability. Despite these limited CN^- sources, an exploration of other user-friendly organic CN^- source for direct cyanation of indole would be highly favorable. In the recent years, Wang and co-workers firstly reported palladium-catalyzed cyanation of aryl halides,[18] Copper-mediated cyanation of arenes,[19] aryl halides,[20] indole derivatives[21] and arylboronic acids[22] using benzyl cyanide as a CN^- surrogate. This notable reagent is commercially available, hazardless, inexpensive and highly soluble in common organic solvents. In view of the beneficial features associating with this CN^- source as well as our current interest in cyanation reactions,[23] herein we disclose our efforts on copper-mediated direct

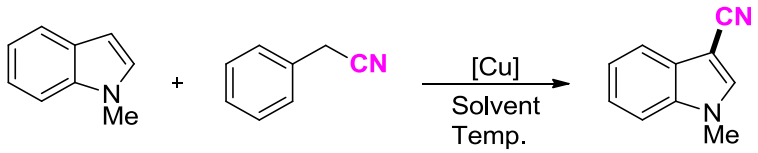
cyanation of indole using benzyl cyanide in a highly regioselective manner.

4.2 Results and discussion

4.2.1 Preliminary evaluation of copper-mediated direct C3-cyanation of indole derivatives

In order to achieve the C-3 indole functionalization for cyanation, a series of reaction parameter optimization were deployed (Table 4.1). *N*-Methylindole was chosen as the benchmark substrate. Commercially available copper salts were investigated (Table 4.1, entries 2-8). CuI showed successful cyanation of indole while other Cu complexes did not. A screening of solvent revealed that DMF was the solvent of choice (Table 4.1, entries 6, 9-12). When the reaction temperature was increased from 110 ^{o}C to 130 ^{o}C and the reaction time was extended to 24 h, the product yield was improved (Table 4.1, entries 1 and 2, 2 and 6).

Table 4.1 Initial optimization of direct C3-cyanation of *N*-methylindole[a]



entry	[Cu] (equiv.)	solvent	time (h)	% yield[b]
1[c]	CuI (1)	DMF	20	Trace
2	CuI (1)	DMF	20	51
3	Cu_2O (1)	DMF	20	0
4	Cu(OAc) (1)	DMF	20	Trace

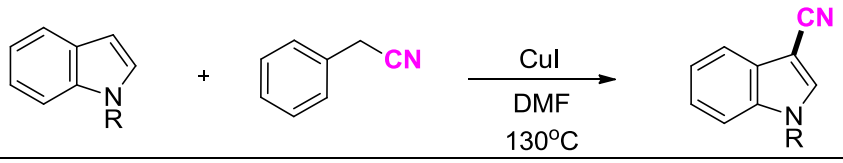
5	$Cu(OAc)_2$ (1)	DMF	20	Trace
6	CuI (1)	DMF	24	89
7	CuBr (1)	DMF	24	Trace
8	CuCl (1)	DMF	24	0
9	CuI (1)	CH_3CN	24	0
10	CuI (1)	dioxane	24	0
11	CuI (1)	toluene	24	0
12	CuI (1)	DMSO	24	Trace
13[d]	CuI (1)	DMF	24	79
14	CuI (1.5)	DMF	24	91

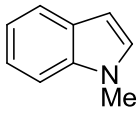
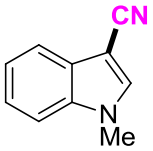
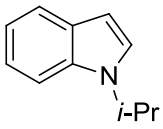
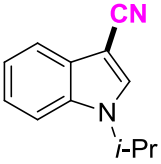
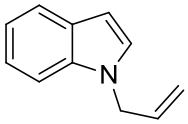
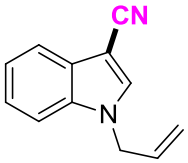
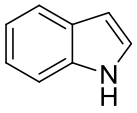
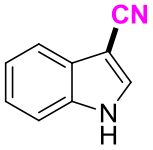
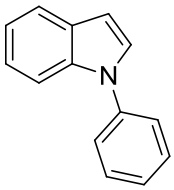
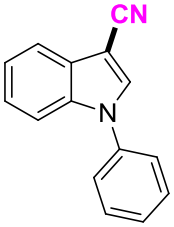
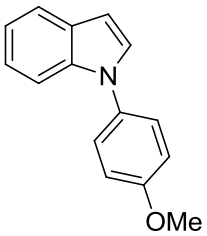
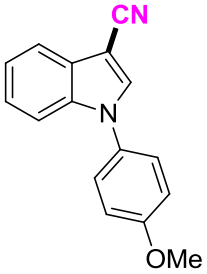
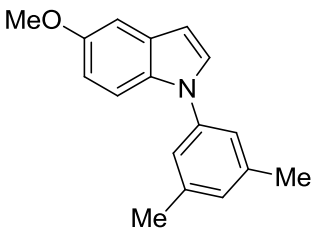
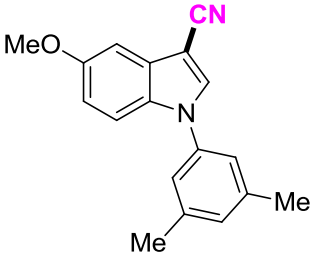
[a] Reaction conditions: copper source (0.5 mmol, 1 equiv), *N*-methylindole (0.5 mmol), $PhCH_2CN$ (0.75 mmol) and solvent (2.0 mL) were stirred under air at 130 ^oC for indicated period of time. [b] Calibrated GC yields were reported using pentadecane as the internal standard. [c] 110 ^oC was used. [d] 140 ^oC was used.

4.2.2 Scope of copper-mediated direct C3-cyanation of indole derivatives

Having the optimized reaction conditions in hand, we next examined the substrate scope of this cyanation reaction (Table 4.2). *N*-Alkylated indoles proceeded smoothly to give the corresponding products in good yields (Table 4.2, entries 1-2). Allyl group remained intact during the course of the reaction (Table 4.2, entry 3). Disappointingly, unprotected NH indole showed poor conversion under these reaction conditions (Table 4.2, entry 4). It is possibly due to the decomposition of unprotected indole. *N*-Arylindoles were also tested (Table 4.2, entries 5-7). Moderate yields were generally obtained.

Table 4.2 Copper-mediated direct C3-cyanation of indoles[a]

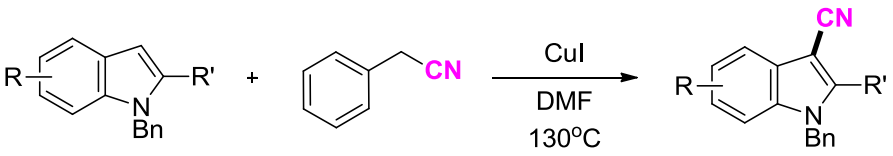


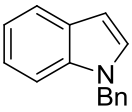
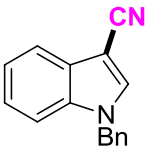
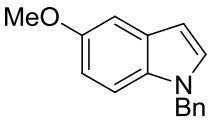
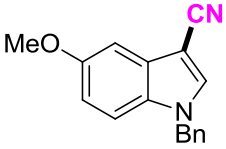
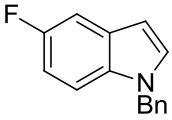
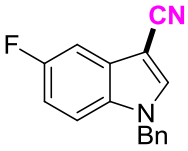
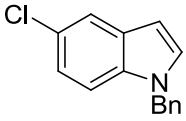
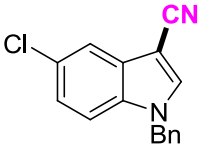
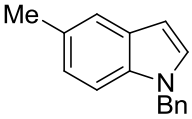
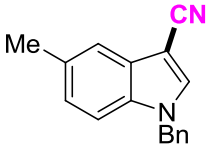
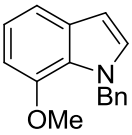
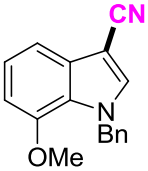
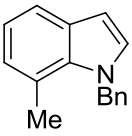
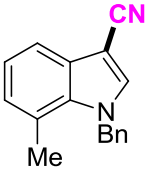
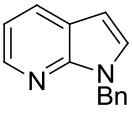
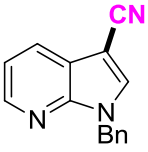
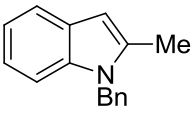
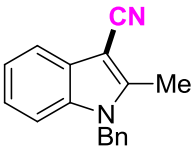
entry	indole	product	time(h)	% yield[b]
1			24 h	86
2			24 h	70
3			24 h	73
4			24 h	17
5[c]			48 h	60
6[c]			46 h	66
7[c]			48 h	57

[a] Reaction conditions: CuI (0.5 mmol), *N*-substituted indole (0.5 mmol), $PhCH_2CN$ (0.75 mmol) and DMF (2.0 mL) were stirred under air at 130 ^oC for indicated time. [b] Isolated yield. [c] 1.5 equiv. of CuI was used.

To further test the generality of the reaction system, a series of substituted *N*-benzylindoles was probed in this cyanation system (Table 4.3). Functional groups such as fluoro, chloro, and methoxy were compatible under these reaction conditions (Table 4.3, entries 2-4). The intact chloro group is beneficial for later functionalization using other coupling protocols.[24] In fact, these nitrile containing products can undergo further organic transformations to afford a variety of potential xanthine oxidase inhibitors, HCV inhibitors and therapeutic estrogen receptor ligands.[3,5,6] *N*-Benzylindoles with 5- and 7-substitutents furnished the desired product smoothly with extended reaction times (Table 4.3, entries 5-7). Azaindole and sterically hindered 2-methyl-*N*-benzylindole were found to be feasible substrates for the cyanation (Table 4.3, entries 8 and 9).

Table 4.3 Copper-mediated direct C3-cyanation of benzylindoles[a]

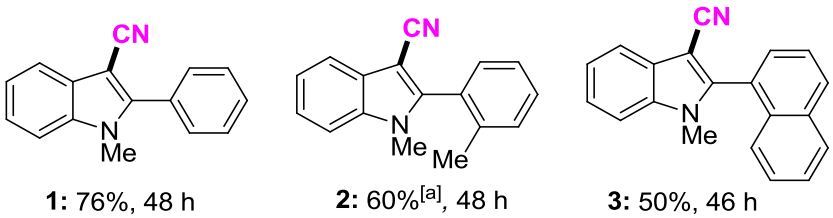


entry	indole	product	time	% yield[b]
1			24 h	82
2			24 h	78
3			28 h	62
4			28 h	73
5			49 h	77
6			46 h	70
7			46 h	60
8			6 h	65
9[c]			48 h	56

[a] Reaction conditions: CuI (0.5 mmol), substituted benzylindole (0.5 mmol),

$PhCH_2CN$ (0.75 mmol) and DMF (2.0 mL) were stirred under air at 130 ^oC for indicated time. [b] Isolated yield. [c] 1.5 equiv. of CuI was used.

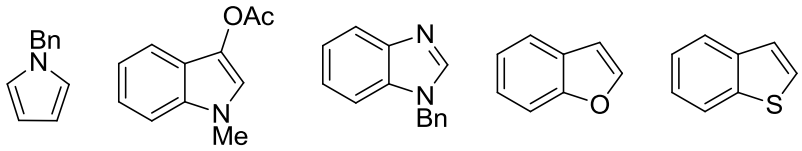
Highly sterically congested 2-aryl-*N*-methylindoles were applicable substrates for direct cyanation (Scheme 4.1). 2-(1-Naphthyl)-*N*-methylindole afforded the desired product in lower yield presumably due to the large steric hindrance of the *ortho*-naphthyl moiety.



1: 76%, 48 h **2:** 60%[a], 48 h **3:** 50%, 46 h

Scheme 4.1 Copper-mediated direct C3-cyanation of *N*-methyl indoles (reaction conditions were the same as in Table 4.2, entry 5). [a] 1.0 mmol $PhCH_2CN$ was used.

Other heteroarenes were used as substrates in this optimized reaction condition (Scheme 4.2). However, no desired products could be obtained.



Scheme 4.2 Unsuccessful examples of copper-mediated direct cyanation of heteroarenes (Reaction conditions were same as Table 4.2, entry 1)

4.3 Conclusion

In summary, we have developed a simple protocol for facile preparation of 3-cyanoindoles. Inexpensive reaction system, copper(I) iodide and benzyl cyanide, is found effective to promote regioselective cyanation of indoles in open-to-air vessel.

This protocol potentially provides a more direct and complementary access of pharmaceutically useful intermediates.

4.4 Experimental section

4.4.1 General considerations

Unless otherwise noted, all reagents were purchased from commercial suppliers and used without purification. All cyanations were performed in an open vessel, a vial (approx. 60 mL volume), fitted with an air condenser and equipped with Teflon coated magnetic stir bar (4 mm x 10 mm). All indole derivatives except indole, *N*-methylindole and *N*-methyl-2-phenylindole, were synthesized according to the literature methods.[25] 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. NMR spectra were recorded on a Brüker spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C and 376 MHz for ^{19}F). 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). ^{19}F NMR chemical shifts were determined relative to $CFCl_3$ as the external standard and low field is positive. 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 (ESI-MS). 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, ^{13}C and/or ^{19}F 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.

4.4.2 General procedure for reaction condition screenings

All reagents were weighted in air and the reactions were performed in an open-to-air vessel. Copper salt (0.25-0.75 mmol), *N*-methylindole (0.5 mmol) and $PhCH_2CN$ (0.75 mmol) were loaded into a 60 mL vial equipped with a Teflon-coated magnetic stir bar. The solvent (2 mL) was added at room temperature. The vial was fitted with an air condenser and then placed into a preheated oil bath with vigorous stirring for the indicated time. After the completion of reaction, the vial was allowed to cool at room temperature. Ethyl acetate (~20 mL) and pentadecane (internal standard) were added. The organic layer was subjected to GC analysis.

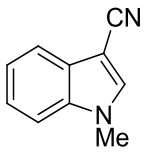
4.4.3 General procedure for cyanation of indoles with benzyl cyanide

Copper(I) iodide (0.5-0.75 mmol), $PhCH_2CN$ (0.75-1.0 mmol), indole derivatives (0.5 mmol) and DMF (2.0 mL) were loaded into a 60 mL vial equipped with an air condenser and Teflon-coated magnetic stir bar under air. The vial was then placed into a preheated oil bath which the temperature was indicated in the table and vigorously stirred in an open system for the indicated time. After the

completion of reaction, the reaction vial was allowed to cool at room temperature. Ethyl acetate (~20 mL) was added for dilution. The organic layer was subjected to GC analysis. After analyzing GC spectra, the crude product was further extracted with ethyl acetate (2 x 10 mL). The filtrate was concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel to afford the desired product.

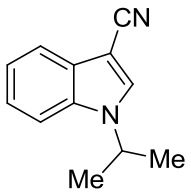
4.4.4 Characterization data of substituted cyanoindole products

1-Methyl-1*H*-indole-3-carbonitrile (Table 4.2, entry 1)[17f]



Eluents (DCM: Hexane = 1: 1, R_f= 0.5) was used for flash column chromatography. 67.1 mg, 86 % yield, brown liquid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.85 (s, 3H), 7.29-7.42 (m, 3H), 7.55 (s, 1H), 7.76 (d, *J*= 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 33.6, 85.3, 110.3, 115.9, 122.1, 123.8, 127.7, 135.5, 136.0.

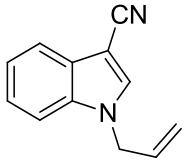
1-Isopropyl-1*H*-indole-3-carbonitrile (Table 4.2, entry 2)



Eluents (DCM: Hexane = 1: 1, R_f= 0.35) was used for flash column chromatography. 64.4 mg, 70 % yield, brown liquid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.59 (d, *J*= 6.8 Hz, 6H), 4.70-4.77 (m, 1H), 7.29-7.38 (m, 2H), 7.48 (d, *J*= 8.0 Hz, 1H), 7.74 (s, 1H), 7.78

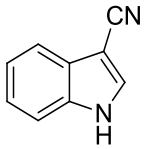
(d, *J*= 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.6, 48.4, 85.6, 110.7, 116.2, 119.9, 122.1, 123.6, 128.0, 131.2, 135.0; HRMS (ESI) calcd. for $C_{12}H_{13}N_2$ [M + H^+]: 185.1079, found 185.1083.

1-Allyl-1*H*-indole-3-carbonitrile (Table 4.2, entry 3)[17i]



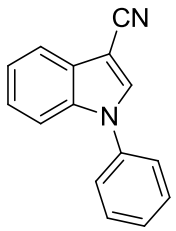
Eluents (DCM: Hexane = 1: 1, R_f= 0.35) was used for flash column chromatography. 64.4 mg, 73 % yield, brown liquid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.79 (d, *J*= 5.6 Hz, 2H), 5.18 (d, *J*= 17.2 Hz, 1H), 5.33 (d, *J*= 10.4 Hz, 1H), 5.96-6.06 (m, 1H), 7.30-7.39 (m, 2H), 7.42 (d, *J*= 7.4 Hz, 1H), 7.63 (s, 1H), 7.79 (d, *J*= 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.4, 86.0, 110.7, 115.8, 119.0, 119.9, 122.2, 123.8, 127.9, 131.6, 134.6, 135.4.

1*H*-Indole-3-carbonitrile (Table 4.2, entry 4)[17f]



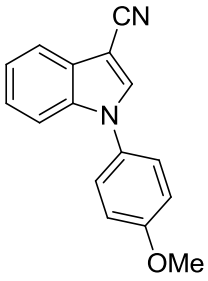
Eluents (DCM: Hexane = 6: 1, R_f= 0.20) was used for flash column chromatography. 12.1 mg, 17 % yield, yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.42 (m, 2H), 7.51 (d, *J*= 8.4 Hz, 1H), 7.76 (s, 1H), 7.81 (d, *J*= 6.4 Hz, 1H), 8.86 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 87.5, 112.0, 115.7, 119.6, 122.3, 124.3, 126.9, 131.7, 134.8.

1-Phenyl-1*H*-indole-3-carbonitrile (Table 4.2, entry 5)[17i]



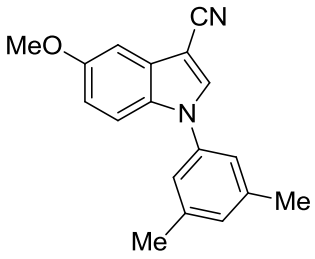
Eluents (DCM: Hexane = 1: 1, R_f= 0.5) was used for flash column chromatography. 65.4 mg, 60 % yield, light orange solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.39 (m, 2H), 7.49-7.56 (m, 4H), 7.59-7.63 (m, 2H), 7.82 (s, 1H), 7.84-7.86 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 88.0, 111.5, 115.4, 119.9, 122.7, 124.5, 124.8, 127.9, 128.3, 130.0, 134.6, 135.5, 137.2.

1-(4-Methoxyphenyl)-1*H*-indole-3-carbonitrile (Table 4.2, entry 6)[17i]



Eluents (DCM: Hexane = 1: 1, R_f= 0.25) was used for flash column chromatography. 81.8 mg, 66 % yield, white solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.92 (s, 3H), 7.09 (d, *J*= 8.8 Hz, 2H), 7.34-7.36 (m, 2H), 7.40 (d, *J*= 8.8 Hz, 2H), 7.43-7.46 (m, 1H), 7.76 (s, 1H), 7.82-7.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.6, 87.4, 111.4, 115.0, 115.6, 119.8, 122.5, 124.3, 126.3, 127.7, 130.5, 134.9, 136.0, 159.4.

1-(3,5-Dimethylphenyl)-5-methoxy-1*H*-indole-3-carbonitrile (Table 4.2, entry 7)

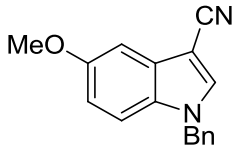


Eluents (DCM: Hexane = 1: 1, R_f= 0.25) was used for flash column chromatography. 78.7 mg, 57 % yield, light orange solid, m.p. 140.7 – 141.8 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 6H), 3.91 (s, 3H), 6.97 (d, *J*= 8.8 Hz, 1H), 7.08 (s, 2H), 7.11 (s, 1H), 7.23 (s, 1H), 7.41 (d, *J*= 8.8 Hz, 1H), 7.72 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 55.8, 87.2, 100.8, 112.7, 115.1, 122.3, 128.9, 129.9, 130.5, 134.5, 137.8, 139.9, 156.3; HRMS (ESI) calcd. for $C_{18}H_{17}N_2O$ [M + H^+]: 277.1341, found 277.1332.

1-Benzyl-1*H*-indole-3-carbonitrile (Table 4.3, entry 1)[17i]

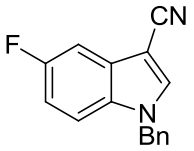
Eluents (DCM: Hexane = 1: 1, R_f= 0.5) was used for flash column chromatography. 95.1 mg, 82 % yield, brown liquid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.36 (s, 2H), 7.16-7.19 (m, 2H), 7.32-7.41 (m, 6H), 7.62 (s, 1H), 7.80-7.82 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 50.8, 86.1, 110.7, 119.9, 122.2, 123.9, 127.0, 127.9, 128.3, 129.0, 134.9, 135.1, 135.5.

1-Benzyl-5-methoxy-1*H*-indole-3-carbonitrile (Table 4.3, entry 2)[26]



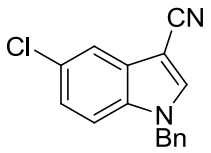
Eluents (DCM: Hexane = 1: 1, R_f= 0.2) was used for flash column chromatography. 102.2 mg, 78 % yield, white solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.88 (s, 3H), 5.30 (m, 2H), 6.95 (dd, *J*= 2.4, 9.2 Hz, 1H), 7.14-7.17 (m, 2H), 7.19 (s, 1H), 7.24 (d, *J*= 9.2 Hz, 1H), 7.34-7.37 (m, 3H), 7.56 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 50.9, 55.6, 85.5, 100.8, 111.7, 114.6, 126.9, 128.3, 128.8, 129.0, 130.4, 134.8, 135.2, 156.0.

1-Benzyl-5-fluoro-1*H*-indole-3-carbonitrile (Table 4.3, entry 3)



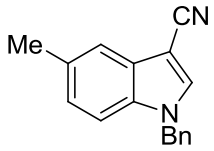
Eluents (DCM: Hexane = 1: 1, R_f= 0.25) was used for flash column chromatography. 77.5 mg, 62 % yield, orange solid, m.p. 93.4-95.2 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.35 (s, 2H), 7.05 (td, *J*= 2.4, 8.8 Hz, 1H), 7.17 (d, *J*= 6.8 Hz, 2H), 7.29-7.34 (m, 1H), 7.36-7.42 (m, 4H), 7.65 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 51.1, 86.1, 104.9, 105.2, 111.9, 112.5, 112.8, 115.2, 127.0, 128.5, 129.1, 132.0, 134.8, 136.1, 157.9, 160.3; ^{19}F NMR (400 MHz, $CDCl_3$) δ -120.3; HRMS (ESI) calcd. for $C_{16}H_{11}N_2F$ [M + Na^+]: 273.0804, found 273.0810.

1-Benzyl-5-chloro-1*H*-indole-3-carbonitrile (Table 4.3, entry 4)



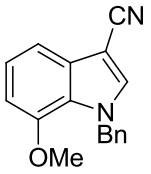
Eluents (DCM: Hexane = 1: 1, R_f= 0.4) was used for flash column chromatography. 97.3 mg, 73 % yield, orange solid, m.p. 117.9-120.0 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.35 (s, 2H), 7.15 (d, *J*= 6.0 H, 2H), 7.25-7.31 (m, 2H), 7.36-7.41 (m, 3H), 7.63 (s, 1H), 7.75 (s, 1H);; ^{13}C NMR (100 MHz, $CDCl_3$) δ 51.0, 85.7, 112.0, 115.0, 119.2, 124.4, 127.0, 128.2, 128.5, 128.8, 129.1, 133.8, 134.7, 135.9; HRMS (ESI) calcd. for $C_{16}H_{12}N_2Cl$ [M + H^+]: 267.0689, found 267.0684.

1-Benzyl-5-methyl-1*H*-indole-3-carbonitrile (Table 4.3, entry 5)[17d]



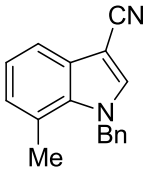
Eluents (DCM: Hexane = 1: 1, R_f= 0.45) was used for flash column chromatography. 94.5 mg, 77 % yield, light orange solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.50 (s, 3H), 5.33 (s, 2H), 7.14-7.17 (m, 3H), 7.26 (d, *J*= 8.4 Hz, 1H), 7.34-7.39 (m, 3H), 7.58 (d, *J*= 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 50.9, 85.6, 110.5, 116.0, 119.6, 125.7, 127.1, 128.3, 128.4, 129.1, 132.1, 134.0, 134.9, 135.4.

1-Benzyl-7-methoxy-1*H*-indole-3-carbonitrile (Table 4.3, entry 6)



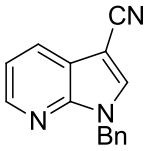
Eluents (DCM: Hexane = 1: 1, R_f= 0.2) was used for flash column chromatography. 90.4 mg, 69 % yield, light orange solid, m.p. 142.8-146.9 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.89 (s, 3H), 5.66 (s, 2H), 6.75 (d, *J*= 8.0 Hz, 1H), 7.15 (d, *J*= 7.2 Hz, 2H), 7.21 (t, *J*= 8.0 Hz, 1H), 7.31-7.38 (m, 4H), 7.50 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.4, 55.4, 86.4, 104.7, 112.3, 115.8, 122.9, 125.4, 126.9, 127.9, 128.8, 130.2, 135.4, 137.2, 147.9; HRMS (ESI) calcd. for $C_{17}H_{15}N_2O$ [M + H^+]: 263.1184, found 263.1191.

1-Benzyl-7-methyl-1*H*-indole-3-carbonitrile (Table 4.3, entry 7)



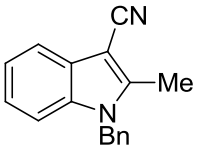
Eluents (DCM: Hexane = 1: 1, R_f= 0.45) was used for flash column chromatography. 71.3 mg, 58 % yield, yellow solid, m.p. 153.7-154.5 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.57 (s, 3H), 5.63 (s, 2H), 6.97 (d, *J*= 7.2 Hz, 2H), 7.04 (d, *J*= 7.2 Hz, 1H), 7.20 (t, *J*= 7.6 Hz, 1H), 7.32-7.38 (m, 3H), 7.56 (s, 1H), 7.67 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.2, 52.9, 86.4, 115.6, 117.9, 122.1, 122.4, 125.5, 126.8, 128.0, 128.9, 129.1, 130.7, 134.4, 136.4, 137.1; HRMS (ESI) calcd. for $C_{17}H_{15}N_2$ [M + H^+]: 247.1235, found 247.1226.

1-Benzyl-1*H*-pyrrolo[2,3-*b*]pyridine-3-carbonitrile (Table 4.3, entry 8)



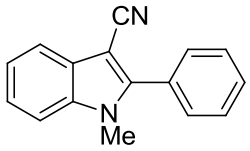
Eluents (DCM: Hexane = 1: 1, R_f= 0.2) was used for flash column chromatography. 75.7 mg, 65 % yield, yellow solid, m.p. 90.3-91.6 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.56 (s, 2H), 7.28-7.38 (m, 6H), 7.71 (s, 1H), 8.12 (dd, *J*= 1.6, 6.4 Hz, 1H), 8.51 (dd, *J*= 1.6, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 48.7, 85.0, 118.3, 120.1, 127.9, 128.4, 128.5, 129.0, 134.9, 135.6, 145.2, 146.4; HRMS (ESI) calcd. for $C_{15}H_{12}N_3$ [M + H^+]: 234.1031, found 234.1041.

1-Benzyl-2-methyl-1*H*-indole-3-carbonitrile (Table 4.3, entry 9)[17d]



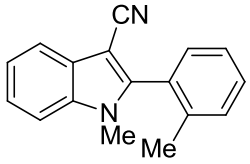
Eluents (DCM: Hexane = 1: 1, R_f= 0.45) was used for flash column chromatography. 68.9 mg, 56 % yield, yellow liquid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.55 (s, 3H), 5.35 (s, 2H), 7.00 (d, *J*= 6.4 Hz, 2H), 7.26-7.33(m, 6H), 7.73 (d, *J*= 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.1, 47.3, 85.7, 110.3, 116.5, 119.1, 122.2, 123.4, 126.0, 127.2, 128.0, 129.1, 135.7, 136.2, 145.8.

1-Methyl-2-phenyl-1*H*-indole-3-carbonitrile (Scheme 4.1, compound 1) [17h]



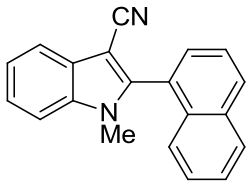
Eluents (DCM: Hexane = 1: 1, R_f= 0.4) was used for flash column chromatography. 88.2 mg, 76 % yield, yellow liquid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.76 (s, 3H), 7.37-7.44 (m, 3H), 7.58 (s, 5H), 7.80 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.6, 85.2, 110.5, 119.2, 119.2, 122.2, 123.7, 127.4, 128.5, 128.8, 129.7, 136.7, 147.9.

1-Methyl-2-(*o*-tolyl)-1*H*-indole-3-carbonitrile (Scheme 4.1, compound 2)



Eluents (DCM: Hexane = 1: 1, R_f= 0.6) was used for flash column chromatography. 73.8 mg, 60 % yield, yellow solid, m.p. 113.9-114.9 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.26 (s, 3H), 3.60 (s, 3H), 7.34-7.44 (m, 5H), 7.46-7.50 (m, 2H), 7.83 (d, *J*= 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.7, 31.0, 86.2, 110.6, 116.3, 119.5, 122.4, 123.7, 126.2, 127.5, 128.4, 130.3, 130.6, 130.7, 136.4, 138.0, 148.1; HRMS (ESI) calcd. for $C_{17}H_{15}N_2$ [M + H^+]: 247.1235, found 247.1229.

1-Methyl-2-(naphthalen-1-yl)-1*H*-indole-3-carbonitrile (Scheme 4.1, compound 3)[17k]



Eluents (DCM: Hexane = 1: 1, R_f= 0.45) was used for flash column chromatography. 70.8 mg, 50 % yield, orange liquid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.55 (s, 3H), 7.39-7.44 (m, 1H), 7.46-7.55 (m, 4H), 7.59 (t, *J*= 7.6 Hz, 1H), 7.65-7.67 (m, 2H), 7.89 (d, *J*= 7.8 Hz, 1H), 8.00 (d, *J*= 8.0 Hz, 1H), 8.08 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.5, 110.5, 119.7, 122.5, 123.9, 124.9, 125.4, 126.6, 127.5, 128.8, 129.6, 130.8, 133.6.

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Chapter 5 Palladium-Catalyzed Direct Arylation of Polyfluoroarenes with Heteroaryl and Aryl Chlorides

5.1 Introduction

Heterobiaryl motifs are commonly found in biologically active compounds, natural products, pharmaceutically effective molecules and functional materials. Particularly, 2-substituted nitrogen-containing compounds constitute high relevance in pharmaceutical chemistry and material sciences.[1] For examples, polymer and hybrid electron accepting materials based on semiconducting perfluorophenylquinoline (P5FQ),[2] the sensitization of TiO_2 nanoparticles and electrodes with perfluoroaryl motif in organic semioconducting dye for photochemical applications (Ph5FQ-TiO_2)[3], and betaine dyes for determination of solvent polarity (eicosanfluoro (F_{20})-substituted betaine dye) (Figure 5.1)

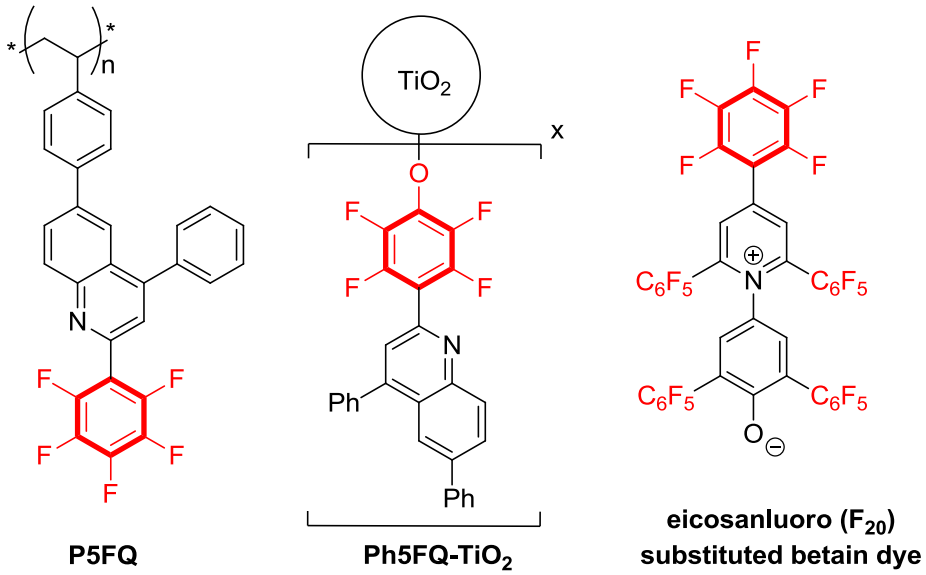
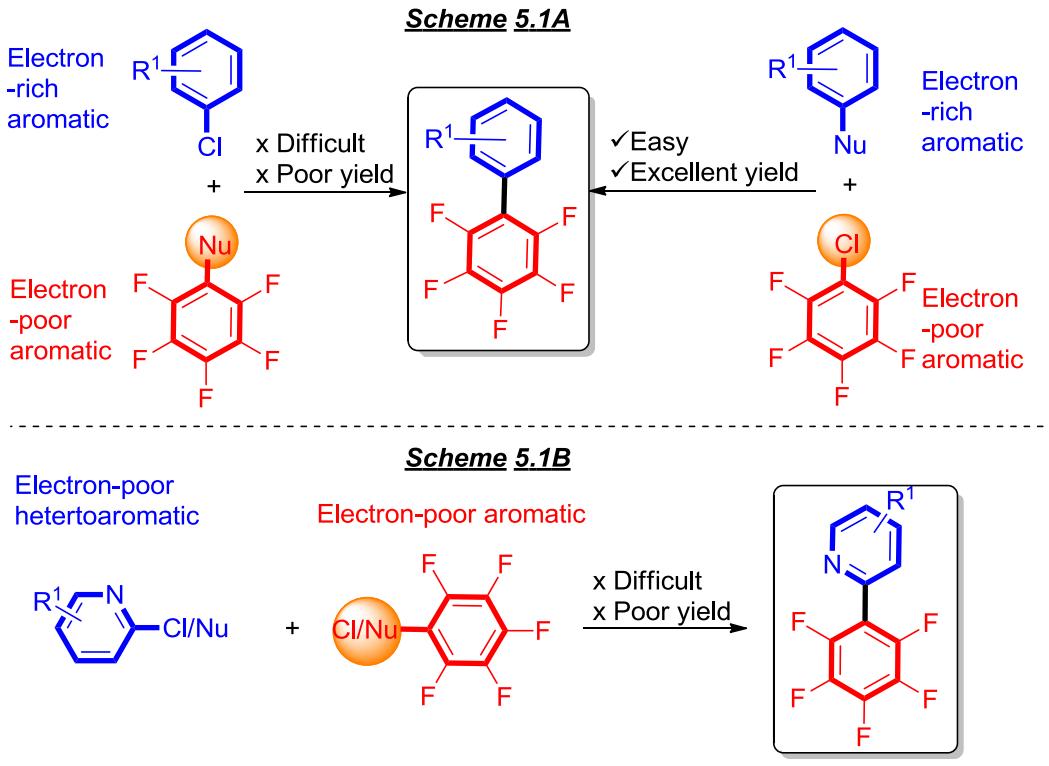


Figure 5.1 Examples of useful heteroaryl-perfluoroaryl-containing molecules

Transition metal-catalyzed cross-coupling constitutes as useful method for connecting two aromatic building blocks together. However, integrating an electron-deficient aromatic fragment to the target molecule has encountered difficulty.

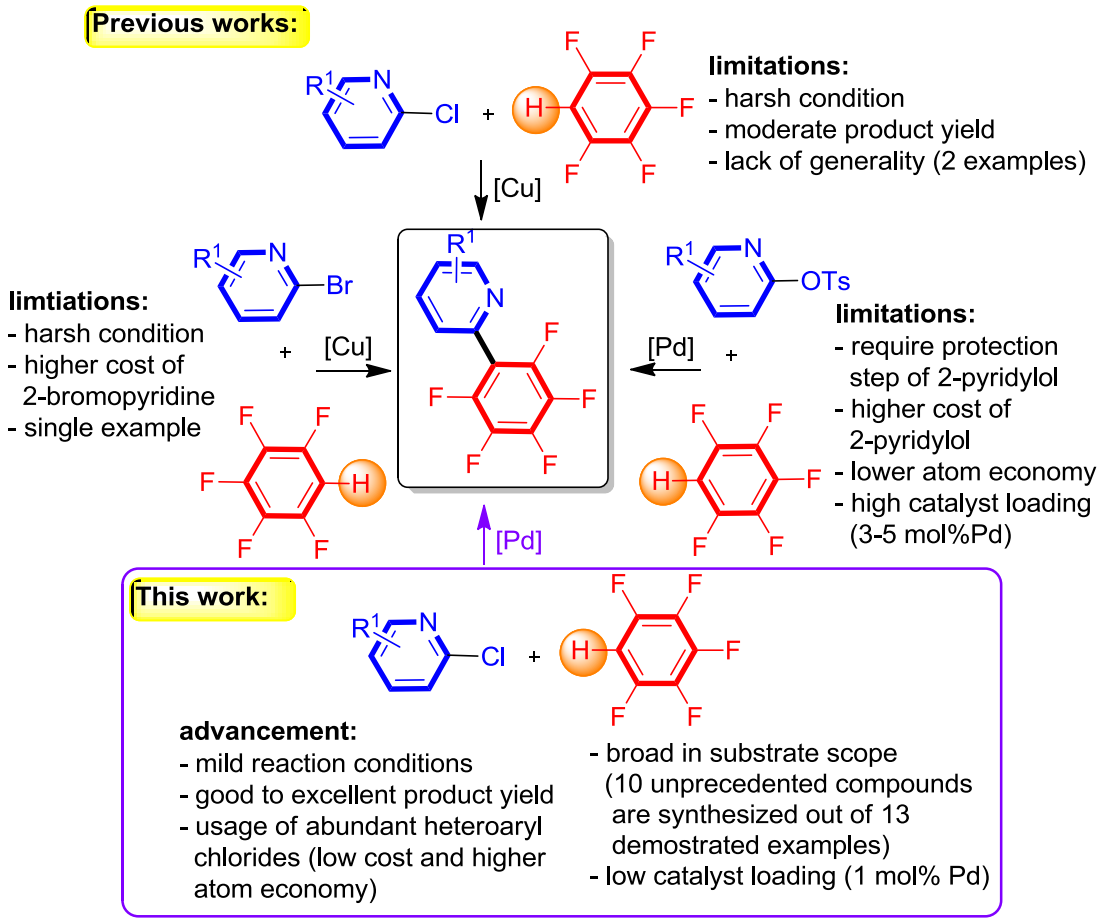
For instance, the general use of highly electron-deficient nucleophilic partners (e.g. $C_6F_5B(OH)_2$) are still problematic. Those challenges may arise from: (1) the preparation of highly electron-deficient nucleophiles is not straightforward;[4] (2) electron-deficient heteroaryl and polyfluoroaryl nucleophiles often undergo transmetallation process at a relatively slower rate; and (3) electron-deficient arylboronic acids are moderately stable and usually decompose via rapid protodeboronation during the course of coupling reactions. Indeed, these problematic issues must be tackled in order to afford target product in a better yield.[4,5] One of the usual solutions is to circumvent the selection of relatively electron-deficient arene as the nucleophilic partner between two coupling components (Scheme 5.1. Nevertheless, this strategy would become a challenge, if both of the coupling partners are electron-deficient aromatics (Scheme 5.1. Hence, effort in seeking efficient protocol for obtaining electron-deficient biaryls is indeed demanded.



Scheme 5.1 Advantages and limitations of interchanging nucleophile strategy

Direct C-H arylation of polyfluoroarenes is an excellent alternative to conventional cross-coupling reactions when heteroaryl and polyfluoroaryl components are used.[6] This synthetic route allows a better atom economy and more streamlined chemical synthesis. For instance, the direct usage of polyfluoroaryl could avoid the multi-step synthesis of unstable heteroarylboronic acid[7] or polyfluoroarylboronic acid and thus eventually improves the step-economy.[8]

Despite the advantages of using direct arylation method, there have been only a few reports regarding the successful direct C-H arylation of polyfluoroarenes with heteroaryl halides and sulfonates, in particular 2-substituted-pyridyl halides and sulfonates (Scheme 5.2). In 2008, Daugulis initially reported a copper-catalyzed arylation of polyfluorobenzenes with aryl and heteroaryl iodides and bromides.[9] One example concerning the coupling of 2-bromopyridine was demonstrated. Later, they employed the same catalyst system and similar reaction conditions for 2-pyridyl chloride coupling.[10] Nevertheless, even under the harsh reaction conditions (120-150 ^{o}C), the yield of the corresponding coupling product from 2-chloropyridine and pentafluorbenzene was moderate. In 2011, Zhang reported a palladium-catalyzed direct arylation of polyfluoroarenes with heteroaryl tosylates.[11] Indeed, aryl sulfonates are the most versatile complementary substrates to aryl halides for various coupling reactions. Yet, the cost of substituted hydroxypyridines (as the precursors for the corresponding tosylates) is exceptionally higher when compared to the direct usage of substituted pyridyl chlorides.[12] Moreover, additional tosylation step of hydroxypyridines is required too. Therefore, the development of a new catalytic system for direct usage of inexpensive and versatile heteroaryl chlorides is still highly desirable.



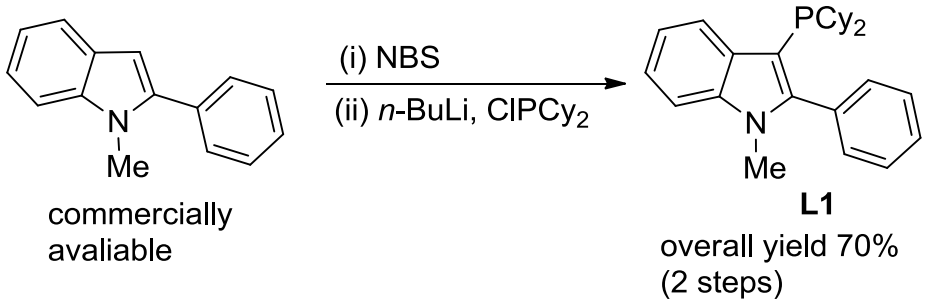
Scheme 5.2 Transition metal-catalyzed direct arylation of polyfluoroarenes with substituted 2-pyridyl halides and sulfonates

In view of current drawbacks and our persisting interests in palladium-catalyzed direct C-H arylation reaction[13] and phosphine ligand synthesis and applications,[14] we aim to develop an efficient protocol for coupling of electron-deficient polyfluoroarenes with heteroaryl chlorides, and especially substituted 2-pyridyl chlorides.

5.2 Results and discussion

5.2.1 Preliminary evaluation of palladium-catalyzed direct arylation of polyfluoroarenes with heteroaryl chlorides

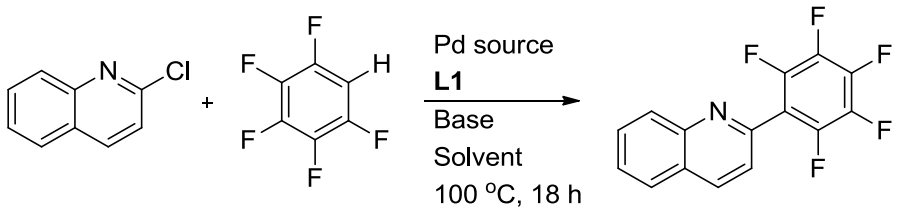
We initially chose the 3-(dicyclohexylphosphino)-2-phenylindole (PCy_2 Phendole-Phos) **L1** to test the feasibility of direct arylation of polyfluoroarenes with heteroaryl chlorides. This ligand features of commercially available and inexpensive starting materials and can be easily prepared in large scale in 2 steps (Scheme 5.3).



Scheme 5.3 Two-step synthesis of indolyl phosphine **L1** from commercially available materials

To evaluate the effectiveness of **L1** for direct arylation of polyfluorobenzenes with heteroaryl chlorides, 2-chloroquinoline and pentafluorobenzene were used as benchmark substrates (Table 5.1). Catalyst loading of 2.0 mol% Pd was initially applied in probing the ligand efficacy. $Pd(OAc)_2$ was found to be superior among $Pd_2(dba)_3$, $PdCl_2(CH_3CN)_2$, $Pd(TFA)_2$ and $Pd(OAc)_2$ screened (Table 5.1, entries 1-4). Addition of 10 mol% PivOH improved the desired product yield from 43% to 84% (Table 5.1, entries 1 and 5). Na_3PO_4, KOAc and Na_2CO_3 provided comparable product yields among the common inorganic bases examined (Table 5.1, entries 6-10). DMA was found to be the best choice of solvent (Table 5.1, entries 1 and 11-13).

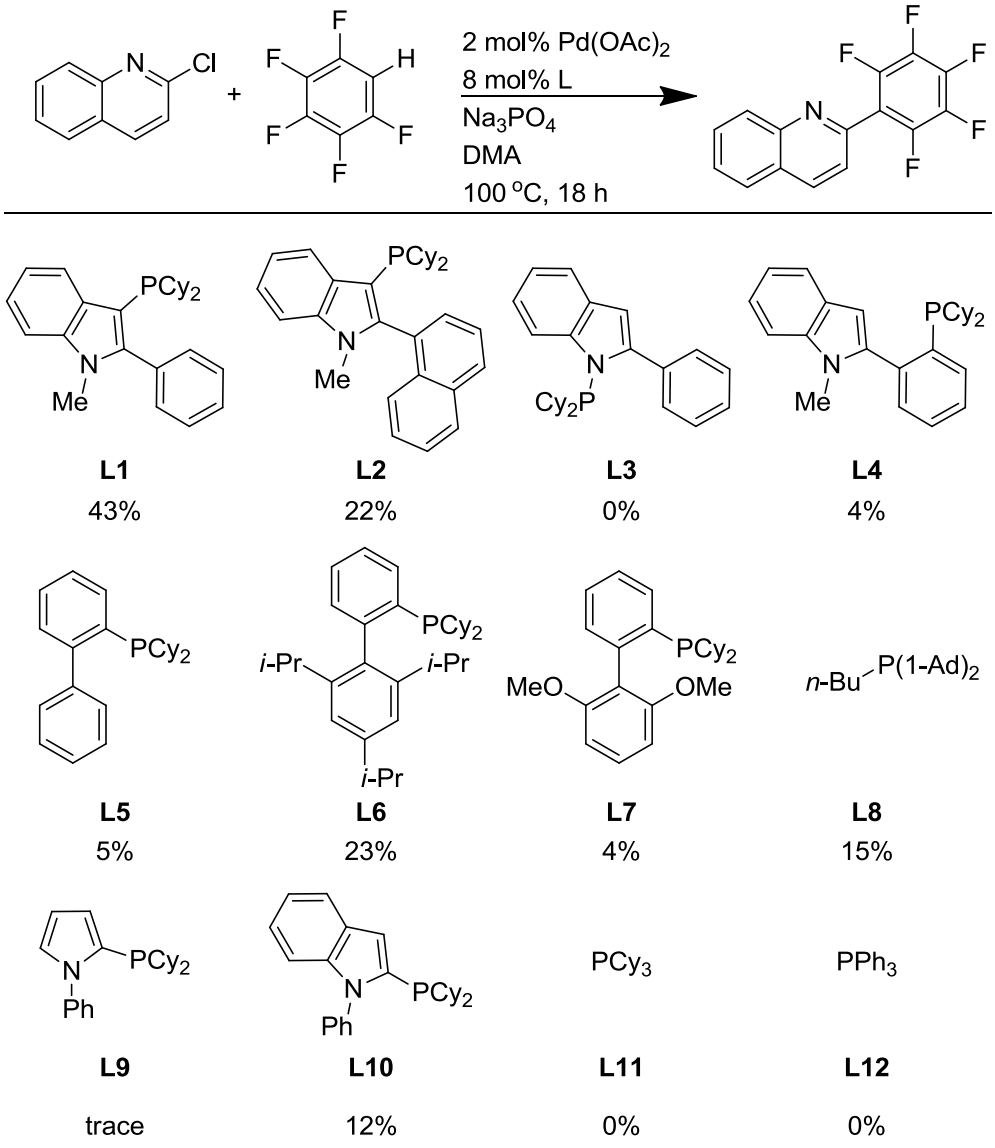
Table 5.1 Initial screening of palladium-catalyzed direct arylation of polyfluoroarenes with heteroaryl chlorides[a]



Entry	Pd source (mol %)	Base	Solvent	Yield %[b]
1	$Pd(OAc)_2$ (2)	Na_3PO_4	DMA	43
2	$Pd(TFA)_2$ (2)	Na_3PO_4	DMA	Trace
3	$PdCl_2(CH_3CN)_2$ (2)	Na_3PO_4	DMA	5
4	$Pd_2(dba)_3$ (2)	Na_3PO_4	DMA	Trace
5	$Pd(OAc)_2$ (2)	Na_3PO_4	DMA	84[c]
6	$Pd(OAc)_2$ (0.5)	Na_3PO_4	DMA	82[c]
7	$Pd(OAc)_2$ (0.5)	NaOAc	DMA	56[c]
8	$Pd(OAc)_2$ (0.5)	KOAc	DMA	82[c]
9	$Pd(OAc)_2$ (0.5)	Na_2CO_3	DMA	79[c]
10	$Pd(OAc)_2$ (0.5)	K_2CO_3	DMA	21[c]
11	$Pd(OAc)_2$ (2)	Na_3PO_4	Toluene	32
12	$Pd(OAc)_2$ (2)	Na_3PO_4	DMF	41
13	$Pd(OAc)_2$ (0.5)	Na_3PO_4	*i*-PrOAc	34[c]

[a] Reaction conditions: 2-Chloroquinoline (0.5 mmol), pentafluorobenzene (1.0 mmol), Pd source (2 mol%), **L1** (8 mol%), base (0.75 mmol) and solvent (1.0 mL) were stirred at 100 ^oC for 18 h under N_2. [b] Calibrated GC yields were reported using dodecane as internal standard. [c] 10 mol% PivOH was added.

With these encouraging results in hand, we next investigated the effect of phosphine ligands in this reaction (Scheme 5.4). Previously reported indolylphosphine ligands where the phosphino group is attached to different positions of the indole ring were examined (**L1**-**L4**). Ligand **L1** was found to be the best ligands for this reaction. A list of commercially available and well-recognized effective phosphine ligands were further evaluated (**L5**-**L12**), such as PCy_3, PPh_3, CataCXium® A, CataCXium® PCy, **cataCXium® PInCy,** SPhos, XPhos and Cy-JohnPhos. Surprisingly, other than XPhos (**L6**) could give a better yield among the ligands examined, poor substrate conversions and product yields were observed from **L5** and **L7**-**L12**. Therefore, catalyst system comprising $Pd(OAc)_2$ and **L1** was employed to test the scope of this reaction.

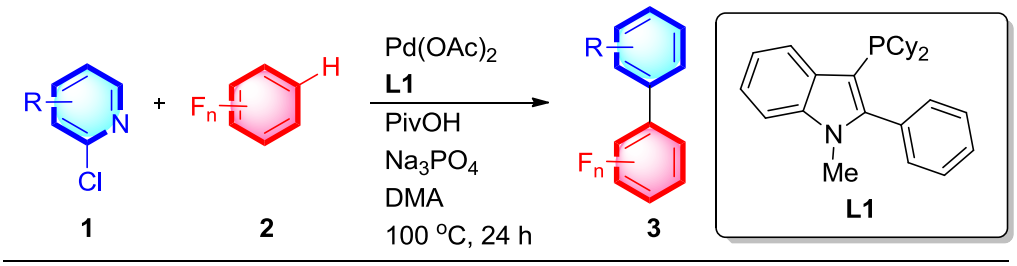


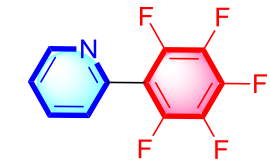
Scheme 5.4 Investigation of phosphine ligands in Pd-catalyzed direct arylation of perfluorobenzene with 2-quinolyl chlorides. Reaction conditions: 2-chloroquinoline (0.50 mmol), pentafluorobenzene (1.0 mmol), $Pd(OAc)_2$ (2 mol%), **L** (8 mol%), Na_3PO_4 (0.75 mmol) and DMA (1.0 mL) were stirred at 100 ^oC for 18 h under nitrogen. Calibrated GC yields were reported using dodecane as internal standard.

5.2.2 Scope of palladium-catalyzed direct arylation of polyfluoroarenes with heteroaryl chlorides

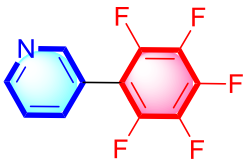
A wide range of heteroaryl chlorides were probed in order to test the efficacy of the new catalytic system (Table 5.2). 2-Chloropyridine, in which it is the most challenging cross-coupling partner [10] showed excellent product yield under these reaction conditions (Table 5.2, **3au**). 6-Substituted-2-chloropyridines were efficiently coupled smoothly with pentafluorobenzene in good yields (Table 5.2, **3cu**-**3gu**). Diphenylation could be done when 2,6-dichloropyridine was used (Table 5.2, **3hu**). Other polyfluoroarenes were also applicable coupling partners (Table 5.2, **3cv**-**3cz**). It should be noted that 10 new compounds were synthesized among the 13 entries which may implies the lack of current effective methods for accessing pyridyl/polyfluoro biaryl compounds, in spite of the usefulness of polyfluoroarene compounds.

Table 5.2 Palladium-catalyzed direct arylation of polyfluoroarenes with heteroaryl chlorides[a,b]

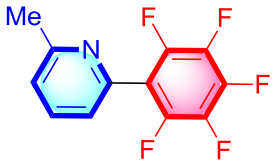




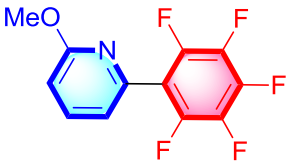
3au 90% (5 mol% Pd)[c]



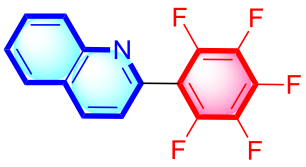
3bu 81% (2 mol% Pd)[d]



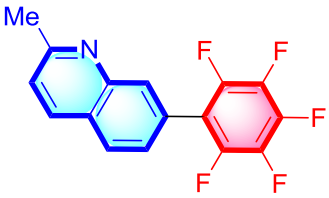
3cu 85% (1 mol% Pd)



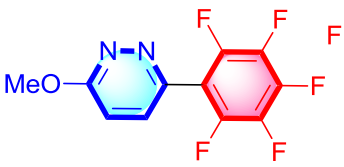
3du 80% (1 mol% Pd)



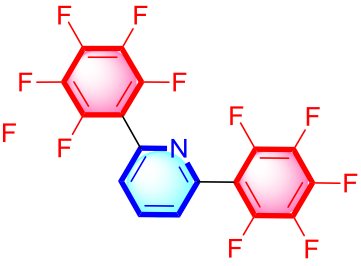
3eu 82% (1 mol% Pd)



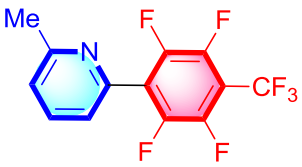
3fu 85% (1 mol% Pd)



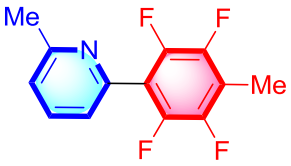
3gu 81% (2 mol% Pd)[e]



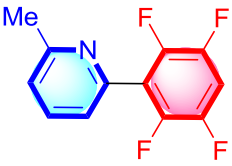
3hu 95% (1 mol% Pd)[e]



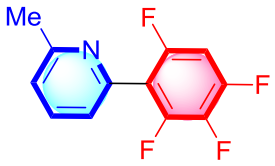
3cv 70% (1 mol% Pd)



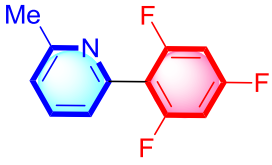
3cw 96% (1 mol% Pd)[f]



3cx 65% (1 mol% Pd)



3cy 65% (1 mol% Pd)[g]



3cz 73% (1 mol% Pd)[h]

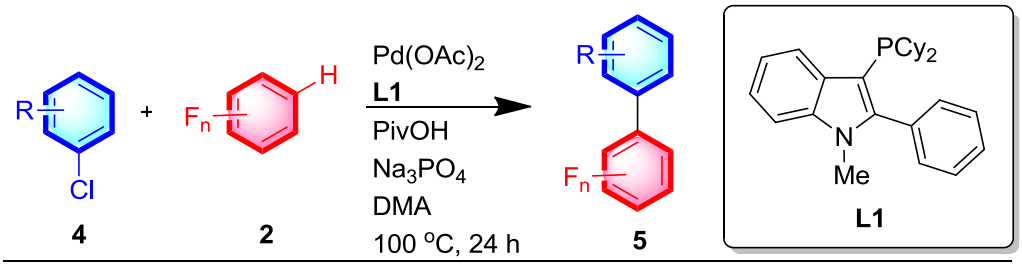
[a] Reaction conditions: Heteroaryl chlorides (0.5 mmol), polyfluorobenzenes (1.0

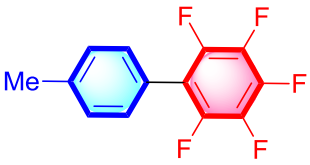
mmol), $Pd(OAc)_2$: **L1** (1 : 4), Na_3PO_4 (0.75 mmol), PivOH (10 mol%) and DMA (1.0 mL) were stirred at 100 ^oC for 24 h under nitrogen. [b] Isolated yields. [c] Dioxane (1.0 mL) was used and stirred at 110 ^oC. [d] Dioxane : DMA (1 : 1, total 1.0 mL) was used and stirred at 110 ^oC. [e] Dioxane : DMA (4 : 1, total 1.0 mL) was used and stirred at 110 ^oC. [f] polyfluorobenzenes (2.0 mmol), $Pd(OAc)_2$: **L1** (1 : 4), Na_3PO_4 (1.50 mmol), PivOH (20 mol%) and dioxane : DMA (4 : 1, total 2.0 mL) were stirred at 110 ^oC. [g] 4 equiv. polyfluorobenzene was used. [h] 3 equiv. polyfluorobenzene was used. [i] 5 equiv. polyfluorobenzene was used.

5.2.3 Scope of palladium-catalyzed direct arylation of polyfluoroarenes with aryl and alkenyl chlorides

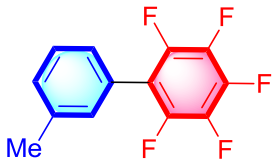
In order to probe the generality of the Pd-**L1** catalyst system, a series of the electron neutral, electron rich and functionalized aryl chlorides were further examined (Table 5.3). Electron rich aryl chlorides were coupled with pentafluorobenzene in excellent yields (Table 5.3, **5eu-5hu**). Functional groups, such as –CHO, –COMe, –COOMe, –COPh, –CN, were compatible under these reaction conditions (Table 5.3, **5iu-5ou**). Particularly, the free amino groups remained intact during the course of the reaction (Table 3, **5qu** and **5ru**). Alkenyl chloride could also serve as an effective substrate for direct arylation of pentafluorobenzene (Table 3, **5su**). To the best of our knowledge, it is the lowest palladium catalyst loading reported to date for this reaction.

Table 5.3 Palladium-catalyzed direct arylation of polyfluoroarenes with aryl chlorides [a, b]

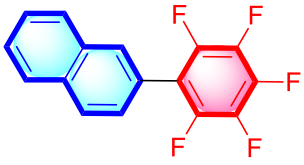




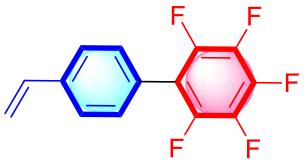
5au 91% (1 mol% Pd)



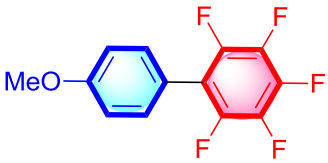
5bu 82% (1 mol% Pd)



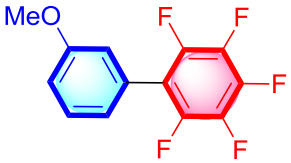
5cu 86% (1 mol% Pd)



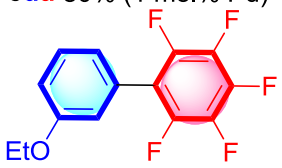
5du 80% (1 mol% Pd)



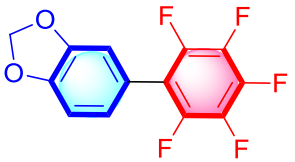
5eu 87% (2 mol% Pd)



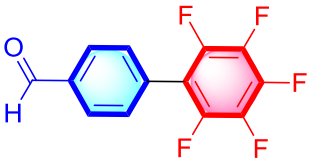
5fu 87% (1 mol% Pd)



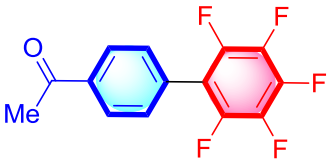
5gu 90% (1 mol% Pd)



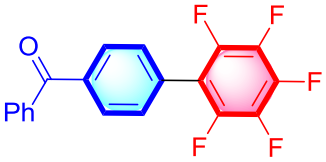
5hu 80% (2 mol% Pd)[c]



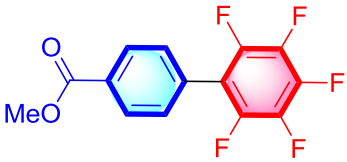
5iu 70% (1 mol% Pd)



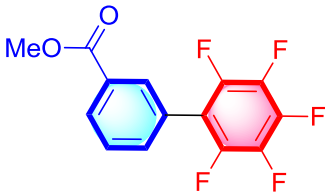
5ju 75% (1 mol% Pd)



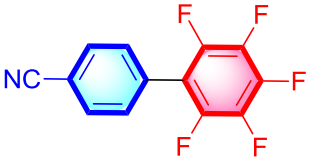
5ku 84% (1 mol% Pd)



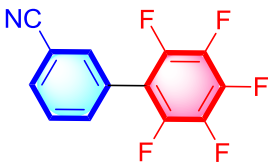
5lu 73% (1 mol% Pd)



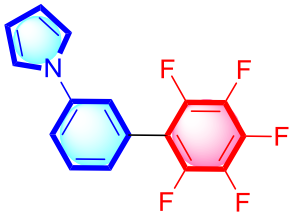
5mu 85% (1 mol% Pd)



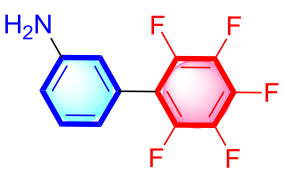
5nu 80% (2 mol% Pd)[c]



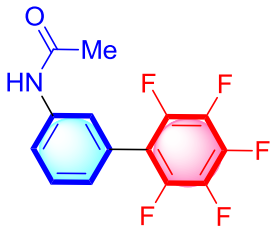
5ou 80% (2 mol% Pd)[c]



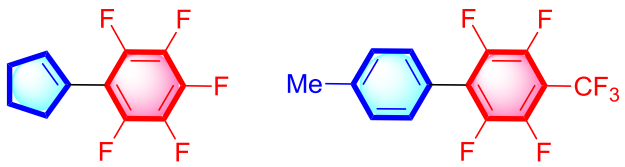
5pu 84% (1 mol% Pd)



5qu 91% (1 mol% Pd)



5ru 93% (1 mol% Pd)



5su 70% (2 mol% Pd) **5av** 80% (1 mol% Pd)

[a] Reaction conditions: Aryl chlorides (0.5 mmol), polyfluorobenzenes (1.0 mmol), $Pd(OAc)_2$: L1 (1 : 4), Na_3PO_4(0.75 mmol), PivOH (10 mol%) and DMA (1.0 mL) were stirred at 100 ^oC for 24 h. [b] Isolated yields. [c] without 10 mol% PivOH.

5.3 Conclusion

In conclusion, we reported the first general palladium-catalyzed direct arylation of polyfluorobenzenes with heteroaryl chlorides especially substituted 2-pyridyl chlorides using the combination of $Pd(OAc)_2$ and indolylphosphine ligand **L1** as catalyst system. Particularly noteworthy is that the reaction conditions were mild and the catalyst loading down to 1 mol% Pd could be achieved. Moreover, the substrate scope can be extended to non-activated and activated aryl chlorides and alkenyl chloride without difficulty. General functional groups such as –CHO, –C(O)Me, –COOMe, –C(O)Ph, –NHC(O)Me, –CN, $–NH_2$ were compatible under these reaction conditions. We believe that this direct heteroarylation protocol provides a useful and facile access to polyfluoro/hetero biaryl compounds that are important in pharmaceutical chemistry and material sciences.

5.4 Experimental section

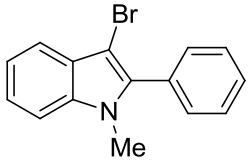
5.4.1 General considerations

Unless otherwise noted, all reagents were purchased from commercial suppliers and used without purification. All arylation reactions were performed in Rotaflo® (England) resealable screw cap Schlenk flask (approx. 20 mL volume) in the presence of Teflon coated magnetic stirrer bar (4 mm × 10 mm). Toluene and dioxane were distilled from sodium and sodium benzophenone ketyl under nitrogen, respectively.[15] Anhydrous *N*, *N*-dimethylformamide (DMF) and anhydrous *N*, *N*-dimethylacetamide (DMA) in Sure/Seal bottles were purchased from Aldrich and used directly. Na_3PO_4, Na_2CO_3, K_2CO_3, NaOAc and KOAc were purchased from chemical supplier and used without grinding. Commercial aryl chlorides (liquid form only) were purified by passed through a short plug (0.5 cm wide×4 cm high) of neutral alumina or distillation. Indolylphosphine ligands **(L1-L4)** were prepared according to the reported procedure.[14b,15d,15h] Ligands **(L5-L12)** were purchased from commercial suppliers. 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. NMR spectra were recorded on a Brüker spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C, 376 MHz for ^{19}F and 162 MHz for ^{31}P). 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). ^{19}F NMR chemical shifts were determined relative to $CFCl_3$ as the external standard and low field is positive. ^{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 FTICR mass spectrometer (ESI-MS). 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, ^{13}C, ^{19}F and/or ^{31}P 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 indolylphosphine ligand L1 in large scale

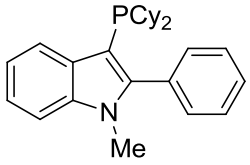
3-Bromo-1-methyl-2-phenyl-1*H*-indole[14d]



The synthesis of 3-bromo-1-methyl-2-phenyl-1*H*-indole was modified from the literature method. [14d] To a solution of *N*-methyl-2-phenyl-1*H*-indole (10.4 g, 50.0 mmol) in chloroform (100 mL), a solution of *N*-bromosuccinimide (8.90 g, 50.0 mmol) in chloroform (200 mL) was added at room temperature. After stirring for 30 min, the reaction mixture was poured onto water (150 mL). The organic layer was washed with water twice, dried with Na_2SO_4 and was then concentrated. The concentrated solution was filtered over a pad of silica (3 × 2 inch) and eluted with DCM/hexane (1:9). The solution was evaporated to give white solid product. The final product 3-bromo-1-methyl-2-phenyl-1*H*-indole was dried under vacuum (13.8 g, 97%) to give

white solid as the desired compound. ^{1}H NMR (400MHz, $CDCl_3$) δ 3.62 (s, 3H), 7.18–7.27 (m, 1H), 7.28–7.33 (m, 2H), 7.43–7.50 (m, 5H), 7.61 (d, *J*= 7.8 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 31.6, 90.1, 109.7, 119.3, 120.5, 122.8, 127.2, 128.4, 128.6, 130.4, 130.7, 136.8, 138.0; MS (EI): *m/z* (relative intensity) 285.1 (M^+, 100), 204.1 (51), 191.1 (16), 178.1 (15).

3-(Dicyclohexylphosphino)-1-methyl-2-phenyl-1*H*-indole (L1)[14d]



3-Bromo-1-methyl-2-phenyl-1*H*-indole (10.3 g, 36.0 mmol) was dissolved in freshly distilled THF (120 mL) at room temperature under nitrogen atmosphere. The solution was cooled to -78 ℃ in dry ice/acetone bath. Titrated *n*-BuLi (39.6 mmol) was added dropwise by syringe. After the reaction mixture was stirred for 30 min at -78℃, chlorodicyclohexylphosphine (9.54 ml, 43.2 mmol) was added dropwise by syringe. The reaction was allowed to warm to room temperature and stirred overnight. Solvent was removed under reduced pressure. After the solvent was removed under vacuum, the product was successively washing with cold MeOH. The product was then dried under vacuum. 3-(Dicyclohexylphosphino)-1-methyl-2-phenyl-1*H*-indole was obtained as a white solid (10.4 g, 72%). ^{1}H NMR (400MHz, CD_2Cl_2) δ 1.03–1.35 (m, 10H), 1.55–1.90 (m, 10H), 2.30–2.35 (m, 2H), 3.53 (s, 3H), 7.17 (t, *J*= 7.4 Hz, 1H), 7.25–7.29 (m, 1H), 7.37–7.49 (m, 6H), 7.88 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (100MHz, CD_2Cl_2) δ 27.1, 27.21, 27.24, 27.3, 30.6, 30.7, 31.0, 32.2, 32.4, 34.3, 34.4, 104.2, 104.4, 109.8, 119.8, 121.6, 121.7, 127.7, 128.0, 128.2, 130.5, 130.6, 131.67, 131.69, 132.95, 132.98, 138.2, 149.7, 150.1 (unresolved complex C-P splittings were observed); ^{31}P NMR (162MHz, CD_2Cl_2) δ -18.26; MS (EI): *m/z* (relative intensity)

403.3 (M^+, 17), 348.3 (4), 321.2 (31), 238.1 (100), 207.1 (12).

5.4.3 General procedures for initial ligand and reaction conditions screening

General Procedure for reaction condition screenings (Pd catalysts loading equal to 2.0 mol%): Pd source (0.010 mmol) and ligand (Pd : L = 1 : 4) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The tubes were evacuated and backfilled with nitrogen (3 cycles). Precomplexation was applied by adding freshly distilled dichloromethane (1.0 mL) and Et_3N (0.10 mL) into the tube. The palladium complex stock solution was stirred and warmed using a hair drier for 1 to 2 minutes until the solvent started boiling. The solvent was then evaporated under high vacuum. 2-Chloroquinoline (0.50 mmol, 0.082 g) and base (0.75 mmol) were loaded into the tube, and the system was further evacuated and flushed with nitrogen for three times. Pentafluorobenzene (1.0 mmol, 111 μL) and solvent (1.0 mL) were added into the tube via syringe and the mixture was stirred at room temperature for several minutes. The tube was then placed into a preheated oil bath (100 ℃) and stirred for 18 h. After the completion of the reaction, the reaction tube was allowed to reach room temperature. Ethyl acetate (~10 mL), dodecane (114 μL, internal standard) and water (~3 mL) 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 screening (Pd catalysts loading lower than 1.0 mol%): A stock solution of $Pd(OAc)_2$ (11.5 mg, 0.050 mmol) with L1 (Pd : L = 1 : 4) in freshly distilled 10 mL DCM (1.0 mol% Pd per 1 mL stock solution) was initially prepared with continuously stirring at room temperature. An array of Schlenk tubes equipped

with a Teflon-coated magnetic stir bar were evacuated and backfilled with nitrogen (3 cycles). The corresponding volume of stock solution and Et_3N (0.10 mL) were transferred to an array of Schlenk tubes *via* syringes. 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. 2-Chloroquinoline (0.50 mmol, 82 mg) and base (0.75 mmol) were loaded into the tube, and the system was further evacuated and flushed with nitrogen for three times. Pentafluorobenzene (1.0 mmol, 111 μL), pivalic acid (5.1 mg, 0.050 mmol, if necessary) and solvent (1.0 mL) were added into the tube via syringe and the mixture was stirred at room temperature for several minutes. The tube was then placed into a preheated oil bath (100 ℃) and stirred for the time as indicated. After the completion of the reaction, the reaction tube was allowed to reach room temperature. Ethyl acetate (~10 mL), dodecane (114 μL, internal standard) and water (~3 mL) were added. The organic layer was subjected to GC analysis. The GC yield was previously calibrated by authentic sample/dodecane calibration curve.

5.4.4 General procedures for direct arylation of polyfluoroarenes with aryl chlorides

General Procedure for direct arylation of polyfluoroarenes with aryl chlorides (Pd catalysts loading equal to or larger than 2.0 mol%): $Pd(OAc)_2$ (Pd loading indicated in the entry table) and L1 (Pd : L = 1 : 4) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The tubes were evacuated and backfilled with nitrogen (3 cycles). Precomplexation was applied by adding freshly distilled dichloromethane (1.0 mL) and Et_3N (0.10 mL) into the tube. The palladium complex stock solution was stirred and warmed using a hair drier for 1 to 2 minutes

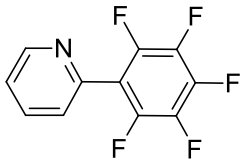
until the solvent started boiling. The solvent was then evaporated under high vacuum. Na_3PO_4 (0.164 g, 0.75 mmol) and solid aryl chlorides (0.50 mmol) were loaded into the tube, and the system was further evacuated and flushed with nitrogen for three times. Polyfluoroarenes (1.0 mmol), liquid aryl chlorides (0.5 mmol), pivalic acid (5.1 mg, 0.050 mmol) and DMA (1.0 mL) were added into the tube via syringe and the mixture was stirred at room temperature for several minutes. The tube was then placed into a preheated oil bath (100 ℃) and stirred for 24 h. After the completion of the reaction, the reaction tube was allowed to reach room temperature. Ethyl acetate (~10 mL) and water (~3 mL) were added. The organic layer was subjected to GC analysis. 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 procedures for direct arylation of polyfluoroarenes with aryl chlorides (Pd catalysts loading equal to 1.0 mol%): A stock solution of $Pd(OAc)_2$ (11.5 mg, 0.050 mmol) with L1 (Pd : L = 1 : 4) in freshly distilled 10 mL DCM (1.0 mol% Pd per 1 mL stock solution) was initially prepared with continuously stirring at room temperature. An array of Schlenk tubes equipped with a Teflon-coated magnetic stir bar were evacuated and backfilled with nitrogen (3 cycles). The corresponding volume of stock solution and Et_3N (0.10 mL) were transferred to an array of Schlenk tubes *via* syringes. 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. Na_3PO_4 (0.164 g, 0.75 mmol) and solid aryl chlorides (0.50 mmol) were loaded into the tube, and the system was further evacuated and flushed with nitrogen for three times. Polyfluoroarenes (1.0 mmol), liquid aryl chlorides (0.5 mmol), pivalic acid (5.1 mg, 0.050 mmol) and DMA (1.0 mL) were added into the

tube via syringe and the mixture was stirred at room temperature for several minutes. The tube was then placed into a preheated oil bath (100 ℃) and stirred for 24 h. After the completion of the reaction, the reaction tube was allowed to reach room temperature. Ethyl acetate (~10 mL) and water (~3 mL) were added. The organic layer was subjected to GC analysis. 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.

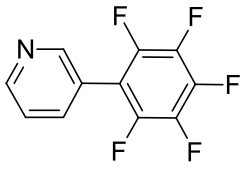
5.4.5 Characterization data for cross-coupling products

2-(Perfluorophenyl)pyridine (Table 5.2, compound 3au)[16]



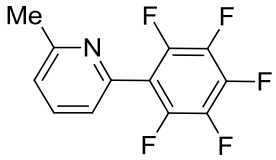
Eluents (Ethyl acetate: Hexane= 1: 9, R_f= 0.30) was used for flash column chromatography. ^{1}H NMR (400MHz, $CDCl_3$) δ 7.35–7.38 (m, 1H), 7.46 (d, *J*= 7.6 Hz, 1H), 7.82 (t, *J*= 8.0 Hz, 1H), 8.75 (d, *J*= 4.4 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 115.2–115.5 (m), 123.8, 125.9, 136.3–136.6 (m), 136.7, 138.7–139.2 (m), 139.7–140.1 (m), 142.2–142.7 (m), 143.1–143.5 (m), 145.6–146.0 (m), 146.8, 150.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -162.0 (m, 2F), -154.0 (t, *J*= 18.8 Hz, 1F), -143.3 (dd, *J*= 22.5 Hz, 7.5 Hz, 2F); MS (EI): *m/z* (relative intensity) 245.0 (M^+, 100), 226.0 (47), 191.9 (19), 116.9 (9), 93.0 (6).

3-(Perfluorophenyl)pyridine (Table 5.2, compound 3bu)[17]



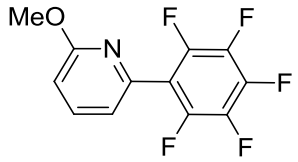
Eluents (Ethyl acetate: Hexane= 1: 4, R_f= 0.45) was used for flash column chromatography. ^{1}H NMR (400MHz, $CDCl_3$) δ 7.44 (dd, *J*= 7.6 Hz, *J*= 4.8 Hz, 1H), 7.77 (d, *J*= 8.0 Hz, 1H), 8.68–8.69 (m, 2H); ^{13}C NMR (100MHz, $CDCl_3$) δ 112.2–112.8 (m), 123.0, 123.6, 136.4–136.9 (m), 137.5, 138.9–139.4 (m), 139.5–139.9 (m), 142.0–142.5 (m), 142.7–143.2 (m), 145.2–145.7 (m), 150.3, 150.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -161.2 (m, 2F), -153.5 (t, *J*= 22.5 Hz, 1F), -143.0 (dd, *J*= 22.5 Hz, 7.5 Hz, 2F) ; MS (EI): *m/z* (relative intensity) 245.0 (M^+, 100), 226.0 (20), 192.0 (34), 122.9 (6), 99.0 (3).

2-Methyl-6-(perfluorophenyl)pyridine (Table 5.2, compound 3cu)



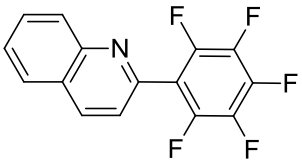
Eluents (Ethyl acetate: Hexane= 1: 9, R_f= 0.60) was used for flash column chromatography. Colorless liquid; ^{1}H NMR (400MHz, CD_2Cl_2) δ 2.61 (s, 3H), 7.27–7.30 (m, 2H), 7.75 (t, *J*= 7.8 Hz, 1H); ^{13}C NMR (100MHz, CD_2Cl_2) δ 24.0, 115.6–116.3 (m), 122.8, 123.4, 136.2–136.7 (m), 136.8, 138.7–139.2 (m), 139.5–140.1 (m), 142.0–142.5 (m), 143.1–143.6 (m), 145.8, 159.3; ^{19}F NMR (376 MHz, CD_2Cl_2) δ -163.1 (m, 2F), -155.6 (t, *J*= 22.5 Hz, 1F), -143.9 (dd, *J*= 22.5 Hz, 7.5 Hz, 2F); MS (EI): *m/z* (relative intensity) 259.0 (M^+, 100), 192.9 (18), 167.9 (6), 90.9 (16), 65.0 (9); HRMS: calcd. for $C_{12}H_7F_5N^+$: 260.0493, found 260.0496.

2-Methoxy-6-(perfluorophenyl)pyridine (Table 5.2, compound 3du)



Eluents (Ethyl acetate: Hexane= 1: 9, R_f= 0.40) was used for flash column chromatography. Colorless liquid; ^{1}H NMR (400MHz, $CDCl_3$) δ 3.94 (s, 3H), 6.81 (d, *J*= 8.4 Hz, 1H), 7.05 (d, *J*= 7.2 Hz, 1H), 7.68 (t, *J*= 7.8 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 53.6, 111.4, 115.4, 115.0–115.7 (m), 118.8, 136.2–136.9 (m), 138.8, 139.5–140.1 (m), 142.1–142.6 (m), 142.2–143.7 (m), 143.8, 145.7–146.3, 164.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -162.5 (m, 2F), -154.8 (t, *J*= 22.5 Hz, 1F), -142.8 (dd, *J*= 22.5 Hz, 7.5 Hz, 2F); MS (EI): *m/z* (relative intensity) 273.9 (M^+, 100), 244.9 (34), 226.1 (44), 191.9 (35), 93.0 (14); HRMS: calcd. for $C_{12}H_7F_5NO^+$: 276.0442, found 276.0443.

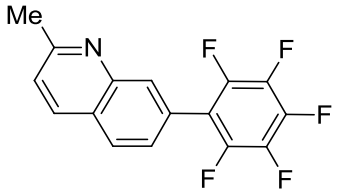
2-(Perfluorophenyl)quinoline (Table 5.2, compound 3eu)[11]



Eluents (Ethyl acetate: Hexane= 1: 4, R_f= 0.45) was used for flash column chromatography. ^{1}H NMR (400MHz, $CDCl_3$) δ 7.53 (d, *J*= 8.4 Hz, 1H), 7.63 (t, *J*= 7.4 Hz, 1H), 7.78 (t, *J*= 8.4 Hz, 1H),7.89 (d, *J*= 8.0 Hz, 1H), 8.16 (d, *J*= 8.4 Hz, 1H), 8.29 (d, *J*= 8.4 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 115.6–115.9 (m), 122.7, 127.4, 127.6, 127.7, 129.7, 130.2, 136.4–136.8 (m), 136.9, 138.9–139.4 (m), 140.0–140.4 (m), 142.5–142.9 (m), 143.3–143.8 (m), 145.8–146.2 (m), 147.0, 148.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -161.6 (m, 2F), -153.5 (t, *J*= 22.5 Hz, 1F), -142.8 (dd, *J*= 22.5 Hz, 7.5 Hz, 2F); MS (EI): *m/z* (relative intensity) 295.0 (M^+, 100), 276.0 (31), 192.9

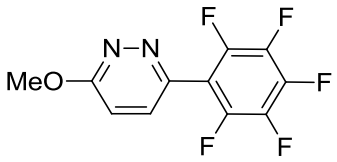
(26), 102.0 (17), 76.0 (14).

2-Methyl-7-(perfluorophenyl)quinoline (Table 5.2, compound 3fu)



Eluents (Ethyl acetate: Hexane= 1: 4, R_f= 0.45) was used for flash column chromatography. White solid; m.p. 148.7 – 150.9 ^{o}C; ^{1}H NMR (400MHz, $CDCl_3$) δ 2.75 (s, 3H), 7.33 (d, *J*= 8.0 Hz, 1H), 7.48 (d, *J*= 8.0 Hz, 1H),7.85 (d, *J*= 8.0 Hz, 1H), 8.05–8.10 (m, 2H); ^{13}C NMR (100MHz, $CDCl_3$) δ 25.3, 115.2–115.7 (m), 123.0, 126.5, 126.9, 127.3, 127.9, 130.8, 135.8, 136.4–136.9 (m), 138.9–139.2 (m), 139.2–139.5 (m), 141.6–142.2 (m), 142.7–143.2 (m), 145.2–145.6 (m), 147.5, 160.1; ^{19}F NMR (376 MHz, $CDCl_3$) *δ* -161.9 (m, 2F), -154.8 (t, *J*= 22.5 Hz, 1F), -142.9 (dd, *J*= 22.5 Hz, 7.5 Hz, 2F); MS (EI): *m/z* (relative intensity) 309.0 (M^+, 100), 290.0 (5), 191.9 (6), 154.5 (9), 63 (5); HRMS: calcd. for $C_{16}H_9F_5N^+$: 310.0650, found 310.0646.

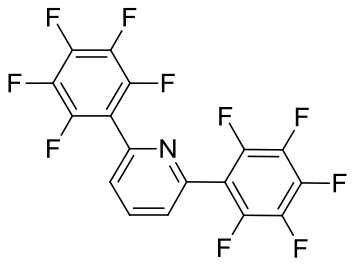
3-Methoxy-6-(perfluorophenyl)pyridazine (Table 5.2, compound 3gu)



Eluents (Ethyl acetate: Hexane= 1: 4, R_f= 0.40) was used for flash column chromatography. White solid; m.p. 88.4 – 90.8 ^{o}C; ^{1}H NMR (400MHz, $CDCl_3$) δ 4.19 (s, 3H), 7.10 (d, *J*= 9.2 Hz, 1H), 7.51 (d, *J*= 9.2 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 55.1, 112.2–112.7 (m), 117.3, 130.9, 136.3–136.7 (m), 138.8–139.2 (m), 140.1–140.5 (m), 142.7–143.1 (m), 143.2–143.6 (m), 145.8–146.0 (m), 146.1, 164.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ-161.4 (m, 2F), -152.6 (t, *J*= 22.5 Hz, 1F), -142.6 (dd, *J*=

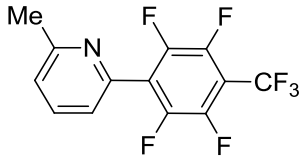
22.5 Hz, 7.5 Hz, 2F); MS (EI): *m/z* (relative intensity) 276.0 (M^+, 36), 205.0 (100), 192.0 (11), 179.0 (11), 117.0 (8) ; HRMS: calcd. for $C_{11}H_6F_5N_2O^+$: 277.0395, found 277.0392.

2,6-Bis(perfluorophenyl)pyridine (Table 5.2, compound 3hu)



Eluents (Ethyl Acetate: Hexane= 1: 9, R_f= 0.60) was used for flash column chromatography. White solid; m.p. 76.9 – 80.5 ^oC; ^1H NMR (400MHz, $CDCl_3$) δ 7.57 (d, *J*= 7.6 Hz, 2H), 8.00 (t, *J*= 8.0 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 114.5–114.8 (m), 125.9, 136.4–136.8 (m), 137.5, 138.9–139.3 (m), 140.1–140.5 (m), 142.6–143.0 (m), 143.2-143.6 (m), 145.7–146.1 (m), 147.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -161.7 (m, 2F), -153.3 (t, *J*= 22.5 Hz, 1F), -143.0 (dd, *J*= 22.5 Hz, 7.5 Hz, 2F); MS (EI): *m/z* (relative intensity) 411.1 (M^+, 100), 392.1 (37), 244.0 (10), 192.0 (35), 93.0 (4); HRMS: calcd. for $C_{17}H_4F_{10}N^+$: 412.0179, found 412.0178.

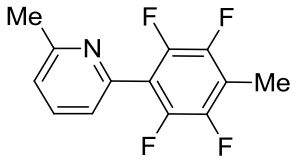
2-Methyl-6-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyridine (Table 5.2, compound 3cv)



Eluents (Ethyl acetate: Hexane= 1: 4, R_f= 0.50) was used for flash column chromatography. White solid; m.p. 54.7 – 57.5 ^oC; ^1H NMR (400MHz, $CDCl_3$) δ 2.62 (s, 3H), 7.26–7.30 (m, 2H), 7.73 (t, *J*= 7.8 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ

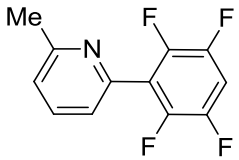
24.4, 108.9–110.1 (m), 119.5, 122.2, 122.7, 124.0, 124.1–124.5 (m), 136.9, 142.8–143.5 (m), 145.6, 145.6–145.9 (m), 159.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -141.1 (m, 2F), -140.6 (m, 2F), -56.5 (m, 3F); MS (EI): *m/z* (relative intensity) 309.0 (M^+, 100), 289.9 (16), 192.9 (10), 90.9 (5), 68.9 (26); HRMS: calcd. for $C_{13}H_7F_7N^+$: 310.0461, found 310.0465.

2-Methyl-6-(2,3,5,6-tetrafluoro-4-methylphenyl)pyridine (Table 5.2, compound 3cw)



Eluents (Ethyl acetate: Hexane= 1: 4, R_f= 0.50) was used for flash column chromatography. White solid; m.p. 72.3 – 75.3 ^{o}C; ^{1}H NMR (400MHz, $CDCl_3$) δ 2.29 (s, 3H), 2.60 (s, 3H), 7.18 (d, *J*= 7.6 Hz, 1H), 7.24 (d, *J*= 7.6 Hz, 1H), 7.66 (t, *J*= 7.8 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 7.5, 24.4, 115.8–116.2 (m), 117.4–117.8 (m), 122.7, 123.0, 136.6, 142.4–142.8 (m), 143.7–144.1 (m), 144.9–145.2 (m), 146.1–146.5 (m), 147.1, 158.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -145.4 (dd, *J*= 22.5 Hz, 11.3 Hz, 2F), -143.9 (dd, *J*= 22.5 Hz, 11.3 Hz, 2F); MS (EI): *m/z* (relative intensity) 255.1 (M^+, 100), 234.0 (11), 213.0 (5), 187.0 (15), 91.0 (32); HRMS: calcd. for $C_{13}H_{10}F_4N^+$: 256.0744, found 256.0742.

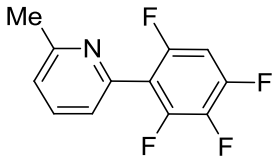
2-Methyl-6-(2,3,5,6-tetrafluorophenyl)pyridine (Table 5.2, compound 3cx)



Eluents (Ethyl acetate: Hexane= 1: 9, R_f= 0.50) was used for flash column

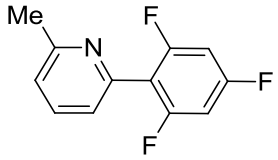
chromatography. Colorless liquid; ^{1}H NMR (400MHz, $CDCl_3$) δ 2.61 (s, 3H), 7.04 – 7.13 (m, 1H), 7.21 (d, *J*= 7.6 Hz, 1H), 7.26 (d, *J*= 7.6 Hz, 1H), 7.69 (t, *J*= 7.8 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 24.4, 105.4–105.9 (m), 120.9–121.2 (m), 122.7, 123.3, 136.7, 142.6–143.0 (m), 144.6–145.0 (m), 145.1–145.5 (m), 146.8, 147.1–147.5 (m), 159.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -143.6 (dd, *J*= 22.5 Hz, 15.0 Hz, 2F), -138.9 (dd, *J*= 22.5 Hz, 11.3 Hz, 2F); MS (EI): *m/z* (relative intensity) 241.0 (M^+, 100), 221.0 (5), 173.9 (12), 91.0 (23), 66.0 (11); HRMS: calcd. for $C_{12}H_8F_4N^+$: 242.0587, found 242.0585.

2-Methyl-6-(2,3,4,6-tetrafluorophenyl)pyridine (Table 5.2, compound 3cy)



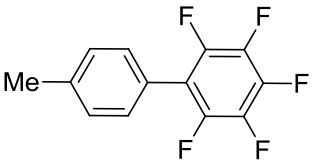
Eluents (Ethyl acetate: Hexane= 1: 4, R_f= 0.70) was used for flash column chromatography. Colorless liquid; ^{1}H NMR (400MHz, $CDCl_3$) δ 2.61 (s, 3H), 6.81–6.88 (m, 1H), 7.19 (d, *J*= 8.0 Hz, 1H), 7.22 (d, *J* =7.6 Hz, 1H), 7.67 (t, *J*= 7.8 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 24.5, 100.8–101.3 (m), 115.7-116.1 (m), 122.8, 123.1, 136.0–136.3 (m), 136.7, 138.4–138.8 (m), 147.0, 147.9–148.3 (m), 149.0–149.4 (m), 150.4–150.8 (m), 151.5–151.9 (m), 153.2–153.5 (m), 155.6–156.0 (m), 158.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -164.9 (m, 1F), 135.2 (dd, *J*= 22.5 Hz, 7.5 Hz, 1F), 132.0 (m, 1F), -117.9 (d, *J*= 11.3 Hz, 1F); MS (EI): *m/z* (relative intensity) 241.0 (M^+, 100), 221.0 (5), 174.0 (15), 91.0 (32), 66.0 (10); HRMS: calcd. for $C_{12}H_8F_4N^+$: 242.0587, found 242.0587.

2-Methyl-6-(2,4,6-trifluorophenyl)pyridine (Table 5.2, compound 3cz)



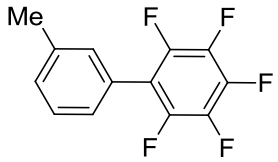
Eluents (Ethyl acetate: Hexane= 1: 4, R_f= 0.70) was used for flash column chromatography. Colorless liquid; ^{1}H NMR (400MHz, $CDCl_3$) δ 2.62 (s, 3H), 6.73–6.78 (m, 2H), 7.18 (d, *J*= 7.8, 1H), 7.23 (d, *J*= 7.6 Hz, 1H), 7.67 (t, *J*= 7.8 Hz,1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 24.4, 100.2–100.7 (m), 114.7–115.2 (m), 122.6, 122.7, 136.5, 147.8, 158.6, 159.2–159.6 (m), 160.9–161.3 (m), 161.7–162.0 (m), 163.4–163.7 (m); ^{19}F NMR (376 MHz, $CDCl_3$) δ -111.2 (d, *J*= 7.5 Hz, 2F), -107.6 (t, *J*= 7.5 Hz, 1F); MS (EI): *m/z* (relative intensity) 223.0 (M^+, 100), 155.9 (10), 90.9 (13), 66.0 (3), 51.0 (2); HRMS: calcd. for $C_{12}H_9F_3N^+$: 224.0682, found 224.0678.

2,3,4,5,6-Pentafluoro-4'-methyl-1,1'-biphenyl (Table 5.3, compound 5au)[6g]



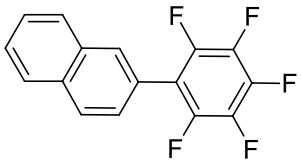
Eluents (Hexane, R_f= 0.5) was used for flash column chromatography. ^{1}H NMR (400MHz, $CDCl_3$) δ 2.44 (s, 3H), 7.31–7.33 (m, 4H); ^{13}C NMR (100MHz, $CDCl_3$) δ 21.3, 115.7–116.2 (m), 123.4, 129.4, 130.0, 136.4–136.7 (m), 138.8–139.3 (m), 139.4, 141.3–141.6 (m), 142.7–143.1 (m), 145.2–145.6 (m); ^{19}F NMR (376 MHz, $CDCl_3$) δ -162.5 (m, 2F), -156.2 (t, *J*= 22.5 Hz, 1F), -143.4 (dd, *J*= 22.5 Hz, *J*= 7.5 Hz, 2F); MS (EI): *m/z* (relative intensity) 258.0 (M^+, 100), 237.0 (54), 219 (24), 187.9 (14), 91.0 (9).

2,3,4,5,6-Pentafluoro-3'-methyl-1,1'-biphenyl (Table 5.3, compound 5bu)[6g]



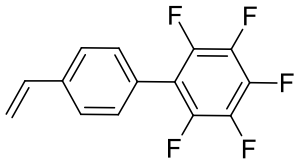
Eluents (Hexane, R_f= 0.5) was used for flash column chromatography. ^{1}H NMR (400MHz, $CDCl_3$) δ 2.45 (s, 3H), 7.23–7.26 (m, 2H), 7.30 (d, *J*= 7.6 Hz, 1H), 7.41 (t, *J*= 7.6 Hz , 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 21.3, 115.8–116.4 (m), 126.3, 127.2, 128.6, 130.1, 130.7, 136.4–136.8 (m), 138.5, 138.7–139.3 (m), 141.2–141.8 (m), 142.8–143.2 (m), 145.2–145.6 (m); ^{19}F NMR (376 MHz, $CDCl_3$) δ -162.5 (m, 2F), -156.0 (t, *J*= 22.5 Hz, 1F), 143.2 (dd, *J*= 22.5 Hz, *J*= 7.5 Hz, 2F) ; MS (EI): *m/z* (relative intensity) 258.0 (M^+, 100), 237.0 (62), 218.9 (33), 188.0 (20), 90.9 (12).

2-(Perfluorophenyl)naphthalene (Table 5.3, compound 5cu)[18]



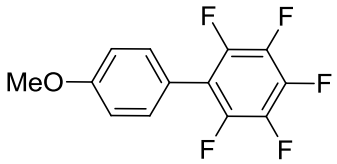
Eluents (Ethyl acetate: Hexane= 1: 9, R_f= 0.70) was used for flash column chromatography. ^{1}H NMR (400MHz, $CDCl_3$) δ 7.48–7.52 (m, 1H), 7.54–7.60 (m, 2H), 7.89–7.92 (m, 2H), 7.94–7.97 (m. 2H); ^{13}C NMR (100MHz, $CDCl_3$) δ 115.7–116.2 (m), 123.7, 126.7, 127.0, 127.8, 128.3, 128.4, 130.1, 133.0, 133.3, 136.4–136.8 (m), 138.9–139.4 (m), 141.5–141.9 (m), 143.0–143.3 (m), 145.3–145.7 (m); ^{19}F NMR (376 MHz, $CDCl_3$) *δ* -162.1 (m, 2F), -155.4 (t, *J*= 22.5 Hz, 1F), -143.0 (dd, *J*= 22.5 Hz, *J*= 7.5 Hz, 2F) ; MS (EI): *m/z* (relative intensity) 294.0 (M^+, 100), 274.0 (30), 243.0 (10), 225.0 (11), 92.9 (3).

2,3,4,5,6-Pentafluoro-4'-vinyl-1,1'-biphenyl (Table 5.3, compound 5du)[18]



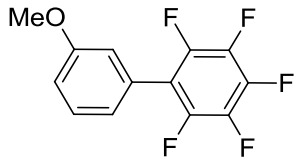
Eluents (Hexane, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400MHz, $CDCl_3$) δ 5.37 (d, *J*= 10.8 Hz, 1H), 5.86 (d, *J*= 17.6 Hz, 1H), 6.78 (dd, *J*= 10.8 Hz, *J*= 17.6 Hz, 1H), 7.41 (d, *J*= 8.0 Hz, 2H), 7.54 (d, *J*= 8.4 Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$) δ 115.3, 115.4–115.9 (m), 125.6, 126.4, 130.3, 136.0, 136.4–136.9 (m), 138.6, 138.9–139.3 (m), 141.6–141.9 (m), 142.7–143.1 (m), 145.2–145.6 (m); ^{19}F NMR (376 MHz, $CDCl_3$) δ -162.3 (m, 2F), -155.7 (t, *J*= 22.5 Hz, 1F), -143.2 (dd, *J*= 22.5 Hz, *J*= 7.5 Hz, 2F) ; MS (EI): *m/z* (relative intensity) 270.1 (M^+, 100), 250.0 (53), 219.0 (67), 201 (41), 135 (14).

2,3,4,5,6-Pentafluoro-4'-methoxy-1,1'-biphenyl (Table 5.3, compound 5eu)[6g]



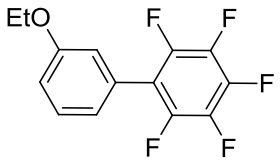
Eluents (Ethyl acetate: Hexane= 1: 50, R_f= 0.45) was used for flash column chromatography. ^{1}H NMR (400MHz, $CDCl_3$) δ 3.87 (s, 3H), 7.02 (d, *J*= 8.8 Hz, 2H), 7.37 (d, *J*= 8.4 Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$) δ 55.3, 114.2, 115.2–116.2 (m), 118.4, 131.4, 136.1–137.0, 138.4–139.5 (m), 140.9–141.6 (m), 142.6–143.4 (m), 145.0–145.7 (m), 160.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -162.7 (m, 2F), -156.6 (t, *J*= 22.5 Hz, 1F), -143.7 (dd, *J*= 22.5 Hz, *J*= 7.5 Hz, 2F); MS (EI): *m/z* (relative intensity) 274.0 (M^+, 100), 230.9 (83), 205.0 (34), 180.9 (18), 92.9 (7).

2,3,4,5,6-Pentafluoro-3'-methoxy-1,1'-biphenyl (Table 5.3, compound 5fu)[6g]



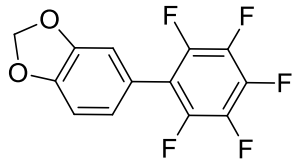
Eluents (Ethyl acetate: Hexane= 1: 50, R_f= 0.45) was used for flash column chromatography. ^{1}H NMR (400MHz, $CDCl_3$) δ 3.85 (s, 3H), 6.96 (s, 1H), 7.00–7.03 (m, 2H), 7.41 (t, *J*= 8.0 Hz , 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 55.3, 114.8, 115.8, 122.4, 127.5, 129.7, 136.3–136.8 (m), 138.8–139.4 (m), 141.5–142.0, 142.6–143.1 (m), 145.1–145.7 (m), 159.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -162.4 (m, 2F), -155.7 (t, *J*= 22.5 Hz, 1F), -142.9 (dd, *J*= 22.5 Hz, *J*= 11.3 Hz, 2F); MS (EI): *m/z* (relative intensity) 274.0 (M^+, 100), 243.9 (33), 230.9 (55), 204.9 (31), 191.9 (12).

3'-Ethoxy-2,3,4,5,6-pentafluoro-1,1'-biphenyl (Table 5.3, compound 5gu)



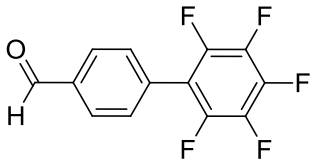
Eluents (Ethyl acetate: Hexane= 1: 50, R_f= 0.50) was used for flash column chromatography. Colorless liquid; ^{1}H NMR (400MHz, $CDCl_3$) δ 1.45 (t, *J*= 6.8 Hz, 3H), 4.08 (q, *J*= 6.8 Hz, 2H), 6.95 (s, 1H), 6.98–7.02 (m, 2H), 7.40 (t, *J*= 8.0 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 14.7, 63.6, 115.4, 115.6–116.2 (m), 116.3, 122.3, 127.4, 129.7, 136.3–136.7 (m), 138.8–139.3 (m), 141.4–141.9 (m), 142.7–143.0 (m), 145.2–145.7 (m), 159.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -162.4 (m, 2F), -155.8 (t, *J*= 22.5 Hz, 1F), -142.9 (dd, *J*= 22.5 Hz, *J*= 7.5 Hz, 2F); MS (EI): *m/z* (relative intensity) 288.0 (M^+, 42), 260.0 (100), 231.0 (26), 204.9 (16), 193.0 (13); HRMS: calcd. for $C_{14}H_9OF_5^+$: 288.0574, found 288.0584.

5-(Perfluorophenyl)benzo[d][1,3]dioxole (Table 5.3, compound 5hu)[17]



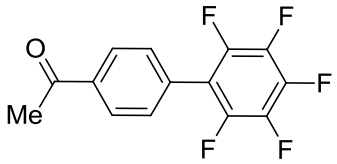
Eluents (Ethyl acetate: Hexane= 1: 20, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400MHz, $CDCl_3$) δ 6.03 (s, 2H), 6.88–6.93 (m, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ 101.5, 108.6, 110.3, 115.4–115.9 (m), 119.4, 124.2, 136.2–136.9 (m), 138.7–139.4 (m), 141.2–141.8 (m), 142.6–143.1 (m), 145.2–145.6 (m), 148.0, 148.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -162.5 (m, 2F), -156.2 (t, *J*= 22.5 Hz, 1F), 143.3 (dd, *J*= 22.5 Hz, *J*= 7.5 Hz, 2F); MS (EI): *m/z* (relative intensity) 288.0 (M^+, 100), 229.0 (22), 211.0 (48), 180.0 (14), 143.6 (18).

2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-4-carbaldehyde (Table 5.3, compound 5iu)[13c]



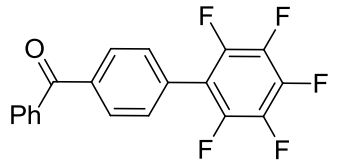
Eluents (Ethyl acetate: Hexane= 1: 20, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400MHz, $CDCl_3$) δ 7.62 (d, *J*= 8.4 Hz, 2H), 8.02 d, *J*= 6.4 Hz, 2H), 10.08 (s, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 114.3–115.2 (m), 129.8, 130.9, 132.4, 136.6, 138.7–139.5 (m), 139.5–140.0 (m), 142.0–142.5(m), 142.5–143.1 (m), 145.0–145.6 (m), 191.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -161.4 (m, 2F), -153.6 (t, *J*= 22.5 Hz, 1F), -142.7 (dd, *J*= 22.5 Hz, *J*= 7.5 Hz, 2F); MS (EI): *m/z* (relative intensity) 271.9 (M^+, 100), 241.9 (45), 223.9 (59), 192.9 (26), 73.9 (11).

1-(2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-4-yl)ethanone (Table 5.3, compound 5ju)[18]



Eluents (Ethyl acetate: Hexane= 1: 20, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400MHz, $CDCl_3$) δ 2.64 (s, 3H), 7.53 (d, *J*= 8.0 Hz, 2H), 8.06 (d, *J*= 8.4 Hz , 2H); ^{13}C NMR (100MHz, $CDCl_3$) δ 26.5, 114.6–115.1 (m), 128.5, 130.4, 131.0, 136.4–136.9 (m), 137.4, 138.9–139.3 (m), 139.3–139.7 (m), 141.7–142.3 (m), 142.6–143.0 (m), 145.0–145.5 (m), 197.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -161.7 (m, 2F), -154.1 (t, *J*= 22.5 Hz, 1F), -142.9 (dd, *J*= 22.5 Hz, *J*= 7.5 Hz, 2F); MS (EI): *m/z* (relative intensity) 286.0 (M^+, 26), 271.0 (100), 242.0 (34), 224.0 (30), 193.0 (24).

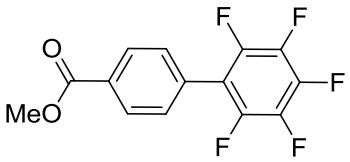
(2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-4-yl)(phenyl)methanone (Table 5.3, compound 5ku)[13c]



Eluents (Ethyl acetate: Hexane= 1: 20, R_f= 0.20) was used for flash column chromatography. ^{1}H NMR (400MHz, $CDCl_3$) δ 7.49–7.63 (m, 5H), 7.84 (d, *J*= 7.2 Hz , 2H), 7.92 (d, *J*= 8.0 Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$) δ 114.5–115.3 (m), 128.3, 129.9, 130.1, 130.3, 132.7, 136.4–136.9 (m), 137.1, 138.1, 138.7–139.2 (m), 139.2–139.9 (m), 141.8–142.2 (m), 142.8–143.1 (m), 145.1–145.5 (m), 195.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -161.6 (m, 2F), -154.2 (t, *J*= 18.8 Hz, 1F), -142.8 (dd, *J*= 22.5 Hz, *J*= 7.5 Hz, 2F); MS (EI): *m/z* (relative intensity) 348.0 (M^+, 100), 270.9 (74),

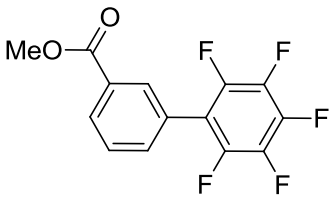
242.0 (53), 193.0 (38), 105 (72).

Methyl 2',3',4',5',6'-pentafluoro-[1,1'-biphenyl]-4-carboxylate (Table 5.3, compound 5lu)[17]



Eluents (Ethyl acetate: Hexane= 1: 10, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400MHz, $CDCl_3$) δ 3.95 (s, 3H), 7.50 (d, *J*= 8.0 Hz, 2H), 8.14 (d, *J*= 8.0 Hz , 2H); ^{13}C NMR (100MHz, $CDCl_3$) δ 52.3, 114.7–115.1 (m), 129.8, 130.2, 130.9, 136.4–136.9 (m), 138.9–139.3 (m), 139.3–139.7 (m), 141.8–142.3 (m), 142.6–143.0 (m), 145.1–145.6 (m), 166.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -161.7 (m, 2F), -153.3 (t, *J*= 22.5 Hz, 1F), -142.9 (dd, *J*= 22.5 Hz, *J*= 7.5 Hz, 2F); MS (EI): *m/z* (relative intensity) 302.0 (M^+, 43), 270.9 (100), 241.9 (34), 224.0 (29), 193.0 (20).

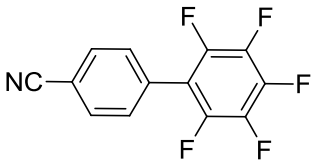
Methyl 2',3',4',5',6'-pentafluoro-[1,1'-biphenyl]-3-carboxylate (Table 5.3, compound 5mu)[17]



Eluents (Ethyl acetate: Hexane= 1: 20, R_f= 0.20) was used for flash column chromatography. ^{1}H NMR (400MHz, $CDCl_3$) δ 3.93 (s, 3H), 7.55–7.61 (m, 2H), 8.11–8.13 (m, 2H); ^{13}C NMR (100MHz, $CDCl_3$) δ 52.3, 114.6–115.1 (m), 126.7, 128.8, 130.3, 130.9, 131.3, 134.4, 136.4–136.8 (m), 138.9–139.2 (m), 139.2–139.6 (m), 141.6–142.1 (m), 142.7–143.1 (m), 145.1–145.5 (m), 166.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -161.9 (m, 2F), -154.8 (t, *J*= 22.5 Hz, 1F), -143.2 (dd, *J*= 22.5 Hz, *J*= 7.5 Hz,

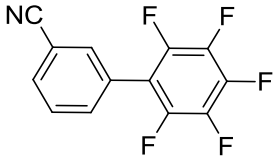
2F); MS (EI): *m/z* (relative intensity) 302.0 (M^+, 54), 270.9 (100), 241.9 (37), 223.9 (30), 192.9 (16).

2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-4-carbonitrile (Table 5.3, compound 5ou)[13c]



Eluents (Ethyl acetate: Hexane= 1: 9, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400MHz, $CDCl_3$) δ 7.56 (d, *J*= 8.0 Hz, 2H), 7.80 (d, *J*= 8.0 Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$) δ 113.3, 113.7–114.5 (m), 118.0, 130.9, 131.1, 132.4, 136.5–137.0 (m), 139.0–139.5 (m), 139.6–140.1 (m), 142.2–142.6 (m), 142.6–143.0 (m), 145.0–145.5 (m); ^{19}F NMR (376 MHz, $CDCl_3$) δ -160.9 (m, 2F), -152.9 (t, *J*= 22.5 Hz, 1F), -142.7 (dd, *J*= 22.5 Hz, *J*= 7.5 Hz, 2F); MS (EI): *m/z* (relative intensity) 268.9 (M^+, 100), 248.9 (12), 217.8 (10), 199.9 (9), 92.9 (8).

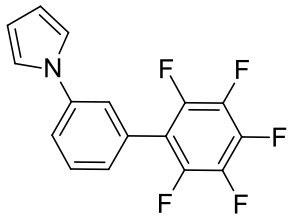
2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-3-carbonitrile (Table 5.3, compound 5ou)[19]



Eluents (Ethyl acetate: Hexane= 1: 9, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400MHz, $CDCl_3$) δ 7.62–7.69 (m, 2H), 7.74–7.78 (m, 2H); ^{13}C NMR (100MHz, $CDCl_3$) δ 113.4, 113.4–113.8 (m), 117.9, 127.8, 129.7, 132.8, 133.6, 134.5, 136.4–137.0 (m), 139.0–139.5 (m), 139.6–140.1 (m), 142.1–142.6 (m), 142.6–143.0 (m), 145.1–145.6 (m); ^{19}F NMR (376 MHz, $CDCl_3$) δ -160.9 (m, 2F),

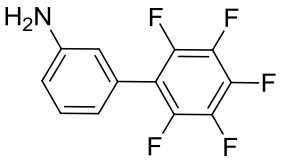
-153.0 (t, *J*= 22.5 Hz, 1F), -143.0 (dd, *J*= 22.5 Hz, *J*= 7.5 Hz, 2F); MS (EI): *m/z* (relative intensity) 268.9 (M^+, 100), 248.9 (13), 217.9 (6), 192.0 (10), 92.9 (5).

1-(2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-3-yl)-1H-pyrrole (Table 5.3, compound 5pu)



Eluents (Ethyl acetate: Hexane= 1: 4, R_f= 0.70) was used for flash column chromatography. Orange solid; m.p. 98.3 – 99.3 ^oC; ^1H NMR (400MHz, $CDCl_3$) δ 6.41–6.42 (m, 2H), 7.14–7.15 (m, 2H), 7.33 (d, *J*= 7.2 Hz, 1H), 7.49 – 7.53 (m, 2H), 7.56–7.58 (m, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 110.9, 114.9–115.4 (m), 119.2, 121.2, 122.1, 127.2, 127.7, 129.9, 136.3–136.9 (m), 138.8–139.7 (m), 141.1, 141.7–142.1 (m), 142.7–143.2 (m), 145.1–145.6 (m); ^{19}F NMR (376 MHz, $CDCl_3$) δ -161.8 (m, 2F), -154.7 (t, *J*= 22.5 Hz, 1F), -142.8 (dd, *J*= 22.5 Hz, *J*= 7.5 Hz, 2F); MS (EI): *m/z* (relative intensity) 309.1 (M^+, 100), 281.0 (16), 261.0 (9), 242.0 (9), 154.5 (8); HRMS: calcd. for $C_{16}H_8NF_5^+$: 309.0577, found 309.0579

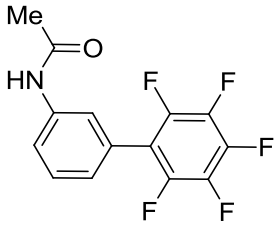
2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-3-amine (Table 5.3, compound 5qu)[13c]



Eluents (Ethyl acetate: Hexane= 1: 1, R_f= 0.70) was used for flash column chromatography. ^1H NMR (400MHz, $CDCl_3$) δ 3.73 (s, 2H), 6.71 (s, 1H), 6.76–6.80 (m, 2H), 7.27 (t, *J*= 7.8 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 115.9, 116.0–116.2 (m), 116.4, 120.2, 127.2, 129.5, 136.2–136.8 (m), 138.6–139.2 (m), 141.2-141.7 (m),

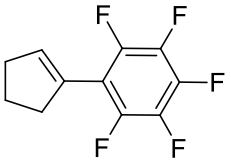
142.6–143.1 (m), 145.1–145.6 (m), 146.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -162.5 (m, 2F), -156.1 (t, *J*= 22.5 Hz, 1F), -142.8 (dd, *J*= 22.5 Hz, *J*= 7.5 Hz, 2F); MS (EI): *m/z* (relative intensity) 258.8 (M^+, 74), 191.9 (60), 160.8 (29), 116.9 (62), 93.0 (45).

_N_-(2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-3-yl)acetamide (Table 5.3, compound 5ru)



Eluents (Ethyl acetate: Hexane= 1: 1, R_f= 0.70) was used for flash column chromatography. White solid; m.p. 184.1 – 185.4 ^{o}C; ^{1}H NMR (400MHz, $(CD_3)_2CO$) δ 2.12 (s, 3H), 7.19 (d, *J*= 7.6 Hz, 1H), 7.48 (t, *J*= 8.0 Hz, 1H), 7.72 (d, *J*= 8.0 Hz, 1H), 7.92 (s, 1H), 9.37 (s, 1H) ; ^{13}C NMR (100MHz, $CDCl_3$) δ 25.3, 115.9–116.5 (m), 121.3, 122.0, 126.7, 127.8, 130.0, 137.0–137.5(m), 139.0, 139.4–140.2 (m), 142.0–142.7 (m) 143.3–143.9 (m), 145.7–146.3 (m), 169.1; ^{19}F NMR (376 MHz, $(CD_3)_2CO$) δ -164.8 (m, 2F), -158.4 (t, *J*= 22.5 Hz, 1F), -144.7 (dd, *J*= 22.5 Hz, *J*= 7.5 Hz, 2F); MS (EI): *m/z* (relative intensity) 301.0 (M^+, 23), 259.0 (100), 231.0 (11), 205.0 (6), 181.0 (4); HRMS: calcd. for $C_{14}H_9NOF_5^+$: 302.0599, found 302.0601.

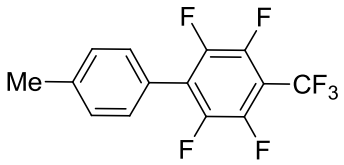
1-(Cyclopent-1-en-1-yl)-2,3,4,5,6-pentafluorobenzene (Table 5.3, compound 5su)



Eluents (Hexane, R_f= 0.50) was used for flash column chromatography. Colorless liquid; ^{1}H NMR (400MHz, $CDCl_3$) δ 1.97–2.05 (m, 2H), 2.52–2.57 (m, 2H), 2.57–2.76 (m, 2H), 6.22 (bs, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 23.3, 33.3, 35.4, 112.6–

113.1 (m), 129.2, 136.1–136.6 (m), 136.7, 138.0–138.6 (m), 138.6–139.2 (m), 140.5–140.9 (m), 143.0–143.5 (m), 145.4–145.9 (m); ^{19}F NMR (376 MHz, $CDCl_3$) δ -163.5 (m, 2F), -157.7 (t, *J*= 22.5 Hz, 1F), -140.5 (dd, *J*= 22.5 Hz, *J*= 7.5 Hz, 2F); MS (EI): *m/z* (relative intensity) 234.0 (M^+, 81), 218.9 (87), 180.9 (38), 87.0 (100), 69 (23); HRMS: calcd. for $C_{11}H_7F_5^+$: 234.0468, found 234.0456.

2,3,5,6-Tetrafluoro-4'-methyl-4-(trifluoromethyl)-1,1'-biphenyl (Table 5.3, compound 5av)[20]



Eluents (Hexane, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400MHz, $CDCl_3$) δ 2.46 (s, 3H), 7.34–7.40 (m, 4H); ^{13}C NMR (100MHz, $CDCl_3$) δ 21.3, 108.0, 116.9, 119.6, 122.3, 123.1, 124.8–125.1 (m), 129.6, 129.8, 140.3, 142.7–143.3 (m), 145.1–146.0 (m); ^{19}F NMR (376 MHz, $CDCl_3$) δ -141.7 (m, 2F), -141.1 (m, 2F), -56.3 (t, *J*= 22.5 Hz, 3F); MS (EI): *m/z* (relative intensity) 308.0 (M^+, 100), 289.0 (25), 219.0 (64), 91.1 (13), 69.0 (42).

5.5 References

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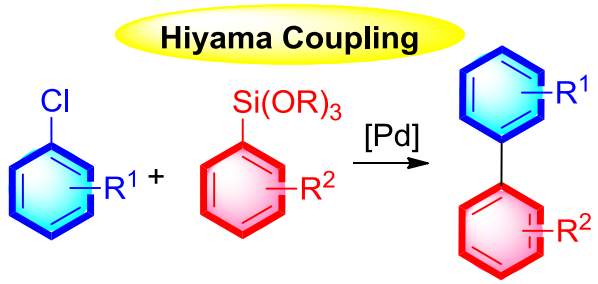
Chapter 6 Palladium-Catalyzed Hiyama Cross-Coupling Reaction of Aryl and Heteroaryl Chlorides under Solvent-Free Reaction Condition

6.1 Introduction

Palladium-catalyzed cross-coupling reactions have become versatile protocols in organic synthesis for construction of carbon-carbon or carbon-heteroatom bonds.[1] Suzuki,[2] Negishi,[3] Kumada,[4] and Stille[5] reactions are common methods for the preparation of biaryls which have numerous applications in pharmaceutical, material, and agricultural chemistry.[6] Hiyama[7] cross-coupling reaction is one of the most attractive methodology to access biaryl compounds because of low cost, low toxicity, commercial availability, easy preparation and handling and high stability to a variety of reaction conditions of organosilicon reagents. However, organosilicons are less reactive electrophiles owing to their less polarized carbon and silicon bonds.

Aryl(alkoxy)silane is one of the most extensively studied organosilicons[8] in Hiyama coupling since the initial report by Shibata and coworkers.[9] Reactive aryl iodides and bromides have been predominantly used as electrophiles in the Hiyama coupling reactions instead of the relatively cheaper and more commercially available aryl chlorides.[10] Since the initial attempt of the use of 10mol% Pd_2dba_3/John-phos system for the Hiyama coupling of $PhSi(OMe)_3$ with 4-chloroacetophenone to give 47% product yield[11], the effectiveness of the Hiyama coupling of aryl chlorides has not been improved significantly comparing with other cross-coupling methodologies. Palladium catalytic systems such as Pd/(*o*-tol)$_3$P [12], Pd/*i*-*Pr*-DPE phos[13],Pd/(4-FC_6H_4)$_3$P[14], Pd/phosphite[15], Pd/phosphonate[16], Pd/carbene ligand[17], Pd/diamine ligand[18], Pd/diimine ligand[19], Pd/thiourea ligand[20], Pd/MIDA ligand[21], ligand free Pd/C systems[22] and SBA-15-supported Pd nanoparticles[23] for the Hiyama coupling of aryl(alkoxy)silane with aryl chlorides have been reported. However, in

general, these reports are commonly suffered from 1) narrow substrate scope (unreactive/poor results for the electron rich aryl chlorides and/or functionalized aryl chlorides); 2) limited examples (only few aryl chlorides are demonstrated in some reports); 3) high catalyst loading (3-5 mol% Pd catalysts are commonly used), 4) long reaction time (10-24 h for conventional heating). Moreover, in some cases, rising the reaction temperature is not the effective mean to improve the yield. [16, 18]



Previous work:

- Conventional heating

1. Medium to high catalyst loading (0.5-5 mol%Pd)
2. Long reaction time (12-24 h)
3. Require solvents (e.g. Toluene, Dioxane)
4. Limited examples for solvent-free conditions of aryl chlorides

- Microwave heating

1. Medium to low catalyst loading (0.5-0.1 mol%Pd)
2. Short reaction time (0.5 h)
3. Require solvents (e.g. H_2O)
4. High instrumental cost

- Common limitations

1. Lack of the use of heteroaryl silanes for heteroaryl-heteroaryl synthesis
2. Limited examples for sterically hindered biaryl synthesis

This work:

- Conventional heating

1. Low catalyst loading (down to 0.05 mol%Pd)
2. Short reaction time (3 h)
3. Solvent-free conditions for most of substrates
4. Wide substrate scope (32 examples)
5. Solventless large-scaled synthesis (100 mmol scale)
6. Success in sterically hindered *di*-ortho substituted biaryl synthesis
7. First report of heteroaryl-heteroaryl synthesis
8. Demonstrate acid or water protocol to minimize side products

Figure 6.1 General limitations of Hiyama-coupling of aryl chlorides by conventional heating.

Recently, breakthrough such as lowering the catalyst loading to 0.5 mol% Pd, shorter reaction time, wider substrate scope (steric hindered aryl chlorides) have been made by Verkade and coworker's Pd/ $^{t}Bu_2P$-N=P($^{i}BuNCH_2CH_2)_3N$ catalyst[24], Jin and coworker's β-diketiminatophosphane Pd complex[19b] and wang and coworker's dinuclear NHC/Pd complex[17c]. Yet, catalyst loading remains high and the heteroaryl-heteraryl Hiyama coupling keep silent. Microwave irradiation is found to be an alternative to improve the catalytic activity of the Hiyama coupling of aryl chlorides. [25,26] Despite of the high cost, the availability of the microwave instrument and technical concerns such as solvent and heat control especially for large scale synthesis[27], aryl bromides are still predominantly used in current microwave irradiated Hiyama coupling reaction. Therefore, development of highly effective catalyst for the Hiyama coupling reactions by all means is highly desired.

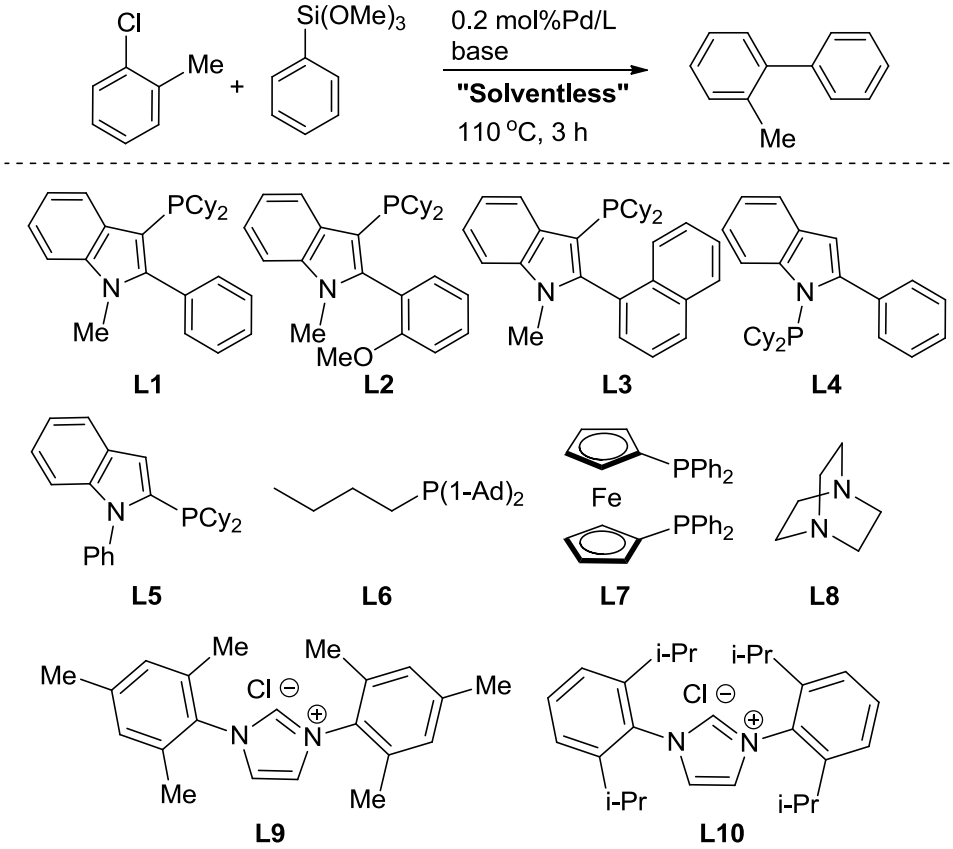
In view of the current limitations and our persisting interests in the palladium-catalyzed coupling reactions, we would like to develop a highly active catalytic system and environmental friendly solvent-free condition with conventional heating to achieve multi-target of Hiyama coupling reaction such as lowering the catalyst loading[28], expending the substrate scope, and applying the catalysis to pilot scale (50- 200 mmol[28]). Indole-scaffolded phosphine ligands, which are developed by our group, showed excellent activities towards a board range of palladium-catalyzed coupling reactions.[29] Among them, the 3-(dicyclohexylphosphino)-2-phenylindole **L1** is effective ligand in various coupling reactions with aryl chlorides.[30] We believed that the indolyl scaffold may provide effective steric and electronic influence[31] towards palladium center and increase the catalytic activity of the catalytic system. Herein, we report the highly efficient indolyl phosphine ligand **L2** to the solvent-free Hiyama coupling reaction of aryl/heteroaryl chlorides with aryl/heteroaryl tri(alkoxy)silanes.

6.2 Results and discussion

6.2.1 Preliminary evaluation of palladium-catalyzed Hiyama cross-coupling reaction of aryl chlorides

In order to investigate the feasibility of palladium-catalyzed Hiyama cross-coupling reaction of aryl chlorides, sterically hindered 2-chlorotoluene and phenyltrimethoxysilane were chosen as the benchmark substrates. The results are promising, under 0.2 mol% Pd, indolyl phosphine ligands that the phosphino group attached to the 3-position of indole ring (Table 6.1, entries 1-3) are highly active towards the Hiyama coupling reaction. The results (Table 6.1, entries 1-5) also shows that the Hiyama coupling reaction is sensitive to the steric (product yield increase along with increasing the ortho steric hindrance of the indole bottom ring, (**L1**-**L3**)) and electronic factors (product yield significantly decrease, if attaching the phosphino group to the nitrogen position, (**L1** and **L4**)) of the phosphine ligands and the 2-arylindole provided an excellent scaffold (**L1** and **L5**) to affect the Hiyama coupling reaction. Commercially available and well recognized ligands such as phosphine ligands **L6** (CataCXiumA), **L7** (dppf), dinitrogen ligand **L8** (DABCO), and NHC carbine ligands **L9** (IMes•HCl), **L10** (IPr•HCl) were examined. However, they were found to be inactive ligands towards the Pd-catalyzed Hiyama coupling reaction. Commonly used fluoride bases were screened (Table 6.1, entries 1, 11 and 12). TBAF•$3H_2O$ was found to be the best base while KF and CsF hardly promoted the Hiyama reaction. Upon surveying the Pd sources (Table 6.1, entries 1, 11 and 12), $Pd(OAc)_2$ afforded the best product yield. It is worthy to note that Pd/**L2** system gives the best result among **L1**-**L10** under solvent-free condition and also achieved the lowest catalyst loading so far for this entry in Hiyama coupling reaction (Table 6.1, entry 2).

Table 6.1 Initial screenings of palladium-catalyzed Hiyama cross-coupling reaction of 2-chlorotoluene with phenyltrimethoxysilane[a]



entry	Pd source	promotor/base	ligand	% yield[b]
1	$Pd(OAc)_2$	$TBAF\cdot 3H_2O$	L1	69
2	$Pd(OAc)_2$	$TBAF\cdot 3H_2O$	L2	87
3	$Pd(OAc)_2$	$TBAF\cdot 3H_2O$	L3	77
4	$Pd(OAc)_2$	$TBAF\cdot 3H_2O$	L4	0
5	$Pd(OAc)_2$	$TBAF\cdot 3H_2O$	L5	33
6	$Pd(OAc)_2$	$TBAF\cdot 3H_2O$	L6	4
7	$Pd(OAc)_2$	$TBAF\cdot 3H_2O$	L7	0[c]
8	$Pd(OAc)_2$	$TBAF\cdot 3H_2O$	L8	0
9	$Pd(OAc)_2$	$TBAF\cdot 3H_2O$	L9	0
10	$Pd(OAc)_2$	$TBAF\cdot 3H_2O$	L10	0

11	$Pd(OAc)_2$	KF	L1	0
12	$Pd(OAc)_2$	CsF	L1	Trace
13	$Pd_2(dba)_3$	$TBAF\cdot 3H_2O$	L1	61
14	$PdCl_2(CH_3CN)_2$	$TBAF\cdot 3H_2O$	L1	82

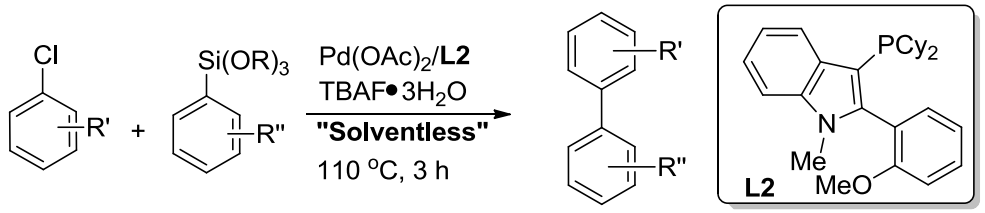
[a] Reaction condition: 2-Chlorotoluene (0.5 mmol), phenyltrimethoxysilane (1.0 mmol), Pd source/ L = 1:4 and base (1.0 mmol) were stirred for 3 h at 110 ^oC under nitrogen. [b] Calibrated GC yields were reported using dodecane as internal standard. [c] Pd source:L = 1:2

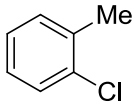
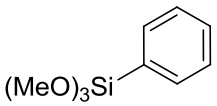
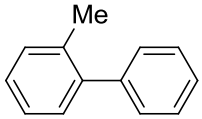
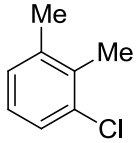
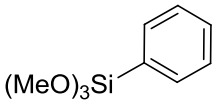
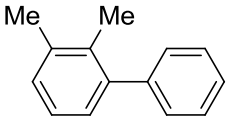
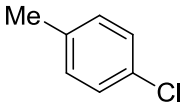
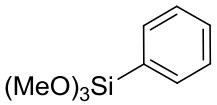
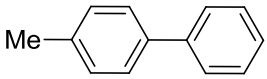
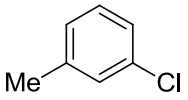
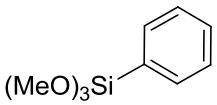
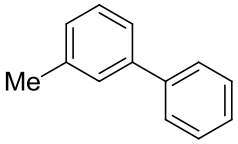
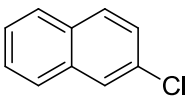
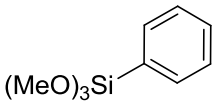
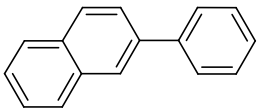
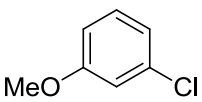
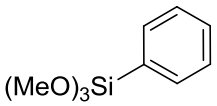
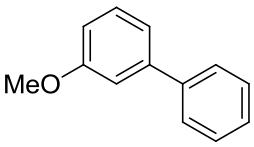
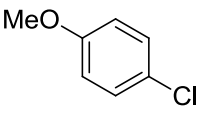
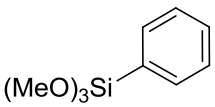
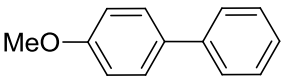
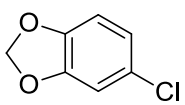
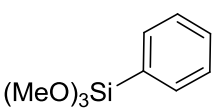
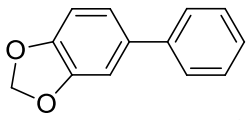
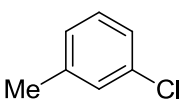
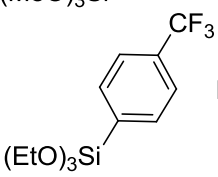
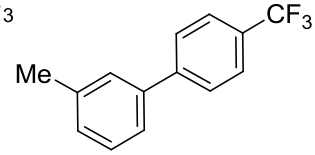
6.2.2 Scope of palladium-catalyzed Hiyama cross-coupling reaction of aryl chlorides

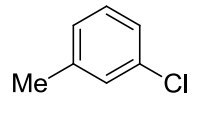
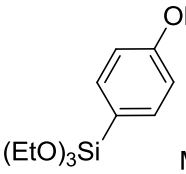
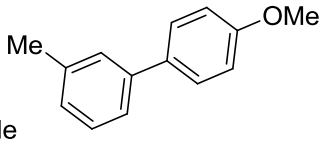
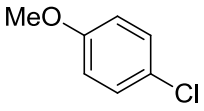
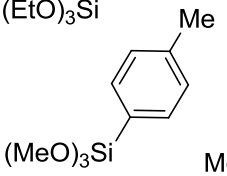
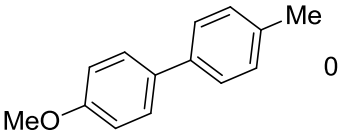
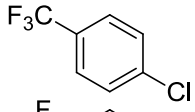
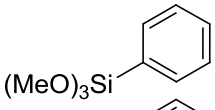
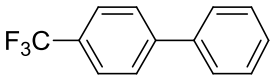
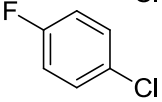
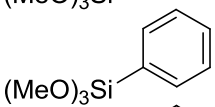
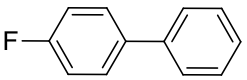
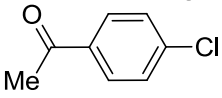
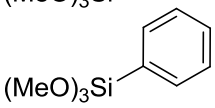
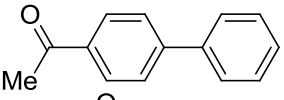
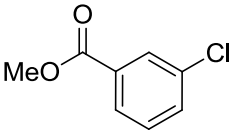
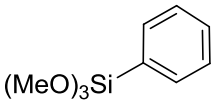
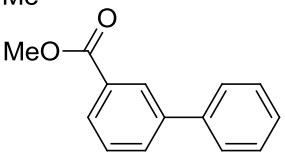
With the preliminary optimized reaction conditions in hand, a wide range of electron rich, electron neutral and functionalized aryl chlorides were used to test the efficiency of the Pd/**L2** system. Sterically hindered, electron neutral and electron rich aryl chlorides were coupled with phenyl(trimethoxy)silane to give excellent yields (Table 6.2, entries 1-8). Apart from aryl chlorides, electron-deficient and –rich trialkoxysilanes were also able to couple and gave products in good yields (Table 6.2, entries 9-11). An array of common function groups such as $-CF_3$, -F, -COMe, $-CO_2Me$, -COPh and -CN were compatible and afforded excellent product yields (Table 6.2, entries 12-22). A free $-NH_2$ group in 3-chloroaniline was remained intact under this optimized reaction condition (Table 6.2, entry 23). During the study of the Hiyama reaction, we observed lower yield for the ArCl baring an ester functional group (Table 6.2, entries 15 and 19) and corresponding benzoic acid. The addition of acetic acid to the reaction mixture was found to able to neutralize the methoxide anion[32], and thus to reduce the possibility of alkaline hydrolysis of ester group and improve the product

yield (Table 6.2, entries 15-20). The catalyst loading could be down to 0.2-0.05 mol% Pd. To our best knowledge, this is the lowest catalyst loading reported for the Hiyama coupling of aryl chlorides with aryl(trialkoxy)silanes.[33]

Table 6.2 Palladium-catalyzed Hiyama cross-coupling reaction of aryl chlorides[a]



entry	ArCl	Ar'Si(OR)$_3$	product	mol% Pd	% yield[b]
1				0.2	86
2				0.2	80
3				0.067	86
4				0.1	99
5				0.1	92
6				0.2	97
7				0.2	98
8				0.2	95
9				0.2	65

10				0.2	70
11				0.2	82
12				0.05	93
13				0.05	86
14				0.05	75
15				0.05	53
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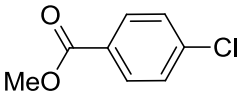
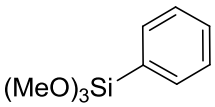
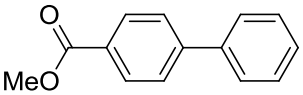
19				0.05	64
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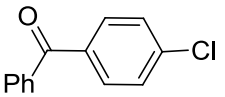
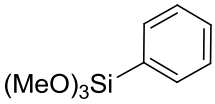
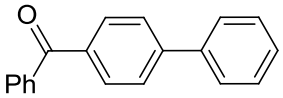
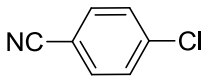
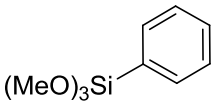
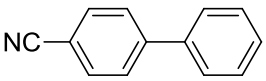
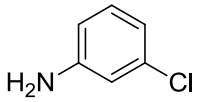
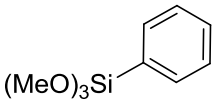
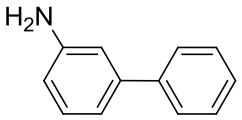
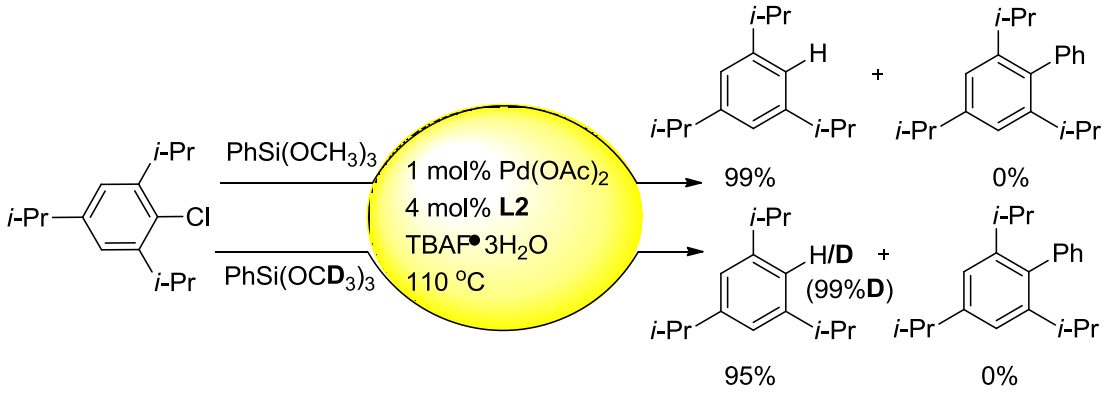
21				0.05	99[g]
22				0.2	88[g]
23				0.2	73

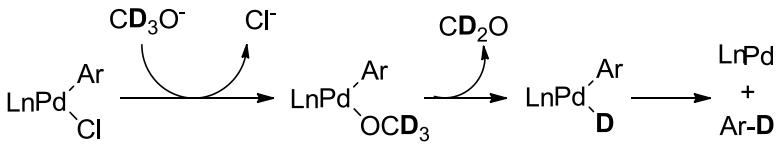
[a] Reaction condition: ArCl (0.5 mmol), Ar'Si(OR)$_3$ (1.0 mmol), Pd(OAc)$_2$/ L1 = 1:4 and TBAF·3H$_2$O (1.0 mmol) were stirred for 3 h at 110 ^{o}C under nitrogen. [b] Isolated yields. [c] 0.35 equiv. AcOH was added. [d] 0.25 equiv. AcOH was added. [e] 0.25 equiv. AcOH and toluene (0.5 mL) were added. [f] 0.50 equiv. AcOH was added. [g] Toluene (0.5 mL) was added.

6.2.3 Investigation of proton source of reduced product of sterically hindered aryl chloride and scope of palladium-catalyzed Hiyama cross-coupling reaction of sterically hindered aryl chlorides

Sterically hindered di-*ortho*-substituted aryl chlorides were found to be extremely difficult substrates in Hiyama coupling with aryl(alkoxy)silanes, which only has single report up to date.[19b] With the excellent results, we attempted to apply the highly active Pd/**L2** system to the Hiyama coupling of extremely sterically hindered 1-chloro-2,4,6-triisopropylbenzene. However, without the desired coupling product, we obtain reduced 1,3,5-triisopropylbenzene as sole product (Scheme 6.1). We think the methoxide anion which generated from the phenyl(trimethoxy)silane may compete with the transmetalation step of the corresponding silane to undergo the ligand substitution of chloride anion and following the -hydride elimination and reductive elimination to give the reduced arene (Scheme 6.2). We synthesized the $SiPh(OCD_3)_3$ to perform the deuterium experiment and the reduced 1,3,5-triisopropylbenzene has 99%D at the reduction position which support our hypothesis (Scheme 6.1).



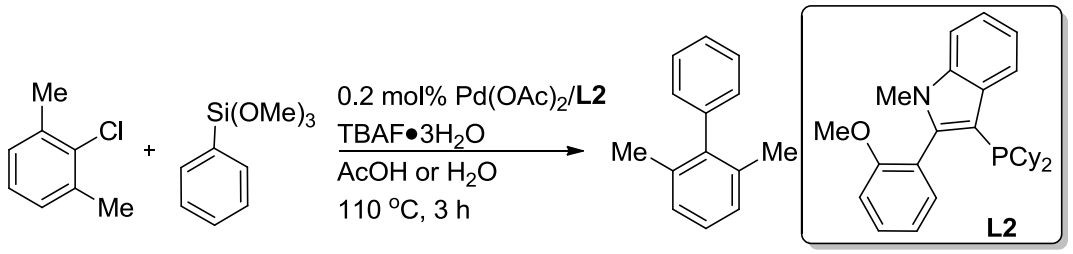
Scheme 6.1 Deuterium experiment of Hiyama coupling reaction of 1-chloro-2,4,6-triisopropylbenzene.



Scheme 6.2 Proposed mechanism for the generation of reduced arenes.

Addition of 0.25-0.50 equivalent of acetic acid to neutralize the methoxide anion was successfully suppressed the generation of 1,3-dimethylbenzene and increased the yield of desired coupling product (Table 6.3, entries 2-4). Since certain amount of 1,3-dimethylbenzene still observed (Table 6.3, entries 2-4) and excess acetic acid reduced the rate of reaction (Table 6.3, entries 4 and 5), we attempted to use water as a mild proton source to protonate the methoxide anion meanwhile the reaction rate is able to remain intact (Table 6.3, entires 6-9). The addition of 10 equiv of water is highly sufficient to suppress the formation of 1,3-dimethylbenzene so as to greatly improve the desired yield (Table 6.3, entries 1 and 8). The highly sterically congested di-*ortho*-substituted aryl chlorides were found to be feasible coupling partners in the Hiyama coupling reaction with this new reaction protocol (Table 6.4, entries 1-5). Fair yield could also be obtained in the tri-*ortho*-subsitiuted Hiyama coupling reaction (Table 6.4, entry 6).

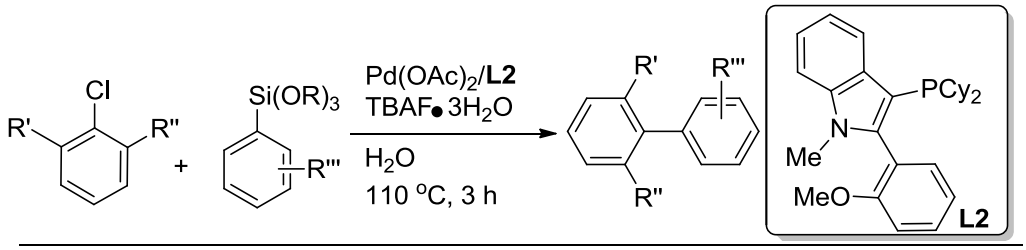
Table 6.3 Investigation of water and acid effect on Hiyama cross-coupling reaction of sterically hindered aryl chlorides[a]

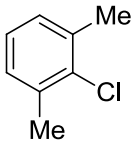
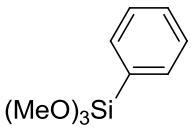
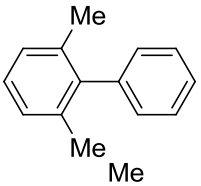
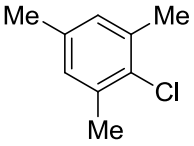
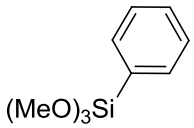
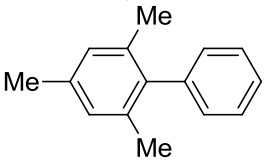
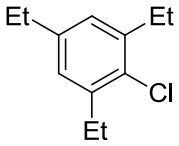
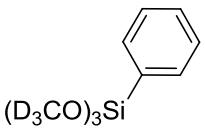
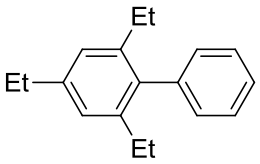
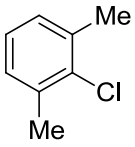
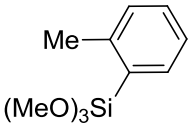
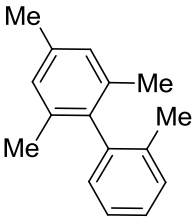


entry	AcOH (equiv.)	H_2O (equiv.)	% yield[b]
1	-	-	56[c]
2	0.25	-	67
3	0.35	-	74[d]
4	0.50	-	73
5	1.0	-	22
6	-	2.5	69
7	-	5.0	81
8	-	10	97
9	-	20	49

[a] Reaction condition: 1,3-dimethyl-2-chlorobenzene (0.5 mmol), phenyltrimethoxysilane (1.0 mmol), $Pd(OAc)_2$/ L1 =1:4, $TBAF\cdot 3H_2O$ and acetic acid or water additive were stirred at 110 ^oC for 3 h. [b] FID yield calibrated using dodecane as internal standard. [c] 0.5 mol%$Pd(OAc)_2$. [d] Isolated yield.

Table 6.4 Palladium-catalyzed Hiyama cross-coupling reaction of steric hindered aryl chlorides[a]



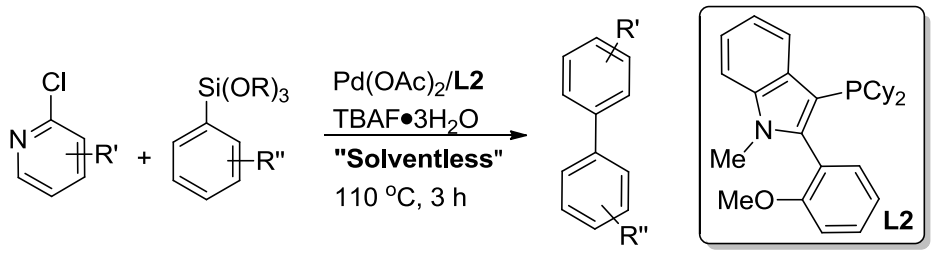
entry	ArCl	Ar'Si(OR)$_3$	product	mol% Pd	% yield[b]
1				0.2	97
2				0.2	74[c]
3				0.5	80
4				0.5	70[c]
5				1.0	66[d]
6				1.0	36[c,d]

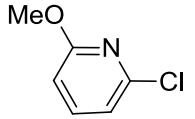
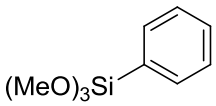
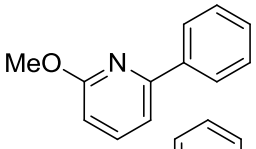
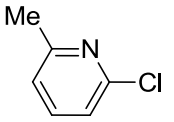
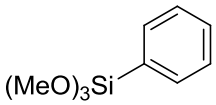
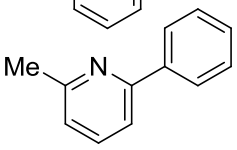
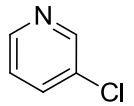
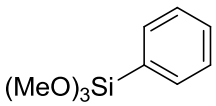
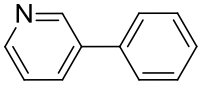
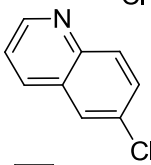
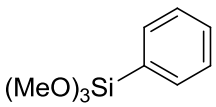
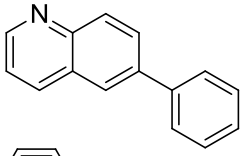
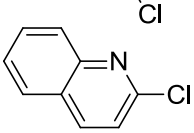
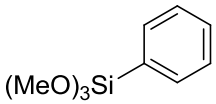
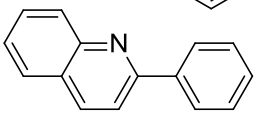
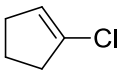
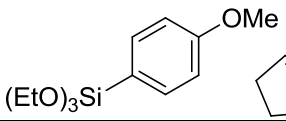
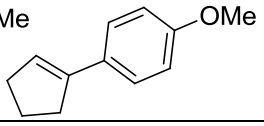
[a] Reaction condition: ArCl (0.5 mmol), Ar'Si(OR)$_3$ (1.0 mmol), Pd(OAc)$_2$/ L1 =1:4, TBAF·3H$_2$O (1.0 mmol), and 10 equivalent of H$_2$O were stirred for 3 h at 110 ^{o}C under nitrogen. [b] Isolated yields. [c] 0.35 equivalent of AcOH was used instead of H$_2$O. [d] NMR yield.

6.2.4 Scope of palladium-catalyzed Hiyama cross-coupling reaction of heteroaryl chlorides and alkenyl chloride

Apart from electron rich and steric hindered aryl chlorides, heteroaryl chlorides are another difficult class of substrates in Hiyama coupling reaction. In general, even assisting with the microwave irradiation, 0.5-1.0 mol%Pd is still necessary to affect the Hiyama coupling reaction of heteroaryl chlorides to obtain good to excellent product yield. However, using Pd/**L2** system, a range of heteroaryl chlorides can be smoothly coupled with aryltrialkyoxysilanes to give good to excellent yields of the corresponding produces under solvent-free condition and the catalyst loading can be down to 0.05mol%Pd (Table 6.5, entries 1-5). Alkenyl chloride is also a feasible coupling partner for the Hiyama coupling reaction (Table 6.5, entry 6).

Table 6.5 Palladium-catalyzed Hiyama cross-coupling reaction of heteroaryl chlorides and alkenyl chloride with aryltrialkyoxysilanes[a]



entry	Het-ArCl	Ar'Si(OR)$_3$	product	mol% Pd	% yield[b]
1				0.05	99
2				0.1	97
3				0.2	88
4				0.2	83
5				0.1	81
6				0.2	63

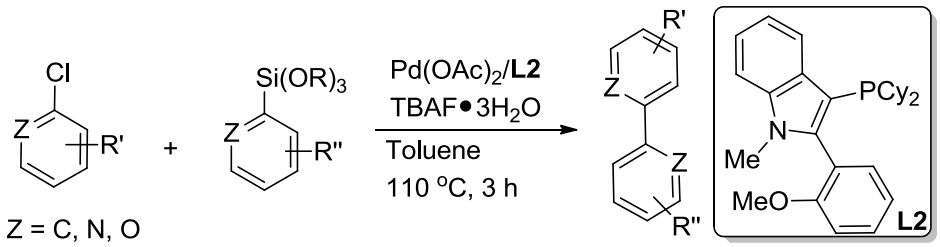
[a] Reaction condition: ArCl (0.5 mmol), Ar'Si(OR)$_3$ (1.0 mmol), Pd(OAc)$_2$/ L1 =1:4 and TBAF·3H$_2$O (1.0 mmol) were stirred for 3 h at 110 ^{o}C under nitrogen. [b] Isolated yields.

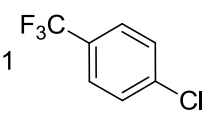
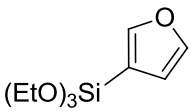
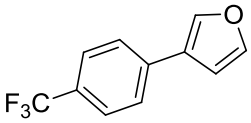
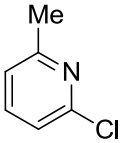
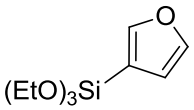
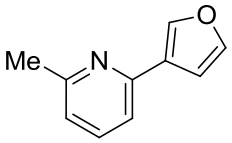
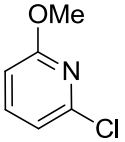
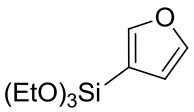
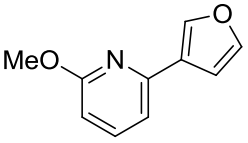
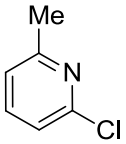
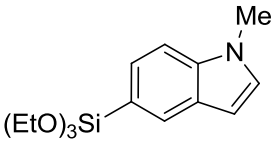
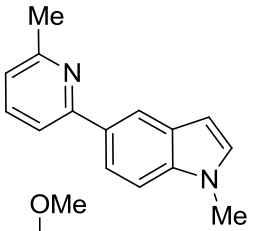
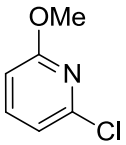
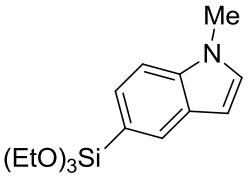
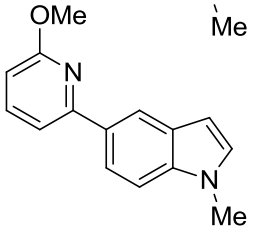
6.2.5 Scope of palladium-catalyzed Hiyama cross-coupling reaction of heteroaryl trialkoxysilanes

Heteroaryl-heteroaryl cross-coupling reaction is found to be one of the most difficult coupling reactions. Since both of the coupling partners are electron-deficient

aromatic compounds which the electron-deficient nuclephiles are usually unstable and often undergo a transmetallation process at a relatively slower rate. With 1mol%Pd catalyst of Pd/**L2** system and toluene as solvent[34], electron-deficient and heteroaryl chlorides were coupled with heteroaryl (ethoxy)silanes for the first time in Hiyama coupling reaction (Table 6.6, entries 1-5).

Table 6.6 Palladium-catalyzed Hiyama cross-coupling reaction of aryl- or hetero- aryl chlorides with heteroaryl trialkyoxysilanes[a]



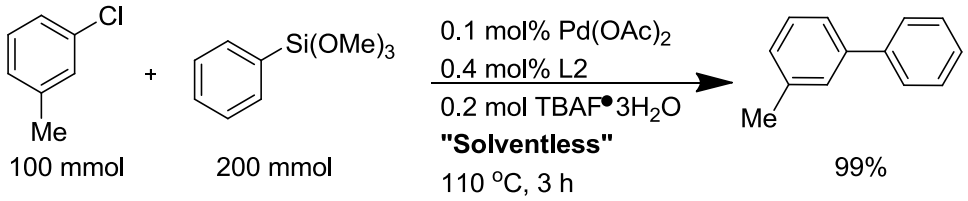
entry	Het-ArCl	Het-Ar'Si(OR)$_3$	product	mol% Pd	% yield[b]
1				1	67
2				1	81
3				1	87
4				1	60
5				1	54

[a] Reaction condition: ArCl (0.5 mmol), Ar'Si(OR)$_3$ (1.0 mmol), Pd(OAc)$_2$/ L1 =1:4,

TBAF·$3H_2O$ (1.0 mmol), and 1mL toluene were stirred for 3 h at 110 ^oC under nitrogen. [b] Isolated yields.

6.2.6 Application in large-scaled biaryl synthesis

To test the feasibility of scaling up the current reaction condition and to magnify the advantages of conventional heating for the routine application, a large scale Hiyama cross-coupling reaction was conducted (Scheme 6.3). Notably, without degasification and purification of the reactants, 3-chlorotoluene and phenyltrimethoxysilane was directly scaled up 200 times as Table 6.2 conditions to give the coupling product without any diminishing of the yield (Table 6.2, entry 4 and scheme 6.3).



Scheme 6.3 Large scale solvent-free Hiyama cross-coupling reaction of 3-chlorotoluene and phenyltrimethoxysilane.

6.3 Conclusion

In conclusion, the Pd/**L2** system is highly efficient towards Hiyama cross-coupling reaction. Aryl and heteroaryl chlorides are smoothly coupled with aryltrialkoxysilanes under solvent-free condition to give excellent yields within 3h. A wide range of aryl chlorides bearing common functional groups such as cyano, ketone, ester, and amine were compatible in the mild reaction conditions and the catalyst loading can be down to 0.05mol%Pd for the first time. The deuterium experiment reveals the possible pathway of the formation of reduced arenes and implies an

addition of acid or water protocol which improves the yield of Hiyama coupling of the stercally hindered aryl chlorides dramatically. Particularly noteworthy is that the Hiyama coupling of heteroaryl chlorides with heteroaryltrialkoxysilanes are reported for the first time. Under the conventional heating, the reaction can be easily scale up 200 times (100mmol) without degasification and purification of reactants. We are anticipating this highly efficient protocol to be widely adapted in routine synthesis.

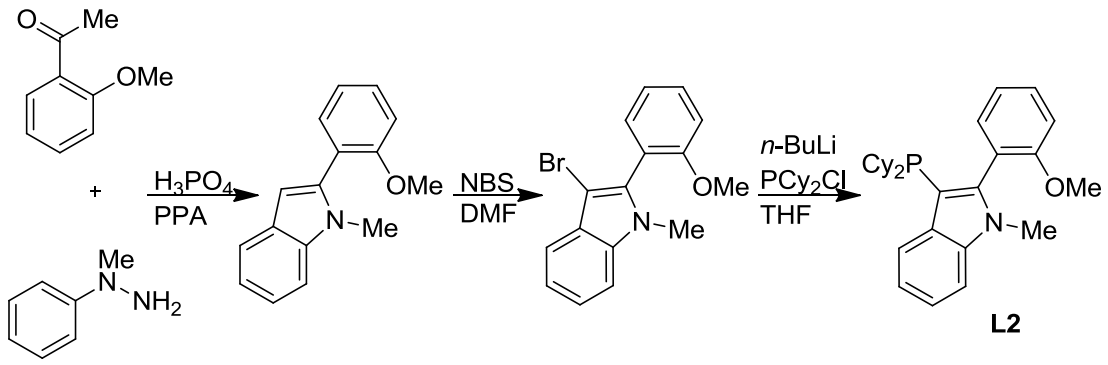
6.4 Experimental section

6.4.1 General considerations

Unless otherwise noted, all reagents were purchased from commercial suppliers and used without purification. All Hiyama cross-coupling reactions were performed in resealable screw cap Schlenk tube (approx. 15 mL volume) in the presence of Teflon-coated magnetic stirrer bar (4 mm × 10 mm). A blast shield was applied to all close-capped reactions. Toluene and tetrahydrofuran (THF) were distillated from sodium and sodium benzophenone ketyl under nitrogen, respectively. [35] Indolylphosphine ligand **L1**, **L3** and **L4** were prepared according to the reported procedures.[30a, 36] Ligands **L5** – **L10** were purchased from commercial suppliers. Tetrabutylammonium fluoride trihydrate ($TBAF \cdot 3H_2O$) was purchased from Fluka. KF and CsF were purchased from Aldrich. Aryl silanes except for 1*H*-indole, 1-methyl-5-(triethoxysilyl) and silane, tri(methoxy-d_3)phenyl- (9CI) were purchased from commercial suppliers and used directly. 1*H*-indole, 1- methyl-5-(triethoxysilyl) and silane, tri(methoxy-d_3)phenyl- (9CI) were synthesized according to the reported procedures.[37] New bottle of *n*-butyllithium was used (*Note*: since the concentration of *n*-BuLi may vary, we recommend performing a titration prior to use). Thin layer chromatography was performed on 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. NMR spectra were recorded on a Brüker spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C, 376 MHz for ^{19}F and 162 MHz for ^{31}P). Spectra were referenced internally to the residual proton resonance in $CDCl_3$ (δ 7.26 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). ^{19}F NMR chemical shifts were determined relative to $CFCl_3$ as the external standard and low field is positive. ^{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 FTICR mass spectrometer (ESI-MS). 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, ^{13}C and/or ^{19}F 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.

6.4.2 Preparation of indolylphosphine ligand L2



Indolylphosphine ligand **L2** was prepared according to the reported procedures without modification.[36b]

3-(Dicyclohexylphosphino)-2-(2-methoxyphenyl)-1-methyl-1-*H*-indole (L2)

3-Bromo-2-(2-methoxyphenyl)-1-methyl-1*H*-indole (10 mmol), *n*-BuLi (11 mmol) and chlorodicyclohexylphosphine (12 mmol) in THF (25 ml) were given white solid product (3.1 g, 71%). ^{1}H NMR (400 MHz, C_6D_6) δ 1.02-1.39 (m, 10H), 1.50-2.01 (m, 10H), 2.31-2.37 (m, 1H), 2.47-2.54 (m, 1H), 3.09 (s, 3H), 3.23 (s, 3H), 7.09-7.13 (m, 1H), 7.14-7.16 (m, 1H), 7.22-7.26 (m, 2H), 7.44 (d, *J*= 7.4 Hz, 1H), 8.07 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 27.2, 27.3, 29.9, 30.2, 30.3, 30.8, 30.9, 31.8, 32.0, 32.2, 32.4, 33.9, 34.0, 34.5, 34.7, 54.5, 104.5, 104.7, 109.7, 110.4, 119.7, 119.9, 121.3, 121.5, 122.1, 129.8, 130.9, 131.0, 134.01, 134.04, 138.3, 146.5, 146.9, 158.2; ^{31}P NMR (162 MHz, C_6D_6) δ -17.87; MS (EI): *m/z* (relative intensity) 433.3 (M^+, 5), 402.3 (100), 320 (10), 268.1 (30).

6.4.3 General procedure for initial ligand and reaction conditions screening

An array of stock solutions of Pd metal sources (0.010 mmol) with ligand (Pd:L =1:4) in freshly distilled THF (4.0 mL) were initially prepared with continuously stirring at room temperature for 1 min. An array of Schlenk tubes were charged with

magnetic stirrer bar (4 mm x 10 mm) and were evacuated and backfilled with nitrogen (3 cycles). The stock solutions (0.40 mL, 0.20 mol% Pd) were added by syringe to the array of Schlenk tubes respectively. The solvent in Schlenk tubes were removed under reduced pressure. The Schlenk tubes were charged with bases and were again evacuated and backfilled with nitrogen (3 cycles). The Schlenk tubes were then added with trimethoxyphenylsilane (0.19 mL, 1.0 mmol) via autopipette. The reaction mixtures were allowed stir for 1 min and 2-chlorotoluene (59 L, 0.50 mmol) was added to each Schlenk tubes via autopipette. This batch of Schlenk tube was resealed and magnetically stirred in a preheated 110 ^{o}C oil bath for 3 h. The reactions were allowed to reach room temperature. Ethyl acetate (~8 mL), dodecane (113 μL, internal standard) and water (~2 mL) were added. The organic layer was subjected to GC analysis. The GC yield was previously calibrated by authentic sample/dodecane calibration curve.

6.4.4 General procedure for palladium-catalyzed Hiyama coupling of aryl chlorides

$Pd(OAc)_2$ (2.3 mg, 0.010 mmol) with ligand **L2** (17.3mg, 0.040 mmol) in freshly distilled 10 mL THF (0.2 mol% Pd per 1 mL stock solution) were initially prepared with continuously stirring at room temperature for 1 min. Schlenk tube was charged with magnetic stirrer bar (4 mm x 10 mm) and was evacuated and backfilled with nitrogen (3 cycles). The corresponding volume of stock solution was added by syringe to the tube. The solvent was removed under reduced pressure. TBAF•$3H_2O$ (0.32 g, 1.0 mmol) and solid aryl chlorides (0.50 mmol) was added to the tube which was again evacuated and backfilled with nitrogen (3 cycles). trimethoxyphenylsilane (0.19 mL, 1.0 mmol) was then added to the tube via

autopipette and the reaction mixture was allowed stir for 1 min. Liquid aryl chlorides (0.50 mmol) was added to the tube via autopipette. Acetic acid and/or toluene (0.50 mL) were then added via autopipette and syringe respectively (if needed, as indicated in Table 2 and 3). The tube was resealed and magnetically stirred in a preheated 110 ^{o}C oil bath for 3 h. The reaction was allowed to reach room temperature. Ethyl acetate (~8 mL), water (~2 mL) were added. The organic layers were combined and concentrated. The crude products were purified by column chromatography on silica gel (230-400 mesh).

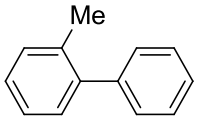
6.4.5 General procedure for large-scale Hiyama coupling of aryl chlorides

$Pd(OAc)_2$ (23 mg, 0.10 mmol) and ligand **L2** (0.173 g, 0.40 mmol) were loaded to a 250 mL Schlenk flask (with a glass stopcock and 24/29 joint with hooks) which equipped with a magnetic stirrer bar (30 mm x 6 mm) and fitted with septum. The flask was carefully evacuated and backfilled with nitrogen for three cycles. Precomplexation was accomplished by adding 10 mL freshly distilled THF in to the flask and the solution was allowed to stir at room temperature for 1 min. The solvent was removed under reduced pressure. $TBAF•3H_2O$ (63 g, 0.20 mol) was quickly charged to the flask which was evacuated and backfilled with nitrogen for other three cycles. Trimethoxyphenylsilane (38 mL, 0.20 mol) was then added to the tube by syringe and the reaction mixture was allowed to stir for 10 min. 3-chlorotoluene (11.8 mL, 0.10 mol) was added to the flask by syringe and allowed to stir for another 5 min. The septum was replaced with a 24/29 stopper with hooks which was then fixed with wire to the flask. The stopcock was closed and the flask was placed in a preheated 110 ^{o}C oil bath for 3 h. The reaction was allowed to reach room temperature. Ethyl acetate and water were added to the flask and the mixture was transferred to

separating funnel and subjected to extraction. The organic layers were combined and concentrated. The crude product was filtered through a pad of silica gel (10 cm x 20 cm, 230-400 mesh) and eluted with hexane to yield the pure 3-methylbiphenyl (16.6 g, 99%).

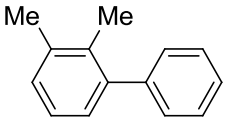
6.4.6 Characterization data for cross-coupling products

2-Methyl-1,1'-biphenyl (Table 6.2, entry 1)[36a]



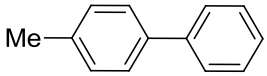
Eluents (Hexane, R_f= 0.55) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (s, 3H), 7.32–7.36 (m, 4H), 7.40–7.43 (m, 3H), 7.47–7.51 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.4, 125.7, 126.7, 127.2, 128.0, 129.2, 129.8, 130.3, 135.3, 141.9, 142.0; MS (EI): *m/z* (relative intensity) 168.1 (M^+, 100), 153.0 (40), 139.0 (8), 115.0 (14), 77.0 (4).

2,3-Dimethyl-1,1'-biphenyl (Table 6.2, entry 2)[38]



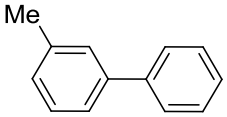
Eluents (Hexane, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.55 (s, 3H), 2.44 (s, 3H), 7.18-7.27 (m, 3H), 7.39–7.44 (m, 3H), 7.49 (t, *J*= 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.9, 20.7, 125.2, 126.6, 127.6, 128.8, 129.4, 134.0, 137.1, 142.2, 142.6; MS (EI): *m/z* (relative intensity) 182.1 (M^+, 95), 167.1 (100), 152.0 (26), 128.0 (8), 76.0 (8).

4-Methyl-1,1'-biphenyl (Table 6.2, entry 3)[36a]



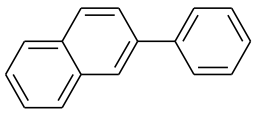
Eluents (Hexane, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.48 (s, 3H), 7.33 (d, *J*= 7.6 Hz, 2H), 7.40 (t, *J*= 7.6 Hz, 1H), 7.50 (t, *J*= 7.6 Hz, 2H), 7.58 (d, *J*= 8.0 Hz, 2H), 7.66 (d, *J*= 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 126.9, 127.0, 128.7, 129.4, 137.0, 138.3, 141.1; MS (EI): *m/z* (relative intensity) 168.0 (M^+, 100),139.0 (8), 115.0 (15), 91.0 (6), 62.9 (9).

3-Methyl-1,1'-biphenyl (Table 6.2, entry 4)[39]



Eluents (Hexane, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400MHz, $CDCl_3$) δ 2.48 (s, 3H), 7.29 (d, *J*= 7.6 Hz, 1H), 7.46 (t, *J*= 7.6 Hz, 2H), 7.52–7.57 (m, 4H), 7.72 (d, *J*= 7.8 Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$) δ 21.5, 124.2, 127.1, 127.2, 127..9, 128.0, 128.6, 128.7, 138.3, 141.2, 141.3; MS (EI): *m/z* (relative intensity) 168.1 (M^+, 100), 152.0 (23), 139.0 (5), 115.0 (8), 89.0 (4).

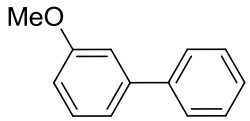
2-Phenylnaphthalene (Table 6.2, entry 5)[32]



Eluents (Hexane, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.48 (s, 3H), 7.47–7.51 (m, 1H), 7.57–7.63 (m, 4H), 7.82–7.87 (m, 3H), 7.96–8.02 (m, 3H), 8.16 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 125.5, 125.7, 125.9, 126.2, 127.3, 127.4, 127.6, 128.2, 128.4, 128.8, 132.6, 133.6, 138.5, 141.1; MS (EI): *m/z* (relative intensity) 204.1 (M^+, 100), 176.0 (3), 152.1 (3), 126.0 (3), 101.0

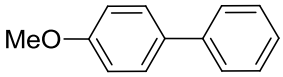
(7).

3-Methoxy-1,1'-biphenyl (Table 6.2, entry 6)[40]



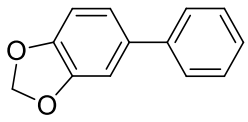
Eluents (Ethyl acetate: Hexane= 1: 50, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.96 (s, 3H), 7.03 (d, *J*= 8.2 Hz, 1H), 7.29 (s, 1H), 7.33 (d, *J*= 8.0 Hz, 1H), 7.46–7.50 (m, 2H), 7.56 (t, *J*= 7.6 Hz, 2H), 7.73. (d, *J*= 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.1, 112.6, 112.8, 119.6, 127.1, 127.3, 128.7, 129.7, 141.0, 142.7, 159.9; MS (EI): *m/z* (relative intensity) 184.0 (M^+, 100), 154.1 (28), 141.0 (51), 115.0 (92), 76.1 (17).

4-Methoxy-1,1'-biphenyl (Table 6.2, entry 7)[36a]



Eluents (Ethyl acetate: Hexane= 1: 20, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.90 (s, 3H), 7.05 (d, *J*= 8.8 Hz, 2H), 7.38 (t, *J*= 7.6 Hz, 1H), 7.49 (t, *J*= 7.6 Hz, 1H), 7.59–7.65 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.2, 114.2, 126.6, 126.7, 128.1, 128.7, 133.7, 140.8, 159.1; MS (EI): *m/z* (relative intensity) 184.0 (M^+, 100), 169.0 (47), 141.0 (57), 115.0 (52), 89.1 (7).

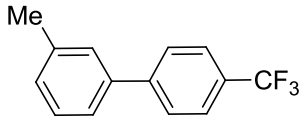
5-Phenylbenzo[d][1,3]dioxole (Table 6.2, entry 8)[32]



Eluents (Ethyl acetate: Hexane= 1: 9, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.03 (s. 3H), 6.94 (d, *J*= 8.0 Hz, 1H),

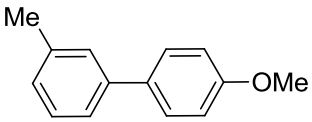
7.11-7.15 (m, 2H), 7.37 (t, *J*= 7.4 Hz, 1H), 7.47 (t, *J*= 7.6 Hz, 2H), 7.58 (d, *J*= 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 101.0, 107.6, 108.5, 120.5, 126.8, 126.9, 128.7, 135.5, 140.8, 147.0, 148.0; MS (EI): *m/z* (relative intensity) 198.0 (M^+, 100), 139.0 (44), 115.0 (4), 98.8 (4), 77.0 (2).

3-Methyl-4'-(trifluoromethyl)-1,1'-biphenyl (Table 6.2, entry 9)[41]



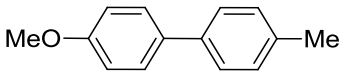
Eluents (Hexane, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.48 (s, 3H), 7.26 (d, *J*= 7.4 Hz, 1H), 7.38-7.45 (m, 3H), 7.72 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 124.36 (q, *J*= 270 Hz), 124.37, 125.6 (q, *J*= 4.0 Hz), 127.4, 128.0, 128.88, 128.92, 129.2 (q, *J*= 32 Hz), 138.6, 139.8, 144.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.3; MS (EI): *m/z* (relative intensity) 236.0 (M^+, 100), 217.1 (13), 165.0 (45), 152.0 (16), 91.1 (6).

4'-Methoxy-3-methyl-1,1'-biphenyl (Table 6.2, entry 10)[42]



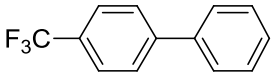
Eluents (Ethyl acetate: Hexane= 1: 50, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.47 (s, 3H), 3.89 (s, 3H), 7.03 (d, *J*= 8.8 Hz, 2H), 7.19 (d, *J*= 7.6 Hz, 1H), 7.37 (t, *J*= 7.4 Hz, 1H), 7.41–7.44 (m, 2H), 7.59 (d, *J*= 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 55.2, 114.1, 123.8, 127.4, 127.5, 128.1, 128.6, 133.8, 138.2, 140.8, 159.0; MS (EI): *m/z* (relative intensity) 198.1 (M^+, 100), 183.0 (51), 155.0 (40), 128.0 (16), 89.0 (4).

4-Methoxy-4'-methyl-1,1'-biphenyl (Table 6.2, entry 11)[40]



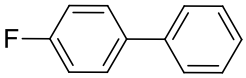
Eluents (Ethyl acetate: Hexane= 1: 9, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.46 (s, 3H), 3.90 (s, 3H), 7.04 (d, *J*= 8.4 Hz, 2H), 7.30 (d, *J*= 7.6 Hz, 2H), 7.53 (d, *J*= 6.4 Hz, 2H), 7.59 (d, *J*= 7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 55.3, 114.2, 126.6, 127.9, 129.4, 133.7, 136.3, 138.0, 158.9; MS (EI): *m/z* (relative intensity) 198.1 (M^+, 100), 183.1 (61), 155.0 (45), 128.0 (19), 77.1 (6).

4-(Trifluoromethyl)-1,1'-biphenyl (Table 6.2, entry 12)[43]



Eluents (Hexane, R_f= 0.60) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J*= 7.2 Hz. 1H), 7.52 (t, *J*= 7.6 Hz, 2H), 7.64 (d, *J*= 7.6 Hz, 2H), 7.71-7.75 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 124.3 (q, *J*= 270.0 Hz), 125.7 (q, *J*= 4.0 Hz), 127.3, 127.4, 128.1, 129.0, 129.3 (q, *J*= 33.0 Hz), 139.7, 144.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.3; MS (EI): *m/z* (relative intensity) 222.1 (M^+, 100), 201.0 (12), 172.0 (4), 152.0 (24), 75.0 (3).

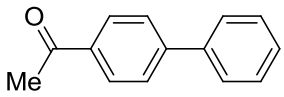
4-Fluoro-1,1'-biphenyl (Table 2, entry 13)[43]



Eluents (Hexane, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (t, *J*= 8.6 Hz, 2H), 7.36 (t, *J*= 7.4 Hz, 1H), 7.45 (t, *J*= 7.4 Hz, 2H), 7.55-7.57 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 115.6 (d, *J*= 22.0 Hz), 126.9, 127.2, 128.6 (d, *J*= 8.0 Hz), 128.8, 137.3 (d, *J*= 3.0 Hz), 140.2, 162.4 (d, *J*= 244.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -115.7; MS (EI): *m/z* (relative intensity) 172.0 (M^+,

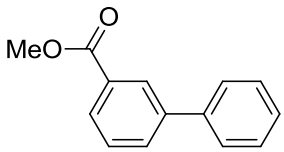
100), 146.0 (6), 120.0 (3), 74.0 (4), 51.0 (3).

1-([1,1'-Biphenyl]-4-yl)ethanone (Table 6.2, entry 14)[44]



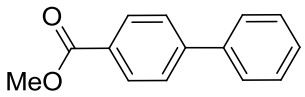
Eluents (Ethyl acetate: Hexane= 1: 9, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.63 (s, 3H), 7.41 (t, *J*= 7.4 Hz, 1H), 7.47 (t, *J*= 7.4 Hz, 2H), 7.63 (d, *J*= 7.2 Hz, 2H), 7.68 (d, *J*= 8.4 Hz, 2H), 8.03 (d, *J*= 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.5, 127.0, 127.1, 128.1, 128.8, 128.9, 135.7, 139.7, 145.6, 197.6; MS (EI): *m/z* (relative intensity) 196.0 (M^+, 43), 181.0 (100), 152.0 (65), 126.9 (6), 76.0 (10).

Methyl [1,1'-biphenyl]-3-carboxylate (Table 6.2, entry 15-18)[45]



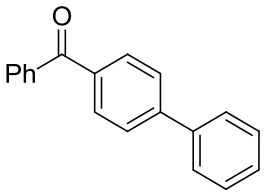
Eluents (Ethyl acetate: Hexane= 1: 9, R_f= 0.50) was used for flash column chromatography.; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.96 (s, 3H), 7.39 (t, *J*= 7.2 Hz, 1H), 7.46-7.54 (m, 3H), 7.64 (d, *J*= 7.2 Hz, 2H), 7.80 (d, *J*= 7.6 Hz, 1H), 8.04 (d, *J*= 7.6 Hz, 1H), 8.31 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.1, 127.1, 127.7, 128.2, 128.3, 128.8, 128.9, 130.6, 131.5, 140.0, 141.4, 167.0 ; MS (EI): *m/z* (relative intensity) 212.0 (M^+, 87), 196.0 (8), 181.0 (100), 152.0 (92), 76.0 (19).

Methyl [1,1'-biphenyl]-4-carboxylate (Table 6.2, entry 19-20)[40]



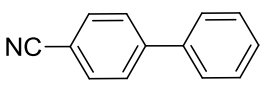
Eluents (Ethyl acetate: Hexane= 1: 9, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.95 (s, 3H), 7.40 (t, *J*= 7.2 Hz, 1H), 7.47 (t, *J*= 7.4 Hz, 2H), 7.62-7.67 (m, 4H), 8.13 (d, *J*= 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 51.9, 126.9, 127.1, 128.0, 128.7, 128.8, 130.0, 139.8, 145.4, 166.8; MS (EI): *m/z* (relative intensity) 212.1 (M^+, 72), 181.0 (100), 152.0 (56), 126.0 (5), 76.0 (9).

[1,1'-Biphenyl]-4-yl(phenyl)methanone (Table 6.2, entry 21)[40]



Eluents (Ethyl acetate: Hexane= 1: 4, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J*= 7.2 Hz, 1H), 7.47-7.53 (m, 4H), 7.58-7.63 (m, 1H), 7.67 (d, *J*= 8.0 Hz, 2H), 7.72 (d, *J*= 8.4 Hz, 2H), 7.82-7.86 (m, 2H), 7.92 (d, *J*= 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 126.8, 127.1, 128.1, 128.2, 128.8, 129.9, 130.6, 132.2, 136.1, 137.6, 139.8, 145.0, 196.2; MS (EI): *m/z* (relative intensity) 258.1 (M^+, 75), 181.0 (100), 152.0 (64), 105.0 (24), 77.0 (40).

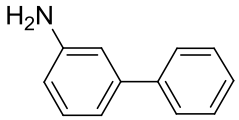
[1,1'-Biphenyl]-4-carbonitrile (Table 6.2, entry 22)[46]



Eluents (Ethyl acetate: Hexane= 1: 4, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.45 (m, 1H), 7.49 (t, *J*= 7.4 Hz,

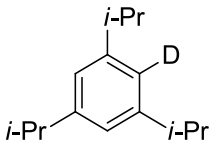
2H), 7.59-7.61 (m, 2H), 7.67-7.73 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 110.8, 118.8, 127.1, 127.6, 128.6, 129.0, 132.5, 139.0, 145.5; MS (EI): *m/z* (relative intensity) 179.1 (M^+, 100), 151.0 (14), 126.0 (3), 100.0 (2), 76.0 (6).

[1,1'-Biphenyl]-3-amine (Table 6.2, entry 23)[47]



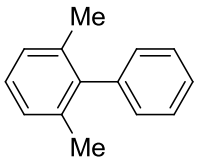
Eluents (Ethyl acetate: Hexane= 1: 2, R_f= 0.60) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.62 (s, 2H), 6.71 (d, *J*= 7.2 Hz,1H), 6.94 (s, 1H), 7.04 (d, *J*= 7.6 Hz, 1H), 7.27 (t, *J*= 7.6 Hz, 2H), 7.37 (t, *J*= 7.2 Hz, 1H), 7.46 (t, *J*= 7.6 Hz, 2H), 7.61 (d, *J*= 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 113.8, 114.0, 117.6, 127.0, 127.1, 128.6, 129.6, 141.3, 142.4, 146.6 ; MS (EI): *m/z* (relative intensity) 169.0 (M^+, 100), 141.0 (11), 115.0 (11), 89.0 (4), 71.6 (3).

Benzene-*d*, 2,4,6-tris(1-methylethyl)- (Scheme 6.1)



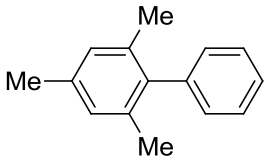
Eluents (Hexane, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (d, *J*= 6.8 Hz, 18H), 2.93-3.03 (m, 3H), 7.02 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.1, 34.2, 34.3, 122.1, 148.6, 148.7; MS (EI): *m/z* (relative intensity) 205.2 (M^+, 27), 190.1 (100), 162.1 (51), 106.0 (20), 92.0 (11); HRMS: calcd. for $C_{15}H_{24}D^+$: 206.2019, found 206.2016.

2,6-Dimethyl-1,1'-biphenyl (Table 6.4, entry 1-2)[36a]



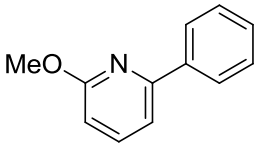
Eluents (Hexane, R_f= 0.55) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.11 (s, 6H), 7.17-7.26 (m, 5H), 7.40 (t, *J*= 7.4 Hz, 1H), 7.49 (t, *J*= 7.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 126.6, 127.0, 127.2, 128.4, 129.0, 136.0, 141.0, 141.8; MS (EI): *m/z* (relative intensity) 182.0 (M^+, 72), 167.0 (100), 152.0 (30), 115.0 (21), 77.0 (15).

2,4,6-Trimethyl-1,1'-biphenyl (Table 6.4, entry 3-4)[48]



Eluents (Hexane, R_f= 0.55) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.07 (s, 6H), 2.40 (s, 3H), 7.01 (s, 2H), 7.20 (d, *J*= 7.8 Hz, 2H), 7.38 (t, *J*= 7.4 Hz, 1H), 7.47 (t, *J*= 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 21.0, 126.5, 128.0, 128.3, 129.3, 135.9, 136.5, 139.0, 141.1; MS (EI): *m/z* (relative intensity) 196.1 (M^+, 100), 165.0 (66), 141.0 (7), 115.0 (15), 89.0 (13).

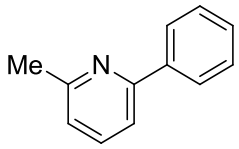
2-Methoxy-6-phenylpyridine (Table 6.5, entry 1)[49]



Eluents (Ethyl acetate: Hexane= 3: 7, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.09 (s, 3H), 6.74 (d, *J*= 8.0 Hz, 1H), 7.37 (d, *J*= 7.6 Hz, 1H), 7.44 (t, *J*= 7.2 Hz, 1H), 7.51 (t, *J*= 7.4 Hz, 2H), 7.64 (t,

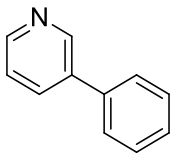
J= 7.8 Hz, 1H), 8.11 (d, *J*= 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.1, 109.2, 112.7, 126.6, 128.5, 128.8, 139.0, 139.1, 154.6, 163.7 ; MS (EI): *m/z* (relative intensity) 184.0 (M^+, 100), 154.0 (60), 127.0 (10), 102.0 (6), 77.0 (8).

2-Methyl-6-phenylpyridine (Table 6.5, entry 2)[40]



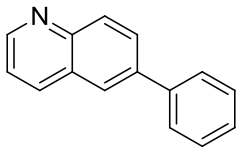
Eluents (Ethyl acetate: Hexane= 1: 4, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.65 (s, 3H), 7.08 (d, *J*= 7.6 Hz, 1H), 7.42 (t, *J*= 7.2 Hz, 1H), 7.47-7.52 (m, 3H), 7.61 (t, *J*= 7.6 Hz, 1H), 8.02 (d, *J*= 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.6, 117.5, 121.4, 126.9, 128.5, 128.6, 136.7, 139.6, 156.8, 158.2; MS (EI): *m/z* (relative intensity) 169.1 (M^+, 100), 154.0 (8), 127.0 (6), 115.0 (5), 77.0 (6).

3-Phenylpyridine (Table 6.5, entry 3)[40]



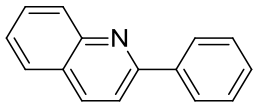
Eluents (Ethyl acetate: Hexane= 1: 2, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.35 (m, 1H), 7.37-7.41 (m, 1H), 7.46 (t, *J*= 7.4 Hz, 2H), 7.56 (d, *J*= 7.2 Hz, 2H), 7.85 (d, *J*= 7.6 Hz, 1H), 8.58 (d, *J*= 3.6 Hz, 1H), 8.85 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 123.4, 127.0, 128.0, 129.0, 134.2, 136.5, 137.7, 148.2, 148.3; MS (EI): *m/z* (relative intensity) 155.1 (M^+, 100), 127.0 (16), 102.0 (14), 76.0 (7), 51.0 (9).

6-Phenylquinoline (Table 6.5, entry 4)[50]



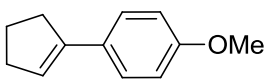
Eluents (Ethyl acetate: Hexane= 1: 4, R_f= 0.25) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.41 (m, 2H), 7.48 (t, *J*= 7.6 Hz, 2H), 7.69 (d, *J*= 7.6 Hz, 2H), 7.95-7.97 (m, 2H), 8.13-8.19 (m, 2H), 8.89-8.91 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 121.3, 125.3, 127.3, 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 intensity) 205.1 (M^+, 100), 176.0 (12), 151.0 (6), 102.1 (8), 76.0 (5).

2-Phenylquinoline (Table 6.5, entry 5)[51]



Eluents (Ethyl acetate: Hexane= 1: 2, R_f= 0.30) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.57 (m, 4H), 7.75 (t, *J*= 7.8 Hz, 1H), 7.81 (d, *J*= 8.0 Hz, 1H), 7.85 (d, *J*= 8.8 Hz, 1H), 7.17-8.24 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 118.9, 126.2, 127.1, 127.4, 127.5, 128.7, 129.2, 129.5, 129.6, 136.7, 139.5, 148.2, 157.2; MS (EI): *m/z* (relative intensity) 205.1 (M^+, 100), 176.0 (6), 151.0 (3), 102.1 (6), 75.0 (4).

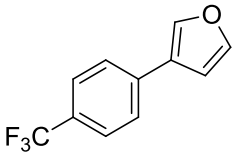
1-Cyclopentenyl-4-methoxybenzene (Table 6.5, entry 6)[36b]



Eluents (Hexane, R_f= 0.30) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.99-2.07 (m, 2H), 2.51-2.56 (m, 2H), 2.67-2.72 (m, 2H), 3.82 (s, 3H), 6.06-6.08 (m, 1H), 6.87 (d, *J*= 8.8 Hz, 2H), 7.40 (d, *J*= 8.8 Hz, 2H); ^{13}C NMR

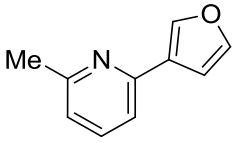
(100 MHz, $CDCl_3$) δ 23.4, 33.2, 33.3, 55.2, 113.6, 123.9, 126.7, 129.7, 141.8, 158.6 ; MS (EI): *m/z* (relative intensity) 174.1 (M^+, 100), 159.0 (37), 143.1 (54), 128.0 (35), 91.0 (20).

3-(4-(Trifluoromethyl)phenyl)furan (Table 6.6, entry 1)[52]



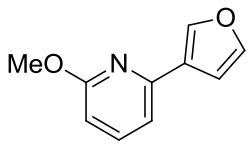
Eluents (Ethyl acetate: Hexane= 1: 20, R_f= 0.80) was used for flash column chromatography. ^1H NMR (400 MHz, $CDCl_3$) δ 6.73 (d, *J*= 0.8 Hz, 1H), 7.52 (dd, *J*=1.6 Hz, 1.6 Hz, 1H), 7.58 (d, *J*= 8.0 Hz, 2H), 7.63 (d, *J*= 8.4 Hz, 2H), 7.80 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.5; MS (EI): *m/z* (relative intensity) 212.0 (M^+, 100), 183.0 (40), 164.0 (15), 133.0 (29), 115.0 (76).

2-(Furan-3-yl)-6-methylpyridine (Table 6.6, entry 2)



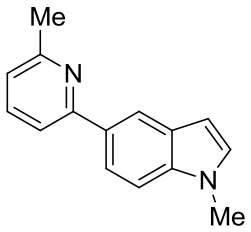
Eluents (Ethyl acetate: Hexane= 1: 9, R_f= 0.35) was used for flash column chromatography. ^1H NMR (400 MHz, $CDCl_3$) δ 2.56 (s, 3H), 6.88 (d, *J*= 1.2 Hz, 1H), 6.99 (d, *J*= 7.6 Hz, 1H), 7.24 (d, *J*= 7.6 Hz, 1H), 7.47 (dd, *J*= 1.8 Hz, 1.6 Hz, 1H), 7.54 (t, *J*= 7.6 Hz, 1H), 8.02 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.5, 108.7, 117.1, 121.2, 127.2, 136.7, 141.1, 143.6, 151.1, 158.4 ; MS (EI): *m/z* (relative intensity) 159.0 (M^+, 100), 130.0 (100), 118.0 (4), 103.0 (13), 77.0 (17); HRMS: calcd. for $C_{10}H_{10}NO^+$: 160.0757, found 160.0757.

2-(Furan-3-yl)-6-methoxypyridine (Table 6.6, entry 3)[53]



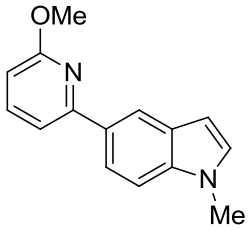
Eluents (Ethyl acetate: Hexane= 1: 9, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.98 (s, 3H), 6.61 (d, *J*= 8.4 Hz, 1H), 6.87 (d, *J*= 0.8 Hz, 1H), 7.03 (d, *J*= 7.2 Hz, 1H), 7.48 (dd, *J*= 1.6 Hz, 1.6 Hz, 1H), 7.54 (t, *J*= 8.0 Hz, 1H), 8.03 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.1. 108.5, 108.6, 112.4, 127.0, 138.9, 141.2, 143.6, 149.2, 163.7; MS (EI): *m/z* (relative intensity) 175.0 (M^+, 100), 146.0 (32), 117.0 (49), 90.0 (26), 77.0 (10).

1-Methyl-5-(6-methylpyridin-2-yl)-1H-indole (Table 6.6, entry 4)



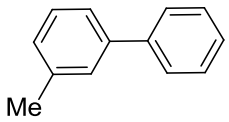
Eluents (Ethyl acetate: Hexane= 1: 9, R_f= 0.45) was used for flash column chromatography. Yellow solid; m.p.= 129.9-132.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.65 (s, 3H), 3.82 (s, 3H), 6.57 (d, *J*= 2.8 Hz, 1H), 7.03-7.08 (m, 2H), 7.39 (d, *J*= 8.8 Hz, 1H), 7.56-7.63 (m, 2H), 7.91 (d, *J*= 8.8 Hz, 1H), 8.27 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.8, 32.9, 101.8, 109.3, 117.4, 119.7, 120.5, 121.0, 128.8, 129.4, 131.4, 136.7, 137.2, 158.0, 158.3; MS (EI): *m/z* (relative intensity) 222.1 (M^+, 100), 206.1 (6), 180.1 (5), 155.0 (5), 111.0 (3); HRMS: calcd. for $C_{15}H_{15}N_2^+$: 223.1230, found 223.1231.

5-(6-Methoxypyridin-2-yl)-1-methyl-1H-indole (Table 6.6, entry 5)



Eluents (Ethyl acetate: Hexane= 1: 9, R_f= 0.30) was used for flash column chromatography. Yellow solid; m.p.= 117.3-120.8; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.83 (s, 3H), 4.09 (s, 3H), 6.58 (d, *J*= 2.8 Hz, 1H), 6.64 (d, *J*= 8.0 Hz, 1H), 7.08 (d, *J*= 2.8 Hz, 1H), 7.37-7.41 (m, 2H), 7.62 (t, *J*= 8.0 Hz, 1H), 7.98 (d, *J*= 8.8 Hz, 1H); 8.35 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.9, 53.2, 101.8, 107.7, 109.2, 112.4, 119.5, 120.8, 128.8, 129.5, 130.7, 139.0, 163.6; MS (EI): *m/z* (relative intensity) 238.1 (M^+, 100), 207.1 (31), 192.0 (11), 155.0 (8), 103.1 (6); HRMS: calcd. for $C_{15}H_{15}N_2O^+$: 239.1179, found 239.1181.

3-Methyl-1,1'-biphenyl (Scheme 6.3)[39]



Eluents (Hexane, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.68 (s, 3H), 7.43 (d, *J*= 7.6 Hz, 1H), 7.59 (t, *J*= 7.6 Hz, 2H), 7.67–7.70 (m, 4H), 7.87 (d, *J*= 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 124.2, 127.1, 127.8, 127.9, 128.4, 128.60, 128.62, 138.2, 141.2, 141.3; MS (EI): *m/z* (relative intensity) 168.1 (M^+, 100), 152.0 (26), 115.0 (10), 82.8 (5), 63.0 (5).

6.5 References

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Chapter 7 Palladium-Catalyzed Borylation of Aryl Chlorides with Pinacol Borane

7.1 Introduction

Arylboronic acids, boronate esters, and potassium trifluoroborate salts are commonly used organoboron intermediates in metal-catalyzed cross-coupling reactions. Suzuki-Miyaura cross-coupling reaction is one of the most significant methodologies ultizing organoboron nucleophiles for the synthesis of biaryl compounds which are important structural motifs in biological active molecules and pharmaceutical compounds.[1] Although arylboronic acids, boronate esters and potassium trifluoroborate salts are highly stable and non-toxic, their syntheses sometimes are challenging. The traditional method for preparing arylboronic acids and boronate esters is via the halogen-metal exchange (e.g. Mg or Li) of aryl bromides or iodides and subsequent trapping with trialkylborates. However, this synthetic route is incompatible with base-sensitive functional groups (e.g. aldehyde, ketone, nitrile, etc.)[1d] Therefore, additional protection and deprotection steps are usually required for this synthetic method. Moreover, this protocol is incompatible with relatively inexpensive and broadly available aryl chlorides. Hence, to solve the limitations of the conventional method for preparing arylboronic reagents, transition metal-catalyzed borylation of aryl halides and sulfonates with alkoxyboranes has been developed.[2] Another approach for constructing $C_{(sp2)}$-B bonds involves Re, Ru, Rh and especially Ir-catalyzed direct C-H borylation of arenes.[3] However, it is difficult to control the regioselectivity. In 1995, Miyaura pioneered a palladium-catalyzed borylation of aryl halides with bis(pinacolato)diborane.[4] Since then, a number of palladium-catalyzed borylation has emerged for converting aryl halides and sulfonates to corresponding arylboronate esters. Nickel-catalyzed borylations being other

protocols for generating arylboronic sources have been reported by Perce and co-workers.[5] Although recent notable findings showed great achievements in palladium-catalyzed borylation of aryl halides and sulfonates with tetraalkoxydiboranes, limited palladium catalyst system are effective for borylation of relatively inexpensive and commercially available aryl chlorides with dialkoxyboranes. Dialkoxyboranes such as pinacolborane are more attractive because of relatively low cost, commercial availability and high atom economy.

In 1997, Masuda and coworkers reported palladium-catalyzed borylation of aryl iodides and bromides with dialkoxyhydroborane.[6] Since then, there are great advancements in developing palladium catalyst system for converting aryl iodides, bromides and triflates to corresponding arylboranate esters.[7] Until to 2006, Masuda and coworkers demonstrated that the combination of $Pd(dba)_2$ and *t*-Bu-DPEphos was efficient for coupling of pinacolborane with aryl bromides and chlorides.[8] However, 5 mol% Pd catalyst loading was required and only two examples of aryl chlorides were demonstrated successfully. In 2008, Buchwald and coworkers developed the first general catalyst system consisting of $PdCl_2(CH_3CN)_2$ and Sphos that converting aryl and heteroaryl chlorides with pinacolborane to corresponding boronate esters successfully.[9] Nevertheless, 3 mol% Pd catalyst loading was required and the substrate scope was limited. Aryl chlorides bearing electron-withdrawing groups were incompatible in that reaction condition. To solve the issue of substrate scope, Masuda and coworkers reported the borylation of electron-deficient aryl chlorides with pinacolborane in the presence of NBu_4I as an additive using $Pd(dba)_2$ and *t*-Bu-DPEphos as a catalyst system.[10] Although the aryl chlorides bearing electron-deficient groups were effective substrates under that reaction condition, 5 mol% Pd catalyst loading was required and only activated aryl chlorides were feasible cross-coupling partners. In 2011, Watanabe and coworkers reported the

palladium-catalyzed borylation of arylsulfonates with pinacolborane utilizing $Pd(dba)_2$ and d-*t*-bpf as a catalyst system.[11] Aryl sulfonates are the most versatile complementary substrates to aryl halides for various coupling reactions. However, additional protection step of substituted phenols is required. The atom economy is lower compared with that of aryl chlorides. Besides, 5 mol% Pd catalyst loading was required and only activated aryl sulfonates were converted to corresponding arylboronate esters successfully.

To the best of our knowledge, a general protocol for borylation of both non-activated and activated aryl chlorides with pinacolborane under low catalyst loading has been sporadically reported to date. As a result, developing an effective catalyst system for converting a broad range of aryl chlorides to corresponding arylboronate esters using pinacolborane is worthwhile.

Our group has developed two series of C-P type indolylphosphine ligands previously. One is the phosphine group attached to the bottom ring (**CM-phos**). Another one is the phosphine group incorporated into C-3 position of the indole ring. They are good matching partners with palladium precursors that compose effective catalyst systems for serval cross-coupling reactions (Scheme 7.1, **L1**, **L11**, **L16** and **L2**).[12] They are prepared by simple and straightforward Fischer indolization, bromination (for the indolylphospine ligands in which the phosphine group attached to C-3 position of the indole ring) and phosphination. Apart from simple and straightforward ligand preparation, the starting materials are inexpensive and readily available. The indolylphosphine ligands are purified easily by single crystallization after phosphination. This type of ligands exhibits high air and moisture stability in both solid and solution states. Particular noteworthy is that the ligand diversity is easily accessed by changing different substituents in different positions of indolyl scaffold for providing a high level of steric and electronic fine-tuning (Figure 7.1 and

7.2). With our previous experiences in dealing with indolylphosphine ligands, we plan to apply well developed Fischer Indolization as our protocol for a new ligand synthesis. With respect to the indolyl scaffold in which the phosphine group attached to the bottom ring, different substituents of the bottom ring are changed, the alkyl groups at the *N*-position of indolyl scaffold are altered and a variety of substituents attached to the indolyl ring are adjusted for providing additional steric and electronic effects (Scheme 7.1, **L2**-**L9**). In regard to the indolyl scaffold in which the phosphine group attached to C-3 position of the indole ring, the bottom ring of indolyl scaffold is fine-tuned by using different substituted acetophenones and the alkyl groups at the *N*-position of indolyl scaffold are expanded for offering potential of steric and electronic properties fine tuning (Scheme 7.1, **L10**, **L12-L15**, **L17-L20** and **L22-L24**).

In continuing our research interests in development of indolylphosphine ligands[12h, 12i, 13] and palladium-catalyzed borylation of aryl sulfonates and chlorides with bis(pinacolato)boron,[12j,14] herein, we report our effort in developing general catalyst system for coupling aryl chlorides with pinacolborane at 1.0 mol% Pd catalyst loading.

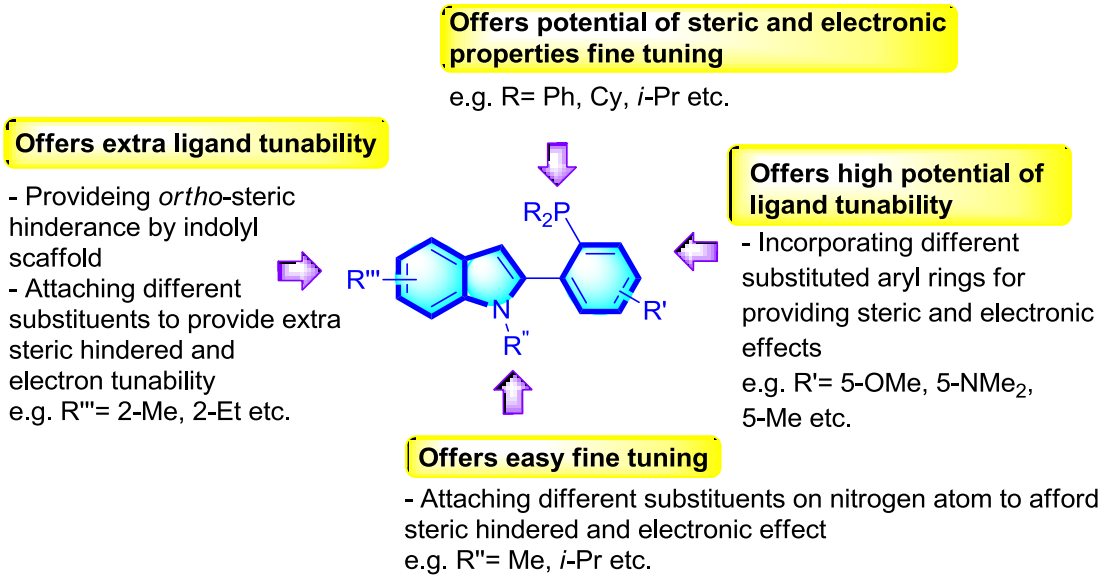


Figure 7.1 Proposed ligand design with high potential of tunability for indolylphosphine ligands in which the phosphine group attached to the bottom ring

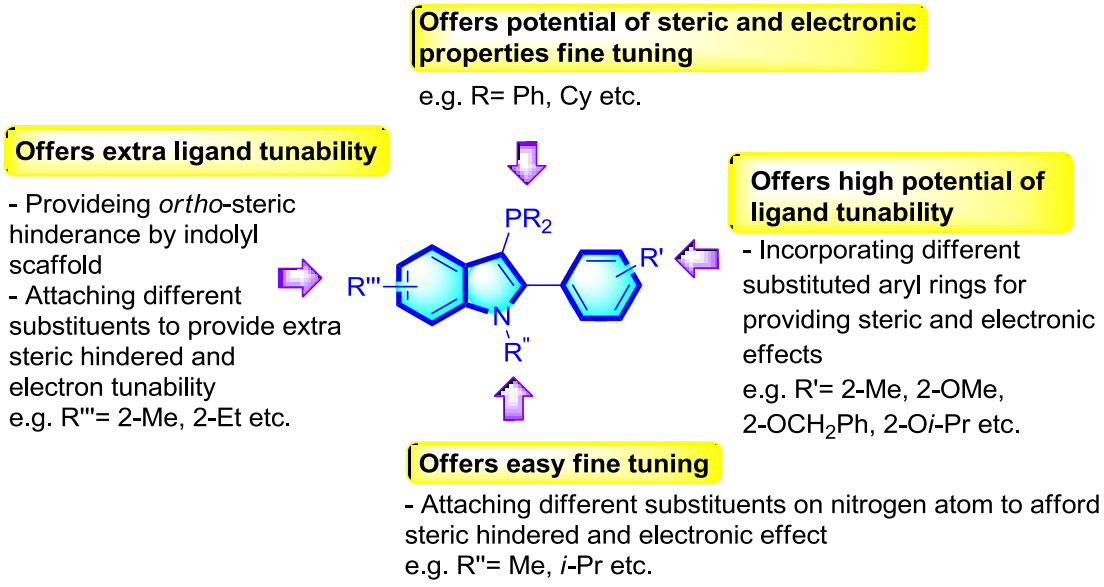
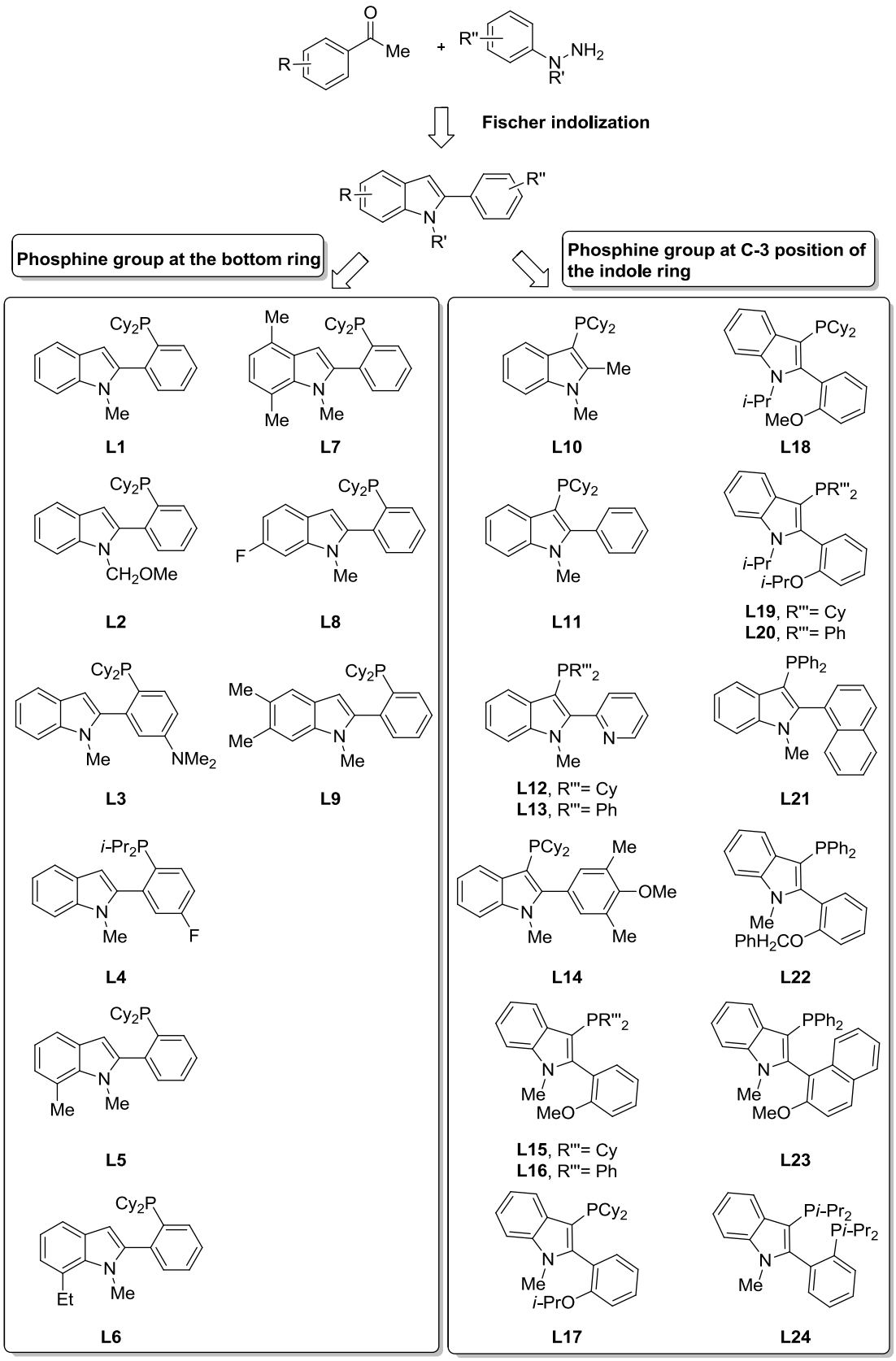


Figure 7.2 Proposed ligand design with high potential of tunability for indolylphosphine ligands in which the phosphine group attached to C-3 position of the indole ring



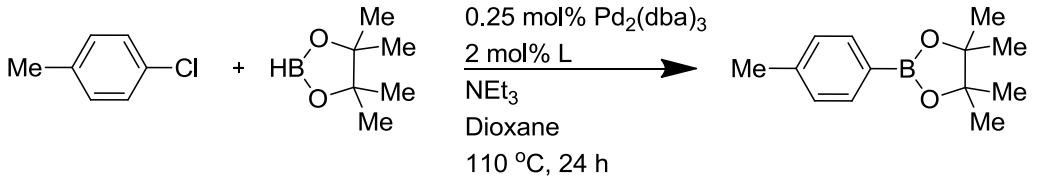
Scheme 7.1 Exploration of two series of indolylphosphine ligands in which the phosphine group attached to the bottom ring and at C-3 position of the indole ring

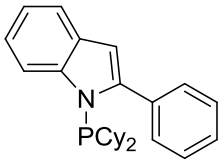
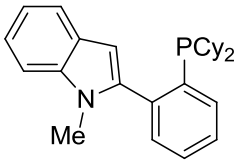
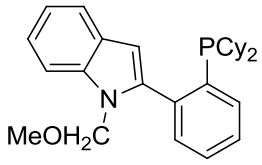
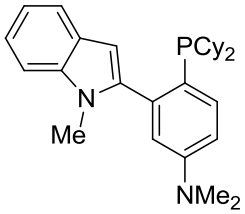
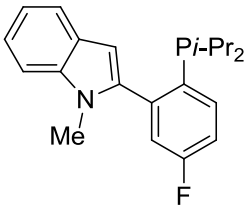
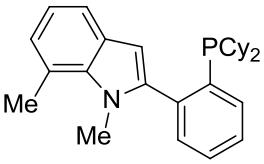
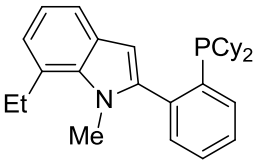
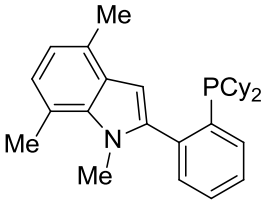
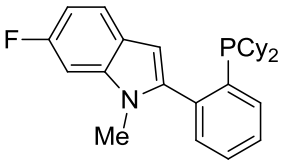
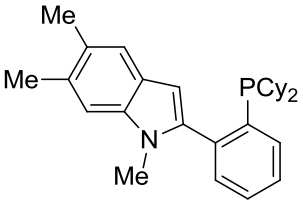
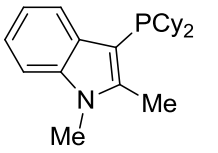
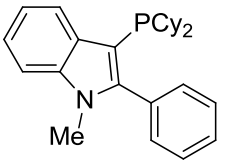
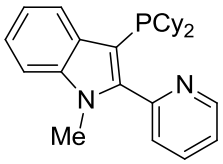
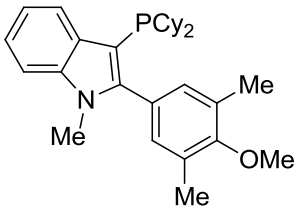
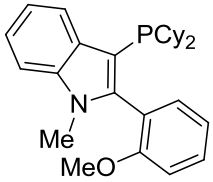
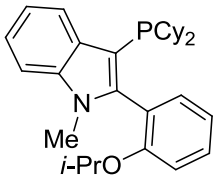
7.2 Results and discussion

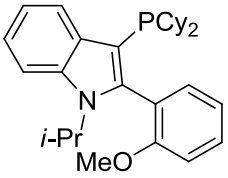
7.2.1 Preliminary evaluation of palladium-catalyzed borylation of aryl chlorides with pinacol borane

In order to investigate the feasibility of palladium-catalyzed borylation of aryl chlorides with pinacol borane, a series of screening experiments was carried out. 4-chlorotoluene and pinacolborane were used as benchmark substrates. Commercially available and well recognized ligands and our group developed indolylphosphine ligands were examined (Table 7.1). *N*-phosphine substituted ligand **L1** showed no product conversion. A variety of the indolylphosphine ligands based on CM-phos ligand scaffold was investigated and afforded poor to moderate product yields (Table 7.1, **L2**-**L10**). C3-phosphine-substituted indolylphosphine ligands were then examined (Table 7.1, **L11**-**L27**). **L18** was the best choice of the indolylphosphine ligands. Changing the substituents of the bottom ring and the *N*-position of C3-indolyl scaffold simultaneously enhanced the catalytic efficiency of the reaction. Disappointingly, ligand **L19**-**L26** with a diphenylphosphine moiety exhibited no product conversion. Buchwald-type ligands **L28-L30** and Beller-type ligands **L31-L33** showed poor to good catalytic performance. As a result, the catalyst system comprising of Pd_2dba_3 and **L18** was chosen for further optimization of the reaction conditions.

Table 7.1 Investigation of ligand effect on palladium-catalyzed borylation of 4-chlorotoluene with pinacol borane[a,b]



			
L1 2%	**L2** 62% (1 mol% Pd)[c]	**L3** 7% (1 mol% Pd)[c]	**L4** 29% (1 mol% Pd)[c]
			
L5 56% (1 mol% Pd)[c]	**L6** 45% (1 mol% Pd)[c]	**L7** 53% (1 mol% Pd)[c]	**L8** 44% (1 mol% Pd)[c]
			
L9 34% (1 mol% Pd)[c]	**L10** 51% (1 mol% Pd)[c]	**L11** trace (1 mol% Pd)[c]	**L12** 9%
			
L13 trace (1 mol% Pd)[c]	**L14** 24% (1 mol% Pd)[c]	**L15** 31%	**L16** 34%



L17
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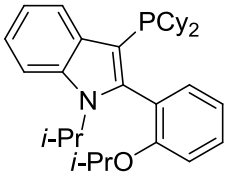

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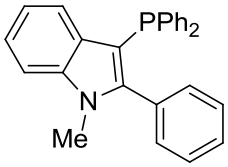

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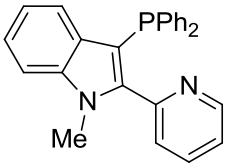

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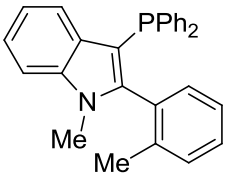

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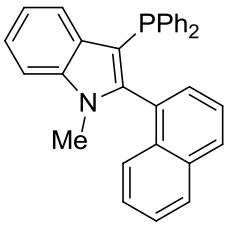

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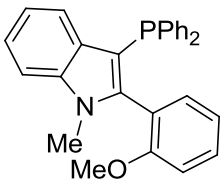

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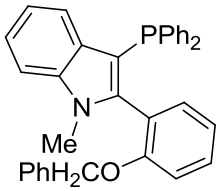

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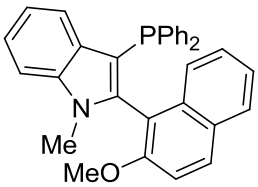

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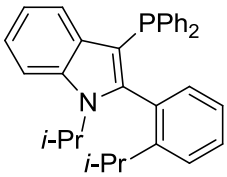

L26
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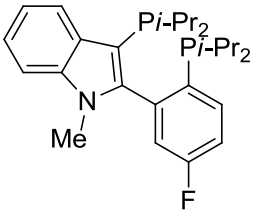

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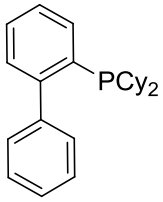

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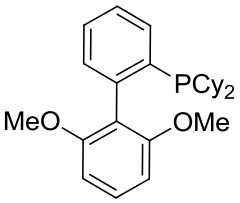
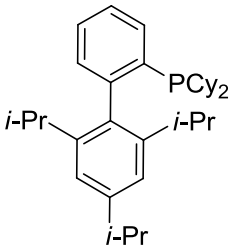
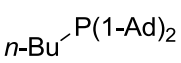


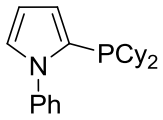
L29
62%
65% (1 mol% Pd)[c]



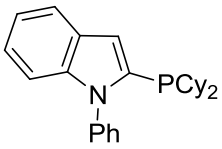
L30
60%
78% (1 miol% Pd)[c]



L31
3%



L32
23%

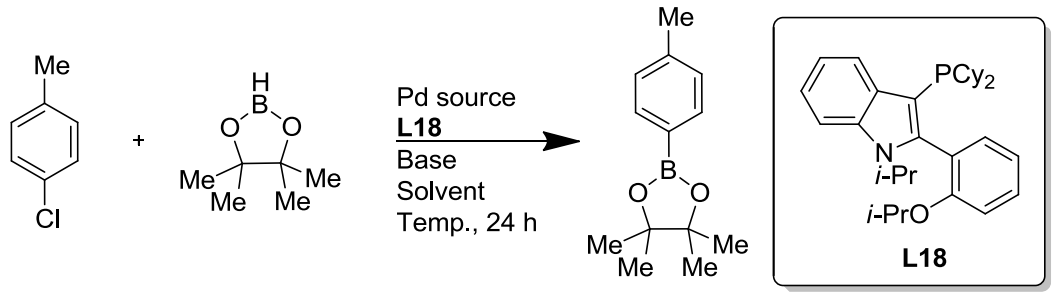


L33
32%

[a] Reaction condition: 4-chlorotoluene (1.0 mmol), HBpin (1.5 mmol), $Pd_2(dba)_3$ (0.25 mol%), L (2.0 mol%), NEt_3 (3.0 mmol) and dioxane (3.0 mL) were stirred at 110 ^oC for 24 h. [b] FID-Calibrated yield using dodecane as internal standard [c] Reaction condition: 4-chlorotoluene (0.5 mmol), HBpin (0.75 mmol), $Pd_2(dba)_3$ (0.5 mol%), L (4.0 mol%), NEt_3 (1.5 mmol) and dioxane (1.5 mL) were stirred at 110 ^oC for 24 h.

A variety of palladium sources, bases and solvents were examined and the results were summarized in Table 7.2. Upon surveying the palladium sources (Table 7.2, entries 1, 3-6 and 8), $Pd(dba)_2$ (Table 7.2, entry 3) gave the best result with the product yield of 88% while $Pd_2(dba)_3$, $PdCl_2(CH_3CN)_2$ and $Pd(TFA)_2$ (Table 7.2, entries 1, 6 and 8) also provided compatible yields. Commonly used solvents were examined (Table 7.2, entries 1 and 9-15). Dioxane was the best choice of solvents (Table 7.2, entry 1). An inferior result was obtained when NEt_3 was chosen as solvent (Table 7.2, entry 15). Other organic and inorganic bases were investigated (Table 7.2, entries 1 and 16-19). NEt_3 was found to be a superior base (Table 7.1, entry 1). NE*t*-Pr_2 afforded poorer result due to the steric bulkiness causing the difficulty in coordination of Pd precursor when compared with NEt_3 (Table 7.1, entry 19). Reaction temperatures (90-120 ℃) have been studied (Table 7.2, entry1 and 20-23). The product yields increased from 35% to 84% when the temperature was raised from 90 ^oC to 110 ^oC. The slightly decreased yield was obtained when the reaction temperature was further increased to 120 ^oC (Table 7.2, entry 23). The temperature of 110℃ gave the best yield and thus was chosen as a reaction temperature for further investigation (Table 7.2, entry 1).

Table 7.2 Investigation of reaction parameters on palladium-catalyzed borylation of 4-chlorotoluene with pinacol borane[a]



Entry	Pd source	Temp. (^oC)	Base	Solvent	Pd Loading (mol%), Time (h)	Yield (%)[b]
1	$Pd_2(dba)_3$	110	NEt_3	Dioxane	1 (24)	85
2	$Pd_2(dba)_3$	110	NEt_3	Dioxane	0.5 (24)	64
3	$Pd(dba)_2$	110	NEt_3	Dioxane	1 (24)	88
4	$Pd(OAc)_2$	110	NEt_3	Dioxane	1 (24)	70
5	$PdCl_2$	110	NEt_3	Dioxane	1 (24)	15
6	$PdCl_2(CH_3CN)_2$	110	NEt_3	Dioxane	1 (24)	85
7	$PdCl_2(CH_3CN)_2$	110	NEt_3	NEt_3	1 (24)	43
8	$Pd(TFA)_2$	110	NEt_3	Dioxane	1 (24)	82
9	$Pd_2(dba)_3$	110	NEt_3	CH_3CN	1 (24)	30
10	$Pd_2(dba)_3$	110	NEt_3	Toluene	1 (24)	80
11	$Pd_2(dba)_3$	110	NEt_3	DMF	1 (24)	trace
12	$Pd_2(dba)_3$	110	NEt_3	*t*-BuOH	1 (24)	0
13	$Pd_2(dba)_3$	110	NEt_3	H_2O	1 (24)	0
14	$Pd_2(dba)_3$	110	NEt_3	THF	1 (24)	42
15	$Pd_2(dba)_3$	110	NEt_3	NEt_3	1 (24)	38
16	$Pd_2(dba)_3$	110	DMAP	Dioxane	1 (24)	0

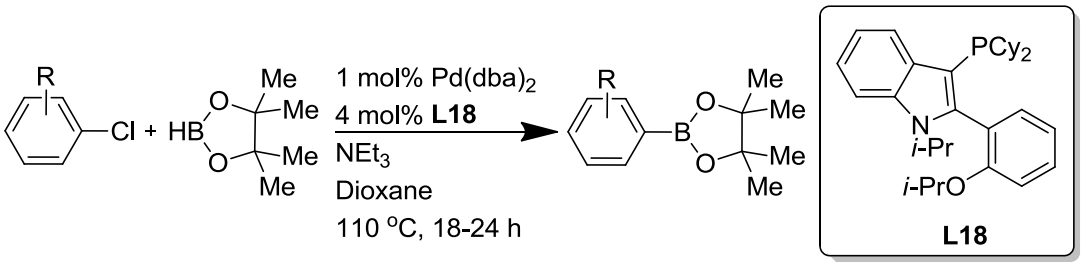
17	$Pd_2(dba)_3$	110	DBU	Dioxane	1 (24)	0
18	$Pd_2(dba)_3$	110	KOAc	Dioxane	1 (24)	0
19	$Pd_2(dba)_3$	110	NE*t*-Pr_2	Dioxane	1 (24)	73
20	$Pd_2(dba)_3$	90	NEt_3	Dioxane	1 (24)	35
21	$Pd_2(dba)_3$	90	NEt_3	Dioxane	2 (24)	50
22	$Pd_2(dba)_3$	100	NEt_3	Dioxane	1 (24)	45
23	$Pd_2(dba)_3$	120	NEt_3	Dioxane	1(24)	78

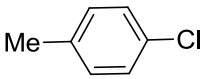
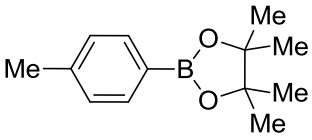
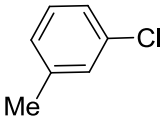
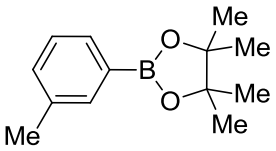
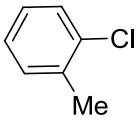
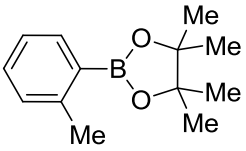
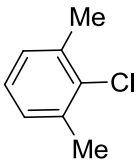
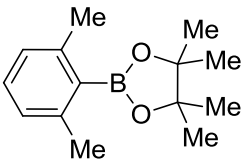
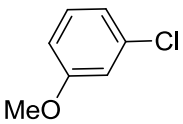
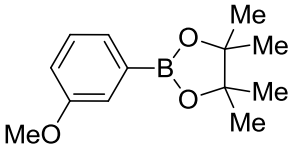
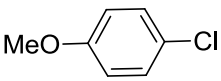
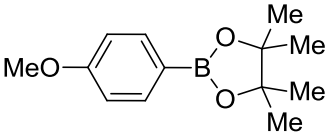
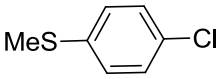
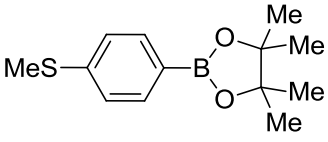
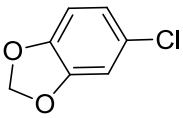
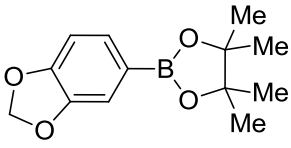
[a] Reaction condition: 4-chlorotoluene (0.5 mmol), HBpin (0.75 mmol), Pd source (1.0 mol%), L18 (4.0 mol%), base (1.5 mmol) and solvent (1.5 mL) stirred at indicated temperature for 24 h. [b] FID-Calibrated yield using dodecane as internal standard.

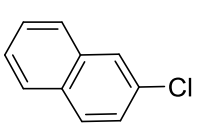
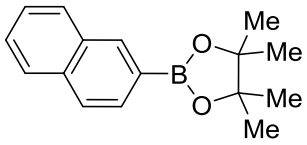
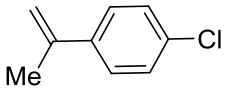
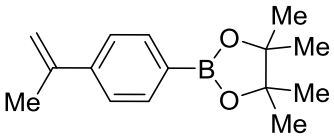
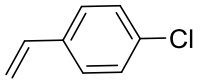
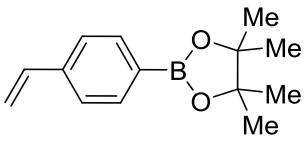
7.2.2 Scope of palladium-catalyzed borylation of aryl chlorides with pinacol borane

With the optimized reaction conditions in hand, we next examined the scope of this reaction. A wide range of non-activated aryl chlorides was investigated under this optimized reaction condition and the results are listed in Table 7.3. The aryl chloride containing *ortho*-methyl group was found to be feasible cross-coupling partner and furnished good product yield (Table 7.3, entry 3). Electron-rich 4-chloroanisole was coupled with pincolborane to corresponding product in excellent yield. The alkenyl groups attached on aryl chlorides were remained intact in this optimized reaction condition and afforded moderate to good product yields (Table 7.3, entry 10 and 11).

Table 7.3 Palladium-catalyzed borylation of non-activated aryl chlorides with pinacol borane[a]



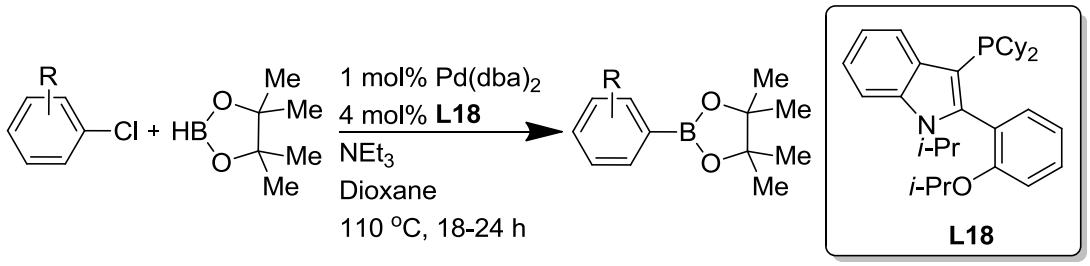
Entry	ArCl	Product	Pd (mol%)	Time (h)	Yield (%)[b]
1			1	24	82
2			1	24	81
3			1	24	64
4			1	24	11
5			1	24	71
6			1	24	92
7			1	24	60
8			1	24	70

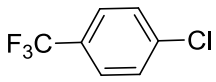
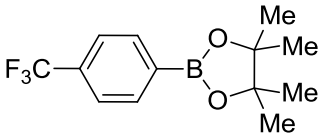
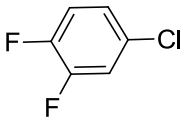
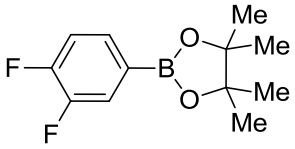
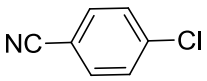
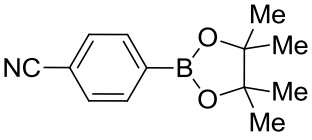
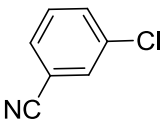
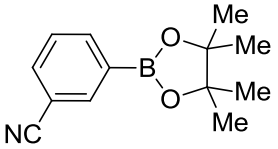
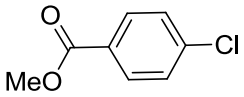
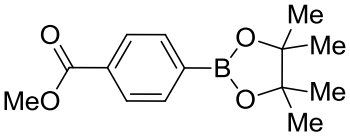
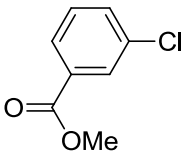
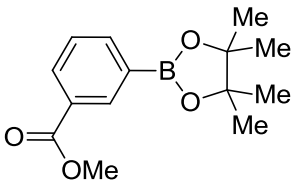
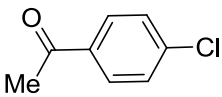
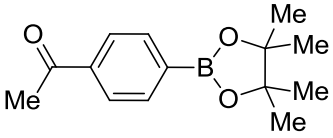
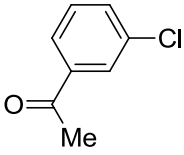
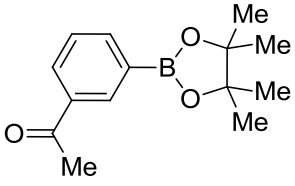
9			1	24	64
10			1	24	60
11			1	24	50

[a] Reaction condition: ArCl (0.5 mmol), HBpin (0.75 mmol), $Pd(dba)_2$ (1.0 mol%), L18 (4 mol%), NEt_3 (1.5 mmol) and dioxane (1.5 mL) stirred at 110 ^oC for 24 h. [b] Isolated yields.

Apart from non-activated aryl chlorides, activated aryl chlorides also were applicable substrates in this $Pd(dba)_2$ and **L18** catalytic system (Table 7.4). Addition of tetrabutylammonium iodide (TBAI) was found to be afforded better product yields for borylation of activated aryl chlorides with pinacol borane (Table 7.4, entry 1 and 2). Common functional groups such as -CN, -COOMe and -COMe were compatible under this mild reaction condition (Table 7.4, entries 4-11). Good to excellent product yields were obtained.

Table 7.4 Palladium-catalyzed borylation of activated aryl chlorides with pinacol borane[a]



Entry	ArCl	Product	Pd (mol%)	Time (h)	Yield (%)[b]
1			1	24	trace
2			1	18	60[c]
3			1	18	50[c]
4			1	24	trace
5			1	18	70[c]
6			1	18	80[c]
7			1	18	74[c]
8			1	19	80[c]
9			1	24	trace
10			1	18	66[c]
11			1	18	77[c]

[a] Reaction condition: ArCl (0.5 mmol), HBpin (0.75 mmol), $Pd(dba)_2$ (1.0 mol%), L18 (4 mol%), NEt_3 (1.5 mmol) and dioxane (1.5 mL) stirred at 110 ^oC for 18-24 h. [b] Isolated yields. [c] TBAI (0.75 mmol) was added.

7.3 Conclusion

In conclusion, new ligand design based on our group previously developed C3-indolyl scaffold (**L18**) was synthesized. The palladium catalyst system comprising of $Pd(dba)_2$ and novel indolyphosphine ligand (**L18**) was found to be effective for borylation of aryl chlorides with cheaper and more atom economical pinacol borane. A wide range of non-activated and activated aryl chlorides can be converted to corresponding arylboronate esters under this optimized reaction condition. Notably, it is the first general report of borylation of both electron-rich and –deficient aryl chlorides using pinacol borane as the boron source. The catalyst loading can be down to 1 mol% Pd that is the lowest compared with the previous reports.

7.4 Experimental section

7.4.1 General considerations

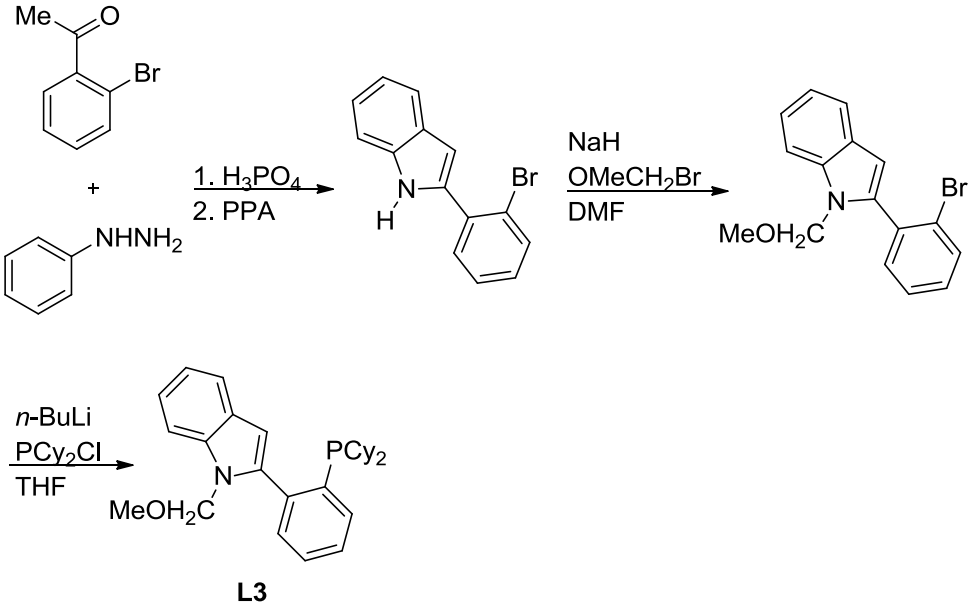
Unless otherwise noted, all reagents were purchased from commercial suppliers and used without purification. All borylation reactions were performed in Rotaflo® (England) resealable screw cap Schlenk flask (approx. 20 mL volume) in the presence of Teflon coated magnetic stirrer bar (4 mm × 10 mm). Toluene, tetrahydrofuran (THF) and dioxane were distilled from sodium and sodium benzophenone ketyl under nitrogen,[15] respectively. *tert*-Butanol was distilled from sodium under nitrogen and stored with calcium hydride. Triethylamine and acetonitrile were distillated from

calcium hydride under nitrogen. Water was distillated under nitrogen. Anhydrous *N*, *N*-dimethylformamide (DMF) in Sure/Seal bottles were purchased from Aldrich and used directly. The indolylphosphine ligands **L1**-**L2**, **L12, L15-L19**, **L21**-**L23** and **L26** were synthesized by the reported procedures.[12h, 12i, 13a, 13b,16] Ligands **L28**-**L33** were purchased from commercial suppliers. Commercially available aryl chlorides (liquid form only) were purified by passed through a short plug (0.5 cm width × 4 cm height) of neutral alumina or distillation. New bottle of *n*-butyllithium was used (Note: since the concentration of *n*-BuLi from old bottle may vary, we recommend performing a titration prior to use). 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. NMR spectra were recorded on a Brüker spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C, 376 MHz for ^{19}F and 162 MHz for ^{31}P). 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). ^{19}F NMR chemical shifts were determined relative to $CFCl_3$ as the external standard and low field is positive. ^{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. 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, ^{13}C, ^{19}F and/or ^{31}P 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.

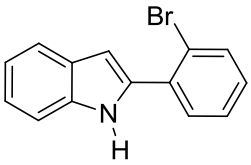
7.4.2 Preparation of indolylphosphine ligands L3-L11, L13-L14, L20, L24-L25 and L27

7.4.2.1 Preparation of indolylphosphine ligand **L3**



L3

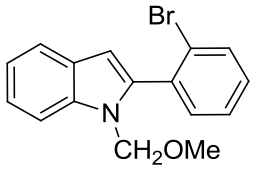
2-(2-Bromophenyl)-1*H*-indole



A general procedure for Fischer-indole synthesis of 2-(2-bromophenyl)-1*H*-indole was used according to the previous report.[13b] 2'-Bromoacetophenone (20 mmol), phenylhydrazine (24 mmol), H_3PO_4 (10 mL) and PPA (60 g) were given the desired product as an off-white powder (3.3 g, 61%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86 (s, 1H), 7.17-7.23 (m, 1H), 7.25-7.30 (m, 2H), 7.40-7.47 (m, 2H), 7.63-7.66 (m, 1H), 7.70-7.74 (m, 2H), 8.66 (s, 1H); ^{13}C NMR (100

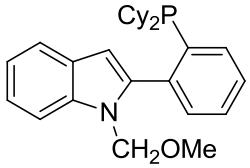
MHz, $CDCl_3$) δ 103.6, 110.9, 120.1, 120.8, 121.3, 122.6, 127.7, 128.1, 129.2, 131.4, 133.4, 133.9, 136.2; MS (EI): *m/z* (relative intensity) 271 (M^+, 100), 191 (19), 165 (49), 95 (13).

2-(2-Bromophenyl)-1-(methoxymethyl)-1*H*-indole



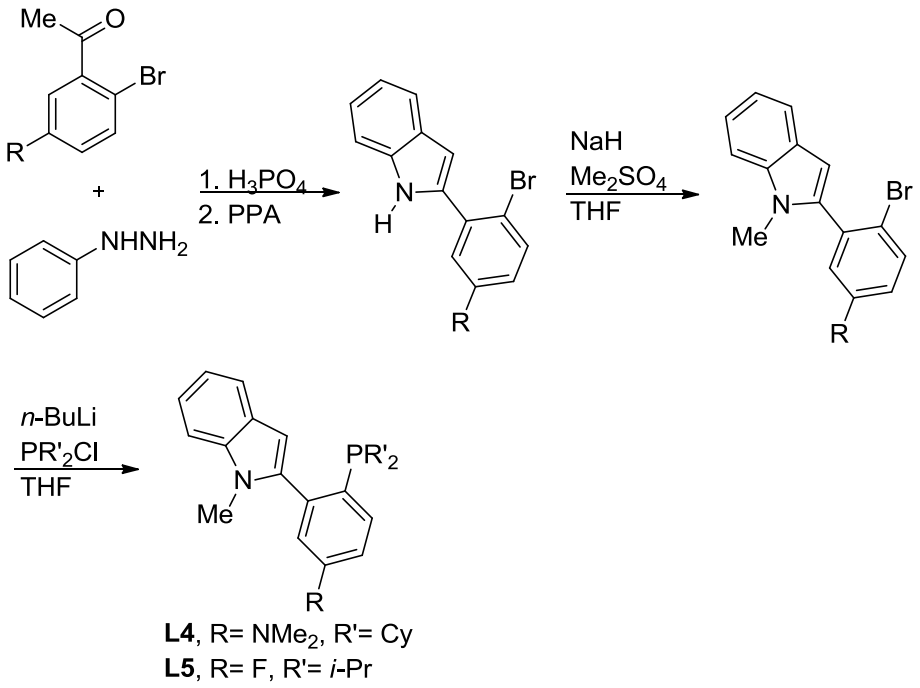
2-(2-bromophenyl)-1*H*-indole (5.0 mmol) was dissolved in 15 mL anhydrous DMF in dropping funnel and added dropwise to the 10 mL anhydrous DMF solution contained NaH (15 mmol, 60% in mineral oil) at room temperature under nitrogen atmosphere. NaH was washed with hexane (10 mL x3) under N_2. The mixture was stirred for 30 min at room temperature. $BrCH_2OMe$ (6.0 mmol) was then added to the mixture dropwise. After the mixture was stirred at room temperature for overnight, EtOAc and water was added to the mixture and the organic phase was separated. The organic phase was washed with large amount of water and was then concentrated. The concentrated mixture was purified by column chromatography on silica gel (25 × 3 cm) and eluted with EtOAc/hexane (1:9). The solution was evaporated in vacuum to give the desired product as a pale yellow liquid (0.79 g, 50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.10 (s, 3H), 5.36 (s, 2H), 6.59 (s, 1H), 7.23 (t, *J*= 8.0 Hz, 1H), 7.28-7.37 (m, 2H), 7.44 (t, *J*= 8.0 Hz, 1H), 7.51 (d, *J*= 8.0 Hz, 1H), 7.59 (d, *J*= 8.0 Hz, 1H), 7.70 (d, *J*= 8.0 Hz, 1H), 7.74 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.7, 74.9, 104.3, 110.5, 120.6, 120.8, 122.4, 125.1, 127.2, 128.1, 130.2, 132.9, 133.1, 133.7, 136.9, 139.2; MS (EI): *m/z* (relative intensity) 315 (M^+, 100), 286 (41), 205 (69), 190 (32); HRMS: calcd. for $C_{16}H_{14}NOBrH^+$: 316.0332, found 316.0330.

2-(2-(Dicyclohexylphosphino)phenyl)-1-(methoxymethyl)-1*H*-indole L3

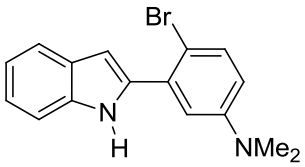


2-(2-Bromophenyl)-1-(methoxymethyl)-1*H*-indole (2.93 mmol) was dissolved in freshly distilled THF (20 mL) at room temperature under nitrogen atmosphere. The solution was cooled to -78 ^{o}C in dry ice/acetone bath. Titrated *n*-BuLi (3.3 mmol) was added dropwise by syringe. After the reaction mixture was stirred for 30 min at 78 ^{o}C, chlorodicyclohexylphosphine (3.3 mmol) in THF (5 mL) was added. The reaction was allowed to warm to room temperature and stirred overnight. Solvent was removed under reduced pressure. After the solvent was removed under vacuum, the product was successively washing with cold MeOH. The product was then dried under vacuum. 2-(2-(Dicyclohexylphosphino)phenyl)-1-(methoxymethyl)-1*H*-indole was obtained as an off-white solid (0.58 g, 50%). ^{1}H NMR (400 MHz, C_6D_6) δ 0.95-1.25 (m, 10H), 1.56-1.73 (m, 12H), 2.81 (s, 3H), 5.35 (bs, 1H), 6.62 (s, 1H), 7.10-7.14 (m, 1H), 7.17-7.29 (m, 3H), 7.43-7.46 (m, 2H), 7.60 (d, *J*= 8.0 Hz, 1H), 7.70 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 26.4, 27.2, 30.3, 55.0, 75.2, 75.3, 105.5, 110.8, 120.46, 120.55, 122.1, 127.8, 128.1, 128.5, 132.28, 132.31, 132.59, 132.65, 137.0, 137.6, 140.6, 140.88, 140.94; ^{31}P NMR (162 MHz, C_6D_6) δ -10.37; MS (EI): *m/z* (relative intensity) 433 (M^+, 55), 418 (24), 368 (100), 350 (85), 236 (67); HRMS: calcd. for $C_{28}H_{36}NOPH^+$: 434.2613, found 434.2633.

7.4.2.2 Preparation of indolylphosphine ligand **L4**-**L5**



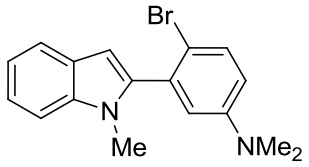
4-Bromo-3-(1*H*-indol-2-yl)-*N*,*N*-dimethylaniline



A general procedure for Fischer-indole synthesis of 4-bromo-3-(1*H*-indol-2-yl)-*N*,*N*-dimethylaniline was used according to the previous report with a slight modification.[13b] 1-(2-Bromo-5-(dimethylamino)phenyl)ethanone (5.7 mmol), phenylhydrazine (6.84 mmol), H_3PO_4 (2.0 mL) and PPA (20 g) were given the reaction mixture. The mixture was poured into crashed ice cube and then neutralized with 2 M NaOH and extracted with CH_2Cl_2. The combined organic extracts were dried over anhydrous Na_2SO_4 and then concentrated under reduced pressure. The crude product was purified according to the previous report[13b] to give the desired product as a light yellow powder (1.04 g, 58%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.03 (s, 6H), 6.67 (d, *J*= 8.0 Hz, 1H). 6.90 (s, 1H), 6.98 (s, 1H), 7.24-7.35

(m, 2H), 7.48 (d, *J*= 8.0 Hz, 1H), 7.56 (d, *J*= 8.0 Hz, 1H), 7.78 (d, *J*= 8.0 Hz, 1H), 8.68 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.4, 102.9, 107.4, 110.9, 113.6, 114.9, 119.9, 120.5, 122.2, 128.1, 133.4, 133.9, 135.9, 137.2, 149.6; MS (EI): *m/z* (relative intensity) 314 (M^+, 100), 235 (36), 220 (32), 207 (28), 191 (28); HRMS: calcd. for $C_{16}H_{15}N_2BrH^+$: 315.0497, found 315.0495.

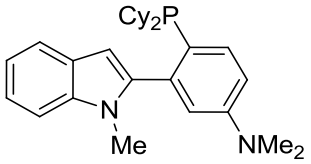
4-Bromo-*N*,*N*-dimethyl-3-(1-methyl-1*H*-indol-2-yl)aniline



4-Bromo-3-(1*H*-indol-2-yl)-*N*,*N*-dimethylaniline (3.2 mmol) was dissolved in 10 mL freshly distilled THF in dropping funnel and added dropwise to the 5 mL freshly distilled THF solution contained NaH (4.8 mmol, 60% in mineral oil) at room temperature. NaH was washed with hexane (10 mL x3) under N_2. The mixture was stirred for 15 min at room temperature. Me_2SO_4 (3.36 mmol) was then added to the mixture dropwise. After the mixture was stirred at room temperature for overnight, solvent was removed by vacuum. EtOAc and water was added to the mixture and the organic phase was separated. The combined organic phase was washed with brine several times and concentrated. The concentrated mixture was purified by column chromatography on silica gel (10 × 3 cm) and eluted with EtOAc/hexane (1:9). The solution was evaporated in vacuum to give the desired product as a white powder (0.84 g, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.99 (s, 6H), 3.62 (s, 3H), 6.53 (s, 1H), 6.72 (d, *J*= 8.7 Hz, 1H), 6.79 (s, 1H), 7.17 (t, *J*= 8.0 Hz, 1H), 7.28 (t, *J*= 8.0 Hz, 1H), 7.39 (d, *J*= 8.0 Hz, 1H), 7.52 (d, *J*= 8.0 Hz, 1H), 7.68 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.6, 40.7, 101.6, 109.5, 114.4, 116.9, 119.7, 120.6, 121.6, 127.7, 132.0, 132.9, 134.4, 137.2, 140.7, 143.4; MS (EI): *m/z* (relative intensity) 328

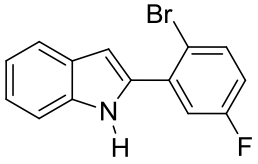
(M^+, 100), 249 (44), 233 (30), 204 (50); HRMS: calcd. for $C_{17}H_{17}N_2BrH^+$: 329.0653, found 329.0650.

4-(Dicyclohexylphosphino)-N,N-dimethyl-3-(1-methyl-1*H*-indol-2-yl)aniline L4



The general procedure for the synthesis of 2-(2-(Dicyclohexylphosphino)phenyl)-1-(methoxymethyl)-1*H*-indole **L3** was followed. 4-Bromo-*N*,*N*-dimethyl-3-(1-methyl-1H-indol-2-yl)aniline (1.42 mmol) in 10 mL THF, *n*-BuLi (1.56 mmol) and PCy_2Cl (1.56 mmol) in 3 mL THF were given the desired product as a white solid (0.44 g, 69%). ^{1}H NMR (400 MHz, C_6D_6) δ 1.13-1.30 (m, 11H), 1.69-1.80 (m, 11 H), 2.48 (s, 6H), 3.40 (s, 3H), 6.64 (d, *J*= 10.0 Hz, 1H), 6.74 (s, 1H), 6.78 (t, *J*= 4.0 Hz, 1H), 7.23-7.30 (m, 3H), 7.48 (d, *J*= 8.0 Hz, 1H), 7.79 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 26.4, 27.3, 30.4, 30.5, 39.2, 102.9, 109.4, 111.9, 115.47, 115.5, 119.4, 120.2, 120.9, 121.5, 121.6, 127.4, 128.2, 133.26, 133.3, 136.9, 142.0, 142.3, 142.46, 142.5, 149.9; ^{31}P NMR (162 MHz, C_6D_6) δ -13.30; MS (EI): *m/z* (relative intensity) 446 (M^+, 37), 431 (6), 363 (100), 281 (88), 265 (25); HRMS: calcd. for $C_{29}H_{39}N_2PH^+$: 447.2929, found 447.2913.

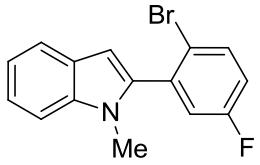
2-(2-Bromo-5-fluorophenyl)-1*H*-indole



A general procedure for Fischer-indole synthesis of 2-(2-bromo-5-fluorophenyl)-1*H*-indole was used according to the previous report.[13b]

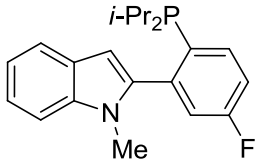
1-(2-bromo-5-fluorophenyl)ethanone (10 mmol), phenylhydrazine (15 mmol), H_3PO_4 (4.0 mL) and PPA (30 g) were given the desired product as a white solid (1.68 g, 58%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.89 (s, 1H), 6.95-7.00 (m, 1H), 7.18 (d, *J*= 6.0 Hz, 1H), 7.28 (t, *J*= 8.0 Hz, 2H), 7.35-7.39 (m, 1H), 7.46 (d, *J*= 8.0 Hz, 1H), 7.65-7.71 (m, 2H), 8.70 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 104.3, 111.1, 114.1, 116.2, 116.4, 117.9, 118.2, 120.4, 120.9, 123.0, 128.0, 134.9, 135.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -144.28; MS (EI): *m/z* (relative intensity) 289 (M^+, 100), 208 (21), 183 (67); HRMS: calcd. for $C_{14}H_9NFBrH^+$: 289.9981, found 289.9987.

2-(2-Bromo-5-fluorophenyl)-1-methyl-1*H*-indole



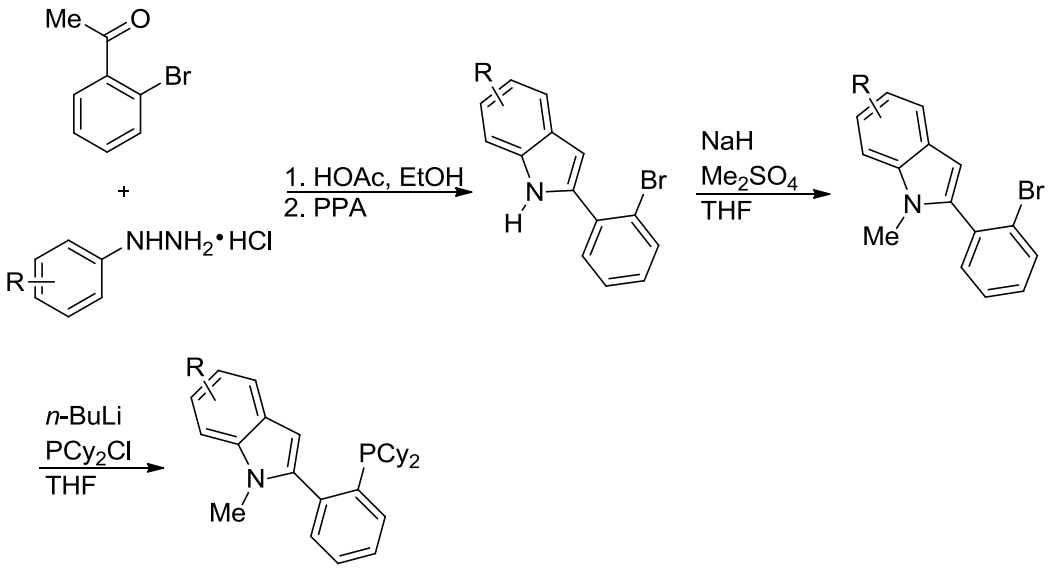
The general procedure for the synthesis of 4-bromo-*N*,*N*-dimethyl-3-(1-methyl-1*H*-indol-2-yl)aniline was followed. 2-(2-Bromo-5-fluorophenyl)-1*H*-indole (5.5 mmol) in 15 mL THF, NaH (8.3 mmol) in 5 mL THF and Me_2SO_4 (5.8 mmol) were given the desired product as a white solid (1.33 g, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.62 (s, 3H), 6.56 (s, 1H), 7.06-7.11 (m, 1H), 7.17-7.22 (m, 2H), 7.32 (t, *J*= 8.0 Hz, 1H), 7.41 (d, *J*= 8.0 Hz, 1H), 7.67-7.71 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.7, 102.5, 109.6, 117.3 (d, *J*= 22.0 Hz), 119.5, 119.8 (d, *J*= 22.0 Hz), 119.9, 120.9, 122.1, 127.5, 134.0 (d, *J*= 8.0 Hz), 136.0 (d, *J*= 8.0 Hz), 137.3, 138.4, 161.4 (d, *J*= 247.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.70; MS (EI): *m/z* (relative intensity) 305 (M^+, 100), 222 (100), 208 (22), 196 (39), 111 (44); HRMS: calcd. for $C_{15}H_{11}NFBrH^+$: 304.0151, found 304.0137.

2-(2-(Diisopropylphosphino)-5-fluorophenyl)-1-methyl-1*H*-indole L5



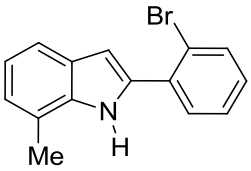
The general procedure for the synthesis of 2-(2-(dicyclohexylphosphino)phenyl)-1-(methoxymethyl)-1*H*-indole **L3** was followed. 2-(2-bromo-5-fluorophenyl)-1-methyl-1*H*-indole (4.30 mmol) in 15 mL THF, *n*-BuLi (4.73 mmol) and P*i*-Pr$_2$Cl (4.73 mmol) in 5 mL THF were given the desired product as a white solid (0.73 g, 50%). ^{1}H NMR (400 MHz, C_6D_6) δ 0.77-0.82 (m, 6H), 0.84-0.89 (m, 6H), 1.65-1.80 (m, 2H), 3.15 (s, 3H), 6.47 (s, 1H), 6.82-6.87 (m, 1H), 6.97-7.00 (m, 1H), 7.09-7.13 (m, 1H), 7.22-7.30 (m, 2H), 7.72 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 18.8, 19.5, 19.7, 23.6, 30.2, 30.3, 103.77, 103.79, 109.4, 114.7, 114.9, 118.65, 118.71, 118.85, 118.91, 119.6, 120.4, 121.4, 132.9, 133.1, 133.83, 133.86, 133.91, 133.94, 136.9, 139.33, 139.36, 142.91, 142.99, 143.2, 143.3, 161.2, 163.7; ^{31}P NMR (162 MHz, C_6D_6) δ -3.28; ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.67; MS (EI): *m/z* (relative intensity) 341 (M^+, 19), 298 (100), 254 (46), 240 (31); HRMS: calcd. for $C_{21}H_{25}NFPH^+$: 342.1787, found 342.1798.

7.4.2.3 Preparation of indolylphosphine ligand **L6-L10**



L6, R= 2-Me
L7, R= 2-Et
L8, R= 2,5-diMe
L9, R= 3-F
L10, R= 3,4-diMe

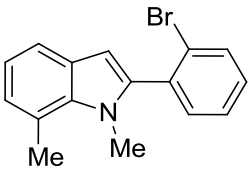
2-(2-Bromophenyl)-7-methyl-1*H*-indole



A general procedure for Fischer-indole synthesis of 2-(2-bromophenyl)-7-methyl-1*H*-indole was used according to the previous reports with a slight modification.[13a, 13b] 2'-Bromoacetophenone (10 mmol), 2-methylphenylhydrazine hydrochloride (12 mmol), ethanol (5 mL), glacial acetic acid (a few drops) were stirred at 80 ^{o}C for 3 h. Solvent was evaporated to yield the phenylhydrazone intermediate. PPA (30 g) was added to the phenylhydrazone intermediate. The mixture was heated slowly 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 phases were combined, dried over Na_2SO_4 and concentrated under reduced

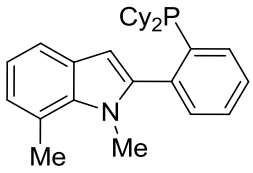
pressure. The crude product was purified by column chromatography on silica gel (20 × 4 cm) and eluted with EtOAc/hexane (1:9). The solution was evaporated in vacuum to give the desired product as a yellow liquid (1.52 g, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.62 (s, 3H), 6.92 (s, 1H), 7.11-7.19 (m, 2H), 7.27 (t, *J*= 8.0 Hz, 1H), 7.45 (t, *J*= 8.0 Hz, 1H), 7.62 (d, *J*= 8.0 Hz, 1H), 7.70 (d, *J*= 8.0 Hz, 1H), 7.77 (d, *J*= 8.0 Hz, 1H), 8.65 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.5, 104.0, 118.4, 120.1, 120.3, 121.2, 123.0, 127.58, 127.6, 129.0, 131.3, 133.4, 133.9, 135.79, 135.83; MS (EI): *m/z* (relative intensity) 285 (M^+, 100), 204 (28), 190 (6), 179 (14); HRMS: calcd. for $C_{15}H_{12}NBrH^+$:286.0231, found 286.0226.

2-(2-Bromophenyl)-1,7-dimethyl-1*H*-indole



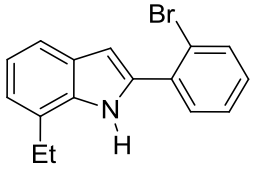
The general procedure for the synthesis of 4-bromo-*N*,*N*-dimethyl-3-(1-methyl-1*H*-indol-2-yl)aniline was followed. 2-(2-Bromophenyl)-7-methyl-1*H*-indole (5.34 mmol) in 10 mL THF, NaH (10.67 mmol) in 5 mL THF and Me_2SO_4 (5.6 mmol) were given the desired product as a light yellow solid (1.33 g, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.86 (s, 3H), 3.84 (s, 3H), 6.50 (s, 1H), 6.98-7.06 (m, 2H), 7.32-7.36 (m, 1H), 7.41-7.45 (m, 1H), 7.52 (d, *J*= 8.0 Hz, 1H), 7.74 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.1, 33.9, 102.6, 118.9, 119.9, 121.3, 124.7, 125.4, 127.2, 128.5, 130.0, 132.7, 132.9, 134.6, 136.2, 140.4; MS (EI): *m/z* (relative intensity) 299 (M^+, 100), 284 (95), 217 (14), 204 (40), 191 (19); HRMS: calcd. for $C_{16}H_{14}NBrH^+$: 300.0388, found 300.0390.

2-(2-(Dicyclohexylphosphino)phenyl)-1,7-dimethyl-1H-indole L6



The general procedure for the synthesis of 2-(2-(dicyclohexylphosphino)phenyl)-1-(methoxymethyl)-1*H*-indole **L3** was followed. 2-(2-Bromo-5-fluorophenyl)-1-methyl-1*H*-indole (4.0 mmol) in 15 mL THF, *n*-BuLi (4.4 mmol) and PCy_2Cl (4.4 mmol) in 5 mL THF were given the desired product as a white solid (0.98 g, 59%). ^{1}H NMR (400 MHz, C_6D_6) δ 0.94-1.36 (m, 10H), 1.46-1.82 (m, 12H), 2.48 (s, 3H), 3.53 (s, 3H), 6.62 (s, 1H), 6.95 (d, *J*= 8.0 Hz, 1H), 7.11-7.22 (m, 3H), 7.37-7.40 (m, 1H), 7.47-7.50 (m, 1H), 7.63 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 19.7, 26.1, 26.4, 26.8, 27.3, 28.4, 29.9, 30.4, 32.5, 33.80, 33.87, 35.4, 104.1, 118.6, 119.6, 120.9, 124.3, 127.3, 127.5, 127.8, 128.1, 128.9, 132.05, 132.11, 132.21, 132.24, 135.9, 137.5, 137.7, 141.46, 141.50, 141.6, 141.8; ^{31}P NMR (162 MHz, C_6D_6) δ -10.04; MS (EI): *m/z* (relative intensity) 417 (M^+, 14), 402 (7), 334 (100), 252 (43), 236 (36); HRMS: calcd. for $C_{28}H_{36}NPH^+$: 418.2664, found 418.2656.

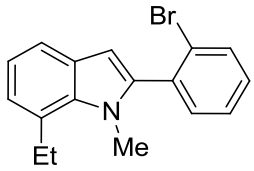
2-(2-Bromophenyl)-7-ethyl-1*H*-indole



The general procedure for the synthesis of 2-(2-bromophenyl)-7-methyl-1*H*-indole was followed. 2'-Bromoacetophenone (10 mmol), 2-ethylphenylhydrazine hydrochloride (12 mmol), ethanol (10 mL), glacial acetic acid (a few drops) and PPA (30 g) were given the desired product as a yellow

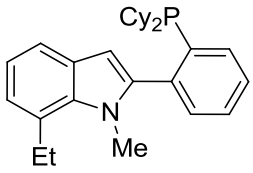
liquid (1.54 g, 52%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.48 (t, *J*= 6.0 Hz, 3H), 2.95-3.01 (m, 2H), 6.89 (s, 1H), 7.12-7.19 (m, 2H), 7.26 (t, J= 8.0 Hz, 1H), 7.44 (t, *J*= 8.0 Hz, 1H), 7.60 (d, *J*= 4.0 Hz, 1H), 7.68-7.76 (m, 2H), 8.71 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 24.2, 104.0, 118.6, 120.5, 121.1, 121.3, 126.4, 127.7, 127.9, 129.1, 131.5, 133.6, 134.0, 135.2, 135.8; MS (EI): *m/z* (relative intensity) 299 (M^+, 100), 284 (75), 218 (18), 204 (55), 191 (20); HRMS: calcd. for $C_{16}H_{13}NBrH^+$: 300.0388, found 300.0387.

2-(2-Bromophenyl)-7-ethyl-1-methyl-1*H*-indole



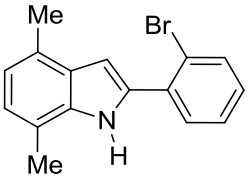
The general procedure for the synthesis of 4-bromo-*N*,*N*-dimethyl-3-(1-methyl-1*H*-indol-2-yl)aniline was followed. 2-(2-Bromophenyl)-7-ethyl-1*H*-indole (5.2 mmol) in 10 mL THF, NaH (10.4 mmol) in 5 mL THF and Me_2SO_4 (5.5 mmol) were given the desired product as a light yellow solid (1.38 g, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42 (t, *J*= 8.0 Hz, 3H), 3.18-3.23 (m, 2H), 3.80 (s, 3H), 6.53 (s, 1H), 7.08-7.12 (m, 2H), 7.34 (t, *J*= 8.0 Hz, 1H), 7.43-7.47 (m, 2H), 7.53 (d, *J*= 8.0 Hz, 1H), 7.74 (t, *J*= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.8, 25.7, 33.7, 102.8, 118.8, 120.0, 123.0, 125.4, 127.2, 128.0, 128.8, 130.0, 132.7, 132.9, 134.6, 140.6; MS (EI): *m/z* (relative intensity) 313 (M^+, 100), 298 (21), 219 (91), 204 (39); HRMS: calcd. for $C_{17}H_{15}NBrH^+$: 314.0544, found 314.0544.

2-(2-(Dicyclohexylphosphino)phenyl)-7-ethyl-1-methyl-1*H*-indole L7



The general procedure for the synthesis of 2-(2-(dicyclohexylphosphino)phenyl)-1-(methoxymethyl)-1*H*-indole **L3** was followed. 2-(2-Bromophenyl)-7-ethyl-1-methyl-1*H*-indole (3.0 mmol) in 10 mL THF, *n*-BuLi (3.3 mmol) and PCy_2Cl (3.3 mmol) in 5 mL THF were given the desired product as a white solid (0.82 g, 63%). ^{1}H NMR (400 MHz, C_6D_6) δ 0.81-1.31 (m, 13H), 1.37-1.81 (m, 12H), 2.88-2.93 (m, 2H), 3.55 (s, 3H), 6.64 (s, 1H), 7.04 (d, *J*= 8.0 Hz, 1H), 7.17-7.22 (m, 3H), 7.38-7.41 (m, 1H), 7.49 (d, *J*= 8.0 Hz, 1H), 7.65 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 26.4, 26.8, 27.3, 28.3, 29.8, 30.0, 30.2, 32.4, 32.5, 33.7, 33.8, 35.4, 35.6, 104.3, 118.6, 119.7, 122.6, 128.1, 129.3, 131.9, 132.0, 132.25, 132.27, 135.1, 137.5, 137.7, 141.5, 141.7, 141.8; ^{31}P NMR (162 MHz, C_6D_6) δ -9.86; MS (EI): *m/z* (relative intensity) 431 (M^+, 17), 416 (8), 348 (100), 266 (33), 236 (33); HRMS: calcd. for $C_{29}H_{38}NPH^+$: 432.2820, found 432.2813.

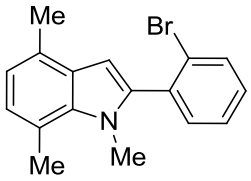
2-(2-Bromophenyl)-4,7-dimethyl-1*H*-indole



The general procedure for the synthesis of 2-(2-bromophenyl)-7-methyl-1*H*-indole was followed. 2'-Bromoacetophenone (5.0 mmol), 2,5-dimethylphenylhydrazine hydrochloride (6.0 mmol), ethanol (10 mL), glacial acetic acid (a few drops) were stirred at 80 ^{o}C for 1 h. PPA (15 g) was added and given the desired product as a yellow liquid (0.68 g, 48%). ^{1}H NMR (400 MHz,

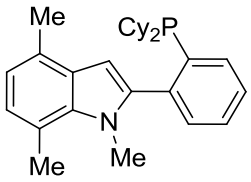
$CDCl_3$) δ 2.78 (s, 3H), 2.94 (s, 3H) 7.19-7.24 (m, 2H), 7.28 (d, *J*= 8.0 Hz, 1H), 7.40 (t, *J*= 8.0 Hz, 1H), 7.59 (t, *J*= 8.0 Hz, 1H), 7.89 (d, *J*= 8.0 Hz, 1H), 7.94 (d, *J*= 8.0 Hz, 1H), 8.91 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.2, 18.5, 102.5, 117.4, 120.2, 121.0, 123.0, 127.4, 127.5, 127.6, 128.7, 131.1, 133.4, 133.7, 135.1, 135.4; MS (EI): *m/z* (relative intensity) 301 (M^+, 100), 284 (29), 218 (16), 204 (20); HRMS: calcd. for $C_{16}H_{14}NBrH^+$: 300.0388, found 300.0381.

2-(2-Bromophenyl)-1,4,7-trimethyl-1*H*-indole



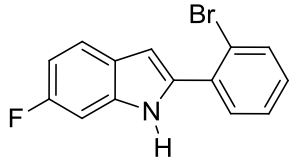
The general procedure for the synthesis of 4-bromo-*N*,*N*-dimethyl-3-(1-methyl-1*H*-indol-2-yl)aniline was followed. 2-(2-Bromophenyl)-4,7-dimethyl-1*H*-indole (4.9 mmol) in 20 mL THF, NaH (9.7 mmol) in 5 mL THF and Me_2SO_4 (5.2 mmol) were given the desired product as a light yellow solid (1.23 g, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.56 (s, 3H), 2.83 (s, 3H), 3.84 (s, 3H), 6.51 (s, 1H), 6.85 (d, *J*= 8.0 Hz, 1H), 6.91 (d, *J*= 8.0 Hz, 1H), 7.32-7.36 (m, 1H), 7.42-7.47 (m, 2H), 7.74 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.4, 19.8, 33.8, 99.9, 101.1, 118.9, 119.9, 124.7, 125.4, 127.2, 128.0, 129.9, 132.7, 133.0, 134.8, 135.8, 139.9; MS (EI): *m/z* (relative intensity) 315 (M^+, 100), 300 (29), 232 (29), 218 (37), 204 (15); HRMS: calcd. for $C_{17}H_{15}NBrH^+$: 314.0544, found 314.0540.

2-(2-(Dicyclohexylphosphino)phenyl)-1,4,7-trimethyl-1*H*-indole L8



The general procedure for the synthesis of 2-(2-(dicyclohexylphosphino)phenyl)-1-(methoxymethyl)-1*H*-indole **L3** was followed. 2-(2-Bromophenyl)-7-ethyl-1-methyl-1*H*-indole (2.6 mmol) in 10 mL THF, *n*-BuLi (2.9 mmol) and PCy_2Cl (2.9 mmol) in 5 mL THF were given the desired product as a white solid (0.46 g, 41%). ^{1}H NMR (400 MHz, C_6D_6) δ 0.97-1.34 (m, 10H), 1.46-1.81 (m, 12H), 2.50 (s, 3H), 2.57 (s, 3H), 3.55 (s, 3H), 6.61 (s, 1H), 6.91-6.97 (m, 2H), 7.18-7.23 (m, 2H), 7.40-7.43 (m, 1H), 7.40-7.50 (m, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 18.4, 19.7, 26.5, 27.0, 27.5, 28.8, 30.1, 32.5, 33.9, 34.0, 35.7, 102.8, 104.5, 118.6, 120.0, 124.5, 127.2, 127.9, 128.1, 128.8, 132.2, 132.29, 132.32, 135.6, 137.8, 138.1, 140.9, 141.0, 141.7, 142.0, 145.3; ^{31}P NMR (162 MHz, C_6D_6) δ -9.94; MS (EI): *m/z* (relative intensity) 431 (M^+, 20), 348 (100), 266 (47), 250 (27), 236 (20); HRMS: calcd. for $C_{29}H_{38}NPH^+$: 432.2820, found 432.2839.

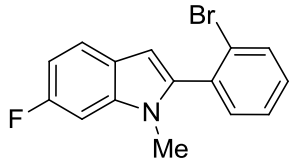
2-(2-Bromophenyl)-6-fluoro-1*H*-indole



The general procedure for the synthesis of 2-(2-bromophenyl)-7-methyl-1*H*-indole was followed. 2'-Bromoacetophenone (10.0 mmol), 3-fluorophenylhydrazine hydrochloride (12.0 mmol), ethanol (15 mL), glacial acetic acid (a few drops) and PPA (30 g) was added and given the desired product as a white solid (1.56 g, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (s, 1H), 6.94 (d, *J*= 8.0

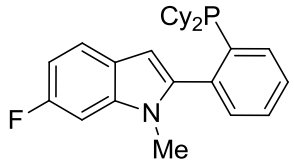
Hz, 1H), 7.14 (d, *J*= 8.0 Hz, 1H), 7.25 (t, *J*= 8.0 Hz, 1H), 7.42 (t, *J*= 6.0 Hz, 1H), 7.58-7.62 (m, 2H), 7.72 (d, *J*= 8.0 Hz, 1H), 8.68 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 97.3 (d, *J*= 26.0 Hz), 103.5, 109.0 (d, *J*= 24.0 Hz), 121.2, 121.6 (d, *J*= 10.0 Hz), 124.7, 127.7, 129.3, 131.2, 133.1, 134.0, 136.1 (d, *J*= 4.0 Hz), 136.7 (d, *J*= 21.0 Hz), 160.1 (d, *J*= 237.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.92; MS (EI): *m/z* (relative intensity) 288 (M^+, 100), 209 (21), 183 (59), 104 (10); HRMS: calcd. for $C_{14}H_9NFBrH^+$: 289.9981, found 289.9972.

2-(2-Bromophenyl)-6-fluoro-1-methyl-1*H*-indole



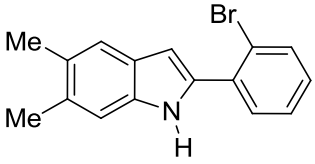
The general procedure for the synthesis of 4-bromo-*N*,*N*-dimethyl-3-(1-methyl-1*H*-indol-2-yl)aniline was followed. 2-(2-Bromophenyl)-4,7-dimethyl-1*H*-indole (3.4 mmol) in 10 mL THF, NaH (5.1 mmol) in 5 mL THF and Me_2SO_4 (3.6 mmol) were given the desired product as a light yellow solid (1.01 g, 98%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.55 (s, 3H), 6.51 (s, 1H), 6.95 (t, *J*= 8.0 Hz, 1H), 7.07 (d, *J*= 8.0 Hz, 1H), 7.33-7.37 (m, 1H), 7.44 (d, *J*= 4.0 Hz, 2H), 7.57-7.61 (m, 1H), 7.74 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.8, 95.9 (d, *J*= 26.0 Hz), 100.0, 102.1, 108.4 (d, *J*= 24.0 Hz), 121.4 (d, *J*= 10.0 Hz), 124.0, 125.2, 127.2, 130.2, 132.8, 133.9, 137.3 (d, *J*= 11.0 Hz), 140.1, 159.8 (d, *J*= 236.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.51; MS (EI): *m/z* (relative intensity) 303 (M^+, 100), 222 (79), 208 (14), 194 (11), 111 (20); HRMS: calcd. for $C_{15}H_{11}NBrFH^+$: 304.0137, found 304.0125.

2-(2-(Dicyclohexylphosphino)phenyl)-6-fluoro-1-methyl-1*H*-indole L9



The general procedure for the synthesis of 2-(2-(dicyclohexylphosphino)phenyl)-1-(methoxymethyl)-1*H*-indole **L3** was followed. 2-(2-Bromophenyl)-6-fluoro-1-methyl-1*H*-indole (3.28 mmol) in 10 mL THF, *n*-BuLi (3.6 mmol) and PCy_2Cl (3.9 mmol) in 5 mL THF were given the desired product as a white solid (1.11 g, 81%). ^{1}H NMR (400 MHz, C_6D_6) δ 0.91-1.25 (m, 11H), 1.48-1.78 (m, 11H), 3.06 (s, 3H), 6.52 (s, 1H), 6.89 (d, *J*= 10.0 Hz, 1H), 6.97 (t, *J*= 10.0 Hz, 1H), 7.11 (t, *J*= 8.0 Hz, 1H), 7.19 (d, *J*= 8.0 Hz, 1H), 7.26-7.29 (m, 1H), 7.42-7.46 (m, 2H); ^{13}C NMR (100 MHz, C_6D_6) δ 26.4, 27.2, 30.47, 30.55, 95.9, 96.2, 103.5, 107.9, 108.2, 121.0, 121.1, 124.5, 137.0, 137.2, 137.5, 137.8, 140.8, 141.1, 141.7, 158.8, 161.1; ^{31}P NMR (162 MHz, C_6D_6) δ -9.96; ^{19}F NMR (376 MHz, $CDCl_3$) δ -121.38; MS (EI): *m/z* (relative intensity) 421 (M^+, 30), 338 (100), 256 (70), 240 (40); HRMS: calcd. for $C_{27}H_{33}NFPH^+$: 422.2413, found 422.2408.

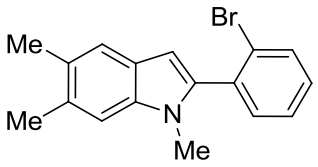
2-(2-Bromophenyl)-5,6-dimethyl-1*H*-indole



The general procedure for the synthesis of 2-(2-bromophenyl)-7-methyl-1*H*-indole was followed. 2'-Bromoacetophenone (10.0 mmol), 3,4-dimethylphenylhydrazine hydrochloride (12.0 mmol), ethanol (15 mL), glacial acetic acid (a few drops) and PPA (30 g) was added and given the product. The product was washing with small amount of hexane for further purification. The

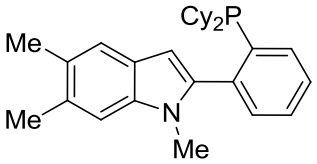
desired product was given as a light yellow solid (1.49 g, 50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.40 (s, 3H), 2.42 (s, 3H), 6.74 (s, 1H), 7.19-7.24 (m, 2H), 7.39 (t, *J*= 8.0 Hz, 1H), 7.45 (s, 1H), 7.63 (d, *J*= 8.0 Hz, 1H), 7.70 (d, *J*= 8.0 Hz, 1H), 8.50 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 20.5, 102.9, 111.3, 120.7, 121.1, 126.5, 127.5, 128.8, 131.2, 131.7, 133.7, 133.9, 135.25, 135.33; MS (EI): *m/z* (relative intensity) 299 (M^+, 100), 286 (35), 218 (13), 204 (20); HRMS: calcd. for $C_{16}H_{14}NBrH^+$: 300.0388, found 300.0376.

2-(2-Bromophenyl)-1,5,6-trimethyl-1*H*-indole



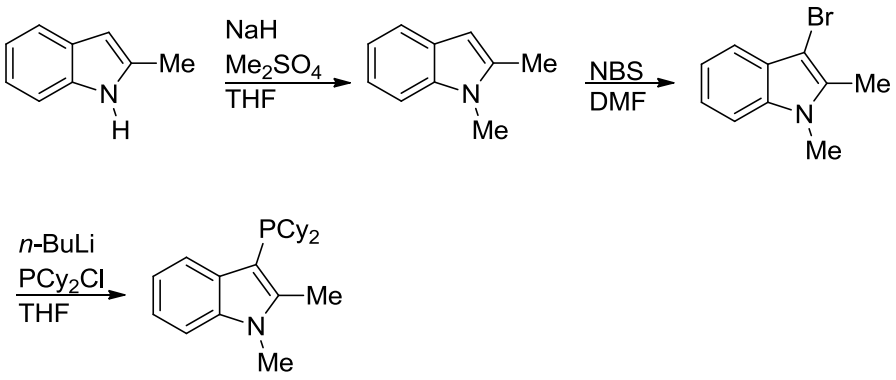
The general procedure for the synthesis of 4-bromo-*N*,*N*-dimethyl-3-(1-methyl-1*H*-indol-2-yl)aniline was followed. 2-(2-Bromophenyl)-4,7-dimethyl-1*H*-indole (2.54 mmol) in 10 mL THF, NaH (3.8 mmol) in 5 mL THF and Me_2SO_4 (2.67 mmol) were given the desired product as a light yellow solid (0.66 g, 83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3H), 2.46 (s, 3H), 3.55 (s, 3H), 6.42 (s, 1H), 7.18 (s, 1H), 7.30-7.34 (m, 1H), 7.39-7.45 (m, 3H), 7.72 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 20.7, 30.6, 101.3, 109.9, 120.7, 125.3, 125.9, 127.1, 128.4, 129.9, 130.8, 132.7, 132.8, 134.5, 136.3, 138.9; MS (EI): *m/z* (relative intensity) 313 (M^+, 100), 300 (24), 232 (18), 218 (24), 204 (11); HRMS: calcd. for $C_{17}H_{16}NBrH^+$: 314.0544, found 314.0551.

2-(2-(Dicyclohexylphosphino)phenyl)-1,5,6-trimethyl-1*H*-indole L10

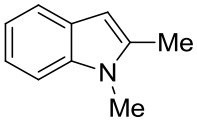


The general procedure for the synthesis of 2-(2-(dicyclohexylphosphino)phenyl)-1-(methoxymethyl)-1*H*-indole **L3** was followed. 2-(2-Bromophenyl)-1,5,6-trimethyl-1*H*-indole (1.79 mmol) in 8 mL THF, *n*-BuLi (2.0 mmol) and PCy_2Cl (2.0 mmol) in 5 mL THF were given the desired product as a white solid (0.45 g, 60%). ^{1}H NMR (400 MHz, C_6D_6) δ 0.95-1.25 (m, 10H), 1.52-1.85 (m, 12H), 2.34 (s, 3H), 2.37 (s, 3H), 2.28 (s, 3H), 7.58 (s, 1H), 7.04 (s, 1H), 7.11-7.21 (m, 2H), 7.35-7.38 (m, 1H), 7.47-7.50 (m, 2H); ^{13}C NMR (100 MHz, C_6D_6) δ 20.0, 20.6, 26.5, 27.3, 29.4, 30.2, 30.4, 30.5, 30.6, 103.01, 103.03, 110.1, 120.8, 126.7, 127.5, 1281.1, 129.2, 129.6, 132.1, 132.2, 132.29, 132.31, 136.4, 137.6, 137.8, 140.2, 140.3, 141.5, 141.8; ^{31}P NMR (162 MHz, C_6D_6) δ -9.78; MS (EI): *m/z* (relative intensity) 431 (M^+, 11), 348 (100), 266 (32), 250 (23), 236 (14); HRMS: calcd. for $C_{29}H_{38}NPH^+$: 432.2820, found 432.2837.

7.4.2.4 Preparation of indolylphosphine ligand **L11**

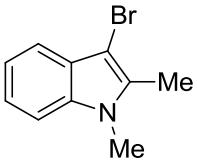


1,2-Dimethyl-1*H*-indole[17]



The general procedure for the synthesis of 4-bromo-*N*,*N*-dimethyl-3-(1-methyl-1*H*-indol-2-yl)aniline was followed. 2-Methyl-1*H*-indole (10 mmol) in 15 mL THF, NaH (15.0 mmol) in 5 mL THF and Me_2SO_4 (10.5 mmol) were given the desired product as a white solid (1.30 g, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.50 (s, 3H), 3.72 (s, 3H), 5.83 (s, 1H), 7.16 (t, *J*= 8.0 Hz, 1H), 7.24 (t, *J*= 8.0 Hz, 1H), 7.33 (d, *J*= 8.0 Hz, 1H), 7.61 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.7, 99.4, 108.6, 119.1, 119.5, 120.3, 127.9, 136.7, 137.2; MS (EI): *m/z* (relative intensity) 144 (M^+, 100), 127 (9), 114 (22), 102 (22), 77 (18).

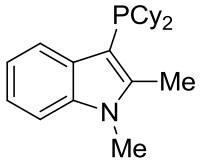
3-Bromo-1,2-dimethyl-1*H*-indole[18]



To a solution of 1,2-dimethyl-1*H*-indole (7.5 mmol) in anhydrous DMF (15 mL), a solution of *N*-bromosuccinimide (7.88 mmol) in anhydrous DMF (10 mL) was added dropwise at room temperature under nitrogen atmosphere. After stirring for 2 h,

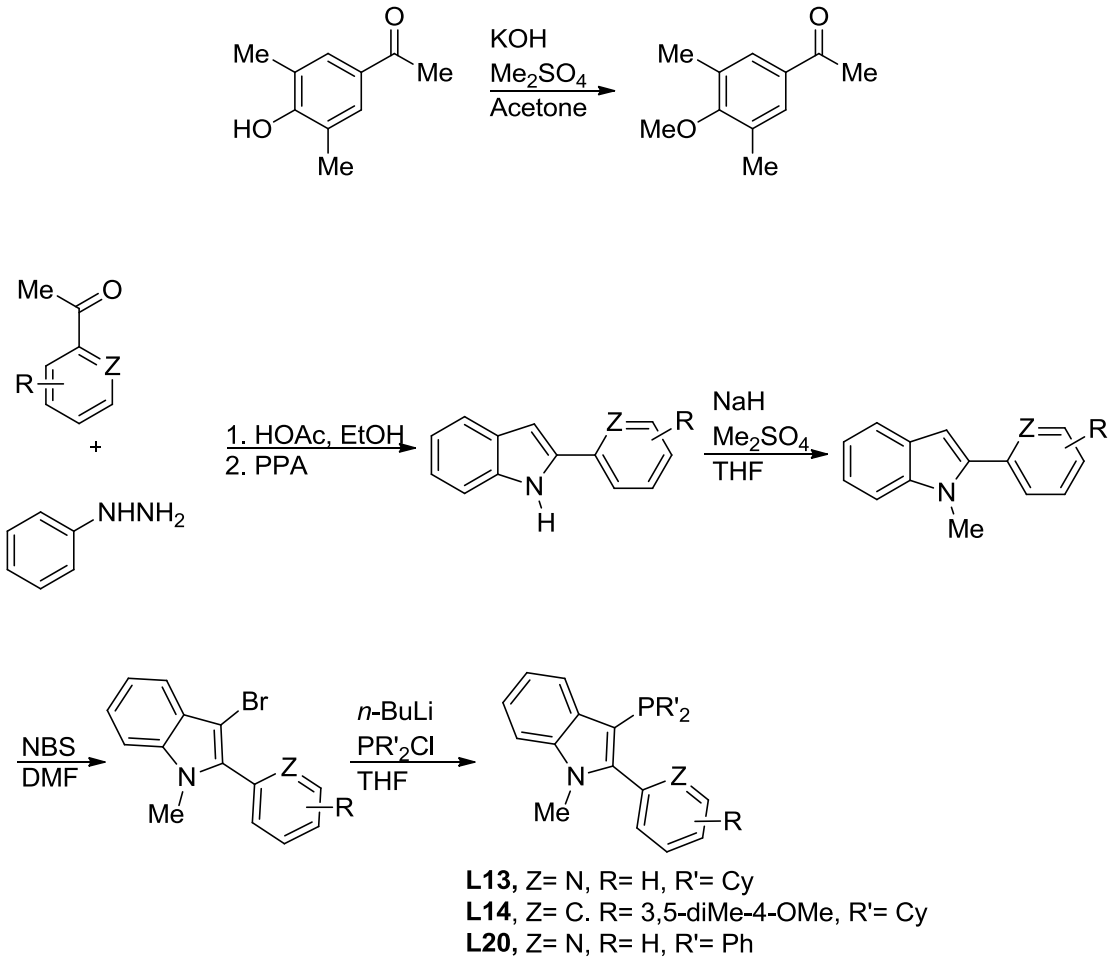
the reaction mixture was poured onto crushed ice and CH_2Cl_2 was added to the flask followed by water. The organic phase was washed with large amount of water and then concentrated. The concentrated solution was filtered over a pad of silica (15 x 3 cm) and washed with EtOAc/hexane (1:20). The solution was evaporated to give the desired product as a white solid (0.84 g, 50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.46 (s, 3H), 3.72 (s, 3H), 7.16-7.29 (m, 3H), 7.52 (d, *J*= 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.0, 30.2, 89.0, 108.8, 118.3, 119.9, 121.6, 126.8, 134.0, 136.1; MS (EI): *m/z* (relative intensity) 224 (M^+, 100), 144 (82), 128 (47), 102 (34), 76 (24).

3-(Dicyclohexylphosphino)-1,2-dimethyl-1H-indole L11



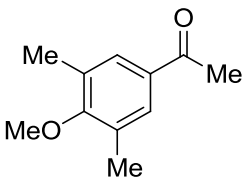
The general procedure for the synthesis of 2-(2-(dicyclohexylphosphino)phenyl)-1-(methoxymethyl)-1*H*-indole **L3** was followed. 3-Bromo-1,2-dimethyl-1*H*-indole (3.0 mmol) in 6 mL THF, *n*-BuLi (3.3 mmol) and PCy_2Cl (3.3 mmol) in 3 mL THF were given the desired product as a white solid (0.72 g, 70%). ^{1}H NMR (400 MHz, C_6D_6) δ 1.02-1.44 (m, 10H), 1.51-1.61 (m, 4H), 1.72-1.88 (m, 4H), 2.04-2.17 (m, 2H), 2.41 (s, 3H); 2.43-2.52 (m, 2H), 2.81 (s, 3H); 7.03 (d, *J*= 6.0 Hz, 1H), 7.20-7.26 (m, 2H), 7.97 (d, *J*= 4.0 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 26.5, 27.08, 27.12, 27.2, 28.8, 30.3, 30.4, 32.0, 32.2, 33.7, 33.8, 101.5, 101.6, 109.0, 119.8, 120.8, 120.9, 131.2, 138.0; ^{31}P NMR (162 MHz, C_6D_6) δ -18.04; MS (EI): *m/z* (relative intensity) 341 (M^+, 15), 259 (23), 176 (100); HRMS: calcd. for $C_{22}H_{32}NPH^+$: 342.2351, found 342.2361.

7.4.2.5 Preparation of substituted acetophenone and indolylphosphine ligand **L13,** **L14** and **L20**



L13, Z= N, R= H, R'= Cy
L14, Z= C. R= 3,5-diMe-4-OMe, R'= Cy
L20, Z= N, R= H, R'= Ph

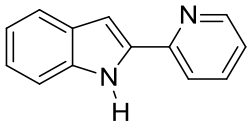
1-(4-Methoxy-3,5-dimethylphenyl)ethanone



A general procedure for synthesis of 1-(4-methoxy-3,5-dimethylphenyl)ethanone was used according to the previous reports with a slight modification. [19] 1-(4-Hydroxy-3,5-dimethylphenyl)ethanone (20 mmol) dissolved in 50 mL acetone. KOH (60 mmol) and Me_2SO_4 (21 mmol) were added and then stirred at room temperature for 4 h. After the completion of the reaction, extraction and purification

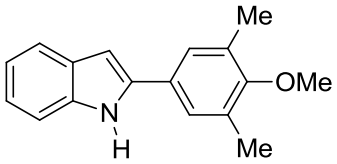
according to the previous report,[19] the desired product as a colorless oil was given (3.58 g, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.31 (s, 6H), 2.53 (s, 3H), 3.74 (s, 3H), 7.62 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.0, 26.3, 59.5, 129.2, 130.9, 132.7, 161.1, 197.4; MS (EI): *m/z* (relative intensity) 178 (M^+, 65), 163 (100), 105 (52), 91 (55), 77 (23).

2-(Pyridin-2-yl)-1*H*-indole[20]



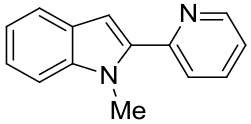
The general procedure for the synthesis of 2-(2-bromophenyl)-7-methyl-1*H*-indole was followed. 1-(Pyridin-2-yl)ethanone (20 mmol), phenylhydrazine (24 mmol), ethanol (10 mL) and glacial acetic acid (a few drops) were stirred at 80 ^{o}C for 1 h. Solvent was evaporated under reduced pressure. PPA (20 g) was added to yield the reaction mixture. After the reaction, extraction and purification by column chromatography according to the previous procedure, the solution was evaporated in vacuum to give the desired product. The product was recrystallized by small amount of CH_2Cl_2 and cold hexane for further purification. The product was then dried under vacuum to afford a yellow solid (3.10 g, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (s, 1H), 7.16-7.25 (m, 3H), 7.38 (d, *J*= 8.0 Hz, 1H), 7.71-7.77 (m, 2H), 7.85 (d, *J*= 8.0 Hz, 1H), 8.63 (d, *J*= 8.0 Hz, 1H), 10.23 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 100.6, 111.4, 119.9, 120.0, 121.1, 121.9, 123.1, 129.0, 136.65, 136.68, 136.73, 149.0, 150.4; MS (EI): *m/z* (relative intensity) 194 (M^+, 100), 167 (100), 139 (48), 114 (20), 89 (88).

2-(4-Methoxy-3,5-dimethylphenyl)-1*H*-indole



The general procedure for the synthesis of 2-(2-bromophenyl)-7-methyl-1*H*-indole was followed. 1-(4-Methoxy-3,5-dimethylphenyl)ethanone (15 mmol), phenylhydrazine (18 mmol), ethanol (10 mL) and glacial acetic acid (a few drops) were stirred at 80 ^{o}C for 2 h. Solvent was evaporated under reduced pressure. PPA (30 g) was added to yield the reaction mixture. After the reaction, extraction and purification by column chromatography according to the previous procedure, the solution was evaporated in vacuum to give the desired product and small amount of cold hexane was used to further wash the product. The product was then dried under vacuum to afford a light yellow solid (3.27 g, 87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.39 (s, 6H), 3.81 (s, 3H), 6.78 (s, 1H), 7.14-7.24 (m, 2H), 7.36-7.42 (m, 3H), 7.66 (d, *J*= 8.0 Hz, 1H), 8.34 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.2, 40.3, 59.7, 99.2, 110.7, 120.1, 120.4, 121.9, 125.6, 127.9, 129.3, 131.5, 136.6, 137.9, 156.8; MS (EI): *m/z* (relative intensity) 251 (M^+, 87), 236 (100), 220 (5), 193 (15); HRMS: calcd. for $C_{17}H_{17}NOH^+$: 252.1388, found 252.1379.

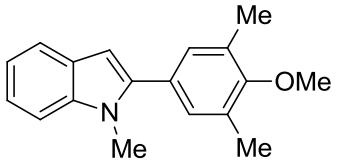
1-Methyl-2-(pyridin-2-yl)-1*H*-indole[21]



The general procedure for the synthesis of 4-bromo-*N*,*N*-dimethyl-3-(1-methyl-1*H*-indol-2-yl)aniline was followed. 2-(Pyridin-2-yl)-1*H*-indole (8.5 mmol) in 20 mL THF, NaH (12.8 mmol) in 5 mL THF

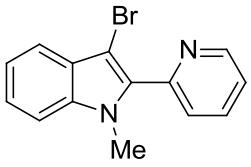
and Me_2SO_4 (9 mmol) were given the desired product as a light yellow solid (1.74 g, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.1 (s, 3H), 6.92 (s, 3H), 7.17 (t, *J*= 8.0 Hz, 1H), 7.26-7.33 (m, 2H), 7.44 (d, *J*= 8.0 Hz, 1H), 7.69 (d, *J*= 8.0 Hz, 1H), 7.14-7.83 (m, 2H), 8.74 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.9, 103.4, 109.8, 119.9, 120.9, 121.7, 122.5, 123.5, 127.4, 136.5, 139.0, 139.3, 149.0, 152.5; MS (EI): *m/z* (relative ntensity) 207 (M^+, 100), 192 (4), 180 (13), 130 (17), 78 (19).

2-(4-Methoxy-3,5-dimethylphenyl)-1-methyl-1*H*-indole



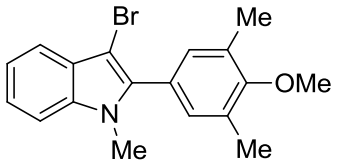
The general procedure for the synthesis of 4-bromo-*N*,*N*-dimethyl-3-(1-methyl-1*H*-indol-2-yl)aniline was followed. 2-(4-Methoxy-3,5-dimethylphenyl)-1*H*-indole (12 mmol) in 20 mL THF, NaH (24 mmol) in 5 mL THF and Me_2SO_4 (12.6 mmol) were given the desired product as a light yellow solid (2.99 g, 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.40 (s, 6H), 3.78 (s, 3H), 3.83 (s, 3H), 6.53 (s, 1H), 7.15-7.20 (m, 3H), 7.27 (t, *J*= 8.0 Hz, 1H), 7.39 (d, *J*= 8.0 Hz, 1H), 7.66 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.2, 31.1, 59.7, 101.1, 109.5, 119.7, 120.3, 121.3, 127.9, 128.3, 129.8, 131.0, 138.1, 141.5, 156.9; MS (EI): *m/z* (relative ntensity) 265 (M^+, 100), 250 (100), 234 (4), 207 (11); HRMS: calcd. for $C_{18}H_{19}NOH^+$: 266.1545, found 266.1542.

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



The general procedure for the synthesis of 3-bromo-1,2-dimethyl-1*H*-indole was followed. 1-Methyl-2-(pyridin-2-yl)-1*H*-indole (8 mmol) in 15 mL DMF and *N*-bromosuccinimide (8.4 mmol) in 15 mL DMF were given the desired product as a light yellow solid (2.19 g, 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.91 (s, 3H), 7.27 (t, *J*= 6.0 Hz, 1H), 7.34-7.38 (m, 2H), 7.42 (d, *J*= 8.0 Hz, 1H), 7.67 (d, *J*= 8.0 Hz, 1H), 7.85-7.91 (m, 2H), 8.82 (d, *J*= 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.0, 91.4, 110.0, 119.8, 120.6, 122.7, 123.7, 126.7, 127.1, 135.7, 136.4, 137.4, 149.5, 150.0; MS (EI): *m/z* (relative intensity) 286 (M^+, 63), 207 (100), 180 (29), 152 (25), 78 (46); HRMS: calcd. for $C_{14}H_{11}N_2BrH^+$: 287.0184, found 287.0195.

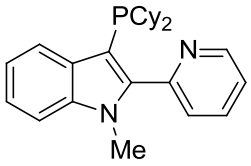
3-Bromo-2-(4-methoxy-3,5-dimethylphenyl)-1-methyl-1*H*-indole



The general procedure for the synthesis of 3-bromo-1,2-dimethyl-1*H*-indole was followed. 2-(4-Methoxy-3,5-dimethylphenyl)-1-methyl-1*H*-indole (9.5 mmol) in 18 mL DMF and *N*-bromosuccinimide (10 mmol) in 15 mL DMF were given the desired product as a white solid (3.25 g, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 6H), 3.69 (s, 3H), 3.85 (s, 3H), 7.17 (s, 2H), 7.24-7.38 (m, 3H), 7.63 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.2, 31.6, 59.7, 89.7, 109.6, 119.2, 120.4, 122.6, 125.7, 127.2, 131.0, 131.1, 136.7, 138.0, 157.3; MS (EI): *m/z* (relative intensity) 345 (M^+, 5), 331 (5), 300 (100), 285 (11); HRMS: calcd. for $C_{18}H_{18}NOBrH^+$: 344.0650,

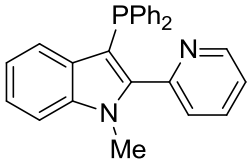
found 344.0656.

3-(Dicyclohexylphosphino)-1-methyl-2-(pyridin-2-yl)-1*H*-indole L13



The procedure of preparation of 2-(2-(dicyclohexylphosphino)phenyl)-1-(methoxymethyl)-1*H*-indole **L3** was followed. 3-Bromo-1-methyl-2-(pyridin-2-yl)-1*H*-indole (3.5 mmol) in 10 mL THF, *n*-BuLi (3.9 mmol) and PCy_2Cl (3.9 mmol) in 5 mL THF were given the desired product as a white solid (0.56 g, 40%). ^{1}H NMR (400 MHz, C_6D_6) δ 0.98-1.43 (m, 10H), 1.44-2.00 (m, 10H), 2.42-2.53 (m, 2H), 3.37 (s, 3H), 6.66-6.69 (m, 1H), 7.10-7.14 (m, 1H), 7.21-7.30 (m, 3H), 7.80 (d, *J*= 8.0 Hz, 1H), 8.07-8.09 (m, 1H), 8.58 (d, *J*= 4.0 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 26.3, 26.85, 26.97, 26.98, 27.0, 30.5, 30.6, 30.7, 32.1, 32.3, 34.5, 34.6, 105.1, 105.3, 110.1, 114.2, 120.1, 121.81, 121.83, 122.2, 128.4, 128.5, 130.4, 130.5, 134.5, 138.6, 147.8, 148.2, 148.7, 152.1; ^{31}P NMR (162 MHz, C_6D_6) δ -17.72; MS (EI): *m/z* (relative intensity) 404 (M^+, 6), 321 (100), 239 (73), 223 (33); HRMS: calcd. for $C_{26}H_{33}N_2PH^+$: 405.2459, found 405.2446.

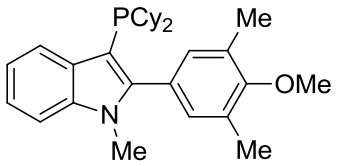
3-(Diphenylphosphino)-1-methyl-2-(pyridin-2-yl)-1*H*-indole L20



The procedure of preparation of 2-(2-(dicyclohexylphosphino)phenyl)-1-(methoxymethyl)-1*H*-indole **L3** was followed. 3-Bromo-1-methyl-2-(pyridin-2-yl)-1*H*-indole (3.5 mmol) in 10 mL THF, *n*-BuLi (3.9

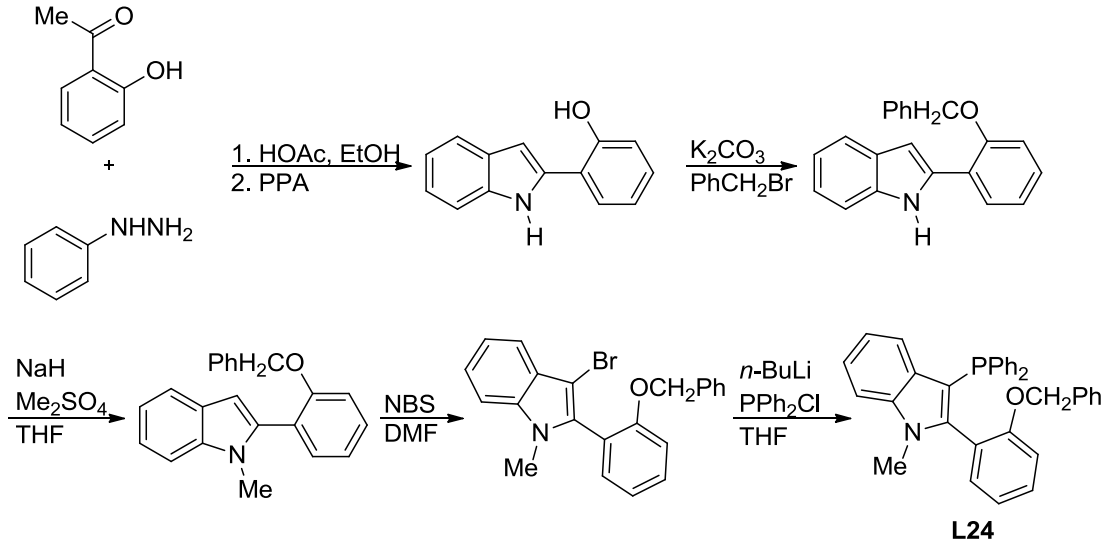
mmol) and PPh_2Cl (3.9 mmol) in 5 mL THF were given the desired product as a white solid (1.01 g, 76%). ^{1}H NMR (400 MHz, C_6D_6) δ 3.48 (s, 3H), 6.61-6.65 (m, 1H), 6.92-7.17 (m, 10H), 7.36 (d, *J*= 8.0 Hz, 1H), 7.52 (d, *J*= 8.0 Hz, 1H), 7.58-7.62 (m, 4H), 8.54 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 31.0, 105.2, 110.2, 120.5, 122.3, 122.6, 122.7, 129.79, 129.8, 132.5, 132.7, 135.0, 138.3, 138.4, 139.2, 147.4, 147.9, 149.0, 151.2; ^{31}P NMR (162 MHz, C_6D_6) δ -27.22; MS (EI): *m/z* (relative intensity) 392 (M^+, 33), 315 (100), 238 (13), 223 (25); HRMS: calcd. for $C_{26}H_{21}N_2PH^+$: 393.1521, found 393.1519.

3-(Dicyclohexylphosphino)-2-(4-methoxy-3,5-dimethylphenyl)-1-methyl-1*H*-indole L14

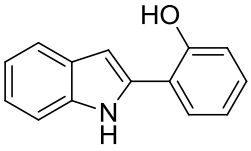


The procedure of preparation of 2-(2-(dicyclohexylphosphino)phenyl)-1-(methoxymethyl)-1*H*-indole **L3** was followed. 3-Bromo-2-(4-methoxy-3,5-dimethylphenyl)-1-methyl-1*H*-indole (9.3 mmol) in 20 mL THF, *n*-BuLi (10.3 mmol) and PCy_2Cl (10.3 mmol) in 5 mL THF were given the desired product as a white solid (3.06 g, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99-1.38 (m, 9H), 1.52-1.92 (m, 11H), 2.21-2.37 (m, 2H), 2.36 (s, 6H), 3.52 (s, 3H), 3.82 (s, 3H), 6.97 (s, 2H), 7.18 (t, *J*= 8.0 Hz, 1H), 7.28 (t, *J*= 8.0 Hz, 1H), 7.37 (d, *J*= 8.0 Hz, 1H), 7.88 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.4, 27.2, 27.27, 27.32, 27.4, 30.5, 30.6, 31.0, 31.9, 32.1, 34.2, 34.3, 59.7, 109.5, 119.6, 121.4, 121.7, 127.6, 130.2, 130.7, 131.9, 138.1, 157.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ -17.83; MS (EI): *m/z* (relative intensity) 461 (M^+, 23), 379 (31), 296 (100), 265 (23), 250 (19); HRMS: calcd. for $C_{30}H_{40}NOPH^+$: 462.2926, found 462.2921.

7.4.2.6 Preparation of indolylphosphine ligand **L24**

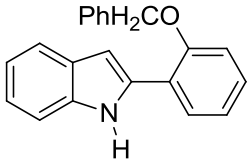


2-(1*H*-Indol-2-yl)phenol



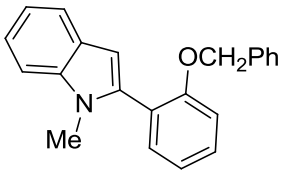
A general procedure for Fischer-indole synthesis of 2-(1*H*-Indol-2-yl)phenol was used according to the previous reports.[22] 1-(2-Hydroxyphenyl)ethanone (100 mmol), phenylhydrazine (110 mmol), ethanol (50 mL), glacial acetic acid (a few drops) and PPA (100 g) were given the desired product as light brown solid (15.0 g, 72%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.83 (t, *J*= 7.5 Hz, 1H), 6.89-6.93 (m, 2H), 6.96-7.01 (m, 2H), 7.06 (t, *J*= 7.8 Hz, 1H), 7.43 (t, *J*= 8.5 Hz, 2H), 7.66 (d, *J*= 7.8 Hz, 1H), 11.01 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 101.2, 112.0, 117.1, 119.4, 119.8, 120.3, 120.4, 121.8, 128.1, 128.8, 129.0, 136.1, 136.8, 154.7; MS (EI) cannot detect the products.

2-(2-(Benzyloxy)phenyl)-1*H*-indole[23]



After 2-(1*H*-indol-2-yl)phenol (10 mmol) was dissolved in 20 ml DMF, K_2CO_3 (30 mmol) was then added and stirred at room temperature for 30 min. Benzyl bromide (15 mmol) was added dropwise and stirred at room temperature for overnight. After stirring for overnight, the reaction mixture was poured onto crushed ice and CH_2Cl_2 was added to the flask followed by water. The organic phase was washed with large amount of water and then concentrated. The concentrated solution was isolated by flash column chromatography on silica gel (25 x 4 cm) and eluted with CH_2Cl_2/hexane (3:7). The solution was evaporated to give the desired product as a light brown solid (2.39 g, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.27 (s, 2H), 6.98 (s, 1H), 7.12-7.25 (m, 5H), 7.28-7.35 (m, 1H), 7.46-7.56 (m, 5H), 7.69 (d, *J*= 7.9 Hz, 1H), 7.94 (d, *J*= 7.6 Hz, 1H), 9.78 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 71.2, 99.7, 110.8, 113.5, 119.7, 120.2, 120.9, 121.7, 121.9, 127.7, 127.9, 128.2, 128.4, 128.5, 128.9, 135.8, 136.0, 136.3, 154.9; MS (EI): *m/z* (relative intensity) 299 (M^+, 38), 222 (19), 208 (100), 180 (38), 152 (25).

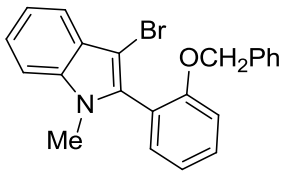
2-(2-(Benzyloxy)phenyl)-1-methyl-1*H*-indole[24]



The general procedure for the synthesis of 4-bromo-*N*,*N*-dimethyl-3-(1-methyl-1*H*-indol-2-yl)aniline was followed. 2-(2-(benzyloxy)phenyl)-1*H*-indole (8 mmol) 20 mL THF, NaH (12 mmol) in 5 mL

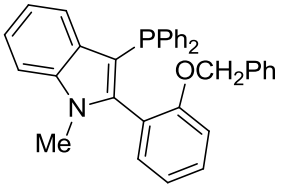
THF and Me_2SO_4 (8.4 mmol) were given the desired product as a white solid (2.59 g, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.66 (s, 3H), 5.14 (s, 3H), 6.61 (s, 1H), 7.11-7.16 (m, 2H), 7.21 (t, *J*= 8.0 Hz, 1H), 7.28-7.33 (m, 6H), 7.40-7.48 (m, 3H), 7.73 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.0, 70.5, 101.9, 109.3, 113.3, 119.3, 120.3, 121.2, 122.8, 126.8, 127.7, 128.0, 128.4, 129.9, 132.7, 136.8, 137.7, 138.6, 156.6; MS (EI): *m/z* (relative intensity) 313 (M^+, 2), 251 (64), 209 (100), 180 (47).

2-(2-(Benzyloxy)phenyl)-3-bromo-1-methyl-1*H*-indole



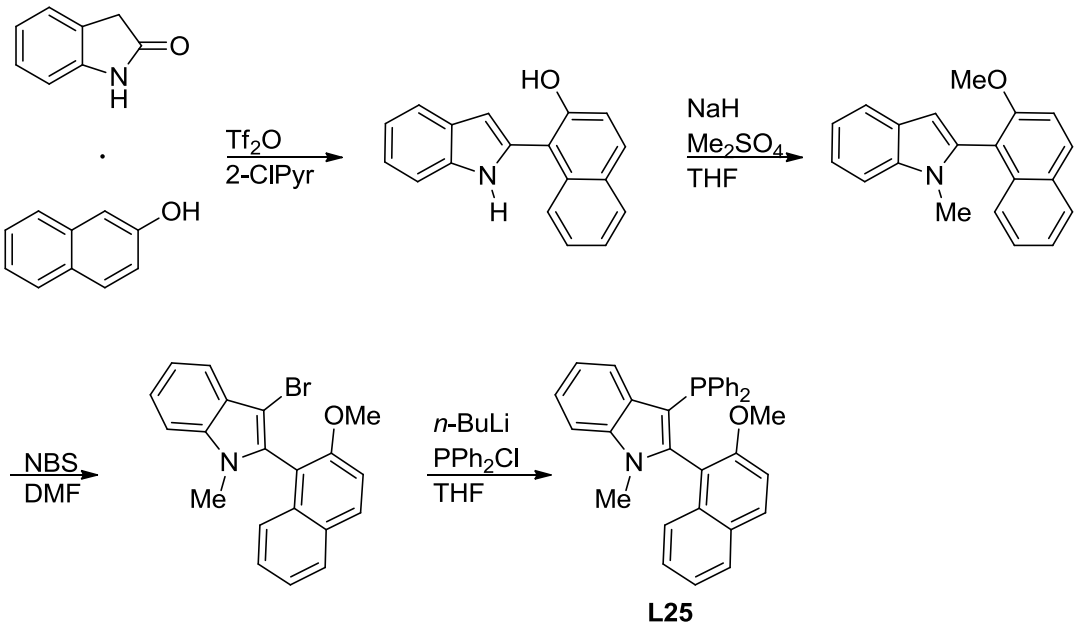
The general procedure for the synthesis of 3-bromo-1,2-dimethyl-1*H*-indole was followed. 2-(2-(Benzyloxy)phenyl)-1-methyl-1*H*-indole (6.5 mmol) in 15 mL DMF and *N*-bromosuccinimide (6.9 mmol) in 10 mL DMF were given the desired product as a white solid (2.4 g, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.06 (s, H), 5.1 (s, 2H), 7.10-7.17 (m, 2H), 7.22-7.30 (m, 6H), 7.31-7.37 (m, 2H), 7.42-7.48 (m, 2H), 7.66 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.5, 70.7, 109.5, 113.8, 119.2, 120.1, 120.4, 121.2, 122.4, 126.9, 127.8, 128.5, 130.8, 133.5, 136.8; MS (EI): *m/z* (relative intensity) 391 (M^+, 8), 312 (34), 221 (10), 91 (61); HRMS: calcd. for $C_{22}H_{18}NOBrH^+$: 392.0650, found 392.0668.

2-(2-(Benzyloxy)phenyl)-3-(diphenylphosphino)-1-methyl-1*H*-indole L24



The procedure of preparation of 2-(2-(dicyclohexylphosphino)phenyl)-1-(methoxymethyl)-1*H*-indole **L3** was followed. 2-(2-(Benzyloxy)phenyl)-3-bromo-1-methyl-1*H*-indole (2.31 mmol) in 5 mL THF, *n*-BuLi (2.55 mmol) and PPh_2Cl (2.55 mmol) in 3 mL THF were given the desired product as a white solid (0.77 g, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.68 (s, 3H), 5.04-5.15 (m, 2H), 6.99 (t, *J*= 8.0 Hz, 1H), 7.06-7.13 (m, 3H), 7.16-7.31 (m, 9H), 7.32-7.50 (m, 8H), 7.56-7.65 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.9, 70.2, 103.8, 109.6, 113.1, 119.8, 120.7, 121.5, 121.6, 121.8, 126.6, 127.1, 127.5, 127.6, 127.8, 127.9, 128.07, 128.13, 128.13, 128.4, 129.6, 130.6, 131.9, 132.1, 132.6, 132.8, 133.6, 136.8, 138.2, 138.5, 146.8, 147.3, 157.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ -28.01; MS (EI): *m/z* (relative intensity) 497 (M^+, 7), 406 (20), 390 (100), 252 (20); HRMS: calcd. for $C_{34}H_{28}NOPH^+$: 498.1987, found 498.2003.

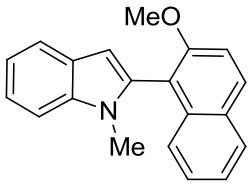
7.4.2.7 Preparation of indolylphosphine ligand **L25**



L25

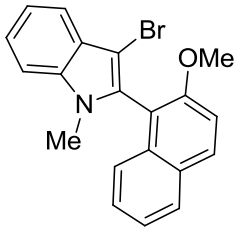
1-(1*H*-Indol-2-yl)naphthalen-2-ol was prepared according to the previous report.[25]

2-(2-Methoxynaphthalen-1-yl)-1-methyl-1*H*-indole



The general procedure for the synthesis of 4-bromo-*N*,*N*-dimethyl-3-(1-methyl-1*H*-indol-2-yl)aniline was followed. 1-(1*H*-indol-2-yl)naphthalen-2-ol (10 mmol) in 15 mL THF, NaH (24.0 mmol) in 10 mL THF and Me_2SO_4 (21.0 mmol) were given the desired product as a white solid (2.78 g, 97%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.50 (s, 3H), 3.90 (s, 3H), 6.61 (s, 1H), 7.20 (t, *J*= 8.0 Hz, 1H), 7.31 (d, *J*= 8.0 Hz, 1H), 7.36-7.45 (m, 4H), 7.63 (t, *J*= 4.0 Hz, 1H), 7.73 (d, *J*= 8.0 Hz, 1H), 7.88 (t, *J*= 8.0 Hz, 1H), 8.01 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.1, 56.5, 103.1, 109.4, 113.1, 119.3, 120.5, 121.0, 123.8, 125.3, 126.9, 127.8, 130.7; MS (EI): *m/z* (relative intensity) 287 (M^+, 100), 270 (15), 254 (18), 228 (15).

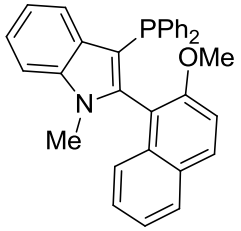
3-Bromo-2-(2-methoxynaphthalen-1-yl)-1-methyl-1*H*-indole



The general procedure for the synthesis of 3-bromo-1,2-dimethyl-1*H*-indole was followed. 2-(2-Methoxynaphthalen-1-yl)-1-methyl-1*H*-indole (9.0 mmol) in 25 mL DMF and *N*-bromosuccinimide (9.5 mmol) in 20 mL DMF were given the desired product as a white solid (3.1 g, 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.54 (s, 3H), 3.93 (s, 3H), 7.31-7.48 (m, 7H), 7.63 (d, *J*= 7.7 Hz, 1H), 7.93-7.95 (m, 1H), 8.05 (d, *J*= 9.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.9. 56.6. 92.0. 109.6, 113.1, 113.2, 113.4, 120.1, 122.3, 124.0, 124.9, 127.2, 127.3, 128.1, 128.8, 131.6, 133.4, 133.8,

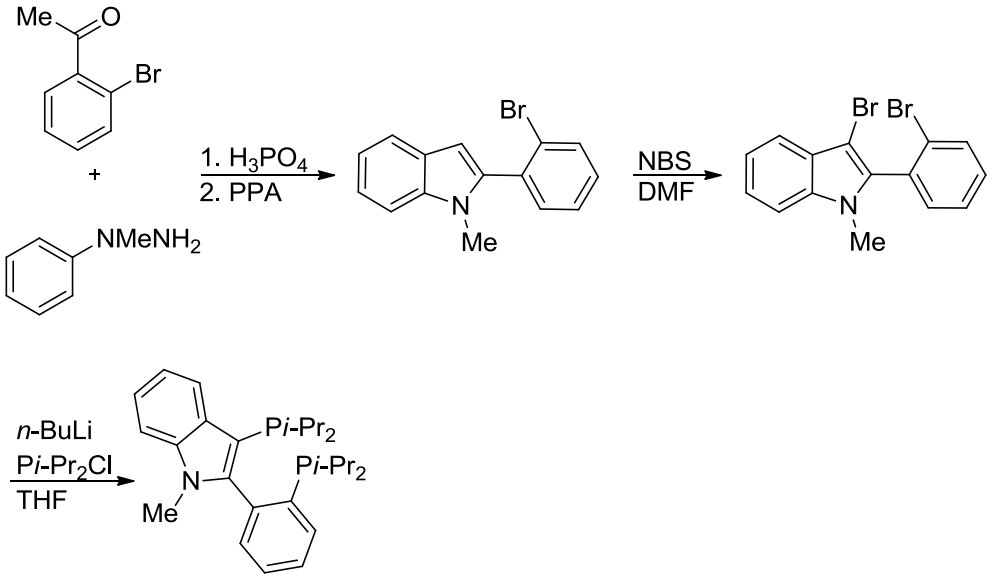
136.7, 156.4; MS (EI): *m/z* (relative intensity) 365 (M^+, 86), 296 (100), 271 (84), 255 (28), 241 (37), 143 (23); HRMS: calcd. for $C_{20}H_{16}NBrOH^+$: 366.0488, found 366.0491.

3-(Diphenylphosphino)-2-(2-methoxynaphthalen-1-yl)-1-methyl-1*H*-indole L25



The general procedure for the synthesis of 2-(2-(dicyclohexylphosphino)phenyl)-1-(methoxymethyl)-1*H*-indole **L3** was followed. 3-Bromo-2-(2-methoxynaphthalen-1-yl)-1-methyl-1*H*-indole (8.5 mmol) in 20 mL THF, *n*-BuLi (9.4 mmol) and PPh_2Cl (10.2 mmol) in 5 mL THF were given the desired product as a white solid (2.8 g, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.55 (s, 3H), 3.69 (s, 3H), 7.07 (t, J= 8.0 Hz, 1H), 7.23 (d, J= 8.0 Hz, 1H), 7.29-7.56 (m, 16H), 7.93 (d, J= 8.0 Hz, 1H), 8.07 (d, J= 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.6, 55.9, 105.0, 109.7, 112.9, 114.3, 119.9, 121.5, 121.7, 123.7, 124.7, 127.1, 127.28, 127.33, 127.78, 127.82, 127.84, 127.88, 128.0, 128.5, 129.7, 129.8, 131.3, 132.3, 132.4, 132.5, 132.6, 134.4, 137.85, 137.92, 138.1, 138.81, 138.84, 144.1, 144.6, 158.2; ^{31}P NMR (162 MHz, $CDCl_3$) δ -27.54; MS (EI): *m/z* (relative intensity) 471 (M^+, 36), 440 (100), 348 (7), 286 (14), 235 (18); HRMS: calcd. for $C_{32}H_{26}NOPH^+$: 472.1825, found 472.1838.

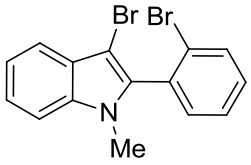
7.4.2.8 Preparation of indolylphosphine ligand **L27**



L27

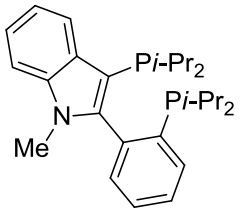
2-(2-Bromophenyl)-1-methyl-1*H*-indole was prepared according to the previous report.[13b]

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



The general procedure for the synthesis of 3-bromo-1,2-dimethyl-1*H*-indole was followed. 2-(2-Bromophenyl)-1-methyl-1*H*-indole (15 mmol) in 20 mL DMF and *N*-bromosuccinimide (16 mmol) in 15 mL DMF were given the desired product as a light yellow solid (2.8 g, 77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.61 (s, 3H),7.28-7.31 (m, 1H), 7.35-7.52 (m, 5H), 7.67-7.69 (m, 1H), 7.78-7.81 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.22, 90.68, 109.69, 119.39, 120.43, 122.90, 125.45, 126.73, 127.39, 130.87, 132.11, 132.89, 133.23, 136.23, 137.06; MS (EI): *m/z* (relative intensity) 365 (M^+, 100), 283 (10), 204 (95); HRMS: calcd. for $C_{15}H_{11}NBr_2^+$: 363.9349, found 363.9337.

3-(Diisopropylphosphino)-2-(2-(diisopropylphosphino)phenyl)-1-methyl-1*H*-indole L27



The general procedure for the synthesis of 2-(2-(dicyclohexylphosphino)phenyl)-1-(methoxymethyl)-1*H*-indole **L3** was followed. 3-Bromo-2-(2-bromophenyl)-1-methyl-1*H*-indole (5.0 mmol) in 15 mL THF, *n*-BuLi (11.0 mmol) and P*i*-Pr_2Cl (12.0 mmol) in 5 mL THF were given the desired product as a white solid (1.51 g, 70%). ^{1}H NMR (400 MHz, C_6D_6) δ 0.86-1.28 (m, 27H), 1.85-2.05 (m, 2H), 2.22-2.34 (m, 1H), 2.77-2.88 (m, 1H), 3.12 (s, 3H), 7.17-7.20 (m, 3H), 7.25-7.29 (m, 3H), 7.40 (d, *J*= 8.0 H, 1H), 7.97 (s, *J*= 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.1, 18.2, 20.2, 20.4, 20.9, 21.1, 21.5, 21.6, 21.7, 21.9, 22.3, 22.4, 22.5, 22.7, 22.9, 23.1, 23.8, 23.9, 25.8, 25.9, 26.7, 26.8, 31.5, 31.6, 84.3, 105.9, 109.9, 119.5, 121.4, 121.8, 127.8, 128.2, 130.3, 131.9, 132.0, 133.6, 137.9, 139.4, 139.5, 139.7, 157.8; ^{31}P NMR (162 MHz, C_6D_6) δ -7.82, -2.47; MS (EI): *m/z* (relative intensity) 438 (M^+, 0), 396 (100), 236 (74); HRMS: calcd. for $C_{27}H_{39}NP_2H^+$: 440.2636, found 440.2622.

7.4.3 General procedures for initial ligands and reaction conditions screening

General procedure for initial ligands screening (Pd catalysts loading equal to 0.5 mol%): Ligand (Pd : L = 1 : 4) was loaded into the Schlenk tube with a Telfon-coated magnetic stir bar. A stock solution of Pd_2dba_3 (0.025 mmol) in freshly distilled 10 mL dioxane (0.5 mol% Pd per 1 mL stock solution) was initially prepared with continuously stirring at room temperature. An array of Schlenk tubes

containing ligands equipped with a Teflon-coated magnetic stir bar were evacuated and backfilled with nitrogen for three times. The corresponding volume of stock solution was transferred to an array of Schlenk tubes *via* syringes. The palladium complex stock solution was stirred for 10 minutes. 4-chlorotoluene (1.0 mmol), pinacol borane (0.22 mL, 1.5 mmol) and NEt_3 (0.42 mL, 3.0 mmol) were loaded into the tube subsequently. Dioxane (2.0 mL) was added into the reaction system with continuous stirring. The Schlenk tube was resealed and placed into a pre-heated oil bath (110 ^{o}C) for 24 h. After completion of the reaction, the tube was allowed to cool down at room temperature. Ethyl acetate (~8.0 mL), dodecane (113 μL, internal standard) and water (~2.0 mL) 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 reaction conditions screening (Pd catalysts loading equal to 1.0 mol%): Pd source (0.005 mmol) and ligand (Pd : L = 1 : 4) were loaded subsequently into the Schlenk tube with a Telfon-coated magnetic stir bar. The Schlenk tube was evacuated and backfilled with nitrogen for three times. Precomplexation was applied by adding freshly distilled solvent (0.5 mL) into the tube. The palladium complex stock solution was stirred for 10 minutes. 4-chlorotoluene (0.5 mmol), pinacol borane (0.11 mL, 0.75 mmol) and base (1.5 mmol) were loaded into the tube subsequently. The solvent (1.0 mL) was added into the reaction system with continuous stirring. The Schlenk tube was resealed and placed into a pre-heated oil bath (reaction temperature as noted in Table 3) for 24 h. After completion of the reaction, the tube was allowed to cool down at room temperature. Ethyl acetate (~8.0 mL), dodecane (113 μL, internal standard) and water (~2.0 mL) were added. The organic layer was subjected to GC analysis. The GC yield

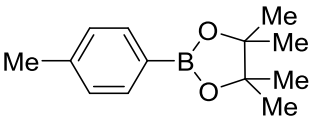
was previously calibrated by authentic sample/dodecane calibration curve.

7.4.3 General procedures for borylation of aryl chlorides

Indolyphosphine ligand **L18** (0.0098 g, 0.02 mmol) and $Pd(dba)_2$ (0.0029 g, 0.005 mmol) were loaded subsequently into the Schlenk tube with a Telfon-coated magnetic stir bar. The Schlenk tube was evacuated and flushed with nitrogen for three times. Precomplexation was applied by adding dioxane (0.5 mL) into the tube. The palladium complex stock solution was stirred for 10 minutes. Tetrabutylammonium iodide (0.2770 g, 0.75 mmol) was added if necessary. Aryl chlorides (0.5 mmol), pinacol borane (0.11 mL, 0.75 mmol) and triethylammine (0.21 mL, 1.5 mmol) were loaded into the tube subsequently. Dioxane (1.0 mL) was added into the reaction system. After continue stirring for another 5 minutes, the tube was put into a pre-heated oil bath (110 ℃) for 18-24 h. After completion of the reaction, the tube was allowed to cool down to room temperature. Ethyl acetate (~8.0 mL), water (~2.0 mL) were added. The organic layers were combined and concentrated. The crude products were purified by column chromatography on silica gel (230-400 mesh).

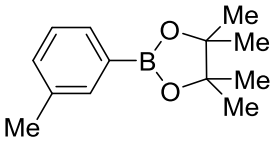
7.4.4 Characterization data for coupling products

4,4,5,5-Tetramethyl-2-(*p*-tolyl)-1,3,2-dioxaborolane (Table 7.3, Entry 1)[12j]



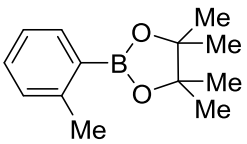
Eluents (Ethyl acetate: Hexane= 1: 50, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (s, 12H), 2.39 (s, 3H), 7.22 (d, *J*= 7.6 Hz, 2H), 7.75 (d, *J*= 7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 24.8, 83.5, 128.5, 134.8, 141.3; MS (EI): *m/z* (relative intensity) 218.1 (M^+, 21), 203.1 (31), 132.1 (59), 119.0 (100), 91.0 (13), 65.0 (5), 41.1 (21).

4,4,5,5-Tetramethyl-2-(*m*-tolyl)-1,3,2-dioxaborolane (Table 7.3, Entry 2)[12j]



Eluents (Ethyl acetate: Hexane= 1: 50, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (s, 12H), 2.39 (s, 3H), 7.30 (d, *J*= 4.9 Hz, 2H), 7.65 (t, *J*= 3.9 Hz, 1H), 7.68 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 24.8, 83.6, 127.6, 11.8, 132.0, 135.3, 137.1; MS (EI): *m/z* (relative intensity) 218.1 (M^+, 30), 203.1 (39), 161.1(9), 132.1 (79), 119.1 (100), 91.1 (14) 41.1 (7).

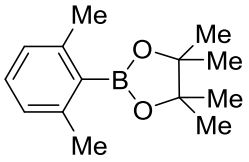
4,4,5,5-Tetramethyl-2-(*o*-tolyl)-1,3,2-dioxaborolane (Table 7.3, Entry 3)[12j]



Eluents (Ethyl acetate: Hexane= 1: 50, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38 (s, 12H), 2.58 (s, 3H), 7.18-7.21

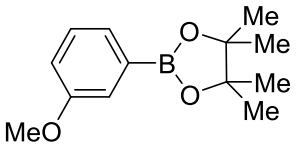
(m, 2H), 7.35 (t, *J*= 7.6 Hz, 1H), 7.81 (d, *J*= 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.2, 24.9, 83.3, 124.7, 129.7130.7, 135.8, 144.8; MS (EI): *m/z* (relative intensity) 218.1 (M^+, 15), 203.1 (26), 161.1(79), 132.1 (13), 119.1 (100), 91.1 (16), 41.1 (7).

2-(2,6-Dimethylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Table 7.3, Entry 4)[12j]



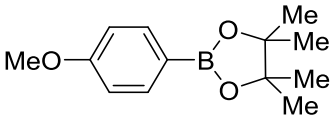
Eluents (Ethyl acetate: Hexane= 1: 50, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39 (s, 12H), 2.40 (s, 6H), 6.94 (d, *J*= 7.6 Hz, 2H), 7.13 (t, *J*= 7.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.2, 25.0, 83.6, 126.4, 141.7; MS (EI): *m/z* (relative intensity) 232.1 (M^+, 22), 175.1 (100), 132.0 (74), 117.0 (13), 105.0 (16), 91.0 (20), 43.0 (20), 28.1 (82).

2-(3-Methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Table 7.3, Entry 5)[26]



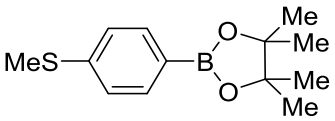
Eluents (Ethyl acetate: Hexane= 1: 20, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 12H), 3.84 (s, 3H), 7.02 (d, *J*= 8.2 Hz, 1H), 7.31 (t, *J*= 7.4 Hz, 1H), 7.35 (s, 1H), 7.43 (d, *J*= 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.8, 55.2, 83.8, 117.8, 118.7, 127.1, 128.9, 159.0; MS (EI): *m/z* (relative intensity) 234.1 (M^+, 66), 219.1 (28), 148.1 (87), 134.0 (100), 104.0 (12), 91.0 (11), 77.0 (9), 41.1 (9).

2-(4-Methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Table 7.3, Entry 6)[26]



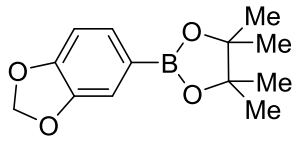
Eluents (Ethyl acetate: Hexane= 1: 20, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 12H), 3.82 (s, 3H), 6.91 (d, *J*= 8.7 Hz, 2H), 7.78 (d, *J*= 8.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.8, 55.0, 83.5, 113.2, 136.5, 162.1; MS (EI): *m/z* (relative intensity) 234.1 (M^+, 53), 219.1 (33), 148.1 (45), 134.0 (100), 104.0 (9), 91.0 (7), 77.0 (7), 41.1 (6).

4,4,5,5-Tetramethyl-2-(4-(methylthio)phenyl)-1,3,2-dioxaborolane (Table 7.3, Entry 7)[27]



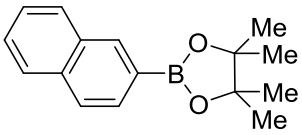
Eluents (Ethyl acetate: Hexane= 1: 20, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 2.49 (s, 3H), 7.23 (d, *J*= 8.4 Hz, 2H), 7.72 (d, *J*= 8.3Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.0, 24.8, 83.7, 124.9, 135.0, 142.5; MS (EI): *m/z* (relative intensity) 250.1 (M^+, 71), 235.1 (18), 164.0 (27), 150.0 (100), 136.0 (10), 117.0 (10), 43.1 (9), 28.1 (9).

2-(Benzo[d][1,3]dioxol-5-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Table 7.3, Entry 8)[27]



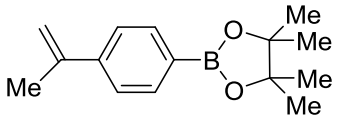
Eluents (Ethyl acetate: Hexane= 1: 20, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (s, 12H), 5.94 (s, 2H), 6.83 (d, *J*= 7.7 Hz, 1H), 7.25 (s, 1H), 7.37 (d, *J*= 7.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.8, 83.6, 100.7, 108.2, 113.9, 129.7, 147.1, 150.1; MS (EI): *m/z* (relative intensity) 248.1 (M^+, 87), 233.1 (29), 162.1 (70), 148.1 (100), 116.8 (8), 91.0 (11), 41.1 (11).

4,4,5,5-Tetramethyl-2-(naphthalen-2-yl)-1,3,2-dioxaborolane (Table 7.3, Entry 9)[12j]



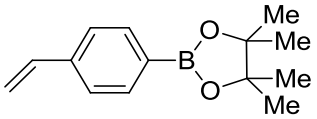
Eluents (Ethyl acetate: Hexane= 1: 50, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42 (s, 12H), 7.48-7.56 (m, 2H), 7.85-7.93 (m, 4H), 8.43 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.9, 83.9, 125.8, 127.0, 127.0, 127.7, 128.6, 130.4, 132.8, 135.0, 136.2; MS (EI): *m/z* (relative intensity) 254.1 (M^+, 36), 239.1 (9), 168.1 (66), 154.1 (100), 127.0 (7), 41.1 (5).

4,4,5,5-Tetramethyl-2-(4-(prop-1-en-2-yl)phenyl)-1,3,2-dioxaborolane (Table 7.3, Entry 10)[28]



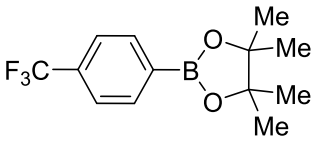
Eluents (Ethyl acetate: Hexane= 1: 50, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 12H), 2.17 (s, 3H), 5.13 (s, 2H), 7.48 (d, *J*= 8.3 Hz, 2H), 7.80 (d, *J*= 8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 24.8, 83.7, 1132, 124.8, 134.8, 143.2, 144.0; MS (EI): *m/z* (relative intensity) 244.1 (M^+, 59), 229.1 (34), 158.1 (90), 145.1 (100), 129.0 (10), 115.0 (19), 85.1 (10), 77.0 (15), 41.1 (14), 28.1 (13).

4,4,5,5-Tetramethyl-2-(4-vinylphenyl)-1,3,2-dioxaborolane (Table 7.3, Entry 11)[27]



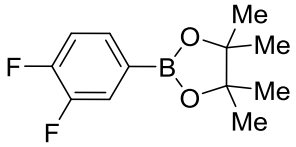
Eluents (Ethyl acetate: Hexane= 1: 50, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 12H), 5.30 (d, *J*= 10.9 Hz, 1H), 5.82 (d, *J*= 17.6 Hz, 1H), 6.70-6.77 (m, 1H), 7.42 (d, *J*= 8.0 Hz, 2H), 7.78 (d, *J*= 8.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.8, 83.7, 114.8, 125.5, 135.0, 136.8, 140.2; MS (EI): *m/z* (relative intensity) 230.1 (M^+, 41), 215.1 (33), 144.1 (77), 130.0 (100), 103.0 (9), 85.1 (10), 77.0 (15), 43.1 (15), 28.1 (19).

4,4,5,5-Tetramethyl-2-(4-(trifluoromethyl)phenyl)-1,3,2-dioxaborolane (Table 7.4, Entry 1 and 2)[12j]



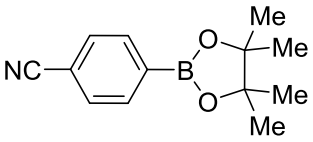
Eluents (Ethyl acetate: Hexane= 1: 50, R_f= 0.50) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 12H), 7.62 (d, *J*= 7.7 Hz, 2H), 7.92 (d, *J*= 7.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.8, 84.3, 124.1 (q, *J*= 270 Hz), 124.3 (q, *J*= 3.0 Hz), 132.8 (q, J= 32.0 Hz), 135.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.0 (s, 3F); MS (EI): *m/z* (relative intensity) 272.1 (M^+, 6), 257.1 (95), 229.1 (9), 186.1 (94), 173.0 (100), 154.0 (9), 142.2 (9), 85.1 (19), 58.1 (25), 43.1 (42), 28.1 (23).

2-(3,4-Difluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Table 7.4, Entry 3)[29]



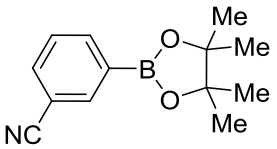
Eluents (Ethyl acetate: Hexane= 1: 50, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 7.11-7.17 (m, 1H), 7.51-7.61 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.8, 84.2, 116.9 (d, *J*= 16.0 Hz), 123.3 (d, *J*= 15.0 Hz), 128.4 (d, *J*= 12.0 Hz), 131.4 (dd, *J*= 6.0 Hz, 4.0 Hz), 152.6 (dd, *J*= 251 Hz, 12 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -139.5 (d, *J*= 18.8 Hz, 1F), -133.9 (d, *J*= 18.8 Hz, 1F); MS (EI): *m/z* (relative intensity) 240.2 (M^+, 22), 225.2 (100), 197.1 (9), 154.1 (66), 141.1 (87), 85.1 (13), 75.1 (5), 58.1 (13), 43.1 (17).

4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (Table 7.4, Entry 4 and 5)[12j]



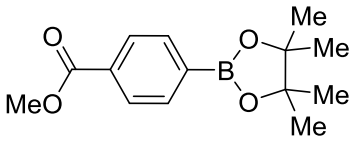
Eluents (Ethyl acetate: Hexane= 1: 20, R_f= 0.30) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 7.62 (d, *J*= 8.3 Hz, 2H), 7.87 (d, *J*= 8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.8, 84.4, 114.5, 118.8, 131.0, 135.0; MS (EI): *m/z* (relative intensity) 229.1 (M^+, 8), 214.1 (100), 186.1 (13), 172.0 (6), 143.1 (100), 130.0 (69), 103.0 (13), 85.1 (16), 58.1 (27), 43.1 (41), 28.1 (26).

3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (Table 7.4, Entry 6)[12j]



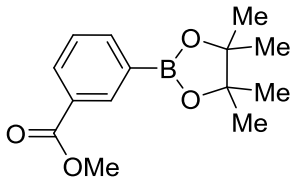
Eluents (Ethyl acetate: Hexane= 1: 20, R_f= 0.30) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 7.45 (t, *J*= 7.6 Hz, 1H), 7.70 (d, *J*= 7.8 Hz, 1H), 8.00 (d, *J*= 7.5 Hz, 1H), 8.08 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.8, 84.4, 128.3, 134.3, 138.3, 138.7; MS (EI): *m/z* (relative intensity) 229.1 (M^+, 19), 214.1 (94), 143.1 (100), 130.1 (61).

Methyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (Table 7.4, Entry 7)[12j]



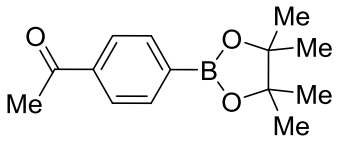
Eluents (Ethyl acetate: Hexane= 1: 20, R_f= 0.30) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 12H), 3.90 (s, 3H), 7.86 (d, *J*= 8.2 Hz, 2H), 8.01 (d, *J*= 8.3Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.8, 52.0, 84.1, 128.5, 132.2, 134.6, 167.0; MS (EI): *m/z* (relative intensity) 262.1 (M^+, 16), 247.2 (69), 231.2 (16), 177.1 (89), 163.1 (100), 131.1 (17), 103.1 (17), 85.1 (11), 59.1 (8), 43.1 (10).

Methyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (Table 7.4, Entry 8)[12j]



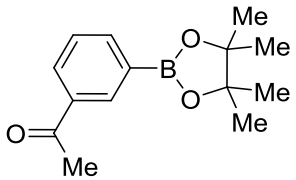
Eluents (Ethyl acetate: Hexane= 1: 20, R_f= 0.30) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 12H), 3.92 (s, 3H), 7.45 (t, *J*= 7.6 Hz, 1H), 7.98 (d, *J*= 6.8 Hz, 1H), 8.13 (d, *J*= 7.9 Hz, 1H), 8.47 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.9, 52.0, 84.1, 127.8, 129.6, 132.2, 35.8, 139.1, 167.1; MS (EI): *m/z* (relative intensity) 262.1 (M^+, 10), 247.1 (27), 231.1 (14), 219.1 (100), 163.1 (79), 131.0 (29), 103.1 (29).

1-(4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethan-1-one (Table 7.4, Entry 9 and 10)[12j]



Eluents (Ethyl acetate: Hexane= 1: 20, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38 (s, 12H), 2.63 (s, 3H), 7.90-7.96 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.7, 26.6, 84.1, 127.1, 134.8, 138.9; MS (EI): *m/z* (relative intensity) 246.1 (M^+, 21), 231.2 (100), 203.1 (8), 189.1 (12), 160.1 (41), 147.1 (98), 131.0 (24), 103.0 (16), 85.1 (12), 59.1 (7), 43.1 (22).

1-(3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethan-1-one (Table 7.4, Entry 11)[28]



Eluents (Ethyl acetate: Hexane= 1: 20, R_f= 0.40) was used for flash column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 12H), 2.63 (s, 3H), 7.47 (t, *J*= 7.4 Hz, 1H), 8.00 (d, *J*= 7.3 Hz, 1H), 8.06 (d, *J*= 7.8 Hz, 1H), 8.37 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.8, 84.1, 128.0, 130.7, 134.8, 136.4, 139.4; MS (EI): *m/z* (relative intensity) 246.1 (M^+, 9), 231.1 (94), 203.0 (49), 185.0 (14), 160.0 (16), 147.0 (100), 131.0 (32), 103.0 (23), 85.0 (18), 59.0 (12), 43.0 (61), 28.0 (21).

7.5 References

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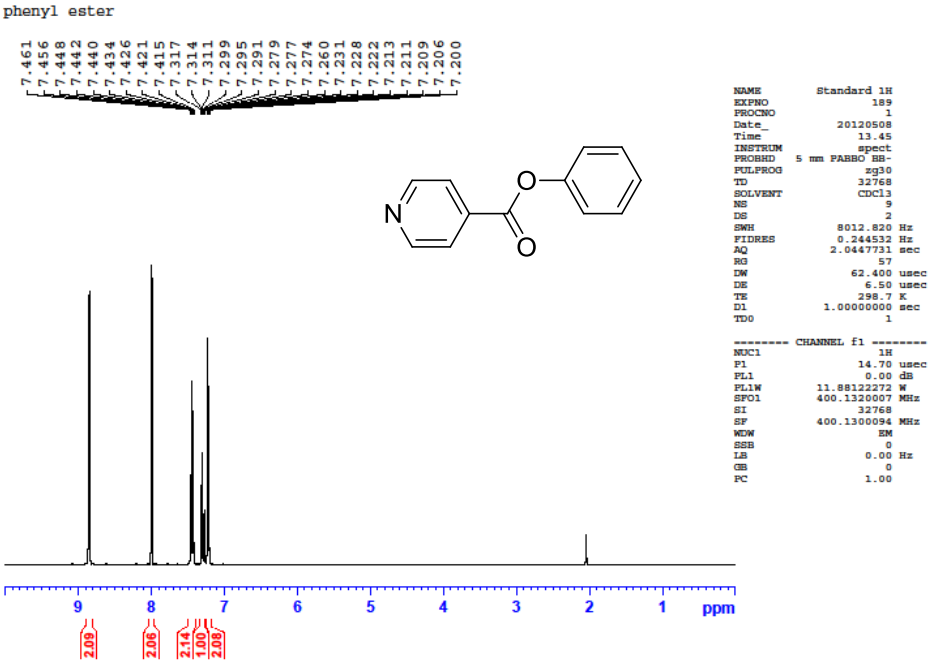
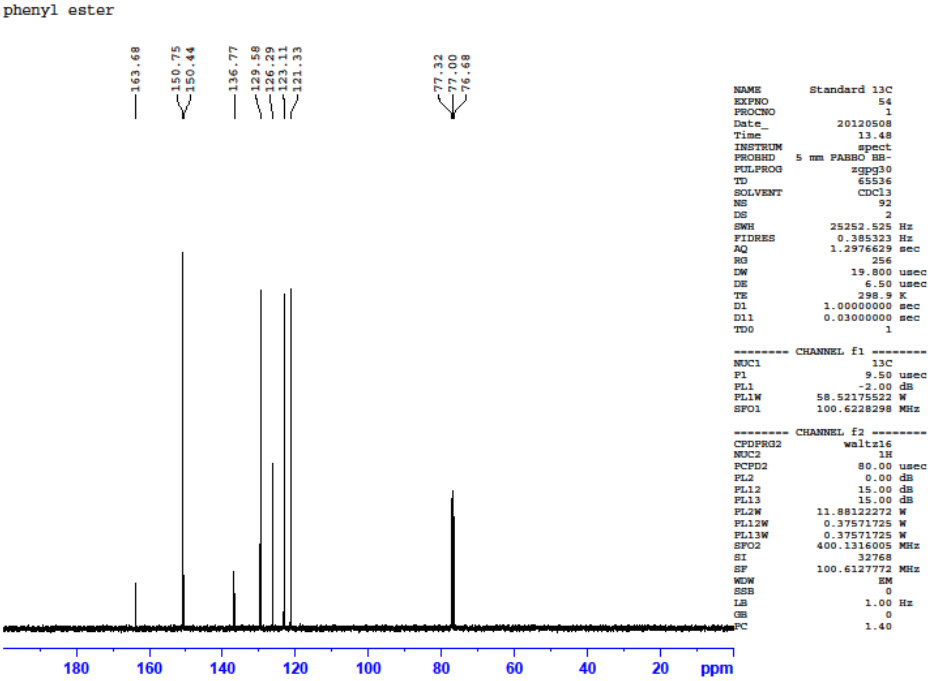
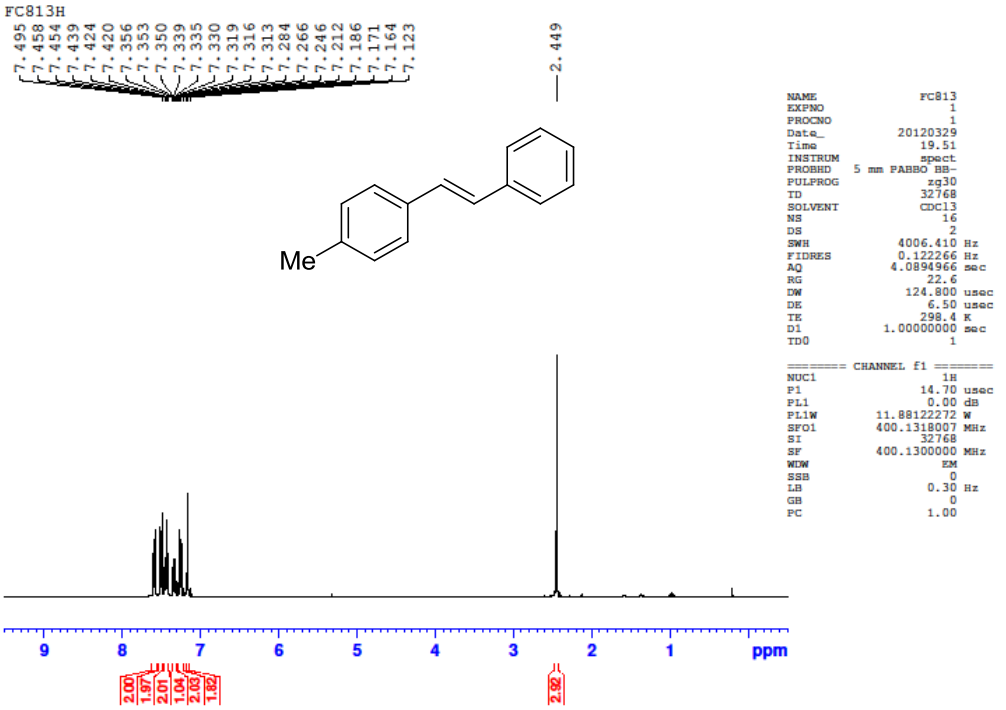
Appendix

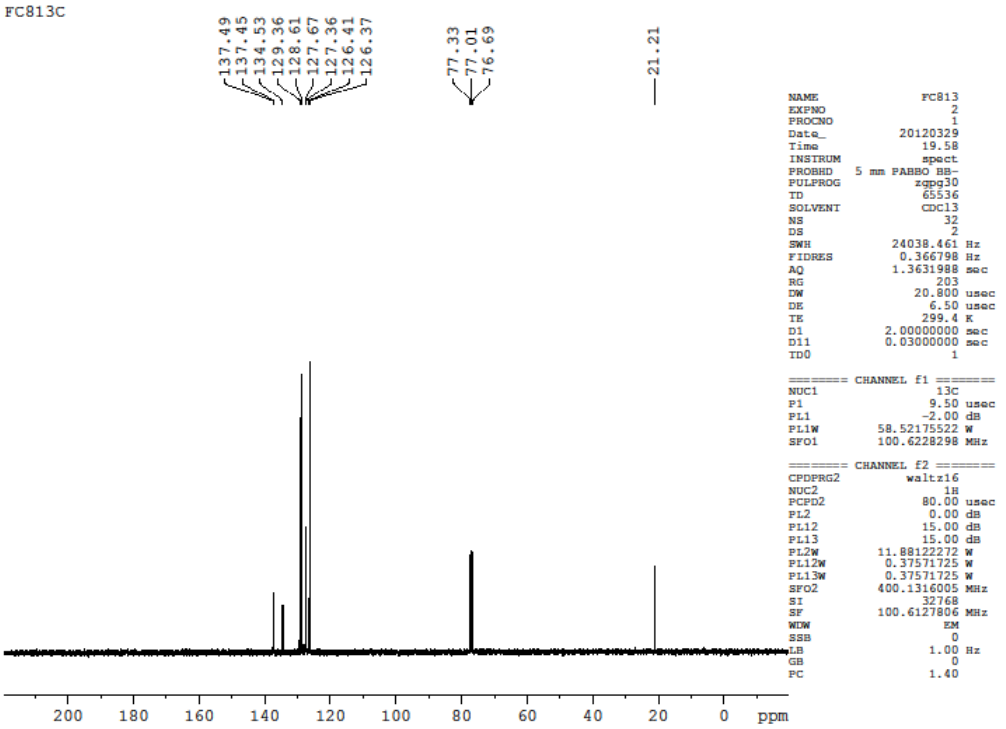
Phenyl isonicotinate (Table 2.2, L9)



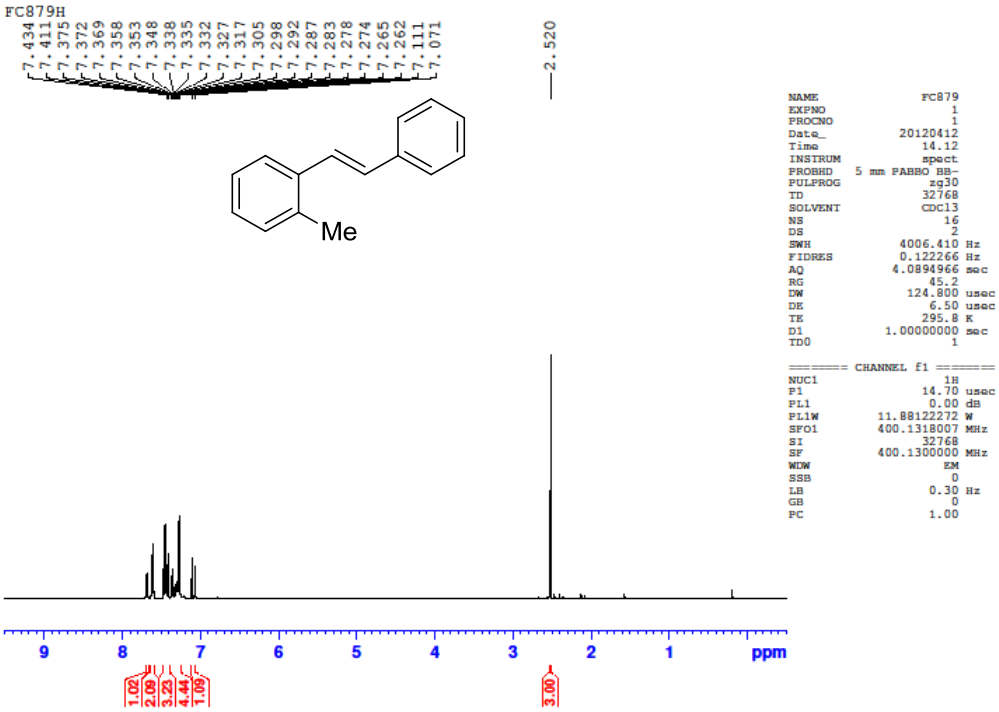


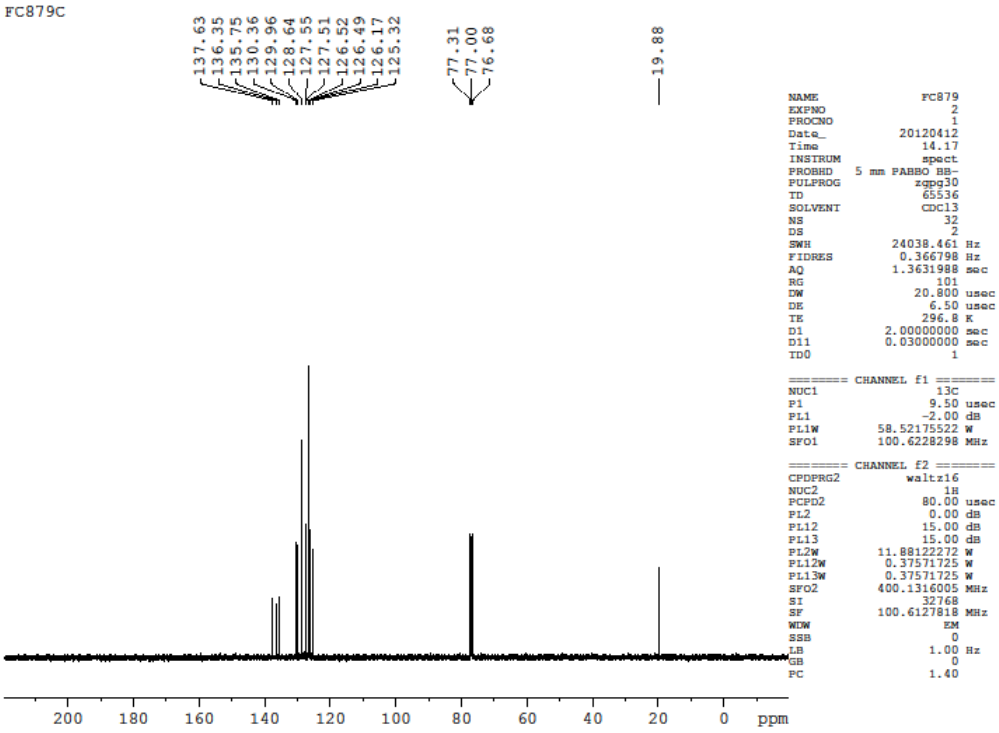
Benzene, 1-methyl-4-[(1*E*)-2-phenylethenyl]- (Table 2.3, compound 3ak)



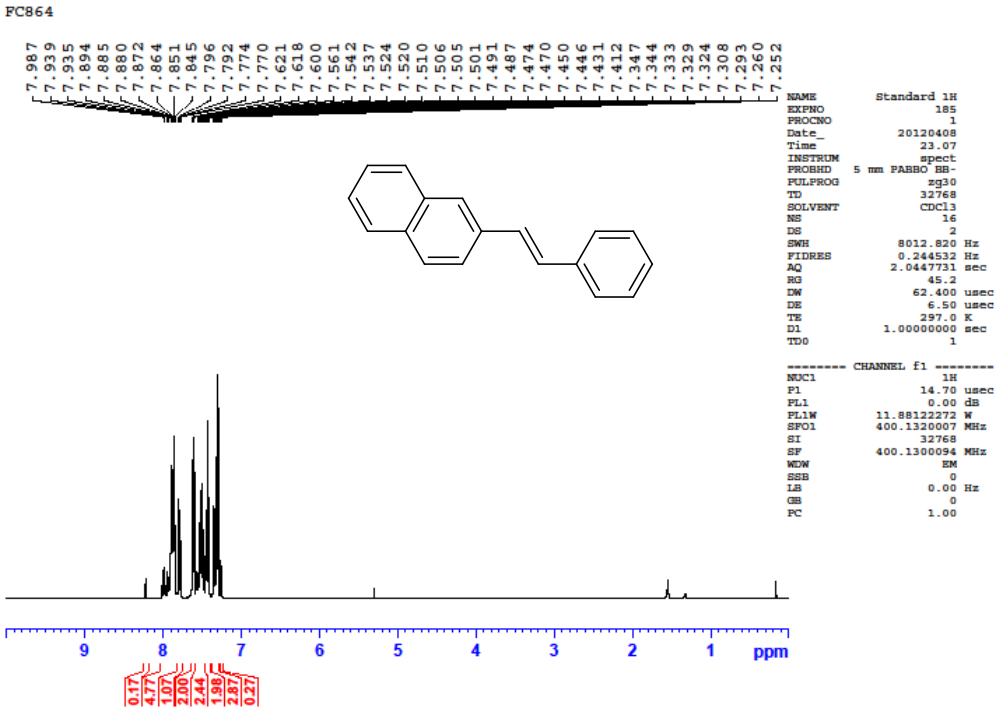


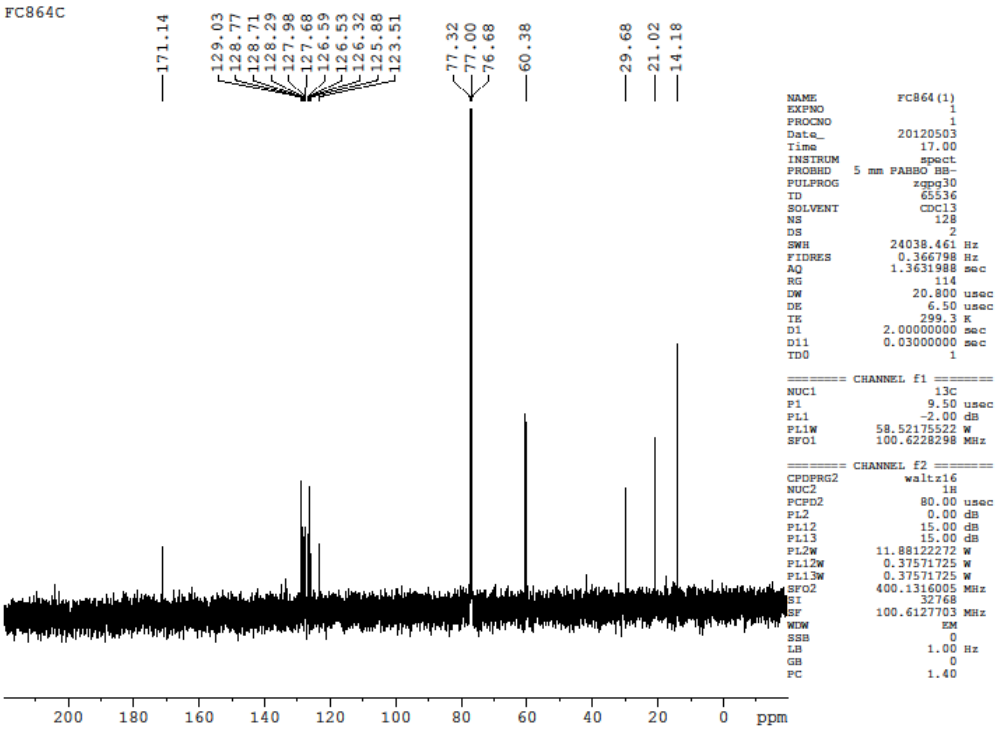
Benzene, 1-methyl-2-[(1*E*)-2-phenylethenyl]- (Table 2.3, compound 3bk)



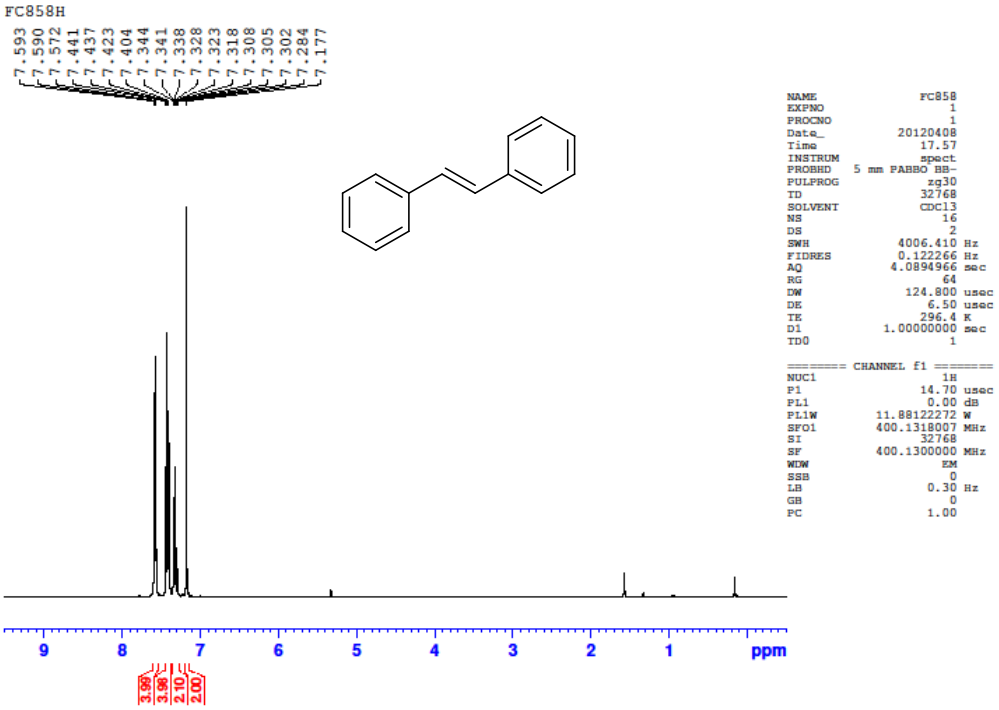


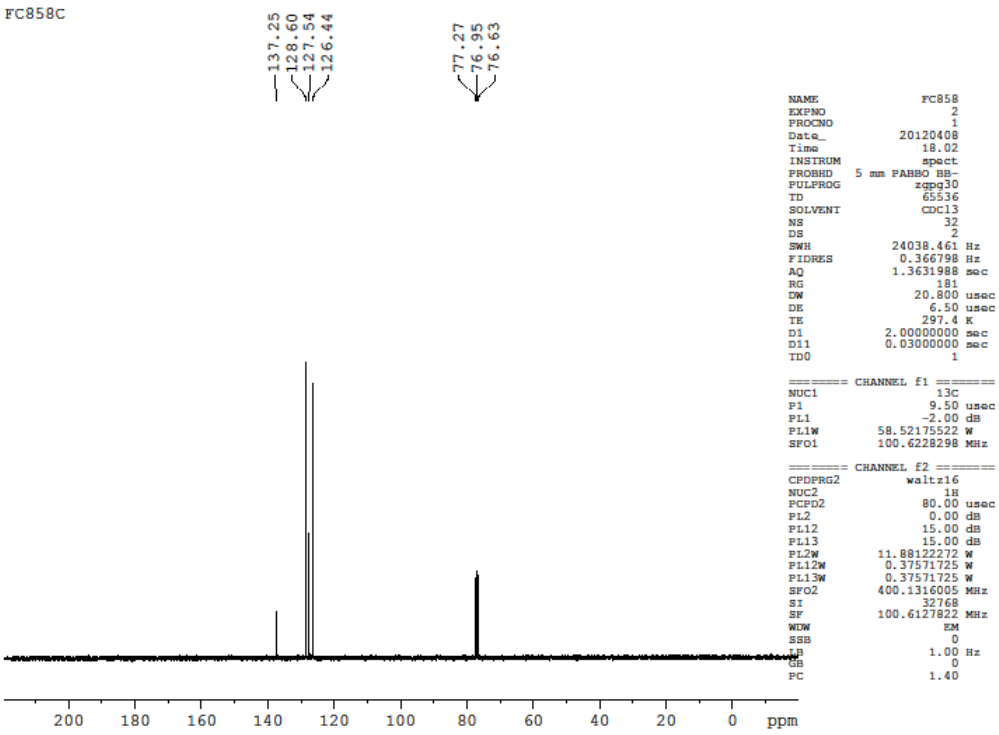
Naphthalene, 2-[(1*E*)-2-phenylethenyl]- (Table 2.3, compound 3ck)



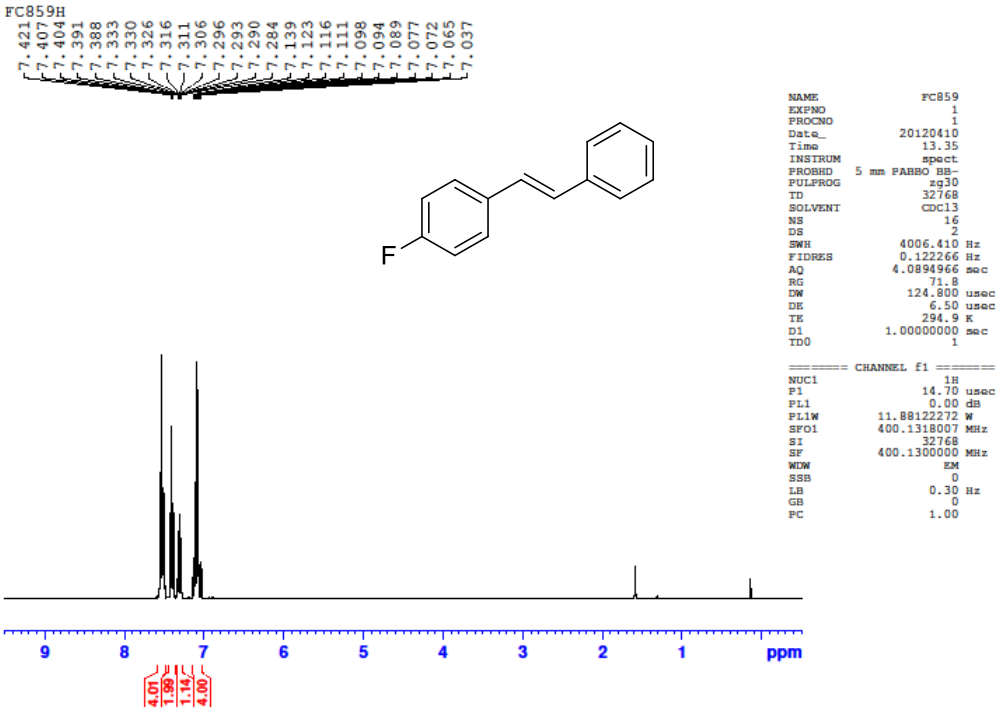


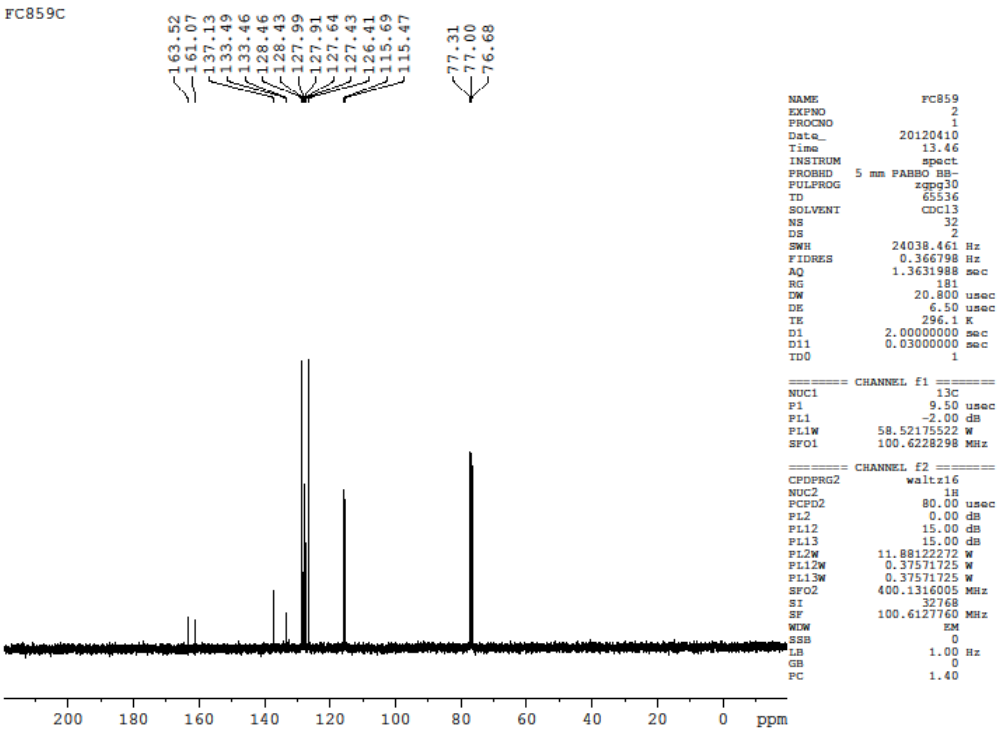
Benzene, 1,1'-(1*E*)-1,2-ethenediylbis- (Table 2.3, compound 3dk)



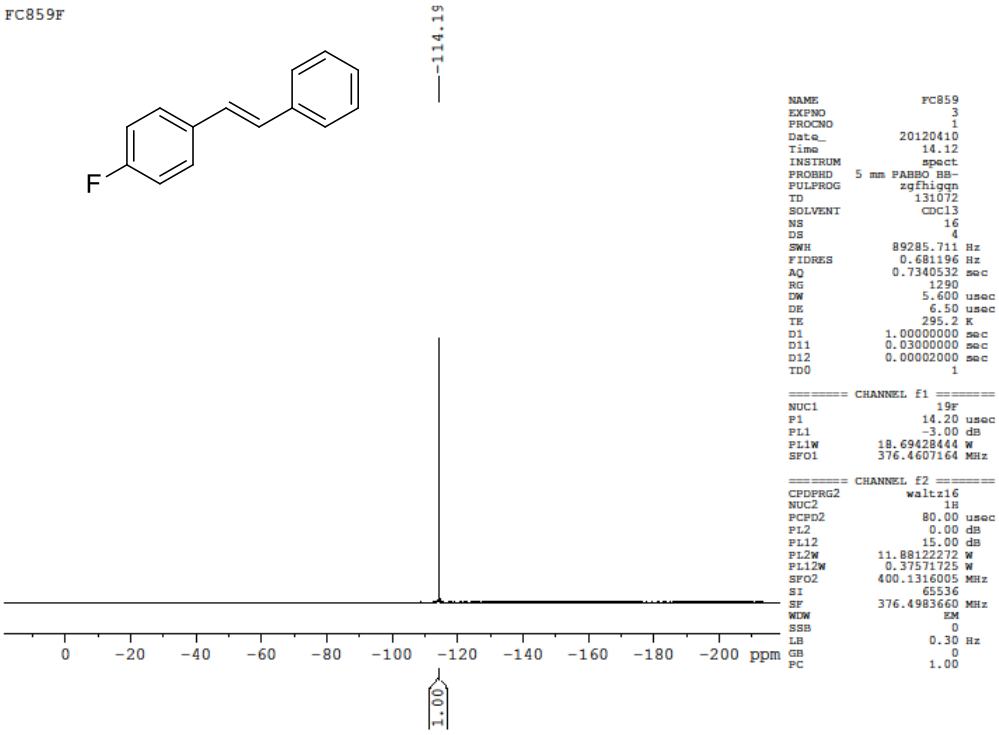


Benzene, 1-fluoro-4-[(1*E*)-2-phenylethenyl]- (Table 2.3, compound 3ek)

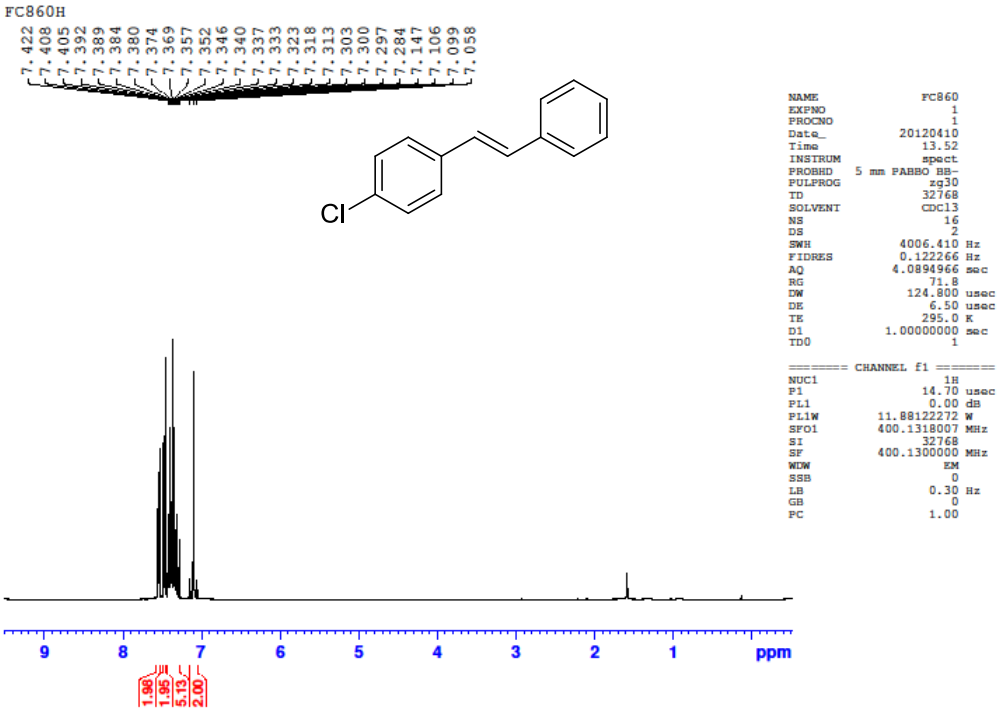


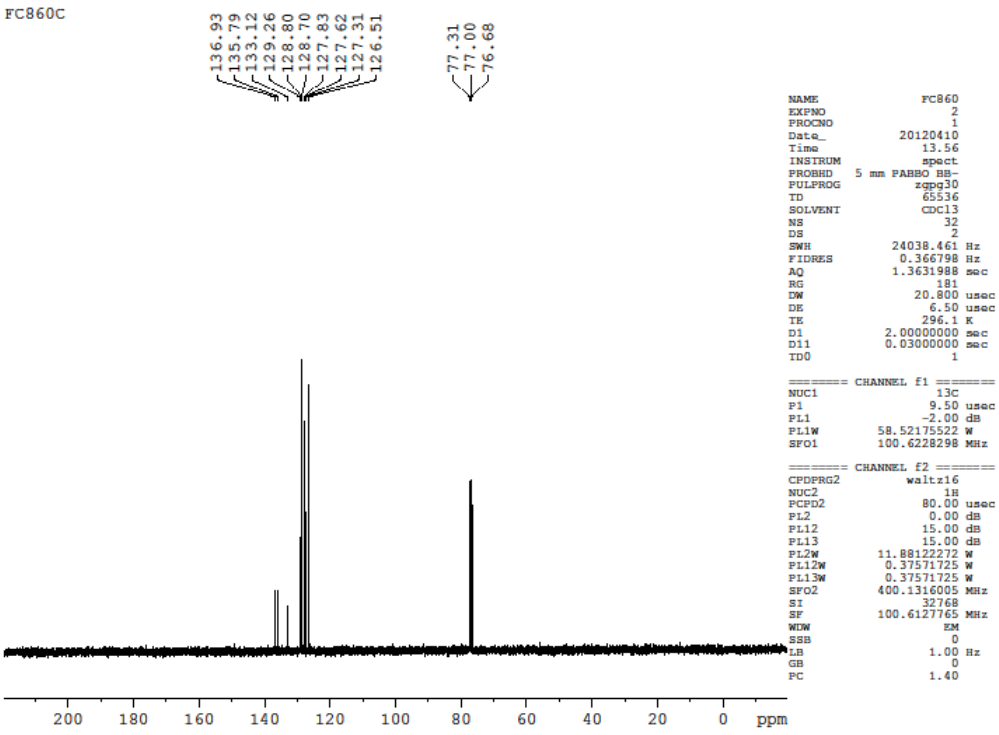


Benzene, 1-fluoro-4-[(1*E*)-2-phenylethenyl]- (Table 2.3, compound 3ek)

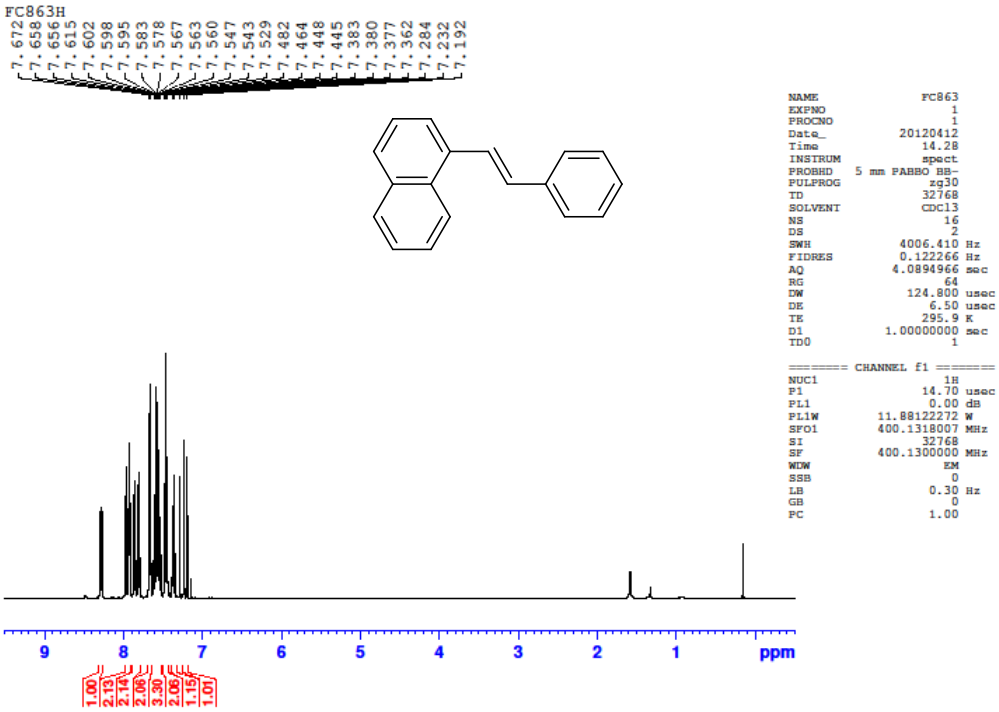


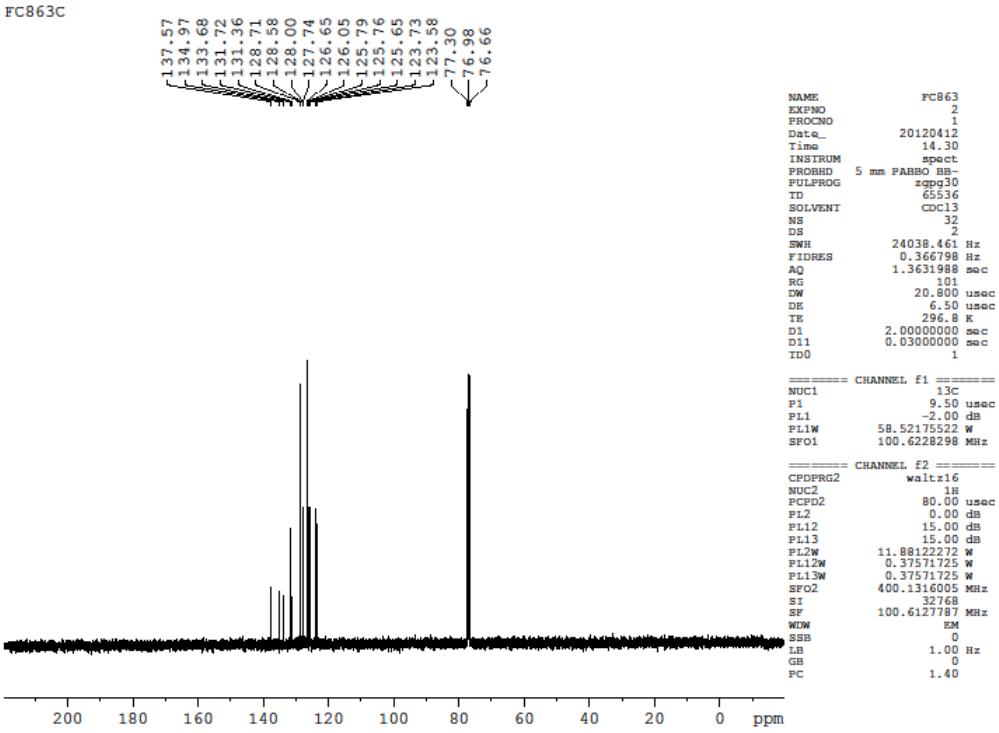
Benzene, 1-chloro-4-[(1*E*)-2-phenylethenyl]- (Table 2.3, compound 3fk)



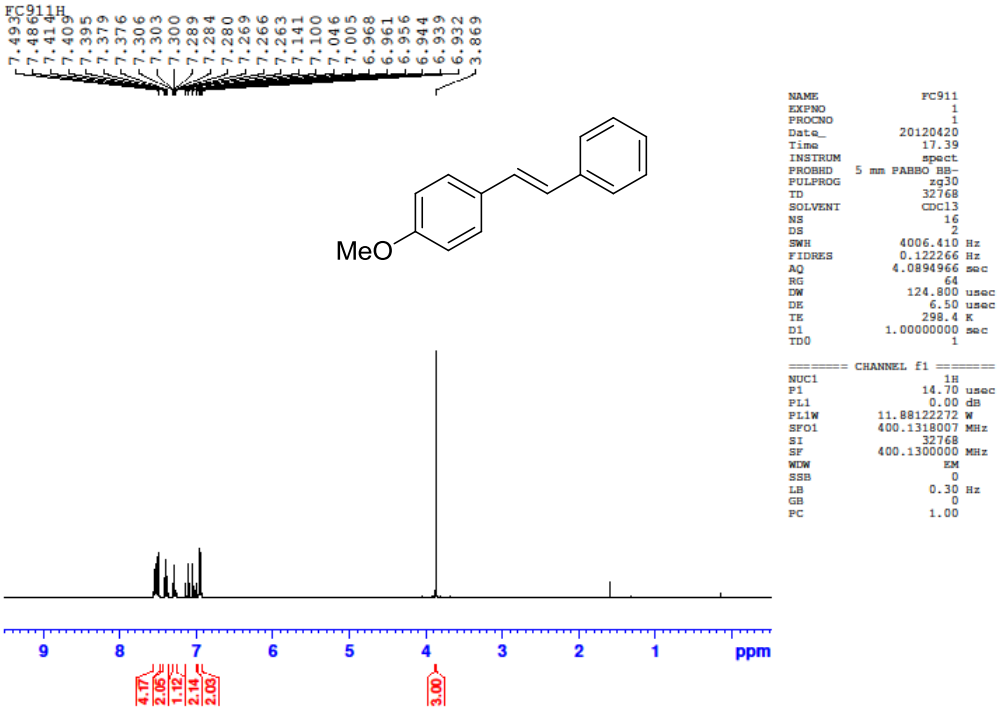


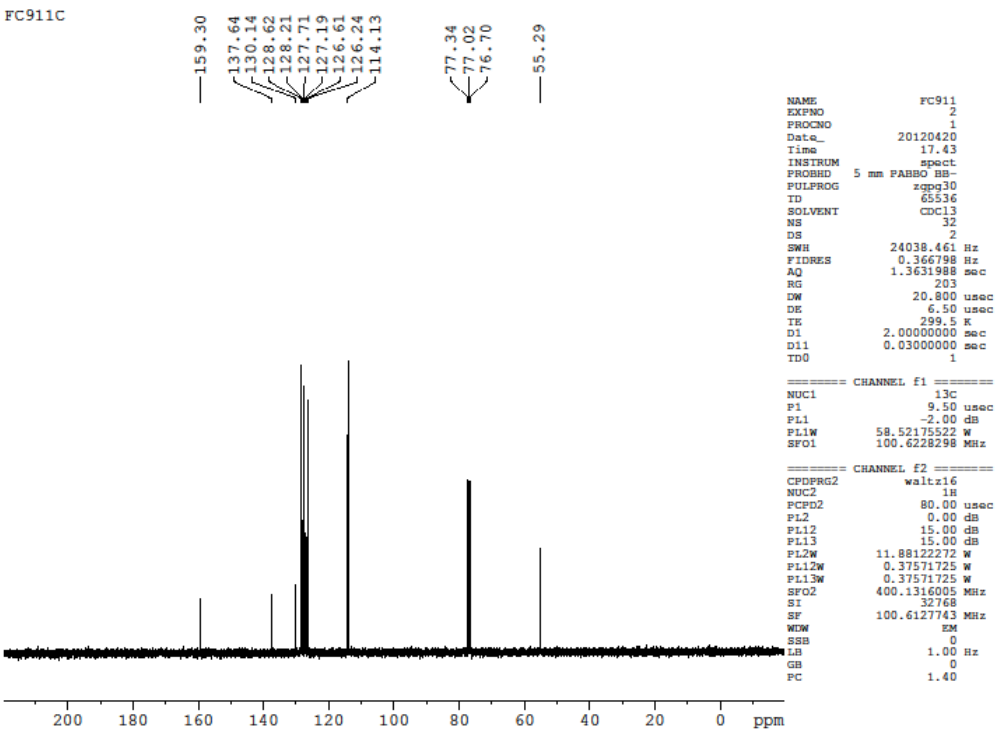
Naphthalene, 1-[(1*E*)-2-phenylethenyl]- (Table 2.3, compound 3gk)



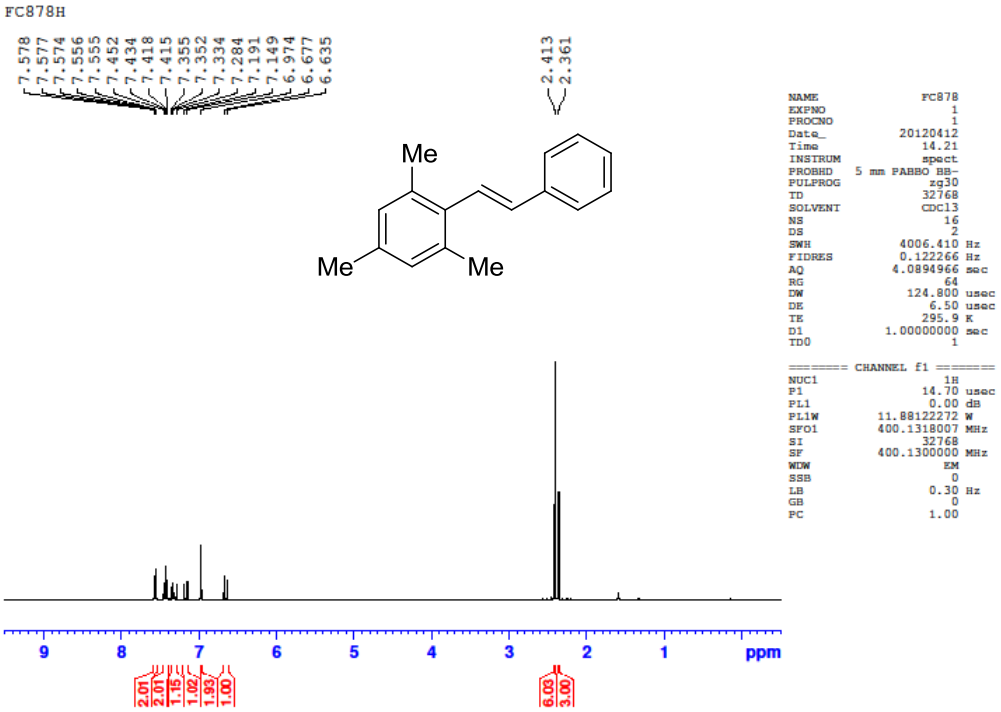


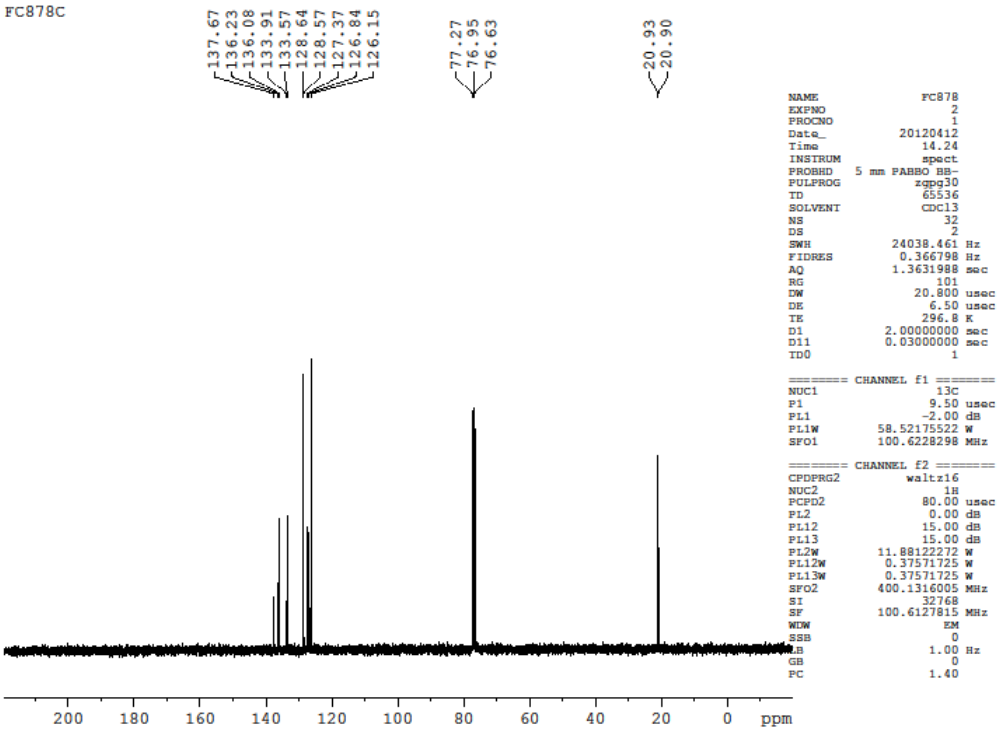
Benzene, 1-methoxy-4-[(1*E*)-2-phenylethenyl]- (Table 2.3, compound 3hk)



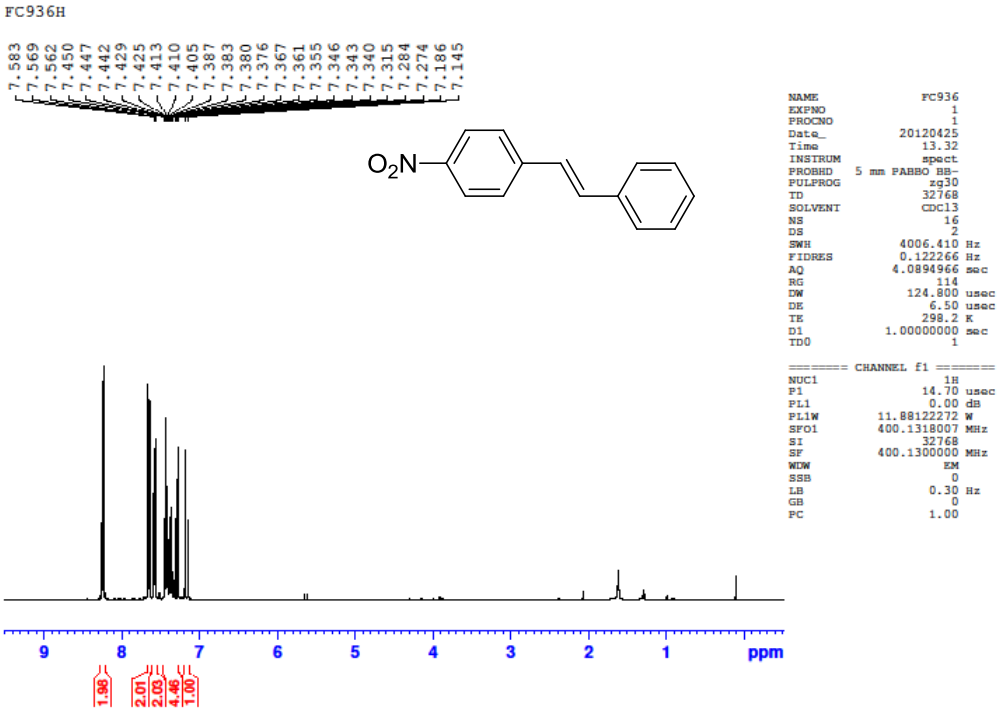


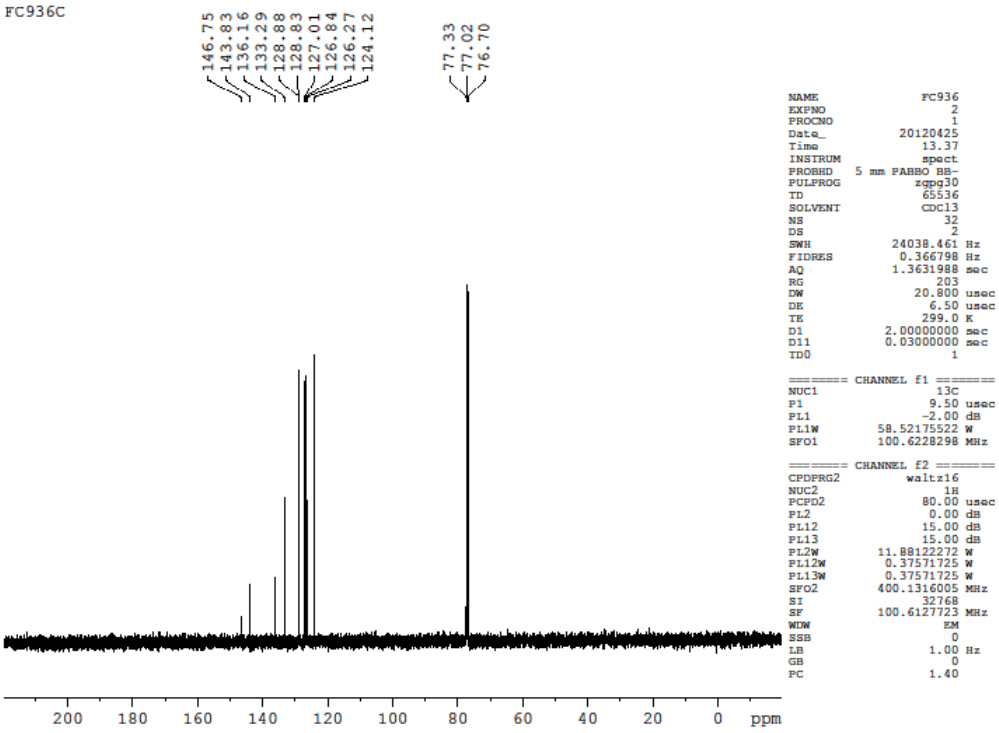
Benzene, 1,3,5-trimethyl-2-[(1*E*)-2-phenylethenyl]- (Table 2.3, compound 3ik)



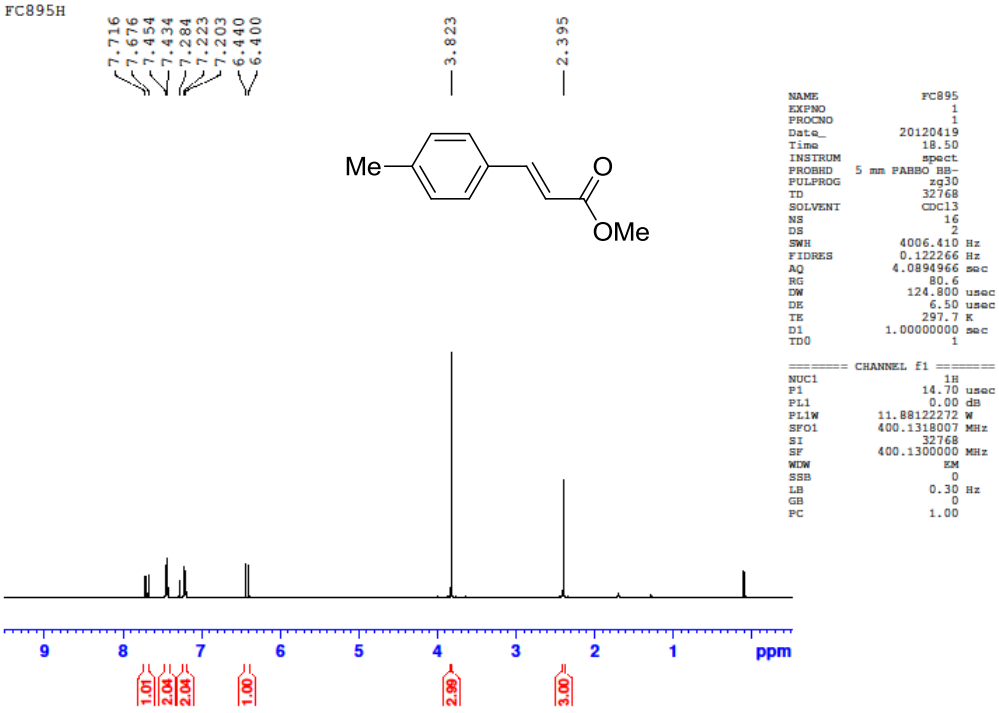


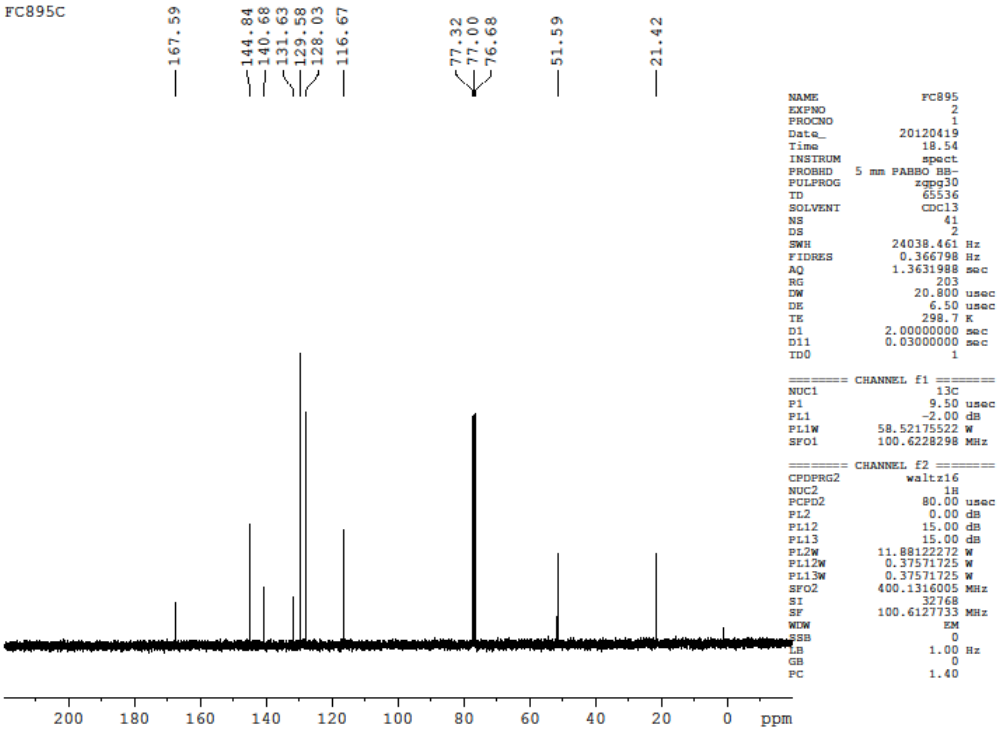
Benzene, 1-nitro-4-[(1*E*)-2-phenylethenyl]- (Table 2.3, compound jk)



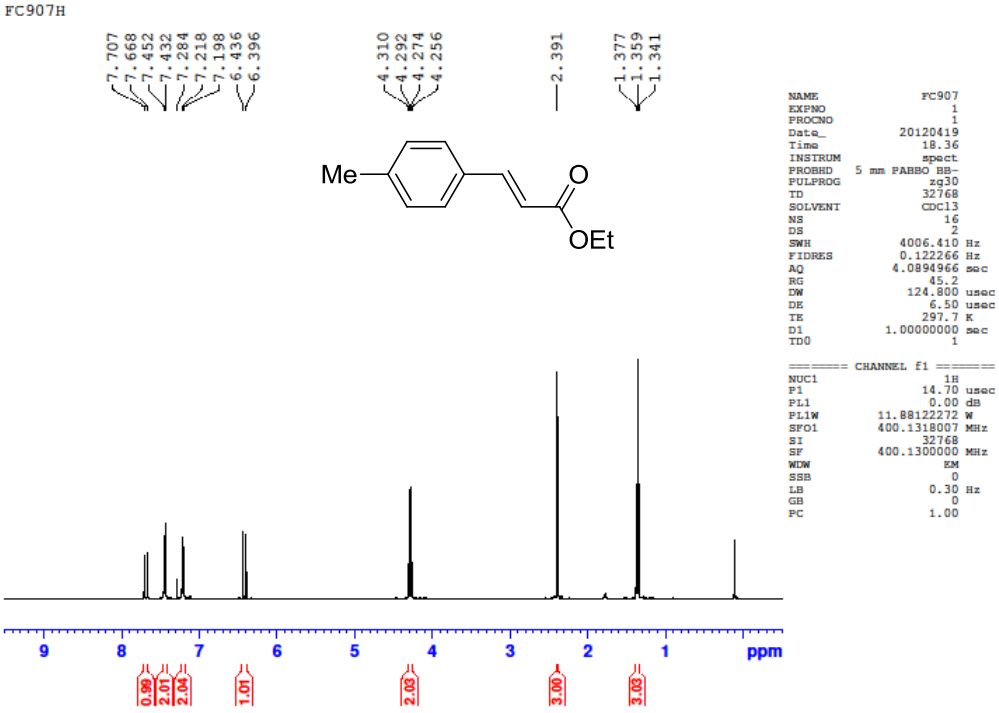


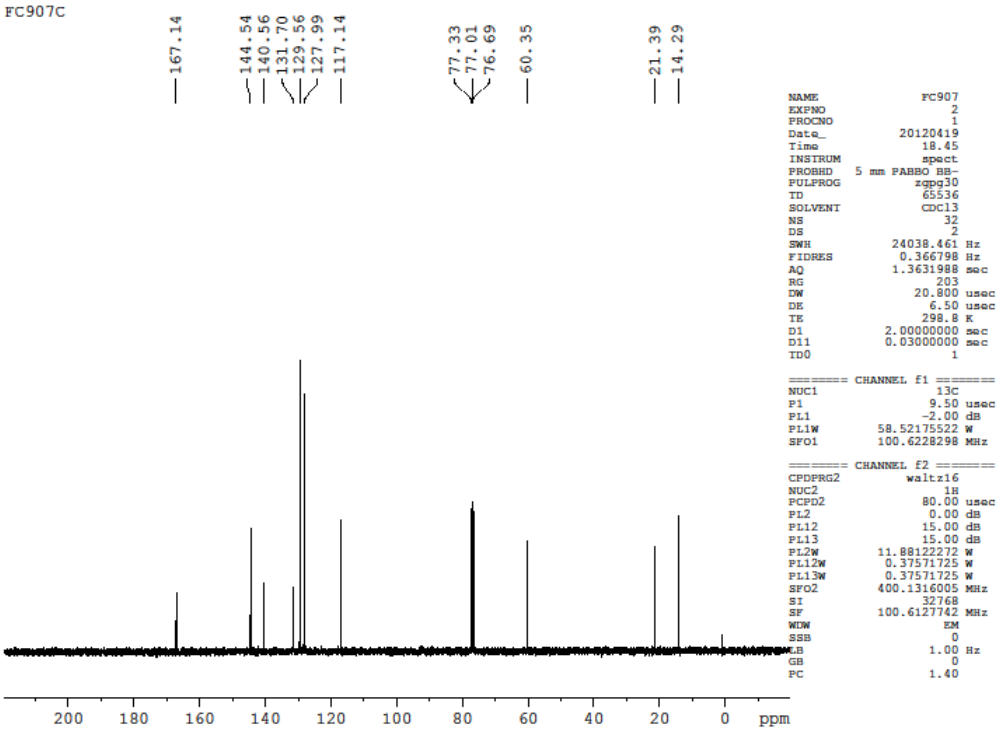
2-Propenoic acid, 3-(4-methylphenyl)-, methyl ester, (2*E*)- (Table 2.3, compound 3al)



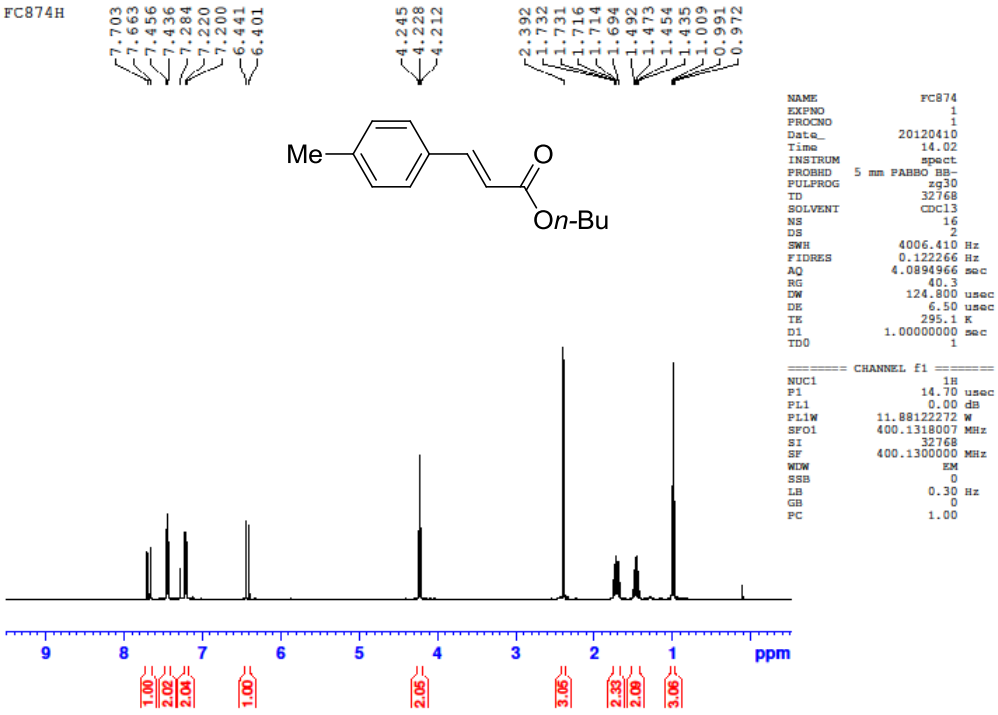


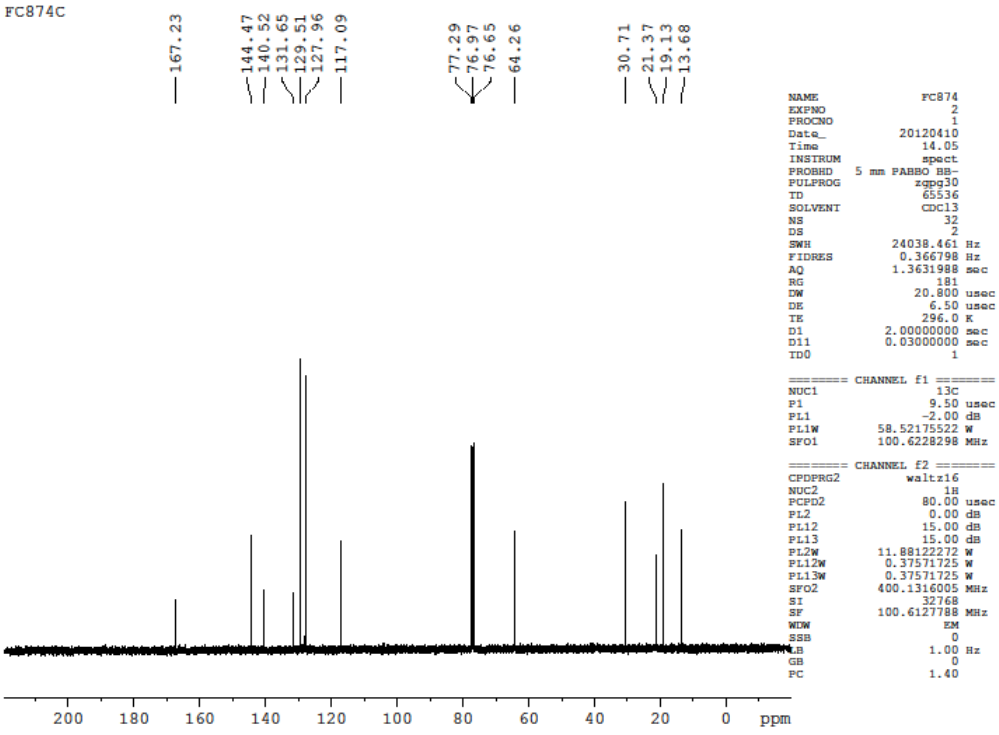
2-Propenoic acid, 3-(4-methylphenyl)-, ethyl ester, (2*E*)- (Table 2.3, compound 3am)



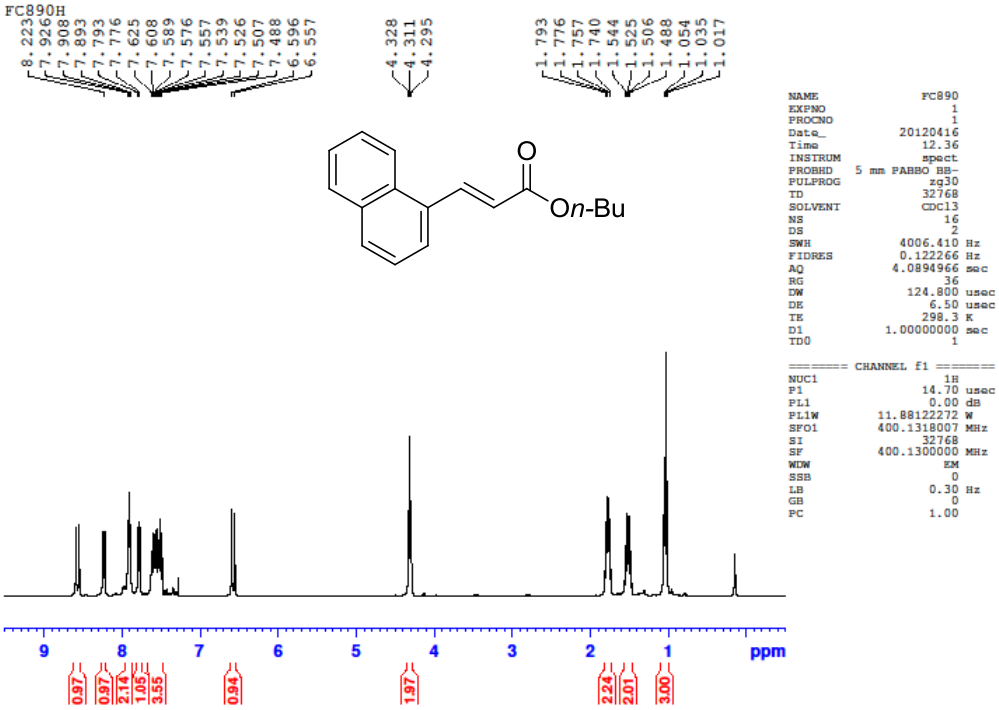


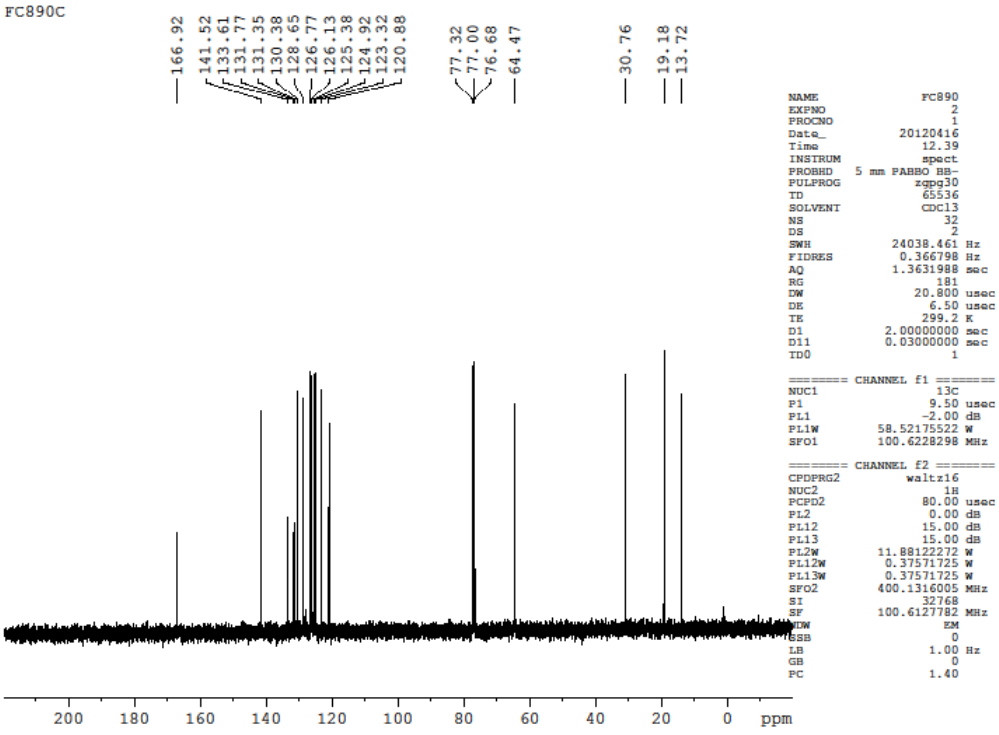
2-Propenoic acid, 3-(4-methylphenyl)-, butyl ester, (2*E*)- (Table 2.3, compound 3an)



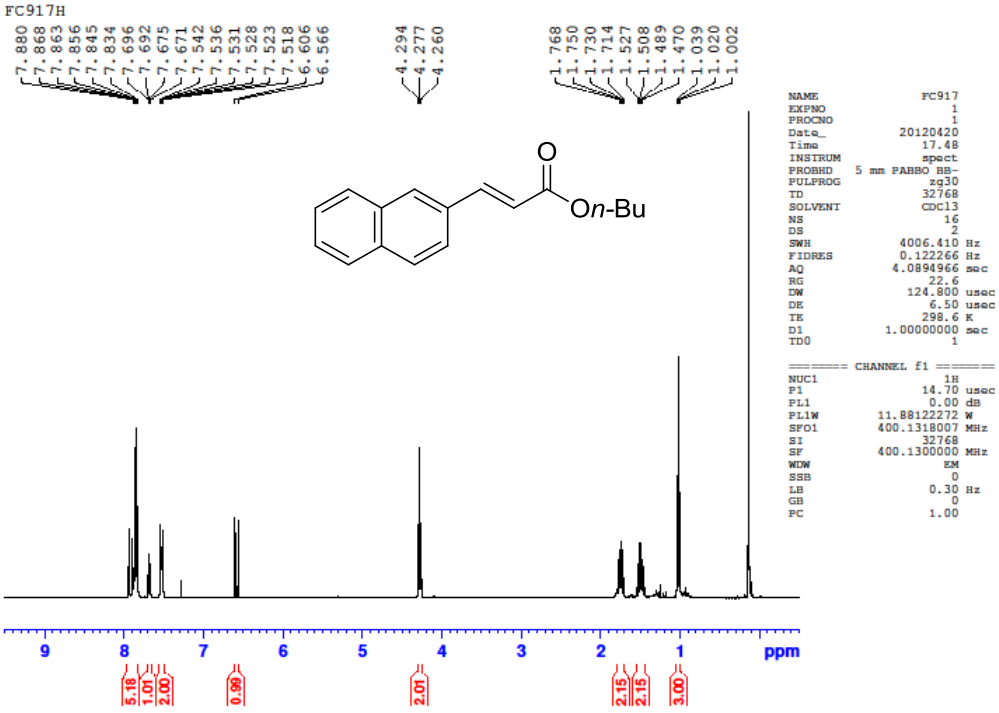


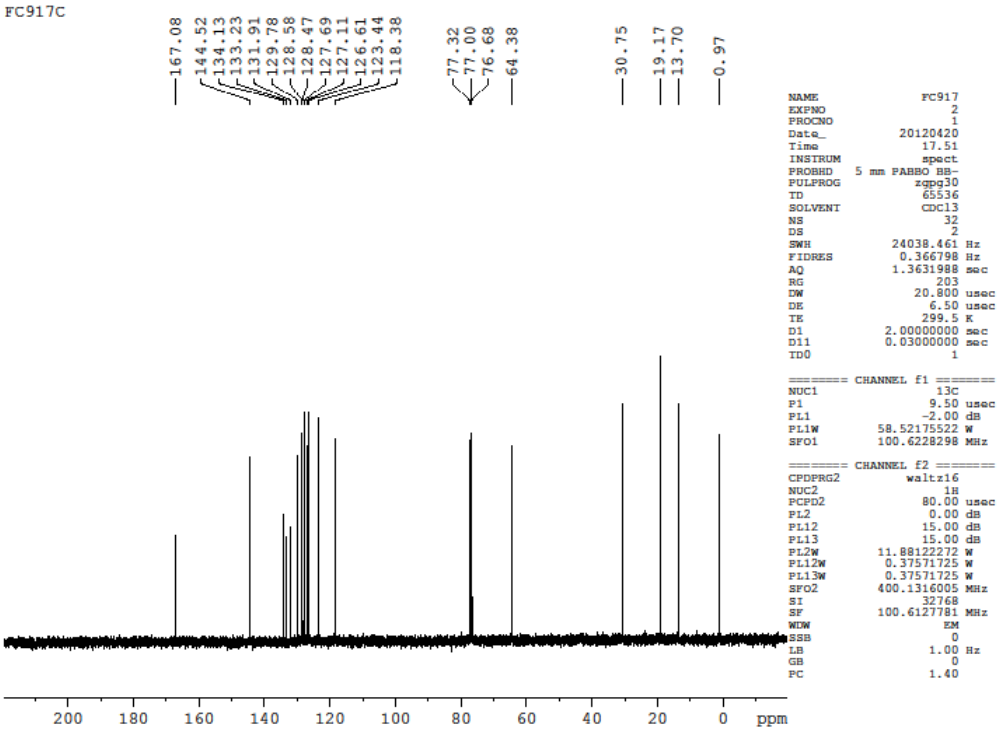
2-Propenoic acid, 3-(1-naphthalenyl)-, butyl ester, (2*E*)- (Table 2.3, compound 3gn)



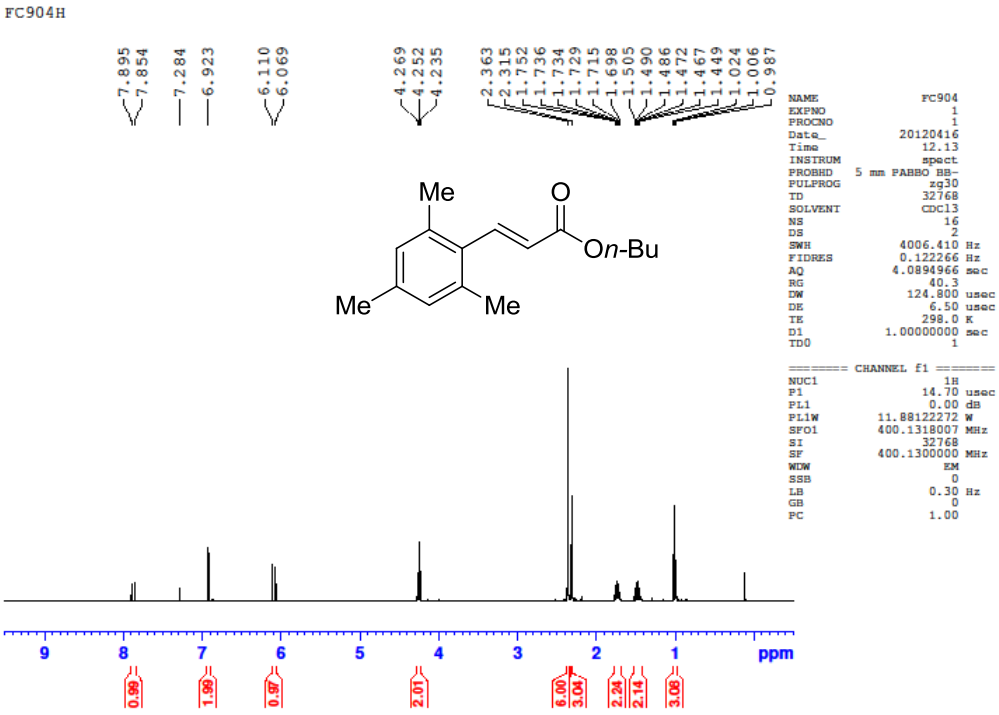


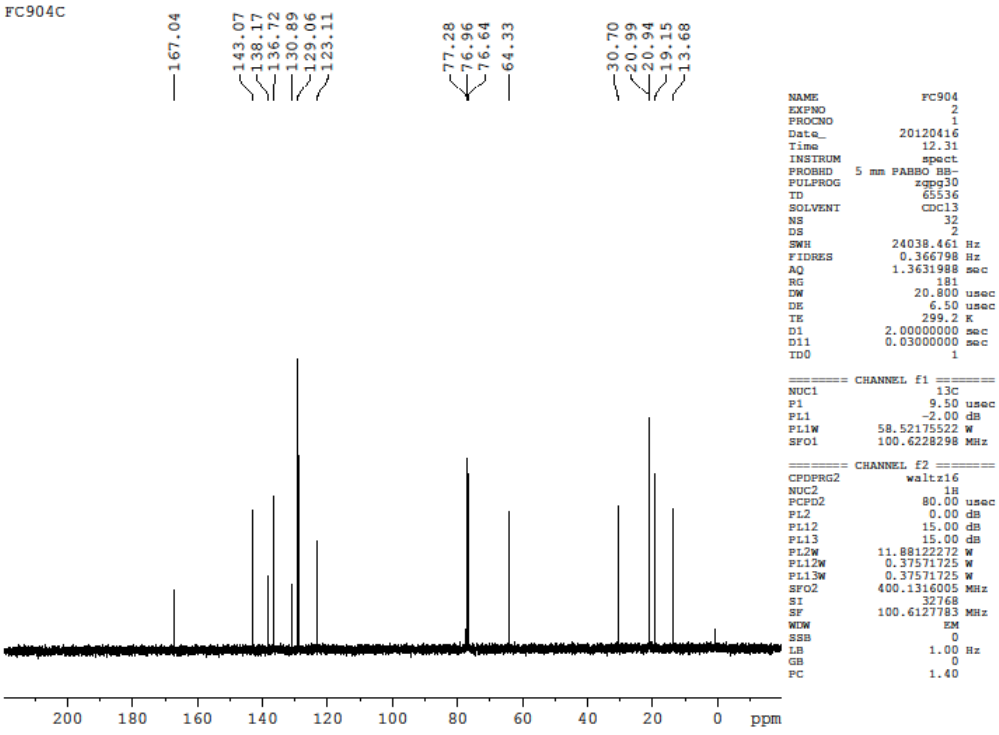
2-Propenoic acid, 3-(2-naphthalenyl)-, butyl ester, (2*E*)- (Table 2.3, compound 3cn)



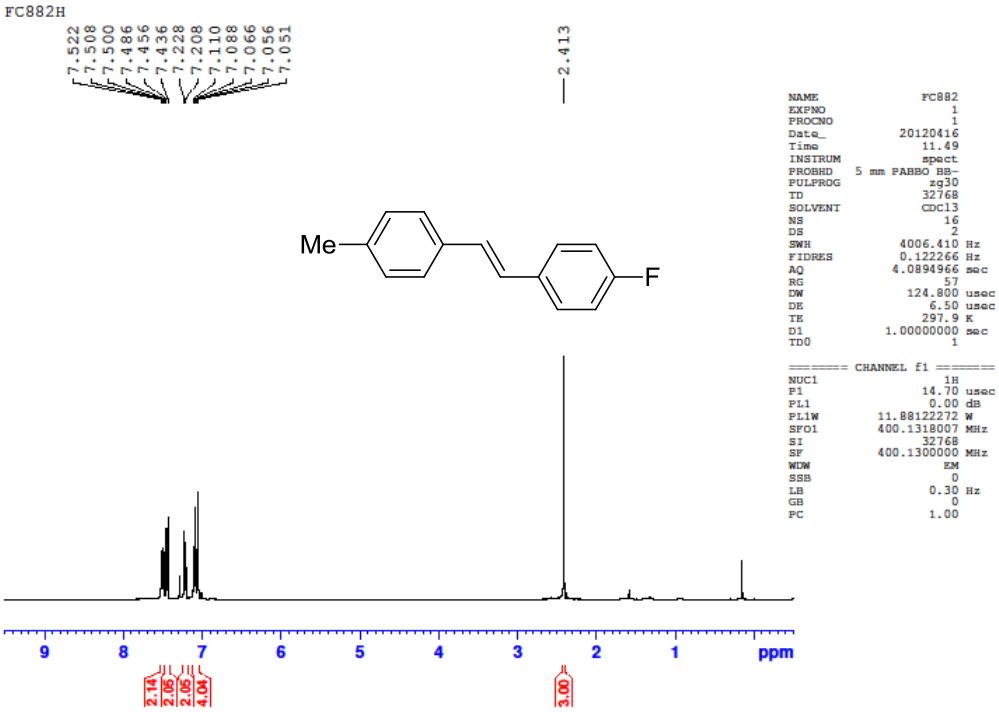


2-Propenoic acid, 3-(2,4,6-trimethylphenyl)-, butyl ester, (2*E*)- (Table 2.3, compound 3in)





Benzene, 1-fluoro-4-[(1*E*)-2-(4-methylphenyl)ethenyl]- (Table 2.3, compound 3ao)

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EXPNO                   1
PROCNO                  1
Date_            20120416
Time                11.49
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 32768
SOLVENT             CDCl3
NS                     16
DS                      2
SWH              4006.410 Hz
FIDRES           0.122266 Hz
AQ               4.0894966 sec
RG                     57
DW                124.800 usec
DE                  6.50 usec
TE                297.9 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 =======
NUC1                   1H
P1                  14.70 usec
PL1                  0.00 dB
PL1W           11.88122272 W
SFO1           400.1318007 MHz
SI                   32768
SF             400.1300000 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
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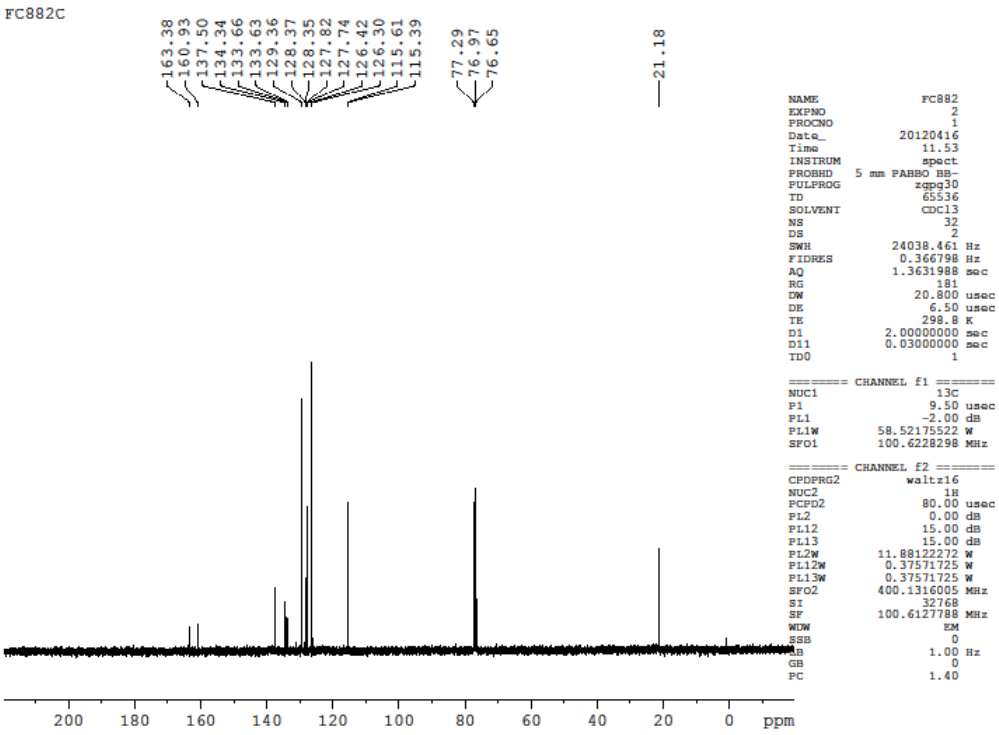


```
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PROCNO                  1
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INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                 65536
SOLVENT             CDCl3
NS                     32
DS                      2
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                    181
DW                 20.800 usec
DE                  6.50 usec
TE                298.8 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1

======== CHANNEL f1 =======
NUC1                   13C
P1                   9.50 usec
PL1                 -2.00 dB
PL1W           58.52175522 W
SFO1           100.6228298 MHz

======== CHANNEL f2 =======
CPDPRG2            waltz16
NUC2                   1H
PCPD2               80.00 usec
PL2                  0.00 dB
PL12                15.00 dB
PL13                15.00 dB
PL2W           11.88122272 W
PL12W           0.37571725 W
PL13W           0.37571725 W
SFO2           400.1316005 MHz
SI                   32768
SF             100.6127788 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
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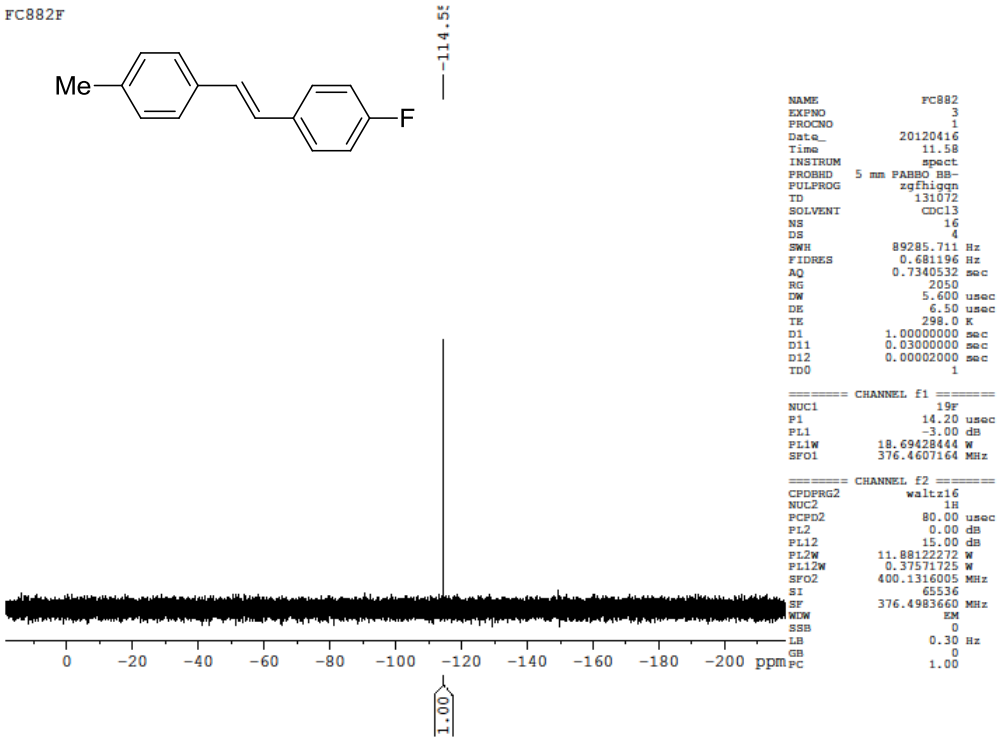
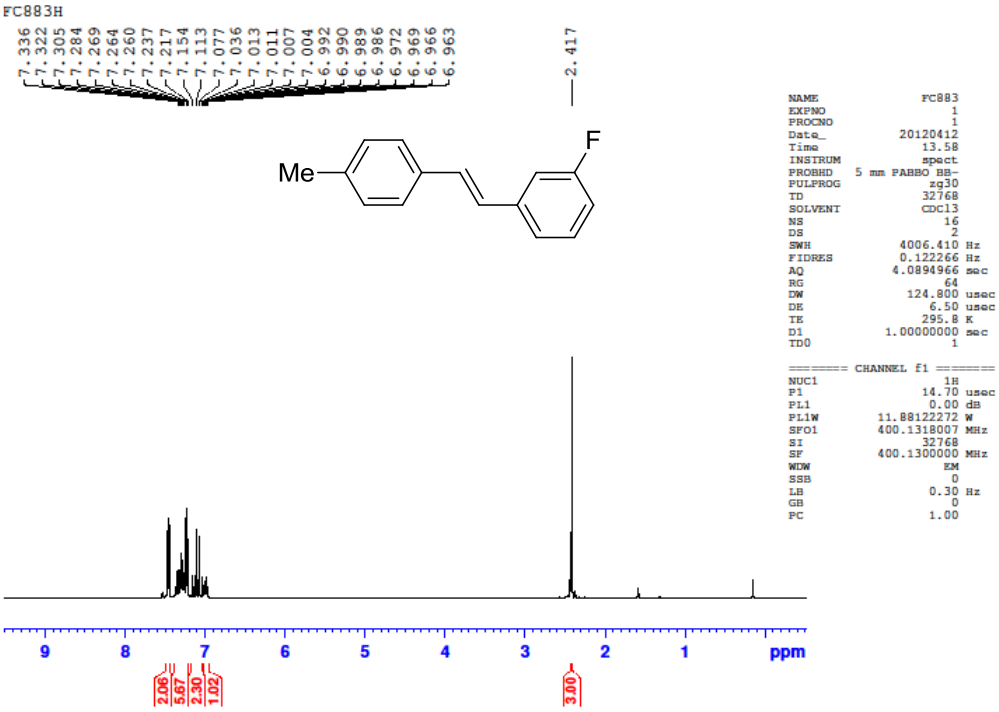
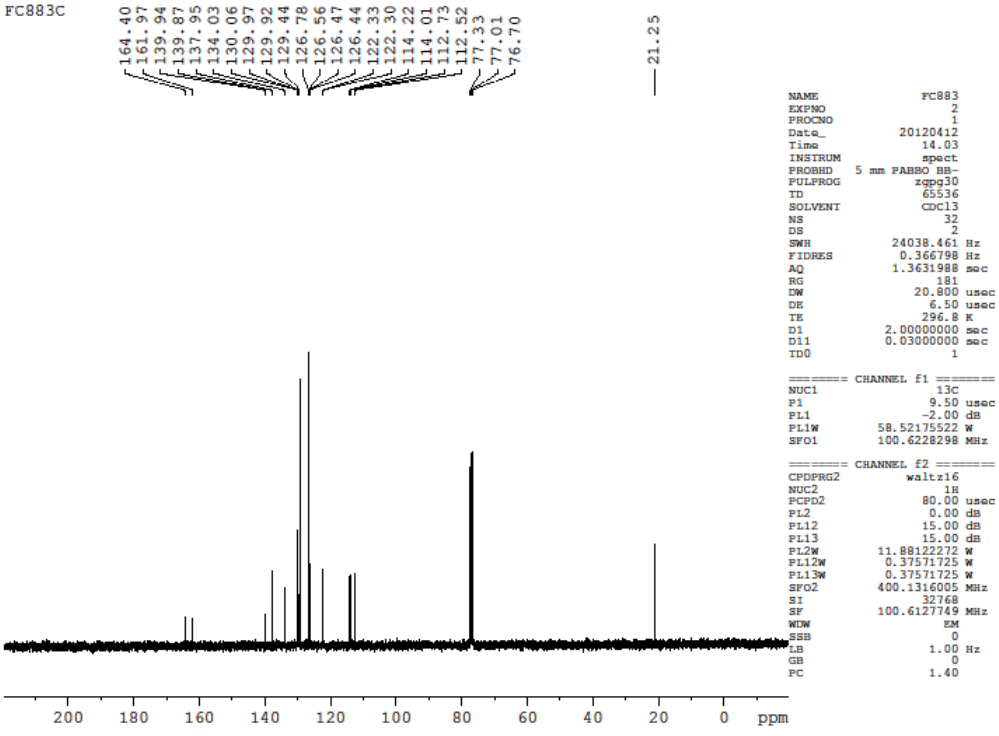
Benzene, 1-fluoro-4-[(1*E*)-2-(4-methylphenyl)ethenyl]- (Table 2.3, compound 3ao)

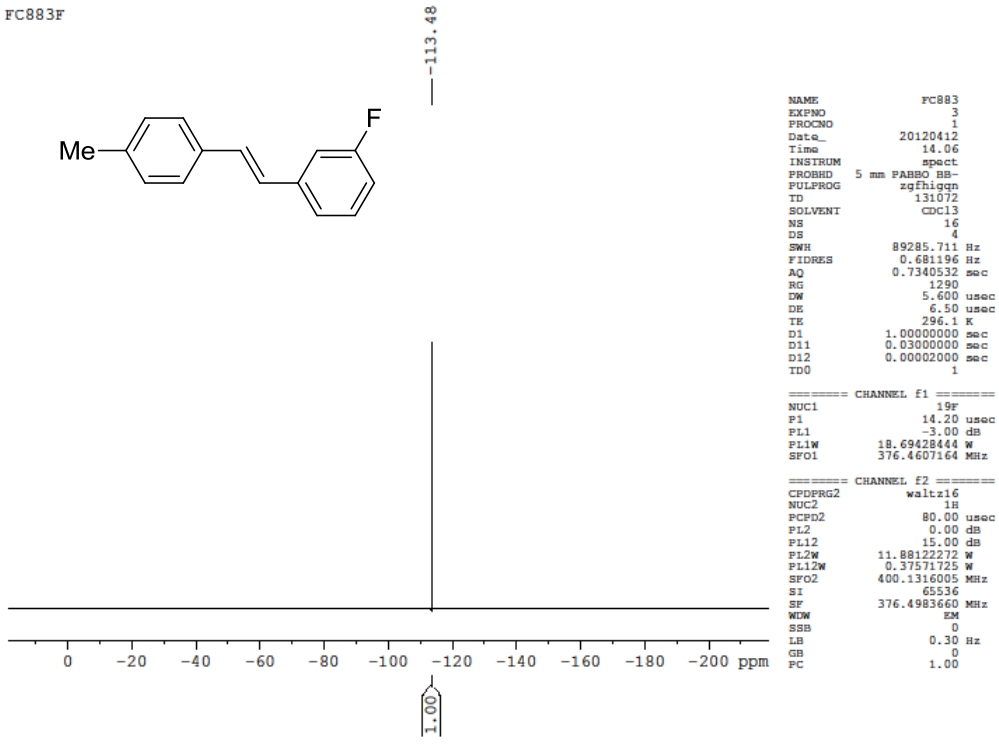


Benzene, 1-fluoro-3-[2-(4-methylphenyl)ethenyl]-, (*E*)- (Table 2.3, compound 3ap)





Benzene, 1-fluoro-3-[2-(4-methylphenyl)ethenyl]-, (*E*)- (Table 2.3, compound 3ap)



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PROCNO	1
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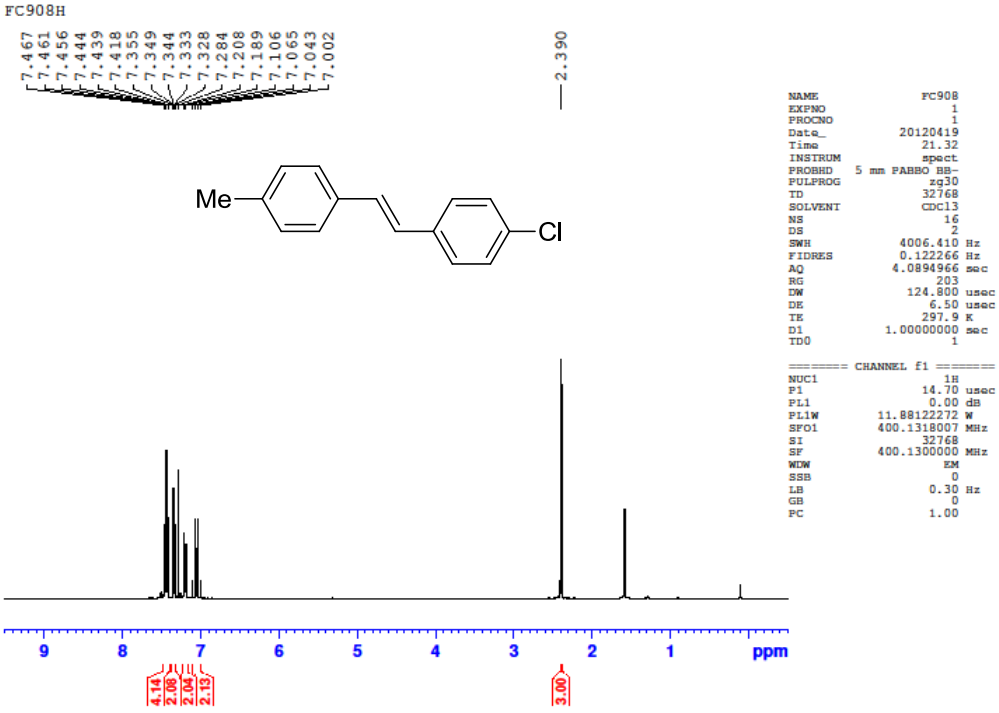
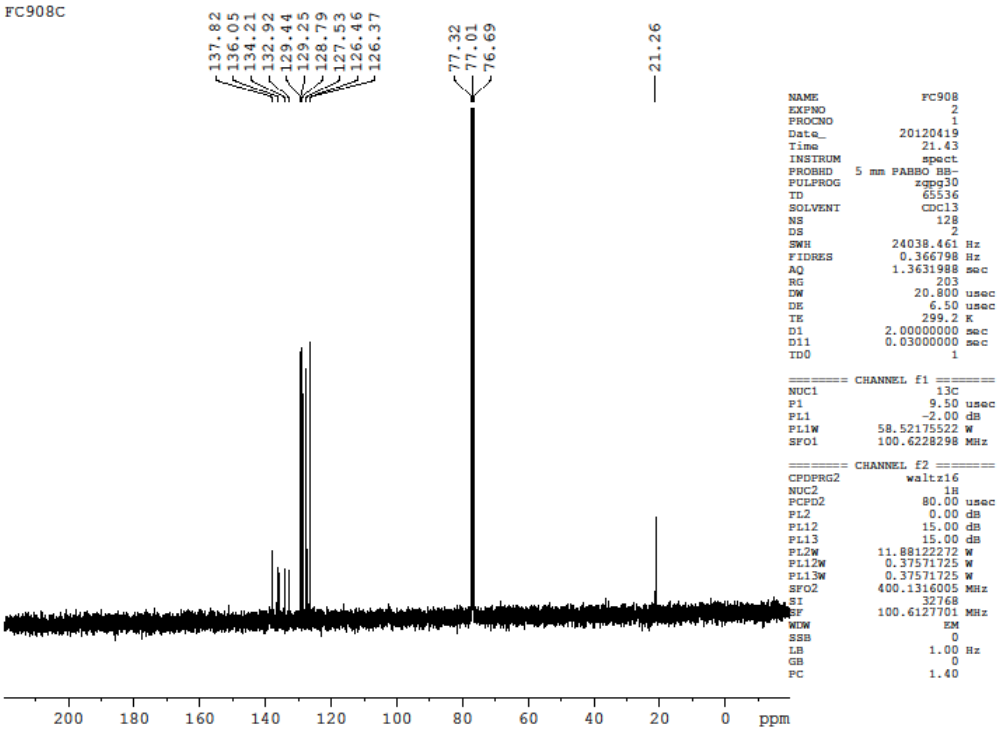
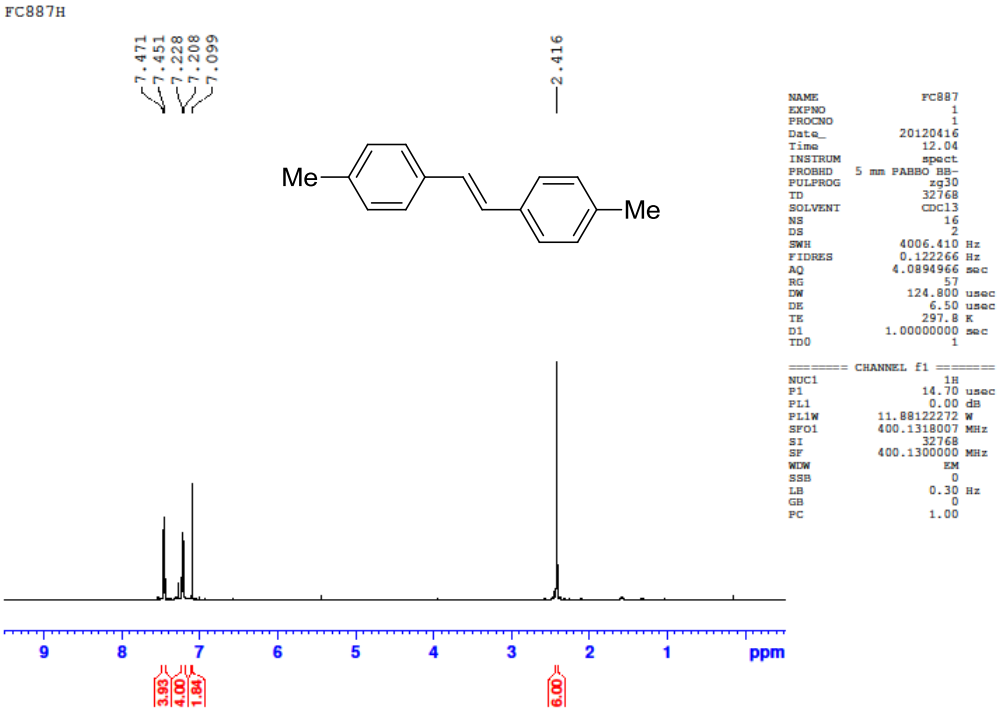
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgfhigqn
TD	131072
SOLVENT	CDCl3
NS	16
DS	4
SWH	89285.711 Hz
FIDRES	0.681196 Hz
AQ	0.7340532 sec
RG	1290
DW	5.600 usec
DE	6.50 usec
TE	296.1 K
D1	1.00000000 sec
D11	0.03000000 sec
D12	0.00002000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	19F
P1	14.20 usec
PL1	-3.00 dB
PL1W	18.69428444 W
SFO1	376.4607164 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	0.00 dB
PL12	15.00 dB
PL2W	11.88122272 W
PL12W	0.37571725 W
SFO2	400.1316005 MHz
SI	65536
SF	376.4983660 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

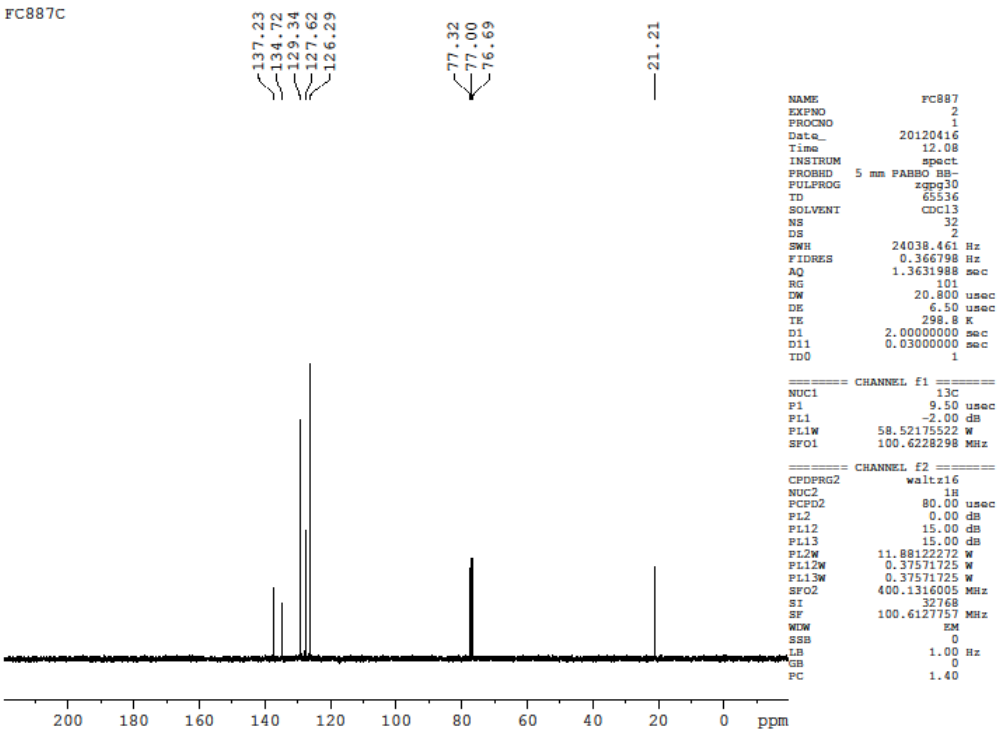
Benzene, 1-chloro-4-[(1*E*)-2-(4-methylphenyl)ethenyl]- (Table 2.3, compound 3aq)



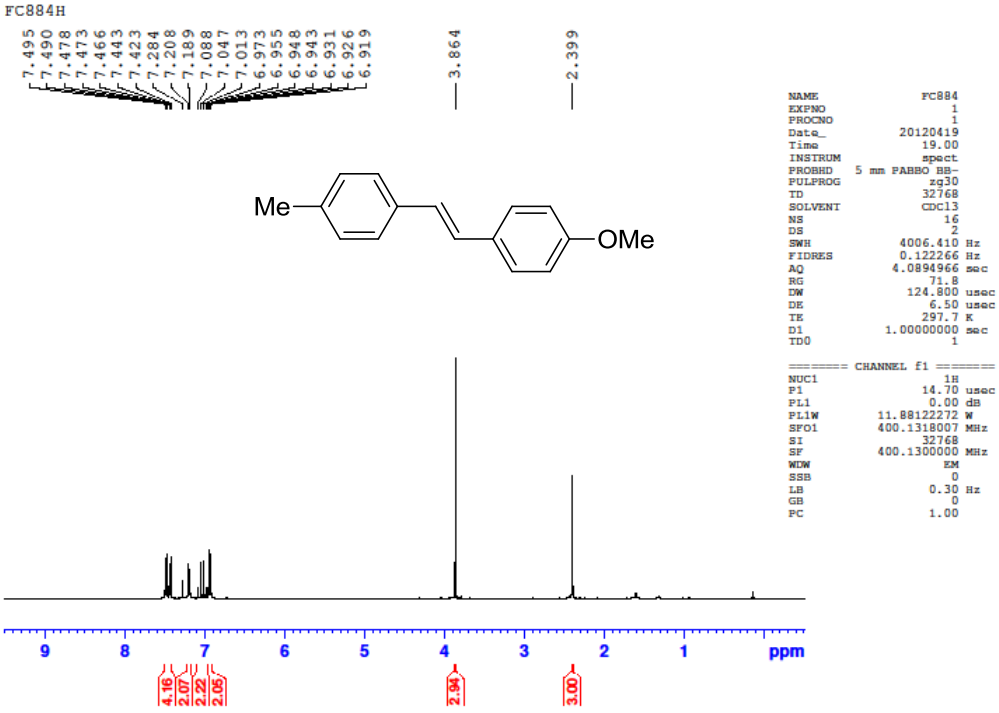


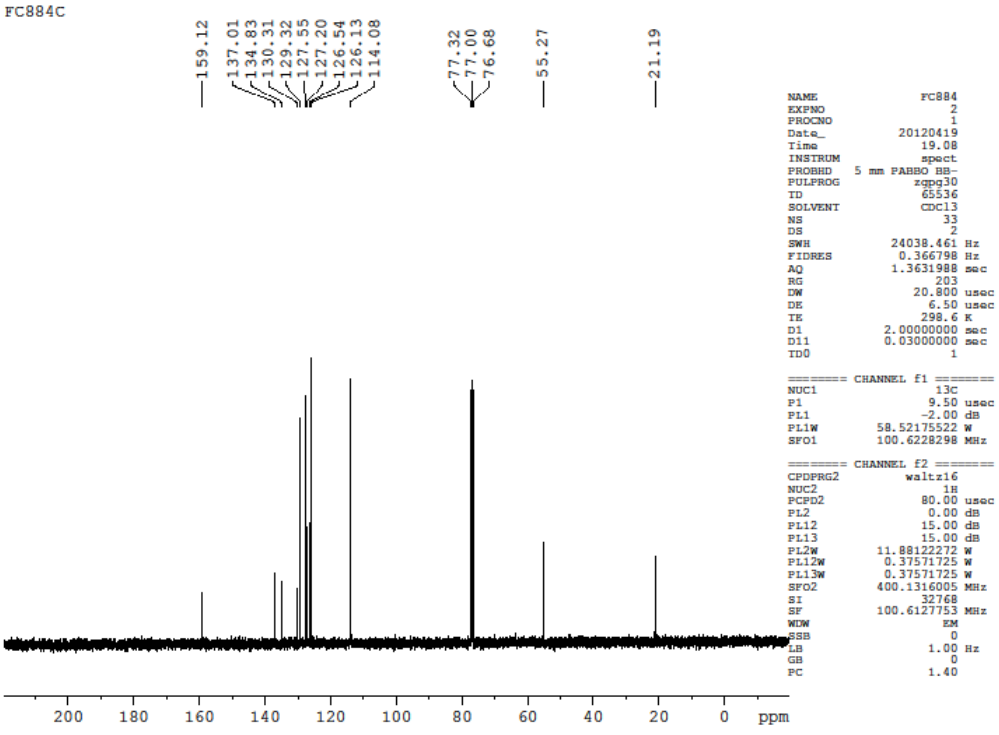
Benzene, 1,1'-(1*E*)-1,2-ethenediylbis[4-methyl- (Table 2.3, compound 3ar)



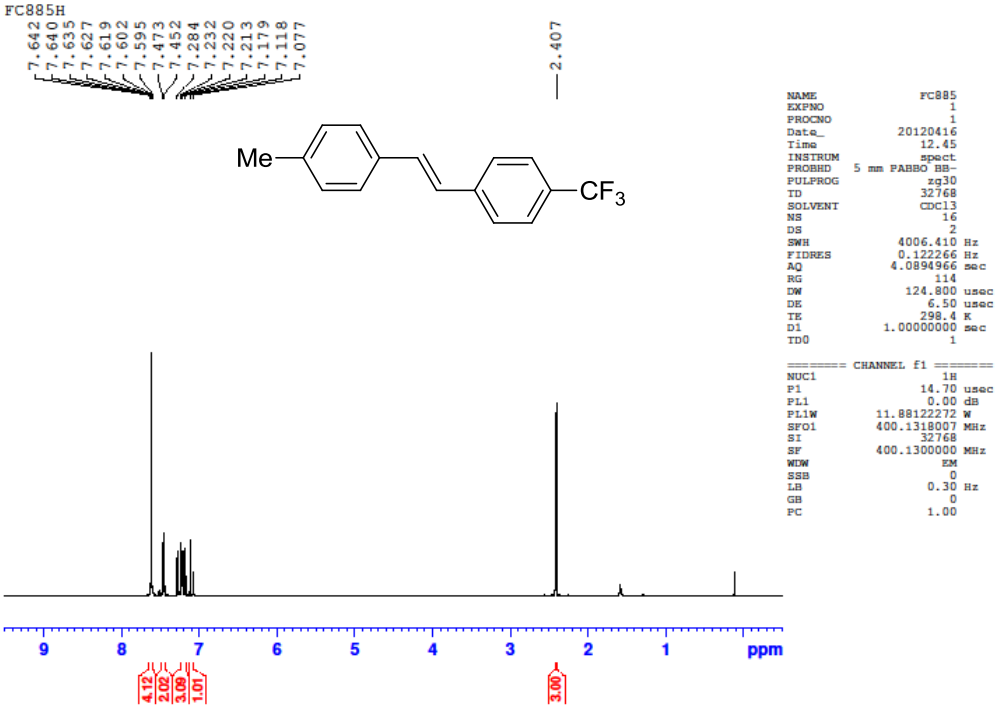


Benzene, 1-methoxy-4-[(1*E*)-2-(4-methylphenyl)ethenyl]- (Table 2.3, compound 3as)





Benzene, 1-[(1*E*)-2-(4-methylphenyl)ethenyl]-4-(trifluoromethyl)- (Table 2.3, compound 3at)

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PROCNO                  1
Date_            20120416
Time                12.45
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PULPROG              zg30
TD                  32768
SOLVENT             CDCl3
NS                     16
DS                      2
SWH              4006.410 Hz
FIDRES           0.122266 Hz
AQ               4.0894966 sec
RG                    114
DW                124.800 usec
DE                  6.50 usec
TE                298.4 K
D1               1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  1H
P1                 14.70 usec
PL1                0.00 dB
PL1W         11.88122272 W
SFO1         400.1318007 MHz
SI                  32768
SF           400.1300000 MHz
WDW                   EM
SSB                    0
LB                 0.30 Hz
GB                     0
PC                 1.00
```

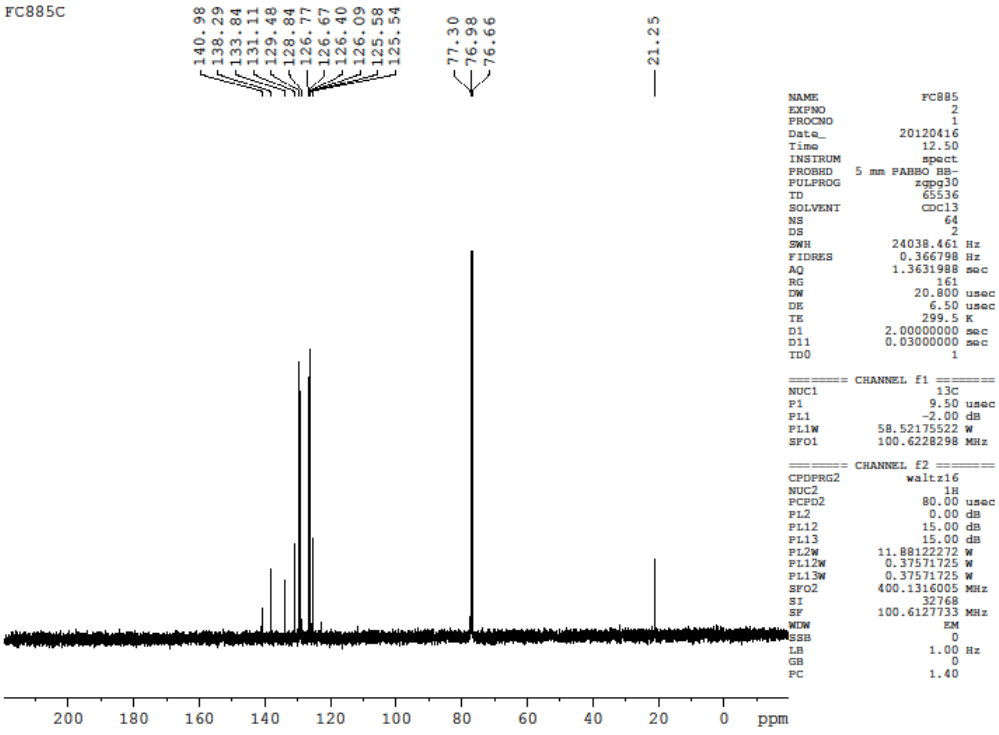


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PROCNO                  1
Date_            20120416
Time                12.50
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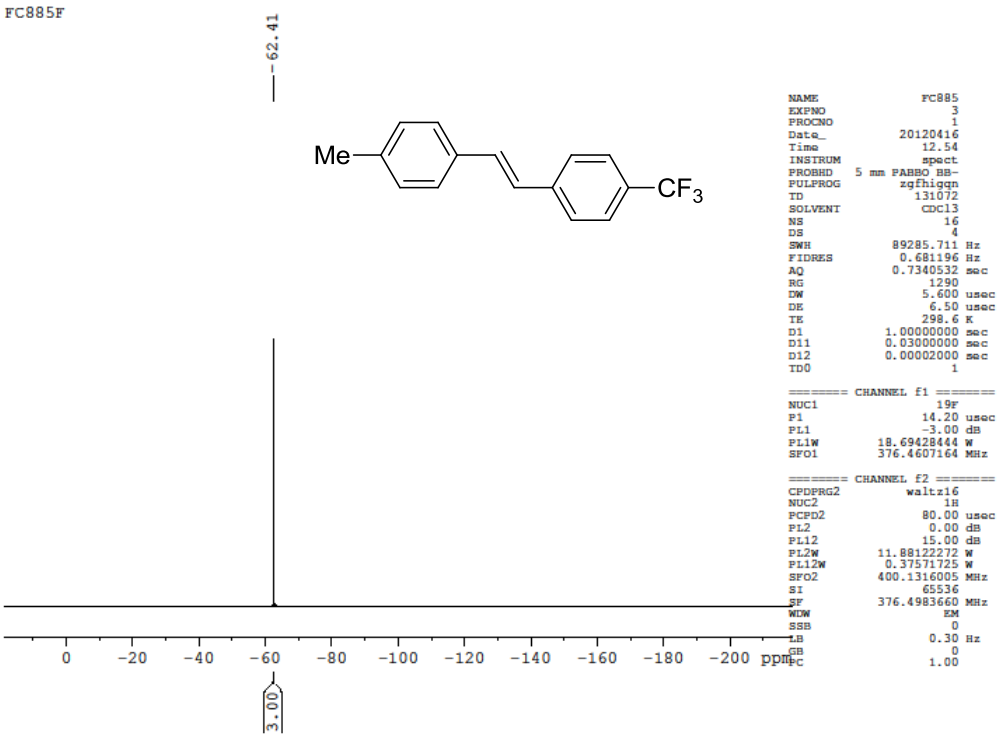
PROBHD   5 mm PABBO BB-
PULPROG             zgpg30
TD                  65536
SOLVENT             CDCl3
NS                     64
DS                      2
SWH              24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                    161
DW                 20.800 usec
DE                  6.50 usec
TE                299.5 K
D1               2.00000000 sec
D11              0.03000000 sec
TD0                     1

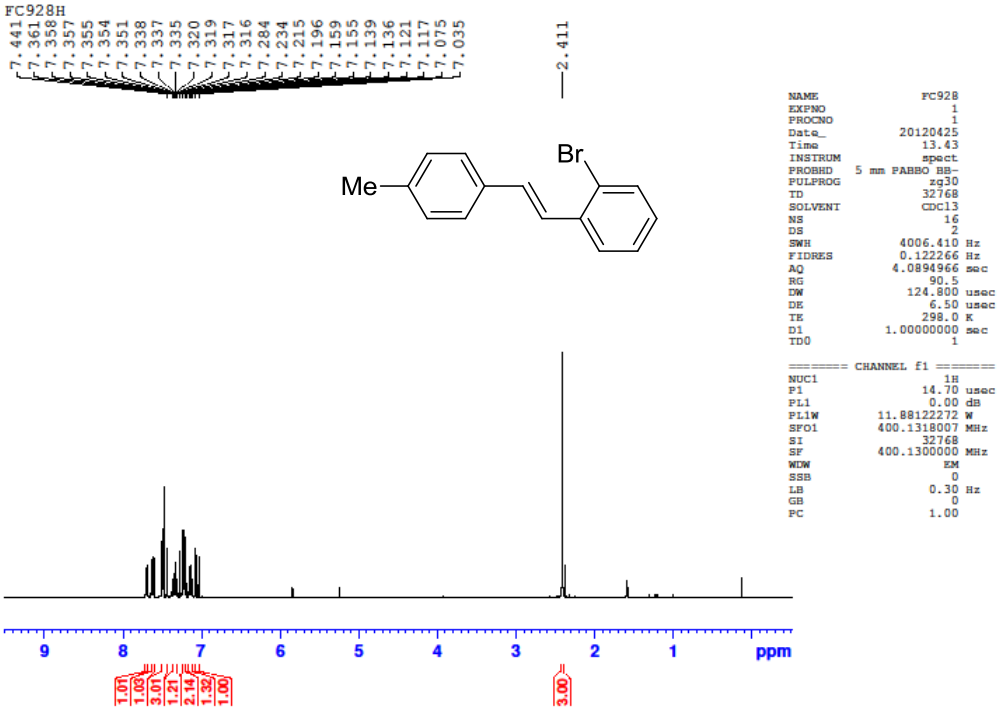
======== CHANNEL f1 ========
NUC1                  13C
P1                  9.50 usec
PL1                -2.00 dB
PL1W         58.52175522 W
SFO1         100.6228298 MHz

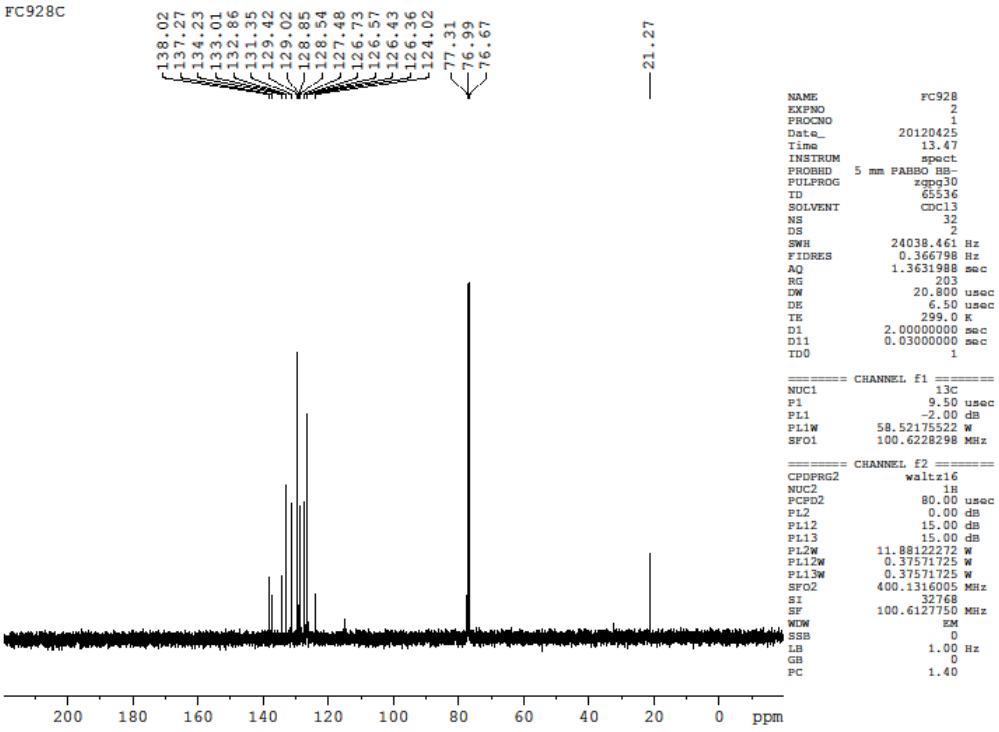
======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                  1H
PCPD2              80.00 usec
PL2                 0.00 dB
PL12               15.00 dB
PL13               15.00 dB
PL2W         11.88122272 W
PL12W         0.37571725 W
PL13W         0.37571725 W
SFO2         400.1316005 MHz
SI                  32768
SF           100.6127733 MHz
WDW                   EM
SSB                    0
LB                 1.00 Hz
GB                     0
PC                 1.40
```

Benzene, 1-[(1*E*)-2-(4-methylphenyl)ethenyl]-4-(trifluoromethyl)- (Table 2.3, compound 3at)

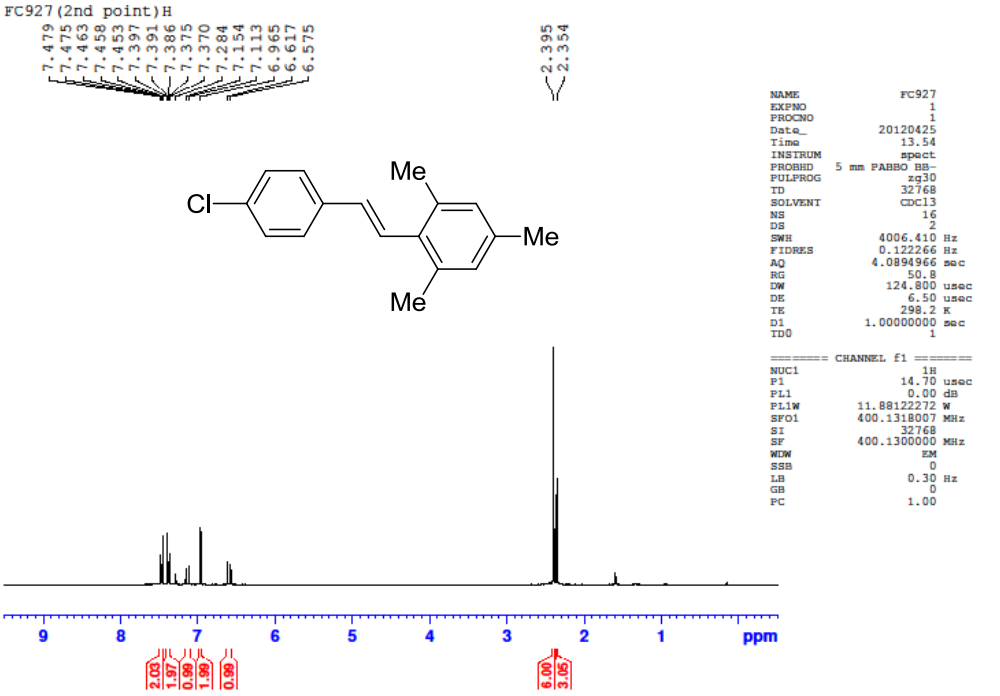


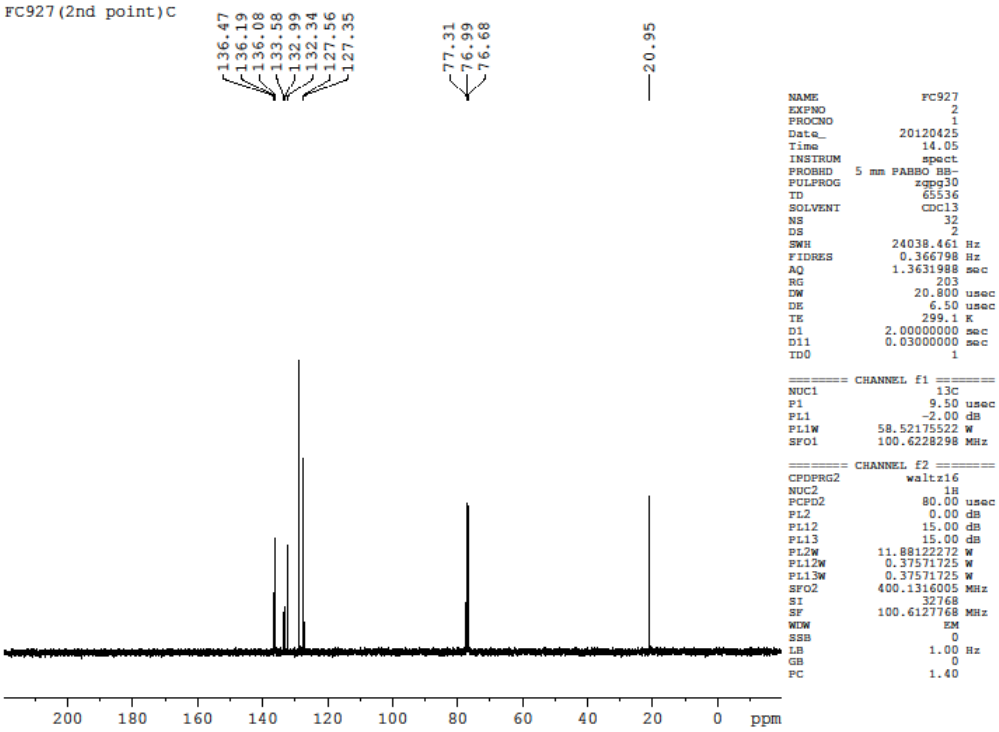
Benzene, 1-bromo-2-[(1*E*)-2-(4-methylphenyl)ethenyl]- (Table 2.3, compound 3au)





Benzene, 1-chloro-4-[(1*E*)-2-(1,3,5-trimethylphenyl)ethenyl]- (Table 2.3, compound 3fv)





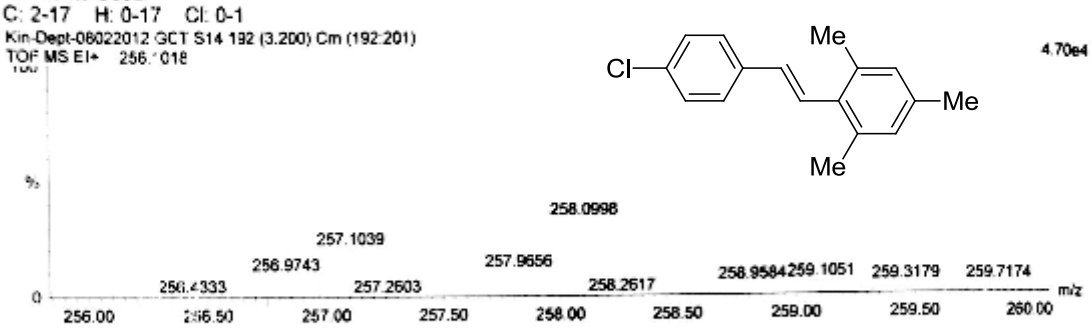
Benzene, 1-chloro-4-[(1*E*)-2-(1,3,5-trimethylphenyl)ethenyl]- (Table 2.3, compound 3fv)

Elemental Composition Report Page 1

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Selected filters: None

Monoisotopic Mass, Odd and Even Electron Ions
2 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 2-17 H: 0-17 Cl: 0-1

Kin-Dept-08022012 GCT S14 192 (3.200) Cm (192:201)
TOF MS EI+ 256.1018



Minimum:		5.0	5.0	-1.5		
Maximum:				50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
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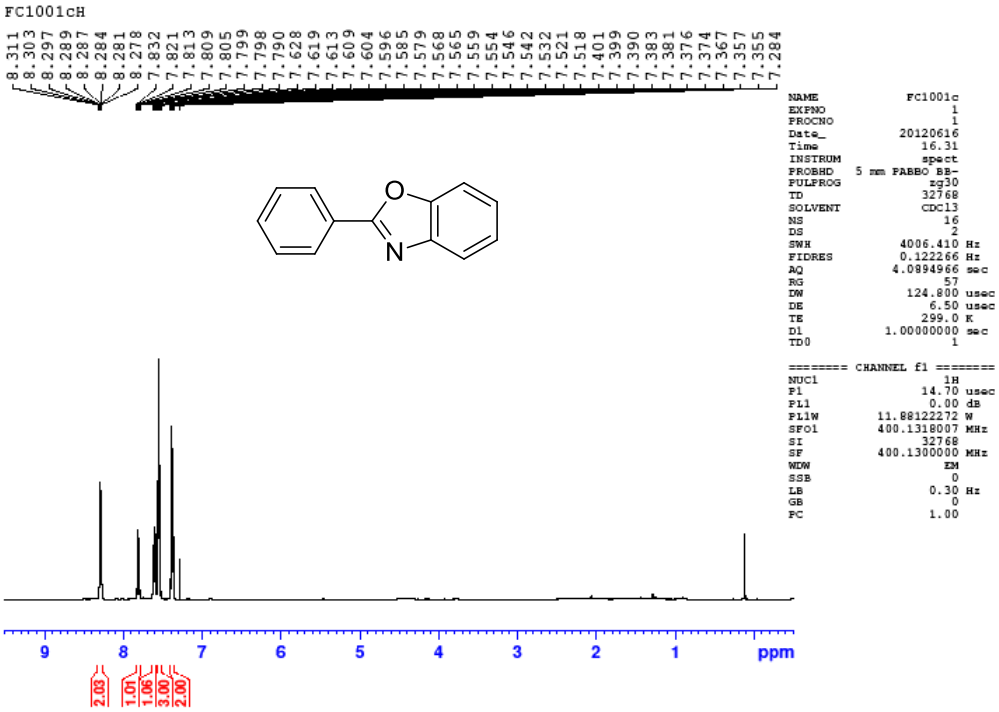
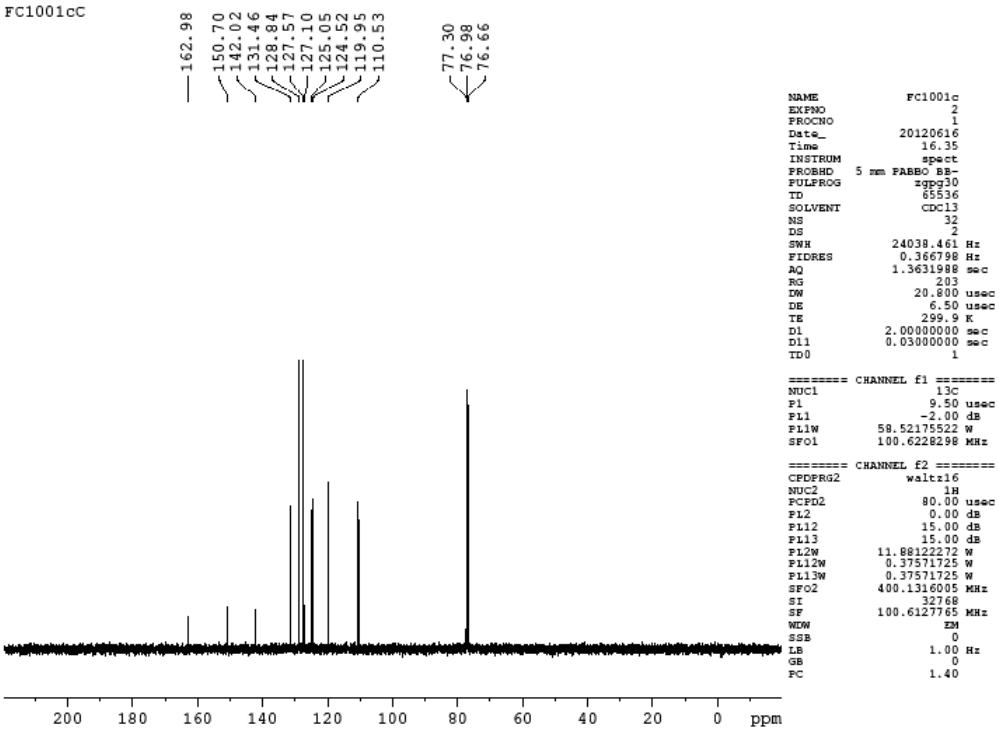
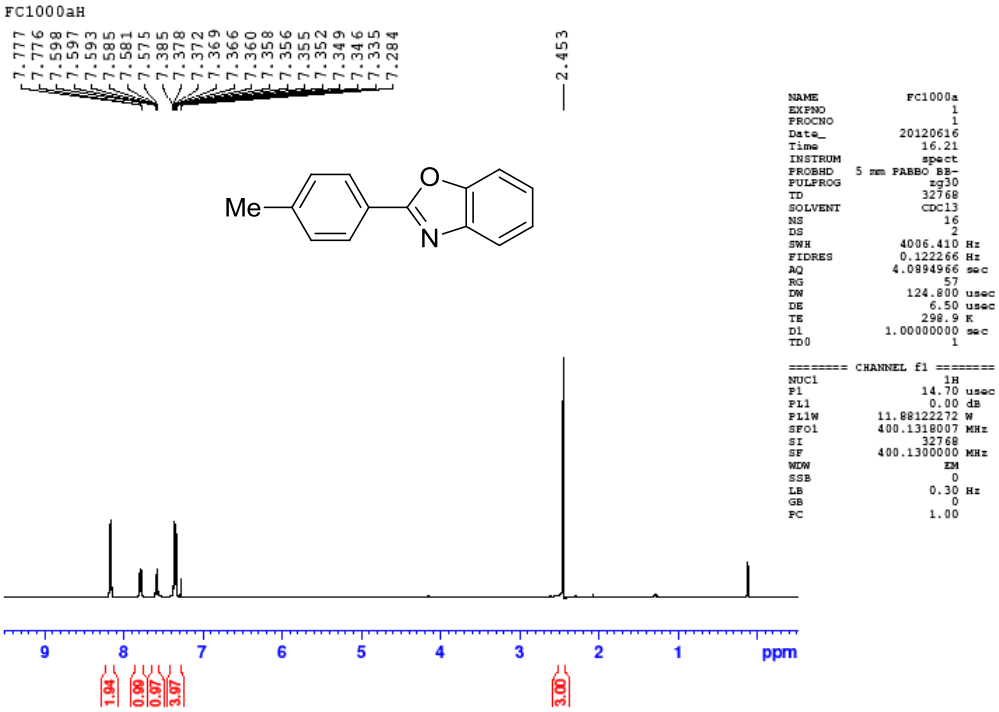
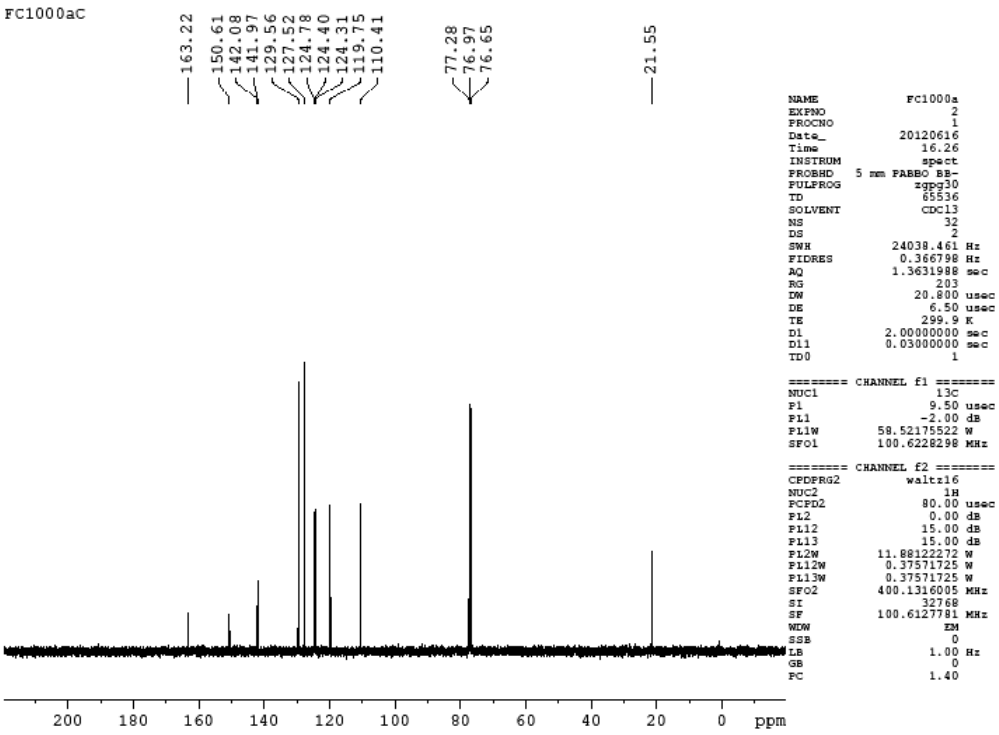
2-Phenylbenzoxazole (Table 3.2, entry 1)



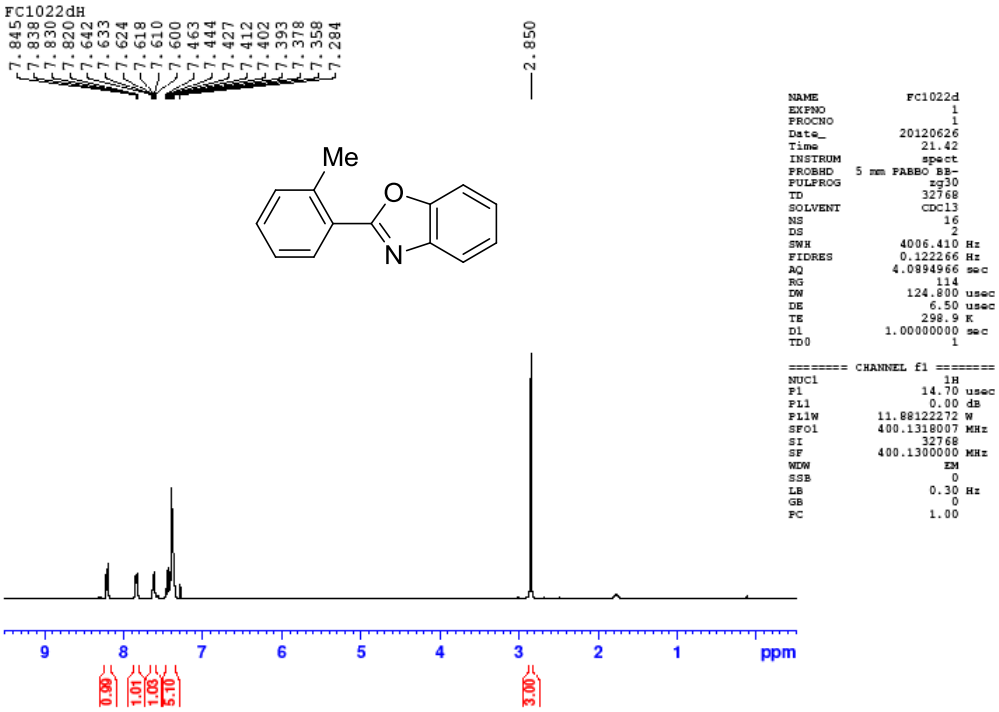


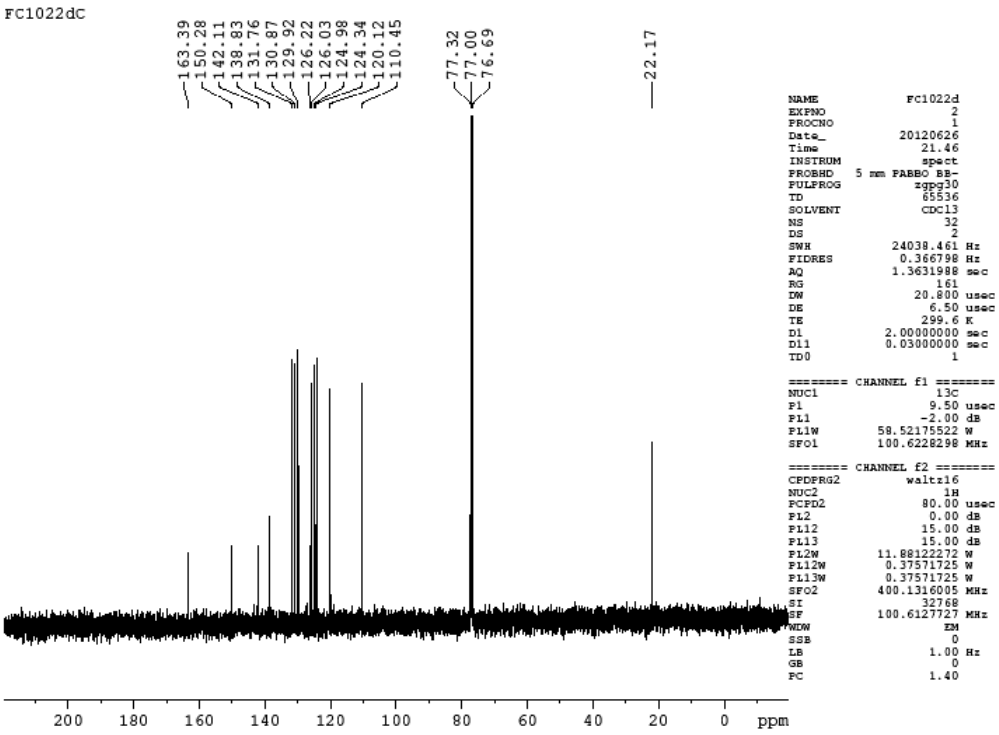
2-(4-Methylphenyl)benzoxazole (Table 3.2, entry 2)



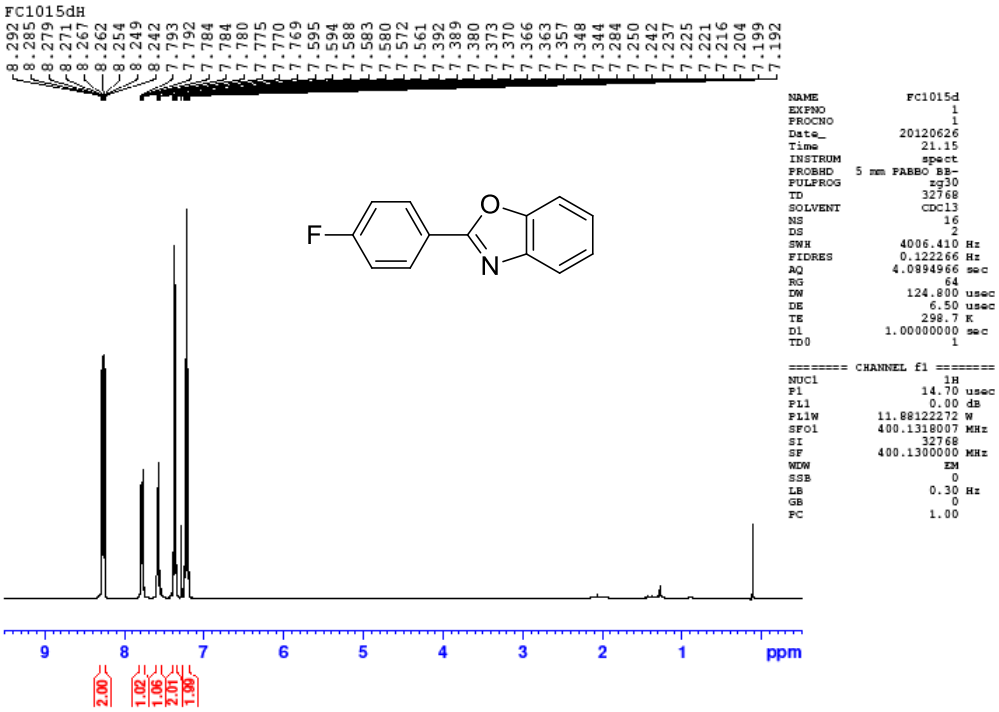


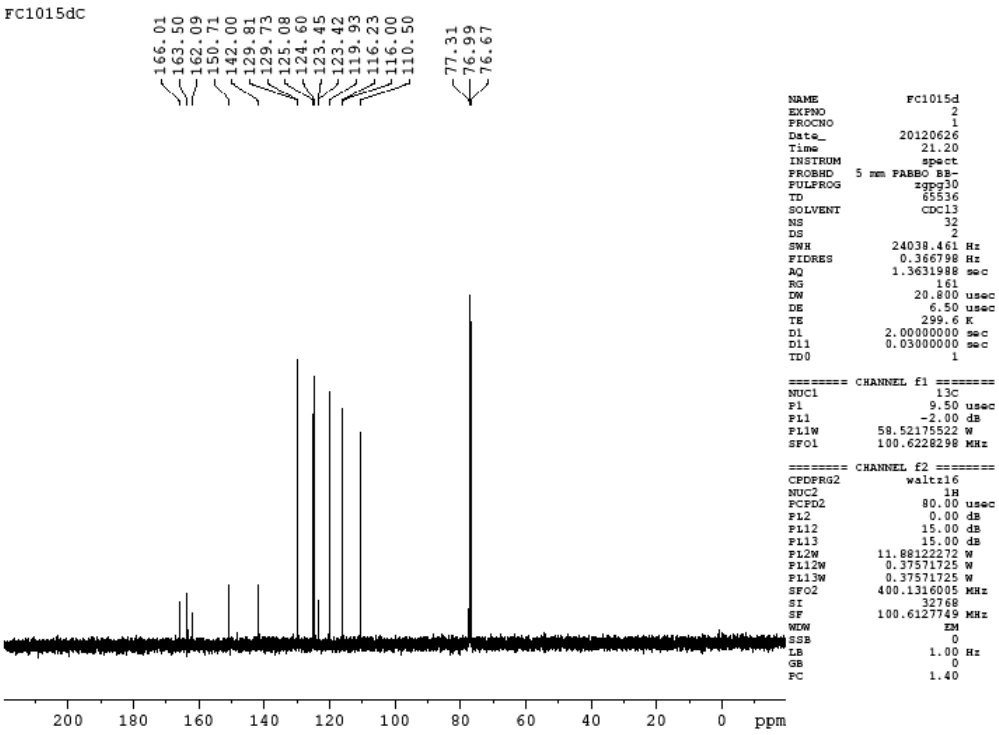
2-(2-Methylphenyl)benzoxazole (Table 3.2, entry 3)



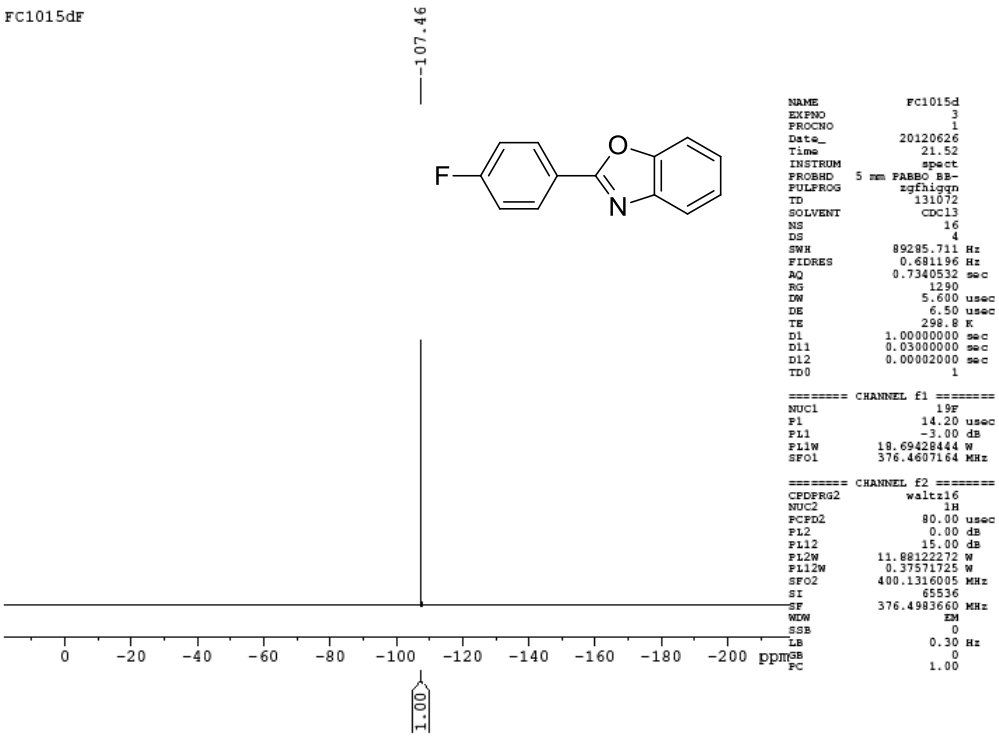


2-(4-Fluorophenyl)benzoxazole, (Table 3.2, entry 4)





2-(4-Fluorophenyl)benzoxazole, (Table 3.2, entry 4)



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PROCNO	1
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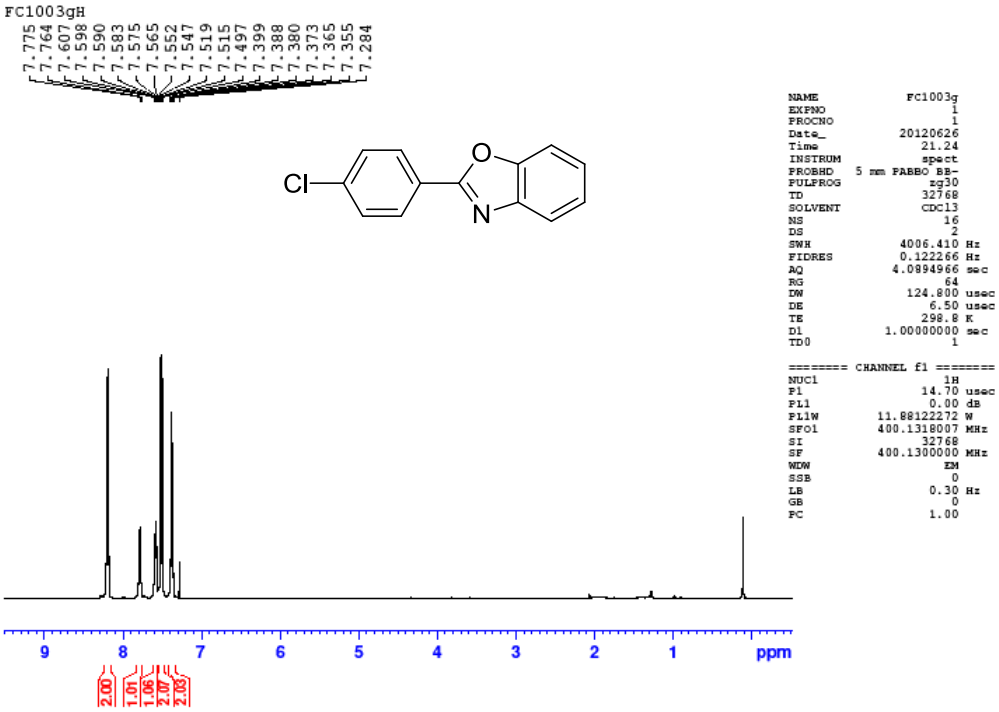
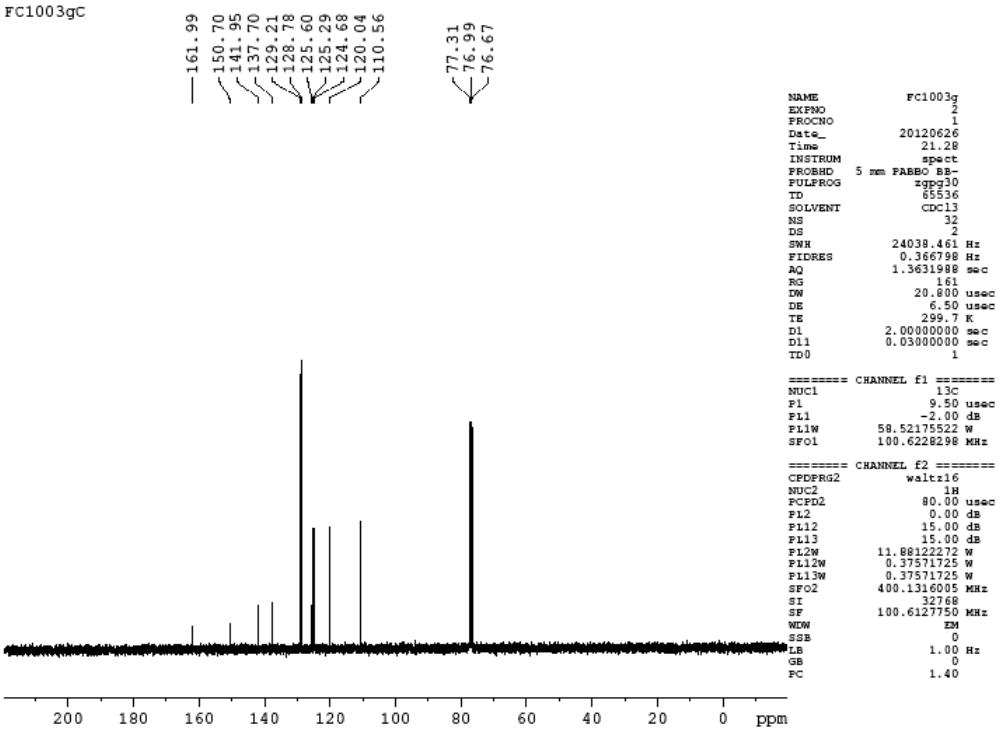
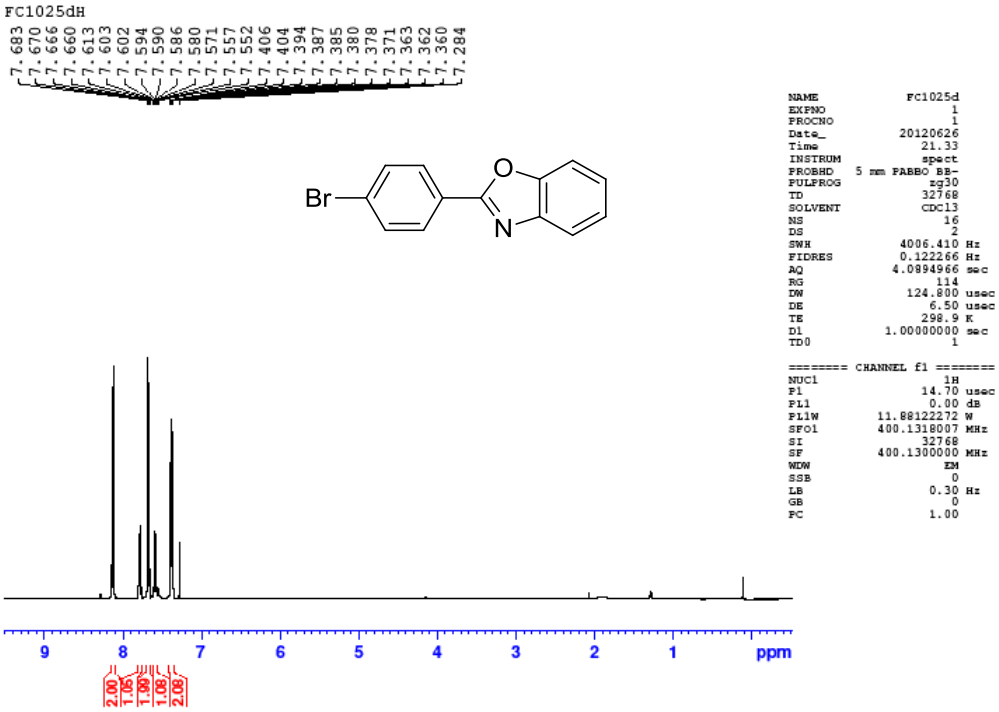
Time	21.52
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgfhigqn
TD	131072
SOLVENT	CDCl3
NS	16
DS	4
SWH	89285.711 Hz
FIDRES	0.681196 Hz
AQ	0.7340532 sec
RG	1290
DW	5.600 usec
DE	6.50 usec
TE	298.8 K
D1	1.00000000 sec
D11	0.03000000 sec
D12	0.00002000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	19F
P1	14.20 usec
PL1	-3.00 dB
PL1W	18.69428444 W
SFO1	376.4607164 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	0.00 dB
PL12	15.00 dB
PL2W	11.88122272 W
PL12W	0.37571725 W
SFO2	400.1316005 MHz
SI	65536
SF	376.4983660 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

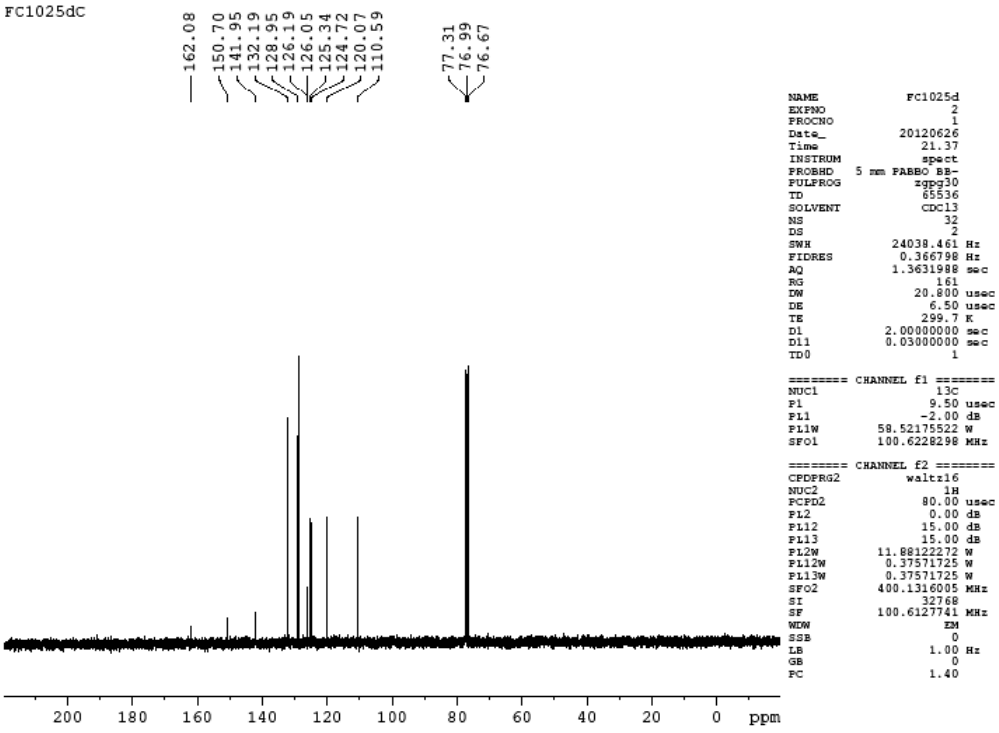
2-(4-Chlorophenyl)benzoxazole (Table 3.2, entry 5)



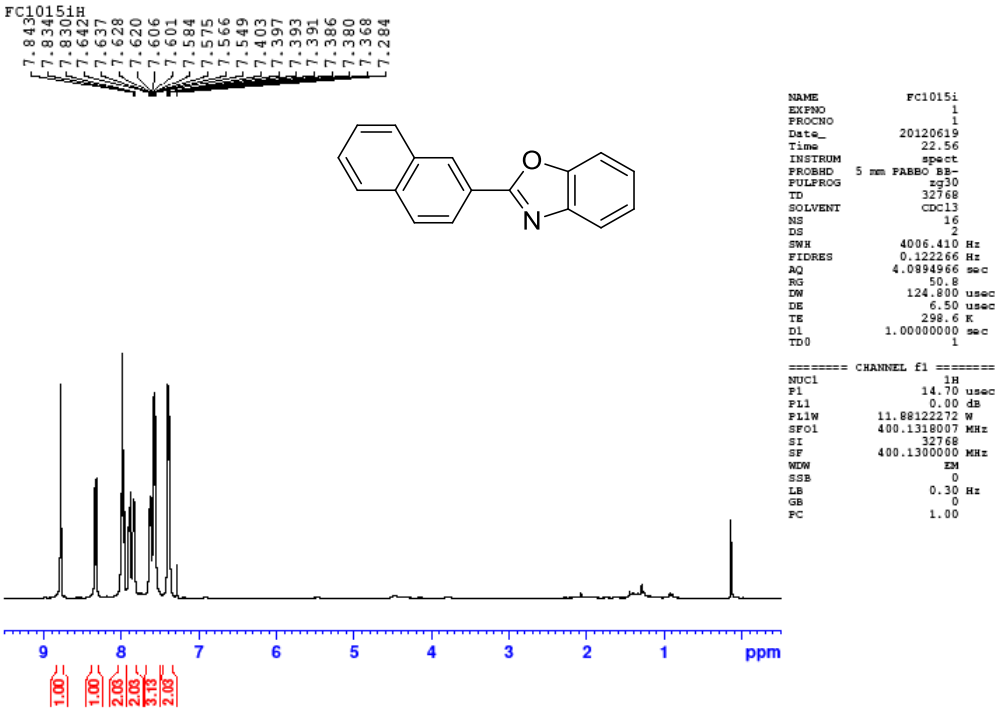


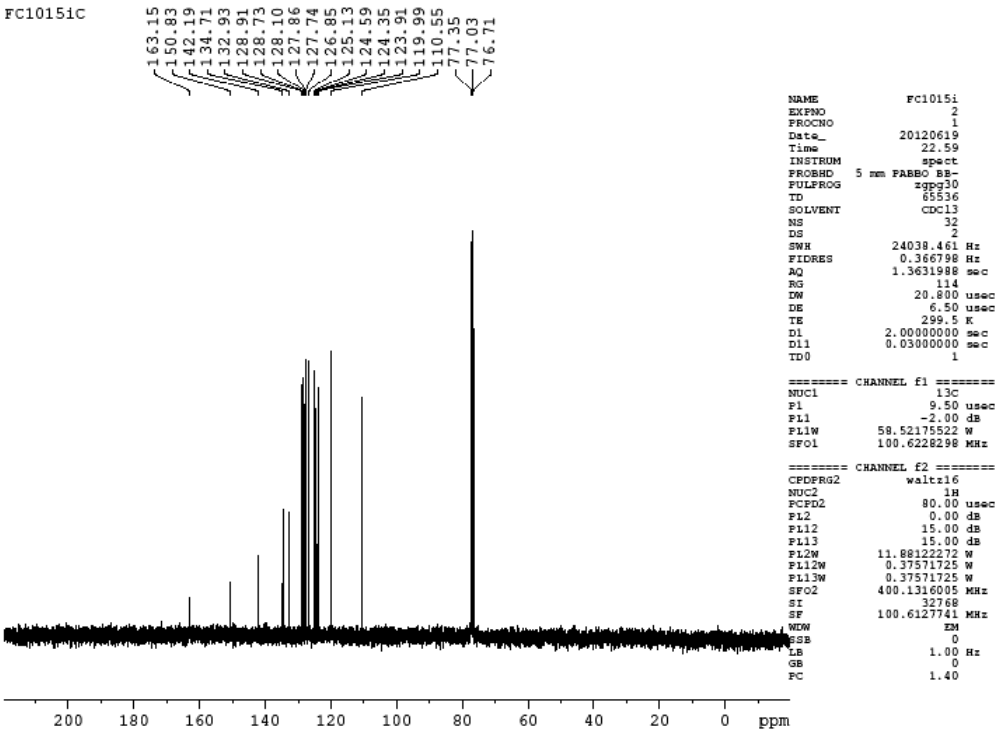
2-(4-Bromophenyl)benzoxazole (Table 2, entry 6, compound 3fa)



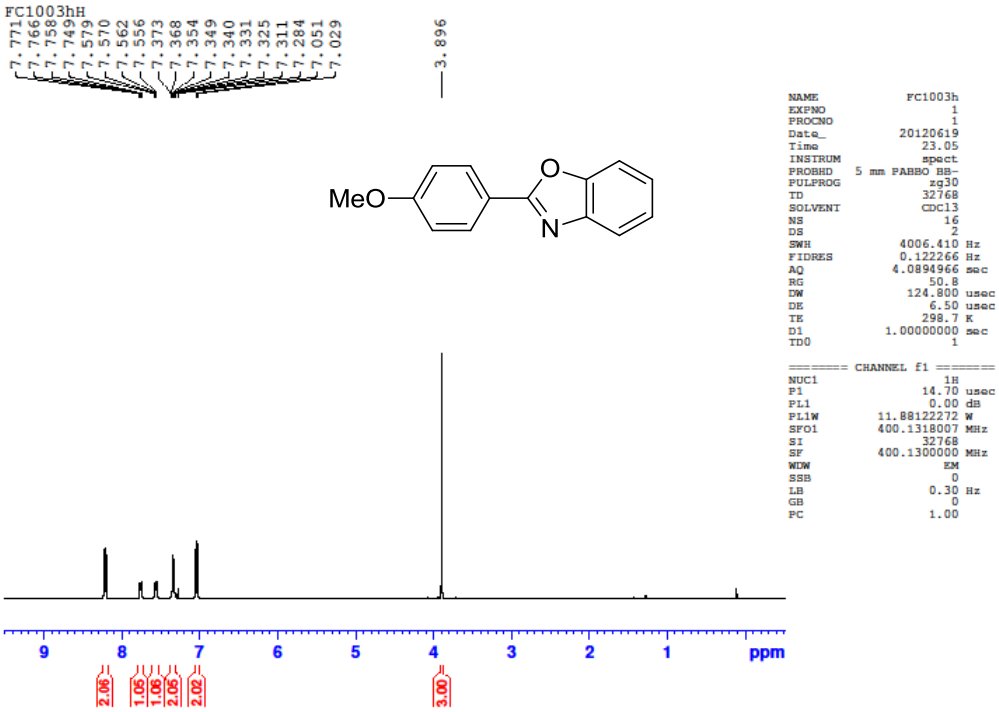


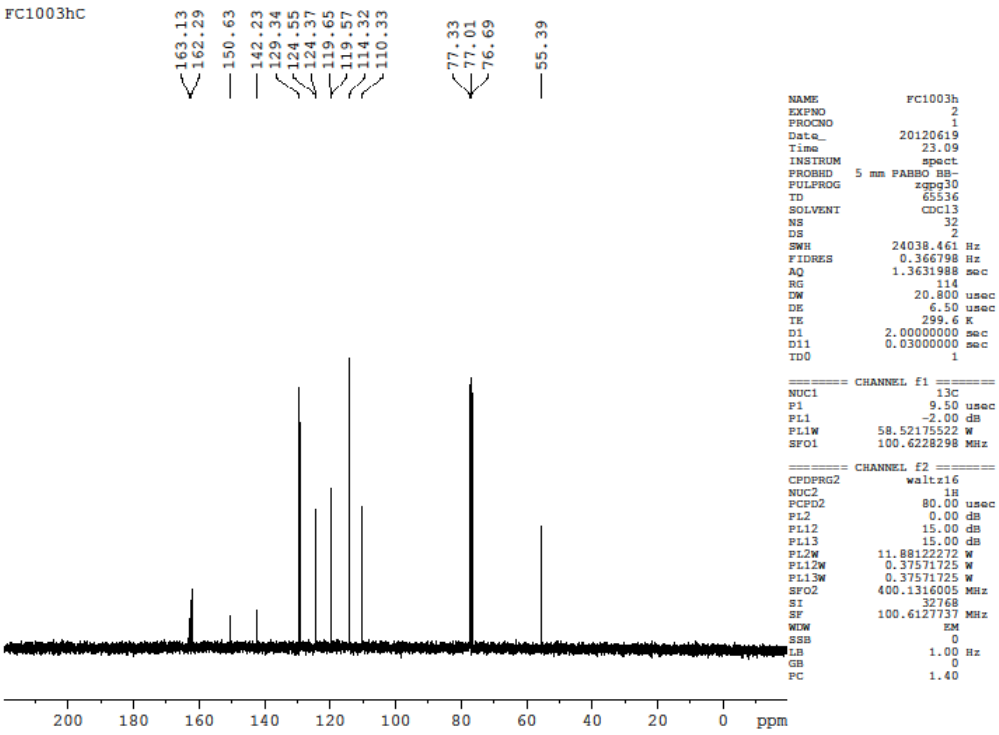
2-(2-Naphthalenyl)benzoxazole (Table 3.2, entry 7)



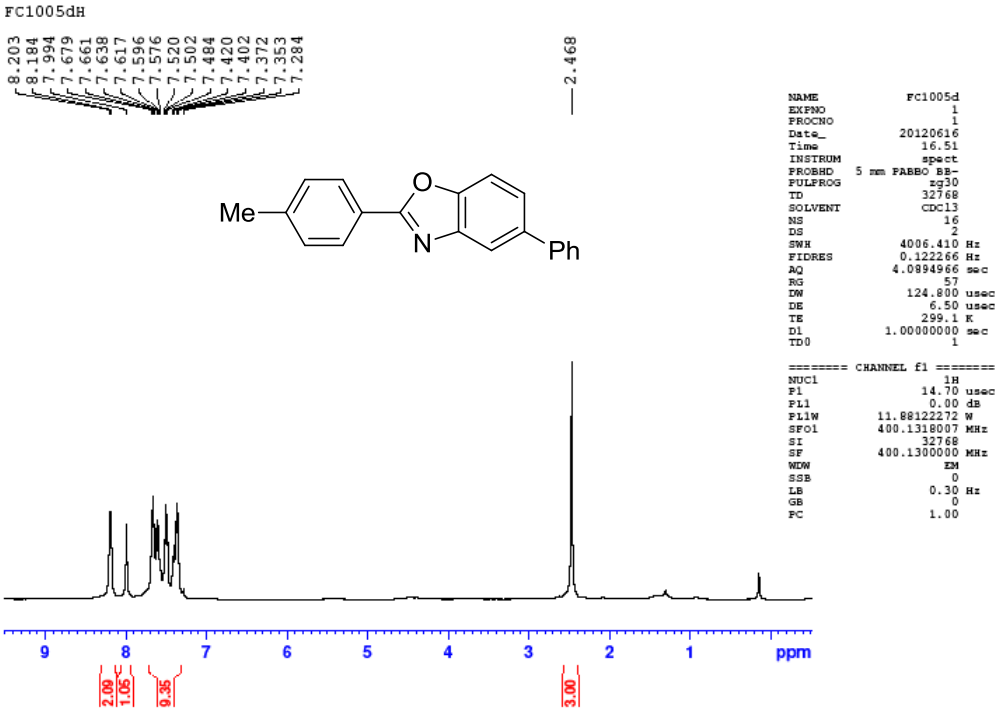


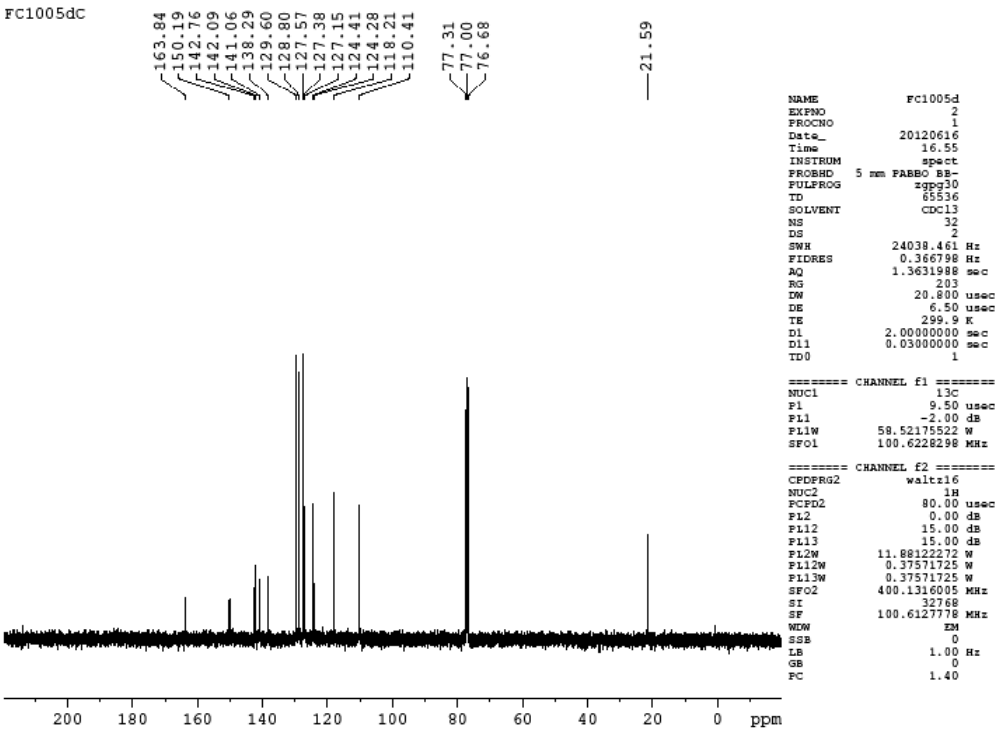
2-(4-Methoxyphenyl)benzoxazole (Table 3.2, entry 8)



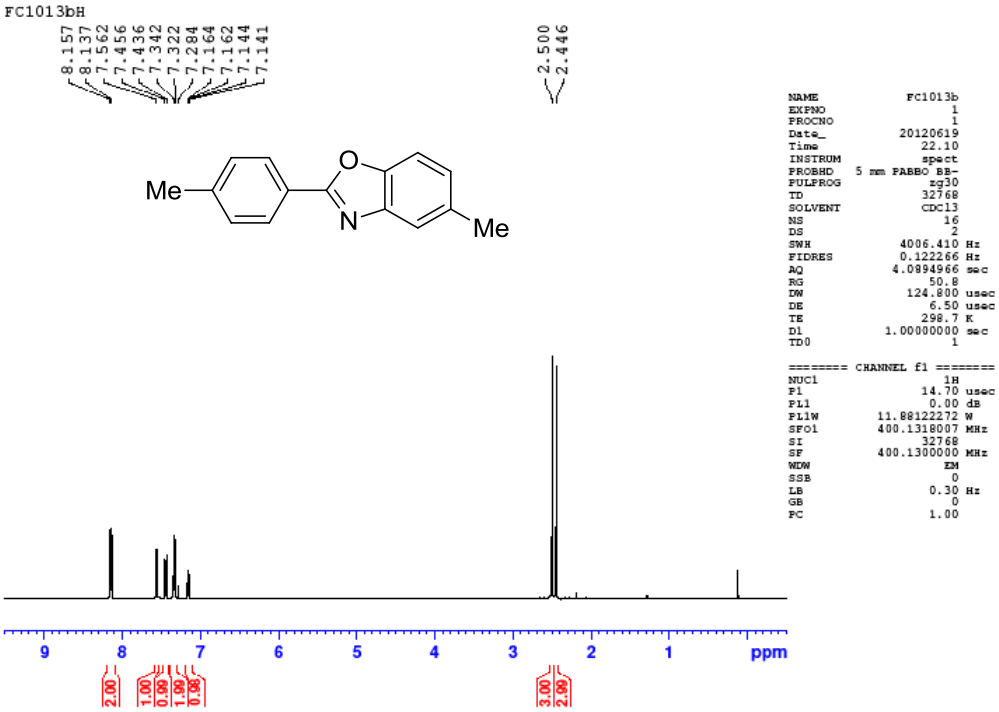


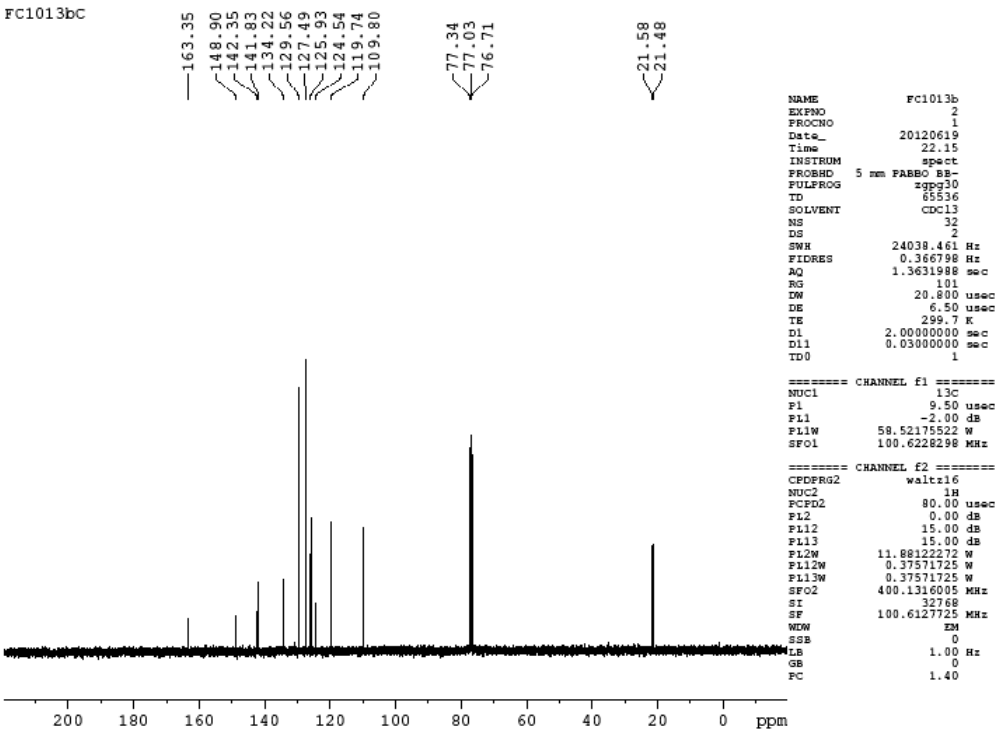
2-(4-Methylphenyl)-5-phenylbenzoxazole (Table 3.3, entry 1)



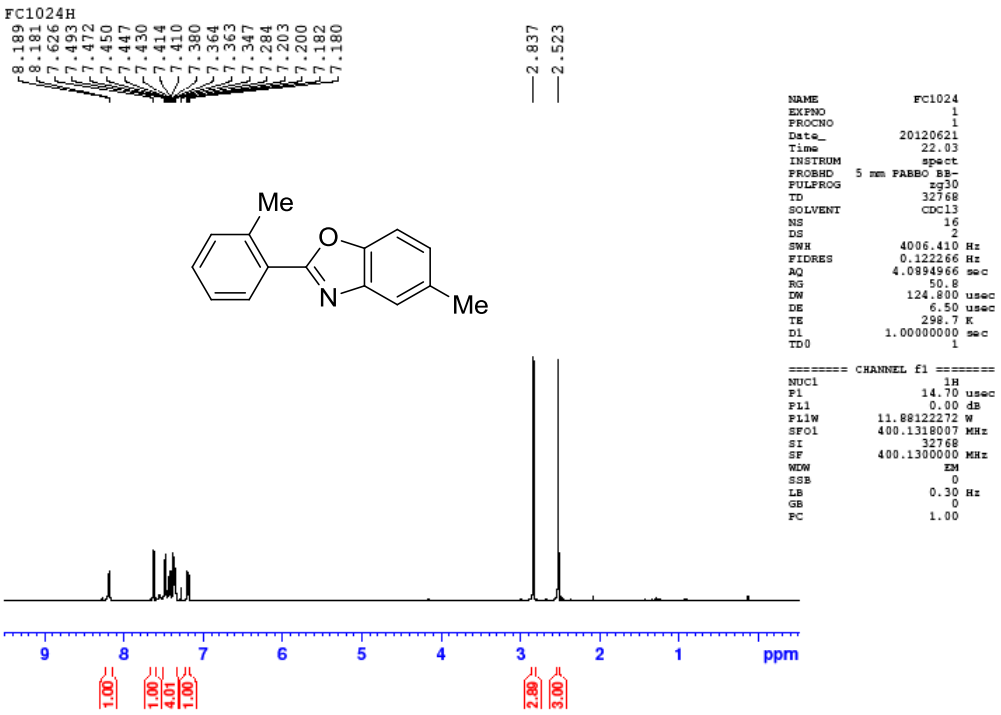


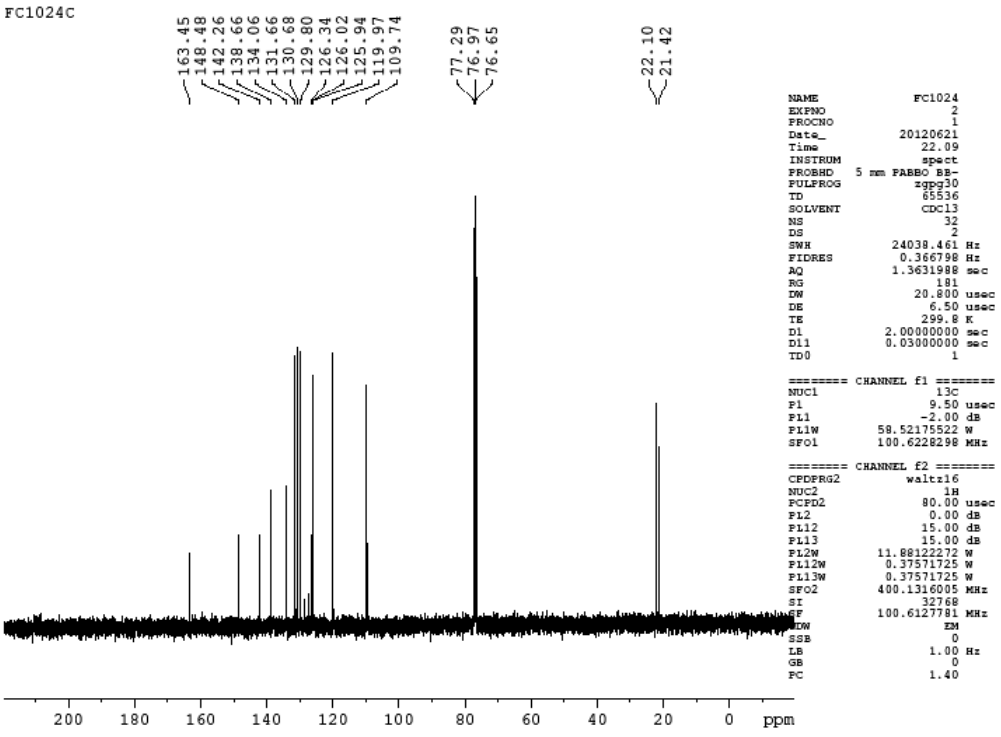
5-Methyl-2-(4-methylphenyl)benzoxazole (Table 3.3, entry 2)





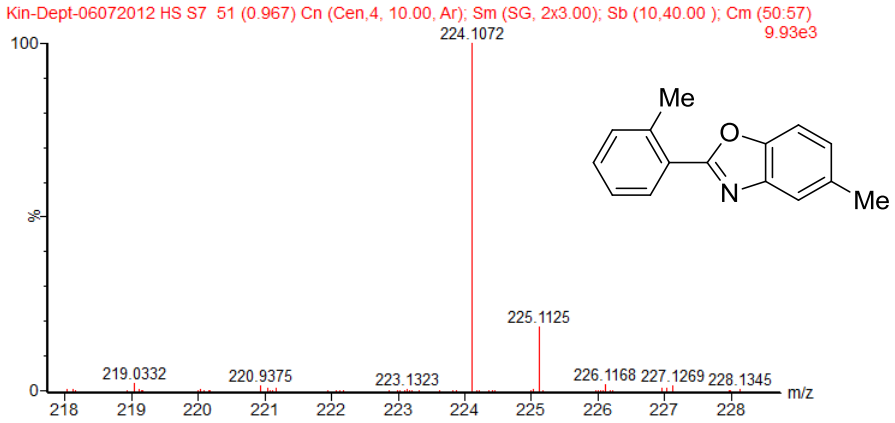
5-Methyl-2-(2-methylphenyl)benzoxazole (Table 3.3, entry 3)





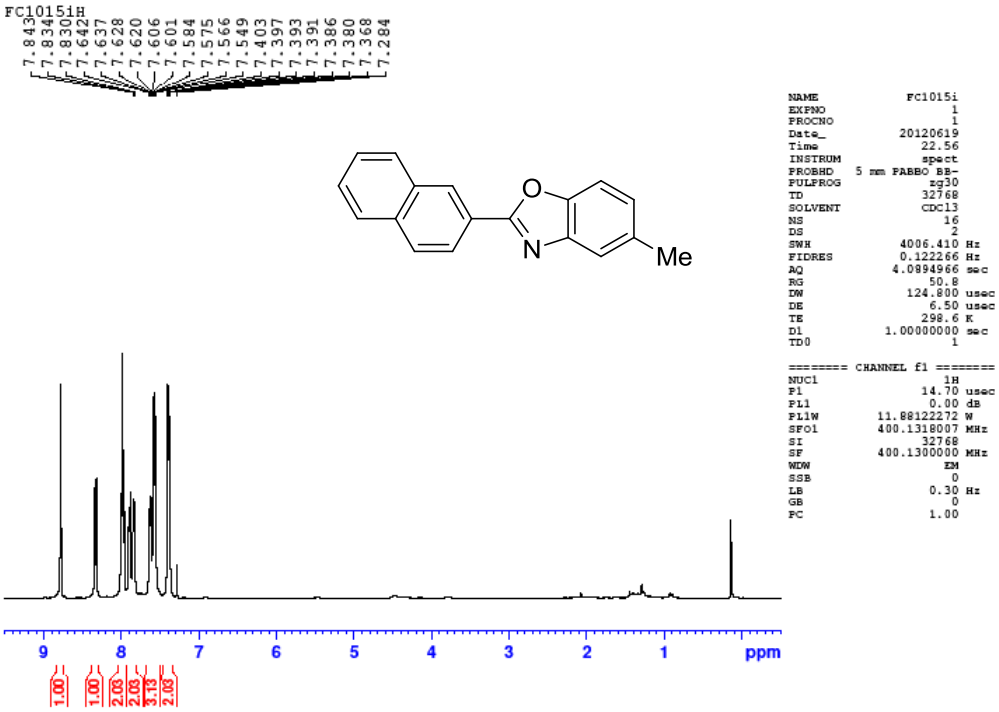
5-Methyl-2-(2-methylphenyl)benzoxazole (Table 3.3, entry 3)

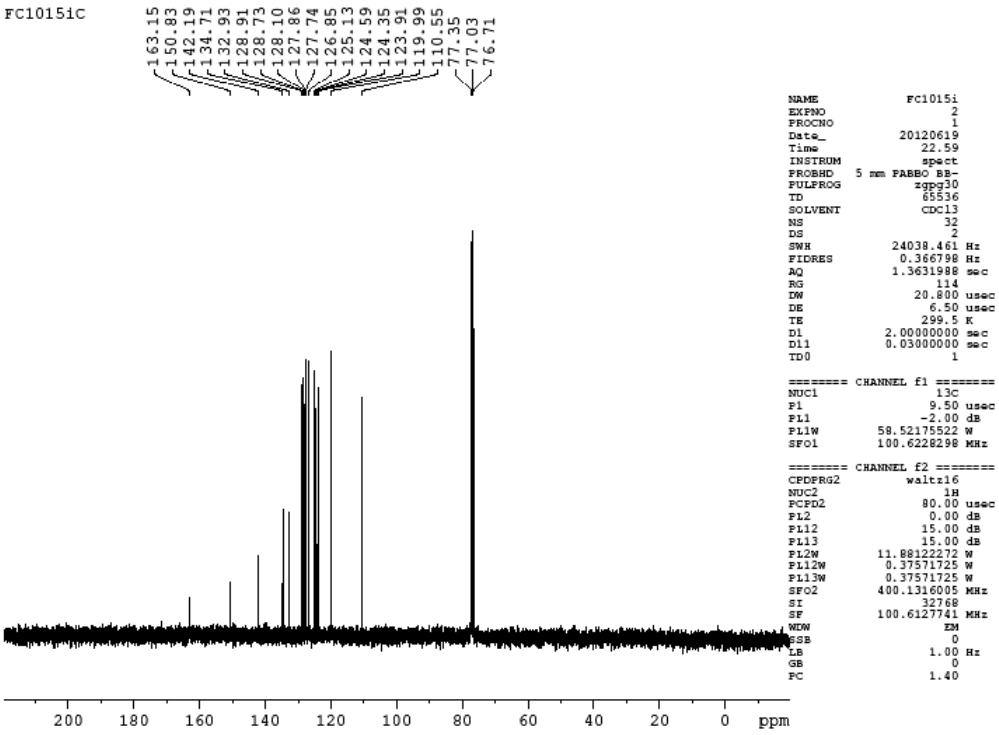
HS



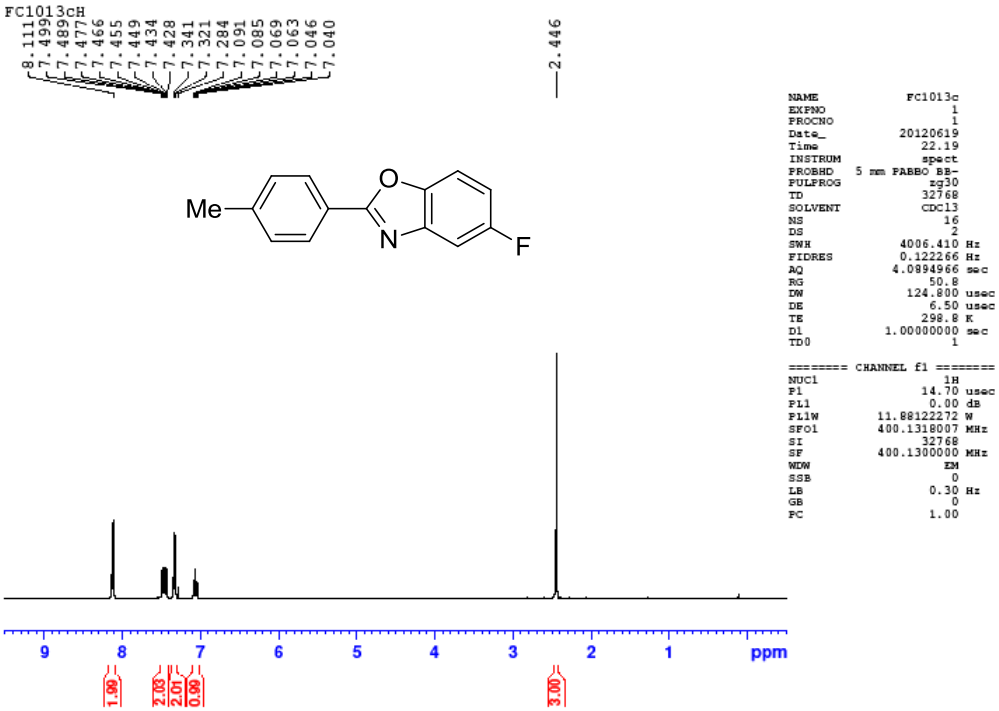
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
224.1072	224.1075	-0.3	-1.3	9.5	5.4	C15 H14 N O

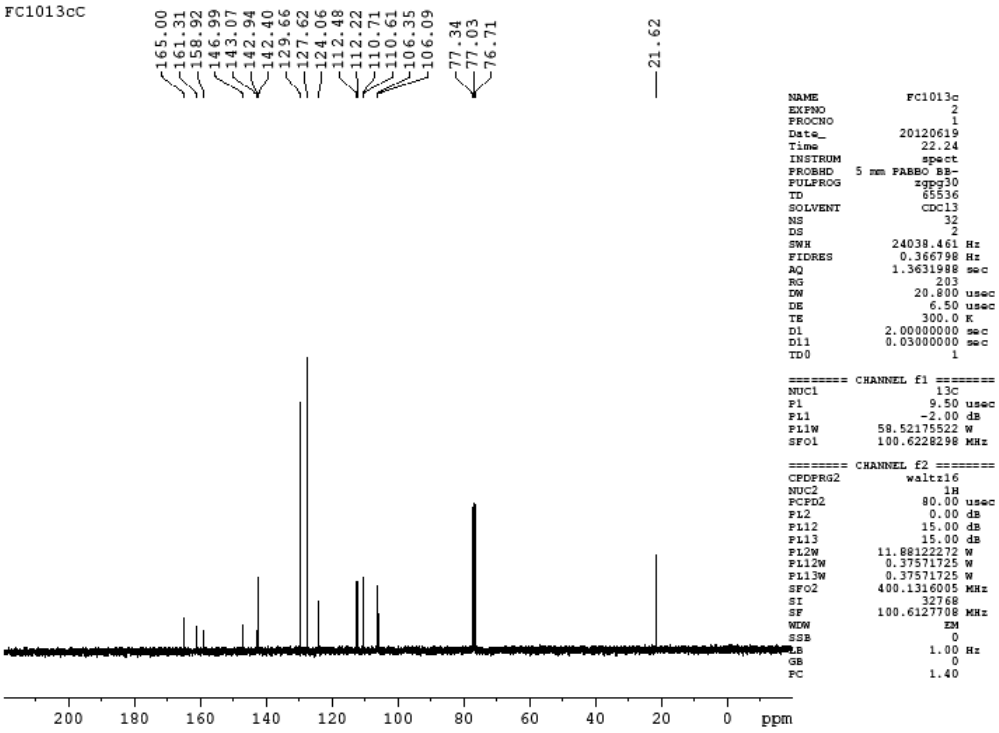
5-Methyl-2-(2-naphthalenyl)benzoxazole (Table 3.3, entry 4)



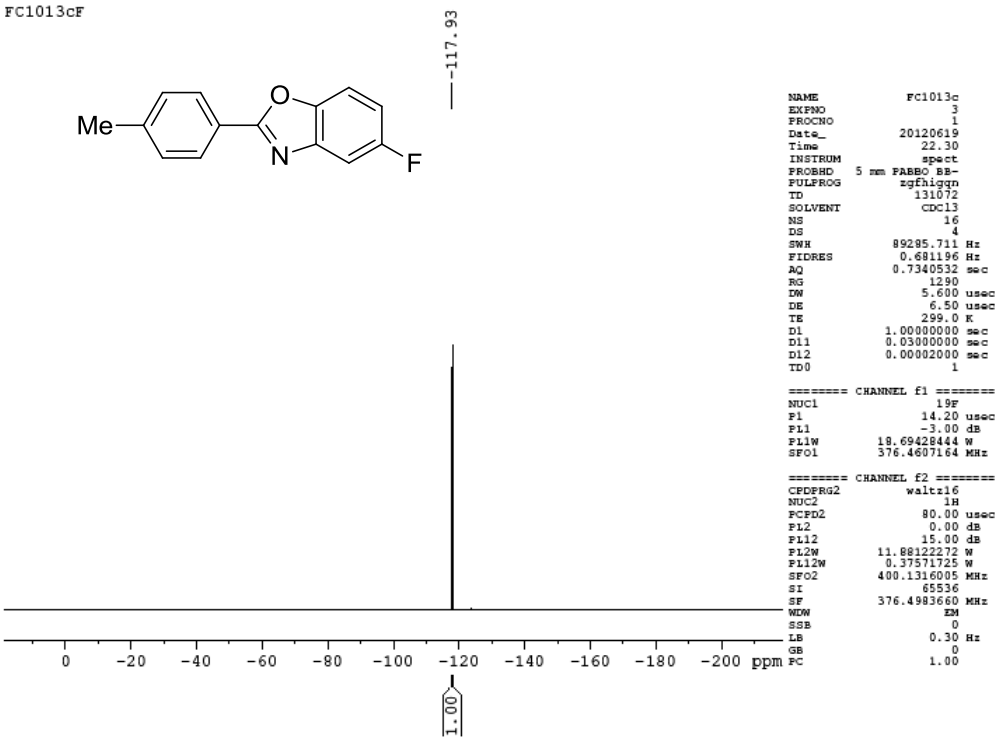


5-Fluoro-2-(4-methylphenyl)benzoxazole (Table 3.3, entry 5)

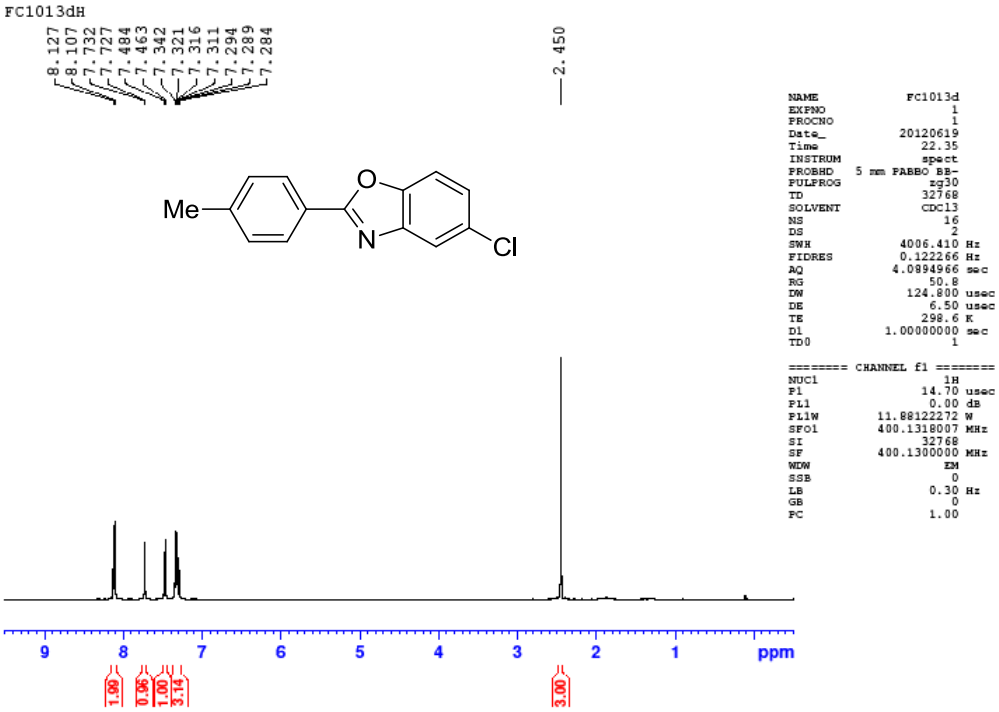


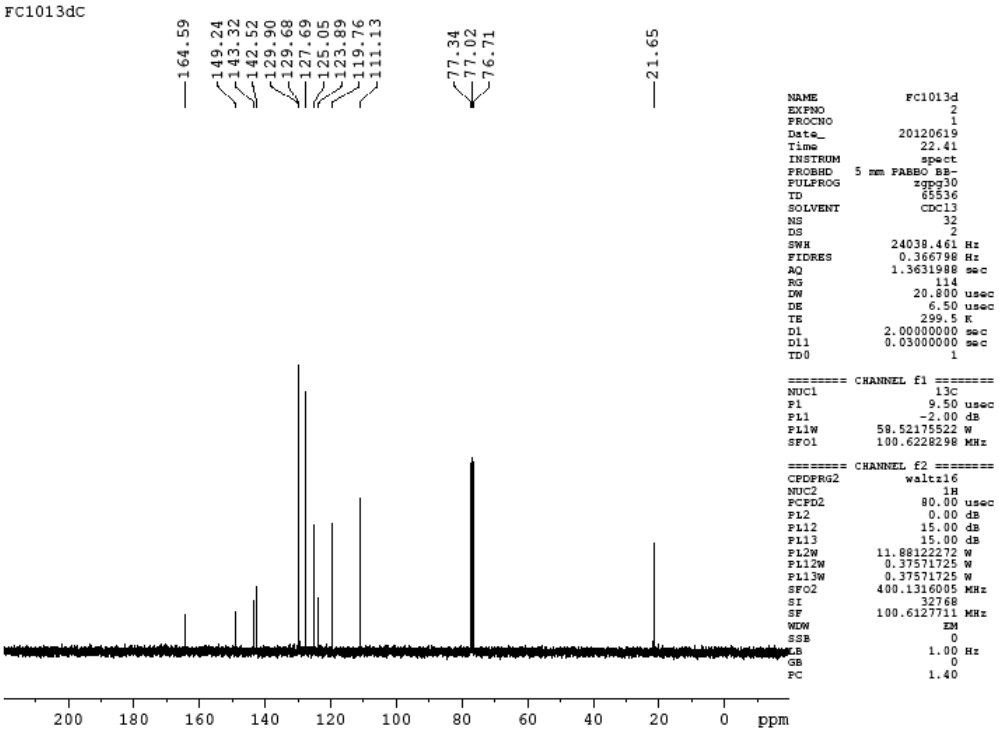


5-Fluoro-2-(4-methylphenyl)benzoxazole (Table 3.3, entry 5)



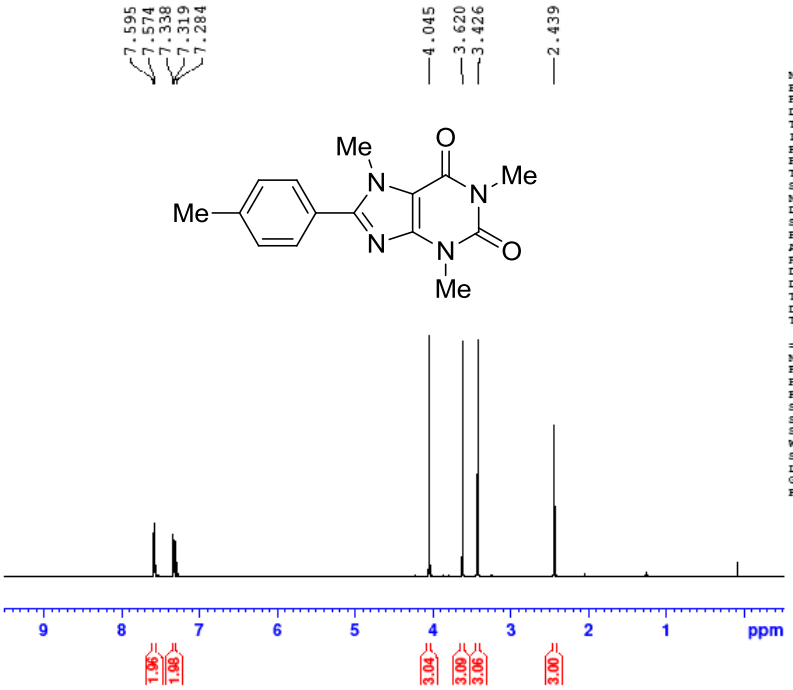
5-Chloro-2-(4-methylphenyl)benzoxazole (Table 3.3, entry 6)





1,3,7-Trimethyl-8-(4-tolyl)-xanthine (Scheme 3.3, compound 1)

FC1004aH



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PROCNO	1
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Time	16.40
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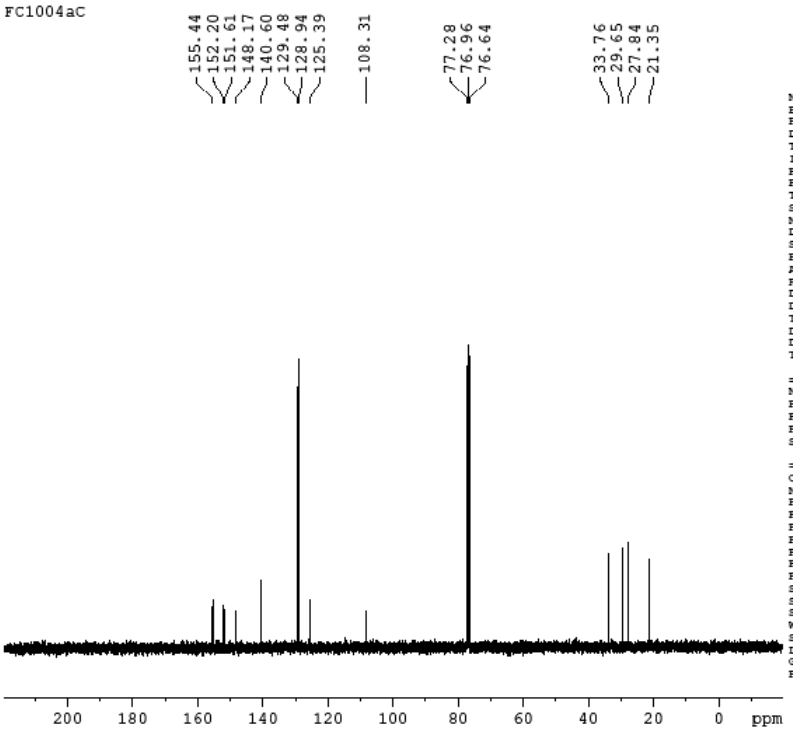
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	16
DS	2
SWH	4006.410 Hz
FIDRES	0.122266 Hz
AQ	4.0894966 sec
RG	57
DW	124.800 usec
DE	6.50 usec
TE	299.1 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	14.70 usec
PL1	0.00 dB
PL1W	11.88122272 W
SFO1	400.1318007 MHz
SI	32768
SF	400.1300000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

FC1004aC



NAME	FC1004a
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PROCNO	1
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Time	16.44
INSTRUM	spect
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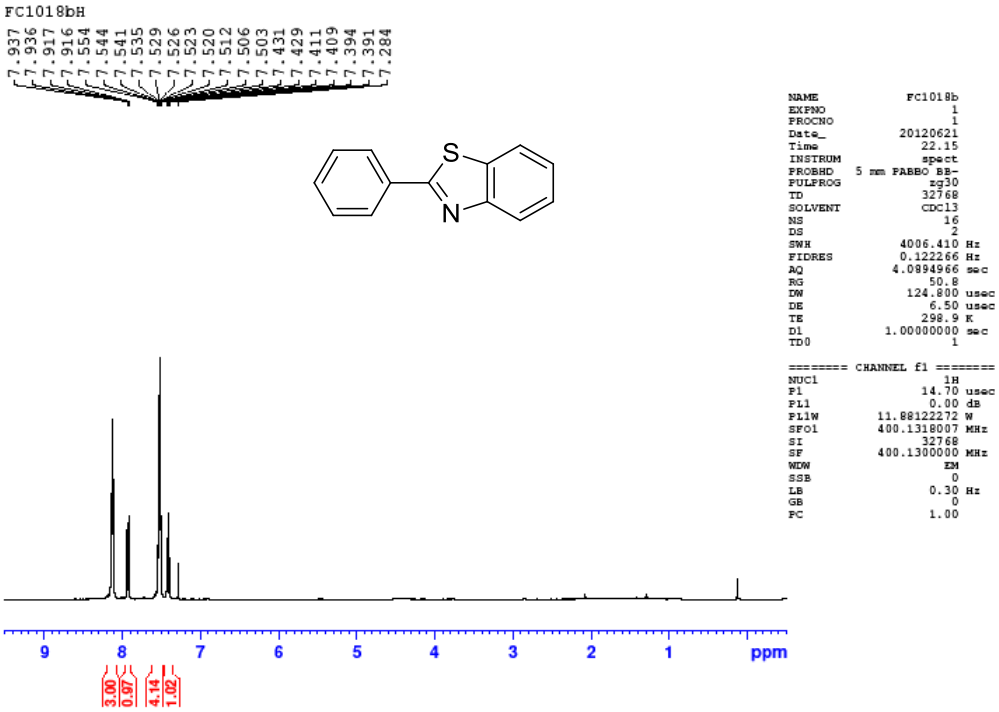
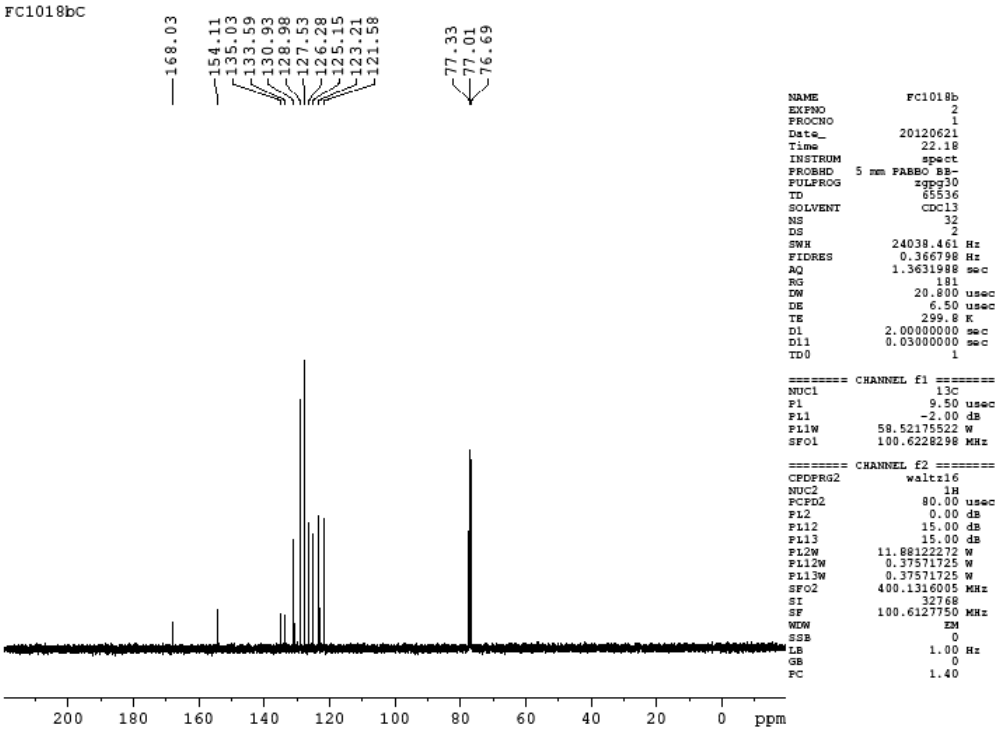
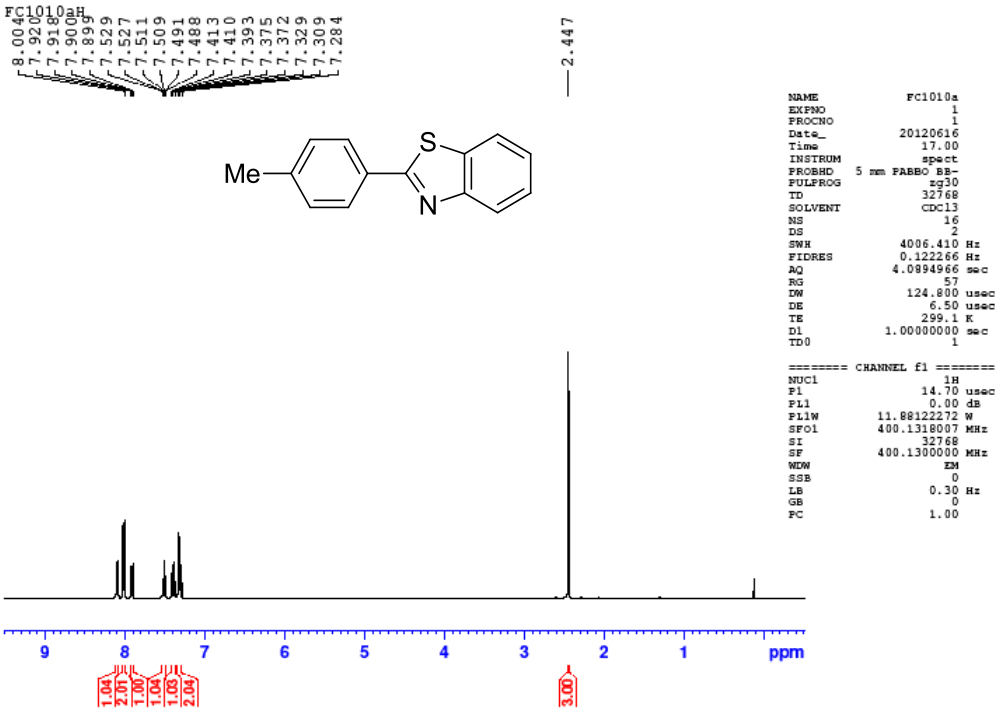
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	32
DS	2
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	299.9 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.50 usec
PL1	-2.00 dB
PL1W	58.52175522 W
SFO1	100.6228298 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	0.00 dB
PL12	15.00 dB
PL13	15.00 dB
PL2W	11.88122272 W
PL12W	0.37571725 W
PL13W	0.37571725 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127796 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

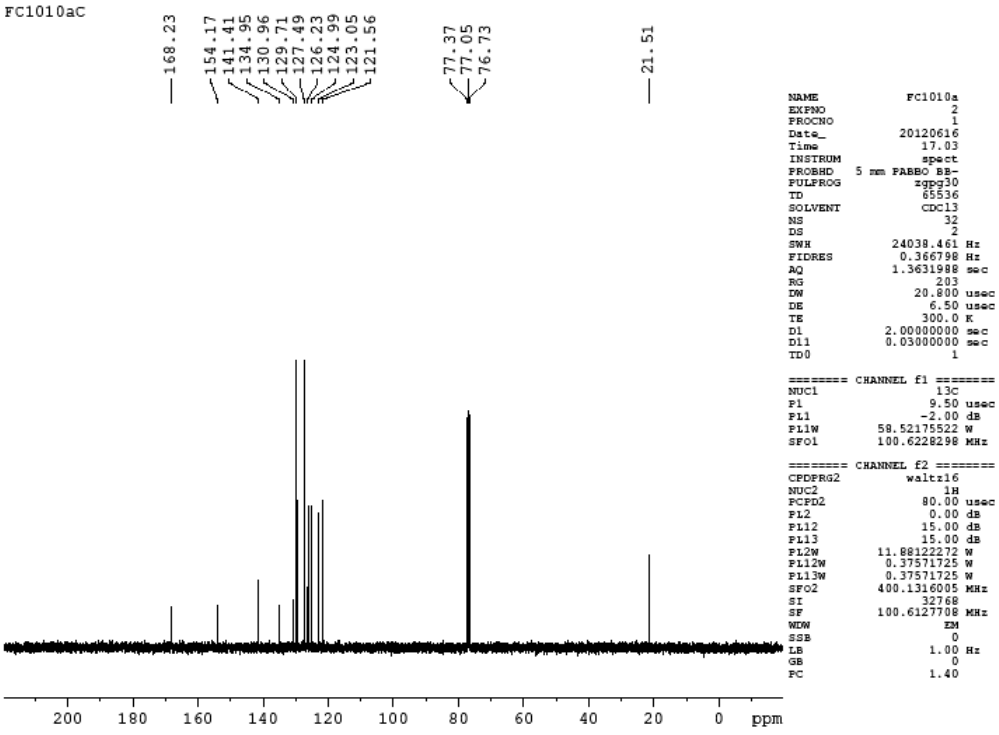
2-Phenylbenzothiazole (Scheme 3.3, compound 2)



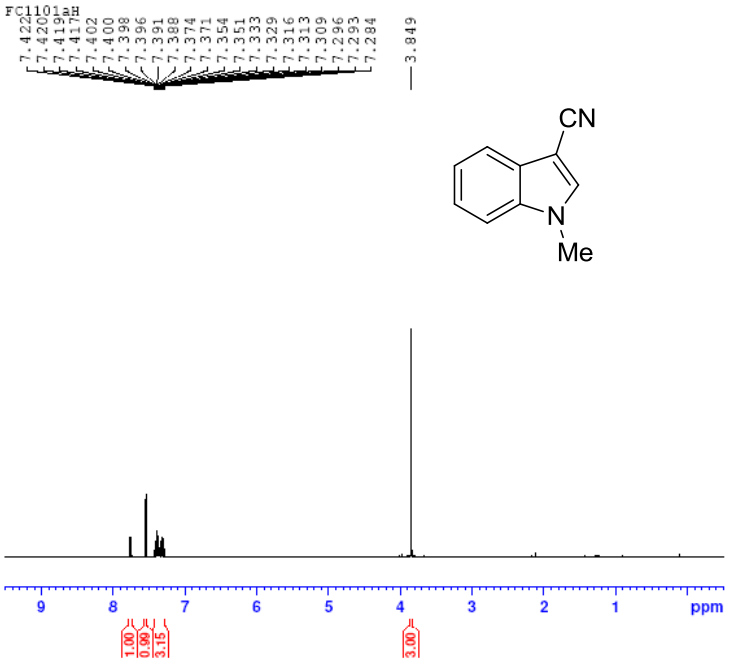


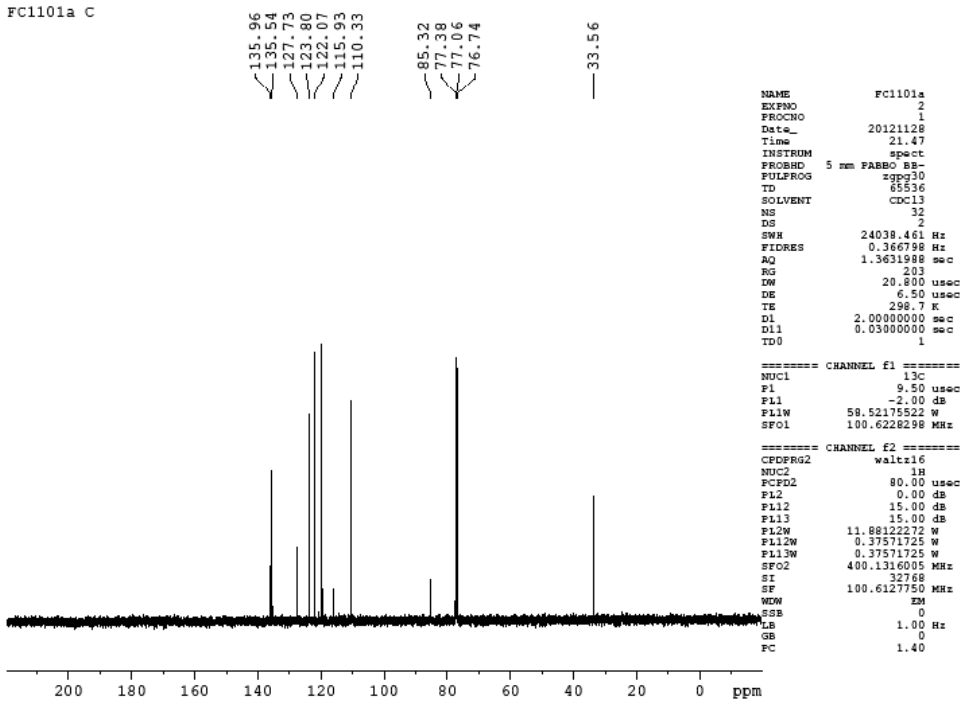
2-(4-Methylphenyl)benzothiazole (Scheme 3.3, compound 3)



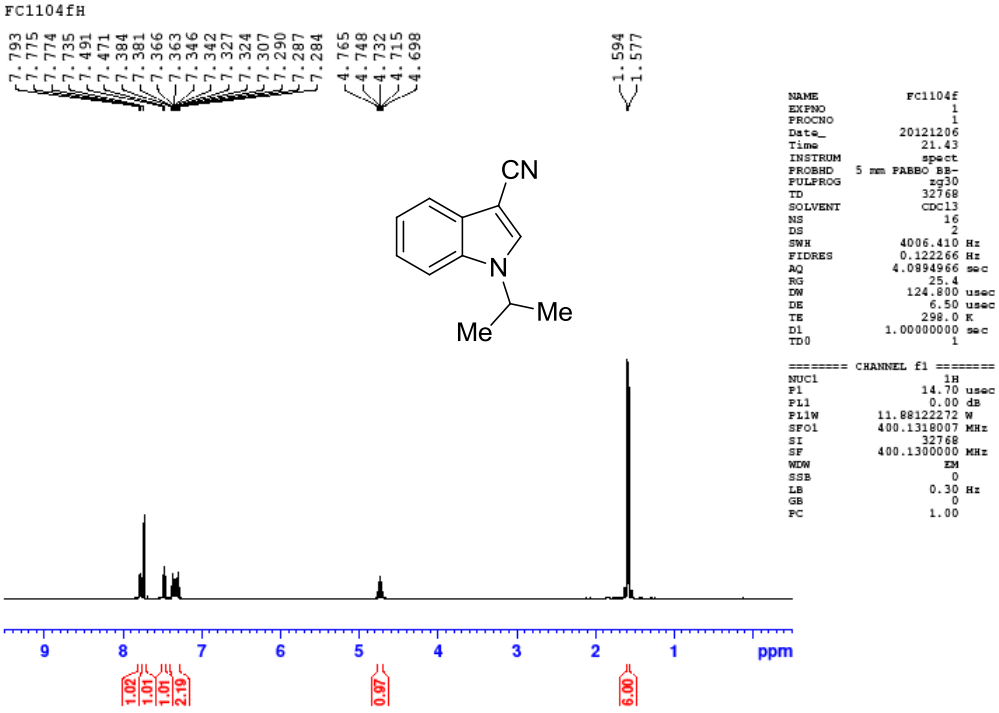


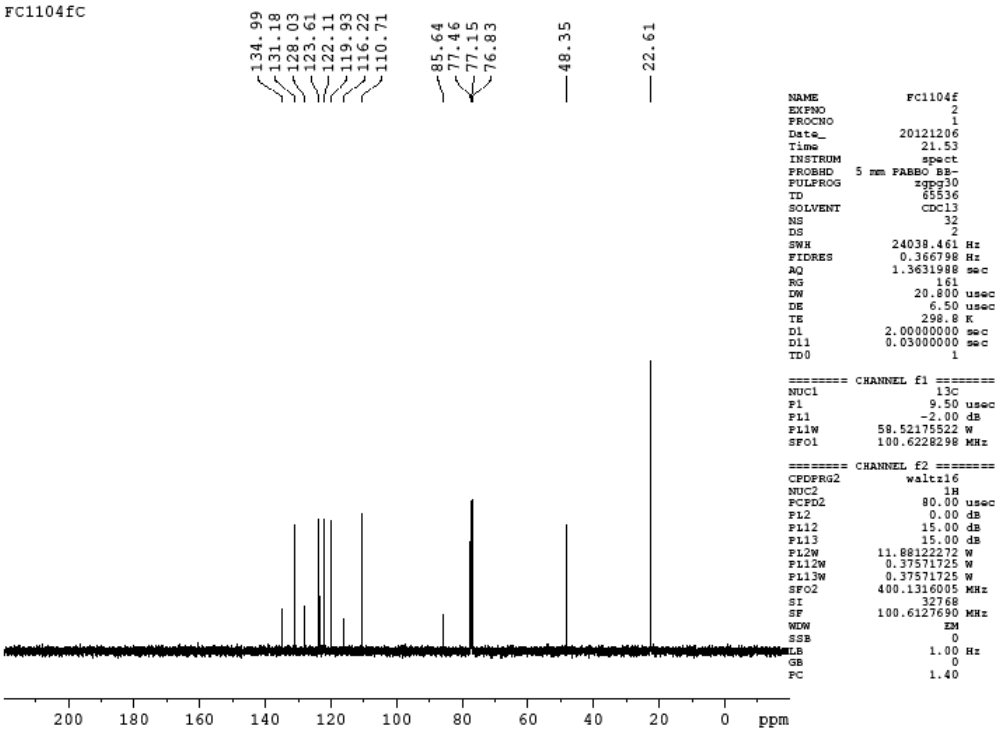
1-Methyl-1*H*-indole-3-carbonitrile (Table 4.2, entry 1)





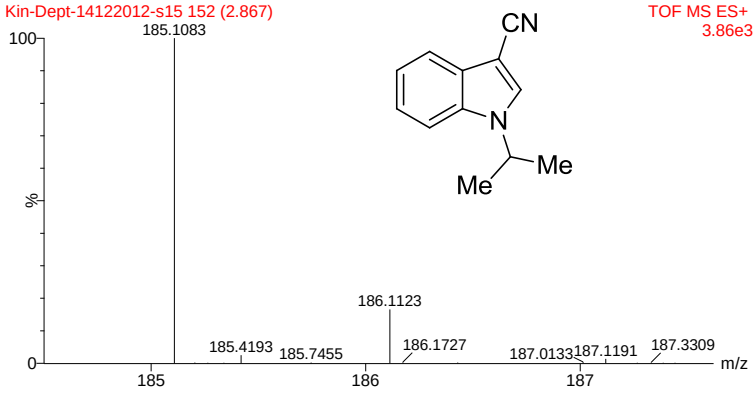
1-Isopropyl-1*H*-indole-3-carbonitrile (Table 4.2, entry 2)





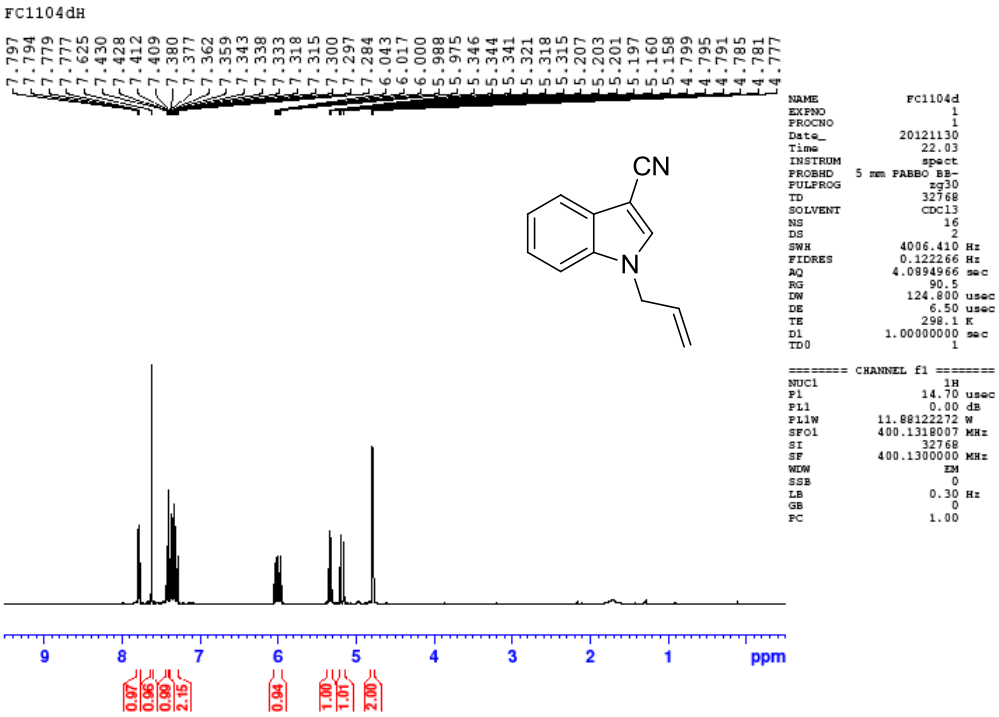
1-Isopropyl-1*H*-indole-3-carbonitrile (Table 4.2, entry 2)

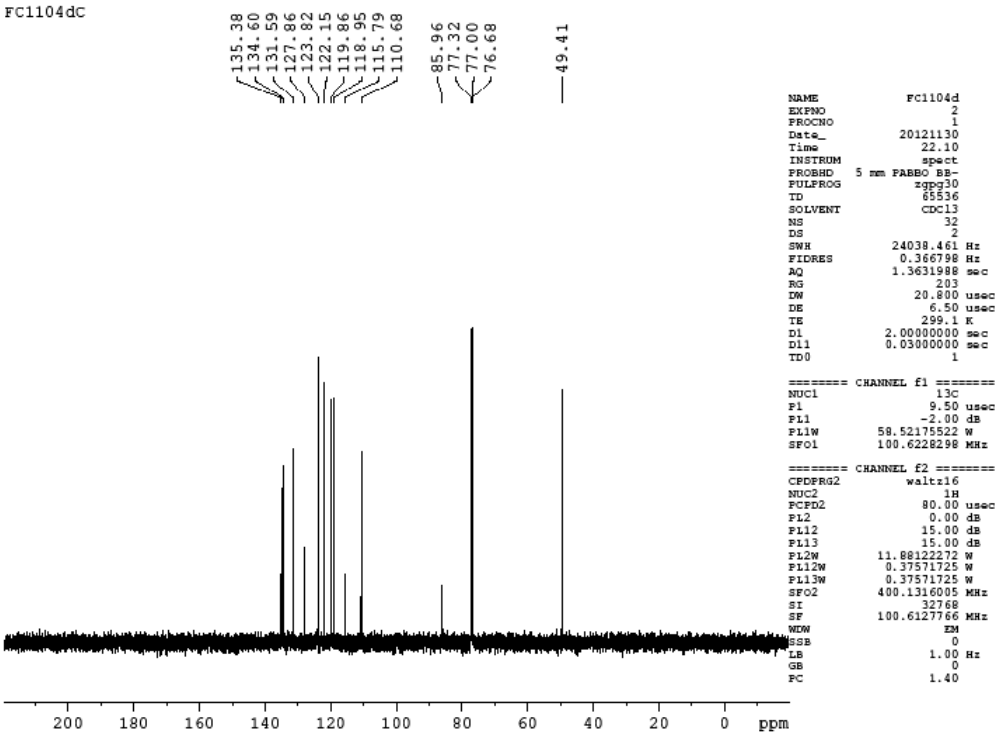
HS



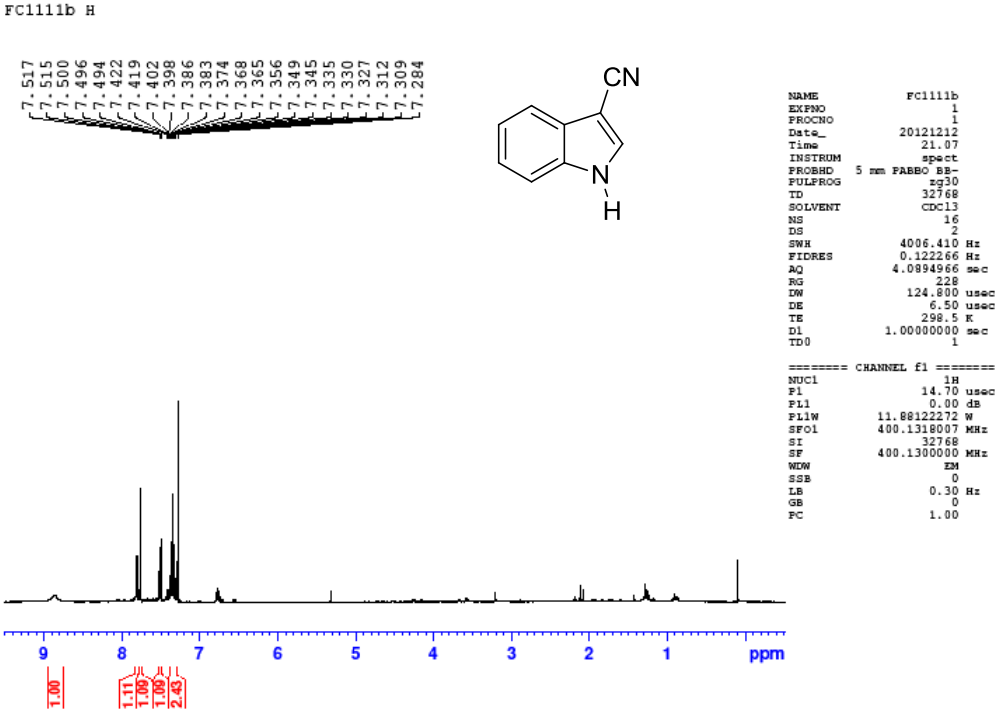
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
185.1083	185.1079	0.4	2.2	7.5	7.0	C12 H13 N2

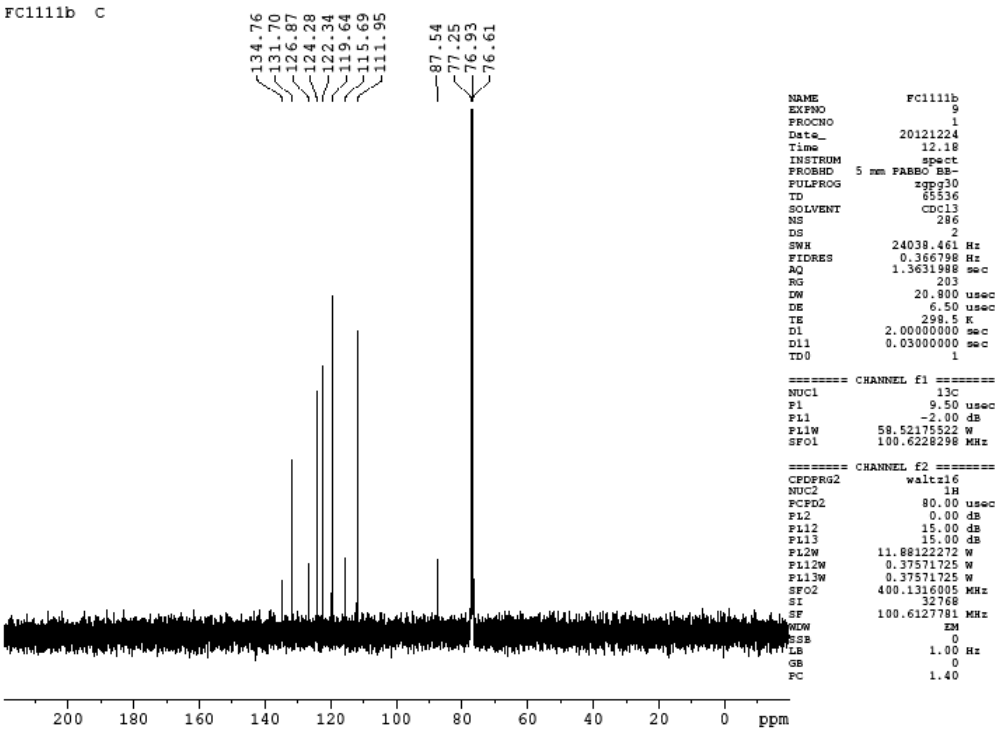
1-Allyl-1*H*-indole-3-carbonitrile (Table 4.2, entry 3)



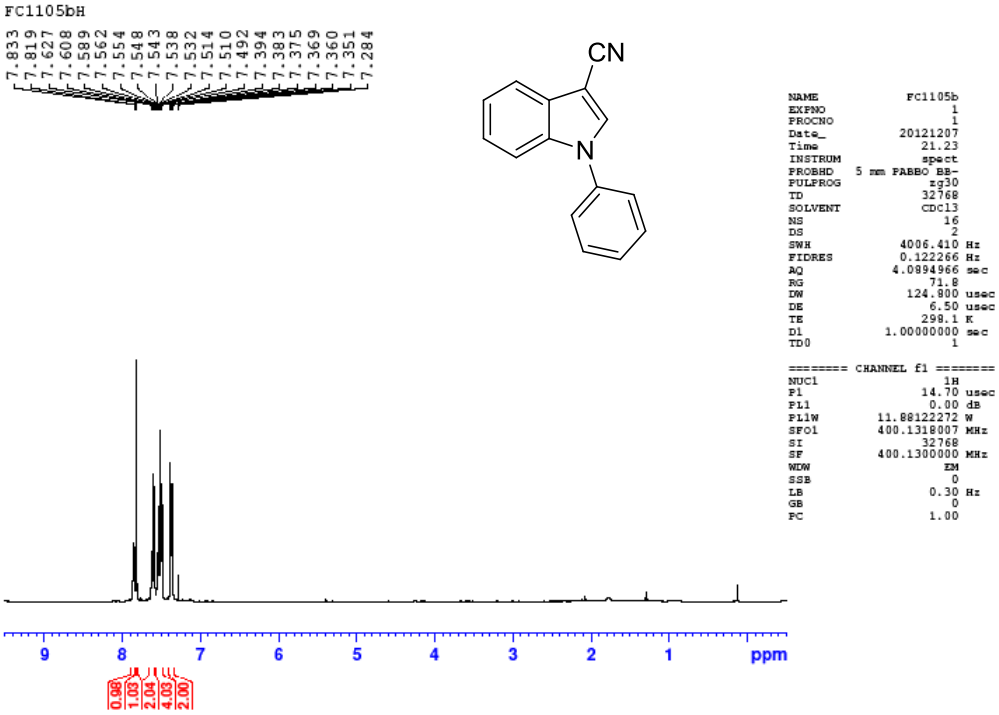


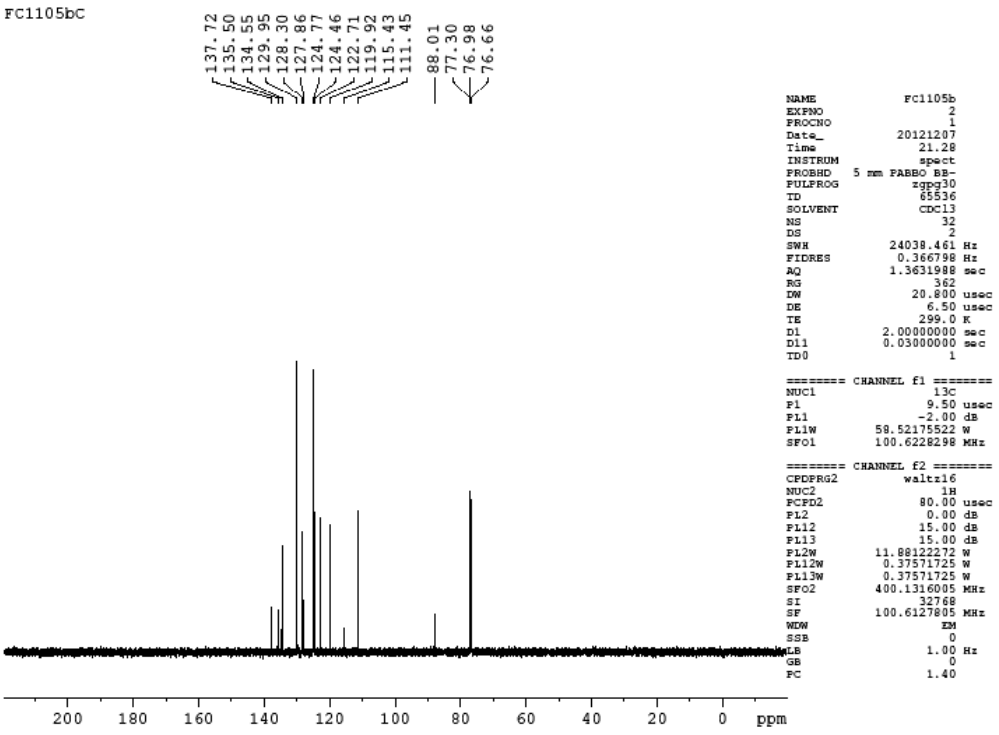
1*H*-Indole-3-carbonitrile (Table 4.2, entry 4)



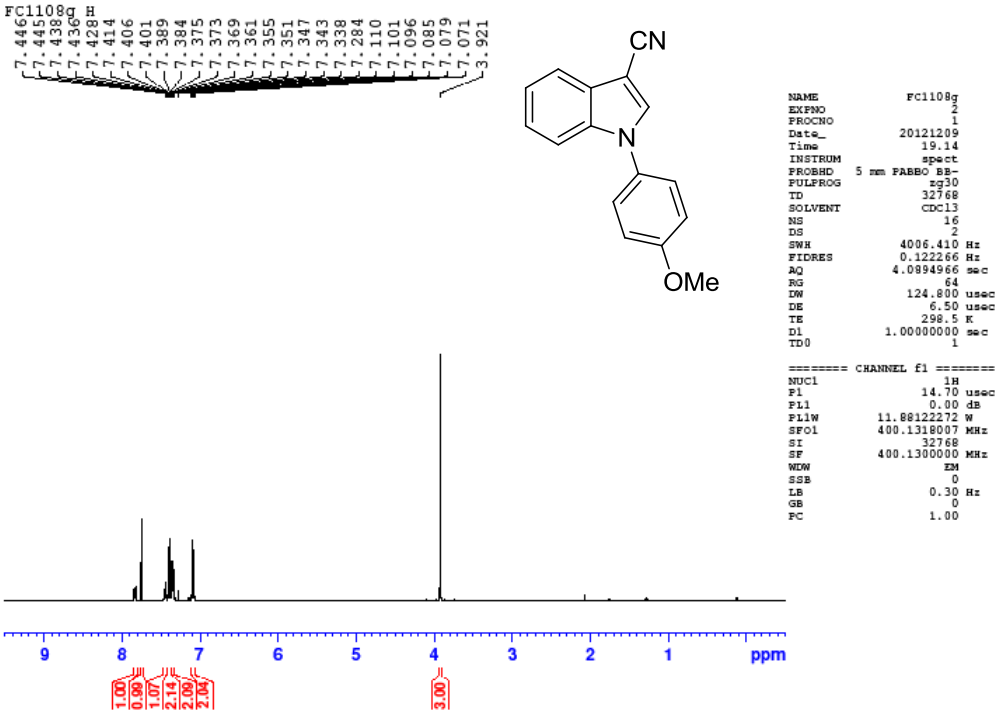


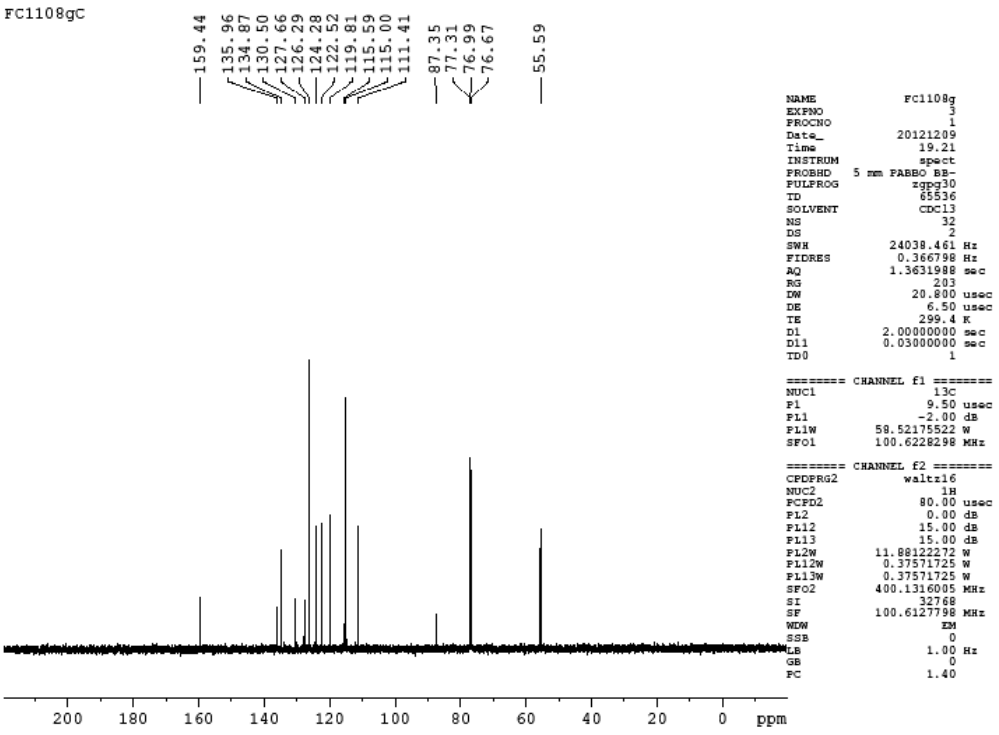
1-Phenyl-1*H*-indole-3-carbonitrile (Table 4.2, entry 5)



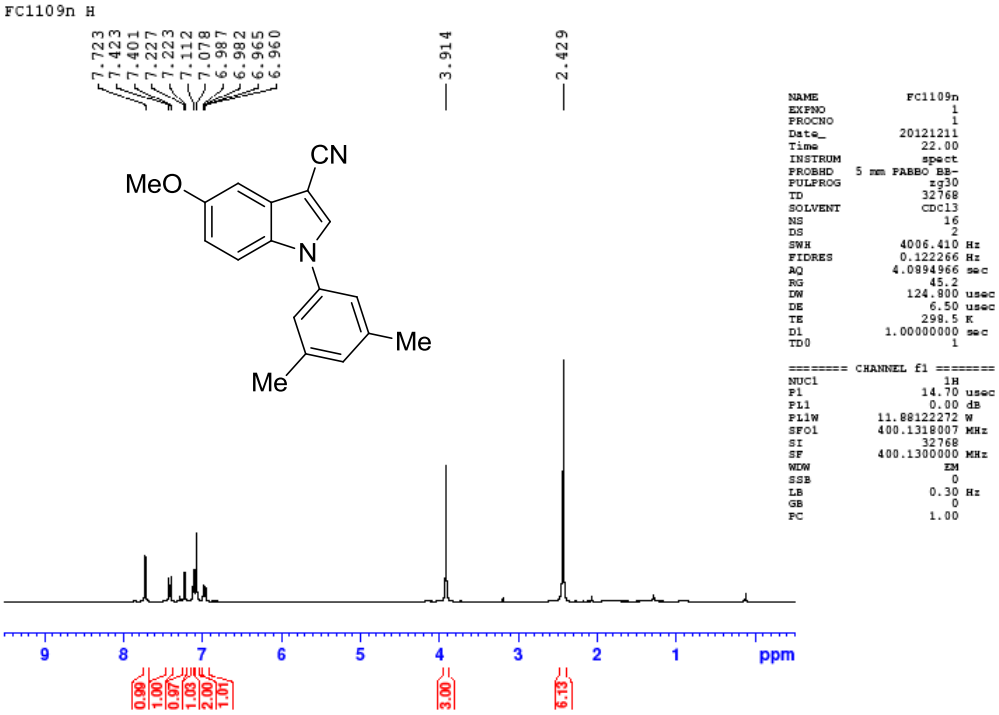


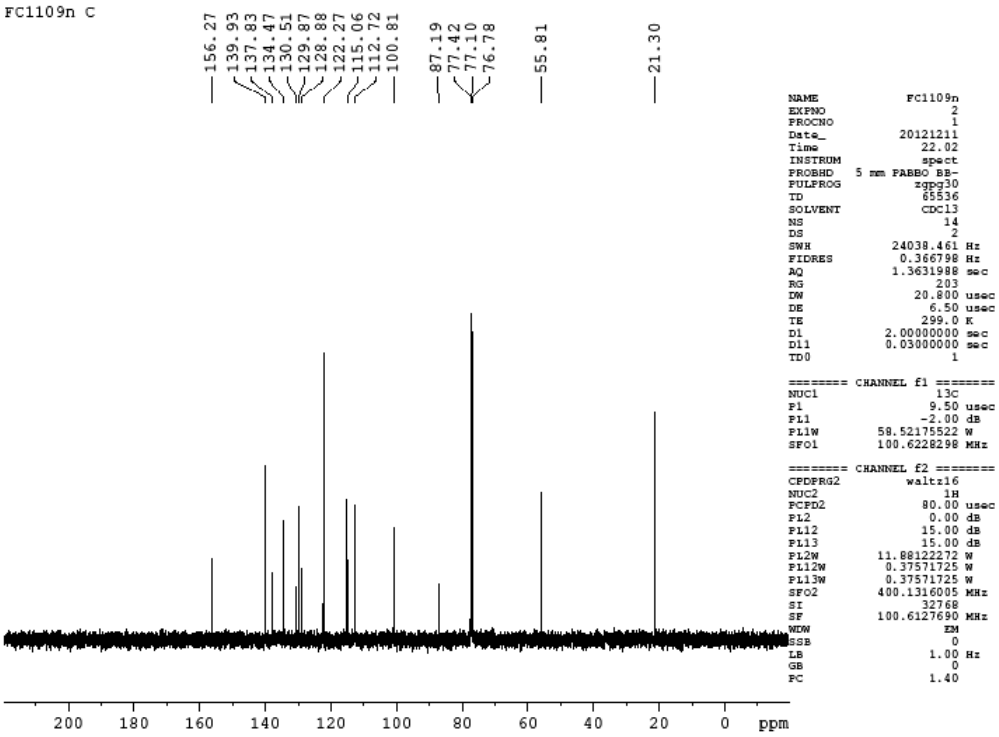
1-(4-Methoxyphenyl)-1*H*-indole-3-carbonitrile (Table 4.2, entry 6)



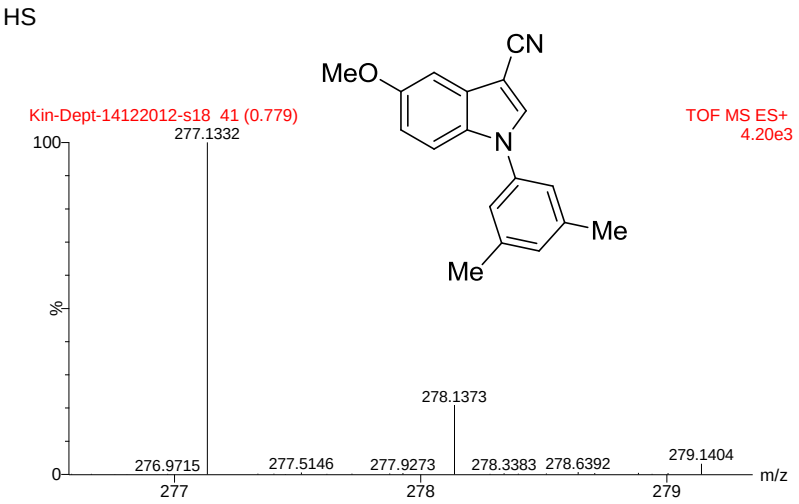


1-(3,5-Dimethylphenyl)-5-methoxy-1*H*-indole-3-carbonitrile (Table 4.2, entry 7)



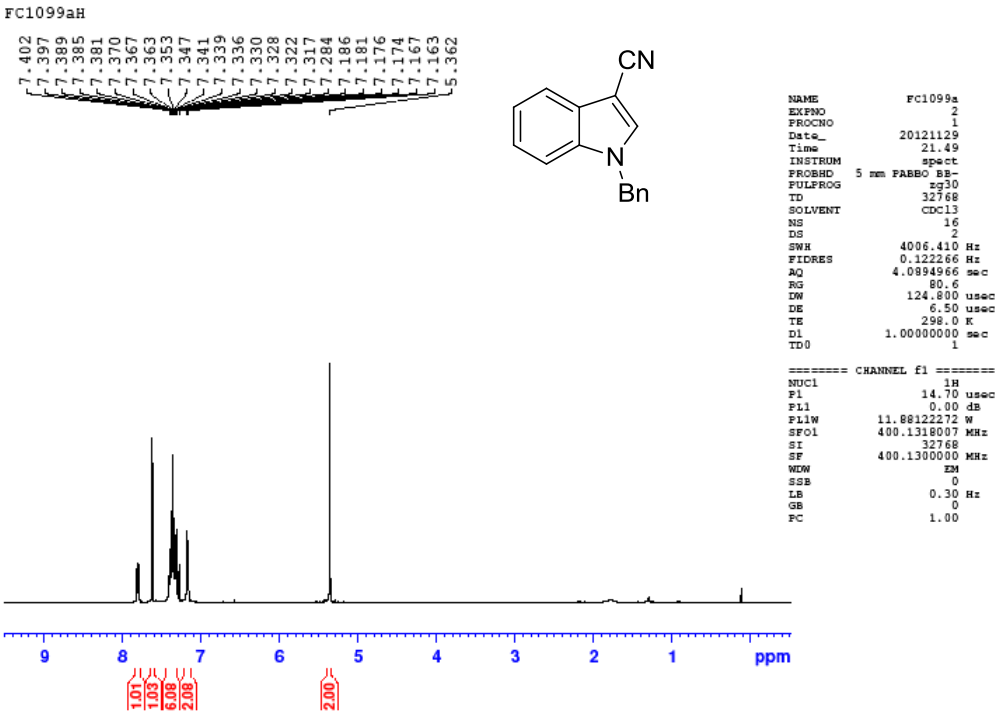


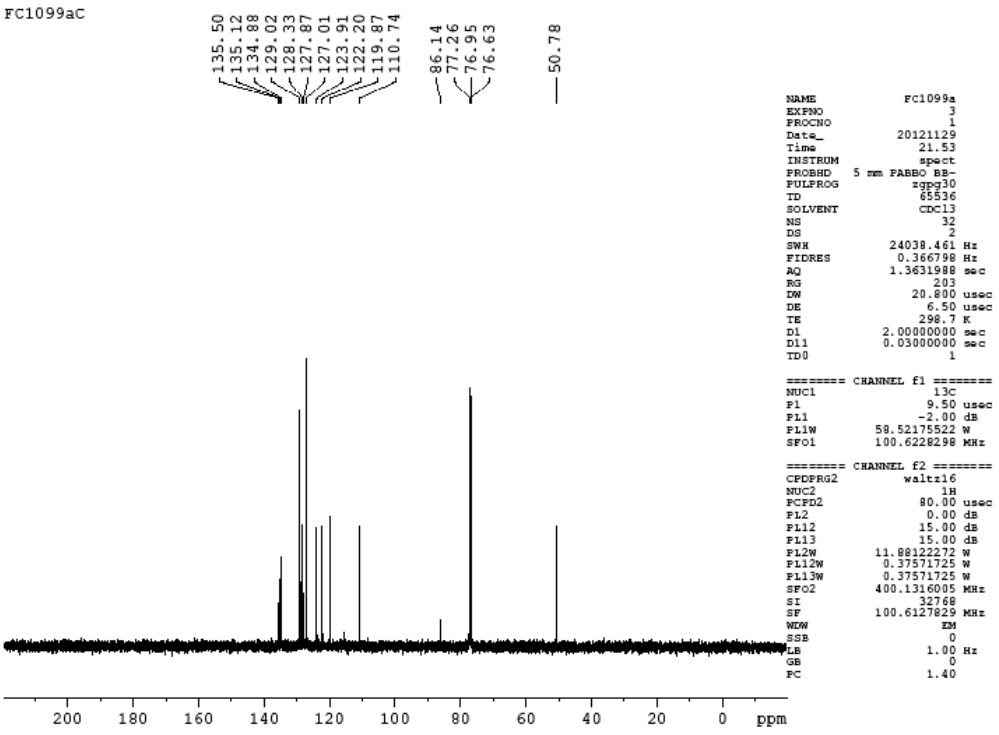
1-(3,5-Dimethylphenyl)-5-methoxy-1*H*-indole-3-carbonitrile (Table 4.2, entry 7)



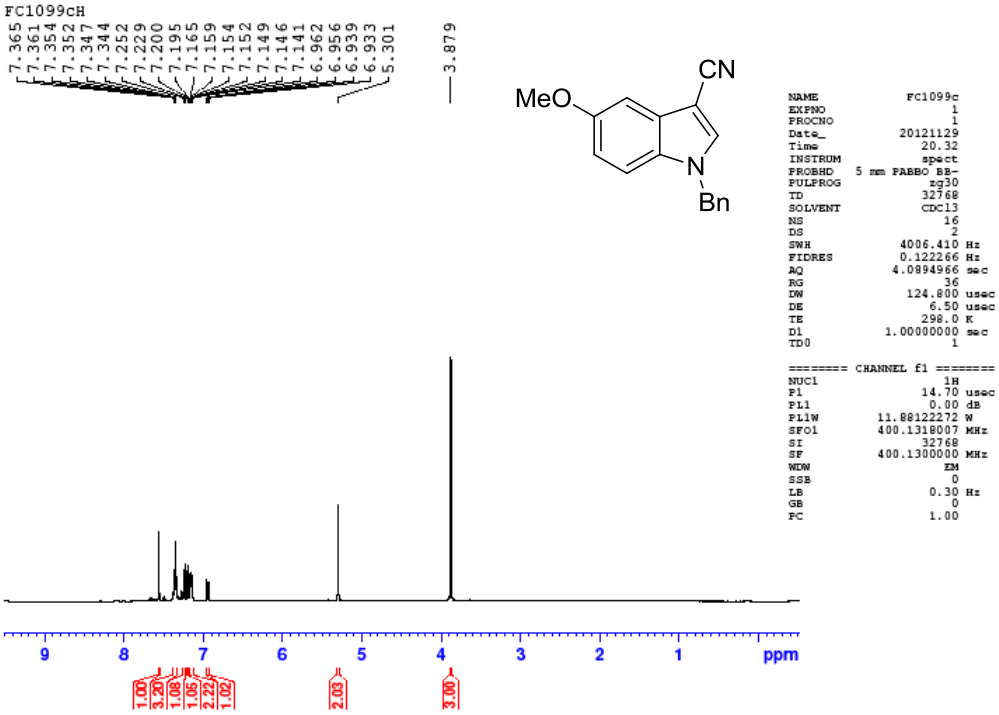
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
277.1332	277.1341	-0.9	-3.2	11.5	5.1	C18 H17 N2 O

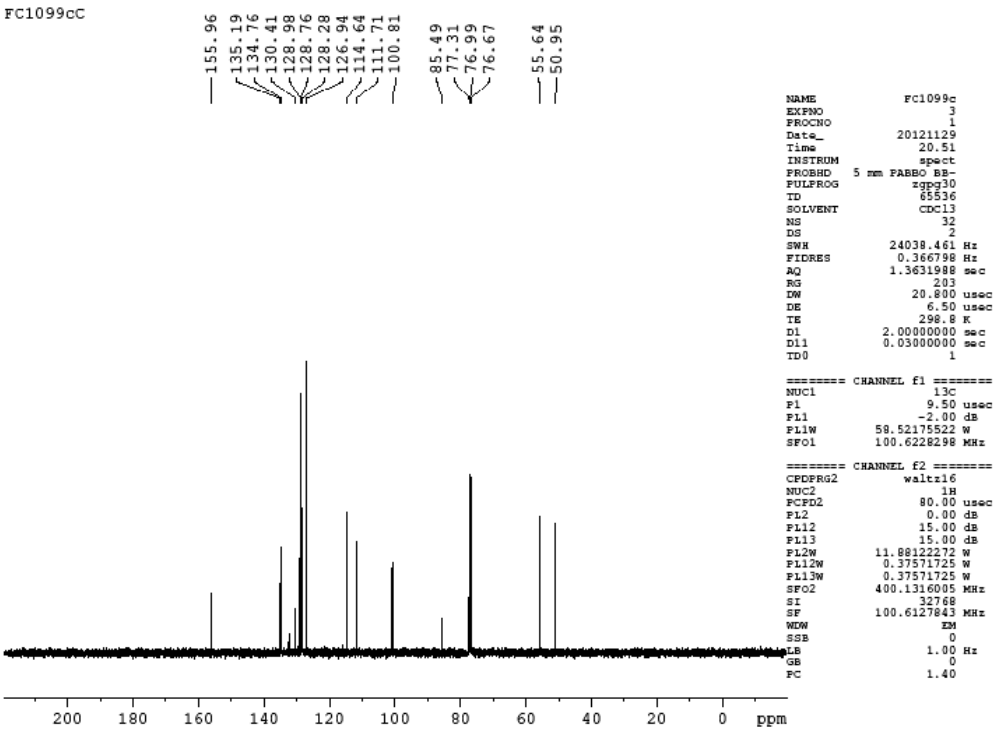
1-Benzyl-1*H*-indole-3-carbonitrile (Table 4.3, entry 1)



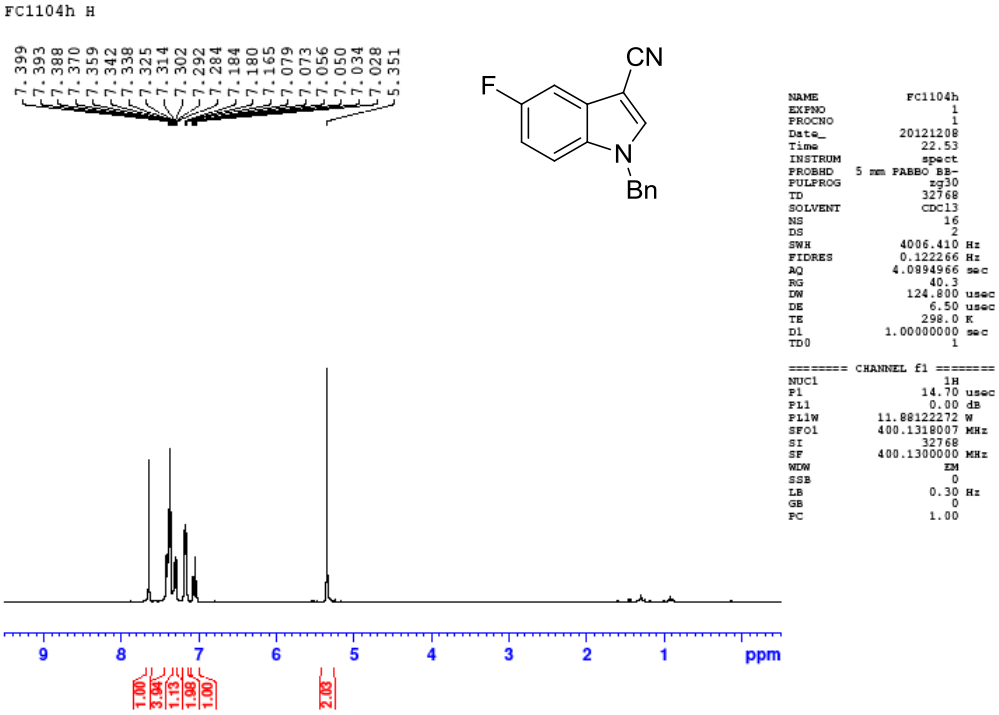


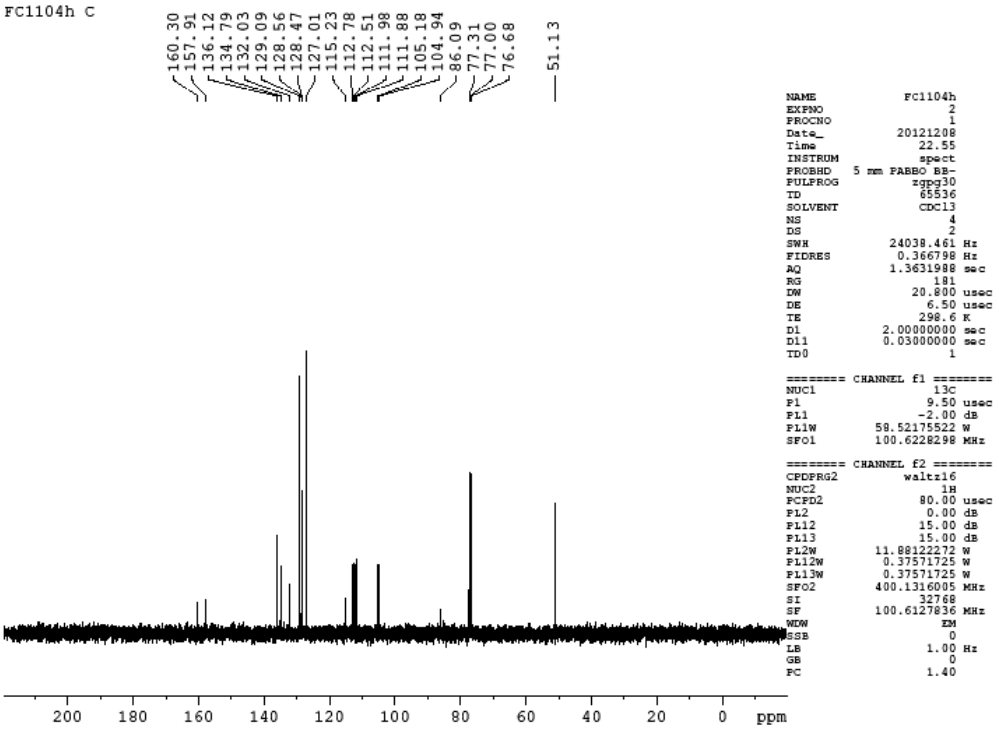
1-Benzyl-5-methoxy-1*H*-indole-3-carbonitrile (Table 4.3, entry 2)



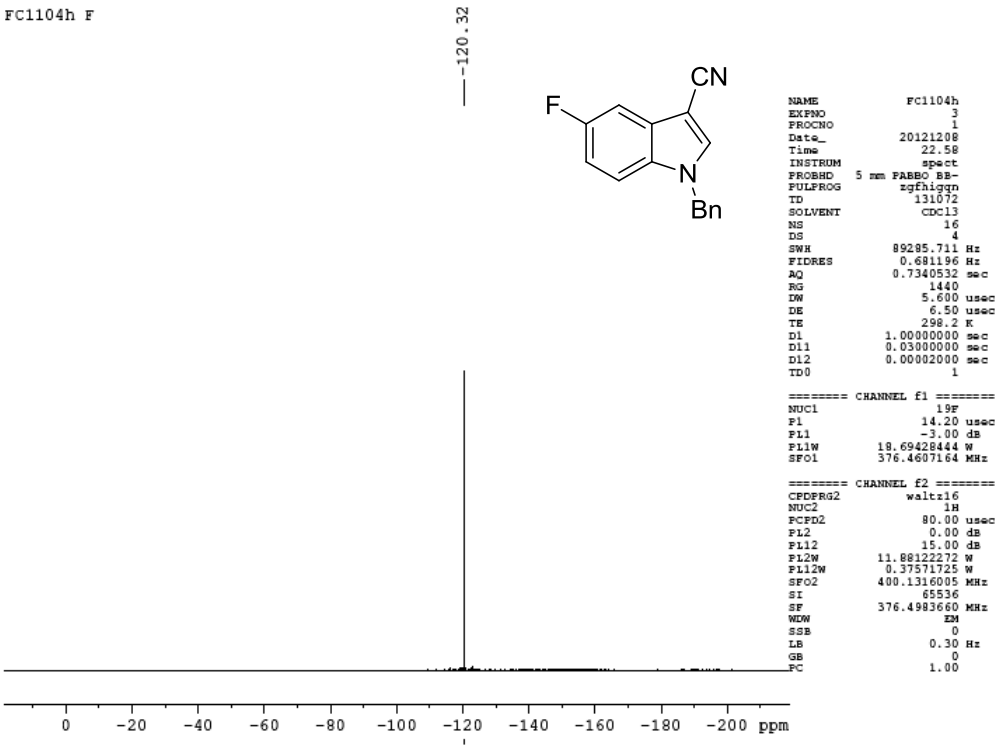


1-Benzyl-5-fluoro-1*H*-indole-3-carbonitrile (Table 4.3, entry 3)

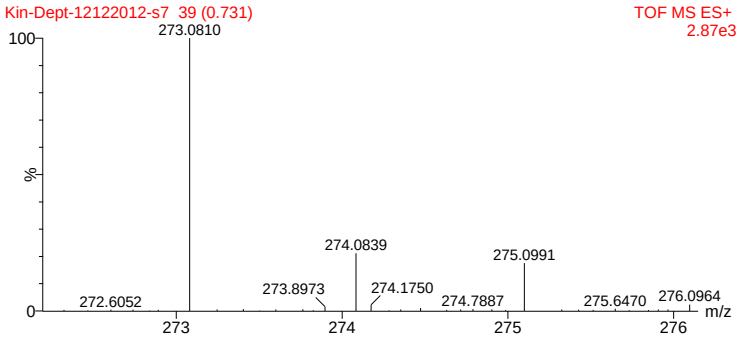




1-Benzyl-5-fluoro-1*H*-indole-3-carbonitrile (Table 4.3, entry 3)

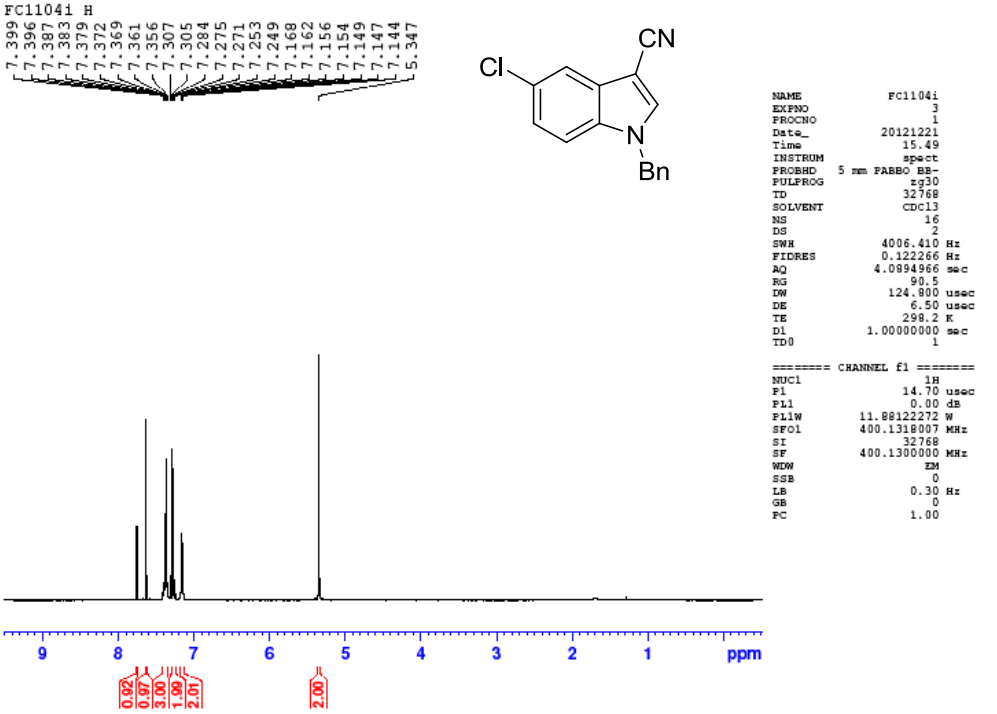


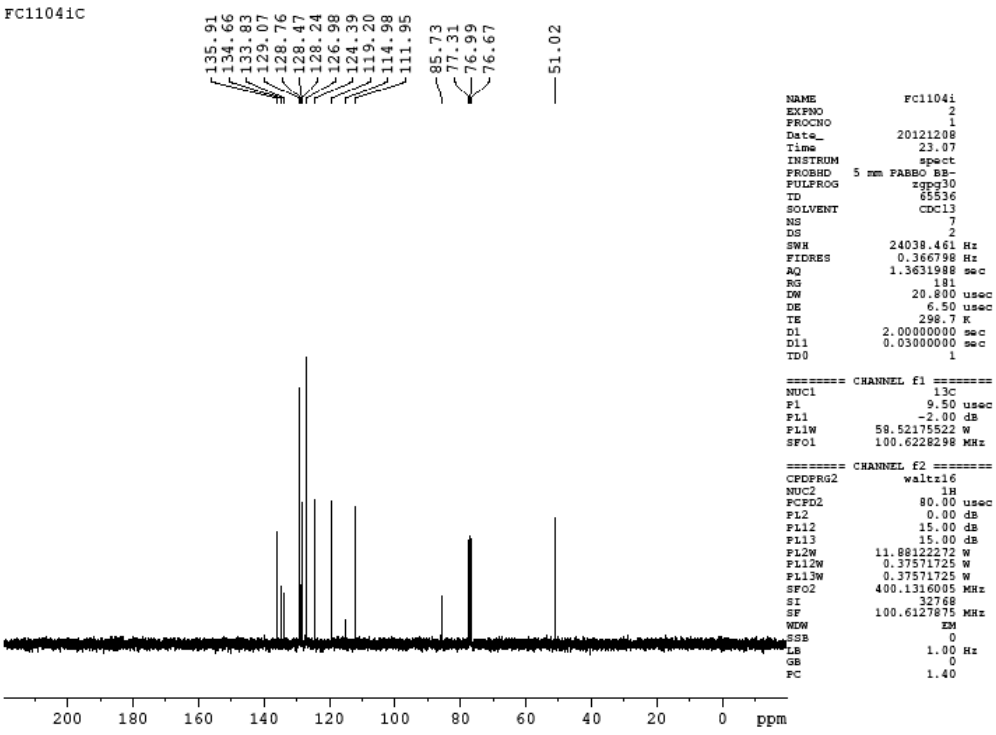
HS



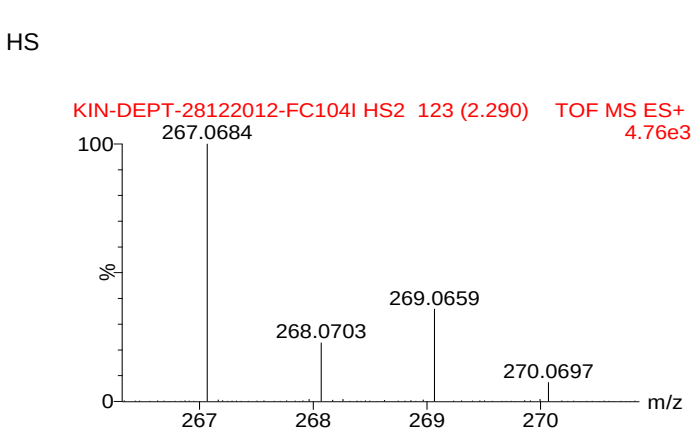
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
273.0810	273.0804	0.6	2.2	11.5	211.4	C16 H11 N2 F Na

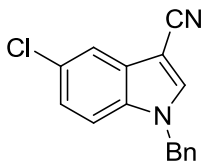
1-Benzyl-5-chloro-1*H*-indole-3-carbonitrile (Table 4.3, entry 4)





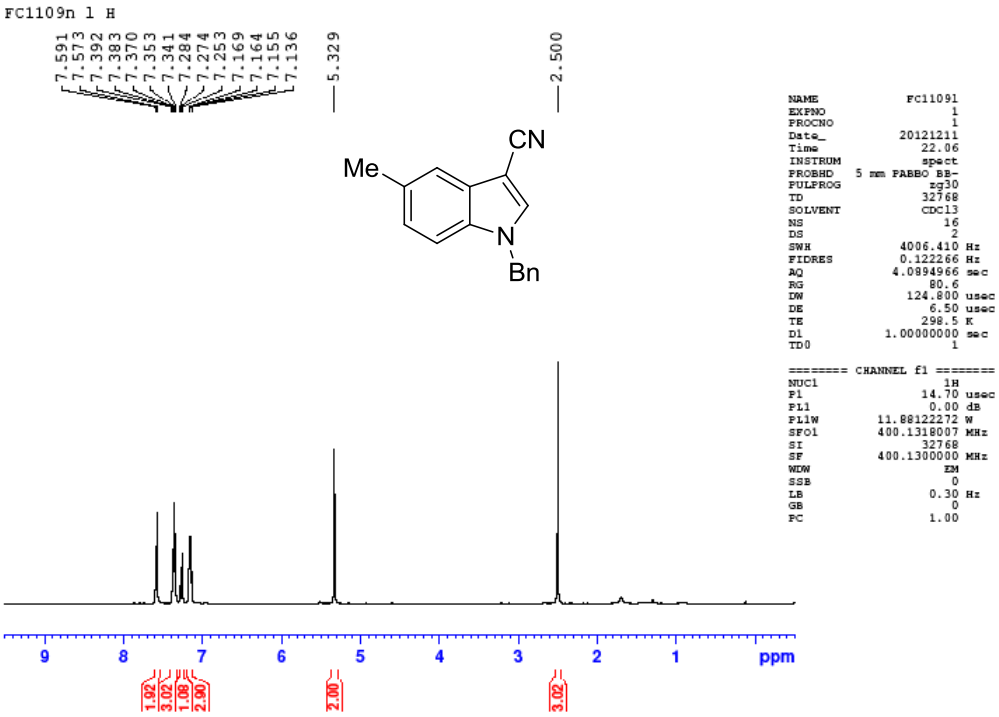
1-Benzyl-5-chloro-1*H*-indole-3-carbonitrile (Table 4.3, entry 4)

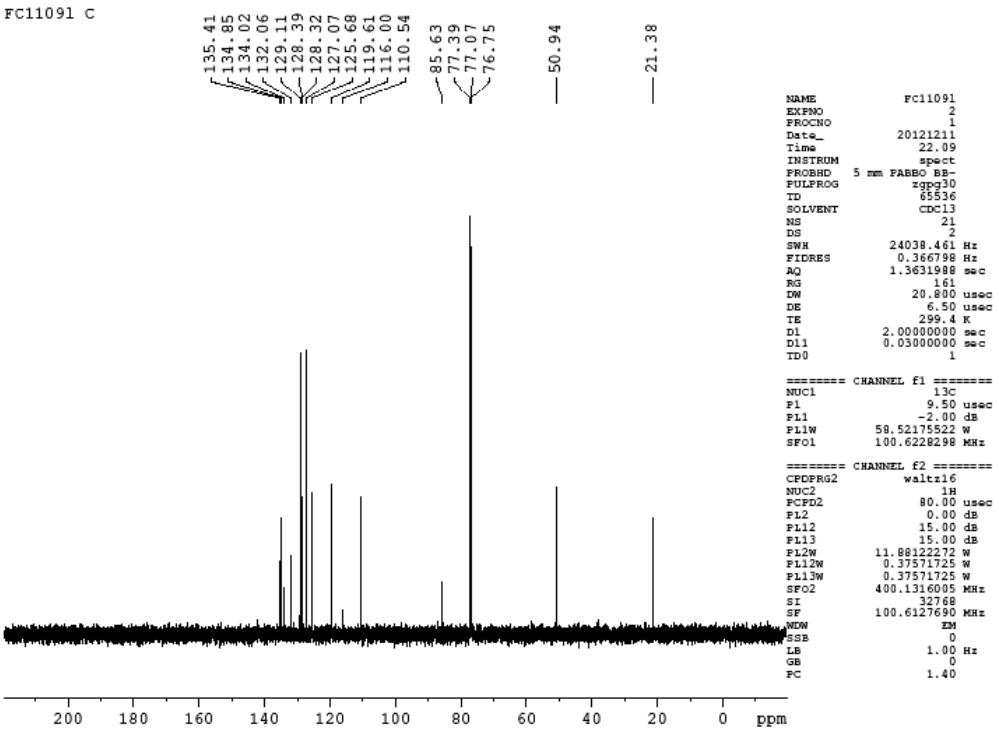




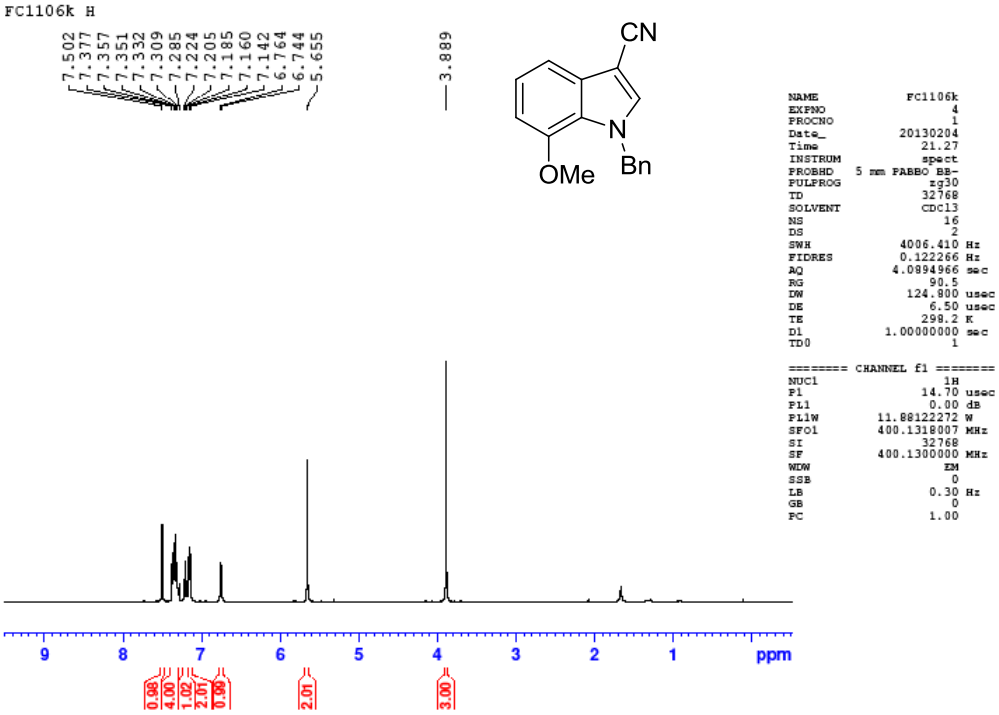
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
267.0684	267.0689	-0.5	-1.9	11.5	16.2	C16 H12 N2 Cl

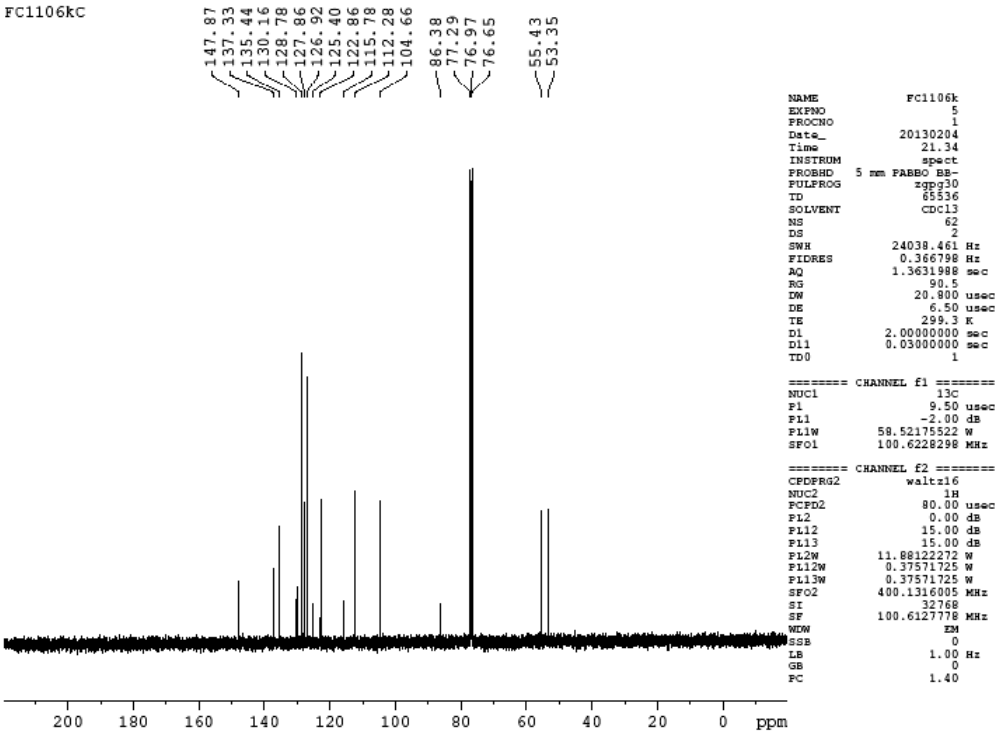
1-Benzyl-5-methyl-1*H*-indole-3-carbonitrile (Table 4.3, entry 5)





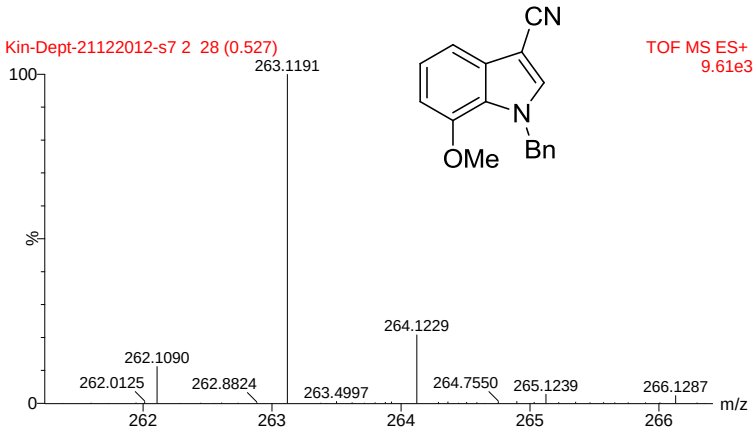
1-Benzyl-7-methoxy-1*H*-indole-3-carbonitrile (Table 4.3, entry 6)





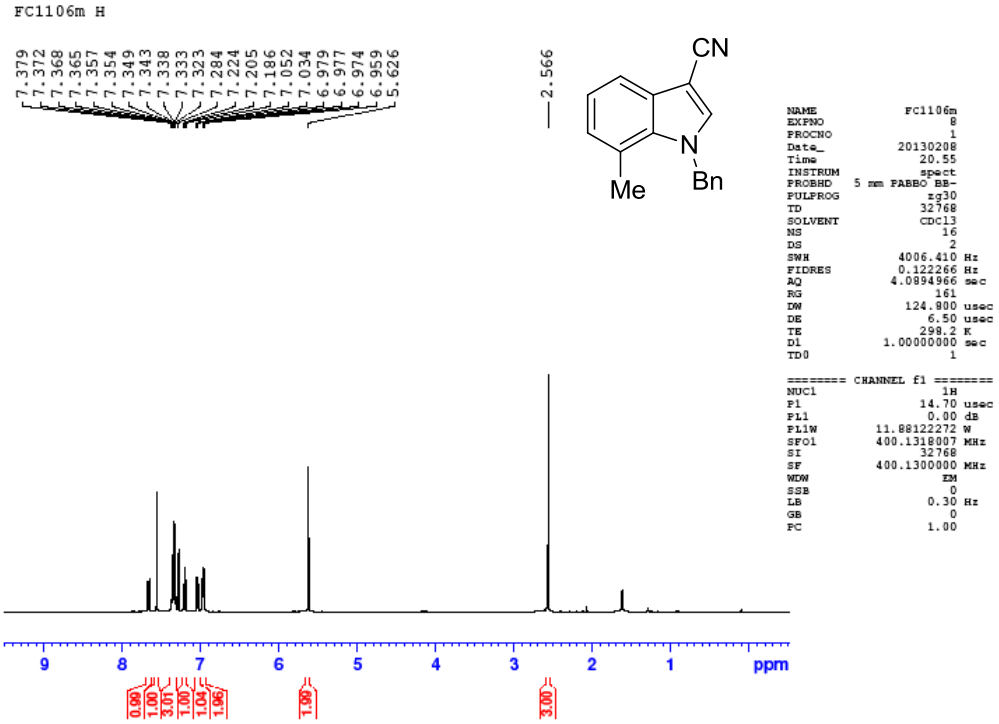
1-Benzyl-7-methoxy-1*H*-indole-3-carbonitrile (Table 4.3, entry 6)

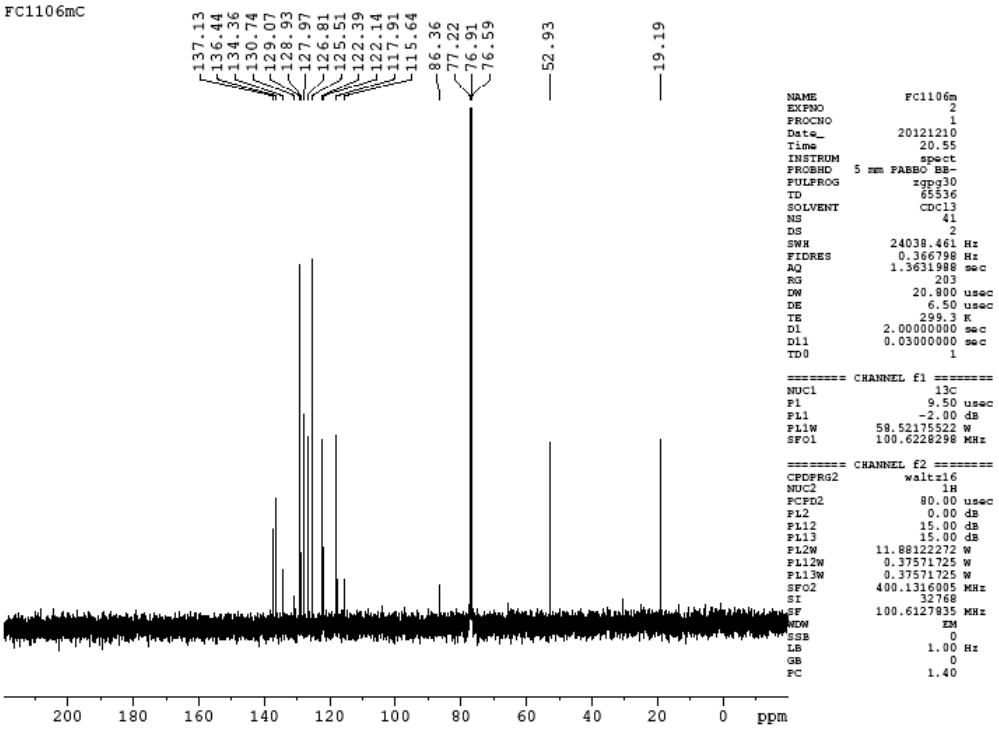
HS



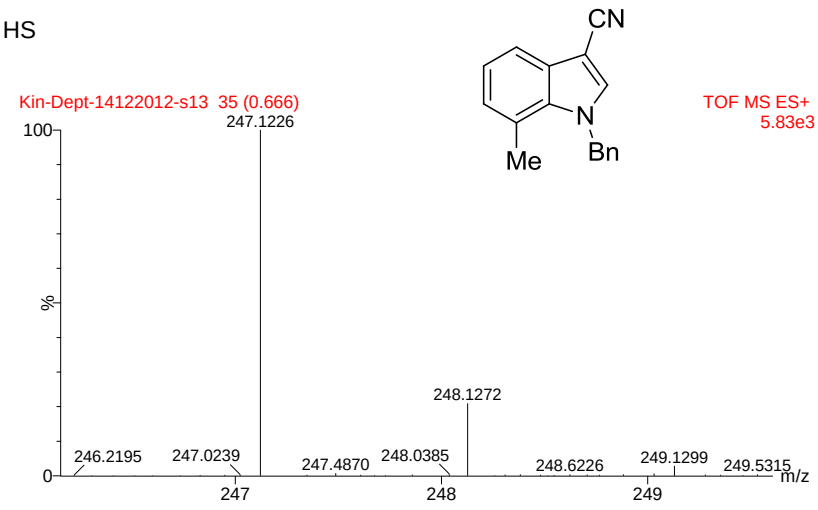
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
263.1191	263.1184	0.7	2.7	11.5	10.4	C17 H15 N2 O

1-Benzyl-7-methyl-1*H*-indole-3-carbonitrile (Table 4.3, entry 7)



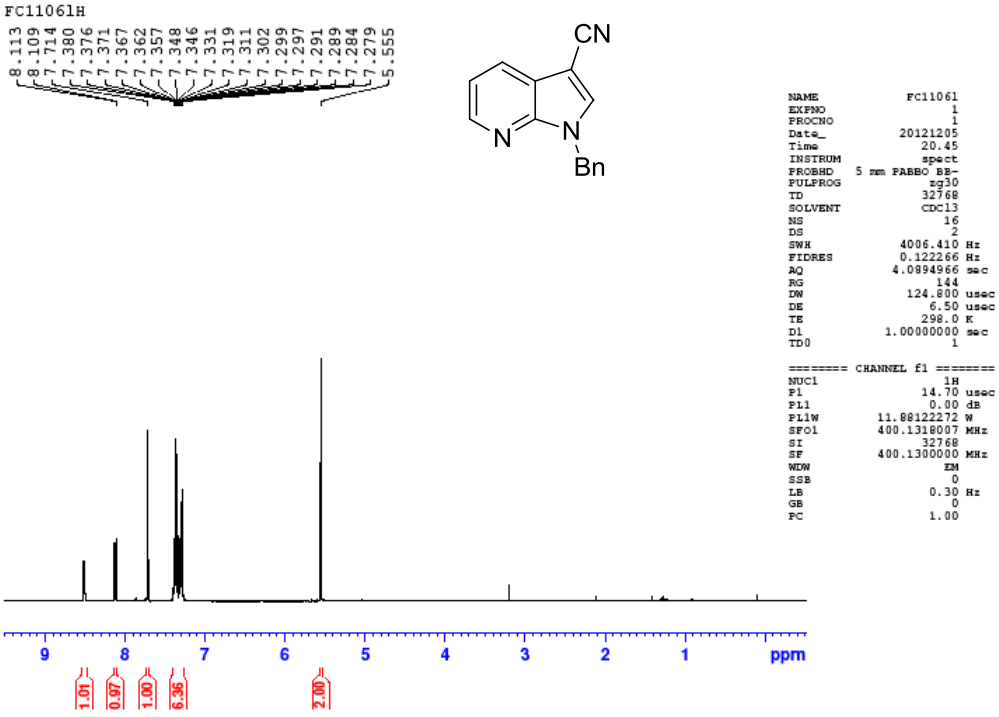


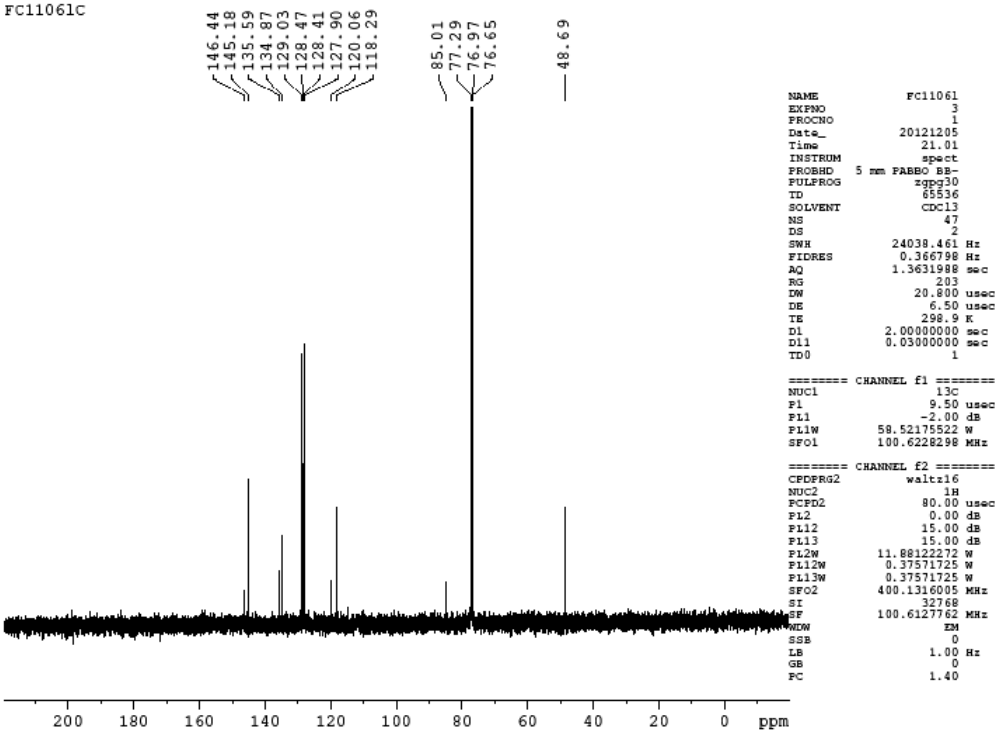
1-Benzyl-7-methyl-1*H*-indole-3-carbonitrile (Table 4.3, entry 7)



Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
247.1226	247.1235	-0.9	-3.6	11.5	10.4	C17 H15 N2

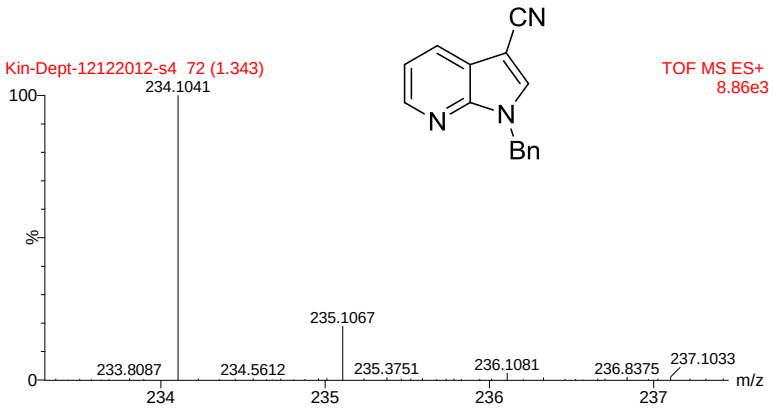
1-Benzyl-1*H*-pyrrolo[2,3-*b*]pyridine-3-carbonitrile (Table 4.3, entry 8)





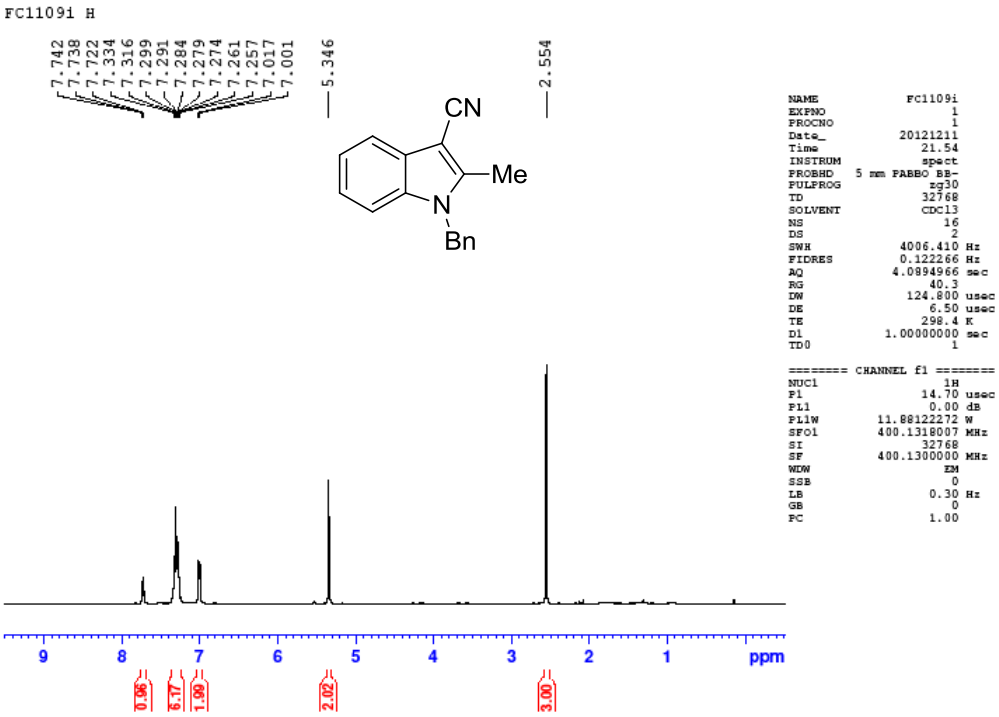
1-Benzyl-1*H*-pyrrolo[2,3-*b*]pyridine-3-carbonitrile (Table 4.3, entry 8)

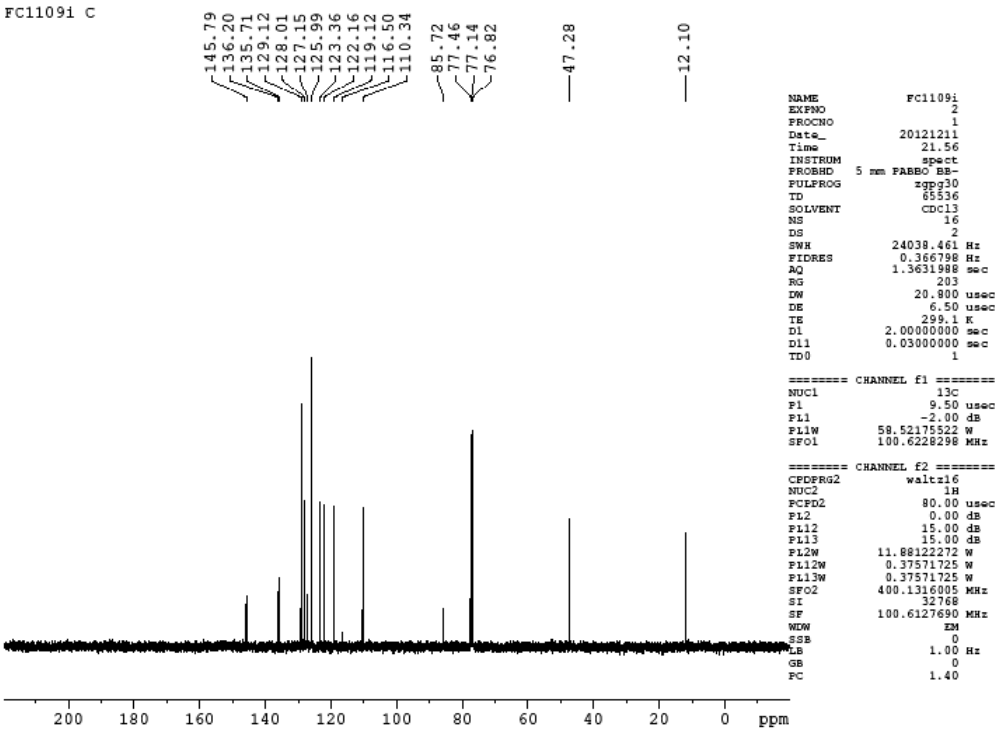
HS



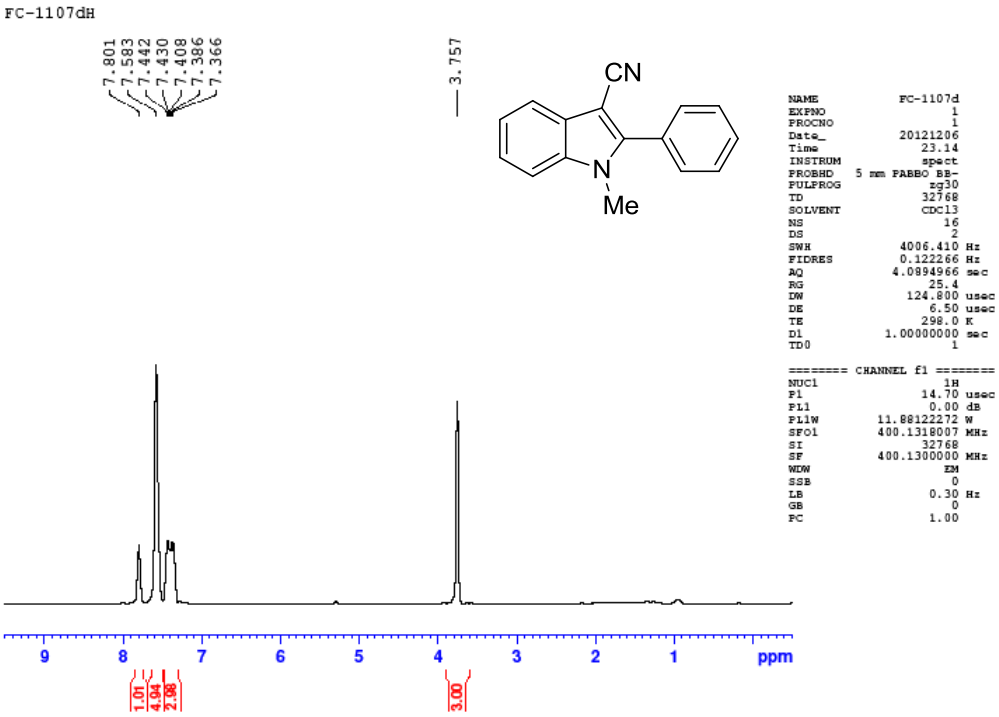
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
234.1041	234.1031	1.0	4.3	11.5	15.8	C15 H12 N3

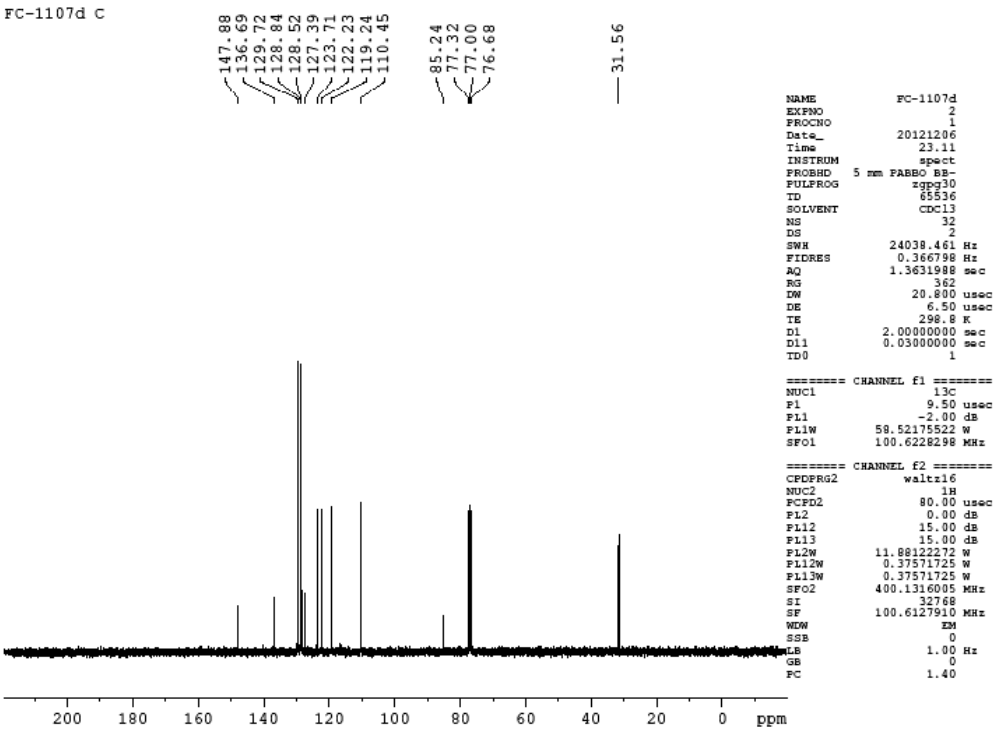
1-Benzyl-2-methyl-1*H*-indole-3-carbonitrile (Table 4.3, entry 9)



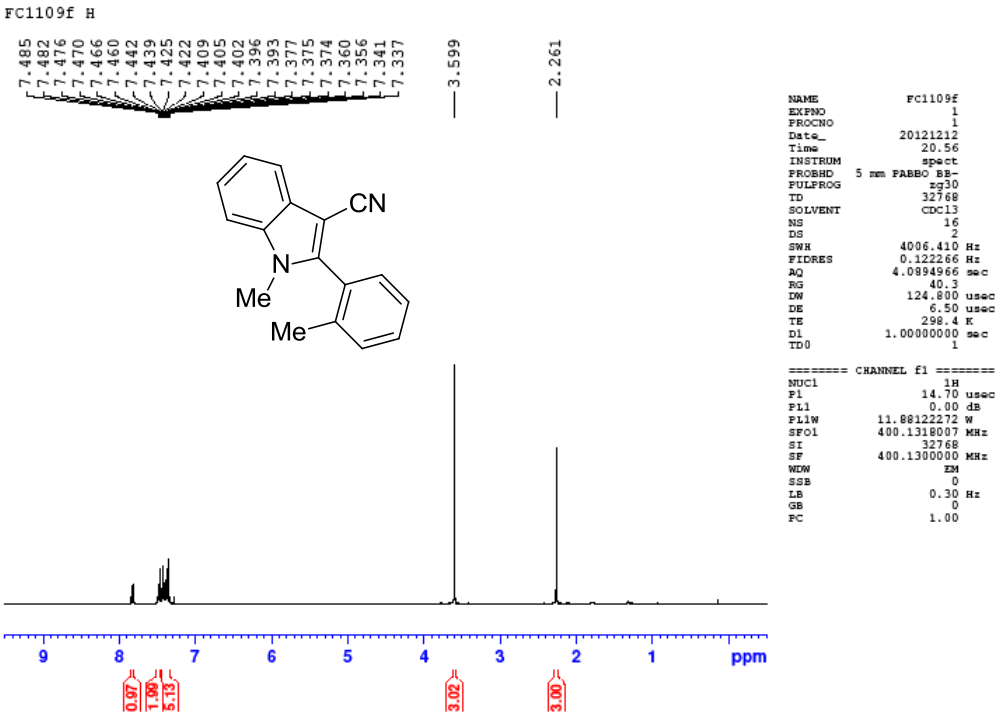


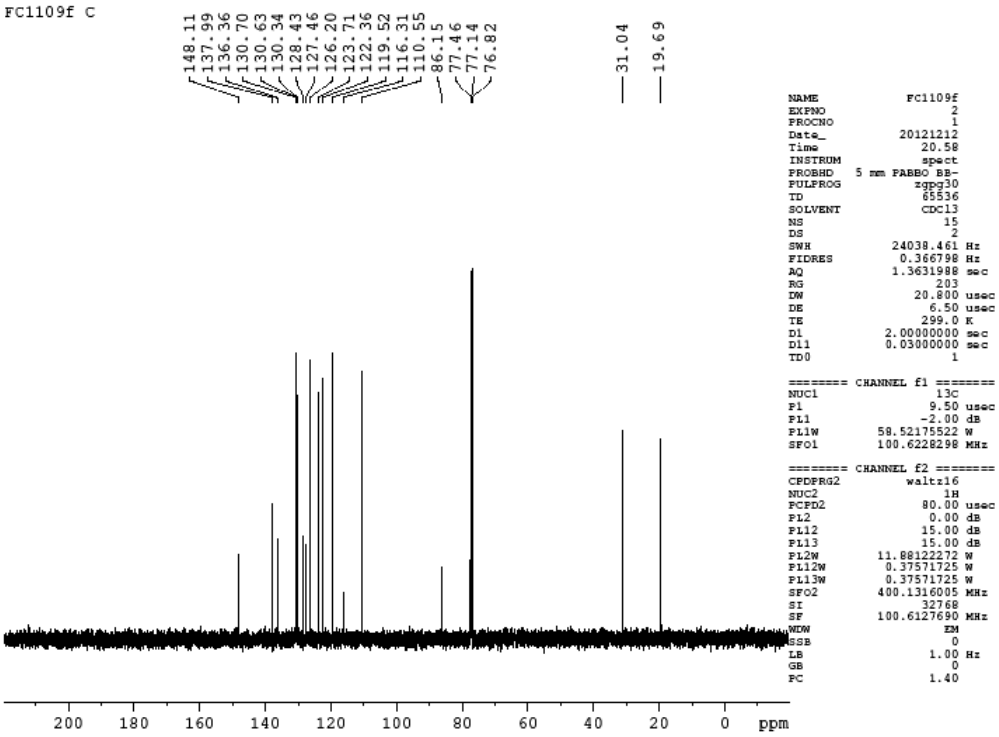
1-Methyl-2-phenyl-1*H*-indole-3-carbonitrile (Scheme 4.1, compound 1)





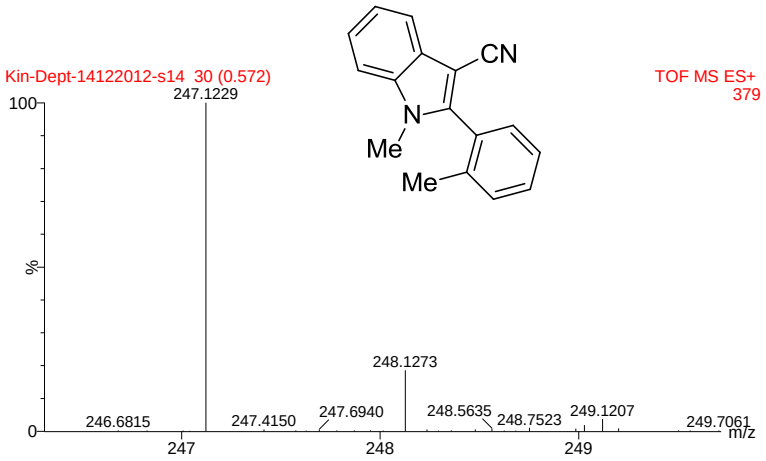
1-Methyl-2-(*o*-tolyl)-1*H*-indole-3-carbonitrile (Scheme 4.1, compound 2)





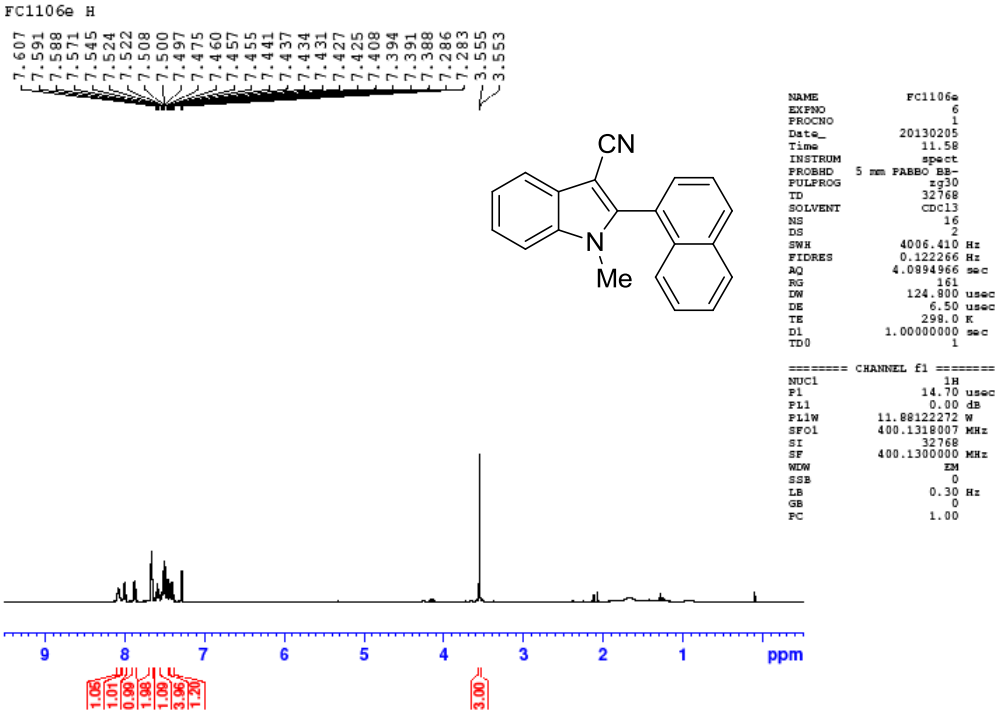
1-Methyl-2-(*o*-tolyl)-1*H*-indole-3-carbonitrile (Scheme 4.1, compound 2)

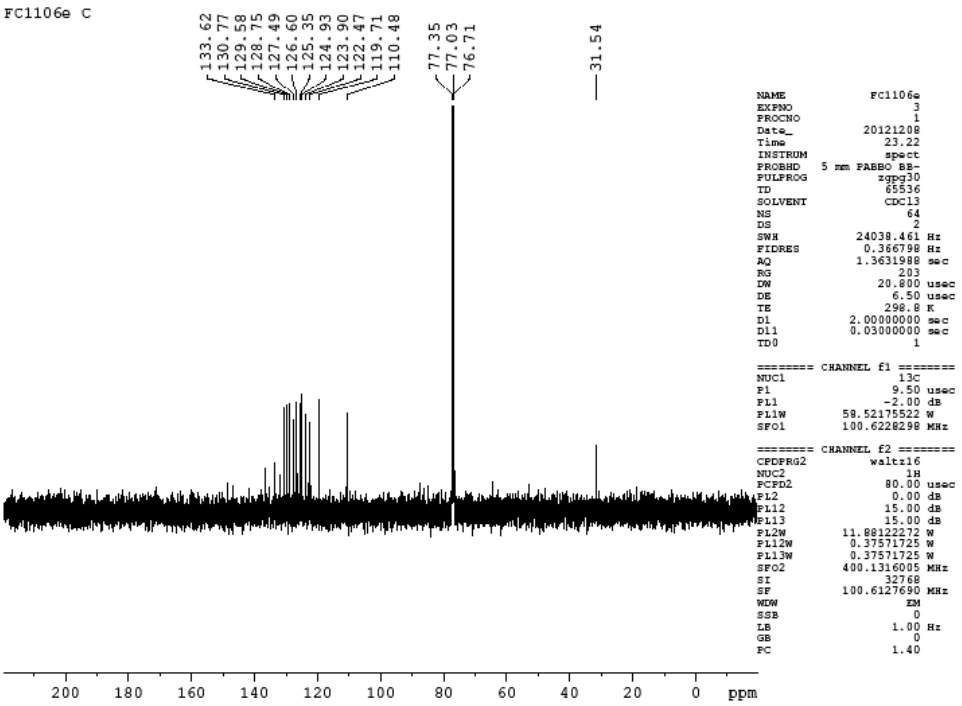
HS



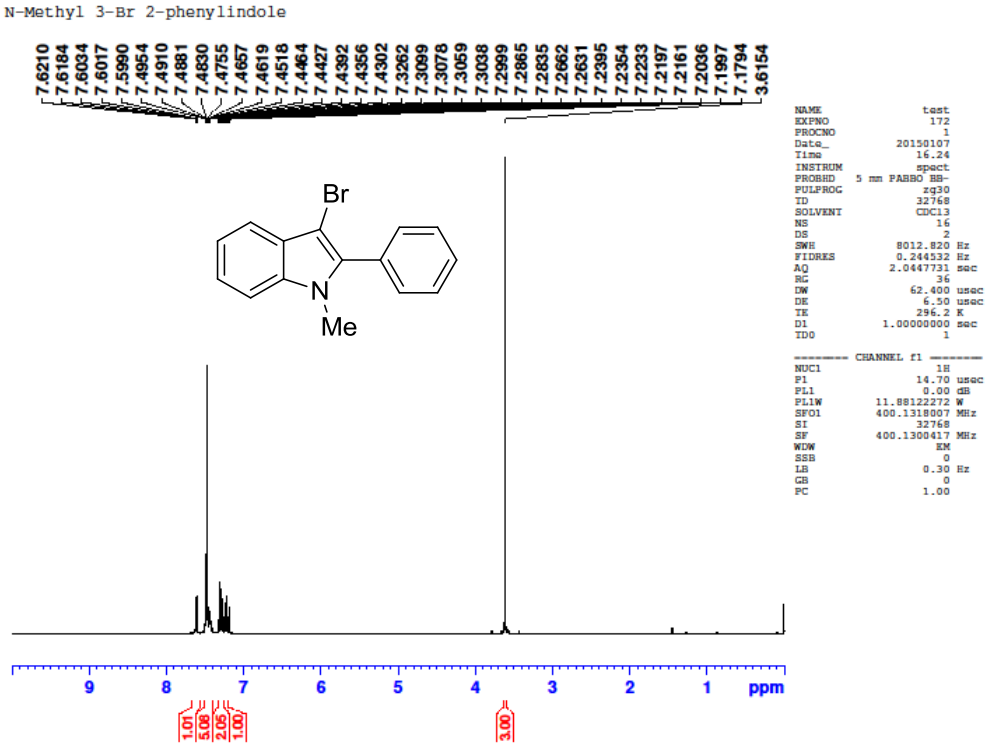
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
247.1229	247.1235	-0.6	-2.4	11.5	1.9	C17 H15 N2

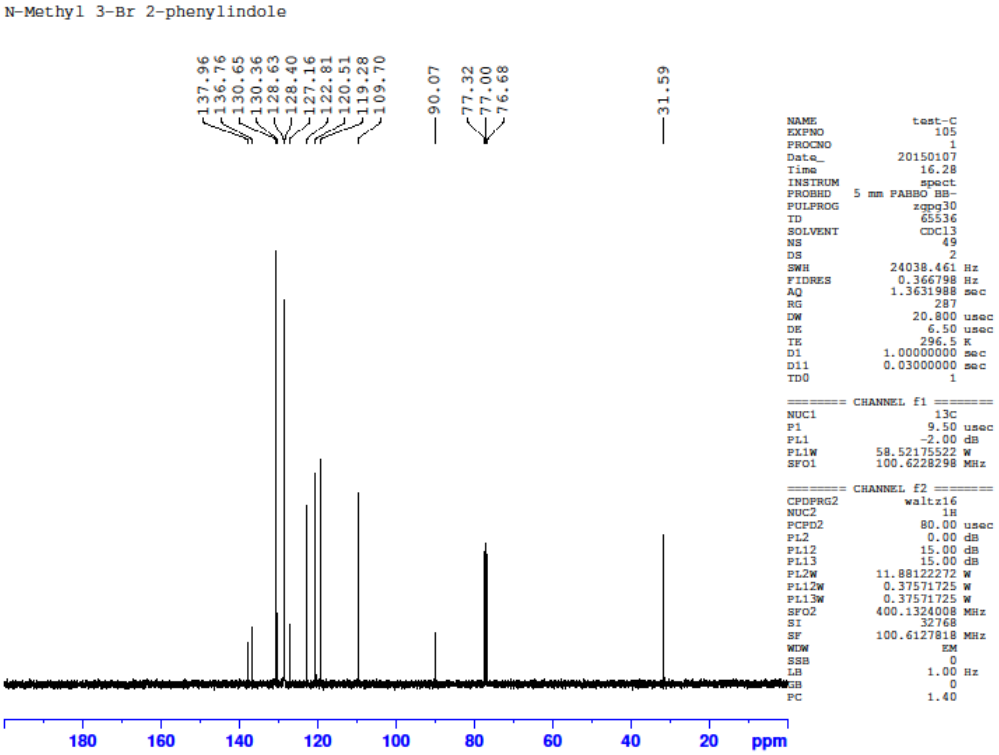
1-Methyl-2-(naphthalen-1-yl)-1*H*-indole-3-carbonitrile (Scheme 4.1, compound 3)



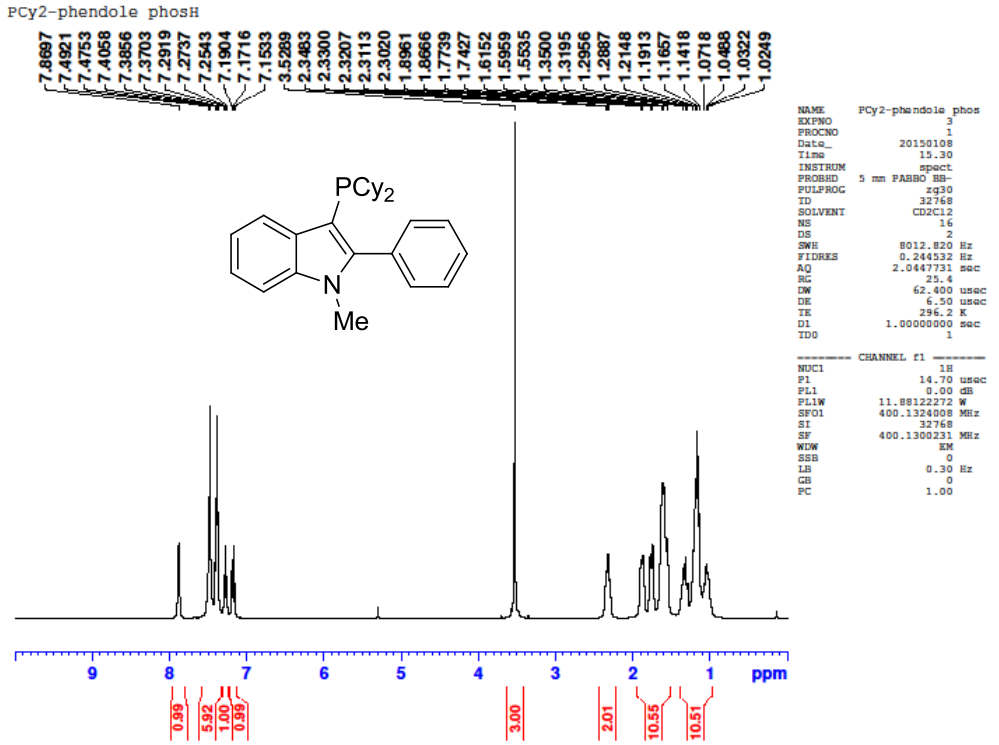


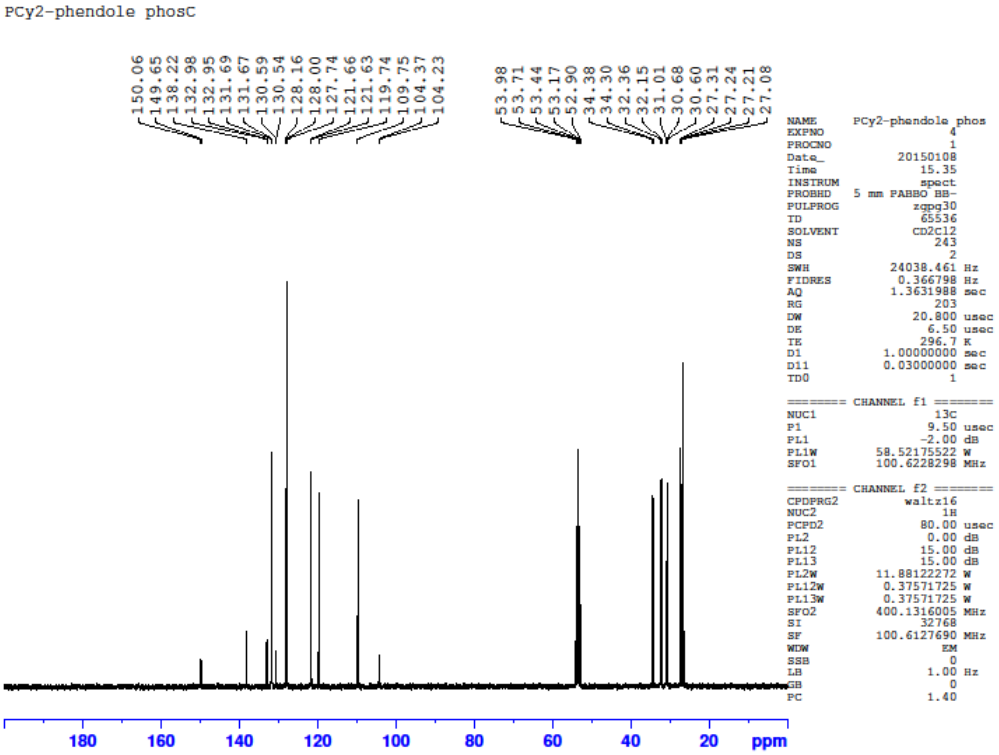
3-Bromo-1-methyl-2-phenyl-1*H*-indole (Scheme 5.4, L1 precursor)



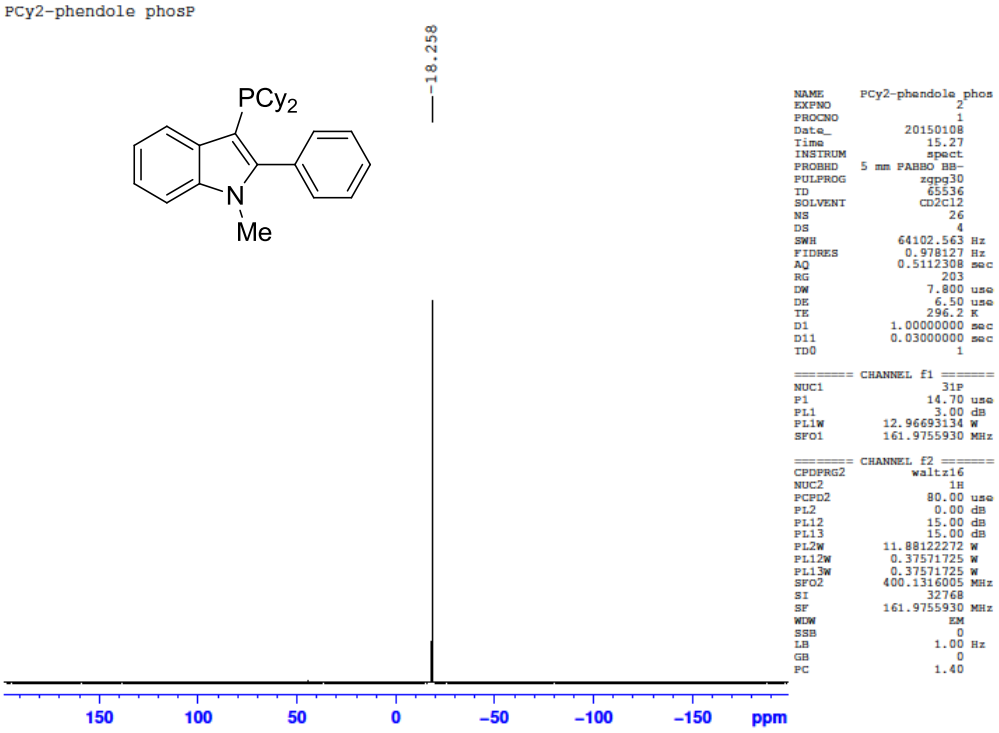


3-(Dicyclohexylphosphino)-1-methyl-2-phenyl-1*H*-indole (Scheme 5.4, L1)

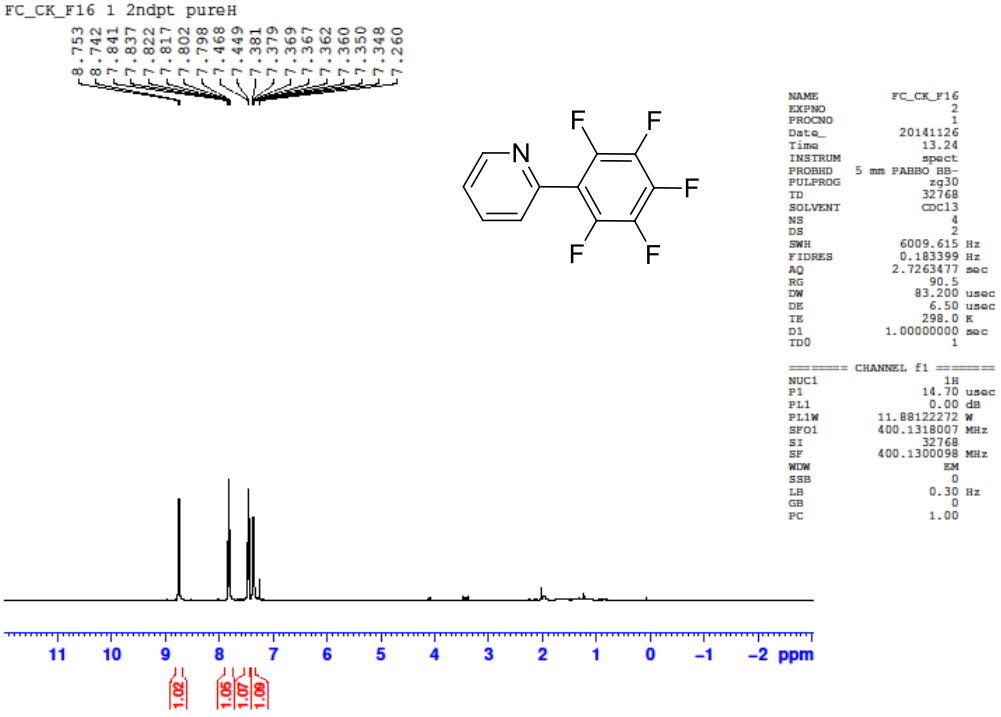


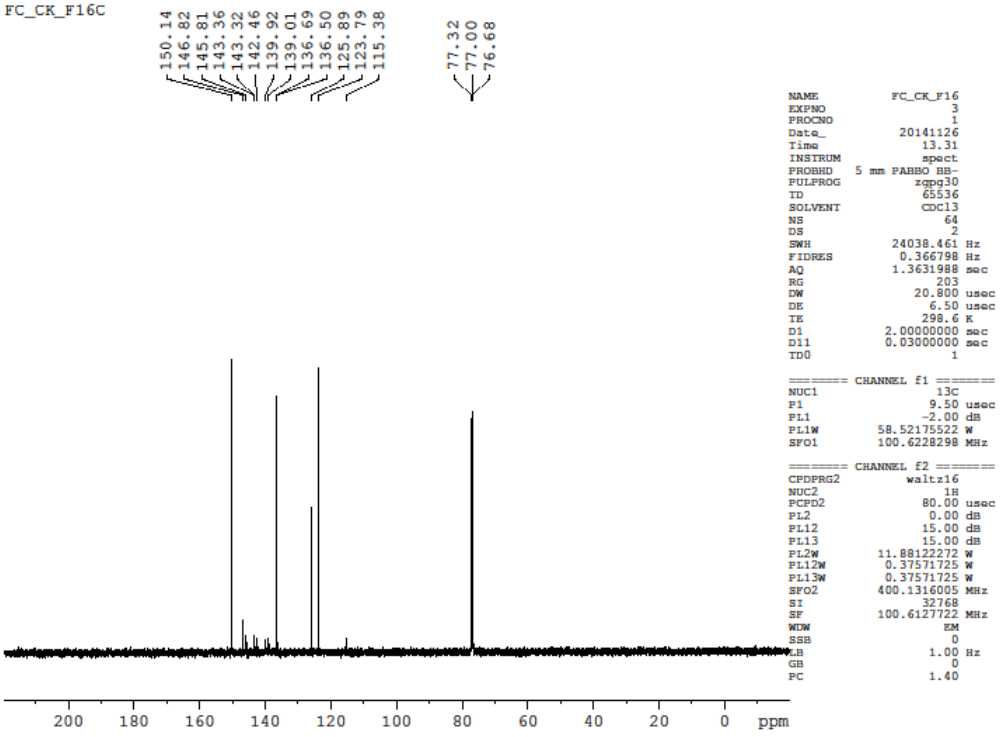


3-(Dicyclohexylphosphino)-1-methyl-2-phenyl-1*H*-indole (Scheme 5.4, L1)

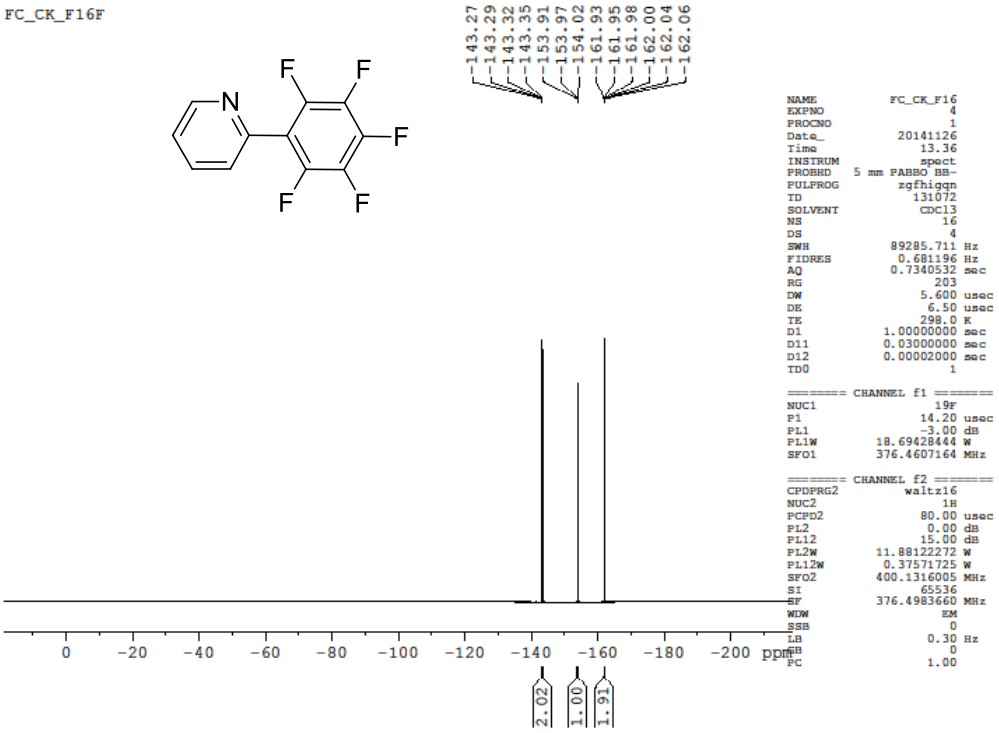


2-(Perfluorophenyl)pyridine (Table 5.2, compound 3au)

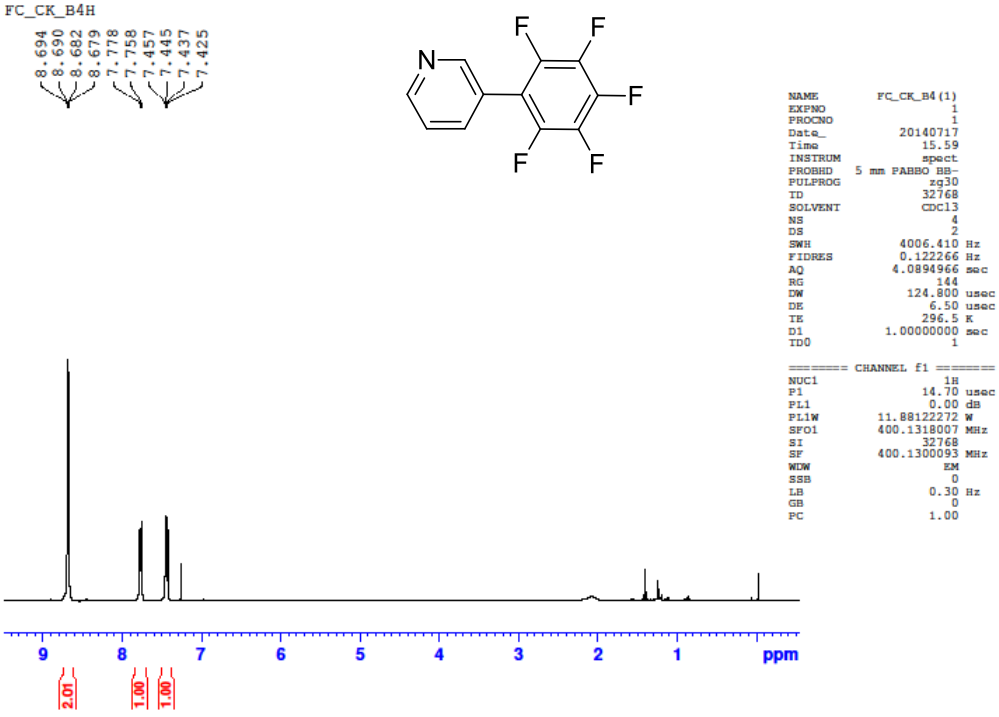


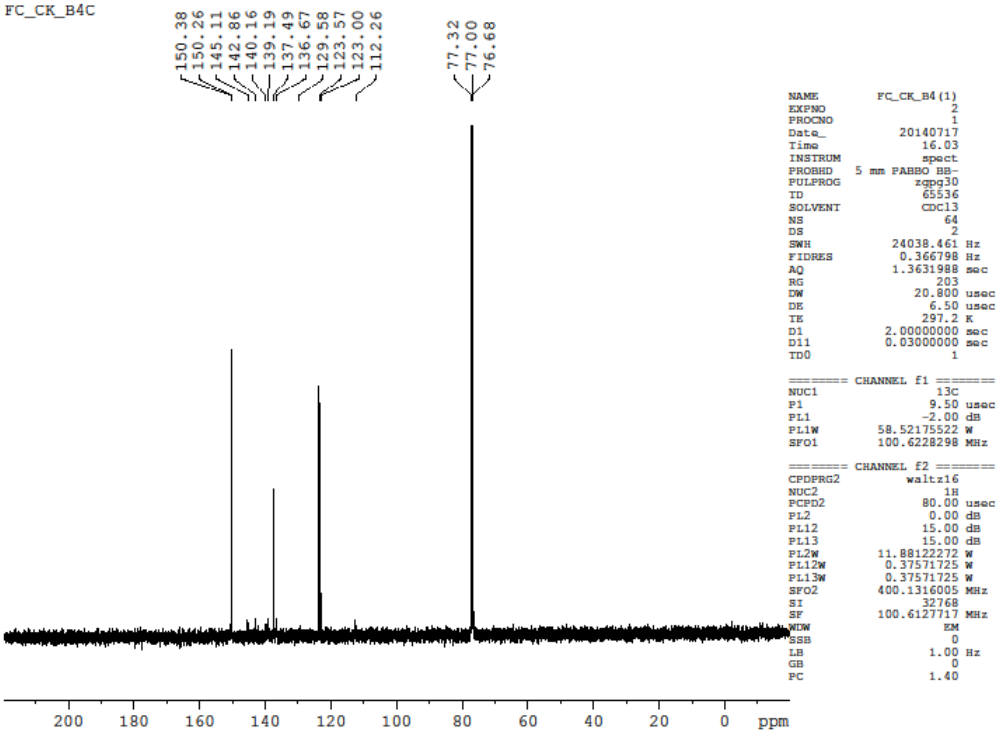


2-(Perfluorophenyl)pyridine (Table 5.2, compound 3au)

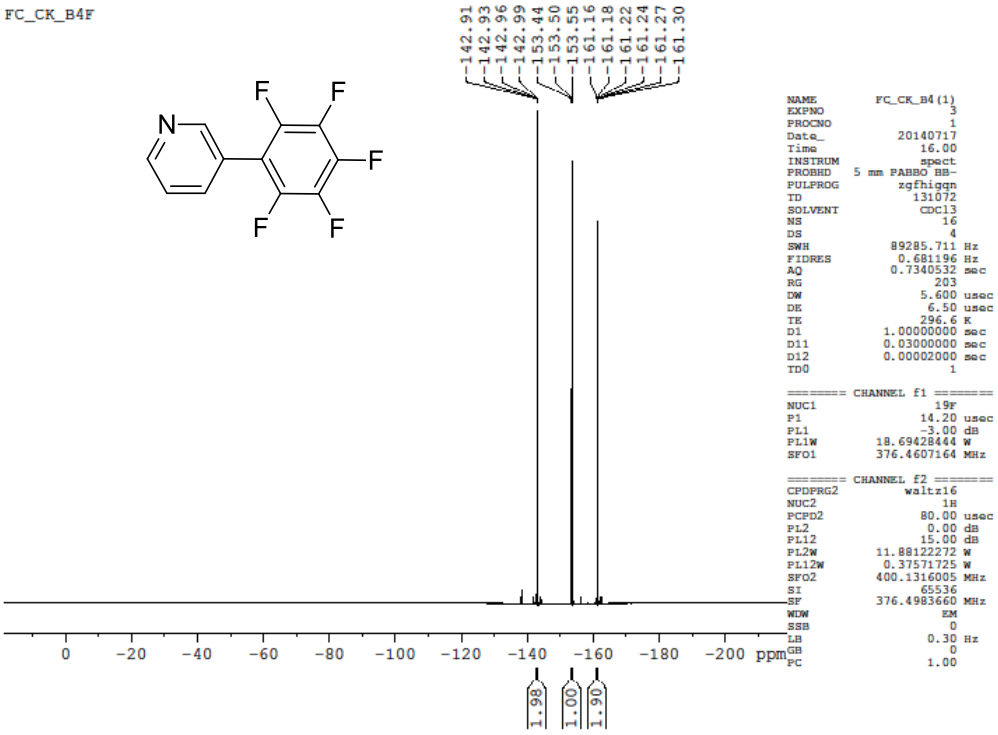


3-(Perfluorophenyl)pyridine (Table 5.2, compound 3bu)

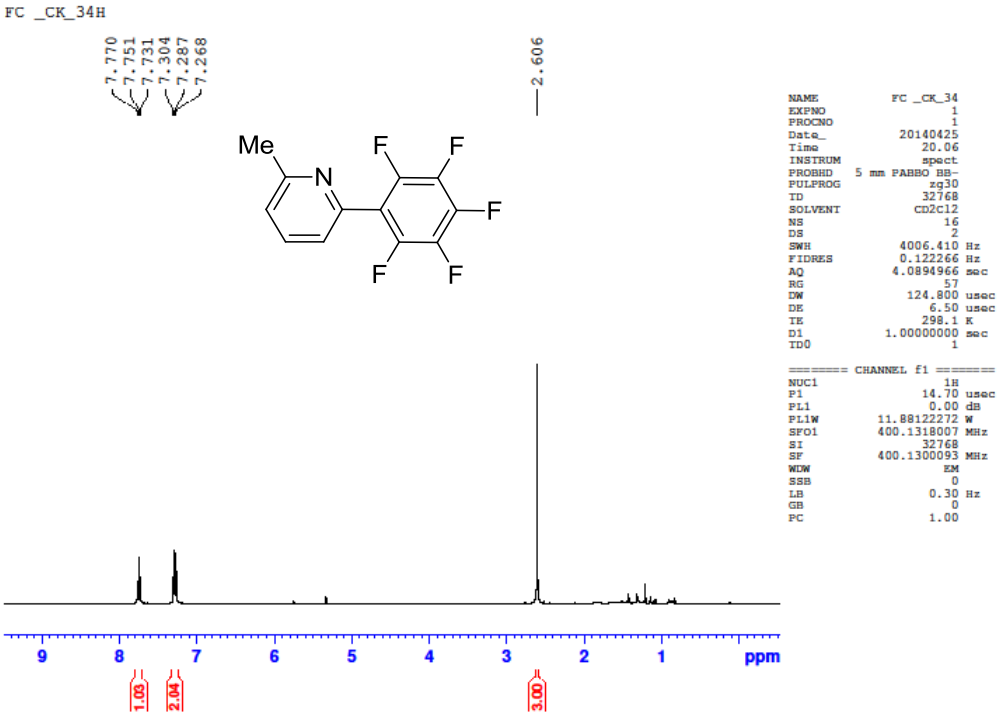


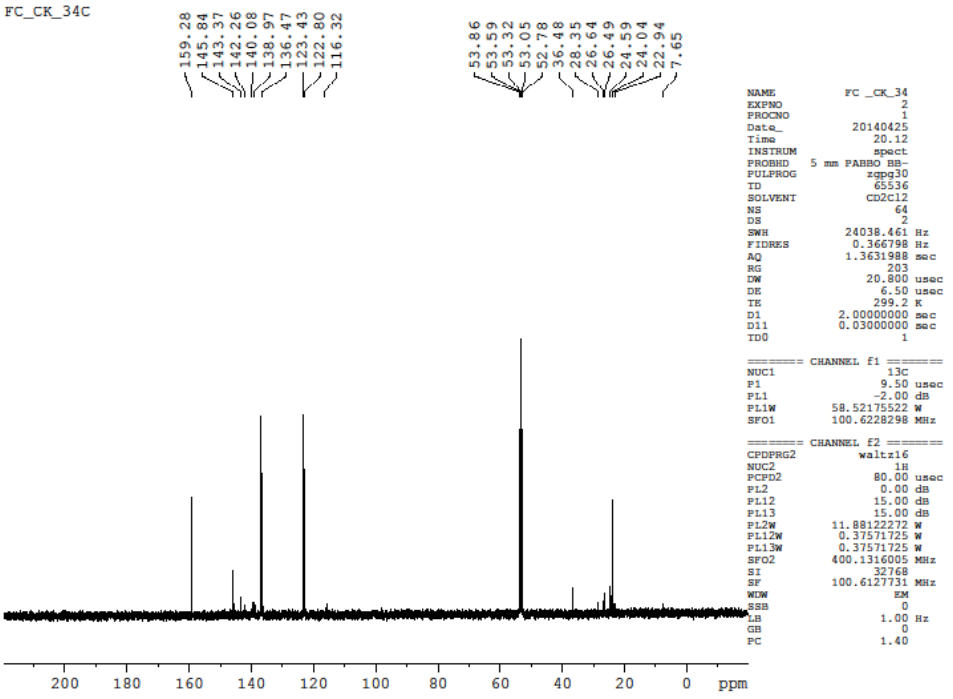


3-(Perfluorophenyl)pyridine (Table 5.2, compound 3bu)

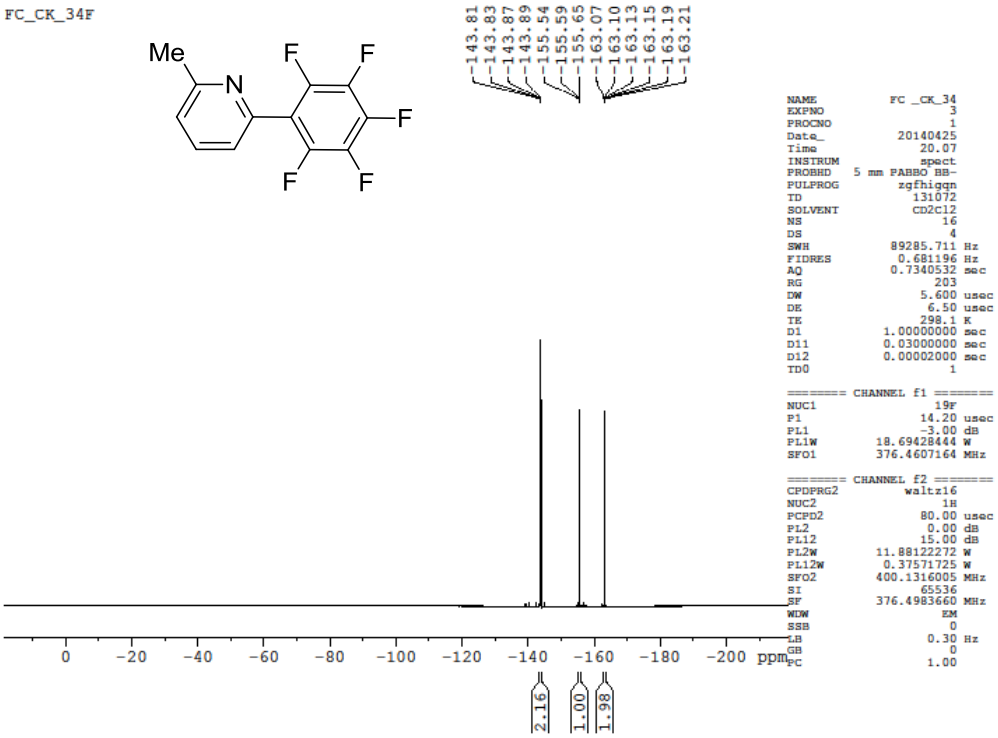


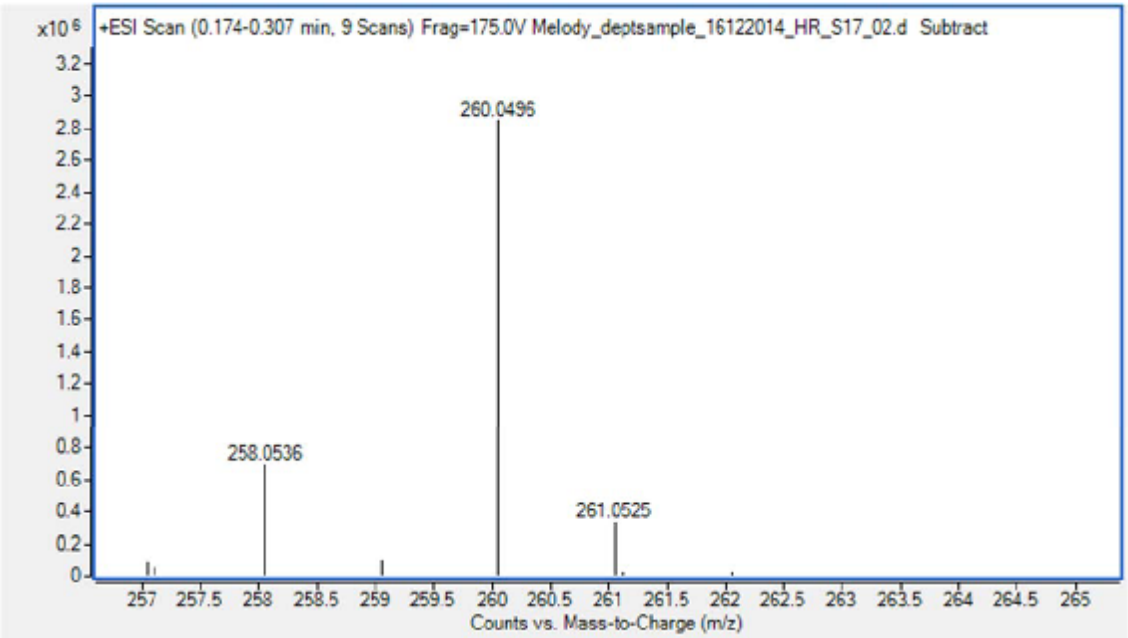
2-Methyl-6-(perfluorophenyl)pyridine (Table 5.2, compound 3cu)





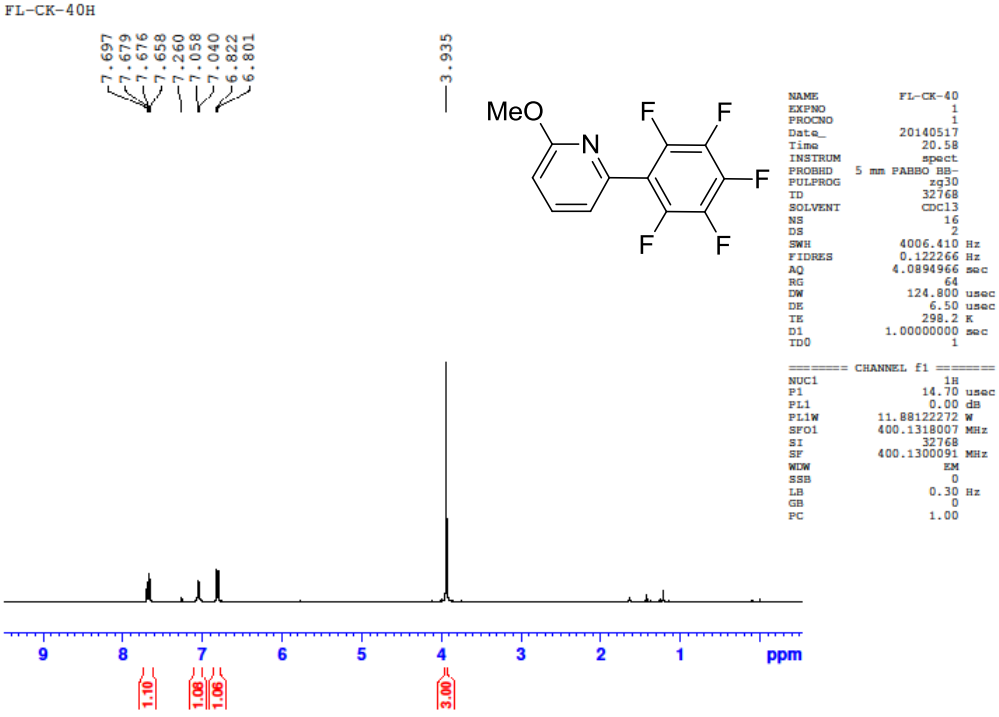
2-Methyl-6-(perfluorophenyl)pyridine (Table 5.2, compound 3cu)

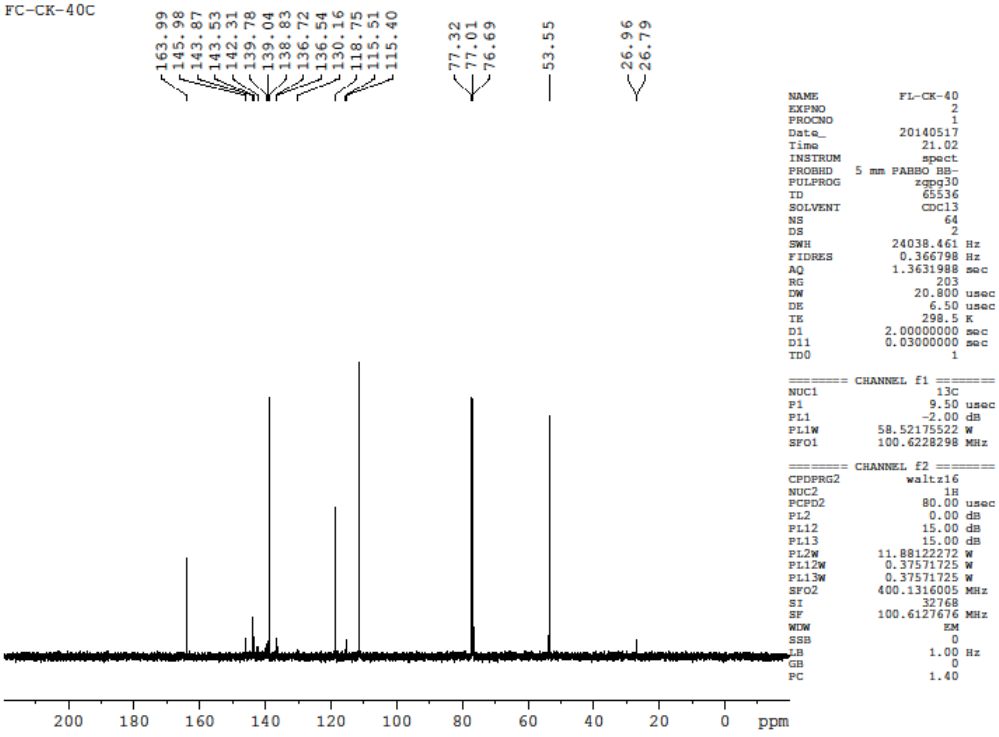




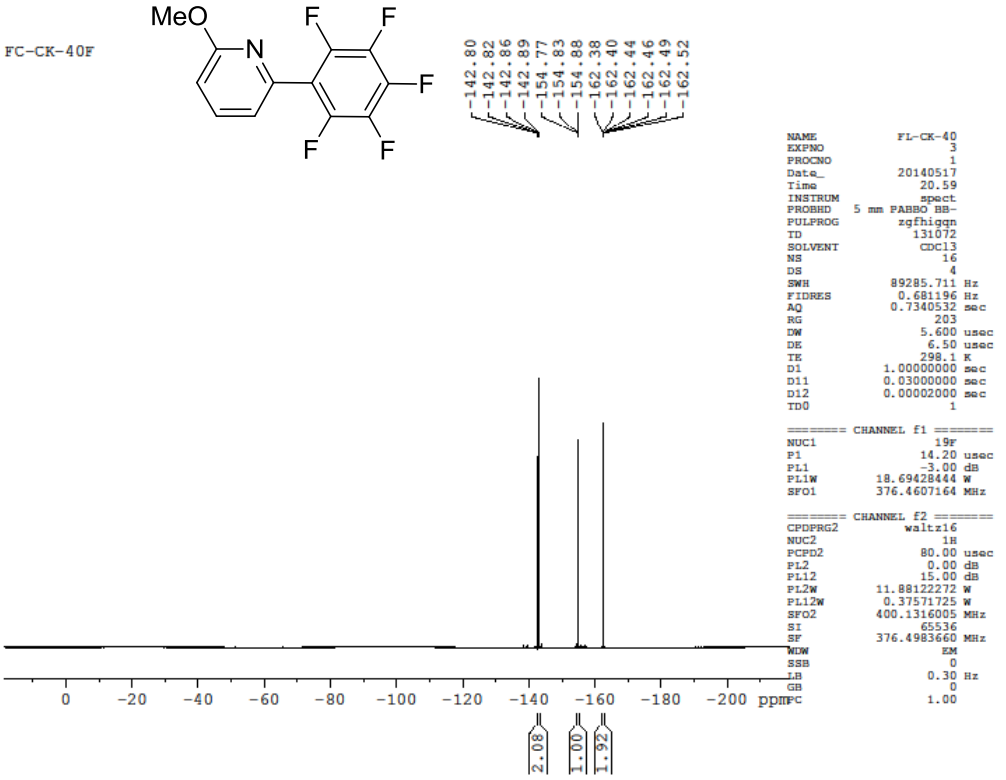
Mass	Calc. Mass	mDa	PPM	Formula
260.0496	260.0493	0.3	1.2	C12 H7 F5 N

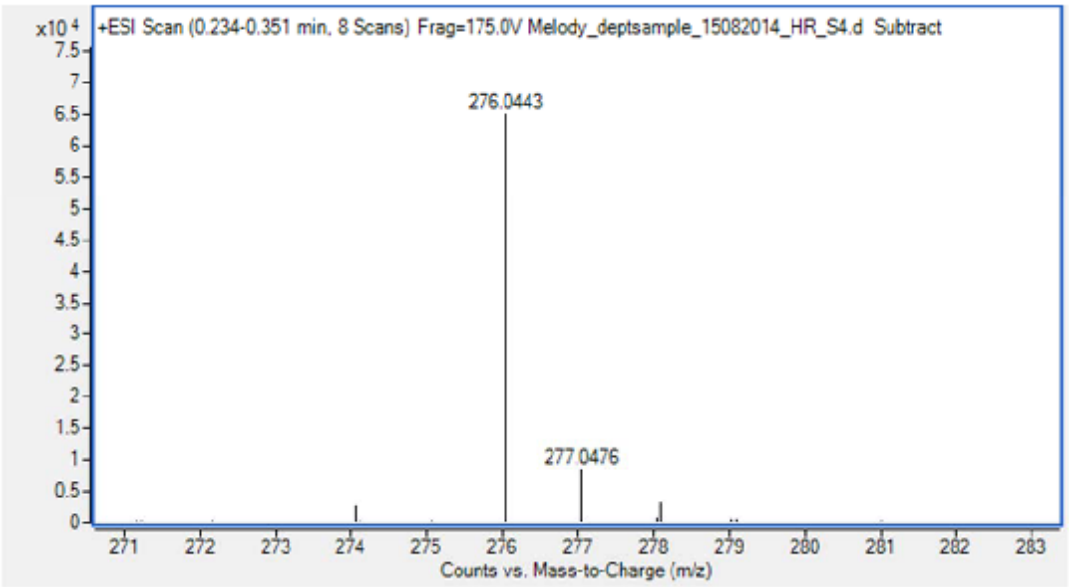
2-Methoxy-6-(perfluorophenyl)pyridine (Table 5.2, compound 3du)





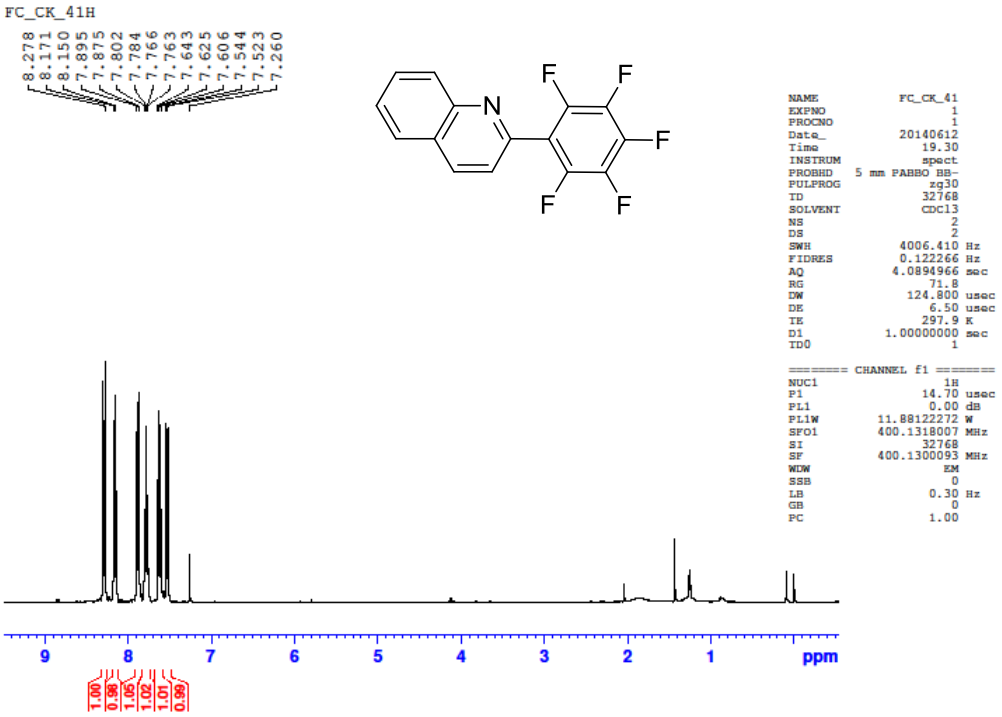
2-Methoxy-6-(perfluorophenyl)pyridine (Table 5.2, compound 3du)

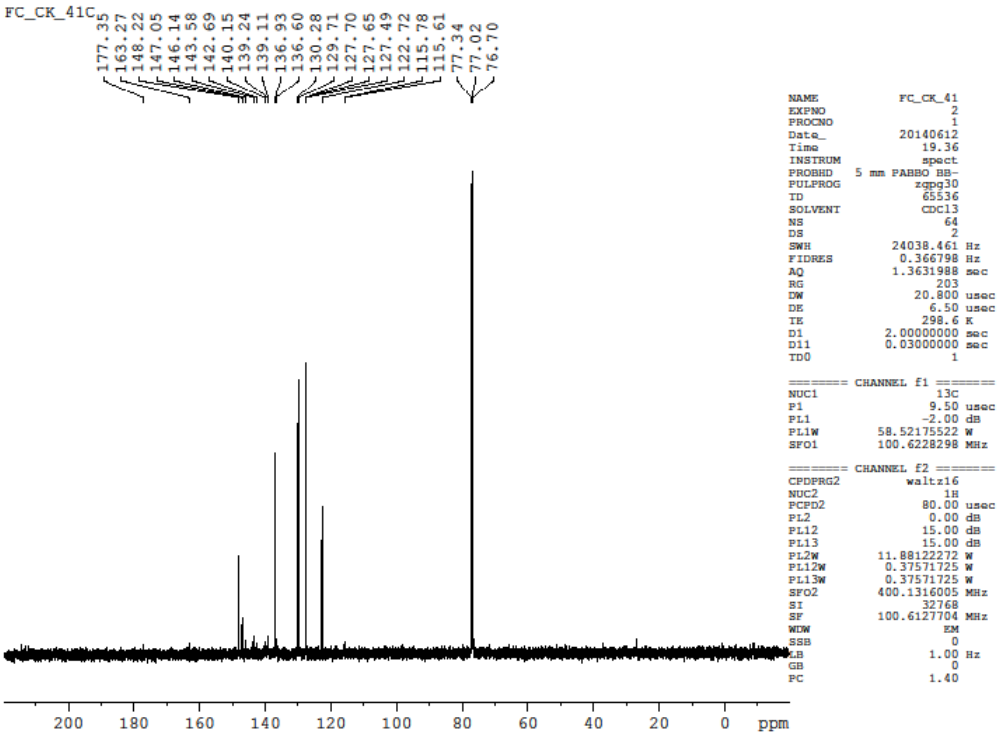




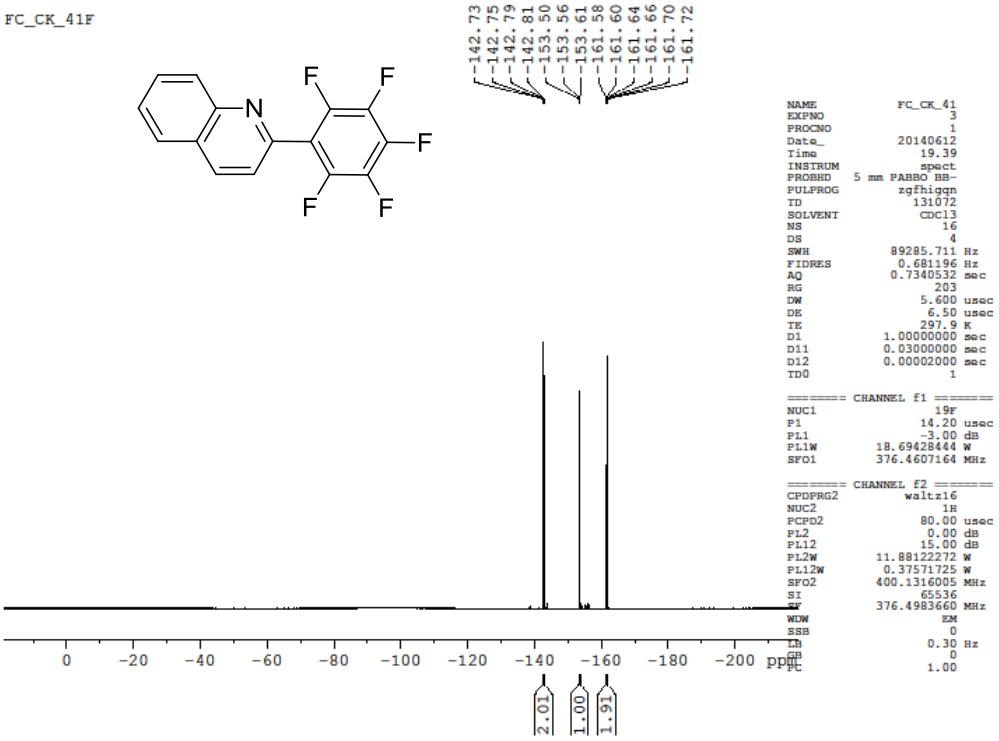
Mass	Calc. Mass	mDa	PPM	Formula
276.0443	276.0442	0.1	0.4	C12 H7 F5 N O

2-(Perfluorophenyl)quinoline (Table 5.2, compound 3eu)

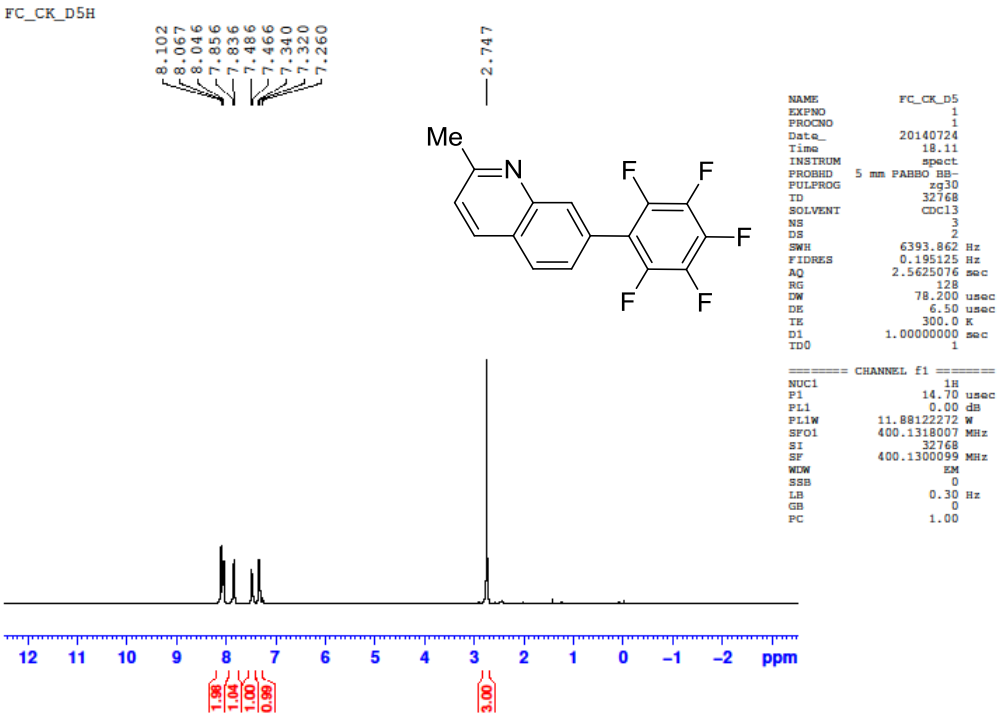


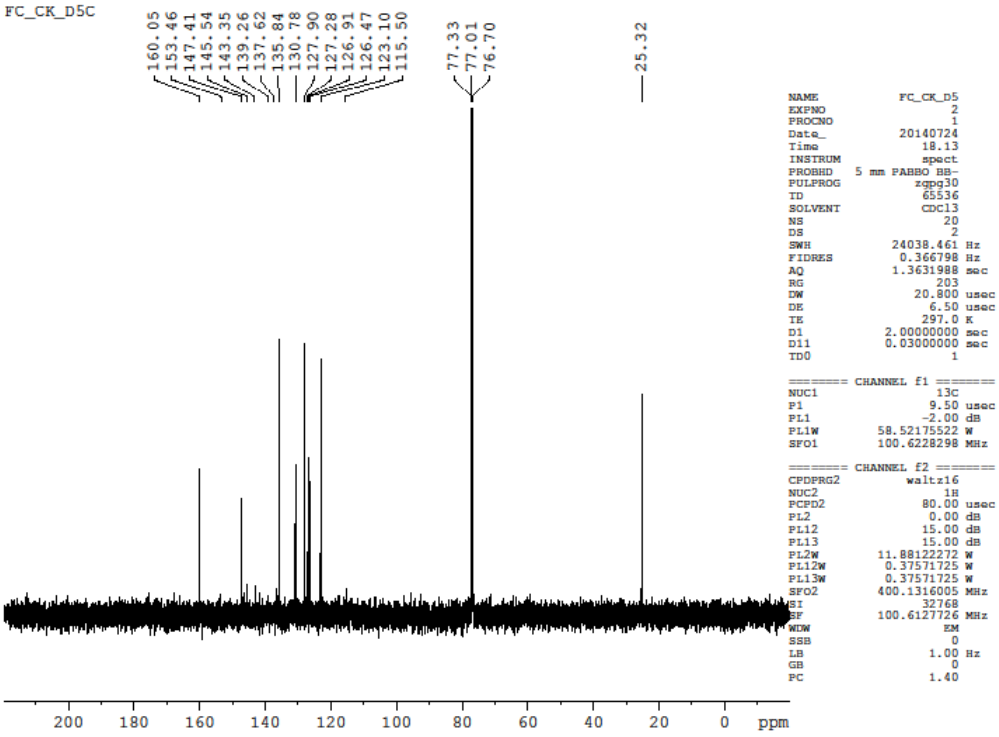


2-(Perfluorophenyl)quinoline (Table 5.2, compound 3eu)

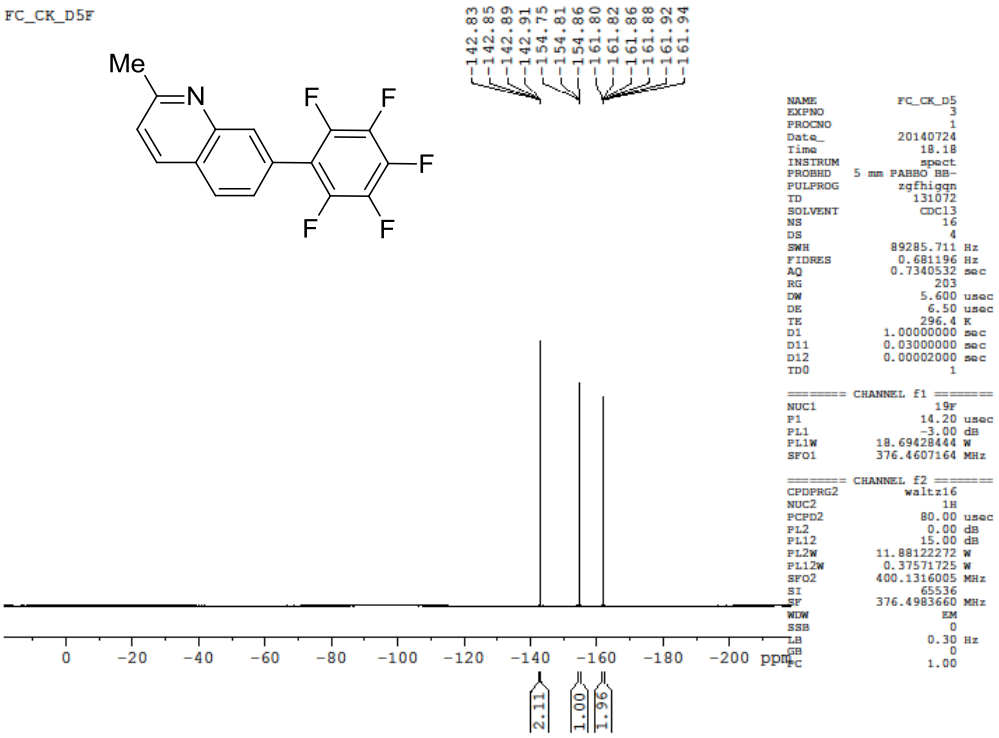


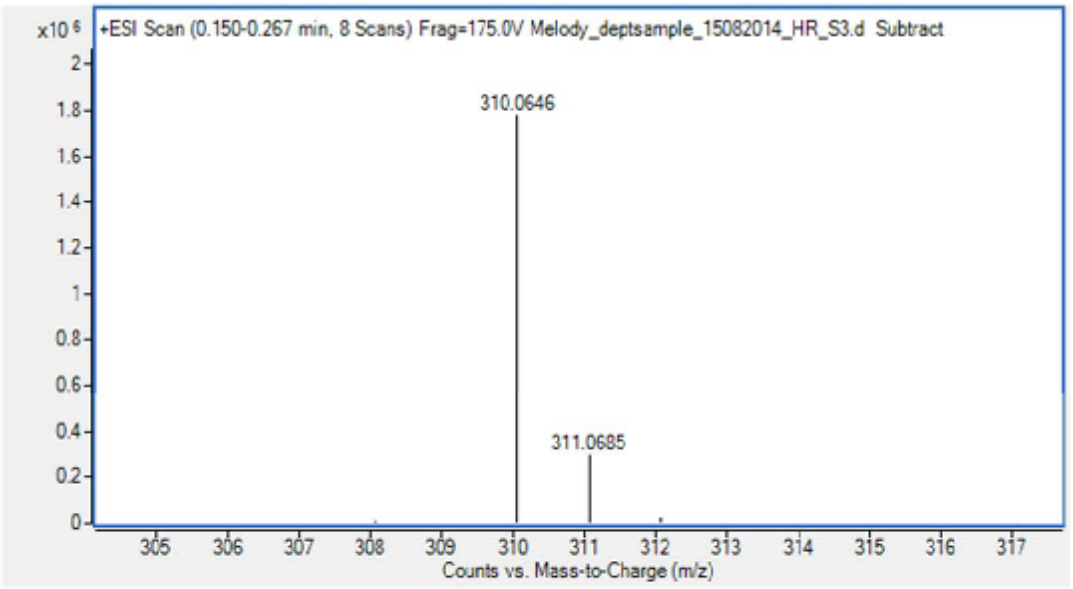
2-Methyl-7-(perfluorophenyl)quinoline (Table 5.2, compound 3fu)





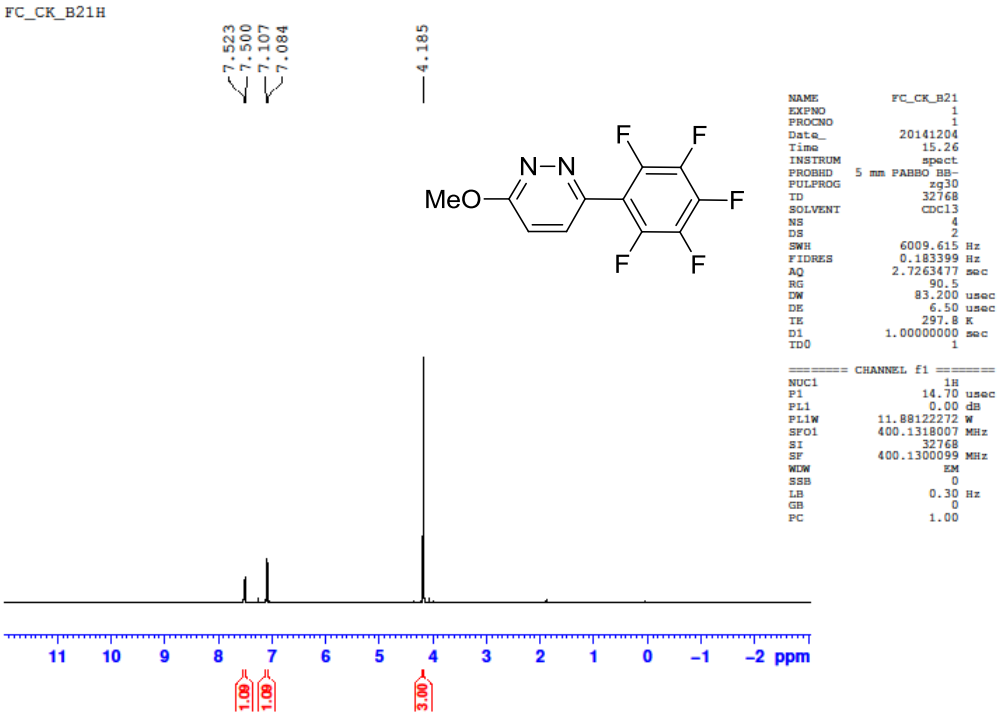
2-Methyl-7-(perfluorophenyl)quinoline (Table 5.2, compound 3fu)

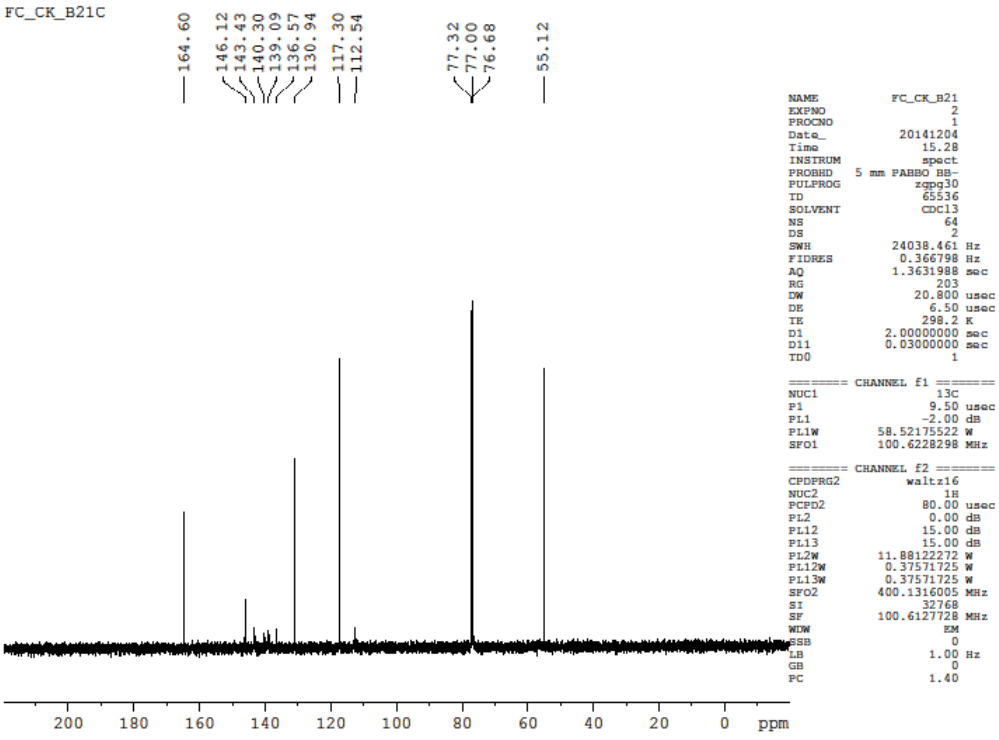




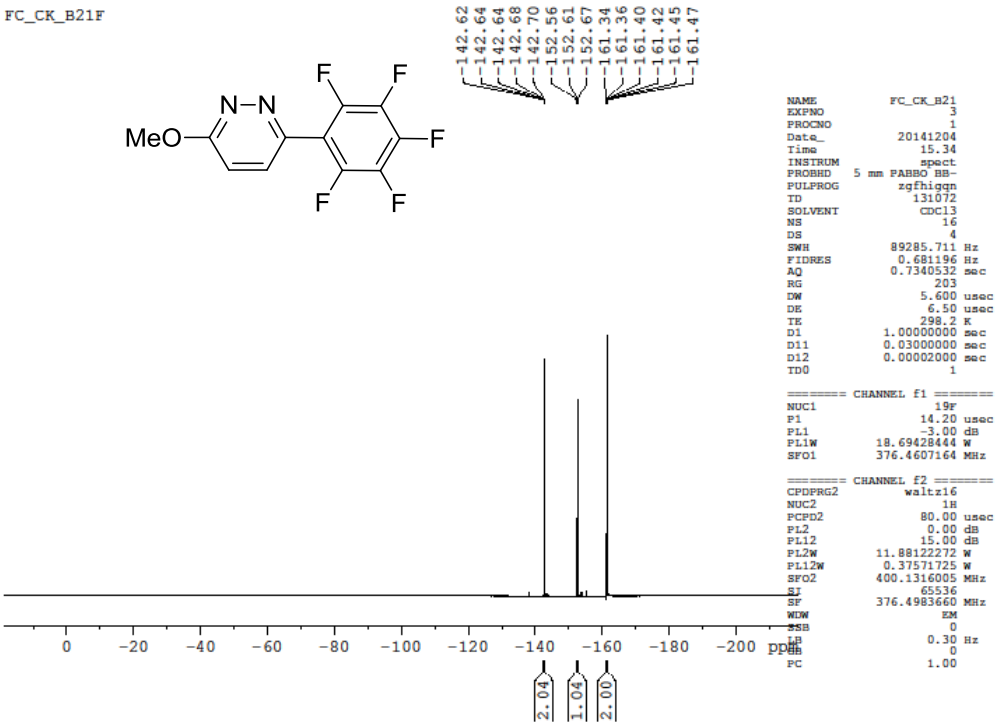
Mass	Calc. Mass	mDa	PPM	Formula
310.0646	310.0650	-0.4	-1.3	C16 H9 F5 N

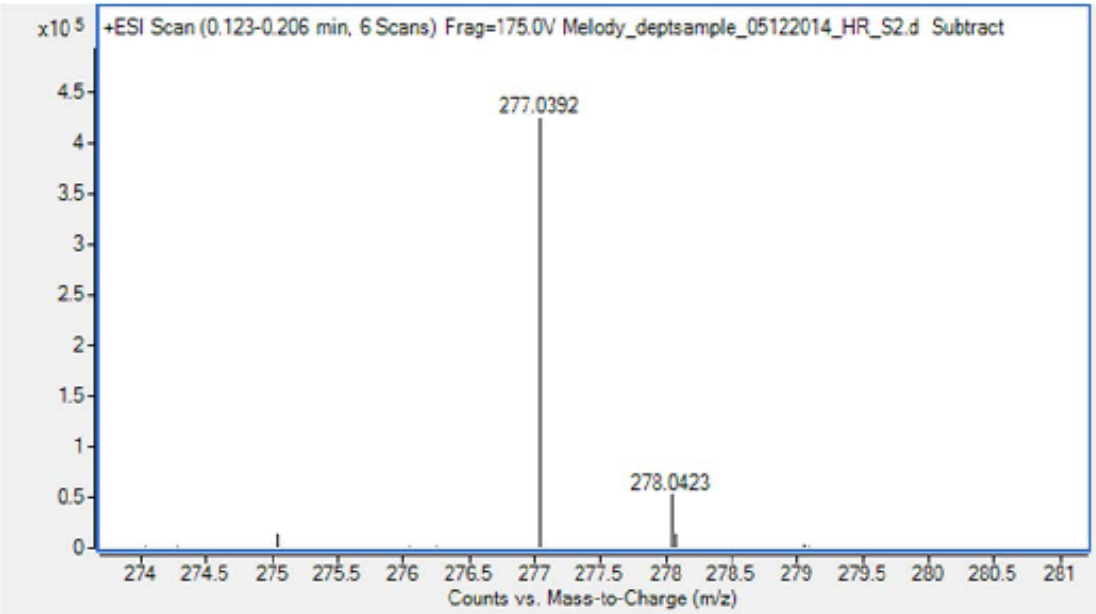
3-Methoxy-6-(perfluorophenyl)pyridazine (Table 5.2, compound 3gu)





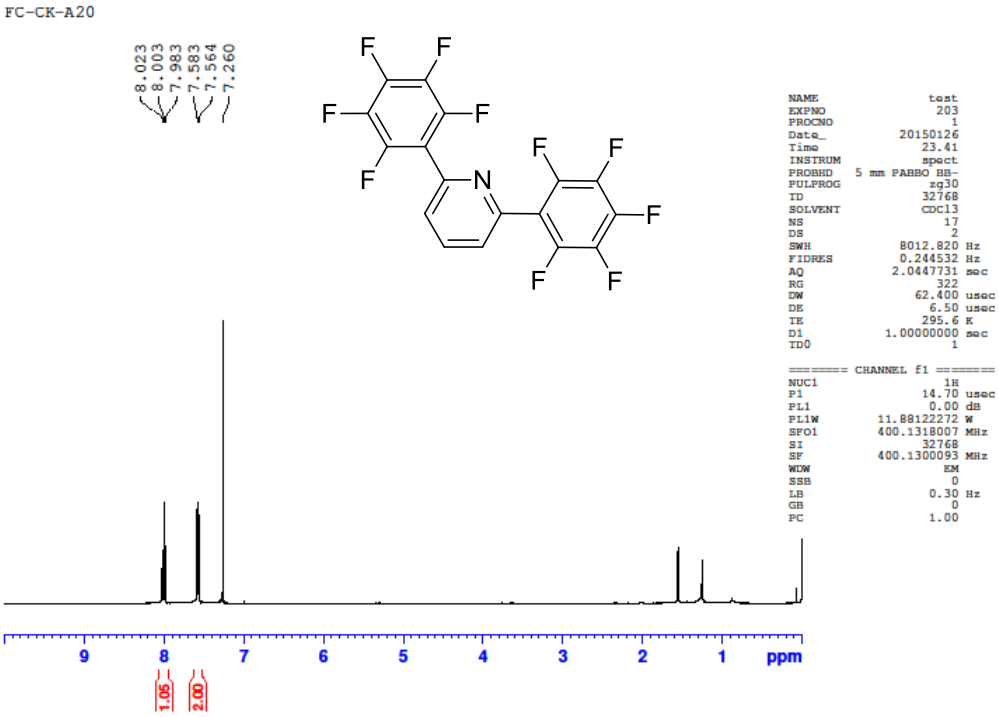
3-Methoxy-6-(perfluorophenyl)pyridazine (Table 5.2, compound 3gu)

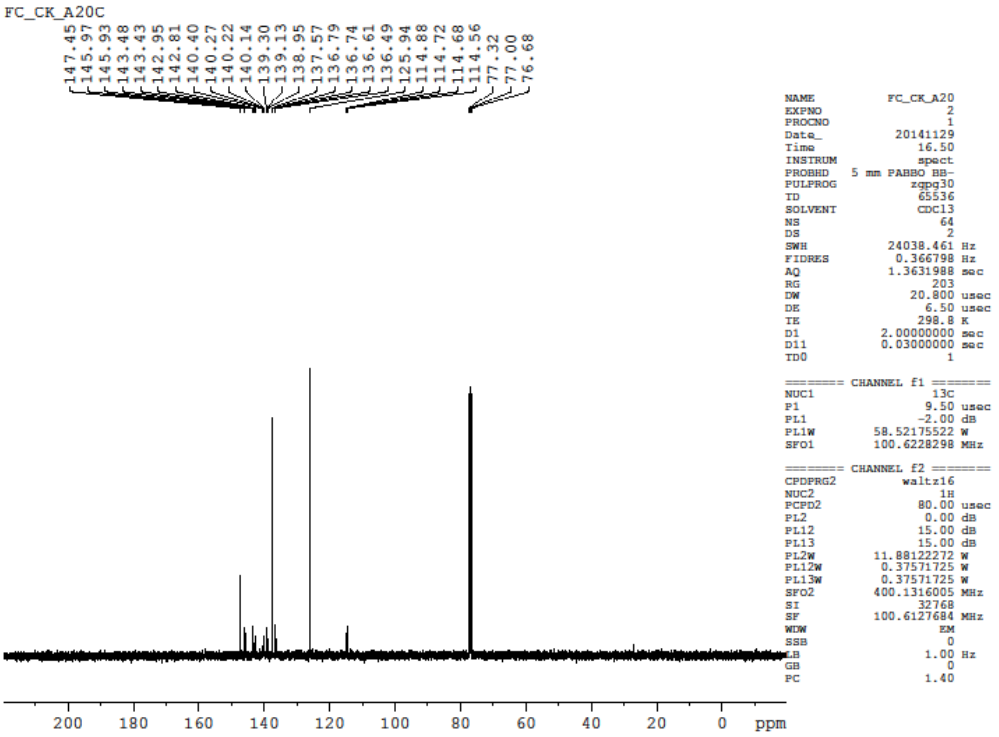




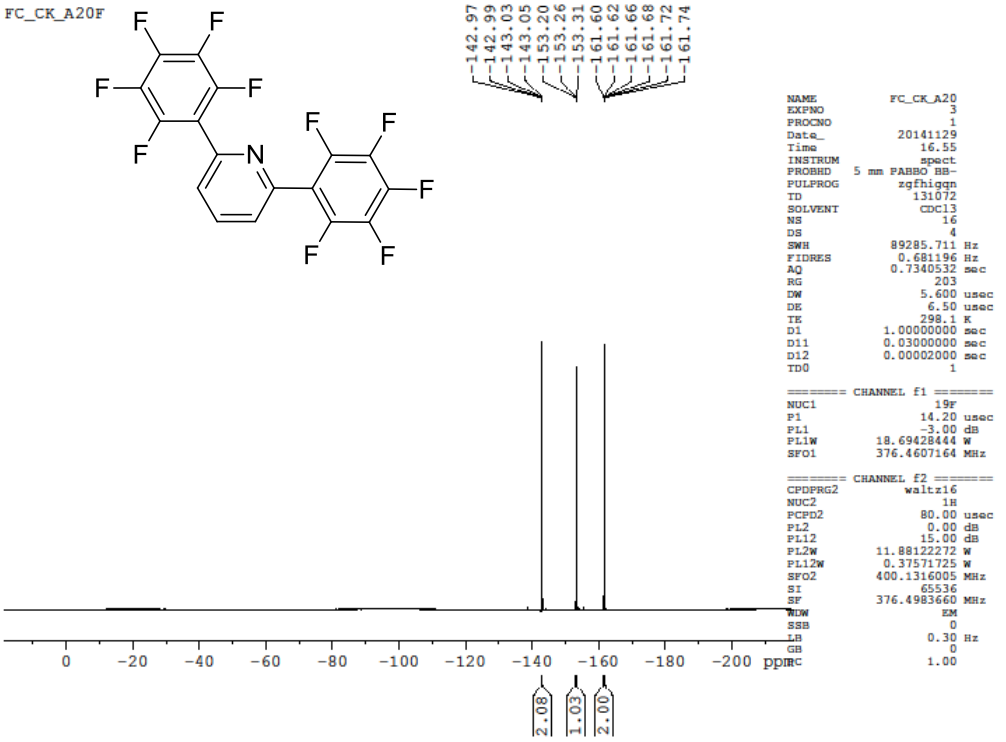
Mass	Calc. Mass	mDa	PPM	Formula
277.0392	277.0395	-0.3	-1.1	C11 H6 F5 N2 O

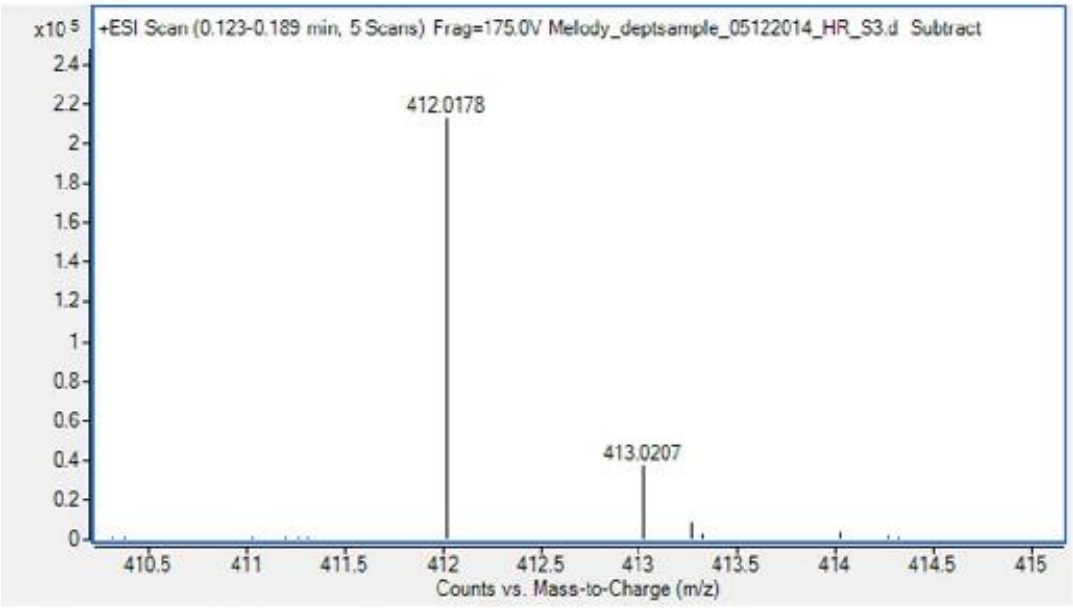
2,6-Bis(perfluorophenyl)pyridine (Table 5.2, compound 3hu)





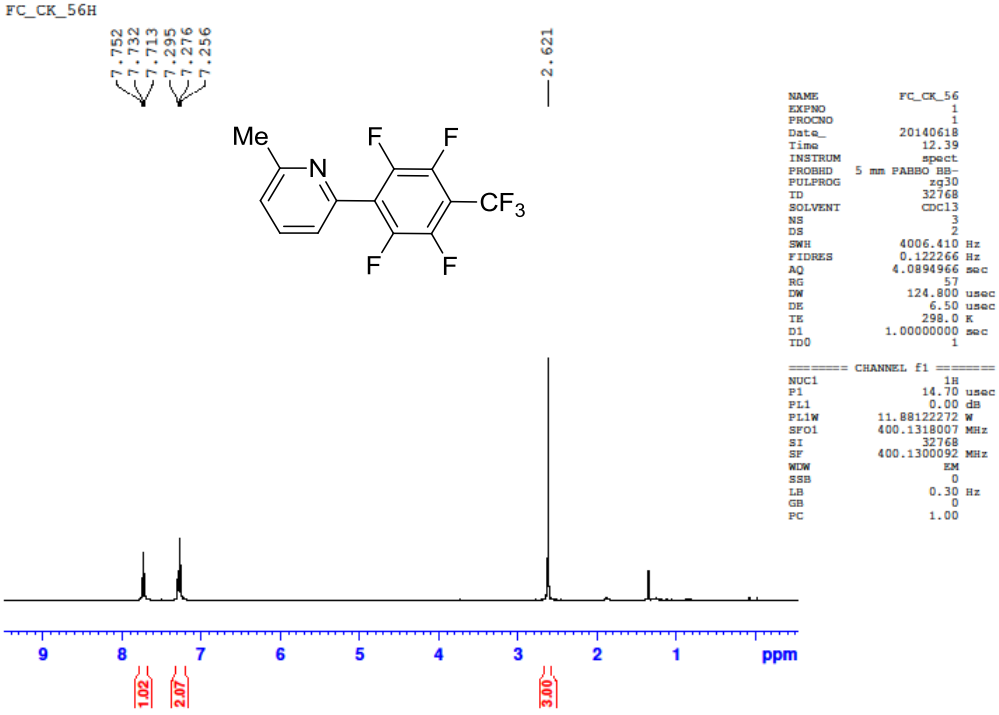
2,6-Bis(perfluorophenyl)pyridine (Table 5.2, compound 3hu)

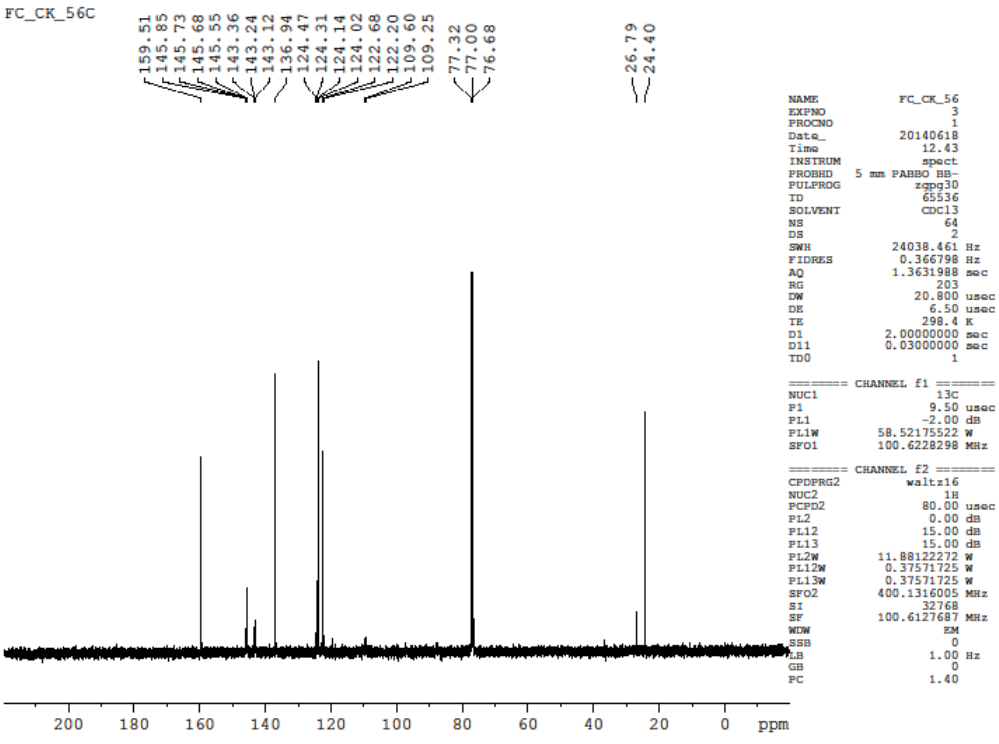




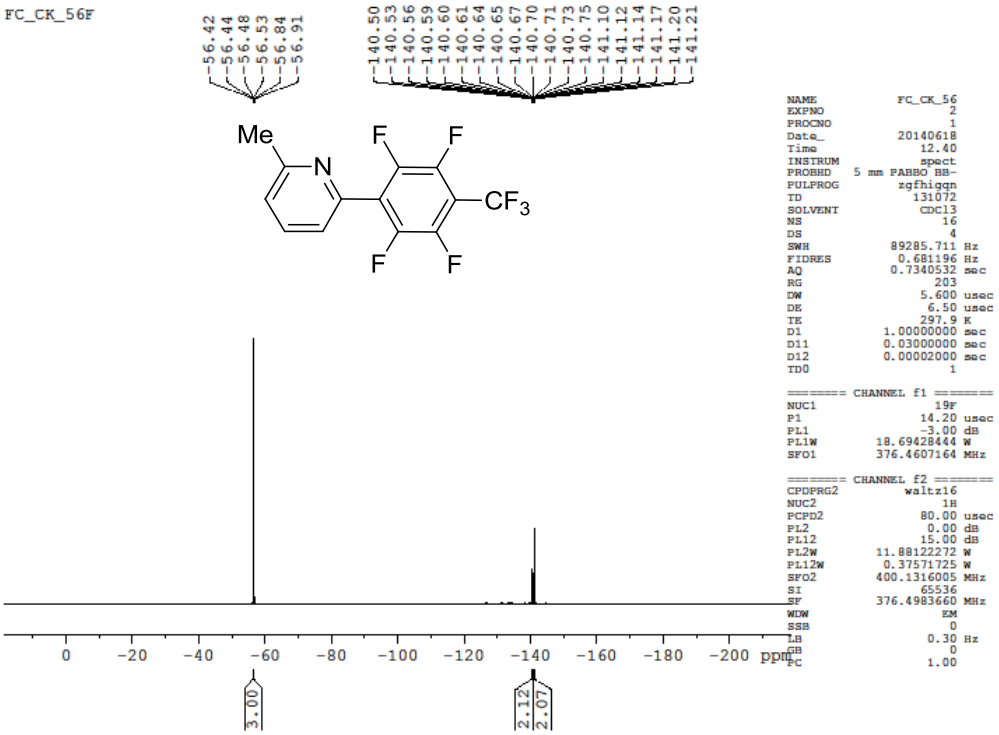
Mass	Calc. Mass	mDa	PPM	Formula
412.0178	412.0179	-0.1	-0.2	C17 H4 F10 N

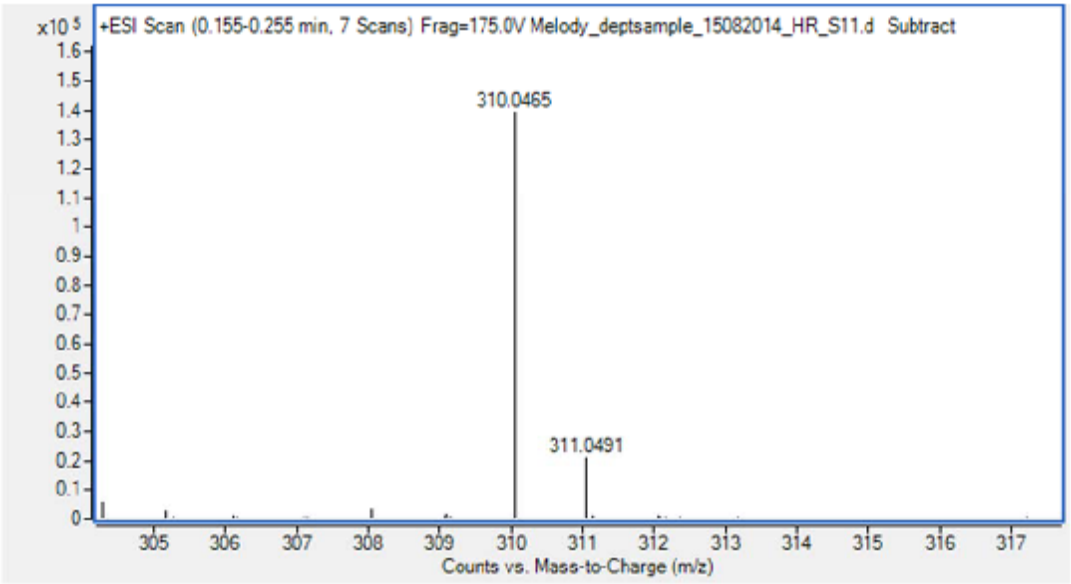
2-Methyl-6-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyridine (Table 5.2, compound 3cv)





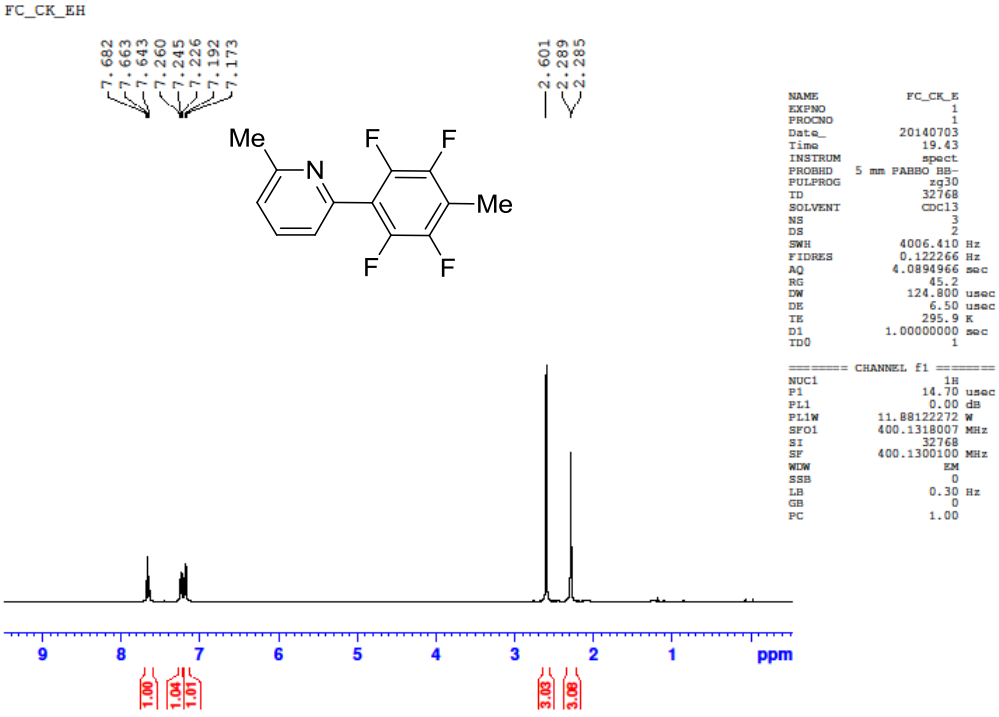
2-Methyl-6-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyridine (Table 5.2, compound 3cv)

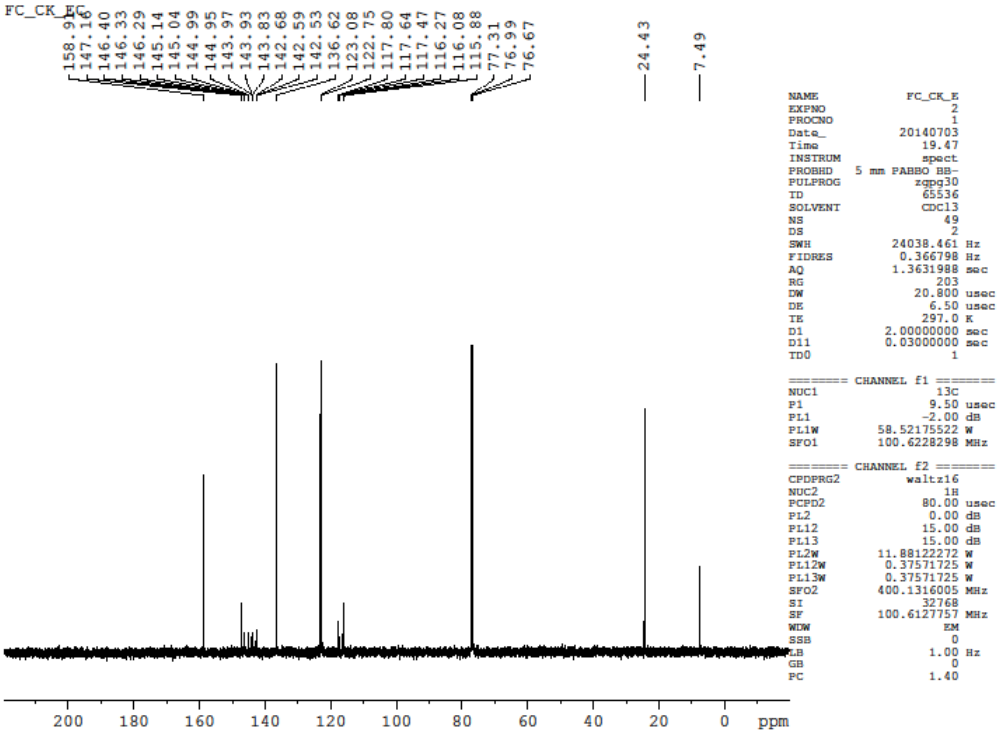




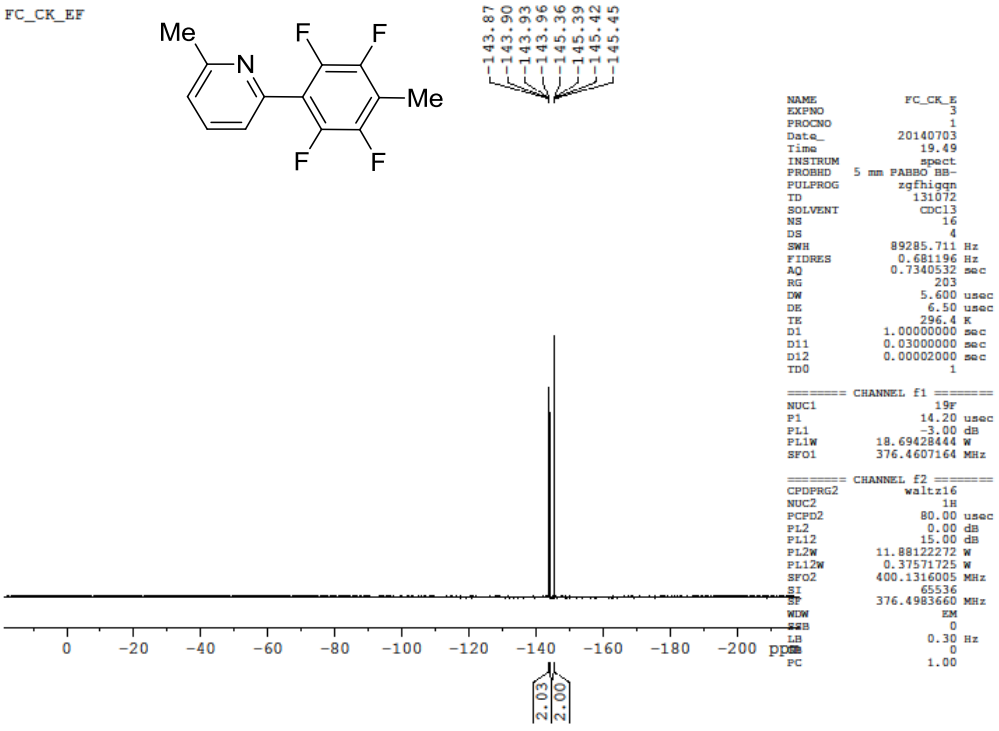
Mass	Calc. Mass	mDa	PPM	Formula
310.0465	310.0461	0.4	1.3	C13 H7 F7 N

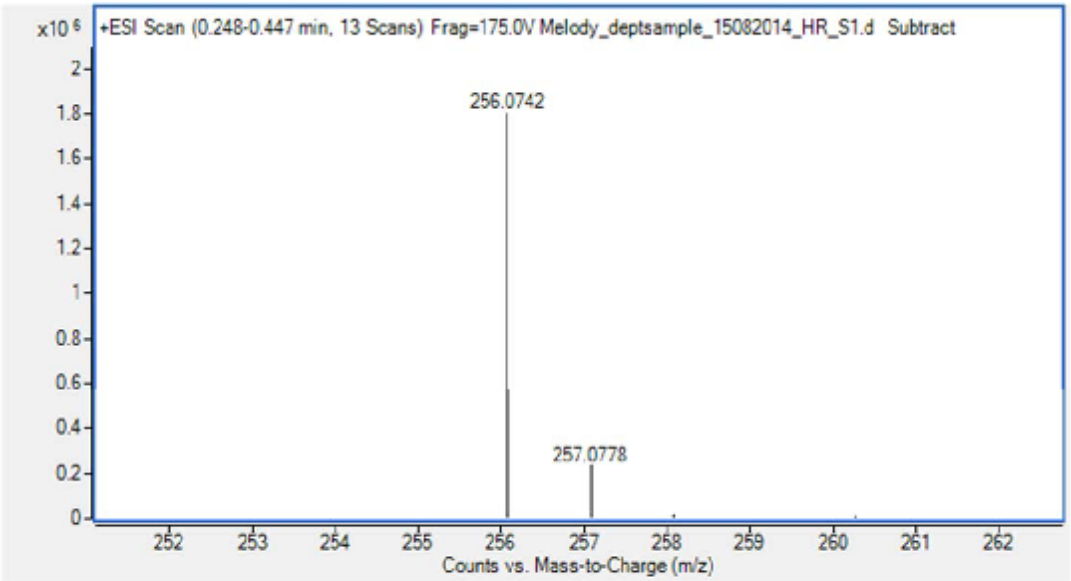
2-Methyl-6-(2,3,5,6-tetrafluoro-4-methylphenyl)pyridine (Table 5.2, compound 3cw)





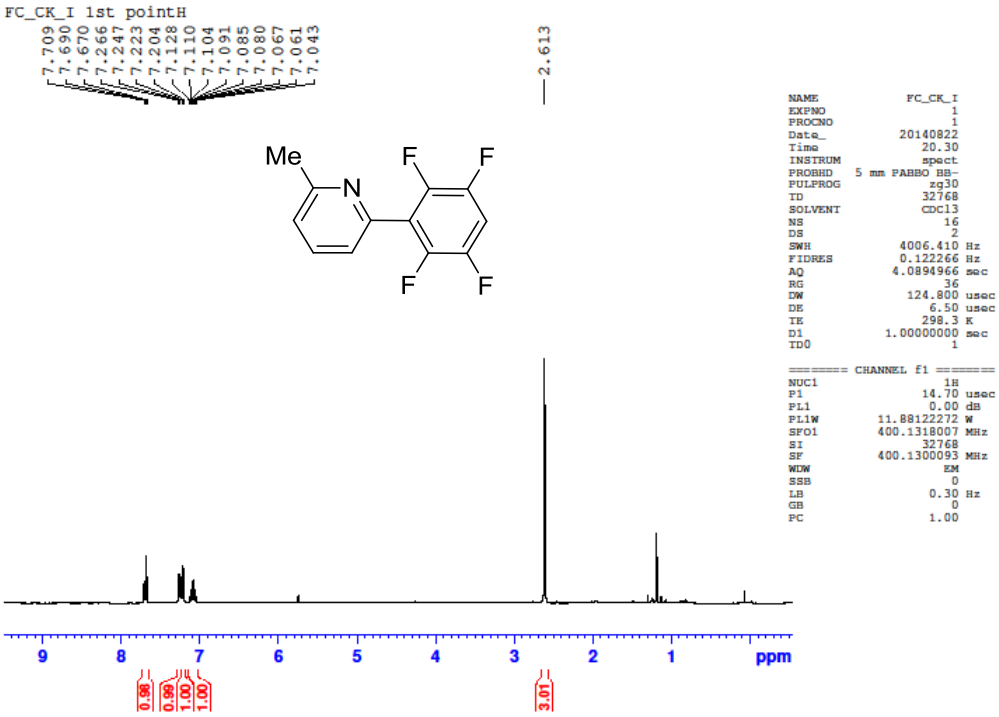
2-Methyl-6-(2,3,5,6-tetrafluoro-4-methylphenyl)pyridine (Table 5.2, compound 3cw)

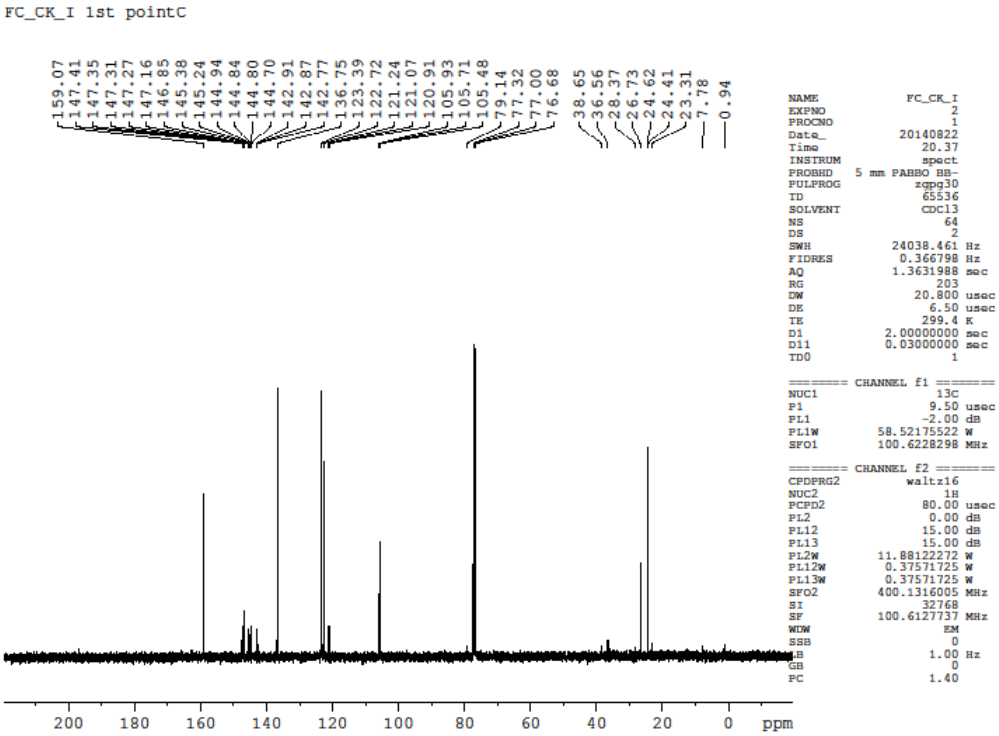




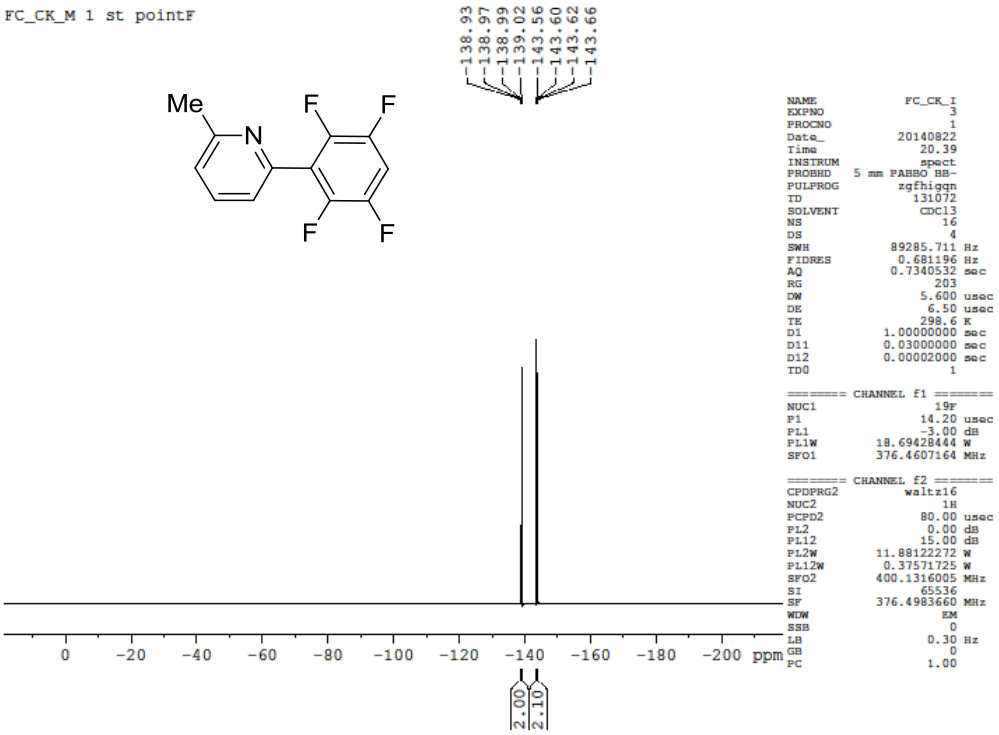
Mass	Calc. Mass	mDa	PPM	Formula
256.0742	256.0744	-0.2	-0.8	C13 H10 F4 N

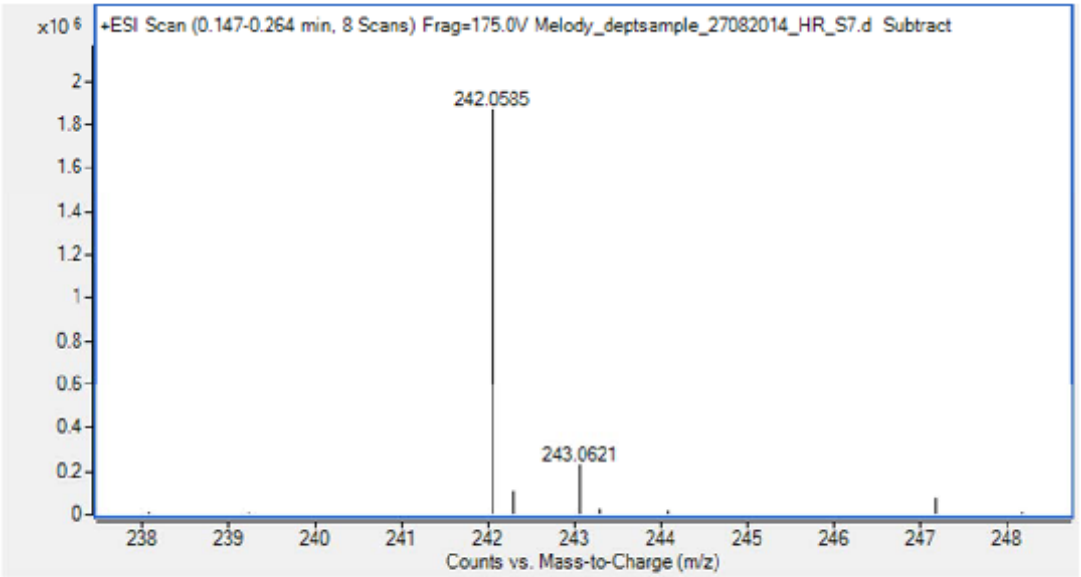
2-Methyl-6-(2,3,5,6-tetrafluorophenyl)pyridine (Table 5.2, compound 3cx)





2-Methyl-6-(2,3,5,6-tetrafluorophenyl)pyridine (Table 5.2, compound 3cx)

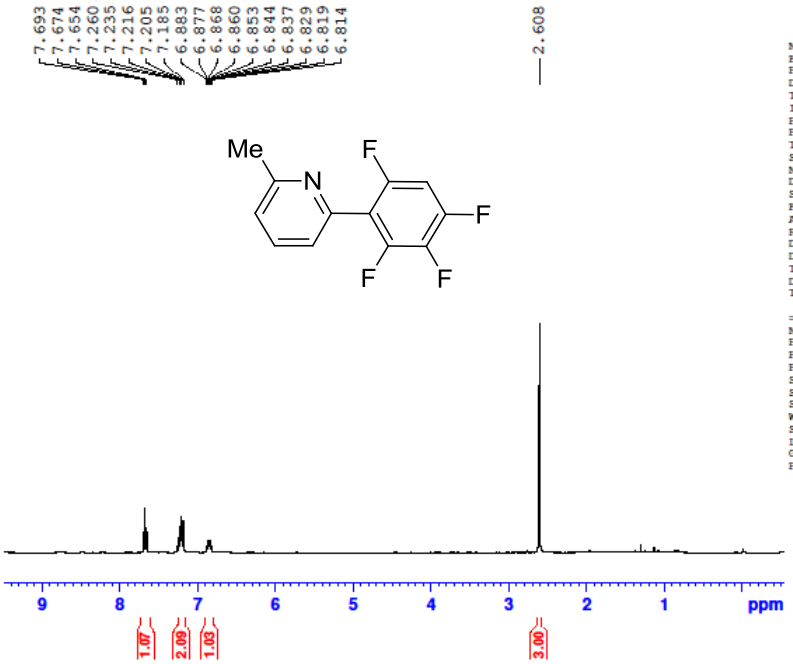




Mass	Calc. Mass	mDa	PPM	Formula
242.0585	242.0587	-0.2	-0.8	C12 H8 F4 N

2-Methyl-6-(2,3,4,6-tetrafluorophenyl)pyridine (Table 5.2, compound 3cy)

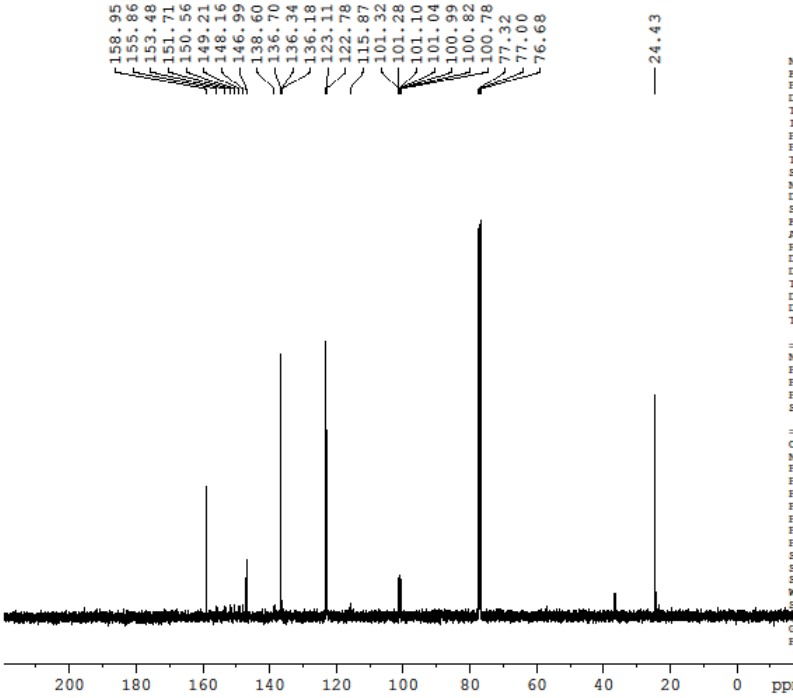
FC_CK_K_2nd ptH




```
NAME                FC_CK_K
EXPNO                     1
PROCNO                    1
Date_              20140715
Time                 13.34
INSTRUM              spect
PROBHD     5 mm PABBO BB-
PULPROG              zg30
TD                   32768
SOLVENT              CDCl3
NS                        3
DS                        2
SWH               4006.410 Hz
FIDRES               0.122266 Hz
AQ                4.0894966 sec
RG                       64
DW                 124.800 usec
DE                   6.50 usec
TE                  298.1 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 =======
NUC1                     1H
P1                   14.70 usec
PL1                   0.00 dB
PL1W            11.88122272 W
SFO1           400.1318007 MHz
SI                    32768
SF             400.1300098 MHz
WDW                      EM
SSB                       0
LB                    0.30 Hz
GB                        0
PC                    1.00
```

FC_CK_K_2ndptC

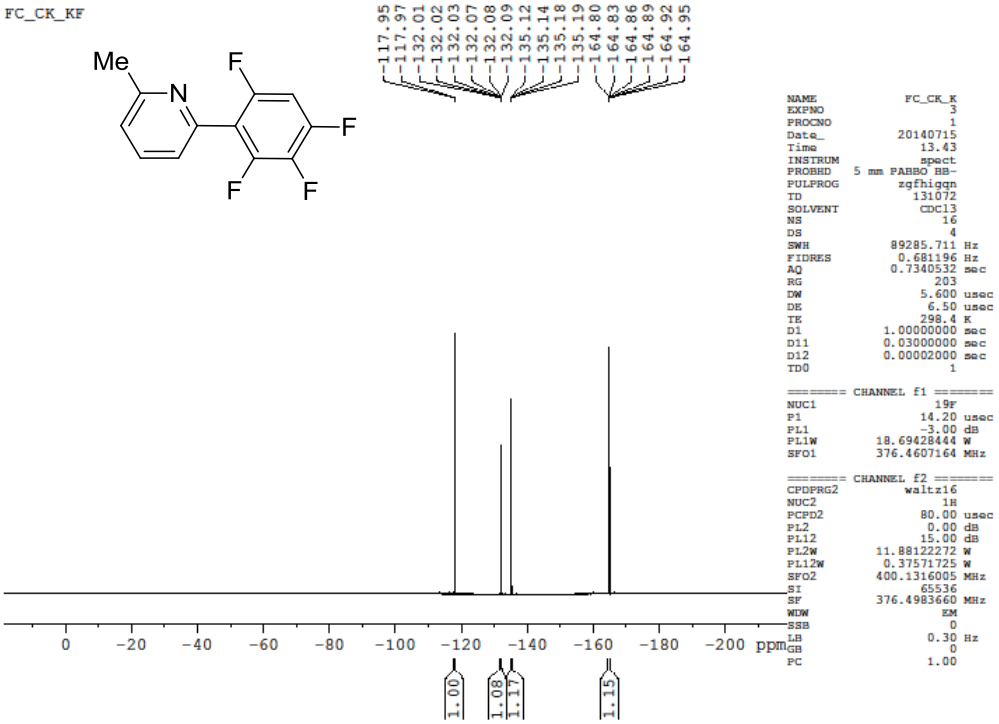


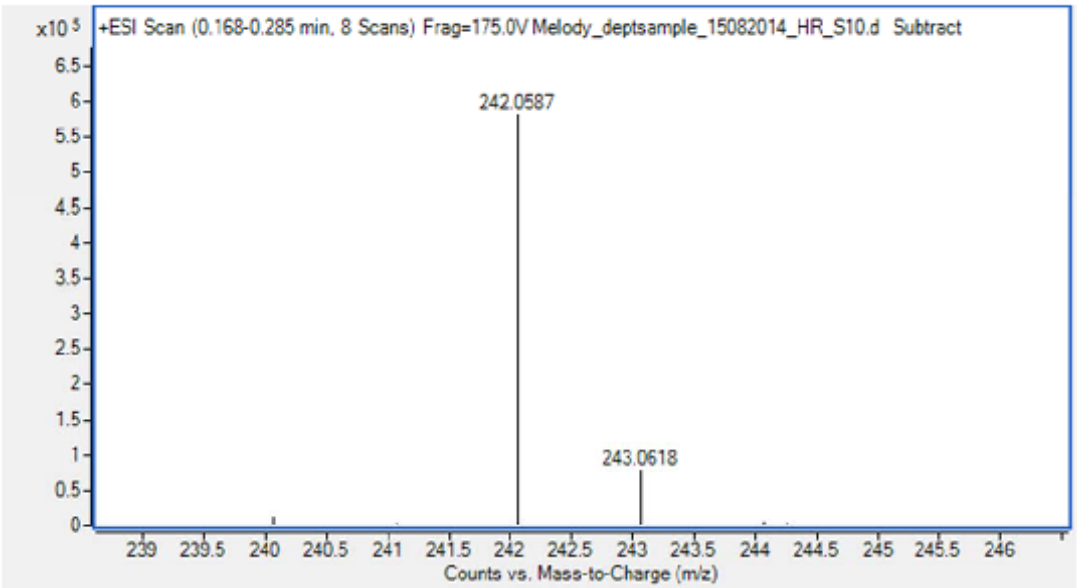

```
NAME                FC_CK_K
EXPNO                     2
PROCNO                    1
Date_              20140715
Time                 13.37
INSTRUM              spect
PROBHD     5 mm PABBO BB-
PULPROG            zgpg30
TD                   65536
SOLVENT              CDCl3
NS                       64
DS                        2
SWH              24038.461 Hz
FIDRES               0.366798 Hz
AQ                1.3631988 sec
RG                      203
DW                  20.800 usec
DE                   6.50 usec
TE                  299.0 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                       1

======== CHANNEL f1 =======
NUC1                     13C
P1                    9.50 usec
PL1                  -2.00 dB
PL1W            58.52175522 W
SFO1           100.6228298 MHz

======== CHANNEL f2 =======
CPDPRG2              waltz16
NUC2                     1H
PCPD2                80.00 usec
PL2                   0.00 dB
PL12                 15.00 dB
PL13                 15.00 dB
PL2W            11.88122272 W
PL12W            0.37571725 W
PL13W            0.37571725 W
SFO2           400.1316005 MHz
SI                    32768
SF             100.6127729 MHz
WDW                      EM
SSB                       0
GB                        0
PC                    1.40
```

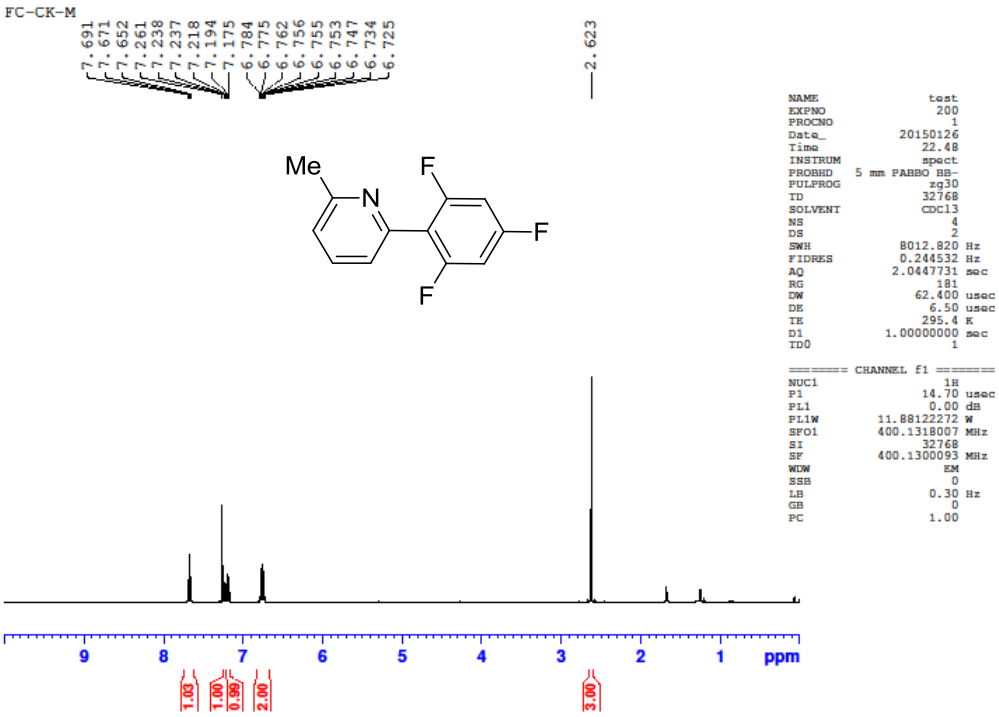
2-Methyl-6-(2,3,4,6-tetrafluorophenyl)pyridine (Table 5.2, compound 3cy)

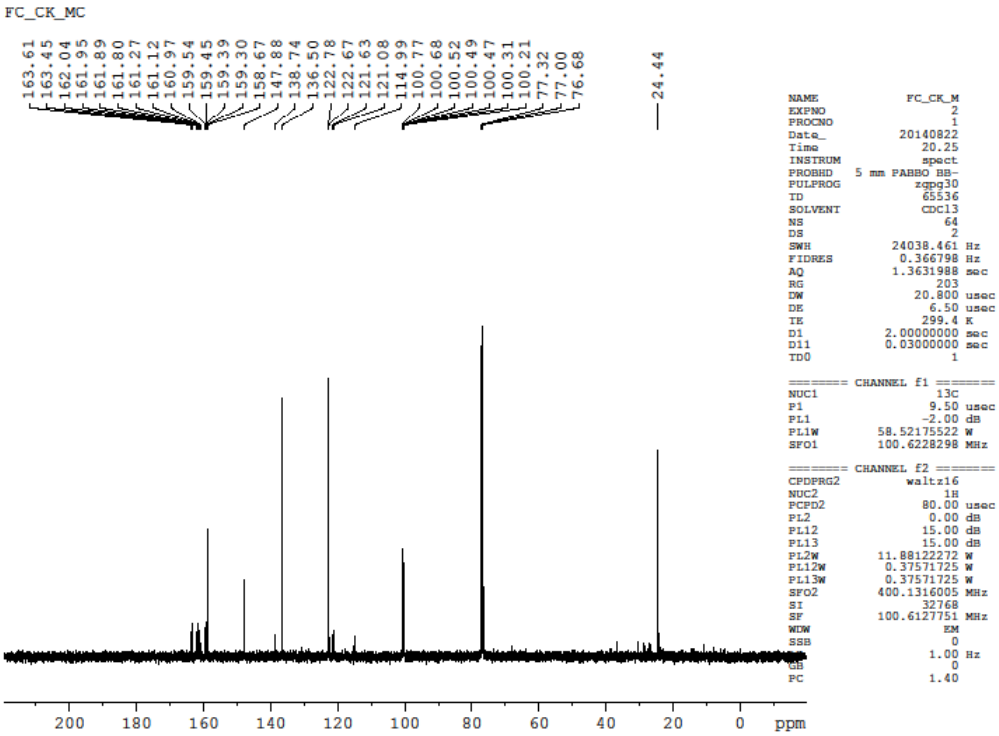




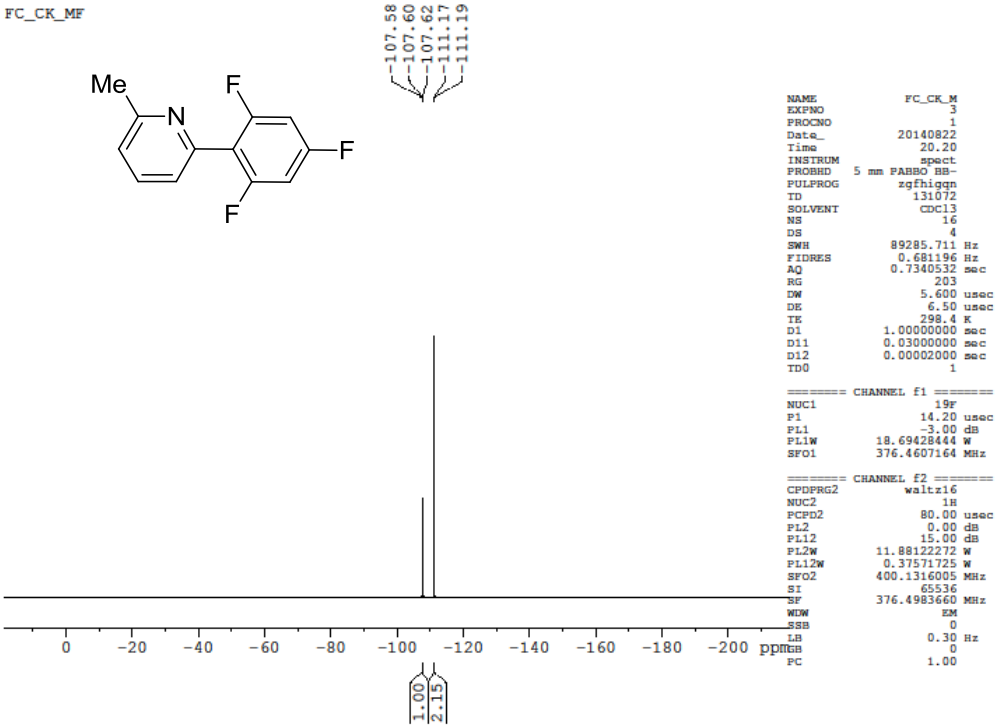
Mass	Calc. Mass	mDa	PPM	Formula
242.0587	242.0587	0.0	0.0	C12 H8 F4 N

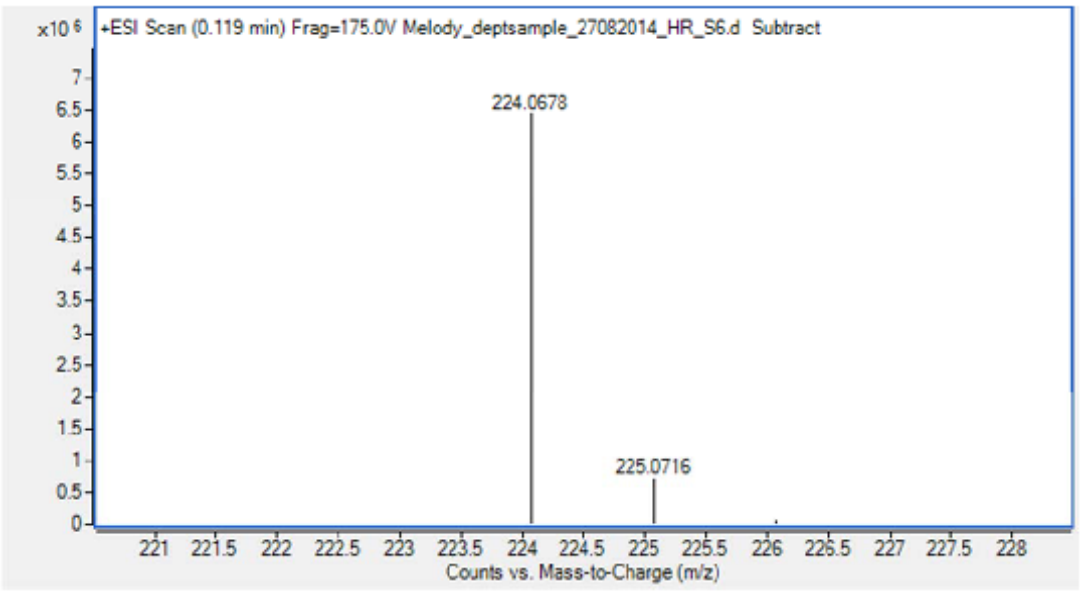
2-Methyl-6-(2,4,6-trifluorophenyl)pyridine (Table 5.2, compound 3cz)





2-Methyl-6-(2,4,6-trifluorophenyl)pyridine (Table 5.2, compound 3cz)

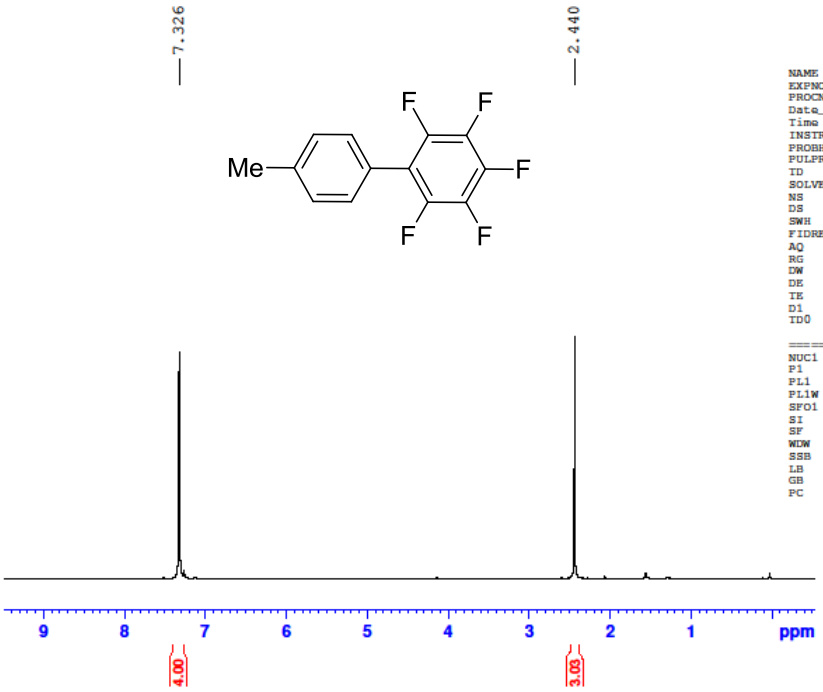




Mass	Calc. Mass	mDa	PPM	Formula
224.0678	224.0682	-0.4	-1.8	C12 H9 F3 N

2,3,4,5,6-Pentafluoro-4'-methyl-1,1'-biphenyl (Table 5.3, compound 5au)

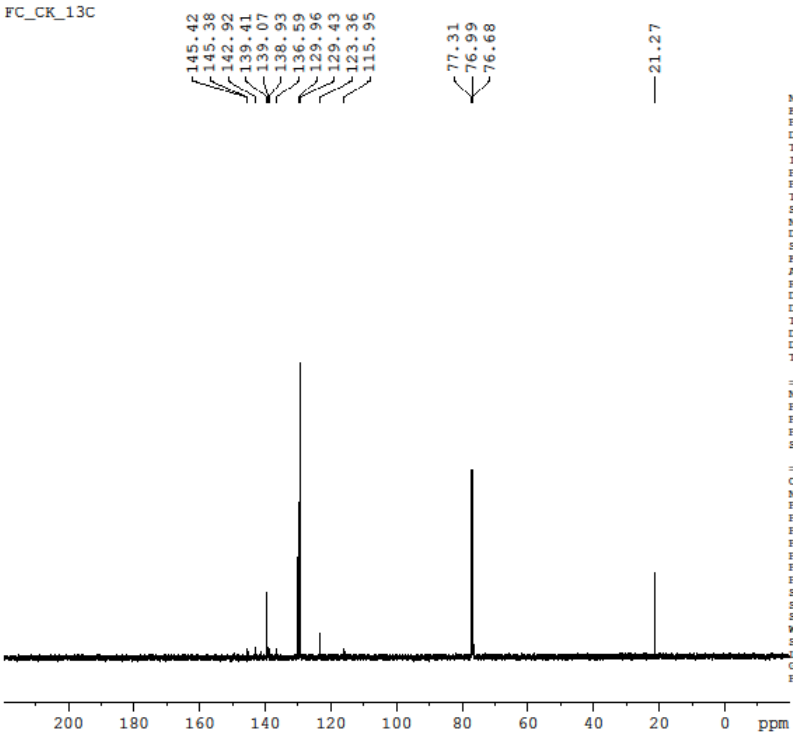
FC_CK_13H




```
NAME            FC_CK_13
EXPNO                  1
PROCNO                 1
Date_           20140409
Time                14.03
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             4006.410 Hz
FIDRES          0.122266 Hz
AQ              4.0894966 sec
RG                  80.6
DW                124.800 usec
DE                  6.50 usec
TE                298.2 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 =======
NUC1                  1H
P1                 14.70 usec
PL1                0.00 dB
PL1W          11.88122272 W
SFO1          400.1318007 MHz
SI                 32768
SF            400.1300098 MHz
WDW                   EM
SSB                    0
LB                 0.30 Hz
GB                     0
PC                 1.00
```

FC_CK_13C

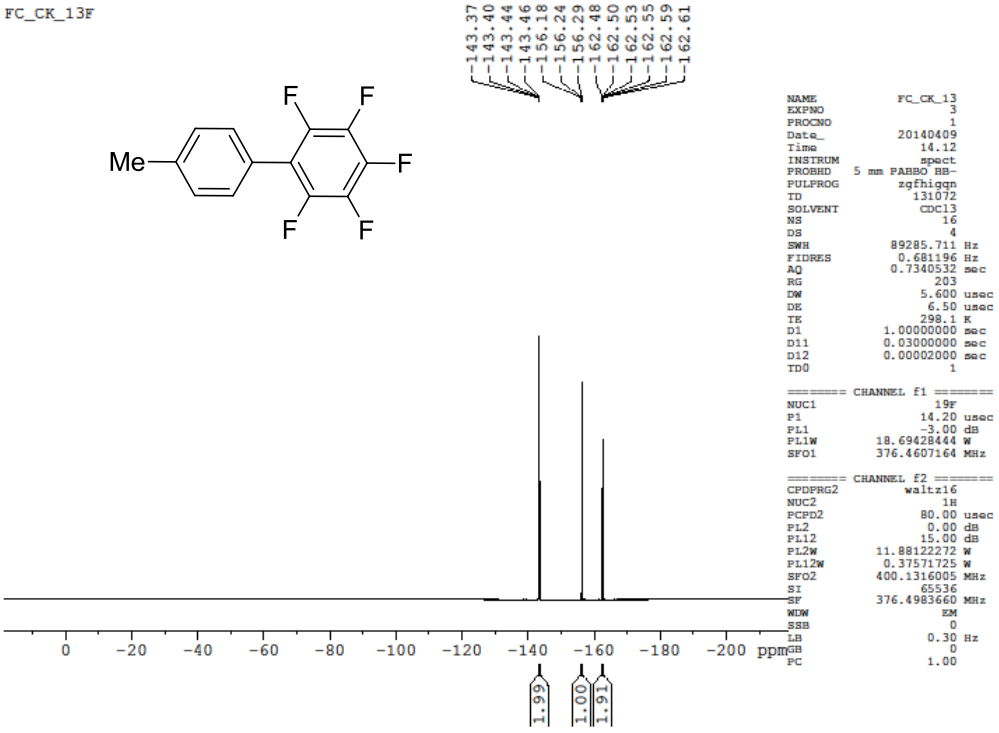



```
NAME            FC_CK_13
EXPNO                  2
PROCNO                 1
Date_           20140409
Time                14.07
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                    64
DS                     2
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631988 sec
RG                   203
DW                20.800 usec
DE                  6.50 usec
TE                298.6 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                    1

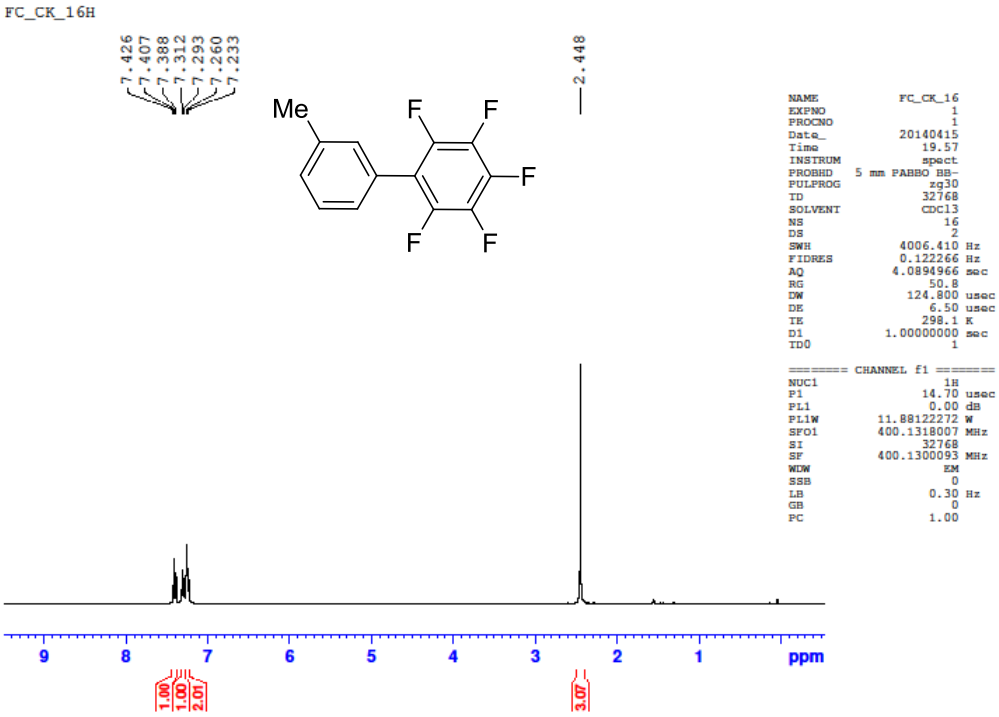
======== CHANNEL f1 =======
NUC1                 13C
P1                  9.50 usec
PL1                -2.00 dB
PL1W          58.52175522 W
SFO1          100.6228298 MHz

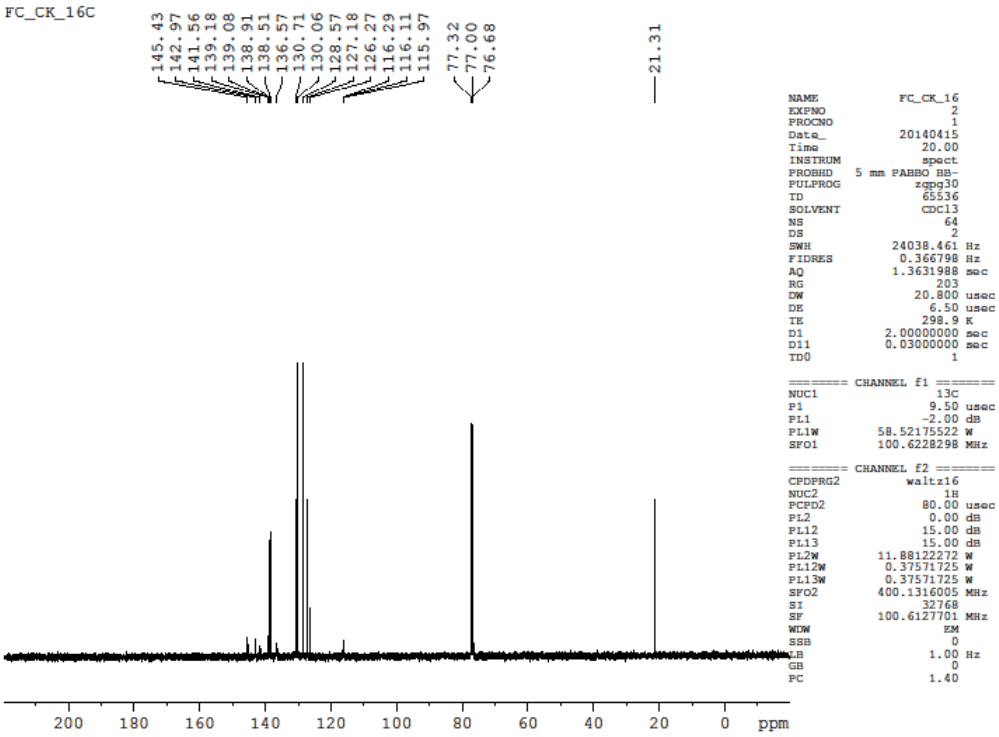
======== CHANNEL f2 =======
CPDPRG2          waltz16
NUC2                  1H
PCPD2              80.00 usec
PL2                0.00 dB
PL12               15.00 dB
PL13               15.00 dB
PL2W          11.88122272 W
PL12W          0.37571725 W
PL13W          0.37571725 W
SFO2          400.1316005 MHz
SI                 32768
SF            100.6127708 MHz
WDW                   EM
SSB                    0
LB                 1.00 Hz
GB                     0
PC                 1.40
```

2,3,4,5,6-Pentafluoro-4'-methyl-1,1'-biphenyl (Table 5.3, compound 5au)

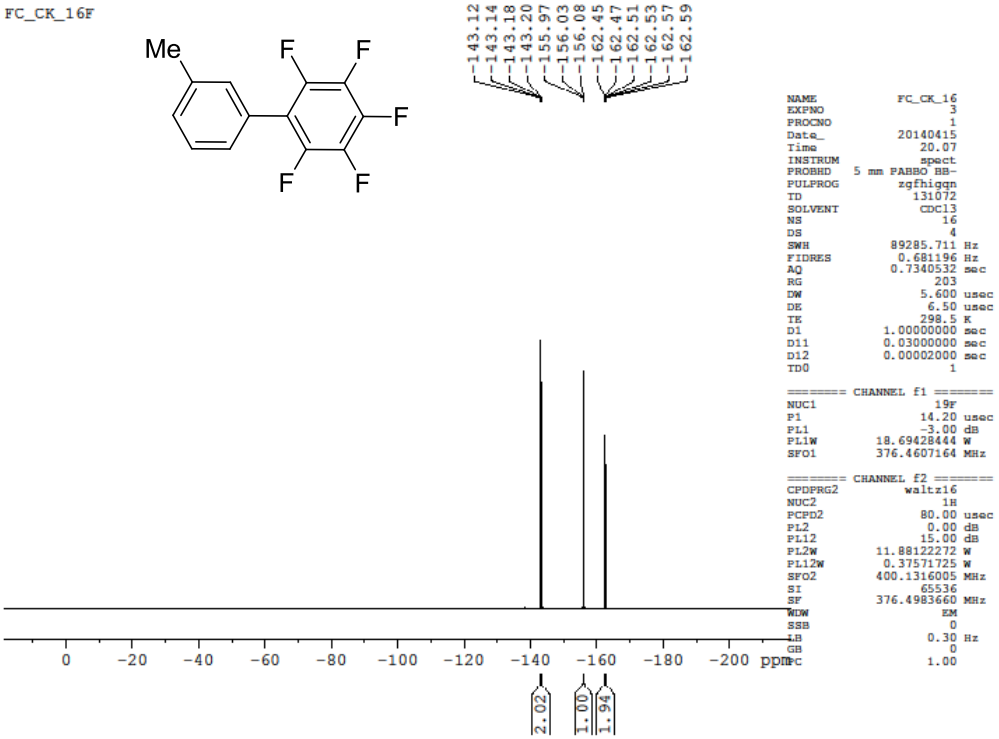


2,3,4,5,6-Pentafluoro-3'-methyl-1,1'-biphenyl (Table 5.3, compound 5bu)

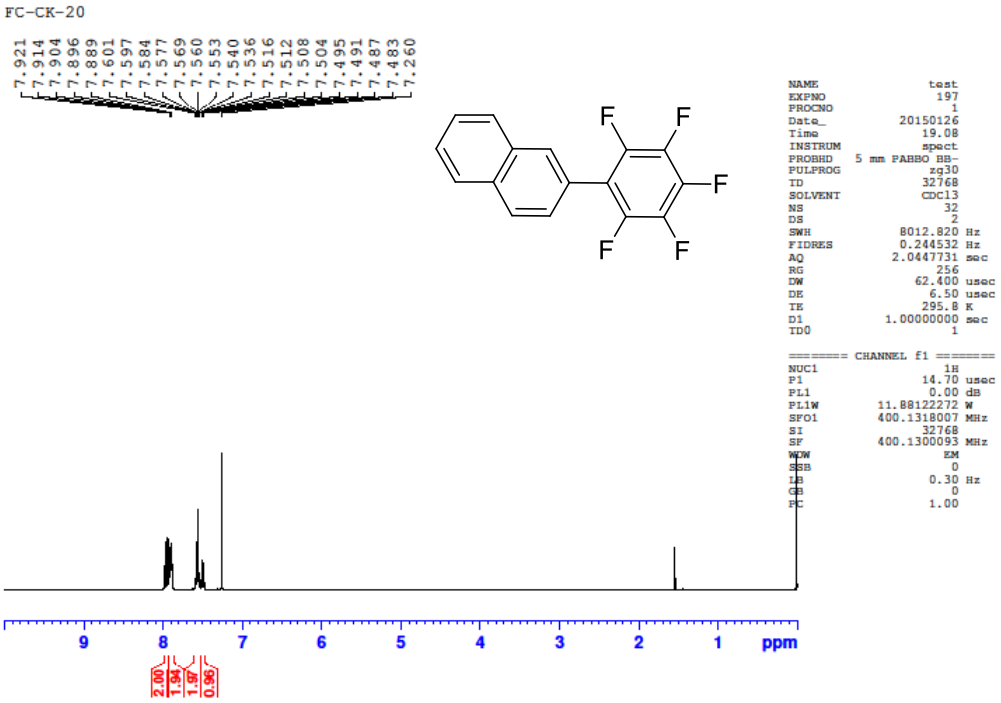


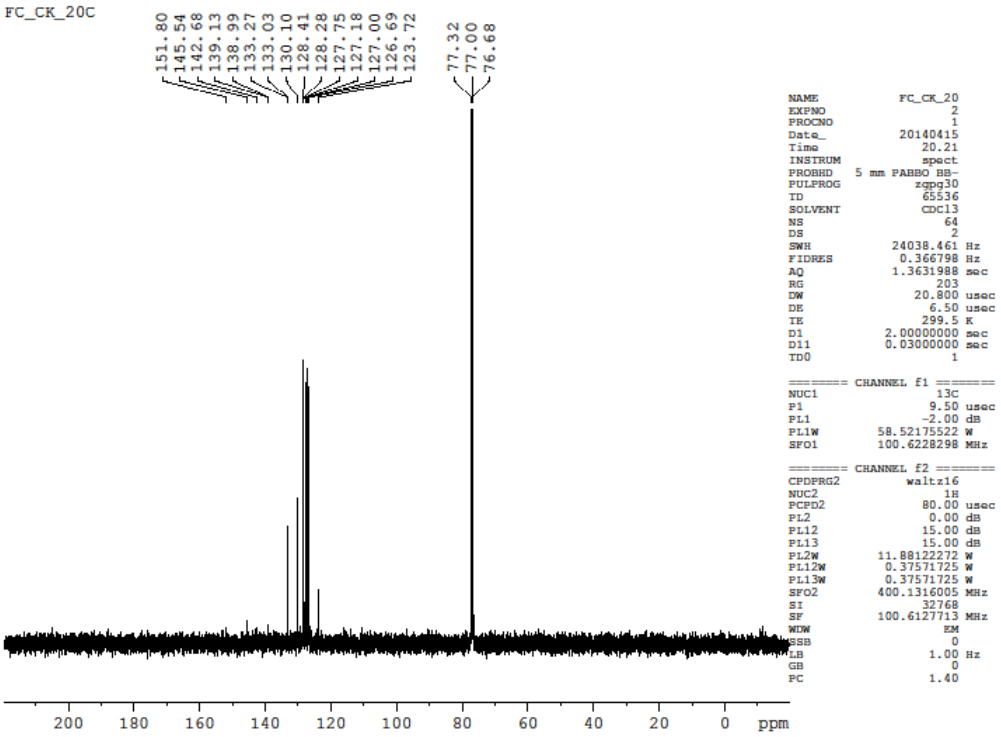


2,3,4,5,6-Pentafluoro-3'-methyl-1,1'-biphenyl (Table 5.3, compound 5bu)

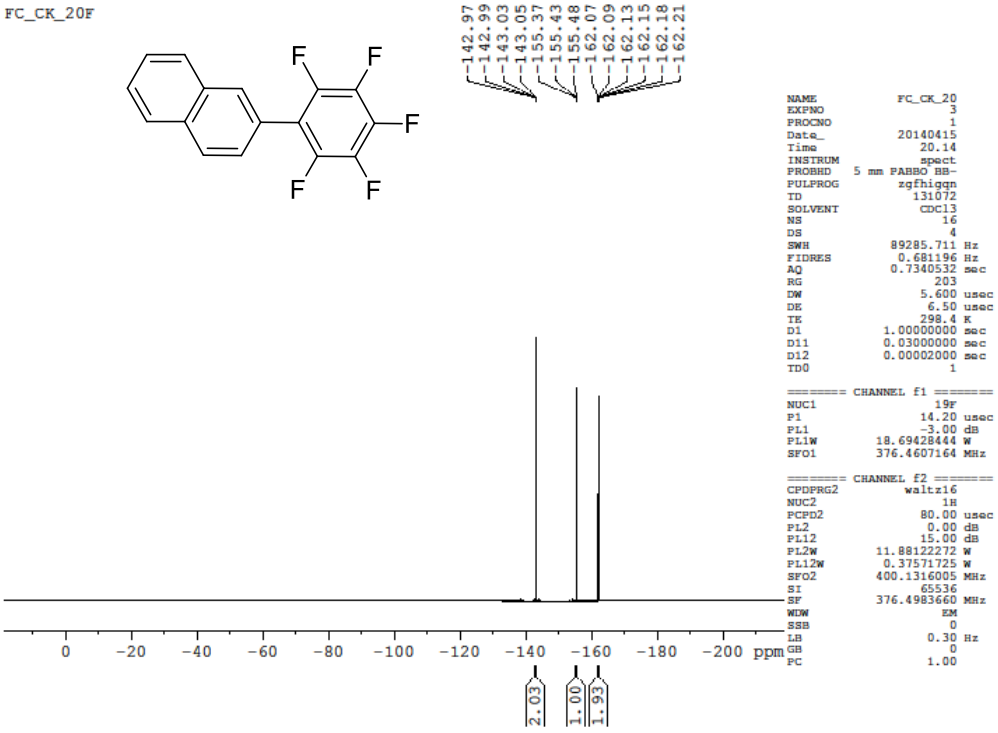


2-(Perfluorophenyl)naphthalene (Table 5.3, compound 5cu)

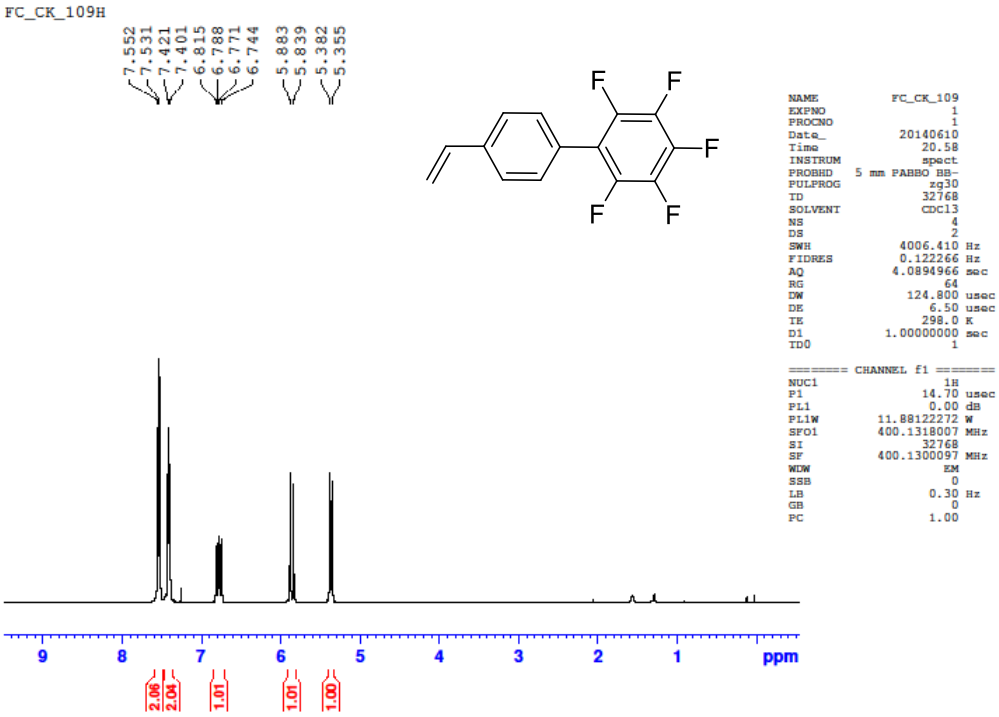


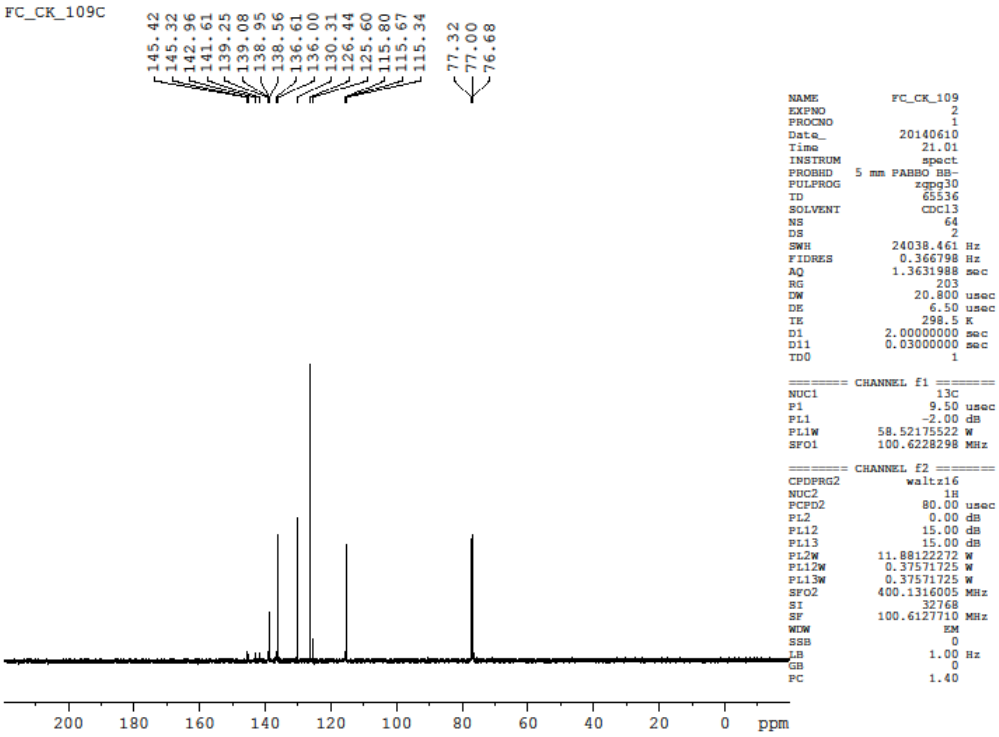


2-(Perfluorophenyl)naphthalene (Table 5.3, compound 5cu)

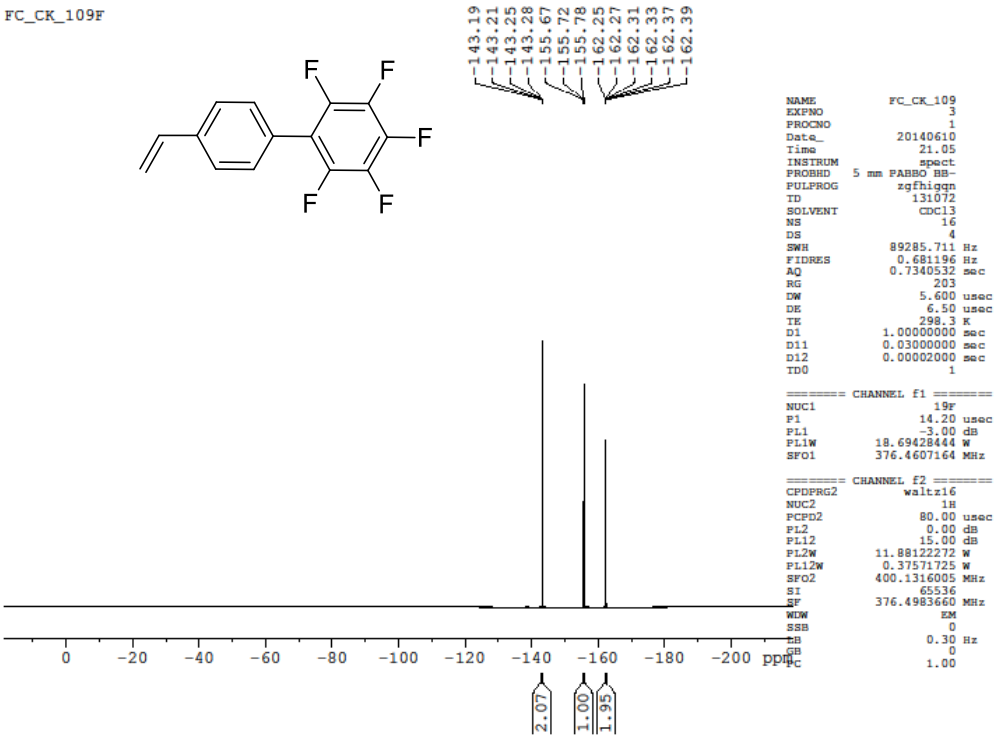


2,3,4,5,6-Pentafluoro-4'-vinyl-1,1'-biphenyl (Table 5.3, compound 5du)

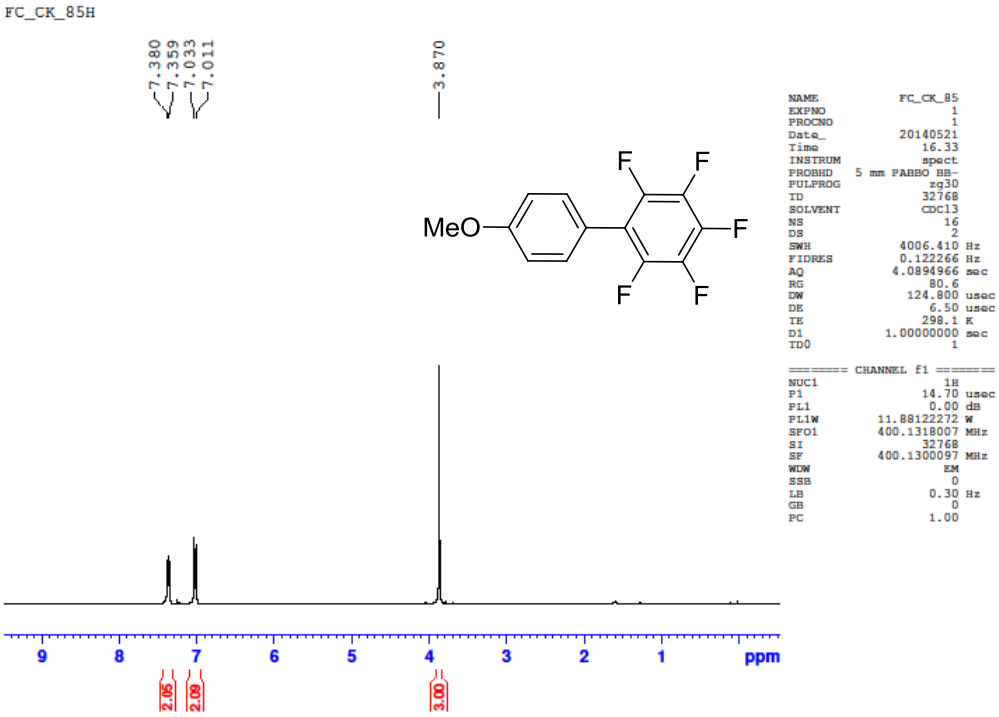


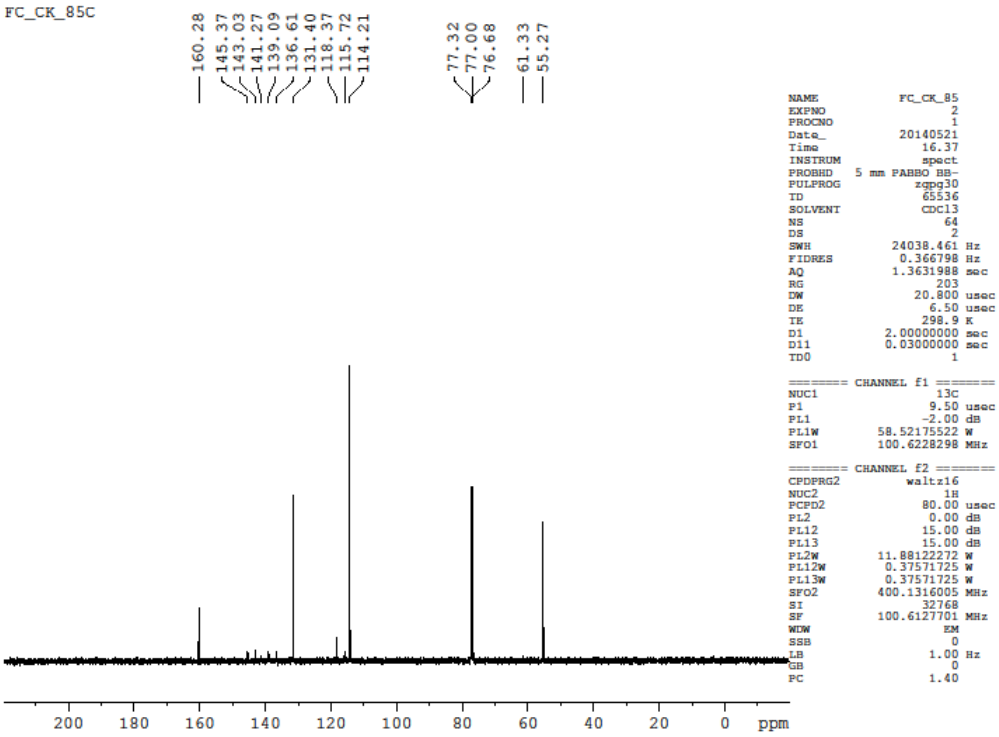


2,3,4,5,6-Pentafluoro-4'-vinyl-1,1'-biphenyl (Table 5.3, compound 5du)

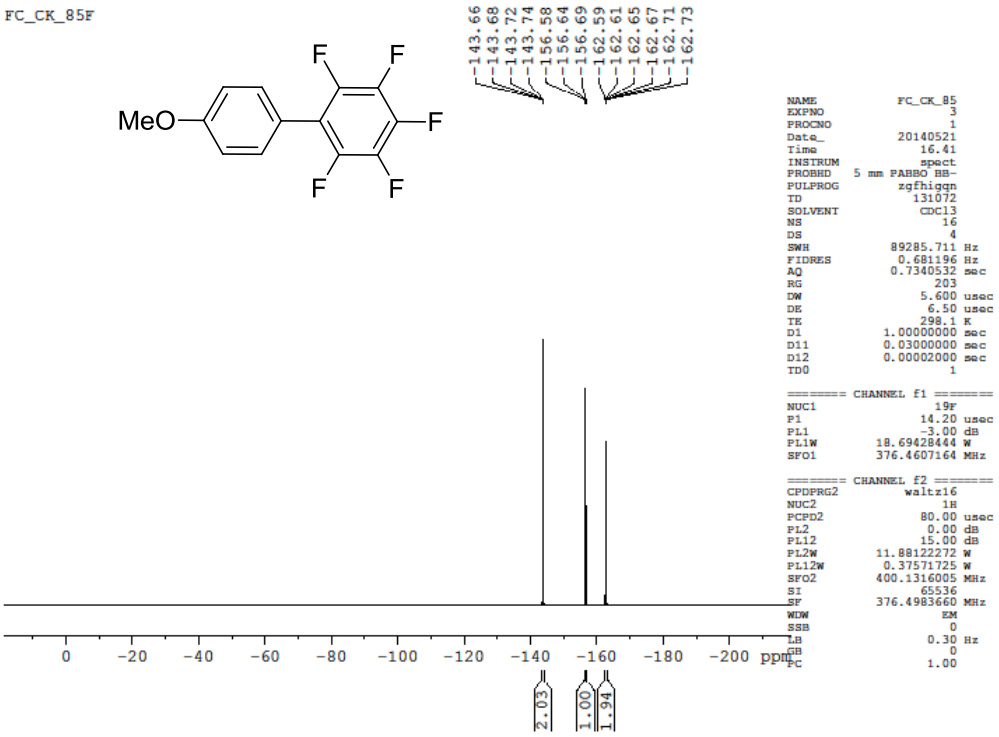


2,3,4,5,6-Pentafluoro-4'-methoxy-1,1'-biphenyl (Table 5.3, compound 5eu)



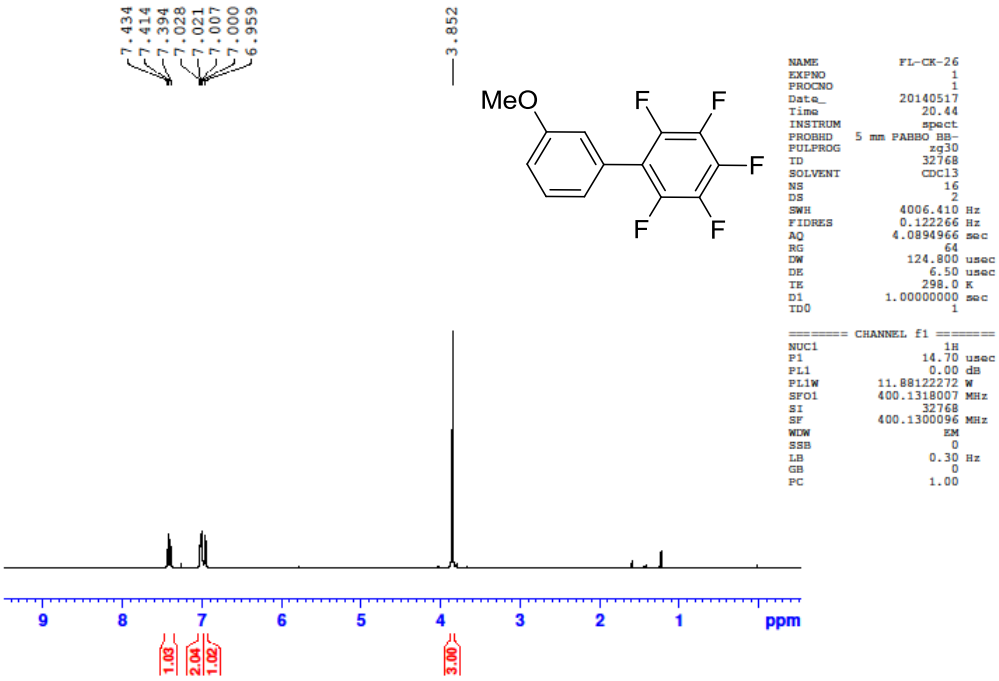


2,3,4,5,6-Pentafluoro-4'-methoxy-1,1'-biphenyl (Table 5.3, compound 5eu)



2,3,4,5,6-Pentafluoro-3'-methoxy-1,1'-biphenyl (Table 5.3, compound 5fu)

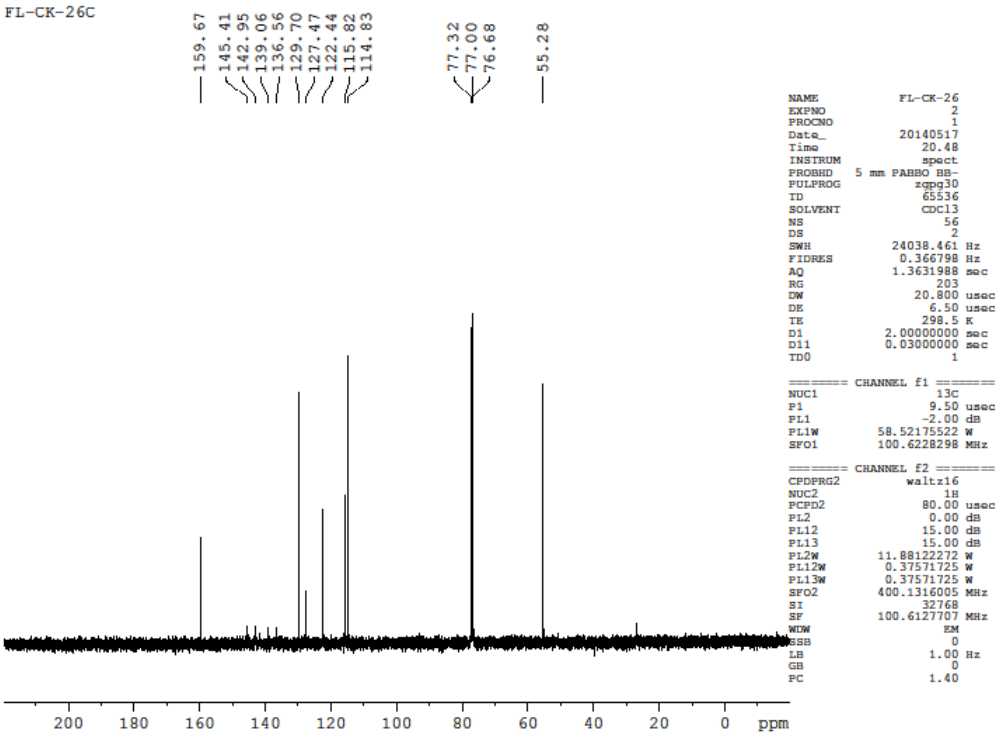
FL-CK-26H




```
NAME            FL-CK-26
EXPNO                1
PROCNO               1
Date_         20140517
Time             20.44
INSTRUM          spect
PROBHD   5 mm PABBO BB-
PULPROG          zg30
TD              32768
SOLVENT          CDCl3
NS                  16
DS                   2
SWH           4006.410 Hz
FIDRES        0.122266 Hz
AQ            4.0894966 sec
RG                  64
DW             124.800 usec
DE               6.50 usec
TE              298.0 K
D1            1.00000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                1H
P1               14.70 usec
PL1               0.00 dB
PL1W        11.88122272 W
SFO1        400.1318007 MHz
SI                32768
SF          400.1300096 MHz
WDW                EM
SSB                 0
LB               0.30 Hz
GB                  0
PC               1.00
```

FL-CK-26C

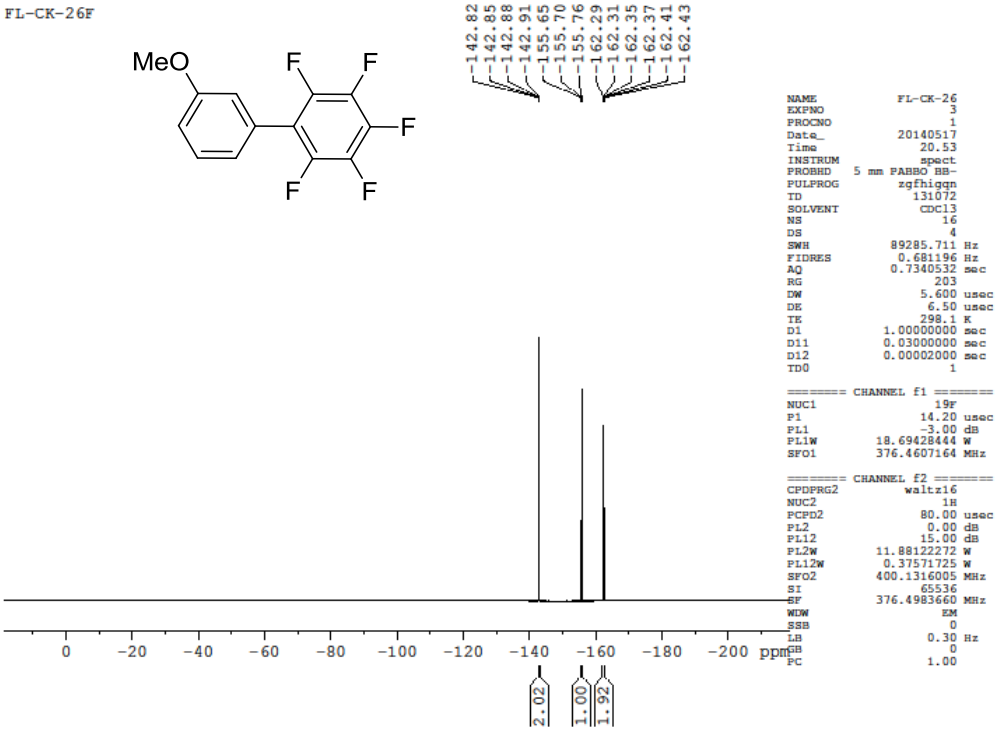



```
NAME            FL-CK-26
EXPNO                2
PROCNO               1
Date_         20140517
Time             20.48
INSTRUM          spect
PROBHD   5 mm PABBO BB-
PULPROG        zgpg30
TD              65536
SOLVENT          CDCl3
NS                  56
DS                   2
SWH          24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631988 sec
RG                 203
DW             20.800 usec
DE               6.50 usec
TE              298.5 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1               13C
P1               9.50 usec
PL1              -2.00 dB
PL1W        58.52175522 W
SFO1        100.6228298 MHz

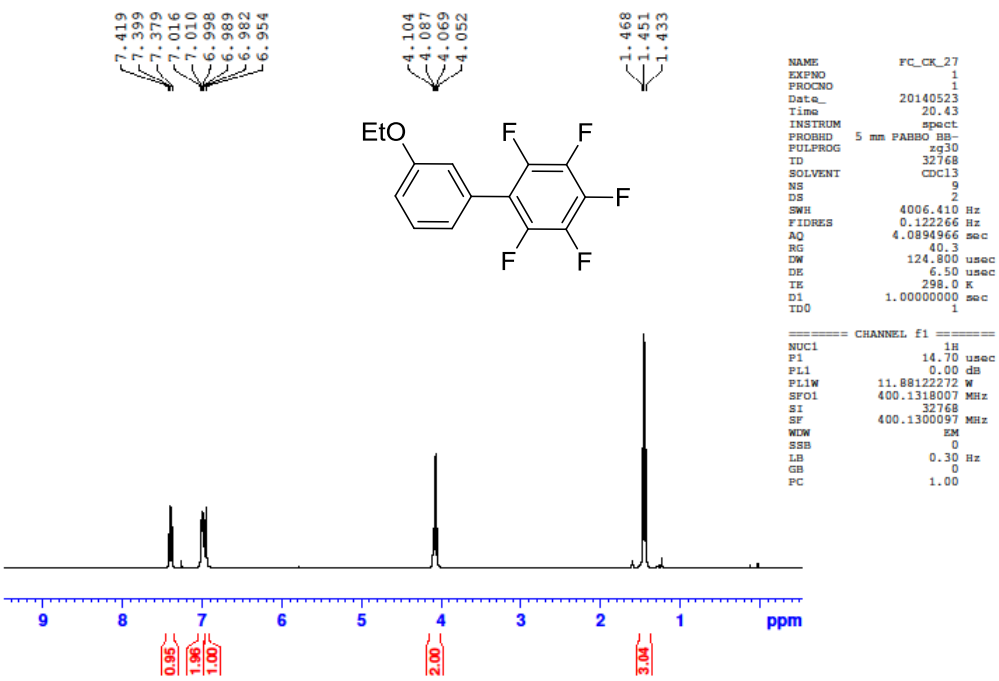
======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                1H
PCPD2            80.00 usec
PL2               0.00 dB
PL12             15.00 dB
PL13             15.00 dB
PL2W        11.88122272 W
PL12W        0.37571725 W
PL13W        0.37571725 W
SFO2        400.1316005 MHz
SI                32768
SF          100.6127707 MHz
WDW                EM
SSB                 0
LB               1.00 Hz
GB                  0
PC               1.40
```

2,3,4,5,6-Pentafluoro-3'-methoxy-1,1'-biphenyl (Table 5.3, compound 5fu)



3'-Ethoxy-2,3,4,5,6-pentafluoro-1,1'-biphenyl (Table 5.3, compound 5gu)

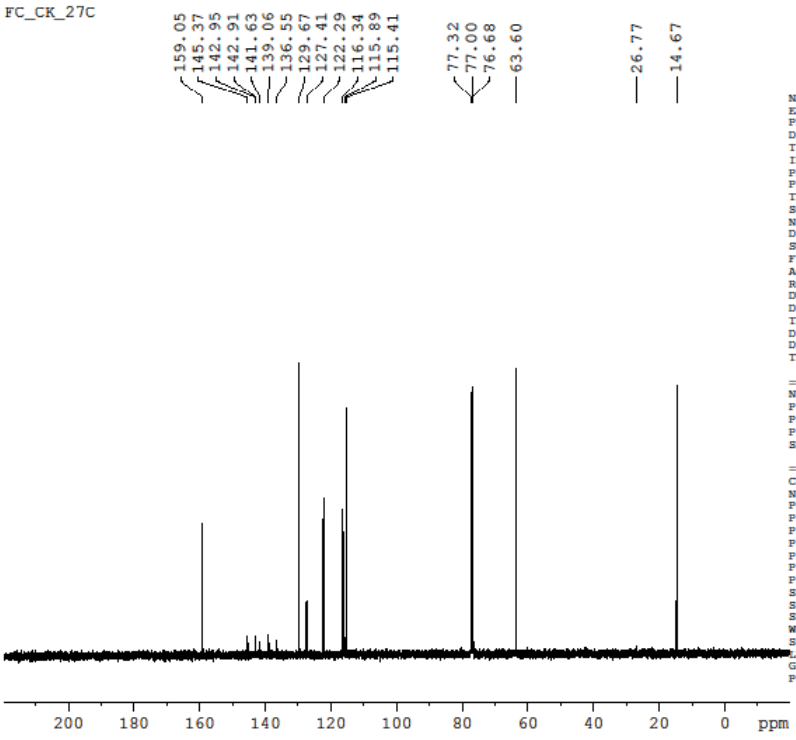
FC_CK_27H




```
NAME                FC_CK_27
EXPNO                      1
PROCNO                     1
Date_               20140523
Time                   20.43
INSTRUM                spect
PROBHD   5 mm PABBO BB-
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                         9
DS                         2
SWH                4006.410 Hz
FIDRES             0.122266 Hz
AQ                 4.0894966 sec
RG                      40.3
DW                   124.800 usec
DE                     6.50 usec
TE                   298.0 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     14.70 usec
PL1                     0.00 dB
PL1W              11.88122272 W
SFO1              400.1318007 MHz
SI                        32768
SF                400.1300097 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00
```

FC_CK_27C

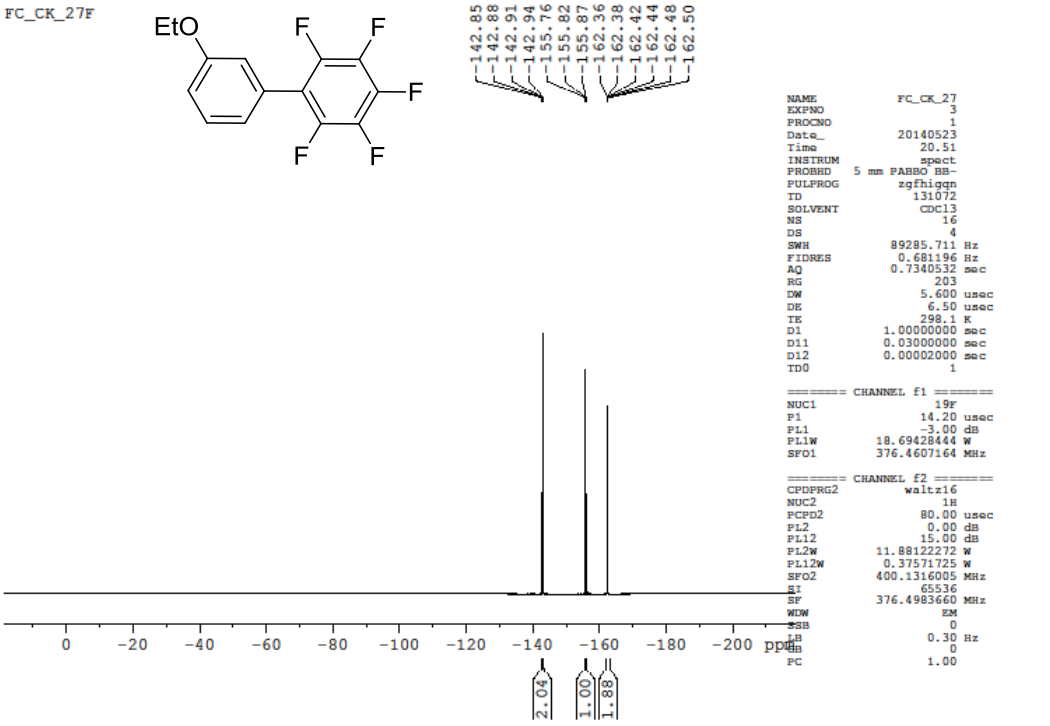


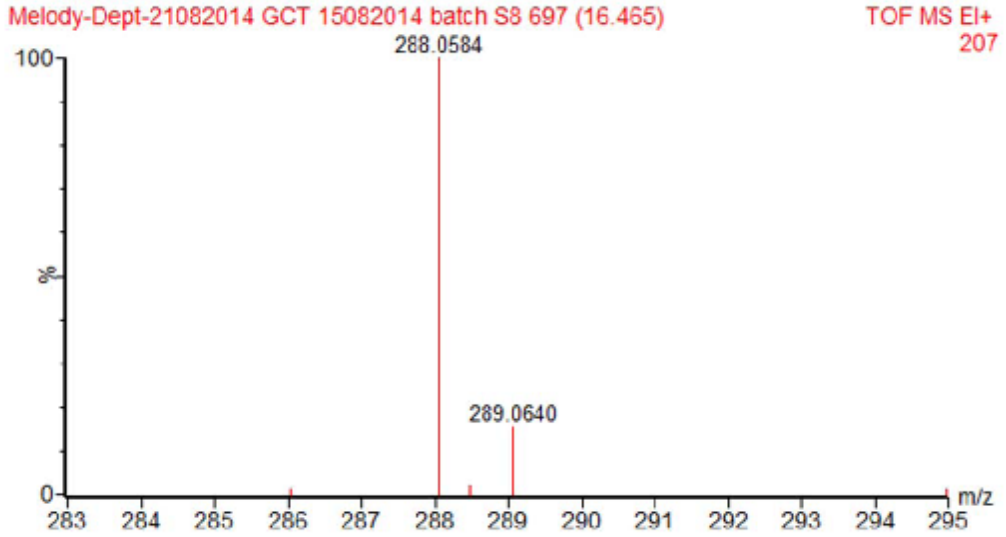

```
NAME                FC_CK_27
EXPNO                      2
PROCNO                     1
Date_               20140523
Time                   20.47
INSTRUM                spect
PROBHD   5 mm PABBO BB-
PULPROG             zgpg30
TD                    65536
SOLVENT               CDCl3
NS                        46
DS                         2
SWH               24038.461 Hz
FIDRES             0.366798 Hz
AQ                 1.3631988 sec
RG                       203
DW                   20.800 usec
DE                     6.50 usec
TE                   298.8 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      13C
P1                      9.50 usec
PL1                    -2.00 dB
PL1W              58.52175522 W
SFO1              100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                      1H
PCPD2                  80.00 usec
PL2                     0.00 dB
PL12                   15.00 dB
PL13                   15.00 dB
PL2W              11.88122272 W
PL12W              0.37571725 W
PL13W              0.37571725 W
SFO2              400.1316005 MHz
SI                        32768
SF                100.6127705 MHz
WDW                       EM
SSB                        0
LB                      1.00 Hz
GB                         0
PC                      1.40
```

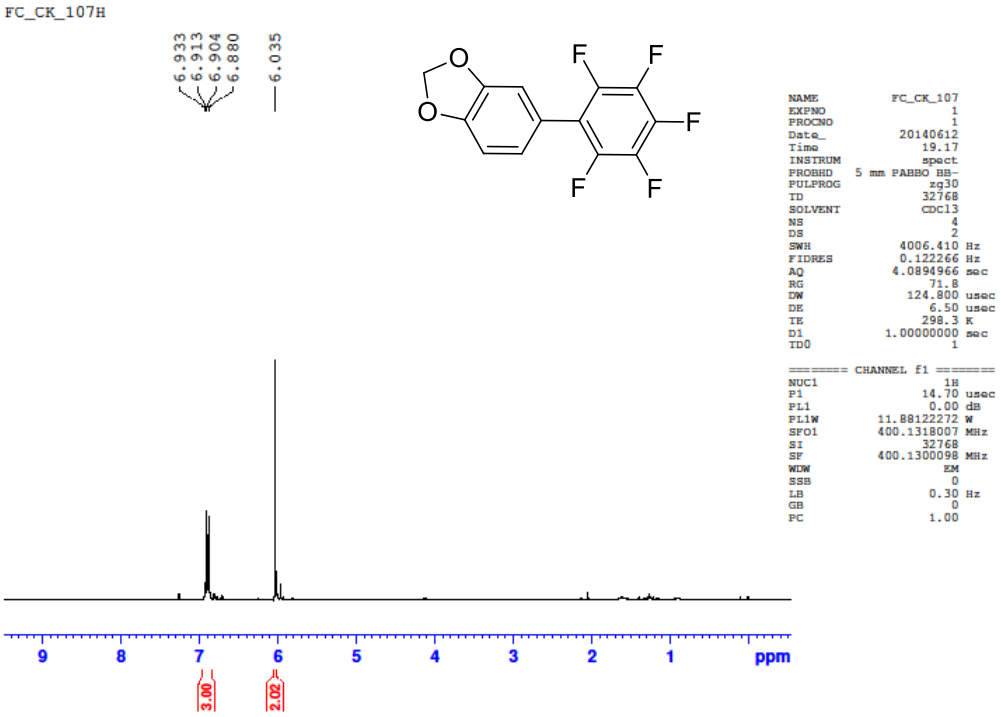
3'-Ethoxy-2,3,4,5,6-pentafluoro-1,1'-biphenyl (Table 5.3, compound 5gu)

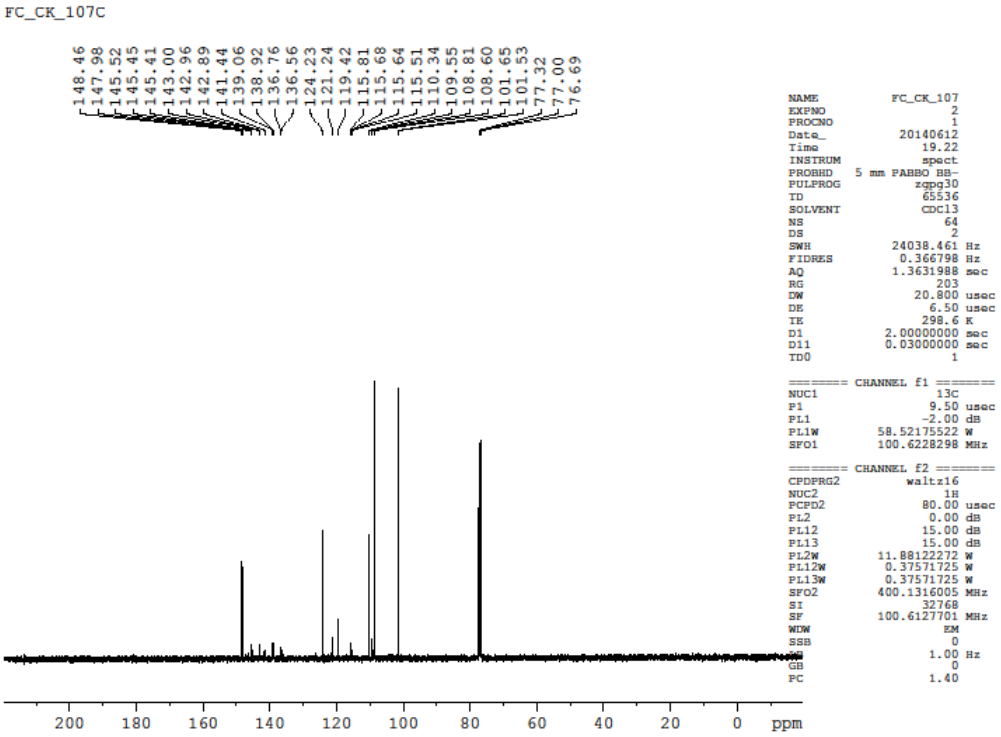




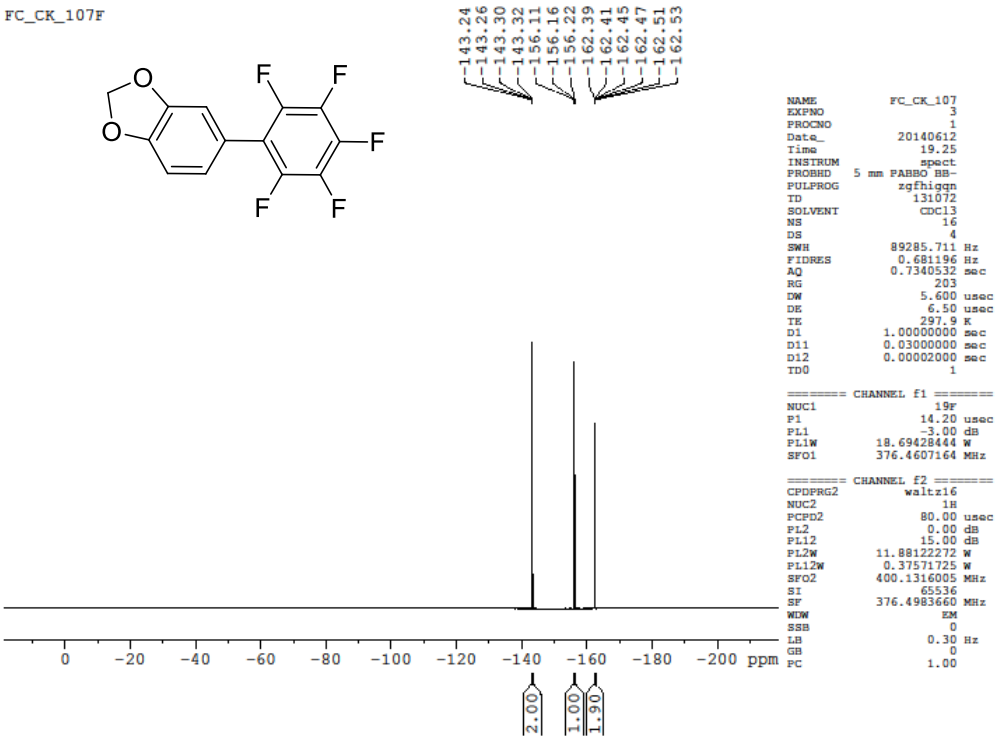
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
288.0584	288.0574	1.0	3.5	8.0	2773014.0	C14 H9 O F5

5-(Perfluorophenyl)benzo[d][1,3]dioxole (Table 5.3, compound 5hu)

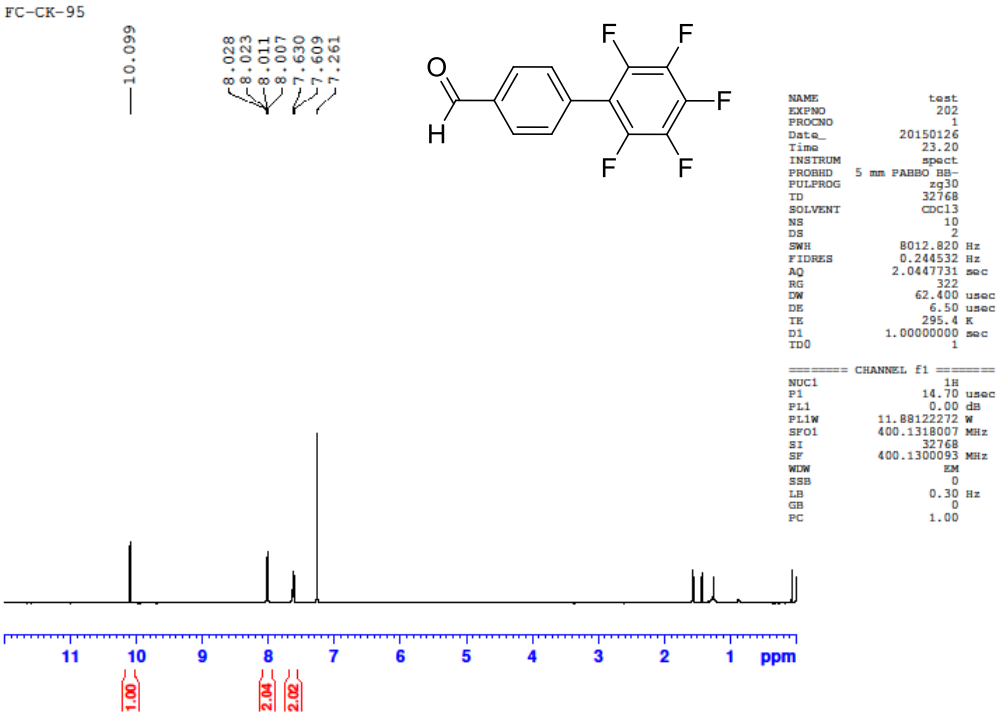


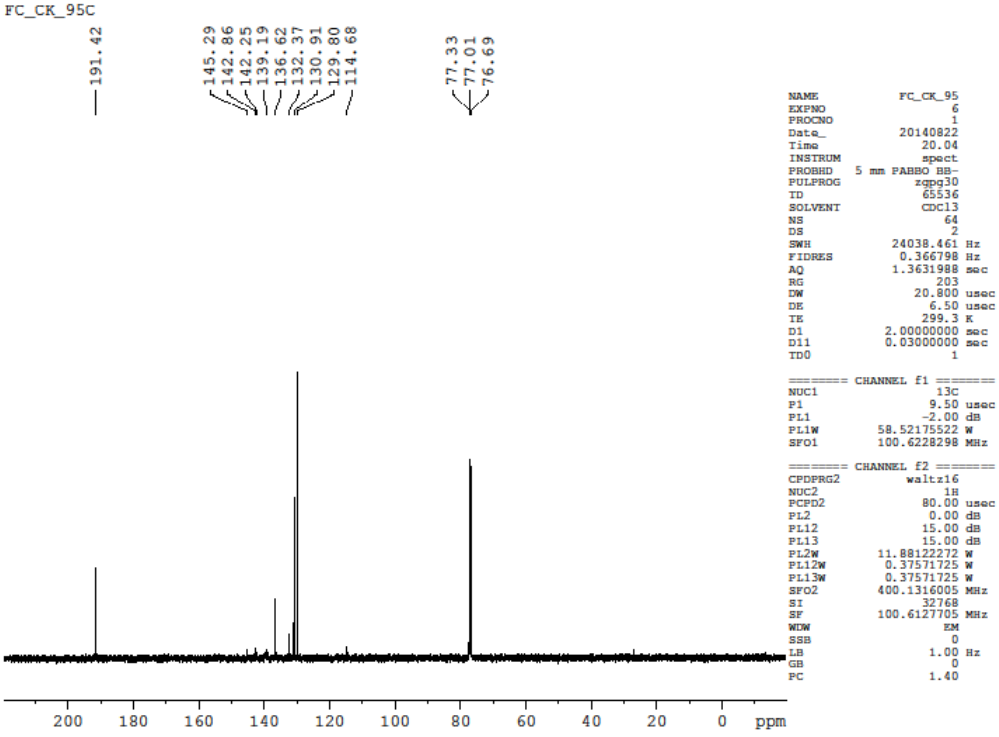


5-(Perfluorophenyl)benzo[d][1,3]dioxole (Table 5.3, compound 5hu)

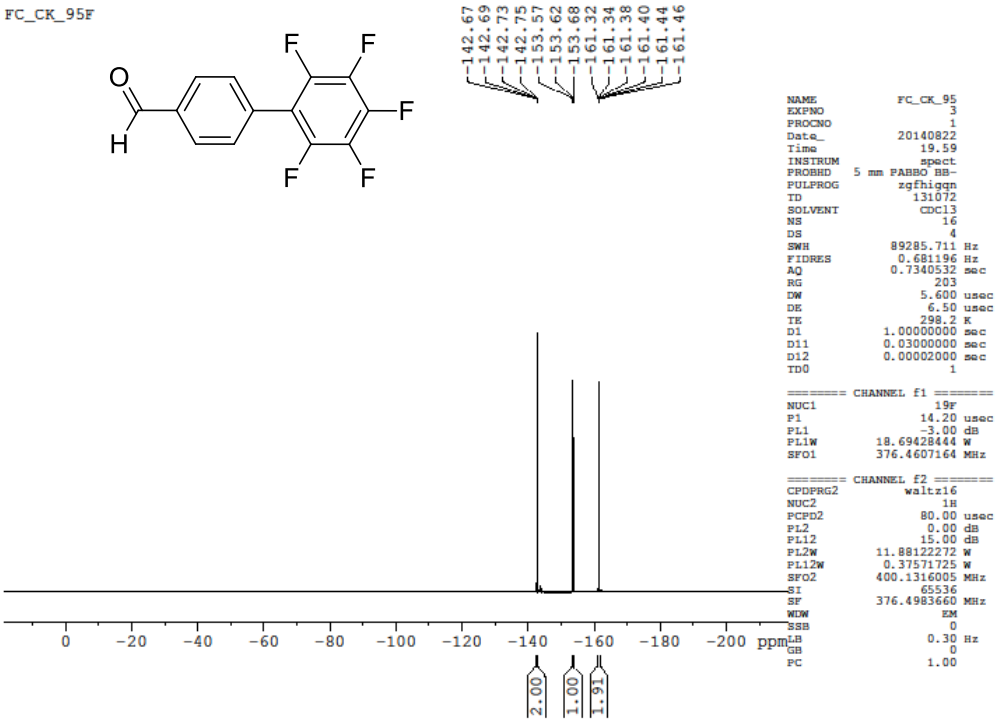


2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-4-carbaldehyde (Table 5.3, compound 5iu)

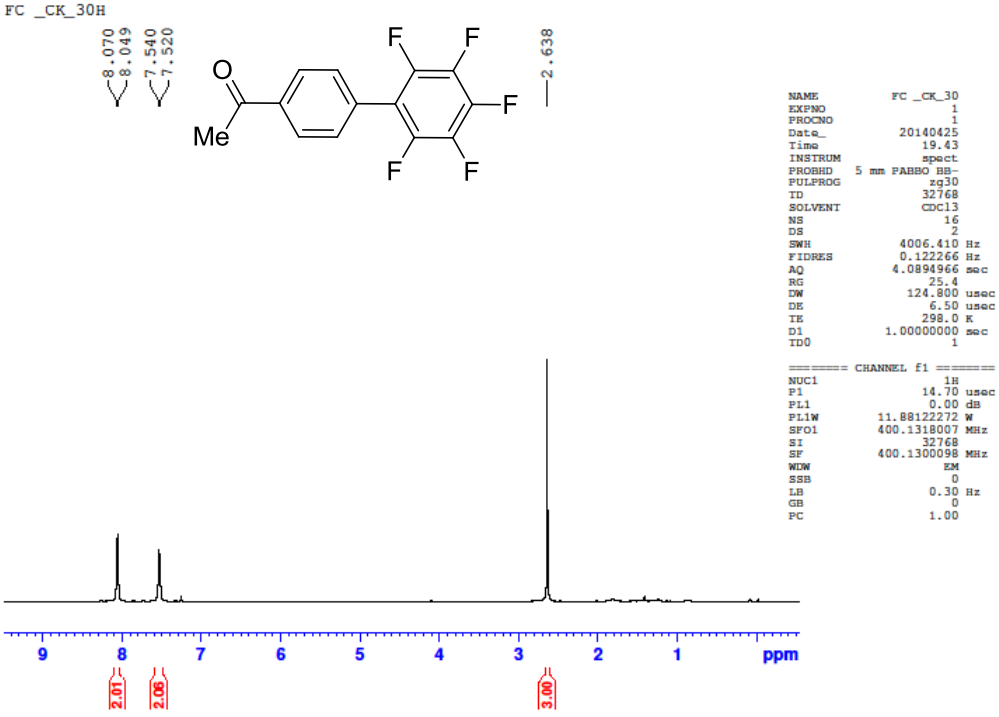


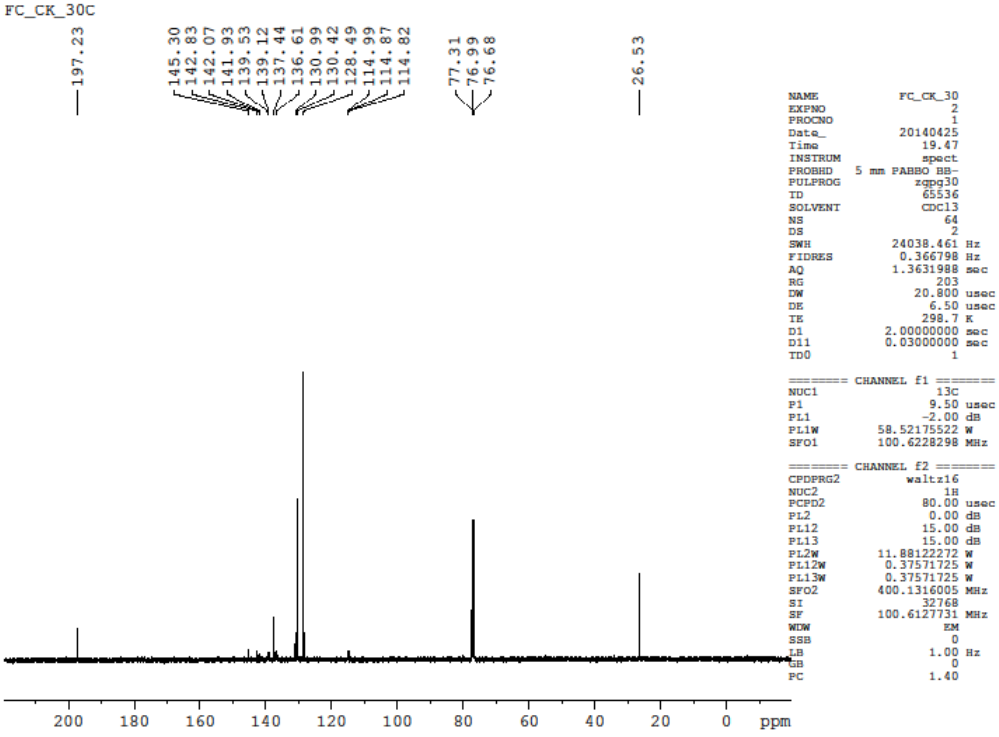


2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-4-carbaldehyde (Table 5.3, compound 5iu)

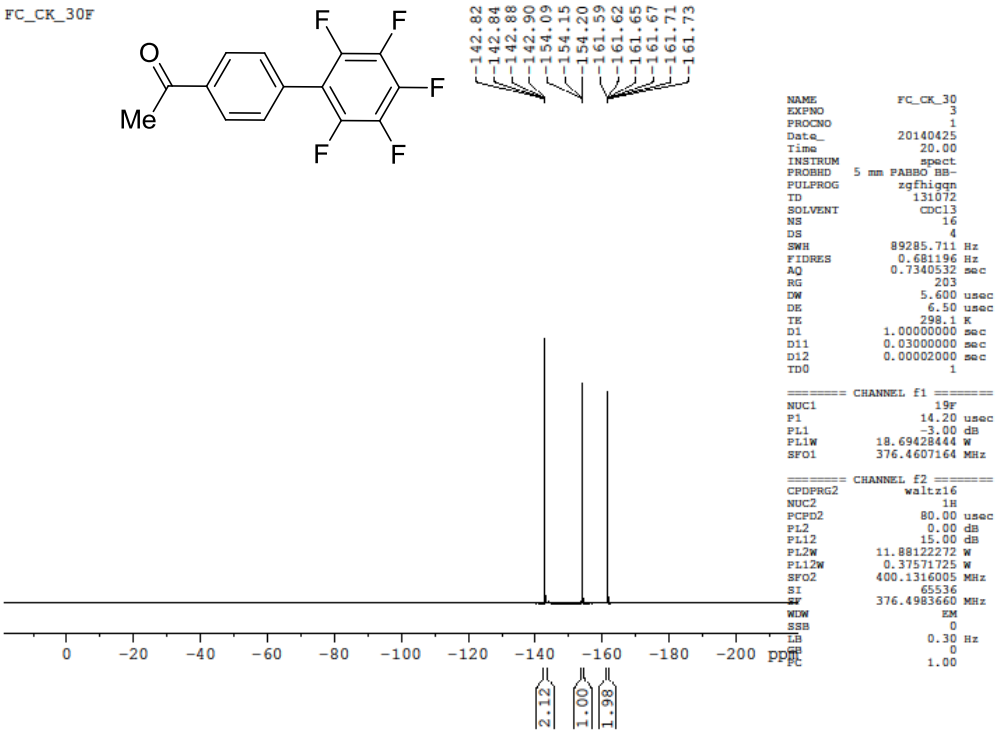


1-(2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-4-yl)ethanone (Table 5.3, compound 5ju)



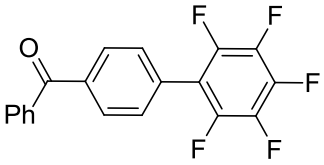


1-(2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-4-yl)ethanone (Table 5.3, compound 5ju)



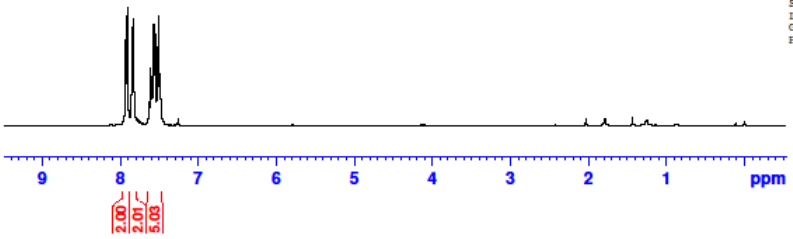
(2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-4-yl)(phenyl)methanone (Table 5.3, compound 5ku)

FC_CK_35H

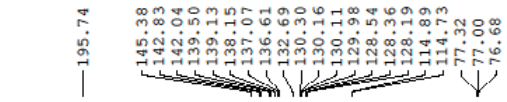



```
NAME            FC_CK_35
EXPNO                  1
PROCNO                 1
Date_           20140417
Time                17.36
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             4006.410 Hz
FIDRES             0.122266 Hz
AQ                4.0894966 sec
RG                     45.2
DW                124.800 usec
DE                  6.50 usec
TE                297.9 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 =======
NUC1                   1H
P1                 14.70 usec
PL1                 0.00 dB
PL1W           11.88122272 W
SFO1           400.1318007 MHz
SI                 32768
SF             400.1300095 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```



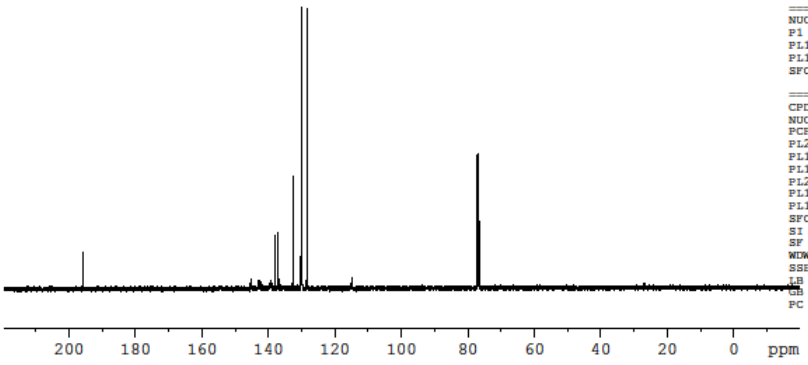
FC_CK_35C



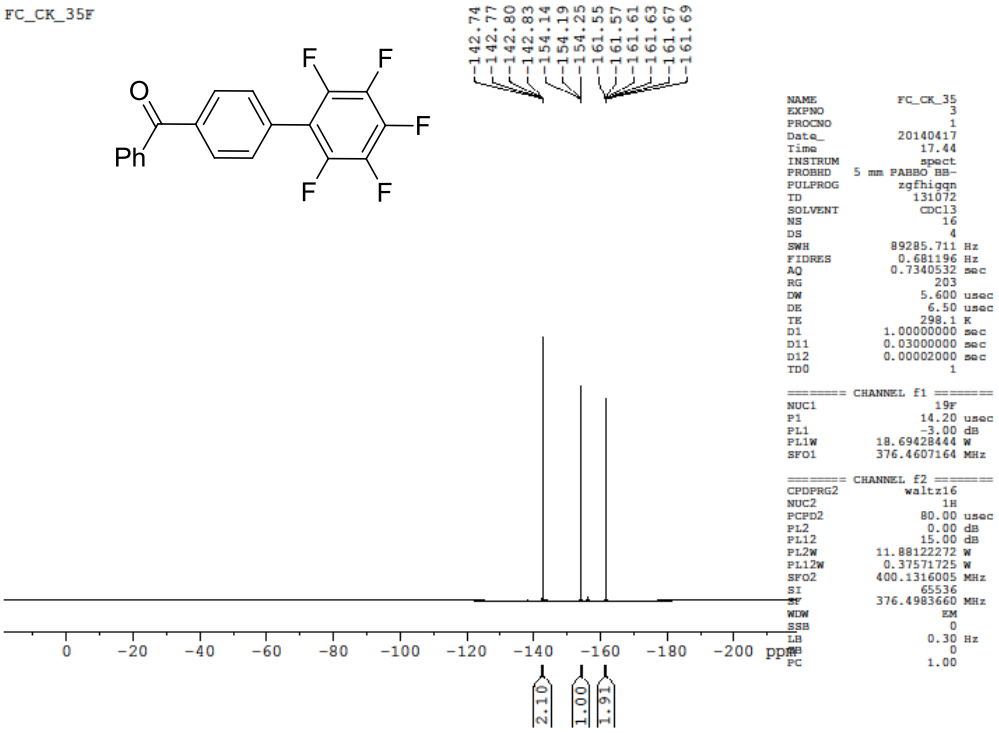

```
NAME            FC_CK_35
EXPNO                  2
PROCNO                 1
Date_           20140417
Time                17.42
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                    64
DS                     2
SWH            24038.461 Hz
FIDRES             0.366798 Hz
AQ                1.3631988 sec
RG                   203
DW                20.800 usec
DE                  6.50 usec
TE                298.9 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                    1

======== CHANNEL f1 =======
NUC1                   13C
P1                  9.50 usec
PL1                -2.00 dB
PL1W           58.52175522 W
SFO1           100.6228298 MHz

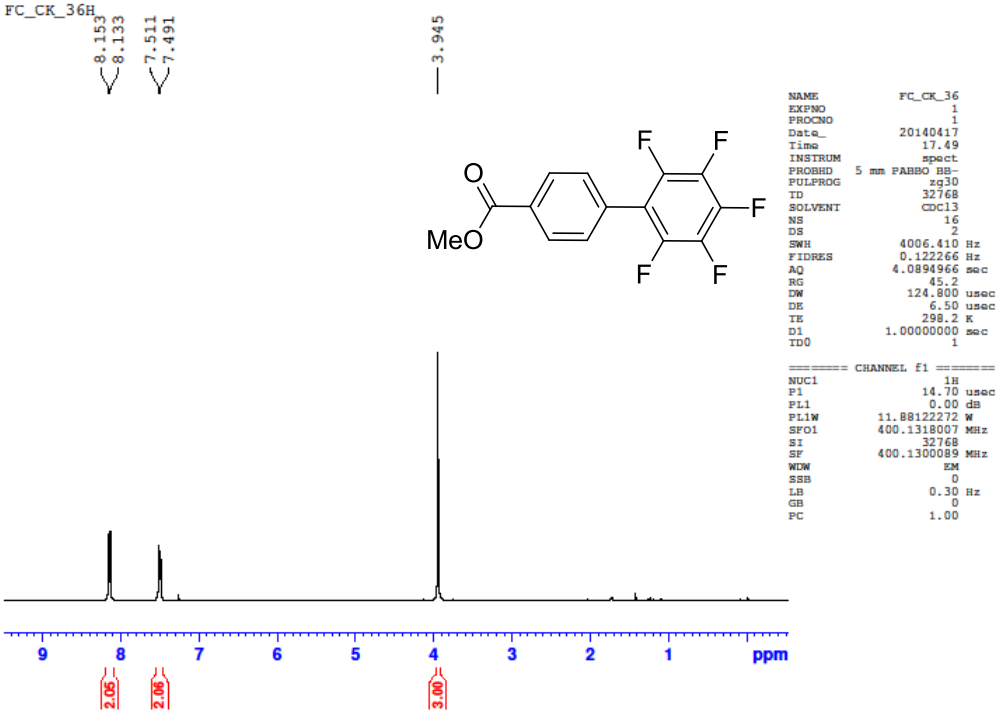
======== CHANNEL f2 =======
CPDPRG2            waltz16
NUC2                   1H
PCPD2              80.00 usec
PL2                 0.00 dB
PL12               15.00 dB
PL13               15.00 dB
PL2W           11.88122272 W
PL12W           0.37571725 W
PL13W           0.37571725 W
SFO2           400.1316005 MHz
SI                 32768
SF             100.6127756 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
```

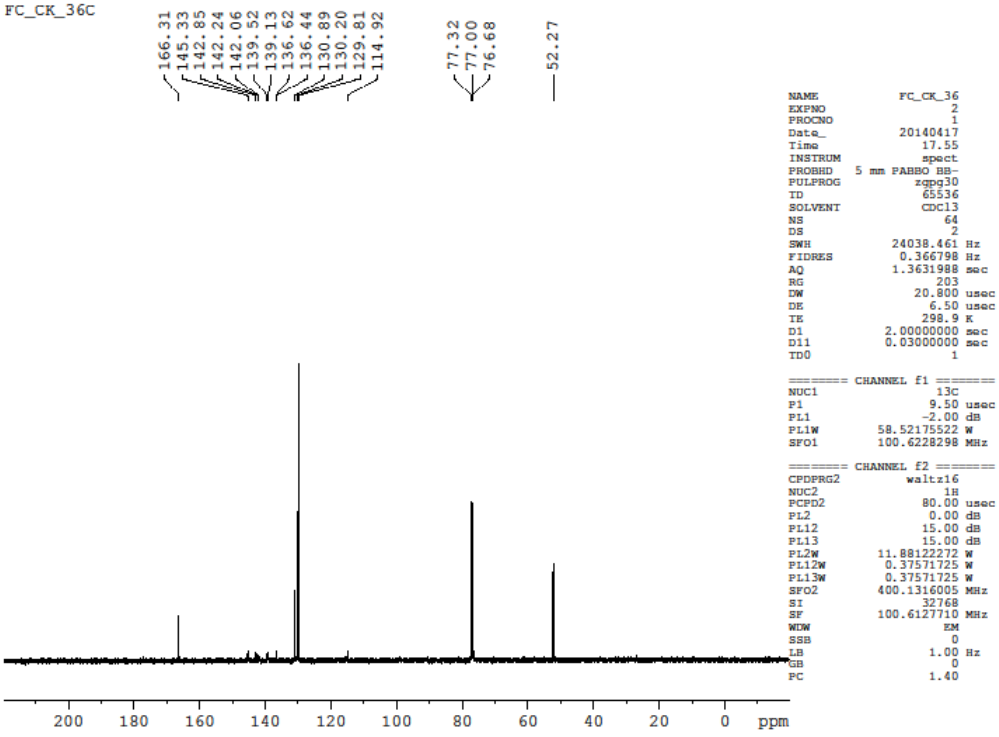


(2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-4-yl)(phenyl)methanone (Table 5.3, compound 5ku)

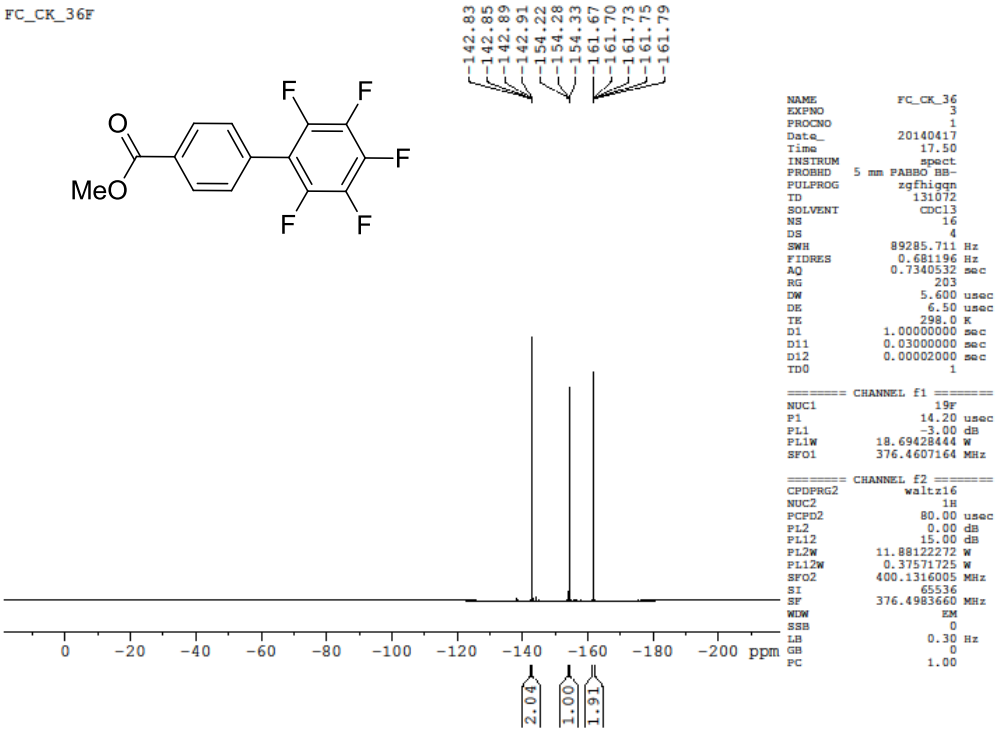


Methyl 2',3',4',5',6'-pentafluoro-[1,1'-biphenyl]-4-carboxylate (Table 5.3, compound 5lu)

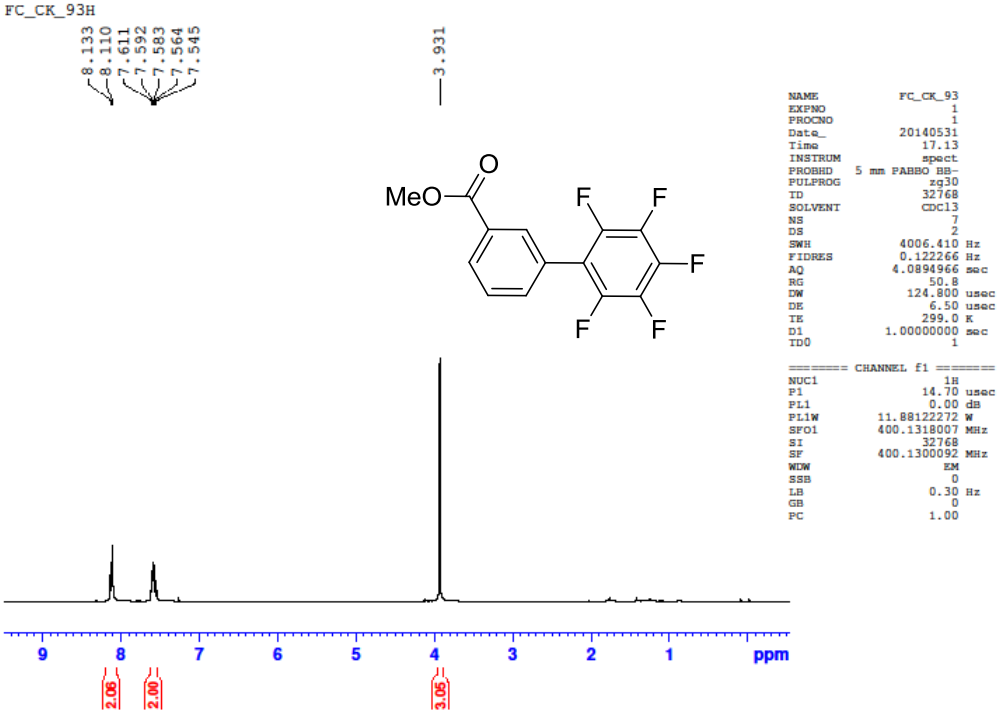


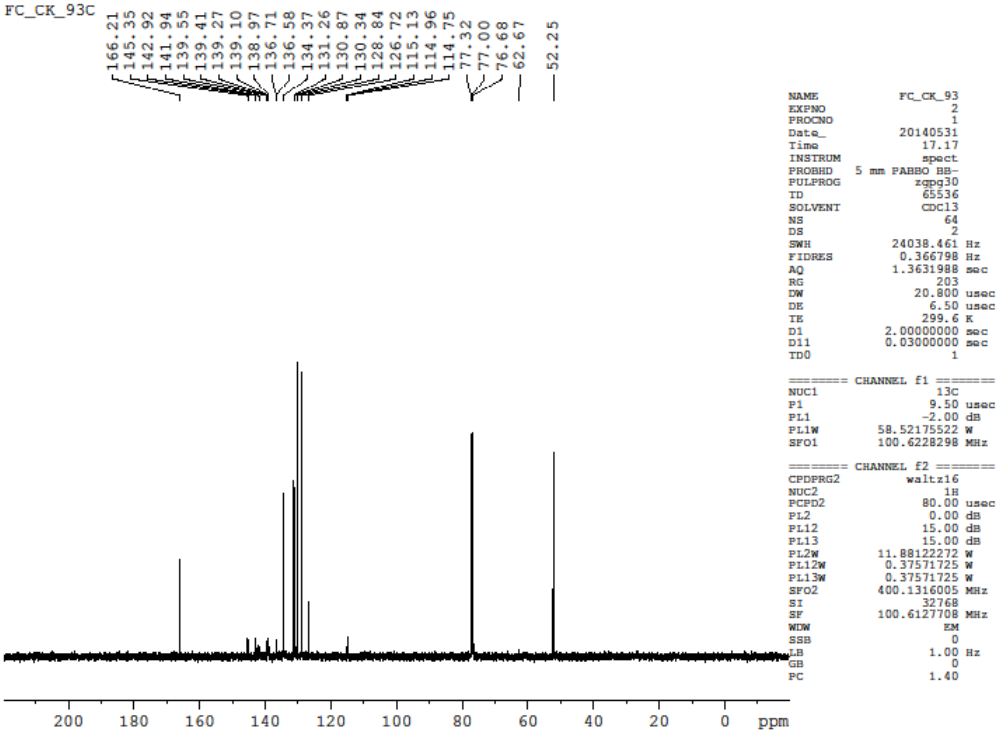


Methyl 2',3',4',5',6'-pentafluoro-[1,1'-biphenyl]-4-carboxylate (Table 5.3, compound 5lu)

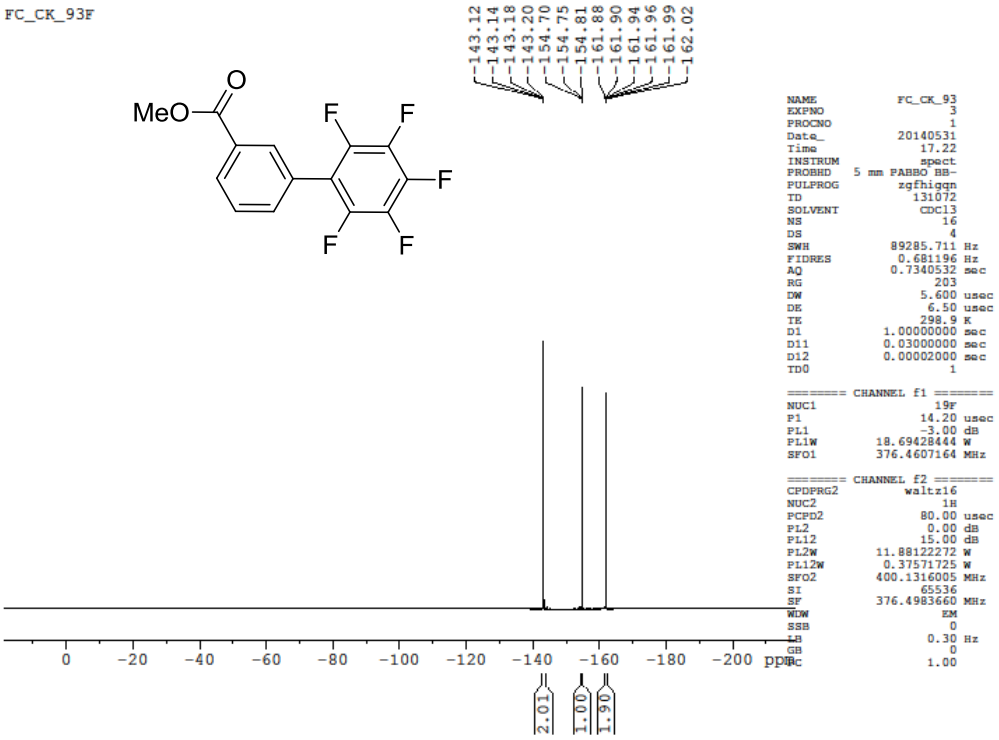


Methyl 2',3',4',5',6'-pentafluoro-[1,1'-biphenyl]-3-carboxylate (Table 5.3, compound 5mu)

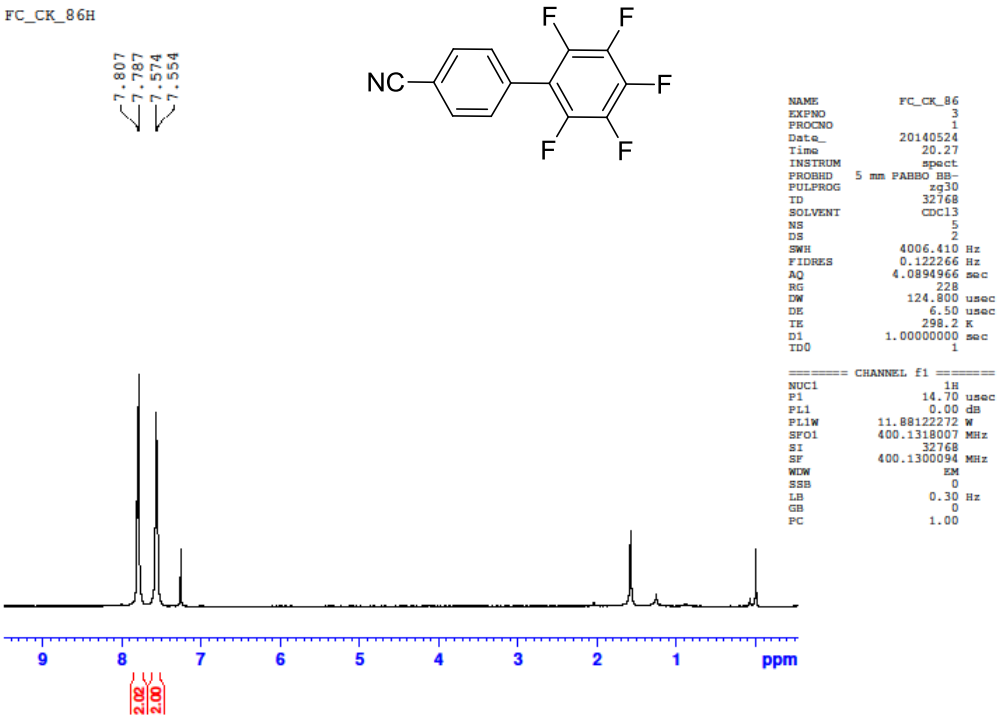


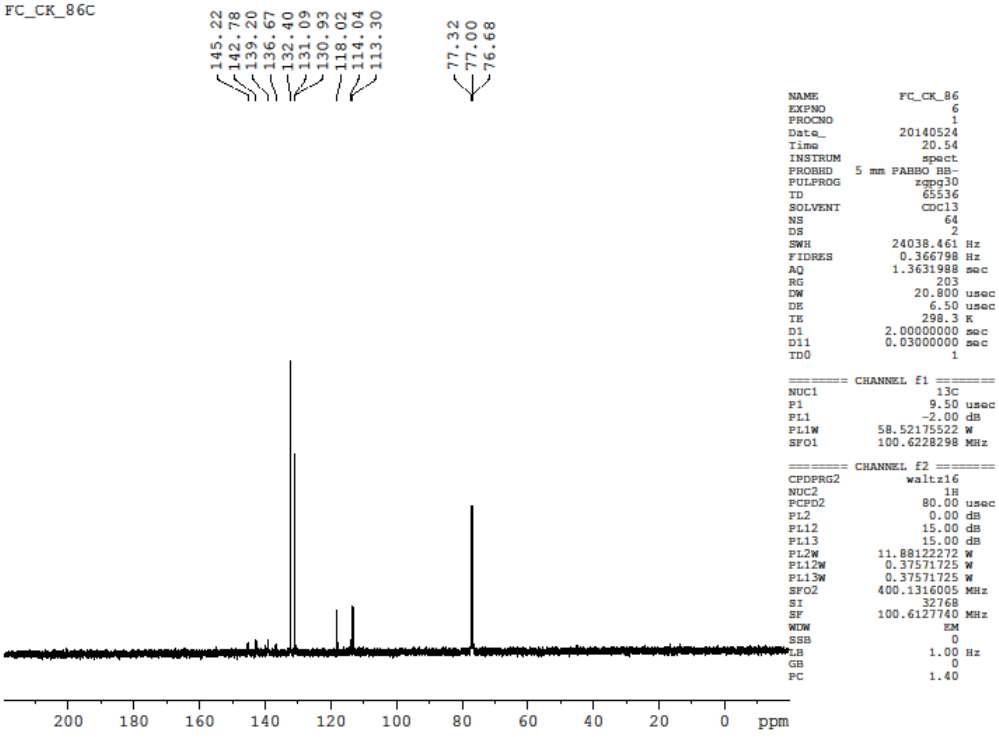


Methyl 2',3',4',5',6'-pentafluoro-[1,1'-biphenyl]-3-carboxylate (Table 5.3, compound 5mu)

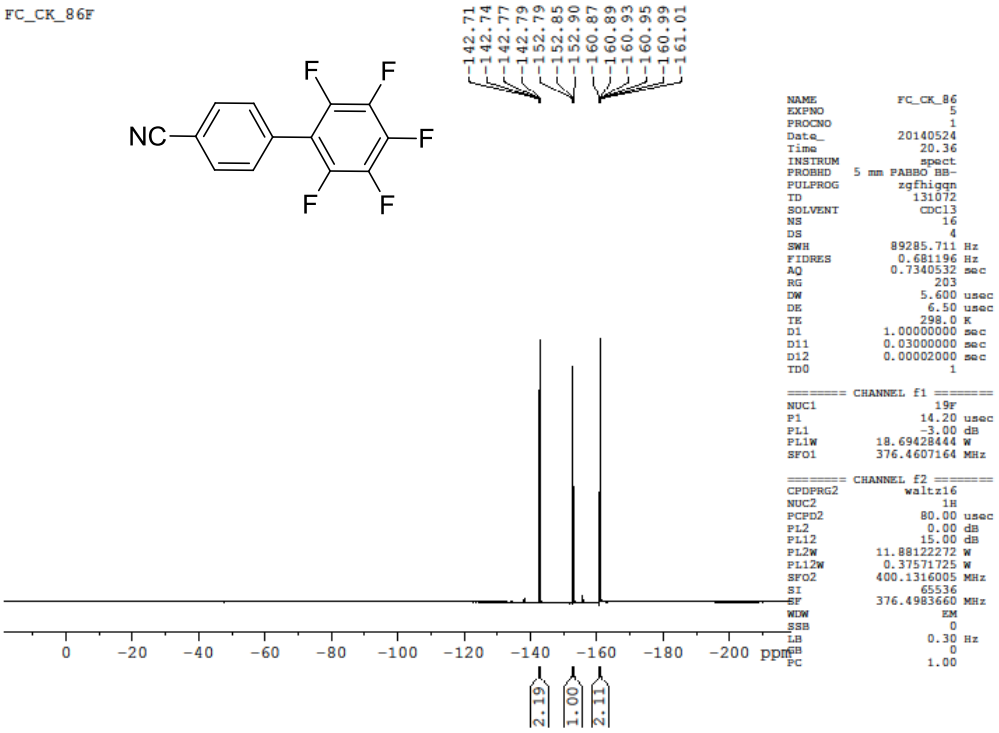


2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-4-carbonitrile (Table 5.3, compound 5ou)

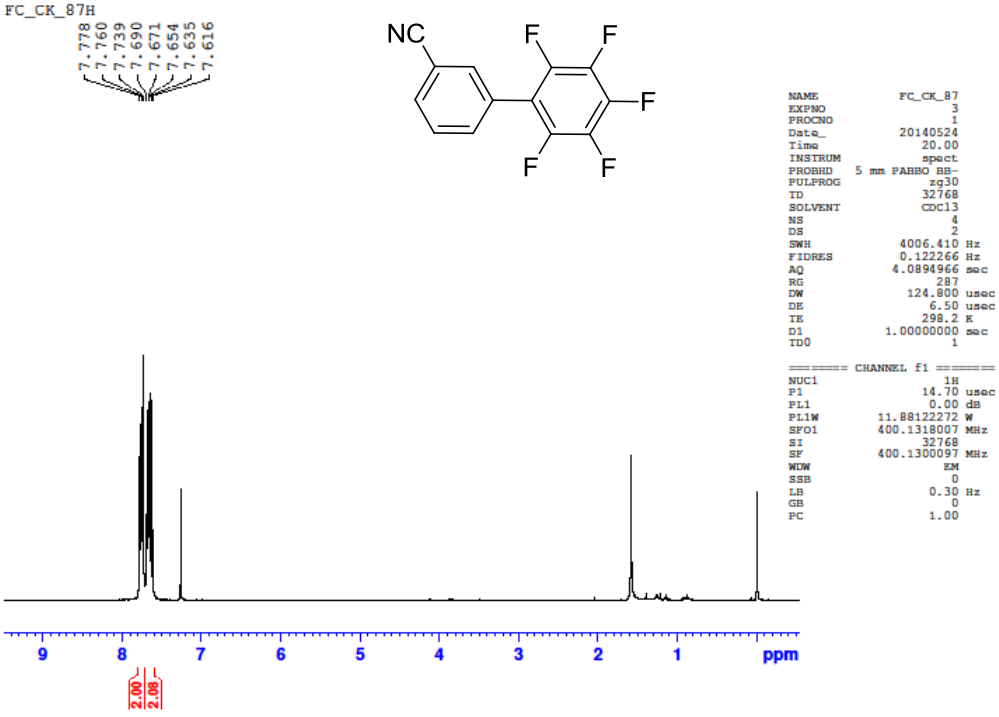


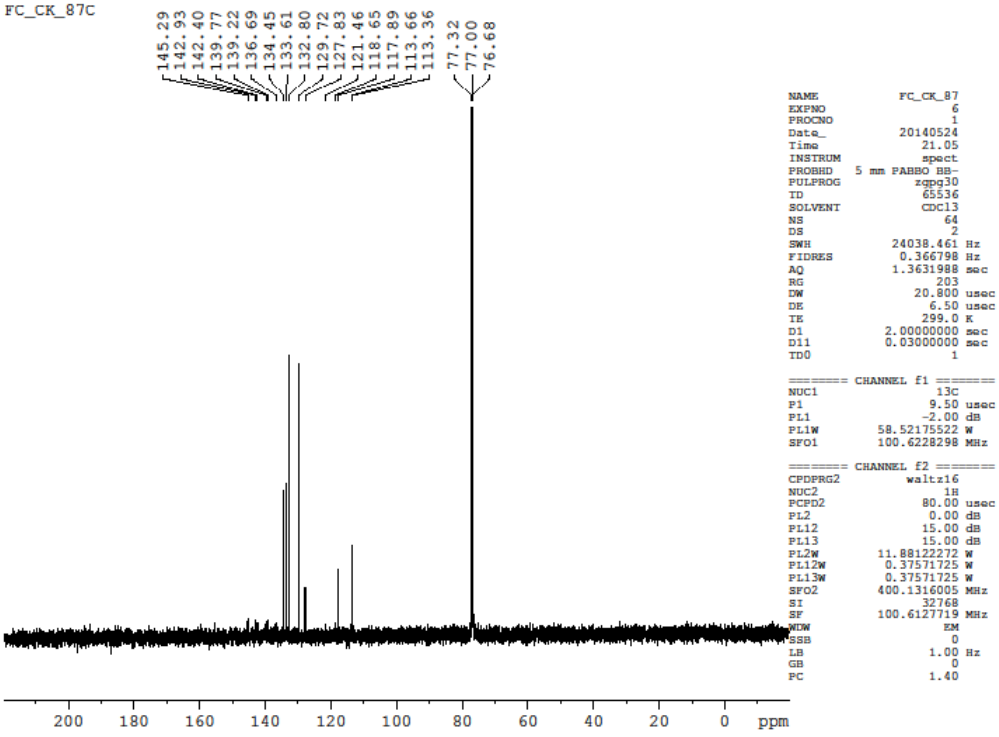


2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-4-carbonitrile (Table 5.3, compound 5ou)

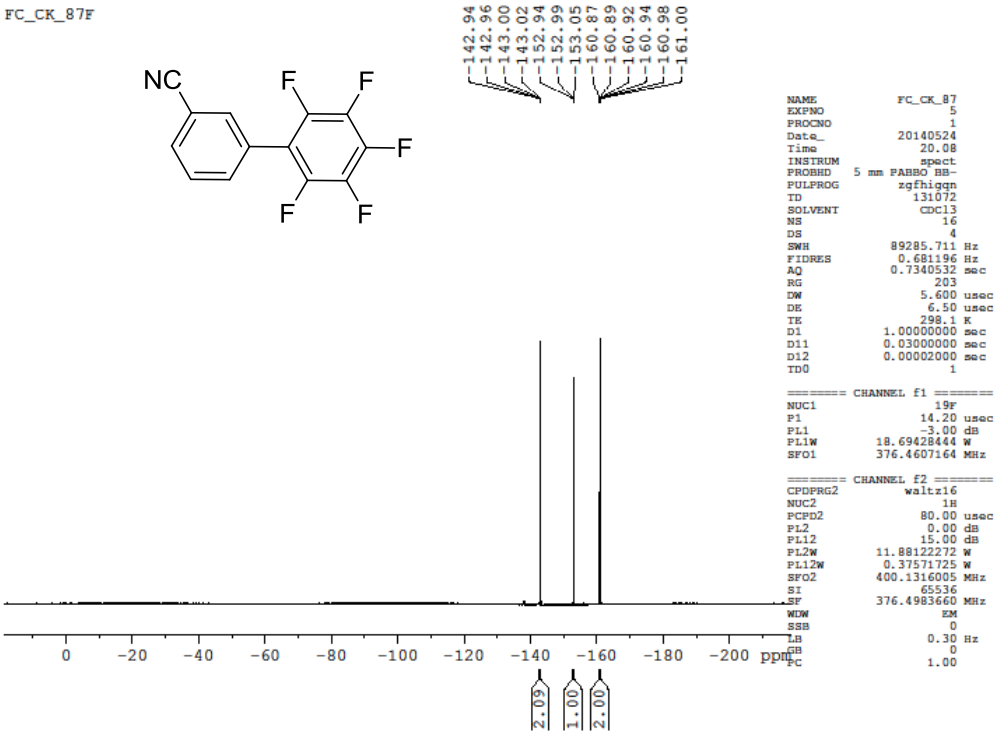


2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-3-carbonitrile (Table 5.3, compound 5ou)

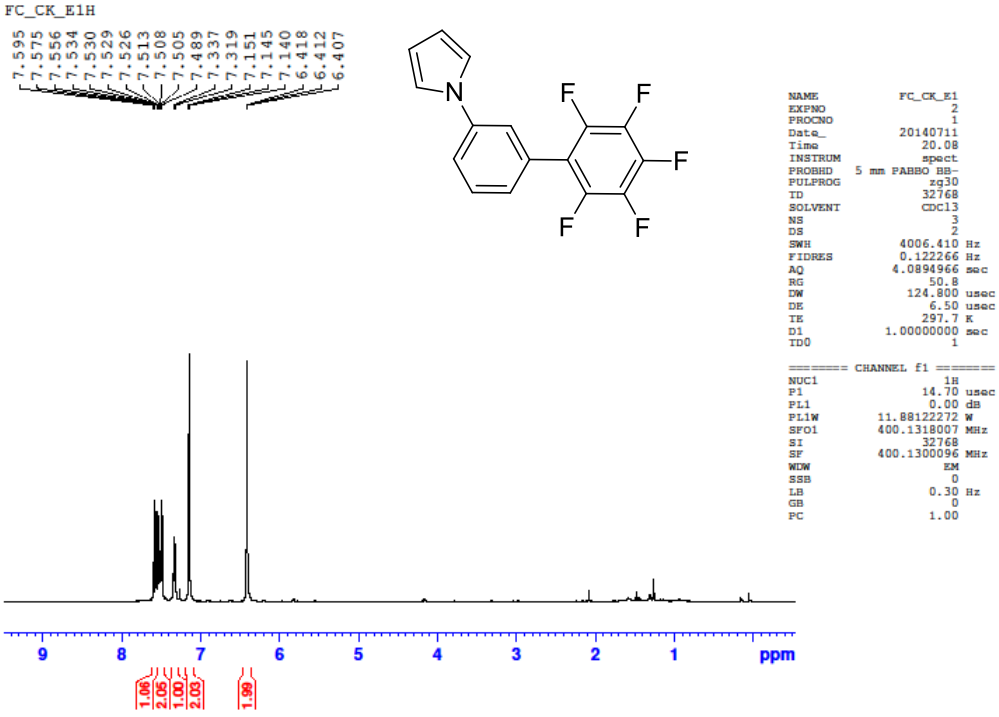


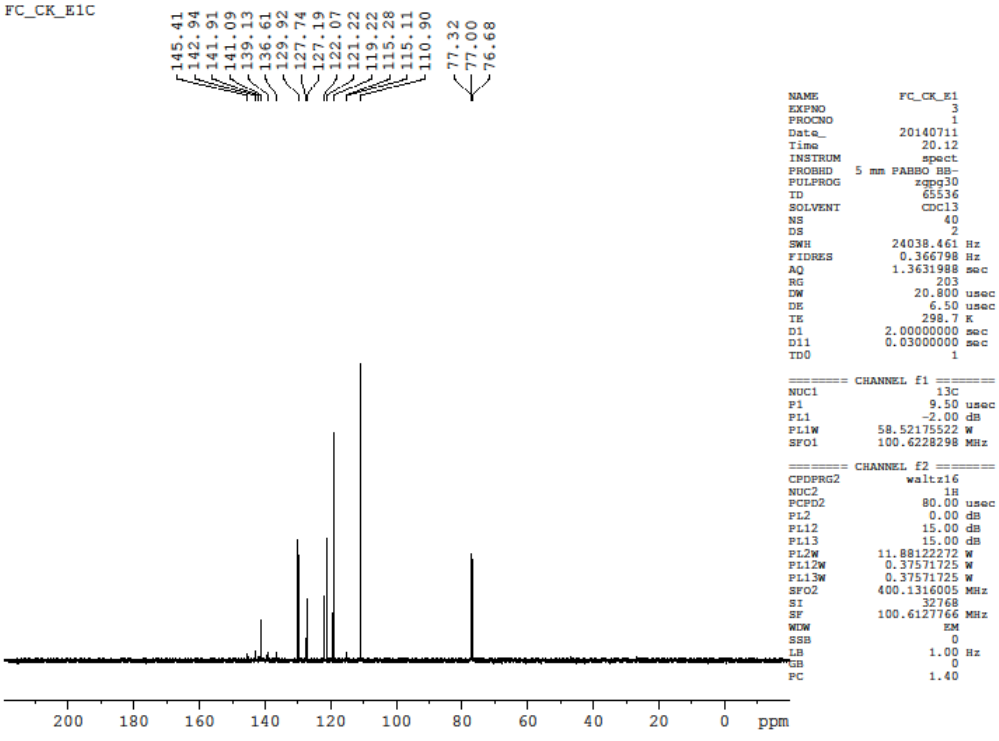


2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-3-carbonitrile (Table 5.3, compound 5ou)

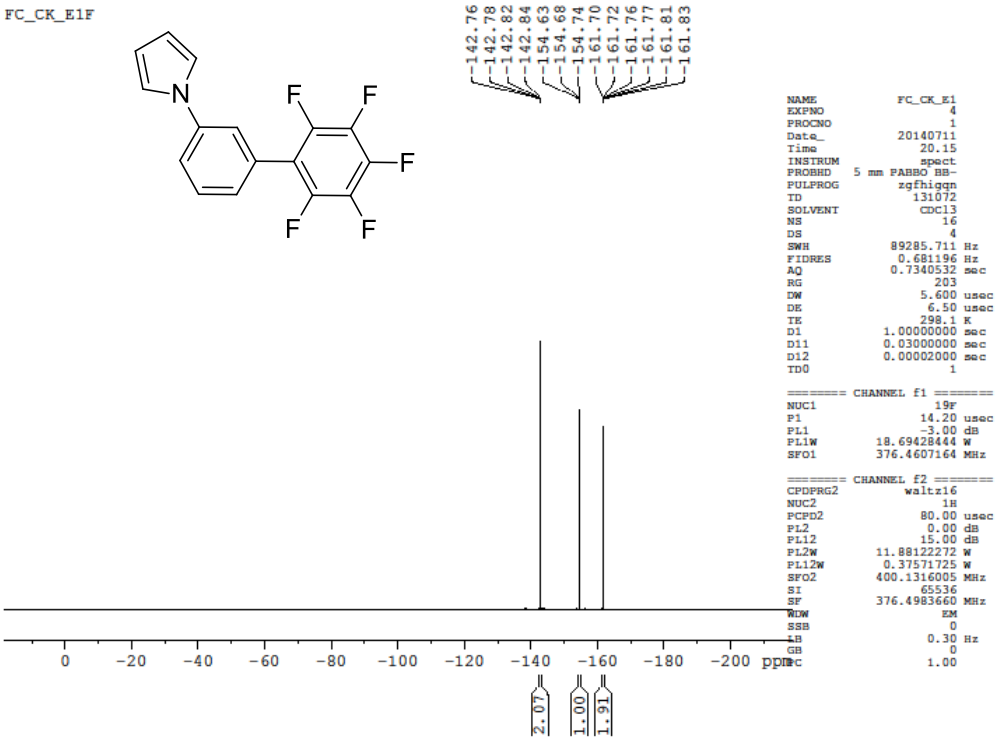


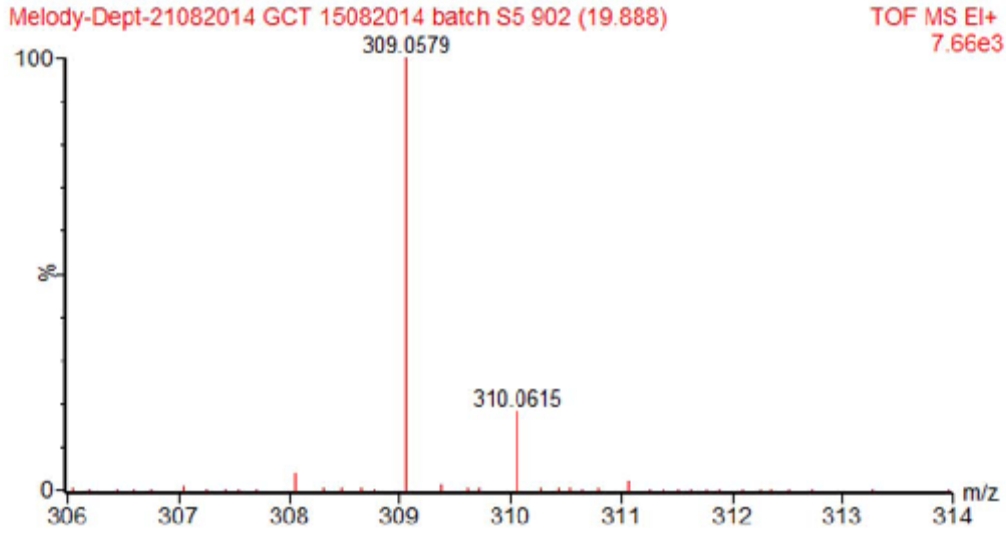
1-(2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-3-yl)-1H-pyrrole (Table 5.3, compound 5pu)





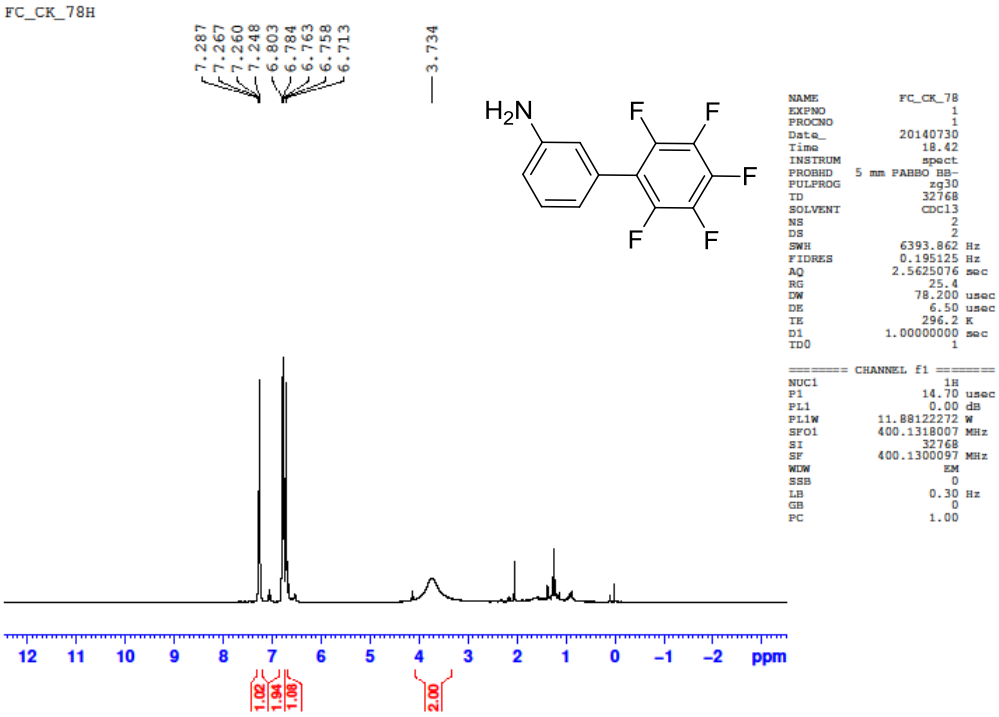
1-(2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-3-yl)-1H-pyrrole (Table 5.3, compound 5pu)

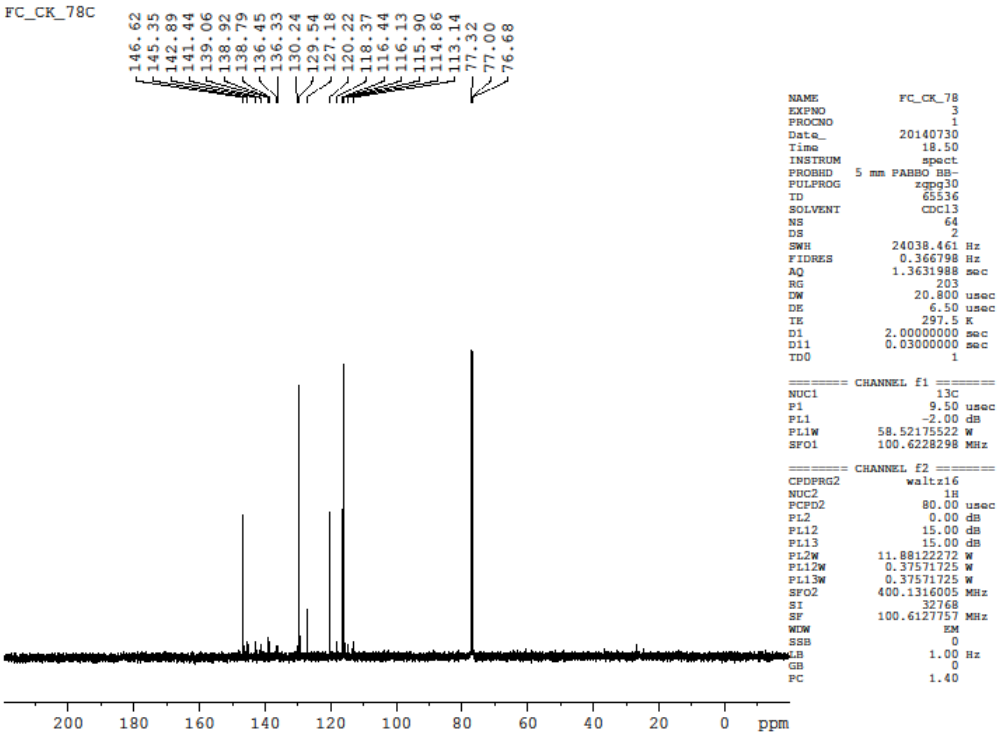




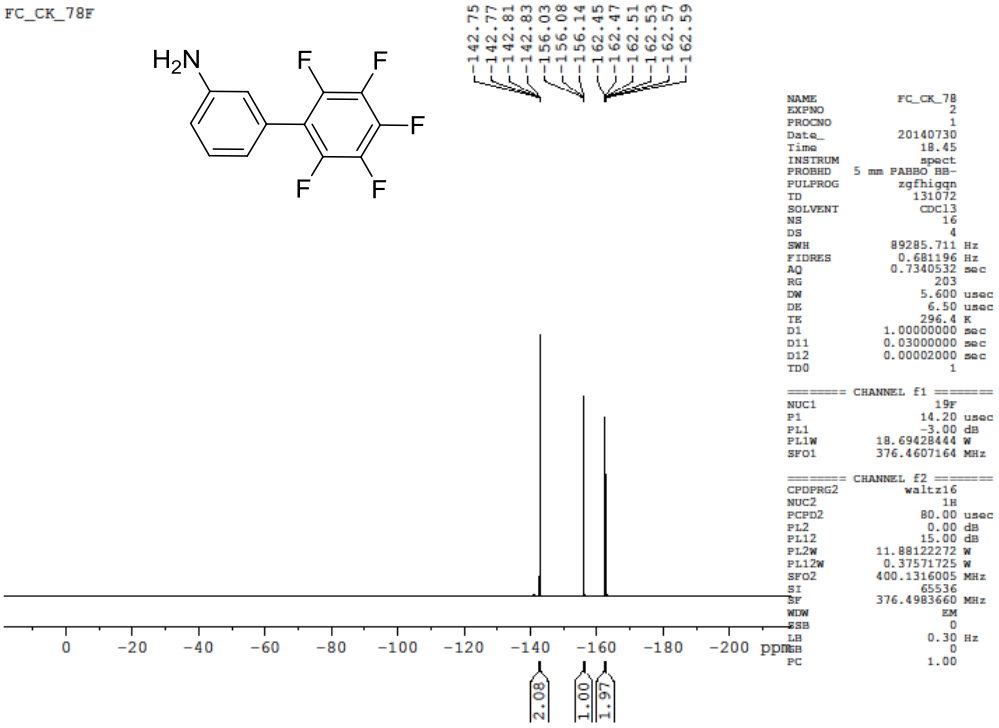
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
309.0579	309.0577	0.2	0.6	11.0	2.3	C16 H8 N F5

2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-3-amine (Table 5.3, compound 5qu)

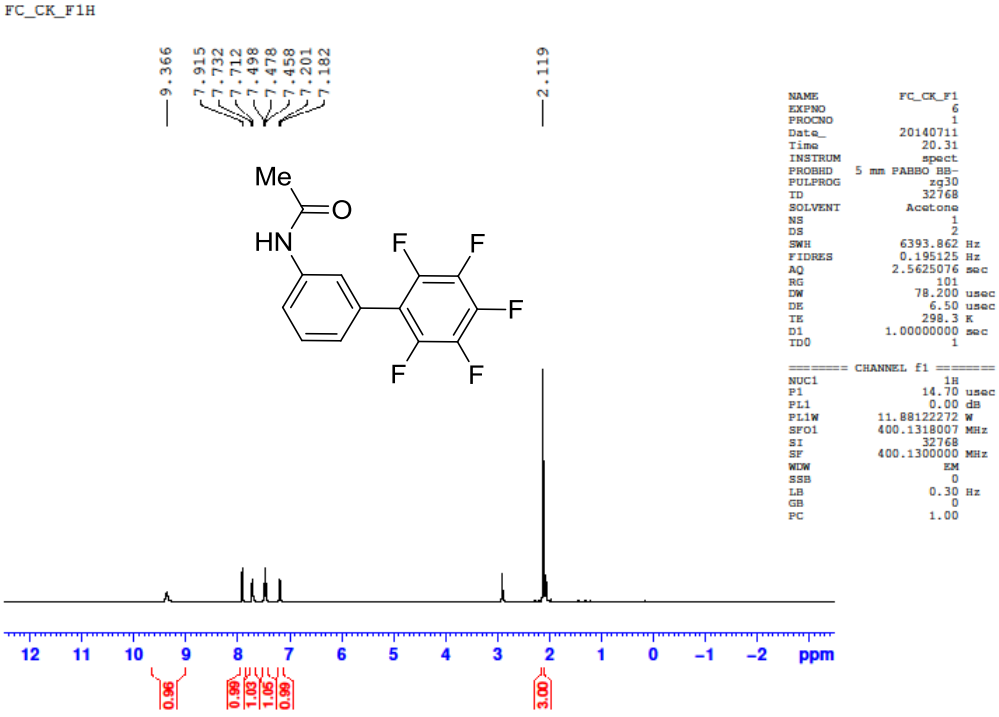


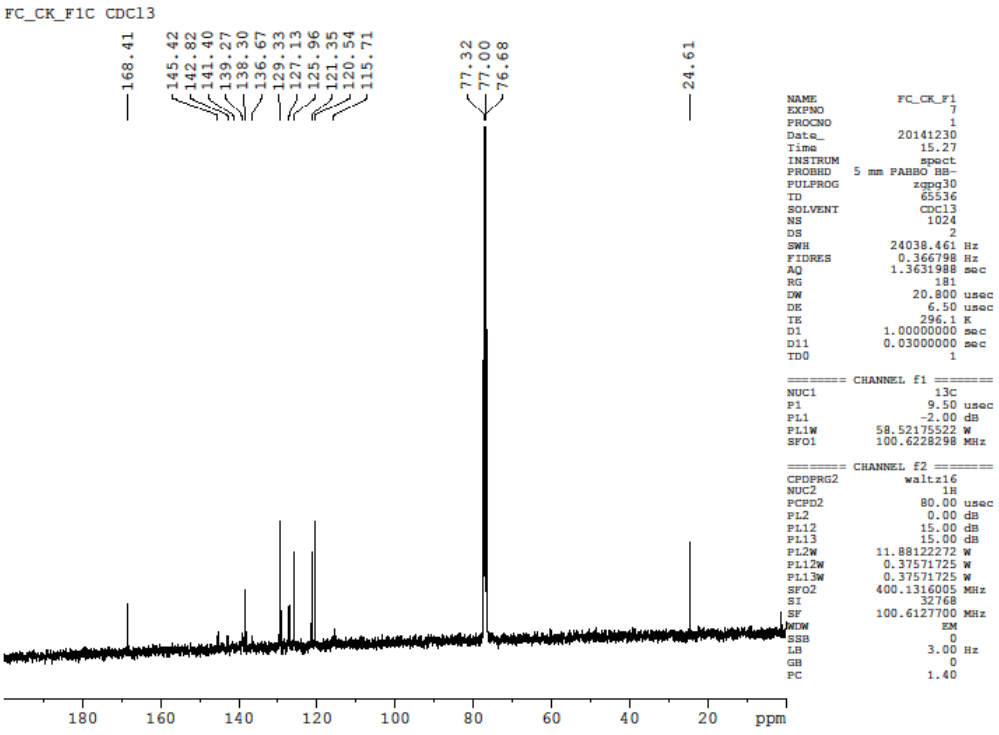


2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-3-amine (Table 5.3, compound 5qu)

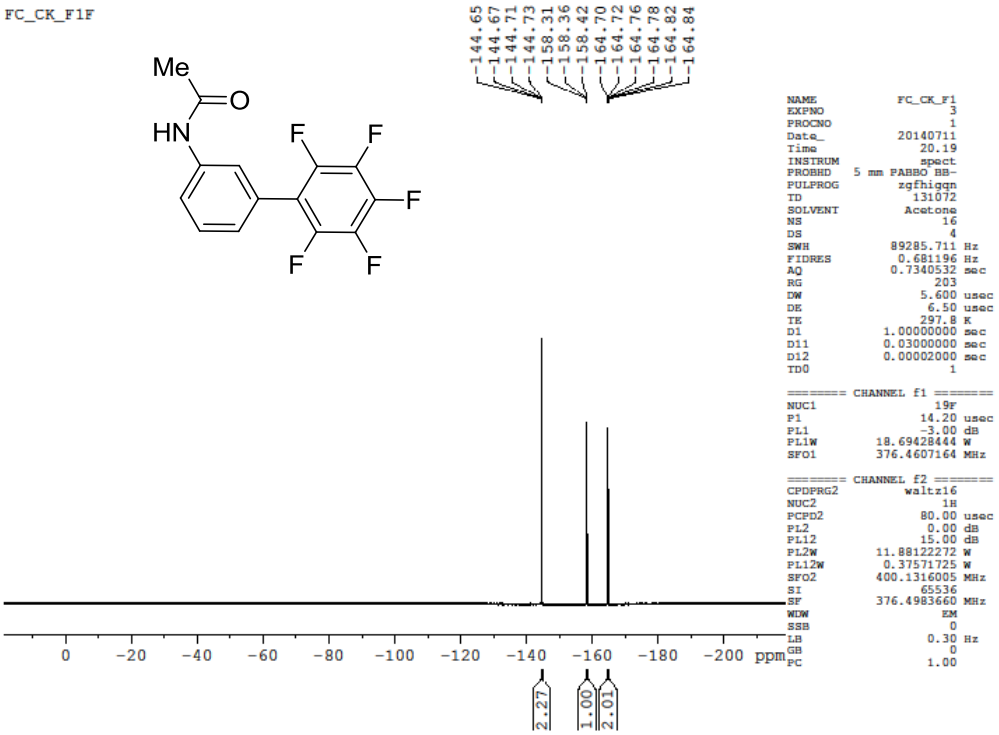


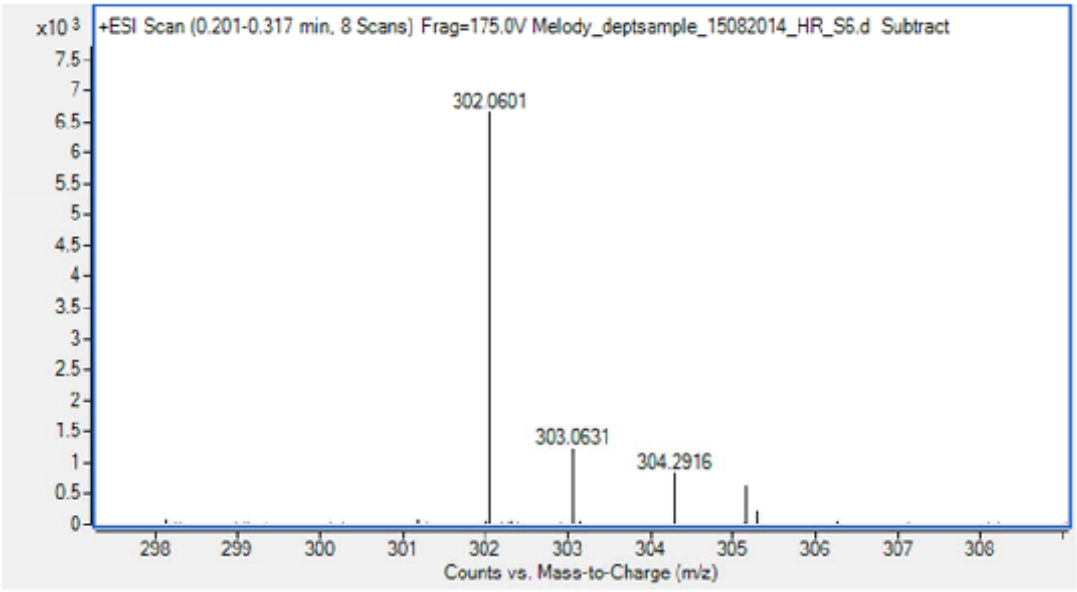
***N*-(2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-3-yl)acetamide (Table 5.3, compound 5ru)**





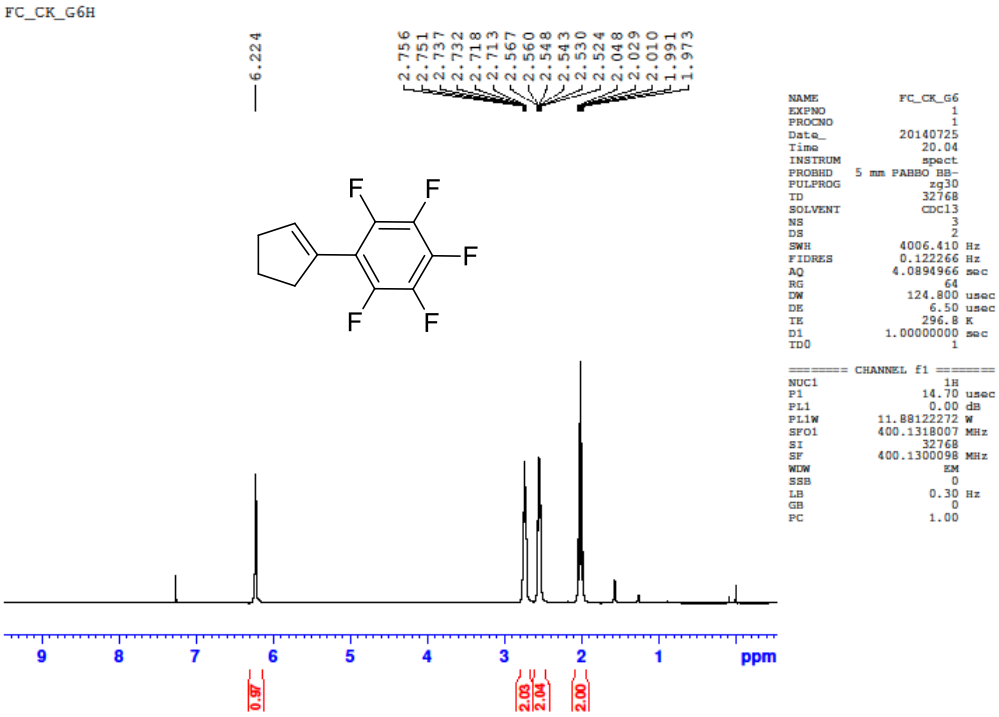
_N_-(2',3',4',5',6'-Pentafluoro-[1,1'-biphenyl]-3-yl)acetamide (Table 5.3, compound 5ru)

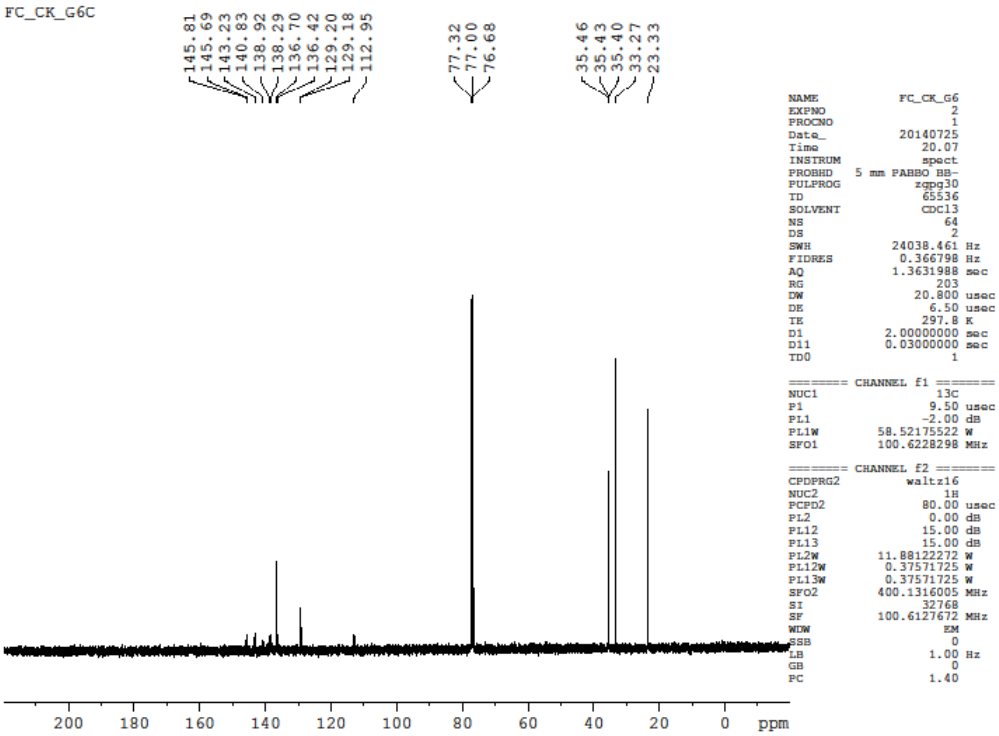




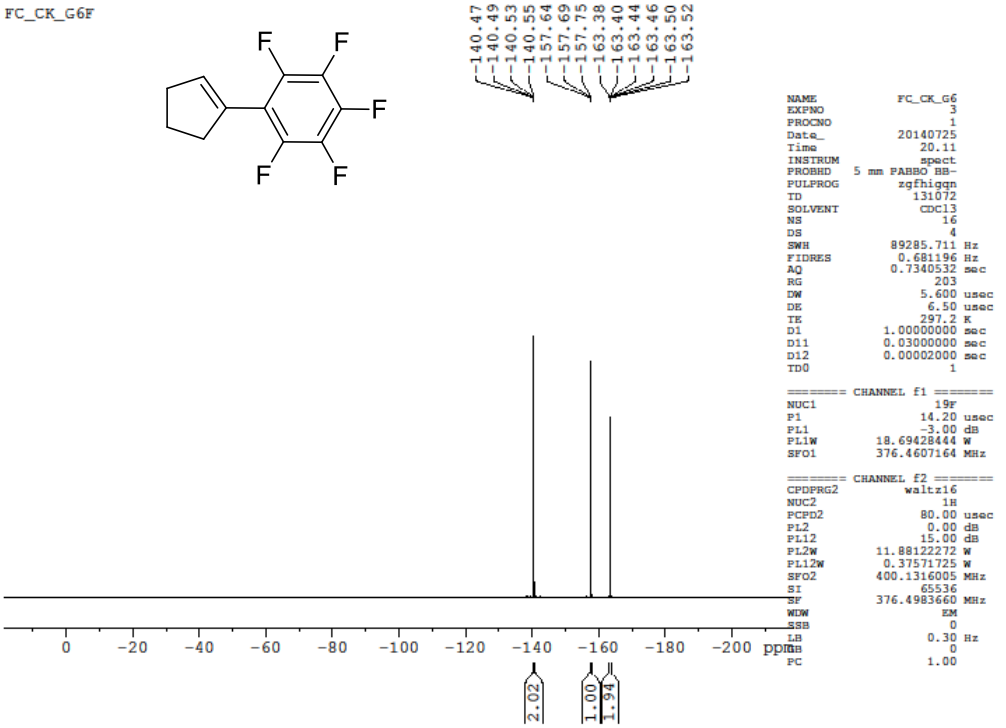
Mass	Calc. Mass	mDa	PPM	Formula
302.0601	302.0599	0.2	0.7	C14 H9 F5 N O

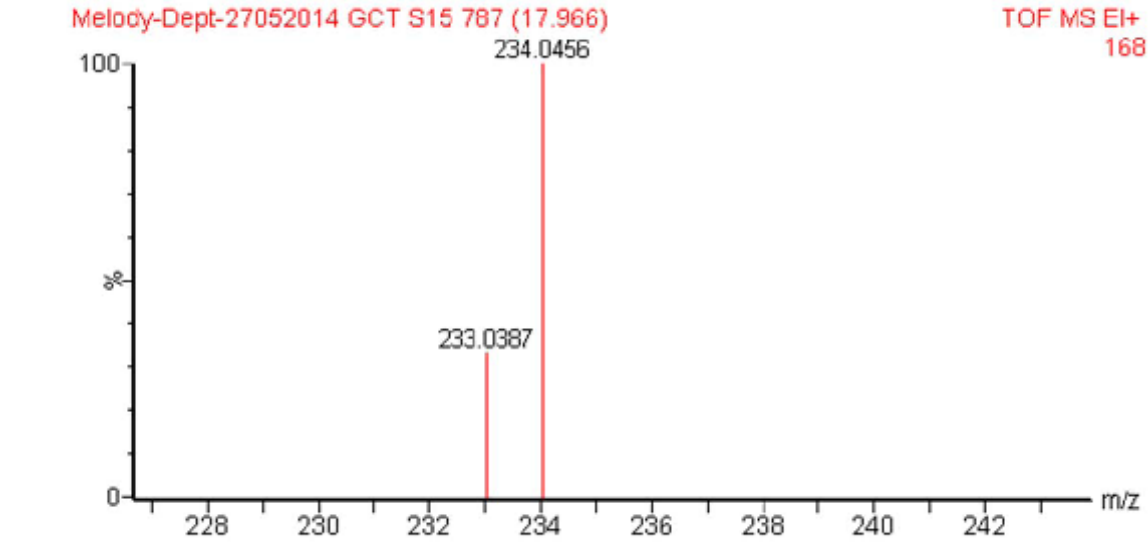
1-(Cyclopent-1-en-1-yl)-2,3,4,5,6-pentafluorobenzene (Table 5.3, compound 5su)





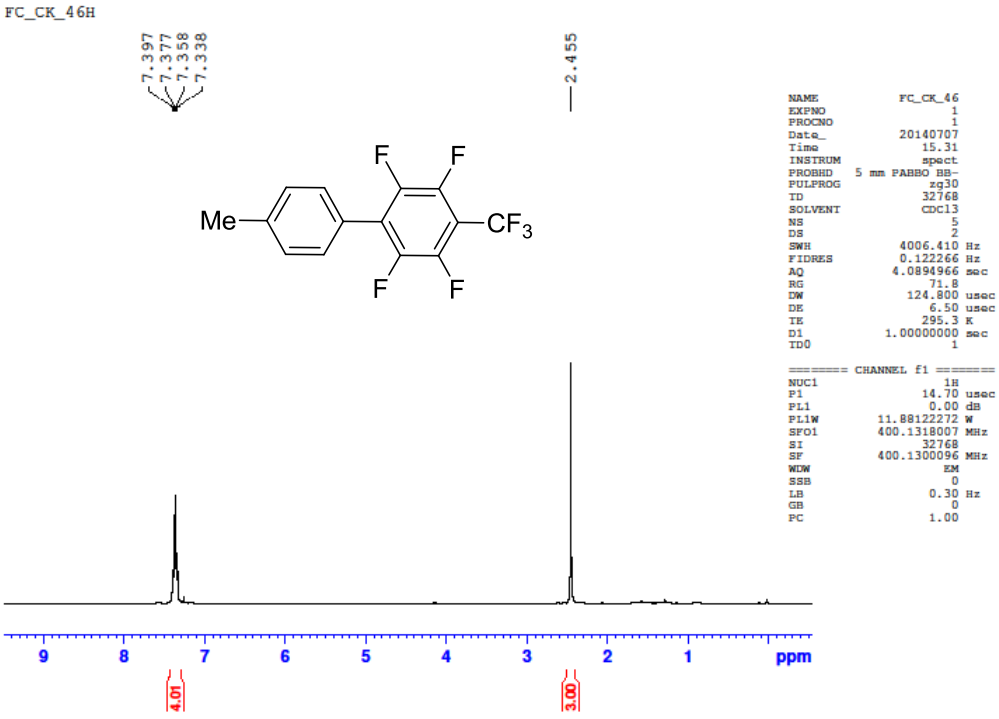
1-(Cyclopent-1-en-1-yl)-2,3,4,5,6-pentafluorobenzene (Table 5.3, compound 5su)

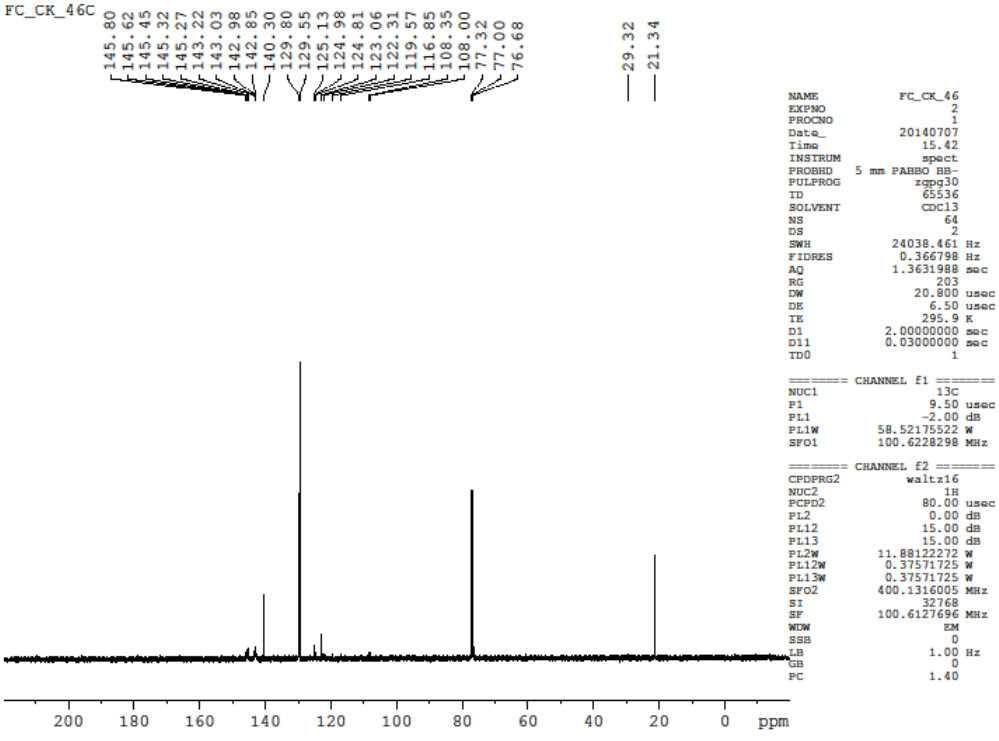




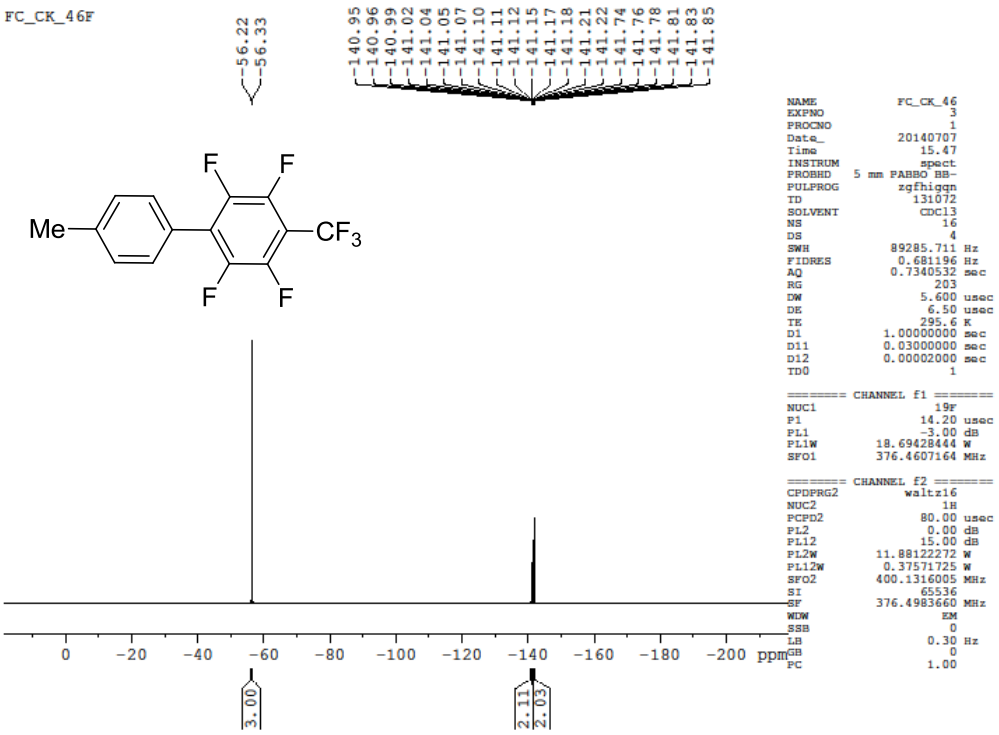
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
234.0456	234.0468	-1.2	-5.1	6.0	5546080.0	C11 H7 F5

2,3,5,6-Tetrafluoro-4'-methyl-4-(trifluoromethyl)-1,1'-biphenyl (Table 5.3, compound 5av)

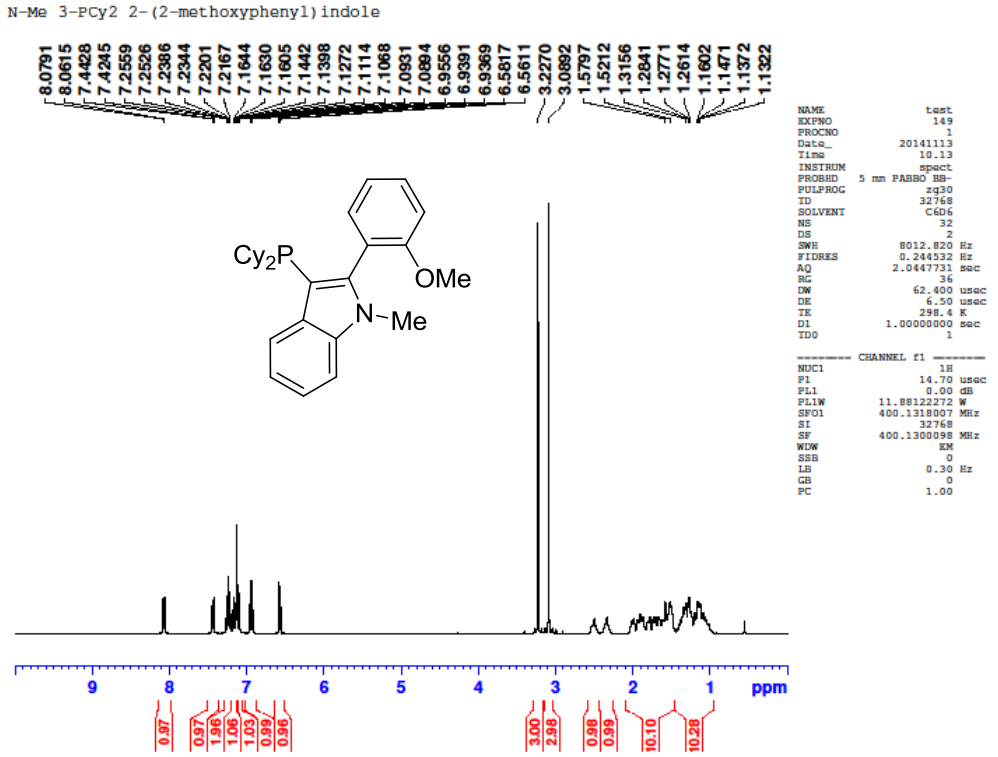


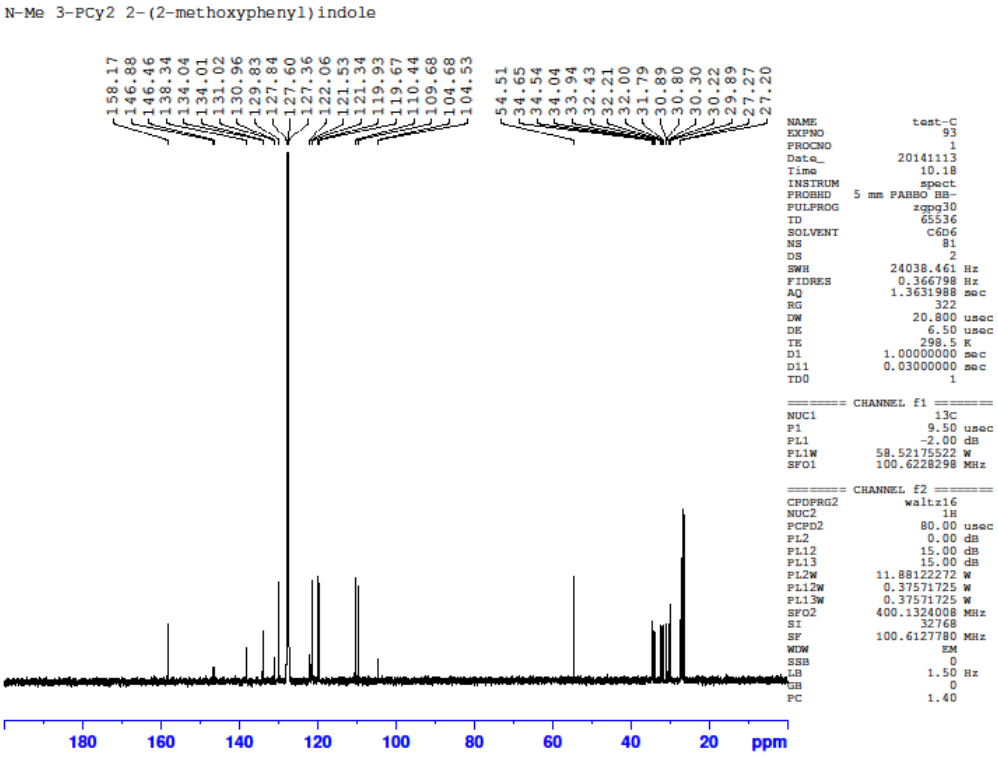


2,3,5,6-Tetrafluoro-4'-methyl-4-(trifluoromethyl)-1,1'-biphenyl (Table 5.3, compound 5av)

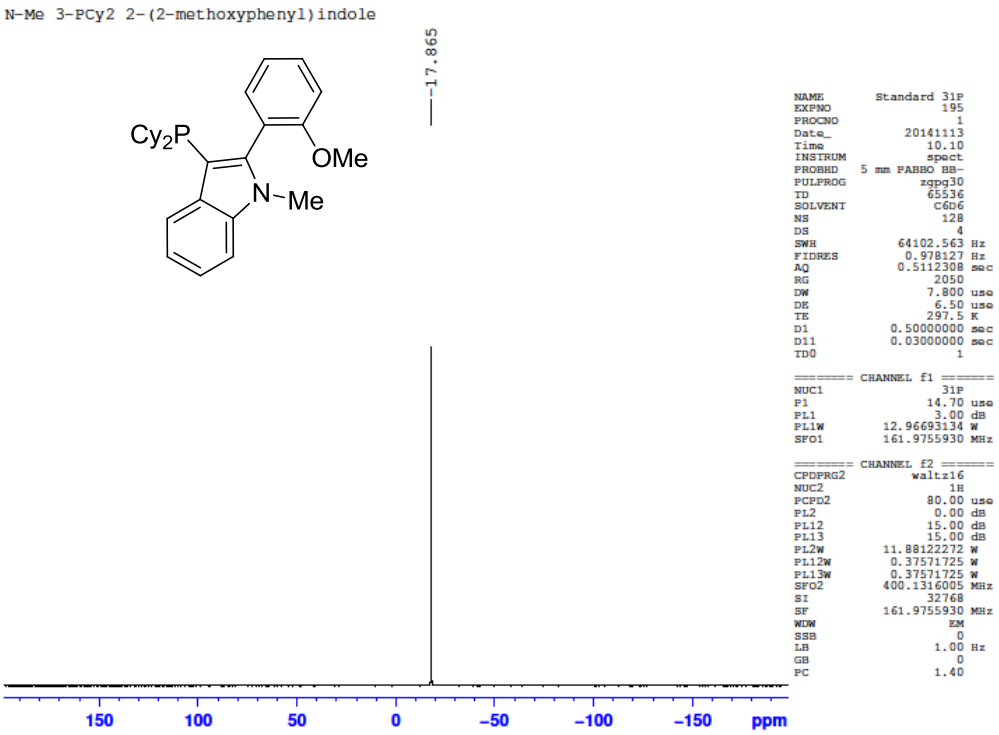


3-(Dicyclohexylphosphino)-2-(2-methoxyphenyl)-1-methyl-1-*H*-indole (Table 6.1, L2)





3-(Dicyclohexylphosphino)-2-(2-methoxyphenyl)-1-methyl-1-*H*-indole (Table 6.1, L2)



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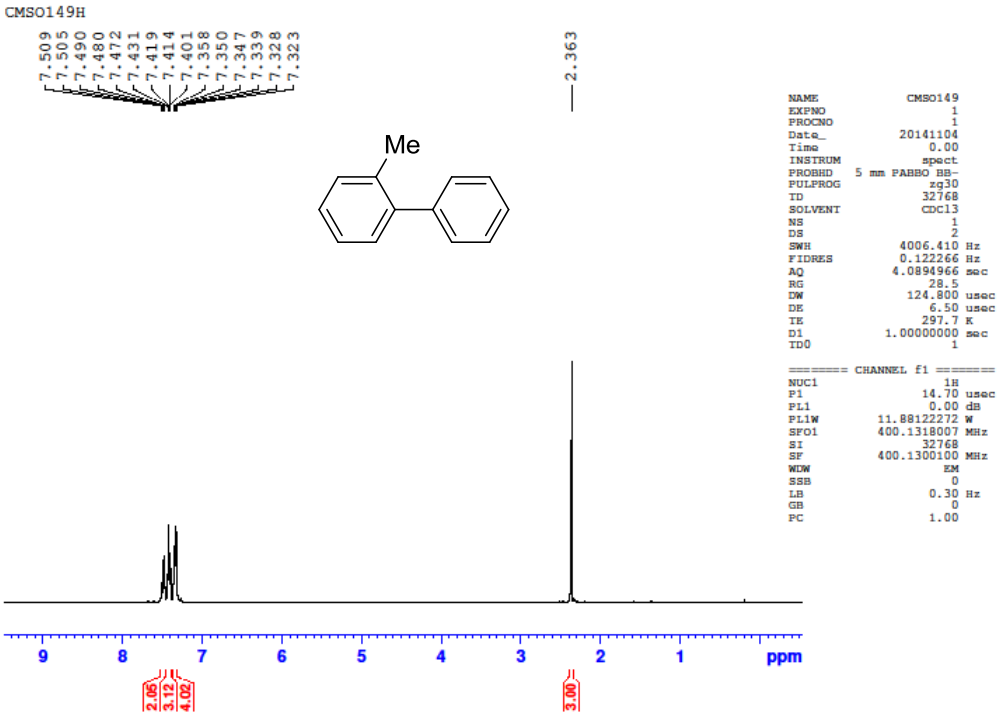
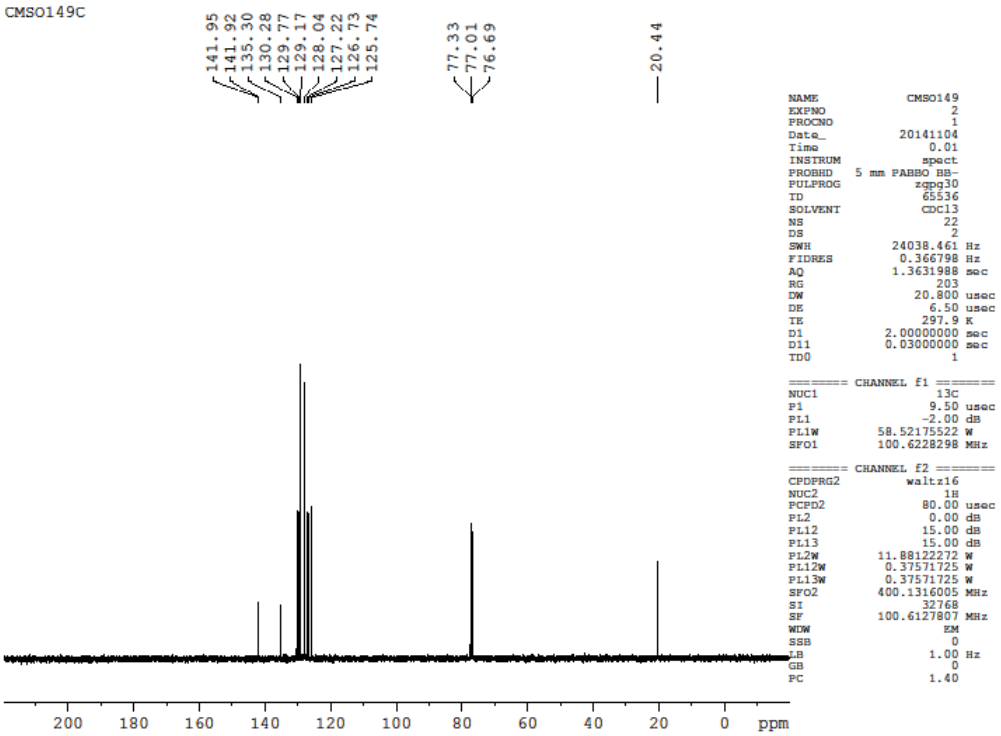
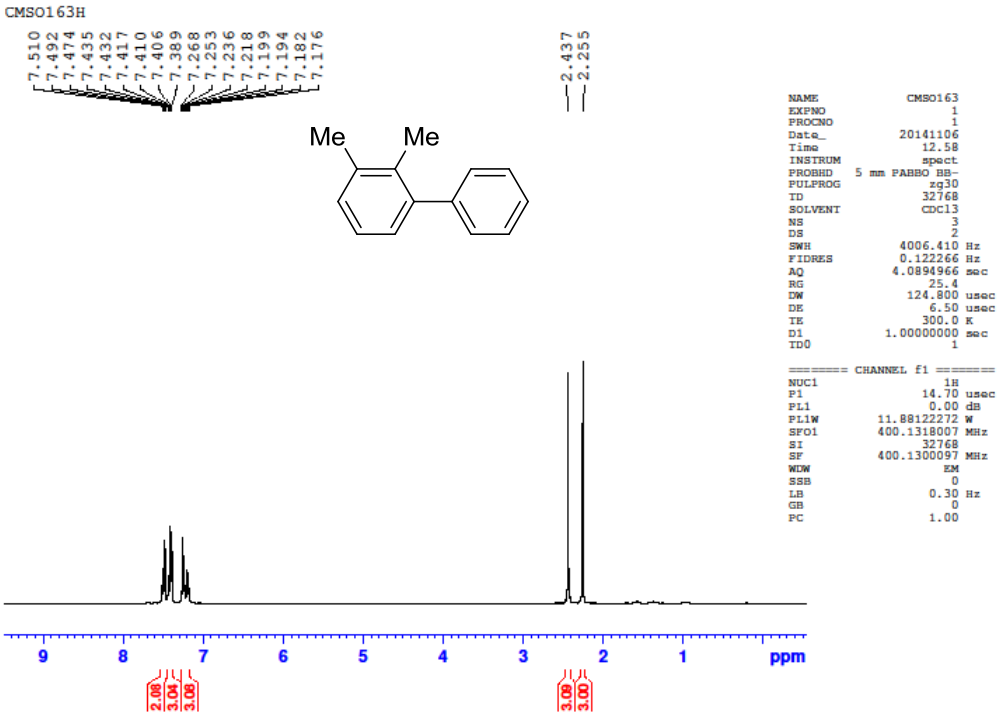
PROCNO	1
Date_	20141113
Time	10.10
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	C6D6
NS	128
DS	4
SWH	64102.563 Hz
FIDRES	0.978127 Hz
AQ	0.5112308 sec
RG	2050
DW	7.800 use
DE	6.50 use
TE	297.5 K
D1	0.50000000 sec
D11	0.03000000 sec
TD0	1
======= CHANNEL f1 ======	
NUC1	31P
P1	14.70 use
PL1	3.00 dB
PL1W	12.96693134 W
SFO1	161.9755930 MHz
======= CHANNEL f2 ======	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 use
PL2	0.00 dB
PL12	15.00 dB
PL13	15.00 dB
PL2W	11.88122272 W
PL12W	0.37571725 W
PL13W	0.37571725 W
SFO2	400.1316005 MHz
SI	32768
SF	161.9755930 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

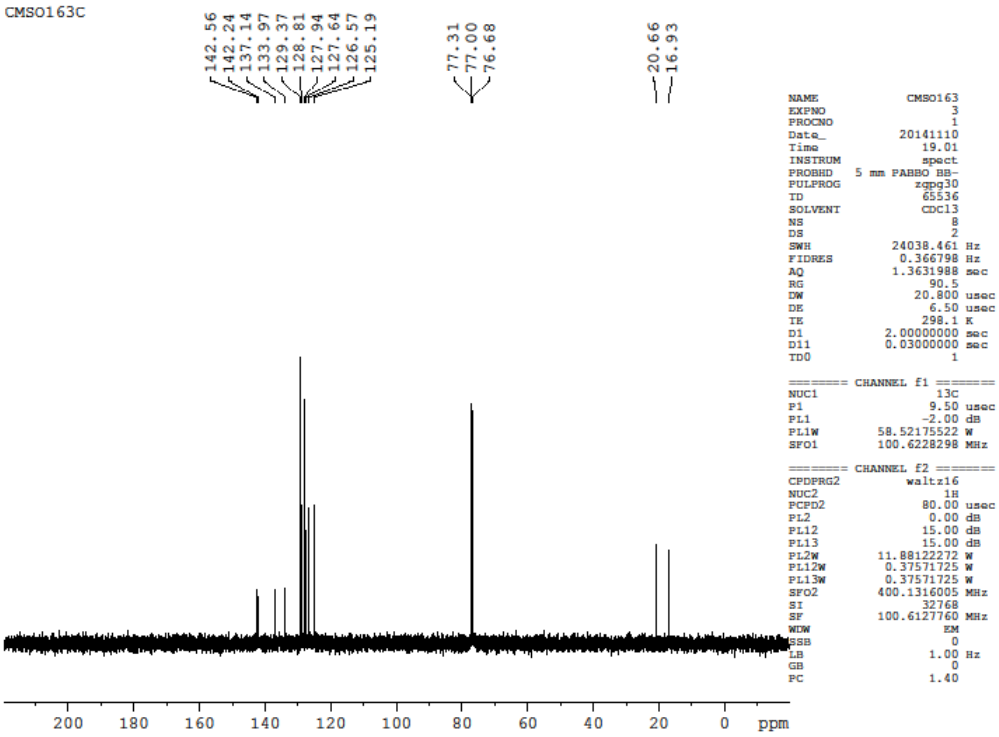
2-Methyl-1,1'-biphenyl (Table 6.2, entry 1)



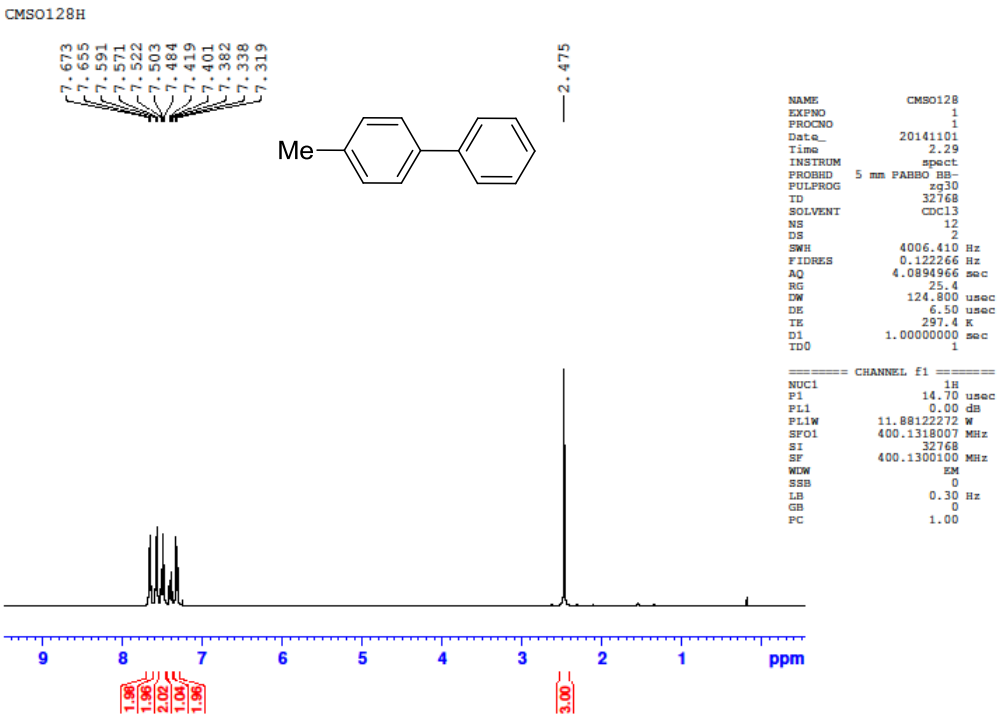


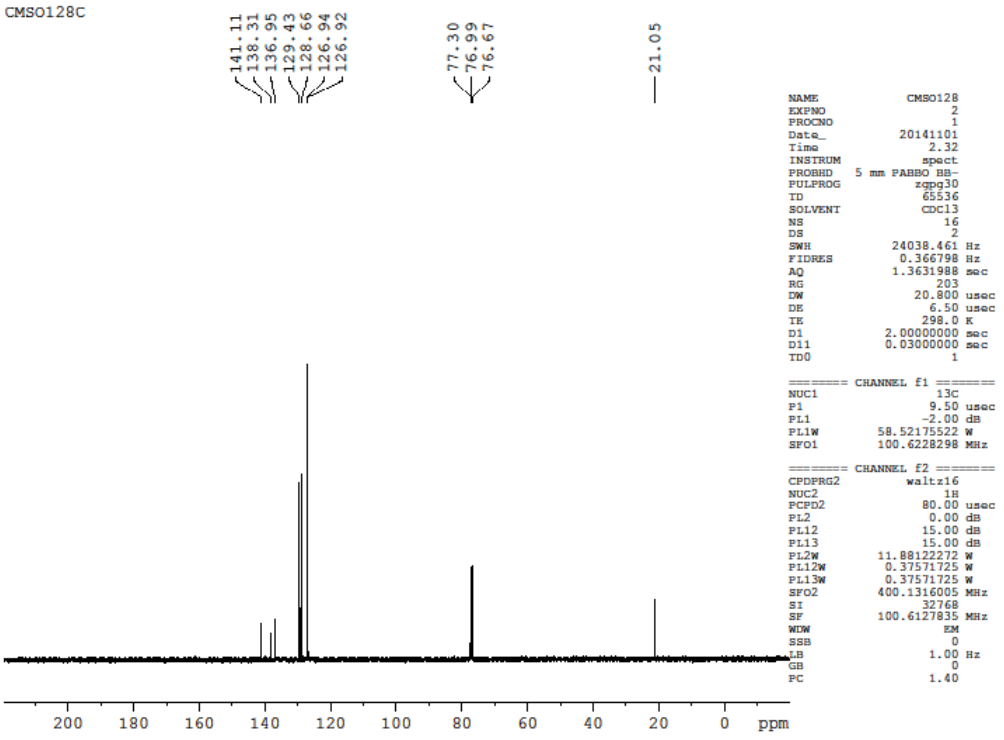
2,3-Dimethyl-1,1'-biphenyl (Table 6.2, entry 2)



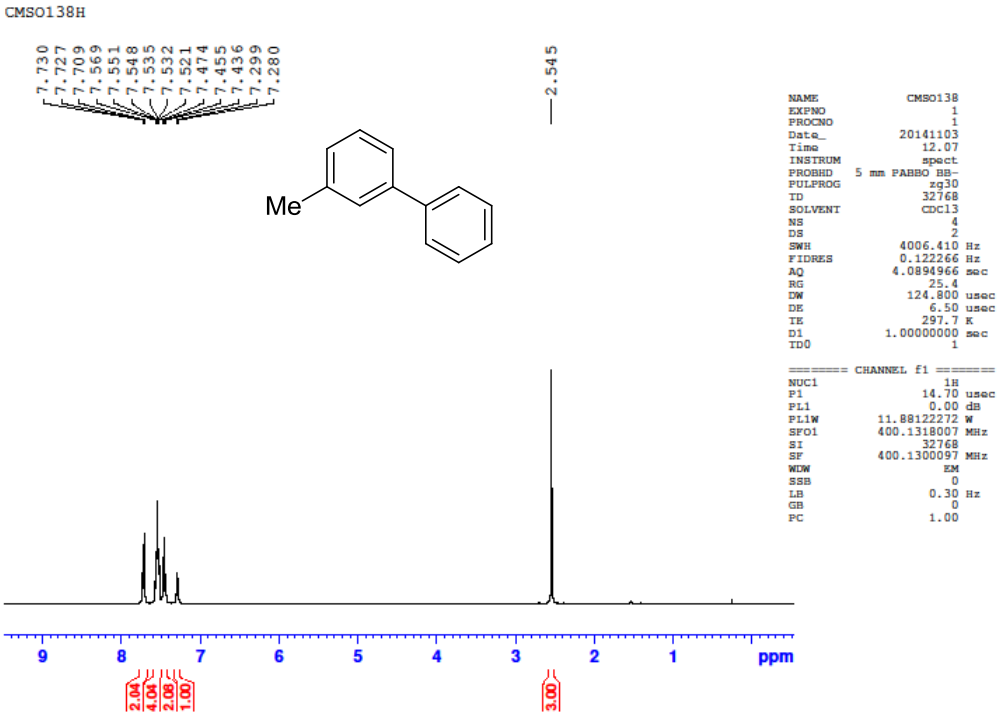


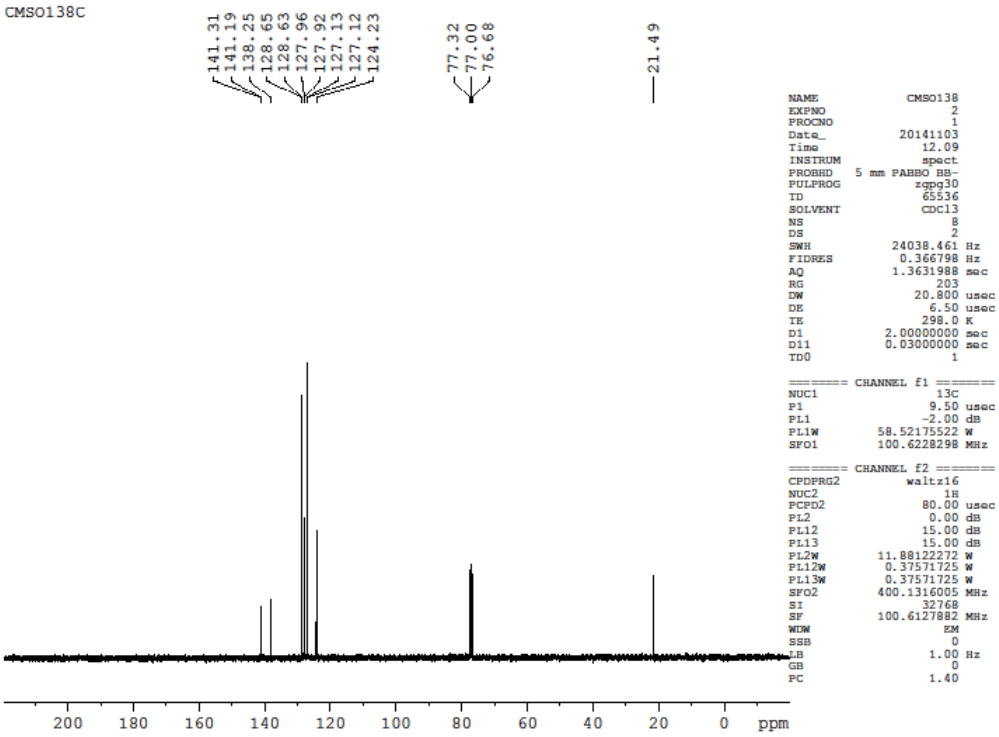
4-Methyl-1,1'-biphenyl (Table 6.2, entry 3)



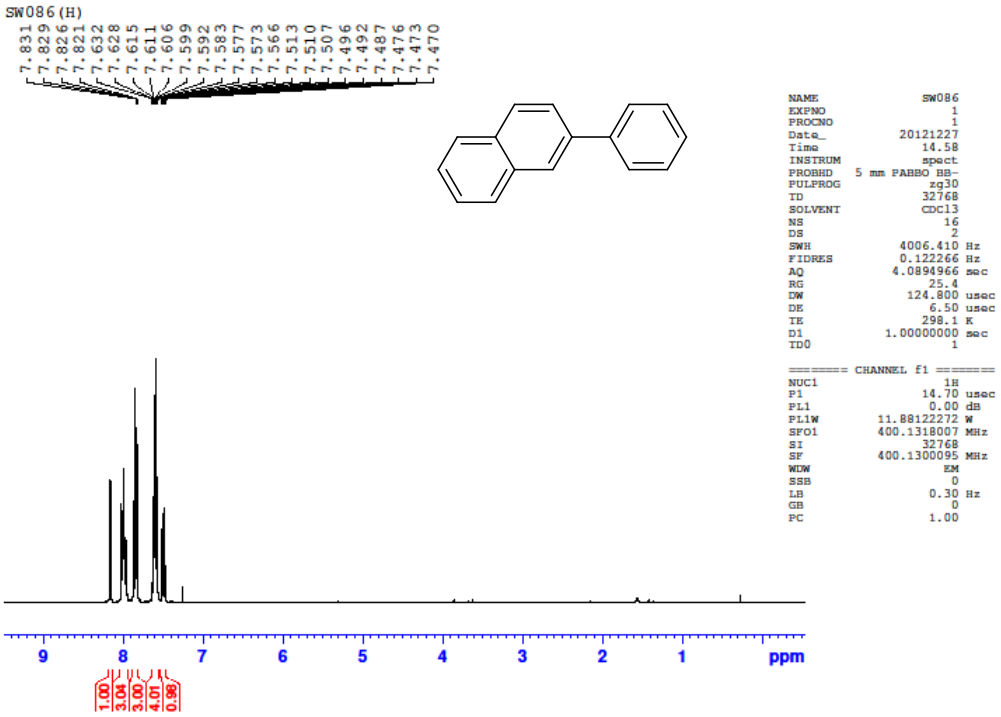


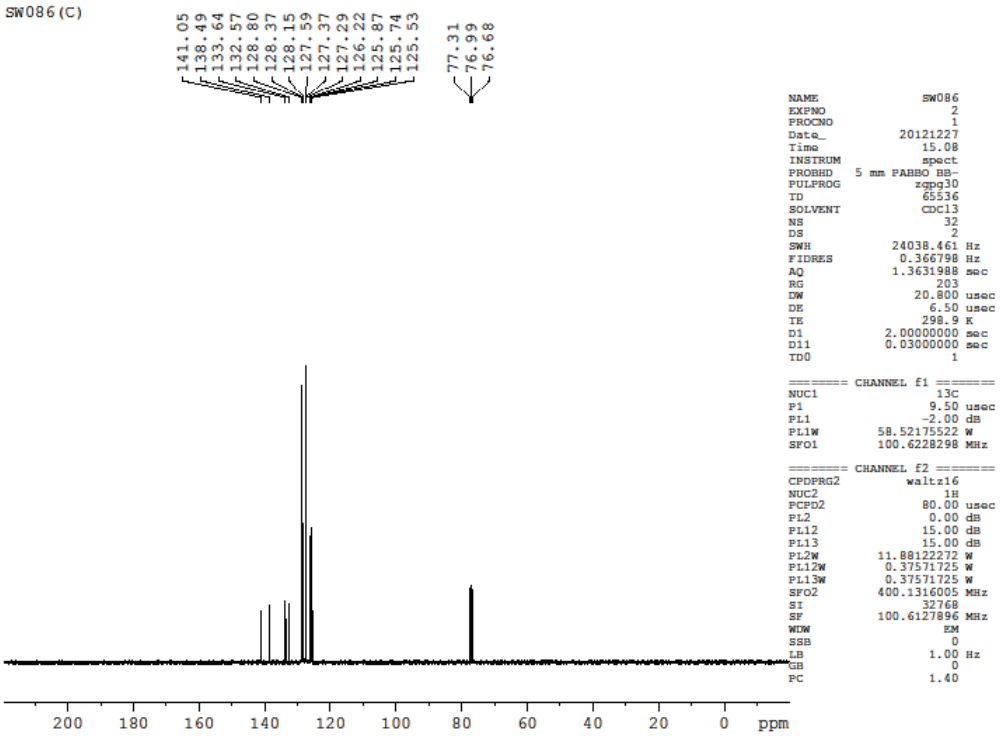
3-Methyl-1,1'-biphenyl (Table 6.2, entry 4)



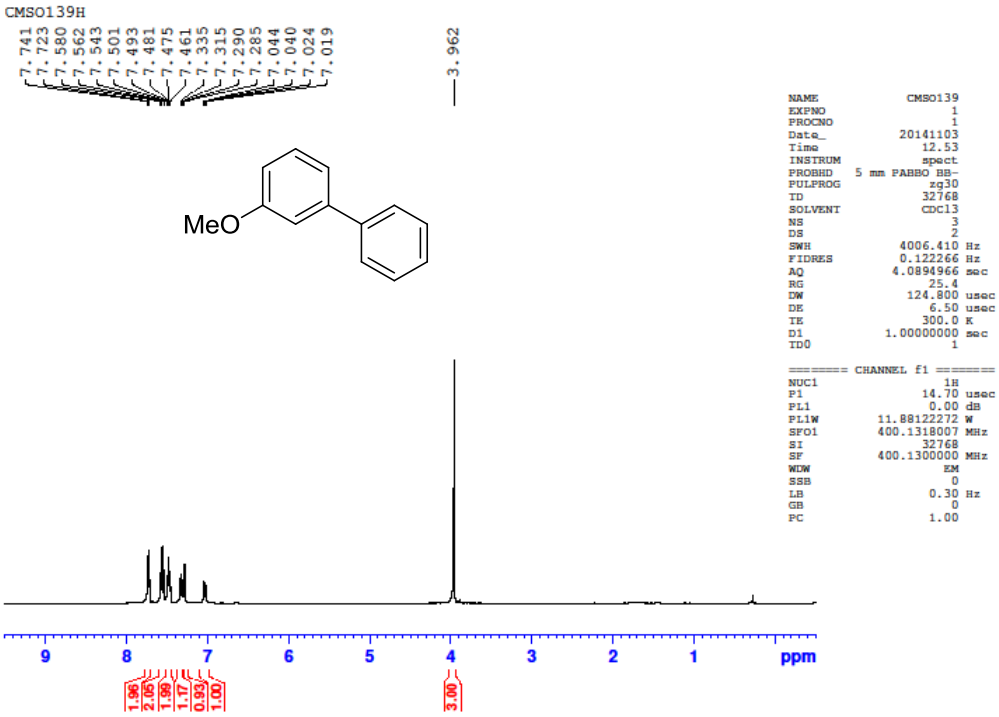


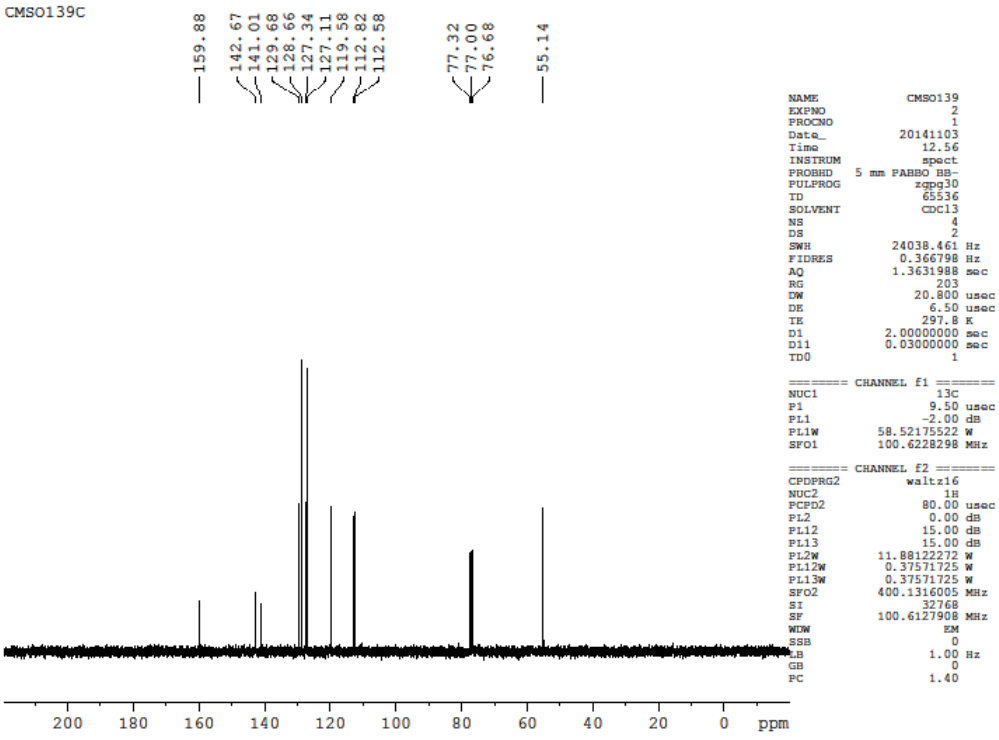
2-Phenylnaphthalene (Table 6.2, entry 5)



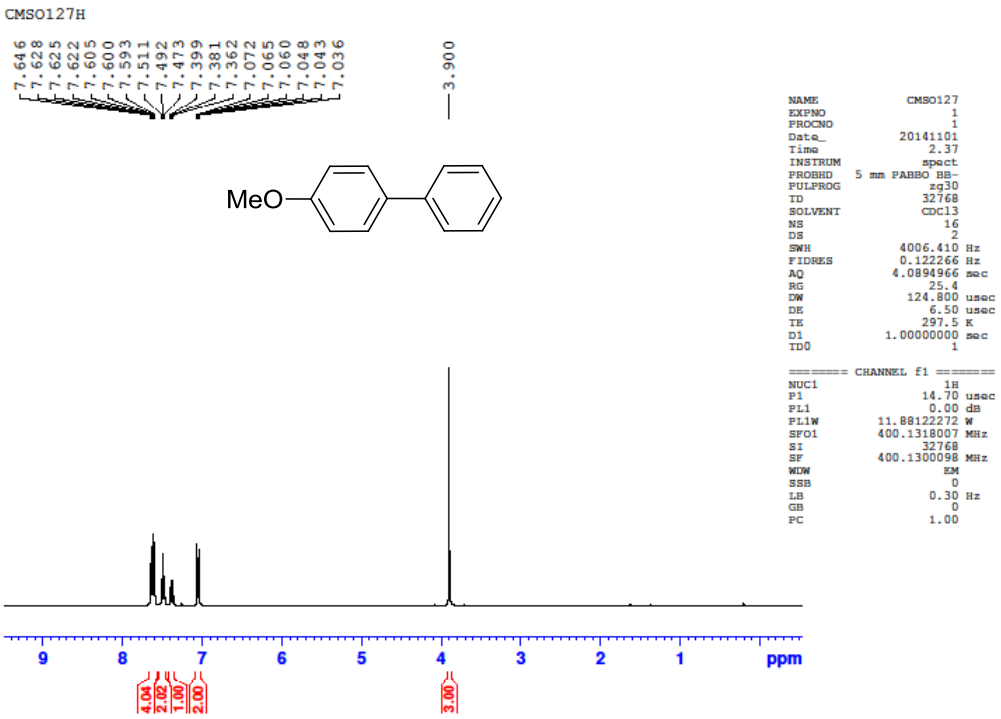


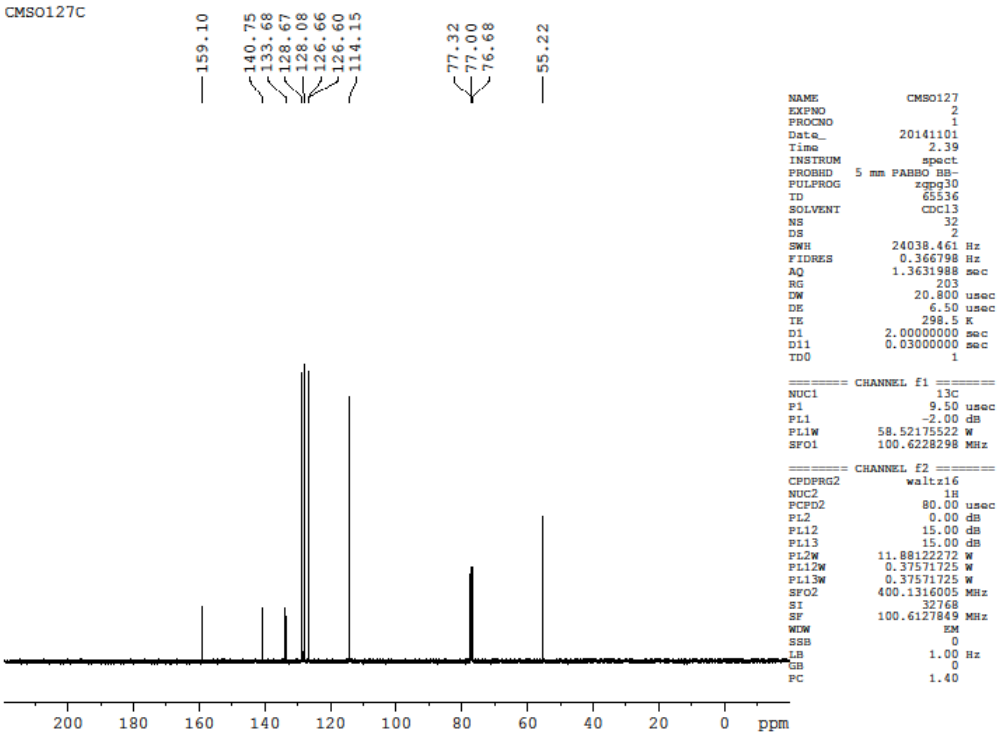
3-Methoxy-1,1'-biphenyl (Table 6.2, entry 6)





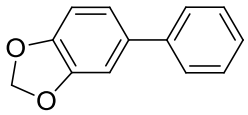
4-Methoxy-1,1'-biphenyl (Table 6.2, entry 7)





5-Phenylbenzo[d][1,3]dioxole (Table 6.2, entry 8)

CMSO141H



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PROCNO                    1
Date_              20141103
Time                  12.59
INSTRUM               spect
PROBHD   5 mm PABBO BB-
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                        2
DS                        2
SWH                4006.410 Hz
FIDRES             0.122266 Hz
AQ                 4.0894966 sec
RG                      25.4
DW                   124.800 usec
DE                     6.50 usec
TE                   297.8 K
D1                 1.00000000 sec
TD0                       1

======== CHANNEL f1 =======
NUC1                      1H
P1                     14.70 usec
PL1                     0.00 dB
PL1W              11.88122272 W
SFO1              400.1318007 MHz
SI                      32768
SF                400.1300095 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00
```
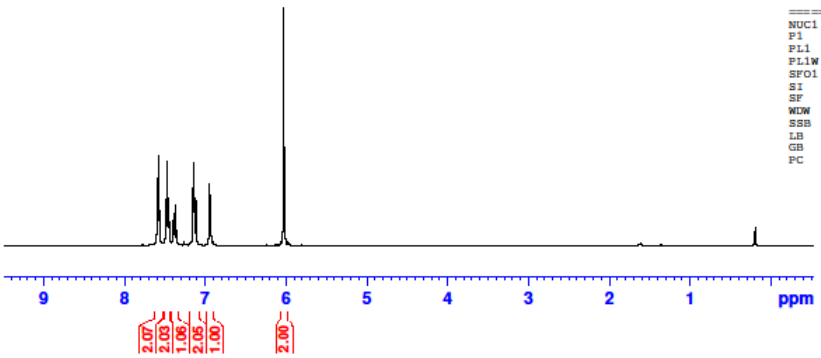
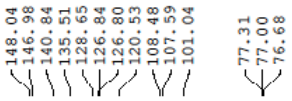



CMSO141C




```
NAME                CMSO141
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PROCNO                    1
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Time                  13.00
INSTRUM               spect
PROBHD   5 mm PABBO BB-
PULPROG             zgpg30
TD                    65536
SOLVENT               CDCl3
NS                        6
DS                        2
SWH               24038.461 Hz
FIDRES             0.366798 Hz
AQ                 1.3631988 sec
RG                      203
DW                   20.800 usec
DE                     6.50 usec
TE                   298.1 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                       1

======== CHANNEL f1 =======
NUC1                      13C
P1                      9.50 usec
PL1                    -2.00 dB
PL1W              58.52175522 W
SFO1              100.6228298 MHz

======== CHANNEL f2 =======
CPDPRG2                waltz16
NUC2                      1H
PCPD2                  80.00 usec
PL2                     0.00 dB
PL12                   15.00 dB
PL13                   15.00 dB
PL2W              11.88122272 W
PL12W              0.37571725 W
PL13W              0.37571725 W
SFO2              400.1316005 MHz
SI                      32768
SF                100.6127859 MHz
WDW                       EM
SSB                        0
LB                      1.00 Hz
GB                         0
PC                      1.40
```
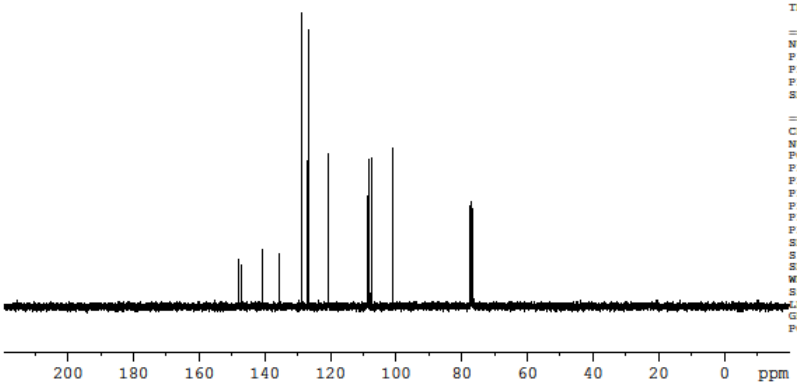
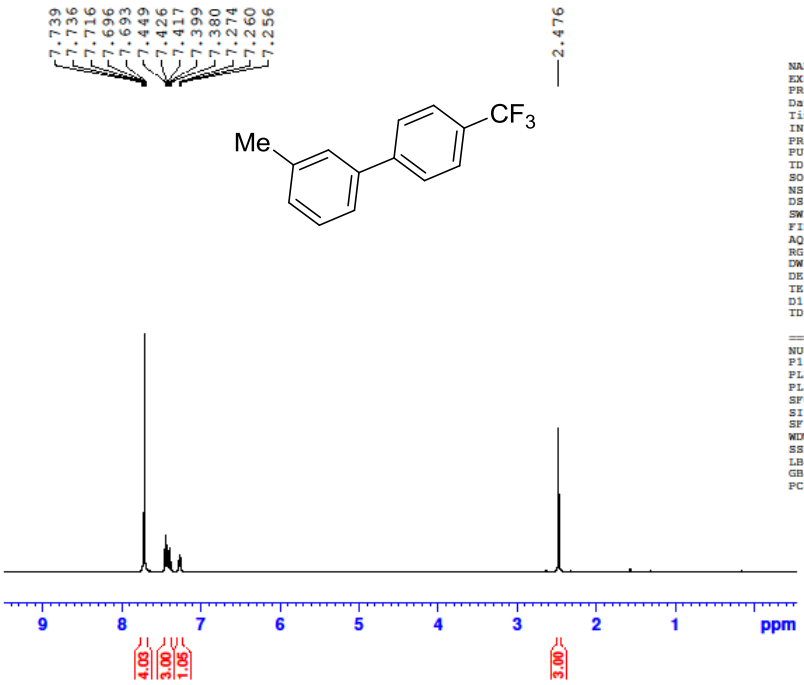



3-Methyl-4'-(trifluoromethyl)-1,1'-biphenyl (Table 6.2, entry 9)

CMSO157H




```
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PROCNO                  1
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Time                13.38
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG               zg30
TD                   32768
SOLVENT              CDCl3
NS                       8
DS                       2
SWH              4006.410 Hz
FIDRES           0.122266 Hz
AQ               4.0894966 sec
RG                    25.4
DW                124.800 usec
DE                  6.50 usec
TE                 297.3 K
D1               1.00000000 sec
TD0                      1

======== CHANNEL f1 =======
NUC1                    1H
P1                   14.70 usec
PL1                   0.00 dB
PL1W         11.88122272 W
SFO1         400.1318007 MHz
SI                   32768
SF           400.1300096 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```
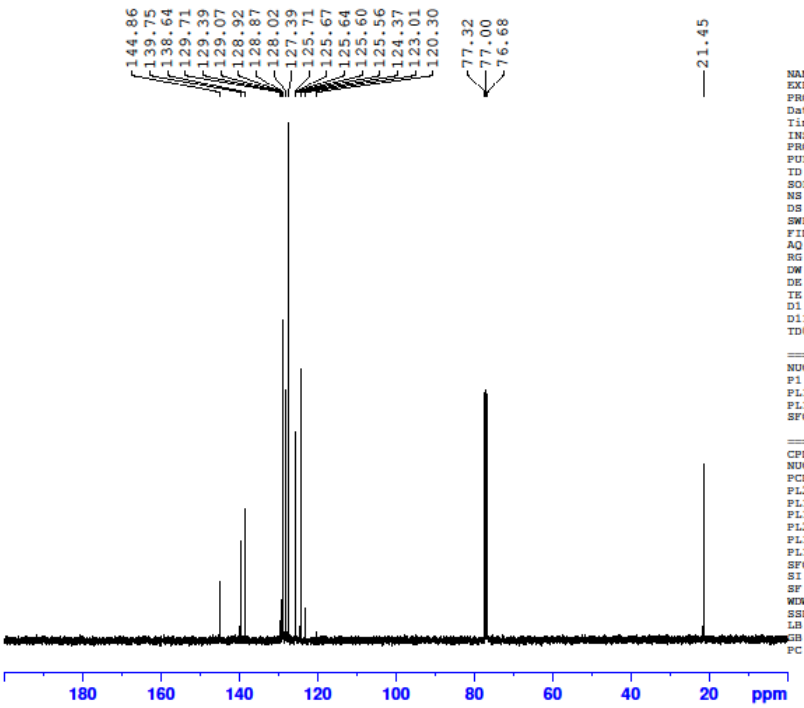

CMSO157C




```
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PROCNO                  1
Date_            20141106
Time                13.44
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                      64
DS                       2
SWH              24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                     203
DW                 20.800 usec
DE                  6.50 usec
TE                 298.7 K
D1               2.00000000 sec
D11              0.03000000 sec
TD0                      1

======== CHANNEL f1 =======
NUC1                   13C
P1                    9.50 usec
PL1                  -2.00 dB
PL1W         58.52175522 W
SFO1         100.6228298 MHz

======== CHANNEL f2 =======
CPDPRG2             waltz16
NUC2                    1H
PCPD2                80.00 usec
PL2                   0.00 dB
PL12                 15.00 dB
PL13                 15.00 dB
PL2W         11.88122272 W
PL12W         0.37571725 W
PL13W         0.37571725 W
SFO2         400.1316005 MHz
SI                   32768
SF           100.6127739 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.40
```
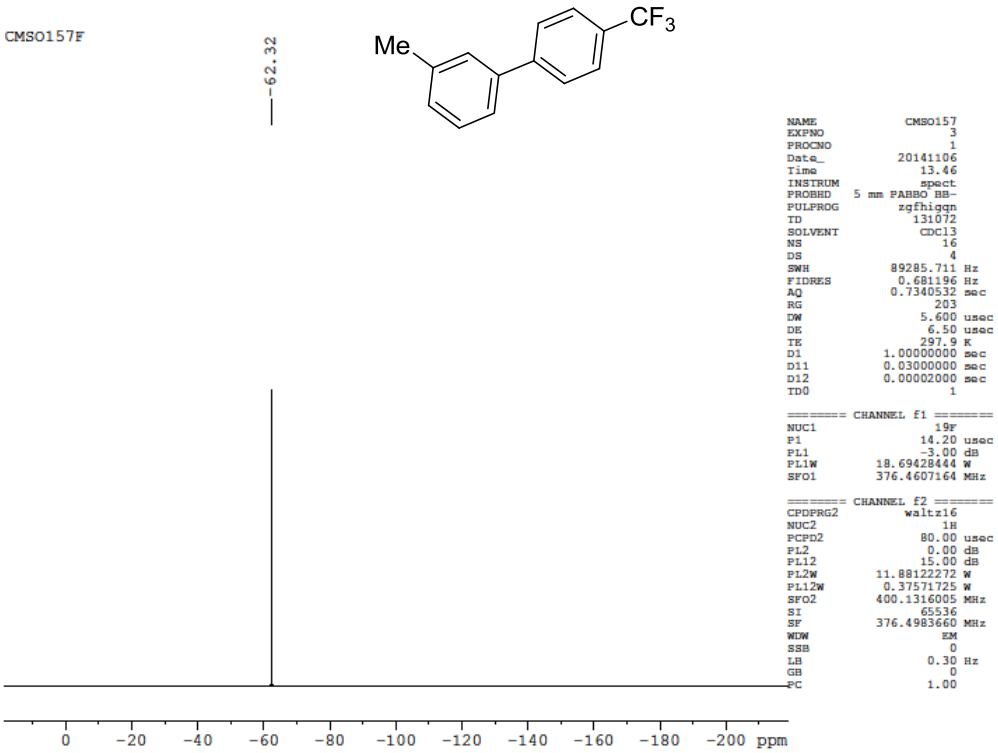
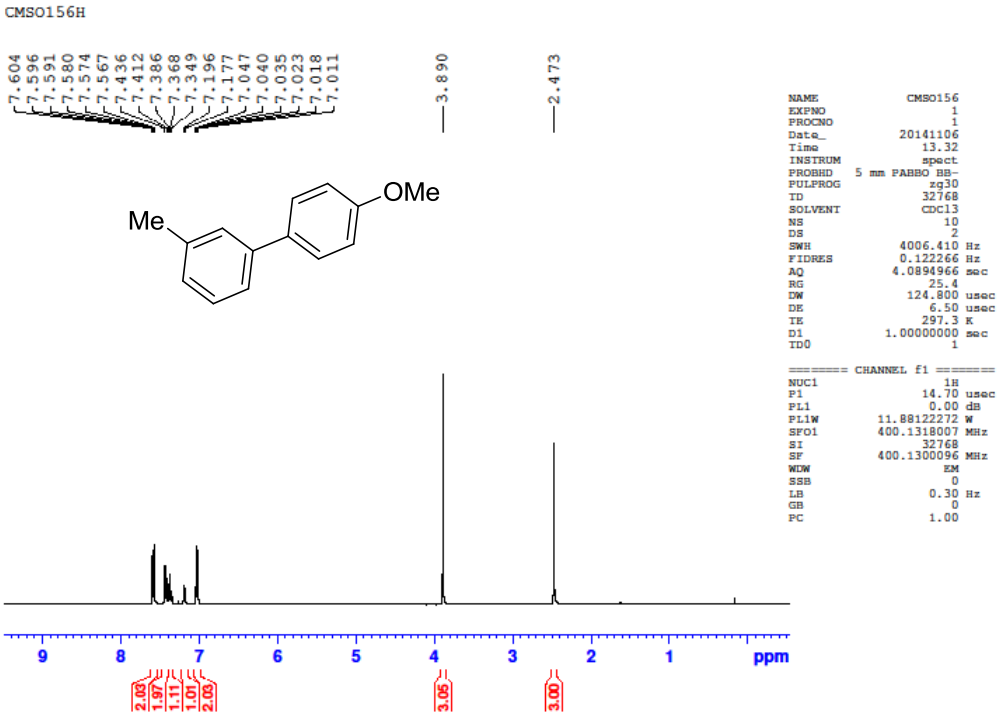
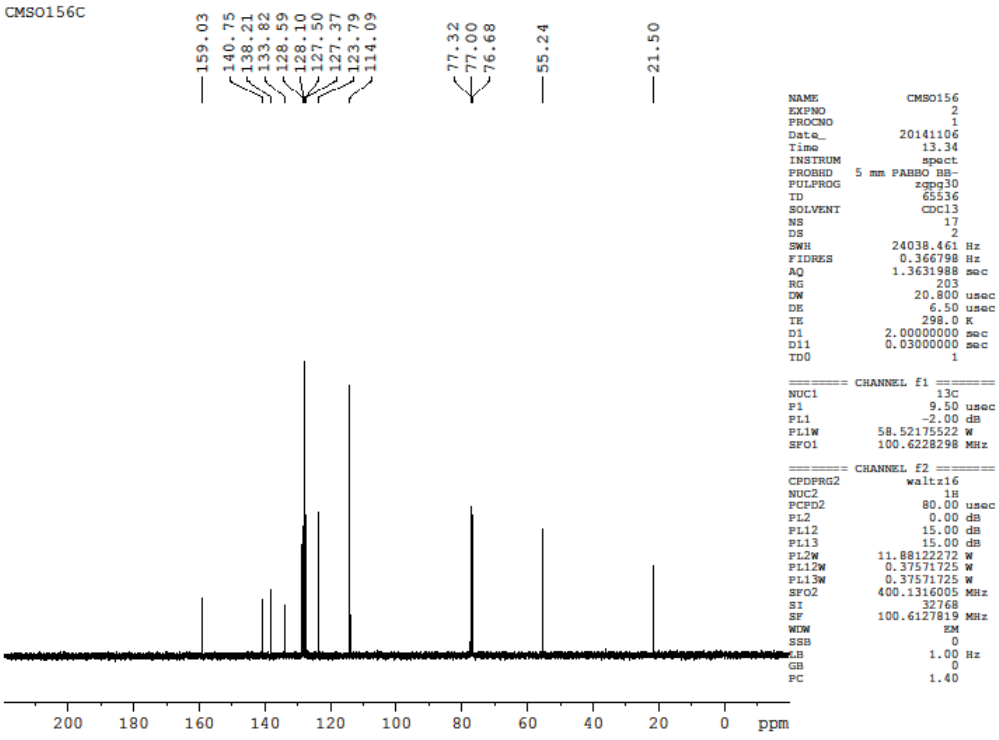

3-Methyl-4'-(trifluoromethyl)-1,1'-biphenyl (Table 6.2, entry 9)

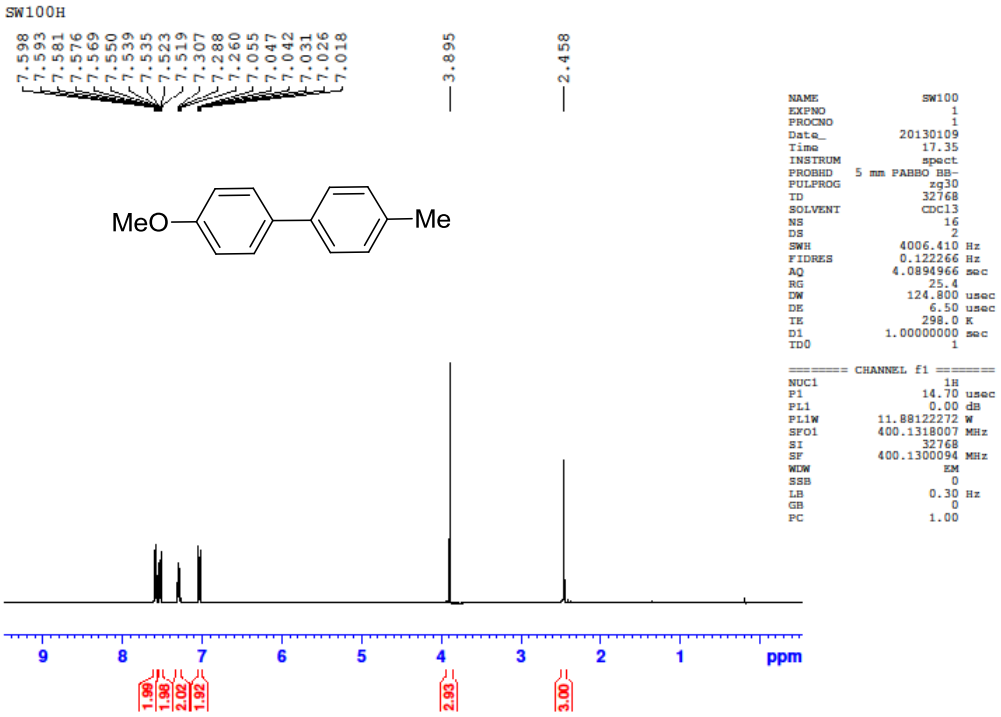


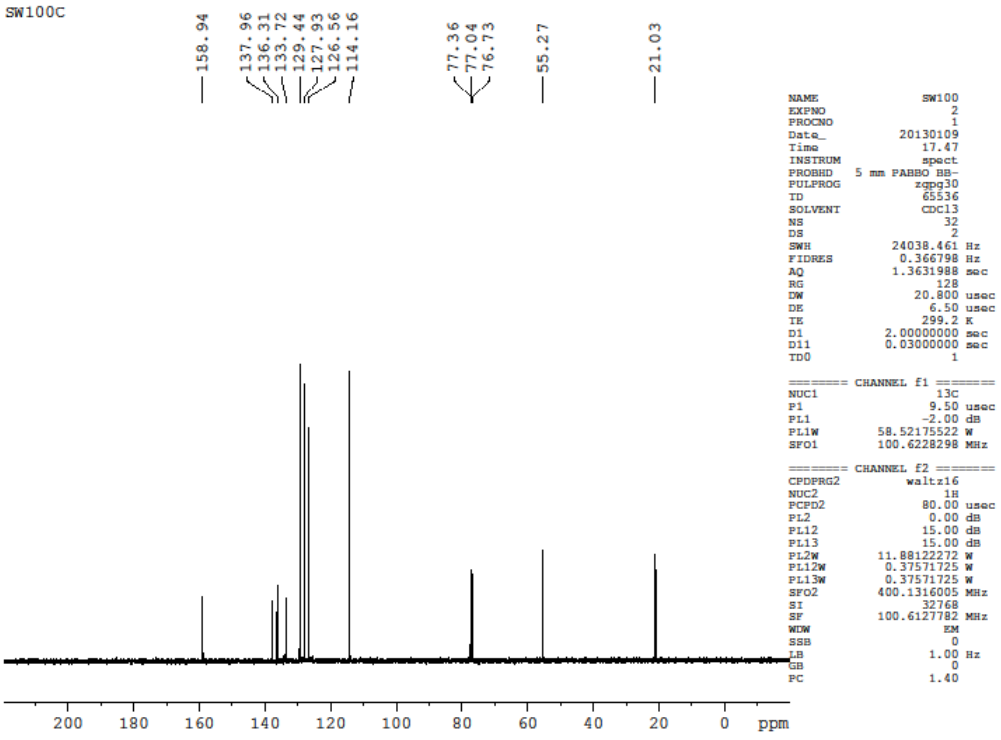
4'-Methoxy-3-methyl-1,1'-biphenyl (Table 6.2, entry 10)





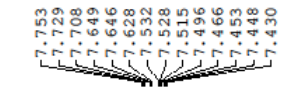
4-Methoxy-4'-methyl-1,1'-biphenyl (Table 6.2, entry 11)

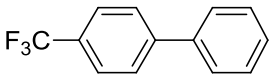




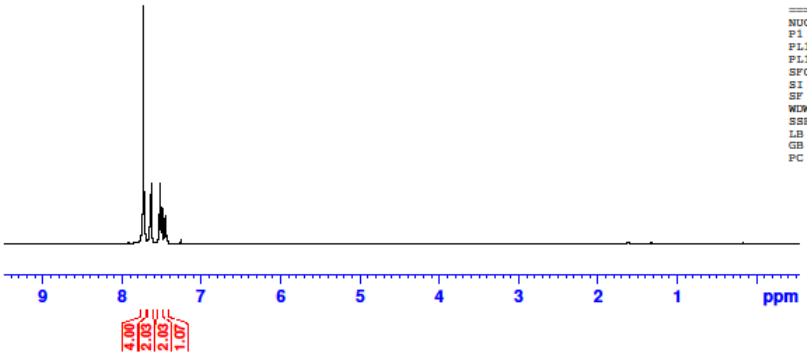
4-(Trifluoromethyl)-1,1'-biphenyl (Table 6.2, entry 12)

CMSO123H

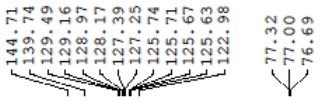




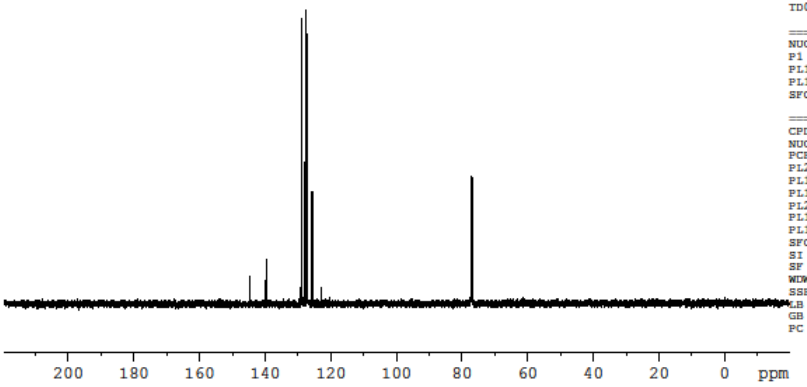

```
NAME                CMSO123
EXPNO                     1
PROCNO                    1
Date_              20141103
Time                  12.21
INSTRUM               spect
PROBHD   5 mm PABBO BB-
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                        3
DS                        2
SWH                4006.410 Hz
FIDRES             0.122266 Hz
AQ                 4.0894966 sec
RG                      45.2
DW                   124.800 usec
DE                     6.50 usec
TE                   297.8 K
D1                 1.00000000 sec
TD0                       1

======== CHANNEL f1 =======
NUC1                    1H
P1                   14.70 usec
PL1                   0.00 dB
PL1W           11.88122272 W
SFO1           400.1318007 MHz
SI                    32768
SF             400.1300097 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```



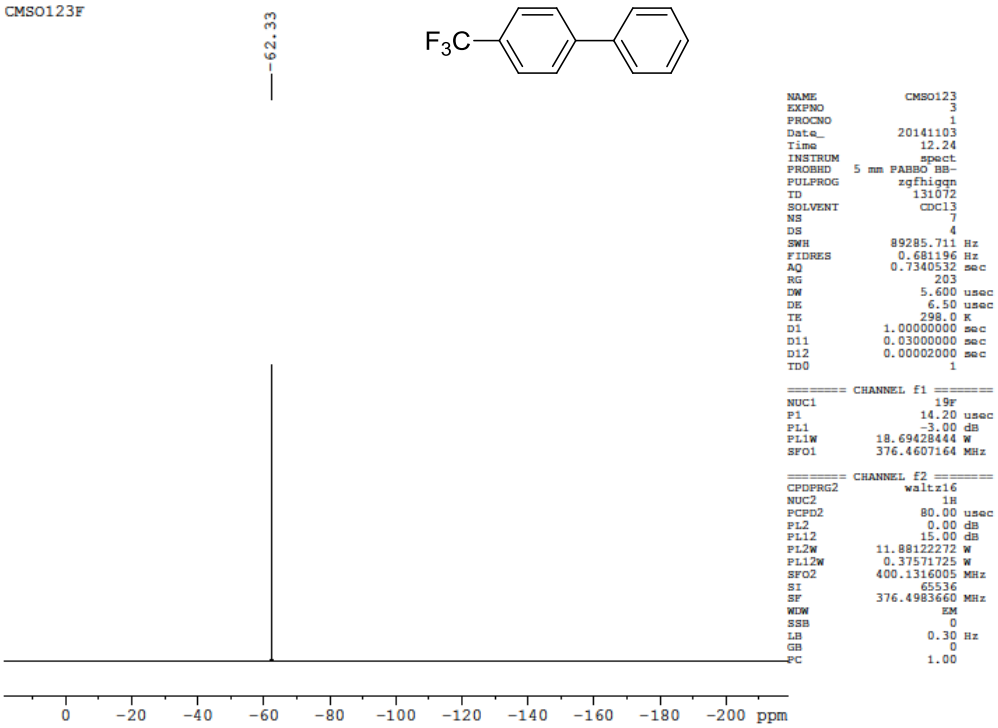
CMSO123C



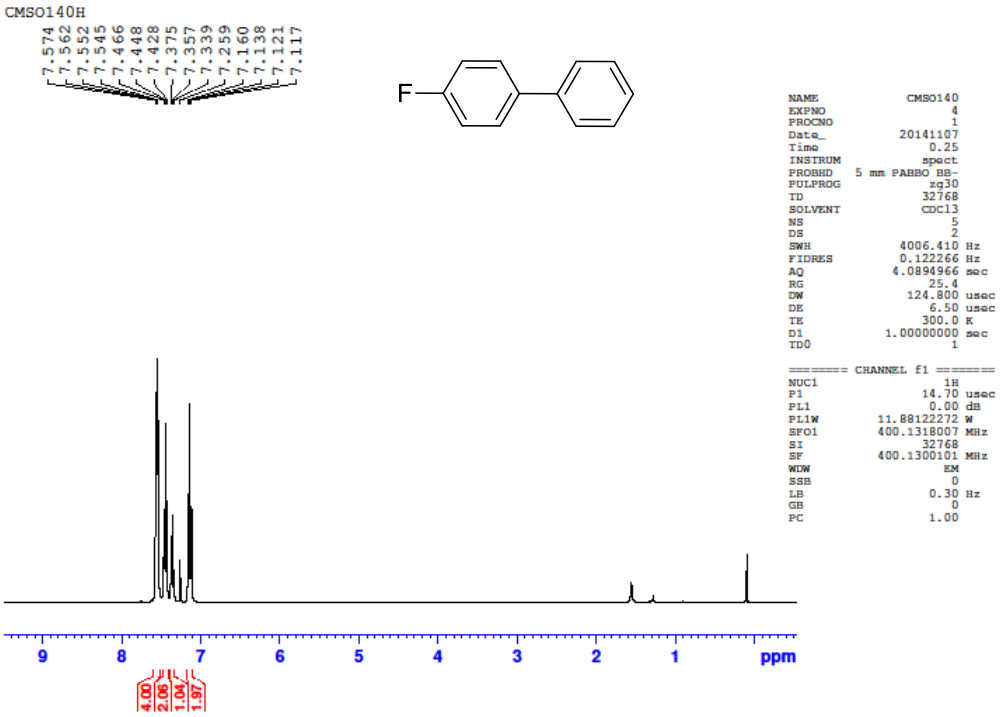

```
NAME                CMSO123
EXPNO                     2
PROCNO                    1
Date_              20141103
Time                  12.22
INSTRUM               spect
PROBHD   5 mm PABBO BB-
PULPROG             zgpg30
TD                    65536
SOLVENT               CDCl3
NS                       17
DS                        2
SWH                24038.461 Hz
FIDRES             0.366798 Hz
AQ                 1.3631988 sec
RG                      203
DW                   20.800 usec
DE                     6.50 usec
TE                   298.4 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                       1

======== CHANNEL f1 =======
NUC1                   13C
P1                    9.50 usec
PL1                  -2.00 dB
PL1W           58.52175522 W
SFO1           100.6228298 MHz

======== CHANNEL f2 =======
CPDPRG2            waltz16
NUC2                    1H
PCPD2                80.00 usec
PL2                   0.00 dB
PL12                 15.00 dB
PL13                 15.00 dB
PL2W           11.88122272 W
PL12W           0.37571725 W
PL13W           0.37571725 W
SFO2           400.1316005 MHz
SI                    32768
SF             100.6127751 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.40
```

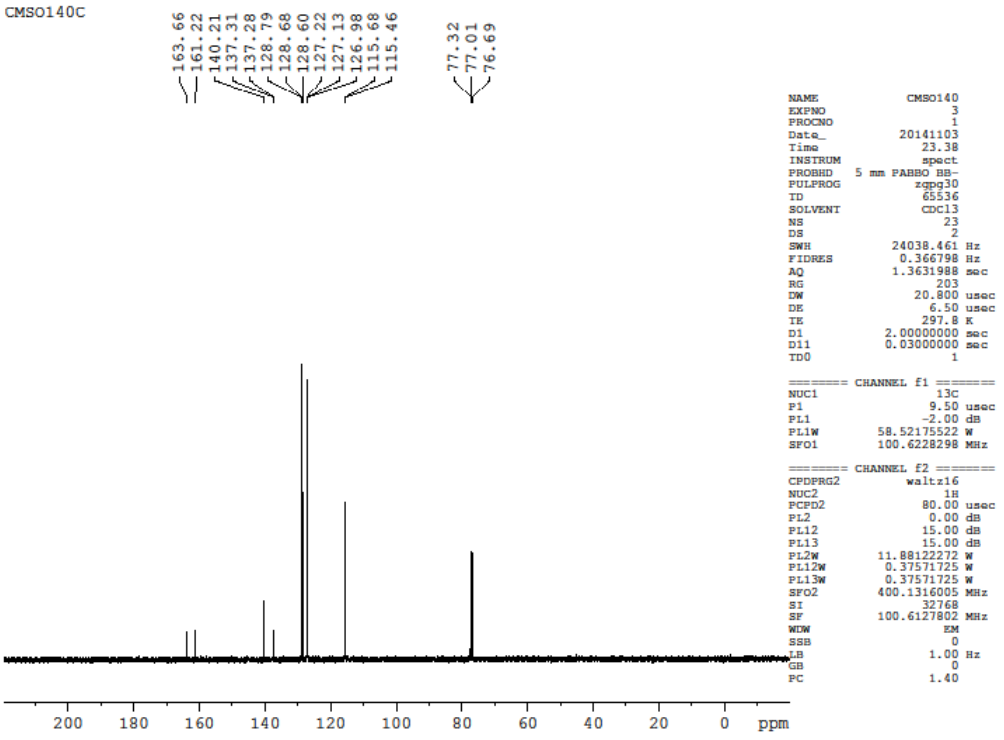


4-(Trifluoromethyl)-1,1'-biphenyl (Table 6.2, entry 12)

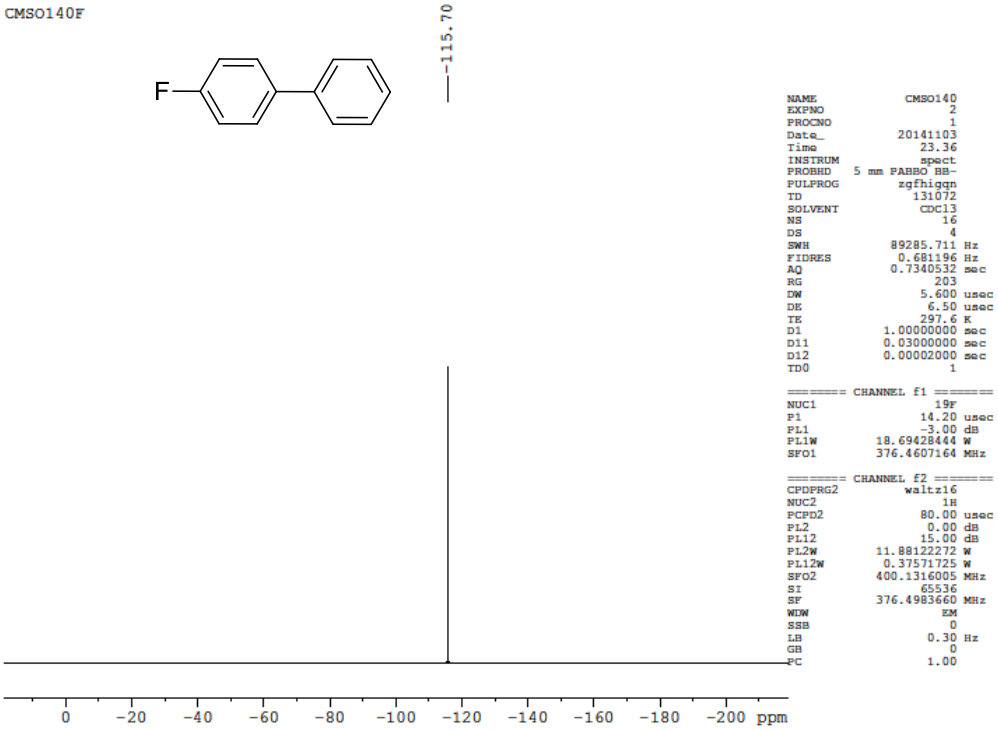


4-Fluoro-1,1'-biphenyl (Table 2, entry 13)



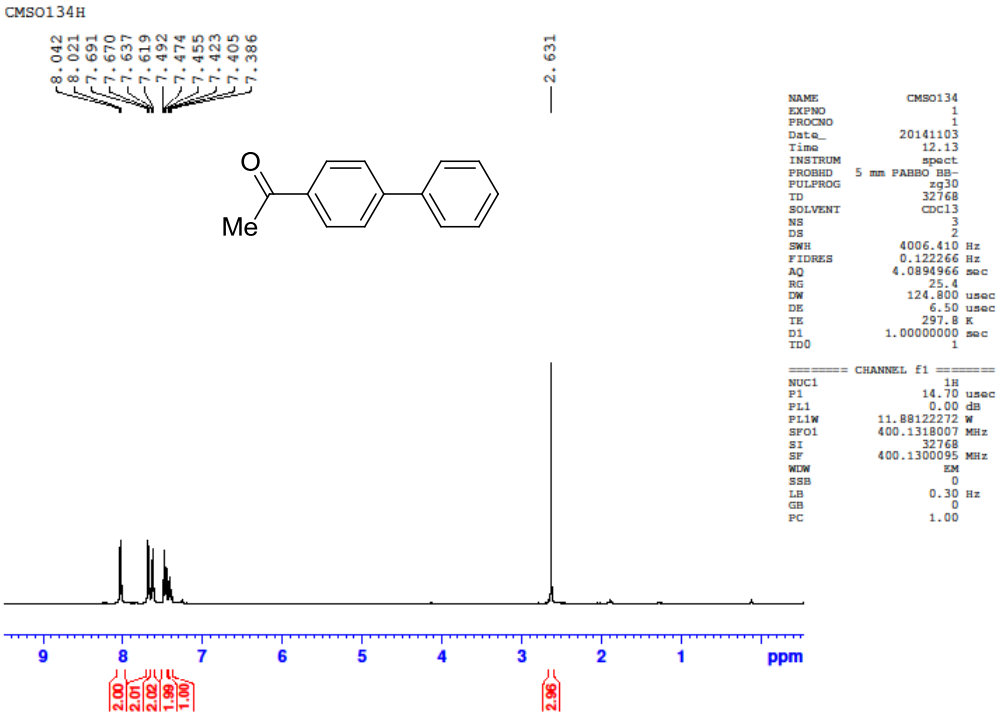


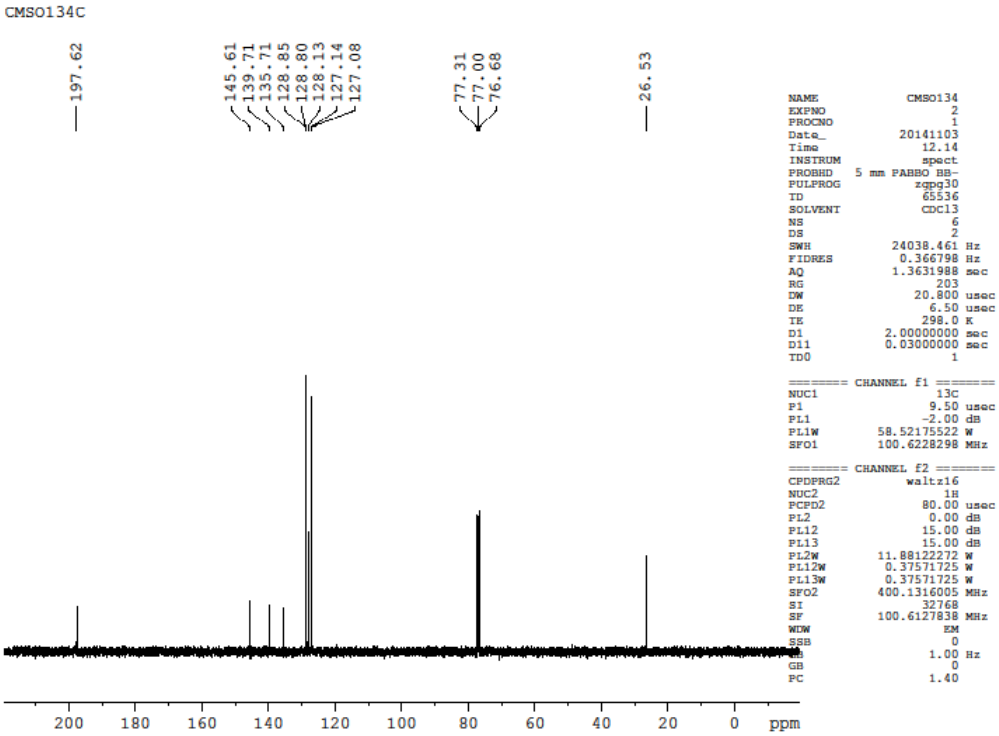
4-Fluoro-1,1'-biphenyl (Table 2, entry 13)



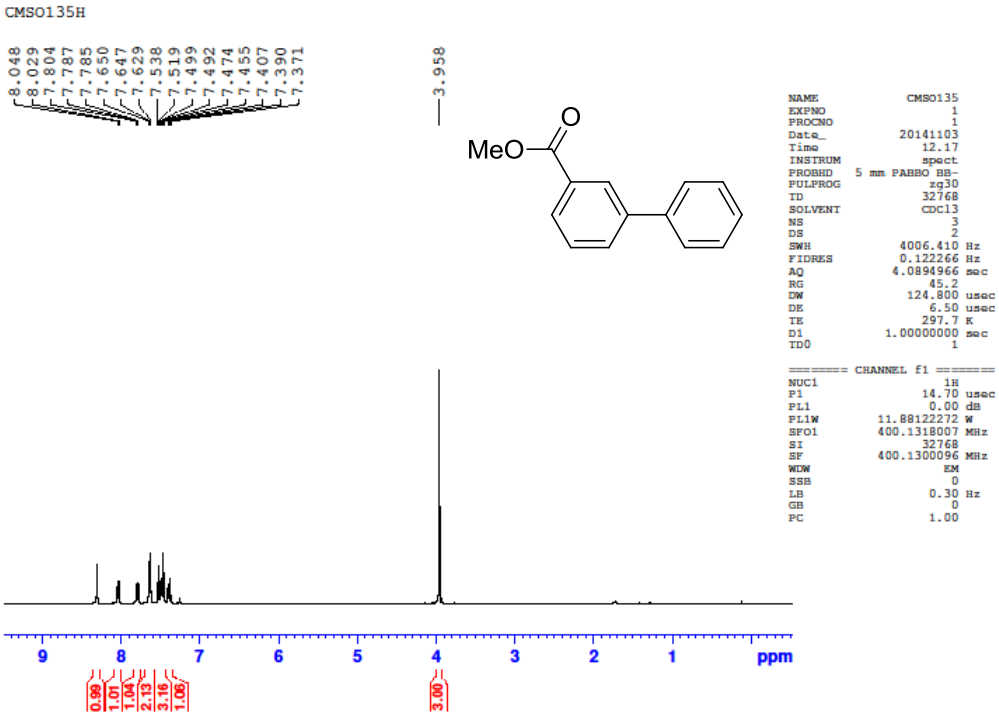
NAME	CMSO140
EXPNO	2
PROCNO	1
Date_	20141103
Time	23.36
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgfhigqn
TD	131072
SOLVENT	CDCl3
NS	16
DS	4
SWH	89285.711 Hz
FIDRES	0.681196 Hz
AQ	0.7340532 sec
RG	203
DW	5.600 usec
DE	6.50 usec
TE	297.6 K
D1	1.00000000 sec
D11	0.03000000 sec
D12	0.00002000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	19F
P1	14.20 usec
PL1	-3.00 dB
PL1W	18.69428444 W
SFO1	376.4607164 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	0.00 dB
PL12	15.00 dB
PL2W	11.88122272 W
PL12W	0.37571725 W
SFO2	400.1316005 MHz
SI	65536
SF	376.4983660 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

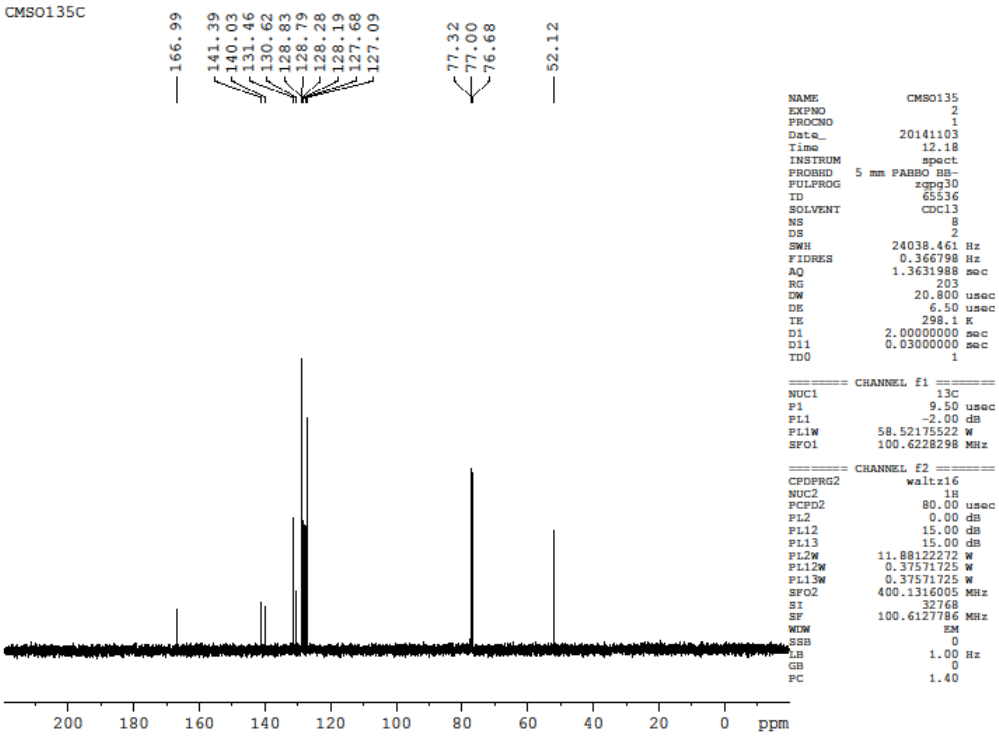
1-([1,1'-Biphenyl]-4-yl)ethanone (Table 6.2, entry 14)



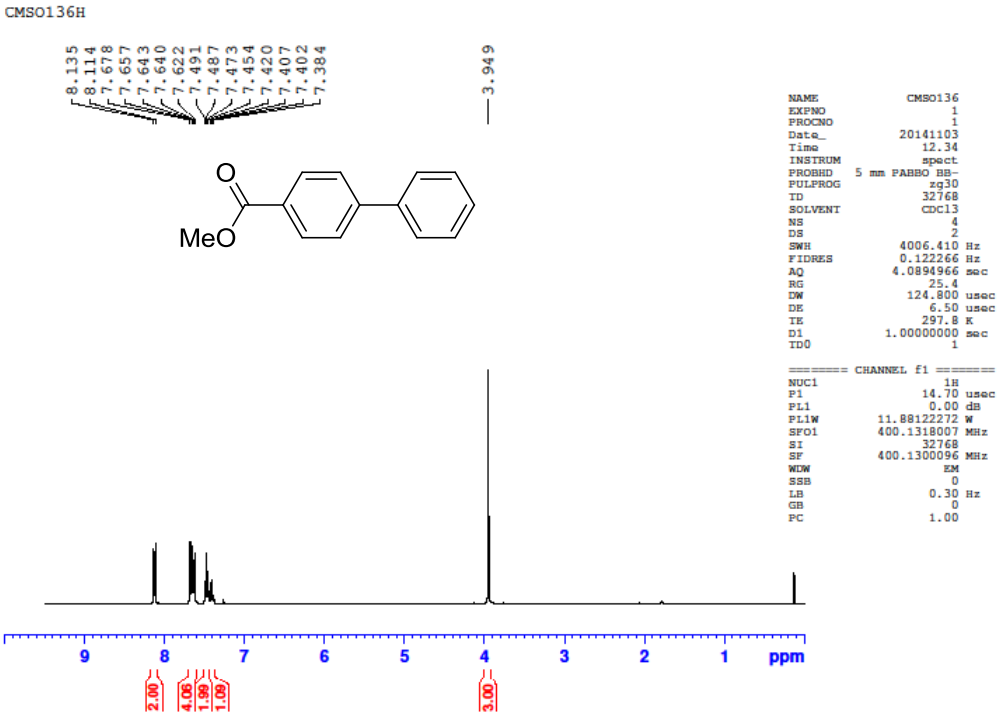


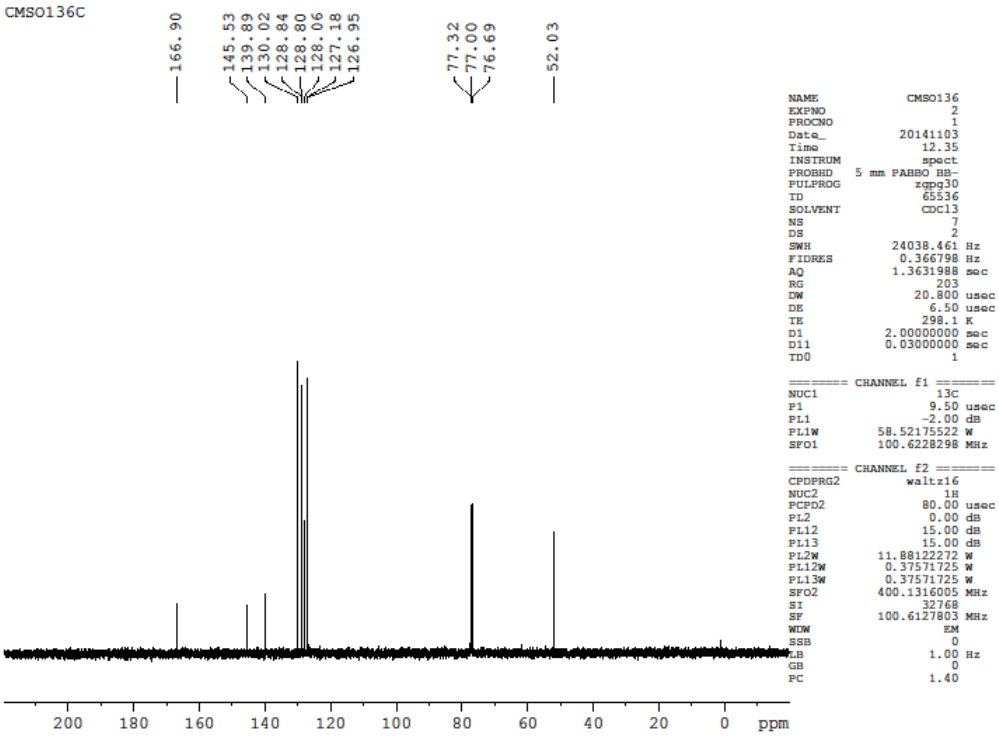
Methyl [1,1'-biphenyl]-3-carboxylate (Table 6.2, entry 15-18)





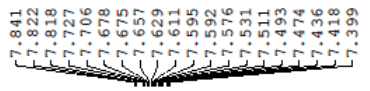
Methyl [1,1'-biphenyl]-4-carboxylate (Table 6.2, entry 19-20)

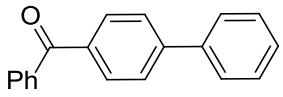




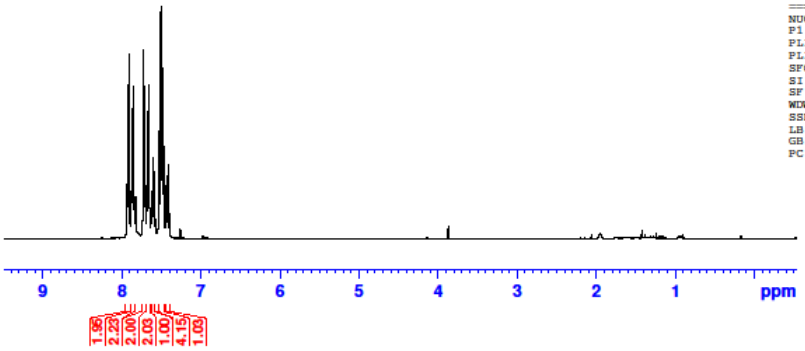
[1,1'-Biphenyl]-4-yl(phenyl)methanone (Table 6.2, entry 21)

CMSO169H



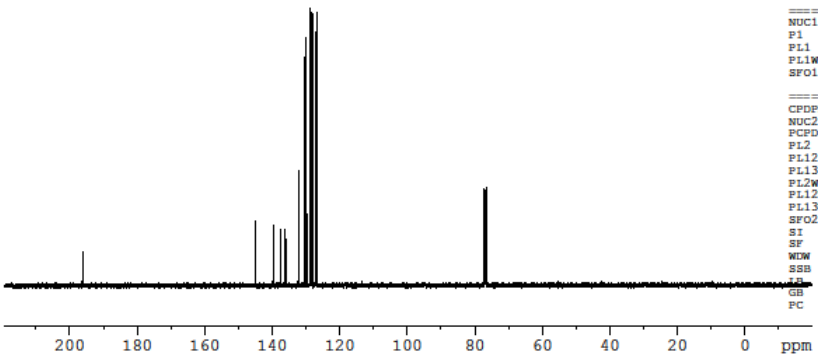



```
NAME              CMSO169
EXPNO                   1
PROCNO                  1
Date_            20141106
Time                14.06
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  32768
SOLVENT             CDCl3
NS                      8
DS                      2
SWH              4006.410 Hz
FIDRES           0.122266 Hz
AQ               4.0894966 sec
RG                   25.4
DW                124.800 usec
DE                  6.50 usec
TE                 300.0 K
D1              1.00000000 sec
TD0                     1

======== CHANNEL f1 =======
NUC1                   1H
P1                  14.70 usec
PL1                  0.00 dB
PL1W           11.88122272 W
SFO1           400.1318007 MHz
SI                   32768
SF             400.1300093 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

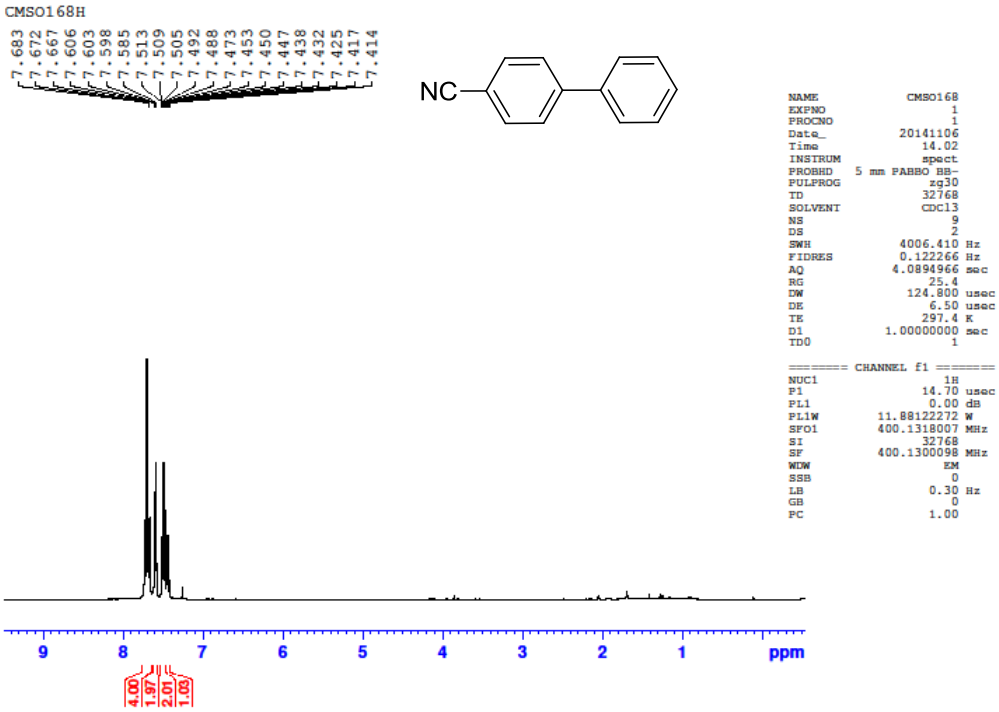


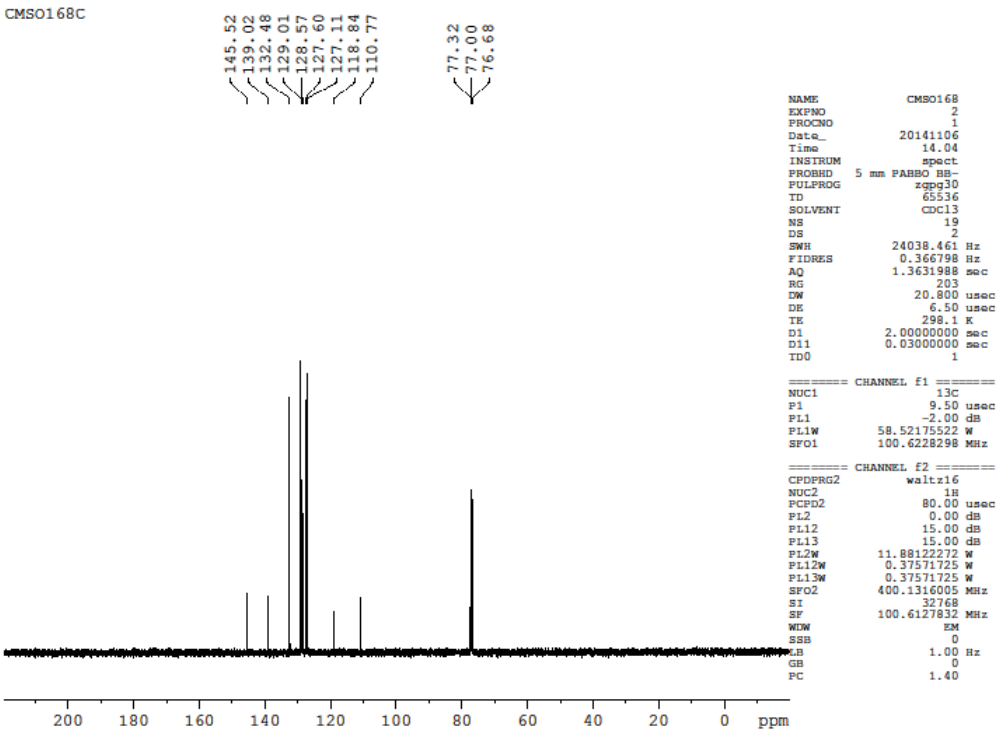
CMSO169C


```
NAME              CMSO169
EXPNO                   2
PROCNO                  1
Date_            20141106
Time                14.09
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                  65536
SOLVENT             CDCl3
NS                     24
DS                      2
SWH              24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                    203
DW                20.800 usec
DE                  6.50 usec
TE                 298.2 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                     1

======== CHANNEL f1 =======
NUC1                   13C
P1                   9.50 usec
PL1                 -2.00 dB
PL1W           58.52175522 W
SFO1           100.6228298 MHz

======== CHANNEL f2 =======
CPDPRG2            waltz16
NUC2                   1H
PCPD2               80.00 usec
PL2                  0.00 dB
PL12                15.00 dB
PL13                15.00 dB
PL2W           11.88122272 W
PL12W           0.37571725 W
PL13W           0.37571725 W
SFO2           400.1316005 MHz
SI                   32768
SF             100.6127895 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```



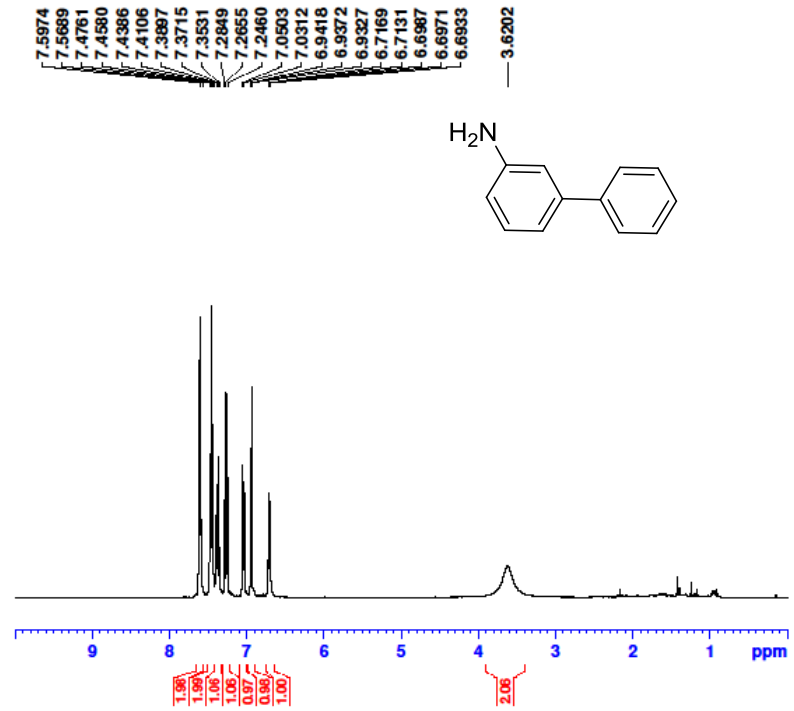
[1,1'-Biphenyl]-4-carbonitrile (Table 6.2, entry 22)





[1,1'-Biphenyl]-3-amine (Table 6.2, entry 23)

CMSO145H




```
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EXPNO                   1
PROCNO                  1
Date_            20141106
Time                13.15
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  32768
SOLVENT             CDCl3
NS                      4
DS                      2
SWH              6393.862 Hz
FIDRES           0.195125 Hz
AQ               2.5625076 sec
RG                   40.3
DW                 78.200 usec
DE                  6.50 usec
TE                 297.4 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  14.70 usec
PL1                  0.00 dB
PL1W          11.88122272 W
SFO1          400.1318007 MHz
SI                  32768
SF            400.1300098 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```
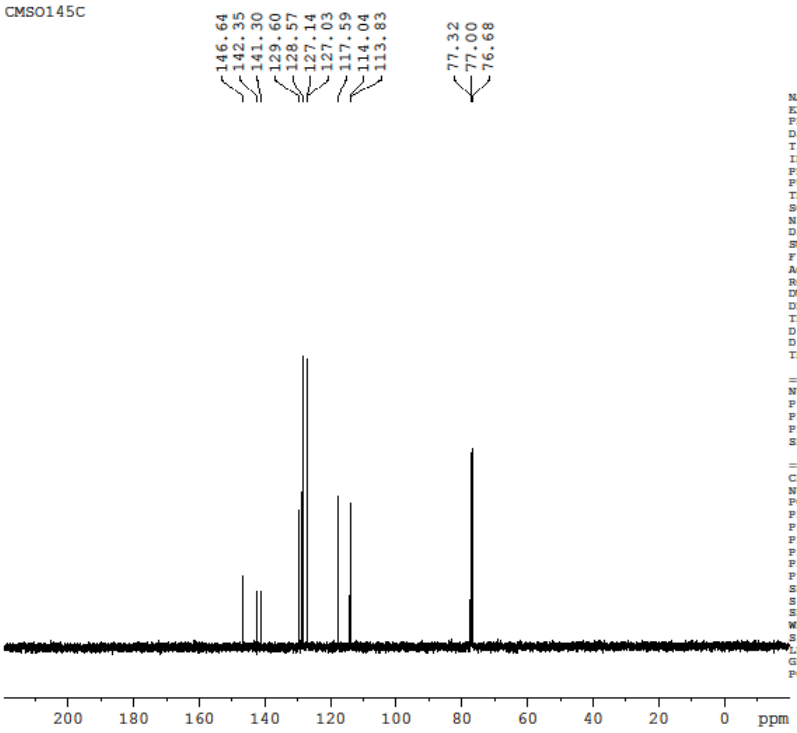
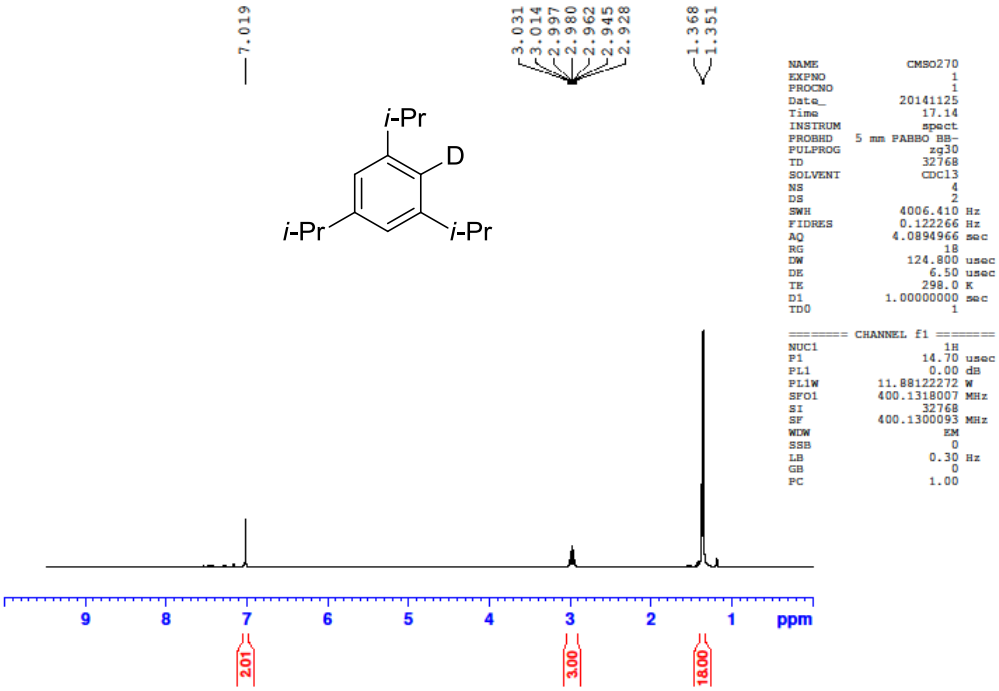

CMSO145C



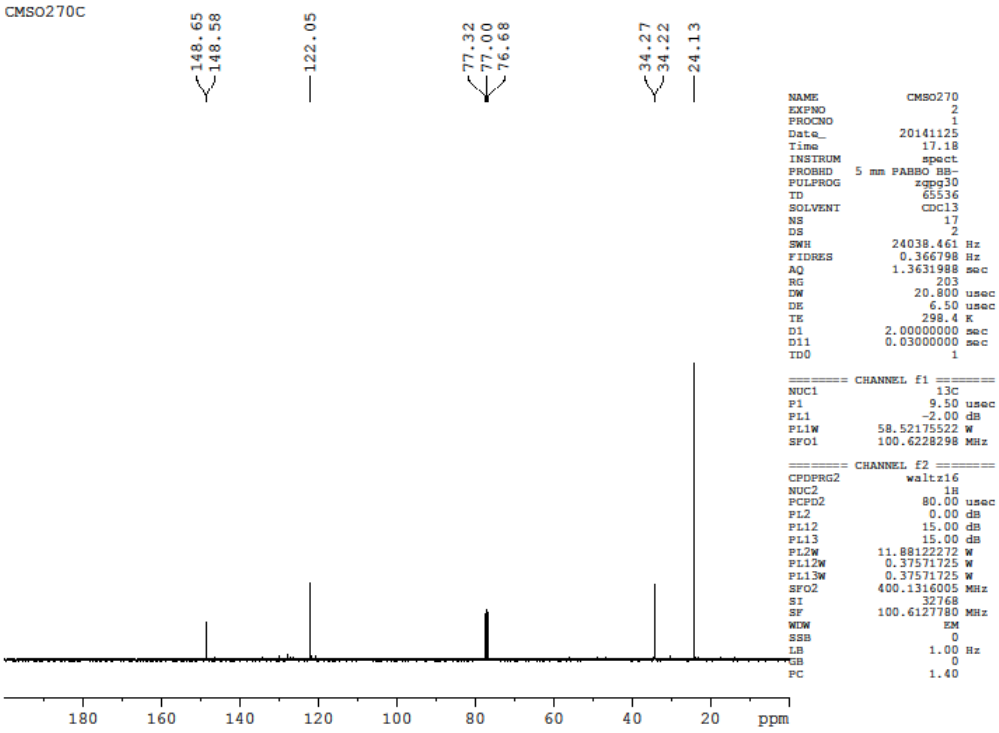

```
NAME              CMSO145
EXPNO                   2
PROCNO                  1
Date_            20141106
Time                13.16
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                  65536
SOLVENT             CDCl3
NS                     18
DS                      2
SWH              24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                    203
DW                 20.800 usec
DE                  6.50 usec
TE                 298.0 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   13C
P1                   9.50 usec
PL1                 -2.00 dB
PL1W          58.52175522 W
SFO1          100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2            waltz16
NUC2                   1H
PCPD2               80.00 usec
PL2                  0.00 dB
PL12                15.00 dB
PL13                15.00 dB
PL2W          11.88122272 W
PL12W          0.37571725 W
PL13W          0.37571725 W
SFO2          400.1316005 MHz
SI                  32768
SF            100.6127831 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```

Benzene-*d*, 2,4,6-tris(1-methylethyl)- (Scheme 6.1)

CMSO270H

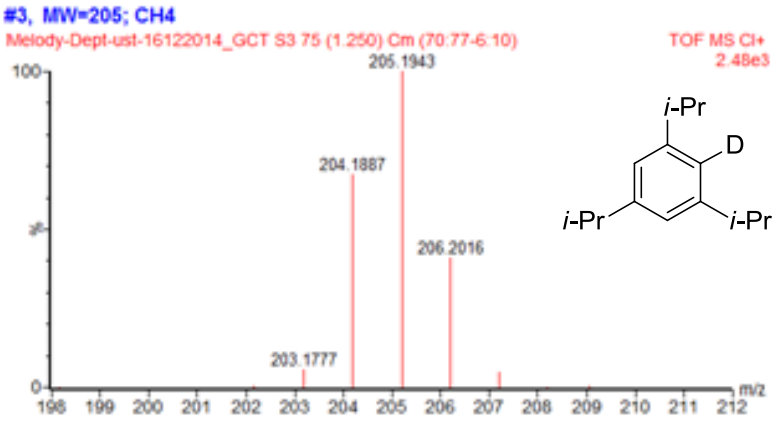


CMSO270C



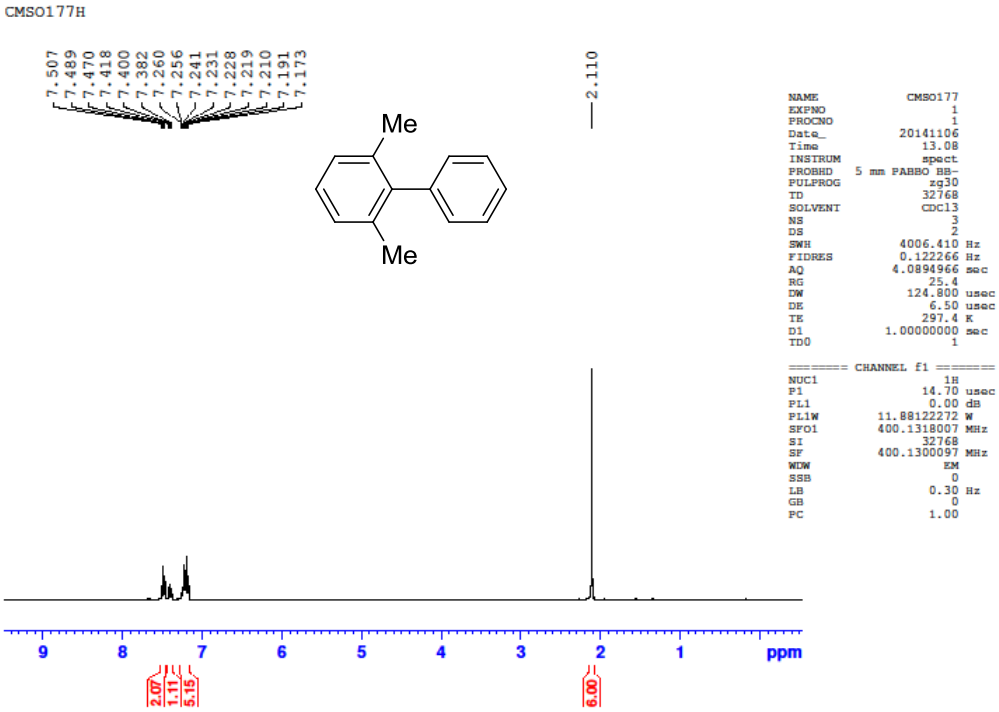
Benzene-*d*, 2,4,6-tris(1-methylethyl)- (Scheme 6.1)

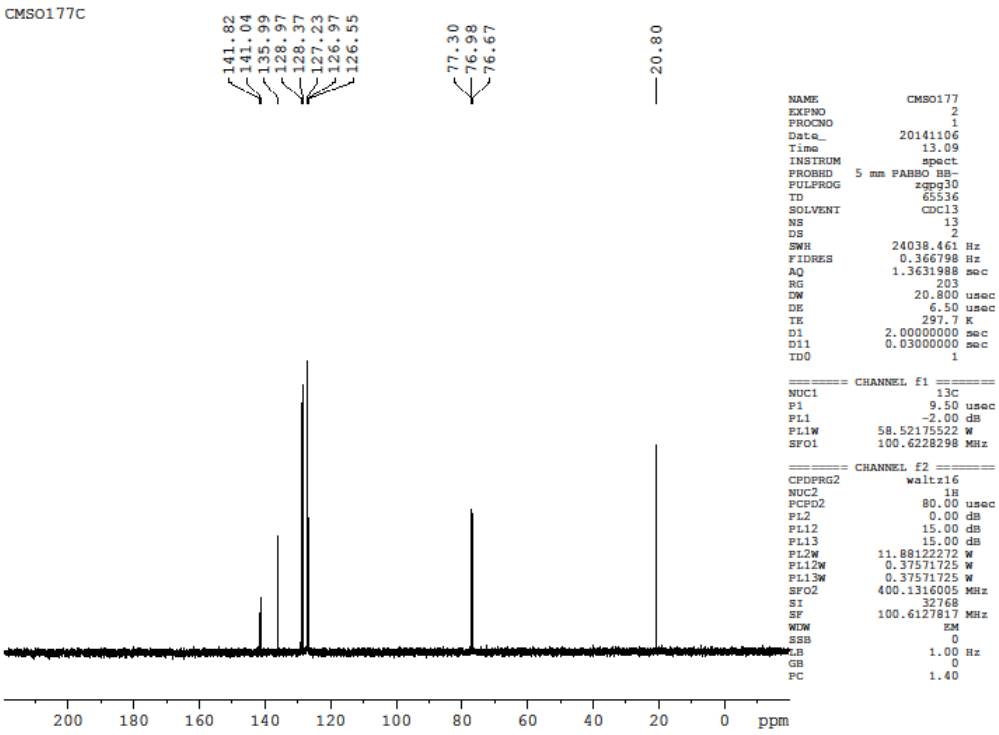
HS



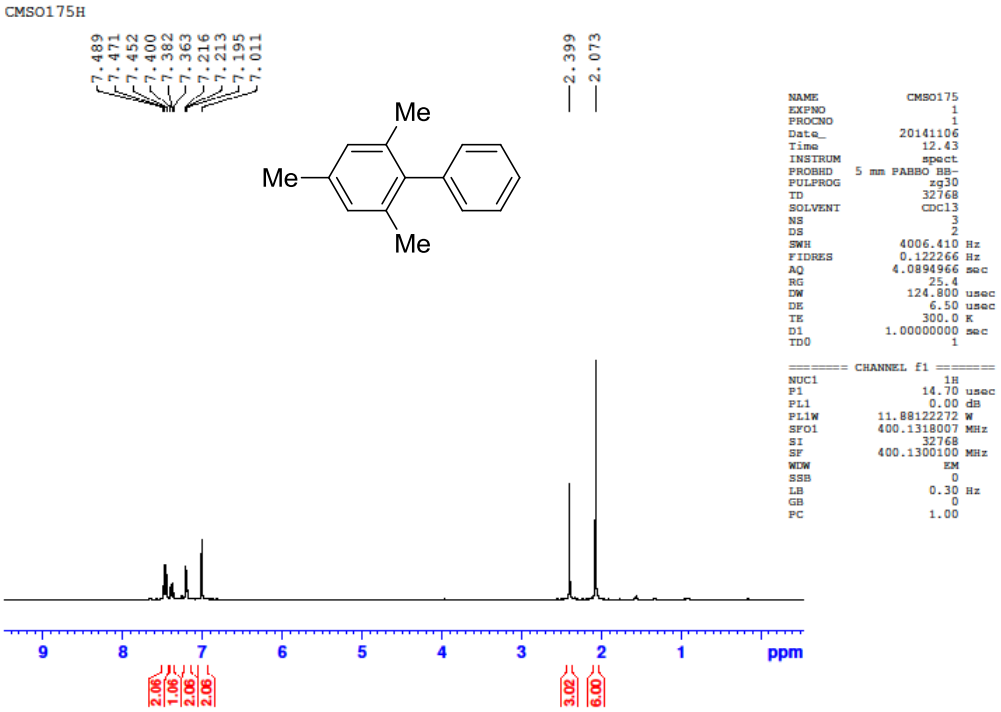
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
206.2016	206.2019	-0.3	-1.5	3.5	5.9	C15 H24 D

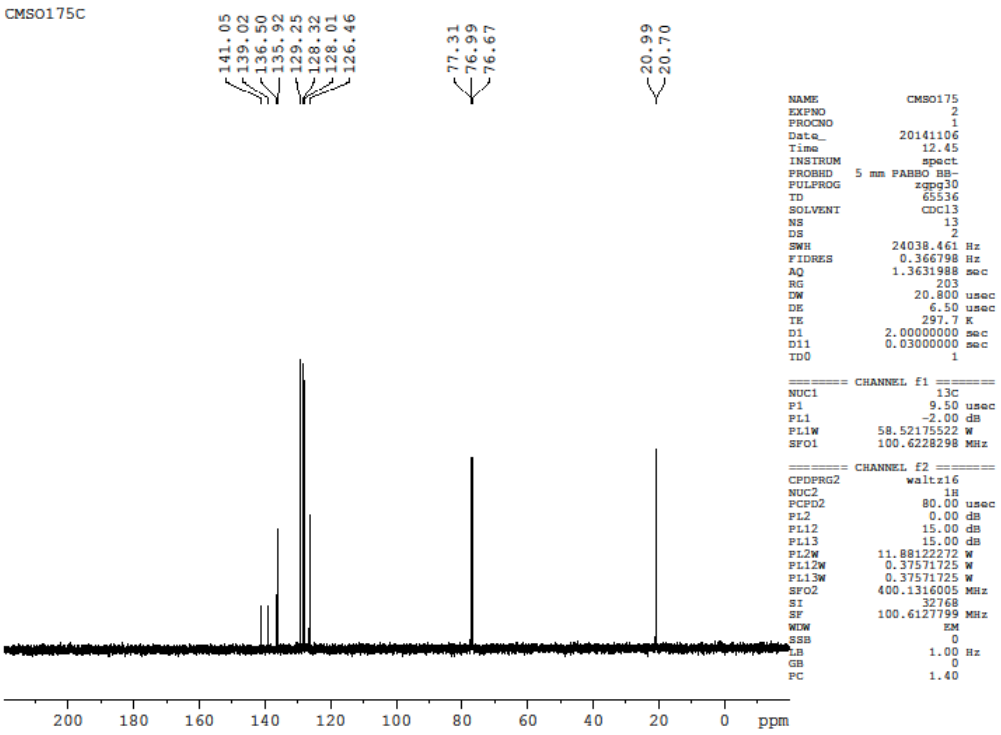
2,6-Dimethyl-1,1'-biphenyl (Table 6.4, entry 1-2)



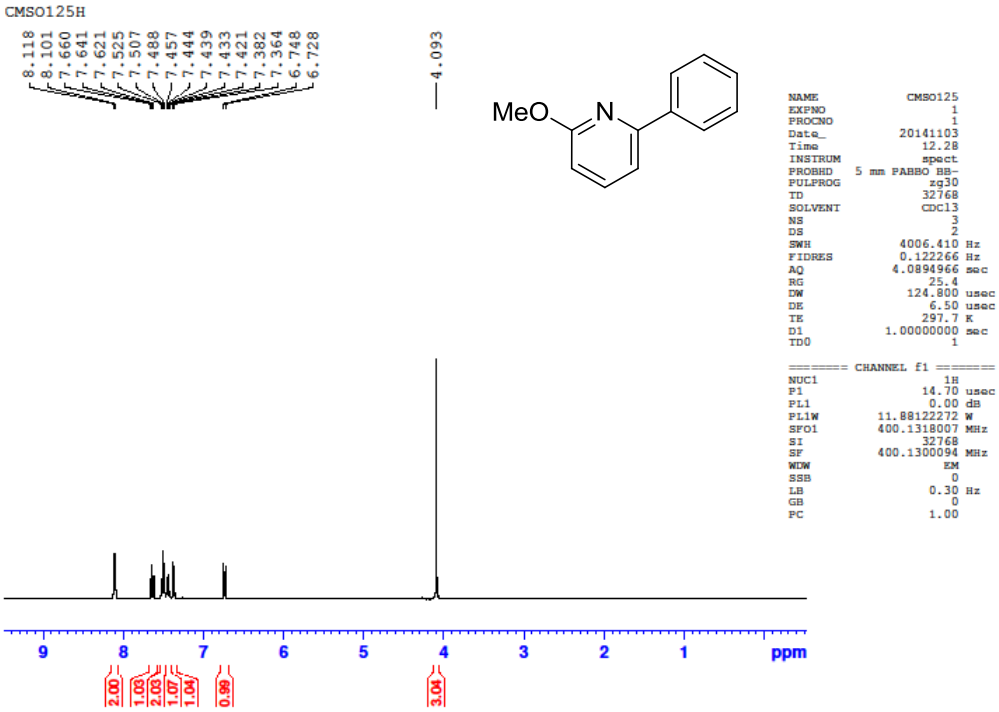


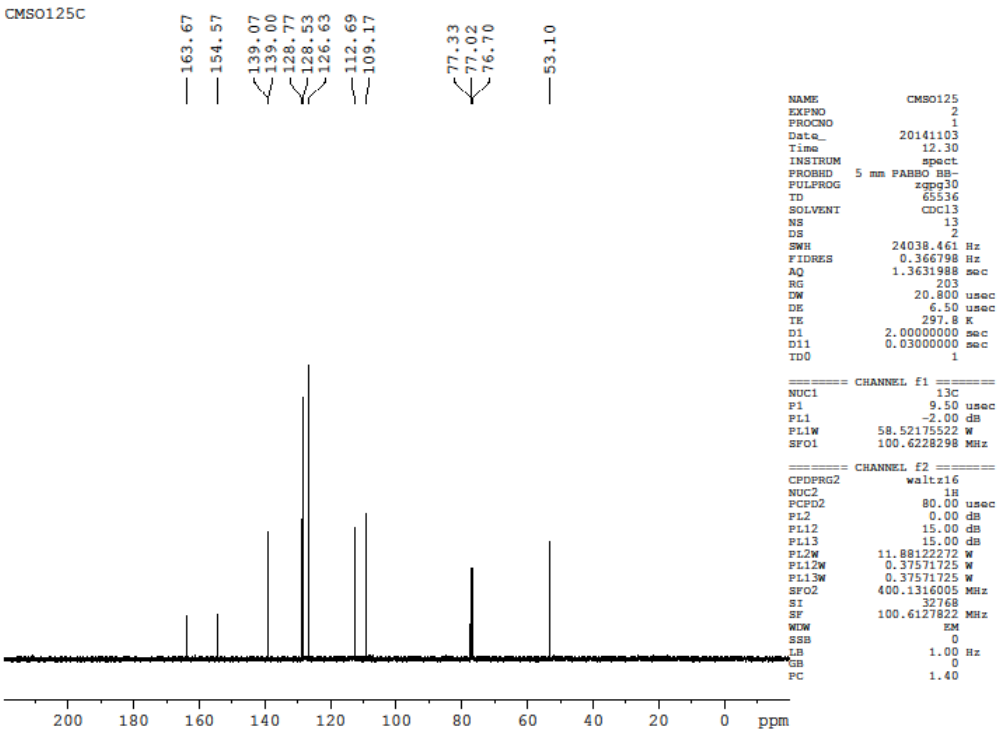
2,4,6-Trimethyl-1,1'-biphenyl (Table 6.4, entry 3-4)



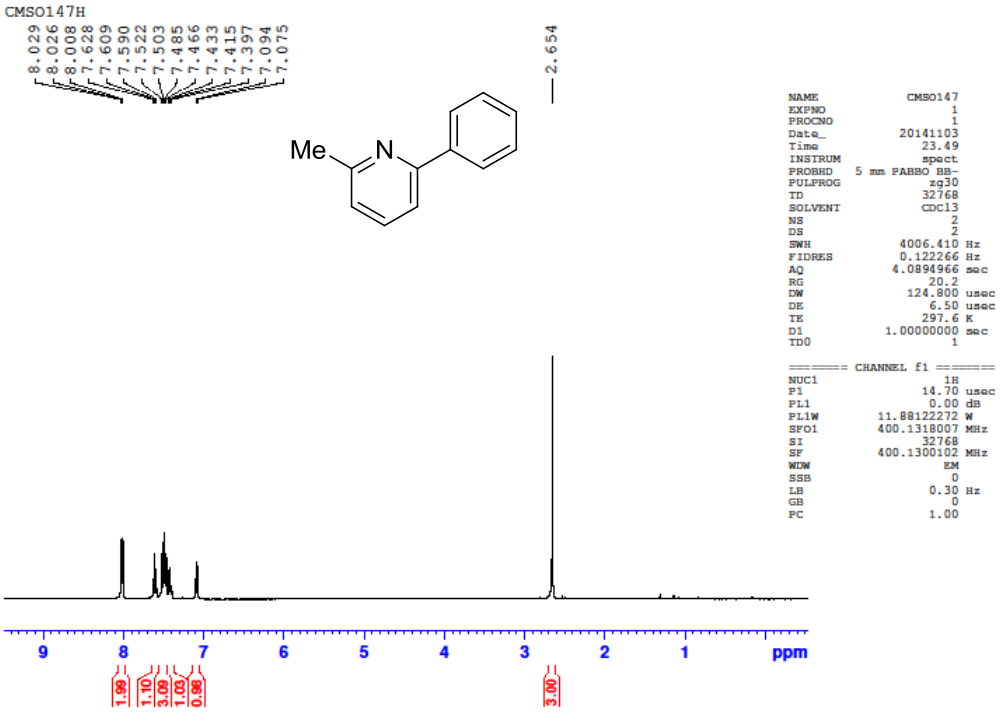


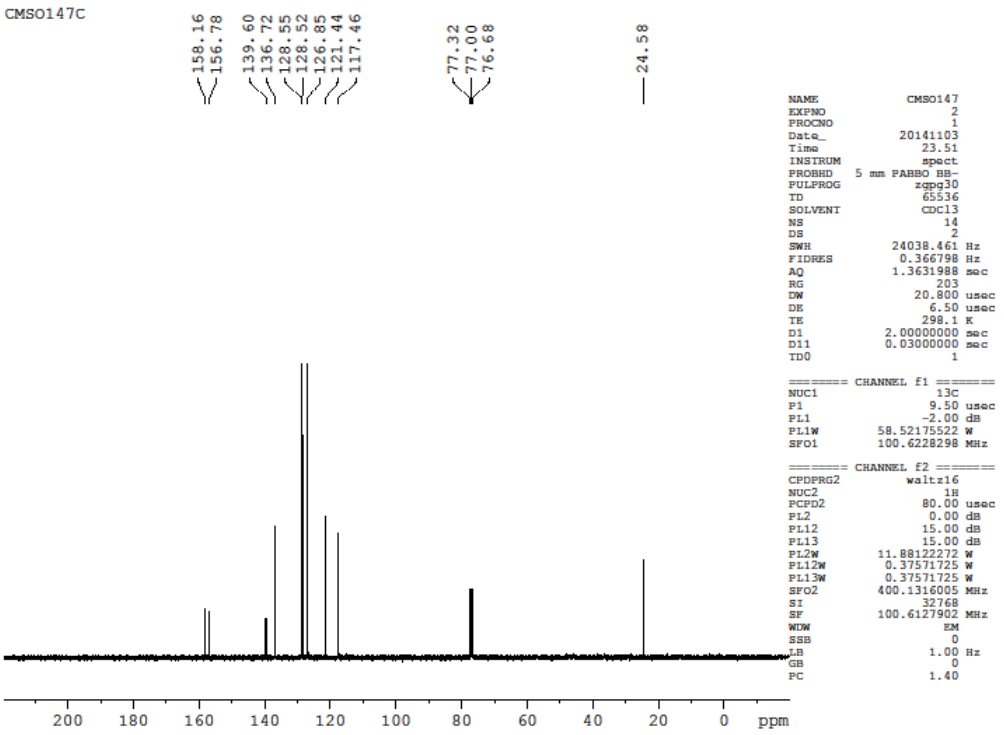
2-Methoxy-6-phenylpyridine (Table 6.5, entry 1)





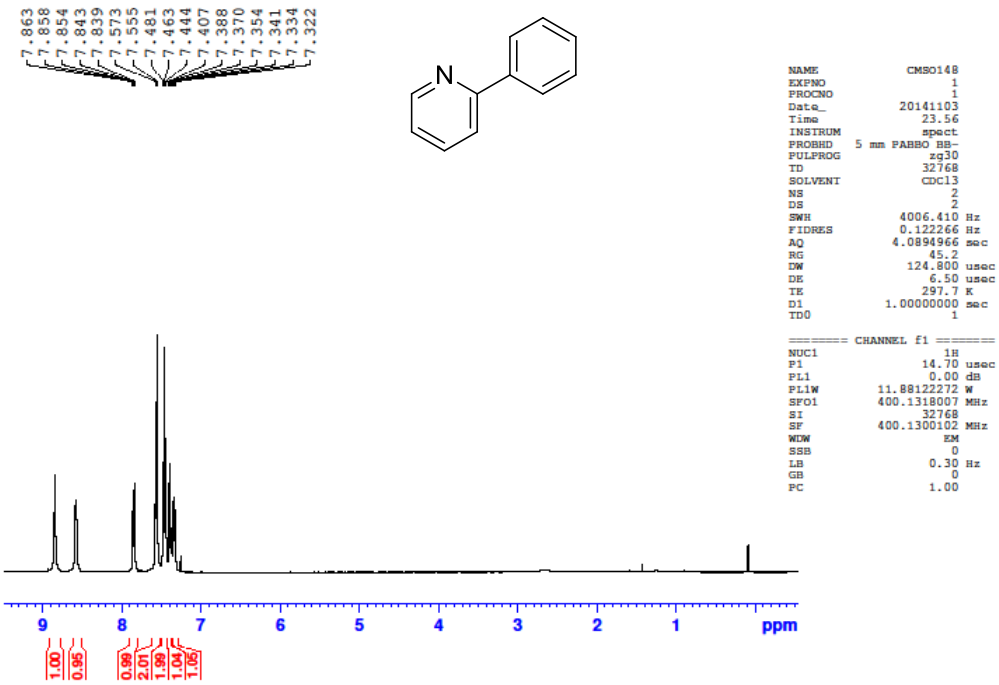
2-Methyl-6-phenylpyridine (Table 6.5, entry 2)





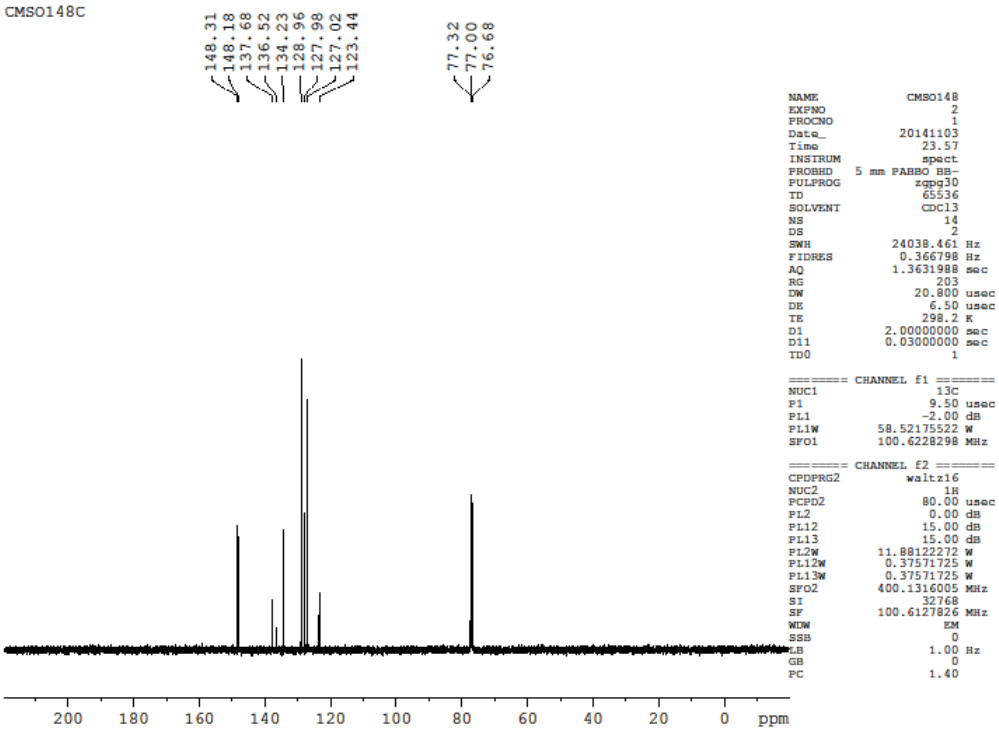
3-Phenylpyridine (Table 6.5, entry 3)

CMSO148H




```
NAME              CMSO148
EXPNO                   1
PROCNO                  1
Date_            20141103
Time                23.56
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  32768
SOLVENT             CDCl3
NS                      2
DS                      2
SWH              4006.410 Hz
FIDRES           0.122266 Hz
AQ               4.0894966 sec
RG                   45.2
DW                124.800 usec
DE                  6.50 usec
TE                 297.7 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 =======
NUC1                  1H
P1                 14.70 usec
PL1                0.00 dB
PL1W        11.88122272 W
SFO1        400.1318007 MHz
SI                 32768
SF          400.1300102 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```

CMSO148C




```
NAME              CMSO148
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PROCNO                  1
Date_            20141103
Time                23.57
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                  65536
SOLVENT             CDCl3
NS                     14
DS                      2
SWH              24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                    203
DW                 20.800 usec
DE                  6.50 usec
TE                 298.2 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1

======== CHANNEL f1 =======
NUC1                  13C
P1                  9.50 usec
PL1                -2.00 dB
PL1W        58.52175522 W
SFO1        100.6228298 MHz

======== CHANNEL f2 =======
CPDPRG2           waltz16
NUC2                  1H
PCPD2              80.00 usec
PL2                0.00 dB
PL12              15.00 dB
PL13              15.00 dB
PL2W        11.88122272 W
PL12W        0.37571725 W
PL13W        0.37571725 W
SFO2        400.1316005 MHz
SI                 32768
SF          100.6127826 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```
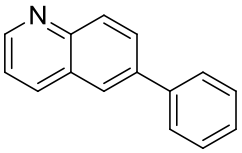
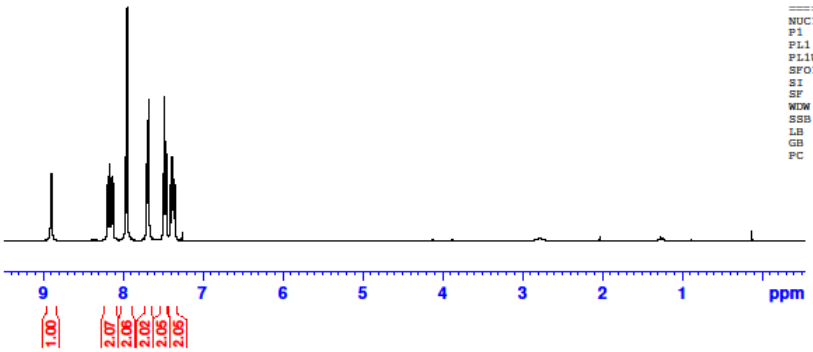

6-Phenylquinoline (Table 6.5, entry 4)

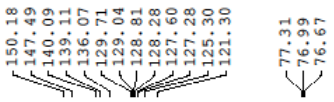
CMSO155H



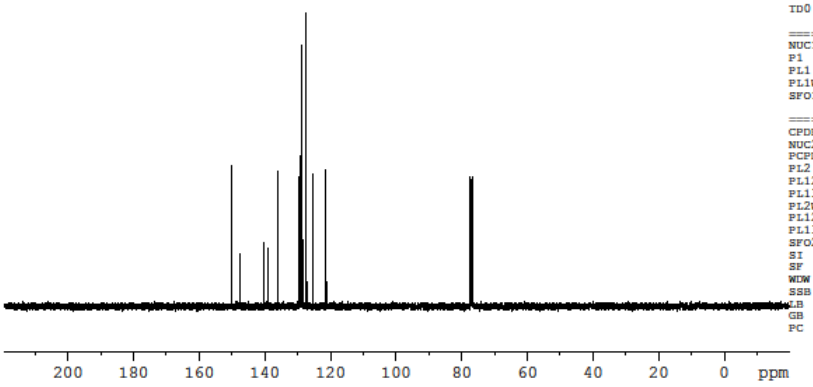

```
NAME                CMSO155
EXPNO                     1
PROCNO                    1
Date_              20141106
Time                  12.48
INSTRUM               spect
PROBHD   5 mm PABBO BB-
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                        3
DS                        2
SWH                4006.410 Hz
FIDRES             0.122266 Hz
AQ                 4.0894966 sec
RG                     25.4
DW                   124.800 usec
DE                     6.50 usec
TE                    300.0 K
D1                 1.00000000 sec
TD0                       1

======== CHANNEL f1 =======
NUC1                      1H
P1                     14.70 usec
PL1                     0.00 dB
PL1W              11.88122272 W
SFO1              400.1318007 MHz
SI                      32768
SF                400.1300098 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00
```



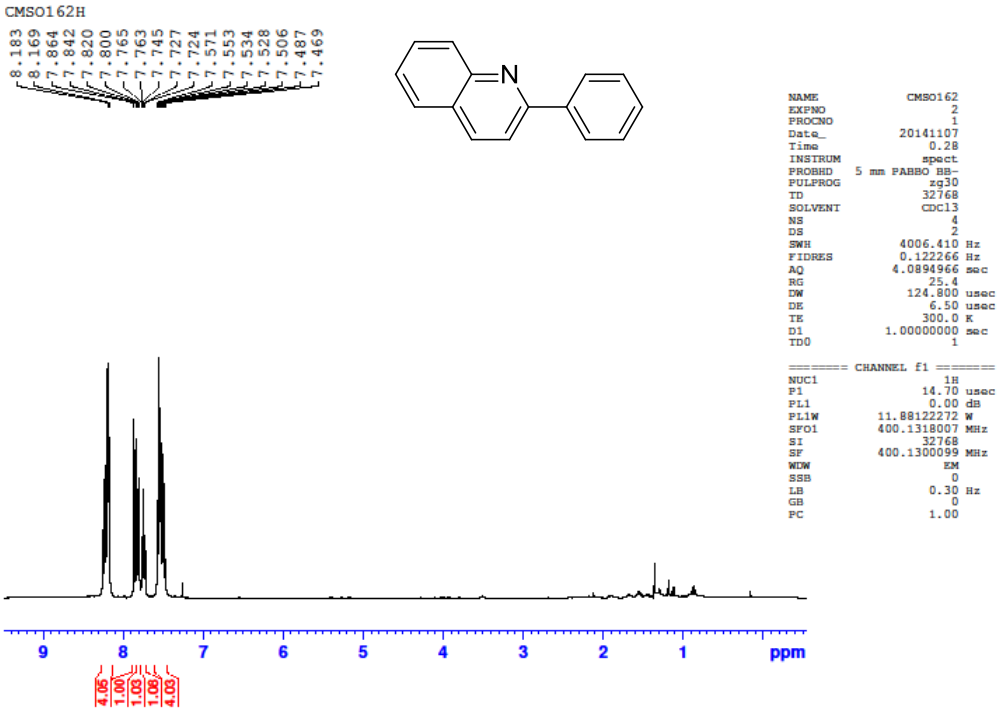
CMSO155C

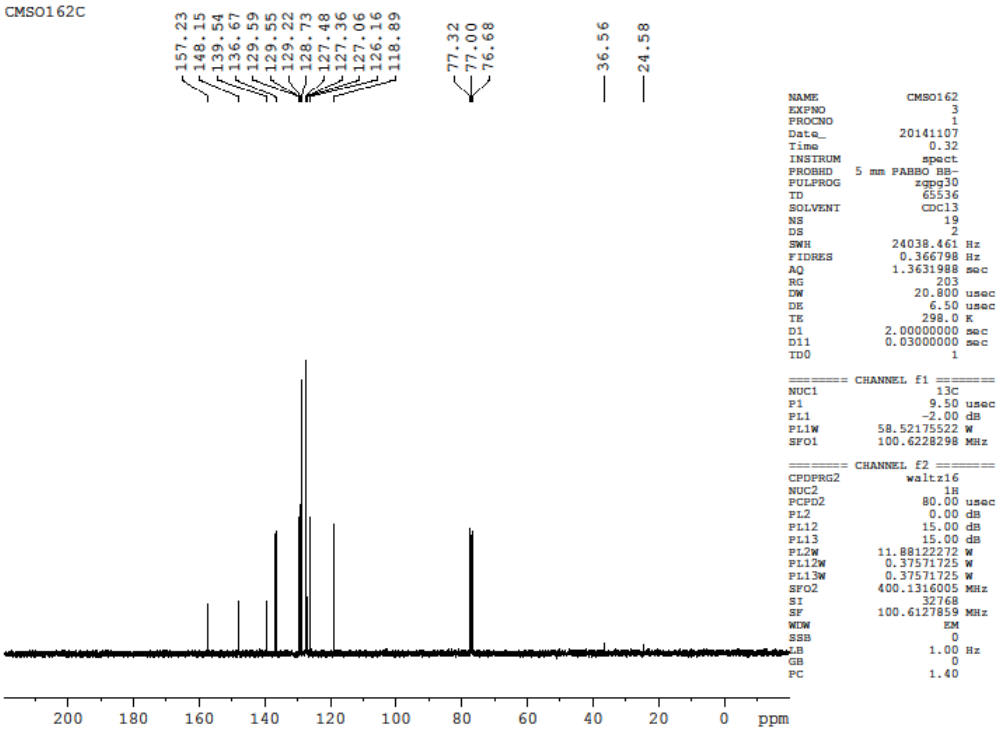



```
NAME                CMSO155
EXPNO                     2
PROCNO                    1
Date_              20141106
Time                  12.49
INSTRUM               spect
PROBHD   5 mm PABBO BB-
PULPROG             zgpg30
TD                    65536
SOLVENT               CDCl3
NS                       15
DS                        2
SWH               24038.461 Hz
FIDRES             0.366798 Hz
AQ                 1.3631988 sec
RG                      203
DW                   20.800 usec
DE                     6.50 usec
TE                    297.8 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                       1

======== CHANNEL f1 =======
NUC1                      13C
P1                      9.50 usec
PL1                    -2.00 dB
PL1W              58.52175522 W
SFO1              100.6228298 MHz

======== CHANNEL f2 =======
CPDPRG2                waltz16
NUC2                      1H
PCPD2                  80.00 usec
PL2                     0.00 dB
PL12                   15.00 dB
PL13                   15.00 dB
PL2W              11.88122272 W
PL12W              0.37571725 W
PL13W              0.37571725 W
SFO2              400.1316005 MHz
SI                      32768
SF                100.6127873 MHz
WDW                       EM
SSB                        0
LB                      1.00 Hz
GB                         0
PC                      1.40
```

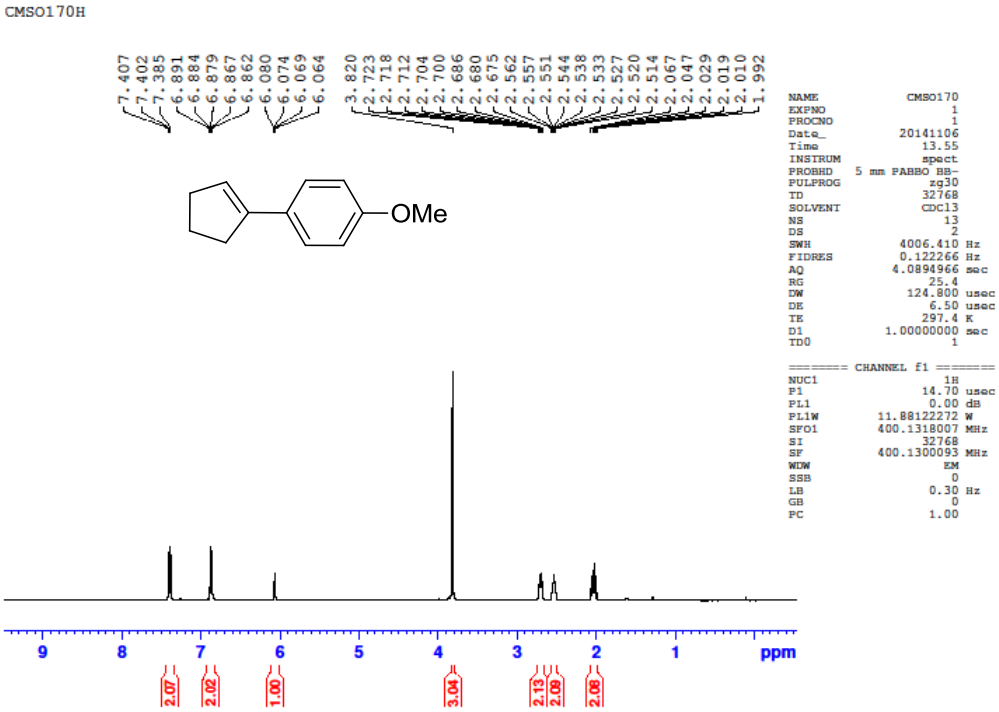


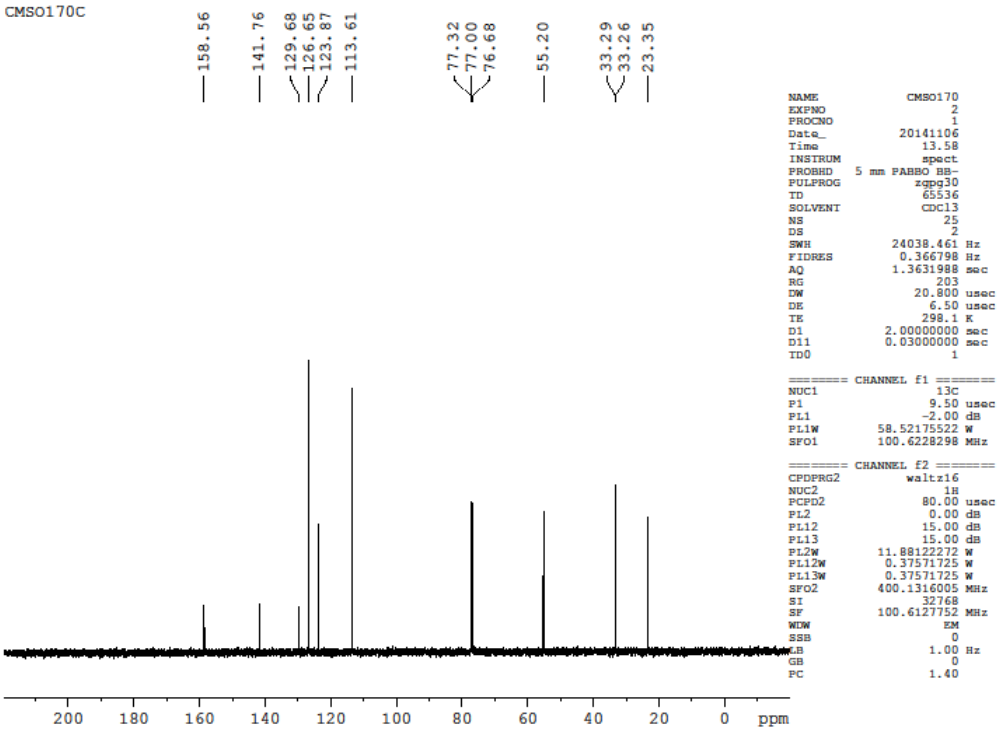
2-Phenylquinoline (Table 6.5, entry 5)





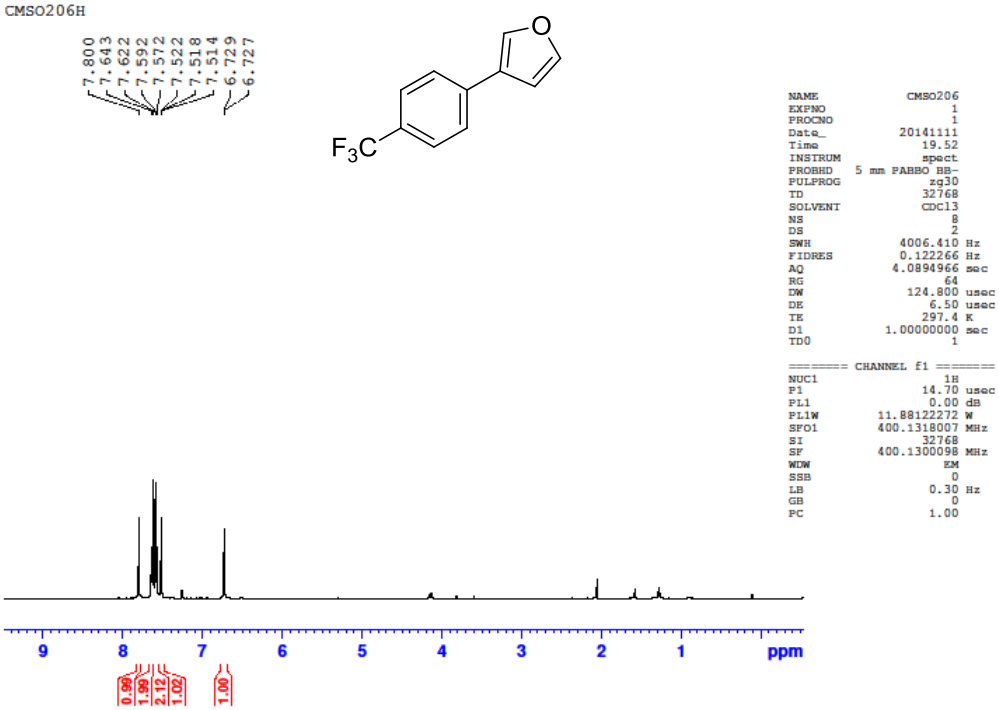
1-Cyclopentenyl-4-methoxybenzene (Table 6.5, entry 6)



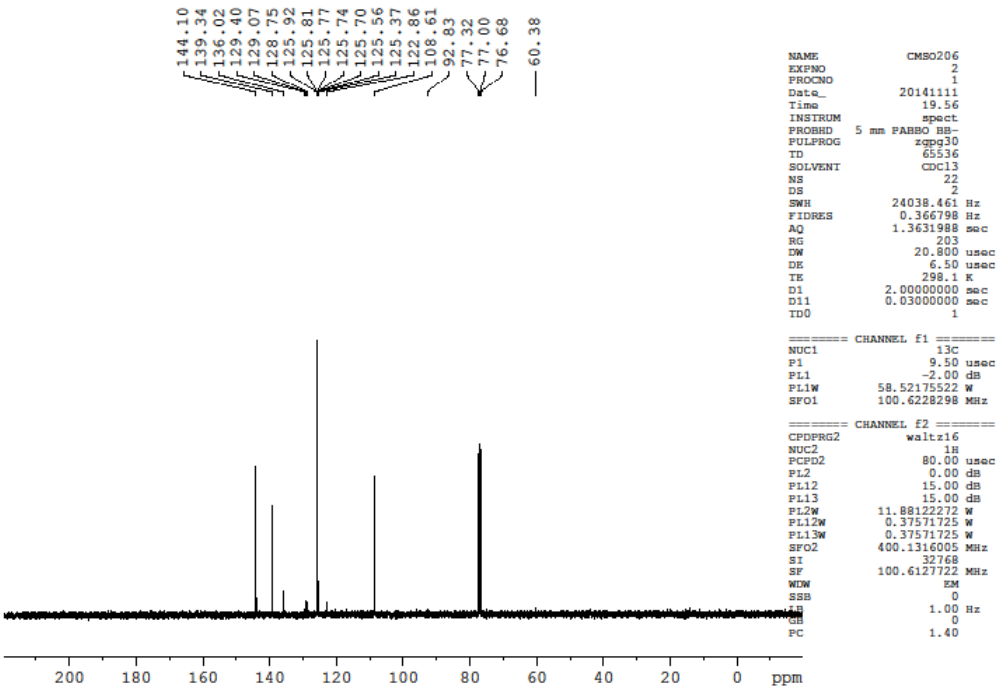


3-(4-(Trifluoromethyl)phenyl)furan (Table 6.6, entry 1)

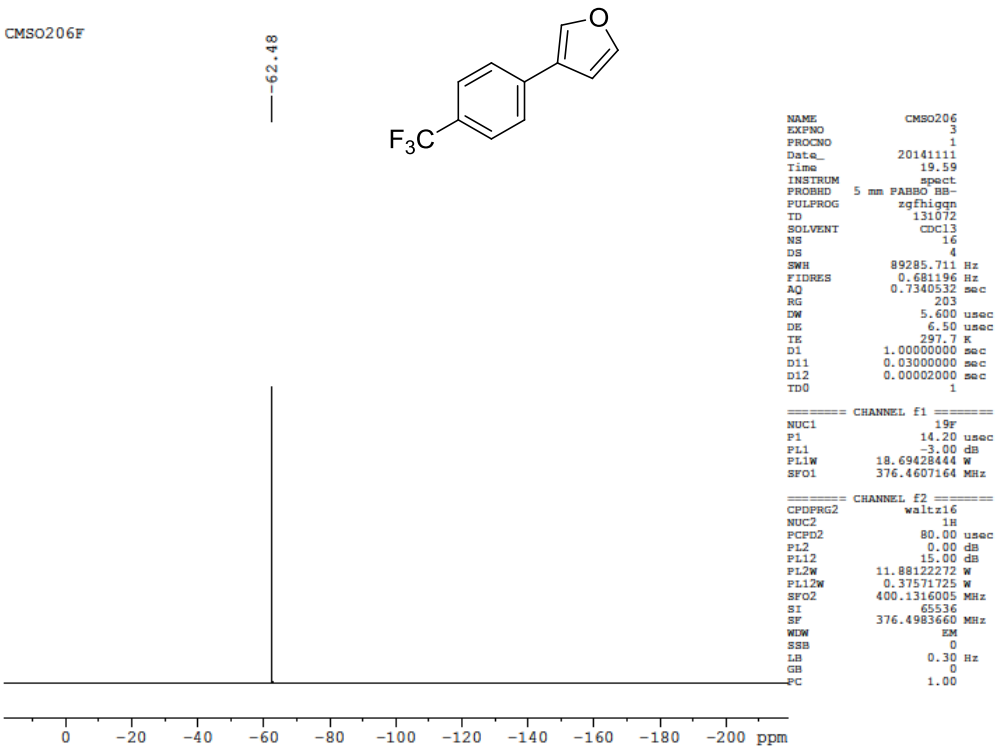
CMSO206H



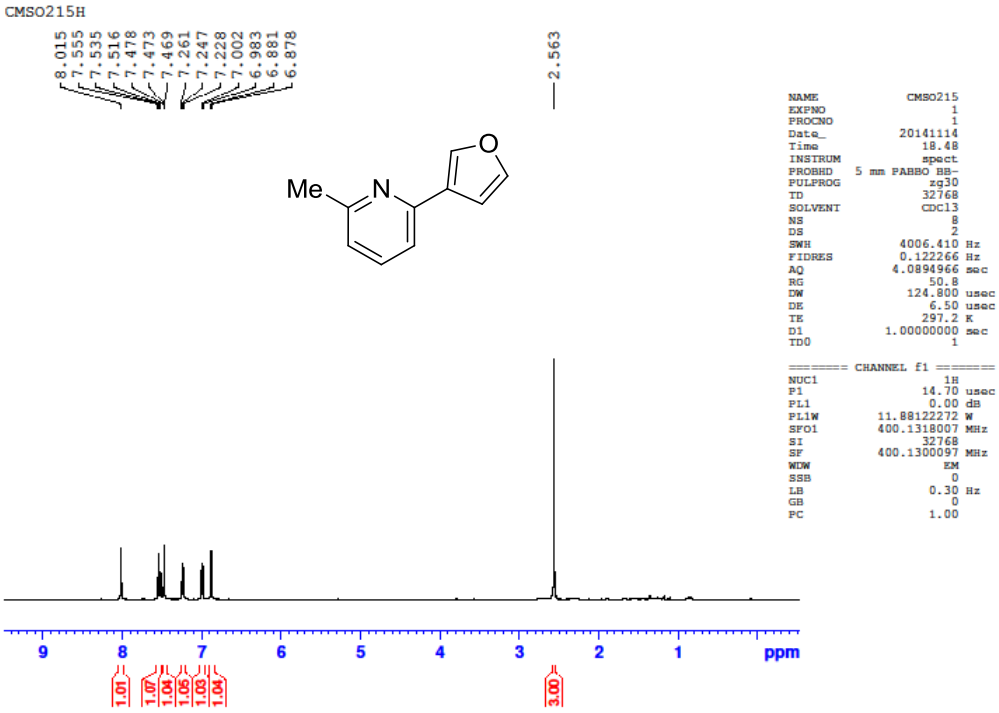
CMSO206C

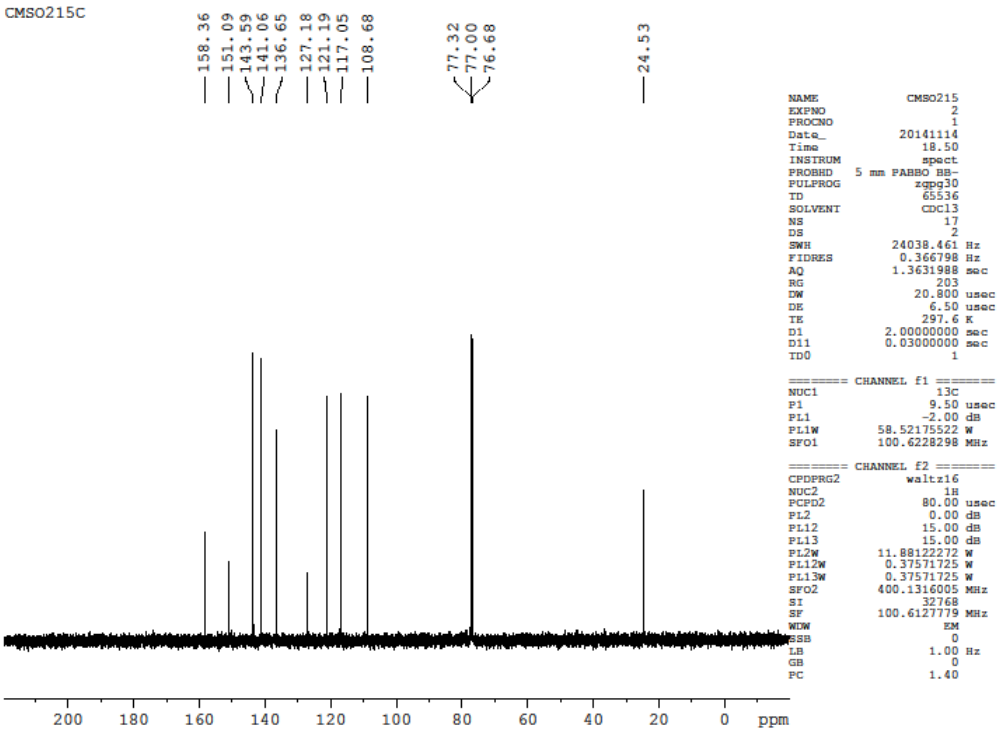


3-(4-(Trifluoromethyl)phenyl)furan (Table 6.6, entry 1)



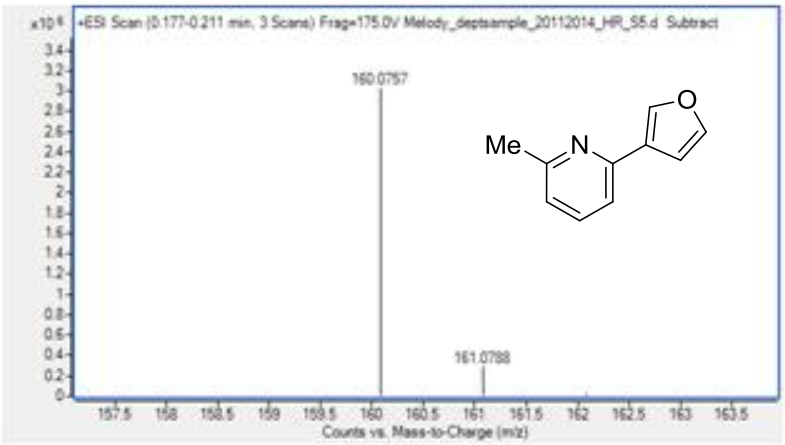
2-(Furan-3-yl)-6-methylpyridine (Table 6.6, entry 2)





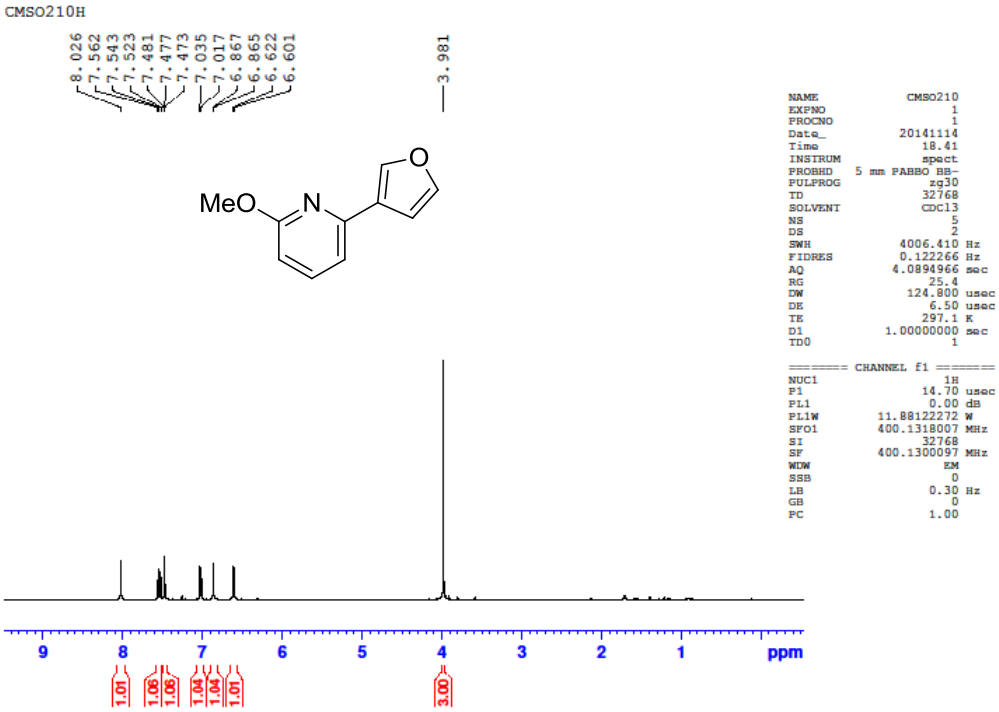
2-(Furan-3-yl)-6-methylpyridine (Table 6.6, entry 2)

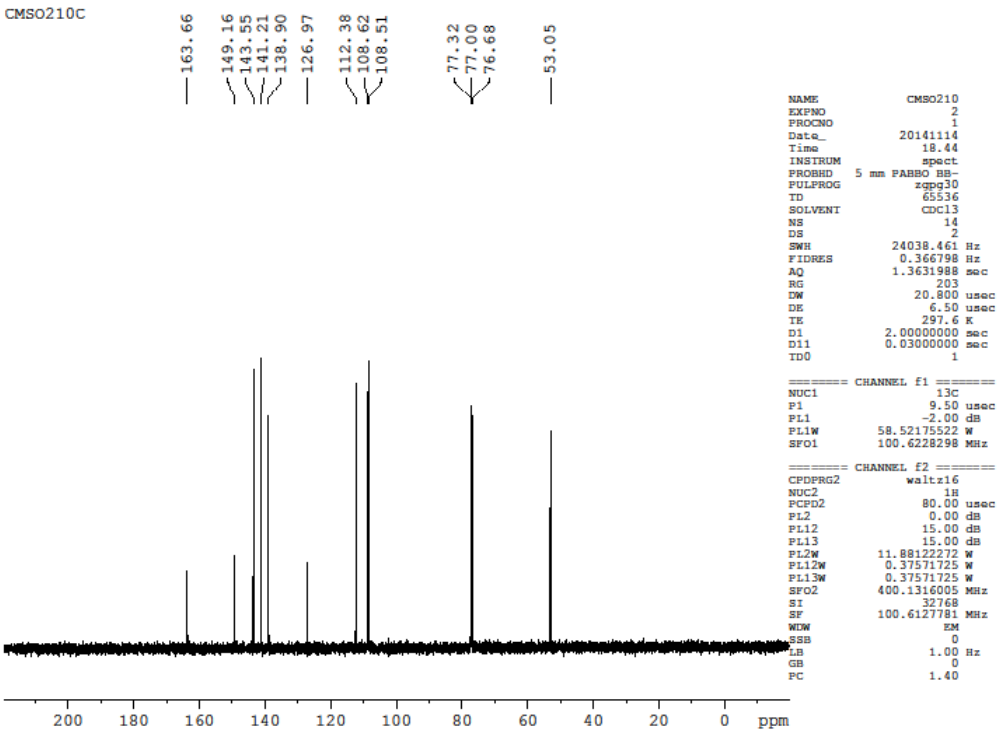
HS



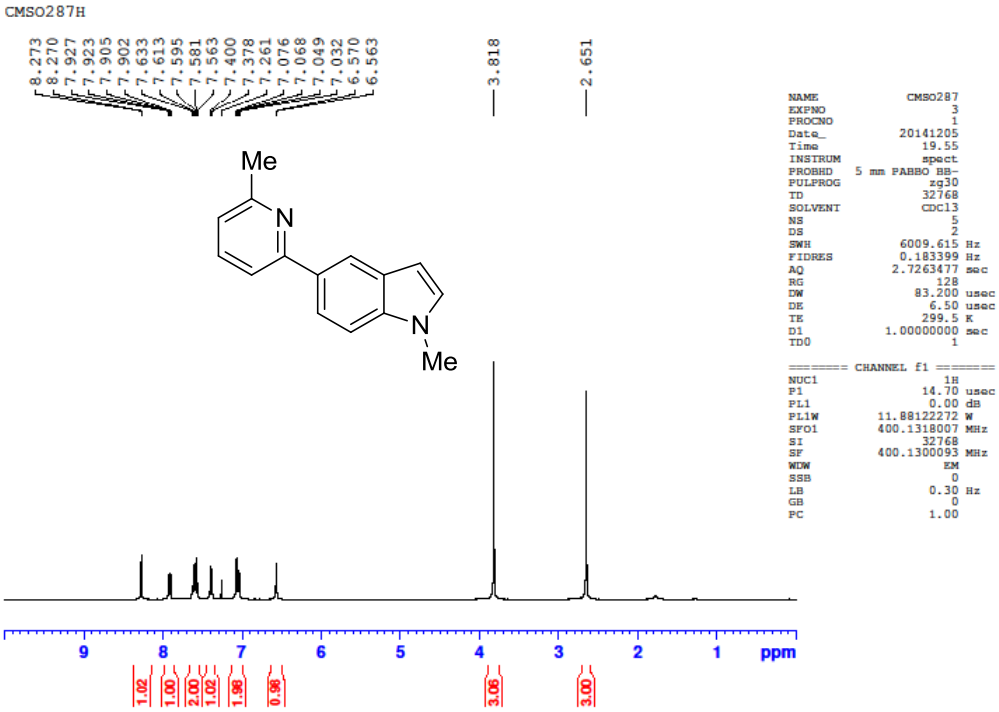
Mass	Calc. Mass	mDa	PPM	Formula
160.0757	160.0757	0	0	C10 H10 N O

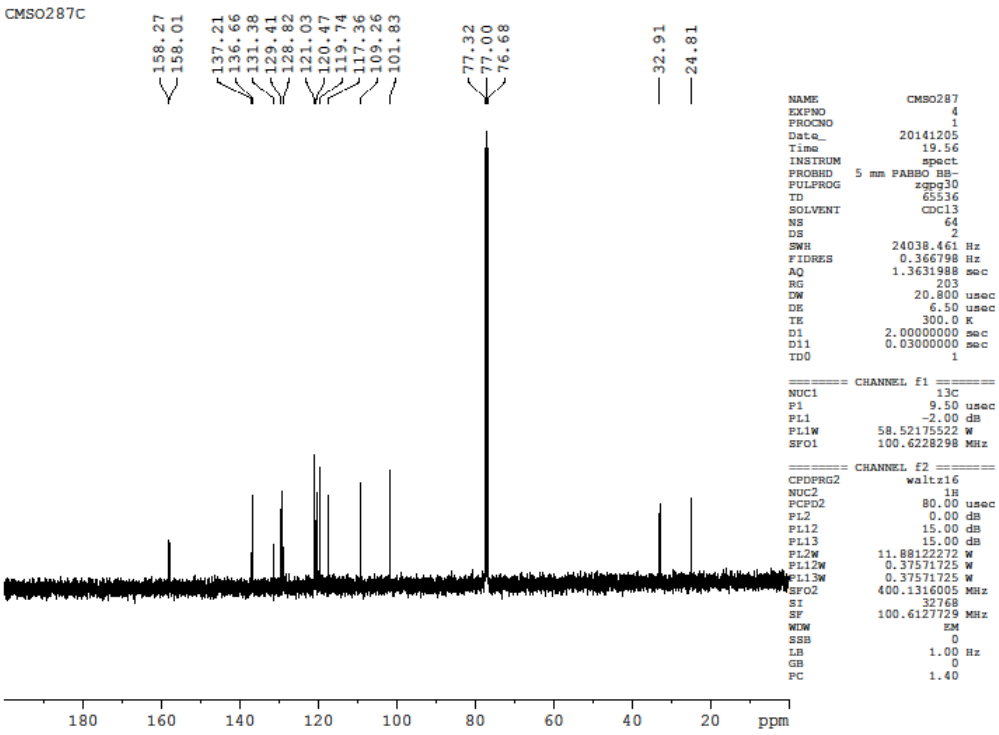
2-(Furan-3-yl)-6-methoxypyridine (Table 6.6, entry 3)





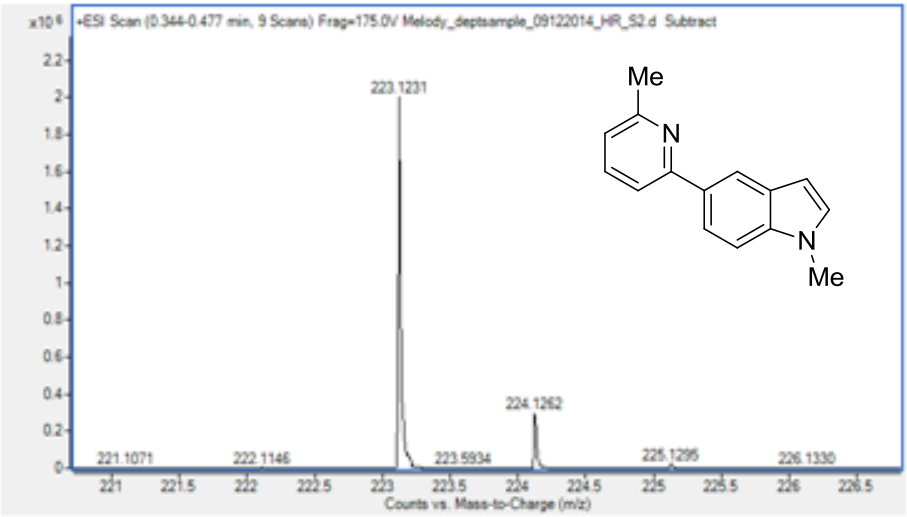
1-Methyl-5-(6-methylpyridin-2-yl)-1H-indole (Table 6.6, entry 4)





1-Methyl-5-(6-methylpyridin-2-yl)-1H-indole (Table 6.6, entry 4)

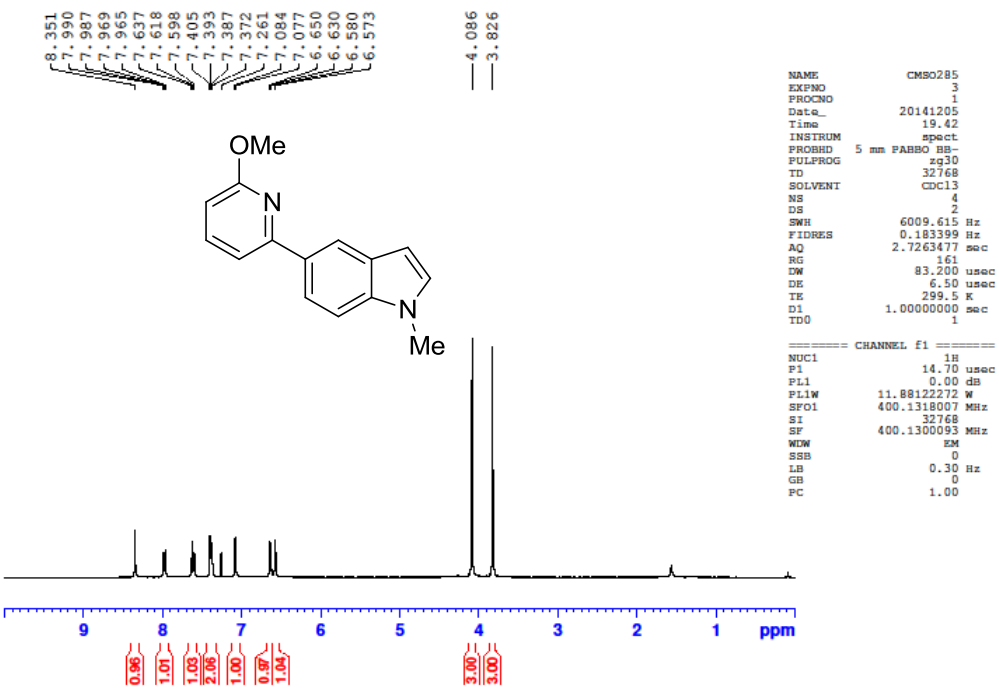
HS



Mass	Calc. Mass	mDa	PPM	Formula
223.1231	223.1230	0.1	0.4	C15 H15 N2

5-(6-Methoxypyridin-2-yl)-1-methyl-1H-indole (Table 6.6, entry 5)

CMSO285H



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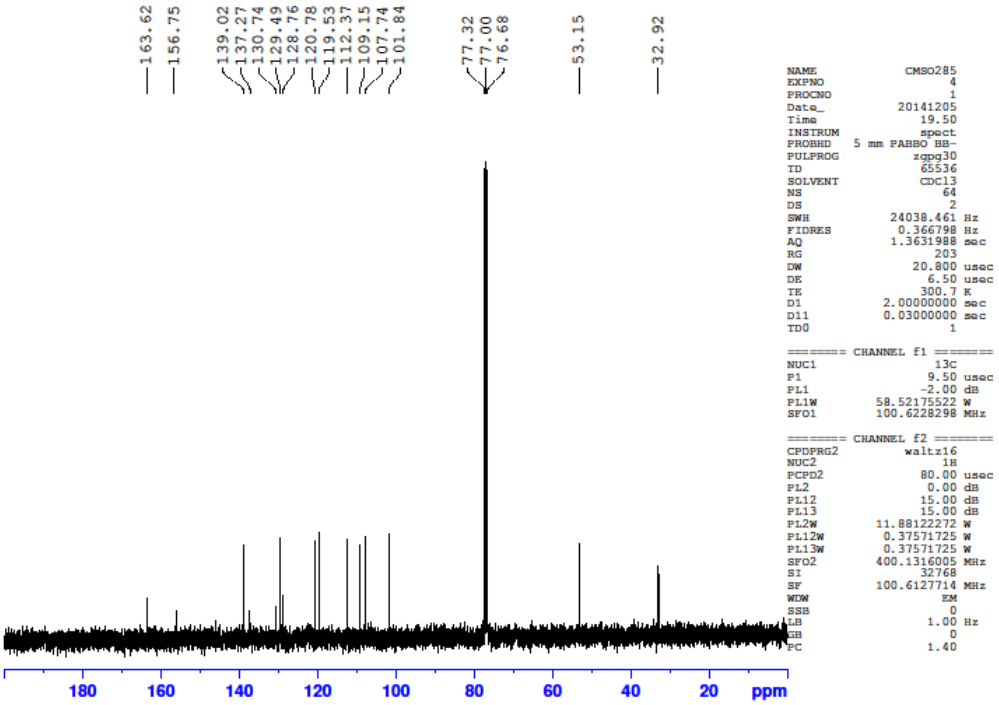
EXPNO	3
PROCNO	1
Date_	20141205
Time	19.42
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	4
DS	2
SWH	6009.615 Hz
FIDRES	0.183399 Hz
AQ	2.7263477 sec
RG	161
DW	83.200 usec
DE	6.50 usec
TE	299.5 K
D1	1.00000000 sec
TD0	1
======= CHANNEL f1 =======	
NUC1	1H
P1	14.70 usec
PL1	0.00 dB
PL1W	11.88122272 W
SFO1	400.1318007 MHz
SI	32768
SF	400.1300093 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

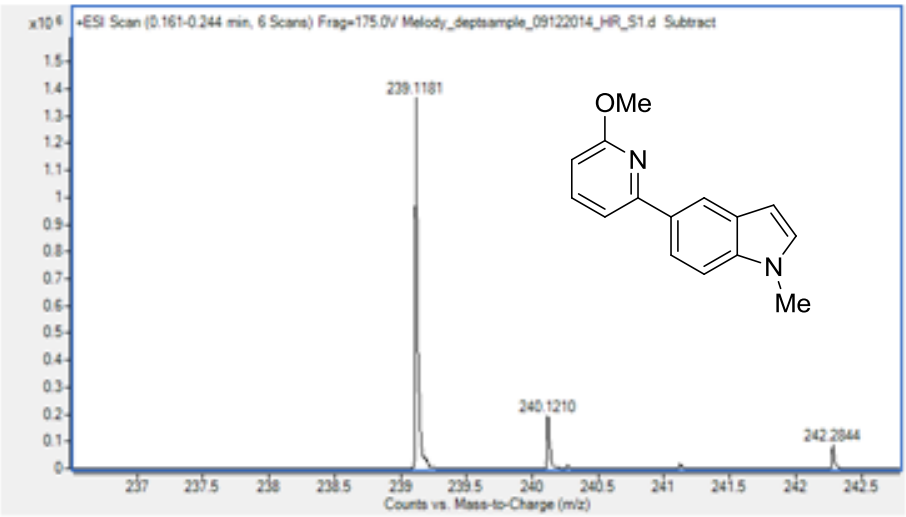
CMSO285C



NAME	CMSO285
EXPNO	4
PROCNO	1
Date_	20141205
Time	19.50
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	64
DS	2
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	300.7 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======= CHANNEL f1 =======	
NUC1	13C
P1	9.50 usec
PL1	-2.00 dB
PL1W	58.52175522 W
SFO1	100.6228298 MHz
======= CHANNEL f2 =======	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	0.00 dB
PL12	15.00 dB
PL13	15.00 dB
PL2W	11.88122272 W
PL12W	0.37571725 W
PL13W	0.37571725 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127714 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

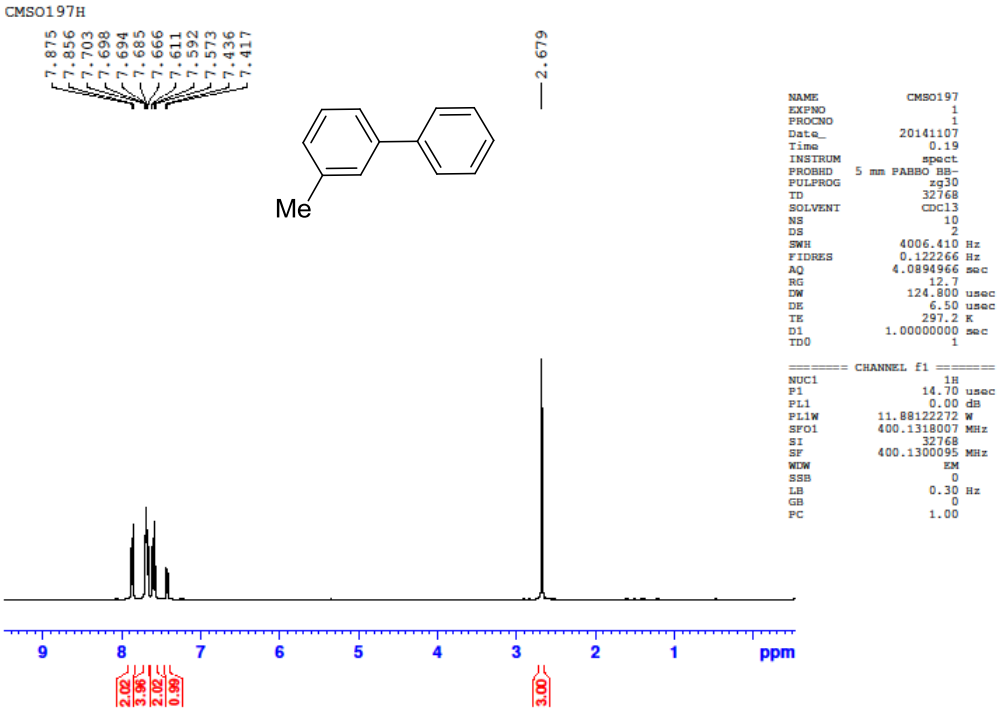
5-(6-Methoxypyridin-2-yl)-1-methyl-1H-indole (Table 6.6, entry 5)

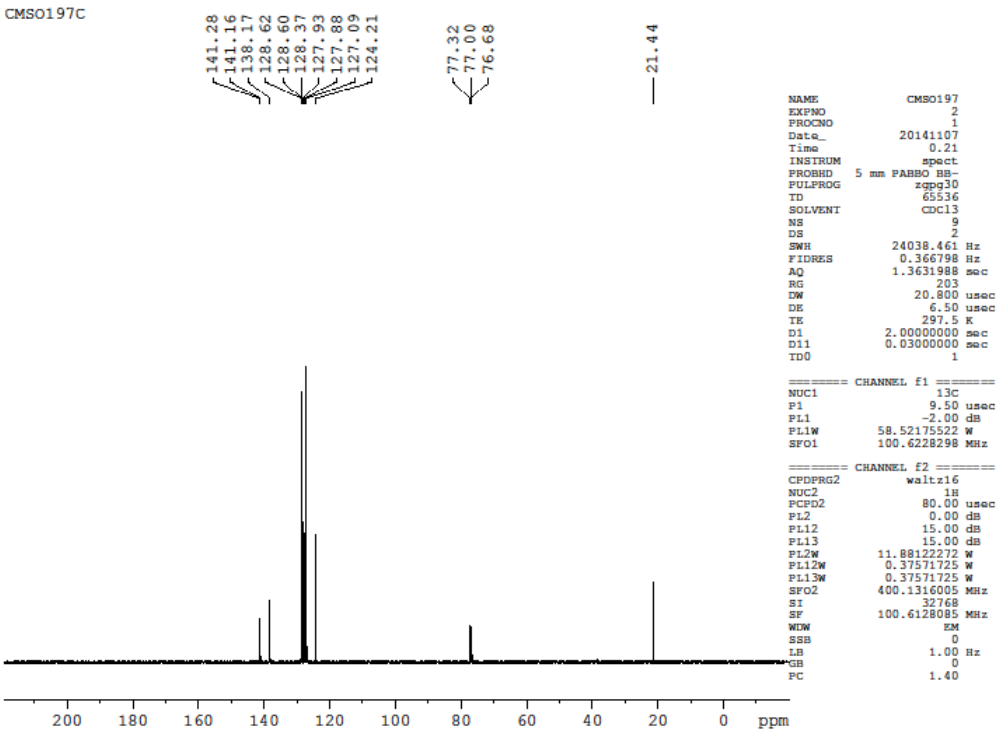
HS



Mass	Calc. Mass	mDa	PPM	Formula
239.1181	239.1179	0.2	0.8	C15 H15 N2 O

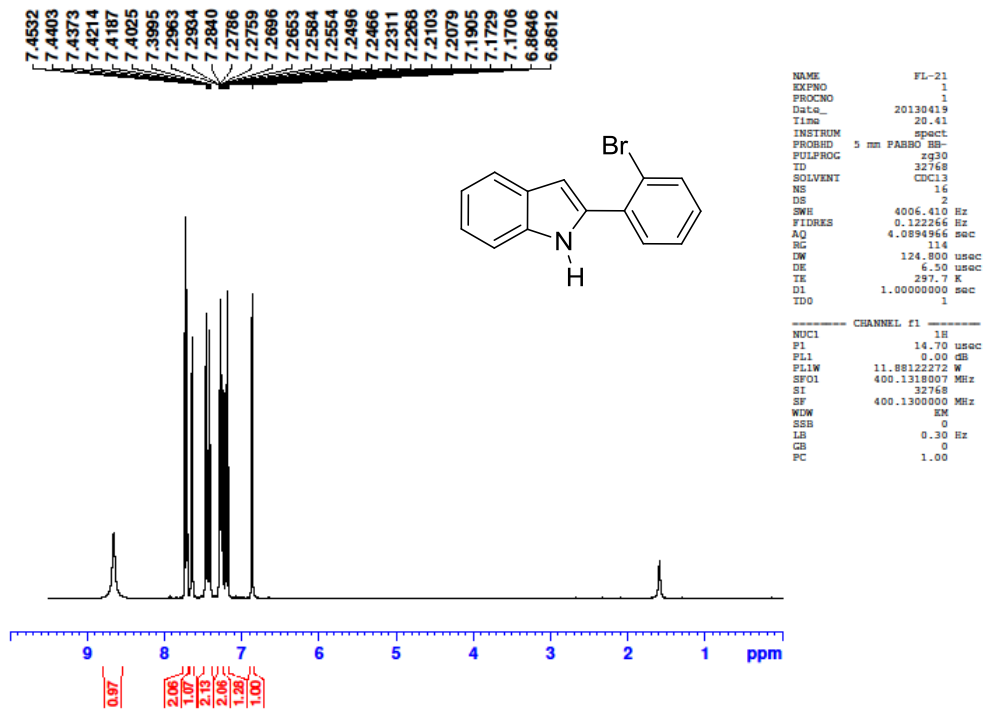
3-Methyl-1,1'-biphenyl (Scheme 6.3)





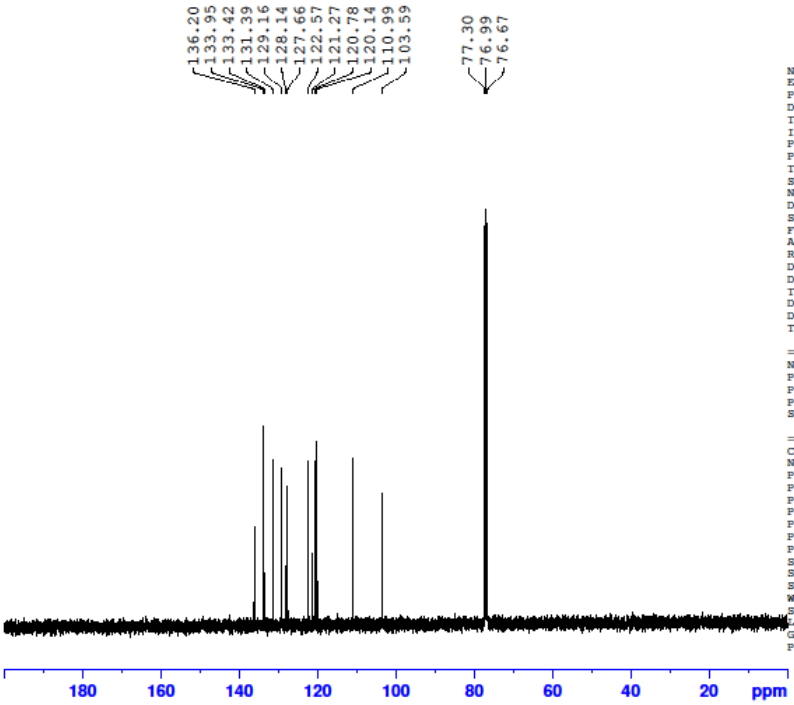
2-(2-Bromophenyl)-1*H*-indole (Table 7.1, L3 precursor)

FL-21H



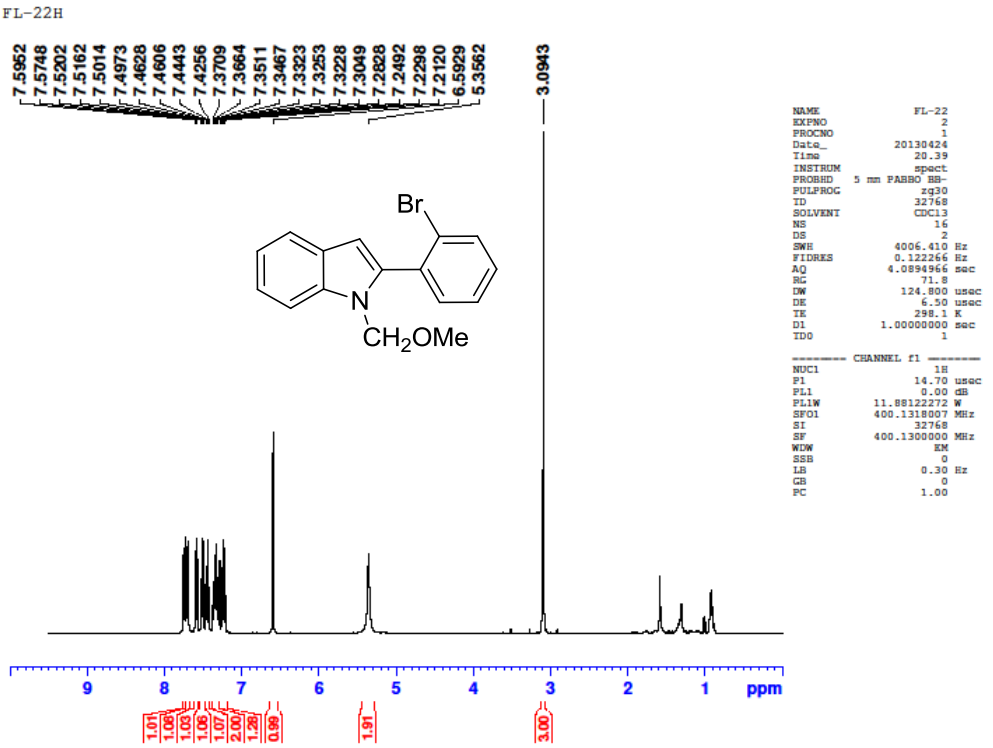

```
NAME                FL-21
EXPNO                   1
PROCNO                  1
Date_            20130419
Time                20.41
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  32768
SOLVENT             CDCl3
NS                     16
DS                      2
SWH              4006.410 Hz
FIDRES           0.122266 Hz
AQ               4.0894966 sec
RG                    114
DW                124.800 usec
DE                  6.50 usec
TE                 297.7 K
D1              1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                 14.70 usec
PL1                 0.00 dB
PL1W          11.88122272 W
SFO1          400.1318007 MHz
SI                  32768
SF            400.1300000 MHz
WDW                    EM
SSB                     0
LB                 0.30 Hz
GB                      0
PC                  1.00
```

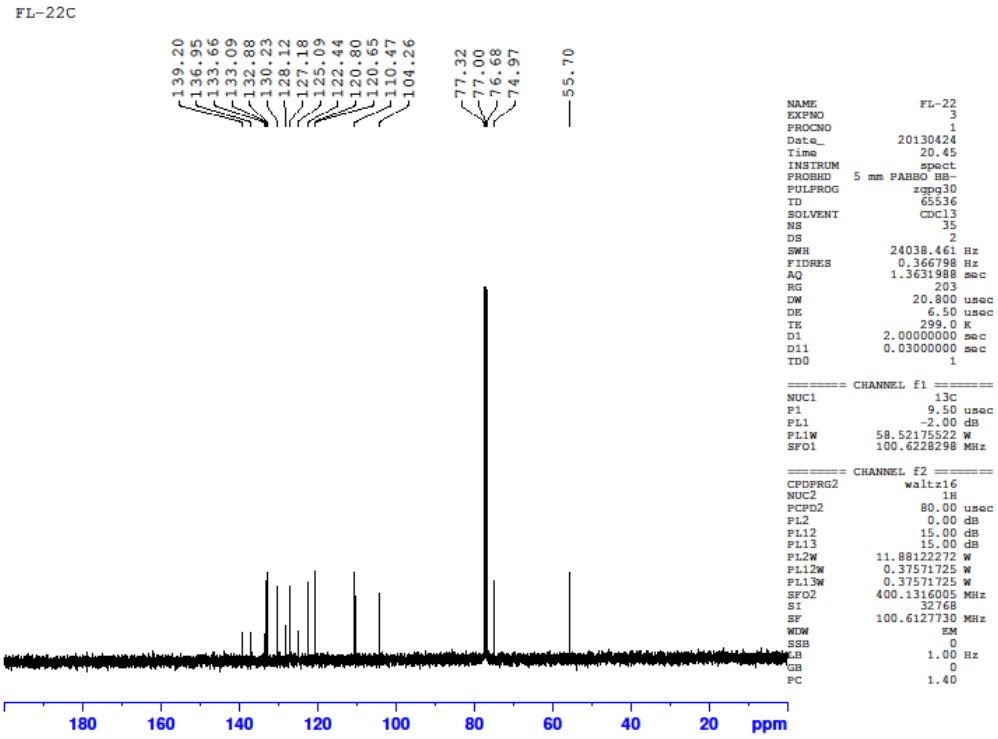
FL-21C




```
NAME                FL-21
EXPNO                   2
PROCNO                  1
Date_            20130419
Time                20.47
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                  65536
SOLVENT             CDCl3
NS                     56
DS                      2
SWH              24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                    181
DW                 20.800 usec
DE                  6.50 usec
TE                 298.8 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   13C
P1                  9.50 usec
PL1                -2.00 dB
PL1W          58.52175522 W
SFO1          100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                   1H
PCPD2              80.00 usec
PL2                 0.00 dB
PL12               15.00 dB
PL13               15.00 dB
PL2W          11.88122272 W
PL12W          0.37571725 W
PL13W          0.37571725 W
SFO2          400.1316005 MHz
SI                  32768
SF            100.6127757 MHz
WDW                    EM
SSB                     0
LB                 1.00 Hz
GB                      0
PC                  1.40
```

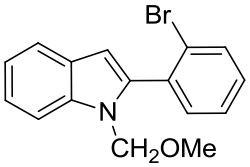
2-(2-Bromophenyl)-1-(methoxymethyl)-1*H*-indole (Table 7.1, L3 precursor)

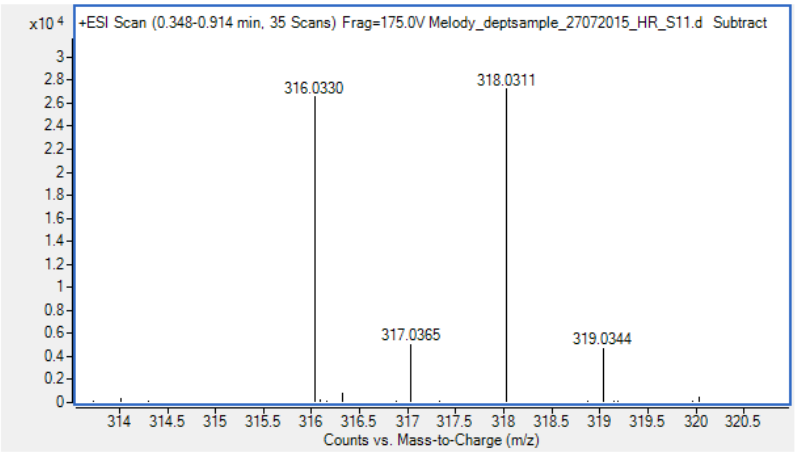




2-(2-Bromophenyl)-1-(methoxymethyl)-1*H*-indole (Table 7.1, L3 precursor)

HS

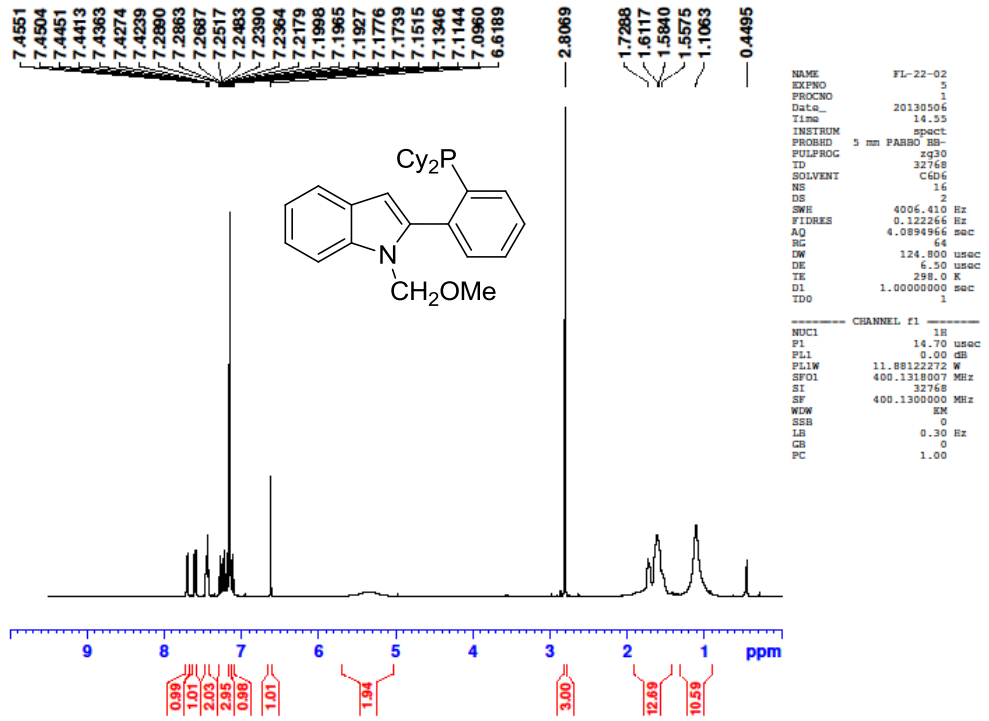




Mass	Calc. Mass	mDa	PPM	Formula
316.0330	316.0332	-0.2	-0.6	C16 H15 Br N O

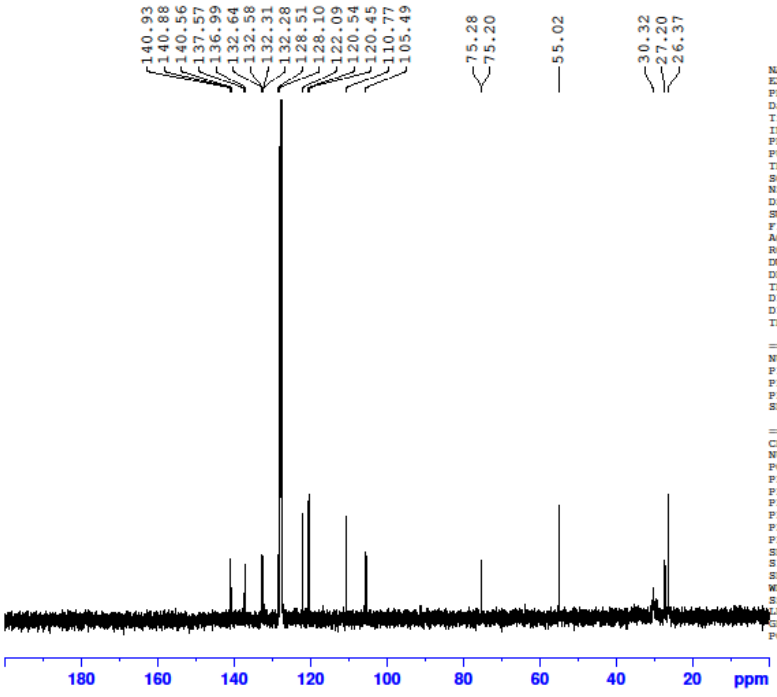
2-(2-(Dicyclohexylphosphino)phenyl)-1-(methoxymethyl)-1*H*-indole (Table 7.1, L3)

FL-22-02H



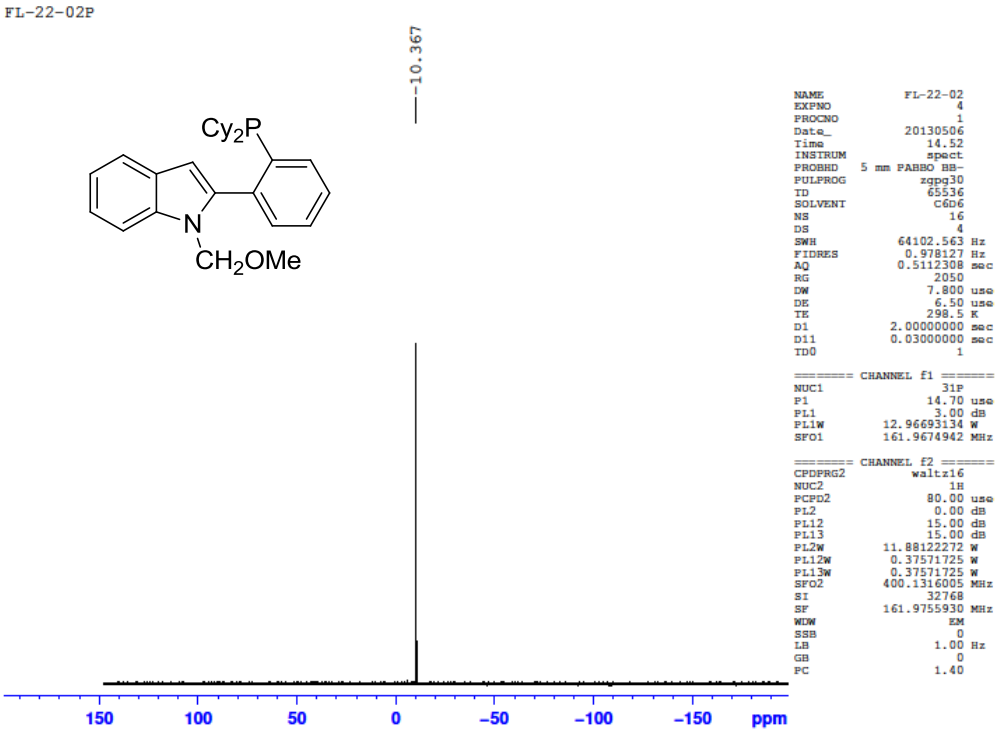

```
NAME                FL-22-02
EXPNO                      5
PROCNO                     1
Date_               20130506
Time                   14.55
INSTRUM                spect
PROBHD   5 mm PABBO BB-
PULPROG                zg30
TD                    32768
SOLVENT                C6D6
NS                       16
DS                        2
SWH                4006.410 Hz
FIDRES             0.122266 Hz
AQ                 4.0894966 sec
RG                        64
DW                   124.800 usec
DE                     6.50 usec
TE                   298.0 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                       1H
P1                     14.70 usec
PL1                     0.00 dB
PL1W               11.88122272 W
SFO1               400.1318007 MHz
SI                        32768
SF                 400.1300000 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00
```

FL-22-02C

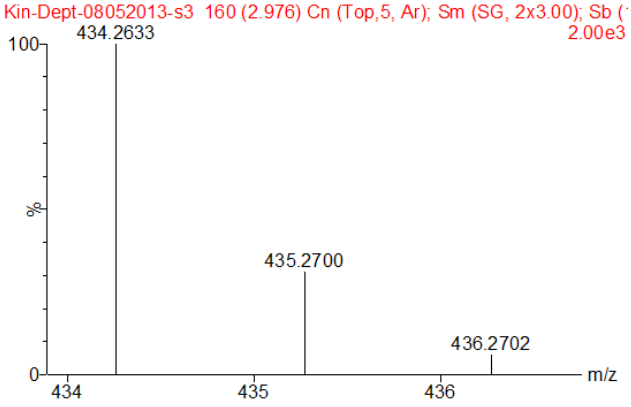



```
NAME                FL-22-02
EXPNO                      3
PROCNO                     1
Date_               20130813
Time                   21.41
INSTRUM                spect
PROBHD   5 mm PABBO BB-
PULPROG             zgpg30
TD                    65536
SOLVENT                C6D6
NS                       64
DS                        2
SWH               24038.461 Hz
FIDRES             0.366798 Hz
AQ                 1.3631988 sec
RG                      203
DW                   20.800 usec
DE                     6.50 usec
TE                   297.1 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                       13C
P1                      9.50 usec
PL1                    -2.00 dB
PL1W               58.52175522 W
SFO1               100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                  80.00 usec
PL2                     0.00 dB
PL12                   15.00 dB
PL13                   15.00 dB
PL2W               11.88122272 W
PL12W               0.37571725 W
PL13W               0.37571725 W
SFO2               400.1316005 MHz
SI                        32768
SF                 100.6127690 MHz
WDW                       EM
SSB                        0
LB                      1.00 Hz
GB                         0
PC                      1.40
```

2-(2-(Dicyclohexylphosphino)phenyl)-1-(methoxymethyl)-1*H*-indole (Table 7.1, L3)



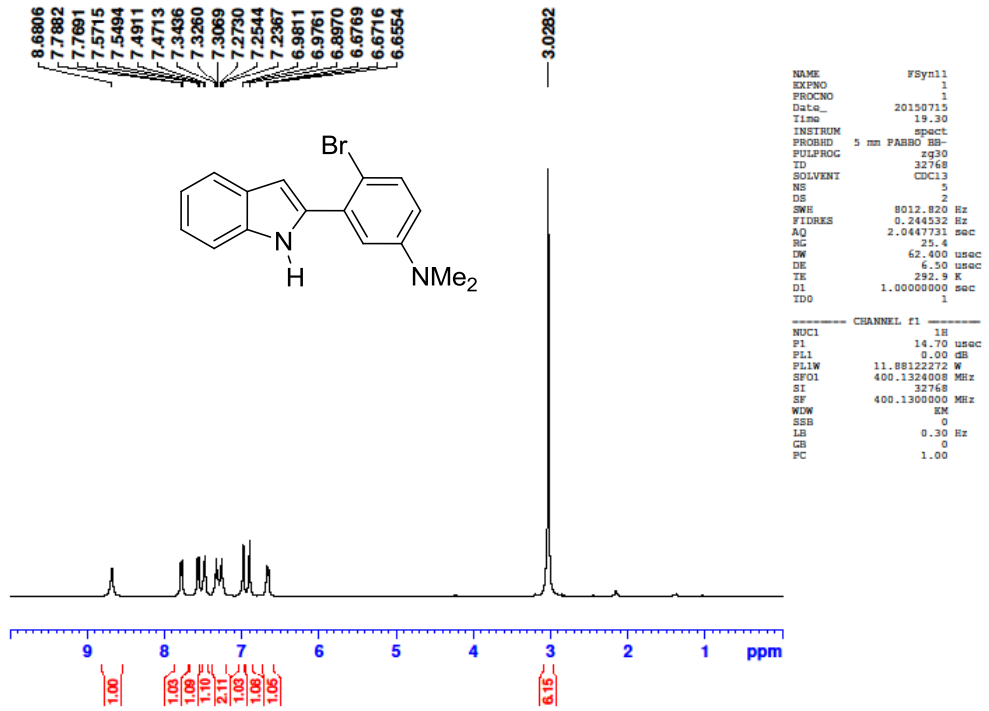
HS



Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
434.2633	434.2613	2.0	4.6	11.5	1.8	C28 H37 N O P

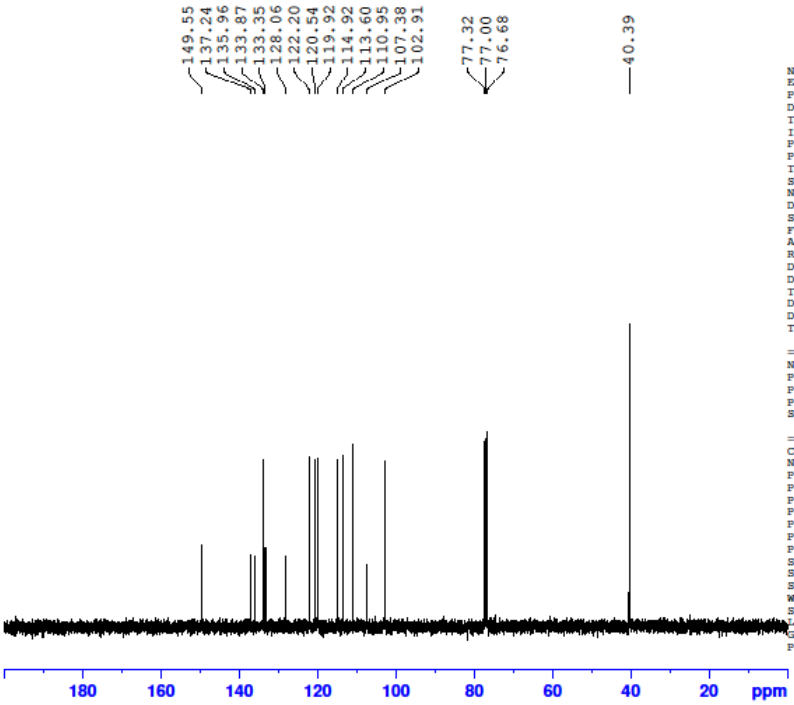
4-Bromo-3-(1*H*-indol-2-yl)-*N*,*N*-dimethylaniline (Table 7.1, L4 precursor)

FSyn111H




```
NAME                FSyn11
EXPNO                    1
PROCNO                   1
Date_             20150715
Time                 19.30
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                        8
DS                        2
SWH                8012.820 Hz
FIDRES             0.244532 Hz
AQ                 2.0447731 sec
RG                      25.4
DW                    62.400 usec
DE                     6.50 usec
TE                    292.9 K
D1                 1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                    14.70 usec
PL1                    0.00 dB
PL1W              11.88122272 W
SFO1              400.1324008 MHz
SI                    32768
SF                400.1300000 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

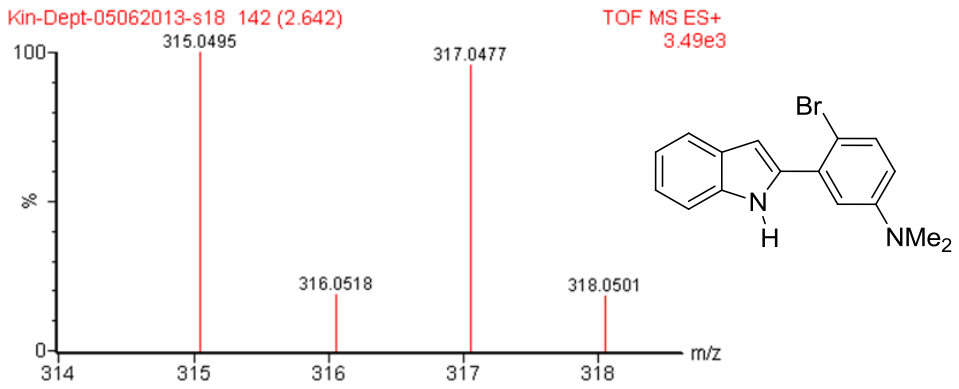
FSyn11C




```
NAME                FSyn11
EXPNO                    2
PROCNO                   1
Date_             20150715
Time                 19.32
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG             zgpg30
TD                    65536
SOLVENT               CDCl3
NS                       10
DS                        2
SWH               24038.461 Hz
FIDRES             0.366798 Hz
AQ                 1.3631988 sec
RG                      203
DW                    20.800 usec
DE                     6.50 usec
TE                    293.1 K
D1                 1.00000000 sec
D11                0.03000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                     9.50 usec
PL1                   -2.00 dB
PL1W              58.52175522 W
SFO1              100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2              waltz16
NUC2                     1H
PCPD2                 80.00 usec
PL2                    0.00 dB
PL12                  15.00 dB
PL13                  15.00 dB
PL2W              11.88122272 W
PL12W              0.37571725 W
PL13W              0.37571725 W
SFO2              400.1316005 MHz
SI                    32768
SF                100.6127940 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.40
```

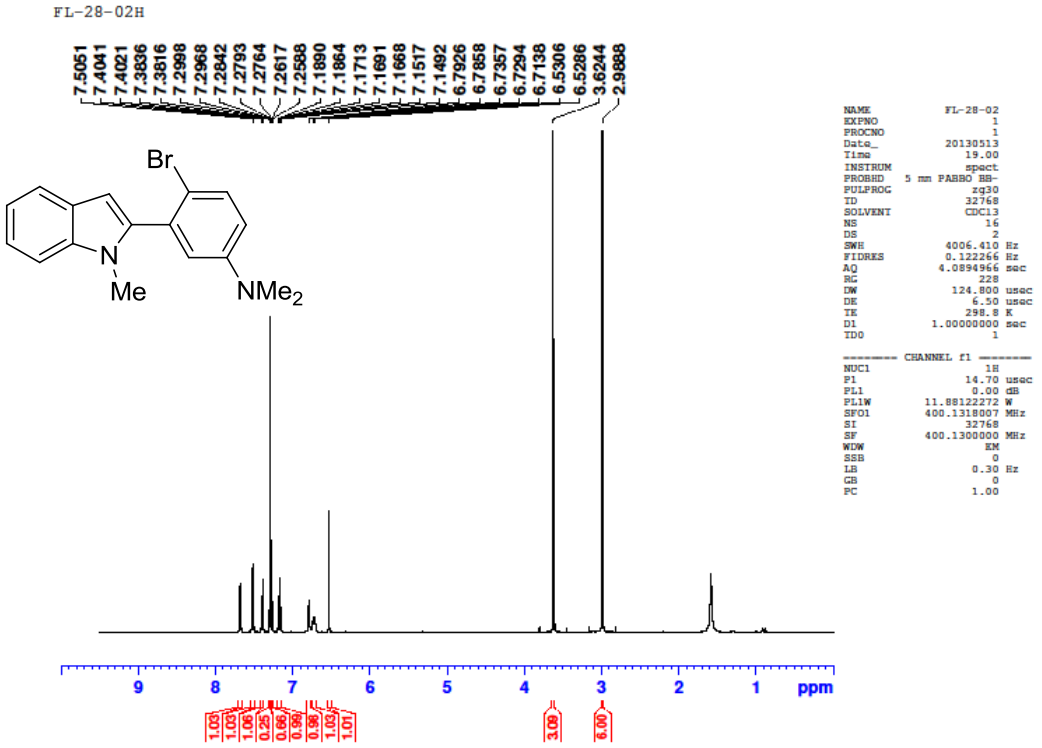
4-Bromo-3-(1*H*-indol-2-yl)-*N*,*N*-dimethylaniline (Table 7.1, L4 precursor)

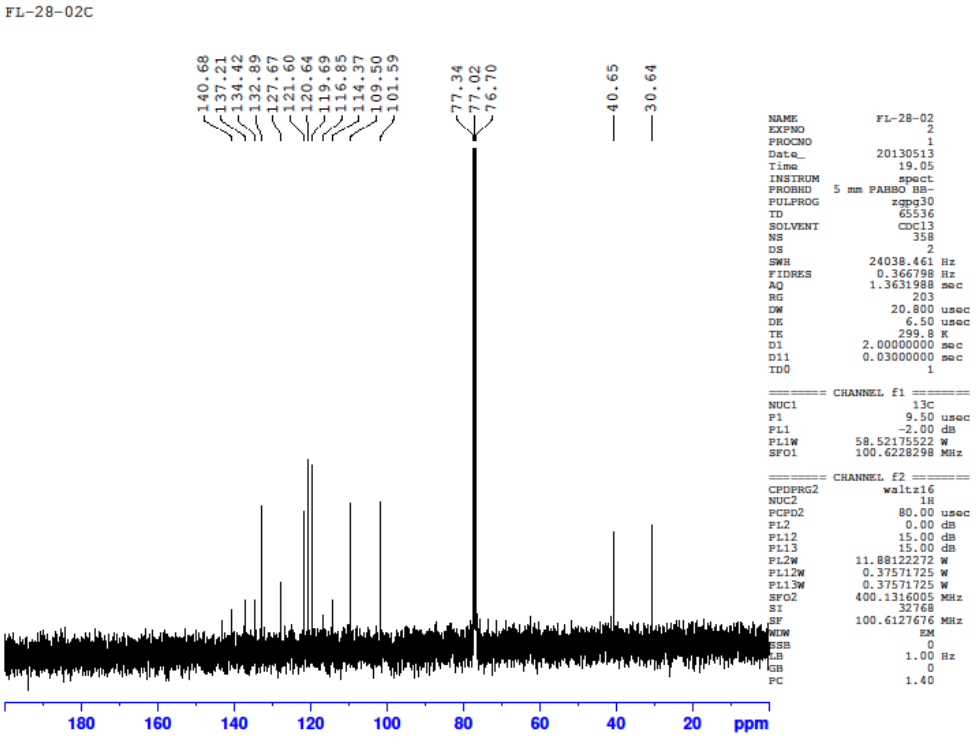
HS



Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
315.0495	315.0497	-0.2	-0.6	9.5	1	C16 H16 N2 Br

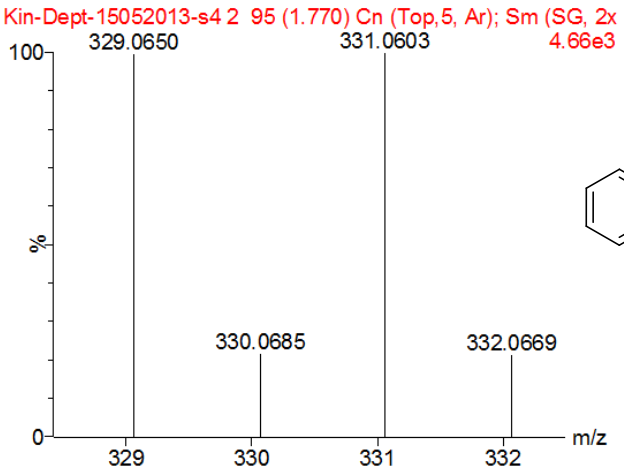
4-Bromo-*N*,*N*-dimethyl-3-(1-methyl-1*H*-indol-2-yl)aniline (Table 7.1, L4 precursor)





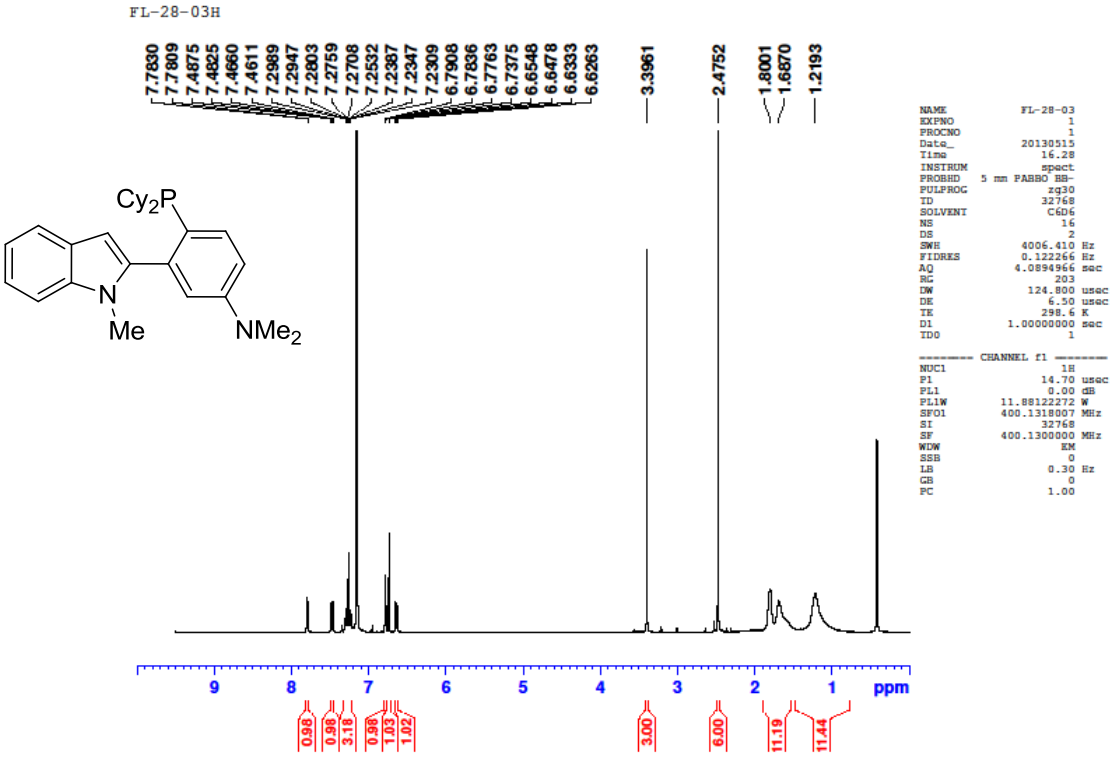
4-Bromo-*N*,*N*-dimethyl-3-(1-methyl-1*H*-indol-2-yl)aniline (Table 7.1, L4 precursor)

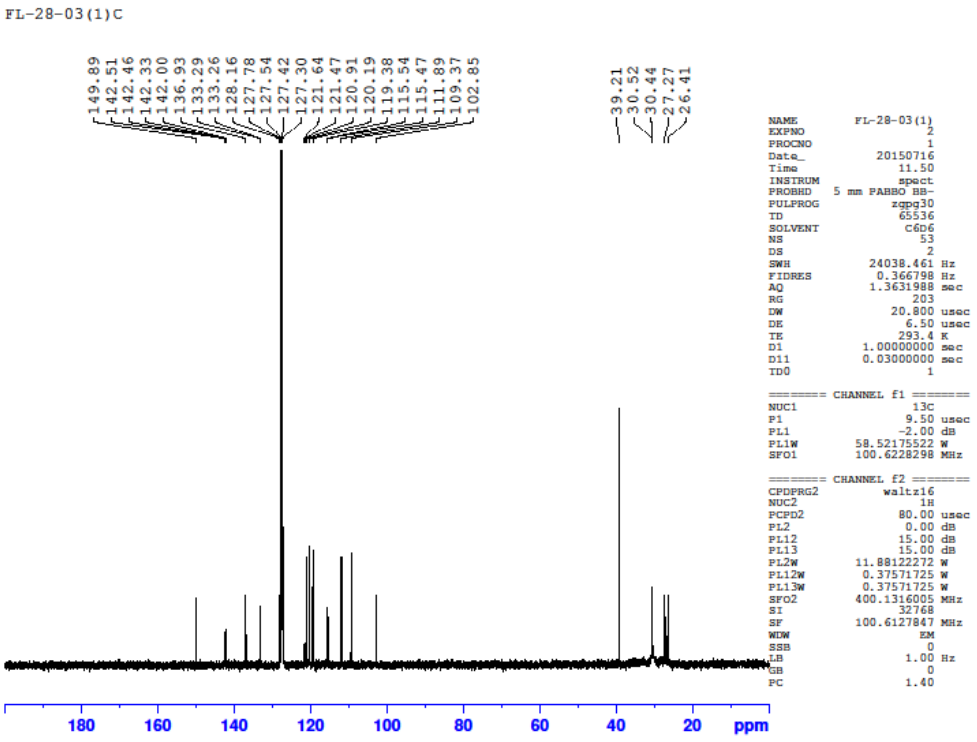
HS



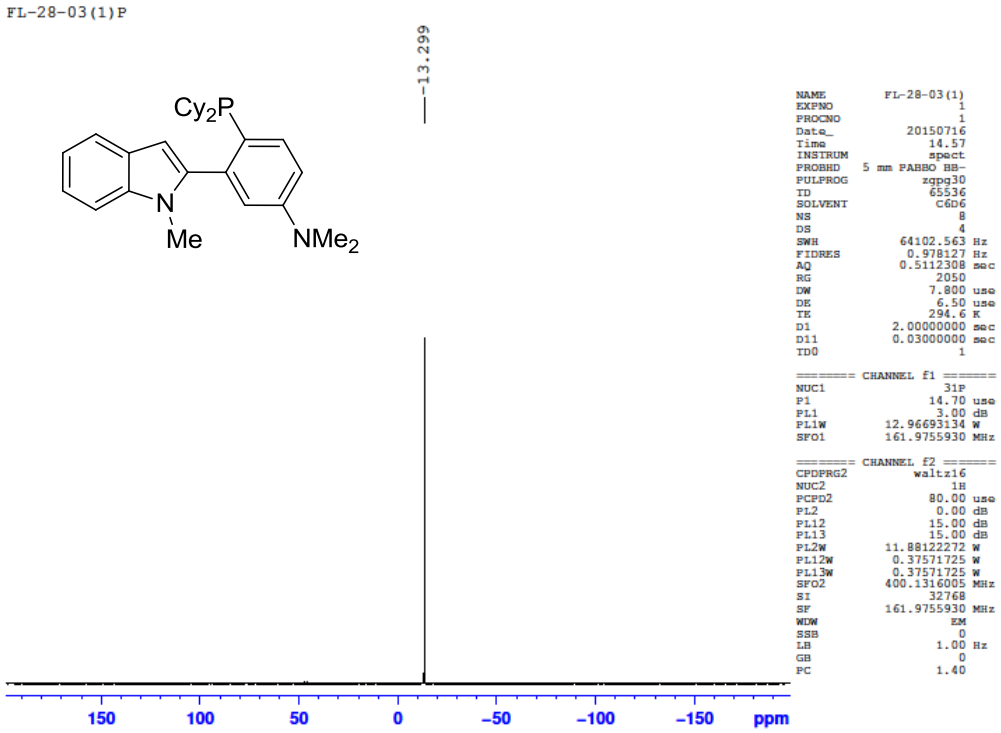
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
329.0650	329.0653	-0.3	-0.9	9.5	4.2	C17 H18 N2 Br

4-(Dicyclohexylphosphino)-N,N-dimethyl-3-(1-methyl-1*H*-indol-2-yl)aniline (Table 7.1, L4)

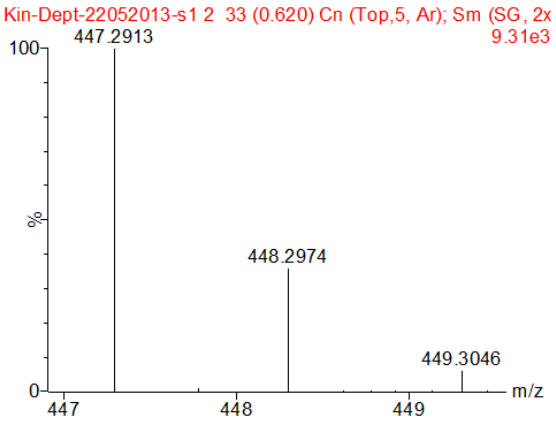




4-(Dicyclohexylphosphino)-N,N-dimethyl-3-(1-methyl-1*H*-indol-2-yl)aniline (Table 7.1, L4)



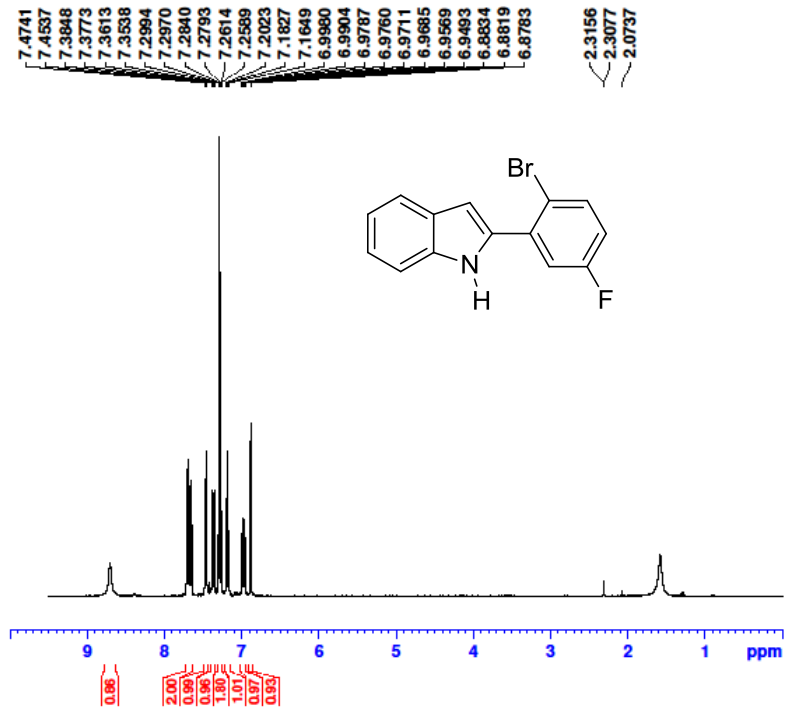
HS



Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
447.2913	447.2929	-1.6	-3.6	11.5	10.1	C29 H40 N2 P

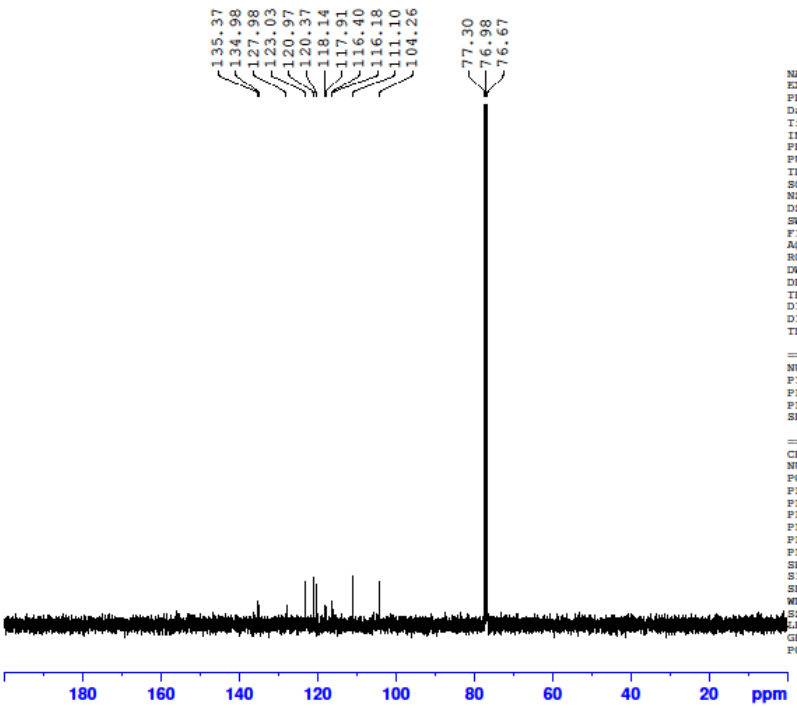
2-(2-Bromo-5-fluorophenyl)-1*H*-indole (Table 7.1, L5 precursor)

FL-59H



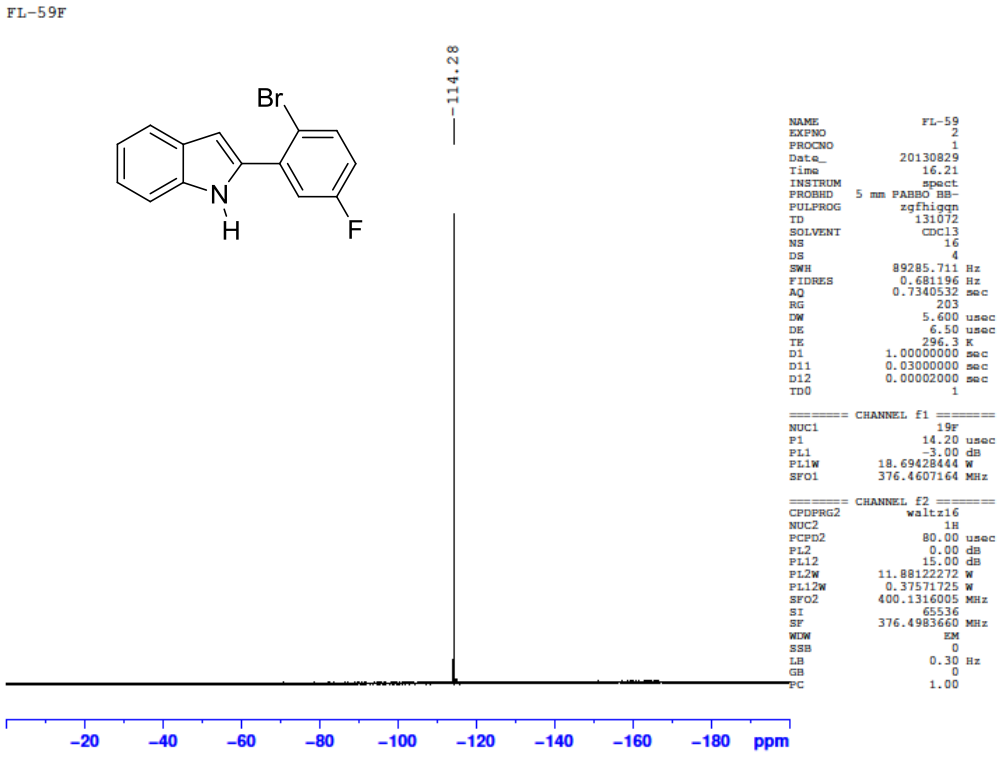

```
NAME                FL-59
EXPNO                  1
PROCNO                 1
Date_           20130829
Time               16.17
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             4006.410 Hz
FIDRES          0.122266 Hz
AQ              4.0894966 sec
RG                   287
DW                124.800 usec
DE                  6.50 usec
TE                 296.2 K
D1              1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 14.70 usec
PL1                0.00 dB
PL1W          11.88122272 W
SFO1          400.1318007 MHz
SI                 32768
SF            400.1300000 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

FL-59C

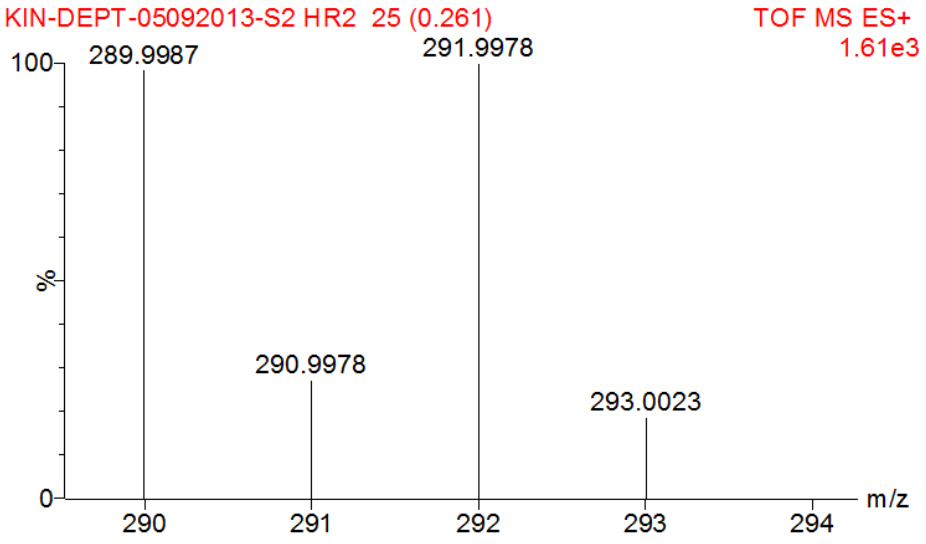



```
NAME                FL-59
EXPNO                  3
PROCNO                 1
Date_           20130829
Time               16.23
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                    64
DS                     2
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631988 sec
RG                   203
DW                 20.800 usec
DE                  6.50 usec
TE                 296.9 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  13C
P1                  9.50 usec
PL1                -2.00 dB
PL1W          58.52175522 W
SFO1          100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                  1H
PCPD2              80.00 usec
PL2                 0.00 dB
PL12               15.00 dB
PL13               15.00 dB
PL2W          11.88122272 W
PL12W          0.37571725 W
PL13W          0.37571725 W
SFO2          400.1316005 MHz
SI                 32768
SF            100.6127728 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
```

2-(2-Bromo-5-fluorophenyl)-1*H*-indole (Table 7.1, L5 precursor)

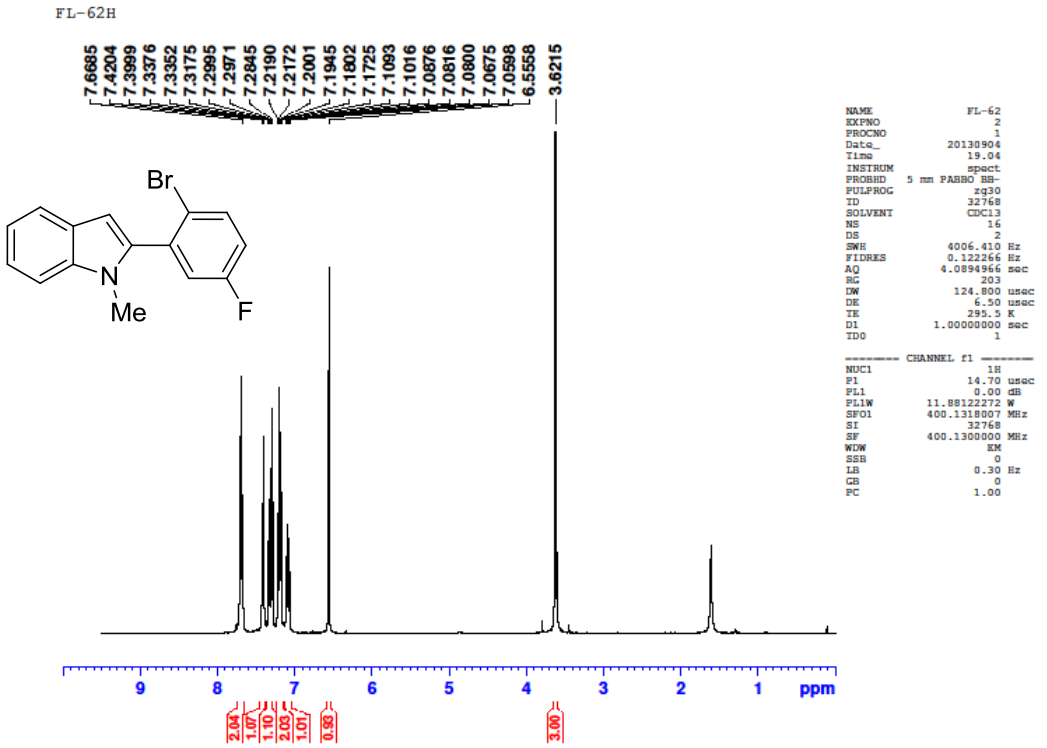


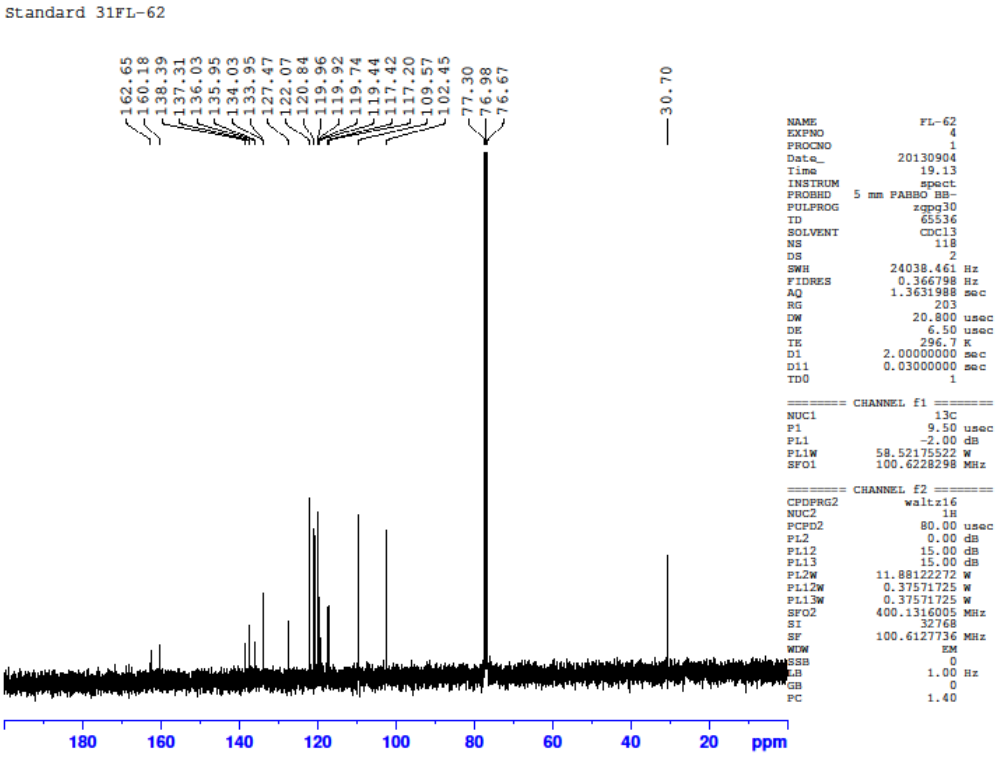
HR



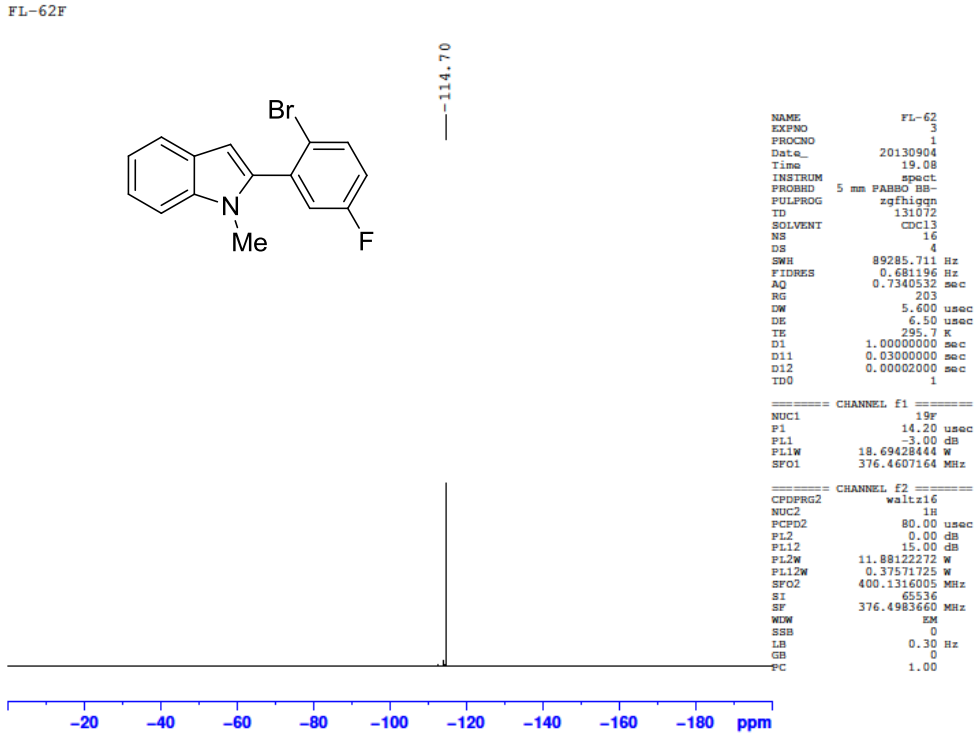
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
289.9987	289.9981	0.6	2.1	9.5	36.3	C14 H10 N F Br

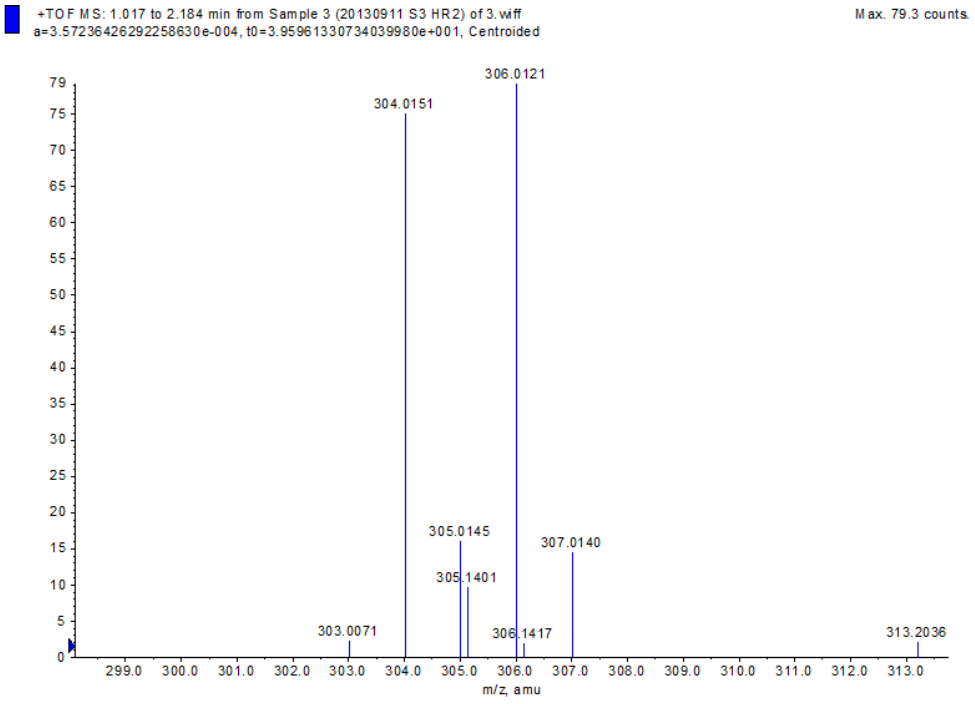
2-(2-Bromo-5-fluorophenyl)-1-methyl-1*H*-indole (Table 7.1, L5 precursor)





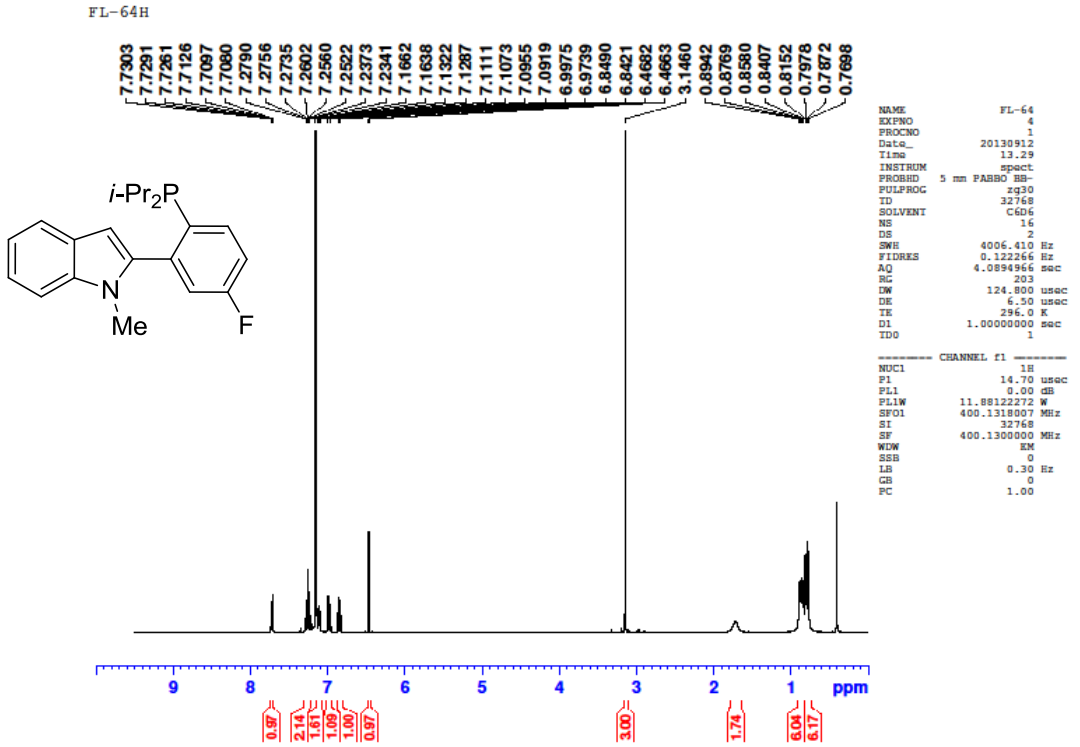
2-(2-Bromo-5-fluorophenyl)-1-methyl-1*H*-indole (Table 7.1, L5 precursor)

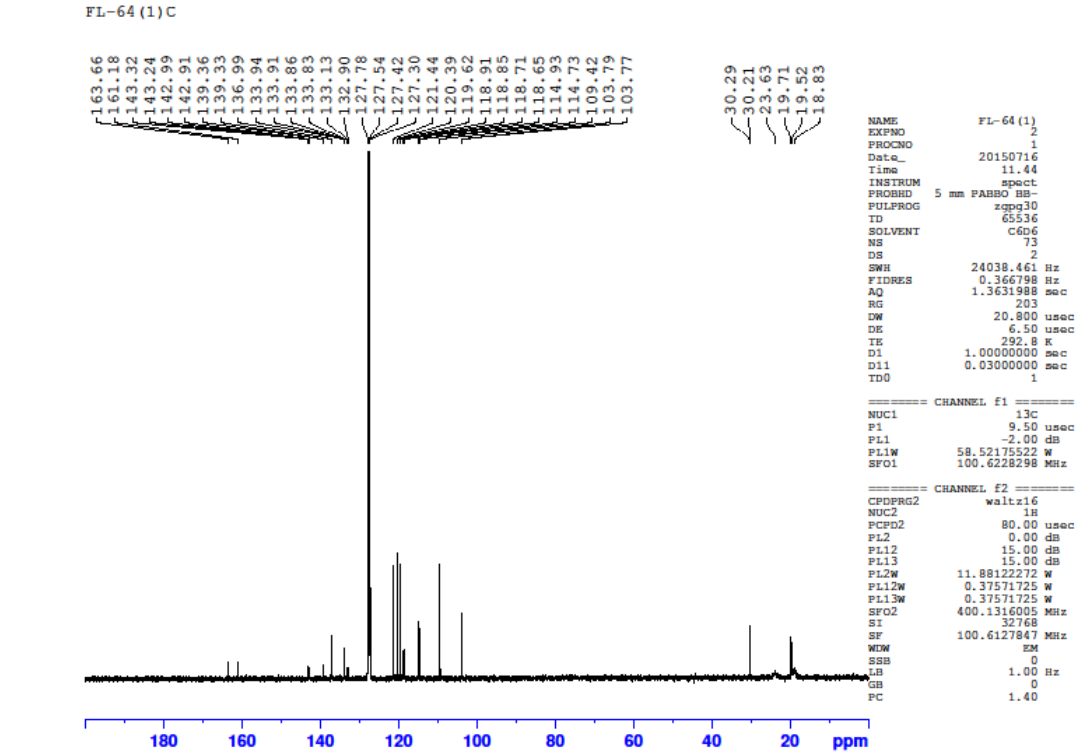




Formula: [C15H12BrFN]
Measured mass: 304.0137
Calculated mass: 304.0151
PPM: 4.6

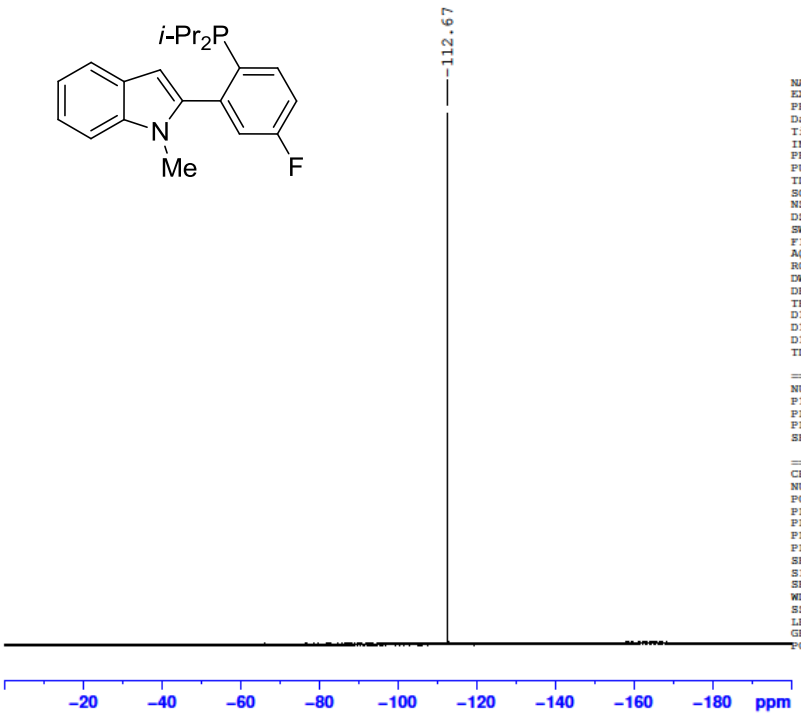
2-(2-(Diisopropylphosphino)-5-fluorophenyl)-1-methyl-1*H*-indole (Table 7.1, L5)





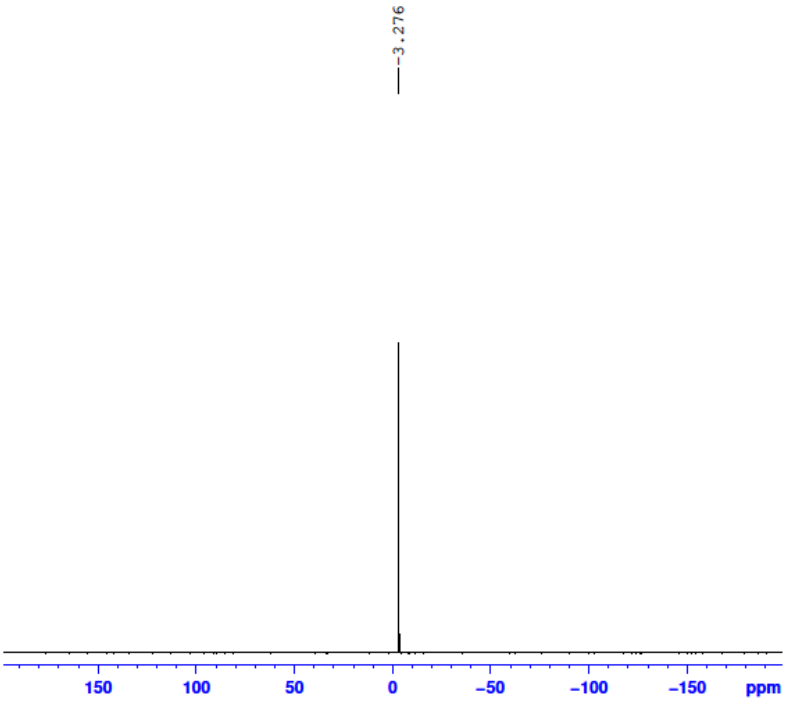
2-(2-(Diisopropylphosphino)-5-fluorophenyl)-1-methyl-1*H*-indole (Table 7.1, L5)

FL-64F




```
NAME                FL-64
EXPNO                  6
PROCNO                 1
Date_           20130912
Time                13.34
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG         zgfhigqn
TD                131072
SOLVENT             C6D6
NS                    16
DS                     4
SWH           89285.711 Hz
FIDRES        0.681196 Hz
AQ            0.7340532 sec
RG                   203
DW                 5.600 usec
DE                 6.50 usec
TE                296.2 K
D1            1.00000000 sec
D11           0.03000000 sec
D12           0.00002000 sec
TD0                    1

======== CHANNEL f1 =======
NUC1                  19F
P1                 14.20 usec
PL1                -3.00 dB
PL1W         18.69428444 W
SFO1         376.4607164 MHz

======== CHANNEL f2 =======
CPDPRG2           waltz16
NUC2                  1H
PCPD2              80.00 usec
PL2                0.00 dB
PL12              15.00 dB
PL2W         11.88122272 W
PL12W         0.37571725 W
SFO2         400.1316005 MHz
SI                 65536
SF           376.4983660 MHz
WDW                   EM
SSB                    0
LB                 0.30 Hz
GB                     0
PC                 1.00
```

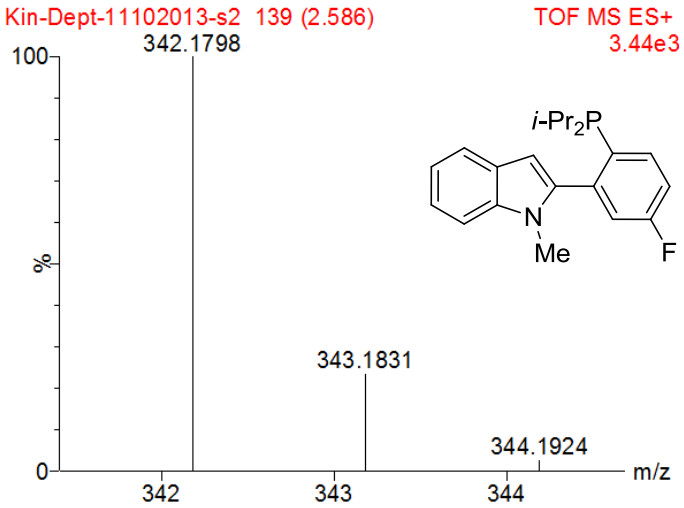
FL-64(1)P




```
NAME             FL-64(1)
EXPNO                   3
PROCNO                  1
Date_            20150716
Time                14.49
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG          zgpg30
TD                 65536
SOLVENT             c6d6
NS                    10
DS                     4
SWH           64102.563 Hz
FIDRES        0.978127 Hz
AQ            0.5112308 sec
RG                  2050
DW                 7.800 use
DE                 6.50 use
TE                294.7 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 =======
NUC1                  31P
P1                 14.70 use
PL1                3.00 dB
PL1W         12.96693134 W
SFO1         161.9755930 MHz

======== CHANNEL f2 =======
CPDPRG2           waltz16
NUC2                  1H
PCPD2              80.00 use
PL2                0.00 dB
PL12              15.00 dB
PL13              15.00 dB
PL2W         11.88122272 W
PL12W         0.37571725 W
PL13W         0.37571725 W
SFO2         400.1316005 MHz
SI                 32768
SF           161.9755930 MHz
WDW                   EM
SSB                    0
LB                 1.00 Hz
GB                     0
PC                 1.40
```

2-(2-(Diisopropylphosphino)-5-fluorophenyl)-1-methyl-1*H*-indole (Table 7.1, L5)

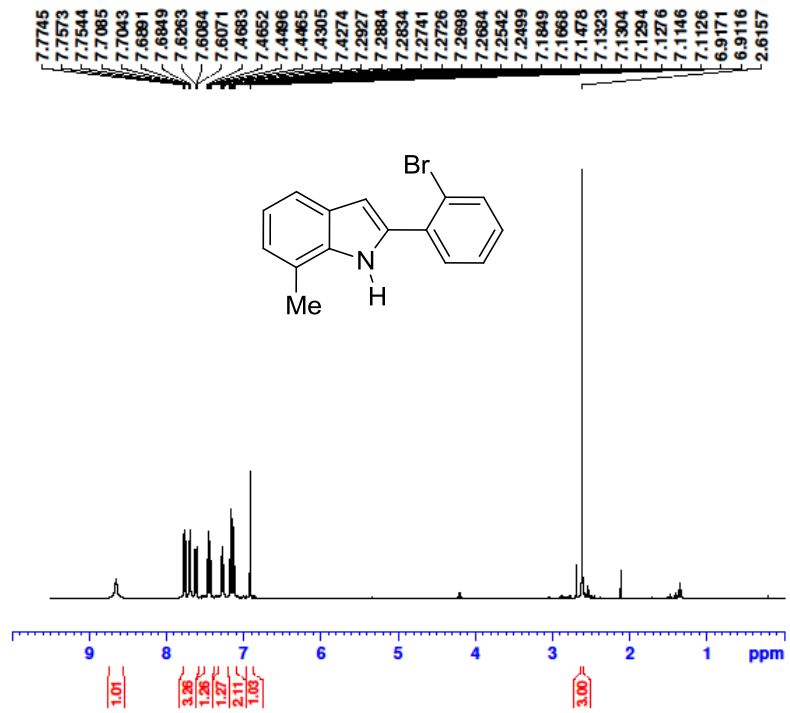
HS



Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
342.1798	342.1787	1.1	3.2	9.5	0.4	C21 H26 N F P

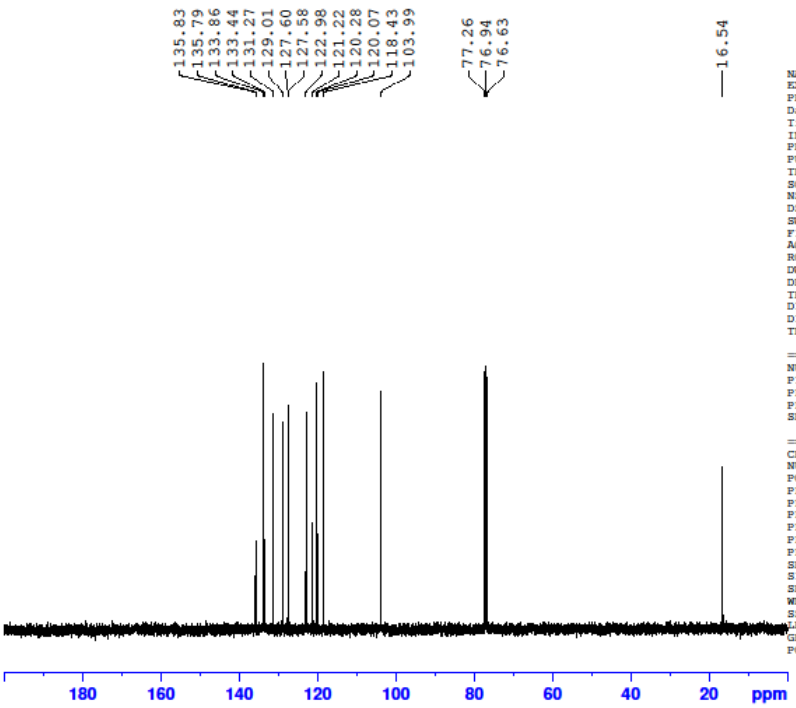
2-(2-Bromophenyl)-7-methyl-1*H*-indole (Table 7.1, L6 precursor)

FL-35H




```
NAME                FL-35
EXPNO                  3
PROCNO                 1
Date_           20130619
Time                19.48
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH           4006.410 Hz
FIDRES        0.122266 Hz
AQ            4.0894966 sec
RG                  45.2
DW             124.800 usec
DE               6.50 usec
TE              299.0 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1             14.70 usec
PL1             0.00 dB
PL1W       11.88122272 W
SFO1       400.1318007 MHz
SI                 32768
SF         400.1300000 MHz
WDW                   EM
SSB                    0
LB              0.30 Hz
GB                     0
PC                  1.00
```

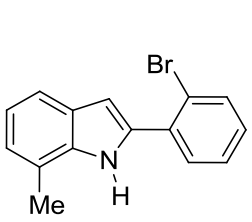
FL-35C

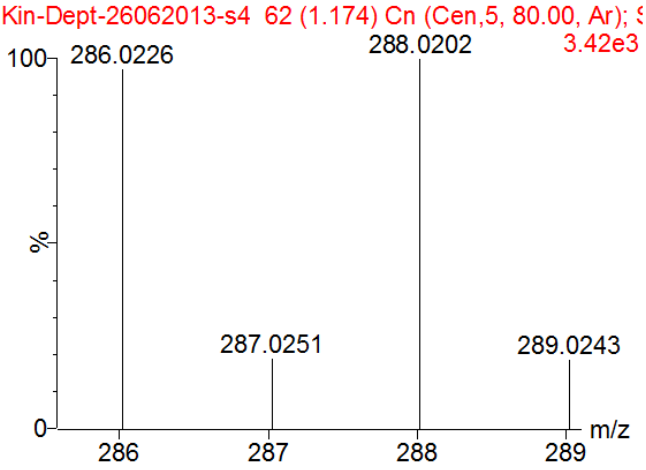



```
NAME                FL-35
EXPNO                  4
PROCNO                 1
Date_           20130619
Time                19.54
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                    29
DS                     2
SWH           24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631988 sec
RG                   203
DW             20.800 usec
DE               6.50 usec
TE              299.8 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  13C
P1              9.50 usec
PL1             -2.00 dB
PL1W       58.52175522 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2          80.00 usec
PL2             0.00 dB
PL12           15.00 dB
PL13           15.00 dB
PL2W       11.88122272 W
PL12W       0.37571725 W
PL13W       0.37571725 W
SFO2       400.1316005 MHz
SI                 32768
SF         100.6127888 MHz
WDW                   EM
SSB                    0
LB              1.00 Hz
GB                     0
PC                  1.40
```

2-(2-Bromophenyl)-7-methyl-1*H*-indole (Table 7.1, L6 precursor)

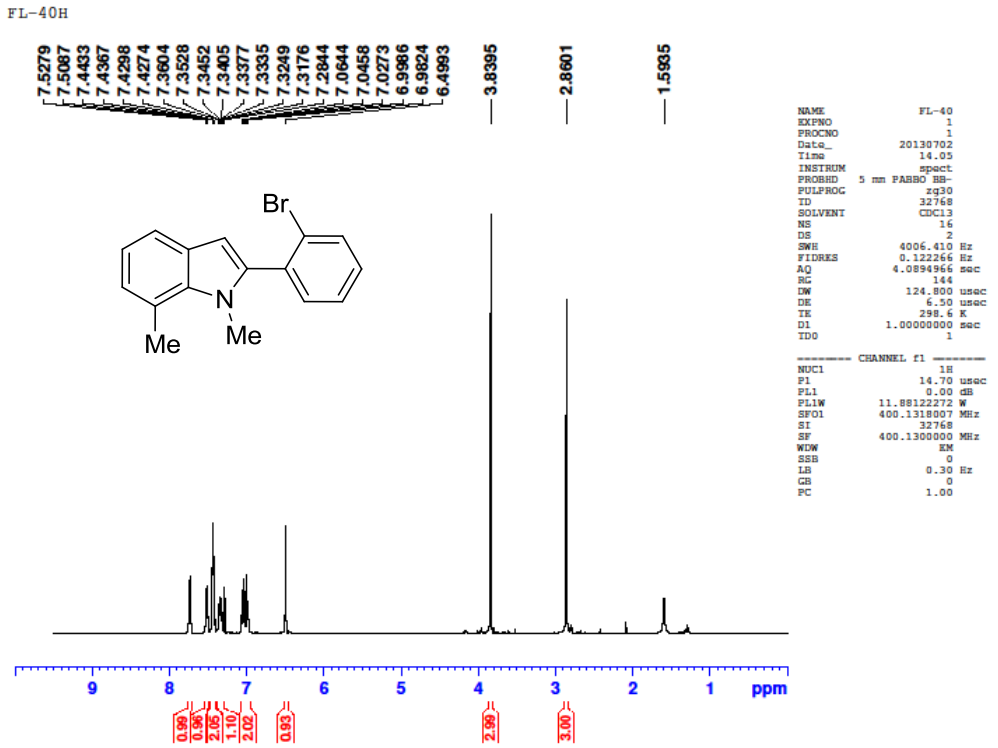
HS

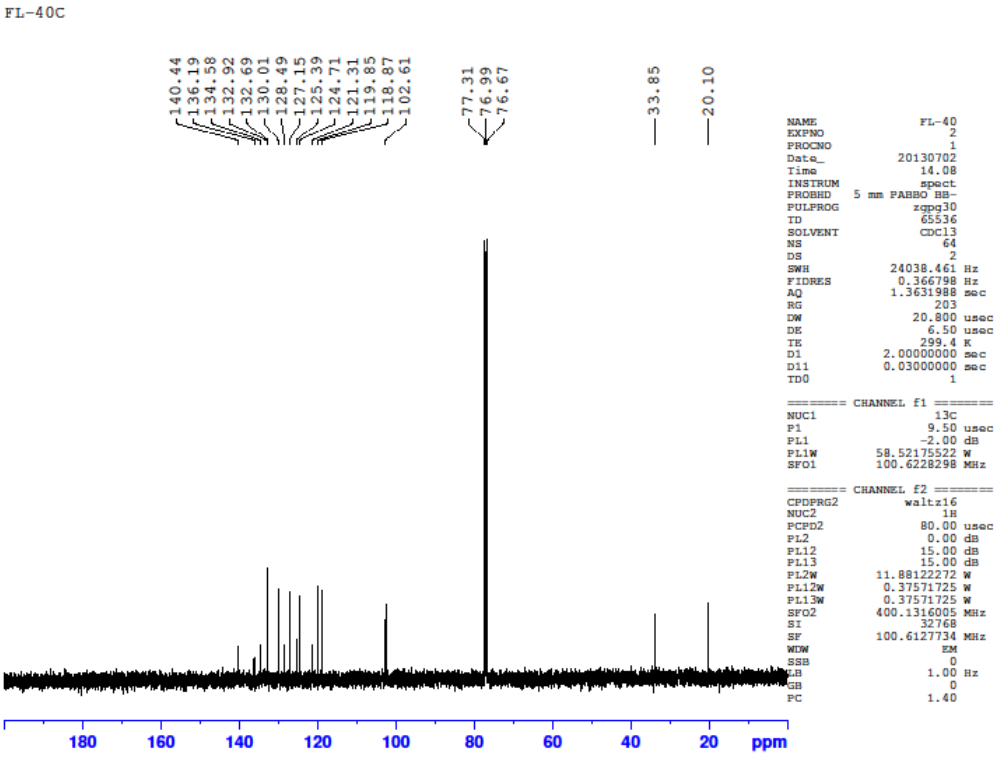




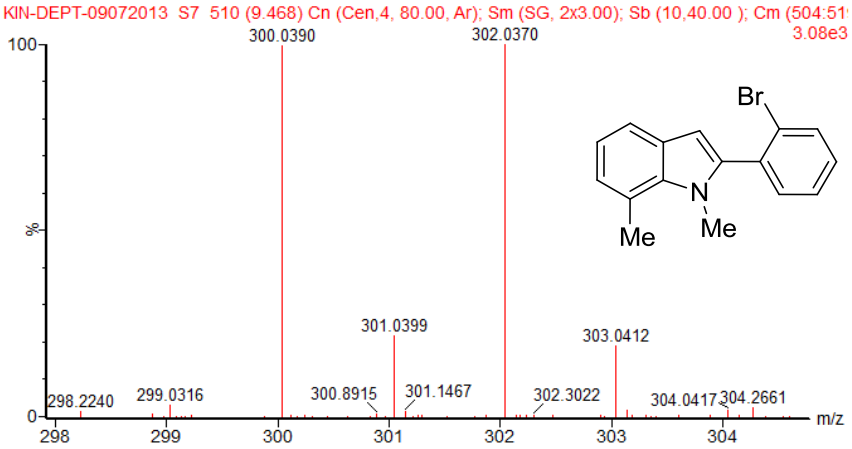
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
286.0226	286.0231	-0.5	-1.7	9.5	4.4	C15 H13 N Br

2-(2-Bromophenyl)-1,7-dimethyl-1*H*-indole (Table 7.1, L6 precursor)



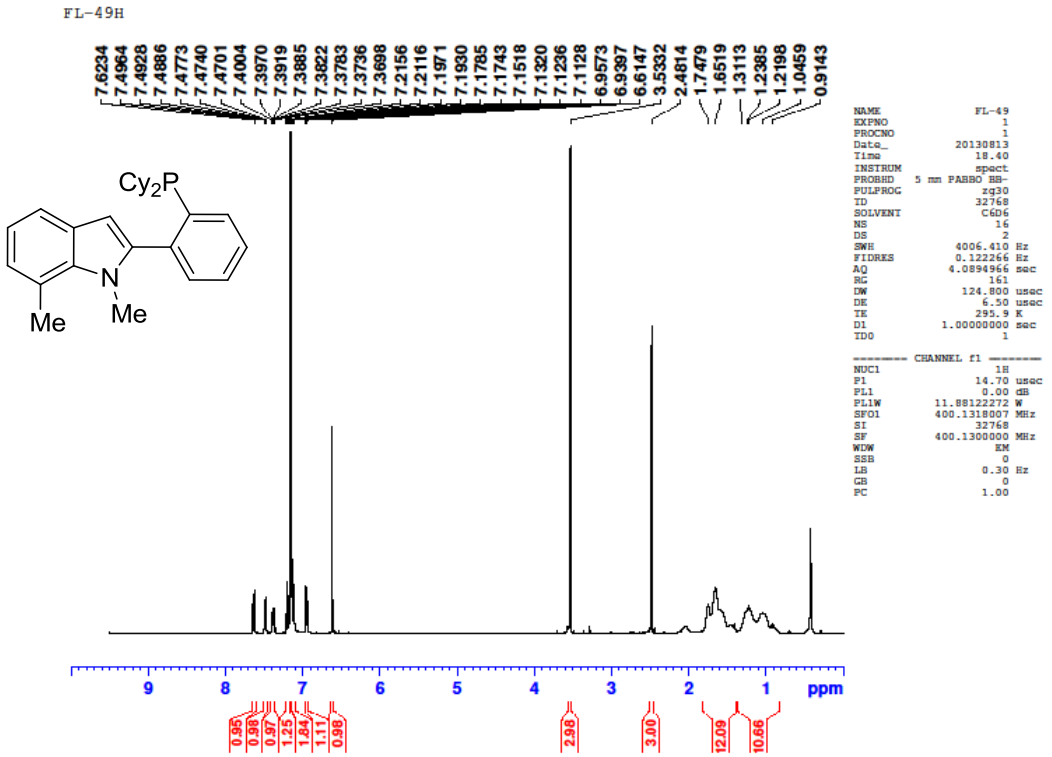


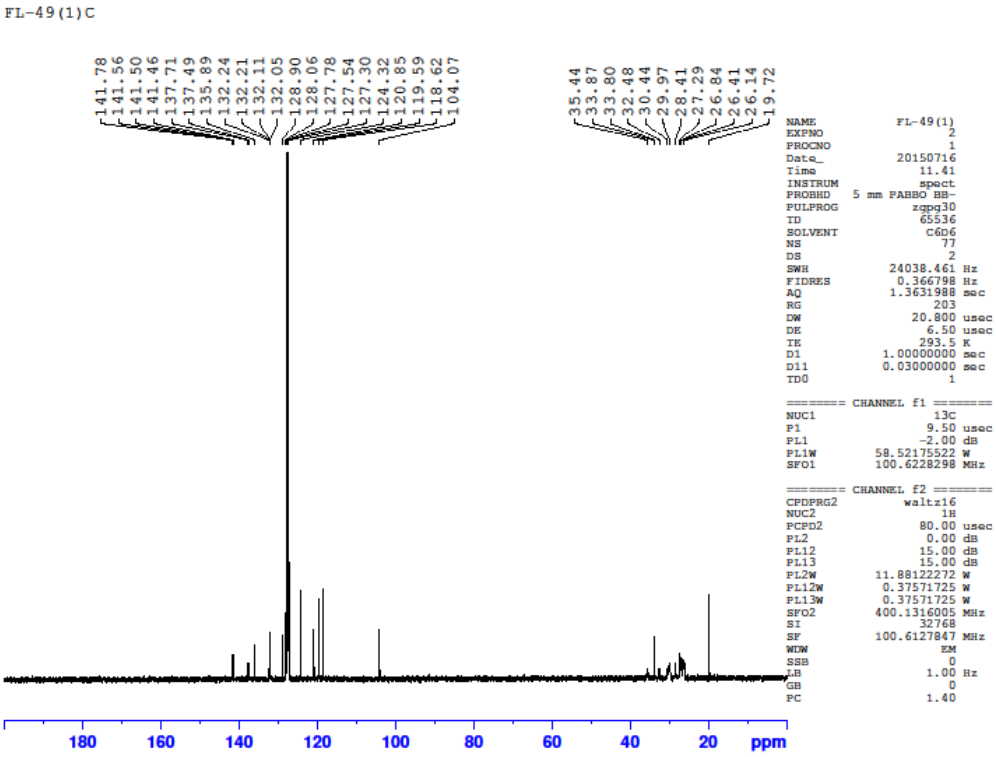
2-(2-Bromophenyl)-1,7-dimethyl-1*H*-indole (Table 7.1, L6 precursor)



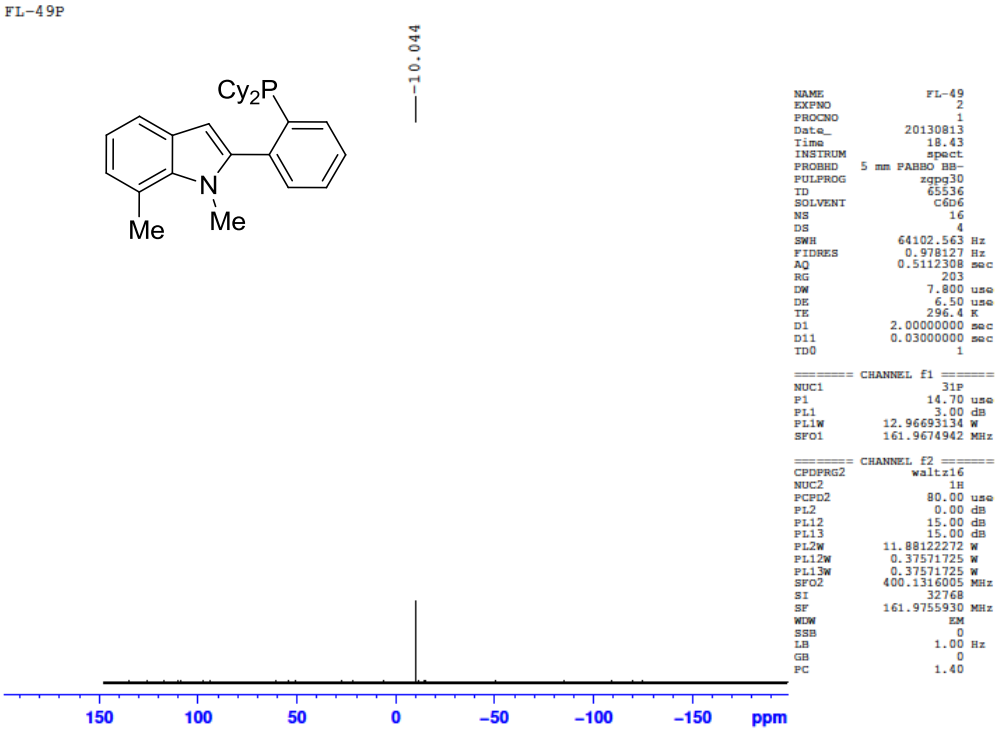
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
300.0390	300.0388	0.2	0.7	9.5	6.7	C16 H15 N Br

2-(2-(Dicyclohexylphosphino)phenyl)-1,7-dimethyl-1*H*-indole (Table 7.1, L6)

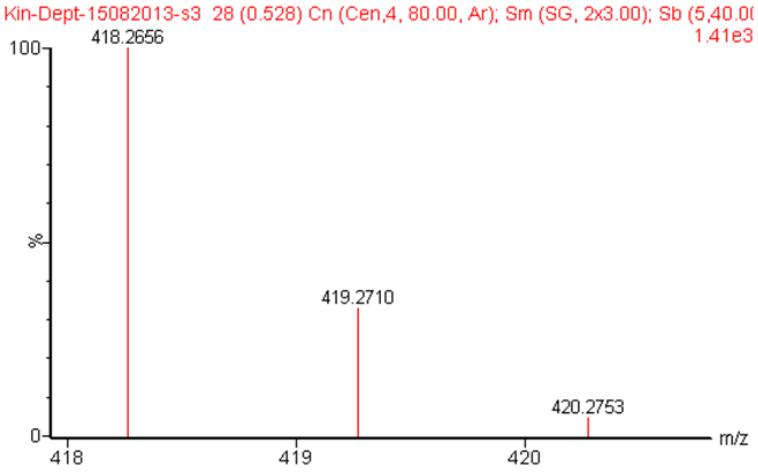




2-(2-(Dicyclohexylphosphino)phenyl)-1,7-dimethyl-1*H*-indole (Table 7.1, L6)

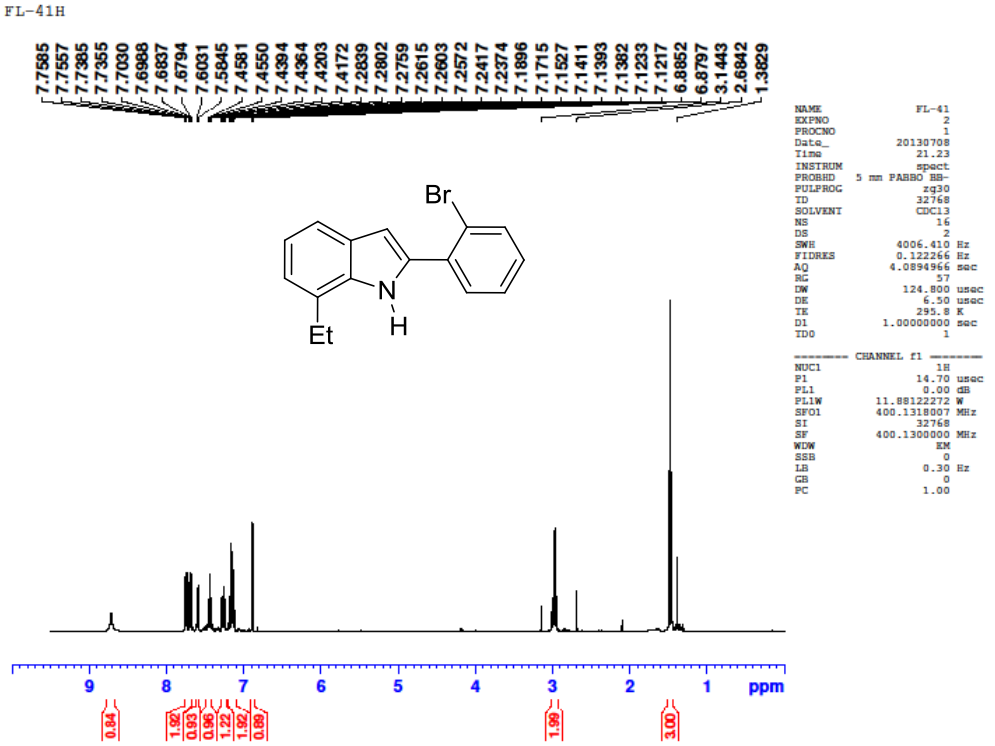


HS



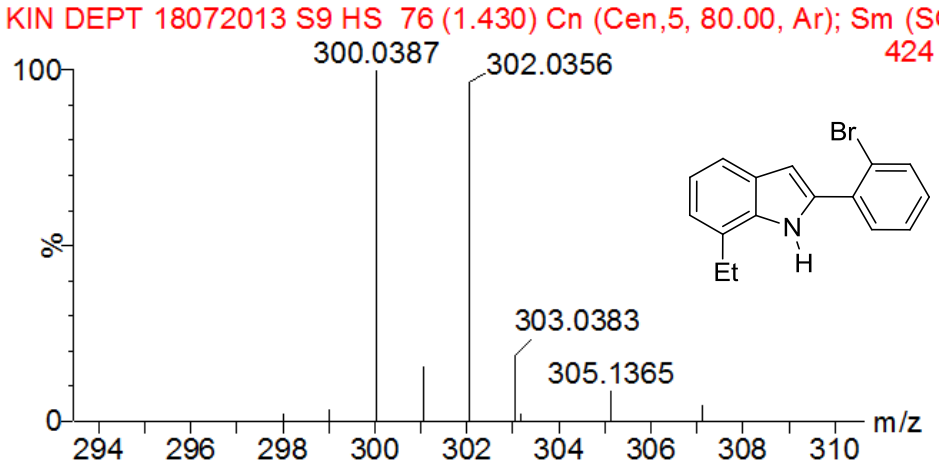
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
418.2656	418.2664	-0.8	-1.9	11.5	0.2	C28 H37 N P

2-(2-Bromophenyl)-7-ethyl-1*H*-indole (Table 7.1, L7 precursor)



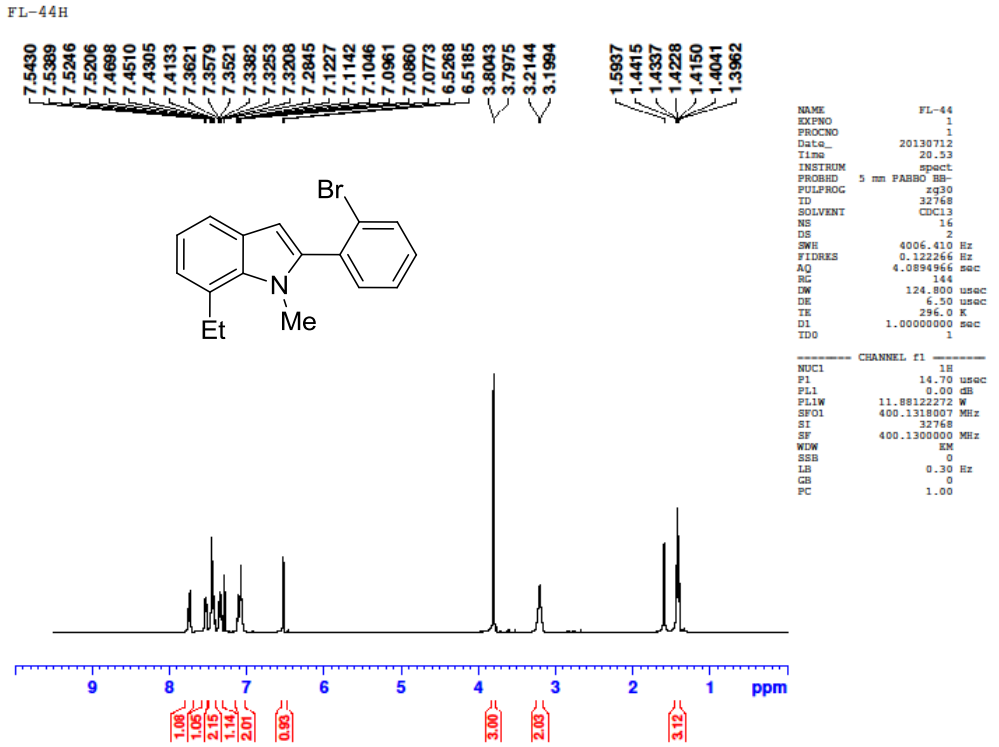
2-(2-Bromophenyl)-7-ethyl-1*H*-indole (Table 7.1, L7 precursor)

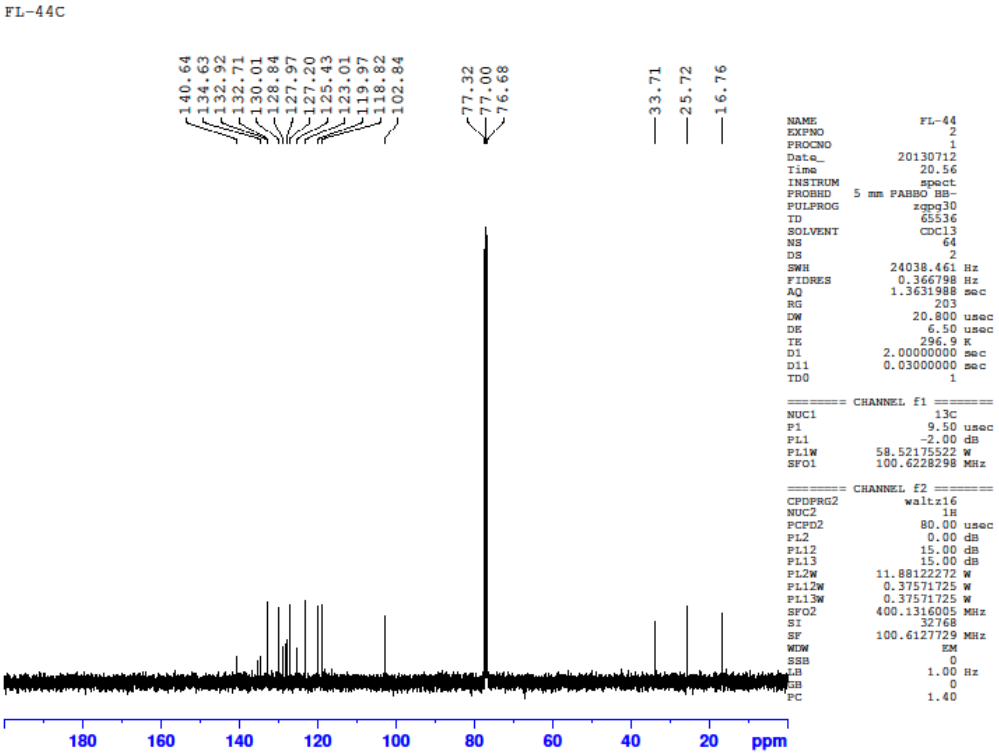
HS



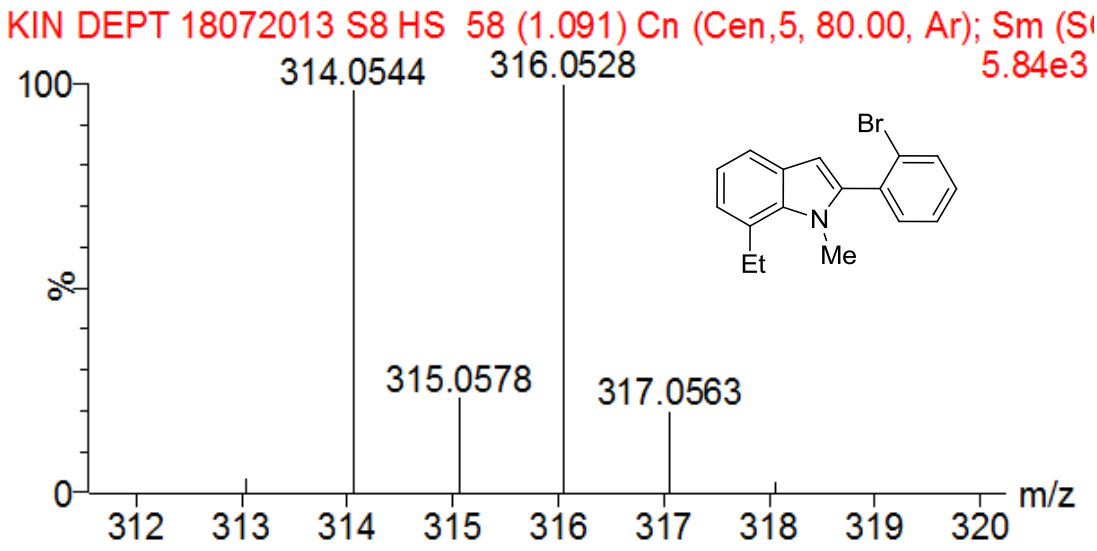
Mass	Calc. Mass	PPM	Formula
300.0387	300.0388	-0.3	C16H14NBr

2-(2-Bromophenyl)-7-ethyl-1-methyl-1*H*-indole (Table 7.1, L7 precursor)



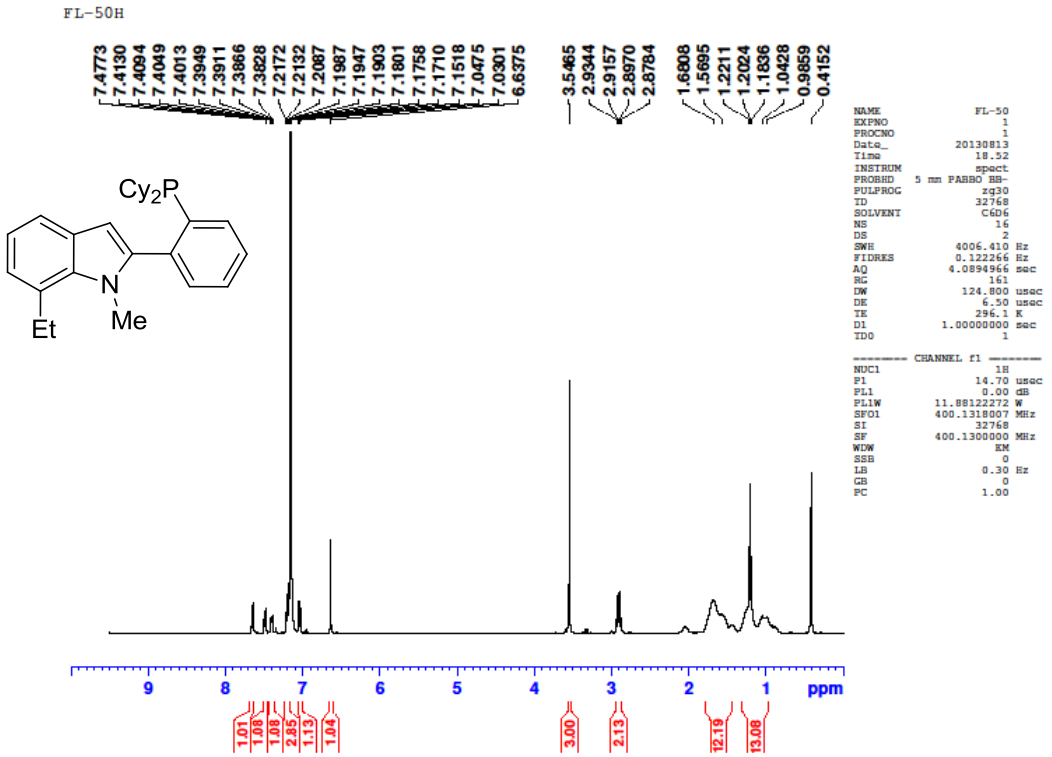


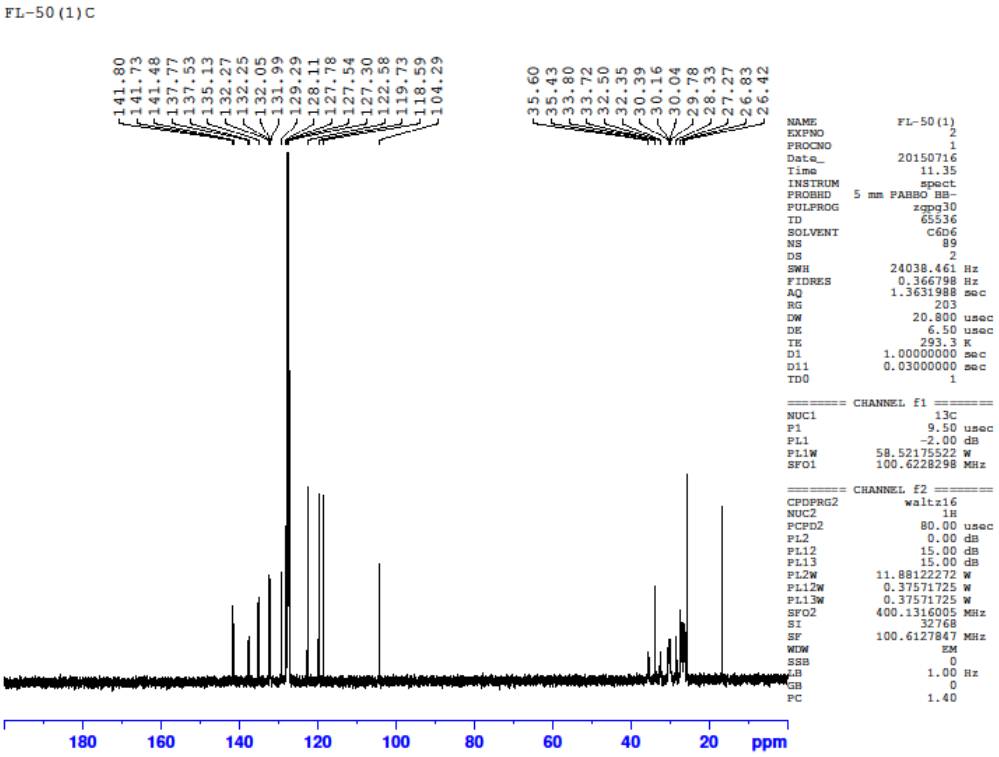
2-(2-Bromophenyl)-7-ethyl-1-methyl-1*H*-indole (Table 7.1, L7 precursor)



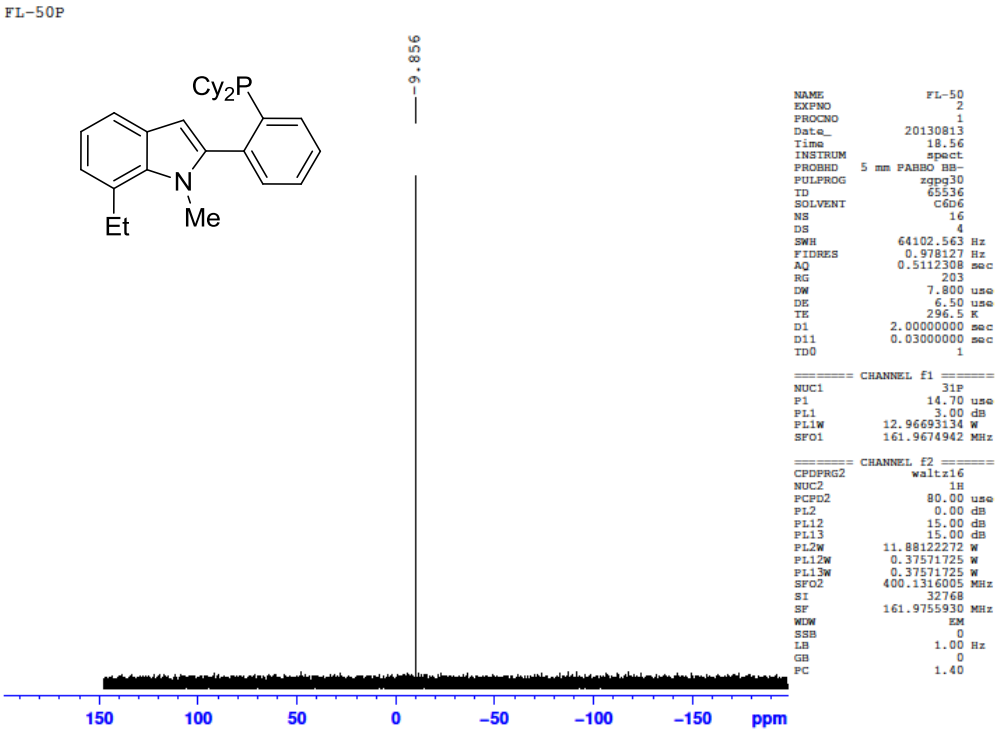
Mass	Calc. Mass	PPM	Formula
314.0544	314.0544	0	C17H16NBr

2-(2-(Dicyclohexylphosphino)phenyl)-7-ethyl-1-methyl-1*H*-indole (Table 7.1, L7)

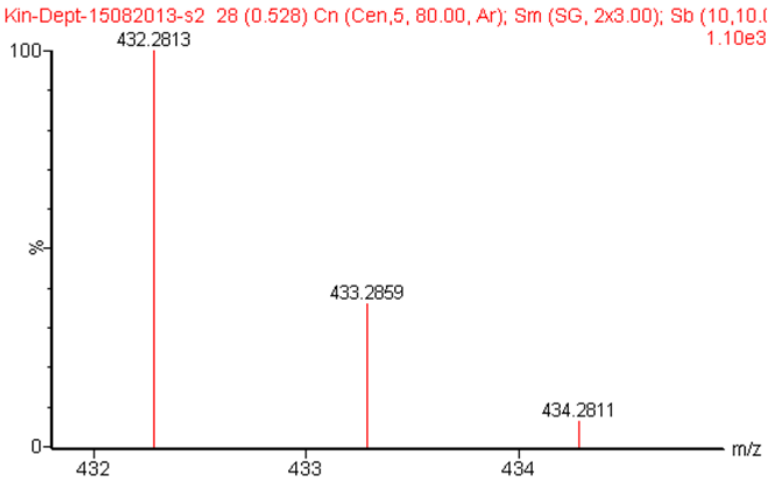




2-(2-(Dicyclohexylphosphino)phenyl)-7-ethyl-1-methyl-1*H*-indole (Table 7.1, L7)

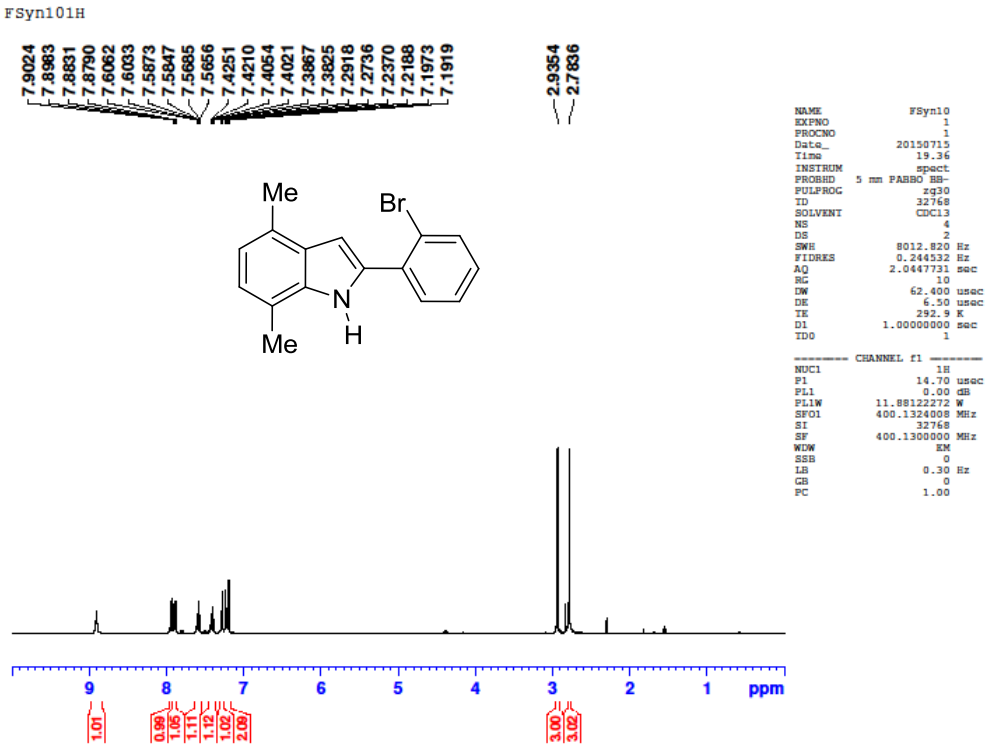


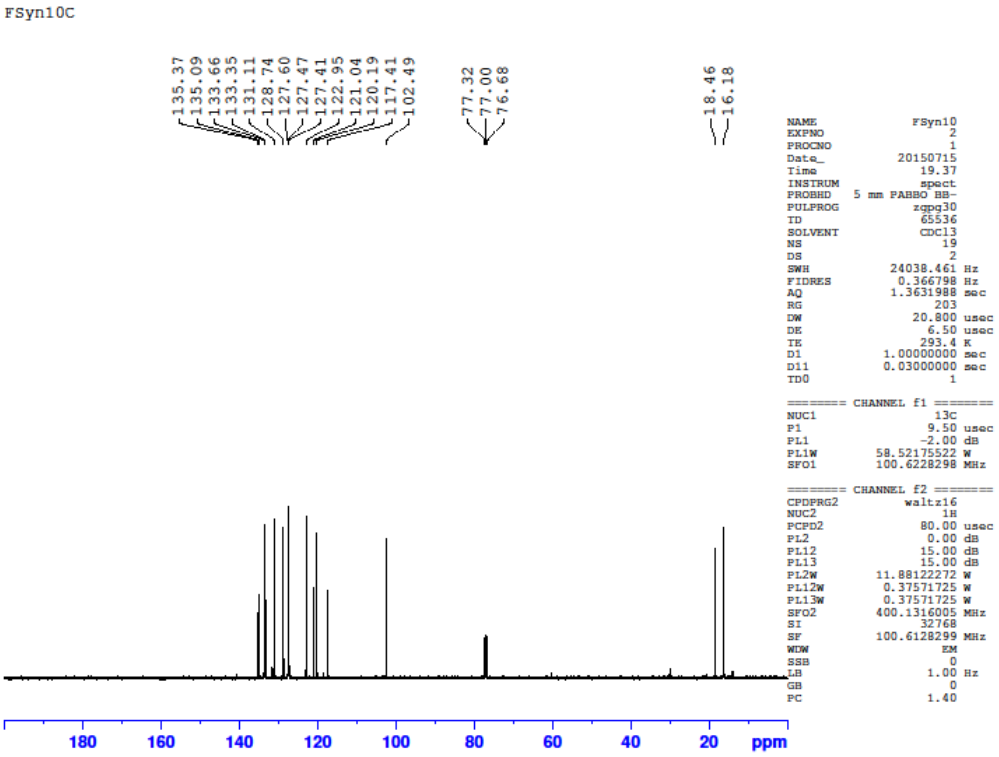
HS



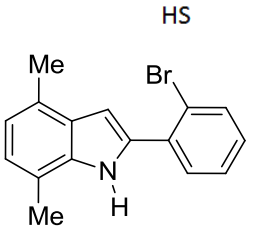
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
432.2813	432.2820	-0.7	-1.6	11.5	1.6	C29 H39 N P

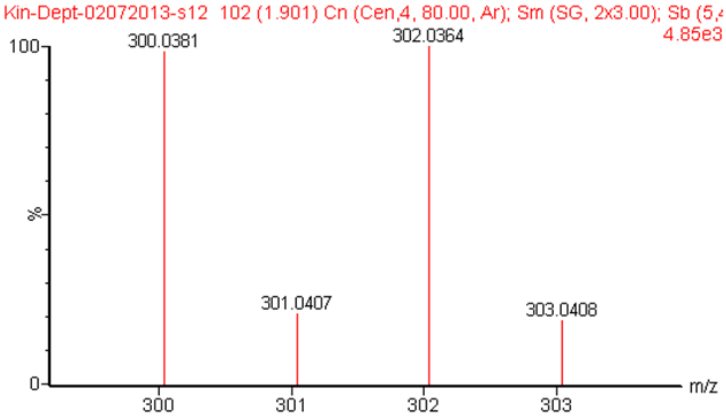
2-(2-Bromophenyl)-4,7-dimethyl-1*H*-indole (Table 7.1, L8 precursor)





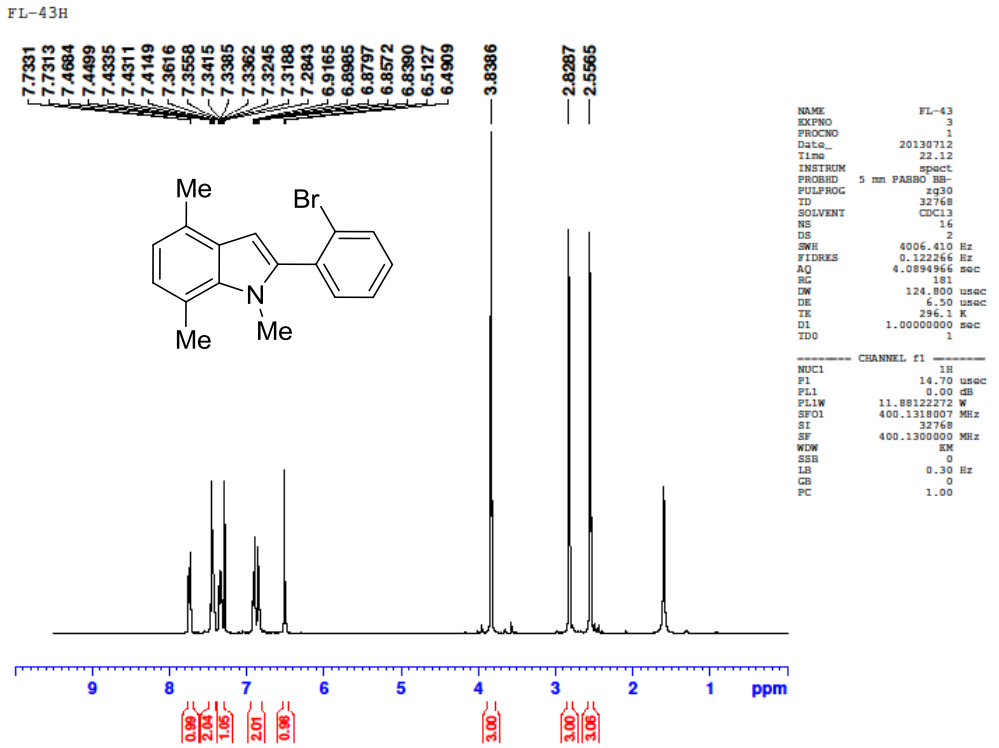
2-(2-Bromophenyl)-4,7-dimethyl-1*H*-indole (Table 7.1, L8 precursor)

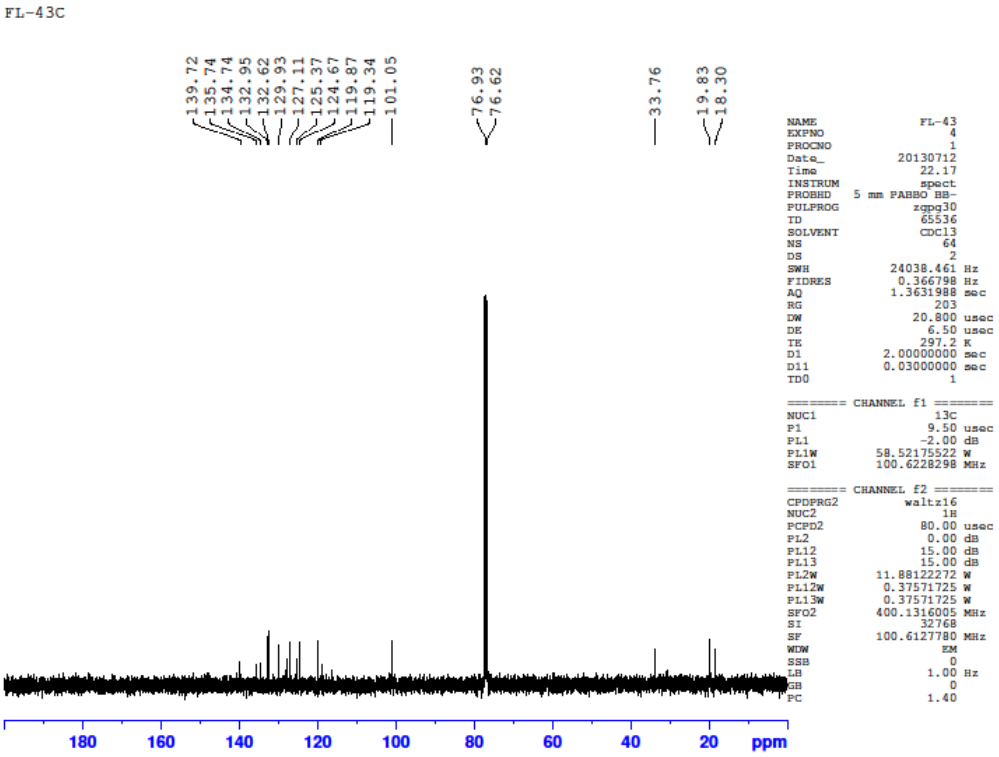




Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
300.0381	300.0388	-0.7	-2.3	9.5	6.8	C16 H15 N Br

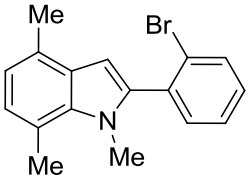
2-(2-Bromophenyl)-1,4,7-trimethyl-1*H*-indole (Table 7.1, L8 precursor)

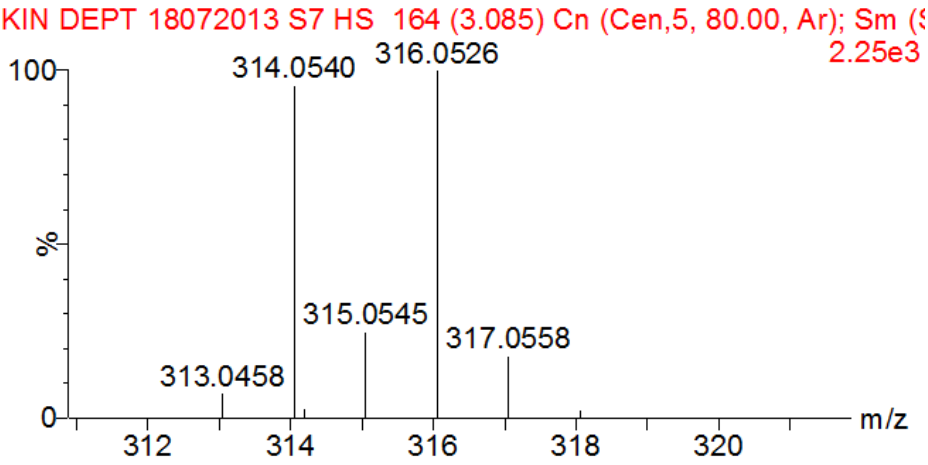




2-(2-Bromophenyl)-1,4,7-trimethyl-1*H*-indole (Table 7.1, L8 precursor)

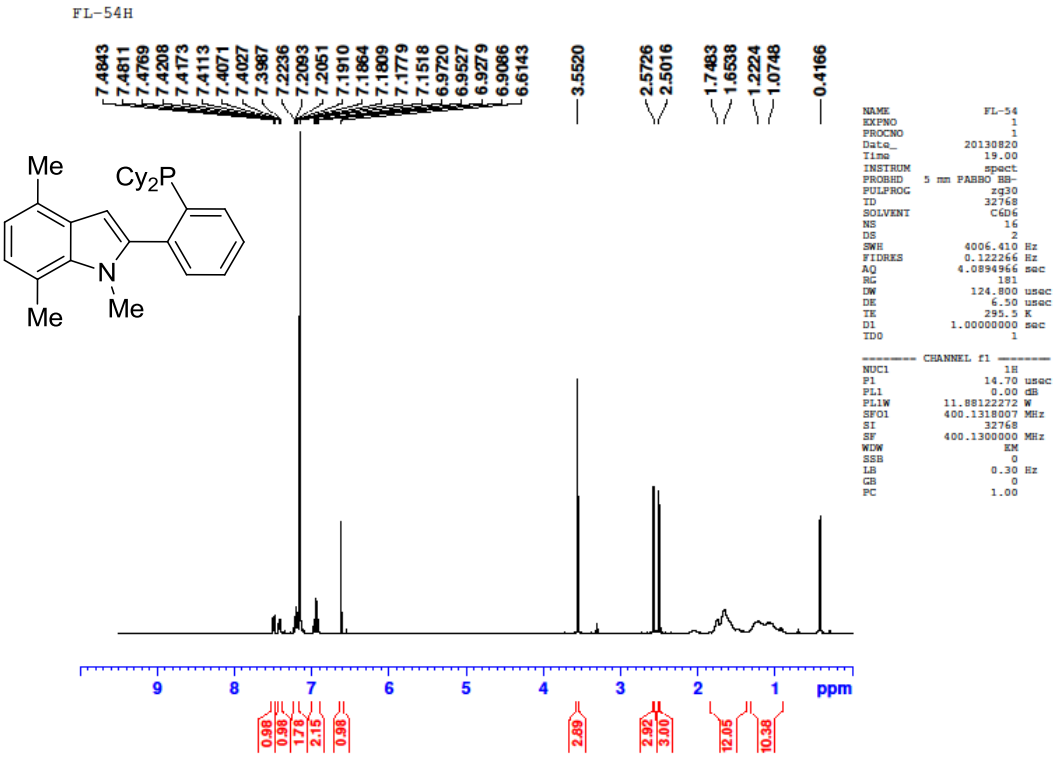
HS

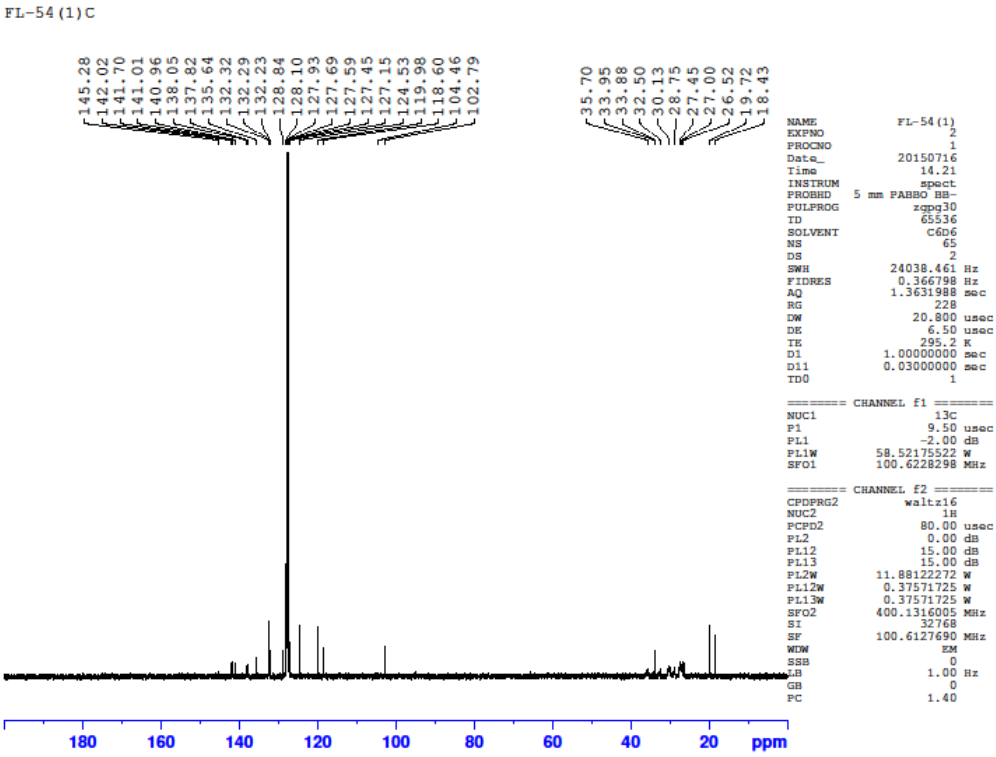




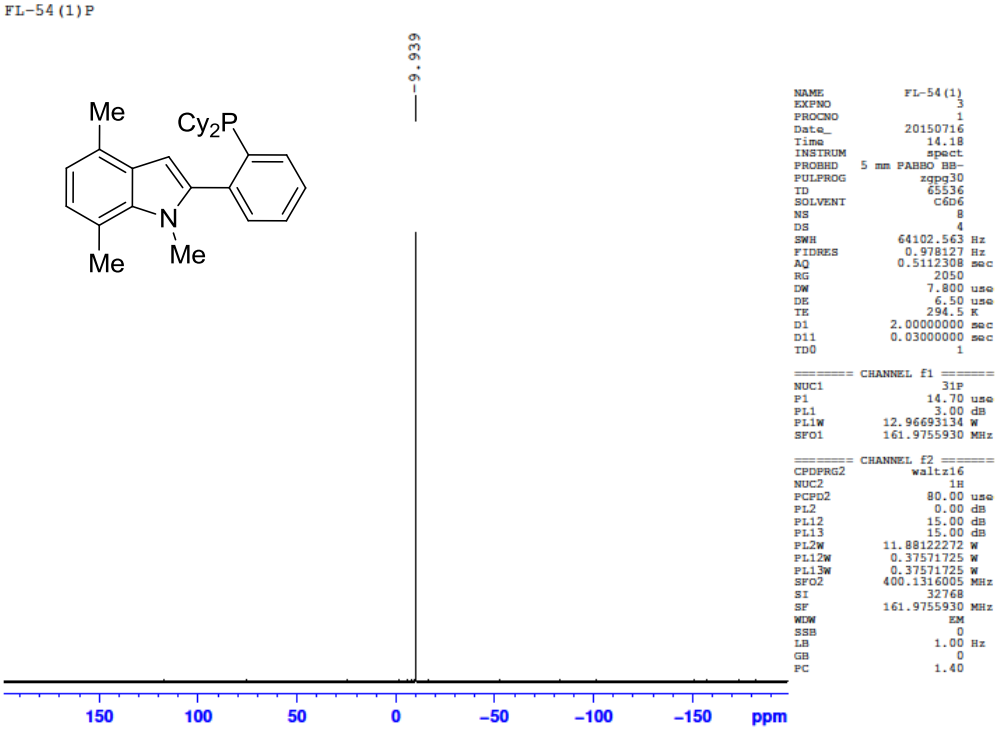
Mass	Calc. Mass	PPM	Formula
314.0540	314.0544	-1.3	C17H16NBr

2-(2-(Dicyclohexylphosphino)phenyl)-1,4,7-trimethyl-1*H*-indole (Table 7.1, L8)



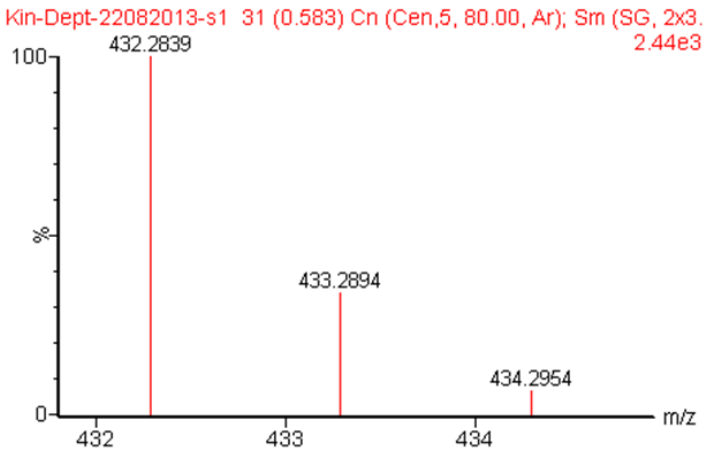


2-(2-(Dicyclohexylphosphino)phenyl)-1,4,7-trimethyl-1*H*-indole (Table 7.1, L8)




```
NAME            FL-54(1)
EXPNO                 3
PROCNO                1
Date_          20150716
Time              14.18
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG         zgpg30
TD                65536
SOLVENT            C6D6
NS                    8
DS                    4
SWH           64102.563 Hz
FIDRES        0.978127 Hz
AQ            0.5112308 sec
RG                 2050
DW                7.800 use
DE                6.50 use
TE               294.5 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                   1

======== CHANNEL f1 ======
NUC1                31P
P1                14.70 use
PL1                3.00 dB
PL1W        12.96693134 W
SFO1       161.9755930 MHz

======== CHANNEL f2 ======
CPDPRG2         waltz16
NUC2                1H
PCPD2             80.00 use
PL2                0.00 dB
PL12              15.00 dB
PL13              15.00 dB
PL2W        11.881222272 W
PL12W        0.37571725 W
PL13W        0.37571725 W
SFO2       400.1316005 MHz
SI                32768
SF         161.9755930 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```

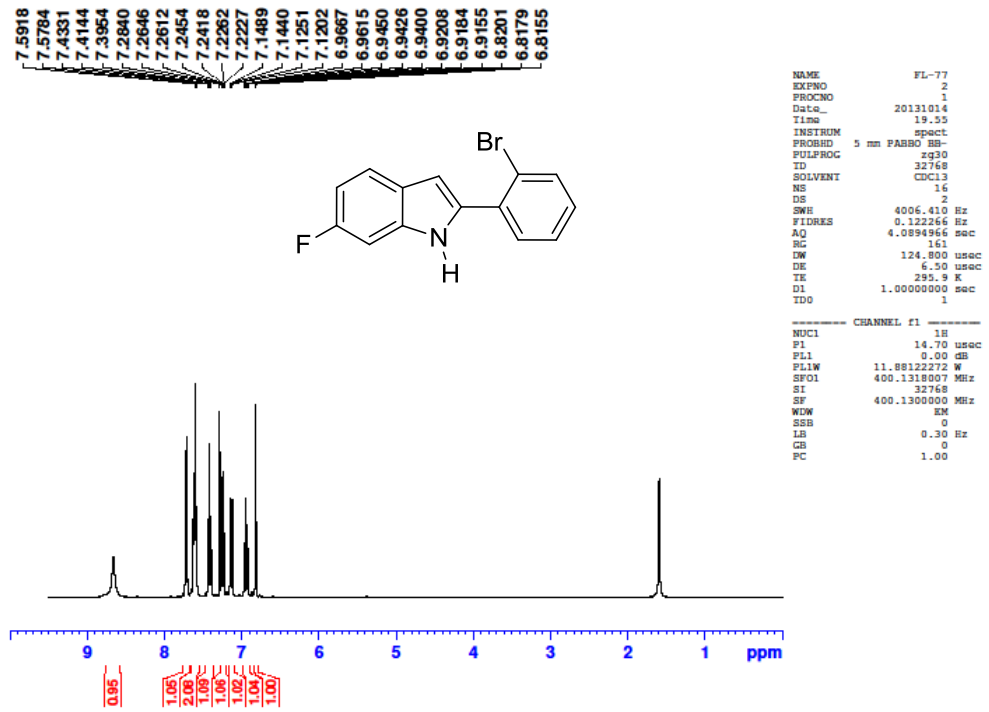
HR



Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
432.2839	432.2820	1.9	4.4	11.5	2.4	C29 H39 N P

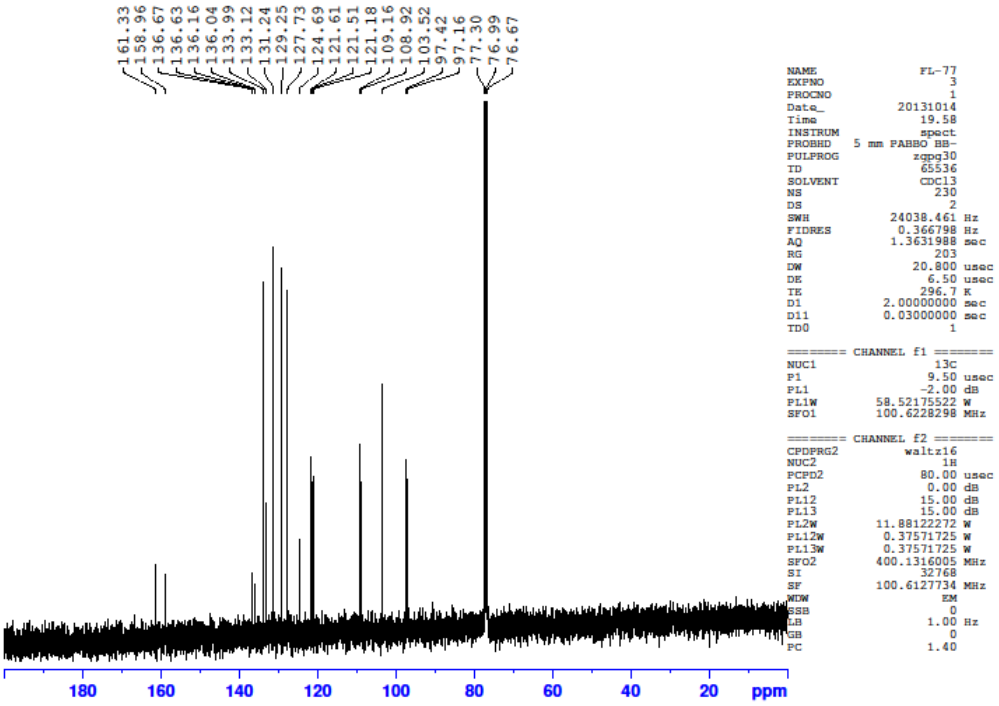
2-(2-Bromophenyl)-6-fluoro-1*H*-indole (Table 7.1, L9 precursor)

FL-77H



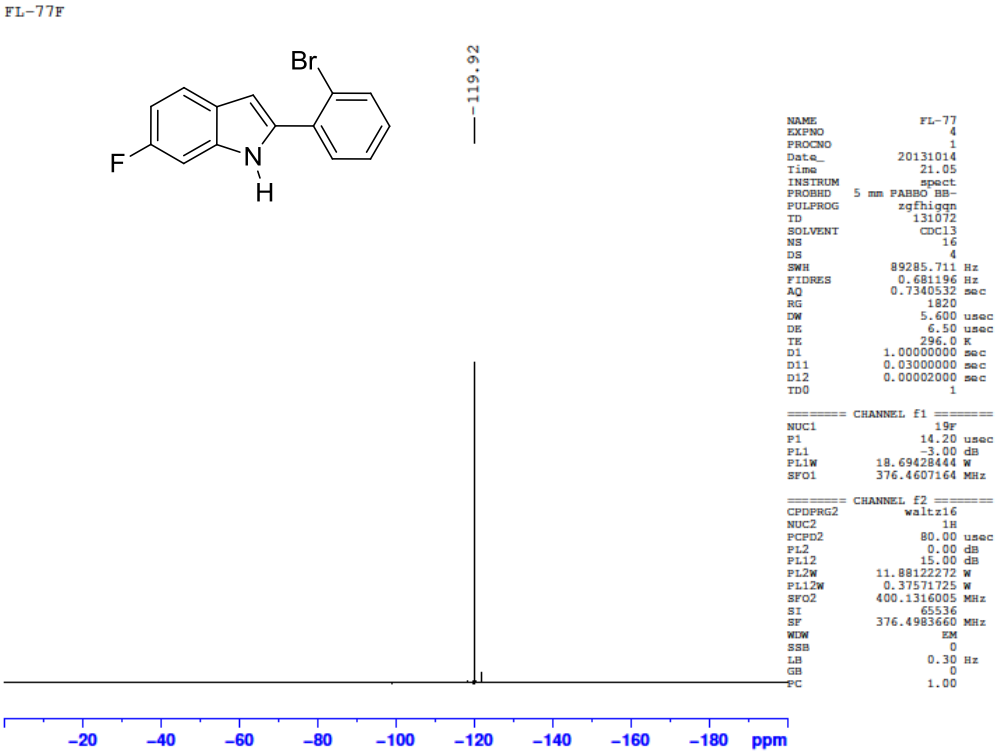

```
NAME                FL-77
EXPNO                  2
PROCNO                 1
Date_           20131014
Time                19.55
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             4006.410 Hz
FIDRES          0.122266 Hz
AQ              4.0894966 sec
RG                   161
DW                124.800 usec
DE                  6.50 usec
TE                 295.9 K
D1              1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 14.70 usec
PL1                 0.00 dB
PL1W         11.88122272 W
SFO1         400.1318007 MHz
SI                 32768
SF           400.1300000 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

FL-77C

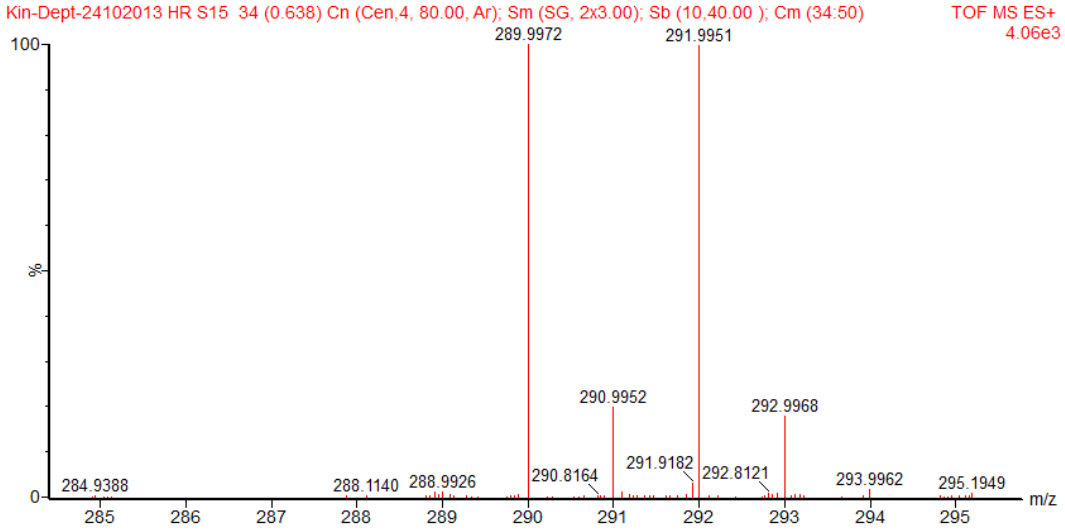



```
NAME                FL-77
EXPNO                  3
PROCNO                 1
Date_           20131014
Time                19.58
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                   230
DS                     2
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631988 sec
RG                   203
DW                20.800 usec
DE                  6.50 usec
TE                 296.7 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                  9.50 usec
PL1                -2.00 dB
PL1W         58.52175522 W
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2              80.00 usec
PL2                 0.00 dB
PL12               15.00 dB
PL13               15.00 dB
PL2W         11.88122272 W
PL12W         0.37571725 W
PL13W         0.37571725 W
SFO2         400.1316005 MHz
SI                 32768
SF           100.6127734 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
```

2-(2-Bromophenyl)-6-fluoro-1*H*-indole (Table 7.1, L9 precursor)



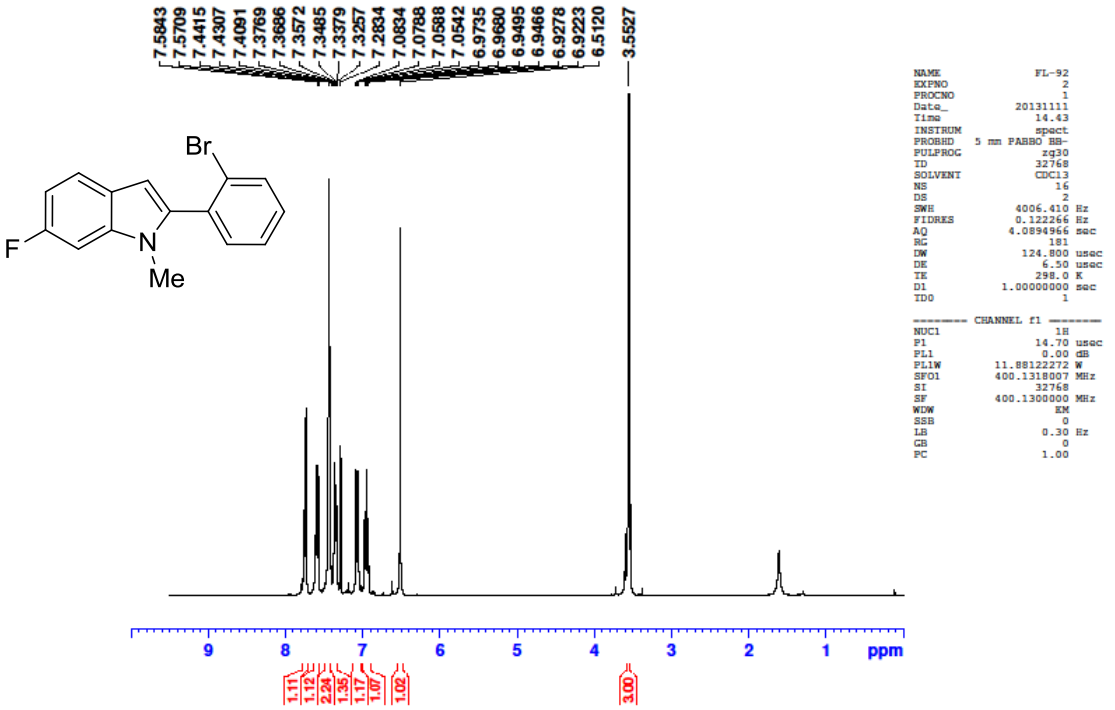
HS



Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
289.9972	289.9981	-0.9	-3.1	9.5	14.9	C14 H10 N Br F

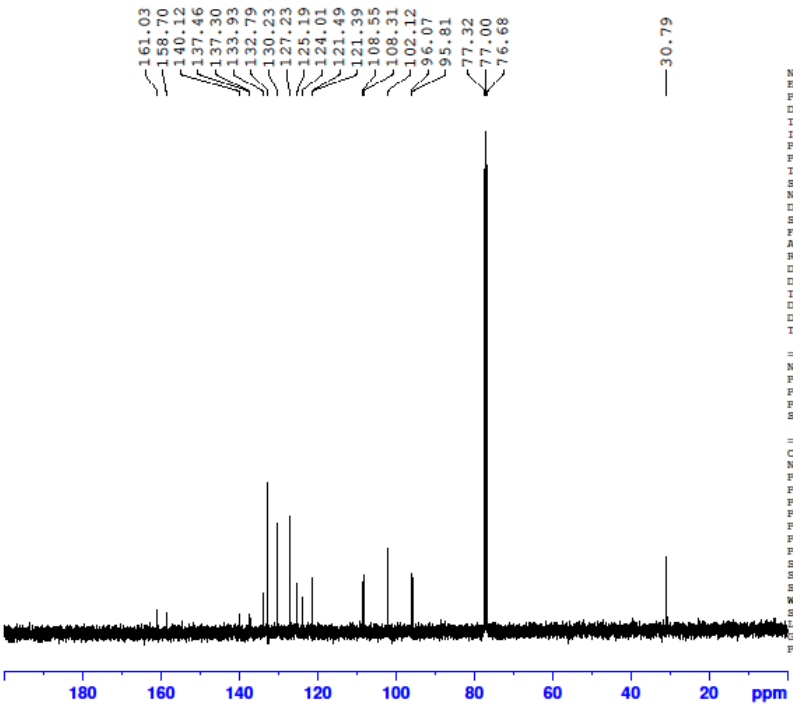
2-(2-Bromophenyl)-6-fluoro-1-methyl-1*H*-indole (Table 7.1, L9 precursor)

FL-92H



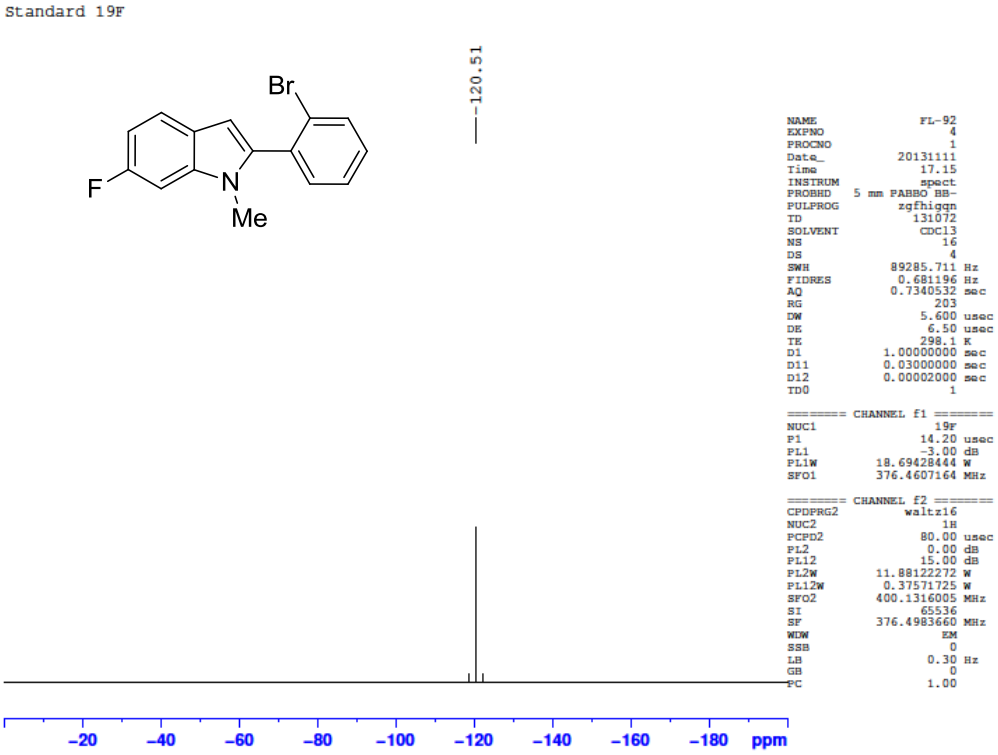

```
NAME                FL-92
EXPNO                  2
PROCNO                 1
Date_           20131111
Time               14.43
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             4006.410 Hz
FIDRES          0.122266 Hz
AQ              4.0894966 sec
RG                   181
DW                124.800 usec
DE                  6.50 usec
TE                298.0 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 14.70 usec
PL1                0.00 dB
PL1W          11.88122272 W
SFO1          400.1318007 MHz
SI                 32768
SF            400.1300000 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

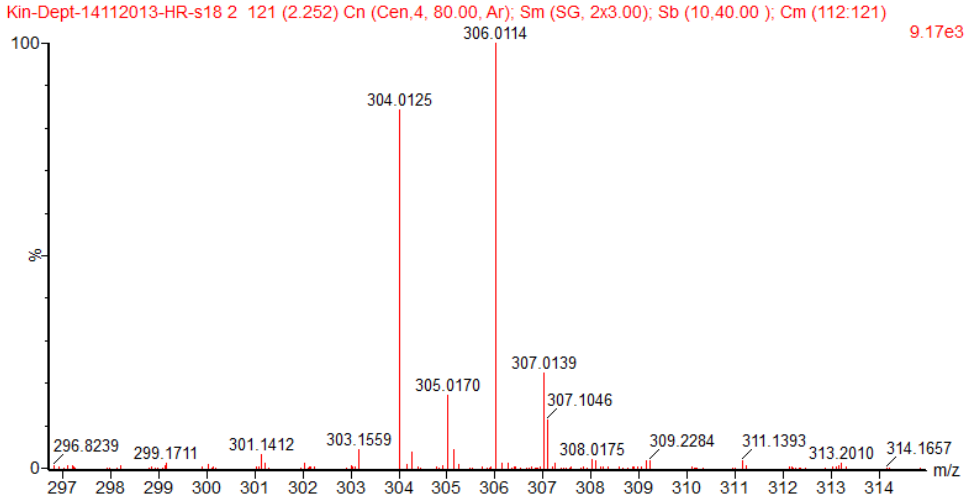
FL-92C




```
NAME                FL-92
EXPNO                  3
PROCNO                 1
Date_           20131111
Time               17.10
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                    64
DS                     2
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631988 sec
RG                   181
DW                20.800 usec
DE                  6.50 usec
TE                298.3 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  13C
P1                  9.50 usec
PL1                -2.00 dB
PL1W          58.52175522 W
SFO1          100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                  1H
PCPD2              80.00 usec
PL2                 0.00 dB
PL12               15.00 dB
PL13               15.00 dB
PL2W          11.88122272 W
PL12W          0.37571725 W
PL13W          0.37571725 W
SFO2          400.1316005 MHz
SI                 32768
SF            100.6127721 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
```

2-(2-Bromophenyl)-6-fluoro-1-methyl-1*H*-indole (Table 7.1, L9 precursor)

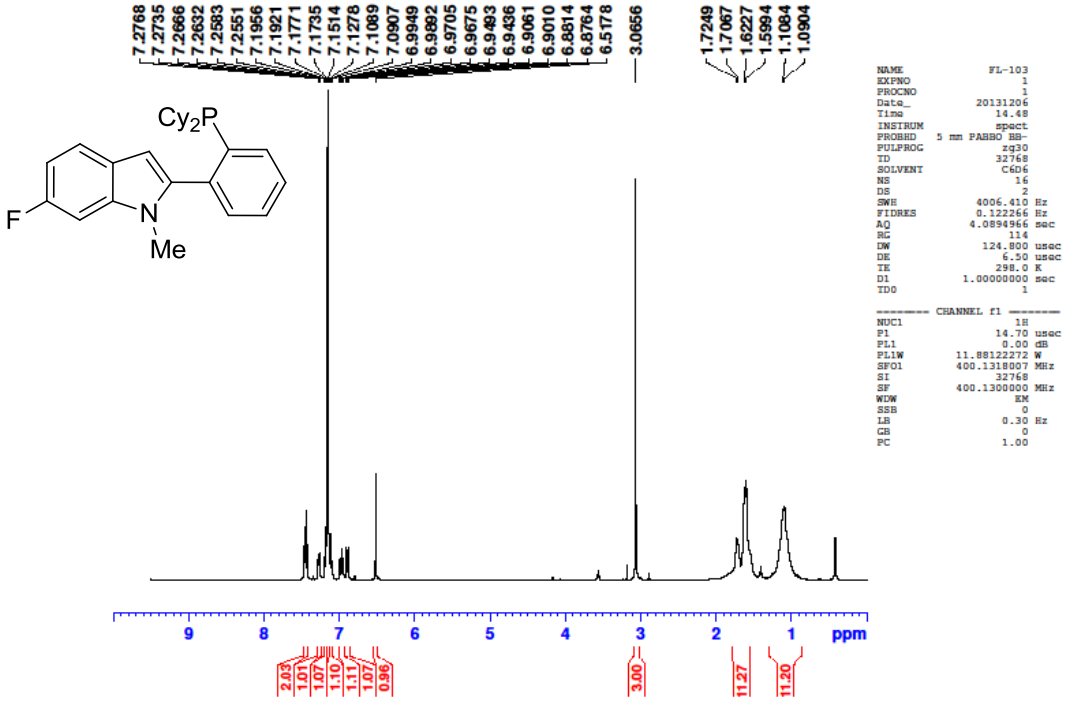




Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
304.0125	304.0137	-1.2	-3.9	9.5	74.6	C15 H12 N F Br

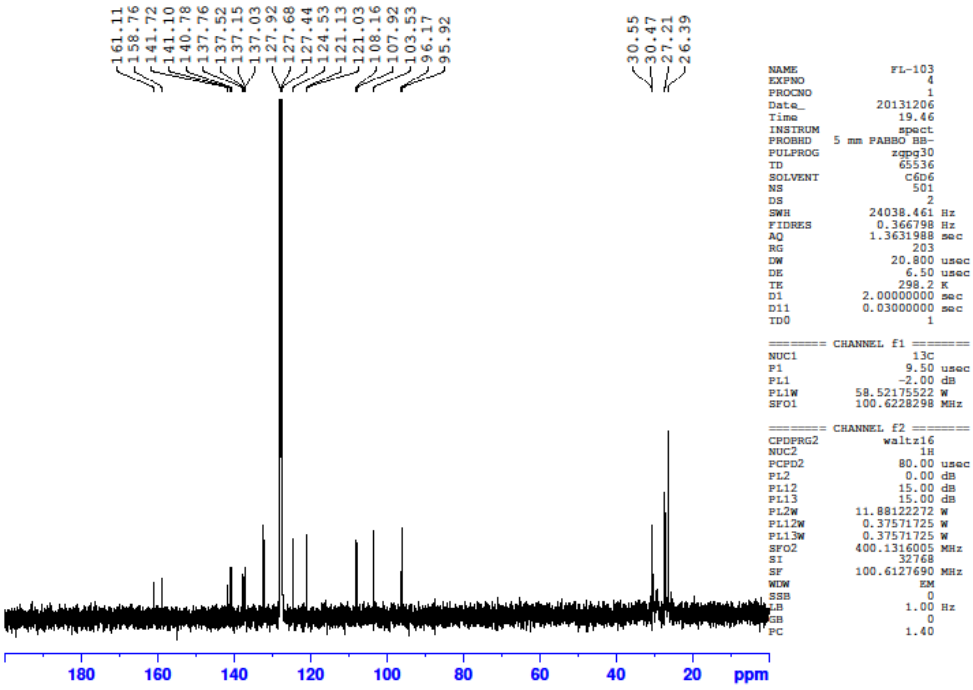
2-(2-(Dicyclohexylphosphino)phenyl)-6-fluoro-1-methyl-1*H*-indole (Table 7.1, L9)

FL-103H



NAME	FL-103
EXPNO	1
PROCNO	1
Date_	20131206
Time	14.48
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	32768
SOLVENT	C6D6
NS	16
DS	2
SWH	4006.410 Hz
FIDRES	0.122266 Hz
AQ	4.0894966 sec
RG	114
DW	124.800 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	14.70 usec
PL1	0.00 dB
PL1W	11.88122272 W
SFO1	400.1318007 MHz
SI	32768
SF	400.1300000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

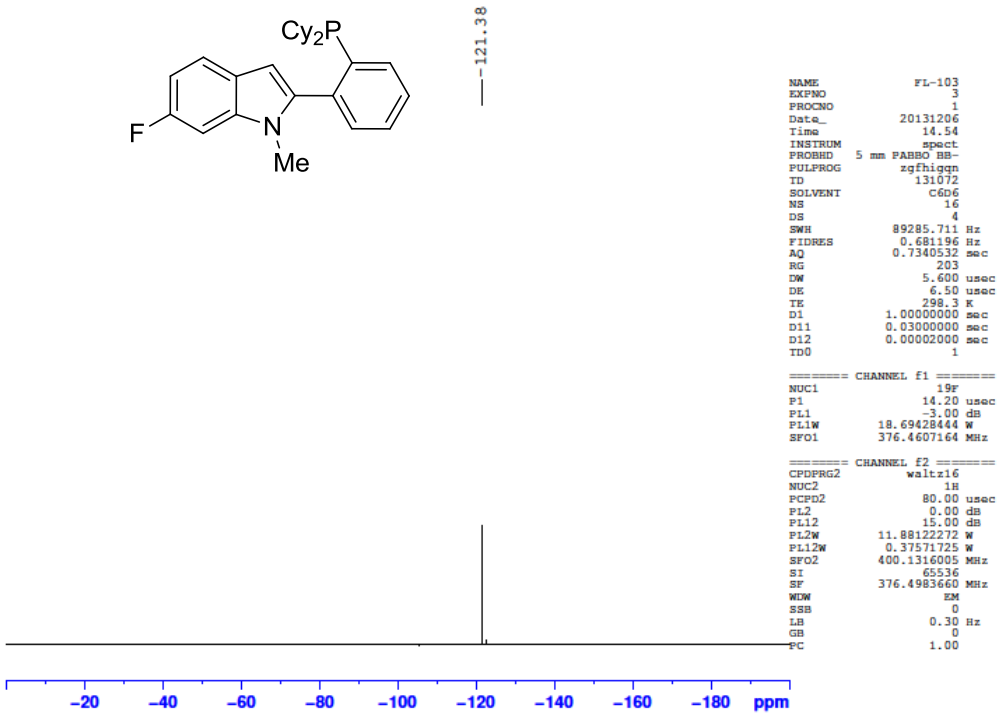
FL-103C



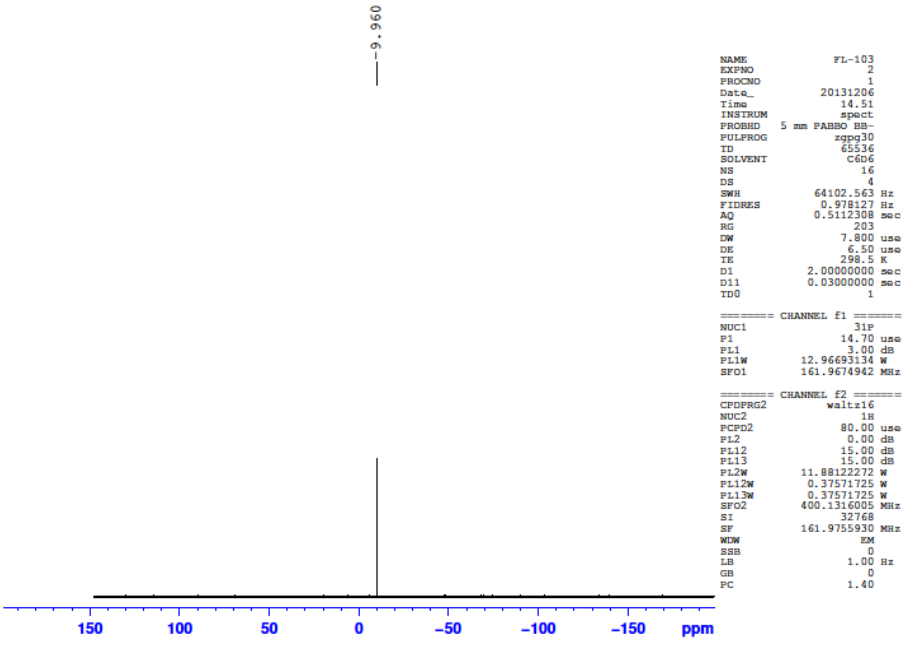
NAME	FL-103
EXPNO	4
PROCNO	1
Date_	20131206
Time	19.46
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	C6D6
NS	501
DS	2
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	298.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.50 usec
PL1	-2.00 dB
PL1W	58.52175522 W
SFO1	100.6228298 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	0.00 dB
PL12	15.00 dB
PL13	15.00 dB
PL2W	11.88122272 W
PL12W	0.37571725 W
PL13W	0.37571725 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127690 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

2-(2-(Dicyclohexylphosphino)phenyl)-6-fluoro-1-methyl-1*H*-indole (Table 7.1, L9)

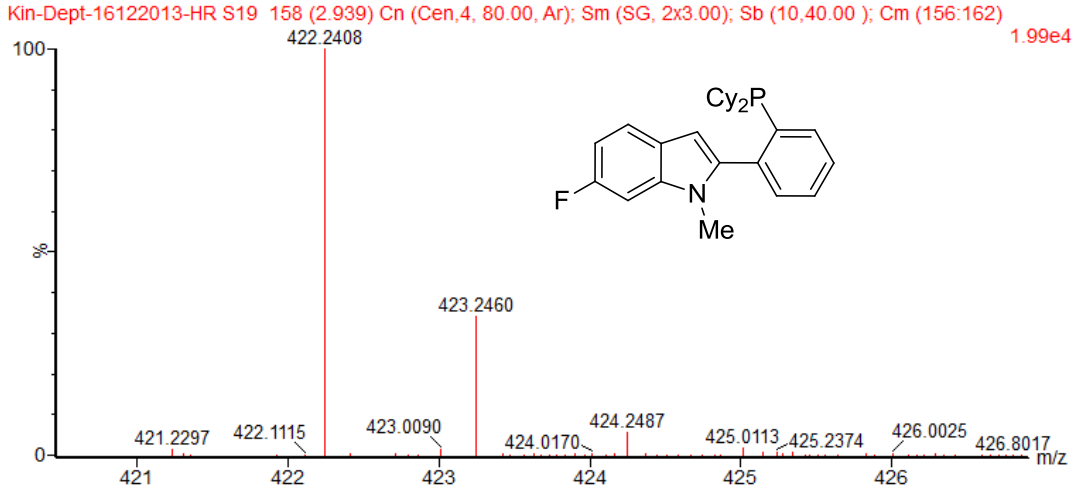
FL-103F



FL-103P

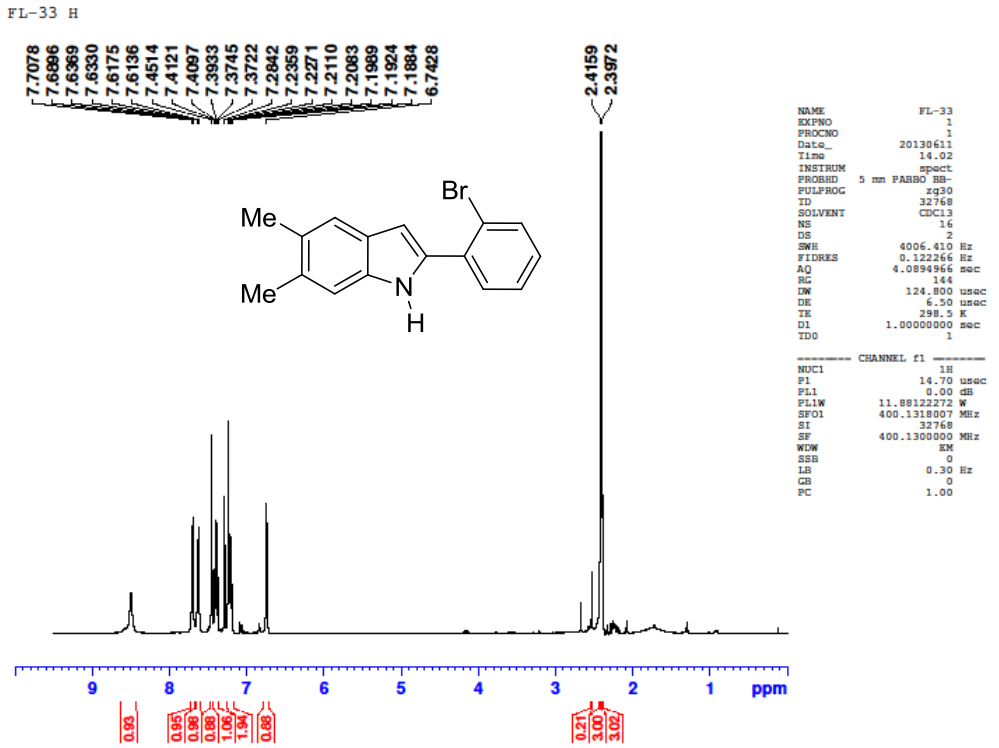


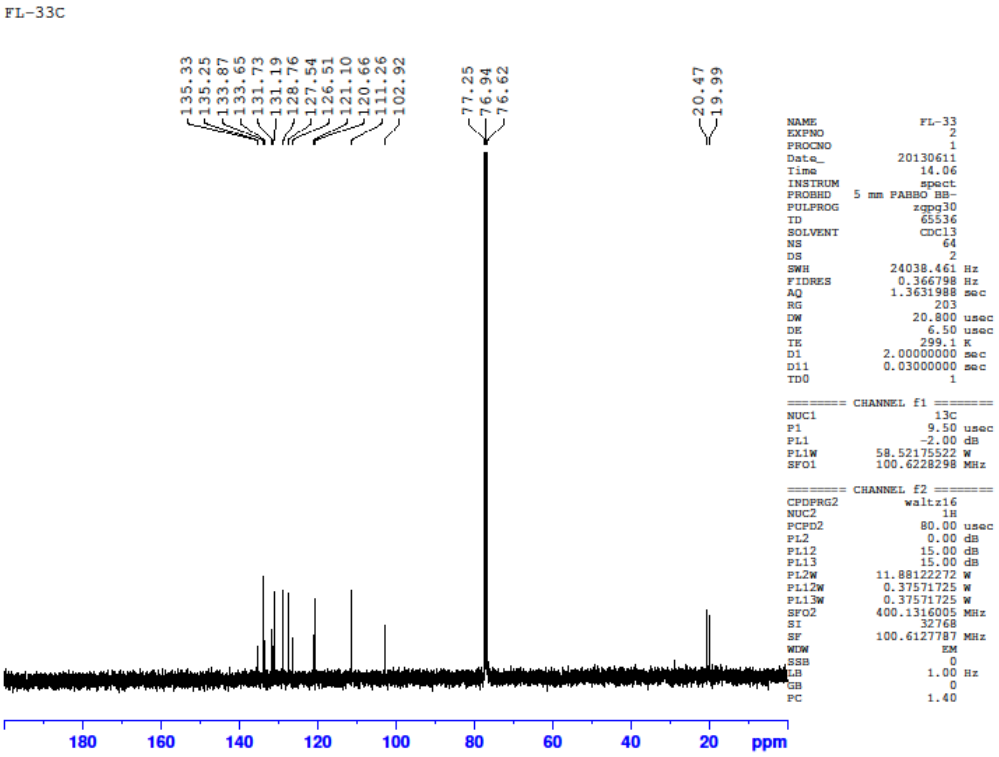
2-(2-(Dicyclohexylphosphino)phenyl)-6-fluoro-1-methyl-1*H*-indole (Table 7.1, L9)



Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
422.2408	422.2413	-0.5	-1.2	11.5	38.5	C27 H34 N F P

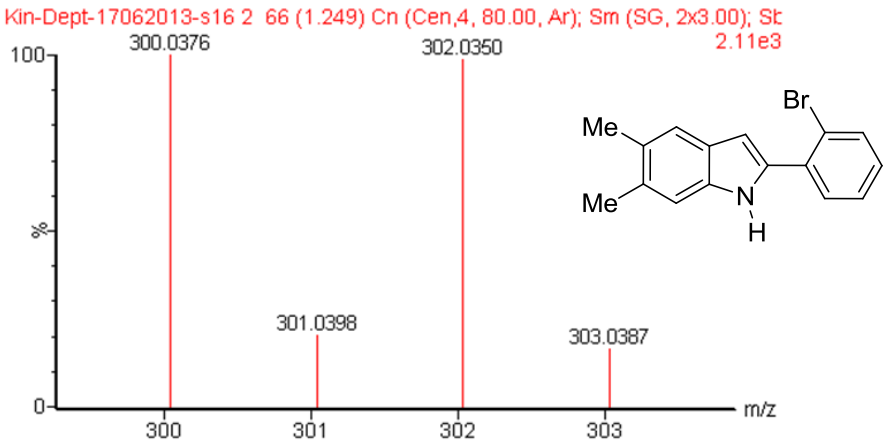
2-(2-Bromophenyl)-5,6-dimethyl-1*H*-indole (Table 7.1, L10 precursor)





2-(2-Bromophenyl)-5,6-dimethyl-1*H*-indole (Table 7.1, L10 precursor)

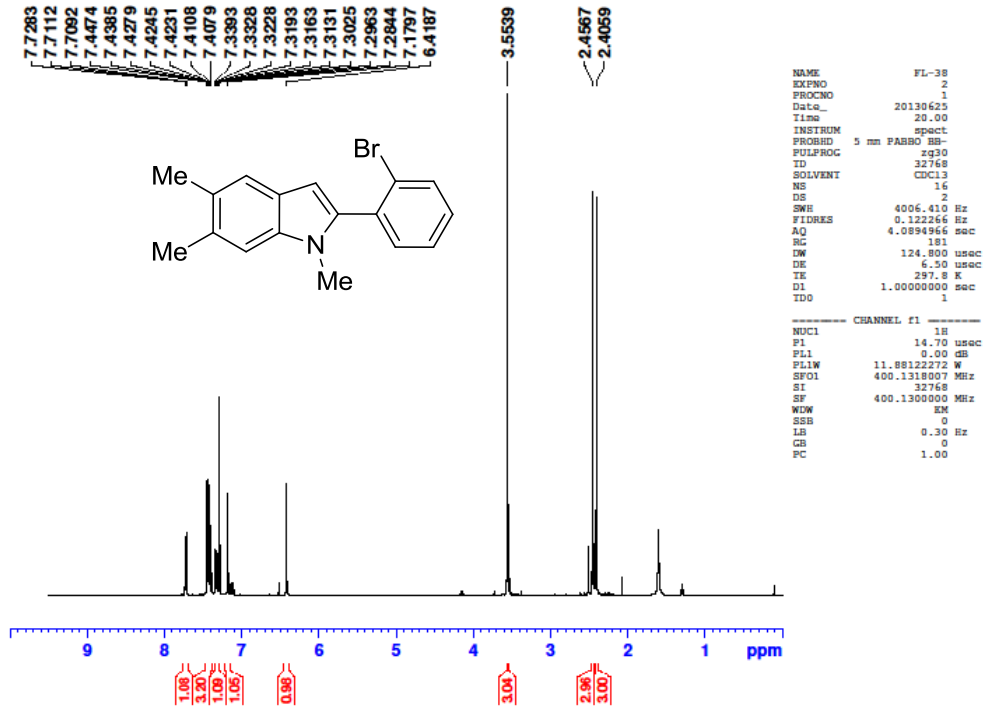
HS



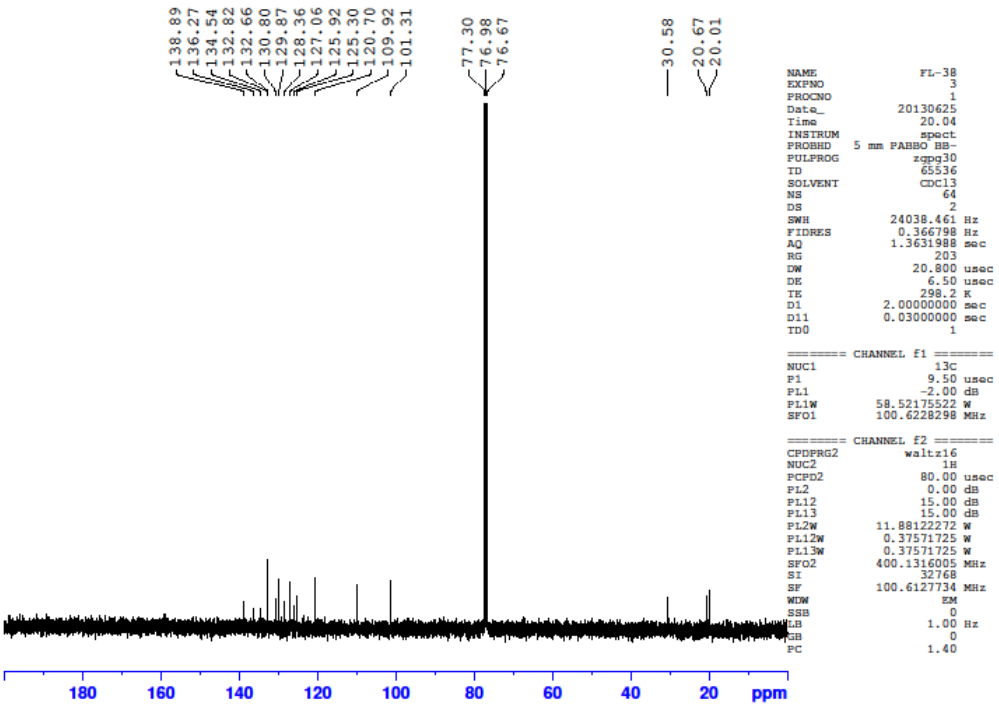
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
300.0376	300.0388	-1.2	-4.0	9.5	1.9	C16 H15 N Br

2-(2-Bromophenyl)-1,5,6-trimethyl-1*H*-indole (Table 7.1, L10 precursor)

FL-38H

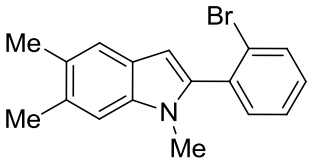


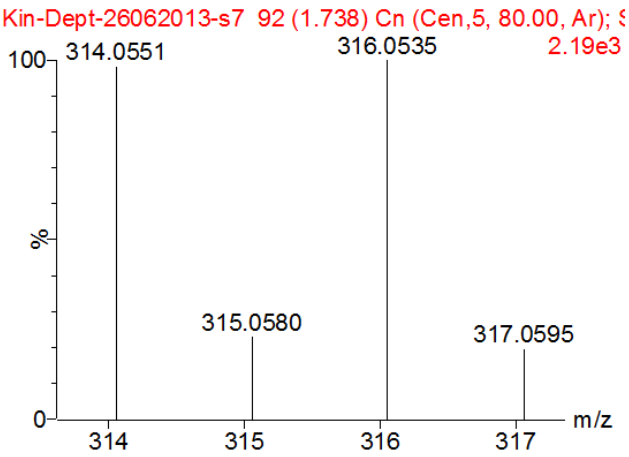
FL-38C



2-(2-Bromophenyl)-1,5,6-trimethyl-1*H*-indole (Table 7.1, L10 precursor)

HS

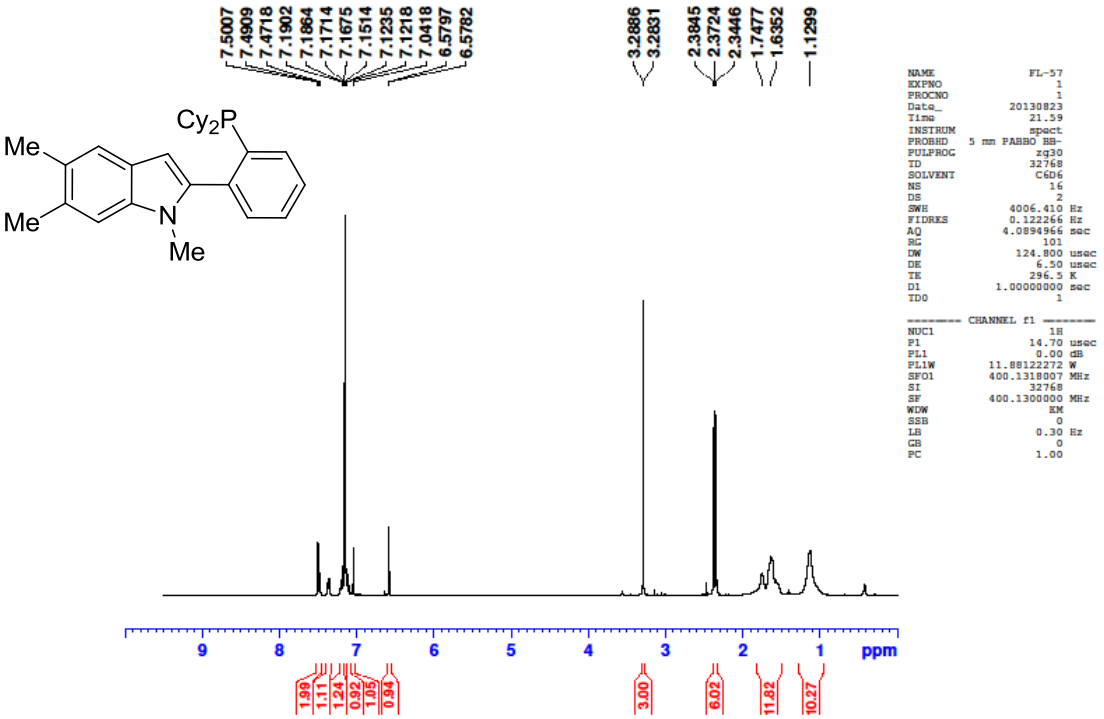




Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
314.0551	314.0544	0.7	2.2	9.5	6.3	C17 H17 N Br

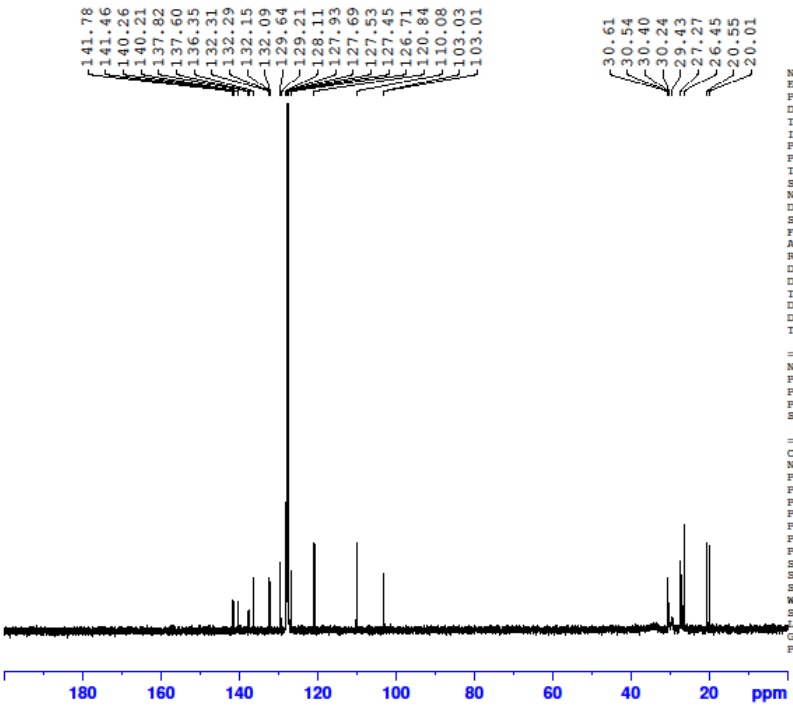
2-(2-(Dicyclohexylphosphino)phenyl)-1,5,6-trimethyl-1*H*-indole (Table 7.1, L10)

FL-57H



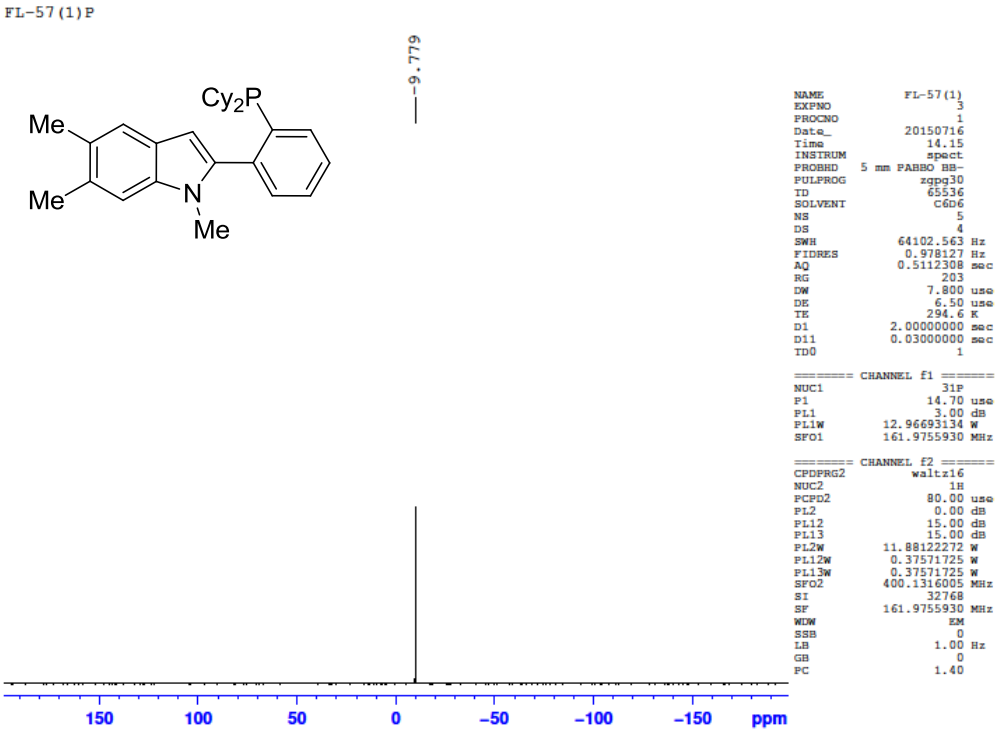

```
NAME                FL-57
EXPNO                   1
PROCNO                  1
Date_            20130823
Time                21.59
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  32768
SOLVENT              C6D6
NS                     16
DS                      2
SWH              4006.410 Hz
FIDRES           0.122266 Hz
AQ               4.0894966 sec
RG                    101
DW                124.800 usec
DE                  6.50 usec
TE                 296.5 K
D1               1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  14.70 usec
PL1                  0.00 dB
PL1W           11.88122272 W
SFO1           400.1318007 MHz
SI                  32768
SF             400.1300000 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

FL-57(1)C

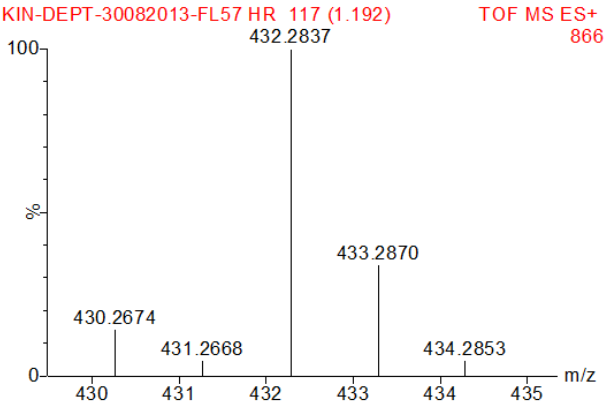



```
NAME              FL-57(1)
EXPNO                    2
PROCNO                   1
Date_             20150716
Time                 14.12
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                65536
SOLVENT            C6D6
NS                   44
DS                    2
SWH           24038.461 Hz
FIDRES         0.366798 Hz
AQ             1.3631988 sec
RG                  228
DW               20.800 usec
DE                6.50 usec
TE               294.9 K
D1             1.00000000 sec
D11            0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 13C
P1                9.50 usec
PL1              -2.00 dB
PL1W        58.52175522 W
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                 1H
PCPD2             80.00 usec
PL2               0.00 dB
PL12             15.00 dB
PL13             15.00 dB
PL2W        11.88122272 W
PL12W        0.37571725 W
PL13W        0.37571725 W
SFO2        400.1316005 MHz
SI                32768
SF          100.6127690 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```

2-(2-(Dicyclohexylphosphino)phenyl)-1,5,6-trimethyl-1*H*-indole (Table 7.1, L10)



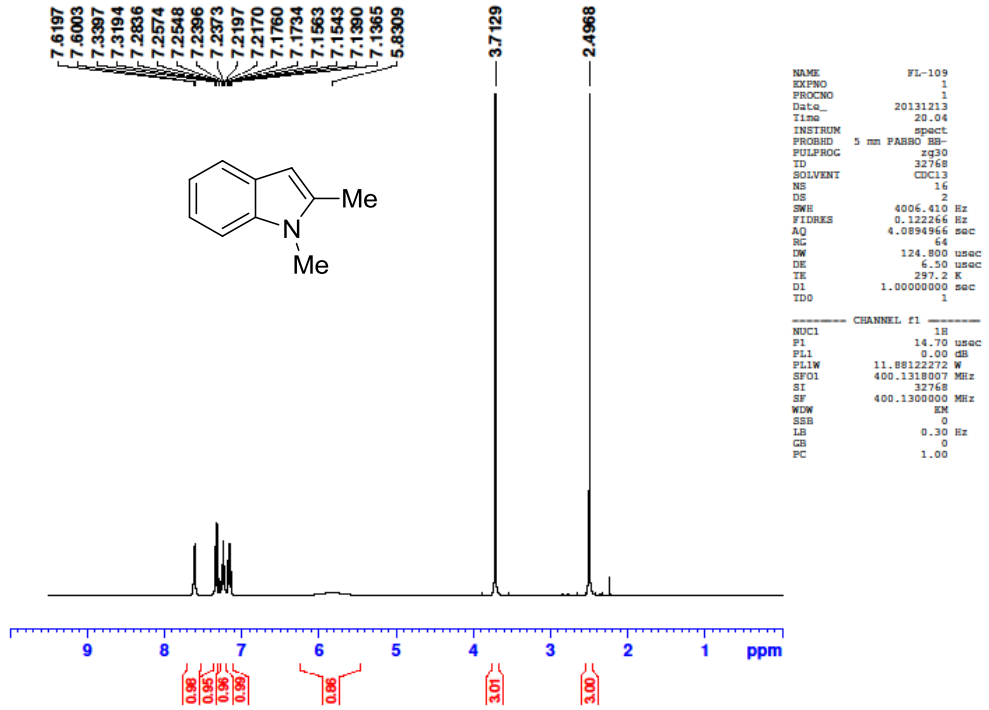
HR



Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
432.2837	432.2820	1.7	3.9	11.5	0.6	C29 H39 N P

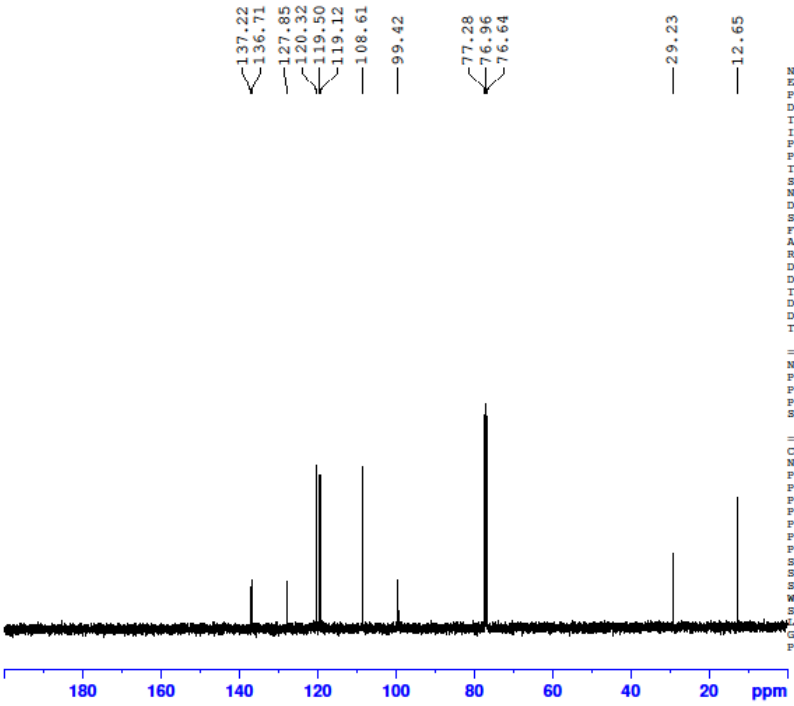
1,2-Dimethyl-1*H*-indole (Table 7.1, L11 precursor)

FL-109H




```
NAME                FL-109
EXPNO                    1
PROCNO                   1
Date_             20131213
Time                 20.04
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                   32768
SOLVENT              CDCl3
NS                      16
DS                       2
SWH               4006.410 Hz
FIDRES            0.122266 Hz
AQ                4.0894966 sec
RG                      64
DW                 124.800 usec
DE                   6.50 usec
TE                  297.2 K
D1                1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   14.70 usec
PL1                   0.00 dB
PL1W         11.88122272 W
SFO1         400.1318007 MHz
SI                   32768
SF           400.1300000 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```

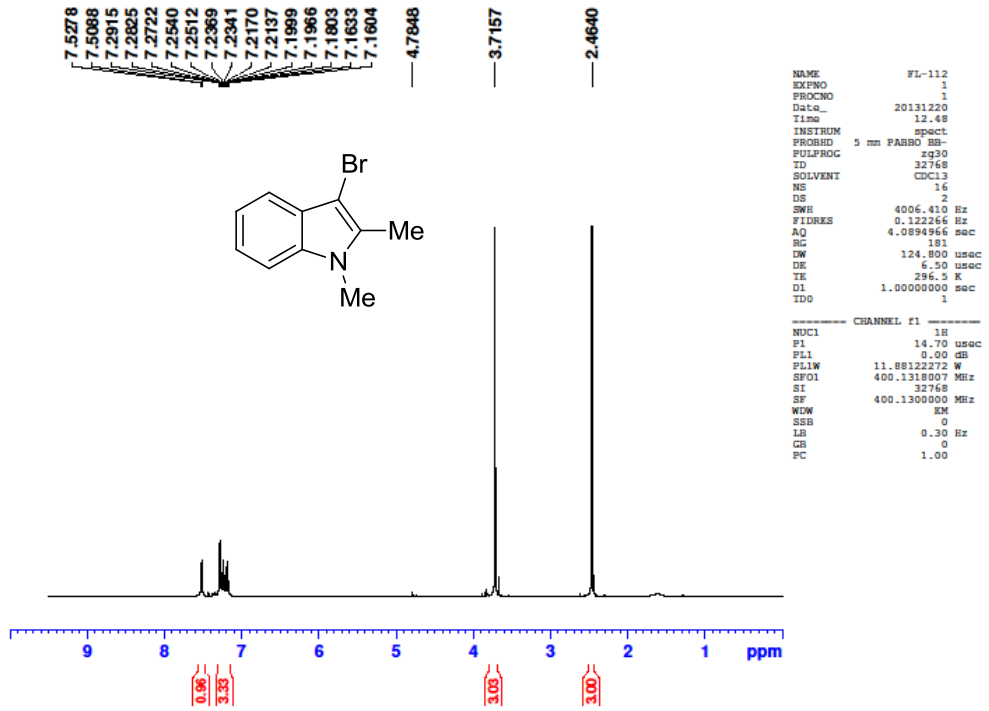
FL-109C




```
NAME                FL-109
EXPNO                    2
PROCNO                   1
Date_             20131213
Time                 20.06
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG            zgpg30
TD                   65536
SOLVENT              CDCl3
NS                      25
DS                       2
SWH              24038.461 Hz
FIDRES            0.366798 Hz
AQ                1.3631988 sec
RG                     203
DW                 20.800 usec
DE                   6.50 usec
TE                  297.6 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    13C
P1                    9.50 usec
PL1                  -2.00 dB
PL1W         58.52175522 W
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                    1H
PCPD2                80.00 usec
PL2                   0.00 dB
PL12                 15.00 dB
PL13                 15.00 dB
PL2W         11.88122272 W
PL12W         0.37571725 W
PL13W         0.37571725 W
SFO2         400.1316005 MHz
SI                   32768
SF           100.6127849 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.40
```

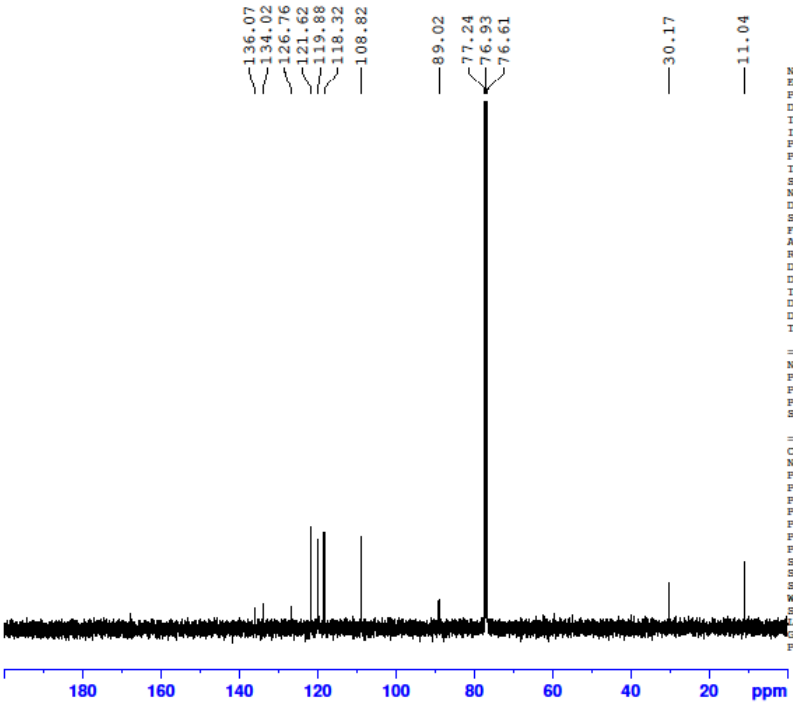
3-Bromo-1,2-dimethyl-1*H*-indole (Table 7.1, L11 precursor)

FL-112H



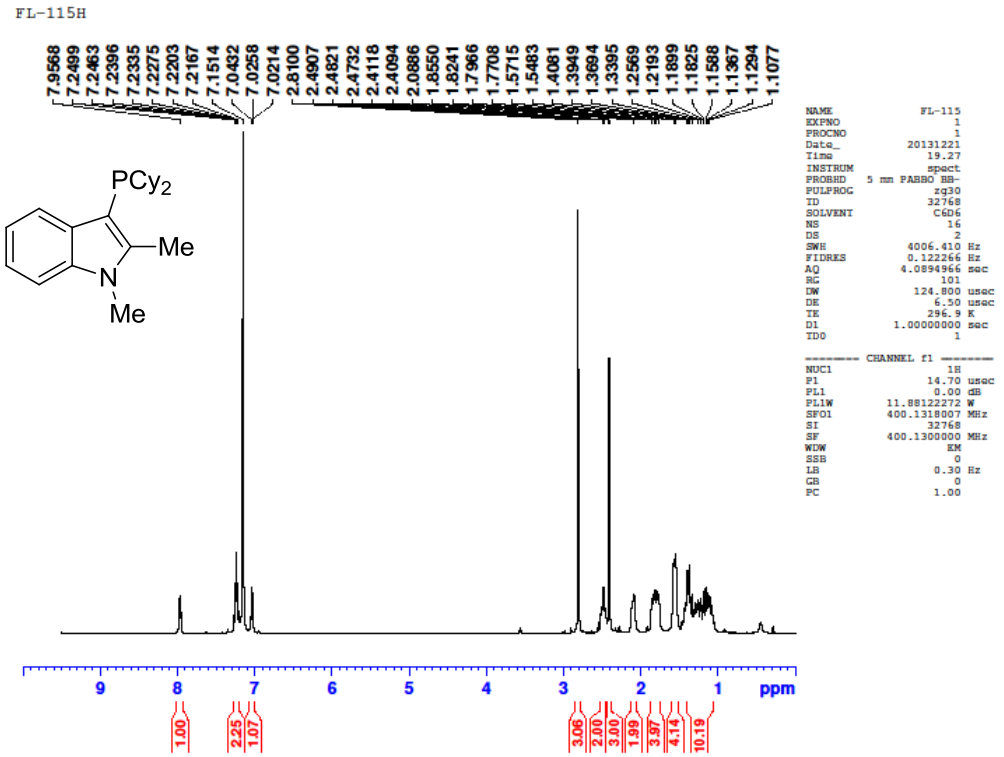

```
NAME                FL-112
EXPNO                    1
PROCNO                   1
Date_             20131220
Time                 12.48
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                   32768
SOLVENT              CDCl3
NS                      16
DS                       2
SWH               4006.410 Hz
FIDRES            0.122266 Hz
AQ                4.0894966 sec
RG                     181
DW                 124.800 usec
DE                   6.50 usec
TE                  296.5 K
D1                1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                  14.70 usec
PL1                  0.00 dB
PL1W           11.88122272 W
SFO1          400.1318007 MHz
SI                   32768
SF            400.1300000 MHz
WDW                     EM
SSB                      0
LB                  0.30 Hz
GB                       0
PC                    1.00
```

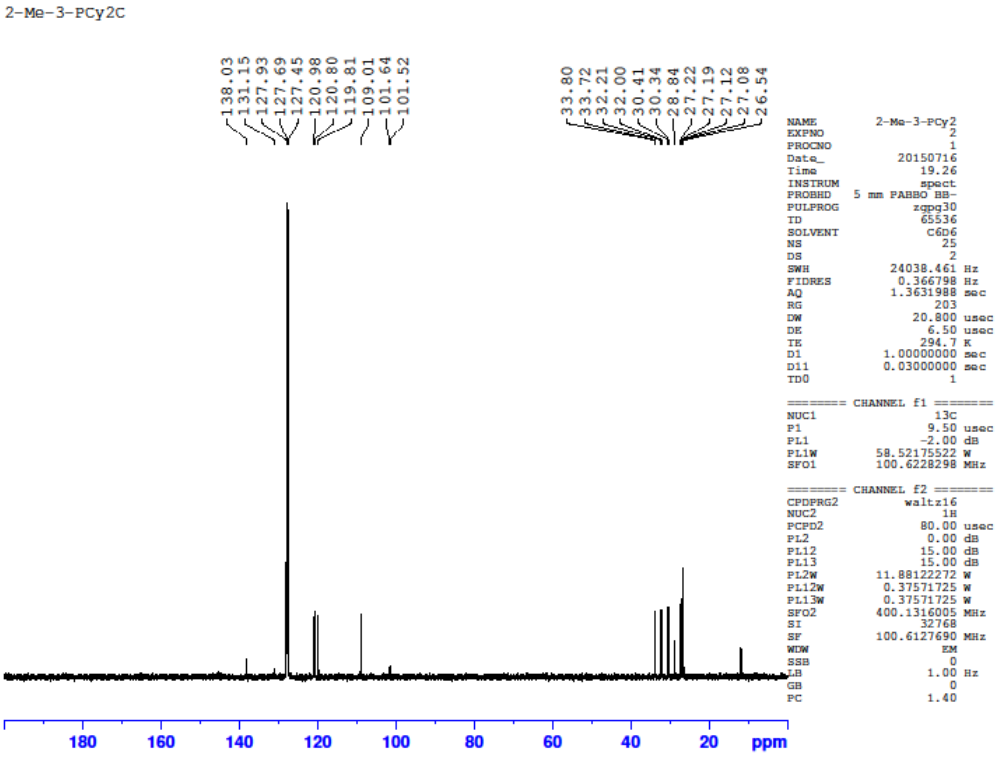
FL-112C



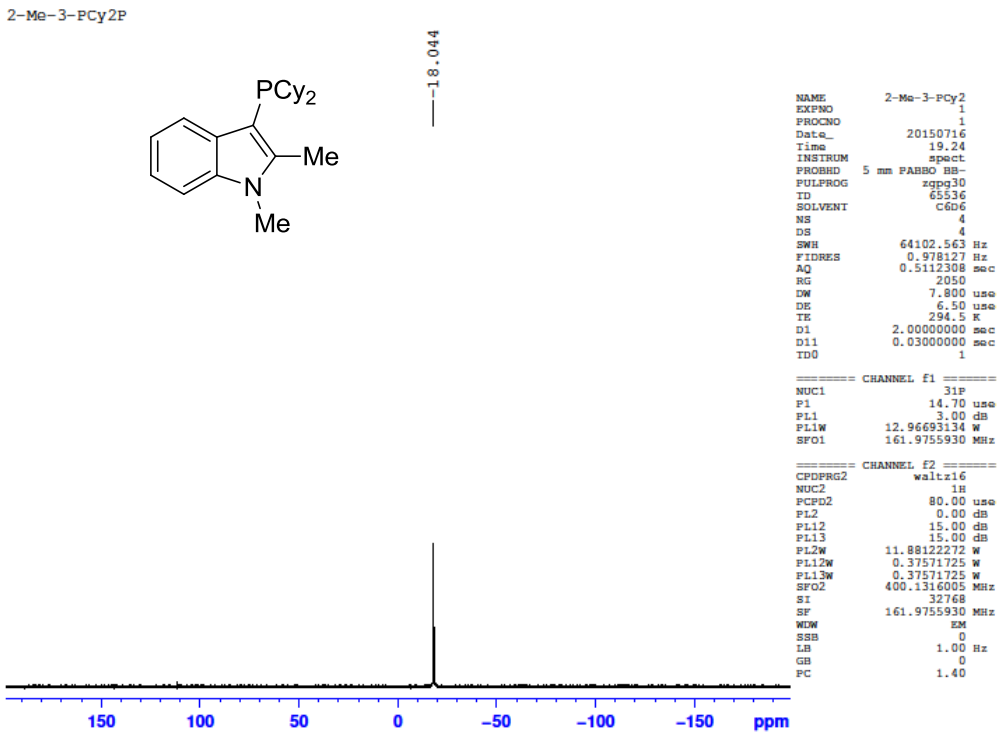

```
NAME                FL-112
EXPNO                    2
PROCNO                   1
Date_             20131220
Time                 12.52
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                   65536
SOLVENT              CDCl3
NS                      64
DS                       2
SWH              24038.461 Hz
FIDRES            0.366798 Hz
AQ                1.3631988 sec
RG                     203
DW                 20.800 usec
DE                   6.50 usec
TE                  297.4 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    13C
P1                   9.50 usec
PL1                  -2.00 dB
PL1W          58.52175522 W
SFO1          100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2              waltz16
NUC2                    1H
PCPD2                80.00 usec
PL2                   0.00 dB
PL12                 15.00 dB
PL13                 15.00 dB
PL2W           11.88122272 W
PL12W           0.37571725 W
PL13W           0.37571725 W
SFO2          400.1316005 MHz
SI                   32768
SF            100.6127798 MHz
WDW                     EM
SSB                      0
LB                  1.00 Hz
GB                       0
PC                    1.40
```

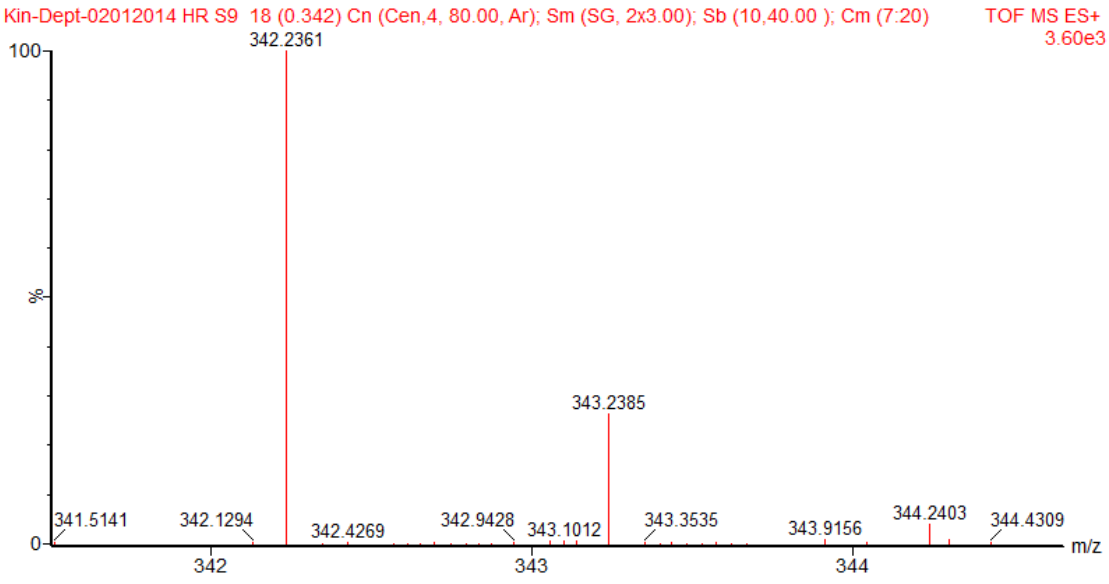
3-(Dicyclohexylphosphino)-1,2-dimethyl-1*H*-indole (Table 7.1, L11)





3-(Dicyclohexylphosphino)-1,2-dimethyl-1*H*-indole (Table 7.1, L11)

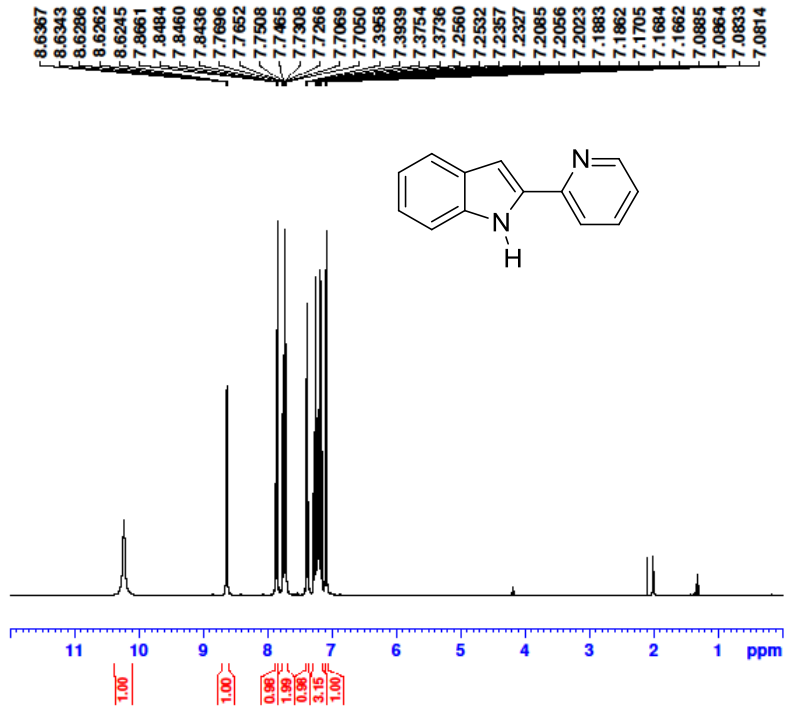




Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
342.2361	342.2351	1.0	2.9	7.5	3.6	C22 H33 N P

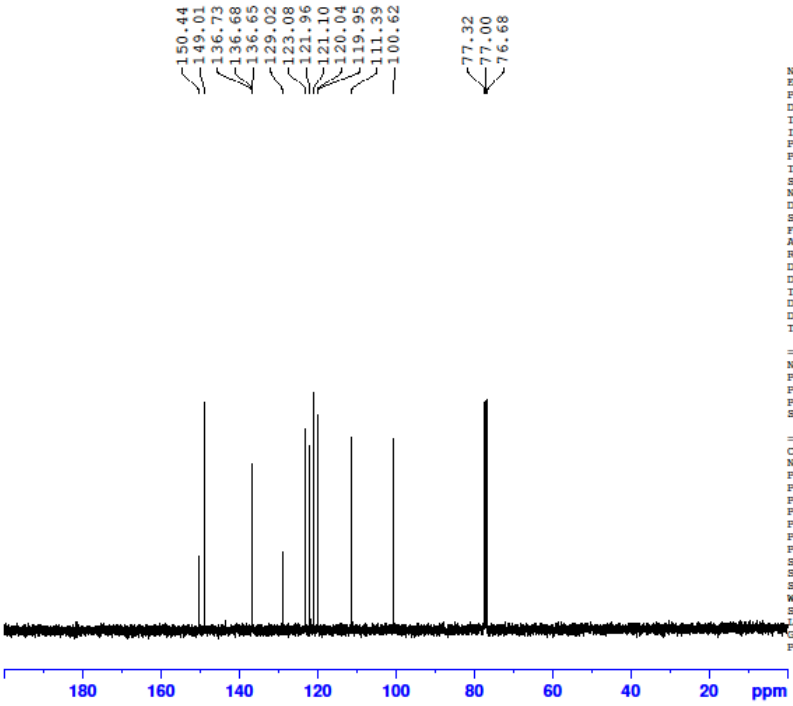
2-(Pyridin-2-yl)-1*H*-indole (Table 7.1, L13 and L20 precursor)

FL-76(1)H



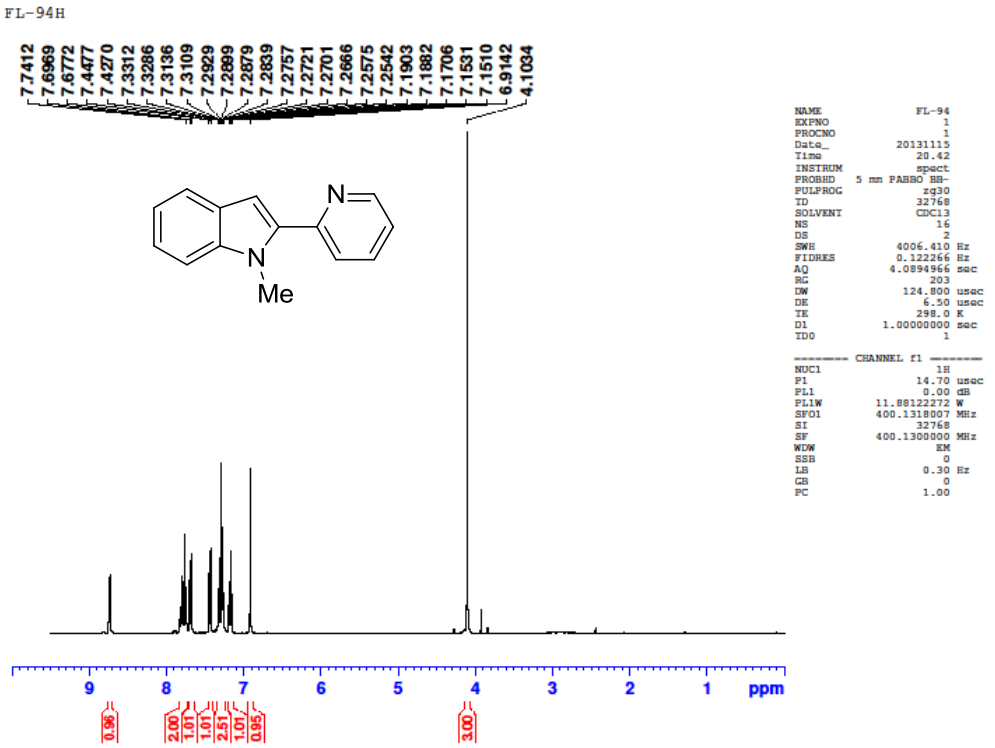
NAME	FL-76(1)
EXPNO	2
PROCNO	1
Date_	20150728
Time	11.49
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	16
DS	2
SWH	8012.820 Hz
FIDRES	0.244532 Hz
AQ	2.0447731 sec
RG	25.4
DW	62.400 usec
DE	6.50 usec
TE	295.3 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	14.70 usec
PL1	0.00 dB
PL1W	11.88122272 W
SFO1	400.1324008 MHz
SI	32768
SF	400.1300000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

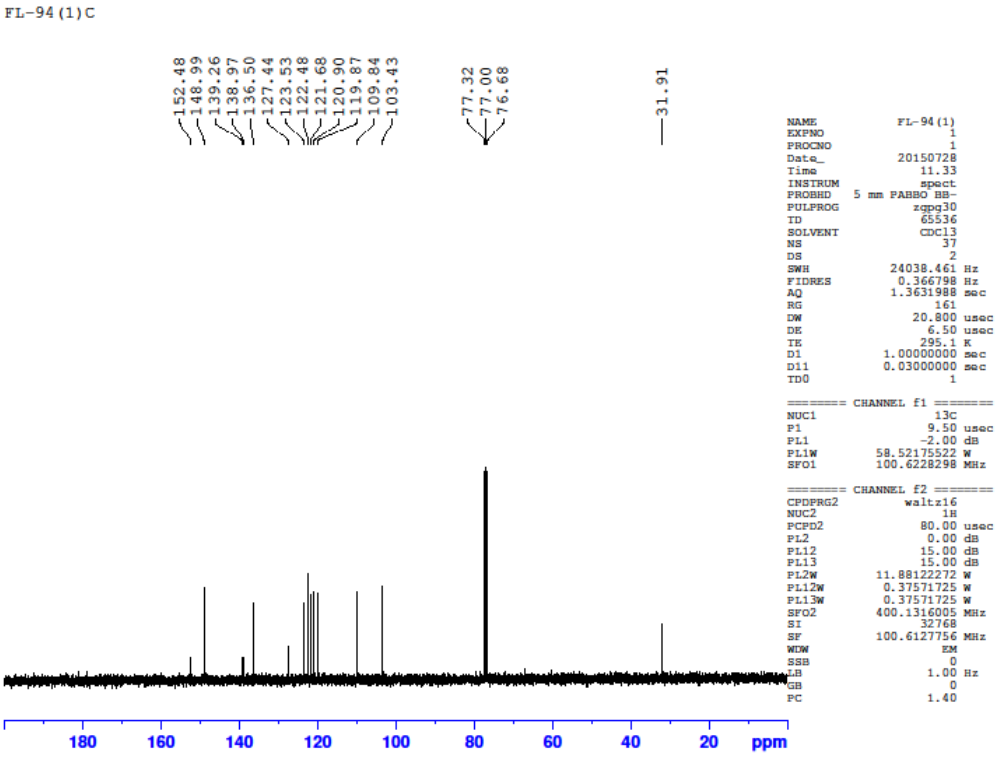
FL-76(1)C



NAME	FL-76(1)
EXPNO	1
PROCNO	1
Date_	20150728
Time	11.47
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	38
DS	2
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	161
DW	20.800 usec
DE	6.50 usec
TE	295.0 K
D1	1.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.50 usec
PL1	-2.00 dB
PL1W	58.52175522 W
SFO1	100.6228298 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	0.00 dB
PL12	15.00 dB
PL13	15.00 dB
PL2W	11.88122272 W
PL12W	0.37571725 W
PL13W	0.37571725 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127795 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

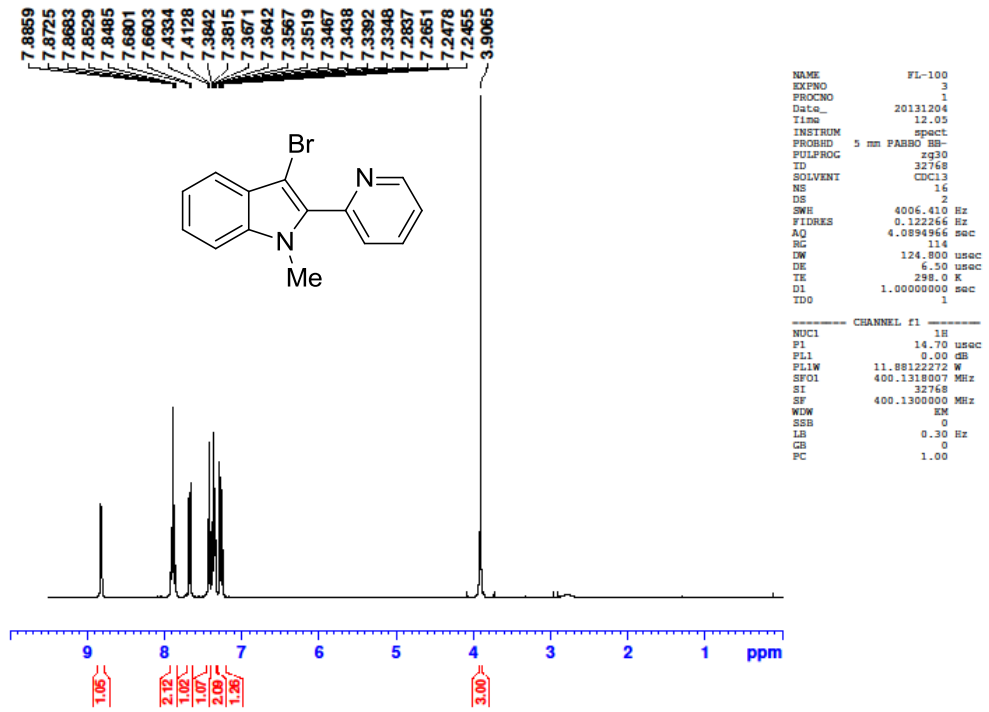
1-Methyl-2-(pyridin-2-yl)-1*H*-indole (Table 7.1, L13 and L20 precursor)





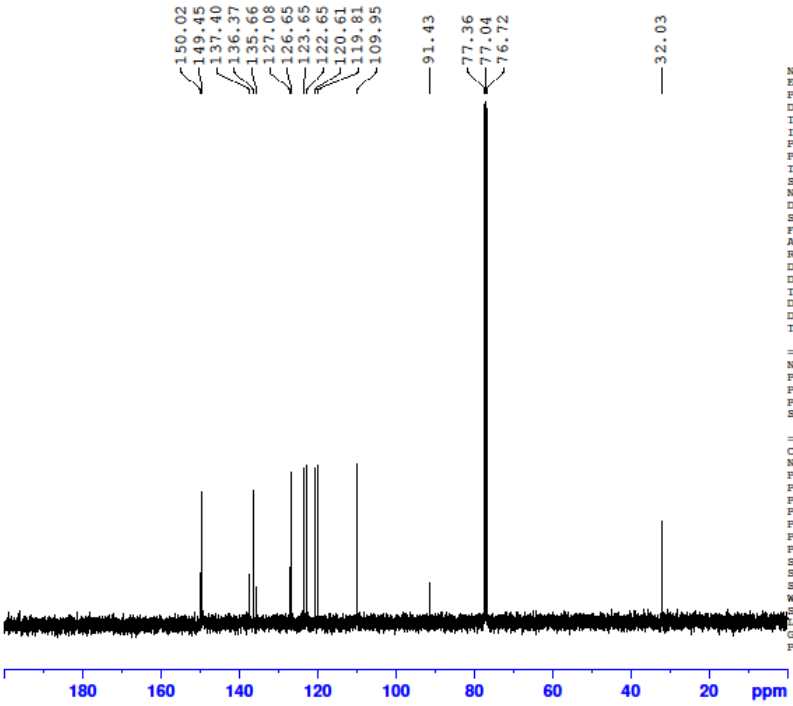
3-Bromo-1-methyl-2-(pyridin-2-yl)-1*H*-indole (Table 7.1, L13 and L20 precursor)

FL-100H



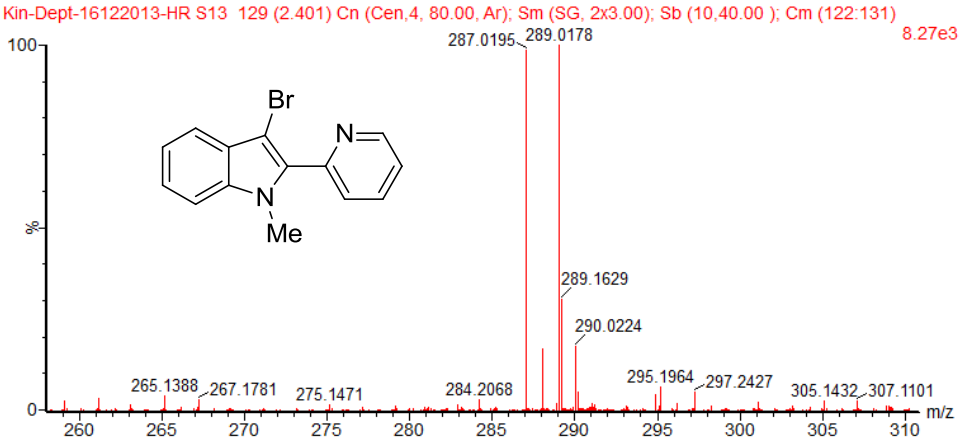
NAME	FL-100
EXPNO	3
PROCNO	1
Date_	20131204
Time	12.05
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	16
DS	2
SWH	4006.410 Hz
FIDRES	0.122266 Hz
AQ	4.0894966 sec
RG	114
DW	124.800 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	14.70 usec
PL1	0.00 dB
PL1W	11.88122272 W
SFO1	400.1318007 MHz
SI	32768
SF	400.1300000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

FL-100C



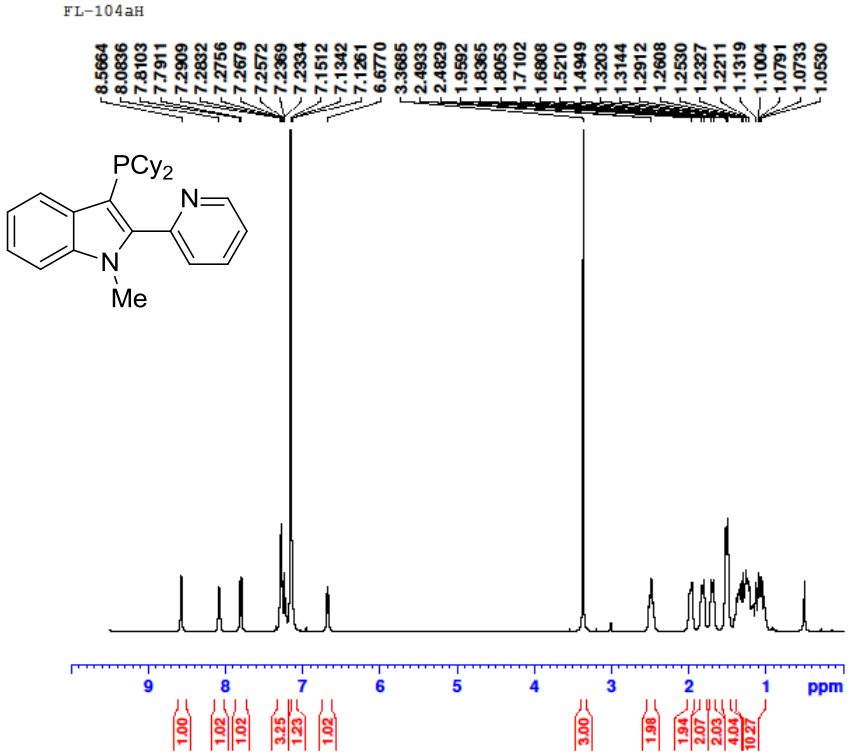
NAME	FL-100
EXPNO	2
PROCNO	1
Date_	20131204
Time	11.48
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	64
DS	2
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	298.4 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.50 usec
PL1	-2.00 dB
PL1W	58.52175522 W
SFO1	100.6228298 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	0.00 dB
PL12	15.00 dB
PL13	15.00 dB
PL2W	11.88122272 W
PL12W	0.37571725 W
PL13W	0.37571725 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127702 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

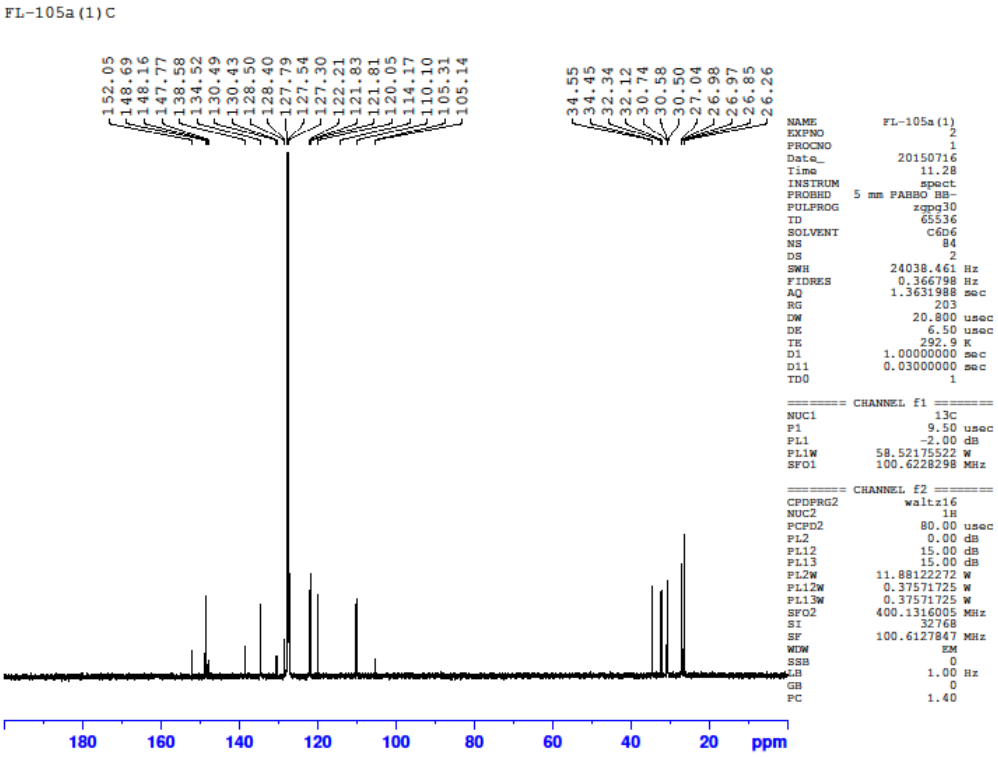
3-Bromo-1-methyl-2-(pyridin-2-yl)-1*H*-indole (Table 7.1, L13 and L20 precursor)



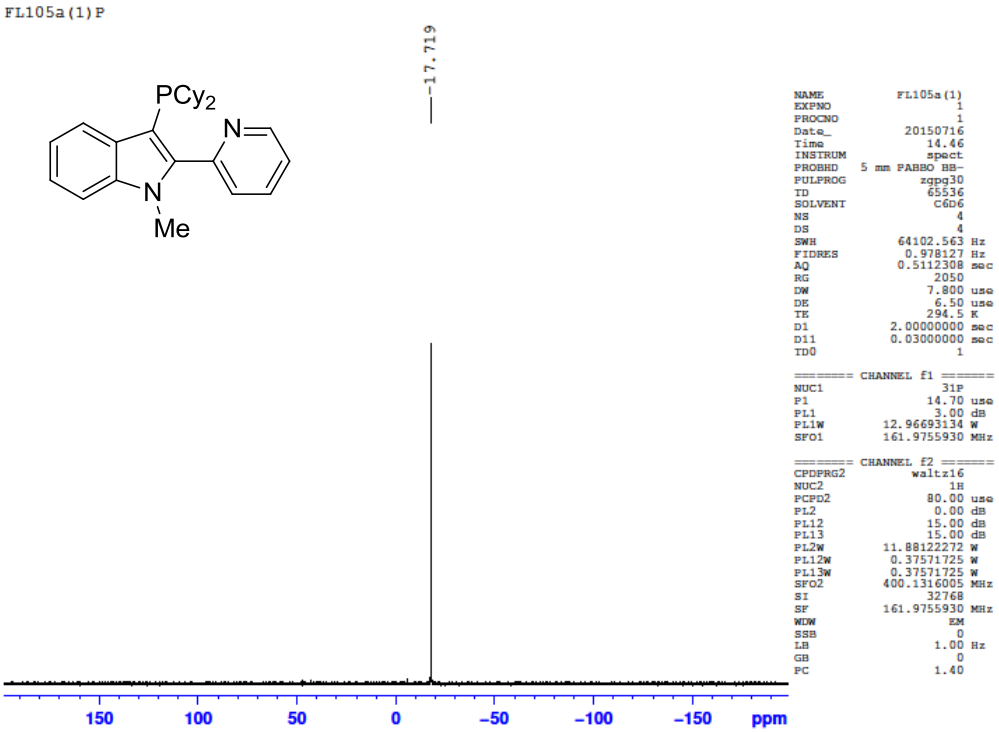
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
287.0195	287.0184	1.1	3.8	9.5	2.7	C14 H12 N2 Br

3-(Dicyclohexylphosphino)-1-methyl-2-(pyridin-2-yl)-1*H*-indole (Table 7.1, L13)

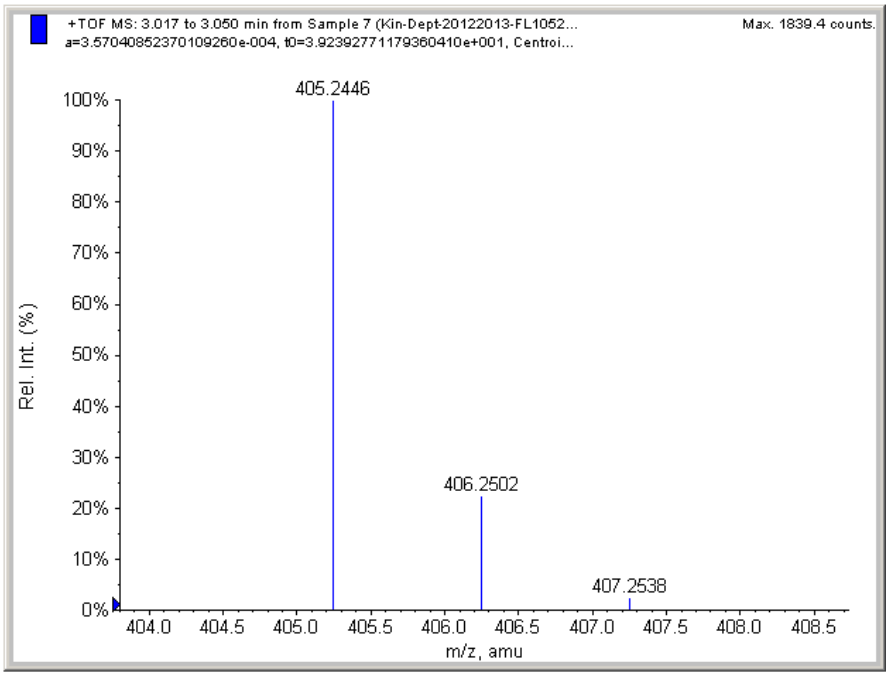




3-(Dicyclohexylphosphino)-1-methyl-2-(pyridin-2-yl)-1*H*-indole (Table 7.1, L13)

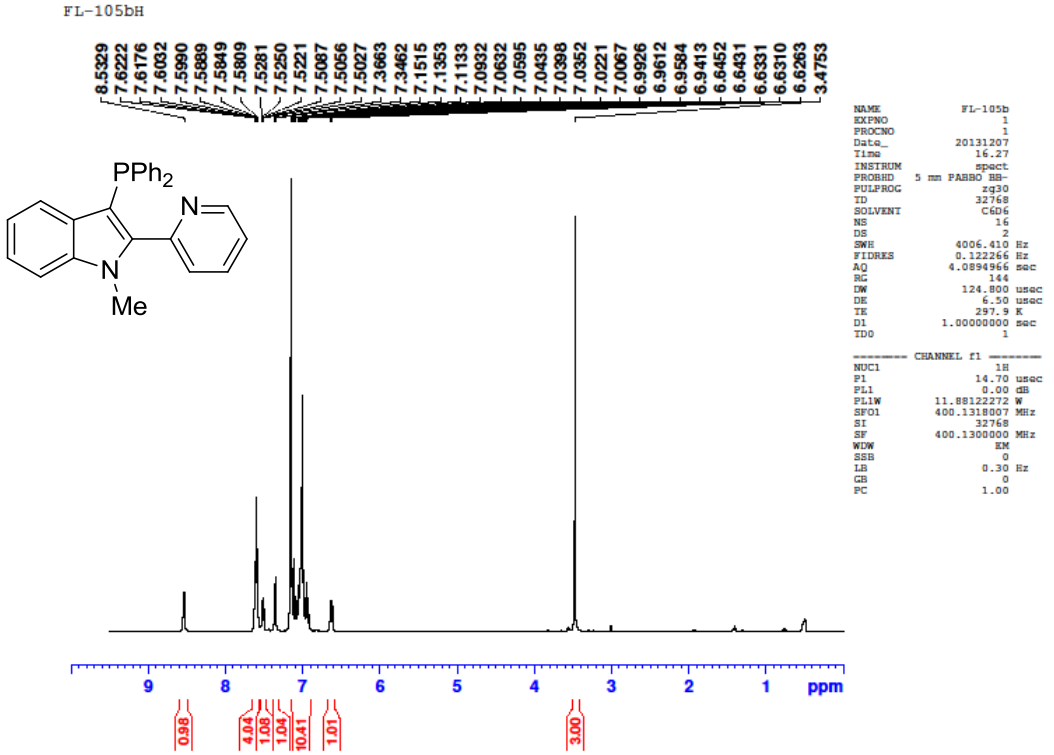


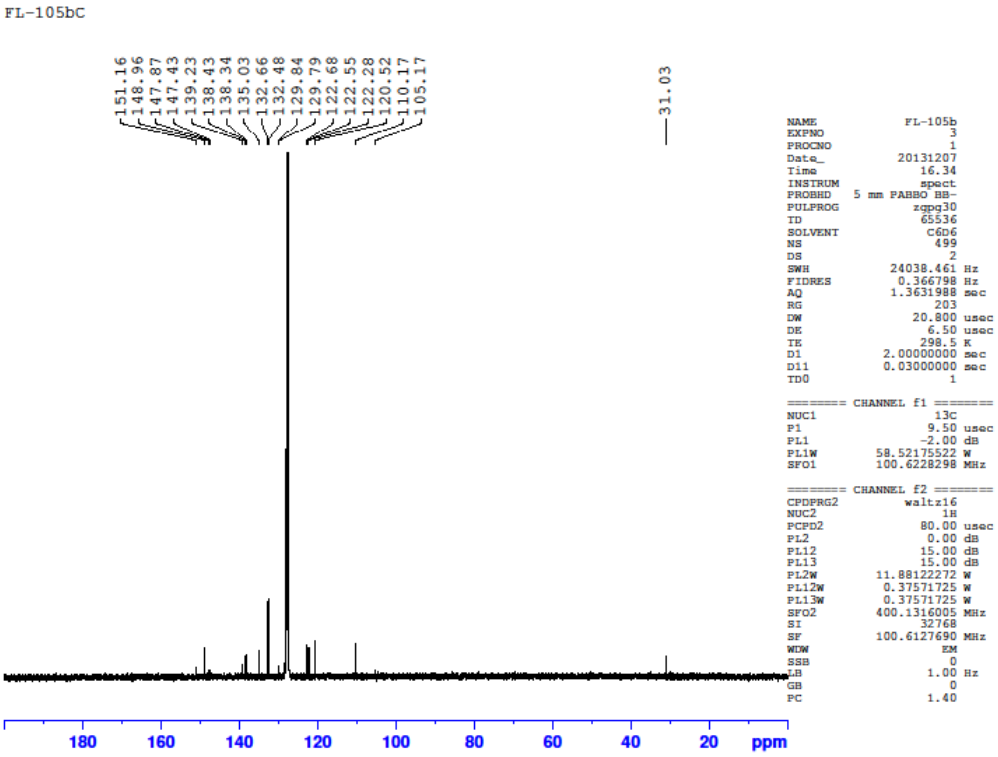
HR



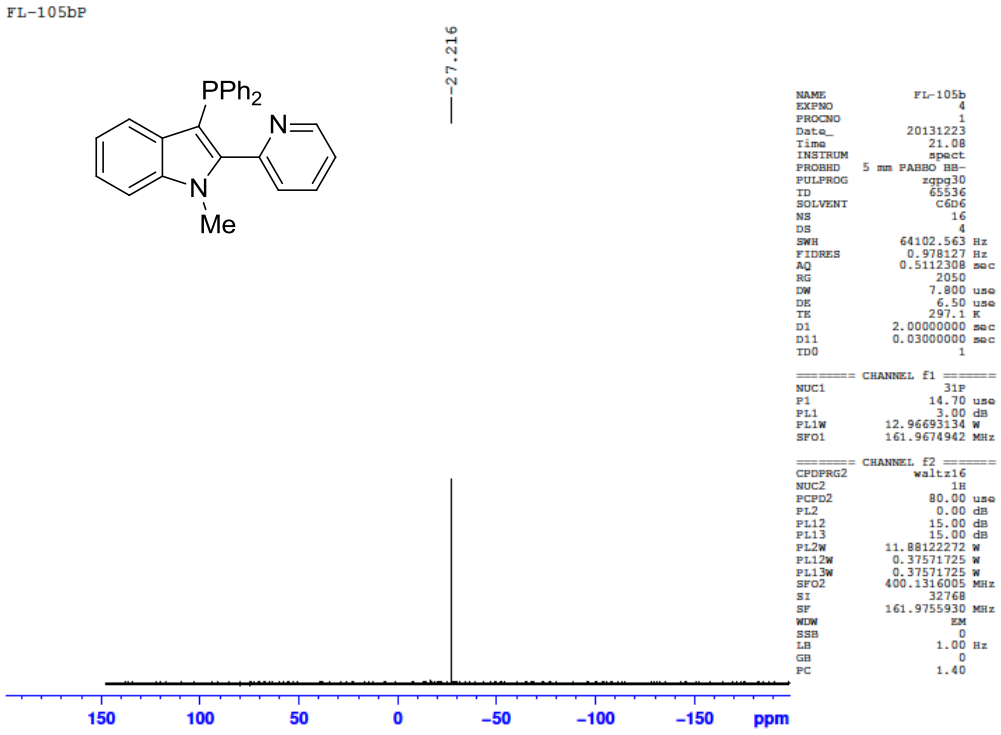
Formula: C26H34N2P
Measured mass: 405.2446
Calculated mass: 405.2459
PPM: -3.4

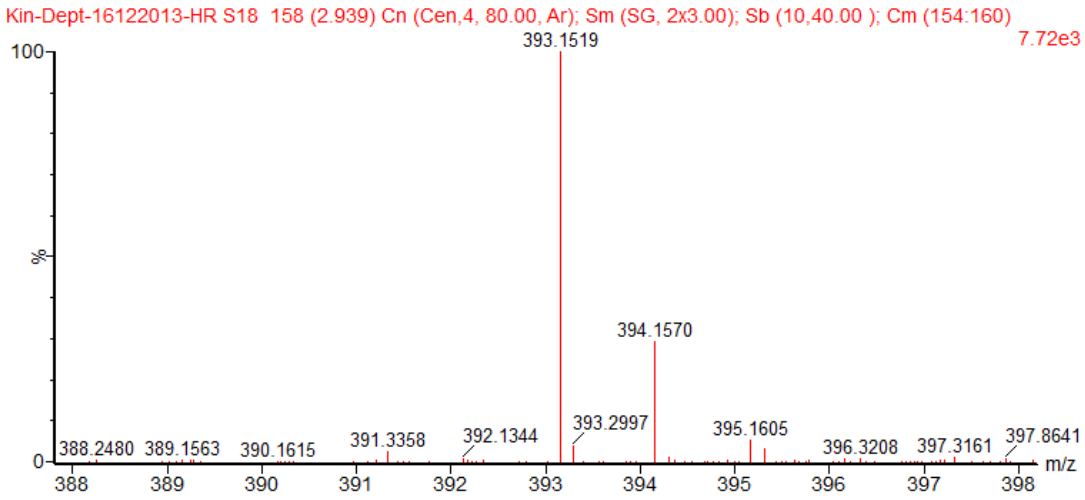
3-(Diphenylphosphino)-1-methyl-2-(pyridin-2-yl)-1*H*-indole (Table 7.1, L20)





3-(Diphenylphosphino)-1-methyl-2-(pyridin-2-yl)-1*H*-indole (Table 7.1, L20)

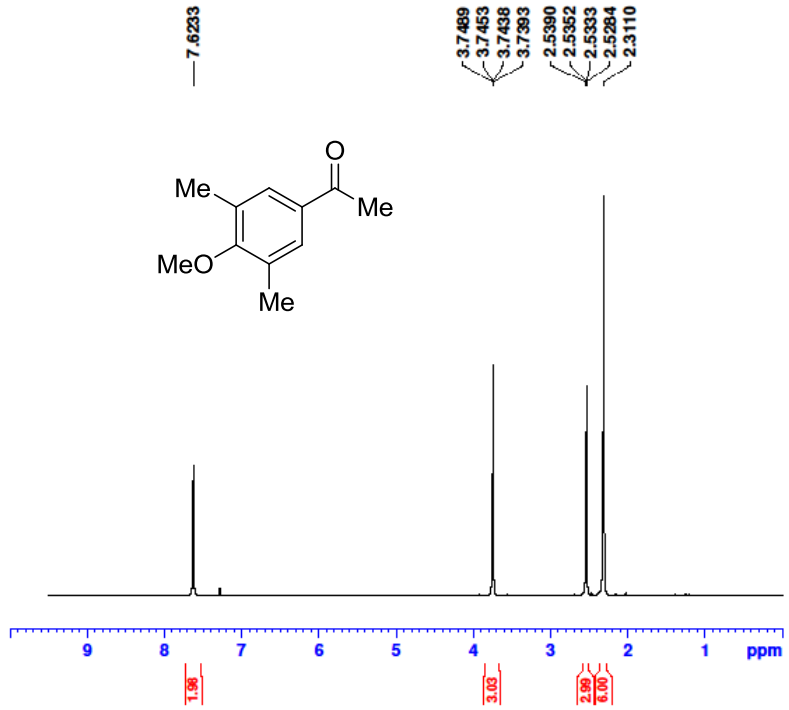




Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
393.1519	393.1521	-0.2	-0.5	17.5	8.5	C26 H22 N2 P

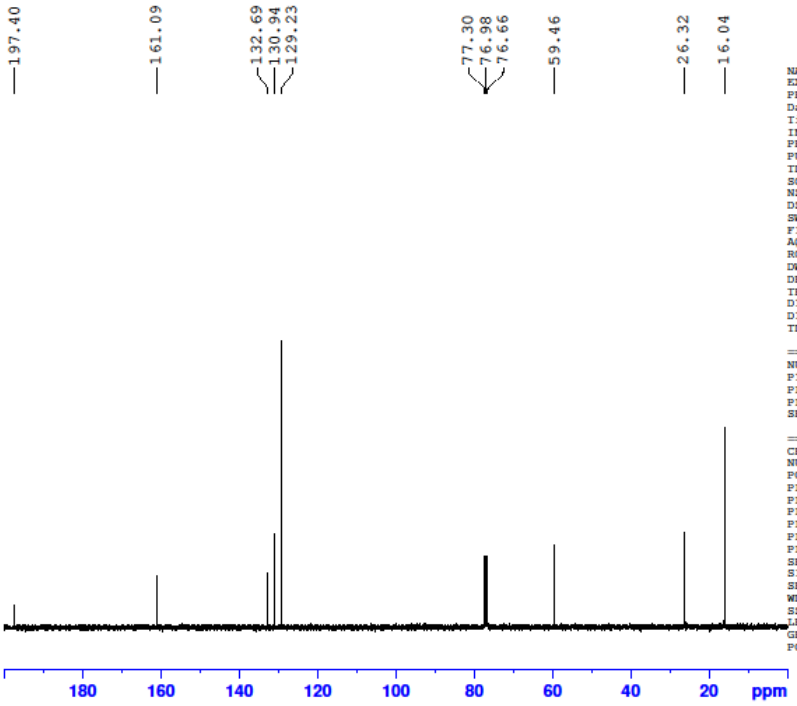
1-(4-Methoxy-3,5-dimethylphenyl)ethanone (Table 7.1, L14 precursor)

FS-44H



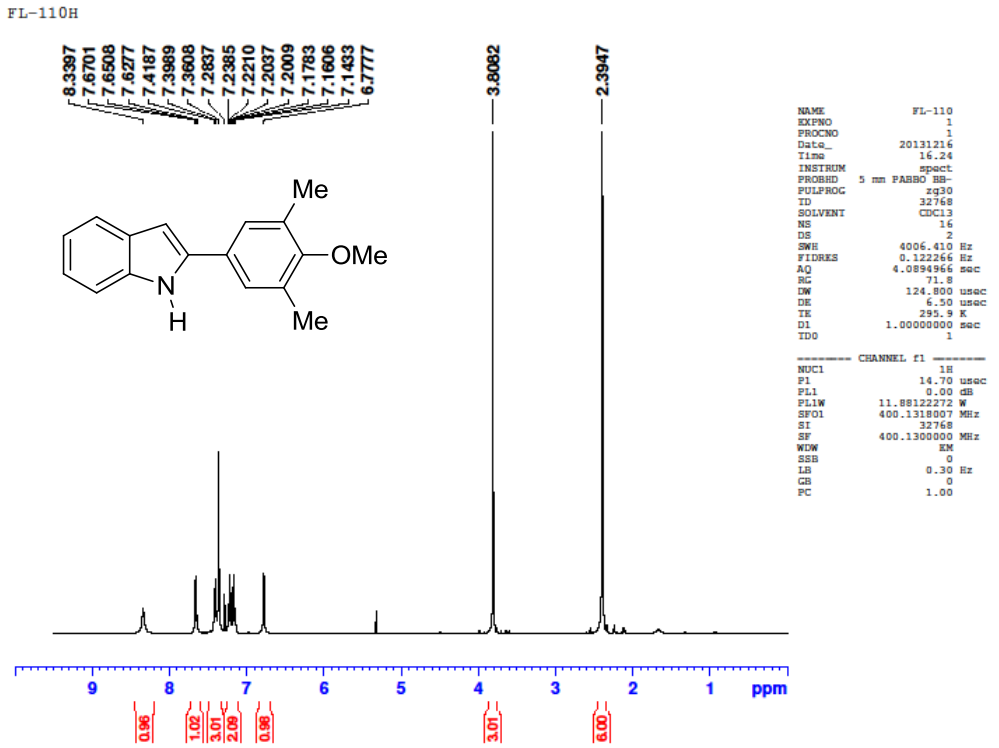

```
NAME                FS-44
EXPNO                  1
PROCNO                 1
Date_           20131113
Time               19.35
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             4006.410 Hz
FIDRES          0.122266 Hz
AQ              4.0894966 sec
RG                  25.4
DW                124.800 usec
DE                  6.50 usec
TE                298.0 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                1H
P1                14.70 usec
PL1                0.00 dB
PL1W        11.88122272 W
SFO1        400.1318007 MHz
SI                 32768
SF          400.1300000 MHz
WDW                EM
SSB                 0
LB               0.30 Hz
GB                  0
PC                1.00
```

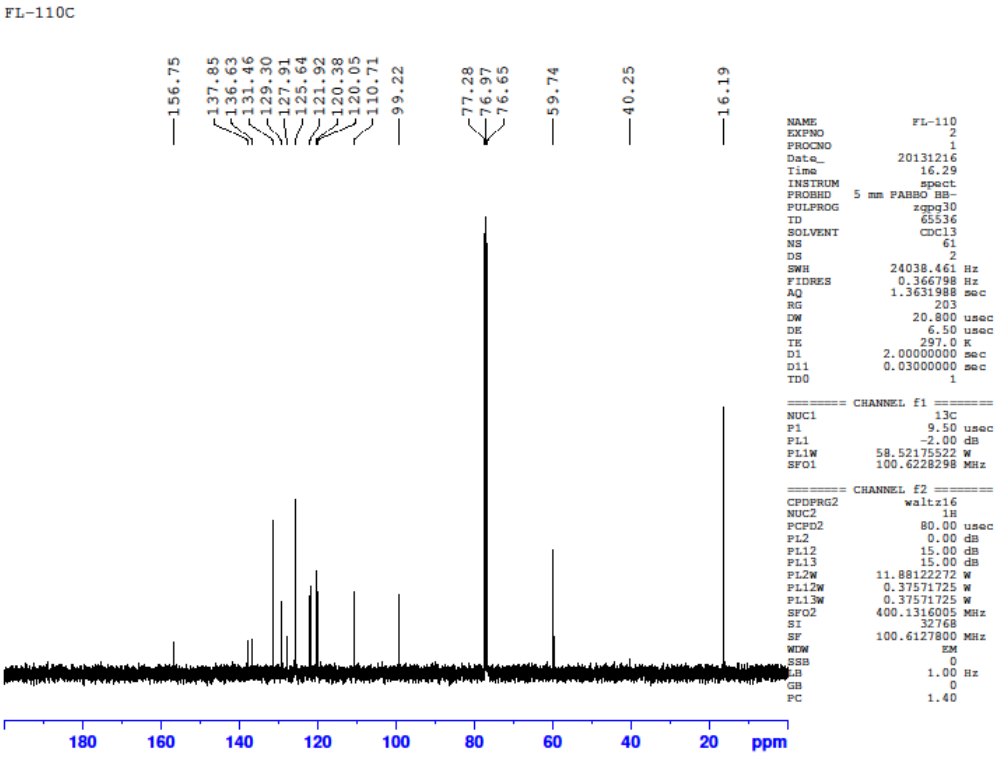
FS-44C



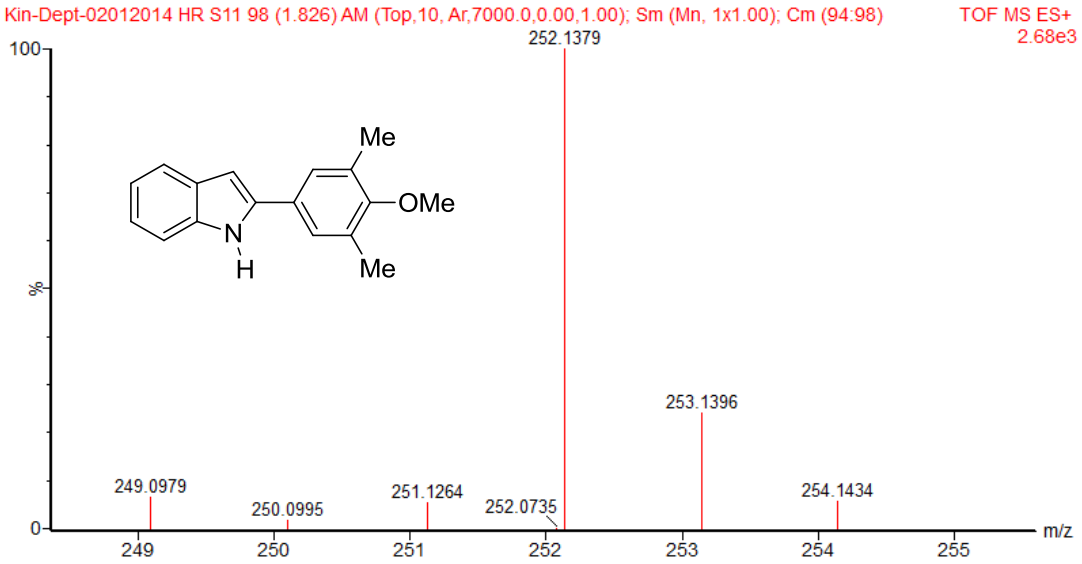

```
NAME                FS-44
EXPNO                  2
PROCNO                 1
Date_           20131113
Time               19.38
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                    22
DS                     2
SWH             24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631988 sec
RG                   203
DW                20.800 usec
DE                  6.50 usec
TE                298.5 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                13C
P1                 9.50 usec
PL1               -2.00 dB
PL1W        58.52175522 W
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                1H
PCPD2             80.00 usec
PL2                0.00 dB
PL12              15.00 dB
PL13              15.00 dB
PL2W        11.88122272 W
PL12W       0.37571725 W
PL13W       0.37571725 W
SFO2        400.1316005 MHz
SI                 32768
SF          100.6127831 MHz
WDW                EM
SSB                 0
LB               1.00 Hz
GB                  0
PC                1.40
```

2-(4-Methoxy-3,5-dimethylphenyl)-1*H*-indole (Table 7.1, L14 precursor)



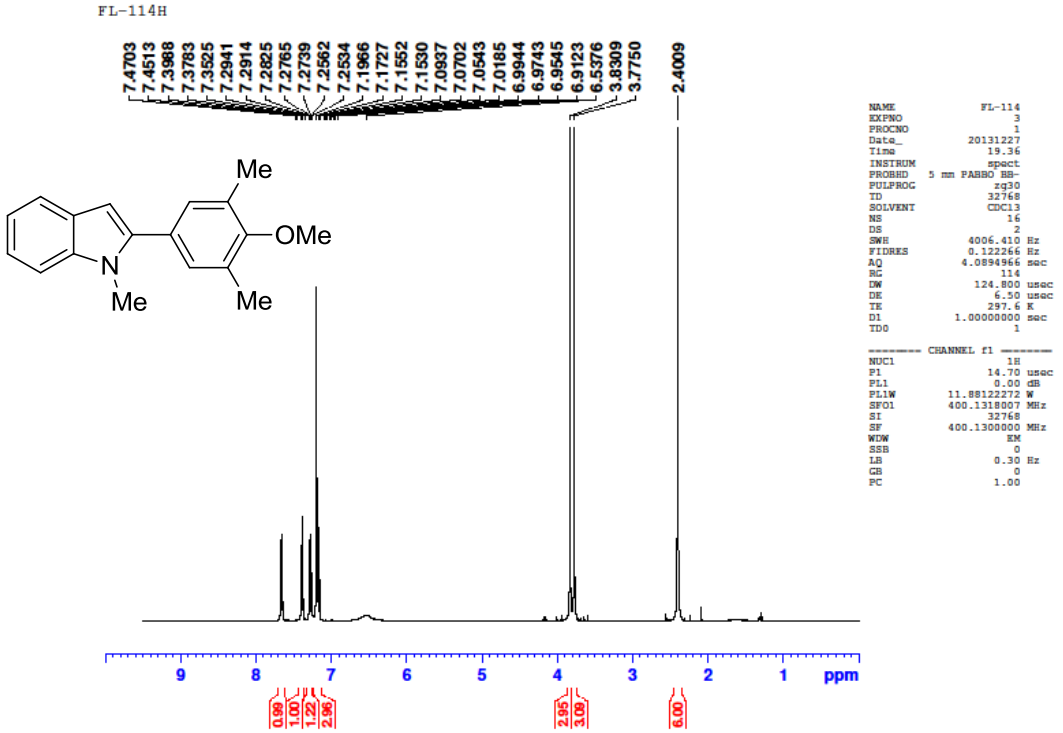


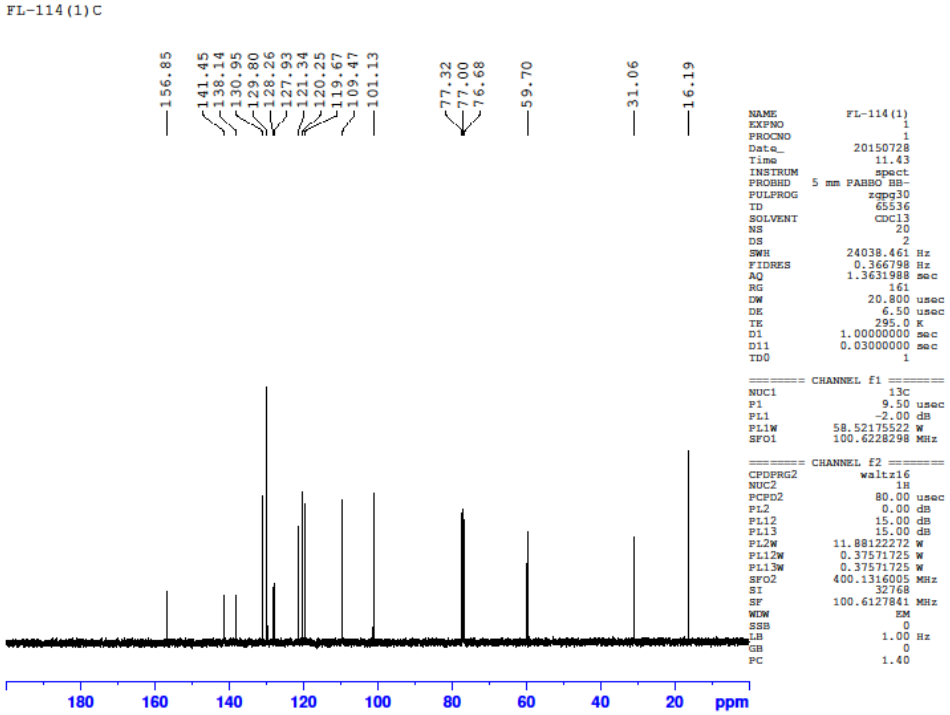
2-(4-Methoxy-3,5-dimethylphenyl)-1*H*-indole (Table 7.1, L14 precursor)



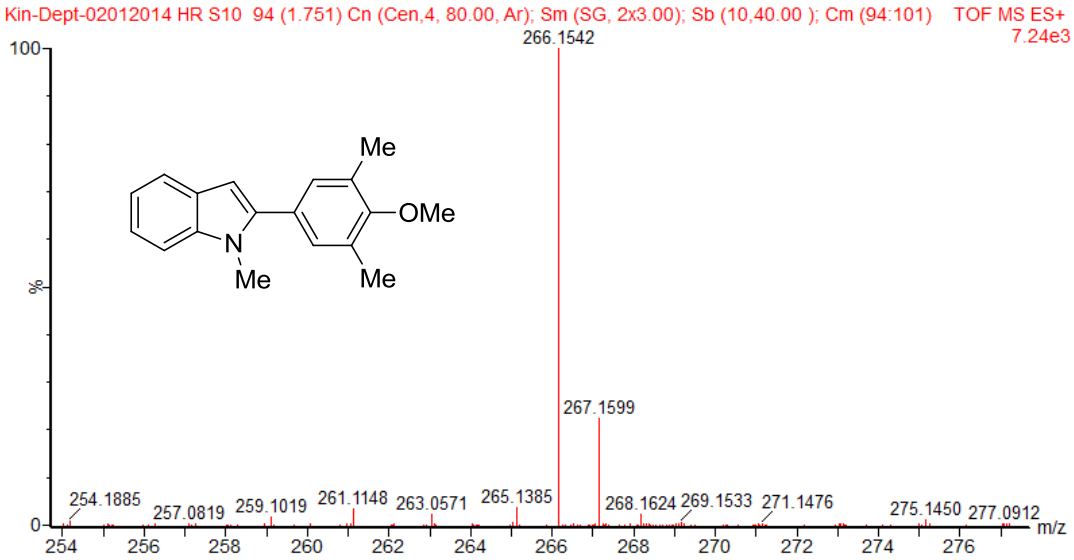
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
252.1379	252.1388	-0.9	-3.6	9.5	39.8	C17 H18 N O

2-(4-Methoxy-3,5-dimethylphenyl)-1-methyl-1*H*-indole (Table 7.1, L14 precursor)



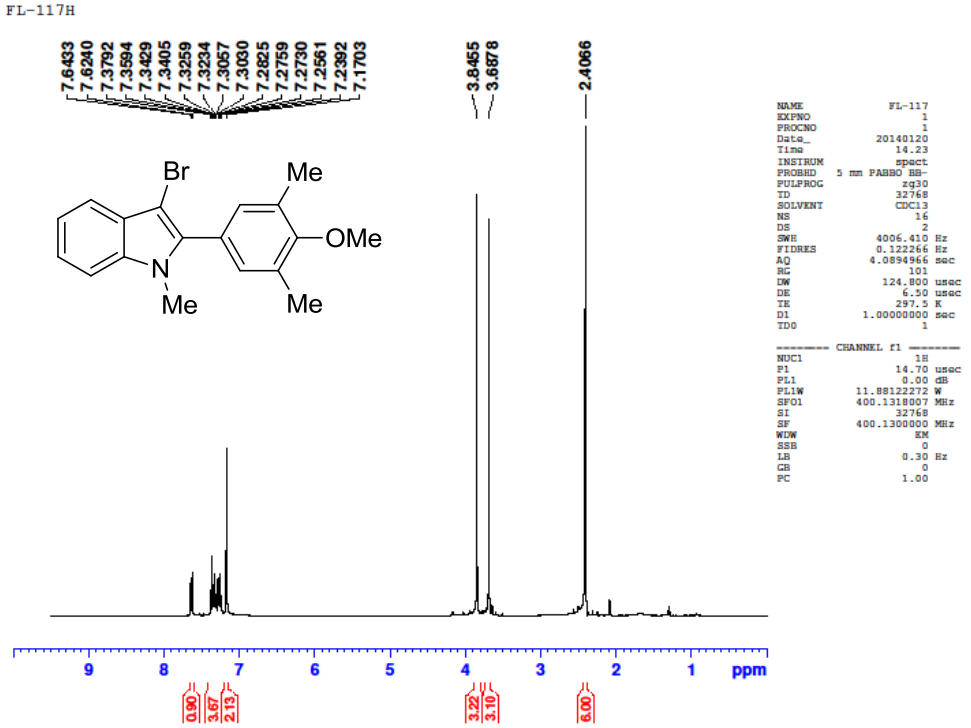


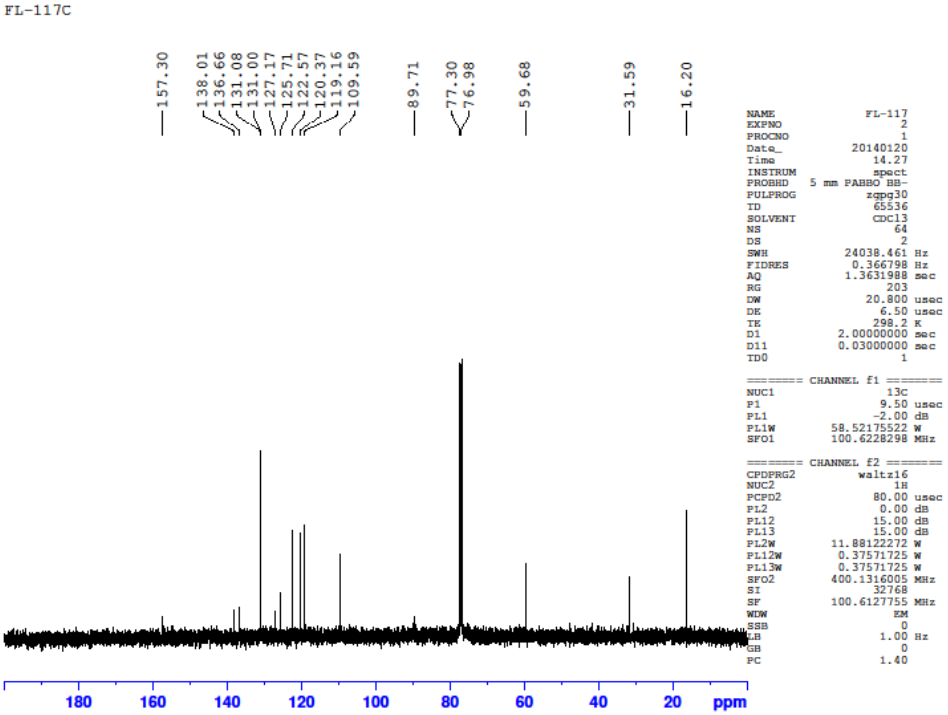
2-(4-Methoxy-3,5-dimethylphenyl)-1-methyl-1*H*-indole (Table 7.1, L14 precursor)



Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
266.1542	266.1545	-0.3	-1.1	9.5	4.6	C18 H20 N O

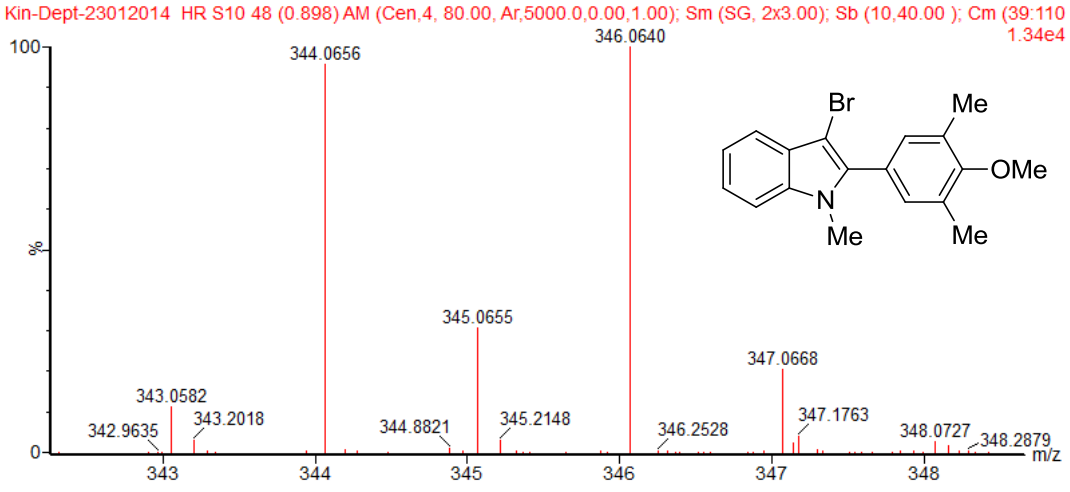
3-Bromo-2-(4-methoxy-3,5-dimethylphenyl)-1-methyl-1*H*-indole (Table 7.1, L14 precursor)





3-Bromo-2-(4-methoxy-3,5-dimethylphenyl)-1-methyl-1*H*-indole (Table 7.1, L14 precursor)

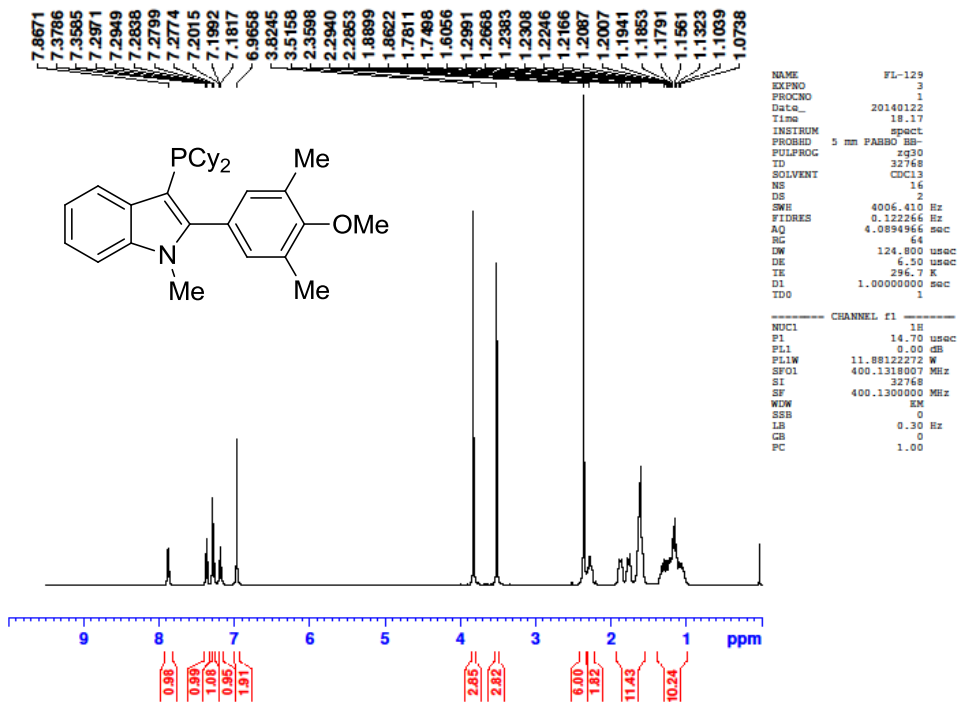
HS



Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
344.0656	344.0650	0.6	1.7	9.5	233.2	C18 H19 N O Br

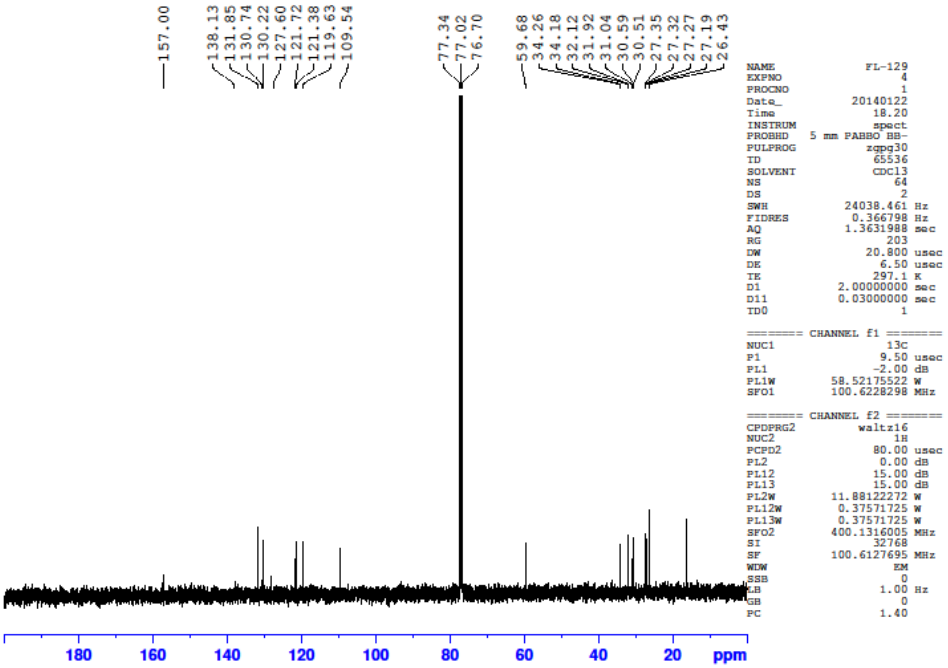
3-(Dicyclohexylphosphino)-2-(4-methoxy-3,5-dimethylphenyl)-1-methyl-1*H*-indole (Table 7.1, L14)

FL-129H



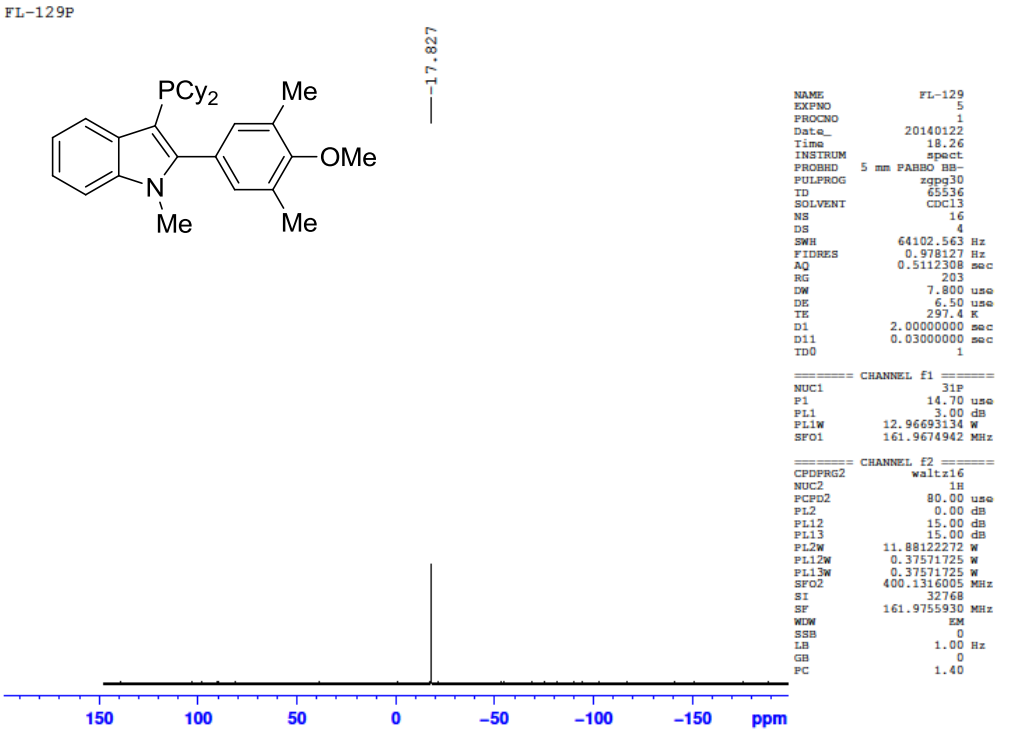

```
NAME                FL-129
EXPNO                    3
PROCNO                   1
Date_             20140122
Time                 18.17
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  32768
SOLVENT              CDCl3
NS                      16
DS                       2
SWH              4006.410 Hz
FIDRES           0.122266 Hz
AQ               4.0894966 sec
RG                      64
DW                124.800 usec
DE                  6.50 usec
TE                 296.7 K
D1              1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                  14.70 usec
PL1                  0.00 dB
PL1W            11.88122272 W
SFO1            400.1318007 MHz
SI                   32768
SF              400.1300000 MHz
WDW                     EM
SSB                      0
LB                  0.30 Hz
GB                       0
PC                    1.00
```

FL-129C

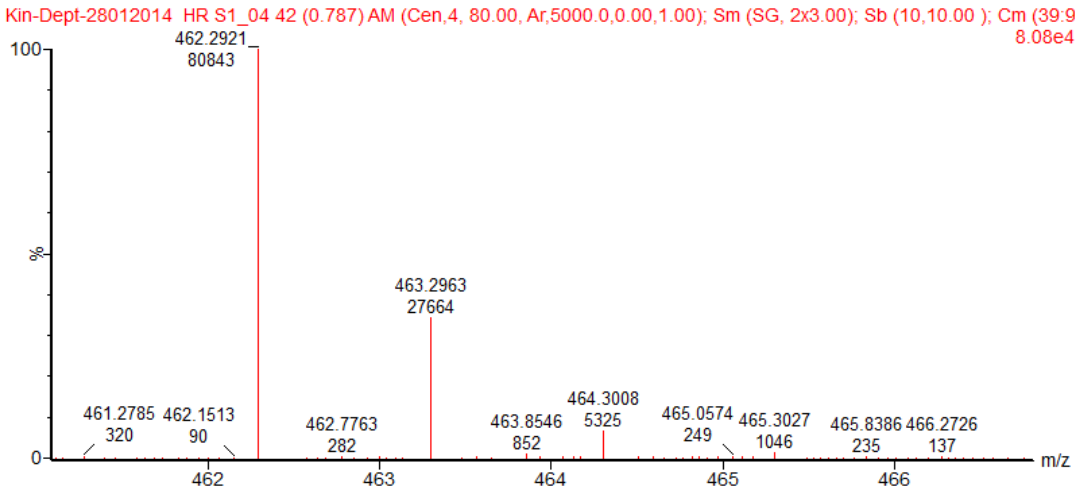



```
NAME                FL-129
EXPNO                    4
PROCNO                   1
Date_             20140122
Time                 18.20
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG             zgpg30
TD                  65536
SOLVENT              CDCl3
NS                      64
DS                       2
SWH              24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                     203
DW                20.800 usec
DE                  6.50 usec
TE                 297.1 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13c
P1                   9.50 usec
PL1                 -2.00 dB
PL1W            58.52175522 W
SFO1            100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                    1H
PCPD2               80.00 usec
PL2                  0.00 dB
PL12                15.00 dB
PL13                15.00 dB
PL2W            11.88122272 W
PL12W            0.37571725 W
PL13W            0.37571725 W
SFO2            400.1316005 MHz
SI                   32768
SF              100.6127695 MHz
WDW                     EM
SSB                      0
LB                  1.00 Hz
GB                       0
PC                    1.40
```

3-(Dicyclohexylphosphino)-2-(4-methoxy-3,5-dimethylphenyl)-1-methyl-1*H*-indole (Table 7.1, L14)

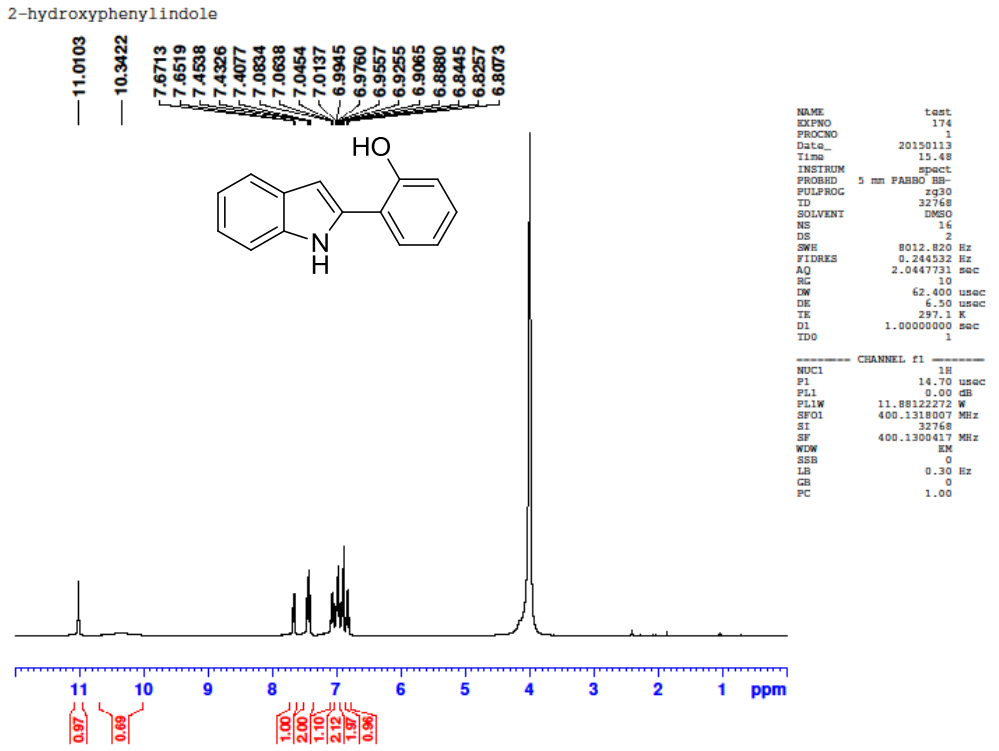


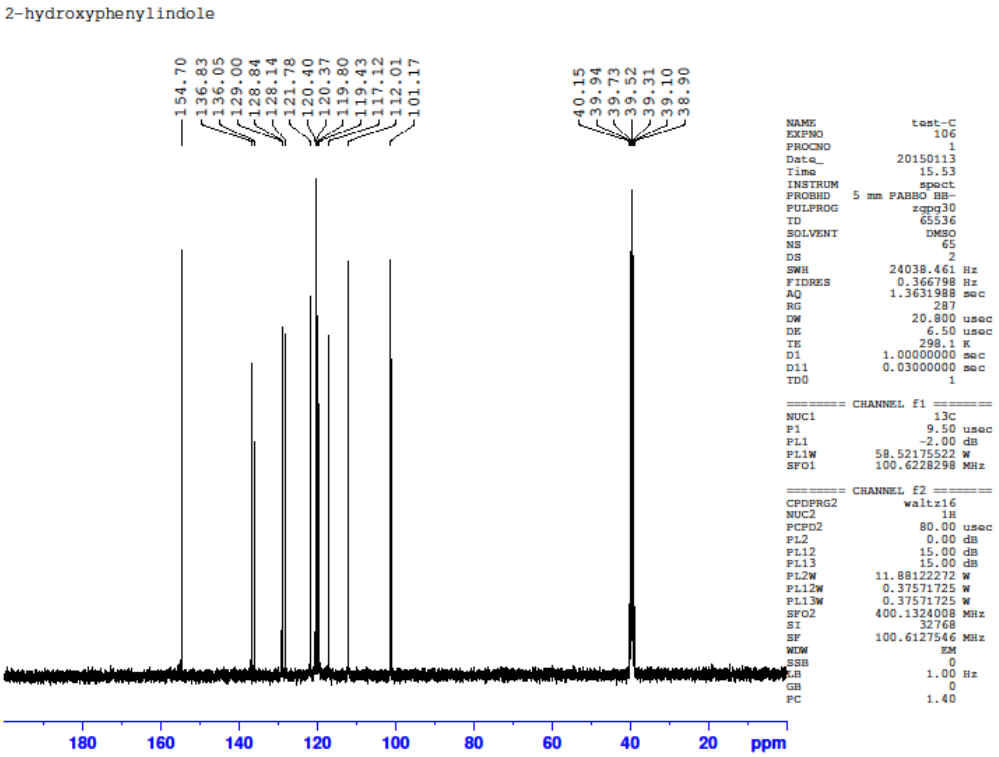
HS



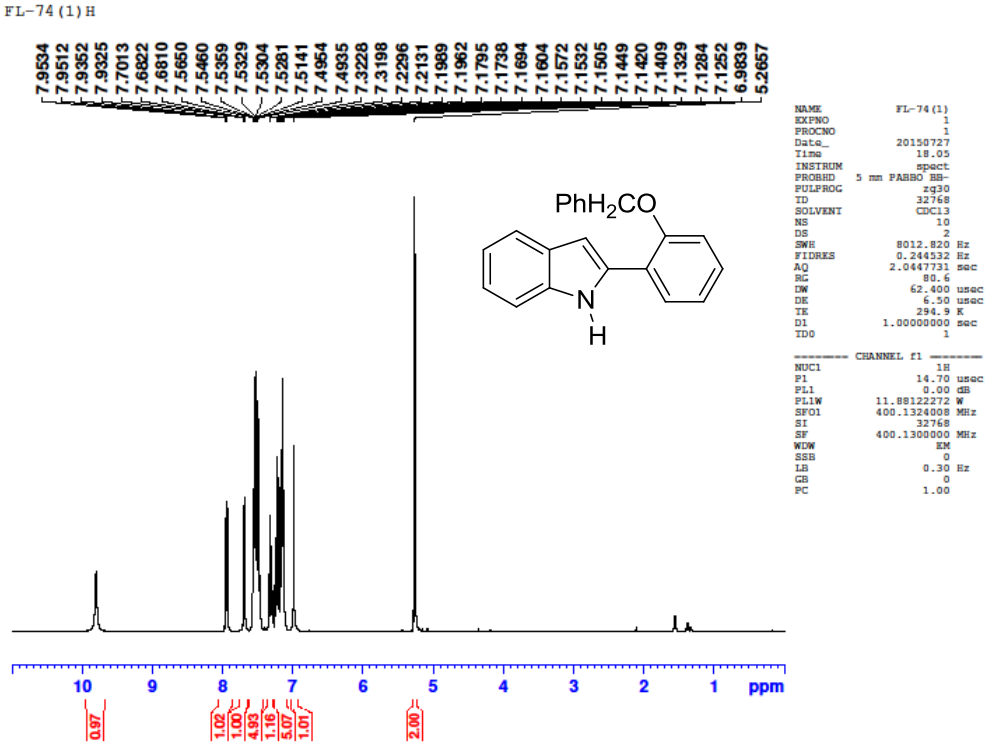
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
462.2921	462.2926	-0.5	-1.1	11.5	27.0	C30 H41 N O P

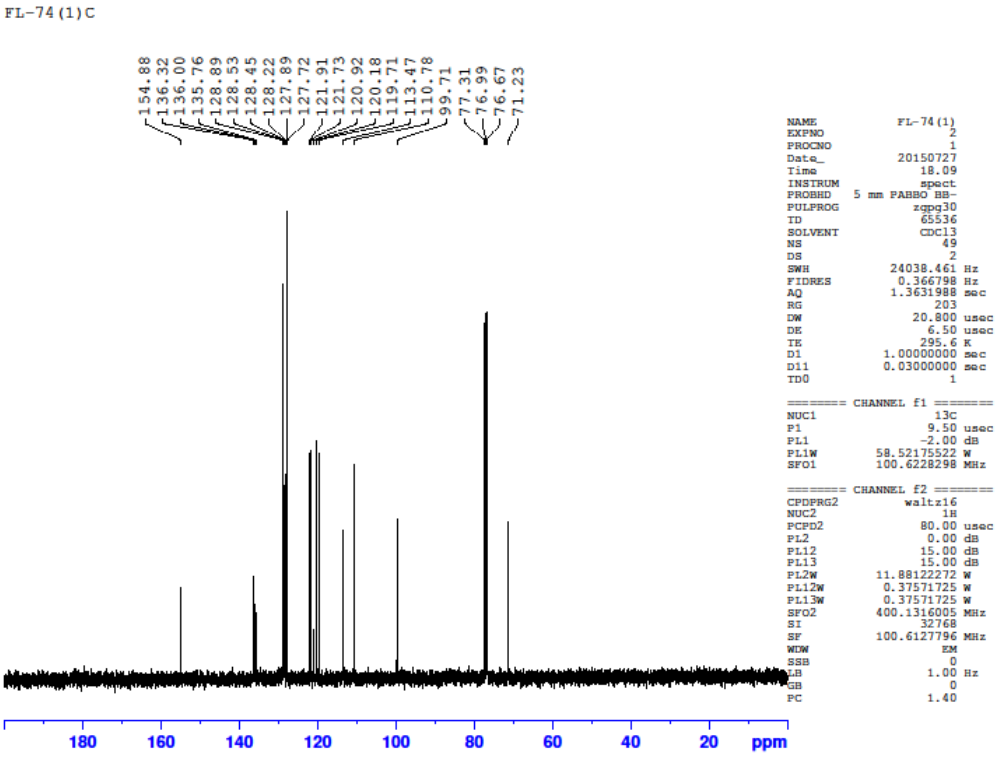
2-(1*H*-Indol-2-yl)phenol (Table 7.1, L24 precursor)



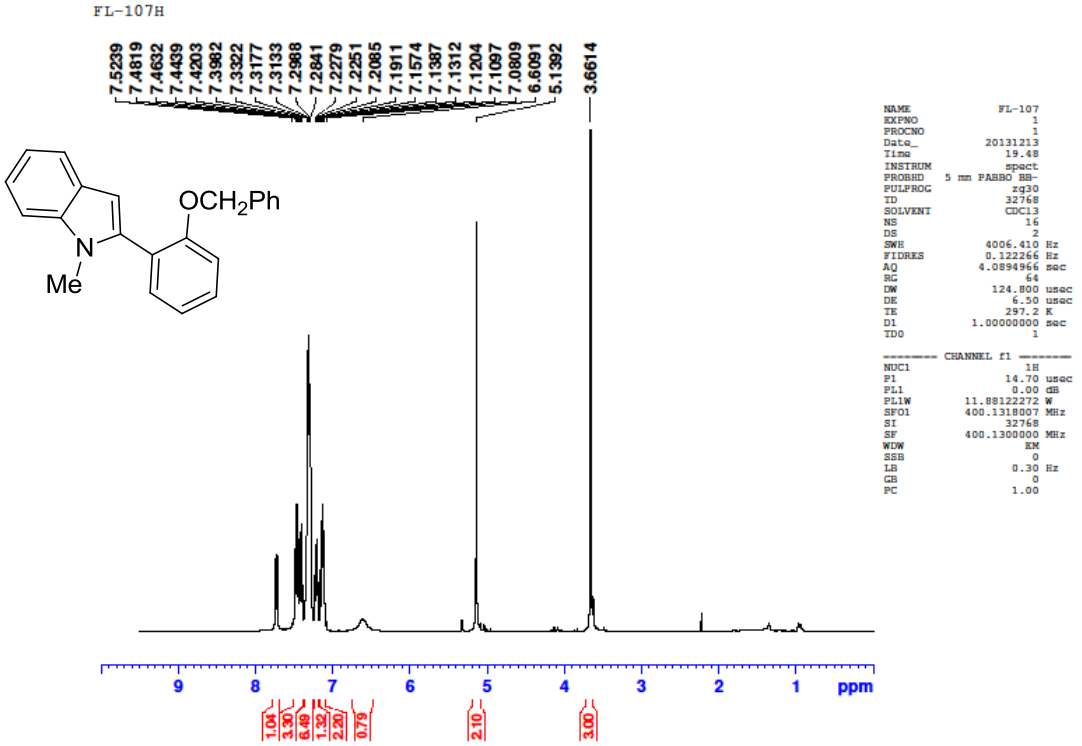


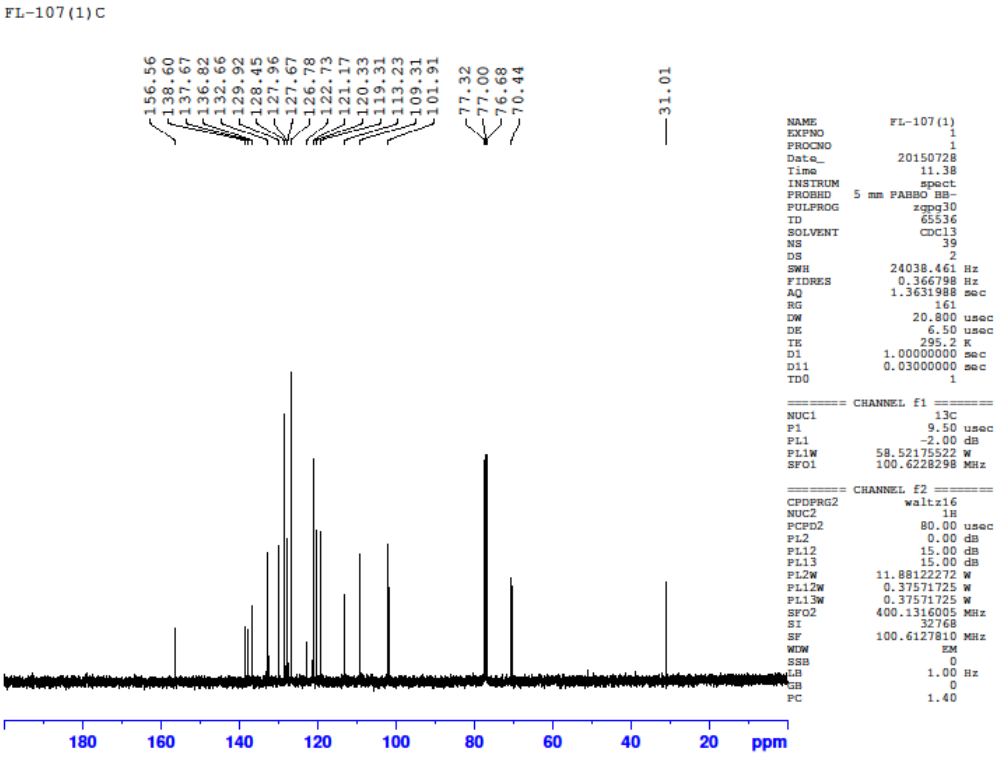
2-(2-(Benzyloxy)phenyl)-1*H*-indole (Table 7.1, L24 precursor)



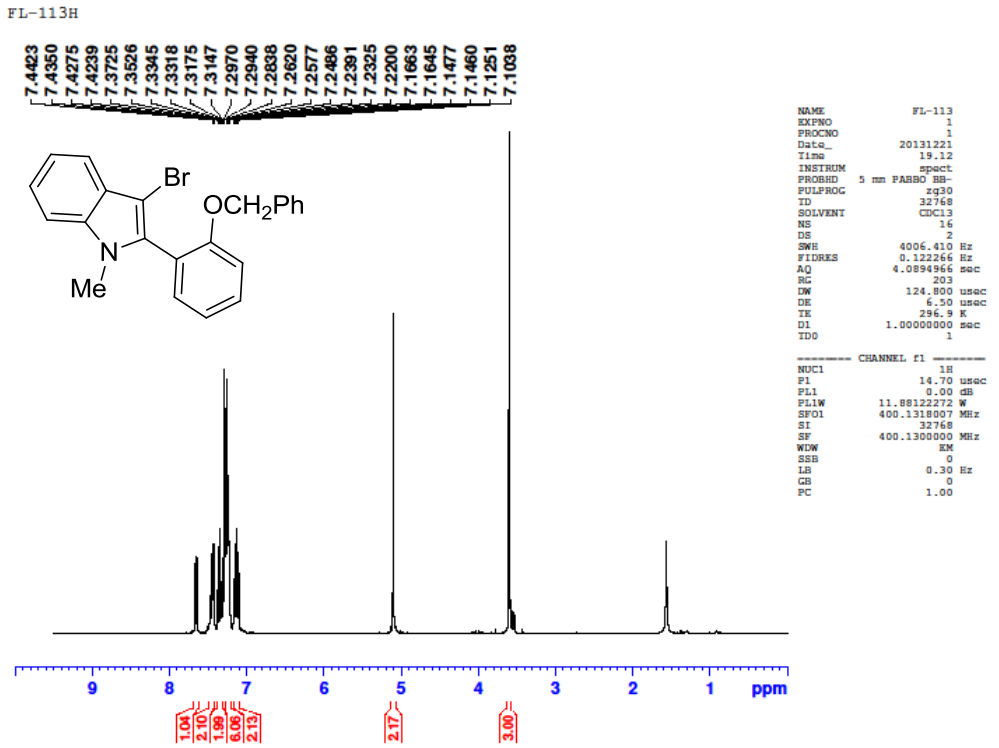


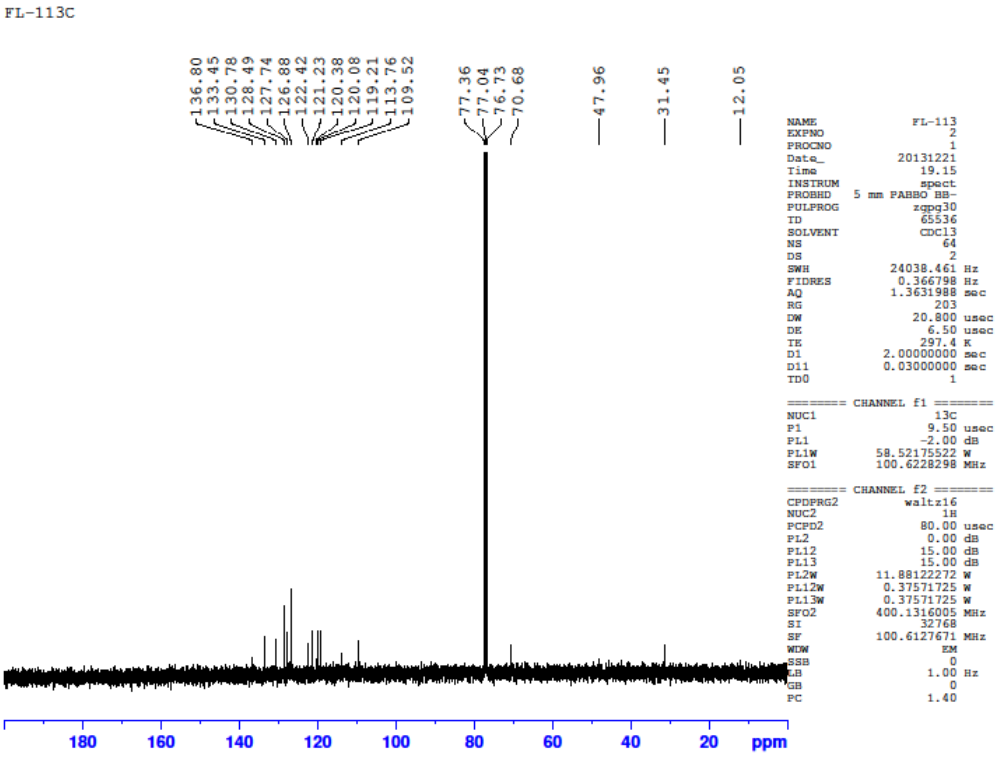
2-(2-(Benzyloxy)phenyl)-1-methyl-1*H*-indole (Table 7.1, L24 precursor)



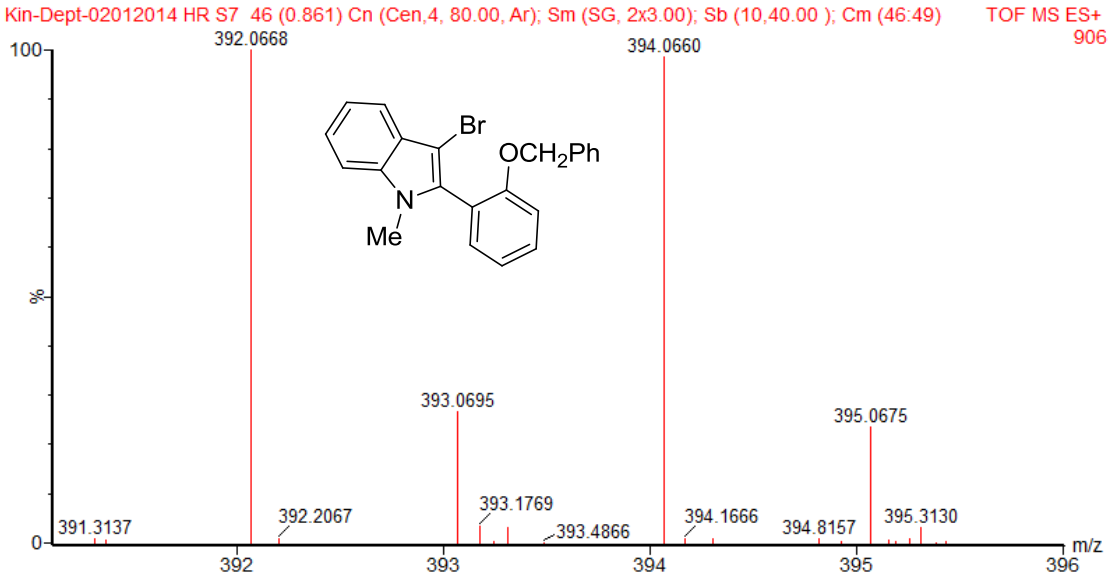


2-(2-(Benzyloxy)phenyl)-3-bromo-1-methyl-1*H*-indole (Table 7.1, L24 precursor)



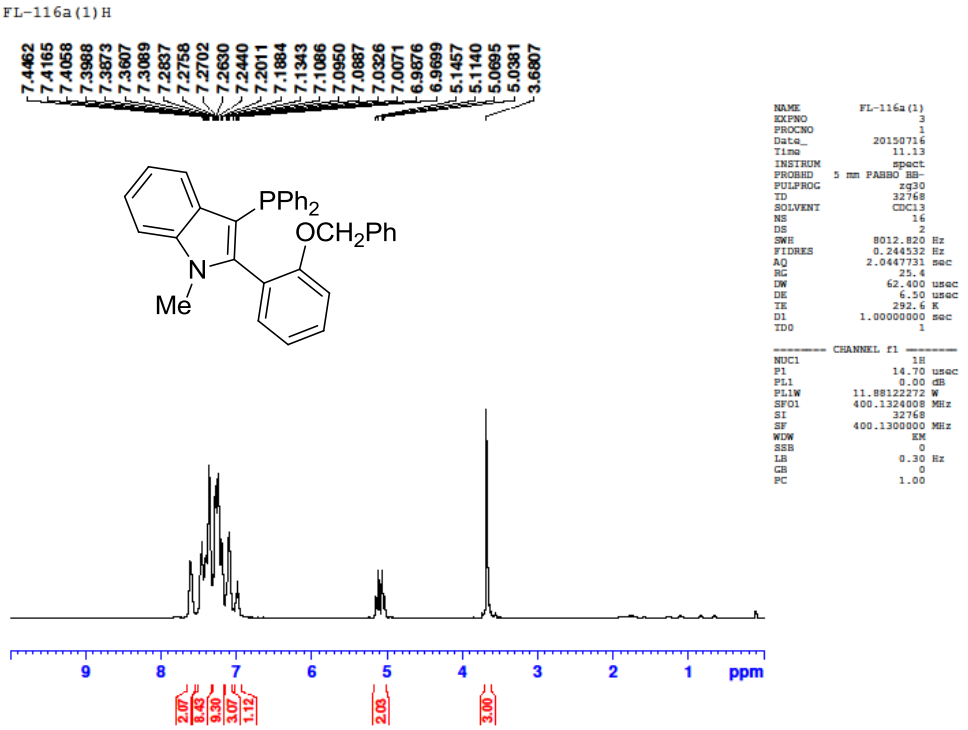


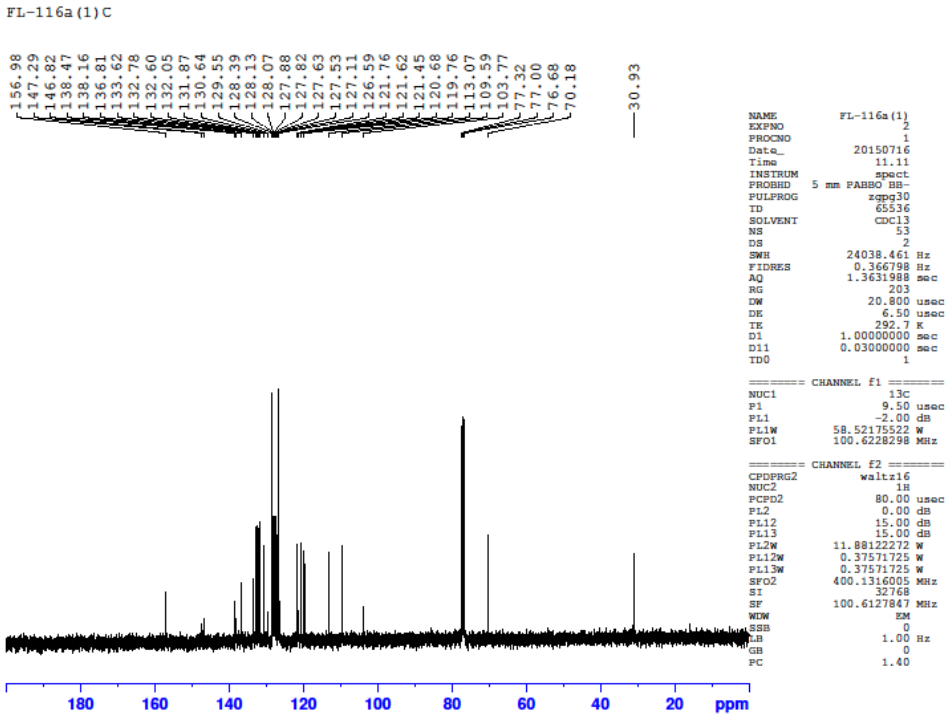
2-(2-(Benzyloxy)phenyl)-3-bromo-1-methyl-1*H*-indole (Table 7.1, L24 precursor)



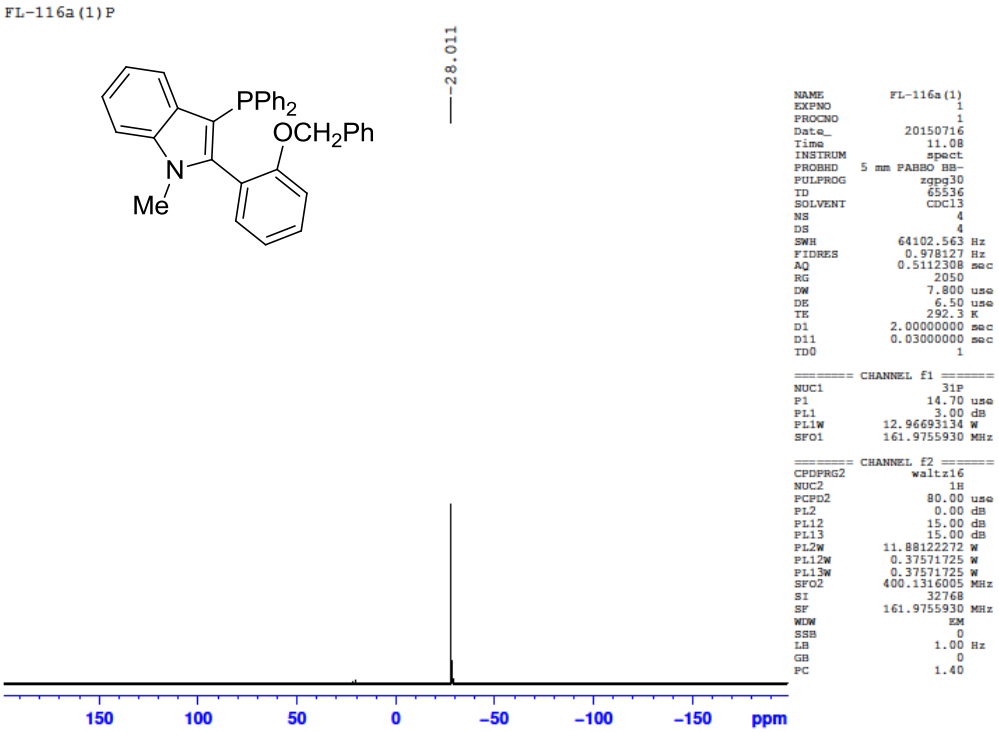
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
392.0668	392.0650	1.8	4.6	13.5	0.8	C22 H19 N O Br

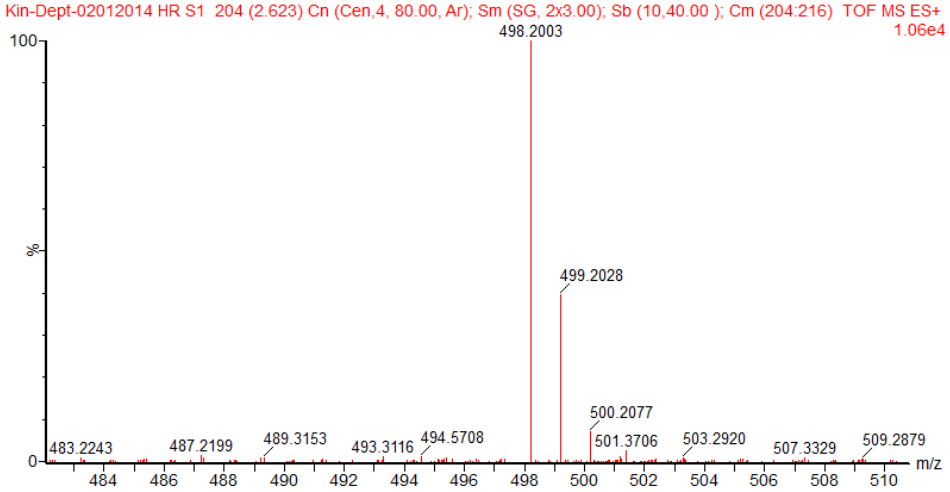
2-(2-(Benzyloxy)phenyl)-3-(diphenylphosphino)-1-methyl-1*H*-indole (Table 7.1, L24)





2-(2-(Benzyloxy)phenyl)-3-(diphenylphosphino)-1-methyl-1*H*-indole (Table 7.1, L24)

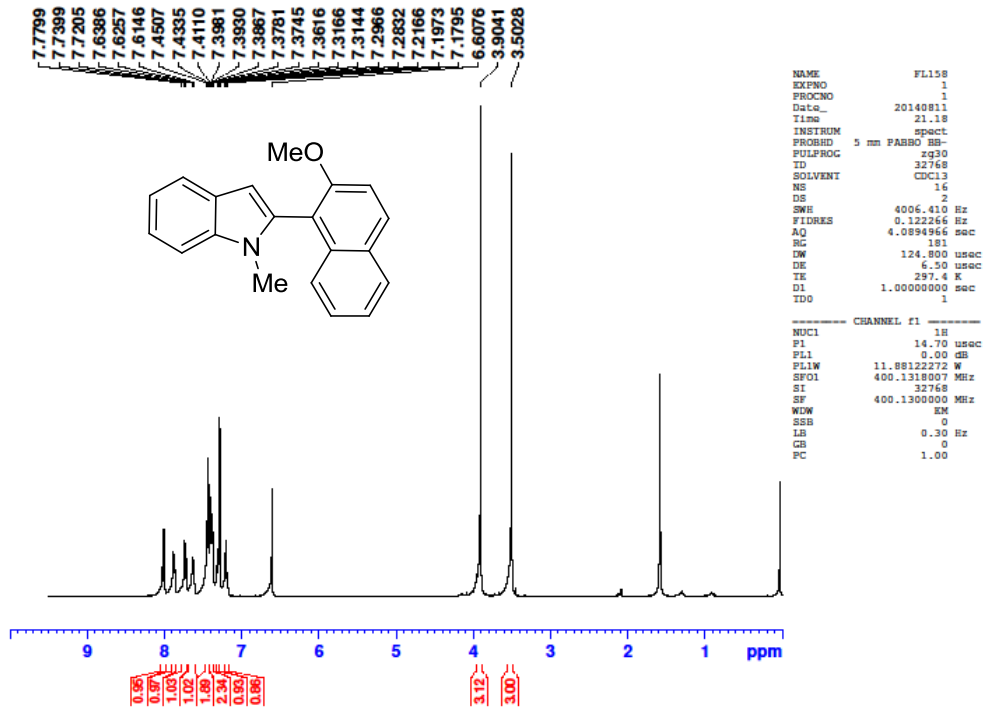




Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
498.2003	498.1987	1.6	3.2	21.5	2.2	C34 H29 N O P

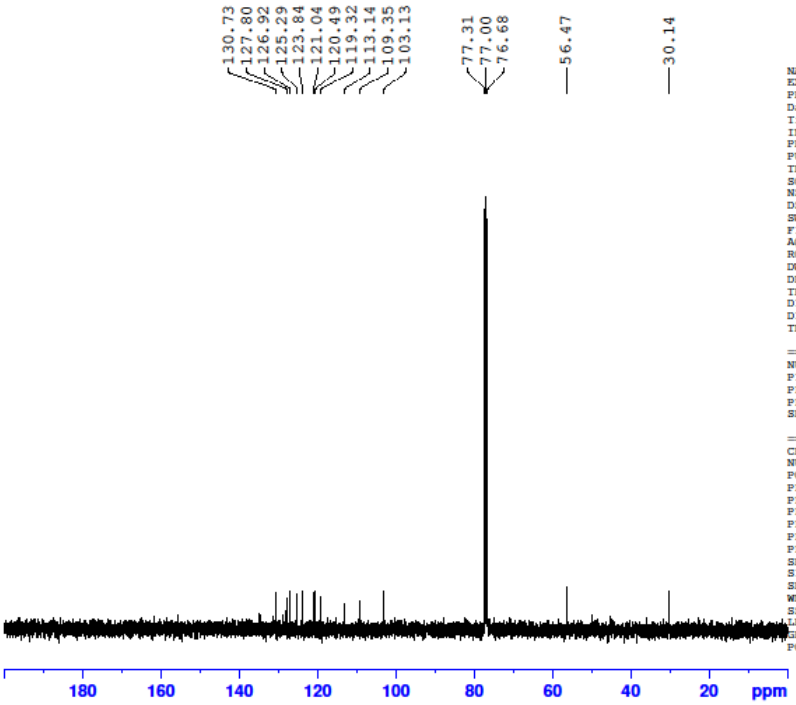
2-(2-Methoxynaphthalen-1-yl)-1-methyl-1*H*-indole (Table 7.1, L25 precursor)

FL158H



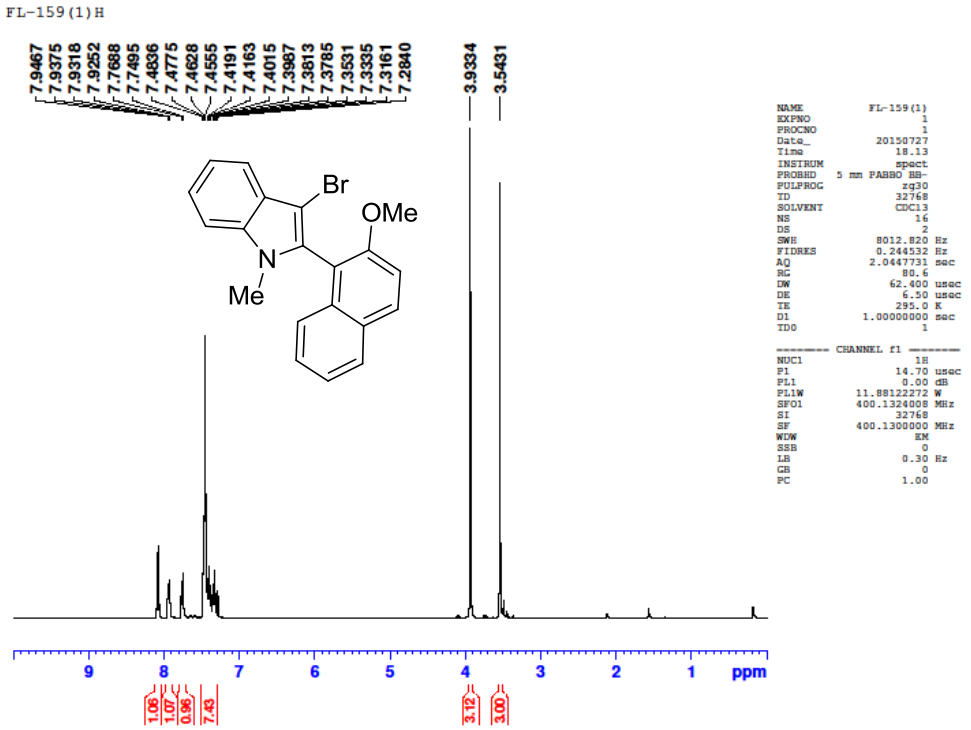

```
NAME                FL158
EXPNO                   1
PROCNO                  1
Date_            20140811
Time                21.18
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  32768
SOLVENT             CDCl3
NS                     16
DS                      2
SWH              4006.410 Hz
FIDRES           0.122266 Hz
AQ               4.0894966 sec
RG                    181
DW                124.800 usec
DE                  6.50 usec
TE                 297.4 K
D1               1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                 14.70 usec
PL1                 0.00 dB
PL1W           11.88122272 W
SFO1           400.1318007 MHz
SI                  32768
SF             400.1300000 MHz
WDW                    EM
SSB                     0
LB                 0.30 Hz
GB                      0
PC                   1.00
```

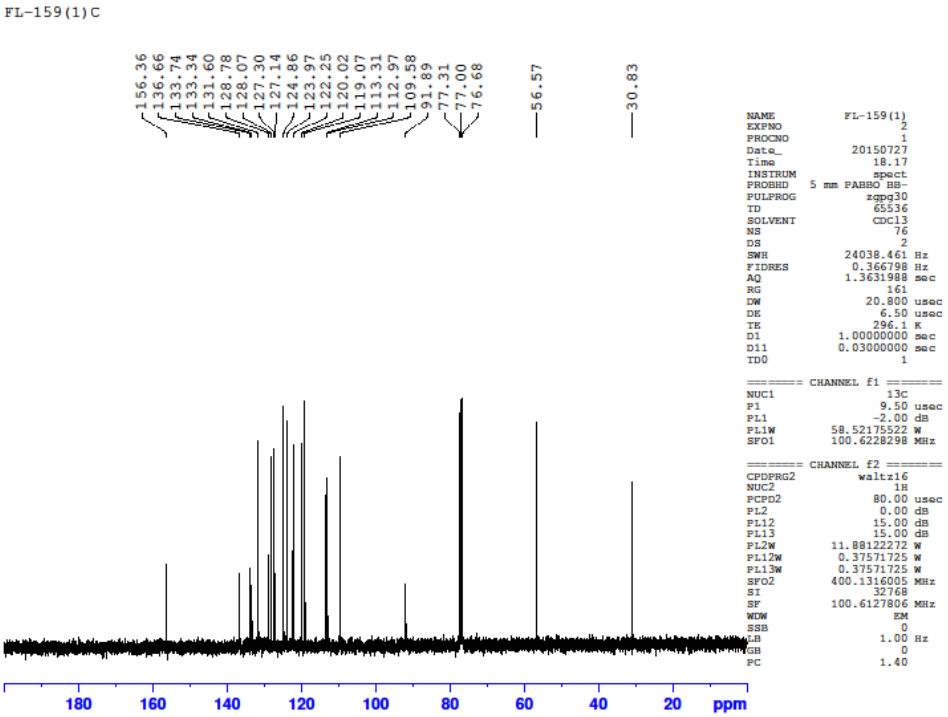
FL158C




```
NAME                FL158
EXPNO                   2
PROCNO                  1
Date_            20140811
Time                21.21
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                  65536
SOLVENT             CDCl3
NS                     64
DS                      2
SWH              24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                    203
DW                 20.800 usec
DE                  6.50 usec
TE                 297.6 K
D1               2.00000000 sec
D11              0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   13C
P1                  9.50 usec
PL1                -2.00 dB
PL1W           58.52175522 W
SFO1           100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2            waltz16
NUC2                   1H
PCPD2              80.00 usec
PL2                 0.00 dB
PL12               15.00 dB
PL13               15.00 dB
PL2W           11.88122272 W
PL12W           0.37571725 W
PL13W           0.37571725 W
SFO2           400.1316005 MHz
SI                  32768
SF             100.6127719 MHz
WDW                    EM
SSB                     0
LB                 1.00 Hz
GB                      0
PC                   1.40
```

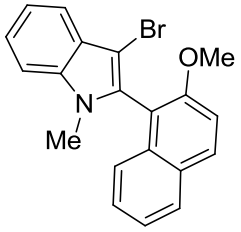
3-Bromo-2-(2-methoxynaphthalen-1-yl)-1-methyl-1*H*-indole (Table 7.1, L25 precursor)

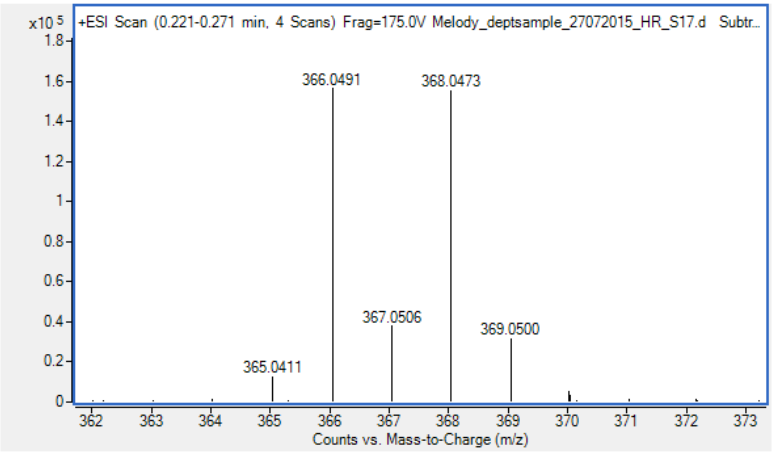




3-Bromo-2-(2-methoxynaphthalen-1-yl)-1-methyl-1*H*-indole (Table 7.1, L25 precursor)

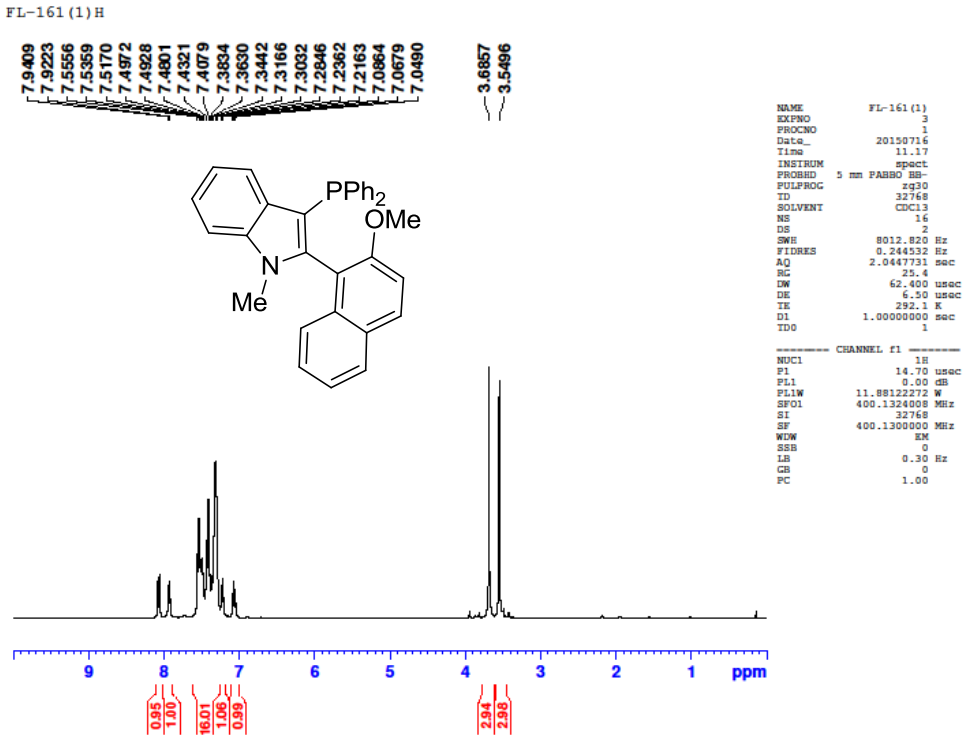
HS

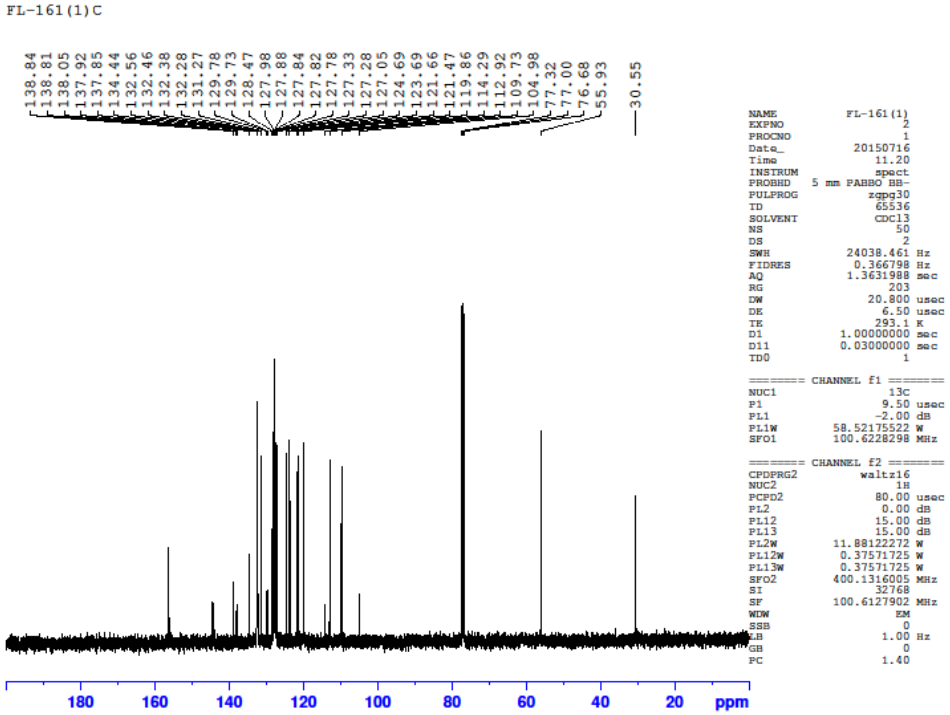




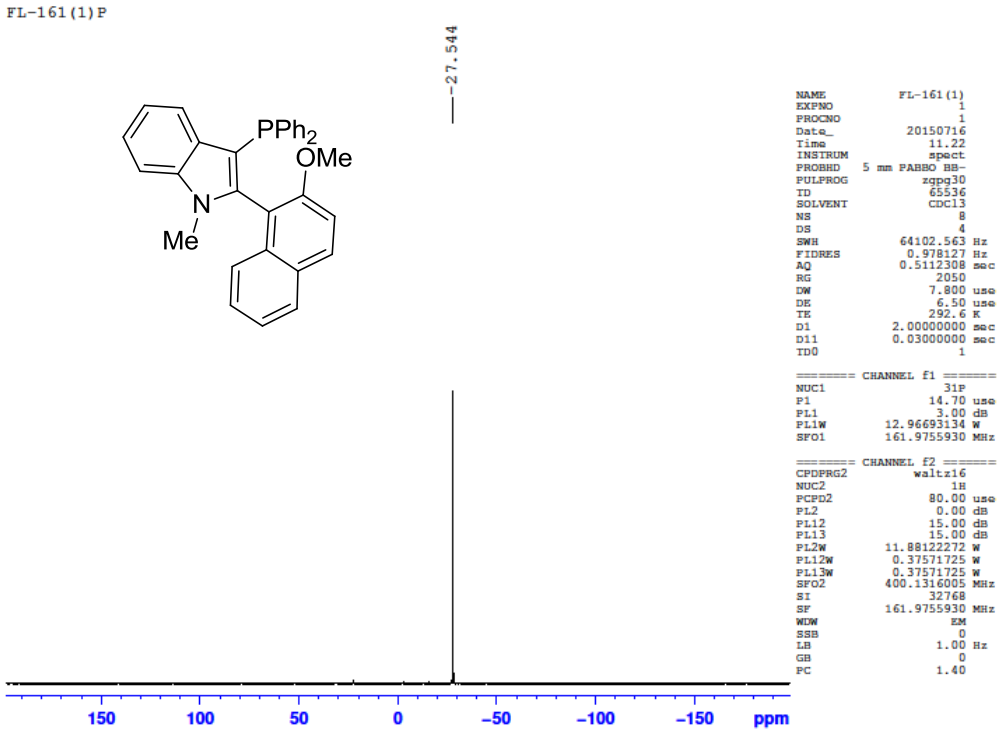
Mass	Calc. Mass	mDa	PPM	Formula
366.0491	366.0488	0.3	0.8	C20 H17 Br N O

3-(Diphenylphosphino)-2-(2-methoxynaphthalen-1-yl)-1-methyl-1*H*-indole (Table 7.1, L25)

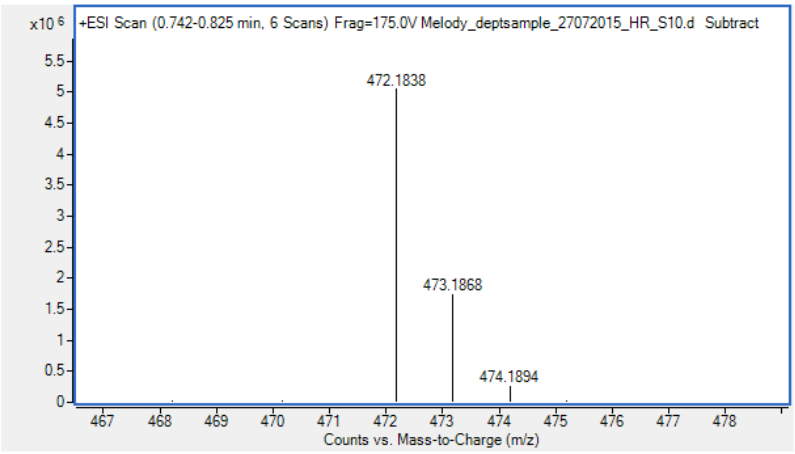




3-(Diphenylphosphino)-2-(2-methoxynaphthalen-1-yl)-1-methyl-1*H*-indole (Table 7.1, L25)

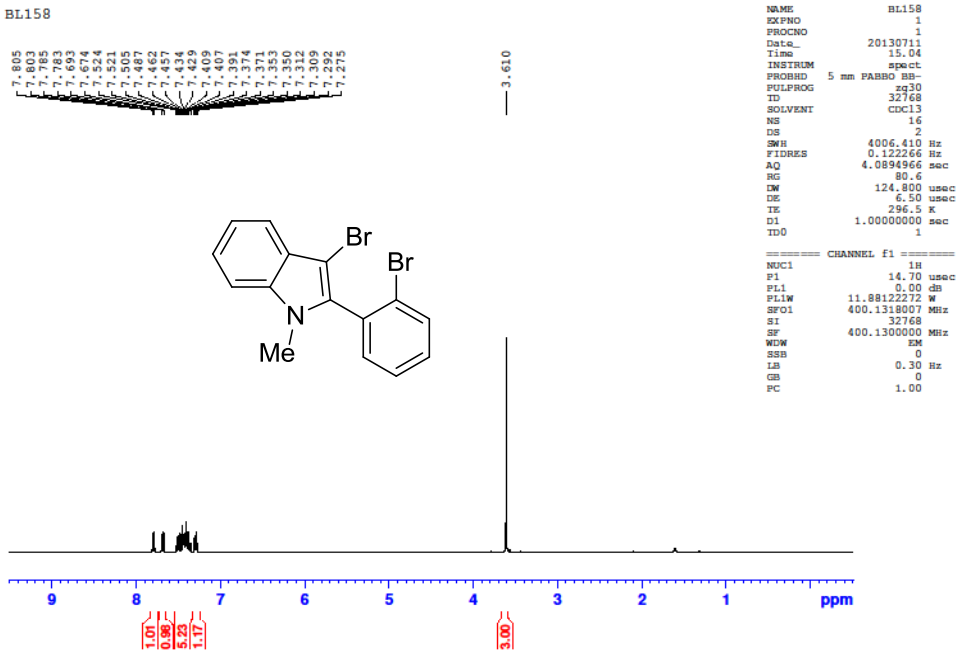


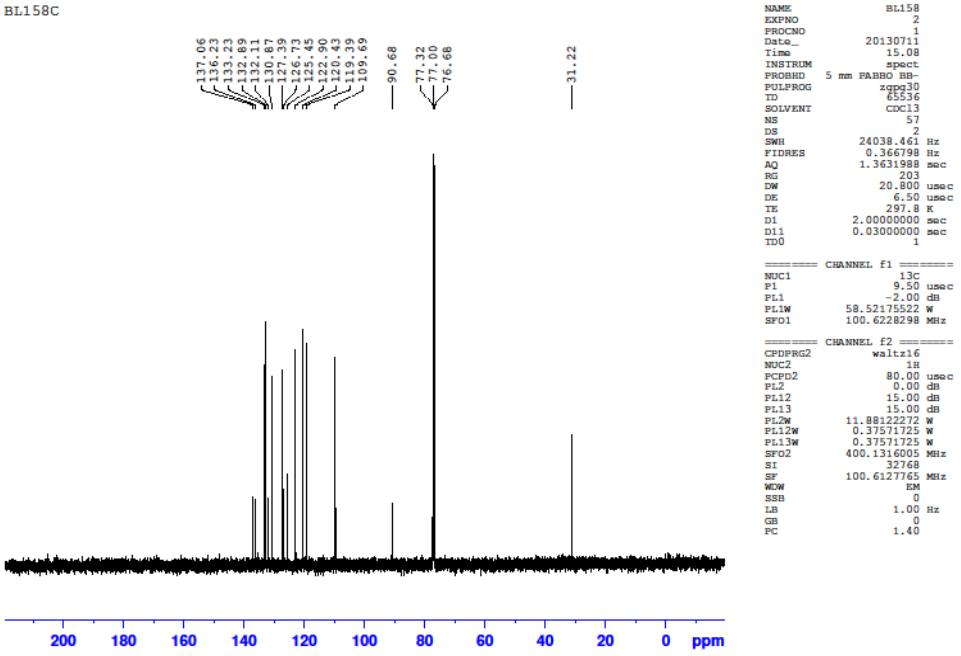
HS



Mass	Calc. Mass	mDa	PPM	Formula
472.1838	472.1825	1.3	2.8	C32 H27 N O P

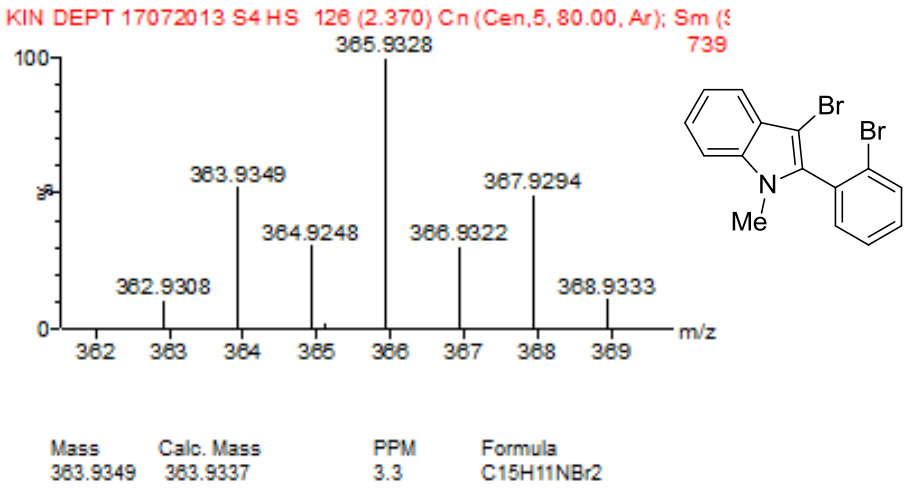
3-Bromo-2-(2-bromophenyl)-1-methyl-1*H*-indole (Table 7.1, L27 precursor)





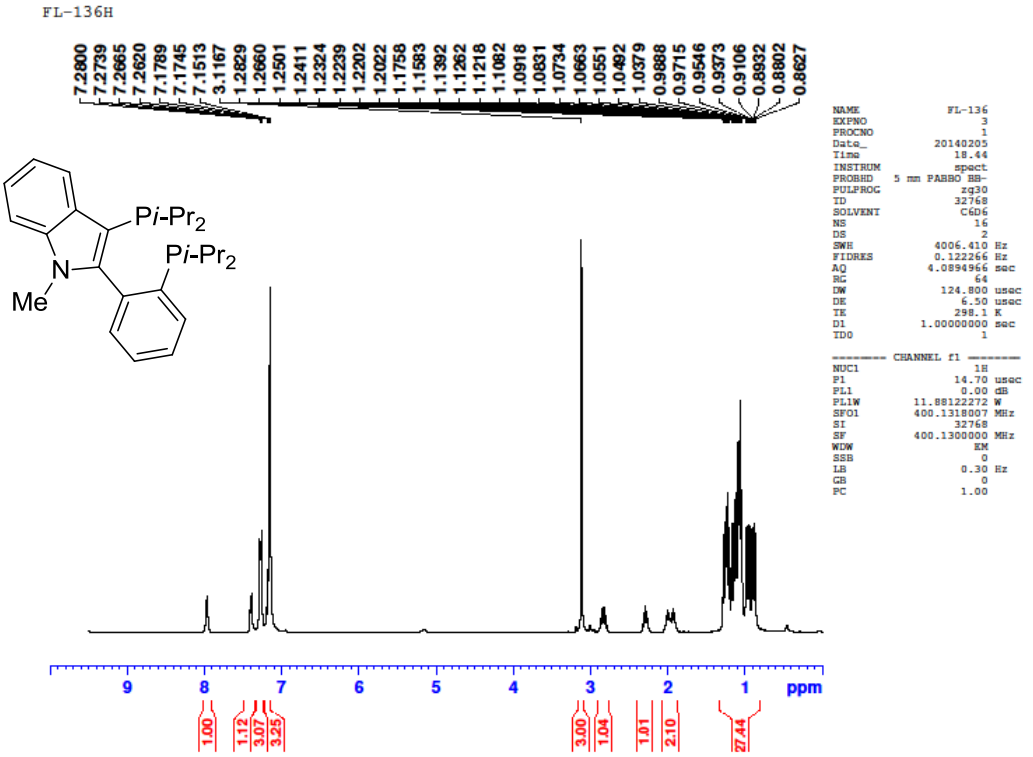
3-Bromo-2-(2-bromophenyl)-1-methyl-1*H*-indole (Table 7.1, L27 precursor)

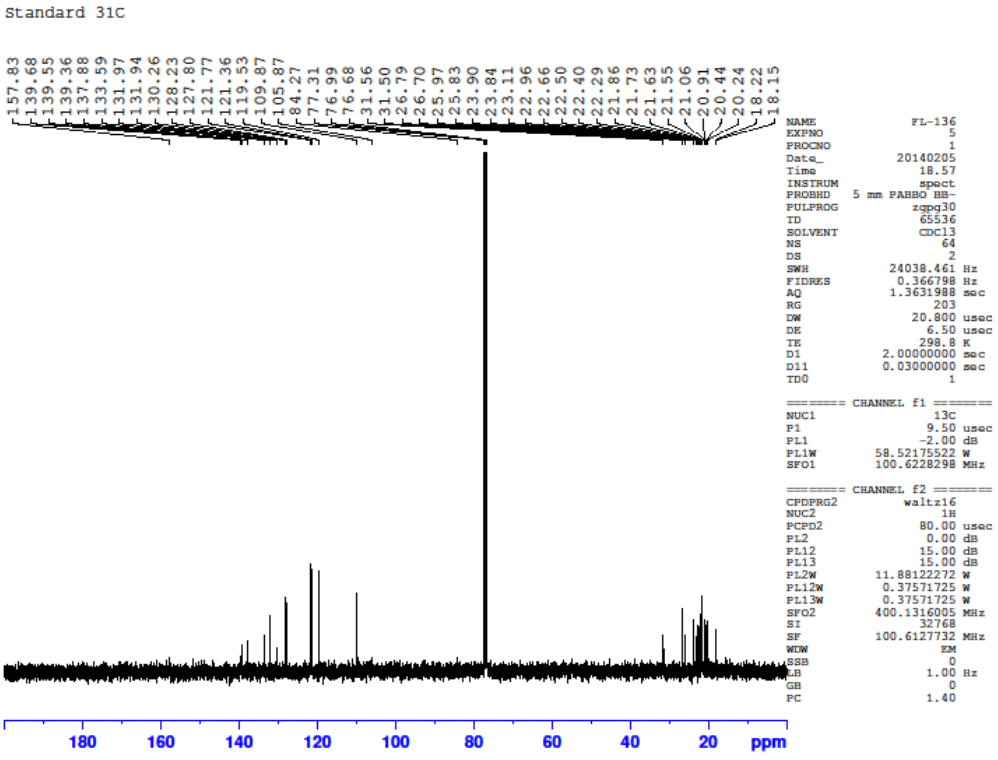
HS



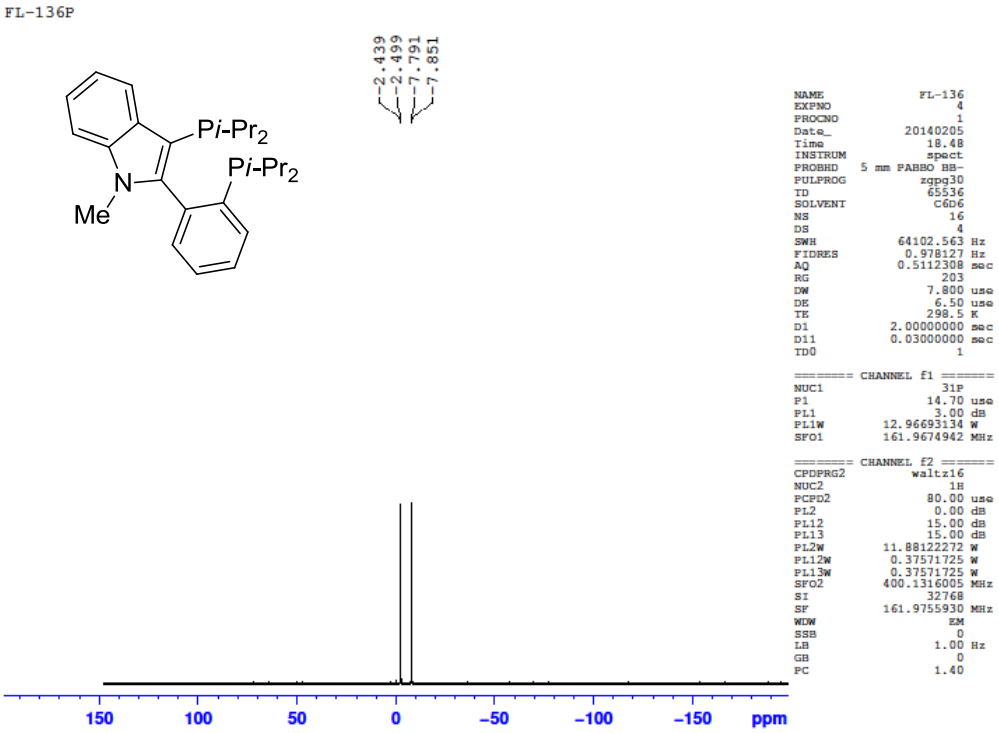
Mass	Calc. Mass	PPM	Formula
363.9349	363.9337	3.3	C15H11NBr2

3-(Diisopropylphosphino)-2-(2-(diisopropylphosphino)phenyl)-1-methyl-1*H*-indole (Table 7.1, L27)

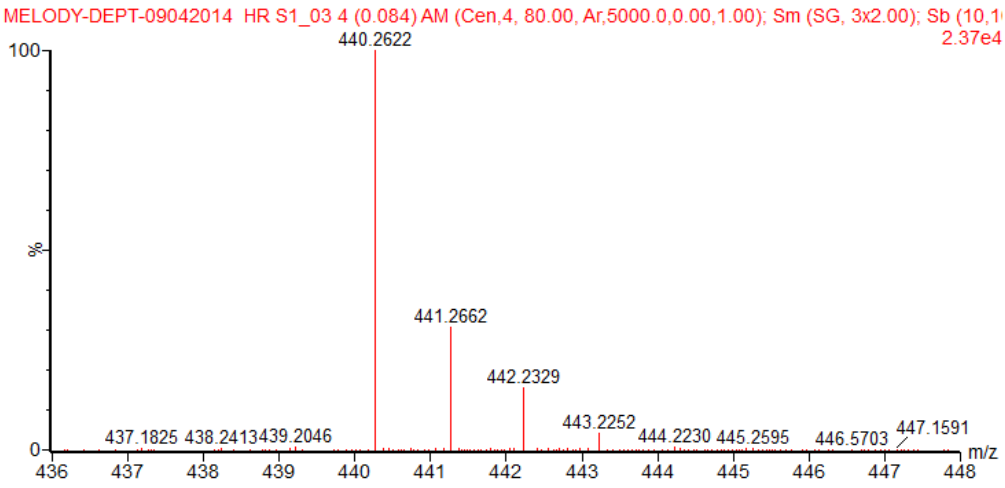




3-(Diisopropylphosphino)-2-(2-(diisopropylphosphino)phenyl)-1-methyl-1*H*-indole (Table 7.1, L27)



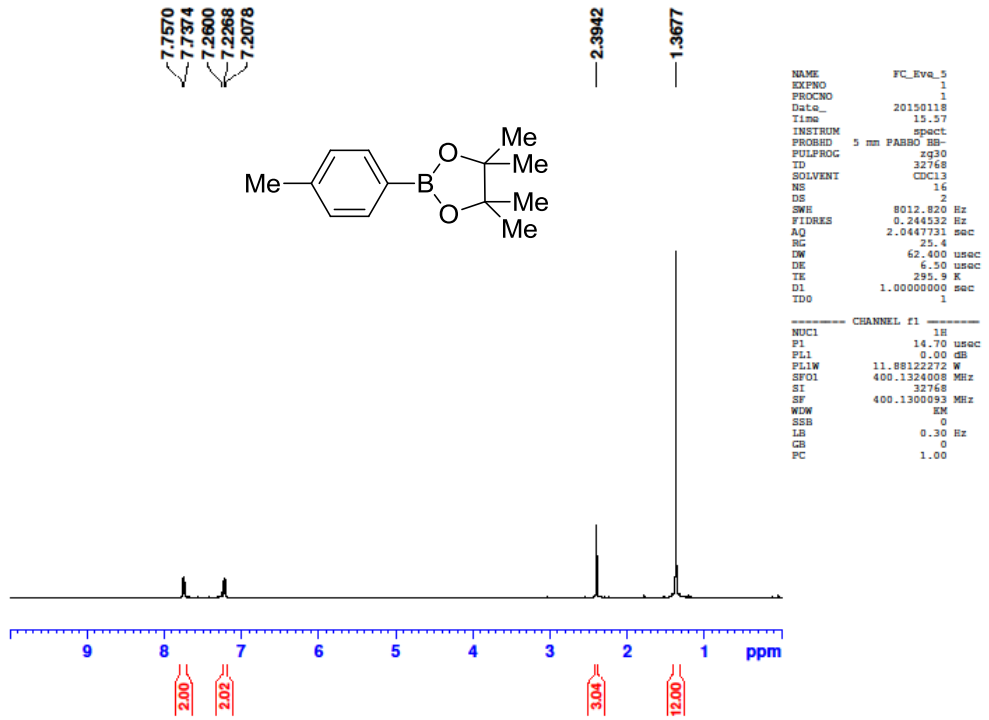
HS



Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
440.2622	440.2636	-1.4	-3.2	9.5	973.4	C27 H40 N P2

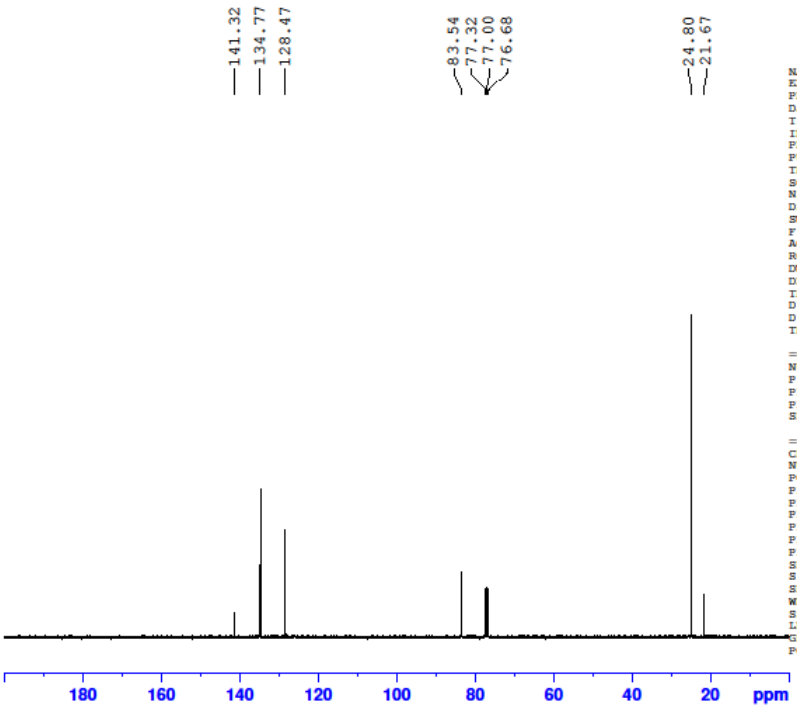
4,4,5,5-Tetramethyl-2-(*p*-tolyl)-1,3,2-dioxaborolane (Table 7.3, Entry 1)

FC_Eve_5H




```
NAME            FC_Eve_5
EXPNO                  1
PROCNO                 1
Date_           20150118
Time                15.57
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ              2.0447731 sec
RG                  25.4
DW                62.400 usec
DE                 6.50 usec
TE                295.9 K
D1              1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 14.70 usec
PL1                0.00 dB
PL1W          11.88122272 W
SFO1          400.1324008 MHz
SI                 32768
SF            400.1300093 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

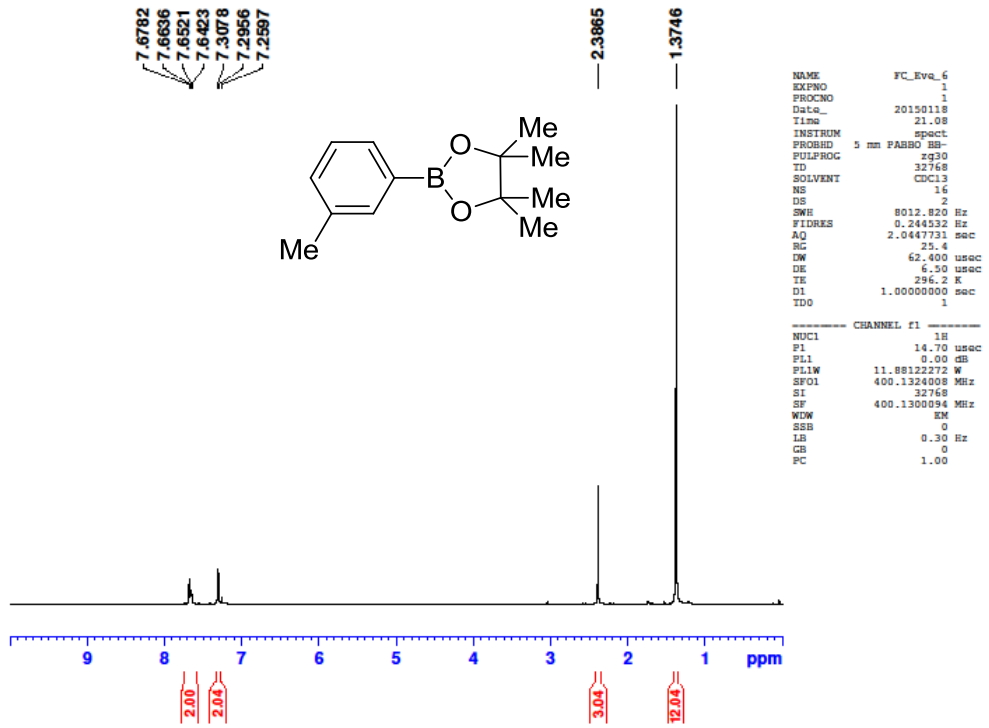
FC_Eve_5C




```
NAME            FC_Eve_5
EXPNO                  2
PROCNO                 1
Date_           20150118
Time                16.01
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                    37
DS                     2
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631988 sec
RG                   203
DW                20.800 usec
DE                 6.50 usec
TE                296.1 K
D1              1.00000000 sec
D11             0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  13C
P1                  9.50 usec
PL1                -2.00 dB
PL1W          58.52175522 W
SFO1          100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                  1H
PCPD2              80.00 usec
PL2                0.00 dB
PL12              15.00 dB
PL13              15.00 dB
PL2W          11.88122272 W
PL12W          0.37571725 W
PL13W          0.37571725 W
SFO2          400.1316005 MHz
SI                 32768
SF            100.6127780 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
```

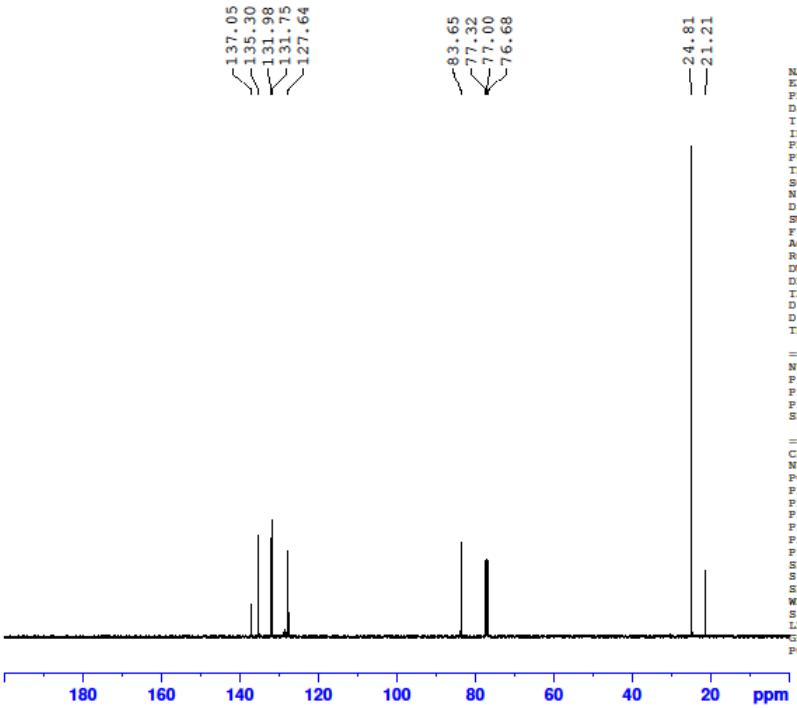
4,4,5,5-Tetramethyl-2-(*m*-tolyl)-1,3,2-dioxaborolane (Table 7.3, Entry 2)

FC_Eve_6H



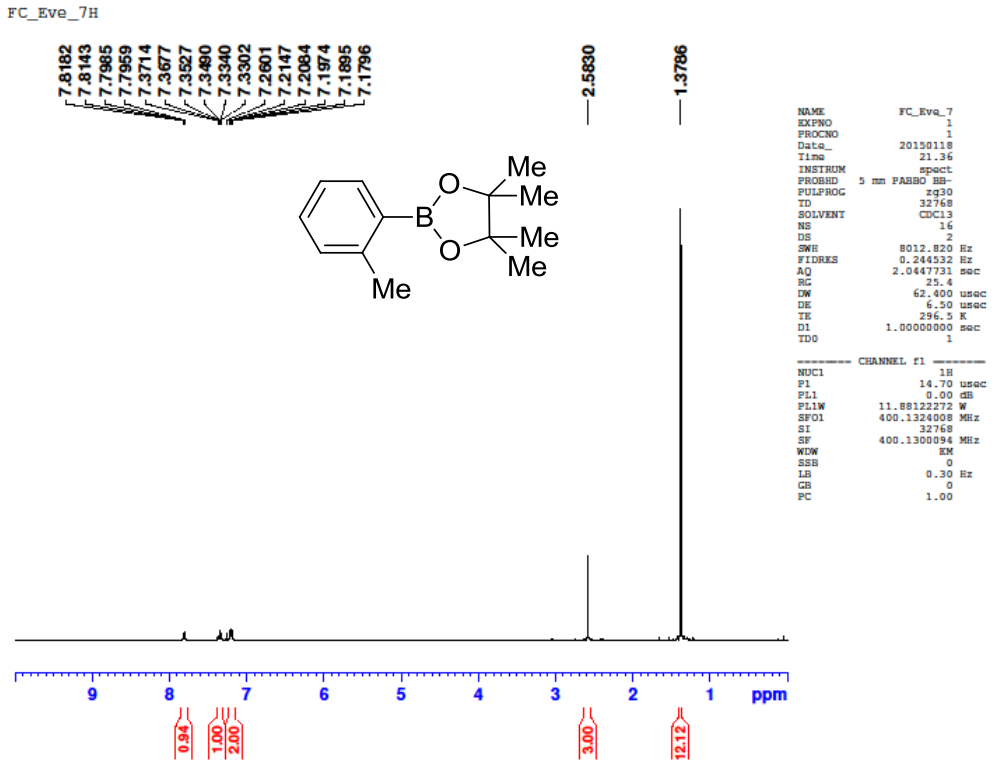

```
NAME            FC_Eve_6
EXPNO                  1
PROCNO                 1
Date_           20150118
Time                21.08
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ              2.0447731 sec
RG                  25.4
DW                62.400 usec
DE                 6.50 usec
TE                296.2 K
D1              1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                14.70 usec
PL1                0.00 dB
PL1W          11.88122272 W
SFO1          400.1324008 MHz
SI                 32768
SF            400.1300094 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                 1.00
```

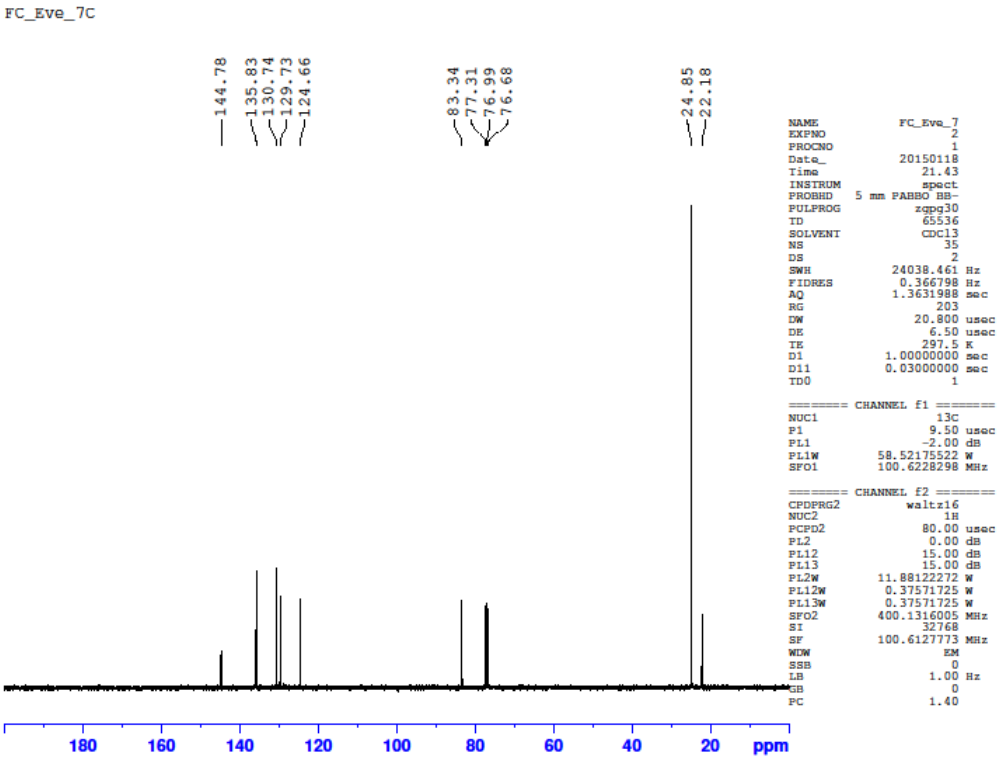
FC_Eve_6C




```
NAME            FC_Eve_6
EXPNO                  2
PROCNO                 1
Date_           20150118
Time                21.13
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                   127
DS                     2
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631988 sec
RG                   203
DW                20.800 usec
DE                 6.50 usec
TE                297.0 K
D1              1.00000000 sec
D11             0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  13C
P1                 9.50 usec
PL1               -2.00 dB
PL1W          58.52175522 W
SFO1          100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2             80.00 usec
PL2                0.00 dB
PL12              15.00 dB
PL13              15.00 dB
PL2W          11.88122272 W
PL12W          0.37571725 W
PL13W          0.37571725 W
SFO2          400.1316005 MHz
SI                 32768
SF            100.6127773 MHz
WDW                   EM
SSB                    0
LB                1.00 Hz
GB                     0
PC                 1.40
```

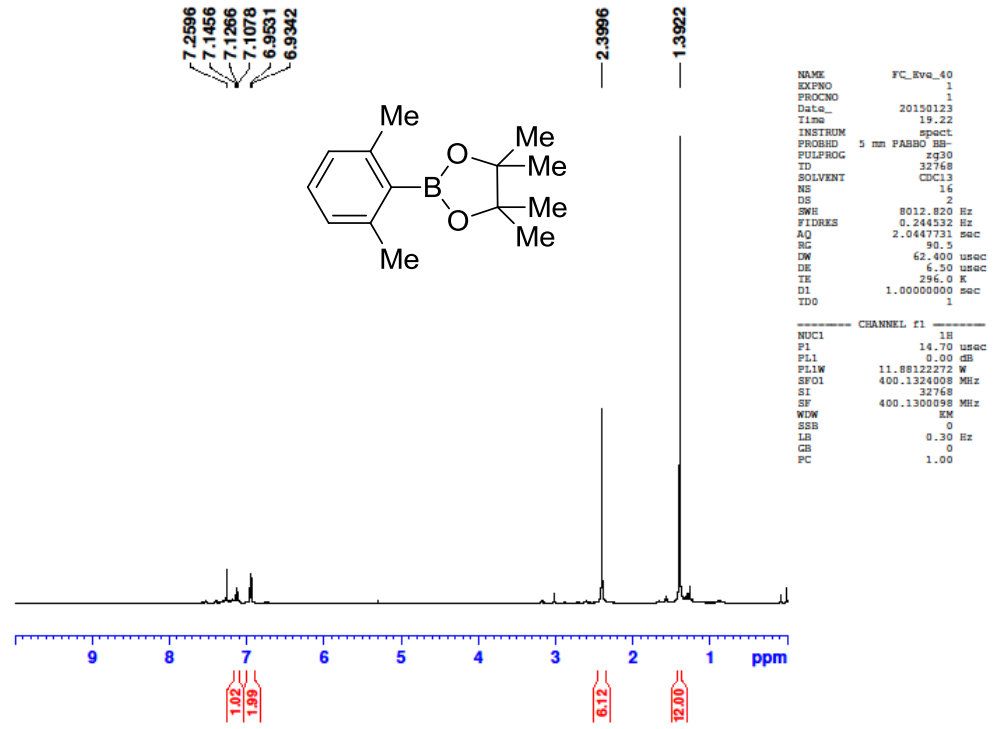
4,4,5,5-Tetramethyl-2-(*o*-tolyl)-1,3,2-dioxaborolane (Table 7.3, Entry 3)





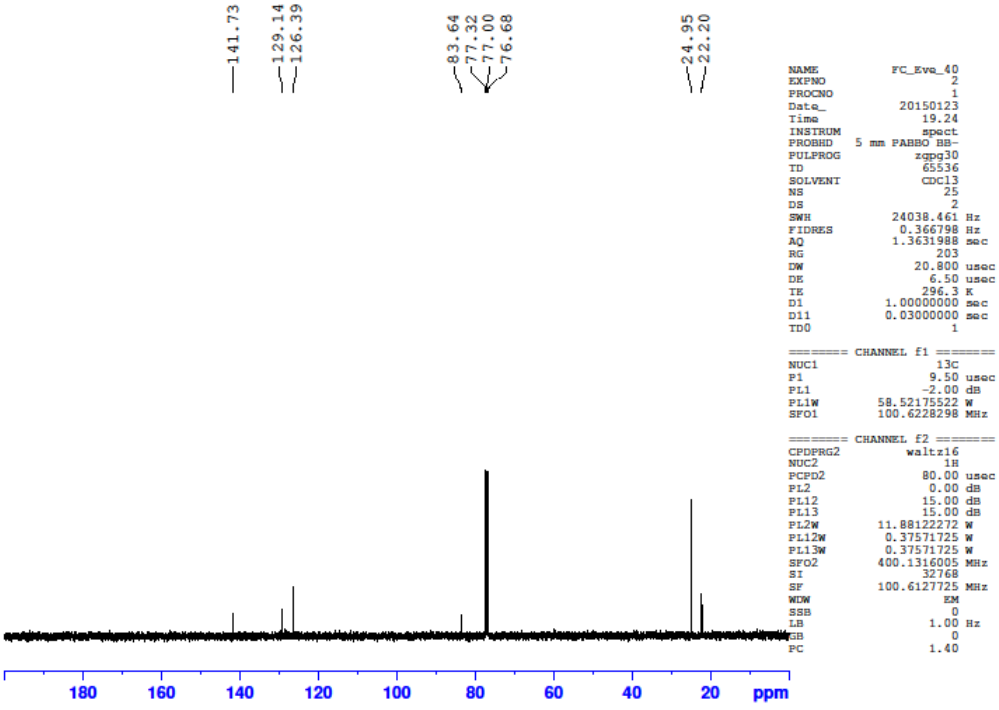
2-(2,6-Dimethylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Table 7.3, Entry 4)

FC_Eve_40H




```
NAME            FC_Eve_40
EXPNO                   1
PROCNO                  1
Date_            20150123
Time                19.22
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                     16
DS                      2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ              2.0447731 sec
RG                  90.5
DW                62.400 usec
DE                 6.50 usec
TE                296.0 K
D1              1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                 14.70 usec
PL1                 0.00 dB
PL1W           11.88122272 W
SFO1           400.1324008 MHz
SI                  32768
SF             400.1300098 MHz
WDW                    EM
SSB                     0
LB                 0.30 Hz
GB                      0
PC                 1.00
```

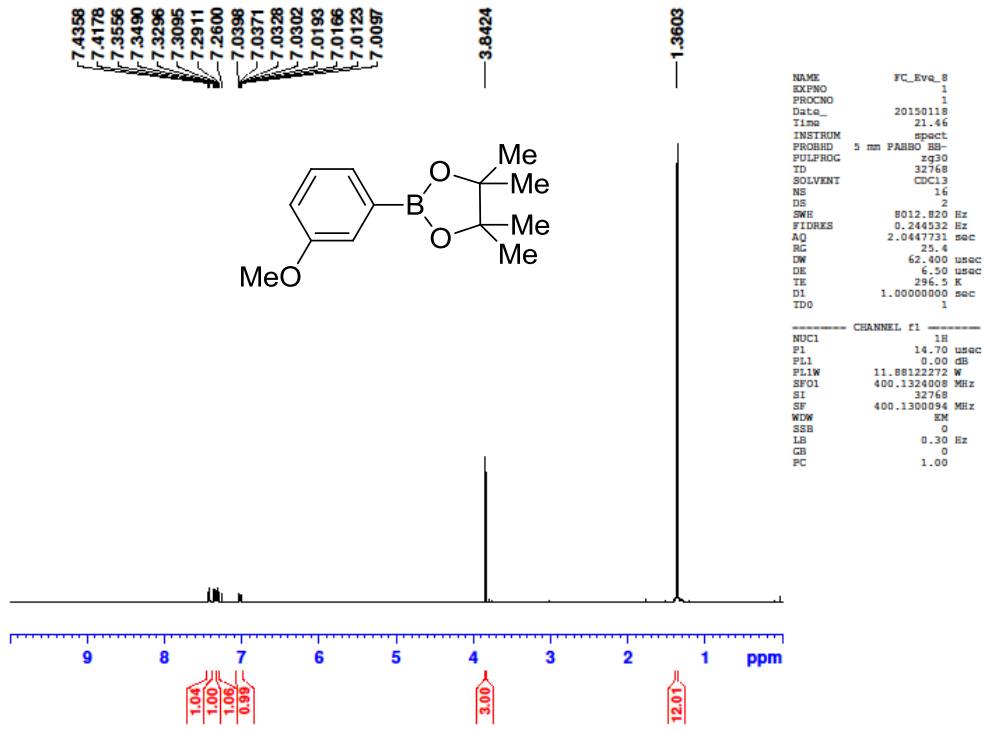
FC_Eve_40C




```
NAME            FC_Eve_40
EXPNO                   2
PROCNO                  1
Date_            20150123
Time                19.24
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                     25
DS                      2
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631988 sec
RG                    203
DW                20.800 usec
DE                 6.50 usec
TE                296.3 K
D1              1.00000000 sec
D11             0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   13C
P1                  9.50 usec
PL1                -2.00 dB
PL1W           58.52175522 W
SFO1           100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2            waltz16
NUC2                   1H
PCPD2              80.00 usec
PL2                 0.00 dB
PL12               15.00 dB
PL13               15.00 dB
PL2W           11.88122272 W
PL12W           0.37571725 W
PL13W           0.37571725 W
SFO2           400.1316005 MHz
SI                  32768
SF             100.6127725 MHz
WDW                    EM
SSB                     0
LB                 1.00 Hz
GB                      0
PC                 1.40
```

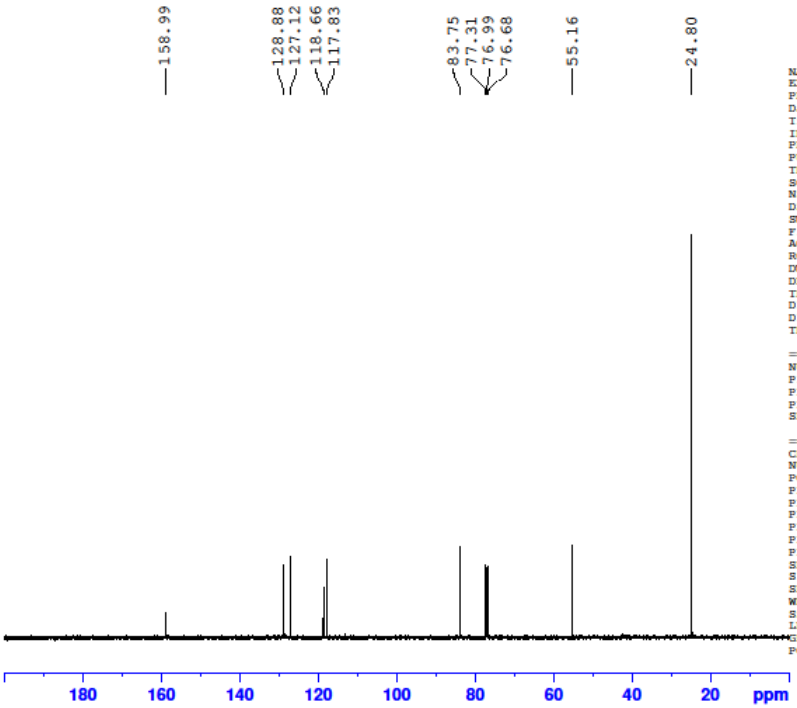
2-(3-Methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Table 7.3, Entry 5)

FC_Eve_8H




```
NAME            FC_Eve_8
EXPNO                  1
PROCNO                 1
Date_           20150118
Time                21.46
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ              2.0447731 sec
RG                  25.4
DW                62.400 usec
DE                 6.50 usec
TE                296.5 K
D1              1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 14.70 usec
PL1                0.00 dB
PL1W          11.88122272 W
SFO1          400.1324008 MHz
SI                 32768
SF            400.1300094 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

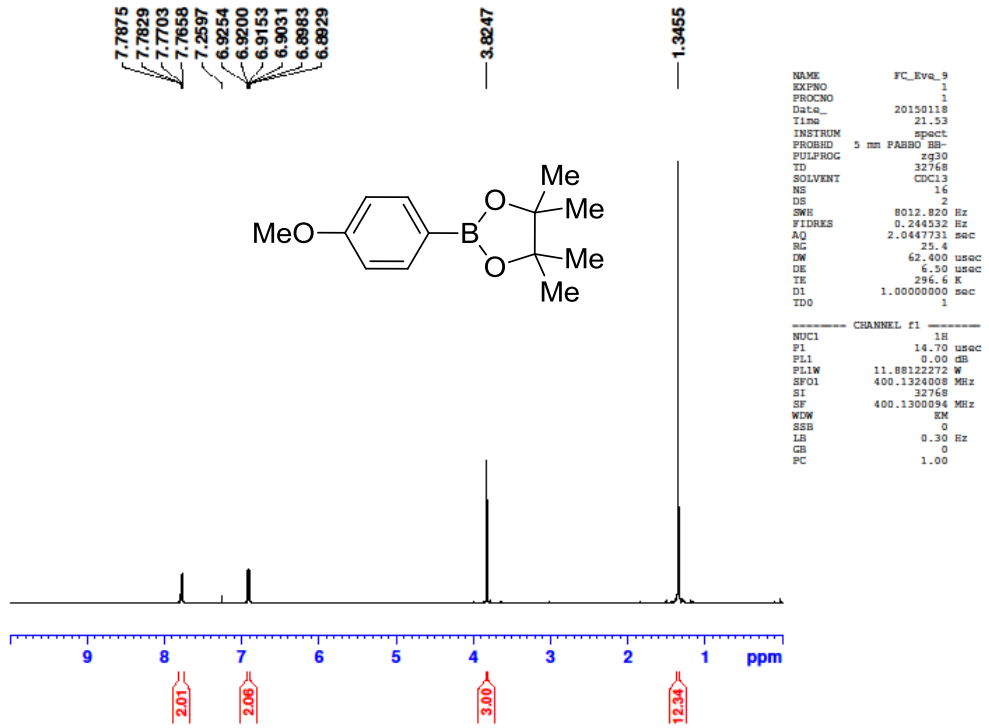
FC_Eve_8C




```
NAME            FC_Eve_8
EXPNO                  2
PROCNO                 1
Date_           20150118
Time                21.49
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                    41
DS                     2
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631988 sec
RG                   203
DW                20.800 usec
DE                 6.50 usec
TE                297.4 K
D1              1.00000000 sec
D11             0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  13C
P1                  9.50 usec
PL1                -2.00 dB
PL1W          58.52175522 W
SFO1          100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                  1H
PCPD2              80.00 usec
PL2                0.00 dB
PL12              15.00 dB
PL13              15.00 dB
PL2W          11.88122272 W
PL12W          0.37571725 W
PL13W          0.37571725 W
SFO2          400.1316005 MHz
SI                 32768
SF            100.6127773 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
```

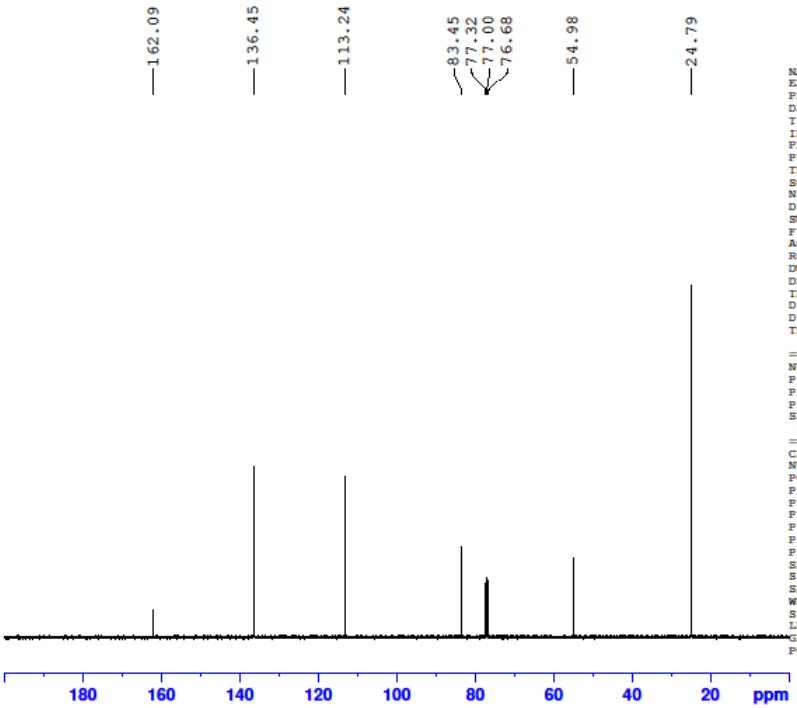
2-(4-Methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Table 7.3, Entry 6)

FC_Eve_9H



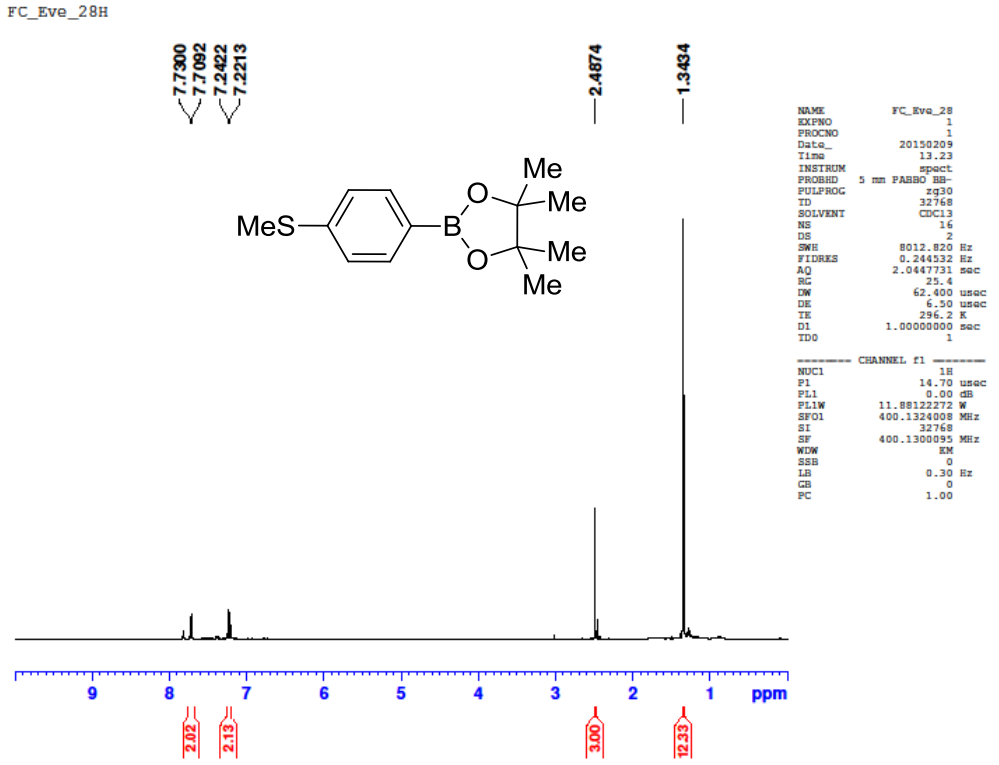

```
NAME            FC_Eve_9
EXPNO                  1
PROCNO                 1
Date_           20150118
Time                21.53
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ              2.0447731 sec
RG                  25.4
DW                62.400 usec
DE                 6.50 usec
TE                296.6 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 14.70 usec
PL1                0.00 dB
PL1W          11.88122272 W
SFO1          400.1324008 MHz
SI                 32768
SF            400.1300094 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

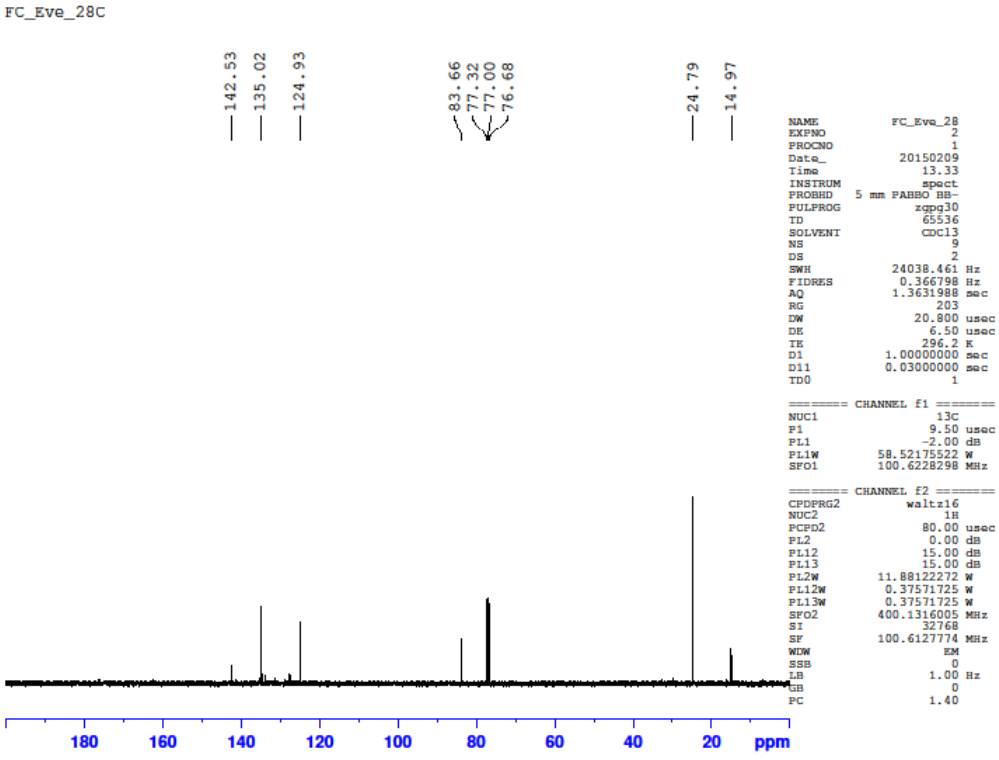
FC_Eve_9C



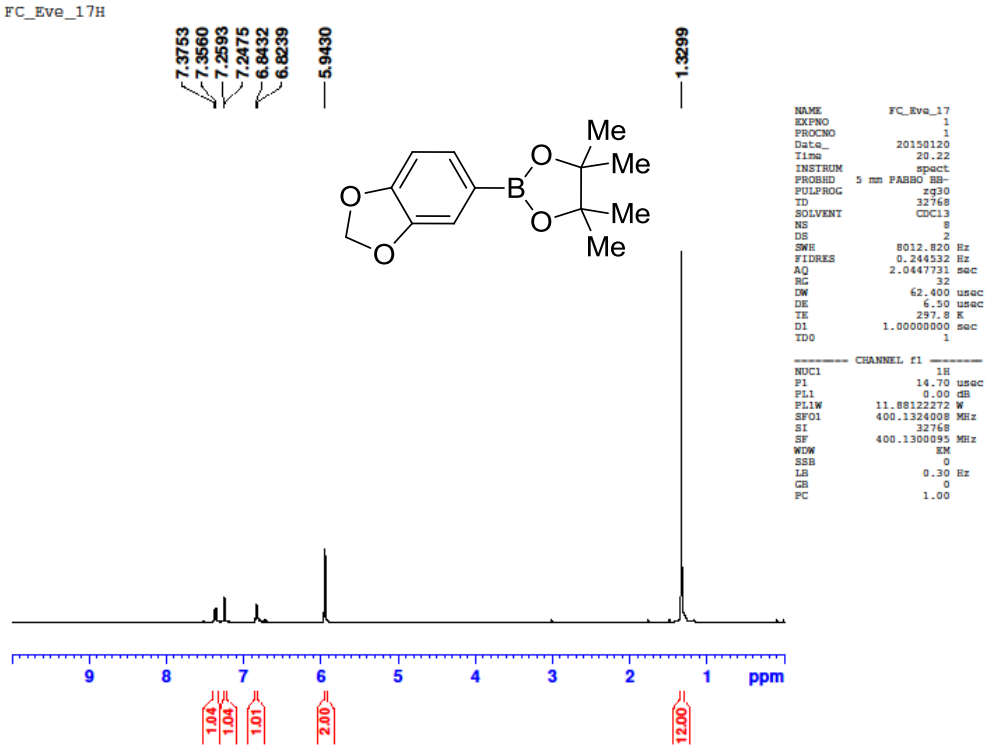

```
NAME            FC_Eve_9
EXPNO                  2
PROCNO                 1
Date_           20150118
Time                21.55
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                    33
DS                     2
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631988 sec
RG                   203
DW                20.800 usec
DE                 6.50 usec
TE                297.4 K
D1             1.00000000 sec
D11            0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  13C
P1                  9.50 usec
PL1                -2.00 dB
PL1W          58.52175522 W
SFO1          100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2              80.00 usec
PL2                 0.00 dB
PL12               15.00 dB
PL13               15.00 dB
PL2W          11.88122272 W
PL12W          0.37571725 W
PL13W          0.37571725 W
SFO2          400.1316005 MHz
SI                 32768
SF            100.6127781 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
```

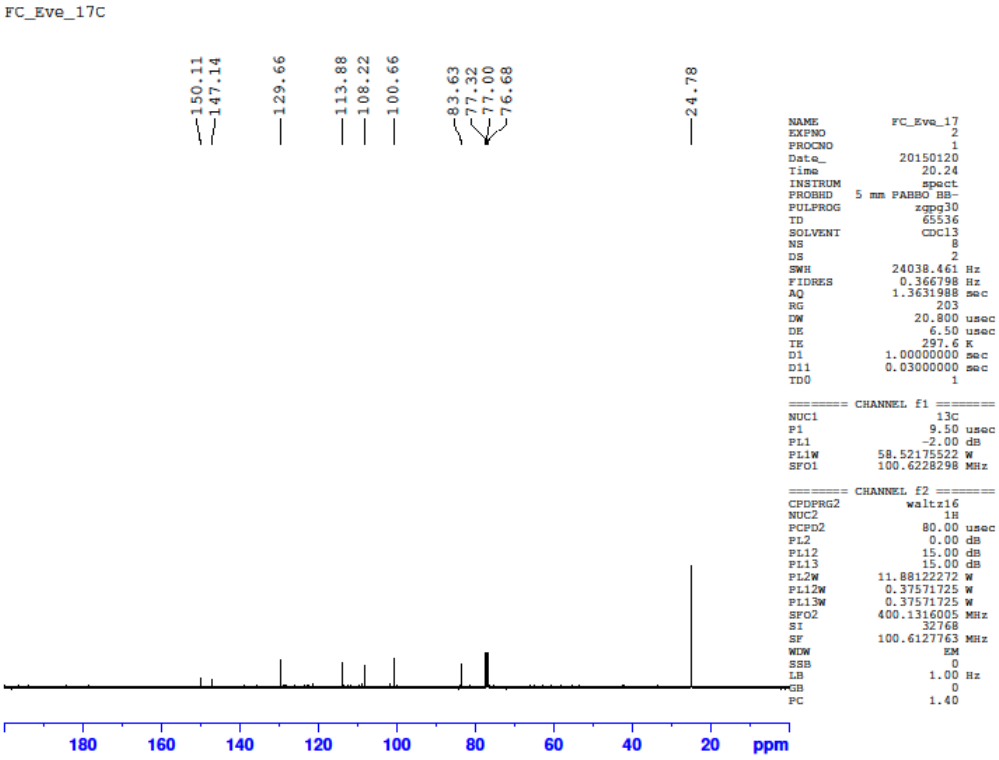
4,4,5,5-Tetramethyl-2-(4-(methylthio)phenyl)-1,3,2-dioxaborolane (Table 7.3, Entry 7)



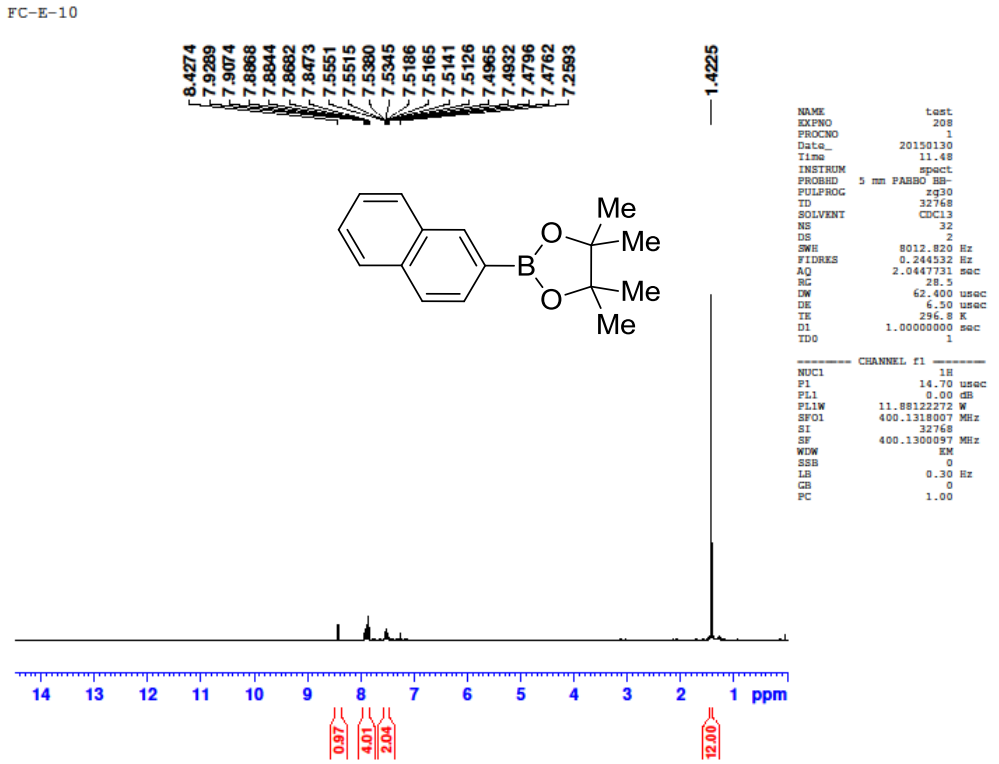


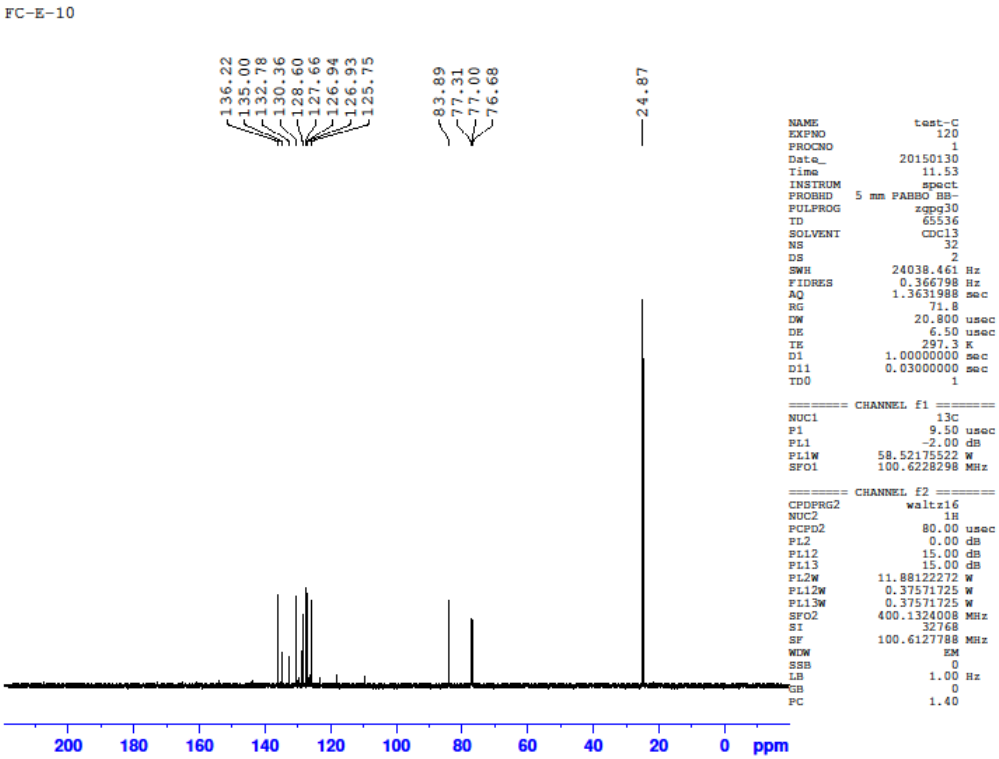
2-(Benzo[d][1,3]dioxol-5-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Table 7.3, Entry 8)





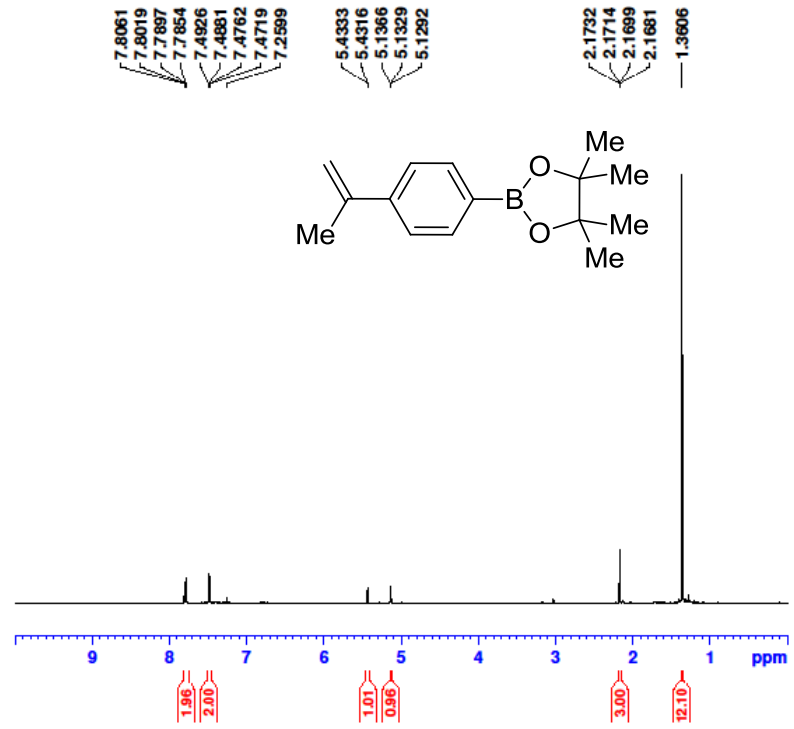
4,4,5,5-Tetramethyl-2-(naphthalen-2-yl)-1,3,2-dioxaborolane (Table 7.3, Entry 9)





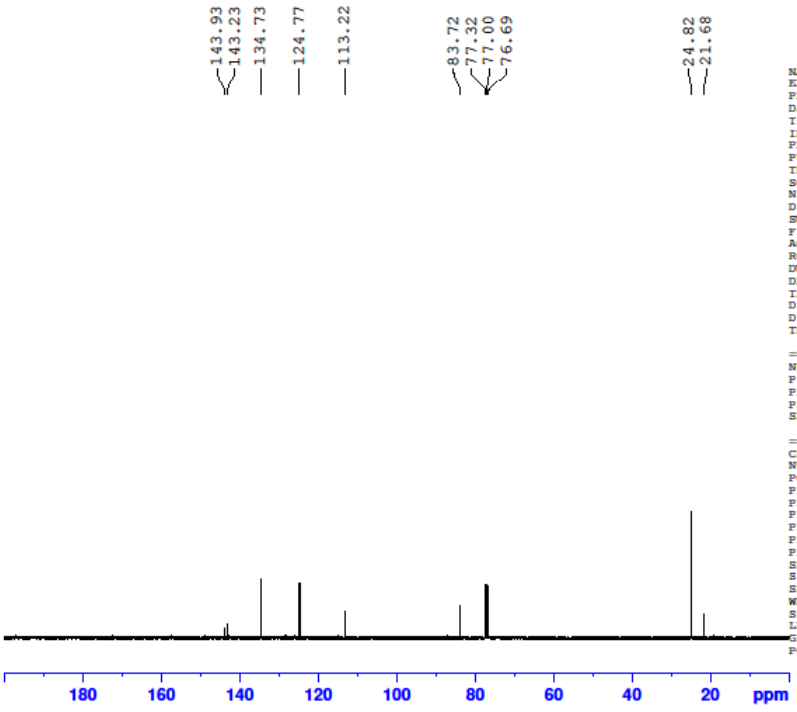
4,4,5,5-Tetramethyl-2-(4-(prop-1-en-2-yl)phenyl)-1,3,2-dioxaborolane (Table 7.3, Entry 10)

FC_Eve_34H




```
NAME            FC_Eve_34
EXPNO                   1
PROCNO                  1
Date_            20150204
Time                15.46
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                  32768
SOLVENT             CDCl3
NS                     16
DS                      2
SWH              8012.820 Hz
FIDRES           0.244532 Hz
AQ               2.0447731 sec
RG                   28.5
DW                62.400 usec
DE                 6.50 usec
TE                296.3 K
D1               1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                 14.70 usec
PL1                 0.00 dB
PL1W           11.88122272 W
SFO1           400.1324008 MHz
SI                  32768
SF             400.1300096 MHz
WDW                    EM
SSB                     0
LB                 0.30 Hz
GB                      0
PC                 1.00
```

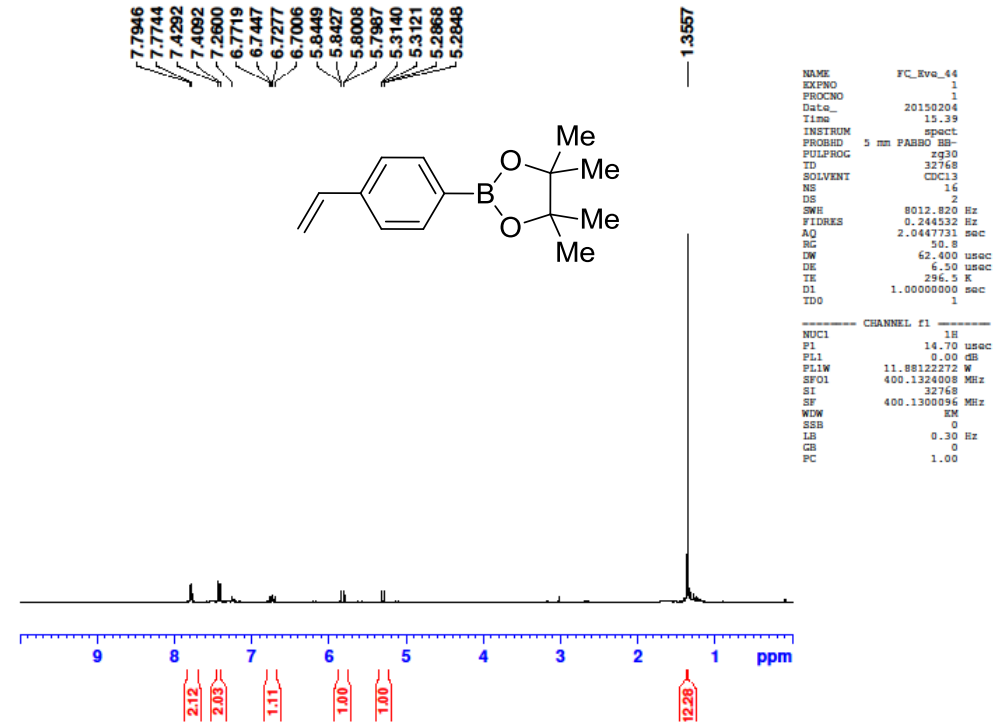
FC_Eve_34C




```
NAME            FC_Eve_34
EXPNO                   2
PROCNO                  1
Date_            20150204
Time                15.46
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                  65536
SOLVENT             CDCl3
NS                     15
DS                      2
SWH              24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                    203
DW                20.800 usec
DE                 6.50 usec
TE                296.6 K
D1               1.00000000 sec
D11              0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   13C
P1                  9.50 usec
PL1                -2.00 dB
PL1W           58.52175522 W
SFO1           100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                   1H
PCPD2              80.00 usec
PL2                 0.00 dB
PL12               15.00 dB
PL13               15.00 dB
PL2W           11.88122272 W
PL12W           0.37571725 W
PL13W           0.37571725 W
SFO2           400.1316005 MHz
SI                  32768
SF             100.6127751 MHz
WDW                    EM
SSB                     0
LB                 1.00 Hz
GB                      0
PC                 1.40
```

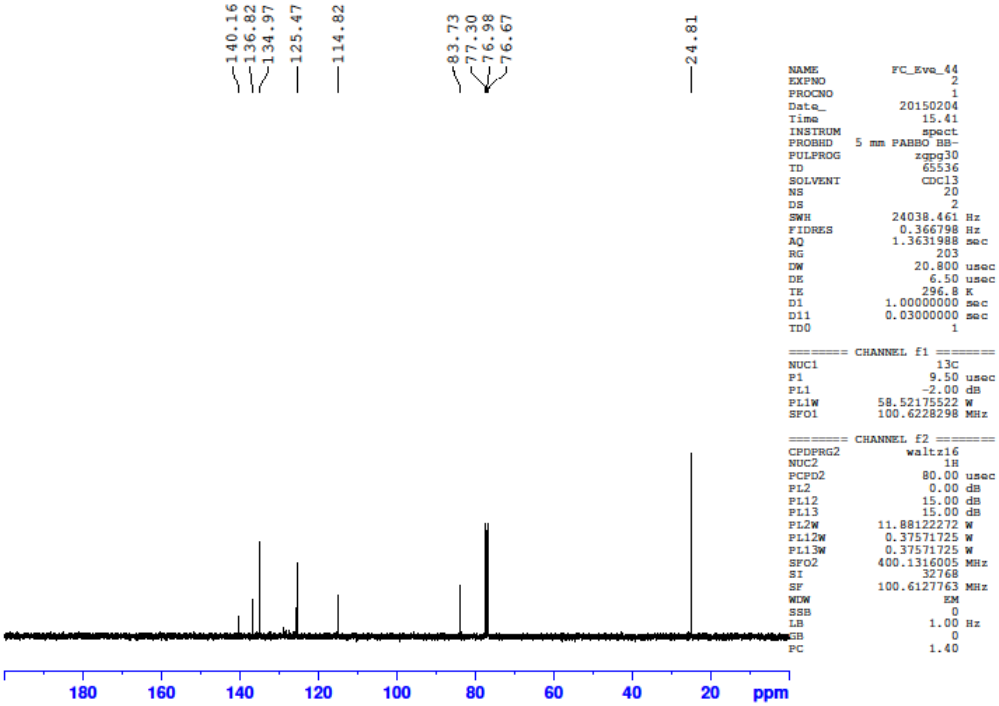
4,4,5,5-Tetramethyl-2-(4-vinylphenyl)-1,3,2-dioxaborolane (Table 7.3, Entry 11)

FC_Eve_44H




```
NAME            FC_Eve_44
EXPNO                   1
PROCNO                  1
Date_            20150204
Time                15.39
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  32768
SOLVENT             CDCl3
NS                     16
DS                      2
SWH              8012.820 Hz
FIDRES           0.244532 Hz
AQ               2.0447731 sec
RG                   50.8
DW                62.400 usec
DE                 6.50 usec
TE                296.5 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                 14.70 usec
PL1                0.00 dB
PL1W           11.88122272 W
SFO1           400.1324008 MHz
SI                  32768
SF             400.1300096 MHz
WDW                    EM
SSB                     0
LB                 0.30 Hz
GB                      0
PC                 1.00
```

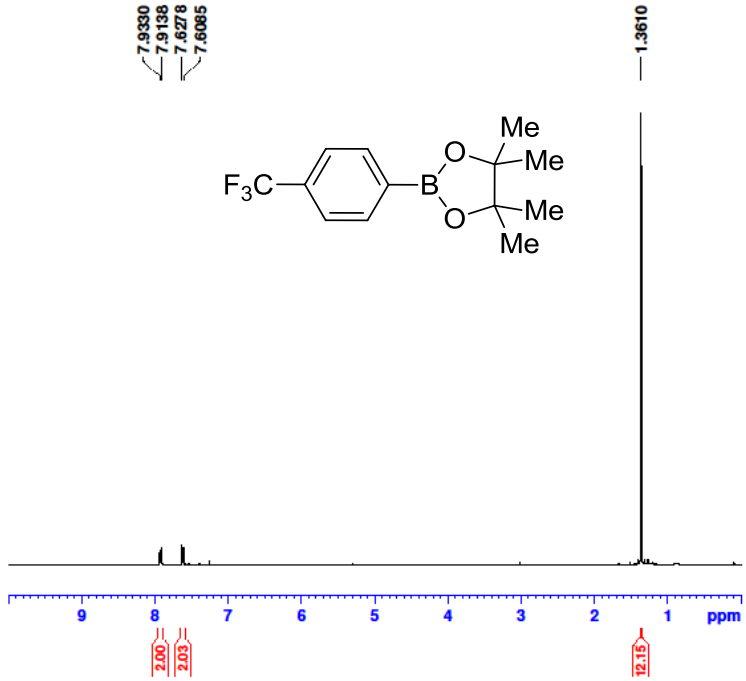
FC_Eve_44C




```
NAME            FC_Eve_44
EXPNO                   2
PROCNO                  1
Date_            20150204
Time                15.41
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                  65536
SOLVENT             CDCl3
NS                     20
DS                      2
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                    203
DW                20.800 usec
DE                 6.50 usec
TE                296.8 K
D1             1.00000000 sec
D11            0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   13C
P1                 9.50 usec
PL1               -2.00 dB
PL1W           58.52175522 W
SFO1           100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2            waltz16
NUC2                   1H
PCPD2             80.00 usec
PL2                0.00 dB
PL12              15.00 dB
PL13              15.00 dB
PL2W           11.88122272 W
PL12W           0.37571725 W
PL13W           0.37571725 W
SFO2           400.1316005 MHz
SI                  32768
SF             100.6127763 MHz
WDW                    EM
SSB                     0
LB                 1.00 Hz
GB                      0
PC                 1.40
```

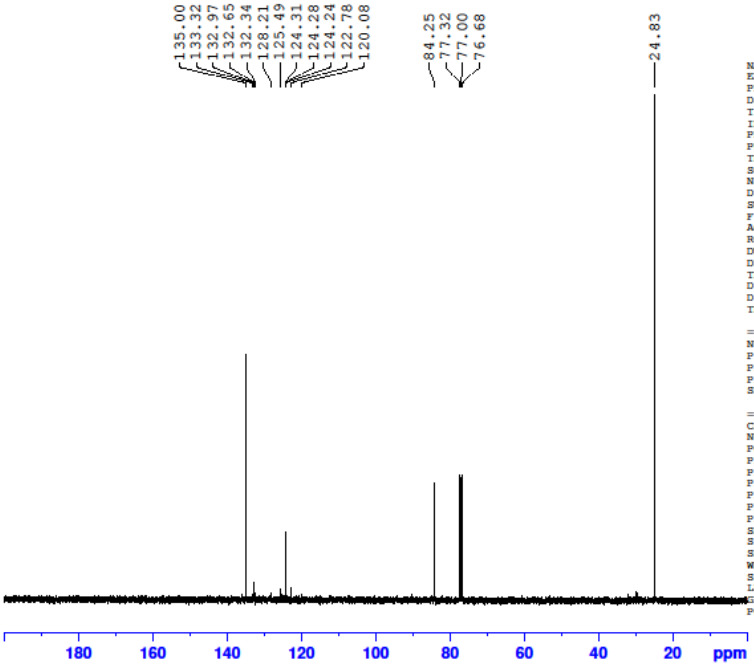
4,4,5,5-Tetramethyl-2-(4-(trifluoromethyl)phenyl)-1,3,2-dioxaborolane (Table 7.4, Entry 1 and 2)

FC_Eve_56H



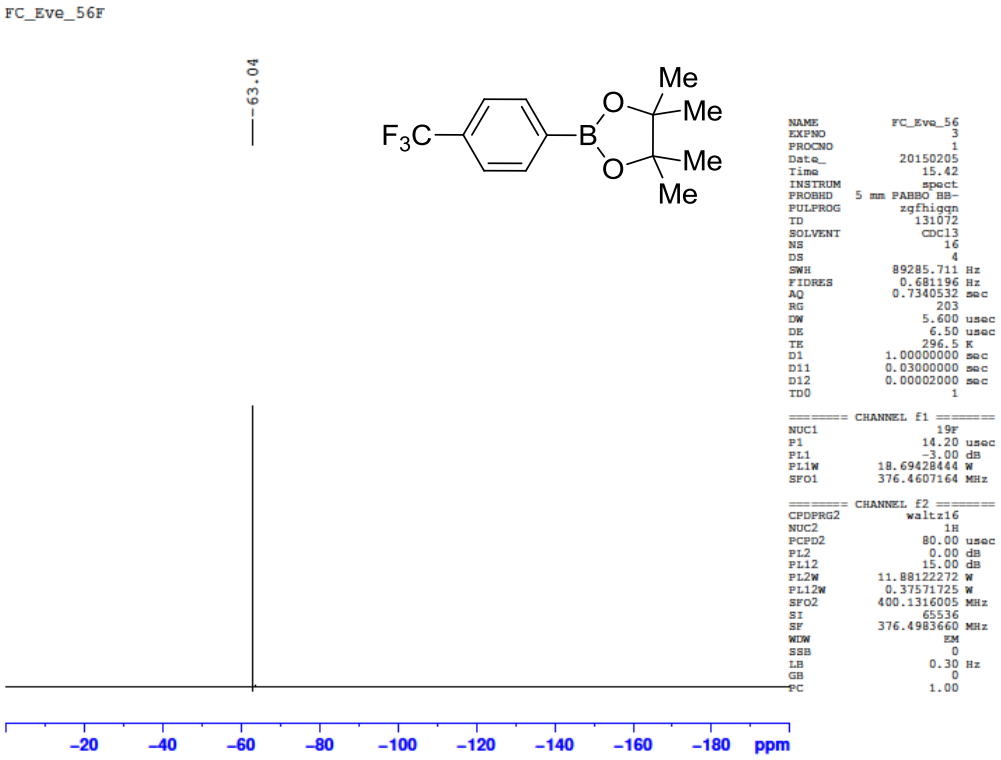
NAME	FC_Eve_56
EXPNO	1
PROCNO	1
Date_	20150205
Time	15.37
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	16
DS	2
SWH	8012.820 Hz
FIDRES	0.244532 Hz
AQ	2.0447731 sec
RG	36
DW	62.400 usec
DE	6.50 usec
TE	296.4 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	14.70 usec
PL1	0.00 dB
PL1W	11.88122272 W
SFO1	400.1324008 MHz
SI	32768
SF	400.1300091 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

FC_Eve_56C

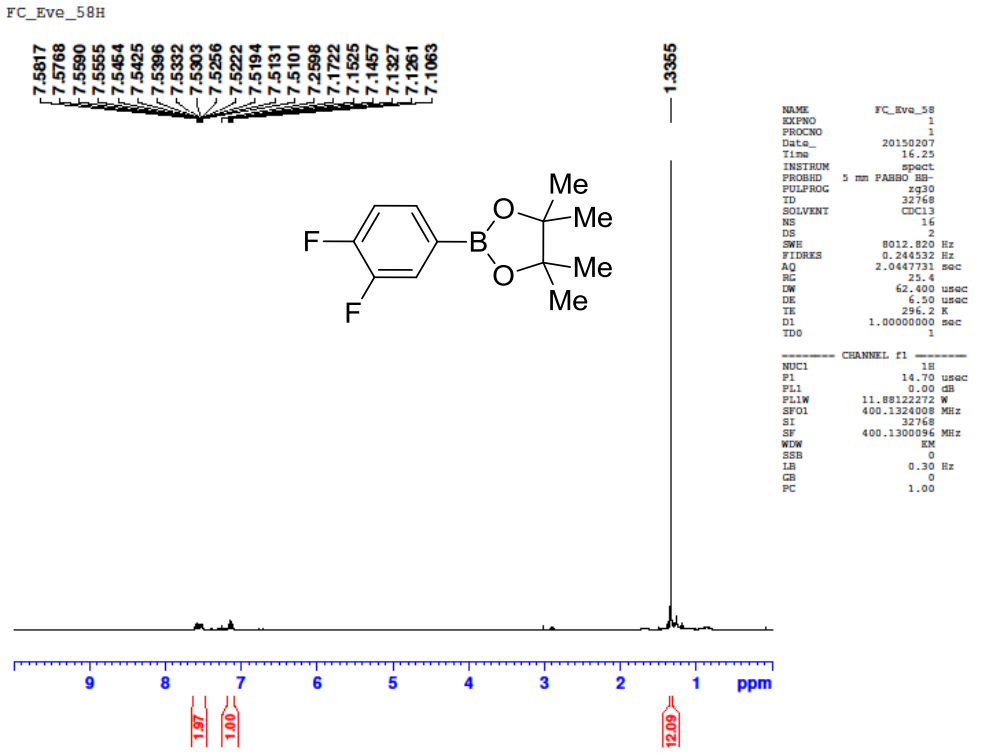


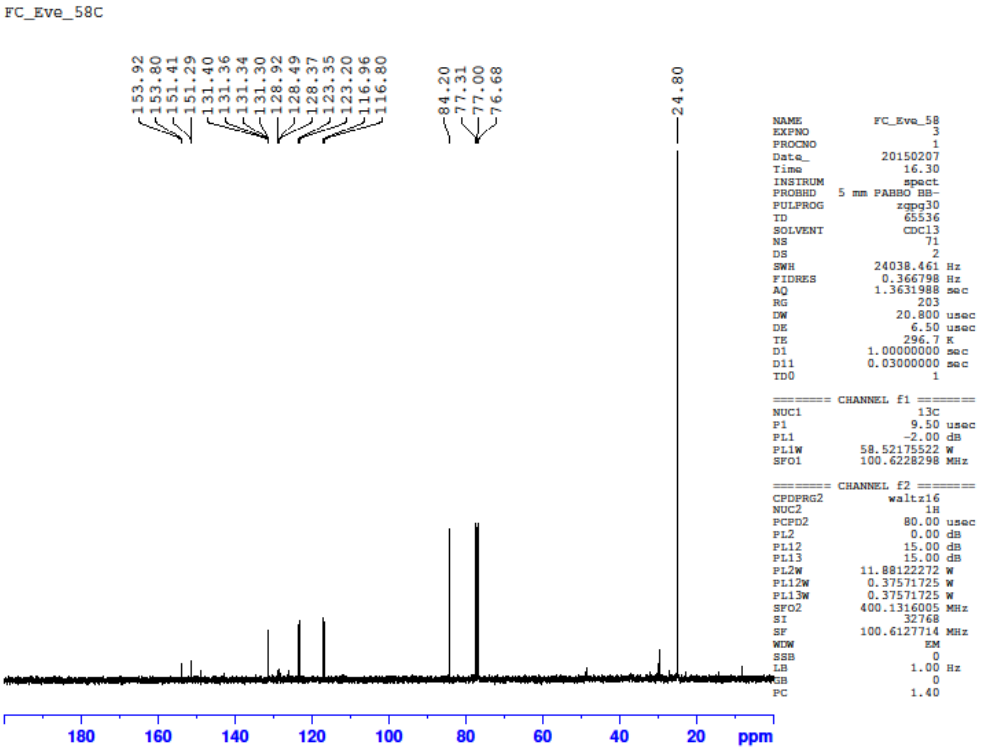
NAME	FC_Eve_56
EXPNO	2
PROCNO	1
Date_	20150205
Time	15.39
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	25
DS	2
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	297.0 K
D1	1.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.50 usec
PL1	-2.00 dB
PL1W	58.52175522 W
SFO1	100.6228298 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	0.00 dB
PL12	15.00 dB
PL13	15.00 dB
PL2W	11.88122272 W
PL12W	0.37571725 W
PL13W	0.37571725 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127702 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

4,4,5,5-Tetramethyl-2-(4-(trifluoromethyl)phenyl)-1,3,2-dioxaborolane (Table 7.4, Entry 1 and 2)

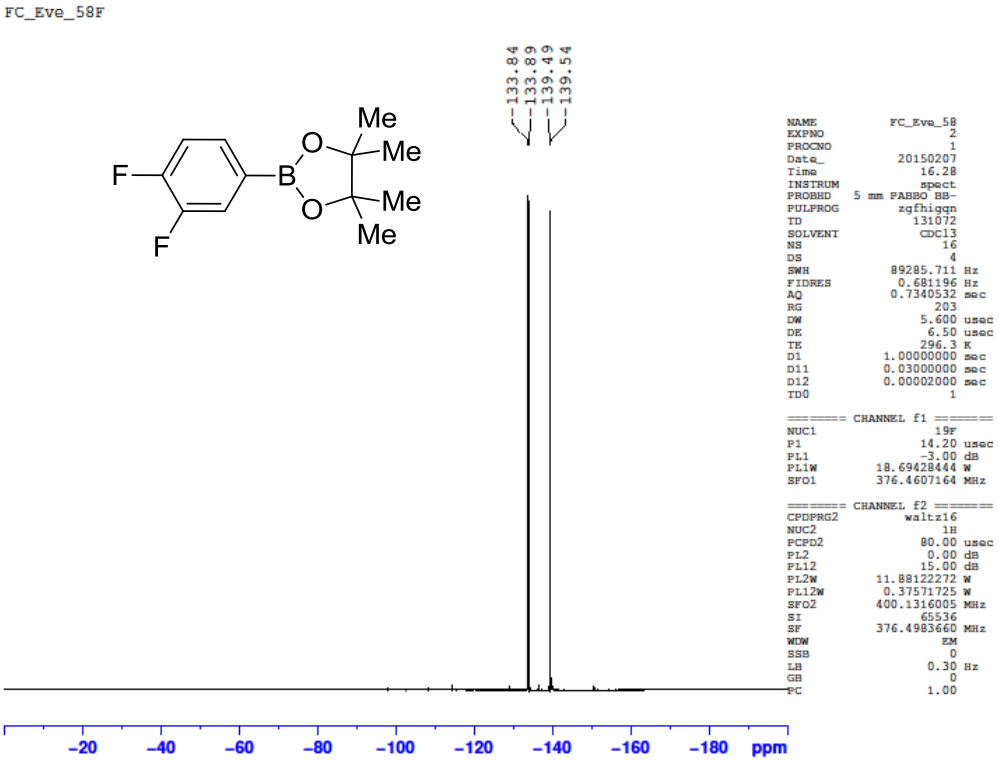


2-(3,4-Difluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Table 7.4, Entry 3)



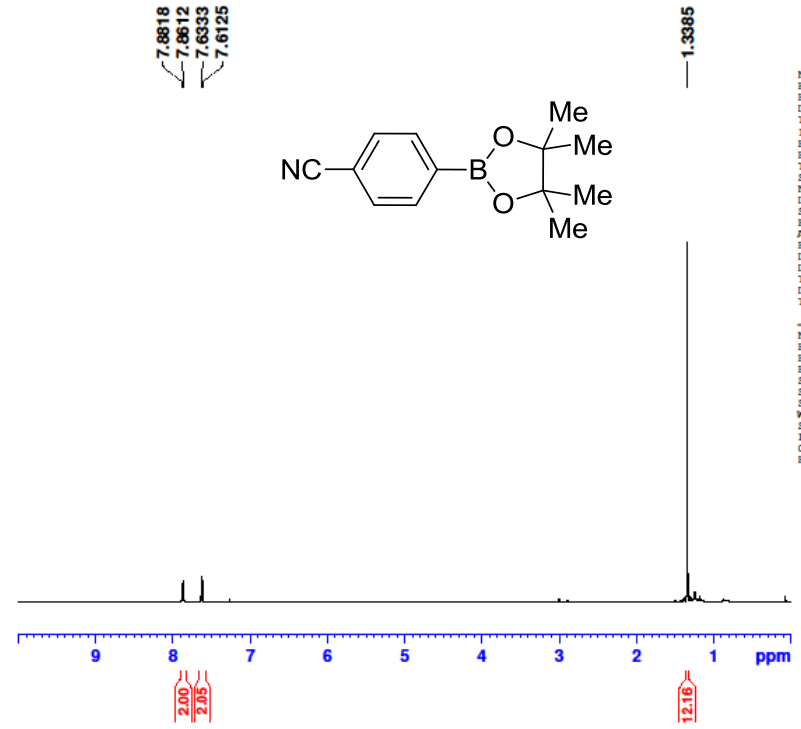


2-(3,4-Difluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Table 7.4, Entry 3)



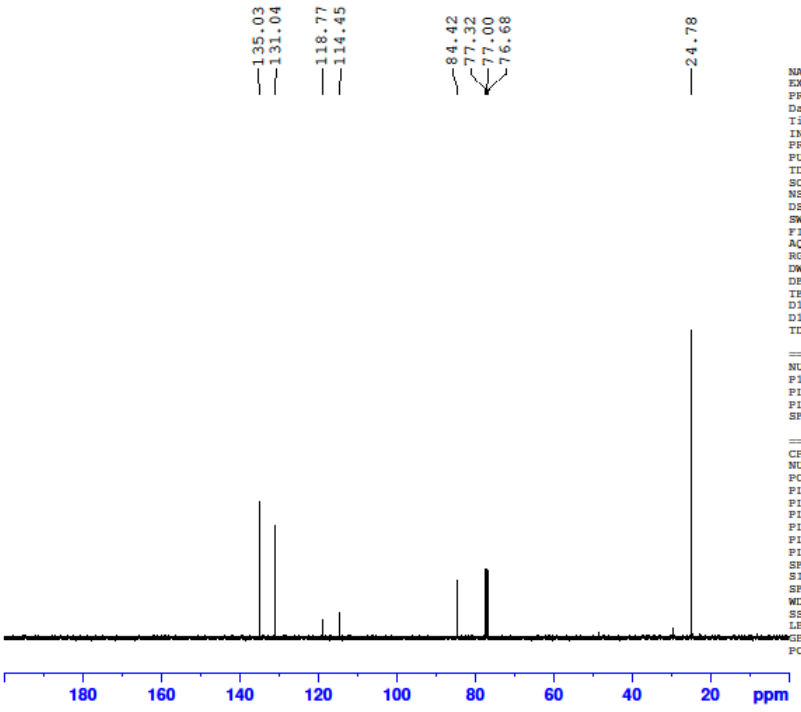
4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (Table 7.4, Entry 4 and 5)

FC_Eve_62H



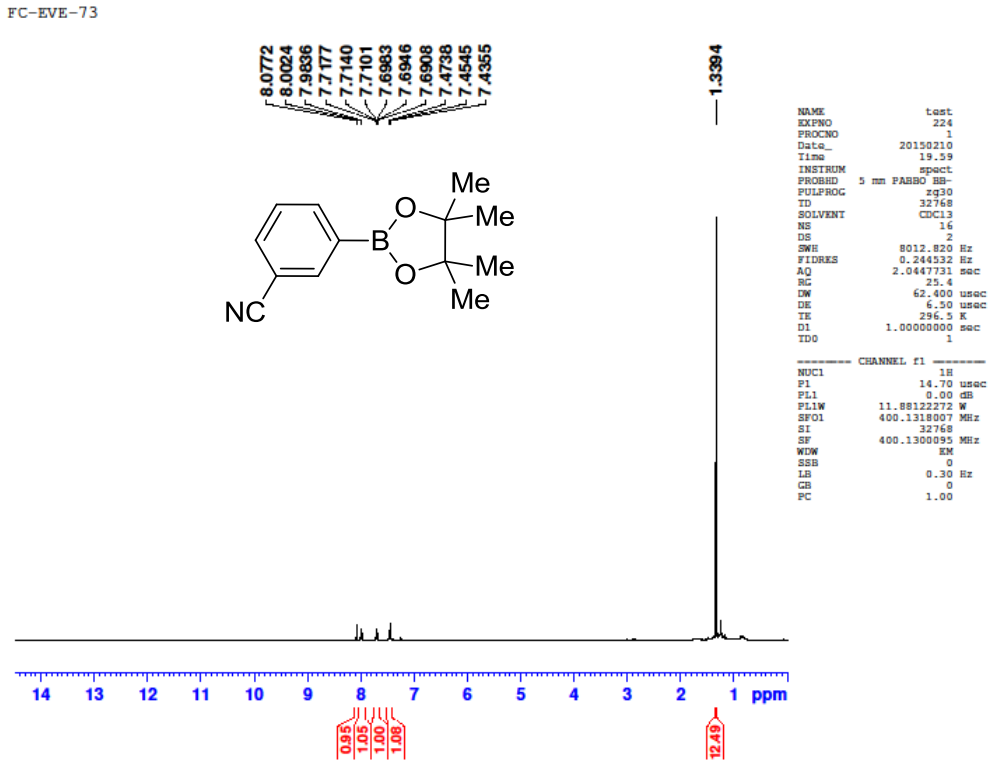

```
NAME            FC_Eve_62
EXPNO                   1
PROCNO                  1
Date_            20150207
Time                16.40
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                  32768
SOLVENT             CDCl3
NS                     12
DS                      2
SWH              8012.820 Hz
FIDRES           0.244532 Hz
AQ               2.0447731 sec
RG                   25.4
DW                62.400 usec
DE                 6.50 usec
TE                296.4 K
D1               1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                 14.70 usec
PL1                 0.00 dB
PL1W           11.88122272 W
SFO1           400.1324008 MHz
SI                  32768
SF             400.1300096 MHz
WDW                    EM
SSB                     0
LB                 0.30 Hz
GB                      0
PC                 1.00
```

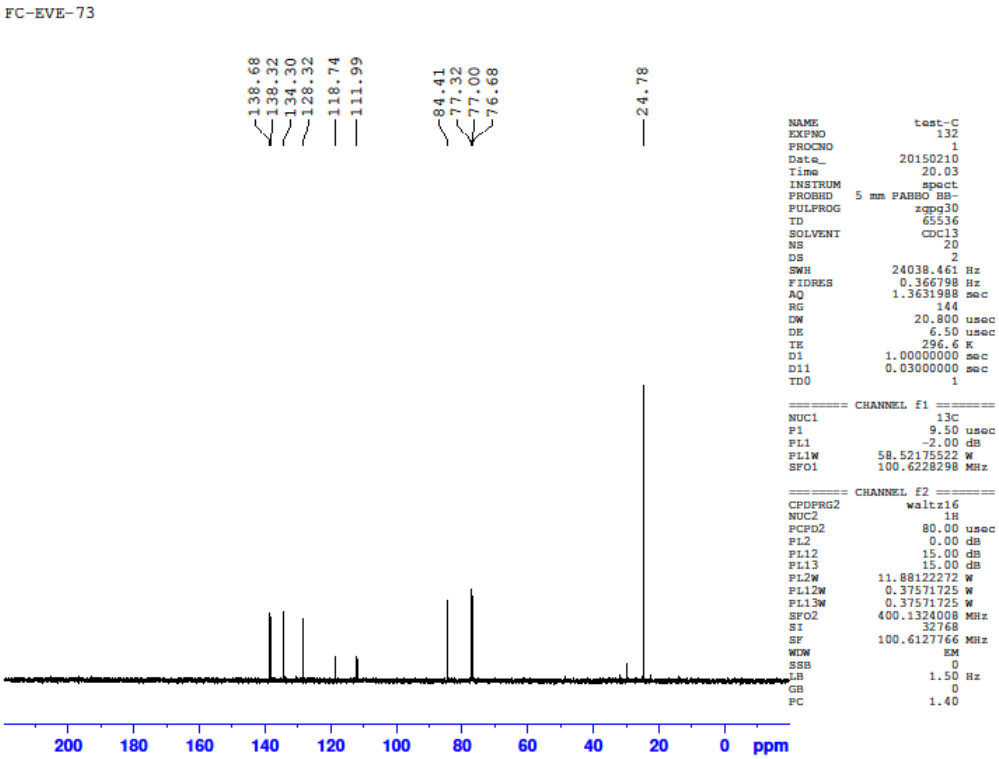
FC_Eve_62C



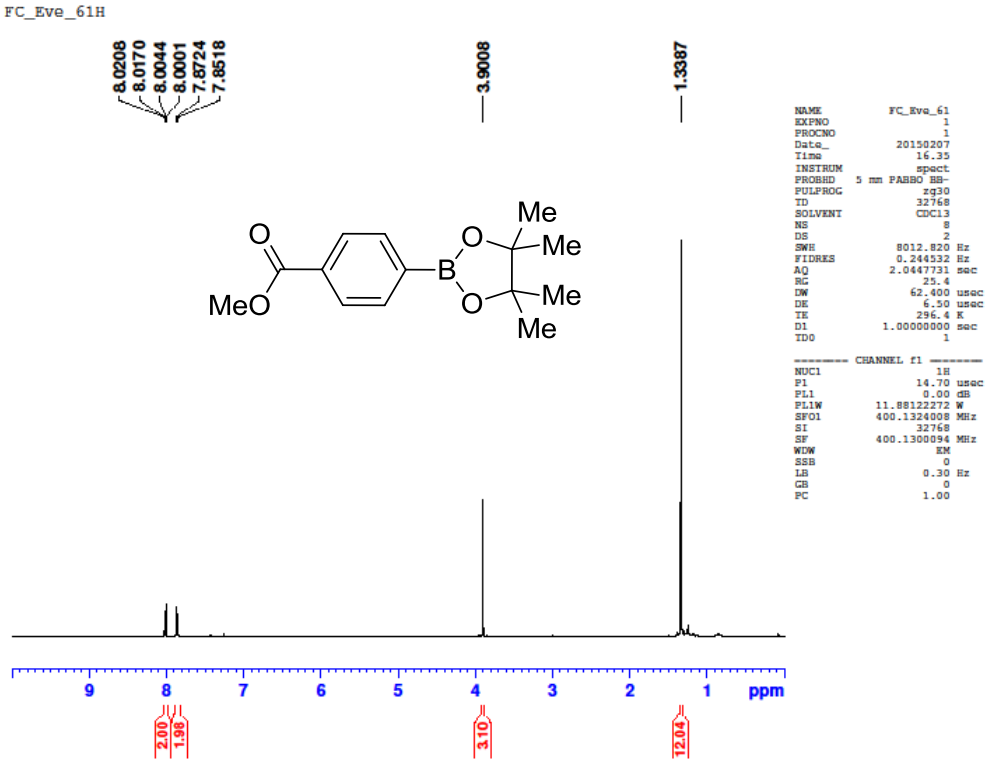

```
NAME            FC_Eve_62
EXPNO                   2
PROCNO                  1
Date_            20150207
Time                16.42
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                  65536
SOLVENT             CDCl3
NS                     22
DS                      2
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                    203
DW                20.800 usec
DE                 6.50 usec
TE                296.9 K
D1               1.00000000 sec
D11              0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   13C
P1                  9.50 usec
PL1                -2.00 dB
PL1W           58.52175522 W
SFO1           100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                   1H
PCPD2              80.00 usec
PL2                 0.00 dB
PL12               15.00 dB
PL13               15.00 dB
PL2W           11.88122272 W
PL12W           0.37571725 W
PL13W           0.37571725 W
SFO2           400.1316005 MHz
SI                  32768
SF             100.6127768 MHz
WDW                    EM
SSB                     0
LB                 1.00 Hz
GB                      0
PC                 1.40
```

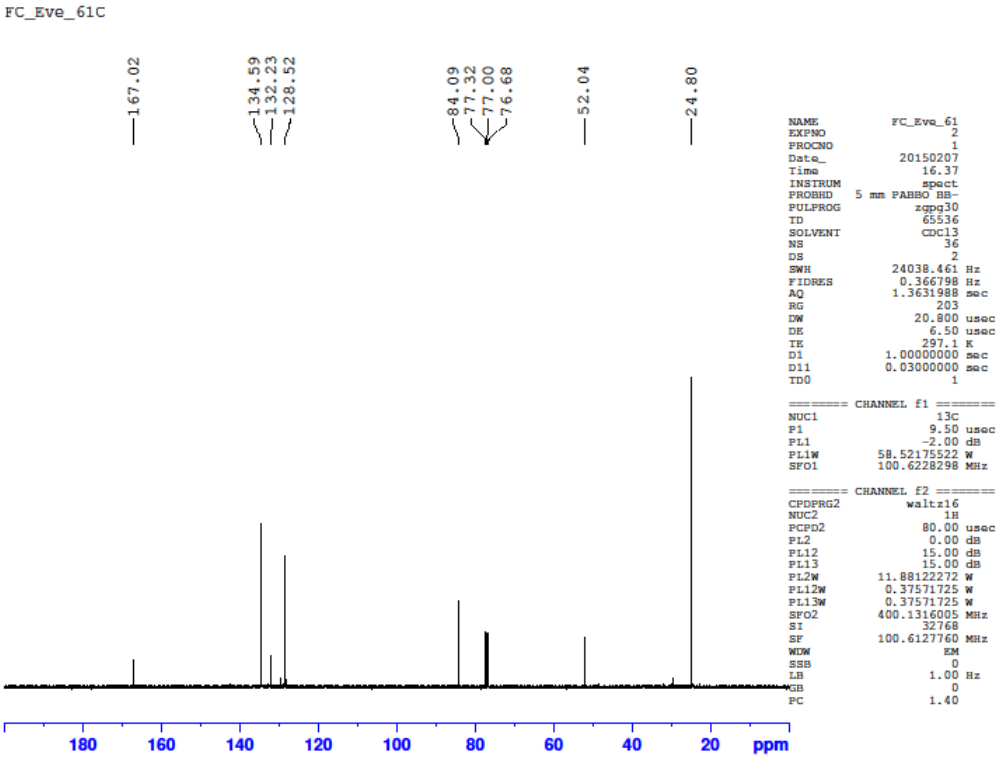
3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (Table 7.4, Entry 6)



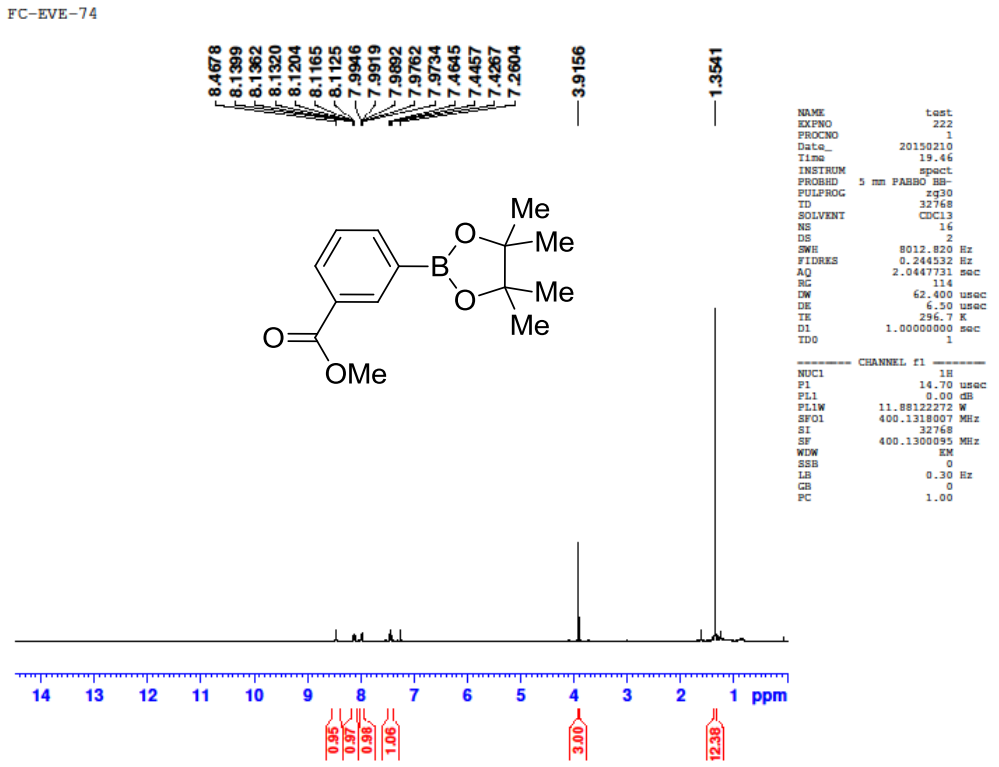


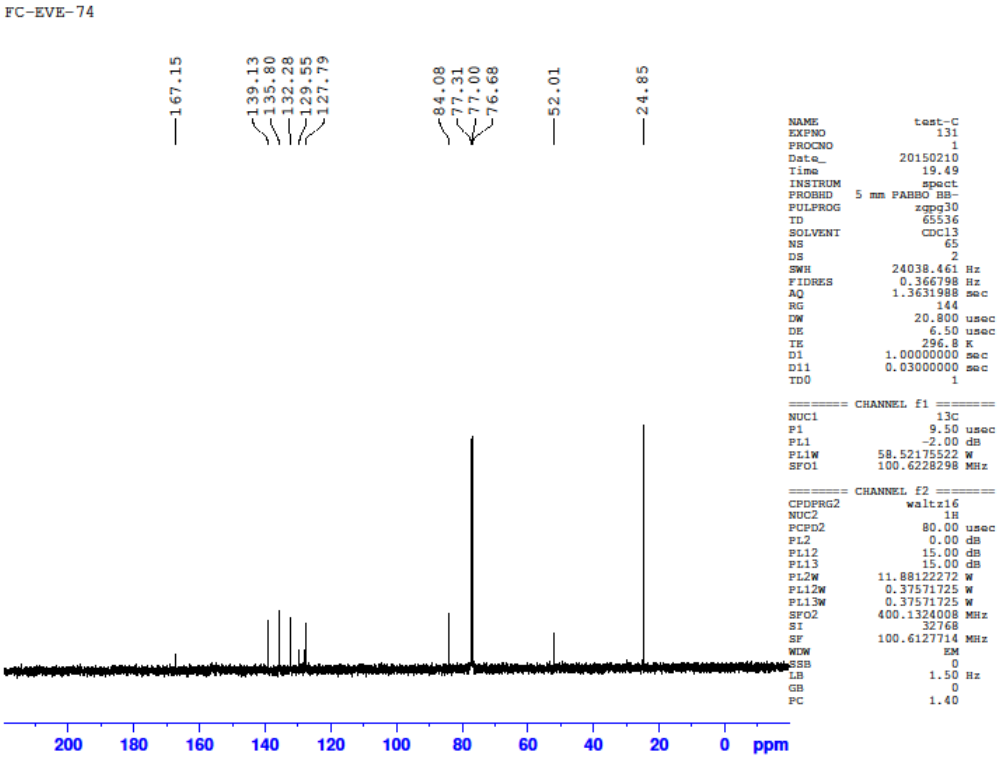
Methyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (Table 7.4, Entry 7)



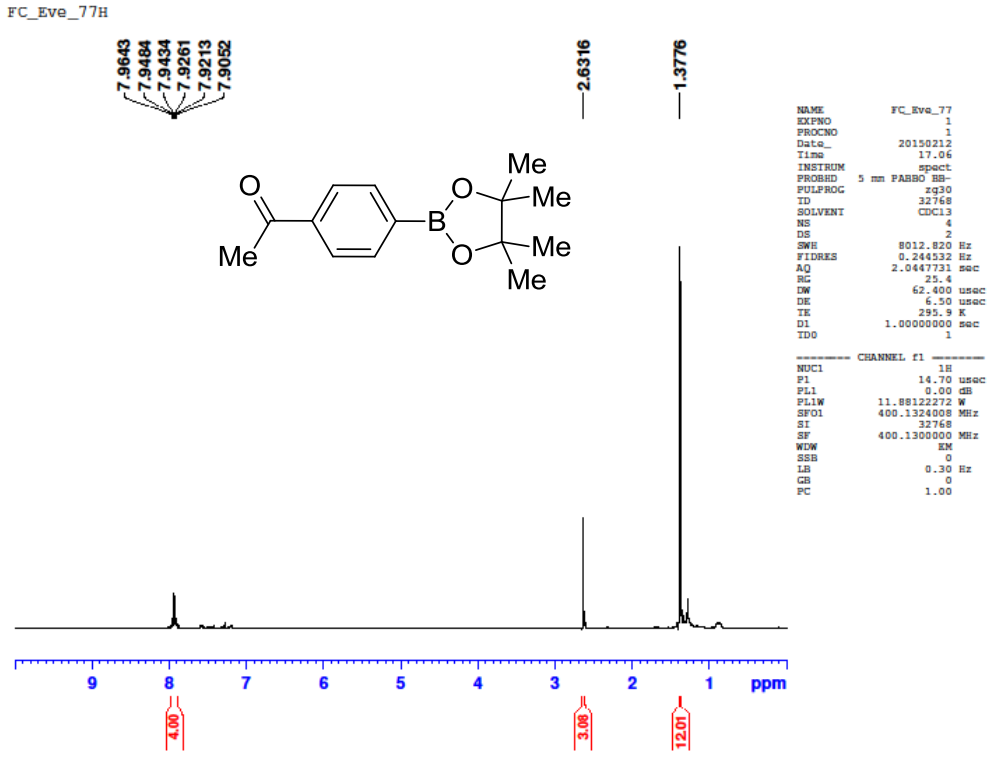


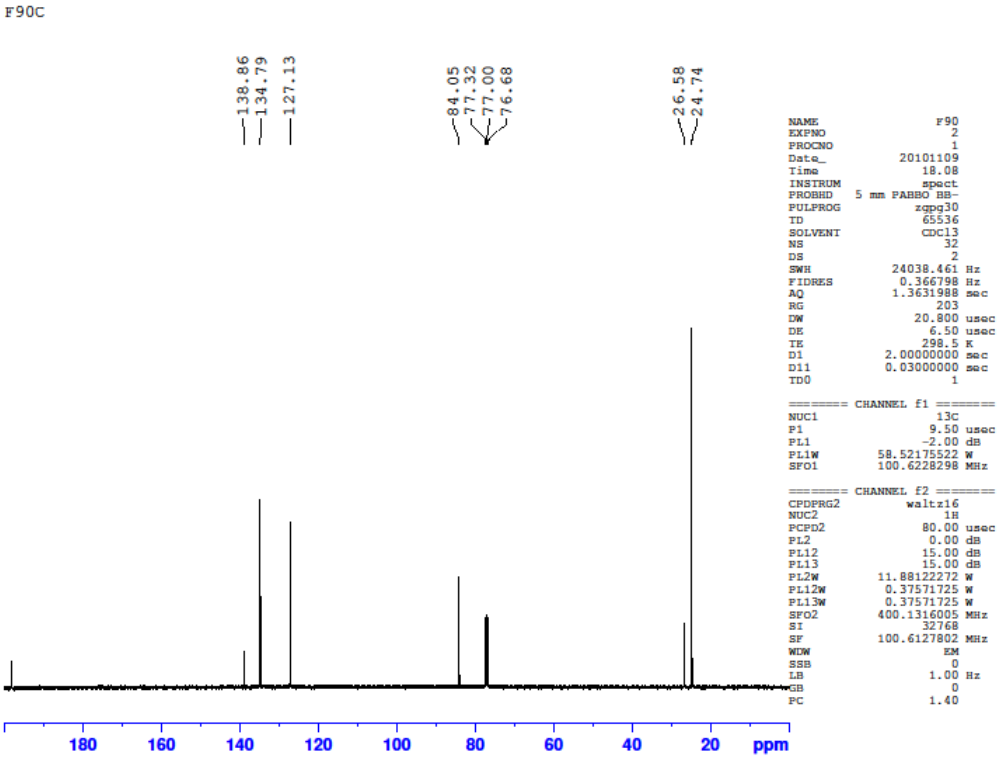
Methyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (Table 7.4, Entry 8)





1-(4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethan-1-one (Table 7.4, Entry 9 and 10)





1-(3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethan-1-one (Table 7.4, Entry 11)