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The Hong Kong Polytechnic University

Department of Applied Biology and

Chemical Technology

Exploration of a new face of catalysts in general C-C and C-N bond-construction processes

Chung Kin Ho

A Thesis Submitted in Partial Fulfillment of the

Requirements for the Degree of Master of Philosophy

June 2011

Certification of originality

I hereby declare that this thesis is my own research work carried out since my registration at The Hong Kong Polytechnic University for the degree of Master of Philosophy in September, 2009, and that, to the best of my knowledge and belief, it reproduces no material previously published or neither written, nor material that has been accepted for the award of any other degree or diploma, except where due acknowledgement has been made in the text.

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Chung Kin Ho

June, 2011

Abstract

"Exploration of a new face of catalysts in general C-C and C-N bond-construction processes"

Submitted by Chung Kin Ho

For the Degree of Master of Philosophy

At The Hong Kong Polytechnic University in June, 2011

Palladium-catalyzed amination is a powerful tool for synthesizing nitrogen containing compounds in material science, pharmaceuticals as well as organic synthesis. Our research group reported a palladium-catalyzed amination of aryl mesylate in 2008. The substrate scope expanding to aryl tosylates has been attempted. An efficient method for synthesis of amines via palladium-catalyzed amination of aryl tosylates with amines is hereby reported. The investigations on the effect of solvents and bases in palladium catalyzed amination of aryl tosylate will be described and the experimental results on substrate scopes will be discussed. Current study shows that a great diversity of aryl tosylates and amines can be used for C-N bond formation. The reaction conditions are not only restricted to the organic solvents used, solvent-free conditions and aqueous

medium can also be accomplished. Good to excellent yields of the desired products can be achieved.

The next part of my research study is the development of a new class of phosphine ligand for general carbon-carbon and carbon-nitrogen bond formation reactions. The preliminary results showed that the phenyl imidazolidinyl backbone ligands were less effective for catalytic reaction. Thus, we modified the ligand scaffold to phenyl benzimidazolyl backbone. It can be easily synthesized from inexpensive and commercial available materials. Hemilabile phenyl benzimidazolyl ligand is an effective ligand for catalytic synthesis. The scope of aryl chlorides and amines via palladium-catalyzed amination utilizing benzimidazolyl ligand is described. Primary and secondary aromatic/aliphatic amines are effective substrates in this catalytic system. Functional group such as keto and esters are also compatible in this system. Good to excellent yields of the desired products can be achieved. Catalyst loading down to 0.1 mol% Pd can also be accomplished.

Publications

Chung, K. H.; So, C. M.; Wong, S. M.; Luk. C. H.; Zhou, Z.; Lau, C. P.; Kwong, F. Y. *Chemical Communications* DOI: 10.1039/c2cc15972d.

Yeung, P. Y.; Chung, K. H.; Kwong, F. Y. *Organic Letters* **2011**, *13*, 2912.

Wong, P. Y.; Chow, W. K.; Chung, K. H.; So, C. M.; Lau, C. P.; Kwong, F. Y. *Chemical. Communications* **2011**, *47*, 8328.

Liu, W.; Cao, H.; Zhang, H.; Zhang, H.; Chung, K. H.; He, C.; Wang, H.; Kwong, F. Y.; Lei, A. *Journal of the American Chemical Society* **2010**, *132*, 16737.

Chung, K. H.; So, C. M.; Kwong, F. Y. Palladium-Catalyzed Amination of Aryl Tosylate. Manuscript in preparation.

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Abbreviation

%	percentage
℃	degree of Celsius
1-Ad	1-adamantyl
acac	acetylacetnate
Ar	Aryl
BINAP	2,2’-bis(diphenylphosphanyl)-1,1’-binaphthyl
Br	Bromo
Bu	butyl
Cl	Chloro
CMPhos	2-[2-(dicyclohexylphosphino)phenyl]-1-methyl-1H-indole
COD	cyclooctadiene
Cy	cyclohexyl
CyPF-t-Bu	1-(dicyclohexylphosphino)-2-[1-(tert-butylphosphino)ethyl]-Ferrocene
DavePhos	2-Dicyclohexylphosphino-2'-(N,N-dimethylamino)bihenyl

dba	dibenzylideneactone
DME	1,2-dimethoxyethane
dmeda	N,N’-diemthylethylenediamine
DMF	N,N-Dimethylformamide
dppf	1,1’-bis(diphenylphosphino)ferrocene
DtBPF	1,1'-bis(ditertbutylphosphino)ferrocene
ee	enantiomeric excess
Et	ethyl
GC	Gas Chromatography
h	hour(s)
I	iodo
IPA	iso-propyl alcohol,
iPr	iso-propyl
IPr.HCl	1,3-bis(2,6-diisopropylphenyl)imidazolium chloride
JohsPhos	(2-Biphenyl)di-tert-butylphosphine
L	ligand
LiHMDS	Lithium bis(trimethylsilyl)amide
M	metal
Me	methyl

Me-Cy-JohnPhos	2-Dicyclohexylphosphino-2'-methylbiphenyl
Me-DalPhos	2-[di(adamantan-1-yl)phosphino]- N,N-dimethylaniline
Mor-DalPhos	N-[2-(1-diadamantanyl phosphino)phenyl]morpholine
n-BuLi	normal-butyl lithium
OAc	acetate
o-tol	ortho-tolyl, 2-methylphenyl
Pd	Palladium
Ph	phenyl
phen	1,10-phenanthroline
PPF-A	1-(diphenylphosphino)-2- [1-(methylamino)ethyl]-Ferrocene
PPF-OMe	1-(diphenylphosphino)-2-(1-methoxyethyl)-Ferrocene
rt	room temperature
Sn	Tin
tBu	tert-butyl
tBu-Bphos	2-(di-tert-butylphosphino)-N,N-diethylbenzamide
Ts	tosyl, 4-toluenesulfonyl
X	halide

X-Phos	2-Dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl

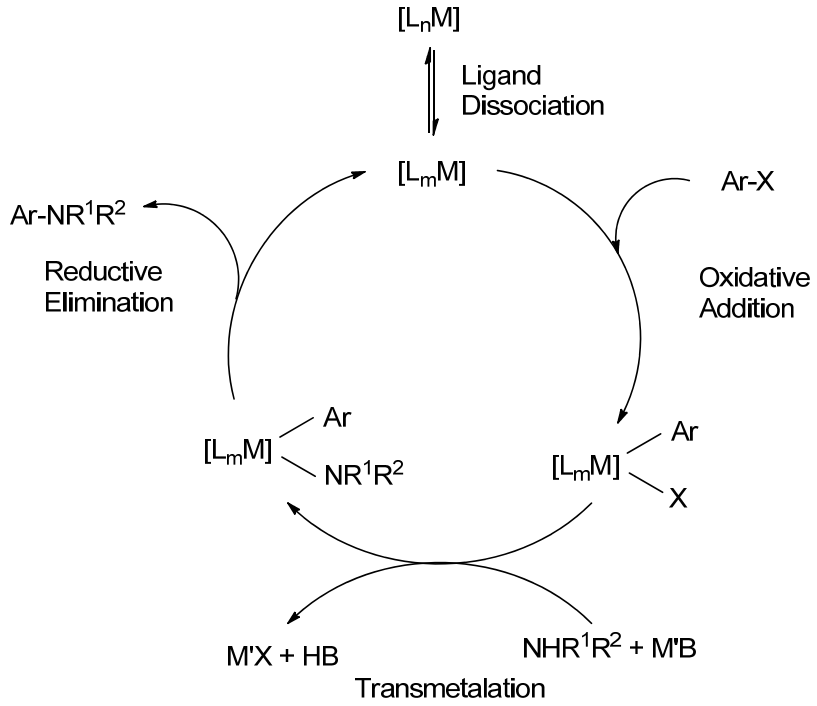
Chapter 1: Introduction

1.1. Buchwld-Hartwig amination

Transition metal-catalyzed reactions are the most powerful tool for the carbon-carbon and carbon-heteroatom bond formations.[1] Among these types of bond formation, we particularly are interested in the carbon-nitrogen bond formation reaction which is also called amination. Amination was firstly reported by Migita and Kosugi in 1983.[2] A number of research groups paid effort to further invent new methodology for these reactions. The most famous reactions are Buchwald-Hartwig reaction and Ullmann-type reaction, which utilized palladium and copper metal complexes, respectively. Carbon-nitrogen bond formation is synthetically attractive and highly versatile in pharmaceuticals, material sciences, and organic synthesis.[1d,3] The *N*-arylated product can be regarded as nucleophilic substitution of amine to aryl halide. Such cross-coupling reaction takes places only in the presence of suitable catalyst.[4] The transition metals currently used for amination are iron[5], copper[4], nickel, and palladium.[6] They play important roles in oxidative addition, transmetalation, as well as reductive elimination reaction. In the following sections, we will discuss

the general mechanism of amination, availability of transition metals in catalysis, substrate scopes, and ligands employed in coupling reactions.

1.2. Mechanism



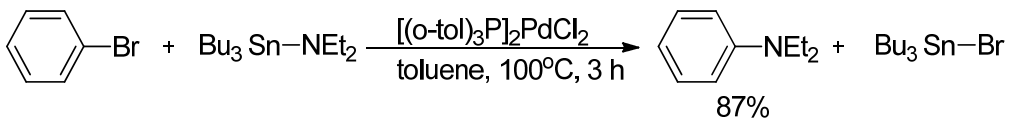
A current mechanism of amination was proposed in detail by Hartwig, Blackmond, and Buchwald in 2006.[1a,6-7] It uses aryl halides and amines in the present of palladium-BINAP. The catalytic cycle involves three steps which include oxidative addition of aryl halide, transmetalation of halide and amine, and reductive elimination of desired product. Ligand dissociation from catalyst precursor ($[L_nM]$) which generates vacant site for oxidative addition. The active catalyst ($[L_mM]$) is oxidized by donating two electrons to aryl halide bond. A

base (M'B) eliminates halide and proton from amine (NHR^1R^2), then deprotonated amine coordinates to metal complex. Finally, the Ar and NR^1R^2 moieties from metal complex undergo reductive elimination to generate new C-N bond. Metal complex is eventually regenerated back to the initial states and start another catalytic cycle again.

1.3. Transition metals for amination

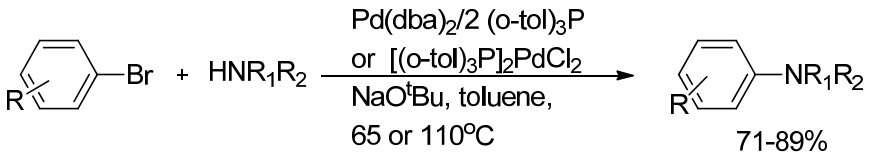
1.3.1. Palladium

Palladium is one of the most widely used metals for catalytic system. The first palladium-catalyzed amination was reported by Migita in 1983.[2a] Aniline derivatives were synthesized in the present of $PdCl_2[(o\text{-}tol)_3P]_2$ from aryl bromides (Scheme 1.1). Yields were moderate to good. However, handling of organostannyl compounds requires extra care due to the toxicities of the substrates and because of side product formation, this method was not widely used at that time.



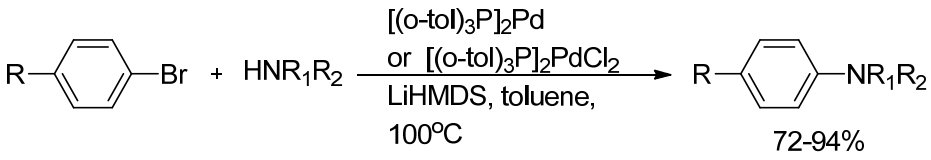
Scheme 1.1: The first palladium-catalyzed amination reported by Migita

The problems were overcome via the introduction of a special base in the catalytic system in 1995. Buchwald and Hartwig concurrently reported a new tin-free catalytic system by using different bases. Buchwald and coworkers utilized NaO^{t}Bu as a base to effectively couple aryl bromides and amine (Scheme 1.2).[8] $PdCl_2[(o\text{-tol})_3P]_2$ or mixing $Pd(dba)_2$ and $(o\text{-tol})_3P$ were showed total comparable efficiency to generate corresponding amine products.



Scheme 1.2: Tin-free catalytic system was reported by Buchwald

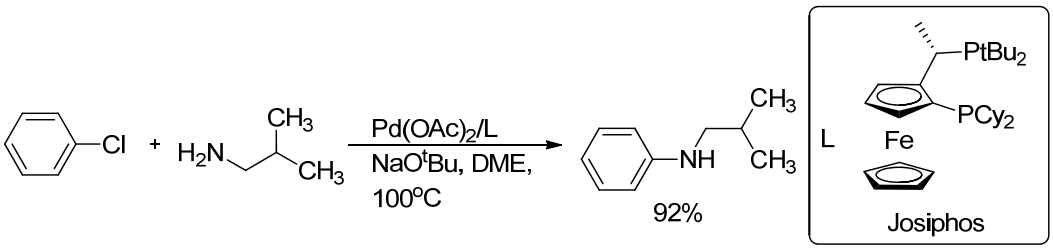
Hartwig and coworkers reported similar catalytic system using LiHMDS instead of NaO^{t}Bu (Scheme 1.3).[9] Both $PdCl_2[(o\text{-tol})_3P]_2$ and $Pd[(o\text{-tol})_3P]_2$ were effectively catalyzed amination in the present of LiHMDS.



Scheme 1.3: Tin-free catalytic system was reported by Hartwig

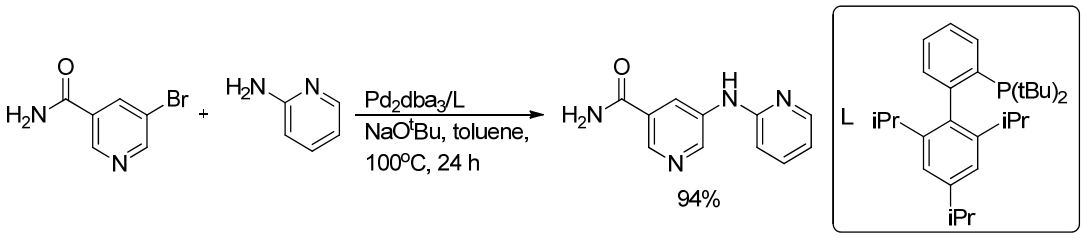
Although these publications expanded the scope of amine *N*-arylation, substrate scope was still narrow. Among the efforts to increase the scope and efficiency of the reaction, development of new ligand has shown the biggest impact. Palladium-catalyzed coupling processes tolerate various functional groups, thus the synthesis of highly complex molecules becomes practically feasible.[1e,2b,10] Among substrates used for amination, organic bromides, iodides, and triflates are common coupling partners. Although organic chloride is the most attractive class of substrate due to great diversity of compounds and low cost, aryl chlorides are not reactive under the same conditions as bromides, iodides, and triflates. The inertness of chloride is due to its high bond dissociation energy, 96 kcalmol^{-1}. This reluctates bond cleavage of Ar-Cl to Pd(0) through oxidative addition. A introduction of two main classes of ligand (chelating bisphosphine ligands and biaryl monophosphine ligands) leads aryl chloride oxidative add to metal possible. Thus the cross-coupling of aryl chloride has become more popular. Hartwig reported a highly reactive, general, and

long-lived catalysts for coupling heteroaryl and aryl chlorides.[11] Aryl chlorides react with primary alkylamines in the combination of Josiphos ligand and $Pd(OAc)_2$ to afford secondary amines (Scheme 1.4). Steric hindrance, strong electron donation, and tight chelation properties of Josiphos ligand made the catalyst long lifetime and highly reactive.



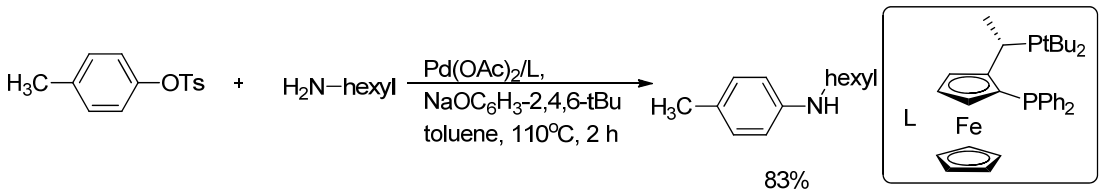
Scheme 1.4: The combination of Josiphos ligand and $Pd(OAc)_2$ to afford secondary amines

Buchwald showed monodentate biaryl ligand bulky and electron rich is an effective catalyst system towards amination.[6] This system catalyzed a wide scope of amine and aryl halides. A complex of Pd_2dba_3 and biaryl ligand allows the reaction of aryl/heteroaryl halides bearing primary amides and 2-aminoheterocycles to generate various amines in good yield (Scheme 1.5).[12]



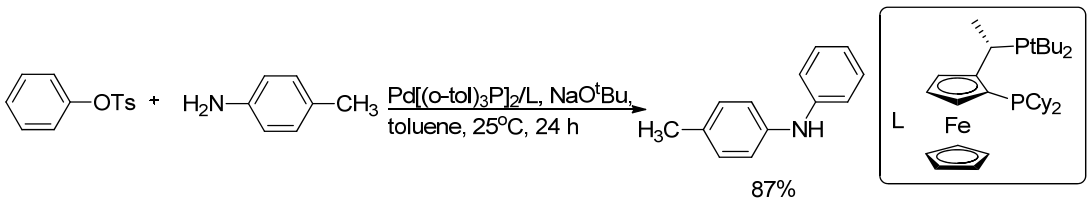
Scheme 1.5: Palladium-catalyzed amination of aryl bromides

Beside aryl halides, aryl sulfonates are useful coupling partners in palladium catalyzed amination.[1e,13] Hartwig reported first amination of aryl tosylates by using sterically hindered chelating alkyl phosphines.[14] Two examples illustrated success coupling of aryl tosylates with aniline and hexylamine in combination of Pd salt and phosphine ligand (Scheme 1.6).



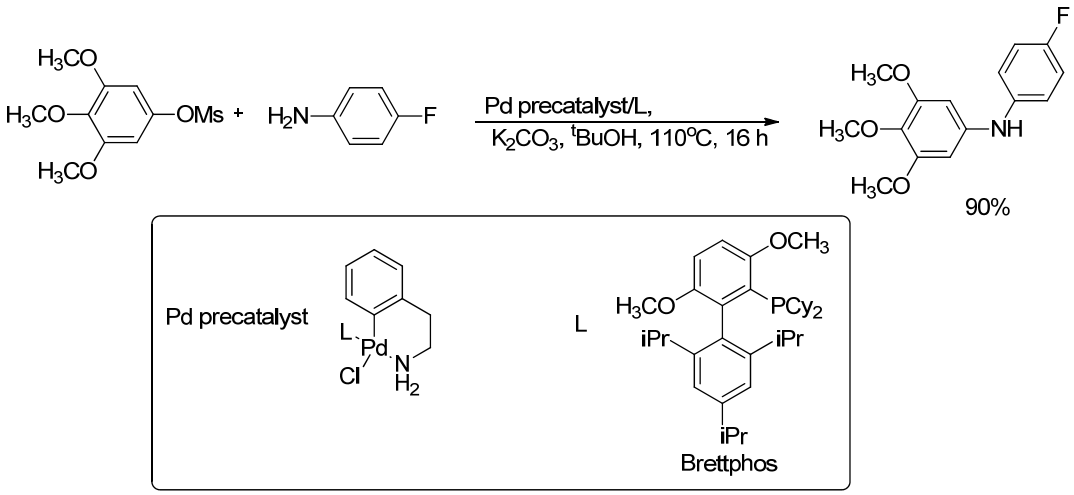
Scheme 1.6: The first palladium-catalyzed amination of aryl tosylate

Hartwig's group modified the Josiphos type ligands to effectively catalyzed amination of aryl and heteroaryl tosylates at room temperature. Coupling of tosylates with primary alkylamines and arylamines catalyzed by $Pd[(o\text{-}tol)_3P]_2$ and CyPF-^{t}Bu give good to excellent yield (Scheme 1.7).[15]



Scheme 1.7: The first palladium-catalyzed amination of aryl tosylate under room temperature

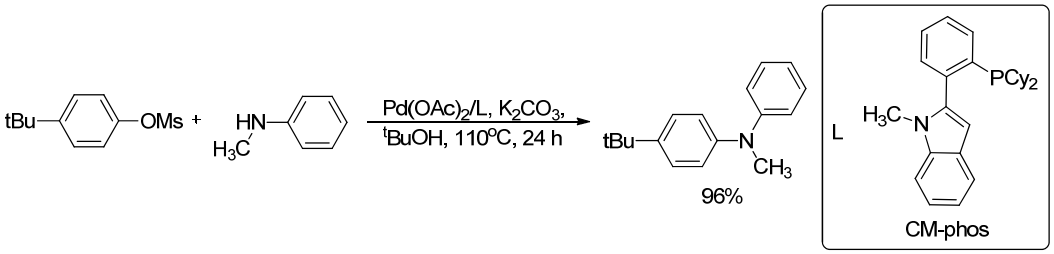
Buchwald published a highly active biaryl phosphine ligand Brettphos for palladium-catalyzed amination reaction. Seven examples were reported using BrettPhos to catalyze aryl mesylates and primary amine (Scheme 1.8).[16]



Scheme 1.8: Palladium-catalyzed amination of aryl mesylate

Kwong reported palladium catalyzed amination of aryl mesylates in the present of indolyl phohphine type ligand. The ligand was developed to catalyze the amination aryl mesylates and aromatic and *N*-heterocycle amines (Scheme

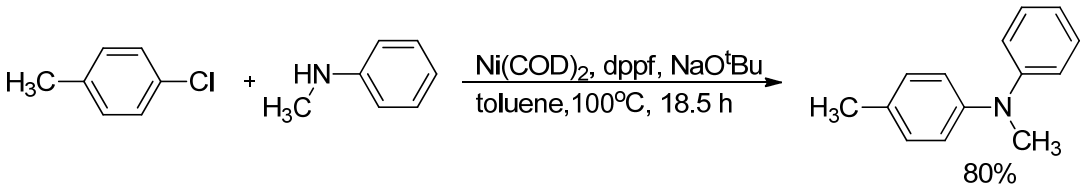
1.9).[17]



Scheme 1.9: $Pd(OAc)_2$ and CMPhos catalytic system for amine synthesis

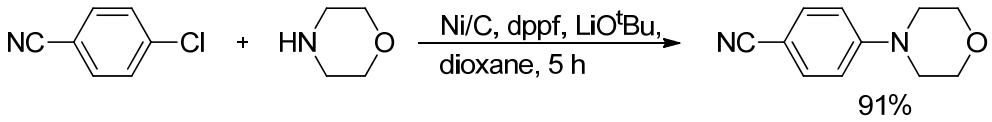
1.3.2. Nickel

Although palladium complexes are the most widely used class of catalyst, they often require specially designed ligands. Moreover, cost and environmental factors limit their use in industries.[1d,18] Nickel-based catalytic systems have been considered as alternative. Nickel inserts effectively into aryl chloride without tailor-made ligands. In 1997, Buchwald and Wolfe had published the first nickel-catalyzed amination of aryl chlorides.[19] Combination of $Ni(COD)_2$ and dppf in the present of NaO^tBu generated corresponding amine under 70-100 ℃ (Scheme 1.10).



Scheme 1.10: The first nickel-catalyzed amination of aryl chloride

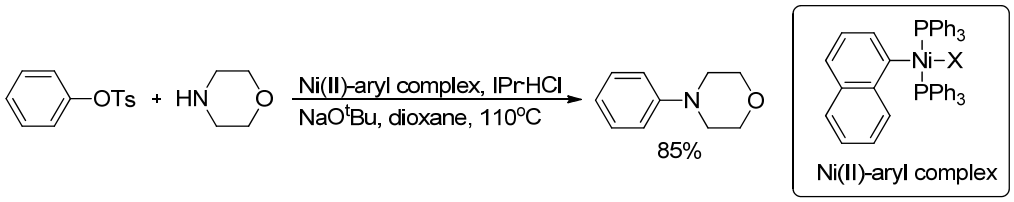
In 2000, an industrially attractive catalyst system was developed by Lipshutz and coworker.[20] This system showed high efficiency for C-N bond formation with advantage of ease workup and recovery of metal.[21] The catalyst precursor was prepared by reacting $Ni(NO_3)_2 \cdot 6H_2O$ water and activated carbon. Nickel metal embedded within carbon or so called nickel-in-charcoal (Ni(II)/C) was then generated to phosphine-ligated active Ni(0)/C in the present of dppf (Scheme 1.11). A wide variety of functionalized aryl halides were transformed into desired products by active Ni(0)/C.



Scheme 1.11: Ni/C catalyzed amination of aryl chloride

The catalyst can be stored, filtered off, and reused after completion of reaction. Thus, Ni/C is environmentally benign in organic synthesis. Gao and Yang utilized Ni(II)-aryl complex to perform amination of aryl tosylates.[13]

Combination of $Ni(PPh_3)_2$(1-naphthyl)Cl and IPr·HCl successfully couple aryl tosylates with amine at elevated temperatures to give corresponding amines (Scheme 1.12).



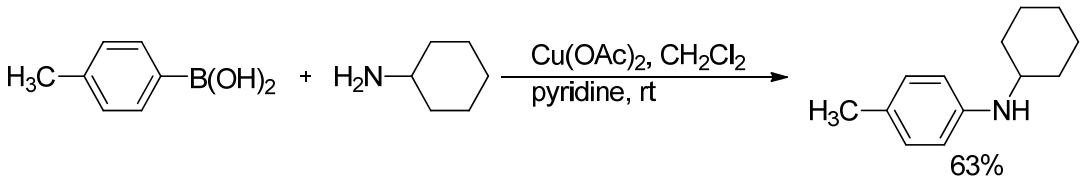
Scheme 1.12: Nickel-catalyzed amination was reported by Gao and Yang

Despite remarkable advantages of nickel catalysts, these reactions are still underdeveloped.[22]

1.3.3. Copper

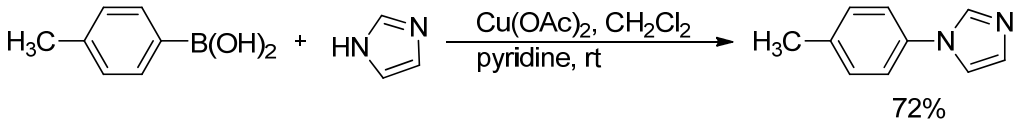
Efficient palladium-catalyzed amination is a great discovery in organic synthesis.[23] Although it is a major breakthrough, limitation such as air and moisture sensitive of metal sources, as well as high cost of palladium still exist. These limitations forced chemists to rediscover other metal catalysts. Recently, Ullmann coupling reaction was reexamined. Copper-catalyzed *N*-arylation was first reported by Ullmann over hundred years ago.[24] The harsh reaction condition

(high temperature, strong base, stoichiometric amount of metal, and extended reaction time) and poor substrate scope limited their applications in natural product synthesis.[4,23] In the past ten years, highly efficient catalytic systems with milder conditions and enhanced product yield have been achieved. Chan reported a protocol for *N*-arylation using aryl boronic acids instead of aryl halides as coupling partner in 1998 (Scheme 1.13).[25]



Scheme 1.13: Copper-catalyzed amination using aryl boronic acid

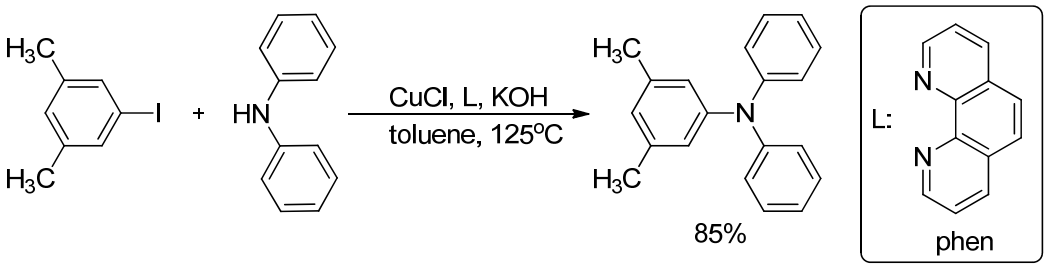
At the same year, Lam published a similar protocol for *N*-arylated heterocycles with aryl boronic acids (Scheme 1.14).[26]



Scheme 1.14: Copper-catalyzed amination using heterocycles amine

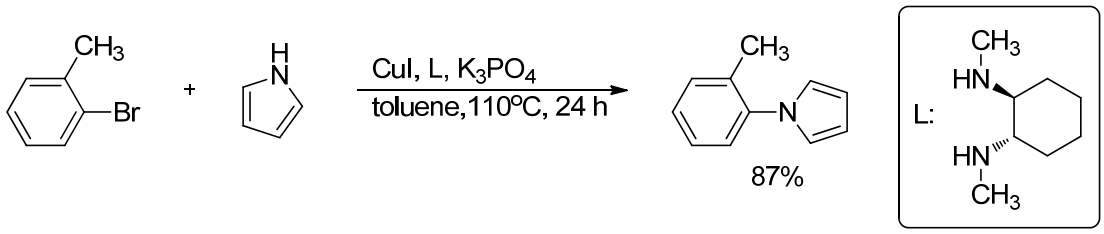
This revolutionized protocol has been found useful for copper-catalyzed *N*-arylation of amines with boronic acids. Apart from boronic acid, simpler and

more accessible aryl halides were successfully applied in the present of bidentate ligands. Goodbrand et al. found that using phen as chelating ligand could improve Ullmann reaction dramatically (Scheme 1.15).[27]



Scheme 1.15: Cu/phen modified Ullmann reaction

There have been an impressive number of publications for *N*-arylation of aryl amine. Copper catalysts provide the most general system for wide range of nitrogen heterocycles (imidazoles, imidazoles, pyrroles, etc.). Among the procedures available,[23] Buchwald developed a general and effective system for *N*-arylation of heterocycles.[28] A combination of copper (I) iodide and diamine is a successful system for various nitrogen heterocycles in generating corresponding amine products (Scheme 1.16).

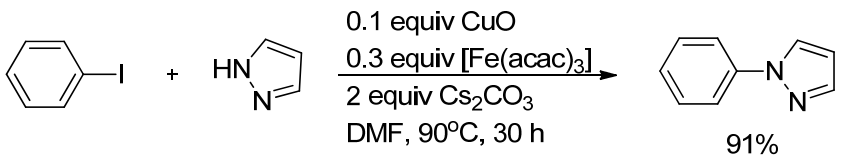


Scheme 1.16: The most general copper-catalyzed amination of heterocyclic amine

Although aryl halides are easy accessible, elevated temperature is required for most reactiona. Owing to the previous reaction in room temperature, Chan and Lam protocol using boronic acid is still an excellent alternative for synthesis of di- or tri-arylamines.

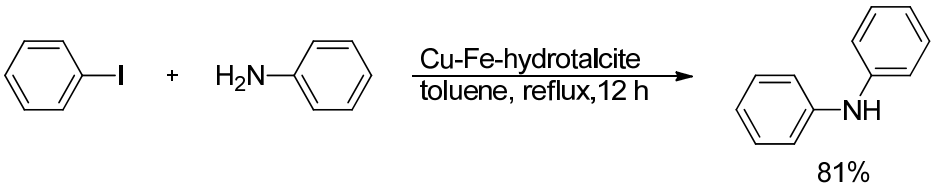
1.3.4. Iron

Despite the well development of palladium and copper catalyzed coupling reactions, new methods that use cheap and environmentally friendly catalyst is still in demand.[5,29] Iron has significant advantages which includes low cost, readily availablility, and environmentally benign character. Recently, Taillefer's group described a CuO and $Fe(acac)_3$ cooperative catalyst system which provides *N*-aryl heterocycles from aryl iodide and pyrazole (Scheme 1.17).[30]



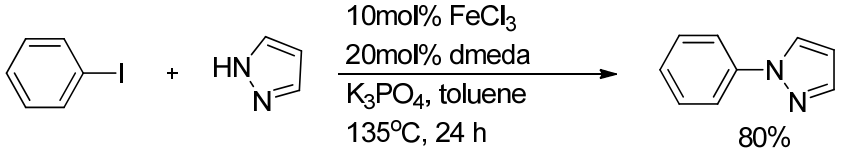
Scheme 1.17: Fe/Cu cocatalyzt for amination of aryl iodide

In the same year, Wakharkar et al. reported *N*-arylation in the present of Cu-Fe-hydrotalcite (Scheme 1.18).[31]



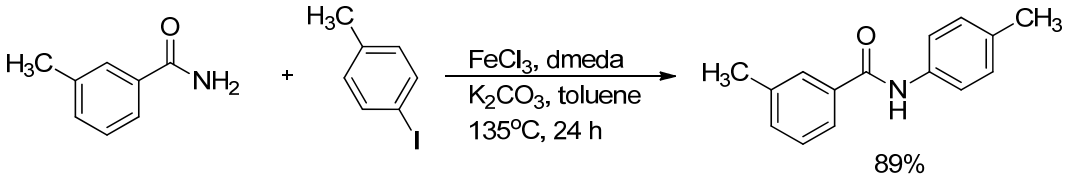
Scheme 1.18: Cu-Fe-hydrotalcite catalytic system for amine synthesis

Although the above system is efficient, the major drawback is the use of copper salt. Bolm et al. overcame this problem and reported the first genuine iron-catalyzed *N*-arylation of nitrogen nucleophiles.[5] By coupling of pyrzaole with aryl iodides in the present of $FeCl_3$ and dmeda (Scheme 1.19).



Scheme 1.19: The first iron-catalyzed amination of aryl iodide

In addition, Bolm et al. published the iron-catalyzed *N*-arylation of amides using the same conditions as previous described (Scheme 1.20).[29b]



Scheme 1.20: Iron-catalyzed *N*-arylation of amides

The coupling partners mainly were aryl iodides, therefore iron is relatively underexplored transition metal in the catalytic cross coupling reaction.

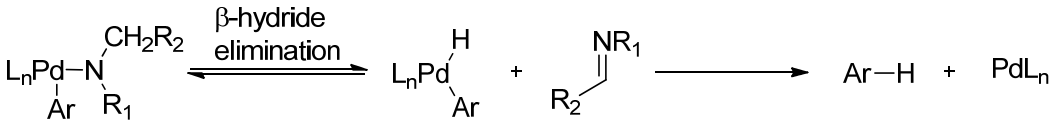
1.4. Phosphine Ligand for amination

1.4.1. Phosphine Ligand

Phosphine ligand plays important roles in palladium catalyzed C-N bond formation.[1a,1e] It alters not only electronic property but also bulkiness of metal center. Electron rich ligand increases electron density around Pd center to facilitate oxidative addition. Bulky ligand accelerates the rate of reductive elimination. However, ligand coordination is not effective with bulky aryl which

lead to palladium back precipitation.

A plethora of ligands are available for palladium catalyzed amination. Each ligand targets specific reaction condition and use different coupling partner. Tertiary phosphine such as triphenylphosphine and tricyclohexylphosphine were employed initially. They were fairly effective for reaction at the early development of catalytic systems. Although tricyclohexylphosphine appears enhancing oxidative addition step, it probably promotes *β*–hydride elimination over reductive elimination. Amine contained *β*-hydrogen suffers *β*-hydride elimination seriously, which results in imine formation and hydrodehalogenation of the aryl halide (Scheme 1.21).[2b,10] Thus, major challenge of ligand development is to inhibit the undesired side reaction.



Scheme 1.21: *β*-hydride elimination pathway

The development of chelating bisphosphine ligands and biaryl monophosphine ligands are shown to be effective for catalytic protocol. Chelating bisphosphine

ligands provide steric hindrance, strong electron donation, and tight chelation to palladium center. The extensive use of this type ligand was based on the assumptions that it also accelerates reductive elimination. JosiPhos type ligand, dppf, DtBPF, and CyPF-t-Bu were the examples of bisphosphine ligand (Figure 1.1).

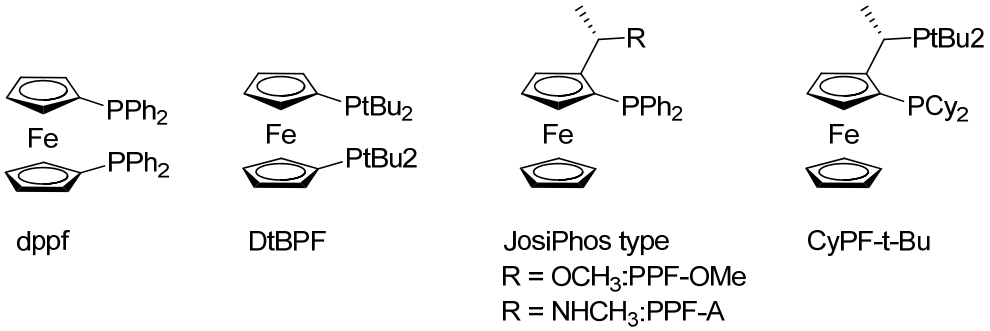


Figure 1.1: Examples of Josiphos type ligand

A range of highly active, bulky, and electron rich biaryl monophosphine ligand can also be successfully applied to amination. This ligand system was the most active class in major amine synthesis.[6] X-Phos is probably the most active ligand of this type (Figure 1.2).

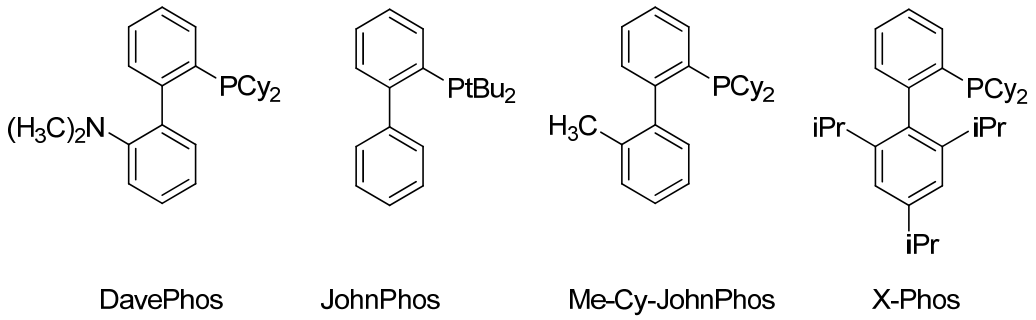


Figure 1.2: Examples of biaryl monophosphine ligand

In general, ligands design is currently governed by the ease preparation, stability, and minimal catalyst loading.

1.4.2. Hemilabile Ligand

Beside the two major classes of ligands developed for coupling reactions, hemilabile ligand is a unique class not belongs to both. Hemilabile ligands are polydentate ligand which contains two or more donor atoms capable of binding to metal centers.[32] These donor atoms are chosen to be different from each other to enhance their ability to interact with various metal centers. In fact, these donor atoms influence the bonding and reactivity of the other ligands bind to metal particularly in trans position. Hemilabile ligands should have at least one substitutionally labile donor and one donor firmly bond to metal. The substitutionally labile donor can be dissociated and remain available for

recoordination (Figure 1.3). The energy different between open and close situations should be relatively small.

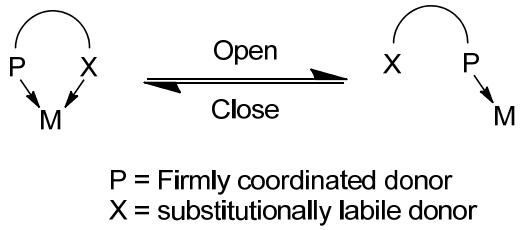


Figure 1.3: Hemilabile ligand dissociation and recoordination mechanism

The metal ligand coordination is governed by hard and soft acid base principle.[33] Combining hard and soft donors in the same ligand provides novel and unprecedented properties of the resulting metal complexes. Metal catalyst needs to enter the catalytic cycle through ligand dissociation.[34] Such low coordination and low valent 14-electron active catalyst is unstable and its formation is energetically unfavorable. The use of electronically and coordinatively tunable hemilabile ligands can solve these problems. Ligand interacts with metal dynamically in different stages of catalytic cycle. Indeed, switching between saturated and unsaturated states not only protect catalytic intermediate but also activate the key intermediate steps.

Hemilabile ligand should fulfill the following features.[34] (1) It must be a

bifunctional ligand with at least two donor atoms that has different donating character. (2) The electronic properties of donor atoms can be fine-tuned by chemical alteration of its attached or nearby substituents. (3) Two donating sites are separated by ligand moiety that is stereogeometrically flexible and redox active. (4) It must act as unidentate, chelating, and bridging ligand. (5) It can stabilize unsaturated metal through its electronic and spatial effects. "P,O-type" and "P,N-type" ligands meet these requirements and show catalytic active species in catalytic cycle (Figure 1.4). Guram et al. reported phenyl backbone derived P,O ligand for aryl bromides and chlorides.[35] Kwong et al. introduced benzamide derived P,O ligand (Bphos) for aryl chlorides.[1c] Stradiotto et al. recently reported P,N ligands (Me-DalPhos and Mor-DalPhos) which are effective for cross coupling of aryl chlorides and amines.[36]

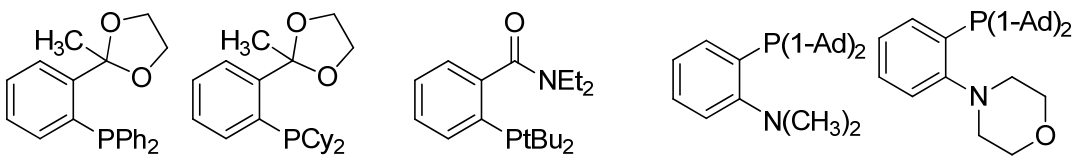
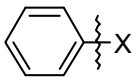


Figure 1.4: Examples of hemilabile ligands

1.5. Substrate

1.5.1. Aryl Chloride

Aryl halides were the first intensively studied electrophilic partners. They were well developed in coupling reactions.[1e] Aryl chlorides should be the choice of coupling partner in pharmaceutical and industrial processes. They are lower cost and ready available when comparing to aryl bromides and iodides. However aryl chlorides have poor reactivity towards coupling reactions. The low reactivity is due to the strength of the C-Cl bond, which is significantly higher than both C-Br and C-I bonds (Figure 1.5).[37]



X =		
	Cl	96 kcal mol^{-1}
	Br	81 kcal mol^{-1}
	I	65 kcal mol^{-1}

Figure 1.5: Bond dissociation energy of aryl halides

1.5.2. Aryl Tosylate

An alternative class of synthetic equivalents of aryl halides is aryl sulfonates[1e,13] which are regarded as pseudo-halides by chemists in traditional

organic synthesis and easily obtained from corresponding phenols. In fact, good availability and low cost of phenols are the advantage of using sulfonates. In fact, they Among them, aryl tosylates are particular useful, because they can be easily prepared with additional advantages of simple handling, pronounced stability to hydrolysis, and stable crystalline solids. However aryl tosylate is a challenging coupling substrate due to their low activity towards oxidation addition.

1.6. Summary

In summary, transition metal catalyzed carbon-nitrogen bond formation is highly attractive and useful in pharmaceutical, material sciences, and organic synthesis. Chemists continue research on the method improvement and expansion of the scope of coupling partners. There are a number of journals reported on carbon-nitrogen bond formation. Among the factors affecting the effectiveness of reaction conditions, ligands play an important role in catalytic cycle. The electron rich and bulky ligands show high effective in the reaction. Recently, hemilabile P,O- and P,N- type ligands are introduced to switch between saturated and unsaturated states. They not only protecting the catalytic intermediate but also can activate all the key steps.

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Chapter 2: Palladium-catalyzed amination of aryl tosylates

2.1. Introduction

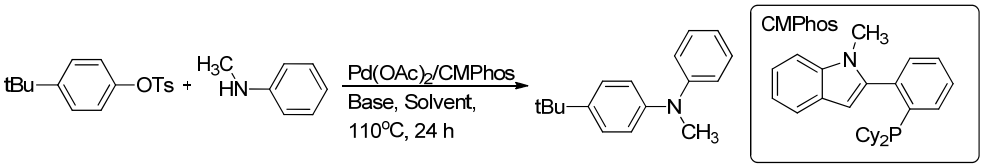
In 2008, our research group reported the first palladium-catalyzed amination of aryl mesylates using indolyl phosphine ligand.[1] However, amination of aryl sulfornates remain underdevelopment due to the inertness of aryl mesylates and tosylates. This area is highly challenging, and only limited examples of aryl sulfonates were reported.[1-5]

Indolyl phosphine ligand moiety is highly effective for amination of aryl mesylates under mild conditions. We attempted to explore the possibility of amination using aryl tosylates as coupling partner. This study was focus on palladium-catalyzed amination of aryl tosylates using indolyl phosphine ligand. The reaction conditions were firstly screened, and the substrate scopes of aryl tosylates and amines were then examined under optimal reaction conditions.

2.2. Results and discussion

2.2.1. Optimization of reaction conditions

Table 2.1: Screening of reaction condition for palladium-catalyzed amination of aryl tosylates[a]



entry	Base	Solvent	Yield (%)[b]
1	NaO^tBu	^{t}BuOH	0
2	Cs_2CO_3	^{t}BuOH	14
3	K_3PO_4	^{t}BuOH	85
4	K_2CO_3	^{t}BuOH	81
5	Na_2CO_3	^{t}BuOH	39
6	K_3PO_4	Dioxane	41
7	K_3PO_4	DMF	>99
8	K_3PO_4	IPA	0
9	K_3PO_4	*tert*-Amyl alcohol	0
10[c]	K_3PO_4	^{t}BuOH	0

11[d]	K_3PO_4	^tBuOH	0

[a] Reaction conditions: ArOTs (1.0 mmol), *N*-methyl aniline (1.5 mmol), Base (2.5 mmol), $Pd(OAc)_2$ (0.5 mol%), CMPhos (2 mol%) (Pd/P atom = 1:4), $PhB(OH)_2$ (0.04 mmol), solvent (3 mL), at 110℃ under N_2 for 24 h. [b] Determined by calibrated GC analysis with dodecane as internal standard. [c] Absent of ligand and without pretreatment of catalyst, $Pd(OAc)_2$ (1 mol%). [d] Tricyclohexyl phosphine (PCy_3) (Pd/phosphine atom = 1:4) was used in place of CMPhos, without pretreatment of catalyst, $Pd(OAc)_2$ (1 mol%).

With reference to our previous report on palladium-catalyzed amination of aryl mesylate,[1] a general reaction condition was obtained by screening of bases and solvent. As shown in Table 2.1, the screening began with the coupling of p-*tert*-butyl benzyl tosylate and *N*-methyl aniline using $Pd(OAc)_2$ and CMPhos system. Strongly basic NaO^tBu (entry 1) and Cs_2CO_3 (entry 2) undesirably promote decomposition of aryl tosylate through alkaline hydrolysis. Sulfur atom in aryl tosylates is easily attacked by strong nucleophiles. The undesired phenolic product is formed via sulfur-oxygen bond cleavage.[6-10] Thus, weak base are generally chosen to avoid hydrolysis of aryl tosylate. Although the decomposition product to phenol was still observed, weaker base K_3PO_4 (entry 3)

offered the best yield among other bases used for screening. The formation of phenol was not detected when K_2CO_3 was used (entry 4). Na_2CO_3 (entry 5) did not promote product formation. It only gave modest 39% yield. The reaction was found sensitive to solvent. IPA (entry 8) and *tert*-Amyl alcohol (entry 9) were inefficient. By replacing *tert*-butyl alcohol to DMF (entry 7), the product yield was higher. However *tert*-butyl alcohol is preferred due to the treatment, handling, high toxicity and hazard of DMF. Ligand plays important role in catalytic system. No product formation was detected in the absent of ligand (entry 10). Moreover, ligand moiety was another factor influencing the reaction efficiency. Use of PCy_3 (entry 11) failed to provide the corresponding product. Based on these findings, the optimal reactions were set as entry 4 in Table 2.1.

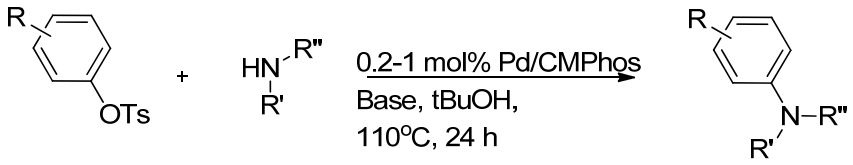
2.3. Substrate scope in amination

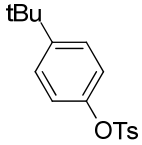
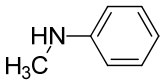
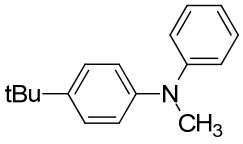
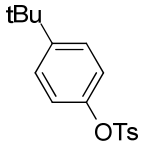
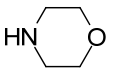
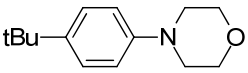
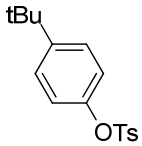
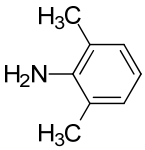
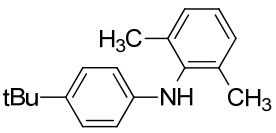
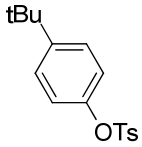
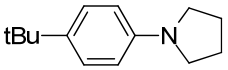
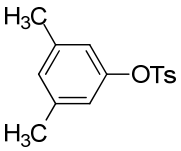
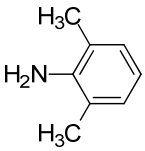
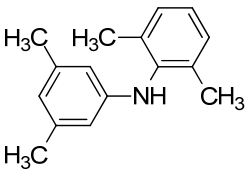
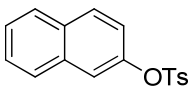
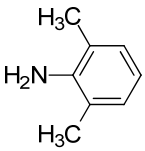
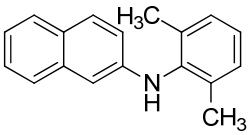
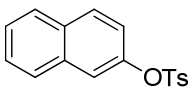
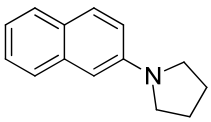
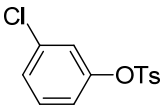
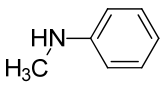
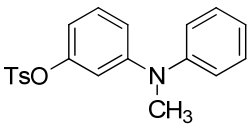
2.3.1. Amination of aromatic and secondary cyclic amines

The optimal conditions were used to investigate scope of aryl and secondary cyclic amines (Table 2.2). Yields were generally good under low palladium

loading. Both weakly basic K_2CO_3 and K_3PO_4 were suitable for the amination. Slightly improved yield was obtained when K_3PO_4 was used. Thus, the cross coupling of amine was conducted under K_3PO_4 in some examples.

Table 2.2: Palladium-catalyzed amination of aromatic and secondary cyclic amines[a]



entry	ArOTs	Amine	Product	Pd (mol%)	Yield (%)[b]
1[c]				0.2	90
2[c]				0.25	96
3				2	89
4[c]				0.5	88
5				0.5	83
6				0.5	77
7[c]				1	91
8[c,d]				1	85

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

Catalyst loading was governed by nature of tosylates and amines. Electron-rich p-*tert*-butyl phenyl tosylate coupled with *N*-methyl aniline to give good yield (entry 1) while increasing the electron density and bulkiness of aniline such as using 2,6-dimethyl aniline required more catalyst to enhance product formation (entry 3). The reaction was strongly influenced by the electronic properties of aryl tosylates.[11] Less-electron-rich 3,5-dimethyl tosylate and electron-neutral 2-naphthyl tosylate aminated by 2,6-dimethyl aniline under low palladium loading (entries 5-6). Diarylation of amine was restricted since bulky aniline product did not undergo further amination reaction. As for secondary cyclic amines, they generally have highly basic nitrogen atom. The metal loading is higher than aryl amine. p-*tert*-Butyl phenyl tosylate and 2-naphthyl tosylate were successfully arylated to corresponding pyrrolidine derivatives with good yields (entries 4 and 7). Morpholine was effectively coupled with p-*tert*-butyl phenyl tosylate in excellent yield (entry 2). The reason of low catalyst loading may come from the electron withdrawing oxygen atom, so morpholine is less basic. In fact secondary cyclic amines easily undergo *β*–hydride elimination. However none of the *β*-eliminated product was detected in our catalytic system. The selectivity of palladium-catalyzed amination of aryl chloride and tosylate was also

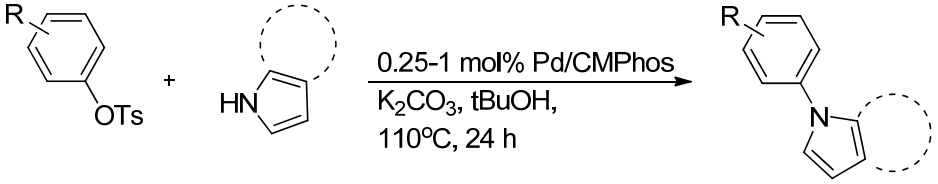
demonstrated. 3-Chloro phenyl tosylate was examined due to minimal influence of bond energy. Halide coupling was preferred to tosylate coupling (entry 8). Since halide groups are suggested to be a better leaving group than tosylate, oxidation addition favors cleavage of C-Cl bond.

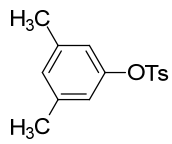
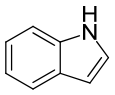
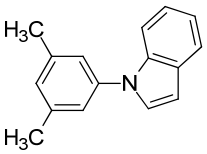
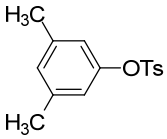
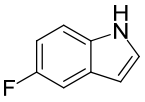
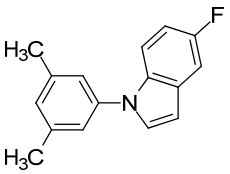
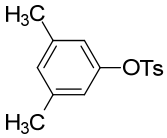
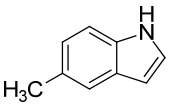
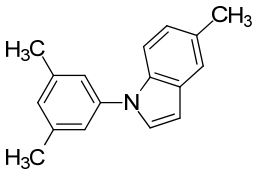
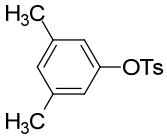
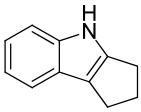
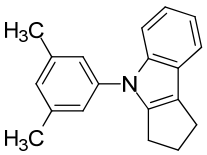
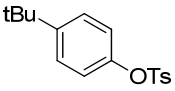
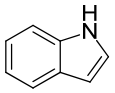
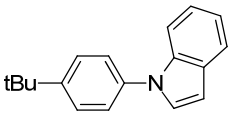
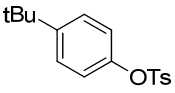
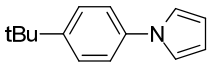
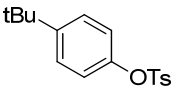
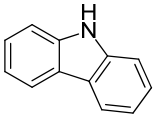
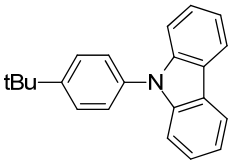
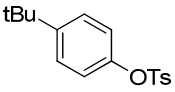
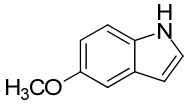
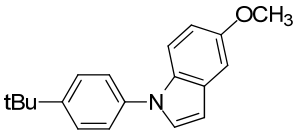
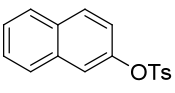
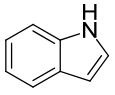
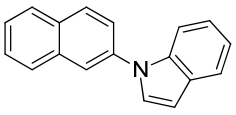
2.3.2. *N*-Arylation of nitrogen heterocycles

Indole derivatives play a very important role in the pharmaceutical synthesis. Indole moiety was found in many biological active and pharmaceutical compounds.[12,13] Examples include preparation of antipsychotic agents[14], synthesis of biological active heterocyclic agents[15] and synthesis of pharmacological active diindolemethane.[16] *N*-Heterocyclic amines are classes of analogue of the aromatic cyclopentadiene. It could be nonsubstituted as pyrrole or substituted as indole. They are weakly basic and easily attacked through electrophilic substitution in the five-member ring.[17] The electrophilic attack at weak *N*-basicity nitrogen atom would not occur due to destruction of aromaticity of the five-member ring. By this reason, formation of *N*-arylindole involving less-reactive nitrogen nucleophile remains challenging. Limited journals were reported palladium-catalyzed *N*-arylindolation with aryl chlorides,

bromides, iodides, triflates and mesylates. We are pleasured to find that indole was effectively aminated with aryl tosylate under our catalytic system (Table 2.3).

Table 2.3: Palladium-catalyzed *N*-arylation of nitrogen heterocycles[a]



entry	ArOTs	*N*-heterocycle	Product	Pd (mol%)	Yield (%)[b]
1				0.25	99
2				0.5	88
3				0.5	90
4				1	77
5				0.5	97
6				0.5	78
7[c]				1	96
8				0.5	91
9				0.5	90

[a] Reaction conditions: ArOTs (1.0 mmol), *N*-heterocycle amine (1.5 mmol), K_2CO_3 (2.5 mmol), $Pd(OAc)_2$/CMPhos (mol% as indicated) (Pd/P atom = 1:4),

$PhB(OH)_2$ (0.04 mmol), ^tBuOH (3 mL), at 110℃ under N_2 for 24 h. [b] Yield of isolated product. [c] ArOTs (1.5 mmol), carbazole (1.0 mmol) were used.

Palladium-catalyzed *N*-arylation of *N*-heterocycle often produces a mixture of three products. *C*-Arylated indole and *N,C*-diarylated indole were formed as well as *N*-arylated indole. Selection of an appropriate ligand was able to minimize the formation of the unwanted side products.[12] Our system showed that indole was effectively and selectively *N*-arylated to give corresponding indole derivative without the formation of undesired products. The reaction of 3,5-dimethyl phenyl tosylate (entry 1), p-*tert*-butyl phenyl tosylate (entry 5), and 2-naphthyl tosylate (entry 9) with indole processed in excellent yield up to nearly completed conversion. For the coupling of substituted indoles, 5-substituted indole with activating or deactivating effects showed similar reactivity with respected to indole. The nucelophilicity of nitrogen atom did not influence by substitution groups. Deactivating 5-fluoroindole coupled well with 3,5-dimethyl phenyl tosylate (entry 2) to give good yield while coupling with electron-neutral 5-methylindole (entry 3) afforded similar yield. Moreover, activated 5-methoxyindole (entry 8) did not further promote product formation. The catalyst loading in 5-substituted indole is more or less the same. As indole

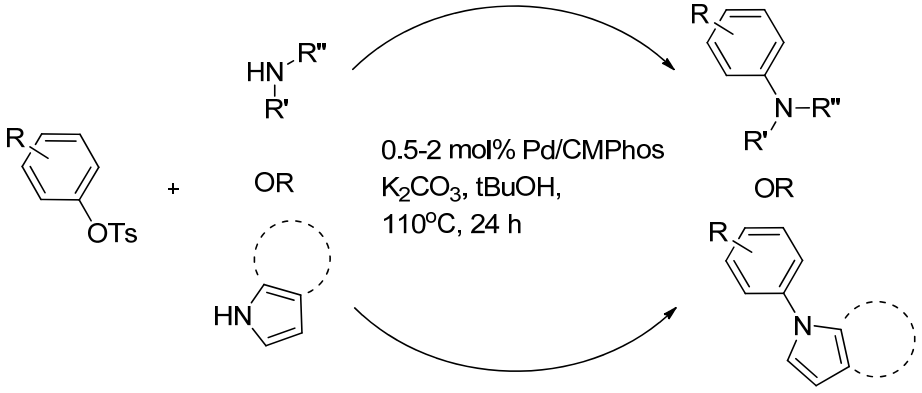
becomes hindered, 1,2,3,4-tetrahydrocyclopentaindole (entry 4) required an increase of catalyst loading to obtain desired product in 77% yield. To expand the scope of *N*-heterocycle amines, an attempt to react pyrrole (entry 6) with *tert*-butyl phenyl tosylate produced the *N*-arylated product in 78% yield. For the coupling of *tert*-butyl phenyl tosylate with carbazole (entry 7), enhanced catalyst loading was needed to afford excellent yield probably due to bulkiness of carbazole. In this case, it was difficult to completely isolate the products by fresh column chromatography. Thus, the substrate amount of coupling partners was reversed (i.e. 1.5 mmole *tert*-butyl tosylate and 1.0 mmole carbazole). Although mono-heteroatom *N*-heterocycles were successfully coupled to aryl tosylate, mulit-heteroatom *N*-heterocycles were not compatible.

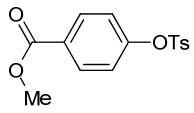
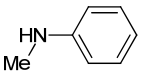
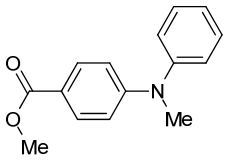
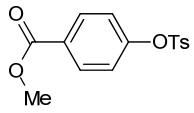
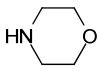
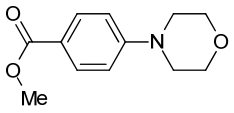
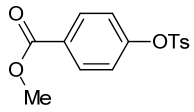
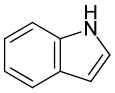
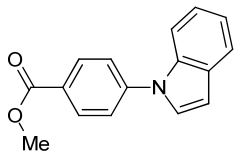
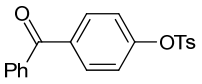
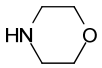
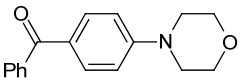
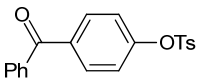
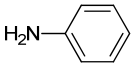
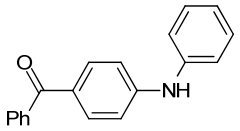
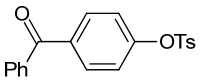
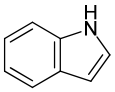
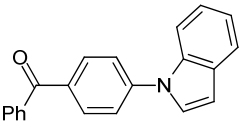
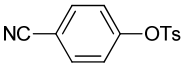
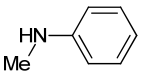
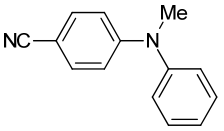
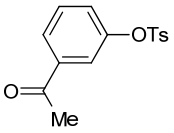
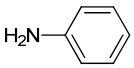
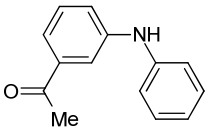
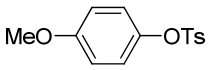
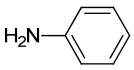
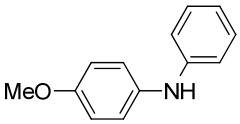
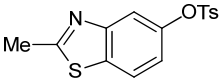
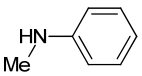
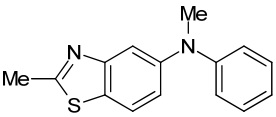
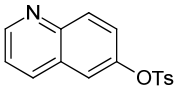
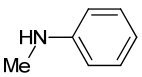
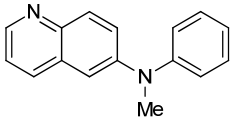
2.3.3. Amination of functionalized aryl tosylates

With the success of the *N*-arylation of amines, we attempted to tackle wider variety of functionalized aryl tosylates. K_2CO_3 was found to be the most effective base, while strongly basic such as NaO^tBu promoted decomposition of aryl tosylate via S-O bond cleavage as well as decomposition of functionality. Limited aminatioin examples were reported by Buchwald's

group[3] and Hartwig's groups[2,4] due to the employment of strong base. To this, our catalytic system showed a wider functional group tolerance than previous publications.

Table 2.4: Palladium-catalyzed amination of functionalized aryl tosylates[a]



entry	ArOTs	Amine	Product	Pd (mol%)	Yield (%)[b]
1				0.5	90
2				0.5	83
3				0.5	72
4				0.5	95
5				0.5	92
6				0.5	93
7				0.5	87
8				1	75
9				1	77
10				2	80
11				1	94

[a] Reaction conditions: ArOTs (1.0 mmol), *N*-heterocycle or amine (1.5 mmol), K_2CO_3 (2.5 mmol), $Pd(OAc)_2$/CMPhos (mol% as indicated) (Pd/P atom = 1:4),

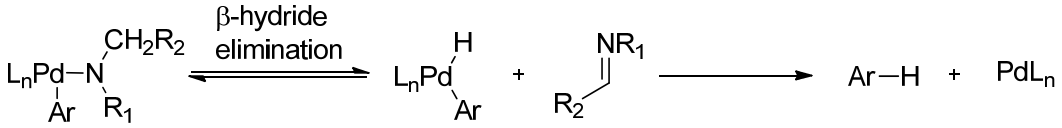
$PhB(OH)_2$ (0.04 mmol), ^tBuOH (3 mL), at 110℃ under N_2 for 24 h. [b] Yield of isolated product.

Amination of aryl tosylate bearing various base sensitive functional groups was accomplished using $Pd(OAc)_2$ and CMPhos catalyst system in the present of weak base K_2CO_3 (Table 2.4). The reaction conditions tolerated nitrile, methoxy and carbonyl derivative including benzoate, acetophenone, and benzophenone groups. Electron-withdrawing functional groups in para position activate aryl tosylates by weaken the C-O bond. Therefore low catalyst loading was generally required. Methyl 4-tosyloxybenzoate and 4-tosyloxybenzophenone were effectively coupled to aniline, *N*-methyl aniline, morphiline, and indole (entries 1-6) in good to excellent yields. 4-Tosyloxybenzonitrile (entry 7) was aminated by *N*-methyl aniline in 87% yield. The activation effect did not found in meta position, for instance, 3-acetylphenyl tosylate (entry 8) was converted to amine product in good yield using higher metal loading. As for electron-donating properties, 4-methoxyphenyl tosylate (entry 9) was effectively coupled with aniline using 1 mol% Pd. Heterocyclic aryl tosylates were also good coupling partners in amination. Catalytic amination of 6-tosyloxyquinoline (entry 10) and

5-tosyloxy-2methylbenzo[*d*]thiazole (entry 11) were also effectively coupled in good yields.

2.3.4. *N*-Arylation of alkylamine

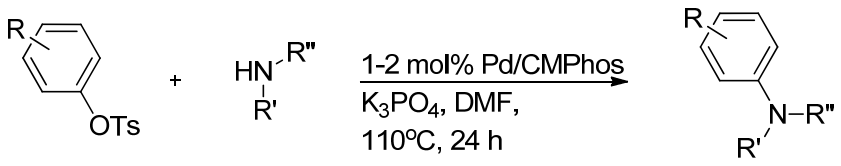
The catalytic system was further examined to include alkylamines. However the catalyst system was less successful even under best conditions. Fortunately, DMF was the best alternative with increased amount of catalyst. Alkylamine particularly acyclic secondary amines often are the most challenging substrates for amination due to propensity of β-hydride elimination.[18]

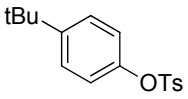
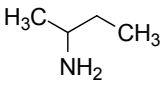
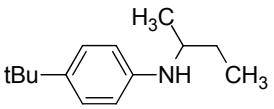
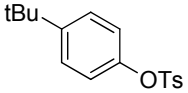
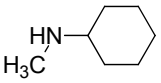
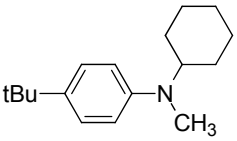
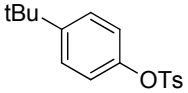
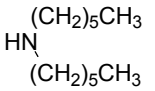
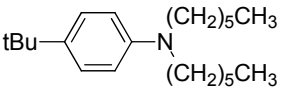
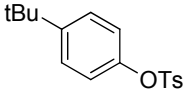
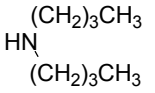
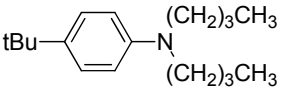
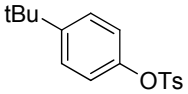
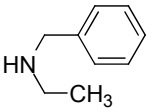
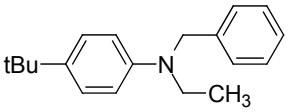
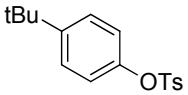
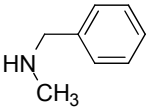
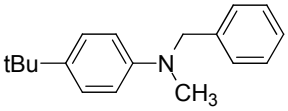
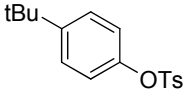
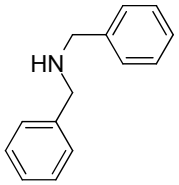
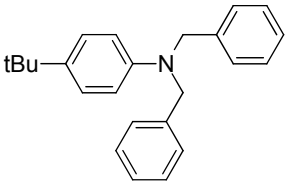


Scheme 2.1: β-hydride elimination pathway

This catalytic system effectively minimizes the undesired arene by-products. The results were summarized in Table 2.5.

Table 2.5: Palladium-catalyzed *N*-arylation of alkylamines[a]



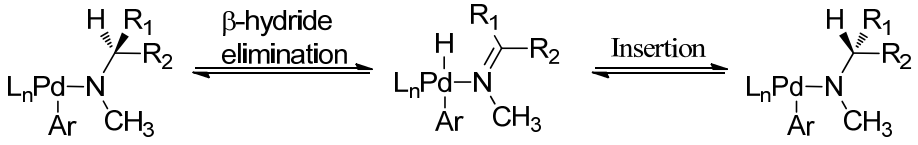
entry	ArOTs	Amine	Product	Pd (mol%)	Yield (%)[b]
1				2	91
2				2	79
3				2	62
4				2	74
5				2	68
6				2	87
7[c]				1	84

[a] Reaction conditions: ArOTs (1.0 mmol), amine (1.5 mmol), K_3PO_4 (2.5 mmol), $Pd(OAc)_2$/CMPhos (mol% as indicated) (Pd/P atom = 1:4), $PhB(OH)_2$ (0.04 mmol), DMF (3 mL), at 110℃ under N_2 for 24 h. [b] Yield of isolated product. [c] ^{t}BuOH (3mL) as solvent.

Reaction of *sec*-butylamines (entry 1) and cyclohexylamine (entry 2), which are hindered α-branched amines, occurred in up to 91% yield. However, reactions of linear secondary amines were less effective. p-*tert*-Butyl phenyl tosylate coupled with dihexylamine (entry 3) and dibutylamine (entry 4) in moderate yields. The reduction by-product *tert*-butyl benzene was found. For reaction of benzyl amines, altering the second substituent did not contribute to any effect. *N*-Arylation of p-*tert*-butyl phenyl tosylate with *N*-methyl benzylamine, *N*-ethyl benzylamine, and dibenzylamine (entries 5-7) afforded good yields.

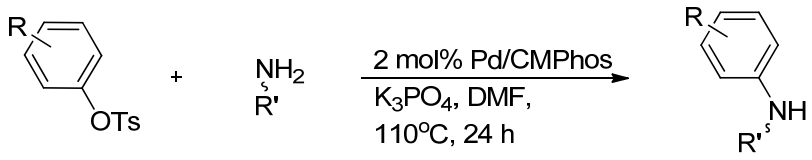
2.3.5. Reaction of chiral amines with aryl tosylates

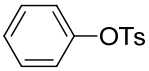
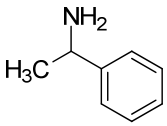
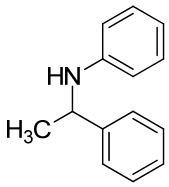
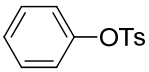
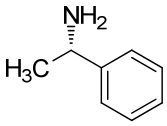
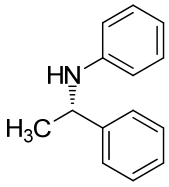
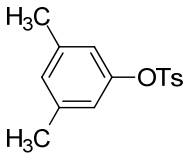
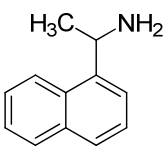
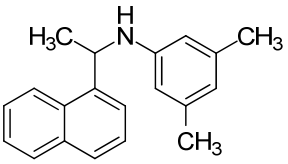
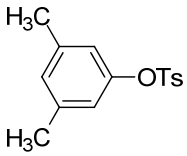
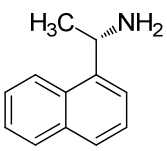
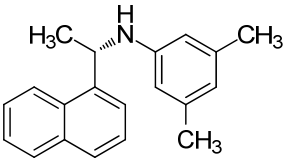
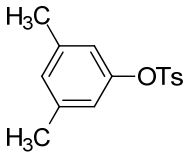
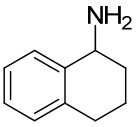
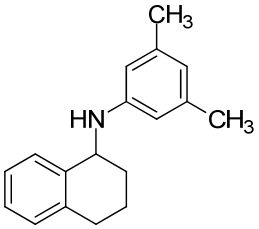
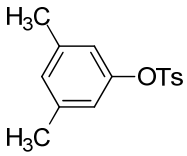
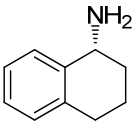
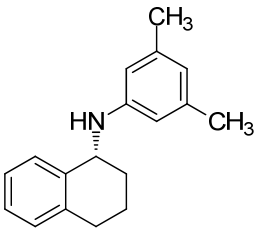
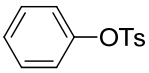
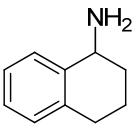
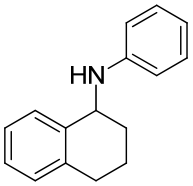
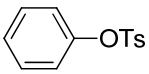
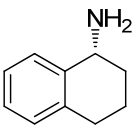
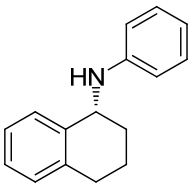
Use of monophosphine such as P(o-tolyl)$_3$ gave the product with erosion of enantiomeric excess due to the availability of free vacant coordination site. Whereas use of bulky BINAP as ligand results in essentially preservation of stereochemical integrity. The loss of sterochemical integrity through insertion after β-hydride elimination was well studied (Scheme 2.2).[19,20] *N*-Arylation of enantiomerically enriched α-substituted amines was attempted in Table 2.6.



Scheme 2.2: The erosion of enantiomeric excess of chiral amine

Table 2.6: Palladium-catalyzed *N*-arylation of optically active *α*-substituted amines[a]



entry	ArOTs	Amine	Product	Yield (%)[b]	ee (%)[c]
1				78	
2				72	97 (R)
3				91	
4				76	99 (S)
5				75	
6				74	93 (R)
7				67	
8				60	95 (R)

[a] Reaction conditions: ArOTs (1.0 mmol), amine (1.5 mmol), K_3PO_4 (2.5 mmol), 2 mol% $Pd(OAc)_2$/CMPhos (Pd/P atom = 1:4), $PhB(OH)_2$ (0.04 mmol), DMF (3 mL), at 110℃ under N_2 for 24 h. [b] Yield of isolated product. [c] Determined by HPLC on a OD-H column.

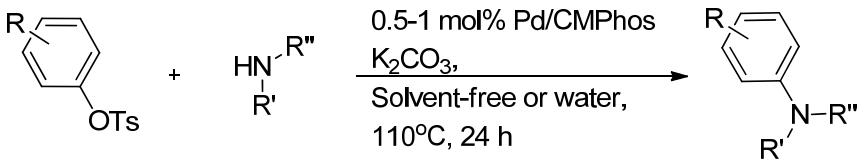
The use of $Pd(OAc)_2$/CMPhos protocol to cross-couple optically active *α*-substituted amines[21] with aryl tosylates was successful. (R)-(+)-*α*-Methylbenzylamine (98% ee) (entry 2) was coupled with phenyl tosylate with 97% ee. The enantiomeric excess of (S)-(−)-1-(1-Naphthyl)ethylamine (99% ee) (entry 4) was fully retained. The ee remains high when *N*-arylation of (R)-(−)-1,2,3,4-Tetrahydro-1-naphthylamine (97% ee) with 3,5-dimethyl phenyl tosylate (entry 6) and phenyl tosylate (entry 8). Racemic amines experiments were carried out for HPLC retention time determination and comparison (entries 1, 3, 5, and 7).

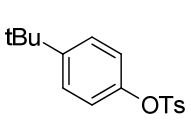
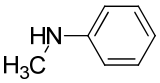
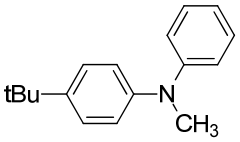
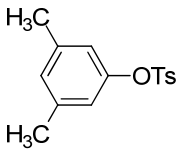
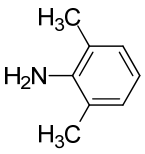
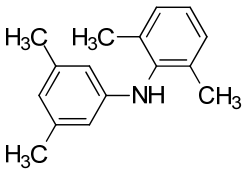
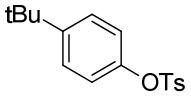
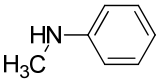
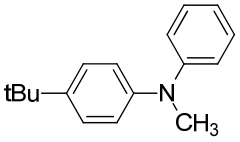
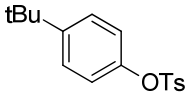
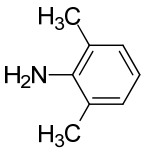
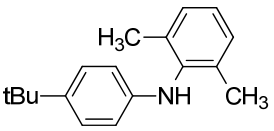
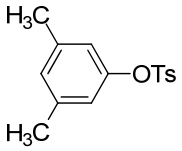
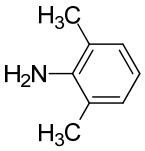
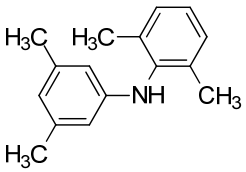
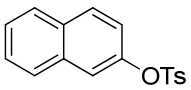
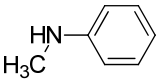
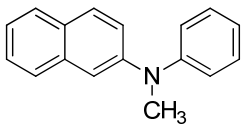
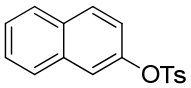
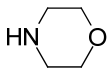
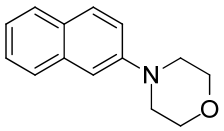
2.3.6. Catalytic amination in solvent-free and water conditions

Encourage by the results of *N*-arylation, the possibility of using solvent-free

and aqueous medium were examined. The classical metal-catalyzed amination applying organic solvents are generally toxic and polluting environment. Recently, green synthesis and sustainable chemistry proposed use of environmental friendly catalyst system for C-N coupling.[22-24]

Table 2.7: Palladium-catalyzed amination in solvent-free and water[a]



entry	ArOTs	Amine	Product	Pd (mol%)	Yield (%)[b]
1[c]				0.5	95
2[c]				0.5	97
3				1	95
4				1	82
5				1	94
6				1	90
7				1	87

[a] Reaction conditions: ArOTs (1.0 mmol), amine (2.0 mmol), K_2CO_3 (2.5 mmol), $Pd(OAc)_2$/CMPhos (mol% as indicated) (Pd/P atom = 1:4), $PhB(OH)_2$ (0.04 mmol), water (3mL), at 110℃ under N_2 for 24 h. [b] Yield of isolated product. [c] Amine (5.0 mmol) reaction in solvent-free condition.

The challenge of these conditions is the homogeneity of catalyst and substrates.

No detrimental effects were observed under solvent-free conditions. In addition, the rate of reaction is slightly higher due to the higher effective concentration of reactants. The reaction was conducted in slightly excess of amine (Table 2.7). *N*-Methyl aniline (entry 1) was effectively coupled with p-*tert*-butylphenyl tosylate in comparable yield (compare to Table 2.2, entry 1). Excellent yield was obtained from coupling of 3,5-dimethylphenyl tosylate and 2,6-dimethyl aniline (compare to Table 2.2, entry 5). Aqueous metal-catalyzed reaction has become more popular.[25-27] The use of water as a "green solvent" for amination often induces difficulty. Since the solubility of catalyst in water is low, a phase transfer catalyst and toluene as co-solvent were required.[28,29] Additionally, aryl tosylate under aqueous conditions is more challenging due to the ease of decomposition of substrate through alkaline hydrolysis. To our delight, the use of $Pd(OAc)_2$/CMPhos catalytic protocol in water without using co-solvent gave good to excellent results. Amination of various aryl tosylates with anilines provided corresponding amine derivatives in up to 95% yield (entries 3-7).

2.4. Conclusion

In summary, we have developed the first efficient, mild, and general catalytic

protocol for amination of aryl tosylates. Significantly expanded substrate scopes of aryl tosylates and amine derivatives have achieved. The first *N*-arylindoles using aryl tosylates is reported. A variety of functionalized aryl tosylates are compatible with this reaction conditions. The use of $Pd(OAc)_2$/CMPhos as catalyst preserves the stereochemical integrity to give high yield of aminated products. It is the first time, aryl tosylates could be aminated under solvent-free condition with superior results. This reaction could be performed under aqueous conditions that do not necessitate the use of co-solvents.

2.5. Experimental section

2.5.1. General procedure for amination of aryl tosylates

General procedure for amination of aryl tosylate: $Pd(OAc)_2$ (2.3 mg, 0.010 mmol) and ligand L (Pd:L = 1:4) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The tube was evacuated and flushed with nitrogen for several times. Precomplexation was applied by adding freshly distilled dichloromethane and Et_3N into the tube. The solution was stirred and

warmed using hair drier for about 1 to 2 minutes until the solvent started boiling. The solvent was then evaporated under high vacuum. Aryl tosylate (1.0 mmol), K_2CO_3 (2.5 mmol), solid amines (1.5 mmol) and phenyl boronic acid (0.04 mmol) were loaded into the tube, and the system was further evacuated and flushed with nitrogen for several times. Liquid amines (1.5 mmol) were also loaded into the tube. The solvent *tert*-butanol (3 mL) was then added. The tube was stirred at room temperature for several minutes and then placed into a preheated oil bath (110 ℃) for 24 hours. After completion of reaction as judged by GC analysis, the reaction tube was allowed to cool to room temperature and quenched with water and diluted with EtOAc. The organic layer was separated and the aqueous layer was washed with EtOAc. The filtrate was concentrated under reduced pressure. The crude products were purified by flash column chromatography on silica gel (230-400 mesh) to afford the desired product.

2.6. Reference

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(21) Purchased from Sigma-Aldrich. (R)-(+)-α-Methylbenzylamine, 98%, 115541-25mL, Lot. No.: 06601BE; (S)-(−)-1-(1-Naphthyl)ethylamine, ≥99%, 237450-1g, Lot. No.:01712JH; (R)-(−)-1,2,3,4-Tetrahydro-1-naphthylamine, 97%, 668818-5g, Lot No.:MKBD4387.

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Chapter 3: Development of new P,N-type hemilabile ligand

3.1. Introduction

The catalytic cross-coupling reactions are among one the most straightforward and practical protocols in preparing pharmaceutically useful compounds. While synthetic chemists have been remarkably adept at coming up brilliantly creative methods in refining specific bond constructions, the extension of these reactions into truly general methodology by the application of simple and highly effective catalyst is still in great demand. In fact, the high tunability of the catalyst is of significance to deal with various libraries of lead compound in the diversified drug discovery processes since different molecules usually require a particular fine-tuned catalyst for optimization.

The improvement of current methodologies and exploration of new technology for versatile bond construction process are of fundamental importance. The purpose of this research is to rationally develop a new class of simple and highly efficient phosphine ligands (and their potential chiral

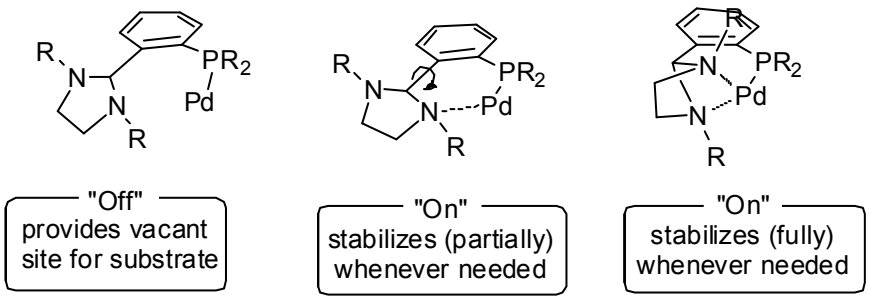
variants) with high potential of tunablity and to explore the scope of new ligands in tackling problematic/unexplored substrates.

Recently, classes of hemilabile ligand were developed utilizing two different donor atoms toward metal coordination. We attempted to design a new class of potentially hemilabile phosphine ligands, which enjoy the electron-richness and bulkiness. Additionally, it is designed to be easily prepared and highly diversified. For a better economic prospective, we planned to choose inexpensive and readily available benzaldehyde or acetophenone with diamines as starting materials. The research idea of using imidazolidine as ligand scaffold is come from Guram,[1,2] who published the use of dioxolane and phenyl backbone-derived P,O-ligands for palladium-catalyzed Suzuki-Miyaura coupling and Buchwald-Hartwig amination in 1999.

3.2. Results and discussion

3.1.1. Preparation of phenyl imidazolidinyl backbone ligands

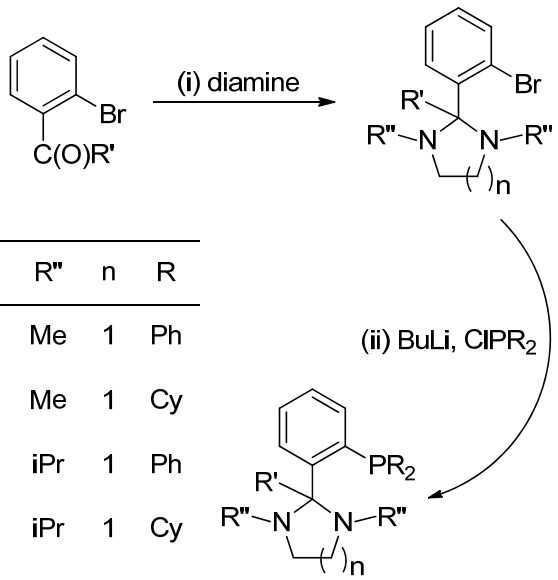
The potential of high activity may arise from the hemiability of the ligand skeleton, which can stabilize the palladium metal center as well as provide vacant site for bulky substrates. This type of ligand is anticipated to be highly efficient as it possesses a weak coordinating hemilabile group, which exerts a dynamic "on and off mechanism": coordinating to metal center or providing a vacant site for substrate binding (Scheme 3.1).[3,4]



Scheme 3.1: A dynamic on and off mechanism

Synthesis of imidazolidinyl-based ligands was based on two synthetic steps. First, 2-bromobenzaldehyde was reacted with diamine such as dmeda through condensation in high yield. Then purified precursors were lithiated by *n*-BuLi at -78℃, followed by trapping of dialkylphosphine to generate a

variety ligands (Scheme 3.2). The yield of precursors and ligands are shown in Table 3.1



	R'	R"	n
1a	H	Me	1
1b	H	iPr	1
1c	H	tBu	1
1d	H	Me	2
1e	Me	Me	1

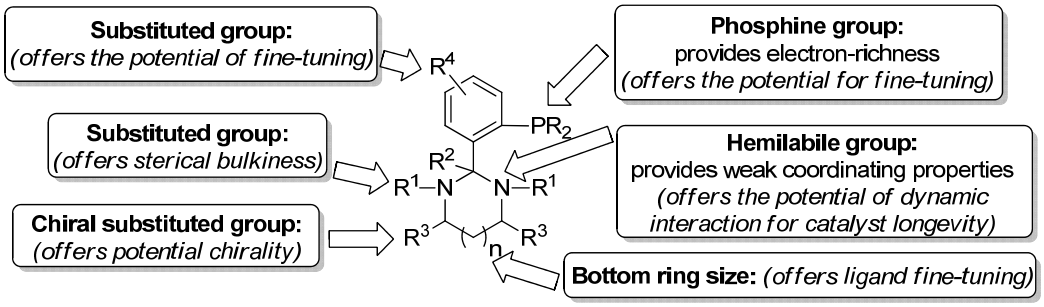
	R'	R"	n	R
2a	H	Me	1	Ph
2b	H	Me	1	Cy
2c	H	iPr	1	Ph
2d	H	iPr	1	Cy
2e	H	tBu	1	Ph
2f	H	tBu	1	Cy
2g	H	Me	2	Cy
2h	Me	Me	1	Ph
2i	Me	Me	1	Cy

Scheme 3.2: Synthetic pathways for the phenyl imidazolidinyl phosphine ligands

Table 3.1: Yield of precursors and ligands

entry	Precursor	Yield (%)	Ligand	Yield (%)
1	**1a**	75	**2a**	46
2	–	–	**2b**	40
3	**1b**	98	**2c**	49
4	–	–	**2d**	30
5	**1c**	95	**2e**	28
6	–	–	**2f**	28
7	**1d**	96	**2g**	49
8	**1e**	45	**2h**	44
9	–	–	**2i**	14

Particularly noteworthy is that the ligand scaffold can be fine-tuned by using different substituted benzaldehyde, acetophenone and diamine derivatives. These characteristics offer us a great potential of ligand skeleton fine-tuning.

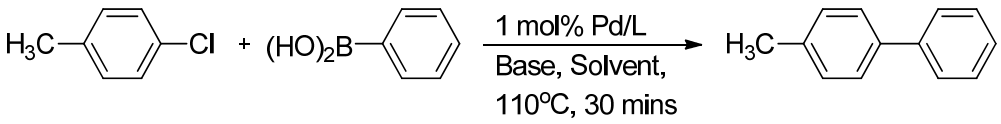


Scheme 3.3: Strategic design of a phenyl imidazolidinyl backbone ligands

3.1.2. Initial screening of model reaction

In our initial screening experiments, p-chlorotoluene and phenyl boronic acid were chosen to optimize reaction conditions. The reaction conditions were investigated a combination of various metals, ligands, solvents as well as bases. Results are summarized in Table 3.2.

Table 3.2: Optimization of model reaction[a]



entry	Pd	Ligand	Solvent	Base	GC Yield (%)[b]
1	$Pd(OAc)_2$	**2b**	Toluene	$K_3PO_4 \cdot H_2O$	5
2	$Pd(OAc)_2$	**2d**	Toluene	$K_3PO_4 \cdot H_2O$	41
3	$Pd(OAc)_2$	**2f**	Toluene	$K_3PO_4 \cdot H_2O$	2

4	$Pd(OAc)_2$	**2g**	Toluene	$K_3PO_4 \cdot H_2O$	80
5	$Pd(OAc)_2$	**2i**	Toluene	$K_3PO_4 \cdot H_2O$	0
6	$(CNCH2)_2PdCl_2$	**2g**	Toluene	$K_3PO_4 \cdot H_2O$	13
7	$Pd(TFA)_2$	**2g**	Toluene	$K_3PO_4 \cdot H_2O$	20
8	$PdCl_2(cod)$	**2g**	Toluene	$K_3PO_4 \cdot H_2O$	20
9	$Pd(dba)_2$	**2g**	Toluene	$K_3PO_4 \cdot H_2O$	40
10	$Pd(OAc)_2$	**2g**	tBuOH	$K_3PO_4 \cdot H_2O$	40
11	$Pd(OAc)_2$	**2g**	THF	$K_3PO_4 \cdot H_2O$	67
12	$Pd(OAc)_2$	**2g**	Dioxane	$K_3PO_4 \cdot H_2O$	40
13	$Pd(OAc)_2$	**2g**	DMF	$K_3PO_4 \cdot H_2O$	0
14	$Pd(OAc)_2$	**2g**	Toluene	CsF	40
15	$Pd(OAc)_2$	**2g**	Toluene	KOAc	7
16	$Pd(OAc)_2$	**2g**	Toluene	Cs_2CO_3	34
17	$Pd(OAc)_2$	**2g**	Toluene	K_3PO_4	47
18	**$Pd(OAc)_2$**	**2g**	**Toluene**	**K_2CO_3**	**97**

[a] Reaction conditions: Aryl chloride (1.0mmol), Boronic acid (1.5 mmol), Base (3mmol), 1mol% Pd, 1mol% Ligand, Solvent (3mL), at 110℃ under N_2 for 30mins. [b] Determined by calibrated GC analysis with dodecane as internal standard.

We firstly tested a number of cyclohexyl phosphine based ligands in the model reaction. Increase the steric bulkiness of *N*-substituted from methyl (entry 1) to *iso*-propyl (entry 2) gave a great product yield enhancement, however, to *tert*-butyl (entry 3) the yield sharply dropped. Increase the bottom ring size from 5- to 6- membered ring gave the best result (entry 4). While replacing the cyclohexyl by phenyl group, poorer levels of conversion were found (not shown in Table 3.2). An array of palladium sources (entries 6-9) was then examined. Reduced product yields were observed using common palladium sources other than $Pd(OAc)_2$. Thus the catalytic protocol was effective performed in the present of $Pd(OAc)_2$ and ligand **2g**. By replacing solvent toluene with tBuOH (entry 10), THF (entry 11), dioxane (entry 12), or DMF (entry 13) did not contribute to the reaction. No significant effect was observed in product formation by changing bases (entries 14-17). Nevertheless, K_2CO_3 (entry 18) was the best among other bases screened.

3.1.3. Examination the best metal-to-ligand ratio

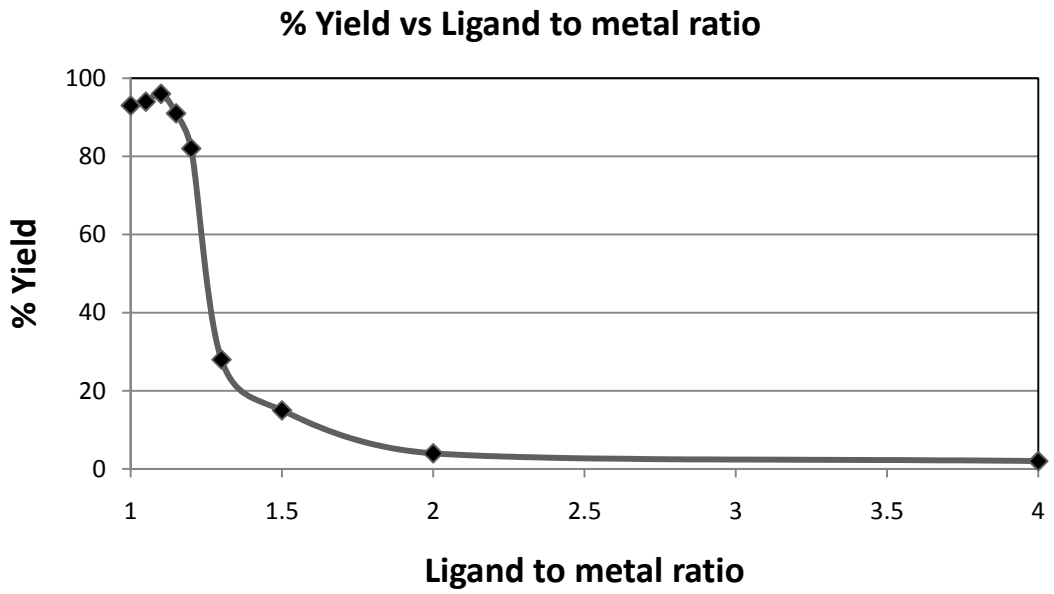


Figure 3.1: % Yield vs Ligand to metal ratio.

Reaction conditions: p-chlorotoluene (1.0 mmol), phenylboronic acid (1.5 mmol), K_2CO_3 (3.0 mmol), 1 mol% $Pd(OAc)_2$, **2g** (Pd/P atom as indicated), toluene (3 mL), at 110℃ under N_2 for 30 mins. Yield was determined by calibrated GC analysis with dodecane as internal standard.

After successful of tuning the reaction conditions, metal-to-ligand ratio was then investigated. Results were highly sensitive to ligand ratio (Figure 3.1) which was tested among 1 to 4. Notable, yields were suddenly decreased from 1.3. Thus the ligand amount was probably too high. All palladium vacant sites were fully coordinated to ligand. A deactivated saturated palladium species dose not enters catalytic cycles. As the ratio reduced to 1.1, the catalytic system

was highly effective. p-Chlorotoluene was nearly completely converted to biaryl product. The high accuracy of ligand ratio was required for effective Suzuki-Miyaura cross coupling. The coordination ability of hemilabile donor N atoms probably too strong, the Pd-N bond dose not easily be broken down.

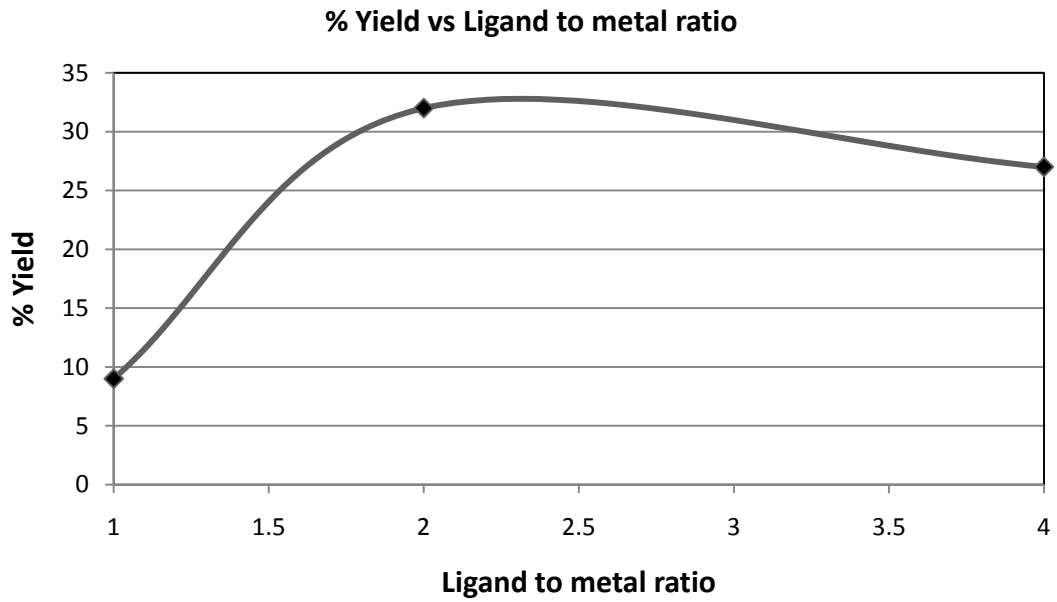


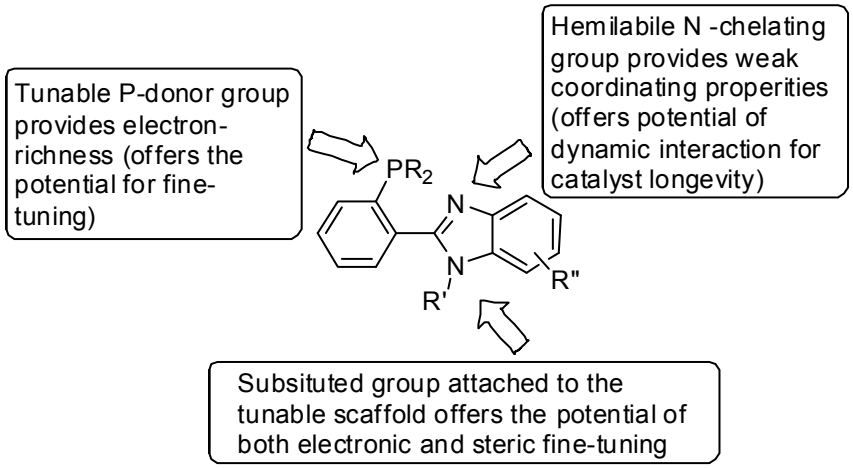
Figure 3.2: % Yield vs Ligand to metal ratio.

Reaction conditions: p-chlorotoluene (1.0 mmol), phenylboronic acid (1.5 mmol), K_2CO_3 (3.0 mmol), 0.1 mol% $Pd(OAc)_2$, **2g** (Pd/P atom as indicated), toluene (3 mL), at 110℃ under N_2 for 12h. Yield was determined by calibrated GC analysis with dodecane as internal standard.

The catalyst system picture was different in low palladium concentration circumstance. As Figure 3.2 demonstrated reversed results in 0.1 mol% $Pd(OAc)_2$, the highly effective ligand ratio around 1 was not observed here. However, ligand ratio among 2 to 4 gave similar results. We speculated that concentration effect plays a role for these interesting results. The ratio of substrate to catalyst enhancement led to high possibility of substrate coordination. Thus excess amount of ligand were needed. Based on these findings, this catalyst system is highly influenced by the substrate to catalyst ratio too.

3.1.4. Preparation of phenyl benzimidazolyl backbone ligands

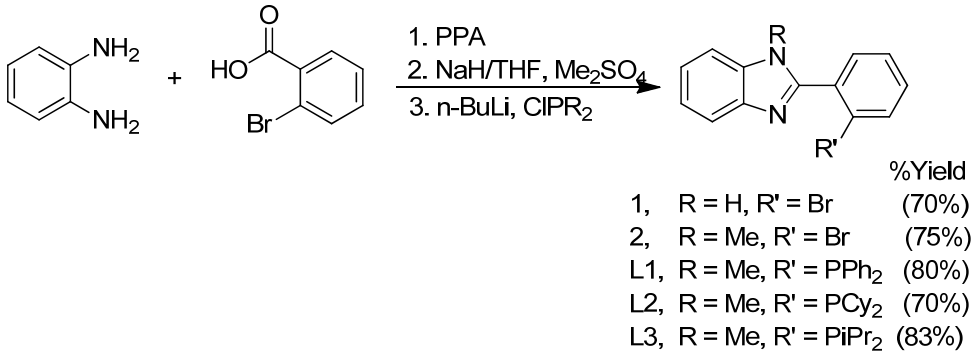
For the reason of strong N donor atoms, we attempted to weaken the nucleophilicity of N atoms by introducing the extended aromaticity. Benzimidazolyl scaffold consists of two N atoms in 5 member ring. This structure has planar and aromatic properties. Thus, this scaffold prevents two N atoms coordinated to metal vacant sites at the same time (Scheme 3.4).



Scheme 3.4: Strategic design of phenyl benzimidazolyl backbone ligands

Ligand precursor of this new class of benzimidazolyl phosphine ligands was efficiently synthesized from the condensation between the commercially available and inexpensive o-phenylenediamine and 2-bromobenzoic acid in the present of polyphosphoric acid.[5] Notably, 2-(2-bromophenyl)-1H-benzoimidazole can be easily synthesized at large scale with good yield but without any difficulties for the both synthesis and purification process. The ligand precursor was deprotonated with sodium hydride and strategically chosen the simplest methyl group as the substituent in order to rapid synthesize and examine the catalytic activity of this new class of ligand in this study. Finally, the methylated ligand precursors were than lithiated by *n*-BuLi and trapping the lithiated intermediate by $ClPR_2$ afforded the corresponding benzimidazolyl phosphines in good to excellence yields

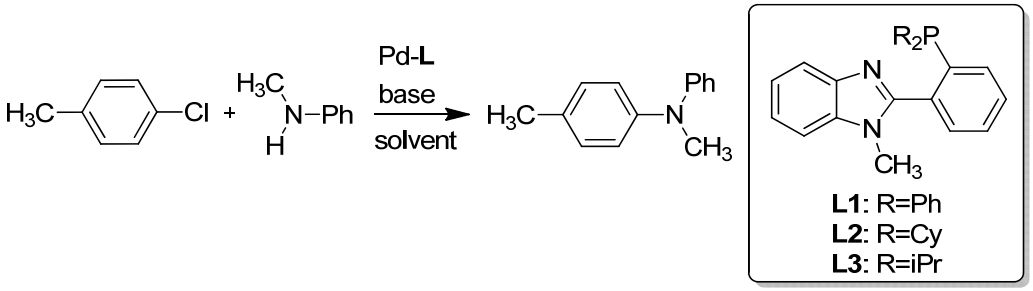
(Scheme 3.5). It is noteworthy to note that this class of ligand exhibits high air stability in both solid and solution states.[6] Large synthetic scale and easy purification of this new class of ligands is also attractive feature for the potential industrial applications.



Scheme 3.5:Synthetic pathways of the benzimidazolyl phosphine ligands

3.1.5. Initial screening of model reaction

Table 3.3: Screening of the effectiveness of the benzimidazolyl phosphine ligands[a]



entry	Pd source	Pd (mol%)	base	solvent	Yield (%)[b]
1[c]	$Pd(OAc)_2$	0.5	*t*-BuONa	Toluene	84
2[c]	$Pd(dba)_2$	0.5	*t*-BuONa	Toluene	86
3[c]	$Pd_2(dba)_3$	0.5	*t*-BuONa	Toluene	99
4[c]	$PdCl_2(CH_3CN)_2$	0.5	*t*-BuONa	Toluene	84
5[d]	$Pd(OAc)_2$	0.5	*t*-BuONa	Toluene	62
6[e]	$Pd(OAc)_2$	0.5	*t*-BuONa	Toluene	92
7	$Pd(OAc)_2$	0.5	*t*-BuONa	Toluene	96
8	$Pd(OAc)_2$	0.2	*t*-BuONa	Toluene	83
9	$Pd_2(dba)_3$	0.2	*t*-BuONa	Toluene	94
10	$Pd_2(dba)_3$	0.2	*t*-BuONa	Dioxane	93
11	$Pd_2(dba)_3$	0.1	*t*-BuONa	Toluene	74
12	$Pd_2(dba)_3$	0.1	*t*-BuONa	Dioxane	66
13	$Pd_2(dba)_3$	0.1	*t*-BuONa	*p*-Xylene	67
14	$Pd_2(dba)_3$	0.1	K_3PO_4	Toluene	65
15	$Pd_2(dba)_3$	0.2	K_3PO_4	Toluene	85
16	$Pd_2(dba)_3$	0.1	Cs_2CO_3	Toluene	34
17	$Pd_2(dba)_3$	0.1	K_2CO_3	Toluene	4
18[f]	$Pd_2(dba)_3$	0.2	*t*-BuONa	Toluene	1

19[g]	$Pd_2(dba)_3$	0.2	*t*-BuONa	Toluene	81

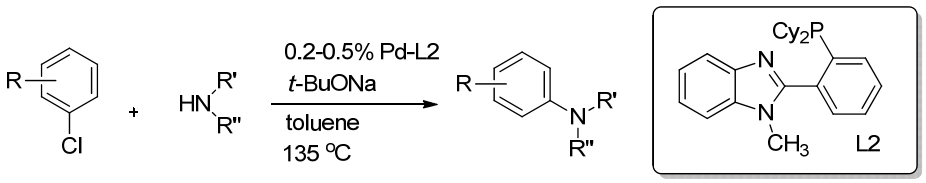
[a] Reaction conditions: Pd, ligand L2, Pd: L=1:4 ArCl (1.0 mmol), *N*-methylaniline (1.5 mmol), base (2.5 mmol), solvent (3.0 mL) were stirred for 20 h at 135 °C under N_2. [b] Calibrated GC yields were reported using dodecane as the internal standard. [c] Pd:L=1:2. [d] Pd:L=1:1. [e] Pd:L=1:3. [f] Ligand=L1. [g] Ligand=L3.

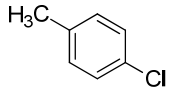
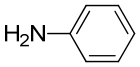
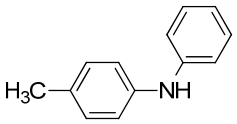
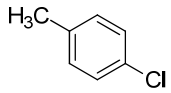
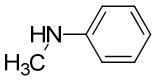
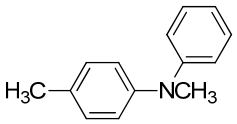
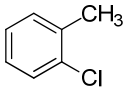
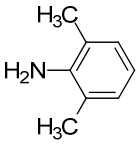
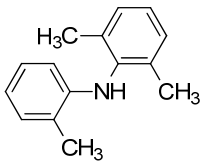
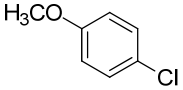
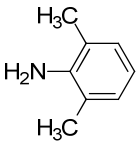
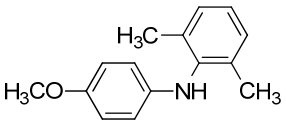
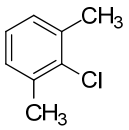
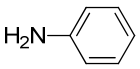
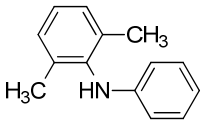
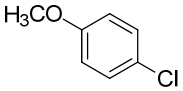
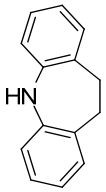
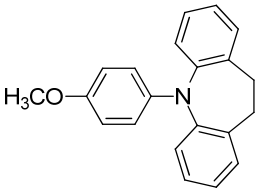
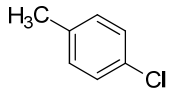
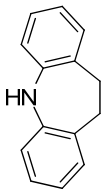
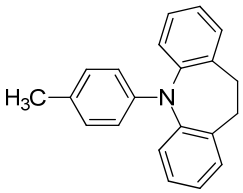
To test the effectiveness of the new ligands, amination of 4-chlorotoluene with *N*-methylaniline were used as the model entry. A catalyst loading of 0.5 mol% Pd was initially applied in probing the ligand efficacy (Table 3.3). The metal to ligand ratio and metal sources were subsequently investigated using toluene as the solvent and *t*-BuONa as the base. For the metal source, $Pd_2(dba)_3$ gave the best result among $Pd(OAc)_2$, $Pd(dba)_2$, $Pd_2(dba)_3$, and $PdCl_2(CH_3CN)_2$ (entries 1-4). Upon investigating the metal/ligand ratio from 1:1 to 1:4, the ratio of 1:4 provided the highest yield (entries 1, 5-7). The use of $Pd_2(dba)_3$ and metal/ligand ratio 1:4 were then choose for the further screening process. Among the commonly used organic solvents examined, toluene gave the best result (entries 9-13). Moreover, using higher boiling point solvent cannot improve the desired yield (entry 13). Several bases were examined in the presence of ligand **L2**.

t-BuONa were found to be the best base of choice in this catalytic system (entries 11, 14-17). It is worthy to note that K_3PO_4 was also an effective base in this system. It is important for the substrates that containing reactive functional groups such as keto and esters. Ligand **L1** with a diphenylphosphino moiety provided trace conversion while the dicyclohexylphosphino analogue, **L2**, gave the best catalytic activity (entries 9, 18-19). Ligand **L3** bearing a diisopropylphosphino moiety showed a lower catalytic activity towards the amination reaction.

3.1.6. Amination of ArCl with aromatic amines

Table 3.4: Palladium-catalyzed amination of ArCl and aromatic amine[a]



entry	ArCl	Amine	Product	Pd (mol%)	Yield (%)[b]
1				0.2	99
2				0.2	90
3				0.2	99
4				0.2	90
5[c]				0.5	90
6				0.2	99
7				0.2	94

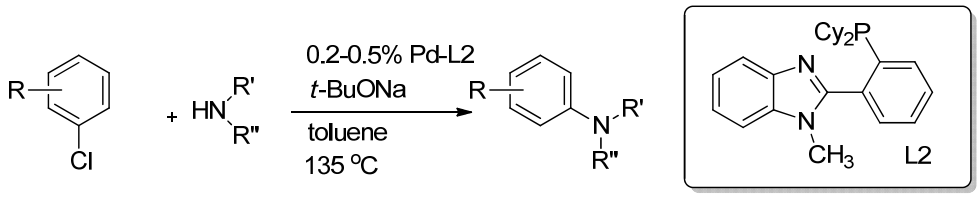
[a] Reaction conditions: ArCl (1.0 mmol), Amine (1.5 mmol), *t*-BuONa (2.5 mmol), $Pd_2(dba)_3$/L2 = 1:4, Toluene (3.0 mL) were stirred for 20 h at 135 °C

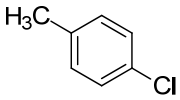
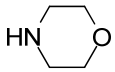
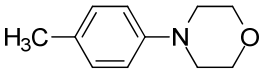
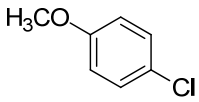
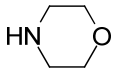
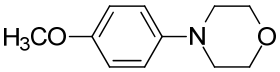
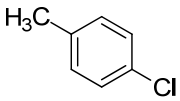
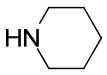
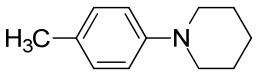
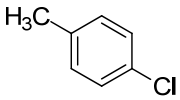
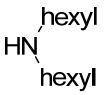
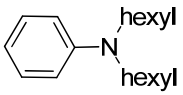
under N_2. [b] Isolated yields. [c] Reaction time was 24 h.

The preliminary optimized reaction conditions were employed for the amination of aryl chlorides with aromatic amines (Table 3.4). Aniline and *N*-methylaniline were effective substrates to give the corresponding products in excellent yields (entries 1-2). Amination of deactivated aryl chloride were not diminishing the desired product yields compare with the amination of neutral aryl chloride. (entry 3) Amination of sterically hindered aryl chlorides with/or bulky amines were proceed smoothly. (entries 5-7)

3.1.7. Amination of ArCl with aliphatic amines

Table 3.5: Palladium-catalyzed amination of ArCl and aliphatic amine[a]



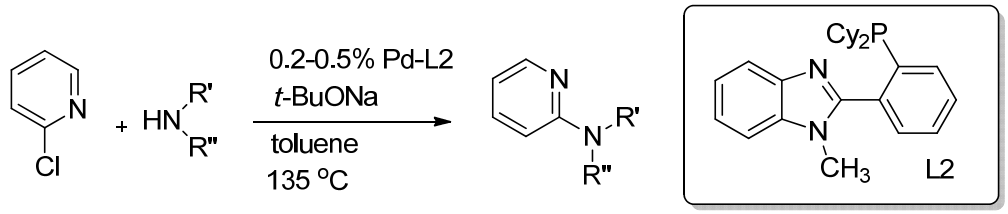
entry	ArCl	Amine	Product	Pd (mol%)	Yield (%)[b]
1				0.2	90
2				0.2	90
3				0.5	85
4				0.5	81

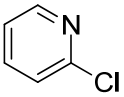
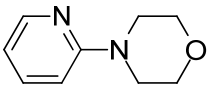
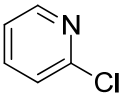
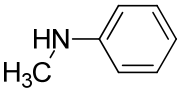
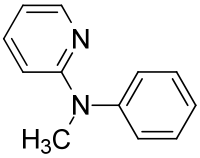
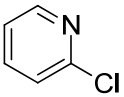
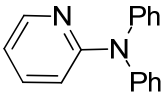
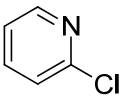
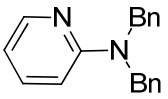
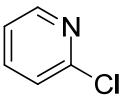
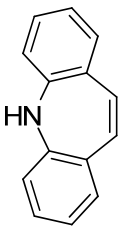
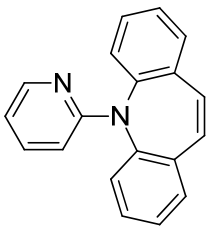
[a] Reaction conditions: ArCl (1.0 mmol), Amine (1.5 mmol), *t*-BuONa (2.5 mmol), $Pd_2(dba)_3$/L2 = 1:4, Toluene (3.0 mL) were stirred for 20 h at 135 °C under N_2. [b] Isolated yields.

The reactivity of Pd-**L2** system towards the amination of arylchlorides with cyclic and aliphatic amines was examined (Table 3.5). Morpholine and piperidine show excellent reactivity in the amination reaction (entries 1-3). Difficult amines such as dibenzylamine were also compatible in this system (entry 4).

3.1.8. Amination of heteroaryl and functionalized aryl chlorides

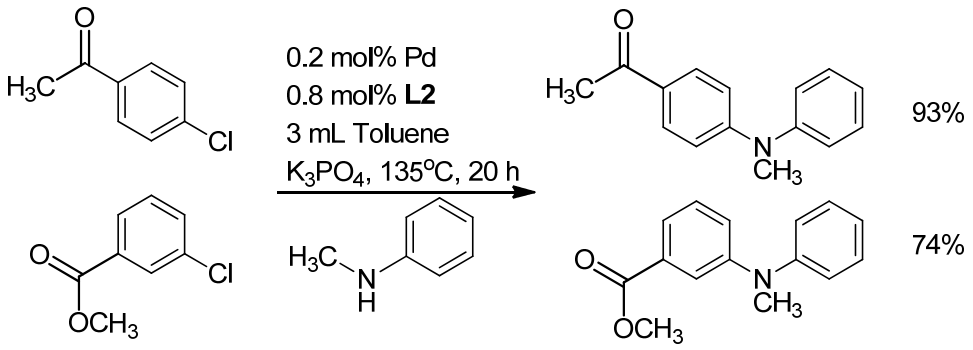
Table 3.6: Palladium-catalyzed amination of heteroaryl chloride[a]



entry	ArCl	Amine	Product	Pd (mol%)	Yield (%)[b]
1[c]				0.2	92
2[c]				0.2	99
3				0.5	98
4				0.5	95
5				0.5	97

[a] Reaction conditions: ArCl (1.0 mmol), Amine (1.5 mmol), *t*-BuONa (2.5 mmol), $Pd_2(dba)_3$/L2 = 1:4, Toluene (3.0 mL) were stirred for 24 h at 135 °C under nitrogen. [b] Isolated yields. [c] Reaction time was 20 h.

Apart from non-functionalized aryl chlorides, the coupling of heteroaryl chloride was also studied. The results showed that the heteroaryl chlorides are also effective substrate for amination reaction (Table 3.6). Under 0.5 mol% Pd loading conditions, cyclic, aromatic and aliphatic amines were transformed to corresponding products in excellent yields.



Scheme 3.6: Palladium-catalyzed amination of functionalized arylchloride

Functional group compatibility is one of the major concerns for accounting the effectiveness of an amination system since one of the important applications of amination reaction is to synthesize pharmaceutically useful intermediates that usually contain reactive functional groups. In this system, using K_3PO_4 as base, reactive functional groups such as keto and ester were also compatible and gave the desired products in good yield (Scheme 3.6)

3.2. Conclusion

In summary, we have developed a new series of efficient hemilabile phosphine ligands. These ligands can be easily synthesized in large scale using inexpensive and commercially available starting materials. Palladium complexes derived from these ligands provide highly active catalysts for amination of aryl chlorides with aromatic and aliphatic amines. Functional groups such as keto and ester were compatible in the use of K_3PO_4 as base. In view of the simplicity of the ligand synthesis as well as the high potential in modifying the ligand skeleton, we anticipate that further enhancements in reactivity and versatility of the ligand series will be attainable.

3.3. Experimental section

3.3.1. General procedures for initial screening and metal-to-ligand ratio of phenyl imidazolidine backbone ligands

General procedures for initial screening and metal-to-ligand ratio for phenyl

imidazolidine backbone ligands: Pd source (0.010 mmol), ligand (mol% as indicated), and base (3 mmol) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The tube was evacuated and flushed with nitrogen for several times. Aryl chloride (1.0 mmol) and solvent (3 mL) were loaded into the tube. The tube was stirred at room temperature for several minutes. Boronic acid (1.5 mmol) was then added. The tube was stirred at room temperature for several minutes and then placed into a preheated oil bath (110 ℃) for times as indicated. After completion of reaction, the reaction tube was allowed to cool to room temperature. EtOAc (~10 mL), dodecane (227 μL, internal standard) and water were added. The organic layer was subjected to GC analysis. The GC yield obtained was previously calibrated by authentic sample / dodecane calibration curve.

3.3.2. General procedures for initial ligand and reaction conditions screening of phenyl benzoimidazole backbone ligands

General procedure for screening: $Pd_2(dba)_3$ (0.023 g, 0.10 mmol) and ligand L (Pd:L = 1:4) were loaded into a reaction tube equipped with a

Teflon-coated magnetic stir bar. The tube was evacuated and flushed with nitrogen (3 cycles). A stock solution was prepared by adding 5.0 mL freshly distilled toluene. Bases (2.5 mmol) were loaded into an array of Schlenk tubes. The tubes were evacuated and flushed with nitrogen (3 cycles). 4-chlorotoluene (1.0 mmol), *N*-methylaniline (1.5 mmol) and the stock solution (0.1mol% Pd per 0.5 mL stock solution) were loaded into the tubes. Toluene was then added to give a total volume of 3.0 mL in each tube. The solutions were stirred at room temperature for several minutes and then placed into a preheated oil bath (135℃) for 20 hours. After completion of reaction, the reaction tube was allowed to cool to room temperature. Ethyl acetate (~10 mL), dodecane (227 μL, internal standard) and water were added. The organic layer was subjected to GC analysis. The GC yield obtained was previously calibrated by authentic sample/dodecane calibration curve.

3.3.3. General procedures for amination of aryl chlorides

General procedure for amination of aryl chloride: A stock solution of $Pd_2(dba)_3$ (0.023 g, 0.10 mmol) and ligand L (Pd:L = 1:4) were loaded into a reaction tube

equipped with a Teflon-coated magnetic stir bar. The tube was evacuated and flushed with nitrogen (3 cycles). A stock solution was prepared by adding 5.0 mL freshly distilled toluene. Bases (2.5 mmol) were loaded into an array of Schlenk tubes. The tubes were evacuated and flushed with nitrogen (3 cycles). Aryl chlorides (1.0 mmol), amines (1.5 mmol) and the stock solution (0.1mol% Pd per 0.5 mL stock solution) were loaded into the tubes. Toluene was then added to give a total volume of 3.0 mL in each tube. The solutions were stirred at room temperature for several minutes and then placed into a preheated oil bath (135℃) for the time period as indicated in Tables. After completion of reaction as judged by GC analysis, the reaction tube was allowed to cool to room temperature and quenched with water and diluted with EtOAc. The organic layer was separated and the aqueous layer was washed with EtOAc. The filtrate was concentrated under reduced pressure. The crude products were purified by flash column chromatography on silica gel (230-400 mesh) to afford the desired product.

3.4. Reference

(1) Liu, Z.-J.; Vors, J.-P.; Gesing, E. R. F.; Bolm, C. *Green Chemistry* **2011**, *13*, 42.

(2) Bei, X.; Uno, T.; Norris, J.; Turner, H. W.; Weinberg, W. H.; Guram, A. S.; Petersen, J. L. *Organometallics* **1999**, *18*, 1840.

(3) Braunstein, P.; Naud, F. *Angewandte Chemie International Edition* **2001**, *40*, 680.

(4) Bassetti, M. *European Journal of Inorganic Chemistry* **2006**, *2006*, 4473.

(5) According to the list price from Aldrich (21-2-2011), o-phenylenediamine is cost 0.18 USD/G and 2-bromobenzoic acid is cost 0.88 USD/G.

(6) There were no detectable phosphine oxide signal of L2 from 31P NMR, when the solid-form ligand was stand under air for a month.

Chapter 4: Summary

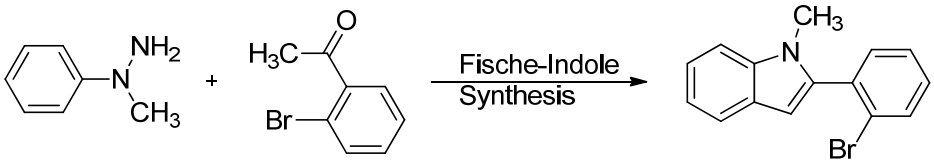
In conclusion, efficient, mild, and general catalytic methods for palladium-catalyzed amination of aryl tosylates have been investigated. The substrate scopes are expanded to functionalized aryl tosylates, aryl/alkyl amines, and optically active α-substituted amines. The reaction medium is not restricted to organic solvent, solvent-free and aqueous conditions are also found to be efficient described. The catalyst loading is generally low with good to excellent product yields.

As for ligand development, phenyl imidazolidine backbone ligands are less effective. Modified phenyl benzoimidazole ligands scaffolds are effective for coupling of primary and secondary aryl/alkyl amines. Good to excellent yields of the desired products can be achieved in low catalyst loading (down to 0.1 mol% Pd).

Appendix

1. Supporting data for chapter 2

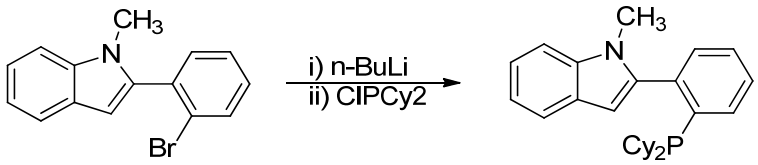
1.1. Preparation of indolyl phosphine liagnd



General procedure for Fischer-indole synthesis:[1] 2'-Bromoacetophenone (1.31 mL, 10 mmol) was mixed with *N*-methylphenylhydrazine (1.3 mL, 11 mmol) in phosphoric acid (5 mL) and stirred at room temperature for 30 min. PPA (25-30 g) was added to the mixture and an exothermic reaction ensured whereupon the mixture was heated slowly to 120 ℃ and kept at this temperature for 1 h. The mixture was poured into ice water and then extracted with Et_2O (3 x ~150 mL). The organic phases were combined, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was filtered through a short silica pad (3 x ~10 cm) and washed with hexane then EA/Hexane (1:9). The solution was evaporated to yield a light yellow solid. Small amount of cold hexane was used to further wash the product. The product was then dried under vacuum to

afford *N*-methyl-2-(2'-bromophenyl)indole (2.35 g, 75%) as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.61 (s, 3H), 6.56 (s, 1H), 7.20-7.45 (m, 6H), 7.70-7.75 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.5, 102.0, 109.4, 119.7, 120.6, 121.6, 125.0, 127.1, 127.5 130.0, 132.6 132.7, 134.1, 137.1, 139.5; IR (cm-1) 3049.43, 2933.63, 1536.35, 1457.76, 1431.08, 1382.94, 1337.55, 1309.58, 1164.78, 1061.55, 1023.56, 791.60, 749.44, 662.83, 578.63, 536.74, 454.92; MS (EI): *m/z* (relative intensity) 285 (M^+, 100), 204 (75), 190 (10), 178 (20).

_N_-Methyl-2-(2'-Dicyclohexylphosphinophenyl)indole (CMPhos)

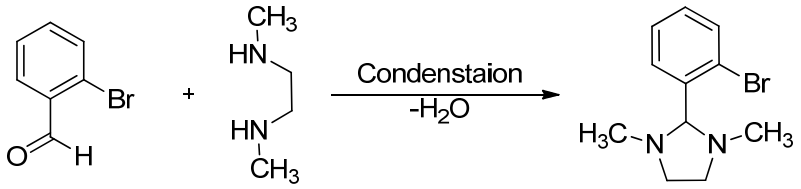


General procedure for ligand synthesis: *N*-methyl-2-(2'-bromophenyl)indole (2.2 g, 7.7 mmol) was dissolved in freshly distilled THF (25 mL) at room temperature under a nitrogen atmosphere. The solution was cooled to -78 °C in dry ice/acetone bath. Titrated *n*-BuLi (8.47 mmol) was added dropwise by syringe. After the reaction mixture was stirred for 30 min at -78 ℃, chlorodicyclohexylphosphine (1.87 mL, 8.47 mmol) in THF (5 mL) was

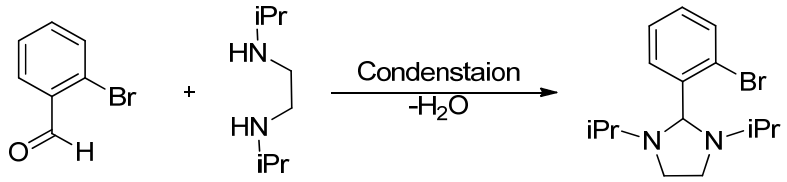
added. The reaction was allowed to warm to room temperature and stirred overnight. Solvent was removed under reduced pressure. After the solvent was removed under vacuum, the product was successively washed with cold MeOH/EtOH mixture. The product was then dried under vacuum. White solid of *N*-methyl-2-(2'-dicyclohexylphosphinophenyl)indole **(CMPhos)** (2.75g, 88%) were obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20-1.80 (m, 22H), 3.53 (s, 3H), 6.44 (s, 1H), 7.15 (t, *J* = 7.4 Hz, 1H), 7.24-7.27 (m, 1H), 7.36-7.50 (m, 4H), 7.66 (d, *J* =7.7 Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$) δ 25.5, 26.2, 27.1, 28.9, 29.3, 29.5, 30.1, 30.7, 103.2, 109.3, 119.3, 120.2 121.0, 127.6, 127.8, 128.0, 128.2, 128.4, 131.8, 131.9, 132.7, 136.6 (unresolved complex C-P splittings were observed); ^{31}P NMR (162 MHz, C_6D_6) δ -9.87; MS (EI): *m/z* (relative intensity) 403 (M^+, 25), 348 (5), 321 (30), 238 (100), 222 (30), 207 (20).

2. Supporting data for chapter 3

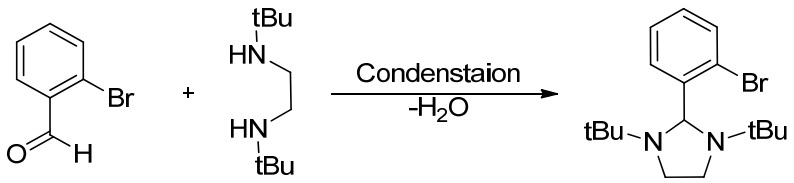
2.1. Preparation of phenyl imidazolidine backbone ligands



2-(2-bromophenyl)-1,3-dimethylimidazolidine (1a): A solution of 2-Bromobenzaldehyde (2.33 mL, 20 mmol), *N,N'*-dimethylehtylenediamine (2.36 mL, 22 mmol) and anhydrous toluene (40 mL) was heated at reflux for 6 h using a Dean Stark setup to remove water. The mixture was extracted with Et_2O (100 mL) and 0.5M NaOH (3 x 100 mL). The organic phases were dried over Na_2SO_4 and concentrated under vacuum to afford 2-(2-bromophenyl)-1,3-dimethylimidazolidine (3.77 g, 75%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.22 (s, 6H), 2.61-2.65 (m, 2H), 3.35-3.39 (m, 2H), 4.06 (s, 1H), 7.12-7.16 (m, 1H), 7.31-7.35 (m, 1H), 7.49-7.51 (m, 1H), 7.70-7.73 (m, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 39.4, 53.5, 88.3, 125.5, 127.9, 129.6, 131.0, 132.2, 138.7; MS (EI): *m/z* (relative intensity) 225 (M^+, 27), 253 (27), 212 (17), 210 (17), 99 (100).

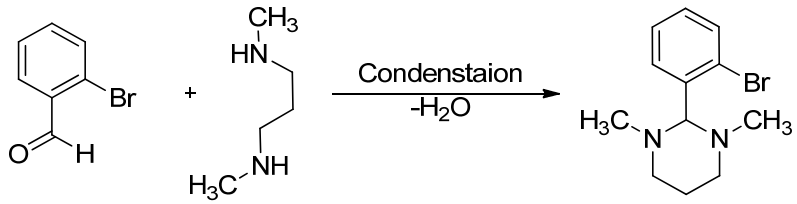


2-(2-bromophenyl)-1,3-diisopropylimidazolidine (1b): Similar procedure for the synthesis of 1a were followed. 2-Bromobenzaldehyde (2.33 mL, 20 mmol) and *N,N'*-diisopropylehtylenediamine (3.97 mL, 22 mmol) were used to afford 2-(2-bromophenyl)-1,3-diisopropylimidazolidine (4.68 g, 75%) as a reddish oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (d, J = 6.8 Hz, 6H), 1.00 (d, J = 6.4 Hz, 6H), 2.72-2.75 (m, 2H), 2.81-2.82 (m, 2H), 3.16-3.17 (m, 2H), 4.70 (s, 1H), 7.07-7.11 (m, 1H), 7.26-7.27 (m, 1H), 7.29-7.31 (m, 1H), 7.31-7.44 (m, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 16.7, 22.0, 44.6, 48.0, 78.9, 124.8, 127.5, 128.9, 131.7, 132.1, 142.7; MS (EI): *m/z* (relative intensity) 311 (M^+, 5), 309 (5), 240 (5), 238 (5), 155 (100); HRMS: cald. for $C_{15}H_{23}N_2BrH^+$: 311.1123, found 311.1119.



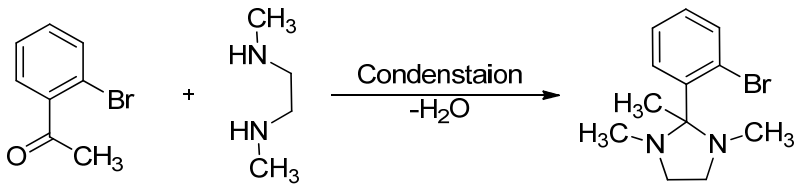
2-(2-bromophenyl)-1,3-di-*tert*-butylimidazolidine (1c): Similar

procedure for the synthesis of 1a were followed. 2-Bromobenzaldehyde (2.33 mL, 20 mmol) and *N,N'*-di-*tert*-butylehtylenediamine (4.74 mL, 22 mmol) were used to afford 2-(2-bromophenyl)-1,3-di-*tert*-butylimidazolidine (5.35 g, 79%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.03 (s, 18H), 2.95-2.98 (m, 2H), 3.23-3.27 (m, 2H), 4.91 (s, 1H), 7.00-7.04 (m, 1H), 7.27-7.30 (m, 1H), 7.33-7.35 (m, 1H), 7.81-7.83 (m, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 27.7, 47.1, 53.9, 75.3, 123.0, 127.2, 127.8, 131.7, 133.0; MS (EI): *m/z* (relative intensity) 339 (M^+, 0), 269 (12), 267 (12), 183 (100), 127 (11), 71 (32); HRMS: cald. for $C_{17}H_{27}N_2BrH^+$: 339.1436, found 339.1426.



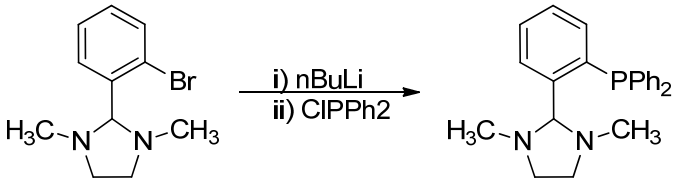
2-(2-bromophenyl)-1,3-dimethylhexahydropyrimidine (1d): Similar procedure for the synthesis of 1a were followed. 2-Bromobenzaldehyde (2.33 mL, 20 mmol) and *N,N'*-dimethyl-1,3-propanediamine (2.75 mL, 22 mmol) were used to afford 2-(2-bromophenyl)-1,3-dimethylhexahydropyrimidine (4.23 g, 79%) as a milky oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.61-1.65 (m, 1H), 1.94 (s, 6H),

2.02-2.14 (m, 1H), 2.19-2.26 (m, 2H), 3.01-3.06 (m, 2H), 3.68 (s, 1H), 7.10-7.14 (m, 1H), 7.31-7.34 (m, 1H), 7.48-7.50 (m, 1H), 7.707.72 (m, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 25.1, 41.9, 55.4, 87.7, 125.4, 128.0, 138.2, 130.7, 131.9, 140.1; MS (EI): *m/z* (relative intensity) 269 (M^+, 12), 267 (12), 198 (17), 196 (17), 113 (100); HRMS: cald. for $C_{12}H_{17}N_2BrH^+$: 269.0653, found 269.0644.



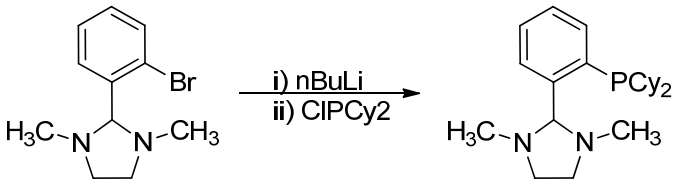
2-(2-bromophenyl)-1,2,3-trimethylimidazolidine (1e): A solution of 2'-Bromoacetophenone (2.69 mL, 20 mmol), *N,N'*-dimethylehtylenediamine (21.45 mL, 100 mmol) and acetic acid (0.2 mL, 3.5 mmol) was mixed into a reaction tube and stirred at room temperature for 2 d. The mixture was extracted with Et_2O (mL) and 0.5M NaOH (3 x mL). The organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The product was separated through fractional distillation to afford 2-(2-bromophenyl)-1,2,3-trimethylimidazolidine (2.41 g, 45%) as a yellowish oil. ^{1}H NMR (400 MHz, C_6D_6) δ 1.30 (s, 3H), 2.07 (s, 6H),

2.53-2.57 (m, 2H), 3.07-3.11 (m, 2H), 6.72-6.76 (m, 1H), 6.96-7.00 (m, 1H), 7.52-7.54 (m, 1H), 7.59-7.61 (m, 1H); ^{13}C NMR (100MHz, C_6D_6) δ 14.1, 35.6, 36.2, 51.1, 51.4, 82.5, 123.2, 126.2, 127.1, 128.4, 128.8, 130.7, 131.2, 133.5, 136.0, 142.6; MS (EI): *m/z* (relative intensity) 269 (M^+, 0), 255 (33), 253 (33), 226 (98), 224 (100), 214 (84), 212 (88); HRMS: cald. for $C_{12}H_{17}N_2BrH^+$: 269.0653, found 269.0643.



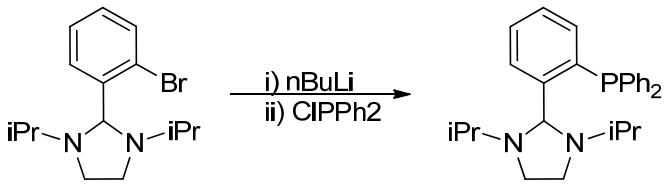
2-(2-(diphenylphosphino)phenyl)-1,3-dimethylimidazolidine (2a): 2-(2-bromophenyl)-1,3-dimethylimidazolidine (1.02 mL, 4 mmol) was dissolved in freshly distilled THF (10 mL) at room temperature under a nitrogen atmosphere. The solution was cooled to -78 °C in dry ice/acetone bath. Titrated *n*-BuLi (4.4 mmol) was added dropwise by syringe. After the reaction mixture was stirred for 30 min at -78 ℃, chlorodiphenylphosphine (0.83 mL, 4.4 mmol) in THF (7 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 crystal of

2-(2-(diphenylphosphino)phenyl)-1,3-dimethylimidazolidine (0.66 g, 46%) was obtained by recrystallization. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.05 (s, 6H), 2.56-2.60 (m, 2H), 3.38-3.42 (m, 2H), 4.52 (d, *J* =7.2 Hz, 1H), 6.97-7.00 (m, 1H), 7.21-7.36 (m, 10H), 7.40-7.44 (m, 1H), 7.27-7.36 (m, 10H), 7.40-7.44 (m, 1H), 7.78-7.82 (m, 1H), ; ^{13}C NMR (100MHz, $CDCl_3$) δ 39.4, 53.5, 86.9, 87.1, 128.2, 128.3, 128.4, 128.5, 129.2, 129.3, 129.5, 133.5, 133.8, 140.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ -19.14; MS (EI): *m/z* (relative intensity) 360 (M^+, 11), 359 (33), 283 (39), 173 (100); HRMS: cald. for $C_{23}H_{25}N_2PH^+$: 361.1834, found 361.1848.



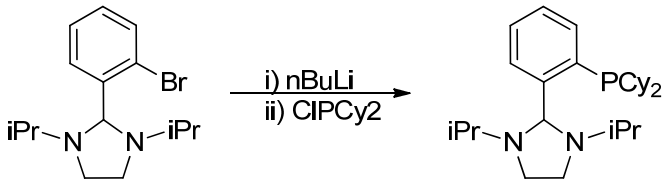
2-(2-cyclohexylphosphino)phenyl)-1,3-dimethylimidazolidine (2b): Similar procedure for the synthesis of 2a were followed. 2-(2-bromophenyl)-1,3-dimethylimidazolidine (1.02 mL, 4 mmol), chlorodicyclohexylphosphine (1.0 mL, 4.4 mmol) were used to afford 2-(2-cyclohexylphosphino)phenyl)-1,3-dimethylimidazolidine (0.66 g, 46%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98-1.30 9m, 11H), 1.49-1.76 (m, 9H), 1.86-1.93 (m, 4H), 2.20 (s, 6H), 2.63-2.64 (m, 2H), 3.37-3.38 (m,

2H), 4.85 (d, *J* = 8.0Hz, 1H), 7.25-7.29 (m, 1H), 7.36-7.40 (m, 1H), 7.45-7.48 (m, 1H), 7.79-7.82 (m, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 9.0, 25.8, 26.4, 27.1, 27.2, 27.3, 29.6, 29.7, 31.0, 31.1, 35.4, 35.5, 39.6, 53.4, 56.0, 85.1, 85.3, 127.2, 129.2, 129.3, 131.9, 132.0, 136.1, 136.3, 146.7, 146.9; ^{31}P NMR (162 MHz, $CDCl_3$) δ -20.22; MS (EI): *m/z* (relative intensity) 372 (M+, 1), 290 (20), 289 (100), 205 (13), 173 (19); HRMS: cald. for $C_{23}H_{37}N_2PH^+$: 373.2773, found 373.2756.



2-(2-(diphenylphosphino)phenyl)-1,3-diisopropylimidazolidine (2c): Similar procedure for the synthesis of 2a were followed. 2-(2-bromophenyl)-1,3-diisopropylimidazolidine (1.04 mL, 4 mmol), chlorodiphenylphosphine (0.83 mL, 4.4 mmol) were used to afford 2-(2-(diphenylphosphino)phenyl)-1,3-diisopropylimidazolidine (0.75 g, 45%). ^{1}H NMR (400 MHz, C_6D_6) δ 0.89 (d, *J* = 6.0Hz, 6H), 0.94 (d, *J* = 6.8Hz, 6H), 2.66-2.70 (m, 2H), 2.81-2.87 (m, 2H), 3.11-3.15 (m, 2H), 5.44 (d, *J* = 8.0Hz, 1H), 6.96-7.08 (m, 7H), 7.20-7.26 (m, 2H), 7.36-7.40 (m, 4H), 8.13-8.16 (m, 1H); ^{13}C NMR (100MHz, C_6D_6) δ 15.0, 15.1, 22.4,

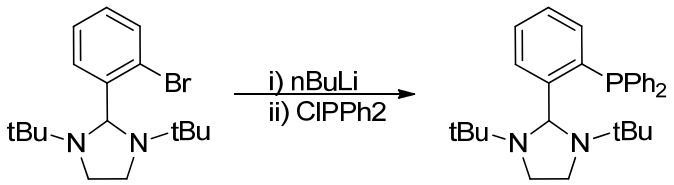
43.4, 46.9, 77.6, 77.8, 127.7, 128.2, 128.3, 128.4, 129.2, 130.6, 130.7, 133.6, 133.8, 134.1, 134.2, 136.6, 136.8, 138.5, 138.6, 149.9, 150.1; ^{31}P NMR (162 MHz, C_6D_6) δ -19.55; MS (EI): *m/z* (relative intensity) 416 (M^+, 14), 415 (41), 372 (56), 339 (58), 229 (100); HRMS: cald. for $C_{27}H_{33}N_2PH^+$: 417.2460, found 417.2465.



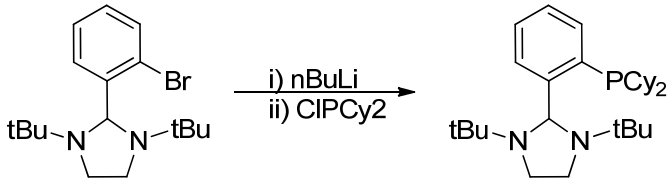
2-(2-(dicyclohexylphosphino)phenyl)-1,3-diisopropylimidazolidine

(2d): Similar procedure for the synthesis of 2a were followed. 2-(2-bromophenyl)-1,3-diisopropylimidazolidine (1.04 mL, 4 mmol), chlorodicyclohexylphosphine (1.0 mL, 4.4 mmol) were used to afford 2-(2-(dicyclohexylphosphino)phenyl)-1,3-diisopropylimidazolidine (0.51 g, 30%). ^{1}H NMR (400 MHz, C_6D_6) δ 1.03 (d, *J* = 6.8Hz, 6H), 1.13-1.40 (m, 17H), 1.55-1.73 (m, 8H), 1.82-1.88 (m, 2H), 2.01-2.05 (m, 2H), 2.74-2.75 (m, 2H), 2.97-3.00 (m, 2H), 3.11-3.12 (m, 2H), 7.09-7.13 (m, 1H), 7.28-7.32 (m, 1H), 7.38-7.41 (m, 1H), 8.27-8.28 (m, 1H); ^{13}C NMR (100MHz, C_6D_6) δ 15.3, 15.4, 22.7, 26.5, 27.2, 27.3, 27.4, 27.5, 30.4, 30.5, 31.0, 31.2, 36.2, 36.4, 42.7, 46.0, 76.0, 76.2, 126.7, 128.9, 130.8, 130.9,

131.0, 136.4, 136.6, 151.2, 151.4; ^{31}P NMR (162 MHz, C_6D_6) δ -18.63; MS (EI): *m/z* (relative intensity) 248 (M^+, 1), 427 (4), 385 (7), 345 (100), 229 (13).

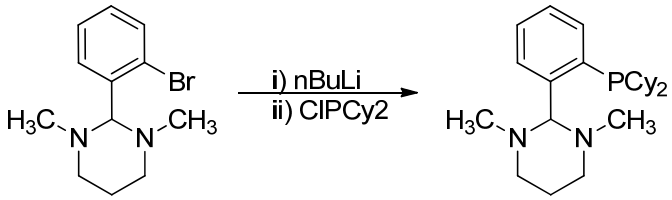


1,3-di-*tert*-butyl-2-(2-(diphenylphosphino)phenyl)imidazolidine (2e): Similar procedure for the synthesis of 2a were followed. 2-(2-bromophenyl)-1,3-di-*tert*-butylimidazolidine (1.15 mL, 4 mmol), chlorodiphenylphosphine (0.83 mL, 4.4 mmol) were used to afford 1,3-di-*tert*-butyl-2-(2-(diphenylphosphino)phenyl)imidazolidine (0.51 g, 28%). ^{1}H NMR (400 MHz, C_6D_6) δ 0.92 (s, 18H), 2.75-2.79 (m, 2H), 3.43 (bs, 2H), 6.92-6.96 (m, 1H), 7.02-7.12 (m, 7H), 7.40-7.73 (m, 1H), 7.46-7.50 (m, 5H); ^{13}C NMR (100MHz, C_6D_6) δ 27.8, 46.9, 47.0, 54.1, 126.6, 128.1, 128.2, 128.3, 131.4, 131.5, 133.4, 133.6, 136.9, 140.0, 140.2; ^{31}P NMR (162 MHz, C_6D_6) δ -17.75; MS (EI): *m/z* (relative intensity) 444 (M^+, 1), 387 (100), 331 (52), 302 (51), 288 (77), 183 (57); HRMS: cald. for $C_{29}H_{37}N_2PH^+$: 445.2773, found 445.2787.



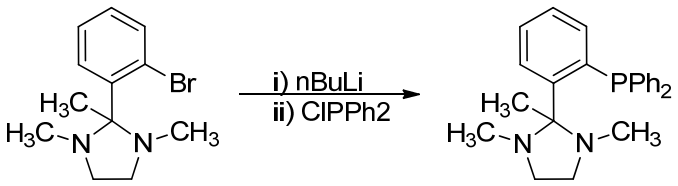
1,3-di-*tert*-butyl-2-(2-(dicyclohexylphosphino)phenyl)imidazolidine

(2f): Similar procedure for the synthesis of 2a were followed. 2-(2-bromophenyl)-1,3-di-*tert*-butylimidazolidine (1.15 mL, 4 mmol), chlorodicyclohexylphosphine (1.0 mL, 4.4 mmol) were used to afford 1,3-di-*tert*-butyl-2-(2-(dicyclohexylphosphino)phenyl)imidazolidine (0.51 g, 28%). ^{1}H NMR (400 MHz, C_6D_6) δ 0.90-1.19 (m, 24H), 1.50-1.90 (m, 16H), 2.54 (s, 2H), 3.39 (s, 1H), 7.09-7.20 (m, 3H), 7.38-7.39 (m, 1H), 8.09 (s, 1H), 11.36 (s, 1H); ^{13}C NMR (100MHz, C_6D_6) δ26.2, 26.7, 27.0, 27.4, 27.5, 27.8, 27.9, 28.9, 30.3, 36.2, 43.1, 46.9, 54.4, 125.9, 132.1; ^{31}P NMR (162 MHz, C_6D_6) δ -21.72; MS (EI): *m/z* (relative intensity) 456 (M^+, 2), 399 (100), 373 (30), 358 (30), 343 (32), 314 (79), 300 (49).



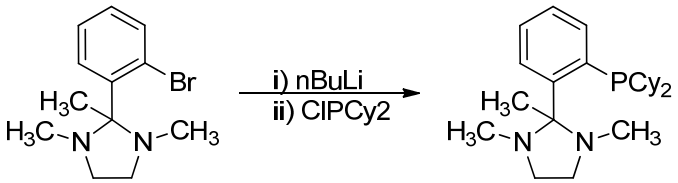
2-(2-(dicyclohexylphosphino)phenyl)-1,3-dimethylhexahydropyrimidi ne (2g): Similar procedure for the synthesis of 2a were followed. 2-(2-bromophenyl)-1,3-dimethylhexahydroprimidine (0.83 mL, 4 mmol),

chlorodicyclohexylphosphine (1.0 mL, 4.4 mmol) were used to afford 2-(2-(dicyclohexylphosphino)phenyl)-1,3-dimethylhexahydropyrimidine (0.81 g, 49%). ^{1}H NMR (400 MHz, C_6D_6) δ 1.09-1.41 (m, 13H), 1.60-1.74 (m, 9H), 1.85-1.92 (m, 2H), 2.00-2.35 (m, 13H), 2.89-2.92 (m, 2H), 4.88-4.90 (m, 1H), 7.09-7.13 (m, 1H), 7.23-7.27 (m, 1H), 7.41-7.43 (m, 1H), 8.23-8.24 (m, 1H); ^{13}C NMR (100MHz, C_6D_6) δ 24.6, 26.5, 27.2, 27.3, 27.4, 27.5, 30.5, 30.6, 31.1, 31.2, 36.1, 36.3, 42.6, 55.7, 84.1, 84.4, 126.7, 128.8, 130.2, 130.3, 131.7, 136.8, 137.1, 148.8, 149.0; ^{31}P NMR (162 MHz, C_6D_6) δ -19.73; MS (EI): *m/z* (relative intensity) 386 (M^+, 1), 304 (20), 303 (100), 187 (18).



2-(2-(diphenylphosphino)phenyl)-1,2,3-trimethylimidazolidine (2h): Similar procedure for the synthesis of 2a were followed. 2-(2-bromophenyl)-1,2,3-trimethylimidazolidine (0.97 mL, 4.8 mmol), chlorodiphenylphosphine (0.75 mL, 4 mmol) were used to afford 2-(2-(diphenylphosphino)phenyl)-1,2,3-trimethylimidazolidine (0.10 g, 23%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38 (s, 3H), 1.83 (s, 6H), 2.59-2.62

(m, 2H), 3.26-3.30 (2H), 7.14-7.16 (m, 1H), 7.17-7.23 (m, 4H), 7.25-7.29 (m, 8H), 7.44-7.47 (m, 1H), ; ^{13}C NMR (100MHz, $CDCl_3$) δ 14.1, 35.6, 50.9, 51.0, 82.3, 127.2, 127.4, 127.8, 127.9, 128.0, 132.9, 133.1, 137.5, 138.0, 141.8, 142.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ -11.95; MS (EI): *m/z* (relative intensity) 304 (100), 227 (68), 183 (24), 165 (13), 149 (17).

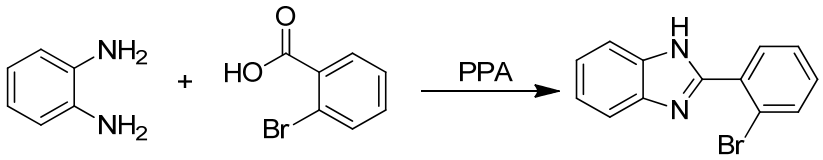


2-(2-(dicyclohexylphosphino)phenyl)-1,2,3-trimethylimidazolidine

(2i): Similar procedure for the synthesis of 2a were followed. 2-(2-bromophenyl)-1,2,3-trimethylimidazolidine (0.97 mL, 4.8 mmol), chlorodicyclohexylphosphine (0.91 mL, 4 mmol) were used to afford 2-(2-(dicyclohexylphosphino)phenyl)-1,2,3-trimethylimidazolidine (0.51 g, 11%). ^{1}H NMR (400 MHz, C_6D_6) δ 1.20-1.48 (m, 18H), 1.68 (s, 9H), 1.80-1.82 (m, 5H), 2.08 (s, 9H), 2.49-2.51 (m, 2H), 3.29-3.30 (m, 2H), 7.10-7.12 (m, 1H), 7.38-7.41 (m, 2H), 7.64-7.66 (m, 1H); ^{13}C NMR (100MHz, C_6D_6) δ 13.4, 13.5, 26.5, 26.8, 27.3, 27.5, 27.6, 27.8, 27.9, 30.8, 31.0, 31.3, 31.4, 35.7, 36.8, 37.0, 51.1, 51.2, 82.4, 82.5, 126.5, 127.7, 127.8, 134.0, 134.1; ^{31}P NMR (162 MHz, C_6D_6) δ -6.81; HRMS: cald. for

$C_{24}H_{39}N_2PH^+$: 387.2929, found 387.2940.

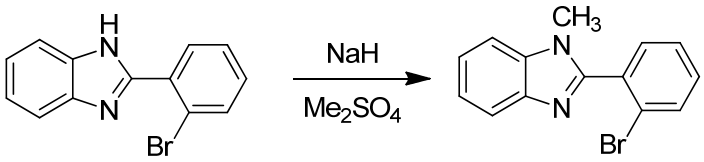
2.2. Preparation of phenyl benzoimidazole backbone ligands



2-(2-bromophenyl)-1H-benzoimidazole was synthesized according to the literature method.[2] 2-bromobenzoic acid (100 mmol) and 1,2-phenylenediamine (100 mmol) were taken in polyphosphoric acid (~120 g) and heated to 150 ^oC for 6 h. The reaction mixture was poured over crushed ice and kept in a refrigerator overnight. The resulting violet solid precipitate was filtered and added to 0.5 M Na_2CO_3 solution (500 mL), stirred for 30 min and filtered. The precipitate was dissolved in methanol (300 mL), and filtered through celite. The solution was evaporated to yield a white solid. Hexane was used to further wash the product. The product was then dried under vacuum to afford 2-(2-bromophenyl)-1H-benzoimidazole (20 g, 70%) as a white solid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.28-7.35 (m, 3H), 7.43-7.47 (m, 1H), 7.53-7.56 (m, 1H), 7.70 (d, *J* =8.0 Hz, 1H), 7.85-7.87 (m, 1H), 8.25 (d, 1H), 10.52 (s,

1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 114.6, 121.7, 122.5, 127., 131.1, 131.7, 131.8, 133.1, 138.0, 150.7; MS (EI): *m/z* (relative intensity) 272.0 (M^+, 100), 193.0 (53), 90.0 (28).

2-(2-bromophenyl)-1-methyl-1H-benzoimidazole

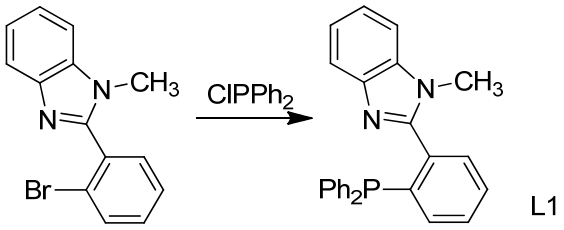


General procedure for methylation of 2-(2-bromophenyl)-1H-benzoimidazole:

2-(2-bromophenyl)-1H-benzoimidazole (10.9 g, 40 mmol) was dissolved in 500 ml THF in dropping funnel and added dropwisely to the 1 L THF solution contained 1.2 equiv NaH (60% in mineral oil, 1.92 g, 48 mmol) at room temperature. NaH was washed with hexane (10 mL × 3) under N_2. The mixture stirred for 1 h at room temperature. Dimethylsulfate (4.16 mL 44 mmol) was then added to the mixture dropwisely. The mixture was refluxed for 30 min and stirred at room temperature for 3 h. 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 applied to 3

× 3 cm silca pad and eluted with EtOAc. The organic solvent was dried over Na_2SO_4 and evaporated in vacuum. The white solid of 2-(2-bromophenyl)-1-methyl-1H-benzoimidazole[3] (8.6 g, 75%) was obtained. ^{1}HNMR (400 MHz, $CDCl_3$) δ 3.66 (s, 3H), 7.34-7.49 (m, 5H), 7.55 (dd, *J* =7.4 Hz, 1.6Hz, 1H), 7.72 (dd, *J* =8.0 Hz, 1.2Hz, 1H), 7.85-7.89 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.7, 109.6, 120.0, 122.3, 122.8, 123.7, 127.4, 131.3, 132.0, 132.3, 132.7, 135.4, 142.7, 152.4; MS (EI): *m/z* (relative intensity) 286.0 (M^+, 100), 207.1 (93), 103.1 (22), 77.0 (43).

1-methyl-2-(2-(diphenylphosphino)phenyl)-1H-benzoimidazole (L1)



L1

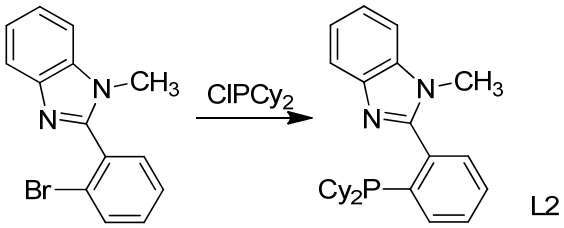
General procedure for ligand synthesis:

2-(2-bromophenyl)-1-methyl-benzoimidazole (0.86 g, 3.0 mmol) was dissolved in freshly distilled THF (20 mL) at room temperature under a nitrogen atmosphere. The solution was cooled to -78 °C in dry ice/acetone bath. Titrated *n*-BuLi (3.0 mmol) was added dropwise by syringe. After the reaction mixture was stirred for 30 min at -78 °C, chlorodiphenylphosphine (0.55 mL, 3.0 mmol) was added. The reaction

was allowed to warm to room temperature and stirred for 5 h. Solvent was removed under reduced pressure. DCM 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 applied to 2 × 10 cm silica pad and eluted with 200ml EA:Hexane (1:9). This fraction was discarded and further eluted with EA: Hexane (4:6). The collected solvent was removed under vacuum and the solid product was further purified by washing with small amount of cold diethyl ether. The product was then dried under vacuum. White solid of 2-(2-(dicyclohexylphosphino)phenyl)-1-methyl-benzoimidazole **(L1)** (0.95g, 80%) were obtained. Melting point: 174.2-176.2°C; ^{31}P NMR (161MHz, CD_2Cl_2) δ -11.7; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.46 (s, 3H), 7.25-7.38 (m, 14H), 7.49-7.55 (m, 3H), 7.72-7.74 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.5, 109.3, 119.5, 121.7, 122.2, 128.1, 128.2, 128.5, 129.5, 130.4, 130.5, 133.5, 133.7, 133.8, 135.4, 136.0, 136.3, 136.6, 136.7, 139.5, 139.7, 142.7, 153.1 (unresolved complex C-P splittings were observed); IR (cm^{-1}): 3051.12, 1613.13, 1478.90, 1462.03, 1424.04, 1377.53, 1327.71, 1282.58, 1244.50, 1148.55, 1125.98, 1093.06, 1027.09, 1005.94, 773.97, 745.88, 695.76, 521.56, 493.47, 469.17; MS (EI): *m/z* (relative intensity)

392.1 (M^+, 2), 315.1 (100), 223.0 (22), 207.0 (26); HRMS: calcd. for $C_{26}H_{21}N_2PH^+$: 393.1521, found 393.1524.

1-methyl-2-(2-(dicyclohexylphosphino)phenyl)-1H-benzoimidazole (L2)

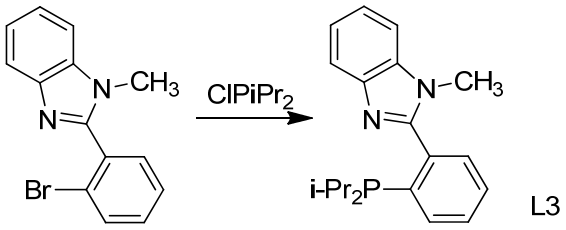


L2

General procedures for the synthesis of ligand **L1** were followed. 2-(2-bromophenyl)-1-methyl-benzoimidazole (2.86 g, 10.0 mmol), *n*-BuLi (10.0 mmol), chlorodicyclohexylphosphine (2.20 mL, 10.0 mmol), and 40 mL THF were used to afford 1-methyl-2-(2-(dicyclohexylphosphino)phenyl)-1H-benzoimidazole (**L2**) (2.85 g, 70%) as a white solid. Small amount of cool hexane instead of diethyl ether was used for washing the products. Melting point: 155.7-158.1 ºC; ^{31}P NMR (161MHz, CD_2Cl_2) δ -8.07; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10-1.31(m, 10H), 1.67-1.78 (m, 10H), 1.91-1.94 (m, 2H), 3.56 (s, 3H), 7.30-7.37 (m, 2H), 7.43-7.61 (m, 4H), 7.71-7.79 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.3, 27.1, 27.1, 27.2, 29.2, 29.3, 30.0, 30.2, 30.6, 30.7, 33.6, 33.7, 109.4, 119.3, 121.5, 122.0, 128.5, 128.8, 130.5, 1306, 132.6,

132.7, 135.3, 137.0, 137.2, 138.8, 139.1, 142.9, 154.6, 154.6 (unresolved complex C-P splittings were observed); IR (cm^{-1}): 3049.23, 2922.74, 2846.49, 1444.05, 1420.25, 1380.93, 1323.98, 1279.02, 1236.37, 1179.81, 1150.92, 1121.29, 1041.62, 1001.29, 885.48, 849.19, 773.73, 746.94, 526.06, 457.22; MS (EI): *m/z* (relative intensity) 404.2 (M^+, 0), 321.1 (100), 238.0 (39), 223.0 (28), 55.1 (7); HRMS: calcd. for $C_{26}H_{33}N_2PH^+$: 405.2460, found 405.2445.

1-methyl-2-(2-(diisopropylhexylphosphino)phenyl)-1H-benzoimidazole (L3)

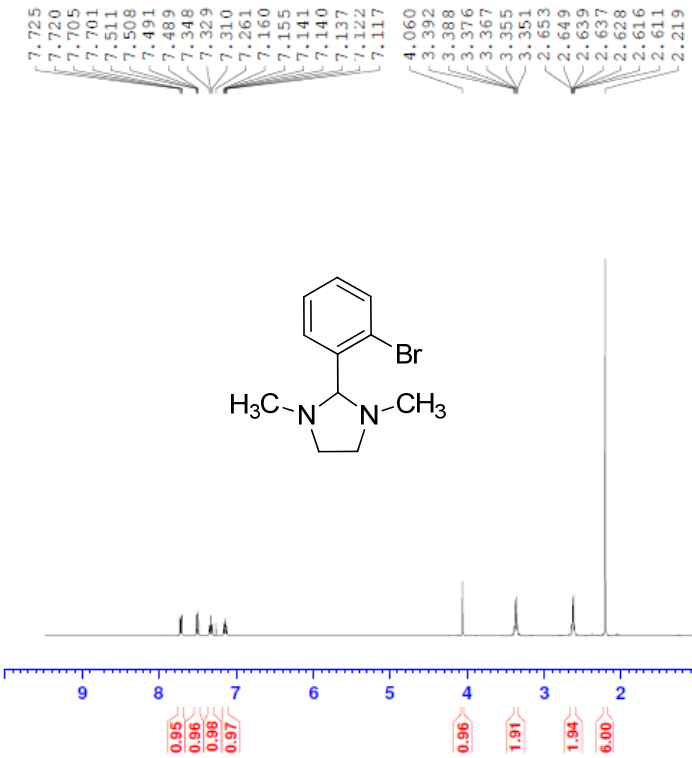


L3

General procedures for the synthesis of ligand **L1** were followed. 2-(2-bromophenyl)-1-methyl-benzoimidazole (0.86 g, 3.0 mmol), *n*-BuLi (3.0 mmol), chlorodiisopropylphosphine (0.47 mL, 10.0 mmol) were used to afford 1-methyl-2-(2-(diisopropylphosphino)phenyl)-1H-benzoimidazole (**L2**) (0.802 g, 83%) as a white solid. Small amount of cool hexane instead of diethyl ether was used for washing the products. Melting point: 147.7-149.7

ºC; ^{31}P NMR (161MHz, CD_2Cl_2) δ 0.45; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.02-1.09 (m, 12H), 2.14-2.18 (m, 2H), 3.59 (s, 3H), 7.31-7.38 (m, 2H), 7.44- 7.46 (m, 1H), 7.50-7.63 (m, 3H), 7.71-7.73 (m, 1H), 7.78-7.80 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.1, 19.2, 19.5, 19.6, 23.6, 23.8, 30.5, 30.6, 109.3, 119.3, 121.5, 122.1, 128.6, 128.9, 130.5, 130.6, 132.2, 132.3, 135.2, 137.4, 137.6, 138.5, 138.8, 142.9, 154.4, 154.5 (unresolved complex C-P splittings were observed); IR (cm^{-1}): 2959.77, 2941.70, 2859.58, 1441.13, 1421.73, 1382.81, 1325.73, 1279.50, 1239.22, 1150.84, 1119.29, 1032.32, 1002.00, 881.61, 775.91, 749.74, 653.87, 609.59, 596.19, 515.71; MS (EI): *m/z* (relative intensity) 324.2 (M^+, 0), 281.1 (100), 238.0 (56), 223.0 (51), 207.0 (48); HRMS: calcd. for $C_{26}H_{33}N_2PH^+$: 325.1834, found 325.1822.

3. ^{1}H, ^{13}C, ^{31}P NMR, MS, HRMS and IR spectra

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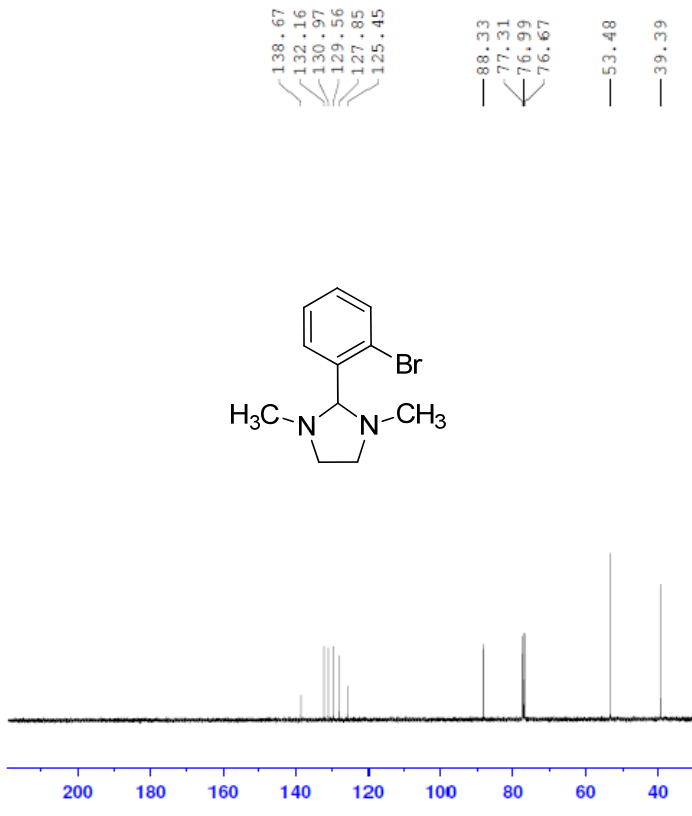


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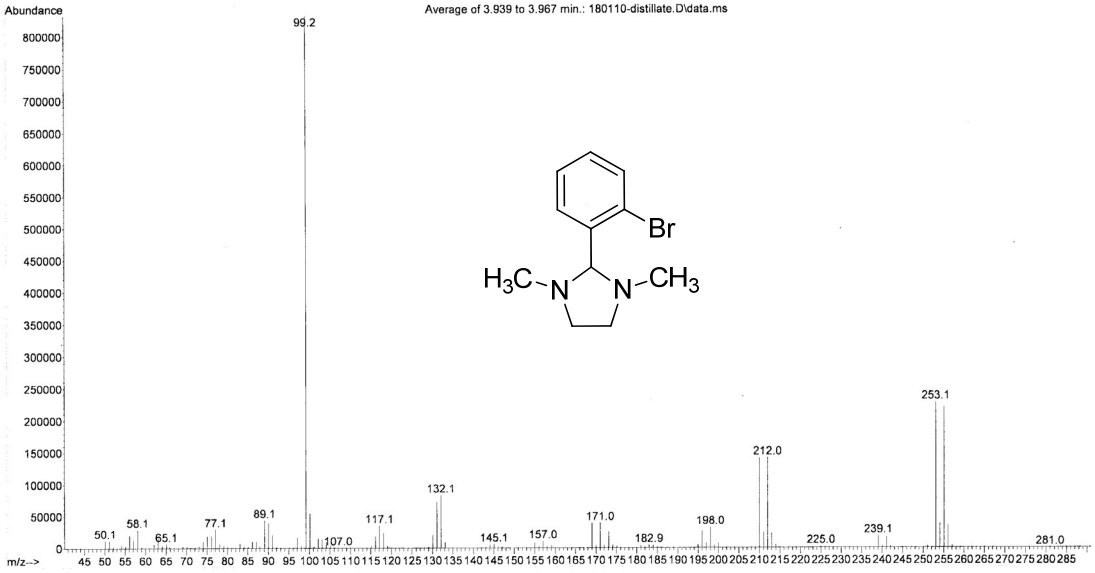
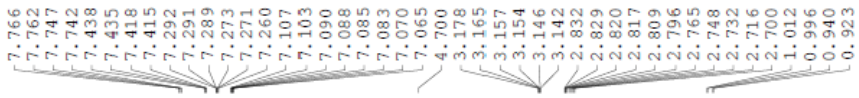
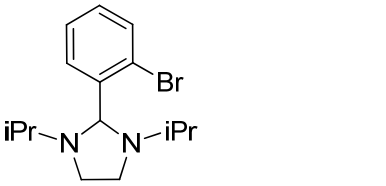
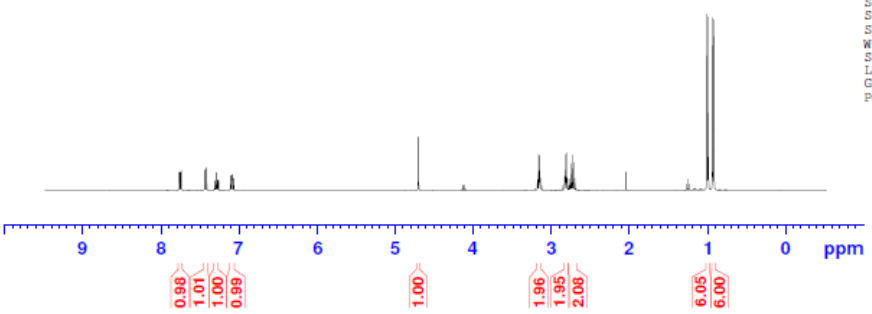


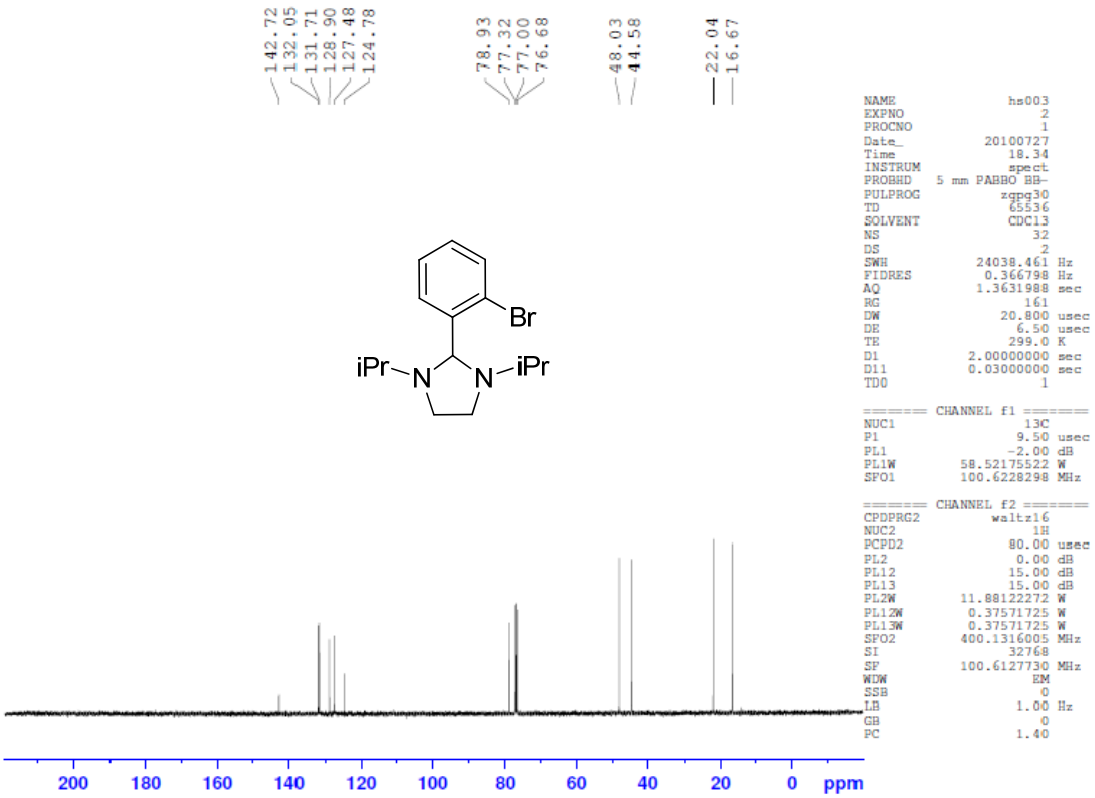



```
NAME                 hs003
EXPNO                    1
PROCNO                   1
Date_             20100727
Time                 18.26
INSTRUM              spect
PROBHD     5 mm PABBO BB-
PULPROG              zg30
TD                   32768
SOLVENT              CDCl3
NS                       8
DS                       2
SWH              4006.410 Hz
FIDRES           0.122266 Hz
AQ               4.0894966 sec
RG                      36
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            400.1300100 MHz
WDW                    EM
SSB                     0
LB                 0.30 Hz
GB                      0
PC                 1.00
```





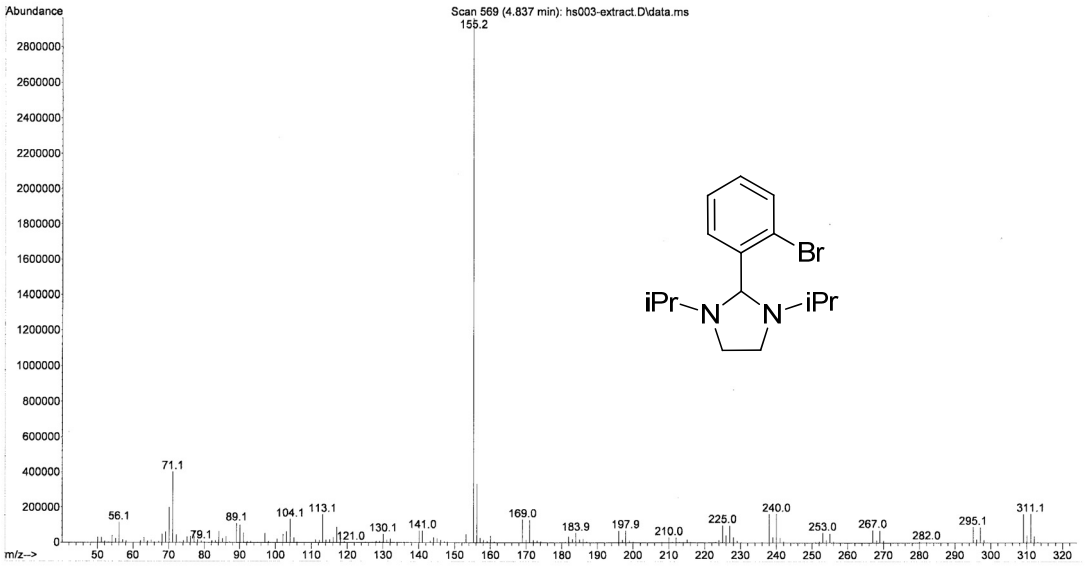



```
NAME                hs003
EXPNO                   2
PROCNO                  1
Date_            20100727
Time                18.34
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                 65536
SOLVENT             CDCl3
NS                     32
DS                      2
SWH          24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631988 sec
RG                   161
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

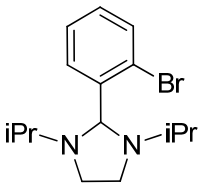
======== CHANNEL f2 ======
CPDPRG2         waltz16
NUC2                1H
PCPD2              80.00 usec
PL2                0.00 dB
PL12              15.00 dB
PL13              15.00 dB
PL2W        11.88122272 W
PL12W        0.37571725 W
PL13W        0.37571725 W
SFO2       400.1316005 MHz
SI                 32768
SF         100.6127730 MHz
WDW                EM
SSB                 0
LB                1.00 Hz
GB                  0
PC                1.40
```

```
File       :C:\msdchem\1\DATA\Ho\Synthesis\hs003-extract.D
Operator   : fbm
Acquired   : 27 Jul 2010  15:07     using AcqMethod METHOD2.M
Instrument :   5973N
Sample Name:
Misc Info  :
Vial Number: 6
```



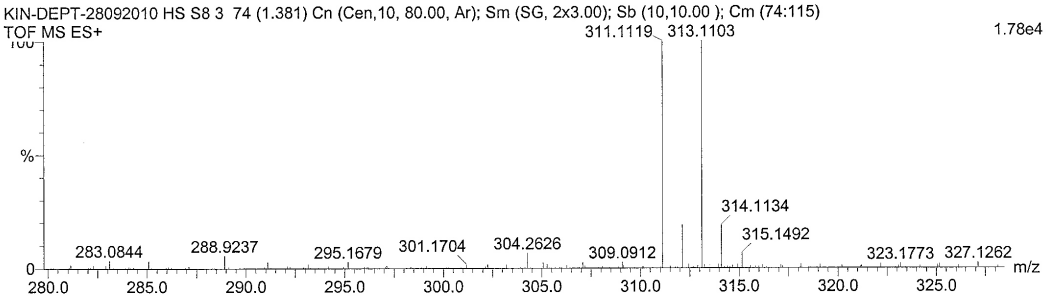
ental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -100.0, max = 1000.0
Selected filters: None

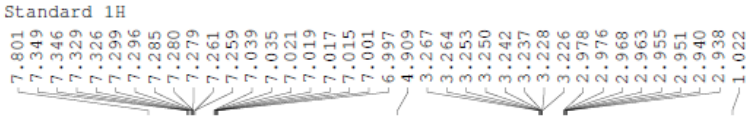


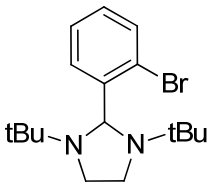
Monoisotopic Mass, Even Electron Ions
59 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-29 H: 0-38 N: 0-2 Na: 0-1 Br: 0-2

KIN-DEPT-28092010 HS S8 3 74 (1.381) Cn (Cen,10, 80.00, Ar); Sm (SG, 2x3.00); Sb (10,10.00); Cm (74:115)
TOF MS ES+ 1.78e4

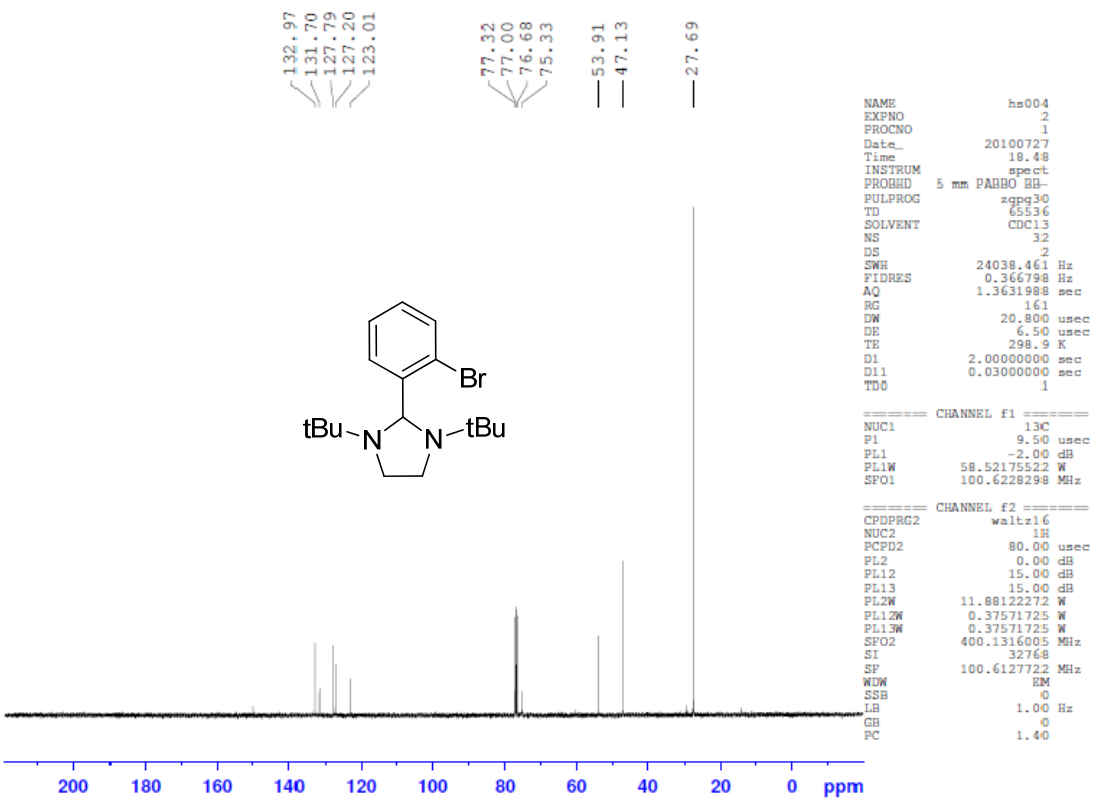


Minimum:				-100.0		
Maximum:		5.0	5.0	1000.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
311.1119	311.1123	-0.4	-1.3	4.5	4.8	C15 H24 N2 Br





NAME	hs004
EXPNO	1
PROCNO	1
Date_	20100727
Time	18.43
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	8
DS	2
SWH	5597.015 Hz
FIDRES	0.170807 Hz
AQ	2.9273248 sec
RG	32
DW	89.333 usec
DE	6.50 usec
TE	298.3 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	400.1300000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

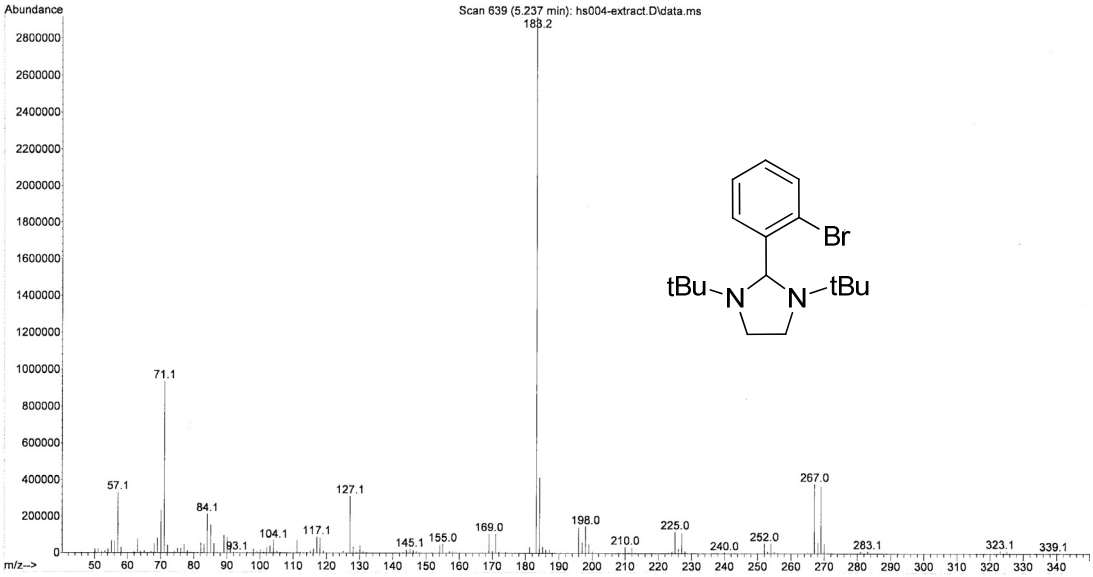



```
NAME                hs004
EXPNO                   2
PROCNO                  1
Date_            20100727
Time                18.48
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                    32
DS                     2
SWH          24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631988 sec
RG                   161
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         100.6127722 MHz
WDW                  EM
SSB                   0
LB                1.00 Hz
GB                    0
PC                1.40
```

```
File       :C:\msdchem\1\DATA\Ho\Synthesis\hs004-extract.D
Operator   : fbm
Acquired   : 27 Jul 2010  15:23     using AcqMethod METHOD2.M
Instrument :   5973N
Sample Name:
Misc Info  :
Vial Number: 3
```

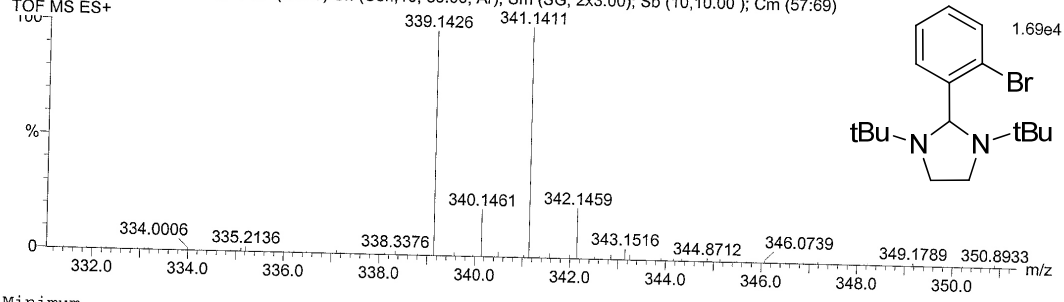


.nental Composition Report **Page 1**

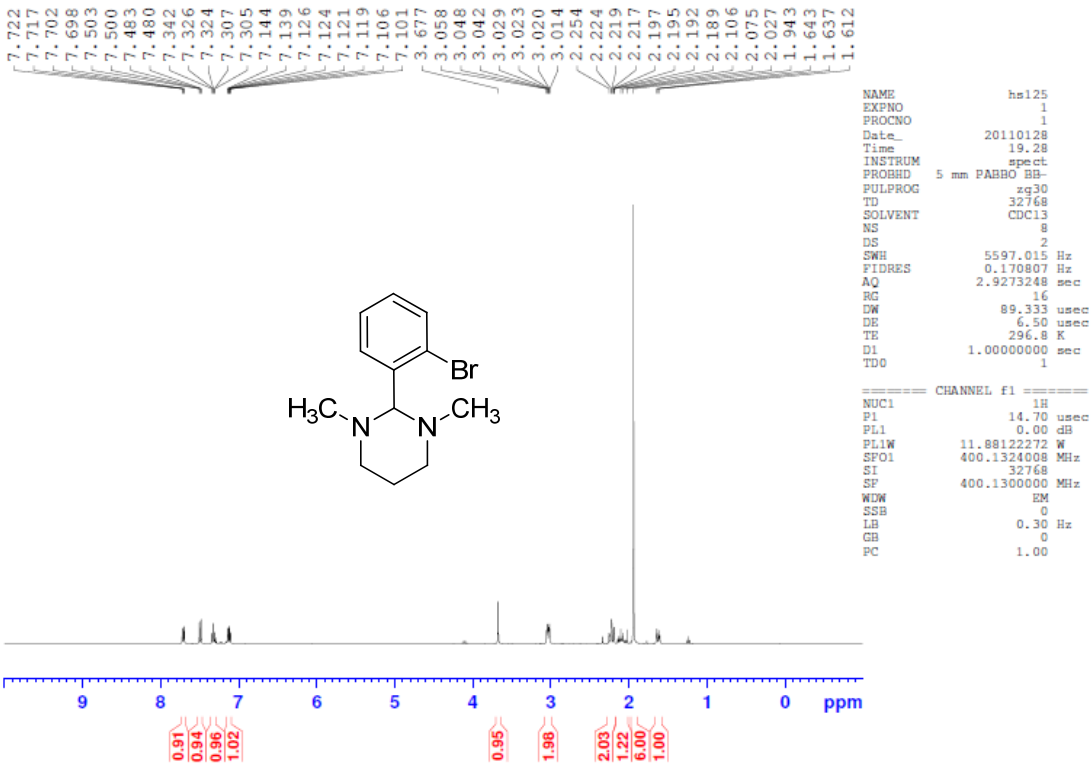
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -100.0, max = 1000.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
47 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-29 H: 0-28 N: 0-2 Na: 0-1 Br: 0-2

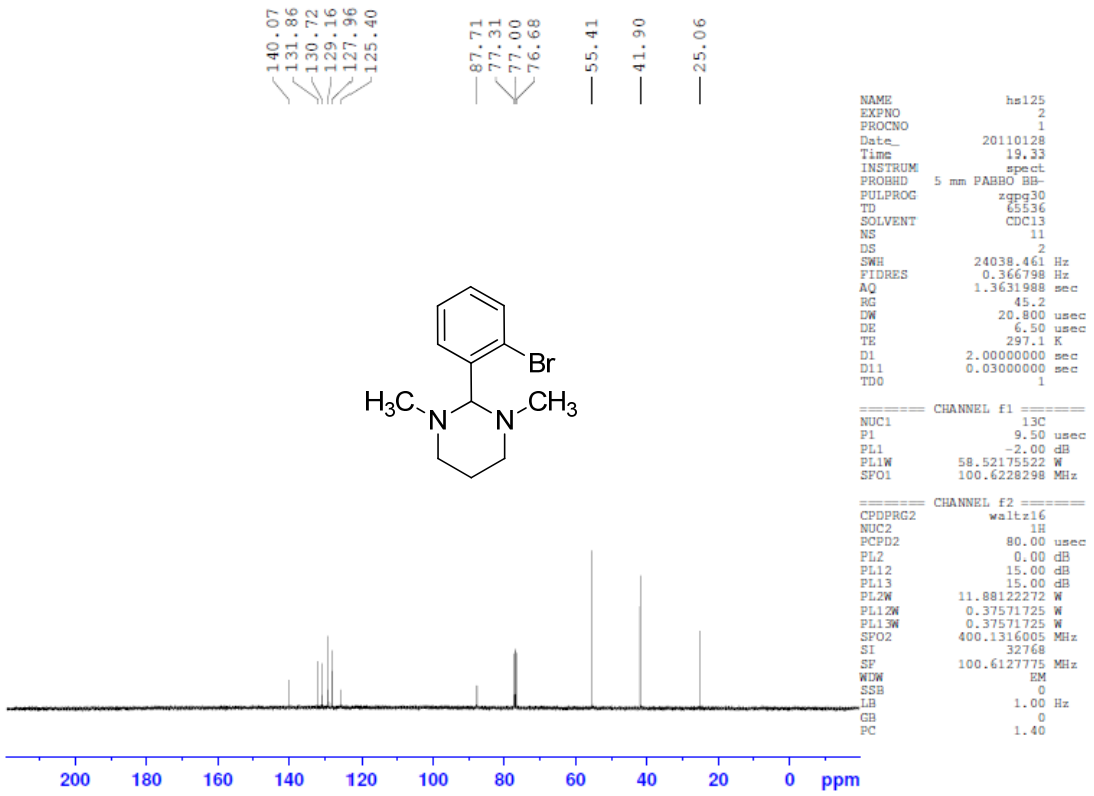
KIN-DEPT-28092010 HS S17 4 57 (1.065) Cn (Cen,10, 80.00, Ar); Sm (SG, 2x3.00); Sb (10,10.00); Cm (57:69)
TOF MS ES+



Minimum:				-100.0		
Maximum:		5.0	5.0	1000.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
339.1426	339.1436	-1.0	-2.9	4.5	6.2	C17 H28 N2 Br



NAME	hs125
EXPNO	1
PROCNO	1
Date_	20110128
Time	19.28
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	8
DS	2
SWH	5597.015 Hz
FIDRES	0.170807 Hz
AQ	2.9273248 sec
RG	16
DW	89.333 usec
DE	6.50 usec
TE	296.8 K
D1	1.00000000 sec
TD0	1
====== CHANNEL f1 ======	
NUC1	1H
P1	14.70 usec
PL1	0.00 dB
PL1W	11.88122272 W
SFO1	400.1324008 MHz
SI	32768
SF	400.1300000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

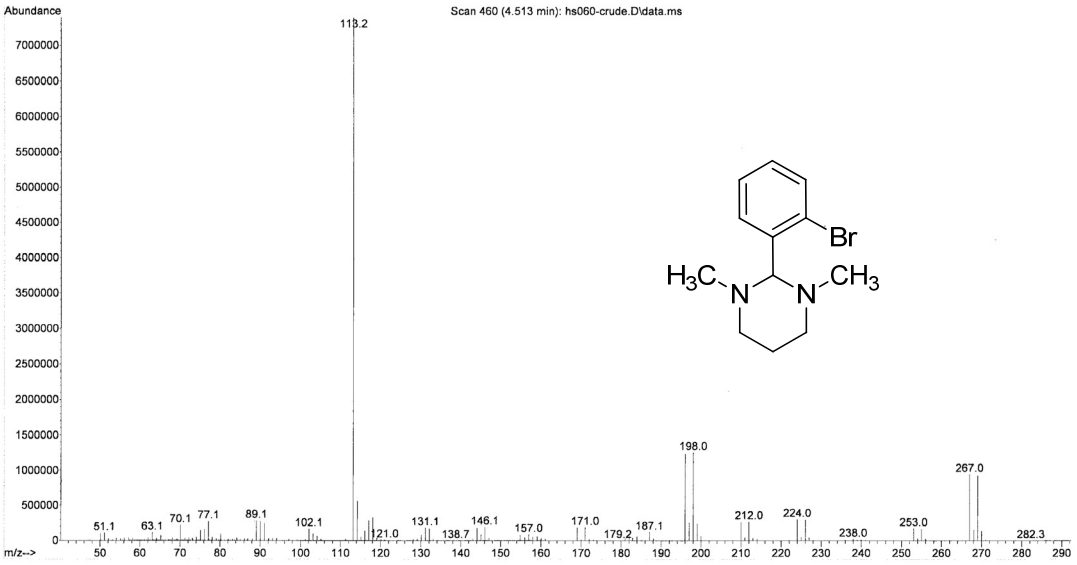



```
NAME                hs125
EXPNO                   2
PROCNO                  1
Date_            20110128
Time                19.33
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG          zgpg30
TD                  65536
SOLVENT             CDCl3
NS                     11
DS                      2
SWH             24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631988 sec
RG                   45.2
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           100.6127775 MHz
WDW                    EM
SSB                     0
LB                 1.00 Hz
GB                      0
PC                  1.40
```

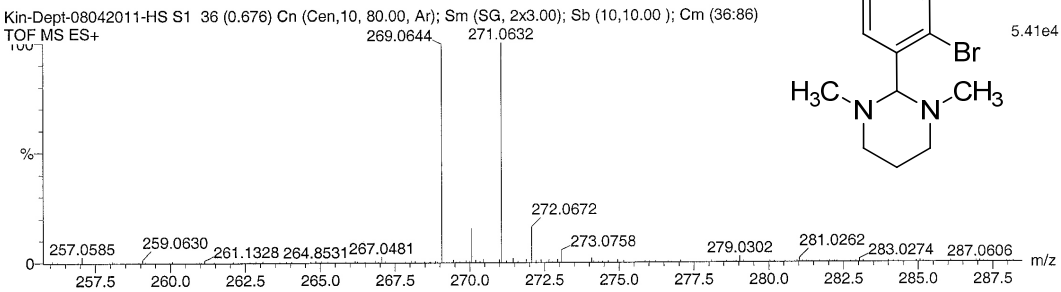
```
File       :C:\msdchem\1\DATA\Ho\Synthesis\hs060-crude.D
Operator   : Seam
Acquired   :  5 Oct 2010  15:53     using AcqMethod METHOD2.M
Instrument :   5973N
Sample Name:
Misc Info  :
Vial Number: 8
```



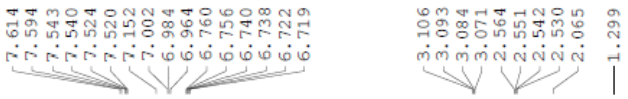
ental Composition Report **Page 1**

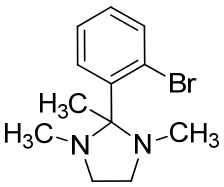
Single Mass Analysis
Tolerance = 20.0 PPM / DBE: min = -100.0, max = 1000.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
43 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-12 H: 0-18 N: 0-4 Na: 0-1 39K: 0-1 Br: 0-1

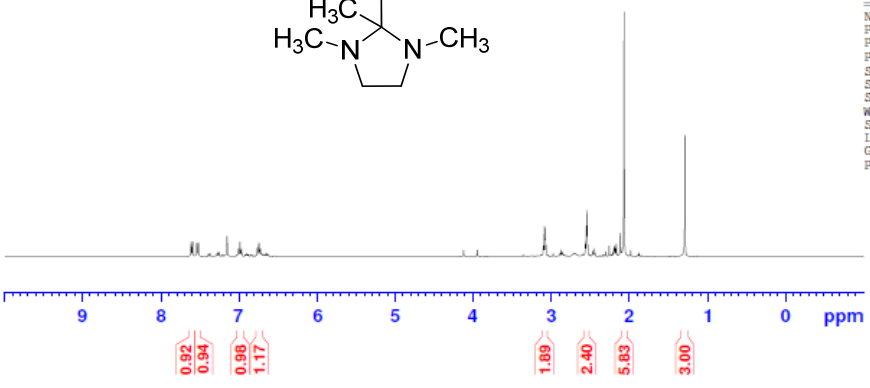


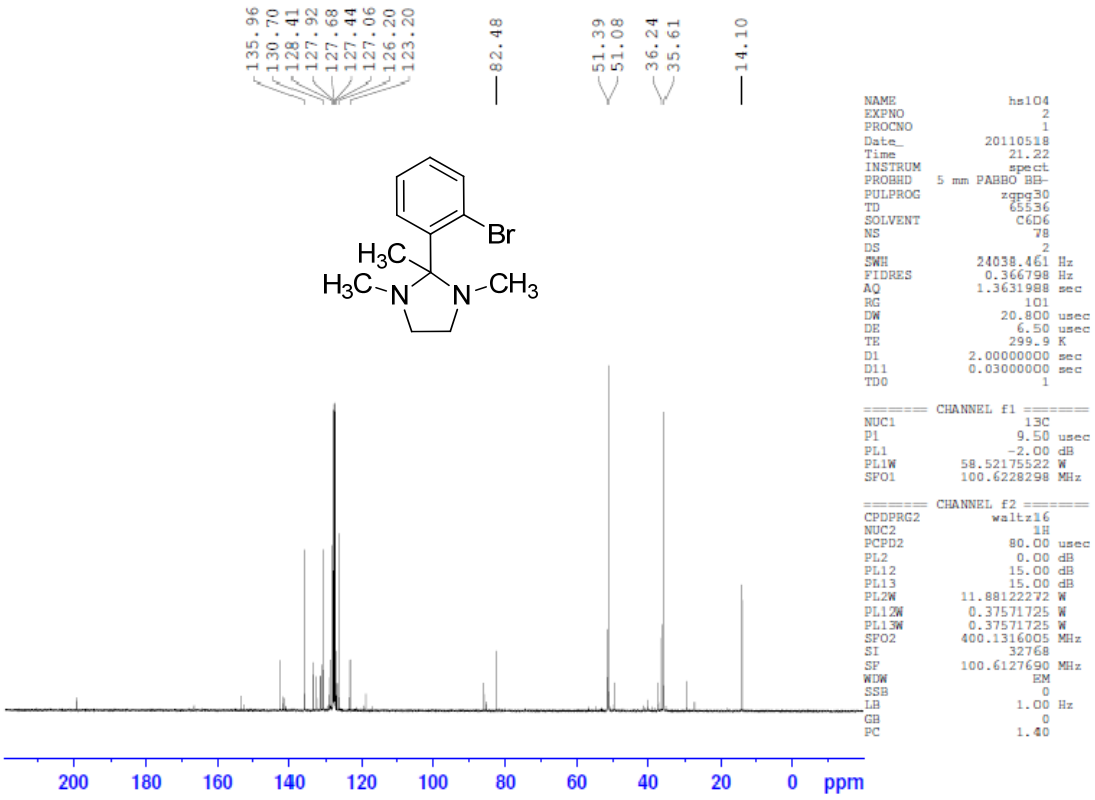
Minimum:				-100.0		
Maximum:		5.0	20.0	1000.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
269.0644	269.0653	-0.9	-3.3	4.5	24.8	C12 H18 N2 Br





NAME	hs104
EXPNO	1
PROCNO	1
Date_	20101129
Time	15.18
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	32768
SOLVENT	C6D6
NS	8
DS	2
SWH	5597.015 Hz
FIDRES	0.170807 Hz
AQ	2.9273248 sec
RG	22.6
DW	89.333 usec
DE	6.50 usec
TE	296.9 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



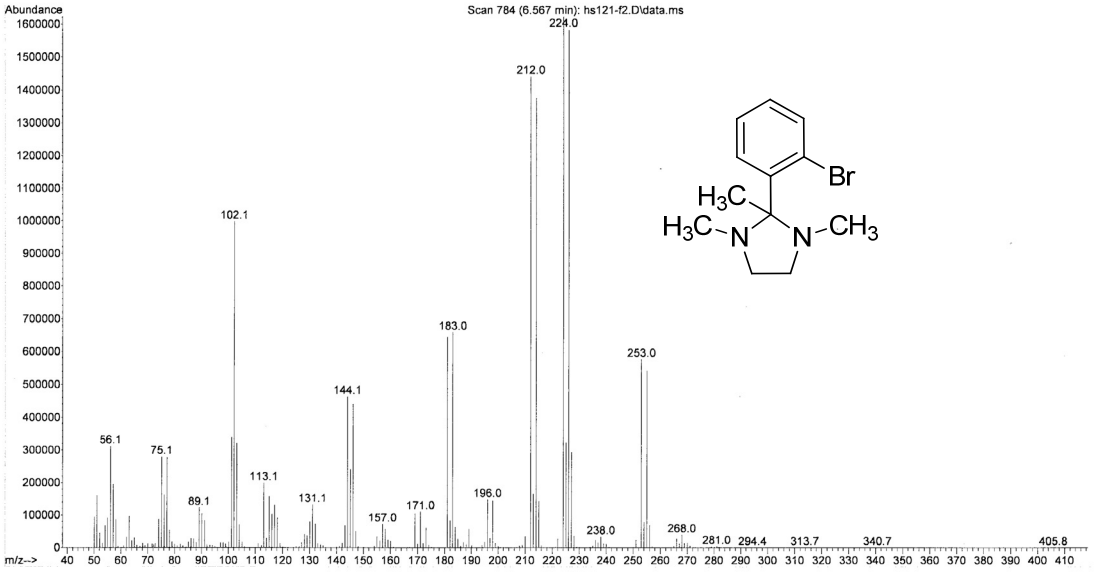



```
NAME                hs104
EXPNO                   2
PROCNO                  1
Date_            20110518
Time                21.22
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                 65536
SOLVENT             C6D6
NS                    78
DS                     2
SWH            24038.461 Hz
FIDRES         0.366798 Hz
AQ             1.3631988 sec
RG                   101
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          100.6127690 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```

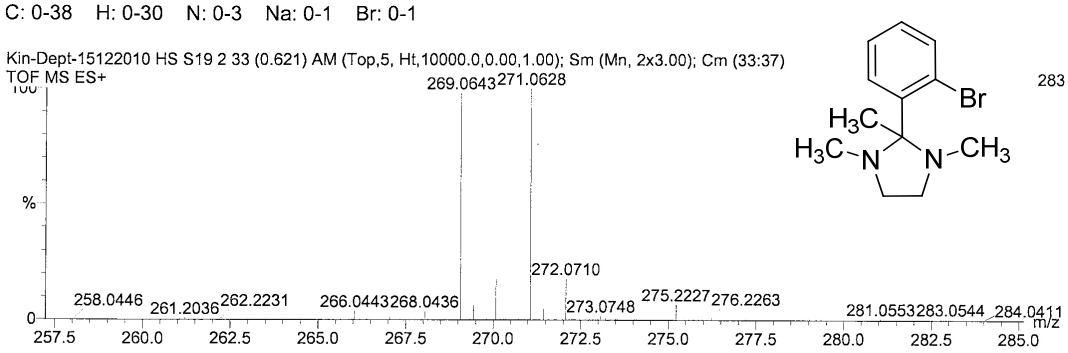
```
File        :C:\msdchem\1\DATA\Ho\Synthesis\hs121-f2.D
Operator    :
Acquired    :  9 Dec 2010  20:02     using AcqMethod METHOD2D.M
Instrument  :   5973N
Sample Name:
Misc Info   :
Vial Number: 1
```



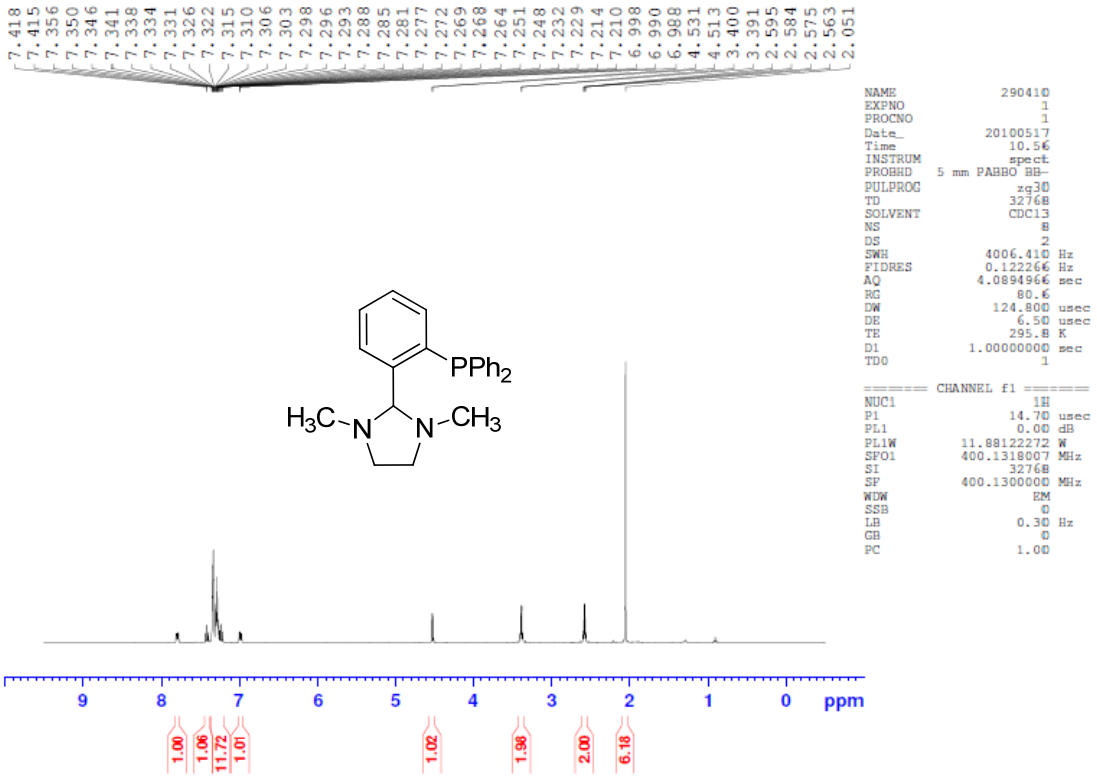
...ental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -100.0, max = 1000.0
Selected filters: None

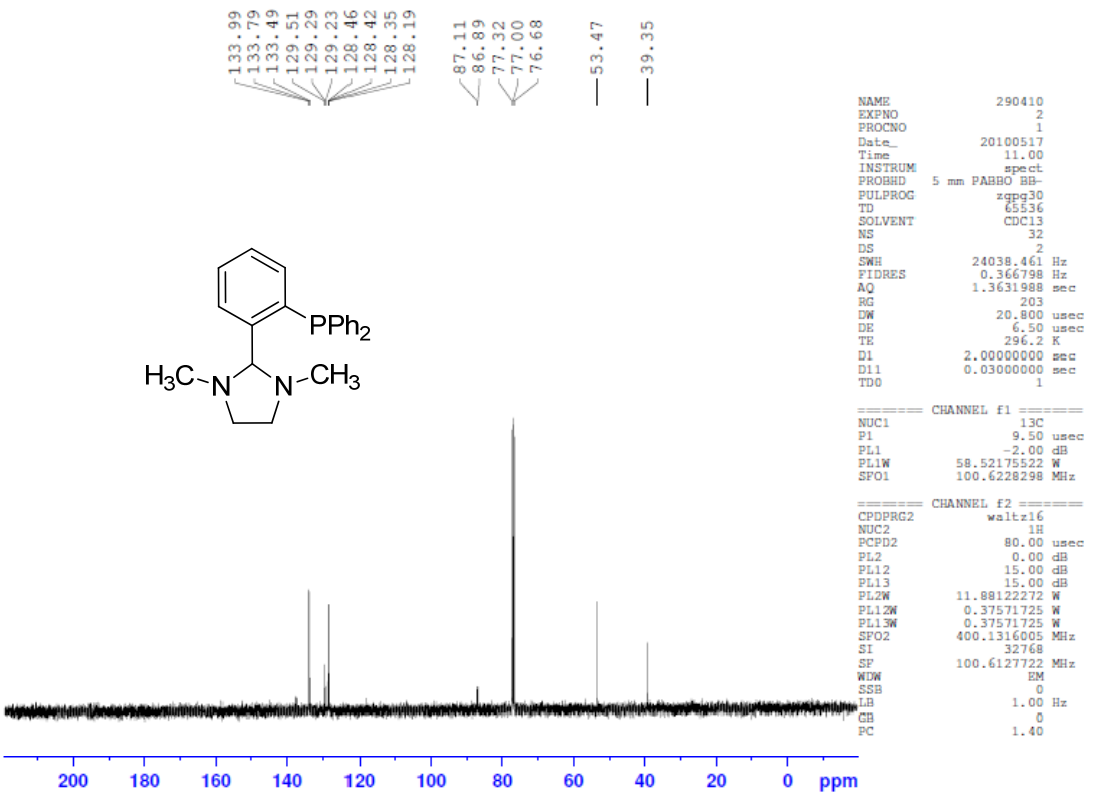
Monoisotopic Mass, Even Electron Ions
44 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-38 H: 0-30 N: 0-3 Na: 0-1 Br: 0-1



Minimum:				-100.0		
Maximum:		5.0	5.0	1000.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
269.0643	269.0653	-1.0	-3.7	4.5	1.0	C12 H18 N2 Br



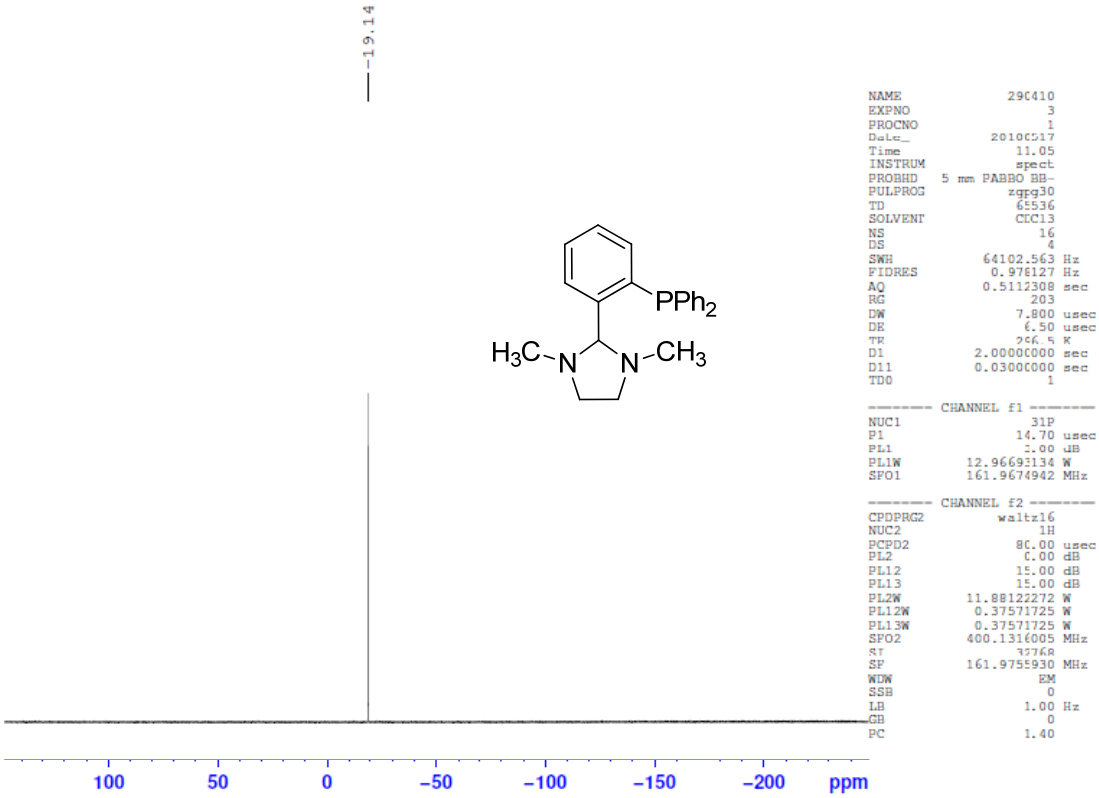
NAME	290410
EXPNO	1
PROCNO	1
Date_	20100517
Time	10.56
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	8
DS	2
SWH	4006.410 Hz
FIDRES	0.122266 Hz
AQ	4.0894966 sec
RG	80.6
DW	124.800 usec
DE	6.50 usec
TE	295.8 K
D1	1.00000000 sec
TD0	1
====== CHANNEL f1 ======	
NUC1	1H
P1	14.70 usec
PL1	0.00 dB
PL1W	11.88122272 W
SFO1	400.1318007 MHz
SI	32768
SF	400.1300000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00




```
NAME                290410
EXPNO                    2
PROCNO                   1
Date_             20100517
Time                 11.00
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                     203
DW                 20.800 usec
DE                  6.50 usec
TE                 296.2 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            100.6127722 MHz
WDW                     EM
SSB                      0
LB                  1.00 Hz
GB                       0
PC                  1.40
```

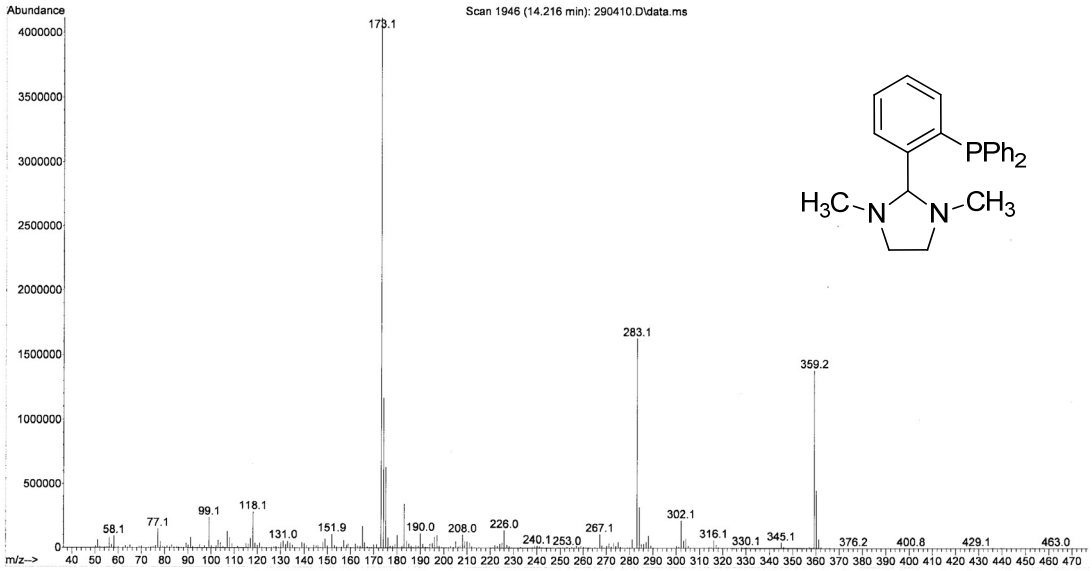



```
NAME                290410
EXPNO                    3
PROCNO                   1
Date_             20100517
Time                 11.05
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       4
SWH              64102.563 Hz
FIDRES           0.978127 Hz
AQ               0.5112308 sec
RG                     203
DW                  7.800 usec
DE                  6.50 usec
TE                 296.5 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                      1

======== CHANNEL f1 =======
NUC1                   31P
P1                 14.70 usec
PL1                 2.00 dB
PL1W           12.96693134 W
SFO1          161.9674942 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            161.9755930 MHz
WDW                     EM
SSB                      0
LB                  1.00 Hz
GB                       0
PC                  1.40
```

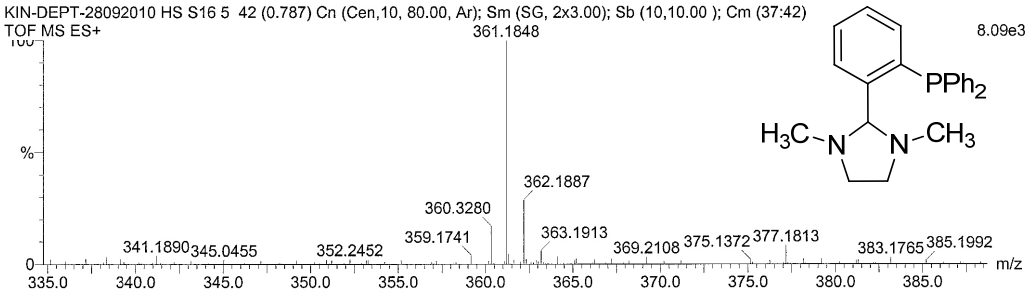
```
File       :C:\msdchem\1\DATA\Ho\Synthesis\290410.D
Operator   : fbm
Acquired   :  2 May 2010  16:29     using AcqMethod WANGJUN.M
Instrument :   5973N
Sample Name:
Misc Info  :
Vial Number: 6
```



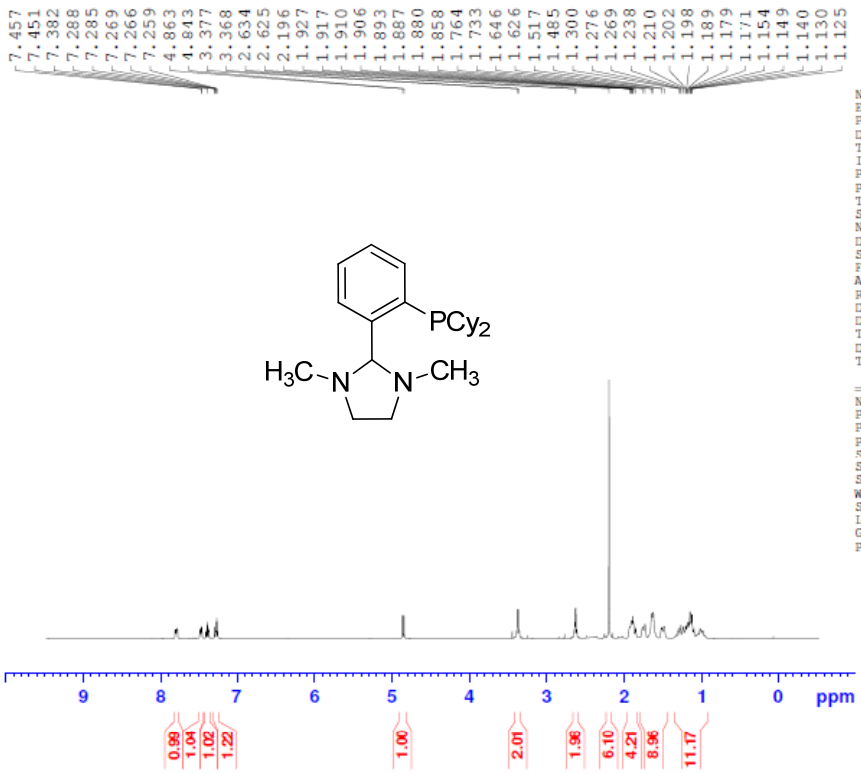
ıtal Composition Report **Page 1**

ɔingle Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -100.0, max = 1000.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
5 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-23 H: 0-26 N: 0-2 Na: 0-1 P: 0-1

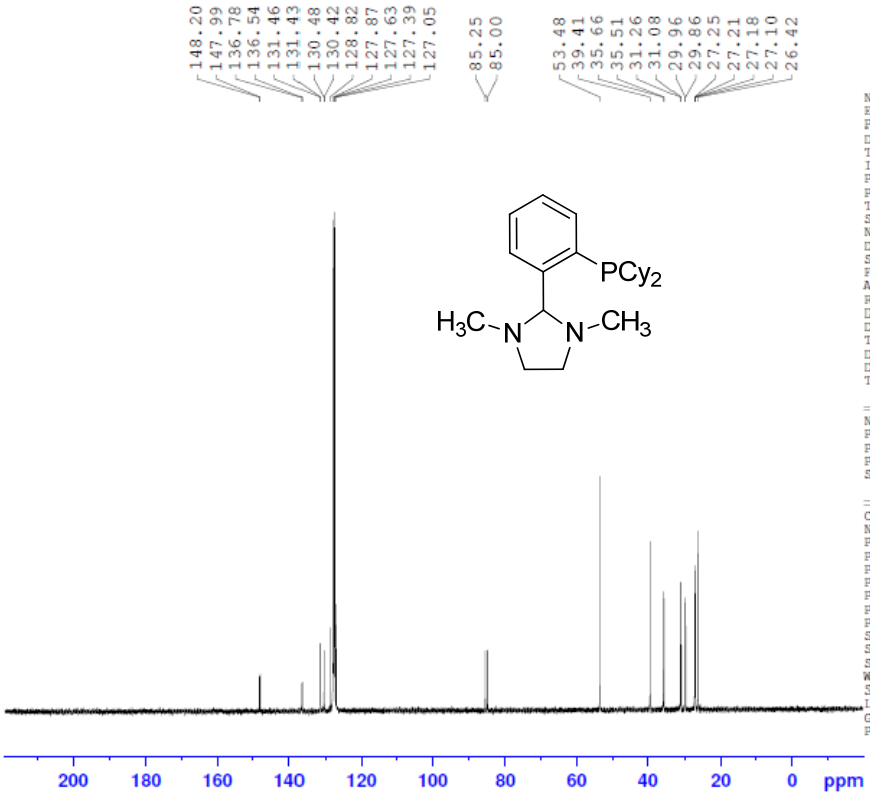


Minimum:				-100.0		
Maximum:		5.0	5.0	1000.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
361.1848	361.1834	1.4	3.9	12.5	45.1	C23 H26 N2 P




```
NAME            030610-3
EXPNO                  1
PROCNO                 1
Date_           20100610
Time               17.21
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 32768
SOLVENT            CDC13
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                 296.5 K
D1              1.00000000 sec
TD0                    1

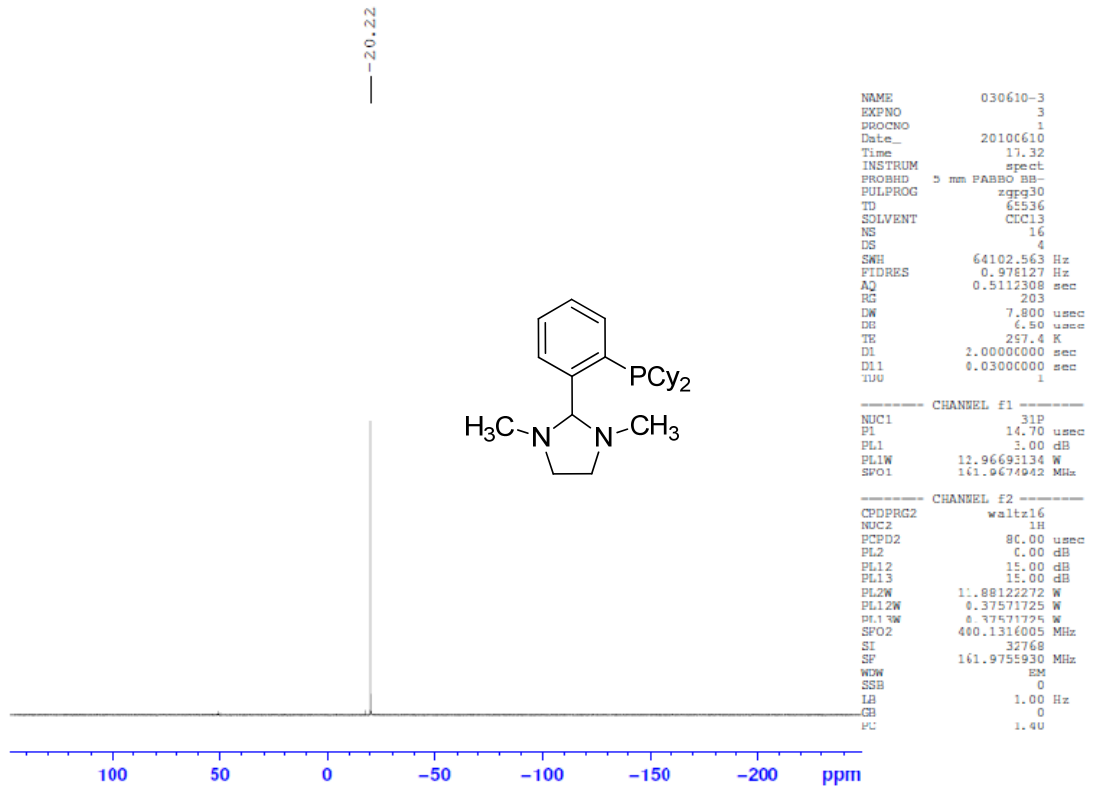
====== CHANNEL f1 ======
NUC1                1H
P1                14.70 usec
PL1                0.00 dB
PL1W         11.88122272 W
SFO1         400.1318007 MHz
SI                 32768
SF           400.1300102 MHz
WDW                EM
SSB                 0
LB                0.30 Hz
GB                  0
PC                1.00
```




```
NAME            030610-3
EXPNO                  4
PROCNO                 1
Date_           20110518
Time               21.50
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                 65536
SOLVENT             C6D6
NS                    63
DS                     2
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631988 sec
RG                   144
DW                20.800 usec
DE                  6.50 usec
TE                 299.7 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           100.6127730 MHz
WDW                EM
SSB                 0
LB                1.00 Hz
GB                  0
PC                1.40
```

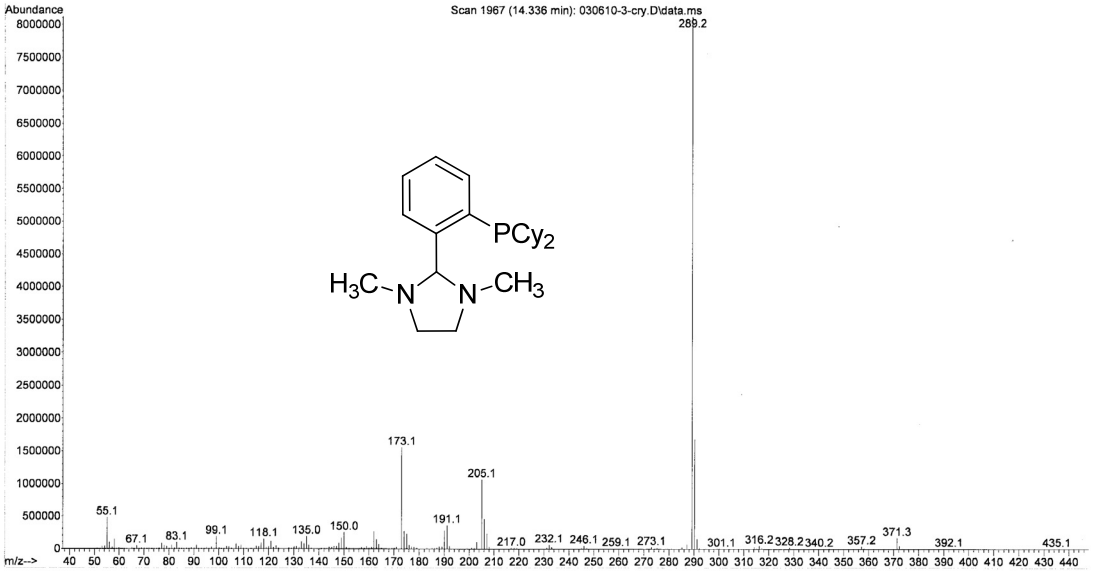



```
NAME                030610-3
EXPNO                      3
PROCNO                     1
Date_               20100610
Time                   17.32
INSTRUM                spect
PROBHD   5 mm PABBO BB-
PULPROG                zgpg30
TD                      65536
SOLVENT                CDCl3
NS                         16
DS                          4
SWH                64102.563 Hz
FIDRES             0.978127 Hz
AQ                 0.5112308 sec
RG                        203
DW                    7.800 usec
DE                    6.50 usec
TE                    297.4 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      31P
P1                      14.70 usec
PL1                      3.00 dB
PL1W               12.96693134 W
SFO1              161.9674942 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                161.9755930 MHz
WDW                       EM
SSB                        0
LB                      1.00 Hz
GB                         0
PC                      1.40
```

```
File       :C:\msdchem\1\DATA\Ho\Synthesis\030610-3-cry.D
Operator   : fbm
Acquired   : 10 Jun 2010  19:03     using AcqMethod WANGJUN.M
Instrument :   5973N
Sample Name:
Misc Info  :
Vial Number: 3
```

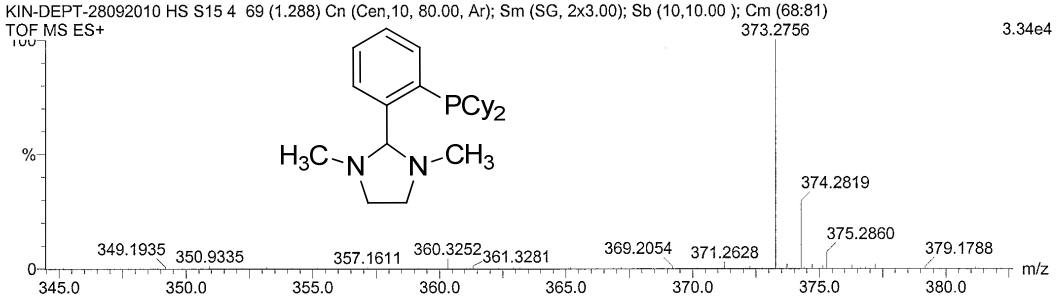


ɜmental Composition Report **Page 1**

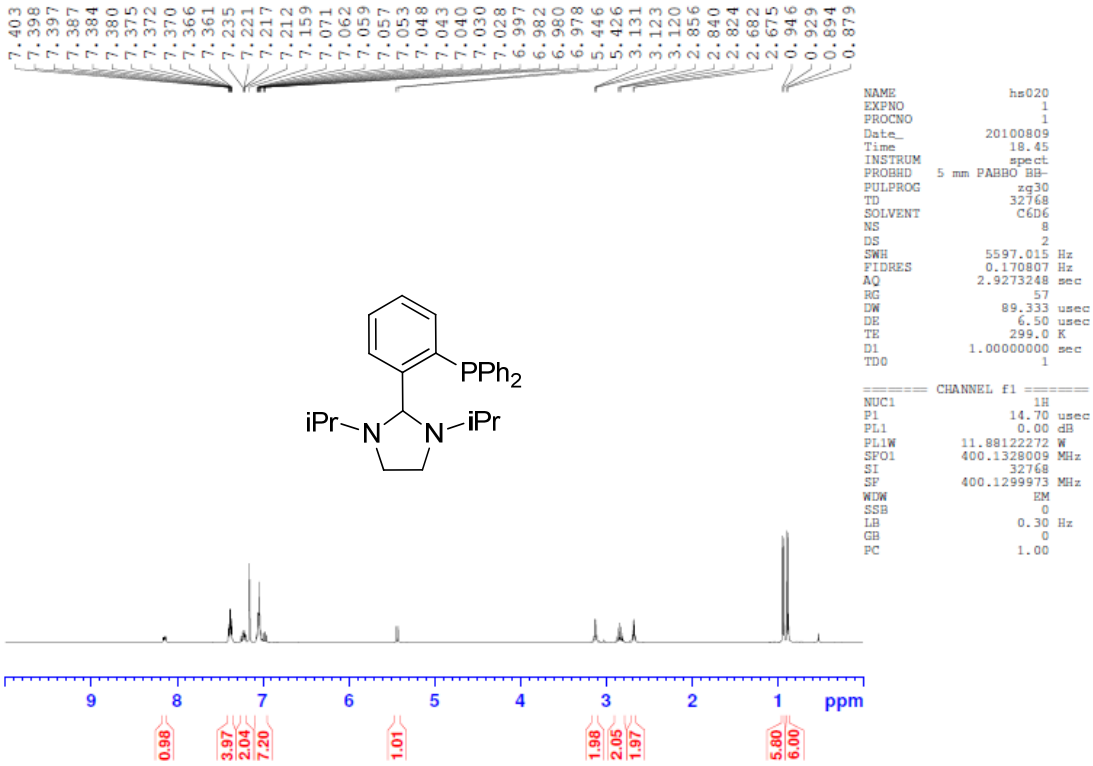
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -100.0, max = 1000.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
38 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-29 H: 0-38 N: 0-2 Na: 0-1 P: 0-1

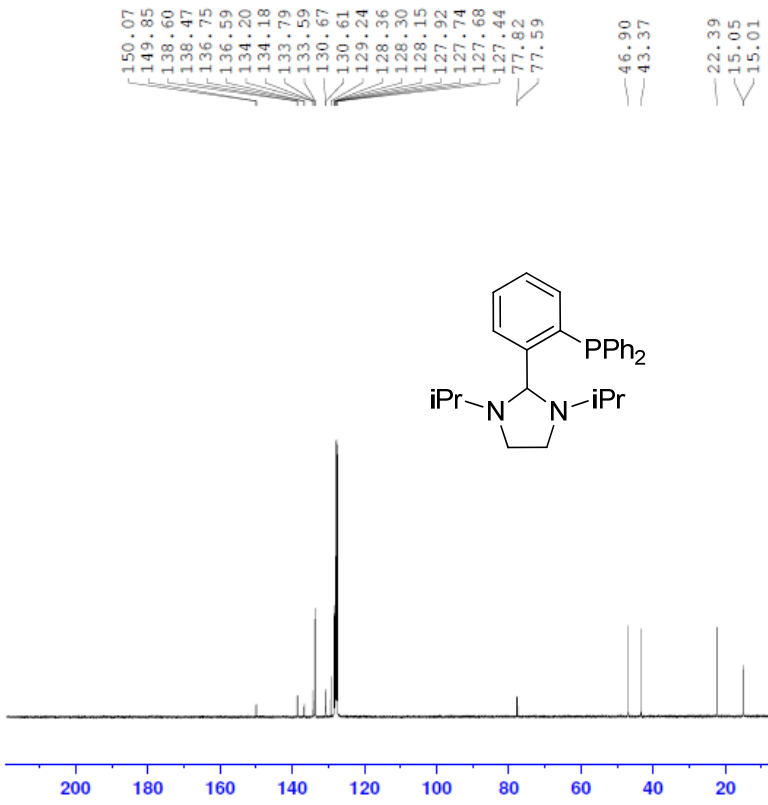
KIN-DEPT-28092010 HS S15 4 69 (1.288) Cn (Cen,10, 80.00, Ar); Sm (SG, 2x3.00); Sb (10,10.00); Cm (68:81)
TOF MS ES+ 3.34e4



Minimum:				-100.0		
Maximum:		5.0	5.0	1000.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
373.2756	373.2773	-1.7	-4.6	6.5	310.5	C23 H38 N2 P



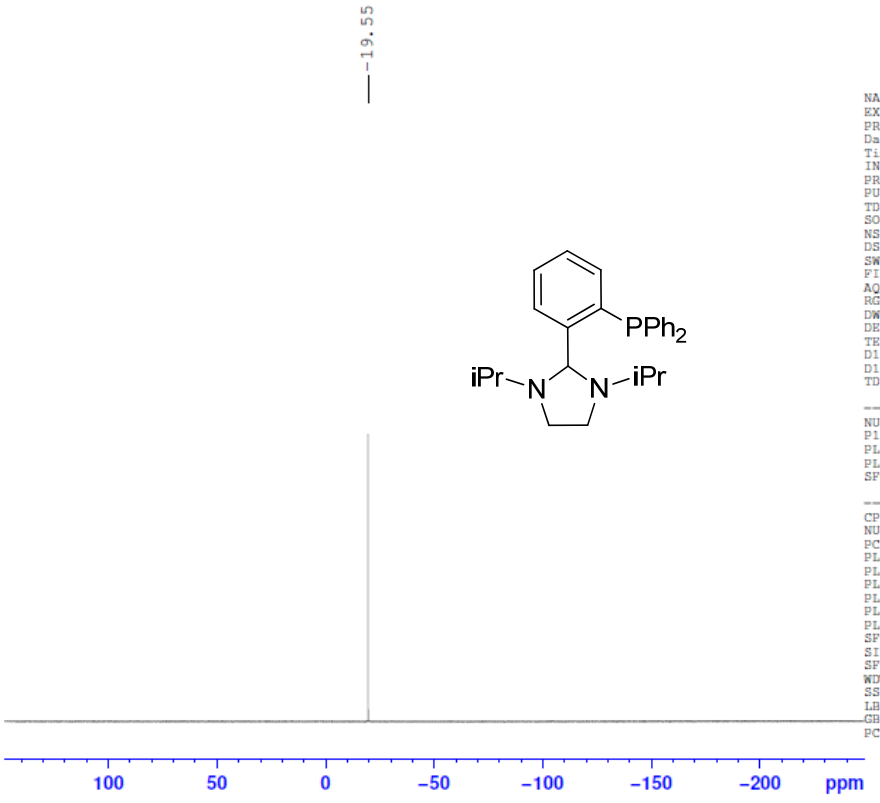
NAME	hs020
EXPNO	1
PROCNO	1
Date_	20100809
Time	18.45
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	32768
SOLVENT	C6D6
NS	8
DS	2
SWH	5597.015 Hz
FIDRES	0.170807 Hz
AQ	2.9273248 sec
RG	57
DW	89.333 usec
DE	6.50 usec
TE	299.0 K
D1	1.00000000 sec
TD0	1
====== CHANNEL f1 ======	
NUC1	1H
P1	14.70 usec
PL1	0.00 dB
PL1W	11.88122272 W
SFO1	400.1328009 MHz
SI	32768
SF	400.1299973 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00




```
NAME                hs020
EXPNO                   4
PROCNO                  1
Date_            20110518
Time                21.43
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG           zgpg30
TD                 65536
SOLVENT              C6D6
NS                     95
DS                      2
SWH             24038.461 Hz
FIDRES              0.366798 Hz
AQ                  1.363198 sec
RG                    101
DW                 20.800 usec
DE                  6.50 usec
TE                  299.5 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
```

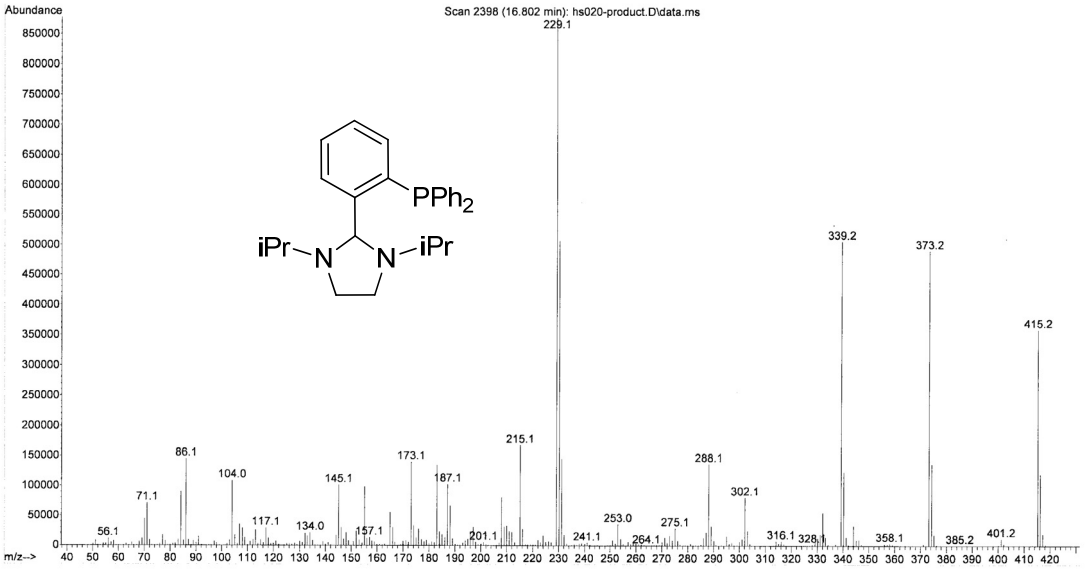



```
NAME                hs020
EXPNO                   3
PROCNO                  1
Date_            20100809
Time                18.55
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG           zgpg30
TD                 65536
SOLVENT              C6D6
NS                     16
DS                      4
SWH             64102.563 Hz
FIDRES              0.978127 Hz
AQ                  0.5112308 sec
RG                    203
DW                 7.800 usec
DE                  6.50 usec
TE                  299.5 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  31P
P1                 14.70 usec
PL1                 3.00 dB
PL1W           12.96693134 W
SFO1          161.9674942 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            161.9755930 MHz
WDW                    EM
SSB                     0
LB                  1.00 Hz
GB                      0
PC                  1.40
```

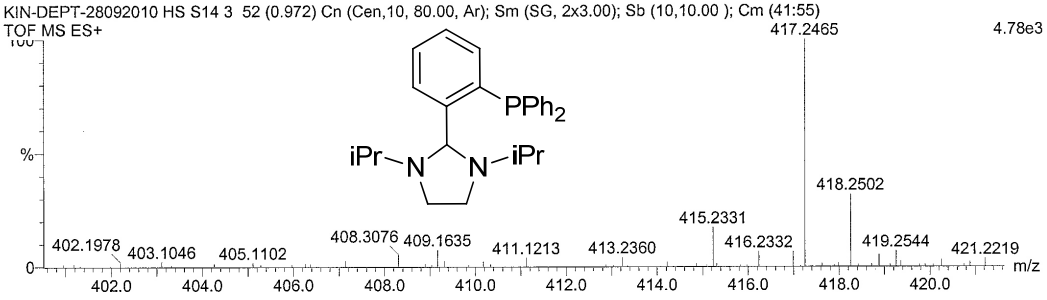
```
File       :C:\msdchem\1\DATA\Ho\Synthesis\hs020-product.D
Operator   : Seam
Acquired   : 11 Aug 2010  10:48     using AcqMethod WANGJUN.M
Instrument :   5973N
Sample Name:
Misc Info  :
Vial Number: 6
```



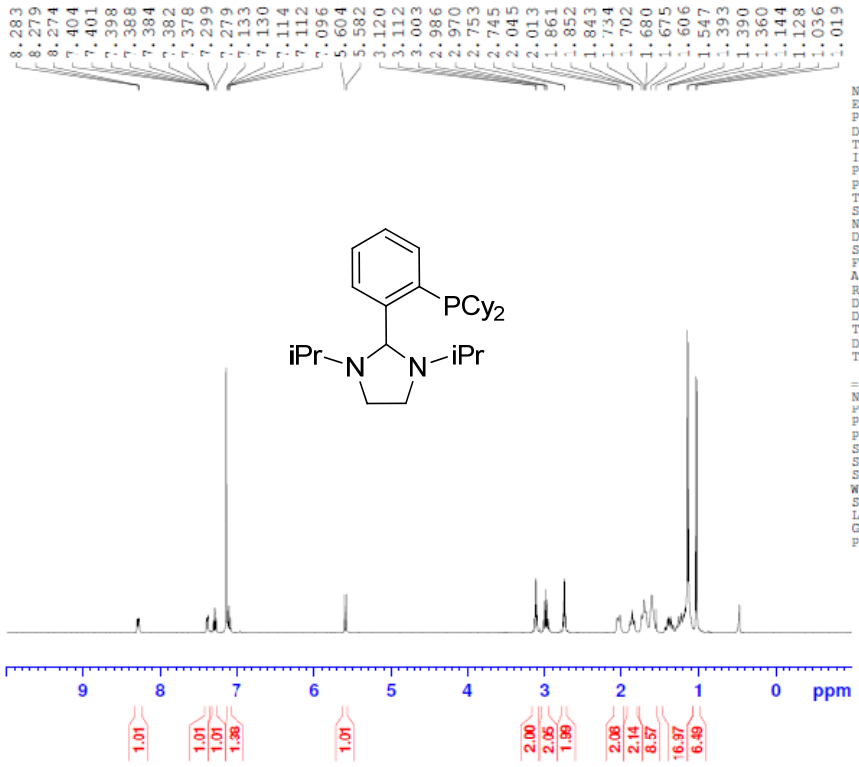
Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -100.0, max = 1000.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
19 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-29 H: 0-38 N: 0-2 Na: 0-1 P: 0-1

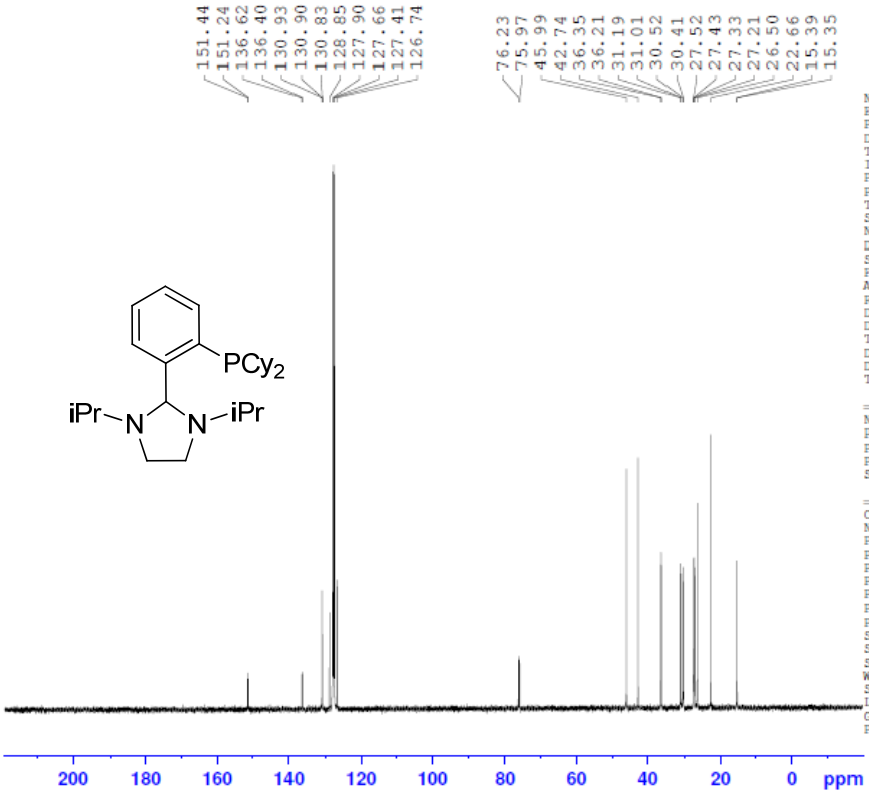


Minimum:				-100.0		
Maximum:		5.0	5.0	1000.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
417.2465	417.2460	0.5	1.2	12.5	15.2	C27 H34 N2 P




```
NAME                hs049
EXPNO                   1
PROCNO                  1
Date_            20100910
Time                16.40
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG              zg30
TD                  32768
SOLVENT              C6D6
NS                      8
DS                      2
SWH           5597.015 Hz
FIDRES        0.170807 Hz
AQ            2.9273248 sec
RG                   71.8
DW               89.333 usec
DE                6.50 usec
TE                298.6 K
D1            1.00000000 sec
TD0                     1

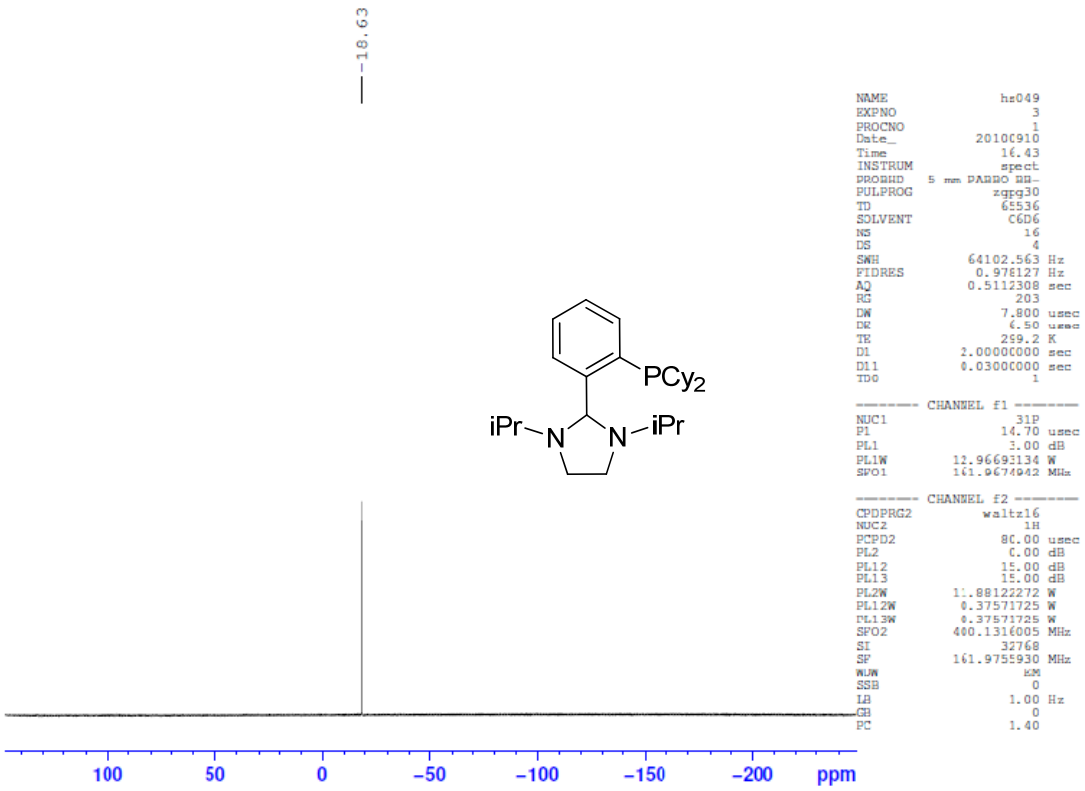
====== CHANNEL f1 ======
NUC1                  1H
P1                14.70 usec
PL1                0.00 dB
PL1W        11.88122272 W
SFO1       400.1324008 MHz
SI                  32768
SF         400.1300000 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.00
```




```
NAME                hs049
EXPNO                   6
PROCNO                  1
Date_            20110518
Time                22.00
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG          zgpg30
TD                  65536
SOLVENT              C6D6
NS                     57
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                299.6 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         100.6127690 MHz
WDW                   EM
SSB                    0
LB                1.00 Hz
GB                     0
PC                1.40
```

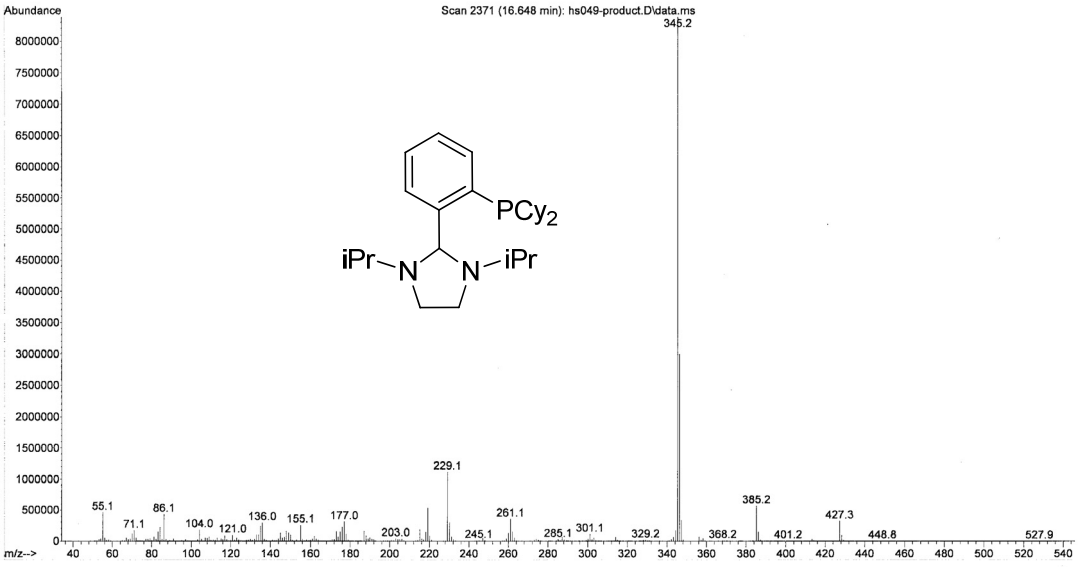


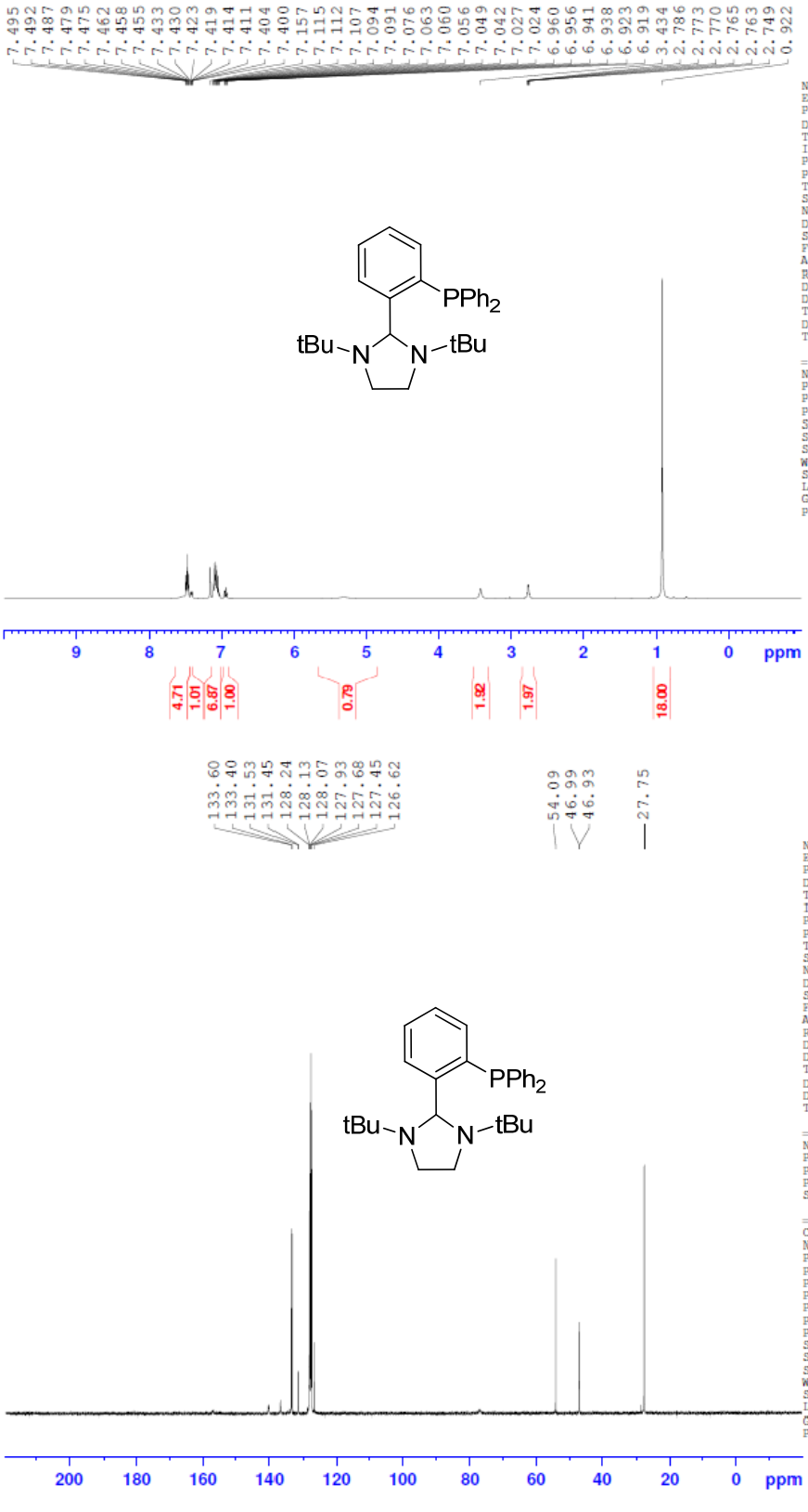

```
NAME                hs049
EXPNO                   3
PROCNO                  1
Date_            20100910
Time                16.43
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG             zgpg30
TD                   65536
SOLVENT               C6D6
NS                      16
DS                       4
SWH              64102.563 Hz
FIDRES           0.978127 Hz
AQ               0.5112308 sec
RG                     203
DW                  7.800 usec
DE                  6.50 usec
TE                  298.2 K
D1               2.00000000 sec
D11              0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   31P
P1                  14.70 usec
PL1                  3.00 dB
PL1W           12.96693134 W
SFO1           161.9674942 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             161.9755930 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```

```
File       :C:\msdchem\1\DATA\Ho\Synthesis\hs049-product.D
Operator   : Seam
Acquired   : 10 Sep 2010  14:28     using AcqMethod WANGJUN.M
Instrument :   5973N
Sample Name:
Misc Info  :
Vial Number: 5
```





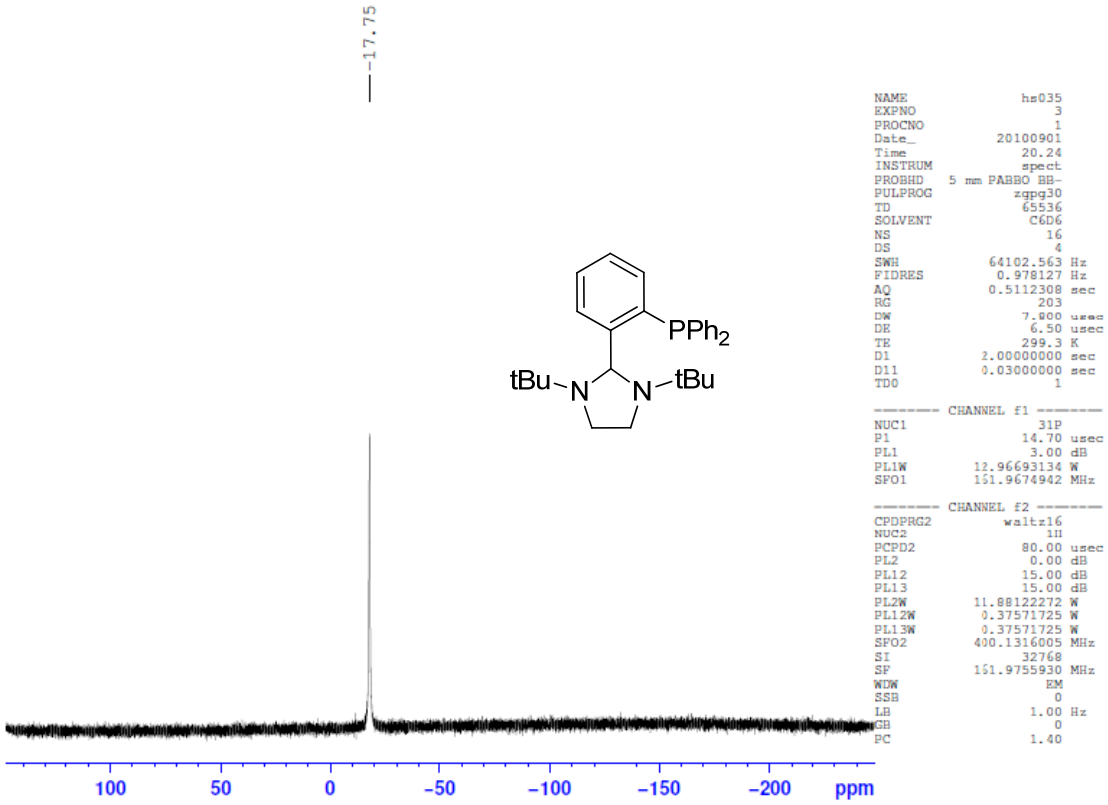

```
NAME                hs035
EXPNO                   1
PROCNO                  1
Date_            20100901
Time                20.13
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  32768
SOLVENT              C6D6
NS                      8
DS                      2
SWH              5597.015 Hz
FIDRES           0.170807 Hz
AQ               2.9273248 sec
RG                   28.5
DW                89.333 usec
DE                  6.50 usec
TE                298.5 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           400.1299981 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

```
NAME                hs035
EXPNO                   7
PROCNO                  1
Date_            20110518
Time                21.54
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                  65536
SOLVENT              C6D6
NS                     74
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               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
```

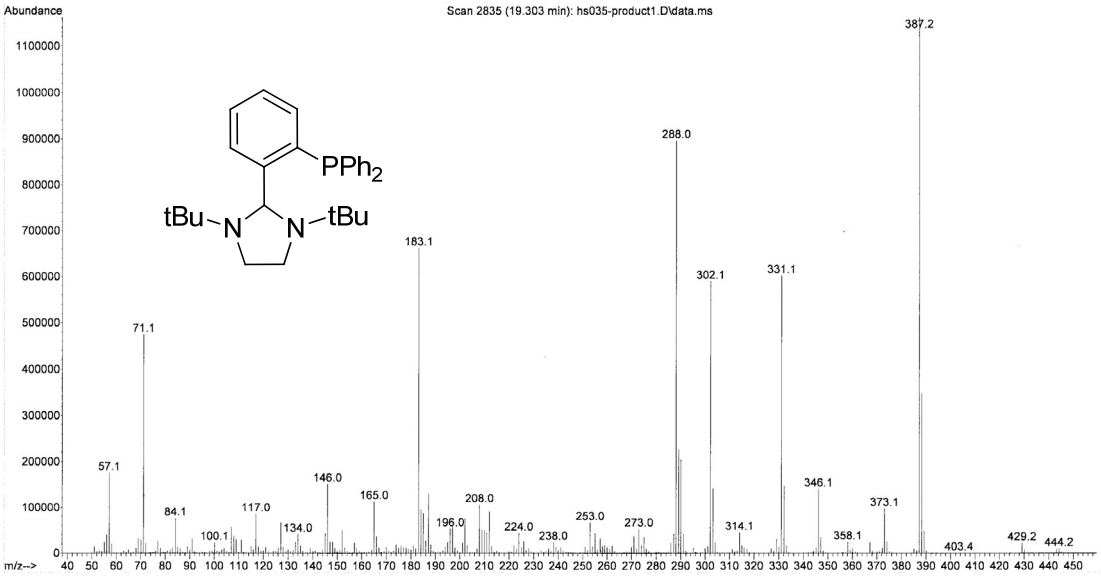



```
NAME                hs035
EXPNO                   3
PROCNO                  1
Date_            20100901
Time                20.24
INSTRUM             spect
PROBHD    5 mm PABBO BB-
PULPROG           zgpg30
TD                 65536
SOLVENT              C6D6
NS                     16
DS                      4
SWH            64102.563 Hz
FIDRES         0.978127 Hz
AQ             0.5112308 sec
RG                    203
DW                7.800 usec
DE                 6.50 usec
TE                299.3 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  31P
P1                 14.70 usec
PL1                3.00 dB
PL1W          12.96693134 W
SFO1         161.9674942 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           161.9755930 MHz
WDW                   EM
SSB                    0
LB                1.00 Hz
GB                     0
PC                 1.40
```

```
File       :C:\msdchem\1\DATA\Ho\Synthesis\hs035-product1.D
Operator   : Seam
Acquired   :  5 Sep 2010  12:29     using AcqMethod WANGJUN.M
Instrument :   5973N
Sample Name:
Misc Info  :
Vial Number: 2
```

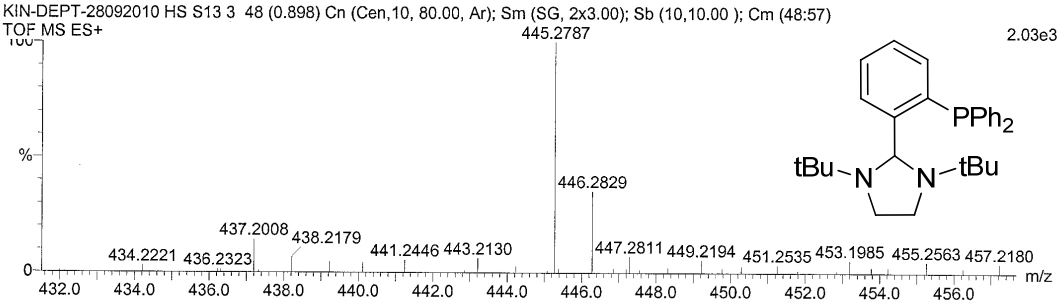


ɹnental Composition Report **Page 1**

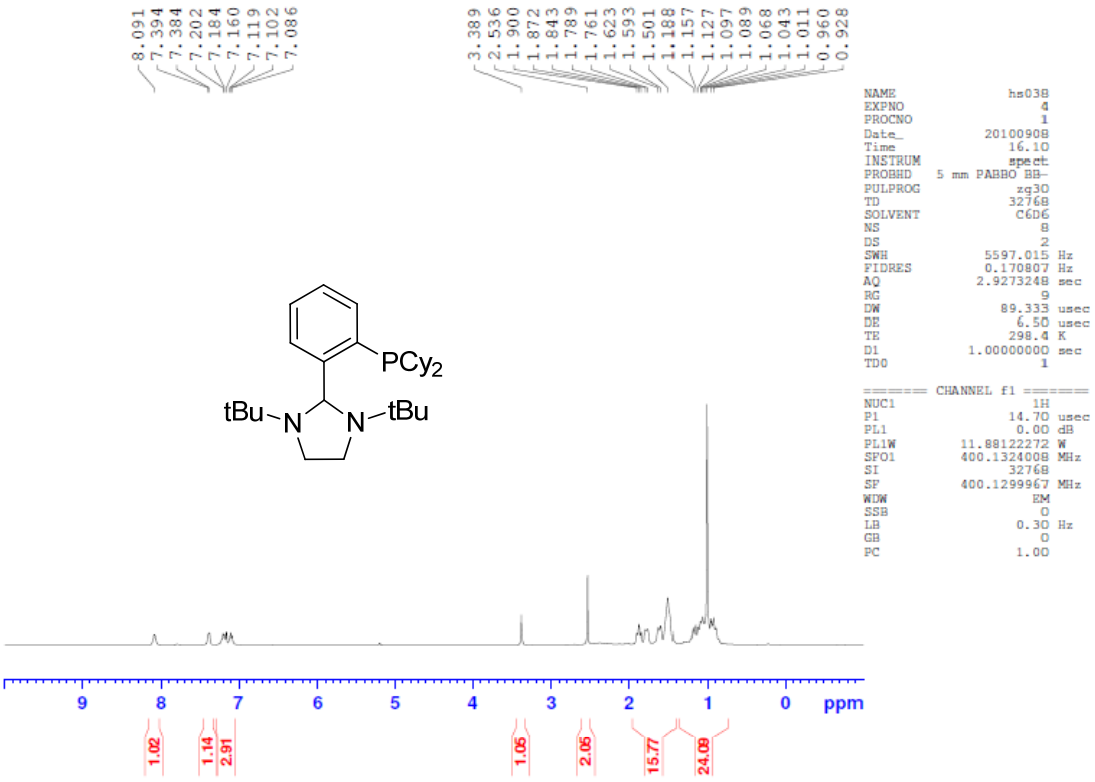
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -100.0, max = 1000.0
Selected filters: None

Monoisotopic Mass, Even Electron Ions
4 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-29 H: 0-38 N: 0-2 Na: 0-1 P: 0-1

KIN-DEPT-28092010 HS S13 3 48 (0.898) Cn (Cen,10, 80.00, Ar); Sm (SG, 2x3.00); Sb (10,10.00); Cm (48:57)
TOF MS ES+

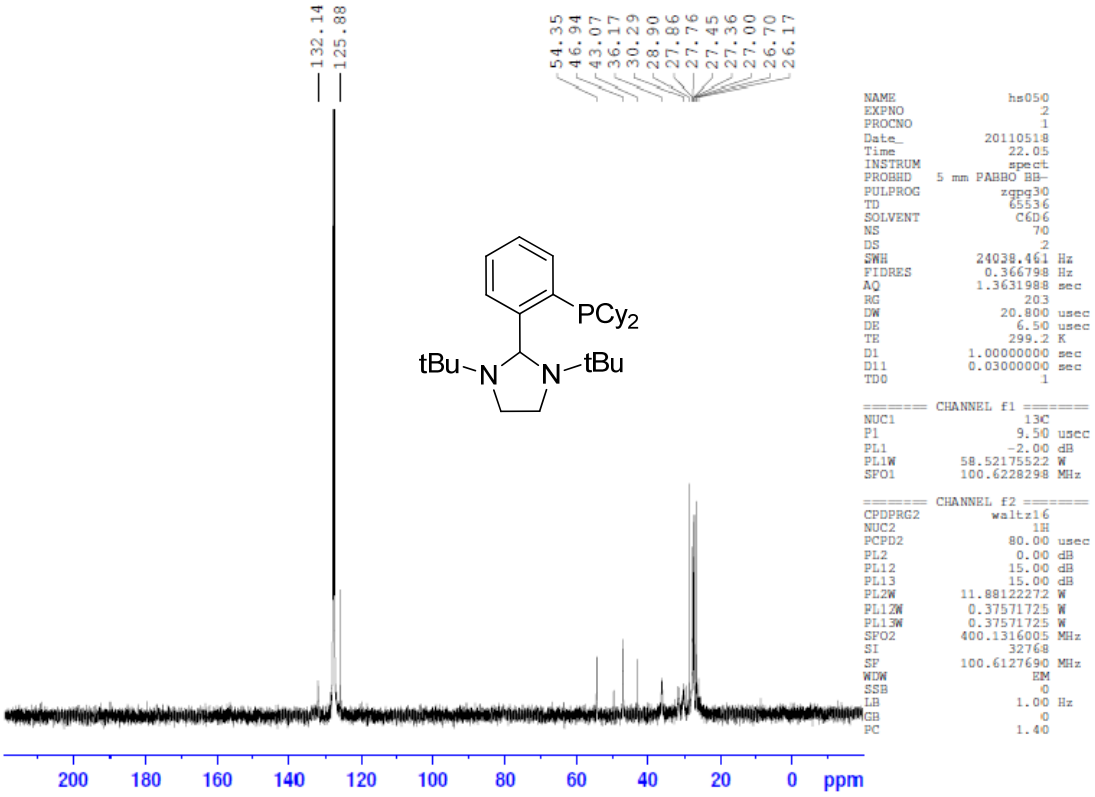


Minimum:		5.0	5.0	-100.0		
Maximum:				1000.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
445.2787	445.2773	1.4	3.1	12.5	3.9	C29 H38 N2 P




```
NAME                 hs038
EXPNO                   4
PROCNO                  1
Date_             20100908
Time                16.10
INSTRUM               spect
PROBHD     5 mm PABBO BB-
PULPROG              zg30
TD                  32768
SOLVENT              C6D6
NS                      8
DS                      2
SWH              5597.015 Hz
FIDRES           0.170807 Hz
AQ               2.9273248 sec
RG                      9
DW                 89.333 usec
DE                   6.50 usec
TE                 298.4 K
D1               1.00000000 sec
TD0                     1

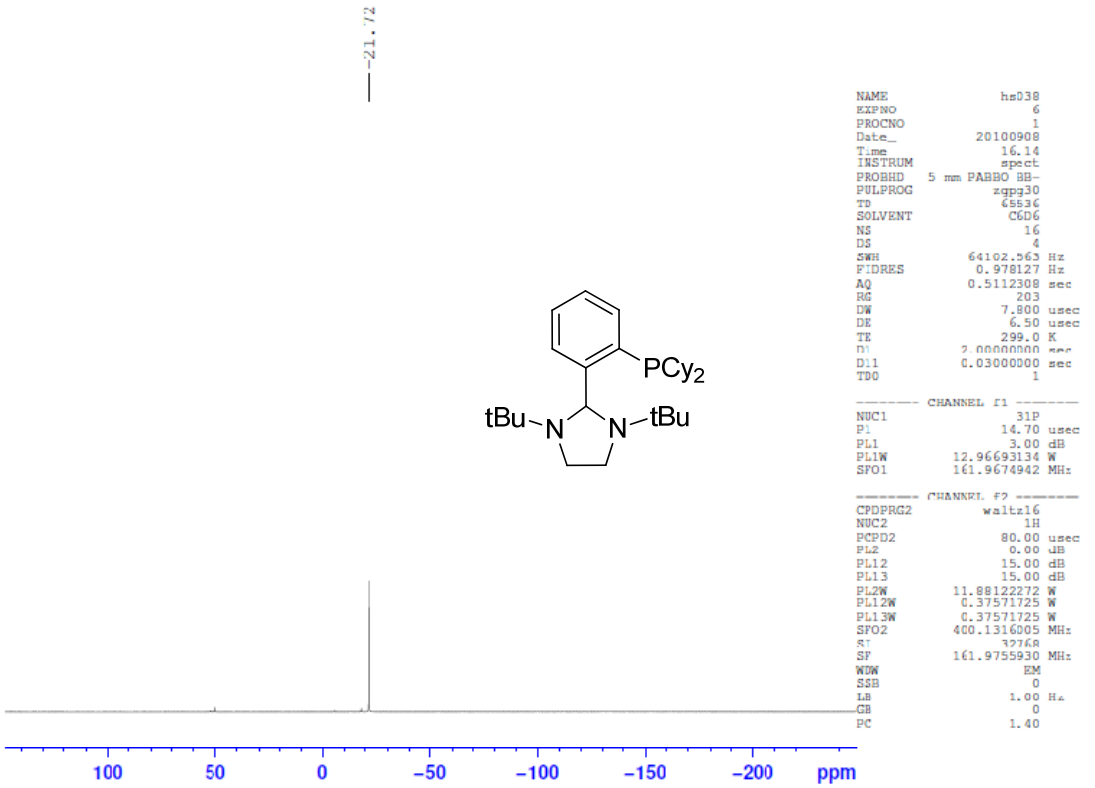
====== CHANNEL f1 ======
NUC1                   1H
P1                  14.70 usec
PL1                  0.00 dB
PL1W          11.88122272 W
SFO1          400.1324008 MHz
SI                  32768
SF            400.1299967 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```




```
NAME                hs050
EXPNO                   2
PROCNO                  1
Date_            20110518
Time                22.05
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                 65536
SOLVENT              C6D6
NS                     70
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                299.2 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
```

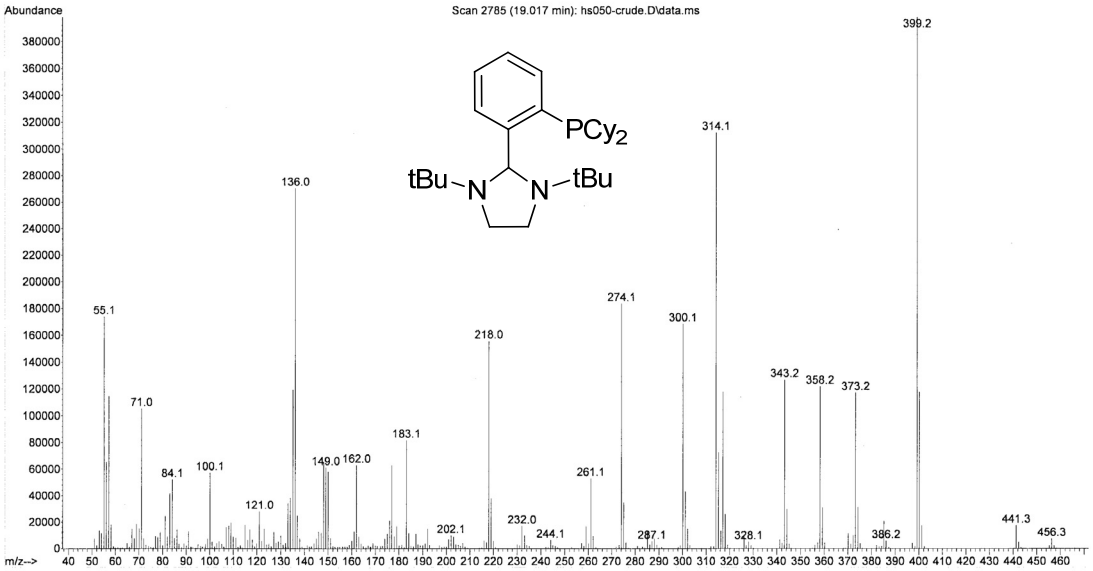


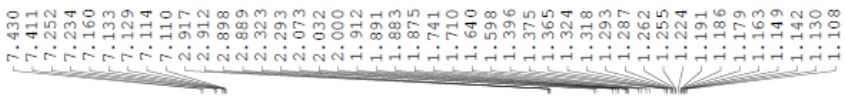

```
NAME                hs038
EXPNO                   6
PROCNO                  1
Date_            20100908
Time                16.14
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                 65536
SOLVENT              C6D6
NS                     16
DS                      4
SWH           64102.563 Hz
FIDRES         0.978127 Hz
AQ             0.5112308 sec
RG                    203
DW                 7.800 usec
DE                 6.50 usec
TE                299.0 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1

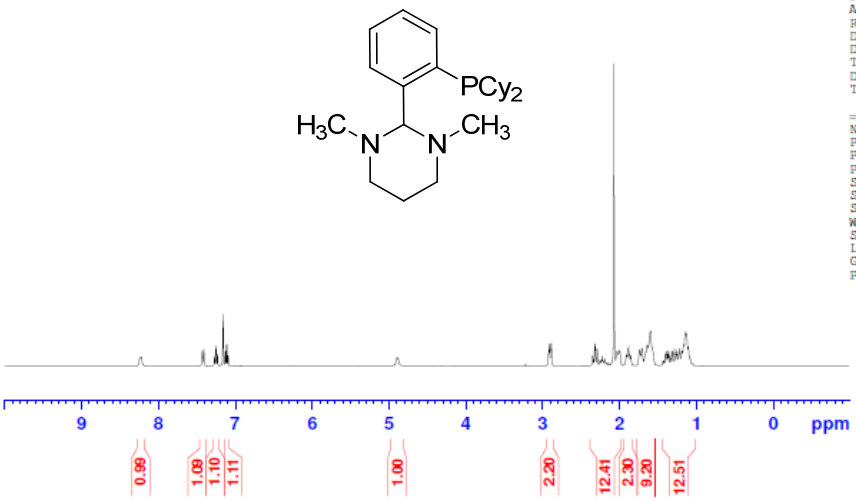
====== CHANNEL f1 ======
NUC1                  31P
P1                 14.70 usec
PL1                 3.00 dB
PL1W          12.96693134 W
SFO1         161.9674942 MHz

====== 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           161.9755930 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
```

```
File       :C:\msdchem\1\DATA\Ho\Synthesis\hs050-crude.D
Operator   : Seam
Acquired   : 13 Sep 2010  12:14     using AcqMethod WANGJUN.M
Instrument :   5973N
Sample Name:
Misc Info  :
Vial Number: 1
```

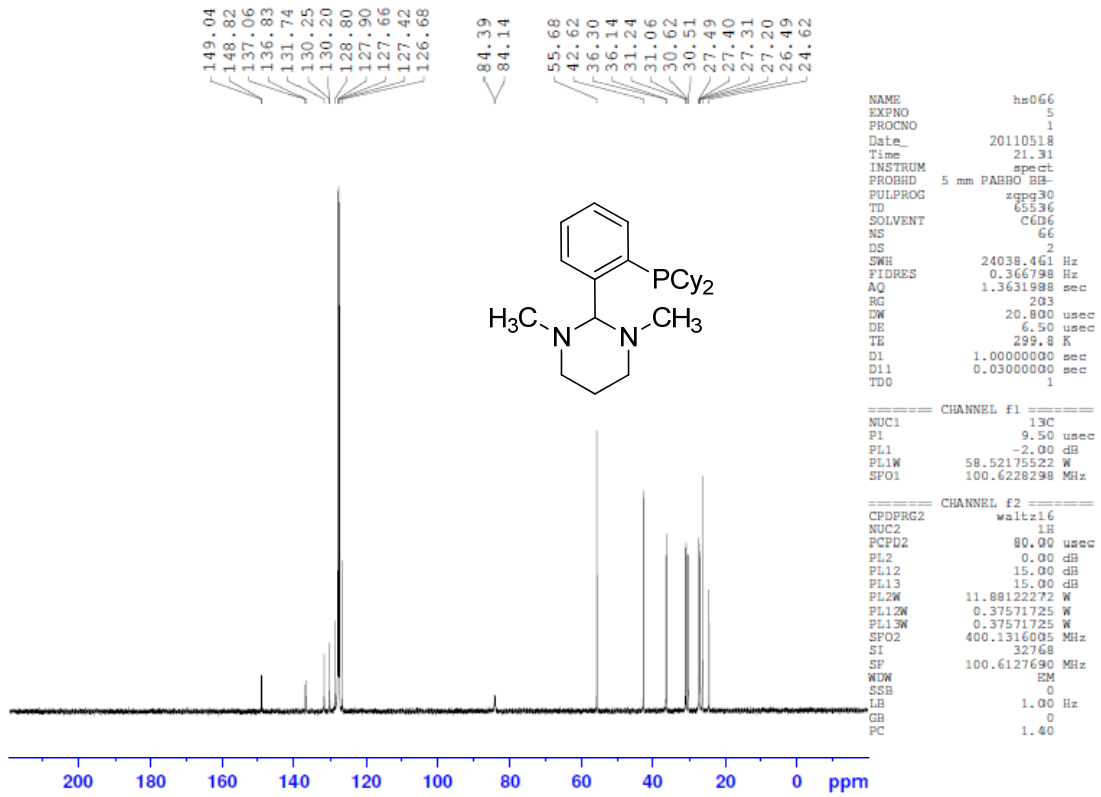


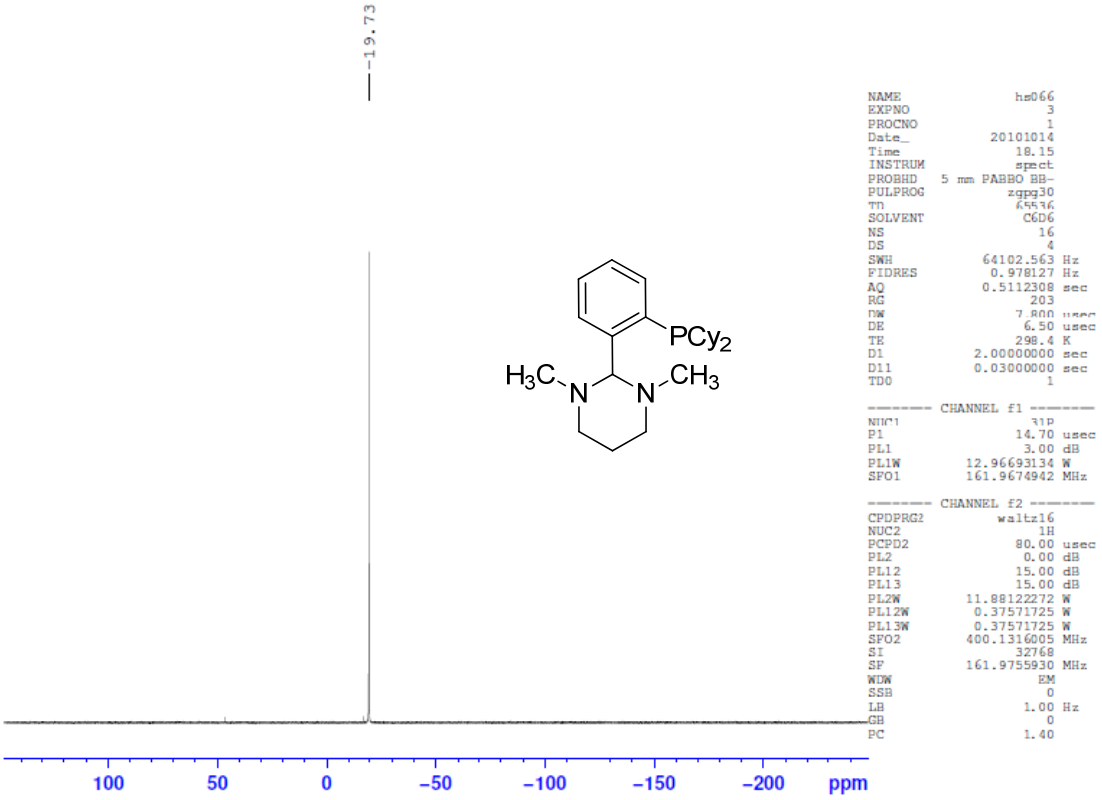




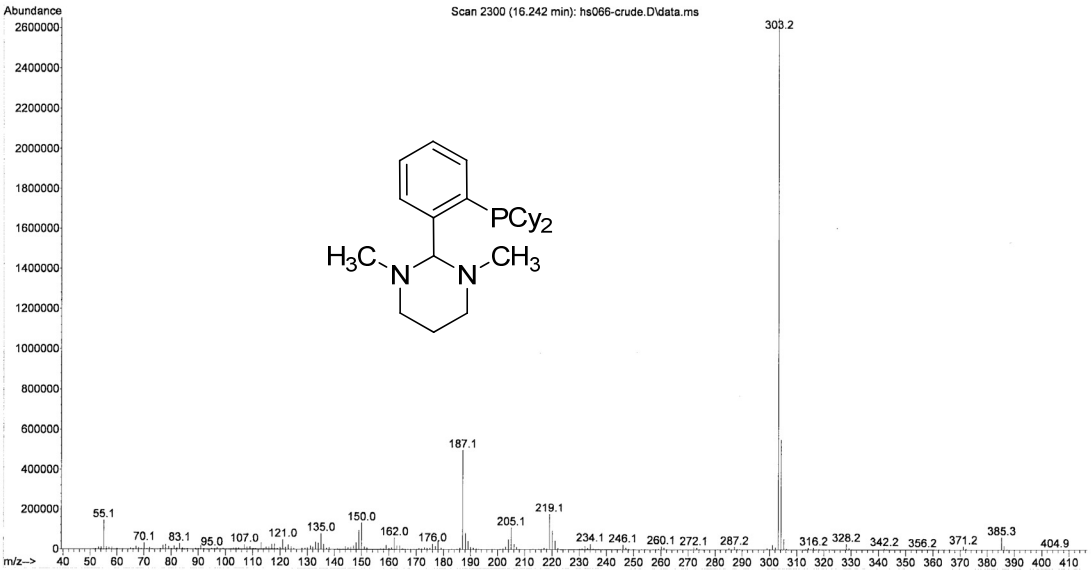

```
NAME                 hs066
EXPNO                    1
PROCNO                   1
Date_             20101014
Time                 18.05
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG              zg30
TD                  32768
SOLVENT              C6D6
NS                       8
DS                       2
SWH              5597.015 Hz
FIDRES           0.170807 Hz
AQ               2.9273248 sec
RG                    22.6
DW                 89.333 usec
DE                   6.50 usec
TE                 297.8 K
D1               1.00000000 sec
TD0                      1

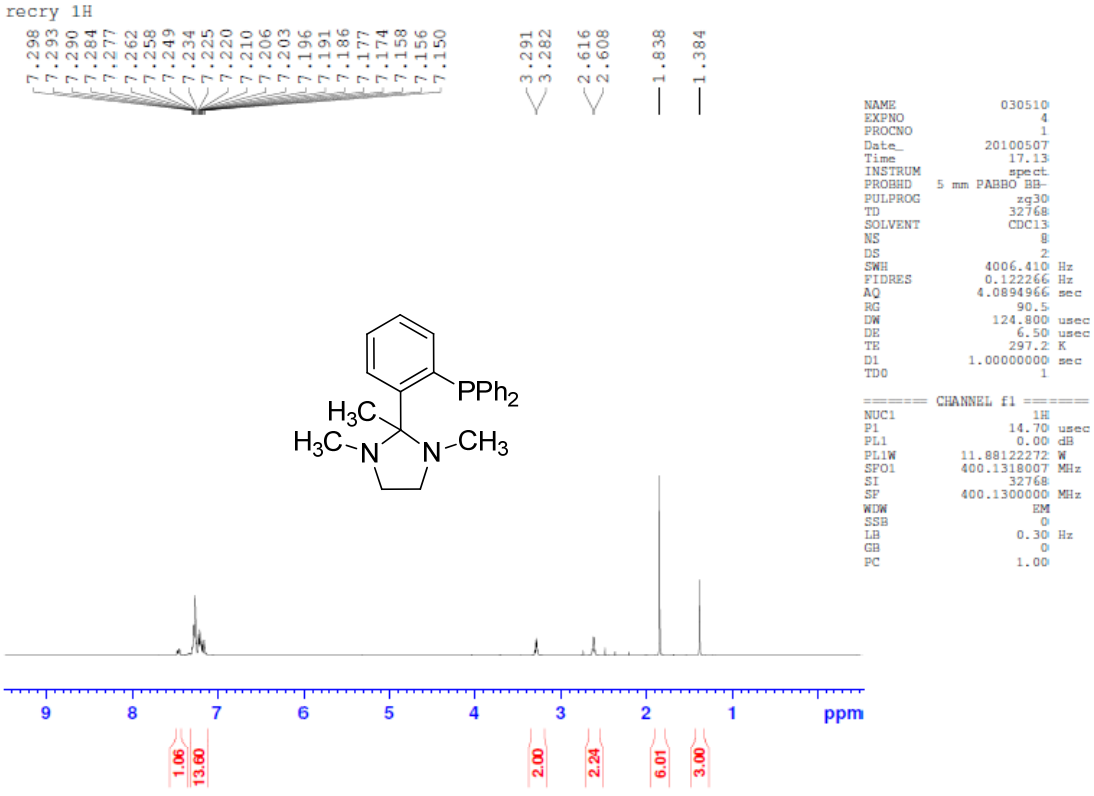
======= CHANNEL f1 =======
NUC1                    1H
P1                   14.70 usec
PL1                   0.00 dB
PL1W          11.88122272 W
SFO1          400.1324008 MHz
SI                   32768
SF            400.1299967 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```


149.04
148.82
137.06
136.83
131.74
130.25
130.20
128.80
127.90
127.66
127.42
126.68
84.39
84.14
55.68
42.62
36.30
36.14
31.24
31.06
30.62
30.51
27.49
27.40
27.31
27.20
26.49
24.62
PCy2
H3C
N
N
CH3
200
180
160
140
120
100
80
60
40
20
0
ppm
NAME hs066
EXPNO 5
PROCNO 1
Date_ 20110518
Time 21.31
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT C6D6
NS 66
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 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


19.73
PCy2
H3C
N
N
CH3
100
50
0
-50
-100
-150
-200
ppm
NAME hs066
EXPNO 3
PROCNO 1
Date_ 20101014
Time 18.15
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT C6D6
NS 16
DS 4
SWH 64102.563 Hz
FIDRES 0.978127 Hz
AQ 0.5112308 sec
RG 203
DW 7.800 usec
DE 6.50 usec
TE 298.4 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
====== CHANNEL f1 ======
NUC1 31P
P1 14.70 usec
PL1 3.00 dB
PL1W 12.96693134 W
SFO1 161.9674942 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 161.9755930 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

```
File       :C:\msdchem\1\DATA\Ho\Synthesis\hs066-crude.D
Operator   : Seam
Acquired   : 13 Oct 2010  13:14      using AcqMethod WANGJUN.M
Instrument :   5973N
Sample Name:
Misc Info  :
Vial Number: 4
```

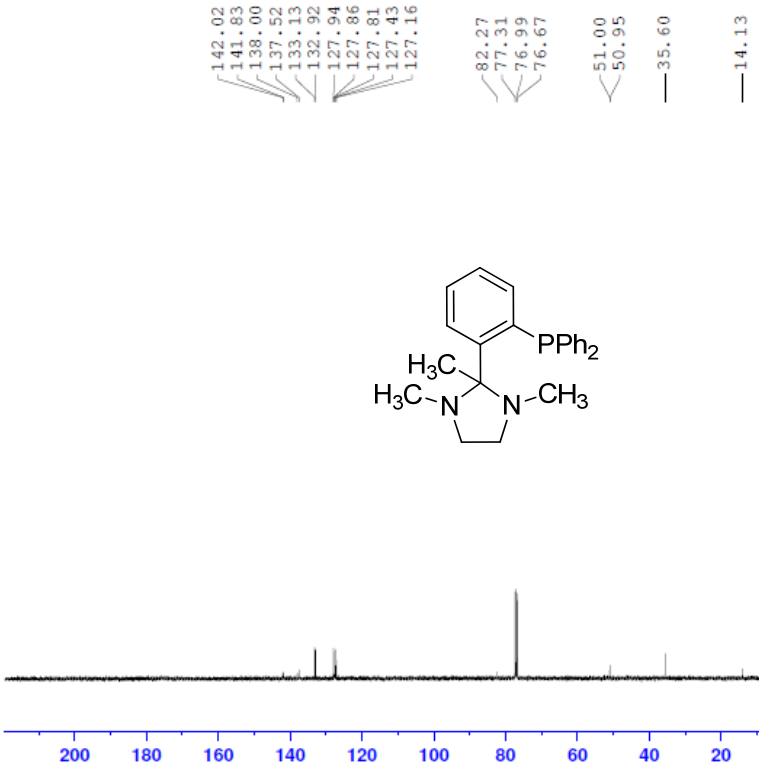





```
NAME                 030510
EXPNO                     4
PROCNO                    1
Date_              20100507
Time                  17.13
INSTRUM                spect
PROBHD   5 mm PABBO BB-
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                        8
DS                        2
SWH                4006.410 Hz
FIDRES             0.122266 Hz
AQ                 4.0894966 sec
RG                     90.5
DW                   124.800 usec
DE                     6.50 usec
TE                    297.2 K
D1                 1.00000000 sec
TD0                       1

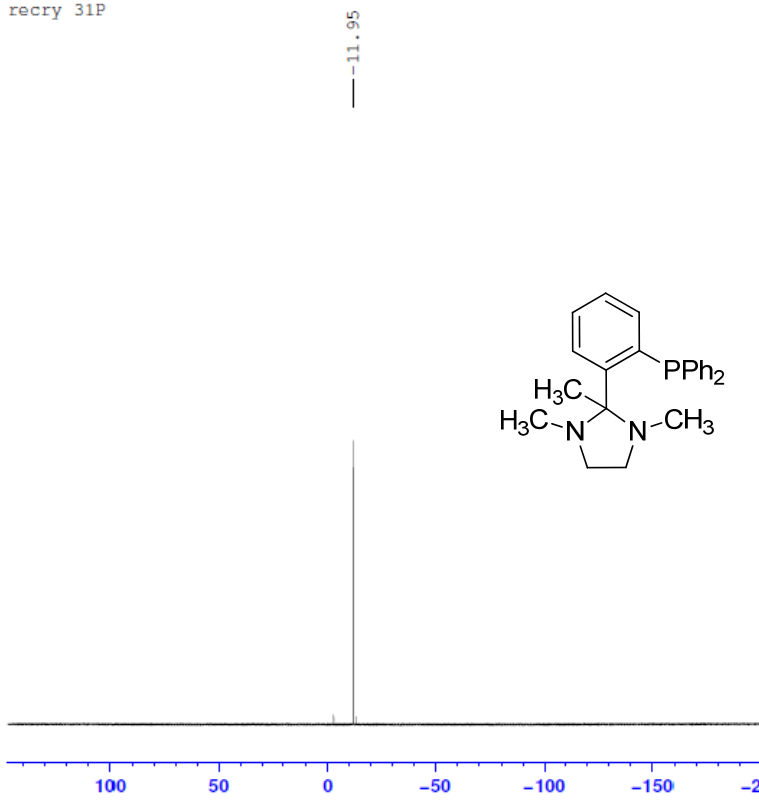
====== CHANNEL f1 ======
NUC1                     1H
P1                    14.70 usec
PL1                    0.00 dB
PL1W           11.88122272 W
SFO1           400.1318007 MHz
SI                    32768
SF             400.1300000 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

recry 13C



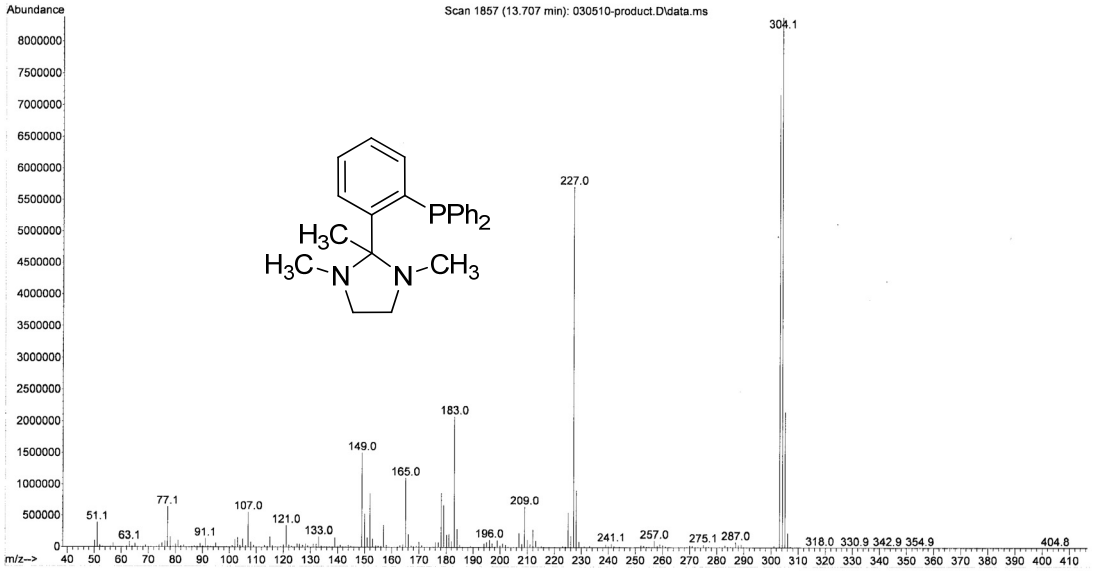
NAME	030510
EXPNO	5
PROCNO	1
Date_	20100507
Time	17.18
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	32
DS	2
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	297.7 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
====== CHANNEL f1 ======	
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	100.6127724 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

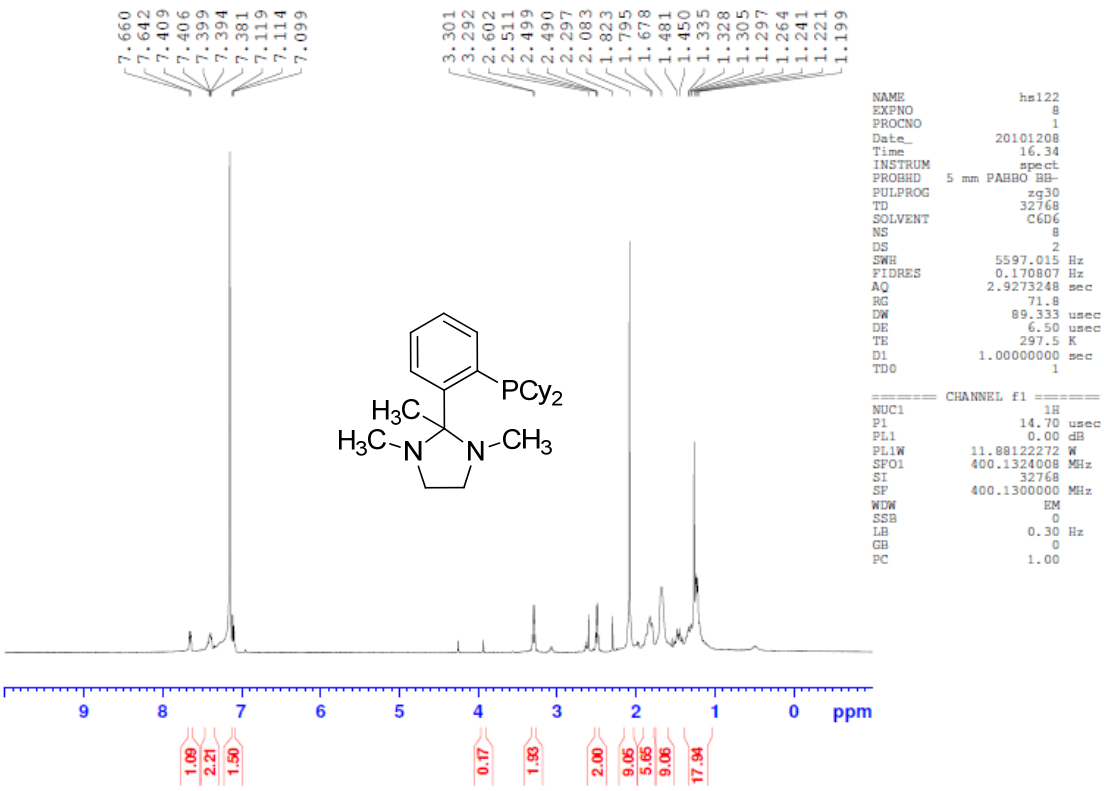
recry 31P

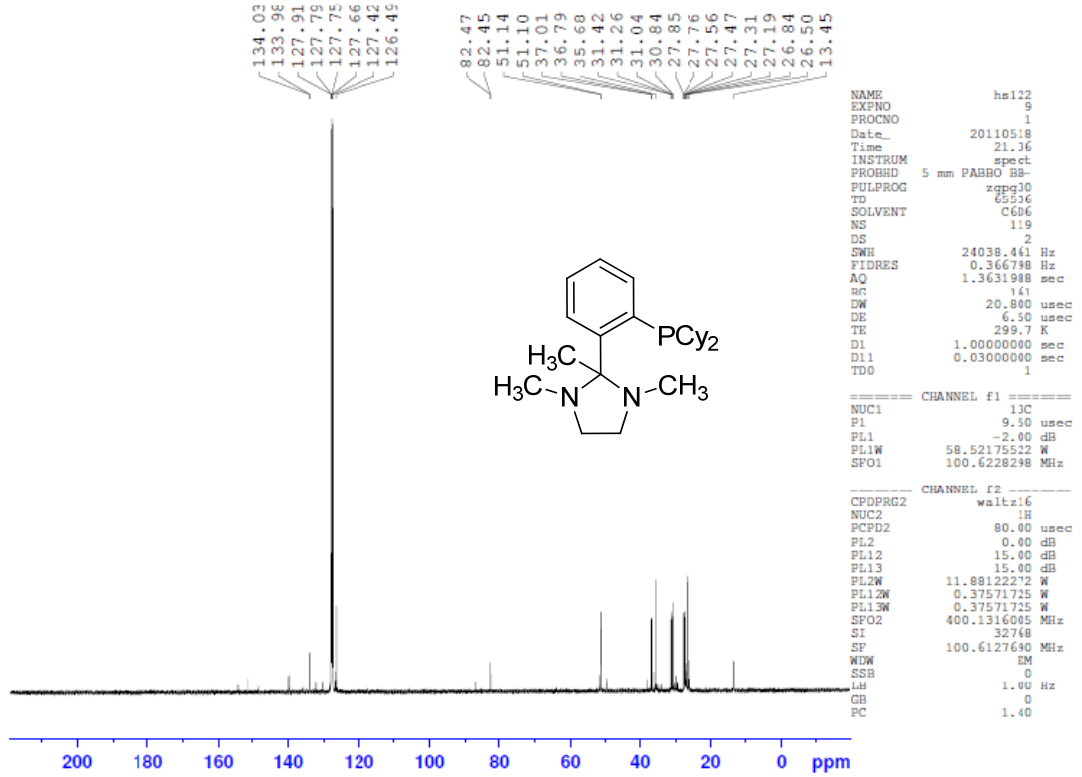


NAME	030510
EXPNO	6
PROCNO	1
Date_	20100507
Time	17.23
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	4
SWH	64102.563 Hz
FIDRES	0.978127 Hz
AQ	0.5112308 sec
RG	203
DW	7.800 usec
DE	6.50 usec
TE	297.9 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
====== CHANNEL f1 ======	
NUC1	31P
P1	14.70 usec
PL1	3.00 dB
PL1W	12.96693134 W
SFO1	161.9674942 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	161.9755930 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

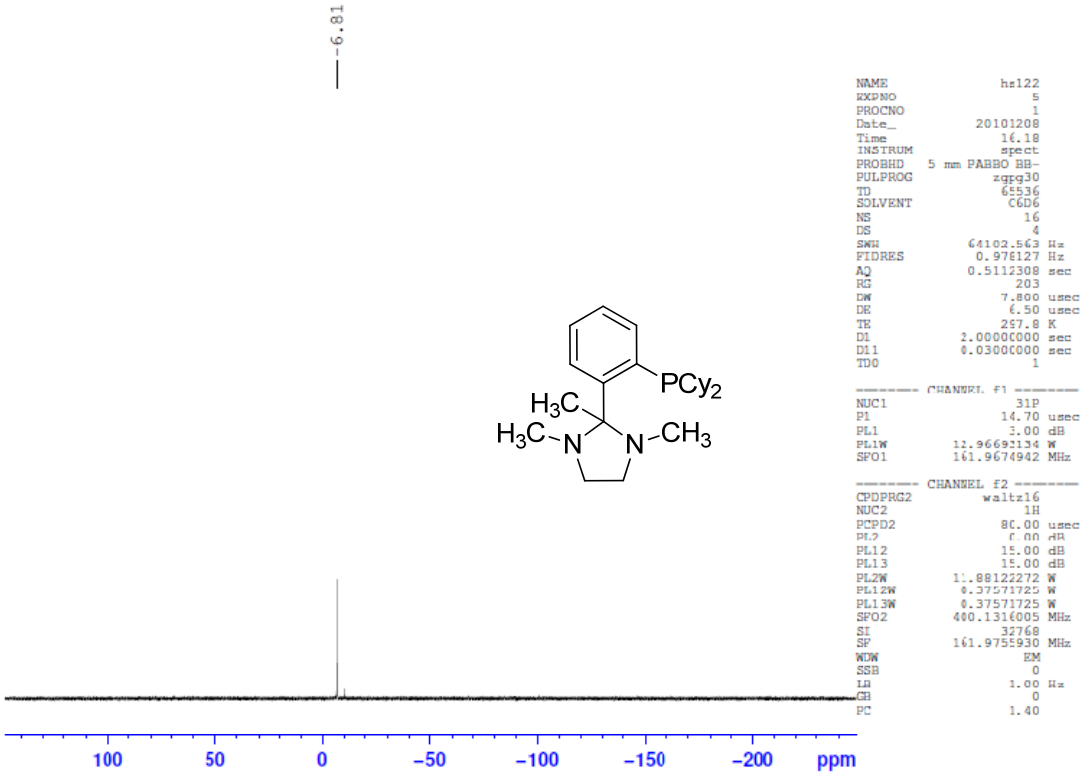
```
File       :C:\msdchem\1\DATA\Ho\Synthesis\030510-product.D
Operator   : Seam
Acquired   : 30 Aug 2010  17:30     using AcqMethod WANGJUN.M
Instrument :   5973N
Sample Name:
Misc Info  :
Vial Number: 4
```







NAME	hs122
EXPNO	9
PROCNO	1
Date_	20110518
Time	21.36
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	C6D6
NS	119
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	299.7 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



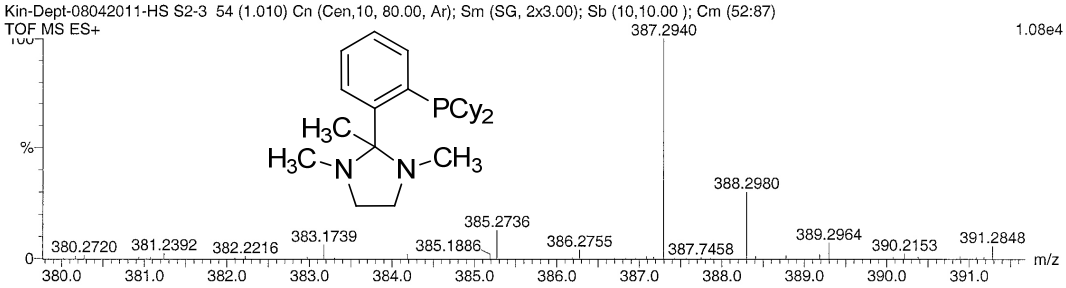
NAME	hs122
EXPNO	5
PROCNO	1
Date_	20101208
Time	16.18
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	C6D6
NS	16
DS	4
SWH	64102.563 Hz
FIDRES	0.976127 Hz
AQ	0.5112308 sec
RG	203
DW	7.800 usec
DE	6.50 usec
TE	297.8 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	31P
P1	14.70 usec
PL1	3.00 dB
PL1W	12.96693134 W
SFO1	161.9674942 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	161.9755930 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

ɜmental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -100.0, max = 1000.0
Selected filters: None

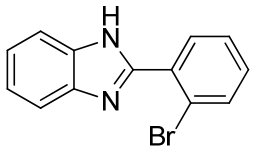
Monoisotopic Mass, Even Electron Ions
605 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-24 H: 0-401 N: 0-2 Na: 0-1 P: 0-2 39K: 0-1

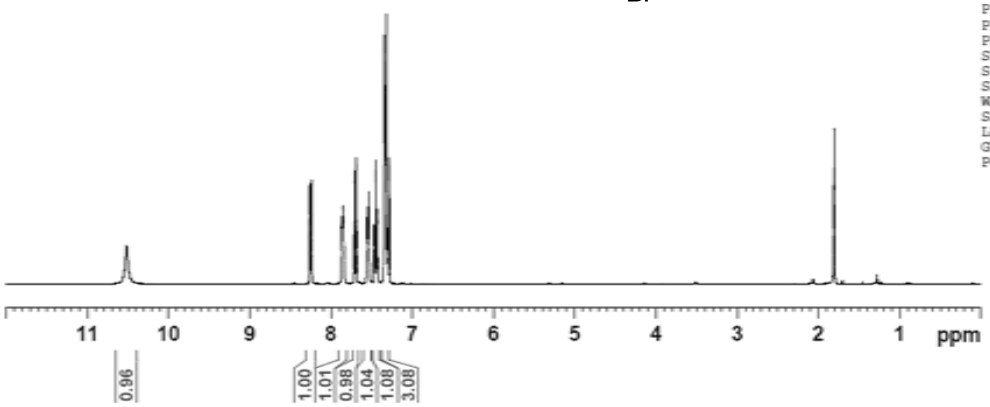
Kin-Dept-08042011-HS S2-3 54 (1.010) Cn (Cen,10, 80.00, Ar); Sm (SG, 2x3.00); Sb (10,10.00); Cm (52:87)

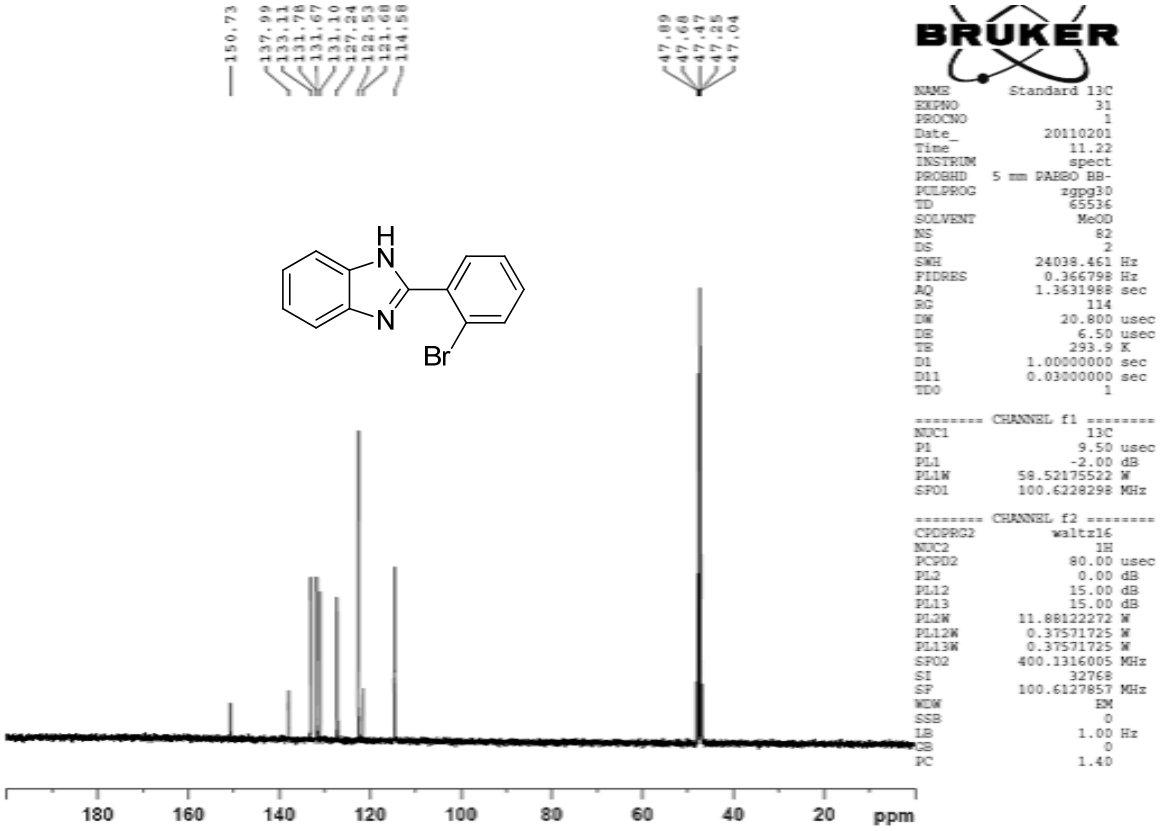


Minimum:				-100.0		
Maximum:		5.0	5.0	1000.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
387.2940	387.2929	1.1	2.8	6.5	79.5	C24 H40 N2 P

NAME	Standard 1H
EXPNO	126
PROCNO	1
Date_	20110124
Time	18.15
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	10
DS	2
SWH	8012.820 Hz
FIDRES	0.244532 Hz
AQ	2.0447731 sec
RG	181
DW	62.400 usec
DE	6.50 usec
TE	296.8 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	14.70 usec
PL1	0.00 dB
PL1W	11.88122272 W
SFO1	400.1336012 MHz
SI	32768
SF	400.1300000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



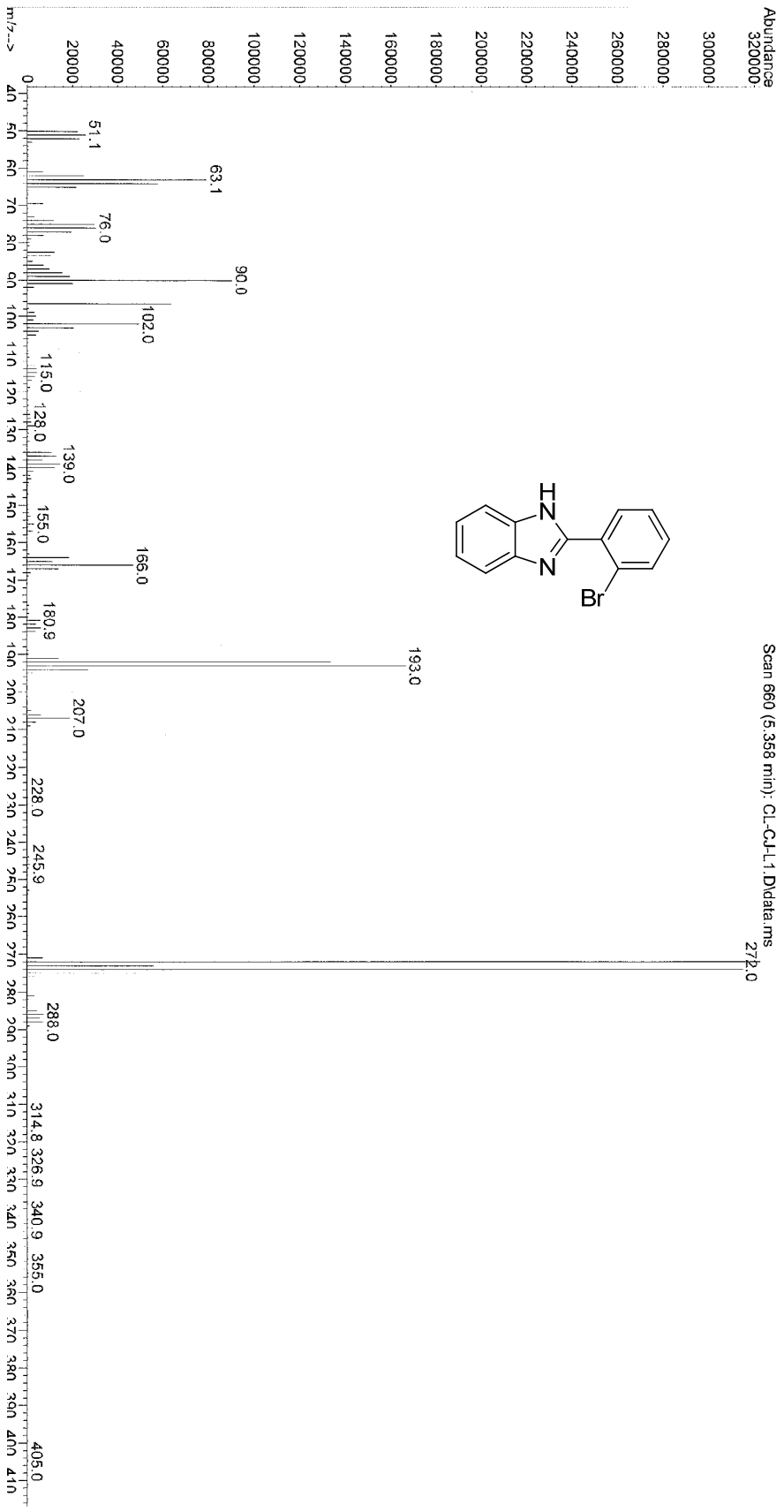


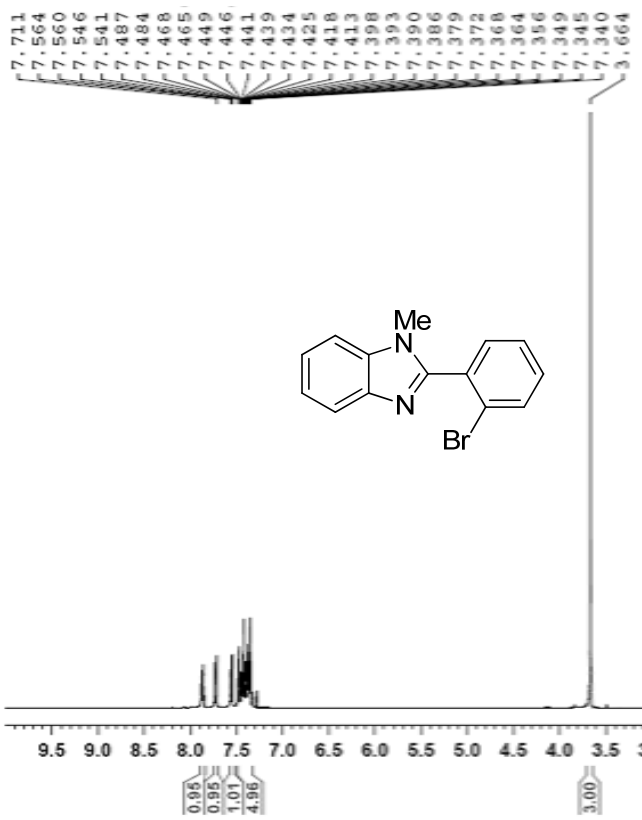


BRUKER

NAME	Standard 13C
EXPNO	31
PROCNO	1
Date_	20110201
Time	11.22
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	MeOD
NS	82
DS	2
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	114
DW	20.800 usec
DE	6.50 usec
TE	293.9 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	100.6127857 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

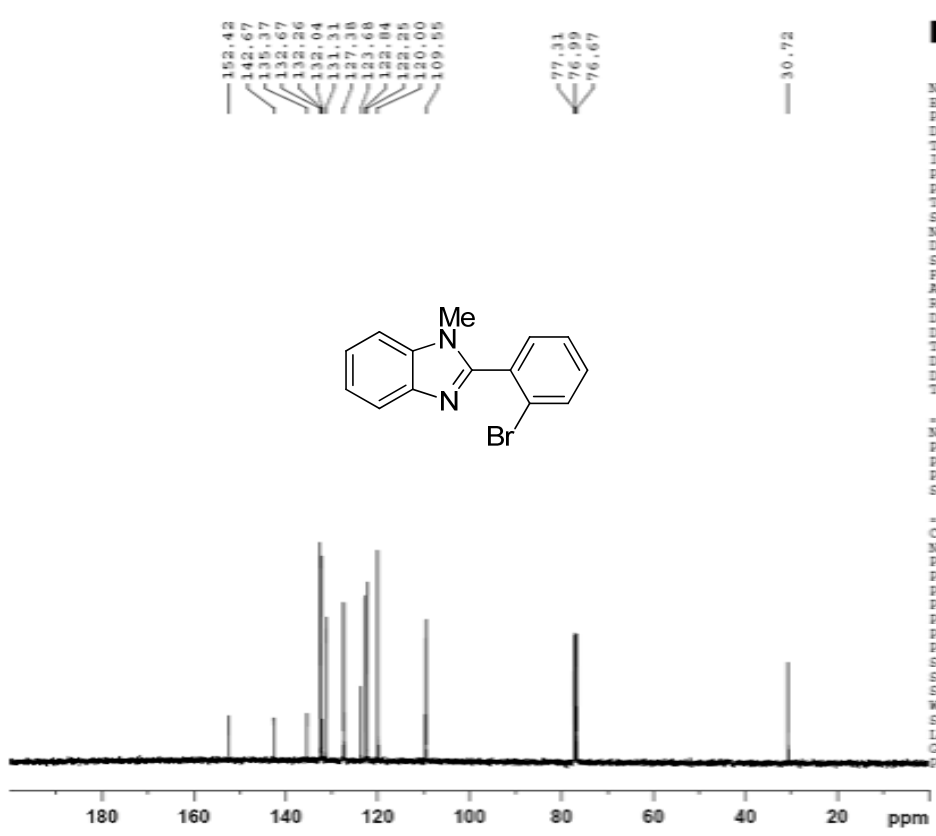
File :C:\MSDCHEM\1\DATA\HO\Snapshot\CL-CJ-L1.D
Operator : Seam
Acquired : 26 Jan 2011 13:51 using AcqMethod METHOD2A.M
Instrument : 5973N
Sample Name:
Misc Info :
Vial Number: 2






```
NAME            Standard 1H
EXPNO                  127
PROCNO                   1
Date_             20110125
Time                13.48
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                   40.3
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         400.1336012 MHz
SI                  32768
SF           400.1300000 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

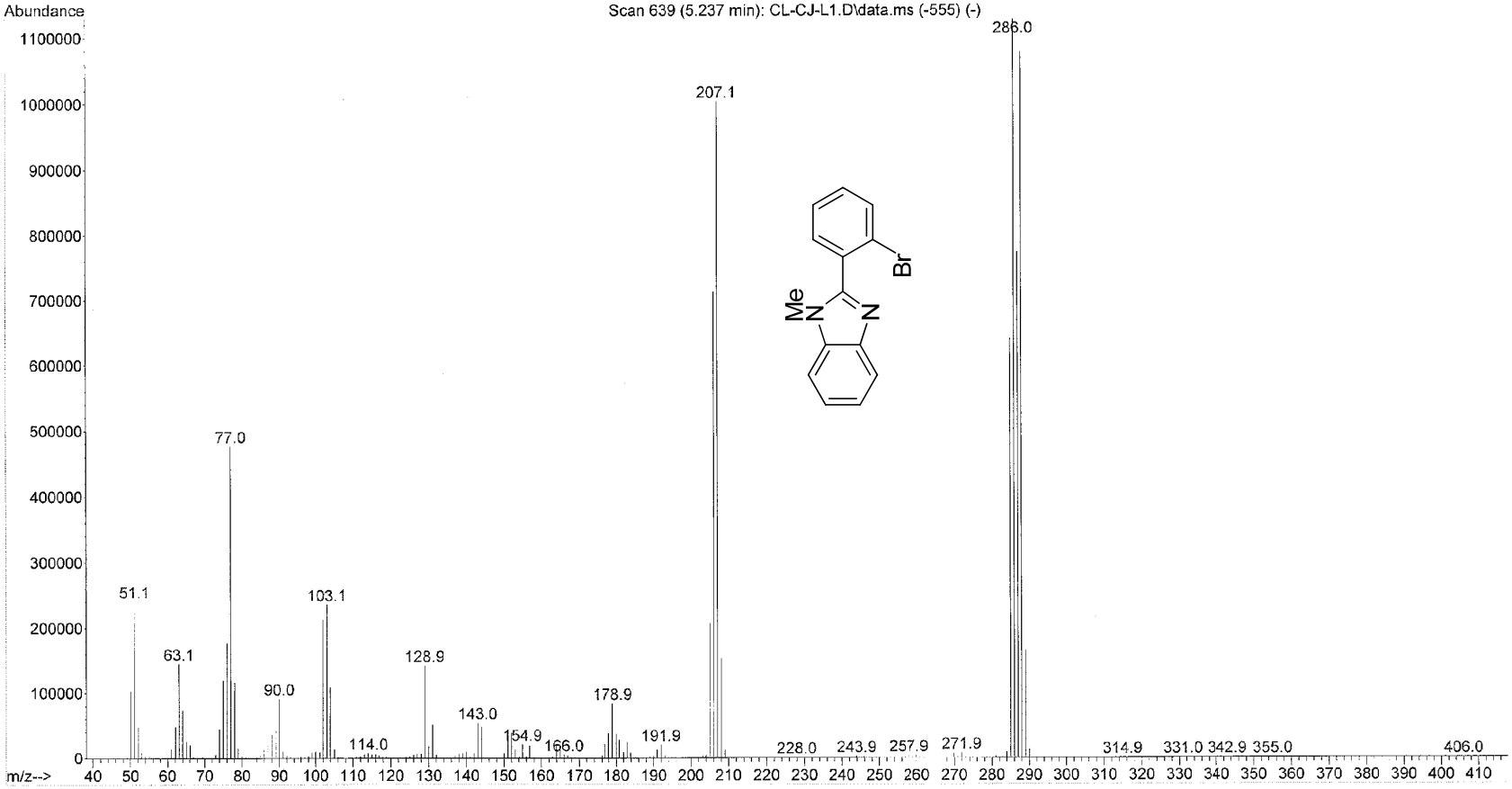


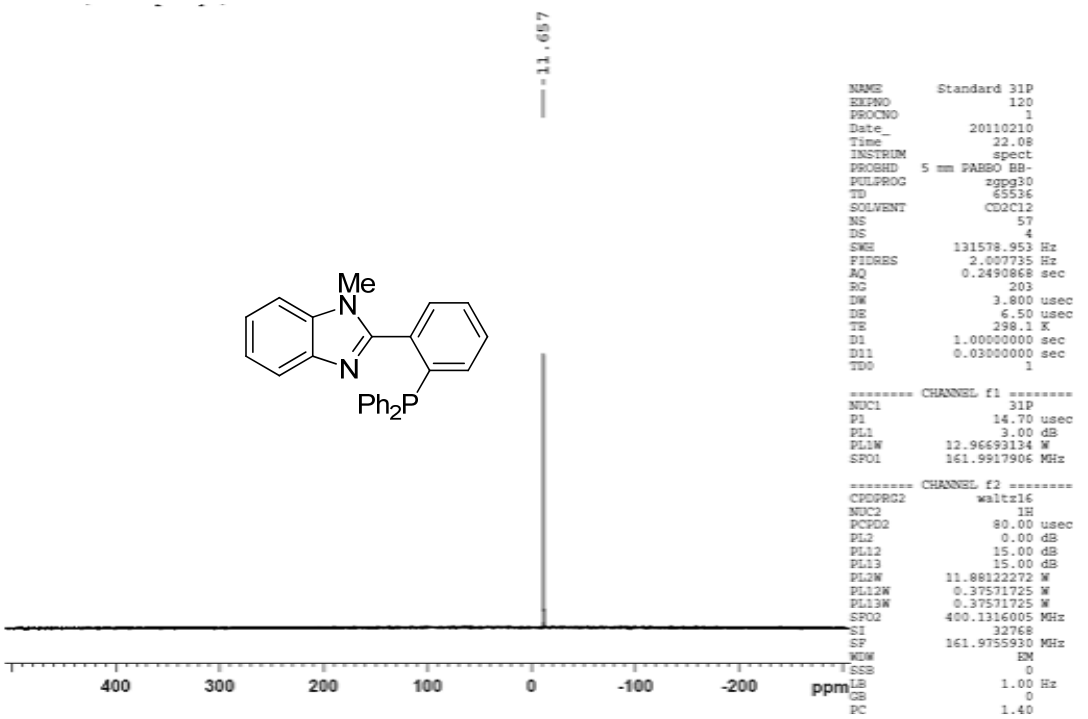

```
NAME            Standard 13C
EXPNO                   29
PROCNO                   1
Date_             20110125
Time                13.53
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG            zgpg30
TD                  65536
SOLVENT             CDCl3
NS                     59
DS                      2
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631988 sec
RG                    144
DW                20.800 usec
DE                 6.50 usec
TE                295.4 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           100.6127857 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
```

```
File       :C:\MSDCHEM\1\DATA\HO\Snapshot\CL-CJ-L1.D
Operator   : Seam
Acquired   : 26 Jan 2011  13:51     using AcqMethod METHOD2A.M
Instrument :   5973N
Sample Name:
Misc Info  :
Vial Number: 2
```

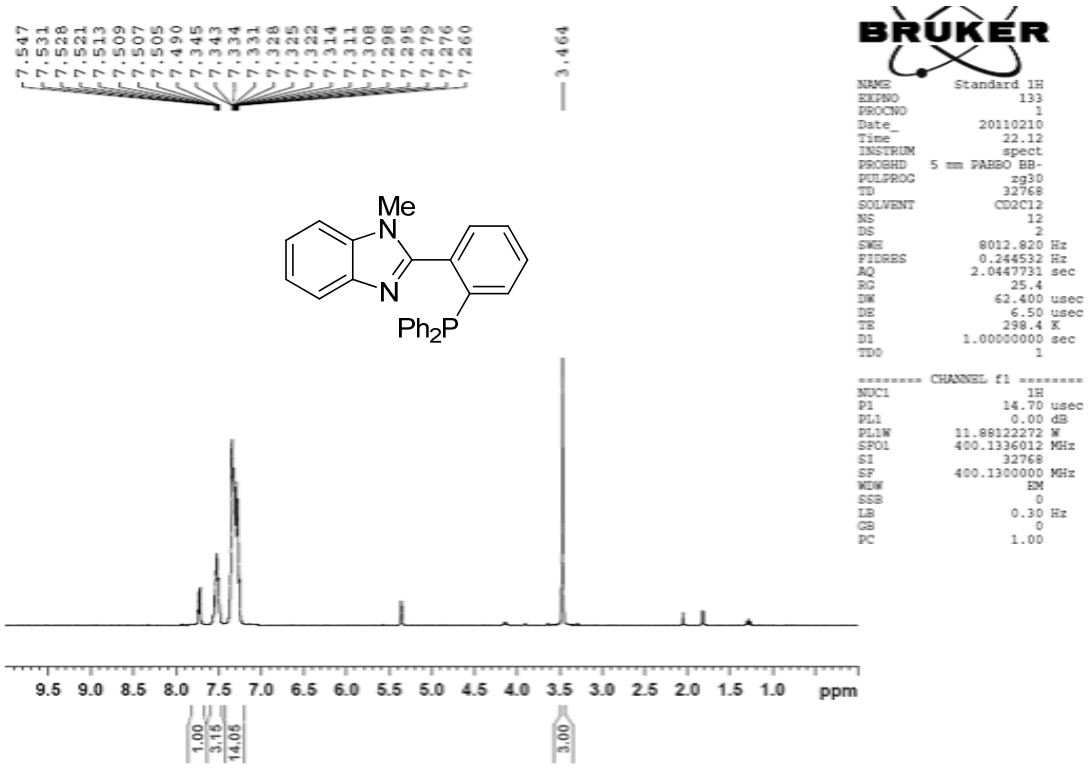





```
NAME            Standard 31P
EXPNO                    120
PROCNO                     1
Date_               20110210
Time_                  22.08
INSTRUM                spect
PROBHD   5 mm PABBO BB-
PULPROG                zgpg30
TD                      65536
SOLVENT                CD2C12
NS                         57
DS                          4
SWH              131578.953 Hz
FIDRES             2.007735 Hz
AQ                 0.2490868 sec
RG                       203
DW                   3.800 usec
DE                   6.50 usec
TE                   298.1 K
D1                1.00000000 sec
D11               0.03000000 sec
TD0                        1

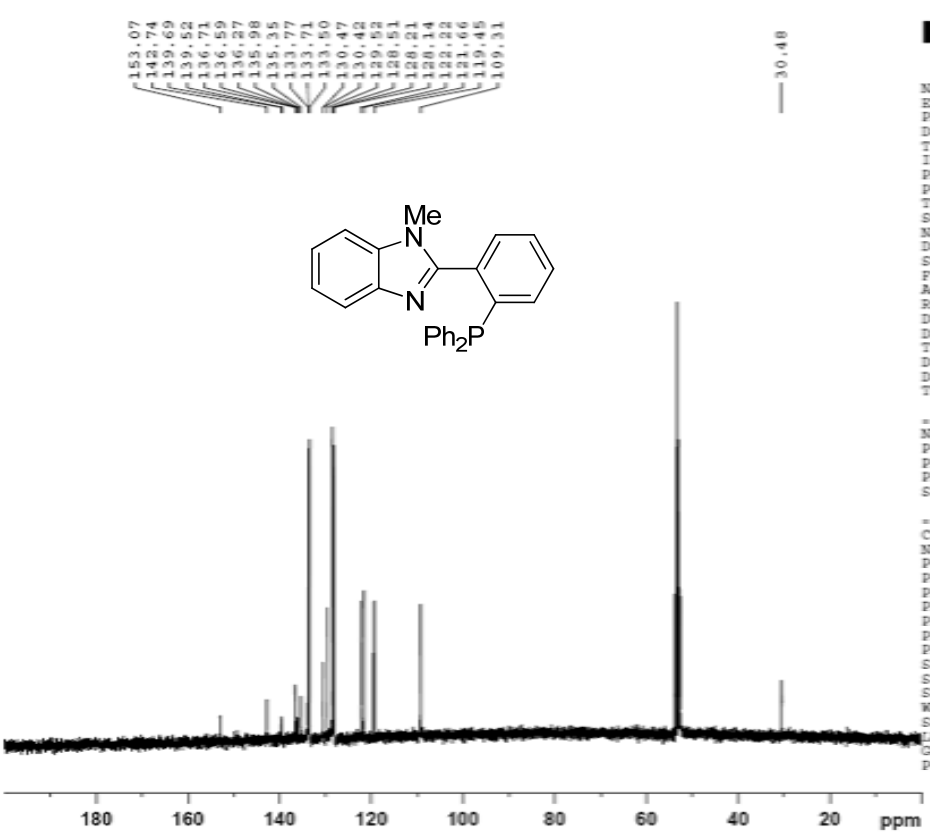
======== CHANNEL f1 ========
NUC1                     31P
P1                   14.70 usec
PL1                   3.00 dB
PL1W             12.96693134 W
SFO1            161.9917906 MHz

======== 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              161.9755930 MHz
WDW                       EM
SSB                        0
LB                    1.00 Hz
GB                         0
PC                      1.40
```




```
NAME            Standard 1H
EXPNO                    133
PROCNO                     1
Date_               20110210
Time_                  22.12
INSTRUM                spect
PROBHD   5 mm PABBO BB-
PULPROG                zg30
TD                      32768
SOLVENT                CD2C12
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                   298.4 K
D1                1.00000000 sec
TD0                        1

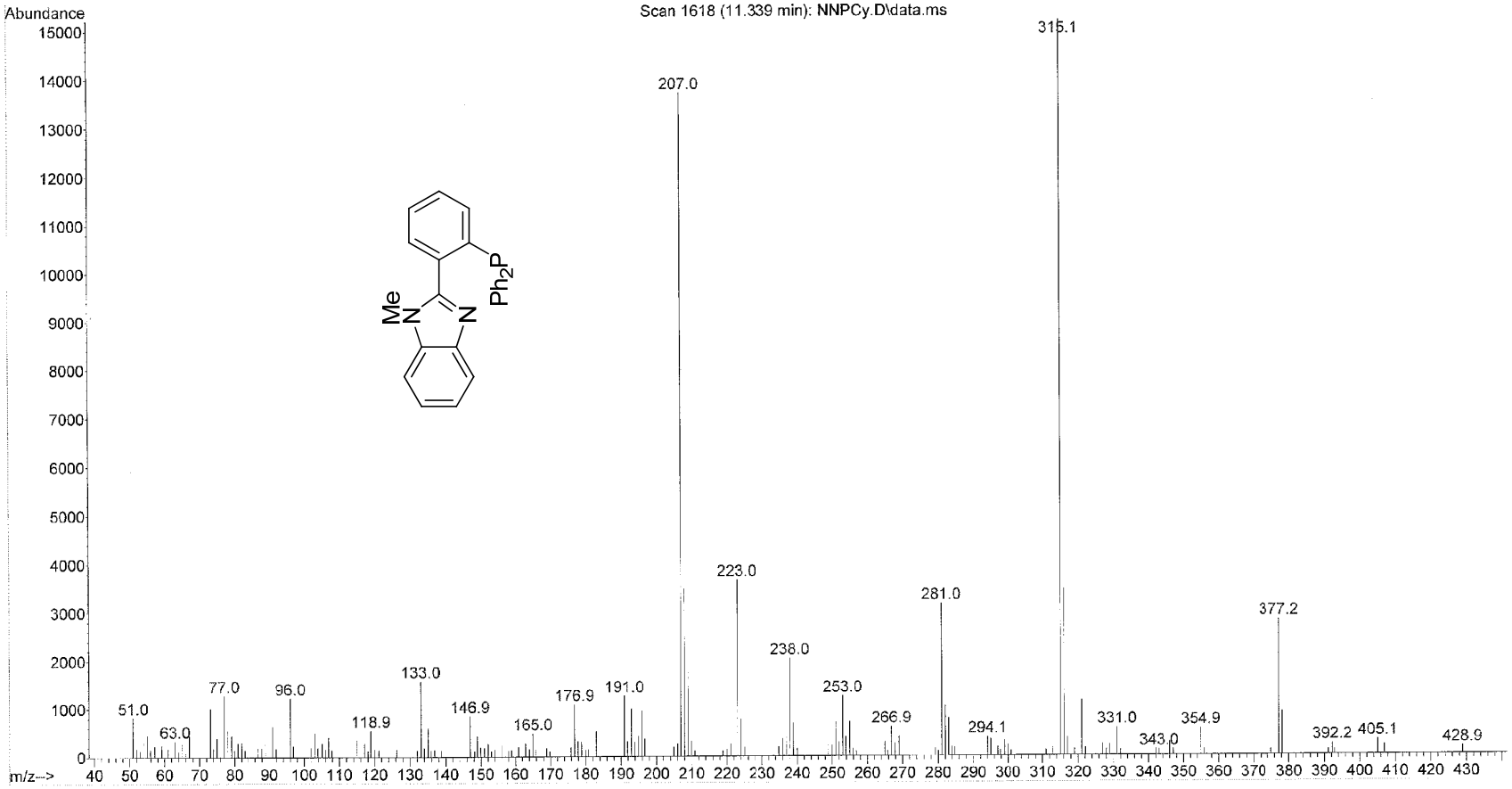
======== CHANNEL f1 ========
NUC1                      1H
P1                   14.70 usec
PL1                   0.00 dB
PL1W             11.88122272 W
SFO1            400.1336012 MHz
SI                     32768
SF              400.1300000 MHz
WDW                       EM
SSB                        0
LB                    0.30 Hz
GB                         0
PC                      1.00
```

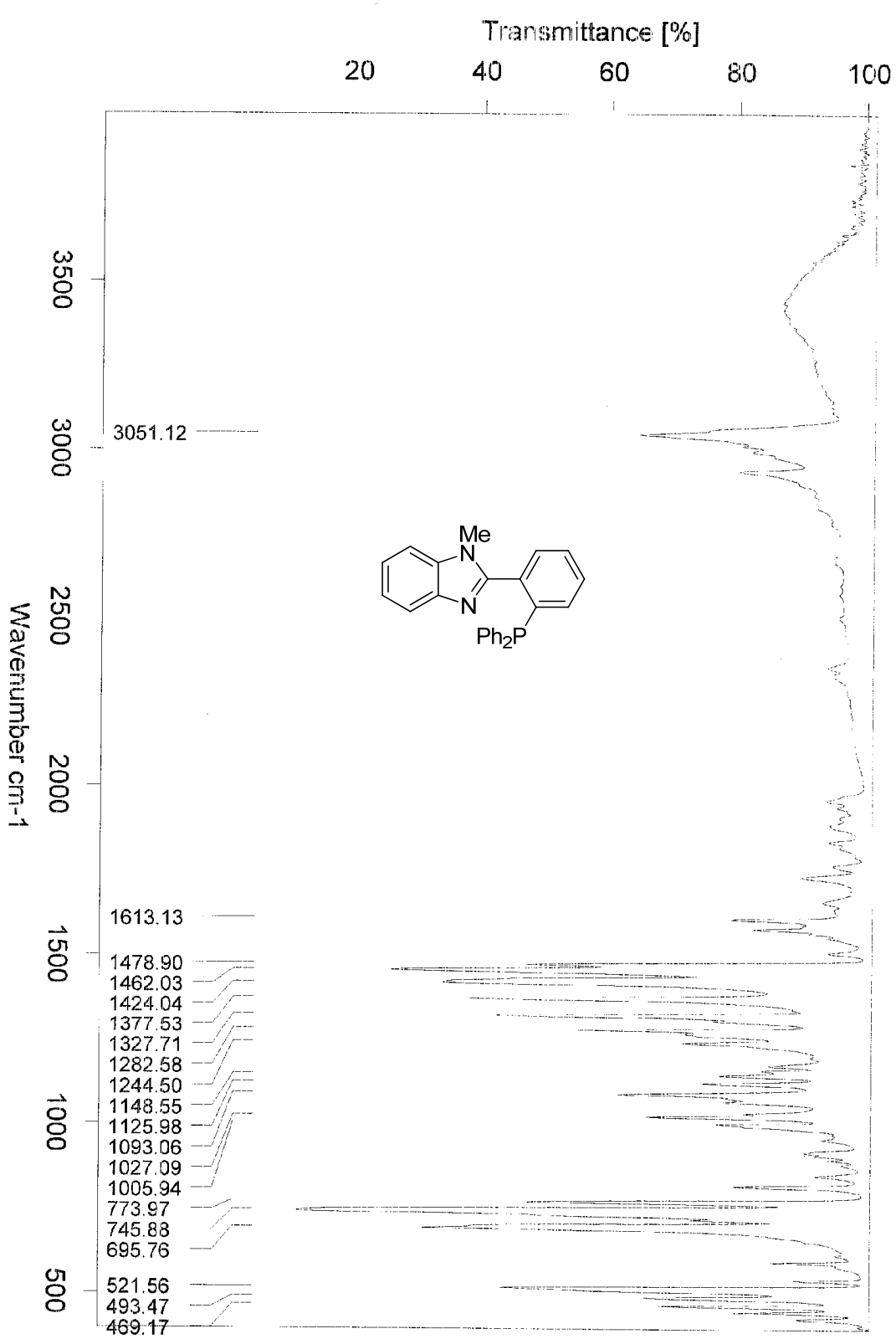


BRUKER

NAME	Standard 13C
EXPNO	32
PROCNO	1
Date_	20110210
Time	22.17
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CD2C12
NS	204
DS	2
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	114
DW	20.800 usec
DE	6.50 usec
TE	299.0 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	100.6127857 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

```
File       :C:\msdchem\1\DATA\DIC\NNPCy.D
Operator   : Seam
Acquired   : 10 Feb 2011  16:48     using AcqMethod METHOD2F.M
Instrument :   5973N
Sample Name:
Misc Info  :
Vial Number: 3
```

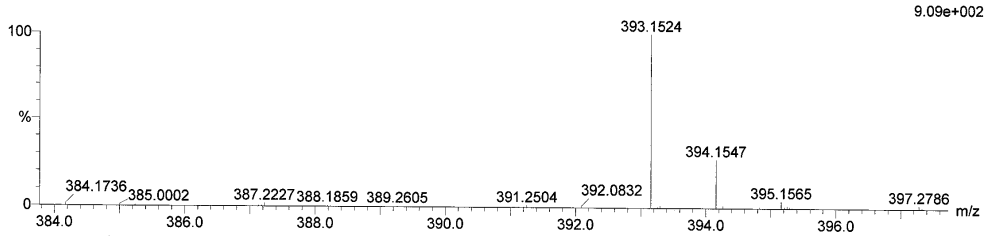



Transmittance [%]
20
40
60
80
100
Wavenumber cm-1
3500
3000
2500
2000
1500
1000
500
3051.12
1613.13
1478.90
1462.03
1424.04
1377.53
1327.71
1282.58
1244.50
1148.55
1125.98
1093.06
1027.09
1005.94
773.97
745.88
695.76
521.56
493.47
469.17
Me
N
N
Ph2P

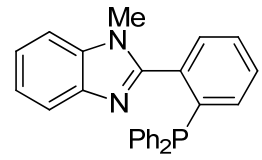
mental Composition Report **Page 1**

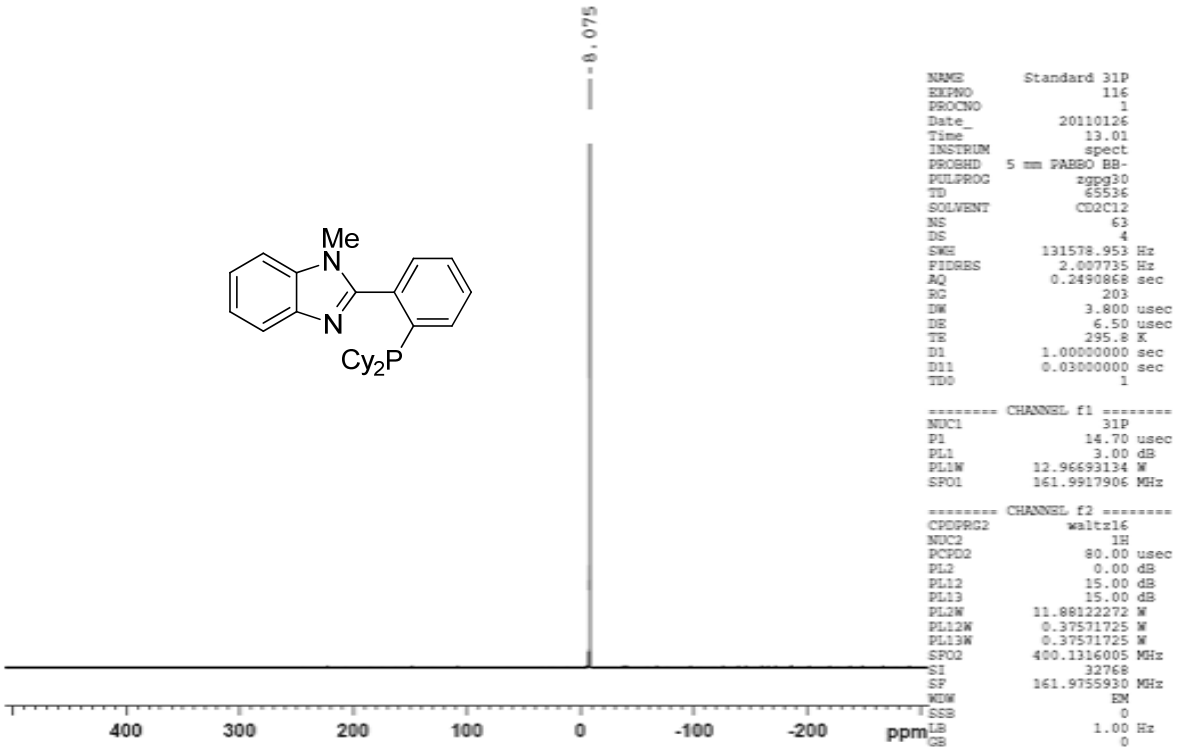
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Even Electron Ions
13 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-26 H: 0-26 N: 0-3 Na: 0-1 P: 0-1
Kin-Dept-16022011-HS S10 51 (0.967) Cn (Cen,4, 80.00, Ar); Sm (SG, 2x3.00); Sb (5,40.00); Cm (40:58)
TOF MS ES+

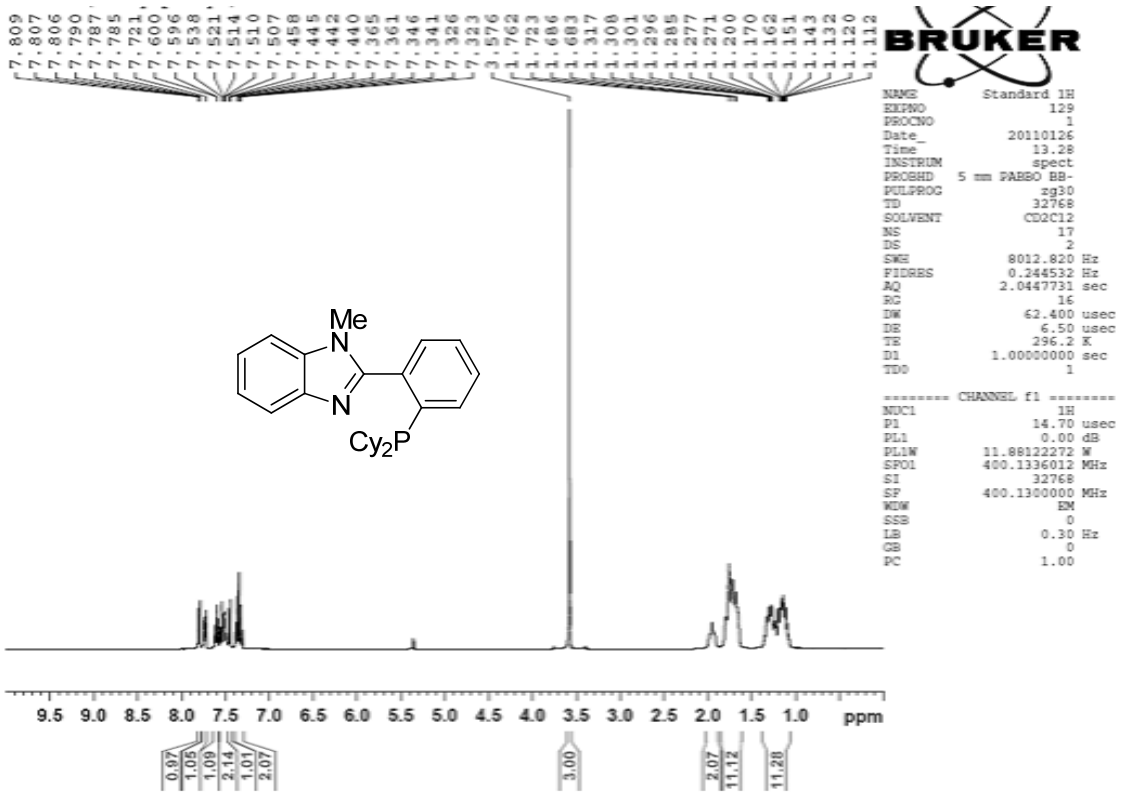


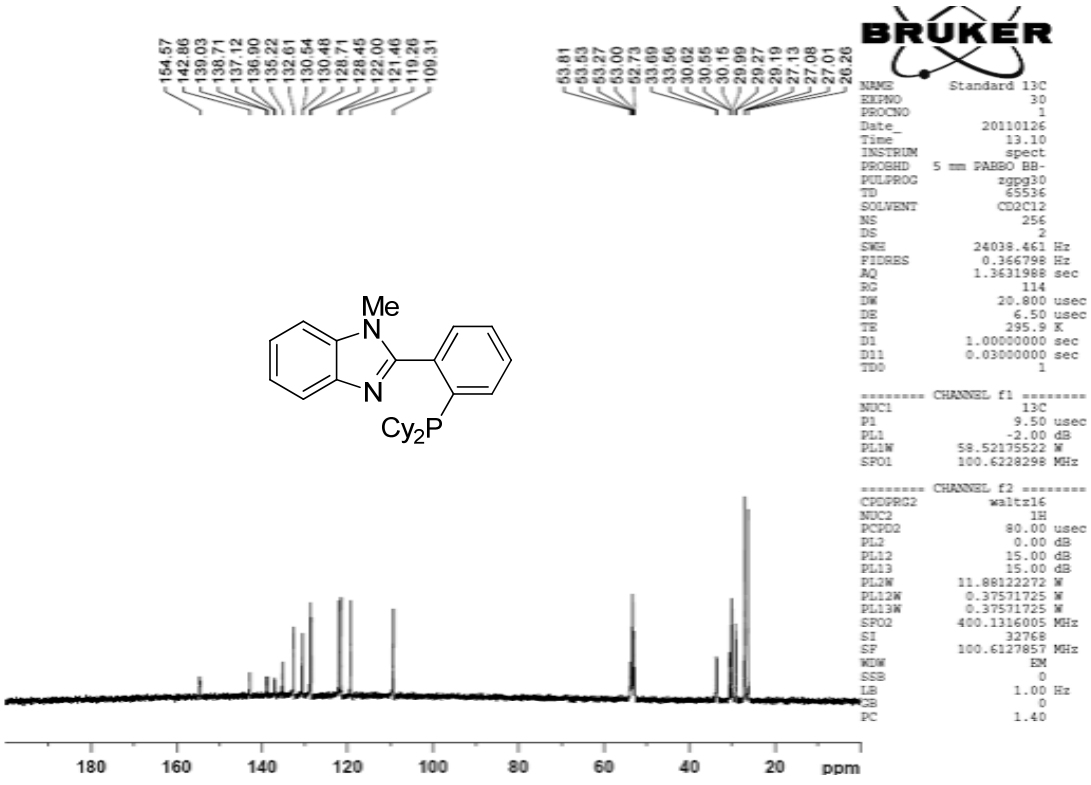
Minimum:				-1.5		
Maximum:		5.0	5.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
393.1524	393.1521	0.3	0.8	17.5	1.0	C26 H22 N2 P



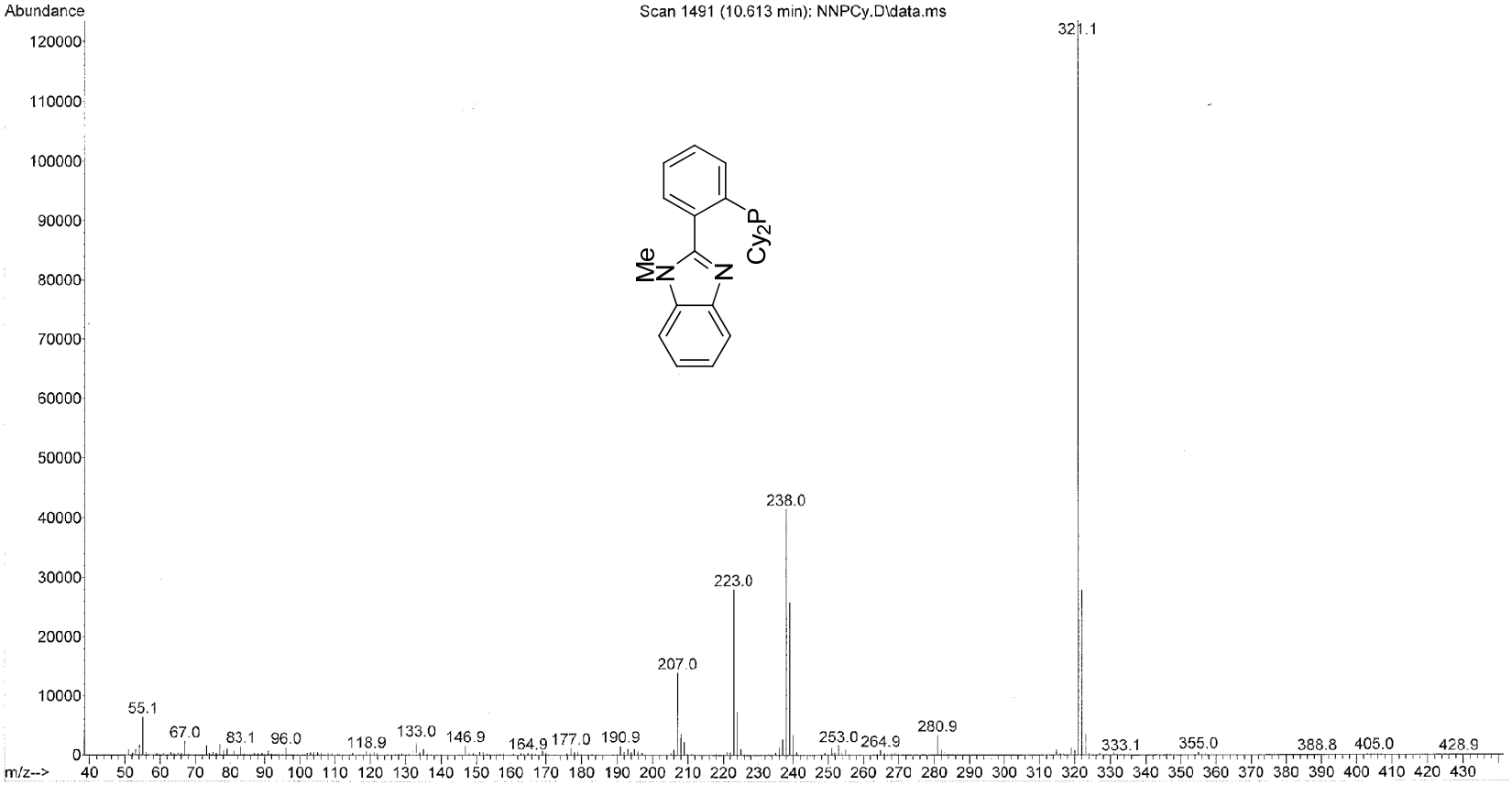


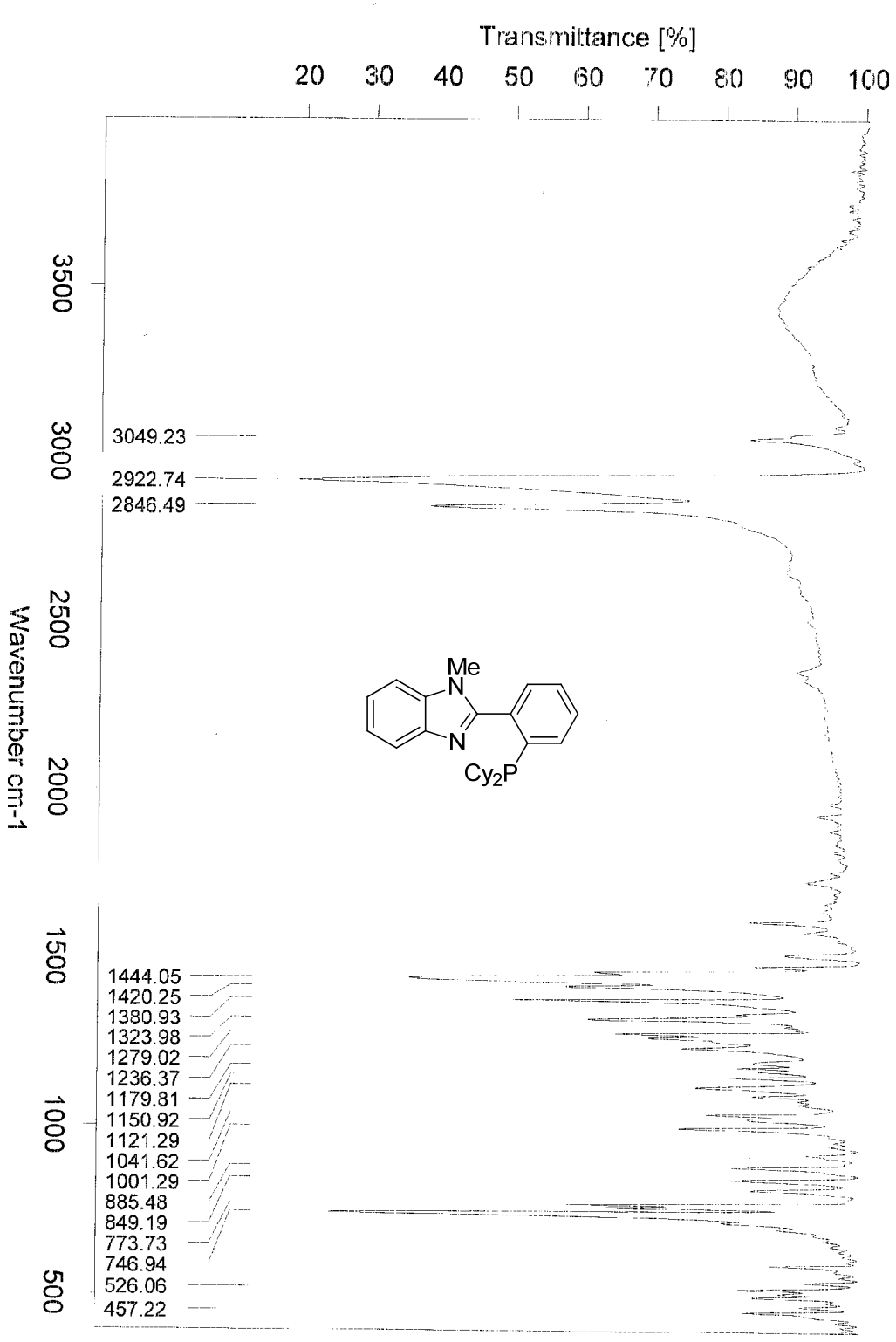
NAME	Standard 31P
EXPNO	116
PROCNO	1
Date_	20110126
Time	13.01
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CD2C12
NS	63
DS	4
SWH	131578.953 Hz
FIDRES	2.007735 Hz
AQ	0.2490868 sec
RG	203
DW	3.800 usec
DE	6.50 usec
TE	295.8 K
D1	1.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	31P
P1	14.70 usec
PL1	3.00 dB
PL1W	12.96693134 W
SFO1	161.9917906 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	161.9755930 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0


7.809 7.807 7.806 7.790 7.787 7.785 7.721 7.600 7.596 7.538 7.521 7.514 7.510 7.507 7.458 7.445 7.442 7.440 7.365 7.361 7.346 7.341 7.326 7.323 3.576 1.762 1.723 1.686 1.683 1.317 1.308 1.301 1.296 1.285 1.277 1.271 1.200 1.170 1.162 1.151 1.143 1.132 1.120 1.112
BRUKER
NAME Standard 1H
EXPNO 129
PROCNO 1
Date_ 20110126
Time 13.28
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CD2C12
NS 17
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 2.0447731 sec
RG 16
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 400.1336012 MHz
SI 32768
SF 400.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
Me
N
N
Cy2P
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
0.97 1.05 1.09 2.14 1.01 2.07 3.00 2.07 11.12 11.28


154.57 142.86 139.03 138.71 137.12 136.90 135.22 132.61 130.54 130.48 128.71 128.45 122.00 121.46 119.26 109.31
53.81 53.53 53.27 53.00 52.73 33.69 33.56 30.62 30.55 30.15 29.99 29.27 29.19 27.13 27.08 27.01 26.26
BRUKER
NAME Standard 13C
EXPNO 30
PROCNO 1
Date_ 20110126
Time 13.10
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CD2C12
NS 256
DS 2
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631988 sec
RG 114
DW 20.800 usec
DE 6.50 usec
TE 295.9 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 100.6127857 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
Me
N
N
Cy2P
180 160 140 120 100 80 60 40 20 ppm

```
File       :C:\msdchem\1\DATA\DIC\NNPCy.D
Operator   : Seam
Acquired   : 10 Feb 2011  16:48     using AcqMethod METHOD2F.M
Instrument :   5973N
Sample Name:
Misc Info  :
Vial Number: 3
```



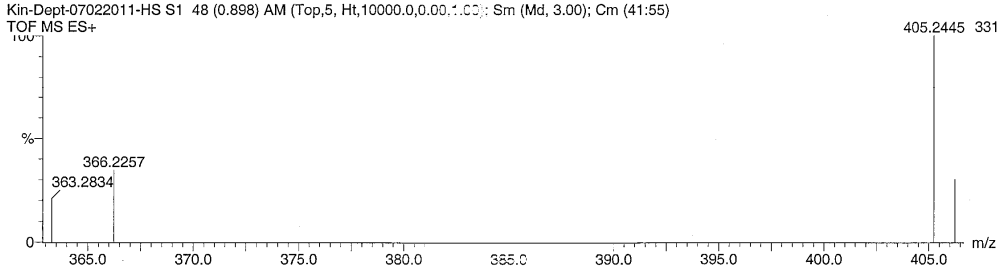

Transmittance [%]
20
30
40
50
60
70
80
90
100
Wavenumber cm-1
3500
3000
2500
2000
1500
1000
500
3049.23
2922.74
2846.49
1444.05
1420.25
1380.93
1323.98
1279.02
1236.37
1179.81
1150.92
1121.29
1041.62
1001.29
885.48
849.19
773.73
746.94
526.06
457.22
Me
N
N
Cy2P

ental Composition Report **Page 1**

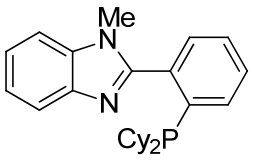
Single Mass Analysis
Tolerance = 20.0 PPM / DBE: min = -100.0, max = 1000.0
Selected filters: None

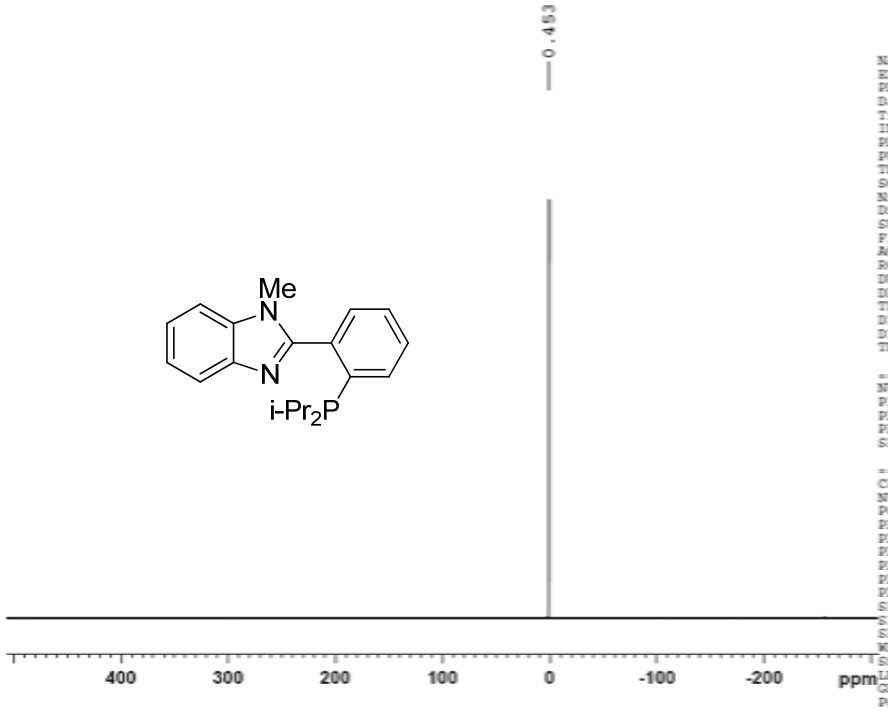
Monoisotopic Mass, Even Electron Ions
45 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-26 H: 0-34 N: 0-4 Na: 0-1 P: 0-2

Kin-Dept-07022011-HS S1 48 (0.898) AM (Top,5, Ht,10000.0,0.00:1.00); Sm (Md, 3.00); Cm (41:55)

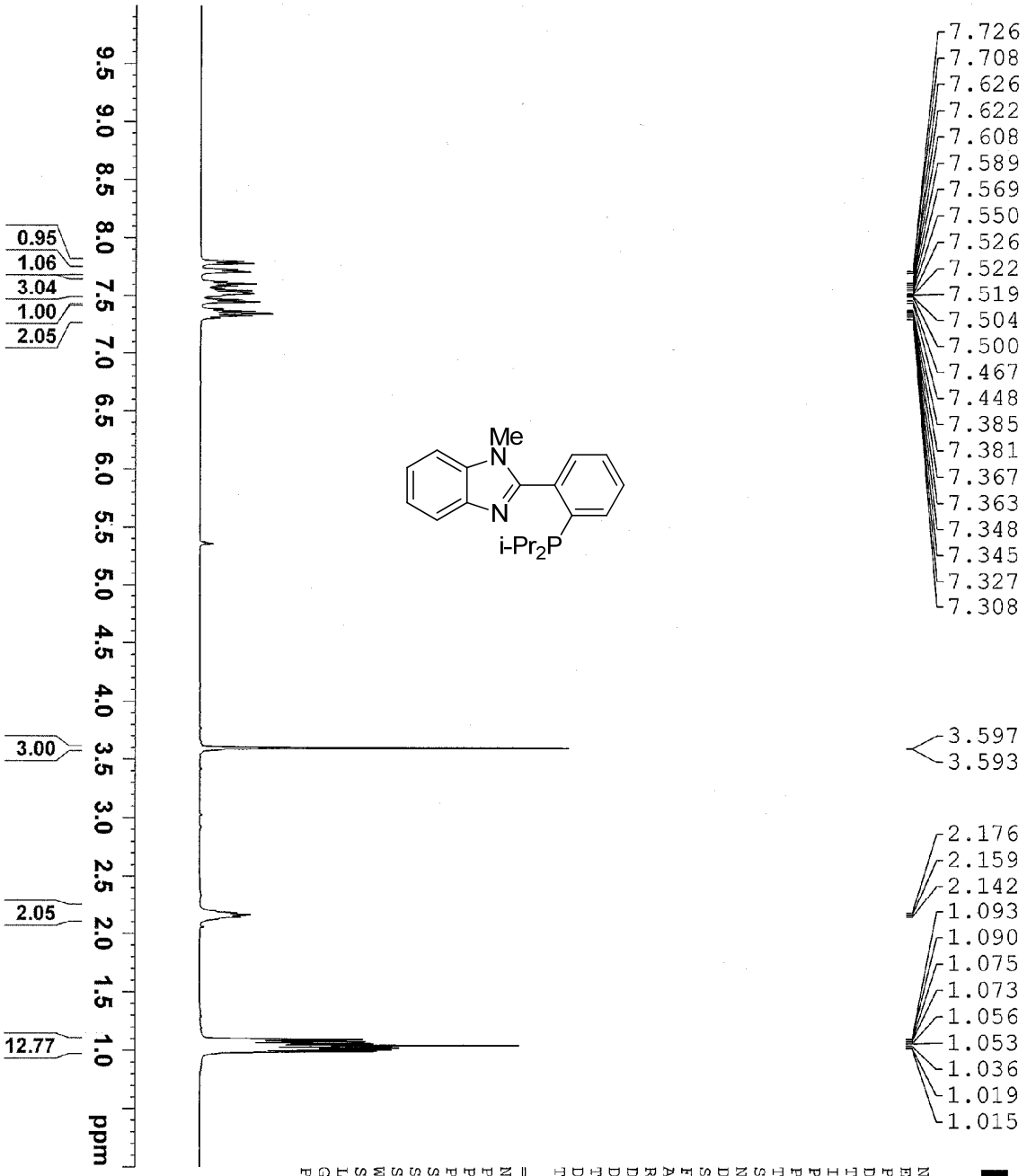


Minimum:				-100.0		
Maximum:		5.0	20.0	1000.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
405.2445	405.2460	-1.5	-3.7	11.5	2773074.0	C26 H34 N2 P





NAME	Standard 31P
EXPNO	121
PROCNO	1
Date_	20110211
Time	15.22
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CD2C12
NS	5
DS	4
SWH	131578.953 Hz
FIDRES	2.007735 Hz
AQ	0.2490868 sec
RG	203
DW	3.800 usec
DE	6.50 usec
TE	296.3 K
D1	1.00000000 sec
D11	0.03000000 sec
TD0	1
========	CHANNEL f1 ========
NUC1	31P
P1	14.70 usec
PL1	3.00 dB
PL1W	12.96693134 W
SFO1	161.9917906 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	161.9755930 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40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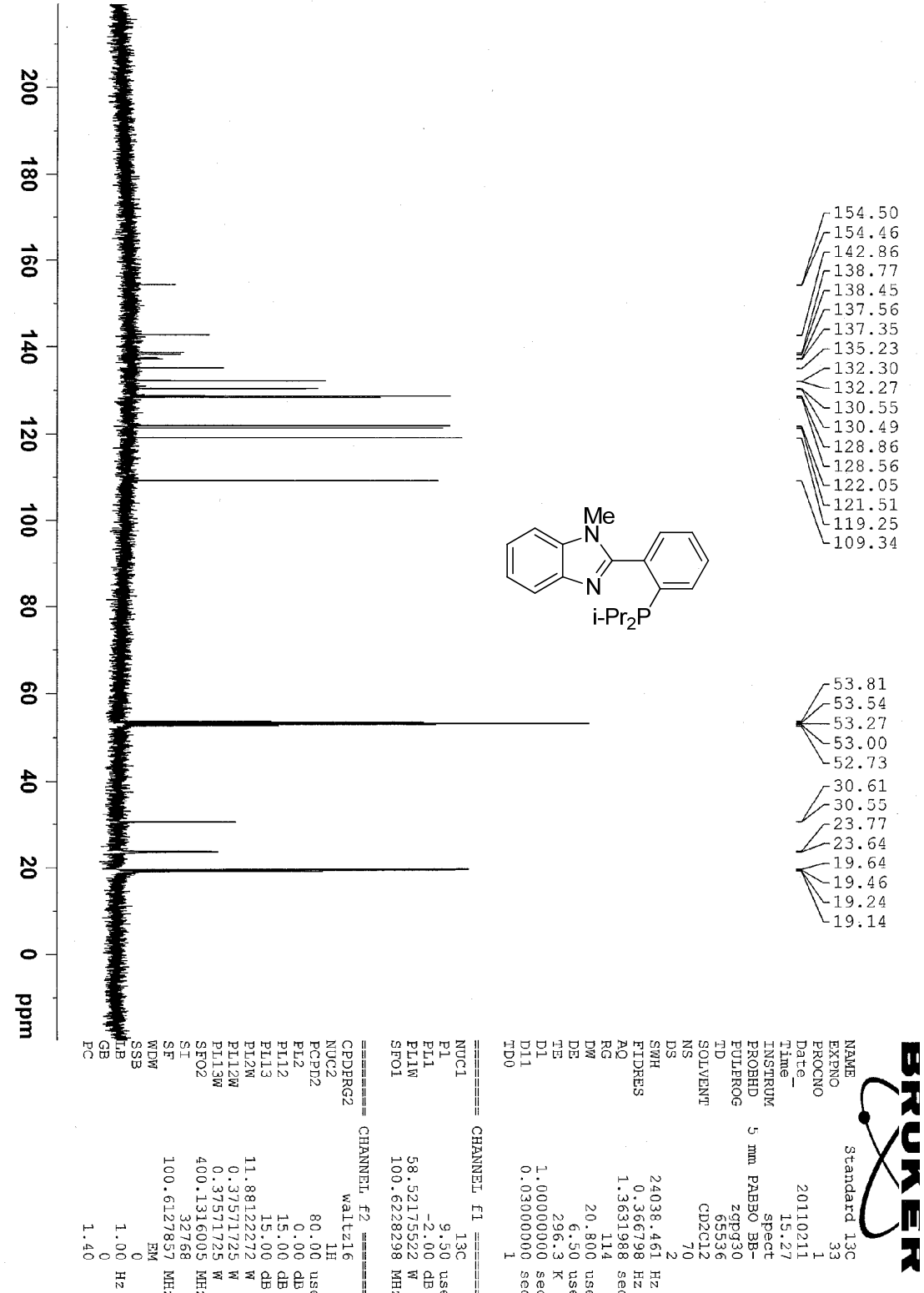
7.708
7.626
7.622
7.608
7.589
7.569
7.550
7.526
7.522
7.519
7.504
7.500
7.467
7.448
7.385
7.381
7.367
7.363
7.348
7.345
7.327
7.308
3.597
3.593
2.176
2.159
2.142
1.093
1.090
1.075
1.073
1.056
1.053
1.036
1.019
1.015
Me
N
N
i-Pr2P
0.95
1.06
3.04
1.00
2.05
3.00
2.05
12.77
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
ppm
BRUKER
NAME Standard 1H
EXPNO 134
PROCNO 1
Date_ 20110211
Time_ 15.24
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CD2C12
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 2.0447731 sec
RG 14.2
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 400.1336012 MHz
SI 32768
SF 400.1300000 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 1.00


154.50
154.46
142.86
138.77
138.45
137.56
137.35
135.23
132.30
132.27
130.55
130.49
128.86
128.56
122.05
121.51
119.25
109.34
Me
N
N
i-Pr2P
53.81
53.54
53.27
53.00
52.73
30.61
30.55
23.77
23.64
19.64
19.46
19.24
19.14
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
Standard 13C
NAME
EXPNO 33
PROCNO 1
20110211
Date_
Time_ 15.27
spect
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PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CD2Cl2
NS 70
DS 2
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631988 sec
RG 114
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 100.6127857 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

```
File       :C:\MSDCHEM\1\DATA\CMSO\Snapshot\NNPBu.D
Operator   : Seam
Acquired   : 10 Feb 2011  17:46      using AcqMethod METHOD2.M
Instrument :   5973N
Sample Name:
Misc Info  :
Vial Number: 5
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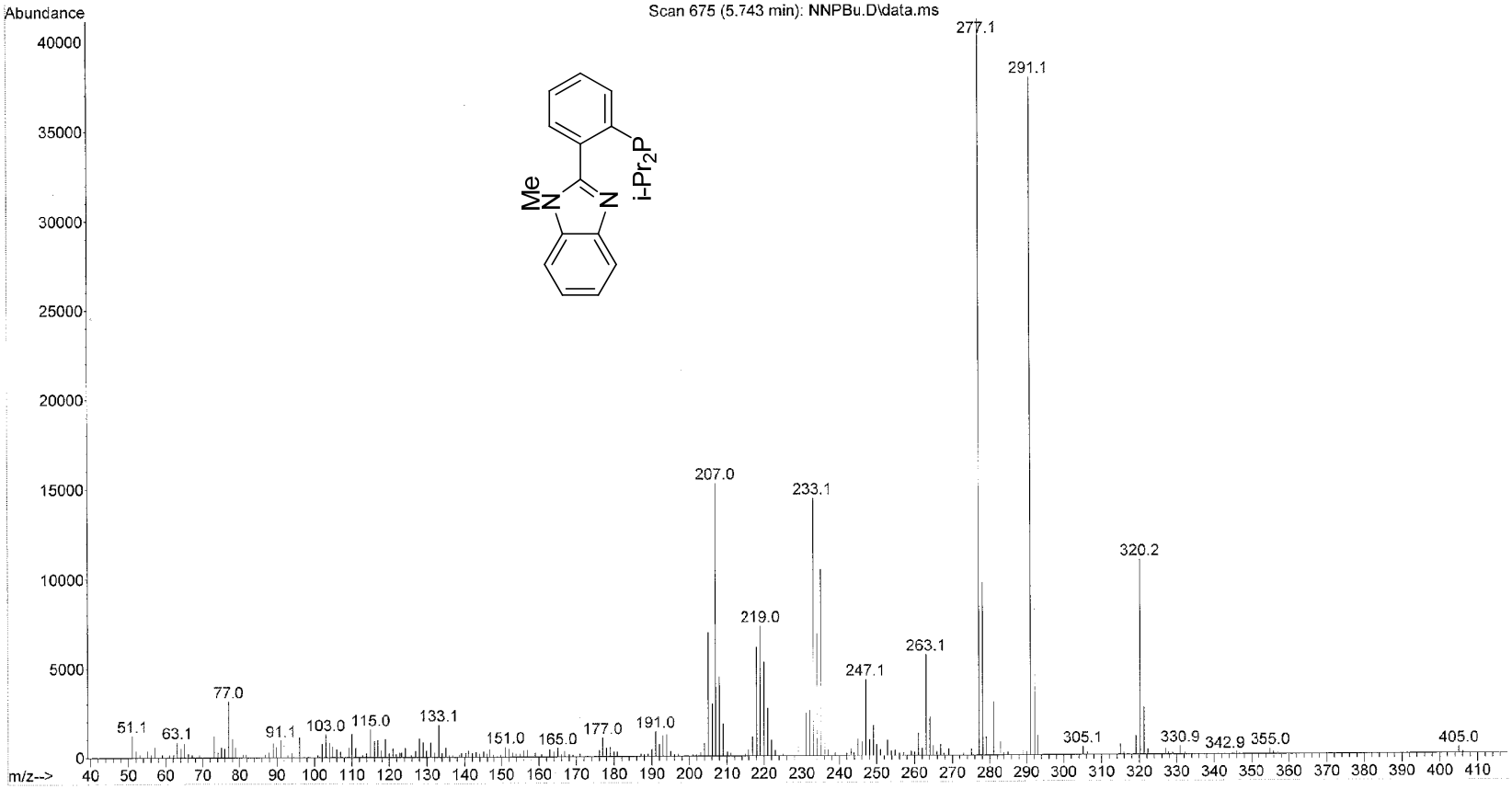
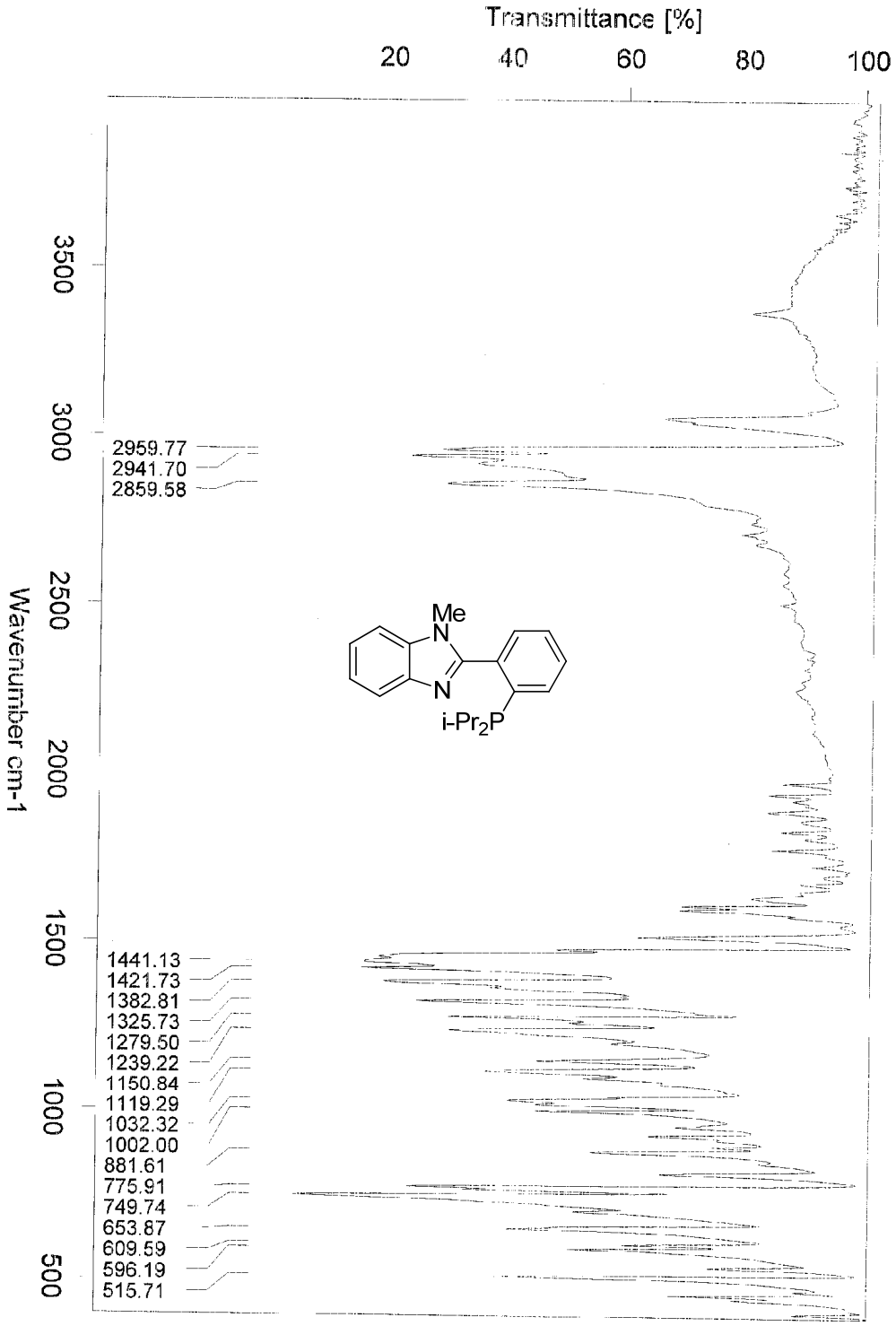



Transmittance [%]
20
40
60
80
100
Wavenumber cm-1
3500
3000
2500
2000
1500
1000
500
2959.77
2941.70
2859.58
1441.13
1421.73
1382.81
1325.73
1279.50
1239.22
1150.84
1119.29
1032.32
1002.00
881.61
775.91
749.74
653.87
609.59
596.19
515.71
Me
N
N
i-Pr2P

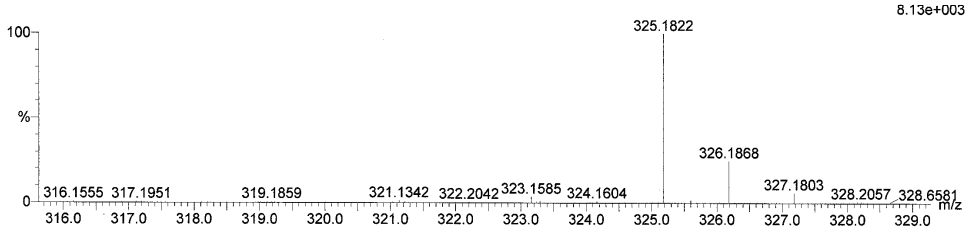
Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off

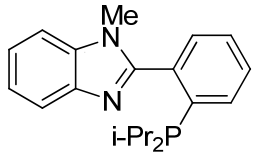
Monoisotopic Mass, Even Electron Ions
38 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-26 H: 0-26 N: 0-3 Na: 0-1 P: 0-1

Kin-Dept-16022011-HS_2 S9 59 (1.117) Cn (Cen,4, 80.00, Ar); Sm (SG, 2x3.00); Sb (5,40.00); Cm (58:65)
TOF MS ES+

8.13e+003



Minimum:				-1.5		
Maximum:		5.0	5.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
325.1822	325.1834	-1.2	-3.7	9.5	76.6	C20 H26 N2 P



4. Reference

(1) So, C. M.; Zhou, Z.; Lau, C. P.; Kwong, F. Y. *Angewandte Chemie International Edition* **2008**, *47*, 6402.

(2) Reddy, K. R.; Krishna, G. G. *Tetrahedron Letters* **2005**, *46*, 661.

(3) Letsinger, R. L.; MacLean, D. B. *Journal of the American Chemical Society* **1963**, *85*, 2230.