TRANSITION METAL NITRENES-SYNTHETIC APPLICATIONS IN AZIRIDINATION AND BICYCLIC N-HETEROCYCLES AND USE OF NITROGEN LIGANDS IN HECK, SUZUKI-COUPLING AND AMINATION REACTIONS

A THESIS

SUBMITTED TO THE

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IN

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BY

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C E R T I F I C A T E

Certified that the work incorporated in the thesis entitled ***"Transition Metal Nitrenes-Synthetic Applications In Aziridination And Bicyclic N-Heterocycles And Use Of Nitrogen Ligands In Heck, Suzuki-Coupling And Amination Reactions"*** *by* ***Mr. Girish M. Kulkarni*** *was carried out by the candidate under my guidance in the National Chemical Laboratory, Pune. Such material has been obtained from other sources has been duly acknowledged in the thesis.*

Date :

Dr. Suresh Iyer

(Research Guide)

D E C L A R A T I O N

I hereby declare that the thesis entitled ***"Transition Metal Nitrenes-Synthetic Applications In Aziridination And Bicyclic N-Heterocycles And Use Of Nitrogen Ligands In Heck, Suzuki-Coupling And Amination Reactions "*** *submitted for my Ph.D. degree to the* ***University of Pune*** *has been carried out at National Chemical Laboratory, under the guidance of* ***Dr. Suresh Iyer****. The work is original and has not been submitted in part or full by me for any degree or diploma to this or any other University.*

Date :

Girish M. Kulkarni

(Research Student)

Dedicated

To My

Parents

AKNOWLEDGEMENTS

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Girish M. Kulkarni

"The discovery of truly new reactions is likely to be limited to the realm of transition-metal organic chemistry, which will almost certainly provide us with additional "miracle reagents" in the years to come."

D. Seebach

Angew Chem.1990,102, 1363.

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Chapter-2 Reactions of azides nitro compounds and nitrene precursors with metal carbonyls and DBT and DCT as nitrene precursors, route to β-lactams through nitrenes

Section-A Reaction of azides, nitro compounds and nitrene precursors with metal carbonyls and route to β-lactams through nitrenes

Section-B DBT and DCT as nitrene precursors and their reaction with olefins and hydrocarbons

GENERAL REMARKS

1. All solvents were distilled and dried before use.
2. Petroleum ether refers to the fraction collected in the boiling range 60-80^{o}C.
3. Organic layers after every extraction were dried over anhydrous sodium sulfate.
4. Column Chromatography was performed over silica gel (60-120 mesh).
5. TLC analyses were performed over glass plates coated with silica gel (5-25 m) containing UV active G-254 additive.
6. IR spectra were recorded on a Perkin-Elmer model 683 B or 1605 FT-IR and absorptions were expressed in cm-^{1}.
7. ^{1}H and ^{13}C-NMR spectra were recorded on Brucker FT AC-200 and MSL-300 MHz instruments using TMS as an internal standard. The following abbreviations were used. s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, bs = broad singlet, and dd = doublet of doublet.
8. Mass spectra (MS) were recorded on an automated finnigan MAT 1020C mass spectrometer using ionization energy of 70eV.
9. All melting points and boiling points are uncorrected and the temperatures are in centigrade scale.
10. Elemental analysis was done on Carlo ERBA EA 110B instrument.

LIST OF ABBREVIATIONS

Ac	Acetyl
Ar	Aryl
Aq	Aqueous
BINAP	(1,1'-binaphthalene-2,2'-diphenyl)-phosphane
Boc	tertiary butyloxy carbonyl
b.p.	Boiling Point
^{n}Bu	n-butyl
cat	catalyst
Cp	Cyclopentadienyl
COD	Cyclooctadiene
DCM	Dichloromethane
DMSO	Dimethyl Sulfoxide
DMF	Dimethyl Formamide
DAB	Diazabutadiene
^{0}C	degree centigrade
g	Grams
h	Hour
IR	Infrared
L	Ligand
LTA	Lead tetraacetate
ml	Millilitre
mg	Milligrams
min	Minutes
mmole	millimole

m.p.	Melting Point
M^+	Molecular Ion
MS	Mass Spectrum
NMR	Nuclear Magnetic Resonance
NMP	N-methyl pyrrolidone
P.E.	Petroleum ether
RBF or rbf	Round Bottom flask
r.t.	Room Temperature
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
Ts	Tosyl
TMS	Trimethylsilane

ABSTRACT

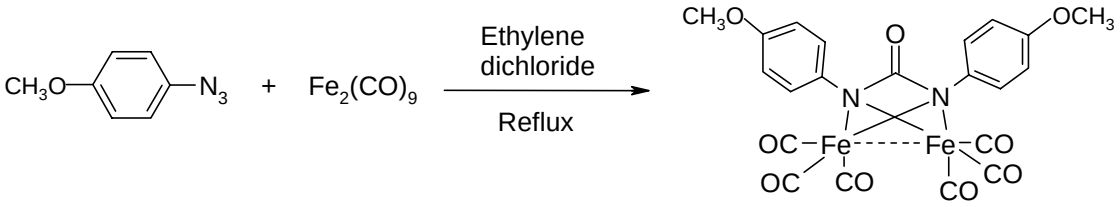
Chapter-1 Synthesis of transition metal nitrenes and Aziridination

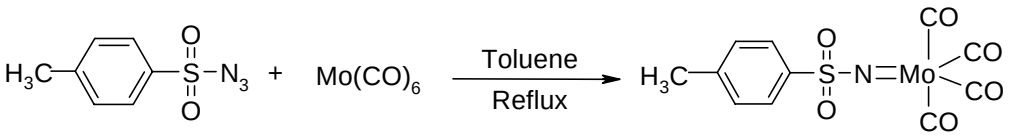
Section-A Synthesis of transition metal nitrenes

Nitrogen atom transfer reactions constitute an important area of research in bioinorganic and organic chemistry. The importance of alkene aziridination reactions in the construction carbon-nitrogen bonds is well documented in the literature. Transition metal imido complexes plays an important role in nitrogen transfer reactions. Imido complexes of ruthenium, molybdenum, vanadium and titanium are well studied and characterized in the literature.

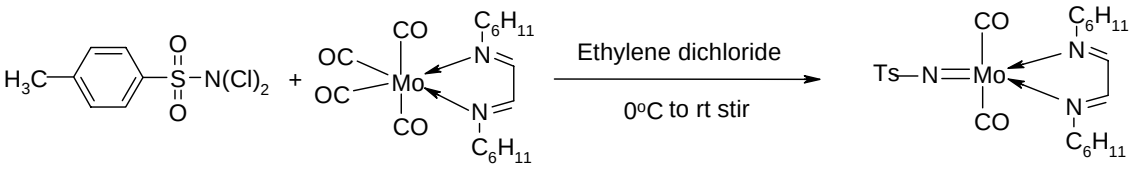
Scheme-1

A. Synthesis of metal imido complexes by the reaction of aryl azides with metal carbonyls

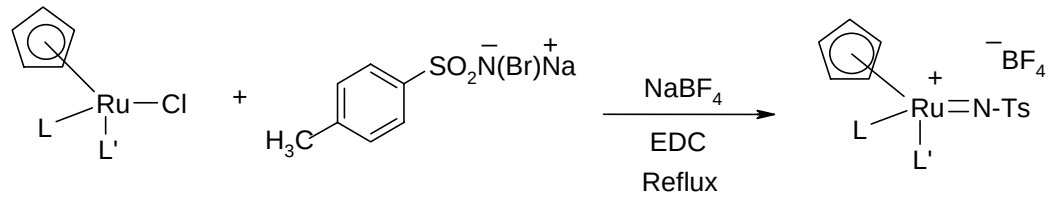




B. By the reaction of N, N-dihalocompounds with metal carbonyls



C. Synthesis of Ruthenium nitrene complexes



L = $P(C_6H_5)_3$, CH_3CN

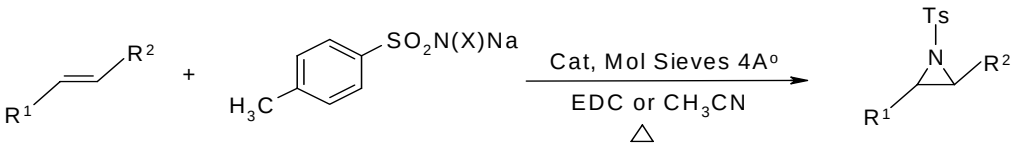
L' = $P(OCH_3)_3$, $P(C_6H_5)_3$, CH_3CN

Section-B Transition metal catalyzed aziridination of olefins

The intermolecular cycloaddition of an electron-deficient species such as a nitrene, a nitrenium ion or a carbene (or their formal equivalents) to the Π-bond of an alkene, alkyne, imine or nitrile is a significant approach to aziridines and azines. The development of metal catalyzed coupling of simple organic molecules to give higher functionalised molecules is a field of rapid progress. Aziridines can be used as versatile precursors for the synthesis of a variety of organic compounds of biological importance. Various methods are available for the preparation of enantiomerically pure aziridines, but most of are laborious multi-step reactions, where either optically pure starting materials or stiochiometric amounts of chiral auxillaries were used. The simplest catalytic formation of aziridines is in principle, either the addition of a carbene fragment to an imine or the addition of a nitrene fragment to an alkene.

Transition metal catalyzed of bromamine-T, chloramines-T and other nitrene precursors were carried out with olefins (Scheme-2).

Scheme-2



$R^1 = C_6H_5$,

$R^2 = H, COOCH_2CH_3$

X = Cl, Br

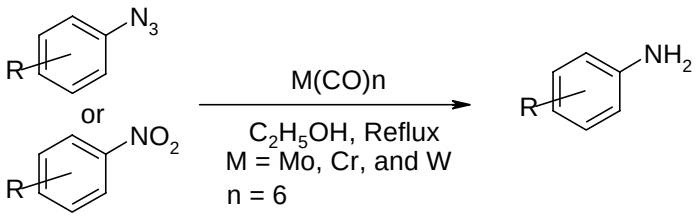
Chapter-2 Reactions of azides, nitro compounds and nitrene precursors with metal carbonyls, DBT and DCT as nitrene precursors, route to β-lactams through nitrenes

Section-A Reaction of azides, nitro compounds and nitrene precursors with metal carbonyls and route to β-lactams through nitrenes

Since azide ion is an excellent nucleophile it is often the reagent of choice for introducing a nitrogen functional group. The reduction of azido group to a 1° amino group is consequently often an important step in a reaction sequence. A wide range of reduction methods were available including several of which are claimed to permit selective reduction of azido group in the presence of other functional groups. Many of the methods fall into one of the broad categories: 1) Involving the use of hydrogen and metal catalysts. 2) Involving low-valent metals and 3) Involving the use of nucleophiles with attack of the terminal nitrogen of the azide with the formation of triazine.

Reactions of aryl azides and aryl nitro compounds were carried out in the presence of metal carbonyls in refluxing ethanol (Scheme-3).

Scheme-3



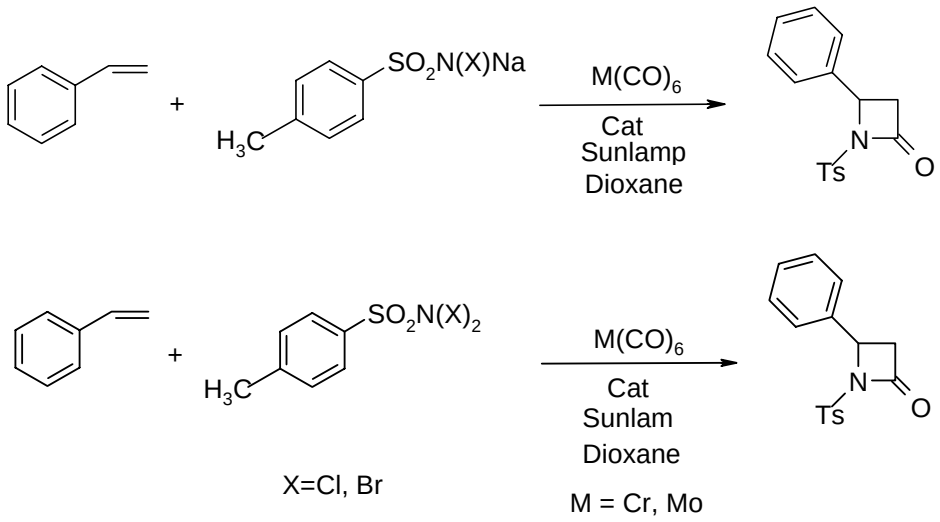
Reaction of Nitrene precursors with metal carbonyls-Route to β-lactams

The four membered cyclic amide derivatives of 3-amino propionic acids known as β-lactams, are first synthesized by Staudinger in 1907. The recognition of the β-lactam moiety as the key pharmacophoric component of the penum antibiotics initiated a flurry of synthetic activity. Intensive research has generated numerous

methods of synthesizing the β-lactam skeleton. Commonly, the lactam ring is formed through either ketene-imine cyclizations (Staudinger reaction) or ester enolate-imine condensations (Gilman-Speeter reaction). However other notable methods are sometimes employed, including photoinduced rearrangements, and radical cyclizations.

Reactions of bromamine-T, chloramines-T and tosyl azide were carried out with styrene in the presence of $Cr(CO)_6$ under thermal and photolytic conditions (Scheme-4).

Scheme-4



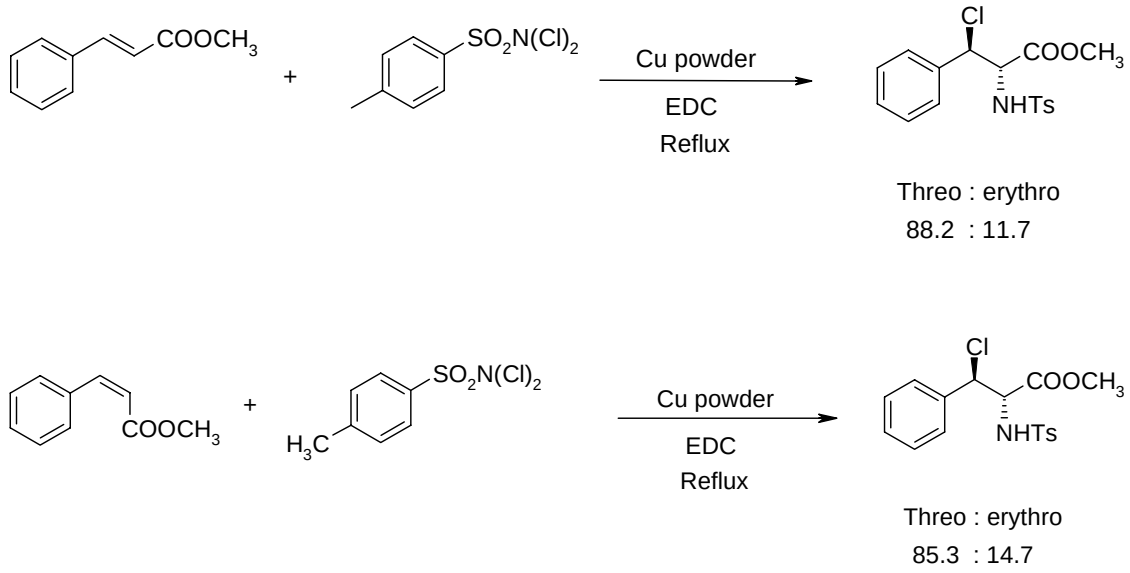
Section-B DBT and DCT as nitrene precursors and their reaction with olefins and hydrocarbons

The functionalization of olefins by the addition of two different functional groups in a single step provides access to wide range of functional group manipulation in organic synthesis. Variety of reactions such as aminohalogenation, halohydration, haloazidation and azidohydroxylation are some of the examples of this kind of synthetic transformation. The ionic addition of N-halosulfonamides and

Cu catalyzed radical addition of N, N-dichloro-4-toluenesulphonamide and N, N-dichlorourethane to olefins and hydrocarbons to give amino halogenation and amination products has been described by Kharasch and others. DCT and N, N-dichlorourethane react with cyclic ethers in the presence of Cu catalysts to form amination products.[8] These reactions are known to proceed by radical or nitrenoid and nitrene intermediates. $Mo(CO)_6$ and $W(CO)_6$ reacts with N, N-dichlorophenylsulphonamide to form nitrene complexes. Azides and chloramine-T react with olefins to form aziridines in the presence of Cu catalysts via nitrene and nitrenoid intermediates. Cu and Pd (II) complexes catalyze the regiospecific and stereoselective addition of DCT to ethyl cinnamate forming halo amines.

Reactions of α, β-unsaturaed olefins with DCT and DBT were carried out in the presence of metal powders (Scheme-5).

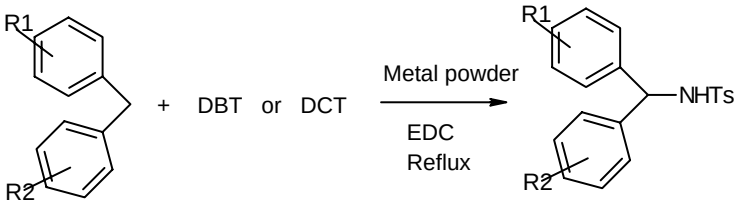
Scheme-5



C-H insertion reaction using dibromamine-T and dichloramine-T

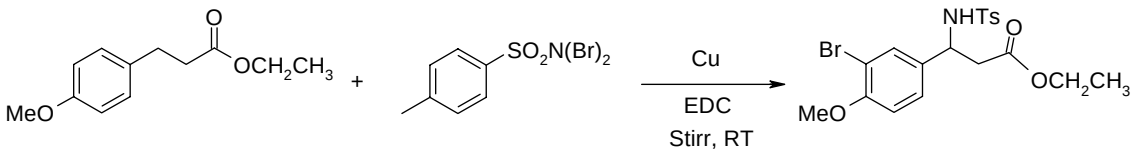
Dibromamine-T and dichloramine-T were reacted with various hydrocarbons and 3-phenyl propinoic ester and formed aminated products. Reaction of DBT with 3-phenyl propinoic ester gave both benzylic amination and aromatic halogenated product in one step. Different substituted 3-phenyl propinoic esters were prepared for the reaction of benzylic amination by DBT (Scheme-6) and (Scheme-7).

Scheme-6



R1=H, COMe, Cl
R2=H, COMe,

Scheme-7



Chapter-3

Synthesis of N-heterocycle bicyclic compounds using transition metal complexes

Nitrogen heterocycles especially pyrrolidine derivatives are wide spread among both natural products and medicinally important synthetic compounds. Bicyclic derivatives of these compounds, basically 3-azabicyclo[3,3,0]octane framework, on the other hand are quite rare and only known from a few synthetic analogues such as prostacyclin(PGI_2) antidiabetic glyclazide and some antibacterial quinonecarboxylic acid derivatives. Besides their physiological activity bicyclic pyrrolidine derivatives also serve as chiral auxillaries in asymmetric transformations. There is also a

considerable interest in development of new methods for preparing cage-like oxaheterocycles and rigid amine containing heterocycles (azacycles).

Reactions of bromamine-T with 1, 6-diene in the presence of various transition metal complexes were carried out in refluxing EDC or CH_3CN (Scheme-8).

Scheme-8

$R = COOC_2H_5$, CN X = Cl, Br

$R' = COOC_2H_5$

Chapter-4

Use of nitrogen ligands in the Heck, Amination and Suzuki-Coupling reactions

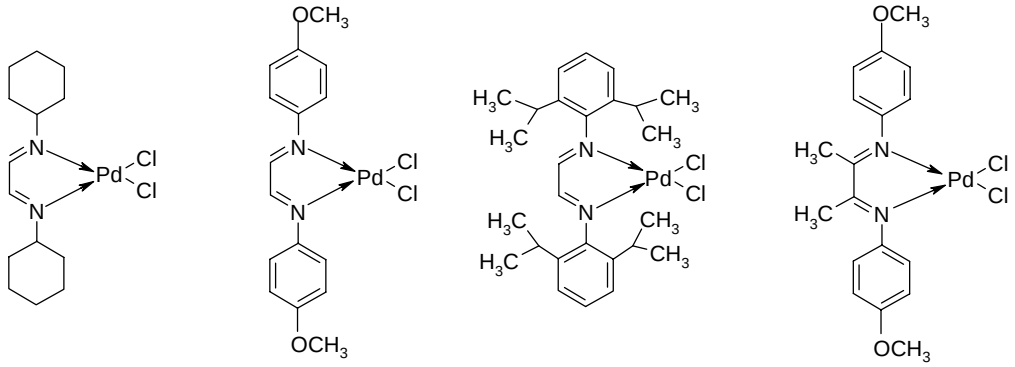
Several new ligands and Pd complexes have been reported for the Heck reaction in recent years. The emphasis on the activation of bromides and chlorides for the Heck reaction has led to the discovery of new ligands and metal complexes. The use of dimethylglycine as additive for activating aryl bromides has been reported by Reetz et.al. $^tBu_3P$ and triphenyl phosphite as ligands and the use of tetraphenylphosphonium salts as additive has been reported for the activation of chlorides ligands.

While the activation of activated bromides and chlorides has been made easy with the above mentioned ligands and additives but there still remains a need for better catalysts for the activation of unactivated bromides and chlorides. Another aspect of the Heck reaction is the use of phosphine, which are easily oxidizable and undergo side reactions.

Nitrogen compounds are commonly used ligands in transition metal chemistry and equal in number and reactions to P-ligands. The diazabutadiene ligands can be

readily synthesized form the condensation of amines and aldehydes or ketones (compared to the tedious synthesis of phosphines). The Pd complexes can be easily synthesized from the reaction of $PdCl_2$ with these ligands. The strong σ donor and π acceptor properties of the diazabutadienes make them excellent ligands for the Heck reaction. We thought that the strong basic nature of these ligands might assist the activation of aryl bromides and chlorides.

$PdCl_2$(DAB) complexes



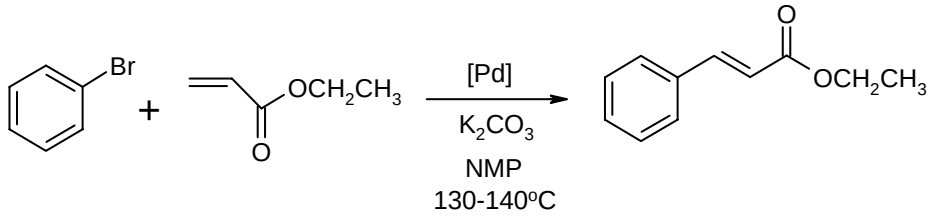
1 2 3 4

Mizoroki-Heck Reaction

The Pd-catalyzed arylation of olefins with aryl halides generally refered to as the Heck reaction, has received increasing attention in the last two decades. This is primarily due to the enormous synthetic potential of this versatile method for generating new C-C bonds. This reaction represents a powerful and popular method for the formation of C-C bonds. In particular Heck reaction is an important method for the preparation of aryl functionalized alkenes in synthetic organic chemistry as applicable to pharmaceutical industry. Thus organopalladium compounds play an important role in homogeneous catalysis due to their versatility and non-toxicity.

Mizoroki-Heck reaction of aryl bromides with olefins was carried out in the presence of different $PdCl_2$(DAB) complexes (Scheme-9).

Scheme-9

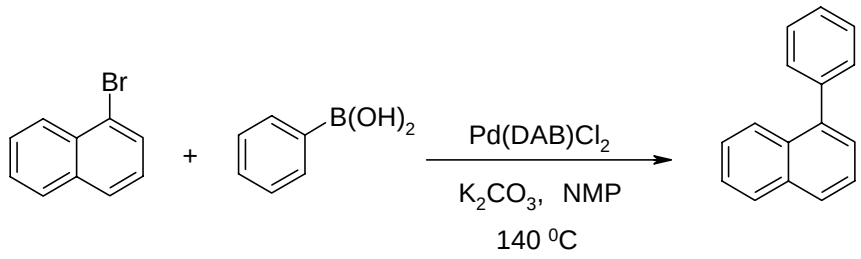


Suzuki-Miyaura Coupling

The Pd-catalyzed cross-coupling reaction between organoboron compounds and org. halides or triflates provides a powerful and general methodology for the formation of C-C bonds. Recently, this reaction was called as the Suzuki-Miyaura coupling. This is a versatile method for synthesizing unsymmetrical biaryls. The availability of the reagents and the mild reaction conditions all contribute to the versatility of this reaction. The coupling reaction offers several additional advantages, such as being largely unaffected by the presence of H_2O, tolerating a broad range of functional groups, and proceeding generally regio and stereoselectively. Also, the inorganic byproduct of the reaction is nontoxic and easily removed from the reaction mixture thereby making the Suzuki coupling suitable not only for laboratory but also for industrial processes. As a consequence the Suzuki coupling have been used extensively in the synthesis of natural products, nucleoside analogs and pharmaceuticals.

Suzuki coupling reactions of aryl bromides with phenylboronic acid were carried out in the presence of diazabutadiene based Palladium catalysts (Scheme-10).

Scheme-10

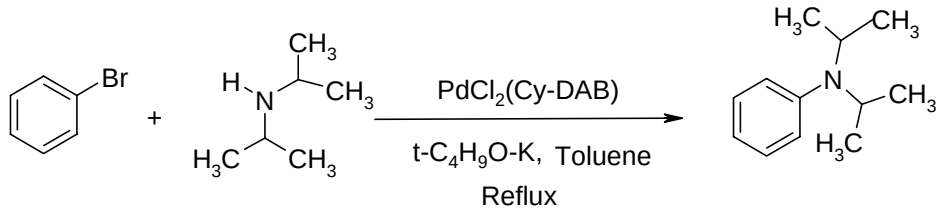


Buchwald-Hartwig aryl amination

Aromatic and aliphatic amines such as aniline and piperidine derivatives are an important class of fine chemicals, which are presently produced via stoichiometric methods. Arylamines are commonly prepared by acidic nitration, followed by an often troublesome reduction and subsequent alkylation of the aniline. In the recent years, the work by Buckwald and Hartwig in palladium catalyzed carbon-heteroatom bond formation can be regarded as an important breakthrough.

Buchwald-Hartwig aryl amination reactions of aryl bromides with different amines were carried out in the presence of diazabutadiene based Palladium catalysts (Scheme-11).

Scheme-11



Chapter-1 Synthesis of transition metal nitrenes

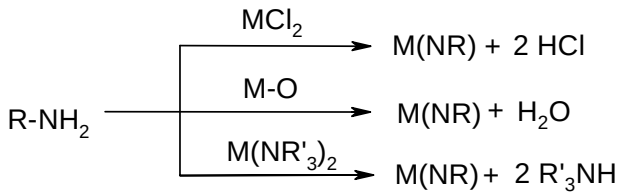
1.1.1 Introduction and Background

One of the most fascinating fields of organometallic chemistry is concerned with the stabilization of labile organic species by coordination to a transition metal. More generally, some classes of transition metal complexes able to generate these species in situ from the precursors under mild conditions. Once formed, they can be trapped on the metal or can give place to a reaction with another ligand bound to the metal or finally they can be involved in a reaction with organic substrates, sometimes in a catalytic sequence. Among these species, carbenes have been widely studied as ligands in organometallic complexes.[1] On the other hand, nitrenes are the important labile organic intermediates which are stabilized by various transition metals.

Preparation of organoimido complexes

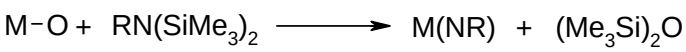
A number of synthetic routes to organoimido complexes have been used, in the past years. Most frequently deprotonation of primary amines with non co-ordinating base is used as common route for the synthesis of imido complexes[2, 3] (Scheme-1).

Scheme-1



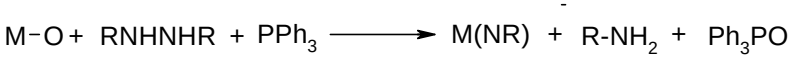
Silylated derivatives of primary amines have been used to react with metal oxo complexes. The great strength of Si-O and Si-F bonds makes silylamines especially effective for replacing oxo or fluoro ligands (Scheme-2).

Scheme-2



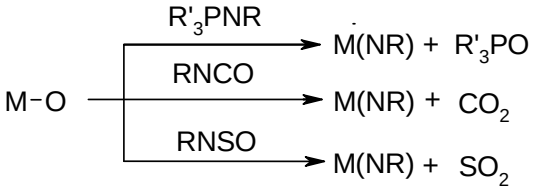
By disproportion of 1, 2-disubstituted hydrazines reacting with metal oxo compound and triphenyl phosphine. Procedure is restricted to Rhenium complexes[4] (Scheme-3).

Scheme-3



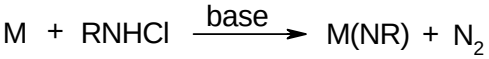
Metal imido complexes could also be prepared by the reaction of metal oxo compounds with phosphinimines, isocyanates and sulfinylamines[5] (Scheme-4).

Scheme-4



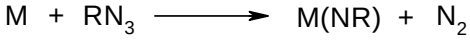
Tetrakis Osmiumimido complex $Os(NR)_4$ were prepared by the reaction of chloramines with metal in the presence of base [6] (Scheme-5).

Scheme-5



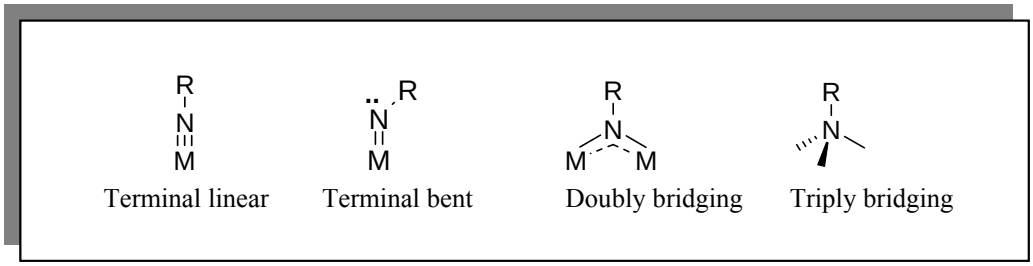
Palladium, platinum and rhodium organoimido complexes were prepared by this method. Formation of dinitrogen molecule is the driving force for the formation of metal imido complex [7] (Scheme-6).

Scheme-6



Stereochemistry

There are four modes of bonding so far known.



The majority of mononuclear organoimido complexes exhibit psuedotetrahedral or psuedooctahedral co-ordination geometries. The idealized geometries of the latter complexes are frequently owing to the presence of the short metal-nitrogen bond. The terminal linear arrangement was the bonding mode most commonly observed for e.g. $Mo(NC_6H_5)_2(S_2CN(C_2H_5)_2]_2$. Other known complexes possess the terminal bent structure [e.g. $Ru(NR_f)(CO)_2\ \{P(C_6H_5)_2\}_3$]. In general a bent M-N-R geometry can be expected when a linear, 4-electron donor NR ligand would cause the electron count (EAN rule) of the complex to exceed 18 electrons.

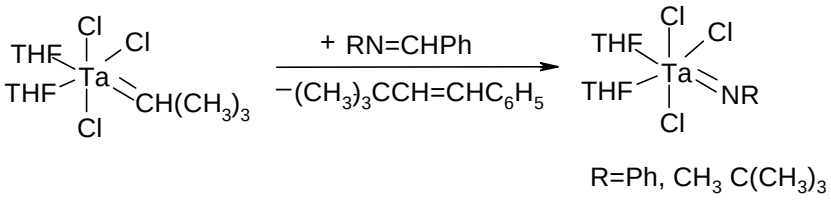
A number of early transition metal organoimido complexes fall in the doubly bridging category for e.g. $[Zr(N\ ^tBu)\{N(CH_3)_2\}_2]_2$. The triply bridging coordination mode is found in a number of cluster complexes of the iron triad for e.g. $Fe_3\{N\ Si(CH_3)_3\}(CO)_{10}$.

Background

Most of the organoimido complexes prepared to date contain 2nd and 3rd row transition metals. Such complexes have now been prepared for all 13 naturally occurring metals.

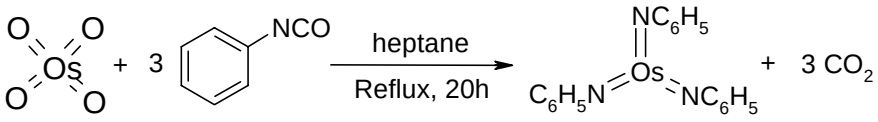
In 1980, tantalum imido complexes[7] have been synthesized by reacting tantalum neo pentylidene complexes with imines. The procedure is high yielding and straightforward route for variety of tantalum imido derivatives (Scheme-1).

Scheme-1



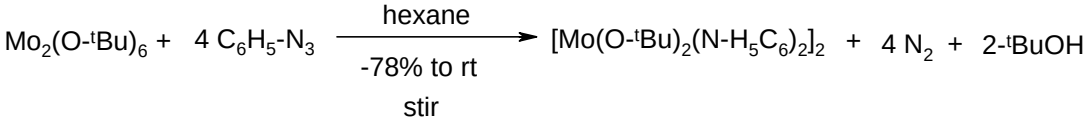
In the year 1991, osmium organoimido[8] complexes have been prepared by the reaction of osmium tetroxide with 3 equivalents of 2, 6-diisopropyl phenyl isocyanate in refluxing heptane over a period of 20 h (Scheme-2).

Scheme-2



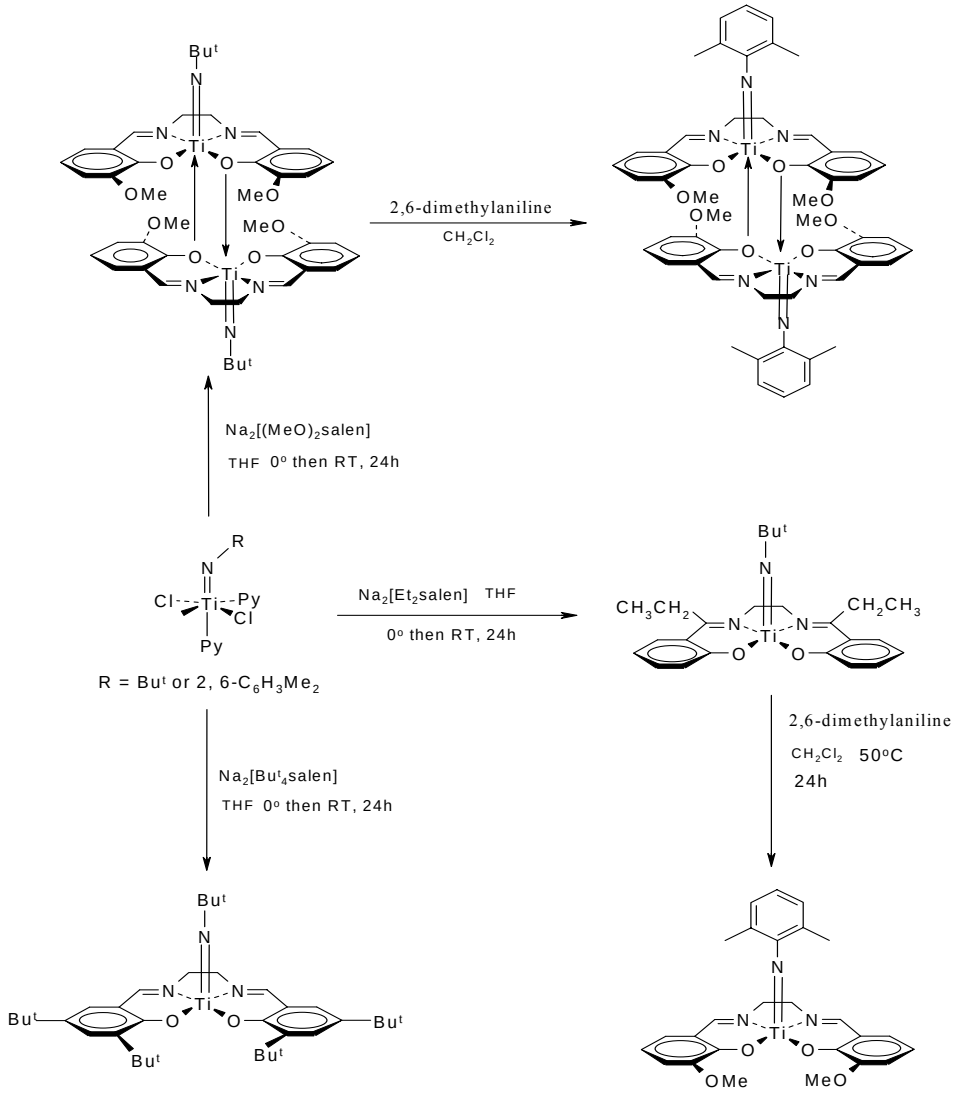
In the year 1982, bisimido molybdenum complexes[9] have been synthesized by reacting aryl azides with $Mo_2(OR)_6$ (Scheme-3).

Scheme-3



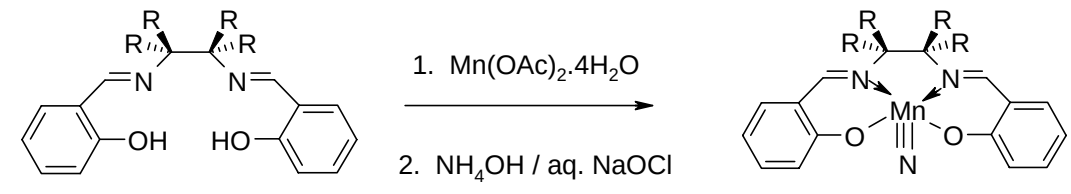
In the year 1998, new mono- and binuclear titanium imido complexes supported by tetradentate, have been synthesized with dianionic N_2O_2-donor Schiff base ligands from readily available $Ti(NBu^t)Cl_2(Py)$[10] (Scheme-4).

Scheme-4



In the year 1996, Erick M. Carreira[11] et al have reported facile preparation of two novel nitridomanganese(V) salen-derived complexes that serve as reagents for the amination of electron-rich enol ethers (Scheme-5).

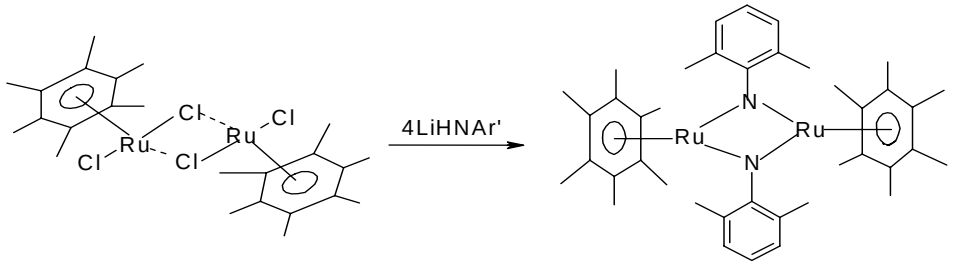
Scheme-5



R= H, CH_3

In 1997 a number of ruthenium imido complexes[12] have been synthesized by the reaction of $[(\eta^6\text{-arene})RuCl_2]_2$ with LiNH-R (R = 2, 6-diisopropylphenyl, 2, 6-dimethylphenyl, 2, 4, 6-tri-tert butylphenyl) (Scheme-6).

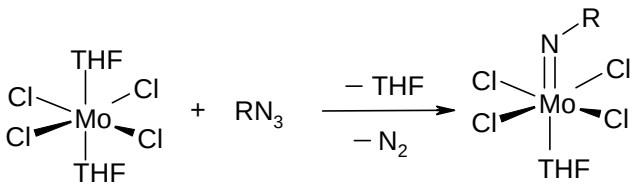
Scheme-6



Ar' = 2, 6-dimethylphenyl

In recent year, R. R. Schrock[13] have reported the preparation of several new Molybdenum imido complexes of the type $Mo(NR)Cl_4(THF)$ via the treatment of $MoCl_4(THF)_2$ with azides (Scheme-7).

Scheme-7



R = C_6F_5, 3, 5-$(CF_3)_2$-C_6H_3, 1-adamantyl, $C(C_6H_5)_3$, and 2, 6-$^{i}Pr_2$-C_6H_3

Objective

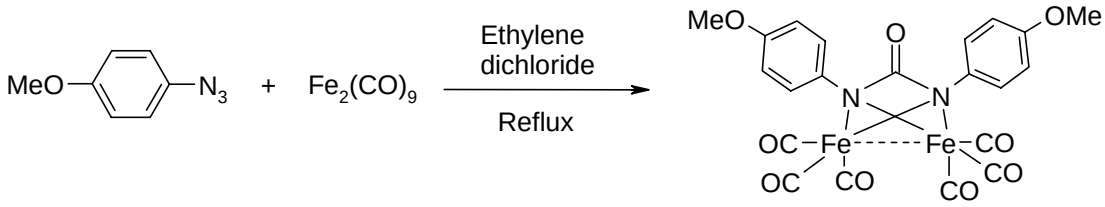
Our aim was to prepare metal nitrene (imido) complexes of molybdenum and iron by the reaction of aryl azides with metal carbonyls. Metal carbonyls like $Mo(CO)_6$, $Fe_2(CO)_9$, $Mo(CO)_4$(DAB) were treated with various aryl azides.

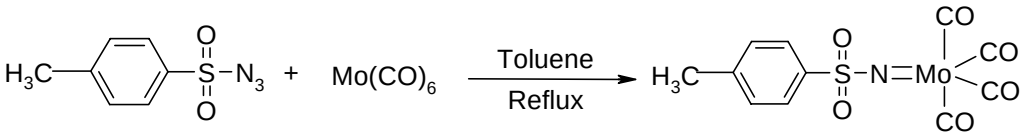
$(\eta^5\text{-}C_5H_5)Ru\{P(C_6H_5)_3\}_2Cl$ with bromamine-T in the presence of $NaBF_4$ or NH_4PF_6.

1.1.2 Present work

A. Synthesis of metal imido complexes by the reaction of aryl azides with metal carbonyls

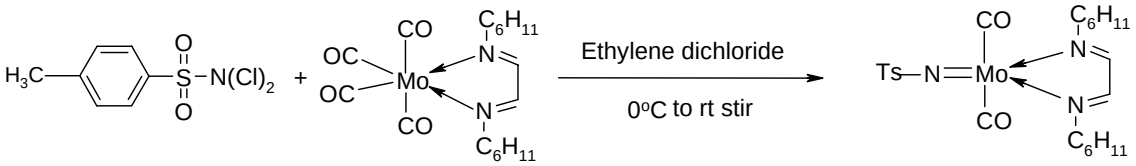
Scheme-1





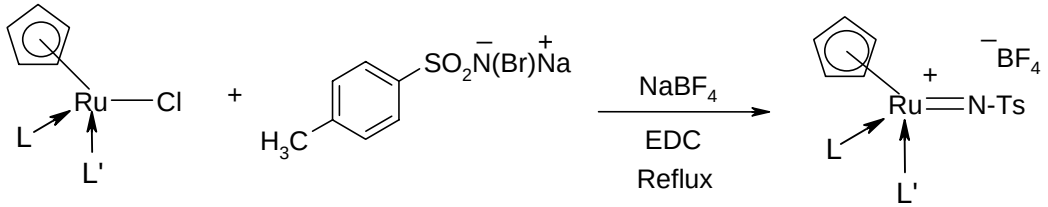
B. By the reaction of N, N-dihalocompounds with metal carbonyls

Scheme-2



C. Synthesis of Ruthenium Nitrene complexes

Scheme-3



L = $P(C_6H_5)_3$, CH_3CN

L' = $P(OCH_3)_3$,PPh_3, CH_3CN

Results and Discussion

First, reactions of aryl azides with metal carbonyls were attempted for the synthesis of metal nitrene complexes. In the process, we used p-toluenesulphonyl azide and also p-methoxyphenyl azide as nitrene precursors. p-toluenesulphonyl azide gives stable nitrene intermediate compared to other aryl azides. The reactions were carried out in refluxing toluene or ethylene dichloride but we couldn't get the required metal nitrene complex. In the case of p-methoxyphenyl azide, p-anisidine was obtained as the product. p-toluenesulphonyl azide was not undergone any change during the reaction and it was recovered back. Synthesis of ruthenium nitrene complexes were also tried using other ruthenium complexes like $(\eta^5\text{-}C_5H_5)Ru\{P(C_6H_5)_3P(OCH_3)\}Cl$, $(\eta^5\text{-}C_5H_5)Ru\{P(C_6H_5)_3CH_3CN\}^+ {}^-BF_4$ with bromamine-T with NH_4PF_6 and $NaBF_4$. The ^{1}H-NMR was complex in these cases.

Ruthenium nitrene complexes were attempted to synthesize by the reaction of $(\eta^5\text{-}C_5H_5)$ $Ru\{P(C_6H_5)_3\}_2Cl$ with bromamine-T in the presence of NH_4BF_4 or NH_4PF_6 in refluxing EDC. Ruthenium metal nitrene complex was synthesized by the reaction of $(\eta^5\text{-}C_5H_5)$ $Ru\{P(C_6H_5)_3\}_2Cl$ and bromamine-T as nitrene source and in the presence of $NaBF_4$ or NH_4BF_4. The formation of metal nitrene complex could be proposed on the basis of ^{1}H NMR of reaction mixture although some impurity was there and we couldn't able to isolate the pure product. The purification of the mixture was tried by several methods such as crystallization and column chromatography on silica gel, neutral alumina and flurosil.

The ^{1}H-NMR of the mixture shows two methyl peaks at δ 2.43 and δ 2.30 which are due to methyl groups from metal nitrene complex and phosphinime. One of the peaks at δ 5.44 and δ 5.41 was due to cyclopentadienyl protons of the Ruthenium nitrene complex and other peak would be due to cyclopentadienyl protons of some other ruthenium metal complex formed during the reaction. One of

the other evidence that metal nitrene complex was formed, was the shift in the chemical shift of the cyclopentadienyl protons in the ^{1}H-NMR of the reaction mixture. The reason was the deshielding of cyclopentadienyl protons in the cationic nitrene complex. Since in the ^{1}H-NMR of the starting ruthenium complex, the cyclopentadienyl protons are at δ 4.10. The integration of the aromatic peaks was coming more than the desired numbers of protons. This was due to some amount of phosphinimine formed by the dissociated triphenyl phosphine and tosyl nitrene. The integration of doublet at δ 6.99 was coming around five protons corresponding to two ortho protons of tosyl phenyl group nearby tosyl methyl group. Due to the presence of 20% of phosphinimine the intrgration was high. A multiplet and two doublets at δ 7.50 and δ 7.75 (*J*=10 Hz) respectively were due to aromatic protons of triphenylphosphine of the product and phosphinimine. Doublets at δ 7.46 (*J*=10 Hz) and δ 7.03 (*J*=!0 Hz) were due to protons of tosyl groups with A_2B_2 pattern. Obviously the integration was high due to mixture. According to calculation and comparison of the ratios of protons due to the product (Ruthenium nitrene) and phosphinimine it shows that 80:20 mixture was present.

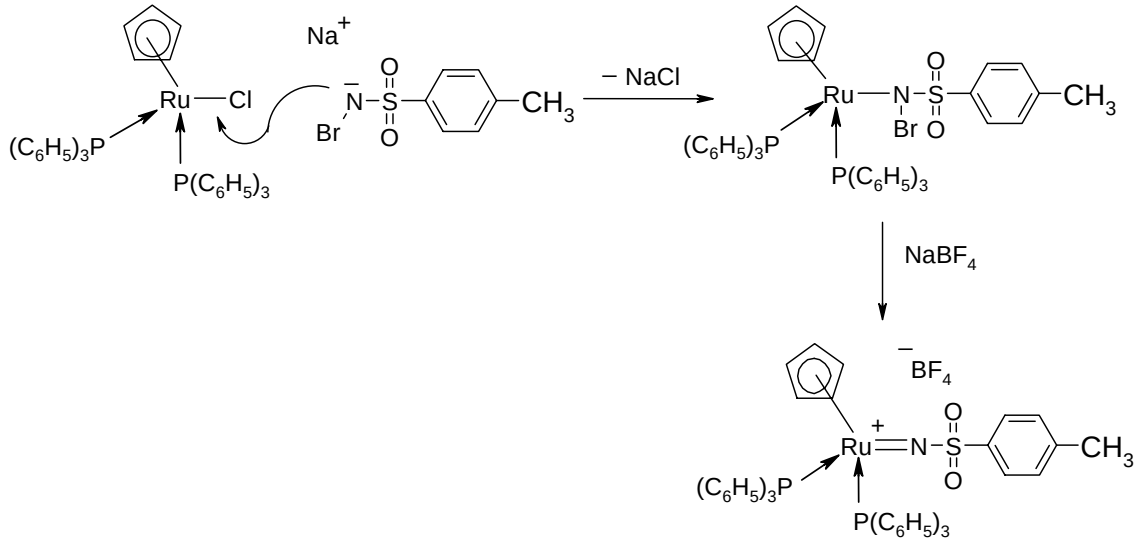
The ^{13}C-NMR shows peaks due to tosyl methyl carbons of the product and phosphinimine at δ 21.26, δ 21.67. Cyclopentadienyl carbons were at δ 92. The aromatic carbons were from δ 125.78 to δ 144.62. The spectrum contains peaks due to both the product and phosphinimine.

The mass spectra the molecular ion peak at 431 indicates the pesence of phosphinimine. The molecular ion peak (946) due ruthenium nitrene complex was not there in the spectra but the peaks at 885, 863, 671, 584 could be assigned due to fragments of the nitrene complex.

One of the major problem occurred during the synthesis of ruthenium metal nitrene complex was to get the metal complex in pure form. We have tried to purify by column chromatography on silica gel, alumina and flurosil using various eluting solvents like ethyl acetate, acetone and then methanol but couldn't able to get the product. The product was eluting along with phosphinimine. The coordination of phosphinimine with product (Ruthenium nitrene) could also be possible. Therefore through the column chromatography we obtained the mixture of phosphinime and the product.

Thus by studying this reaction we concluded that the cationic ruthenium nitrene complex was formed by the reaction of $(\eta^5\text{-}C_5H_5)\ Ru\{P(C_6H_5)_3\}_2Cl$ with bromamine-T.

Mechanism



1.1.3 Experimental

1. Preparation of $Mo(CO)_4DAB$

$Mo(CO)_6$ (0.786 g, 3 m mol) was added to a solution of glyoxal (0.435 g, 3 mmol) and cyclohexylamine (0.594 g, 6mmol) in 5 ml of benzene and 3 ml of methanol and stirred overnight. A dark brown crystals were obtained.

Yield : 82%

M. P. : 190^0C

IR (Nujol, cm^{-1}) : 2923, 2854, 2019, 1928, 1884, 1820, 1514, 1461, 1377.

^{1}H-NMR ($CDCl_3$, δ ppm) : 1.36 - 2.09 (m, 20H, Cy-C$\underline{H}_2$), 3.69–3.79 (m, 2H, Cy-C$\underline{H}$), 8.24 (s, 2H,)

2. Preparation of (η^5-C_5H_5) $Ru\{P(C_6H_5)_3\}_2Cl$

(η^5-C_5H_5) $Ru\{P(C_6H_5)_3\}_2Cl$ was prepared according to known methods. To a boiling solution of triphenylphosphine (3.114 g, 3mmol) in 95% ethanol (200 ml) was added a solution of $RuCl_3.3H_2O$ in 95% ethanol (80 ml). After 5 min refluxing freshly distilled cyclopentadiene (1.188 g, 18 mmol) and 95% ethanol (10 ml) were added. The solution was refluxed for 1 hour and cooled to give orange crystals, which were collected and washed with ethanol. Recrystallization from dichloromethane/n-hexane mixture gave the compound.

Yield : 82%

M. P. : 236-248 °C

IR : ν(Ru-Cl) 280 m, 275 m cm-l.

^{1}H-NMR ($CDCl_3$, δ ppm) : 4.10 (s, 3H, η-$C_5\underline{H}_5$), 7.12-1.35 (m, Ar-$\underline{H}$)

C-H analysis : Found; C, 67.4; H, 4.7; Cl, 4.8

Calcd.: C, 67.8; H, 4.86; Cl, 4.88%.

3. Preparation of Bromamine-T

Preparation of Dibromamine-T

Recrystallized Chloramine-T (1.0 g, 4 mmol) was dissolved in water (20 ml) and liquid bromine (2 ml, 12 mmol) was added dropwise from a burette with constant stirring of the solution. The golden yellow precipitate of the Dibromamine-T was thoroughly washed with water, filtered under suction and dried in a vacuum dessicator for 24 hours.

Yield : 89 %

M.P. : 92 ^{o}C (Lit M.P. 92-93 ^{o}C)

Dibromamine-T (3.3 g, 11 m mol) was dissolved in small lots at a time with stirring, in aqueous solutions of sodium hydroxide (0.8 g, 20 mmol) in 50 ml of water, and the solution was cooled in ice. Pale yellow crystals of BromamineT separated out. The solid was filtered under suction, washed quickly with minimum quantity of water and dried over P_2O_5 in a dessicator.

Yield : 2.8 g (86 %)

^{1}H NMR (D_2O) : δ 2.4 (s, 3H), 7.4(d , *J* = 1.9 Hz, 2H), 7.7(d, *J* = 1.9Hz, 2H).

MS m/z (%) : 274 (M^{+2}, 21), 272(M^{+}, 7), 185 (5), 171 (18), 155 (22), 107 (17), 91 (100), 77 (4).

C-H Analysis : Calculated for $C_7H_7NO_2SBrNa$; Br =24.4 %, N = 4.4 %, S = 9.5 %

Found Br = 24.0 %, N = 4.1 %, S = 9.4 %

Drying of Bromamine-T

The Bromamine-T trihydrate obtained in the above step was dried to constant weight at 80°C under vacuum. Accurate control of temperature is essential for effective drying.

4. Reaction of Bromamine-T with (η^5-C_5H_5) Ru{$P(C_6H_5)_3$}$_2$Cl

To a 25ml RBF, Bromamine-T (0.068g, 0.25 mmol) and (η^5-C_5H_5) Ru{$P(C_6H_5)_3$}$_2$Cl (0.180g, 0.25 mmol) $NaBF_4$ (0.050g, 0.5 mmol) were added. To this 10 ml of dry EDC was added and kept for reflux. Reaction was monitored by TLC. After the completion EDC was evaporated on rotary evaporator. The mixture was tried for the purification on different adsorbing material like silica gel, neutral alumina and flurosil.

^{1}H-NMR ($CDCl_3$, δ ppm) : 7.79 (d, 6H, Ar-H) 7.69 (d, 2H J=10Hz, 2H); 7.50 (m, 15 H); 7.03 (d 2H, Ar-H); 5.44 and 5.41 (5H cyclopentadienyl-H); 2.43 and 2.30(s, 6H, CH_3)

^{13}C NMR ($CDCl_3$, δ ppm) : 21.26, 21.67, 29.68, 91.81, 92.72, 125.78, 127.15, 128.64, 129.64, 132.71, 133.21, 140.43, 143.62, 144.62.

Mass Spectra (m/z, % intensity) : 885, 863, 671, 584, 453, 431, 277, 147, 84.

Conclusion

In conclusion, cationic ruthenium nitrene complexes could be prepared by simple precursors like (η^5-C_5H_5) Ru{$P(C_6H_5)_3$}$_2$Cl and Bromamine-T.

1.1 References

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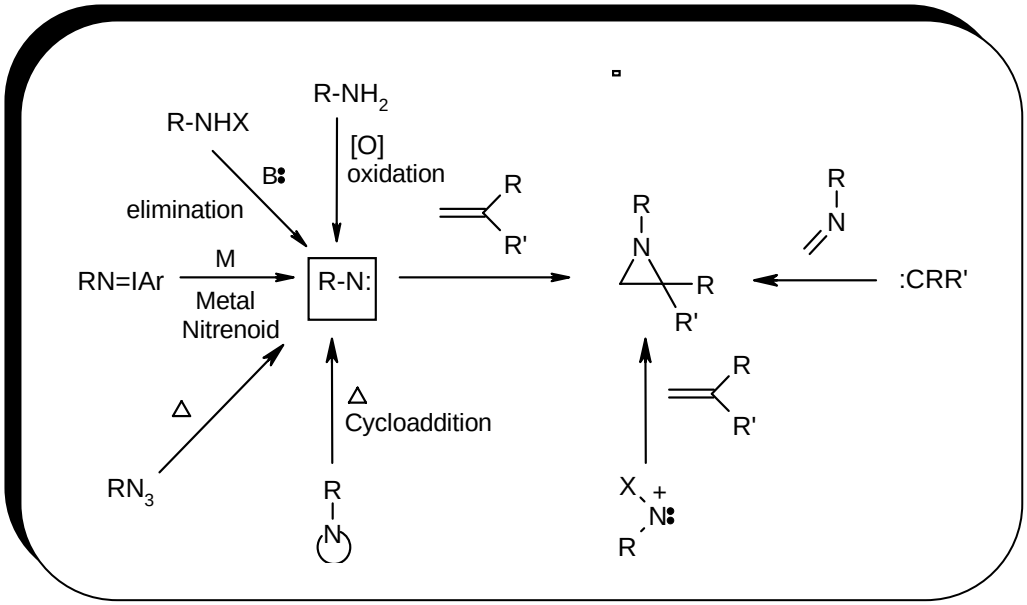
AZIRIDINATION

1.2.1 Introduction

The intermolecular cycloaddition of an electron-deficient species such as a nitrene, a nitrenium ion or a carbene (or their formal equivalents) to the π-bond of an alkene, alkyne, imine or nitrile is a significant approach to aziridines and azines.

Electrophilic nitrogen compounds, such as arenesulfonyloxyamines, can convert alkenes to aziridines without the intervention of free nitrenes. The ylide Ph_2S^+ NH^- adds stereospecifically to E and Z conjugated alkenes and chiral sulfiimides can transfer chirality to the aziridine formed. These reactions are often named "aziridinations".



The development of metal catalyzed coupling of simple organic molecules to give higher functionalized molecules is a field of rapid progress. Aziridines can be used as versatile precursors for the synthesis of a variety of organic compounds of

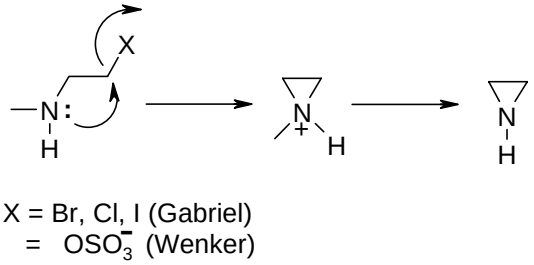
biological importance. Various methods are available for the preparation of enantiomerically pure aziridines, but most of are laborious multi-step reactions, where either optically pure starting materials or stoichiometric amounts of chiral auxillaries were used. The simplest catalytic formation of aziridines is, in principle, either the addition of a carbene fragment to an imine or the addition of a nitrene fragment to an alkene.

Background

Aziridine is synthesized by many catalytic and noncatalytic methods. The most obvious and oldest approach to aziridine synthesis involves internal (neighboring group) cyclization of an amino group situated β to a living group. There are many reports on the asymmetric synthesis of aziridines.

Gabriel and Wenkert method of the synthesis of aziridines is one of the oldest method via 1, 2-elimination of hydrogen halide or hydrogen sulphite (Scheme-1).

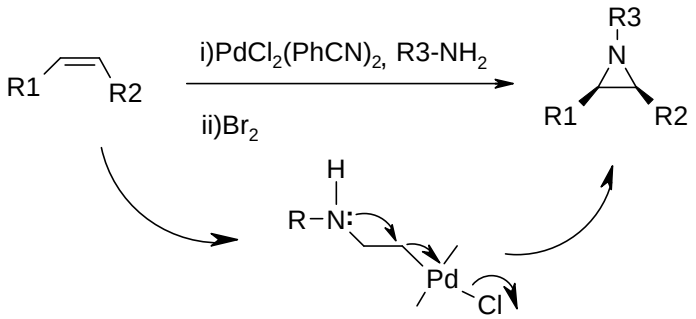
Scheme-1



X = Br, Cl, I (Gabriel)
= OSO_3^- (Wenker)

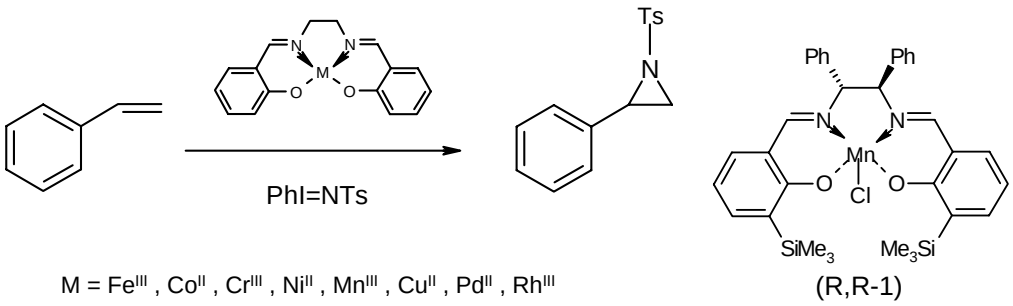
In the year 1977, J. E. Backvall[1] et al have reported Pd-promoted amination of olefins using primary amines followed by oxidation by bromine, resulting in the formation of N-substituted aziridines (Scheme-2).

Scheme-2



In the year 1992, new chiral metal salen complexes with bulky silyl groups (TMS, TBDMS) in the 3rd position have been synthesized by Burrows et al group.[2] Although some of these complexes catalyzed the epoxidation reaction in high ee's. These complexes catalyzed the aziridination of cis-β-methylstyrene without any asymmetric induction (Scheme-3).

Scheme-3

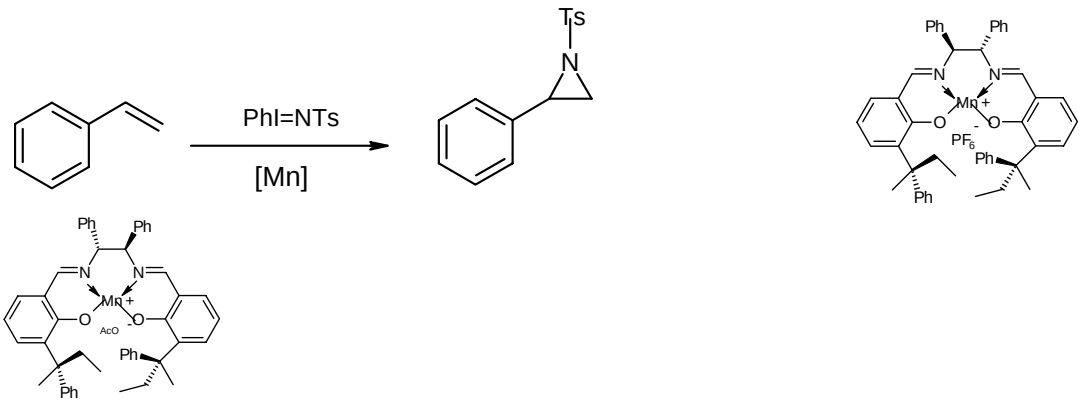


M = Fe^{III} , Co^{II} , Cr^{III} , Ni^{II} , Mn^{III} , Cu^{II} , Pd^{II} , Rh^{III}

(R,R-1)

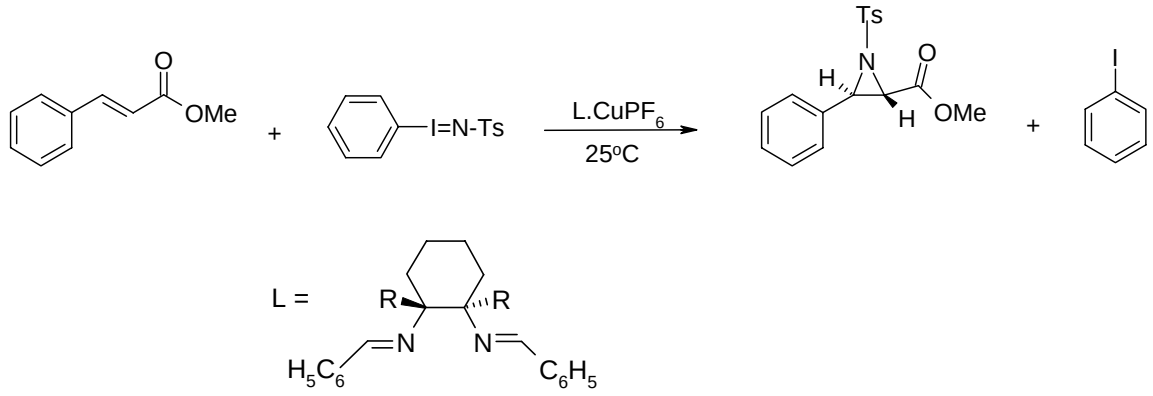
In the year 1993, optically active (salen)manganese (III) complex was found to show moderate level of asymmetric induction in the aziridination of styrene, though chemical yield was poor[3] (Scheme-4).

Scheme-4



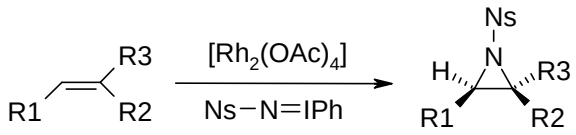
In 1995, it has been shown that Cu(I) complexes are the most effective catalysts for aziridination. Aziridination proceed via a Cu-nitrenoid intermediate[4] (Scheme-5).

Scheme-5



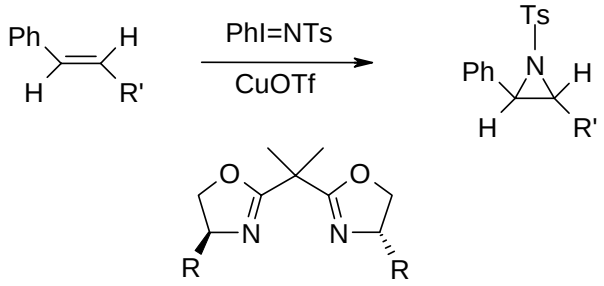
In the year 1996, a new methodology has been found by using dirhodiumacetate. Dirhodiumacetate catalyzed decomposition of [N-(p-nitrobenzene sulfonyl imino)] phenyl iodinane (C_6H_5I=N-Ts), which in the presence of olefins affords aziridines. The reaction was stereospecific, with chiral catalysts and asymmetric induction was up to 73% ee[5] (Scheme-6).

Scheme-6



Evans[6] et al showed that soluble copper metal complexes are the metal catalysts of choice in the aziridination of olefins with C_6H_5I=N-Ts. Preliminary evidence indicates that, chiral 4, 4'-disubstituted bis(oxazoline) are excellent ligands for the copper catalyzed cyclopropanation of olefins and are also effective in enantioselective aziridination reactions (Scheme-7).

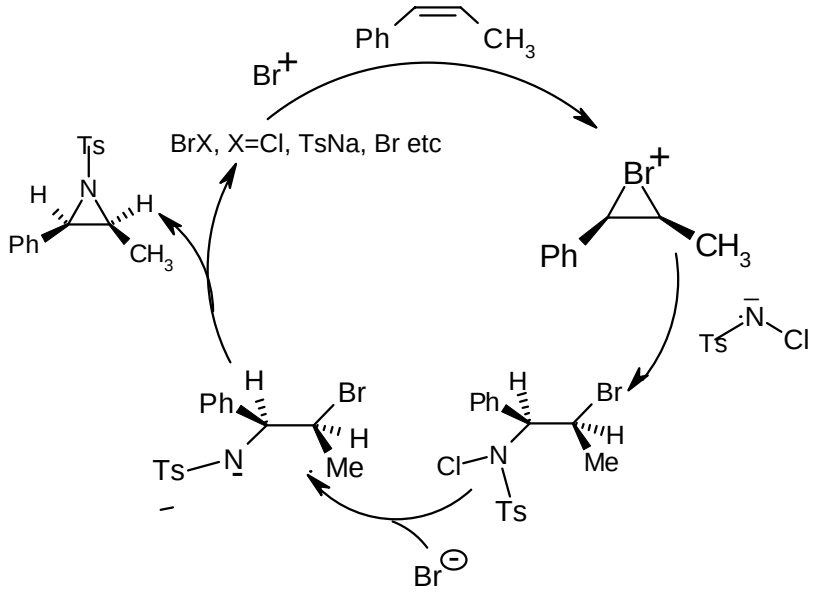
Scheme-7



2a, R=$CH(CH_3)_2$
2b, R=C_6H_5
2c, R=$C(CH_3)_3$
2d, R=$C(CH_3)_2Ph$
2e, R=$C(CH_3)Ph_2$

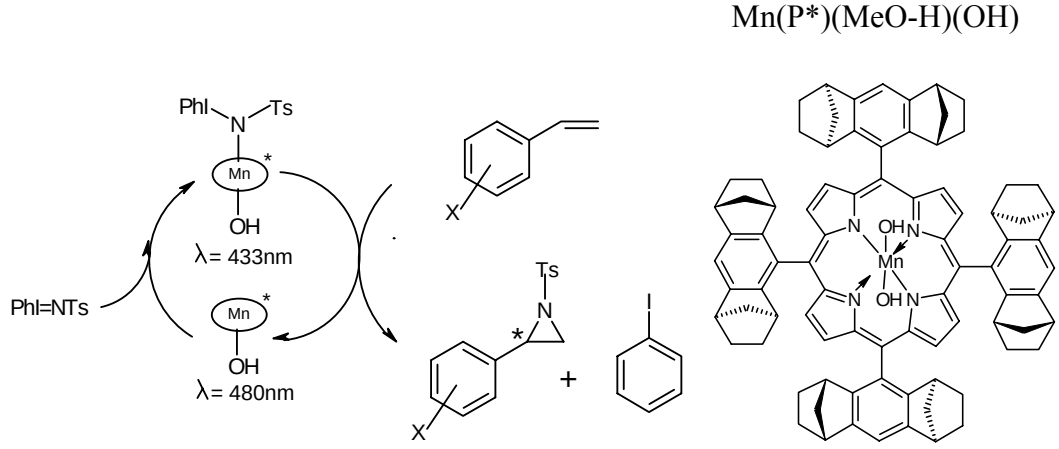
In 1998, K. B. Sharpless[7] have shown that a wide range of bromine sources for example $ZnBr_2$, $HgBr_2$, $FeBr_2$, $CuBr_2$, Br_2 and NBS can be used as catalysts for aziridination of simple olefins using chloramine-T (Scheme-8).

Scheme-8



In the year 1998, a D_4-manganese(III) porphyrin was utilized to catalyze aziridination of styrene type substrates with enantiomeric excess ranging from 43 to 68%, evidence for a Mn (IV) reactive intermediate in the catalysis was obtained from spectroscopic studies and organic product analysis[8] (Scheme-9).

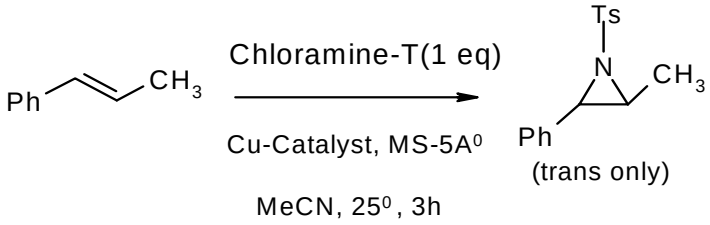
Scheme-9



In the year 1998, for the first time Komatsu[9] et al showed that chloramine-T, a well-known commercially available oxidant can be used as a nitrogen source. Chloramine-T and its analogs can be used as nitrogen transfer reagents for the

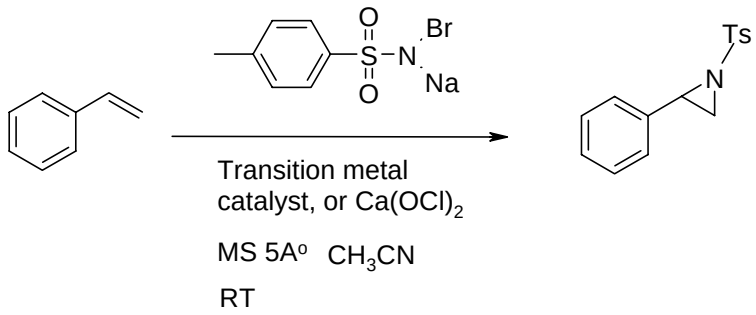
catalytic aziridination of alkenes. Copper catalysts were found to work well for this reaction.

Scheme-10



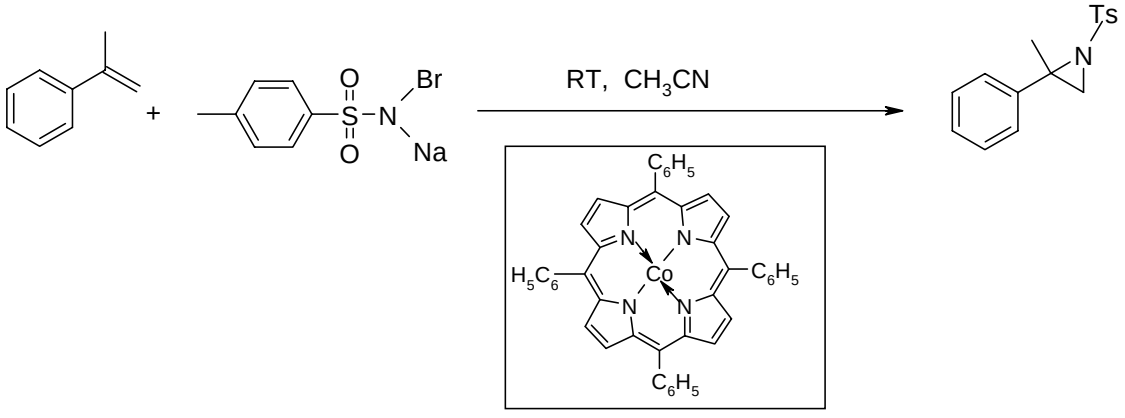
In the year 2001, it was shown that bromamine-T could be efficiently used for the aziridination reaction as nitrogen source. The copper catalyzed reactions of bromamine-T with various olefins gave good yields of the aziridine compared to chloramine-T[10] (Scheme-11).

Scheme-11



Recently in 2005, Co(porphyrin) complexes are found very efficient catalysts for aziridination of wide variety of alkenes[11] (Scheme-12).

Scheme-12



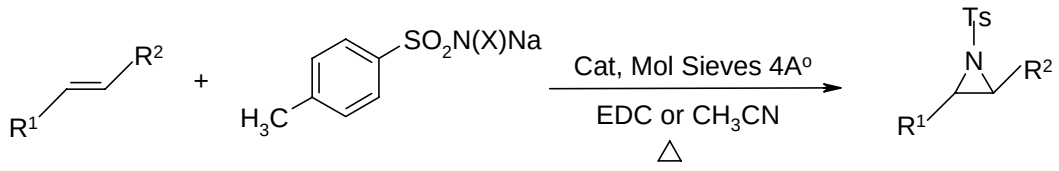
Objective

Our objective was to use simple and effective metal complexes using variety of transition metals for the catalysis of aziridination reaction. For this purpose we used many class of ligands and metal salts. Apart from these metal complexes we used many transition metal carbonyls and simple metal salts. Under the study, we screened many classes of ligands. For example nitrogen based ligands like salen, diazabutadiene, phthalocyanin and DMG etc. Oxygen based ligands like acac with various transition metals have been screened for the aziridination reaction.

1.2.2 Present Work

Aziridination reaction of chloramine-T, bromamine-T and other nitrene precursors with olefins was carried out in the presence of various transition metal catalysts (Scheme-1).

Scheme-1



$R^1 = C_6H_5$,

X = Cl, Br

R^2 = H, $COOCH_2CH_3$

Table-1- Aziridination using various transition metal complexes

Sl.No	Nitrene Source	Olefin	Catalyst	Time (hrs)	Yield (%)
1.	4-$CH_3.C_6H_5SO_2N_3$	$C_6H_5.CH=CH_2$	$C_5H_4CH_3.Mn(CO)_3$	24	6
2.	4-$CH_3.C_6H_5SO_2N_3$	-do-	CoCl(DMG)(Py)	-do-	5
3.	4-$CH_3.C_6H_5SO_2N(Cl)Na$	-do-	$(TMEDA)PdCl_2$	-do-	21
4.	4-$CH_3.C_6H_5SO_2N(Cl)Na$	-do-	Cu(TMEDA)OH.Cl	-do-	17
5.	4-$CH_3.C_6H_5SO_2N(Cl)Na$	-do-	$Fe(CO)_5$	-do-	42
6.	4-$CH_3.C_6H_5SO_2N(Br)Na$	-do-	CoCl(DMG)(C_5H_5N), $AgNO_3$	-do-	26
7.	4-$CH_3.C_6H_5SO_2N(Br)Na$	-do-	$Mn(acac)_2Br$, $AgNO_3$	-do-	30
8.	4-$CH_3.C_6H_5SO_2N(Br)Na$	-do-	Fe(Pc)	- do-	82
9.	4-$CH_3.C_6H_5SO_2N(Br)Na$	-do-	$CuCl(Bz_2O_2)(Py)_2$	-do-	24
10.	4-$CH_3.C_6H_5SO_2N(Br)Na$	-do-	η^5-$C_5H_5)Ru\{P(C_6H_5)_3\}_2Cl$	-do-	6
11.	4-$CH_3.C_6H_5SO_2N(Br)Na$	-do-	$Pd(dba)_2$+ Cy-DAB	-do-	19
12.	4-$CH_3.C_6H_5SO_2N(Br)Na$	-do-	$ZrOCl_2$	-do-	31
13.	4-$CH_3.C_6H_5SO_2N(Br)Na$	-do-	$Mn(acac)_2Br$ $AgNO_3$	-do-	31

Reaction conditions : Bromamine-T(1.2 mmol) + Styrene(1 mmol)+ cat (10 mg-30 mg)+ EDC or CH_3CN (10 ml) Reflux

Results and Discussion

Various transition metal catalysts containing different kinds of ligands and different metal salts are used for the catalysis of aziridination reaction. Transition metals containing different kinds of ligands like salen-Fe(salen), Fe(salphen),

Fe(salen)Cl, Mn(salen)Cl, Cu(salen), acac-Fe(acac), $Mn(acac)_3$, $Mn(acac)_2Br$ metal carbonyls- $Fe(CO)_5$, $Mo(CO)_6$, $Cr(CO)_6$, $Fe_2(CO)_9$, $(\eta^5\text{-}C_5H_5)_2Fe_2(CO)_2$ were tried for the aziridination reaction using Chloramine-T and Bromamine-T as nitrene source.

Pd(0) and Pd (II) complexes like, $Pd(TMEDA)Cl_2$ and $Pd(dba)_2$, $Pd_2(dba)_3.CHCl_3$ with cyclohexyldiimine, 2, 6-diisopropyldiimine and bipyridil ligands, were also used for the reaction. Other metal complexes for example, $Ni\{P(OC_6H_5)_3\}_4$ Cu(OH)Cl(TMEDA), $CuCl(Bz_2O_2)(C_6H_5N)_2$, $AuCl.P(C_6H_5)_3$, Fe(Phthalocyanin), $(\eta^5\text{-}C_5H_5)Ru\{P(C_6H_5)_3\}_2Cl$ $RuCl_2(DMSO)$, Cu/Al_2O_3 Cu/Hy, Fe/Hy, sulphated Fe, $Co(DMG)(C_6H_5N)Cl$, $Cu(OAc_2)$/Binol and Cu(Tc) were used for the catalysis of the reaction. Some of metal salts, $FeCl_2$, $ZrOCl_2$, $Mn(OAc)_3$ were used for the reaction.

The reaction of chloramine-T with styrene was catalyzed by stoichiometric amount of $Fe(CO)_5$ gave the aziridine in moderate yields. $Mo(CO)_6$ gave 4-toluenesulphonamide while with $Cr(CO)_6$ less amount of aziridine was formed. Tosyl azide gave about 6 % of the aziridine when reacted with styrene in the presence of stoichiometric amount of Methylcyclopentadienyl (I) manganese tricarbonyl. $Fe_2(CO)_9$, $(\eta^5\text{-}C_5H_5)_2Fe_2(CO)_2$ didn't gave the product with chloramine-T, bromamine-T and tosyl azide. The study shows that iron and manganese carbonyls can stabilize the nitrene intermediate formed in situ better than does the molybdenum carbonyl which readily undergoes protonation to give $Ts\text{-}NH_2$.

Stereoselectivity of the aziridination reaction and the effect of catalysts was shown in the reaction of stilbene and also provides some clue to the reaction mechanism as well as specificity of catalysis in these reactions. One can easily vary the catalyst to get cis isomer $Fe(CO)_5$, trans isomer with Mn(Salen)Cl or a mixture of

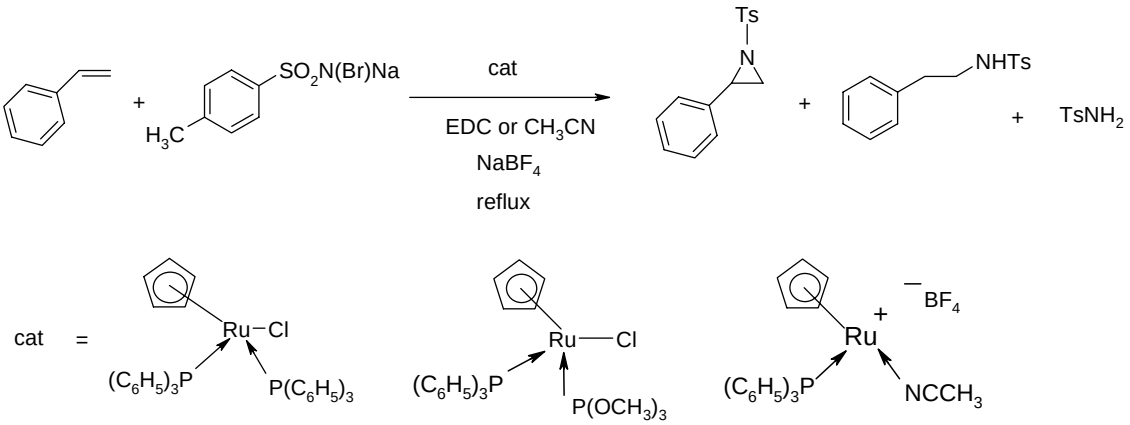
cis-trans isomers (5 : 1) with Fe(Phthc). Electron rich styrene is the only olefin which reacted under most of the above conditions described, while electron deficient olefins, ethyl acrylate, methyl cinnamate and simple unsubstituted olefins, cyclohexene, cycloctene gave no reaction. Among the acac complexes, Fe(acac), $Mn(acac)_3$ gave less amount of aziridine, while $Mn(acac)_2Br$ in the presence of $AgNO_3$ gives 26 - 30 % yield of aziridine. The reason was in the presence of $AgNO_3$, the Mn-Br bond got polarized and a cationic complex was formed which can stabilize the nitrene intermediate and transfer to olefin efficiently to form aziridine.

Fe(salen), Fe(salen)Cl, Cu(salen) catalyzed reactions of chloramine-T and bromamine-T gave trace amount of the aziridine. Mn(salen)Cl complexes gave the highest yield of aziridination with $AgNO_3$ as co-catalyst in ethylene dichloride as solvent (Mn – 47.6 %, Fe – 19 %). In acetonitrile the yields were lower (8 – 10.9 %). $NaBF_4$ gave lower yield of aziridination in both the solvents studied. The reason for the higher yield of aziridine can be attributed to the polarization of metal-chloride bond. $Pd(dba)_2$ and $Pd_2(dba)_3.CHCl_3$, both Pd(0) complexes, similarly catalyzed reaction of chloramine-T with styrene in the presence of cyclohexyldiimine, 2,6-diisopropyldiimine and bipyridyl to form the aziridine in moderate yields. $PdCl_2$(TMEDA) gave the good yield i.e. 21% among the Pd-complexes. $Ni\{P(OC_6H_5)_3\}_4$ caused formation of 4-toluene sulphonamide and the phosphinimine by reaction of the ligand with the bromamine-T or a nitrene intermediate. $Co(DMG)(C_6H_5N)Cl$ in the presence of $AgNO_3$ gives 26 % yield of aziridine. Cu(OH)Cl(TMEDA), $CuCl(Bz_2O_2)(C_6H_5N)_2$, $AuCl.P(C_6H_5)_3$, Cu(Tc) also gave only low to moderate yields of the aziridine. $RuCl_2(DMSO)_4$, Cu/Al_2O_3 Cu/Hy, Fe/Hy, sulphated Fe gave very trace amount of aziridine. The Fe(Phthalocyanine) gave a very high yield of 81% in the absence of $NaBF_4$. $ZrOCl_2$ gave 31% yield of the aziridine. $FeCl_2$ catalyzed the reaction of tosyl azide with styrene gave

chloroaminated product in 27% yield. The co-catalyst effect was studied for $ZrOCl_2$ catalyzed aziridination reaction. Thus reactions with styrene were carried out in the presence of $AgNO_3$, $NaBF_4$ and NH_4BF_4 but to our disappointment there was no increase in the yield of the product observed. This may be due to under these conditions ionization of metal halide bond may not be possible.

CpRu(LL')Cl catalyzed Aziridination reactions

Scheme-2



With cyclopentadienyl Ru complexes, the yield was higher with trimethyl phosphite as ligand, in ethylene dichloride (16 – 21 %). The higher yield of the aziridine in the case of cyclopentadienyl Ruthenium with trimethylphosphite ligand may attributed to better stabilization of in situ formed nitrene intermediate. The co-catalyst $AgNO_3$ gave low yield (8.4 %). $NaBF_4$ gave the best yield with arene Ru complexes in ethylene dichloride (15 %). $NaBF_4$, NH_4PF_6 and $AgNO_3$ cause ionization of the halide forming a cationic intermediate, increasing the reactivity to generate the metal nitrene.

Reaction of tosyl azide with styrene, methylcinnamate, stilbene in the presence of $(\eta^5\text{-}C_5H_5)Ru\{P(C_6H_5)_3\}_2Cl$, $(\eta^5\text{-}C_5H_5)Ru\{P(C_6H_5)_3P(OCH_3)\}Cl$, $(\eta^5\text{-}C_5H_5)Ru\{P(C_6H_5)_3CH_3CN\}^+ {}^-BF_4$, and co-catalysts like $AgNO_3$, CuCl, $NaBF_4$,

NH_4BF_4, didn't yield the aziridine product. The reaction was studied with different conditions like different solvents (CH_3CN, EDC Toluene) and with thermal, photolytic conditions. In most of the cases tosyl azide was recovered back. Under the conditions the azide was not able to form tosyl nitrene. (η^5-C_5H_5)Ru{$P(C_6H_5)_3$}$_2$Cl catalyzed reaction of bromamine-T with styrene gave 6% of aziridine and 15% of styrene hydroaminated product, the rest was Ts-NH_2. (η^5-C_5H_5)Ru{$P(C_6H_5)_3CH_3CN$}$^+$ $^-BF_4$ catalyzed reaction of benzoyl azide with styrene gave diphenylurea.

Various sulfur ligands and its metal complexes, for example Cu(thiophenecarboxylate), DMSO and dimethylsulfide are also tried for the reaction. Imine complexes derived from thiophene carboxaldehyde with Fe, Mn, are screened for the reaction. In these cases there was no formation of aziridine. Probably the sulphur ligands retard the reaction under these conditions by forming sulfinylimines. Dibromamine-T with Cu-powder with styrene also gave 10% of the aziridine. Other major product was Ts-NH_2.

Conclusion

In conclusion, various kinds of metal complexes with different kinds of ligands are tried for the aziridination reaction and in most of the cases low yield of aziridine is obtained. Metal carbonyl i.e. $Fe(CO)_5$ catalyzed aziridination using chloramine-T shows the presence of metal nitrene intermediate. Use of sulfur ligands gave either no reaction or no improvement in the reaction, the formation of sufinylamine will retard the reaction. In the case of Mn(salen)Cl along with $AgNO_3$ as co-catalyst, the yield of the aziridine was increased to 45% compared to Mn(Salen)Cl catalyzed reaction. The reason for increased yield may be attributed to Mn-Cl bond

polarization in the presence of Ag+ ions, thus facilitating easy formation of transient metal nitrene intermediate.

1.2.3 Experimental

The metal carbonyls, $Fe(CO)_5$, $(\eta^5\text{-}C_5H_5)_2Fe(CO)_2$, $Mo(CO)_6$, $Fe_2(CO)_9$ Fe(Pc) were purchased from Aldrich chemicals. $ZrOCl_2.4H_2O$ was purchased from Loba chemicals. All other metal complexes were prepared from well known literature methods.

Preparation of M(Salen) complexes

The metallic chelate complexes of bivalent copper, nickel, cobalt with different o-hydroxyaldehyde and o-phenylene diamine or ethylene diamine were obtained as usual by interaction of 2-hydroxyaldehyde (2 mol), amine (1.2 mol) and the corresponding metal chelates (1 mol) in hot aqueous ethanol mixture. Also prepared by the action of the different Schiff's bases obtained by the condensation of the aldehyde and amines, with metal chelates in hot ethanol. The products were crystallized from hot ethanol, cupric acetate monohydrate, nickel acetate tetrahydrate and cobalt acetate in methanol, ferrous ammonium sulphate in water were used respectively for the copper, nickel, cobalt and iron salen complexes.

Preparation of $Co(DMG)_2(C_5H_5N)Cl$

Dimethyl glyoxime (0.232 g, 2 mmol) and $CoCl_2.6H_2O$ (0.237 g, 1 mmol) were dissolved in 95% ethanol (100 ml) and heated to 70 ^{0}C. Pyridine (0.158 g, 2 mmol) was added and heating was stopped, but vigorous stirring open to air was continued. After cooling, air was bubbled for 45 mins. and then stirred for another 3-4h. again cooled to 0 ^{0}C, water was added, tan colored ppt obtained was collected by vacuum filtration and washed with water, dried.

Yield : 78.5%

M.P. : 240-242 ^{0}C

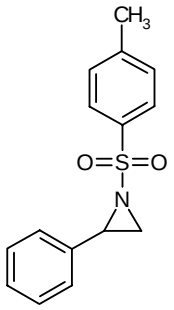
^{1}H-NMR ($CDCl_3$, δ ppm) : 2.41(s, 12H -C<u>H</u>$_3$), 7.25 (d, 2H Py-H), 7.71 (m, 1H,
Py-H) 8.29 (d, 2H, Py-H)

C-H Analysis : Calculated : C (38.56 %) ; H (4.94 %) ; N (17.30 %)
Found : C (38. 74 %) ; H (4.17 %) ; N (16.89 %)

1. Reaction of chloramine-T with styrene in the presence of $Fe(CO)_5$

Styrene (0.104 g, 1 mmol) and chloramine-T (0.227 g, 1.0 mmol) were taken in a 25 ml of round bottomed flask to which 10 ml of dry CH_3CN was added. Then $Fe(CO)_5$ (0.200 g, 1 mmol) was added dropwise at 0 ^{0}C.Then reaction mixture was allowed to stir at room temperature and then kept for reflux. Reaction was monitored by TLC. After completion of the reaction, the mixture was concentrated on rotovap. The mixture was purified on silica gel column chromatography to give 42 % of pure aziridine.

1-(4-Methylphenylsulfonyl)-2-phenyl azirane



M.P. : 88-90 °C

IR ($CHCl_3$ cm^{-1}) : 665, 696 715, 769, 783, 916, 1161, 1217, 1327, 3017

^{1}H-NMR ($CDCl_3$, δ ppm) : 2.40 (d, 1H), 2.42 (s, 3H), 2.99 (d, 1H), 3.80 (dd, 1H), 7.33 (m, 7H), 7.88 (d, 2H)

^{13}C NMR ($CDCl_3$, δ ppm) : 21.83, 35.76, 40.76, 126.44, 126.91, 128.13, 128.42, 129.56, 135.08, 135.37 144.16.

Mass Spectra (m/z, % intensity) : 273 (M^+, 8), 171 (18), 155 (10), 118 (75), 91 (100)

2. Reaction of tosyl azide with styrene in the presence of Cu/Al_2O_3

Styrene (0.104 g, 1 mmol) and Cu/Al_2O_3 (0.025 g) are taken in a 25 ml of round bottomed flask to which 10 ml of dry CH_3CN was added. Then $Ts\text{-}N_3$ (0.197 g, 1 mmol) was added dropwise at room temperature. The reaction mixture was then kept for reflux. Reaction was monitored by TLC. After the reaction, the reaction mixture was concentrated on rotovap. The mixture was purified on silica gel column chromatography to give 12 % of pure 1-(4-methylphenylsulfonyl)-2-phenyl azirane.

3. Reaction of tosyl azide with styrene in the presence of η^5-$(CH_3C_5H_4)Mn(CO)_3$ Styrene (0.104 g, 1 mmol) and η^5-$(CH_3C_5H_4)Mn(CO)_3$ (0.218 g, 1mmol)) were taken in a 25 ml of round bottomed flask to which 10 ml of dry CH_3CN was added. Then $Ts\text{-}N_3$ (0.197 g, 1 mmol) was added dropwise at room temperature. The reaction mixture was then kept for reflux. Reaction was monitored by TLC After the completion, the reaction mixture was concentrated on rotovap. The mixture was purified on silica gel column chromatography to give 6 % of pure 1-(4-methylphenylsulfonyl)-2-phenyl azirane.

4. Reaction of tosyl azide with styrene in the presence of $Ti(^iOPr)_4$

Styrene (0.104 g, 1 mmol) and $Ts\text{-}N_3$ (0.197 g, 1 mmol) were taken in a 25 ml of round bottomed flask to which 10 ml of dry CH_3CN was added. Then $Ti(^iOPr)_4$ in 1 ml of dry CH_3CN was added dropwise at room temperature. The reaction mixture was then kept for reflux. Reaction was monitored by TLC. After the reaction, the mixture was concentrated on rotovap. The mixture was purified on silica gel column chromatography to give 10% of pure 1-(4-methylphenylsulfonyl)-2-phenyl azirane.

5. Reaction of tosyl azide with styrene in the presence of $Mn(acac)_3$

Styrene (0.104 g, 1 mmol) and $Mn(acac)_3$ (0.032 g, 0.1 mmol) were taken in a 25 ml of round bottomed flask to which 10 ml of dry CH_3CN was added. Then Ts-N_3 (0.197 g, 1 mmol) was added dropwise at room temperature. The reaction mixture was refluxed. Reaction was monitored by TLC. After the completion, the reaction mixture was concentrated on rotovap. The mixture was purified on silica gel column chromatography to give 12 % of pure 1-(4-methylphenylsulfonyl)-2-phenyl azirane.

6. Reaction of bromamine-T with styrene in the presence of $Mn(acac)_2Br$

Styrene (0.104 g, 1 mmol) and $Mn(acac)_2Br$ (0.032 g, 0.1 mmol) were taken in a 25 ml of round bottomed flask to which 10 ml of dry ethylene dichloride was added. Then bromamine-T (0.326 g, 1.2 mmol) was added portionwise followed by addition of $AgNO_3$ (0.017 g, 0.1 mmol) at room temperature. The reaction mixture was then kept for reflux. Reaction was monitored by TLC. After completion, the reaction mixture was concentrated by rotary evaporation. The mixture was purified by silica gel column chromatography to give 30 % of pure 1-(4-methylphenylsulfonyl)-2-phenyl azirane.

7. Reaction of chloramine-T with stilbene in the presence of $Fe(CO)_5$

Stilbene (0.180 g, 1 mmol) and Chloramine-T (0.227 g, 1.0 mmol) are taken in a 25 ml of round bottomed flask to which 10 ml of dry CH_3CN was added. Then Fe $(CO)_5$ (0.200 g, 1 mmol) was added dropwise at 0 ^{0}C.Then reaction mixture was allowed to stir at room temperature and then refluxed. Reaction was monitored by TLC. After the reaction, the mixture was concentrated on rotovap. The mixture was purified on silica gel column chromatography to give 5% of pure 1-(4-methylphenylsulfonyl)-2, 3-diphenyl azirane.

8. Reaction of bromamine-T with styrene in the presence of $ZrOCl_2$: Styrene (0.250 g, 2.5 mmol) and dehydrated $ZrOCl_2$ (0.038 g, 0.2 mmol) were taken in a 25 ml of round bottomed flask to which 10 ml of dry CH_3CN was added. Then bromamine-T (0.163 g, 0.5 mmol) was added portionwise at room temperature. The reaction mixture was then refluxed. Reaction was monitored by TLC. After the reaction, the reaction mixture was concentrated on rotovap. The mixture was purified on silica gel column chromatography to give 24 % of pure 1-(4-methylphenylsulfonyl)-2-phenyl azirane.

9. Reaction of chloramine-T with styrene in the presence of $Cu(OAc)_2$/binol

Styrene (0.104 g, 1 mmol), $Cu(OAc)_2$ (0.038 g) and binol (0.05 g, 0.2 mmol) were taken in a 25 ml of round bottomed flask to which 10 ml of dry CH_3CN was added. Then chloramine-T (0.227 g, 1 mmol) was added portionwise at room temperature. The reaction mixture was then kept for reflux. Reaction was monitored by TLC. After the reaction, the reaction mixture was concentrated on rotovap. The mixture was purified by column chromatography to give 12 % of pure 1-(4-methylphenylsulfonyl)-2-phenyl azirane.

10. Reaction of chloramine-T with styrene in the presence of $PdCl_2$(TMEDA)

Styrene (0.104 g, 1 mmol) and $PdCl_2$(TMEDA) (0.010 g) were taken in a 25 ml of round bottomed flask to which 10 ml of dry CH_3CN was added. Then chloramine-T (0.227 g, 1 mmol) was added portionwise at room temperature. The reaction mixture was then kept for reflux. Reaction was monitored by TLC. After

completion, the reaction mixture was concentrated on rotovap. The mixture was purified by column chromatography to give 20 % of pure 1-(4-methylphenylsulfonyl)-2-phenyl azirane.

11. Reaction of chloramine-T with styrene in the presence Cu(TMEDA).OH.Cl : Styrene (0.104 g, 1 mmol) and Cu(TMEDA).OH.Cl(0.023 g, 0.1 mmol) were taken in a 25 ml of round bottomed flask to which 10 ml of dry CH_3CN was added. Then chloramine-T (0.227 g, 1 mmol) was added portionwise at room temperature. The reaction mixture was then refluxed. Reaction was monitored by TLC. After completion of the reaction, the mixture was concentrated on rotovap. The mixture was purified by column chromatography to give 17 % of pure 1-(4-methylphenylsulfonyl)-2-phenyl azirane.

12. Reaction of Chloramine-T with Styrene in the presence CuTc

Styrene (0.104 g, 1 mmol) and CuTc (0.038 g, 0.2 mmol) were taken in a 25 ml of round bottomed flask to which 10 ml of dry CH_3CN was added. Then chloramine-T (0.227 g, 1 mmol) was added portionwise at room temperature. The reaction mixture was then kept for reflux. Reaction was monitored by TLC. After copletion of the reaction, the mixture was concentrated on rotovap. The mixture was purified on silica gel column chromatography to give 10 % of pure 1-(4-methylphenylsulfonyl)-2-phenyl azirane.

13. Reaction of bromamine-T with styrene in the presence of $CuCl(Bz_2O)_2(C_5H_5N)_2$: Styrene (0.250 g, 2.5 mmol) and $CuCl(Bz_2O)_2(C_5H_5N)_2$ (0.038 g, 0.2 mmol) were taken in a 25 ml of round bottomed flask to which 10 ml of dry CH_3CN was added. Then bromamine-T (0.163 g, 0.5 mmol) was added

portionwise at room temperature. The reaction mixture was then refluxed. Reaction was monitored by TLC. After completion of the reaction, the mixture was concentrated on rotovap. The mixture was purified on silica gel column chromatography to give 24 % of pure 1-(4-methylphenylsulfonyl)-2-phenyl azirane.

14. Reaction of bromamine-T with styrene in the presence of η^5-C_5H_5)Ru{$P(C_6H_5)_3$}$_2$Cl : Styrene (0.104 g, 1 mmol), (η^5-C_5H_5)Ru{$P(C_6H_5)_3$}$_2$Cl (0.015 g, 0.02 mmol) and $NaBF_4$ (0100 g, 0.1 mmol) were taken in a 25 ml of round bottomed flask to which 10 ml of dry CH_3CN was added. Then Bromamine-T (0.136 g, 0.5 mmol) was added portionwise at room temperature. The reaction mixture was then refluxed. Reaction was monitored by TLC. After copletion of the reaction, the mixture was concentrated on rotovap. The mixture was purified on silica gel column chromatography to give 6 % of pure 1-(4-methylphenylsulfonyl)-2-phenyl azirane.

15. Reaction of bromamine-T with styrene in the presence of η^5-C_5H_5)Ru{$P(C_6H_5)_3P(OCH_3)_3$}Cl : Styrene (0.104 g, 1 mmol), (η^5-C_5H_5)Ru{$P(C_6H_5)_3$}$_2$Cl (0.015 g, 0.02 mmol) and $NaBF_4$ (0100 g, 0.1 mmol) were taken in a 25 ml of round bottomed flask to which 10 ml of dry CH_3CN was added. Then bromamine-T (0.272 g, 1 mmol) was added portionwise at room temperature. The reaction mixture was then kept for reflux. Reaction was monitored by TLC. After the reaction, the reaction mixture was concentrated on rotovap. The mixture was purified by column chromatography to give 21.5 % of pure 1-(4-methylphenylsulfonyl)-2-phenyl azirane.

16. Reaction of dibromamine-T with styrene in the presence of Cu powder

Styrene (0.104 g, 1 mmol) and Cu (0.063 g, 1 mmol) were taken in a 25 ml of round bottomed flask to which 8 ml of dry CH_3CN was added. Then dibromamine-T (0.397 g, 1 mmol) was dissolved in 2 ml of dry CH_3CN and added dropwise through syringe at room temperature. The reaction mixture was stirred, then kept for reflux. Reaction was monitored by TLC. After completion of the reaction, the mixture was concentrated on rotovap. The mixture was purified on silica gel column chromatography to give 12 % of pure 1-(4-methylphenylsulfonyl)-2-phenyl azirane.

1.2 References

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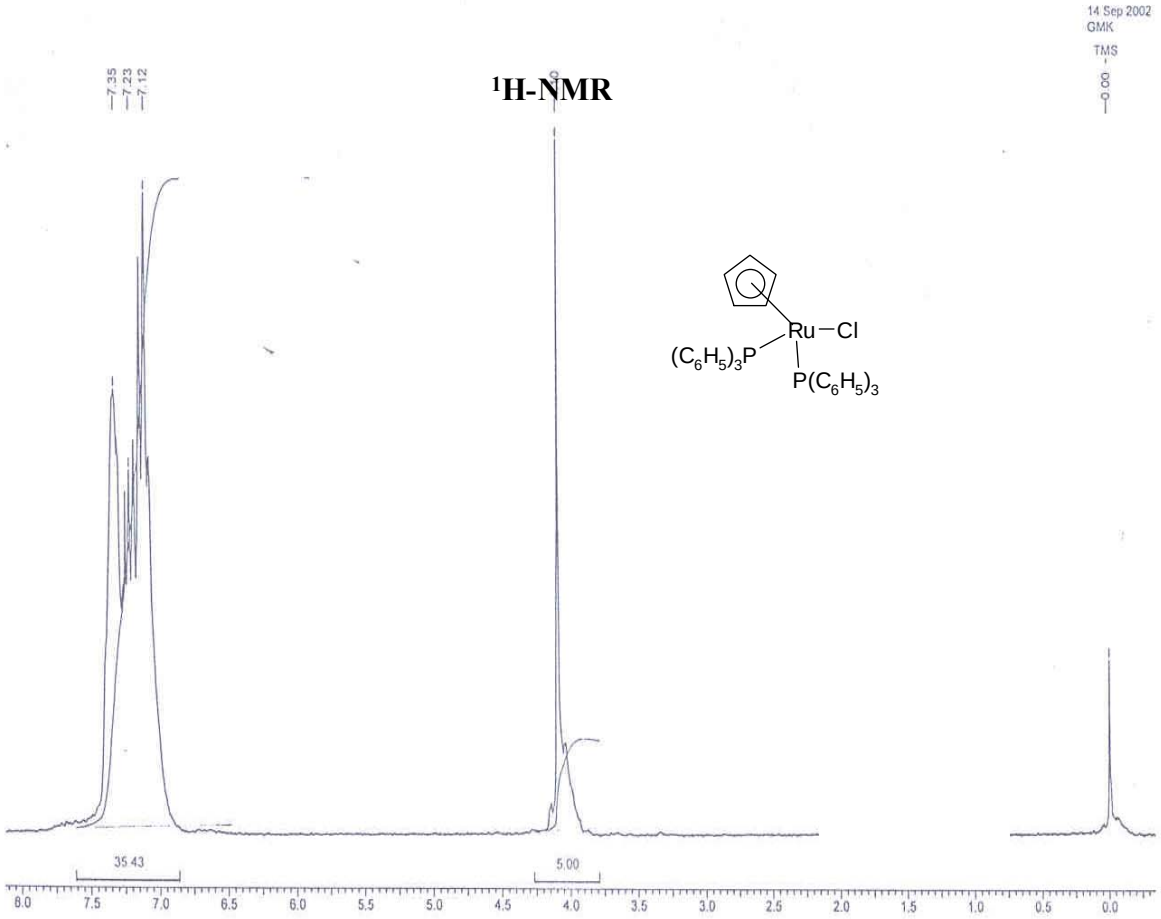
SPECTRA

^{1}H-NMR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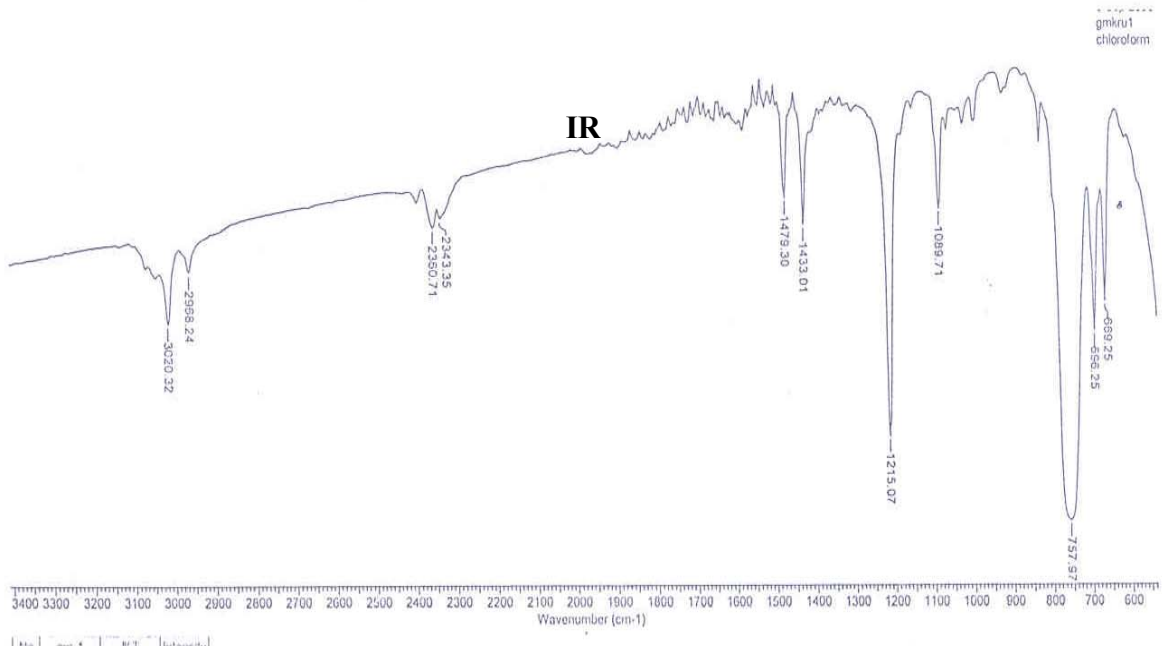
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689.25
Wavenumber (cm-1)

^{1}H-NMR

8 Oct 2002
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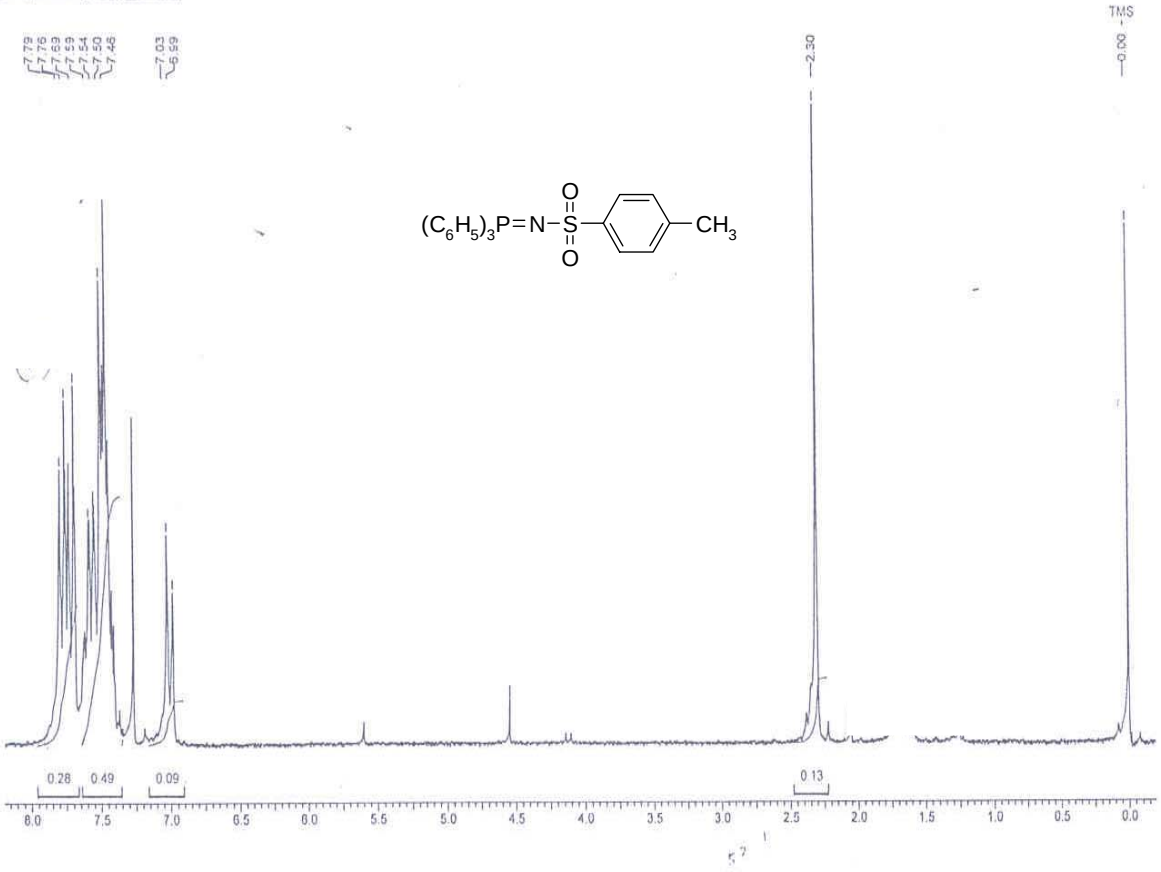

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7 Oct 2002
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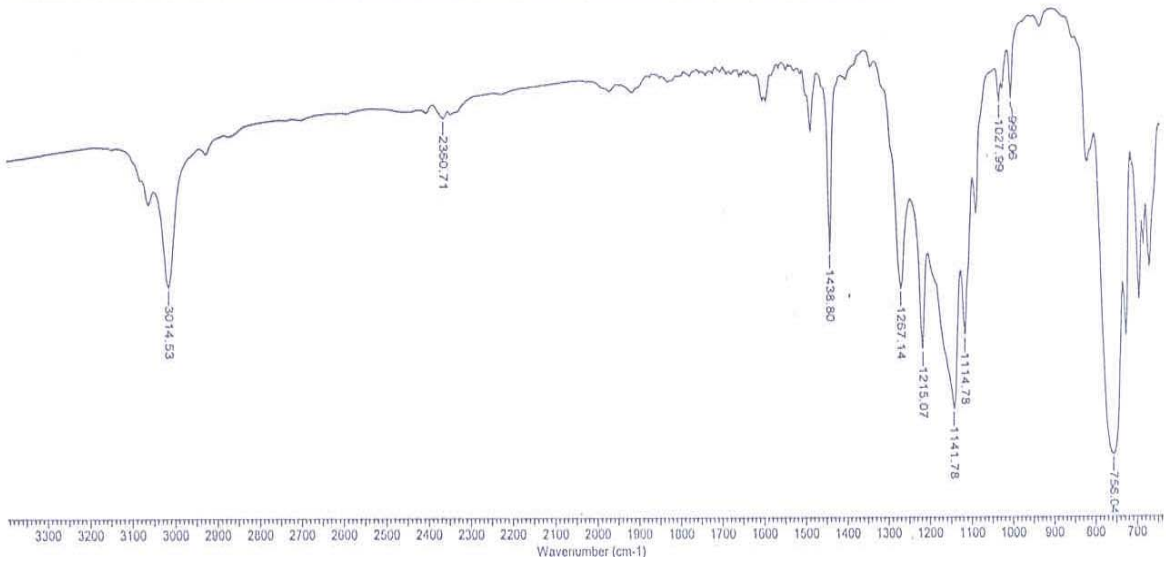

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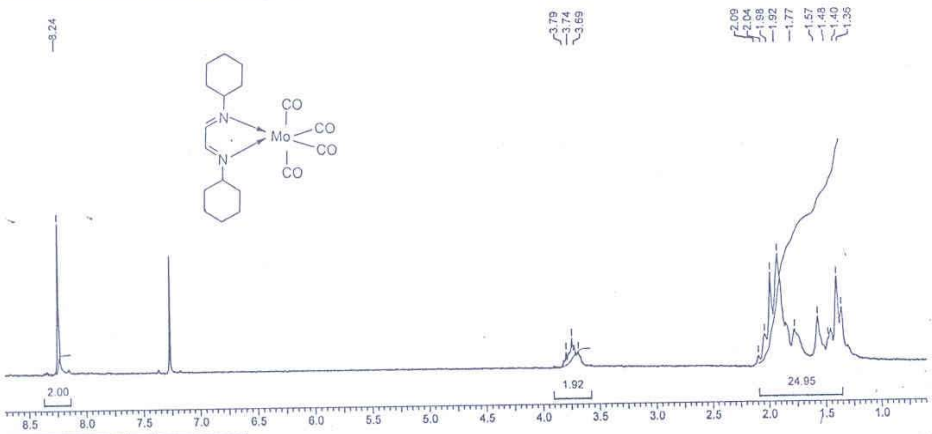

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4	1.48	0.082	11	3.69	0.046
5	1.57	0.150	12	3.74	0.089
6	1.77	0.109	13	3.79	0.044
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IR

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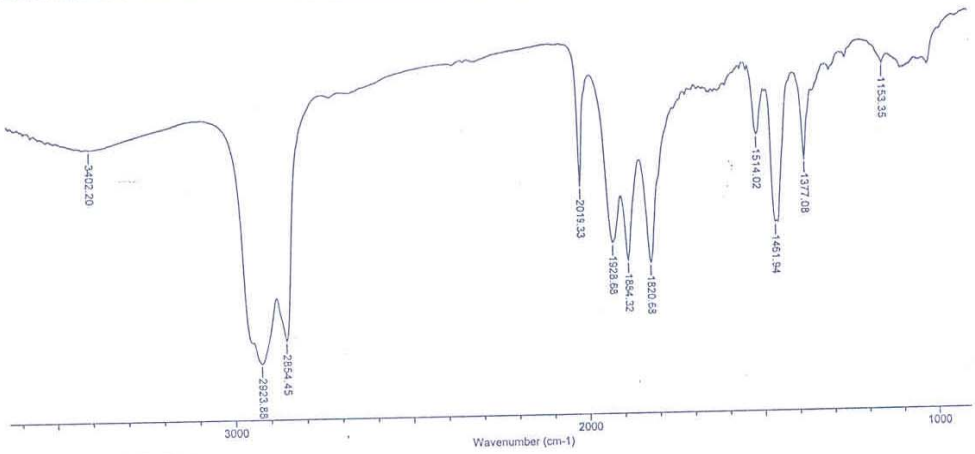

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5	1820.68	0.212	S
6	1884.32	0.217	S
7	1928.68	0.254	S
8	2019.33	0.372	M
9	2854.45	0.062	VS
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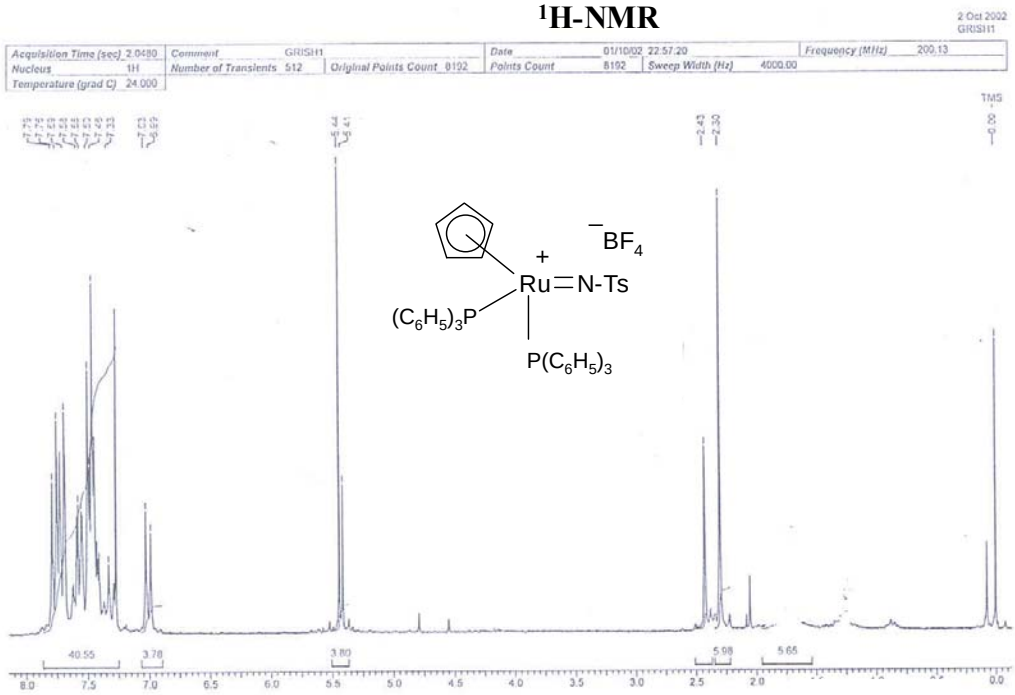
^{1}H-NMR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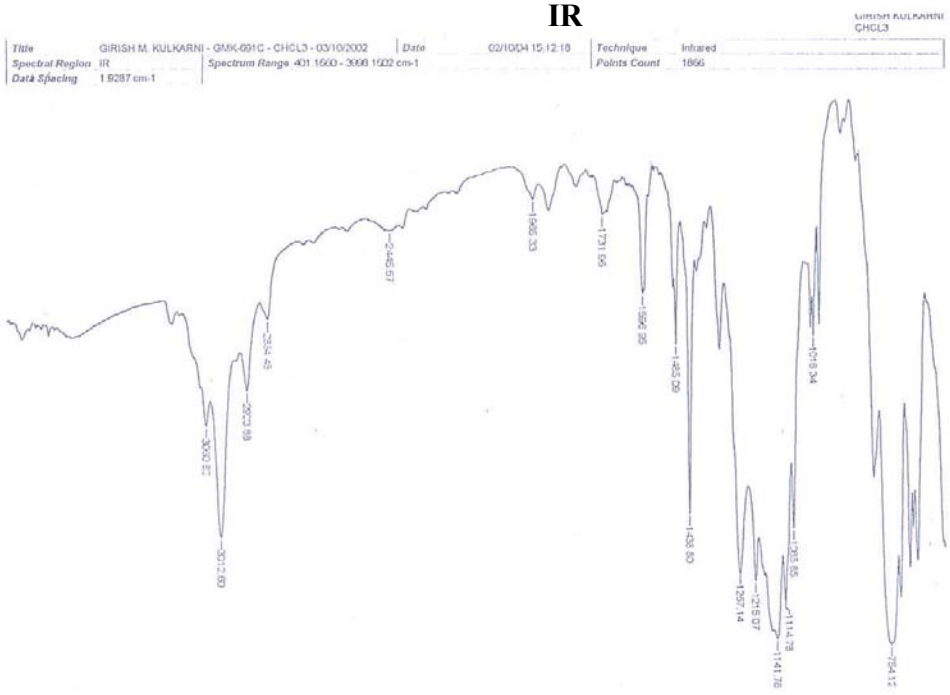
3.80
5.98
5.65

IR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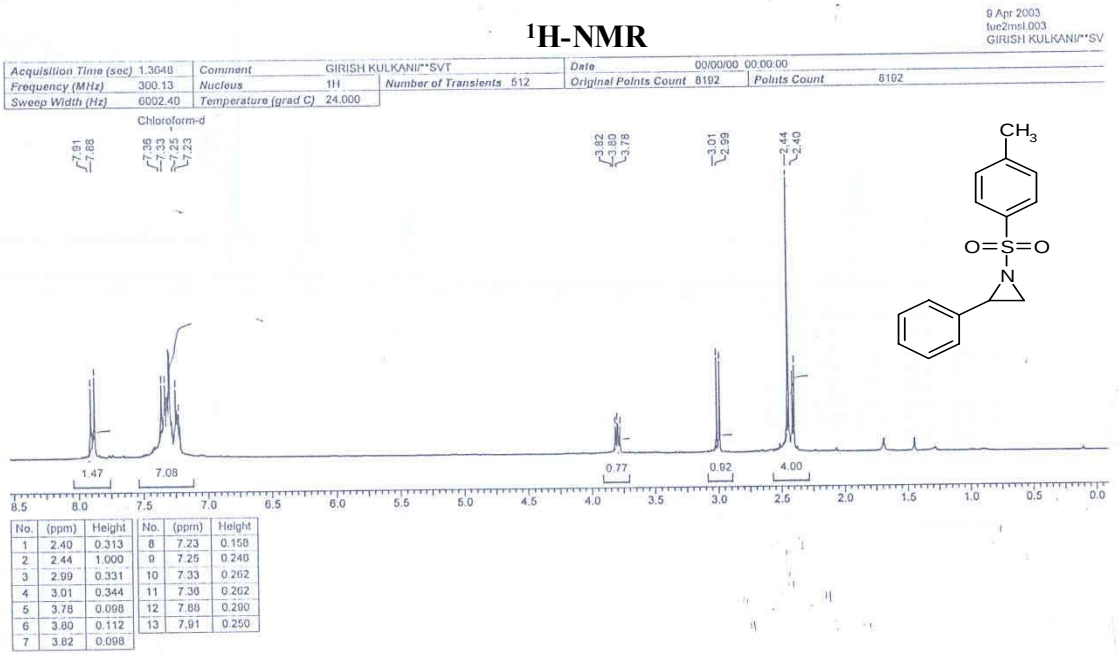
^{1}H-NMR



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4	3.01	0.344	11	7.36	0.262
5	3.78	0.098	12	7.88	0.290
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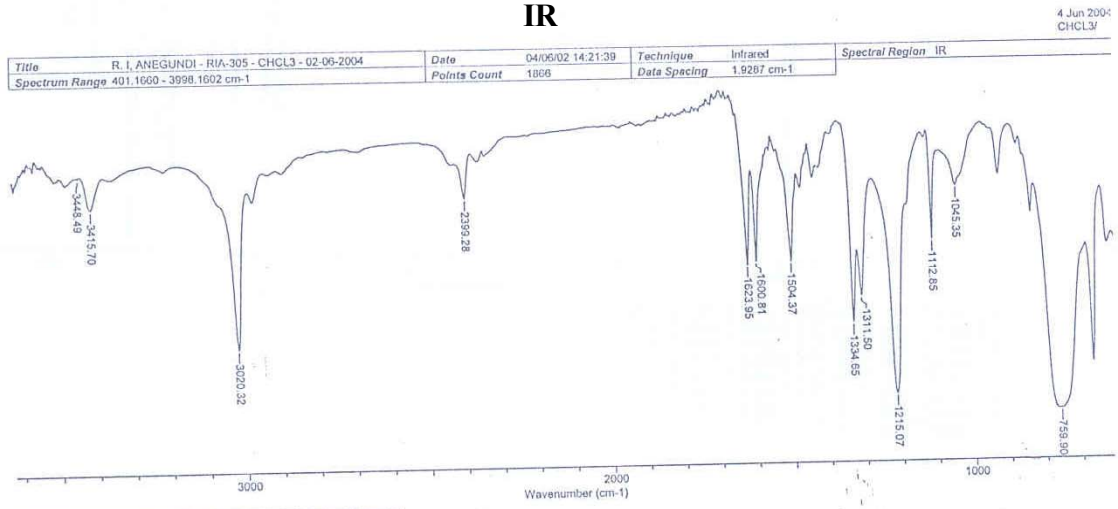
7	3.82	0.098			

A:\GMK-820(.003

IR



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5	1311.50	0.272	S	12	3415.70	0.476	M
6	1334.65	0.218	S	13	3448.49	0.543	W
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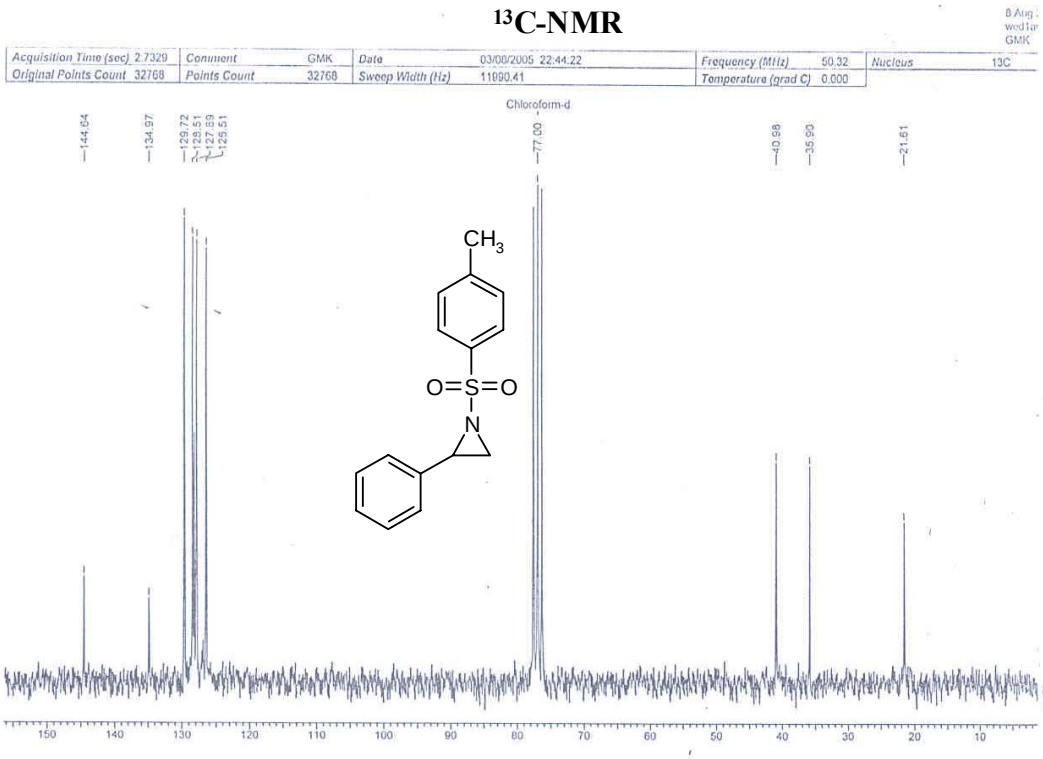

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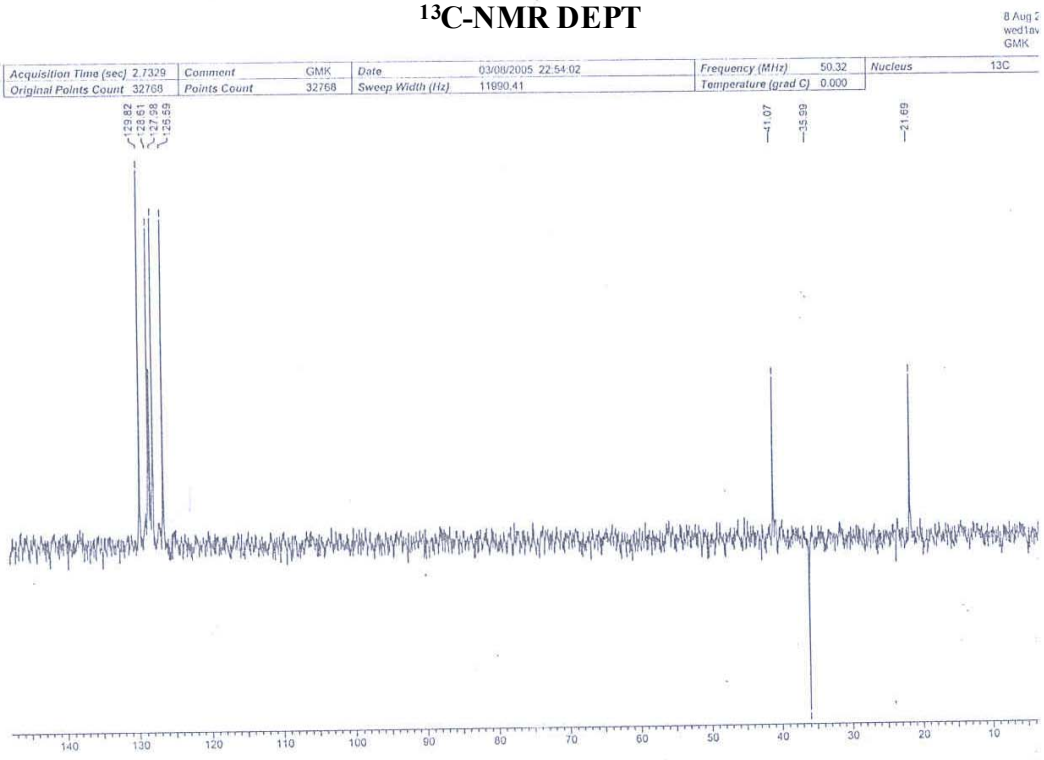

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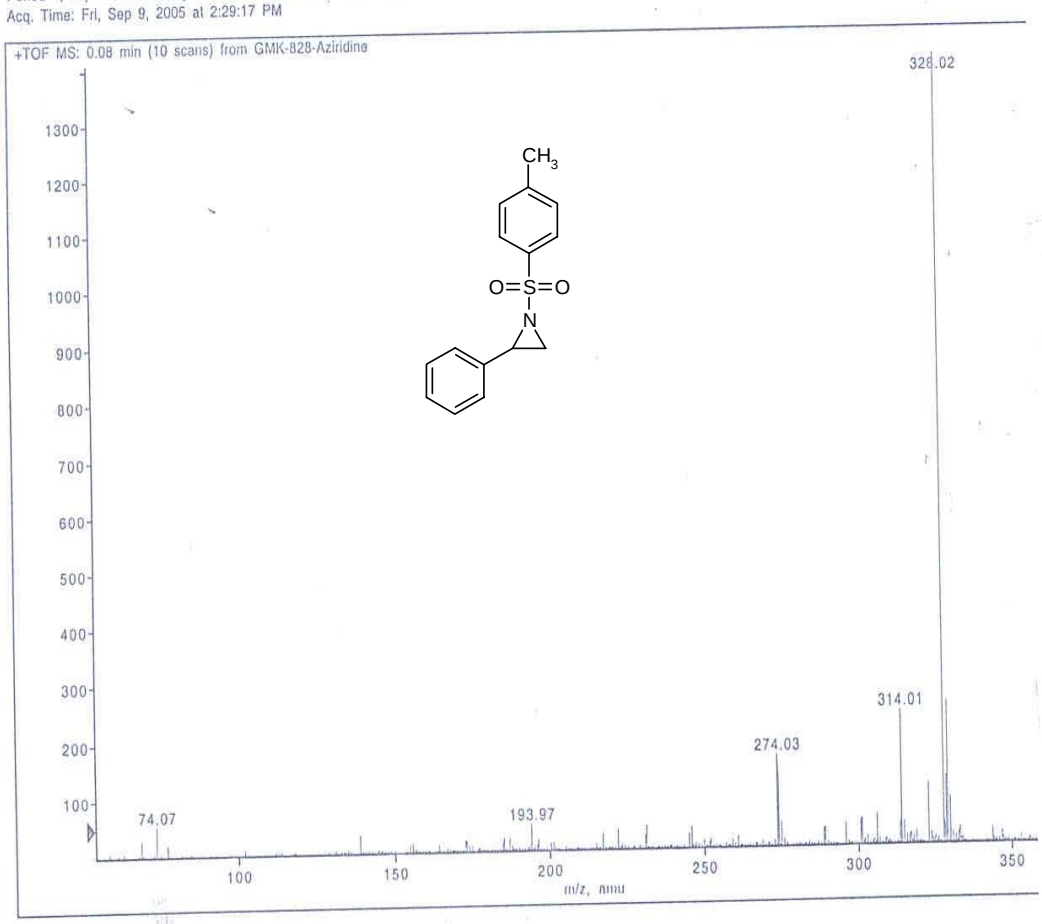


Chapter-2

Section : A Metal carbonyl mediated selective reduction of azides and nitro compounds

2.1.1 Introduction

Since azide ion is an excellent nucleophile it is often the reagent of choice for introducing a nitrogen functional group. The reduction of azido group to a 1° amino group is consequently often an important step in a reaction sequence. A wide range of reduction methods are available including several of which are claimed to permit selective reduction of azido group in the presence of other functional groups. Many of the methods fall into one of the broad categories : 1) Involving the use of hydrogen and metal catalysts. 2) Involving low-valent metals and 3) Involving the use of nucleophiles with attack of the terminal nitrogen of the azide with the formation of triazine.

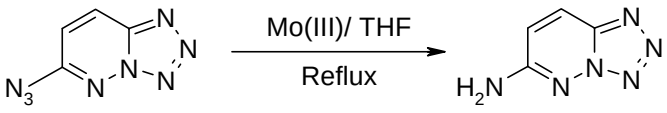
There are large numbers of reagents available in the literature for the conversion of azides and aromatic nitro compounds to amines. Pd/C-$HCOONH_4$, triphenylphosphine in water, boranes, Zn/NH_4Cl, Sm-$AlCl_3$./H_2O, $FeCl_3$/NaI, $FeCl_3$/Zn, LiCl/$NaBH_4$, Sm/TMSCl/H_2O, Fe/NH_4Cl, Zn/$HCOONH_4$, catalytic transfer hydrogenation, catalytic hydrogenation, Fe(porphyrin)/$NaBH_4$, Fe Phthalocyanine/$NaBH_4$, In/HCl, transfer hydrogenation catalyzed by metal oxides in i-C_3H_7OH, FeS-NH_4Cl in methanol-water mixture are some of the recent and traditional methods of selective reductions of azides and nitro compounds.[1] Aryl nitro compounds undergo deoxygenation and reduction in the presence of metal carbonyls. Phenyl azide reacts with $Fe_2(CO)_9$ to form aniline and diphenyl urea in acetonitrile / water mixture.[2] Other examples are Raney Ni, $RhCl_3$/CO, $SnCl_2$,

aq.VCl_2, aq.$TiCl_2$, Mo(III) catalyst generated from Mo(V) Chloride and Zinc. Various metal hydrides like $LiAlH_4$, $NaBH_4$ and $\{(C_6H_5)_3P\}_2CuBH_4$.

Background

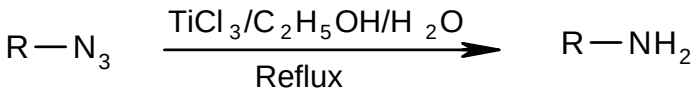
Heterocyclic azido and hydrazido compounds were reduced by a Mo (III) species prepared by the reaction of Molybdenum (V) chloride and Zn dust in THF[3] (Scheme-1).

Scheme-1



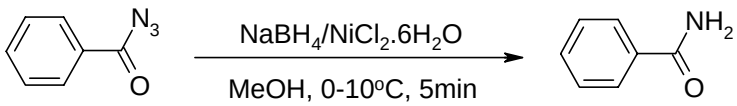
Olah[5] *et al*. described a homogeneous reduction of aryl azides to aryl amines with V(II)chloride but the method was limited to aryl azides. A wide range of heterocyclic azides were reduced by $TiCl_3$ in ethanol/H_2O at reflux temperature (Scheme-2).

Scheme-2



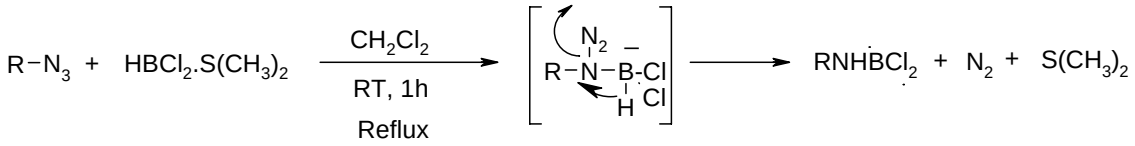
Aroyl azides generally are reduced to the corresponding amides in very high yield and under mild conditions using $NaBH_4$ / $NiCl_2$ system[6] (Scheme-3).

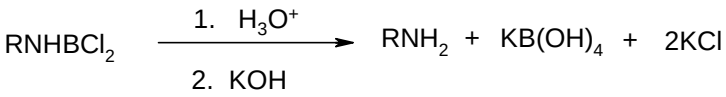
Scheme-3



In 2003, it has been showed that $BHCl_2.S(CH_3)_2$ is a suitable reagent for the reduction of organyl azides in the presence of various other functional groups like esters, halides, nitriles and nitro group[8] (Scheme-4).

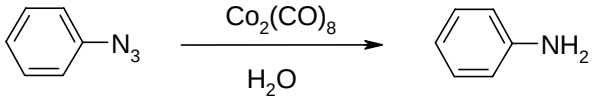
Scheme-4





Azides were readily converted into their corresponding amines using catalytic amount of Co_2CO_8 under mild conditions[10] (Scheme-5).

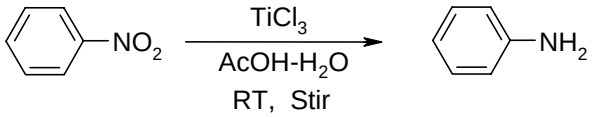
Scheme-5



Reduction of aromatic nitro compounds

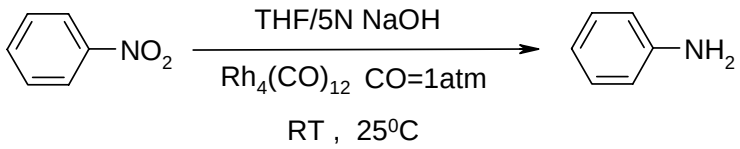
In the year 1980, an improved procedure which avoids prolonged reaction at high temperature and handling under reduced pressure was reported for the reduction of heteroaromatic and nitro compounds with aq. $TiCl_3$[11] (Scheme-6).

Scheme-6



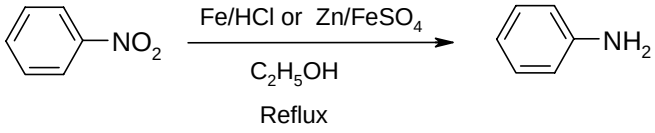
In 1991, Kotohiro Nomura[13] *et al*. have developed selective reduction of aromatic nitro compounds to amines by using catalytic amount of catalytic amount of $Rh_4(CO)_{12}$/Chelate posphine ligand (dppe, dppm etc) under the atmosphere of carbon monoxide (Scheme-7).

Scheme-7



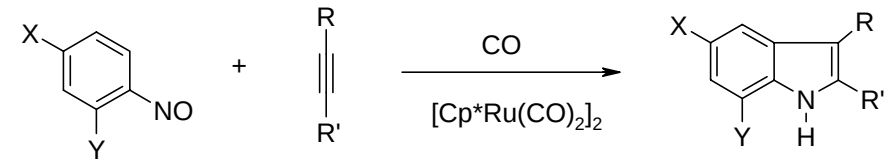
In the year 2005, aromatic nitro compounds with variety of functional groups are reduced to amines using activated iron generated from Fe/HCl or Zn/$FeSO_4$ [14] (Scheme-8).

Scheme-8



In the year 2002, Kenneth M. Nicholas[15] *et al*. have reported regioselective synthesis of indoles from the $[Cp^*Ru(CO)_2]_2$ catalyzed reaction of nitrosoaromatics (ArNO) with alkynes under carbon monoxide (Scheme-9).

Scheme-9



X = H, Br, Cl R = C_6H_5, $CO_2C_2H_5$

Y = H, CH_3 R' = H, $CO_2C_2H_5$

Objective

Our aim was to prepare metal nitrene complexes using simple nitrene precursors, Ts-N_3, aryl nitro compounds and bromamine-T by treating with metal

carbonyls. There were good numbers of literature methods[15] for the preparation of transition metal nitrene complexes by the reactions of azides and isocyanates in the presence of various metal complexes. We aimed to prepare different nitrene complexes with metal carbonyls, but instead we observed the selective reduction of azides and nitro compounds with very good yields. So we have intended to study the reduction of azides and nitro compounds in the presence of various functional groups in a fuller length.

2.1.2 Present Work

Reactions of aryl azides and aryl nitro compounds were carried out in the presence of metal carbonyls in refluxing ethanol. Aryl azides and aryl nitro compounds having different functional groups were used for the reduction in the presence of different metal carbonyls.

Scheme-1

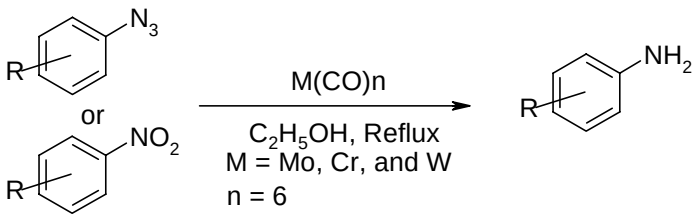


Table - 1 Reduction of azides to amines

Sl. No.	Azides	Amines	Time, h	Yield %
1.	$C_6H_5.N_3$	$C_6H_5.NH_2$	2.5	59
2.	4-$CH_3O.C_6H_4.N_3$	4-$CH_3O.C_6H_4.NH_2$	3	84
3.	4-$Cl.C_6H_4.N_3$	4-$Cl.C_6H_4.NH_2$	2	88

4.	$4\text{-}NO_2.C_6H_4.N_3$	$4\text{-}NO_2.C_6H_4.NH_2$	6.5	74
5.	$2\text{-}COOH.C_6H_4.N_3$	$2\text{-}COOH.C_6H_4.NH_2$	6.5	96
6.	$1\text{-}C_{10}H_7.N_3$	$1\text{-}C_{10}H_7.NH_2$	24	90
7.	$C_6H_5.CH_2.N_3$	$C_6H_5.CH_2.NH_2$	1.5	56
8.	$C_6H_5.CON_3$	$C_6H_5.CONH_2$	6	43
9.	$4\text{-}CH_3.C_6H_4.SO_2N_3$	$4\text{-}CH_3.C_6H_4.SO_2NH_2$	24	80
10.	$C_6H_5.CH=CH.CH_2.N_3$	$C_6H_5.CH=CH.CH_2.NH_2$	24	NR
11.	$C_6H_{11}.N_3$	$C_6H_{11}.NH_2$	24	86
12.	$2\text{-}NO_2.C_6H_4.N_3$	$2\text{-}NO_2.C_6H_4.NH_2$	6	45
13.	$4\text{-}CH_3O.C_6H_4.N_3$	$4\text{-}CH_3O.C_6H_4.NH_2$	4	12[b]
14.	$4\text{-}CH_3O.C_6H_4.N_3$	$4\text{-}CH_3O.C_6H_4.NH_2$	24	11[c]
15.	$4\text{-}CH_3O.C_6H_4.N_3$	$4\text{-}CH_3O.C_6H_4.NH_2$	24	14[d]

Reaction conditions : ArN_3 (1mmol) + $Mo(CO)_6$ (1mmol), Ethanol (10ml) reflux

[b]$Fe(CO)_5$; [c]$W(CO)_6$; [d]$Cr(CO)_6$.

Table-2 : Reduction of aromatic nitro compounds

Sl No.	Nitro Compound	Amine	Time, h	Yield %
1.	$4\text{-}CH_3.C_6H_5.NO_2$	$4\text{-}CH_3.C_6H_5.NH_2$	24	54
2.	$4\text{-}Cl.C_6H_5.NO_2$	$4\text{-}Cl.C_6H_5.NH_2$	24	83
3.	$4\text{-}NO_2.C_6H_4.CH=CH.C_6H_4$	$4\text{-}NH_2.C_6H_4.CH=CH.C_6H_4$	24	84
4.	$2\text{-}NO_2.C_6H_4.CH=CH.COOC_2H_5$	$2\text{-}NH_2.C_6H_4.CH=CH.COOC_2H_5$	24	17.5
5.	$2\text{-}I.C_6H_4.NO_2$	$2\text{-}I.C_6H_4.NH_2$	24	96

Reaction Conditions: $ArNO_2$ (1mmol): $Mo(CO)_6$ (1mmol), Ethanol (10ml), reflux

Results and Discussion

Refluxing solutions of the azides and nitro compounds in the presence of stoichiometric quantity of $Mo(CO)_6$ (1eq.) in ethanol, produces the amines in high yields (80-95%). The azides could be selectively reduced in the presence of Cl, COOH, and NO_2. Cinnamyl azide could not be reduced under these conditions. Benzoyl azide and 4-toluenesulphonyl azide gave good yields of the reduced amide. The reductions were complete in 1.5-24 h, with longer reaction times for the TsN_3,

cyclohexyl and 1-napthyl azide. Reductions of 4-methoxy-phenyl azide in the presence of $Fe(CO)_5$, $W(CO)_6$ and $Cr(CO)_6$ gave low yields of 4-anisidine. Aryl nitro compounds could be reduced in the presence of stoichiometric $Mo(CO)_6$, in refluxing ethanol. Aromatic nitro compounds with chloro and iodo substitution gave good yields of the amino compound (83% and 96%). 4-Nitro stilbene gave selectively 4-amino stilbene in 84% yield, while 4-nitro ethyl cinnamate gave low yield (17.5%) of the reduced product.

The $Mo(CO)_6$ reduction of the aryl azides and nitro compounds probably proceeds through the formation of metal nitrenes. The formation of metal nitrene complex in the reaction of cyclopentadienyl Mo dicarbonyl dimer with aryl nitro compounds, iron carbonyl reaction with azides and nitro compounds to form iron nitrenes and $W(CO)_5$.THF reaction with bulky azides. These could be very good evidence for formation of metal nitrene complex in our reactions. The oxygen of nitro group combines with metal carbonyl to form CO_2 with formation of metal nitrene, which gets protonolyzed to form the amine. Azide similarly forms metal nitrene by the loss of nitrogen followed by protonolysis. Photochemical reduction by irradiating with an Hg coated lamp gave low yields of the reduction product from both tosylazide and 4-nitrotoluene.

We also attempted for partial reduction of nitro compounds to nitroso compounds with $Mo(CO)_4[P(C_6H_5)]_3$ catalyst, but couldn't get the product the starting material recovered back.

Conclusion

Thus aromatic azides and nitro compounds are selectively and efficiently reduced to corresponding amines using stoichiometric amount of metal carbonyls, especially $Mo(CO)_6$, under neutral conditions. The method is cleaner and good for

selective reduction of aromatic azides and nitro compounds compare to other available reagents and reactions.

2.1.3 Experimental

Preparation of aryl azides

In general, all aryl azides are prepared by diazotization of corresponding aryl amines and the treatment with 1.1 equivalents of NaN_3. Then extraction with ethyl acetate and purification on column chromatography gave the product.

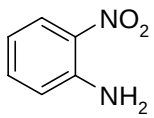
General procedure for reduction of azides and nitro compounds

To a 25 ml RBF 1 mmol of azide or nitro compound is taken in 10 ml of ethanol. To this 1 mmol of $Mo(CO)_6$ was added and kept for reflux. Reaction was monitored by TLC. After completion of the reaction, ethanol was evaporated on a rotary evaporator and crude mixture was purified on silica gel (60-120 mesh) column.

1. Reduction of 2-nitro phenyl azide using $Mo(CO)_6$

To a 25 ml of RBF 2-nitro phenyl azide (164 g, 1 mmol) and $Mo(CO)_6$ (0.132 g, 0.5 mmol) were added along with 10 ml of ethyl alcohol. The reaction refluxed for the completion (6h). The reaction mixture was purified on silica gel chromatography to get 0.062 g (45%) of 2-nitro aniline.

2-Nitroaniline



M.P. : 73^0 C

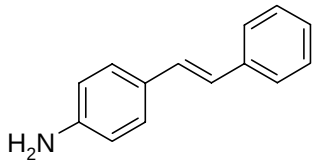
IR ($CHCl_3$ cm^{-1}) : 3515, 3396, 3020, 2399, 2358, 1623, 1573, 1510, 1438, 1344, 1259, 1215, 1105, 757.

^{1}H NMR (δ, $CDCl_3$, 200 MHz) : 4.0 (s, -NH_2, 2H); 6.75 (m, Ar-H 1H); 6.91 (m, Ar-H, 1H); 7.36 (m, Ar-H); 7.56 (m, Ar-H, 1H).

2. Reduction of 4-nitro stilbene using $Mo(CO)_6$

In a 25 ml RBF 4-nitro stilbene (0.193 g, 1 mmol) and $Mo(CO)_6$ (0.201 g, 1 mmol) were taken with 10 ml of ethanol. The mixture was refluxed for completion (24h). The reaction was purified on silica gel chromatoghraphy to get 0.163 g of 4-amino stilbene.

4-(2-Phenyl ethenyl) benzenamine



M.P. : 151^0 C

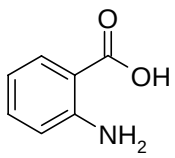
IR ($CHCl_3$ cm^{-1}) : 3446, 3363, 3020, 1618, 1595, 1342, 1217, 1178, 964.

^{1}H NMR (δ, $CDCl_3$, 200 MHz) : 5.52 (s, Ar-N<u>H</u>$_2$); 6.92 (d, Ar-CH=C<u>H</u>-Ar'12Hz 1H); 7.51 (d, Ar-CH=C<u>H</u>-Ar')

3. Reduction of 2-azido benzoic acid using $Mo(CO)_6$

In a 25 ml RBF 2-azido benzoic acid (0.193 g, 1 mmol) and $Mo(CO)_6$ (0.201 g, 1 mmol) were taken with 10 ml of ethanol. The mixture was refluxed for completion (24h). The reaction was purified on silica gel chromatoghraphy to get 0.109 g of 2-amino benzoic acid.

2-Amino benzoic acid



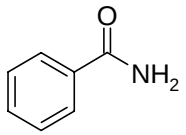
M.P. : 148 ^{0}C

IR ($CHCl_3$ cm^{-1}) : 3510, 3364, 3018, 2360, 1676, 1616, 1589, 1217, 1161, 1045, 757.

^{1}H NMR (δ, $CDCl_3$, 200 MHz) : 4.0 (s, Ar-N$\underline{H_2}$); 6.67 (m, Ar-H, 1H); 6.83 (m, Ar-H 1H); 7.35 (m, Ar-H, 1H); 7.88 (m, Ar-H, 1H); 11.0 (s, -OH, 1H).

4. Reduction of benzoyl azide using $Mo(CO)_6$

In a 25 ml RBF benzoyl azide (0.142 g, 1 mmol) and $Mo(CO)_6$ (0.201 g, 1 mmol) were taken with 10 ml of ethanol. The mixture was refluxed for completion (24 h). The reaction was purified on silica gel chromatography to get 0.054 g of benzamide.



M.P. : 128 ^{0}C

IR ($CHCl_3$ cm^{-1}) : 3446, 3363, 3020, 1618, 1595, 1342, 1217, 1178, 964.

^{1}H NMR (δ, $CDCl_3$, 200 MHz) : 6.0 (s, -NH_2, 2H); 7.44 (d, Ar-H 2H); 7.51(m, Ar-H, 1H); 7.95 (d, Ar-H, 2H)

Route to β-lactams through nitrenes- Reactions of nitrene precursors with metal carbonyls

2.2.1 Introduction

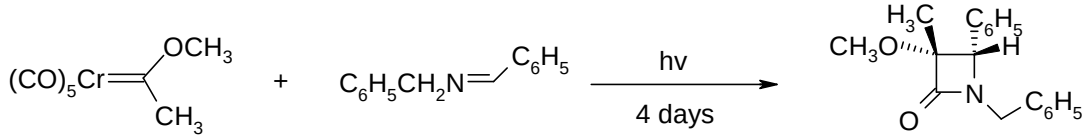
The four membered cyclic amide derivatives of 3-amino propionic acids known as

β-lactams, are first synthesized by Staudinger in 1907.[15] The recognition of the β-lactam moiety as the key pharmacophoric component of the penam antibiotics initiated a flurry of synthetic activity. Intensive research has generated numerous methods of synthesizing the β-lactam skeleton. Commonly, the lactam ring is formed through either ketene-imine cyclizations (Staudinger reaction) or ester enolate-imine condensations (Gilman-Speeter reaction).[16] However other notable methods are sometimes employed, including photo induced rearrangements, and radical cyclizations.

There are numerous methods of transition metal catalyzed synthesis of β-lactam in the literature.

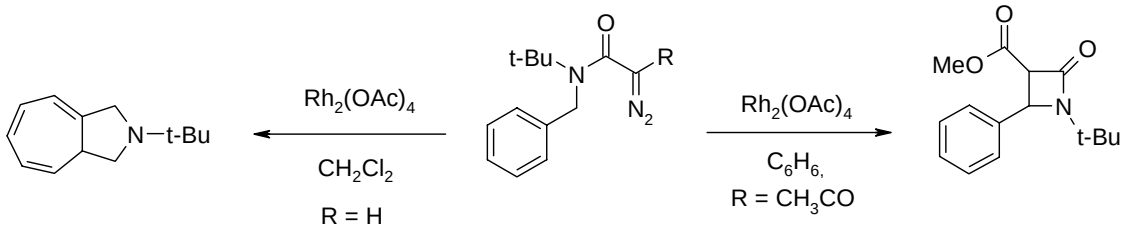
In the year 1985 Louis S. Hegedus[17] *et al*. have synthesized a variety of substituted β-lactams including a cepham analog by photochemical reaction of [(methoxy) (methyl) carbene] chromium complexes with substituted imines. Oxazines were converted to bicyclic β-lactams by the photolytic reaction of molybdenum carbene complexes (scheme-1).

Scheme-1



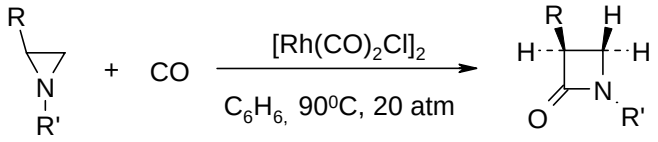
In the year 1988, Micheal P Doyle[18] have shown synthesis of β-lactam via an intramolecular β-C-H insertion by rhodium (II) carboxylate catalyzed decomposition of diazoacetamides (Scheme-2).

Scheme-2



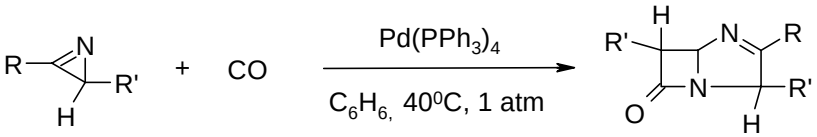
In the year 1989 β-lactams are synthesized in high optical purity from recemic aziridines using chloro (1, 5-cyclooctadiene) rhodium (I) as catalyst and d or l-menthol as chiral agent[19] (Scheme-3).

Scheme-3



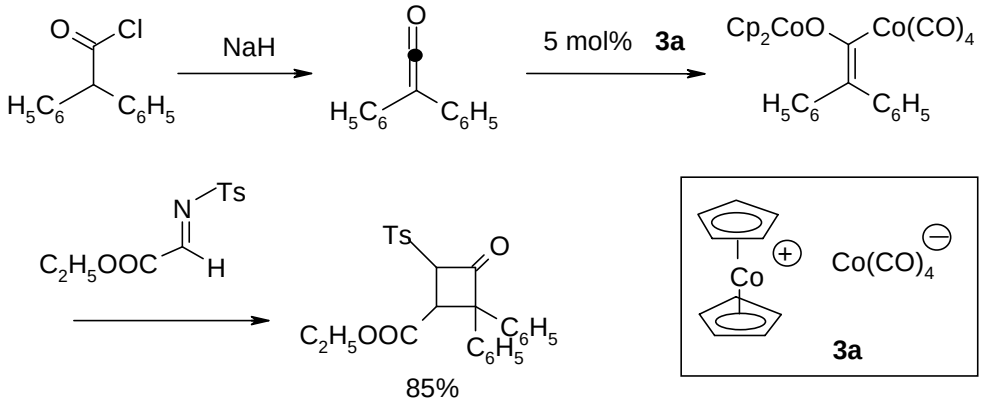
In the year 1981 Howard Alper[20] have shown the synthesis of β-lactams via remarkable Pd (0)-catalyzed carbonylation of azirines (Scheme-4).

Scheme-4



In 2004, France[21] *et al*. have reported cobalt carbonyl catalyzed bifunctional β-lactam formation (Scheme-5).

Scheme-5



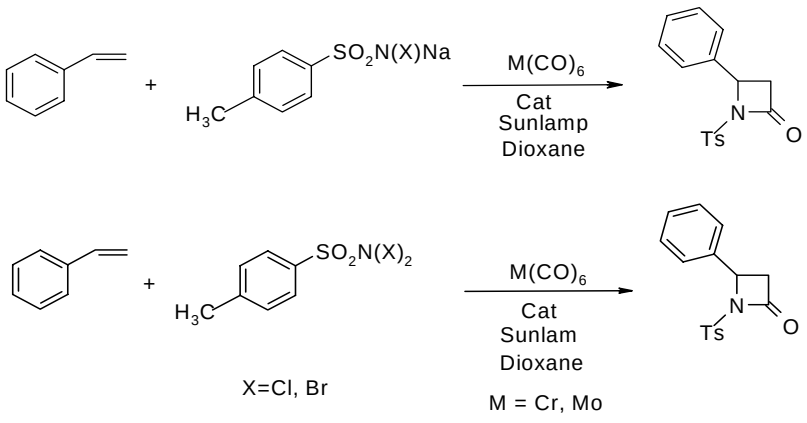
Objective

Our aim was to design other new route for the synthesis of β-lactams via carbonyl insertion in the reaction of nitrene precursors with olefin. Thus dichloramine-T, chloramine-T and bromamine-T were reacted with olefins in the presence of metal carbonyls for e.g. $Cr(CO)_6$, $Mo(CO)_6$ etc. under thermal and photolytic conditions (Scheme-1).

2.2.2.1 Present work

Reactions of bromamine-T, chloramines-T and tosyl azide were carried out with styrene in the presence of $Cr(CO)_6$ under thermal and photolytic conditions.

Scheme-1



Results and Discussion

The reaction between nitrene precursors and the olefin in the presence of metal carbonyls were carried out under thermal and photolytic conditions. The β-lactam formation was expected by in situ carbonyl insertion into aziridine ring. p-Toluene phenyl iodinane, chloramine-T, bromamine-T, dibromamine-T, dichloramine-T and tosyl azides were used as nitrene precursors. Olefins used are styrene, methyl cinnamate, 4-methoxy stilbene, stilbene and $Cr(CO)_6$ was used as CO source. The reactions were carried out in dioxane or acetonitrile as solvent. In the reaction of p-Toluene phenyl iodinane with stilbene in dioxane, while adding $Cr(CO)_6$ initially effervescence observed, but no product formation was there. In most of the reactions the starting material remained unchanged, and p-toluene sulfonamide was obtained as product.

In the case of dihaloamides, moderate yields of amino halogenated compounds are obtained along with starting material and p-toluene sulfonamide. Reactions also tried with additives like DMSO and NMO, which promotes CO cleavage. But there was no reaction observed with these conditions.

Reactions of $Cr(CO)_6$ with nitrene precursors, PhI=NTs, bromamine-T, chloramine-T, DCT and DBT with different olefins like, styrene, methylcinnamate and with additives like, Cu metal powder, TBAB and $CuCl_2$ both under thermal and photolytic conditions were tried. The ^{1}H-NMR and IR spectra were complex and shows the presence of β-lactam product but was not clear.

2.2.3 Experimental

1. Photo-reaction of dichloramine-T with styrene in the presence of $Cr(CO)_6$

In a 25 ml RBF styrene (0.052 g, 0.5 mmol) and $Cr(CO)_6$ (0.11 g, 0.5 mmol) were taken in 10 ml of dry acetonitrile. DCT (0.12 g, 0.5 mmol) was added

portionwise and the solution was stirred under Hg coated sunlamp under argon. Reaction was monitored by TLC. After the completion of reaction, mixture was concentrated on rotovap. The mixture was purified on silica gel chromatography. The ^{1}H-NMR was complex.

^{1}H NMR (δ, $CDCl_3$, 200 MHz) : 7.72 (d, 2H, Ar-H); 7..30 (m, Ar-H 7H); 6.97 (d, Ar-H, 1H); 5..90(d, 1H); 5.07 (q, 1H); 3.68 (m, 4H) 3.22 (t, 2H); 2.41 (s, 3H tosyl-C$\underline{H}_3$)

2. Photo-reaction of Ts-N_3 with styrene in the presence of $Cr(CO)_6$

In a 25 ml RBF Styrene (0.052 g, 0.5 mmol) and $Cr(CO)_6$ (0.11 g, 0.5 mmol) were taken in 10 ml of dry acetonitrile. Ts-N_3 (0.12 g, 0.5 mmol) was added dropwise and the solution was stirred under Hg coated sunlamp under argon. Reaction was monitored by TLC. After the completion of reaction, mixture was concentrated on rotovap. The mixture was purified on silica gel chromatography. The ^{1}H-NMR was complex.

^{1}H NMR (δ, $CDCl_3$, 200 MHz) : 7.84(d, 2H, Ar-H); 7..30 (m, Ar-H 7H); 6.97 (d, Ar-H, 1H); 4.79 (s, 1H); 2.41 (s, 3H tosyl-C$\underline{H}_3$)

3. Photo - reaction of chloramine-T with styrene in the presence of $Cr(CO)_6$

In a 25 ml RBF Styrene (0.052 g, 0.5 mmol) and $Cr(CO)_6$ (0.11 g, 0.5 mmol) were taken in 10 ml of dry acetonitrile. Chloramine-T (0.136 g, 0.5 mmol) was added portionwise and the solution was stirred under Hg coated sunlamp under argon. Reaction was monitored by TLC. After the reaction, mixture was concentrated on rotovap. The mixture was purified on silica gel chromatography.

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Section B : DBT and DCT as nitrene precursors and their reaction with olefins and hydrocarbons

2.3.1 Introduction

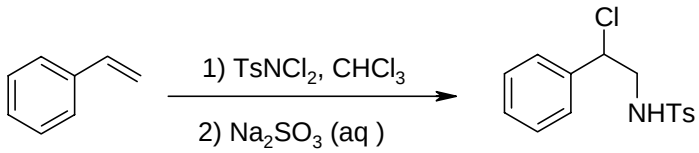
The functionalization of olefins by the addition of two different functional groups in a single step provides access to wide range of functional group manipulation in organic synthesis. Variety of reactions such as aminohalogenation, halo hydration, haloazidation and azidohydroxylation are some of the examples of this kind of synthetic transformation. The ionic addition of N-halo sulfonamides and Cu catalyzed radical addition of N, N-dichloro-4-toluenesulphonamide and N, N-dichlorourethane to olefins and hydrocarbons to give amino halogenation and amination products has been described by Kharasch and others.[1] DCT and N, N-dichlorourethane react with cyclic ethers in the presence of Cu catalysts to form amination products.[2] These reactions are known to proceed by radical or nitrenoid and nitrene intermediates. $Mo(CO)_6$ and $W(CO)_6$ reacts with N, N-dichlorophenylsulphonamide to form nitrene complexes.[3] Azides and chloramine–T react with olefins to form aziridines in the presence of Cu catalysts via nitrene and nitrenoid intermediates.[4, 5] Cu and Pd (II) complexes catalyze the regiospecific and stereoselective addition of DCT to ethyl cinnamate forming halo amines.[6]

C-H insertion reactions of nitrenes are well known in the literature. Nitrenes reacts with hydrocarbons and forms C-H inserted products i.e. amines.

Background

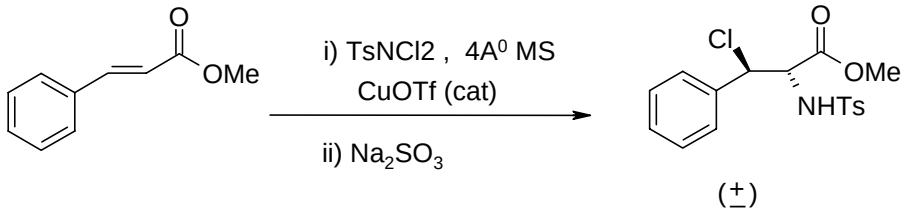
In the year 1968 R. W. Turner et al[7] have described the reactions of N, N-dichloro-p-toluenesulphonamide with styrene, trans stilbene, and indene. A free-radical mechanism was proposed which contrasts with the apparent addition of N, N-dichlorosulphonamides to olefins (Scheme-1).

Scheme-1



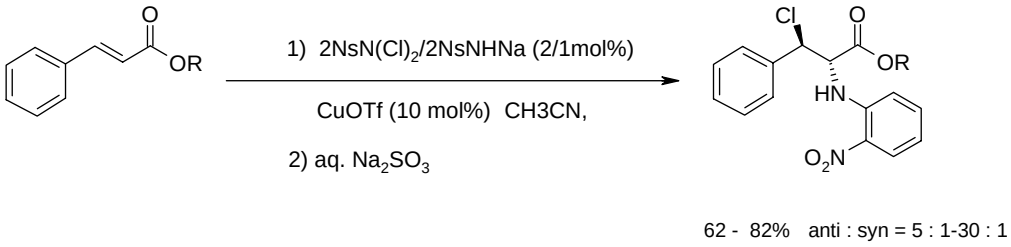
In the year 1999, a new aminohalogenation process has been developed for the synthesis of vicinal haloamine derivatives using cinnamic esters as substrates. The reaction was performed in CH_3CN using $ZnCl_2$ or $Cu(OTf)_2$ as catalyst and N, N-dichloro-*p*-toluenesulfonamide as chlorine/nitrogen source[8] (Scheme-2).

Scheme-2



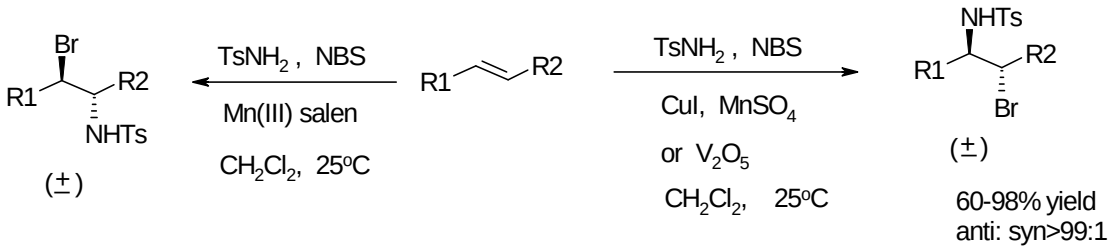
In the year 2000, new regio and stereo selective aminohalogenation of cinnamic esters has been developed using the combination of 2-$NsNCl_2$/2-NsNHNa as the nitrogen and chlorine sources and copper (I) triflate as the catalyst[9] (Scheme-3).

Scheme-3



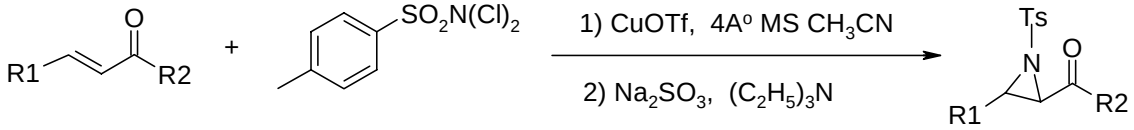
In 2003, a new synthetic procedure for aminohalogenation of olefins has been developed for the preparation of vicinal haloamine derivatives in high yields by using Cu, Mn, or V catalysts with *p*-toluenesulfonamide ($TsNH_2$) and *N*-bromosuccinimide (NBS) as nitrogen and bromine sources[10] (Scheme-4).

Scheme-4



Recently in 2005, an efficient and practical synthesis of N-*p*-tosyl-aziridine-2-ketones and carboxylates through the use of α, β-unsaturated esters and ketones has been reported. Triethylamine was found to be an effective base for the in situ cyclization for most substrates[11] (Scheme-5).

Scheme-5



2.3.2 Present Work

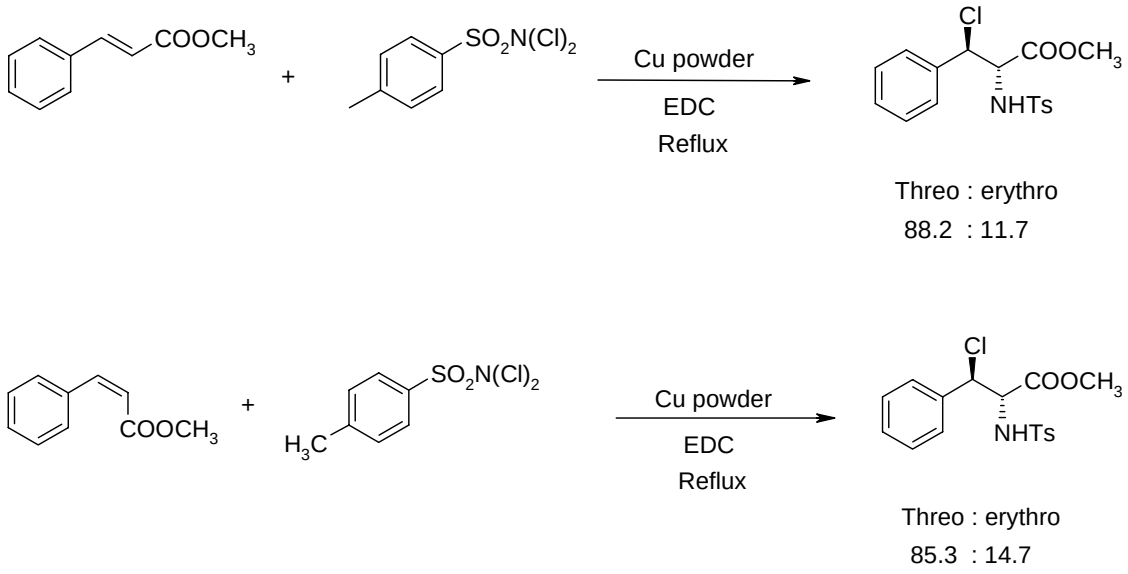
DBT and DCT react with olefins and hydrocarbons in the presence of Cu, Zn, Mg and Al powders to give amino halogenations and amination products in high yields. The reactions are regiospecific, forming products with anti-Markownikoff orientation. E- and Z- Methyl cinnamate and stilbene react stereoselectivitely to give

mixtures of erythro (major) : threo and threo (major) : erythro isomers respectively. The stereoselctivity is increased in the presence of Cu catalyst (72.4: 27.5) for the uncatalyzed reaction to (88.2:11.7) and chloride DCT/DBT.

Reaction of DBT/DCT with Olefins

Reactions of α, β-unsaturaed olefins with DCT and DBT were carried out in the presence of metal powders (Scheme-1).

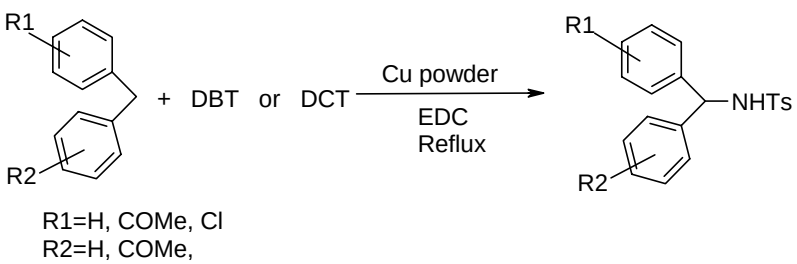
Scheme-1



Benzylic amination of hydrocarbons using DBT/DCT

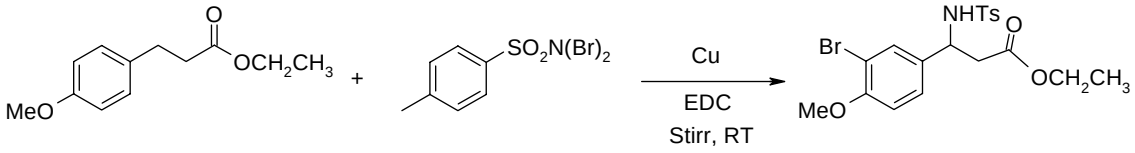
Reactions of aromatic hydrocarbons with DBT and DCT were carried out in the presence of metal powders (Scheme-2).

Scheme-2



Aromatic bromination and benzylic amination by dibromamine-T-A new reaction Reaction of DBT with 3-phenyl propanoic ester gave both benzylic amination and aromatic halogenations in one step at room temperature in the presence of Cu powder (Scheme-3).

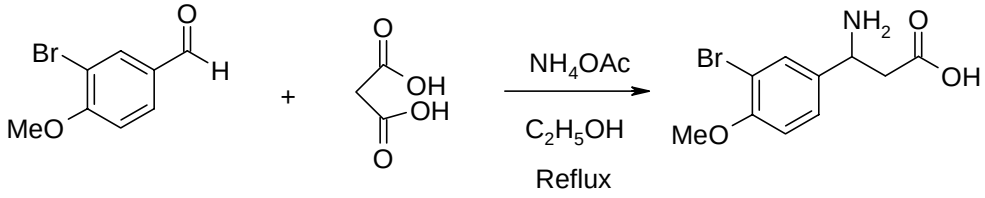
Scheme-3



Preparation of β–amino acid

β–amino acid was prepared by the reaction of bromoanisaldehyde with malonic acid in the presence of ammonium acetate in ethanol at refluxing condition (Scheme-4).

Scheme-4



Esterification and tosylation of β–amino acid-Synthesis of final product

The final product was prepared by esterification of β–amino acid with $SOCl_2$ and ethanol followed by tosylation using tosyl chloride, triethylamine in dry DCM (Scheme-5).

Scheme-5

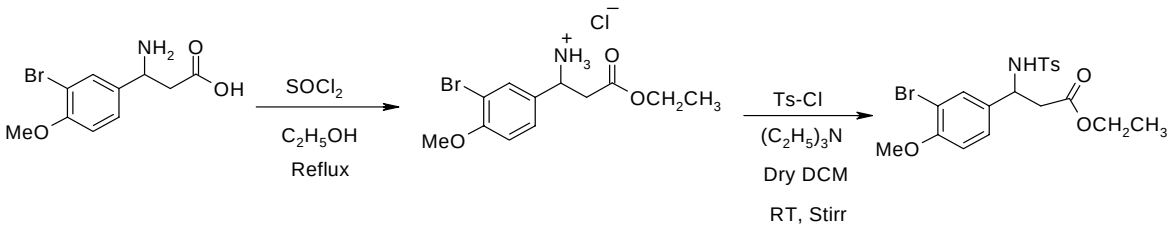


Table 1 : The reaction of DBT and DCT with olefins in the presence of Cu powder

Sl. No.	Olefin	Product	DBT or DCT	Time h	Yield %
1.	E-C_6H_5.CH:CH.$COOCH_3$	C_6H_5.CH(Br).CH.(NHTs).$COOCH_3$ (erythro : threo) (74 : 26)	DBT	4	65
		C_6H_5.CH(Cl).CH.(NHTs).$COOCH_3$ (erythro : threo) (88.2 : 11.7)	DCT	2	80.5
2.	Z-C_6H_5.CH:CH.$COOCH_3$	C_6H_5.CH(Cl).CH.(NHTs).$COOCH_3$ (erythro : threo) (85.3 : 14.6)	DCT	5	80.4
		C_6H_5.CH(Br).CH.(NHTs).$COOCH_3$ (erythro: threo) (68 : 32)	DBT	16	47
3.	E-C_6H_5.CH:CH.C_6H_5	C_6H_5.CH(Cl).CH.(NHTs).C_6H_5 (threo:erythro) (71.7 : 28.3)	DCT	2.25	31
4.	Z-C_6H_5.CH:CH.C_6H_5	C_6H_5.CH(Cl).CH.(NHTs).C_6H_5 (threo : erythro) (57.3 : 42.6)	DCT	1	57
5.	CH_2:CH.$COOCH_2CH_3$	TsNH.CH_2.CH.(Br).$COOCH_2CH_3$	DBT	1.5	65
		TsNH.CH_2.CH.(Cl).$COOCH_2CH_3$	DCT	3.15	75.4
6.	CH_2:C(CH_3).$COOCH_3$	TsNH.CH_2.C.Br.(CH_3).$COOC_2H_5$	DBT	2.45	40
		TsNH.CH_2.C.Cl.(CH_3). $COOC_2H_5$	DCT	6.5	91
7.	CH_2:CH.CN	TsNH.CH_2.CH.Br.CN	DBT	2	40
8.	4-$CH_3OC_6H_5$.CH:CH.COO.CH_2CH_3	4-$CH_3OC_6H_5$.CH (Br).CH. (NHTs). $COOCH_2CH_3$	DBT	2	35
9.	E-C_6H_5.CH:CH.CH.CO.CH_3	E-C_6H_5CH(Br)CH(NHTs)$COCH_3$	DCT	15	42
10.	C_6H_5.CH:CH_2	NR	DBT	24	NR
	,,	C_6H_5.CH.Cl.CH_2.NHTs	DCT	5	50
11.	Cyclohexene	C_6H_{10}Cl.NHTs	DCT	7	42

12.	Isophorone	NR	DBT	24	NR
13.	$C_6H_5.CH:C(CN).COO.CH_2CH_3$	NR	DBT	24	NR
14.	E-$C_6H_5.CH:CH.NO_2$	NR	DBT	24	NR
15	$C_6H_5.CH=CH_2$	$C_6H_5.CH.Cl.CH_2.NHTs$	DCT	5	50

Reaction conditions : DCT (0.288 g, 1.2 mmol) + Methylcinnamate (0.162 g, 1 mmol) + Cu (0.063 g, 1 mmol) + EDC (10 ml) + Mol. Sieves(3 A^0) (50 mg); reflux.

Table 2 : The reaction of DBT and DCT with hydrocarbons in the presence of Cu powder

Sl. No.	Olefin	Product	DBT/ DCT	Time h	Yield %
1.	$C_6H_5.CH_2.C_6H_5$	$C_6H_5.CH.NHTs.C_6H_5$	DBT	5	60
2.	Fluorene	9-$C_{13}H_9$.NHTs	DBT	10	75
3.	$C_6H_5.CH_2.CH_3$	$C_6H_5.CH.NHTs.CH_3$	DBT	4	76.5
4.	2-$CH_3CO.C_6H_5.CH_2.C_6H_5$	2-$CH_3CO.C_6H_5.CH.NHTs.C_6H_5$	DBT	7	82
5.	4-$CH_3CO.C_6H_5.CH_2.C_6H_5$	4-$CH_3CO.C_6H_5.CH.NHTs.C_6H_5$	DBT	3	38
			DCT	8	56.5
6.	4, 4'-$CH_3CO.C_6H_5.CH_2.C_6H_5$	4,4'-$CH_3CO.C_6H_5.CH.NHTs.C_6H_5$	DBT	2.5	83
7.	Tetralin	NR	DBT	24	NR
		2-$C_{10}H_{11}$.NHTs	DCT	2.5	48
8.	Indan	NR	DBT	24	NR
9.	$C_6H_5.CH_3$	NR	DBT	24	NR
			DCT	9	NR

Reaction conditions : DCT (0.288 g, 1.2 mmol) + Methylcinnamate (0.162 g, 1 mmol) + Cu (0.063 g, 1 mmol) + EDC (10 ml) + Mol. Sieves(3 A^0) (50 mg); reflux.

Results and Discussion

Ethyl acrylate gave 3-N-tosylamido-2-halo propionate while methyl cinnamate forms the 2-N-tosylamido–3-chloro-phenyl propionate. The MS of 3-halo-2-N-tosyl amido propionate and 3-chlorophenethyl-N-tosylamide showed $TsNHCH_2$ (184) and C_6H_5CHCl (125) confirming the regiochemistry of the products. The non catalyzed reaction of E-methyl cinnamate with DCT gave a mixture of isomers (erythro: threo

– 72.4: 27.6). The reaction of DCT in the presence of Cu powder with E- and Z-methyl cinnamate gave 88.2: 11.7 and 85.3: 14.6 ratio of erythro and threo 3-chloro-2-N-p-toluenesulfonamido phenylmethylpropionate. The reaction was regiospecific and stereo selective. The similar reaction with DBT gave 74: 26 and 68: 32 ratio of the erythro, threo mixture of 2-N-p-toluenesulfonamido-3-bromo phenylmethylpropionate (Major: erythro – 8 Hz; Minor: threo - 4 Hz). The slight increase in the ratio of stereoisomers is due to the Cu powder. Both the E and Z isomers gave the same major isomer indicating stereo selectivity of the reaction. Stereo selectivity is higher for chloride compared to bromide (DCT/DBT). The reaction of DCT in the presence of Cu powder with E- stilbene and Z-stilbene gave 71.7: 28.3 and 57.3: 42.6 ratio of threo: erythro isomers. The stereochemistry of the isomers was assigned from the coupling constant (Major isomer: threo - 6 Hz, Minor isomer: erythro - 8 Hz; for the vicinal H-$CClC_6H_5$- CHC_6H_5NHTs of the amino halogenated product). The major isomer with stilbene was threo, compared to the erythro isomer obtained with methyl cinnamate. E-Stilbene gave a higher threo: erythro isomer ratio compared to the Z-stilbene.[1b]

The reaction of DCT with tetralin, ethyl benzene and diphenyl methane gave 48 – 56 % yield in 2 – 14 h. No reaction was observed with toluene. DBT gave higher yields with the hydrocarbons but surprisingly no reaction with tetralin, toluene and indane due to competitive protonation Vs amination for the doubly activated substrates (**Table-2**, S.No.1–6). The higher yields with DBT could be due to the difference in stability and reactivity of DCT Vs DBT. The results are shown in **Table-2.** The reaction of methyl cinnamate with DCT was also carried out in the presence of by Fe, Al, Mg and Zn powders to give 3-chloro-2-N-(4-toluenesulphonyl amido)- phenyl methyl propionate in 75–86 % yield in 24–48 h. Surprisingly, these metal powders inhibit the reaction showing longer reaction times of 48 h for

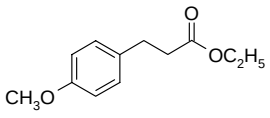
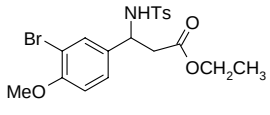
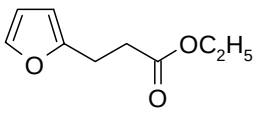
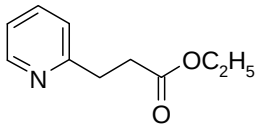
completion, compared to the short reaction times observed with the Cu catalyzed reaction (2 h– DCT; 4 h–DBT) and the non catalyzed reaction (2 h – 24 h).

The reactions of β-nitro styrene and isophorone with DCT didn't yield amino halogenated product. Only Ts-NH_2 was formed. DCT reacted with styrene in the presence of Cu-powder, where the reaction was carried out on silica gel by adsorbing the reactants and gave 12% of amino halogenated product. Also in the presence of Na_2MoO_4 and benzyl triethylammonium chloride in CH_3CN gave 15% yield of the product.

C-H insertion reactions by bromamine-T, chloramine-T, DBT and DCT were tried for different kinds of substrates, the products of which have great importance from synthetic chemistry point of view. Thus the C-H insertion reactions of nitrenes generated from above mentioned nitrene precursors were tried for diethyl malonate, ethyl phenyl acetate, methyl phenyl acetate, 1,2-diphenylethanol, 2-picoline, cumene, N, N-dimethylbenzylamine and dihydromethylcinnamate and also with hydrocarbons like toluene, dioxane and ethylbenzene. These reactions were tried using different catalysts like Cu-powder, $PdCl_2$(Cyclohexyl-DAB), $Pd(dba)_2$+dppe, $PdCl_2[P(C_6H_5)_3]_2$+Cu, $Mo(CO)_6$+Na(DETC), $W(CO)_6$+ Na(DETC), Fe(Pc) and Fe(TPP)Cl and EDC or CH_3CN as solvent. To our disappointment, none of the reactions yielded the desired product.

Table-3 : The reaction of DBT with 3-aryl ethyl propanoic esters in the presence of

Cu powder

S.No	Substrate	N/Br source	Product	Time h	Yield %
1.		DBT		12	13%
2.		DBT	NR	24	--
3.		DBT	NR	24	--

Reaction conditions: DBT (1.2 mmol) + 3-aryl ethyl propinoate (1 mmol) + MS 4 A^{o} (50 mg); EDC, 25 ^{o}C, Stir.

Reaction of dibromamine-T with ethyl 3-(4-methoxy phenyl) propionate in the presence of copper powder at room temperature stirring yielded 34% of ring brominated product, 12% of bromo aminated product and rest was p-toluene sulphonamide (Table-3)**. The structure of the product was confirmed by the spectral analysis and also by preparation of the product by known method.**

The ^{1}H-NMR of product shows A_2B_2 pattern of the p-toluene sulphonamide group at δ7.55 and δ7.18) and NH protons attached to benzylic position (δ5.85). ABX system of the aromatic protons of bromine containing phenyl group appeared at δ7.17, δ7.08 and

δ6.71. The benzylic proton attached to –NH group was at δ4.65 which was changed to triplet after D_2O exchange. Two dd due to methylene protons between benzylic proton and ester group were at 2.73. The IR spectrum shows the presence of sulphonamide –NH at 3290 cm^{-1}. The carbonyl stretching was at 1726cm^{-1}. The absorption due to SO_2 of sulphonamide was at 1373 cm^{-1} and 1166 cm^{-1}. The absorption due to C-Br bond was at 1051 cm^{-1} showing the presence of bromine attached to phenyl ring. The mass spectrum shows molecular ion peak at 458. The presence of bromine attached to phenyl ring was strongly evidenced by the molecular ion peak at 284 in the LC-Mass spectrum, which was due to [4-CH_3O(2-Br.C_6H_4)–CH-CH_2-$COOCH_2CH_3$]$^+$.

To confirm the structure of β-amino ester, the final compound was prepared by unambiguous method. First β-amino acid was easily prepared by the reaction of 3-bromo anisaldehyde with malonic acid and ammonium acetate in ethanol at reflux condition (Scheme-4)**.**

The amino acid obtained then esterified by treating with thionyl chloride in ethanol. The ester amine hydrochloride then treated with tosyl chloride in dry dichloromethane and triethylamine to get the final β-amino ester **(Scheme-5)**. Then all the spectral data was compared with the product obtained by the reaction of DBT with 3-(4-methoxyphenyl)ethylpropionate. Both the compounds were found one and the same.

Conclusion

DBT and DCT react with olefins and hydrocarbons in the presence of Cu, Zn, Mg and Al powders to give amino halogenations and amination products in high yields. The reactions are regiospecific, forming products with anti-Markownikoff orientation.

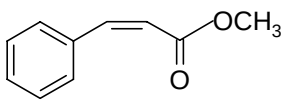
DBT gave higher yields C-H inserted products with the hydrocarbons. With 3-(4-methoxytphenyl) ethyl propionate and copper powder, DBT gave both aromatic bromination and benzylic amination product in one pot.

2.3.3 Experimental

The olefins, hydrocarbons and chloramine-T were purchased form Sigma-Aldrich, Loba Chemie, S.D.Fine Chemicals and SRL. Z-Methyl cinnamate, Z-stilbene (transfer hydrogenation of alkynes),[7] 2-acetyldiphenyl methane, 4-acetyldiphenylmethane, 4,4'-bis acetyl diphenyl methane (acetylation of diphenylmethane),[8] 4-methoxy ethylcinnamate,[9] 2-cyanoethyl cinnamate,[10] E-nitro styrene,[8] N,N-dichloro-4-toluenesulphonamide,[11] N,N-dibromo-4-toluenesulphonamide,[12] 4-methoxyphenylethyl-propionate[7] were synthesized according to known procedures. 3-bromo anisaldehyde was prepared according to literature.[12] The reactions were monitored by TLC using GF-254 grade silica gel on glass plates. Silica gel (100-200 mesh) was used for column chromatography. ^{1}H, ^{13}C NMR spectra were recorded in $CDCl_3$ on Varian 200 MHz and Brucker-300 MHz instruments. All reactions were carried out under Ar atmosphere.

1. Preparation of methyl –3-phenyl -(Z)-2-propenoate

In a 250 ml hydrogenation bulb 3-phenyl methyl propynoate (0.669 g, 4.18 mmol) was taken in 20 ml of hexane. To this solution $Pd/BaSO_4$ (0.040 g 10 %) was added and hydrogenated in a par reactor at 60-70 psi of hydrogen. The reaction was monitored by TLC. Since the RF values of the product and starting material are almost same, the reaction was allowed to continue overnight. After completion, the contents of the hydrogenating bulb was transferred to a 100 ml RBF by filtration on cilite (to remove $Pd/BaSO_4$) and concentrated by rotary evaporation. The mixture was purified by filtration column using pet. ether to get 0.612 g, (90%) of the pure Z-methylcinnamate.



Methyl –3-phenyl -(Z)-2-propenoate

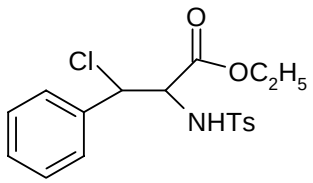
Yield : (0.612 g) 90%

^{1}H NMR (δ, $CDCl_3$, 200 MHz) : 7.19 (d, 1H, J=12Hz, Ar-CH=CH-COO); 6.02 (d, 1H, J=12Hz, Ar-CH=CH-COO); 7.51 (d, Ar-CH=CH-Ar')

2. Reaction of (DCT) N, N-dichlorotoluenesulfonamide with (E) - methyl cinnamate in the presence of Cu powder

(E)-Ethyl cinnamate (0.162 g, 1 mmol), Cu powder (0.063 g, 1 mmol) were taken in 10 ml of ethylene dichloride and kept for reflux. N, N-dichlorotoluenesulfonamide (0.288 g, 1.2 mmol) was added in portions to the above refluxing solution. The reaction was completed in 3 h. Filtration, concentration of the filtrate on rotary evaporator and purification by column

chromatography gave 0.310 g (80.5 %, erythro: threo - 88.2: 11.7) of the 3-chloro-2-N-p-toluenesulfonamido phenyl methyl propionate.



3-Chloro-2-N-p-toluenesulfonamido phenyl methyl propionate

Yield : 80.5 %

IR (cm^{-1}) : 3282, 2923, 2854, 1730, 1596, 1454, 1344, 1228, 1161, 1093, 966, 810.

^{1}H NMR (δ - $CDCl_3$, 200 MHz) : 7.63 (d, 8 Hz, 2 H), 7.31 (m, 8H), 5.25 (d, 10 Hz,

1H, D_2O exchanges), 5.14 (d, 6 Hz, 1 H, major –erythro), 4.43 (dd, 10, 6 Hz, 1 H, major - erythro), 3.61 (s, 3 H, threo - minor), 3.51 (s, 3 H, major - erythro), 2.42 (s, 3 H, major - erythro), 2.39 (s, 3H, minor - threo)

^{13}C NMR (δ, $CDCl_3$, 200 MHz) : 168.9, 143.6, 136.5, 135.89, 129.45, 128.5, 128, 127.51, 127.10, 61.86, 61.56, 52.42, 21.31

MS m/z (%) : 367, 308, 276, 242, 228, 189, 155, 125, 103, 91, 77, 65.

3. Reaction of N, N-dichlorotoluenesulfonamide with (Z) - methyl cinnamate in the presence of Cu powder

(Z) - Methyl cinnamate (0.162 g, 1 mmol), Cu powder (0.063 g, 1 mmol) were taken in 10 ml of ethylene dichloride and kept for reflux. N, N-Dichlorotoluenesulfonamide (0.288 g, 1.2 mmol) was added in portions to the above refluxing solution. The reaction was

completed in 4 h. Filtration, concentration of the filtrate on rotary evaporator and purification by column chromatography gave 0.295 g (80.4 %, 85.3: 14.6) of the 3-chloro-2-N-p-toluenesulfonamido phenyl methyl propionate.

Yield : 80.5 %

IR (cm^{-1}) : 3282, 2923, 1730, 1454, 1375, 1344, 1228, 1161, 1093, 810

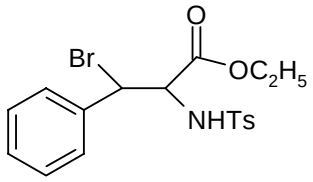
^{1}H NMR (δ, $CDCl_3$, 200 MHz) : 7.63 (d, 8 Hz, 2 H), 7.23 (m, 8H), 5.27 (d, 10Hz, 1H, D_2O exchanges), 5.13 (d, 6 Hz, 1 H, erythro - major), 4.40 (dd, 10, 6 Hz, 1 H, erythro - major), 3.62 (s, 3 H, threo - minor), 3.51 (s, 3 H, major - erythro), 2.41 (s, 3H,

Major - erythro), 2.39 (s, 3H, minor - threo)

^{13}C NMR (δ, $CDCl_3$, 200 MHz) : 168.9, 143.6, 136.6, 135.9, 129.45, 128.9, 128.5, 127.5, 127.14, 61.89, 52.41, 21.31

MS : m/z (%) : 367, 342, 332, 308, 276, 242, 228, 189, 155, 125, 103, 91, 77, 65.

4. Reaction of (DBT) N, N-Dibromotoluenesulfonamide with (E) - methyl cinnamate in the presence of Cu powder: (E) - Methyl cinnamate (0.162 g, 1 mmol), Cu powder (0.063 g, 1 mmol) and 10 ml ethylene dichloride were taken in a flask and kept for reflux. N, N-Dibromotoluenesulfonamide (0.319 g, 1 mmol) was added in portions to the above refluxing solution. The reaction was completed in 4 h. Filtration, concentration of the filtrate on rotary evaporator and purification by column chromatography gave 0.269 g (65 %, 74: 26) of the 3-bromo-2-N-p-toluenesulfonamido phenyl methyl propionate.



3-bromo-2-N-p-toluenesulfonamido phenyl methyl propionate

Yield : 65 %

^{1}H NMR (δ, $CDCl_3$, 300 MHz) : 7.62 (d, 4 Hz, 2 H), 7.41 - 7.18 (m, 7H), 5.46 - 5.43 (d, 9 Hz, 1 H, D_2O exchanges, threo, minor), 5.33 - 5.31 (d, 4 Hz, 1H, threo, minor), 5.22 – 5.19 (d, 9 Hz, 1 H, D_2O exchanges, erythro, major), 5.13 - 5.11 (d, 8 Hz, 1 H, erythro, major), 4.51 - 4.46 (dd, 9, 6 Hz, 1H, erythro, major, D_2O - d), 4.41 - 4.37 (dd, 9, 4 Hz, 1 H, threo, minor, D_2O - d), 3.57 (s, 3H, threo, minor), 3.52 (s, 3H, erythro, major), 2.41 (s, 3H, erythro, major), 2.40 (s, 3H, threo, minor)

^{13}C NMR (δ, $CDCl_3$, 300 MHz) : 169.34, 168.77, 143.55, 136.58, 136.22, 129.38, 128.87, 128.78, 128.50, 128.09, 127.10, 126.92, 62.11, 61.60, 53.47, 52.78, 52.45, 51.23, 31.38, 29.47, 21.28

MS (m/e) : 413, 352, 322, 301, 242, 171, 155, 131, 118, 91.

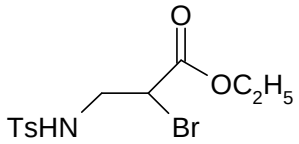
5. Reaction of (DBT) N, N-dibromotoluenesulfonamide with (Z) - methyl cinnamate in the presence of Cu powder : (Z) - Methyl cinnamate (0.162 g, 1 mmol), Cu powder (0.063 g, 1 eq.) and 10 ml ethylene dichloride were taken in a flask and kept for reflux. N, N-Dibromotoluenesulfonamide (0.320 g, 1 mmol) was added in portions to the above refluxing solution. The reaction was completed in 16 h. Filtration, concentration of the filtrate on rotary evaporator and purification by column chromatography gave 0.194 g (47 %, 68: 32) of the 3-bromo-2-N-p-toluenesulfonamido phenyl methyl propionate.

Yield : 65 %

^{1}H NMR (δ, $CDCl_3$, 200 MHz) : 7.61 (d, 4 Hz, 2H), 7.17 - 7.58 (m, 7 H), 5.51 - 5.47 (d, 8 Hz, 1H, D_2O exchanges, minor), 5.33 - 5.31 (d, 4 Hz, 1H, minor-threo), 5.30 - 5.25 (d, 10 Hz, 1H, D_2O exchanges, major-erythro), 5.13 - 5.10 (d, 6 Hz, 1H, major - erythro), 4.52 - 4.47 (dd, 10, 6 Hz, 1H, major - erythro, D_2O - doublet), 4.40 - 4.35 (dd, 10, 4 Hz, 1H, minor-threo, D_2O - doublet), 3.58 (s, 3H, minor - threo), 3.52 (s,3H, major-erythro), 2.41(s, 3H, major - erythro), 2.39 (s, 3H, minor - threo)

^{13}C NMR (δ, $CDCl_3$, 200 MHz) : 169.34, 168.77, 143.55, 136.58, 136.22, 129.38, 128.87, 128.78, 128.50, 128.09, 127.10, 126.92, 62.11, 61.60, 53.47, 52.78, 52.45, 51.23, 31.38, 29.47, 21.28.

6. Reaction of (DBT) N, N-dibromotoluenesulfonamide with ethyl acrylate in the presence of Cu powder: Ethyl acrylate (0.1 g, 1 mmol), Cu powder (0.076 g, 1.2 eq.) and 10 ml ethylene dichloride were taken in a flask and kept for reflux. N, N-Dibromotoluenesulfonamide (0.395 g, 1.2 mmol) was added in portions to the above refluxing solution. The reaction was completed in 1.5 h. Filtration, concentration of the filtrate on rotary evaporator and purification by column chromatography gave 0.228 g (65 %) of the 3-N-p-toluenesulfonamido-2-bromo ethyl propionate.



3-N-p-toluenesulfonamido-2-bromo ethyl propionate

Yield : 65 %

IR (cm^{-1}) : 3612, 3286, 2983, 1731, 1444, 1332, 1159, 1093, 815, 665

^{1}H NMR (δ, $CDCl_3$, 200 MHz) : 7.73 (d, 8 Hz, 2H), 7.31 (d, 10 Hz, 2H), 5.11 (t, 8 Hz, 1-N-H, D_2O exchanges), 4.37 - 4.30 (dd, 6 Hz, 1H), 4.28 - 4.18 (q, 6 Hz, 2 H), 3.58 -3.36 (m, 2H), 2.44 (s, 3H), 1.33 - 1.26 (t, 6 Hz, 3H)

^{13}C NMR (δ, $CDCl_3$, 200 MHz) : 168.38, 143.65, 136.85, 129.71, 126.87, 62.35, 45.72, 21.30, 14.01, 13.64

MS m/z (%) : 351 (2), 304 (22.3), 270 (13.1), 224 (23), 184(41.4), 171 (1.3), 155 (82.8), 139 (4.6), 116 (3.9), 91 (100), 65 (35.5).

7. The reaction of (DCT) N, N-dichlorotoluenesulfonamide with E-Stilbene and Z-Stilbene in the presence of Cu powder

E-Stilbene (0.153 g, 1 mmol) or Z-Stilbene (0.153 g, 1 mmol), Cu powder (0.063g, 1 mmol) and 10 ml ethylene dichloride were taken in a flask and kept for reflux. N, N-dichlorotoluenesulfonamide (0.240 g, 1 mmol) was added in portions to the above refluxing solution. The reaction was completed in 2 h. Filtration, concentration of the filtrate on rotary evaporator and purification by column chromatography gave 0.296 g (80.5 %, threo: erythro - 71.7: 28.3) of the 3-N-p-toluenesulfonamido-2-chloro dibenzyl (from E-Stilbene) and 0.187 g (57.2 %, threo: erythro - 57.3: 42.6) of the 3-N-p-toluenesulfonamido-2-chloro dibenzyl (from Z-Stilbene).

(a) E-Stilbene - 3-N-p-toluenesulfonamido-2-chloro dibenzyl

Yield : 65 %

IR (cm^{-1}) : 3236, 2923, 1458, 1377, 1330, 1153, 1087, 931, 923

^{1}H NMR (δ, $CDCl_3$, 200 MHz) : 7.46 - 6.79 (m, 14 H), 5.6 - 5.4 (d, 8Hz, 1H),

5.19-5.17 (d, 6 Hz, 1H, major, threo), 5.04 - 5.0 (d, 8Hz, 1H, minor, erythro), 4.83 - 4.71 (dd-m, 6, 8 Hz, 1H, erythro, threo mixture), 2.32 (s, 3H, major), 2.30 (s, 3H, minor).

^{13}C NMR (δ, $CDCl_3$, 200 MHz) : 168.9, 143.6, 136.5, 135.89, 129.45, 128.5, 128, 127.51, 127.10, 61.86, 61.56, 52.42, 21.31

MS m/z (%) : 385, 372, 349, 294, 260, 194, 155, 139, 125, 104, 91, 77, 65.

(b) Z-Stilbene - 3-N-p-toluenesulfonamido-2-chloro dibenzyl

IR (cm^{-1}) : 3257, 2924, 2854, 1458, 1377, 1330, 1153, 1087, 923

^{1}H NMR (δ, $CDCl_3$, 200 MHz) : 7.46 – 6.79 (m, 14 H), 5.57 (d, 6 Hz, 1- N-H, minor), 5.46 – 5.42 (d, 8 Hz, 1-N-H, major), 5.20 –5.17 (d, 4 Hz, 1H), 5.04 –5.01 (d, 6 Hz, 1H), 4.40- 4.48 (dd, 6 Hz, 4 Hz, 1H), 2.33 (s, 3 H)

MS m/z (%) : 385, 349, 294, 283, 260, 194, 155, 139, 125, 104, 91, 77, 65.

8. Cu catalyzed reaction of (DBT) N, N-dibromotoluenesulfonamide with methyl methacrylate : Methyl methacrylate (0.1 g, 1 mmol), Cu powder (0.076 g, 1.2 eq.) and 10 ml ethylene dichloride were taken in a flask and kept for reflux. N, N-Dibromotoluenesulfonamide (0.395 g, 1.2 mmol) was added in portions to the above refluxing solution. The reaction was completed in 2.45 h. Filtration, concentration of the filtrate on rotary evaporator and purification by column chromatography gave 0.146 g (40 %) of the 2-N-p-toluenesulfonamido-3-bromomethylpropionate.[13]

Yield : 65 %

IR (cm-1) : 3247, 2921, 2852, 1730, 1598, 1454, 1342, 1307, 1143, 1056, 1000, 850, 700

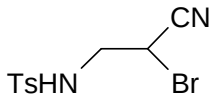
^{1}H NMR (δ, $CDCl_3$, 200 MHz) : 7.73 (d, 6 Hz, 2H), 7.32 (d, 6 Hz, 2H), 5.08 (t, 1-N-H, D_2O exchanges), 3.78 (s, 3 H), 3.58. 3.35 (dd, 34 Hz, 32 Hz, 2H, D_2O exchanges), 2.44 (s, 3H), 1.96 (s, 3H)

^{13}C NMR (δ, CDCl3, 200 MHz) : 170.60, 143.62, 137.06, 129.77, 126.90, 57.03,

53.32, 51.97, 25.54, 21.26

MS m/z (%) : 351 (1.6), 270 (11.9), 238 (15.2), 184 (100), 155 (92.7), 139 (5.9), 114 (8.6), 91 (74.8), 82 (9.2), 65(22.5).

9. Cu catalyzed reaction of N, N-dibromotoluenesulfonamide (DBT) with acrylonitrile : Acrylonitrile (0.053 g, 1 mmol), Cu powder (0.076 g, 1.2 eq.) and 10 ml ethylene dichloride were taken in a flask and kept for reflux. N, N-Dibromotoluenesulfonamide (0.395 g, 1.2 mmol) was added in portions to the above refluxing solution. The reaction was completed in 2 h. Filtration, concentration of the filtrate on rotary evaporator and purification by column chromatography gave 0.121 g (40 %) of the 3-N-p-toluenesulfonamido-2-bromo propionitrile.[13]



3-N-p-toluenesulfonamido-2-bromo propionitrile

Yield : 65 %

IR (cm-1) : 3315, 2921, 2254, 1596, 1458, 1411, 1336, 1153, 1091, 815, 659;

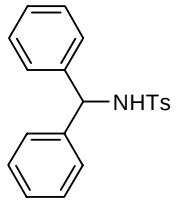
^{1}H NMR (δ, $CDCl_3$, 200 MHz) : 7.75 (d, 8 Hz, 2H), 7.33 (d, 8 Hz, 2 H), 5.47 (t, 1H), 4.43 (t, 8 Hz, 1-N-H, D2O exchanges), 3.47 - 3.56 (dd, 8, 4 Hz, 2H), 2.45 (s, 3H)

^{13}C NMR (CDCl3, 200 MHz) : 144.38, 136.51, 130.04, 127.03, 115.71, 47.01, 26.35, 21.42

MS m/z (%) : 302 (2), 184 (22.8), 171 (18.1), 155 (51), 107(14), 91 (100), 80 (10), 65 (44.9).

10. Reaction of DBT with diphenylmethane in the presence of Cu powder

Diphenylmethane (0.168 g, 1 mmol), Cu powder (0.063 g, 1 mmol) and 10 ml ethylene dichloride were taken in a flask and kept for reflux. N, N-Dichlorotoluenesulfonamide (0.329 g, 1 mmol) was dissolved in 2 ml of ethylene dichloride and added in portions through syringe to the above refluxing solution. The reaction was completed in 5 h. Filtration, concentration of the filtrate on rotary evaporator and purification by column chromatography gave 0.346 g (60 %) of the Diphenylmethyl-N-toluenesulphonamide.



Yield : 65 %

IR (cm^{-1}) : 4214, 3348, 3020, 2401, 1680, 1606, 1454, 1415, 1332, 1269, 1215, 1161, 1093, 1053, 929, 756

^{1}H NMR (δ, $CDCl_3$, 200 MHz) : 7.63 (d, 8 Hz, 2H), 7.43 (d, 8 Hz, 2H), 7.13 (m, 9H), 6.19 (d, 8 Hz, 1H – D_2O exchanges), 5.51 (d, J = 8 Hz, 1H), 2.42 (s, 3 H), 2.26 (s, 3H)

^{13}C NMR (δ, $CDCl_3$, 200 MHz) : 145.78, 143.13, 139.71, 139.20, 136.99, 135.78, 129.97, 129.38, 129.20, 128.46, 127.14, 126.88,126, 60.86, 26.35, 21.2.

11. The reaction of N, N-dichlorotoluenesulfonamide (DBT) with 2'-acetyldiphenylmethane in the presence of Cu powder: 2-Acetyldiphenylmethane (0.210 g, 1 mmol), Cu powder (0.063 g, 1 mmol) and 10 ml ethylene dichloride were taken in a flask and kept for reflux. N, N-Dichlorotoluenesulfonamide (0.329 g, 1 mmol) was added in portions to the above refluxing solution. The reaction was completed in 2 h. Filtration, concentration of the filtrate on rotary evaporator and purification by column chromatography gave 0.311 g (82 %) of the 2-acetyldiphenylmethyl-N-toluenesulphonamide.

Yield : 65 %

IR (cm^{-1}) : 4214, 3348, 3020, 2401, 1680, 1606, 1454, 1415, 1332, 1269, 1215, 1161, 1093, 1053, 929, 756

^{1}H NMR (δ, $CDCl_3$, 200 MHz) : 7.63 (d, 8 Hz, 2H), 7.43 (d, 8 Hz, 2H), 7.13 (m, 9H), 6.19 (d, 8 Hz, 1H – D_2O exchanges), 5.51 (d, J = 8 Hz, 1H), 2.42 (s, 3 H), 2.26 (s, 3H)

^{13}C NMR (δ, $CDCl_3$, 200 MHz) : 145.78, 143.13, 139.71, 139.20, 136.99, 135.78, 129.97, 129.38, 129.20, 128.46, 127.14, 126.88,126, 60.86, 26.35, 21.2.

12. The reaction of N, N-dichlorotoluenesulfonamide (DCT) with 4,4'-acetyldiphenylmethane in the presence of Cu powder

4, 4'-Acetyldiphenylmethane (0.240 g, 1 mmol), Cu powder (0.063 g, 1 mmol) and 10 ml ethylene dichloride were taken in a flask and kept for reflux. N, N-Dichlorotoluenesulfonamide (0.329 g, 1 mmol) was added in portions to the above refluxing solution. The reaction was completed in 2 h. Filtration, concentration of the filtrate on rotary evaporator and purification by column chromatography gave 0.346 g (83 %) of the 4, 4'-(bis) acetyldiphenylmethyl-N-toluenesulphonamide.

Yield : 65 %

IR (cm^{-1}) : 4214, 3265, 3020, 2401, 1681, 1604, 1413, 1359, 1267, 1215, 1161, 929, 757

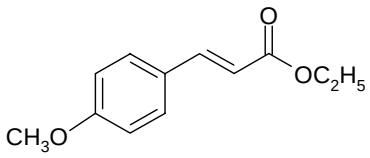
^{1}H NMR (δ, $CDCl_3$, 200 MHz) : 7.76 (d, 8 Hz, 2H), 7.55 (d, 8 Hz, 2H), 7.22 (m, 8H), 6.01 (d, 8 Hz, 1H – D_2O exchanges), 5.62 (d, 8Hz, 1H), 2.54 (s, 3H), 2.37 (s, 6H)

^{13}C NMR (δ, $CDCl_3$, 200 MHz) : 197.42, 144.93, 143.20, 137.21, 136.20, 129.16, 128.35, 127.36, 126.81, 60.61, 26.13, 21.02

MS m/z (%) : 406, 370, 341, 302, 266, 251, 222, 155, 107, 91.

13. Preparation of ethyl-3-(4-methoxyphenyl)-(E)-2-propenoate

In a 100 ml RBF, $(C_6H_5)_2P=CH-COOC_2H_5$ (8.70g, 25 mmol) was dissolved in 60 ml of THF. To this solution 4-methoxybenzaldehyde (2.72g, 20 mmol) was added slowly at cooling condition. Then the solution was stirred and refluxed overnight. After the completion of the reaction, the triphenylphosphine oxide was filtered off and filtrate was concentrated and purified on column chromatography to get 4.50 g (87%) yield.



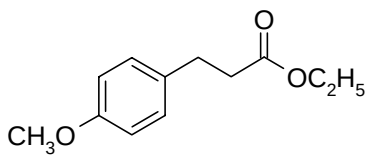
Ethyl-3-(4-methoxyphenyl)-(E)-2-propenoate

Yield : 4.5 g, 87%

^{1}H-NMR (δ ppm, 200 MHz, $CDCl_3$) : 7.6 (d, 1H, J=17Hz,); 7.5 (d, 2H, J= 8Hz,); 6.9 (d, 2H, J=8Hz,); 6.3 (d, 1H, J=17Hz); 4.2 (q, 2H, J=8Hz); 3.8 (s, 3H,); 1.32 (t, 3H, J=8Hz, $OCH_2C\underline{H}_3$)

14. Preparation of ethyl- 3-(4-methoxyphenyl)propionate

In 50 ml RBF 3-(4-methoxyphenyl)-ethylacrylate (1 g, 5 mmol) and Pd/C (0.100 g, 10 % w/w) were taken in 20 ml of ethyl alcohol. To this hydrazine hydrate (0.162 g, 5 mmol) was added dropwise at cooling condition. Then reaction was kept for reflux with stirring for overnight. After the completion of reaction, contents were filtered, washed with cold ethanol and purified on silica gel column chromatography.



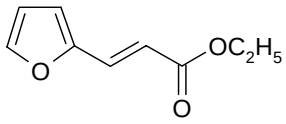
Ethyl 3-(4-methoxyphenyl)propionate

Yield : 0.98 g, 98 %

^{1}H-NMR (δ ppm, 200 MHz, $CDCl_3$) : 7.59 (d, 2H, 10Hz, Ar-H); 7.29 (d, 2H, 10Hz, Ar-H); 4.59 (q, 2H, -OC$\underline{H}_2$$CH_3$); 4.23 (s, 3H, -OC$\underline{H}_3$); 3.34 (t, 2H, 8Hz, -C$\underline{H}_2$-$CH_2$-COO); 3.02 (t, 2H, 8Hz, -CH_2-C$\underline{H}_2$-COO); 1.68 (t, 3H, 8Hz -OCH_2C$\underline{H}_3$).

15. Preparation of ethyl-3-(2-furyl)-(E)-2-propenoate

In a 100 ml RBF, $(C_6H_5)_2P$=CH-$COOC_2H_5$ (8.70g, 25 mmol) was dissolved in 60 ml of THF. To this solution furfural (1.92 g, 20 mmol) added slowly at cooling condition. Then the solution was stirred and kept for refluxed overnight. After completion of the reaction, the triphenylphosphine oxide was filtered off and filtrate was concentrated and purified on column chromatography to get 2.60 g (67%) yield.



Ethyl 3-(2-furyl)-(E)-2-propenoate

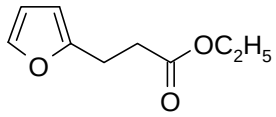
Yield : 2.5 g, 67%

^{1}H NMR (δ, $CDCl_3$, 200 MHz) : 7.80 (d, 1H, *furyl*-H); 6.65 (d, 1H, *furyl*-H); 7.00 (d, 1H, *furyl*-H); 7.65 (d, 1H, 15Hz, -C$\underline{H}$=CH-COO); 6.39 (d, 1H, 15Hz, -CH=C$\underline{H}$-COO 4.19 (q, 2H, -OC$\underline{H}_2$$CH_3$); 1.30 (t, 3H, 9Hz OCH_2C$\underline{H}_3$)

16. Preparation of Ethyl-3-(2-furyl)propionate

In a 50 ml RBF formic acid (1.15 ml, 30 mmol) was taken and cooled to 0 ^{0}C. To this triethylamine (4.2 ml 30 mmol) was added dropwise to neutralize the formic acid at 0 ^{0}C. To this solution Pd/C (0.066 g, 10 %) and ethyl 3-(2-furyl)-(E)-2-propenoate (0.664 g, 4 mmol) was added and kept for reflux. After completion of the reaction the triethylamine and formic acid mixture was distilled under reduced

pressure. The mixture was treated with water and extracted with ethyl acetate (3 X 15 ml). The pure product was obtained by silica gel chromatography.



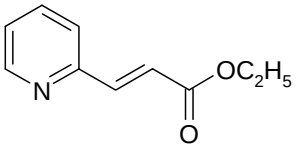
Ethyl-3-(2-furyl)propionate

Yield : 0.98 g, 98 %

^{1}H-NMR (δ ppm, 200 MHz, $CDCl_3$) : 7.32 (d, 1H, *furyl*-H); 6.28 (d, 1H, *furyl*-H); 6.03 (d, 1H, *furyl*-H); 4.17 (q, 2H, -OCH_2CH_3); 2.97 (t, 2H, -CH2-CH2-COO-); 2.65 (t, 2H, -CH2-CH2-COO-); 1.25 (t, 3H, OCH_2CH_3)

17. Preparation of Ethyl-3-(2-pyridyl)-(E)-2-propenoate

In a 100 ml RBF, $(C_6H_5)_2P{=}CH\text{-}COOC_2H_5$ (8.70g, 25 mmol) was dissolved in 60 ml of THF. To this solution pyridine-2-aldehyde (2.34 g, 20 mmol) added slowly at cooling condition. Then the solution was stirred and refluxed overnight. After the reaction the triphenyl phosphine oxide was filtered off and filtrate was concentrated and purified on column chromatography to get 2.47 g (70%) yield.



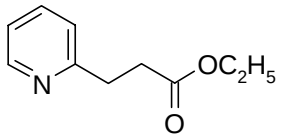
Ethyl-3-(2-pyridyl)-(E)-2-propenoate

Yield : 2.47 g, 70 %

^{1}H-NMR (δ ppm, 200 MHz, $CDCl_3$) : 8.55 – 8.50 (m, 1H,); 7.6 (m, 1H); 7.55 (d, 1H); 7.3 (d, 1H, J=6Hz); 7.2 – 7.1 (m, 1H); 6.8 (d, J=17, 1H); 4.2 (q, 2H, J=7.4Hz); 1.34 (t J=7.5Hz, 3H)

18. Preparation of Ethyl- 3-(2-pyridyl)propionate

In a 50 ml RBF formic acid (1.15 ml, 30 mmol) was taken and cooled to 0 ^{0}C. To this triethylamine (4.2 ml 30 mmol) was added dropwise to neutralize the formic acid at 0 ^{0}C. To this solution Pd/C (0.066 g, 10 %) and ethyl (2-pyridyl) acrylate (0.489 g, 3 mmol) was added and kept for reflux. After completion of the reaction excess of triethylamine and formic acid mixture was distilled under reduced pressure. The mixture was treated with water and extracted with ethyl acetate (3 X 15 ml). The pure product was obtained by silica gel chromatography.



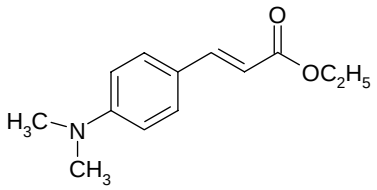
Ethyl-3-(2-pyridyl)propionate

Yield : 0.224 g, 50 %

^{1}H NMR (δ, $CDCl_3$, 200 MHz) : 7.71 (t, 1H, pyridil-H); 7.31 (m, 3H, pyridil-H); 4.14 (q, 2H, $OC\underline{H}_2CH_3$); 3.16 (t, 2H, $-C\underline{H}_2CH_2-$); 2.79 (t, 2H, $-CH_2C\underline{H}_2-$); 1.23 (t, 3H, $-CH_3$)

19. Preparation of Ethyl 3-(4-N, N-dimethylphenyl)-(E)-2-propeonate

In a 100 ml RBF, $(C_6H_5)_2P{=}CH\text{-}COOC_2H_5$ (16.32 g, 48 mmol) was dissolved in 60 ml of THF. To this solution 4-N, N-dimethylbenzaldehyde (7.45 g, 50 mmol) added slowly at cooling condition. Then the solution was stirred and refluxed overnight. After completion of the reaction, the triphenylphosphine oxide was filtered off and filtrate was concentrated and purified on column chromatography to get 4.50 g (87%) yield.



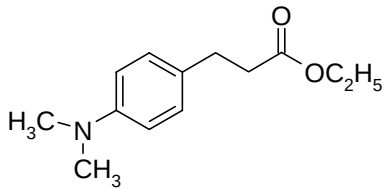
Ethyl 3-(4-N, N-dimethylphenyl)-(E)-2-propenoate

Yield : 8 g, 73%

^{1}H NMR (δ, $CDCl_3$, 200 MHz) : 7.65 (d, 1H, 15Hz, -CH=CH-COO); 7.43 (d, 2H, 8Hz, Ar-H); 6.88 (d, 2H, 8Hz, Ar-H); 6.25 (d, 1H, 15Hz, -CH=CH-COO); 4.25 (q, 2H, $-OCH_2CH_3$); 3.01 (s, 6H, $-N(CH_3)_2$); 1.32 (t, 3H, 9Hz OCH_2CH_3)

20. Preparation of Ethyl- 3-(4-N, N-dimethylphenyl)propionate

A 250 ml of hydrogenation bulb was charged with Ethyl-3-(4-N, N-dimethylphenyl)-propeonate (3 g, 13.6 mmol) and Pd/C (0.080 g) in 75 ml of methanol. The mixture was hydrogenated at 80 psi of hydrogen in par apparatus for about 3-4 h. After completion of the reaction, the contents of the hydrogenation bulb transferred to 100 ml RBF by filtration. The filtrate was concentrated on rotary evaporator and purified on silica gel chromatography to get 1.837 g, (60 %) of the product.



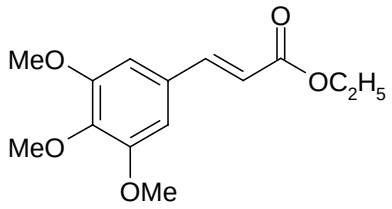
Ethyl- 3-(4-N, N-dimethylphenyl)propionate

Yield : 1.837 g, (60 %)

^{1}H NMR (δ, $CDCl_3$, 200 MHz) : 7.10 (d, 2H, Ar-H); 6.73 (d, 2H, 8Hz, Ar-H); 4.14 (q, 2H, -OCH_2CH_3); 2.91 (s, 6H, -$N(CH_3)_2$); 2.86 (t, 2H, 8Hz –CH_2-CH_2-COO); 2.57 (t, 2H, 8Hz, –CH_2-CH_2-COO); 1.24 (t, 3H, 9Hz OCH_2CH_3)

21. Preparation of Ethyl-3-(3, 4, 5-trimethoxyphenyl)-(E)-2-propenoate

In a 100 ml RBF, $(C_6H_5)_2P{=}CH\text{-}COOC_2H_5$ (9.7 g, 28 mmol) was dissolved in 60 ml of THF. To this solution 3, 4, 5-trimethoxybenzaldehyde (4.9 g, 25 mmol) added slowly at cooling condition. Then the solution was stirred and refluxed overnight. After the reaction the triphenyl phosphine oxide was filtered off and filtrate was concentrated and purified on column chromatography to get 5 g (76%) yield.



Ethyl-3-(3, 4, 5-trimethoxyphenyl)-(E)-2-propenoate

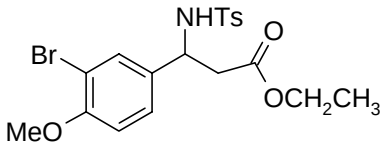
Yield : 5 g, 76 %

^{1}H-NMR (δ ppm, 200 MHz, $CDCl_3$) : 6.17 (d, 1H, 8Hz, Ar-H); 6.64 (d, 1H, 8Hz, Ar-H); 7.91 (d, 1H, 16Hz, -CH=CH-COO); 6.22 (d, 1H, 16Hz, -CH=CH-COO); 4.19 (q, 2H, -OCH_2CH_3); 1.30 (t, 3H, 8Hz -OCH_2CH_3)

22. Reaction of N, N-Dibromo p-toluene sulphonamide with Ethyl-3-(4-methoxyphenyl)propionate

Ethyl-3-(4-Methoxyphenyl)-propionate (0.296 g, 1.42 mmol) and Cu (0.063 g, 1 mmol) are taken in a 25 ml RBF in 8 ml of ethylene dichloride. To this mixture dibromamine-T (0.528 g, 1.6 mmol) was added by dissolving in 2 ml of ethylene dichloride dropwise via syringe at room temperature. The reaction was allowed to

stir at room temperature. After completion of the reaction (monitored by TLC), reaction mixture was concentrated on rotary evaporator. The mixture was purified on silica gel column chromatography to get pure product. 0137 g (34 %) of aromatic halogenated (i.e. Ethyl-3-(3-bromo-4-methoxyphenyl)-propionate and 0.080 g, (12 %) of Ethyl-3-(2-bromo-4-methoxyphenyl)-3-(4-methylphenylsulphonylamino)-propionate was obtained. 0.152 g, (63 %) of Ts-NH_2 was obtained.



Ethyl-3-(3-bromo-4-methoxyphenyl)-3-(4-methylphenylsulphonylamino) propionate

M.P. : 100-102 ^{o}C

IR (Nujol, cm^{-1}) : 3290, 2954, 2923, 2852, 1726, 1602, 1498, 1463, 1373, 1328, 1290, 1166, 1051, 1020, 954, 815, 673.

^{1}H-NMR (δ ppm, 200 MHz, $CDCl_3$) : 1.16 (t, 3H, -OCH_2**CH_3**); 2.38 (s, 3H, Ar-**CH_3**); 2.73 (dd, 4Hz, 4Hz, 2H,-**CH_2**) 3.83 (s, 3H, -O**CH_3**); 4.02 (q, 2H, -C**H**$_2$$CH_3$); 4.65 (dd, 1H, 4Hz, -CH); 5.83 (d, 1H, 4Hz, NH); 6.68 (d, 6Hz, 1H, Ar-H) 7.04 (dd, 1H, Ar-H, 2Hz, 8Hz); 7.14 (d, 1H, 2Hz, Ar-H); 7.15 (d, 8Hz, 2H, Ar-H); 7.55 (d, 8Hz, 2H, Ar-H)

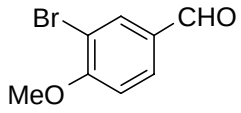
^{13}C NMR (δ, $CDCl_3$, 200 MHz) : 170.46, 155.27, 143.36, 137.21, 132.68, 131.54, 129.41, 126.99, 111.54, 61.02, 56.20, 53.40, 41.14, 29.65, 21.46, 13.98.

LC-MS : 458 (M+2), 456 (M+), 300, 285, 269, 255, 194

Preparation of Ethyl 3-(3-bromo 4-methoxy phenyl) 3-(4-methyl phenyl sulphonyl) amino propionate by known method :

23. Preparation of 3-bromo-4-methoxybenzaldehyde

3-Bromoanisaldehyde was prepared by known literature procedure.[12] It was obtained by treating pure p-anisaldehyde with bromine in the presence of anhydrous $AlCl_3$ under neat conditions.



Yield : 67%

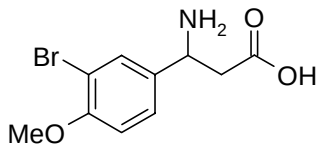
M.P. : 58 ^{o}C

IR (in cm^{-1}) : 3020, 1693, 2399, 1595, 1494, 1269, 1215 1161.

^{1}H-NMR (in $CDCl_3$ δ ppm) : 4.00 (s, 3H, OCH_3); 7.00 (d, 1H, 8Hz, Ar-H) 7.80 (dd, 1H, Ar-H, 2Hz, 8Hz Ar-H); 8.08 (d, 1H, 2Hz, Ar-H); 9.85 (s, 1H, -CHO)

24. Preparation of 3-amino-3-(3-bromo-4-methoxy)phenylpropionic acid

In a 50 ml of RBF 3-bromo-4-methoxybenzaldehyde (3.5 g, 16.2 mmol), malonic acid (1.68 g, 16.2 mmol), ammonium acetate (2.695 g, 35 mmol) were taken and 25 ml of ethyl alcohol was added. The reaction mixture refluxed for 12 h (monitored by TLC). After completion of the reaction, the β-amino acid precipitates out as white solid which was filtered, washed with cold ethanol and dried under vacuum to get (2.43g) 52 % of the product.



3-Amino-3-(3-bromo-4-methoxy)phenylpropionic acid (1)

Yield : (2.43 g) 52 %

M.P. : 216-218 ^{o} C

IR (KBr, cm^{-1}) : 3276, 2948, 2921, 1745, 1666, 1542, 1461, 1375, 1257, 1166, 1053.

^{1}H-NMR (δ ppm, D_2O/K_2CO_3, 200 MHz) : 2.48 (d, 2H, -CH_2); 3.83 (s, 3H, -OCH_3); 4.14 (t, 1H, -CH); 6.99 (d, 1H, 8Hz, Ar-H); 7.27 (dd, 1H, Ar-H, 2Hz, 8Hz); 7.54 (d, 1H, 2Hz, Ar-H)

C-H Analysis : Calculated : C (43.79 %), H (4.37 %), N (5.10 %), Br (29.19 %)

Found : C (43.58 %), H (4.20 %), N (5.15) Br (29.30 %)

25. Preparation of β -amino acid ethyl ester

In a 50 ml of RBF β-amino acid **(1)** (2.3 g, 8.39 mmol) was taken in 20 ml of ethanol. To this solution thionyl chloride (0.74 g 10 mmol) was added dropwise through addition funnel at 0 ^{0}C and the mixture was allowed to stir overnight. The ester hydrochloride was obtained by distilling out the ethanol and excess thionyl chloride. 2.93 g, of acid hydrochloride was obtained.

26. Tosylation of β -amino acid ethyl ester

In a 50 ml of RBF β-aminoacid ester hydrochloride (0.664 g, 1.96 mmol), tosyl chloride (0.394 g, 2 mmol) were taken in 15 ml of dry dichloromethane. To this solution, triethylamine (0.5 ml, 3 mmol) was added by dissolving in 2-3 ml of dry dichloromethane through syringe at 0 ^{0}C. The reaction kept for stirring overnight. After the completion of the reaction (monitored by TLC), the mixture was concentrated on rotary evaporator. The crude mixture was purified on silica gel (100-200 mesh) chromatography to get (0.534 g) 62 % of the product.

^{1}H NMR (δ, $CDCl_3$, 200 MHz) : 7.32 (d, 1H, furan-H); 6.28 (d, furan-H 2Hz 1H); 6.03 (d, 1H, furan-H); 4.17 (q, 2H, OCH_2CH_3); 2.97 (t, 2H, 6Hz, -CH_2CH_2-); 2.65 (t, 2H, 6Hz, -CH_2CH_2-); 1.25 (t, 3H –CH_3).

27. Reaction of Ethyl-3-(2-pyridyl)-propionate with DBT in the presence of Cu powder

In a 25 ml RBF 3-(2-pyridyl) ethyl propionate (0.179 g, 1 mmol), Cu (0.075 g, 1.2 mmol) were taken in 10 ml of ethylene dichloride. Then DBT (0.391 g, 1.2 mmol) was added by dissolving in CH_3CN through syringe. The reaction was stirred at room temperature first, then kept for reflux. After completion of the reaction, the reaction mixture was concentrated on rotary evaporator. The crude mixture was purified on silica gel chromatography.

2.3 References

1. (a) Kharasch, M. S.; Priestley, H. M. *J. Amer. Chem. Soc*., *61*, 3425 **1939**; (b) Seden, T. P.; Turner, R.W. *J. Chem. Soc. (C),* , 876 **1968**; (c) Torimoto, N.; Shingaki, T.; Nagai, T. *Bull. Chem. Soc. Jpn., 50 (10),* 2780 **1977**; (d) Breslow, D. S.; Sloan. M. F. *Tetrahedron Lett.*, *51*, 5349 **1968**; (e) Torimoto, N.; Shingaki, T. Nagai, T. *Bull. Chem. Soc. Jpn*., *51 (10)*, 2983 **1978**.
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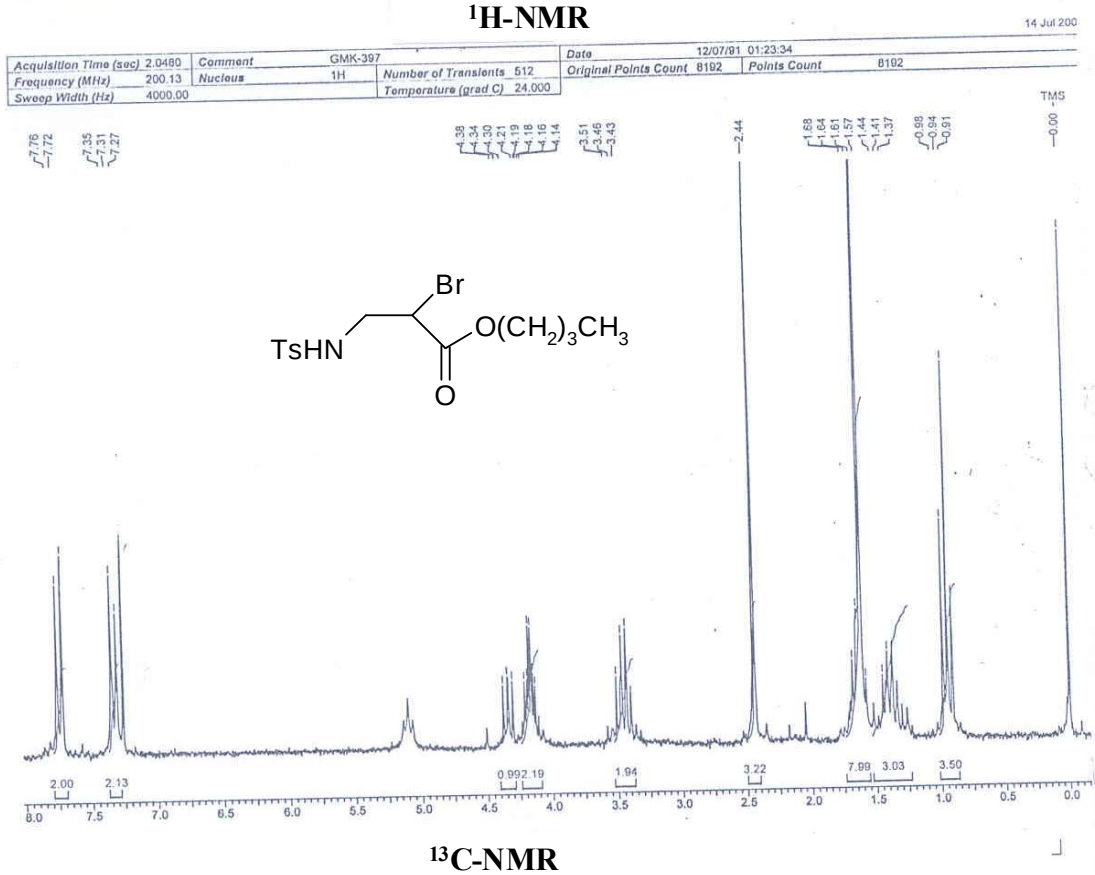
11. Dianjun, C.; Timmons, C.; Guo, Li.; Xin, Xu.; Guigen, Li., *Synthesis,* (15), 2479, **2004**.

SPECTRA

^{1}H-NMR



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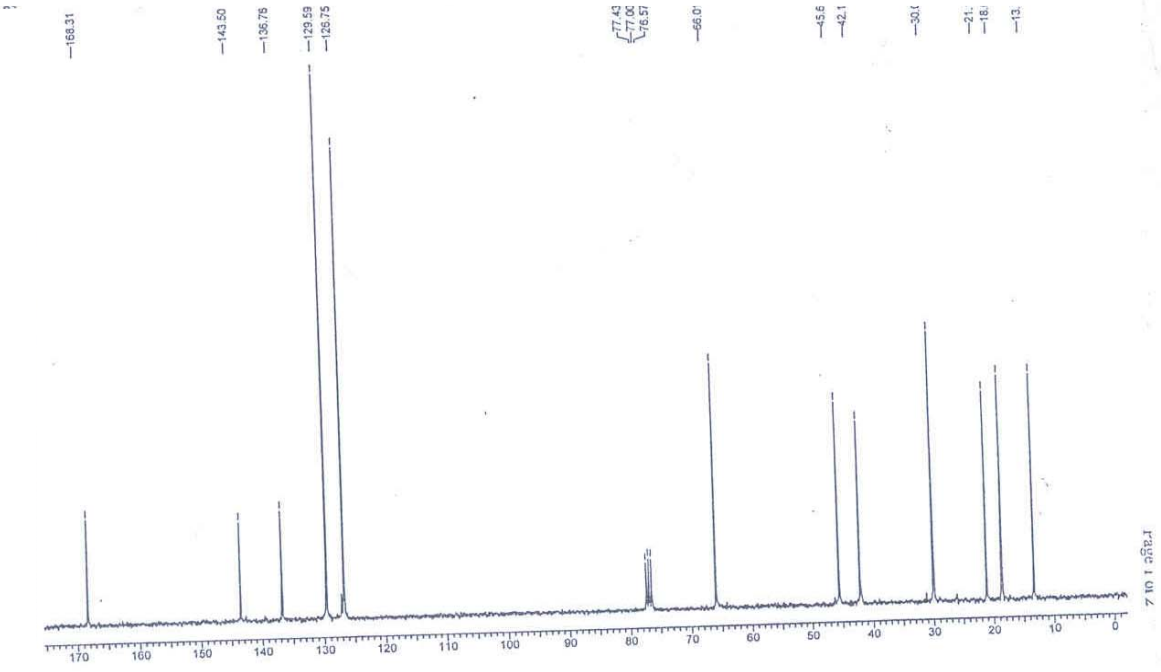

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17 Jul 2001

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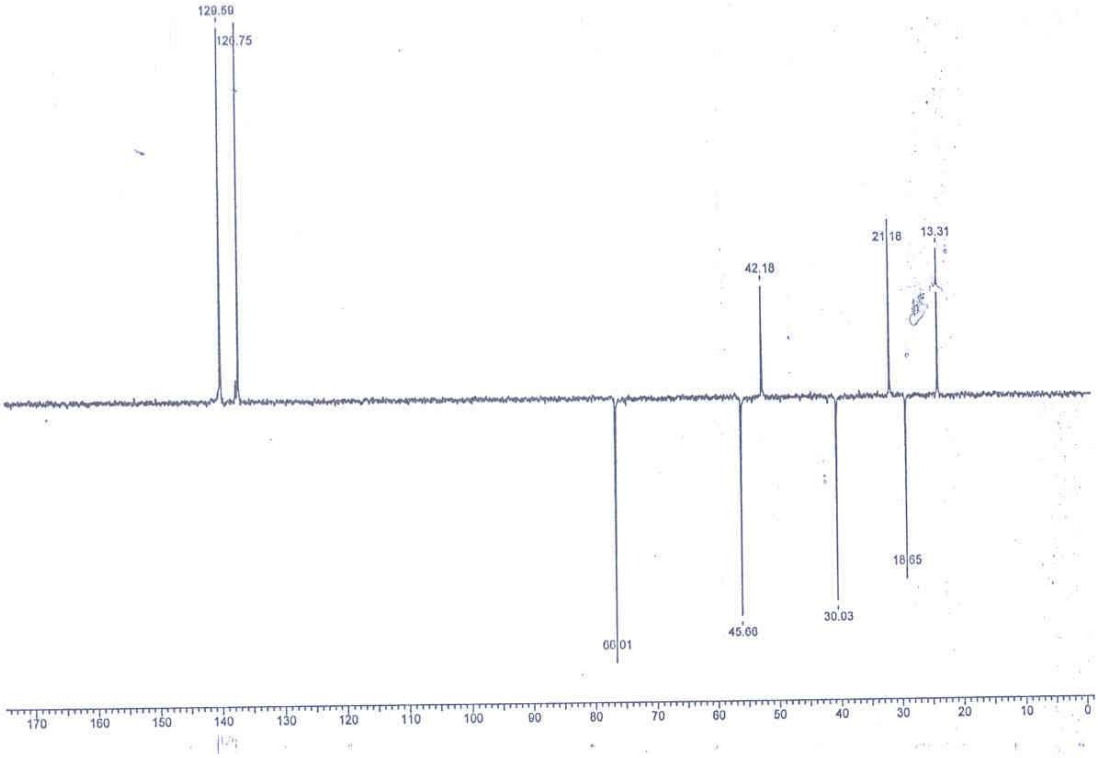

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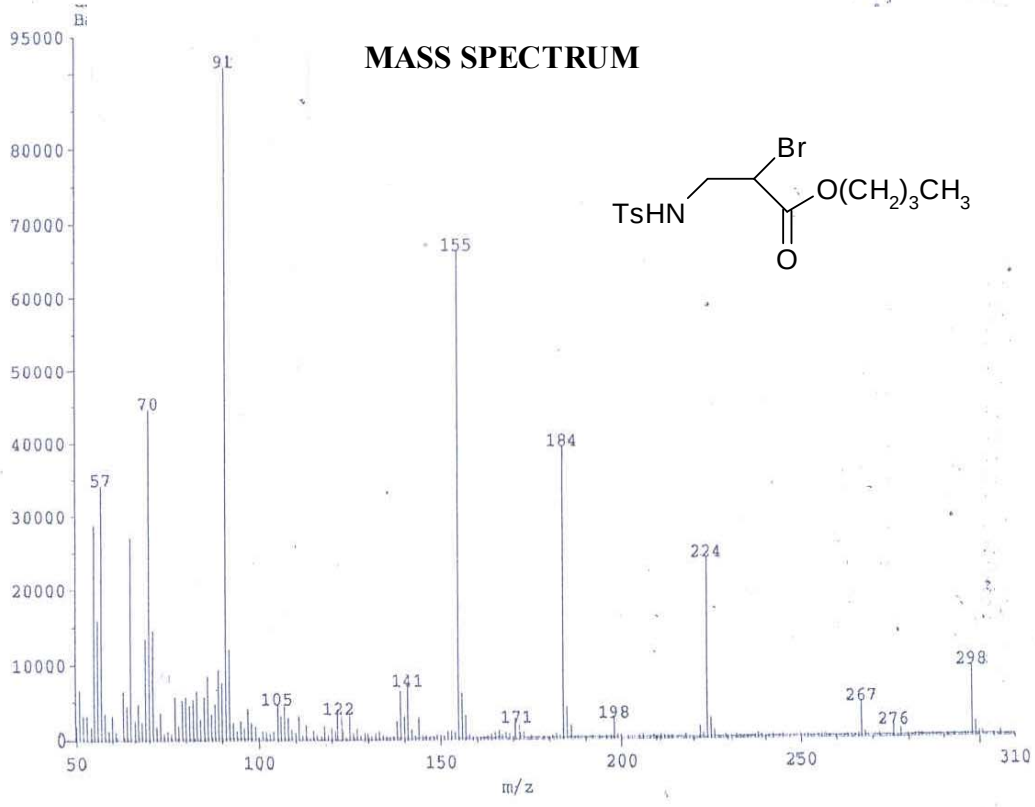

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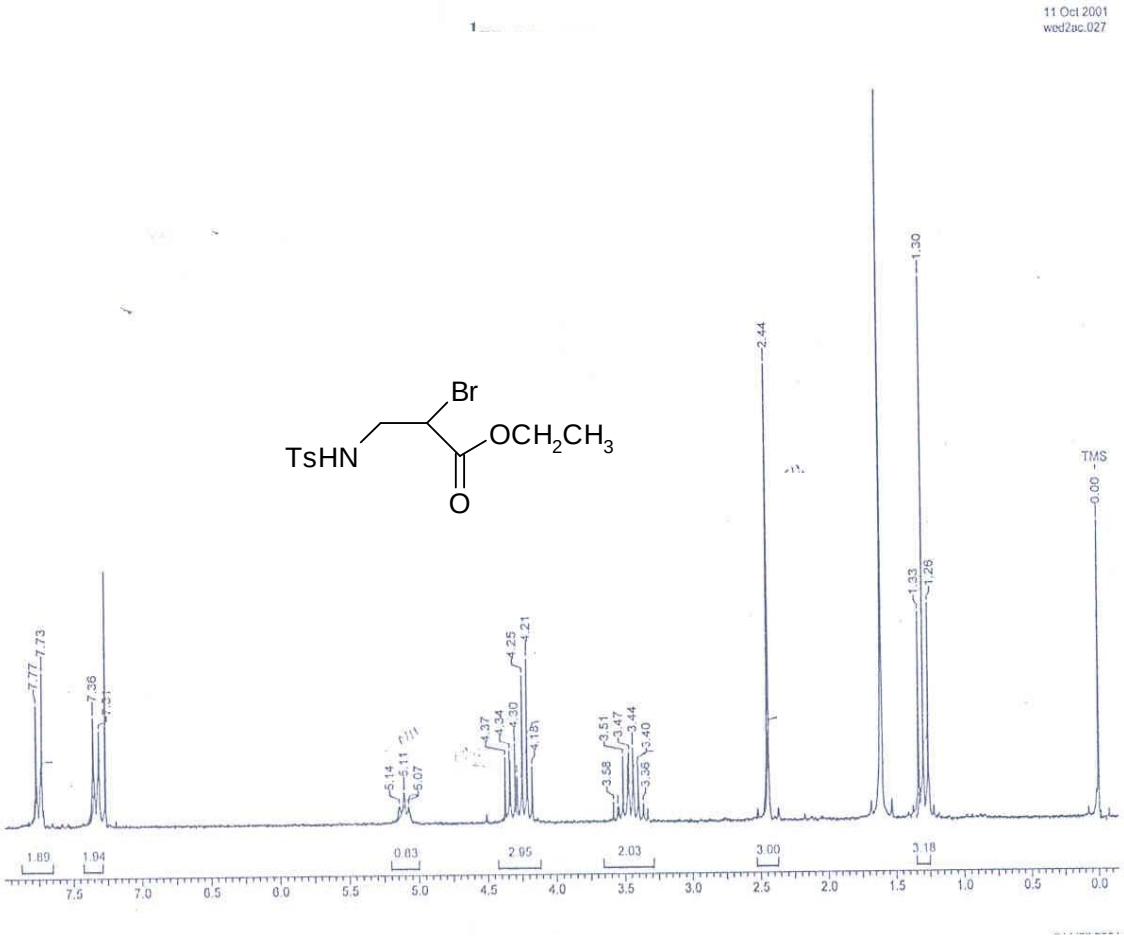
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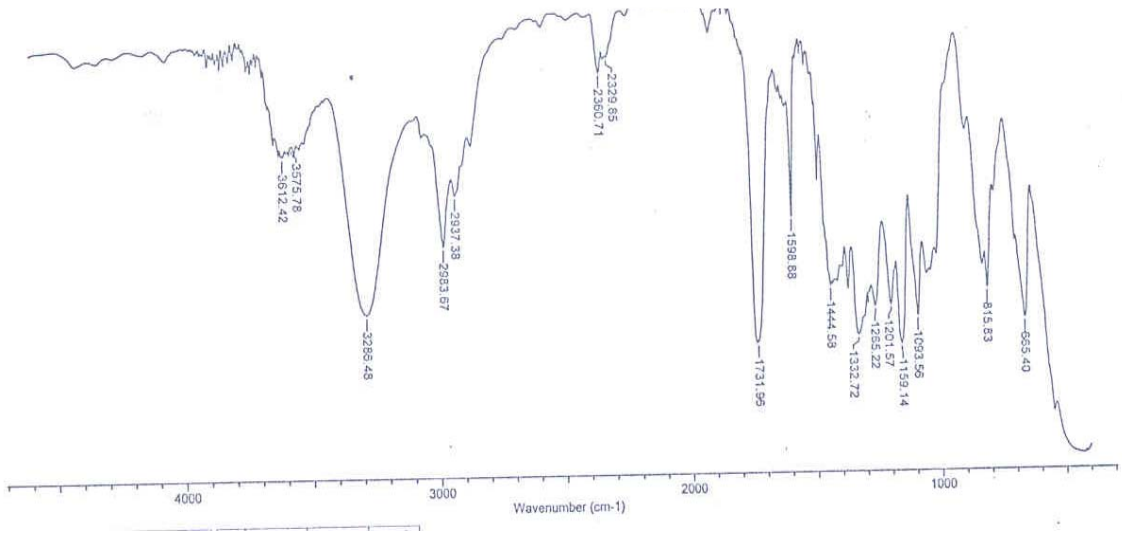
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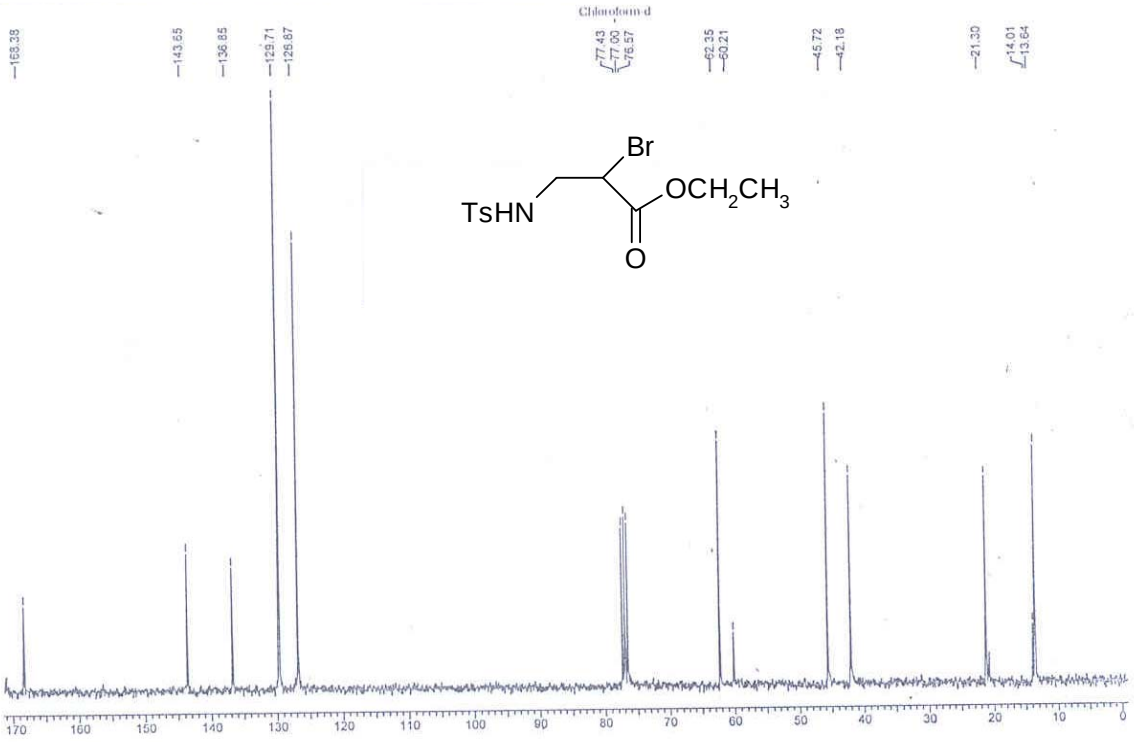

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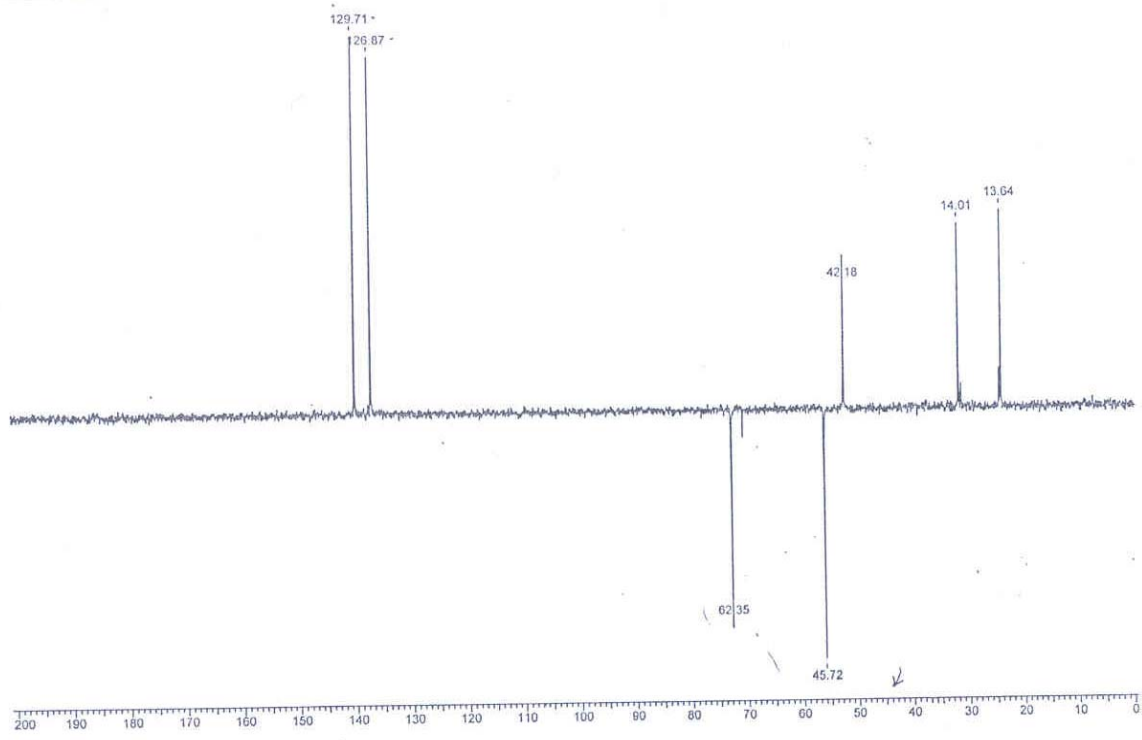

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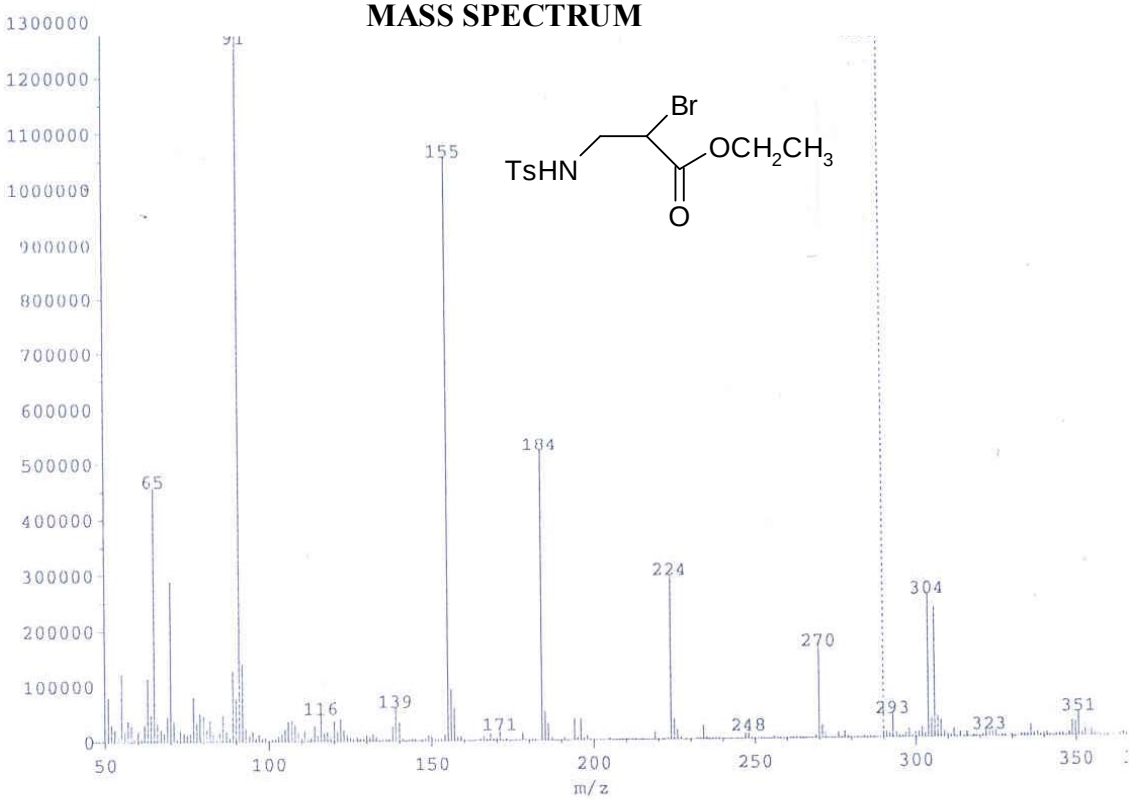

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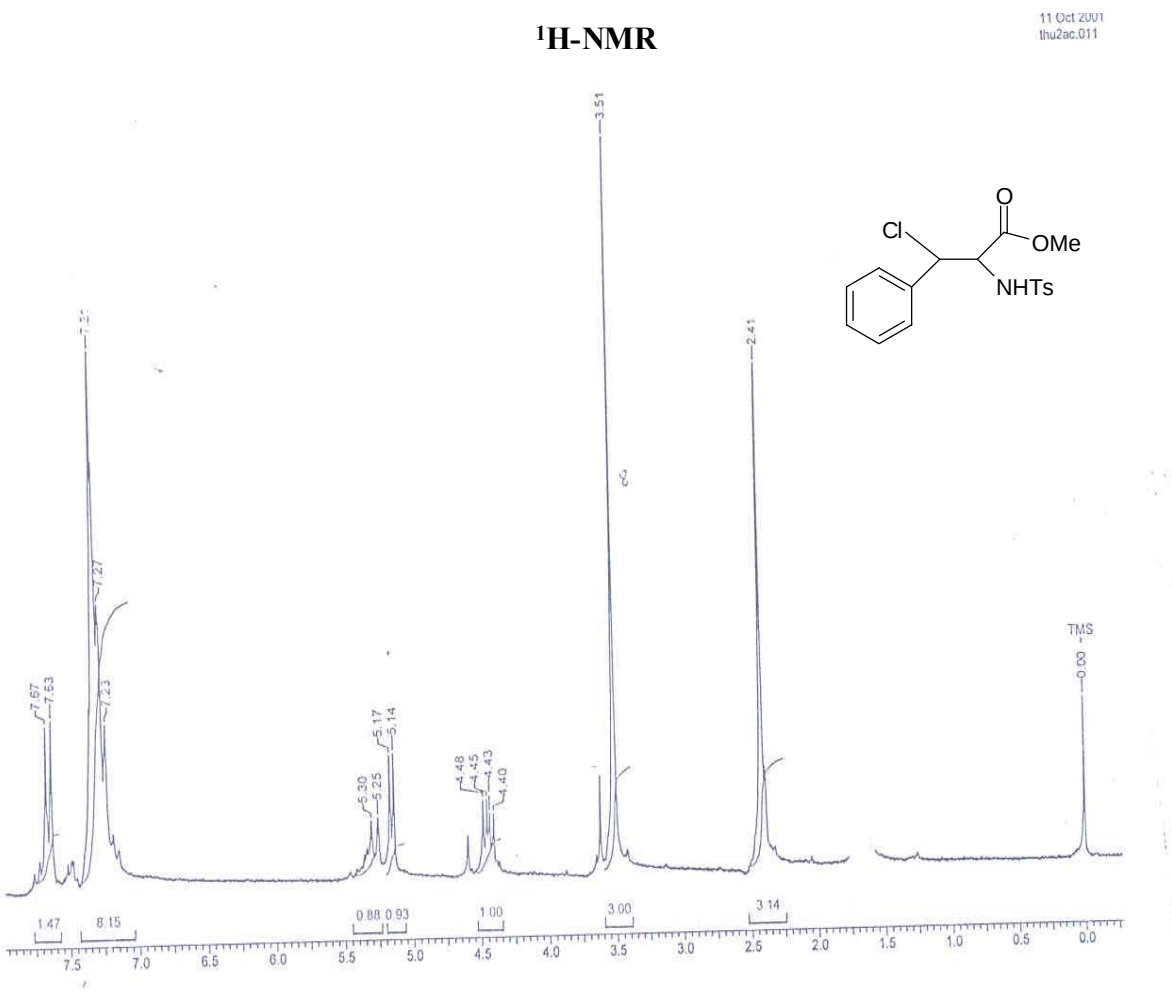
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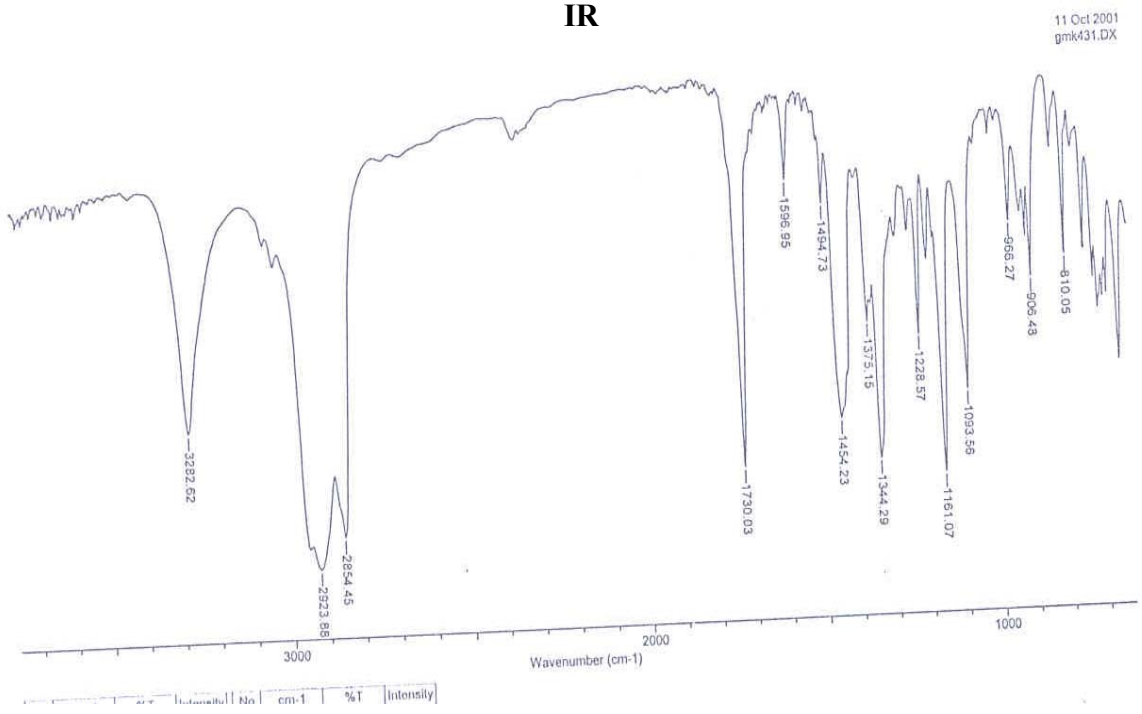
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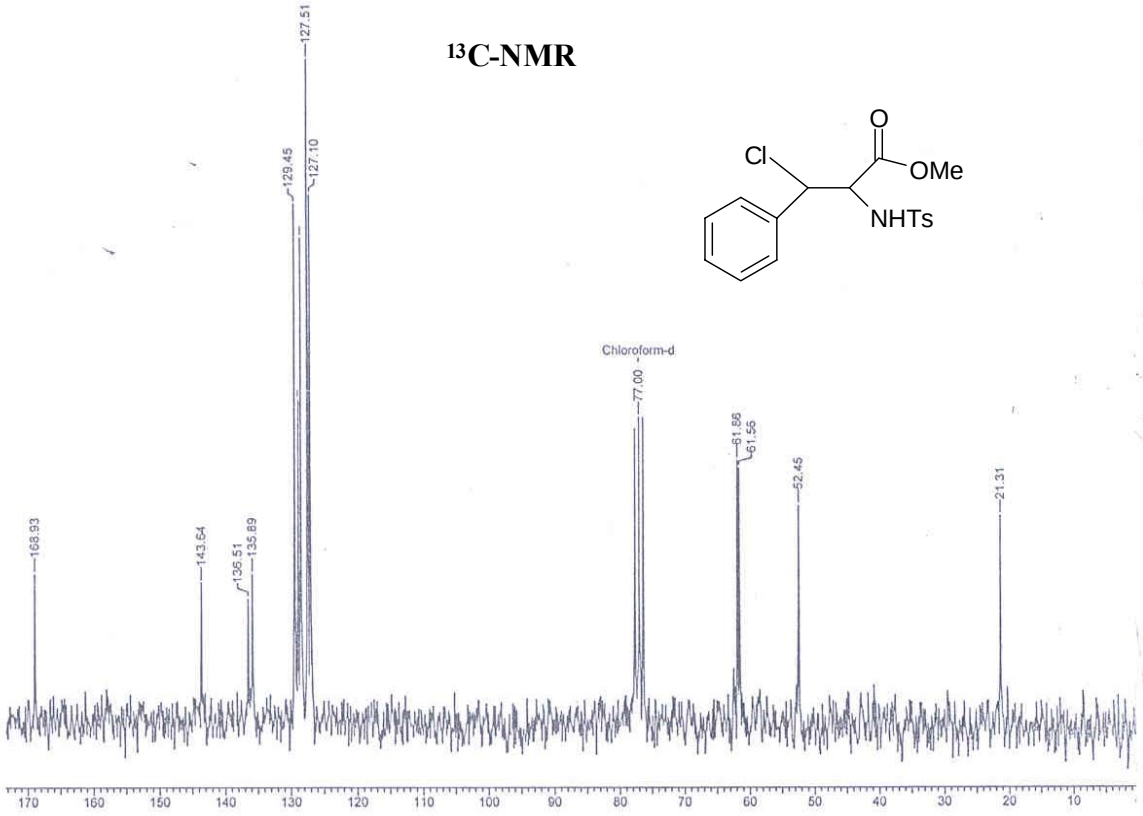

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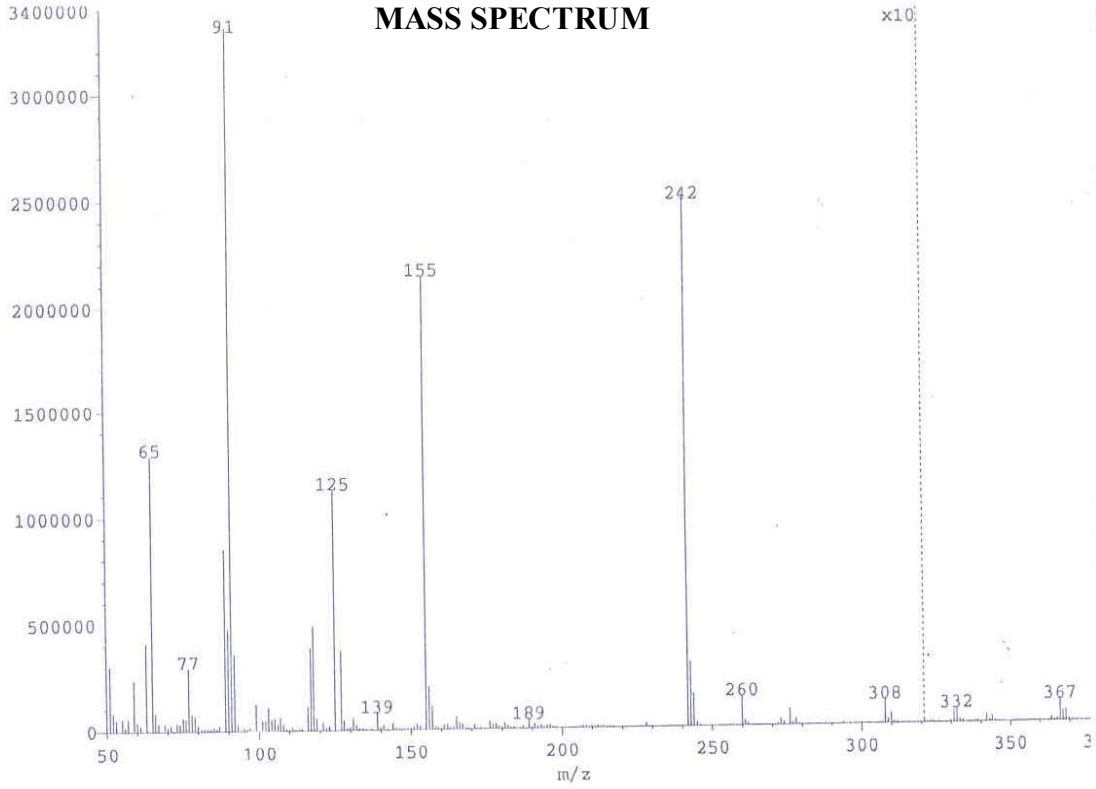

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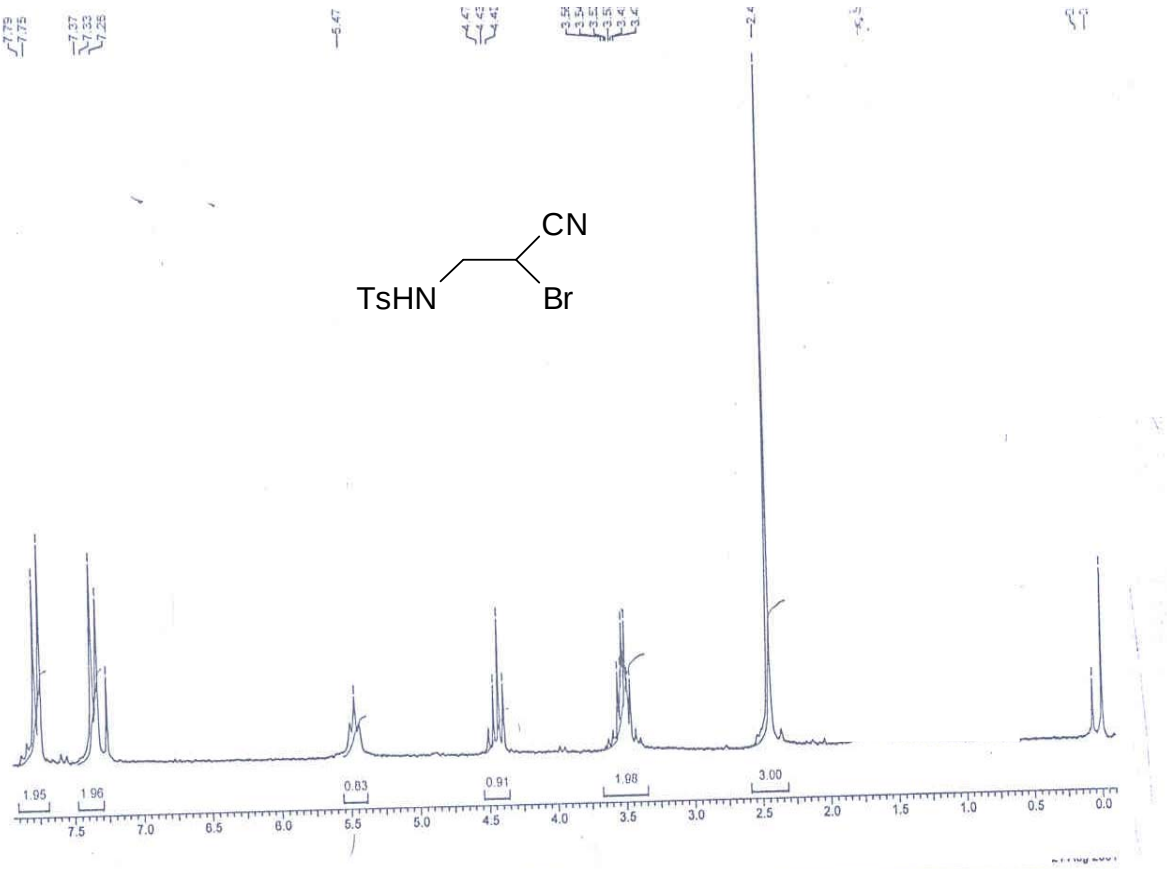
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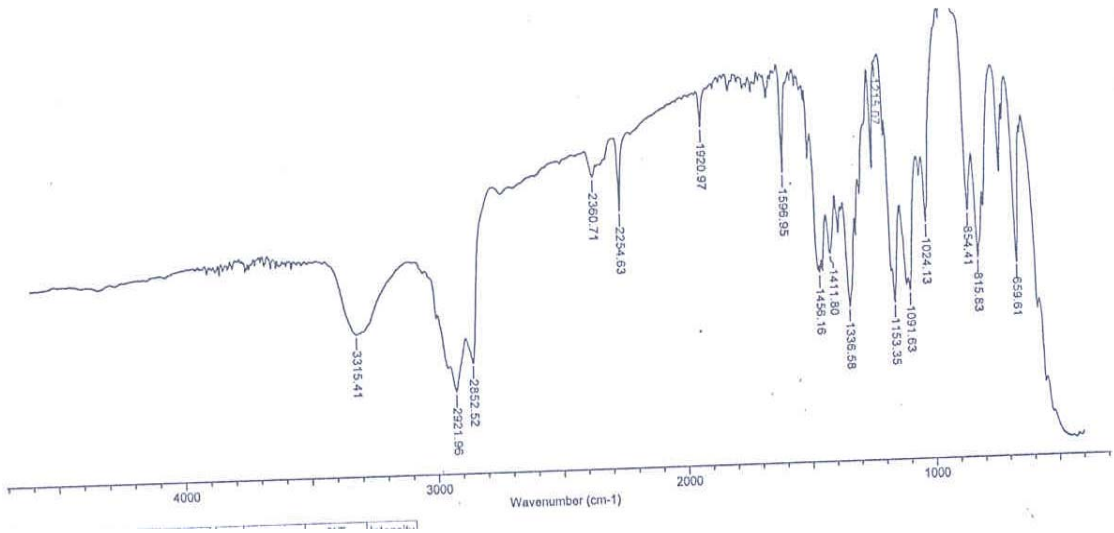
IR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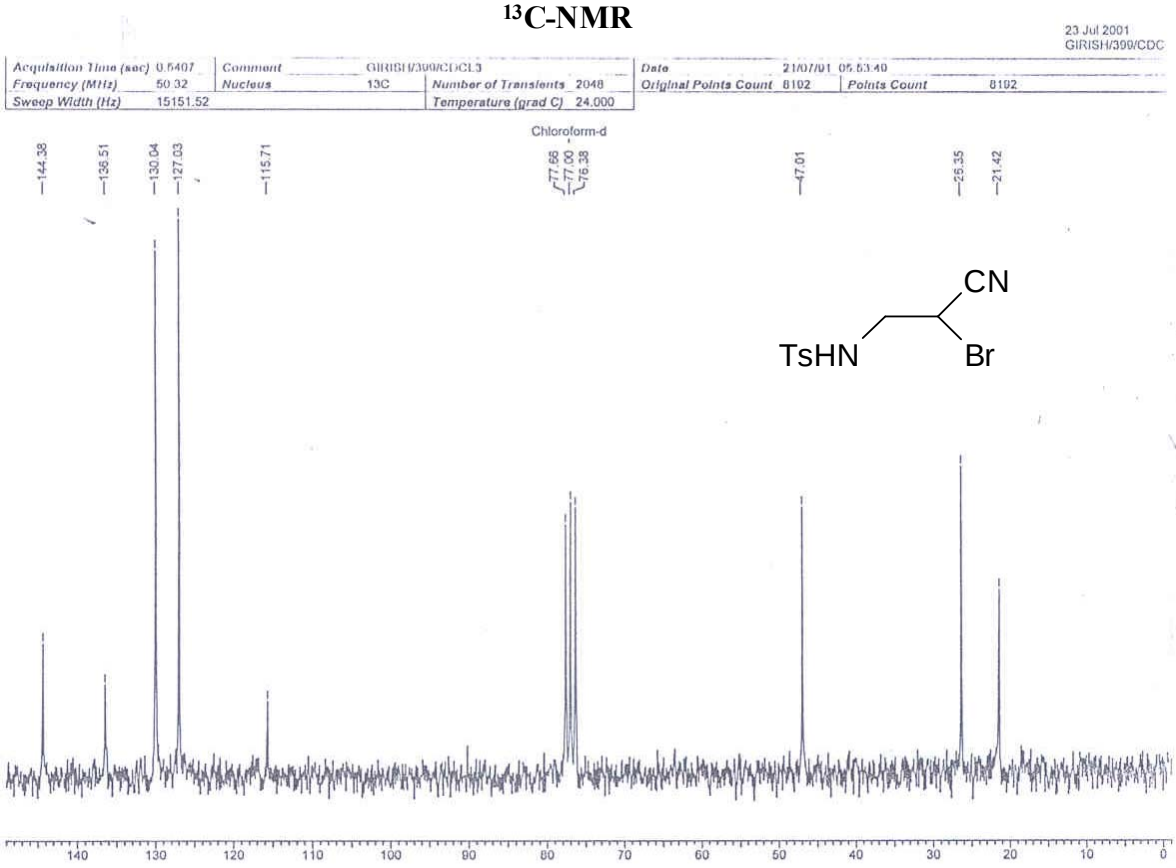
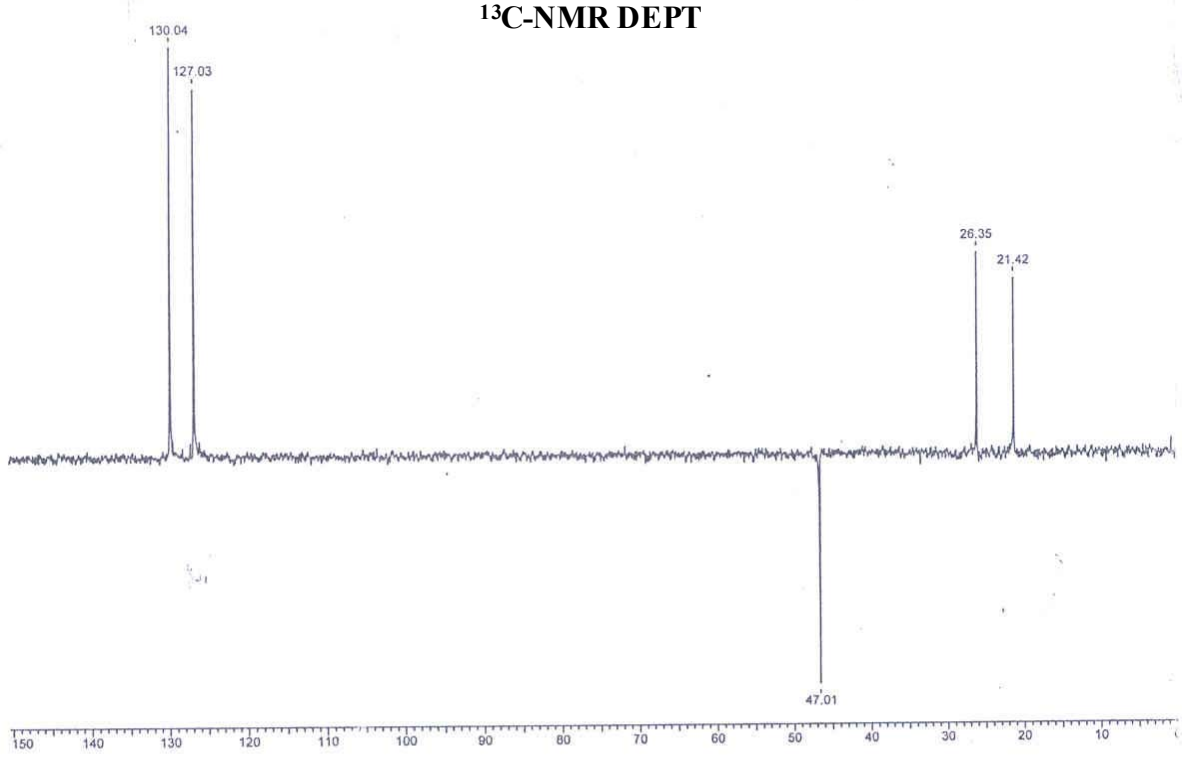
2852.52
2360.71
2254.63
1920.97
1599.95
1455.16
1411.80
1336.58
1153.35
1091.63
1024.13
854.41
815.83
659.61
4000
3000
2000
1000
Wavenumber (cm-1)

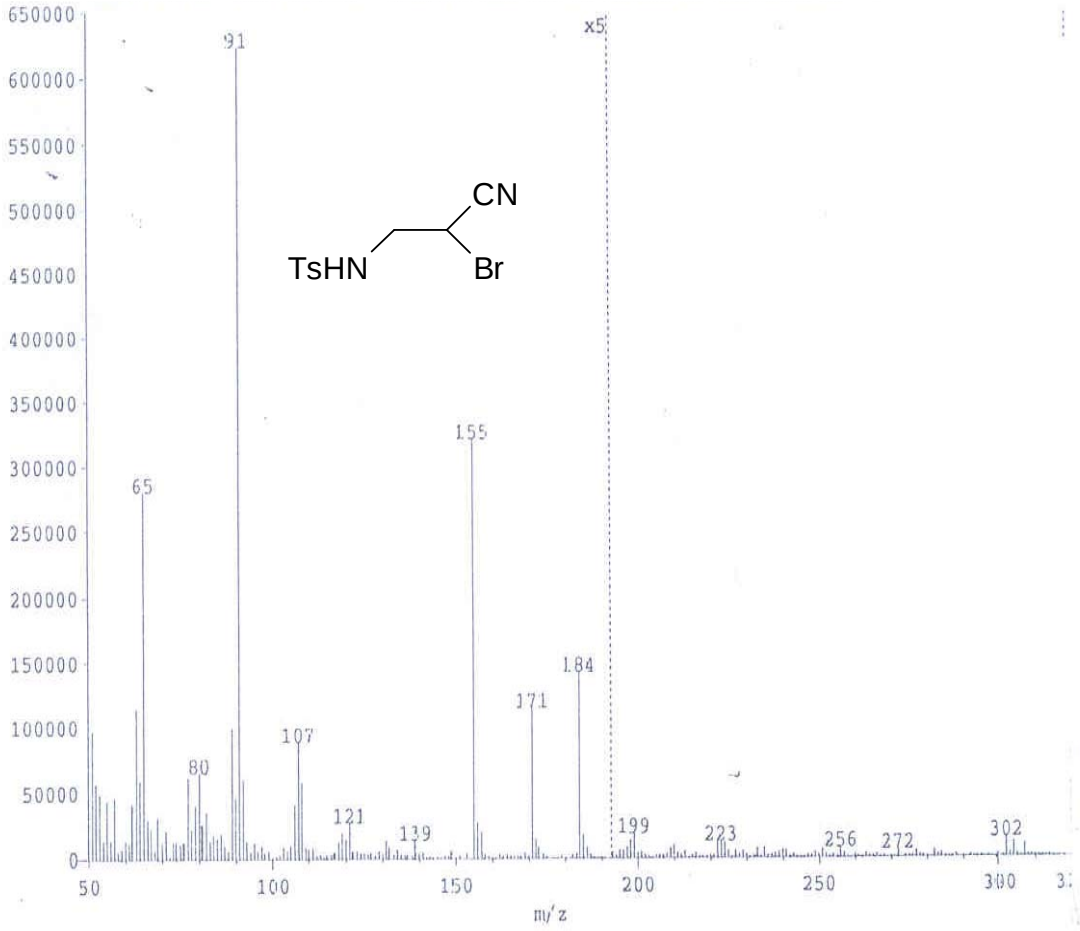
^{13}C-NMR



^{13}C-NMR DEPT



MASS SPECTRUM



^{1}H-NMR

1 Jun 2001
GIRISH/CDCL3

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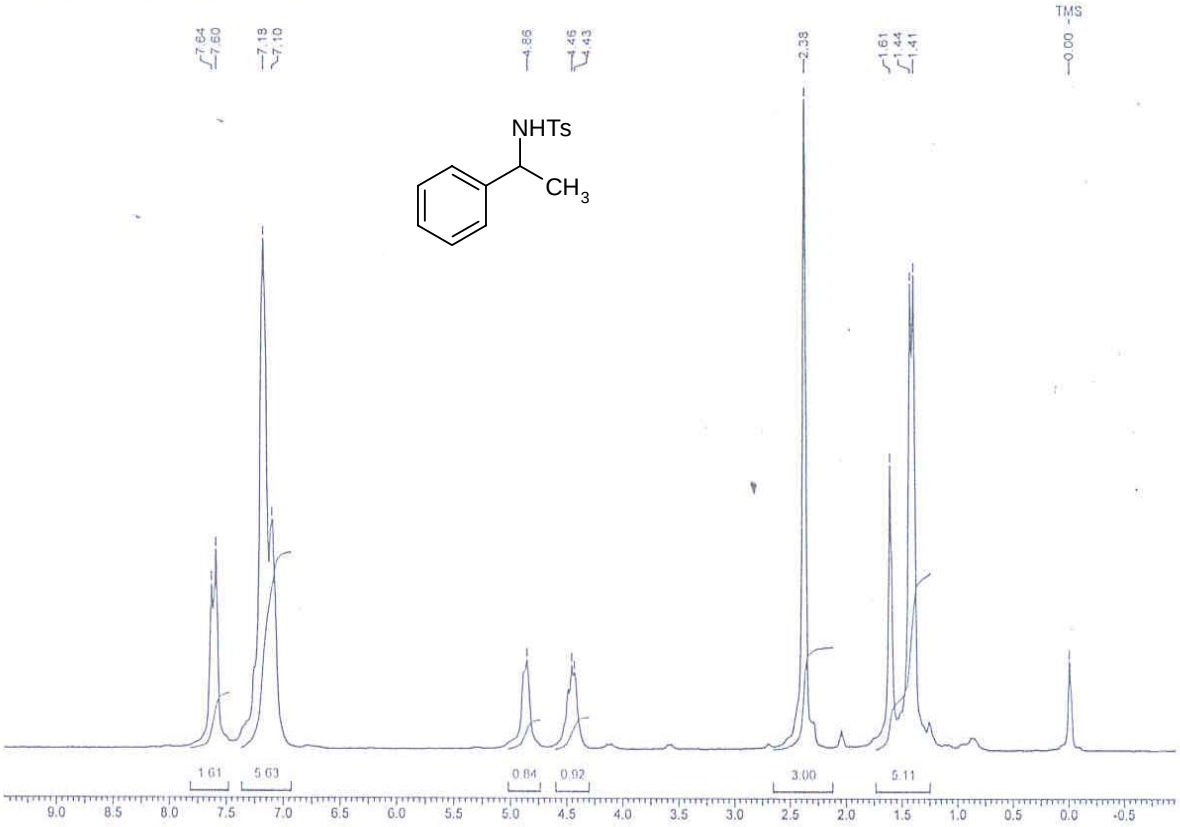
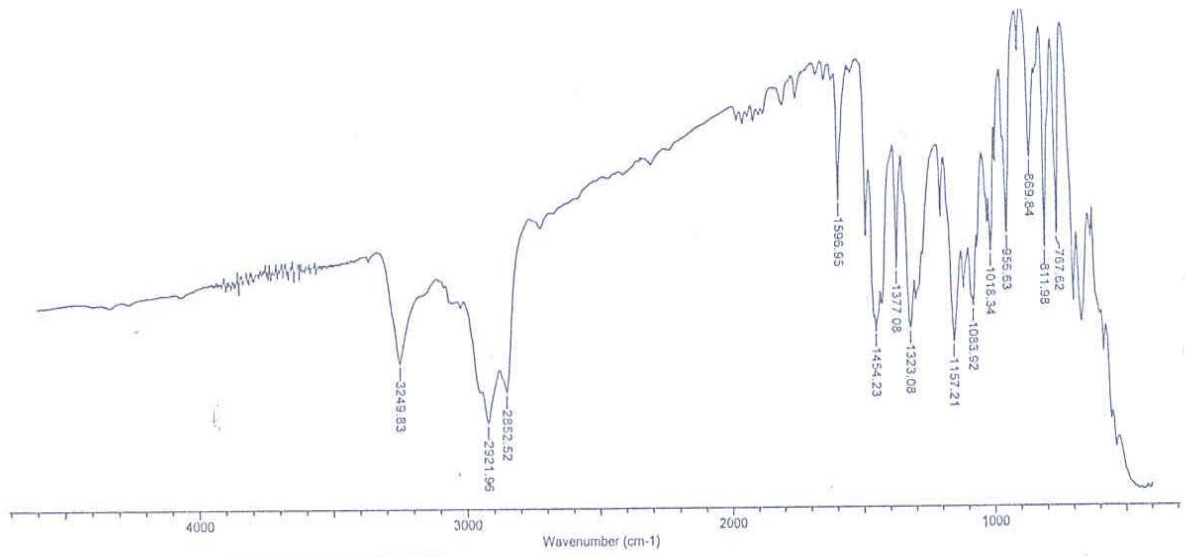
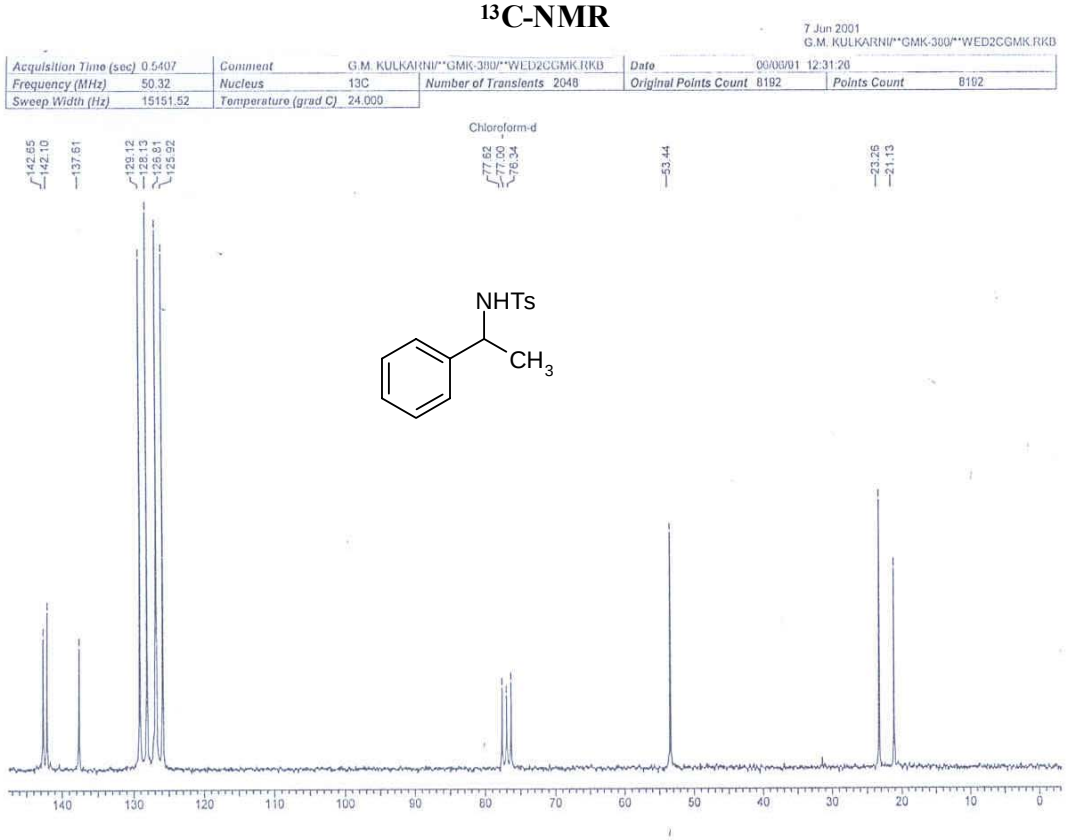


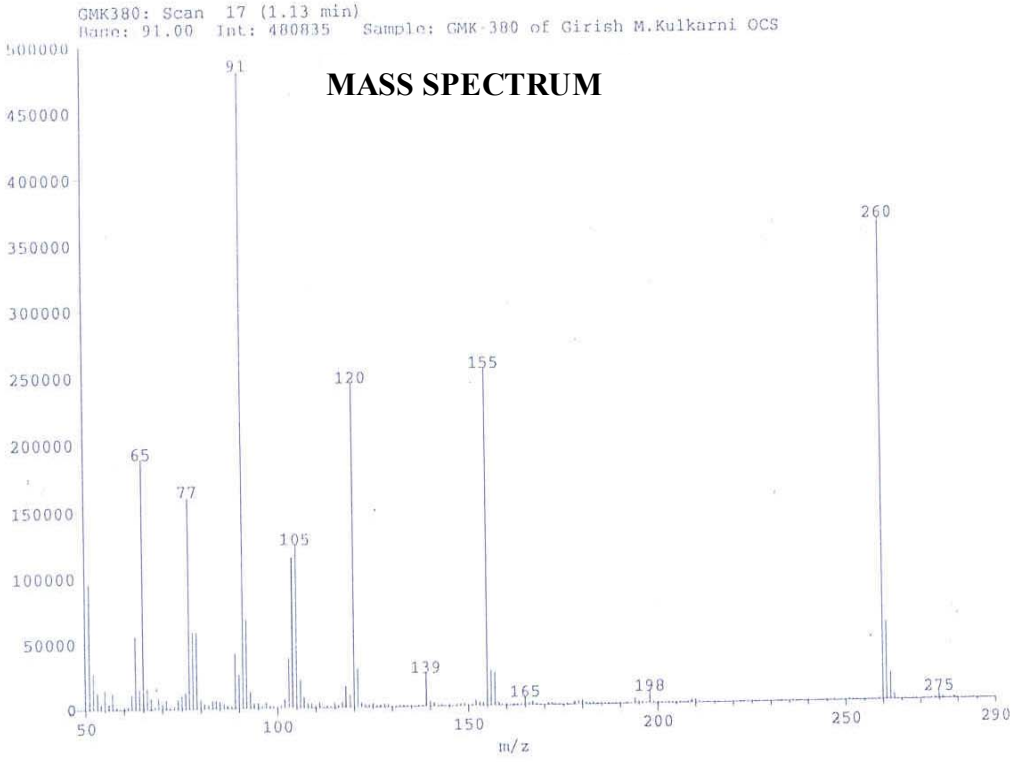
IR



^{13}C-NMR



MASS SPECTRUM



^{1}H-NMR

18 Apr 2001

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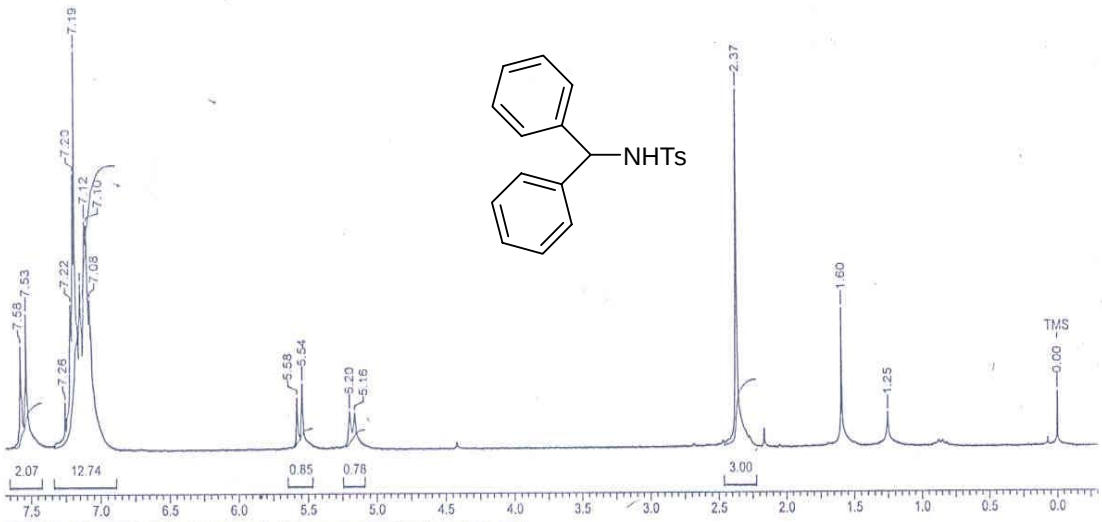

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1	0.00	0.135	10	7.10	0.565
2	1.25	0.082	11	7.12	0.573
3	1.60	0.349	12	7.15	0.415
4	2.37	0.097	13	7.19	1.000
5	5.16	0.086	14	7.20	0.692
6	5.20	0.090	15	7.22	0.364
7	5.54	0.161	16	7.26	0.115
8	5.58	0.125	17	7.53	0.341
9	7.08	0.374	18	7.58	0.258

No.	Annotation	(ppm)
1	TMS	0.00

IR

Title	G . M . KULKARNI - GMK - 350 - NUJOL - 24/ 8/2001	Date	01/08/24 11:37:13	Technique	Infrared
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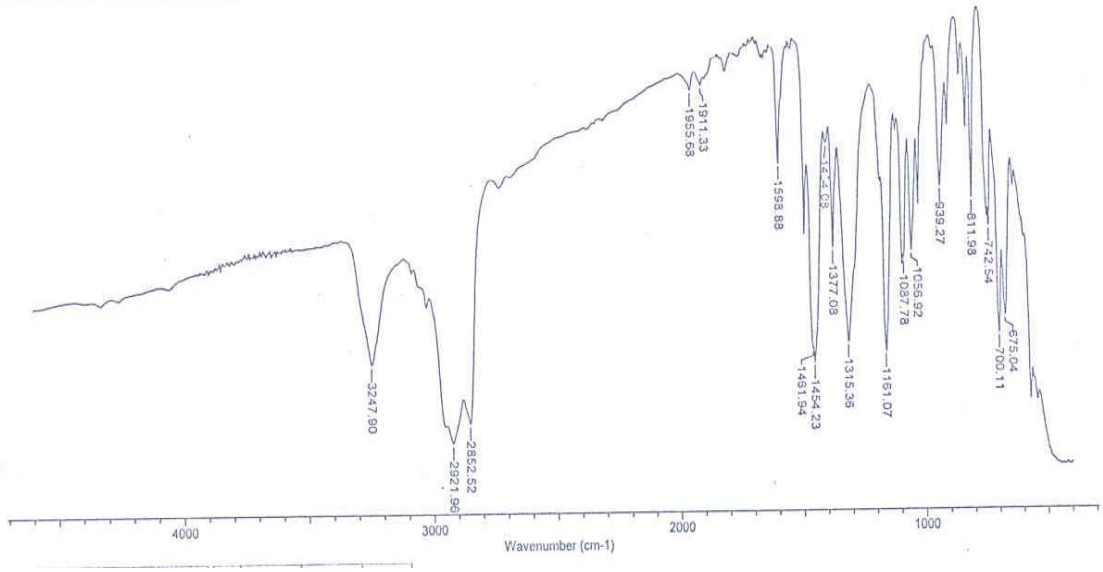

^{13}C-NMR

26 Apr 200

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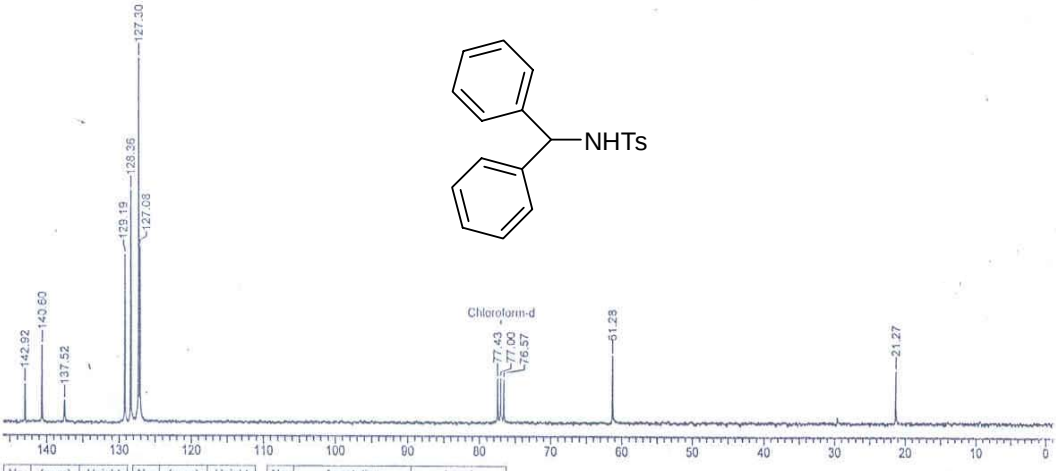

No.	(ppm)	Height	No.	(ppm)	Height
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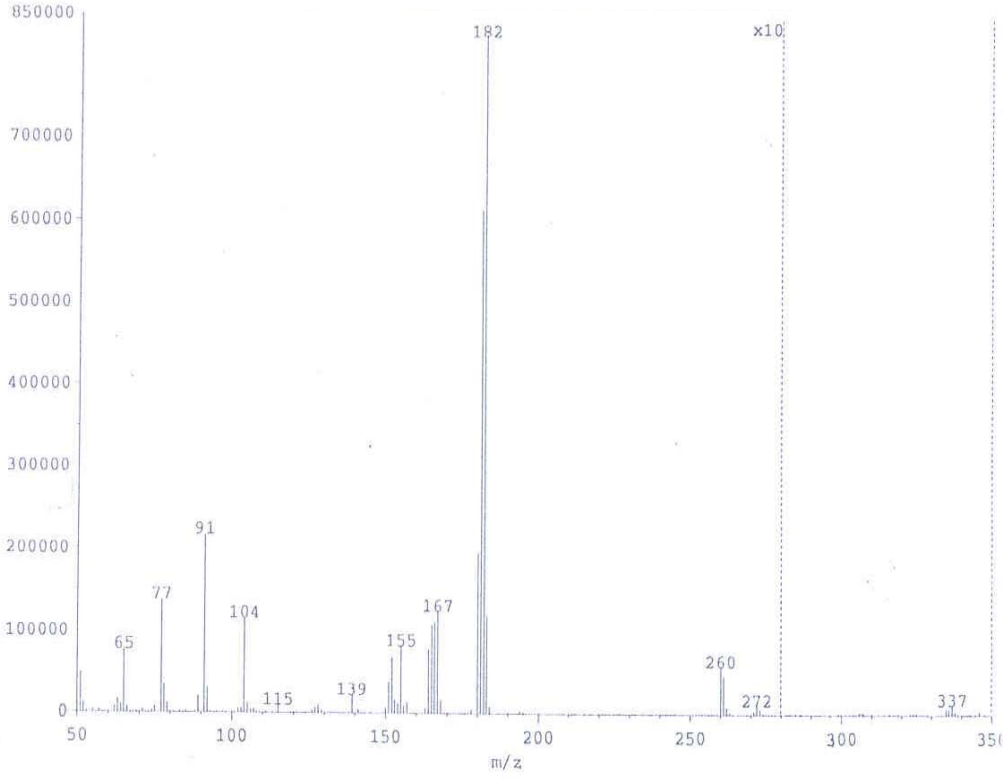
2	61.28	0.181	8	128.36	0.634
3	76.57	0.115	9	129.19	0.456
4	77.00	0.118	10	137.52	0.056
5	77.43	0.119	11	140.60	0.206
6	127.08	0.479	12	142.92	0.100

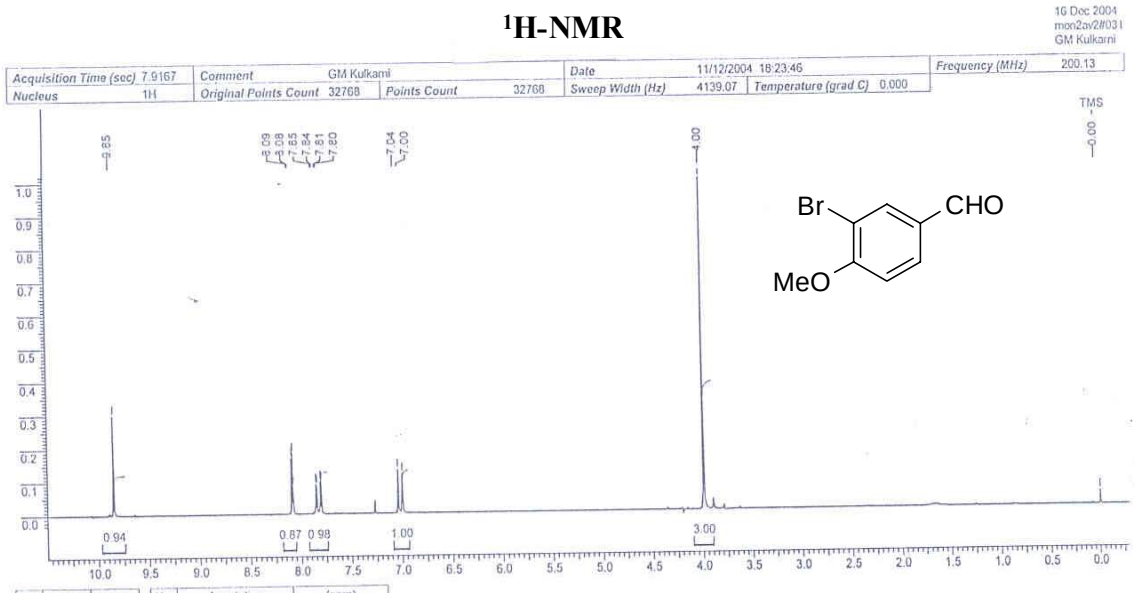
No.	Annotation	(ppm)
1	Chloroform-d	77.00

G:\thu4cgmk.rkb

MASS SPECTRUM



^{1}H-NMR



No.	(ppm)	Height
1	0.00	0.041
2	4.00	1.000
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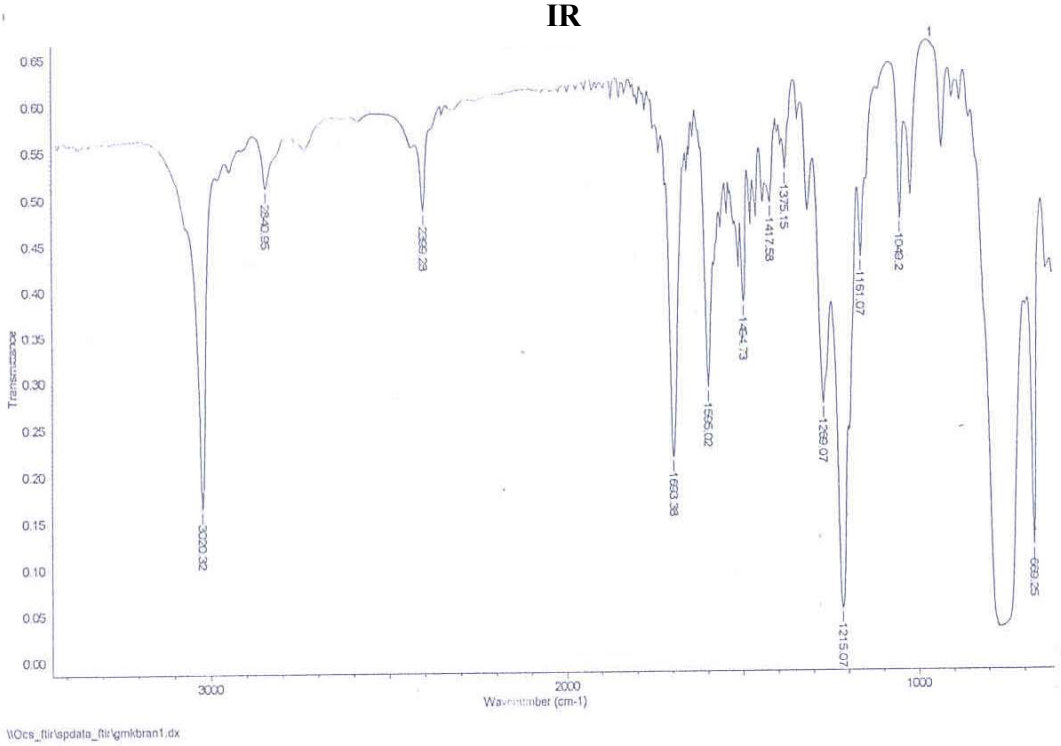
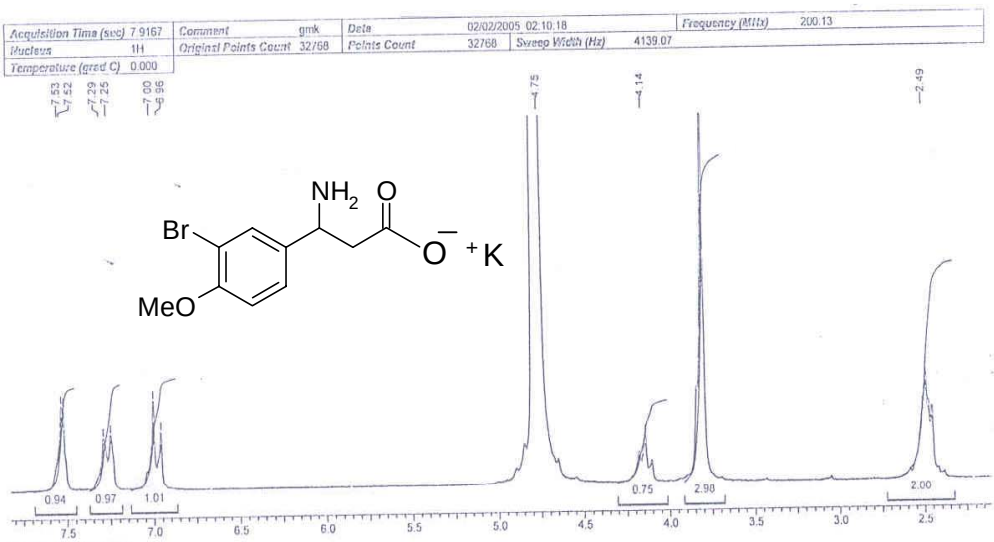
4	7.04	0.130
5	7.80	0.093
6	7.81	0.099
7	7.84	0.083
8	7.85	0.088
9	8.08	0.183
10	8.09	0.168
11	9.85	0.298

No.	Annotation	(ppm)
1	TMS	0.00

IR



^{1}H-NMR



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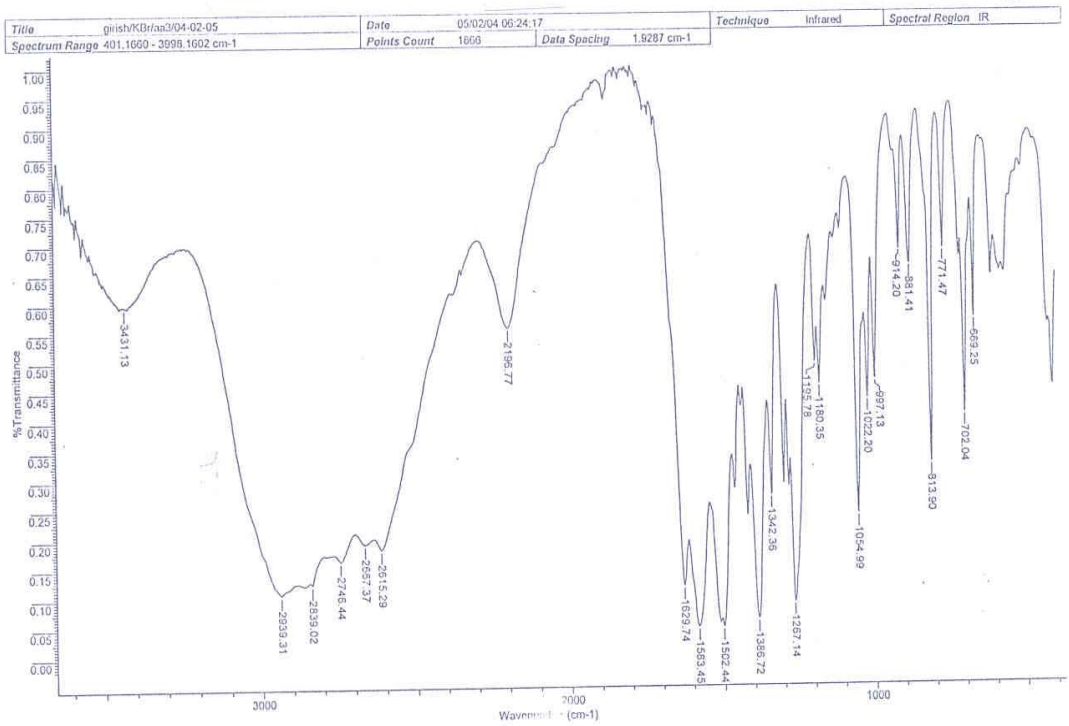
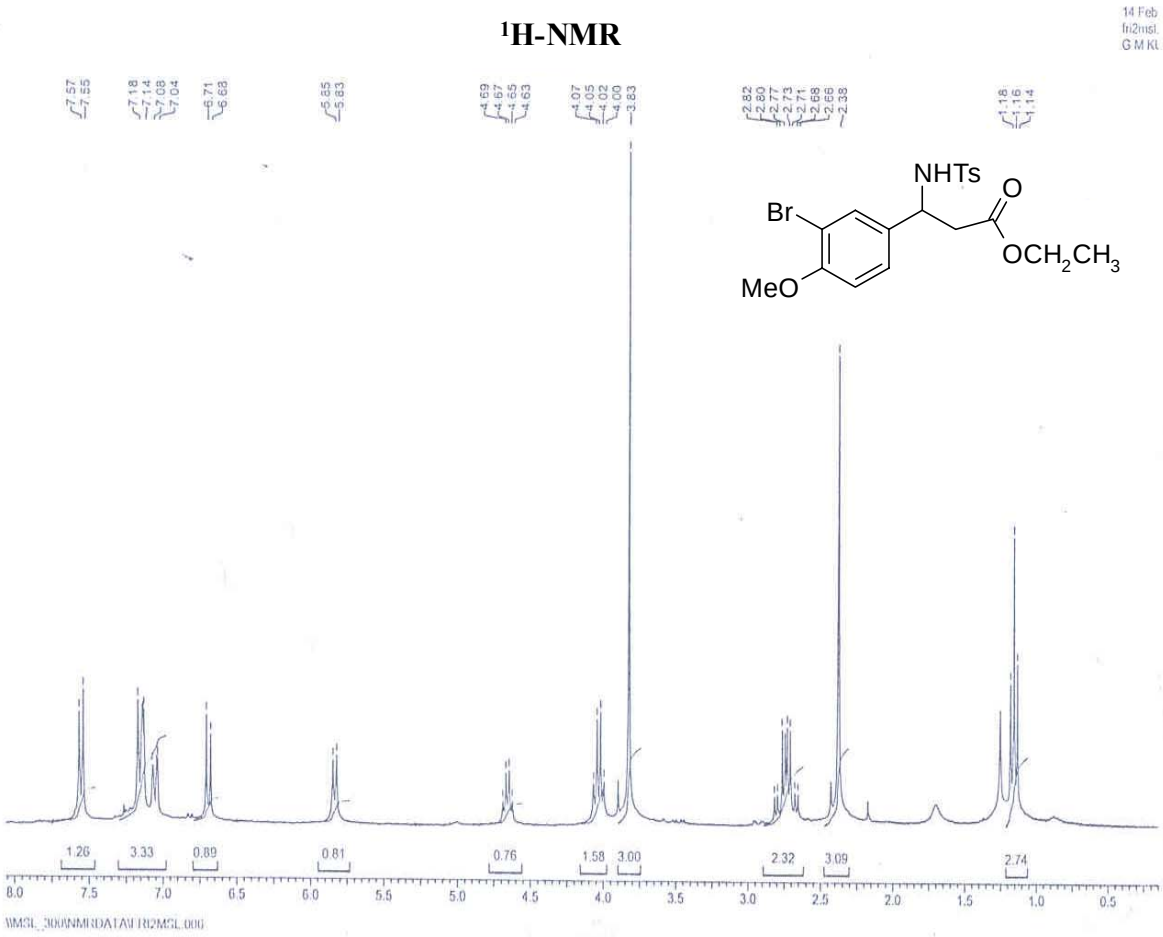
5	7.00	0.031
6	7.25	0.020
7	7.29	0.019
8	7.52	0.029
9	7.53	0.030

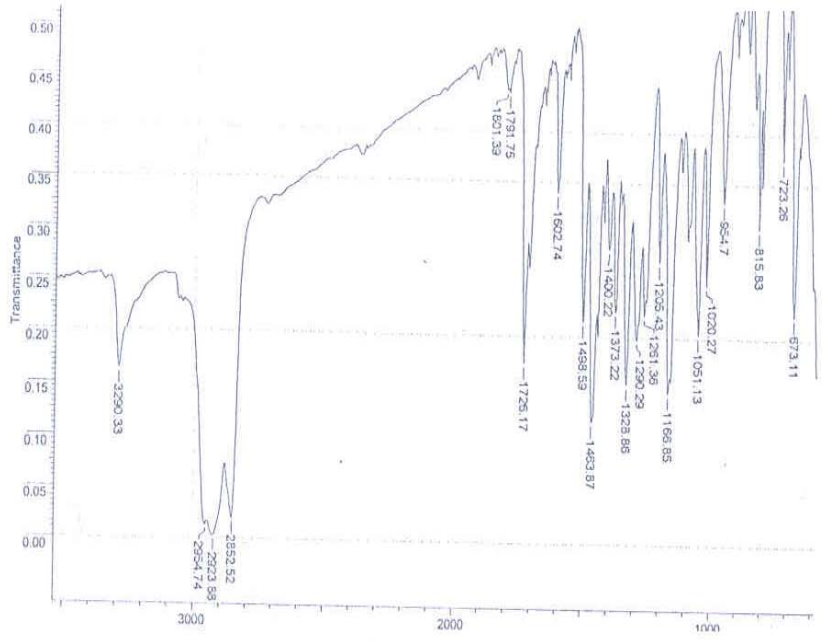
IR



^{1}H-NMR


14 Feb
fri2mst.
GMKL
NHTs
O
Br
OCH2CH3
MeO
1.26
3.33
0.89
0.81
0.76
1.58
3.00
2.32
3.09
2.74
WMSL_300NMRDATA\FR2MSL.000

IR


Transmittance
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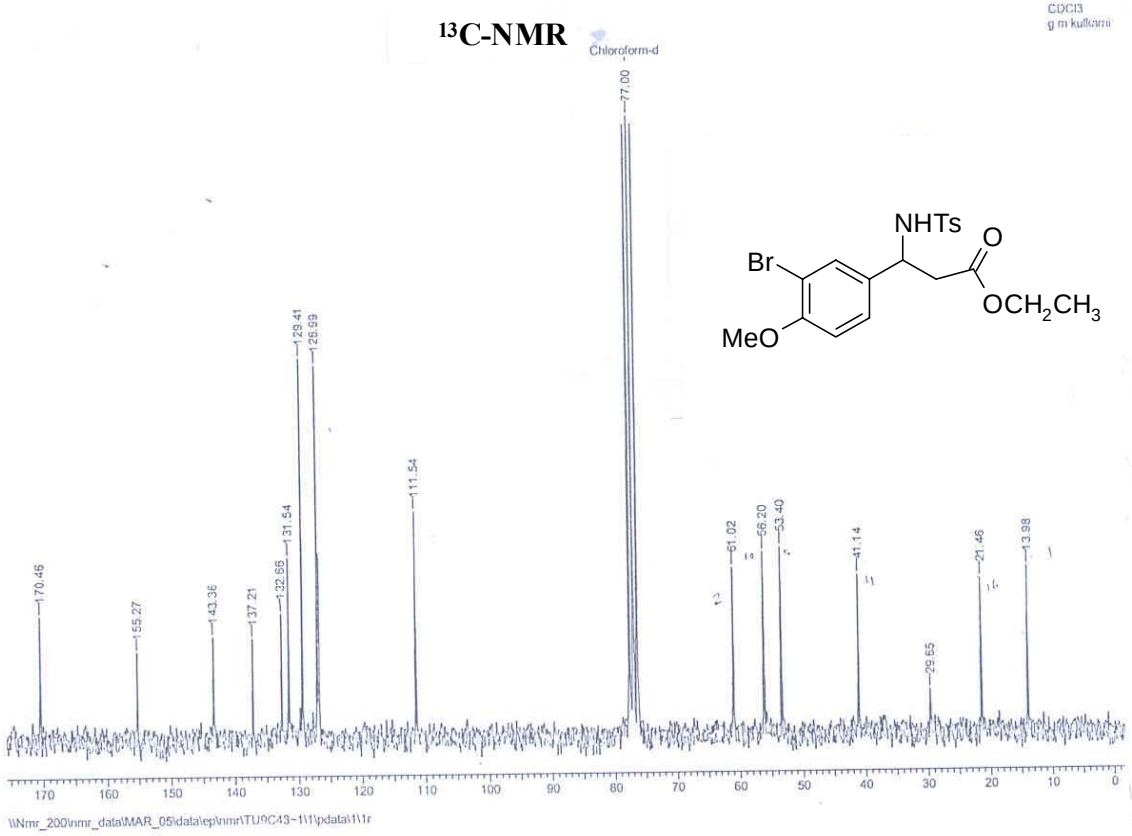
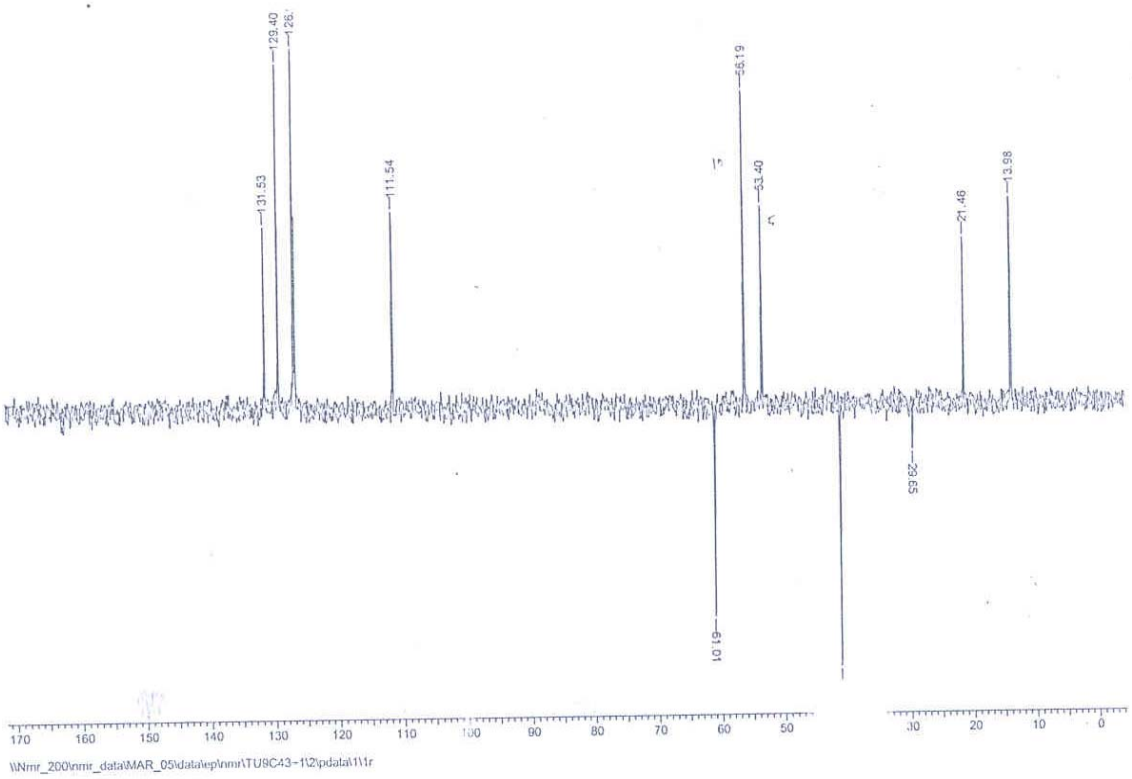
2954.74
2923.58
2852.52
1791.75
1601.39
1725.17
1602.74
1498.59
1463.87
1400.22
1373.22
1328.86
1290.29
1261.36
1205.43
1168.85
1051.13
1020.27
864.7
815.83
723.26
673.11
3000
2000

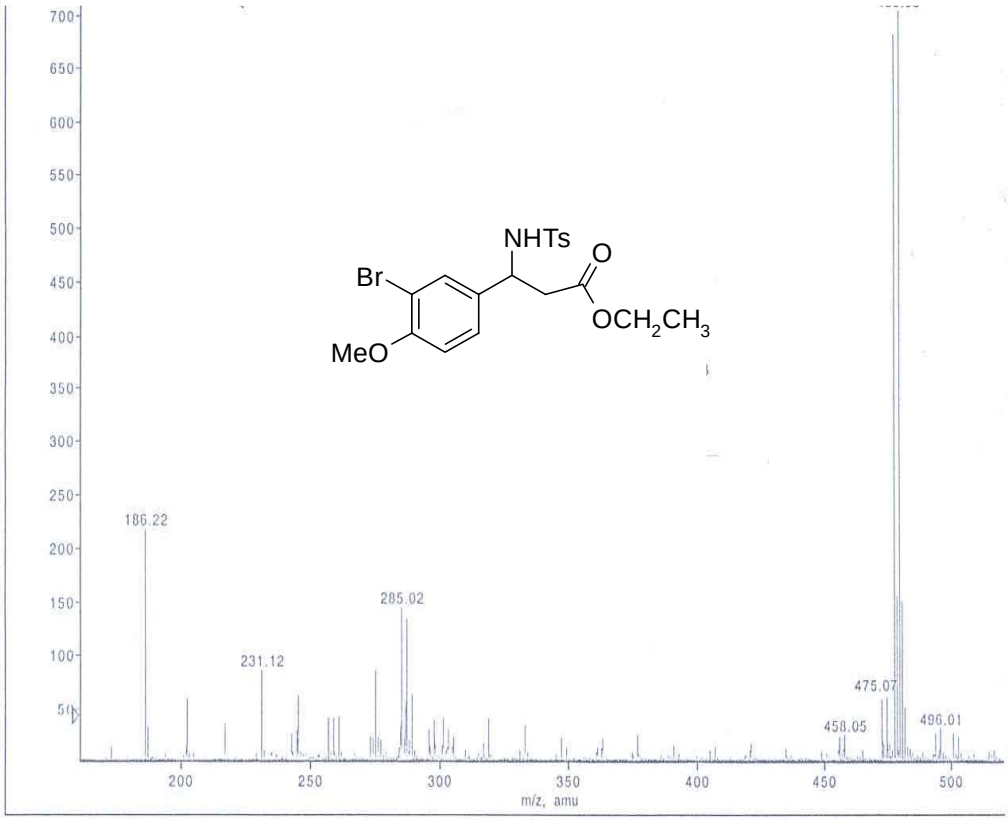
^{13}C-NMR



^{13}C-NMR DEPT



MASS SPECTRUM



^{1}H-NMR

31 Oct 2002

Acquisition Time (sec) 1.3648	Comment		Date	00/00/00 00:00:00		Frequency (MHz)	300.13
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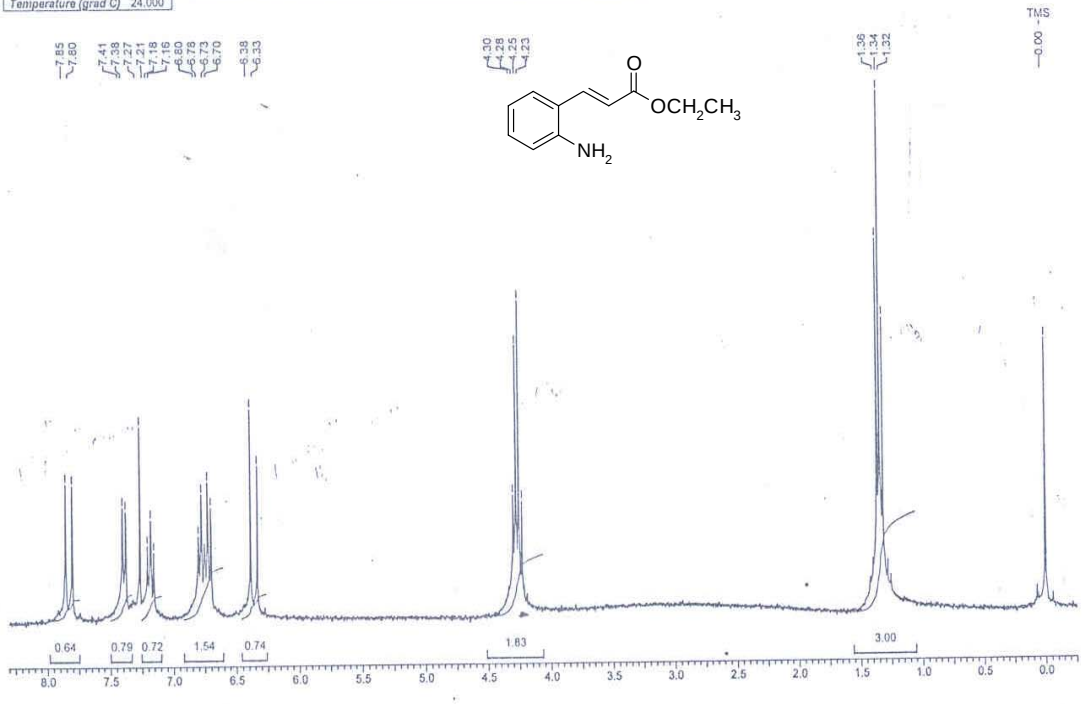

IR

CHCL3

Title GIRISH M. KULKARNI - GMK-716 - CHCL3 - 01-06-2004		Date	04/06/01 11:19:57	Technique	Infrared	Spectral Region	IR
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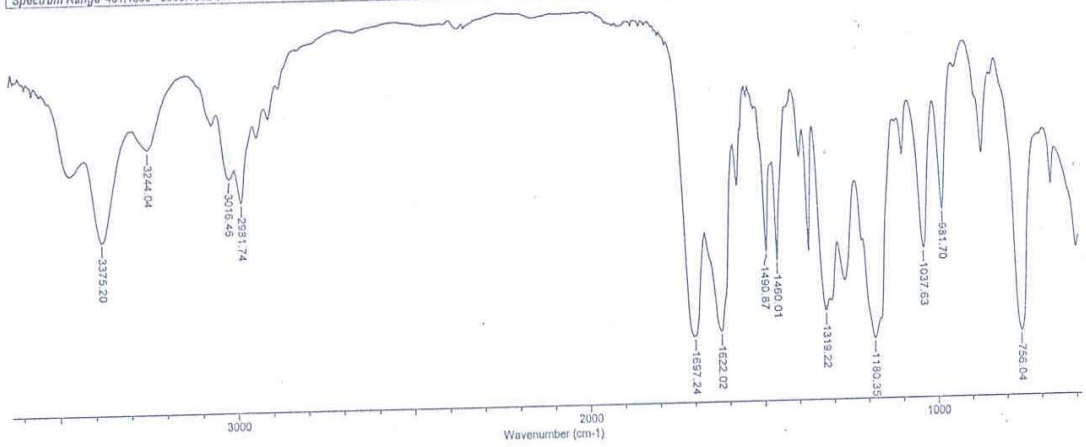


Chapter-3

Transition metal nitrenes - Application in the synthesis of N-heterocycle bicyclic compounds

3.1.1 Introduction

Cycloaddition reactions involving π-components containing transition metal-carbon multiple bonds have become increasingly popular for the synthesis of natural products.[1] The vast majority of these cycloadditions involve metallacarbenoids and lead to unstable metallacyclic intermediates that subsequently undergo reductive elimination[2]

or ligand-promoted reorganization.[3] Cycloadducts derived from metalcarbene complexes are relatively stable and have been found useful for selective carbon-carbon bond formation. Chromium carbene complexes or Fischer carbenes have wide variety applications in the synthesis of several heterocycles. For example Fischer carbenes have been used in the benzannulation reactions for e.g. Dotz benzannulation[4], formation of furan, pyrrole, indole, indene, cyclobutanone, beta-lactam, gamma-lactone, gamma-lactam and 3-hydroxypyridine.

Similarly, metallanitrenoids have been extensively used in C-N bond formation and synthesis of nitrogen containing heterocycles.[5, 6]

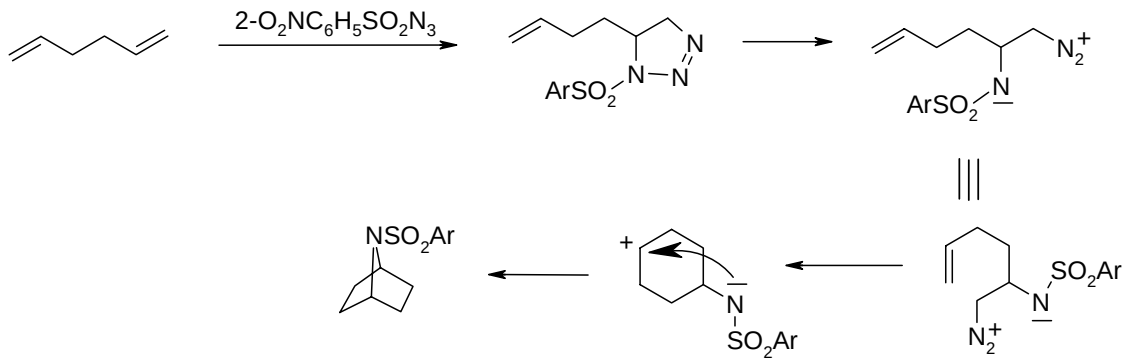
Nitrogen heterocycles especially pyrrolidine derivatives are wide spread among both natural products and medicinally important synthetic compounds.[7] Bicyclic derivatives of these compounds, basically 3-azabicyclo[3.3.0]octane framework, on the other hand are quite rare and only known from a few synthetic analogues such as prostacyclin (PGI_2)[8] antidiabetic glyclazide[9] and some antibacterial

quinonecarboxylic acid derivatives.[10] Besides their physiological activity bicyclic pyrrolidine[11] derivatives also serve as chiral auxillaries[13] in asymmetric transformations. There is also a considerable interest in the development of new methods for preparing cage-like oxaheterocycles[12] and rigid amine containing heterocycles (azacycles).[14]

Background

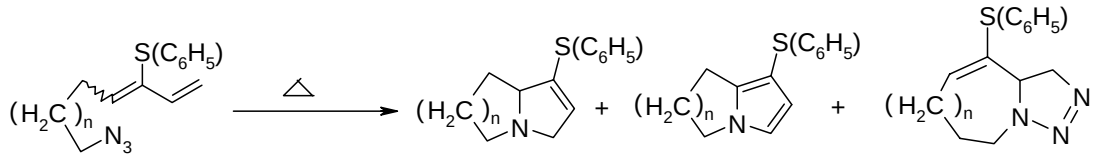
In the year 1981, it has been shown that the addition of aromatic sulfonyl azides to nonconjugated dienes lead to 2–azabicyclo[2.2.1]heptane derivatives via formation of triazoline then nitrogen extrusion and finally intramolecular substitution reaction[15] (Scheme-1).

Scheme-1



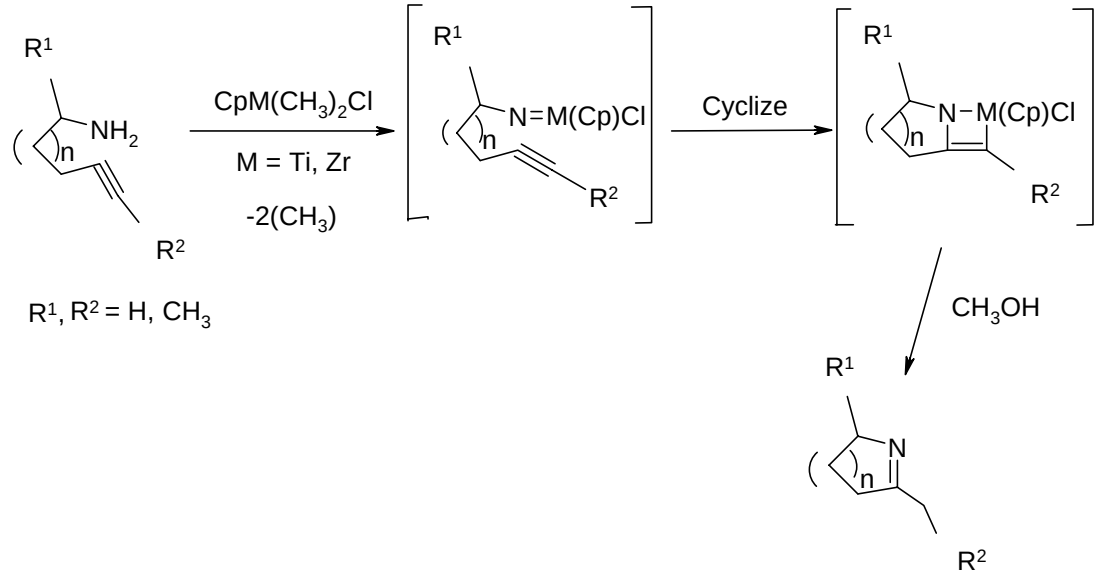
In the year 1986, William H. Pearson[16] have shown that cyclization of heterosubstituted ω-azidodienes provides fused bicyclic 3-pyrrolines in one operation. These pyrrolines are potentially useful intermediates for natural product synthesis (Scheme-2).

Scheme-2



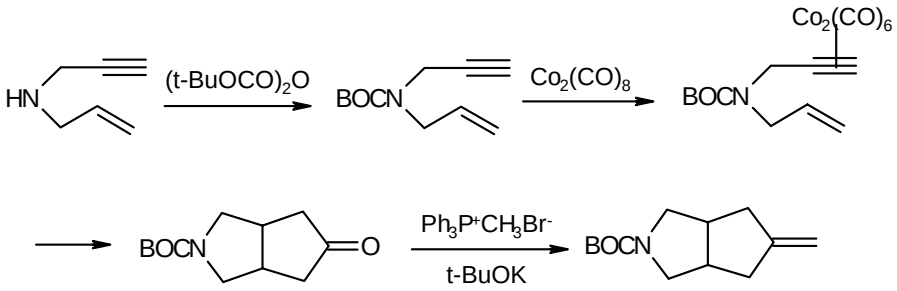
In the year 1992, Tom Livinghouse[17] et al have reported the synthesis of dihydropyrrole and tetrahydropyridine derivatives by the reaction of group (IV) imido complexes and alkylamine (Scheme-3).

Scheme-3



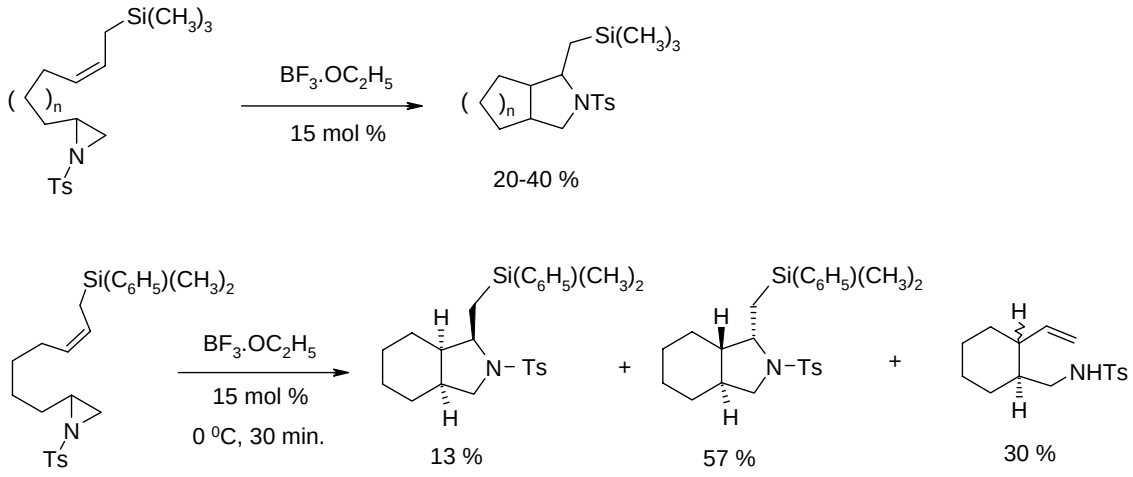
In the year 1993, Daniel P. Becker[18] et al have shown that an intramolecular reductive Pauson-Khand reaction of the hexacarbonyl complex of N-(tert-butyloxycarbonyl) allylpropargylamine under dry state adsorption conditions directly afforded the saturated N-boc-3-azabicyclo [3.3.0] octan-7-one when the reaction was performed under an inert atmosphere (Scheme-4).

Scheme-4



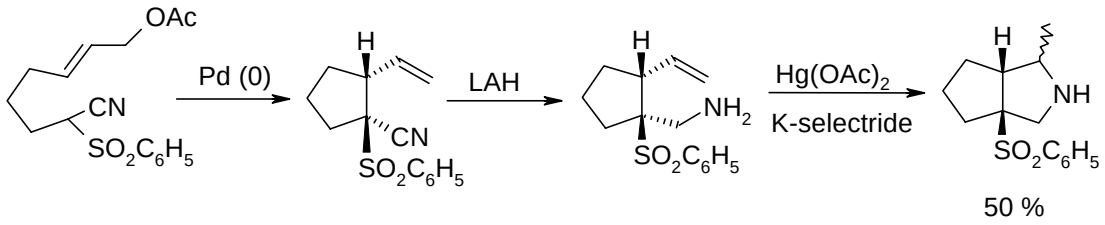
In the year 1999, bicyclic proline analogs using a formal [3+2] intramolecular aziridine –allylsilane cycloaddition reaction were synthesized. This synthesis allows for the preparation of both 5-5 and 6-5 fused ring systems and amenable to the preparation of analogs with substitution on the carbacyclic ring[19] (Scheme-5).

Scheme-5



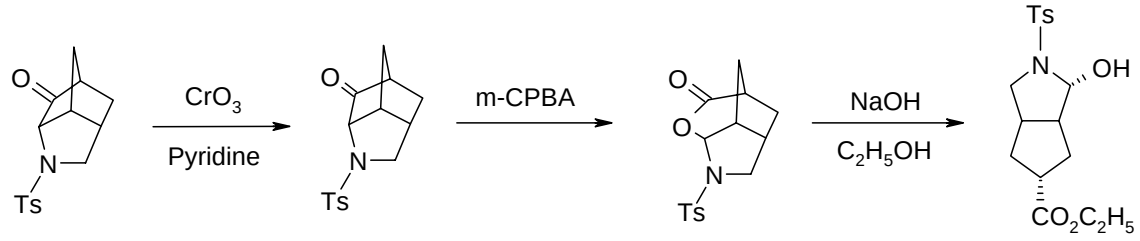
In the year 2000, Young-Ger Suh[20] et al. have developed Palladium catalyzed 1, 2-diastereoselective cyclization of the allylic precursors based on the steric nature of anion stabilizing groups. 1, 1, 2-trisubstituted cycloalkane products have been efficiently transformed into the azacyclic systems (Scheme-6).

Scheme-6



In the year 2003, the efficient synthesis of 3-azabicyclo[3.3.0]octane derivative has been achieved using commercially available starting materials and commonly used reagents by Ozdemir Dogan group[21] (Scheme-7).

Scheme-7



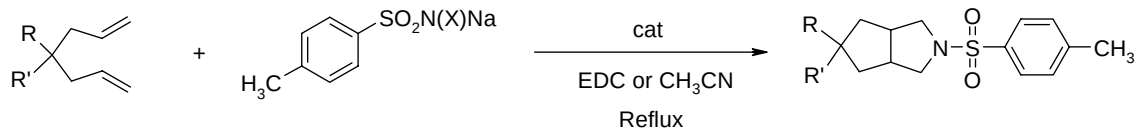
Objective

Our aim was to study the transition metal catalyzed formation of metal nitrenes by activating chloramine-T, bromamine-T, DBT and DCT to develop a methodology towards the synthesis of nitrogen containing heterocyclic compounds. In literature there were some reports on the generation of nitrenes from chloramine-T and transfer of nitrogen atom to olefins to form aziridines. Our strategy was to generate metal nitrenes from easily available simple precursors, chloramines-T, bromamine-T and study their application to the synthesis of new and novel heterocycles by reacting with 1, 6-dienes in the presence of various transition metal catalysts (Scheme-1).

3.1.2 Present work

Reactions of bromamine-T with 1, 6-diene in the presence of various transition metal complexes were carried out in refluxing EDC or CH_3CN.

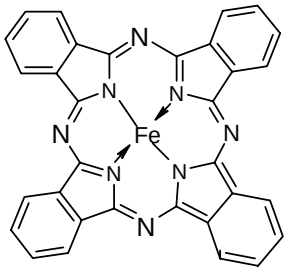
Scheme-1



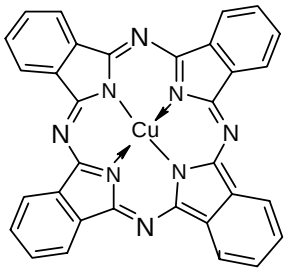
R = $COOC_2H_5$, CN
R' = $COOC_2H_5$

X = Cl, Br

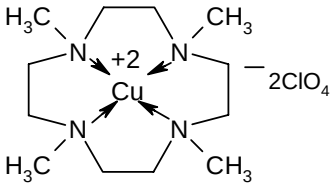
Catalysts



Fe(Pc)



Cu(Pc)

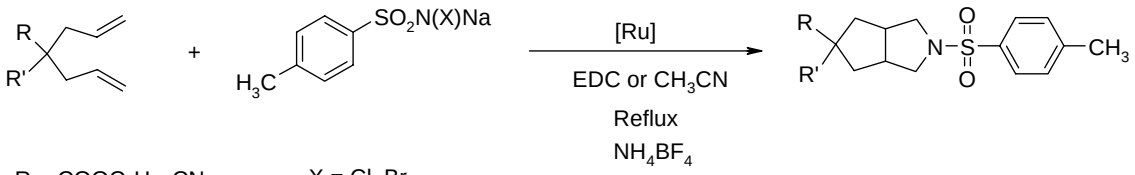


Cu(TMCyclam)

Ruthenium catalyzed reaction of bromamine-T with 1, 6-diene

Various cyclopentadienyl ruthenium complexes were also used for the reaction of bromamine-T with 1, 6-diene.

Scheme-2

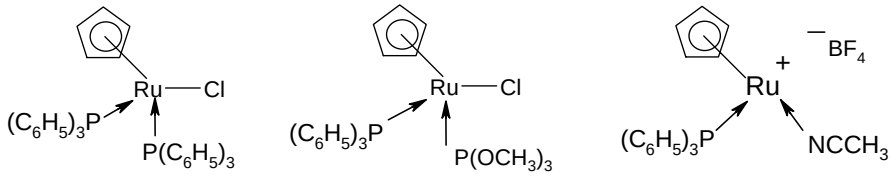


R = $COOC_2H_5$, CN

R' = $COOC_2H_5$

X = Cl, Br

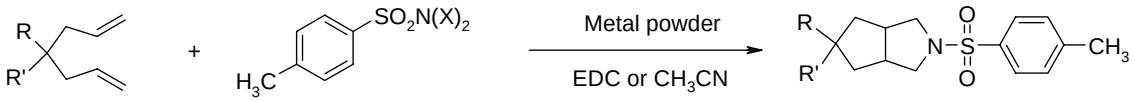
[Ru] =



Cu, Zn metal powder catalyzed reaction of DCT/DBT with 1, 6-diene

Metal powder catalyzed reactions of dihaloamines (e.g. DBT and DCT) with 1, 6-dienes were carried out in EDC or CH_3CN at refluxing condition.

Scheme-3



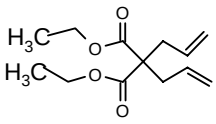
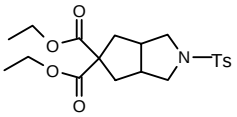
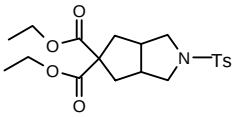
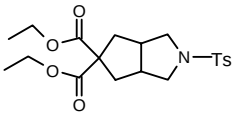
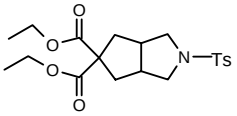
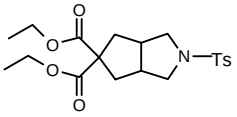
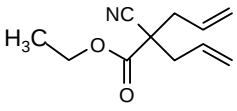
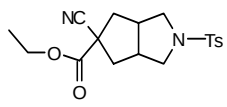
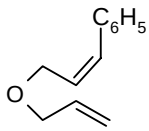
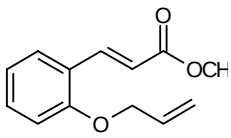
R = $COOC_2H_5$, CN

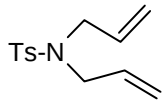
R' = $COOC_2H_5$

X = Cl, Br

Metal powder = Cu, Zn

TABLE : 1 Transition Metal Catalyzed formation of pyrrolidines

Sl. No.	Nitrogen Source	Substrate	Catalyst	Product	Yield (%)
1.	Bromamine-T		$ZrOCl_2$[a]		41
2	Bromamine-T	,,	Fe(Pc) [b]		46
3	Bromamine-T	,,	Cu(Pc)[a]		41
4	Bromamine-T	,,	$CaOCl_2$[a]		25
5	Bromamine-T	,,	Cu(tmcyclam) [a]		34
6	Bromamine-T		Fe(Pc) [b]		20
7	Bromamine-T		Fe(Pc)	–	–
8.	Bromamine-T		Fe(Pc)	–	–

9.	Bromamine-T		Fe(Pc)	–	–

Reaction conditions:1, 6-diene(1mmol)+Bromamine-T(1.2mmol)+Cat(30mg-stoichiometric)+Molecular sieves 4A°+Solvent; Reflux ; [a]CH_3CN, [b]EDC

Results and Discussion

Initially, the copper chloride catalyzed reactions of nitrene precursors especially chloramine-T with 1, 6-dienes has been started by our group[22]. These reactions were studied for insertion and cyclization of metal nitrenes to form azacycles. The catalysts that we chose have already been found to catalyze aziridination reaction. Fe(Pc)[23], $CaOCl_2$ [24] have been used for the aziridination reaction of bromamine-T and olefins.

The reaction of bromamine-T with 1, 6-diene was carried out in the presence of various transition metal catalysts and metal salts for example Fe(Phthalocyanin), $ZrOCl_2$, Cu(Pthalocyanin), $CaOCl_2$, Cu(Tmcyclam) under inert atmosphere and at reflux condition in the acetonitrile or dichloroethane as solvent. The yield of the bicyclic pyrrolidines was moderate. Out of these catalysts Fe(Pc) gave the highest yield of the product i.e. 46%. The reason could be the better stabilization of the in situ formed nitrene intermediate by the phthalocyanin ligand and thereby transfer to bis olefin to form the bicyclic compound. In the case of other catalysts the yield of the product was between 20-45%. In all the reactions the rest was starting material obtained back.

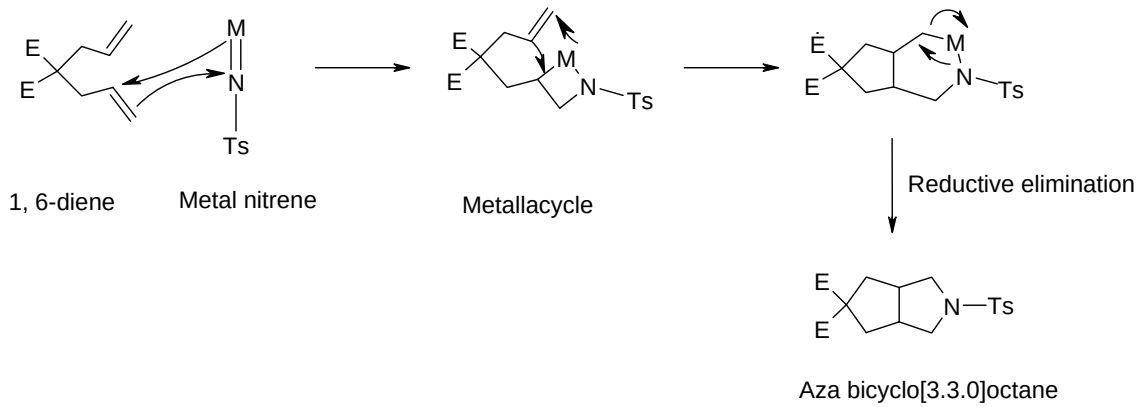
In the case of Fe (Pthalocyanin) catalyzed reaction, the bicyclic product obtained when EDC used as solvent, whereas in acetonitrile some other product obtained but could not able to identify as the 1H-NMR was complex.

Other reactions of 1, 6-diene and dibromamine-T, dichloramine-T in the presence of Cu, Zn powder were tried. In the reaction of DBT and 1, 6-diene in the presence of copper powder in EDC, poor yields of bicyclic pyrrolidines was obtained. The reaction shows that under these conditions the metal nitrene formed by DBT and copper powder insert into bis olefin to give the product. Zn-powder catalyzed reactions of DBT and DCT failed to give the product. Bromamine-T gave 32 % yield of the bicyclic pyrrolidine when treated with 1, 6-diene in the presence of copper chloride. Our group have reported copper chloride catalyzed reaction chloramine-T with 1, 6-diene for the formation of azetidines.[22]

Reactions of 1, 6-diene with bromamine-T in the presence of $(\eta^5\text{-}C_5H_5)Ru\{P(C_6H_5)_3\}_2Cl$ and NH_4BF_4 or thiophene as co-catalyst didn't yield the expected pyrrolidine product. $TsNH_2$ obtained as major product. In the $Pb(OAc)_4$ catalyzed reaction of 1, 6-diene and $TsNH_2$ failed to yield the product. The starting material was recovered back. $Fe(CO)_5$ catalyzed reaction of 1, 6-diene with p-nitrotoluene didn't yield the desired product.

Other dienes were also tried for the cyclization with various nitrogen sources. allylcinnamate, 2-(O-allyl) ethyl cinnamate with bromamine-T and $ZrOCl_2$, Fe (Pc) as catalyst didn't yield the product. No bicyclic product was obtained in the case of CuCl catalyzed reaction of [N-(p-tolylsulfonyl)imino]phenyliodinane and 1, 6-diene. Various dienes like diallylether, N, N-diallyl p-toluene sulphonamide, allyl cinnamyl ether and 2-(O-allyl) ethyl cinnamate were used for cyclization with different nitrene sources but to our disappointment there was no product formation found.

Mechanism



The pathway for the formation of azabicyclo compound was schematically shown in the mechanism above. First, the metal nitrene formed by the reaction of nitrene precursor and the catalyst undergoes [2+2] cycloaddition reaction with one of the double bonds of diene to form metallacycle. Then subsequent insertion of other double bond into metallacycle and reductive elimination lead the azabicyclo (pyrrolidine derivative) compound.

Spectral Analysis

The spectral analysis of Diethyl-N-[(4-methylphenyl)sulphonyl]-3-azabicyclo[3.3.0]octane-7, 7-dicarboxylate **(Fig-1)** explained as follows.

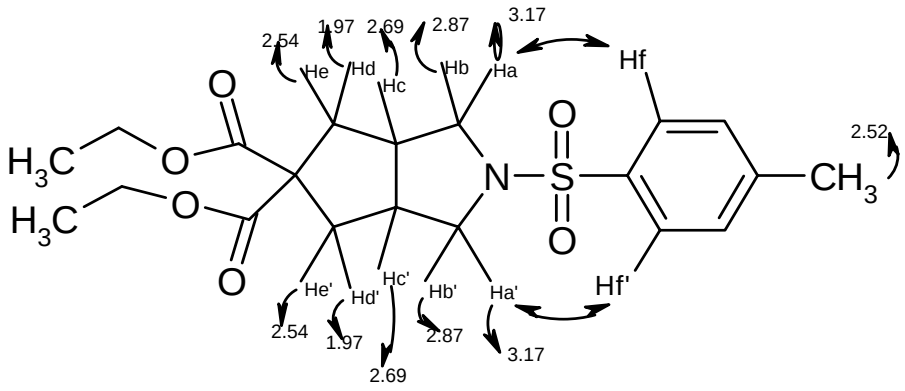
The IR spectrum of diethyl-N-(4-methylphenylsulphonyl)-3-azabicyclo[3.3.0] octane-7, 7- dicarboxylate **(1)** shows the presence of ester group at 1726 cm^{-1}. The absence of absorption frequency around 1640 cm^{-1} indicates the absence of –CH=CH- stretching which was 1643 cm^{-1} in the starting diene. Strong absorption due to SO_2 stretching was at 1344 cm^{-1}. Strong absorption due to methylene groups of bicyclic ring was at 2981 cm^{-1}. A medium absorption due to C-H bending vibrations of cyclopentane ring was at 1446 cm^{-1}.

The ^{13}C-NMR shows six carbons of pertaining to aromatic and carbonyl carbons. In the aliphatic region there were six peaks corresponding to methyl and methylene and methyne carbons. The values of ^{13}C carbons were given in the experimental section. The ^{13}C-NMR indicates that the carbon skeletal structure of the

product was bicyclic pyrrolidine ring which contains two five membered rings, with N-tosyl group at 3-position of one ring and diethyl dicarboxylate at 3-position of the other ring. This was so because then the methyl, methylene and methyne carbons becomes equivalent and fit the number of carbons obtained in the spectrum. This fact was further evidenced by DEPT experiment which shows presence of three methylene carbons, two methyl and one methyne carbon.

The LC-Mass spectrum of compound **(1)** shows the molecular ion (M+1) peak at 410. A peak at 353 was due to fragment molecule with loss of C_4H_9 (M-57). Another peak at 279 was due to further fragmentation with loss of OH (M-74). We could not able to assign the peak at 208 and 130.

2-D COSY and NOESY experiments

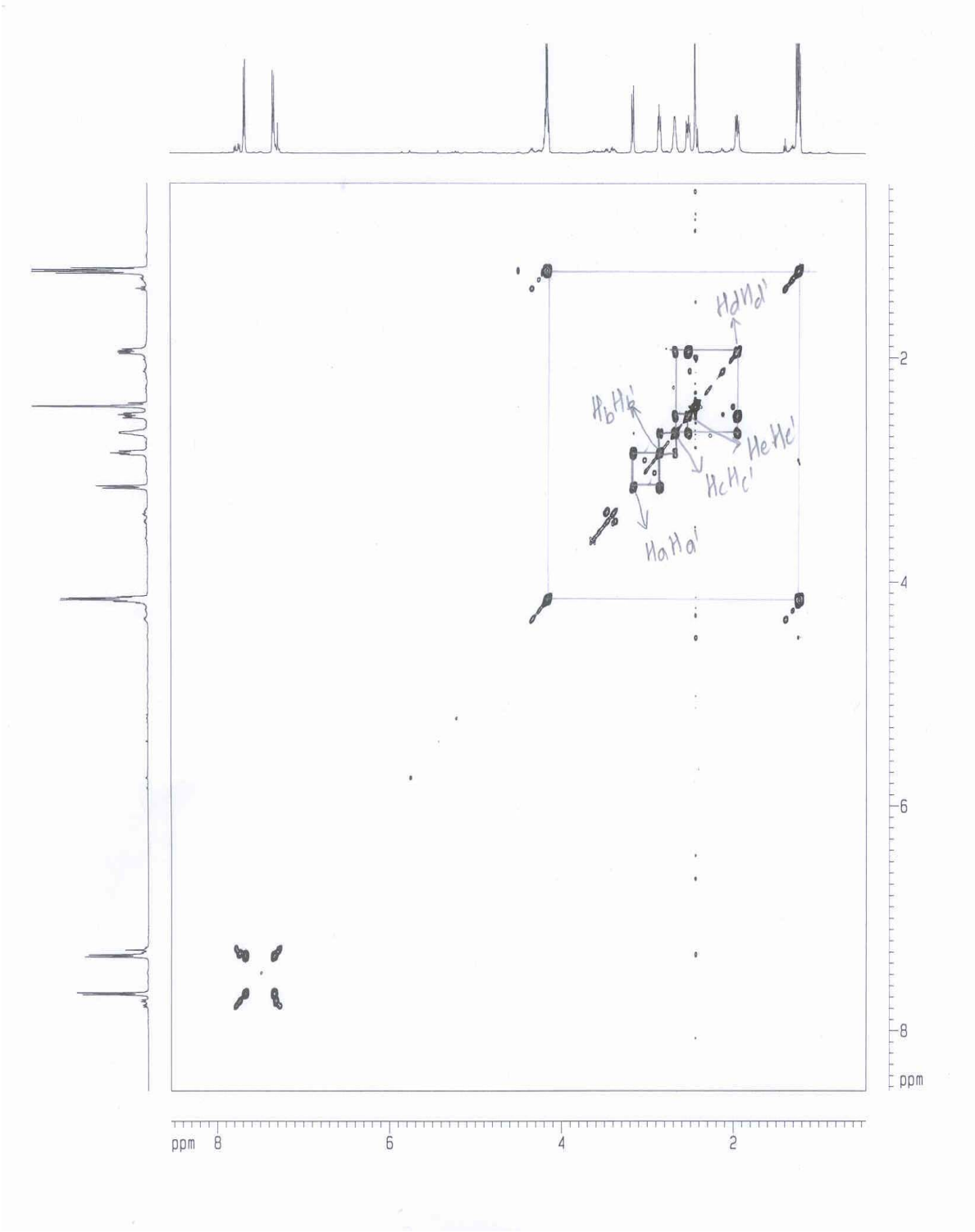


(Fig-1)

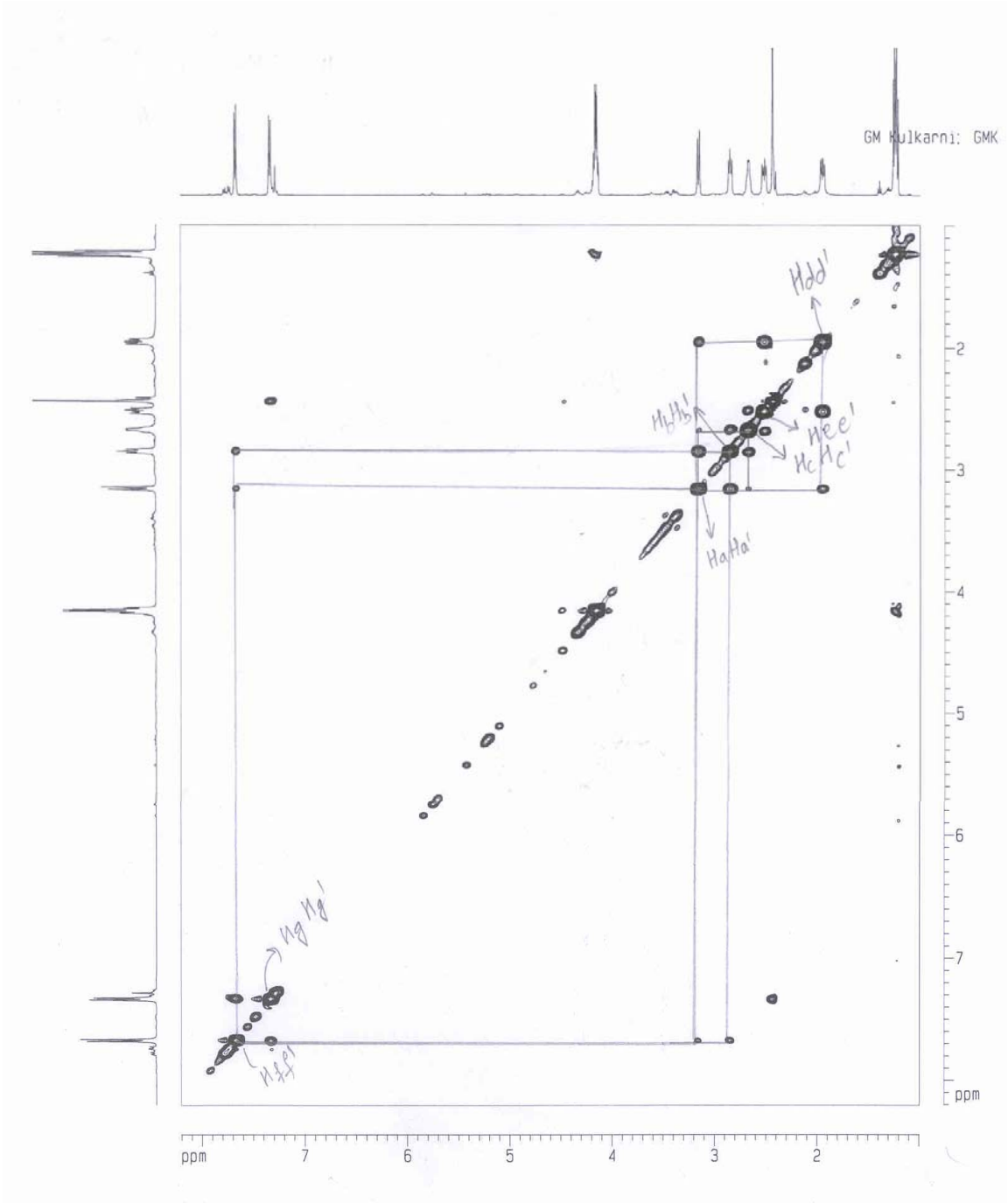
The peak due to HaHa' was at δ 3.17. The coupling between Ha Ha' with Hb Hb' and Hc Hc' was clearly identified by COSY and NOESY correlation spectra. Similarly a doublet of doublet at δ 2.87 due to HbHb' coupled with both HaHa' and HcHc'. The peak due to bridgehead protons (Hc Hc') was at δ 2.69. These protons

were coupled with Hb Hb’ and not with HaHa’. The coupling could be clearly seen in the COSY and NOESY spectra.

2D COSY spectrum of Diethyl-N-[(4-methylphenyl)sulphonyl]-3-azabicyclo[3.3.0]octane-7, 7-dicarboxylate



2D NOESY spectrum of Diethyl-N-[(4-methylphenyl)sulphonyl]-3-azabicyclo[3.3.0] octane-7, 7- dicarboxylate



In the NOESY spectrum it was evidenced that the couplings between HaHa' and HbHb'; Hb Hb' and Hc Hc'; Ha Ha' and Hd Hd'. The aromatic protons Hf and

Hf' were coupled through space with nitrogen attached methylene protons i.e. HaHa' and HbHb' which could be clearly seen by NOESY spectra.

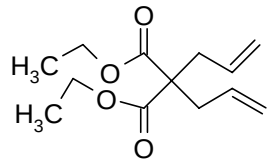
Conclusion

In conclusion, the reaction of bis-olefin, diethyl 2, 2-diallyl malonate and ethyl-2-allyl-2-cyano-4-pentenoate with chloramine-T and bromamine-T catalyzed by various transition metal catalysts and salts afforded the expected product in good yields. The reactions of other bis-olefins failed under various modified conditions, catalyst, solvent temperature and co-catalyst.

3.1.3 Experimental

1. Preparation of diethyl 2,2-diallylmalonate

A 250 ml RB flask equipped with magnetic stirring bar was charged with diethylmalonate (4.0 g, 25 mmol), tetrabutylammoniumbromide (1 g) and allyl bromide (6.6 g, 55 mmol) in 25 ml dichloromethane. To this, 10 % sodium hydroxide (50 ml) was added slowly with stirring at room temperature. The reaction mixture was allowed to stir for overnight. The reaction mixture was neutralized with dil.HCl and extracted with dichloromethane (3 x 15 ml). The combined organic layer dried over anhydrous sodium sulphate and concentrated under reduced pressure. The crude product obtained was purified by silica gel column chromatography using 60-120 mesh silica gel and a mixture of pet ether and ethyl acetate (9:1)



Yield : 1.8 g (30 %)

IR (neat) (cm^{-1}) : 2981, 1735, 1599, 1470, 960, 870

^{1}H-NMR (δ ppm, 200MHz, $CDCl_3$) : 5.75-5.6 (m, 2 H), 5.1 (d, J=11.0 Hz, 4 H), 4.2 (q, J=8 Hz, 4 Hz), 2.6 (d, J=7.4 Hz, 4 H), 1.3 (t, J=8.0 Hz, 6 H)

^{13}C-NMR (δ ppm, 200MHz, $CDCl_3$) : 170.68,131.86, 118.92, 60.20, 58.08, 38.20,

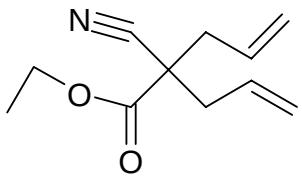
16.82.

Mass(m/z) : 240 (5), 199 (10), 153 (64), 125 (37), 93 (100), 79 (70), 67 (25).

2. Preparation of ethyl-2-allyl-2-cyano-4-pentenoate

A mixture of ethylcyano acetate (2.8 g, 25 mmol), allyl bromide (6.6 g, 55 mmol) and tetrabutylammonium bromide (0.350g, 1mmol) charged into a 250 ml RB flask equipped with magnetic stirring bar. To this, dichloromethane (25 ml) was

added followed by slow addition of 10% aqueous sodium hydroxide (50 ml) with stirring at room temperature. The reaction mixture was allowed to stir overnight. The reaction was quenched by addition of dil.HCl (10% v/v) and the product was extracted with dichloromethane (3 x 15 ml). The combined organic layer washed with brine solution, dried over anhydrous sodium sulphate and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using ethyl acetate-petroleum ether mixture (9:1).



Yield : 1.45 g, (31%)

IR(Neat)(cm^{-1}) : 3014, 2301, 1735, 1605, 1470, 1280, 960

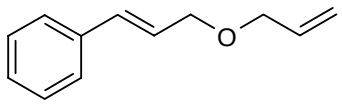
^{1}H-NMR (δ ppm, 200 MHz, $CDCl_3$) : 6.0-5.85 (m,2H), 5.3-5.2 (2s, 4H), 4.2 (q, J=6.0Hz, 2H), 2.75-2.45 (m, 4H). 1.3 (t, J=6.0Hz, 3H).

Mass (m/z) : 192 (M^+, 1), 164 (14), 154 (13), 146 (10), 124 (100), 93 (77)

3. Preparation of 1-[3-allyloxy-(E)-1-propenyl benzene

A 25 ml two necked flask equipped with magnetic stirring bar was charged with sodium hydride (0.96 g, 40 mmol), in dry tetrahydrofuran (10 ml). To this, cinnamyl alcohol (1.34 g, 10 ml) was added slowly at ice cold condition for 10 minutes. After that allyl bromide in 6 ml of tetrahydrofuran was added and to stir at room temperature for overnight. The reaction was quenched with ice-cold water, and the product was extracted with ethyl acetate (3 x 10 ml). The combined organic layer washed with brine solution (10 ml) dried over anhydrous sodium sulphate and

concentrated. The silica gel column chromatographic purification of the crude product gave the pure compound.



Yield : 1.56 g, (89 %)

IR (Neat) (cm^{-1}) : 2923, 1597, 1470, 1045, 960

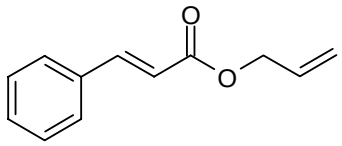
^{1}H NMR (δ ppm, 200MHz, $CDCl_3$) : 7.5-7.20 (m, 5H), 6.65 (d, J=14Hz, 1H), 6.40-

6.20 (m, 1H), 5.4-5.2 (dd, J=15Hz, 6.0Hz, 2H), 4.2 (d, J=6.0Hz, 2H), 4.1 (d, J=6.0Hz, 2H)

Mass (m/z) : 174 (M^+, 2), 156 (2), 143 (3), 133 (25), 115 (50), 105 (100), 91 (48), 77 (50).

4. Preparation of Allyl Cinnamate

A mixture of cinnamic acid (2.96 g, 20 mmol) and allyl alcohol (1.45 g, 25 mmol) was charged into a 25 ml RB flask equipped with magnetic stirring bar. To this thionyl chloride (4 ml) was added slowly at 0°C for about 10 minutes with stirring. The reaction mixture was allowed to stir at room temperature for 1 h. The excess of thionyl chloride was removed by distillation. The crude product was purified by silica gel column chromatography using a mixture of pet. ether and ethyl acetate (9.5:0.5).



Yield : 3.2 g (85%)

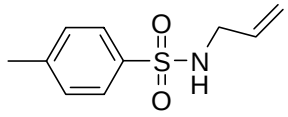
IR (in cm^{-1} Neat) : 3062, 3028, 1712, 1637, 980.

^{1}H NMR(δ ppm, 200Mhz, $CDCl_3$) : 7.8 (d, J=14.5Hz, 1H), 7.50-7.25 (m, 5H), 6.4 (d, J=14Hz, 1H), 6.01-5.95 (m, 1H), 5.2-5.1 (m, 2H), 4.35 (d, J=6.0Hz, 2H).

Mass(m/z) : 188 (M^+,9), 143 (24), 131 (97), 103 (100), 77 (74).

5. Preparation of N-allyl-4-methyl-1-benzene sulphonamide

A 50mL RB flask equipped with magnetic stirring bar was charged with a mixture of allyl amine (1.4 g, 25 mmol) and triethylamine (5 g, 50 mmol) in dry dichloromethane (15 ml). Tosyl chloride (4.75 g, 25 mmol) in dry dichloromethane (5 ml) was added slowly at 0°C for 10 minutes. The reaction mixture neutralized with dil.HCl (10% v/v) and the product extracted with dichloromethane (3 x 10 ml). The combined organic layer dried over anhydrous sodium sulphate, concentrated under reduced pressure. The crude product was purified by silica column chromatography using a mixture of pet-ether and ethyl acetate (9:1).



Yield : 4.6 g (87%)

M.P. : 57° C

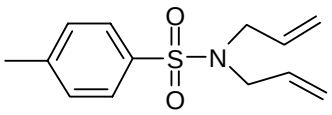
IR (in cm^{-1} Nujol) : 3249, 2923, 1595, 1460, 1321, 1163, 1064, 812, 707

^{1}H NMR (δ ppm, 200MHz, $CDCl_3$) : 7.8 (d, J=8.0 Hz, 2H), 7.3 (d, J=8Hz, 2H),

5.9-5.75(m, 1H), 5.2(s, 1H), 5.1 (s, 1H), 3.6 (m, 2H), 2.4(s, 3H).

6. N, N-Diallyl-4-methyl-1-benzene sulphonamide

A 25 ml RB flask equipped with magnetic stirring bar was charged with a mixture of N-allyl-4-methyl-1-benzene sulphonamide (0.422 g, 2 mmol), allyl bromide (0.484 g, 4 mmol), and tetrabutylammonium bromide (0.05 g, 1.5 mmol) in dichloromethane (10 ml). To this 10 % sodium hydroxide added slowly at 0 °C and allowed to stir at room temperature for overnight. The reaction mixture was neutralized with dilute hydrochloric acid (10 % v/v) and the product extracted with dichloromethane.(3 x 5 ml), the combined organic layer washed with brine solution (1 x 5 ml), dried and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using a mixture of pet. ether and ethyl acetate (9:1).



Yield : 0.376 g, (75 %)

IR ($CHCl_3$ cm^{-1}) : 2981, 2922, 1596, 1442, 1043, 929, 763

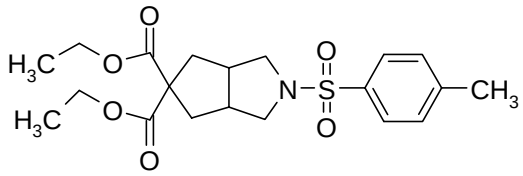
^{1}H-NMR (δ ppm, 200 MHz, $CDCl_3$) : 7.8 (d, J=8.0Hz, 2H), 7.3 (d, J=8.0Hz, 2H), 5.9-5.75 (m, 2H), 5.2 (s, 2H), 5.1 (s, 2H), 3.6 (m, 4H), 2.4(s, 3H).

Mass (m/z) : 251 (M^+,38), 236 (38), 224 (100), 210 (7), 186 (98), 172 (25).

7. Fe(Phthalocyanin) catalyzed reaction of bromamine-T with diethyl 2, 2-diallylmalonate

A 25 ml RB flask equipped with magnetic stirring bar, reflux condenser and argon balloon was charged with bromamine-T (0.191 g, 0.7 mmol), diethyl 2,2-diallylmalonate (0.120 g, 0.5 mmol), $3A^0$ mol. sieves (50 mg) and Fe(Pc) (0.030 g, 0.052 mmol) in dry ethylene dichloride. The reaction mixture was refluxed for 24 hr. After completion of the reaction, the mixture was concentrated under reduced pressure. The crude product was purified by column chromatography using 100-200 mesh silica gel and pet. ether-ethyl acetate (9:1) to get 0.093 g, 46 % of product.

Diethyl N-[(4-methylphenyl)sulphonyl]-3-azabicyclo[3.3.0]octane-7, 7-dicarboxylate (1)



Yield : 0.093 g, (46 %)

^{1}H-NMR (δ ppm, 200 MHz, $CDCl_3$) : 1.25 (q, 6H J=5Hz); 1.97 (dd, 2H J=10Hz,

5Hz); 2.52 (s, 3H); 2.69 (m, 2H); 2.86 (dd, 2H, J=5Hz) 3.17 (d, 2H,).

^{13}C-NMR (in δ ppm, $CDCl_3$) : 13.87, 21.38, 39.51, 41.71, 53.5, 61.39, 62.19, 126.96, 127.09, 127.19, 7.90.129.18, 129.48, 131.87, 132.02.

IR (cm^{-1} , $CHCl_3$) : 2981.74, 2939.31, 1728, 1596.95, 446.51, 1344.44, 1263.29, 1190, 1164.92, 1093.56, 1070.42, 1049.20, 1035.70, 815.83, 665.40.

Mass : 410, 353, 279, 208, 130.

8. $ZrOCl_2$ catalyzed reaction of bromamine-T with diethyl 2,2-diallylmalonate

A 25 ml RB flask equipped with magnetic stirring bar, reflux condenser and argon balloon was charged with bromamine-T (0.166 g, 0.5 mmol), diethyl 2,2-diallylmalonate (0.126 g, 0.5 mmol), $3A^0$ mol. sieves (50mg) and $ZrOCl_2$ (0.089 g, 0.5 mmol)

in dry acetonitrile. The reaction mixture was refluxed for 24hr. After completion of the reaction, the mixture was concentrated under reduced pressure. The crude product was purified by column chromatography using 100-200 mesh silica gel and pet. ether-ethyl acetate (9:1) to get 0.084 g, 41 % of product.

9. Cu(Phthalocyanin) catalyzed reaction of bromamine-T with diethyl 2,2-diallylmalonate : A 25 ml RB flask equipped with magnetic stirring bar, reflux condenser and argon balloon was charged with bromamine-T (0.191 g, 0.7 mmol), diethyl 2,2-diallylmalonate (0.120 g, 0.5 mmol), $3A^0$ mol. sieves (50mg) and Cu(Pc) (0.030 g, 0.052 mmol) in dry acetonitrile. The reaction mixture was refluxed for 24hr. After completion of the reaction, the mixture was concentrated under reduced pressure. The crude product was purified by column chromatography using 100-200 mesh silica gel and pet. ether-ethyl acetate (9:1) to get 0.083 g, 41 % of product.

10. $CaOCl_2$ catalyzed reaction of bromamine-T with diethyl 2,2-diallylmalonate

A 25 ml RB flask equipped with magnetic stirring bar, reflux condenser and argon balloon was charged with bromamine-T (0.166 g, 0.5 mmol), diethyl 2,2-diallylmalonate (0.126 g, 0.5 mmol), $3A^0$ mol. sieves (50 mg) and $CaOCl_2$ (0.089 g, 0.5 mmol) in dry acetonitrile. The reaction mixture was refluxed for 24hr. After completion of the reaction, the mixture was concentrated under reduced pressure. The crude product was purified by column chromatography using 100-200 mesh silica gel and pet. ether-ethyl acetate (9:1) to get 0.051 g, 25 % of product.

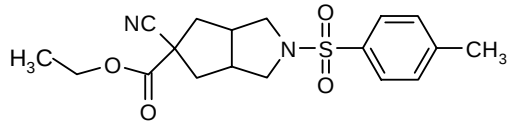
11. Copper powder catalyzed reaction of dibromamine-T with diethyl 2,2-diallylmalonate

A 25 ml two necked RB flask equipped with magnetic stirring bar, reflux condenser and argon balloon was charged with diethyl 2,2-diallylmalonate (0.240 g, 1 mmol), $3A^0$ mol. sieves (50 mg) and copper powder (0.094 g, 1.5 mmol) in dry ethylene dichloride. DBT (0.448 g, 1.5 mmol) was added by dissolving in 2 ml of acetonitrile through syringe dropwise at room temperature. The reaction mixture was stirred at room temperature for an hour and then refluxed for 24hr. After completion of the reaction, the mixture was concentrated under reduced pressure. The crude product was purified by column chromatography using 100-200 mesh silica gel and pet. ether-ethyl acetate (9:1) to get 0.051 g, 15 % of product.

12. Fe(Phthalocyanin) catalyzed reaction of bromamine-T with ethyl-2-allyl-2-cyano-4-pentenoate

A 25 ml RB flask equipped with magnetic stirring bar, reflux condenser and argon balloon was charged with bromamine-T (0.326 g, 1 mmol), ethyl-2-allyl-2-cyano-4-pentenoate (0.193 g, 1 mmol), $3A^0$ mol. sieves (50 mg) and Fe(Pc) (0.030 g, 0.052 mmol) in dry ethylene dichloride was added. The reaction mixture was refluxed for 24hr. After completion of the reaction, the mixture was concentrated under reduced pressure. The crude product was purified by column chromatography using 100-200 mesh silica gel and pet. ether-ethyl acetate to get 0.072 g, 20% of the product.

Ethyl-N-(4-methylphenylsulphonyl)-7-cyano-3-azabicyclo[3.3.0]octane-7-carboxylate



Yield : 0.072 g, (20 %)

M.P. : 105-107 ^{0}C

^{1}H-NMR (δ ppm, 200 MHz, $CDCl_3$) : 1.21(q, 6H J=5Hz); 1.93(dd, 2H J=10Hz,

Hz); 2.33(s, 3H); 2.41(m, 2H); 2.62(dd, 2H, J=5Hz) 2.76(d, 2H,); 3.16(d, 2H); 4.15(q, 2H); 7.22(d, 2H, 9Hz); 7.54(d, 2H, 9Hz).

^{13}C-NMR (δ ppm, 200 MHz, $CDCl_3$) : 13.89, 21.46, 41.20, 42.15, 52.92, 63.00, 119.49, 128.02, 129.64 131.22, 143.97, 167.20

IR ($CHCl_3$, cm^{-1}) : 3022.25, 2983.67, 2360, 2341.42, 243.06,1741.60, 1637.45, 1596.95, 1477.37, 1346.22, 1242.07, 1217.0,1164.92,1093, 757.95.

Mass : 362, 332, 300, 241, 195, 174.

3.1 References

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SPECTRA

^{1}H-NMR

21 May 2003
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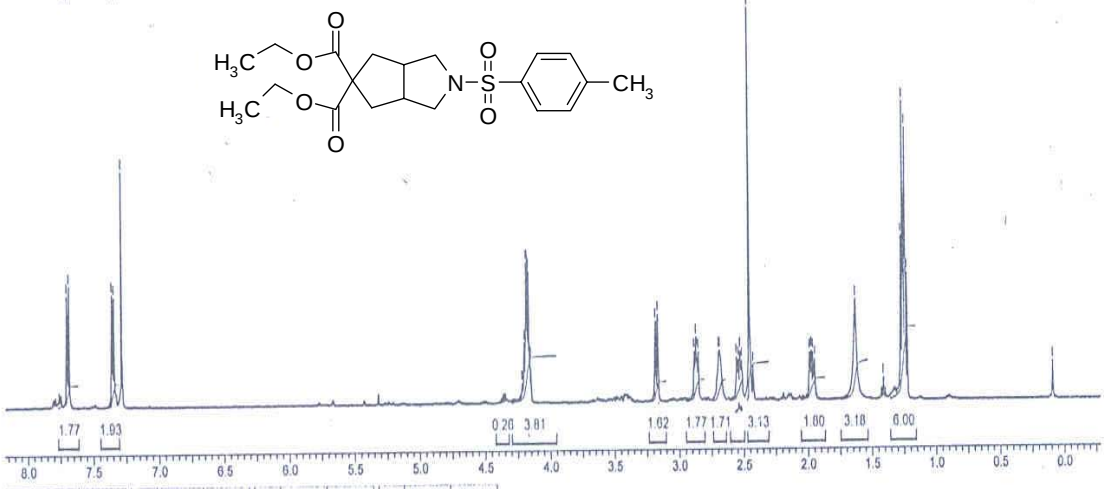

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3	1.24	0.691	14	2.43	0.088	25	2.87	0.161	36	4.20	0.151
4	1.25	0.422	15	2.46	1.000	26	2.89	0.125	37	4.22	0.047
5	1.26	0.425	16	2.52	0.100	27	3.17	0.220	38	7.29	0.597
6	1.26	0.757	17	2.53	0.126	28	3.19	0.201	39	7.34	0.274
7	1.28	0.415	18	2.54	0.103	29	4.15	0.108	40	7.36	0.281
8	1.41	0.053	19	2.56	0.110	30	4.16	0.128	41	7.69	0.304
9	1.63	0.253	20	2.68	0.124	31	4.17	0.330	42	7.70	0.278
10	1.95	0.104	21	2.69	0.127	32	4.17	0.343			
11	1.96	0.121	22	2.70	0.126	33	4.18	0.355			

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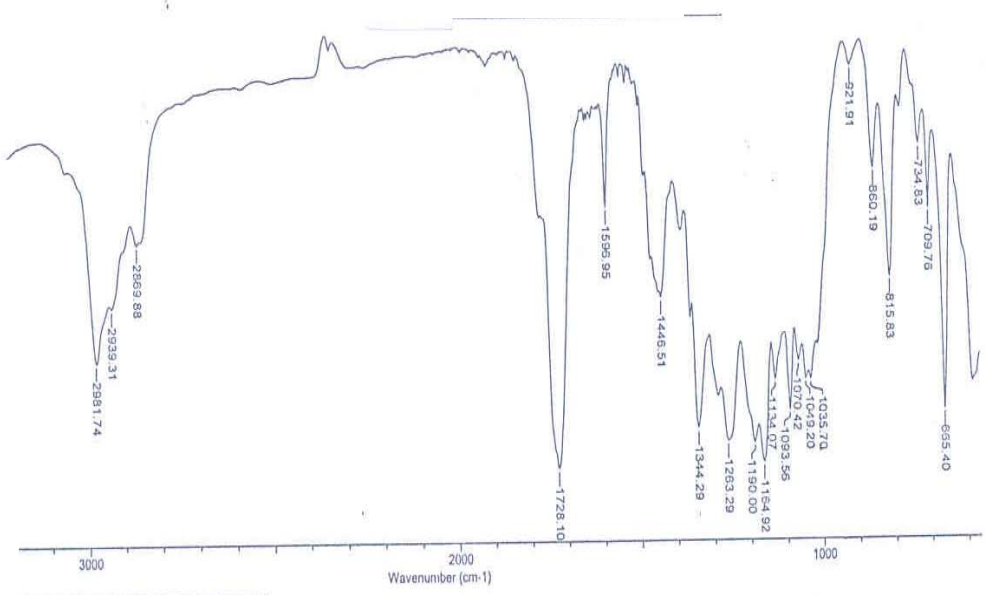

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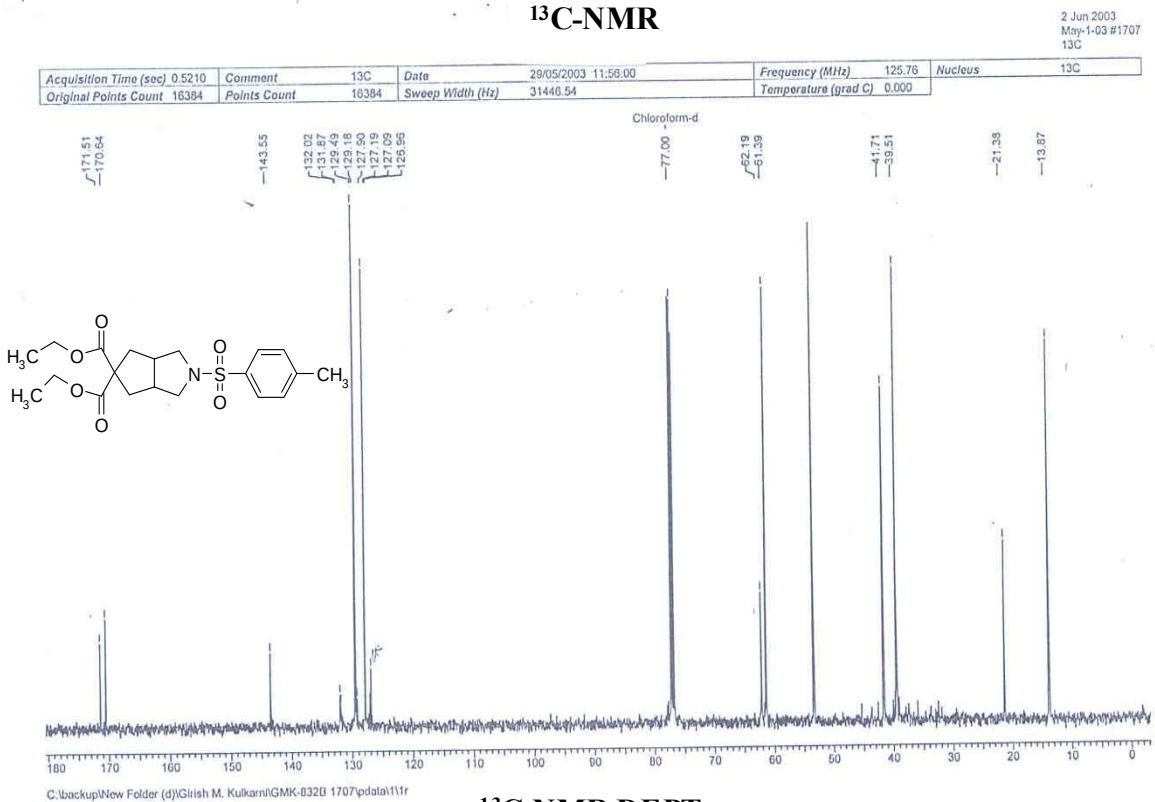

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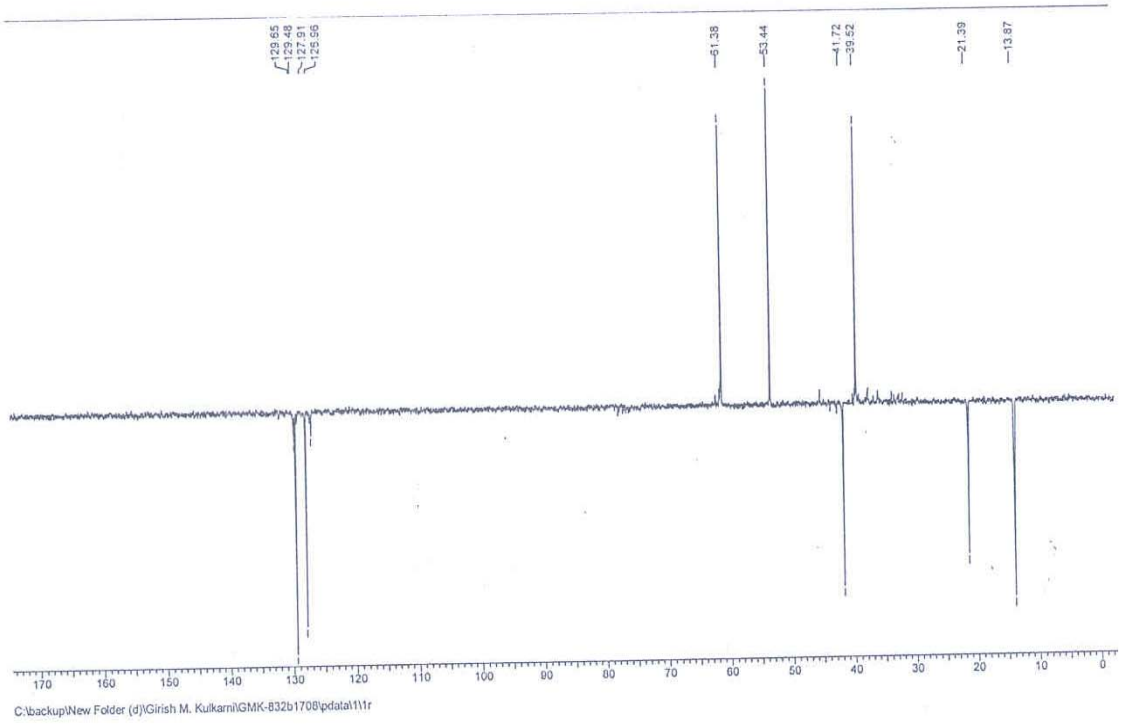

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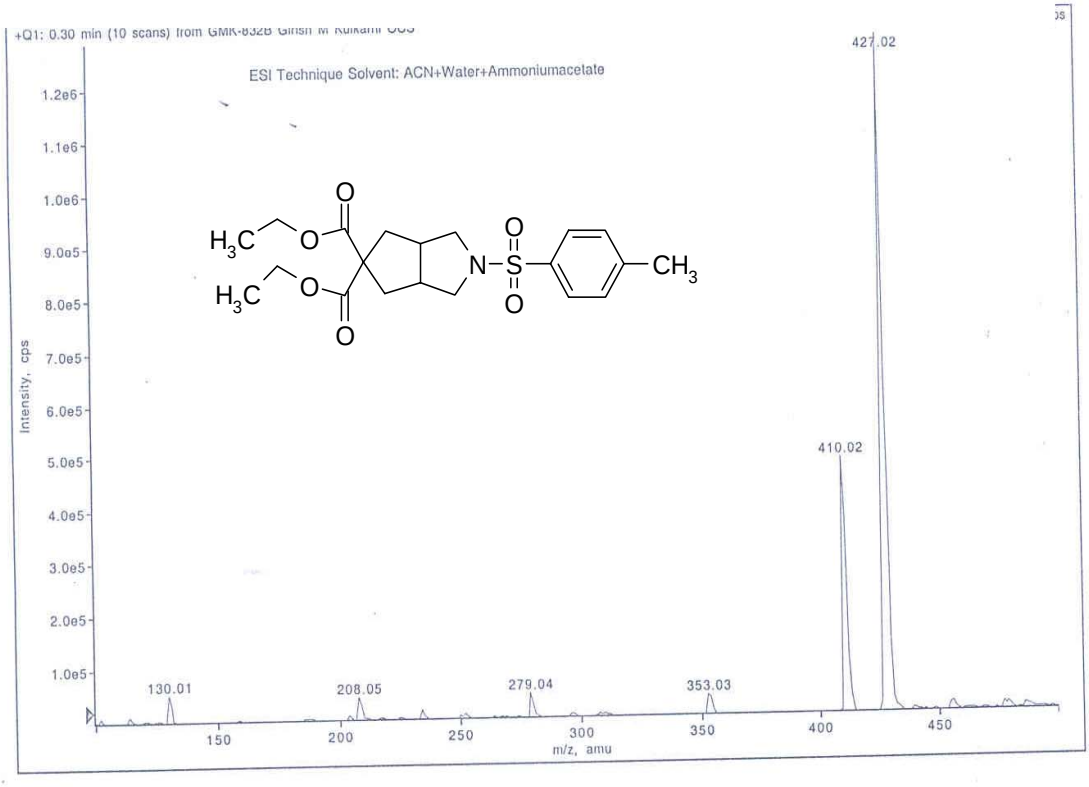

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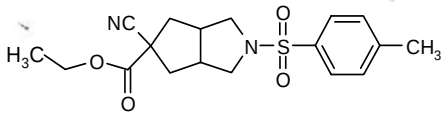

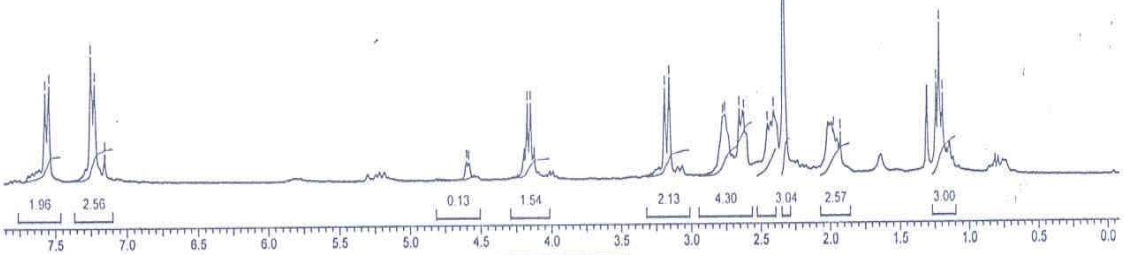

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7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

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2	1.21	0.442	10	2.65	0.196	18	4.60	0.048
3	1.24	0.266	11	2.76	0.180	19	7.15	0.078
4	1.93	0.126	12	2.77	0.174	20	7.22	0.278
5	1.98	0.134	13	3.16	0.287	21	7.25	0.359
6	2.33	1.000	14	3.19	0.256	22	7.54	0.273
7	2.41	0.192	15	4.15	0.217	23	7.57	0.254
8	2.45	0.153	16	4.17	0.215			

No.	Annotation	(ppm)
1	Chloroform-d	7.25

A:\wed3msl.002

IR

CHCl3

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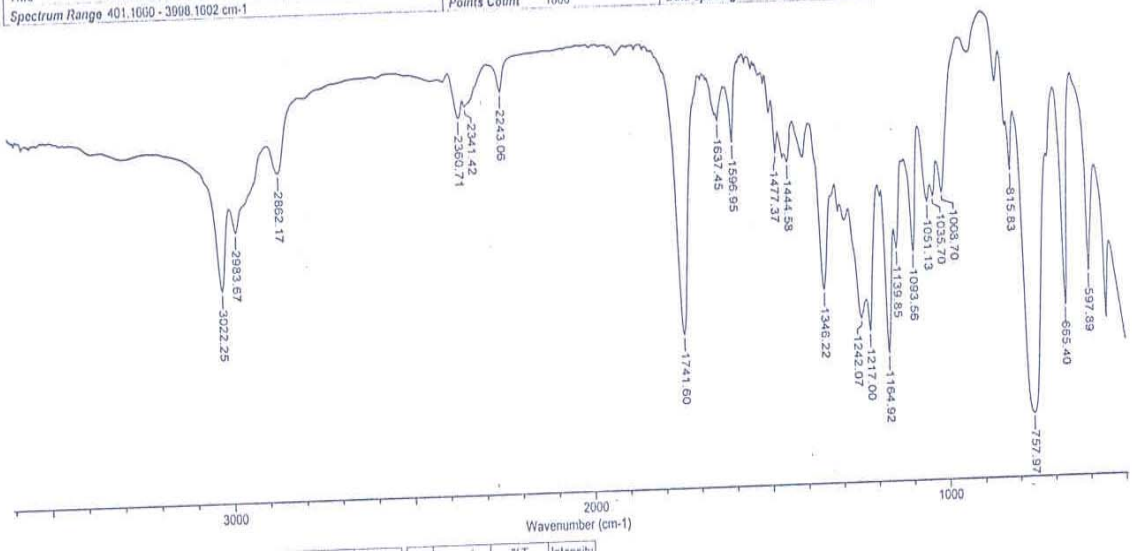

^{13}C-NMR

22 Jan 2004
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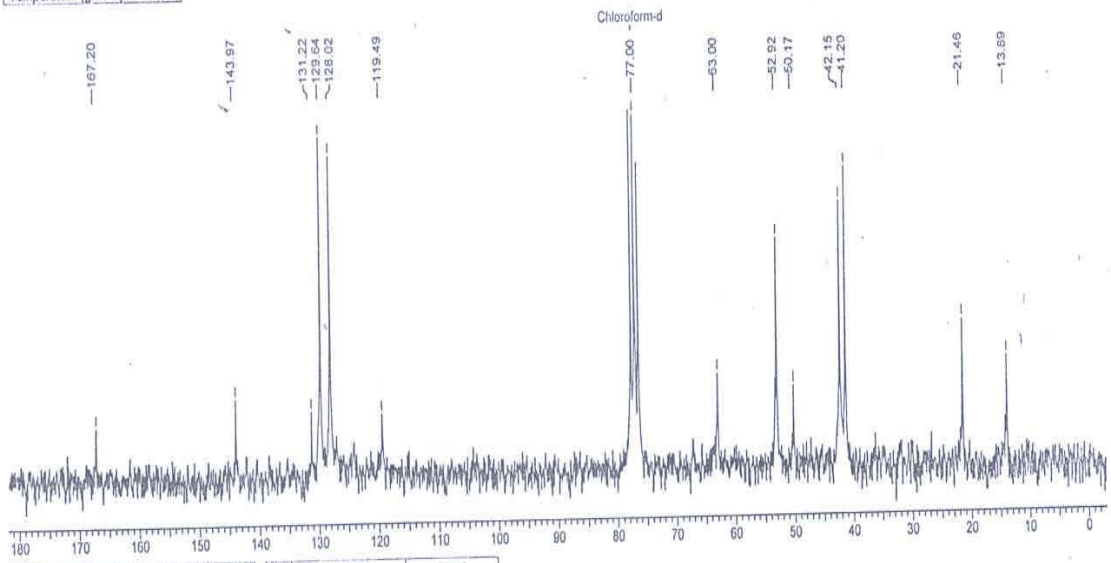

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3	41.20	0.830	10	128.02	0.888
4	42.15	0.731	11	129.64	0.941
5	50.17	0.216	12	131.22	0.170
6	52.92	0.631	13	143.97	0.209
7	63.00	0.255	14	167.20	0.135

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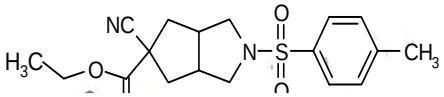

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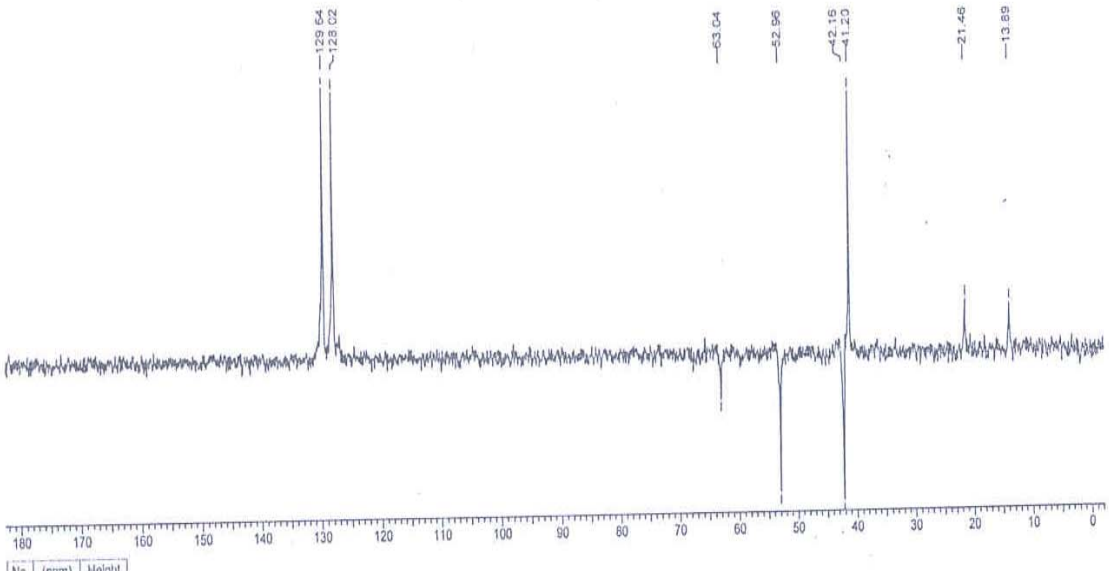

MASS SPECTRUM

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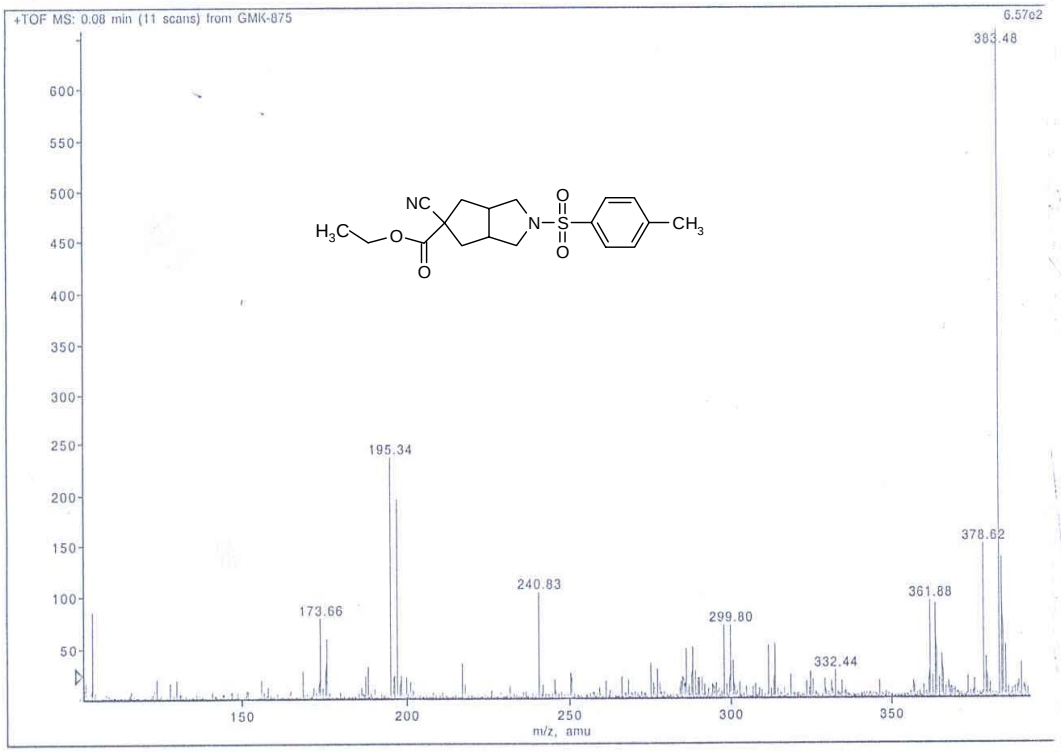


Chapter-3

Transition metal nitrenes - Application in the synthesis of N-heterocycle bicyclic compounds

3.1.1 Introduction

Cycloaddition reactions involving π-components containing transition metal-carbon multiple bonds have become increasingly popular for the synthesis of natural products.[1] The vast majority of these cycloadditions involve metallacarbenoids and lead to unstable metallacyclic intermediates that subsequently undergo reductive elimination[2]

or ligand-promoted reorganization.[3] Cycloadducts derived from metalcarbene complexes are relatively stable and have been found useful for selective carbon-carbon bond formation. Chromium carbene complexes or Fischer carbenes have wide variety applications in the synthesis of several heterocycles. For example Fischer carbenes have been used in the benzannulation reactions for e.g. Dotz benzannulation[4], formation of furan, pyrrole, indole, indene, cyclobutanone, beta-lactam, gamma-lactone, gamma-lactam and 3-hydroxypyridine.

Similarly, metallanitrenoids have been extensively used in C-N bond formation and synthesis of nitrogen containing heterocycles.[5, 6]

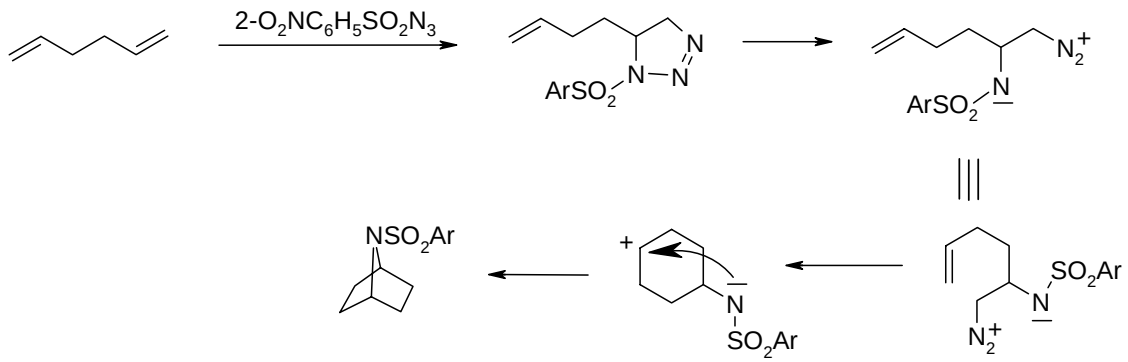
Nitrogen heterocycles especially pyrrolidine derivatives are wide spread among both natural products and medicinally important synthetic compounds.[7] Bicyclic derivatives of these compounds, basically 3-azabicyclo[3.3.0]octane framework, on the other hand are quite rare and only known from a few synthetic analogues such as prostacyclin (PGI_2)[8] antidiabetic glyclazide[9] and some antibacterial

quinonecarboxylic acid derivatives.[10] Besides their physiological activity bicyclic pyrrolidine[11] derivatives also serve as chiral auxillaries[13] in asymmetric transformations. There is also a considerable interest in the development of new methods for preparing cage-like oxaheterocycles[12] and rigid amine containing heterocycles (azacycles).[14]

Background

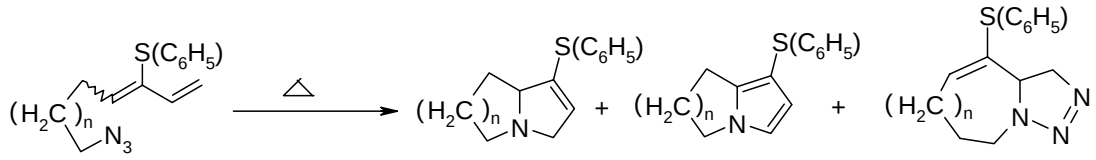
In the year 1981, it has been shown that the addition of aromatic sulfonyl azides to nonconjugated dienes lead to 2–azabicyclo[2.2.1]heptane derivatives via formation of triazoline then nitrogen extrusion and finally intramolecular substitution reaction[15] (Scheme-1).

Scheme-1



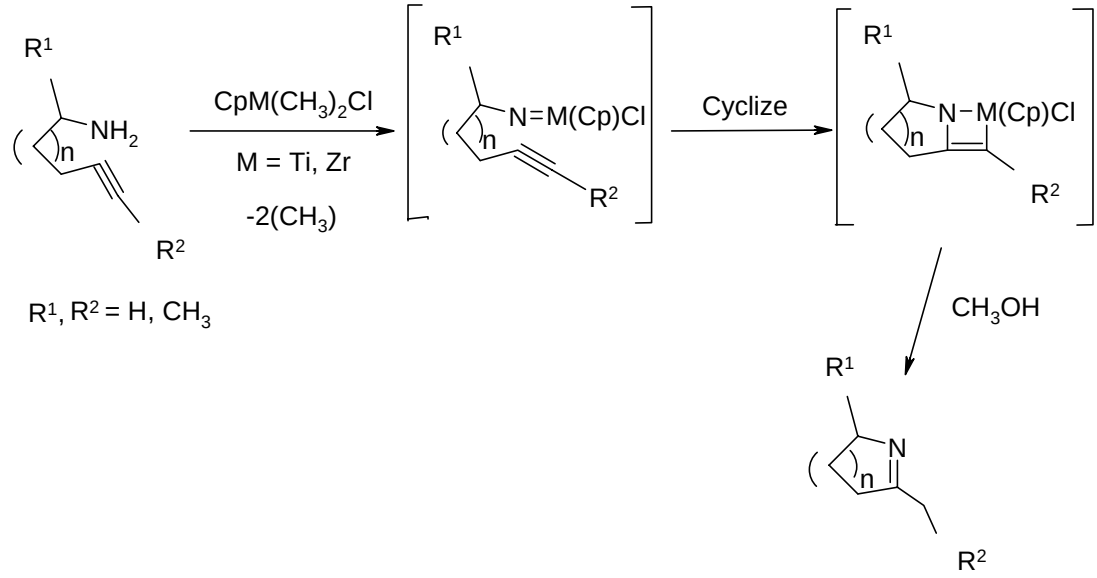
In the year 1986, William H. Pearson[16] have shown that cyclization of heterosubstituted ω-azidodienes provides fused bicyclic 3-pyrrolines in one operation. These pyrrolines are potentially useful intermediates for natural product synthesis (Scheme-2).

Scheme-2



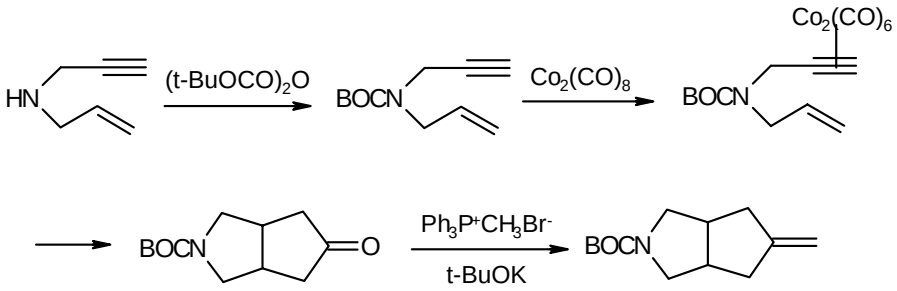
In the year 1992, Tom Livinghouse[17] et al have reported the synthesis of dihydropyrrole and tetrahydropyridine derivatives by the reaction of group (IV) imido complexes and alkylamine (Scheme-3).

Scheme-3



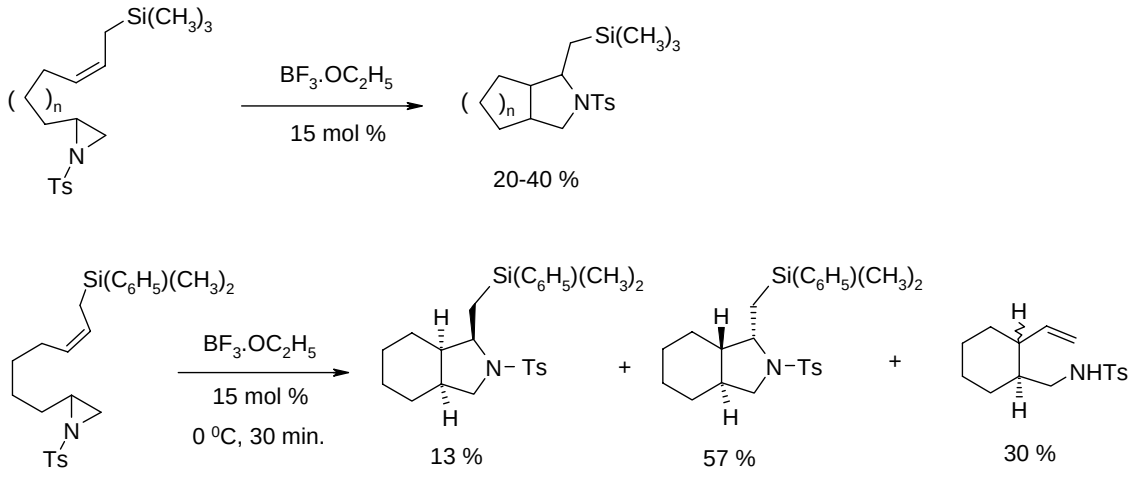
In the year 1993, Daniel P. Becker[18] et al have shown that an intramolecular reductive Pauson-Khand reaction of the hexacarbonyl complex of N-(tert-butyloxycarbonyl) allylpropargylamine under dry state adsorption conditions directly afforded the saturated N-boc-3-azabicyclo [3.3.0] octan-7-one when the reaction was performed under an inert atmosphere (Scheme-4).

Scheme-4



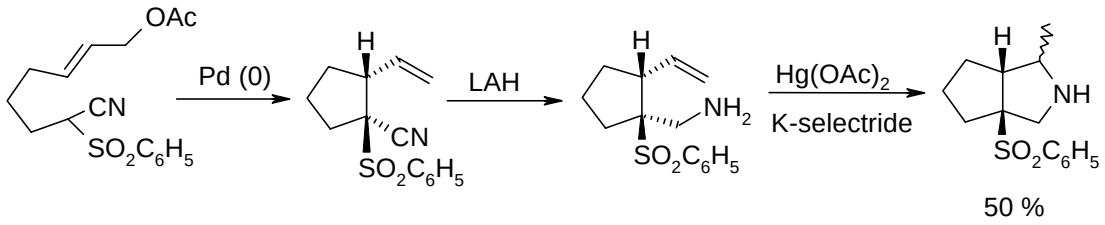
In the year 1999, bicyclic proline analogs using a formal [3+2] intramolecular aziridine –allylsilane cycloaddition reaction were synthesized. This synthesis allows for the preparation of both 5-5 and 6-5 fused ring systems and amenable to the preparation of analogs with substitution on the carbacyclic ring[19] (Scheme-5).

Scheme-5



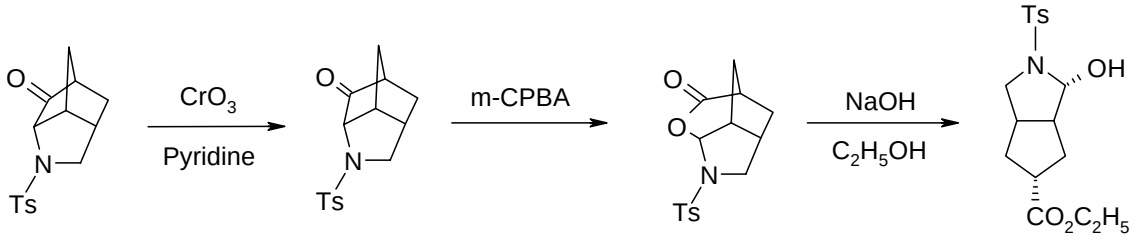
In the year 2000, Young-Ger Suh[20] et al. have developed Palladium catalyzed 1, 2-diastereoselective cyclization of the allylic precursors based on the steric nature of anion stabilizing groups. 1, 1, 2-trisubstituted cycloalkane products have been efficiently transformed into the azacyclic systems (Scheme-6).

Scheme-6



In the year 2003, the efficient synthesis of 3-azabicyclo[3.3.0]octane derivative has been achieved using commercially available starting materials and commonly used reagents by Ozdemir Dogan group[21] (Scheme-7).

Scheme-7



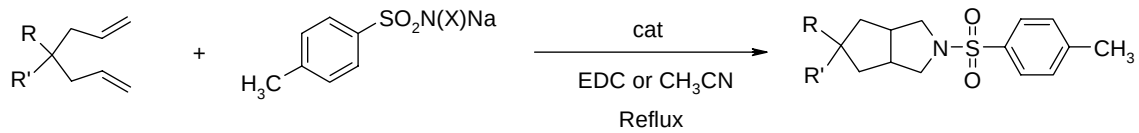
Objective

Our aim was to study the transition metal catalyzed formation of metal nitrenes by activating chloramine-T, bromamine-T, DBT and DCT to develop a methodology towards the synthesis of nitrogen containing heterocyclic compounds. In literature there were some reports on the generation of nitrenes from chloramine-T and transfer of nitrogen atom to olefins to form aziridines. Our strategy was to generate metal nitrenes from easily available simple precursors, chloramines-T, bromamine-T and study their application to the synthesis of new and novel heterocycles by reacting with 1, 6-dienes in the presence of various transition metal catalysts (Scheme-1).

3.1.3 Present work

Reactions of bromamine-T with 1, 6-diene in the presence of various transition metal complexes were carried out in refluxing EDC or CH_3CN.

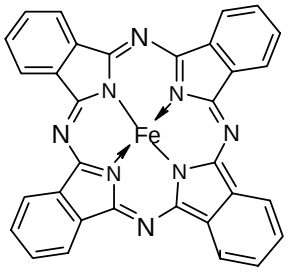
Scheme-1



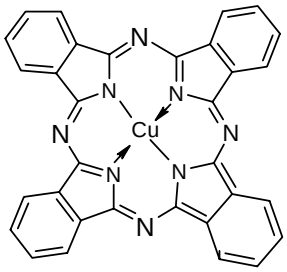
R = $COOC_2H_5$, CN
R' = $COOC_2H_5$

X = Cl, Br

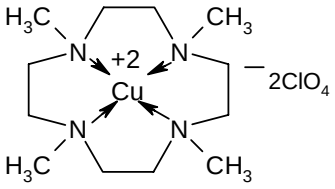
Catalysts



Fe(Pc)



Cu(Pc)

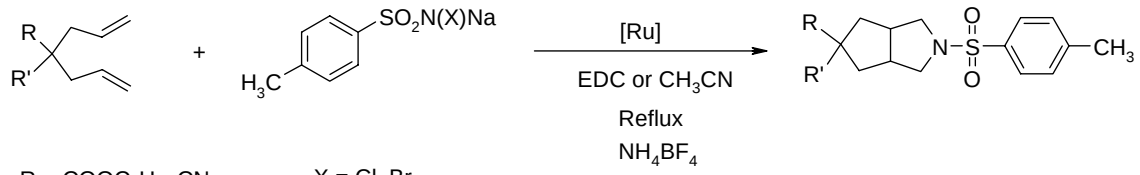


Cu(TMCyclam)

Ruthenium catalyzed reaction of bromamine-T with 1, 6-diene

Various cyclopentadienyl ruthenium complexes were also used for the reaction of bromamine-T with 1, 6-diene.

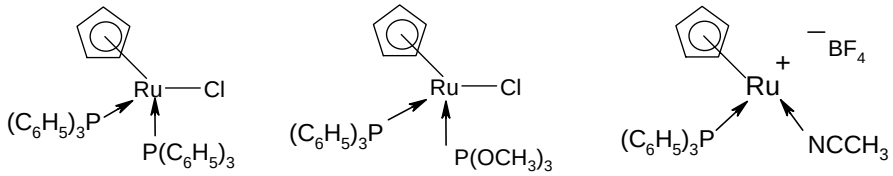
Scheme-2



R = $COOC_2H_5$, CN

R' = $COOC_2H_5$

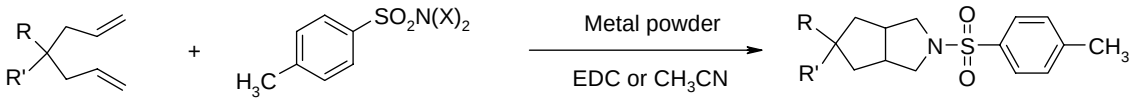
X = Cl, Br

[Ru] = 

Cu, Zn metal powder catalyzed reaction of DCT/DBT with 1, 6-diene

Metal powder catalyzed reactions of dihaloamines (e.g. DBT and DCT) with 1, 6-dienes were carried out in EDC or CH_3CN at refluxing condition.

Scheme-3



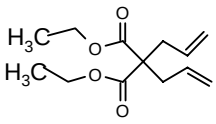
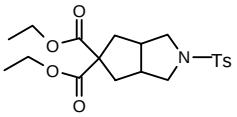
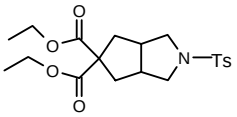
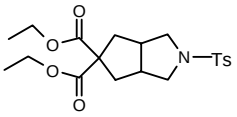
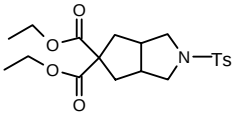
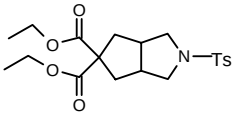
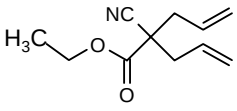
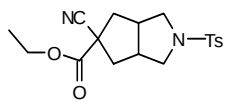
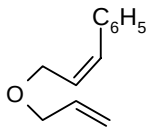
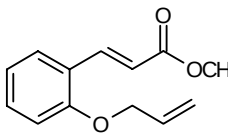
R = $COOC_2H_5$, CN

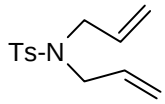
R' = $COOC_2H_5$

X = Cl, Br

Metal powder = Cu, Zn

TABLE : 1 Transition Metal Catalyzed formation of pyrrolidines

Sl. No.	Nitrogen Source	Substrate	Catalyst	Product	Yield (%)
1.	Bromamine-T		$ZrOCl_2$[a]		41
2	Bromamine-T	,,	Fe(Pc) [b]		46
3	Bromamine-T	,,	Cu(Pc)[a]		41
4	Bromamine-T	,,	$CaOCl_2$[a]		25
5	Bromamine-T	,,	Cu(tmcyclam) [a]		34
6	Bromamine-T		Fe(Pc) [b]		20
7	Bromamine-T		Fe(Pc)	–	–
8.	Bromamine-T		Fe(Pc)	–	–

9.	Bromamine-T		Fe(Pc)	–	–

Reaction conditions:1, 6-diene(1mmol)+Bromamine-T(1.2mmol)+Cat(30mg-stoichiometric)+Molecular sieves 4A°+Solvent; Reflux ; [a]CH_3CN, [b]EDC

Results and Discussion

Initially, the copper chloride catalyzed reactions of nitrene precursors especially chloramine-T with 1, 6-dienes has been started by our group[22]. These reactions were studied for insertion and cyclization of metal nitrenes to form azacycles. The catalysts that we chose have already been found to catalyze aziridination reaction. Fe(Pc)[23], $CaOCl_2$ [24] have been used for the aziridination reaction of bromamine-T and olefins.

The reaction of bromamine-T with 1, 6-diene was carried out in the presence of various transition metal catalysts and metal salts for example Fe(Phthalocyanin), $ZrOCl_2$, Cu(Pthalocyanin), $CaOCl_2$, Cu(Tmcyclam) under inert atmosphere and at reflux condition in the acetonitrile or dichloroethane as solvent. The yield of the bicyclic pyrrolidines was moderate. Out of these catalysts Fe(Pc) gave the highest yield of the product i.e. 46%. The reason could be the better stabilization of the in situ formed nitrene intermediate by the phthalocyanin ligand and thereby transfer to bis olefin to form the bicyclic compound. In the case of other catalysts the yield of the product was between 20-45%. In all the reactions the rest was starting material obtained back.

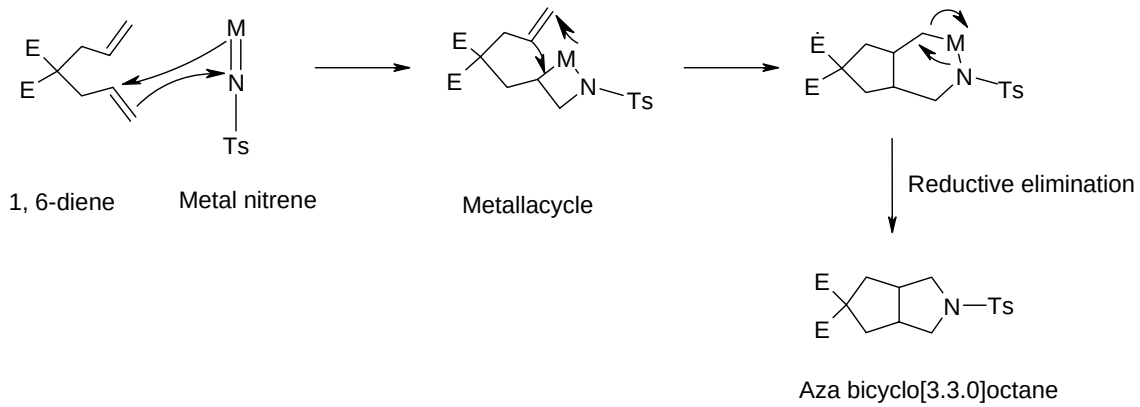
In the case of Fe (Pthalocyanin) catalyzed reaction, the bicyclic product obtained when EDC used as solvent, whereas in acetonitrile some other product obtained but could not able to identify as the 1H-NMR was complex.

Other reactions of 1, 6-diene and dibromamine-T, dichloramine-T in the presence of Cu, Zn powder were tried. In the reaction of DBT and 1, 6-diene in the presence of copper powder in EDC, poor yields of bicyclic pyrrolidines was obtained. The reaction shows that under these conditions the metal nitrene formed by DBT and copper powder insert into bis olefin to give the product. Zn-powder catalyzed reactions of DBT and DCT failed to give the product. Bromamine-T gave 32 % yield of the bicyclic pyrrolidine when treated with 1, 6-diene in the presence of copper chloride. Our group have reported copper chloride catalyzed reaction chloramine-T with 1, 6-diene for the formation of azetidines.[22]

Reactions of 1, 6-diene with bromamine-T in the presence of $(\eta^5\text{-}C_5H_5)Ru\{P(C_6H_5)_3\}_2Cl$ and NH_4BF_4 or thiophene as co-catalyst didn't yield the expected pyrrolidine product. $TsNH_2$ obtained as major product. In the $Pb(OAc)_4$ catalyzed reaction of 1, 6-diene and $TsNH_2$ failed to yield the product. The starting material was recovered back. $Fe(CO)_5$ catalyzed reaction of 1, 6-diene with p-nitrotoluene didn't yield the desired product.

Other dienes were also tried for the cyclization with various nitrogen sources. allylcinnamate, 2-(O-allyl) ethyl cinnamate with bromamine-T and $ZrOCl_2$, Fe (Pc) as catalyst didn't yield the product. No bicyclic product was obtained in the case of CuCl catalyzed reaction of [N-(p-tolylsulfonyl)imino]phenyliodinane and 1, 6-diene. Various dienes like diallylether, N, N-diallyl p-toluene sulphonamide, allyl cinnamyl ether and 2-(O-allyl) ethyl cinnamate were used for cyclization with different nitrene sources but to our disappointment there was no product formation found.

Mechanism



The pathway for the formation of azabicyclo compound was schematically shown in the mechanism above. First, the metal nitrene formed by the reaction of nitrene precursor and the catalyst undergoes [2+2] cycloaddition reaction with one of the double bonds of diene to form metallacycle. Then subsequent insertion of other double bond into metallacycle and reductive elimination lead the azabicyclo (pyrrolidine derivative) compound.

Spectral Analysis

The spectral analysis of Diethyl-N-[(4-methylphenyl)sulphonyl]-3-azabicyclo[3.3.0]octane-7, 7-dicarboxylate **(Fig-1)** explained as follows.

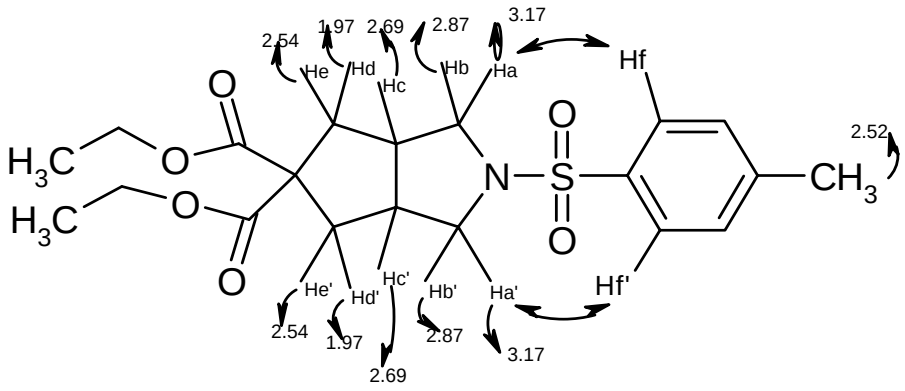
The IR spectrum of diethyl-N-(4-methylphenylsulphonyl)-3-azabicyclo[3.3.0] octane-7, 7- dicarboxylate **(1)** shows the presence of ester group at 1726 cm^{-1}. The absence of absorption frequency around 1640 cm^{-1} indicates the absence of –CH=CH- stretching which was 1643 cm^{-1} in the starting diene. Strong absorption due to SO_2 stretching was at 1344 cm^{-1}. Strong absorption due to methylene groups of bicyclic ring was at 2981 cm^{-1}. A medium absorption due to C-H bending vibrations of cyclopentane ring was at 1446 cm^{-1}.

The ^{13}C-NMR shows six carbons of pertaining to aromatic and carbonyl carbons. In the aliphatic region there were six peaks corresponding to methyl and methylene and methyne carbons. The values of ^{13}C carbons were given in the experimental section. The ^{13}C-NMR indicates that the carbon skeletal structure of the

product was bicyclic pyrrolidine ring which contains two five membered rings, with N-tosyl group at 3-position of one ring and diethyl dicarboxylate at 3-position of the other ring. This was so because then the methyl, methylene and methyne carbons becomes equivalent and fit the number of carbons obtained in the spectrum. This fact was further evidenced by DEPT experiment which shows presence of three methylene carbons, two methyl and one methyne carbon.

The LC-Mass spectrum of compound **(1)** shows the molecular ion (M+1) peak at 410. A peak at 353 was due to fragment molecule with loss of C_4H_9 (M-57). Another peak at 279 was due to further fragmentation with loss of OH (M-74). We could not able to assign the peak at 208 and 130.

2-D COSY and NOESY experiments

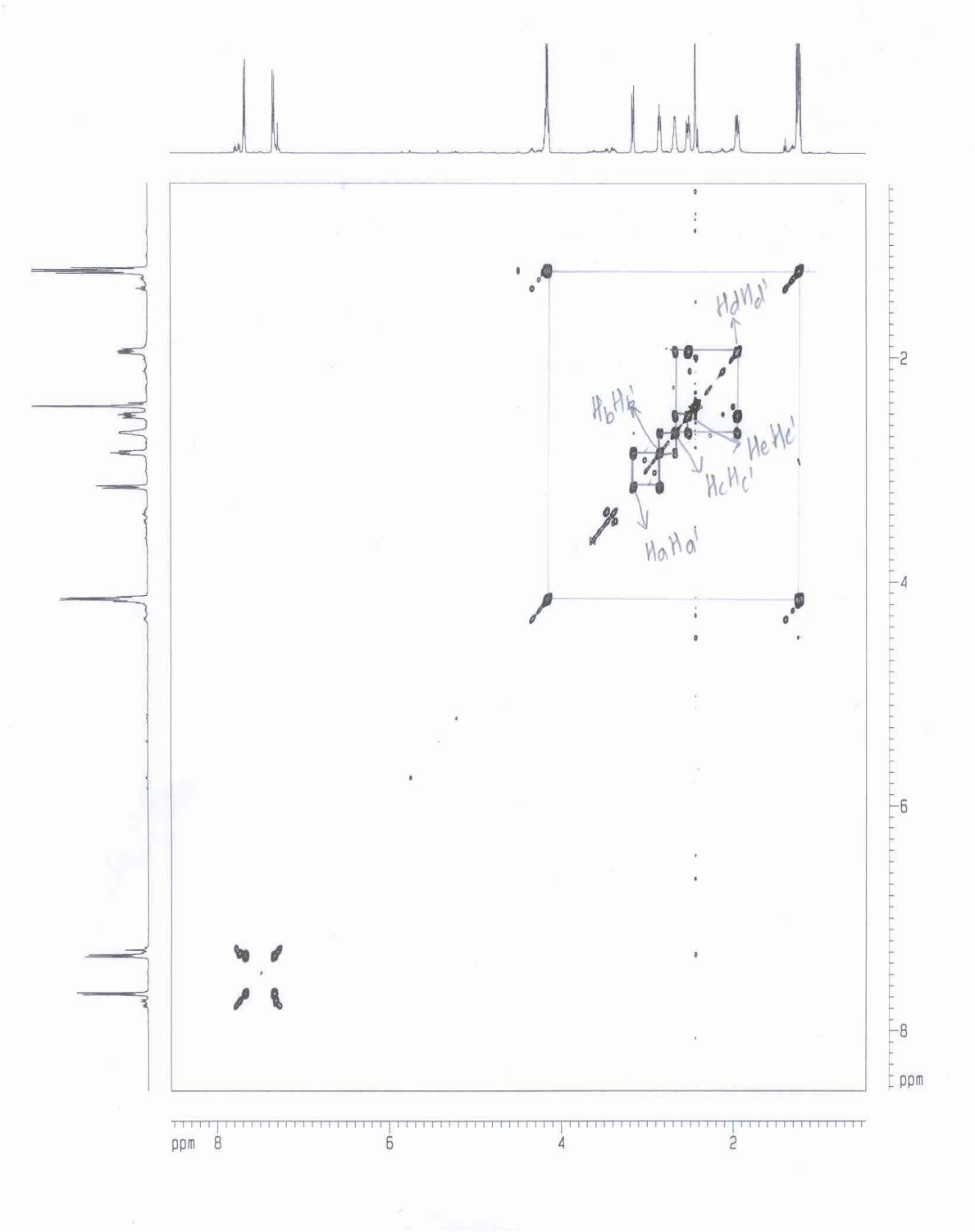


(Fig-1)

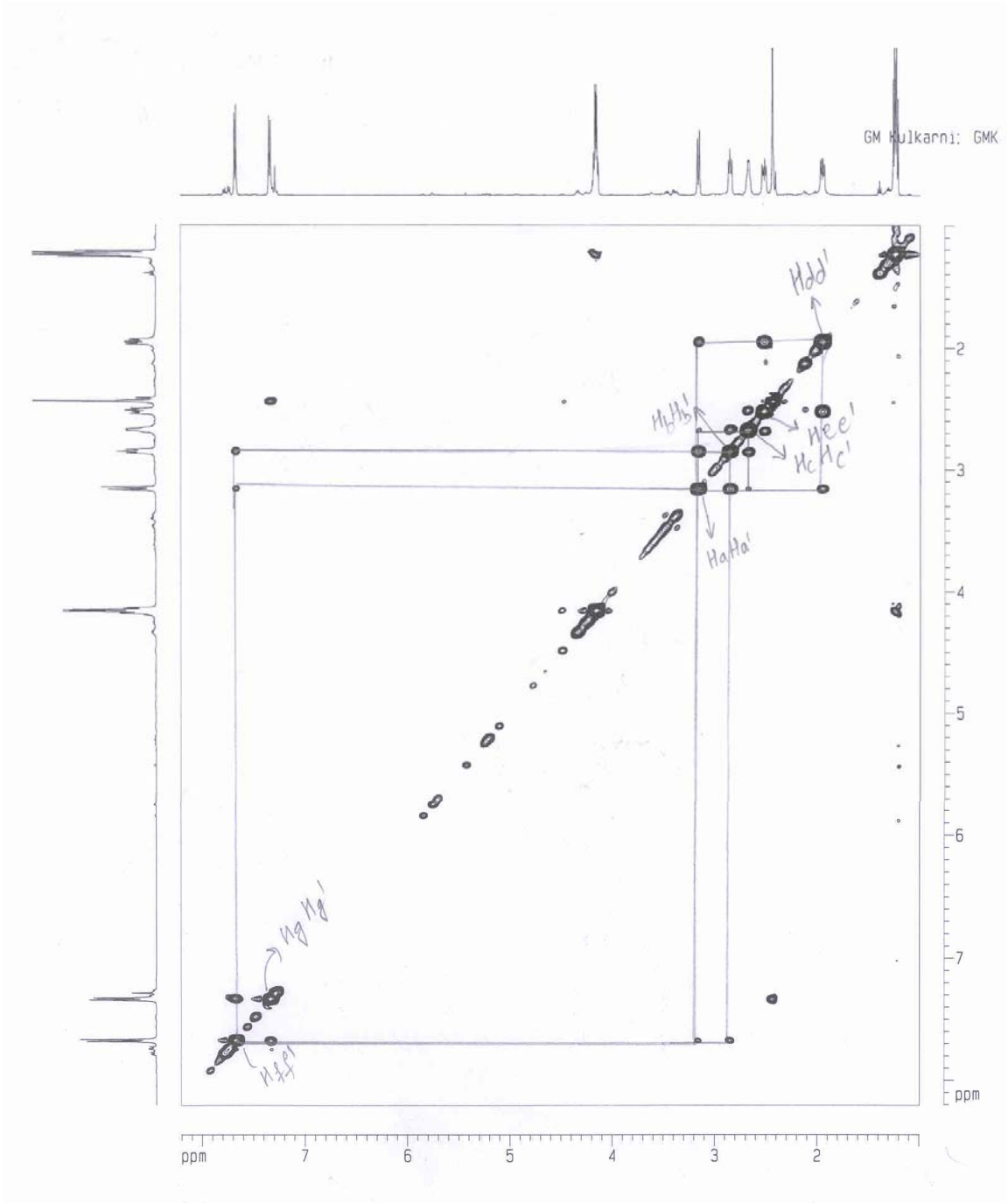
The peak due to HaHa' was at δ 3.17. The coupling between Ha Ha' with Hb Hb' and Hc Hc' was clearly identified by COSY and NOESY correlation spectra. Similarly a doublet of doublet at δ 2.87 due to HbHb' coupled with both HaHa' and HcHc'. The peak due to bridgehead protons (Hc Hc') was at δ 2.69. These protons

were coupled with Hb Hb’ and not with HaHa’. The coupling could be clearly seen in the COSY and NOESY spectra.

2D COSY spectrum of Diethyl-N-[(4-methylphenyl)sulphonyl]-3-azabicyclo[3.3.0]octane-7, 7-dicarboxylate



2D NOESY spectrum of Diethyl-N-[(4-methylphenyl)sulphonyl]-3-azabicyclo[3.3.0] octane-7, 7- dicarboxylate



In the NOESY spectrum it was evidenced that the couplings between HaHa' and HbHb'; Hb Hb' and Hc Hc'; Ha Ha' and Hd Hd'. The aromatic protons Hf and

Hf' were coupled through space with nitrogen attached methylene protons i.e. HaHa' and HbHb' which could be clearly seen by NOESY spectra.

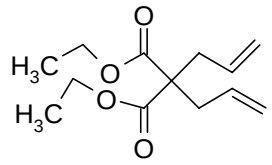
Conclusion

In conclusion, the reaction of bis-olefin, diethyl 2, 2-diallyl malonate and ethyl-2-allyl-2-cyano-4-pentenoate with chloramine-T and bromamine-T catalyzed by various transition metal catalysts and salts afforded the expected product in good yields. The reactions of other bis-olefins failed under various modified conditions, catalyst, solvent temperature and co-catalyst.

3.1.3 Experimental

1. Preparation of diethyl 2,2-diallylmalonate

A 250 ml RB flask equipped with magnetic stirring bar was charged with diethylmalonate (4.0 g, 25 mmol), tetrabutylammoniumbromide (1 g) and allyl bromide (6.6 g, 55 mmol) in 25 ml dichloromethane. To this, 10 % sodium hydroxide (50 ml) was added slowly with stirring at room temperature. The reaction mixture was allowed to stir for overnight. The reaction mixture was neutralized with dil.HCl and extracted with dichloromethane (3 x 15 ml). The combined organic layer dried over anhydrous sodium sulphate and concentrated under reduced pressure. The crude product obtained was purified by silica gel column chromatography using 60-120 mesh silica gel and a mixture of pet ether and ethyl acetate (9:1)



Yield : 1.8 g (30 %)

IR (neat) (cm^{-1}) : 2981, 1735, 1599, 1470, 960, 870

^{1}H-NMR (δ ppm, 200MHz, $CDCl_3$) : 5.75-5.6 (m, 2 H), 5.1 (d, J=11.0 Hz, 4 H), 4.2 (q, J=8 Hz, 4 Hz), 2.6 (d, J=7.4 Hz, 4 H), 1.3 (t, J=8.0 Hz, 6 H)

^{13}C-NMR (δ ppm, 200MHz, $CDCl_3$) : 170.68,131.86, 118.92, 60.20, 58.08, 38.20,

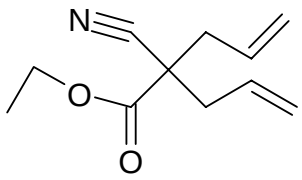
16.82.

Mass(m/z) : 240 (5), 199 (10), 153 (64), 125 (37), 93 (100), 79 (70), 67 (25).

2. Preparation of ethyl-2-allyl-2-cyano-4-pentenoate

A mixture of ethylcyano acetate (2.8 g, 25 mmol), allyl bromide (6.6 g, 55 mmol) and tetrabutylammonium bromide (0.350g, 1mmol) charged into a 250 ml RB flask equipped with magnetic stirring bar. To this, dichloromethane (25 ml) was

added followed by slow addition of 10% aqueous sodium hydroxide (50 ml) with stirring at room temperature. The reaction mixture was allowed to stir overnight. The reaction was quenched by addition of dil.HCl (10% v/v) and the product was extracted with dichloromethane (3 x 15 ml). The combined organic layer washed with brine solution, dried over anhydrous sodium sulphate and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using ethyl acetate-petroleum ether mixture (9:1).



Yield : 1.45 g, (31%)

IR(Neat)(cm^{-1}) : 3014, 2301, 1735, 1605, 1470, 1280, 960

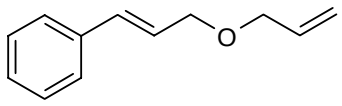
^{1}H-NMR (δ ppm, 200 MHz, $CDCl_3$) : 6.0-5.85 (m,2H), 5.3-5.2 (2s, 4H), 4.2 (q, J=6.0Hz, 2H), 2.75-2.45 (m, 4H). 1.3 (t, J=6.0Hz, 3H).

Mass (m/z) : 192 (M^+, 1), 164 (14), 154 (13), 146 (10), 124 (100), 93 (77)

3. Preparation of 1-[3-allyloxy-(E)-1-propenyl benzene

A 25 ml two necked flask equipped with magnetic stirring bar was charged with sodium hydride (0.96 g, 40 mmol), in dry tetrahydrofuran (10 ml). To this, cinnamyl alcohol (1.34 g, 10 ml) was added slowly at ice cold condition for 10 minutes. After that allyl bromide in 6 ml of tetrahydrofuran was added and to stir at room temperature for overnight. The reaction was quenched with ice-cold water, and the product was extracted with ethyl acetate (3 x 10 ml). The combined organic layer washed with brine solution (10 ml) dried over anhydrous sodium sulphate and

concentrated. The silica gel column chromatographic purification of the crude product gave the pure compound.



Yield : 1.56 g, (89 %)

IR (Neat) (cm^{-1}) : 2923, 1597, 1470, 1045, 960

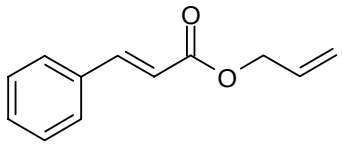
^{1}H NMR (δ ppm, 200MHz, $CDCl_3$) : 7.5-7.20 (m, 5H), 6.65 (d, J=14Hz, 1H), 6.40-

6.20 (m, 1H), 5.4-5.2 (dd, J=15Hz, 6.0Hz, 2H), 4.2 (d, J=6.0Hz, 2H), 4.1 (d, J=6.0Hz, 2H)

Mass (m/z) : 174 (M^+, 2), 156 (2), 143 (3), 133 (25), 115 (50), 105 (100), 91 (48), 77 (50).

4. Preparation of Allyl Cinnamate

A mixture of cinnamic acid (2.96 g, 20 mmol) and allyl alcohol (1.45 g, 25 mmol) was charged into a 25 ml RB flask equipped with magnetic stirring bar. To this thionyl chloride (4 ml) was added slowly at 0°C for about 10 minutes with stirring. The reaction mixture was allowed to stir at room temperature for 1 h. The excess of thionyl chloride was removed by distillation. The crude product was purified by silica gel column chromatography using a mixture of pet. ether and ethyl acetate (9.5:0.5).



Yield : 3.2 g (85%)

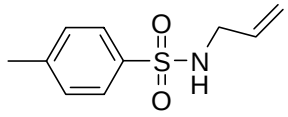
IR (in cm^{-1} Neat) : 3062, 3028, 1712, 1637, 980.

^{1}H NMR(δ ppm, 200Mhz, $CDCl_3$) : 7.8 (d, J=14.5Hz, 1H), 7.50-7.25 (m, 5H), 6.4 (d, J=14Hz, 1H), 6.01-5.95 (m, 1H), 5.2-5.1 (m, 2H), 4.35 (d, J=6.0Hz, 2H).

Mass(m/z) : 188 (M^+,9), 143 (24), 131 (97), 103 (100), 77 (74).

5. Preparation of N-allyl-4-methyl-1-benzene sulphonamide

A 50mL RB flask equipped with magnetic stirring bar was charged with a mixture of allyl amine (1.4 g, 25 mmol) and triethylamine (5 g, 50 mmol) in dry dichloromethane (15 ml). Tosyl chloride (4.75 g, 25 mmol) in dry dichloromethane (5 ml) was added slowly at 0°C for 10 minutes. The reaction mixture neutralized with dil.HCl (10% v/v) and the product extracted with dichloromethane (3 x 10 ml). The combined organic layer dried over anhydrous sodium sulphate, concentrated under reduced pressure. The crude product was purified by silica column chromatography using a mixture of pet-ether and ethyl acetate (9:1).



Yield : 4.6 g (87%)

M.P. : 57° C

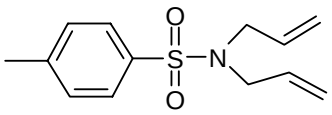
IR (in cm^{-1} Nujol) : 3249, 2923, 1595, 1460, 1321, 1163, 1064, 812, 707

^{1}H NMR (δ ppm, 200MHz, $CDCl_3$) : 7.8 (d, J=8.0 Hz, 2H), 7.3 (d, J=8Hz, 2H),

5.9-5.75(m, 1H), 5.2(s, 1H), 5.1 (s, 1H), 3.6 (m, 2H), 2.4(s, 3H).

6. N, N-Diallyl-4-methyl-1-benzene sulphonamide

A 25 ml RB flask equipped with magnetic stirring bar was charged with a mixture of N-allyl-4-methyl-1-benzene sulphonamide (0.422 g, 2 mmol), allyl bromide (0.484 g, 4 mmol), and tetrabutylammonium bromide (0.05 g, 1.5 mmol) in dichloromethane (10 ml). To this 10 % sodium hydroxide added slowly at 0 °C and allowed to stir at room temperature for overnight. The reaction mixture was neutralized with dilute hydrochloric acid (10 % v/v) and the product extracted with dichloromethane.(3 x 5 ml), the combined organic layer washed with brine solution (1 x 5 ml), dried and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using a mixture of pet. ether and ethyl acetate (9:1).



Yield : 0.376 g, (75 %)

IR ($CHCl_3$ cm^{-1}) : 2981, 2922, 1596, 1442, 1043, 929, 763

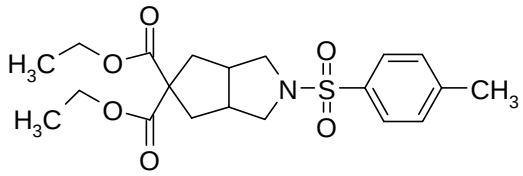
^{1}H-NMR (δ ppm, 200 MHz, $CDCl_3$) : 7.8 (d, J=8.0Hz, 2H), 7.3 (d, J=8.0Hz, 2H), 5.9-5.75 (m, 2H), 5.2 (s, 2H), 5.1 (s, 2H), 3.6 (m, 4H), 2.4(s, 3H).

Mass (m/z) : 251 (M^+,38), 236 (38), 224 (100), 210 (7), 186 (98), 172 (25).

7. Fe(Phthalocyanin) catalyzed reaction of bromamine-T with diethyl 2, 2-diallylmalonate

A 25 ml RB flask equipped with magnetic stirring bar, reflux condenser and argon balloon was charged with bromamine-T (0.191 g, 0.7 mmol), diethyl 2,2-diallylmalonate (0.120 g, 0.5 mmol), $3A^0$ mol. sieves (50 mg) and Fe(Pc) (0.030 g, 0.052 mmol) in dry ethylene dichloride. The reaction mixture was refluxed for 24 hr. After completion of the reaction, the mixture was concentrated under reduced pressure. The crude product was purified by column chromatography using 100-200 mesh silica gel and pet. ether-ethyl acetate (9:1) to get 0.093 g, 46 % of product.

Diethyl N-[(4-methylphenyl)sulphonyl]-3-azabicyclo[3.3.0]octane-7, 7-dicarboxylate (1)



Yield : 0.093 g, (46 %)

^{1}H-NMR (δ ppm, 200 MHz, $CDCl_3$) : 1.25 (q, 6H J=5Hz); 1.97 (dd, 2H J=10Hz,

5Hz); 2.52 (s, 3H); 2.69 (m, 2H); 2.86 (dd, 2H, J=5Hz) 3.17 (d, 2H,).

^{13}C-NMR (in δ ppm, $CDCl_3$) : 13.87, 21.38, 39.51, 41.71, 53.5, 61.39, 62.19, 126.96, 127.09, 127.19, 7.90.129.18, 129.48, 131.87, 132.02.

IR (cm^{-1} , $CHCl_3$) : 2981.74, 2939.31, 1728, 1596.95, 446.51, 1344.44, 1263.29, 1190, 1164.92, 1093.56, 1070.42, 1049.20, 1035.70, 815.83, 665.40.

Mass : 410, 353, 279, 208, 130.

8. $ZrOCl_2$ catalyzed reaction of bromamine-T with diethyl 2,2-diallylmalonate

A 25 ml RB flask equipped with magnetic stirring bar, reflux condenser and argon balloon was charged with bromamine-T (0.166 g, 0.5 mmol), diethyl 2,2-diallylmalonate (0.126 g, 0.5 mmol), $3A^0$ mol. sieves (50mg) and $ZrOCl_2$ (0.089 g, 0.5 mmol)

in dry acetonitrile. The reaction mixture was refluxed for 24hr. After completion of the reaction, the mixture was concentrated under reduced pressure. The crude product was purified by column chromatography using 100-200 mesh silica gel and pet. ether-ethyl acetate (9:1) to get 0.084 g, 41 % of product.

9. Cu(Phthalocyanin) catalyzed reaction of bromamine-T with diethyl 2,2-diallylmalonate : A 25 ml RB flask equipped with magnetic stirring bar, reflux condenser and argon balloon was charged with bromamine-T (0.191 g, 0.7 mmol), diethyl 2,2-diallylmalonate (0.120 g, 0.5 mmol), $3A^0$ mol. sieves (50mg) and Cu(Pc) (0.030 g, 0.052 mmol) in dry acetonitrile. The reaction mixture was refluxed for 24hr. After completion of the reaction, the mixture was concentrated under reduced pressure. The crude product was purified by column chromatography using 100-200 mesh silica gel and pet. ether-ethyl acetate (9:1) to get 0.083 g, 41 % of product.

10. $CaOCl_2$ catalyzed reaction of bromamine-T with diethyl 2,2-diallylmalonate

A 25 ml RB flask equipped with magnetic stirring bar, reflux condenser and argon balloon was charged with bromamine-T (0.166 g, 0.5 mmol), diethyl 2,2-diallylmalonate (0.126 g, 0.5 mmol), $3A^0$ mol. sieves (50 mg) and $CaOCl_2$ (0.089 g, 0.5 mmol) in dry acetonitrile. The reaction mixture was refluxed for 24hr. After completion of the reaction, the mixture was concentrated under reduced pressure. The crude product was purified by column chromatography using 100-200 mesh silica gel and pet. ether-ethyl acetate (9:1) to get 0.051 g, 25 % of product.

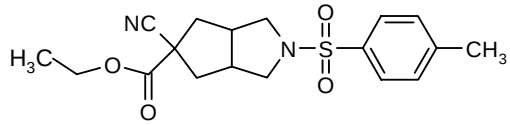
11. Copper powder catalyzed reaction of dibromamine-T with diethyl 2,2-diallylmalonate

A 25 ml two necked RB flask equipped with magnetic stirring bar, reflux condenser and argon balloon was charged with diethyl 2,2-diallylmalonate (0.240 g, 1 mmol), $3A^0$ mol. sieves (50 mg) and copper powder (0.094 g, 1.5 mmol) in dry ethylene dichloride. DBT (0.448 g, 1.5 mmol) was added by dissolving in 2 ml of acetonitrile through syringe dropwise at room temperature. The reaction mixture was stirred at room temperature for an hour and then refluxed for 24hr. After completion of the reaction, the mixture was concentrated under reduced pressure. The crude product was purified by column chromatography using 100-200 mesh silica gel and pet. ether-ethyl acetate (9:1) to get 0.051 g, 15 % of product.

12. Fe(Phthalocyanin) catalyzed reaction of bromamine-T with ethyl-2-allyl-2-cyano-4-pentenoate

A 25 ml RB flask equipped with magnetic stirring bar, reflux condenser and argon balloon was charged with bromamine-T (0.326 g, 1 mmol), ethyl-2-allyl-2-cyano-4-pentenoate (0.193 g, 1 mmol), $3A^0$ mol. sieves (50 mg) and Fe(Pc) (0.030 g, 0.052 mmol) in dry ethylene dichloride was added. The reaction mixture was refluxed for 24hr. After completion of the reaction, the mixture was concentrated under reduced pressure. The crude product was purified by column chromatography using 100-200 mesh silica gel and pet. ether-ethyl acetate to get 0.072 g, 20% of the product.

Ethyl-N-(4-methylphenylsulphonyl)-7-cyano-3-azabicyclo[3.3.0]octane-7-carboxylate



Yield : 0.072 g, (20 %)

M.P. : 105-107 ^{0}C

^{1}H-NMR (δ ppm, 200 MHz, $CDCl_3$) : 1.21(q, 6H J=5Hz); 1.93(dd, 2H J=10Hz,

Hz); 2.33(s, 3H); 2.41(m, 2H); 2.62(dd, 2H, J=5Hz) 2.76(d, 2H,); 3.16(d, 2H); 4.15(q, 2H); 7.22(d, 2H, 9Hz); 7.54(d, 2H, 9Hz).

^{13}C-NMR (δ ppm, 200 MHz, $CDCl_3$) : 13.89, 21.46, 41.20, 42.15, 52.92, 63.00, 119.49, 128.02, 129.64 131.22, 143.97, 167.20

IR ($CHCl_3$, cm^{-1}) : 3022.25, 2983.67, 2360, 2341.42, 243.06,1741.60, 1637.45, 1596.95, 1477.37, 1346.22, 1242.07, 1217.0,1164.92,1093, 757.95.

Mass : 362, 332, 300, 241, 195, 174.

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SPECTRA

^{1}H-NMR

21 May 2003
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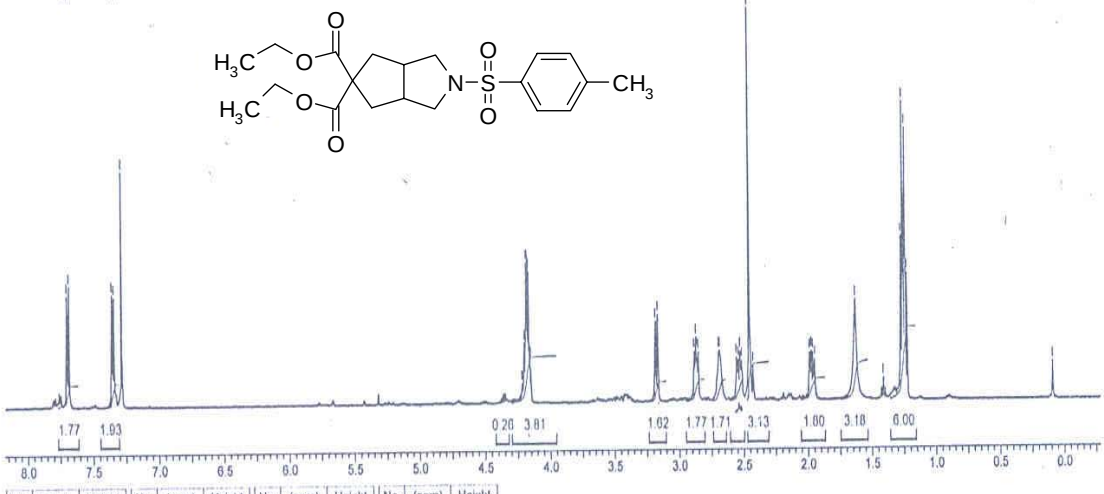

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3	1.24	0.691	14	2.43	0.088	25	2.87	0.161	36	4.20	0.151
4	1.25	0.422	15	2.46	1.000	26	2.89	0.125	37	4.22	0.047
5	1.26	0.425	16	2.52	0.100	27	3.17	0.220	38	7.29	0.597
6	1.26	0.757	17	2.53	0.126	28	3.19	0.201	39	7.34	0.274
7	1.28	0.415	18	2.54	0.103	29	4.15	0.108	40	7.36	0.281
8	1.41	0.053	19	2.56	0.110	30	4.16	0.128	41	7.69	0.304
9	1.63	0.253	20	2.68	0.124	31	4.17	0.330	42	7.70	0.278
10	1.95	0.104	21	2.69	0.127	32	4.17	0.343			
11	1.96	0.121	22	2.70	0.126	33	4.18	0.355			

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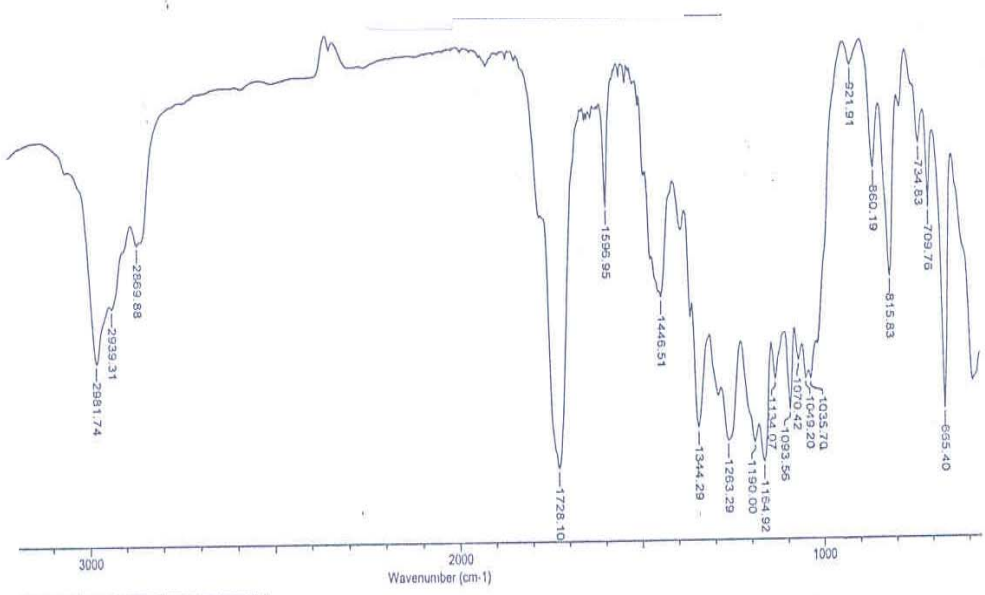

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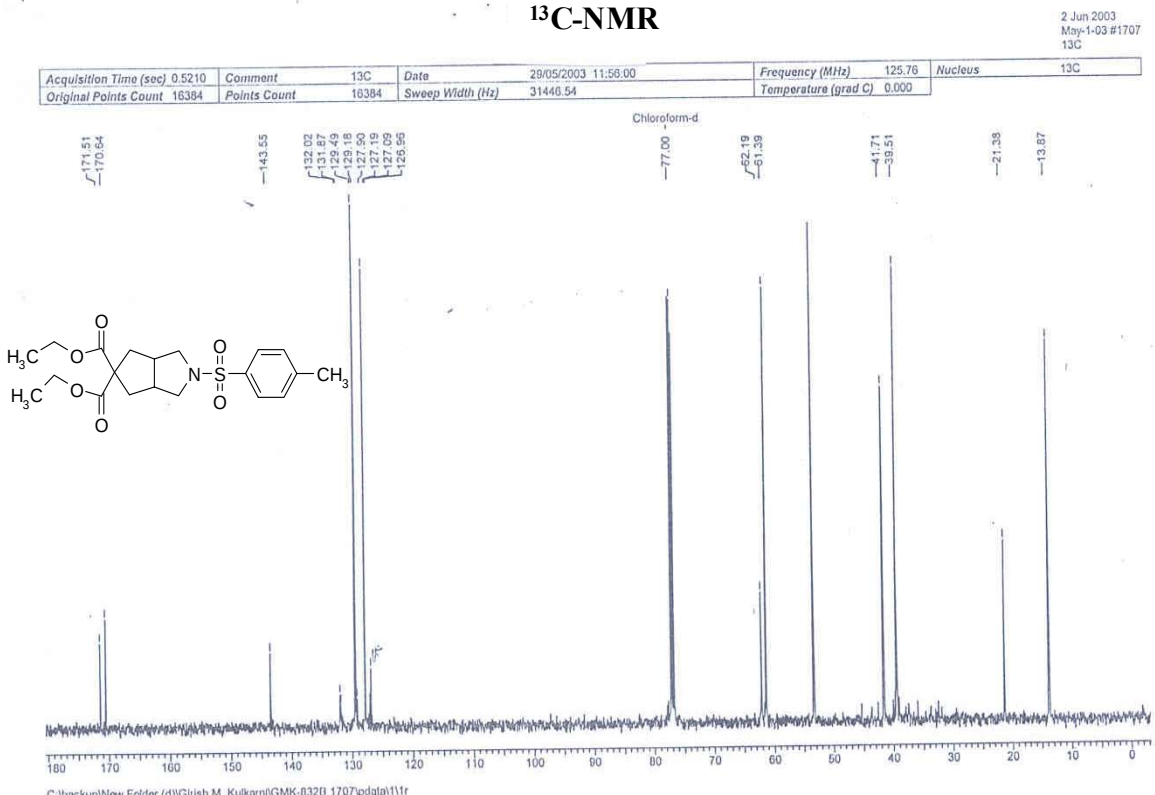

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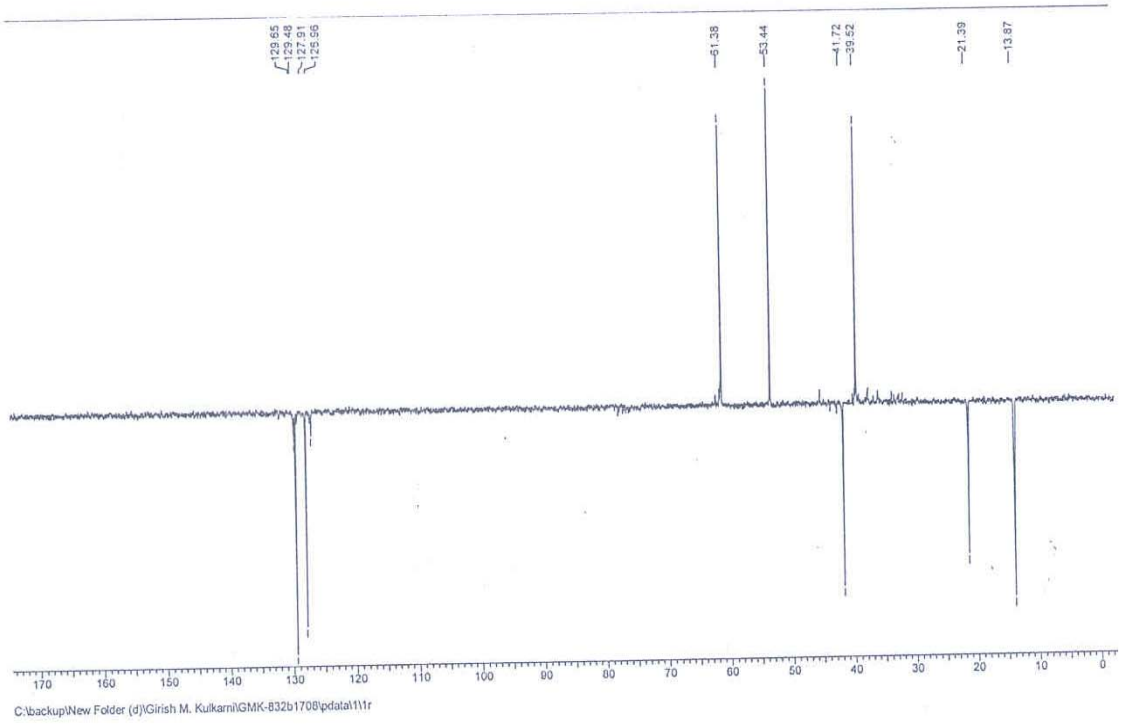

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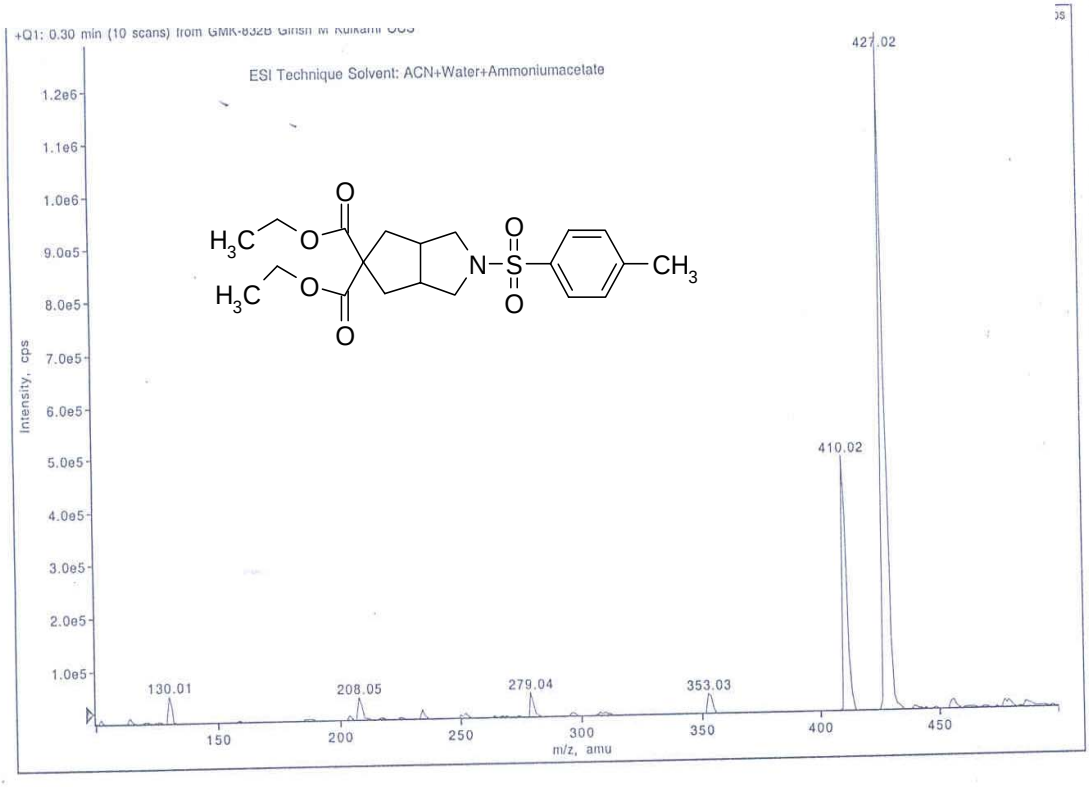

^{1}H-NMR

21 Jan 2004
wed3msl.002
GIRISH/1H

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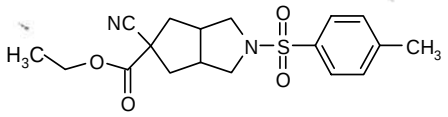

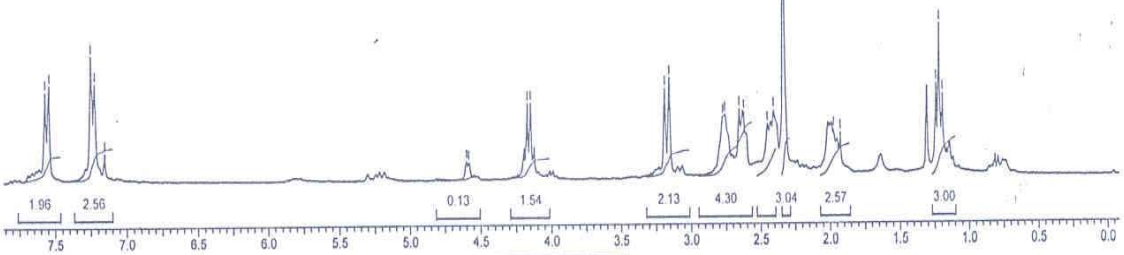

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1	1.19	0.237	9	2.02	0.187	17	4.58	0.045
2	1.21	0.442	10	2.65	0.196	18	4.60	0.048
3	1.24	0.266	11	2.76	0.180	19	7.15	0.078
4	1.93	0.126	12	2.77	0.174	20	7.22	0.278
5	1.98	0.134	13	3.16	0.287	21	7.25	0.359
6	2.33	1.000	14	3.19	0.256	22	7.54	0.273
7	2.41	0.192	15	4.15	0.217	23	7.57	0.254
8	2.45	0.153	16	4.17	0.215			

No.	Annotation	(ppm)
1	Chloroform-d	7.25

A:\wed3msl.002

IR

CHCl3

Title GIRISH M. KULKARNI - GMK-875(C) - CHCL3 - 19-01-2004	Date 04/01/19 14:53:20	Technique Infrared	Spectral Region IR
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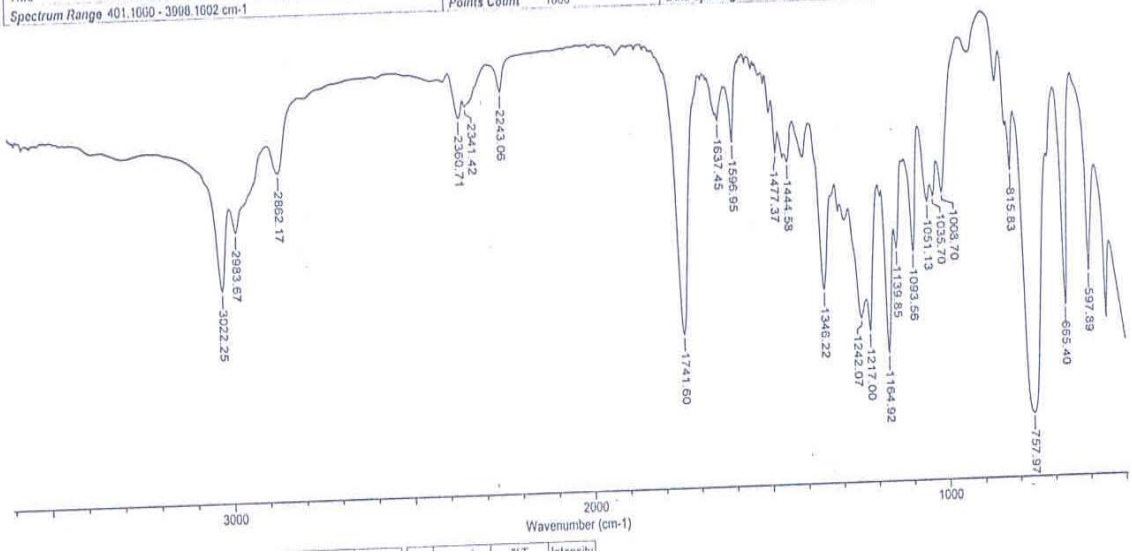

^{13}C-NMR

22 Jan 2004
thu4ac.013
GMK-875C

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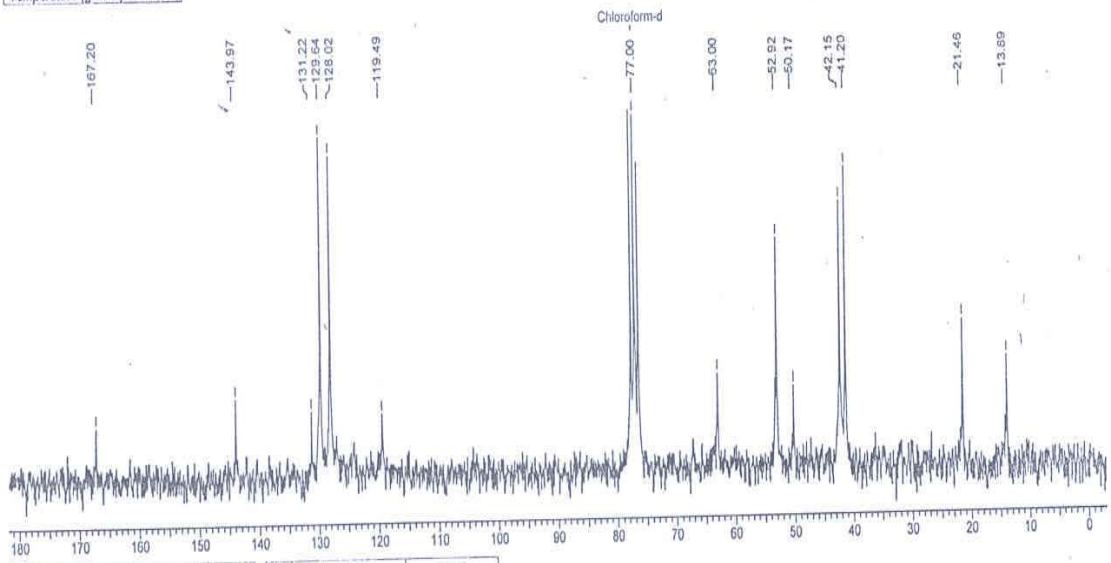
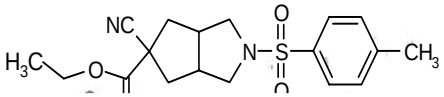
Temperature (grad C) 24.000							



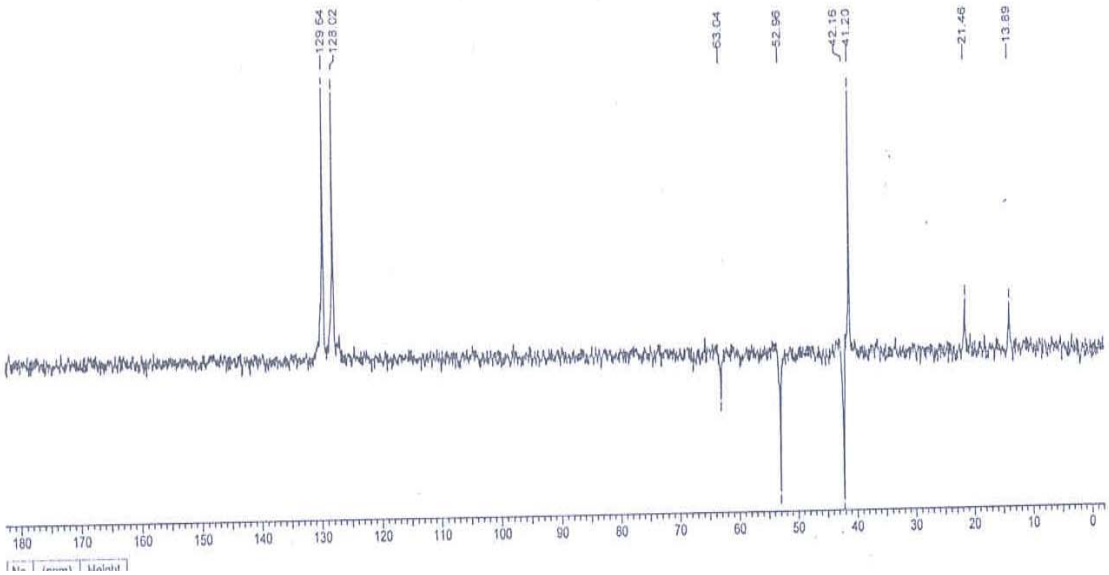
No.	(ppm)	Height	No.	(ppm)	Height
1	13.89	0.289	8	77.00	0.988
2	21.46	0.392	9	119.49	0.161
3	41.20	0.830	10	128.02	0.888
4	42.15	0.731	11	129.64	0.941
5	50.17	0.216	12	131.22	0.170
6	52.92	0.631	13	143.97	0.209
7	63.00	0.255	14	167.20	0.135

No.	Annotation	(ppm)
1	Chloroform-d	77.00



^{13}C-NMR DEPT

A:\thu4ac.013



MASS SPECTRUM

OSTARMultiView 1.5.0
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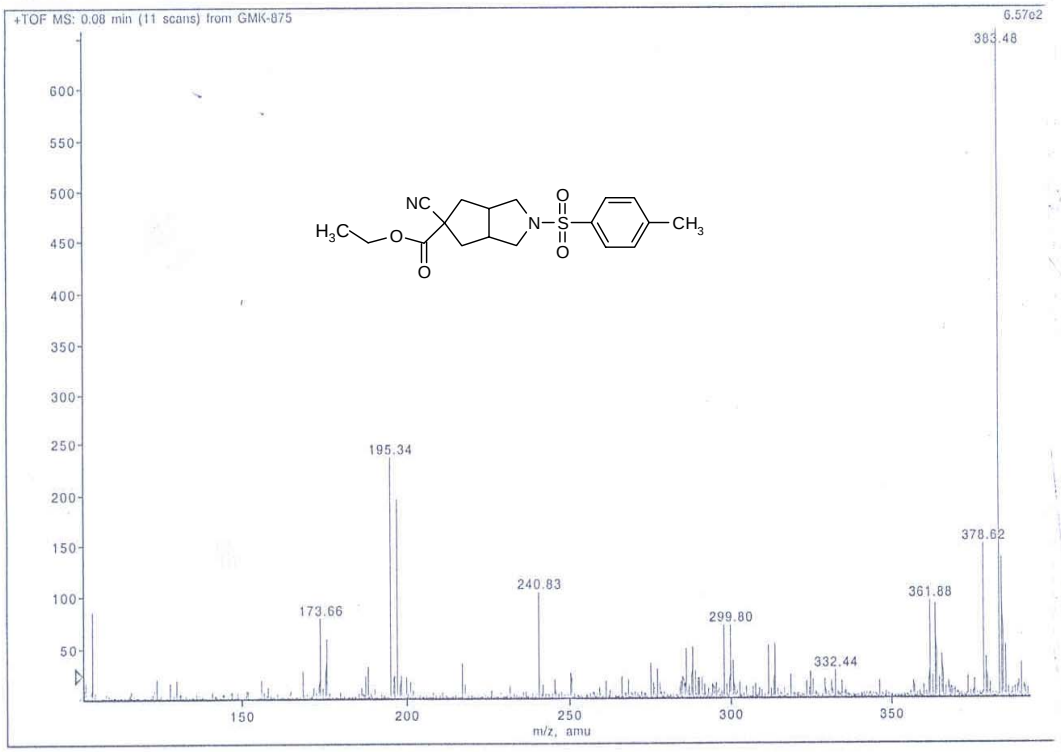


Chapter-4

Use of Nitrogen ligands in Mizoroki-Heck, Buchwald-Hartwig aryl amination and Suzuki-Coupling reactions

Mizoroki-Heck reaction

4.1.1 Introduction

The Pd-catalyzed arylation of olefins with aryl halides generally referred to as the Heck reaction, has received increasing attention in the last two decades.[1, 2] This is primarily due to the enormous synthetic potential of this versatile method for generating new C-C bonds. This reaction represents a powerful and popular method for the formation of C-C bonds. In particular, Heck reaction is an important method for the preparation of aryl functionalized alkenes in synthetic organic chemistry as applicable to pharmaceutical industry. The reaction was discovered by R. F. Heck in the late sixties. Initially, the reaction received much attention for forming C-C bond formation in a single step and the reaction was not well developed in seventies and early eighties. Only few research groups continued to explore the reaction. In mid eighties many research groups focused on developing and exploring the scope and limitations of the reaction.

As shown in the scheme-1**, styrenes and dienes can be prepared from the corresponding alkene and aryl or vinyl compounds substituted with a leaving group X = Cl, Br, I, N_2BF_4, OTf and COCl. This reaction is important owing to the possibility of preparing not only simple terminal or 1, 2-disubstituted olefins but also numerous complex molecular frameworks, e.g. tertiary and quaternary stereo centers. Dienes and alkynes can also be used as unsaturated compounds to get the corresponding coupled products.**

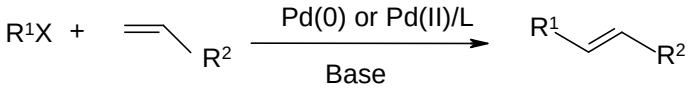
Thus organo-palladium compounds play an important role in homogeneous catalysis due to their versatility and non toxicity. Traditionally, variety of palladium sources such as $Pd(OAc)_2$ $PdCl_2$ $PdCl_2[P(C_6H_5)_3]$, $Pd_2(dba)_3$, etc. were used as catalysts with or without phosphine (for example $P(C_6H_5)_3$) ligands.

However, these catalytic systems suffer from some severe limitations such as non-applicability of this reaction on industrial scale. Typically a relatively large amount of catalyst (1-5 mol %) is

needed for reasonable conversions and catalyst recycling is often hampered by early precipitation of Pd-black.

Scheme-1

Heck Reaction



R^1 = Aryl, Alkenyl

R^2 = Aryl, Alkenyl, $COOC_2H_5$, etc

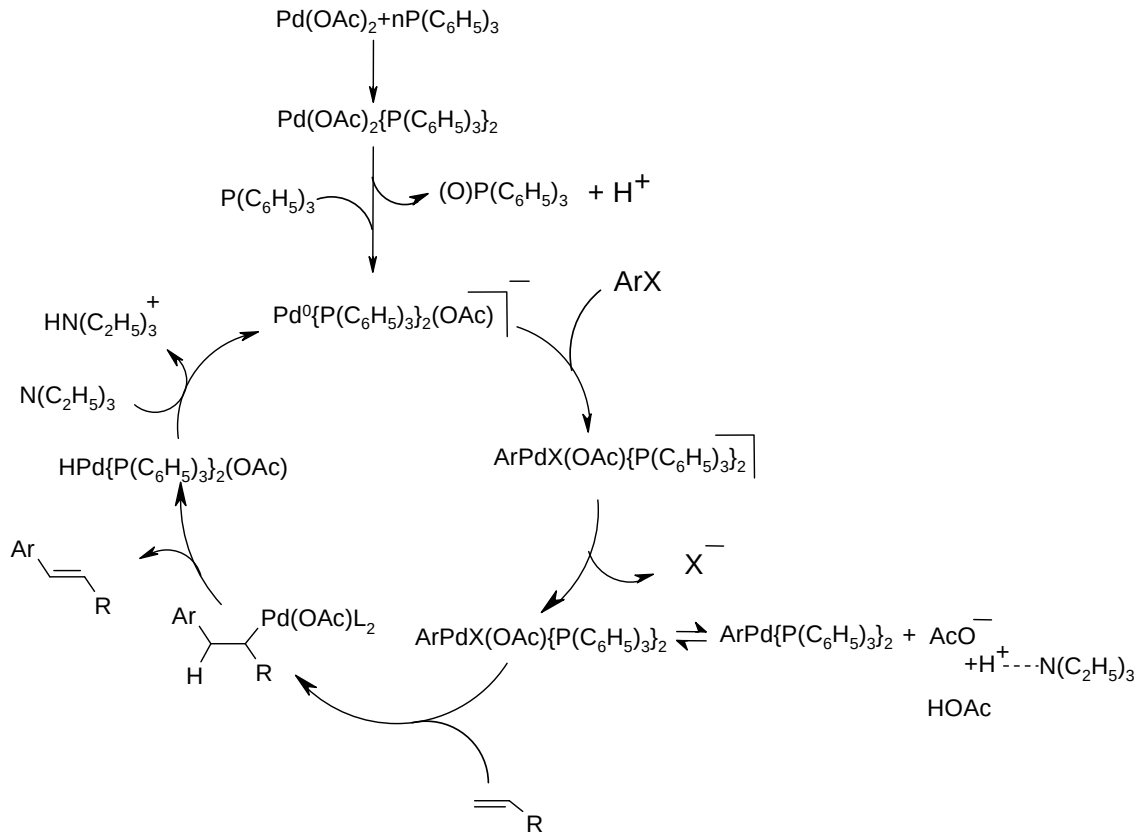
X = I, Br, OSO_2CF_3

Mechanism of the Heck Reaction

The most accepted mechanism of this reaction goes through the following organometallic intermediates. There are two major steps involved in the reaction mechanism, oxidative addition and reductive elimination as shown in (scheme-2**)**.

Mechanism

Scheme-2

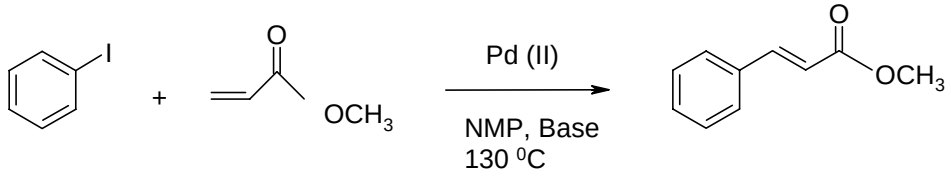


Background

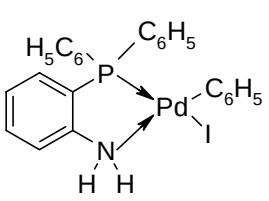
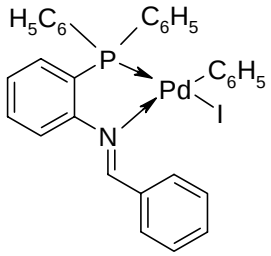
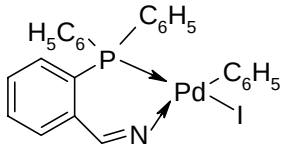
Nitrogen compounds are commonly used ligands in transition metal chemistry and equal in number and reactions to P-ligands.[3] Palladium complexes with various phosphines as ligands have been most commonly used as catalysts for the Mizoroki-Heck reaction.

In the year 2000, Pd (II) complexes of Phosphine-Nitrogen (P-N) bidentate donors have been reported as efficient catalysts for the heck reaction.[4] In a typical reaction between phenyliodide and methyl acrylate in NMP at ca. 130 ^{0}C provides methyl cinnamate with a TON upto 10^6 (Scheme-1).

Scheme-1

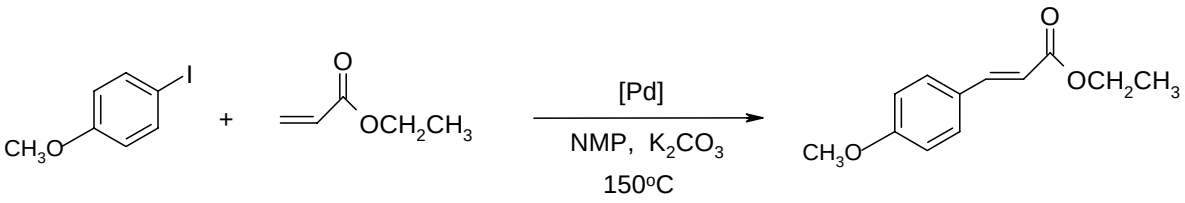


Pd (II) Complexes

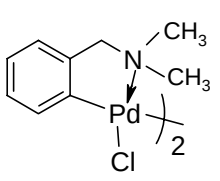




In 2001, Suresh Iyer[5] et al have reported amine and oxime palladacycles with aryl-Pd covalent bond as robust catalysts for the Heck reaction of aryl iodides, bromides and even chlorides. High TON's and TOF's were obtained (Scheme-2).

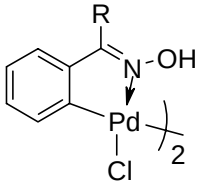
Scheme-2



N, N-Dimethyl benzylamine, Acetophenone and Benzophenone oxime Palladacycles



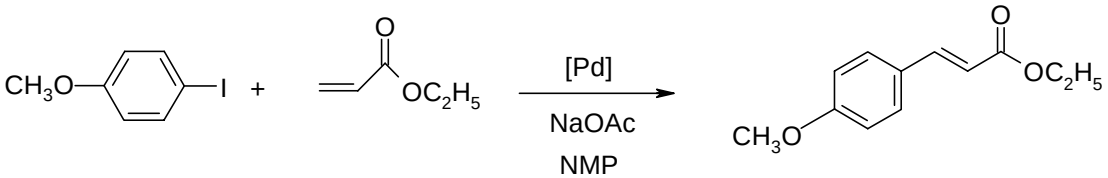
1

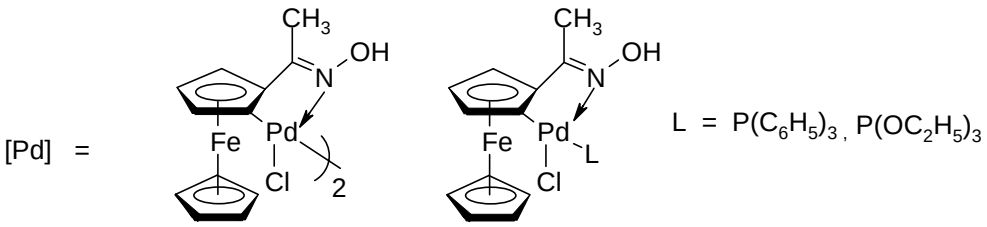


2 R = H, C_6H_5

Acetyl ferrocenyloxime palladacycles have been prepared and used as catalysts for the activation of aryl bromides and aryl chlorides in Heck reaction by Suresh Iyer[6] et al. Good yields of Heck coupled products were obtained with TON of up to 62,000 (Scheme-3).

Scheme-3

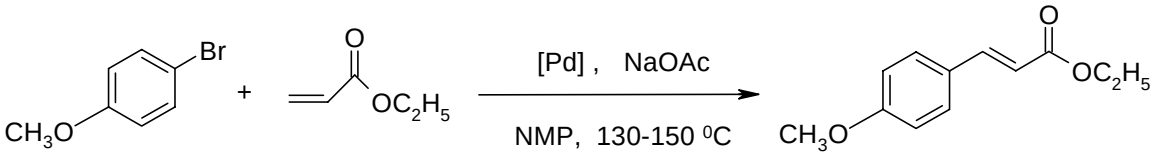


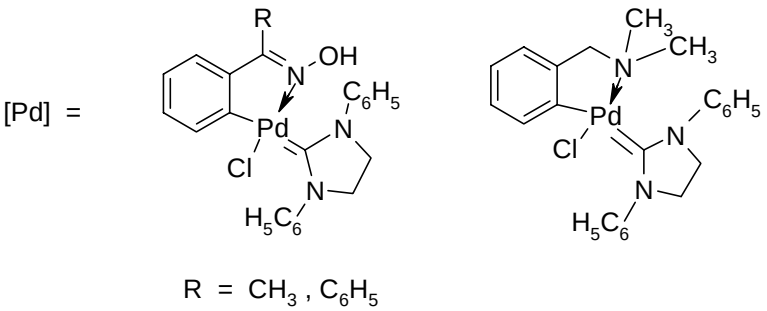


1 **2, 3**

In the year 2003, Suresh Iyer[7] et al have shown that *ortho*-Palladated aryl oxime and amines with a N-heterocyclic carbene ligand catalyze the Mizoroki-Heck and Suzuki reactions with high yields, and moderate TON (2,000-92,000) and TOF (200-4,300 h^{-1}) (Scheme-4).

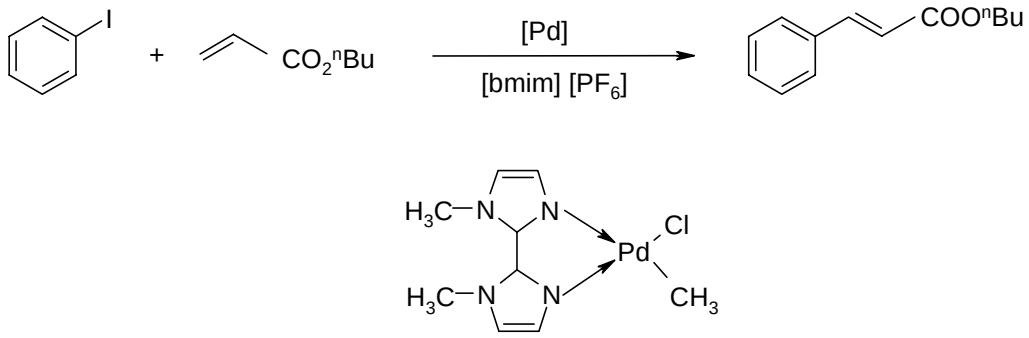
Scheme-4





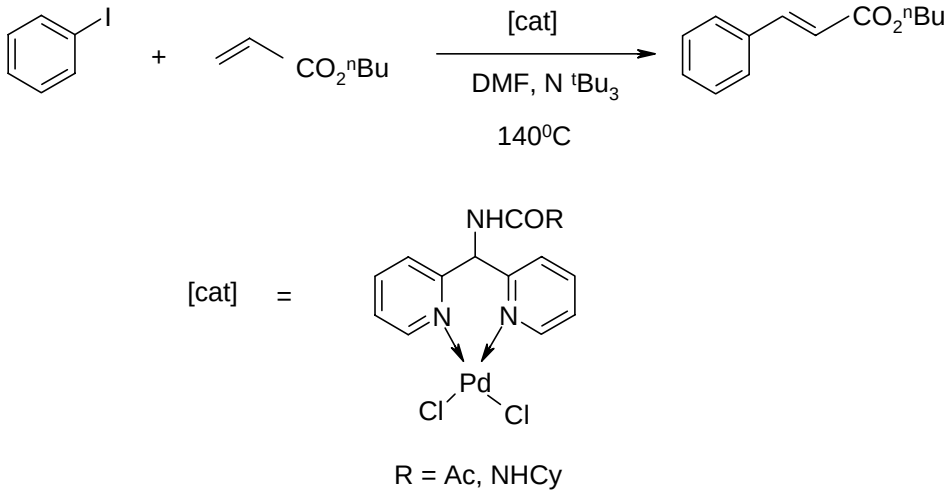
In the year 2003, Howard Alper's[8] group prepared new Pd (II) complexes with bisimidazole ligands and proved as effective catalysts for Heck reaction under phosphine free conditions using ionic liquids as solvent. This system could be recycled about 5 times without any loss of catalytic activity (Scheme-5).

Scheme-5



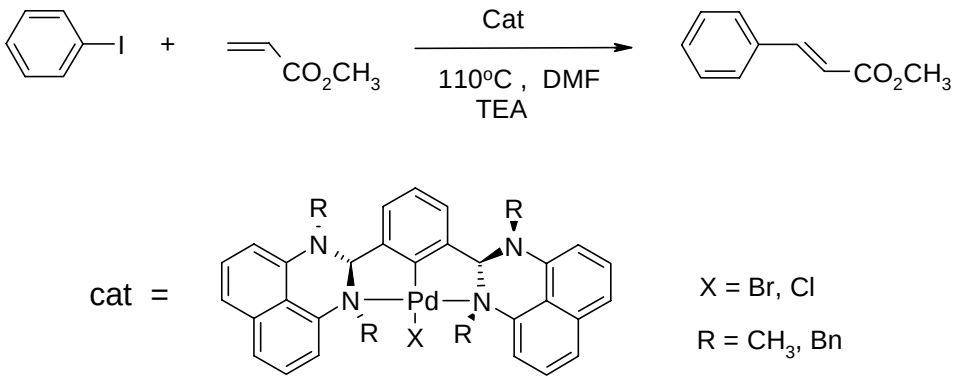
In 2003, it has been shown that a new Pd-dipyridylmethylamine complex is an excellent catalyst for C-C bond forming processes as Heck, Suzuki and Sonogashira reactions both in organic and aqueous solvents under homogeneous conditions[9] (Scheme-6).

Scheme-6



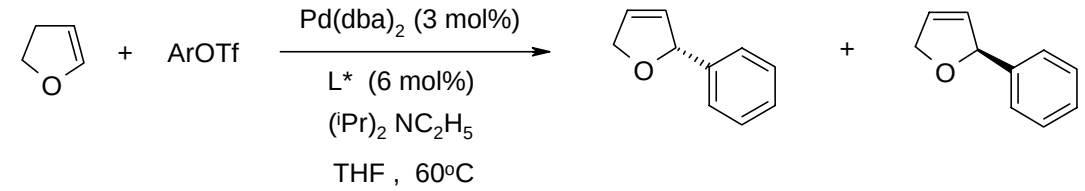
In 2004, a novel Pd-NCN pincer complex[10] bearing two additional nitrogen atoms has been synthesized and used for Heck reaction. The catalyst is quite effective for all aryl iodides with TON of 4.3 X 10^6 (Scheme-7).

Scheme-7

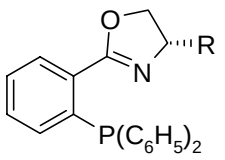


A series new chiral P,N-ligands with substituents at the benzylic position has been prepared and used for asymmetric Heck and allylic substitution reactions, by Xue-long Hou et al[11] (Scheme-8).

Scheme-8



L* =



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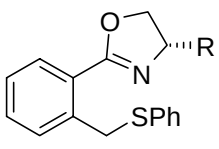

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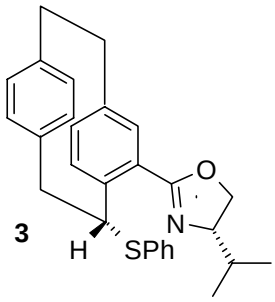
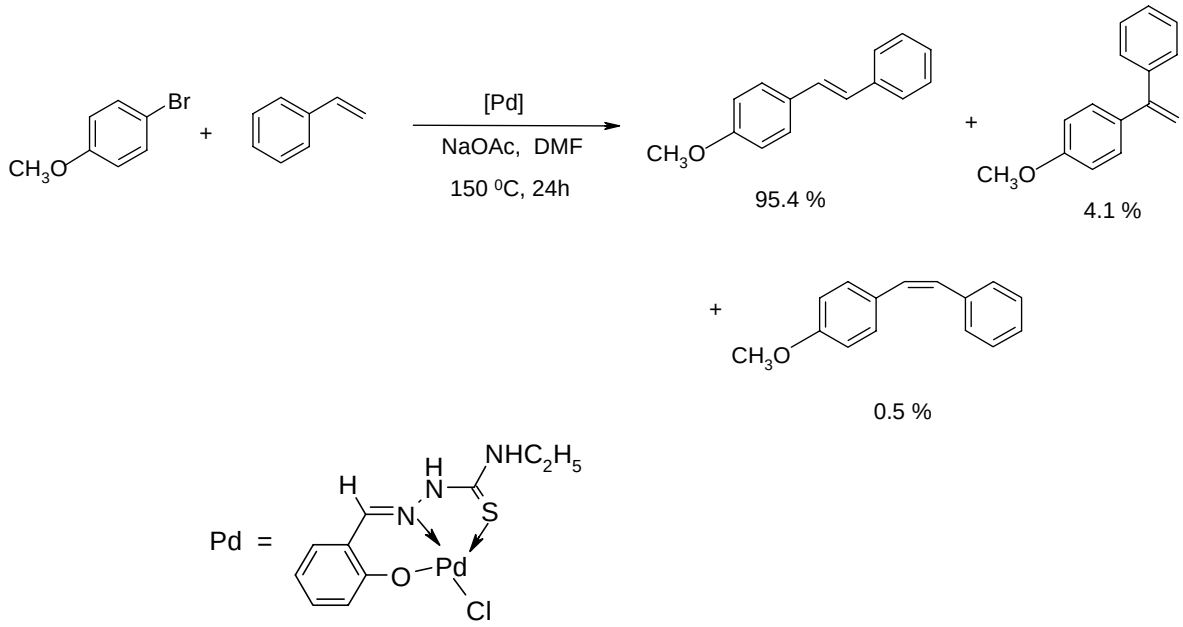


3

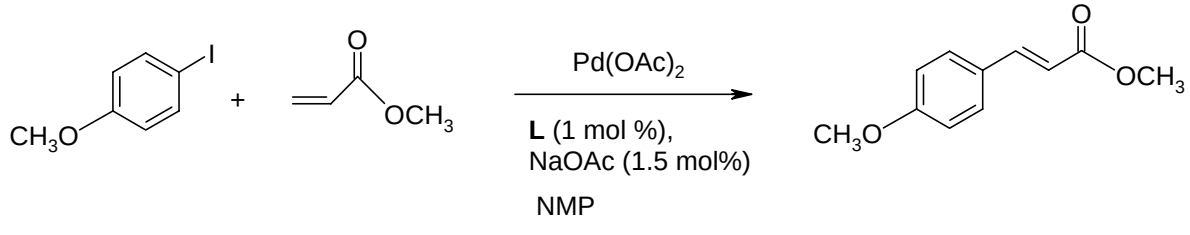
A novel Pd-complex[12] with salicylaldehyde N (4)-ethylthiosemicarbazone has been synthesized and shown that the catalyst effectively catalyzes the Heck reaction of aryl bromides with styrene with TON of up to 43,000 at 150^{0}C after 24h (Scheme-9).

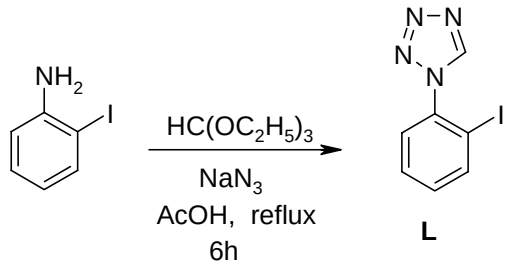
Scheme-9



1-(2-Iodophenyl)-1H-tetrazole was synthesized by the reaction of 2-iodoaniline, sodium azide and triethyl orthoformate in acetic acid and used for catalysis of Heck reaction in the presence of $Pd(OAc)_2$.[13] Excellent yields of cross coupled products were obtained (Scheme-10).

Scheme-10





L

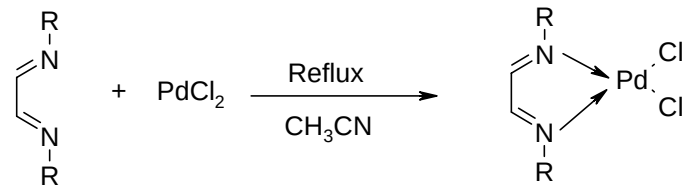
Objective

Our aim was to activate less active aryl bromides in the Heck, Suzuki-coupling and Amination reactions, using Pd-complexes containing nitrogen ligands.

4.1.2 Present work

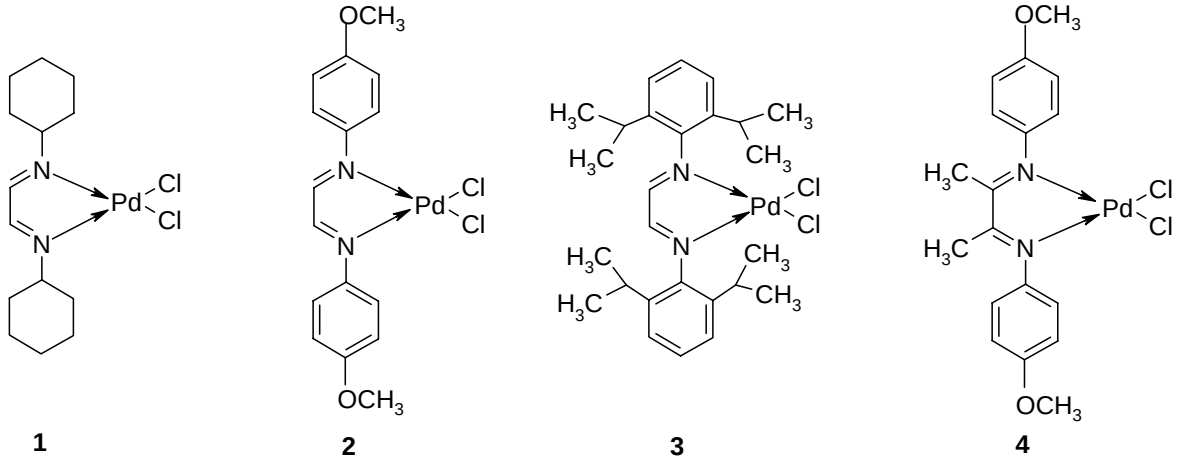
Diazabutadiene Palladium complexes were easily prepared by the addition of corresponding ligands in refluxing acetonitrile $PdCl_2$ solution (Scheme-1).

Scheme-1 Preparation of Diazabutadiene Palladium complexes



R : C_6H_{11}, 4-CH_3O-C_6H_4, 2,6-$(CH_3)_2CH.C_6H_3$

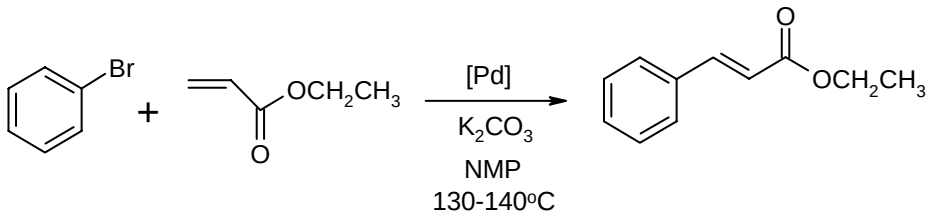
$PdCl_2$(DAB) complexes



$PdCl_2$(DAB) catalyzed Heck Reaction of aryl bromides

Mizoroki-Heck reaction of aryl bromides with olefins was carried out in the presence of different $PdCl_2$(DAB) complexes. Both electron deficient and electron rich aryl bromides and different olefins were used for the reaction.

Scheme-2



$PdCl_2$(DAB) catalyzed Heck Reaction of aryl bromides in TBAB as ionic liquid

Mizoroki-Heck reaction of aryl bromides with olefins in the presence of $PdCl_2$(DAB) complexes was carried out in tetrabutyl ammonium bromide as ionic liquid.

Scheme-3

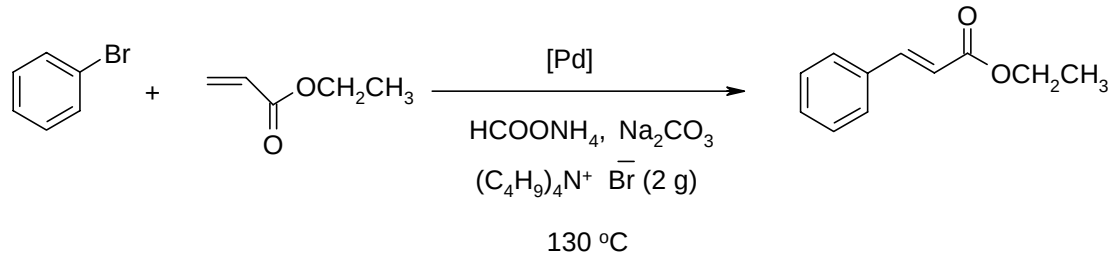


Table - 1 : Mizoroki-Heck reaction with $PdCl_2$(DAB) catalyst

Sl.No	Aryl bromide	Olefin	Catalyst	Time (h)	Yield (%)[a]	TON/TOF
1.	C_6H_5Br	$C_5H_8O_2$[b]	1	24	63	63
			2	45	16	16
			3	20	32	32
			4	24	40	-
2.	C_6H_5Br(10mmol)	$C_7H_{12}O_2$	1	24	20	2666(111)[c]
			1A	24	26.5	132[d](5)
3.	C_6H_5Br(50mmol)	C_8H_8[e](50mmol)	1	24	64	64
			1A	48	15	37,600(783)[f]
			2	24	21	21
			3	29	31	31
			4	24	19	-
4.	1-$C_{10}H_7Br$	$C_5H_8O_2$	1	24	45	45
			2	24	30	30
			3	24	44	44
5.	1-$C_{10}H_7Br$	C_8H_8	1	45mins	89	89
			2	31	44	44
			3	24	78	78
			4	24	22	-
6.	1-$C_{10}H_7Br$ (10mmol)	C_8H_8	1	3	86	17,200(5733)[g]
	1-$C_{10}H_7Br$ (10mmol)		1A	6	76	380(63)[h]

7.	4-HO-C_6H_4.Br	$C_5H_8O_2$	1	24	45	45
			2	42	nr	-
			3	24	nr	-
			4	24	8	-
8.	4-HO-C_6H_4.Br	C_8H_8	1	24	64	64
			2	24	nr	-
			3	24	38	38
			4	24	nr	-
9.	4-$(CH_3)_2N.C_6H_4$.Br	$C_5H_8O_2$	1	24	46	46
			2	48	nr	-
			3	24	25	25
			4	24	nr	-
10.	4-$(CH_3)_2N.C_6H_4$.Br	C_8H_8	1	24	10	10
			2	24	nr	-
			3	24	nr	-
			4	24	nr	-

[a] Reaction Conditions: halide:olefin: base:cat-2:4:4:0.02-temp.:150°C.
[b] $C_5H_8O_2$, Ethyl acrylate.
[c] Reaction conditions:halide:olefin:base : TBAB:Cat-1:10:10:15:0.00075-temp.: 140°C.

[d] Reaction conditions:halide:olefin:base : cat-1A{$Pd(Dba)_2$+Cy-DAB}-10:10:15:0.02:0.04-temp.:140°C.
[e] C_8H_8, Styrene (i) nr, no reation.
[f] Reaction conditions :halide:olefin:base:cat-1A{$Pd(Dba)_2$+Cy-DAB}-50:50:55:0.0002:.0004-temp.:140°C.
[g] Reaction conditions:halide:olefin:base:TBAB:Cat-1 10:10:15:1:0.0005-temp.:120°C.

Table-2: Heck reaction in Ionic Liquid with $PdCl_2$ (DAB) catalysts

S. No.	Aryl Bromide	Olefin	Catalyst	Time, h	Yield %
1.	C_6H_5Br	CH_2=CH.COOBu	1	24	70
		CH_2=CH.COOEt	2	24	68
		CH_2=CH.COOEt	3	20	67
		CH_2=CH.COOBu	4	24	45
2.	C_6H_5Br	Ph.CH=CH_2	2	24	57
		Ph.CH=CH_2	4	24	35
3.	4- HO. C_6H_5.Br	CH_2=CH.COOEt	1	24	46
4.	1- $C_{10}H_7Br$	CH_2=CH.COOEt	1	24	67
			2	24	50
			3	24	85
5.	1- $C_{10}H_7Br$	Ph.CH=CH_2	2	31	87
			4	24	55
6.	4- Br. $C_6H_4.NMe_2$	CH_2=CH.COOEt	2	48	52
			3	24	57

Reaction conditions :

A. ArBr (3 mmol), Butylacrylate (3 mmol), Na_2CO_3 (6 mmol), $HCOONH_4$ (0.1 mmol), Bu_4NBr (6 mmol); Temperature – 130 ^oC

B. ArBr (2 mmol), Styrene (5 mmol), HCOONa (0.147 mmol), NaOAc (2.4 mmol), Bu_4NBr (6 mmol), Temperature – 130 ^oC

Results and Discussion

The results of $PdCl_2$(DAB) catalyzed reaction were given in **Table-1.** The reaction of bromobenzene with ethyl acrylate was catalyzed by $PdCl_2$(cyclohexyl-DAB) to give the E-ethylcinnamate in 63% yield. K_2CO_3 was the base of choice and N-methylpyrrolidinone was used as solvent. With the same catalyst, reaction of bromobenzene with styrene gave the E-stilbene in 64% yield. 4-bromophenol and 4-N, N-dimethyl amino bromobenzene gave only 45 and 46% yields of the substituted ethyl cinnamate while 1-bromonaphthalene and 4-bromophenol gave 89% and 64% yield of the substituted products while 4-N, N-dimethylamino bromobenzene gave only 10% yield. Rate acceleration was observed in the reaction of 1-bromonaphthalene with styrene and reaction was complete in 45mins, compare to long reaction times for other substrates and catalysts. No reaction was observed with 4-chlorotoluene and 4-chloronitrobenzene.

These results are comparable to or better than the results obtained with $PdCl_2$ $\{P(C_6H_5)_3\}_2$ as catalyst (20 - 30 % yield) under similar conditions for the same substrates. The diimine from the condensation of benzaldehyde and ethylenediamine was also used to prepare Pd complex. However, the use of this catalyst also gave

only moderate yields (24 - 55 %) in the reactions of bromo benzene and bromo naphthalene with ethyl acrylate.

Use of other DAB ligands (Cat-2, p-anisidine DAB, Cat-3, 2,6-diisopropylaniline DAB) gave only moderate yields of the substituted products with different aryl bromides. In all these reactions Pd was in +2 oxidation state. For comparison, $Pd(dba)_2$ as catalyst with Cy-DAB as ligand gave comparable yields to $PdCl_2$(DAB) with bromobenzene and butylacrylate (26.5%, TON-132, TOF-5 h^{-1}) and bromonaphthalene and styrene (76%, TON-380, TOF, 63 h^{-1}). Reaction of bromobenzene (50 mmol) with styrene gave 1.354 g stilbene (15%, TON-37,600; TOF-783 h^{-1}).

Recently, the use of ionic liquids has been shown to improve the reactivity and yield of the Mizoroki-Heck reaction.[14] The use of Bu_4NBr as ionic liquid with Pd benzothiazole carbene complex as catalysts shows good reactivity.[15] The vinylation of aryl halides in Bu_4NBr as ionic liquid catalyzed by **1** gave 70 and 66 % yield of the substituted product while the other catalysts **2**, **3** and **4** gave moderate to high yields of the substituted product 52 – 87 % (**Table : 2**).

Multiple reaction - Heck, Suzuki, and Aryl amination in one pot

Heck, Suzuki, and Aryl amination reactions were carried out in the presence of $Pd(dba)_2/P(C_6H_5)_3$ and CuI catalyst. Reaction of 3 equivalents of bromobenzene with styrene, phenylboronic acid and morpholine 1 equivalent each, with sod.tertiarybutoxide as base in dioxane at reflux condition gave very good yields of the products. The

reaction was chemoselective and gave only the Heck, Suzuki and aryl aminated products in high yields. 96 % of biphenyl, 83% of stilbene, 91% of N-phenylmorpholine were obtained. The reaction was clean and there were no side products.

Heck reactions between bromobenzene and ethylacrylate were tried with $Mo(CO)_4$(DAB), $RuCl_2(DMSO)_4$ and $RuCl_2(DMSO)_4$ with $ZnCl_2$ in NMP and K_2CO_3 as base but no Heck coupled products were obtained.

Preparation of pentavalent Pd-complex was attempted by the reaction of p-methoxy iodobenzene and $PdCl_2$(DAB). The reaction was performed by treating p-methoxy iodobenzene with $PdCl_2$(Cyclohexyl-DAB) complex in toluene and 2 drops of NMP at refluxing condition. The reaction of p-methoxy iodobenzene was also tried with $PdCl_2$(DMG) complex. The ^{1}H-NMR was not clear so we couldn't able to assign the structure but peaks corresponding to NMP were also present. It could be possible that NMP might have coordinated with Palladium complex.[17]

Conclusion

Diazabutadiene based Pd-complexes were efficiently catalyze the Mizoroki-Heck reaction of electron rich and electron deficient aryl bromides with moderate to high yields of the products. Electron rich aryl bromides for e.g. p-bromophenol, N, N-

dimethylaniline gave moderately good yields of the Heck reaction products. Reactions in ionic liquid gave increased yields of the products.

4.1.3 Experimental

The aryl halides, styrene, ethyl acrylate, glyoxal, ligands, the metal complexes and catalysts were purchased or prepared according to known procedures.[16] All reactions were carried out under argon atmosphere. Insensitive reactions were carried out in air. NMP, DMSO and DMF were used as solvents and degassed by vacuum purging and flushing with Argon. The reactions were monitored by TLC using GF-

254 grade silica gel on glass plates. Silica gel (100-200 mesh) was used for column chromatography. Fresh round bottom flasks and stirring bars were used to prevent contamination by reactive catalysts like Pd in the studies of the other catalysts. All the reaction products are known compounds and characterized by IR (NaCl plate), ^{1}H NMR ($CDCl_3$, Varian 200 MHz, Bruker 300 MHz) and MS. Representative experimental procedures are described.

General procedure for the Heck reaction catalyzed by $PdCl_2$(DAB)

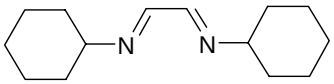
A 25 ml RB flask equipped with magnetic stirring bar, reflux condenser and argon balloon was charged with aryl bromide (5 mmol), olefin (10 mmol), Potassium carbonate (2.75 mmol) and Pd-complex (10 mg, 0.02 mmol) in N-methyl pyrrolidone (10 ml). The reaction mixture was allowed to stir at 140-150 ^{0}C for 4-24 h and neutralized with dil.HCl (10% by volume). The product was extracted with ethyl acetate (3 x 5 ml), the combined organic extracts dried over anhydrous sodium sulphate and concentrated under reduced pressure to yield the crude product. The crude product on silica gel column chromatographic purification using pet. Ether-ethyl acetate mixture gave the pure products.

Large scale reaction for TON and TOF

A 25 ml RB flask equipped with magnetic stirring bar, reflux condenser and argon balloon was charged with aryl bromide (75 mmol), olefin (150 mmol), potassium carbonate (20.7 g, 150 mmol) and Pd-complex (0.010 g, 0.025 mmol)) in N-methyl pyrrolidone (100 ml). The mixture was allowed to stir at 140-150 0C for 4-24 h and neutralized with dil.HCl (10% by volume). The product extracted with ethyl acetate (4 x 50 ml), the combined organic extracts was dried over anhydrous sodium sulphate and concentrated under reduced pressure to yield the crude product. The crude product on silica gel column chromatographic purification using pet.ether-ethyl acetate mixture gave the products.

1. Preparation of N, N-dicyclohexylethylenediimine

A solution of 3 g, (30 mmol) of cyclohexylamine in 10 ml of methanol was mixed with 0.87 g, (15 mmol) of 40% aqueous glyoxal while stirring and cooled to 0 ^{0}C. The white precipitate was separated and collected on filter paper. The solid was washed with cold methanol, and recrystallized from methanol / water, then dried.



N, N-dicyclohexylethylenediimine

Yield : 2.64g, (80%)

M.P. : 150 ^{0}C

IR ($CHCl_3$, cm^{-1}) : 2921, 2852, 2657, 1622, 1452, 1373, 1286, 1151, 1062, 952, 887, 844, 599.

^{1}H NMR (δ ppm, 200MHz, $CDCl_3$) : 7.94 (s, 2H, -CH=N-C_6H_{11}) ; 3.21-3.12 (m, 2H,) 1.85-0.96 (m, 20H, Cy-H).

2. N, N-Biscyclohexyldiimine palladium chloride (II)

A 25 ml RBF was charged with $PdCl_2$ (0.100g, 0.6 mmol) in 10 ml of acetonitrile and kept for reflux along with stirring. Ligand (0.132g, 0.6 mmol) was added and refluxed for another half an hour. The yellow precipitate of catalyst formed was filtered, washed with cold acetonitrile and dried.

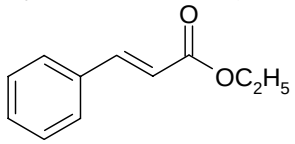
Yield : 0.172g (43%)

M.P. : 218-220 ^{0}C

C H Analysis : Calculated (%) : C (42.31), H(6.04), N (7.05)
Found (%) : C (42.33), H(6.52), N (6.94)

3. $PdCl_2$(DAB) catalyzed Heck reaction of bromobenzene with ethyl acrylate

In a 25 ml RBF, bromobenzene (0.314 g, 2 mmol), ethylacrylate (0.5 ml, 5 mmol), $PdCl_2$(DAB) (0.010 g, 0.025 mmol) and K_2CO_3 (0.552 g, 4 mmol) were taken in 8 ml of NMP. The reaction mixture was degassed under vacuum and simultaneously flushed with argon to exclude oxygen. Then mixture was heated at 140 ^{0}C. The reaction was monitored by TLC and heating continued for 24 h. After the completion, the mixture was neutralized with dil.HCl (10% v/v). The product extracted with ethyl acetate (4 x 50 ml), the combined organic extracts was dried over anhydrous sodium sulphate and concentrated under reduced pressure to yield the crude product. The crude product on silica gel column chromatographic purification using pet.ether-ethyl acetate mixture gave the ethylcinnamate (0.206 g, 63 %).



Ethyl-3-phenyl-(E)-2-propenoate (1)

Mol. F : $C_{11}H_{12}O_2$

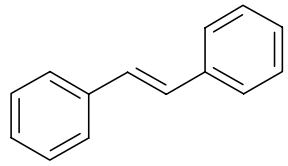
IR (cm $^{-1}$, Neat) : 2980, 1716, 1638, 1592, 1490, 1269, 1173, 883.

^{1}H NMR (δ ppm, 200MHz, $CDCl_3$) : 7.4 (m 1H, Ar-H); 7.3 (m, 2H, Ar-H); 7.21 (m, 2H, Ar-H); 7.64 (d, 1H, 16Hz); 6.39 (d, J=16 Hz, 1H); 4.19 (q, J=8.0Hz, 2H), 1.30 (t, J=8Hz, 3H)

4. $PdCl_2$(DAB) catalyzed Heck reaction of bromobenzene with styrene

In a 25 ml RBF, bromobenzene (0.314 g, 2 mmol), styrene (0.520 g, 5 mmol), $PdCl_2$(DAB) (0.010 g, 0.025 mmol) and K_2CO_3 (0.552 g, 4 mmol) were taken in 8 ml of NMP. The reaction mixture was degassed under vacuum and simultaneously flushed with argon to exclude oxygen. Then mixture was heated at 140 ^{0}C. The reaction was monitored by TLC and heating continued for 24 h. After the completion, the mixture was neutralized with dil.HCl (10% v/v). The product extracted with ethyl acetate (4 x 50 ml), the combined organic extracts was dried over anhydrous sodium sulphate and concentrated under reduced pressure to yield the crude product. The crude product on silica gel column chromatographic

purification using pet.ether-ethyl acetate mixture gave the stilbene (0.230 g, 64 %).



1, 2-Diphenyl-(E)-ethylene (2)

Mol F : $C_{14}H_{12}$

M.P. : 120 ^{0}C

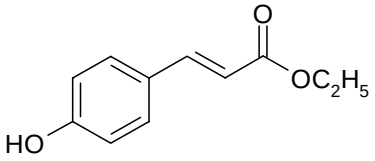
IR (cm $^{-1}$, Nujol) : 2855, 1602, 1506, 1375, 920, 765.

^{1}H NMR (δ ppm, 200MHz, $CDCl_3$) : 7.6 (d, J=14 Hz, 2H), 7.45-7.25 (m, 10H)

Mass (m/z) : 180 (M^+, 100), 104 (42), 77 (100).

5. $PdCl_2$(DAB) catalyzed Heck reaction of 4-bromophenol with ethyl acrylate

In a 25 ml RBF, 4-bromophenol (0.346 g, 2 mmol), ethyl acrylate (0.5 ml, 5 mmol), $PdCl_2$(DAB) (cat-1**) (0.010 g, 0.025 mmol) and K_2CO_3 (0.552 g, 4 mmol) were taken in 8 ml of NMP. The reaction mixture was degassed under vacuum and simultaneously flushed with argon to exclude oxygen. Then mixture was heated at 140 ^{0}C. The reaction was monitored by TLC and heating continued for 24 h. After the completion, the mixture was neutralized with dil.HCl (10% v/v). The product extracted with ethyl acetate (4 x 50 ml), the combined organic extracts was dried over anhydrous sodium sulphate and concentrated under reduced pressure to yield the crude product. The crude product on silica gel column chromatographic purification using pet.ether-ethyl acetate mixture gave the stilbene (0.172 g, 45 %).**



Ethyl-3-(4-hydroxy phenyl)-(E)-2-propionate (3)

Mol. F. : $C_{11}H_{12}O_3$

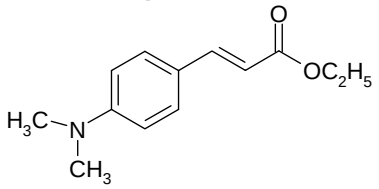
IR (cm $^{-1}$, Nujol) : 3278, 2954, 2854, 1682, 1635, 1604, 1581, 1521, 1458, 1373, 1280, 1188, 1164, 833.

^{1}H NMR (δ ppm, 200MHz, $CDCl_3$) : 7.68 (d, J=16.0 Hz, 1H); 7.44 (d, J=8.0 Hz, 2H); 6.88 (d, J=8.0 Hz, 2H); 6.34(d, J=16.0Hz, 1H); 4.28 (q, -OC<u>H</u>$_2$CH$_3$, 2H), 1.34 (t, J=8Hz, -OCH$_2$C<u>H</u>$_3$ 3H); 1.35 (t, J=8Hz, 3H)

Mass (m/z) : 192 (M^+), 177, 164, 147, 119, 91, 77, 65.

6. $PdCl_2$(DAB) catalyzed Heck reaction of 4-bromo N, N-dimethylaniline with ethyl acrylate

In a 25 ml RBF, 4-Bromo N, N-dimethylaniline (0.400 g, 2 mmol), ethyl acrylate (0.5 ml, 5 mmol), $PdCl_2$(DAB) (cat-1) (0.010 g, 0.025 mmol) and K_2CO_3 (0.552 g, 4 mmol) were taken in 8 ml of NMP. The reaction mixture was degassed under vacuum and simultaneously flushed with argon to exclude oxygen. Then mixture was heated at 140 ^{0}C. The reaction was monitored by TLC and heating continued for 24 h. After the completion, the mixture was neutralized with dil.HCl (10% v/v). The product extracted with ethyl acetate (4 x 50 ml), the combined organic extracts was dried over anhydrous sodium sulphate and concentrated under reduced pressure to yield the crude product. The crude product on silica gel column chromatographic purification using pet.ether-ethyl acetate mixture gave the stilbene (0.201g, 46 %).



Ethyl-3-(4-N, N-dimethyl phenyl)-(E)-2-propionate (4)

Mol F : $C_{13}H_{17}NO_2$

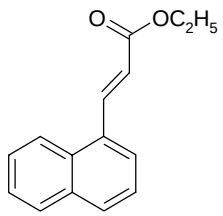
IR (cm $^{-1}$, Nujol) : 2923, 2854, 1704, 1600, 1525, 1456, 1367, 1305, 1220, 1155, 985, 813

^{1}H NMR (δ ppm, 200MHz, $CDCl_3$) : 7.65 (d, 1H, 15Hz, -CH=CH-COO); 7.43 (d, 2H, 8Hz, Ar-H); 6.88 (d, 2H, 8Hz, Ar-H); 6.25 (d, 1H, 15Hz, -CH=CH-COO); 4.25 (q, 2H, $-OCH_2CH_3$); 3.01 (s, 6H, $-N(CH_3)_2$); 1.32 (t, 3H, 9Hz OCH_2CH_3).

Mass (m/z) : 219, 190, 174, 146, 130, 118, 102, 87, 72.

7. $PdCl_2$(DAB) catalyzed Heck reaction of 1-bromonaphthalene with ethyl acrylate

In a 25 ml RBF, 1-Bromonaphthalene (0.400 g, 2 mmol), ethyl acrylate (0.5 ml, 5 mmol), $PdCl_2$(DAB) (**cat-1**) (0.010 g, 0.025 mmol) and K_2CO_3 (0.552 g, 4 mmol) were taken in 8 ml of NMP. The reaction mixture was degassed under vacuum and simultaneously flushed with argon to exclude oxygen. Then mixture was heated at 140 ^{0}C. The reaction was monitored by TLC and heating continued for 24 h. After the completion, the mixture was neutralized with dil.HCl (10% v/v). The product extracted with ethyl acetate (4 x 50 ml), the combined organic extracts was dried over anhydrous sodium sulphate and concentrated under reduced pressure to yield the crude product. The crude product on silica gel column chromatographic purification using pet.ether-ethyl acetate mixture gave the ethyl-3-(1-naphthalenyl)-(E)-2-propionate (0.205 g, 45 %).



Ethyl-3-(1-naphthalenyl)-(E)-2-propionate (5)

Mol F : $C_{15}H_{14}O_2$

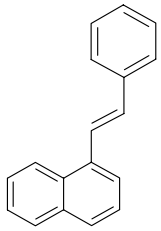
IR (cm $^{-1}$, Nujol) : 3060, 2979, 1712, 1633, 1510, 1367, 1305, 1265, 1178, 1089, 1041, 977, 775.

^{1}H NMR (δ ppm, 200 MHz, $CDCl_3$) : 8.49 (d, J=16Hz, 1H), 7.92-7.55 (m, Ar-H, 7H), 6.57 (d, J=16Hz, 1H), 4.34(q, -C<u>H</u>$_2$CH$_3$, 2H), 1.38 (t, -OCH$_2$C<u>H</u>$_3$, 3H)

Mass (m/z) : 226(M^+), 181, 153, 127, 76, 63.

8. $PdCl_2$(DAB) catalyzed Heck reaction of 1-bromonaphthalene with styrene

In a 25 ml RBF, 1-bromonaphthalene (0.414 g, 2 mmol), styrene (0.520 g, 5 mmol), $PdCl_2$(DAB) (cat-1) (0.010 g, 0.025 mmol) and K_2CO_3 (0.552 g, 4 mmol) were taken in 8 ml of NMP. The reaction mixture was degassed under vacuum and simultaneously flushed with argon to exclude oxygen. Then mixture was heated at 140 ^{0}C. The reaction was monitored by TLC and heating continued for 24 h. After the completion, the mixture was neutralized with dil.HCl (10% v/v). The product extracted with ethyl acetate (4 x 50 ml), the combined organic extracts was dried over anhydrous sodium sulphate and concentrated under reduced pressure to yield the crude product. The crude product on silica gel column chromatographic purification using pet.ether-ethyl acetate mixture gave the stilbene (0.401 g, 89 %).



1-(1-Naphthalenyl)-(E)-2-phenyl ethylene (6)

Mol F : $C_{18}H_{14}$

M.P. : 73 ^{0}C

IR (cm $^{-1}$, Nujol) : 2923, 2854, 1595, 1463, 1377, 1350,1251, 1155 1074.

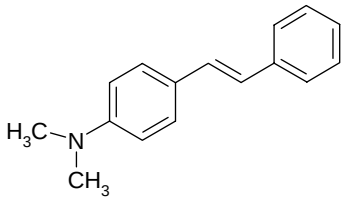
^{1}H NMR (δ ppm, 200 MHz, $CDCl_3$) : 8.25 (d, 16 Hz, 1H), 7.33 – 7.93 (m, 12 H),

7.11 – 7.19 (d, 16 Hz, 1 H).

Mass (m/z) : 230 (M^+), 215, 202,189, 152, 126, 114, 107, 101, 88, 77, 69, 63, 55.

9. $PdCl_2$(DAB) catalyzed Heck reaction of 4-bromo N, N-dimethylaniline with styrene

In a 25 ml RBF, 4-bromo N, N-dimethylaniline (0.400 g, 2 mmol), styrene (0.520 g, 5 mmol), $PdCl_2$(DAB) (Cat-1) (0.010 g, 0.025 mmol) and K_2CO_3 (0.552 g, 4 mmol) were taken in 8 ml of NMP. The reaction mixture was degassed under vacuum and simultaneously flushed with argon to exclude oxygen. Then mixture was heated at 140 ^{0}C. The reaction was monitored by TLC and heating continued for 24 h. After the completion, the mixture was neutralized with dil.HCl (10% v/v). The product extracted with ethyl acetate (4 x 50 ml), the combined organic extracts was dried over anhydrous sodium sulphate and concentrated under reduced pressure to yield the crude product. The crude product on silica gel column chromatographic purification using pet.ether-ethyl acetate mixture gave the product (0.045 g, 10 %).



2-(4-N, N-Dimethyl phenyl)-(E)-1-phenyl ethylene (7)

Mol F : $C_{16}H_{17}N$

M.P. : 76.3 – 77.8 ^{o}C (Lit : 74 – 75 ^{o}C)

IR (cm $^{-1}$, Nujol) : 2923, 2852, 1604, 1519, 1461, 1352, 1222, 966, 810, 748, 690

^{1}H NMR (δ ppm, 200 MHz, $CDCl_3$) : 7.5 – 7.15 (m, 9 H); 7.02 – 6.94 (d, J = 16 Hz,

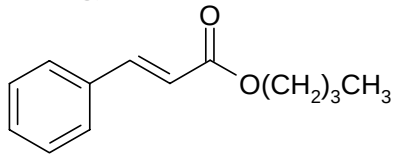
1H); 6.74 – 6.69 (d, J= 10 Hz, 1 H); 2.98 (s, 6H)

Mass (m/z) : 223, 207, 193, 178, 165, 152, 128, 111, 89, 77.

Heck reaction of aryl bromides with olefins in tetrabutyl ammonium bromide as ionic liquid

10. $PdCl_2$(DAB) reaction of bromobenzene with butylacrylate in TBAB

First 2 g of TBAB was taken in 25 ml of round bottomed flask and heated to 130^{0}C. When TBAB becomes molten, $PdCl_2$(DAB) (cat-1) (0.012 g, 0.03 mmol), $HCOONH_4$ (0.012 g, 0.2 mmol), bromobenzene (0.3 ml, 3 mmol), Na_2CO_3 (0.636 g, 6 mmol) and butyl acrylate (10.43 ml, 3 mmol) were added in strict order. The mixture was stirred at 130 ^{0}C for 24 h and neutralized with dil.HCl (10% v/v). The product extracted with ethyl acetate (4 x 50 ml), the combined organic extracts were dried over anhydrous sodium sulphate and concentrated under reduced pressure to yield the crude product. The crude product on silica gel column chromatographic purification using pet.ether-ethyl acetate mixture gave the product (0.430 g) 70 %.



n-Butyl-3-phenyl-(E)-2-propionate (8)

Yield : (0.430 g) 70 %

IR (cm $^{-1}$, Nujol) : 3060, 3028, 2958, 2933, 2873, 1712, 1639, 1311, 1280, 1170, 1066, 979, 864, 767, 709, 684.

^{1}H NMR (δ ppm, 200MHz, $CDCl_3$) : 7.73 – 7.65 (d, 1 H, J = 16 Hz, Ar.C<u>H</u>=), 7.56 –

7.31 (m, 5 H), 6.49 – 6.41 (d, 1 H, J = 16 Hz, =C<u>H</u>.$COOC_4H_9$), 4.25 – 4.18 (t, 2 H, J = 6 Hz, -OOC<u>H</u>$_2$.C_3H_7), 2.05 (s, 3 H), 1.80 – 1.35 (m, 4H, -$COOCH_2$.C<u>H</u>$_2$. C<u>H</u>$_2$.CH_3), 1.01 – 0.93 (t, 3H, J = 8 Hz, -$OOCH_2$ CH_2CH_2.C<u>H</u>$_3$).

11. $PdCl_2$(DAB) catalyzed reaction of p-bromophenol with ethylacrylate in TBAB

First 2g of TBAB was taken in 25 ml of round bottomed flask and heated to 130^{0}C. When TBAB becomes molten, Ferrocenyl Oxime palladacycle (0.012 g, 0.02 mmol), $HCOONH_4$ (0.073g, 0.12 mmol), p-Bromophenol (0.346 g, 2 mmol), NaOAc (0.328 g, 4 mmol) and ethyl acrylate (0.5 ml, 5 mmol) were added in strict order. The mixture was stirred at 130 ^{0}C for 4-24 h and neutralized with dil.HCl (10% by volume). The product extracted with ethyl acetate (4 x 50 ml), the combined organic extracts were dried over anhydrous sodium sulphate and concentrated under reduced pressure to yield the crude product. The crude product on silica gel column chromatographic purification using pet.ether-ethyl acetate mixture gave the product (46 %).

12. Reaction of 1-bromonphthalene with ethylacrylate in TBAB

First 2g of TBAB was taken in 25 ml of round bottomed flask and heated to 130^{0}C. When TBAB becomes molten, $PdCl_2$(DAB) (0.012 g, 0.03 mmol), HCOONa (10.0 g,), p-bromophenol (0.346 g, 2 mmol), NaOAc (0.265 g, 2.5 mmol) and ethyl acrylate (0.5 ml, 5 mmol) were added in strict order. The mixture was allowed to stir at 130 ^{0}C for 4-24 h and neutralized with dil.HCl (10% v/v). The product extracted with ethyl acetate (4 x 50 ml), the combined organic extracts was dried over anhydrous sodium sulphate and concentrated under reduced pressure to yield the crude product. The crude product on silica gel column chromatographic purification using pet.ether-ethyl acetate mixture gave the product (67 %).

13. Palladium catalyzed multiple reaction of bromobenzene with styrene, phenyl boronic acid and morpholine :

In a 50 ml RBF, bromobenzene (0.471 g, 3 mmol), styrene (0.124 g, 1.2 mmol), phenylboronic acid (0.134 g, 1.1 mmol), morpholine (0.095 g, 1.1 mmol), NaO^tBu (0.504 g, 4 mmol) $Pd(dba)_2$ /PPh_3(0.020 g/ 0.052 g) and CuI (0.019 g, 0.1 mmol) were taken in 20 ml of dioxane. The reaction mixture was degassed under vacuum and simultaneously flushed with argon to exclude oxygen. Then mixture was refluxed. The reaction was monitored by TLC and heating continued for 24 h. After

the completion, the mixture was neutralized with dil.HCl (10% v/v). The product extracted with ethyl acetate (4 x 50 ml), the combined organic extracts was dried over anhydrous sodium sulphate and concentrated under reduced pressure to yield the crude product. The crude product on silica gel column chromatographic purification using pet.ether-ethyl acetate mixture gave the stilbene (0.180 g, 91 %), biphenyl (0.154 g, 96%) and N-phenyl morpholine (0.163 g, 83%).

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Suzuki-Miyaura Coupling Reaction

4.2.1 Introduction

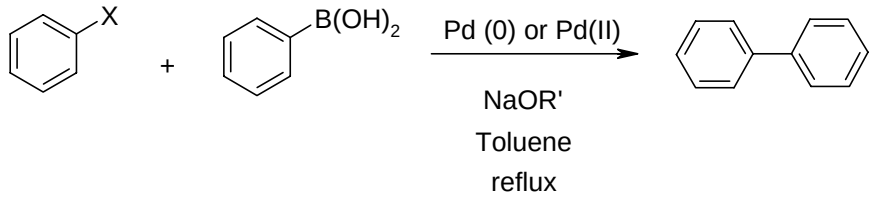
The Pd-catalyzed cross-coupling reaction between organoboron compounds and organic halides or triflates provides a powerful and general methodology for the

formation of C-C bonds. This reaction was called as Suzuki Coupling. This is a versatile method for synthesizing unsymmetrical biaryls. The availability of the reagents and the mild reaction conditions all contribute to the versatility of this reaction. The coupling reaction offers several additional advantages, such as being largely unaffected by the presence of H_2O, tolerating a broad range of functional groups, and proceeding generally regio- and stereoselectively. Also, the inorganic byproduct of the reaction is nontoxic and easily removed from the reaction mixture thereby making the Suzuki coupling suitable not only for laboratory but also for industrial processes. As a consequence the Suzuki coupling have been used extensively in the synthesis of natural products, nucleoside analogs and pharmaceuticals.

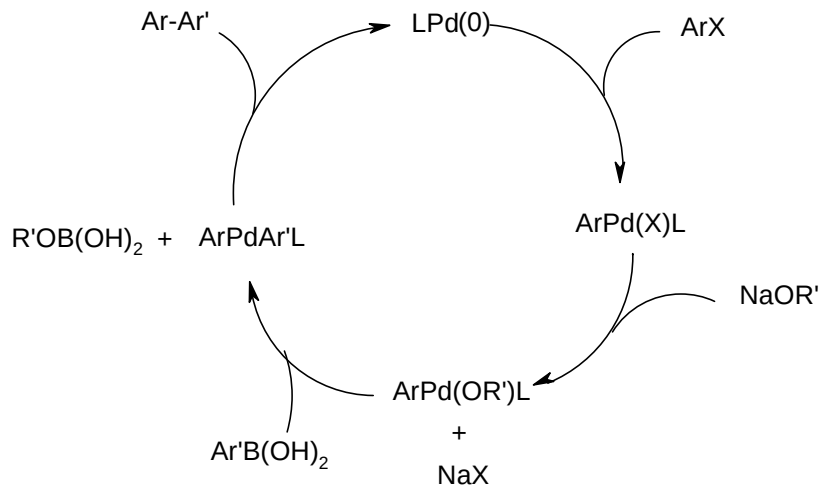
Palladium catalyzed Suzuki-Miyaura coupling

The Suzuki-Miyaura reaction could be represented by following example (Scheme-1). The reaction of aryl halide with phenylboronic acid in the presence of Pd-catalyst and base give the biaryl compound.

Scheme-1



Mechanism

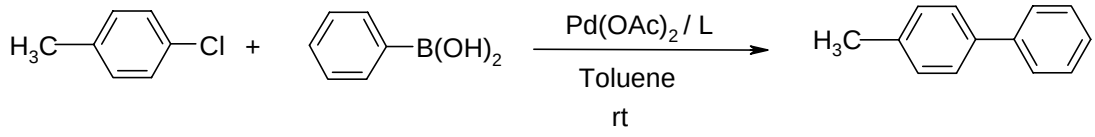


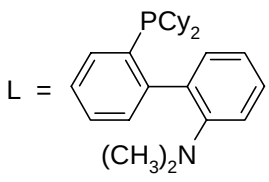
The reaction proceeds via general organometallic steps i.e. oxidative addition, transmetallation and reductive elimination. The reaction proceeds via transmetallation in the presence of bases. No reaction takes place under neutral conditions which is the characteristic feature of boron chemistry compared to other organometallic reagents. The role of the base was explained by activation of either Pd or boranes. Most likely, the formation of Ar-Pd-OR from Ar-Pd-X facilitates the transmetallation with organoboranes.

Background

In the year 1998, Stephen Buchwald group have shown that the biphenyl P-N donor ligands can catalyze Suzuki reaction of aryl chlorides at room temperature[1] (Scheme-1).

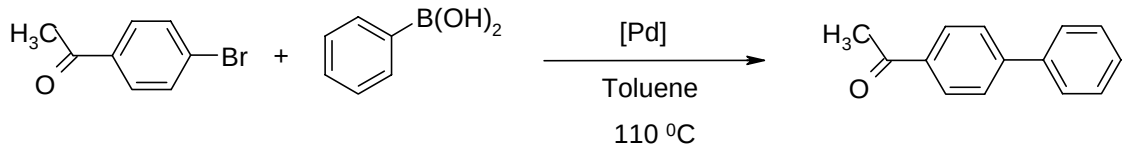
Scheme-1

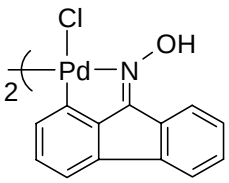




In the year 2000, Carmen Na´jera et al have prepared thermally stable moisture and air insensitive oxime palladacycles from very cheap materials and used for Suzuki coupling. The catalyst efficiently worked and gave excellent yields of the coupled products[2] (Scheme-2).

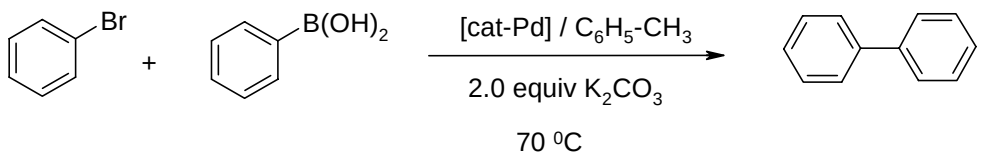
Scheme-2

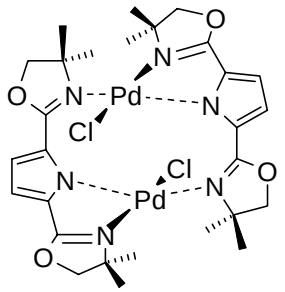




In the year 2001, it was shown that reaction of pyrrole-2, 5-biscarbonitrile[3] with 2-amino-2-methyl-1-propanol gave the bis 2-(4, 4-dimethyl-4, 5-dihydrooxazolyl) pyrrole which was protonated and reacted with $[PdCl_2(COD]$ to give $[Pd_2(dmoxp)_2Cl_2]$ The former was an active catalyst in the Suzuki cross coupling of phenylboronic acid with activated and non activated aryl bromides at 70 ^{0}C and catalyst/substrate ratios of 10^{-4} to 10^{-5} (Scheme-3).

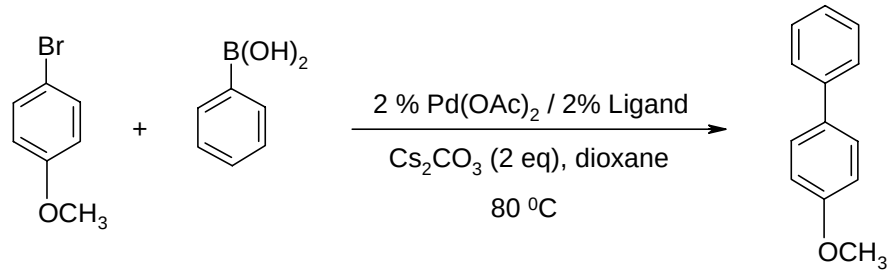
Scheme-3

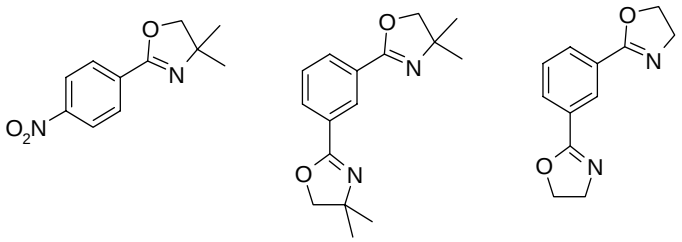


[cat-Pd] = 

A series of 2-aryl-2-oxazolines were prepared and examined by the group of David W. Boykin, as ligands for the Suzuki coupling reaction of aryl bromides and arylboronic acids. 2, 2-(1, 3-Phenylene) bisoxazoline /$Pd(OAc)_2$ was found to be an efficient catalyst for a variety of substrates to afford the coupling products in good to excellent yields[4] (Scheme-4).

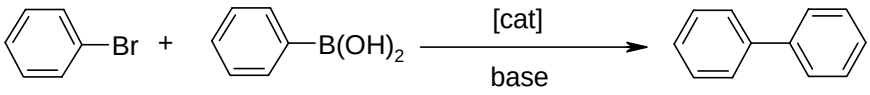
Scheme-4

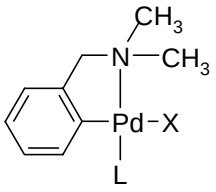


Ligand = 

In the year 2003, triarylphosphine and arsine adducts of imine- and amine-based palladacycles have been produced and the crystal structures of three examples have been determined. The complexes were tested in the Suzuki coupling of an electronically deactivated aryl bromide and the phosphine adducts were found to show much greater activity than the parent palladacycles. Triarylphosphine adducts are preferable to trialkylphosphine adducts as they not only show higher activity but they are also more easily synthesized[5] (Scheme-5).

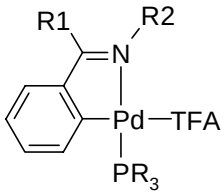
Scheme-5





X = TFA , Cl

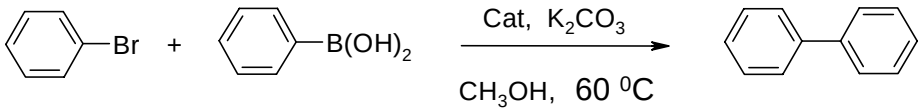
L = $P(C_6H_5)_3$, $As(C_6H_5)_3$



R1 = CH_3 ; R2 = ^{i}Pr ; R_3 = C_6H_5

In the year 2004, It was shown that complexation of the bidentate ferrocenylamine $[\eta^5\text{-}C_5H_4(CH_2)_2N(CH_3)_2]_2Fe$ with $PdCl_2(CH_3CN)_2$ in CH_3OH at room temperature gives air-stable metallamacrocycle $Pd_2Cl_4\{Fe[\eta^5\text{-}C_5H_4(CH_2)_2N(CH_3)_2]\}_2$, which effectively catalyzes Suzuki cross-coupling reactions of aryl bromides with aryl boronic acids in CH_3OH at room temperature and 60 °C, giving generally high yields even under low catalytic loads[6] (Scheme-6).

Scheme-6



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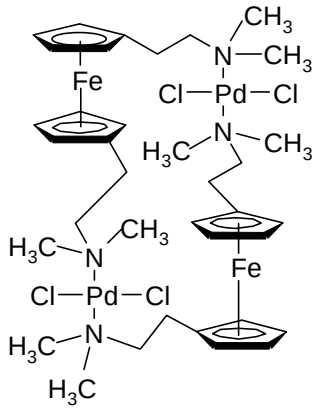
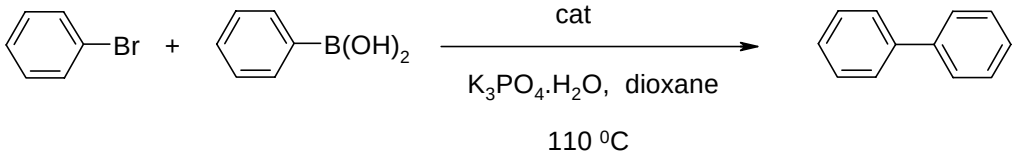
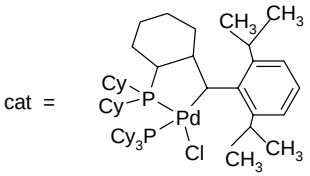


Recently, Lan-Chang Liang et al[7] have shown that treatment of $PdCl_2(PhCN)_2$ with [NP]Li $(THF)_2$ [NP] = *N*-(2-(diphenylphosphino)phenyl)-2,6-diisopropylanilide) in THF affords dimeric $\{[NP]PdCl\}_2$, which reacts with tricyclohexylphosphine to produce $[NP]PdCl(PCy_3)$. Both $\{[NP]PdCl\}_2$ and $[NP]PdCl(PCy_3)$ were highly active catalyst precursors for Suzuki coupling reactions of a wide array of aryl halides, including those featuring electronically deactivated and sterically hindered characteristics (Scheme-7).

Scheme-7





Objective

Our aim was to use nitrogen based ligands and Pd-complexes to activate less active aryl bromides and aryl chlorides for reaction with aryl boronic acids i.e. Miyura Suzuki-coupling (Scheme-1).

4.2.2 Present Work

Suzuki coupling reactions of aryl bromides with phenylboronic acid were carried out in the presence of diazabutadiene based Palladium catalysts

Scheme-1

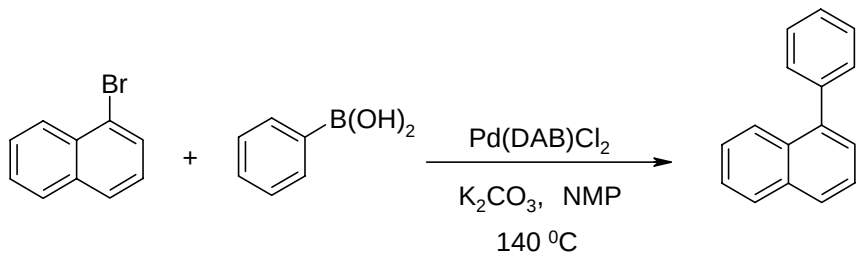


Table-3 $PdCl_2$(DAB) catalyzed Suzuki-coupling reaction of phenyl boronic acid

Sl.No.	Aryl halide	Product	Time (h)	Yield
1.	4-CH_3O-C_4H_4.I	4-CH_3O-C_4H_4.C_6H_5	24	82[a]
2	1-$C_{10}H_7$.Br	1-$C_{10}H_7$.C_5H_5	24	24.5[a]
3.	C_6H_5.CH=C(Br).CONHC_6H_4.4-NO_2	C_6H_5.CH=C(C_6H_5).CONHC_6H_4.4-NO_2	24[b]	NR
4.	C_6H_5.CH=C(Br).COOH	C_6H_5.CH=C(C_6H_5).COOH	24[b]	NR

[a]K_2CO_3 ; [b]K_3PO_4
Reaction Conditions: Aryl halide (1 mmol) + phenylboronic acid (1.2 mmol) + base (2 mmol) + $PdCl_2$(DAB)
(10mg) + Solvent (6 ml) NMP

Results and Discussion

We have carried out suzuki-coupling reactions with aryl bromides, iodides bromoacryl amides and acids using phenyl boronic acid in the prsence of $PdCl_2$(DAB) complexes. The coupled products were obtained in low to moderate yields. The reaction of 1-bromonaphthalene with phenyl boronic acid in the presence of $PdCl_2$(Cyclohexyl-dab) in NMP solvent at 150 ^{0}C gave 25 % of the coupled product.

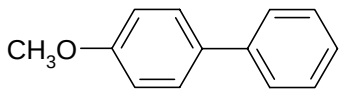
Suzuki coupling reaction of 4-methoxy iodobenzene and phenyl boronic acid in the presence of $Mn(acac)_3$ didn't yield the product. Reaction between 1-bromocinnamic acid and phenylboronic acid in the presence of $Pd_2(dba)_3.CHCl_3$/diisopropyldab, K_3PO_4 in methanol didn't worked and starting material was recovered back.

Conclusion

Diazabutadiene Pd complexes catalyze the Suzuki coupling reaction, but aryl bromide gave less yields of the product.

4.2.3 Experimental

1. $PdCl_2$(DAB) catalyzed Suzuki reaction of phenylboronic acid with 4-methoxy iodobenzene : 4-Methoxy iodobenzene (0.234 g, 1 mmol), phenyl boronic acid (0.122 g, 1 mmol), K_2CO_3 (0.276 g, 2 mmol) and $PdCl_2$(DAB) (**cat-1**) (0.010 g, 0.025 mmol), $(C_4H_9)_4NBr$ (0.161 g, 0.5 mmol) were taken in a round bottomed flask with NMP (5 ml) as solvent and the reaction mixture heated to 150 ^oC for 24h. After completion (monitoring by TLC), the reaction mixture was quenched with dil. HCl, extracted with ethyl acetate, the combined organic extracts washed with brine, dried and concentrated. Purification by column chromatography gave 0.151 g of 4-methoxy biphenyl (82 %)



4-Methoxy biphenyl

Yield : (0.151 g) 82 %

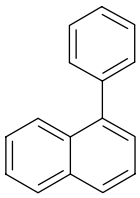
M.P. : 88-89^0C

IR (cm $^{-1}$, Nujol) : 2952, 2921, 2854, 1606, 1521, 1487, 1463, 1377, 1288, 1249, 1201, 1184, 1118, 1035, 833, 759, 688.

^{1}H NMR (δ ppm, 200MHz, $CDCl_3$) : 7.68– 7.41 (m, 7H,) 7.10 – 7.06 (d, 2H, J=8Hz),

Mass (m/z) : 184 (M^+), 169,152, 141, 115, 102, 98, 89, 75, 69, 63, 57.

2. $PdCl_2$(DAB) catalyzed Suzuki reaction of phenylboronic acid with 1-bromonaphthalene : 1-Bromo naphthalene (0.207 g, 1 mmol), phenyl boronic acid (0.122 g, 1 mmol), K_2CO_3 (0.276 g, 2 mmol) and $PdCl_2$(DAB) (**cat-1**) (0.010 g, 0.025 mmol), $(C_4H_9)_4NBr$ (0.161 g, 0.5 mmol) were taken in a round bottomed flask with NMP (5 ml) as solvent and the reaction mixture heated to 150 ^{o}C for 19h. After completion (monitoring by TLC), the reaction mixture was quenched with dil. HCl, extracted with ethyl acetate, the combined organic extracts washed with brine, dried and concentrated. Purification by column chromatography gave 0.056 g of 1-phenylnaphthalene (24.5 %)



1-Phenylnaphthalene

Yield : (0.056 g) 24.5 %

M.P. : 45 ^{0}C

IR (cm $^{-1}$, Nujol) : 3060, 3018, 1593, 1508, 1494, 1446, 1396, 1215, 1074, 1029, 962, 757.

^{1}H NMR (δ ppm, 200 MHz, $CDCl_3$) : 7.93– 7.89 (m, 3H,) 7.57 – 7.39 (m, 9H),

Mass (m/z) : 204 (M^+), 189, 176, 163, 150, 139, 126, 115, 101, 87, 81, 74, 63, 57.

4.2 References

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6. Zhiqiang. Weng., Shihui. Teo., Lip. Lin. Koh.,T. S. Andy Hor., *Organometallics***,** 23, 3603-3609, **2004**.
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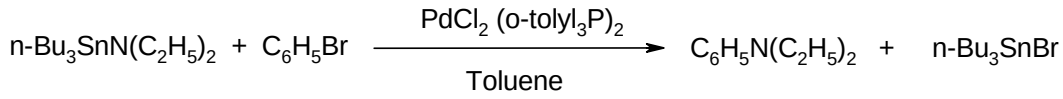
Buchwald-Hartwig aryl amination

4.3.1 Introduction

Aromatic amines play a central role in many areas of modern day organic chemistry, including pharmaceuticals, agrochemicals, photography, xeroxography, pigments and electronic materials. The historical importance of aromatic amines, which is also reflected in their industrial relevance, spurred interest in developing methods for their production. Over the years a number of cleverly designed and extremely useful methods for aryl C-N bond formation have been reported. Among the most important developments in organic synthesis in the last 20 years has been the advent of palladium- and nickel-catalyzed cross-coupling procedures.

In the year 1983, Migita[1] and co-workers reported the first examples of the palladium catalyzed transformation of aryl bromides to aryl amines via the use of aminostannanes. The reaction of N, N-diethylamino tributyltin with aryl bromides in the presence of a catalytic amount of $PdCl_2(o\text{-}tolyl_3P)_2$ gave N, N-diethyl aminobenzene derivatives (Scheme-1).

Scheme -1

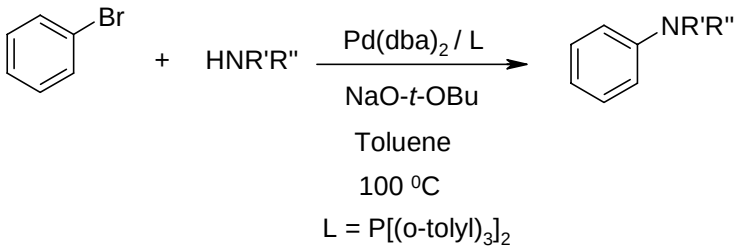


Although a large numbers of synthetic methods for the preparation of aniline derivatives have been reported, general techniques which are applicable for the preparation of a wide variety of structurally different anilines are still of great interest.

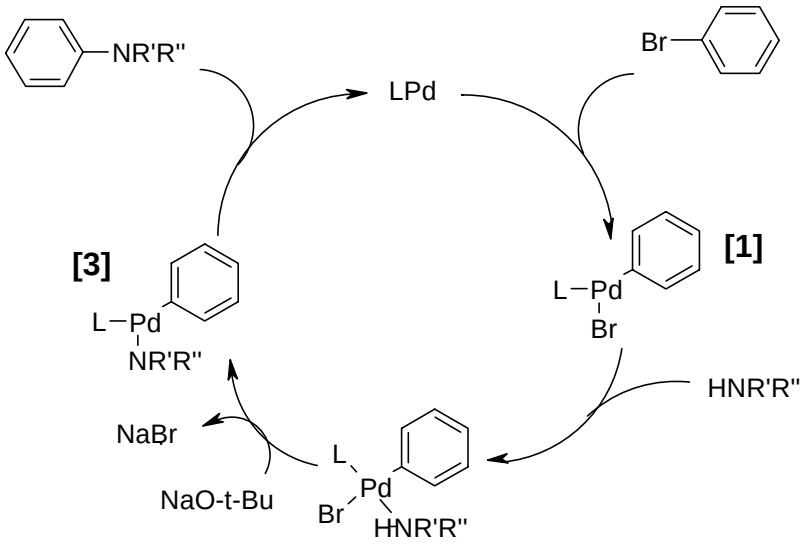
Palladium catalyzed amination of aryl halides

The Palladium catalyzed aryl amination reaction could be represented by following example (scheme-1).

Scheme-1



Mechanism

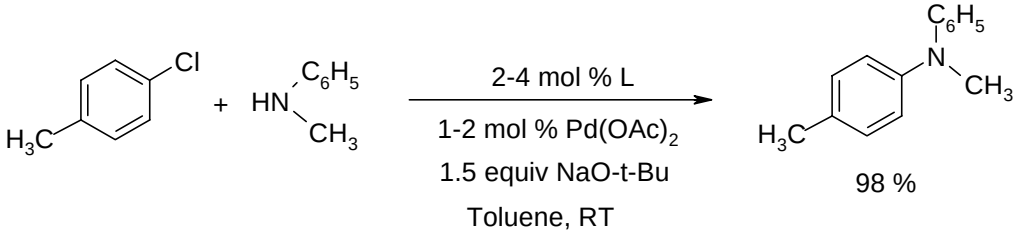


The mechanism of amination reaction proceeds via oxidative addition, coordination and reductive elimination steps. First oxidative addition of Pd (0) into aryl halide leads to aryl palladium complex **[1]**. Then coordination and elimination of HX in the presence of base leads to the complex **[3]**. In the last step, reductive elimination of **[3]** leads to the amination product.

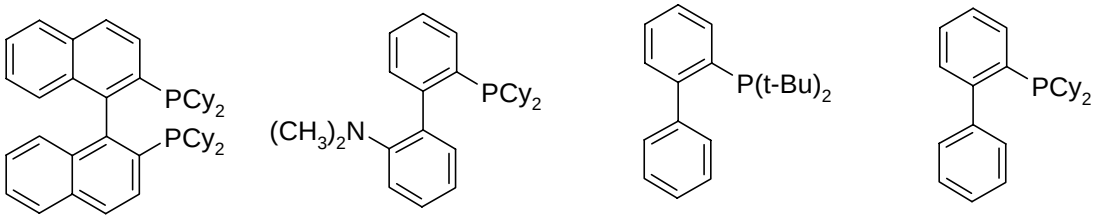
Background

In the year 2000, It has been showed that palladium complexes supported by (*o*-biphenyl)P(*t*-Bu)$_2$ (**3**) or (*o*-biphenyl)PCy$_2$ (**4**) are efficient catalysts[2] for the catalytic amination of a wide variety of aryl halides and triflates. The catalysts perform well for a large number of different substrate combinations at 80-110 °C, including chloro pyridines and functionalized aryl halides and triflates using 0.5-1.0 mol % Pd (Scheme-1).

Scheme-1



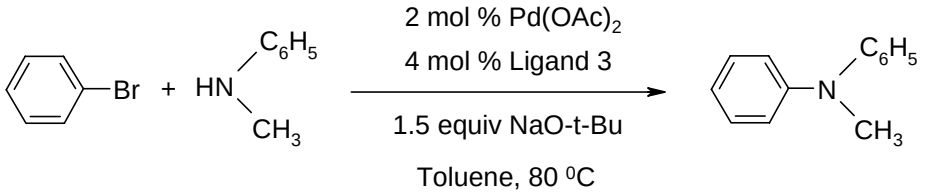
L =

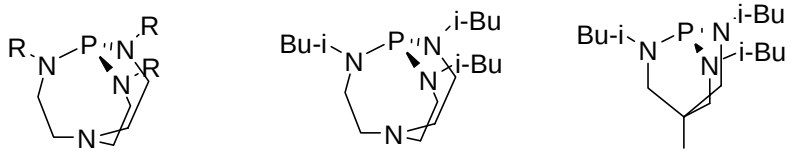


1 **2** **3** **4**

The new bicyclic triamino phosphine ligand P(*i*-BuNCH$_2$)$_3$CMe (**3**) has been synthesized in three steps from commercially available materials and its efficacy in palladium-catalyzed reactions of aryl halides with an array of amines has been demonstrated[3] (Scheme-2).

Scheme-2

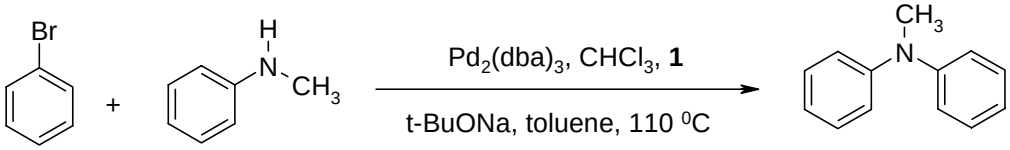


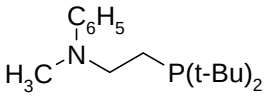


1 **2** **3**

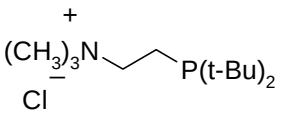
In the year 2005, it has been showed that incorporation of a hemilabile amino group with a bulky, electron-rich phosphorus ligand led to a reversal in the order of aryl bromide reactivity in Pd-catalyzed aryl amination reactions[4] (Scheme-3).

Scheme-3





1



2

Objective

In past, many nitrogen ligand based metal complexes were used for aryl amination reactions using palladium and copper. Our aim was to use diazabutadiene based Pd-complexes for the aryl amination reaction (Scheme-1).

4.3.2 Present work

Scheme-1

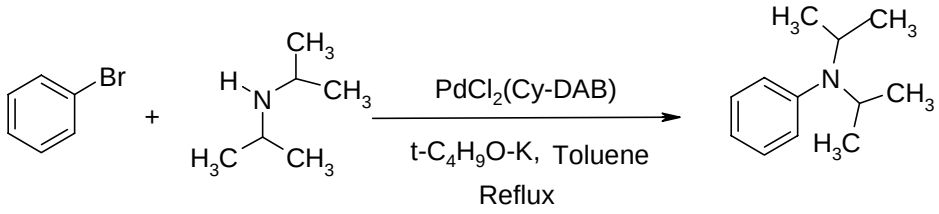


Table – 4 – Amination of aryl halides

Sl. No.	Aryl Halide	Olefin	Co-catalyst	Yield %
1.	$C_6H_5.Br$	C_4H_8ONH	$(C_4H_9)_4NBr$	15
2.	$C_6H_5.Br$	C_4H_8ONH	18-C-6	43
3.	$C_6H_5.Br$	$C_6H_{14}NH$	-	20
4.	$C_6H_5.Br$	C_4H_8ONH	-	22
5.	$4\text{-}Cl.C_6H_4.I$	$C_6H_{14}NH$	18-C-6	12

6.	4-$Cl.C_6H_5.I$	C_4H_8ONH	-	35.5
7.	$C_{10}H_7.Br$	$C_6H_{14}NH$	18-C-6	12
8.	4-$CH_3O.C_6H_4.I$	$C_6H_{11}NH$	18-C-6	5

Reaction conditions : Bromobenzene (1 mmol) + Morpholine (1 mmol) + Catalyst (10 mol%) + Toluene (10 ml); Reflux

Results and Discussion

Amination reactions of aryl bromides with different amines were carried out in the presence of $PdCl_2$(DAB) complex. Both primary and secondary amines, aromatic amines were tried for reaction. Different set of conditions, like change of solvent, change of catalyst, co-catalyst and temperature were observed for the amination reaction. Highest yield of the aminated product (43%) was obtained in the reaction of bromobenzene and morpholine with $PdCl_2$(Cyclohexyl-DAB) and 18-crown-6 as co-catalyst in toluene at 110 ^{0}C. Without 18-crown-6 only 16% of the product was obtained. Different phase transfer catalysts like TBAB, benzyl triethyl ammonium chloride doesn't show any effect on the yield of the product. 36 % of aminated product obtained in the reaction of p-chloro iodobenzene and morpholine. About 12 % of the aminated product was obtained in the reaction of 1-bromonaphthalene and N, N-diisopropylamine.

Different set of haloarenes for e.g. p-methoxy bromobenzene, p-chloro benzonitrile and o-iodophenol with different amines like N-ethyl benzamine, pyrazole, benzotriazole and methyl ester of proline, were tried for the amination reaction in the presence of $PdCl_2$(cyclohexyl-DAB) or $Pd_2(dba)_3$/cyclohexyl-dab. We failed to get the aminated products in these cases. In $PdCl_2$(cyclohexyl-DAB) catalyzed reaction of 4-methoxyiodobenzene with cyclohexylamine, pot tert.butoxide as base gave 5% of the product.

Amination reactions of 4-methoxy iodobenzene with different amines like cyclohexylamine, p-anisidine, N-ethyl aniline in the presence of $PdCl_2$(Cyclohexyl DAB) in tetrabutylammonium bromide as ionic liquid didn't yield the aminated product. The same reactions were tried in different solvents like diglyme, methyl digol and with catalyst Cu(TMEDA)OH.Cl with different base like K_2CO_3, Na_2CO_3 but no aminated product were obtained. No aminated product was observed in the reaction of bromobenzene with morpholine in the presence of Cu (Binol) as catalyst.

Reaction of 1-bromonaphthalene with diisopropylamine in the presence of $PdCl_2$(DAB) gave about 12 % of aminated product. The reaction was carried out with potassium tert-butoxide as base, in toluene. The addition of 18-crown-6 had no effect on the yield.

Conclusion

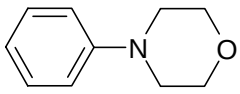
$PdCl_2$(Cyclohexyl-dab) catalyze the aryl amination reaction with moderate yields of the products. Addition of PTC (18-crown-6) increased the yields of

amination product.

4.3.3 Experimental

1. $PdCl_2$(DAB) catalyzed reaction of bromobenzene with morpholine :

Bromobenzene (0.314 g, 2 mmol), morpholine (0.174 g, 2 mmol), K-t-(OC_4H_9) (0.225 g, 2.2 mmol), $PdCl_2$(DAB) **(cat-1)** (0.010 g, 0.025 mmol) and 18–Crown-6 (0.1 g, 0.38 mmol) was taken in a flask containing toluene (10 ml) and refluxed for 24 h. The reaction mixture was concentrated on a rotary evaporator, added water and extracted with ethyl acetate, dried and concentrated. The product was purified by column chromatography to give 0.140 g of N-phenyl morpholine.



N-Phenyl morpholine

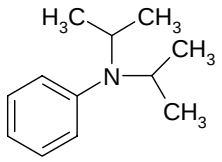
Yield : 42.9 %

IR (Nujol, cm^{-1}) : 3010, 2966, 2858, 2825, 1598, 1498, 1450, 1379,1232, 1120, 927, 756

^{1}H-NMR (δ ppm, 200MHz, $CDCl_3$) : 7.35 – 7.20 (m, 2 H), 6.95 – 6.85 (m, 3 H), 3.89 – 3.84 (m, 4 H), 3.18 – 3.13 (m, 4 H).

2. $PdCl_2$(DAB) catalyzed reaction of bromobenzene with diisopropylamine :

Bromobenzene (0.314 g, 2 mmol), N, N-diisopropylamine (0.250 g, 2.5 mmol), K-t-(OC_4H_9) (0.225 g, 2.2 mmol), $PdCl_2$(DAB) **(cat-1)** (0.010 g, 0.025 mmol) and 18–Crown-6 (0.1 g, 0.38 mmol) was taken in a 25ml round bottomed flask containing toluene (10 ml) and refluxed for completion of the reaction (monitored by TLC) 24 h. The reaction mixture was concentrated on a rotary evaporator, added water and extracted with ethyl acetate, dried and concentrated. The product was purified by column chromatography to give 0.052 g of N, N-diisopropylphenylamine.



N, N-Diisopropylphenylamine

Yield : 20 %

^{1}H-NMR (δ ppm, 200MHz, $CDCl_3$) : 7.25 – 6.88 (m, 5 H, Ar-H), 3.80– 3.73 (sept,

2H) 1.88 (d, 12H, CH_3).

3. Reaction of 1-bromonaphthalene with diisopropylamine :

1-Bromonaphthalene (0.414 g, 2 mmol), N, N-diisopropylamine (0.250 g, 2.5 mmol), K-t-(OC_4H_9) (0.225 g, 2.2 mmol), $PdCl_2$(DAB) **(cat-1)** (0.010 g, 0.025

mmol) and 18–C-6 (0.1 g, 0.38 mmol) was taken in a 25 ml round bottomed flask containing toluene (10 ml) and refluxed under argon atmosphere for completion of the reaction (monitored by TLC) 24 h. The reaction mixture was concentrated on a rotary evaporator, added water and extracted with ethyl acetate, dried and concentrated. The product was purified by column chromatography to give 12% of 1-(N, N-diisopropyl) naphthylamine..

4. $PdCl_2$(DAB) catalyzed reaction of p-methoxyiodobenzene with cyclohexylamine

p-Methoxyiodobenzene (0.234 g, 1 mmol), cyclohexylamine (0.099 g, 1 mmol), K-t-(OC_4H_9) (0.155 g, 1.2 mmol), $PdCl_2$(DAB) **(cat-1)** (0.010 g, 0.025 mmol) and 18–C-6 (0.1 g, 0.38 mmol) was taken in a 25 ml round bottomed flask containing toluene (10 ml) and refluxed for completion of the reaction (monitored by TLC) 24 h. The reaction mixture was concentrated on a rotary evaporator, added water and extracted with ethyl acetate, dried and concentrated. The product was purified by column chromatography to give 5% of N-(4-methoxyphenyl) cyclohexylamine.

4.3 References

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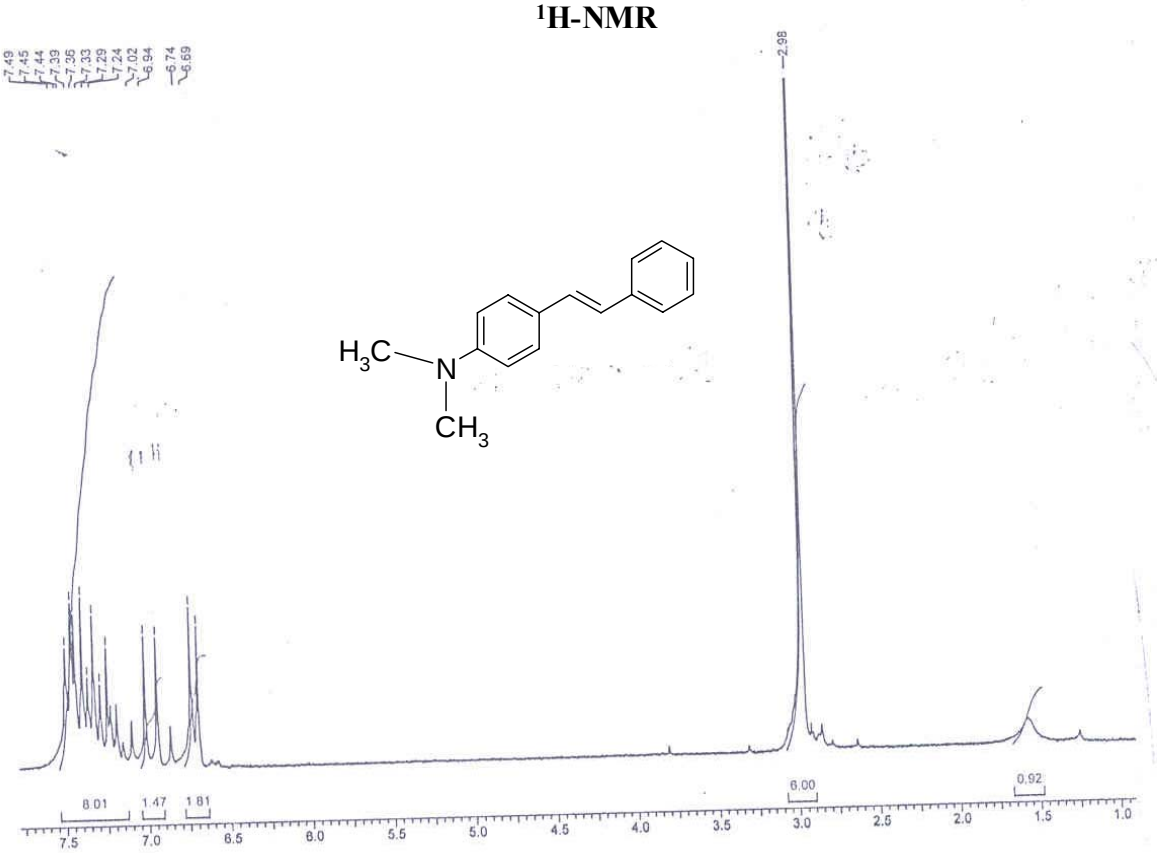
4. Sebastien,. Parisel, L., Luis, Angel, Adrio., Adriana, Amoedo, Pereira., Marta, Marino, Pe´rez., Jose´, Vilab, M., King, Kuok, Hiic., *Tetrahedron* 61, 9822–9826,
   2005.

SPECTRA

^{1}H-NMR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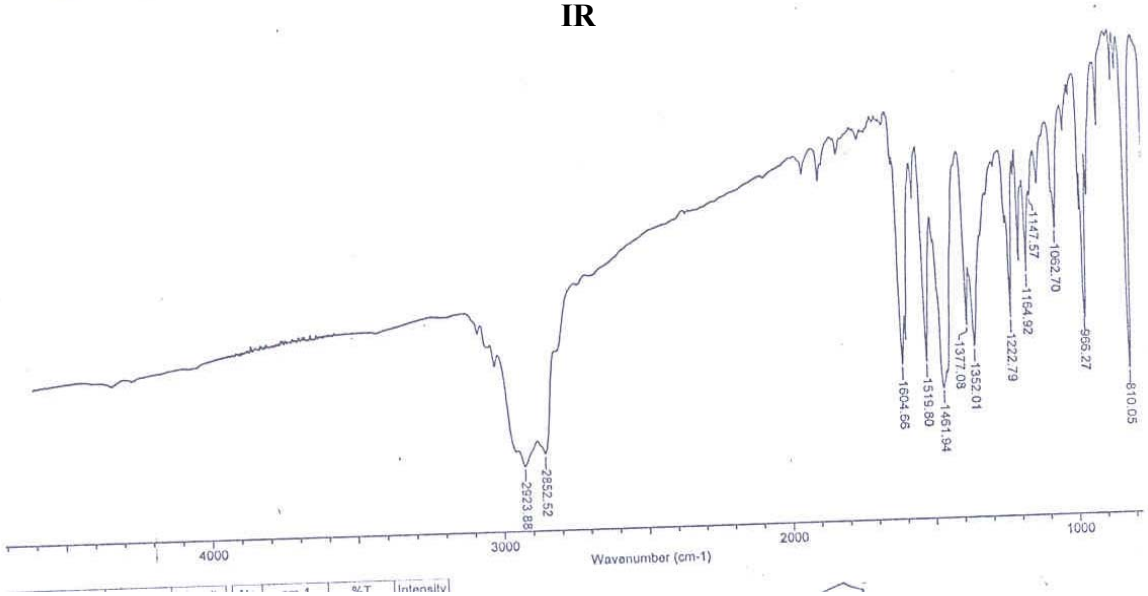
7.45
7.44
7.39
7.36
7.33
7.29
7.24
7.02
6.94
6.74
6.69
2.98
H3C
N
CH3
8.01
1.47
1.81
6.00
0.92

IR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2852.52
1604.65
1519.80
1451.94
1377.08
1352.01
1222.79
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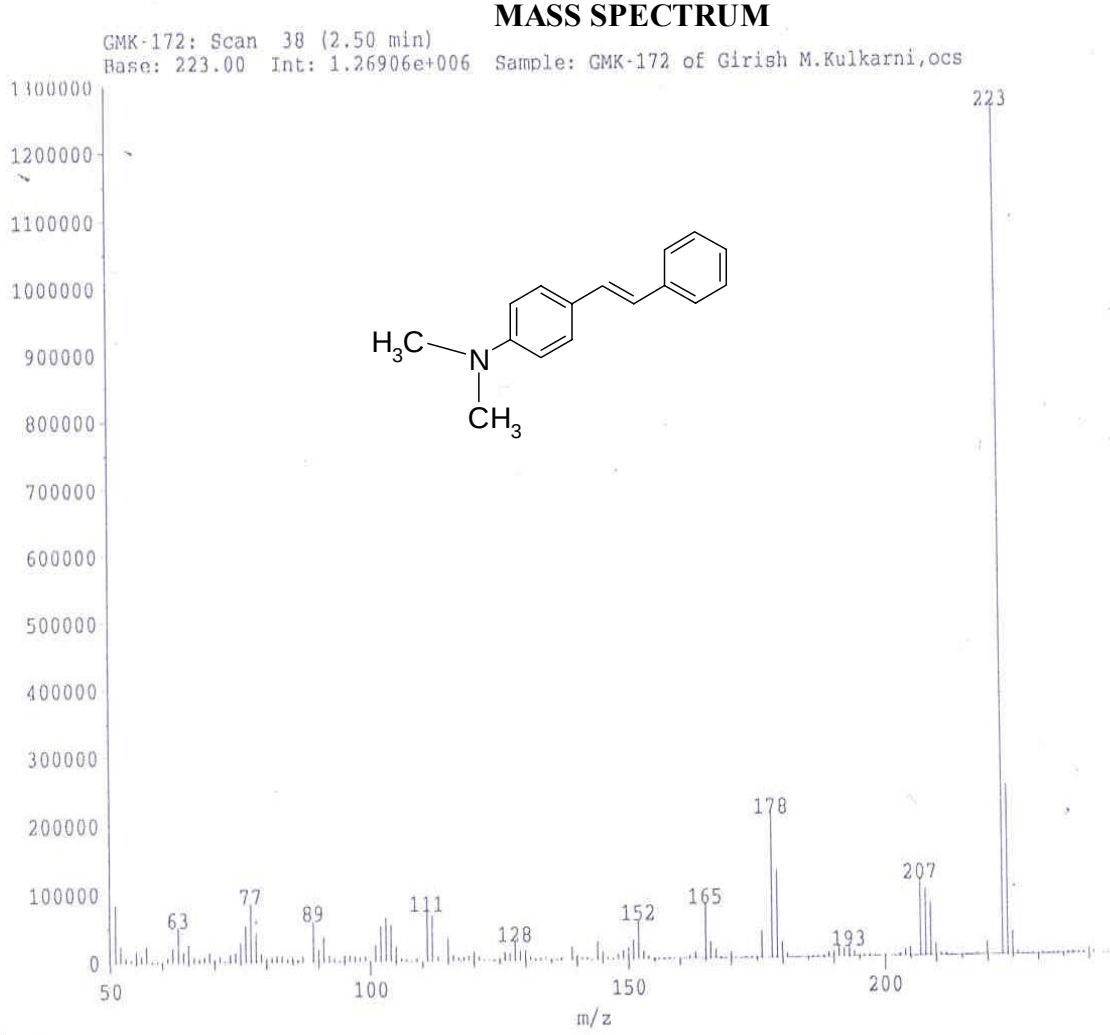
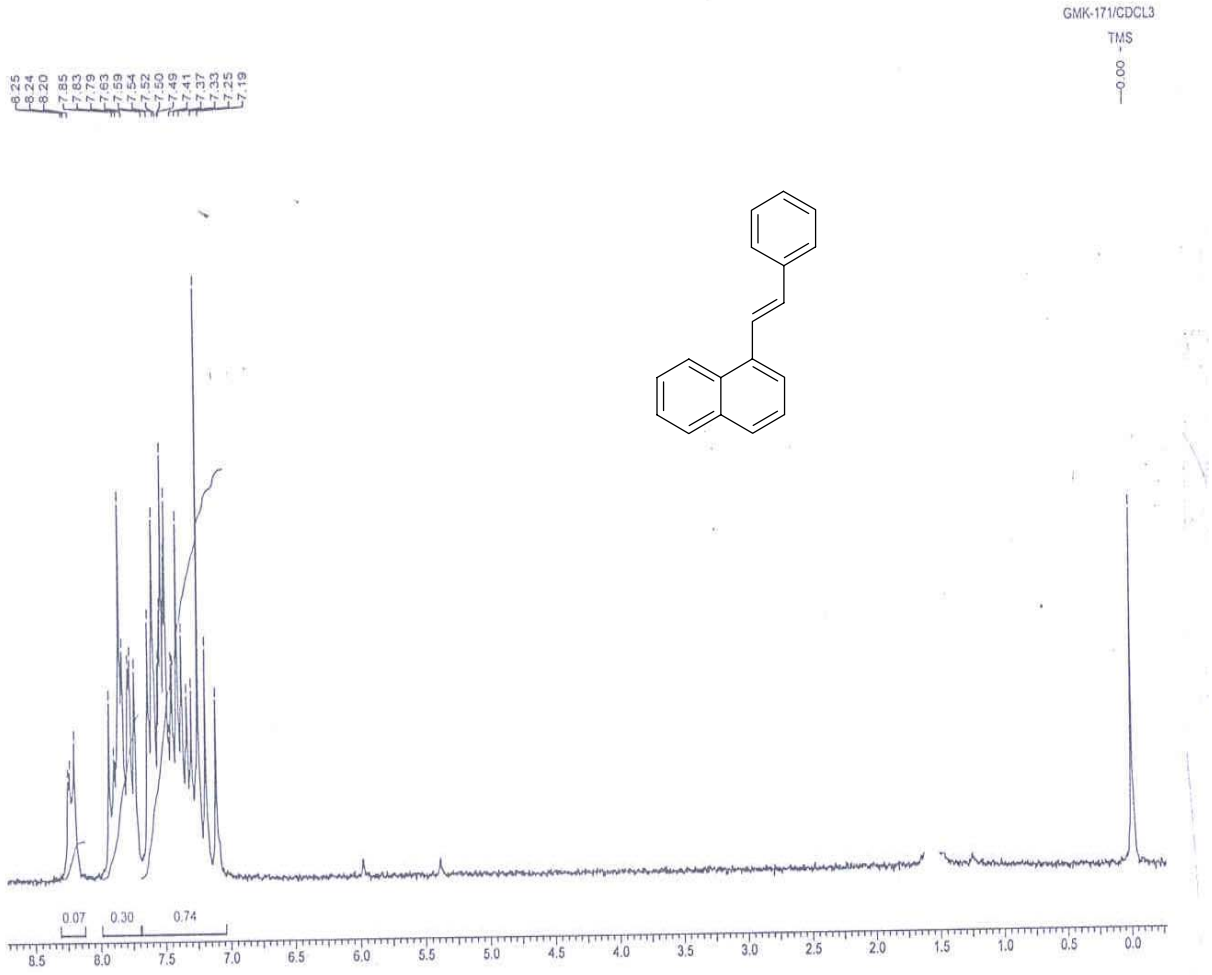
1062.70
955.27
810.05
4000
3000
2000
1000
Wavenumber (cm-1)

MASS SPECTRUM



^{1}H-NMR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8.24
8.20
7.85
7.83
7.79
7.63
7.59
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7.52
7.50
7.49
7.41
7.37
7.33
7.25
7.19
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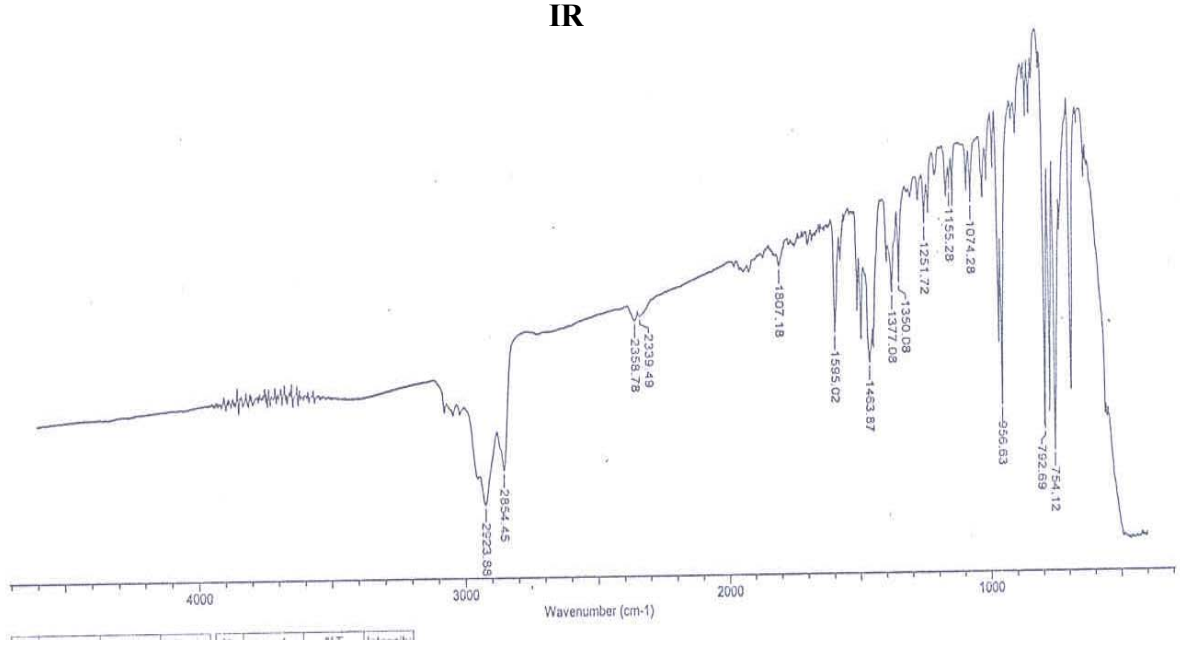
0.30
0.74

IR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2339.49
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1074.28
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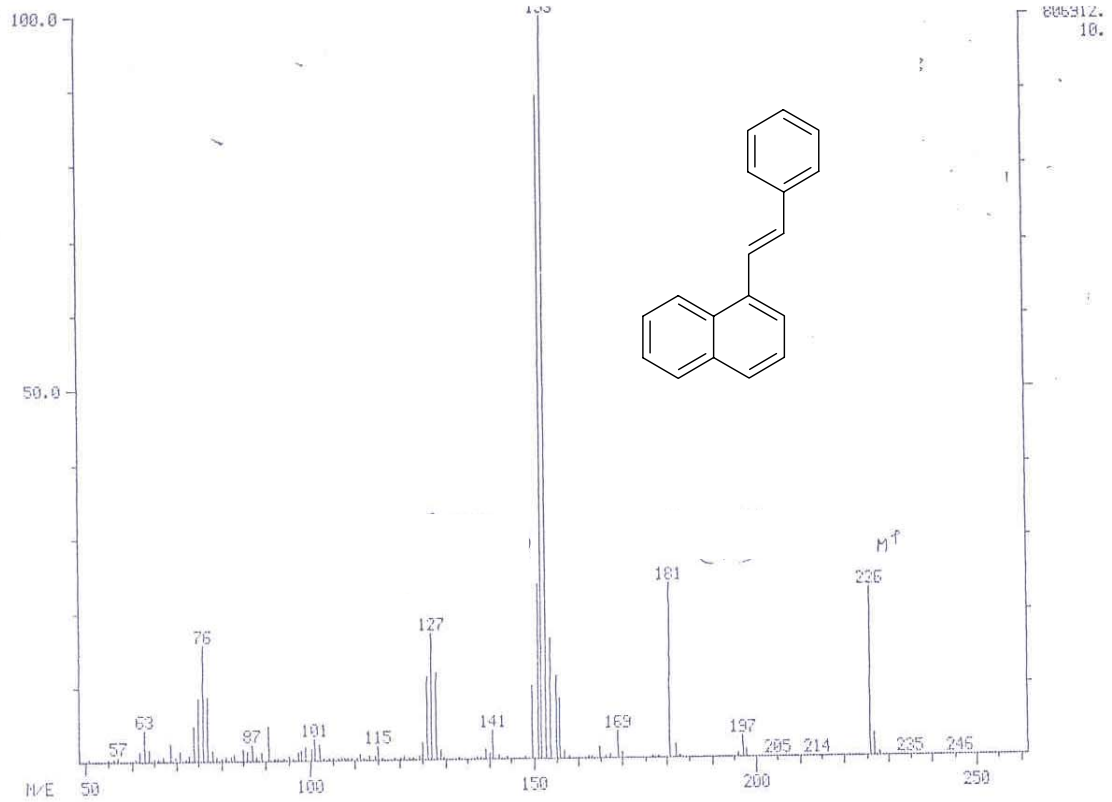
792.69
754.12
Wavenumber (cm-1)

MASS SPECTRUM



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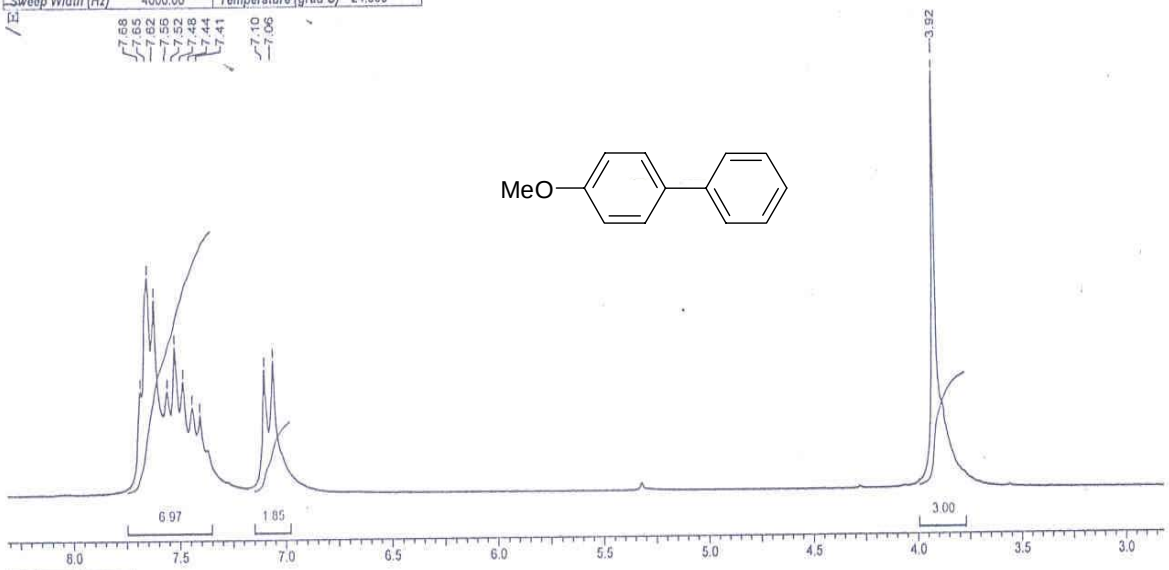

No.	(ppm)	Height
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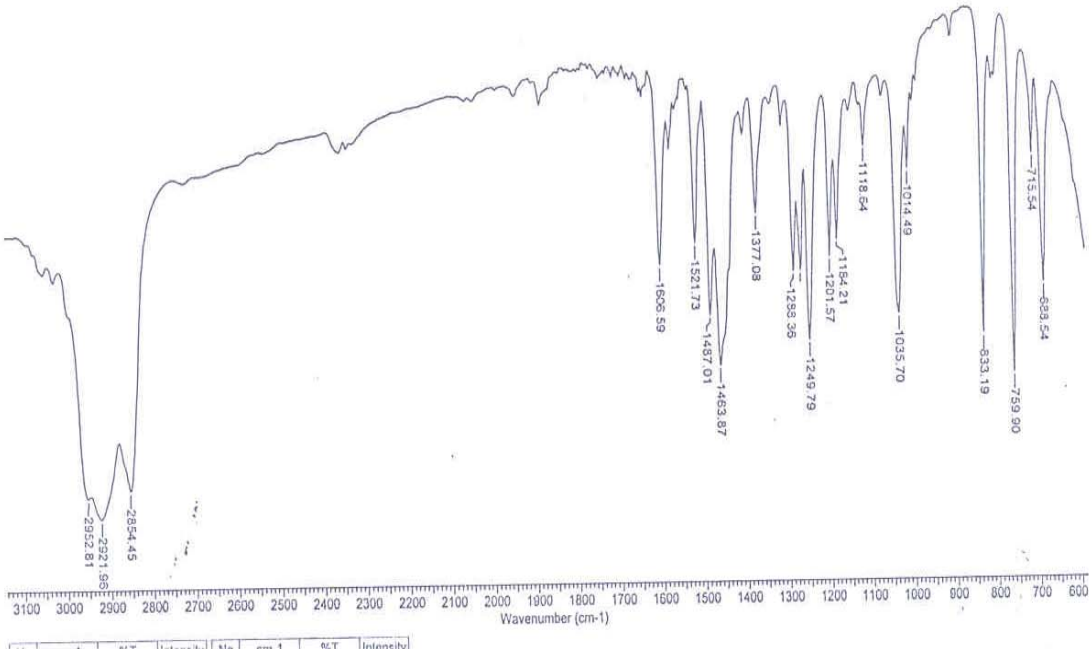
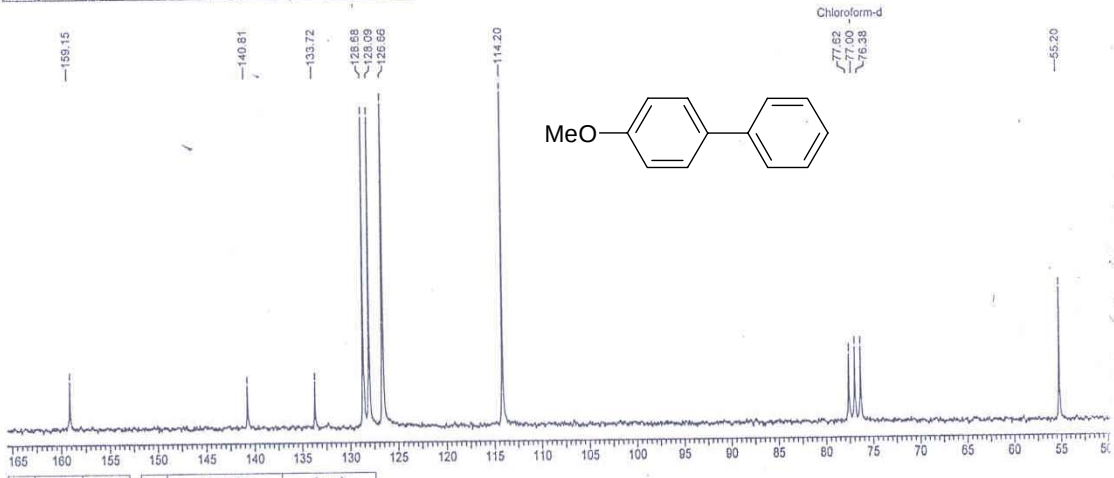
3	7.10	0.292
4	7.41	0.182
5	7.44	0.202
6	7.48	0.264
7	7.52	0.348
8	7.56	0.242
9	7.62	0.462
10	7.65	0.515
11	7.68	0.241

IR



^{13}C-NMR

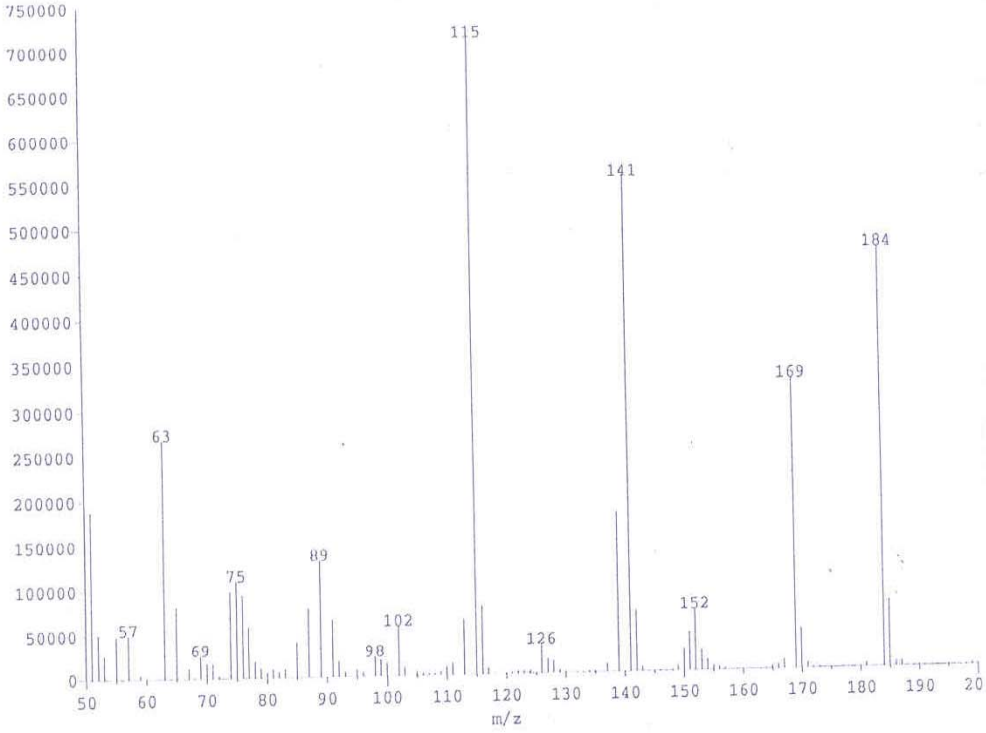
Acquisition Time (sec)	0.5407	Comment		Date	22/11/00 10:50:37
Frequency (MHz)	50.32	Nucleus	13C	Number of Transients	2048
Sweep Width (Hz)	15151.52	Temperature (grad C)	24.000	Original Points Count	8192
				Points Count	8192



No.	(ppm)	Height
1	55.20	0.392
2	76.38	0.223
3	77.00	0.224
4	77.62	0.203
5	114.20	1.000
6	126.66	0.067
7	128.09	0.926
8	128.68	0.927
9	133.72	0.135
10	140.81	0.124
11	159.15	0.140

No.	Annotation	(ppm)
1	Chloroform-d	77.00

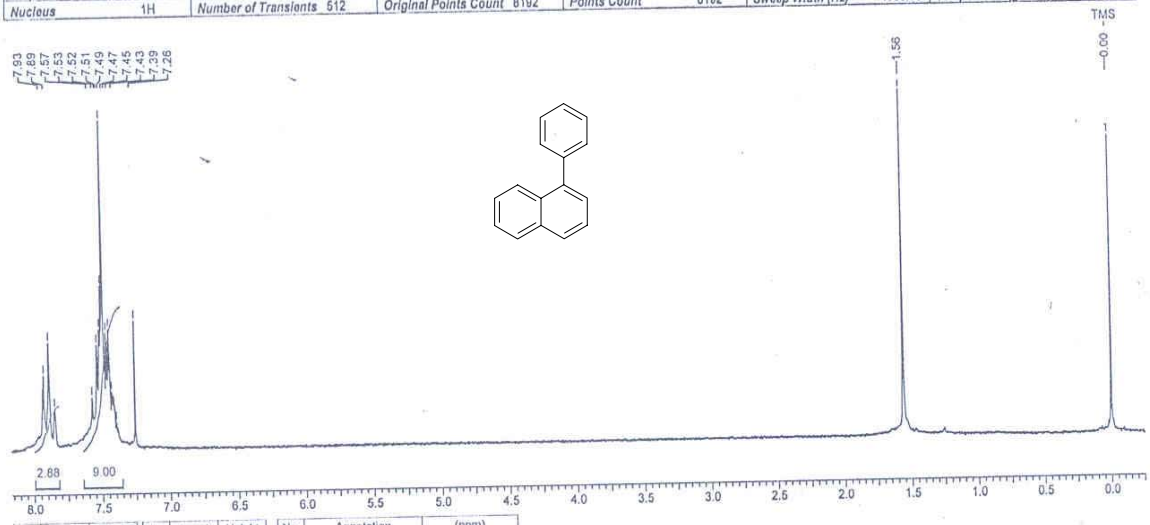
MASS SPECTRUM



^{1}H-NMR

GMK-100/CDCL3

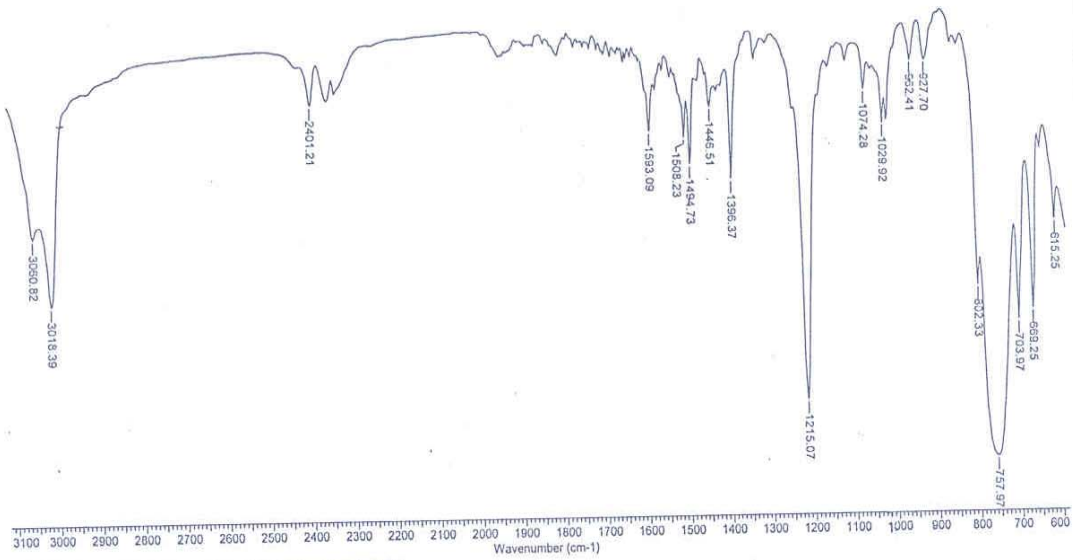
Acquisition Time (sec) 2.0480	Comment GMK-100/CDCL3		Date 17/11/00 10:41:29			Frequency (MHz) 200.13	
Nucleus 1H	Number of Transients 512	Original Points Count 8192	Points Count 8192	Sweep Width (Hz) 4000.00		Temperature (grad C) 24.000	



No.	(ppm)	Height	No.	(ppm)	Height
1	0.00	0.858	9	7.51	0.471
2	1.56	1.000	10	7.52	0.346
3	7.26	0.368	11	7.53	0.302
4	7.39	0.082	12	7.57	0.152
5	7.43	0.168	13	7.85	0.123
6	7.45	0.347	14	7.89	0.309
7	7.47	0.336	15	7.93	0.217
8	7.49	0.948			

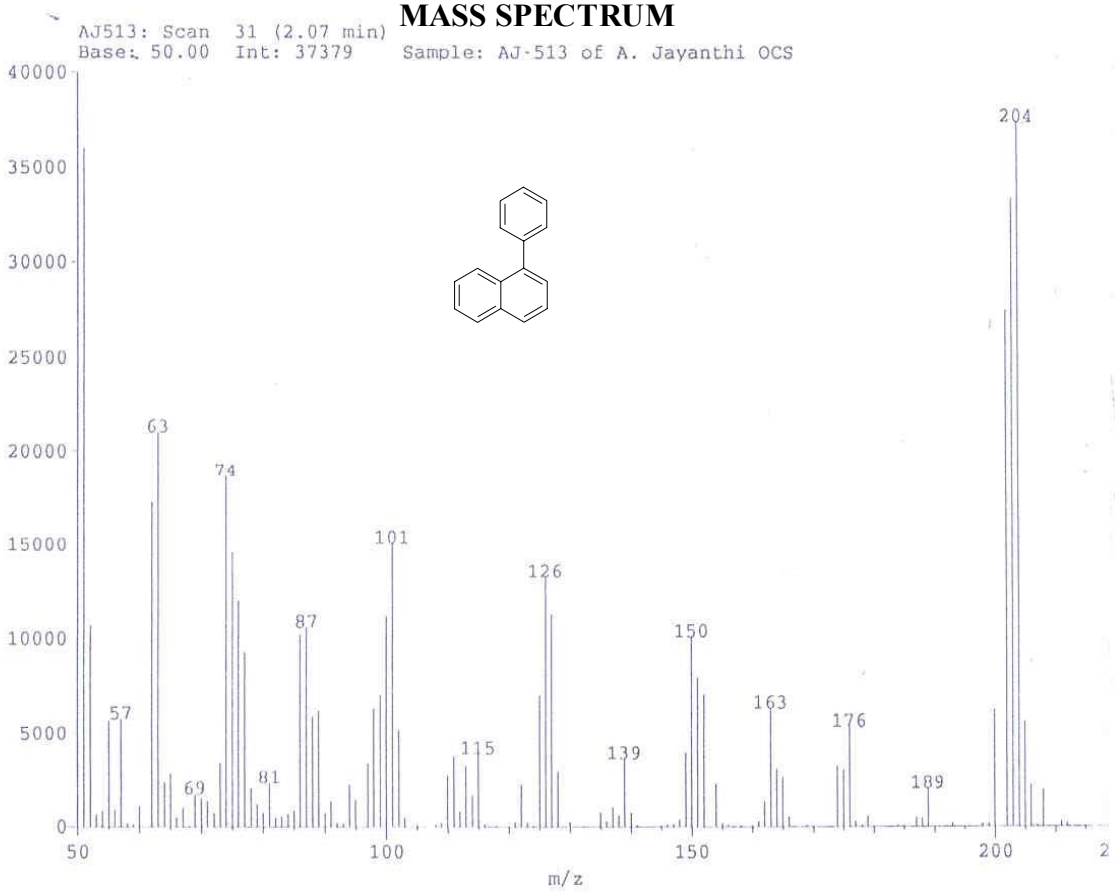
No.	Annotation	(ppm)
1	TMS	0.00

IR



No	cm-1	%T	Intensity	No	cm-1	%T	Intensity
1	615.25	0.388	M	10	1215.07	0.119	S
2	669.25	0.251	S	11	1396.37	0.455	M
3	703.97	0.235	S	12	1446.51	0.563	W
4	757.97	0.030	VS	13	1494.73	0.478	M
5	862.33	0.288	M	14	1508.23	0.518	W
6	927.70	0.631	W	15	1593.09	0.528	W
7	962.41	0.631	W	16	2401.21	0.574	W
8	1029.92	0.536	W	17	3018.39	0.277	
9	1074.28	0.587	W	18	3060.82	0.378	

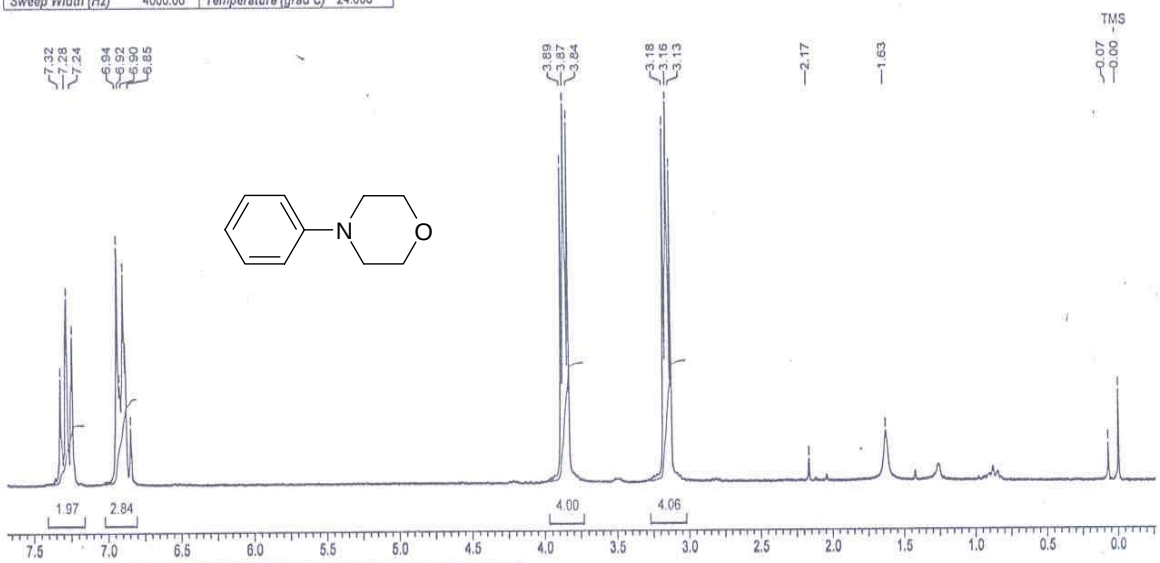
MASS SPECTRUM



^{1}H-NMR

GMK-220/CDCL3/GIRISH

Acquisition Time (sec)	2.0480	Comment	GMK-220/CDCL3/GIRISH		Date	01/12/90 18:07:35	
Frequency (MHz)	200.13	Nucleus	1H	Number of Transients 512	Original Points Count	8192	Points Count 8192
Sweep Width (Hz)	4000.00	Temperature (grad C)	24.000				

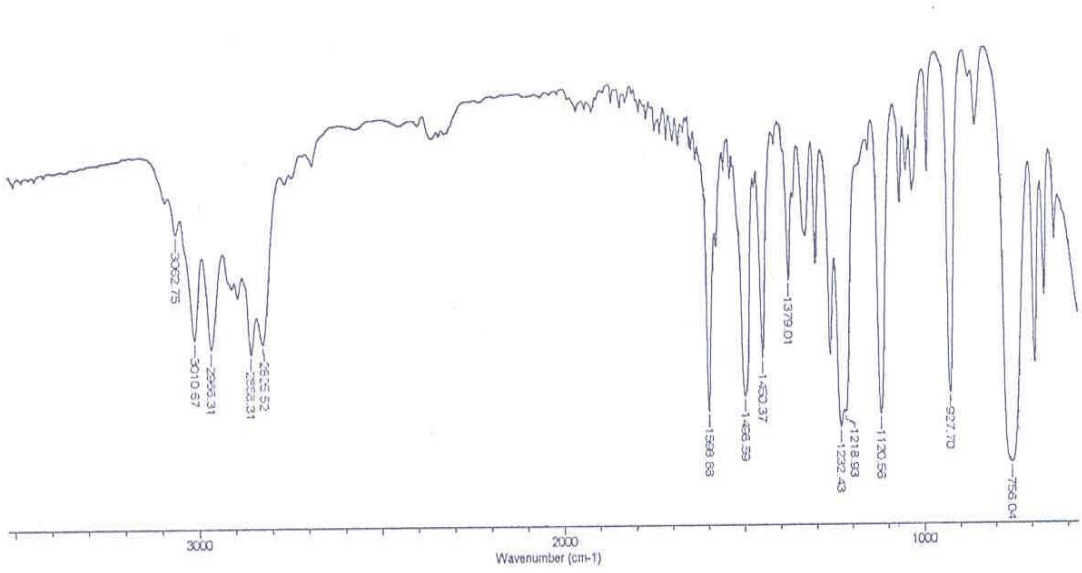


No.	(ppm)	Height
1	0.00	0.226
2	0.07	0.089
3	1.63	0.125
4	2.17	0.053
5	3.13	0.823
6	3.16	1.000
7	3.18	0.933
8	3.84	0.949
9	3.87	0.997

No.	(ppm)	Height
10	3.89	0.832
11	6.85	0.141
12	6.90	0.551
13	6.92	0.251
14	6.94	0.624
15	7.24	0.380
16	7.28	0.484
17	7.32	0.270

No.	Annotation	(ppm)
1	TMS	0.00

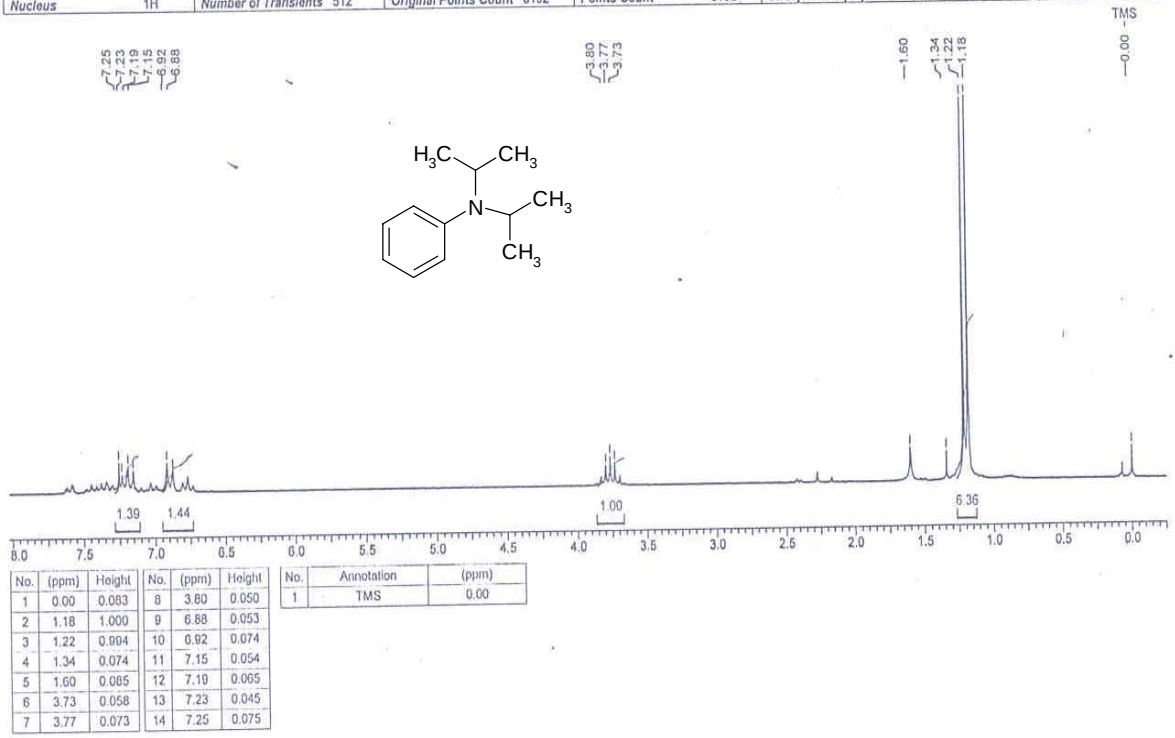
IR



^{1}H-NMR

GMK-215/CDCL3

Acquisition Time (sec) 2.0480	Comment GMK-215/CDCL3		Date 29/11/90 15:05:00			Frequency (MHz) 200.13	
Nucleus 1H	Number of Transients 512	Original Points Count 8192	Points Count 8192	Sweep Width (Hz) 4000.00		Temperature (grad C) 24.000	



No.	(ppm)	Height	No.	(ppm)	Height
1	0.00	0.083	8	3.80	0.050
2	1.18	1.000	9	6.88	0.053
3	1.22	0.994	10	6.92	0.074
4	1.34	0.074	11	7.15	0.054
5	1.60	0.085	12	7.19	0.065
6	3.73	0.058	13	7.23	0.045
7	3.77	0.073	14	7.25	0.075

No.	Annotation	(ppm)
1	TMS	0.00

LIST OF PUBLICATIONS

1. The Pd Catalyzed reactions of γ-bromoacryl amides with 1,3-dienes to form γ-lactams Suresh Iyer, C.Ramesh, **Girish M Kulkarni**
Synlett 2001, No.8, 1241-1244

2. $Mo(CO)_6$ Mediated Selected Reduction of Azides and Nitro Compounds to Amines Under Neutral Conditions. Suresh Iyer and **Girish M Kulkarni**
Synthetic Communications Vol.34, No.4 pp-721-725, 2004

3. Mizoroki-Heck reaction, catalysis by nitrogen ligand Pd-complexes and activation of aryl bromides. Suresh Iyer **Girish M Kulkarni** and C.Ramesh.
Tetrahedron 60 (2004) 2163-2172

4. Nitrogen ligands - The transition metal catalyzed reaction of aryl halides with olefins (Mizoroki-Heck reaction), phenylboronic acid (Suzuki reaction) and amination, new catalysts and co-catalysts - Aryl halide activation - Part - I – Suresh Iyer,* **Girish M. Kulkarni**, C. Ramesh, Aruna K. Sattar
Ind. J. Chem. Sec. B, No.9, (2005) 1894-1908.