Hypervalent Iodine(III) Mediated C-N Bond Formation Reactions

By

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I, hereby declare that the investigation presented in the thesis has been carried out by me. The work is original and has not been submitted earlier as a whole or in part for a degree / diploma at this or any other Institution / University.

Saikat Maiti

List of Publications arising from the thesis

Journal Published

(6) **Maiti, S**.; Mal, P. Dehydrogenative Aromatic Ring Fusion for Carbazole Synthesis via C–C/C–N Bond Formation and Alkyl Migration

Org. Lett. **2017**, *19*, 2454-2457.

(5) **Maiti**, **S**.; Achar, T. K.; Mal, P. An Organic Intermolecular Dehydrogenative Annulation Reaction

Org. Lett. **2017**, *19*, 2006-2009.

(4) Achar, T. K.; **Maiti**, **S**.; Mal, P. PIDA–I_2 mediated direct vicinal difunctionalization of olefins: iodoazidation, iodoetherification and iodoacyloxylation

Org. Biomol. Chem. **2016**, *14*, 4654-4663.

(3) **Maiti**, **S**.; Mal, P. Phenyliodine Diacetate-Mediated Intramolecular C(sp^2)–H Amidation for 1,2-Di-Substituted Benzimidazole Synthesis under Metal-Free Conditions

Adv. Synth. Catal. **2015**, *357*, 1416-1424.

(2) **Maiti**, **S**.; Mal, P. Electron-Rich Aromatics Under Ball Milling: Oxidative Aryl-iodination Using I_2-Oxone and Biarylation with I_2

Synth. Commun. **2014**, *44*, 3461-3469.

(1) Achar, T. K.; **Maiti, S**.; Mal, P. IBX works efficiently under solvent free conditions in ball milling

RSC Adv. **2014**, *4*, 12834-12839.

Communicated

1. **Maiti, S.**; Mal, P. Organocatalytic Intermolecular Dehydrogenative N-Arylation of Sulfonanilides.

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Conferences and Presentation

1. **Poster Presentation:** Indo French Symposium On Functional Metal-Organics: Applications in Materials and Catalysis at NISER, Bhubaneswar on 24th – 26th February, 2014
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4. Science Academies' Lecture Workshop on "Organic and Inorganic Assembly", February 21 – 22, 2015 at Department of Chemistry, Kalinga Institute of Industrial Technology (KIIT), Bhubaneswar, India
5. Indo-European Symposium on Frontiers of Chemistry, November 10 - 12, 2011 at NISER, Bhubaneswar

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Dedicated
To

My Parents

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Dr. Dibyendu Sasmal, Dr. Sudhangshu Maity and Dr. Joydeb Goura, Anupam Manna for their support and encouragement.

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Homi Bhabha National Institute

SYNOPSIS OF Ph. D. THESIS

1. **Name of the Student:** Saikat Maiti
2. **Name of the Constituent Institution:** National Institute of Science Education and Research (NISER)
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SYNOPSIS

Introduction

The formation of C-N bonds are immensely important for the construction of biologically relevant scaffolds.[1] Many chemists have studied metal-catalyzed (transition metal) amination of aryl halides and elucidated mechanism of those reactions. However, many of those transformations have drawbacks e.g., (a) requirement for the preparation of aryl halides (or pseudohalides) or metal reagents prior to the amination (making overall transformation multistep in nature) (b) production of stoichiometric amounts of metal halides as waste after the amination.[2] Contrastingly, by doing direct C−H amination of aromatic compounds (without using aryl halides or prefunctionalized

amines), many amination reactions can be successfully achieved. Such direct C−H amination are of great importance to supply various amine derivatives in higher step economy and waste-free strategy. The Cross-dehydrogenative couplings (CDCs) are particularly attractive because they do not necessitate preactivation of coupling partners and became atom economical. Transition metal mediated CDC methods for C-N bond formation are well studied and may have some drawbacks like using of expensive, toxic reagents and harsh conditions. Toxicity characteristic also require complete removal of residual metal impurities from final products especially in pharmaceutical industries which are again tedious and expensive process.[3] In search of environmentally benign and cost effective method for construction of C-N bonds, hypervalent iodine (III) reagents became popular because of their low toxicity, mild reactivity, easy to handle and environmentally benign nature.[4] Herein, we present the development of hypervalent iodine(III) mediated cross dehydrogenative coupling (CDC) amination methods for the synthesis of heterocycle molecules.[5] Benzimidazole has been synthesized in phenyliodine diacetate (PIDA) mediated inramolecular oxidative amination pathway. Intermolecular CDC amination methods have been developed for the synthesis of multisubstituted carbazole molecules and diarylamine compounds.

Apart from these dehydrogenative C-N bond formation reactions we have also used hypervalent iodine(III) reagents for non-dehydrogenative vicinal difunctionalization of olefins.[6]

Scope and Organization of the Present Thesis

In this thesis, methods have been introduced for (transition) metal free C-N bond formation reactions based on hypervalent iodine(III) reagents. Scope of the reactions including mechanistic studies are described. This thesis has five Chapters and the contents are as follows:

CHAPTER 1: Introduction about Hypervalent Iodine(III) and C-N Bond Formation Reactions

This Chapter mainly focuses on brief introduction about hypervalent iodine(III) reagents, C-N bond formation reactions and divided in two parts: (1) structural aspects, reactivity, preparative methods for hypervalent iodine(III) reagents (2) C-N bond formation reactions. The history and development of C-N bond formation approaches have also been highlighted. Finally this Chapter concludes with our approaches for C-N bond formation reactions to be followed in the present thesis.

CHAPTER 2: Metal-Free Intramolecular C(sp2)-H Amination for N-Substituted Benzimidazole Synthesis

(Ref: S. Maiti and P. Mal; *Adv. Synth. Catal.* **2015**, *357*, 1416-1424)

In this Chapter a metal-free, hypervalent iodine(III) reagent [phenyliodine diacetate (PIDA)]-mediated C(sp^2)-H amination in trifluoroethanol (TFE) has been developed. The intramolecular coupling methodology presented here provides a direct access to 1,2-disubstituted multifunctional benzimidazoles in good to excellent yields. The reactions were performed in the open air, at ambient temperature, and were found to be eco-friendly to atom-economical. A possible mechanistic pathway has also been discussed based on nitrenium ion intermediate formation.

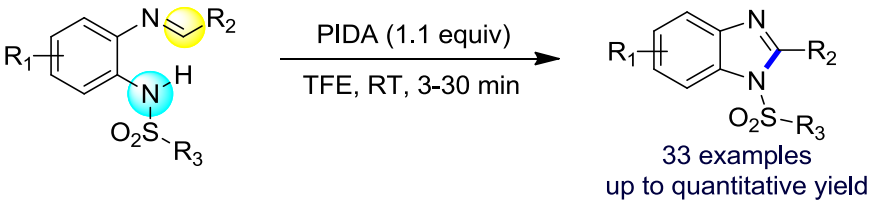

Figure 1. Intramolecular C-H amination by using phenyliodine diacetate (PIDA)

CHAPTER 3 (Part A): Transition-Metal-Free Intermolecular C-H Amination: Construction of Carbazole from Non-Prefunctionalized Arene

(Ref: S. Maiti, T. K. Achar, P. Mal; *Org. Lett.* **2017**, *19*, 2006-2009)

In this Chapter we have shown hypervalent iodine(III) reagent PIDA mediated synthesis of N-substituted carbazole *via* tandem C-C and C-N bond formation reaction. We have performed cross-dehydrogenative coupling (CDC) between anilides and unactivated arenes that are challenging to perform using conventional methods. Three C-H bonds and one N-H bond were functionalized in a single operational method. Stoichiometric as well as organocatalytic methods were developed for intermolecular oxidative amination process. This is also the first report of carbazole synthesis from non-prefunctionalized arene by intermolecular C(sp2)-H amination. Mechanistically reactions were shown to be completed *via* nitrenium ion intermediate and followed by aromatic electrophillic substitution.

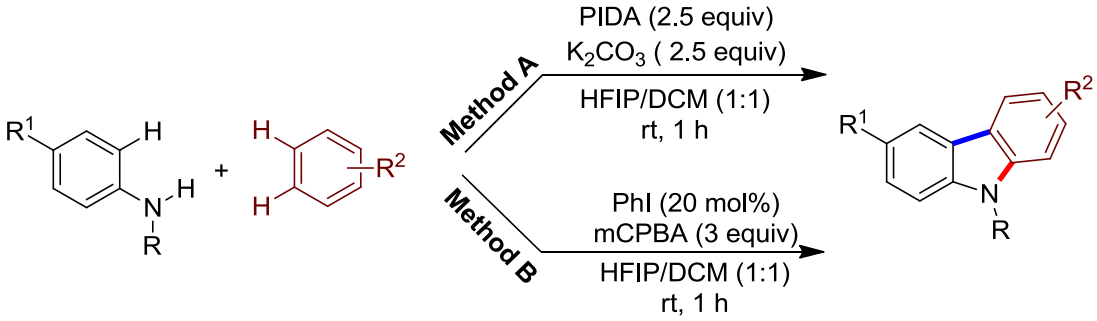

Figure 2. Stoichiometric and organocatalytic approaches for carbazole synthesis

CHAPTER 3 (Part B): Metal-free Intermolecular C(sp^2)-H Amination via Cascade Cross-Dehydrogenative Coupling (CDC)

(Ref: S. Maiti, P. Mal; *Org. Lett.* **2017**, *19*, 2454-2457)

Metal-free hypervalent iodine(III) mediated efficient strategy has been developed for cascade cross-dehydrogenative coupling amination reaction. The intermolecular coupling between para-substituted anilines and mesitylene presented here provides a direct access to 1,2,4-trimethyl substituted carbazoles via cascade cross-dehydrogenative coupling reactio at room temperature. Three new bond formation reactions has been followed for the synthesis of multiple substituted carbazole derivatives with the combination of mesitylene and strategically chosen sulfoanilidies. Proposed mechanism shows that both the product formation follow a cationic pathway and followed by methyl group migration.

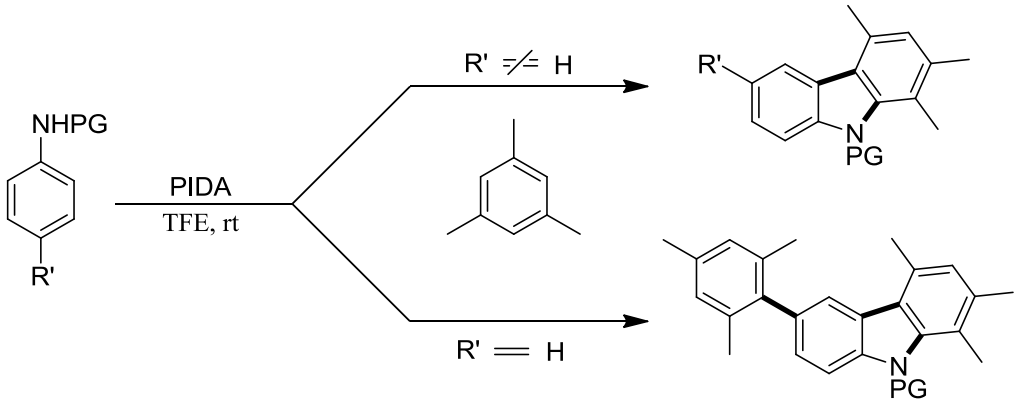

Figure 3. PIDA mediated coupling reactions between anilines and mesitylene.

CHAPTER 4. Organocatalytic Intermolecular N-Arylation of Anilides

(Ref: S. Maiti, P. Mal; Manuscript submitted)

Selective dehydogenative *N*-arylation of para-substituted sulfonanilides under metal-free conditions is shown in this Chapter. The reactions were done using *in situ* generated hypervalent iodine(III) reagent in combination of catalytic amount of iodobenzene and oxidant *m*-chloro perbenzoic acid. For *N*-arylation reactions, biphenyl or diphenylacetylene were used as arenes and the reactions progressed through the formation of nitrenium ion. The nitrenium ions were

presumably generated from nitrogen center of sulfoanilides with electron deficient iodine center of the *in-situ* generated organotrivalent iodine reagent.

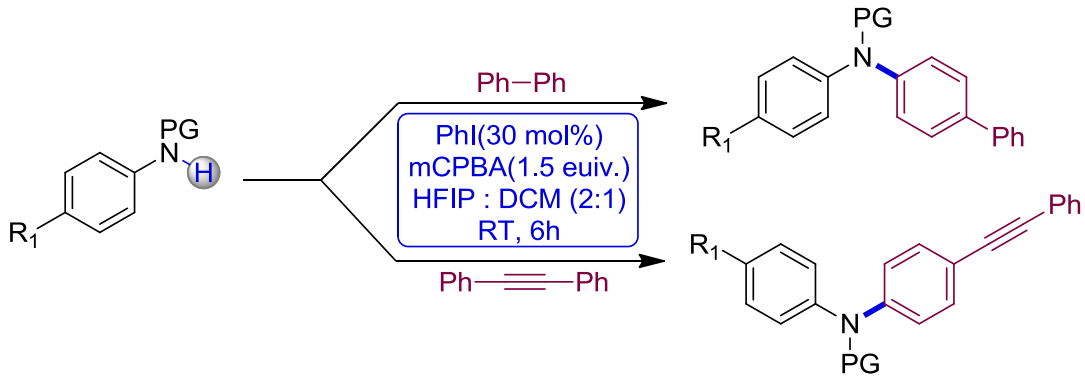

Figure 4. In-situ generated hypervalent iodine (III) mediated intermolecular amination

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CHAPTER 5. PIDA-I_2 Mediated Vicinal Difunctionalization of Olefins

(Ref: T. K. Achar, S. Maiti, P. Mal; *Org. Biomol. Chem.* **2016**, *14*, 4654-4663)

Development of transition metal free vicinal difunctionalization of olefins has been discussed in this Chapter. Iodinium cation (I^+ or IOAc) was produced from the combination of phenyliodine diacetate (PIDA) and molecular iodine(I_2). I^+ facilitated the direct vicinal difunctionalization of olefins to α-azido alkyl iodides via cation–π interaction at room temperature. Sodium azide has been used as azide source. We also performed NMR experiments to confirm the formation of acetyl hypoiodite (IOAc) species in the reaction medium. One of the iodoazidation products have been used for further functionalization for the synthesis of triazole, vinyl azide and isoquinoline products.

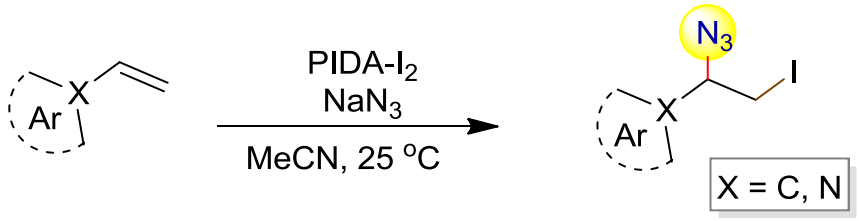

Figure 5. Iodoazidation of olefins using PIDA-Iodine

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6. Achar, T. K.; Maiti, S.; Mal, P., PIDA-I2 mediated direct vicinal difunctionalization of olefins: iodoazidation, iodoetherification and iodoacyloxylation. *Org. Biomol. Chem.* **2016,** *14*, 4654-4663.

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List of Abbreviations Used

Å	Angstrom
Ac	Acetyl
AcOH	Acetic Acid
AcOOH	Peracetic acid
Anal.	Analytically
Anhyd	Anhydrous
aq	Aqueous
Bn	benzyl
bp	Boiling Point
br	Broad
Bz	Benzoyl
ºC	Degree Celcius
Calcd	Calculated
cm	Centimeter
Conc	Concentrated
Cp	Cyclopentadienyl
Cy	Cyclohexyl
d	Doublet, Days
DBU	1,8-diazabiclo[5.4.0]undec-7-ene
DCE	1,2-Dichloroethane
DCM	Dichloromethane
dd	Doublet of a Doublet
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
dil	Dilute
DMA	Dimethylacetamide
DME	1,2-Dimethoxyethane
DMF	*N*,*N*-Dimethyl Formamide
DMSO	Dimethyl Sulfoxide

DTBP	Di-tert-butyl peroxide
equiv	Equivalent
ESI-TOF	Electrospray ionization time-of-flight
Et	Ethyl
EtOAC	Ethyl Acetate
g	Grams
h	Hours
HFIP	1,1,1,3,3,3-Hexafluoro-2-propanol
HRMS	High-Resolution Mass Spectrometry
ICP-OES	Inductively Coupled Plasma Optical Emission Spectroscopy
IR	Infrared
LED	Light Emitting Diode
lit	Liter
m	Multiplet
*m*CPBA	*meta*-chloroperbenzoic acid
*m*CPBA	*meta*-chlorobenzoic acid
M	Molar
MeCN	Acetonitrile
mp	Melting point
Me	Methyl
MHz	Mega Hertz
Min	Minutes
mL	Milliliter
mmol	Millimole
mol	Mole
MS	Mass Spectra, Molecular Sieves
Ms	Methane sulfonyl
M/Z	Mass to charge ratio
N	Normal
nm	Nanometer
NMP	N-Methyl-2-pyrrolidine

NMR	Nuclear Magnetic Resonance
Ns	4-Nitrobenzene sulfonyl
Piv	Pivaloyl
Ppm	Parts per Million
Py	Pyridine
rt	Room Temperature
s	Singlet, Seconds
t	*tert*
TBHP	Tert-Butylhydroperoxide
TEMPO	(2,2,6,6-Tetramethylpiperidin-1-yl)oxyl
TFE	2,2,2-Trifluoroethanol
Tf	Trifluoromethanesulfonyl
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
TMS	Trimethylsilyl
Ts	*p*-Toluenesulfonyl
TFA	Trifluoroacetic acid
XRD	X-Ray Diffraction

Table of Contents

CHAPTER 1

Introduction: Hypervalent Iodine(III) and C-N Bond Formation Reactions

1.1 ABSTRACT

This section mainly focuses on brief introduction about hypervalent iodine(III) reagents, C-N bond formation reactions and divided in two parts: (1) structural aspects, preparative methods of hypervalent iodine(III) reagents and reactivity, (2) C-N bond formation reactions. The history and development of C-N bond formation reactions have also been highlighted along with collection of significant literature reports. Finally this Chapter concludes with conferring the aim of present thesis for C-N bond formation reactions to be followed in the present thesis.

1.2 INTRODUCTION

Iodine was discovered from seaweed ashes in 1811 by French chemist Bernard Courtois and name was given by J. L. Gay Lussac in 1813.[1,2] The name derives from “iodes,” which means violet or purple in Greek. About 2/3 of the total iodine production in the world makes from Chile and almost 1/3 from Japan, together accounting for nearly 90% of the iodine globally.[3] Iodine, an essential trace element in human body is needed for the production of thyroid hormone. The thyroid is responsible for the production of thyroxin, a metabolism-regulating hormone. Iodine deficiency can lead to enlargement of the thyroid (goitre). The body does not make iodine, so it is an essential part of diet. Use of iodized salt is the most cost-effective way to prevent iodine deficiency disorder (IDD).

Iodine is an atom having several unique characteristics. It is the heaviest non-radioactive element in the periodic table classified as a non-metal and it is the largest, the least

electronegative and the most polarizable of the halogens. In natural organic compounds, iodine occurs exclusively in the monovalent state. Iodine is an element with symbol I and atomic number 53. Iodine atom belongs to p-block, group 17, fifth row element with electronic configuration [Kr]$d^{10}s^2p^5$. Therefore, the preferred oxidation state of iodine is -1. Iodine exist in zero (0) oxidation state in molecular iodine and in +1 oxidation state in covalent iodo compound like iodoarene. However, because of its high electropositive nature, largest size and most polarizable of the group 17 elements, iodine can also form stable poly co-ordinated, multivalent compounds with relatively weak bonds to electronegative groups or elements such as oxygen, sulphur, nitrogen or a halide.[4]

1.3 HYPERVALENT IODINE

Compound containing main group elements bearing more than eight electrons in its valance shell are called as hypervalent compound.[5] Iodine can form three types of hypervalent iodine compounds: (i) trivalent iodine compounds (λ^3-iodanes), where iodine atom contains 10 electrons in its valance shell, (ii) pentavalent iodine compounds (λ^5-iodanes), having 12 electrons in valance shell of iodine and (iii) heptavalent iodine compounds (λ^7-iodanes), having 14 electrons in valance shell of iodine. Among these three types, heptavalent iodine compounds are observed in only some inorganic compounds like IF_7, $NaIO_4$ and HIO_4 etc. The six most common structural types of hypervalent iodine species are represented by structures **1-7** (Figure 1.1). Species **2-7** can be generally classified using the Martin-Arduengo N-X-L designation for hypervalent molecules where N is the number of valence electrons formally assignable to the valence shell of the central atom, X, either as unshared pairs of electrons or as pairs of electrons in the sigma bonds joining a number, L, of ligands to the atom X.[6] Structure **1**, the iodonium ion, formally does not belong to hypervalent species since it has only eight valence electrons on the iodine atom. Trivalent and pentavalent iodine compounds are observed in both organic

and inorganic compounds among which organo hypervalent iodine compounds have received considerable attention as an oxidant due to their low toxicity, mild reactivity, ready accessibility, high stability, easy to handle, and so on.[7] The first report of a hypervalent iodine compound in history was in 1886, when iodobenzene dichloride ($PhICl_2$) was accidentally obtained by Willgerodt during his attempt to ring chlorinate iodobenzene by passing chlorine gas to the solution.[8] A predominant use of these organo hypervalent iodine reagents is replacing the highly toxic heavy metal oxidizers, that is, lead(IV), mercury(II), and thallium(III) reagents, as useful alternatives.[9] Extensive applications as stoichiometric oxidants were found to mediate a wide array of bond-forming reactions and other oxidative transformations.

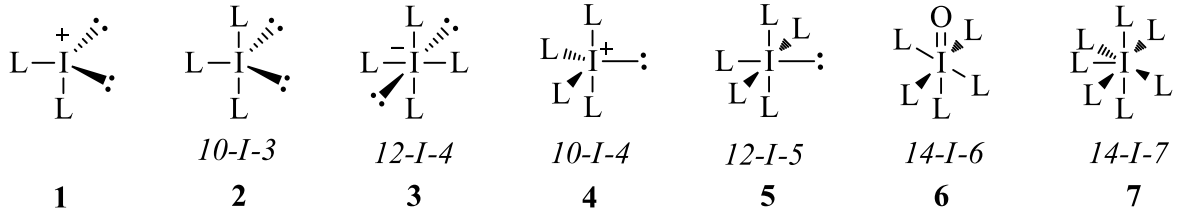
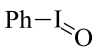
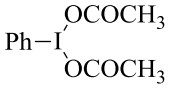
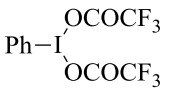
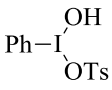
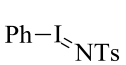
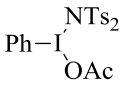


Figure 1.1 Typical structural types of polyvalent iodine compounds.

1.4 ORGANO-HYPERVALENT IODINE (III)

Organoiodine(III) compounds are commonly classified based on the type of ligands attached to the iodine atom. Iodine(III) compounds have found broad application as oxidizing agent in organic synthesis. The most important and commercially available representatives of aryliodine(III) carboxylates is (diacetoxyiodo)benzene $PhI(OAc)_2$, which is commonly abbreviated as PIDA (phenyliodine diacetate) (Table 1.1). Some other representative organoiodine(III) reagents are PhIO, known as iodosylbenzene; $PhI(OCOCF_3)_2$, known as PIFA etc. Sulfonate derivative PhI(OH)(OTs), abbreviated as HTIB is known as Koser's reagent.

Table 1.1 Names and abbreviations of important derivatives of hypervalent organoiodine(III).

Compound	IUPAC names	Common names	Common abbreviations
	(Dichloroiodo)benzene	Iodobenzene dichloride Iodosobenzene dichloride Phenyliodine(III) dichloride	IBD
	Iodosylbenzene	Iodosobenzene	IDB
	(Diacetoxyiodo)benzene	Iodobenzene diacetate Phenyliodo diacetate Iodosobenzene diacetate Phenyliodine(III) diacetate	DIB PIDA IBDA
	[Bis(trifluoroacetoxy)iodo] benzene	Iodobenzene bis(trifluoroacetate) Phenyliodo bis(trifluoroacetate) Phenyliodine(III) bis(trifluoroacetate)	BTI PIFA
	Hydroxy(4-methylphenyl sulfonyloxy)iodo]benzene	[Hydroxy(tolsyloxy)iodo]benz ene Koser's reagent	HTIB, HTI
	[N-(4-Methylphenylsulfonyl) imino]phenyl-l^3-iodane	(N-Tosylimino)phenyliodinane	None
	Acetoxy((4-methyl)-N-tosyl benzene sulfonamidyl)-iodosobenzene	Acetoxy(bistosyl)imido iodobenzene	None

1.5 PREPARATION OF TRIVALENT IODINE(III) COMPOUNDS

In general, the approach to trivalent iodine(III) compound is based on oxidative addition of appropriate ligands to the low valent iodine species. Readily available and inexpensive iodoarene precursors are most commonly used with a suitable oxidant for the preparation of hypervalent organoiodine(III) compounds. (Dichloroiodio)benzene is usually prepared by direct chlorination of iodobenzene with chlorine gas in chloroform or dichloromethane at -3 to +4 ^{o}C (Figure 1.2).[10] (Dichloroiodo)arene compounds are isolated as heat- and light-sensitive yellow crystalline solid, which are insufficiently stable even at low temperature.

The most important, well investigated and practically useful oxidizing agent phenyliodine diacetate (PIDA) is usually prepared by oxidation of iodobenzene with oxidizing agent in acetic acid (Figure 1.2). Frequently used oxidizing agent for synthesis of PIDA are sodium perborate ($NaBO_3.10H_2O$), peracetic acid (AcOOH), *meta*-chloroperbenzoic acid (*m*CPBA), potassium peroxodisulfate ($K_2S_2O_8$).[11,12] The crystal structure of $PhI(OAc)_2$ shows that I-C bond distance is 2.090 Å and the two I-O distances of about 2.156 Å which are longer than the sum of covalent radii of the elements (2.070 Å for I–C and 1.99 Å for I–O).[13]

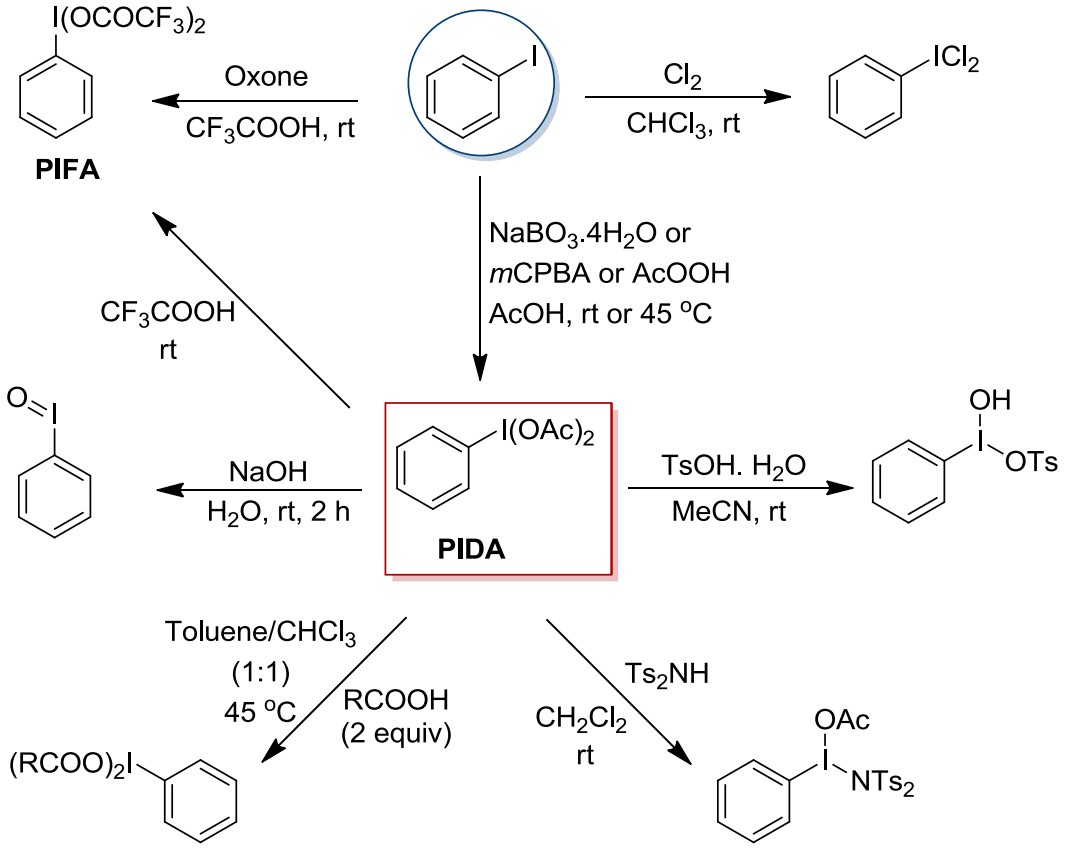


Figure 1.2 Preparation of organoiodine(III) compounds.

Similarly, phenyliodo(bistrifluoroacetate) (PIFA) can be synthesized by oxidation of iodobenzene by oxone in trifluoroacetic acid solvent.[14] PIFA can also be derived from PIDA by ligand exchange with trifluoroacetic acid (Figure 1.2).[15]

The common approach to prepare [bis(aceloxy)iodo]arenes [$PhI(OCOR)_2$] is based on ligand exchange reaction of phenyliodine diacetate (PIDA) with an appropriate carboxylic acid (Figure 1.2). A typical procedure consist of heating of PIDA with a non-volatile carboxylic acid RCOOH (2.0 equiv) in presence of high-boiling solvent like toluene. The equilibrium of this reversible reaction is shifted towards the product formation by distillation of relatively volatile acetic acid (formed during reaction) under reduced pressure.[16]

[Hydroxy(tosyloxy)iodo]benzene (HTIB) which is also known as "Koser's reagent" is synthesized from (diacetoxyiodo)benzene by reacting with *p*-toluenesulfonic acid monohydrate in acetonitrile.[17] Phenyliodine diacetate (PIDA) can be converted to iodosyl benzene by treating with 15% aqueous sodium hydroxide (NaOH) solution at room temperature.[18] Organic iodosyl compounds exist in polymeric structure $(PhIO)_n$, with a typical T-shaped geometry at iodine center. No structural evidence found to support the existence of I=O bond. Most of the iodosyl compounds are thermally unstable and some are explosive upon heating.[19]

Two different hetero atom containing iodine(III) compound acetoxy(bistosyl)imido iodobenzene [$PhI(NTs_2)(OAc)$] is synthesized from PIDA by treating with bis(tosyl)imide in dichloromethane solvent (Figure 1.2).[20]

1.6 STRUCTURE AND BONDING

In principle, there are two possible explanations for the ability of main-group elements to hold more than the octet of electrons within a valence shell: (i) by the involvement of the higher lying d orbitals resulting in dsp^3 or d^2sp^3 hybridization or (ii) by the formation of a new type of highly ionic orbital without involvement of d orbital. In modern literature, it is generally granted that the contribution of d orbital is not crucial to form hypervalent compounds and that

hypervalent bonding is best explained by a molecular orbital description involving a three-center-four-electron bond. In 1951, G. C. Pimentel and R. E. Rundle proposed the idea of three-center-four-electron-bond (3c-4e) based on molecular orbital theory.[21] According to the fundamental description of the 3c-4e bond in hypervalent compound, one bonding electron pair is delocalized to the two ligands resulting in the charge distribution of -0.5 on each ligand and +1.0 on the central atom. In hypervalent iodine(III) compound of type $ArIL_2$, interaction between filled 5p orbital of central iodine and half-filled orbital of two ligands leads to the formation of three molecular orbitals: bonding, nonbonding and antibonding (Figure 1.3). Highest occupied molecular orbital (HOMO) contains a node at the central iodine atom resulting high polarized nature in the hypervalent bonds. Thus the more electronegative atoms shows tendency to occupy the axial positions (Figure 1.4). Carbon substituent R is bound to the iodine atom by normal covalent bond. The overall geometry of the molecule RIL_2 is distorted trigonal bipyramid where two heteroatom ligands L occupy the apical positions and the least electronegative carbon ligand R and both electron pairs exist in equatorial positions (Figure 1.4).

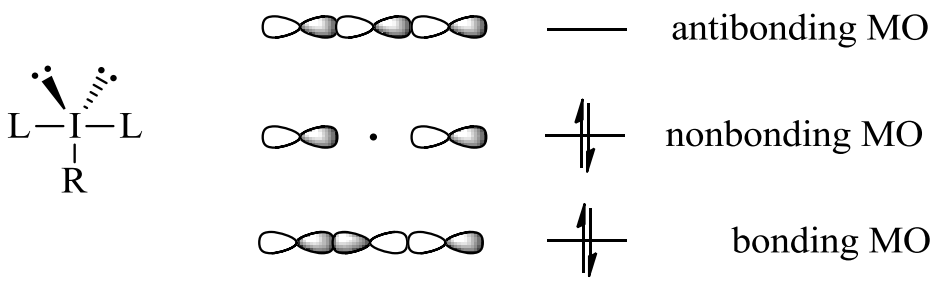


Figure 1.3 Molecular orbital sketch of the three-center-four-electron bond in iodine(III) molecules.

The fundamental feature of these compounds is the highly polarized three-center-four-electron (3c-4e) bond, in which the central atom bears a positive charge and two monovalent ligands share the corresponding negative charge. This type of bonding serves to distinguish hypervalent

compounds from transition metal complexes in which d-orbital hybridization is invoked to account for bonding beyond the stable octet.

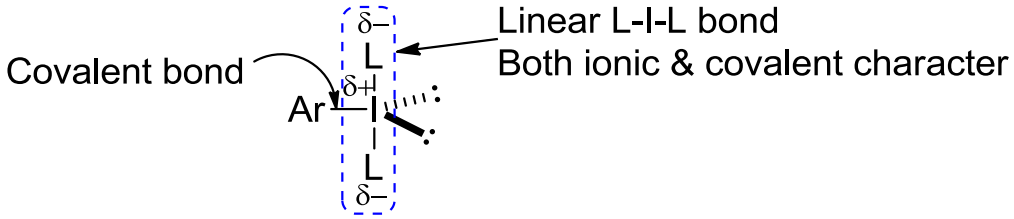
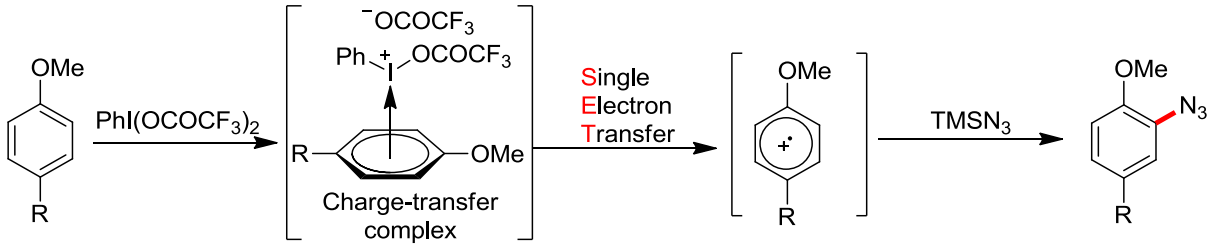


Figure 1.4 Structure of organoiodine(III) compounds of type $ArIL_2$.

1.7 REACTIVITY

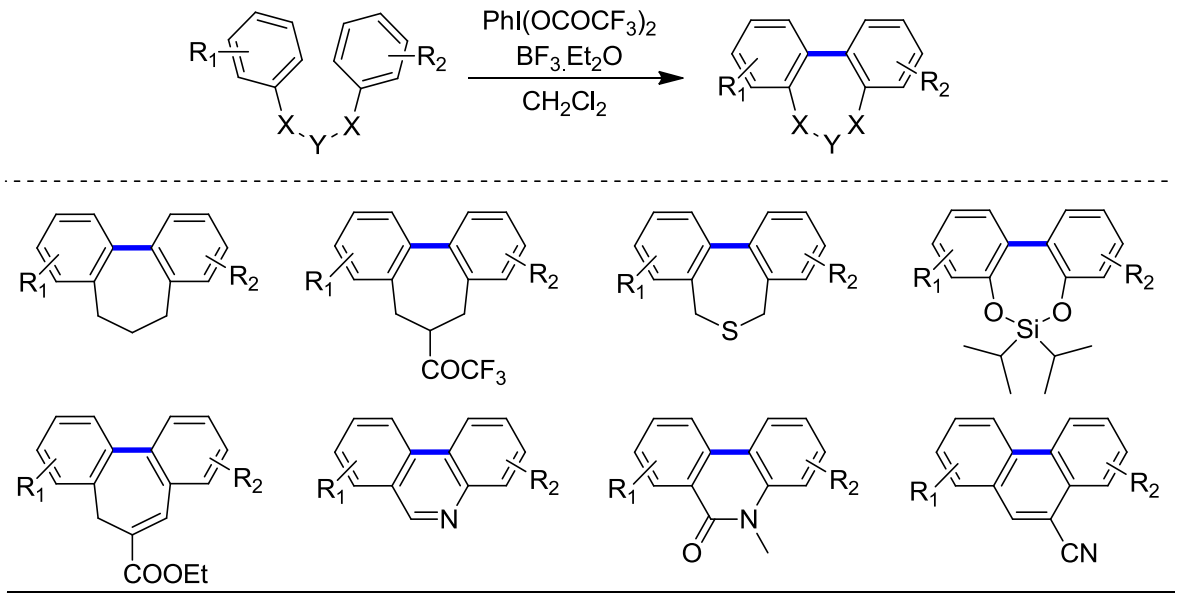
1.7.1 SINGLE-ELECTRON TRANFER REACTIONS

Hypervalent iodine(III) compounds can promote reaction in single-electron transfer pathway by radical-cation intermediate formation with electron-rich aromatic substrates in polar, non-nucleophilic solvents. Kita and co-workers established the reaction of *p*-substituted phenol ethers with [bis(trifluoroacetoxy)iodo]benzene (PIFA) in presence of azide nucleophile in fluorinated alcohol solvents to afford aromatic nucleophilic substituted products (Scheme 1.1).[22] Generation of radical-cation intermediate by SET through charge-transfer complex of phenyl ethers with hypervalent iodine(III) reagent was confirmed with the help of UV and ESR spectroscopic measurements. The requirement of fluorinated alcohol as solvent in these reaction is explained by their unique ability to stabilize the aromatic cation radicals.



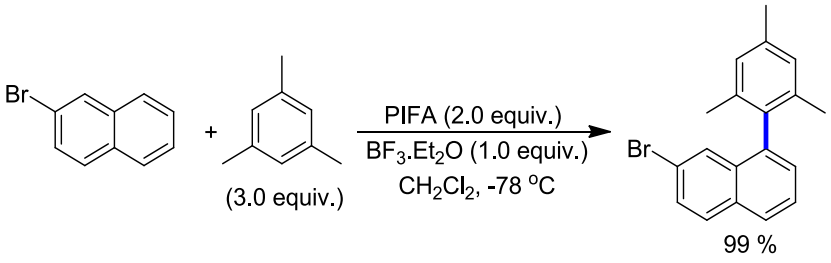
Scheme 1.1 Iodine(III) induced single electron transfer reaction.

The same group developed intramolecular oxidative C-C bond formation reaction for biaryl synthesis using $PhI(OCOCF_3)_2$-$BF_3.Et_2O$ combination as oxidant based on single electron transfer strategy (SET) (Scheme 1.2). Using this protocol a diverse range of tricyclic as well as heterocyclic tricyclic compounds could be achieved under mild conditions. In general, the aryl rings contain electron donating substituents such as methoxy- undergo reaction in more facile way. Reactions proceed through radical cation intermediate formation by SET pathway.[23]



Scheme 1.2 Iodine(III) induced intramolecular C-C bond formation through SET.

In 2008, based on similar SET pathway Kita and co-workers discovered a methodology to obtain intermolecular cross-coupling products of various naphthalene and mesitylene with selection of mesitylene as nucleophilic partner (Scheme 1.3).[24]



Scheme 1.3 Kita's approach for intermolecular C-C bond formation *via* SET.

1.7.2 LIGAND EXCHANGE AND REDUCTIVE ELIMINATION

In general, the reactivity of hypervalent iodine(III) reagents towards nucleophile are discussed in three steps pathways: (a) ligand exchange, (b) reductive elimination and (c) ligand coupling.[25] The mechanistic pathways have been represented in Figure 1.5.

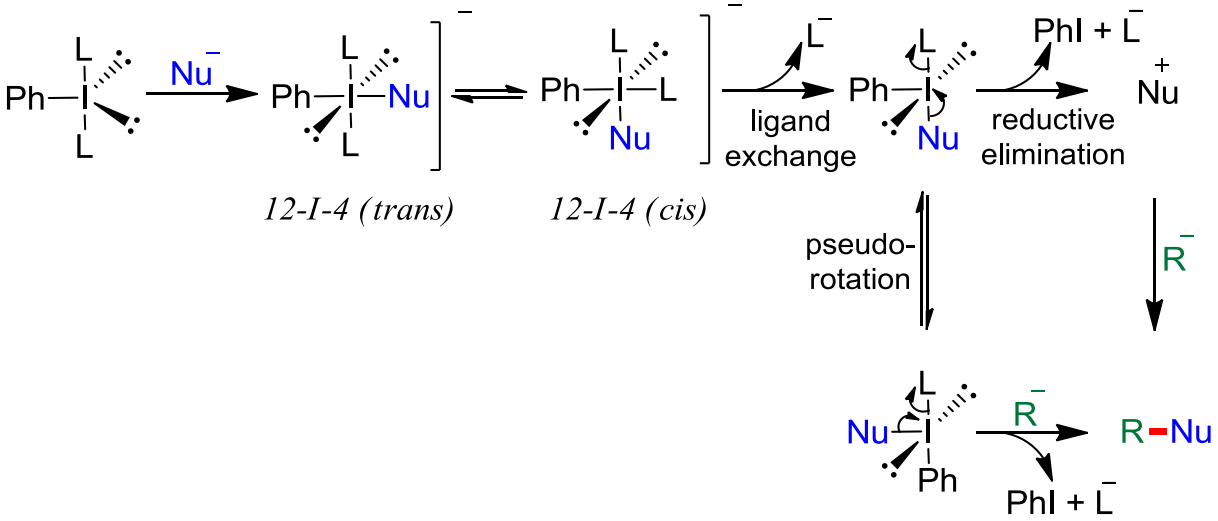
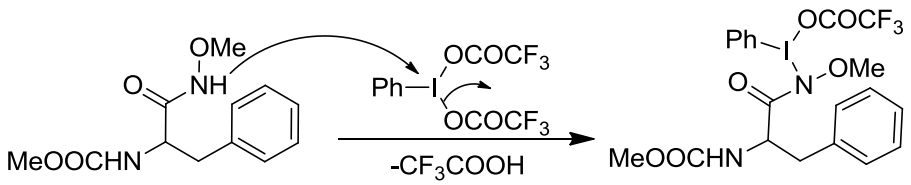


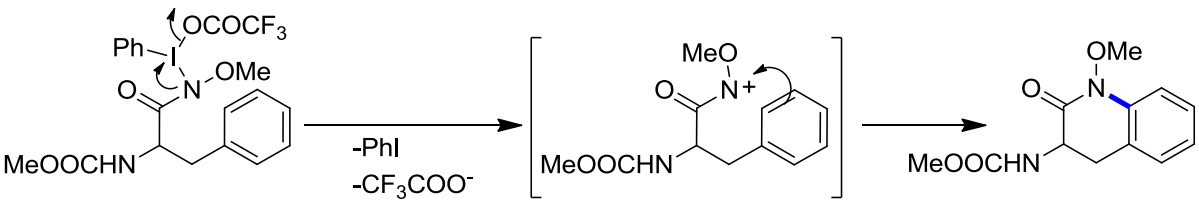
Figure 1.5 Representation of the reactions of λ^3-iodanes of type $ArIL_2$ with nucleophiles Nu.

Firstly, nucleophilic addition take place to electron deficient iodine(III) center in associative pathway to form *trans*- hypervalent 12-I-4 square-planar species. This intermediate species readily isomerizes to *cis* 12-I-4 square-planar intermediate species. Subsequently ligand get eliminated to afford 10-I-3 species (Figure 1.5).



Scheme 1.4 Representative ligand exchange process.

Second step of reaction of hypervalent iodine(III) species with nucleophile includes elimination of iodobenzene or other reduced iodine species. This step is energetically favourable due to very high leaving aptitude of phenyliodino group (-PhIL). Ochiai has suggested calling this phenyliodino group as "hypernucleofuge" since it's million times (10^6) better leaving aptitude than triflet group.[25] Reductive elimination results the formal umpolung of reactivity of the nucleophile, $Nu:^-$ to Nu^+ (Figure 1.5), is a common process in various reactions of hypervalent iodine reagents; it can result in the formation of products of nucleophilic substitution, rearrangement, or fragmentation.



Scheme 1.5 Representative reductive elimination process.

Ligand coupling pathway require initial pseudorotation to bring ligand and nucleophile to apical and equatorial positions favourable for coupling. Usually ligand coupling occurs as a concerted process.

1.8 IN-SITU GENERATION OF IODINE(III)

Iodine center of hypervalent iodine(III) compounds are highly electron deficient in nature, thus it has a natural tendency to accept electron from nucleophilic substrate. In this way iodine(III) convert substrate into oxidized product and itself get reduced into monovalent iodoarene species. So monovalent iodoarene can be used for an oxidative transformation in presence of an appropriate co-oxidant, which is expected to oxidize monovalent iodoarene into trivalent iodoarene *in situ* in the reaction mixture (Figure 1.6). Iodoarene can be used in both stoichiometric as well as in catalytic amount. The process involving *in situ* generation of hypervalent iodine(III) reagent by using catalytic amount of iodoarene may be considered as organocatalytic way. Commonly used oxidizing agents for *in situ* generated hypervalent iodine(III) mediated oxidative transformation are *meta*-chloroperbenzoic acid (*m*CPBA), peracetic acid (AcOOH), oxone ($2KHSO_5.KHSO_4.K_2SO_4$), hydrogen peroxide (H_2O_2) etc.[26]

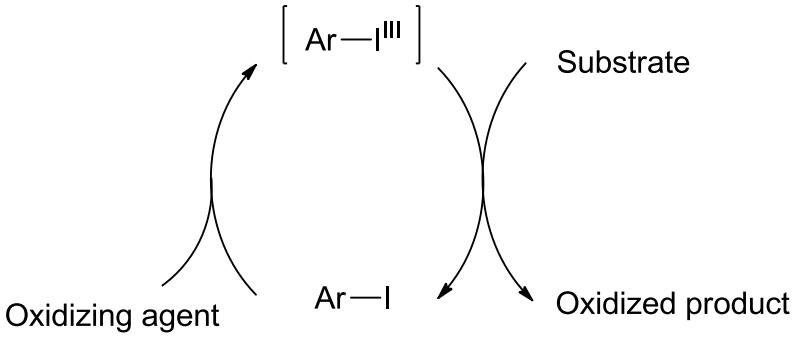


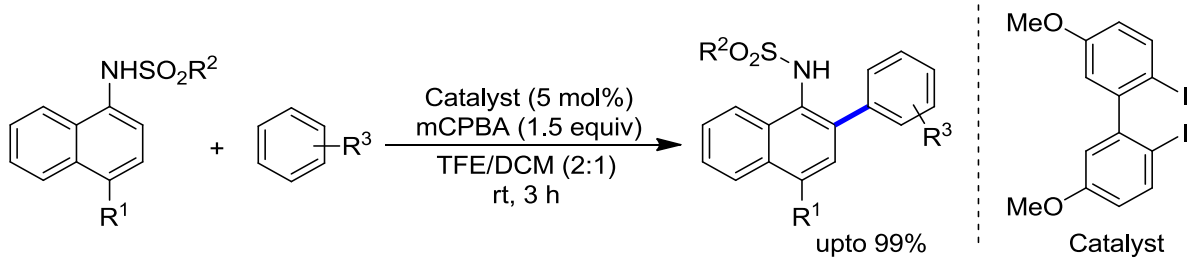
Figure 1.6 In-situ generation of organoiodine(III).

1.9 TRANSFORMATION USING HYPERVALENT IODINE(III) REAGENT

1.9.1 INTERMOLECULAR C(SP^2)-C(SP^2) BOND FORMATION

In situ generated hypervalent iodine(III) mediated C-C selective coupling of anilides with aromatic hydrocarbons was reported by Kita and co-workers (Figure 1.6). Specific 2,2'-diiodobiphenyl compound was used as organocatalyst in presence of oxidant *meta*-

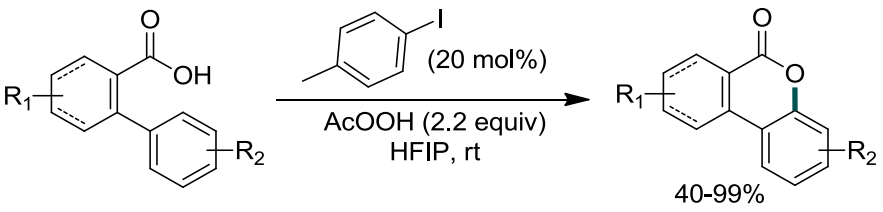
chloroperbenzoic acid (*m*CPBA) for *in situ* generation of iodine(III) species. The reaction proceeds through ligand exchange and reductive elimination steps and followed by attack at carbenium ion center from nucleophilic arene to lead dehydrogenative C-C bond formation.[27]



Scheme 1.6 Kita's approach for hypervalent iodine(III) enabled C-arylation.

1.9.2 C-O BOND FORMATION REACTION

Martin *et. al.*, developed *in situ* generated iodine(III) catalyzed tandem C(sp^2)-O bond-forming process to provide benzolactones under mild conditions (Scheme 1.7). Peracetic acid (AcOOH) was used as oxidizing agent to convert 4-iodotoluene into corresponding iodine(III) species which is responsible for the dehydrogenative C-O bond construction. The authors have proposed a tentative mechanism of oxidative reaction through formation of radical cation with an electron-rich aromatic motif that facilitate the addition of incoming carboxylic acid motif.[28]

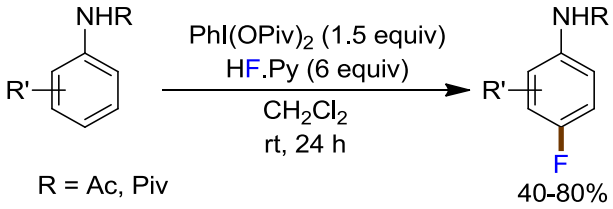


Scheme 1.7 Martin's approach for C-O bond formation.

1.9.3 CARBON-HALOGEN (C-X) BOND FORMATION REACTION

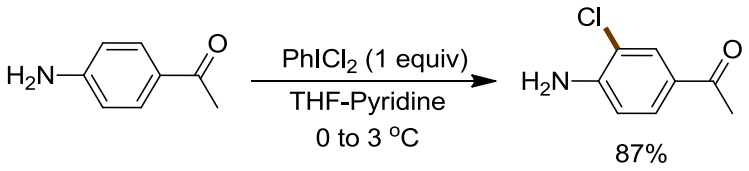
Regioselective fluorination of anilides has been reported by using Py.HF as fluoride source in presence of bis(*tert*-butylcarbonyloxy)-iodobenzene [$PhI(OPiv)_2$] as oxidizeng agent in

dichloromethane solvent at room temperature conditions (Scheme 1.8). Mechanistically, reaction go on through formation of electrophilic nitrenium ion, which is generated by interaction of nitrogen centre of anilide with electron deficient iodine(III) centre of reagent and subsequent nucleophilic attack by fluoride ion.[29]



Scheme 1.8 C-F bond formation using hypervalent iodine(III).

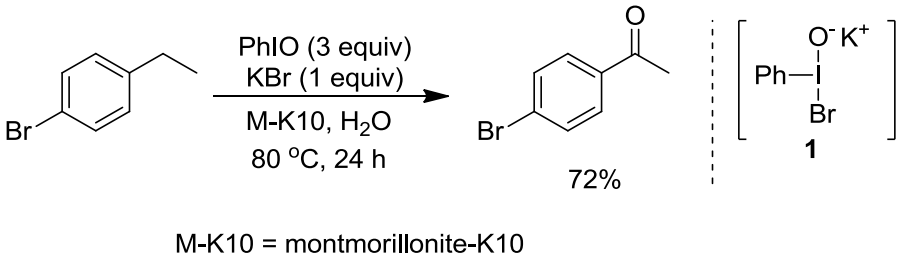
Monochlorination of 4-amino acetophenone could be achieved by using dichloroiodobenzene ($PhICl_2$) in combined solvent system of THF and pyridine (Scheme 1.9). The process was successfully scaled up to afford 24.8 kg of chlorinated product in 87% yield.[10]



Scheme 1.9 Hypervalent iodine(III) enabled C-Cl bond formation.

1.9.4 BENZYLIC C-H OXIDATION

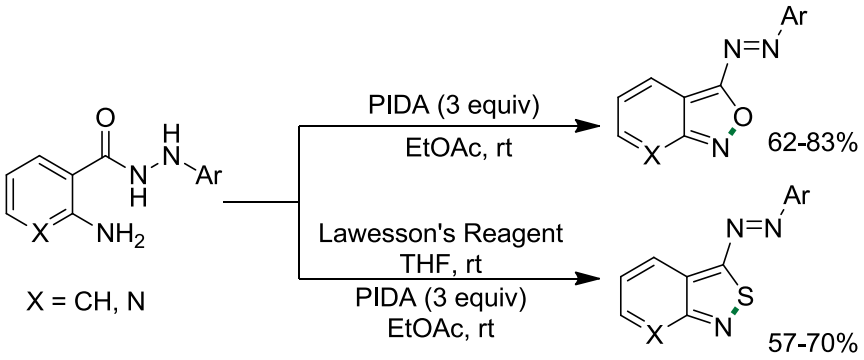
In 2008, Kita and co-workers reported an unprecedented method for benzylic C-H oxidation to give arylketones by using polymeric iodosylbenzene $(PhIO)_n$ in presence of KBr and montmorillonite-K10 clay in aqueous medium (Scheme 1.10). Combination of $(PhIO)_n$ and KBr generate water soluble active species **1**, was considered as key radical initiator during the reaction.[30]



Scheme 1.10 Kita's approach for benzylic oxidation.

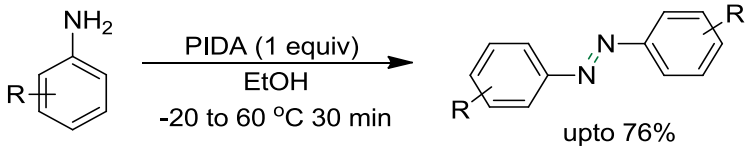
1.9.5 HETEROATOM-HETEROATOM BOND FORMATION

Phenyliodine diacetate (PIDA) has been employed on simple 2-amino-*N'*-arylbenzohydrazides for the synthesis of arylisoxazoles and benzisothiazoles via intramolecular oxidative N-O or N-S bond formation reaction under aerobic conditions (Scheme 1.11). Reaction proceed through nucleophilic attack from oxygen or sulphur on the electrophilic amine, generated with the help of iodine(III) reagent to furnish heterocyclic ring.[31]



Scheme 1.11 Hypervalent iodine(III) enabled N-O and N-S bond formation.

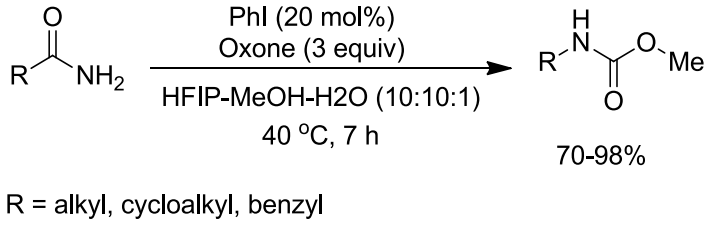
Hajra *et. al.*, developed phenyliodine(III) diacetate (PIDA) mediated oxidative dehydrogenative coupling method for the synthesis of aromatic azo compounds from anilines (Scheme 1.12). The protocol is applicable for both homo-coupling as well as cross-coupling. Mechanistically, the reaction follow ionic pathway.[32]



Scheme 1.12 Hajra's approach for azo formation.

1.9.6 REARRANGEMENT

Hoffmann rearrangement of carboxamides to carbamates has been reported by Zhdankin and co-workers using *in situ* generated hypervalent iodine(III) as catalyst (Scheme 1.13). Iodine(III) species was generated form catalytic amount of iodobenzene in presence of oxidant oxone in combination of 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) and aqueous methanol solvent.[33]



Scheme 1.13 Zhdankin's approach for Hoffmann rearrangement.

1.10 C-N BOND FORMATION

Nitrogen element is crucial to life on earth. It is a component of proteins and it can be found in all living systems. The air we breathe roughly contains 78% nitrogen (molecular nitrogen in gaseous state). Moreover, nitrogen containing organic molecules are widespread in natural products, synthetic pharmaceuticals and organic materials.[34] Thus synthesis of nitrogenous compounds is an interesting branch in organic chemistry with utmost importance. C-N bond constitute the basic framework in most of the nitrogenous compounds. Researchers attempted to develop simpler C-N bond formation methods towards the synthesis of complex molecular

structures. In this thesis two discrete type of C-N bond formation reactions has been discussed: (a) dehydrogenative C(sp^2)-N and (b) non-dehydrogenative C(sp^3)-N bond formation reaction as shown in Figure 1.7. For both type of transformations C(sp^2)-H containing substrates will be used. Nitrogen coupling unit will be used either in intramolecular way or in intermolecular fashion.

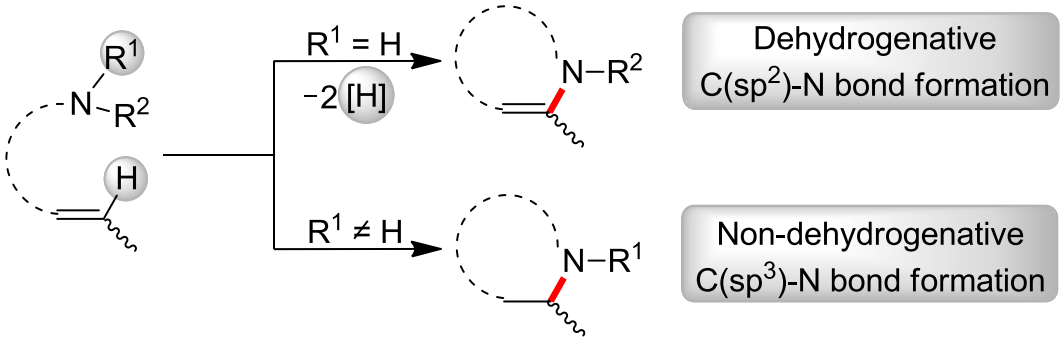


Figure 1.7 Type of C-N bond formation reactions studied in present thesis.

1.10.1 EVALUTION OF C(sp^2)-N BOND FORMATION REACTION

In 1905, Ullman and Goldberg opened new avenue towards organic synthesis with the establishment of copper mediated C(sp^2)-N bond formation reaction from organo-halo compounds (Figure 1.8a).[35] Breakthrough in the field of C-N bond formation reaction was the discovery of transition metal catalyzed cross coupling reaction, independently developed by Buchwald and Hartwig in 1995. This reaction is based on Pd-catalyst, bulky phosphine ligand and base, allows the transformation of aromatic or vinyl C(sp^2)-X (X is halide or pseudohalide) into C(sp^2)-N bond (Figure 1.8b).[36] Both the methods produces stoichiometric amount of haloacid as by-product of the reaction. Notably, these methods have some drawbacks due to requirement of pre-activated substrates for coupling reaction. In recent times, scientific community have explored new strategies for the development of C(sp^2)-N bond creation by (transition) metal catalyzed (or mediated) C-H activation. The term ‘C-H activation’ signify direct transformation of C-H bond into new bond without pre-functionalization of carbon

substrate.[37] Remarkably, pre-activated amine coupling partner is required for C-H activation approach which results in the formation of equimolecular amount of HX (X is either halogen or other functional group) from reaction mixture (Figure 1.8c).

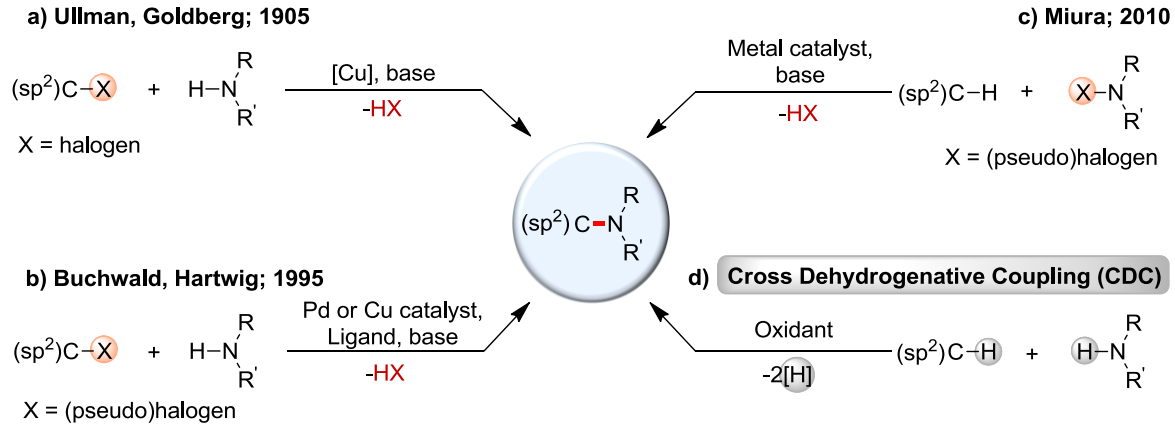
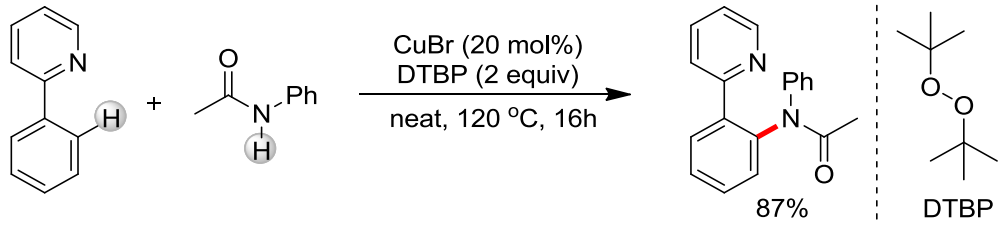


Figure 1.8 Approaches for C(sp^2)-N bond formation reactions.

Cross dehydrogenative coupling (CDC) reaction for the formation of C(sp^2)-N bonds are recently considered as state-of-art practice in organic synthesis (Figure 1.8d). Such a reaction mode is quite attractive caused by non-requirement of pre-activation step on either C-H or N-H coupling partner. Only an external oxidizing agent is required to scavenge the formal hydrogen by-product during the formation of C-N bond. For simplicity of the redox process by-product of the reaction has been mentioned as 'formal hydrogen' although in real H_2 is not formed in the reactions.[37]

1.10.2 METAL CATALYZED DEHYDROGENATIVE C(sp^2)-N BOND FORMATION

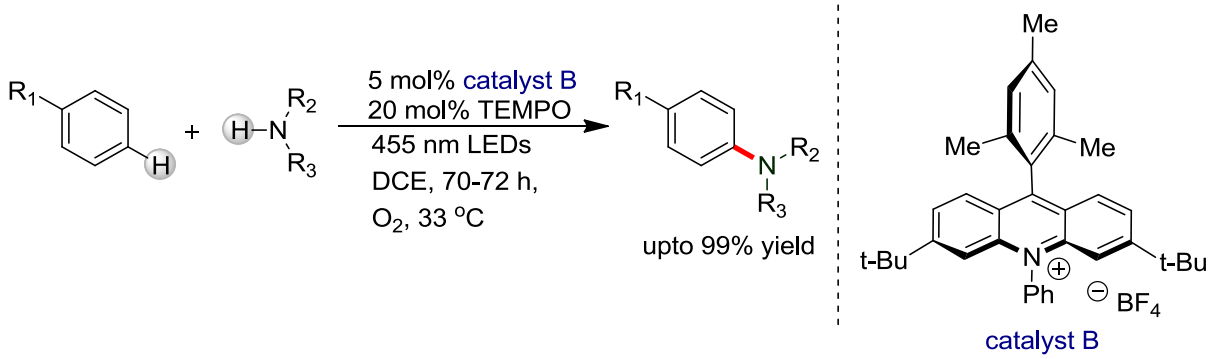
C-J. Li established copper(I) catalyzed dehydrogenative amidation of 2-arylpyridine derivatives with a variety of amides by employing *tert*-butyl peroxide as oxidant (Scheme 1.14). The reaction conditions require neither ligand nor any base for the amidation. DTBP would initiate the catalytic cycle by oxidative addition to the copper (I) pre-catalyst.[38]



Scheme 1.14 Cu(I)-catalyzed intermolecular dehydrogenative amidation.

1.10.3 METAL-FREE DEHYDROGENATIVE C(sp^2)-N BOND FORMATION

Nicewicz and co-workers developed photoredox catalyzed oxidative C(sp^2)-N bond formation strategy for aromatic amination (Scheme 1.15). Acridinium photooxidant (catalyst B) in presence of a nitroxyl radical (TEMPO) promotes site-selective amination on variety of simple and complex aromatics with heteroaromatic azoles. The protocol is highly advantageous for the direct conversion of arene compounds into anilines.[39]



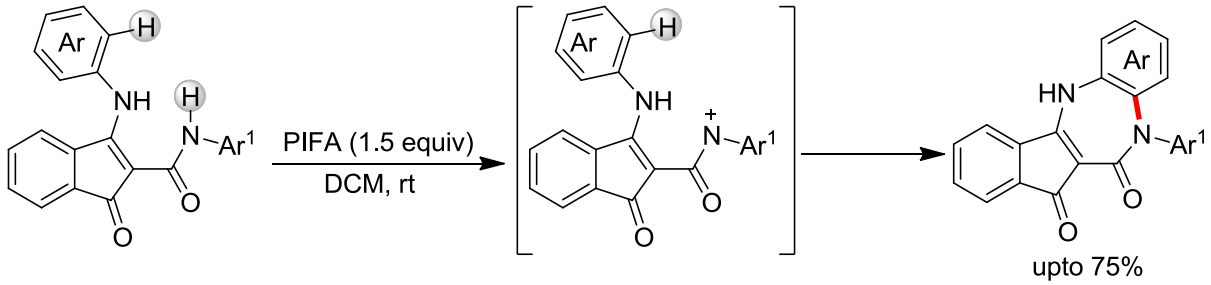
Scheme 1.15 Photocatalyzed intermolecular dehydrogenative amination.

1.10.4 HYPERVALENT IODINE(III) MEDIATED DEHYDROGENATIVE C(sp^2)-N BOND FORMATION

1.10.4.1 INTRAMOLECULAR C(sp^2)-N BOND FORMATION

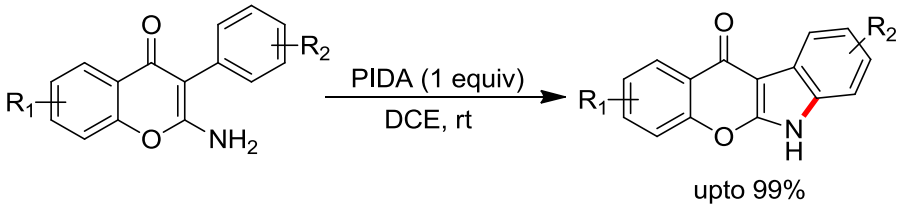
Oxidative C(sp^2)-N bond formation reaction could be achieved by employing phenyliodine bis trifluoroacete (PIFA) for the synthesis of indenodiazepinones (Scheme 1.16). Reaction

proceeds through generation of nitrenium ion intermediate and subsequent nucleophilic attack from aryl ring.[40]



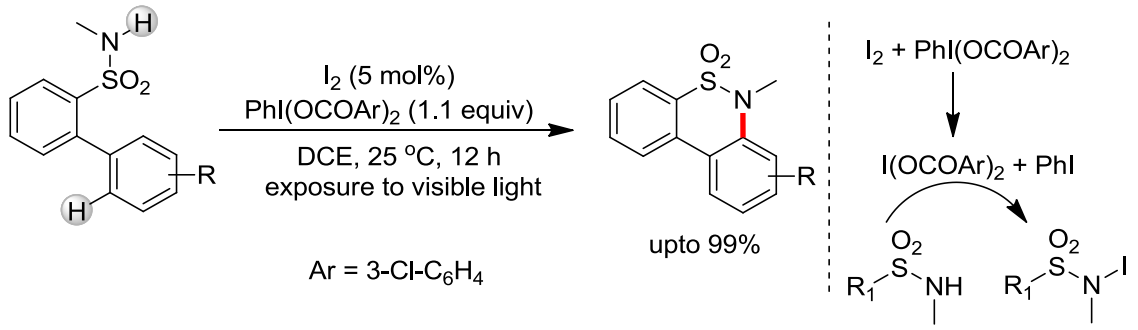
Scheme 1.16 PIFA enabled intramolecular dehydrogenative amination.

Zhao and co-workers developed a Phenyliodine diacetate (PIDA) mediated intramolecular oxidative C(sp^2)-N bond formation reaction for the synthesis of four ring fused heterocycle chromeno[2,3-b]indol-11(6H)-ones at room temperature (Scheme 1.17).[41]



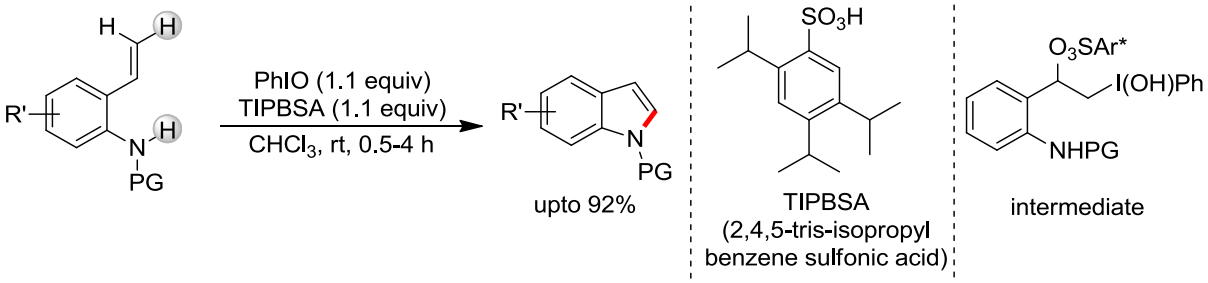
Scheme 1.17 Zhao's approach for substituted indole synthesis.

Recently, Muniz and co-workers have developed a molecular iodine catalysis protocol for mild and selective intramolecular aryl amination reaction in presence of arylacetoxy derivative of hypervalent iodine(III) compound at room temperature conditions (Scheme 1.18). Visible light has been used as initiator to provide differently substituted arylamines. The reaction starts with the formation of $I(OCOAr)_2$ which promote *N*-iodination of sulphonamide substrate and subsequent photolytically assisted homolysis of the N-I bond. The protocol is applicable for both aliphatic as well as aromatic hydrocarbons.[42]



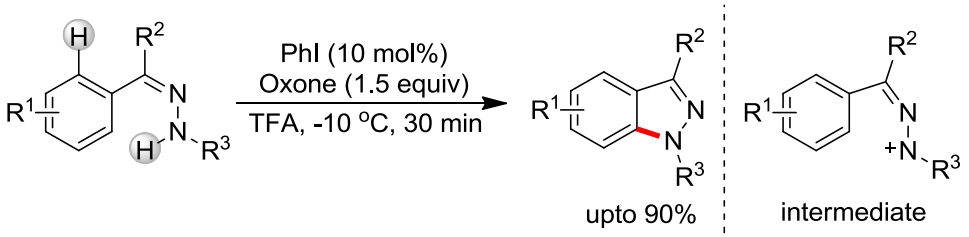
Scheme 1.18 Muniz's approach for intramolecular amination.

The same group have established a metal-free intramolecular dehydrogenative C(sp^2)-N bond formation protocol for the synthesis of indoles from 2-amino styrenes by using hypervalent iodine(III) reagent (Scheme 1.19). The process is based on sterically congested hypervalent iodine compounds of the family of Koser's reagents, and iodosobenzene in combination with 2,4,5-tris-isopropylbenzene sulfonic acid. The reaction is initiated through the interaction between the modified Koser's reagent and alkene group of substrate, leading to 1,2-iodooxygenated intermediate.[43]



Scheme 1.19 Muniz's approach for indole synthesis.

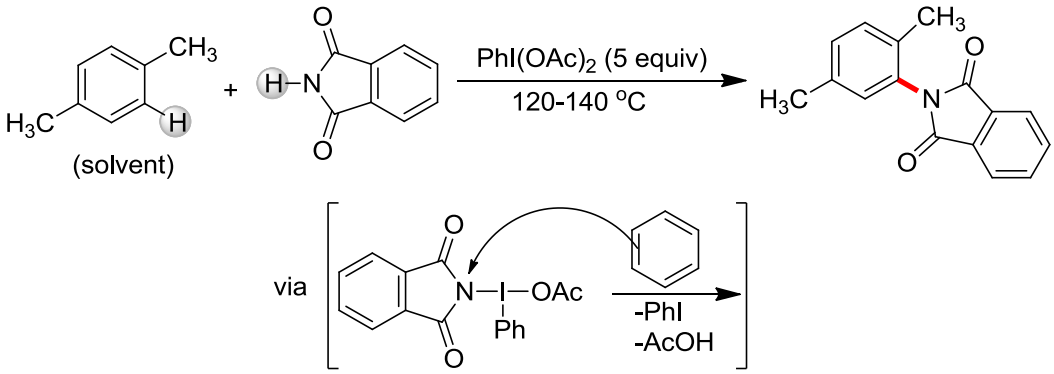
N-aryl substituted indazole could be accomplished on the basis of iodobenzene catalyzed intramolecular oxidative C-H amination of hydrazones (Scheme 1.20). Oxone has been used as oxidant for in-situ generation of hypervalent iodine(III) reagent from iodobenzene in presence of trifluoroacetic acid additive. Reaction proceed through the formation of nitrenium ion intermediate and subsequent aromatic electrophilic substitution reaction.[44]



Scheme 1.20 Organocatalytic indazole synthesis.

1.10.4.2 INTERMOLECULAR C(sp^2)-N BOND FORMATION

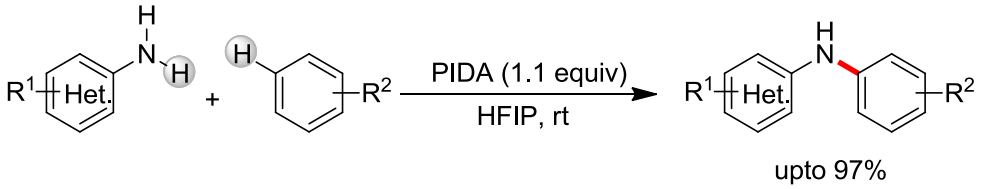
Chang and co-workers reported an intermolecular dehydrogenative coupling reaction between arene and phthalimide by using phenyliodine diacetate (PIDA) at high temperature conditions (Scheme 1.21). The arene molecule acted as C-H coupling substrate as well as solvent for the oxidative C(sp^2)-N bond formation reaction. The transformation starts with the interaction between phthalimide and $PhI(OAc)_2$ to furnish N-iodo(III)-amino complex. Then nucleophilic attack of arene at the iodoimido species afford the C-H imidated product with the elimination of iodobenzene and acetic acid.[45]



Scheme 1.21 Chang's dehydrogenative *N*-arylation approach.

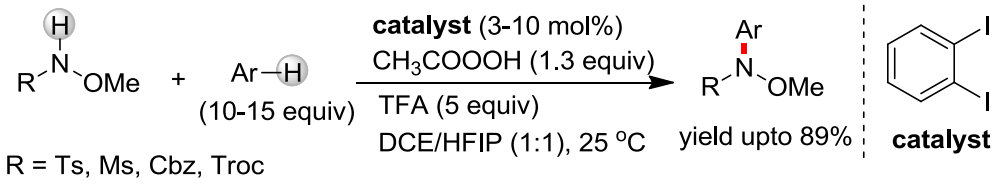
Manna *et. al.*, described a dehydrogenative coupling process between heteroaromatic amines and non-prefunctionalized arenes under hypervalent iodine(III) conditions (Scheme 1.22). Phenyliodine diacetate (PIDA) mediated stoichiometric as well as in-situ generated

organocatalytic conditions from iodobenzene was used for the amination reaction. The reaction proceed through the formation of nitrenium ion intermediate which was stabilized by polar non-nucleophilic solvent like HFIP. The transformation is highly practical because of the diverseness of substrates and ready availability of starting materials.[46]



Scheme 1.22 Antonchick's *N*-arylation approach of heteroaniline.

Very recently, Muniz and co-workers have developed a new catalyst for highly regioselective direct C-H amination of arenes (Scheme 1.23). The catalyst is derived from the oxidation of 1,2-diiodobenzene with peracetic acid. The key of the intermolecular dehydrogenative C-N coupling protocol is the strained µ-oxo-bridged conformation of the bisiodine(III) catalyst.[47]

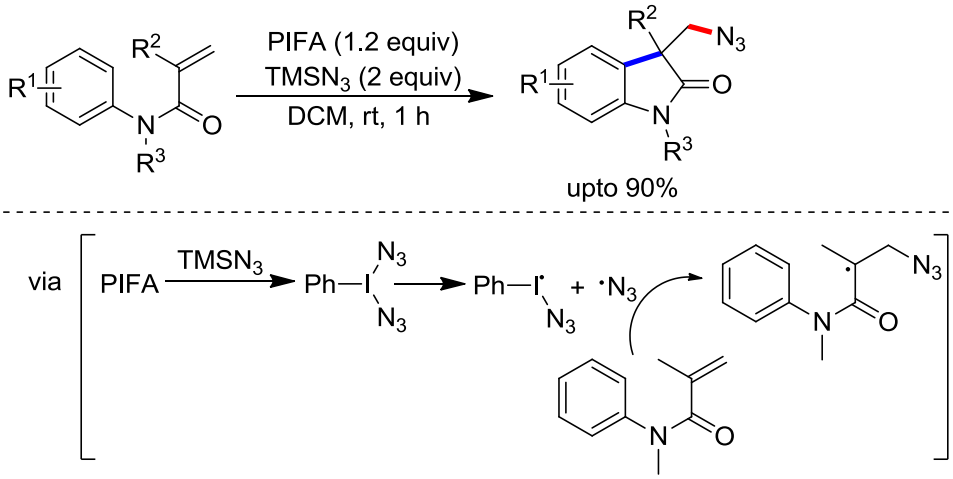


Scheme 1.23 Muniz's N-arylation approach of amide.

1.10.5 NON-DEHYDROGENATIVE C-N BOND FORMATION

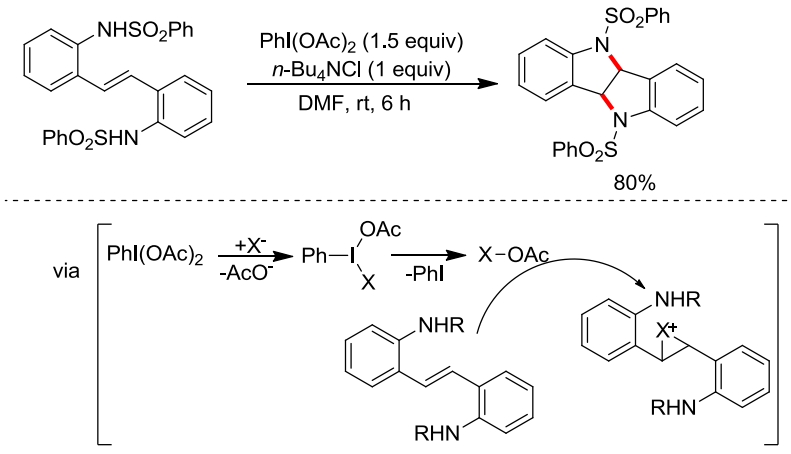
Antonchick and co-workers described the development of functionalization of alkenes by the addition of azide under hypervalent iodine(III) conditions (Scheme 1.24). Use of reagent combination of PIFA and TMSBr provided azidoarylation products by cascade C-N and C-C bond forming reactions. The reaction starts with double ligand exchange between PIFA and

TMSBr to provide diazidoiodonium species which undergoes thermal homolytic cleavage to generate azide radical intermediate. The azide radical attack the alkene to form C(sp^3)-N bond and further radical trap by arene provide oxindole products.[48]



Scheme 1.24 Antonchick's approach for azidoarylation.

Phenyliodine diacetate (PIDA) could be employed for the intramolecular diamination of olefins to furnish bisindoles (Scheme 1.25). Presence of halide additive was crucial for the generation of active hypohalite species with the help of PIDA. Electrophilic addition of olefin to hypohalite afford halonium intermediate. Now two consequent SN^2 displacement reactions lead to the formation of two C(sp^3)-N bonds.[49]



Scheme 1.25 PIDA enabled olefin difunctionalization.

1.11 Objective

The objective of this thesis has been to develop hypervalent iodine(III) enabled synthetic methodologies for:

- **Dehydrogenative C(sp^2)-N bond formation**

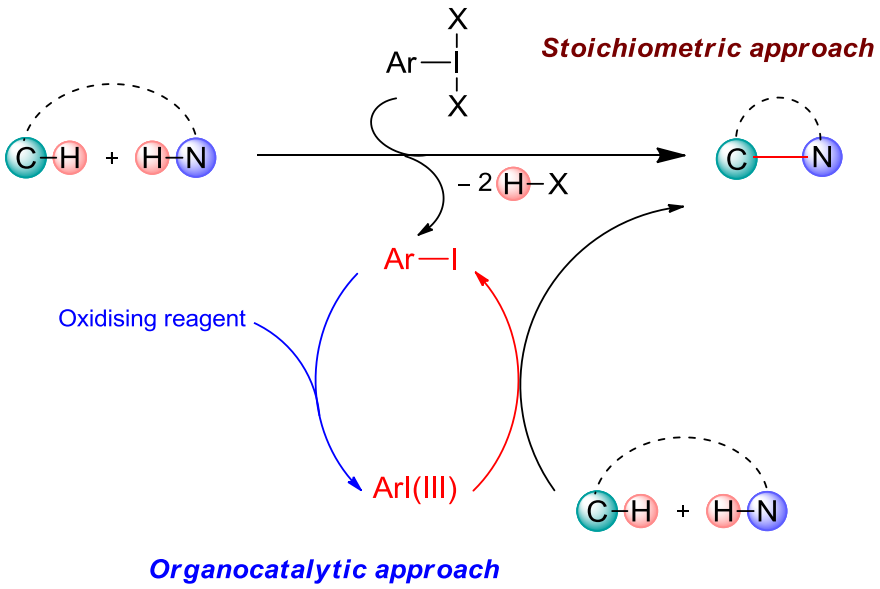


Figure 1.9 Strategy for dehydrogenative C(sp^2)-N bond formation..

- **Non-dehydrogenative C(sp^3)-N bond formation**

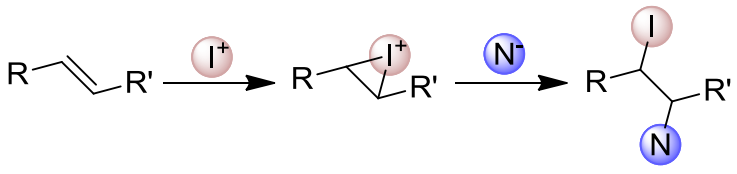


Figure 1.10 Strategy for non-dehydrogenative C(sp^3)-N bond formation..

1.12 Notes and References

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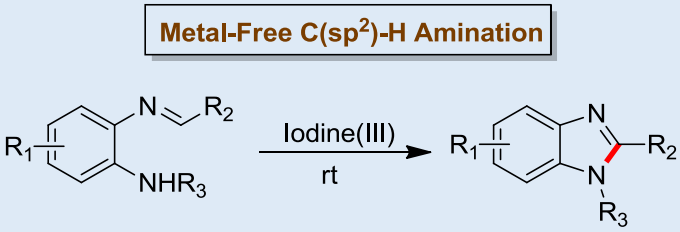
CHAPTER 2

Intramolecular C(sp^2)-H Amination for *N*-Substituted Benzimidazole Synthesis

2.1 ABSTRACT



Hypervalent iodine(III) reagent [phenyliodine diacetate (PIDA)]- mediated C(sp^2)-N bond formation reaction has been developed. The intramolecular dehydrogenative coupling methodology provides a direct access to 1, 2-disubstituted multifunctional benzimidazoles in good to excellent yields. The reactions were performed in the open air and at ambient temperature, and were found to be eco-friendly and atom-economical.

2.2 INTRODUCTION

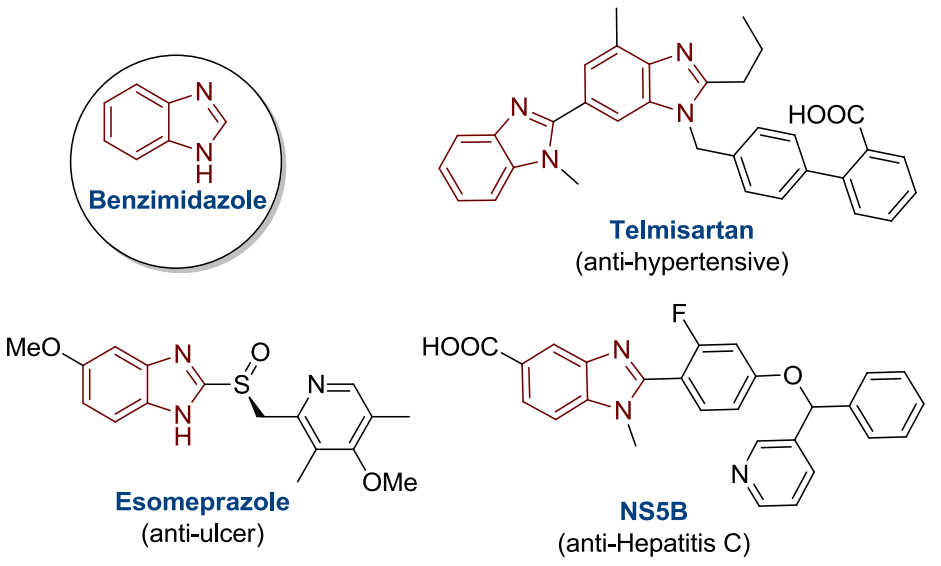
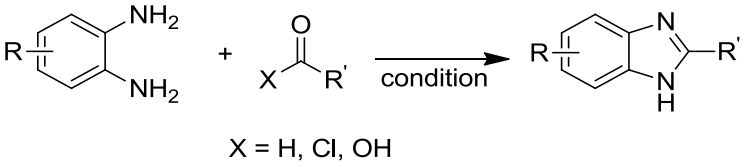


Figure 2.1 Benzimidazole containing drug molecules.

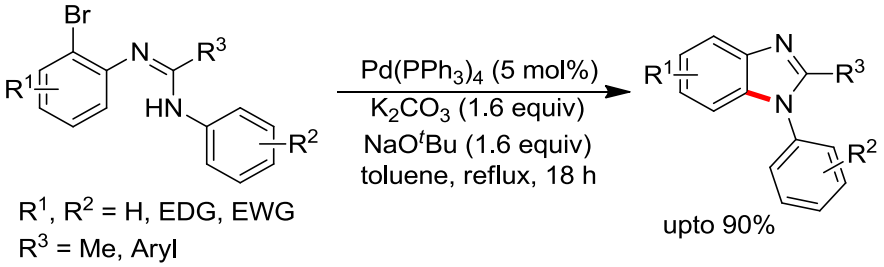
Benzimidazole core is an important class of heterocyclic system with wide range of application in pharmaceutical chemistry and material science.[1] These molecules are known to have anti-infective,[2] anti-hepatitis B,[3] anti-depressant,[4] anti-HIV,[5] anti-inflamatory,[6] anti-cancer[7] and anti-tumor[8] activity. They are also useful as synthetic intermediates for the preparation of dyes and polymers.[9] The benzimidazole core-containing drug esomeprazole (Nexium) was one of the best-selling drugs in 2009 (Figure 2.1).[10] N-substituted benzimidazole derivatives are as well prevalent in a large number of biologically active molecules (Figure 2.1). The wide range of application shown by benzimidazoles inspired chemists to pursue their synthesis in efficient and straightforward way.

The most traditional method for the synthesis of benzimidazole involves the condensation of 1, 2-phenylenediamine with carbonyl derivatives, followed by oxidation (Scheme 2.1).[11]



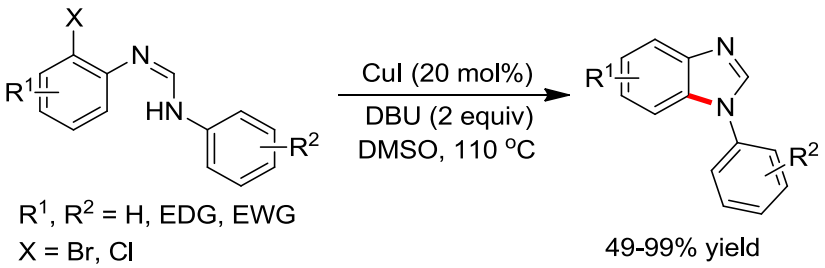
Scheme 2.1 Typical method for synthesis of NH-benzimidazole.

However, very limited methods are available for direct synthesis of *N*-substituted benzimidazoles. Some selected literature reports have been discussed herein. Brain *et. al.*, developed a palladium catalyzed intramolecular C(sp^2)-N bond formation protocol for the synthesis of *N*-substituted benzimidazoles from (o-bromophenyl)amidine precursors (Scheme 2.2). Both electron withdrawing and electron donating groups *para*- to the amidine bromo substituent were well tolerated. Similarly, amidines, which contained a methyl group *ortho* to the bromo substituent also cyclised successfully.[12]



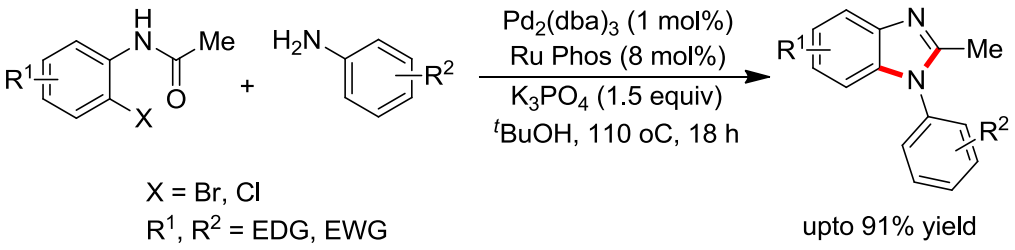
Scheme 2.2 Brain's Pd(II)-catalyzed C(sp^2)-N bond formation approach.

Glorious and co-workers developed an intramolecular *N*-arylation of formamidines for the synthesis of *N*-substituted benzimidazoles by using CuI as catalyst in presence of DBU at high temperature in DMSO solvent (Scheme 2.3).[13]



Scheme 2.3 Glorious's Cu(I)-catalyzed C(sp^2)-N bond formation approach.

Buchwald and co-workers established a Palladium catalyzed intermolecular tandem C(sp^2)-N bond formation reaction by the coupling between 2-haloacetaniolides and anilines for the synthesis of *N*-aryl benzimidazoles in regioisomerically pure form with good functional group tolerance (Scheme 2.4).[14]

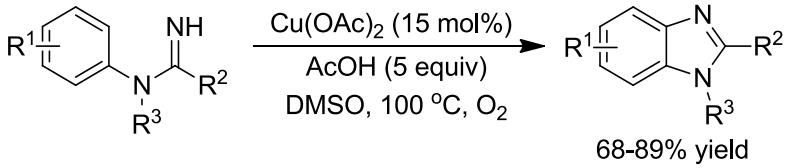


Scheme 2.4 Buchwald's Pd-catalyzed C(sp^2)-N bond formation approach.

Direct synthesis of *N*-substituted benzimidazoles *via* tandem C(sp^2)-N bond formation reaction was achieved by the reaction of imidoyl chlorides with primary amines catalyzed by CuI in presence of K_3PO_4 in DMF solvent under high temperature conditions (Scheme 2.5).[15]

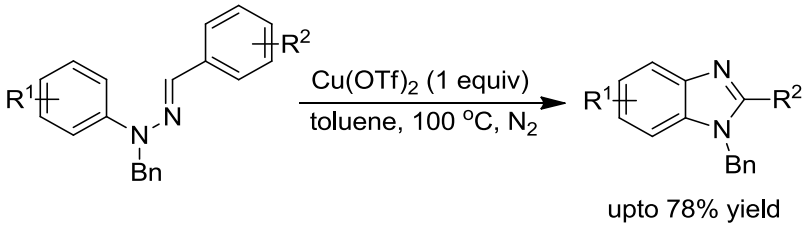
Scheme 2.5 Cu(I)-catalyzed tandem C(sp^2)-N bond formation approach.

Buchwald and co-workers have reported Cu-catalyzed dehydrogenative C(sp^2)-N bond formation method for the synthesis of *N*-substituted benzimidazole in good to excellent yields from amidines (Scheme 2.6).[16]



Scheme 2.6 Buchwald's Cu(II)-catalyzed C(sp^2)-N bond formation approach.

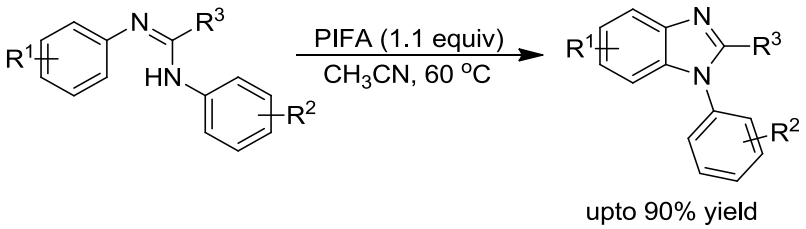
Guru *et. al.*, developed a method for the transformation of *N*-benzylbisarylhydrazones to 2-aryl-*N*-benzylbenzimidazoles by using Cu(II) mediated C-H functionalization and followed by C-N bond formation strategy (Scheme 2.7).[17]



Scheme 2.7 Punniyamurthy's Cu(II) mediated rearrangement approach.

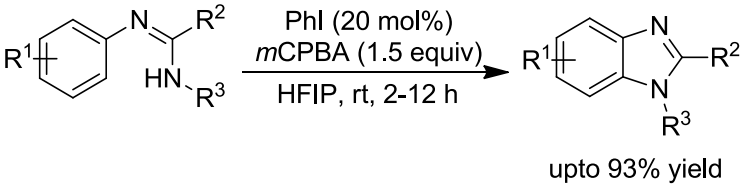
Hypervalent iodine(III) reagent [bis(trifluoroacetoxy)-iodo]benzene (PIFA) mediated intramolecular dehydrogenative C(sp^2)-N bond formation reaction of *N,N′*-disubstituted

ethanimidamides has been developed by Wu and co-workers for the synthesis of *N*-substituted benzimidazoles in metal-free mild conditions (Scheme 2.8). The reaction proceeds through the generation of nitrenium ion intermediate.[18]



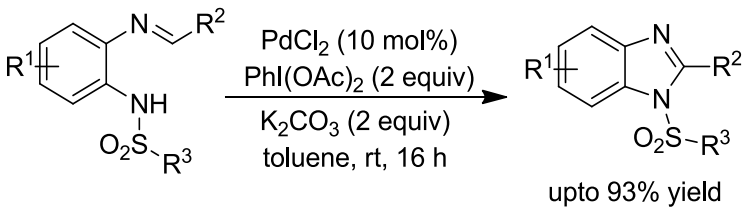
Scheme 2.8 Iodine(III) mediated C(sp^2)-N bond formation approach.

Later, the similar transformation has been established by Punniyamurthy and co-workers by using *in situ* generated hypervalent iodine(III) reagent from catalytic amount of iodobenzene in presence of co-oxidant *meta*-chloroperbenzoic acid in fluorinated alcohol solvent (Scheme 2.9).[19]



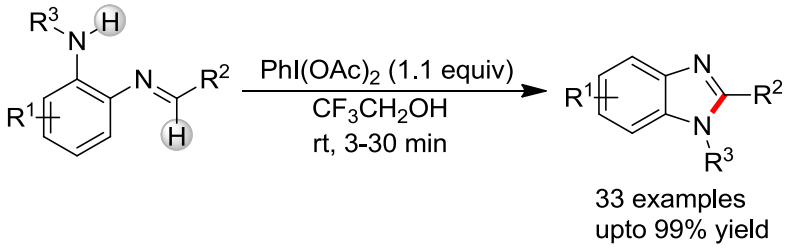
Scheme 2.9 *In situ* iodine(III) mediated C(sp^2)-N bond formation approach.

Zeng and co-workers developed a Pd(II)-catalyzed intramolecular sulfoamidation/oxidation method for the transformation of *o*-sulfonamidophenyldiamines to 1,2-disubstituted benzimidazoles in presence of $PhI(OAc)_2$ and K_2CO_3 at room temperature conditions in toluene solvent (Scheme 2.10). Mechanistically the role of $PhI(OAc)_2$ is to oxidize Pd(II) to Pd(IV) which coordinate with the imine nitrogen and activate the imine carbon, which further undergoes an intramolecular nucleophilic attack by sulphonamide nitrogen and followed by protonation/oxidation-dehydrogenation.[20]



Scheme 2.10 Pd(II)-catalyzed oxidative amidation approach.

However, we have established that neither expensive Pd-catalyst nor any base is required for similar transformation for the synthesis of *N*-substituted benzimidazole from *o*-sulfonamidophenyldiamines. We have developed a absolutely metal-free intramolecular dehydrogenative C(sp^2)-N bond formation protocol by using hypervalent iodine(III) reagent phenyliodine diacetate (PIDA) as sole oxidant for the synthesis of 1,2-disubstituted benzimidazoles in 2,2,2-trifluoroethanol solvent at room temperature under aerobic conditions (Scheme 2.11).[21] The method is an example of metal-free dehydrogenative C(sp^2)-N bond construction via C(sp^2)-H bond functionalization using hypervalent iodine(III) reagents.

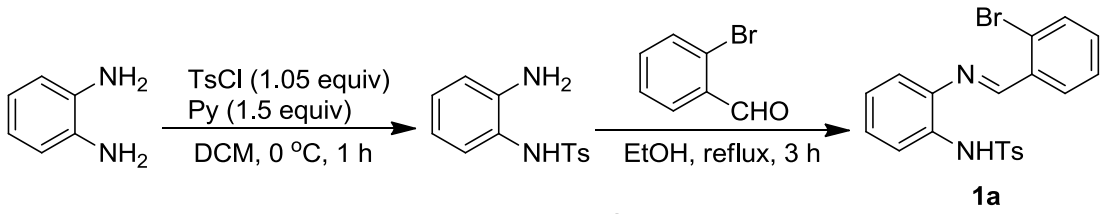


Scheme 2.11 Our metal-free approach using hypervalent iodine(III).

2.3 RESULTS AND DISCUSSIONS

To optimize the reaction conditions, (*E*)-*N*-{2-[(2-bromobenzylidene)amino]phenyl}-4-methylbenzene-sulfonamide (**1a**) was used as a model substrate. Substrate **1a** was prepared following a previous literature report as shown in Scheme 2.12.[20] The most appropriate conditions

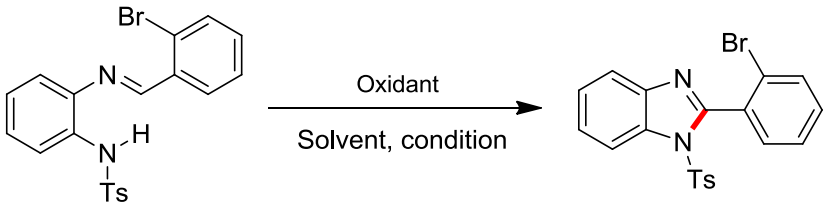
were identified when the reaction was performed for **1a** (0.2 M in TFE) using PIDA (1.1 equiv) in TFE. The product



Scheme 2.12 Preparation of (*E*)-*N*-{2-[(2-bromobenzylidene)amino]phenyl}-4-methylbenzene-sulfonamide (**1a**).

2-(2-bromophenyl)-1-tosylbenzo[d]imidazole (**2a**) was isolated in quantitative (>98%) yield within 5 min at room temperature (Table 2.1, entry 16). PIDA is also recognized as a superior oxidant to the following oxidants: PhI (phenyliodide)–*m*CPBA (*meta*-chloroperbenzoic acid) (entries 3-5), oxone ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$) (entries7 and 8), PIFA [phenyliodine bis(trifluoroacetate)] (entry 12), PhI-oxone (entry 17), PhI-hydrogen peroxide (entry 18), etc. Subsequently, TFE was found to be a more appropriate solvent than HFIP (1,1,1,3,3,3-hexafluoro-2-propanol) (entry 1), TFA (trifluoroacetic acid) (entry 2), acetonitrile (entry 9), ethyl acetate (entry 10), methanol (entry 11) and DCM (dichloromethane) (entry 15). However, no product was obtained with solvents such as DMF (dimethylformamide) (entry 13) and DMSO (dimethyl sulfoxide) (entry 14). The reaction was performed under solvent-free ball milling conditions[22] which did not render a favourable result. As anticipated, TFE, which is polar and non-nucleophilic in nature, appears to be the most suitable solvent for the reaction.[23]

Table 2.1 Optimization for reaction conditions



1a **2a**

entry	oxidant	solvent	time (h)	yield(%)
1	PIDA	HFIP	6 h	64
2	PIDA	AcOH	6 h	70
3	PhI-*m*CPBA	HFIP	8 h	44
4	PhI-*m*CPBA	TFE	8 h	53
5	PhI-*m*CPBA	Solvent free[a]	6 h	31
6	*m*CPBA	DCM	12 h	0
7	Oxone	CH_3CN	12 h	0
8	Oxone	H_2O	12 h	0
9	PIDA	CH_3CN	12 h	11
10	PIDA	EtOEt	12 h	18
11	PIDA	MeOH	12 h	60
12	PIFA	TFE	15 min	50
13	PIDA	DMF	12 h	0
14	PIDA	DMSO	12 h	0
15	PIDA	DCM	30 min	91
16	PIDA	TFE	5 min	>98
17	PhI-Oxone	CH_3CN-H_2O	12 h	0
18	PhI-H_2O_2	TFE	12 h	0

[a] Reactions was performed under solvent-free ball milling conditions.

Furthermore, we focused on the exploration of the scope and generality of the intramolecular dehydrogenative amination method. A wide-ranging 1,2-disubstituted benzimidazole derivatives were isolated in very good to excellent yields (Figure 2.2). A few examples of substitutions at the 2-position of benzimidazole are tolyl (**2b**), 4-fluorophenyl (**2e**), 3,5-dicyanomesityl (**2g**), anisyl (**2h**), perfluorophenyl (**2m**), anthryl (**2o**), pyridyl (**2p**), pyrenyl (**2r**), 3-quinolinyl (**2s**) and 5-nitrofurfuryl (**2t**). The proposed methodology for the synthesis of benzimidazole derivatives with various aromatic systems at 2- position was found to be efficient and convenient. Benzimidazole derivatives with different aliphatic substituents at 2-position were also isolated with quite good yield applying our protocol (Figure 2.3a).

The scope of substrates for this methodology was further extended to different substituents on core benzene ring of benzimidazole (Figure 2.3b). Good yields were obtained for carboxylic acid (**2bb**), naphthalene (**2bc**) and *ortho*-xylyl (**2be**) derivatives. Conversely, nitro (**2ba**) and dichloro (**2bf**) derivatives gave very poor yields. Likewise, substitution at the 1-position or N(sp^3) of benzimidazole was also performed (Figure 2.3c). Products from benzenesulfonyl- (**2ca** and **2cb**) and benzoyl-substituted benzimidazole derivatives (**2cc**) were successfully isolated with good yields. In all the cases, the reactions were completed within 30 min.

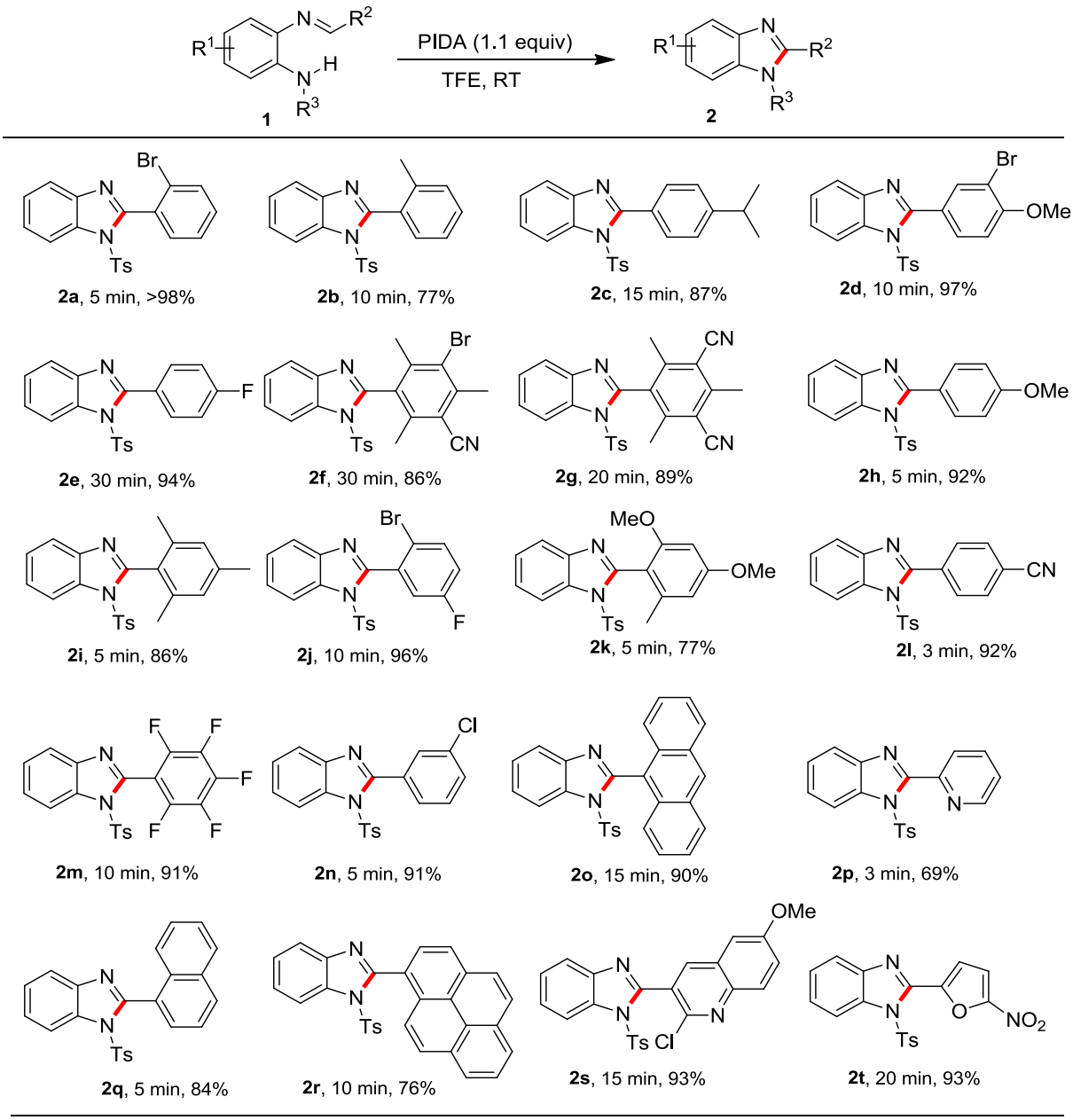


Figure 2.2 Scope of intramolecular dehydrogenative amination reaction.

X-ray crystal structure investigations were carried out for the synthesized benzimidazole **2a** and **2aa**. Good-quality crystals were obtained after slow evaporation of the solvent from an ethyl acetate solution. The structures of compounds **2a** and **2aa** are shown in Figure 2.5.

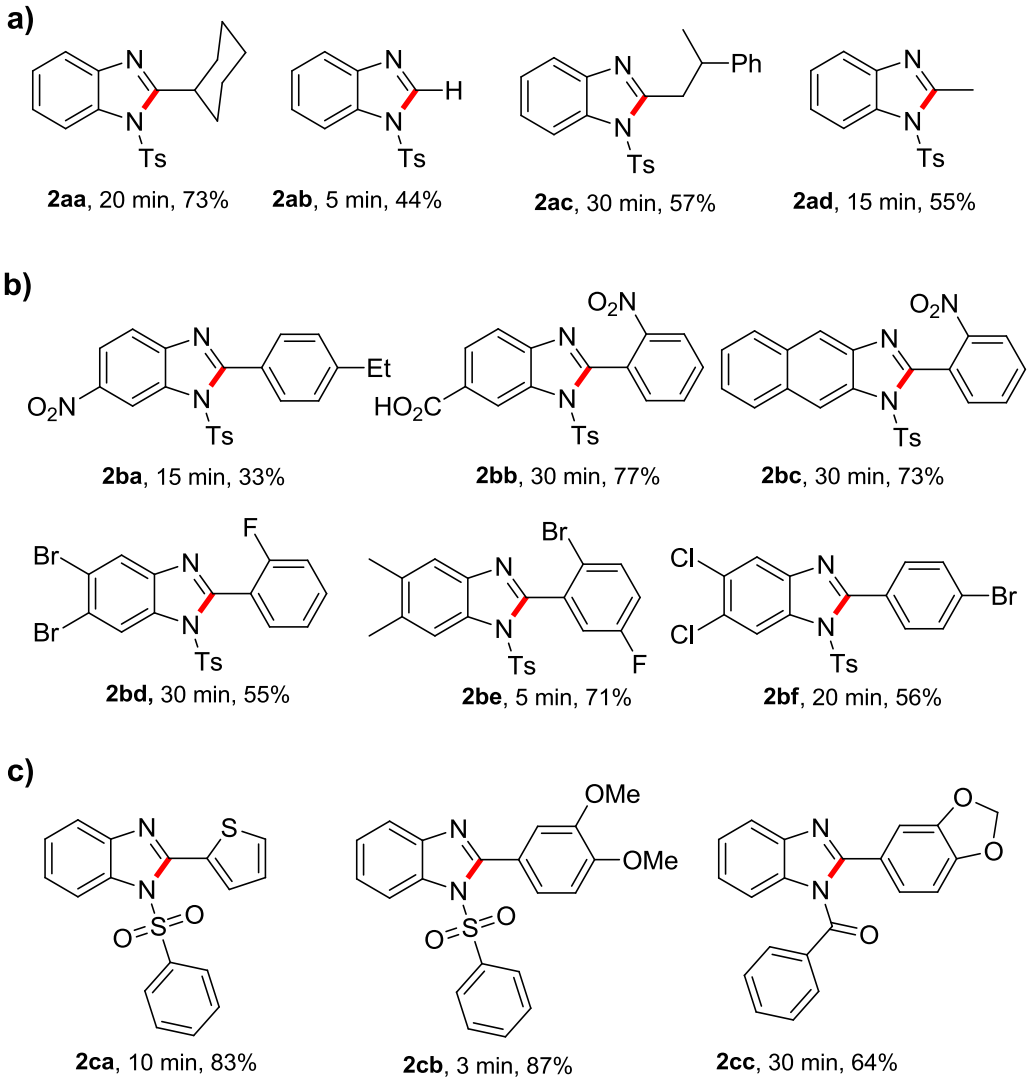


Figure 2.3 Functional group tolerance of amination reaction.

A plausible mechanism for the dehydrogenative C(sp^2)-H amination reaction is described in Figure 2.4. Two possible pathways (path A or path B) were initially rationalized. In path A, the N(sp^3) of the amide unit was expected to coordinate with the iodine atom of hypervalent iodine(III) reagent PIDA. This causes loss of one molecule of acetic acid and intermediate **3** was generated.[24] However, in path B, we assumed that the nitrenium ion intermediate **4** was formed via coordination of the imine N(sp^2) and iodonium ion (from PIDA).[25] Subsequently, **5** was generated from either **3** or **4**. Finally, the acetate anion could abstract one proton from **5** to yield **2**. In path A their must be a nucleophilic attack from the imine bond to the electron deficient nitrenium centre for the ring

construction. Whereas, in path B for the transformation of **4** to **5**, the expected reaction was as follows: three-membered ring opening after nucleophilic attack by amide N atom, followed by reductive elimination of iodobenzene. We assume that the reaction follows path B for cyclization considering that nucleophilic attack from electrophilic carbon centre of imine bond is unlikely to expect.

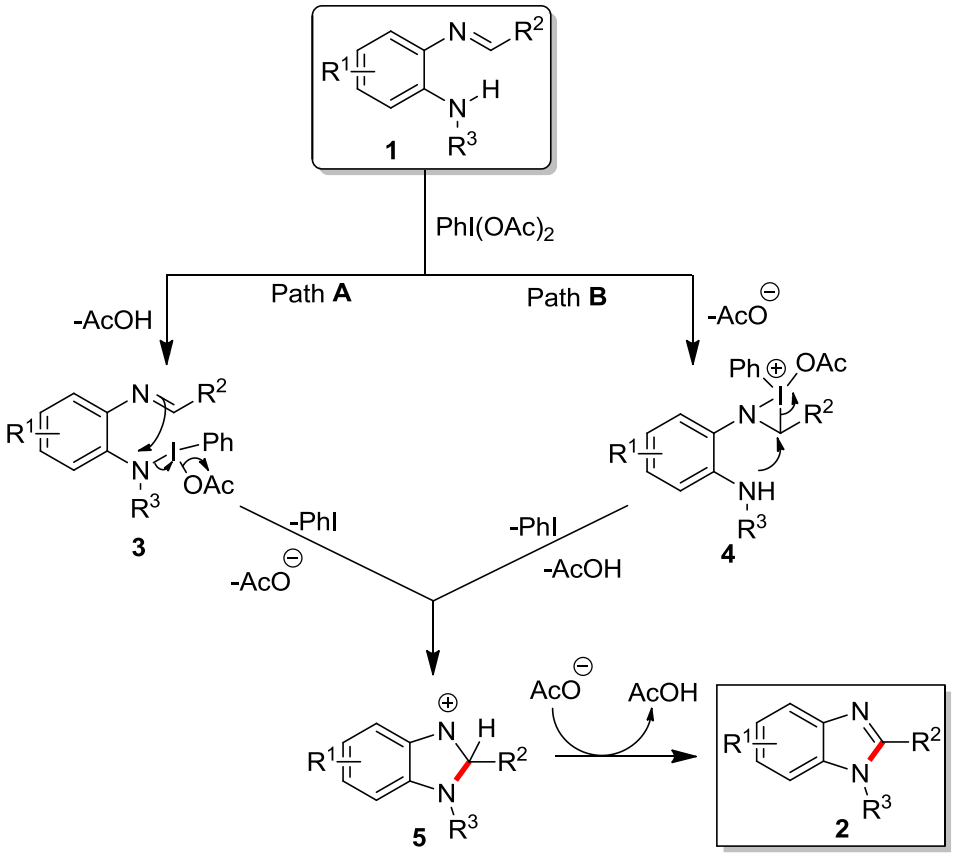
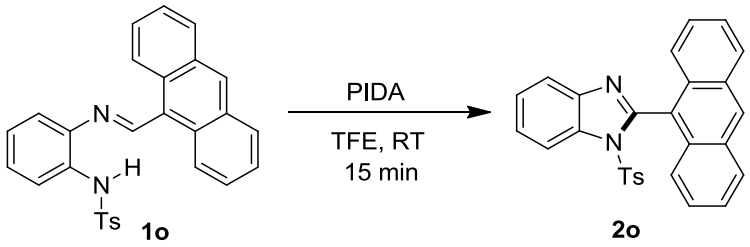


Figure 2.4 Possible reaction mechanism for benzimidazole ring formation.

Furthermore, we confirmed that the presence of Pd catalyst was not necessary for the transformation. Inductively coupled plasma optical emission spectrometry (ICP-OES) analysis was performed for both TFE (solvent) and oxidant PIDA (Table 2.2). The yield and reaction time were standardized for the conversion of **1o** to **2o** (Table 2.2). No Pd impurity was detected in either the TFE or PIDA synthesized by following the PhI-$NaBO_3$-AcOH method.[26] However, some of the PIDA samples had trace amounts (ca. 0.1–1.2 ppm) of a Pd impurity (Table 2.2). Interestingly,

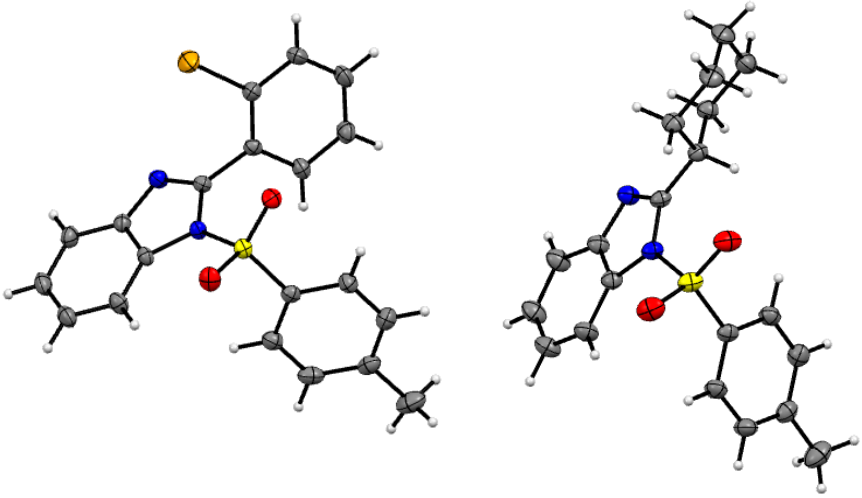
the efficiency of the reaction was unaffected by using PIDA with no Pd (entry 5), by trace Pd impurities (entries 1-4) and in the presence of 500 ppm of externally added Pd (entry 6).

Table 2.2 Standardization of metal-free conditions.



entry	PIDA	Pd (ppm)	Yield(%)
1	**A** (Sigma-Aldrich (98%)	1.2	90
2	**A** and then recrystalization	< 0.1	90
3	PhI-$K_2S_2O_8$-AcOH[27]	0.13	90
4	PhI-MCPBA-AcOH[28]	< 0.1	90
5	PhI-$NaBO_3$-AcOH[26]	0	90
6	**A** + 500 ppm Pd[a]	~500	90

[a] $Pd(OAc)_2$ was added externally before the reaction.



2a (CCDC No. 1032667) **2aa** (CCDC No. 1032666)

Figure 2.5 X-ray structures of compound **2a** and **2aa**.

2.4 CONCLUSIONS

In summary, we have developed a metal-free mild and efficient intramolecular dehydrogenative method for the synthesis of 1,2-disubstituted benzimidazoles. This methodology was found to be well-suited with an extensive range of functional groups and requires easily accessible starting materials. The coupling reaction is a representative demonstration of hypervalent iodine(III) mediated C(sp^2)-H amination. Additionally, performing the reactions in the open atmosphere and at room temperature over shorter reaction times using metal-free conditions may be considered as an example of eco-friendly methodology. This methodology could also be useful in constructing a library of benzimidazoles under metal-free conditions, which would be desirable for medicinal/pharmaceutical chemistry and drug discovery efforts.

2.5 EXPERIMENTAL SECTION

General Methods. Column chromatographic purifications of the synthesized compounds were performed using silica gel (mesh 100–200) and hexane-ethyl acetate mixtures as eluent, unless otherwise specified. NMR spectra were recorded on a 400 MHz instrument at 25 °C. The chemical shift values are reported in parts per million (ppm) with respect to residual chloroform (7.26 ppm for ^{1}H and 77.16 for ^{13}C). High-resolution mass spectra (HR-MS) were recorded on an ESI-TOF (time of flight) mass spectrometer. Infrared spectral data are reported in wave number (cm^{-1}). Melting points of the compounds were determined using a digital melting point apparatus and are uncorrected. X-Ray diffraction data for single crystals of **2a** and **2aa** were collected using a CCD diffractometer equipped with an APEX II detector with graphite-monochromatized Mo-Kα (λ = 0.71073 Å) radiation at 300 K. The structures were solved by direct method using SHELLX-97. FT-IR spectra were recorded after making thin layer of the compounds on the surface of NaCl crystal using dichloromethane. Inductively coupled plasma optical emission spectrometry (ICP-OES) analyses were performed on a Perkin–Elmer Optima 2100 DV instrument.

General procedure for preparation of *N*-substituted benzimidazole: To the solution of imine **1** (0.5 mmol, 1.0 equiv) in TFE (0.5 mL) was added PIDA (0.55 mmol, 1.1 equiv) under open atmosphere. The reaction mixture was stirred at room temperature (27 °C). The progress of the reaction was monitored by TLC using ethyl acetate and hexane as eluent. After complete consumption of the reactant the resulting solution was evaporated to dryness. The resulting residue was purified on silica gel column chromatography using *n*-hexane and ethyl acetate as eluent.

Procedure for preparation of 2-(2-bromophenyl)-1-tosylbenzo[d]imidazole (2a). To a stirred solution of (*E*)-*N*-(2-((2-bromobenzylidene)amino)phenyl)-4-methylbenzenesulfonamide **1a** (0.5 mmol, 1.0 equiv) in TFE (0.5 mL) was added PIDA (0.55 mmol, 1.1 equiv) at room temperature. The progress of the reaction was monitored by TLC using ethyl acetate and hexane as eluent. After complete consumption of the reactant the resulting solution was evaporated to dryness. The resulting residue was purified on silica gel column chromatography using *n*-hexane and ethyl acetate as eluent to isolate 2-(2-bromophenyl)-1-tosylbenzo[d]imidazole (**2a**) in quantitative yield.

Compound characterization data

2-(2-Bromophenyl)-1-tosylbenzo[d]imidazole (2a). Yield quantitative; R_f = 0.5 (hexane : ethyl acetate 4:1); white solid; mp 154-156 °C (no literature report on melting points); IR (KBr) $\tilde{\nu}$ = 2923, 2363, 1647, 1447, 1381, 1307, 1283, 1251, 1189, 1177, 1126, 1087, 1047 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8 Hz, 1H), 7.79 (d, *J* = 8 Hz, 1H), 7.66 (d, *J* = 8 Hz, 1H), 7.54 (d, *J* = 8 Hz, 2H), 7.49-7.39 (m, 5H), 7.20 (d, *J* = 8 Hz, 2H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.7, 146.1, 142.2, 135.1, 132.8, 132.6, 132.5, 132.1, 131.7, 130.0, 127.6, 126.5, 125.8, 125.1, 124.8, 120.9, 114.3, 21.8; HRMS (ESI-TOF) calculated for $C_{20}H_{15}SN_2O_2Br$ ($M + H^+$) 427.0110, found 427.0129.

2-(o-Tolyl)-1-tosylbenzo[d]imidazole (2b). Yield 77%; R_f = 0.5 (hexane : ethyl acetate 4:1); white solid; mp 132-134 °C; IR (KBr) $\tilde{\nu}$ = 3063, 2361, 1594, 1539, 1448, 1380, 1300, 1252, 1230,

1177, 1123, 1072 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8 Hz, 1H), 7.80 (d, *J* = 8 Hz, 1H), 7.52-7.43 (m, 5H), 7.31-7.28 (m, 2H), 7.23-7.18 (m, 3H), 2.41 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.5, 145.9, 142.4, 139.1, 135.4, 133.3, 130.8, 130.4, 130.0, 129.9, 129.8, 127.4, 125.5, 125.0, 124.9, 120.5, 114.5, 21.8, 20.0; HRMS (ESI-TOF) calculated for $C_{21}H_{18}N_2O_2S$ ($M + H^+$) 363.1162, found 363.1175.

2-(4-Isopropylphenyl)-1-tosylbenzo[d]imidazole (2c). Yield 87%; R_f = 0.5 (hexane : ethyl acetate 4:1); white solid; mp 135-137 °C; IR (KBr) $\tilde{\nu}$ = 2961, 2361, 1596, 1495, 1449, 1381, 1304, 1272, 1254, 1189, 1177, 1121, 1076, 1011 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8 Hz, 1H), 7.71 (d, *J* = 8 Hz, 1H), 7.54 (d, *J* = 12 Hz, 2H), 7.42-7.28 (m, 6H), 7.07 (d, *J* = 8 Hz, 2H), 3.01 (sept, *J* = 8 Hz, 1H), 2.32 (s, 3H), 1.32 (d, *J* = 8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 151.7, 145.6, 142.8, 135.1, 134.0, 131.0, 129.7, 127.9, 127.1, 125.9, 125.4, 125.3, 120.4, 115.3, 34.2, 24.0, 21.7; HRMS (ESI-TOF) calculated for $C_{23}H_{22}N_2O_2S$ ($M + H^+$) 391.1475, found 391.1486.

2-(3-Bromo-4-methoxyphenyl)-1-tosylbenzo[d]imidazole (2d). Yield 97%; R_f = 0.4 (hexane : ethyl acetate 4:1); white solid; mp 146-148 °C; IR (KBr) $\tilde{\nu}$ = 2938, 2361, 1609, 1597, 1485, 1450, 1380, 1293, 1269, 1189, 1177, 1121, 1083, 1053, 1015 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8 Hz, 1H), 7.71 (d, *J* = 7.3 Hz, 1H), 7.68-7.63 (m, 2H), 7.46-7.36 (m, 2H), 7.33 (d, *J* = 8 Hz, 2H), 7.13 (d, *J* = 8 Hz, 2H), 7.00 (d, *J* = 8 Hz, 1H), 4.00 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.7, 152.6, 146.0, 142.6, 135.3, 135.0, 134.0, 131.9, 129.9, 127.0, 125.6, 125.5, 123.5, 120.4, 115.3, 110.9, 110.8, 56.5, 21.7; HRMS (ESI-TOF) calculated for $C_{21}H_{17}BrN_2O_3S$ ($M + H^+$) 457.0216, found 457.0199.

2-(4-Fluorophenyl)-1-tosylbenzo[d]imidazole (2e). Yield 94%; R_f = 0.5 (hexane : ethyl acetate 4:1); white solid; mp 118-120 °C; IR (KBr) $\tilde{\nu}$ = 2923, 2364, 1596, 1494, 1450, 1305, 1272, 1229, 1190, 1177, 1159, 1122, 1074, 1012 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8 Hz, 1H),

7.72 (d, J = 8 Hz, 1H), 7.62 (dd, J_1 = 8 Hz, J_2 = 4 Hz, 2H), 7.46-7.38 (m, 2H), 7.32 (d, J = 12 Hz, 2H), 7.18-7.10 (m, 4H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3 (d, $^1J_{CF}$ = 249.9 Hz), 153.2, 146.0, 142.7, 135.0, 134.0, 132.7 (d, $^3J_{CF}$ = 8.7 Hz), 129.9, 127.0, 126.2 (d, $^4J_{CF}$ = 3.4 Hz), 125.7, 125.5, 120.5, 115.3, 115.1 (d, $^2J_{CF}$ = 21.8 Hz), 21.7; HRMS (ESI-TOF) calculated for $C_{20}H_{15}N_2O_2SF$ (M + H^+) 367.0911, found 367.0904.

3-Bromo-2,4,6-trimethyl-5-(1-tosylbenzo[d]imidazol-2-yl)benzonitrile (2f). Yield 86%; R_f = 0.5 (hexane : ethyl acetate 4:1); white solid; mp 195-197 °C; IR (KBr) $\tilde{\nu}$ = 2923, 2361, 2219, 1592, 1447, 1385, 1265, 1250, 1177, 1147, 1089, 1048, 1000 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, J = 8 Hz, 1H), 7.82 (d, J = 8 Hz, 1H), 7.55 (t, J = 7.4 Hz, 1H), 7.51-7.46 (m, 3H), 7.29 (d, J = 4 Hz, 2H), 2.81 (s, 3H), 2.46 (s, 3H), 1.92 (s, 3H), 1.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.9, 146.8, 144.6, 143.9, 142.0, 134.9, 132.9, 130.2, 130.1, 127.6, 126.1, 125.9, 125.2, 120.9, 116.7, 114.2, 112.9, 23.6, 23.1, 21.9, 19.4; HRMS (ESI-TOF) calculated for $C_{24}H_{20}N_3O_2SBr$ (M + H^+) 494.0532, found 494.0531.

2,4,6-Trimethyl-5-(1-tosylbenzo[d]imidazol-2-yl)isophthalonitrile (2g). Yield 89%; R_f = 0.5 (hexane : ethyl acetate 4:1); white solid; mp 214-216 °C; IR (KBr) $\tilde{\nu}$ = 2923, 2360, 2224, 1447, 1384, 1316, 1253, 1173, 1121, 1089, 1050, 814, 749 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 8 Hz, 1H), 7.80 (d, J = 8 Hz, 1H), 7.55 (t, J = 7.5 Hz, 1H), 7.50-7.45 (m, 3H), 7.27 (d, J = 8 Hz, 1H), 2.87 (s, 3H), 2.44 (s, 3H), 2.03 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 147.8, 147.3, 147.2, 142.1, 134.8, 132.9, 130.7, 130.3, 127.4, 126.4, 125.4, 121.0, 115.4, 114.2, 113.5, 21.9, 20.6, 20.1; HRMS (ESI-TOF) calculated for $C_{25}H_{20}N_4O_2S$ (M + H^+) 441.1380, found 441.1423.

2-(4-Methoxyphenyl)-1-tosylbenzo[d]imidazole (2h). Yield 92%; R_f = 0.5 (hexane : ethyl acetate 4:1); white solid; mp 113-116 °C; IR (KBr) $\tilde{\nu}$ = 2942, 2555, 2226, 1579, 1543, 1495, 1450, 1380, 1336, 1304, 1273, 1227, 1152, 1075, 1029 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8 Hz,

1H), 7.69 (d, *J* = 8 Hz, 1H), 7.59 (d, *J* = 8 Hz, 2H), 7.43-7.34 (m, 2H), 7.30 (d, *J* = 8 Hz, 2H), 7.07 (d, *J* = 8 Hz, 2H), 6.98 (d, *J* = 8 Hz, 2H), 3.89 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 154.4, 145.6, 142.8, 135.0, 134.0, 132.6, 129.7, 127.0, 125.3, 125.2, 122.2, 120.2, 115.4, 113.2, 55.4, 21.6; HRMS (ESI-TOF) calculated for $C_{21}H_{18}N_2O_3S$ ($M + H^+$) 379.1111, found 379.1132.

2-Mesityl-1-tosylbenzo[d]imidazole (2i). Yield 86%; R_f = 0.6 (hexane : ethyl acetate 4:1); white solid; mp 145-147 °C; IR (KBr) $\tilde{\nu}$ = 2918, 2361, 1594, 1541, 1449, 1383, 1252, 1228, 1190, 1178, 1121, 1091, 1066, 1013 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8 Hz, 1H), 7.77 (d, *J* = 8 Hz, 1H), 7.48-7.41 (m, 4H), 7.18 (d, *J* = 8 Hz, 2H), 6.88 (s, 2H), 2.39 (s, 3H), 2.37 (s, 3H) 1.76 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 146.0, 142.3, 139.9, 138.8, 135.3, 133.2, 129.8, 127.9, 127.8, 126.9, 125.2, 124.6, 120.5, 114.2, 21.8, 21.5, 20.0; HRMS (ESI-TOF) calculated for $C_{23}H_{22}N_2O_2S$ ($M + H^+$) 391.1475, found 391.1484.

2-(2-Bromo-5-fluorophenyl)-1-tosylbenzo[d]imidazole (2j). Yield 96%; R_f = 0.5 (hexane : ethyl acetate 4:1); white solid; mp 94-96 °C; IR (KBr) $\tilde{\nu}$ = 3063, 2361, 1596, 1578, 1542, 1463, 1448, 1384, 1308, 1288, 1245, 1188, 1175, 1127, 1088, 1045, 1022 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8 Hz, 1H), 7.82 (d, *J* = 8 Hz, 1H), 7.66-7.60 (m, 3H), 7.52-7.43 (m, 2H), 7.24-7.20 (m, 2H), 7.19-7.12 (m, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9 (d, $^1J_{CF}$ = 247.1 Hz), 149.4, 146.4, 142.1, 135.0, 134.0 (d, $^3J_{CF}$ = 8 Hz), 133.7 (d, $^3J_{CF}$ = 8.4 Hz), 132.7, 130.1, 127.4, 126.0, 125.2, 120.9, 119.7 (d, $^2J_{CF}$ = 24 Hz), 119.3 (d, $^4J_{CF}$ = 3.6 Hz), 119.0 (d, $^2J_{CF}$ = 22 Hz), 114.2, 21.7; HRMS (ESI-TOF) calculated for $C_{20}H_{14}N_2O_2SBrF$ ($M + H^+$) 445.0016, found 445.0021.

2-(2,4-Dimethoxy-6-methylphenyl)-1-tosylbenzo[d]imidazole (2k). Yield 77%; R_f = 0.4 (hexane : ethyl acetate 7:3); white solid; mp 178-180 °C; IR (KBr) $\tilde{\nu}$ = 2964, 2363, 1611, 1450, 1379, 1337, 1298, 1253, 1230, 1202, 1189, 1176, 1159, 1092, 1079 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$)

δ 8.17 (d, *J* = 8 Hz, 1H), 7.77 (d, *J* = 4 Hz, 1H), 7.52 (d, *J* = 8 Hz, 2H), 7.42-7.38 (m, 2H), 7.18 (d, *J* = 8 Hz, 2H), 6.40 (s, 1H), 6.27 (s, 1H), 3.87 (s, 3H), 3.44 (s, 3H), 2.37 (s, 3H), 1.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 159.9, 149.7, 145.4, 142.6, 141.7, 135.7, 133.4, 129.6, 127.6, 125.0, 124.4, 120.5, 114.1, 112.0, 106.1, 95.5, 55.4, 55.2, 21.7, 20.2; HRMS (ESI-TOF) calculated for $C_{23}H_{22}N_2O_4S$ ($M + H^+$) 423.1373, found 423.1367.

4-(1-Tosylbenzo[d]imidazol-2-yl)benzonitrile (2l). Yield 92%; R_f = 0.4 (hexane : ethyl acetate 4:1); white solid; mp 146-148 °C; IR (KBr) $\tilde{\nu}$ = 2918, 2356, 2229, 1596, 1492, 1448, 1382, 1306, 1274, 1253, 1190, 1176, 1122, 1080, 1012 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8 Hz, 1H), 7.77-7.73 (m, 5H), 7.50-7.40 (m, 2H), 7.34 (d, *J* = 8 Hz, 2H), 7.13 (d, *J* = 8 Hz, 2H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 146.3, 142.7, 134.8, 134.6, 133.9, 131.6, 131.5, 130.0, 126.9, 126.3, 125.8, 120.8, 118.3, 115.2, 114.3, 21.7; HRMS (ESI-TOF) calculated for $C_{21}H_{15}N_3O_2S$ ($M + H^+$) 374.0958, found 374.0964.

2-(Perfluorophenyl)-1-tosylbenzo[d]imidazole (2m). Yield 91%; R_f = 0.6 (hexane : ethyl acetate 4:1); white solid; mp 103-105 °C; IR (KBr) $\tilde{\nu}$ = 2924, 2360, 1594, 1505, 1449, 1386, 1337, 1242, 1190, 1177, 1123, 1088, 1043, 993 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8 Hz, 1H), 7.81 (d, *J* = 8 Hz, 1H), 7.62 (d, *J* = 8 Hz, 2H), 7.52-7.42 (m, 2H), 7.27 (d, *J* = 8 Hz, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.0 (m), 146.8, 144.4 (m), 142.7, 141.9 (m), 138.6 (m), 136.4 (m), 134.5, 132.9, 130.3, 127.1, 126.7, 125.5, 121.3, 114.1, 106.9 (m), 21.7; HRMS (ESI-TOF) calculated for $C_{20}H_{11}N_2O_2SF_5$ ($M + H^+$) 439.0534, found 439.0537.

2-(3-Chlorophenyl)-1-tosylbenzo[d]imidazole (2n). Yield 91%; R_f = 0.7 (hexane : ethyl acetate 4:1); white solid; mp 100-101 °C; IR (KBr) $\tilde{\nu}$ = 2922, 2360, 1594, 1537, 1449, 1382, 1307, 1272, 1252, 1189, 1177, 1123, 1085, 1032, 1009 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8 Hz, 1H), 7.73 (d, *J* = 8 Hz, 1H), 7.56-7.49 (m, 3H), 7.47-7.38 (m, 3H), 7.36 (d, *J* = 8 Hz, 2H), 7.13 (d, *J* = 8 Hz, 2H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 146.1, 142.5, 134.9, 133.9,

133.7, 131.8, 130.6, 129.9, 129.2, 129.0, 127.0, 125.8, 125.4, 120.6, 115.1, 21.7; HRMS (ESI-TOF) calculated for $C_{20}H_{15}ClN_2O_2S$ ($M + H^+$) 383.0616, found 383.0640.

2-(Anthracen-9-yl)-1-tosylbenzo[d]imidazole (2o). Yield 90%; R_f = 0.45 (hexane : ethyl acetate 4:1); yellow solid; mp 195-197 °C; IR (KBr) $\tilde{\nu}$ = 2918, 2356, 1595, 1535, 1448, 1379, 1346, 1254, 1233, 1175, 1146, 1088, 1044, 1014 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.37 (d, *J* = 8 Hz, 1H), 8.05 (d, *J* = 12 Hz, 2H), 7.92 (d, *J* = 8 Hz, 1H), 7.60-7.50 (m, 2H), 7.45-7.41 (m, 2H), 7.24-7.18 (m, 4H), 6.98 (d, *J* = 8 Hz, 2H), 6.77 (d, *J* = 8 Hz, 2H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 145.6, 142.5, 134.4, 133.6, 131.9, 130.8, 130.3, 130.0, 129.4, 128.5, 127.4, 127.1, 126.6, 125.7, 125.7, 125.3, 125.1, 125.0, 123.6, 120.8, 114.4, 21.6; HRMS (ESI-TOF) calculated for $C_{28}H_{20}N_2O_2S$ ($M + H^+$) 449.1318, found 449.1309.

2-(Pyridin-2-yl)-1-tosylbenzo[d]imidazole (2p). Yield 69%; R_f = 0.4 (hexane : ethyl acetate 7:3); white solid; mp 129-131 °C; IR (KBr) $\tilde{\nu}$ = 3050, 2360, 1592, 14448, 1434, 1375, 1316, 1254, 1189, 1177, 1128, 1087, 790 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, *J* = 4 Hz, 1H), 8.09-8.01 (m, 3H), 7.86-7.78 (m, 3H), 7.46-7.40 (m, 3H), 7.39-7.28 (m, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.7, 149.7, 148.5, 145.6, 142.3, 136.4, 135.8, 133.6, 129.7, 127.9, 125.8, 125.5, 125.0, 124.7, 120.9, 114.4, 21.7; HRMS (ESI-TOF) calculated for $C_{19}H_{15}N_3O_2S$ ($M + H^+$) 350.0958, found 350.0971.

2-(Naphthalen-1-yl)-1-tosylbenzo[d]imidazole (2q). Yield 84%; R_f = 0.5 (hexane : ethyl acetate 4:1); white solid; mp 116-118 °C; IR (KBr) $\tilde{\nu}$ = 3050, 2356, 1595, 1537, 1448, 1379, 1301, 1278, 1254, 1230, 1188, 1175, 1133, 1088, 1042,1014 cm-^{1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8 Hz, 1H), 8.03 (d, *J* = 8 Hz, 1H), 7.87 (d, *J* = 8 Hz, 1H), 7.83 (d, *J* = 8 Hz, 1H), 7.61-7.57 (m, 2H), 7.51-7.44 (m, 3H), 7.28-7.23 (m, 2H), 7.19 (d, *J* = 8 Hz, 2H), 6.88 (d, *J* = 8 Hz, 2H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 145.7, 142.4, 134.9, 133.6, 133.1, 132.5, 130.9, 130.1,

129.5, 128.2, 127.3, 126.8, 126.0, 125.6, 125.3, 125.1, 124.4, 120.6, 114.7, 21.6; HRMS (ESI-TOF) calculated for $C_{24}H_{18}N_2O_2S$ (M + H^+) 399.1162, found 399.1199.

2-(Pyren-1-yl)-1-tosylbenzo[d]imidazole (2r). Yield 76%; R_f = 0.45 (hexane : ethyl acetate 4:1); white solid; mp 190-192 °C; IR (KBr) $\tilde{\nu}$ = 2918, 2360, 1596, 1544, 1448, 1379, 1253, 1188, 1175, 1080, 1047, 1009, 848 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8 Hz, 1H), 8.27(d, *J* = 8 Hz, 2H), 8.20-8.13 (m, 4H), 8.05 (t, *J* = 8 Hz, 1H), 7.89 (d, *J* = 8 Hz, 1H), 7.84 (d, *J* = 12 Hz, 1H), 7.57-7.50 (m, 3H), 7.09 (d, *J* = 12 Hz, 2H), 6.67 (d, *J* = 8 Hz, 2H), 1.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 145.7, 142.6, 134.8, 133.8, 132.8, 131.2, 131.0, 130.7, 129.4, 129.3, 129.0, 128.4, 127.4, 127.2, 126.4, 126.0, 125.8, 125.7, 125.2, 124.4, 124.3, 124.3, 124.1, 123.6, 120.7, 114.9, 21.3; HRMS (ESI-TOF) calculated for $C_{30}H_{20}N_2O_2S$ (M + H^+) 473.1318, found 473.1335.

2-Chloro-6-methoxy-3-(1-tosylbenzo[d]imidazol-2-yl)quinolone (2s). Yield 93%; R_f = 0.4 (hexane : ethyl acetate 7:3); white solid; mp 171-173 °C; IR (KBr) $\tilde{\nu}$ = 2927, 2352, 1615, 1495, 1450, 1380, 1359, 1305, 1254, 1228, 1189, 1176, 1142, 1113, 1088, 1052, 1027 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.19-8.17 (m, 2H), 8.02 (d, *J* = 8 Hz, 1H), 7.83 (d, *J* = 8 Hz, 1H), 7.52-7.43 (m, 5H), 7.19 (d, *J* = 8 Hz, 2H), 7.13 (d, *J* = 4 Hz, 1H), 3.97 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 148.2, 146.7, 146.4, 144.2, 142.3, 140.5, 134.9, 133.0, 130.1, 127.4, 127.2, 126.9, 126.2, 125.3, 124.8, 124.3, 121.0, 114.3, 105.6, 55.9, 21.8; HRMS (ESI-TOF) calculated for $C_{24}H_{18}ClN_3O_3S$ (M + H^+) 464.0830, found 464.0887.

2-(5-Nitrofuran-2-yl)-1-tosylbenzo[d]imidazole (2t). Yield 93%; R_f = 0.5 (hexane : ethyl acetate 4:1); yellow solid; mp 149-151 °C; IR (KBr) $\tilde{\nu}$ = 2914, 2334, 1592, 1541, 1518, 1471, 1382, 1352, 1304, 1277, 1191, 1177, 1130, 1087, 1017 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8 Hz, 1H), 8.06 (d, *J* = 8 Hz, 2H), 7.81 (d, *J* = 8 Hz, 1H), 7.54 (d, *J* = 8 Hz, 1H), 7.51-7.46 (m, 2H), 7.44-7.37 (m, 2H), 7.31 (d, *J* = 4 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ

152.7, 146.8, 145.3, 142.1, 140.4, 134.6, 133.5, 130.4, 127.8, 127.1, 125.7, 121.4, 117.1, 114.4, 112.5, 21.8; HRMS (ESI-TOF) calculated for $C_{18}H_{13}N_3O_5S$ ($M + H^+$) 384.0649, found 384.0647.

2-Cyclohexyl-1-tosylbenzo[d]imidazole (2aa). Yield 73%; R_f = 0.5 (hexane : ethyl acetate 4:1); white solid; mp 107-109 °C; IR (KBr) $\tilde{\nu}$ = 2927, 2360, 1640, 1539, 1452, 1373, 1168, 1121, 1089, 1049, 1004 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05-8.03 (m, 1H), 7.75 (d, *J* = 8 Hz, 2H), 7.68-7.66 (m, 1H), 7.35-7.31 (m, 2H), 7.27 (d, *J* = 8 Hz, 2H), 3.52-3.45 (m, 1H), 2.38 (s, 3H), 1.94-1.84 (m, 4H), 1.75-1.61 (m, 3H), 1.44-1.34 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 145.9, 136.0, 133.0, 130.3, 126.7, 124.8, 124.7, 119.9, 114.1, 38.2, 32.7, 26.4, 25.9, 21.8, 0.1; HRMS (ESI-TOF) calculated for $C_{20}H_{22}N_2O_2S$ ($M + H^+$) 355.1475, found 355.1484.

1-Tosylbenzo[d]imidazole (2ab).[29] Yield 44%; R_f = 0.6 (hexane : ethyl acetate 4:1); white solid; mp 84-86 °C (lit. 85-86 °C); IR (KBr) $\tilde{\nu}$ = 2920, 2359, 1603, 1381, 1254, 1160, 1088 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1H), 7.89-7.85 (m, 3H), 7.77 (d, *J* = 4 Hz, 1H), 7.42-7.38 (m, 2H), 7.36-7.30 (m, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.3, 144.1, 141.3, 134.7, 130.9, 130.4, 127.4, 125.7, 124.9, 121.2, 112.6, 21.8; HRMS (ESI-TOF) calculated for $C_{14}H_{12}N_2O_2S$ ($M + H^+$) 273.0692, found 273.0692.

2-(2-Phenylpropyl)-1-tosylbenzo[d]imidazole (2ac). Yield 57%; R_f = 0.5 (hexane : ethyl acetate 4:1); colourless oil; IR (KBr) $\tilde{\nu}$ = 2963, 2925, 2356, 1597, 1545, 1451, 1376, 1253, 1228, 1168, 1149, 1120, 1089, 1043, 1015 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05-8.03 (m, 1H), 7.73-7.70 (m, 3H), 7.37-7.30 (m, 6H), 7.25-7.21 (m, 3H), 3.74-3.65 (m, 1H), 3.55-3.50 (m 1H), 3.44-3.38 (m, 1H), 2.35 (s, 3H), 1.36 (d, *J* = 8 Hz, 3H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 146.3, 145.8, 142.1, 135.5, 133.1, 130.2, 128.6, 127.0,126.7, 126.4, 124.8, 124.7, 119.9, 113.8, 38.5, 38.3, 21.6, 21.1.; HRMS (ESI-TOF) calculated for $C_{23}H_{22}N_2O_2S$ ($M + H^+$) 391.1475, found 391.1477.

2-Methyl-1-tosylbenzo[d]imidazole (2ad). Yield 55%; R_f = 0.4 (hexane : ethyl acetate 4:1); white solid; mp 112-113 °C (lit. 117 °C); IR (KBr) $\tilde{\nu}$ = 3104, 2920, 2351, 1597, 1546, 1452, 1443, 1425, 1372, 1295, 1274, 1247, 1173, 1188, 1173, 1123, 1089, 1053, 1000 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8 Hz, 1H), 7.81 (d, *J* = 12 Hz, 2H), 7.63 (d, *J* = 8 Hz, 1H), 7.37-7.28 (m, 4H), 2.81 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 146.1, 141.9, 135.5, 133.2, 130.4, 126.9, 124.9, 124.7, 119.7, 113.5, 21.7, 17.0; HRMS (ESI-TOF) calculated for $C_{15}H_{14}N_2O_2S$ ($M + H^+$) 287.0849, found 287.0873.

2-(4-Ethylphenyl)-6-nitro-1-tosylbenzo[d]imidazole (2ba). Yield 33%; R_f = 0.6 (hexane : ethyl acetate 4:1); white solid; mp 139-141 °C; IR (KBr) $\tilde{\nu}$ = 2931, 2360, 2090, 1647, 1541, 1522, 1340, 1272, 1178, 1126, 1080, 1010, 834, 668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.12 (s, 1H), 8.31 (d, *J* = 12 Hz, 1H), 7.79 (d, *J* = 8 Hz, 1H), 7.54 (d, *J* = 8 Hz, 2H), 7.31-7.26 (m, 4H), 7.12 (d, *J* = 8 Hz, 2H), 2.81-2.77 (m, 2H), 2.34 (s, 3H), 1.33 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 148.2, 146.9, 146.6, 145.3, 134.4, 133.6, 131.0, 130.1, 127.5, 127.4, 126.4, 121.0, 120.5, 112.0, 29.0, 21.8, 15.5; HRMS (ESI-TOF) calculated for $C_{22}H_{19}N_3O_4S$ ($M + H^+$) 422.1169, found 422.1162.

2-(2-Nitrophenyl)-1-tosylbenzo[d]imidazole-6-carboxylic acid (2bb). Yield 77%; R_f = 0.4 (hexane : ethyl acetate 1:1); white solid; mp 158-160 °C; IR (KBr) $\tilde{\nu}$ = 2923, 2364, 1697, 1532, 1384, 1347, 1271, 1176, 1134, 1088 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.36 (d, *J* = 8 Hz, 1H), 8.20 (d, *J* = 8 Hz, 1H), 7.84-7.79 (m, 3H), 7.54 (d, *J* = 12 Hz, 3H), 7.24 (d, *J* = 12 Hz, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 151.9, 148.3, 146.8, 146.2, 134.5, 133.2, 133.0, 132.7, 131.9, 130.3, 127.6, 127.1, 126.5, 125.9, 124.9, 120.7, 116.6, 21.8; HRMS (ESI-TOF) calculated for $C_{21}H_{15}N_3O_6S$ ($M + H^+$) 438.0754, found 438.0759.

2-(2-Nitrophenyl)-1-tosylnaphtho[2,3-d]imidazole (2bc). Yield 73%; R_f = 0.4 (hexane : ethyl acetate 7:3); yellow solid; mp 89-91 °C; IR (KBr) $\tilde{\nu}$ = 2923, 2360, 1699, 1592, 1531, 1379, 1348,

1300, 1254, 1175, 1121, 1088, 1066, 1004 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.35 (d, *J* = 9.2 Hz, 1H), 8.23 (s, 1H), 8.07 (d, *J* = 7.8 Hz, 1H), 8.01 (d, *J* = 8.3 Hz, 1H), 7.83-7.76 (m, 2H), 7.58-7.49 (m, 5H), 7.17 (d, *J* = 8.2 Hz, 2H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 148.5, 146.3, 141.8, 134.9, 133.1, 133.0, 132.4, 131.9, 131.7, 131.5, 130.1, 128.5, 128.4, 127.2, 126.3, 125.9, 125.4, 124.8, 118.3, 111.2, 21.8; HRMS (ESI-TOF) calculated for $C_{24}H_{17}N_3O_4S_1$ ($M + H^+$) 444.1013, found 444.1005.

5,6-Dibromo-2-(2-fluorophenyl)-1-tosylbenzo[d]imidazole (2bd). Yield 55%; R_f = 0.5 (hexane : ethyl acetate 4:1); white solid; mp 108-110 °C; IR (KBr) $\tilde{\nu}$ = 2918, 2360, 1625, 1595, 1478, 1447, 1427, 1382, 1304, 1259, 1232, 1190, 1178, 1114, 1085, 1031, 1018 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (s, 1H), 8.02 (s, 1H), 7.61-7.55 (m, 1H), 7.43-7.39 (m, 3H), 7.30-7.27 (m, 1H), 7.22-7.16 (m, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0 (d, $^{1}J_{CF}$ = 251 Hz), 149.6, 146.6, 142.8, 134.5, 133.3, 133.2 (d, $^{3}J_{CF}$ = 8.1 Hz), 132.2, 130.2, 127.3, 125.1, 123.8 (d, $^{4}J_{CF}$ = 3.7 Hz), 121.6, 121.0, 119.1, 118.1 (d, $^{2}J_{CF}$ = 14.7 Hz), 115.8 (d, $^{2}J_{CF}$ = 20.8 Hz), 21.8; HRMS (ESI-TOF) calculated for $C_{20}H_{13}N_2O_2SBr_2F$ ($M + H^+$) 522.9121, found 522.9091.

2-(2-Bromo-5-fluorophenyl)-5,6-dimethyl-1-tosylbenzo[d]imidazole (2be). Yield 71%; R_f = 0.5 (hexane : ethyl acetate 4:1); white solid; mp 121-123 °C; IR (KBr) $\tilde{\nu}$ = 2921, 2356, 1596, 1545, 1460, 1380, 1302, 1256, 1188, 1174, 1117, 1088, 1040, 1021 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.62-7.58 (m, 1H), 7.56 (s, 1H), 7.54 (d, *J* = 4 Hz, 2H), 7.22 (d, *J* = 8 Hz, 2H), 7.15-7.06 (m, 2H), 2.46 (s, 3H), 2.38 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.9 (d, $^{1}J_{CF}$ = 247.1 Hz), 148.6, 146.1, 140.6, 135.5, 135.2, 134.4, 133.9 (d, $^{3}J_{CF}$ = 8.2 Hz), 133.8 (d, $^{3}J_{CF}$ = 8.7 Hz), 131.2, 130.0, 127.4, 120.9, 119.8 (d, $^{2}J_{CF}$ = 24 Hz), 119.4 (d, $^{4}J_{CF}$ = 3.5 Hz), 118.9 (d, $^{2}J_{CF}$ = 22.1 Hz), 114.3, 21.8, 20.9, 20.2; HRMS (ESI-TOF) calculated for $C_{22}H_{18}N_2O_2SBrF$ ($M + H^+$) 473.0329, found 473.0329.

2-(4-Bromophenyl)-5,6-dichloro-1-tosylbenzo[d]imidazole (2bf). Yield 56%; R_f = 0.7 (hexane : ethyl acetate 4:1); white solid; mp 206-208 °C; IR (KBr) $\tilde{\nu}$ = 2971, 2352, 1592, 1432, 1378, 1284, 1234, 1188, 1166, 1083, 1009, 864, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.79 (s, 1H), 7.62 (d, *J* = 8 Hz, 2H), 7.46 (d, *J* = 8 Hz, 2H), 7.29 (d, *J* = 8 Hz, 2H), 7.15 (d, *J* = 8 Hz, 2H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 146.6, 141.9, 134.4, 133.1, 132.5, 131.2, 130.1, 130.0, 129.9, 128.2, 127.1, 126.0, 121.6, 116.8, 21.8; HRMS (ESI-TOF) calculated for $C_{20}H_{13}N_2O_2SBrCl_2$ ($M + H^+$) 494.9331, found 494.9301.

1-(Phenylsulfonyl)-2-(thiophen-2-yl)benzo[d]imidazole (2ca). Yield 83%; R_f = 0.45 (hexane : ethyl acetate 4:1); white solid; mp 96-99 °C; IR (KBr) $\tilde{\nu}$ = 3073, 2364, 1558, 1474, 1448, 1419, 1383, 1337, 1297, 1273, 1233, 1215, 1120, 1088, 1061, 1041 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8 Hz, 1H), 7.81 (d, *J* = 4 Hz, 1H), 7.72 (d, *J* = 8 Hz, 1H), 7.55-7.38 (m, 6H), 7.33-7.27 (m, 2H), 7.21-7.18 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 142.6, 137.8, 134.5, 134.4, 133.4, 130.0, 129.3, 127.6, 126.9, 125.8, 125.6, 120.4, 115.4; HRMS (ESI-TOF) calculated for $C_{17}H_{12}N_2O_2S_2$ ($M + H^+$) 341.0413, found 341.0419.

2-(3,4-Dimethoxyphenyl)-1-(phenylsulfonyl)benzo[d]imidazole (2cb). Yield 87%; R_f = 0.4 (hexane : ethyl acetate 7:3); white solid; mp 129-131 °C; IR (KBr) $\tilde{\nu}$ = 2997, 2835, 2360, 1601, 1585, 1504, 1447, 1379, 1335, 1305, 1271, 1250, 1224, 1187, 1174, 1141, 1121, 1082, 1024 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8 Hz, 1H), 7.72-7.70 (m, 1H), 7.50-7.42 (m, 1H), 7.41-7.39 (m, 4H), 7.32-7.28 (m, 2H), 7.24-7.22 (m, 1H), 7.10 (s, 1H), 6.94 (d, *J* = 8 Hz, 1H), 3.98 (s, 3H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.2, 151.1, 148.1, 142.6, 138.0, 134.4, 134.2, 129.1, 127.0, 125.5, 125.5, 124.5, 122.0, 120.3, 115.4, 113.9, 110.2, 56.1; HRMS (ESI-TOF) calculated for $C_{21}H_{18}N_2O_4S$ ($M + H^+$) 395.1060, found 395.1067.

(2-(Benzo[d][1,3]dioxol-5-yl)benzo[d]imidazol-1-yl)(phenyl)methanone (2cc). Yield 64%; R_f = 0.45 (hexane : ethyl acetate 4 : 1); white solid; mp 158-160 °C; IR (KBr) $\tilde{\nu}$ = 2896, 2363, 1699, 1499, 1474, 1450, 1362, 1307, 1237, 1178, 1107, 1038, 932 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8 Hz, 1H), 7.72-7.70 (m, 2H), 7.57 (t, *J* = 8 Hz, 1H), 7.41 (s, 1H), 7.39-7.38 (m, 3H), 7.31-7.29 (m, 1H), 7.13-7.09 (m, 2H), 6.71 (d, *J* = 8 Hz, 1H), 5.95 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 153.5, 149.4, 147.9, 142.0, 134.7, 134.4, 133.0, 130.7, 129.0, 124.8, 124.8, 124.4, 123.6, 119.9, 113.0, 109.4, 108.5, 101.7; HRMS (ESI-TOF) calculated for $C_{21}H_{14}N_2O_3$ ($M + H^+$) 343.1077, found 343.1096.

2.6 Notes and References

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^{1}H and ^{13}C NMR Spectra of selected compounds

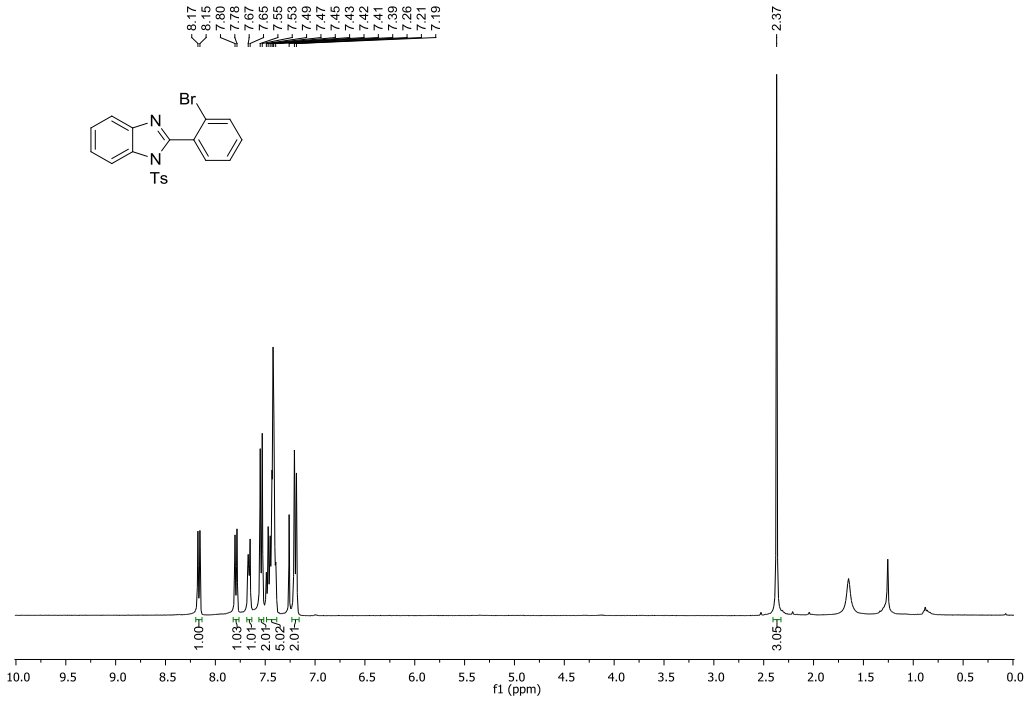


Figure 2.6. ^{1}H NMR spectrum of 2-(2-bromophenyl)-1-tosylbenzo[d]imidazole (**2a**).

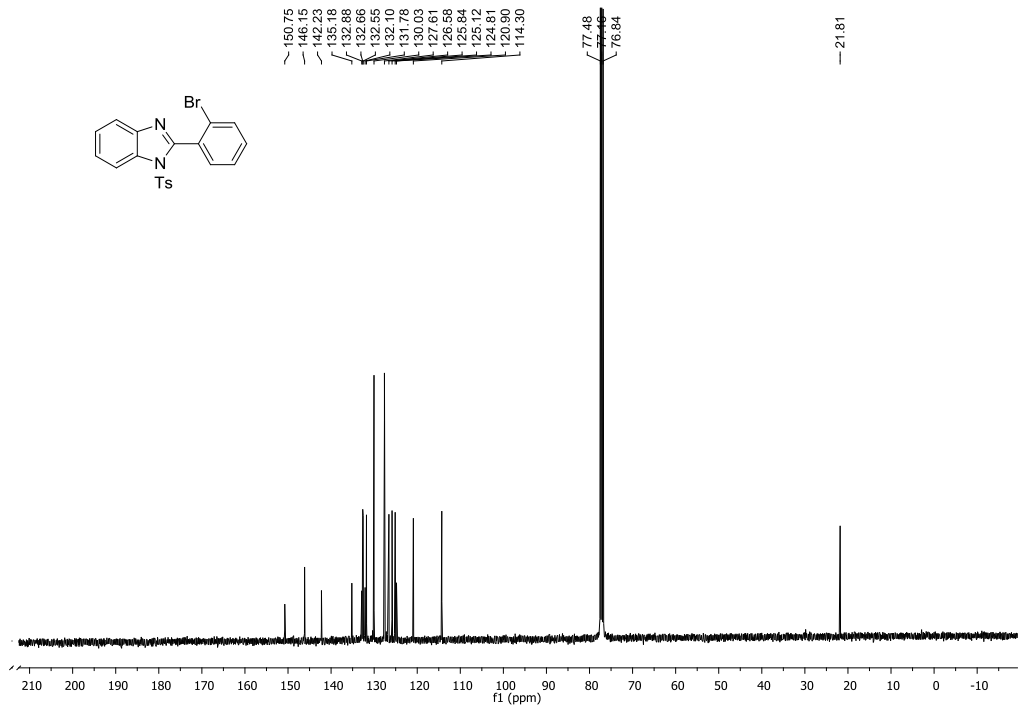


Figure 2.7. ^{13}C NMR spectrum of 2-(2-bromophenyl)-1-tosylbenzo[d]imidazole (**2a**).

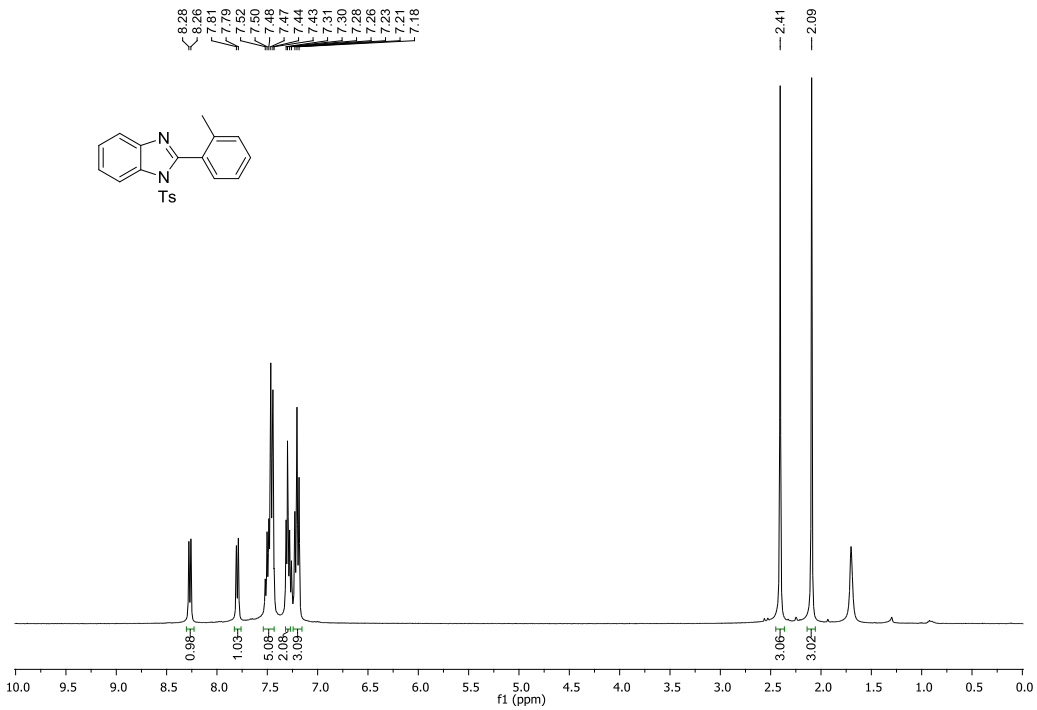


Figure 2.8. ^{1}H NMR spectrum of 2-(o-tolyl)-1-tosylbenzo[d]imidazole (**2b**).

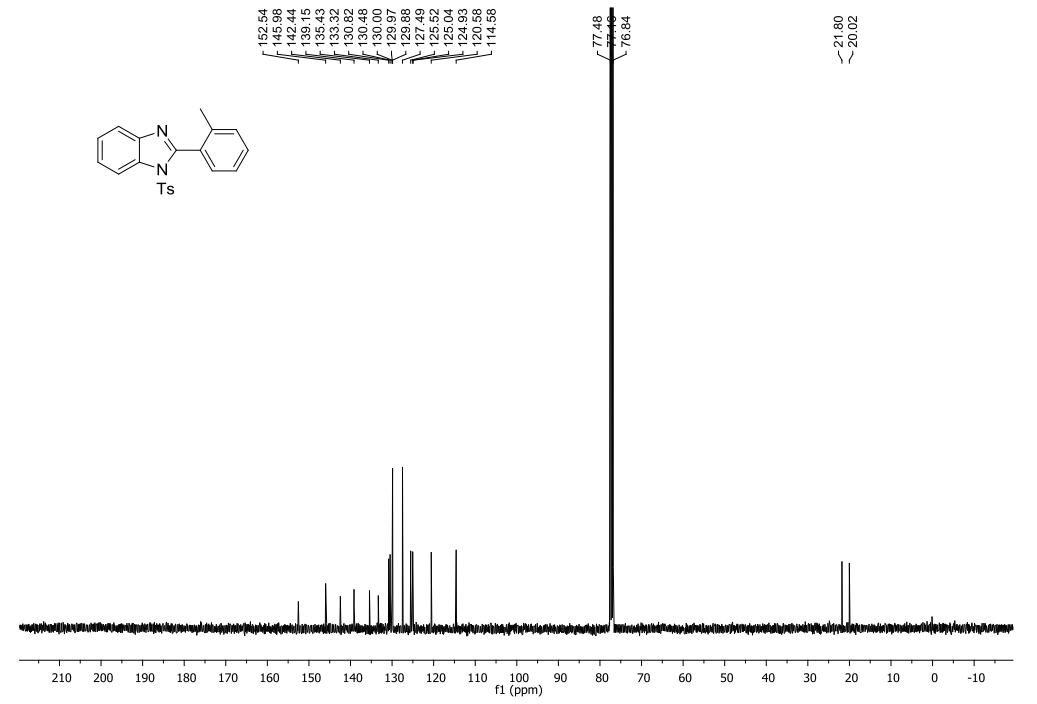


Figure 2.9. ^{13}C NMR spectrum of 2-(o-tolyl)-1-tosylbenzo[d]imidazole (**2b**).

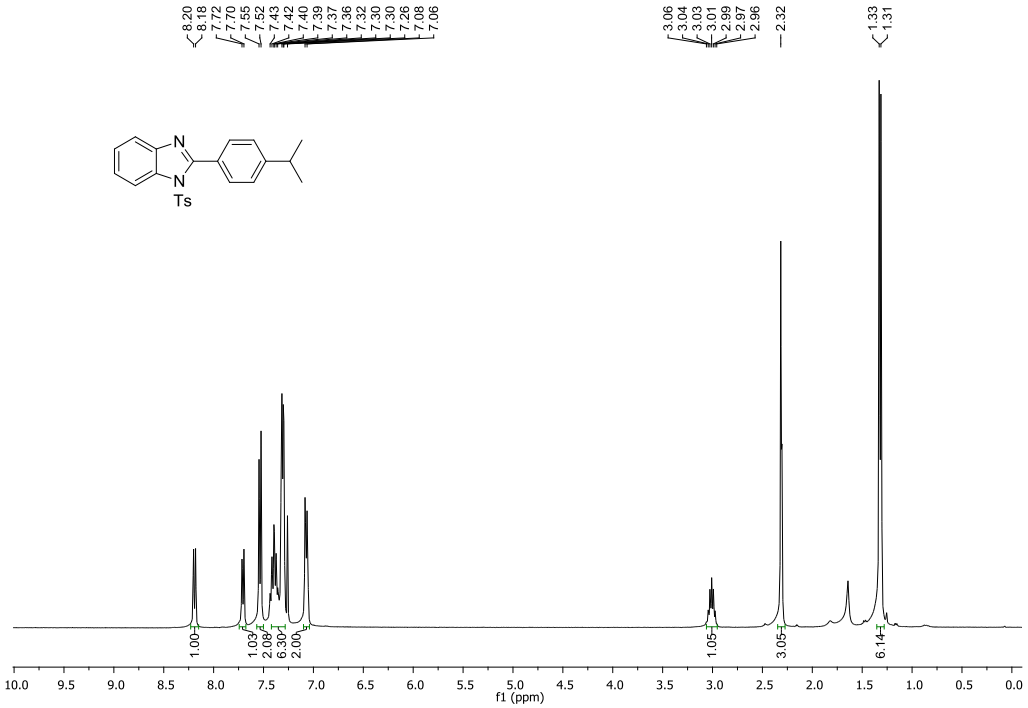


Figure 2.10. ^{1}H NMR spectrum of 2-(4-isopropylphenyl)-1-tosylbenzo[d]imidazole (**2c**).

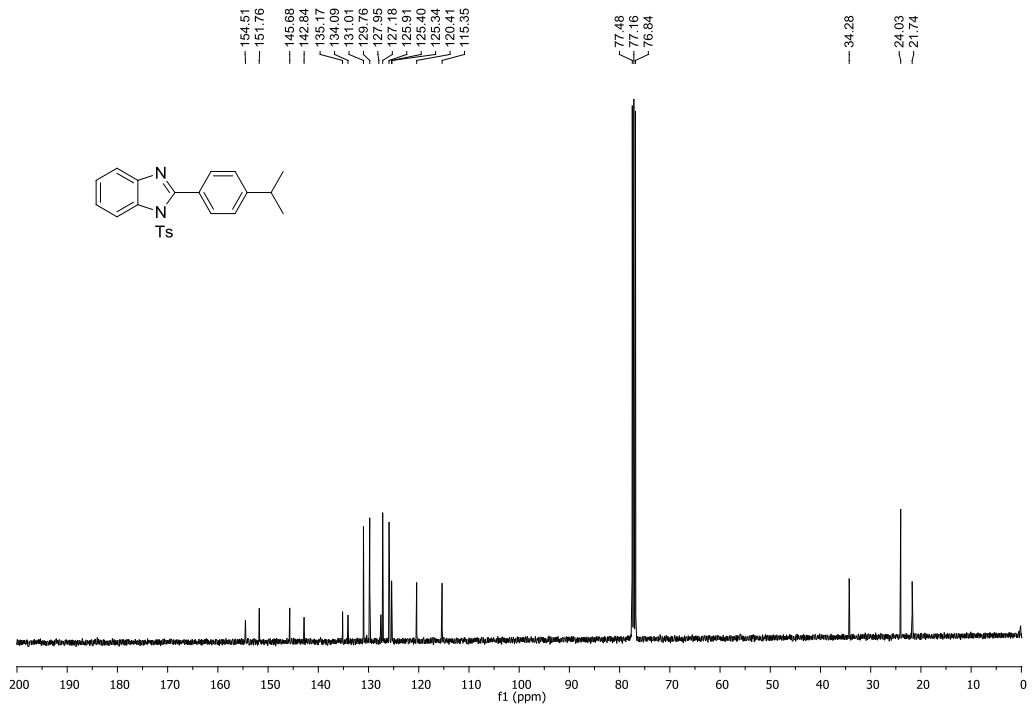


Figure 2.11. ^{13}C NMR spectrum of 2-(4-isopropylphenyl)-1-tosylbenzo[d]imidazole (**2c**).

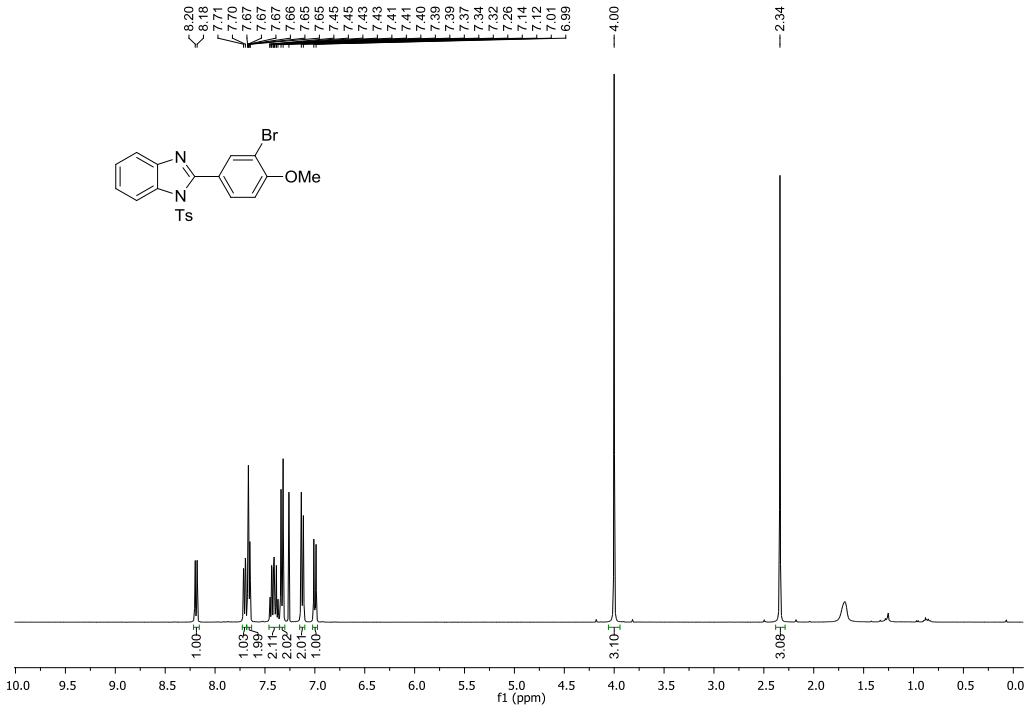


Figure 2.12. ^{1}H NMR spectrum of 2-(3-bromo-4-methoxyphenyl)-1-tosylbenzo[d]imidazole (**2d**).

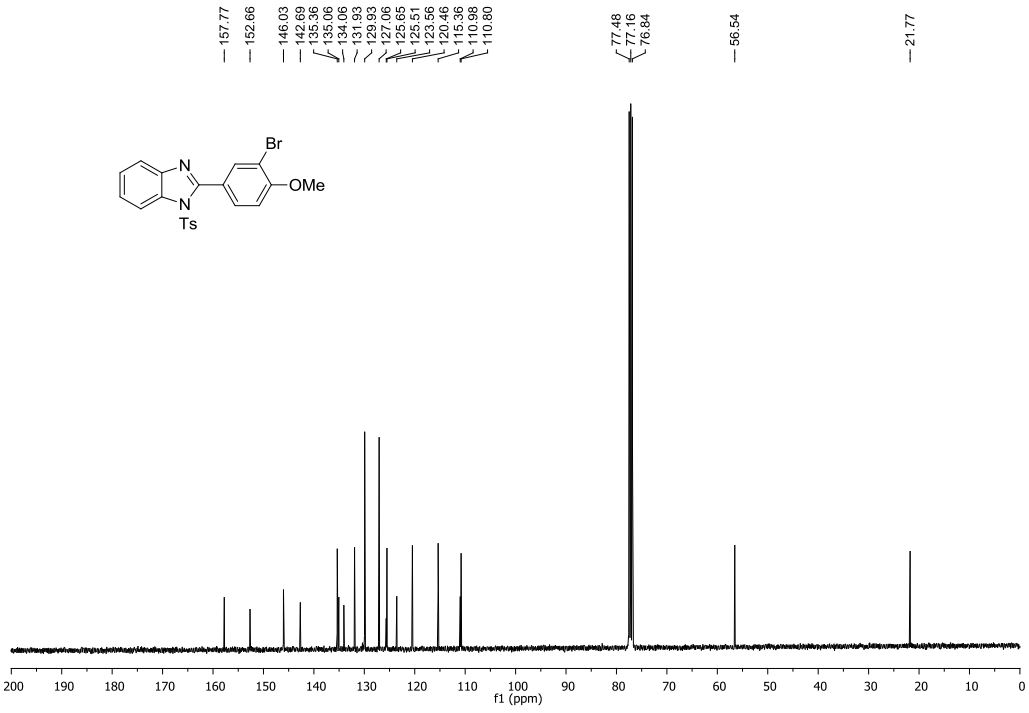


Figure 2.13. ^{13}C NMR spectrum of 2-(3-bromo-4-methoxyphenyl)-1-tosylbenzo[d]imidazole (**2d**).

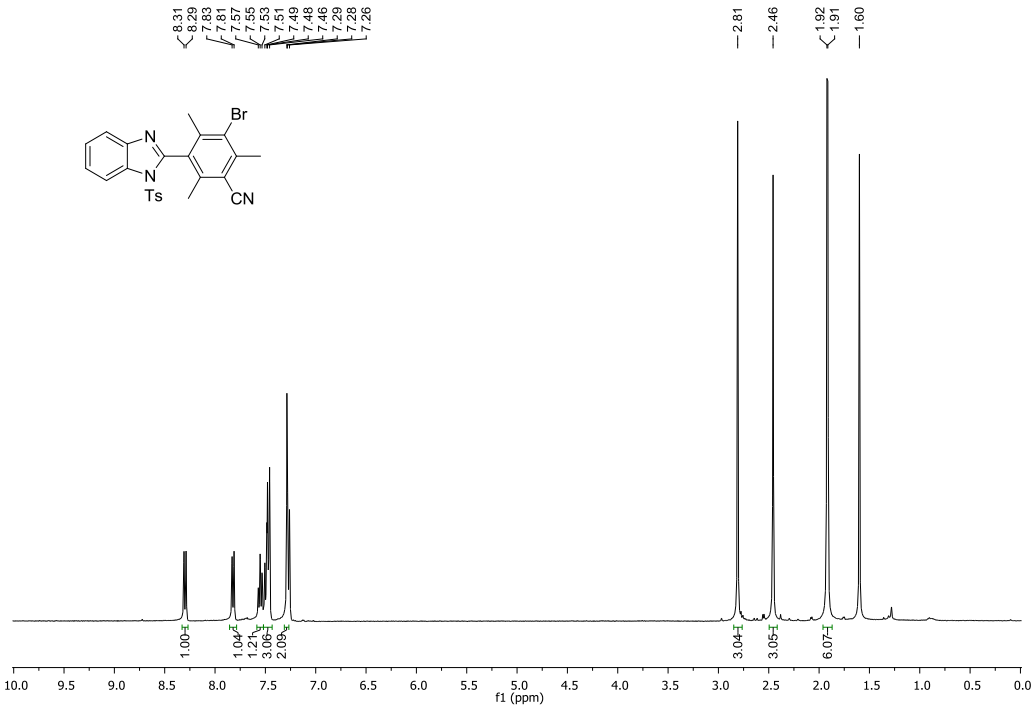


Figure 2.14 ^{1}H NMR spectrum of 3-bromo-2,4,6-trimethyl-5-(1-tosylbenzo[d]imidazol-2-yl)benzonitrile (**2f**).

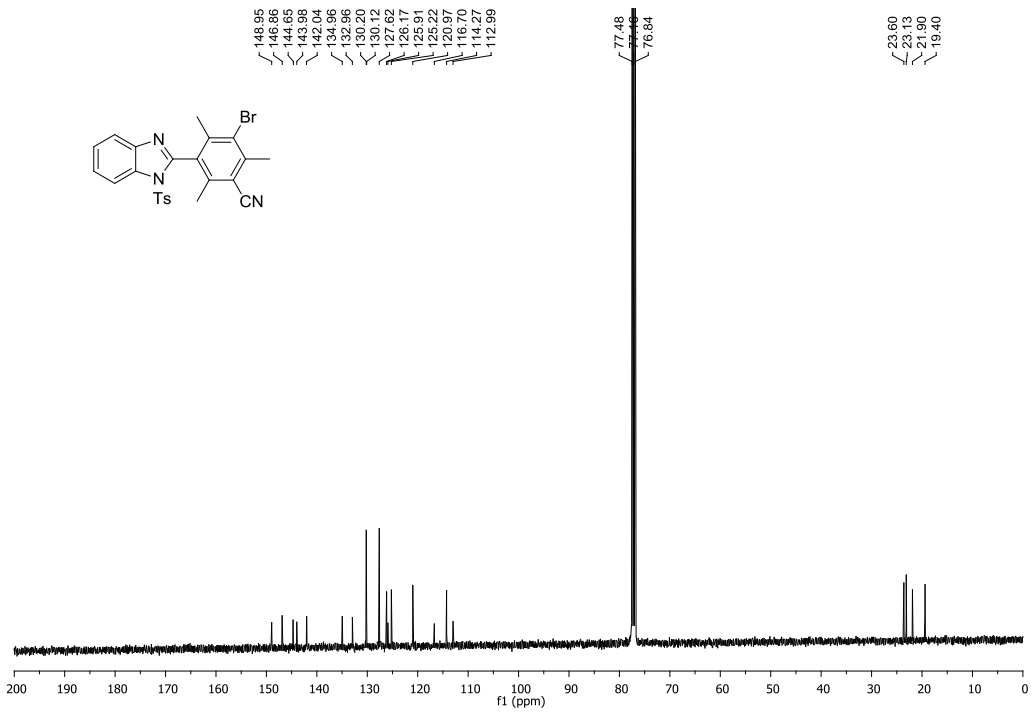


Figure 2.15 ^{13}C NMR spectrum of 3-bromo-2,4,6-trimethyl-5-(1-tosylbenzo[d]imidazol-2-yl)benzonitrile (**2f**).

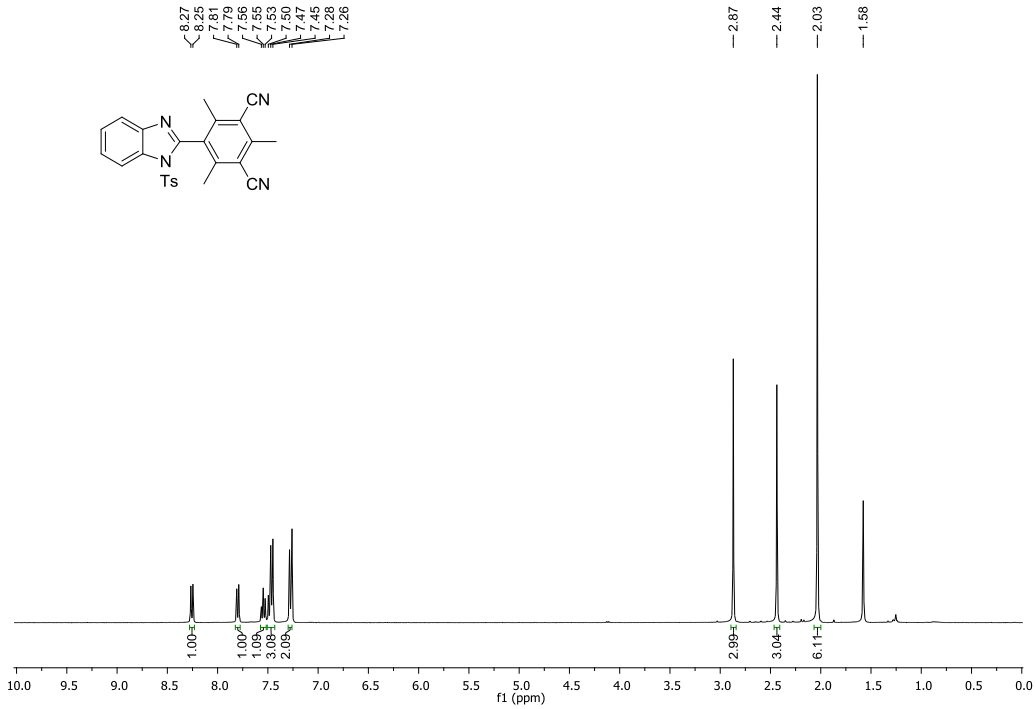


Figure 2.16 ^{1}H NMR spectrum of 2,4,6-trimethyl-5-(1-tosylbenzo[d]imidazol-2-yl)isophthalonitrile (**2g**).

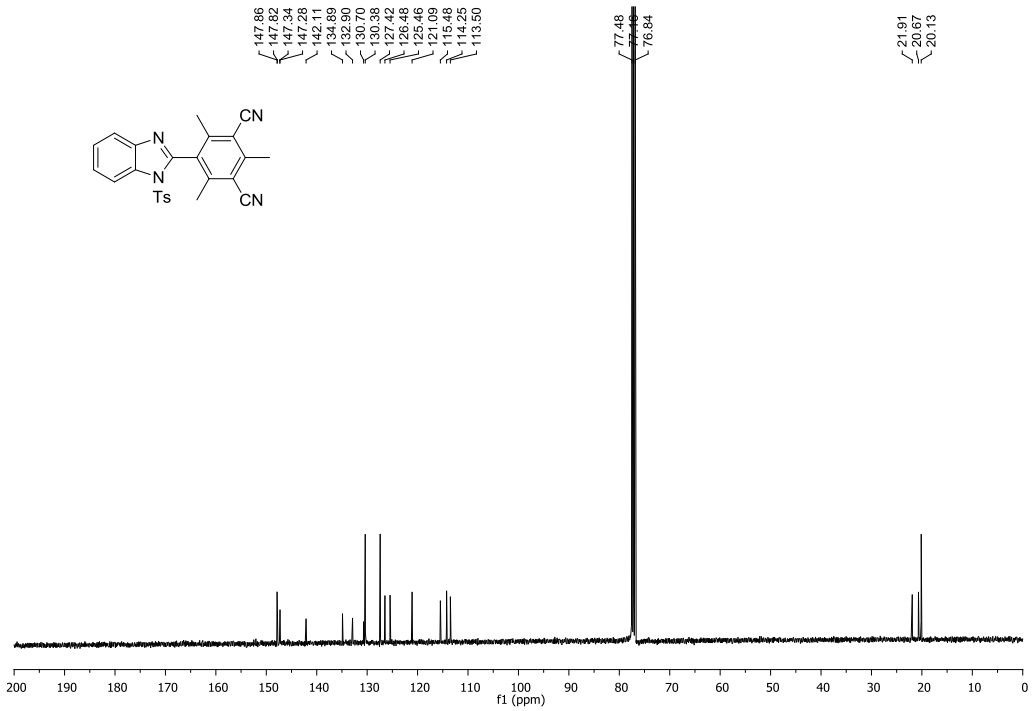


Figure 2.17 ^{13}C NMR spectrum of 2,4,6-trimethyl-5-(1-tosylbenzo[d]imidazol-2-yl)isophthalonitrile (**2g**).

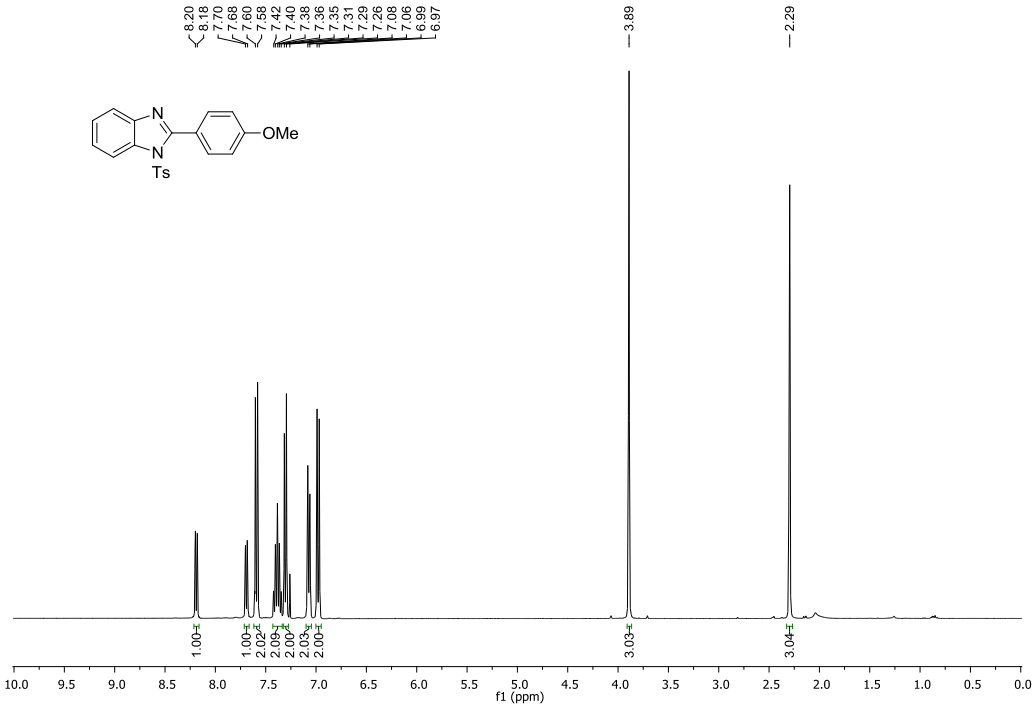


Figure 2.18 ^{1}H NMR spectrum of 2-(4-methoxyphenyl)-1-tosylbenzo[d]imidazole (**2h**).

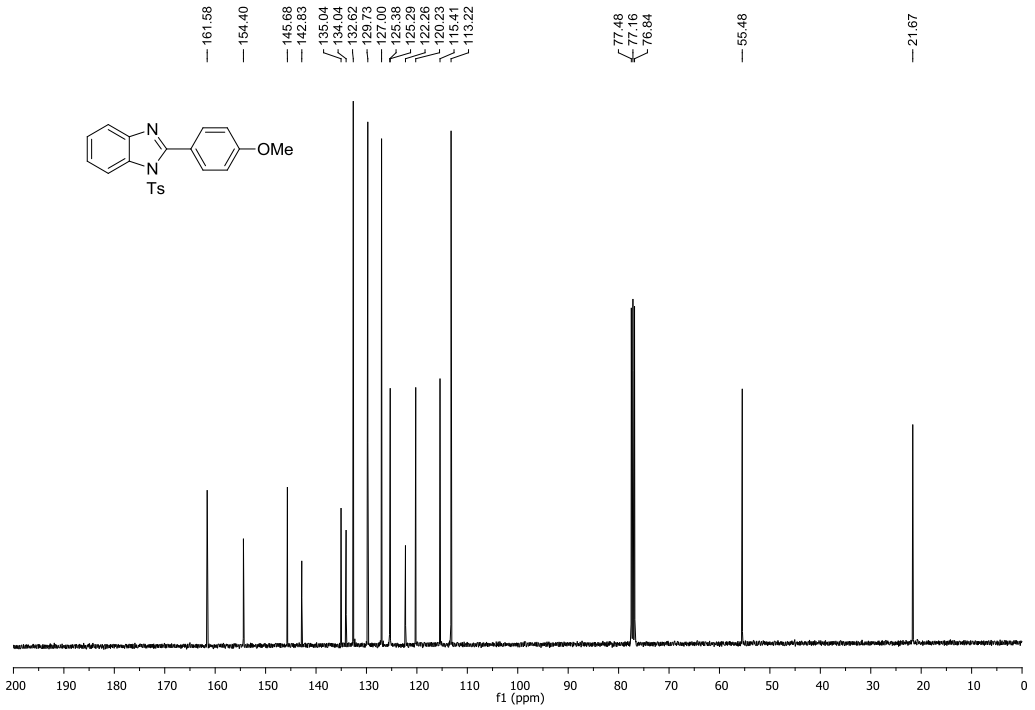


Figure 2.19 ^{13}C NMR spectrum of 2-(4-methoxyphenyl)-1-tosylbenzo[d]imidazole (**2h**).

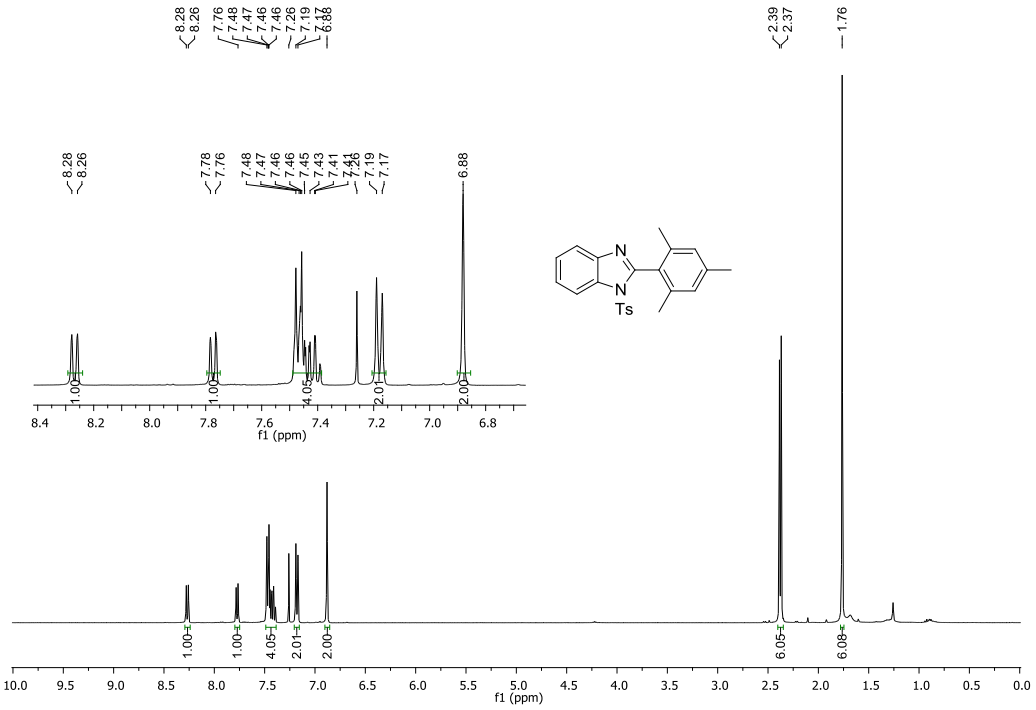


Figure 2.20 ^{1}H NMR spectrum of 2-mesityl-1-tosylbenzo[d]imidazole (**2i**).

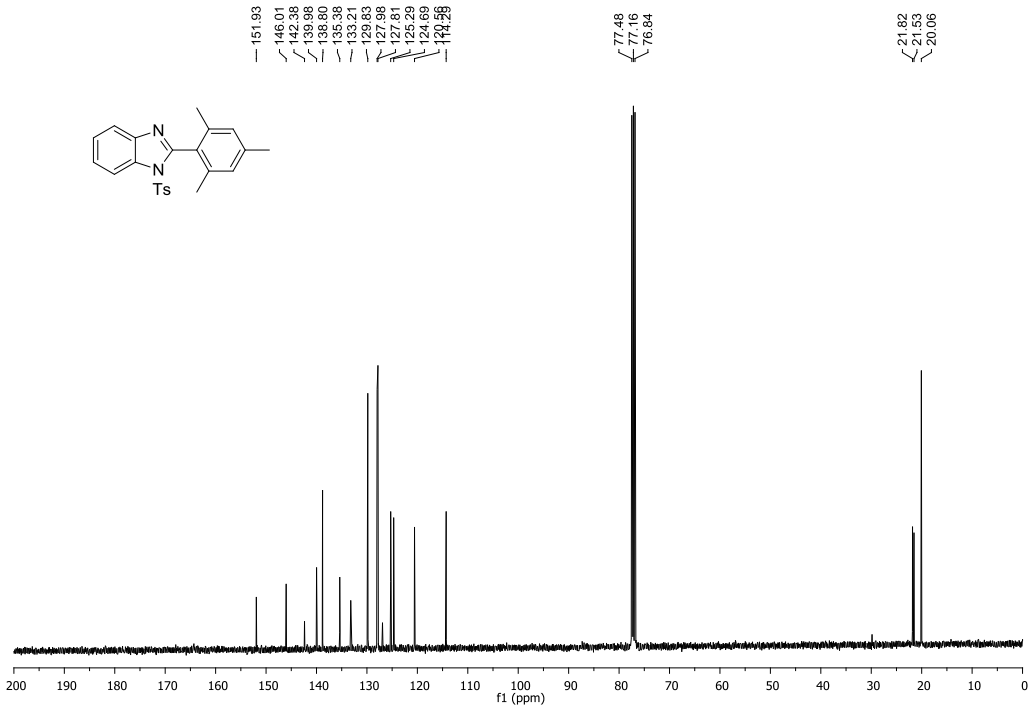


Figure 2.21 ^{13}C NMR spectrum of 2-mesityl-1-tosylbenzo[d]imidazole (**2i**).

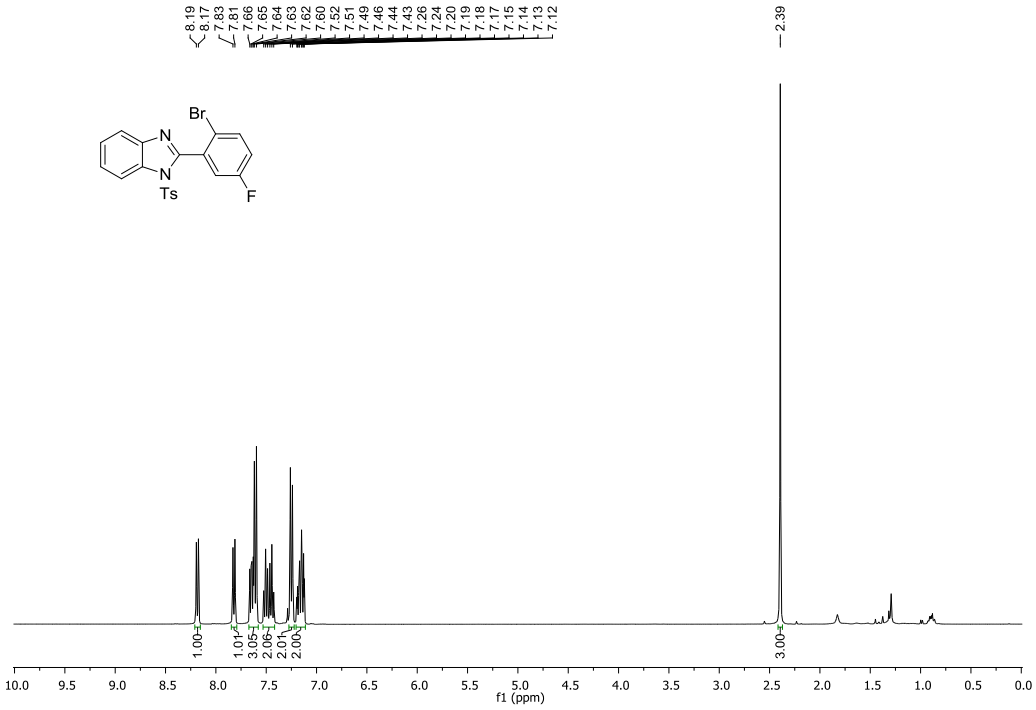


Figure 2.22 ^{1}H NMR spectrum of 2-(2-bromo-5-fluorophenyl)-1-tosylbenzo[d]imidazole (**2j**).

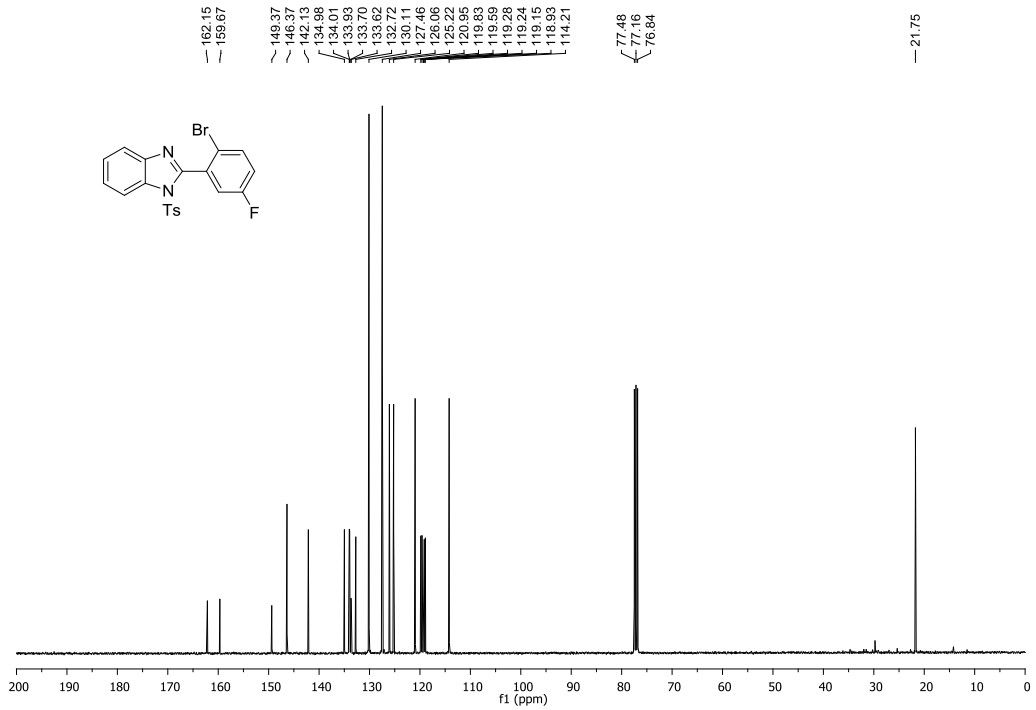


Figure 2.23 ^{13}C NMR spectrum of 2-(2-bromo-5-fluorophenyl)-1-tosylbenzo[d]imidazole (**2j**).

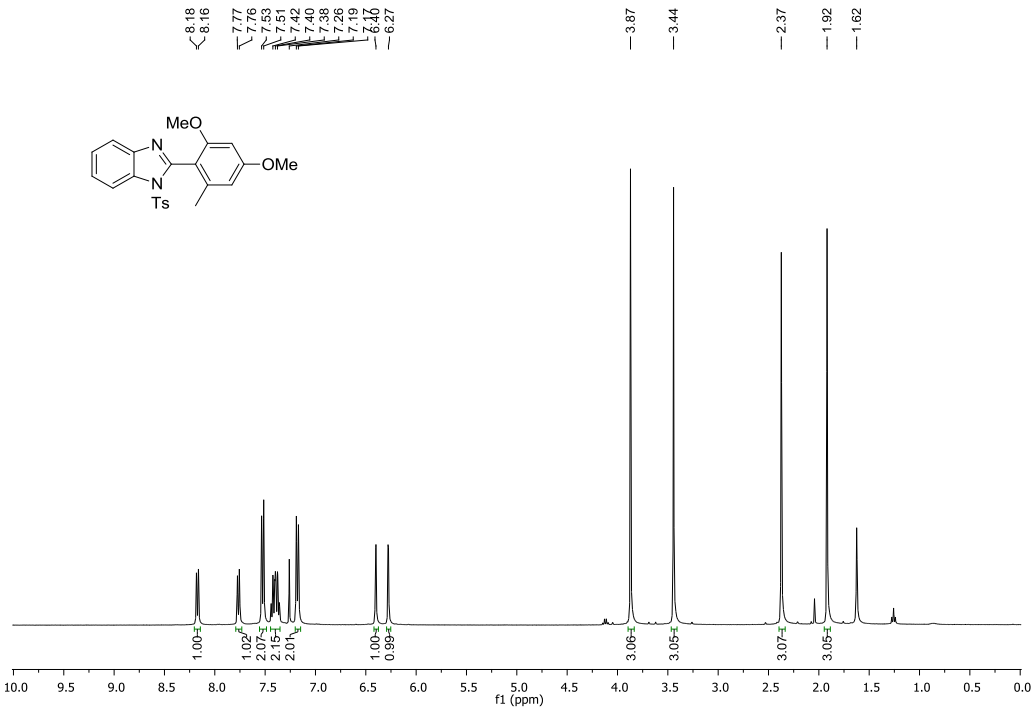


Figure 2.24 ^{1}H NMR spectrum of 2-(2,4-dimethoxy-6-methylphenyl)-1-tosylbenzo[d]imidazole (**2k**).

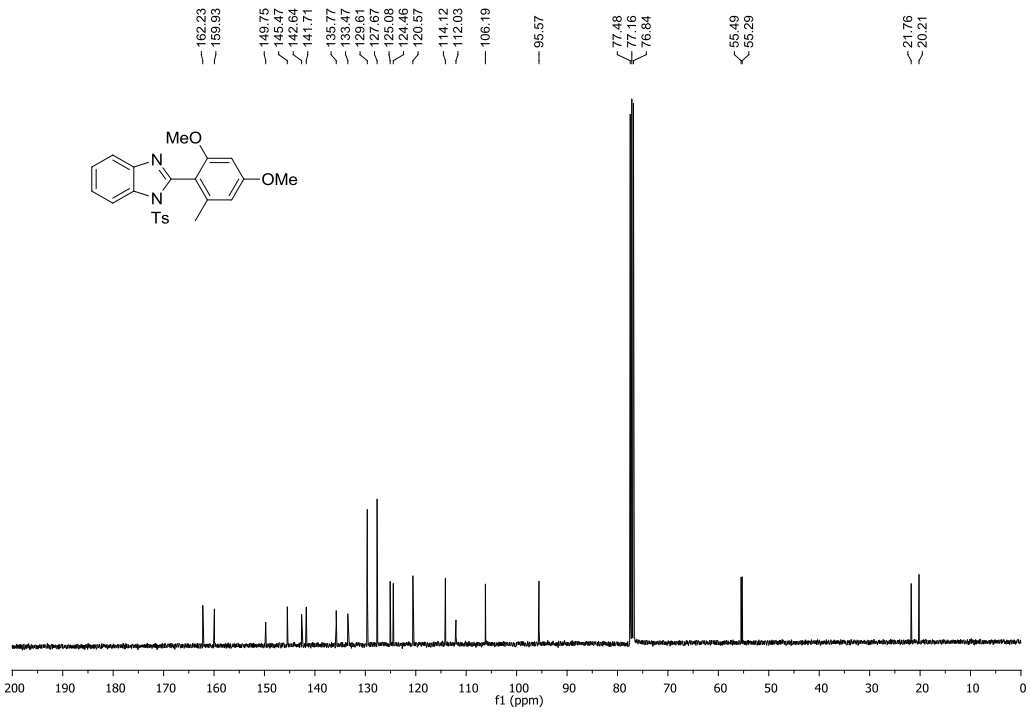


Figure 2.25 ^{13}C NMR spectrum of 2-(2,4-dimethoxy-6-methylphenyl)-1-tosylbenzo[d]imidazole (**2k**).

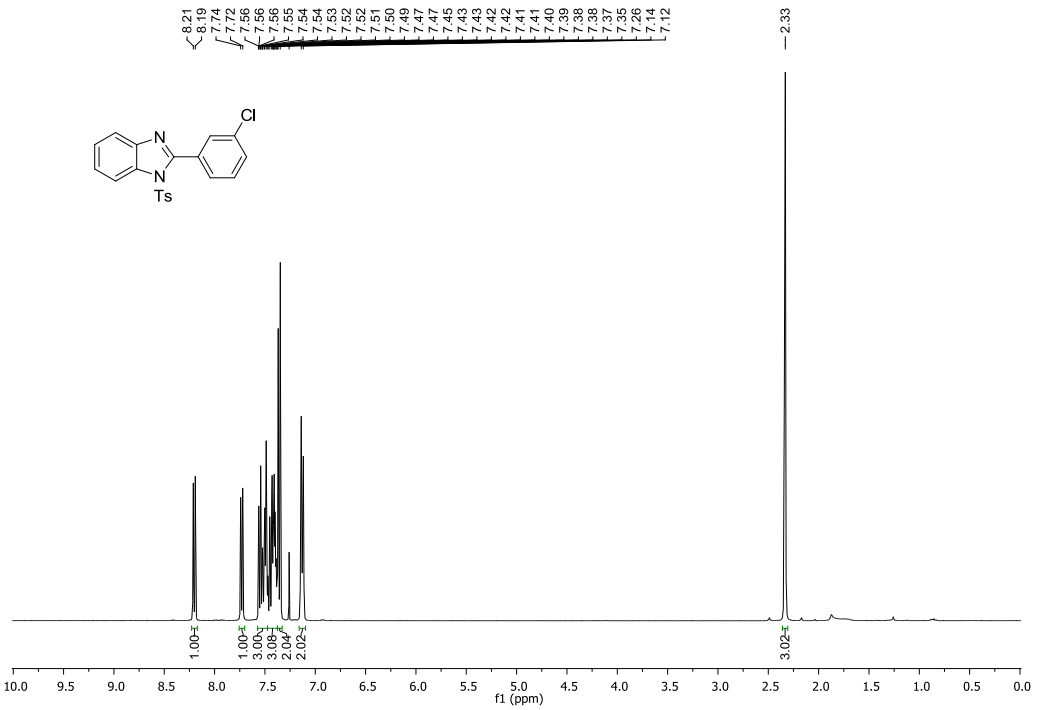


Figure 2.26 ^{1}H NMR spectrum of 2-(3-chlorophenyl)-1-tosylbenzo[d]imidazole (**2n**).

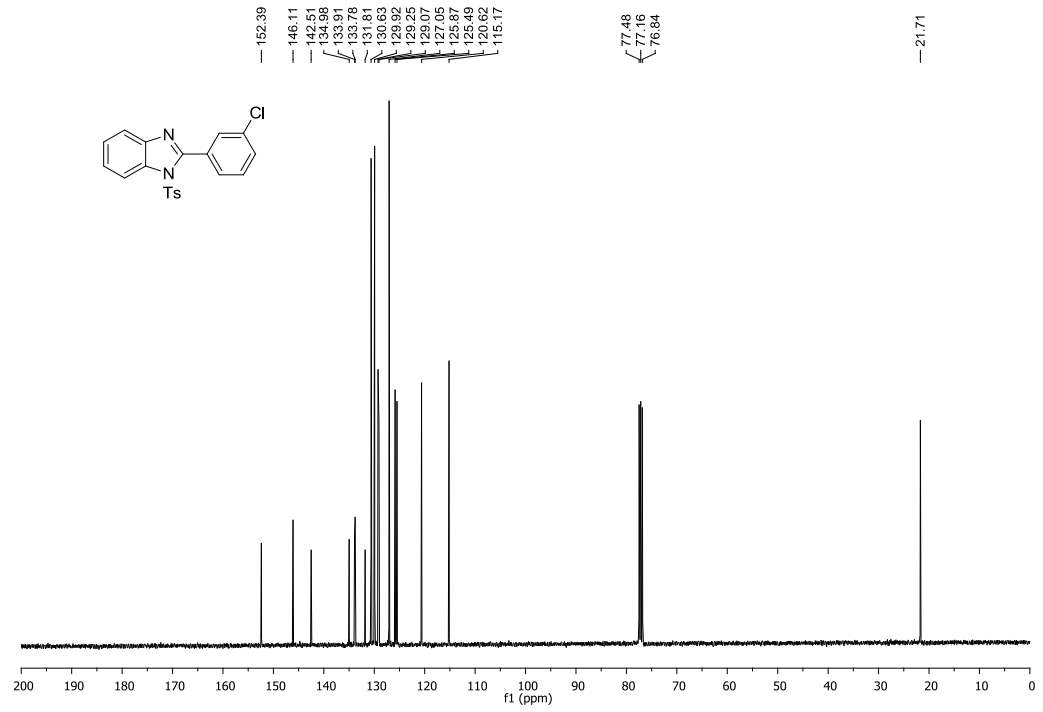


Figure 2.27 ^{13}C NMR spectrum of 2-(3-chlorophenyl)-1-tosylbenzo[d]imidazole (**2n**).

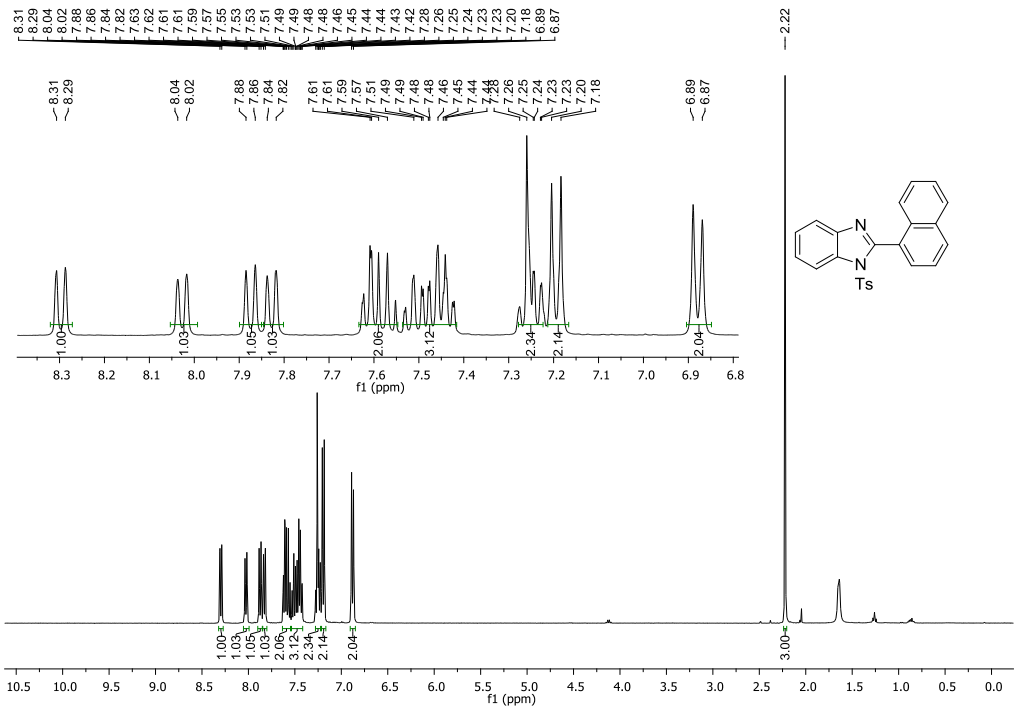


Figure 2.28 ^{1}H NMR spectrum of 2-(naphthalen-1-yl)-1-tosylbenzo[d]imidazole (**2q**).

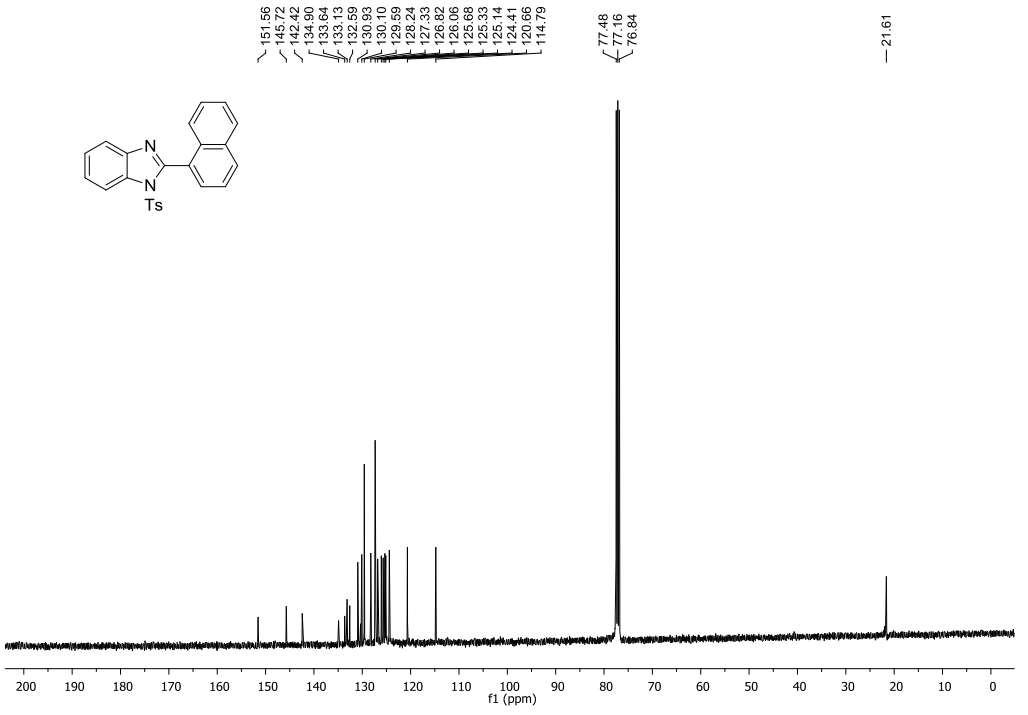


Figure 2.29 ^{13}C NMR spectrum of 2-(naphthalen-1-yl)-1-tosylbenzo[d]imidazole (**2q**).

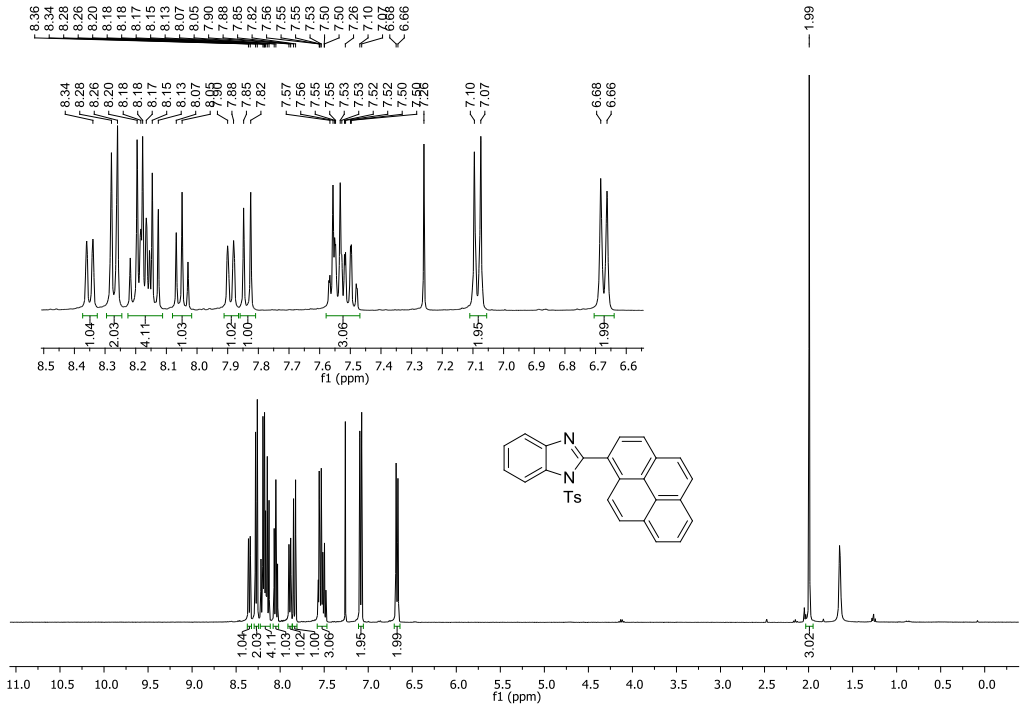


Figure 2.30 ^{1}H NMR spectrum of 2-(pyren-1-yl)-1-tosylbenzo[d]imidazole (**2r**).

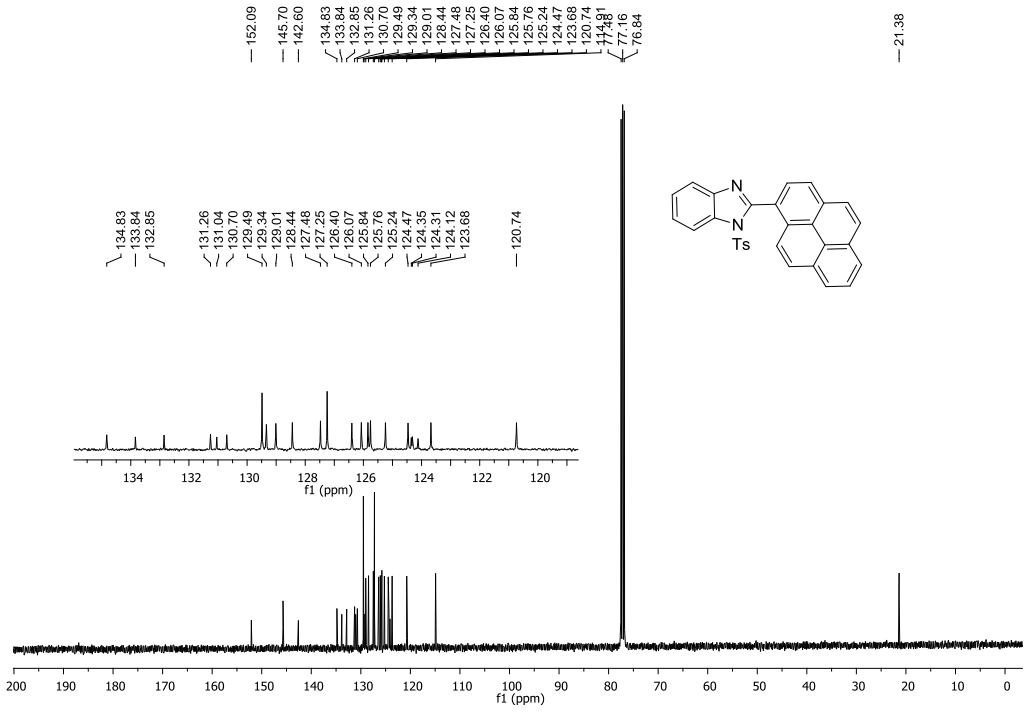


Figure 2.31 ^{13}C NMR spectrum of 2-(pyren-1-yl)-1-tosylbenzo[d]imidazole (**2r**).

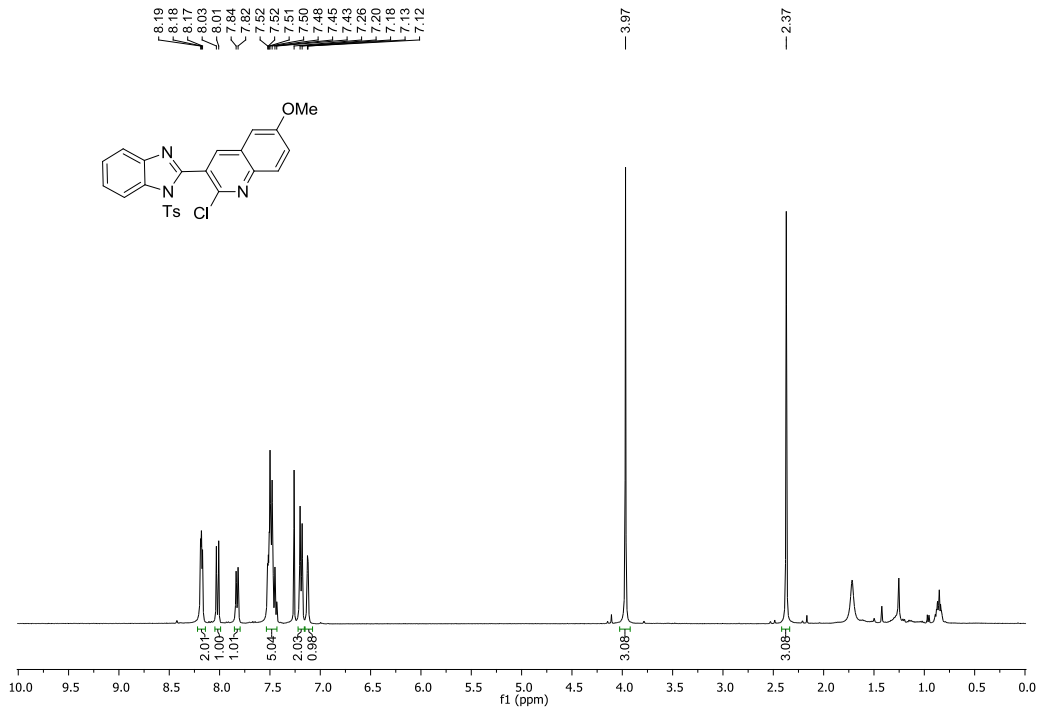


Figure 2.32 ^{1}H NMR spectrum of 2-chloro-6-methoxy-3-(1-tosylbenzo[d]imidazol-2-yl)quinolone (**2s**).

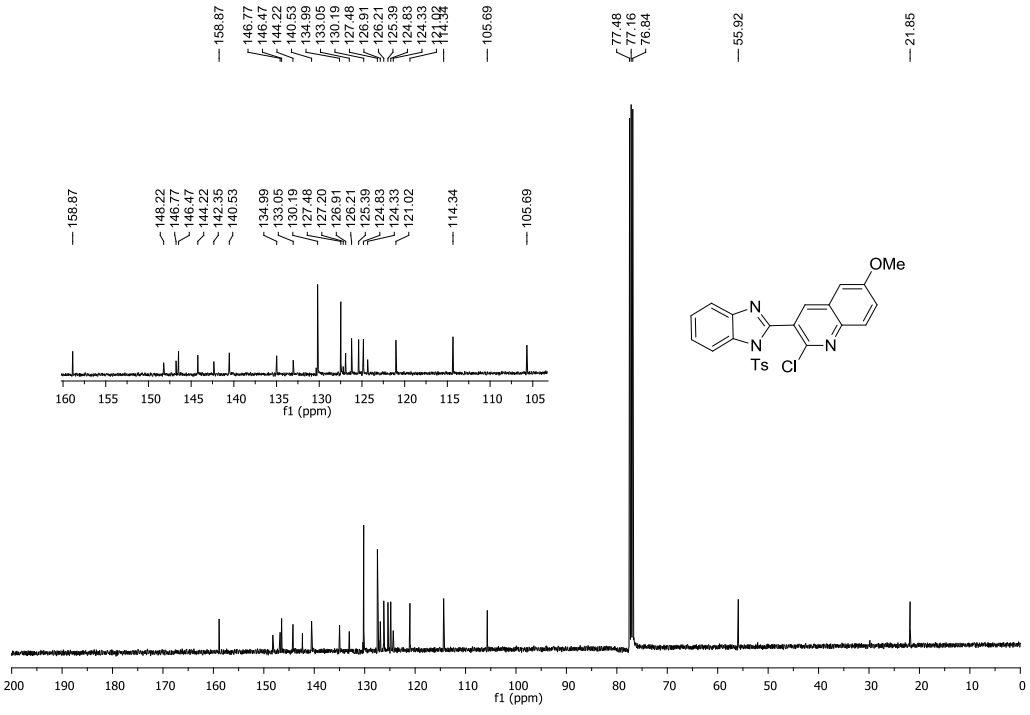


Figure 2.33 ^{13}C NMR spectrum of 2-chloro-6-methoxy-3-(1-tosylbenzo[d]imidazol-2-yl)quinolone (**2s**).

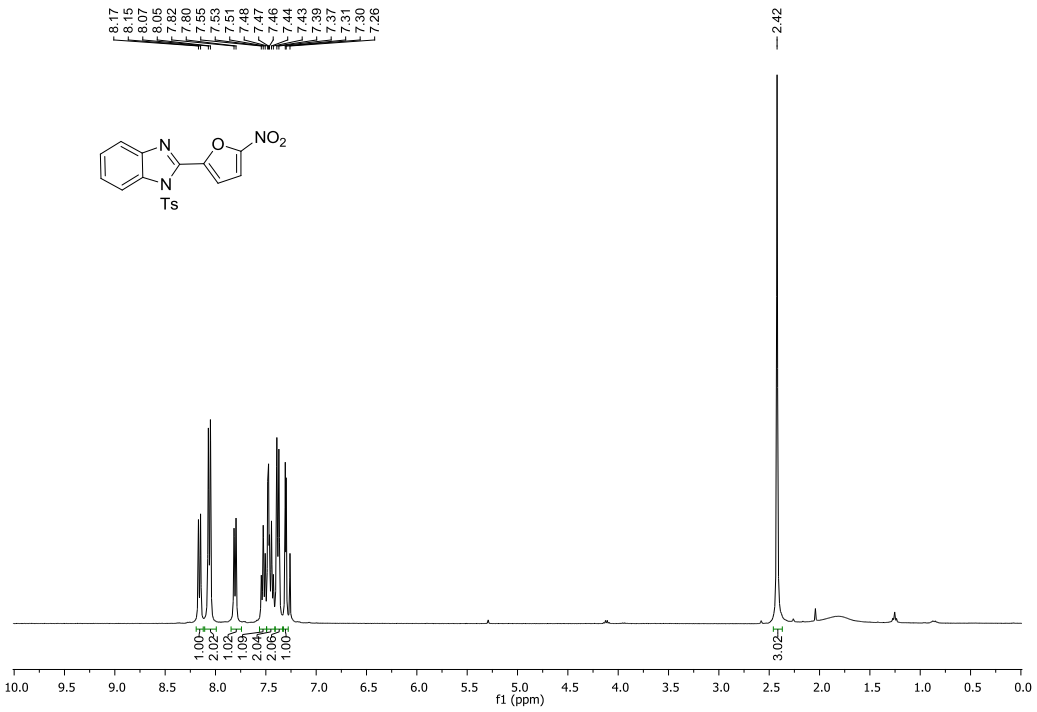


Figure 2.34 ^{1}H NMR spectrum of 2-(5-nitrofuran-2-yl)-1-tosylbenzo[d]imidazole (**2t**).

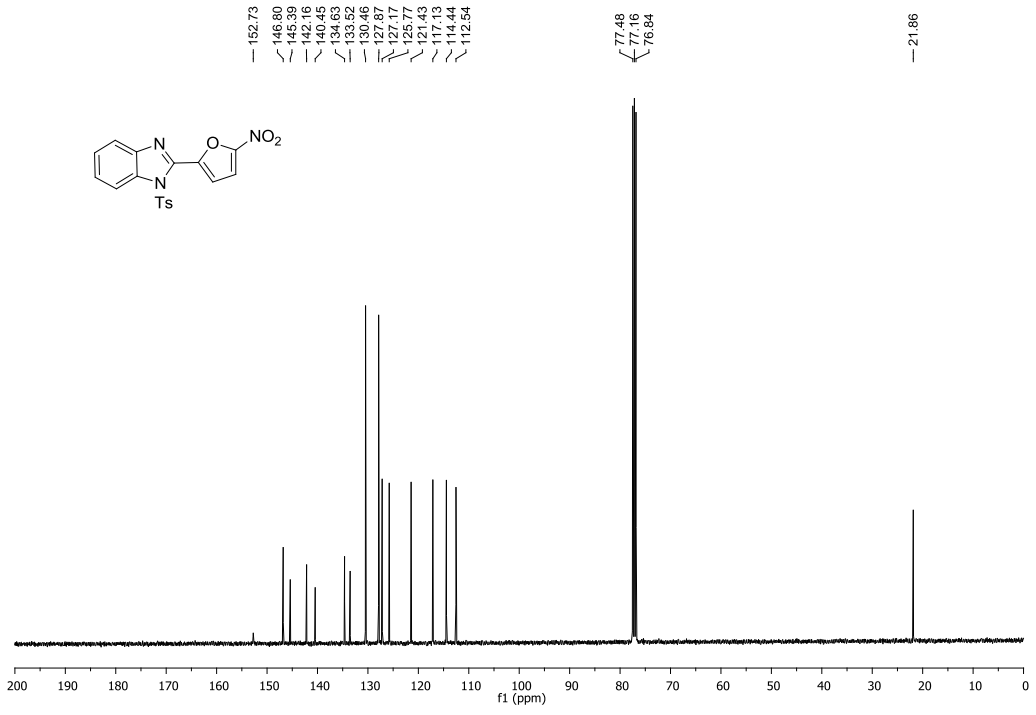


Figure 2.35 ^{13}C NMR spectrum of 2-(5-nitrofuran-2-yl)-1-tosylbenzo[d]imidazole (**2t**).

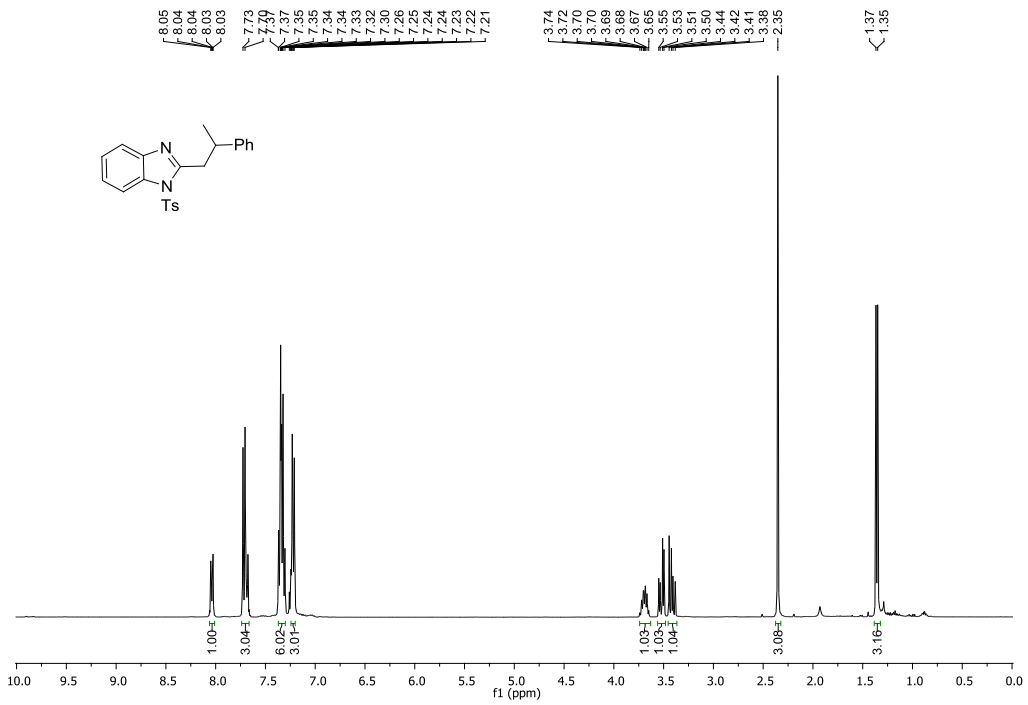


Figure 2.36 ^{1}H NMR spectrum of 2-(2-phenylpropyl)-1-tosylbenzo[d]imidazole (**2ac**).

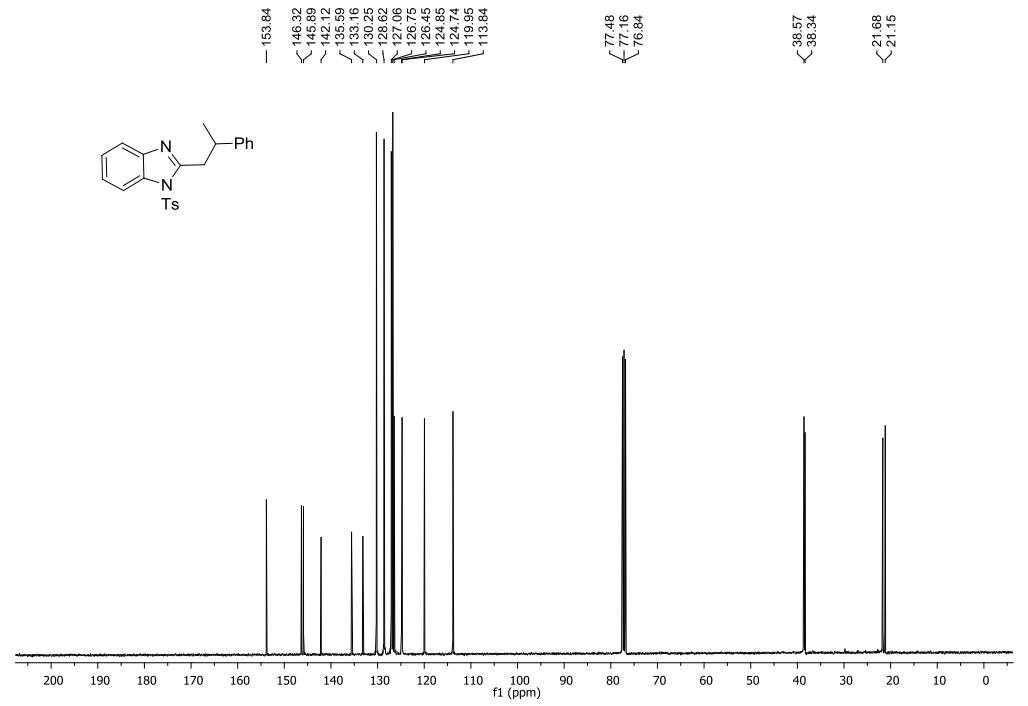


Figure 2.37 ^{13}C NMR spectrum of 2-(2-phenylpropyl)-1-tosylbenzo[d]imidazole (**2ac**).

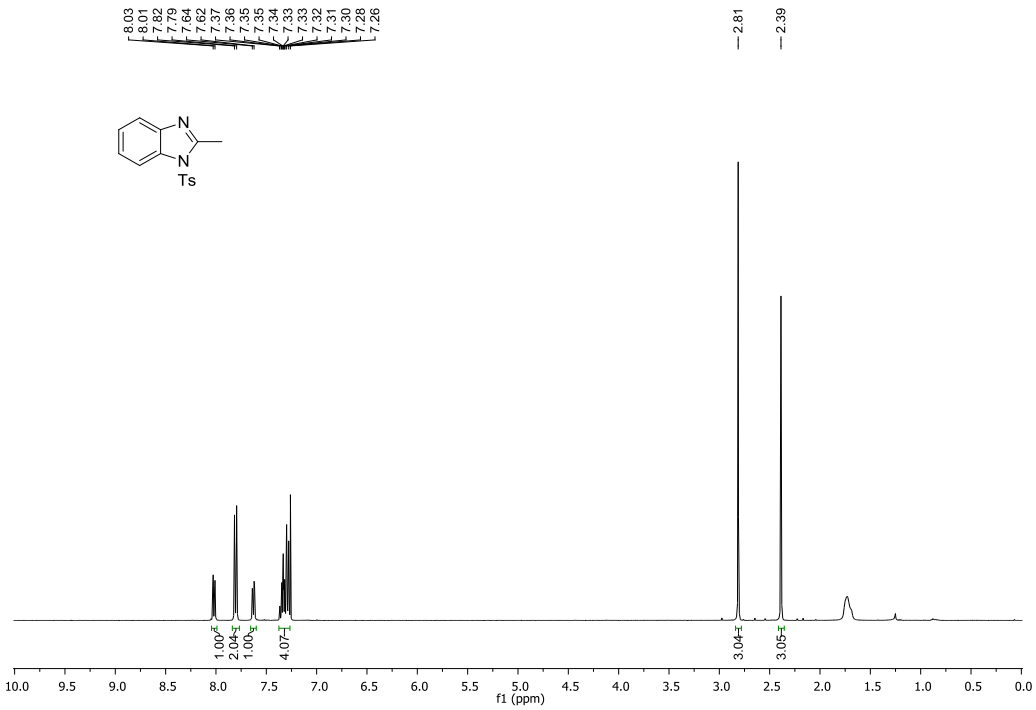


Figure 2.38 ^{1}H NMR spectrum of 2-methyl-1-tosylbenzo[d]imidazole (**2ad**).

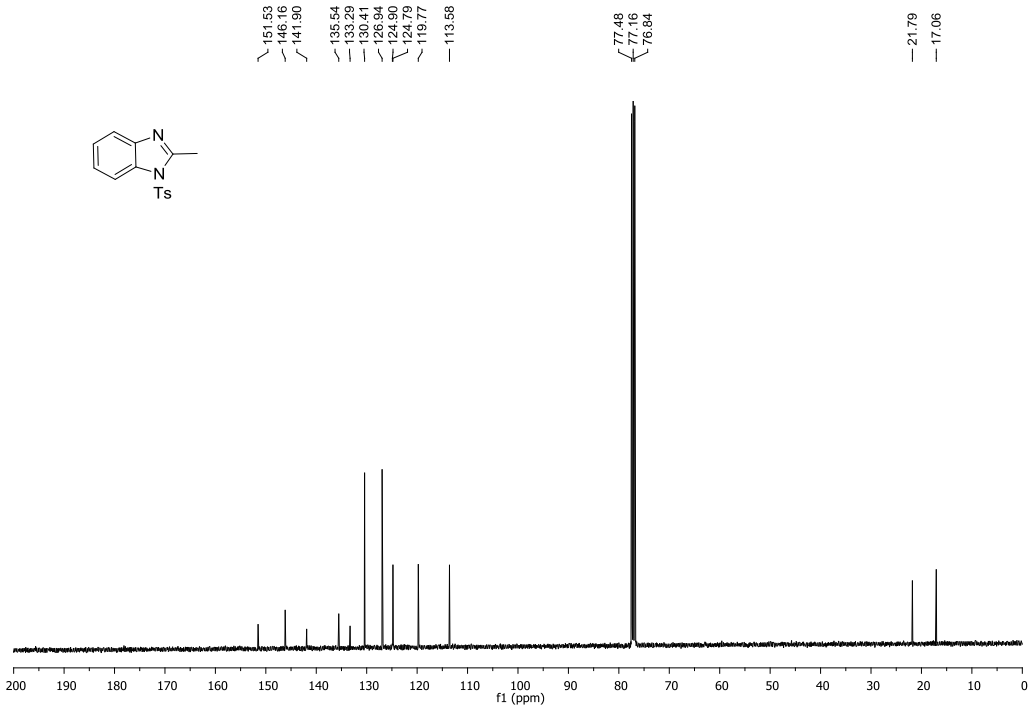


Figure 2.39 ^{13}C NMR spectrum of 2-methyl-1-tosylbenzo[d]imidazole (**2ad**).

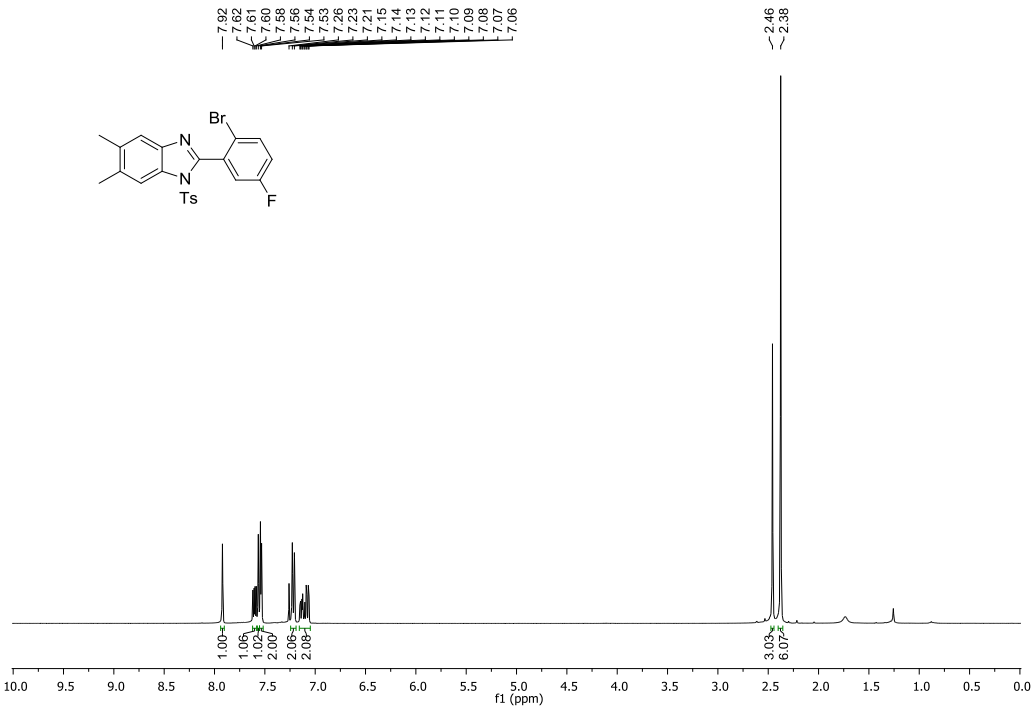


Figure 2.40 ^{1}H NMR spectrum of 2-(2-bromo-5-fluorophenyl)-5,6-dimethyl-1-tosylbenzo[d]imidazole (**2be**).

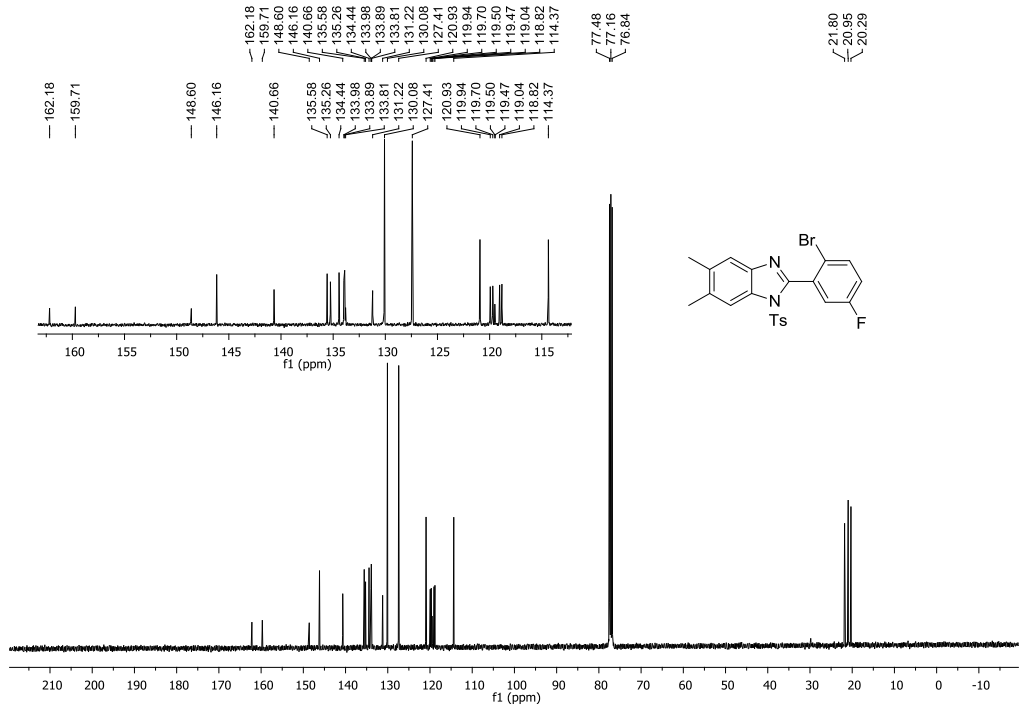


Figure 2.41 ^{13}C NMR spectrum of 2-(2-bromo-5-fluorophenyl)-5,6-dimethyl-1-tosylbenzo[d]imidazole (**2be**).

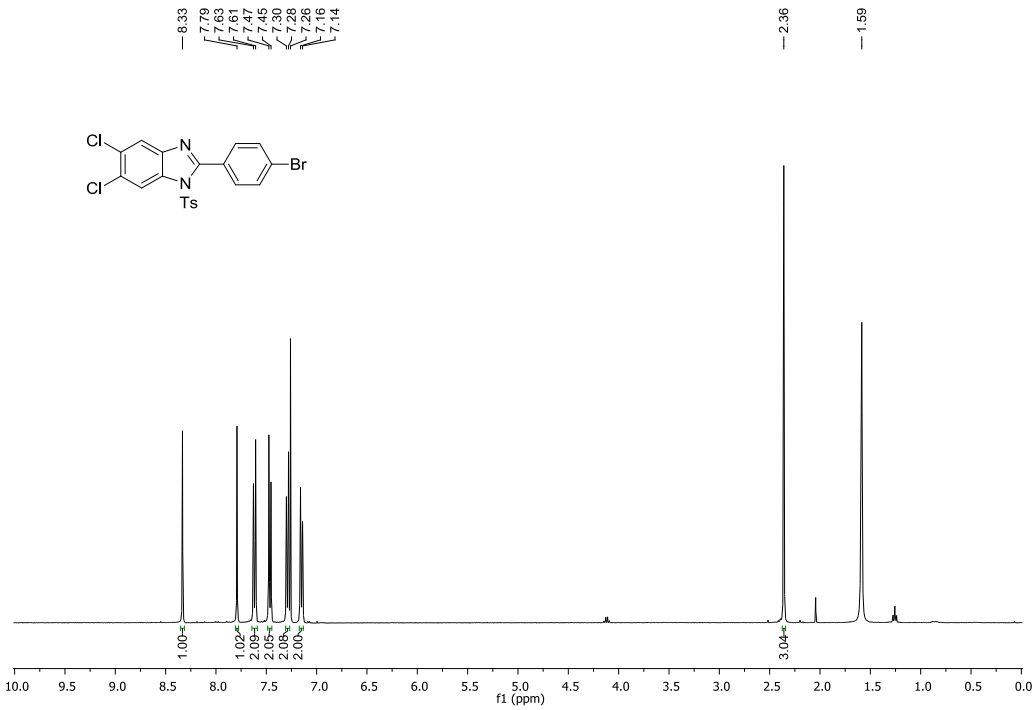


Figure 2.42 ^{1}H NMR spectrum of 2-(4-bromophenyl)-5,6-dichloro-1-tosylbenzo[d]imidazole (**2bf**).

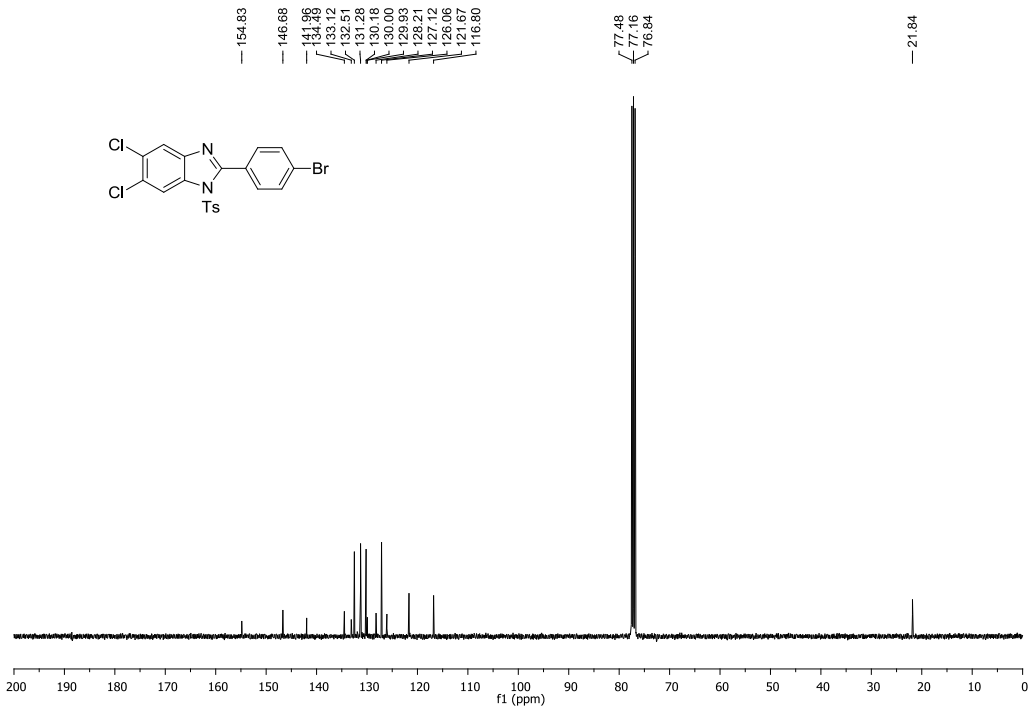


Figure 2.43 ^{13}C NMR spectrum of 2-(4-bromophenyl)-5,6-dichloro-1-tosylbenzo[d]imidazole (**2bf**).

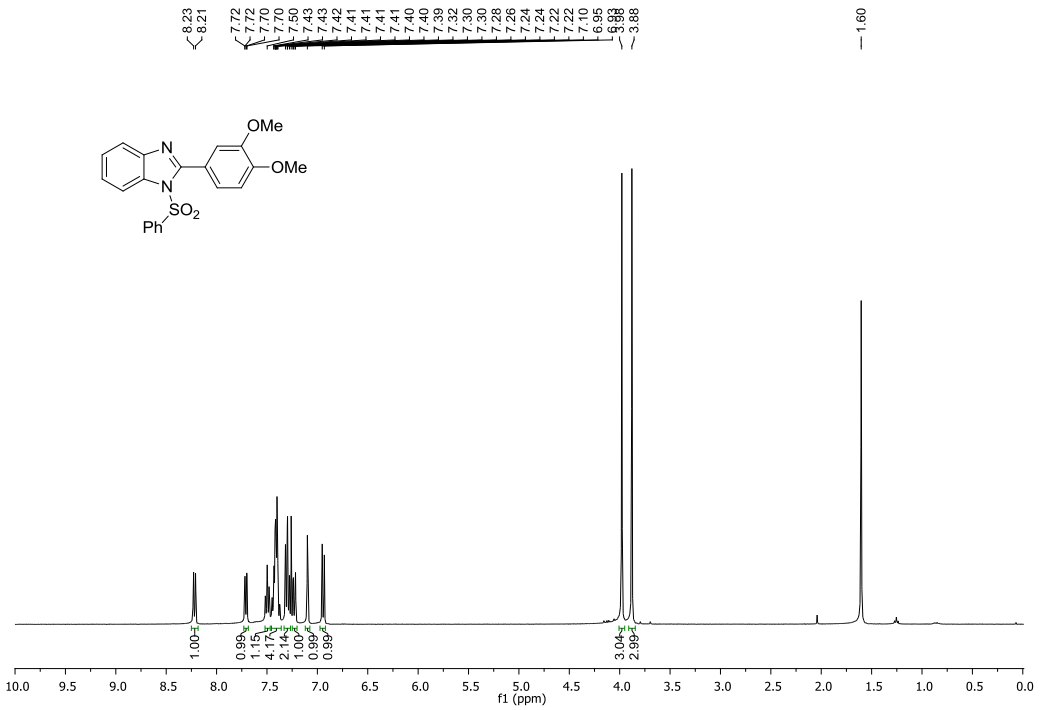


Figure 2.44 ^{1}H NMR spectrum of 2-(3,4-dimethoxyphenyl)-1-(phenylsulfonyl)benzo[d]imidazole (**2cb**).

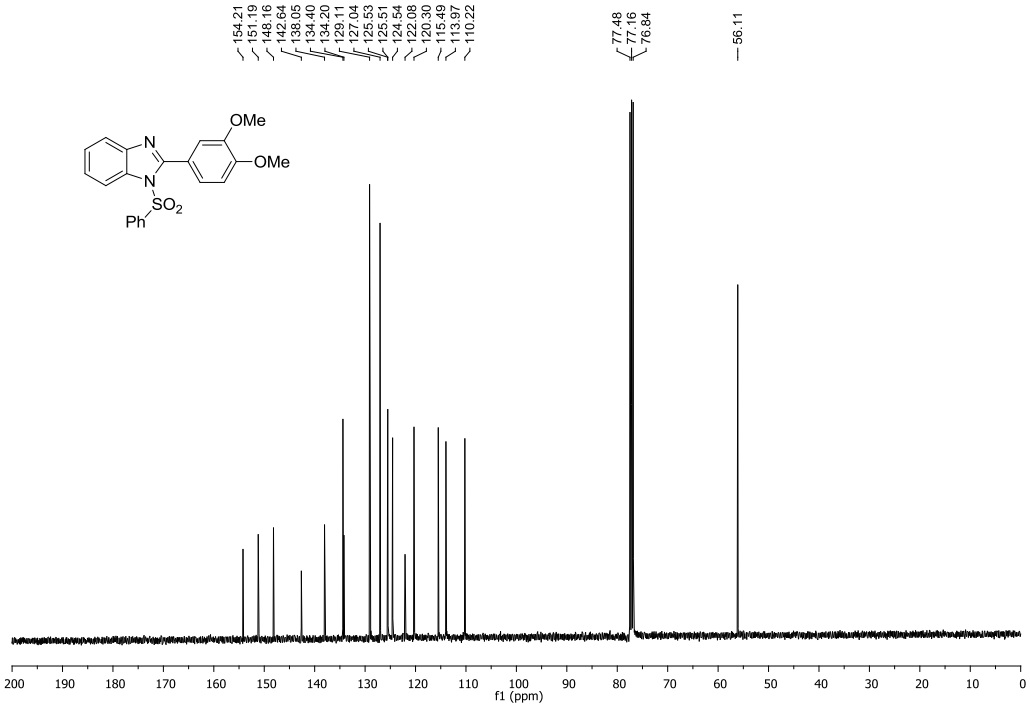


Figure 2.45 ^{13}C NMR spectrum of 2-(3,4-dimethoxyphenyl)-1-(phenylsulfonyl)benzo[d]imidazole (**2cb**).

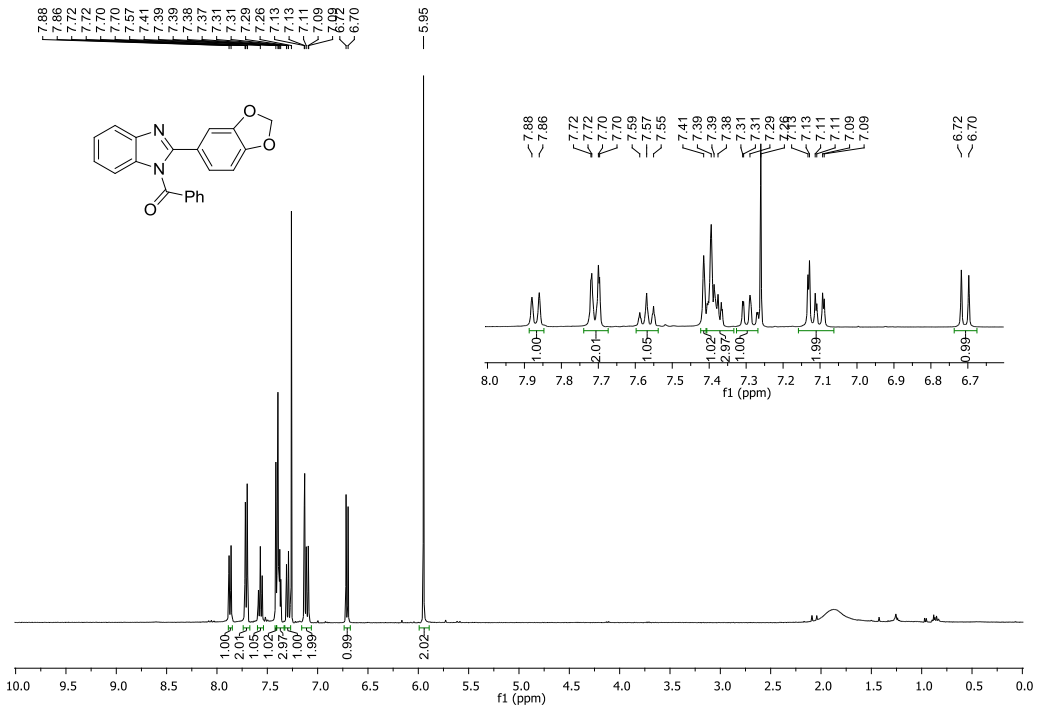


Figure 2.46 ^{1}H NMR spectrum of (2-(benzo[d][1,3]dioxol-5-yl)benzo[d]imidazol-1-yl)(phenyl)methanone (**2cc**).

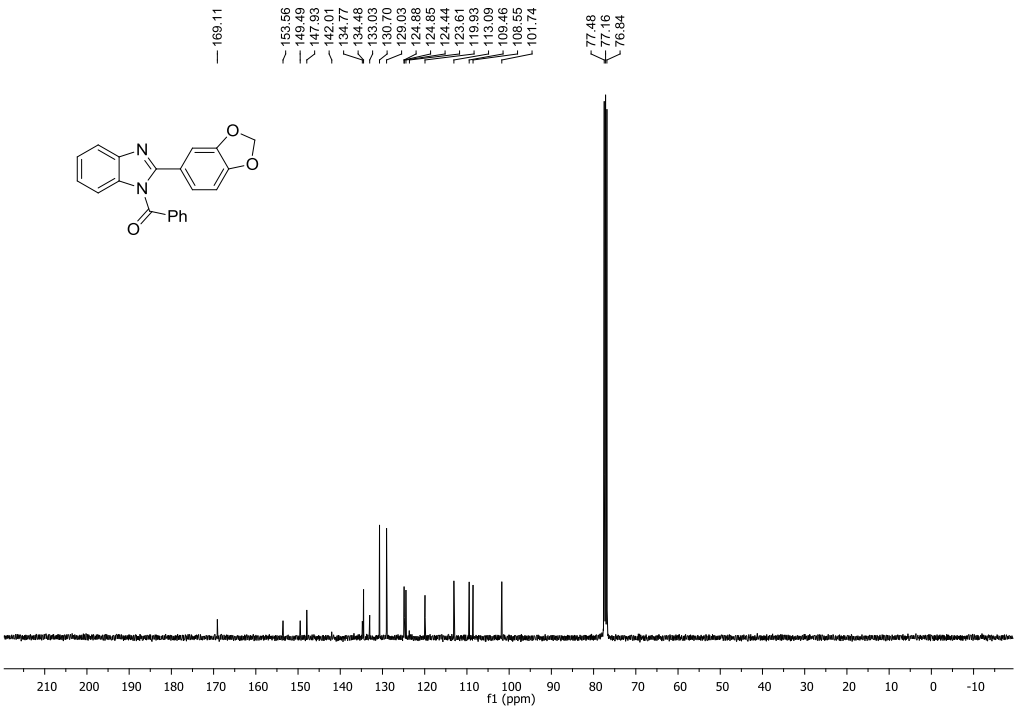
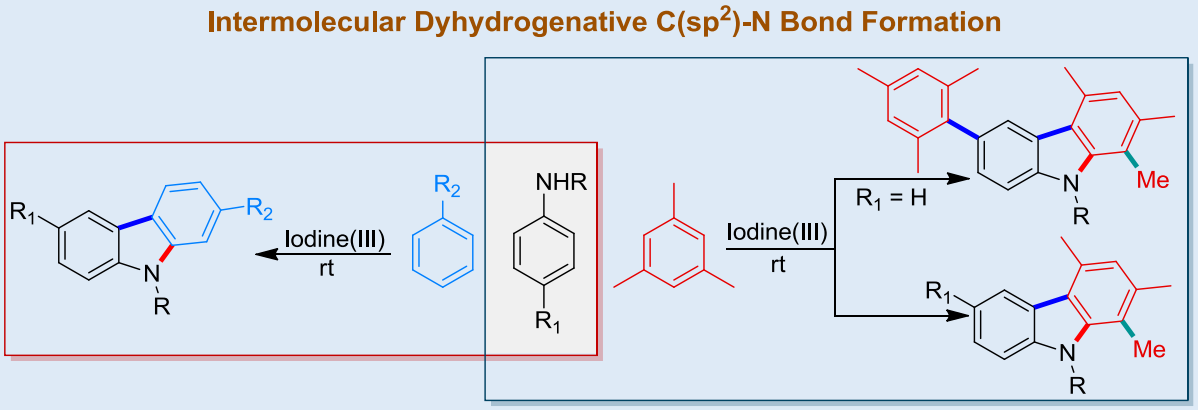


Figure 2.47 ^{13}C NMR spectrum of (2-(benzo[d][1,3]dioxol-5-yl)benzo[d]imidazol-1-yl)(phenyl)methanone (**2cc**).

CHAPTER 3

Carbazole Synthesis: Intermolecular Dehydrogenative C(sp^2)-N Bond Formation Approach

3.1 ABSTRACT



Hypervalent iodine(III) reagent aided intermolecular dehydrogenative C(sp^2)-N and C(sp^2)-C(sp^2) bond formation reaction have been developed for the construction of multisubstituted carbazole derivatives. Readily accessible and simplest precursor non-prefunctionalized anilides and arenes have been employed for coupling reaction to provide three ring heterocycle carbazole through annulation. Iodine(III) reagent was used as sole oxidant from either phenyliodine diacetate (PIDA) or by in-situ generated from catalytic amount iodoarene in presence of co-oxidant *meta*-chloroperbenzoic acid (*m*CPBA).

3.2 INTRODUCTION

Carbazoles are a class of important nitrogen-containing heterocycles, widely exist in several natural products and therapeutic agents.[1] Hence, they are attractive synthetic targets. Structure of some outstandingly important carbazole containing drug molecules have been shown in Figure 3.1. Ellipticine, a DNA intercalating agent is a naturally occurring plant alkaloid holds antitumor

activity.[2] Carvedilol and carazolol were identified for their potential as multiple-action antihypertensive drugs.[3] Carvedilol, a beta blocker is also used to treat heart failure.[4] In addition to their use in medicinal chemistry, carbazoles are also widely used as building blocks for potential organic semiconductors, organic light-emitting diodes, and electroluminescent materials.[5] In view of these important applications, we set out to develop some suitable methods for the synthesis of substituted carbazoles from commonly available feedstock.

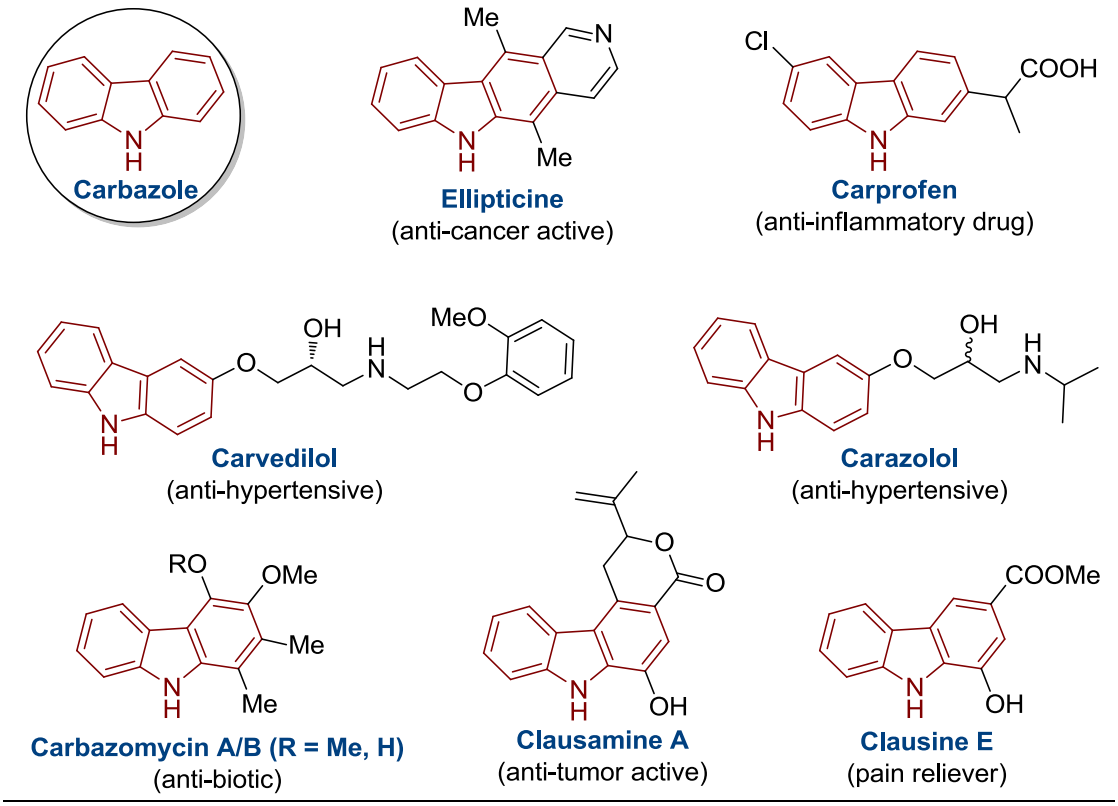


Figure 3.1 Carbazole containing drug molecules.

Commonly used strategies for the synthesis of carbazole molecules have been classified in two types: (a) intramolecular approach and (b) intermolecular approaches (Figure 3.2). In intramolecular approach carbazole molecules are in general derived either through C-C or through C-N bond formation reaction. Traditionally, intramolecular bond constructions are carried out from prefunctionalized substrates with the help of either metal[6] or under meta-free[7] conditions. Recently, with the advent and developed of transition metal chemistry C-H bond

activation approaches are also well practiced for carbazole synthesis through C-C[8] or C-N[9] bond formation. However, intermolecular approaches are relatively less studied for carbazole synthesis. Either two C-C[10] or one C-C and one C-N bond formation reactions can be followed in intermolecular approach.[11]

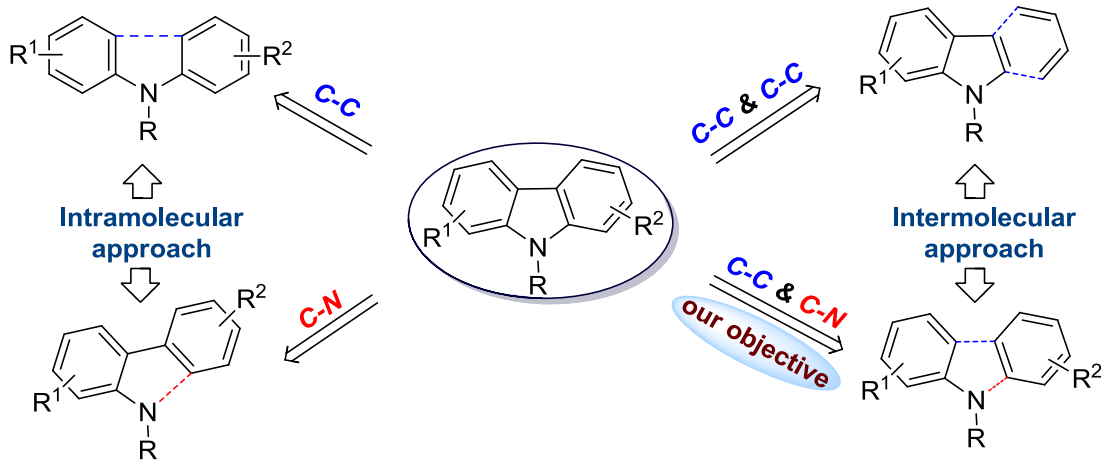
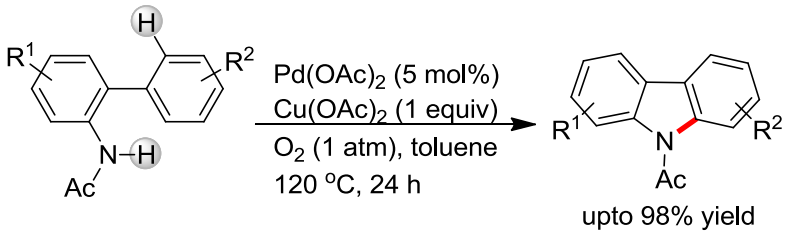


Figure 3.2 Strategies for carbazole synthesis.

Some literature reports for carbazole synthesis through C-N bond formation approach have been discussed here. These approaches have been classified in two types: (a) intramolecular C-N bond formation approach and (b) intermolecular C-N bond formation approach.

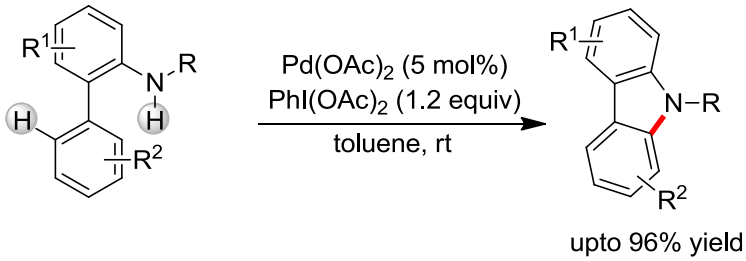
3.2.1 INTRAMOLECULAR C(sp^2)-N BOND FORMATION APPROACH

In 2005, Buchwald and co-workers established a Pd(II)-catalyzed intramolecular dehydrogenative C-N bond formation reaction by employing C-H activation strategy of 2-phenylacetanilides in presence of stoichiometric amount of $Cu(OAc)_2$ in toluene solvent under high temperature conditions (Scheme 3.1). Mechanistically the reaction goes through six membembered palladacycle *via* ortho-palladation process and subsequent reductive elimination of Pd(0). The role of $Cu(OAc)_2$ is to reoxidize Pd(0) to Pd(II).[12]



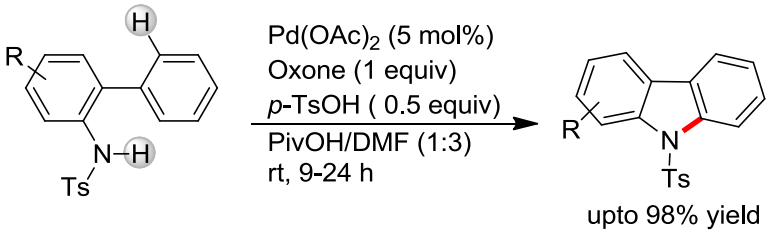
Scheme 3.1 Buchwald's Pd(II)-catalyzed approach.

In 2008, Gaunt *et. al.*, reported Pd(II) catalyzed oxidative C-H amination way for carbazole ring construction at room temperature conditions in toluene solvent (Scheme 3.2). The conversion has been carried out in presence of hypervalent iodine(III) reagent phenyliodine diacetate (PIDA) which oxidize Pd(II) to Pd(IV) and that Pd(IV) species is expected to undergo reductive elimination step more readily to facilitate dehydrogenative C-N bond formation.[13]



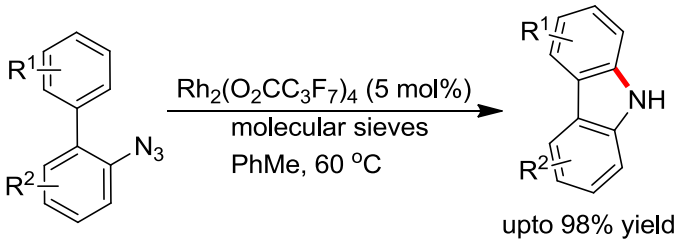
Scheme 3.2 Gaunt's Pd(II)-catalyzed approach.

A Pd(II)-catalyzed dehydrogenative C-H amination of *N*-Ts-2-arylanilines using oxone as an oxidant at ambient temperature has been developed by Youn and co-workers (Scheme 3.3).[14]



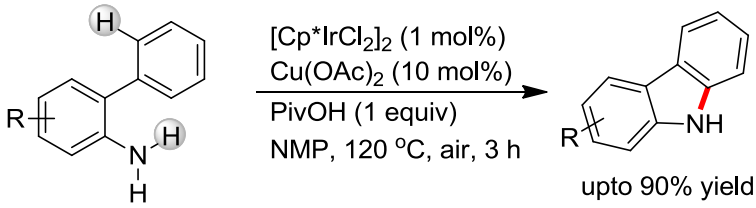
Scheme 3.3 Youn's Pd(II)-catalyzed approach.

In 2009, Driver *et. al.*, described synthesis of carbazoles from substituted biaryl azides using Rh_2(II)-carboxylate catalyst (Scheme 3.4).[15]



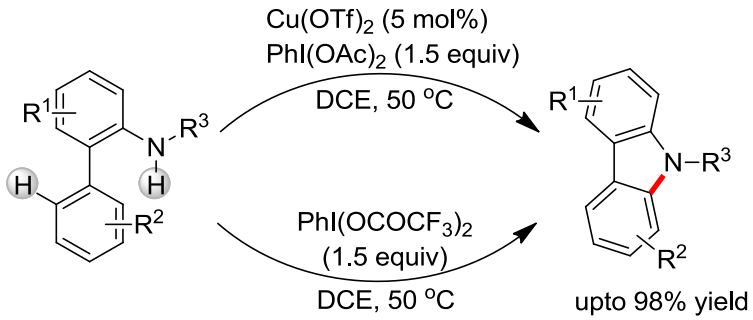
Scheme 3.4 Driver's Rh(II)-catalyzed approach.

Recently, Miura and co-workers have developed an iridium(III) catalyzed dehydrogenative cyclization of 2-aminobiphenyls in presence of copper(II) cocatalyst as terminal oxidant under aerobic conditions through intramolecular C-H bond activation to produce NH-carbazoles (Scheme 3.5). The reaction proceed through six-membered iridacycle intermediate.[16]



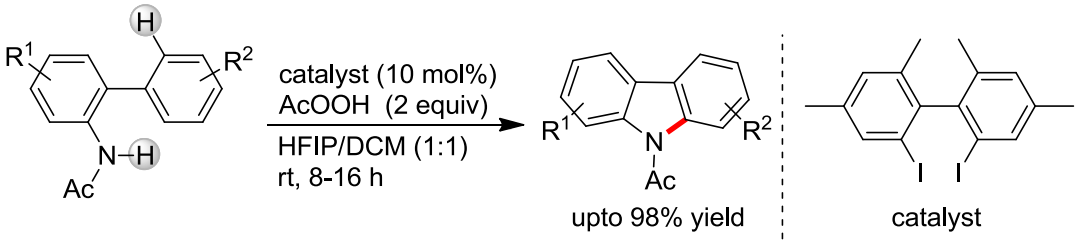
Scheme 3.5 Miura's Ir(III)-catalyzed approach.

In 2011, a new synthetic procedure for intramolecular dehydrogenative C-N bond formation reaction has been established by Chang and co-workers for the construction of carbazoles from *N*-substituted 2-amidobyphenyls under either Cu(II) catalyzed or metal-free conditions using hypervalent iodine(III) as oxidant (Scheme 3.6). Combination of copper(II) triflet and iodine(III) species significantly improves the reaction efficiency than use of only phenyliodine diacete (PIDA) or bis(trifluoroacetoxy)iodobenzene (PIFA). The reaction is believed to operate through a radical mechanism where the Cu(II) species serves as a Lewis acid to activate the hypervalent iodine(III) reagent.[17]



Scheme 3.6 Chang's Cu(II)-catalyzed and metal-free approach.

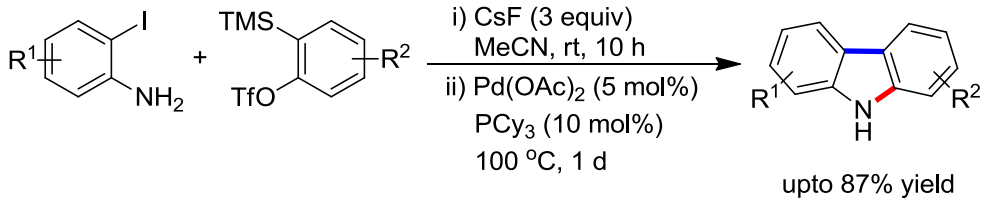
In the same year, Antonchick *et. al.*, developed an atom economical, environmentally friendly organocatalytic method for the synthesis of carbazoles from 2-acetaminobiphenyl substrates through intramolecular C-H amination reaction (Scheme 3.7). *In-situ* generated hypervalent iodine(III) reagent has been used for the dehydrogenative C-N bond formation reaction. Diiodobiphenyl compound acted as catalyst in presence of peracetic acid (AcOOH) to produce μ-oxo-bridged reactive hypervalent iodine(III) species which promote the reaction to proceed through generation of nitrenium ion intermediate and subsequent aromatic electrophilic substitution.[18]



Scheme 3.7 Antonchick's organocatalytic approach.

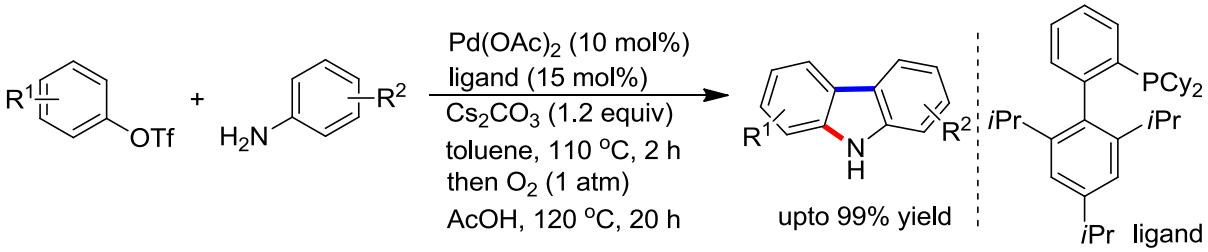
3.2.2 INTERMOLECULAR C(sp^2)-N BOND FORMATION APPROACH

In 2004, Larock and co-workers introduced an intermolecular route to synthesize a variety of carbazoles from the reaction of *o*-iodoanilines and silylaryl triflets in presence of CsF to afford N-arylated products, which subsequently undergo cyclization in presence of Pd-catalyst (Scheme 3.8).[19]



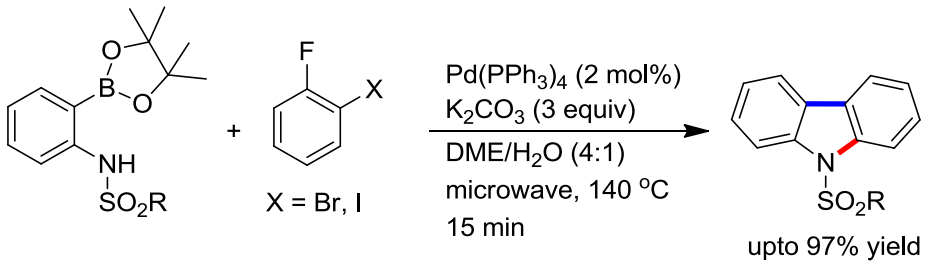
Scheme 3.8 Larock's approach using Pd(II) catalyst.

In 2009, Fujii and co-workers developed a Pd(II)-catalyzed one pot *N*-arylation and oxidative biaryl coupling reaction for the synthesis of carbazole (Scheme 3.9). Readily available anilines and aryl triflets have been operated for the intermolecular approach in presence of bulky phosphine ligand under heating conditions.[20]



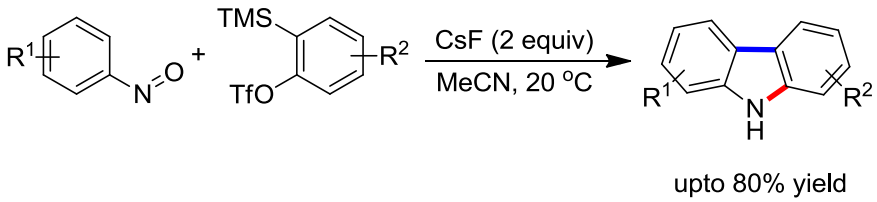
Scheme 3.9 Fujii's approach using Pd(II) catalyst.

A Pd(0)-catalyzed tandem Suzuki cross-coupling/S_NAr protocol was introduced by David *et. al.*, under microwave conditions for the synthesis of functionalized carbazole from anilide boronic esters and 1, 2-dihaloarenes (Scheme 3.10). The process was found to be compatible with a variety of electron-withdrawing groups including aldehydes, esters, and sulfones.[21]



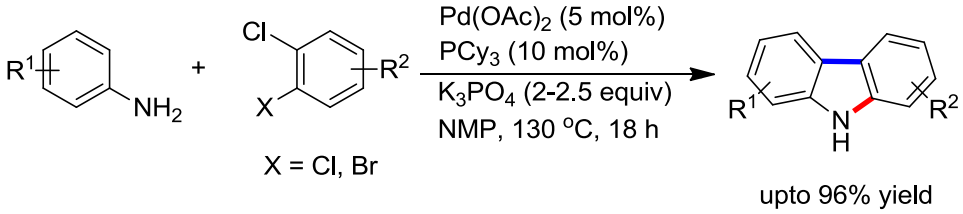
Scheme 3.10 David's approach from anilide boronic ester using Pd(II) catalyst.

Recently, Chakrabarty *et. al.*, established a transition metal-free intermolecular approach for the synthesis of carbazole by reaction of silylaryl triflets and nitrosoarenes at room temperature conditions (Scheme 3.11). CsF has been used as sole reagent for the transformation. Depending on the fluoride source and the solvent, either NH-carbazoles (for CsF in CH_3CN) or N-arylated carbazoles (for TBAT in DME) were obtained.[22]



Scheme 3.11 Studer's approach using Pd(II) catalyst.

In 2007, Ackermann and co-workers have reported a Pd(II)-catalyzed domino N-H/C-H bond activation for synthesis of carbazoles in intermolecular approach (Scheme 3.12). The transition metal catalyzed method involve coupling between substituted anilines and 1, 2-dihaloarenes under heating conditions.[23]



Scheme 3.12 Ackermann's approach using Pd(II) catalyst.

Literature survey reveals that most of the intramolecular approaches are based on preorganized substrates. Intermolecular approaches are relatively advantageous in sense of step economy. But all the reported intermolecular approaches are associated with one common drawback that is requirement of prefunctionalized substrates since those are non-dehydrogenative in nature which makes the ultimate process multistep and cost effective. Moreover, most of the methods require use of toxic and costly (transition) metal as reagent or catalyst. Metal free approaches

are preferable because trace amount of metal may alter the biological activities and physical properties of a compound.[24] To best of our knowledge, transition metal-free intermolecular dehydrogenative annulation approach for carbazole synthesis has so far remained elusive. Therefore development of metal-free method for carbazole synthesis from unfunctionalized arenes was of utmost importance.

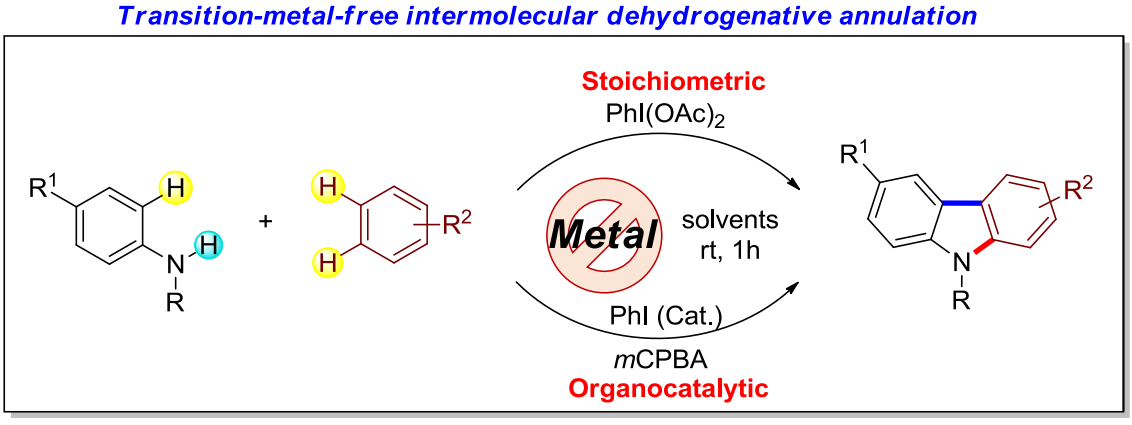
CHAPTER 3: PART A

Transition-Metal-Free Intermolecular C-H Amination : Synthesis of Carbazole from Non-Prefunctionalized Arene

3.A1 ABSTRACT

Herein we demonstrate hypervalent iodine(III) mediated intermolecular dehydrogenative annulation towards synthesis of carbazole derivatives in one pot via oxidative coupling of unprefunctionalized arenes and aniline derivatives (Scheme 3.A1). Three C–H and one N–H bonds were sequentially functionalized in a single operational method from two different molecule for a tandem C–N and C–C bond formation reactions of carbazole synthesis. The iodine(III) could be used either stoichiometrically from phenyleneiodine diacetate (PIDA) or organocatalytically in situ generated from iodobenzene-*m*CPBA. Thus an unprecedented method of carbazole synthesis has been developed from unactivated arenes via intermolecular coupling reaction under transition metal-free conditions.

Herein, we disclose our result on discovery of transition metal-free intermolecular dehydrogenative annulation reaction for *N*-substituted carbazole synthesis *via* tandem C–N/C–C bond formation through sequential C–H/N–H bond functionalization (Scheme 3.A1).



Scheme 3.A1 Our iodine(III) enabled dehydrogenative annulation approach.

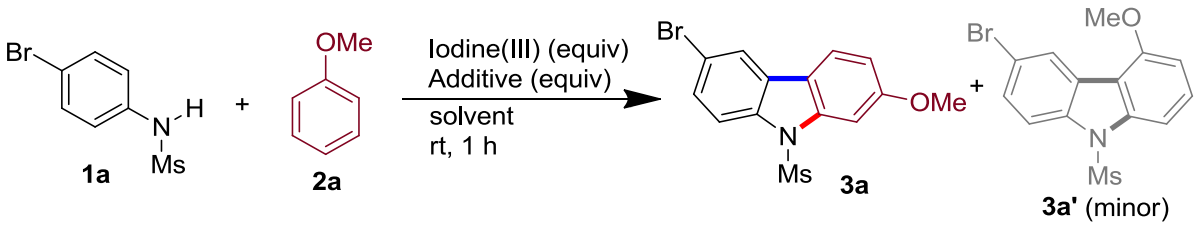
We have utilized unfunctionalized anilines and arenes for hypervalent iodine(III) facilitated intermolecular coupling reactions under stoichiometric as well as oraganocatalytic conditions. We anticipated that adding nitrogen functionalities intermolecularly into unactivated arenes through functionalization of C–H (and N–H) bonds might lead to a powerful approach towards achieving the goal of synthesis of nitrogen based heterocycles in a single operational method.

3.A2 RESULT AND DISCUSSION

N-(4-bromophenyl)methanesulfonamide (**1a**) and anisole (**2a**) were considered as model substrate for optimization of intermolecular dehydrogenative annulation reaction. Substrate **1a** was prepared by the reaction of commercially available 4-bromoaniline and methane sulfonyl chloride in presence of pyridine by following literature report. For stoichiometric optimization (Method A), substrate **1a** and **2a** (3.0 equiv) were treated with 2.5 equiv of phenyliodine diacetate (PIDA) at room temperature in 2,2,2-trifluoroethanol (TFE) (0.2 M) and the desired 6-bromo-2-methoxy-9-(methylsulfonyl)carbazole (**3a**) was obtained in 34% yield (Table 3A.1, entry 1). Nevertheless, 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) was found to be most efficient among the solvents were examined (Table 3A.1, entry 2-4). In addition, we extended our investigation by varying different iodine(III) reagents as oxidant. Stronger oxidant $PhI(OCOCF_3)_2$ (PIFA) could not afford better yield (Table 3A.1, entry 5) of **3a** and iodosylbenzene (PhIO) was found to be ineffective at the studied conditions (Table 3A.1, entry 6). Other oxidants like $PhI(OCOPh)_2$, HTIB or $PhI(OPiv)_2$ were also inefficient to provide promising results than PIDA (Table 3A.1, entry 7, 8, 11). The significant increase in yield was observed by diluting the reaction mixture to 0.1 M using HFIP/DCM (1:1) (Table 3A.1, entry 9). Most appropriate condition was identified when 1.0 equiv of **1a** and 3.0 equiv of **2a** were treated with 2.5 equiv of phenyliodine diacetate (PIDA) in presence of 2.5 equiv of additive K_2CO_3 at 0.1 M in HFIP/DCM (1:1). The desired product **3a** was isolated in 78% yield within

1 h at room temperature under aerobic conditions (Table 3A.1, entry 10). Use of Lewis acid additive like $BF_3.Et_2O$ or acidic additive like AcOH did not offer a more favorable result (Table 3A.1, entry 13-14). Most of the arenes (**2**) are volatile in nature and therefore use of 3 equiv was established as the optimum amount for the reaction (Table 3A.1, entry 15).

Table 3A.1 Optimization of reaction conditions (Method A)

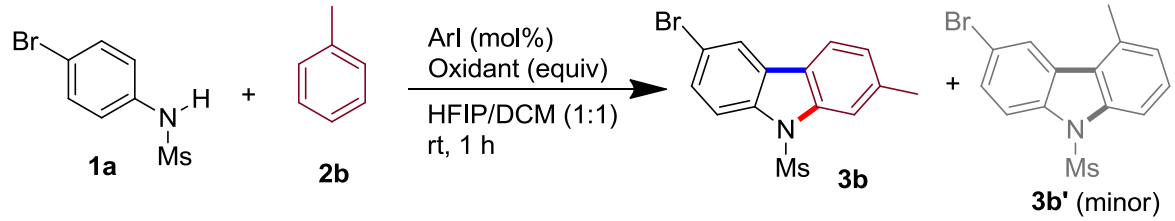


Entry	Iodine(III) (2.5 equiv)	Additive (2.5 equiv)	Solvent	Yield of 3a (%)[b]
1	PIDA	---	CF_3CH_2OH	34
2	PIDA	---	DCM	10
3	PIDA	---	ACN	0
4	PIDA	---	HFIP	57
5	PIFA	---	HFIP	21
6	PhIO	---	HFIP	<5
7	$PhI(OCOPh)_2$	---	HFIP	44
8[c]	HTIB	---	HFIP	18
9	PIDA	---	HFIP:DCM(1:1)	66
10	PIDA	K_2CO_3	HFIP:DCM(1:1)	78
11	$PhI(OPiv)_2$	K_2CO_3	HFIP:DCM(1:1)	41
12	PIDA	K_2CO_3	HFIP	67
13	PIDA	AcOH	HFIP	35
14	PIDA	$BF_3.Et_2O$	HFIP	<5
15[d]	PIDA	K_2CO_3	HFIP:DCM(1:1)	30

[a]Unless mentioned 3.0 equiv of **2a** was used. [b]Yield of isolated product after column chromatography. [c]HTIB = Hydroxy(tosyloxy)iodobezene. [d]1.1 equiv of **2a** was used. HFIP = 1,1,1,3,3,3-hexafluoro-2-propanol.

The organocatalytic approach (Method B) was screened by using various iodoarene in catalytic amount and oxidants which facilitated in situ generation of iodine(III) reagent (Table 3A.2, entry 1-3, 6-7). The desired product 6-bromo-2-methyl-9-(methylsulfonyl)carbazole (**3b**) from **1a** and toluene (**1b**) was isolated in 52% yield when 20 mol% of iodobenzene (PhI) and 3.0 equiv of oxidant *meta*-chloroperbenzoic acid (*m*CPBA) were used at room temperature in HFIP/DCM (1:1). Besides, either increasing the catalyst loading (Table 3A.2, entry 5) or use of additive like K_2CO_3 (Table 3A.2, entry 4) did not lead to any improvement of yield.

Table 3B.1 Optimization of reaction conditions (Method B)



Entry	ArI (mol%)	Oxidant (equiv)	Additives (equiv)	Yield of 3b (%)
1	4-NO_2-C_6H_4I (20)	*m*CPBA (3)	---	trace
2	4-MeO-C_6H_4I (20)	*m*CPBA (3)	---	12
3	C_6H_5I (20)	*m*CPBA (3)	---	52
4	C_6H_5I (20)	*m*CPBA (3)	K_2CO_3 (3)	21
5	C_6H_5I (30)	*m*CPBA (3)	---	49
6	C_6H_5I (20)	TBHP in decane (3)	---	NR
7	C_6H_5I (20)	DTBP (3)	---	NR
8[a]	C_6H_5I (20)	*m*CPBA (3)	---	46

[a]Reaction was carried out at 0 °C

The optimized annulation protocol was subsequently applied to a series of simple arenes and anilides to explore the substrate scope of multi-substituted carbazole synthesis (Figure 3A.1).

Regioselective carbazole derivatives were isolated in good yields under standard conditions. A wide array of simple anilides with different functional groups at *para*-position were compatible here. Electron withdrawing groups like -halo (**3a-3h, 3o-3r, 3w**) or phenyl groups (**3u**) and electron donating alkyl groups (**3j-3n, 3s-3t, 3v, 3y, 3aa**) on anilide substrates were fair yielding as well, under both stoichiometric and organocatalytic conditions. In general, benzene

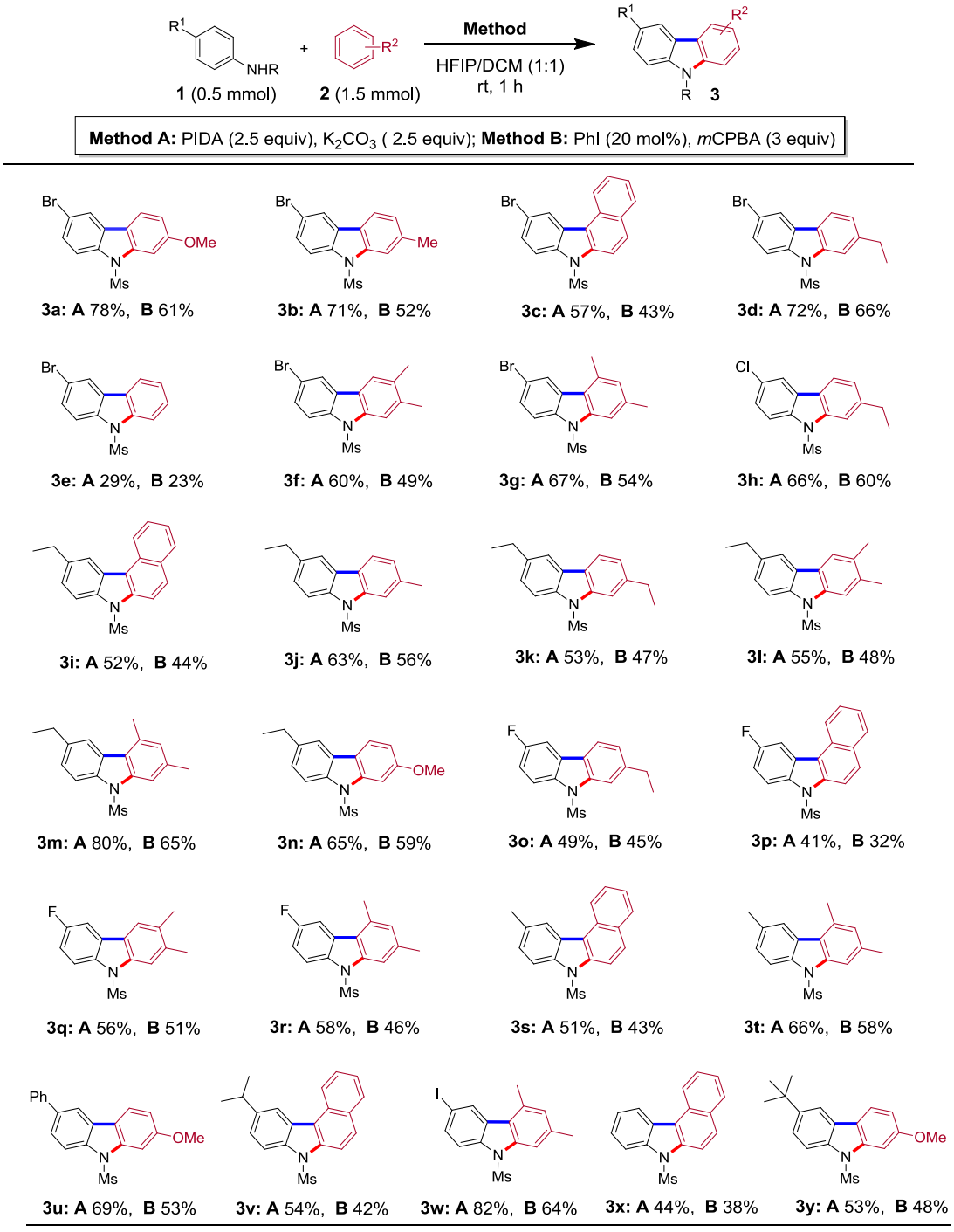


Figure 3A.1 Scope of intermolecular annulation reaction.

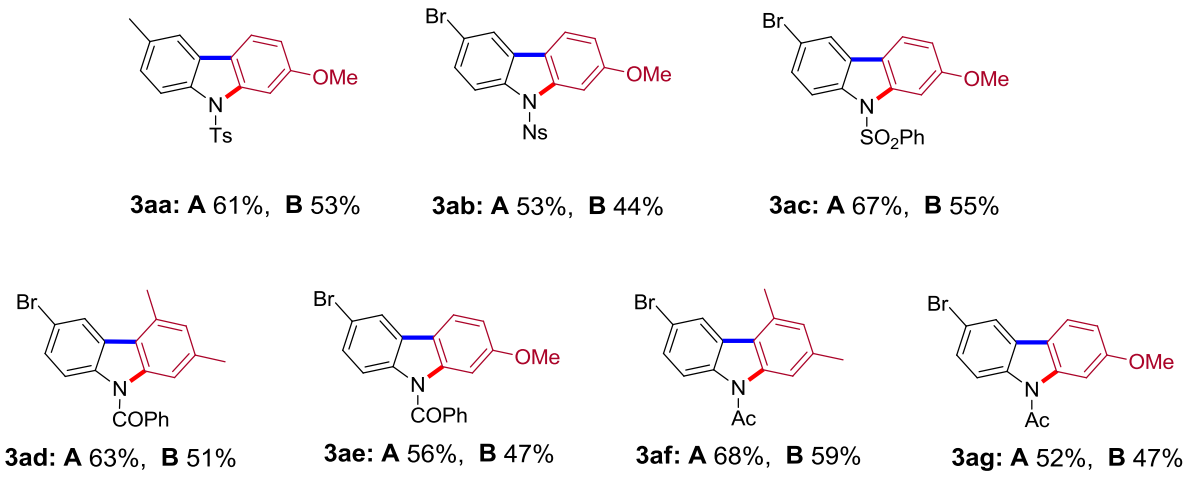


Figure 3A.2 Scope of *N*-substituted carbazole ring construction.

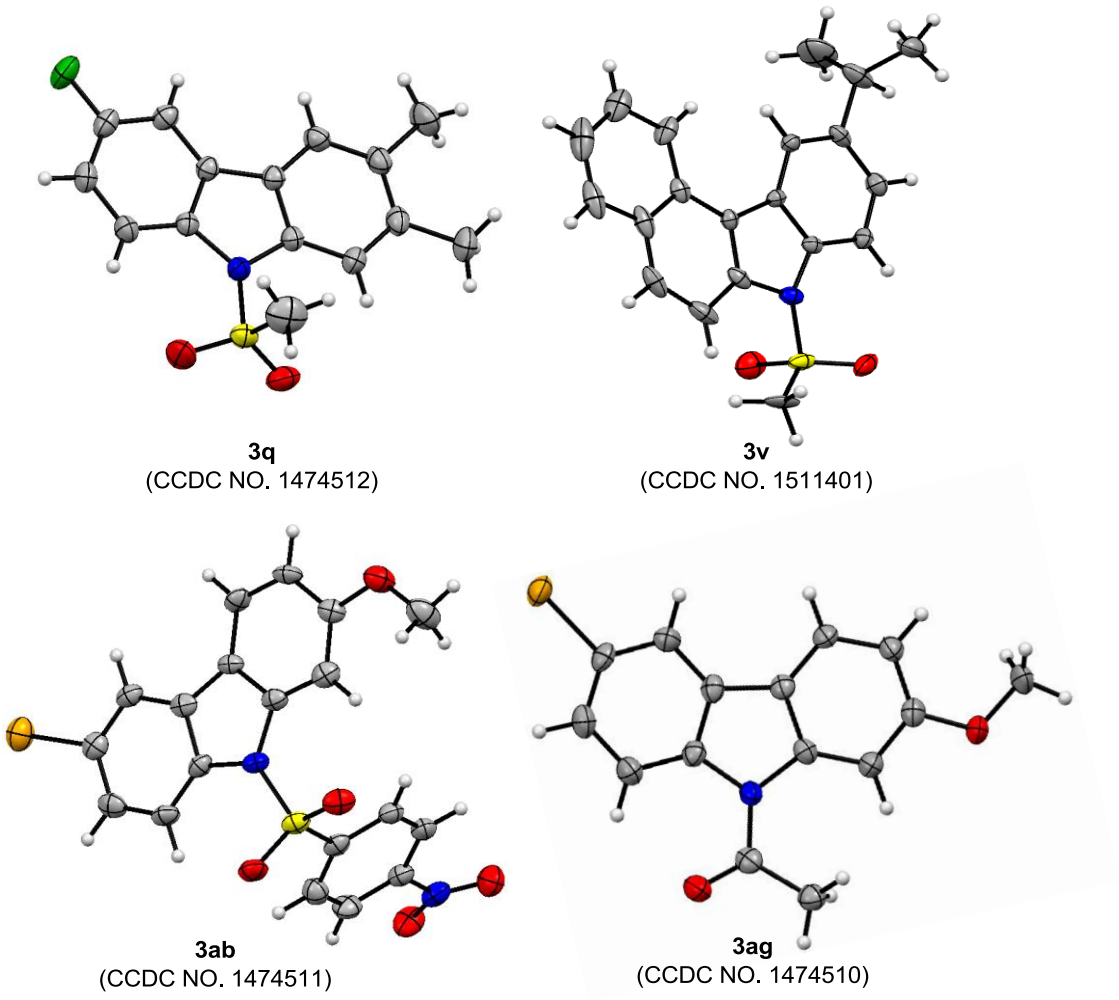


Figure 3A.3 X-ray structure of compound **3q, 3v, 3ab, 3ag**.

substrates with electron donating groups like alkyl or alkoxy undertook cyclization more readily on anilide substrates.

Furthermore, varying substituents at *N*-center of aniline like different sulfonyl, carbonyl groups were also found to be efficient in carbazole synthesis (Figure 3A.2). In all cases better yields were observed for stoichiometric pathway over organocatalytic one. Some of the synthesized carbazole derivatives were characterized by X-ray crystallographic analysis (**3q, 3v, 3ab, 3ag**) (Figure 3A.3).

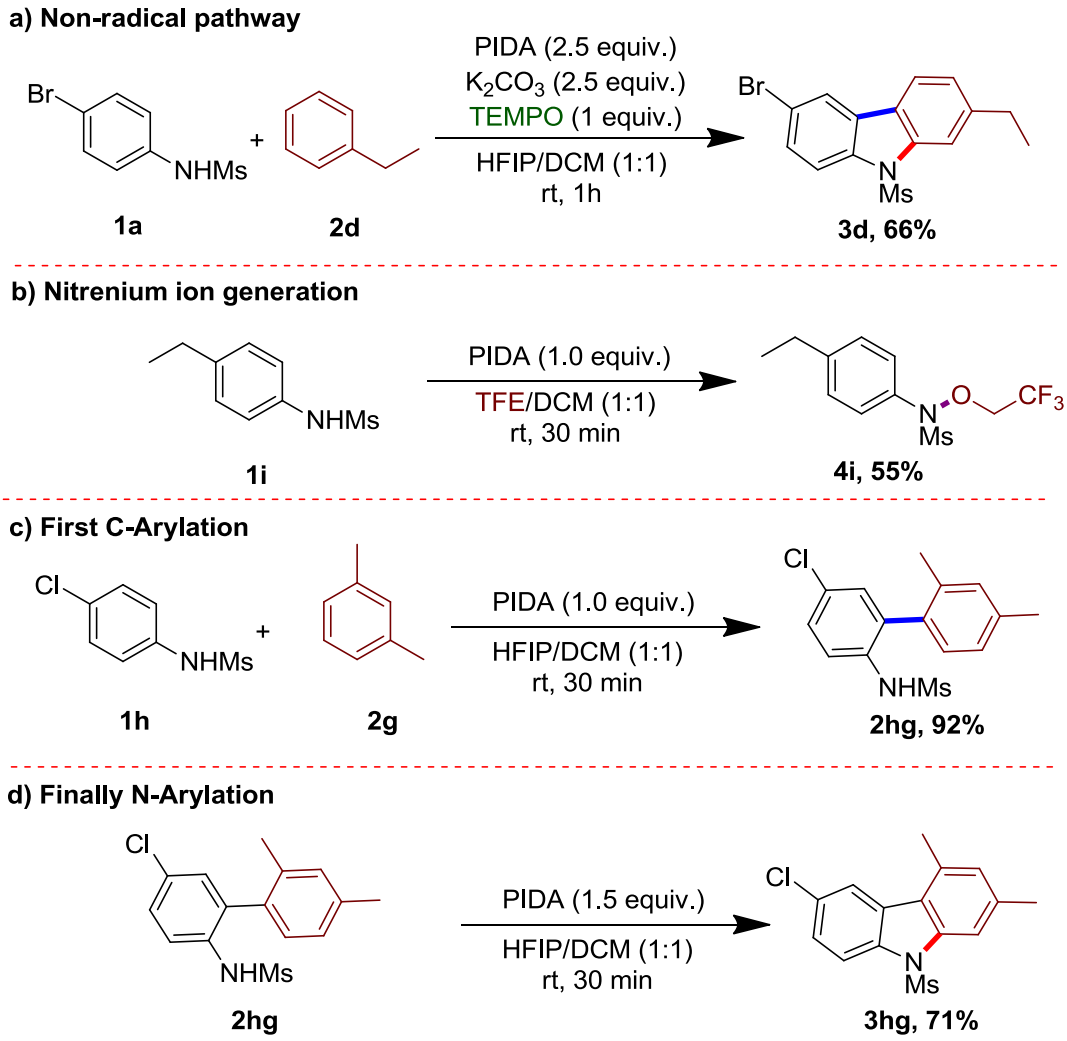


Figure 3A.4 Control experiments.

Based on control experiments (Figure 3A.4) and literature precedence, the plausible mechanism of the intermolecular dehydrogenative annulation reaction is proposed in Figure 3A.5. Upon reaction of *N*-(4-bromophenyl)methanesulfonamide (**1a**) with ethyl benzene (**2d**) under standard conditions and in presence of stoichiometric amount of radical scavenger TEMPO, the product **3d** was isolated in 66% yield (Figure 3A.4a). Absence of any radical trapped product could clearly rule out the possibility of radical pathway. Anilide **1**, upon reaction with PIDA generates nitrenium ion[25] intermediate (**5**) (Figure 3A.5). Formation of nitrenium ion (**5**) was confirmed when sulfoanilide **1i** was treated with 1.0 equiv of PIDA in 2,2,2-trifluoroethanol (TFE) to yield solvent incorporated product *N*-(4-ethylphenyl)-*N*-(2,2,2 trifluoroethoxy)methanesulfonamide (**4i**) in 55% (Figure 3A.4b). Similarly, existence of nitrenium ion is also reported by Kikugawa and co-workers in iodine(III) mediated alkoxylation reaction.[26] Nitrenium ion intermediate expected to get stabilized by charge delocalization to carbenium ion intermediate **6** (Figure 3A.5).[27] Nucleophilic attack from non-prefunctionalized arene possibly took take place to either carbenium ion **6** (C-C bond formation) or to nitrenium ion **5** (C-N bond formation). Reaction of *N*-(4-chlorophenyl)methanesulfonamide (**1h**) with *m*-xylene in presence of 1.0 equiv of PIDA, C-arylated product *N*-(5-chloro-2',4'-dimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2hg**) was isolated in 92% yield (Figure 3A.4c). Following, C-arylated product **2hg**, upon treatment with additional 1.5 equiv of PIDA under standard conditions, was converted to 6-chloro-2,4-dimethyl-9-(methylsulfonyl)carbazole (**3hg**) with 71% yield (Figure 3A.4d). This observation led to a conclusion that the C-C bond was preferentially formed over C-N bond during the carbazole ring construction.[28] From intermediate **7**, the oxidative C-N bond formation went on through iodine (III) mediated nitrenium ion generation and successive nucleophilic attack from phenyl ring.[18] Role of additive K_2CO_3 might be to neutralize the acetic acid released during reaction.[29]

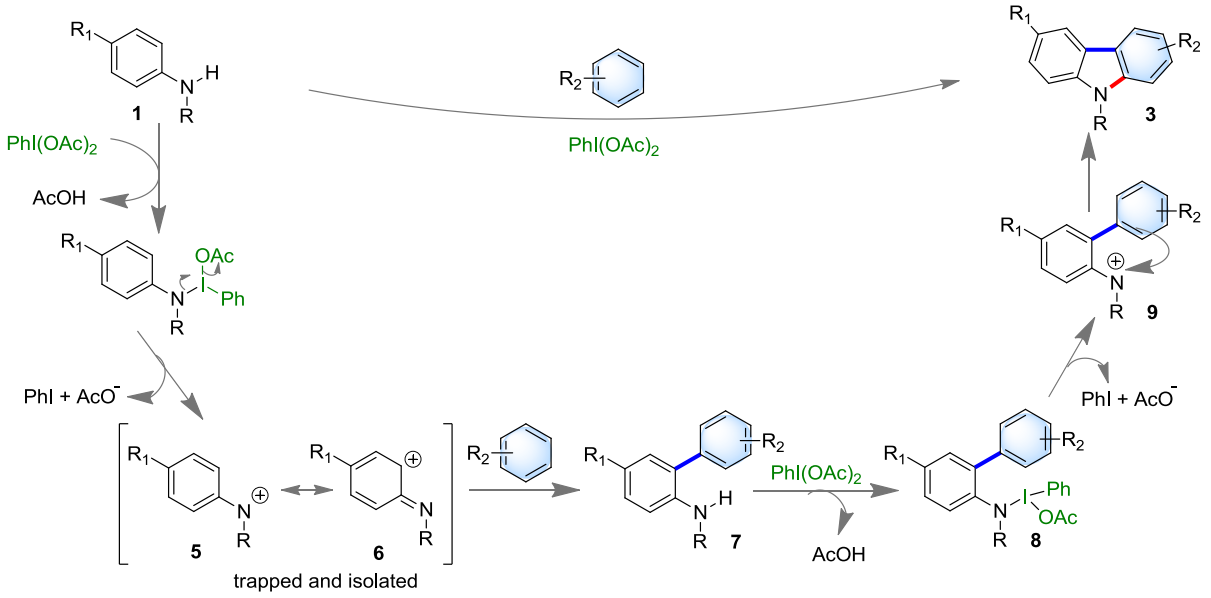


Figure 3A.5 Possible mechanism in stoichiometric method (Method A).

In organocatalytic approach, we believe that iodobenzene was oxidized by *m*CPBA to generate trivalent organoiodine species which enabled the intermolecular annulation of arene and amine to the final product **3** (Figure 3A.6).[18]

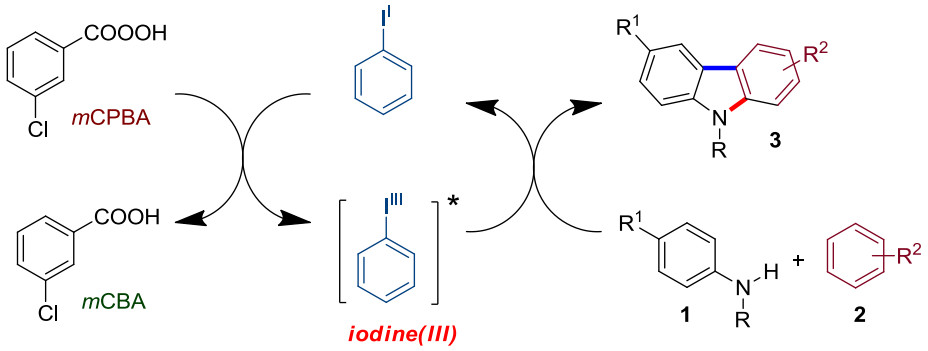


Figure 3A.6 Possible mechanism in organocatalytic method (Method B).

For further synthetic utility, first of all, the compound **3a** was converted into 6-bromo-2-methoxycarbazole (**4a**) with 93% yield (Figure 3A.7a) using 3.0 equiv of Cs_2CO_3 in THF-MeOH (1:1).[30] In addition, synthesis of carbazole alkaloid (±)-mahanimbicine (Figure 3A.7b) can possibly be achieved in two steps from 2-methoxy-6-methyl-9-tosylcarbazole (**3aa**).[31] We have synthesized alkaloid clauszoline-K (**5ah**) herein from *N*-(p-tolyl)benzenesulfonamide

(**1ah**) and anisole (**2a**) (Figure 3A.7c).[17] Moreover, this method might lead to easy synthesis of potent anti-HIV active drug siamenol in two steps from 2-methoxy-6-methyl-9H-carbazole (**4ah**) (Figure 3A.7c).[32] Clauszoline-L, clausine-M and clausine-N alkaloids also could be derived from 7-methoxy-9H-carbazole-3-carbaldehyde (**5ah**) by applying literature known method of transformations.[32]

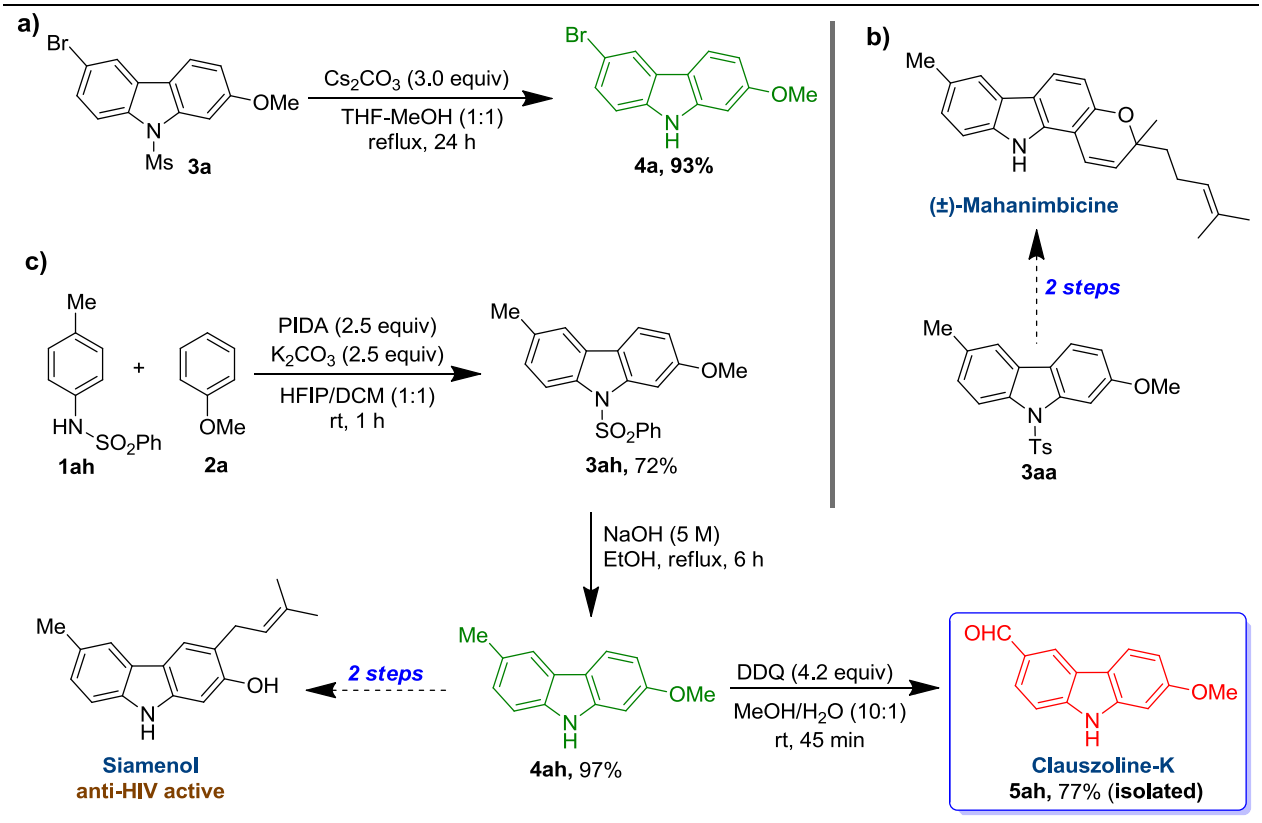


Figure 3A.7 Post synthetic modification.

3A.3 CONCLUSIONS

In summary, we have presented the simplest approach of direct annulation to 3-ring heterocycle carbazoles by fusing two non-prefunctionalized monocyclic arenes via simultaneous functionalization of three C(sp^2)-H and one N(sp^3)-H bonds. Hypervalent iodine(III) reagent was used as the sole reagent and the reactions were done at ambient laboratory conditions. The presented method is a newly discovered metal-free intermolecular dehydrogenative annulation (IDA) reaction for a tandem C-N and C-C bond formation reaction.

The utility of synthesized carbazoles towards synthesis of biologically active natural products are also documented. We anticipate that this generalized annulation approach can provide direct access to the various polycyclic heterocaromatic compounds and might have a major impact on synthesis of complex molecules, functionalized materials and pharmaceuticals.

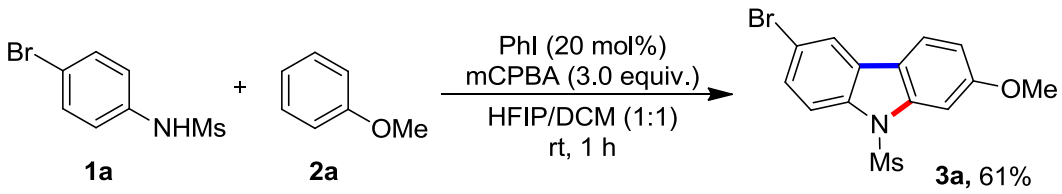
3A.4 EXPERIMENTAL SECTION

General Methods. Column chromatographic purifications of the synthesized compounds were performed using silica gel (mesh 230–400) and hexane-ethyl acetate mixtures as eluent, unless otherwise specified. NMR spectra were recorded on a 400 MHz instrument at 25 ^{o}C. The chemical shift values are reported in parts per million (ppm) with respect to residual chloroform (7.26 ppm for ^{1}H and 77.16 for ^{13}C). High-resolution mass spectra (HR-MS) were recorded on an ESI-TOF (time of flight) mass spectrometer. Infrared spectral data are reported in wave number (cm^{-1}). Melting points of the compounds were determined using a digital melting point apparatus and are uncorrected. X-Ray diffraction data for single crystals of **3q, 3v, 3ab** and **3ag** were collected using a CCD diffractometer equipped with an APEX II detector with graphite-monochromatized Mo-Kα (λ = 0.71073 Å) radiation at 300 K. The structures were solved by direct method using SHELLX-97. FT-IR spectra were recorded after making thin layer of the compounds on the surface of NaCl crystal using dichloromethane.

Materials. $PhI(OAc)_2$ (PIDA), $PhI(OCOCF_3)_2$ (PIFA), $PhI(OPiv)_2$, HTIB, iodobenzene (PhI) and *m*-Chloroperbenzoic acid (*m*CPBA) were purchased from commercial source and used without further purification. $PhI(OCOPh)_2$ and PhIO were prepared from $PhI(OAc)_2$ in a single step according to the literatures. Sulfoanilides were prepared by the reaction of commercially available anilines and sulfonyl chlorides in presence of pyridine in dichloromethane(DCM) solvent. Acetanilides and banzanilides were prepared from anilines by using corresponding

carbonyl chlorides in presence of triethylamine (TEA). Solvents were commercially available and used without further purification.

Representative procedure for preparation of 6-bromo-2-methoxy-9-(methylsulfonyl)carbazole (3a)



Method A

To a stirred solution of *N*-(4-bromophenyl)methanesulfonamide (**1a)** (125 mg, 0.5 mmol), anisole (**2a)** (162 μL, 1.5 mmol) in $(CF_3)_2CHOH$ (HFIP)/CH_2Cl_2 (DCM) (1:1, 3.0 mL), PIDA (403 mg, 1.25 mmol) was added slowly at room temperature and under open air conditions. Then K_2CO_3 (173 mg, 1.25 mmol) was added to the reaction mixture and allowed to stir for 1 h. The progress of the reaction was monitored by TLC using ethyl acetate and hexane as eluent. After the completion of reaction resulting solution was evaporated to dryness. The crude residue was purified on silica gel column chromatography using hexane and ethyl acetate as eluent to obtain 6-bromo-2-methoxy-9-(methylsulfonyl)carbazole (**3a)** (138 mg, 0.389 mmol, yield 78%).

Method B

To a stirred solution of N-(4-bromophenyl)methanesulfonamide (**1a)** (125 mg, 0.5 mmol), anisole (**2a)** (162 μL, 1.5 mmol) and iodobenzene (11 μL, 0.1 mmol) in 1,1,1,3,3,3-hexafluoroisopropanol (HFIP or $(CF_3)_2CHOH$)/dichloromethane (DCM or CH_2Cl_2) (1:1, 3 mL), *m*CPBA (268 mg, 1.5 mmol) was added in one portion at ambient conditions and allowed to stir for additional 1 h at room temperature. The progress of reaction was monitored by TLC using hexane and ethyl acetate mixture as eluent. After completion the solvent was evaporated and saturated aqueous solution of $NaHCO_3$ was added. The aqueous phase was extracted with

ethyl acetate. The organic extract was dried over anhydrous Na_2SO_4 and resulting solution was evaporated to dryness. The residue was purified by column chromatography on silica-gel to give the pure product 6-bromo-2-methoxy-9-(methylsulfonyl)carbazole (**3a)** (108 mg, 0.305 mmol, yield 61%)

Compond characterization data

6-Bromo-2-methoxy-9-(methylsulfonyl)carbazole (3a): R_f = 0.5 (hexane:ethyl acetate 9:1); white solid; mp 164-165 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01-7.97 (m, 2H), 7.82 (d, *J* = 8 Hz, 1H), 7.67 (s, 1H), 7.52-7.49 (m, 1H), 7.04-7.01 (m, 1H), 3.93 (s, 3H), 2.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.7, 140.2, 137.2, 129.0, 128.4, 122.4, 121.2, 118.5, 117.8, 116.2, 113.0, 99.3, 55.9, 38.8; IR (KBr): $\tilde{\nu}$ = 3422, 2926, 2904, 1619, 1495, 1458, 1364, 1280, 1262, 1171, 988, 811, 768 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{14}H_{13}{}^{79}BrNO_3S$ $[M + H]^+$: 353.9794, found: 353.9789, $C_{14}H_{13}{}^{81}BrNO_3S$ $[M + H]^+$: 355.9774, found: 355.9774.

6-Bromo-2-methyl-9-(methylsulfonyl)carbazole (3b): R_f = 0.6 (hexane:ethyl acetate 19:1); white solid; mp 103-104 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (s, 1H), 8.01 (d, *J* = 4 Hz, 1H), 7.94 (s, 1H), 7.81 (d, *J* = 4 Hz, 1H), 7.55-7.53 (m, 1H), 7.25 (d, *J* = 4 Hz, 1H), 2.97 (s, 1H), 2.54 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.1, 137.2, 129.8, 128.3, 125.8, 122.9, 122.8, 120.1, 117.6, 116.2, 115.0, 38.8, 22.3; IR (KBr): $\tilde{\nu}$ = 3016, 2932, 1887, 1746, 1618, 1573, 1445, 1415, 1360, 1254, 1213, 1169, 1147, 1009, 986, 966, 872, 814, 773 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{14}H_{13}NO_2S^{79}Br$ $[M + H]^+$: 337.9845, found: 337.9876, $C_{14}H_{13}NO_2S^{81}Br$ $[M + H]^+$: 339.9825, found: 339.9866.

10-Bromo-7-(methylsulfonyl)benzo[c]carbazole (3c): R_f = 0.7 (hexane:ethyl acetate 9:1); white solid; mp 159-160 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.67-8.66 (m, 2H), 8.38 (d, *J* = 4Hz, 1H), 8.21 (d, *J* = 4Hz, 1H), 8.03 (d, *J* = 4Hz, 1H), 7.99 (d, *J* = 12Hz, 1H), 7.77 (t, $J_1 = J_2$

= 4Hz, 1H), 7.65-7.59 (m, 2H), 3.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.1, 136.9, 131.2, 129.9, 129.5, 129.2, 128.8, 128.0, 125.5, 125.1, 123.4, 118.7, 118.6, 118.1, 116.4, 114.2, 39.4; IR (KBr): $\tilde{\nu}$ = 3012, 2927, 1649, 1541, 1520, 1462, 1429, 1358, 1264, 1237, 1169, 1053, 959, 810, 763, 738 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{17}H_{12}NO_2S^{79}BrNa$ [M + Na]$^+$: 395.9664, found: 395.9653; $C_{17}H_{12}NO_2S^{81}BrNa$ [M + Na]$^+$: 397.9644, found: 397.9646.

***6-Bromo-2-ethyl-9-(methylsulfonyl)carbazole (3d)*:** R_f = 0.65 (hexane:ethyl acetate 19:1); white solid; mp 82-83 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (s, 1H), 8.03 (d, *J* = 8 Hz, 1H), 7.98 (s, 1H), 7.86 (d, *J* = 8 Hz, 1H), 7.55 (d, *J* = 8 Hz, 1H), 7.29 (d, *J* = 8 Hz, 1H), 2.98 (s, 3H), 2.84 (q, *J* = 8 Hz, 2H), 1.33 (t, *J* = 8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.7, 139.2, 137.3, 129.9, 128.4, 124.8, 123.0, 122.9, 120.3, 117.6, 116.3, 114.0, 38.8, 29.7, 16.1; IR (KBr): $\tilde{\nu}$ = 3014, 2966, 2931, 2874, 1619, 1458, 1416, 1366, 1212, 1171, 1148, 995, 974, 876, 819, 767 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{15}H_{15}NO_2S^{79}Br$ [M + H]$^+$: 352.0001, found: 351.9996, $C_{15}H_{15}NO_2S^{81}Br$ [M + H]$^+$: 353.9981, found: 353.9975.

***3-Bromo-9-(methylsulfonyl)carbazole (3e)*:** R_f = 0.65 (hexane:ethyl acetate 19:1); white solid; mp 100-102 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (s, 1H), 8.14-8.13 (m, 1H), 8.05 (d, *J* = 8 Hz, 1H), 7.97 (d, *J* = 8 Hz, 1H), 7.61-7.58(m, 1H), 7.56-7.52(m, 1H), 7.47-7.43(m, 1H), 2.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 130.5, 128.5, 128.2, 125.2, 124.6, 124.1, 123.8, 123.3, 120.5, 117.6, 116.3, 114.9, 39.0; IR (KBr): $\tilde{\nu}$ = 3012, 2960, 2932, 2877, 1617, 1454, 1413, 1369, 1264, 1219, 1162, 1143, 987, 954, 822, 761 cm^{-1}; HR-MS (ESI-TOF): m/z = calculated for $C_{12}H_8N^{79}Br$ [(M–SO_2Me) + H]$^+$: 244.9835, found: 244.9824; $C_{12}H_8N^{81}Br$ [(M–SO_2Me) + H]$^+$: 246.9814, found: 246.9804.

***6-Bromo-2,3-dimethyl-9-(methylsulfonyl)carbazole (3f)*:** R_f = 0.6 (hexane:ethyl acetate 19:1); white solid; mp 72-73 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (s, 1H), 7.91 (d, *J* = 8 Hz, 1H), 7.60 (d, *J* = 8 Hz, 1H), 7.52 (d, *J* = 8 Hz, 1H), 7.28 (d, *J* = 8 Hz, 1H), 2.57 (s, 3H), 2.42 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.3, 140.9, 139.4, 132.1, 130.5, 130.0, 128.5, 127.6, 122.9, 120.7, 119.7, 117.3, 34.6, 20.7, 18.7; IR (KBr): $\tilde{\nu}$ = 3418, 2929, 1609, 1457, 1362, 1318, 1168, 1093, 1073, 961, 819, 789, 755, 733 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{15}H_{15}NO_2S^{79}Br$ $[M + H]^+$: 352.0001, found: 352.0030; $C_{15}H_{15}NO_2S^{81}Br$ $[M + H]^+$: 353.9981, found: 354.0011.

***6-Bromo-2,4-dimethyl-9-(methylsulfonyl)carbazole (3g)*:** R_f = 0.6 (hexane:ethyl acetate 19:1); white solid; mp 149-150 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (s, 1H), 8.09 (d, *J* = 12 Hz, 1H), 7.85 (s, 1H), 7.56 (d, *J* = 8 Hz, 1H), 7.05 (s, 1H), 2.96 (s, 3H), 2.77 (s, 3H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.4, 138.7, 137.3, 133.4, 129.2, 129.0, 127.7, 125.1, 121.3, 117.5, 116.1, 112.5, 38.7, 22.2, 20.9; IR (KBr): $\tilde{\nu}$ = 3397, 2924, 2375, 1611, 1533, 1444, 1396, 1364, 1218, 1170, 1155, 1090, 959, 849, 792 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{15}H_{15}NO_2S^{79}Br$ $[M + H]^+$: 352.0001, found: 351.9993; $C_{15}H_{15}NO_2S^{81}Br$ $[M + H]^+$: 353.9981, found: 353.9974.

***6-Chloro-2-ethyl-9-(methylsulfonyl)carbazole (3h)*:** R_f = 0.65 (hexane:ethyl acetate 19:1); white solid; mp 97-98 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, *J* = 8 Hz, 1H), 7.98 (s, 1H), 7.92 (s, 1H), 7.86 (d, J = 8 Hz, 1H), 7.41 (d, *J* = 8 Hz, 1H), 7.29 (d, *J* = 8 Hz, 1H), 2.08 (s, 3H), 2.84 (q, *J* = 8 Hz, 2H), 1.33 (t, *J* = 8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.7, 139.4, 136.8, 130.0, 127.9, 127.1, 124.8, 123.2, 120.3, 119.9, 115.4, 38.8, 29.7, 16.1; IR (KBr): $\tilde{\nu}$ = 2970, 2928, 2852, 1619, 1455, 1418, 1354, 1284, 1244, 1209, 1164, 1074, 997, 978, 876, 825,

771, 716 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{15}H_{15}NO_2SCl$ $[M + H]^+$: 308.0507, found: 308.0534.

***10-Ethyl-7-(methylsulfonyl)benzo[c]carbazole (3i)*:** R_f = 0.44 (hexane:ethyl acetate 19:1); white solid; mp 125-126 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.81 (d, *J* = 8 Hz, 1H), 8.42-8.38 (m, 2H), 8.24 (d, *J* = 8 Hz, 1H), 8.03 (d, *J* = 8 Hz, 1H), 7.95 (d, *J* = 12 Hz, 1H), 7.76 (t, *J* = 8 Hz, 1H), 7.59 (t, *J* = 8 Hz, 1H), 7.40 (d, *J* = 8 Hz, 1H), 2.98 (s, 3H), 2.93 (q, *J* = 8 Hz, 2H), 1.42 (t, *J* = 8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.9, 136.8, 136.5, 131.2, 129.3, 129.0, 128.7, 127.5, 127.3, 126.70, 125.1, 123.7, 121.5, 119.9, 114.8, 114.5, 39.21, 29.3, 16.4; IR (KBr): $\tilde{\nu}$ = 3054, 2963, 2928, 1666, 1473, 1456, 1359, 1241, 1177, 1162, 1058, 1020, 960, 854, 821, 763, 743 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{19}H_{18}NO_2S$ $[M + H]^+$: 324.1053, found: 324.1055.

***6-Ethyl-2-methyl-9-(methylsulfonyl)carbazole (3j)*:** R_f = 0.5 (hexane:ethyl acetate 19:1); white solid; mp 47-48 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.03 (d, *J* = 8 Hz, 1H), 7.96 (s, 1H), 7.86 (d, *J* = 8 Hz, 1H), 7.77 (s, 1H), 7.30 (d, *J* = 8 Hz, 1H), 7.23 (d, *J* = 8 Hz, 1H), 2.94 (s, 3H), 2.81 (q, *J* = 8 Hz, 2H), 2.54 (s, 3H), 1.33 (t, *J* = 8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.5, 139.1, 138.0, 136.8, 127.3, 126.7, 125.5, 124.2, 119.9, 118.8, 115.1, 114.7, 38.4, 28.9, 22.3, 16.1; IR (KBr): $\tilde{\nu}$ = 3017, 2964, 2928, 2871, 1607, 1475, 1418, 1364, 1325, 1254, 1211, 1168, 1141, 986, 959, 820, 765 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{16}H_{18}NO_2S$ $[M + H]^+$: 288.1053, found: 288.1030.

***2,6-Diethyl-9-(methylsulfonyl)carbazole (3k)*:** R_f = 0.5 (hexane:ethyl acetate 19:1); colourless liquid; ^1H NMR (400 MHz, $CDCl_3$): δ 8.03 (d, *J* = 8 Hz, 1H), 7.98 (s, 1H), 7.88 (d, *J* = 8 Hz, 1H), 7.77 (s, 1H), 7.31-7.27 (m, 2H), 2.94 (s, 3H), 2.85-2.78 (m, 4H), 1.33 (t, *J* = 8 Hz, 6H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 144.6, 140.5, 139.2, 136.8, 127.3, 126.7, 124.4, 124.4, 120.0, 118.9, 114.7, 114.1, 38.4, 28.9, 16.1; IR (KBr): $\tilde{\nu}$ = 3018, 2965, 2930, 2872, 1622, 1606, 1548, 1492, 1475, 1459, 1422, 1365, 1324, 1210, 1169, 1142, 1058, 996, 975, 958, 881, 768, 731 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{17}H_{20}NO_2S$ $[M + H]^+$: 302.1209, found: 302.1259, calculated for $C_{16}H_{17}N$ $[(M–SO_2Me) + H]^+$: 223.1356, found: 223.1325.

***6-Ethyl-2,3-dimethyl-9-(methylsulfonyl)carbazole (3l)*:** R_f = 0.5 (hexane:ethyl acetate 19:1); colourless semi-solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, *J* = 8 Hz, 1H), 7.91 (s, 1H), 7.75 (s, 1H), 7.73 (s, 1H), 7.28 (d, *J* = 8 Hz, 1H), 2.90 (s, 3H), 2.81 (q, *J* = 8 Hz, 2H), 2.43 (S, 3H), 2.41 (S, 3H), 1.33 (t, *J* = 8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.5, 137.5, 136.9, 136.8, 133.0, 127.1, 126.9, 124.6, 120.7, 118.8, 115.5, 114.8, 38.1, 28.9, 20.9, 20.1, 16.1; IR (KBr): $\tilde{\nu}$ = 3017, 2964, 2927, 2855, 1726, 1629, 1478, 1453, 1362, 1323, 1273, 1218, 1159, 1023, 962, 869, 823, 769 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{16}H_{17}N$ $[(M–SO_2Me) + H]^+$: 223.1356, found: 223.1328.

***6-Ethyl-2,4-dimethyl-9-(methylsulfonyl)carbazole (3m)*:** R_f = 0.5 (hexane:ethyl acetate 19:1); white solid; mp 85-86 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (d, *J* = 8 Hz, 1H), 7.87 (d, *J* = 12 Hz, 2H), 7.32-7.29 (m 1H), 7.02 (s, 1H), 2.92 (s, 3H), 2.83 (q, *J* = 8 Hz, 2H), 2.82 (s, 3H), 2.50 (s, 3H), 1.34 (t, *J* = 8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.3, 139.3, 137.5, 136.8, 133.0, 127.5, 127.4, 126.5, 122.5, 121.4, 114.5, 112.6, 38.2, 29.1, 22.1, 21.0, 16.3; IR (KBr): $\tilde{\nu}$ = 3015, 2964, 2928, 2870, 1615, 1473, 1457, 1401, 1363, 1340, 1291, 1221, 1166, 1091, 986, 960, 879, 849, 775, 746 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{17}H_{20}NO_2S$ $[M + H]^+$: 302.1209, found: 302.1206.

***6-Ethyl-2-methoxy-9-(methylsulfonyl)carbazole (3n)*:** R_f = 0.45 (hexane:ethyl acetate 19:1); white solid; mp 75-77 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, *J* = 8 Hz, 1H), 7.85 (d, *J* = 12 Hz, 1H), 7.71 (s, 1H),7.70 (d, J = 4 Hz, 1H), 7.24 (s, 1H), 7.02-6.99 (m, 1H), 3.92 (s, 3H), 2.94 (s, 3H), 2.80 (q, *J* = 8 Hz, 2H), 1.33 (t, *J* = 8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 140.6, 140.1, 136.7, 126.7, 126.4, 120.8, 119.9, 118.4, 114.6, 112.5, 99.5, 55.9, 38.3, 28.9, 16.1; IR (KBr): $\tilde{\nu}$ = 3009, 2964, 2931, 2836, 1621, 1608, 1499, 1477, 1433, 1364, 1274, 1192, 1169, 1115, 1039, 1016, 959, 854, 819, 764 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{16}H_{17}NSO_3Na$ $[M + Na]^+$: 326.0821, found: 326.0814.

***2-Ethyl-6-fluoro-9-(methylsulfonyl)carbazole (3o)*:** R_f = 0.60 (hexane:ethyl acetate 19:1); white solid; mp 103–104 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11-8.08 (m, 1H), 7.98 (s, 1H), 7.85 (d, *J* = 8 Hz, 1H), 7.62-7.59 (m, 1H), 7.29 (d, *J* = 8 Hz, 1H), 7.20-7.14 (m, 1H), 2.05 (s, 3H), 2.83 (q, *J* = 8 Hz, 2H), 1.33(t, *J* = 8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ =160.2 (d, $^1J_{C,F}$ = 241 Hz), 145.6, 139.7, 134.6, 127.9 (d, $^3J_{C,F}$ = 9 Hz), 124.6, 123.7 (d, $^4J_{C,F}$ = 4 Hz), 120.3, 116.1 (d, $^3J_{C,F}$ = 9 Hz), 114.5 (d, $^2J_{C,F}$ = 25 Hz), 114.2, 106.2 (d, $^2J_{C,F}$ = 24 Hz), 38.5, 29.7, 16.1; IR (KBr): $\tilde{\nu}$ = 3015, 2970, 2933, 1620, 1593, 1474, 1423, 1357, 1333, 1292, 1225, 1162, 1124, 996, 979, 880, 864, 826, 766 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{15}H_{15}NO_2SF$ $[M + H]^+$: 292.0802, found: 292.0814.

***10-Fluoro-7-(methylsulfonyl)benzo[c]carbazole (3p)*:** R_f = 0.35 (hexane:ethyl acetate 19:1); white solid; mp 115-116 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.66 (d, *J* = 8 Hz, 1H), 8.39 (d, *J* = 8 Hz, 1H), 8.32–8.28 (m, 1H), 8.22 (d, *J* = 8 Hz, 1H), 8.04 (d, *J* = 8 Hz, 1H), 7.99 (d, *J* = 8 Hz, 1H), 7.77 (t, *J* = 8 Hz, 1H), 7.61 (t, *J* = 8 Hz, 1H), 7.29 (d, *J* = 8 Hz, 1H), 3.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.4 (d, $^1J_{C,F}$ = 240.0 Hz), 137.6, 134.4, 131.2, 129.7, 129.5, 128.8, 128.0, 125.4, 123.3, 119.3 (d, $^4J_{C,F}$ = 4.0 Hz), 116.1 (d, $^3J_{C,F}$ = 9.0 Hz), 114.5, 114.1,

113.9, 108.6 (d, $^{2}J_{C,F}$ = 25.0 Hz), 39.4; IR (KBr): $\tilde{\nu}$ = 3012, 2978, 2932, 2856, 1641, 1474, 1445, 1358, 1177, 1161, 1058, 989, 960, 874, 806 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{17}H_{13}NO_2SF$ $[M + H]^+$: 314.0646, found: 314.0643.

***6-Fluoro-2,3-dimethyl-9-(methylsulfonyl)carbazole (3q)*:** R_f = 0.45 (hexane:ethyl acetate 19:1); white solid; mp 124-125 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01-7.97 (m, 1H), 7.60 (d, *J* = 8 Hz, 1H), 7.51-7.48 (m, 1H), 7.28 (d, *J* = 8 Hz, 1H), 7.15-7.10 (m, 1H), 2.57 (s, 3H), 2.42 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.4 (d, $^{1}J_{C,F}$ = 243.0 Hz), 141.9, 139.3, 138.0, 131.8 (d, $^{3}J_{C,F}$ = 10.0 Hz), 130.7, 128.5, 128.3 (d, $^{4}J_{C,F}$ = 3.0 Hz), 120.7 (d, $^{3}J_{C,F}$ = 9.0 Hz), 117.3, 114.5 (d, $^{2}J_{C,F}$ = 25.0 Hz), 106.5 (d, $^{2}J_{C,F}$ = 24.0 Hz), 34.2, 20.7, 18.7; IR (KBr): $\tilde{\nu}$ = 3014, 2928, 2857, 1733, 1619, 1595, 1478, 1451, 1363, 1324, 1253, 1162, 1111, 1075, 1020, 968, 860, 823, 767 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{15}H_{15}NO_2SF$ $[M + H]^+$: 292.0802, found: 292.0771.

***6-Fluoro-2,4-dimethyl-9-(methylsulfonyl)carbazole (3r)*:** R_f = 0.52 (hexane:ethyl acetate 19:1); white solid; mp 110-111 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16-8.13 (m, 1H), 7.84 (s, 1H), 7.73-7.70 (m, 1H), 7.19-7.14 (m 1H), 7.03 (s, 1H), 2.93 (s, 3H), 2.75 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.0 (d, $^{1}J_{C,F}$ = 239 Hz), 139.8, 138.5, 134.6, 133.3, 128.4 (d, $^{3}J_{C,F}$ = 9 Hz), 127.5, 121.9 (d, $^{4}J_{C,F}$ = 3 Hz), 115.7 (d, $^{3}J_{C,F}$ = 9 Hz), 113.6 (d, $^{2}J_{C,F}$ = 24 Hz), 112.7, 108.6 (d, $^{2}J_{C,F}$ = 25 Hz), 38.4, 22.1, 20.6; IR (KBr): $\tilde{\nu}$ = 3017, 2927, 2865, 1615, 1593, 1473, 1446, 1401, 1363, 1327, 1294, 1164, 1119, 1091, 960, 869, 850, 777, 747 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{15}H_{15}NO_2SF$ $[M + H]^+$: 292.0802, found: 292.0770.

***10-Methyl-7-(methylsulfonyl)benzo[c]carbazole (3s)*:** R_f = 0.35 (hexane:ethyl acetate 19:1); white solid; mp 120-122 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.80 (d, *J* = 8 Hz, 1H), 8.40 (d, *J* = 8 Hz, 1H), 8.36 (s, 1H), 8.21 (d, *J* = 8 Hz, 1H), 8.03 (d, *J* = 8 Hz, 1H), 7.95 (d, *J* = 12 Hz,

1H), 7.75 (t, *J* = 8 Hz, 1H), 7.58 (t, *J* = 8 Hz, 1H), 7.37 (s, 1H), 2.97 (s, 3H), 2.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.8, 136.4, 134.4, 131.2, 129.3, 129.0, 128.8, 127.7, 127.5, 127.3, 125.1, 123.7, 122.6, 119.8, 114.7, 114.6, 39.1, 21.8; IR (KBr): $\tilde{\nu}$ = 3012, 2987, 2942, 2925, 1623, 1585, 1549, 1519, 1446, 1377, 1358, 1267, 1209, 1179, 1116, 1058, 1021, 850, 763, 744 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{18}H_{16}NO_2S$ $[M + H]^+$: 310.0896, found: 310.0920.

***2,4,6-Trimethyl-9-(methylsulfonyl)carbazole (3t)*:** R_f = 0.55 (hexane:ethyl acetate 19:1); white solid; mp 106-107 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, *J* = 8 Hz, 1Hz), 7.85 (s, 2H), 7.27 (d, *J* = 8 Hz, 1Hz), 7.02 (s, 2H), 2.91 (s, 3H), 2.78 (s, 3H), 2.53 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.3, 137.5, 136.6, 133.8, 133.0, 127.5, 127.5, 127.4, 122.6, 122.4, 114.4, 112.6, 38.1, 22.0, 21.6, 20.9; IR (KBr): $\tilde{\nu}$ = 3016, 2924, 2862, 1608, 1585, 1475, 1458, 1362, 1324, 1220, 1166, 1090, 986, 959, 851, 811, 777, 748 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{16}H_{18}NO_2S$ $[M + H]^+$: 288.1053, found: 288.1085.

***2-Methoxy-9-(methylsulfonyl)-6-phenylcarbazole (3u)*:** R_f = 0.35 (hexane:ethyl acetate 19:1); white solid; mp 85-86 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (d, *J* = 8 Hz, 1H), 8.09 (s, 1H), 7.92 (d, *J* = 8 Hz, 1H), 7.72 (s, 1H), 7.69-7.63 (m, 3H), 7.49 (t, *J* = 8 Hz, 2H), 7.39 (t, *J* = 8 Hz, 1H), 7.04 (d, *J* = 8 Hz, 1H), 3.94 (s, 3H), 3.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.2, 141.1, 140.2, 137.9, 137.8, 132.3, 129.0, 127.4, 127.4, 127.1, 125.7, 121.0, 119.7, 117.9, 114.9, 112.7, 99.5, 55.9, 38.6; IR (KBr): $\tilde{\nu}$ = 3059, 2927, 2854, 1734, 1623, 1607, 1495, 1469, 1423, 1366, 1267, 1192, 1172, 1151, 1040, 990, 960, 840, 823, 762, 737, 701 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{20}H_{18}NO_3S$ $[M + H]^+$: 352.1002, found: 352.1003.

***10-Isopropyl-7-(methylsulfonyl)benzo[c]carbazole (3v)*:** R_f = 0.55 (hexane:ethyl acetate 19:1); white solid; mp 113-114 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.82 (d, *J* = 8 Hz, 1H), 8.42 (s, 1H), 8.40 (s, 1H), 8.25 (d, *J* = 8 Hz, 1H), 8.04 (d, *J* = 12 Hz, 1H), 7.95 (d, *J* = 8 Hz, 1H), 7.77 (t, *J* = 8 Hz, 1H), 7.59 (t, *J* = 8 Hz, 1H), 7.44 (d, *J* = 8 Hz, 1H), 3.20 (sept, *J* = 8 Hz, 1H), 2.99 (s, 3H), 1.44 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.6, 136.9, 136.6, 131.2, 129.3, 129.0, 128.7, 127.5, 127.3, 125.2, 125.1, 123.7, 120.0, 119.9, 114.9, 114.6, 39.3, 34.6, 24.6; IR (KBr): $\tilde{\nu}$ = 2959, 2926, 2854, 1735, 1667, 1519, 1473, 1458, 1361, 1241, 1168, 1116, 1058, 984, 959, 819, 763, 745 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{20}H_{20}NO_2S$ $[M + H]^+$: 338.1209, found: 338.1196, calculated for $C_{19}H_{17}N$ $[(M–SO_2Me) + H]^+$: 259.1356, found: 259.1342.

***6-Iodo-2,4-dimethyl-9-(methylsulfonyl)carbazole (3w)*:** R_f = 0.50 (hexane:ethyl acetate 19:1); white solid; mp 131-133 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36 (s, 1H), 7.96 (d, *J* = 8 Hz, 1H), 7.83 (s, 1H), 7.72 (d, *J* = 8 Hz, 1H), 7.04 (s, 1H), 2.95 (s, 3H), 2.75 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.0, 138.6, 137.9, 134.9, 133.3, 131.1, 129.5, 127.7, 121.0, 116.5, 112.4, 88.1, 38.7, 22.1, 20.9; IR (KBr): $\tilde{\nu}$ = 3014, 2924, 2854, 1733, 1651, 1612, 1442, 1365, 1224, 1171, 1136, 1091, 984, 960, 848, 810, 788, 742 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{15}H_{15}INO_2S$ $[M + H]^+$: 399.9863, found: 399.9855.

***7-(Methylsulfonyl)benzo[c]carbazole (3x)*:** R_f = 0.60 (hexane:ethyl acetate 19:1); white solid; mp 62-63 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.81 (d, *J* = 8 Hz, 1H), 8.60-8.58 (m, 1H), 8.41 (d, *J* = 8 Hz, 1H), 8.36-8.34 (m, 1H), 8.05 (d, *J* = 8 Hz, 1H), 7.98 (d, *J* = 12 Hz, 1H), 7.61-7.55 (m, 3H), 3.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.2, 136.6, 131.2, 129.4, 129.0, 127.7, 127.1, 126.5, 125.2, 124.7, 123.7, 122.5, 119.8, 115.1, 114.5, 39.4; IR (KBr): $\tilde{\nu}$ = 3054, 2924,

2853, 1736, 1624, 1585, 1446, 1363, 1268, 1243, 1118, 1030, 1020, 862, 788, 764, 742 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{17}H_{13}NO_2SNa$ $[M + Na]^+$: 318.0559, found: 318.0552.

***6-(tert-Butyl)-2-methoxy-9-(methylsulfonyl)carbazole (3y)*:** R_f = 0.48 (hexane:ethyl acetate 19:1); white solid; mp 108-110 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, *J* = 12 Hz, 1H), 7.90-7.87 (m, 2H), 7.70 (s, 1H), 7.47 (d, *J* = 8 Hz, 1H), 7.01 (d, *J* = 8 Hz, 1H), 3.02 (s, 3H), 2.95 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 151.6, 147.6, 140.1, 136.4, 126.3, 124.1, 120.8, 120.1, 115.8, 114.3, 112.4, 99.5, 55.9, 38.4, 34.9, 31.8; IR (KBr): $\tilde{\nu}$ = 2960, 2867, 2836, 1621, 1606, 1496, 1481, 1365, 1275, 1229, 1192, 1172, 1041, 991, 960, 843, 819, 769 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{18}H_{22}NO_3S$ $[M + H]^+$: 332.1315, found: 332.1309.

***2-Methoxy-6-methyl-9-tosylcarbazole (3aa)*:** R_f = 0.55 (hexane:ethyl acetate 19:1); white solid; mp 143-145 °C (lit. mp 145-148 °C); ^1H NMR (400 MHz, $CDCl_3$): δ 8.13 (d, *J* = 8 Hz, 1H), 7.87 (s, 1H), 7.71 (d, *J* = 8 Hz, 1H), 7.67 (d, *J* = 8 Hz, 2H), 7.57 (s, 1H), 7.20 (d, *J* = 8 Hz, 1H), 7.09 (d, *J* = 8 Hz, 2H), 6.95-6.92 (m, 1H), 3.94 (s, 3H), 2.45 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.8, 140.1, 136.6, 135.0, 133.8, 129.7, 127.3, 126.8, 126.6, 120.5, 120.0, 119.4, 114.9, 112.2, 100.1, 55.9, 21.6, 21.4; IR (KBr): $\tilde{\nu}$ = 3042, 2923, 2854, 1610, 1497, 1458, 1434, 1368, 1269, 1189, 1170, 1152, 1090, 1041, 984, 939, 867, 809, 675 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{21}H_{20}NO_3S$ $[M + H]^+$: 366.1158, found: 366.1162.

***6-Bromo-2-methoxy-9-((4-nitrophenyl)sulfonyl)carbazole (3ab)*:** R_f = 0.45 (hexane:ethyl acetate 9:1); yellow solid; mp 132-134 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, *J* = 12 Hz, 2H), 8.11 (d, *J* = 12 Hz, 2H), 7.93 (s, 1H), 7.91-7.89 (m, 2H), 7.81 (s, 1H), 7.71 (d, *J* = 8 Hz,

1H), 7.52-7.50 (m, 1H), 7.01-6.98 (m, 1H), 3.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.7, 150.9, 142.6, 139.8, 136.8, 129.2, 128.9, 127.8, 124.5, 122.5, 121.3, 119.0, 118.4, 116.6, 113.0, 100.3, 56.0; IR (KBr): $\tilde{\nu}$ = 3445, 3105, 2924, 2853, 1619, 1532, 1496, 1459, 1401, 1380, 1347, 1282, 1262, 1179, 1152, 1088, 1037, 988, 854, 823, 738 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{19}H_{14}N_2O_5S^{79}Br$ $[M + H]^+$: 460.9801, found: 460.9829, $C_{19}H_{14}N_2O_5S^{81}Br$ $[M + H]^+$: 462.9780, found: 417.9806.

***6-Bromo-2-methoxy-9-(phenylsulfonyl)carbazole (3ac)*:** R_f = 0.55 (hexane:ethyl acetate 19:1); colourless solid; mp 147-148 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8 Hz, 1H), 7.87 (d, *J* = 16 Hz, 2H), 7.78 (d, *J* = 8 Hz, 2H), 7.71 (d, *J* = 12 Hz, 1H), 7.50-7.46 (m, 2H), 7.34 (t, *J* = 8 Hz, 2H), 6.96 (d, *J* = 8 Hz, 1H), 3.95 (s, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.5, 140.2, 137.7, 137.2, 134.1, 129.3, 128.9, 128.5, 126.5, 122.2, 121.0, 118.7, 117.6, 116.6, 112.7, 99.9, 56.0; IR (KBr): $\tilde{\nu}$ = 3397, 2924, 2853, 1617, 1494, 1456, 1429, 1369, 1278, 1261, 1228, 1176, 1150, 987, 806, 724 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{19}H_{15}NO_3S^{79}Br$ $[M + H]^+$: 415.9951, found: 415.9932, $C_{19}H_{15}NO_3S^{81}Br$ $[M + H]^+$: 417.9931, found: 417.9908.

***(6-Bromo-2,4-dimethylcarbazol-9-yl)(phenyl)methanone (3ad)*:** R_f = 0.35 (hexane:ethyl acetate 19:1); white solid; mp 122-124 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.70-7.63 (m, 3H), 7.53-7.49 (m, 2H), 7.37-7.31 (m, 2H), 7.20 (s, 1H), 6.97 (s, 1H), 2.77 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.6, 140.1, 138.0, 137.5, 135.5, 132.9, 132.7, 129.3, 129.0, 128.6, 128.2, 126.8, 124.7, 120.9, 116.8, 116.4, 113.6, 22.1, 20.8; IR (KBr): $\tilde{\nu}$ = 3060, 2941, 2854, 1680, 1611, 1446, 1398, 1347, 1310, 1234, 1142, 1120, 1023, 972, 922, 844, 762, 743, 715 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{21}H_{17}NO^{79}Br$ $[M + H]^+$: 378.0488, found: 378.0482, $C_{21}H_{17}NO^{81}Br$ $[M + H]^+$: 380.0468, found: 380.0467.

***(6-Bromo-2-methoxycarbazol-9-yl)(phenyl)methanone (3ae)*:** R_f = 0.5 (hexane:ethyl acetate 19:1); white solid; mp 93-94 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (s 1H), 7.79 (d, *J* = 12 Hz, 1H), 7.71-7.64 (m, 3H), 7.56-7.52 (m, 2H), 7.32-7.28 (m, 2H), 7.00 (s 1H), 6.95 (d, *J* = 4 Hz, 1H), 3.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.5, 159.8, 140.9, 137.9, 135.5, 132.7, 129.1, 129.1, 128.1, 128.1, 122.0, 120.7, 118.3, 117.2, 116.8, 112.4, 100.4, 55.5; IR (KBr): $\tilde{\nu}$ = 3042, 2925, 2833, 1680, 1621, 1495, 1461, 1423, 1353, 1313, 1288, 1222, 1196, 1058, 1012, 973, 863, 808, 707 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{20}H_{15}O_2N^{79}Br$ $[M + H]^+$: 380.0281, found: 380.0279, $C_{20}H_{15}O_2N^{81}Br$ $[M + H]^+$: 382.0261, found: 382.0262.

***1-(6-Bromo-2,4-dimethylcarbazol-9-yl)ethanone (3af)*:** R_f = 0.30 (hexane:ethyl acetate 19:1); white solid; mp 138-139 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21 (d, *J* = 12 Hz, 1H), 8.15 (s, 1H), 7.78 (s, 1H), 7.53 (d, *J* = 8 Hz, 1H), 7.01 (s, 1H), 2.86 (s, 3H), 2.76 (s, 3H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 139.5, 137.9, 137.7, 133.2, 129.0, 128.9, 127.2, 124.7, 121.3, 117.7, 116.9, 113.9, 28.0, 22.3, 21.0; IR (KBr): $\tilde{\nu}$ = 3034, 2919, 2853, 1697, 1610, 1586, 1443, 1397, 1365, 1339, 1305, 1263, 1194, 1007, 865, 829, 749, 694 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{16}H_{15}NO^{79}Br$ $[M + H]^+$: 316.0332, found: 316.0364; $C_{16}H_{15}NO^{81}Br$ $[M + H]^+$: 318.0312, found: 318.0346.

***1-(6-Bromo-2-methoxycarbazol-9-yl)ethanone (3ag)*:** R_f = 0.45 (hexane:ethyl acetate 9:1); white solid; mp 96-98 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, *J* = 12 Hz, 1H), 7.88 (s, 1H), 7.72 (s, 1H), 7.70 (s, 1H), 7.43 (d, *J* = 8 Hz, 1H), 6.94 (d, *J* = 8 Hz, 1H), 3.91 (s, 3H), 2.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.9, 160.3, 140.2, 137.3, 128.5, 128.4, 121.9, 120.6, 118.6, 117.4, 117.0, 111.4, 101.8, 77.48, 55.8, 27.7; IR (KBr): $\tilde{\nu}$ = 3054, 2957, 2925, 2851, 1697, 1621, 1587, 1495, 1463, 1422, 1369, 1310, 1281, 1266, 1205, 1169, 1040, 980, 947, 867,

819, 737 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{15}H_{13}N^{79}BrO_2$ $[M + H]^+$: 318.0124, found: 318.0144, $C_{15}H_{13}N^{81}BrO_2$ $[M + H]^+$: 320.0104, found: 320.0123.

Procedure for the synthesis of *N*-(4-ethylphenyl)-*N*-(2,2,2 trifluoroethoxy)methanesulfonamide (4i)

To a stirred solution of *N*-(4-ethylphenyl)methanesulfonamide (**1b)** (50 mg, 0.25 mmol) in 2,2,2-trifluoroethanol (2.0 mL), PIDA (81 mg, 0.25 mmol) was added at a portion at ambient conditions and allowed to stir for additional 30 mins. After the completion of reaction resulting solution was evaporated to dryness. The crude residue was purified on silica gel column chromatography (10% EtOAc in hexane) to get the pure product *N*-(4-ethylphenyl)-*N*-(2,2,2 trifluoroethoxy)methanesulfonamide (**4i)** (41 mg, 0.138 mmol, Yield 55%).

***N-(4-ethylphenyl)-N-(2,2,2 trifluoroethoxy)methanesulfonamide (4i)*:** Yield 55%; R_f = 0.48 (hexane:ethyl acetate 4:1); yellow liquid; ^{19}F NMR (376.3 MHz, $CDCl_3$): δ -74.5; ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8 Hz, 1H), 6.66 (d, *J* = 12 Hz, 2H), 6.48 (d, *J* = 12 Hz, 1H), 3.64–3.57 (m, 2H), 3.18 (s, 3H), 1.84 (q, *J* = 8 Hz, 2H), 0.85 (t, *J* = 8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 149.0, 147.8, 132.1, 125.7, 123.6 (q, $^1J_{C,F}$ = 276 Hz) 63.5 (q, $^2J_{C,F}$ = 35 Hz), 43.0, 32.3, 7.8; IR (KBr): $\tilde{\nu}$ = 3027, 2976, 2940, 2884, 1656, 1600, 1562, 1460, 1421, 1393, 1310, 1139, 1101, 1064, 967, 875, 841, 773, 706, 679 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{11}H_{14}NO_3SF_3Na$ $[M + Na]^+$: 320.0539, found: 320.0550.

***N-(5-chloro-2',4'-dimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (2hg)*:** Yield 92%; R_f = 0.40 (hexane:ethyl acetate 4:1); white solid; mp 84-85 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, *J* = 8 Hz, 1H), 7.36-7.33 (m, 1H), 7.17 (d, *J* = 4 Hz, 1H), 7.15 (s, 1H), 7.10 (d, *J* = 8 Hz, 1H), 6.99 (d, *J* = 8 Hz, 1H), 6.09 (bs,1H), 2.89 (s, 3H), 2.38 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.4, 136.2, 133.8, 133.4, 132.0, 130.5, 129.8, 129.4, 128.8, 127.7,

120.1, 39.8, 21.2, 19.6; HR-MS (ESI-TOF): m/z calculated for $C_{15}H_{16}NO_2SClNa$ $[M + Na]^+$: 332.0482, found: 332.0487.

6-Chloro-2,4-dimethyl-9-(methylsulfonyl)carbazole (3hg): Yield 71%; R_f = 0.52 (hexane:ethyl acetate 19:1); white solid; mp 177-179 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (d, *J* = 8 Hz, 1H), 7.99 (s, 1H), 7.82 (s, 1H), 7.40 (d, *J* = 8 Hz, 1H), 7.03 (s, 1H), 2.95 (s, 3H), 2.74 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.4, 138.6, 136.7, 133.3, 129.8, 128.5, 127.6, 126.3, 122.0, 121.3, 115.6, 112.5, 38.6, 22.1, 20.8; IR (KBr): $\tilde{\nu}$ = 3030, 2921, 2860, 1879, 1595, 1446, 1345, 1284, 1216, 1155, 1128, 1074, 1006, 966, 823, 803, 749 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{15}H_{14}NO_2SClNa$ $[M + Na]^+$: 330.0326, found: 330.0321.

Pocedure for removal of Ms-group from 6-bromo-2-methoxy-9-(methylsulfonyl)carbazole (3a)

A mixture of 6-bromo-2-methoxy-9-(methylsulfonyl)carbazole **(3a)** (60 mg, 0.169 mmol) and Cs_2CO_3 (165 mg, 0.508 mmol) in THF-MeOH (1:1) was refluxed up to completion (24 h). After completion the solvent was evaporated and saturated aq. solution of NH_4Cl was added. The aqueous phase was extracted with dichloromethane. The organic extract was dried over anhydrous Na_2SO_4 and resulting solution was evaporated to dryness. The residue was purified by column chromatography on silica-gel [eluent: hexane/ethyl acetate (17:3)] to give the pure product 6-bromo-2-methoxy-9H-carbazole **(4a)** (43.5 mg, 0.157 mmol).

***6-Bromo-2-methoxy-9H-carbazole (4a)*:** Yield 93%; R_f = 0.60 (hexane:ethyl acetate 4:1); white solid; mp 218-220 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.27 (s, 1H), 8.22 (s, 1H), 8.02 (d, *J* = 8 Hz, 1H), 7.38 (s, 2H), 6.97 (s, 1H), 6.79 (d, *J* = 8 Hz, 1H), 3.84 (s, 3H); 13C

NMR (100 MHz, DMSO-d_6): δ 159.0, 141.6, 138.4, 126.3, 124.7, 121.8, 121.5, 115.1, 112.5, 110.6, 108.4, 94.4, 55.3.

***2-Methoxy-6-methyl-9-(phenylsulfonyl)carbazole (3ah)*:** Yield 72%; R_f = 0.60 (hexane:ethyl acetate 19:1); white solid; mp 123-125 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8 Hz, 1H), 7.87 (s, 1H), 7.79 (d, *J* = 8 Hz, 2H), 7.71 (d, *J* = 8 Hz, 1H), 7.57 (s, 1H), 7.44 (t, $J_1 = J_2$ = 8 Hz, 1H), 7.31 (t, $J_1 = J_2$ = 8 Hz, 2H), 7.21 (d, *J* = 8 Hz, 1H), 6.94 (d, *J* = 8, 1H), 3.95 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 140.1, 137.9, 136.5, 133.9, 133.8, 129.1, 127.3, 126.8, 126.5, 120.6, 120.0, 119.5, 114.9, 112.2, 100.1, 55.9, 21.4; IR (KBr): $\tilde{\nu}$ = 3395, 2928, 2857, 1877, 1614, 1465, 1307, 1225, 1160, 1110, 1042, 934, 806, 736 cm^{-1}.

Synthesis of 2-methoxy-6-methyl-9H-carbazole (4ah)

2-Methoxy-6-methyl-9-(phenylsulfonyl)carbazole (**3ah**) (330 mg, 0.940 mmol) was dissolved in EtOH and treated with aqueous solution of NaOH (5 M). The resulting solution was stirred at 60 ^{o}C upto completion (6 h). Solvents were evaporated under reduced pressure, diluted with dichloromethane (CH_2Cl_2) and neutralized with 1 M aqueous HCl solution. The aqueous phase was extracted with additional CH_2Cl_2 and combined organic layers were dried over anhydrous Na2SO4 and filtered. The filtrate was concentrated in vacuo and purified by silica gel column chromatography (20% EtOAc in hexane) to get pure 2-methoxy-6-methyl-9H-carbazole (**4ah**) (192 mg, 0.9099 mmole, Yield 97%).

***2-Methoxy-6-methyl-9H-carbazole (4ah)*:** Yield 97%; R_f = 0.45 (hexane:ethyl acetate 9:1); white solid; mp 238-240 °C (lit. mp 227-228 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, *J* = 8 Hz, 1H), 7.86 (bs, 1H), 7.77 (s, 1H), 7.28 (s, 1H), 7.16 (d, *J* = 8 Hz, 1H), 6.89 (s, 1H), 6.83

(d, *J* = 8 Hz, 1H), 3.90 (s, 3H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 141.2, 137.8, 129.0, 125.9, 123.8, 121.0, 119.6, 117.3, 110.1, 108.0, 94.8, 55.7, 21.5.

Synthesis of clauszoline-K (5ah)

Clauszoline-K was synthesized by following literature report. DDQ (587mg, 2.58 mmol) was added to a solution of 2-methoxy-6-methyl-9H-carbazole (4ah, 130 mg, 0.616 mmol) in a solution of MeOH (40 mL) and H_2O (4 mL).Resulting mixture was stirred at room temperature upto complete consumption of starting material (45 min). Diethyl ether was added to reaction mixture and washed with aqueous potassium hydroxide (2 M) and brine several times. The aqueous layers were extracted with diethyl ether. The combined organic layers were dried with anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (25% EtOAc in hexane) to provide pure 7-methoxy-9H-carbazole-3-carbaldehyde (**5ah**, 114 mg, Yield 77%).

***7-Methoxy-9H-carbazole-3-carbaldehyde (5ah)*:** Yield 77%; R_f = 0.40 (hexane:ethyl acetate 4:1); yellow solid; mp 183-184 °C (lit. mp 183-186 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.08 (s, 1H), 8.50 (s, 1H), 8.36 (bs, 1H), 7.99 (d, *J* = 8 Hz, 1H), 7.90 (d, *J* = 8 Hz, 1H), 7.46 (d, *J* = 8 Hz, 1H), 6.96-6.92 (m, 2H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.2, 159.9, 143.5, 141.5, 129.4, 126.6, 123.9, 122.9, 121.6, 117.0, 110.7, 109.5, 95.3, 55.84.

^{1}H and ^{13}C NMR Spectra

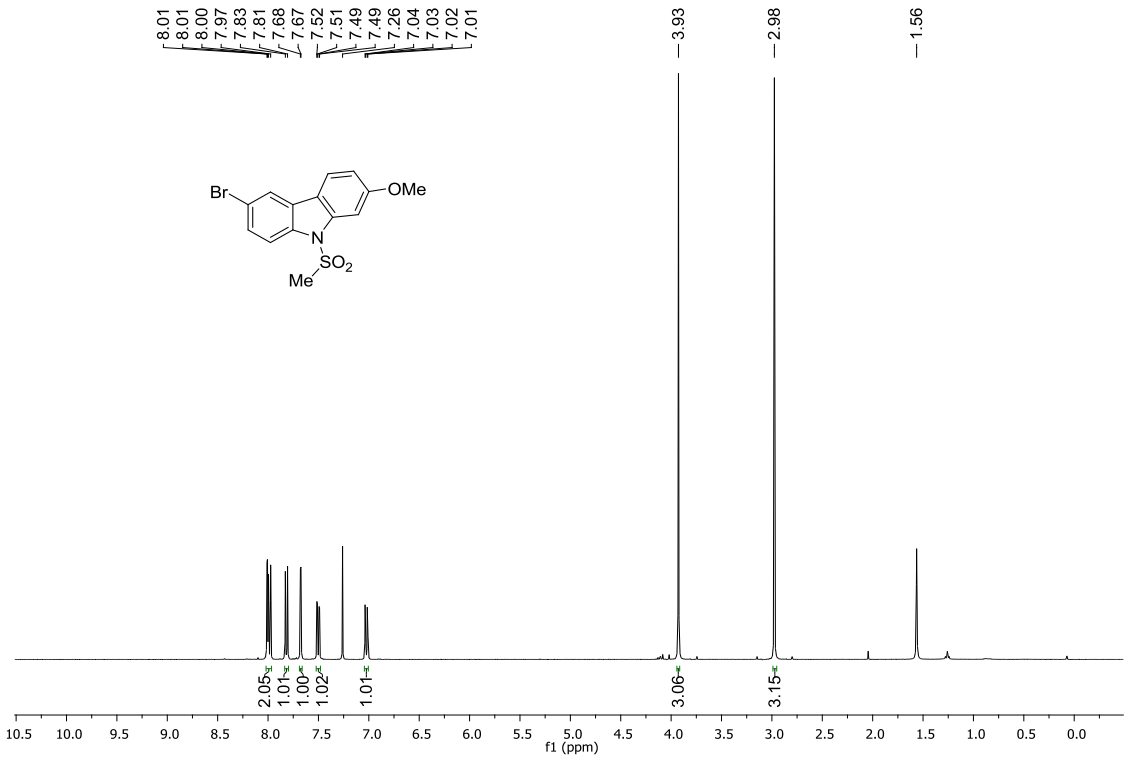


Figure 3A.8 ^{1}H NMR spectrum of 6-bromo-2-methoxy-9-(methylsulfonyl)carbazole **(3a)**

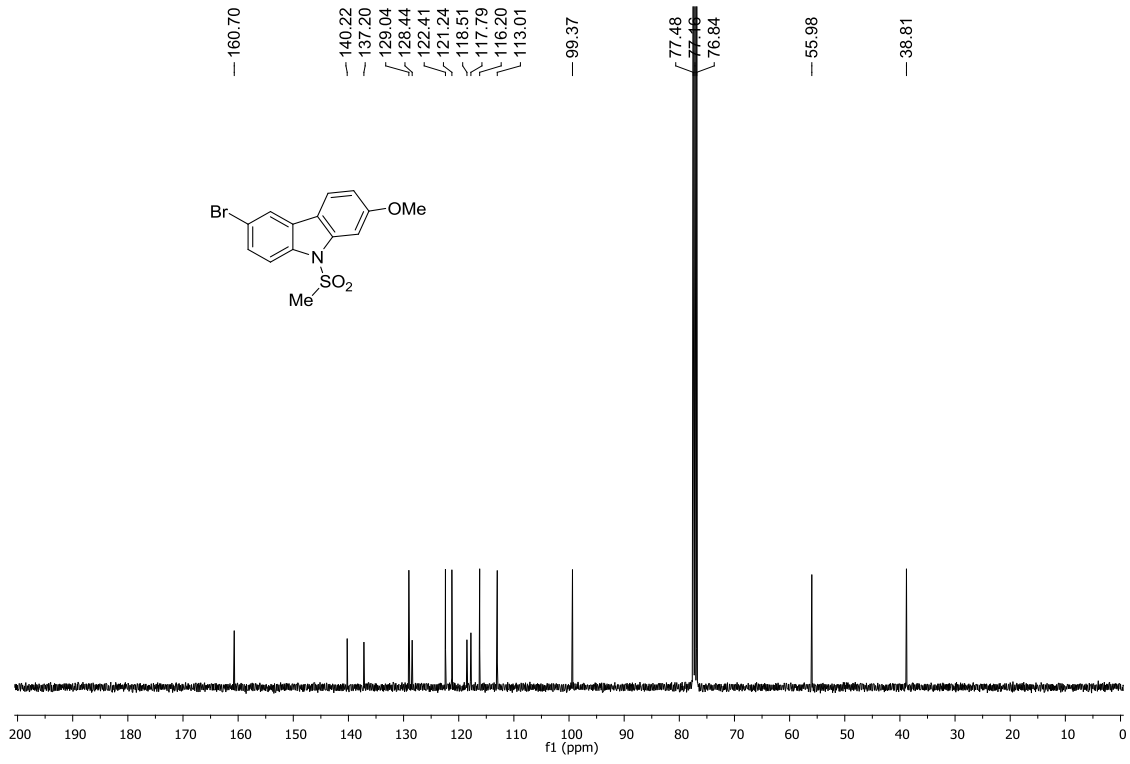


Figure 3A.9 ^{13}C NMR spectrum of 6-bromo-2-methoxy-9-(methylsulfonyl)carbazole **(3a)**

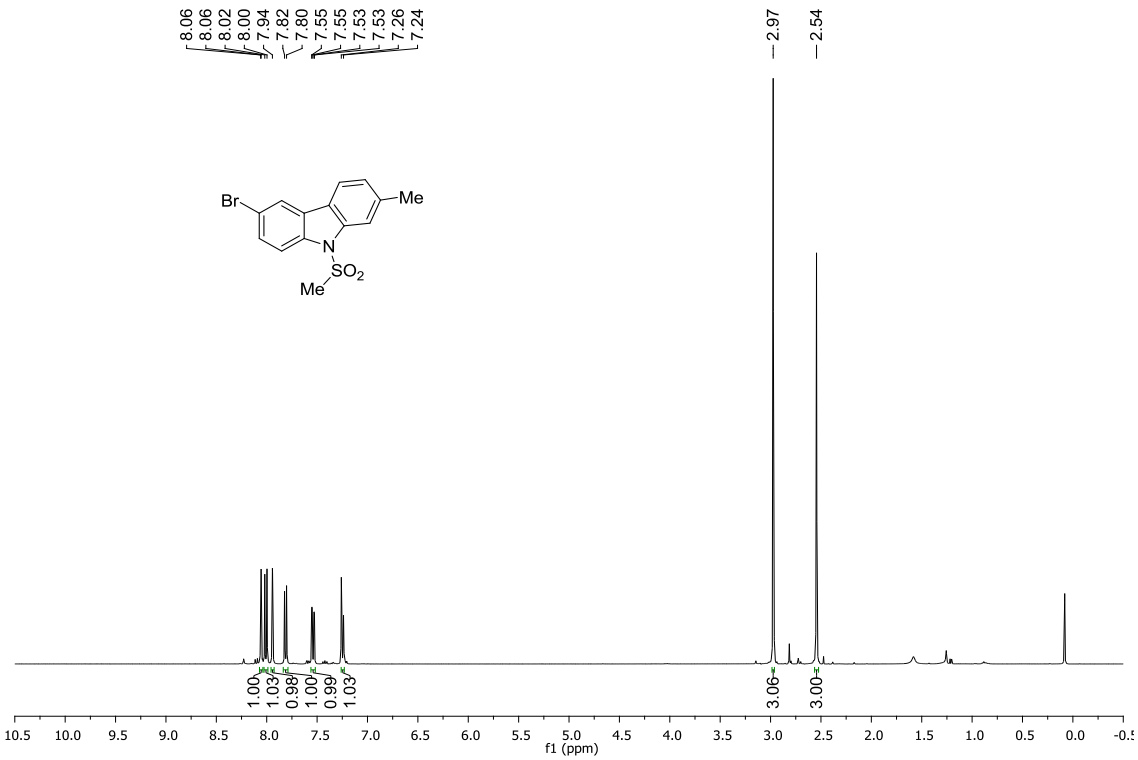


Figure 3A.10 ^{1}H NMR spectrum of 6-bromo-2-methyl-9-(methylsulfonyl)carbazole **(3b)**

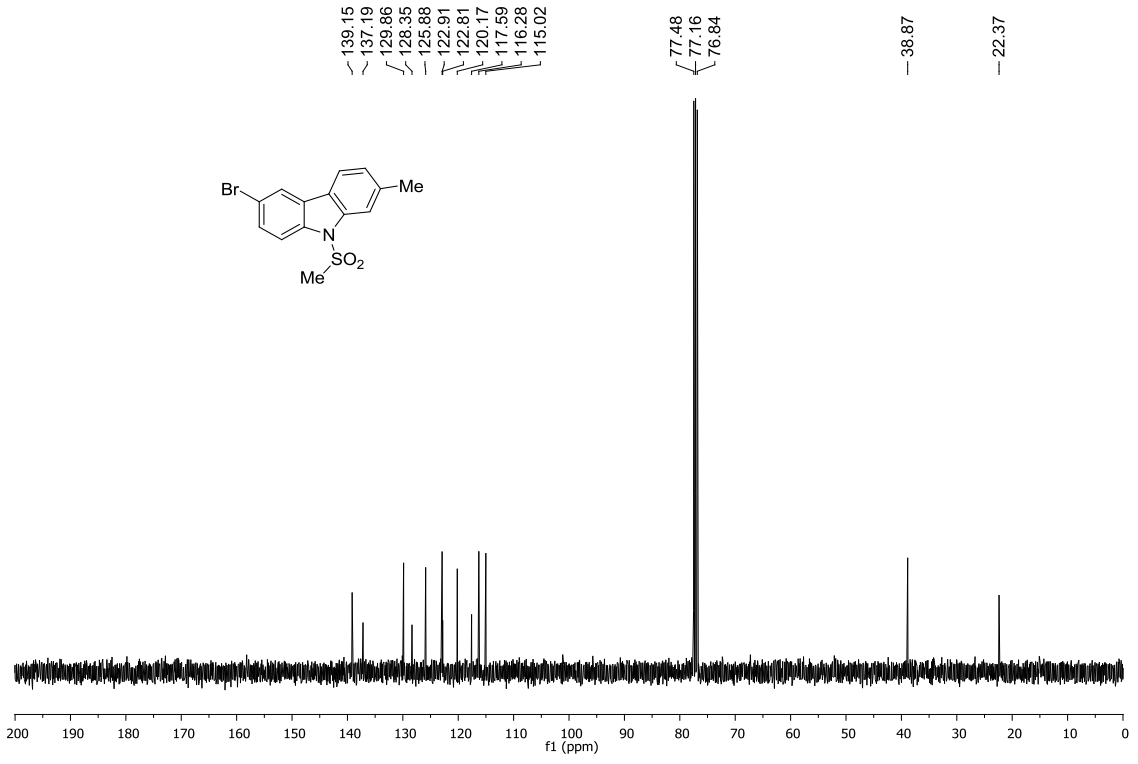


Figure 3A.11 ^{13}C NMR spectrum of 6-bromo-2-methyl-9-(methylsulfonyl)carbazole **(3b)**

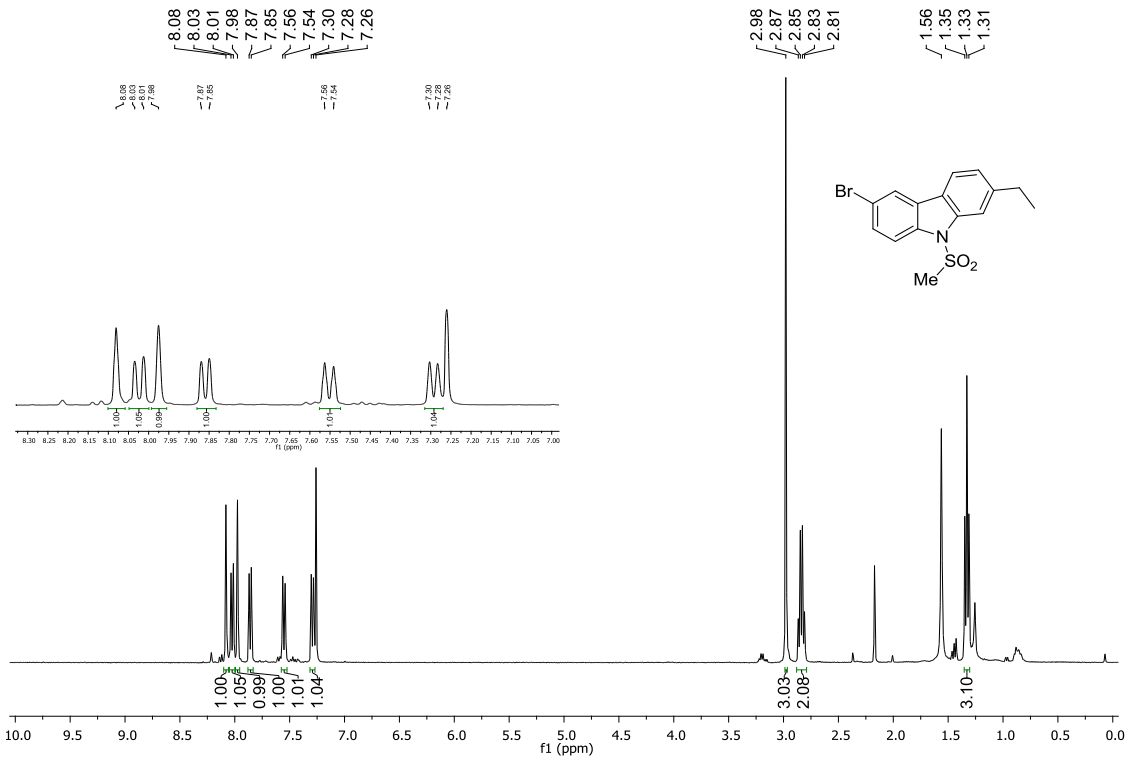


Figure 3A.12 ^{1}H NMR spectrum of 6-bromo-2-ethyl-9-(methylsulfonyl)carbazole **(3d)**

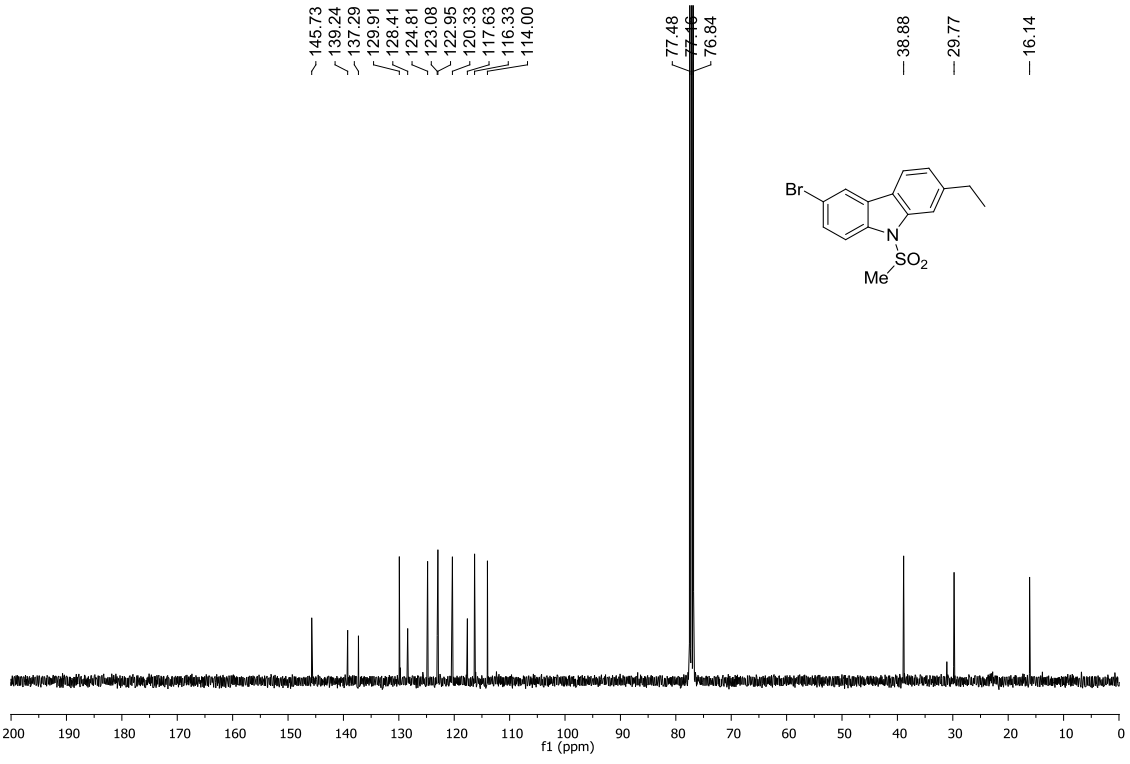


Figure 3A.13 ^{13}C NMR spectrum of 6-bromo-2-ethyl-9-(methylsulfonyl)carbazole **(3d)**

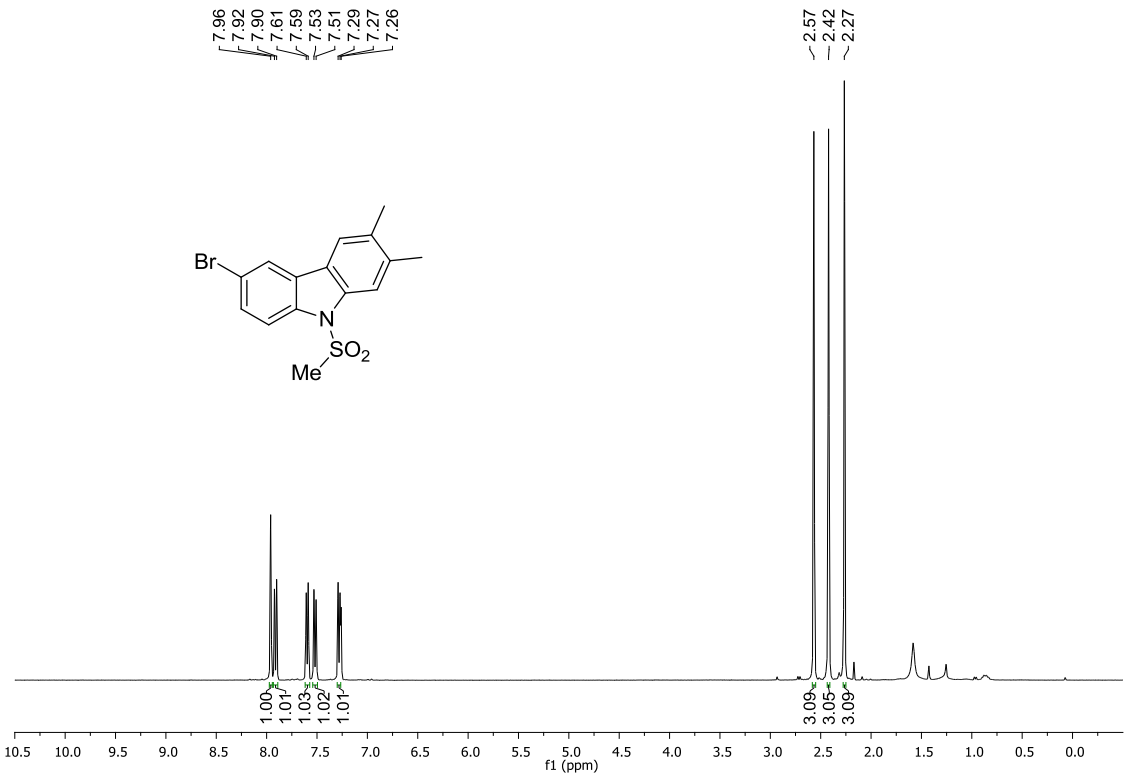


Figure 3A.14 ^{1}H NMR spectrum of 6-bromo-2,3-dimethyl-9-(methylsulfonyl)carbazole **(3f)**

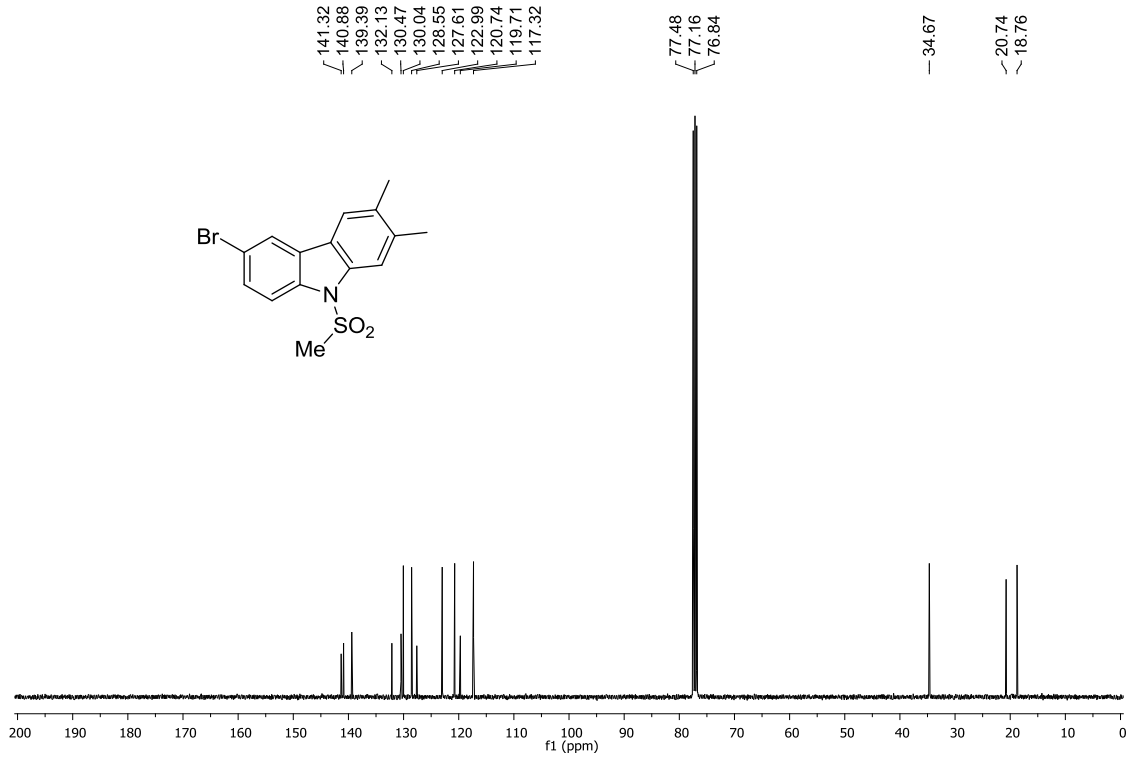


Figure 3A.15 ^{13}C NMR spectrum of 6-bromo-2,3-dimethyl-9-(methylsulfonyl)carbazole **(3f)**

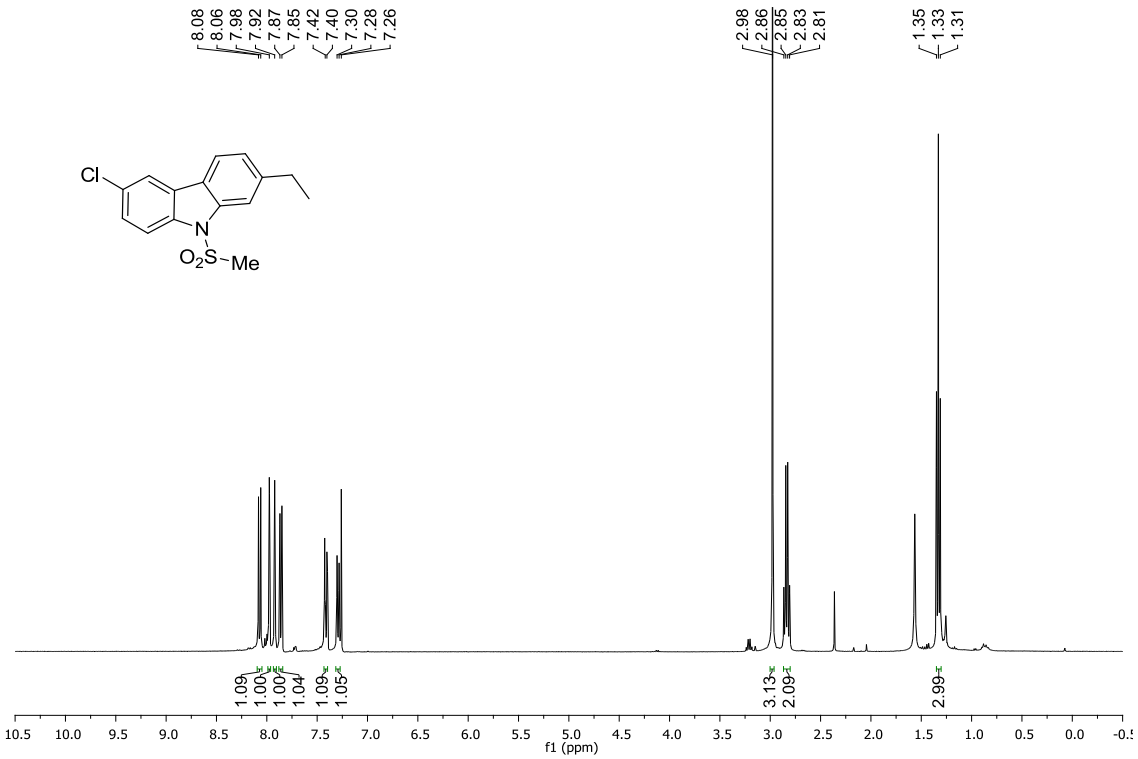


Figure 3A.16 ^{1}H NMR spectrum of 6-chloro-2-ethyl-9-(methylsulfonyl)carbazole **(3h)**

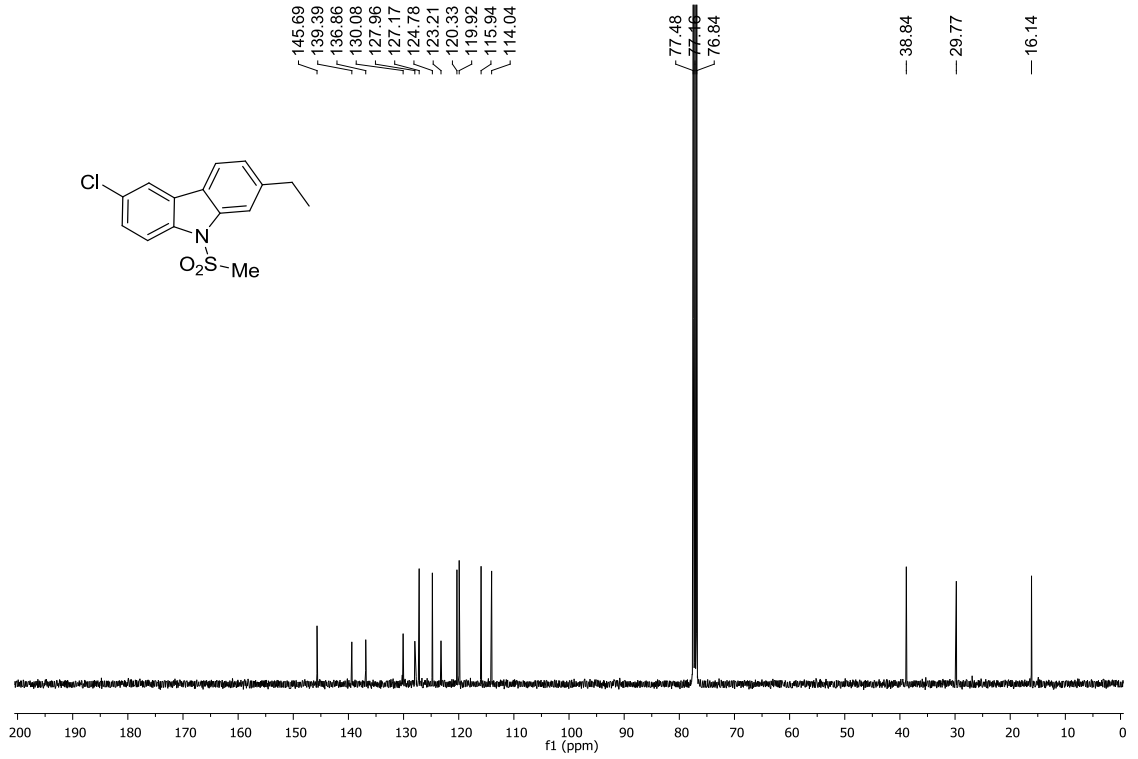


Figure 3A.17 ^{13}C NMR spectrum of 6-chloro-2-ethyl-9-(methylsulfonyl)carbazole **(3h)**

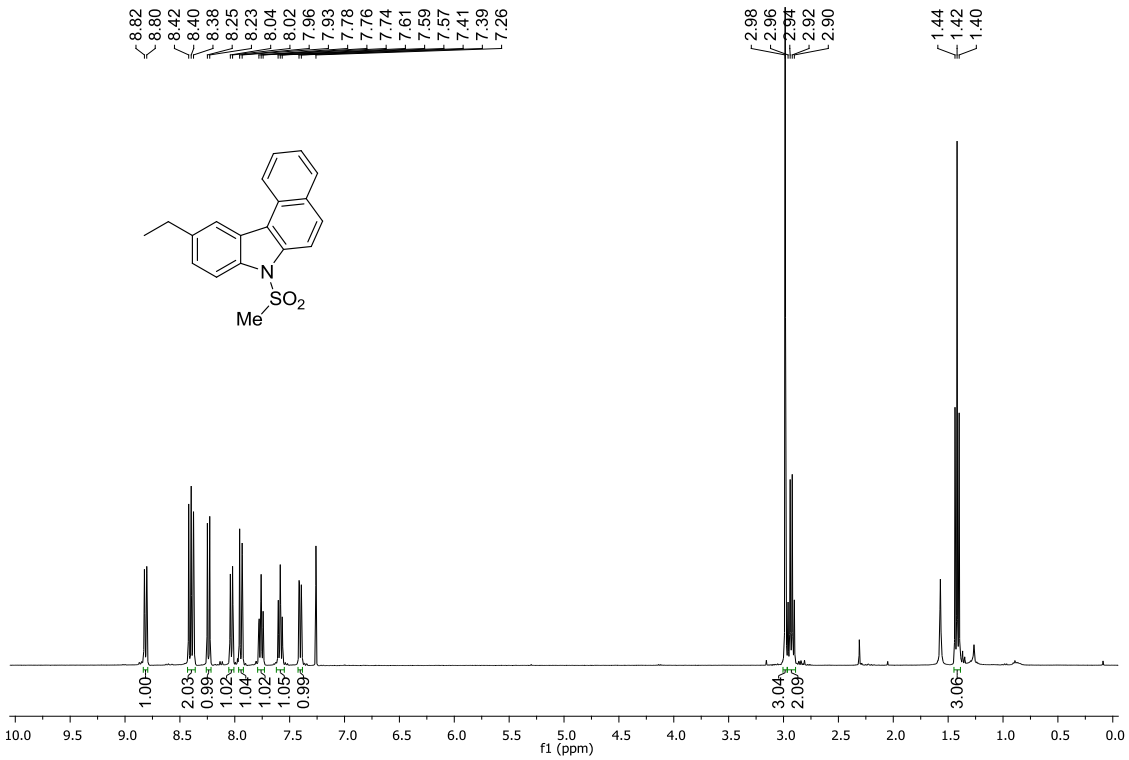


Figure 3A.18 ^{1}H NMR spectrum of 10-ethyl-7-(methylsulfonyl)benzo[c]carbazole **(3i)**

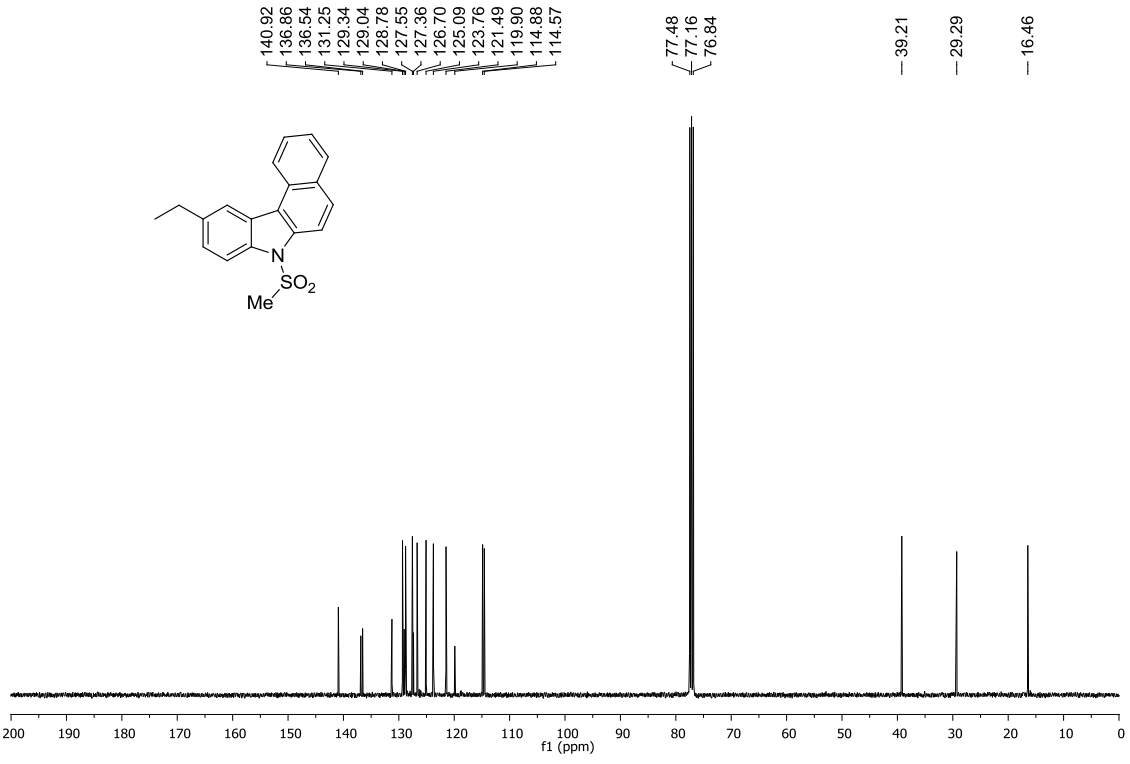


Figure 3A.19 ^{13}C NMR spectrum of 10-ethyl-7-(methylsulfonyl)benzo[c]carbazole **(3i)**

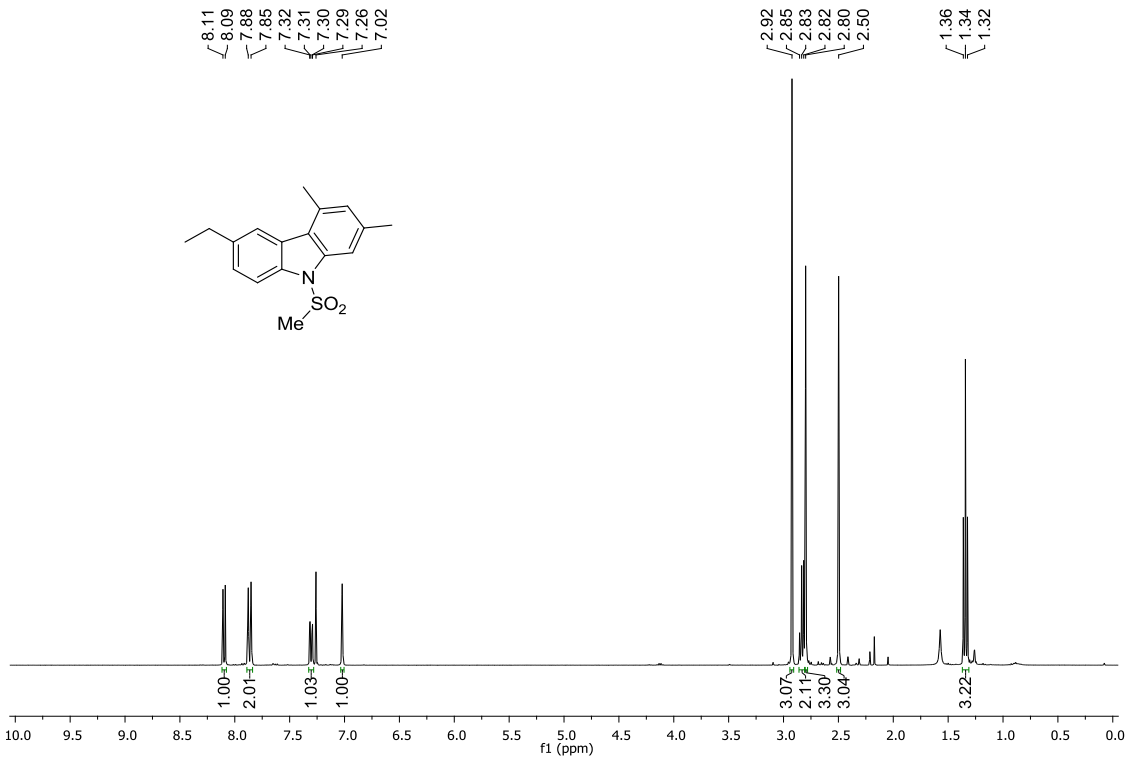


Figure 3A.20 ^{1}H NMR spectrum of 6-ethyl-2,4-dimethyl-9-(methylsulfonyl)carbazole **(3m)**

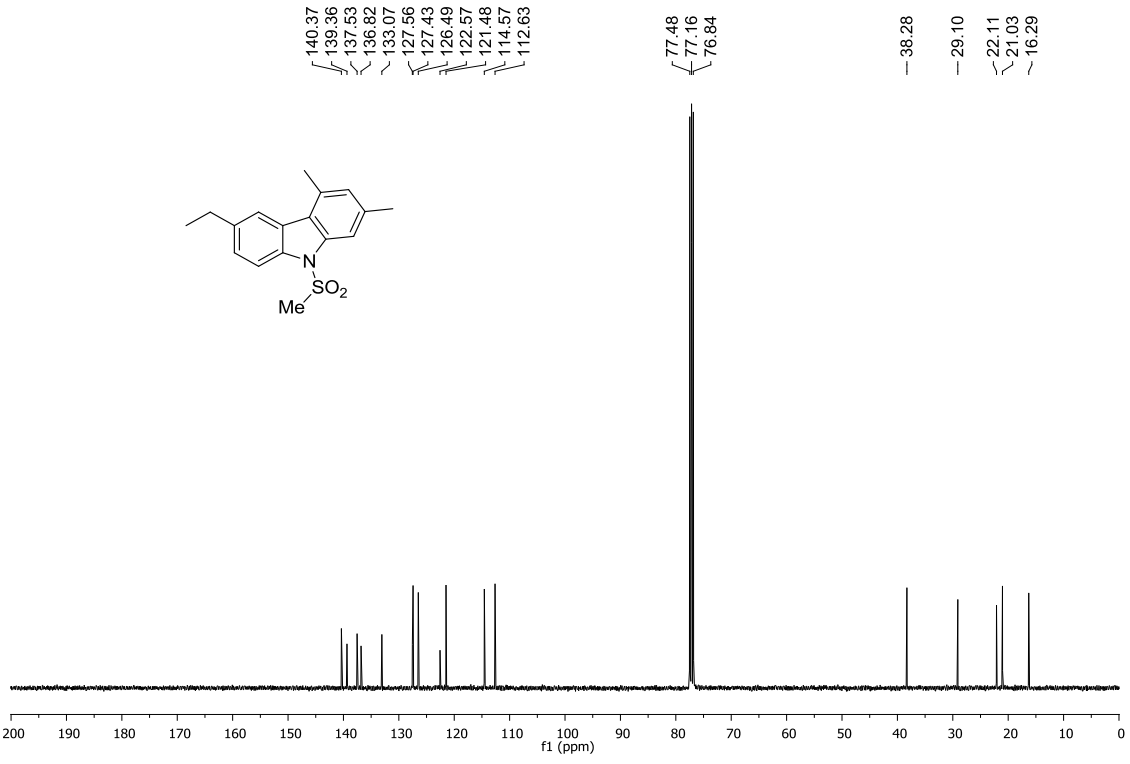


Figure 3A.21 ^{13}C NMR spectrum of 6-ethyl-2,4-dimethyl-9-(methylsulfonyl)carbazole **(3m)**

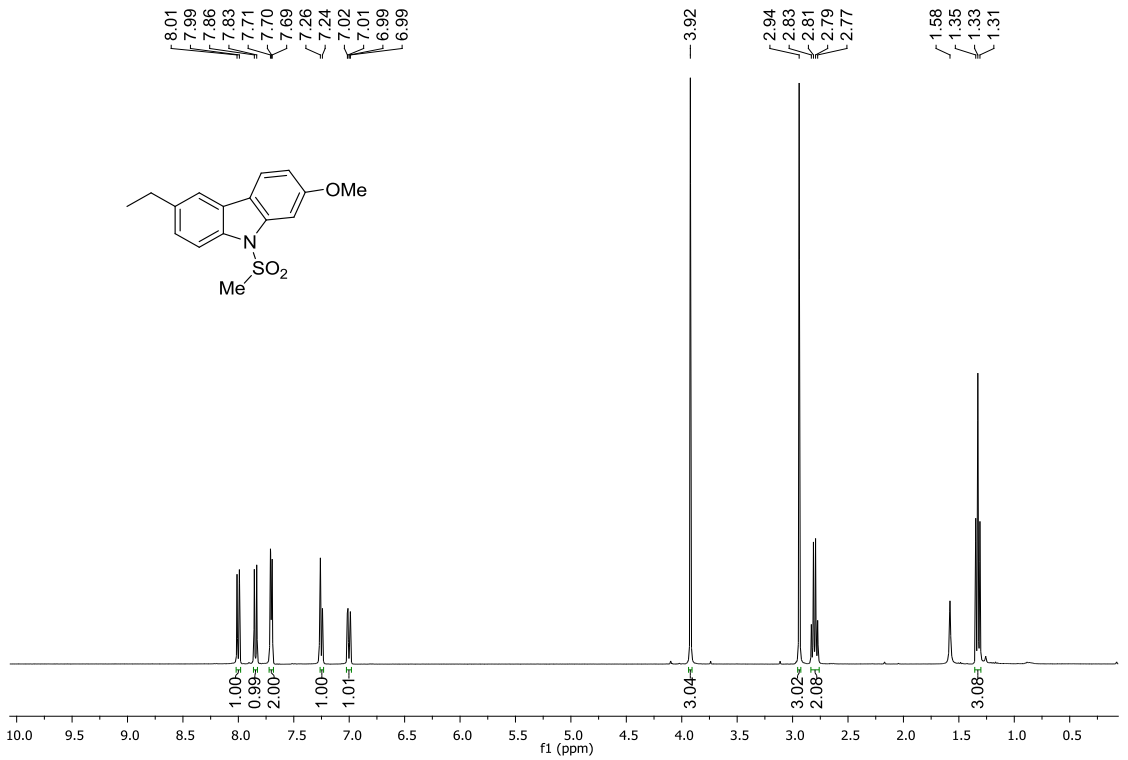


Figure 3A.22 ^{1}H NMR spectrum of 6-ethyl-2-methoxy-9-(methylsulfonyl)carbazole **(3n)**

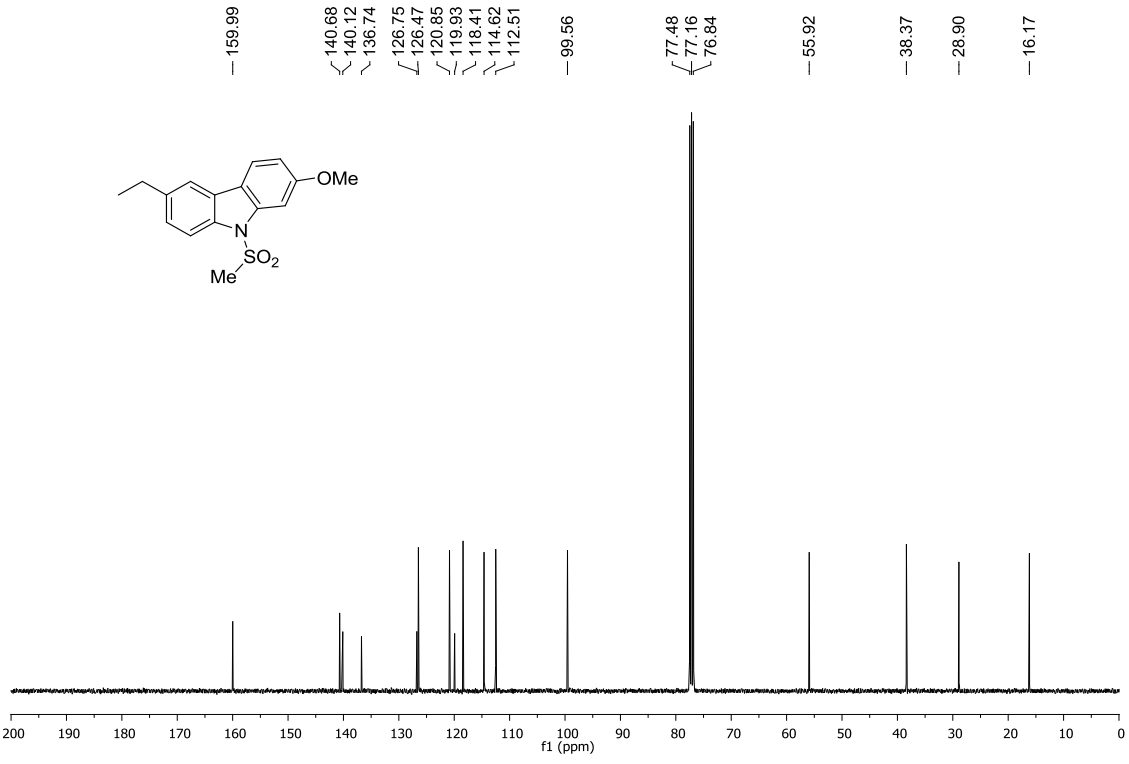


Figure 3A.23 ^{13}C NMR spectrum of 6-ethyl-2-methoxy-9-(methylsulfonyl)carbazole **(3n)**

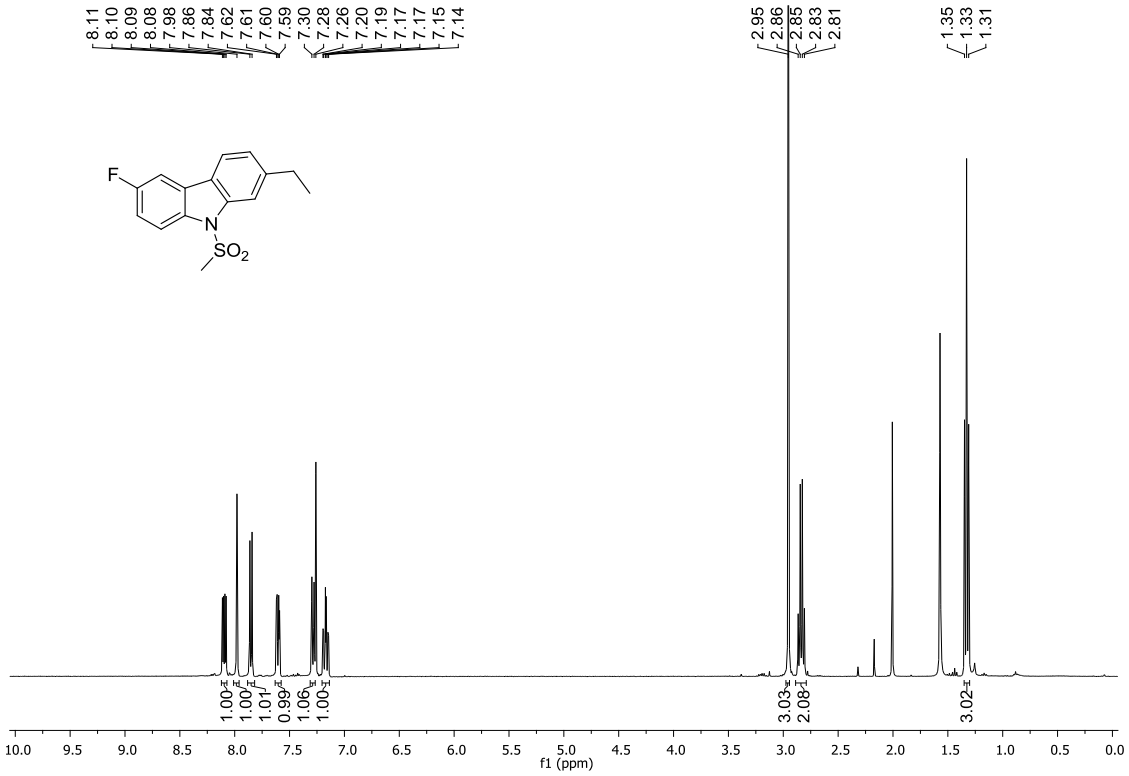


Figure 3A.24 ^{1}H NMR spectrum of 2-Ethyl-6-fluoro-9-(methylsulfonyl)carbazole **(3o)**

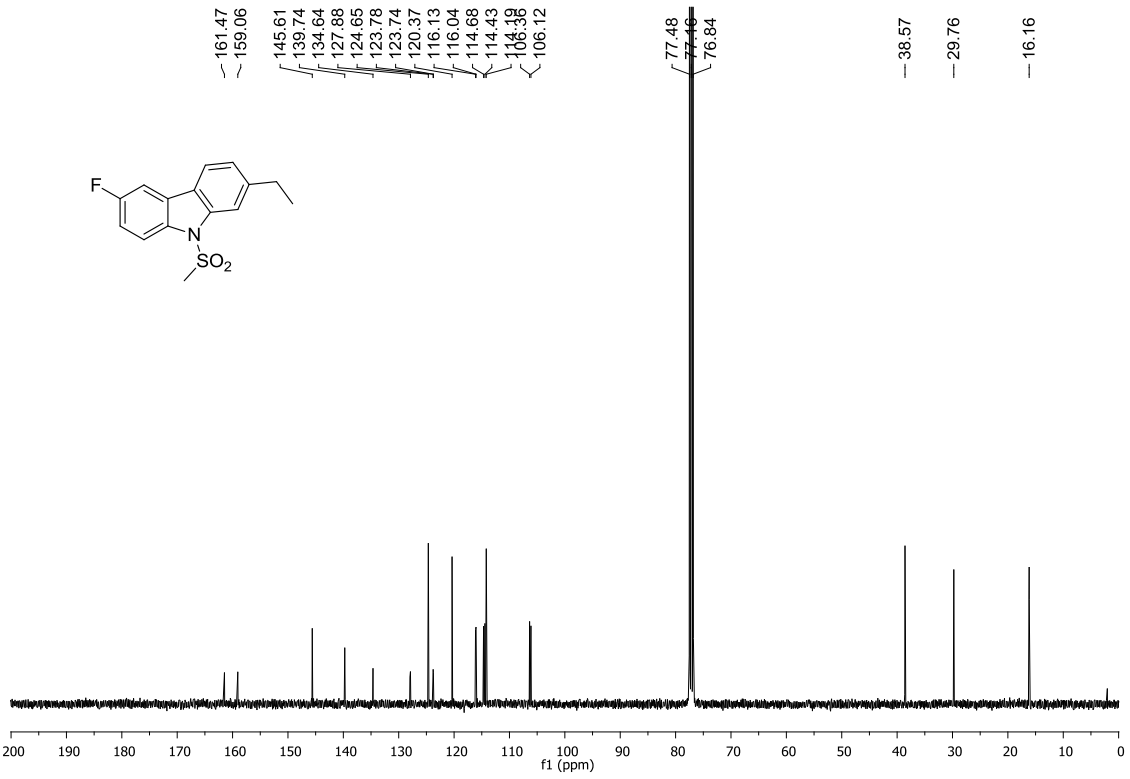


Figure 3A.25 ^{13}C NMR spectrum of 2-Ethyl-6-fluoro-9-(methylsulfonyl)carbazole **(3o)**

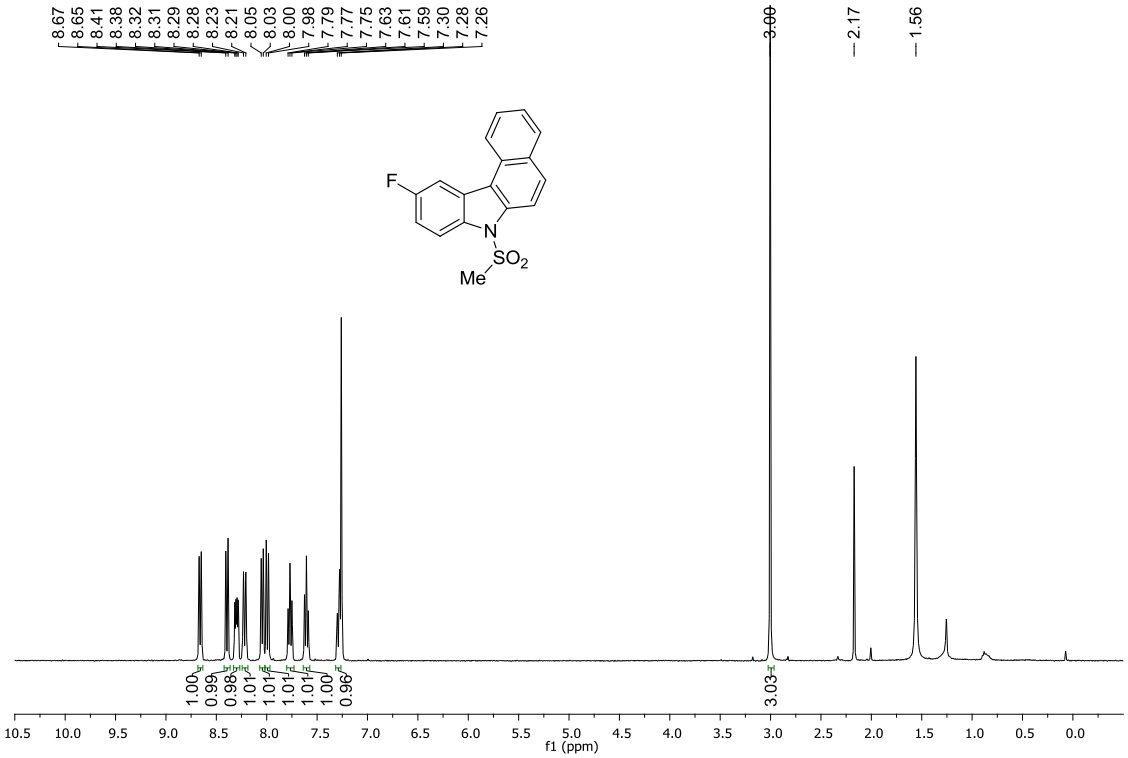


Figure 3A.26 ^{1}H NMR spectrum of 10-fluoro-7-(methylsulfonyl)benzo[c]carbazole **(3p)**

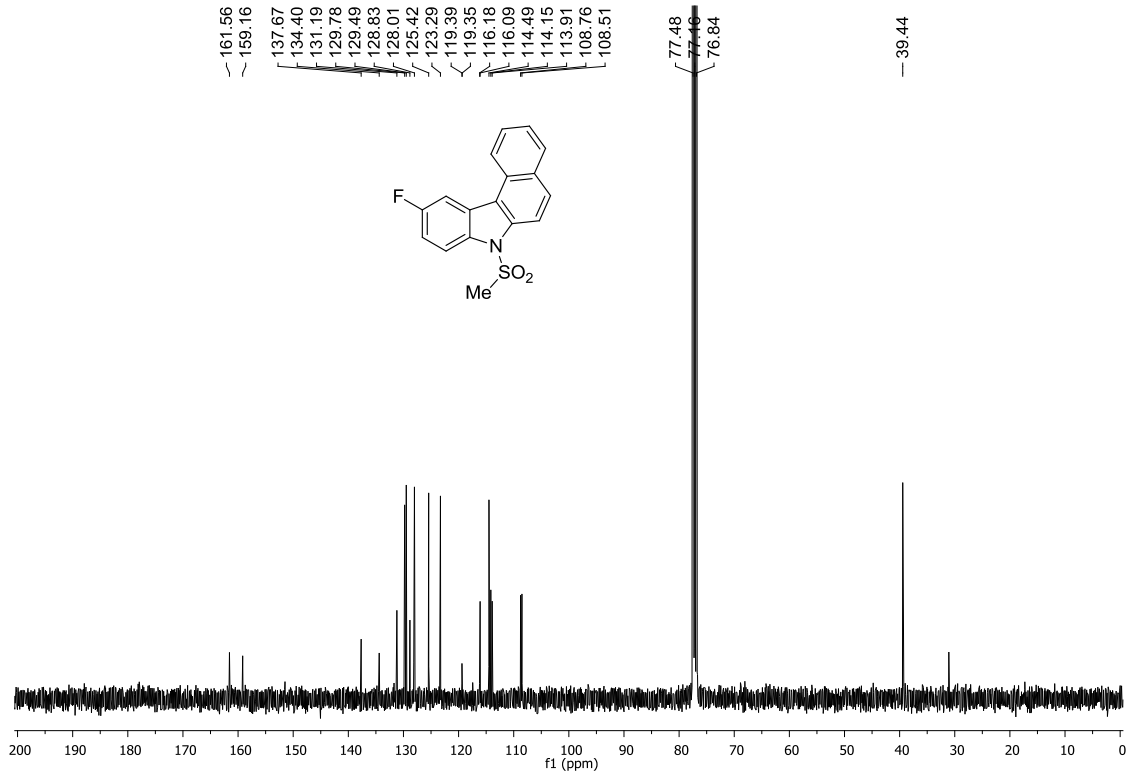


Figure 3A.27 ^{13}C NMR spectrum of 10-fluoro-7-(methylsulfonyl)benzo[c]carbazole **(3p)**

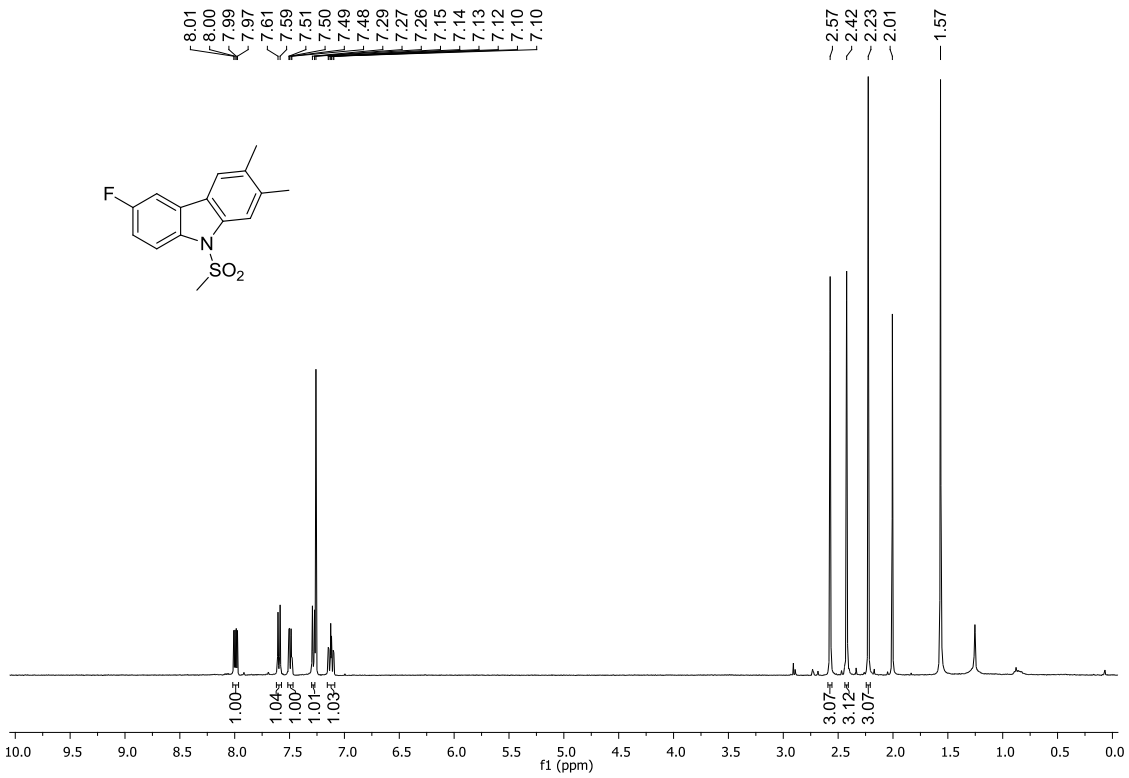


Figure 3A.28 ^{1}H NMR spectrum of 6-Fluoro-2,3-dimethyl-9-(methylsulfonyl)carbazole **(3q)**

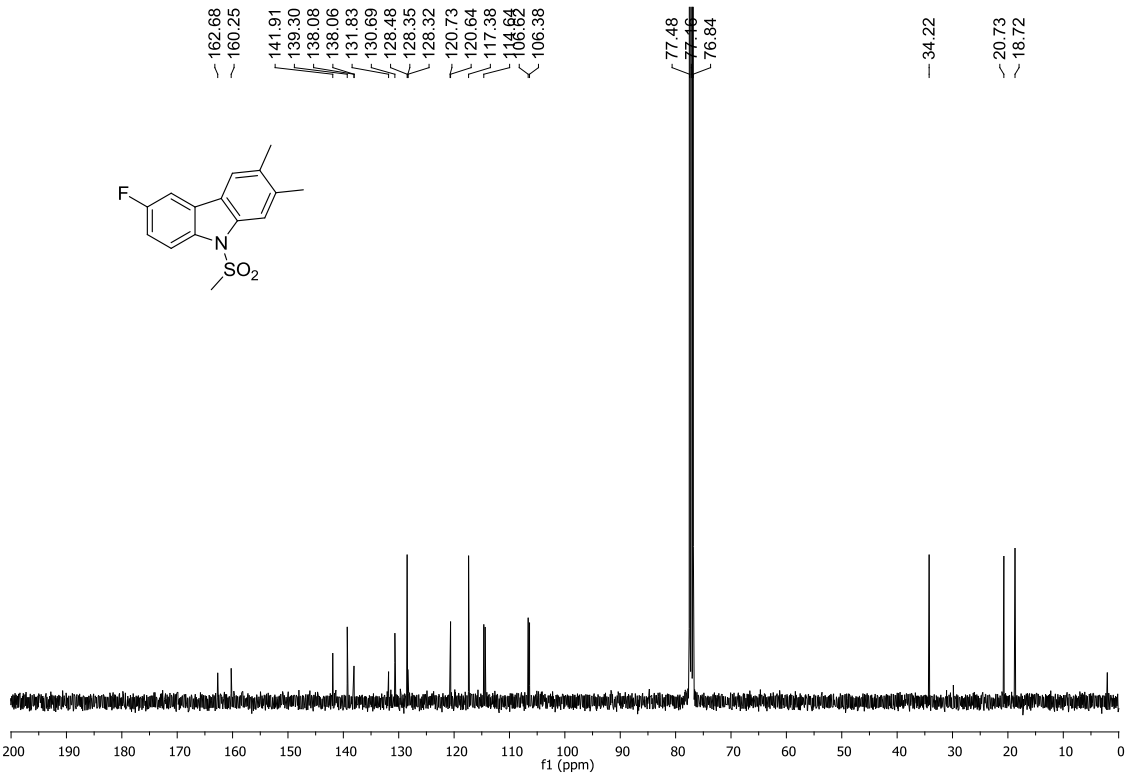


Figure 3A.29 ^{13}C NMR spectrum of 6-Fluoro-2,3-dimethyl-9-(methylsulfonyl)carbazole **(3q)**

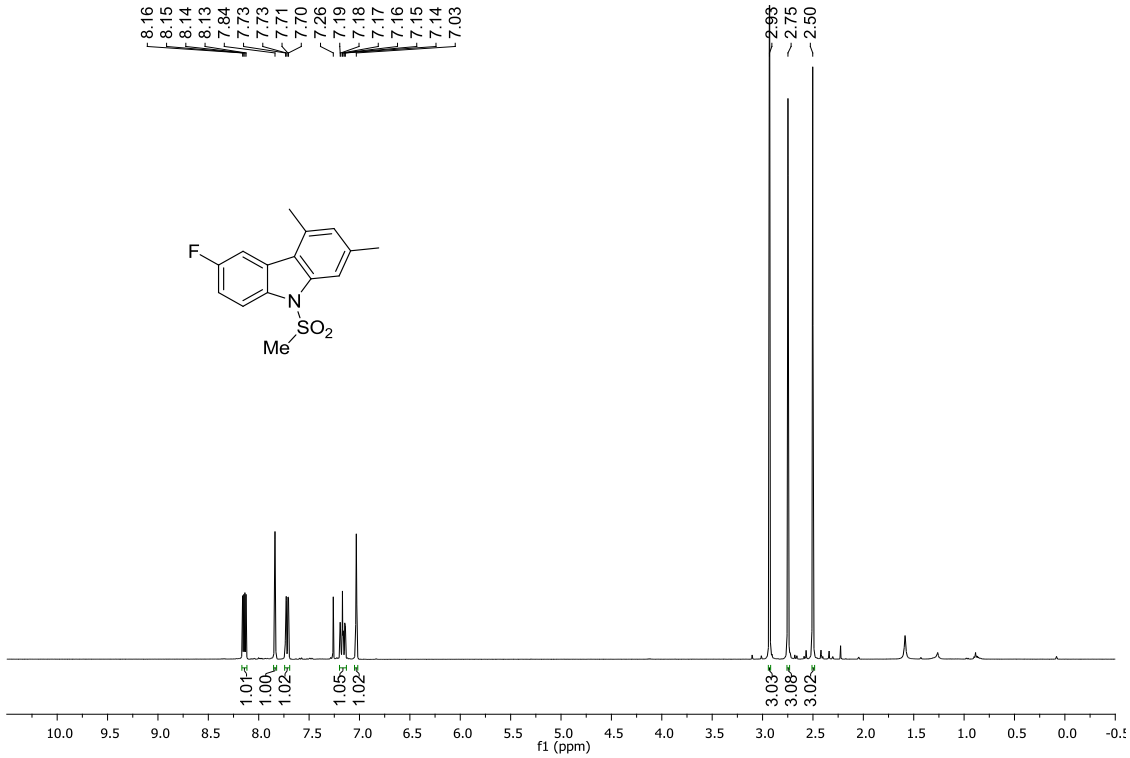


Figure 3A.30 ^{1}H NMR spectrum of 6-fluoro-2,4-dimethyl-9-(methylsulfonyl)carbazole **(3r)**

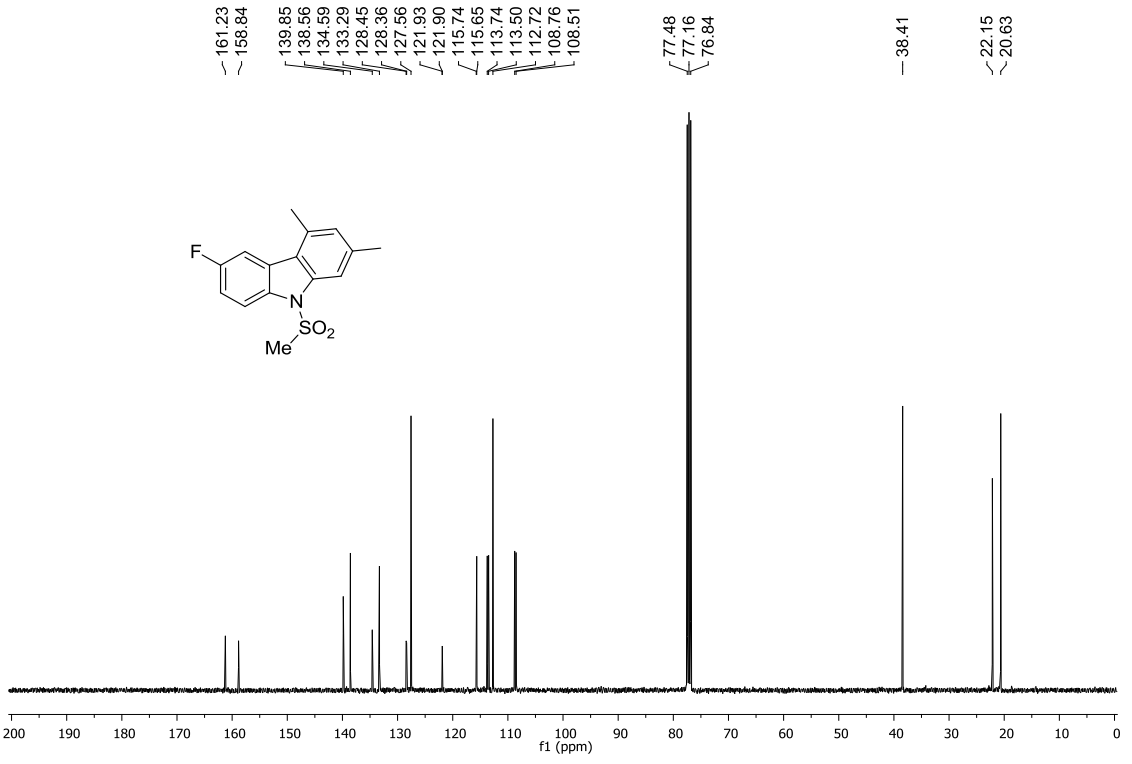


Figure 3A.31 ^{13}C NMR spectrum of 6-fluoro-2,4-dimethyl-9-(methylsulfonyl)carbazole **(3r)**

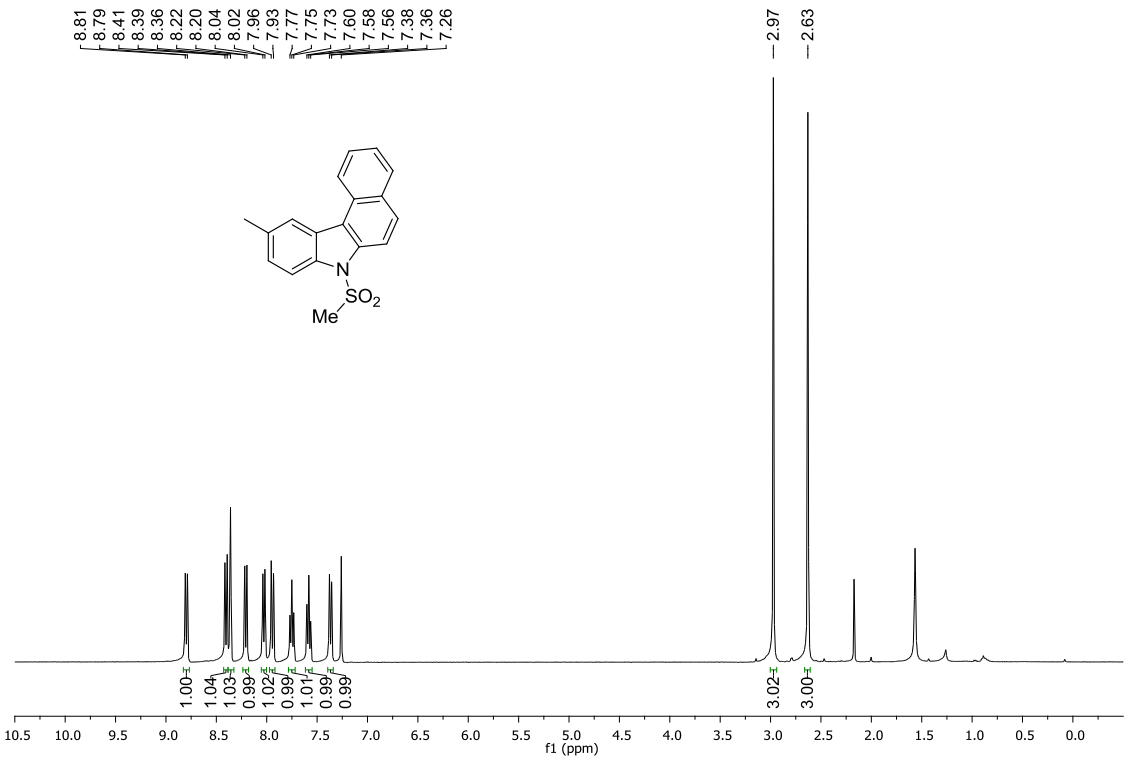


Figure 3A.32 ^{1}H NMR spectrum of 10-methyl-7-(methylsulfonyl)benzo[c]carbazole **(3s)**

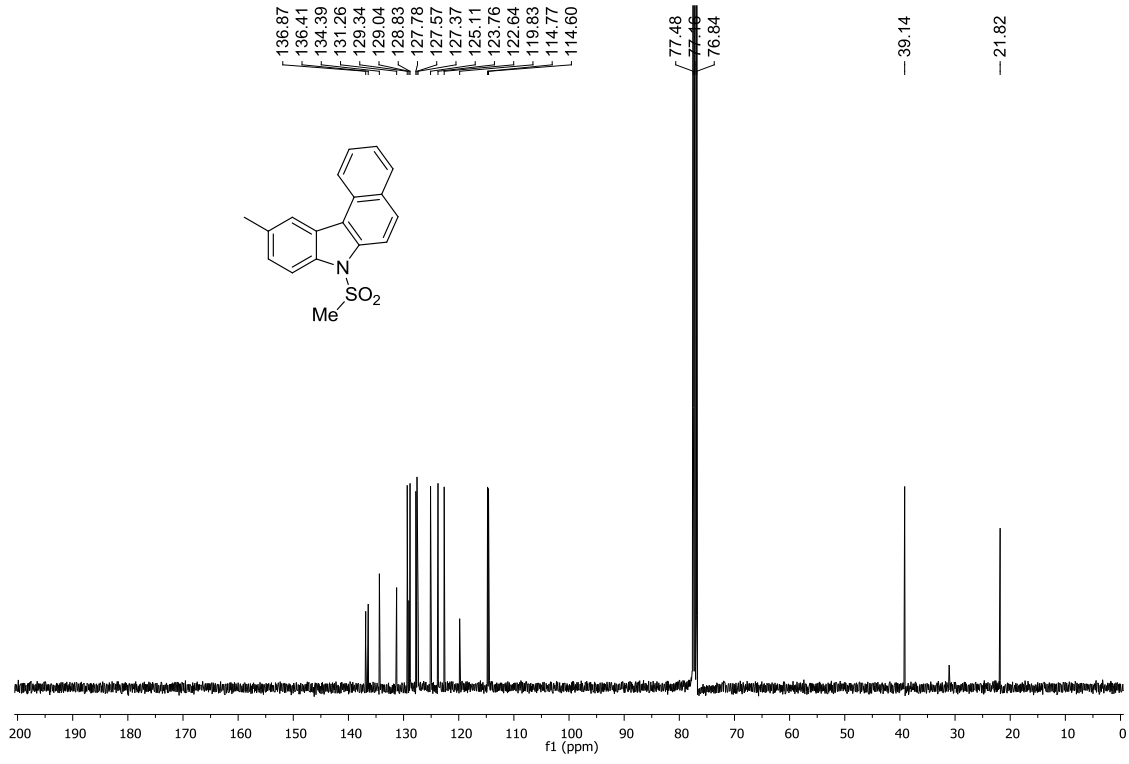


Figure 3A.33 ^{13}C NMR spectrum of 10-methyl-7-(methylsulfonyl)benzo[c]carbazole **(3s)**

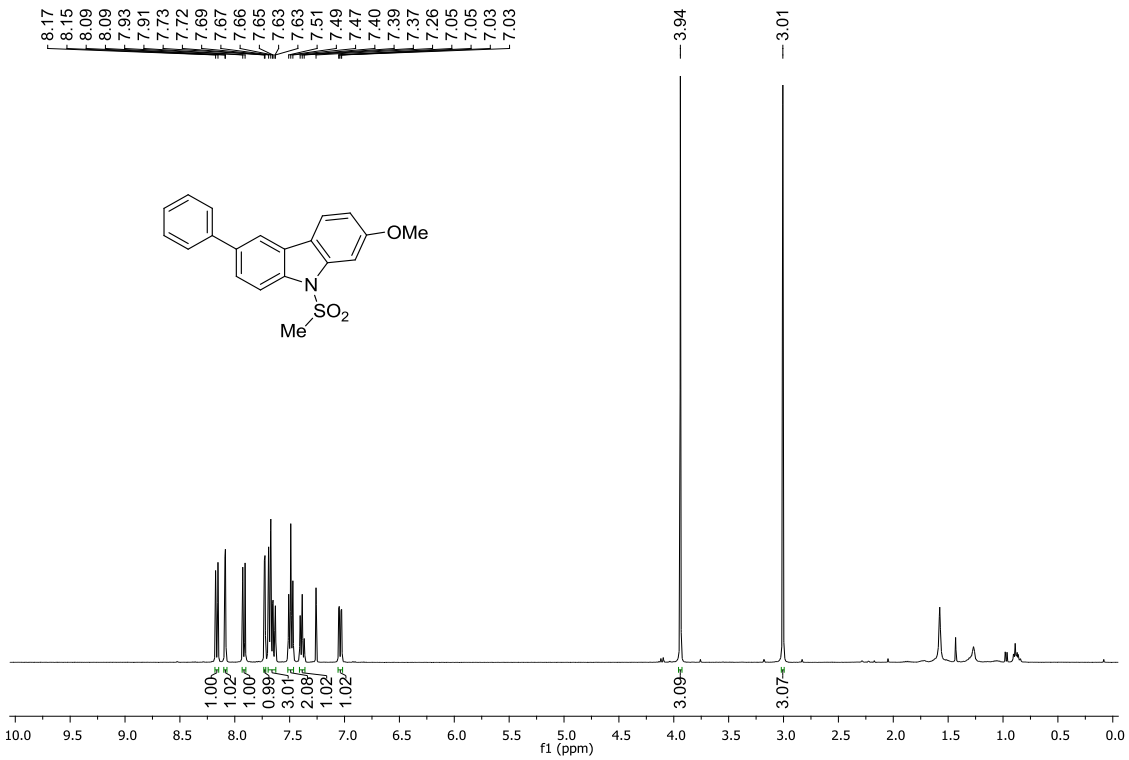


Figure 3A.34 ^{1}H NMR spectrum of 2-methoxy-9-(methylsulfonyl)-6-phenylcarbazole **(3u)**

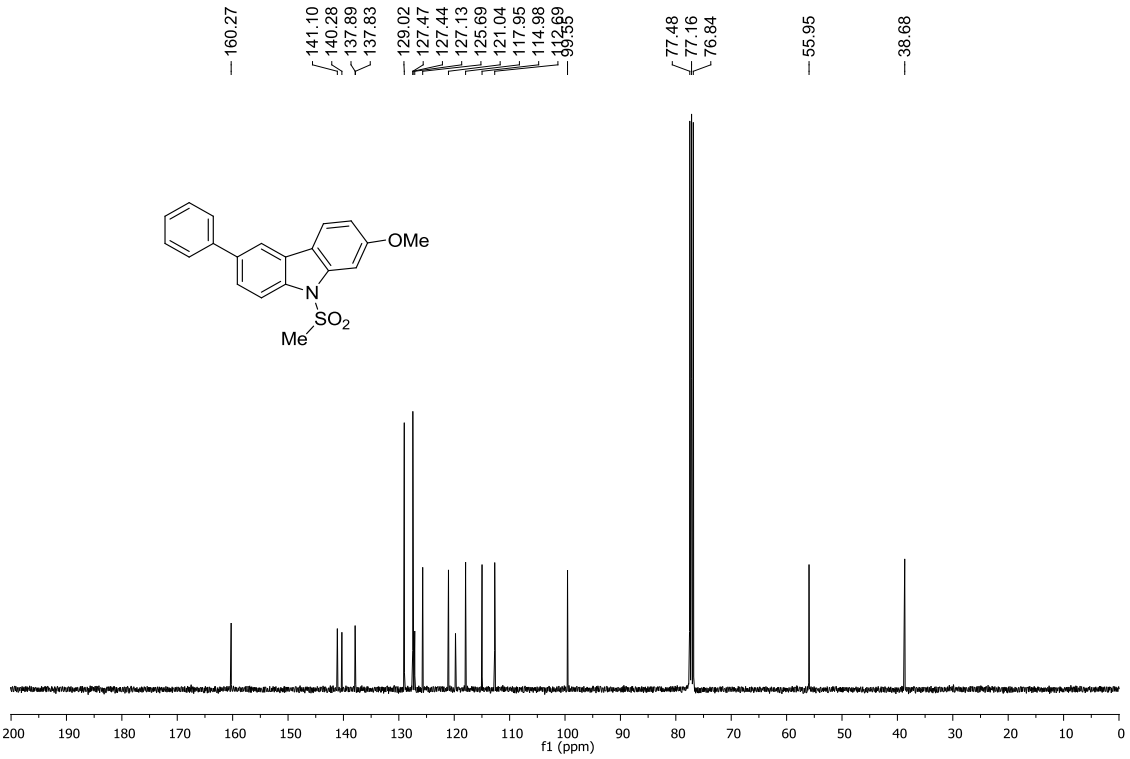


Figure 3A.35 ^{13}C NMR spectrum of 2-methoxy-9-(methylsulfonyl)-6-phenylcarbazole **(3u)**

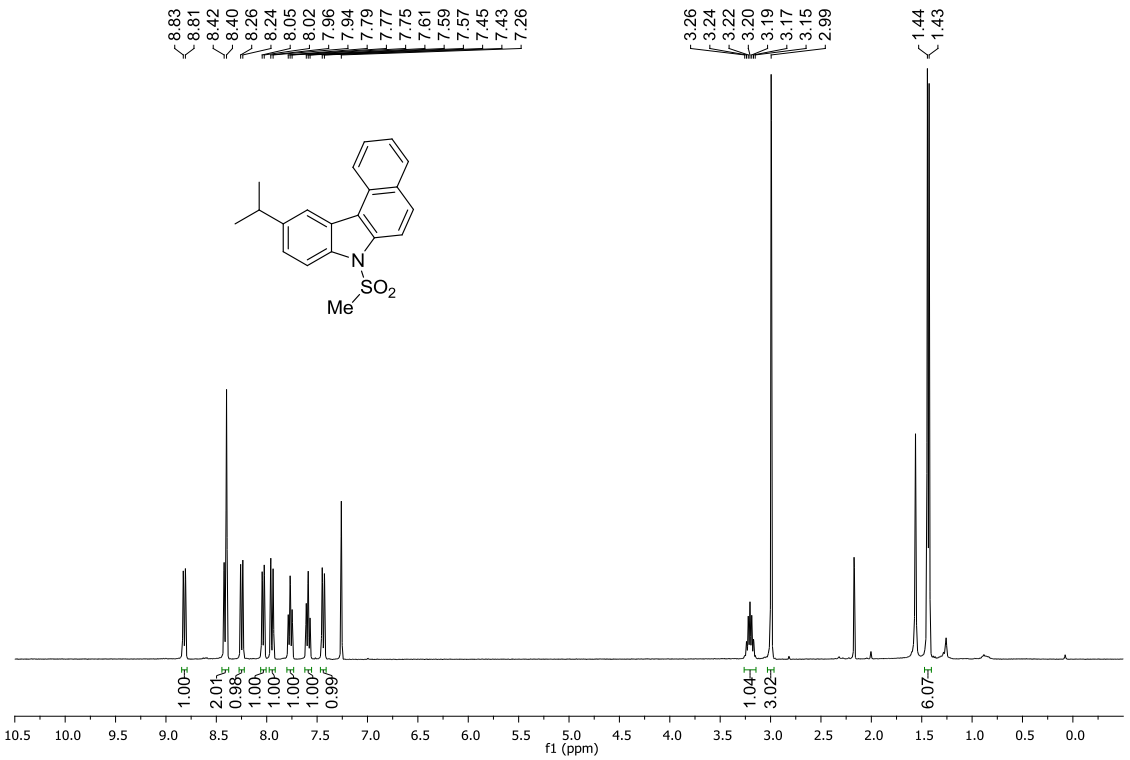


Figure 3A.36 ^{1}H NMR spectrum of 10-isopropyl-7-(methylsulfonyl)benzo[c]carbazole **(3v)**

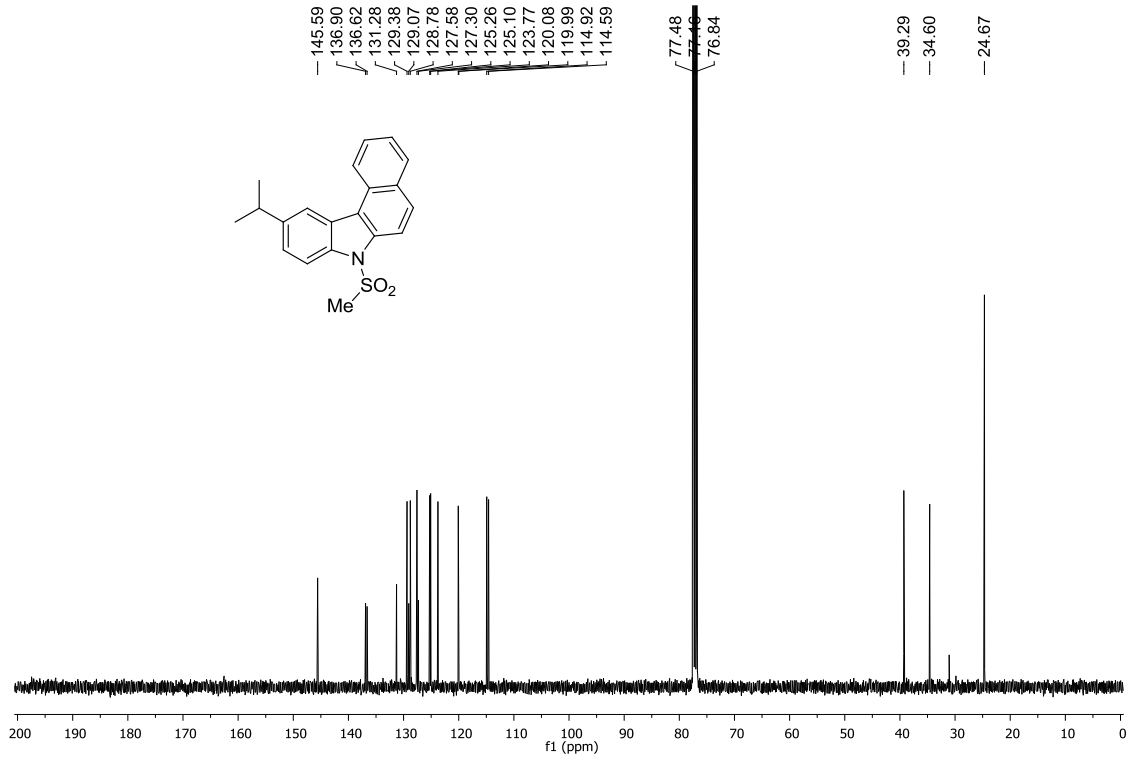


Figure 3A.37 ^{13}C NMR spectrum of 10-isopropyl-7-(methylsulfonyl)benzo[c]carbazole **(3v)**

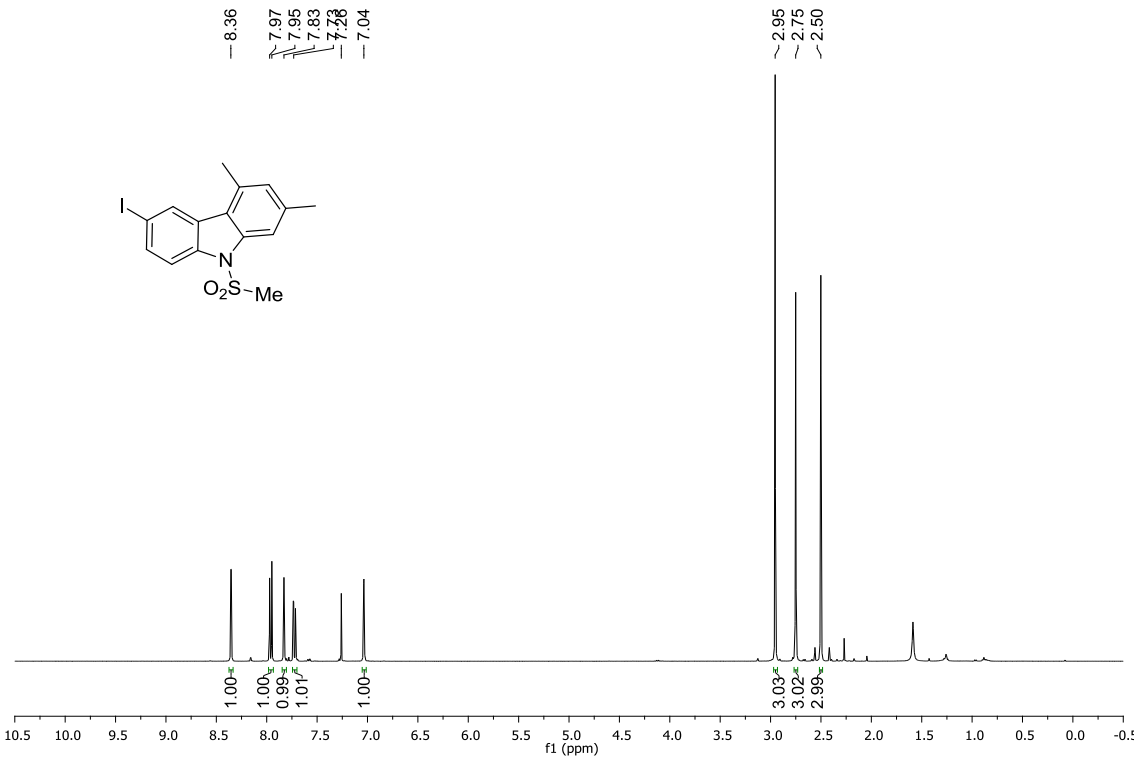


Figure 3A.38 ^{1}H NMR spectrum of 6-iodo-2,4-dimethyl-9-(methylsulfonyl)carbazole **(3w)**

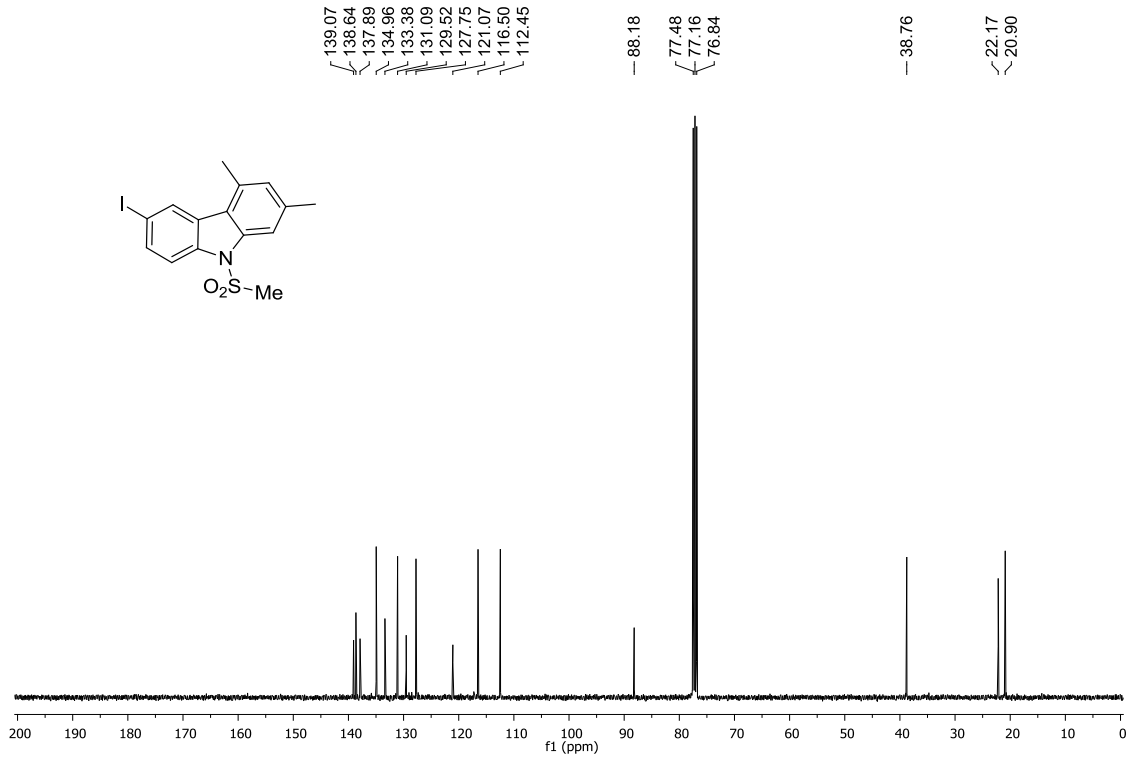


Figure 3A.39 ^{13}C NMR spectrum of 6-iodo-2,4-dimethyl-9-(methylsulfonyl)carbazole **(3w)**

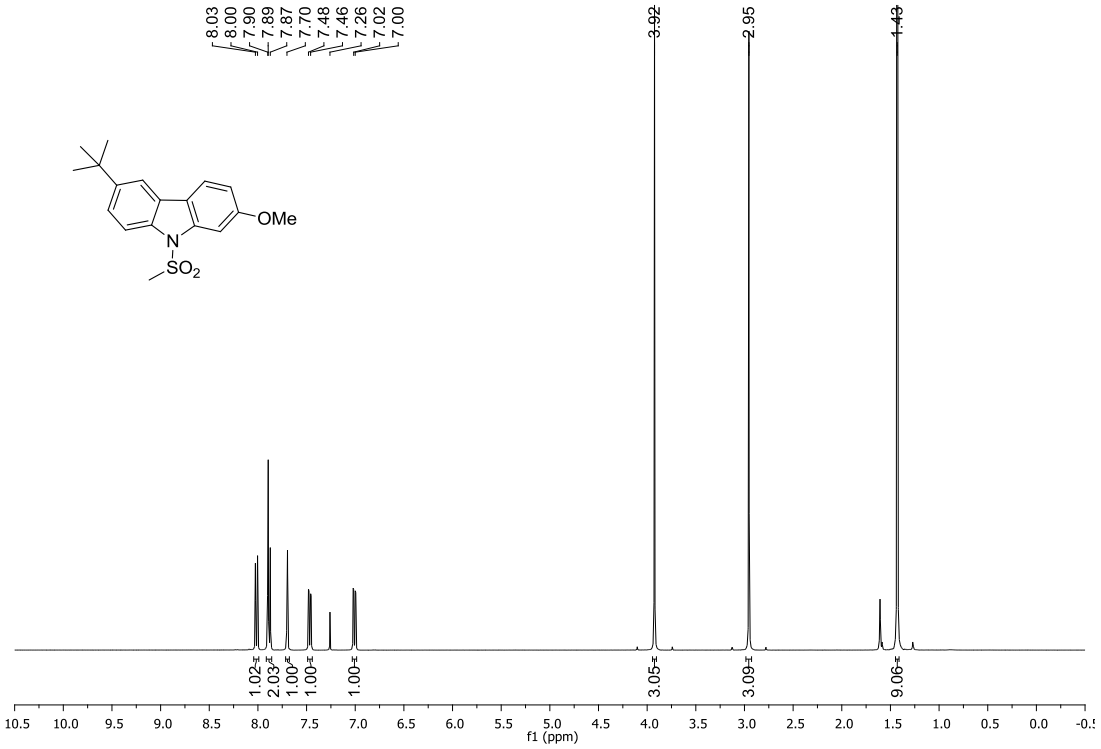


Figure 3A.40 ^{1}H NMR spectrum of 6-(tert-butyl)-2-methoxy-9-(methylsulfonyl)carbazole **(3y)**

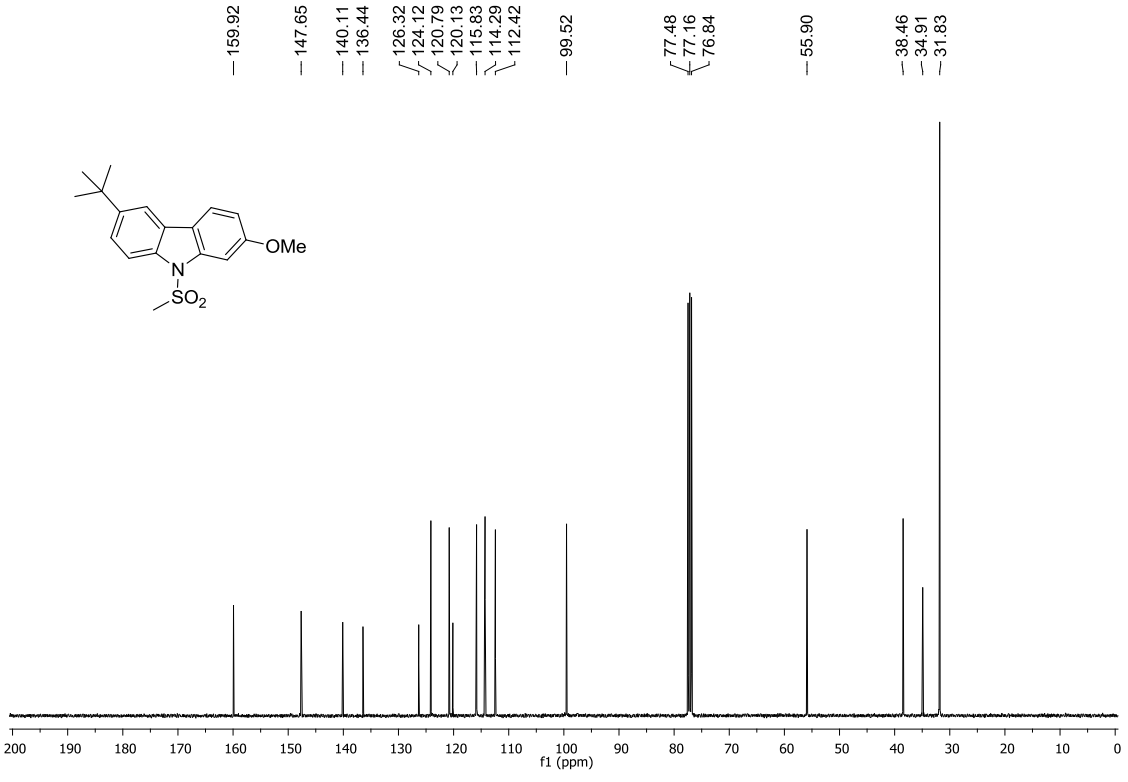


Figure 3A.41 ^{13}C NMR spectrum of 6-(tert-butyl)-2-methoxy-9-(methylsulfonyl)carbazole **(3y)**

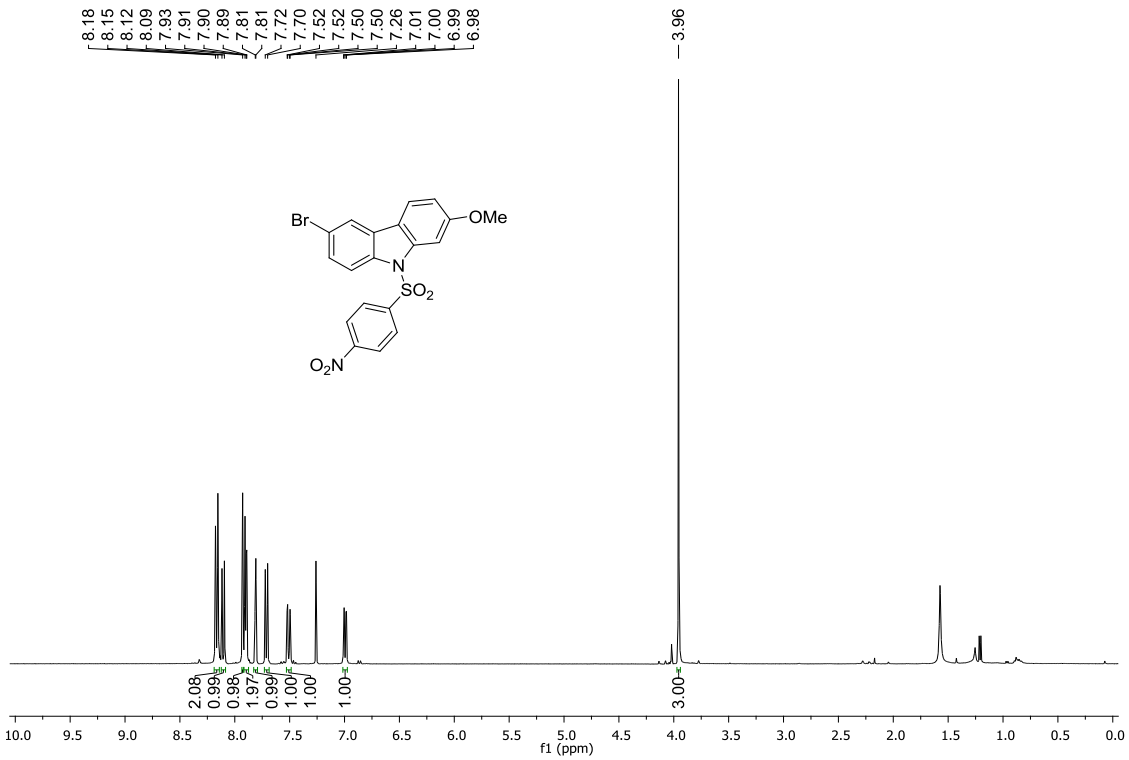


Figure 3A.42 ^{1}H NMR spectrum of 6-bromo-2-methoxy-9-((4-nitrophenyl)sulfonyl)carbazole **(3ab)**

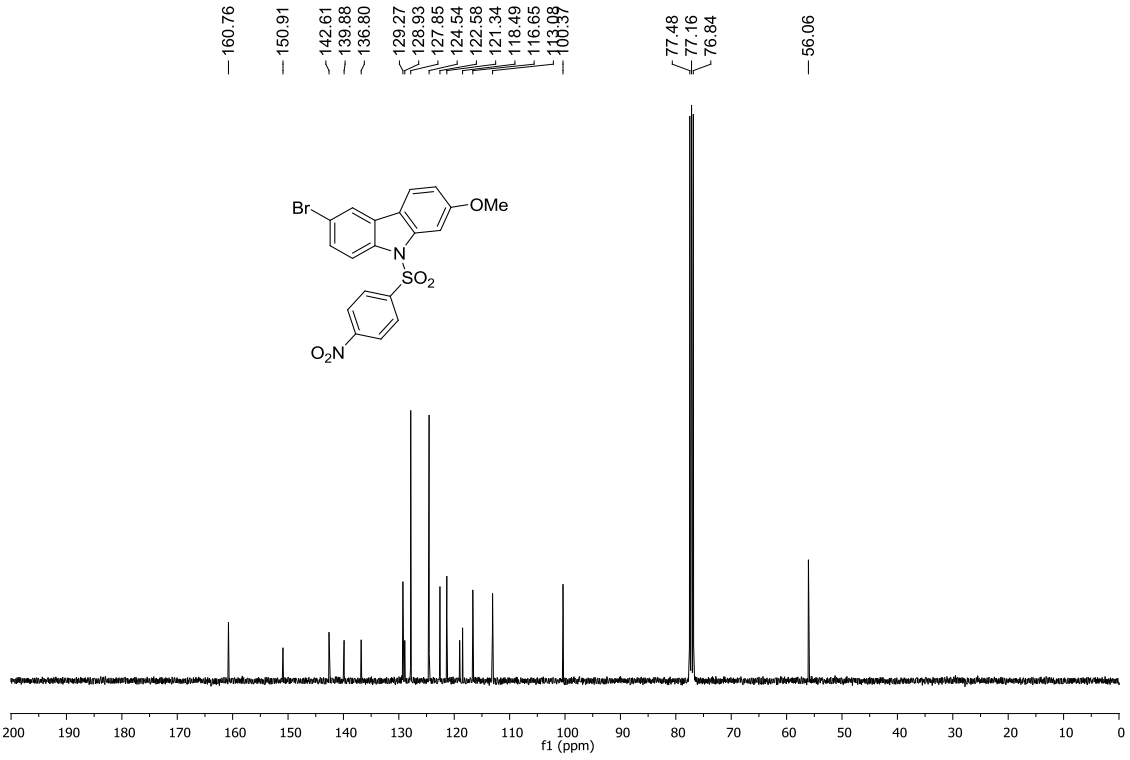


Figure 3A.43 ^{13}C NMR spectrum of 6-bromo-2-methoxy-9-((4-nitrophenyl)sulfonyl)carbazole **(3ab)**

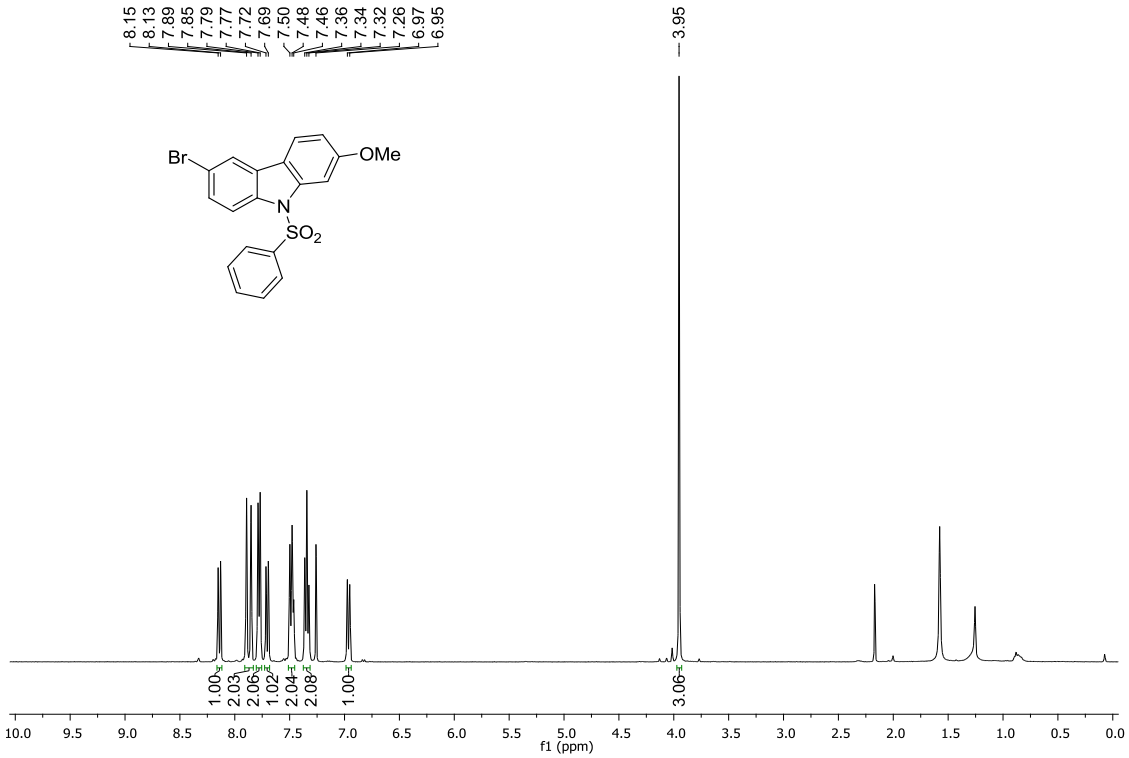


Figure 3A.44 ^{1}H NMR spectrum of 6-bromo-2-methoxy-9-(phenylsulfonyl)carbazole **(3ac)**

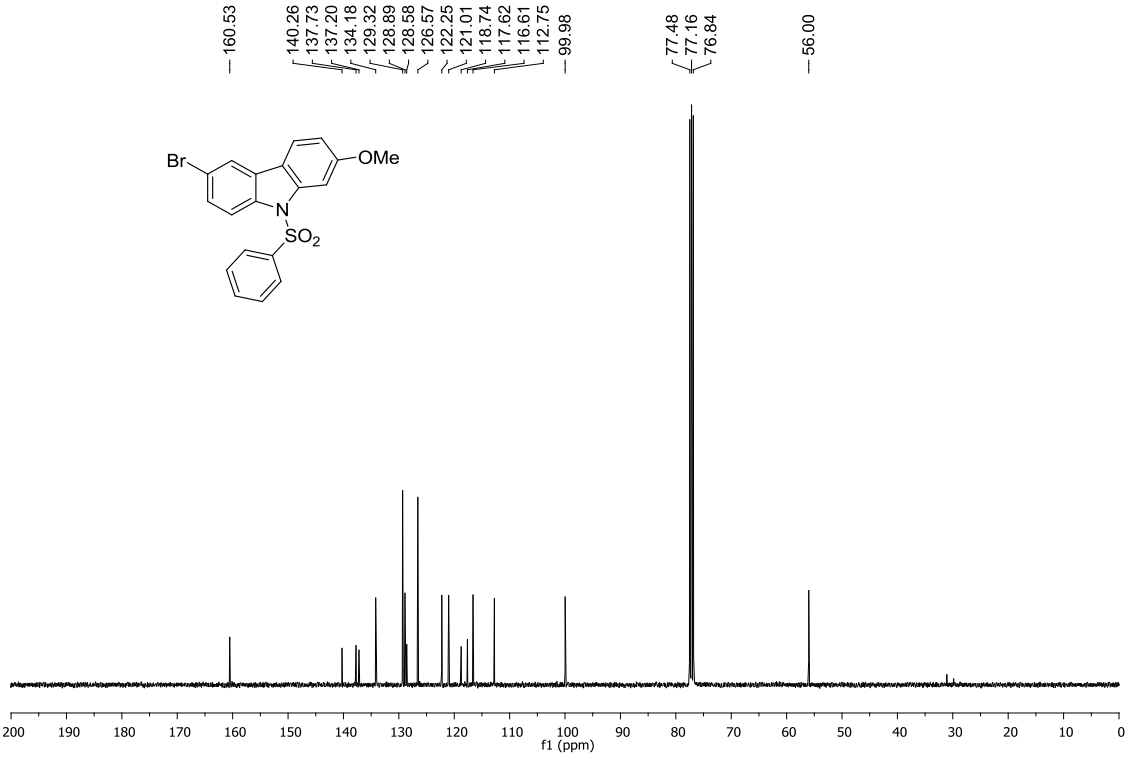


Figure 3A.45 ^{13}C NMR spectrum of 6-bromo-2-methoxy-9-(phenylsulfonyl)carbazole **(3ac)**

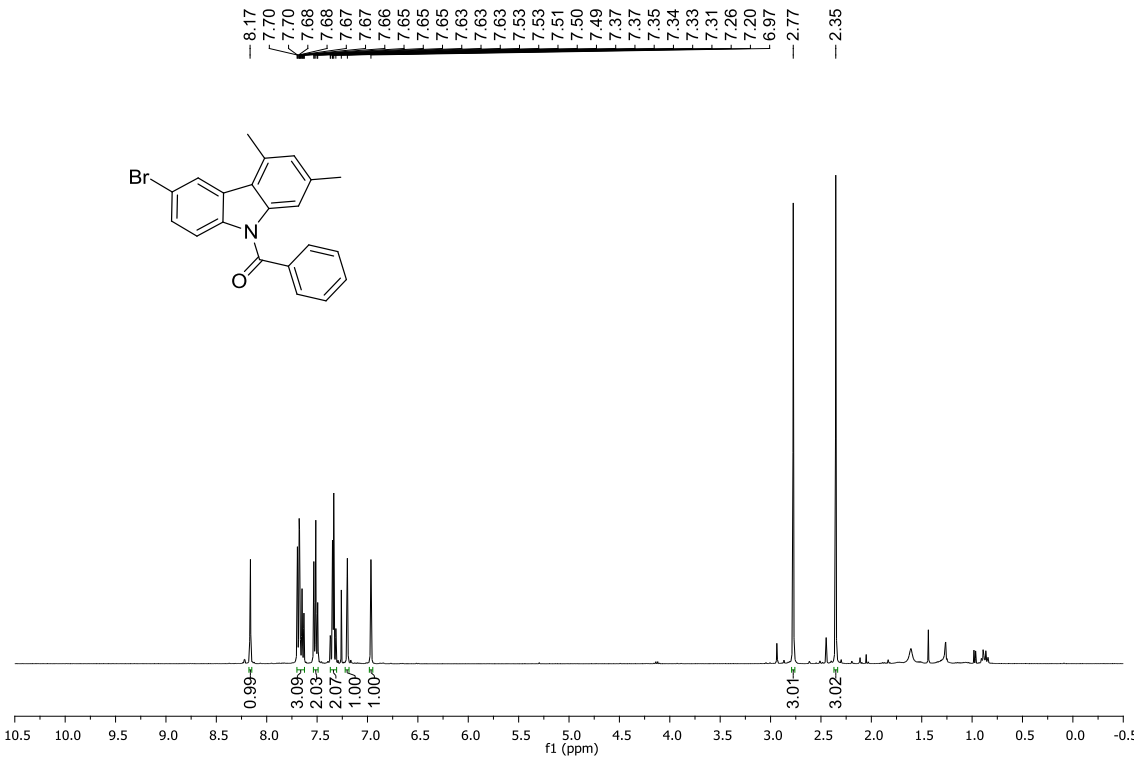


Figure 3A.46 ^{1}H NMR spectrum of (6-bromo-2,4-dimethylcarbazol-9-yl)(phenyl)methanone **(3ad)**

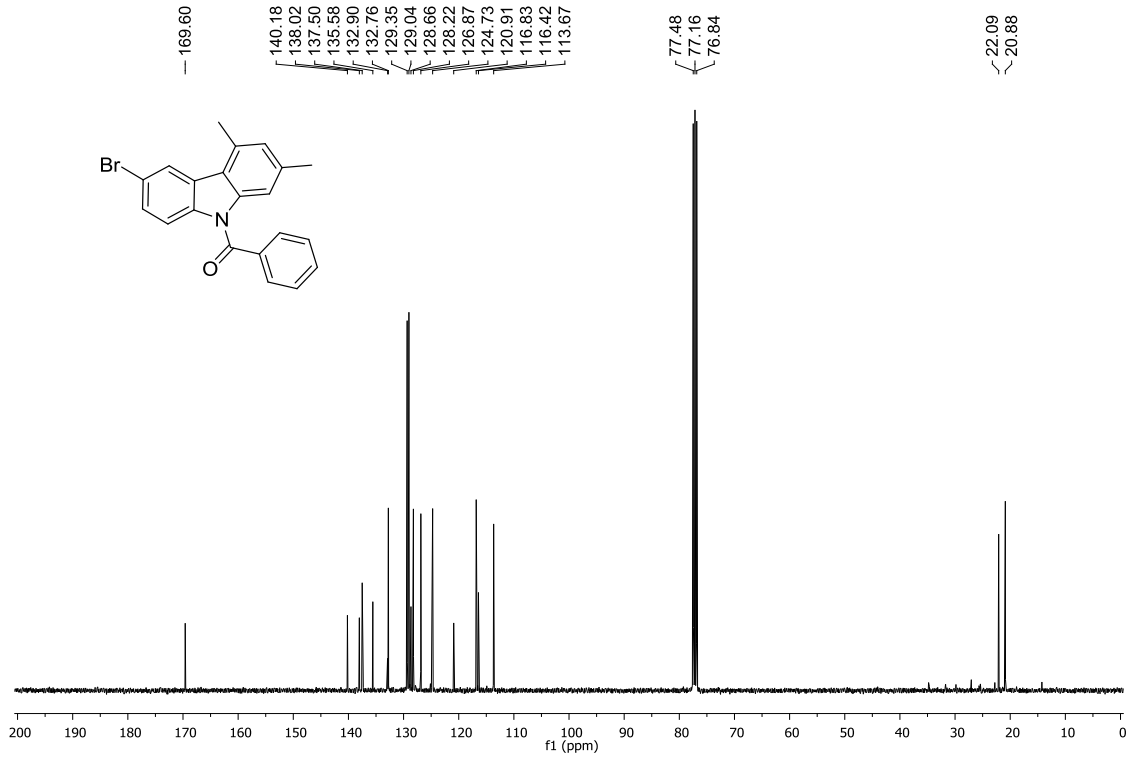


Figure 3A.47 ^{13}C NMR spectrum of (6-bromo-2,4-dimethylcarbazol-9-yl)(phenyl)methanone **(3ad)**

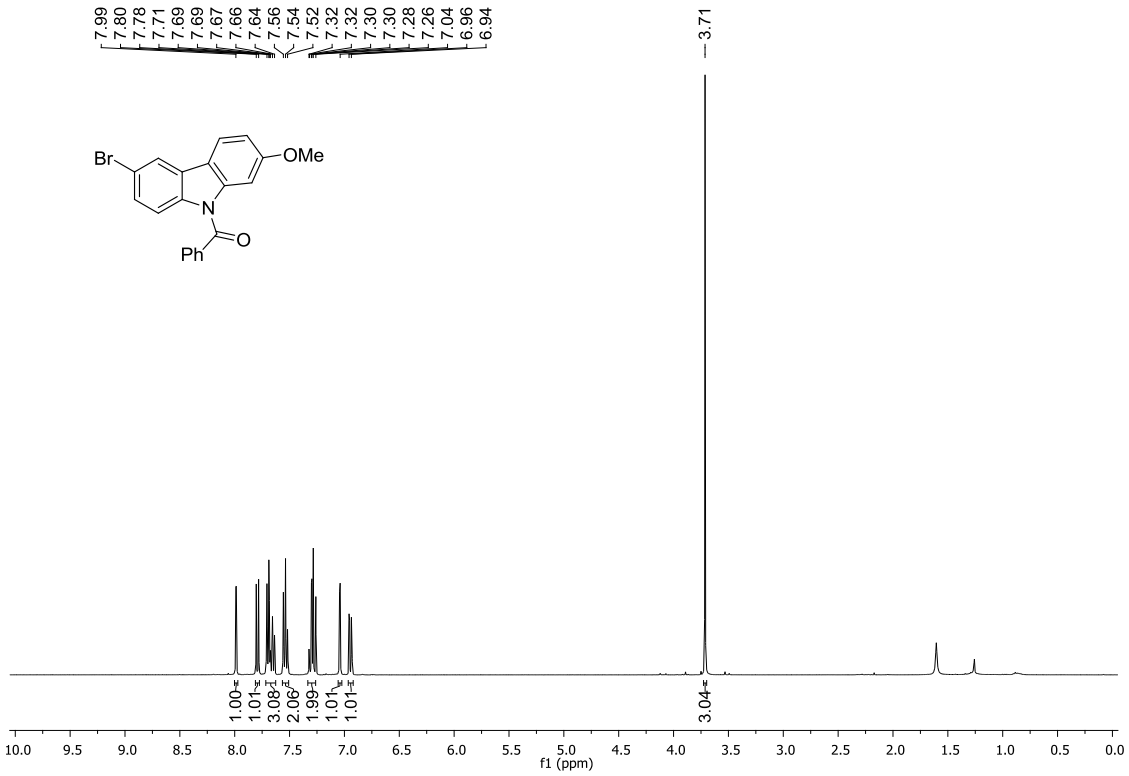


Figure 3A.48 ^{1}H NMR spectrum of (6-bromo-2-methoxycarbazol-9-yl)(phenyl)methanone **(3ae)**

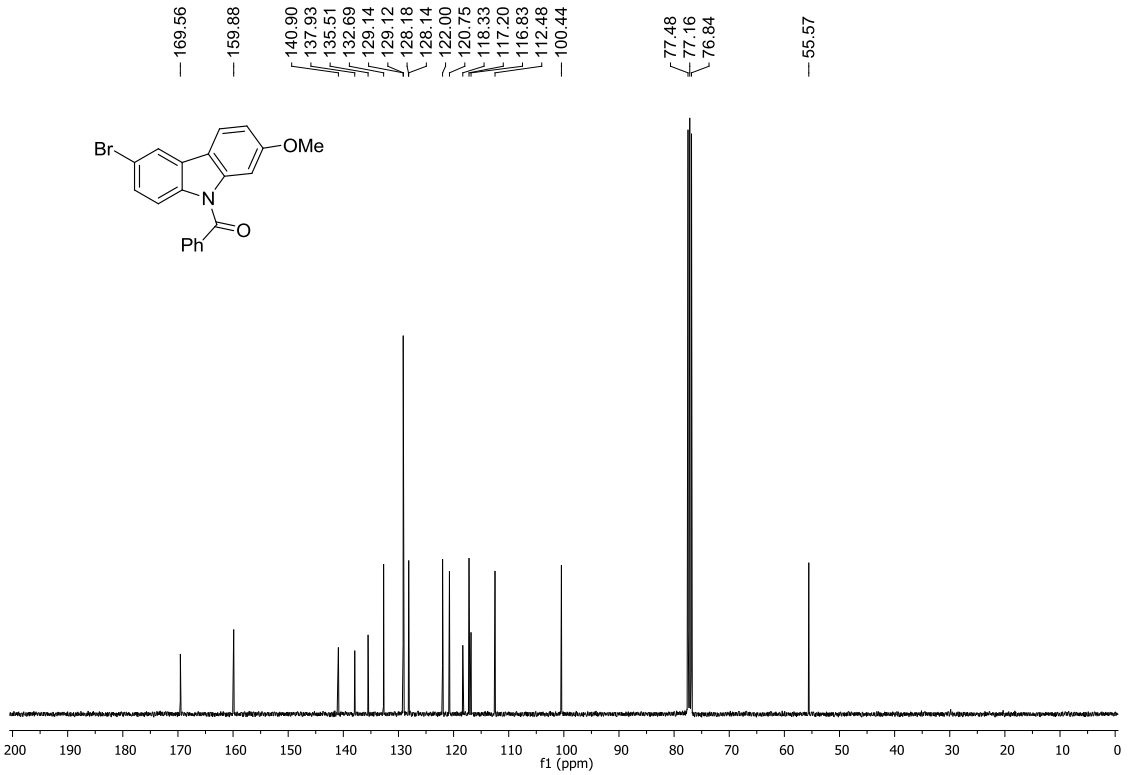


Figure 3A.49 ^{13}C NMR spectrum of (6-bromo-2-methoxycarbazol-9-yl)(phenyl)methanone **(3ae)**

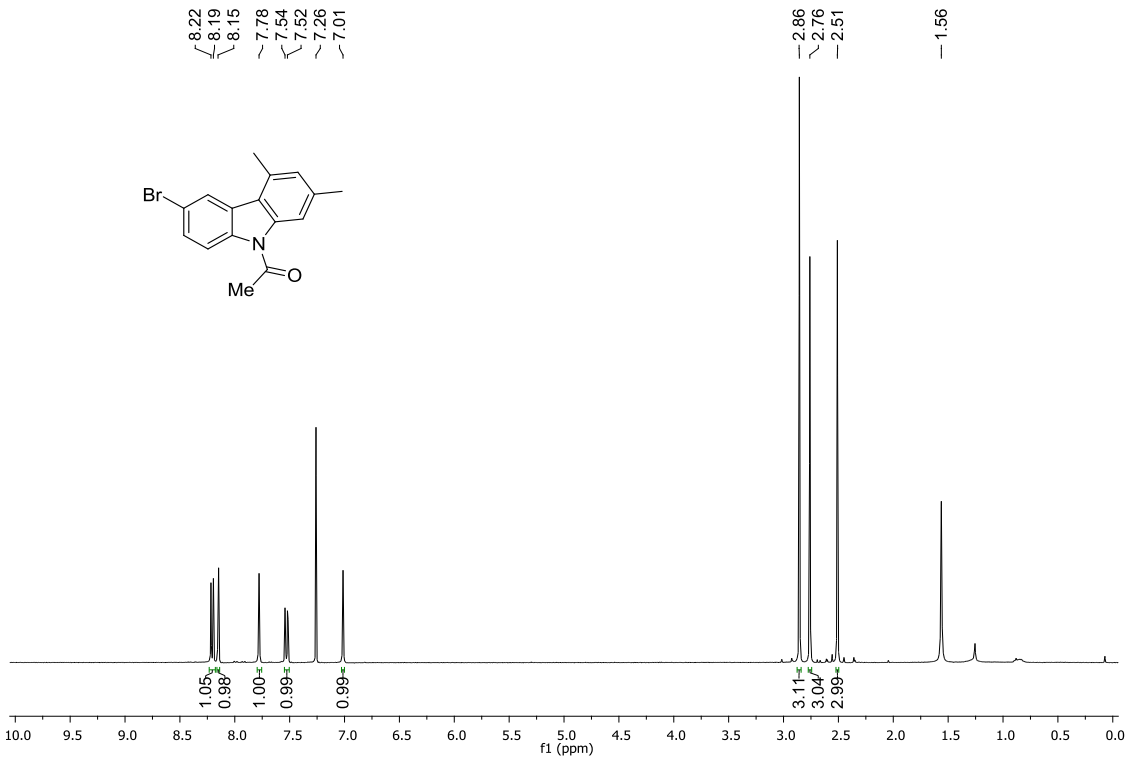


Figure 3A.50 ^{1}H NMR spectrum of 1-(6-bromo-2,4-dimethylcarbazol-9-yl)ethanone **(3af)**

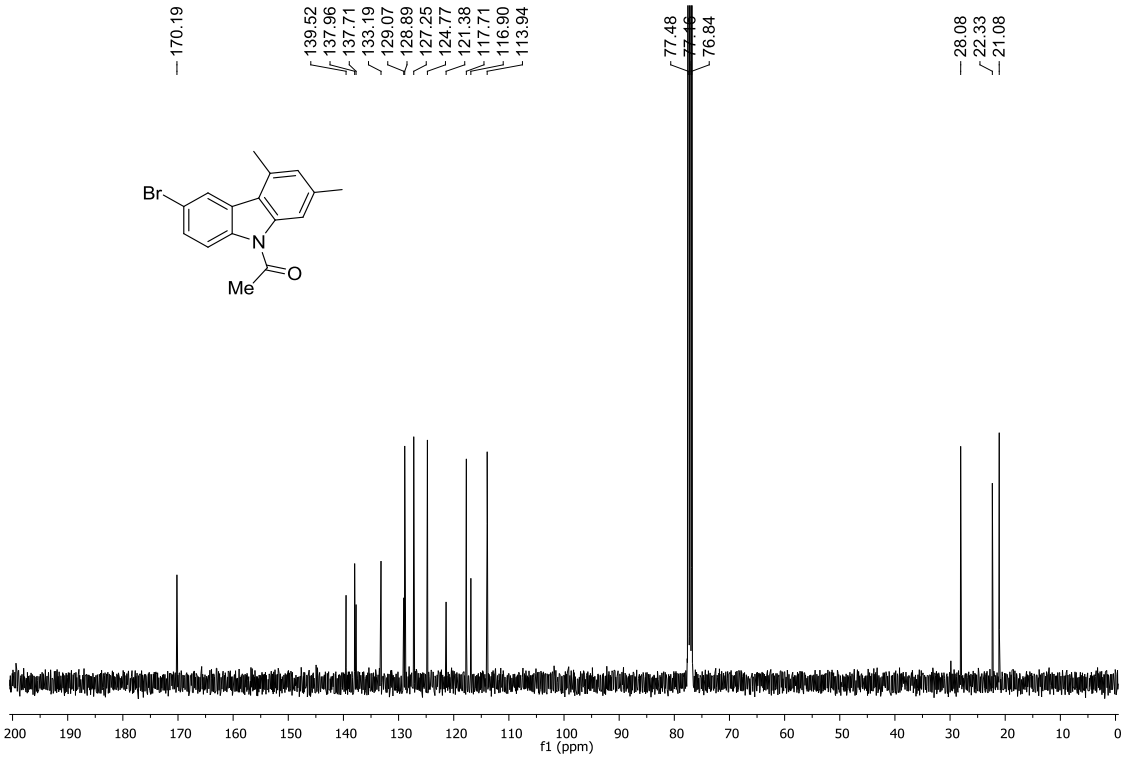


Figure 3A.51 ^{13}C NMR spectrum of 1-(6-bromo-2,4-dimethylcarbazol-9-yl)ethanone **(3af)**

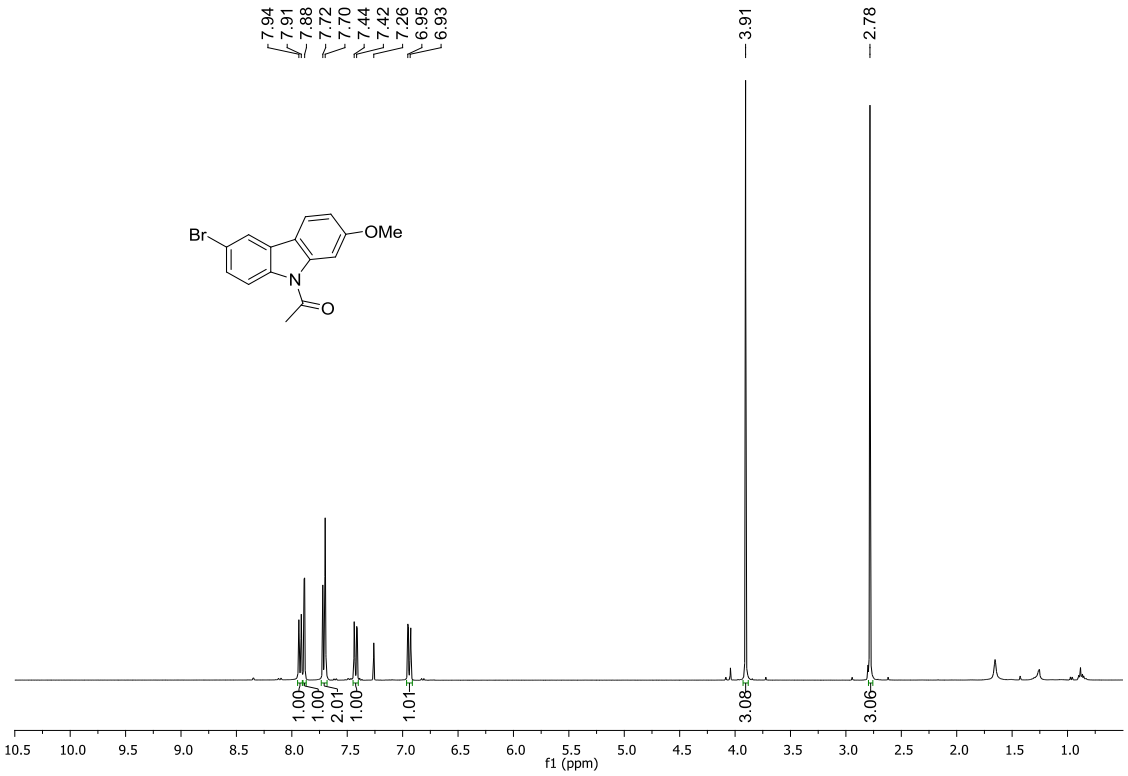


Figure 3A.52 ^{1}H NMR spectrum of 1-(6-bromo-2-methoxycarbazol-9-yl)ethanone **(3ag)**

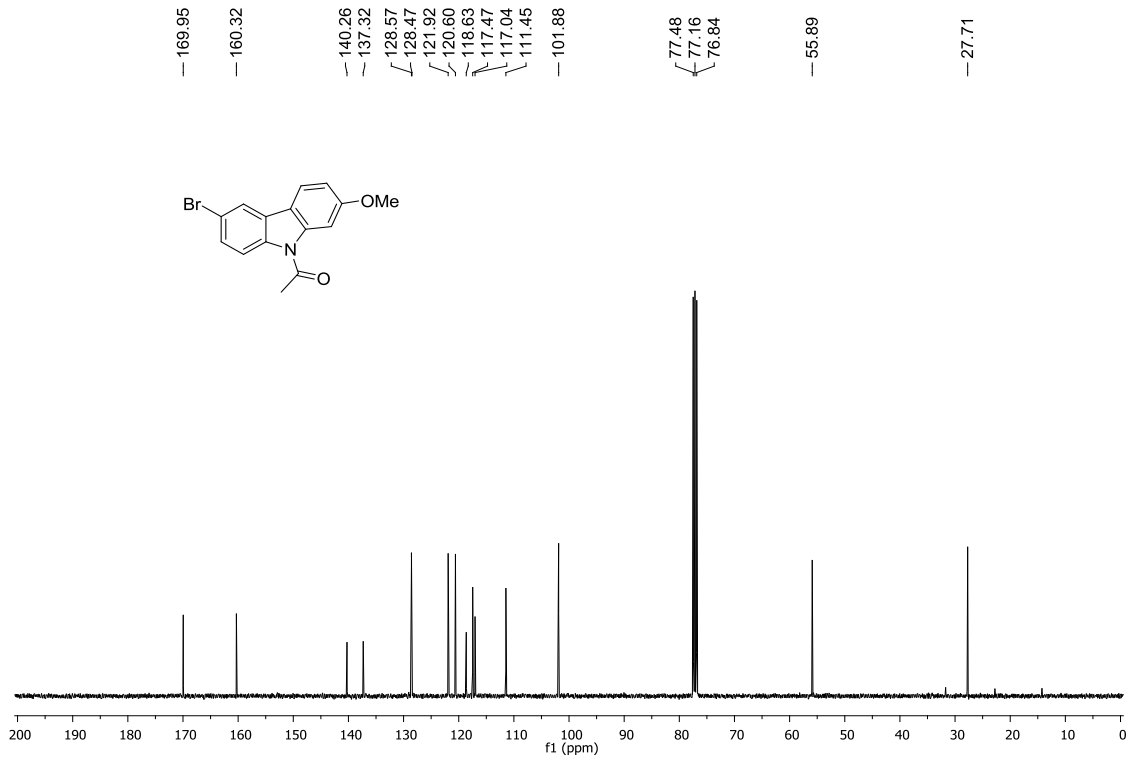


Figure 3A.53 ^{13}C NMR spectrum of 1-(6-bromo-2-methoxycarbazol-9-yl)ethanone **(3ag)**

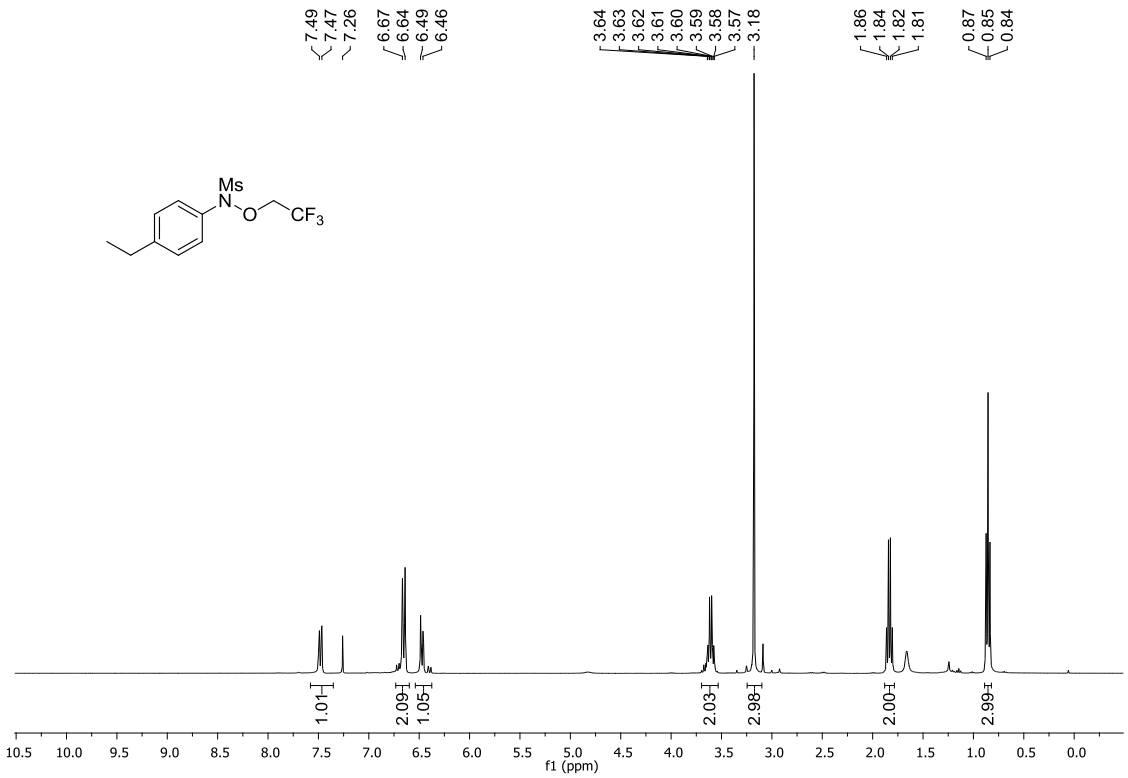


Figure 3A.54 ^{1}H NMR spectrum of N-(4-ethylphenyl)-N-(2,2,2 trifluoroethoxy)methanesulfonamide **(4i)**

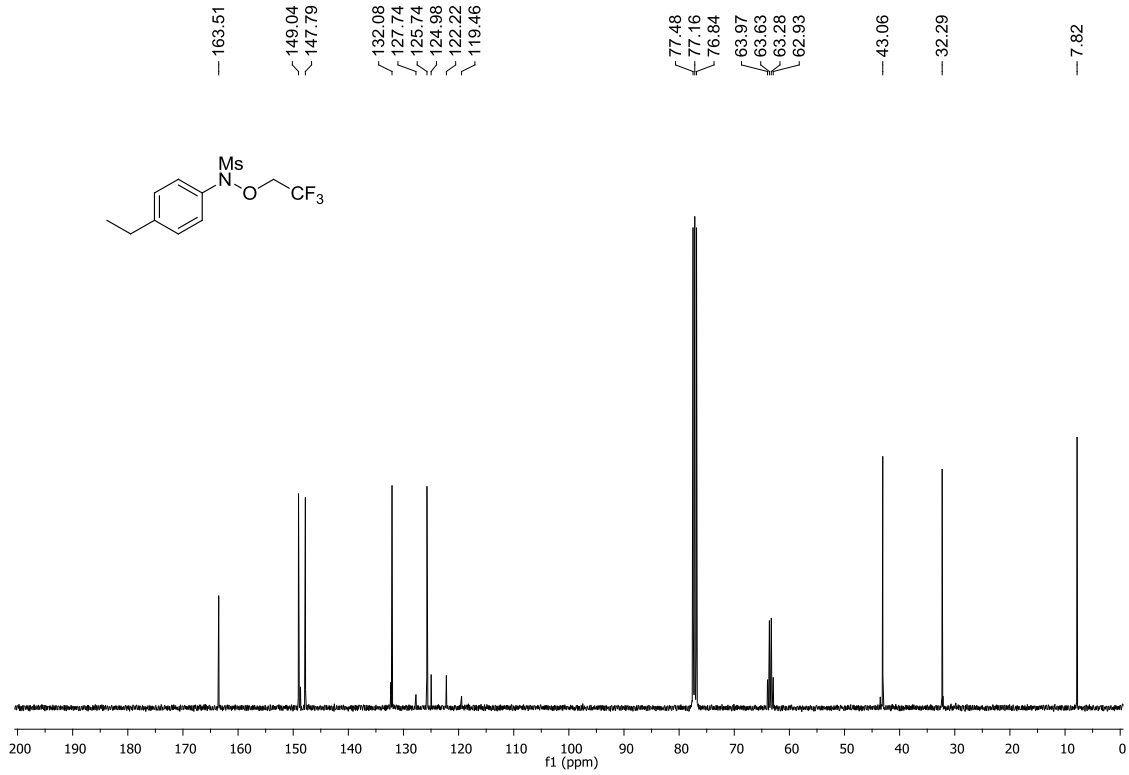


Figure 3A.55 ^{13}C NMR spectrum of N-(4-ethylphenyl)-N-(2,2,2 trifluoroethoxy)methanesulfonamide **(4i)**

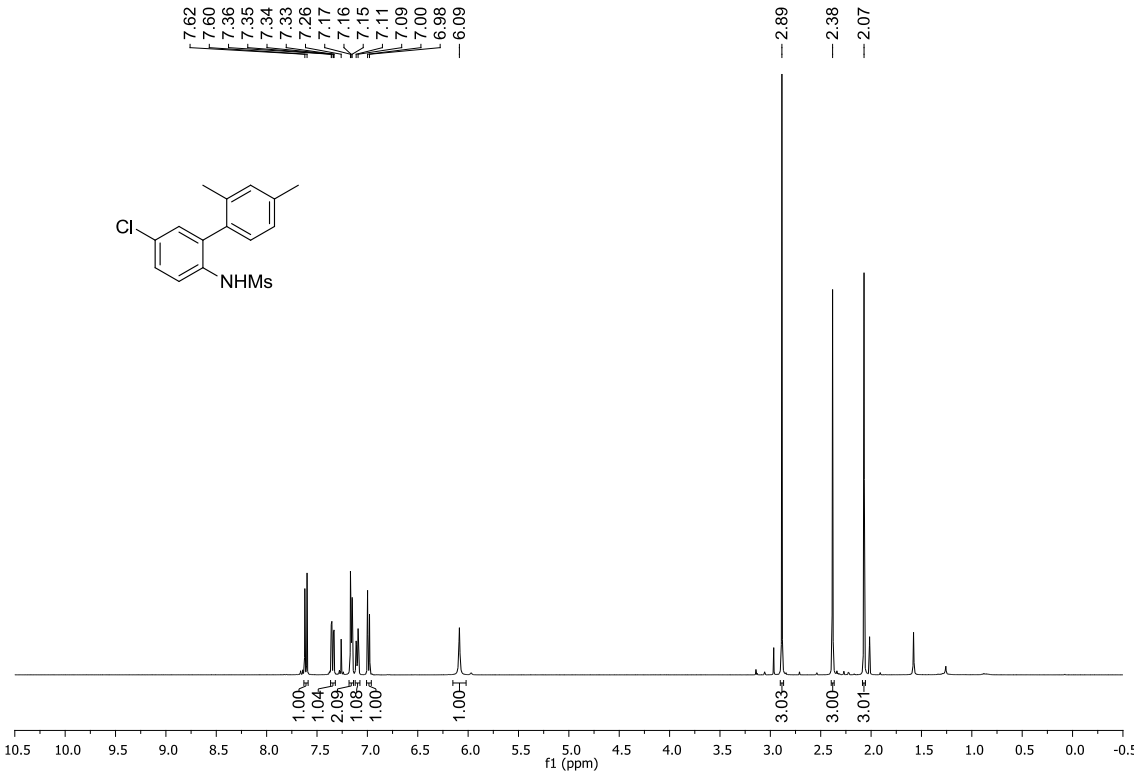


Figure 3A.56 ^{1}H NMR spectrum of N-(5-chloro-2',4'-dimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide **(2hg)**

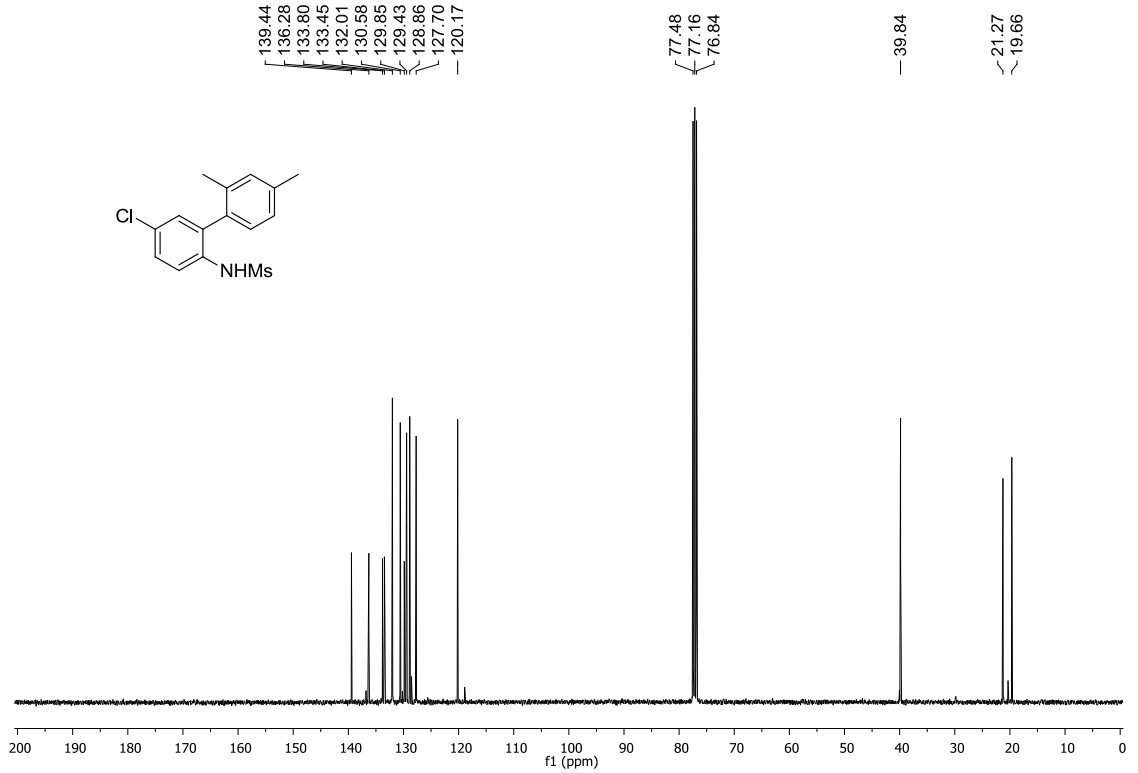


Figure 3A.57 ^{13}C NMR spectrum of N-(5-chloro-2',4'-dimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide **(2hg)**

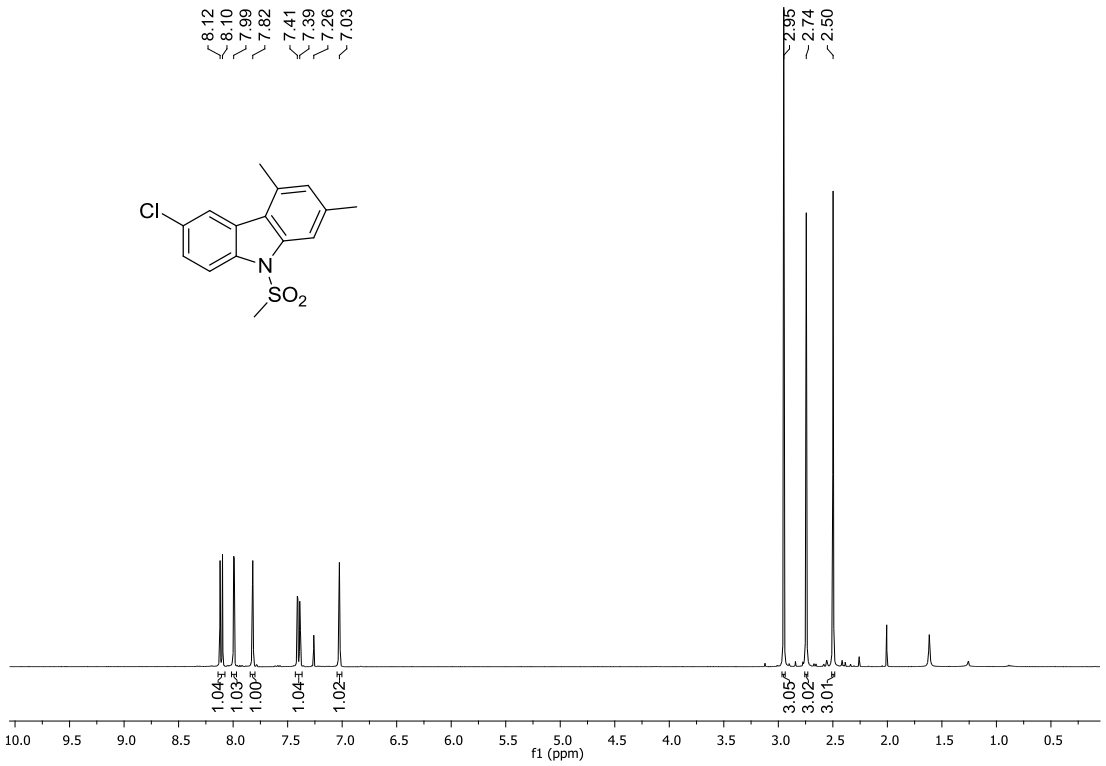


Figure 3A.58 ^{1}H NMR spectrum of 6-chloro-2,4-dimethyl-9-(methylsulfonyl)carbazole **(3hg)**

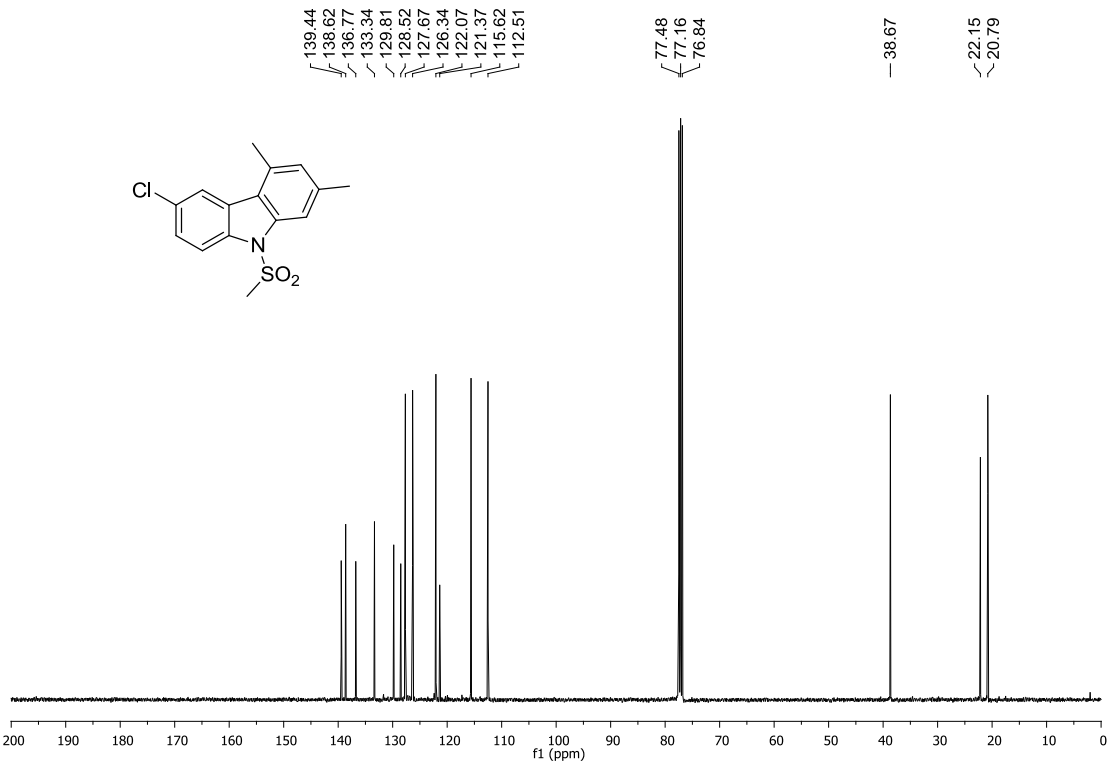


Figure 3A.59 ^{13}C NMR spectrum of 6-chloro-2,4-dimethyl-9-(methylsulfonyl)carbazole **(3hg)**

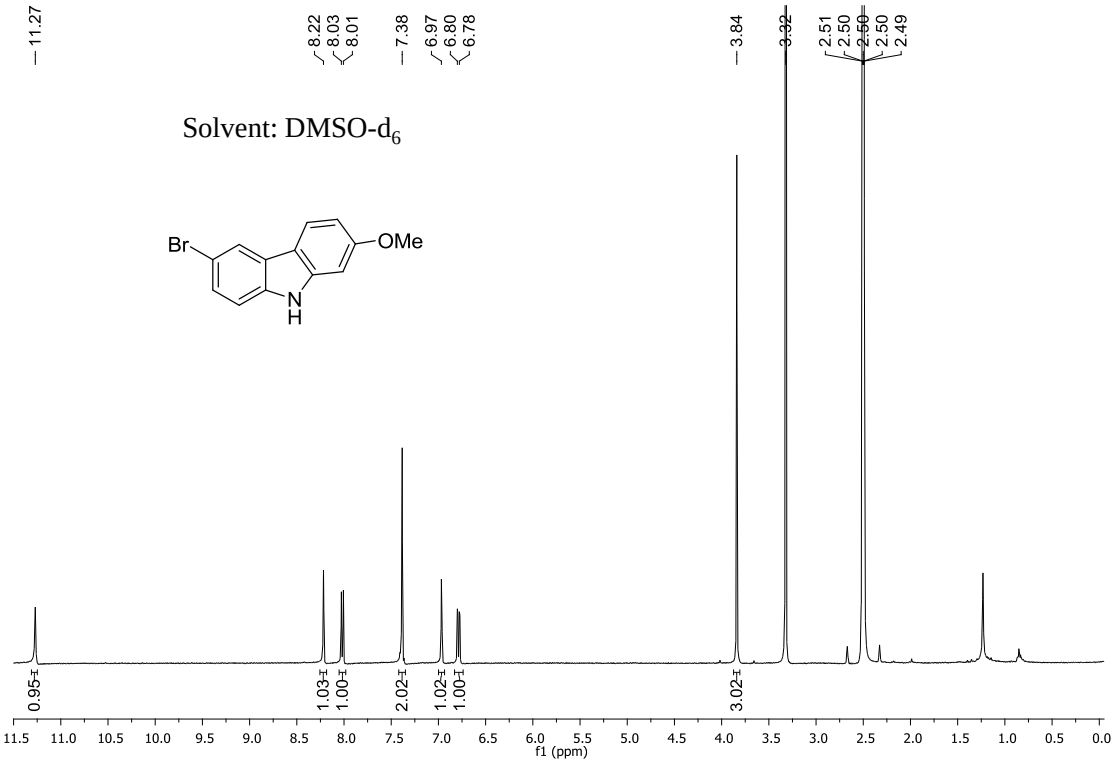


Figure 3A.60 ^{1}H NMR spectrum of 6-bromo-2-methoxy-9H-carbazole **(4a)**

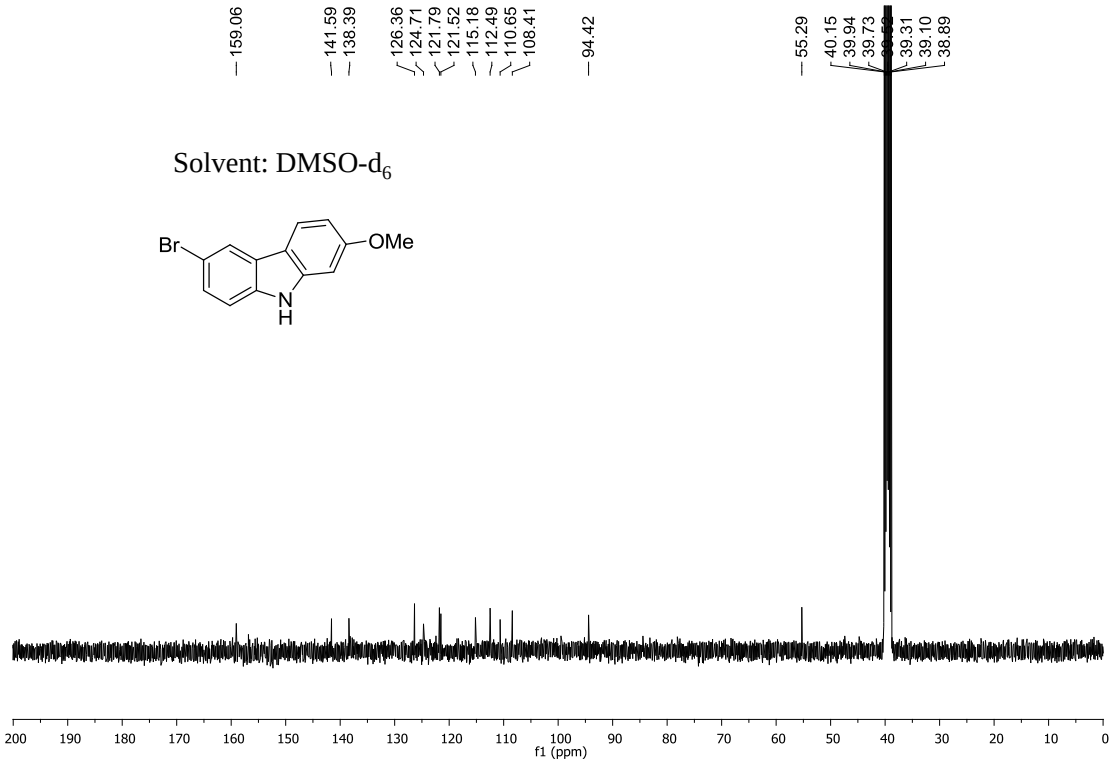


Figure 3A.61 ^{13}C NMR spectrum of 6-bromo-2-methoxy-9H-carbazole **(4a)**

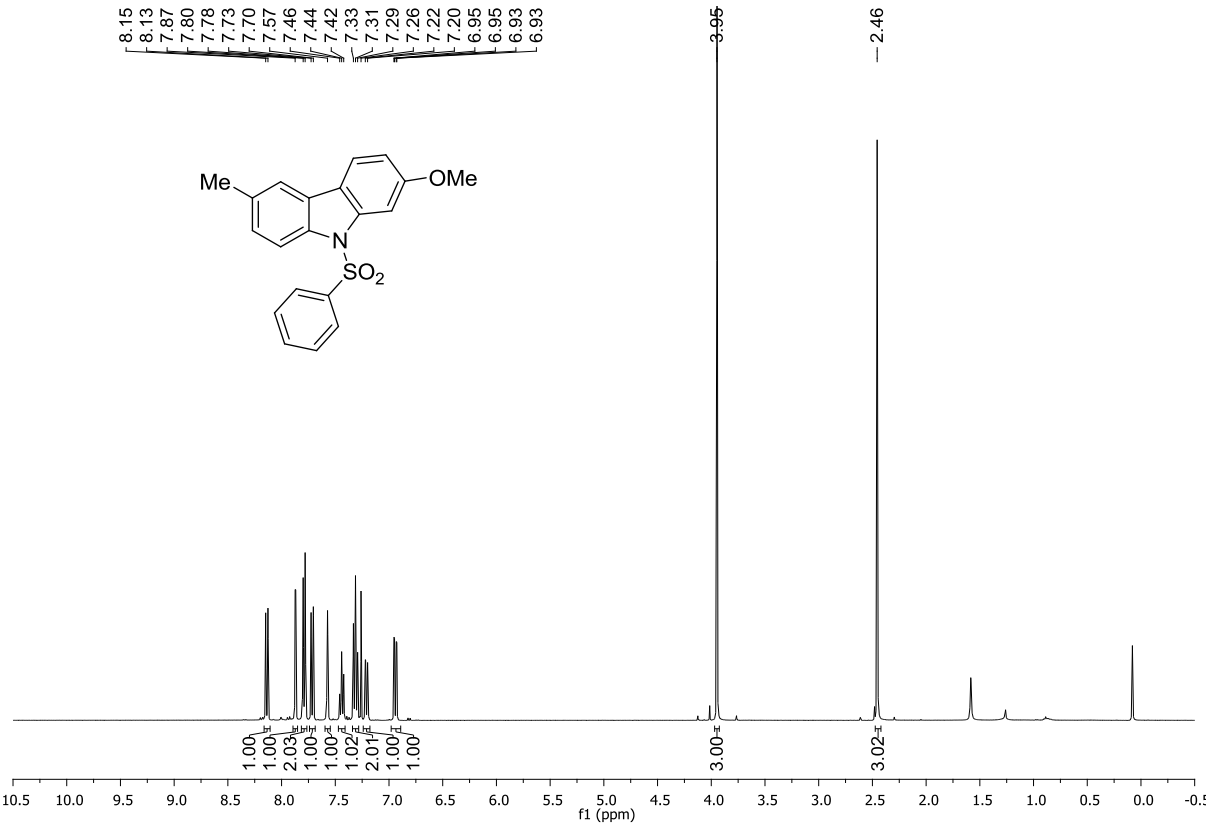


Figure 3A.62 ^{1}H NMR spectrum of 2-methoxy-6-methyl-9-(phenylsulfonyl)carbazole **(3ah)**

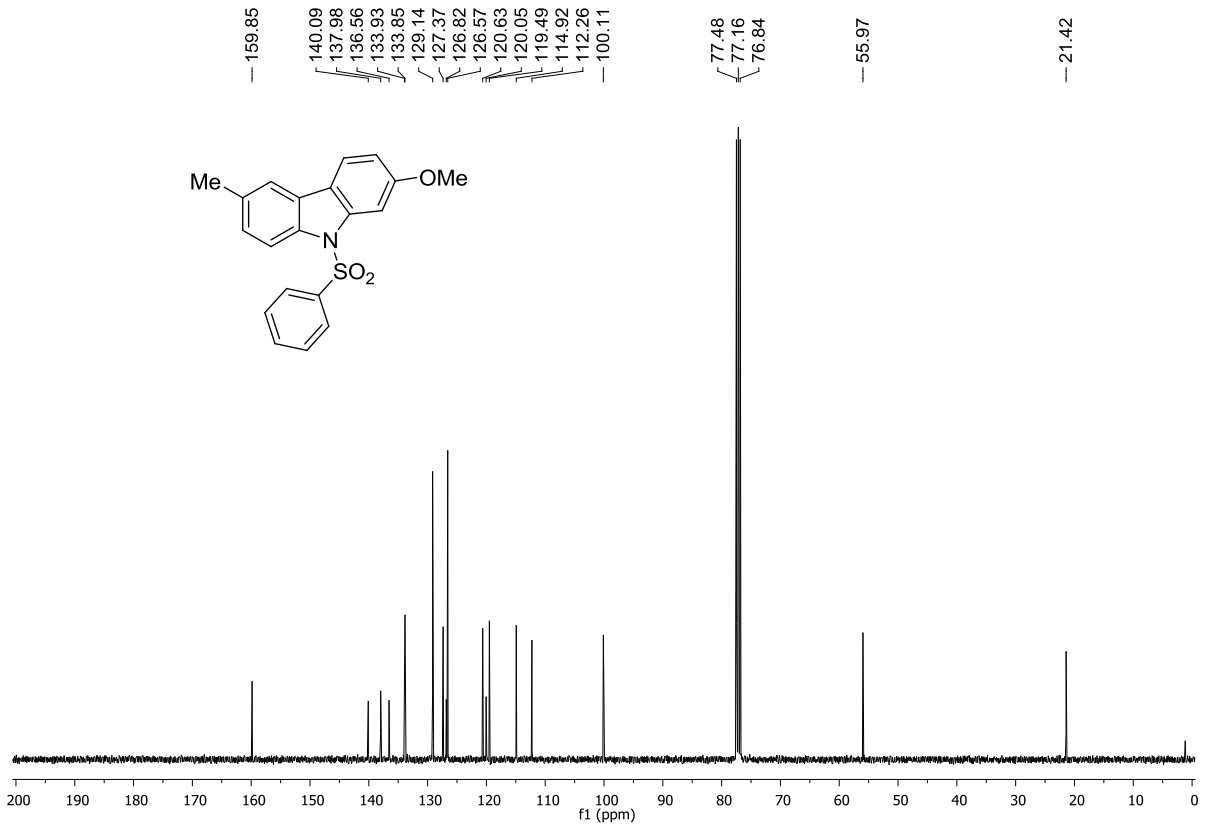


Figure 3A.63 ^{13}C NMR spectrum of 2-methoxy-6-methyl-9-(phenylsulfonyl)carbazole **(3ah)**

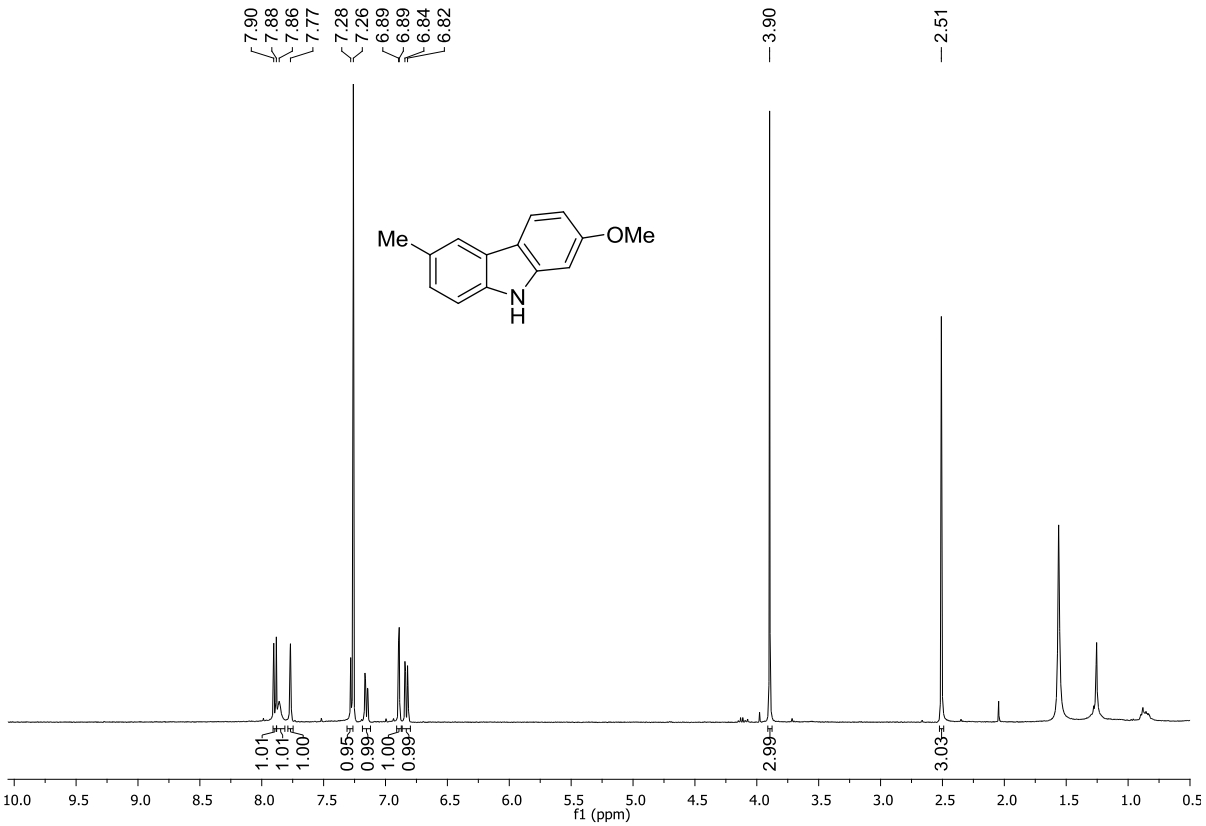


Figure 3A.64 ^{1}H NMR spectrum of 2-methoxy-6-methyl-9H-carbazole **(4ah)**

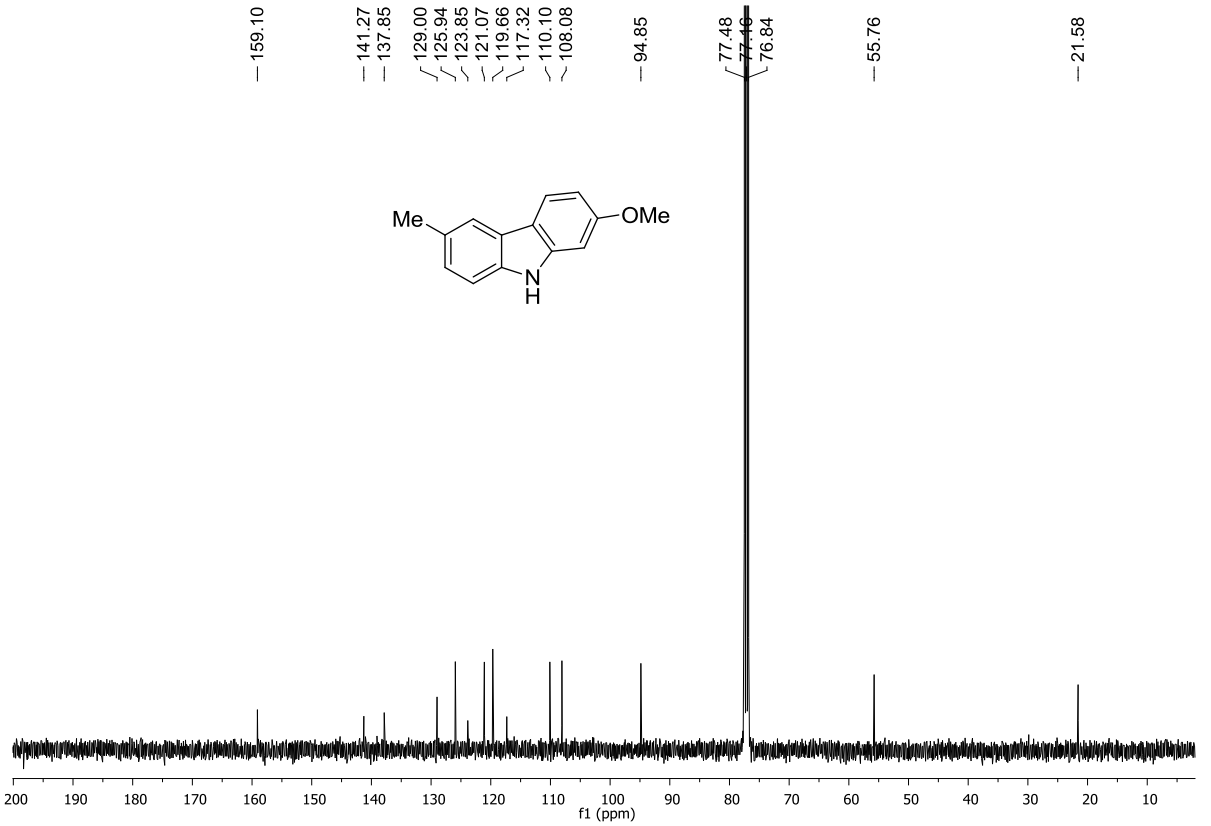


Figure 3A.65 ^{13}C NMR spectrum of 2-methoxy-6-methyl-9H-carbazole **(4ah)**

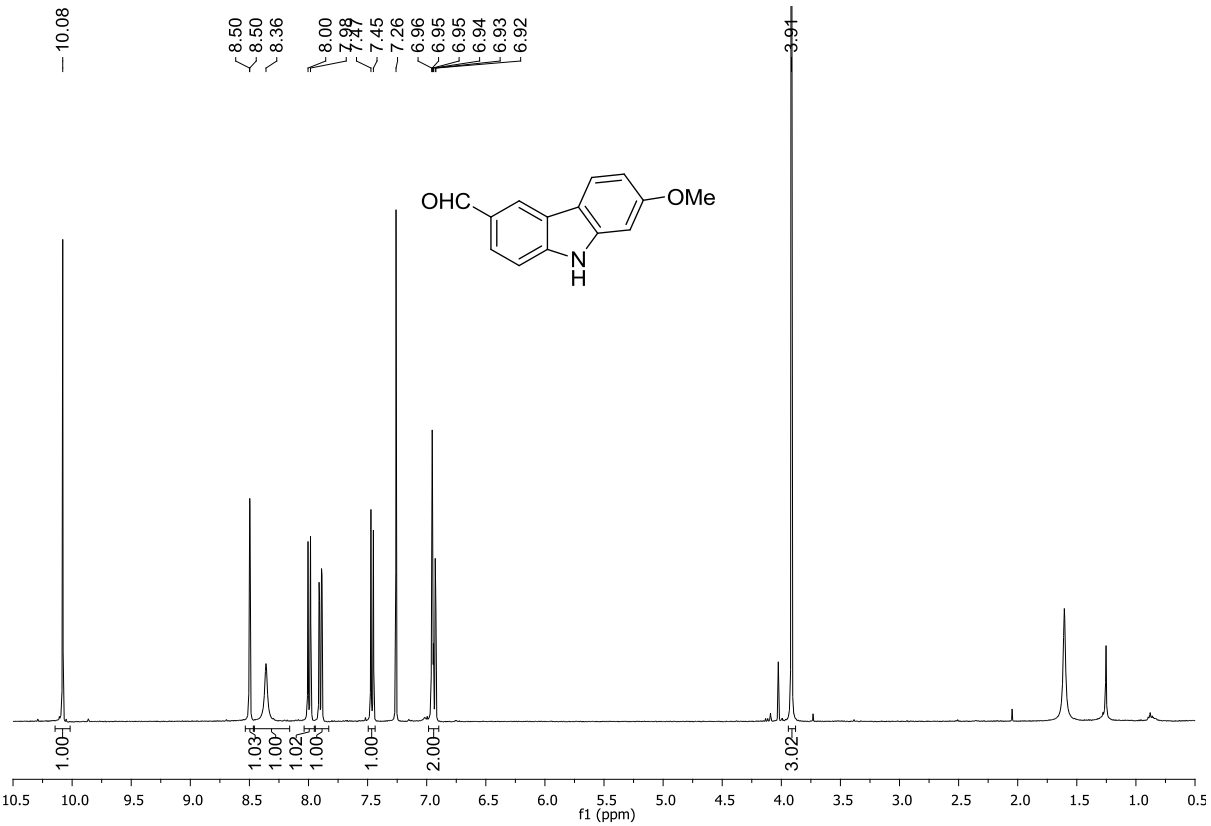


Figure 3A.66 ^{1}H NMR spectrum of 7-methoxy-9H-carbazole-3-carbaldehyde **(5ah)**

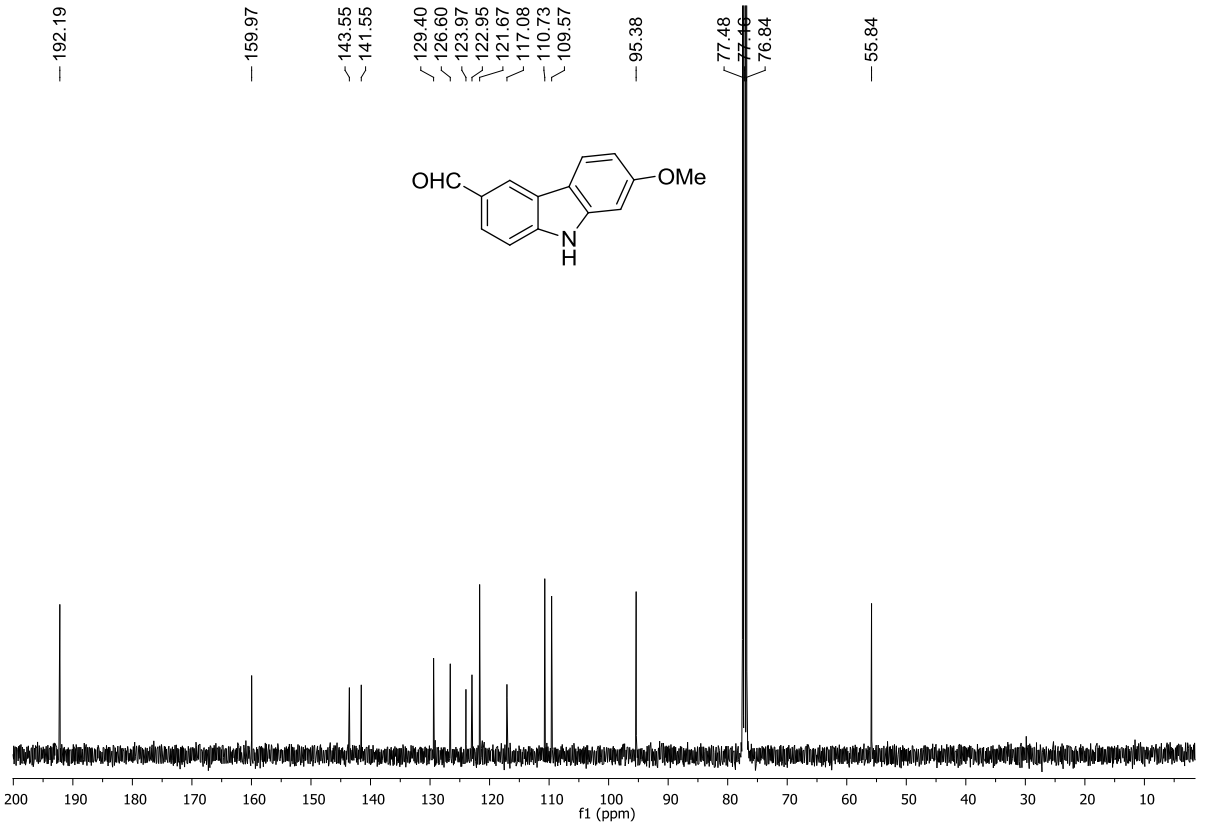


Figure 3A.67 ^{13}C NMR spectrum of 7-methoxy-9H-carbazole-3-carbaldehyde **(5ah)**

CHAPTER 3: PART B

Metal-free Intermolecular C(sp2)-H Amination *via* Cascade Cross-Dehydrogenative Coupling (CDC)

3B.1 ABSTRACT

Hypervalent iodine(III) reagent, phenyliodine diacetate (PIDA) mediated efficient strategy has been developed for cascade cross-dehydrogenative coupling reaction between anilide derivatives and mesitylene under metal-free conditions. The intermolecular annulation reaction provides a direct access to multi-substituted carbazole through sequential C-N/C-C bond formation and selective Me-group migration. Also, regioselective oxidative mesityl incorporation has been described in addition to carbazole ring construction with the strategic choice of anilide substrates.

3B.2 INTRODUCTION

C-C & C-N bonds constitute the basic framework of many pharmaceutically and biologically active natural and unnatural products. Hence development of efficient methods for C-C & C-N bonds formation from easily available feedstock is an area of intense significance. Reaction

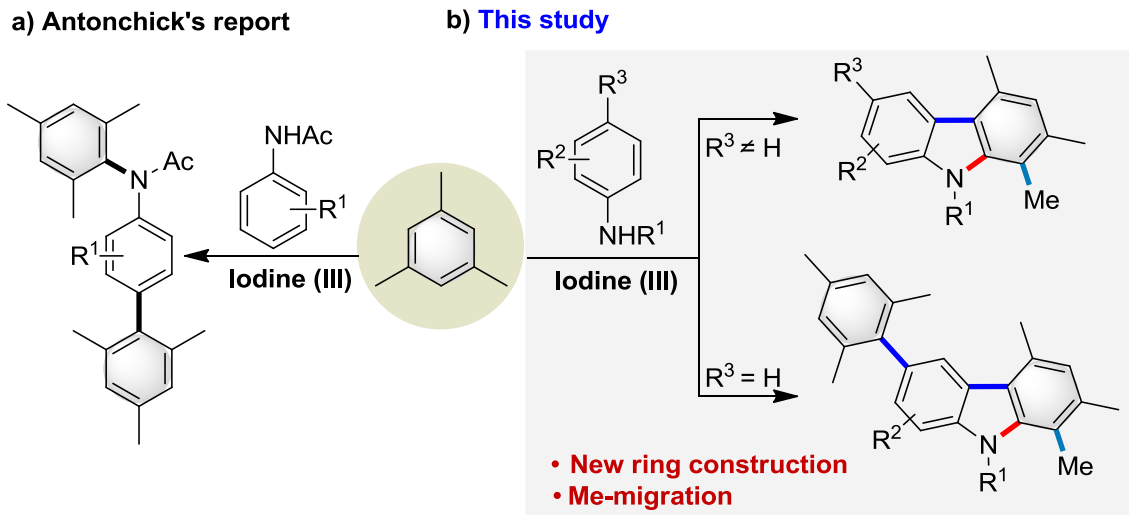


Figure 3B.1 Metal-free Intermolecular dehydrogenative C(sp2)-N bond formation.

involving multiple bonds formation in a single manipulation without isolation or purification of any of the intermediates, recognized as cascade reaction, have received much attention due to high efficiency for generating molecular architecture in a minimum number of steps.[33] Construction of C-C and C-N bonds via direct oxidative functionalization of C-H and N-H bonds, acknowledged as cross dehydrogenative coupling (CDC) reaction has become an extraordinary class of tool in organic synthesis due to ubiquity of C-H and N-H bonds in organic molecules.[34] These coupling reactions are extremely skilful in sense of step economy, atom economy and waste-minimized synthetic alternatives to classical coupling procedures employing prefunctionalized substrates. Limited research has been carried out on iodine(III) facilitated intermolecular dehydrogenative coupling processes for sequential C-C and C-N bond formation.[35] To mention, Antonchick and co-workers have conveyed iodine(III) reagent *para*-tolyliodonium diacetate mediated oxidative route for the incorporation of two aromatic rings on acetanilides.[27] So there is necessity for the development of metal-free intermolecular dehydrogenative coupling reactions which would be an important addition to the field of cascade C-C and C-N bond formation reaction towards the construction of further valuable compounds.

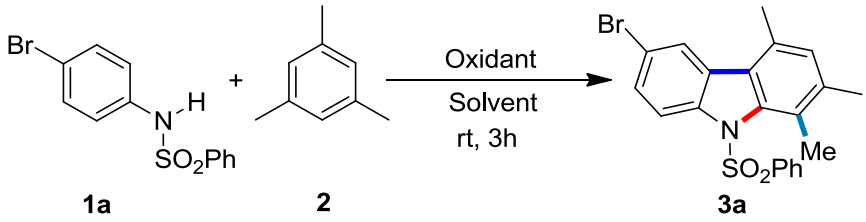
In continuation to our research interest on hypervalent iodine(III) mediated C-H amination, herein we disclose our discovery of method for multi-substituted carbazole synthesis via cascade cross-dehydrogenative coupling reaction under metal-free mild conditions (Figure 3B.1). Mesitylene which is one of the cheapest elementary chemical feedstock was strategically coupled with anilide substrates to provide carbazole molecules. Hypervalent iodine (III) was choice of preference as oxidant because residual contamination by toxic metals is not a concern with this type of reagents.[36] In addition to C-H and N-H bond functionalization, one of the methyl group of mesitylene molecule migrated to its adjacent C-position by C-C bond activation to furnish 1,2,4-trimethyl substituted carbazole products. Regioselective

incorporation of 1,3,5-trimethyl phenyl group to anilides was achieved in addition to annulation with the suitable choice of anilides (Figure 3B.1).

3B.3 RESULTS AND DISCUSSIONS

We initiated our studies by testing the reaction between *N*-(4-bromophenyl)benzenesulfonamide (**1a**) and mesitylene (**2**) at room temperature in presence of 2.5 equiv phenyliodine diacteate (PIDA) as oxidant. After screening different solvents we could find that TFE (2,2,2-trifluoroethanol) (0.2 M) was best to provide 6-bromo-1,2,4-trimethyl-9-(phenylsulfonyl) carbazole (**3a**). However, use of different hypervalent iodine (III) reagents like PIFA, $PhI(OPiv)_2$ or $PhI(OCOPh)_2$ as oxidant could not produce better yield of product (Table 3B.1, entry 4-6). Dilution of solvent with dichloromethane to 0.1 M resulted in reduced yield of desired product **3a** (Table 3B.1, entry 12). Addition of base K_2CO_3 was not profitable in solvent either TFE or HFIP. Yield of product **3a** reduced when 1.5 equivalent of mesitylene (**2**) was used (Table 3B.1, entry 11) as well as when reduced amount of oxidant (Table 3B.1, entry 10) was used. Under optimized condition product **3a** was isolated with 84% yield in 3 h (Table 3B.1, entry 9).

Table 3B.1 Optimization for reaction conditions



1a 2 3a

Entry	Oxidant(equiv.)	Additive(equiv.)	Solvent	Yield (%)
1	PIDA(2.5)	---	DCM	0
2	PIDA(2.5)	---	CH_3CN	54
3	PIDA(2.5)	---	HFIP	76
4	PIFA(2.5)	---	HFIP	<10
5	$PhI(OPiv)_2$(2.5)	---	HFIP	51
6	$PhI(OCOPh)_2$(2.5)	---	HFIP	46
7	PIDA(2.5)	K_2CO_3(2.5)	HFIP	76
8	PIDA(2.5)	K_2CO_3(2.5)	TFE	80
9	PIDA(2.5)	---	TFE	84
10	PIDA(2.0)		TFE	78
11[a]	PIDA(2.5)		TFE	62
12	PIDA(2.5)		TFE:DCM(1:1)	81

[a]: 1.1 equiv of mesitylene was used.

After established optimal reaction conditions, we focused our effort on establishing the generality of our coupling protocol. The PIDA mediated dehydrogenative coupling strategy displays broad substrate capacity and is tolerant of a range of substituent on aryl ring of anilides (Figure 3B.2). Additionally, anilides enclosing with various substituents at *N*-centre also smoothly underwent coupling reaction with mesitylene to provide multi-substituted carbazole. 1,2,4-Trimethyl substituted carbazole products containing electron withdrawing substituents

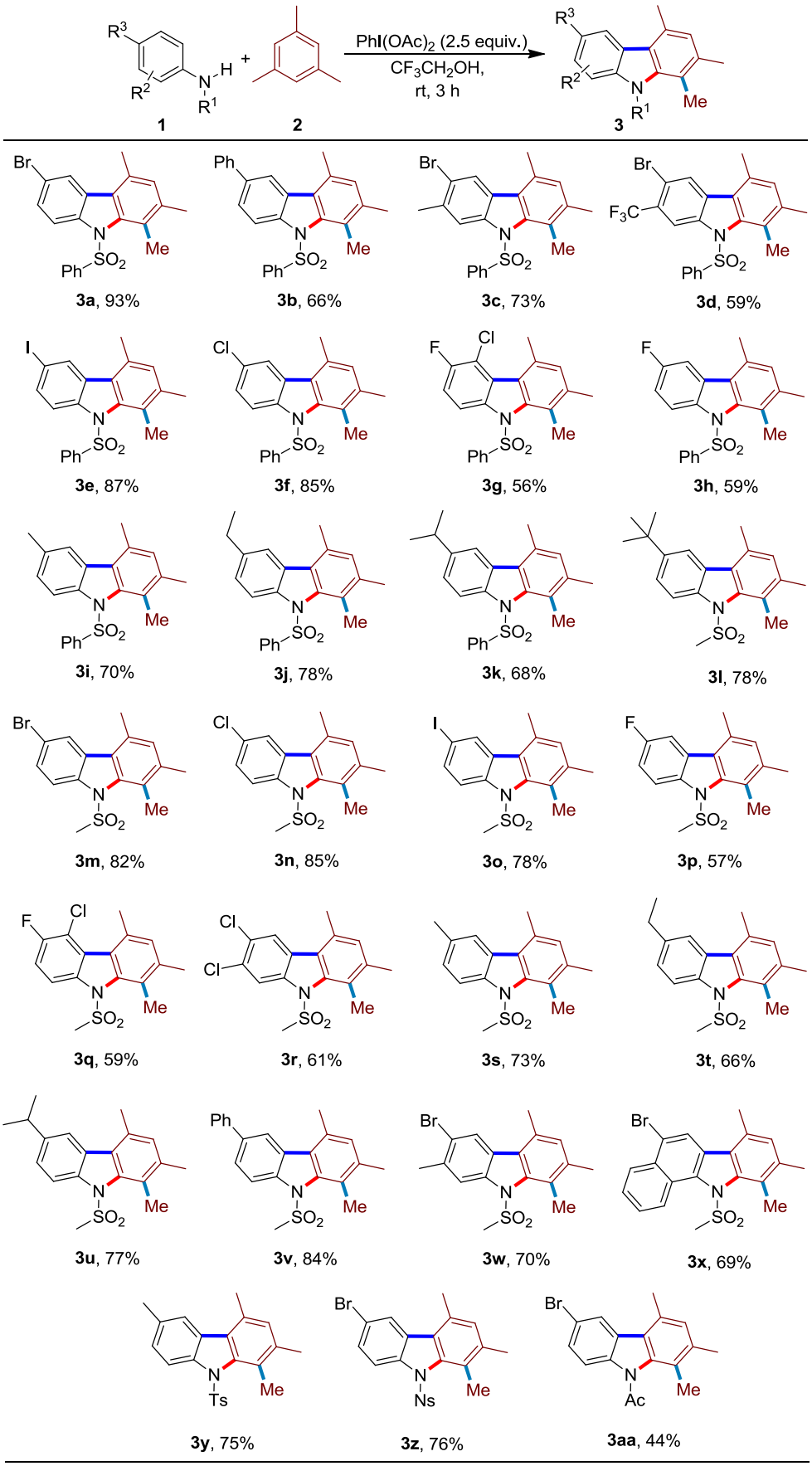


Figure 3B.2 Scope of the dehydrogenative annulation protocol.

like halo and phenyl groups (**3a-3h, 3m-3r, 3v-3x, 3z, 3aa**) as well as electron donating substituents like alkyl groups (**3i-3l, 3t-3u, 3y**) were isolated with good to excellent yield. Subsequently, several disubstituted anilides were tested in the developed cascade method. Delightfully, single regeoisomers of carbazole products were isolated in all cases (**3c-3d, 3g, 3q-3r, 3w**). *N*-(4-bromonaphthalen-1-yl)methanesulfonamide (**1x**) furnished four ring fused heterocycle carbazole derivative 5-bromo-7,9,10-trimethyl-11-(methylsulfonyl)benzo[a]carbazole (**3x**) with 69% yield. Tosyl, 4-nitrobenzenesulfonyl (Ns) as well as acyl groups at *N*-centre of anilines also were responsive to our oxidative protocol (**3y-3aa**) (Figure 3B.2).

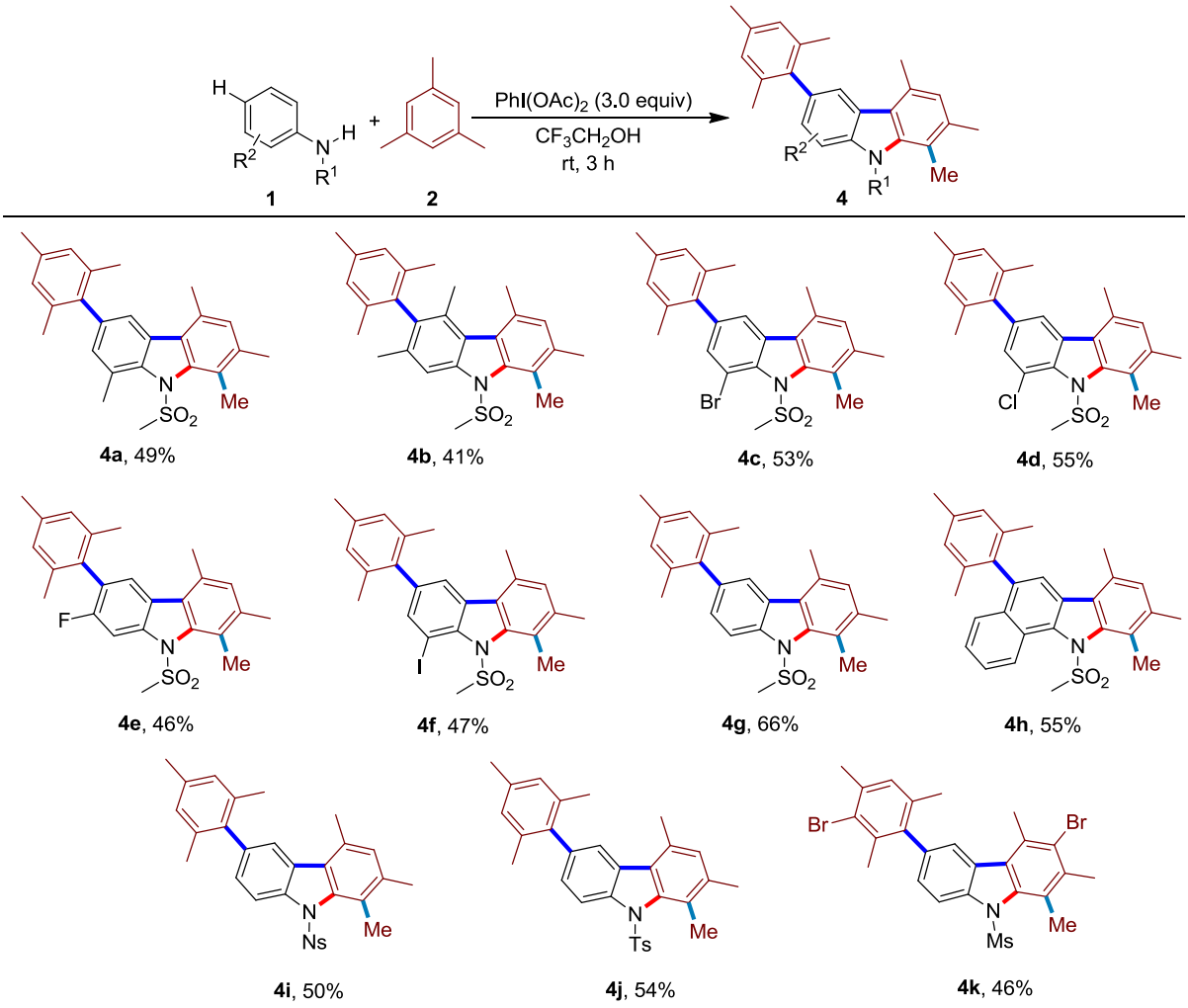


Figure 3B.3 Scope of the dehydrogenative annulation protocol.

We further explored our dehydrogenative coupling protocol with anilide substrates bearing H substituent at *para*-position to amine attached C-centre. Interestingly, a discrete type of carbazole products were isolated with three new bond formation along with anticipated methyl group migration (Figure 3B.3). Use of 3.0 equiv oxidant PIDA under similar metal-free conditions conveyed product with regioselective incorporation of 1,3,5-trimethylphenyl group along with carbazole ring construction through sequential functionalization of five C-H and one N-H bonds. Variety of substituent on arene ring as well as different sulfonyl groups at *N*-centre of anilides were well tolerated to produce desired multi-substituted carbazole products in moderate to good yields (**4a-4j**). Compound **3v** and **4g** were characterized by X-ray crystallographic analysis (Figure 3B.4).

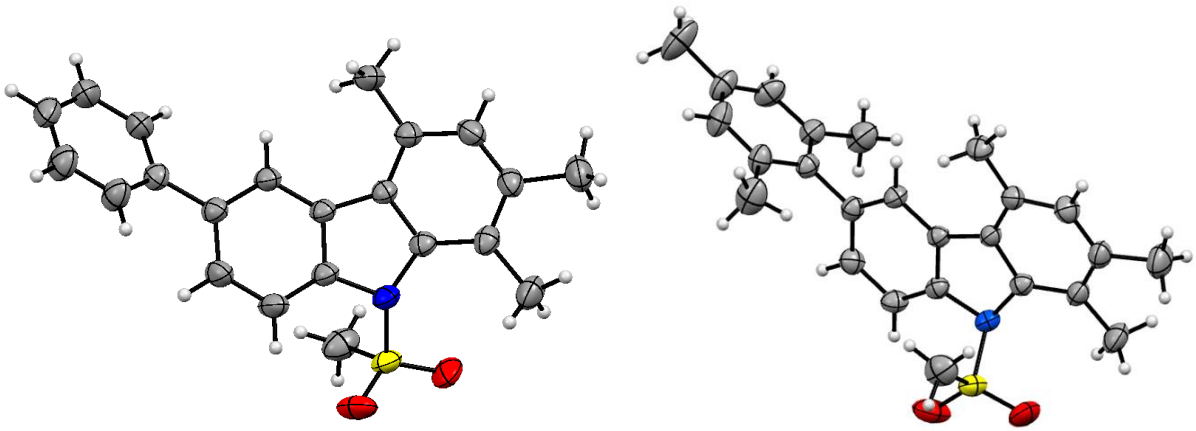
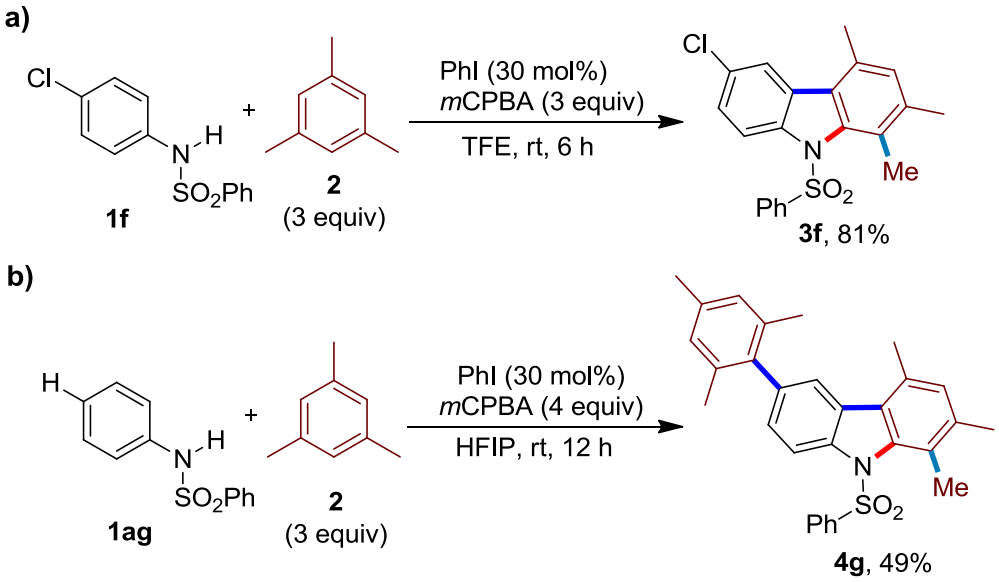


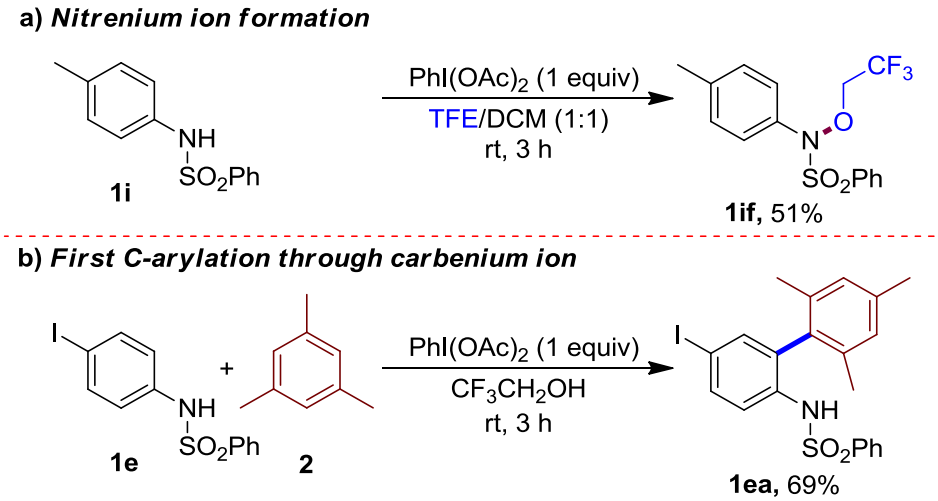
Figure 3B.4 X-ray structure of **3v** and **4g**.

Next, we turned our effort on the development of organocatalytic conditions for the dehydrogenative coupling reaction. Pleasantly, desired product 6-chloro-1,2,4-trimethyl-9-(phenylsulfonyl)carbazole (**3f)** was isolated with 81% yield from coupling between mesitylene (**2**) and *N*-(4-chlorophenyl)benzenesulfonamide (**1f**) by in-situ generation of hypervalent iodine(III) reagent from catalytic amount (30 mol%) of iodobenzene (PhI) in presence of oxidant *meta*-chloroperbenzoic acid (*m*CPBA) in TFE solvent (Scheme 3B.1a). In similar

fashion, carbazole product 6-Mesityl-1,2,4-trimethyl-9-(methylsulfonyl)carbazole (**4g)** was produced by in-situ generation of hypervalent iodine (III) reagent in HFIP solvent (Scheme 3B.1b).



Scheme 3B.1 Organocatalytic cascade cross dehydrogenative coupling reaction.



Scheme 3B.2 Control experiments.

Based on literature precedence and control experiment (Scheme 3B.2) a plausible mechanistic pathway for phenyliodine diacetae (PIDA) mediated cross dehydrogenative coupling reaction

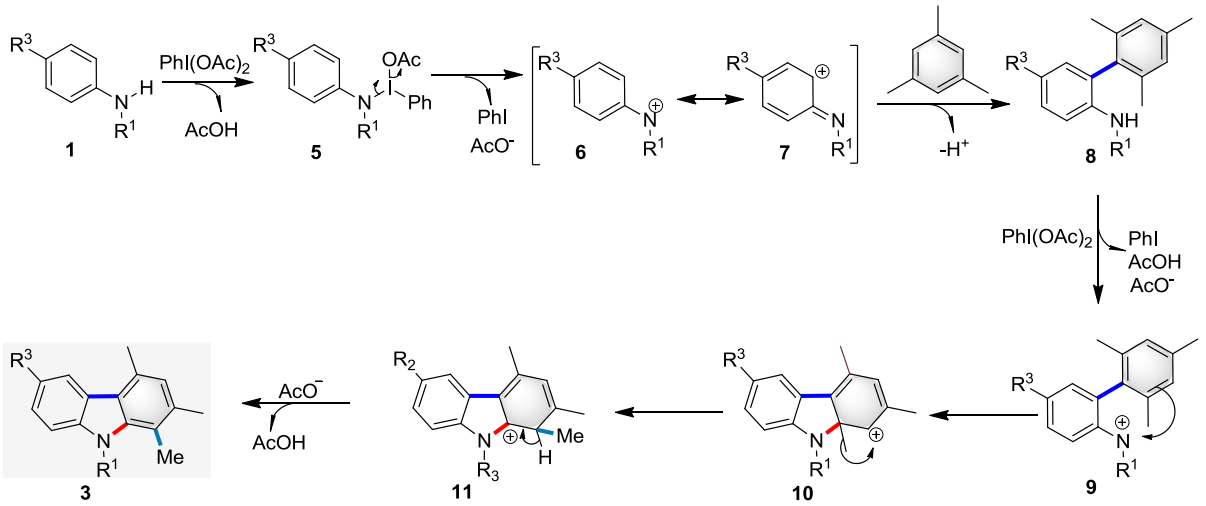


Figure 3B.5 Possible rmechanism for carbazole ring construction.

has been described in Figure 3B.5. First interaction of anilide substrate **1** with $PhI(OAc)_2$ led the formation of nitrenium ion intermediate **6** (Figure 3B.5)**.**[27] The nitrenium ion intermediate could be trapped by nucleophilic addition of solvent molecule in absence of mesitylene**.** Isolation of *N*-(4-iodophenyl)-N-(2,2,2-trifluoroethoxy)benzenesulfonamide (**1if**) with 51% yield from *N*-(4-iodophenyl)benzenesulfonamide (**1i**) in presence of 1.0 equiv of PIDA supports the formation of electrophilic nitrogen species (Scheme 3B.2a). The nitrenium ion intermediate **6** could get stabilized to carbenium ion **7** by charge delocalization (Figure 3B.5). Now both the ionic intermediates (**6** and **7**) could react with nucleophilic arene mesitylene. Carbenium ion was preferred for nuclephillic arene addition to give C-arylated intermediate **8**.[28] Isolation of *N*-(5-iodo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (**1ea**) with 69% yield on treatment of 1.0 equiv PIDA to *N*-(4-iodophenyl)methanesulfonamide (**1e**) and mesitylene (**2**) offered additional confirmation of C-C bond formation over C-N bond formation as initial step of carbazole synthesis (Scheme 3B.2b). Regioselective arylation proved that reaction follows an ionic pathway for the conversion. Intermediate **8** was further oxidized by second molecule of $PhI(OAc)_2$ to generate ionic intermediate **9** (Figure 3B.5). Aromatic electrophilic substitution reaction leads to produce carbenium intermediate **10** which

could further stabilized by adjacent quaternary methyl group migration and provide cationic intermediate **11**.[18] Acetate ion helped to abstract proton to afford desired carbazole product.

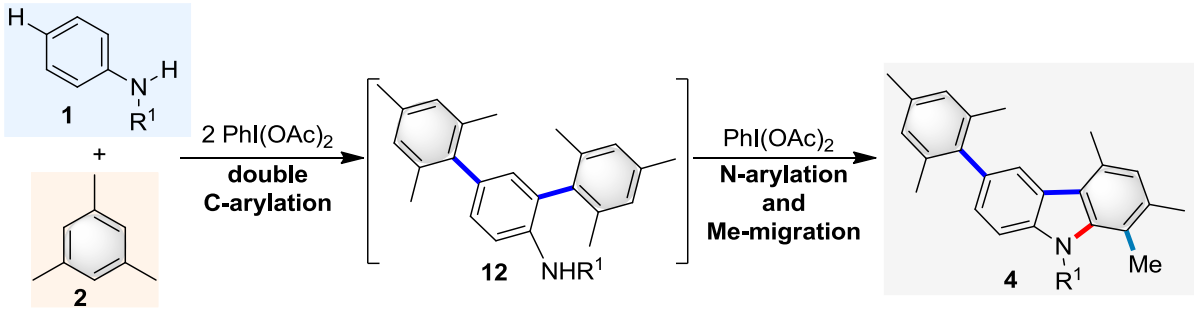
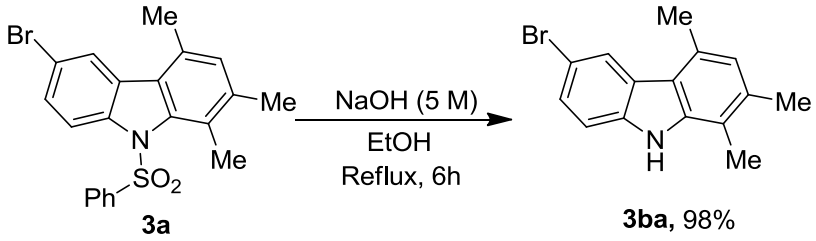


Figure 3B.6 Possible rmechanism for carbazole ring construction and mesityl incorporation.

For *para*- unsubstituted anilide, at initial step 2.0 equiv of PIDA reagent is expected to interact with anilide to create *ortho*- and *para*- mesityl substituted anilide intermediate through nitrenium ion formation (Figure 3B.6).[27] Oxidative C-N bond formation and Me-group migration could be anticipated at the final step with the help of additional 1.0 equiv of $PhI(OAc)_2$.

The sulfonyl group at the *N*-center of carbazole compound **3a** could very easily be removed by treatment with ethanolic NaOH solution to get 6-bromo-1,2,4-trimethyl-9H-carbazole (**3ba**) with 98% yield (Scheme 3B.3).[17]



Scheme 3B.3 Synthesis of NH-carbazole.

3B.4 CONCLUSIONS

In conclusion, a cascade cross dehydrogenative C-N and C-C bond formation reaction has been demonstrated under aerobic and metal-free conditions to yield multi-substituted carbazole products. A broad reactivity scope of anilide substrates has been established. This transformation make direct use of simple and abundant chemical feedstock without requirement of pre-functionalization of substrates. In addition to new ring construction, regioselective incorporation of mesityl ring could achieved with the strategic selection of anilide substrate. We anticipate that this generalized dehydrogenative coupling strategy might have a major impact to unwrap a new direction towards synthesizing complex molecular architectures.

3B.5 EXPERIMENTAL SECTION

Materials Solvents were commercially available and used without further purification. $PhI(OAc)_2$ (PIDA), $PhI(OCOCF_3)_2$ (PIFA), $PhI(OPiv)_2$, iodobenzene (PhI) and *m*-Chloroperbenzoic acid (*m*CPBA) were purchased from commercial source and used without further purification. $PhI(OCOPh)_2$ was prepared from $PhI(OAc)_2$ in a single step according to the literatures. Sulfoanilides were prepared by the reaction of commercially available anilines and sulfonyl chlorides in presence of pyridine in dichloromethane(DCM) solvent. Acetanilides were prepared by using acetyl chlorides in presence of triethylamine (TEA).

Representative Procedure for Preparation of 6-bromo-1,2,4-trimethyl-9-(phenylsulfonyl)carbazole (3a):

To a stirred solution of *N*-(4-bromophenyl)benzenesulfonamide (**1a)** (80 mg, 0.256 mmol), mesitylene (**2a)** (108 µL, 0.769 mmol) in 2,2,2-trifluoroethanol (2.5 mL), PIDA (206 mg, 0.641 mmol) was added slowly at room temperature. The reaction mixture was allowed to stir until completion. Progress of reaction was monitored by TLC using ethyl acetate and hexane as

eluent. After the completion of reaction resulting solution was evaporated to dryness. The crude residue was purified on silica gel column chromatography (1% EtOAc in hexane) to get the pure product 6-bromo-1,2,4-trimethyl-9-(phenylsulfonyl)carbazole (**3a)** (102 mg, 0.238 mmol).

Compound characterization data

***6-Bromo-1,2,4-trimethyl-9-(phenylsulfonyl)carbazole (3a)*:** R_f = 0.65 (hexane:ethyl acetate 19:1); white solid; mp 136-138 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, *J* = 8 Hz, 1H), 7.70 (s, 1H), 7.44 (d, *J* = 8 Hz, 1H), 7.31-7.28 (m, 1H), 7.06-7.02 (m, 2H), 7.00-6.96 (m, 3H), 2.66 (s, 3H), 2.46 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.8, 140.7, 138.4, 134.3, 133.4, 130.4, 129.7, 128.6, 127.9, 127.7, 127.1, 126.6, 124.5, 121.3, 119.3, 20.4, 19.8, 18.5; ; IR (KBr): $\tilde{\nu}$ = 2924, 2851, 1447, 1367, 1181, 1074, 818, 720 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{21}H_{18}NO_2S^{79}BrNa$ $[M + Na]^+$: 450.0134, found: 450.0150, $C_{21}H_{18}NO_2S^{81}BrNa$ $[M + Na]^+$: 452.0114, found: 452.0130.

***1,2,4-Trimethyl-6-phenyl-9-(phenylsulfonyl)carbazole (3b)*:** R_f = 0.60 (hexane:ethyl acetate 19:1); white solid; mp 174-175 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.43 (d, *J* = 8 Hz, 1H), 8.03 (s, 1H), 7.84-7.80 (m, 3H), 7.71-7.68 (m, 2H), 7.62-7.60 (m 1H), 7.52-7.48 (m, 1H), 7.27-7.23 (m, 4H), 2.94 (s, 3H), 2.79 (s, 3H), 2.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.9, 141.9, 141.2, 141.1, 139.0, 137.6, 134.5, 133.1, 132.2, 130.2, 129.5, 128.9, 127.7, 127.7, 127.4, 127.4, 127.2, 125.1, 120.3, 120.1, 20.4, 20.0, 18.5; IR (KBr): $\tilde{\nu}$ = 3062, 2925, 2861, 1582, 1465, 1365, 1266, 1174, 1075, 1041, 958, 870, 795, 763, 724 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{27}H_{24}NO_2S$ $[M + H]^+$: 426.1522, found: 426.1537; $C_{21}H_{19}N$ $[(M – SO_2Ph) + H]^+$: 285.1512, found: 285.1520.

***6-Bromo-1,2,4,7-tetramethyl-9-(phenylsulfonyl)carbazole (3c)*:** R_f = 0.65 (hexane:ethyl acetate 19:1); white solid; mp 166-168 °C; ^{1}HNMR (400 MHz, $CDCl_3$): δ 8.00 (s, 1H), 7.71 (s, 1H), 7.30-7.26 (m, 1H), 7.05-7.01 (m, 2H), 6.98-6.95 (m, 3H), 2.65 (s, 3H), 2.52 (s, 3H), 2.43 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.6, 141.1, 137.8, 135.3, 134.3, 133.3, 131.0, 130.2, 129.3, 127.8, 127.6, 127.1, 126.7, 125.0, 121.9, 121.6, 23.7, 20.4, 19.7, 18.5; IR (KBr): $\tilde{\nu}$ = 2955, 2926, 2864, 1550, 1447, 1364, 1274, 1184, 1143, 1121, 1075, 1041, 878, 815, 718, 671 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{22}H_{20}NO_2S^{79}BrNa$ [M + Na]$^+$: 464.0290, found: 464.0293, $C_{22}H_{20}NO_2S^{81}BrNa$ [M + Na]$^+$: 466.0271, found: 466.0266.

***6-Bromo-1,2,4-trimethyl-9-(phenylsulfonyl)-7-(trifluoromethyl)carbazole (3d)*:** R_f = 0.60 (hexane:ethyl acetate 19:1); white solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.46 (s, 1H), 7.91 (s, 1H), 7.35-7.31 (m, 1H), 7.10-7.06 (m, 3H), 7.01-6.98 (m, 2H), 2.67 (s, 3H), 2.51 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.7, 140.3, 139.9, 135.4, 134.3, 133.8, 130.7, 130.5, 128.2, 127.9, 127.5, 127.0, 125.3, 119.1 (q, $^2J_{C,F}$ = 18 Hz), 116.4 (d, $^3J_{C,F}$ = 10 Hz), 20.6, 19.8, 18.6.

***6-Iodo-1,2,4-trimethyl-9-(phenylsulfonyl)carbazole (3e)*:** R_f = 0.66 (hexane:ethyl acetate 19:1); white solid; mp 122-123 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (s, 1H), 7.88 (s, 1H), 7.62 (d, *J* = 8 Hz, 1H), 7.31-7.28 (m, 1H), 7.06-7.02 (m, 2H), 6.99-6.96 (m, 3H), 2.65 (s, 3H), 2.45 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.5, 141.4, 138.3, 134.5, 134.3, 133.8, 133.4, 130.5, 130.3, 129.7, 127.9, 127.6, 127.1, 126.4, 121.7, 90.3, 20.4, 19.8, 18.5; IR (KBr): $\tilde{\nu}$ = 3058, 2924, 2863, 1641, 1566, 1551, 1446, 1367, 1181, 1112, 1040, 957, 905, 816, 777, 735, 719 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{21}H_{19}INO_2S$ [M + H]$^+$: 476.0176, found: 476.0158.

***6-Chloro-1,2,4-trimethyl-9-(phenylsulfonyl)carbazole (3f)*:** R_f = 0.65 (hexane:ethyl acetate 19:1); white solid; mp 158-159 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, *J* = 8 Hz, 1H), 7.53 (s, 1H), 7.30-7.26 (m, 2H), 7.05-6.95 (m, 5H), 2.66 (s, 3H), 2.45 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.9, 140.2, 138.3, 134.2, 133.3, 132.9, 131.4, 130.3, 129.7, 127.8, 127.7, 127.1, 126.7, 125.8, 121.5, 120.8, 20.4, 19.7, 18.5; IR (KBr): $\tilde{\nu}$ = 2966, 2908, 2861, 1679, 1582, 1512, 1494, 1365, 1275, 1139, 1079, 1041, 964, 820, 753, 741, 704, 686 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{21}H_{19}NO_2SCl$ $[M + H]^+$: 384.0820, found: 384.0804.

***6-Chloro-5-fluoro-1,2,4-trimethyl-9-(phenylsulfonyl)carbazole (3g)*:** R_f = 0.55 (hexane:ethyl acetate 19:1); white solid; mp 158-159 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (d, *J* = 4 Hz, 1H), 7.32-7.29 (m, 2H), 7.08-7.04 (m 2H), 7.00-6.96 (m, 3H), 2.65 (s, 3H), 2.42 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.3 (d, $^1J_{C,F}$ = 244 Hz), 142.2, 138.7, 138.0 (d, $^4J_{C,F}$ = 3 Hz), 134.0, 133.5, 131.2 (d, $^3J_{C,F}$ = 9 Hz), 130.4, 129.6, 128.0, 127.9, 127.2, 126.56 (d, $^4J_{C,F}$ = 3 Hz), 121.6, 118.5 (d, $^2J_{C,F}$ = 20 Hz), 108.9 (d, $^2J_{C,F}$ = 24 Hz), 20.5, 19.5, 18.4; IR (KBr): $\tilde{\nu}$ = 2960, 2927, 2864, 1611, 1583, 1494, 1456, 1369, 1299, 1268, 1217, 1161, 1075, 974, 954, 755, 717, 703, 687 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{21}H_{17}ClFNO_2SNa$ $[M + Na]^+$: 424.0545, found: 424.0546.

***6-Fluoro-1,2,4-trimethyl-9-(phenylsulfonyl)carbazole (3h)*:** R_f = 0.60 (hexane:ethyl acetate 19:1); white solid; mp 160-162 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09-8.06 (m, 1H), 7.29-7.22 (m, 2H), 7.06-6.99 (m, 4H), 6.95-6.92 (m, 2H), 2.67 (s, 3H), 2.44 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.0 (d, $^1J_{C,F}$ = 241 Hz), 142.4, 138.2, 137.9, 134.0, 133.3, 133.1 (d, $^3J_{C,F}$ = 10 Hz), 130.3, 129.7, 127.9, 127.8, 127.3 (d, $^4J_{C,F}$ = 3 Hz), 127.2, 121.1 (d, $^3J_{C,F}$ = 9 Hz), 112.9 (d, $^2J_{C,F}$ = 24 Hz), 108.3 (d, $^2J_{C,F}$ = 25 Hz), 20.4, 19.6, 18.4; IR (KBr): $\tilde{\nu}$ = 3047, 2930, 2851, 1592, 1468, 1448, 1359, 1277, 1170, 1123, 1089, 1070, 1034, 964, 855,

821, 756, 721, 687 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{21}H_{19}FNO_2S$ $[M + H]^+$: 368.1115, found: 368.1079; $C_{15}H_{14}FN$ $[(M – SO_2Ph) + H]^+$: 227.1105, found: 227.1093.

***1,2,4,6-Tetramethyl-9-(phenylsulfonyl)carbazole (3i)*:** R_f = 0.60 (hexane:ethyl acetate 19:1); white solid; mp 144-145 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, *J* = 8 Hz, 1H), 7.37 (s, 1H), 7.26-7.23 (m, 1H), 7.13 (d, *J* = 8 Hz, 1H), 7.01-6.94 (m, 5H), 2.67 (s, 3H), 2.47 (s, 3H), 2.40 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.8, 139.7, 137.2, 135.4, 134.4, 133.0, 131.7, 130.1, 129.4, 127.9, 127.6, 127.2, 126.9, 122.1, 119.6, 21.6, 20.3, 19.95 18.5; IR (KBr): $\tilde{\nu}$ = 2926, 2861, 1583, 1447, 1362, 1174, 1133, 1074, 969, 849, 814, 751, 717, 685 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{22}H_{22}NO_2S$ $[M + H]^+$: 364.1366, found: 364.1312, $C_{16}H_{17}N$ $[M – SO_2Ph) + H]^+$: 223.1356, found: 223.1336.

***6-Ethyl-1,2,4-trimethyl-9-(phenylsulfonyl)carbazole (3j)*:** R_f = 0.65 (hexane:ethyl acetate 19:1); white solid; mp 118-120 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, *J* = 8 Hz, 1H), 7.37 (s, 1H), 7.26-7.22 (m, 1H), 7.16 (d, *J* = 8 Hz, 1H), 7.00-6.93 (m, 5H), 2.69-2.63 (m, 5H), 2.48 (s, 3H), 2.40 (s, 3H), 1.21 (t, *J* = 8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.1, 141.8, 139.9, 137.1, 134.3, 132.9, 131.9, 130.1, 129.3, 128.0, 127.6, 127.5, 127.2, 125.8, 120.9, 119.8, 29.0, 20.3, 19.9, 18.4, 16.2; IR (KBr): $\tilde{\nu}$ = 2964, 2928, 1584, 1473, 1447, 1368, 1174, 1134, 1074, 1038, 956, 870, 835, 753, 734, 686 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{23}H_{24}NO_2S$ $[M + H]^+$: 378.1522, found: 378.1515.

***6-Isopropyl-1,2,4-trimethyl-9-(phenylsulfonyl)carbazole (3k)*:** R_f = 0.60 (hexane:ethyl acetate 19:1); white solid; mp 114-116 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.03 (d, *J* = 8 Hz, 1H), 7.39 (s, 1H), 7.26-7.19 (m, 2H), 6.99-6.92 (m, 5H), 2.93 (sept, *J* = 8 Hz, 1H), 2.66 (s, 3H), 2.48 (s,

3H), 2.40 (s, 3H), 1.24 (d, *J* = 4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.9, 141.8, 140.1, 137.1, 134.2, 132.9, 131.9, 130.1, 129.3, 128.1, 127.6, 127.5, 127.2, 124.2, 119.8, 119.5, 34.3, 24.4, 20.3, 19.9, 18.4; IR (KBr): $\tilde{\nu}$ = 2959, 2867, 1612, 1584, 1549, 1474, 1447, 1365, 1312, 1175, 1088, 1074, 963, 870, 826, 796, 724, 686 cm^{-1}; HR:MS (ESI-TOF): m/z calculated for $C_{24}H_{26}NO_2S$ $[M + H]^+$: 392.1679, found: 392.1663.

***6-(tert-Butyl)-1,2,4-trimethyl-9-(methylsulfonyl)carbazole (3l)*:** R_f = 0.60 (hexane:ethyl acetate 19:1); white solid; mp 132-134 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 9(s, 1H), 7.96 (s, 1H), 7.47 (d, *J* = 8 Hz, 1H), 7.05 (s, 1H), 2.74 (s, 3H), 2.54 (s, 3H), 2.37 (s, 3H), 2.19 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.2, 141.4, 139.9, 137.5, 130.9, 130.3, 129.6, 127.5, 127.4, 124.1, 118.9, 118.6, 34.9, 34.0, 31.7, 20.3, 20.2, 18.5; IR (KBr): $\tilde{\nu}$ = 2961, 2866, 1477, 1458, 1362, 1316, 1203, 1171, 1144, 1076, 966, 854, 827, 790, 755, 740 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{20}H_{26}NO_2S$ $[M + H]^+$: 344.1679, found: 344.1682.

***6-Bromo-1,2,4-trimethyl-9-(methylsulfonyl)carbazole (3m)*:** R_f = 0.70 (hexane:ethyl acetate 19:1); white solid; mp 83-85 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (s, 1H), 7.94 (d, *J* = 12 Hz, 1H), 7.52 (d, *J* = 8 Hz, 1H), 7.07 (s, 1H), 2.69 (s, 3H), 2.52 (s, 3H), 2.38 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.4, 140.9, 138.8, 132.9, 130.6, 130.1, 129.3, 127.6, 125.9, 125.2, 120.6, 119.6, 34.4, 20.4, 20.1, 18.5; IR (KBr): $\tilde{\nu}$ = 3015, 2928, 2863, 1597, 1573, 1448, 1362, 1318, 1276, 1197, 1170, 1113, 1078, 1041, 962, 864, 820, 750, 733, 670 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{16}H_{16}NO_2S^{79}BrNa$ $[M + Na]^+$: 387.9977, found: 387.9983, $C_{16}H_{16}NO_2S^{81}BrNa$ $[M + Na]^+$: 389.9957, found: 389.9959.

***6-Chloro-1,2,4-trimethyl-9-(methylsulfonyl)carbazole (3n)*:** R_f = 0.65 (hexane:ethyl acetate 19:1); white solid; mp 101-103 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, *J* = 8 Hz, 1H), 7.91

(s, 1H), 7.38 (d, *J* = 8 Hz, 1H), 7.07 (s, 1H), 2.69 (s, 3H), 2.53 (s, 3H), 2.38 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.6, 140.5, 138.8, 132.5, 131.8, 130.6, 130.1, 127.7, 126.4, 126.0, 122.2, 120.2, 34.3, 20.4, 20.1, 18.5; IR (KBr): $\tilde{\nu}$ = 3013, 2929, 2864, 1606, 1577, 1493, 1451, 1363, 1318, 1274, 1170, 1140, 1113, 1081, 964, 865, 824, 793, 735, 704, 681 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{16}H_{16}NO_2SClNa$ $[M + Na]^+$: 344.0482, found: 344.0481.

***6-Iodo-1,2,4-trimethyl-9-(methylsulfonyl)carbazole (3o)*:** R_f = 0.50 (hexane:ethyl acetate 19:1); white solid; mp 113-115 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 (s, 1H), 7.81 (d, *J* = 8 Hz, 1H), 7.70 (d, *J* = 8 Hz, 1H), 7.06 (s, 1H), 2.68 (s, 3H), 2.52 (s, 3H), 2.38 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.6, 141, 1, 138.8, 135.1, 133.3, 131.1, 130.6, 130.1, 127.5, 125.6, 120.9, 90.6, 34.5, 20.4, 20.1, 18.5; IR (KBr): $\tilde{\nu}$ = 3012, 2928, 2861, 1592, 1568, 1493, 1362, 1317, 1198, 1170, 1113, 1078, 1041, 961, 866, 818, 786, 746, 733, 699, 666 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{16}H_{16}NSO_2INa$ $[M + Na]^+$: 435.9839, found 435.9827.

***6-Fluoro-1,2,4-trimethyl-9-(methylsulfonyl)carbazole (3p)*:** R_f = 0.45 (hexane:ethyl acetate 19:1); white solid; mp 91-93 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03-7.99 (m, 1H), 7.63-7.60 (m, 1H), 7.14-7.09 (m, 1H), 7.07 (s, 1H), 2.68 (s, 3H), 2.53 (s, 3H), 2.38 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.2 (d, $^1J_{C,F}$ = 242 Hz), 142.0, 138.7, 138.1 (d, $^4J_{C,F}$ = 2 Hz), 132.6 (d, $^3J_{C,F}$ = 10 Hz), 130.5, 130.1, 127.8, 126.5 (d, $^4J_{C,F}$ = 3 Hz), 120.3 (d, $^3J_{C,F}$ = 9 Hz), 113.5 (d, $^2J_{C,F}$ = 24 Hz), 108.9 (d, $^2J_{C,F}$ = 25 Hz), 34.0, 20.4, 19.9, 18.5; IR (KBr): $\tilde{\nu}$ = 3012, 2928, 2863, 1592, 1549, 1470, 1361, 1318, 1274, 1167, 1077, 1040, 857, 819, 768, 734 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{16}H_{17}NO_2SF$ $[M + H]^+$: 306.0959, found: 306.0937.

***5-Chloro-6-fluoro-1,2,4-trimethyl-9-(methylsulfonyl)carbazole (3q)*:** R_f = 0.45 (hexane:ethyl acetate 19:1); white solid; mp 130-131 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (d, *J* = 8Hz, 1H), 7.69 (d, *J* = 8Hz, 1H), 7.08 (s, 1H), 2.66 (s, 3H), 2.52 (s, 3H), 2.38 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.6 (d, $^1J_{C,F}$ = 244 Hz), 141.7, 139.2, 138.1 (d, $^4J_{C,F}$ = 3 Hz), 130.7 (d, $^3J_{C,F}$ = 9 Hz), 130.6, 130.0, 127.8, 125.8 (d, $^4J_{C,F}$ = 3 Hz), 121.0, 119.2 (d, $^2J_{C,F}$ = 20 Hz), 109.6 (d, $^2J_{C,F}$ = 25 Hz), 34.4, 20.5, 19.8, 18.5; IR (KBr): $\tilde{\nu}$ = 3013, 2928, 2856, 1728, 1610, 1550, 1494, 1458, 1365, 1319, 1217, 1175, 1161, 1080, 1015, 880, 826, 776, 737, 703 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{16}H_{15}NO_2SFClNa$ $[M + Na]^+$: 362.0388, found: 362.0401.

***6,7-Dichloro-1,2,4-trimethyl-9-(methylsulfonyl)carbazole (3r)*:** R_f = 0.45 (hexane:ethyl acetate 19:1); white solid; mp 125-126 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (s, 1H), 8.00 (s, 1H), 7.08 (s, 1H), 2.67 (s, 3H), 2.52 (s, 3H), 2.38 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.5, 141.0, 139.2, 130.7, 130.3, 130.2, 130.1, 127.6, 125.3, 123.3, 120.8, 34.7, 20.5, 20.0, 18.5; IR (KBr): $\tilde{\nu}$ = 3013, 2929, 2863, 1724, 1610, 1564, 1493, 1445, 1438, 1269, 1170, 1128, 1077, 1043, 965, 880, 761, 732, 682 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{16}H_{15}NO_2SCl_2Na$ $[M + Na]^+$: 378.0093, found: 378.0033; $C_{15}H_{13}NCl_2$ $[(M–SO_2Me) + H]^+$: 277.0420, found: 277.0396.

***1,2,4,6-Tetramethyl-9-(methylsulfonyl)carbazole (3s)*:** R_f = 0.45 (hexane:ethyl acetate 19:1); white solid; mp 73-75 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, *J* = 8 Hz, 1H), 7.75 (s, 1H), 7.23 (d, *J* = 8 Hz, 1H), 7.05 (s, 1H), 2.71 (s, 3H), 2.53 (s, 3H), 2.51 (s, 3H), 2.37 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.4, 140.1, 137.7, 135.8, 131.3, 130.3, 129.8, 127.6, 127.5, 127.1, 122.8, 118.8, 33.8, 21.7, 20.3, 20.2, 18.5; IR (KBr): $\tilde{\nu}$ = 3010, 2925, 2858, 1549,

1512, 1453, 1360, 1273, 1132, 1077, 1042, 967, 847, 816, 766, 736 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{17}H_{20}NO_2S$ $[M + H]^+$: 302.1209, found: 302.1221.

***6-ethyl-1,2,4-trimethyl-9-(methylsulfonyl)carbazole (3t)*:** R_f = 0.50 (hexane:ethyl acetate 19:1); white solid; mp 103-105 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, *J* = 8 Hz, 1H), 7.77 (s, 1H), 7.26 (d, *J* = 8 Hz, 1H), 7.05 (s, 1H), 2.80 (q, *J* = 8 Hz, 2H), 2.72 (s, 3H), 2.53 (s, 3H), 2.37 (s, 3H), 2.17 (s, 3H), 1.33 (t, *J* = 8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.3, 141.5, 140.3, 137.6, 131.3, 130.3, 129.8, 127.6, 127.2, 126.4, 121.6, 119.0, 33.9, 29.1, 20.3, 20.2, 18.5, 16.1; IR (KBr): $\tilde{\nu}$ = 3012, 2964, 2929, 2867, 1612, 1583, 1456, 1361, 1316, 1198, 1169, 1111, 1040, 1015, 961, 836, 805, 778, 738, 717 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{18}H_{22}NO_2S$ $[M + H]^+$: 316.1366, found: 316.1377.

***6-Isopropyl-1,2,4-trimethyl-9-(methylsulfonyl)carbazole (3u)*:** R_f = 0.55 (hexane:ethyl acetate 19:1); white solid; mp 74-75 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, *J* = 8 Hz, 1H), 7.80 (s, 1H), 7.30 (d, *J* = 12 Hz, 1H), 7.05 (s, 1H), 3.07 (sept, *J* = 8 Hz, 1H), 2.73 (s, 3H), 2.53 (s, 3H), 2.37 (s, 3H), 2.18 (s, 3H), 1.35 (d, *J* = 8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.0, 141.4, 140.3, 137.5, 131.2, 130.3, 129.7, 127.5, 127.3, 124.9, 120.1, 118.9, 34.3, 33.9, 24.4, 20.3, 20.2, 18.5; IR (KBr): $\tilde{\nu}$ = 2959, 2928, 2867, 1474, 1457, 1361, 1315, 1170, 1147, 1111, 1040, 968, 830, 762, 740, 712 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{19}H_{24}NO_2S$ $[M + H]^+$: 330.1522, found: 330.1526.

***6-Bromo-1,2,4,7-tetramethyl-9-(methylsulfonyl)carbazole (3v)*:** R_f = 0.60 (hexane:ethyl acetate 19:1); white solid; mp 96-97 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.94 (s, 1H), 7.05 (s, 1H), 8.09 (s, 1H), 2.67 (s, 3H), 2.54 (s, 3H), 2.52 (s, 3H), 2.37 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.5, 141.3, 138.3, 136.1, 130.6, 130.4, 129.7, 127.7,

126.0, 125.6, 122.4, 120.9, 34.2, 23.8, 20.4, 20.0, 18.5; IR (KBr): $\tilde{\nu}$ = 3011, 2927, 2862, 1455, 1362, 1317, 1174, 1142, 1122, 1042, 1013, 956, 879, 817, 776, 763, 735 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{17}H_{19}NO_2S^{79}Br$ $[M + H]^+$: 380.0314, found: 380.0301, $C_{17}H_{19}NO_2S^{81}Br$ $[M + H]^+$: 382.0294, found: 382.0288.

***1,2,4-Trimethyl-9-(methylsulfonyl)-6-phenyl-carbazole (3w)*:** R_f = 0.50 (hexane:ethyl acetate 19:1); white solid; mp 146-147 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.15-8.12 (m, 2H), 7.69-7.63 (m, 3H), 7.50 (t, *J* = 8 Hz, 2H), 7.40 (t, *J* = 8 Hz, 1H), 7.09 (s, 1H), 2.77 (s, 3H), 2.56 (s, 3H), 2.40 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.5, 141.5, 141.1, 139.5, 138.1, 131.7, 130.5, 129.9, 129.0, 127.7, 127.6, 127.5, 127.0, 125.8, 121.0, 119.3, 34.3, 20.4, 20.3, 18.6; IR (KBr): $\tilde{\nu}$ = 3062, 2951, 2932, 1642, 1455, 1361, 1314, 1169, 1139, 964, 831, 799, 764, 737, 699 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{22}H_{21}NO_2SNa$ $[M + Na]^+$: 386.1185, found: 386.1183.

***5-Bromo-7,9,10-trimethyl-11-(methylsulfonyl)-benzo[a]carbazole (3x)*:** R_f = 0.60 (hexane:ethyl acetate 19:1); white solid; mp 152-154 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.72 (d, *J* = 8 Hz, 1H), 8.40 (s, 1H), 8.33 (d, *J* = 8 Hz, 1H), 7.70-7.61 (m, 2H), 7.10 (s, 1H), 2.77 (s, 3H), 2.61 (s, 3H), 2.40 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.0, 138.9, 138.0, 131.2, 130.7, 130.6, 129.7, 128.6, 127.5, 127.4, 127.4, 127.3, 127.1, 127.1, 124.0, 122.3, 33.1, 20.3, 20.0, 17.9; IR (KBr): $\tilde{\nu}$ = 3054, 2926, 2895, 1588, 1453, 1360, 1266, 1178, 1165, 1091, 1032, 958, 863, 813, 753, 685 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{20}H_{18}{}^{79}BrNO_2SNa$ $[M + Na]^+$: 438.0152, found: 438.0152, $C_{20}H_{18}{}^{81}BrNO_2SNa$ $[M + Na]^+$: 440.0114, found: 440.0154; $C_{19}H_{16}{}^{79}BrN$ $[(M - SO_2Me) + H]^+$: 337.0461, found: 337.0476, $C_{19}H_{16}{}^{81}BrN$ $[(M - SO_2Me) + H]^+$: 339.0441, found: 339.0453.

***1,2,4,6-Tetramethyl-9-tosyl-carbazole (3y)*:** R_f = 0.50 (hexane:ethyl acetate 19:1); white solid; mp 99-100 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, *J* = 8 Hz, 1H), 7.41 (s, 1H), 7.13 (d, *J* = 8 Hz, 1H), 6.96 (s, 1H), 6.86 (d, *J* = 8 Hz, 2H), 6.78 (d, *J* = 8 Hz, 2H), 2.67 (s, 3H), 2.49 (s, 3H), 2.40 (s, 3H), 2.39 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.7, 141.7, 139.8, 137.1, 135.2, 131.8, 131.7, 130.0, 129.3, 128.3, 127.8, 127.5, 127.2, 126.8, 122.1, 119.5, 21.6, 21.5, 20.3, 19.9, 18.5; IR (KBr): $\tilde{\nu}$ = 2924, 2863, 1597, 1493, 1456, 1364, 1269, 1172, 1110, 1076, 1017, 967, 847, 814, 724, 670 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{16}H_{17}N$ $[(M - Ts) + H]^+$: 223.1356, found: 223.1321.

***6-Bromo-1,2,4-trimethyl-9-((4-nitrophenyl)sulfonyl)-carbazole (3z)*:** R_f = 0.50 (hexane:ethyl acetate 19:1); white solid; mp 150-152 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, *J* = 8 Hz, 1H), 7.88 (d, *J* = 8 Hz, 2H), 7.73 (s, 1H), 7.48 (d, *J* = 8 Hz, 1H), 7.14 (d, *J* = 8 Hz, 2H), 7.04 (s, 1H), 2.66 (s, 3H), 2.47 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 141.2, 139.9, 139.6, 138.9, 133.3, 131.0, 130.1, 129.1, 128.5, 127.9, 126.4, 124.9, 123.1, 121.3, 120.0, 20.5, 19.8, 18.5; IR (KBr): $\tilde{\nu}$ = 3104, 2927, 1606, 1531, 1448, 1376, 1348, 1308, 1265, 1177, 1138, 1074, 1040, 959, 854, 819, 781, 740, 682, 638 cm^{-1}.

***1-(6-Bromo-1,2,4-trimethyl-carbazol-9-yl)ethanone (3aa)*:** R_f = 0.55 (hexane:ethyl acetate 19:1); white solid; mp 103-105 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (s, 1H), 7.99 (d, *J* = 8 Hz, 1H), 7.50 (d, *J* = 8 Hz, 1H), 7.03 (s, 1H), 2.73 (s, 3H), 2.50 (s, 3H), 2.41 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 140.2, 139.1, 137.3, 130.5, 129.0, 128.9, 128.5, 124.7, 123.2, 121.3, 116.5, 115.8, 26.6, 20.3, 20.2, 17.7; HR-MS (ESI-TOF): m/z calculated for $C_{17}H_{17}NO^{79}Br$ $[M + Na]^+$: 330.0488, found: 330.0507, $C_{17}H_{17}NO^{81}Br$ $[M + Na]^+$: 332.0468, found: 332.0488.

Representative Procedure for Preparation of 6-Mesityl-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (4h):

To a stirred solution of *N*-phenylmethanesulfonamide **1aa** (100 mg, 0.584 mmol), mesitylene **2a** (245 µL, 1.75 mmol) in 2,2,2-trifluoroethanol (3.0 mL), PIDA (563 mg, 1.75 mmol) was added slowly at ambient conditions and allowed to stir for additional 3 h. Progress of reaction was monitored by TLC using ethyl acetate and hexane as eluent. After the completion of reaction resulting solution was evaporated to dryness. The crude residue was purified on silica gel column chromatography (1% EtOAc in hexane) to get the pure product 6-Mesityl-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole **4h** (156 mg, 0.385 mmol).

***6-Mesityl-1,2,4,8-tetramethyl-9-(methylsulfonyl)-carbazole (4a)*:** R_f = 0.55 (hexane:ethyl acetate 19:1); white solid; mp 116-118 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (s, 1H), 7.07 (s, 1H), 7.05 (s, 1H), 7.02 (s, 2H), 2.77 (s, 3H), 2.63 (s, 3H), 2.59 (s, 3H), 2.40 (s, 6H), 2.25 (s, 3H), 2.10 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.8, 141.5, 139.7, 138.7, 137.5, 136.9, 136.1, 133.8, 131.8, 130.8, 130.6, 129.9, 128.3, 128.2, 120.6, 32.9, 21.1, 20.9, 20.5, 20.2, 20.1, 17.6; IR (KBr): $\tilde{\nu}$ = 3010, 2925, 2859, 1611, 1453, 1359, 1315, 1181, 1164, 1142, 1070, 961, 851, 787, 738, 637 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{26}H_{29}NO_2SNa$ $[M + Na]^+$: 442.1811, found: 442.1844.

***6-Mesityl-1,2,4,5,7-pentamethyl-9-(methylsulfonyl)-carbazole (4b)*:** R_f = 0.65 (hexane:ethyl acetate 19:1); white solid; mp 164-166 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (s, 1H), 7.05 (s, 1H), 6.98 (s, 2H), 2.72 (s, 3H), 2.53 (s, 3H), 2.36 (s, 6H), 2.32 (s, 3H), 2.22 (s, 3H), 1.99 (s, 3H), 1.86 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.8, 141.7, 139.4, 137.1, 137.0, 136.6, 135.7, 135.5, 131.9, 130.1, 129.2, 128.9, 128.6, 128.1, 127.7, 33.5, 25.1, 21.4, 21.2, 21.0, 19.9, 19.8, 18.6; IR (KBr): $\tilde{\nu}$ = 2923, 2854, 1550, 1452, 1361, 1314, 1183, 1166, 1085, 1051, 956,

850, 796, 747 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{27}H_{32}NO_2S$ $[M + H]^+$: 434.2148, found: 434.2150.

***8-Bromo-6-mesityl-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (4c)*:** R_f = 0.65 (hexane:ethyl acetate 19:1); white solid; mp 192-194 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.67 (s, 1H), 7.38 (s, 1H), 7.04 (s, 1H), 7.00 (s, 2H), 3.47 (s, 3H), 2.60 (s, 3H), 2.57 (s, 3H), 2.41 (s, 3H), 2.38 (s, 3H), 2.12 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 140.8, 140.2, 137.5, 137.4, 137.4, 136.4, 136.0, 134.9, 131.8, 130.5, 130.3, 128.3, 126.6, 126.2, 122.2, 113.6, 41.5, 21.1, 21.0, 20.9, 20.3, 17.3; IR (KBr): $\tilde{\nu}$ = 2921, 2861, 1612, 1553, 1459, 1400, 1323, 1266, 1210, 1164, 1072, 1014, 960, 868, 835, 800, 774, 736, 703, 623 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{25}H_{26}N^{79}BrO_2SNa$ $[M + Na]^+$: 506.0760, found: 506.0740, $C_{25}H_{26}N^{81}BrO_2SNa$ $[M + Na]^+$: 508.0740, found: 508.0730; $C_{24}H_{24}N^{79}Br$ $[(M – SO_2Me) + H]^+$: 405.1087, found: 405.1084, $C_{24}H_{24}N^{81}Br$ $[(M – SO_2Me) + H]^+$: 407.1067, found: 407.1060.

***8-Chloro-6-mesityl-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (4d)*:** R_f = 0.65 (hexane:ethyl acetate 19:1); white solid; mp 190-192 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.60 (s, 1H), 7.17 (s, 1H), 7.01 (s, 1H), 6.98 (s, 2H), 3.58 (s, 3H), 2.58 (s, 3H), 2.54 (s, 3H), 2.39 (s, 3H), 2.35 (s, 3H), 1.56 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 139.9, 138.9, 137.6, 137.5, 137.4, 134.6, 130.3, 130.3, 128.6, 128.4, 126.3, 125.8, 124.7, 121.7, 42.2, 21.2, 21.0, 20.4, 20.3, 17.5; IR (KBr): $\tilde{\nu}$ = 3051, 2972, 2944, 2861, 2733, 1612, 1565, 1460, 1324, 1266, 1209, 1165, 1073, 1015, 1000, 962, 907, 849, 804, 737, 703, 666, 625 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{25}H_{26}ClNO_2SNa$ $[M + Na]^+$: 462.1265, found: 462.1241, $C_{24}H_{24}ClN$ $[(M – SO_2Me) + H]^+$: 361.1592, found: 361.1579.

***5-Fluoro-6-mesityl-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (4e)*:** R_f = 0.60 (hexane:ethyl acetate 19:1); white solid; mp 163-165 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, *J* = 8 Hz, 1H), 7.71 (d, *J* = 8 Hz, 1H), 7.06 (s, 1H), 7.02 (s, 2H), 2.62 (s, 3H), 2.56 (s, 3H), 2.39 (s, 3H), 2.37 (s, 3H), 2.34 (s, 3H), 2.07 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.34 (d, $^1J_{C,F}$ = 243 Hz), 142.24 (d, $^3J_{C,F}$ = 12 Hz), 141.5, 137.9, 137.7, 136.8, 132.2, 130.5, 129.5, 128.4, 127.6, 127.3 (d, $^4J_{C,F}$ = 2 Hz), 126.4, 126.2, 124.4 (d, $^3J_{C,F}$ = 5 Hz), 107.3 (d, $^2J_{C,F}$ = 25 Hz), 34.5, 21.2, 20.6, 20.4, 20.2, 18.5; IR (KBr): $\tilde{\nu}$ = 3038, 2971, 2926, 1575, 1495, 1460, 1364, 1272, 1174, 1115, 1037, 957, 866, 821, 778, 764, 738 cm^{-1}; HR-MS (ESI-TOF): m/z = calculated for $C_{25}H_{26}FNO_2S$ $[M + H]^+$: 424.1741, found: 424.1727, calculated for $C_{24}H_{24}FN$ $[(M–SO_2Me) + H]^+$: 345.1887, found: 345.1884.

***8-Iodo-6-mesityl-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (4f)*:** R_f = 0.45 (hexane:ethyl acetate 19:1); white solid; mp 193-195 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (s, 1H), 7.65 (s, 1H), 7.03 (s, 1H), 6.98 (s, 2H), 2.91 (s, 3H), 2.57 (s, 6H), 2.38 (s, 3H), 2.35 (s, 3H), 2.08 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 143.8, 140.8, 138.8, 137.9, 137.5, 137.2, 136.2, 136.1, 134.7, 130.9, 130.4, 128.4, 128.3, 127.4, 127.2, 122.9, 86.6, 38.5, 21.2, 21.0, 20.9, 20.3, 20.2, 17.3; IR (KBr): $\tilde{\nu}$ = 2922, 2857, 1692, 1547, 1512, 1453, 1357, 1275, 1162, 1072, 958, 797, 758 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{25}H_{26}INO_2SNa$ $[M + Na]^+$: 554.0621, found: 554.0618

***5-Mesityl-7,9,10-trimethyl-11-(methylsulfonyl)-benzo[a]carbazole (4g)*:** R_f = 0.50 (hexane:ethyl acetate 19:1); white solid; mp 195-197 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.83 (d, *J* = 8 Hz, 1H), 7.93 (s, 1H), 7.67-7.62 (m, 1H), 7.45-7.39 (m, 2H), 7.12-7.10 (m, 3H), 2.73 (s, 3H), 2.68 (s, 3H), 2.46 (s, 3H), 2.44 (s, 3H), 2.12 (s, 3H), 1.99 (s, 3H), 1.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.1, 138.9, 138.5, 137.4, 137.3, 137.1, 136.8, 136.8, 131.4, 131.0,

130.1, 129.6, 128.6, 128.5, 128.4, 128.3, 126.8, 126.7, 126.3, 125.7, 120.7, 32.8, 21.3, 20.5, 20.4, 20.3, 20.2, 17.9; IR (KBr): $\tilde{\nu}$ = 2924, 2858, 2310, 1641, 1549, 1452, 1387, 1360, 1165, 1036, 959, 755 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{29}H_{29}NO_2SNa$ $[M + Na]^+$: 478.1811, found: 478.1848, calculated for $C_{28}H_{27}N$ $[(M–SO_2Me) + H]^+$: 377.2138, found: 377.2169.

***6-Mesityl-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (4h)*:** R_f = 0.50 (hexane:ethyl acetate 19:1); white solid; mp 177-179 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.11 (d, *J* = 8 Hz, 1H), 7.74 (s, 1H), 7.21 (d, *J* = 8 Hz, 1H), 7.06 (s, 1H), 7.00 (s, 2H), 2.64 (s, 3H), 2.57 (s, 3H), 2.39 (s, 3H), 2.37 (s, 3H), 2.27 (s, 3H), 2.04 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.4, 140.9, 139.0, 138.7, 137.9, 137.1, 136.2, 131.3, 130.4, 129.9, 128.3, 127.8, 127.7, 127.1, 123.1, 119.2, 34.1, 21.12, 20.9, 20.4, 20.3, 18.5; IR (KBr): $\tilde{\nu}$ = 3010, 2925, 2859, 1611, 1462, 1364, 1268, 1195, 1133, 1077, 1040, 965, 834, 796, 760, 738, 705 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{25}H_{28}NO_2S$ $[M + H]^+$: 406.1835, found: 406.1837.

***6-Mesityl-1,2,4-trimethyl-9-((4-nitrophenyl)sulfonyl)-carbazole (4i)*:** R_f = 0.70 (hexane:ethyl acetate 19:1); white solid; mp 92-94 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.15 (d, *J* = 8 Hz, 1H), 7.83 (d, *J* = 8 Hz, 2H), 7.33 (s, 1H), 7.18-7.13 (m, 3H), 7.04 (s, 1H), 6.94 (s, 2H), 2.70 (s, 3H), 2.44 (s, 3H), 2.40 (s, 3H), 2.33 (s, 3H), 1.86 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.1, 141.4, 140.0, 139.6, 139.4, 138.4, 138.1, 137.2, 135.8, 132.1, 130.9, 130.0, 128.7, 128.3, 128.1, 127.8, 127.4, 122.8, 122.6, 120.2, 21.1, 20.7, 20.4, 20.0, 18.3; IR (KBr): = 2997, 2924, 2872, 1607, 1531, 1462, 1400, 1348, 1308, 1177, 1075, 1038, 961, 853, 790, 683, 638 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{24}H_{25}N$ $[(M – SO_2\text{-}C_6H_4\text{-}NO_2) + H]^+$: 327.1982, found: 327.2006.

***6-Mesityl-1,2,4-trimethyl-9-tosyl-carbazole (4j)*:** R_f = 0.65 (hexane:ethyl acetate 19:1); white solid; mp 156-158 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (d, *J* = 8 Hz, 1H), 7.32 (s, 1H), 7.08 (d, *J* = 8 Hz, 1H), 6.99 (s, 1H), 6.94 (s, 2H), 6.88-6.84 (m, 2H), 6.78 (d, *J* = 8 Hz, 2H), 2.69 (s, 3H), 2.42 (s, 3H), 2.41 (s, 3H), 2.34 (s, 3H), 2.17 (s, 3H), 1.89 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 142.1, 140.9, 138.9, 138.6, 137.5, 136.9, 136.0, 132.2, 131.5, 130.1, 129.5, 128.2, 128.1, 128.0, 127.4, 127.2, 127.0, 122.5, 120.1, 21.4, 21.1, 20.7, 20.4, 20.0, 18.4; HR-MS (ESI-TOF): m/z calculated for $C_{31}H_{32}NO_2S$ $[M + H]^+$: 482.2148, found: 482.2138.

N-(p-tolyl)-N-(2,2,2-trifluoroethoxy)benzenesulfonamide (1if): R_f = 0.45 (hexane:ethyl acetate 9:1); white semi-solid; ^{19}F NMR (376.3 MHz, $CDCl_3$): δ -74.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01-7.99 (m, 2H), 7.68-7.60 (m, 2H), 7.57-7.53 (m, 2H), 6.75 (d, *J* = 8 Hz, 1H), 6.67 (d, *J* = 8 Hz, 1H), 6.42 (d, *J* = 8 Hz, 1H), 3.64-3.57 (m, 2H), 1.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 149.8, 148.3, 140.8, 133.2, 131.2, 129.1, 127.3, 124.5, 123.5 (q, $^1J_{C,F}$ = 270 Hz, 73.7, 63.5 (q, $^2J_{C,F}$ = 35 Hz), 25.8.

Synthetic Procedure for Preparation of *N*-(5-iodo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (1ea):

PIDA (89 mg, 0.278 mmol) was added at a time in a mixture of *N*-(4-iodophenyl)benzenesulfonamide **1o** (100 mg, 0.278 mmol) and mesitylene **2a** (117 µL, 0.835 mmol) in 2,2,2-trifluoroethanol (2.5 mL) at room temperature. The reaction was completed after additional stirring of 3 h. Solvent was evaporated to dryness and the crude reaction mixture was purified by silica gel column chromatography (hexane : ethyl acetate 93:7) to get pure *N*-(5-iodo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide **1ea** (92 mg, 0.193 mmol).

***N-(5-Iodo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (1ea)*:** R_f = 0.60 (hexane:ethyl acetate 4:1); white solid; mp 142-143 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74-7.71 (m, 2H), 7.61-7.54 (m, 3H), 7.47-7.43 (m, 2H), 7.27 (s, 1H), 6.90 (s, 2H), 6.17 (s, 1H), 2.33 (s, 3H), 1.63 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.3, 139.0, 138.7, 137.3, 136.8, 134.4, 133.4, 132.6, 130.7, 129.3, 129.1, 127.3, 119.9, 87.9, 21.23, 19.94; IR (KBr): $\tilde{\nu}$ = 3005, 2920, 2852, 1691, 1552, 1468, 1380, 1338, 1280, 1167, 1128, 906, 851, 802, 720, 687 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{21}H_{21}INO_2S$ $[M + H]^+$: 478.0332, found: 478.0318.

Experimental Procedure for the Deprotection Reaction:

***6-Bromo-1,2,4-trimethyl-9H-carbazole (3ab)*:** R_f = 0.70 (hexane:ethyl acetate 4:1); white solid; mp 140-141 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21 (s, 1H), 7.95 (bs, 1H), 7.46 (d, *J* = 8 Hz, 1H), 7.32 (d, *J* = 8 Hz, 1H), 6.87 (s, 1H), 2.77 (s, 3H), 2.43 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.9, 138.2, 134.4, 130.4, 127.3, 126.6, 124.8, 124.0, 118.9, 115.2, 112.2, 111.8, 20.3, 19.7, 13.1; IR (KBr): $\tilde{\nu}$ = 2968, 2914, 2857, 1620, 1512, 1451, 1295, 949, 845, 796 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{15}H_{15}N^{79}Br$ $[M + H]^+$: 288.0382, found: 288.0373, $C_{15}H_{15}N^{81}Br$ $[M + H]^+$: 290.0362, found; 290.0354.

3.3 NOTES AND REFERENCES

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^{1}H and ^{13}C NMR Spectra of selected compounds

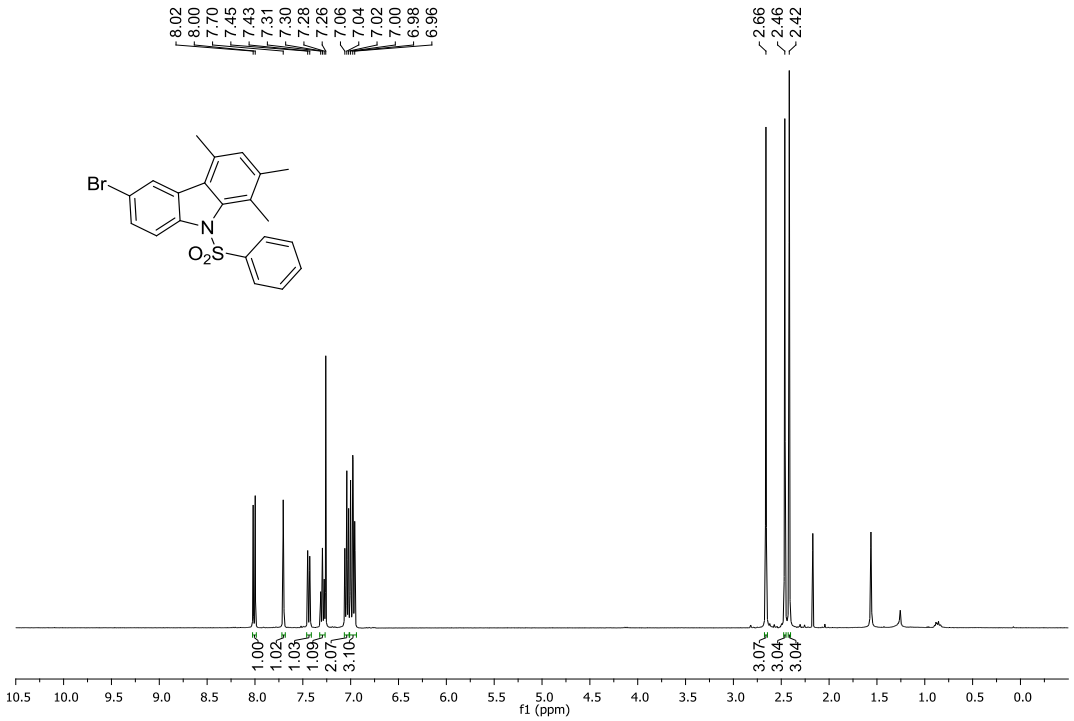


Figure 3B.7 ^{1}H NMR spectrum of 6-bromo-1,2,4-trimethyl-9-(phenylsulfonyl)carbazole **(3a)**

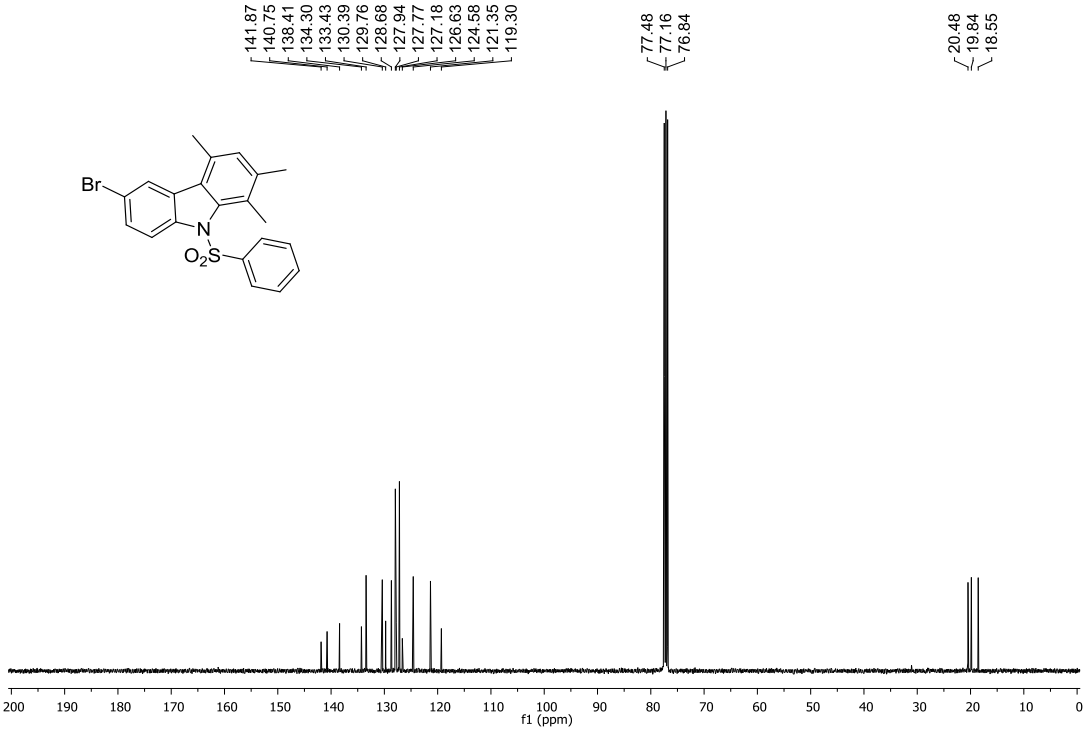


Figure 3B.8 ^{13}C NMR spectrum of 6-bromo-1,2,4-trimethyl-9-(phenylsulfonyl)carbazole **(3a)**

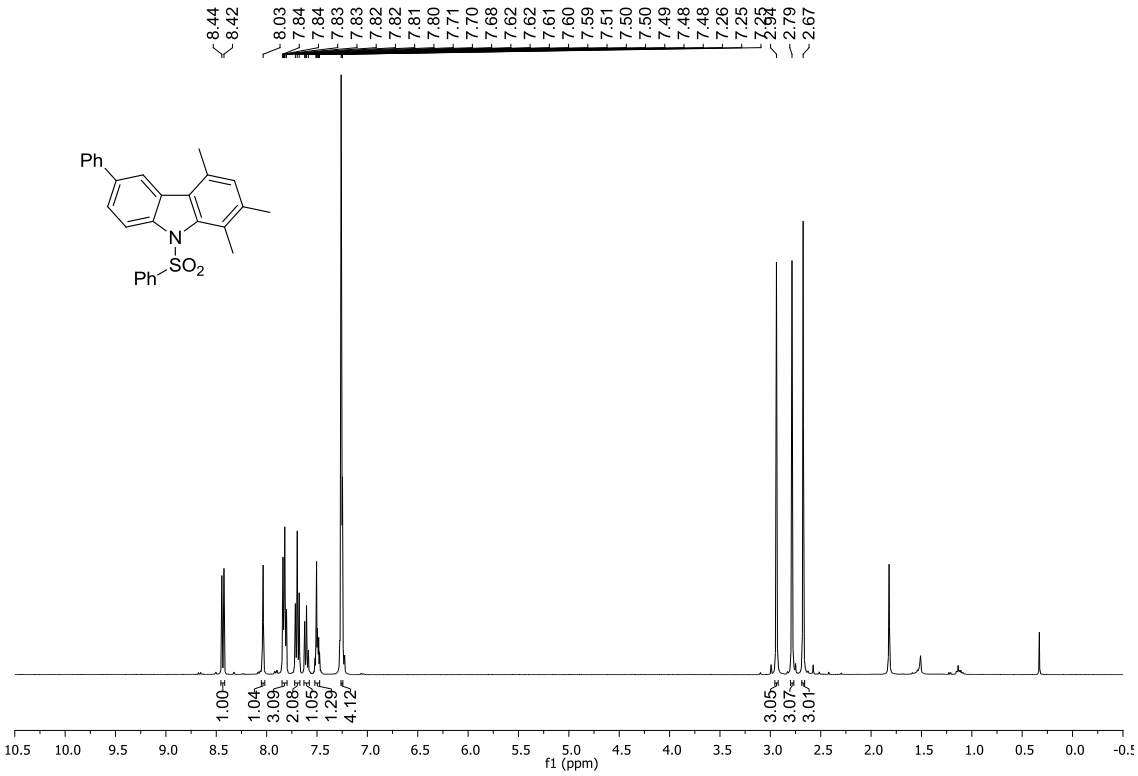


Figure 3B.9 ^{1}H NMR spectrum of 1,2,4-trimethyl-6-phenyl-9-(phenylsulfonyl)carbazole **(3b)**

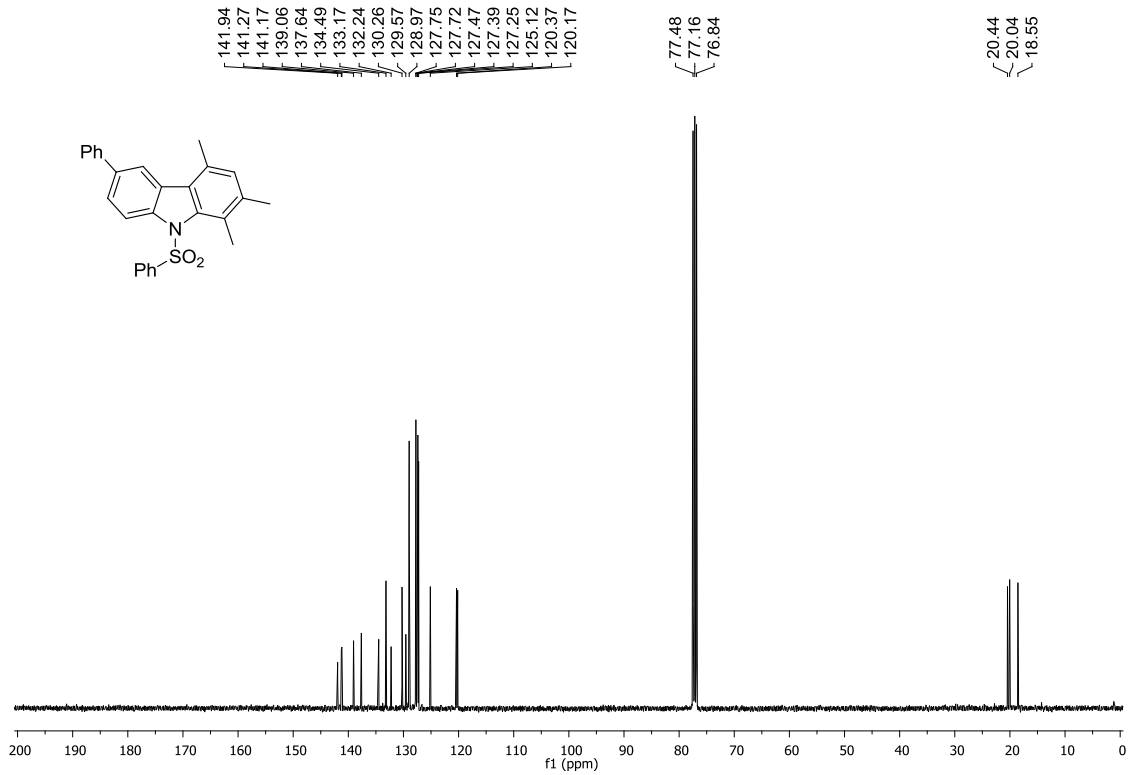


Figure 3B.10 ^{13}C NMR spectrum of 1,2,4-trimethyl-6-phenyl-9-(phenylsulfonyl)carbazole **(3b)**

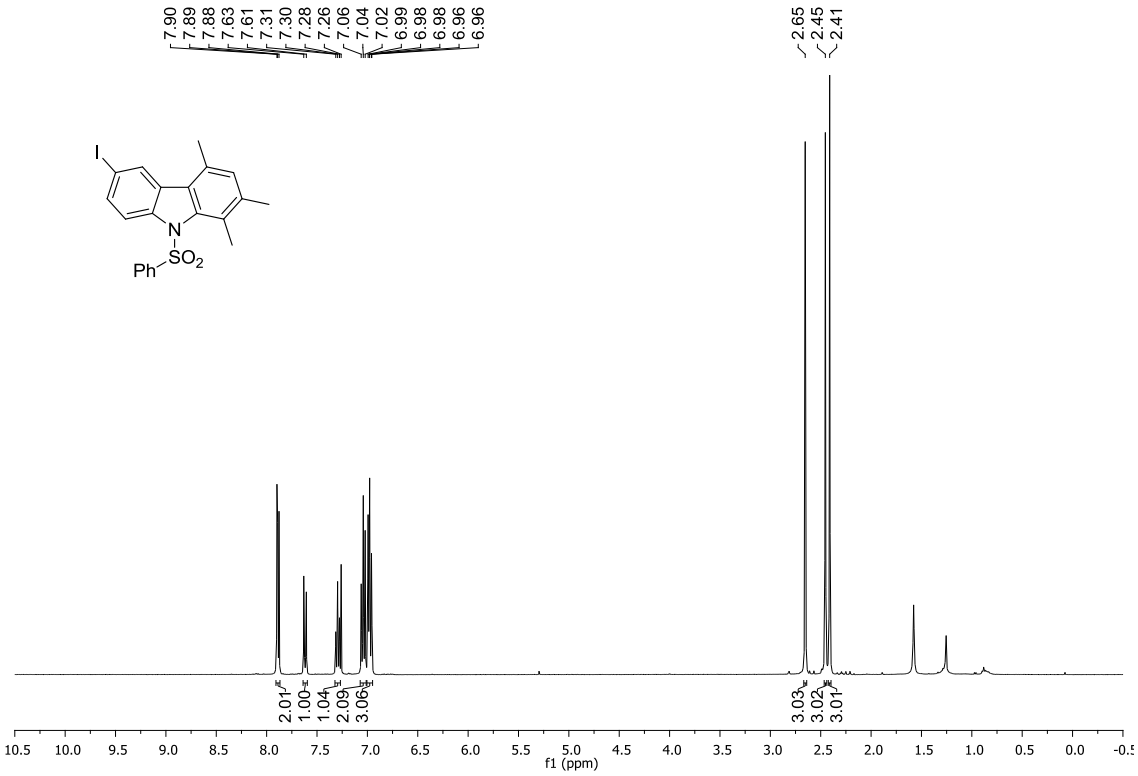


Figure 3B.11 ^{1}H NMR spectrum of 6-iodo-1,2,4-trimethyl-9-(phenylsulfonyl)carbazole **(3e)**

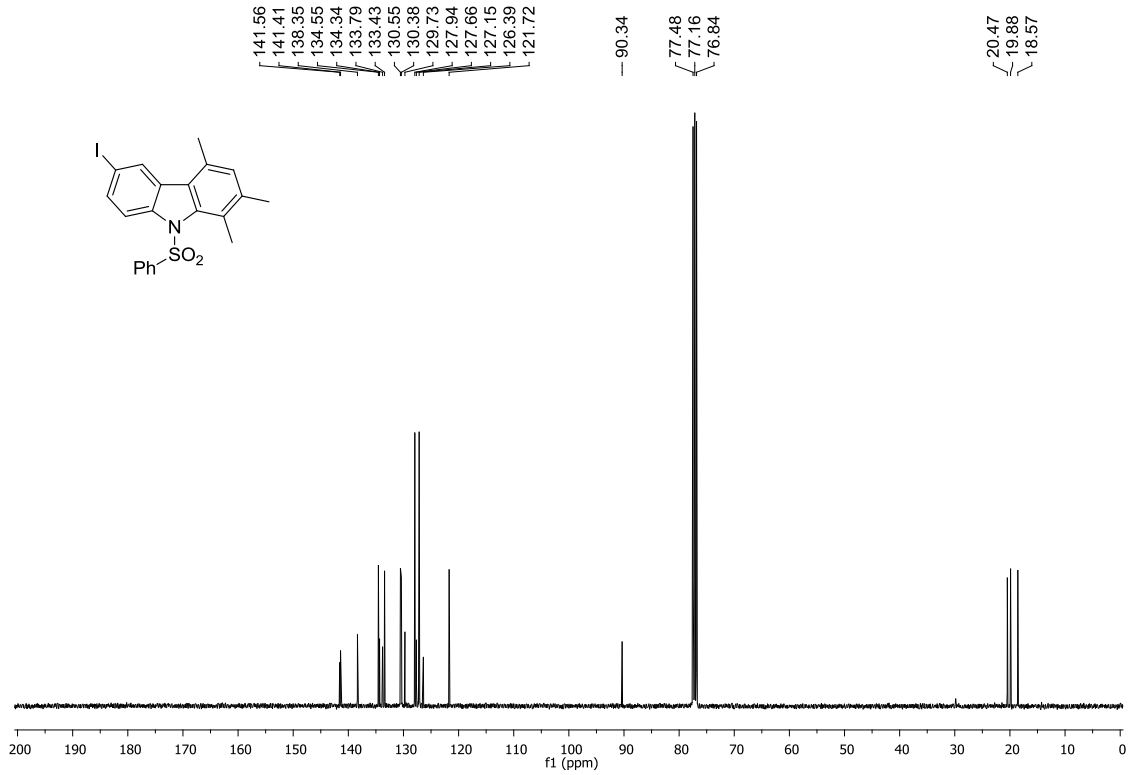


Figure 3B.12 ^{13}C NMR spectrum of 6-iodo-1,2,4-trimethyl-9-(phenylsulfonyl)carbazole **(3e)**

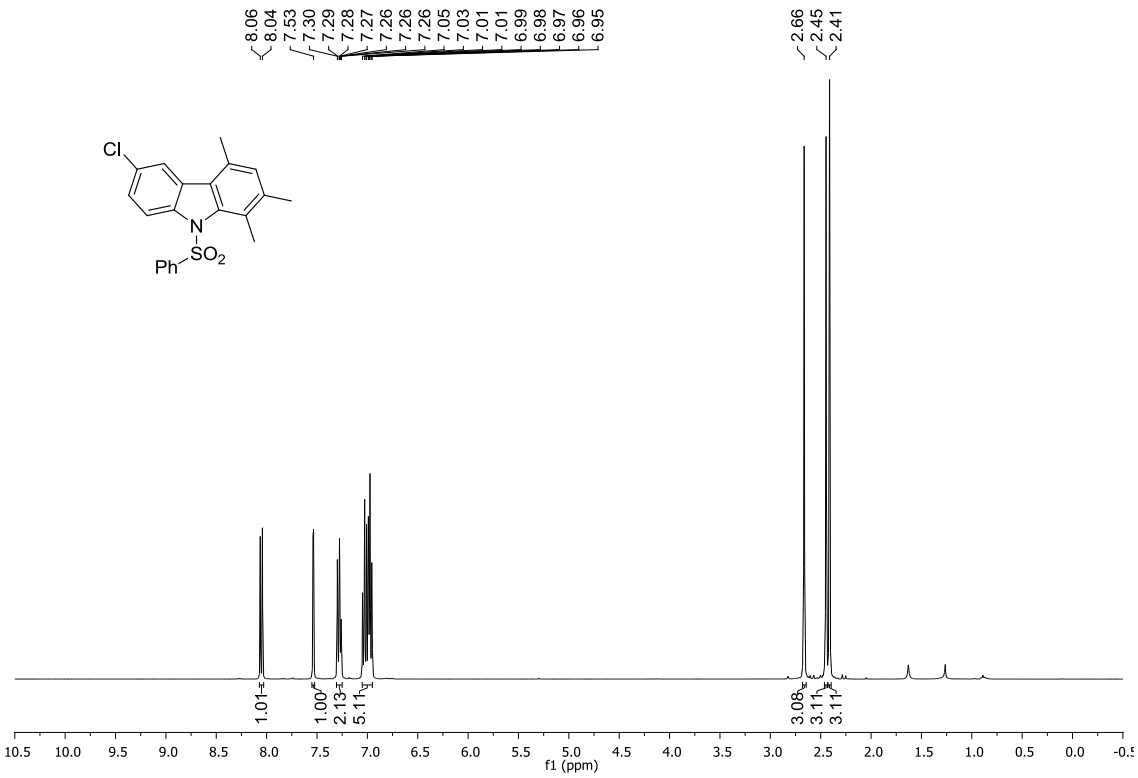


Figure 3B.13 ^{1}H NMR spectrum of 6-chloro-1,2,4-trimethyl-9-(phenylsulfonyl)carbazole **(3f)**

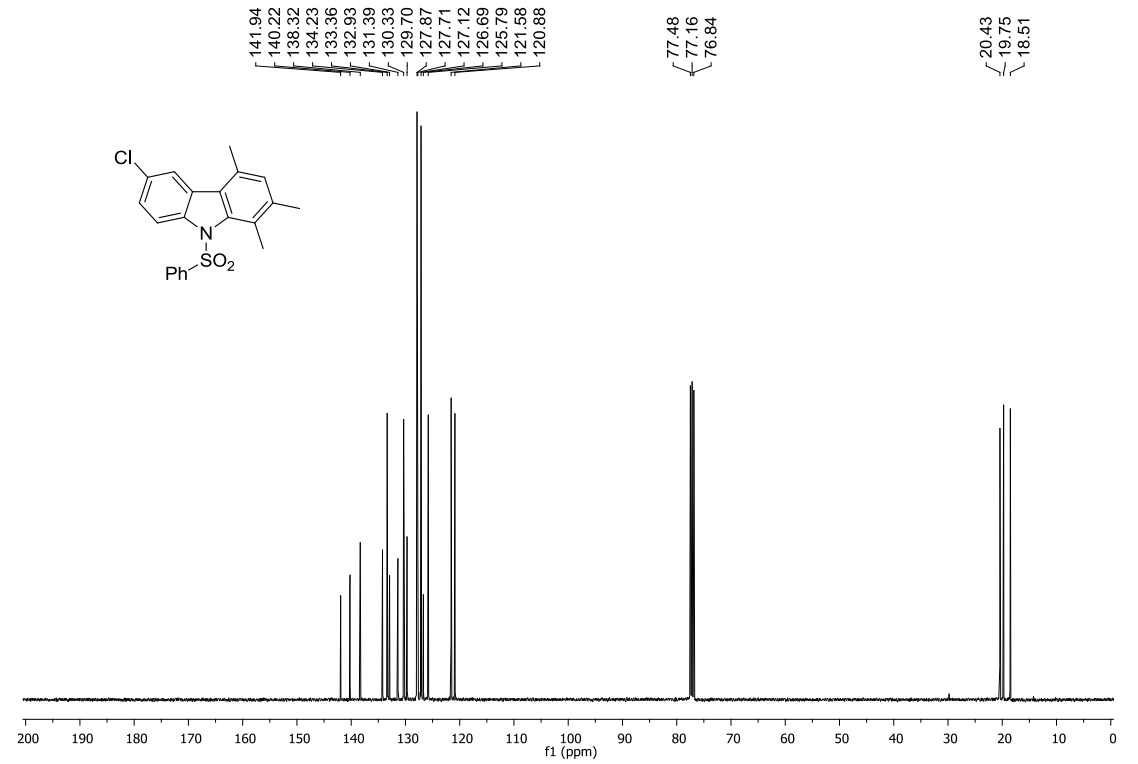


Figure 3B.14 ^{13}C NMR spectrum of 6-chloro-1,2,4-trimethyl-9-(phenylsulfonyl)carbazole **(3f)**

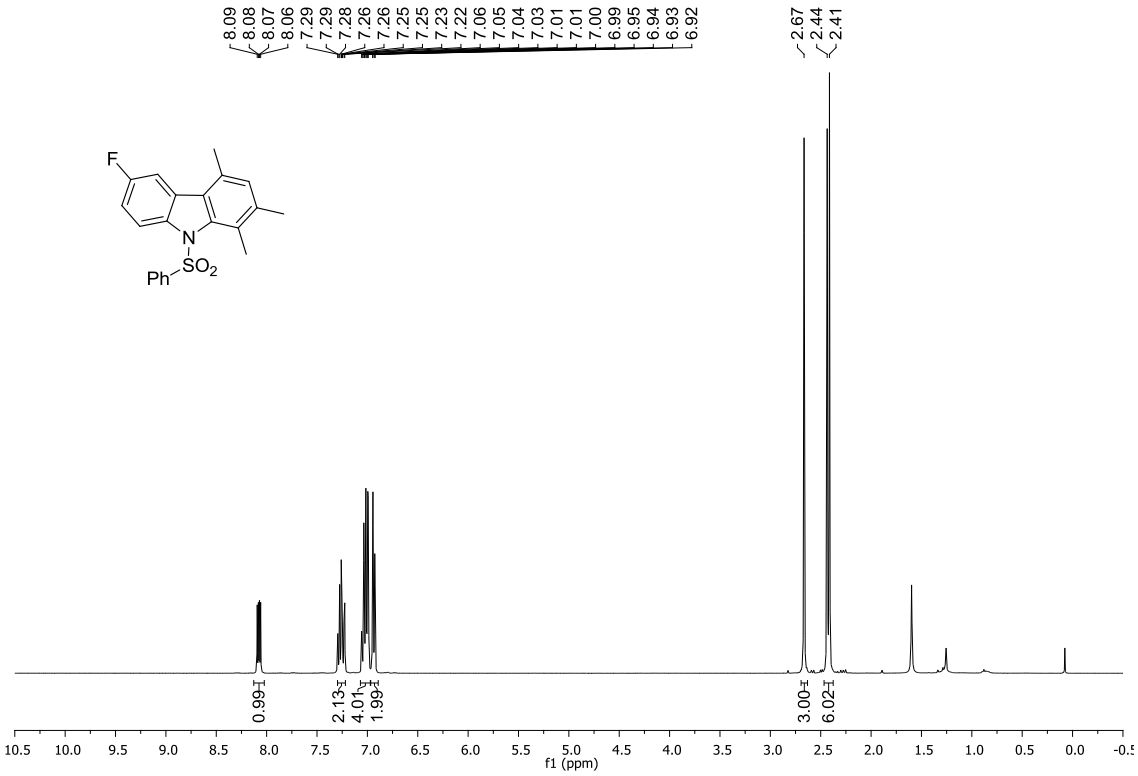


Figure 3B.15 ^{1}H NMR spectrum of 6-fluoro-1,2,4-trimethyl-9-(phenylsulfonyl)carbazole **(3h)**

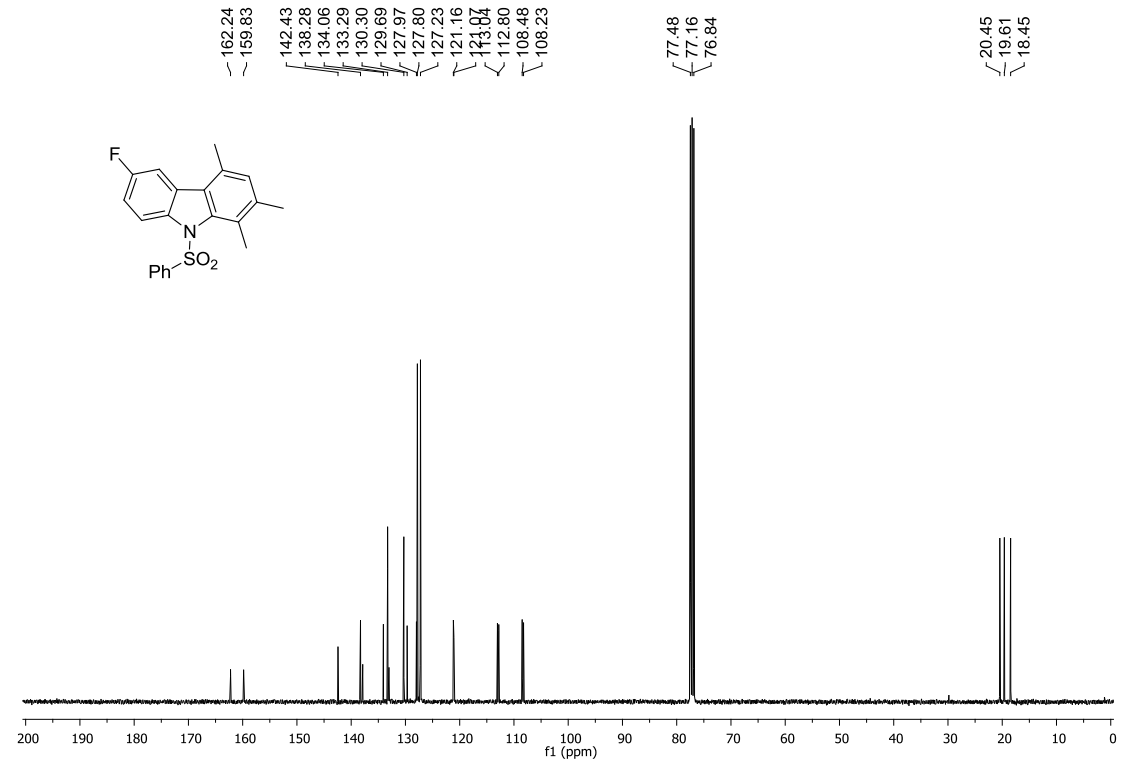


Figure 3B.16 ^{13}C NMR spectrum of 6-fluoro-1,2,4-trimethyl-9-(phenylsulfonyl)carbazole **(3h)**

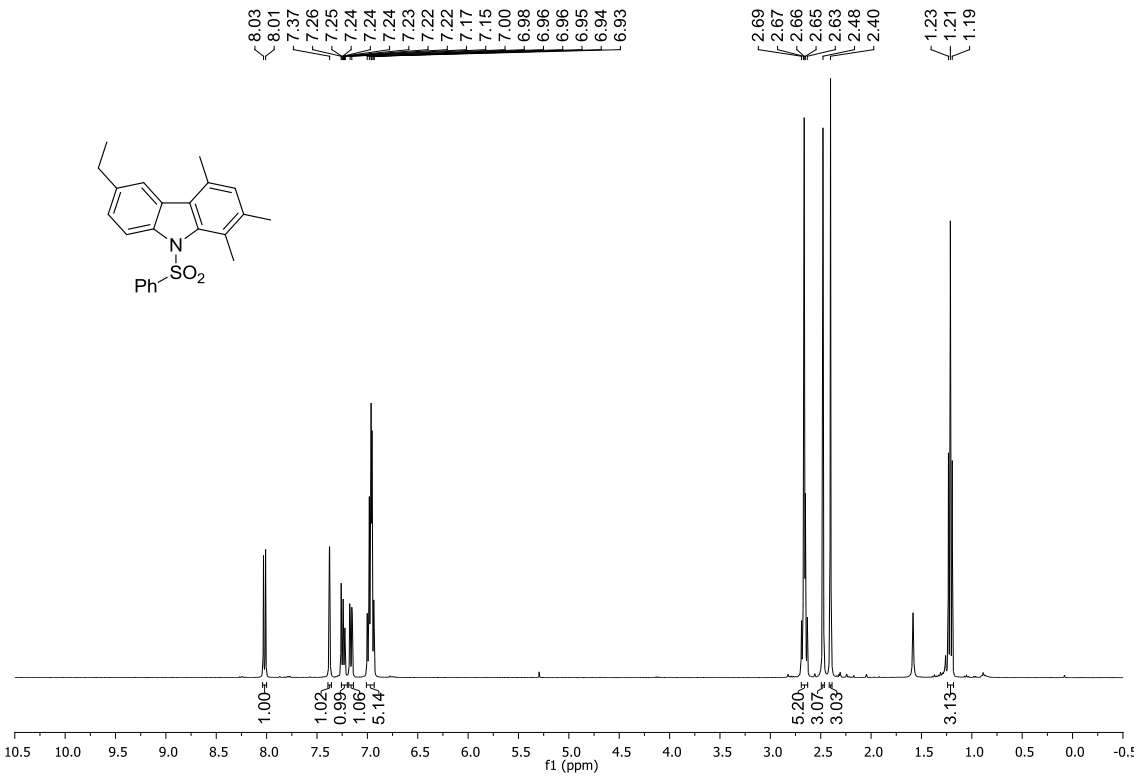


Figure 3B.17 ^{1}H NMR spectrum of 6-ethyl-1,2,4-trimethyl-9-(phenylsulfonyl)carbazole **(3j)**

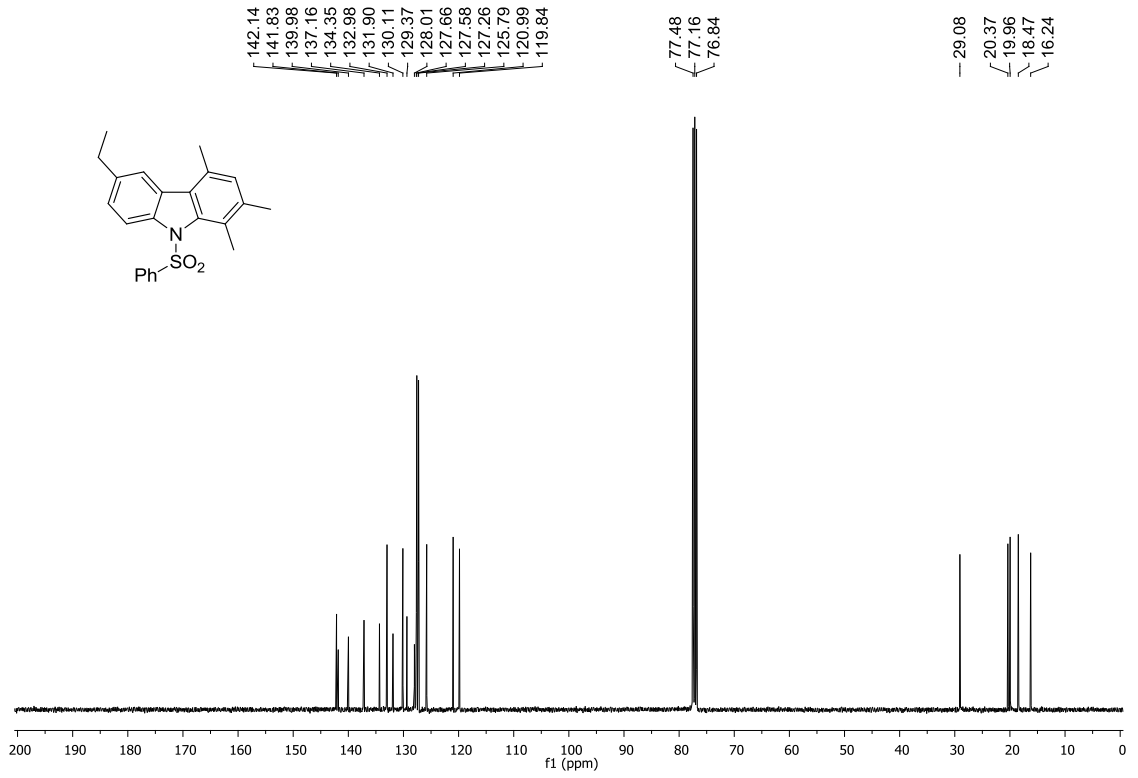


Figure 3B.18 ^{13}C NMR spectrum of 6-ethyl-1,2,4-trimethyl-9-(phenylsulfonyl)carbazole **(3j)**

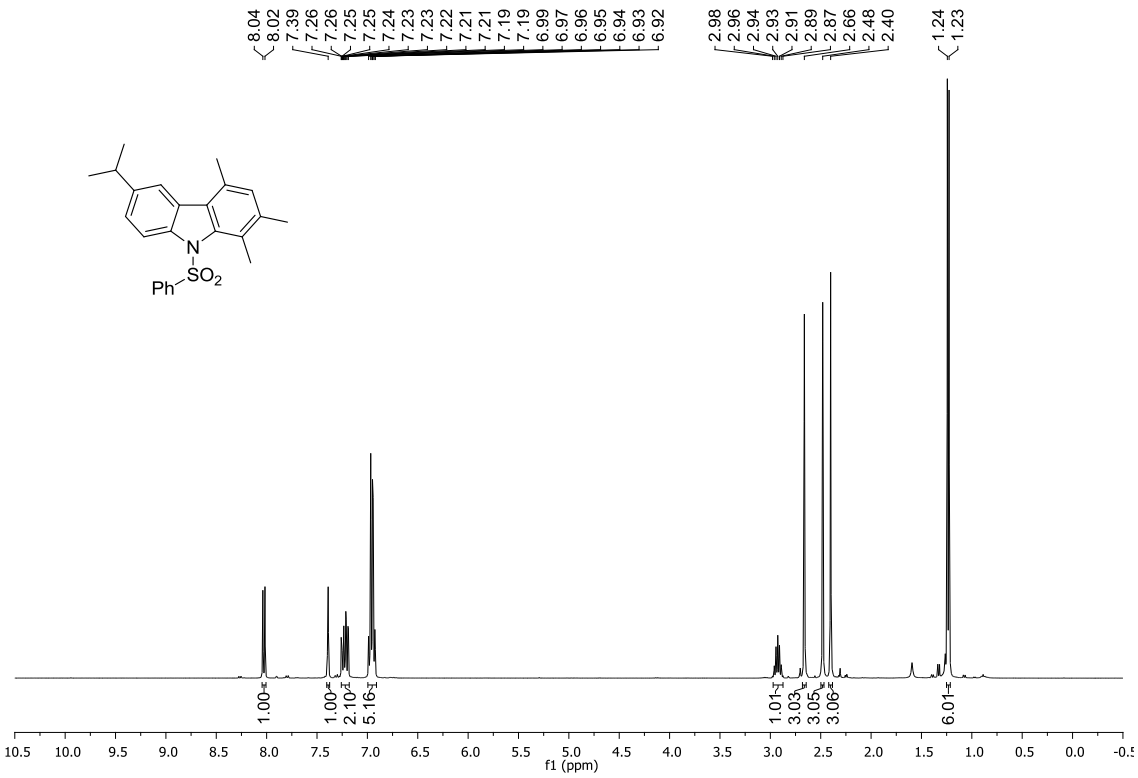


Figure 3B.19 ^{1}H NMR spectrum of 6-isopropyl-1,2,4-trimethyl-9-(phenylsulfonyl)carbazole **(3k)**

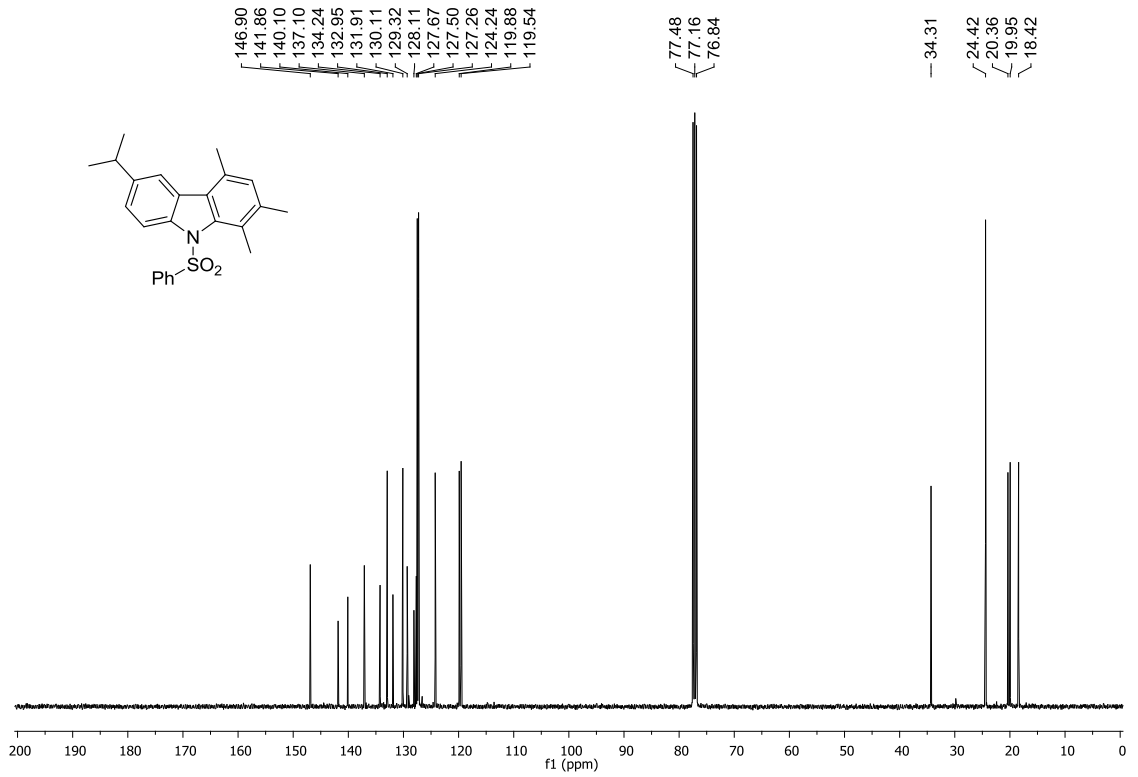


Figure 3B.20 ^{13}C NMR spectrum of 6-isopropyl-1,2,4-trimethyl-9-(phenylsulfonyl)carbazole **(3k)**

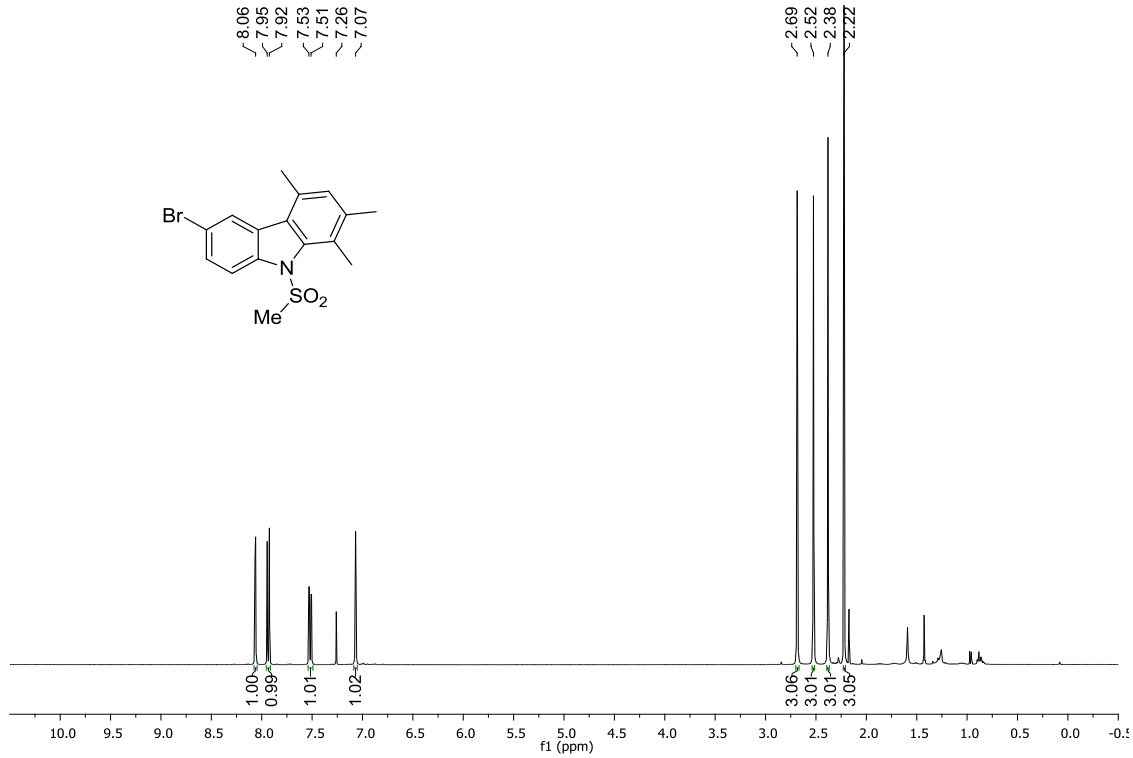


Figure 3B.21 ^{1}H NMR spectrum of 6-bromo-1,2,4-trimethyl-9-(methylsulfonyl)carbazole **(3m)**

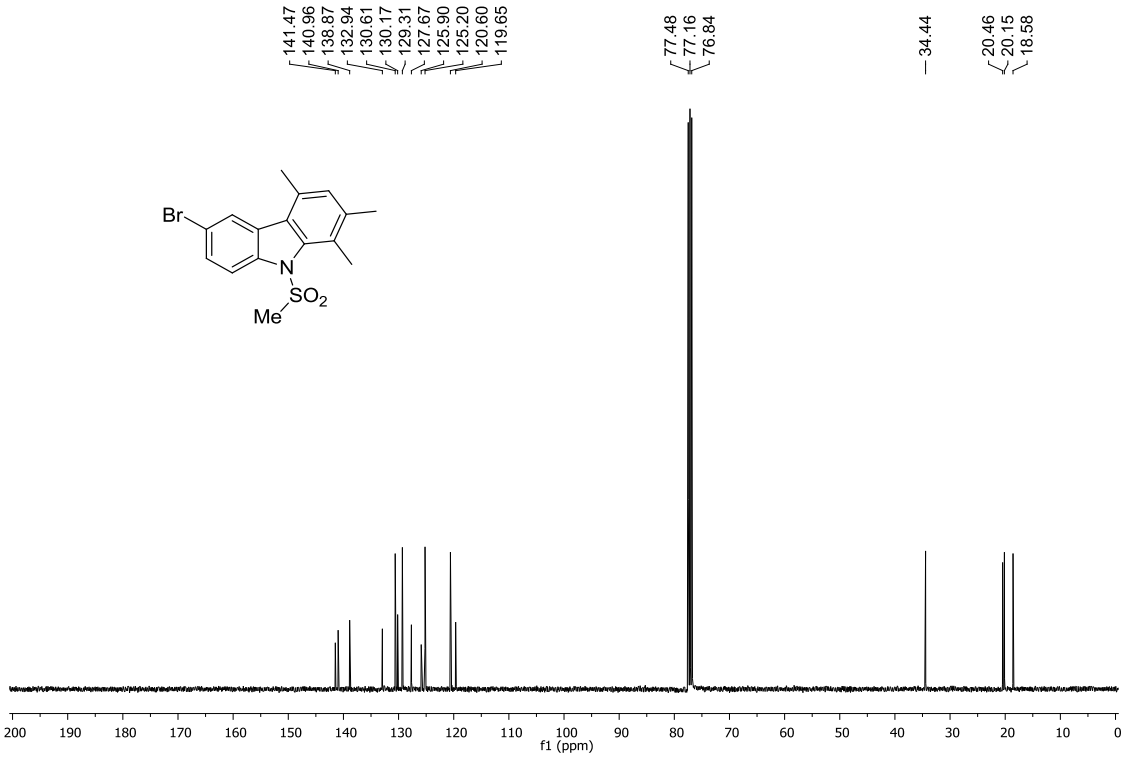


Figure 3B.22 ^{13}C NMR spectrum of 6-bromo-1,2,4-trimethyl-9-(methylsulfonyl)carbazole **(3m)**

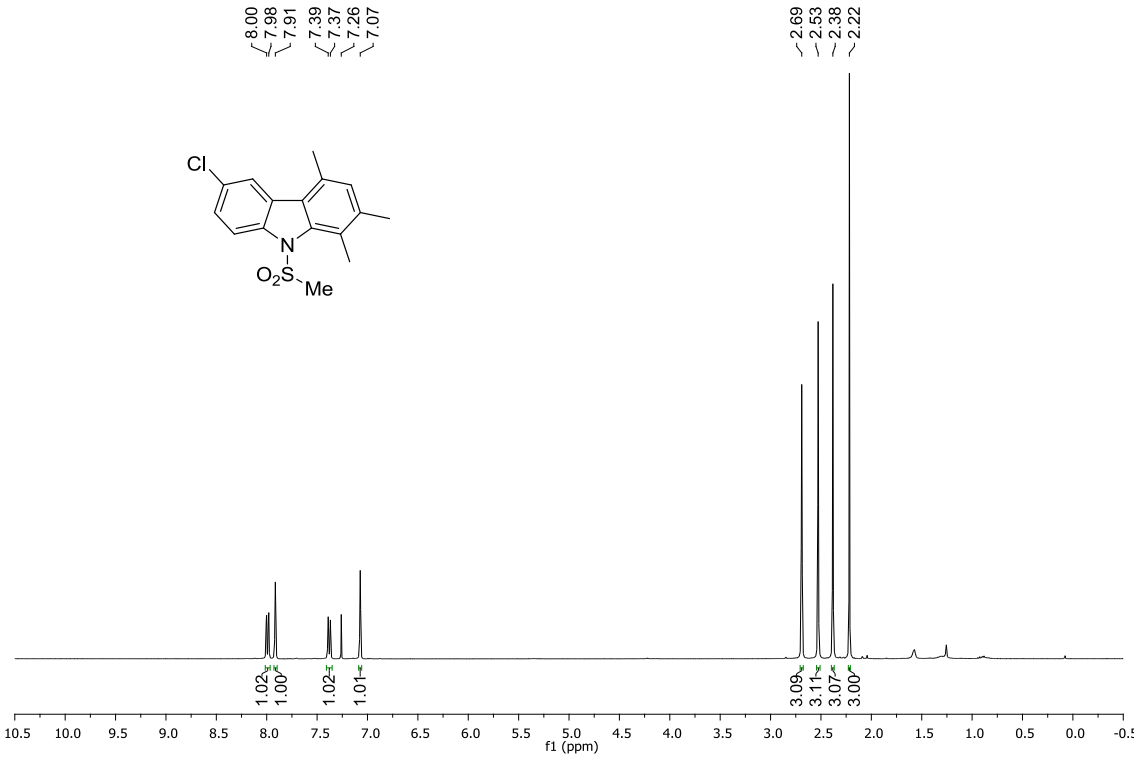


Figure 3B.23 ^{1}H NMR spectrum of 6-chloro-1,2,4-trimethyl-9-(methylsulfonyl)carbazole **(3n)**

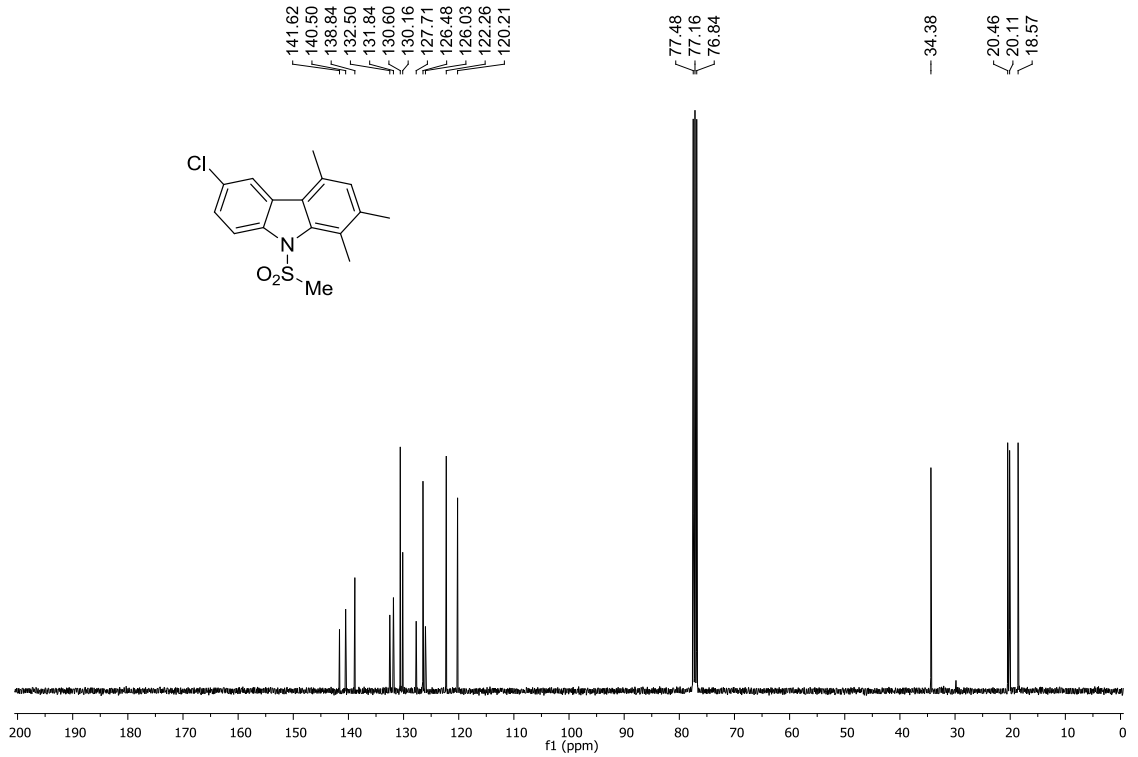


Figure 3B.24 ^{13}C NMR spectrum of 6-chloro-1,2,4-trimethyl-9-(methylsulfonyl)carbazole **(3n)**

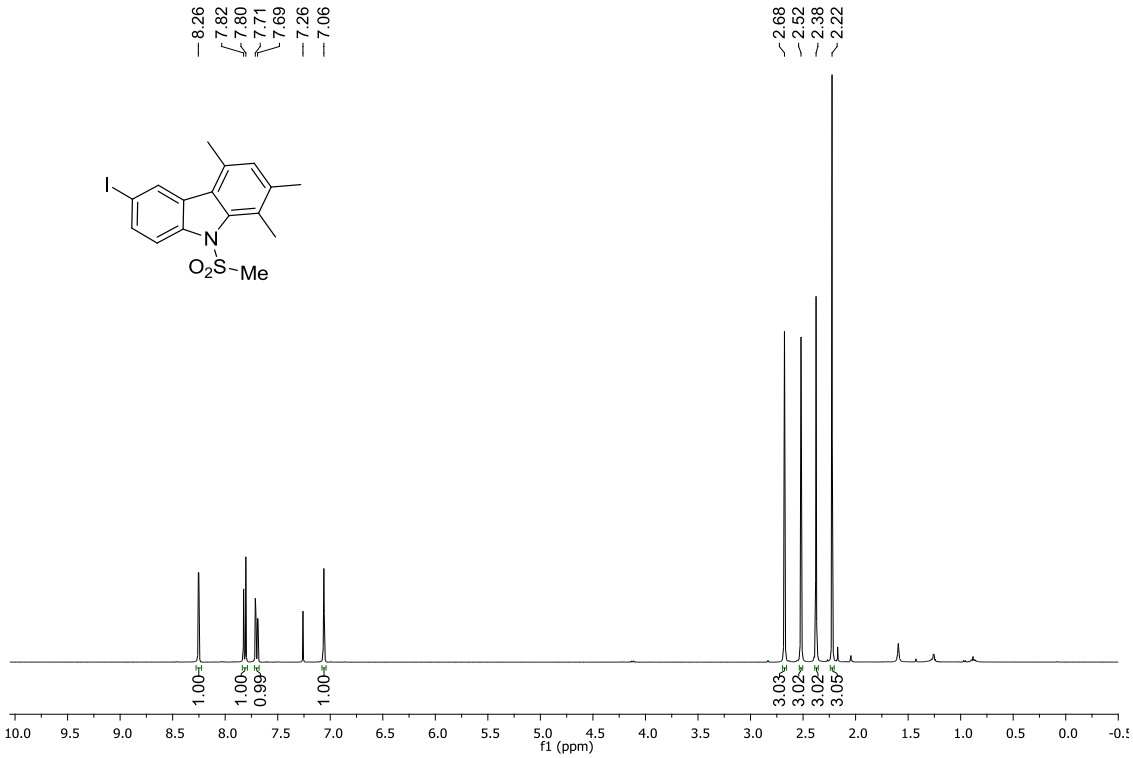


Figure 3B.25 ^{1}H NMR spectrum of 6-iodo-1,2,4-trimethyl-9-(methylsulfonyl)carbazole **(3o)**

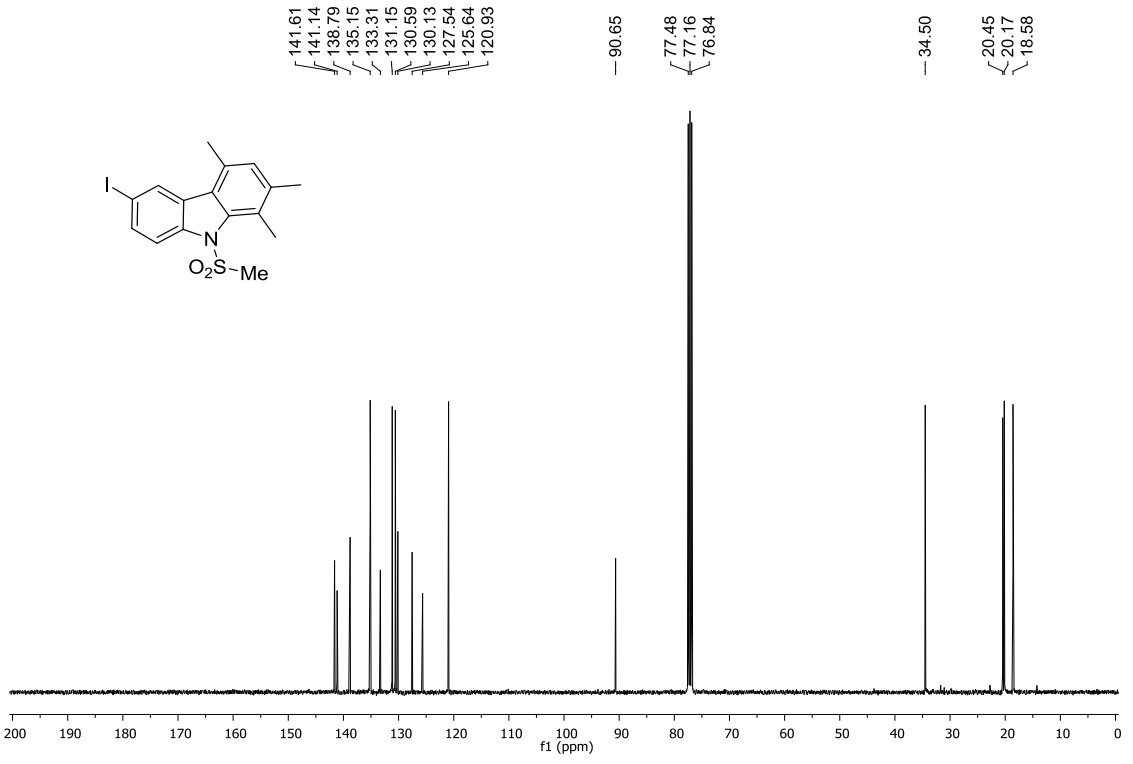


Figure 3B.26 ^{13}C NMR spectrum of 6-iodo-1,2,4-trimethyl-9-(methylsulfonyl)carbazole **(3o)**

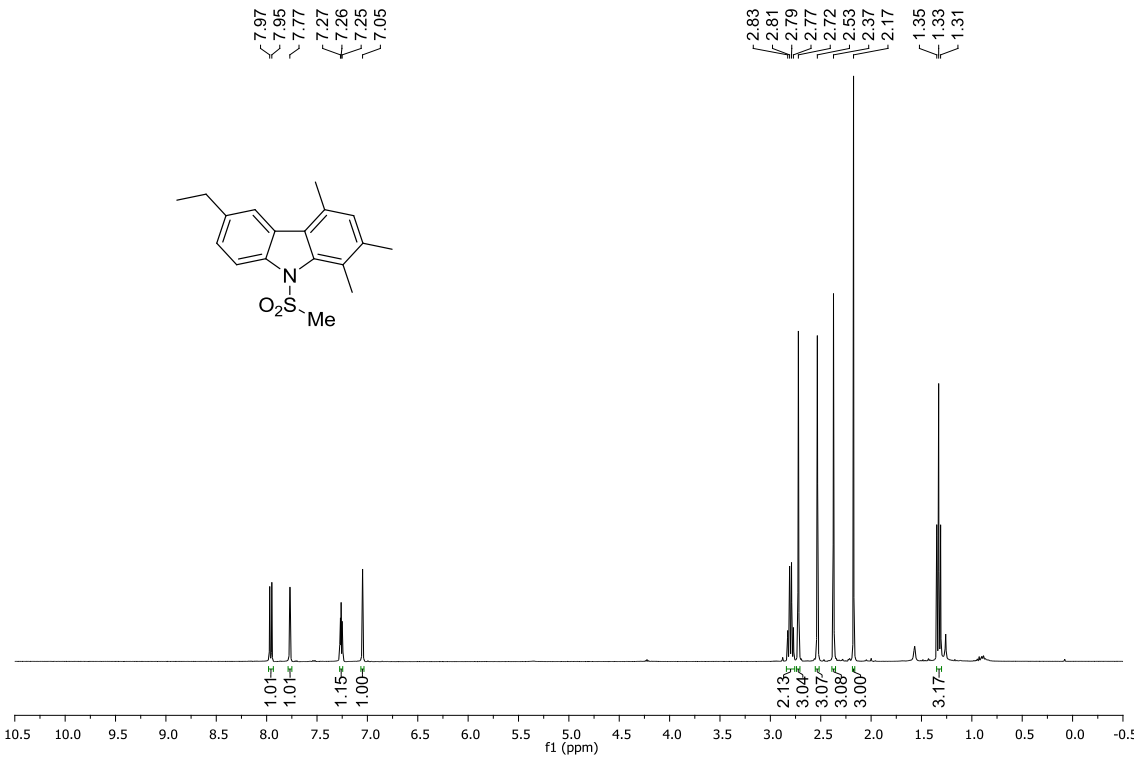


Figure 3B.27 ^{1}H NMR spectrum of 6-ethyl-1,2,4-trimethyl-9-(methylsulfonyl)carbazole **(3t)**

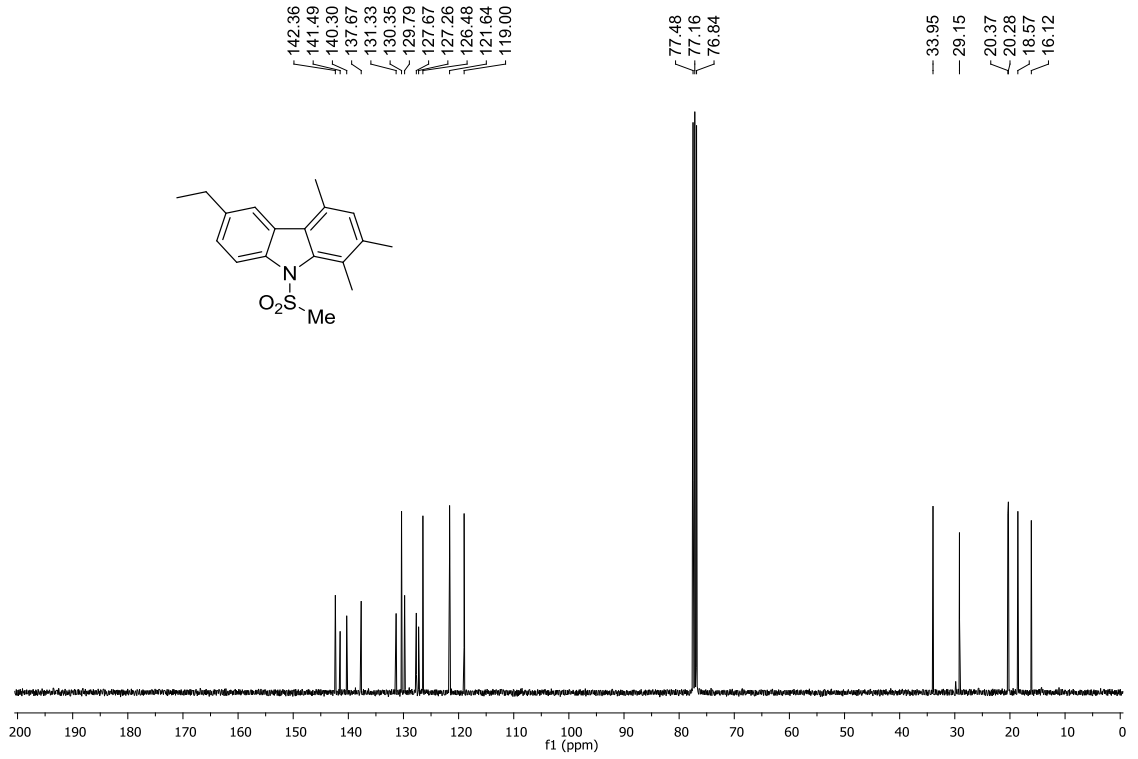


Figure 3B.28 ^{13}C NMR spectrum of 6-ethyl-1,2,4-trimethyl-9-(methylsulfonyl)carbazole **(3t)**

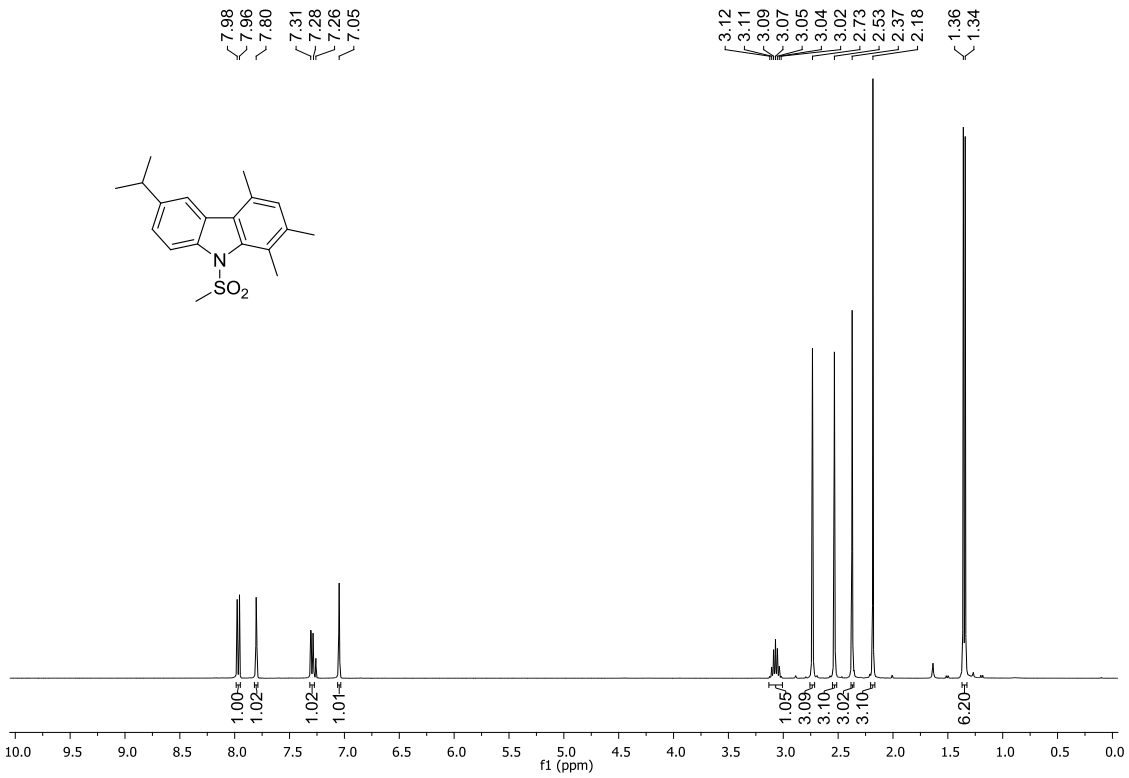


Figure 3B.29 ^{1}H NMR spectrum of 6-isopropyl-1,2,4-trimethyl-9-(methylsulfonyl)carbazole **(3u)**

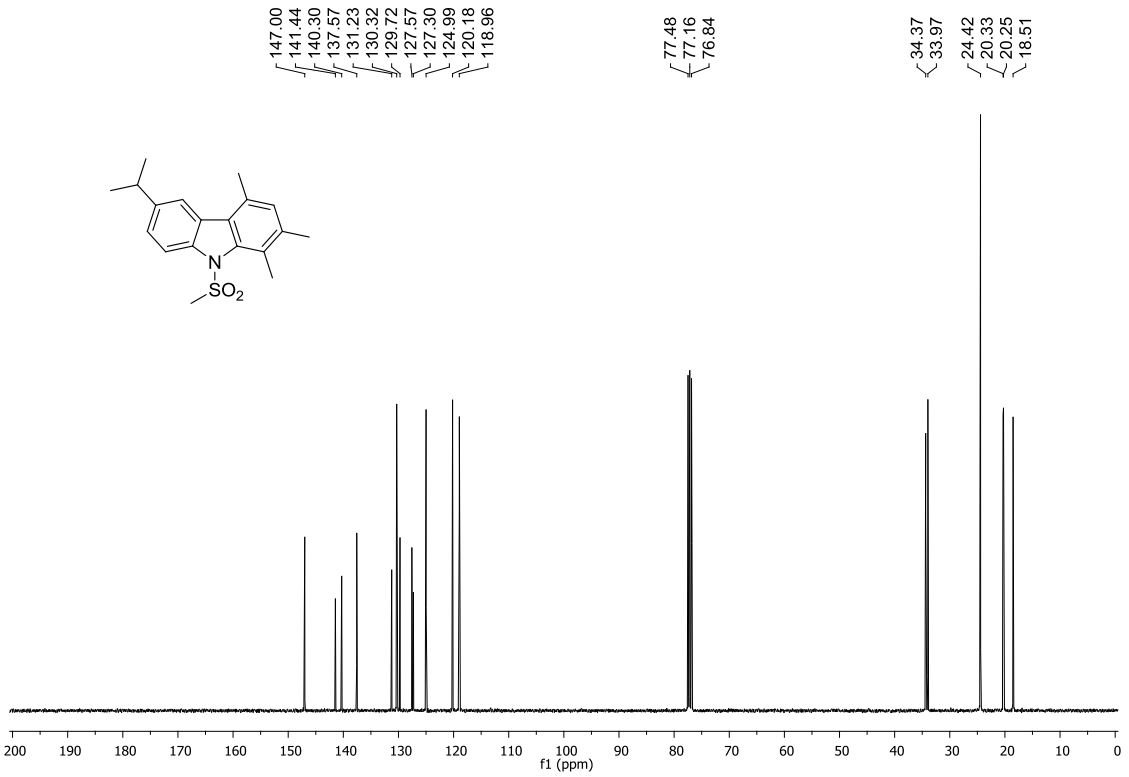


Figure 3B.30 ^{13}C NMR spectrum of 6-isopropyl-1,2,4-trimethyl-9-(methylsulfonyl)carbazole **(3u)**

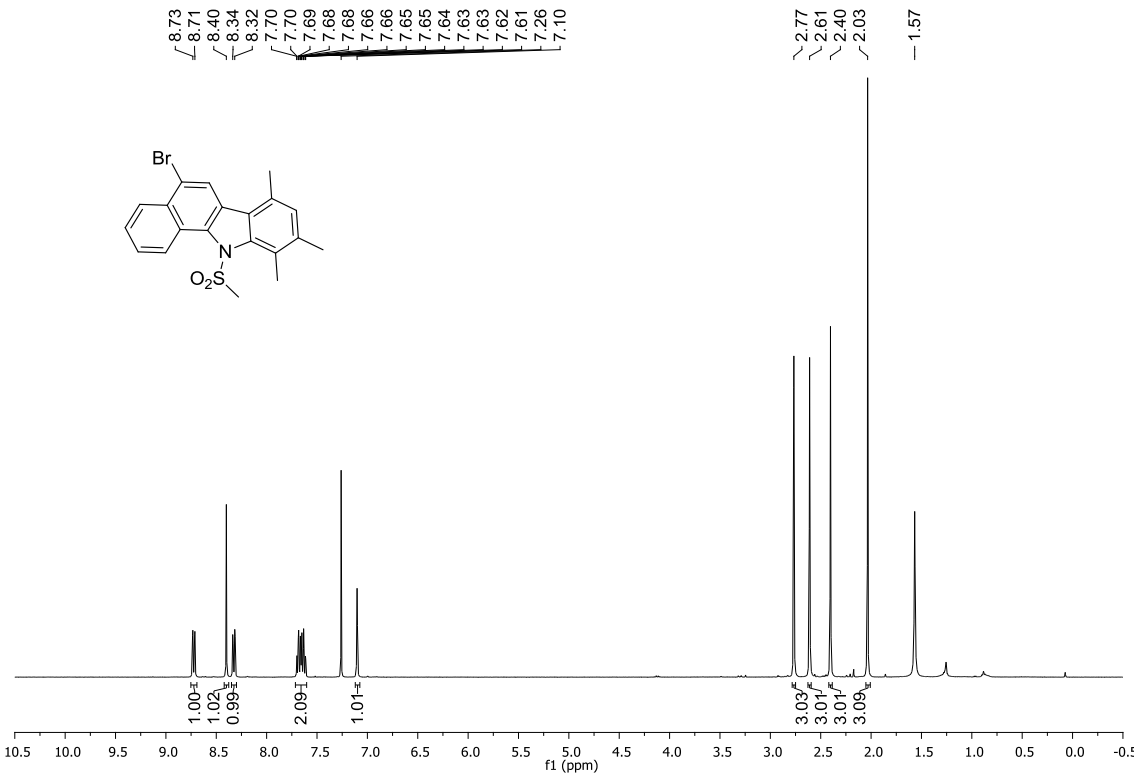


Figure 3B.31 ^{1}H NMR spectrum of 5-bromo-7,9,10-trimethyl-11-(methylsulfonyl)benzo[a]carbazole **(3x)**

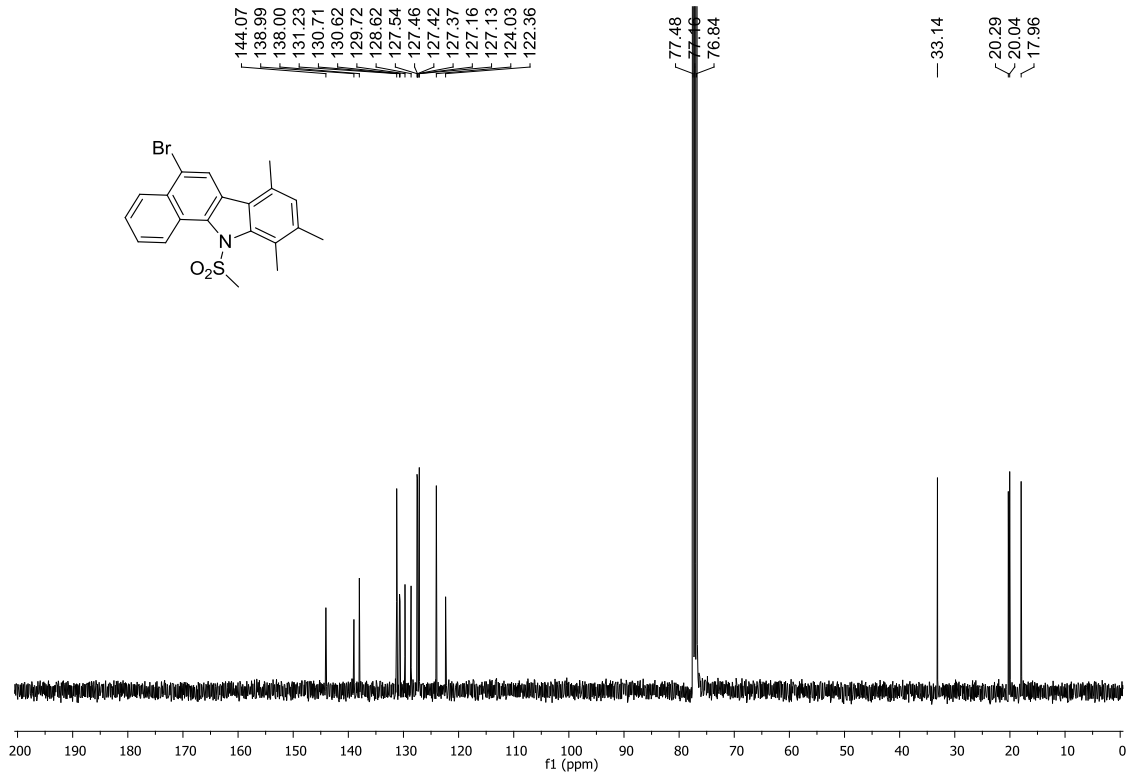


Figure 3B.32 ^{13}C NMR spectrum of 5-bromo-7,9,10-trimethyl-11-(methylsulfonyl)benzo[a]carbazole **(3x)**

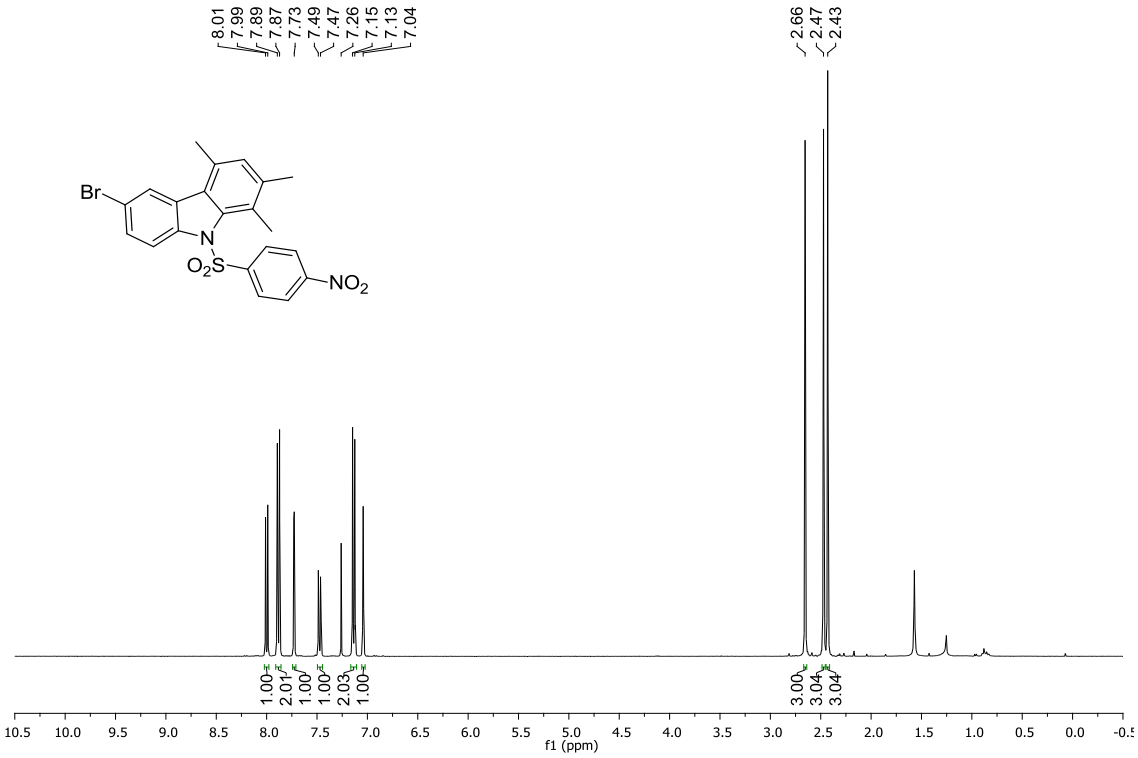


Figure 3B.33 ^{1}H NMR spectrum of 6-bromo-1,2,4-trimethyl-9-((4-nitrophenyl)sulfonyl)carbazole **(3z)**

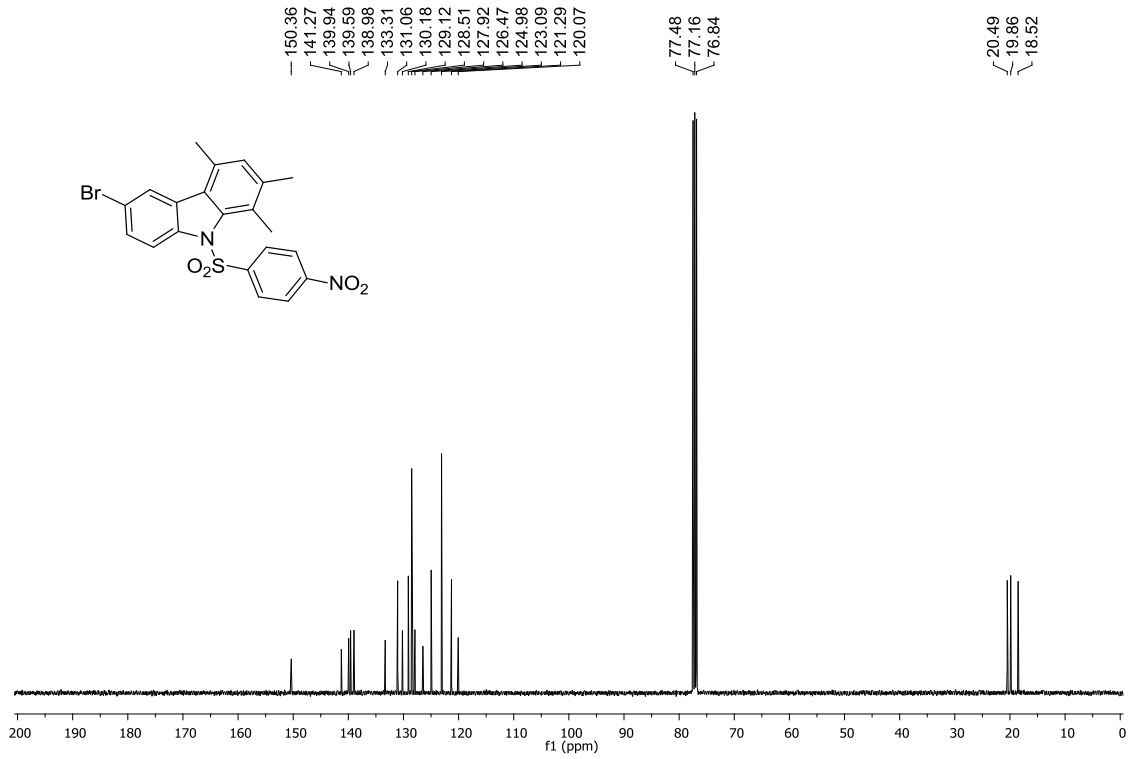


Figure 3B.34 ^{13}C NMR spectrum of 6-bromo-1,2,4-trimethyl-9-((4-nitrophenyl)sulfonyl)carbazole **(3z)**

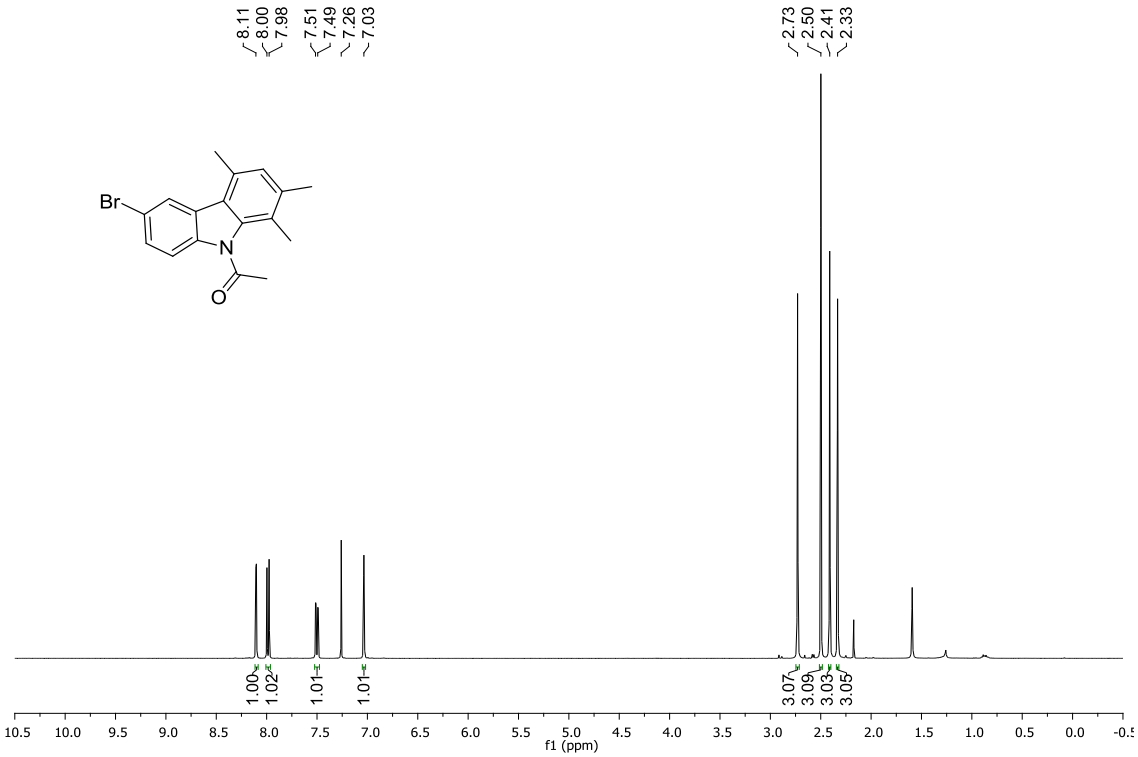


Figure 3B.35 ^{1}H NMR spectrum of 1-(6-bromo-1,2,4-trimethylcarbazol-9-yl)ethanone **(3aa)**

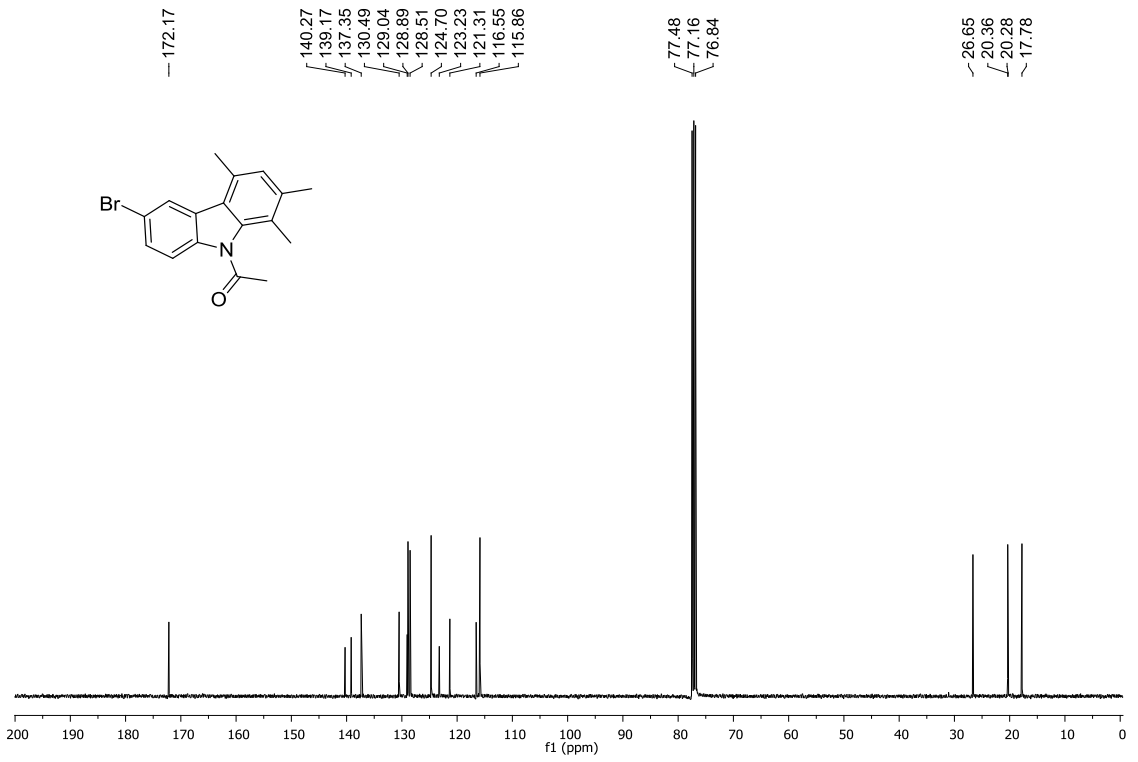


Figure 3B.36 ^{13}C NMR spectrum of 1-(6-bromo-1,2,4-trimethylcarbazol-9-yl)ethanone **(3aa)**

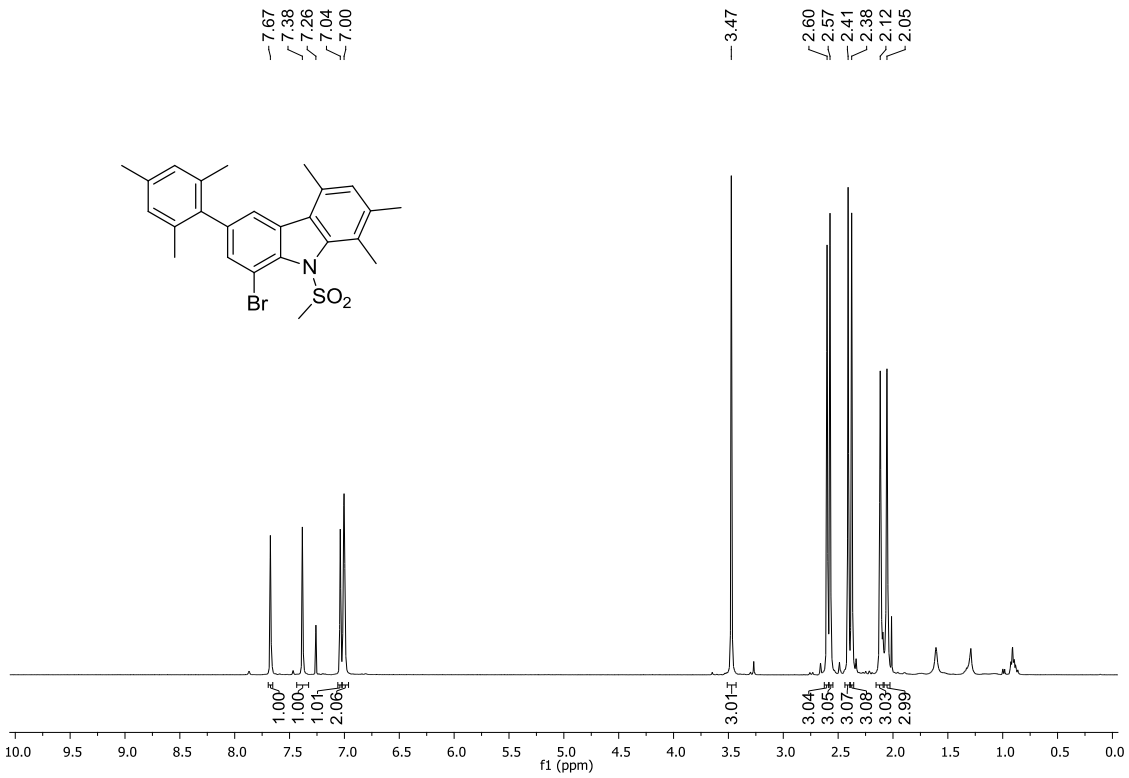


Figure 3B.37 ^{1}H NMR spectrum of 8-bromo-6-mesityl-1,2,4-trimethyl-9-(methylsulfonyl)carbazole **(4c)**

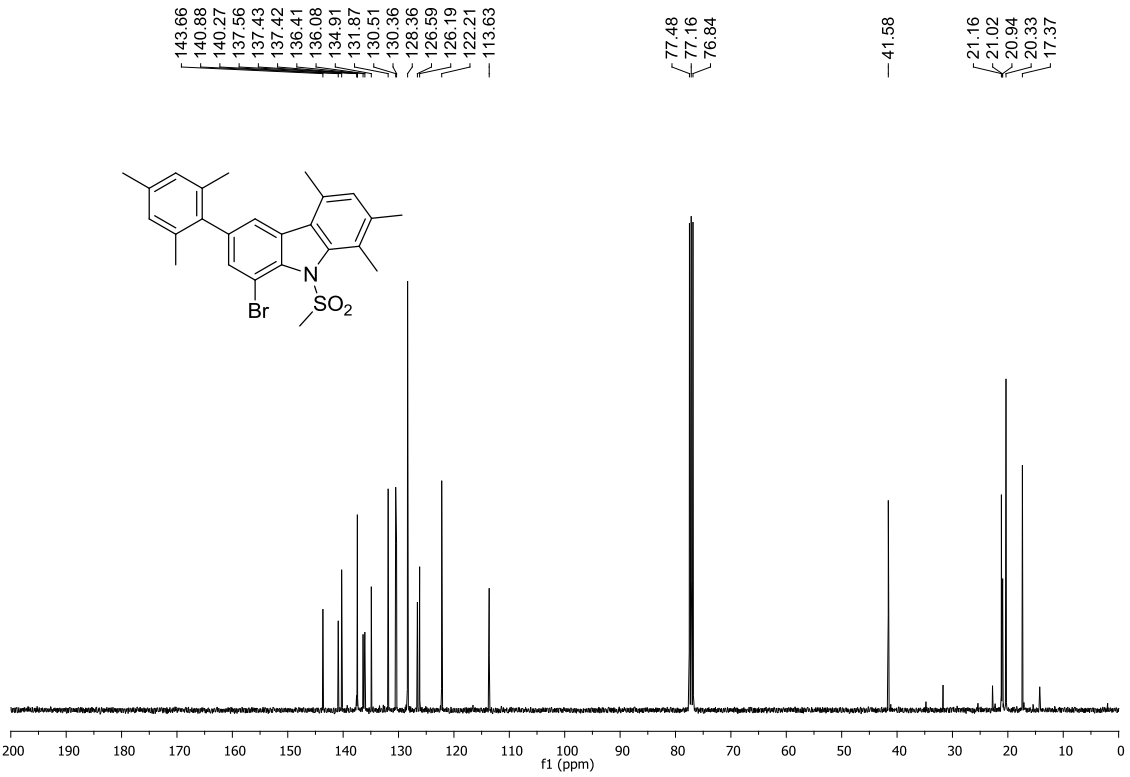


Figure 3B.38 ^{13}C NMR spectrum of 8-bromo-6-mesityl-1,2,4-trimethyl-9-(methylsulfonyl)carbazole **(4c)**

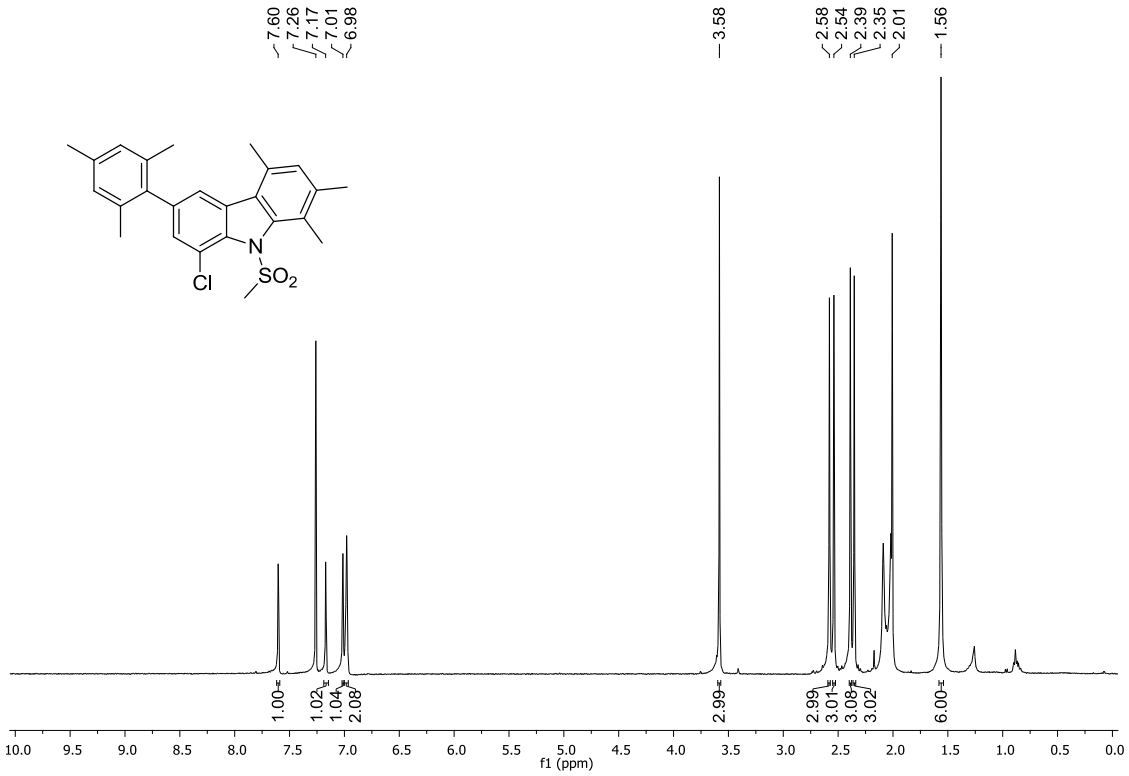


Figure 3B.39 ^{1}H NMR spectrum of 8-chloro-6-mesityl-1,2,4-trimethyl-9-(methylsulfonyl)carbazole **(4d)**

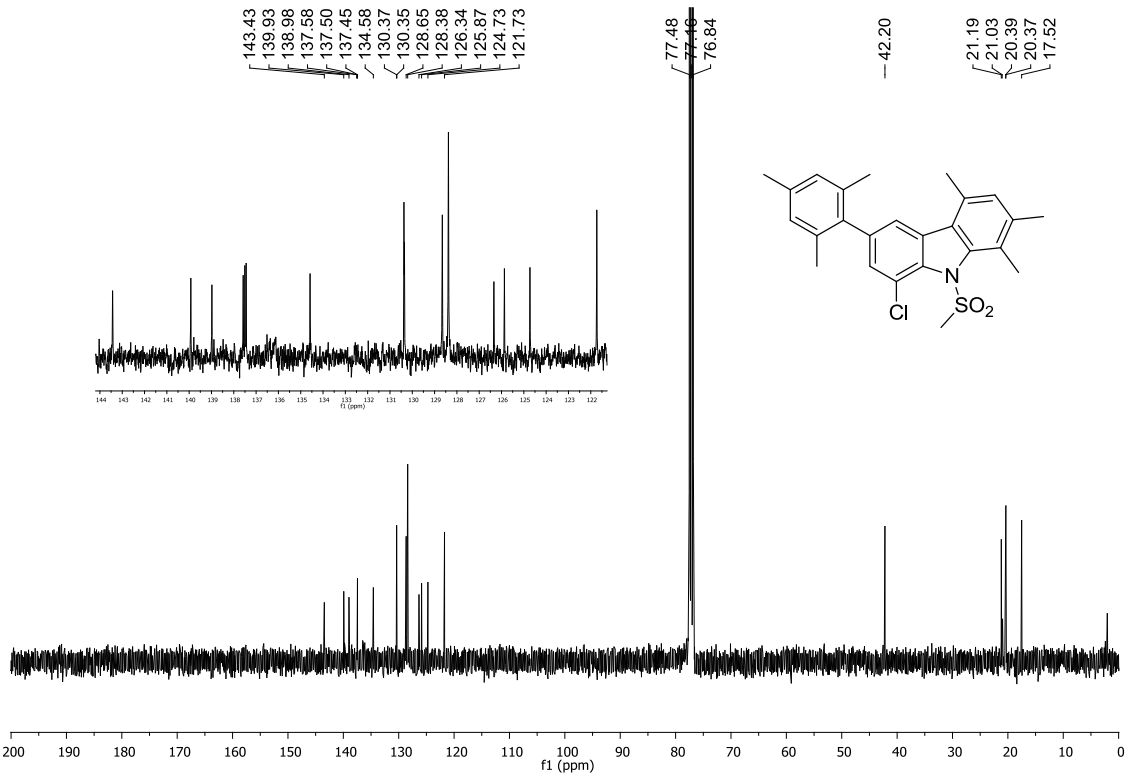


Figure 3B.40 ^{13}C NMR spectrum of 8-chloro-6-mesityl-1,2,4-trimethyl-9-(methylsulfonyl)carbazole **(4d)**

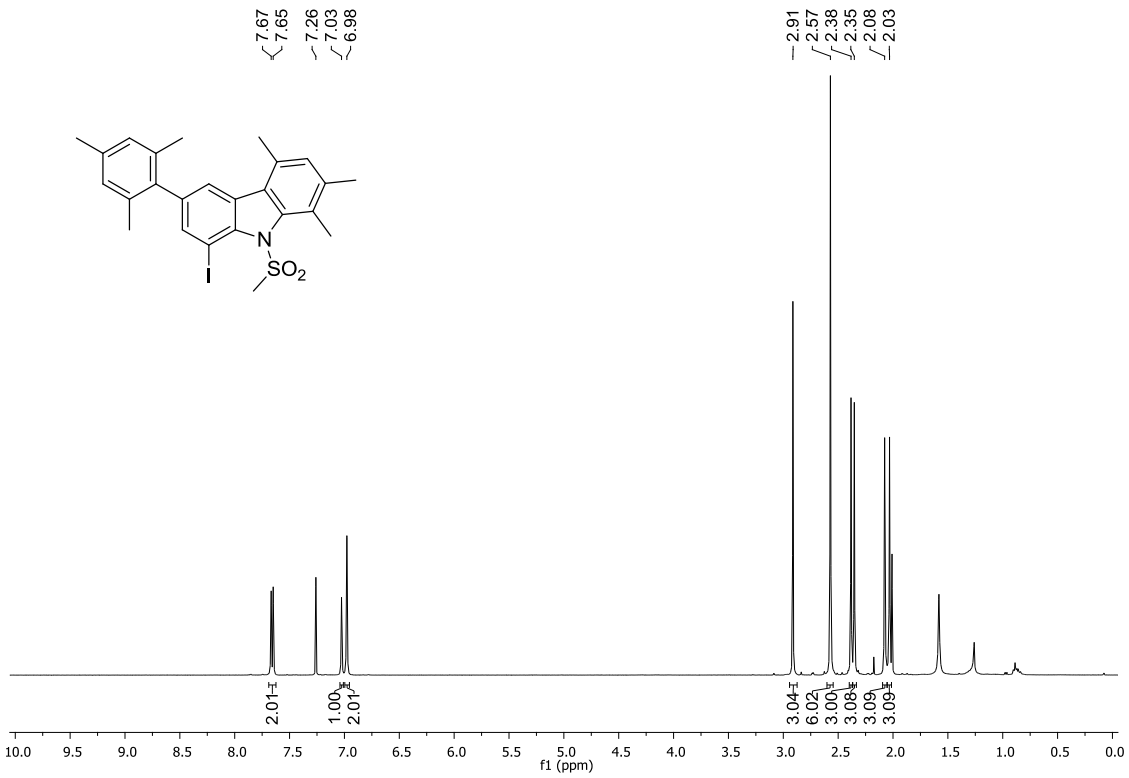


Figure 3B.41 ^{1}H NMR spectrum of 8-iodo-6-mesityl-1,2,4-trimethyl-9-(methylsulfonyl)carbazole **(4f)**

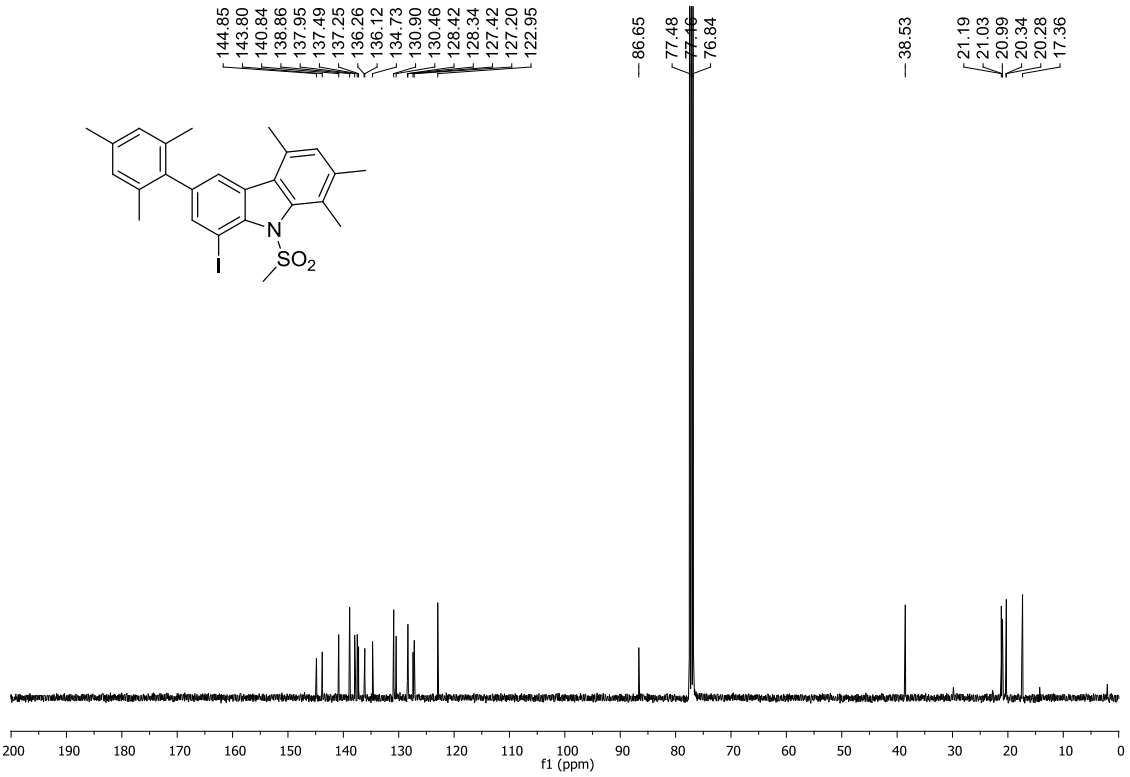


Figure 3B.42 ^{13}C NMR spectrum of 8-iodo-6-mesityl-1,2,4-trimethyl-9-(methylsulfonyl)carbazole **(4f)**

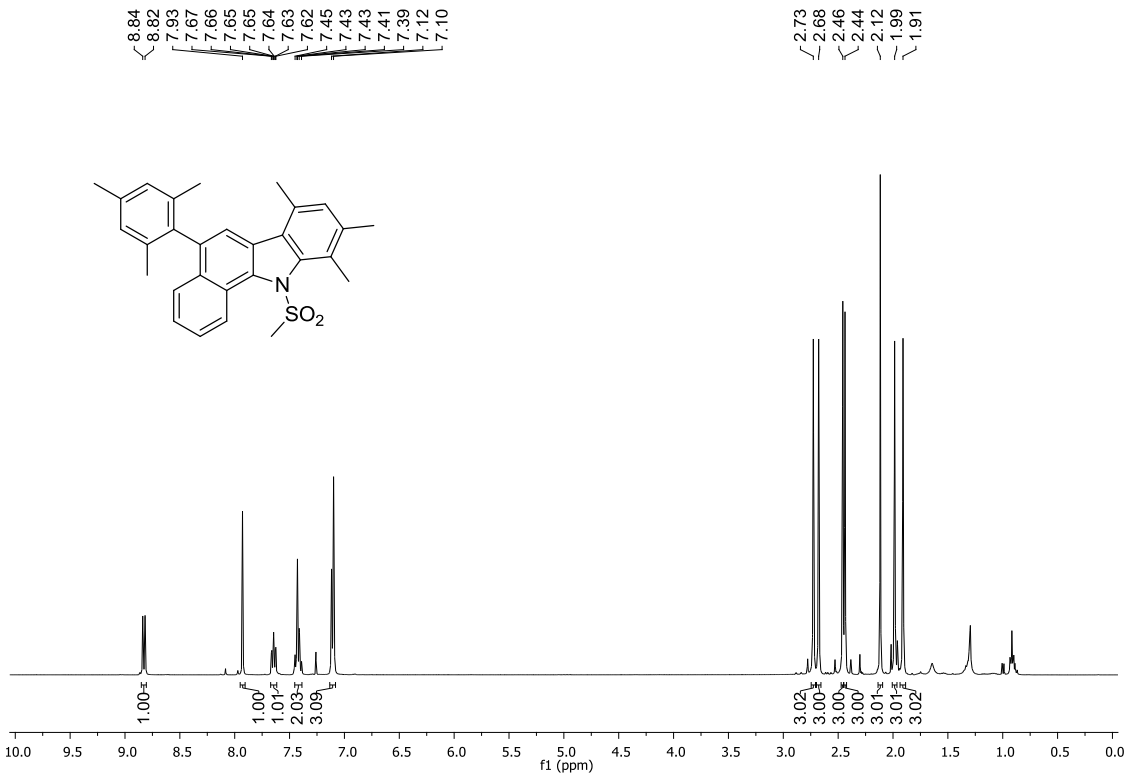


Figure 3B.43 ^{1}H NMR spectrum of 5-mesityl-7,9,10-trimethyl-11-(methylsulfonyl)benzo[a]carbazole **(4g)**

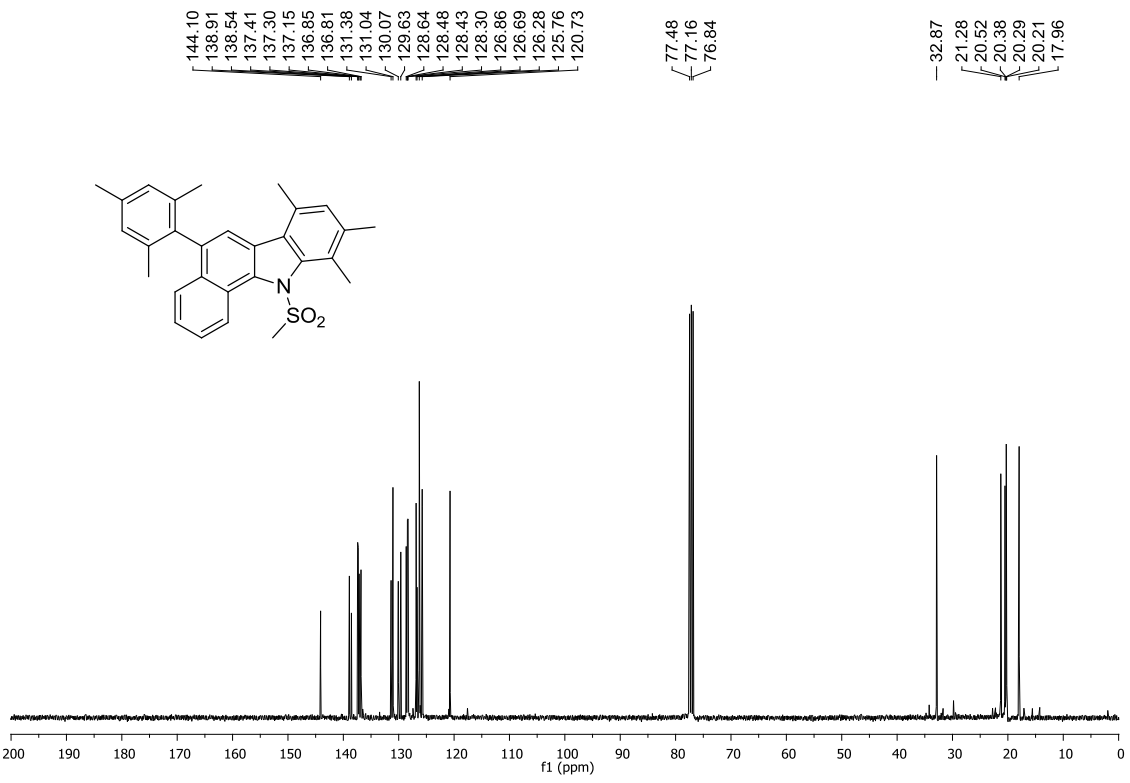


Figure 3B.44 ^{13}C NMR spectrum of 5-mesityl-7,9,10-trimethyl-11-(methylsulfonyl)benzo[a]carbazole **(4g)**

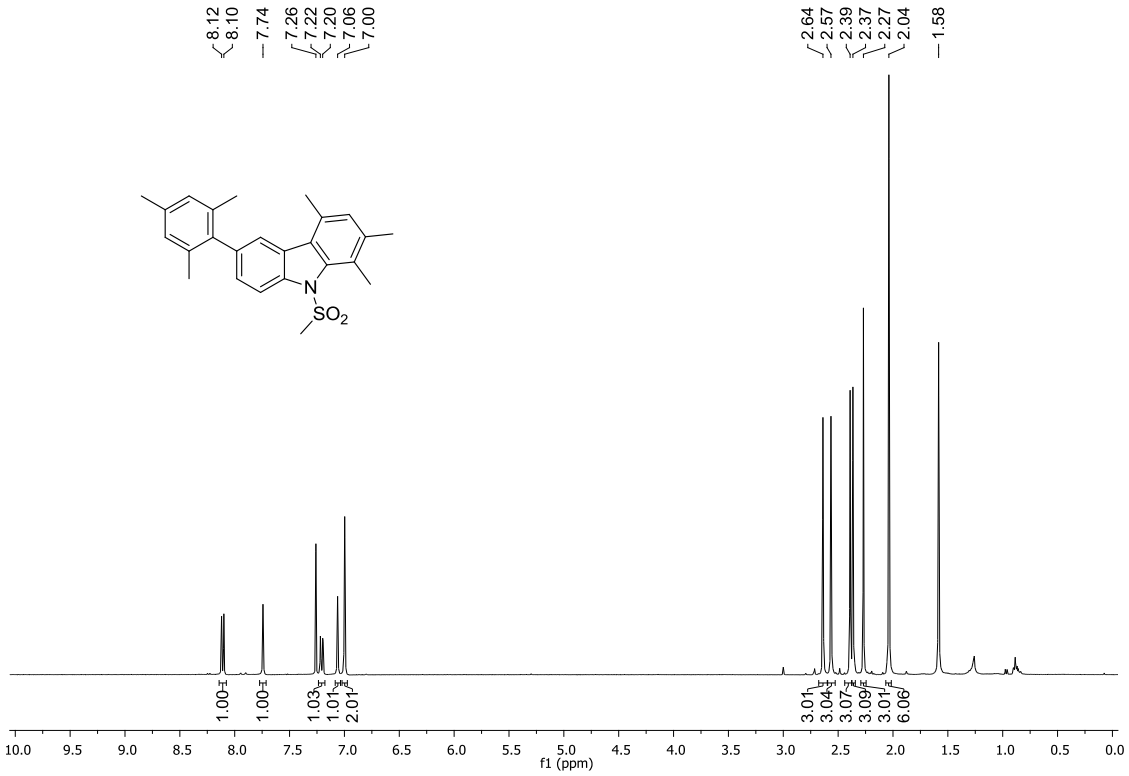


Figure 3B.45 ^{1}H NMR spectrum of 6-mesityl-1,2,4-trimethyl-9-(methylsulfonyl)carbazole **(4h)**

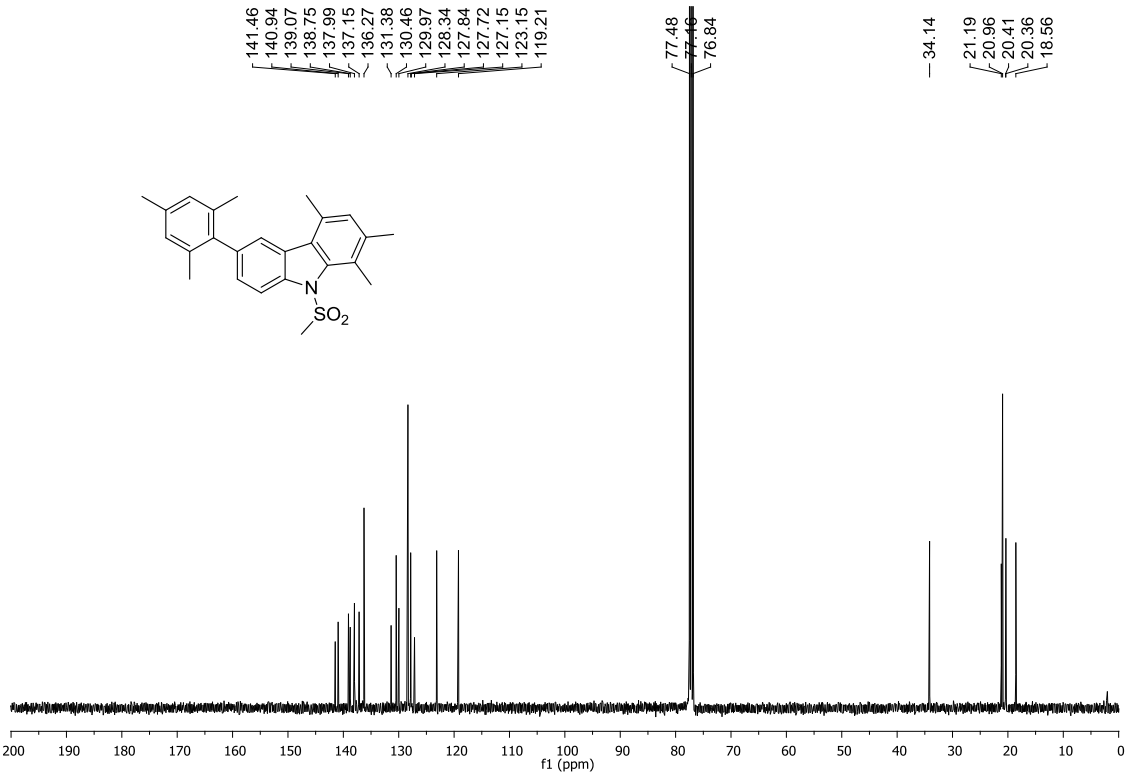


Figure 3B.46 ^{13}C NMR spectrum of 6-mesityl-1,2,4-trimethyl-9-(methylsulfonyl)carbazole **(4h)**

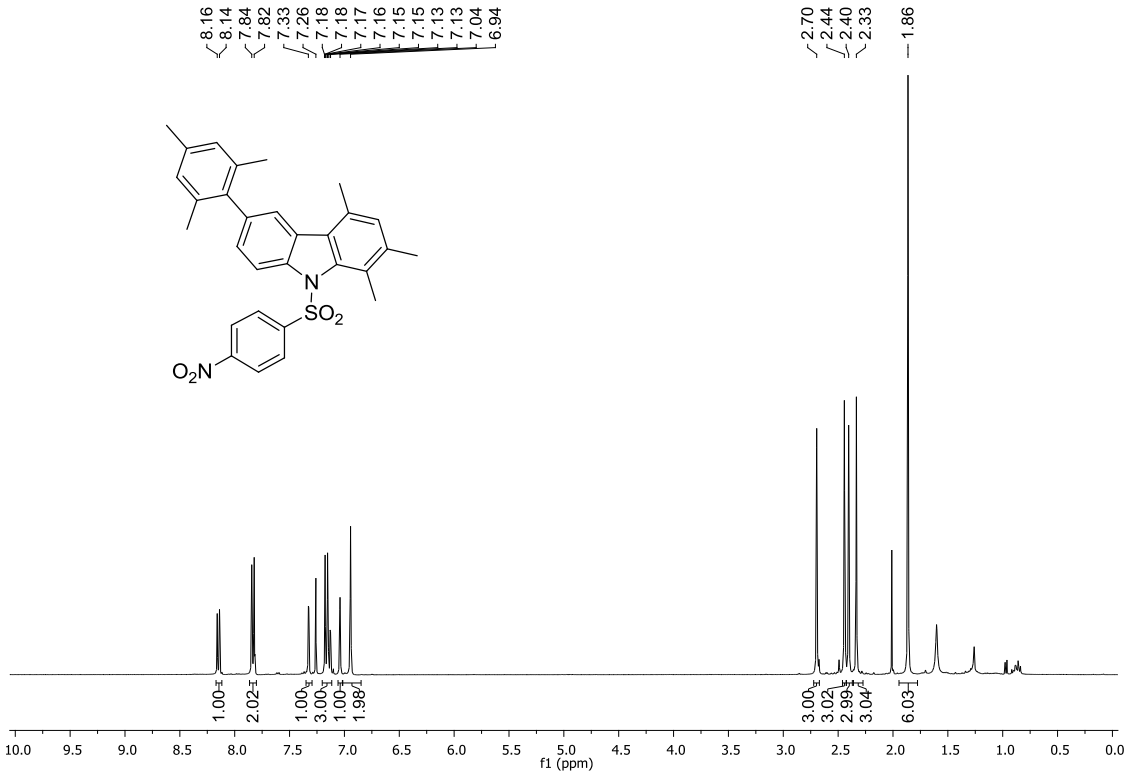


Figure 3B.47 ^{1}H NMR spectrum of 6-mesityl-1,2,4-trimethyl-9-((4-nitrophenyl)sulfonyl)carbazole **(4i)**

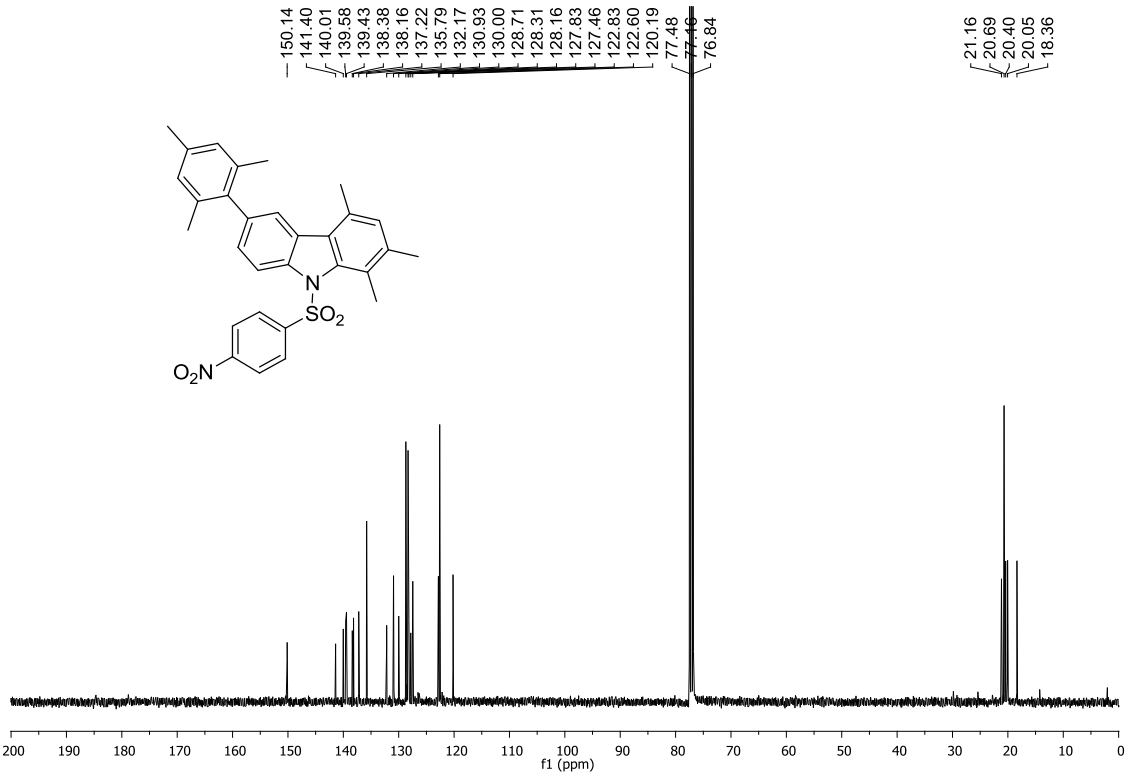


Figure 3B.48 ^{13}C NMR spectrum of 6-mesityl-1,2,4-trimethyl-9-((4-nitrophenyl)sulfonyl)carbazole **(4i)**

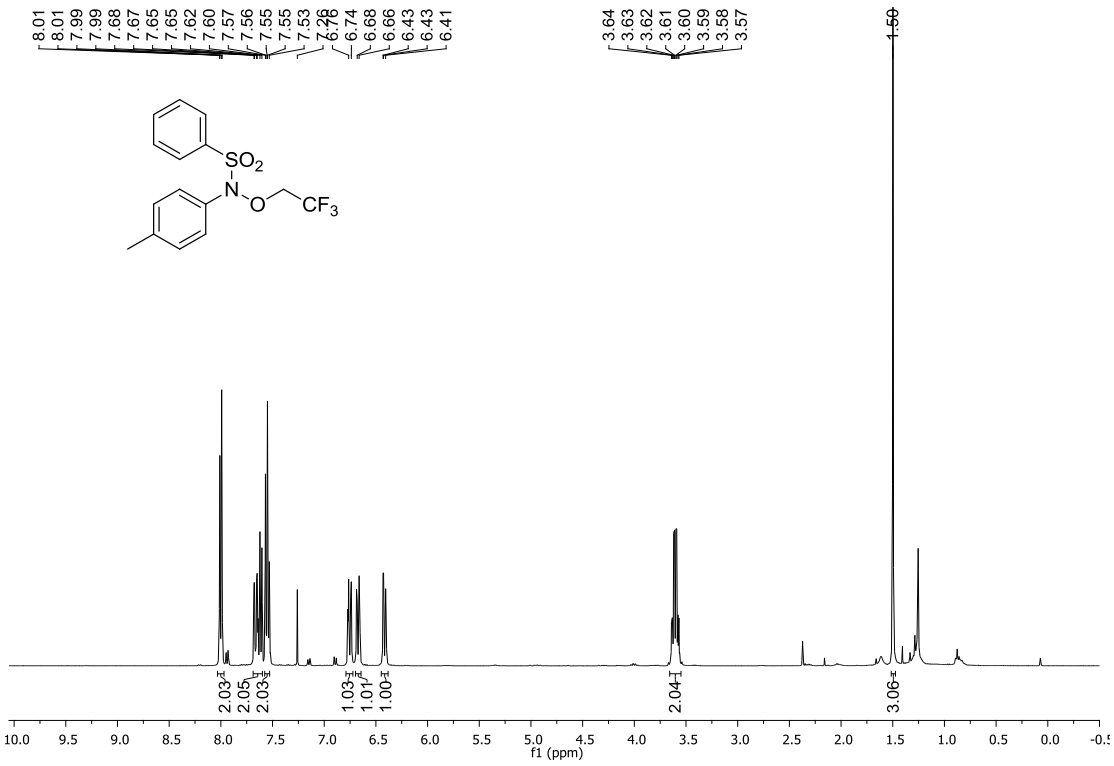


Figure 3B.49 ^{1}H NMR spectrum of N-(p-tolyl)-N-(2,2,2-trifluoroethoxy)benzenesulfonamide **(1if)**

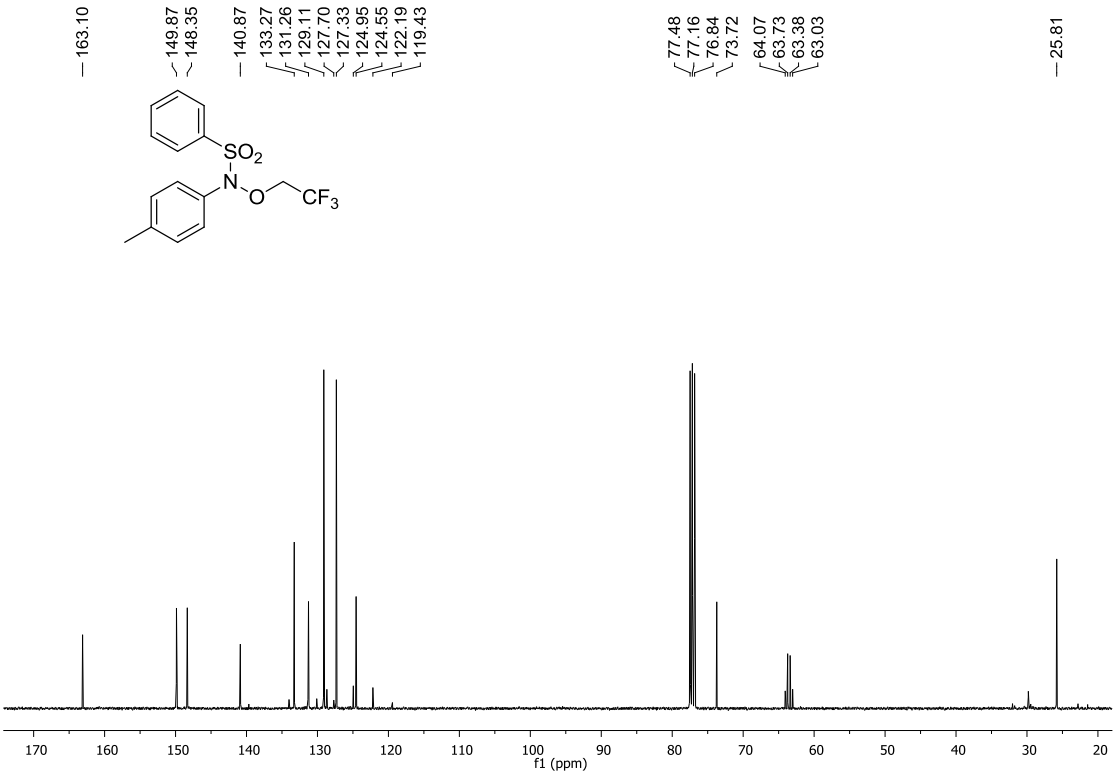


Figure 3B.50 ^{1}H NMR spectrum of N-(p-tolyl)-N-(2,2,2-trifluoroethoxy)benzenesulfonamide **(1if)**

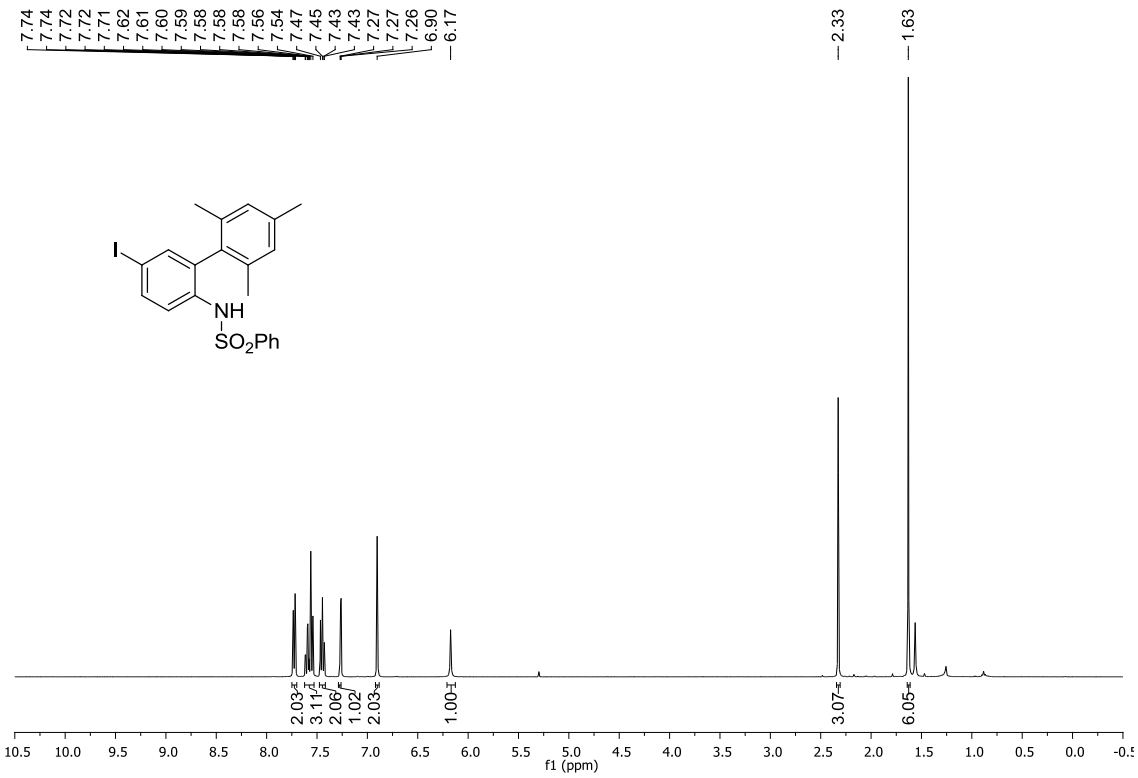


Figure 3B.51 ^{1}H NMR spectrum of N-(5-iodo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide **(1ea)**

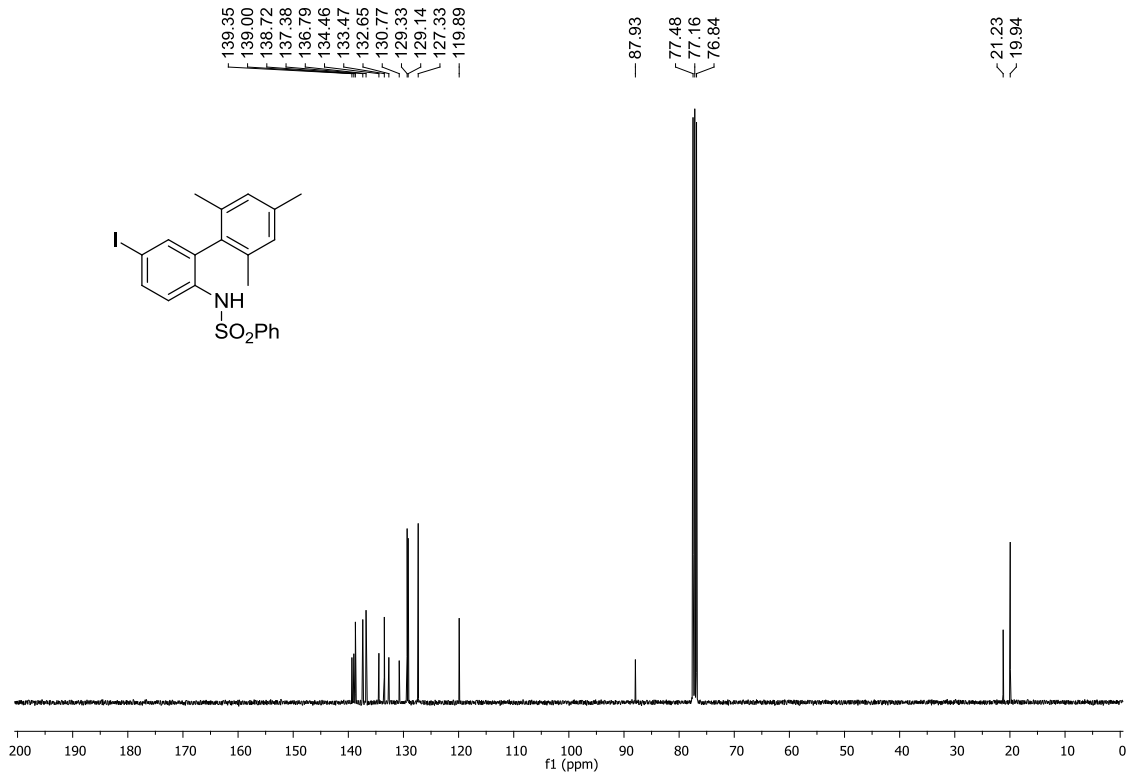


Figure 3B.52 ^{13}C NMR spectrum of N-(5-iodo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide **(1ea)**

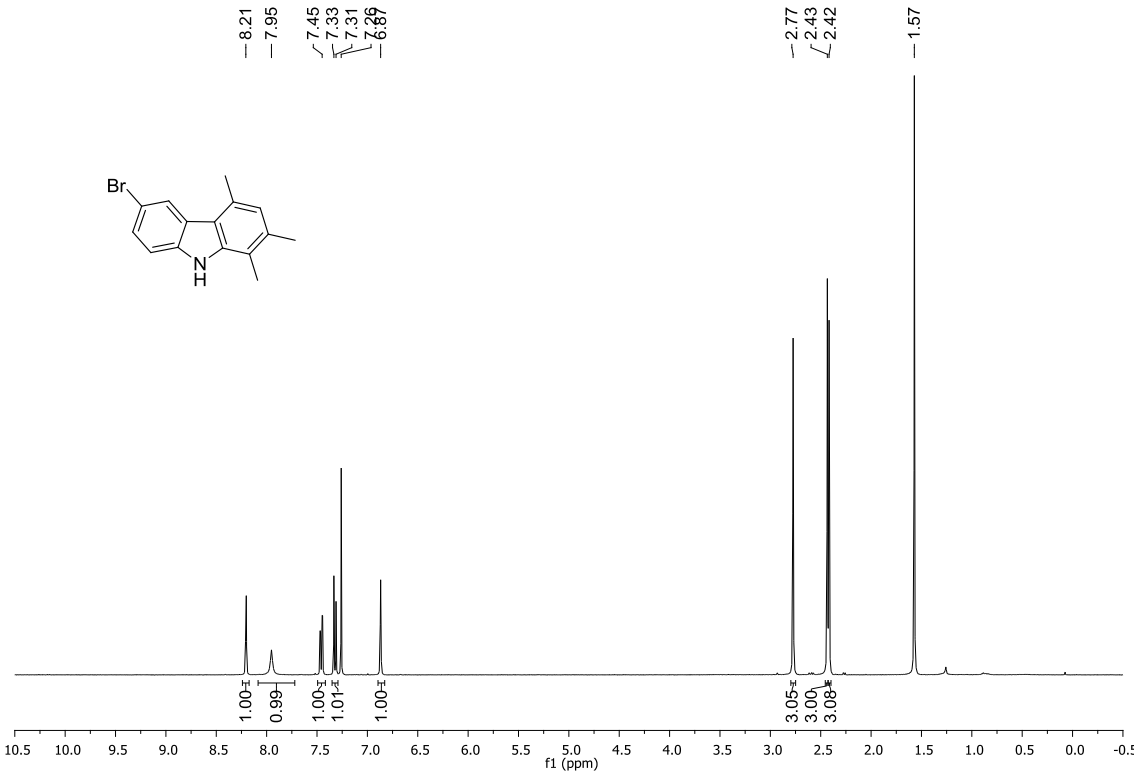


Figure 3B.53 ^{1}H NMR spectrum of 6-bromo-1,2,4-trimethyl-9H-carbazole **(3ab)**

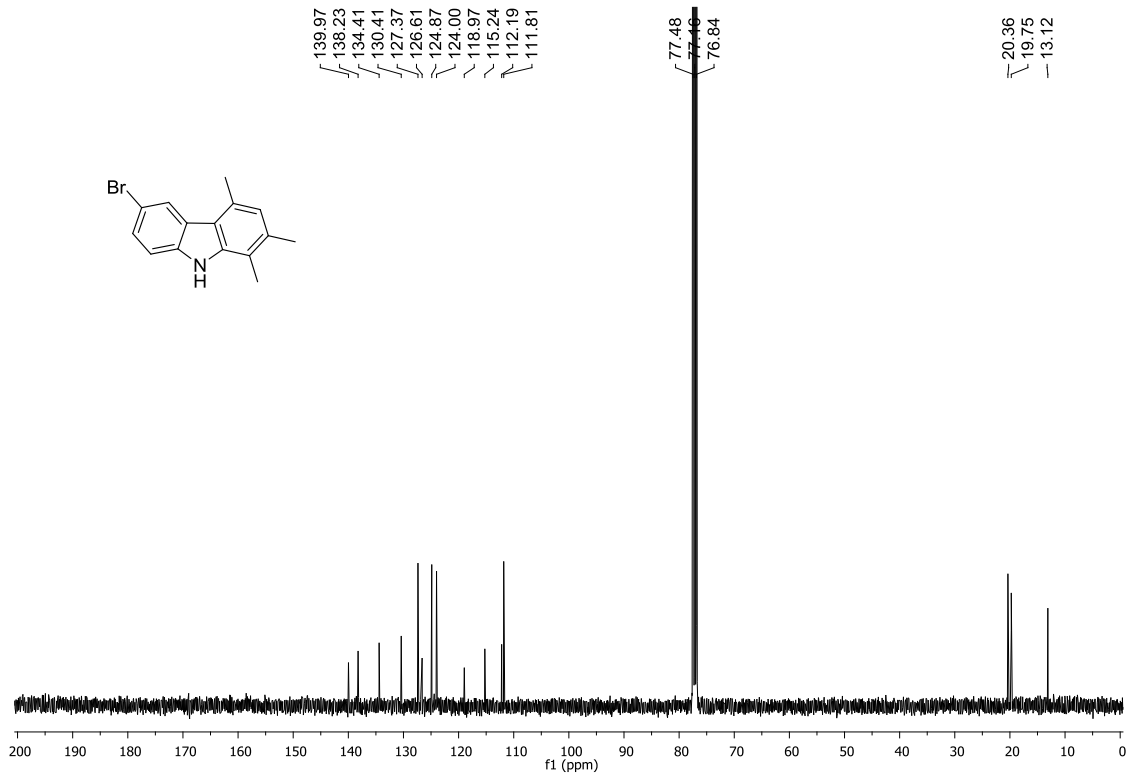
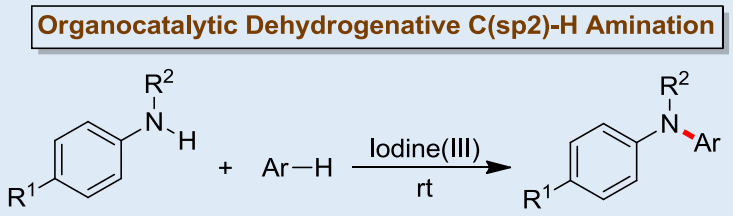


Figure 3B.54 ^{1}H NMR spectrum of 6-bromo-1,2,4-trimethyl-9H-carbazole **(3ab)**

CHAPTER 4

Organocatalytic Intermolecular *N*-Arylation of Anilides

4.1 ABSTRACT



In-situ generated hypervalent iodine (III) enables direct C-H and N-H bond functionalization for intermolecular C(sp2)-N bond construction through selective dehydogenative *N*-arylation of *para*-substituted anilides. The method provides diarylamine compounds under metal-free mild conditions.

4.2 INTRODUCTION

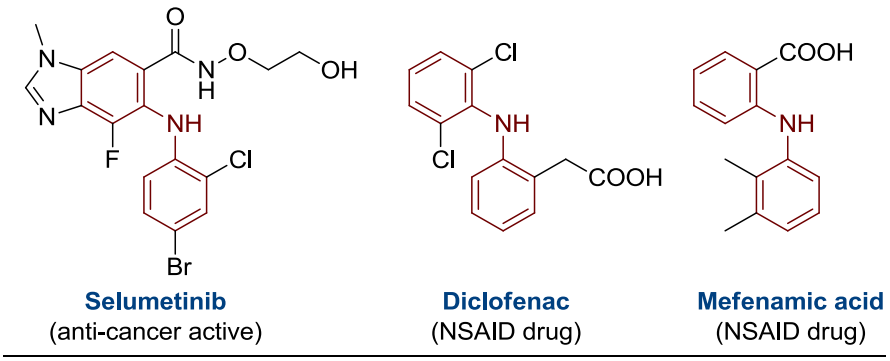
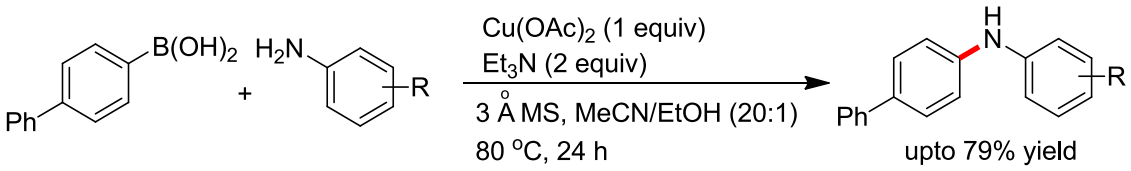


Figure 4.1 Diphenyl amine derived drug molecule

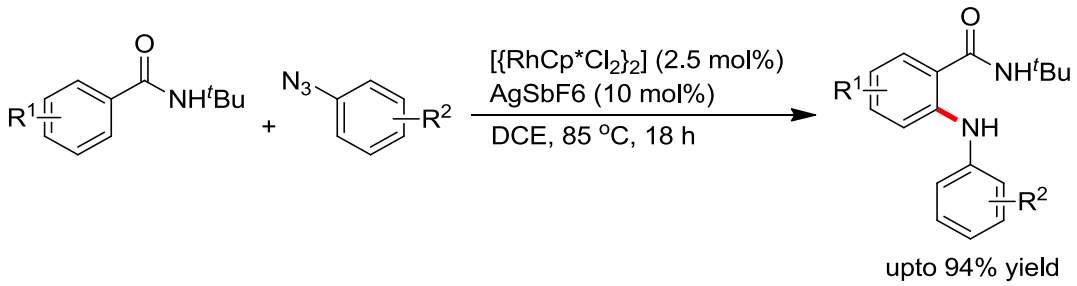
Diarylamine represent an important class of compounds owing to their wide applications in pharmaceuticals, agrochemicals, dyes, and electronic activities (Figure 4.1).[1] Therefore, development of novel and efficient methodologies for the construction of aromatic C-N bon

to access diarylamine derivatives is of great importance. Traditional methods toward diarylamine construction mainly rely on the Cu-mediated Ullmann coupling (reaction of aryl halides with amines in presence of Cu),[23] Buchwald-Hartwig coupling (coupling of aryl halides with primary or secondary amines in presence of Pd-catalyst),[4] Chan-Lam type amination reaction (coupling of an organoboron reagent with N-H functionality).[5] Very recently, Watson and co-workers have developed a Cu(II) mediated Chan-Evan-Lam coupling reaction between aryl BPin with aryl amine to provide diarylamines (Scheme 4.1).[6]



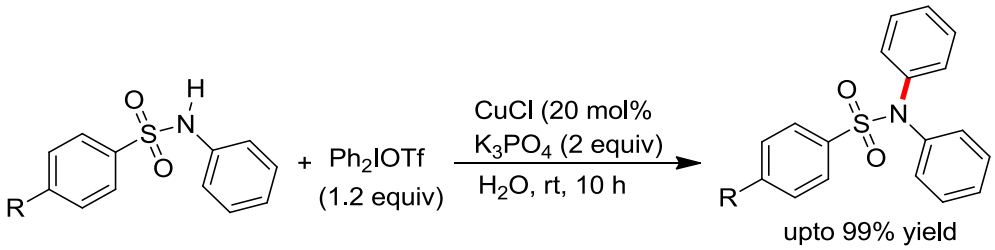
Scheme 4.1 Cu(II)-catalyzed Chan-Evan-Lam coupling reaction.

In 2012, Sukbok Chang and co-workers have developed a Rh-catalyzed C-H amination of benzamides with aryl azides based on directing group strategy (Scheme 4.2). The reaction proceed through the formation of active species $[Cp^*Rh](SbF_6)_2$ in reaction medium by the combination of $[\{RhCp^*Cl_2\}_2]$ and $AgSbF_6$ and followed by formation of five-membered rhodacycle intermediate. The method releases N_2 as by-product.



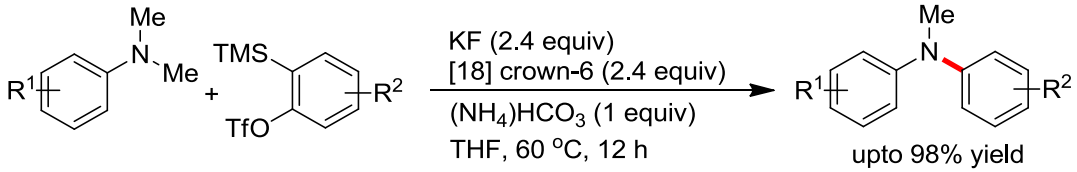
Scheme 4.2 Chang's directing group strategy.

Copper(I) catalyzed *N*-arylation of *N*-aryl sulphonamides in aqueous medium at room temperature conditions have been reported by Geng *et. al.* using hypervalent iodine(III) diaryliodonium salt as a source of arene (Scheme 4.3).[8]



Scheme 4.3 Cu(I)-catalyzed *N*-arylation of *N*-arylsulfonamides.

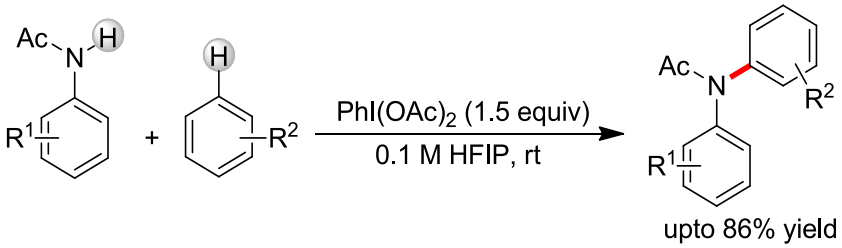
Biju and co-workers have developed a transition-metal-free, monoselective *N*-arylation of aromatic tertiary amines using aryne as the aryl source (Scheme 4.4). The reaction initiates with the nucleophilic addition of *N*,*N*-dimethylaniline to aryne and followed by demethylation induced by fluoride ion.[9]



Scheme 4.4 Biju's approach for *N*-arylation.

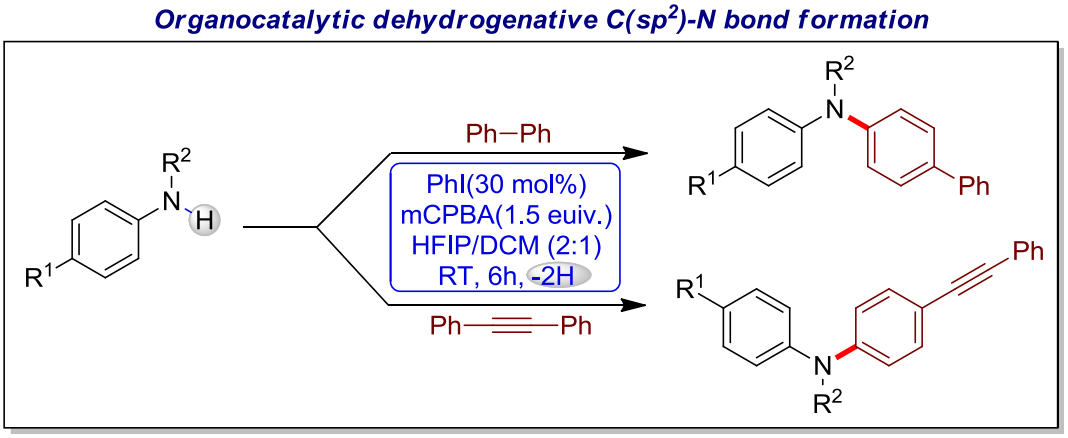
Direct dehydrogenative C-N bond formation method for diarylamine synthesis is a potent alternative synthetic route as it can put a stop to additional prefunctionalization of substrates.

Antonchick and co-workers established phenyliodine diacetate (PIDA) mediated cross-dehydrogenative amination reaction between *para*-substituted acetanilide derivatives with electron rich arenes to provide diarylamines at room temperature conditions (Scheme 4.5). The method breeds stoichiometric amount of iodobenzene as by-product.[10]



Scheme 4.5 Iodine(III) enabled *N*-arylation of acetanilides.

We anticipated that development of organocatalytic method by in-situ generation of hypervalent iodine(III) reagent from iodobenzene will be advantageous in view of trim down of organic waste as by-product.[11] Herein, we have developed a dehydrogenative C(sp^2)-N selective cross-coupling of anilides with selective arenes under organocatalytic conditions to provide *N*-substituted diarylamine derivatives at room temperature.

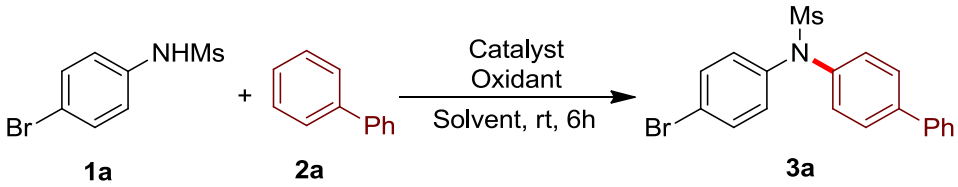


Scheme 4.6 Our approach for organocatalytic *N*-arylation of anilides.

4.3 RESULTS AND DISCUSSION

For optimization of reaction conditions, *N*-(4-bromophenyl)methanesulfonamide (**1a**) and biphenyl (**2a**) were chosen as model substrates. Initially, substrate **1a** and **2a** (1.5 equiv) were treated with 30 mol% PhI in presence of 1.5 equiv oxidant *m*CPBA in 2,2,2-trifluoroethanol (TFE) at room temperature conditions and the desired product *N*-([1,1'-biphenyl]-4-yl)-*N*-(4-bromophenyl)methanesulfonamide (**3a**) was isolated with 69% yield (Table 4.1, entry 2). 1,1,1,3,3,3-Hexafluoro-2-propanol was found to be most efficient among the solvents were

4.1 Optimization of reaction conditions



1a **2a** **3a**

Entry	Catalyst (mol%)	Oxidant (equiv)	Solvent	Yield (%)
1	PhI (30)	*m*CPBA (1.5)	HFIP	83
2	PhI (30)	*m*CPBA (1.5)	TFE	69
3	4-NO_2-C_6H_4-I (30)	*m*CPBA (1.5)	HFIP	35
4	4-Me-C_6H_4-I (30)	*m*CPBA (1.5)	HFIP	75
5	PhI (20)	*m*CPBA (1.5)	HFIP	77
6	PhI (30)	*m*CPBA (1.5)	DCM	27
7	PhI (30)	*m*CPBA (1.5)	ACN	66
8	PhI (30)	*m*CPBA (1.5)	HFIP/DCM (2:1)	87

examined (Table 4.1, entry 1-2, 6-7). By using different iodoarene bearing either electron withdrawing or electron donating substituent did not lead to improvement of yield. Decreasing catalyst loading reduced the product formation. Desired product formation with maximum yield was detected when reaction was performed in solvent system of HFIP/DCM (2:1) (Table 4.1, entry 8).

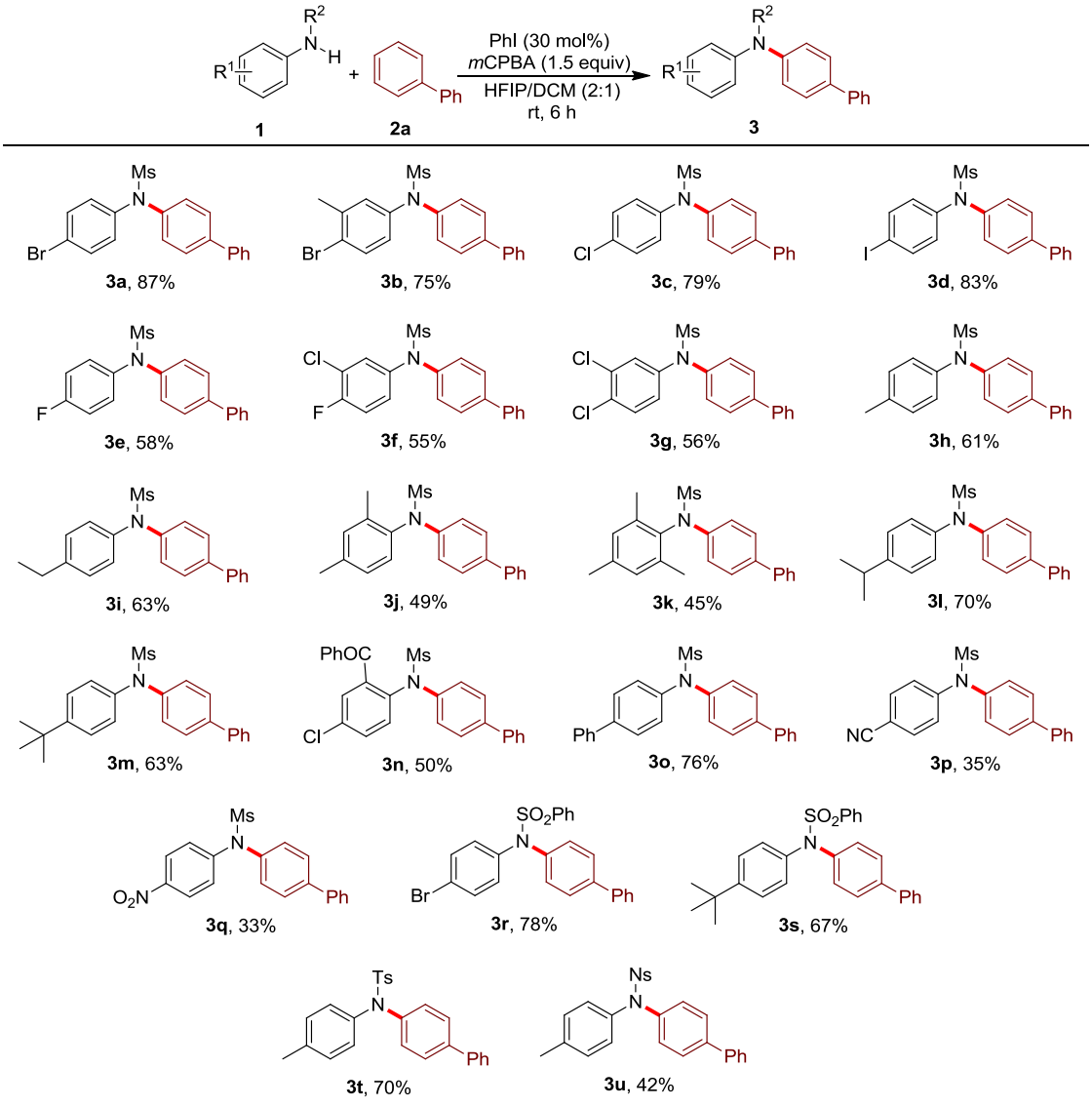


Figure 4.2 Scope of dehydrogenative amination of biphenyl.

With a set of optimized reaction condition in hand, we moved to investigate the generality of our dehydrogenative *N*-arylation protocol. A wide range of sulfoanilide substrates containing

various substituent with different electronic effect were found to be compatible with our method (Figure 4.2). Electron donating alkyl substituents as well as electron withdrawing halo- or phenyl groups containing anilides produced diarylamines smoothly with synthetically useful yield. Notably, much stronger electron withdrawing group –CN or –NO_2 containing sulfoanilides produced product with relatively lower yield (Figure 4.2, **3p-3q**). Pleasingly, anilides with sterically hindered environment also successfully lead to product formation (Figure 4.2, **3j-3k, 3n**). Furthermore, varying substituents at *N*-center of aniline like different sulfonyl groups were also found to be efficient in oxidative C-N bond formation reaction (Figure 4.2, **3r-3u**).

Next, we explored the scope of amination protocol with diphenyl acetylene to undergo oxidative coupling with anilides under our established method (Figure 4.3). Different sulfoanilides as well as acetanilide derivatives were found to be acceptable to provide corresponding *N*-arylated product with quite good yield. Compound **3a** and **5d** were characterized by X-ray crystallographic analysis (Figure 4.4).

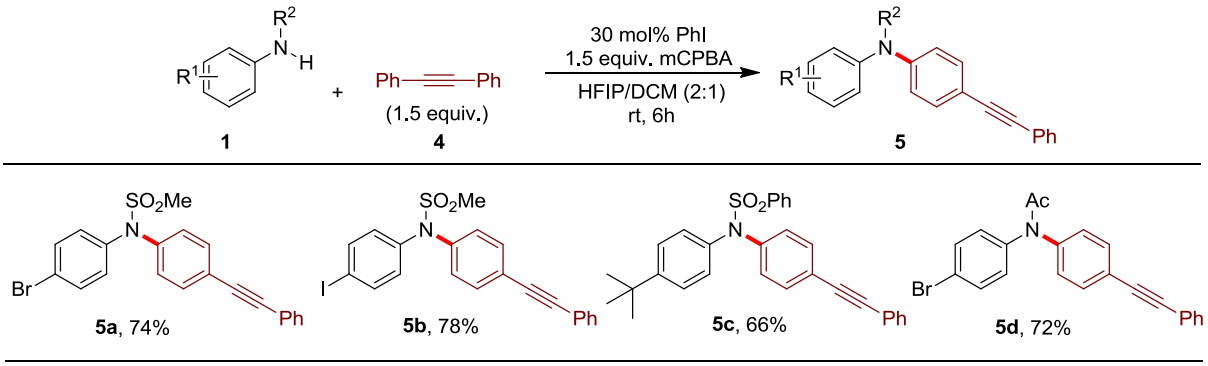
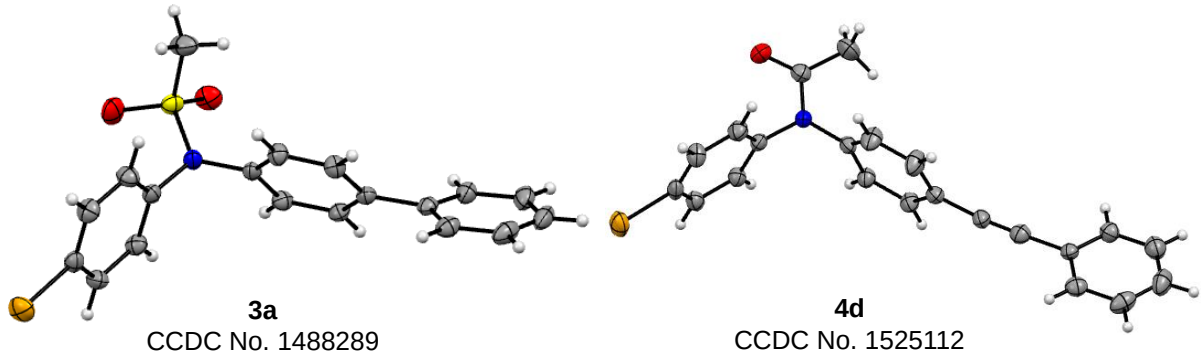


Figure 4.3 Scope of dehydrogenative amination of diphenyl acetylene.



3a
CCDC No. 1488289

4d
CCDC No. 1525112

Figure 4.4 X.-ray structure of **3a** and **4d**.

Based on literature precedence,[12] possible mechanism for the intermolecular dehydrogenative *N*-arylation reaction has been described in Figure 4.5. At first, trivalent organoiodine species is expected to be formed by the oxidation of monovalent iodobenzene in presence of *meta*-chloroperbenzoic acid. In-situ generated iodine(III) interact with anilide through *N*-center to create electrophilic nitrenium ion intermediate **5** by reductive elimination of iodobenzene.[13] Now, nucleophilic attack from arene occurs at the electron deficient *N*-centre to give the desired *N*-arylated product **3** through carbenium intermediate **6**.[14] The by-product of the transformation is *meta*-chlorobenzoic acid (mCBA) and iodobenzene (PhI). Iodobenzene is estimated to be reoxidized by mCPBA to keep active the catalytic cycle to generate hypervalent iodine(III) species (Figure 4.5).[15]

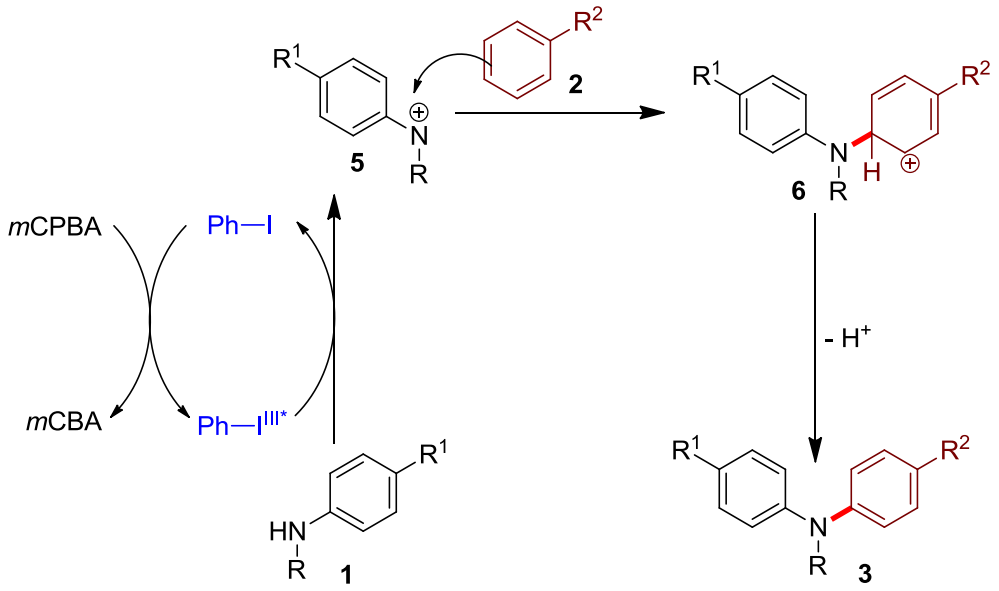


Figure 4.5 Possible reaction mechanism of *N*-arylation.

4.4 CONCLUSIONS

In summary, an intermolecular dehydrogenative C(sp^2)-N bond formation strategy has been developed based on in-situ generated hypervalent iodine(III) reagent. The described transformation is highly practical because of easily accessibility of substrates as well as inexpensive reagents for the straightforward access towards diarylamine compounds.

4.5 EXPERIMENTAL PROCEDURE

Representative procedure for *N*-arylation:

To a stirred solution of *N*-(4-bromophenyl)methanesulfonamide (**1a)** (60 mg, 0.24 mmol), biphenyl (**2a)** (54 mg, 0.36 mmol) and iodobenzene (8 µL, 0.072 mmol) in 1,1,1,3,3,3-hexafluoroisopropanol (HFIP or $(CF_3)_2CHOH$)/dichloromethane (DCM or CH_2Cl_2) (2:1, 3 mL), *m*CPBA (62 mg, 1.5 mmol) was added in one portion at ambient condition and allowed to stir for additional 1 h at room temperature. The progress of reaction was monitored by TLC using hexane and ethyl acetate mixture as eluent. After completion the solvent was evaporated

and saturated aqueous solution of $NaHCO_3$ was added. The aqueous phase was extracted with ethyl acetate. The organic extract was dried over anhydrous Na_2SO_4 and resulting solution was evaporated to dryness. The residue was purified by column chromatography on silica-gel to give the pure product *N*-(4-bromophenyl)-*N*-(4-(phenylethynyl)phenyl)acetamide (**3a)** (81 mg, 0.207 mmol, yield 87%).

Compounds characterization data:

***N-([1,1'-biphenyl]-4-yl)-N-(4-bromophenyl)methanesulfonamide (3a)*:** R_f = 0.45 (hexane:ethyl acetate 4:1); white solid; mp 150-152 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, *J* = 8 Hz, 2H), 7.57-7.50 (m, 4H), 7.46-7.41 (m, 4H), 7.38 (d, *J* = 8 Hz, 1H), 7.29 (d, *J* = 8 Hz, 2H), 3.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.7, 140.5, 140.0, 139.9, 132.8, 129.0, 128.4, 127.9, 127.9, 127.2, 121.1, 40.2; IR (KBr): $\tilde{\nu}$ = 3024, 2927, 2853, 1509, 1447, 1398, 1337, 1276, 1201, 1179, 1104, 1012, 991, 959, 912, 824, 768, 751, 700 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{19}H_{16}NO_2S^{79}BrNa$ $[M + Na]^+$: 423.9977, found: 423.9962; $C_{19}H_{16}NO_2S^{81}BrNa$ $[M + Na]^+$: 425.9957, found: 425.9947.

***N-([1,1'-biphenyl]-4-yl)-N-(4-bromo-3-methylphenyl)methanesulfonamide (3b)*:** R_f = 0.55 (hexane:ethyl acetate 4:1); white solid; mp 98-99 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60-7.53 (m, 5H), 7.46-7.42 (m, 4H), 7.38-7.36 (m, 1H), 7.29-7.27 (m, 1H), 7.13-7.11 (m, 1H), 3.18 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.5, 140.4, 140.2, 140.0, 139.7, 133.4, 130.0, 129.0, 128.4, 127.8, 127.7, 127.2, 126.5, 123.9, 40.2, 23.2; IR (KBr): $\tilde{\nu}$ = 3031, 2926, 2852, 1550, 1515, 1484, 1347, 1251, 1156, 1031, 966, 758, 725, 697 cm-1; HR-MS (ESI-TOF): m/z calculated for $C_{20}H_{18}NO_2S^{79}BrNa$ $[M + Na]^+$: 438.0134, found: 438.0118; $C_{20}H_{18}NO_2S^{81}BrNa$ $[M + Na]^+$: 440.0114, found: 440.0096.

***N-([1,1'-biphenyl]-4-yl)-N-(4-chlorophenyl)methanesulfonamide (3c)*:** R_f = 0.60 (hexane:ethyl acetate 4:1); white solid; mp 151-153 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61-7.59 (m, 2H), 7.57-7.54 (m, 2H), 7.46-7.42 (m, 4H), 7.38-7.36 (m, 5H), 3.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.7, 140.1, 139.9, 139.9, 133.3, 129.9, 129.8, 129.0, 128.8, 128.4, 127.8, 127.2, 122.3, 40.2; IR (KBr): $\tilde{\nu}$ = 3030, 2926, 2854, 1694, 1549, 1512, 1486, 1346, 1275, 1156, 1091, 974, 749 cm-1; HR-MS (ESI-TOF): m/z calculated for $C_{19}H_{16}NO_2SClNa$ $[M + Na]^+$: 380.0482, found: 380.0491.

***N-([1,1'-biphenyl]-4-yl)-N-(4-iodophenyl)methanesulfonamide (3d)*:** R_f = 0.55 (hexane:ethyl acetate 4:1); white solid; mp 158-160 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 8 Hz, 2H), 7.6-7.55 (m, 4H), 7.47-7.41 (m, 4H), 7.39-7.35 (m, 1H), 7.16 (d, *J* = 8 Hz, 2H), 3.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.2, 140.7, 139.9, 139.9, 138.8, 129.1, 129.0, 128.4, 128.0, 127.8, 127.2, 92.2, 40.2; IR (KBr): $\tilde{\nu}$ = 3096, 3030, 2995, 2933, 1679, 1549, 1513, 1483, 1346, 1156, 1007, 979, 764, 748 cm-1; HR-MS (ESI-TOF): m/z calculated for $C_{19}H_{16}NO_2SINa$ $[M + Na]^+$: 471.9839, found: 471.9836.

***N-([1,1'-biphenyl]-4-yl)-N-(4-fluorophenyl)methanesulfonamide (3e)*:** R_f = 0.35 (hexane:ethyl acetate 9:1); white solid; mp 186-188 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60-7.54 (m, 4H), 7.46-7.41 (m, 6H), 7.38-7.34 (m, 1H), 7.12-7.07 (m, 2H), 3.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.85 (d, $^1J_{C,F}$ = 247 Hz), 140.5, 140.4, 140.0, 137.16 (d, $^4J_{C,F}$ = 3 Hz), 130.1 (d, $^3J_{C,F}$ = 9 Hz), 129.0, 128.4, 127.8, 127.4, 127.2, 116.6 (d, $^2J_{C,F}$ = 23 Hz), 40.1; IR (KBr): $\tilde{\nu}$ = 3072, 3028, 2927, 1503, 1484, 1334, 1221, 1144, 1071, 992, 940, 835, 760, 698 cm-1; HR-MS (ESI-TOF): m/z calculated for $C_{19}H_{16}NO_2SFNa$ $[M+Na]^+$: 364.0778, found: 364.0790.

***N-([1,1'-biphenyl]-4-yl)-N-(3-chloro-4-fluorophenyl)methanesulfonamide (3f)*:** R_f = 0.40 (hexane:ethyl acetate 9:1); white solid; mp 145-147 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, *J* = 8 Hz, 2H), 7.56 (d, *J* = 8 Hz, 2H), 7.50-7.46 (m, 1H), 7.45-7.41 (m, 4H), 7.39-7.31 (m, 2H), 7.17 (t, *J* = 8 Hz, 1H), 3.19 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3 (d, $^1J_{C,F}$ = 249 Hz), 140.9, 139.9 (d, $^4J_{C,F}$ = 3 Hz), 137.7 (d, $^3J_{C,F}$ = 4 Hz), 130.1, 129.0, 128.6, 127.9, 127.9, 127.8, 127.8, 127.2, 121.9 (d, $^2J_{C,F}$ = 19 Hz), 117.3 (d, $^2J_{C,F}$ = 22 Hz), 40.3; IR (KBr): $\tilde{\nu}$ = 3097, 3086, 3031, 2939, 1549, 1494, 1398, 1348, 1259, 1230, 1194, 987, 847, 763, 726, 698 cm-1; HR-MS (ESI-TOF): m/z calculated for $C_{19}H_{16}NO_2SClF$ $[M + H]^+$: 376.0569, found: 376.0554.

***N-([1,1'-biphenyl]-4-yl)-N-(3,4-dichlorophenyl)methanesulfonamide (3g)*:** R_f = 0.45 (hexane:ethyl acetate 9:1); white solid; mp 130-131 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (d, *J* = 8 Hz, 2H), 7.57 (d, *J* = 8 Hz, 2H), 7.51 (s, 1H), 7.48-7.38 (m, 6H), 7.29-7.26 (m, 1H), 3.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.2, 140.8, 139.8, 139.5, 133.4, 131.3, 131.1, 129.0, 128.7, 128.6, 128.3, 127.9, 127.2, 126.3, 40.3; IR (KBr): $\tilde{\nu}$ = 3079, 3031, 3011, 2932, 1583, 1550, 1513, 1485, 1472, 1349, 1277, 1160, 1032, 985, 794, 752, 697 cm-1; HR-MS (ESI-TOF): m/z calculated for $C_{19}H_{16}NO_2SCl_2$ $[M + H]^+$: 392.0273, found: 392.0274.

***N-([1,1'-biphenyl]-4-yl)-N-(p-tolyl)methanesulfonamide (3h)*:** R_f = 0.40 (hexane:ethyl acetate 9:1); white solid; mp 178-180 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58-7.54 (m, 4H), 7.45-7.41 (m, 4H), 7.37-7.32 (m, 3H), 7.21 (d, *J* = 8 Hz, 2H), 3.18 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.8, 140.1, 140.0, 138.6, 137.9, 130.4, 128.9, 128.2, 128.1, 127.7, 127.3, 127.2, 40.1, 21.1; IR (KBr): $\tilde{\nu}$ = 3062, 3030, 2987, 2925, 1549, 1510, 1485, 1339, 1155, 760 cm-1; HR-MS (ESI-TOF): m/z calculated for $C_{20}H_{19}NO_2SNa$ $[M + Na]^+$: 360.1029, found: 360.1058.

***N-([1,1'-biphenyl]-4-yl)-N-(4-ethylphenyl)methanesulfonamide (3i)*:** Rf = 0.35 (hexane:ethyl acetate 19:1); white solid; mp 98-100 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59-7.54 (m, 4H), 7.46-7.42 (m, 4H), 7.37-7.34 (m, 3H), 7.24 (d, J = 8 Hz, 2H), 3.18 (s, 3H), 2.67 (q, *J* = 8 Hz, 2H), 1.25 (t, *J* = 8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.0, 140.8, 140.1, 140.0, 138.7, 129.2, 128.9, 128.2, 128.1, 127.7, 127.4, 127.2, 40.1, 28.5, 15.4; IR (KBr): $\tilde{\nu}$ = 3031, 2965, 2931, 2872, 1509, 1486, 1346, 1256, 1157, 977, 834, 757, 697 cm-1; HR-MS (ESI-TOF): m/z calculated for $C_{21}H_{22}NO_2S$ $[M + H]^+$: 352.1366, found: 352.1361.

***N-([1,1'-biphenyl]-4-yl)-N-(2,4-dimethylphenyl)methanesulfonamide (3j)*:** R_f = 0.40 (hexane:ethyl acetate 9:1); white solid; mp 94-96 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55-7.53 (m, 4H), 7.45-7.41 (m, 4H), 7.36-7.33 (m, 2H), 7.14-7.11 (m, 2H), 3.20 (s, 3H), 2.36 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.3, 140.1, 139.1, 138.6, 138.6, 136.4, 132.7, 129.5, 128.9, 128.0, 127.9, 127.5, 127.0, 124.6, 40.1, 21.2, 18.6; IR (KBr): $\tilde{\nu}$ = 3030, 2924, 1485, 1345, 1232, 1152, 975, 763, 697 cm-1; HR-MS (ESI-TOF): m/z calculated for $C_{21}H_{22}NO_2S$ $[M + H]^+$: 352.1366, found: 352.1370.

***N-([1,1'-biphenyl]-4-yl)-N-mesitylmethanesulfonamide (3k)*:** R_f = 0.40 (hexane:ethyl acetate 9:1); semi solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55-7.51 (m, 4H), 7.43 (t, *J* = 8 Hz, 2H), 7.33 (t, *J* = 8 Hz, 1H), 7.25 (d, *J* = 8 Hz, 2H), 7.00 (s, 2H), 3.32 (s, 3H), 2.33 (s, 3H), 2.28 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.1, 139.0, 138.7, 136.4, 134.5, 130.1, 128.9, 128.1, 127.3, 126.9, 119.2, 40.3, 21.2, 19.1; IR (KBr): $\tilde{\nu}$ = 3031, 2923, 2854, 1609, 1549, 1517, 1485, 1342, 1246, 1157, 971, 835, 762, 697 cm-1; HR-MS (ESI-TOF): m/z calculated for $C_{22}H_{23}NSO_2Na$ $[M + Na]^+$: 388.1342, found: 388.1313.

***N-([1,1'-biphenyl]-4-yl)-N-(4-isopropylphenyl)methanesulfonamide (3l)*:** R_f = 0.45 (hexane:ethyl acetate 9:1); white solid; mp 114-116 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58-

7.53 (m, 4H), 7.46-7.41 (m, 4H), 7.37-7.33 (m, 3H), 7.26-7.24 (m, 1H), 3.18 (s, 3H), 2.91 (sept, *J* = 8 Hz, 1H), 1.24 (d, *J* = 4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.6, 140.8, 140.2, 140.1, 138.7, 128.9, 128.2, 128.0, 127.8, 127.7, 127.6, 127.2, 40.1, 33.8, 24.0; IR (KBr): $\tilde{\nu}$ = 3031, 2959, 2930, 2870, 1549, 1508, 1416, 1347, 1277, 1157, 979, 834, 778, 765, 752, 697 cm-1; HR-MS (ESI-TOF): m/z calculated for $C_{22}H_{23}NO_2SNa$ $[M + Na]^+$: 388.1342, found: 388.1339.

***N-([1,1'-biphenyl]-4-yl)-N-(4-(tert-butyl)phenyl)methanesulfonamide (3m)*:** R_f = 0.45 (hexane:ethyl acetate 9:1); white solid; mp 142-144 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59-7.54 (m, 4H), 7.46-7.39 (m, 6H), 7.37-7.33 (m, 3H), 3.19 (s, 3H), 1.31 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.8, 140.7, 140.2, 138.5, 128.9, 128.2, 127.7, 127.5, 127.2, 126.7, 40.1, 34.7, 31.4; IR (KBr): $\tilde{\nu}$ = 3031, 2962, 2868, 1486, 1347, 1158, 979, 750 cm-1; HR-MS (ESI-TOF): m/z calculated for $C_{23}H_{26}NO_2S$ $[M + H]^+$: 380.1679, found: 380.1665.

***N-([1,1'-biphenyl]-4-yl)-N-(2-benzoyl-4-chlorophenyl)methanesulfonamide (3n)*:** R_f = 0.30 (hexane:ethyl acetate 9:1); semi-solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 8 Hz, 2H), 7.61 (d, *J* = 8 Hz, 1H), 7.55-7.50 (m, 1H), 7.46-7.38 (m, 11H), 7.36-7.33 (m, 2H), 3.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.8, 140.2, 140.1, 140.1, 140.0, 137.9, 136.1, 133.8, 133.3, 132.8, 131.5, 130.6, 129.6, 128.9, 128.5, 128.1, 127.7, 127.7, 127.2, 40.64; IR (KBr): $\tilde{\nu}$ = 3068, 3031, 2925, 2853, 1668, 1596, 1516, 1485, 1390, 1349, 1246, 1157, 1116, 979, 888, 806, 736, 633 cm-1; HR-MS (ESI-TOF): m/z calculated for $C_{26}H_{20}NO_3SClNa$ $[M + Na]^+$: 484.0745, found: 484.0736.

***N,N-di([1,1'-biphenyl]-4-yl)methanesulfonamide (3o)*:** R_f = 0.45 (hexane:ethyl acetate 9:1); white solid; mp 170-172 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63-7.56 (m, 8H), 7.51-7.43 (m, 8H), 7.39-7.35 (m, 2H), 3.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.5, 140.4, 140.1,

129.0, 128.4, 127.9, 127.8, 127.2, 40.25; IR (KBr): $\tilde{\nu}$ = 3063, 3031, 2933, 1691, 1550, 1513, 1486, 1342, 1267, 1148, 836, 763, 695 cm-1; HR-MS (ESI-TOF): m/z calculated for $C_{25}H_{21}NO_2SNa$ $[M + Na]^+$: 422.1185, found: 422.1207.

***N-([1,1'-biphenyl]-4-yl)-N-(4-cyanophenyl)methanesulfonamide (3p)*:** R_f = 0.35 (hexane:ethyl acetate 4:1); white solid; mp 180-182 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68-7.65 (m, 2H), 7.64-7.61 (m, 2H), 7.59-7.57 (m, 2H), 7.48-7.37 (m, 7H), 3.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.8, 141.9, 139.6, 138.6, 133.4, 129.4, 129.1, 128.8, 128.1, 127.2, 124.6, 118.3, 109.1, 40.32; IR (KBr): $\tilde{\nu}$ = 3053, 3030, 2932, 1601, 1502, 1485, 1350, 1267, 1158, 965, 835, 755, 698 cm-1; HR-MS (ESI-TOF): m/z calculated for $C_{20}H_{17}NO_2S$ $[M + H]^+$: 349.1005, found: 349.1020.

***N-([1,1'-biphenyl]-4-yl)-N-(4-nitrophenyl)methanesulfonamide (3q)*:** R_f = 0.40 (hexane:ethyl acetate 4:1); white solid; mp 194-196 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20 (d, *J* = 8 Hz, 2H), 7.69 (d, *J* = 12 Hz, 2H), 7.59 (d, *J* = 8 Hz, 2H), 7.49-7.38 (m, 7H), 3.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.6, 144.6, 142.2, 139.6, 138.5, 129.6, 129.1, 129.0, 128.2, 127.3, 125.0, 123.8, 40.3; IR (KBr): $\tilde{\nu}$ = 3079, 3031, 3011, 2993, 2933, 1590, 1515, 1486, 1343, 1267, 1112, 967, 852, 767, 729, 696 cm-1; HR-MS (ESI-TOF): m/z calculated for $C_{19}H_{17}N_2O_4S$ $[M + H]^+$: 369.0904, found: 369.0894.

***N-([1,1'-biphenyl]-4-yl)-N-(4-bromophenyl)benzenesulfonamide (3r)*:** R_f = 0.50 (hexane:ethyl acetate 9:1); white solid; mp 168-170 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8 Hz, 2H), 7.62 (t, *J* = 8 Hz, 1H), 7.56-7.49 (m, 6H), 7.47-7.42 (m, 4H), 7.38-7.34 (m, 1H), 7.30 (d, *J* = 8 Hz, 2H), 7.18 (d, *J* = 8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.8, 140.6, 140.3, 140.2, 140.0, 133.2, 132.6, 129.8, 129.2, 129.0, 128.6, 128.2, 127.8, 127.8, 127.2, 121.5; IR (KBr): $\tilde{\nu}$ = 3057, 3030, 2987, 2924, 1692, 1658, 1549, 1484, 1355, 1273, 1164,

1091, 1010, 764, 689 cm-1; HR-MS (ESI-TOF): m/z calculated for $C_{24}H_{19}NO_2S^{79}Br$ $[M + H]^+$: 464.0314, found: 464.0300; for $C_{24}H_{19}NO_2S^{81}Br$ $[M + H]^+$: 466.0295, found: 466.0282.

***N-([1,1'-biphenyl]-4-yl)-N-(4-(tert-butyl)phenyl)benzenesulfonamide (3s)*:** R_f = 0.45 (hexane:ethyl acetate 9:1); white solid; mp 154-156 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 8 Hz, 2H), 7.61 (t, *J* = 8 Hz, 1H), 7.55-7.48 (m, 6H), 7.43 (t, *J* = 8 Hz, 2H), 7.36-7.32 (m, 5H), 7.21 (d, *J* = 8 Hz, 2H), 1.30 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.8, 140.8, 140.8, 140.4, 140.2, 138.7, 132.8, 129.0, 128.9, 128.6, 128.0, 128.0, 127.9, 127.7, 127.2, 126.4, 34.7, 31.4; IR (KBr): $\tilde{\nu}$ = 3031, 2962, 2903, 2867, 1549, 1510, 1446, 1355, 1268, 1166, 1091, 833, 764, 740, 721, 689 cm-1; HR-MS (ESI-TOF): m/z calculated for $C_{28}H_{27}NSO_2Na$ $[M + Na]^+$: 464.1655, found: 464.1650.

***N-([1,1'-biphenyl]-4-yl)-4-methyl-N-(p-tolyl)benzenesulfonamide (3t)*:** R_f = 0.55 (hexane:ethyl acetate 9:1); white solid; mp 148-150 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, *J* = 8 Hz, 2H), 7.54-7.50 (m, 4H), 7.42 (t, *J* = 8 Hz, 2H), 7.36-7.32 (m, 3H), 7.28 (d, *J* = 8 Hz, 2H), 7.19-7.12 (m, 4H), 2.44 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.7, 141.1, 140.2, 140.1, 138.9, 137.8, 137.8, 130.1, 129.6, 128.9, 128.6, 128.2, 128.0, 127.9, 127.6, 127.2, 21.7, 21.2; IR (KBr): $\tilde{\nu}$ = 3047, 2986, 2943, 2866, 1692, 1549, 1512, 1484, 1351, 1158, 1089, 762, 727, 669 cm-1; HR-MS (ESI-TOF): m/z calculated for $C_{26}H_{24}NO_2S$ $[M + H]^+$: 414.1522, found: 414.1510.

***N-([1,1'-biphenyl]-4-yl)-N-(4-bromophenyl)-4-nitrobenzenesulfonamide (3u)*:** R_f = 0.50 (hexane:ethyl acetate 10:1); white solid; mp 138-140 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36 (d, *J* = 8 Hz, 2H), 7.91 (d, *J* = 8 Hz, 2H), 7.57-7.53 (m, 4H), 7.50-7.44 (m, 5H), 7.28 (d, *J* = 8 Hz, 2H), 7.17 (d, *J* = 8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.4, 145.8, 141.5, 139.9, 139.7, 139.5, 132.9, 129.8, 129.1, 128.6, 128.5, 128.1, 127.2, 127.1, 124.5, 122.3; IR (KBr):

$\tilde{\nu}$ = 3101, 3064, 3031, 2993, 2923, 1528, 1484, 1348, 1310, 1164, 1088, 1010, 853, 764, 737, 698 cm-1.

***N-(4-bromophenyl)-N-(4-(phenylethynyl)phenyl)methanesulfonamide (5a)*:** R_f = 0.50 (hexane:ethyl acetate 9:1); white solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, *J* = 8 Hz, 1H), 7.73-7.72 (m, 1H), 7.53-7.50 (m, 1H), 7.38-7.27 (m, 8H), 7.19-7.17 (m, 2H), 2.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.9, 135.6, 132.0, 131.9, 131.8, 130.3, 129.9, 129.2, 128.6, 128.4, 127.9, 127.5, 123.8, 123.0, 118.1, 117.1, 41.0; IR (KBr): $\tilde{\nu}$ = 3011, 2925, 2853, 1659, 1550, 1513, 1443, 1377, 1173, 1135, 1066, 1008, 919, 847, 766, 699 cm-1; HR-MS (ESI-TOF): m/z calculated for $C_{21}H_{17}NO_2S^{79}Br$ [M + H]+: 426.0158, found: 426.0126; $C_{21}H_{17}NO_2S^{81}Br$ [M + H]+: 428.0138, found: 428.0101.

***N-(4-iodophenyl)-N-(4-(phenylethynyl)phenyl)methanesulfonamide (5b)*:** R_f = 0.50 (hexane:ethyl acetate 9:1); white solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, *J* = 8 Hz, 1H), 7.92-7.91 (m, 1H), 7.70-7.68 (m, 1H), 7.37-7.28 (m, 8H), 7.19-7.16 (m, 2H), 2.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 137.5, 136.3, 134.0, 132.5, 131.9, 131.8, 130.2, 129.9, 129.2, 128.6, 127.9, 127.5, 123.6, 117.5, 88.8, 41.0; IR (KBr): $\tilde{\nu}$ = 3055, 3030, 3013, 2922, 2851, 1550, 1442, 1373, 1223, 1172, 1090, 1007, 960, 808, 767, 748, 700 cm-1; HR-MS (ESI-TOF): m/z calculated for $C_{21}H_{16}O_2SNINa$ $[M + Na]^+$: 495.9839, found: 495.9837.

***N-(4-(tert-butyl)phenyl)-N-(4-(phenylethynyl)phenyl)benzenesulfonamide (5c)*:** R_f = 0.45 (hexane:ethyl acetate 9:1); white solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.33 (d, *J* = 8 Hz, 1H), 7.51-7.45 (m, 5H), 7.32-7.28 (m, 5H), 7.24-7.19 (m, 5H), 7.11-7.09 (m, 2H), 1.35 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.6, 138.5, 136.9, 135.4, 133.5, 132.9, 132.2, 131.0, 130.1, 130.0, 128.8, 128.5, 128.3, 127.4, 127.1, 127.0, 125.1, 123.4, 116.1, 115.8, 34.8, 31.7; IR (KBr): $\tilde{\nu}$ = 3062, 2962, 2867, 1604, 1584, 1460, 1334, 1292, 1230, 1144, 1071, 1009, 996,

864, 793, 725, 704, 686 cm-1; HR-MS (ESI-TOF): m/z calculated for $C_{30}H_{28}NO_2S$ $[M + H]^+$: 466.1835, found: 466.1813.

N-(4-bromophenyl)-N-(4-(phenylethynyl)phenyl)acetamide (5d): R_f = 0.45 (hexane:ethyl acetate 9:1); white solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.5-7.51 (m, 6H), 7.35-7.34 (m, 3H), 7.22 (d, *J* = 4 Hz, 2H), 7.15-7.13 (m, 2H), 2.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.5, 170.2, 167.8, 162.0, 160.6, 142.4, 141.7, 138.7, 132.7, 131.7, 128.5, 127.7, 122.9, 101.1, 88.4, 24.0.

4.5 Notes and References

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^{1}H and ^{13}C NMR Spectra of selected compounds

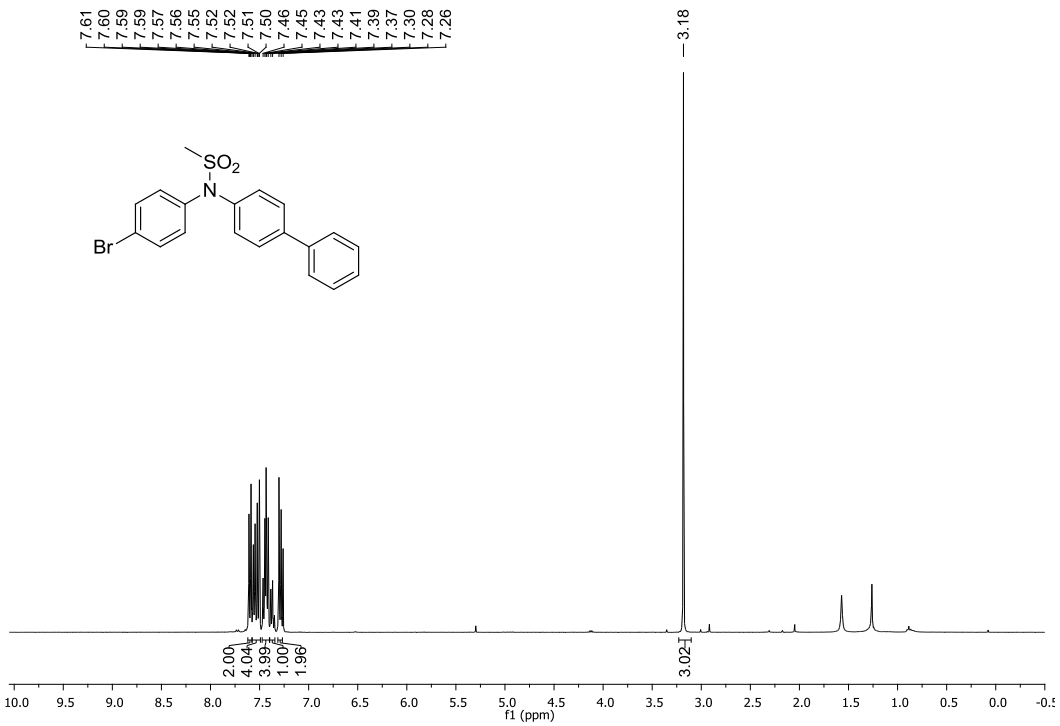


Figure 4.6 ^{1}H NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(4-bromophenyl)methanesulfonamide **(3a)**

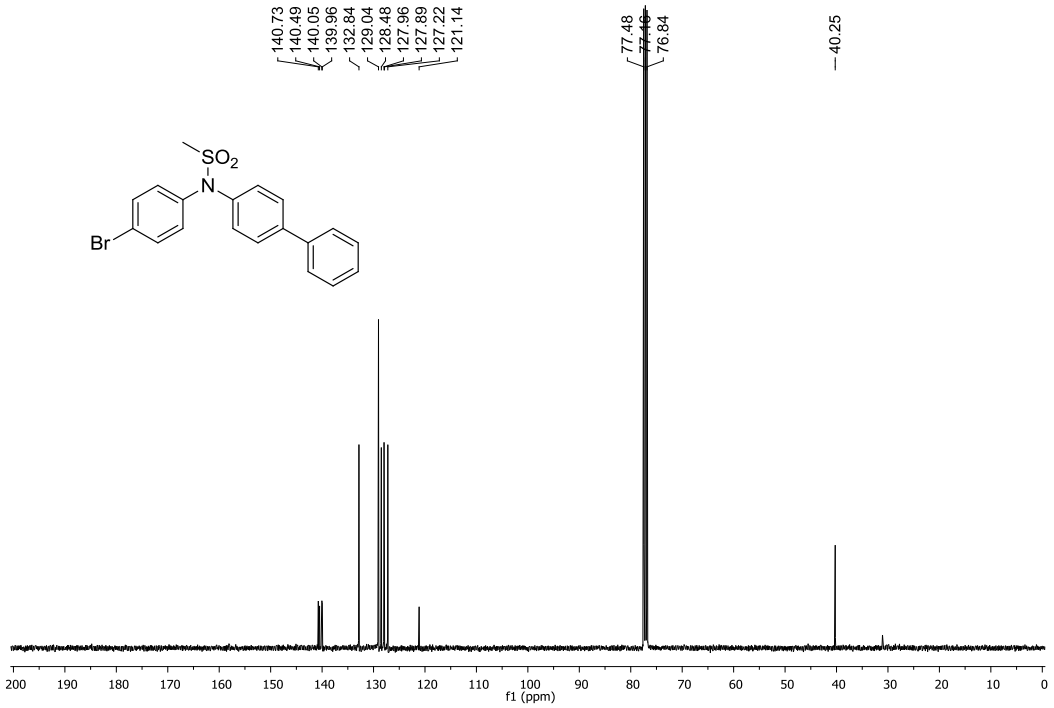


Figure 4.7 ^{13}C NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(4-bromophenyl)methanesulfonamide **(3a)**

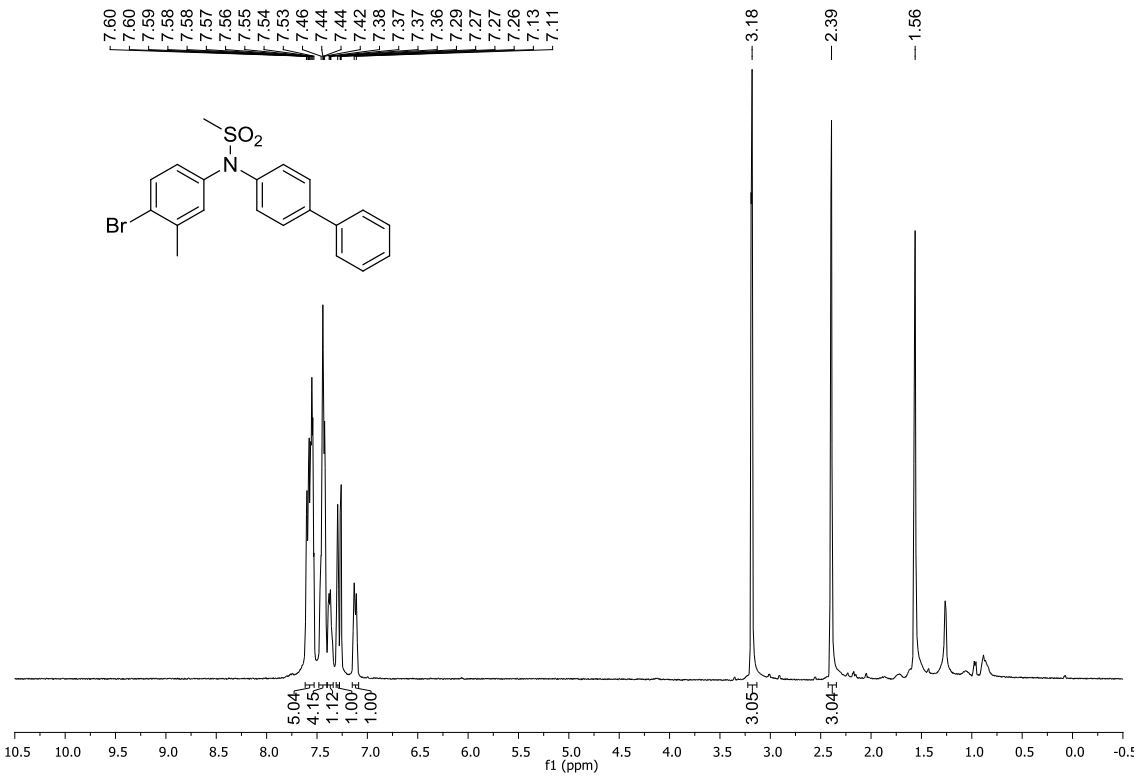


Figure 4.8 ^{1}H NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(4-bromo-3-methylphenyl)methanesulfonamide **(3b)**

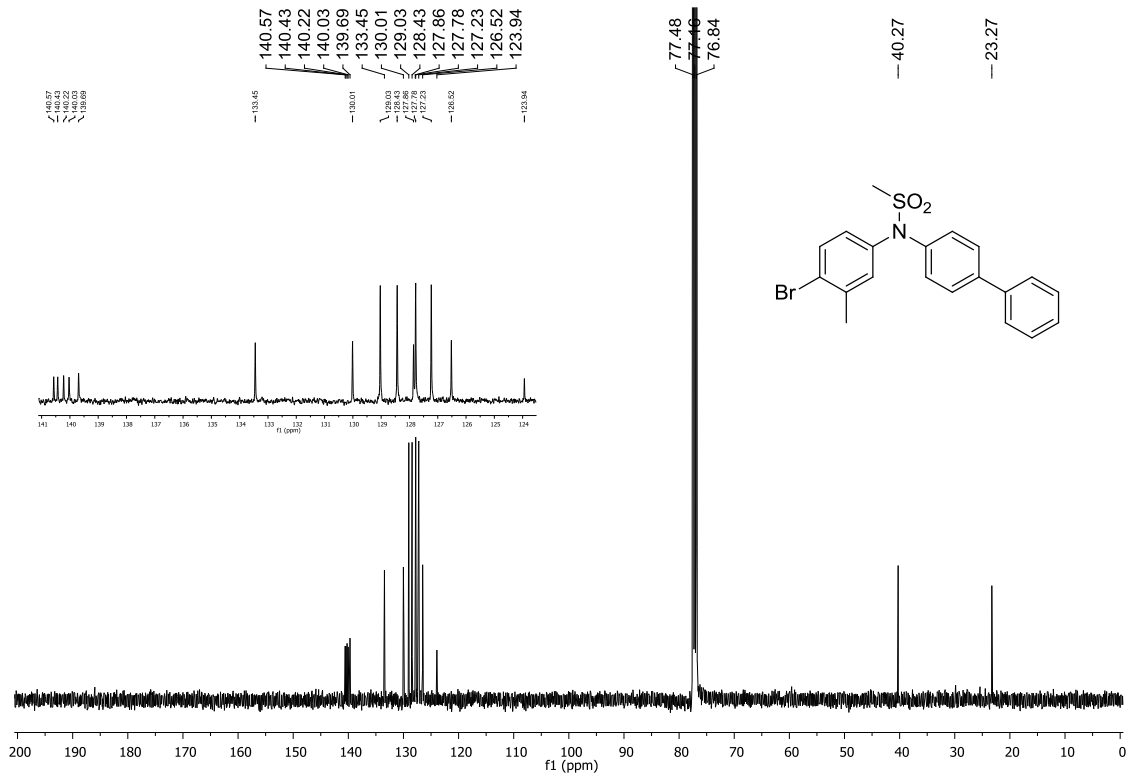


Figure 4.9 ^{13}C NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(4-bromo-3-methylphenyl)methanesulfonamide **(3b)**

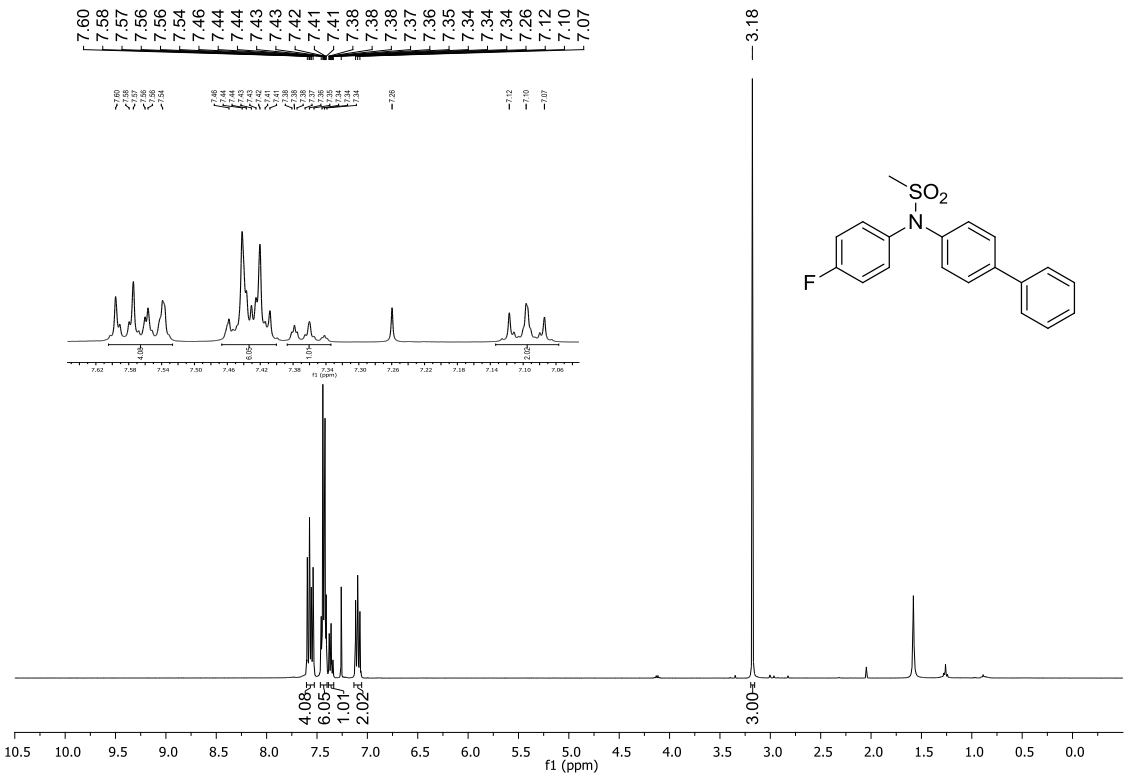


Figure 4.14 ^{1}H NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(4-fluorophenyl)methanesulfonamide **(3e)**

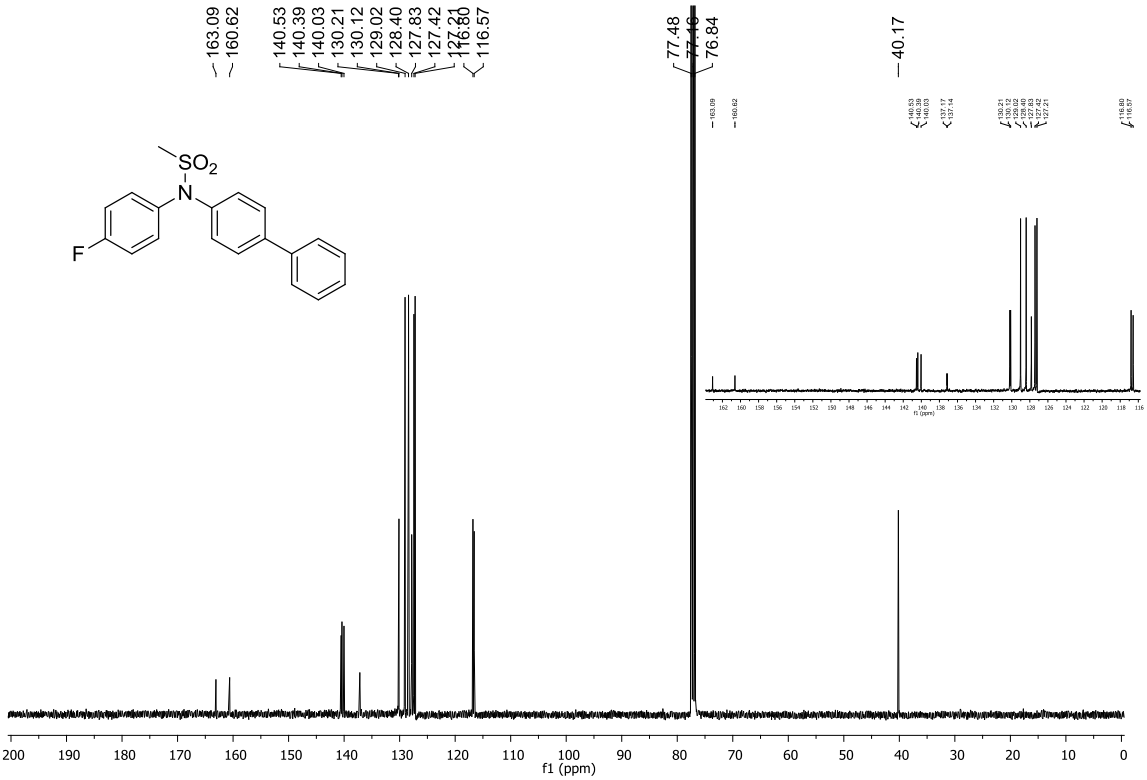


Figure 4.15 ^{13}C NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(4-fluorophenyl)methanesulfonamide **(3e)**

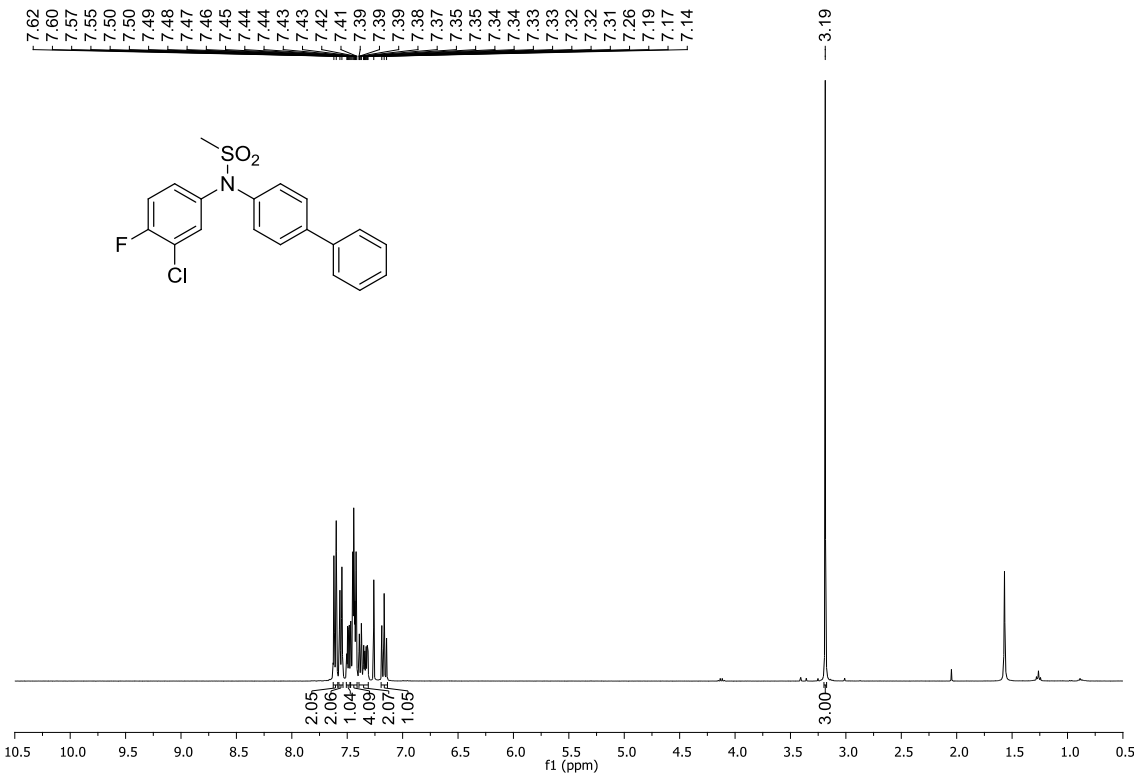


Figure 4.16 ^{1}H NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(3-chloro-4-fluorophenyl)methanesulfonamide **(3f)**

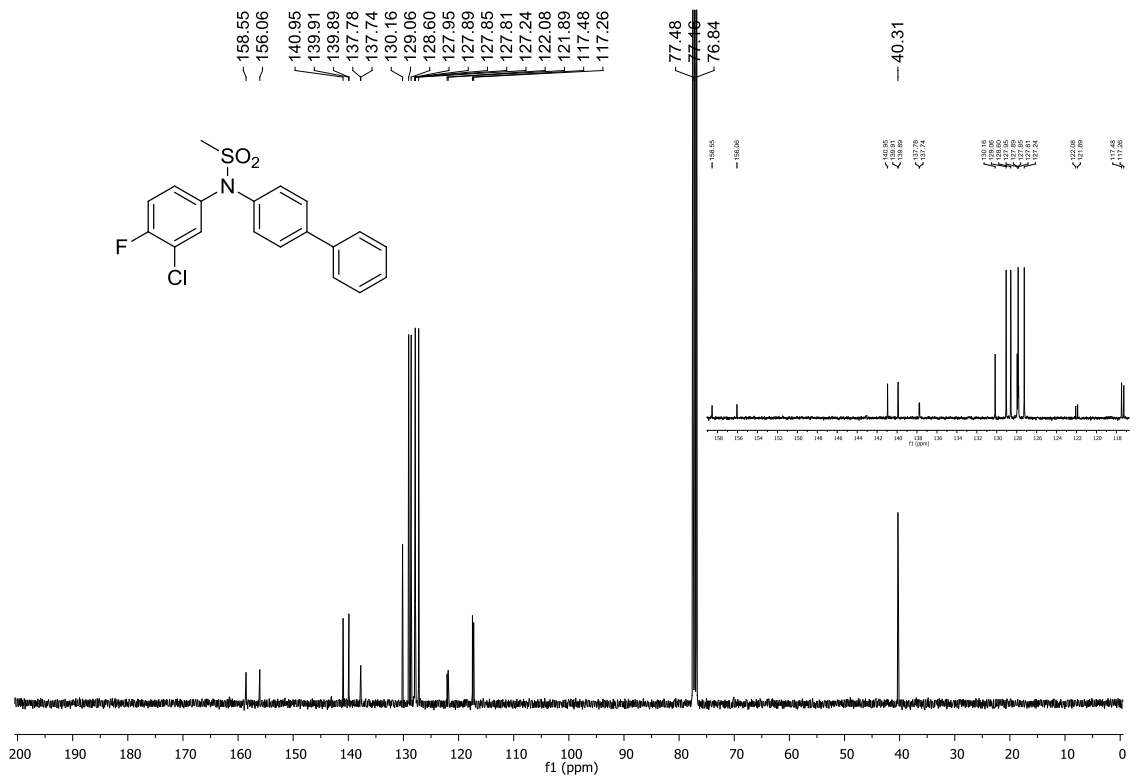


Figure 4.17 ^{13}C NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(3-chloro-4-fluorophenyl)methanesulfonamide **(3f)**

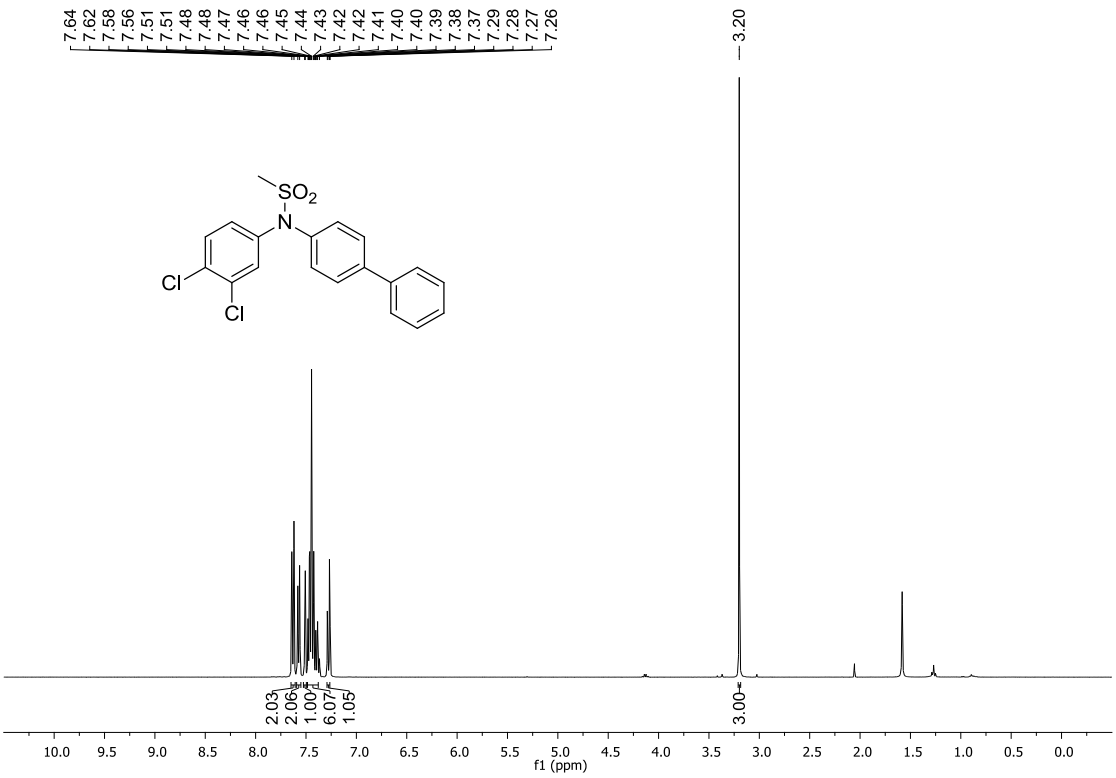


Figure 4.18 ^{1}H NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(3,4-dichlorophenyl)methanesulfonamide **(3g)**

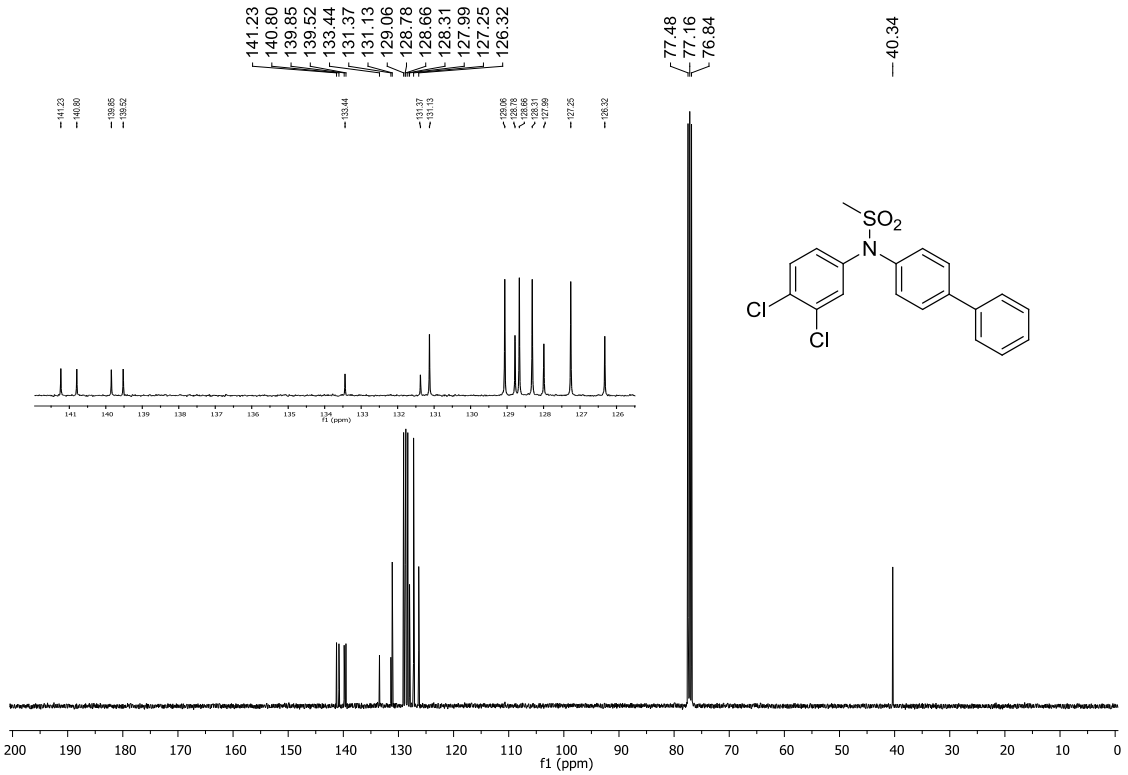


Figure 4.19 ^{13}C NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(3,4-dichlorophenyl)methanesulfonamide **(3g)**

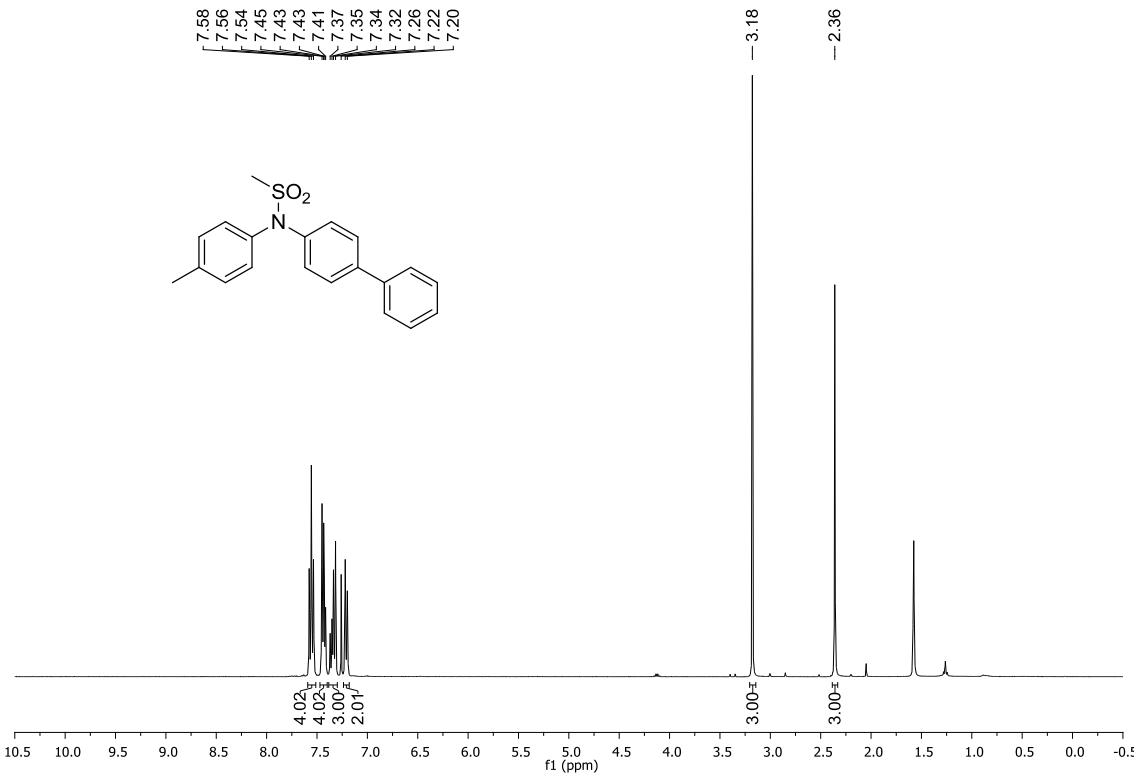


Figure 4.20 ^{1}H NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(p-tolyl)methanesulfonamide **(3h)**

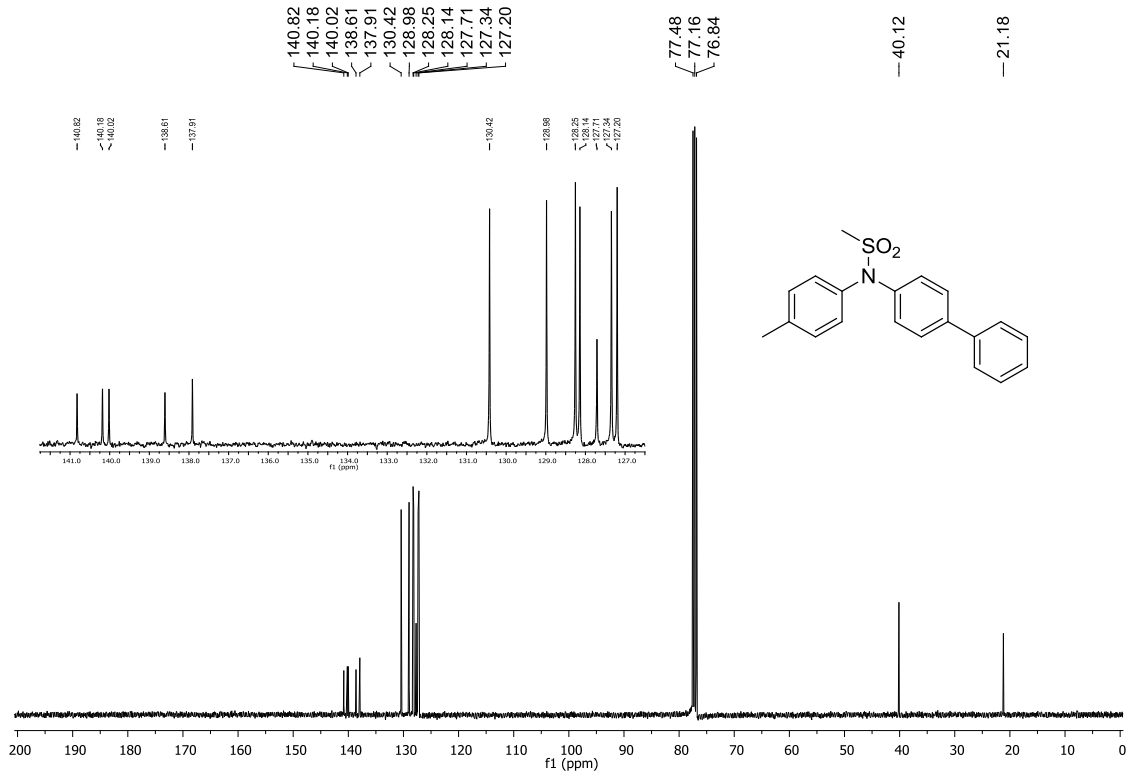


Figure 4.21 ^{13}C NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(p-tolyl)methanesulfonamide **(3h)**

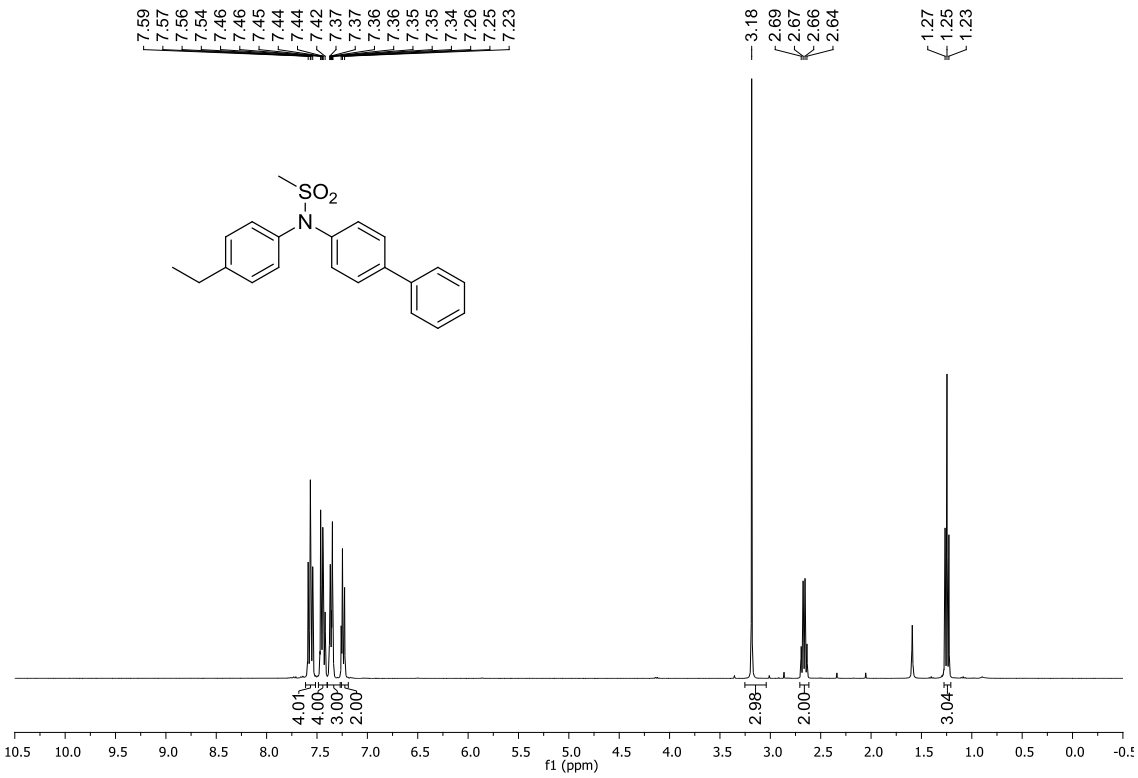


Figure 4.22 ^{1}H NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(4-ethylphenyl)methanesulfonamide **(3i)**

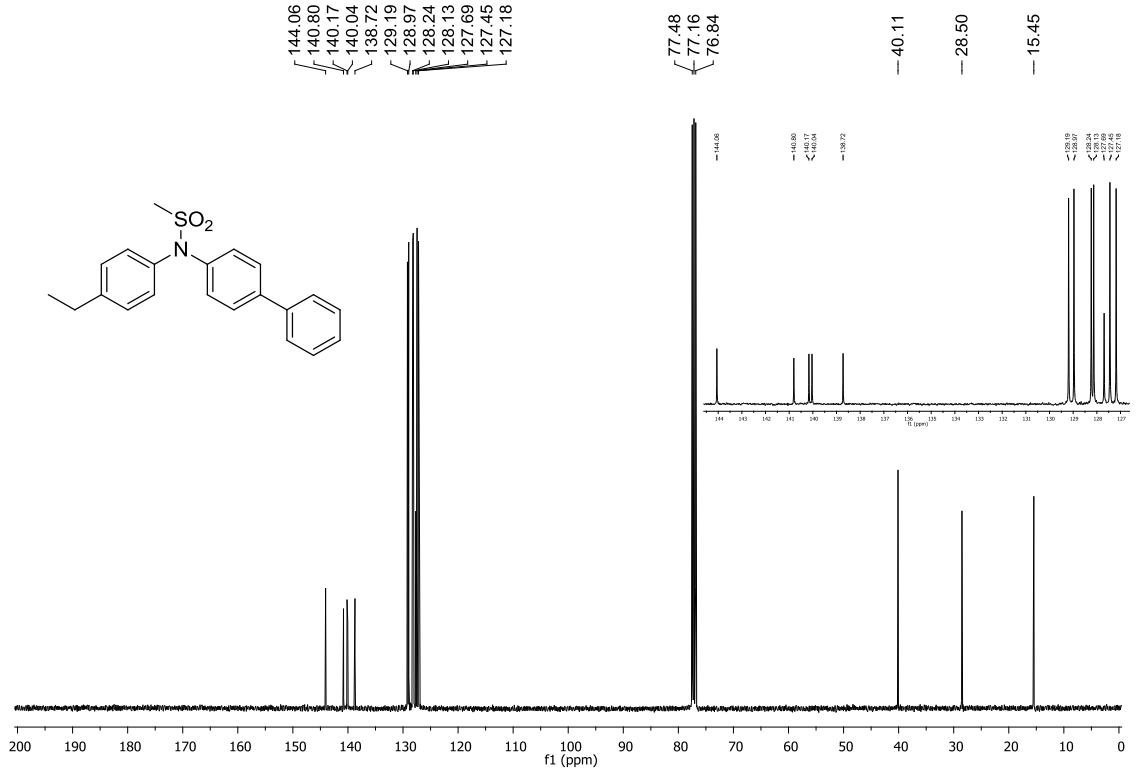


Figure 4.23 ^{13}C NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(4-ethylphenyl)methanesulfonamide **(3i)**

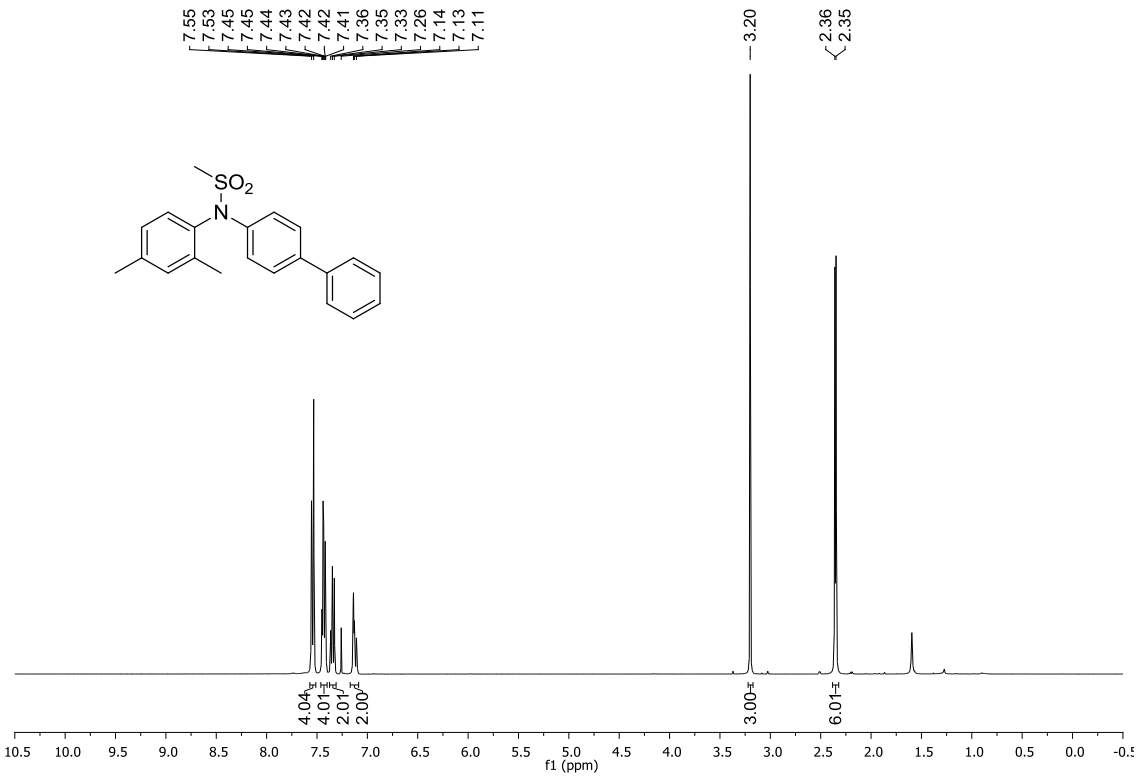


Figure 4.24 ^{1}H NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(2,4-dimethylphenyl)methanesulfonamide **(3j)**

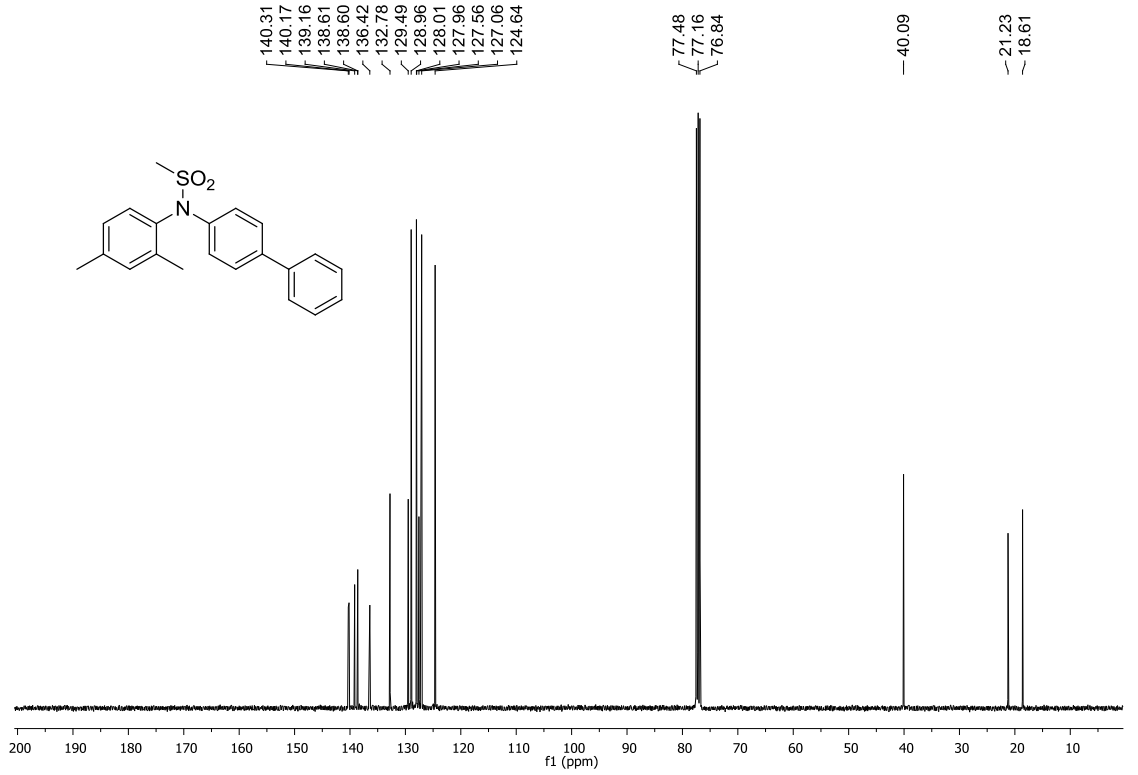


Figure 4.25 ^{13}C NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(2,4-dimethylphenyl)methanesulfonamide **(3j)**

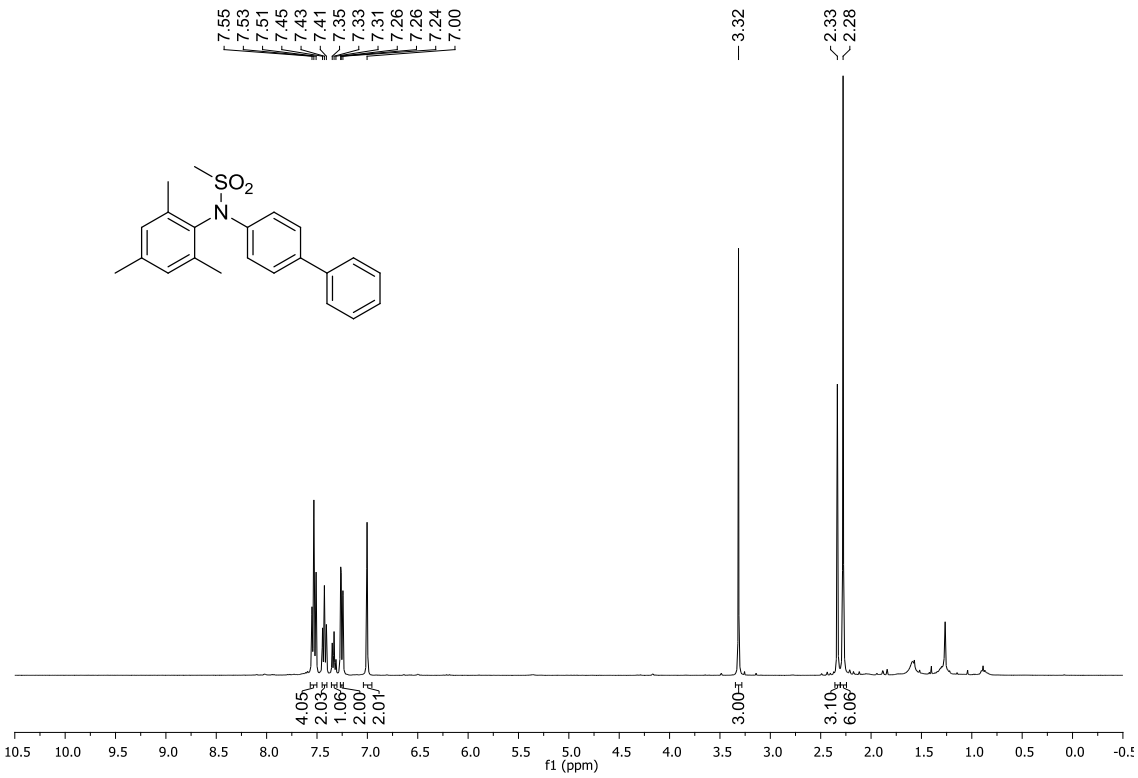


Figure 4.26 ^{1}H NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-mesitylmethanesulfonamide **(3k)**

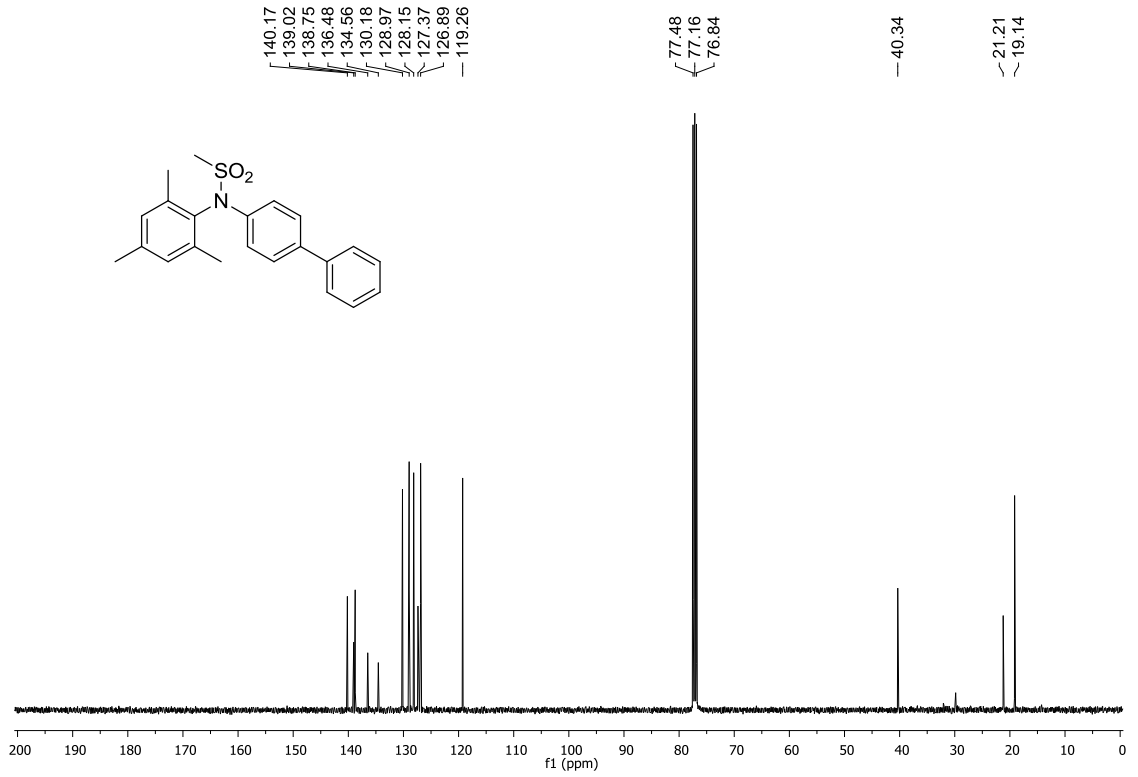


Figure 4.27 ^{1}H NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-mesitylmethanesulfonamide **(3k)**

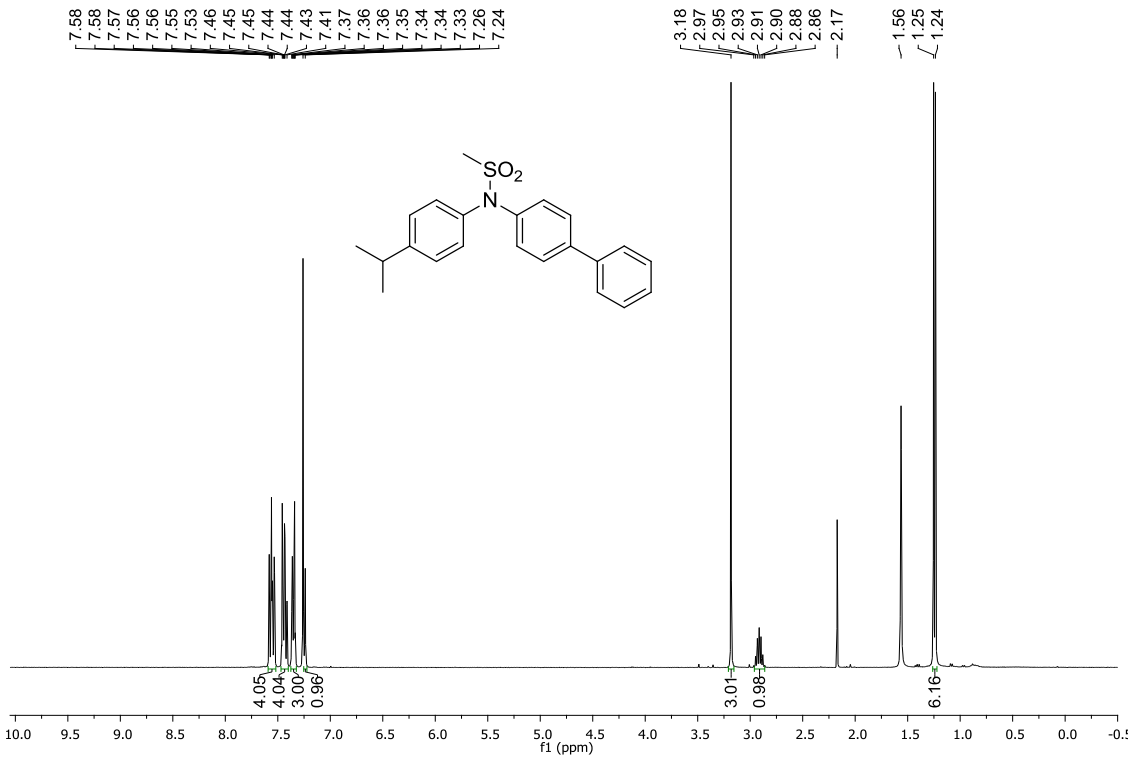


Figure 4.28 ^{1}H NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(4-isopropylphenyl)methanesulfonamide **(3l)**

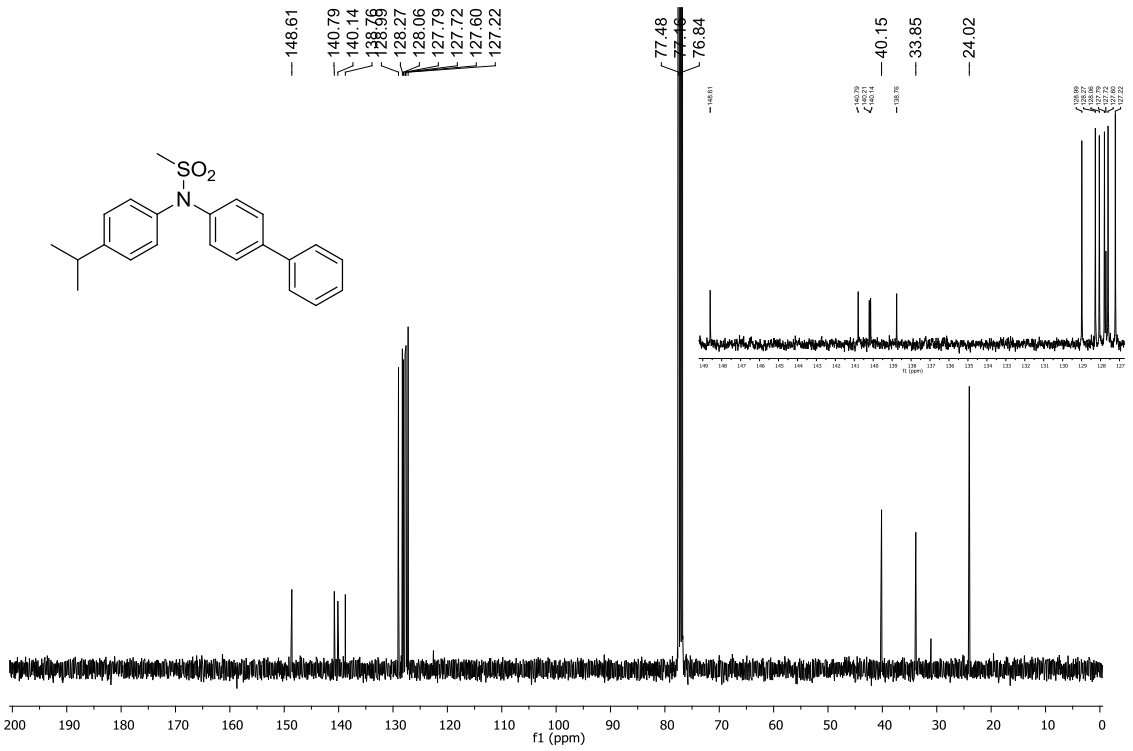


Figure 4.29 ^{13}C NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(4-isopropylphenyl)methanesulfonamide **(3l)**

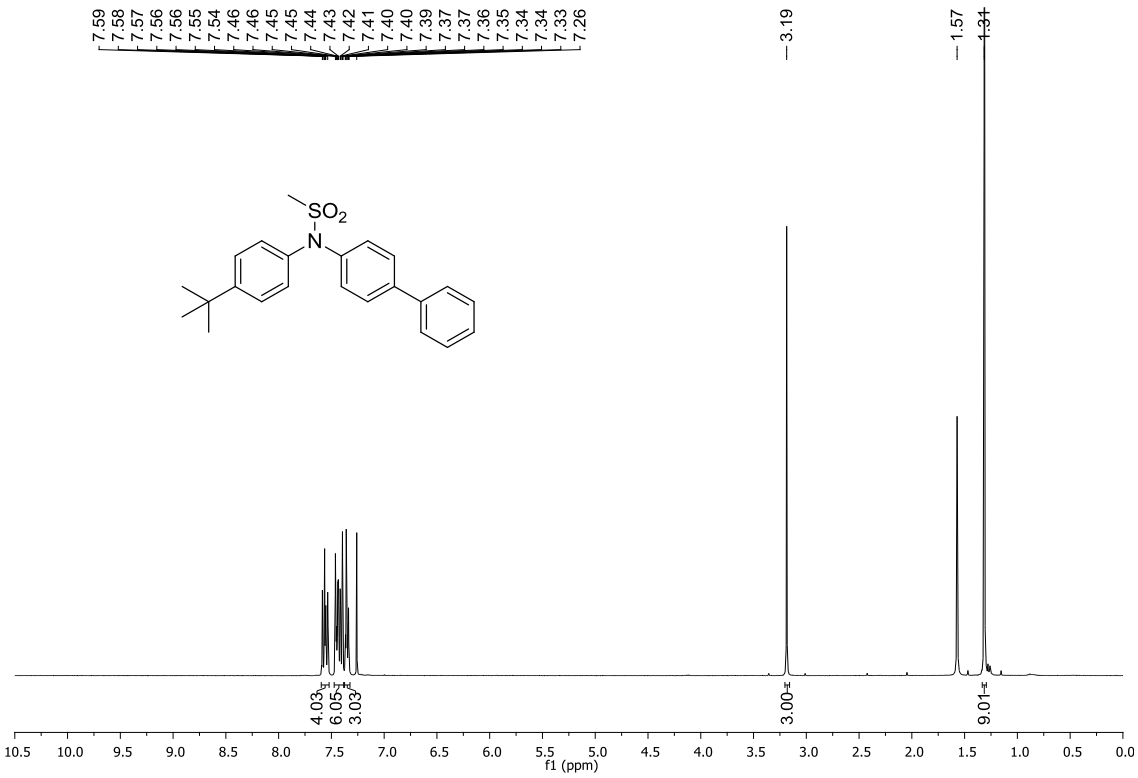


Figure 4.30 ^{1}H NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(4-(tert-butyl)phenyl)methanesulfonamide **(3m)**

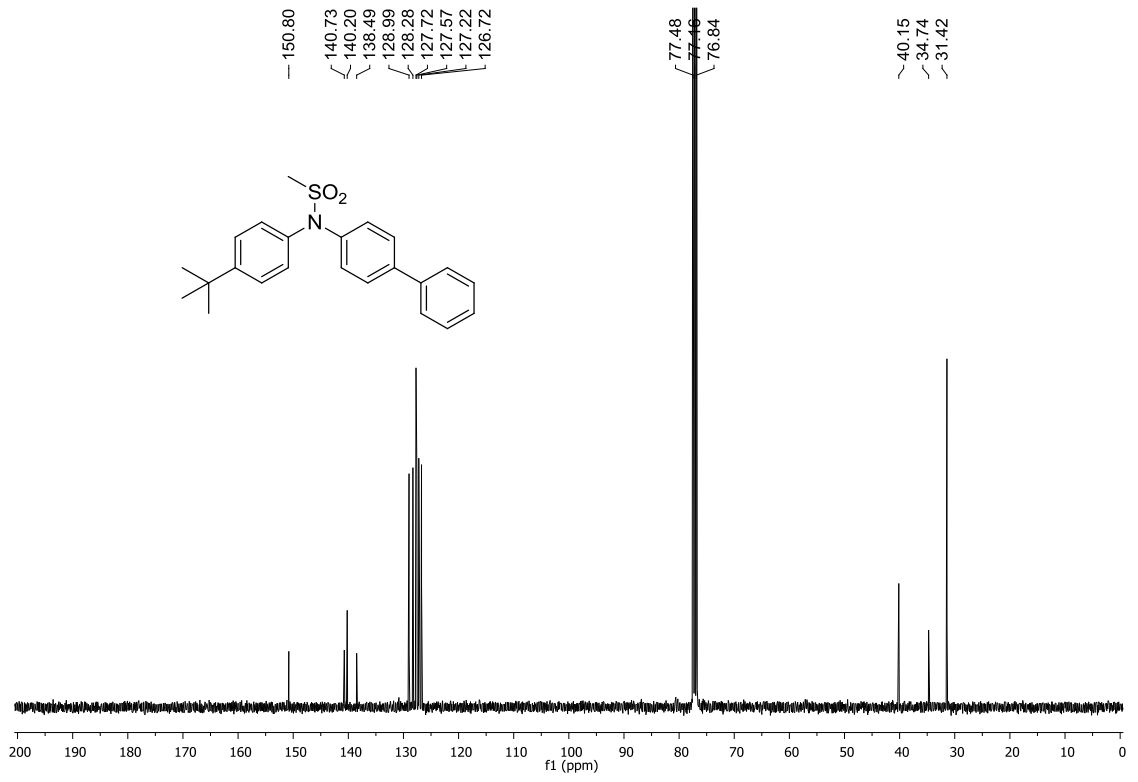


Figure 4.31 ^{13}C NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(4-(tert-butyl)phenyl)methanesulfonamide **(3m)**

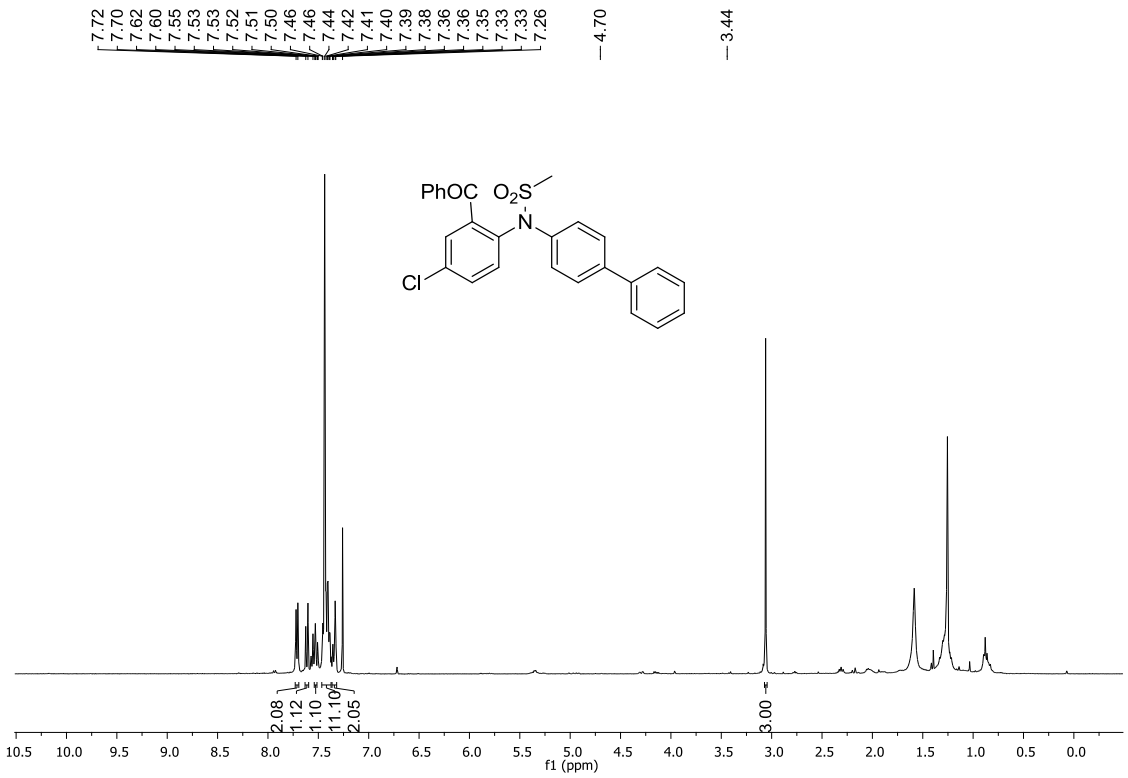


Figure 4.32 ^{1}H NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(2-benzoyl-4-chlorophenyl)methanesulfonamide **(3n)**

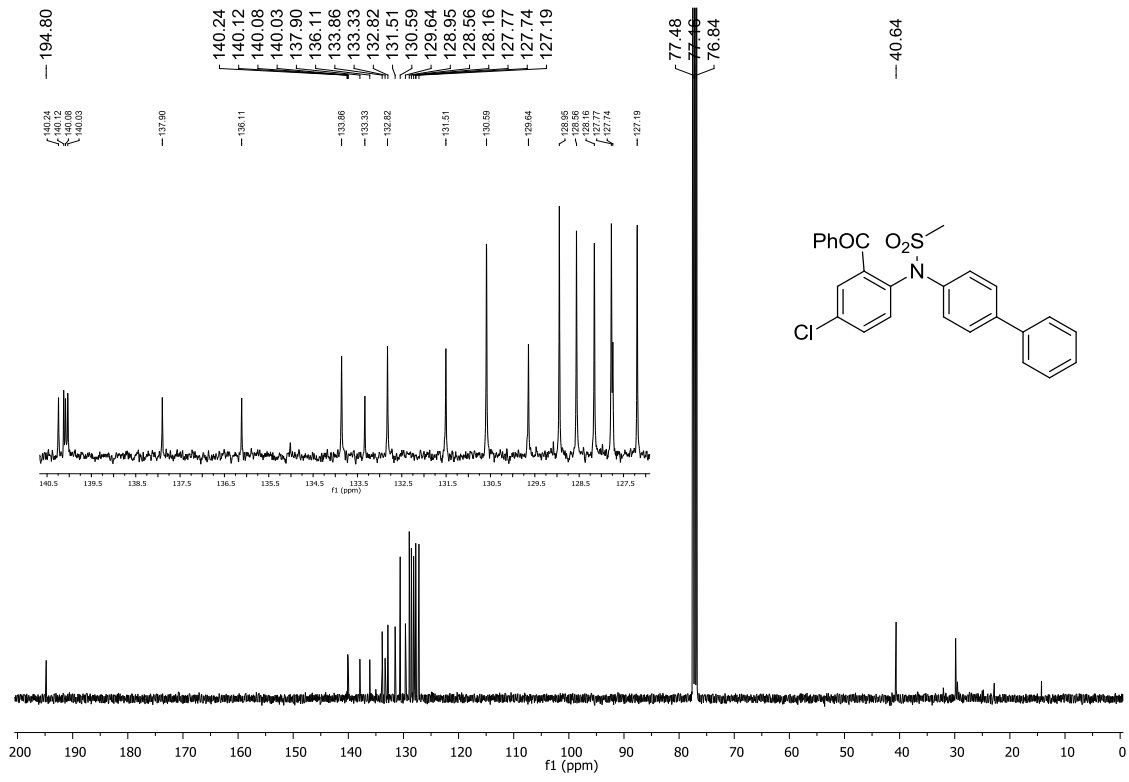


Figure 4.33 ^{13}C NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(2-benzoyl-4-chlorophenyl)methanesulfonamide **(3n)**

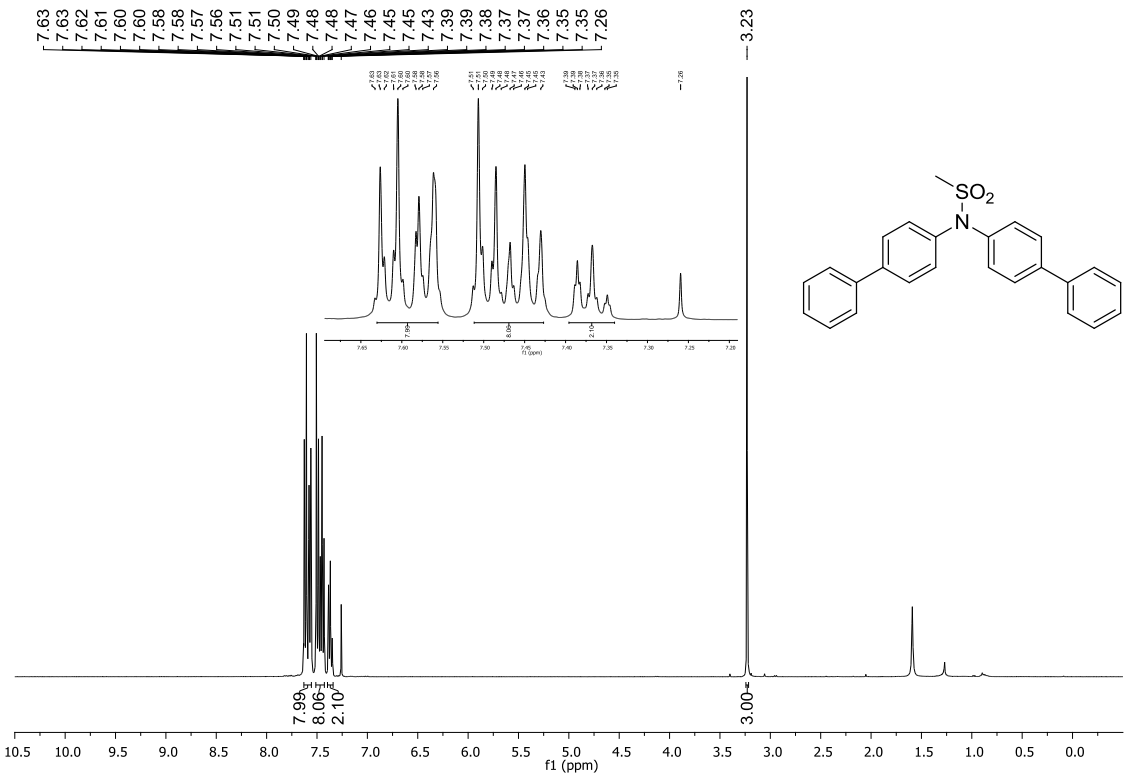


Figure 4.34 ^{1}H NMR spectrum of N,N-di([1,1'-biphenyl]-4-yl)methanesulfonamide **(3o)**

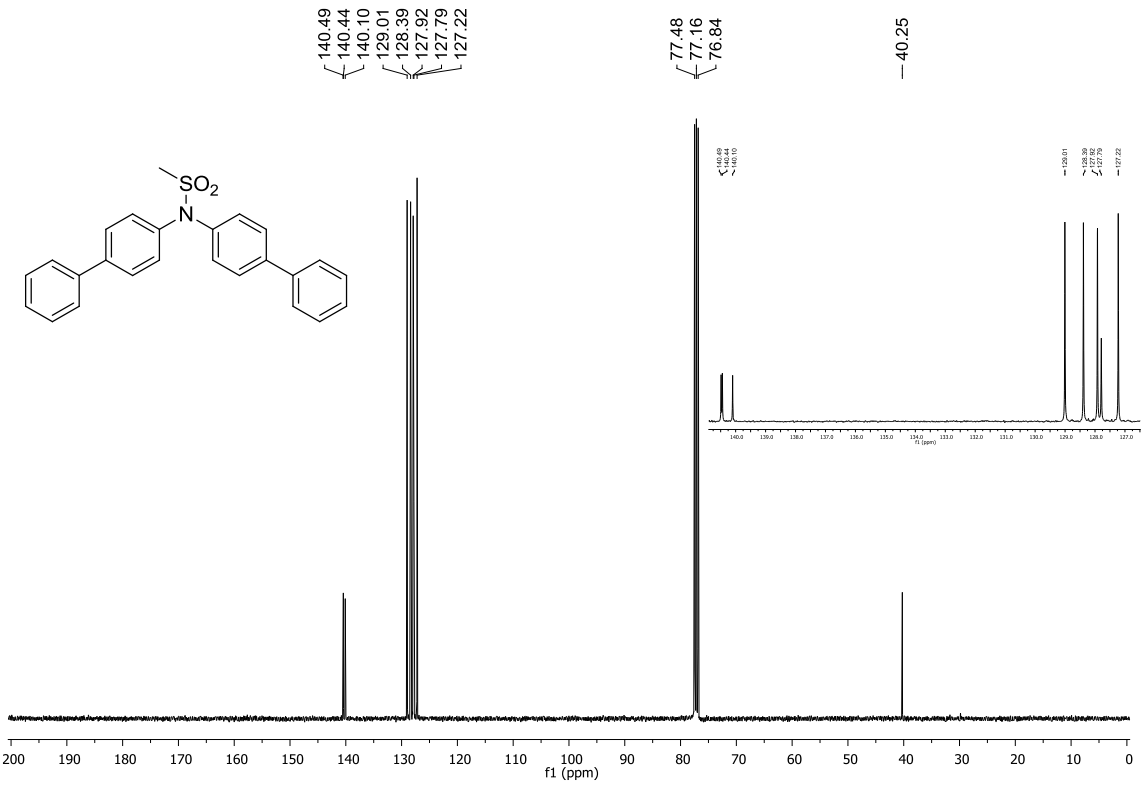


Figure 4.35 ^{13}C NMR spectrum of N,N-di([1,1'-biphenyl]-4-yl)methanesulfonamide **(3o)**

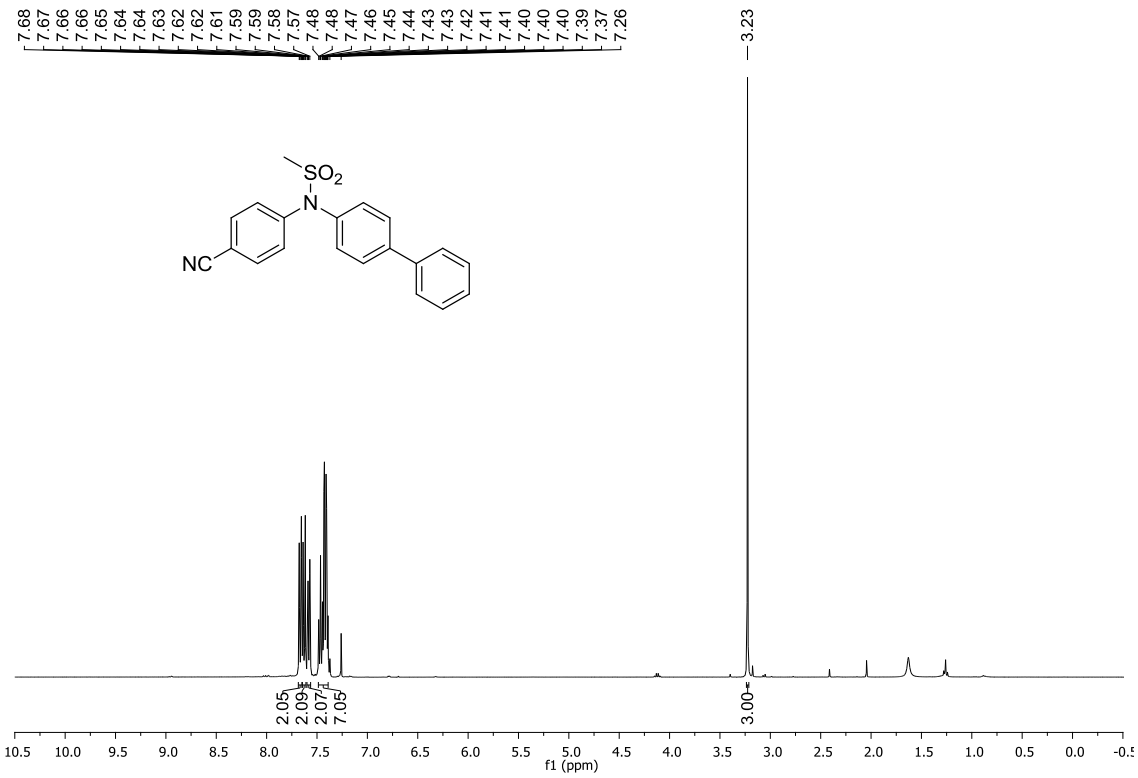


Figure 4.36 ^{1}H NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(4-cyanophenyl)methanesulfonamide **(3p)**

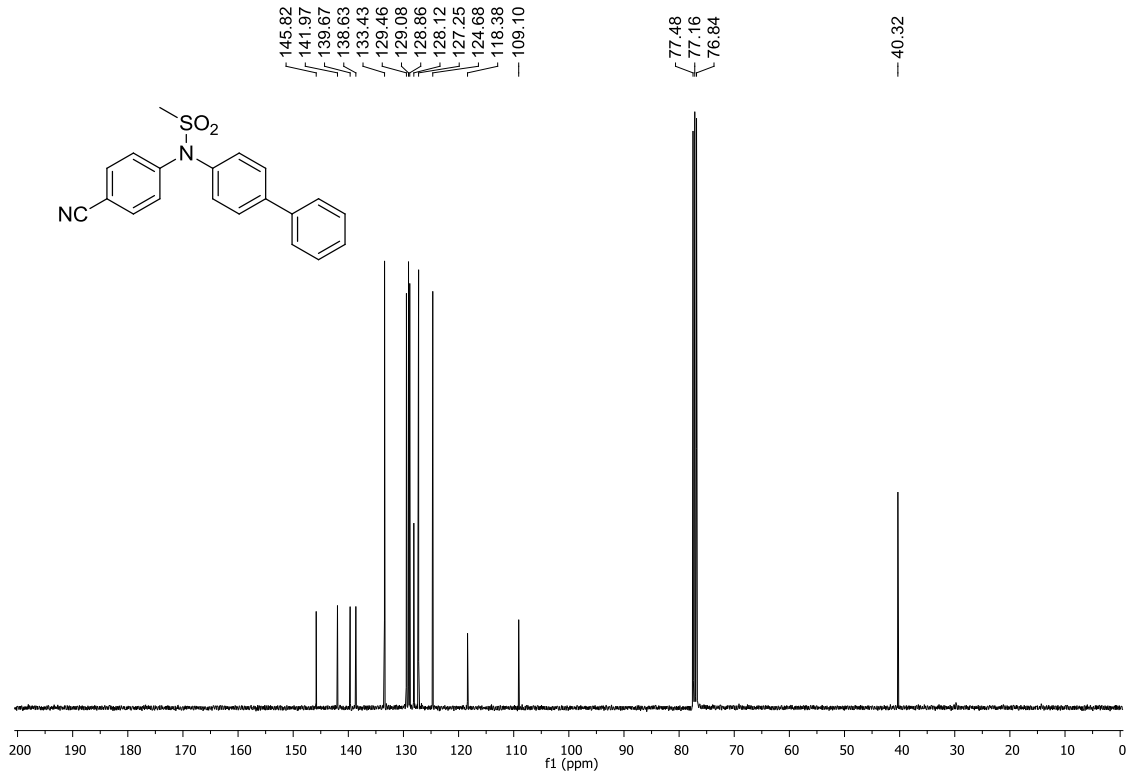


Figure 4.37 ^{13}C NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(4-cyanophenyl)methanesulfonamide **(3q)**

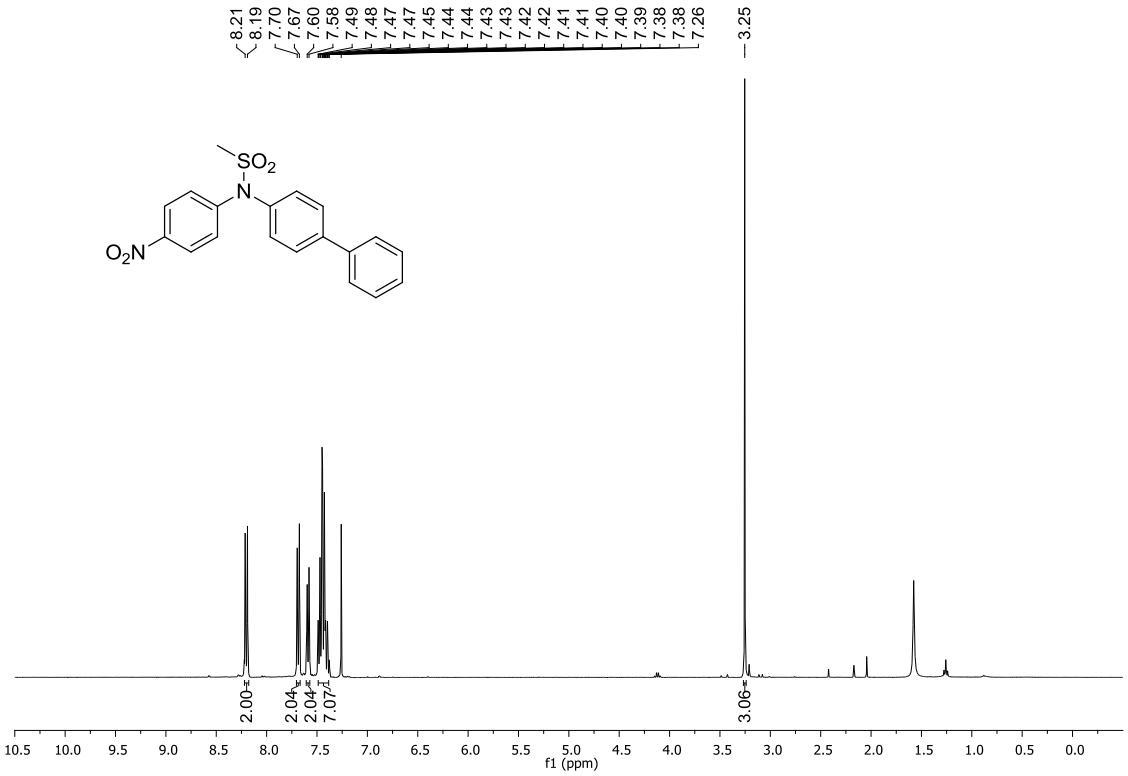


Figure 4.38 ^{1}H NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(4-nitrophenyl)methanesulfonamide **(3q)**

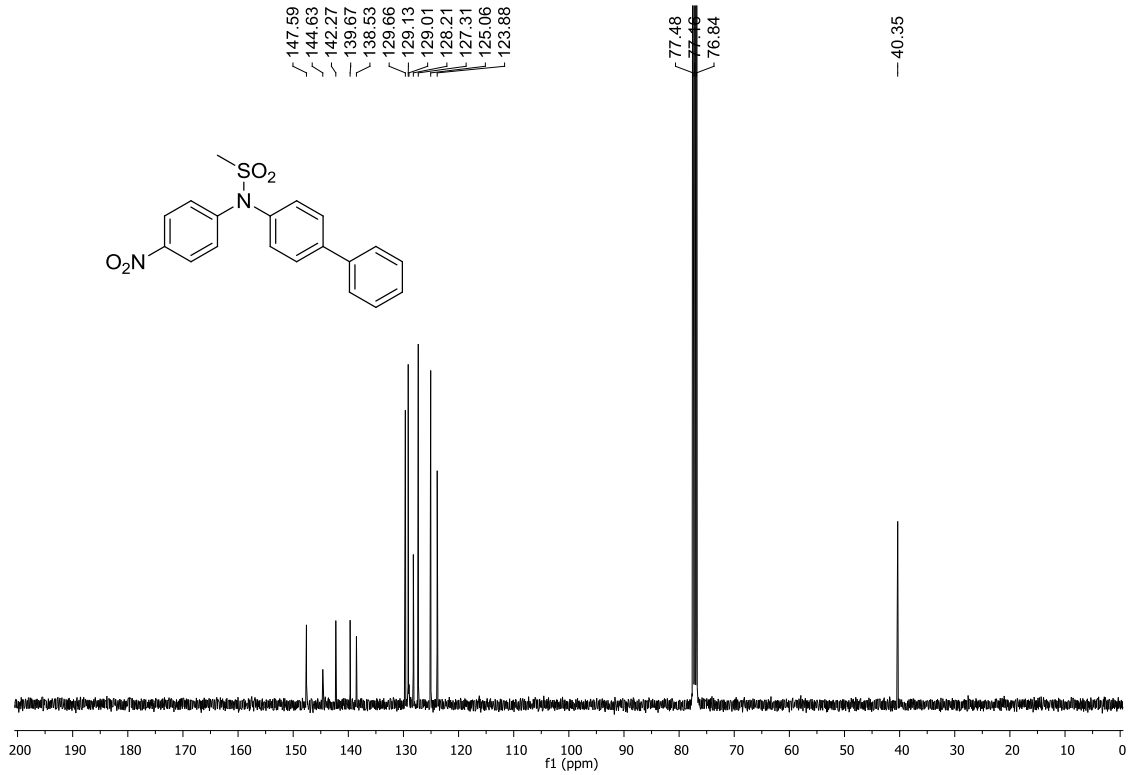


Figure 4.39 ^{13}C NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(4-nitrophenyl)methanesulfonamide **(3q)**

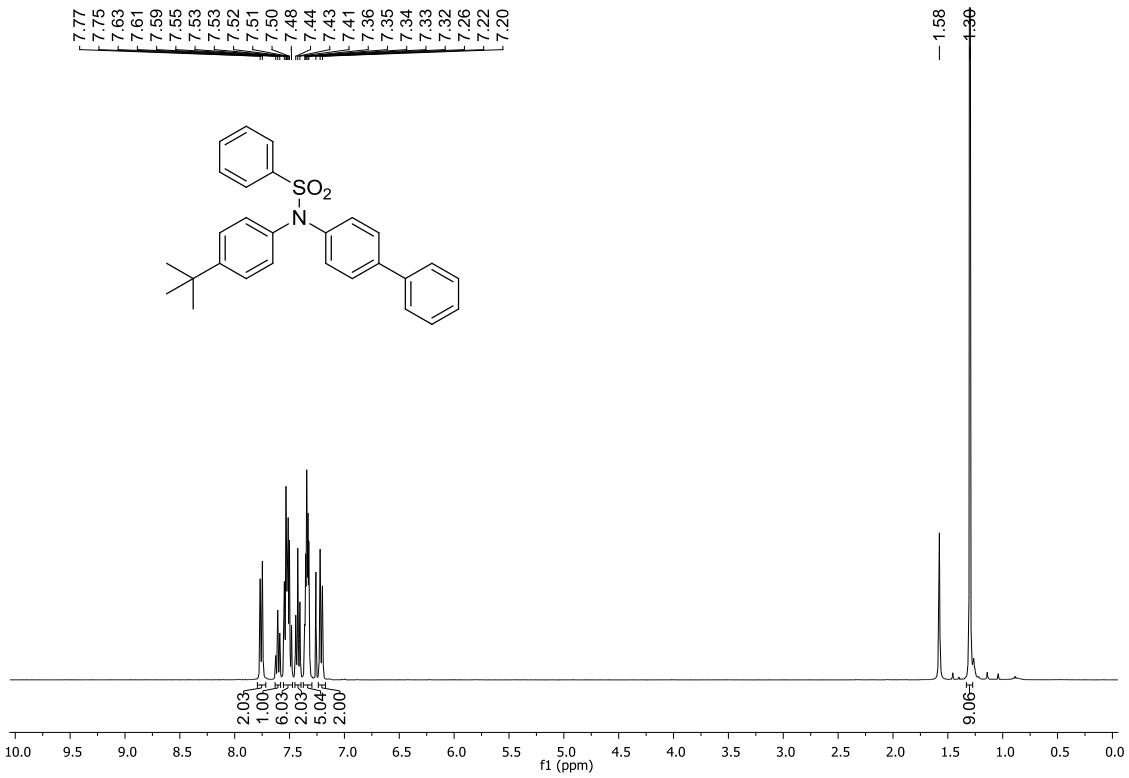


Figure 4.42 ^{1}H NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(4-(tert-butyl)phenyl)benzenesulfonamide **(3s)**

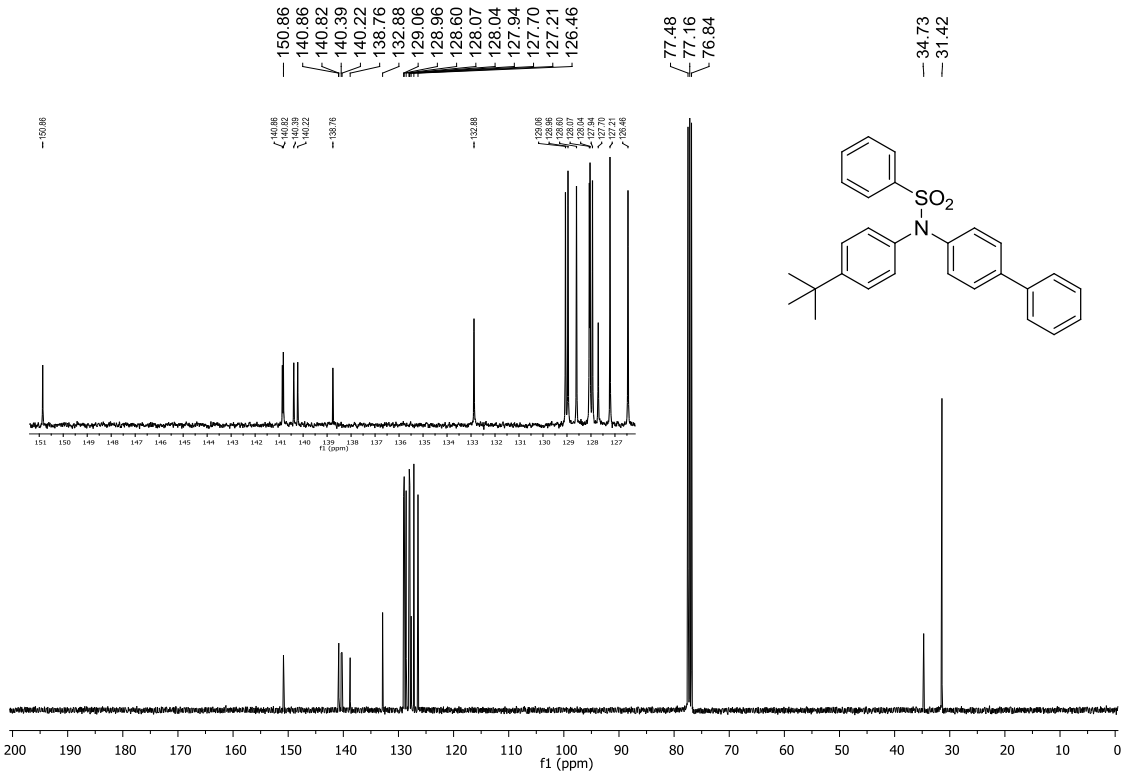


Figure 4.43 ^{13}C NMR spectrum of N-([1,1'-biphenyl]-4-yl)-N-(4-(tert-butyl)phenyl)benzenesulfonamide **(3s)**

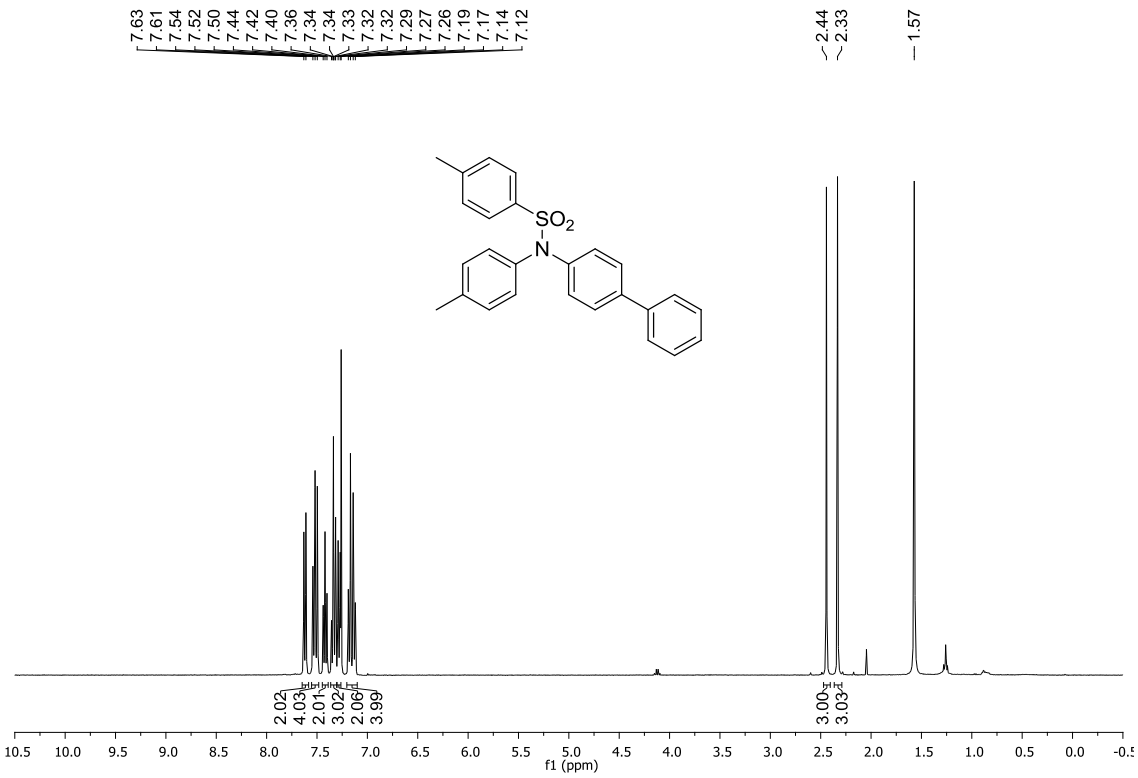


Figure 4.44 ^{1}H NMR spectrum of N-([1,1'-biphenyl]-4-yl)-4-methyl-N-(p-tolyl)benzenesulfonamide **(3t)**

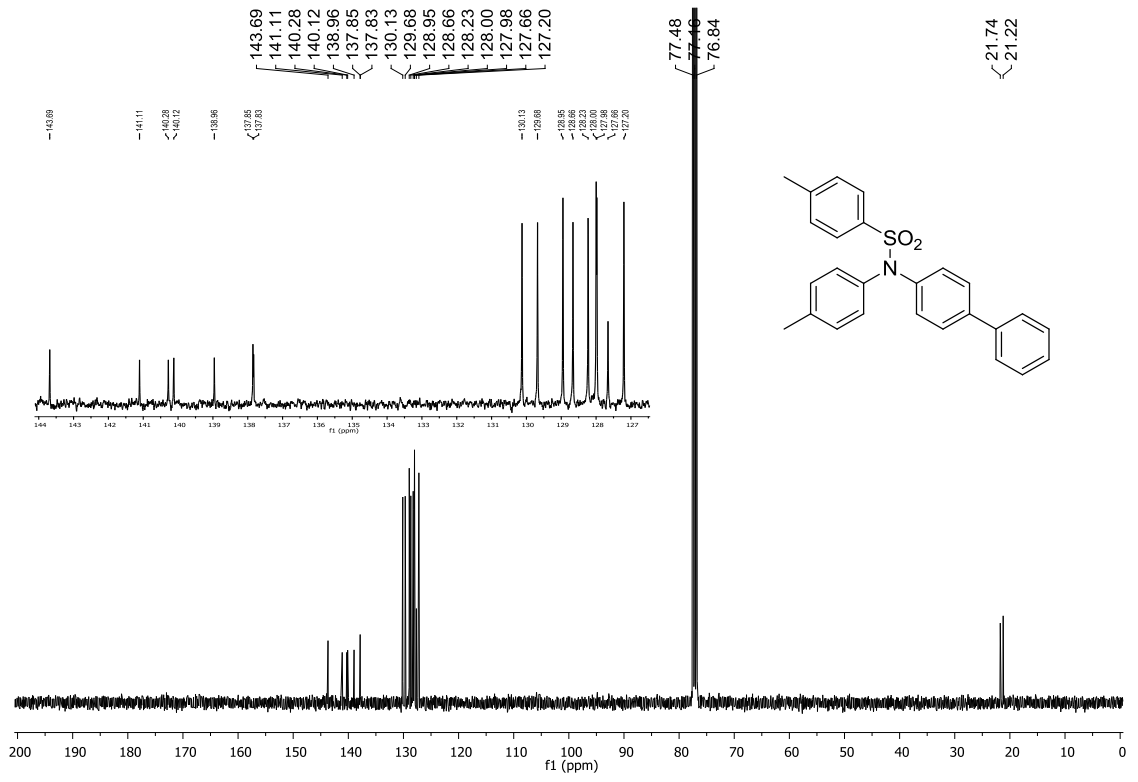


Figure 4.45 ^{13}C NMR spectrum of N-([1,1'-biphenyl]-4-yl)-4-methyl-N-(p-tolyl)benzenesulfonamide **(3t)**

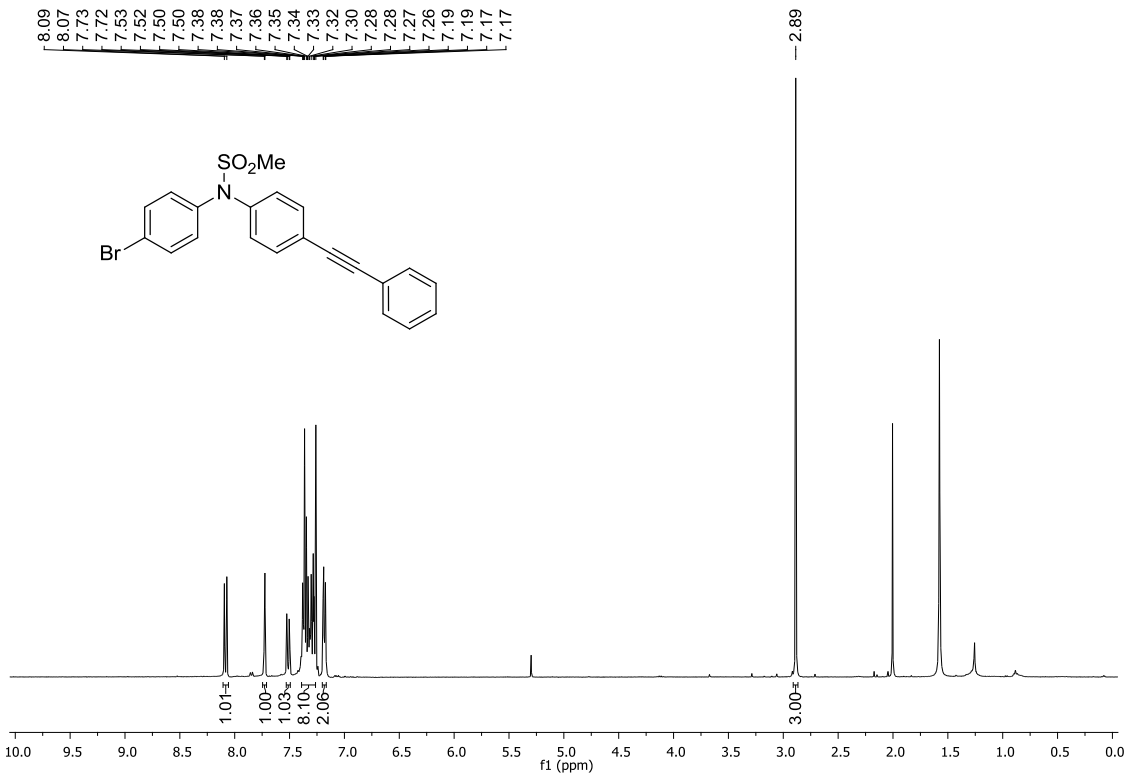


Figure 4.48 ^{1}H NMR spectrum of N-(4-bromophenyl)-N-(4-(phenylethynyl)phenyl)methanesulfonamide **(5a)**

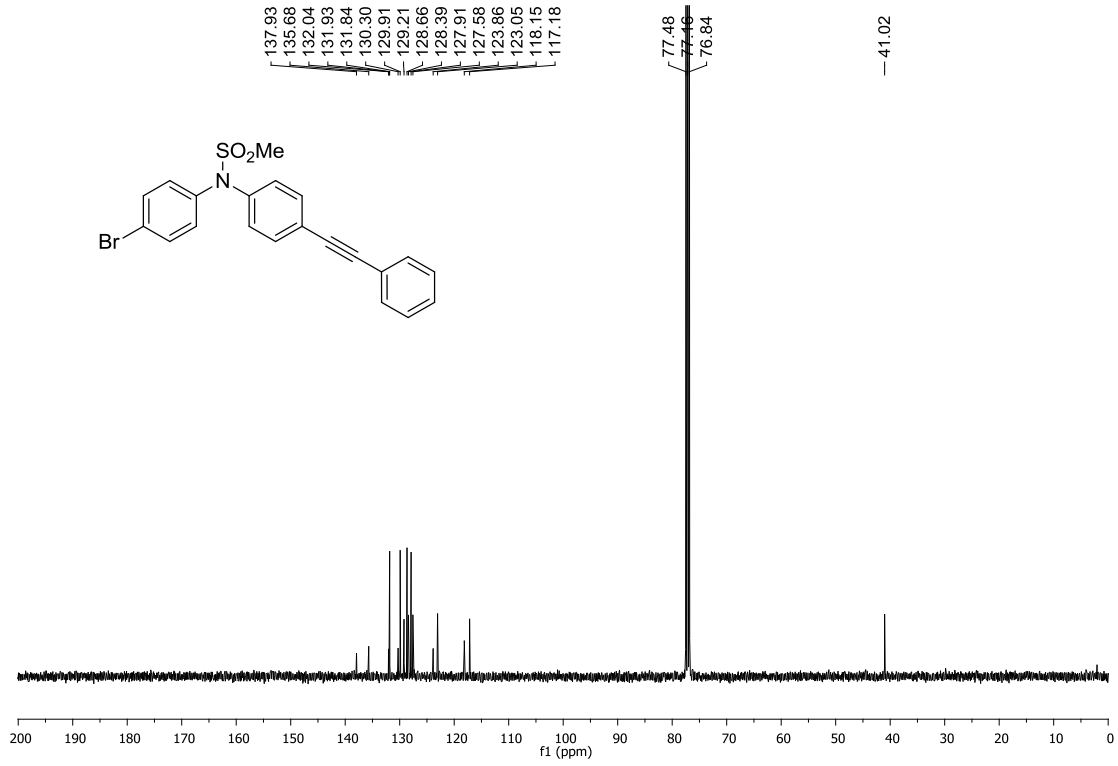


Figure 4.49 ^{13}C NMR spectrum of N-(4-bromophenyl)-N-(4-(phenylethynyl)phenyl)methanesulfonamide **(5a)**

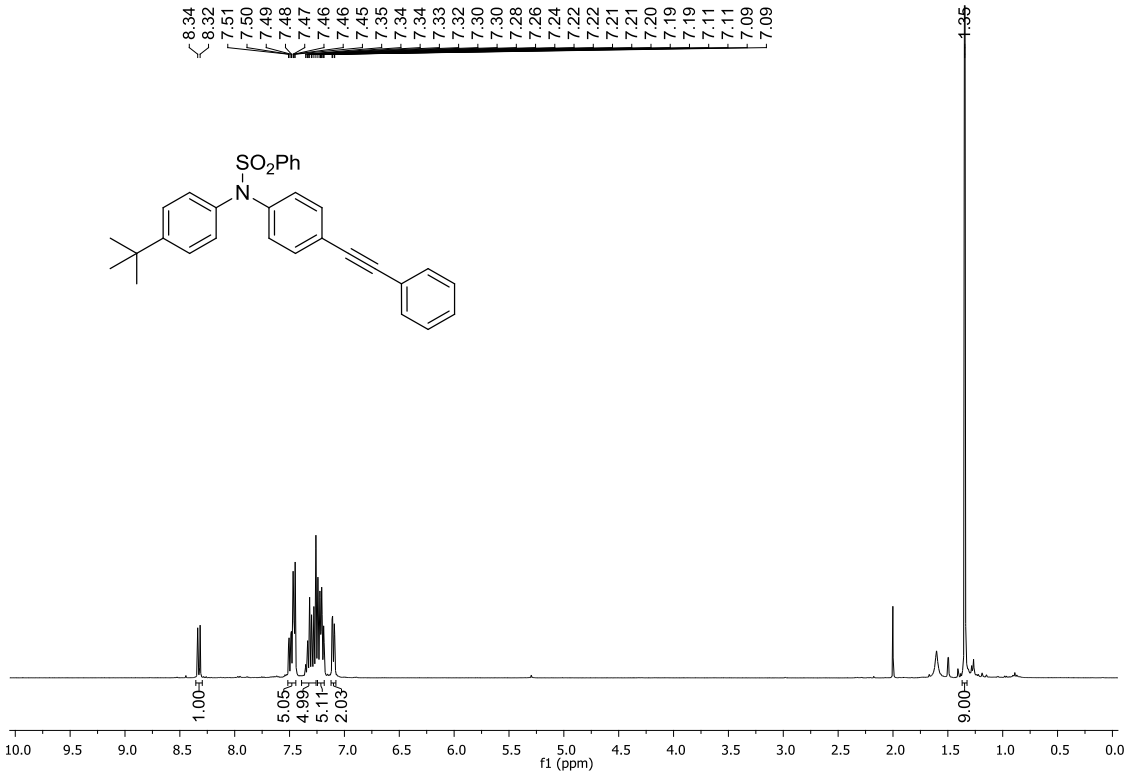


Figure 4.52 ^{1}H NMR spectrum of N-(4-(tert-butyl)phenyl)-N-(4-(phenylethynyl)phenyl)benzenesulfonamide **(5c)**

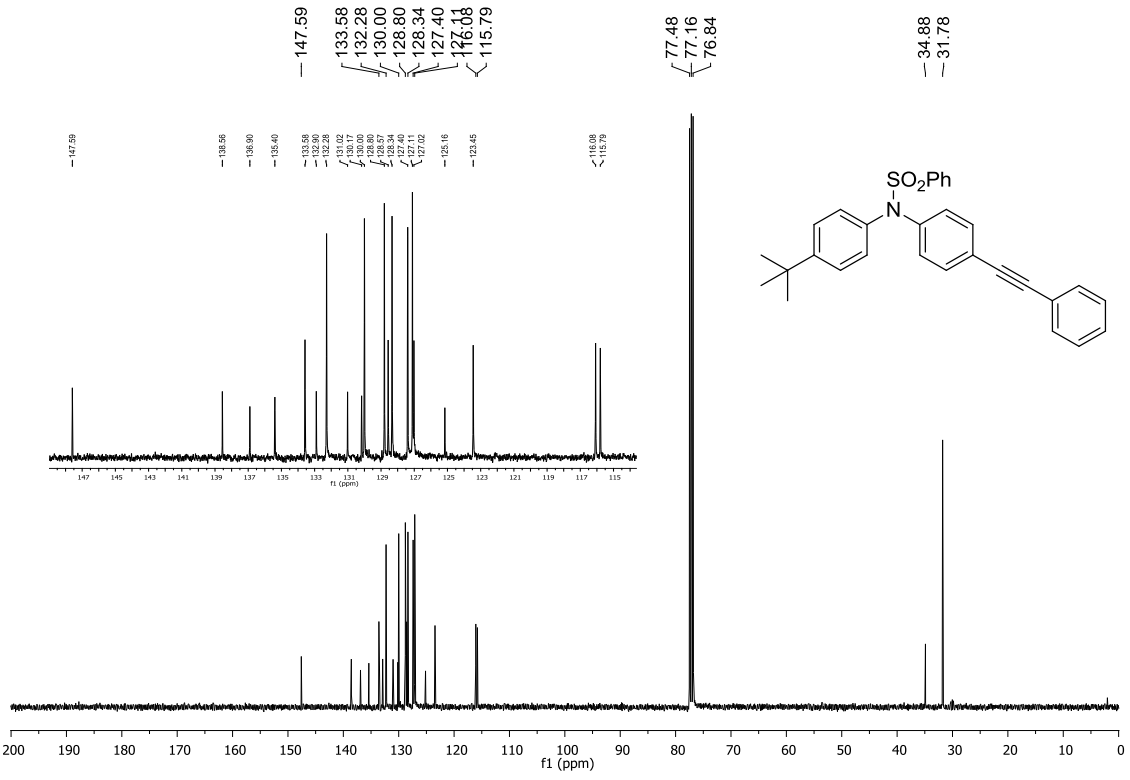
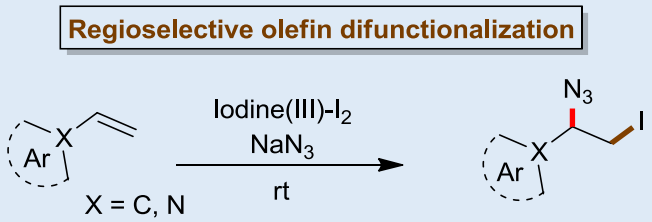


Figure 4.53 ^{13}C NMR spectrum of N-(4-(tert-butyl)phenyl)-N-(4-(phenylethynyl)phenyl)benzenesulfonamide **(5c)**

CHAPTER 5

PIDA-I_2 Mediated Vicinal Difunctionalization of Olefins

5.1 ABSTRACT



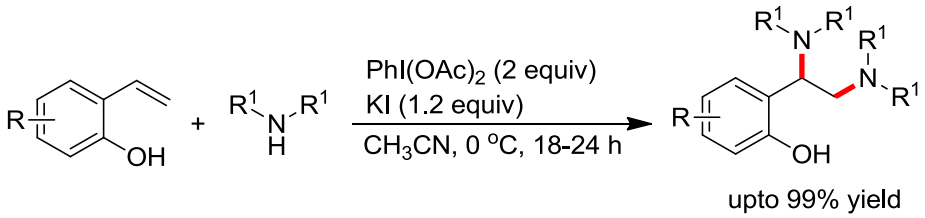
Iodinium cation (I^+ or IOAc) was produced from the combination of phenyliodine diacetate (PIDA) and iodine. I^+ facilitated the direct vicinal difunctionalization of olefins to α-azido alkyl iodides via cation–π interaction at room temperature and under transition-metal free conditions.

5.2 INTRODUCTION

The difunctionalization of olefins is one of the most attractive research areas in organic chemistry[1] and generally more difficult than that of alkynes due to the low polarizability of olefins. Metal free or metal catalyzed olefin difunctionalization reactions have recently been demonstrated as oxyarylation,[2] oxytrifluoromethylation,[3] iodotrifluoromethylation,[4] hydroxyarylation,[5] azido-oxygenation,[6] aminoazidation,[7] iodoazidation,[8] etc. Unactivated olefin difunctionalization reactions via cohalogenation are also considered for carbon heteroatom bond formation in a regio-, chemo- and stereoselective manner.[9] Selective literature reports have been discussed below which contains at least one C-N bond formation reaction.

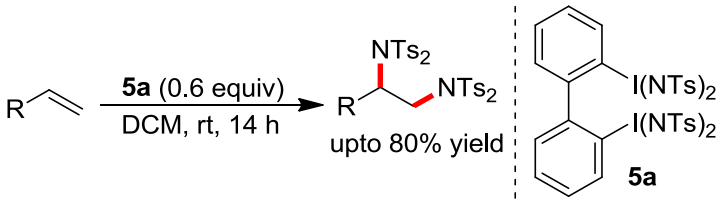
In 2015, Johnston and co-workers developed a double intermolecular diamination of hydroxyl styrenes with electron rich amines by using phenyliodine diacetate in presence of potassium

iodide (Scheme 5.1).[10] The overall transformation provides immediate access to a diverse range of vicinal diamines from commercially available amines and alkenes.



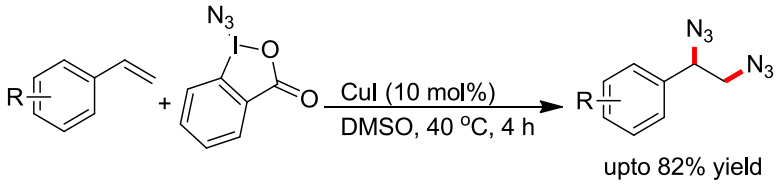
Scheme 5.1 Jonston's approach for vicinal diamination.

Kilian Muniz and co-workers have developed an intermolecular diamination reaction of alkenes with dinuclear iodine(III) reagent (**5a**) based on 2,2'-diiodobiaryl core (Scheme 5.2).[11]



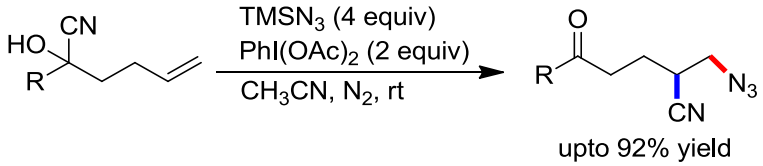
Scheme 5.2 Muniz's approach for diamination.

In synthesis, organic azides[12] have received copious amounts of attention due to their use as a precursor of *N*-containing heterocycles.[13] Owing to their stability under physiological conditions and their unique reactivity, azides are used in bioconjugation via Staudinger ligation,[14] in click chemistry etc.[15] The substitution reaction of primary or secondary alkyl halides with inorganic azides is the most common route to access alkyl azides.[16] Recently, some modified methods have been developed by several research group for azidofunctionalization of unactivated olefins. A copper(I) catalyzed vicinal diazidation of styrene has been developed by Loh and co-workers in 2015 (Scheme 5.3). Azidoiodine(III) reagent has been used as azide source for the reaction. Mechanistic investigation reveals that the transformation follows radical pathway.[17]



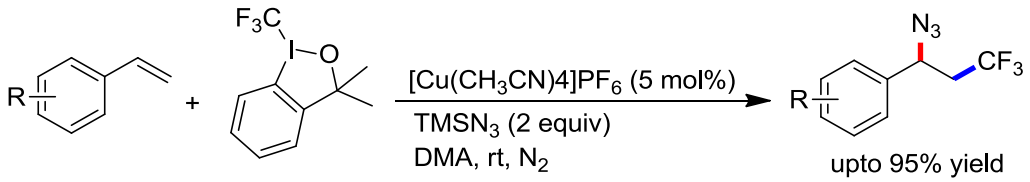
Scheme 5.3 Copper(I) catalyzed vicinal diazidation.

Recently, Zhu and co-workers have described a hypervalent iodine(III) mediated azidocyanation of unactivated alkenes (Scheme 5.4).[18] The strategy involve intramolecular distal cyano group migration combined with alkene difunctionalization. Mechanistic investigation shows that the reaction proceed through the formation of azido radical by the reaction of phenyliodine diacetate with $TMSN_3$. A variety of useful azido-substituted alkyl nitriles have been prepared with exquisite regio- and stereo-selectivities.



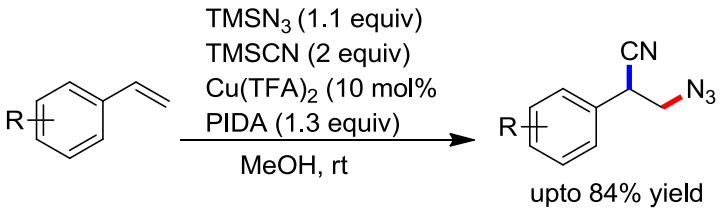
Scheme 5.4 Iodine(III) enabled azidocyanation.

Liu and co-workers have developed a mild reaction conditions for copper-catalyzed intermolecular trifluoromethylazidation reaction of alkenes (Scheme 5.5). Hypervalent iodine(III) compound Togni reagent II has been employed as an oxidant as well as CF_3 source for the reaction.[19]



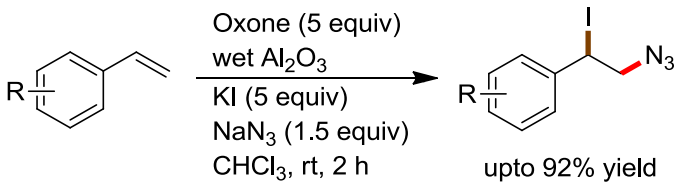
Scheme 5.5 Iodine(III) enabled azidotrifluoromethylation.

Xu *et. al.,* have developed a copper(II) catalyzed Markovnikov type intermolecular azidocyanation reaction of aryl alkenes to give a series of α-azido-propanenitriles (Scheme 5.6). $TMSN_3$ and TMSCN has been used as azoide and cyano source respectively in presence of oxidant phenyliodine diactetate (PIDA). The reaction initiates with hypervalent iodine(III) mediated azide radiacl generation.[20]



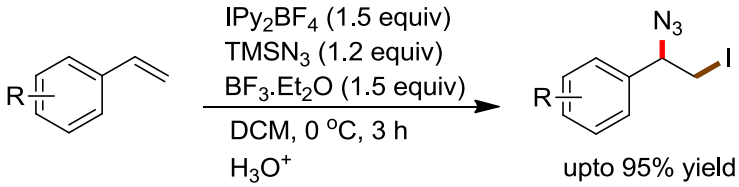
Scheme 5.6 Cu(II) catalyzed azidocyanation.

Curini *et. al.,* have developed a regioselective azidoiodination reaction of alkenes using NaN_3/KI/oxone reagent combination at room temperature conditions (Scheme 5.7). Initially, I^- was oxidized to the iodonium cation (I^+) and it promoted olefin difunctionalization via a bridged iodonium ion intermediate. Finally, nucleophilic addition to the bridged intermediate led to cohalogenated products. The protocol produces selectively *β*-azido iodo compounds.[8]



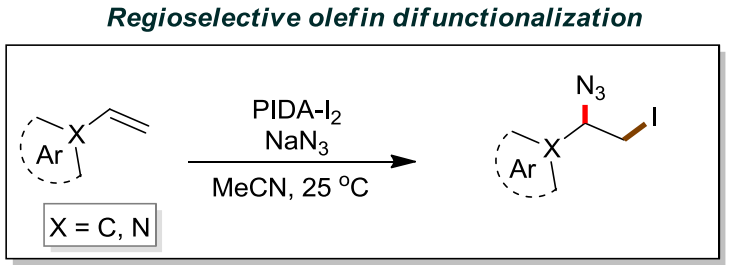
Scheme 5.7 Curini's approach for iodoazidation.

Barluenga and co-workers have developed a reaction of alkenes with IPy_2BF_4 and $TMSN_3$ under the influence of $BF_3.Et_2O$ to provide vicinal azidoiodoalkanes (Scheme 5.8). The method is useful for the preparation of α-azido-iodo alkanes from styrene derivatives.[21]



Scheme 5.8 Barluenga's approach for iodoazidation.

We report here that the PIDA–I_2 combination led to an electrophilic species (I^+) which could activate various olefins via cation–π interaction for regioselective intermolecular vicinal difunctionalization using nucleophiles like sodium azide (NaN_3) (Scheme 5.9).[22]



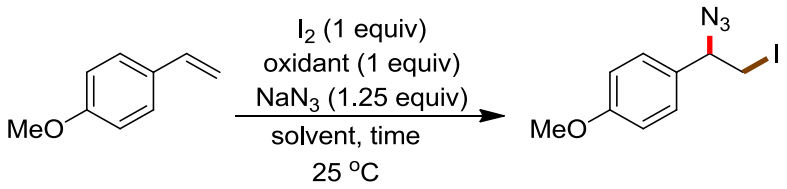
Scheme 5.9 Our approach for regioselective iodoazidation.

5.3 RESULTS AND DISCUSSIONS

4-Vinylanisole (**1a**) was considered as a model substrate for the optimization of olefin difunctionalization under aerobic conditions (Table 5.1). The reaction of **1a**, iodine (I_2), NaN_3 (Caution!!) and $PhI(OAc)_2$ led to **2a** in 37% yield in 1,2-dichloroethane (DCE) (entry 1). NaN_3 is sparingly soluble in DCE and therefore acetonitrile (MeCN), *N*,*N*-dimethylformamide (DMF), dimethylsulfoxide (DMSO) and acetonitrile-water (1 : 1) solvent systems were also used for the study. In acetonitrile, **2a** was obtained in 68% yield and other solvents were not promising for this transformation (entries 3-5). Changing the oxidant from PIDA to phenyliodine-bis(trifluoroacetate) (PIFA) or 2-iodoxybenzoic acid (IBX) did not lead to encouraging results (entries 6 and 7). We have further noticed that NaN_3 was a superior nucleophile than $TMSN_3$ (entry 11). In contrast, the desired product was not observed using I_2

without PIDA (entry 12). Finally, better results were obtained with 1.25 equiv of NaN_3 instead of 1.0 or 1.5 equiv (entries 9 and 10).

Table 5.1 Optimization of reaction conditions



Entry	Oxidant	Solvent	Yield[b] (%)
1	PIDA	DCE	37
2	PIDA	MeCN	68
3	PIDA	DMF	<5
4	PIDA	DMSO	13
5	PIDA	MeCN:H_2O (1:1)	43
6	PIFA	MeCN	51
7	IBX	MeCN	14
8	PIDA	MeCN	59
9[c]	PIDA	MeCN	65
10[d]	PIDA	MeCN	--
11[e]	PIDA	DCE	37
12	---	MeCN	--
13[f]	PIDA	MeOH	--

[a]Conditions: **1a** (0.75 mmol), PIDA (0.75 mmol), I_2 (0.75 mmol), Solvent (2 mL), 25 °C, 1 h; [b]isolated yield [c]NaN_3 (1.0 equiv), [d]NaN_3 (1.5 equiv), [e]$TMSN_3$ (1.2 equiv) were used; [f]instead of N_3, -OMe was incorporated.

Under optimized conditions (Table 5.1, entry 2), azido-iodination reactions of olefins were performed in MeCN under aerobic conditions at room temperature (Figure 5.1). Styrene derivatives with both electron donating and withdrawing substituents provided vicinal iodoazides in good to excellent yields (61–92%). In addition, products obtained with styrenes contained –OMe (**2a**, **2c-d**), –CH3 (**2g**, **2j**, **2m**), –Br (**2b**), –CN (**2h**) and –Cl (**2l**) substitutions and had heterocyclic moieties (**2i**, **2k**). Sterically hindered olefins (**2d, 2g, 2j, 2n, 2o**) also provided the desired azide derivatives in good yields. Exceptionally, in the case of **2f**, two different regioisomers were isolated in the ratio of 1 : 0.55.

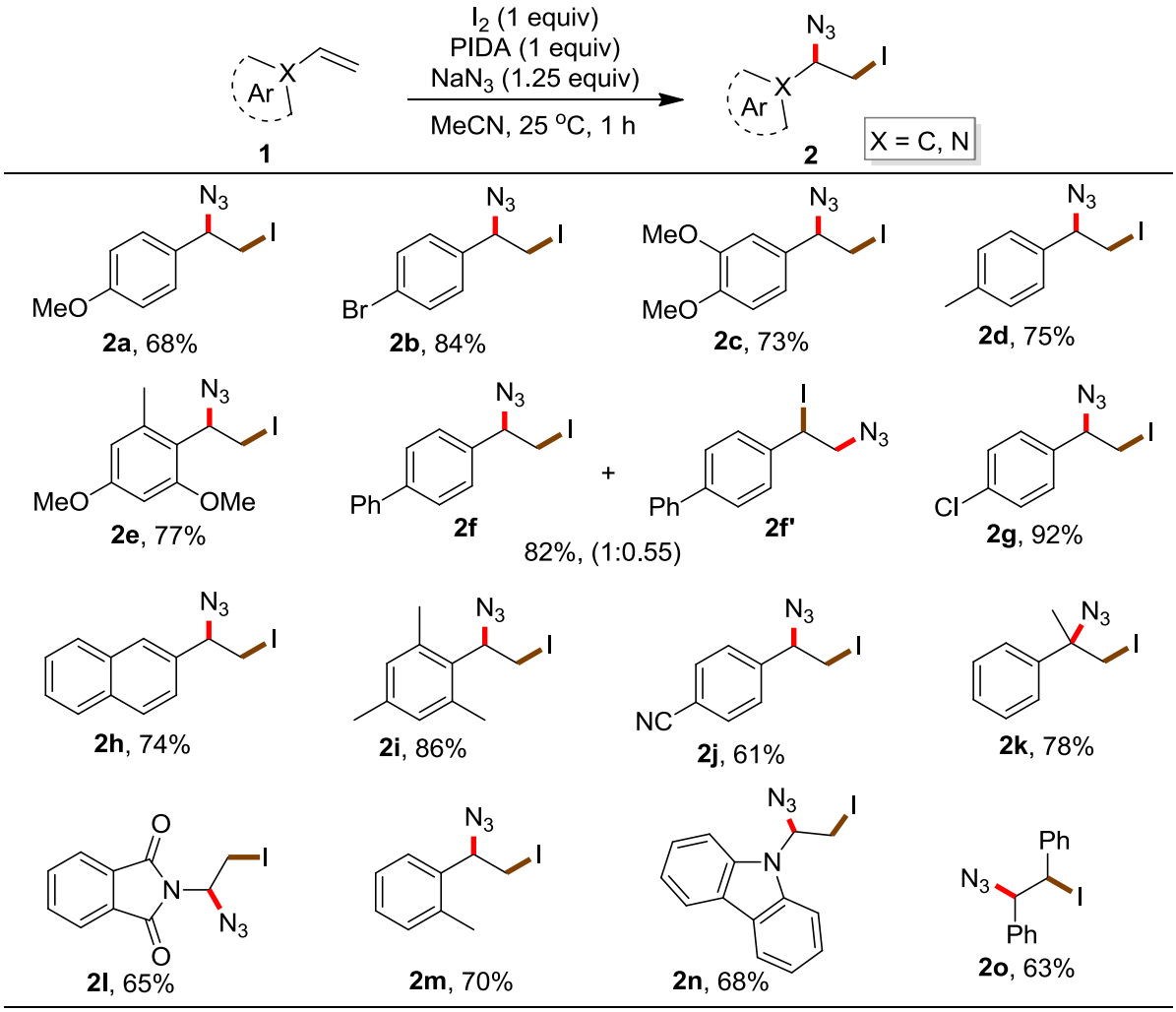


Figure 5.1 Scope of iodoazidation.

To understand the mechanism of the reaction, we examined the role of PIDA and I_2. The iodobenzene obtained from the reactions of PIDA and I_2, led to an identical ^{1}H NMR spectrum (Figure 5.2) as the commercially available sample (CAS no. 591-50-4). Also, the downfield shift of the methyl group of -OAc could confirm the formation of IOAc.[23] This in situ generated I^+ (from IOAc) was expected to form bridged iodonium ions with olefins for the regioselective addition of nucleophiles. Thus the mechanism of the reaction is rationalized and shown in Figure 5.3. Regioselectivity was observed due to the formation of the stable benzylic carbocation intermediate **6** and the reaction followed path **b** (Figure 5.3c).

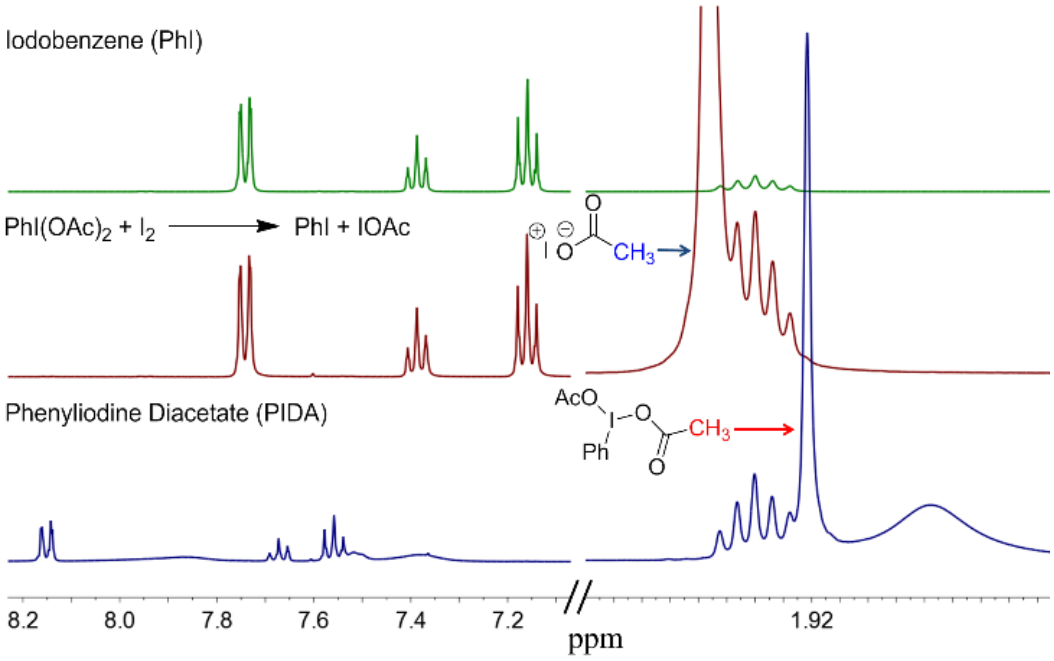


Figure 5.2 ^{1}H experiments for mechanistic investigation.

We hypothesized the formation of bridged-iodonium ion (4, Figure 5.3) and followed by addition of nucleophiles. Therefore in the absence of any other externally added nucleophiles, the methoxide anion from MeOH could act as a nucleophile to result in iodo-methoxylated derivatives. This reaction was found to be very fast (ca. 10 min at 25 °C) and afforded excellent yields of products (Table 5.1). This fact further supported the mechanism of the reaction as proposed in Figure 5.3.

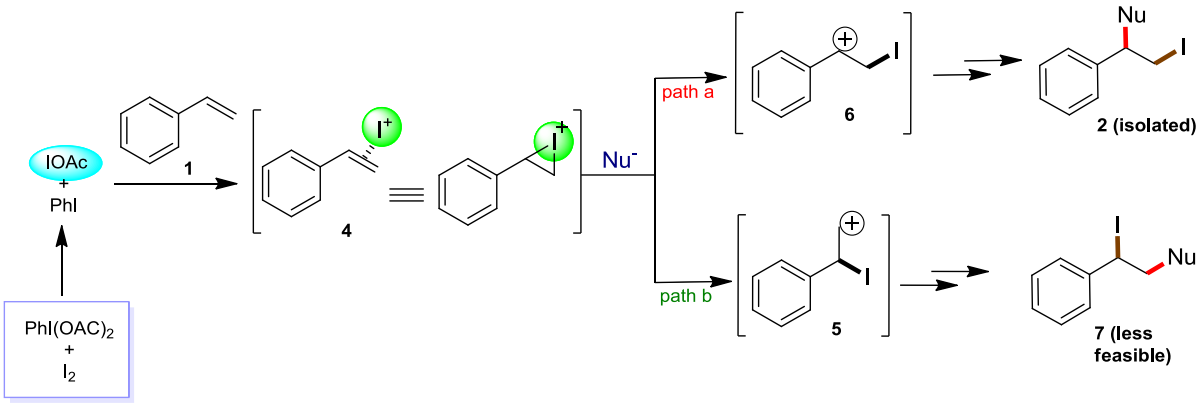
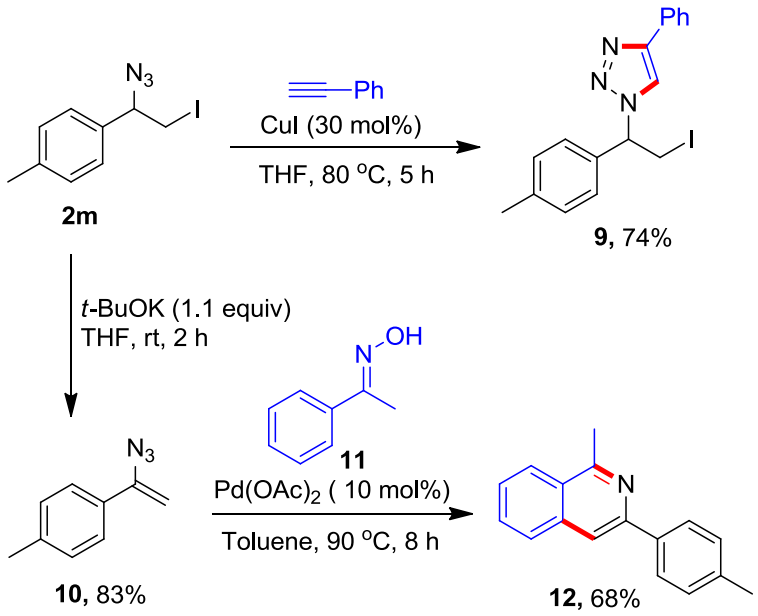


Figure 5.3 Possible reaction mechanism for iodoazidation.

To further exemplify the synthetic utility of iodoazidation products, we successfully used **2m** for the different synthetic transformations (Scheme 5.10). The treatment of **2m** with phenylacetylene using CuI as a catalyst, provided the click product **9** in 74% yield.[24] Azidovinylbenzene (**10**) was prepared from **2m** by treating it with *t*-BuOK in THF at room temperature.[25] Azidovinylbenzene (**10**) was further used for the synthesis of the 3-arylisoquinoline derivative (**12**) by using palladium as a catalyst with oxime (**11**) at 90 °C for



Scheme 5.10 Post synthetic modification.

8 h.[26] Isoquinoline derivatives act as a potential constituent in biologically active molecules,[27] natural products[28] and also in materials science.[29] Hence, our methodology provides a straightforward synthetic protocol for the preparation of synthetically useful compounds.

5.4 CONCLUSIONS

In summary, a vicinal difunctionalization of olefins is developed under transition metal free, room temperature and mild conditions. A series of azido-iodo functionalized derivatives are synthesized. Mechanistically we have shown that I(III) and I_2 led to I^+ which activated the

relatively unactivated olefins via cation–π interaction for nucleophilic addition. Importantly, products obtained could be used as synthetic precursors for pharmaceutical and materials applications. Therefore, we expect that our study may be helpful for a better understanding of mechanistic organic chemistry by exploiting weak and non-covalent interactions.

5.5 EXPERIMENTAL SECTION

General Methods. Dichloroethane (DCE) and acetonitrile were dried by following the standard procedures (dried over anhydrous CaH_2 and followed by distillation). All other reagents were used without further purification. Flash column chromatographic purification of compounds was performed using silica-gel (230-400 mesh) and diethyl ether-hexane/ ethyl acetate-hexane mixtures as solvent eluents. Spectra are reported as values in parts per million (ppm) relative to residual chloroform signal as internal standard (7.26 ppm for ^{1}H and 77.16 ppm for ^{13}C). Analytical thin-layer chromatography was performed with precoated silica gel 60 F254 plates (Merck) and the spots were visualized with UV light at 254 nm or by staining with phosphomolybdic acid (PMA) in methanol (10 gm PMA in 100 mL methanol).

Caution !!!

Azide derivatives are highly toxic (similar toxicity as cyanide ion; LD50 = 27 mg/kg for rats) and therefore during handling of any azide derivatives, personal protective equipment's should be exercised. General safety at laboratory should be carefully implemented and suggested that all reactions should be done in a well-ventilated fume hood behind a blast shield.

Representative procedure for iodoazidation of olefins

To a solution of PIDA (242 mg, 0.75 mmol) and I_2 (190 mg, 0.75 mmol) in acetonitrile (2 mL), NaN_3 (61 mg, 0.94 mmol) was added and stirred for 5 min. Then 4-vinylanisole

1a (100 µL, 0.75 mmol) was added at room temperature (25 °C) and stirring continued until the complete consumption of starting material (TLC analysis), the reaction mixture was diluted with dichloromethane and washed with 10% (w/v) $Na_2S_2O_3$ in water and followed by water. Organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. Crude product was purified through column chromatography using 3% ethyl acetate in hexane as an eluent to obtain the analytically pure compound **2a** (68%, 155 mg) as a colorless oil.

Compond characterization data

1-(1-Azido-2-iodoethyl)-4-methoxybenzene (2a)[30]: R_f = 0.32 (ethyl acetate/hexane = 1:19); colorless oil; yield 68% (155 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.7 Hz, 2H), 6.93 (d, *J* = 8.7 Hz, 2H), 4.68 (t, *J* = 8 Hz, 1H), 3.82 (s, 3H), 3.37 (dd, *J* = 9.5, 3.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2, 130.0, 128.1, 114.5, 66.9, 55.5, 8.6.

1-(1-Azido-2-iodoethyl)-4-bromobenzene (2b): R_f = 0.25 (in hexane); colorless oil; yield 84% (219 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 4.68 (t, *J* = 6.9 Hz, 1H), 3.36 (d, *J* = 6.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.0, 132.4, 128.5, 123.2, 66.5, 7.8.

4-(1-Azido-2-iodoethyl)-1,2-dimethoxybenzene (2c): R_f = 0.25 (ethyl acetate/hexane = 1:19); colorless oil; yield 73% (103 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87 (s, 2H), 6.81 (s, 1H), 4.66 (t, *J* = 7.0 Hz, 1H), 3.90 (s, 3H), 3.88 (s, 3H), 3.37 (d, *J* = 7.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.6, 149.5, 130.4, 119.4, 111.3, 109.5, 67.2, 56.1, 56.0, 8.5.

1-(1-Azido-2-iodoethyl)-4-methylbenzene (2d)[31]: R_f = 0.33 (in hexane); colorless oil; yield 75% (163 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23–7.21 (br, 4H), 4.70 (t, *J* = 7.0

Hz, 1H), 3.39 (d, *J* = 7.1 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0, 134.9, 129.8, 126.6, 67.0, 21.3, 8.4.

2-(1-Azido-2-iodoethyl)-1,5-dimethoxy-3-methylbenzene (2e): R_f = 0.28 (ethyl acetate/hexane = 1:19); pale yellow oil; yield 77% (150 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.36 (s, 1H), 6.35 (s, 1H), 5.10 (t, *J* = 7.7 Hz, 1H), 3.83 (s, 3H), 3.80 (s, 3H), 3.67 (d, *J* = 7.8 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 159.4, 139.3, 115.9, 107.8, 97.0, 61.1, 55.7, 55.3, 20.9, 6.6.

4-(1-Azido-2-iodoethyl)-1,1'-biphenyl (2f): R_f = 0.60 (ethyl acetate/hexane = 1:19); white solid; yield 82% (159 mg); mp 64-67 °C; 1: 0.55 regioisomers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66–7.55 (m, 23H), 7.48–7.44 (m, 12H), 7.41–7.38 (m, 12H), 5.22 (t, *J* = 7.7 Hz, 2H), 4.77 (t, *J* = 7.0 Hz, 3H), 4.04–3.95 (m, 4H), 3.43 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.1, 141.8, 140.4, 140.4, 139.4, 136.9, 129.0, 128.9, 128.1, 127.9, 127.9, 127.8, 127.2, 127.2, 67.1, 58.8, 27.8, 8.2.

1-(1-Azido-2-iodoethyl)-4-chlorobenzene (2g)[30]: R_f = 0.25 (in hexane); colorless oil; yield 92% (235 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.5 Hz, 2H), 7.28 (d, *J* = 8.5 Hz, 2H), 4.71 (t, *J* = 6.9 Hz, 1H), 3.41–3.34 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.5, 135.1, 129.4, 128.2, 66.4, 7.9.

2-(1-Azido-2-iodoethyl)naphthalene (2h)[30]: R_f = 0.75 (ethyl acetate/hexane = 1:19); colorless oil; yield 74% (155 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 12.5, 6.8 Hz, 3H), 7.80 (s, 1H), 7.54 (dd, *J* = 6.3, 3.1 Hz, 2H), 7.42 (dd, *J* = 8.5, 1.7 Hz, 1H), 4.90 (t, *J* = 7.0 Hz, 1H), 3.48 (d, *J* = 6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.4, 133.6, 133.3, 129.3, 128.3, 127.9, 126.9, 126.5, 123.8, 67.5, 8.2.

2-(1-Azido-2-iodoethyl)-1,3,5-trimethylbenzene (2i): R_f = 0.30 (in hexane); colorless oil; yield 86% (168 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.89 (s, 2H), 5.29 (dd, *J* = 10.0, 5.3 Hz, 1H), 3.55 (t, *J* = 10.3 Hz, 1H), 3.38 (dd, *J* = 10.5, 5.3 Hz, 1H), 2.42 (s, 6H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.3, 136.4, 130.9, 130.6, 64.1, 20.9, 20.8, 5.8.

4-(1-Azido-2-iodoethyl)benzonitrile (2j): R_f = 0.40 (ethyl acetate/hexane = 1:9); pale yellow oil; yield 61% (98 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 6.8 Hz, 2H), 7.52 (d, *J* = 8.3 Hz, 2H), 5.12 (dd, *J* = 8.8, 6.5 Hz, 1H), 4.00–3.89 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.6, 132.9, 128.5, 118.3, 112.6, 58.2, 24.8.

(2-Azido-1-iodopropan-2-yl)benzene (2k): R_f = 0.32 (in hexane); colorless oil; yield 78% (172 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46–7.33 (m, 5H), 3.50 (dd, *J* = 14, 12 Hz, 2H), 1.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.8, 128.9, 128.4, 125.7, 65.2, 25.3, 17.9.

2-(1-Azido-2-iodoethyl)isoindoline-1,3-dione (2l): R_f = 0.45 (ethyl acetate/hexane = 1:19); semisolid; yield 65% (128 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.81 (dd, *J* = 5.5, 3.1 Hz, 2H), 5.74 (dd, *J* = 9.3, 6.3 Hz, 1H), 4.10 (dd, *J* = 10.4, 9.4 Hz, 1H), 3.77 (dd, *J* = 10.5, 6.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 134.9, 131.4, 124.2, 66.9, 0.98.

1-(1-Azido-2-iodoethyl)-2-methylbenzene (2m): R_f = 0.35 (in hexane); colorless oil; yield 70% (153 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.46 (m, 1H), 7.24–7.19 (m, 2H), 7.16–7.14 (m, 1H), 5.35 (t, *J* = 7.8 Hz, 1H), 4.04 (d, *J* = 7.7 Hz, 2H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2, 135.5, 131.3, 128.8, 127.1, 126.9, 58.1, 24.7, 19.4.

9-(1-Azido-2-iodoethyl)-9H-carbazole (2n): R_f = 0.33 (in hexane); semisolid, yield 68% (127 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 7.8 Hz, 2H), 7.61 (d, *J* = 8.3 Hz, 2H), 7.51–7.47 (m, 2H), 7.33 (t, *J* = 7.5 Hz, 2H), 6.44 (dd, *J* = 7.8, 6.7 Hz, 1H), 3.80 (dd, *J* = 10.7, 7.9 Hz, 1H), 3.68 (dd, *J* = 10.7, 6.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.8, 126.4, 124.2, 120.8, 120.8, 110.3, 73.0, 2.9.

(1-Azido-2-iodoethane-1,2-diyl)dibenzene (2o)[21]: R_f = 0.30 (in hexane); white solid; yield 63% (122 mg); mp 99–103 °C; E:Z = 1:1, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 6.7 Hz, 2H), 7.42–7.36 (m, 3H), 7.36–7.27 (m, 5H), 7.25–7.20 (m, 5H), 7.20–7.08 (m, 5H), 5.21 (dd, *J* = 15.4, 9.4 Hz, 2H), 5.11 (d, *J* = 9.2 Hz, 1H), 4.94 (d, *J* = 9.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.3, 140.2, 137.8, 136.4, 129.2, 128.8, 128.8, 128.7, 128.6, 128.6, 128.4, 128.4, 127.8, 127.4, 72.9, 72.0, 36.8, 34.5.

Synthesis of 1-(2-iodo-1-(p-tolyl)ethyl)-4-phenyl-1H-1,2,3-triazole (9)[24]:

100 mg (0.34 mmol) of **2m** was taken in a 10 mL sealed tube and dissolved in THF (2 mL). Followed by phenyl acetylene (76 μL, 0.69 mmol) and CuI (19 mg, 0.1 mmol) were added and placed in a pre-heated oil bath at 80 °C. Reaction was monitored by TLC and after completion the reaction was allowed to cool down to room temperature. THF was evaporated under reduced pressure. Then compound was extracted with dichloromethane and washed with water. After drying under anhydrous Na_2SO_4, solvent was removed under reduced pressure and the crude mixture was subjected to column chromatography to obtain the desire product 1-(2-iodo-1-(*p*-tolyl)ethyl)-4-phenyl-1H-1,2,3-triazole (**9**). Yield 98 mg (74%); white solid; mp 112–115 °C; R_f = 0.22 (ethy acetate/hexane = 1:19); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87–7.78 (m, 2H), 7.71 (s, 1H), 7.41 (dd, *J* = 10.3, 4.7 Hz, 2H), 7.36–7.26 (m, 3H), 7.21 (d, *J* = 8.0 Hz, 2H), 5.75 (dd, *J*

= 8.8, 6.4 Hz, 1H), 4.23 (dd, *J* = 10.7, 8.9 Hz, 1H), 3.85 (dd, *J* = 10.7, 6.3 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 139.6, 134.3, 130.5, 130.1, 128.9, 128.4, 126.9, 125.9, 119.6, 66.9, 21.3, 5.3; ESI-MS m/z = 389.8113, calculated for (M + H+) 390.0467.

Synthesis of 1-(1-azidovinyl)-4-methylbenzene (10)[25]:

2m (200 mg, 0.68 mmol) in THF was slowly added to a suspension of *t*-BuOK (116 mg, 1.04 mmol) in dry THF under N_2 atmosphere and allowed to stir for 2 h at room temperature. After completion of reaction THF was removed under reduced pressure. The crude product was dissolved in dichloromethane and washed with water. Finally the compound was purified by column chromatography. Yield 92 mg (83%); pale yellow liquid; R_f = 0.90 (in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.2 Hz, 2H), 7.18 (d, *J* = 8.3 Hz, 2H), 5.39 (d, *J* = 2.3 Hz, 1H), 4.92 (d, *J* = 2.3 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 139.3, 131.6, 129.3, 125.6, 97.3, 21.3; ESI-MS m/z = 160.0604, calculated for ($M + H^+$) 160.0875.

Synthesis of 1-methyl-3-(p-tolyl)isoquinoline (12)[26]:

Acetophenone oxime **11** (60 mg, 0.44 mmol), azidovinylbenzene **10** (84 mg, 0.53 mmol) and $Pd(OAc)_2$ (9 mg, 0.04 mmol) were transferred to a 10 mL sealed tube and dissolved in dry toluene. The reaction vessel was closed with the teflon cap and placed in a pre-heated oil bath at 90 °C for 8 h. After completion of reaction (monitored by TLC), the crude product was cooled to room temperature and concentrated under vacuum. The residue was subjected to column chromatography to afford the desired isoquinoline derivative. Yield 70 mg (68%); colorless liquid, R_f = 0.60 (ethy acetate/hexane = 1:19); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (dd, *J* = 8.4, 0.6 Hz, 1H), 8.05 (d, *J* = 8.2 Hz, 2H), 7.89 (s, 1H), 7.84 (d, *J* = 8.2 Hz, 1H), 7.65 (m, 1H), 7.55 (m, 1H), 7.31 (d, *J* = 7.9 Hz, 2H), 3.04 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 150.2, 138.3,

137.1, 136.9, 130.1, 129.6, 127.7, 126.9, 126.7, 126.6, 125.7, 114.8, 22.8, 21.4; ESI-MS m/z = 234.0419, calculated for ($M + H^+$) 234.1283.

5.6 NOTES AND REFERENCES

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^{1}H and ^{13}C NMR spectra of selected compounds

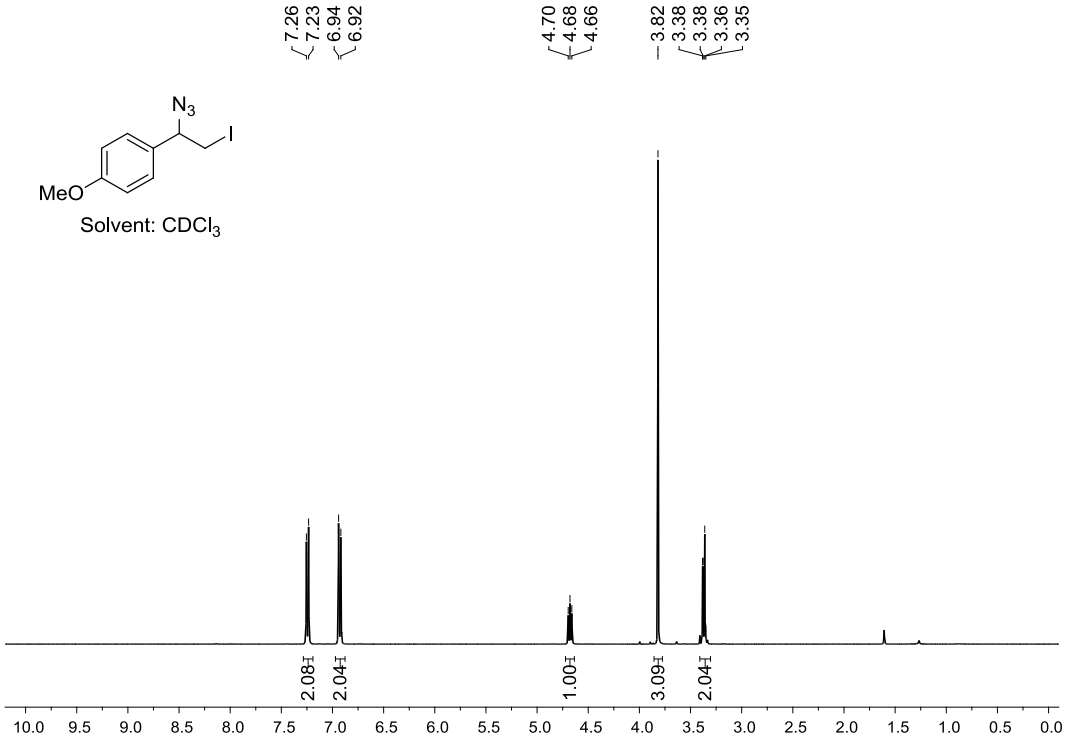


Figure 5.4: ^{1}H NMR spectrum of 1-(1-azido-2-iodoethyl)-4-methoxybenzene (**2a**).

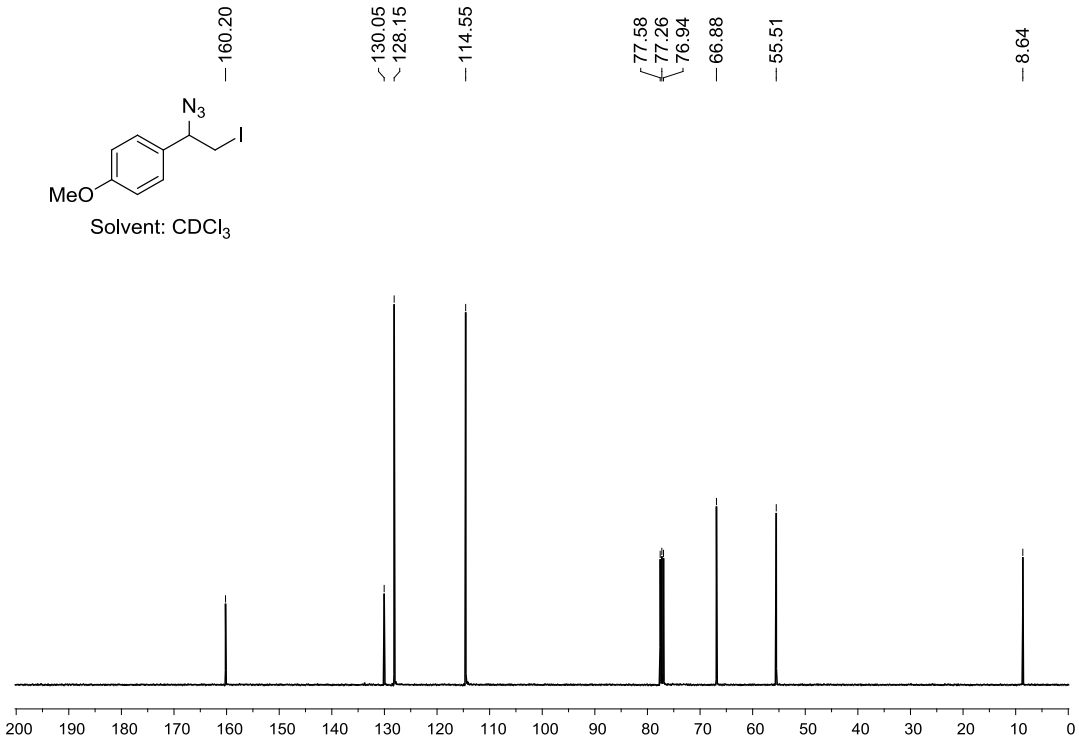


Figure 5.5: ^{13}C NMR spectrum of 1-(1-azido-2-iodoethyl)-4-methoxybenzene (**2a**).

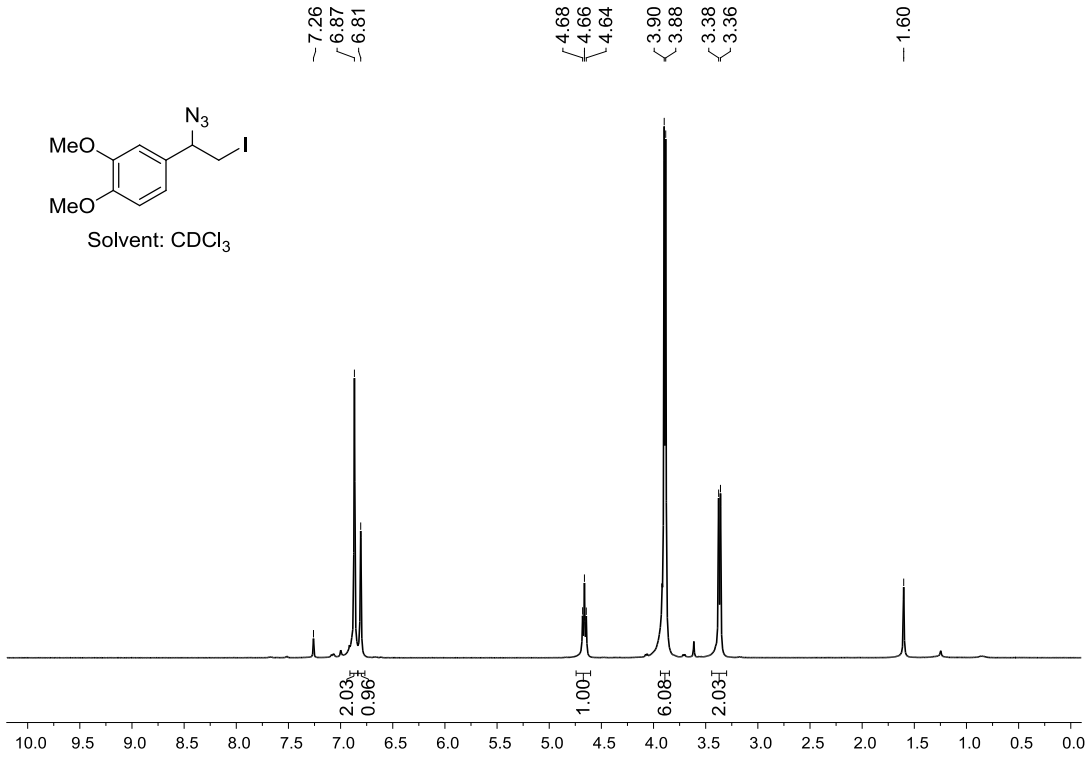


Figure 5.8: ^{1}H NMR spectrum of 4-(1-azido-2-iodoethyl)-1,2-dimethoxybenzene (**2c**).

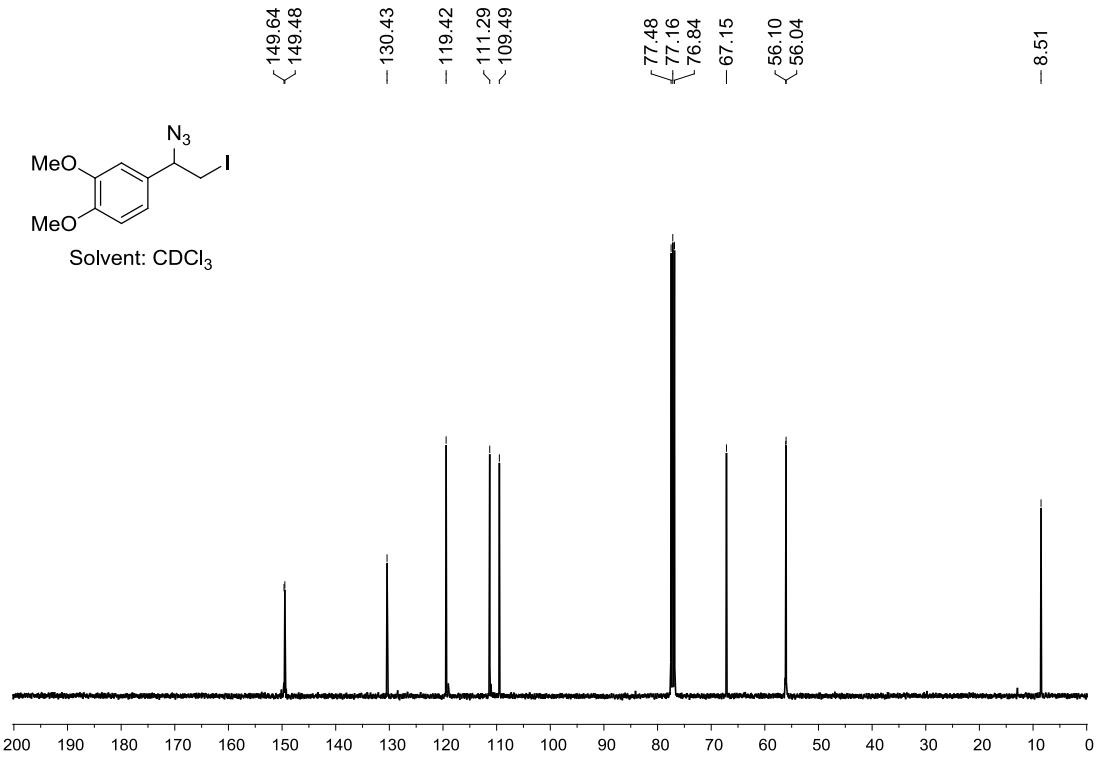


Figure 5.9: ^{13}C NMR spectrum of 4-(1-azido-2-iodoethyl)-1,2-dimethoxybenzene (**2c**).

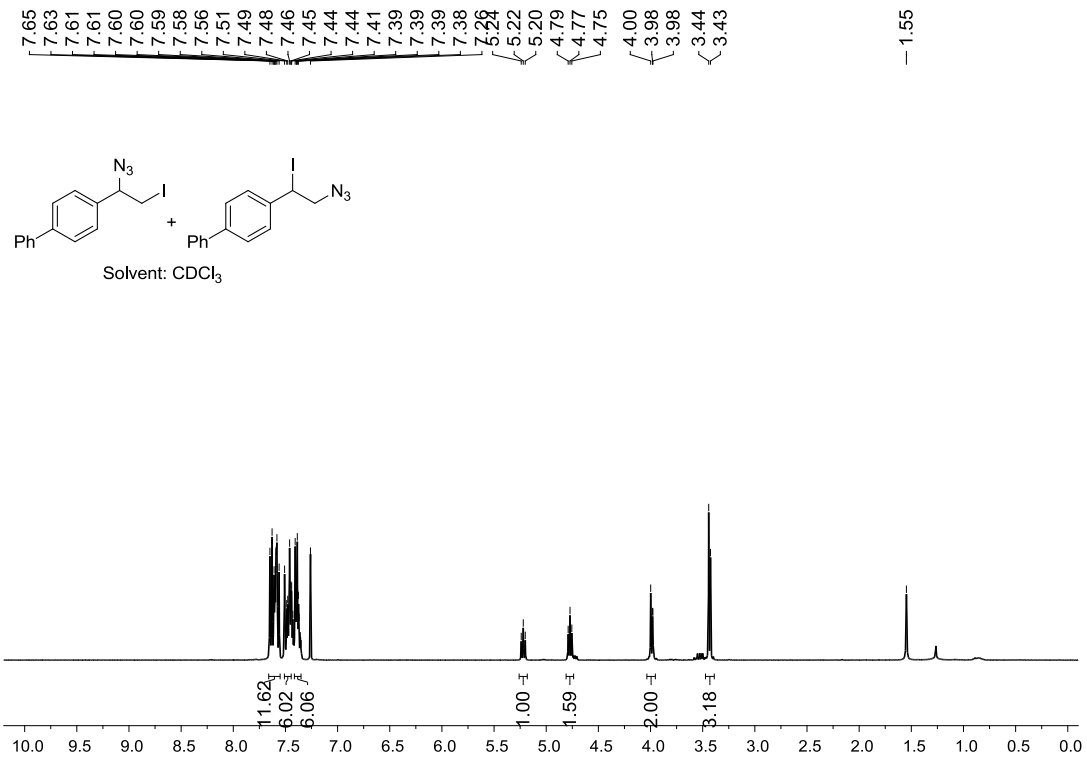


Figure 5.12: ^{1}H NMR spectrum of 4-(1-azido-2-iodoethyl)-1,1'-biphenyl (**2f**).

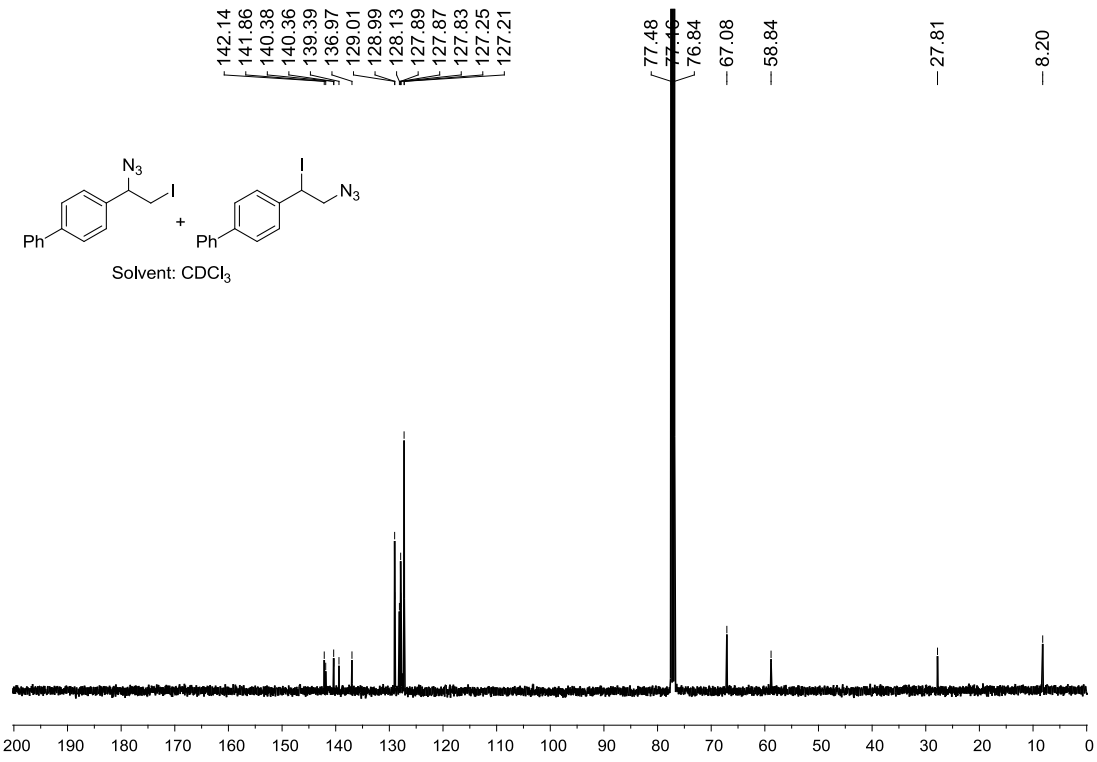


Figure 5.13: ^{13}C NMR spectrum of 4-(1-azido-2-iodoethyl)-1,1'-biphenyl (**2f**).

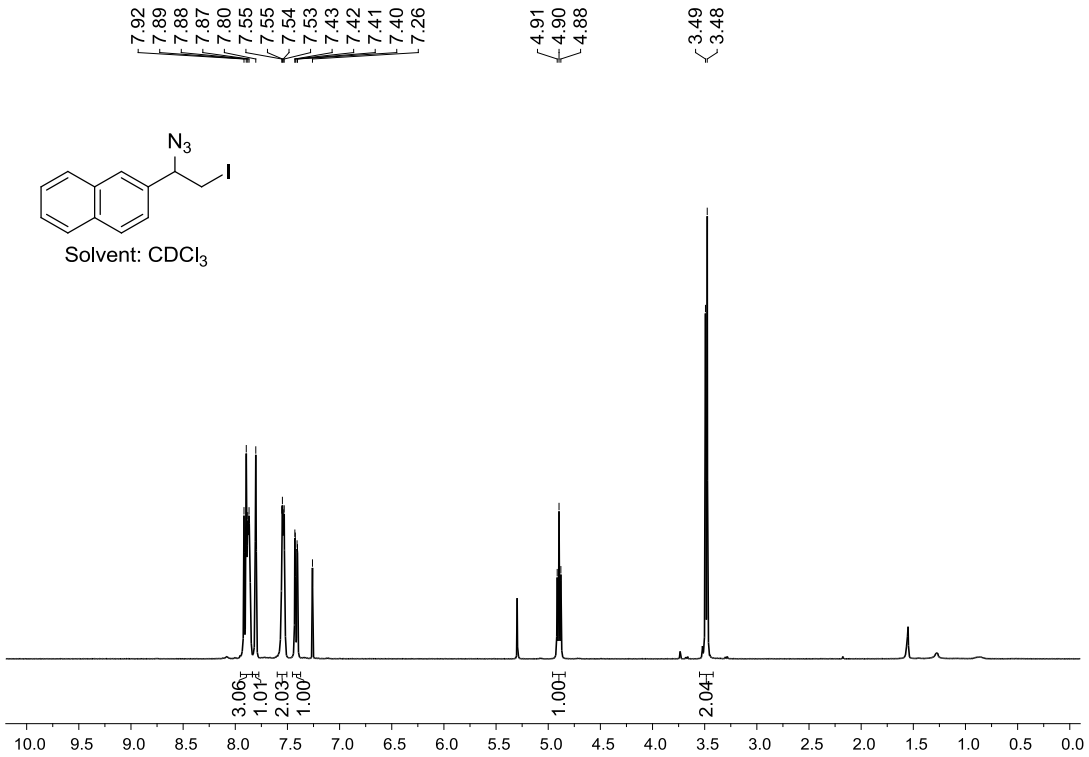


Figure 5.14: ^{1}H NMR spectrum of 2-(1-azido-2-iodoethyl)naphthalene (**2h**).

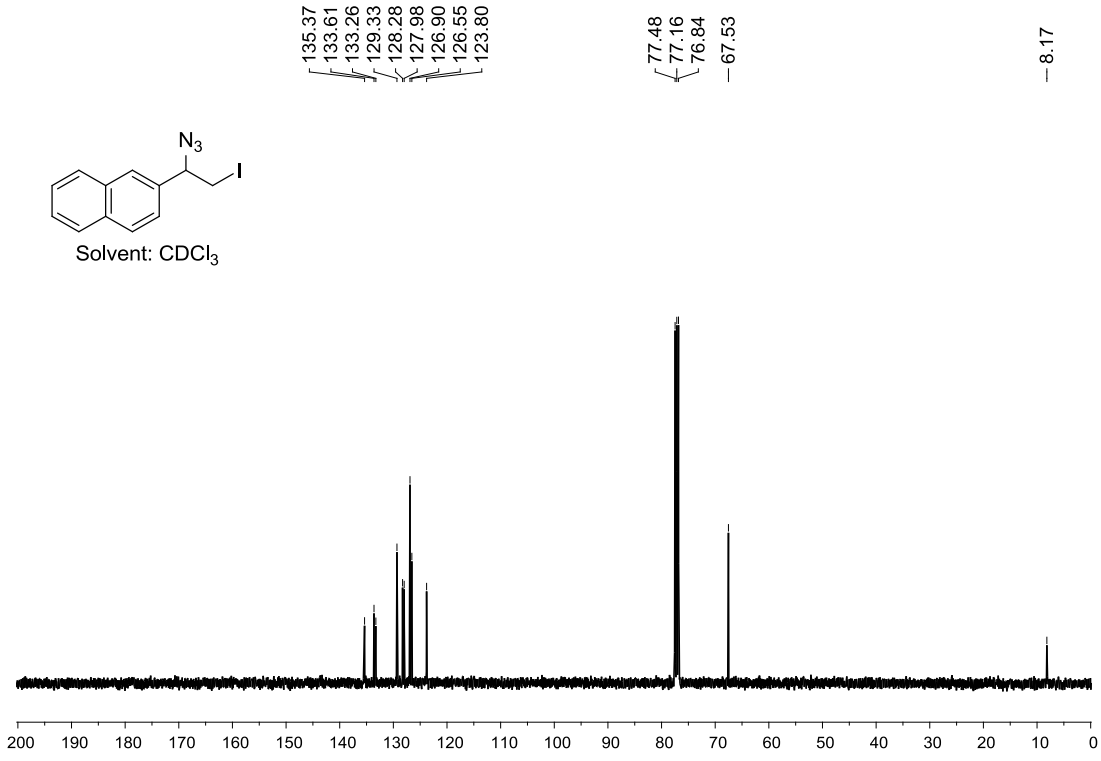


Figure 5.15: ^{13}C NMR spectrum of 2-(1-azido-2-iodoethyl)naphthalene (**2h**).

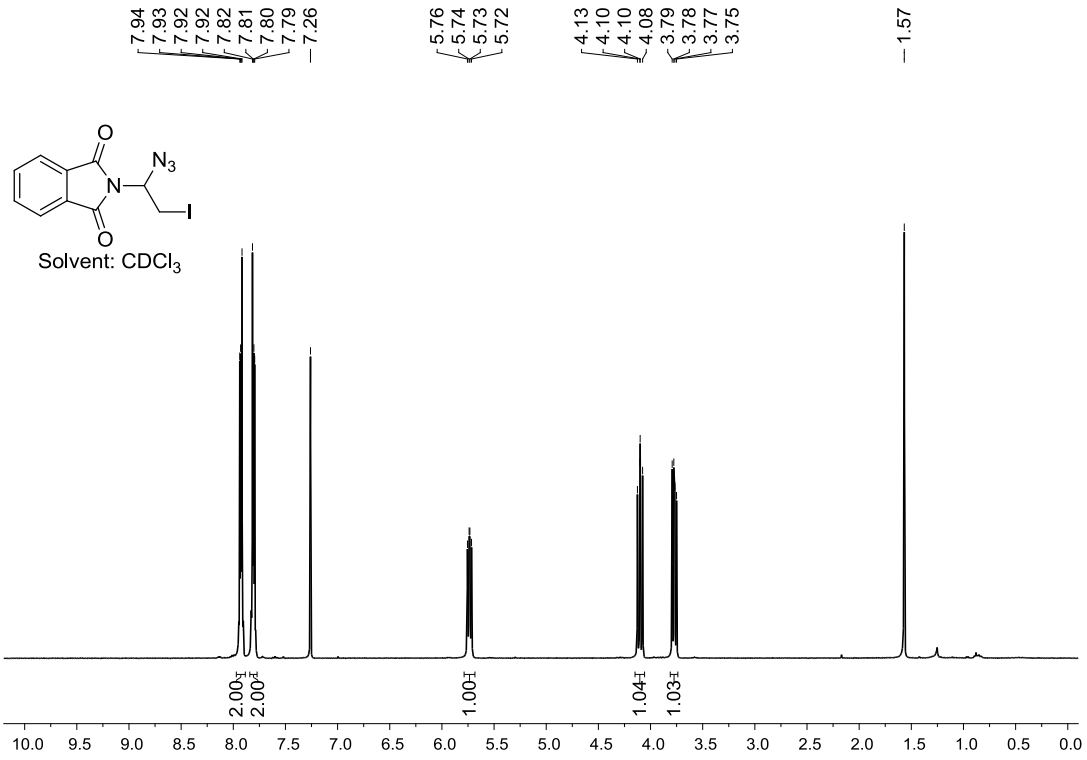


Figure 5.20: ^{1}H NMR spectrum of 2-(1-azido-2-iodoethyl)isoindoline-1,3-dione (**2l**).

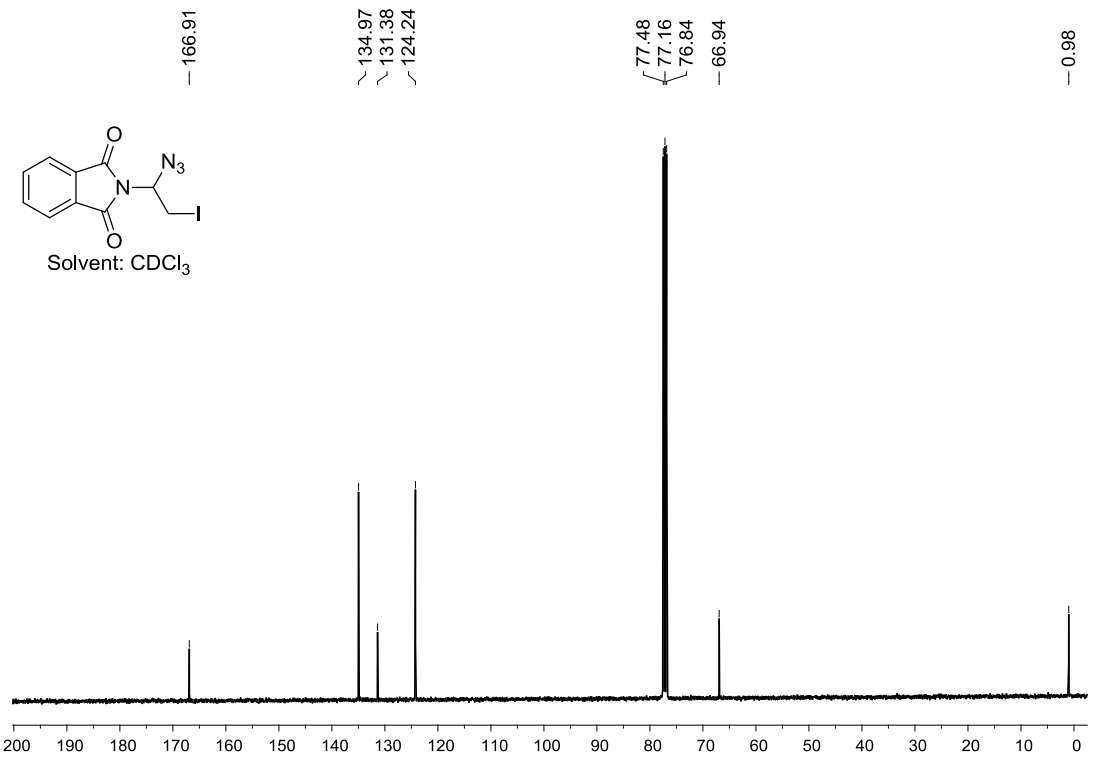


Figure 5.21: ^{13}C NMR spectrum of 2-(1-azido-2-iodoethyl)isoindoline-1,3-dione (**2l**).

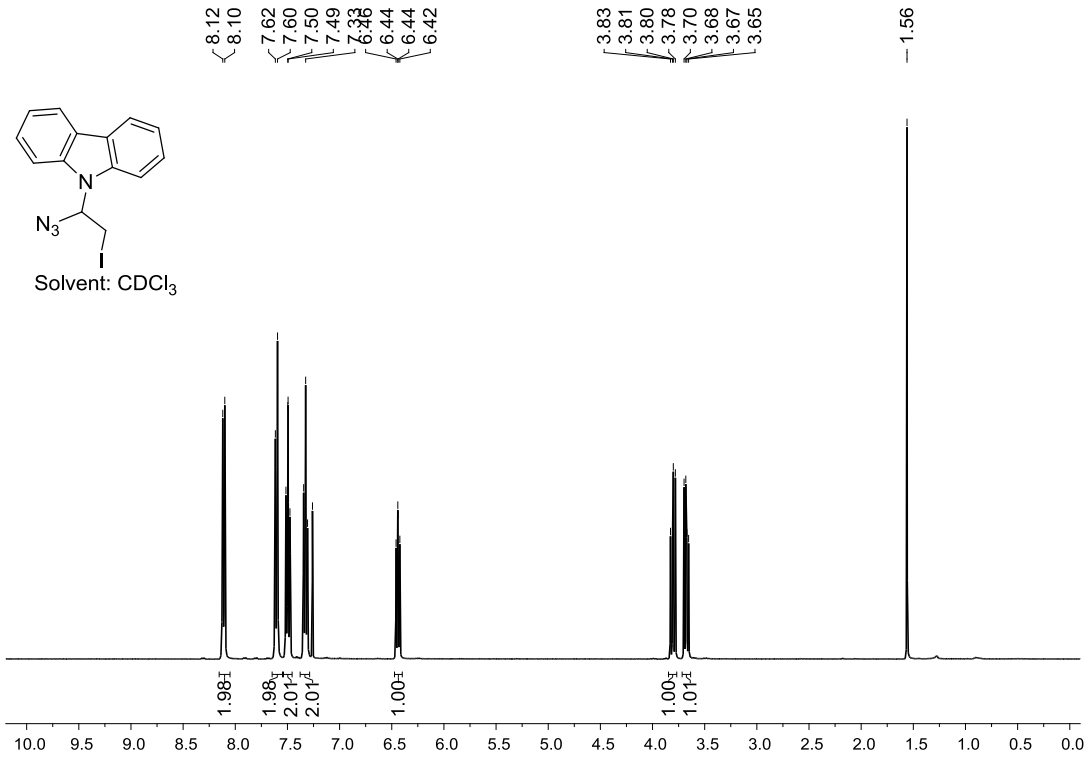


Figure 5.24: ^{1}H NMR spectrum of 9-(1-azido-2-iodoethyl)-9H-carbazole (**2n**).

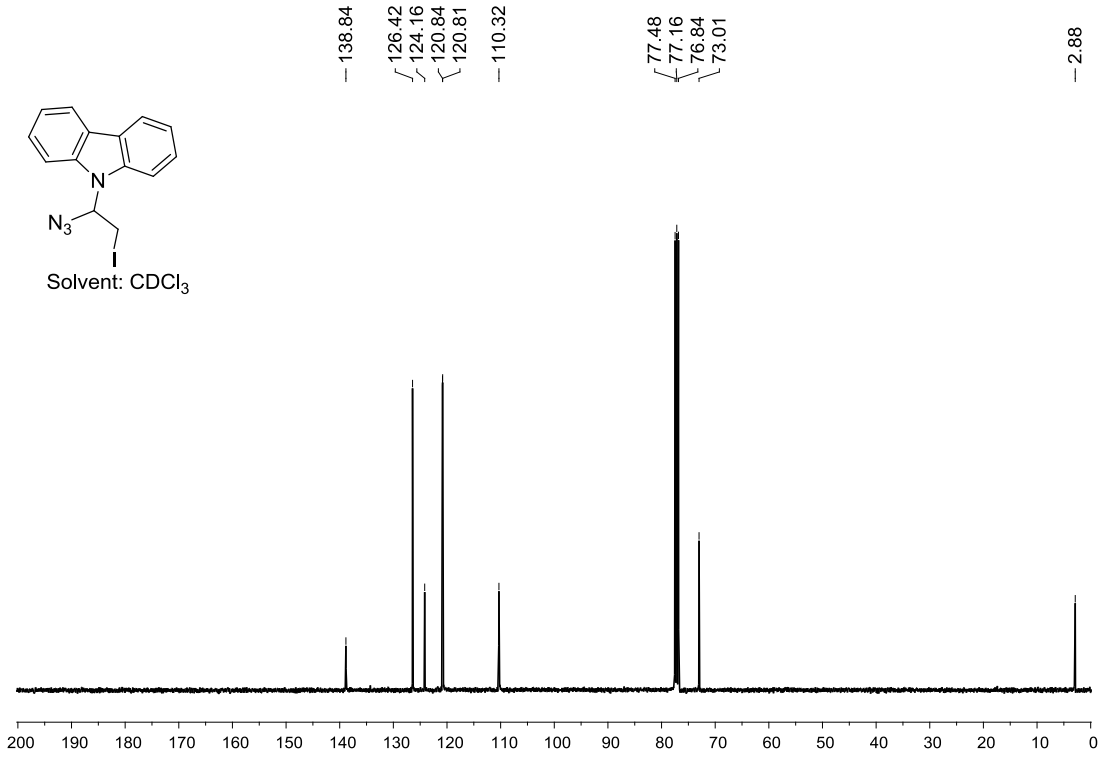


Figure 5.25: ^{13}C NMR spectrum of 9-(1-azido-2-iodoethyl)-9H-carbazole (**2n**).

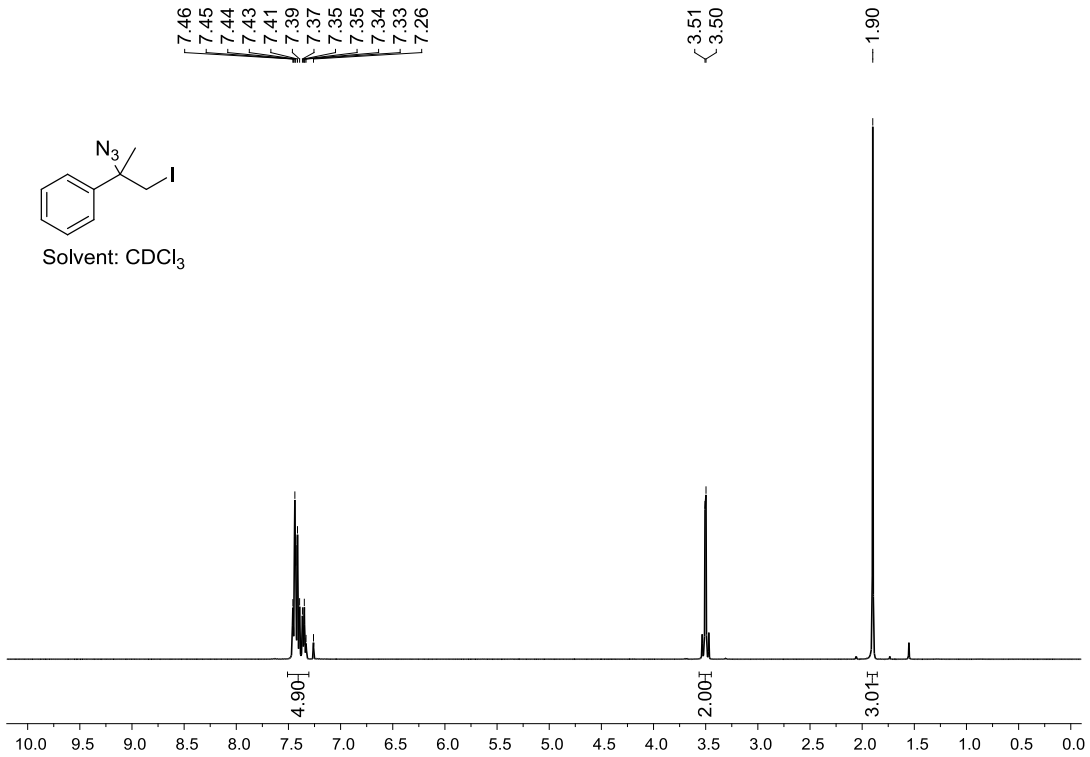


Figure 5.30: ^{1}H NMR spectrum of (2-azido-1-iodopropan-2-yl)benzene (**2k**).

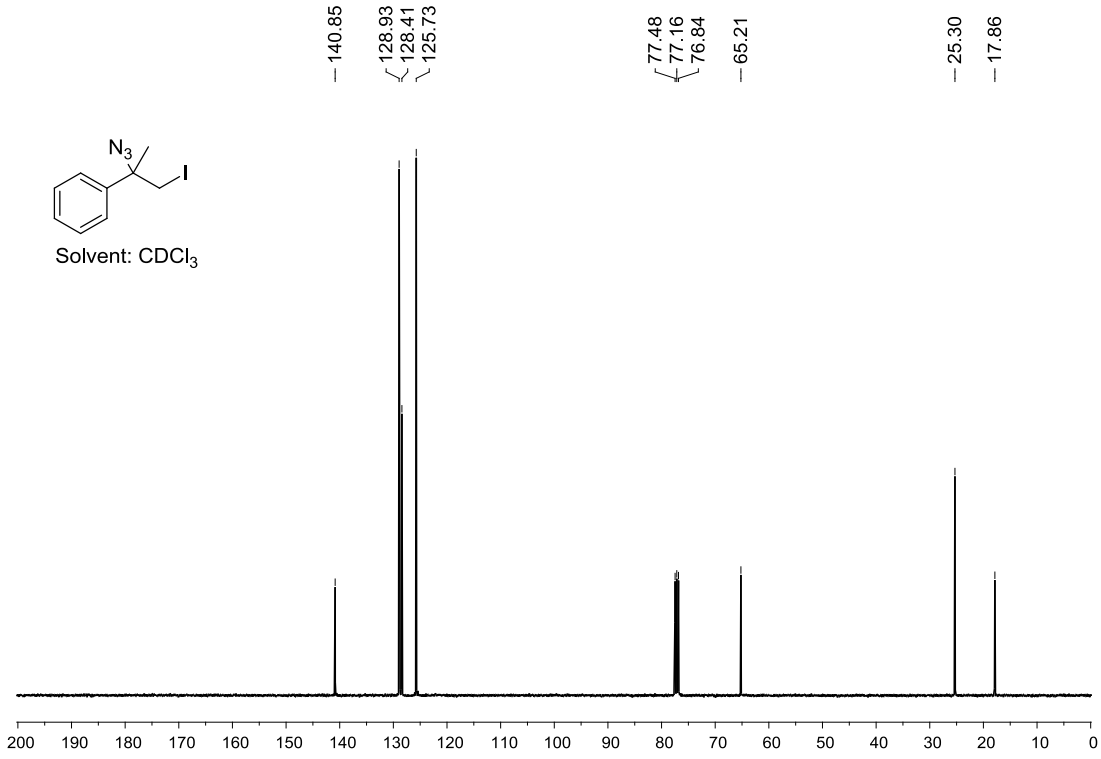


Figure 5.31: ^{13}C NMR spectrum of (2-azido-1-iodopropan-2-yl)benzene (**2k**).

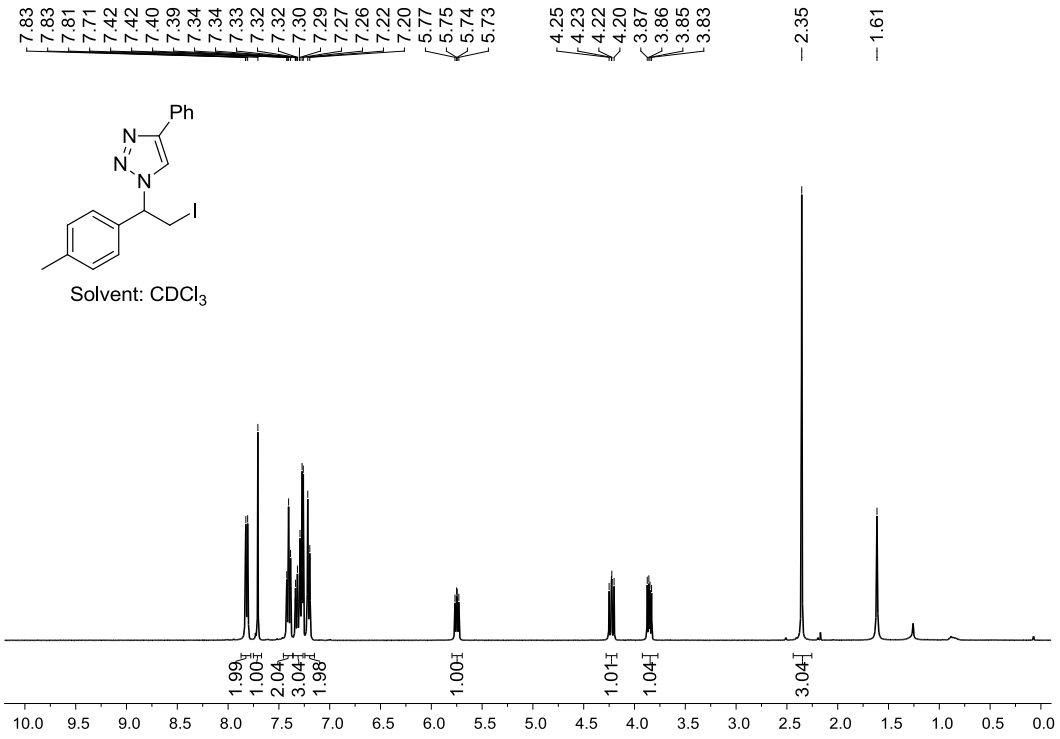


Figure 5.34: ^{1}H NMR spectrum of 1-(2-iodo-1-(*p*-tolyl)ethyl)-4-phenyl-1*H*-1,2,3-triazole (**9**).

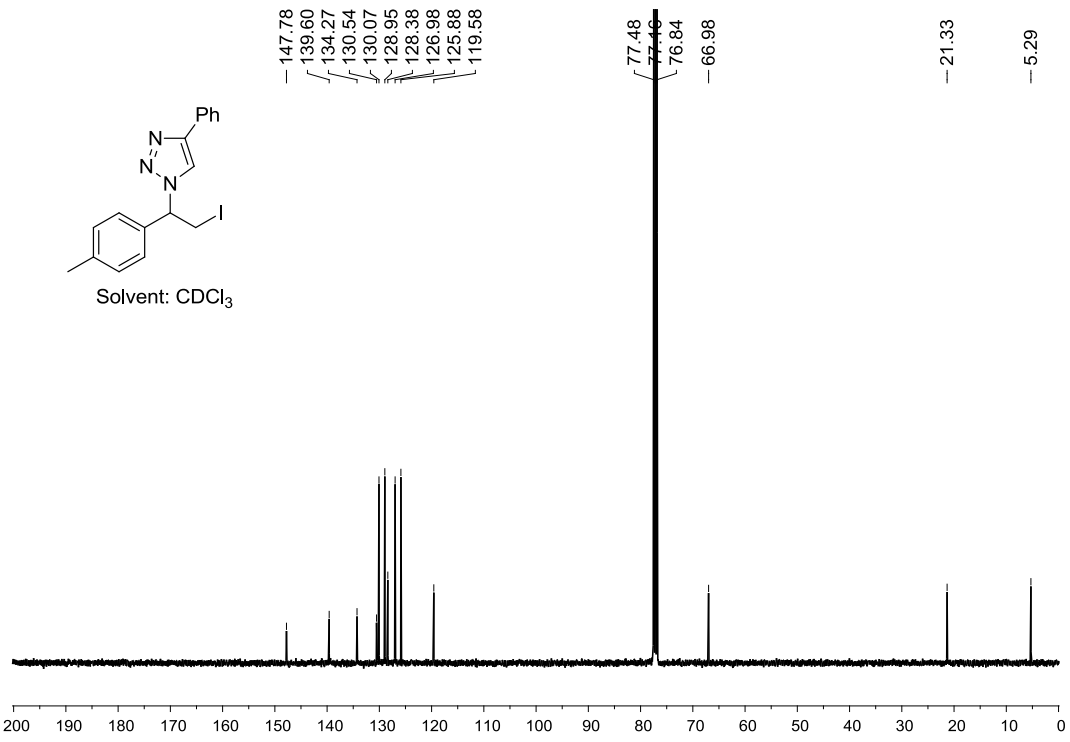


Figure 5.35: ^{13}C NMR spectrum of 1-(2-iodo-1-(*p*-tolyl)ethyl)-4-phenyl-1*H*-1,2,3-triazole (**9**).

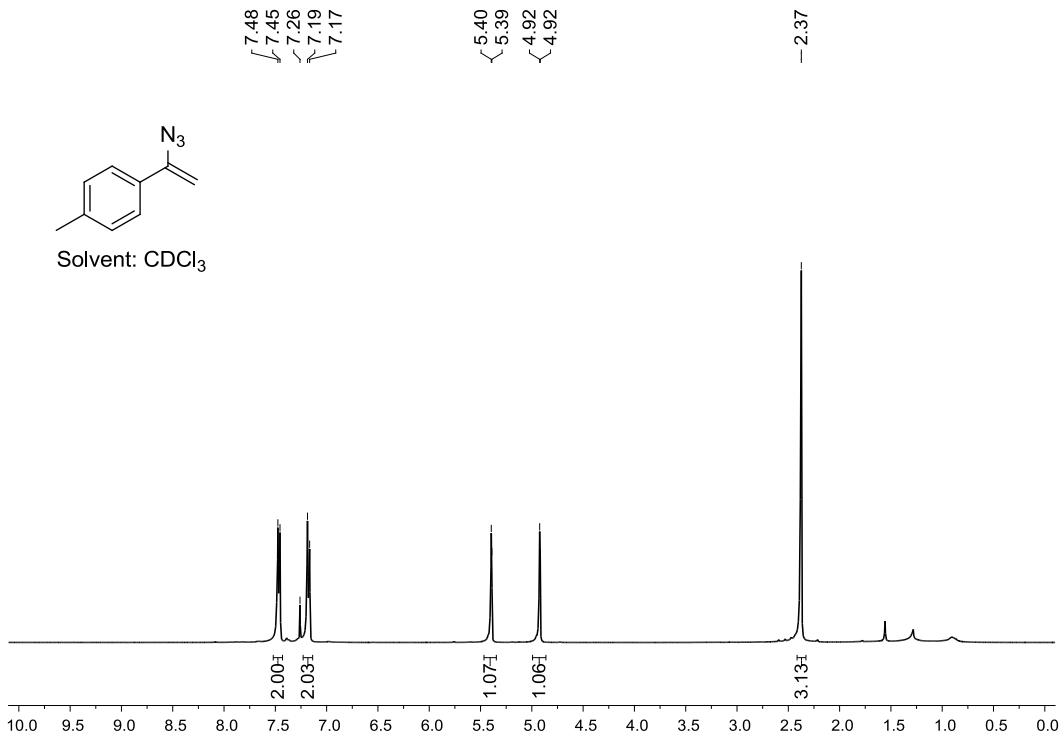


Figure 5.36: ^{1}H NMR spectrum of 1-(1-azidovinyl)-4-methylbenzene (**10**).

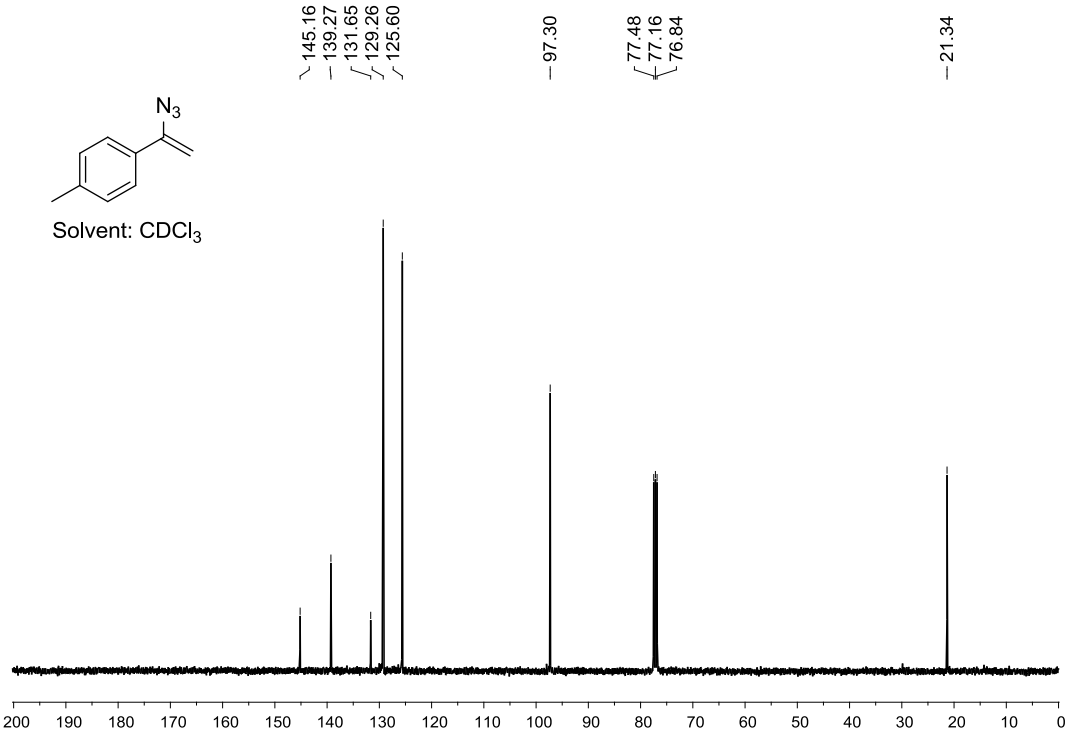


Figure 5.36: ^{13}C NMR spectrum of 1-(1-azidovinyl)-4-methylbenzene (**10**).

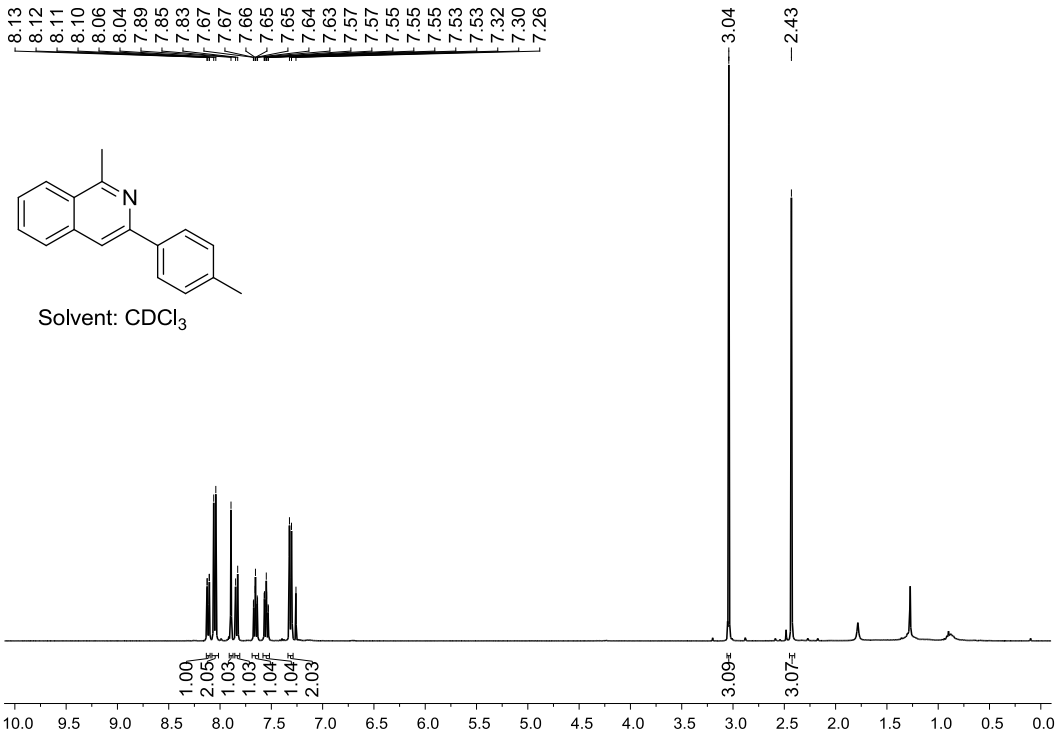


Figure 5.37: ^{1}H NMR spectrum of 1-methyl-3-(*p*-tolyl)isoquinoline (**12**).

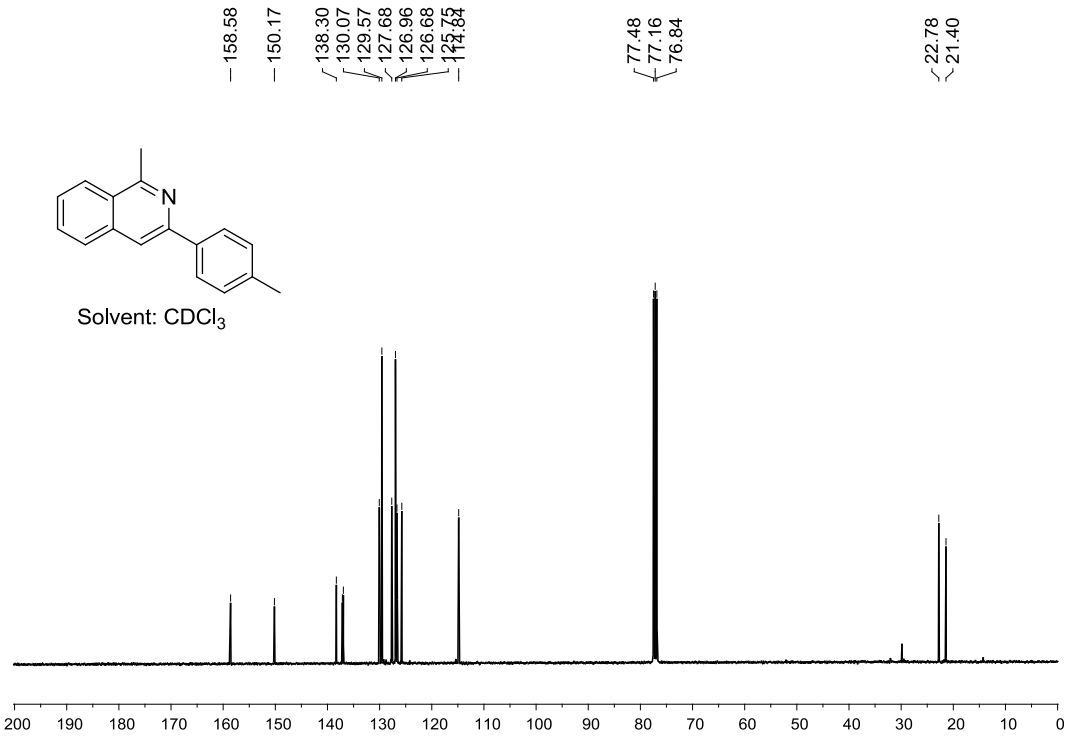
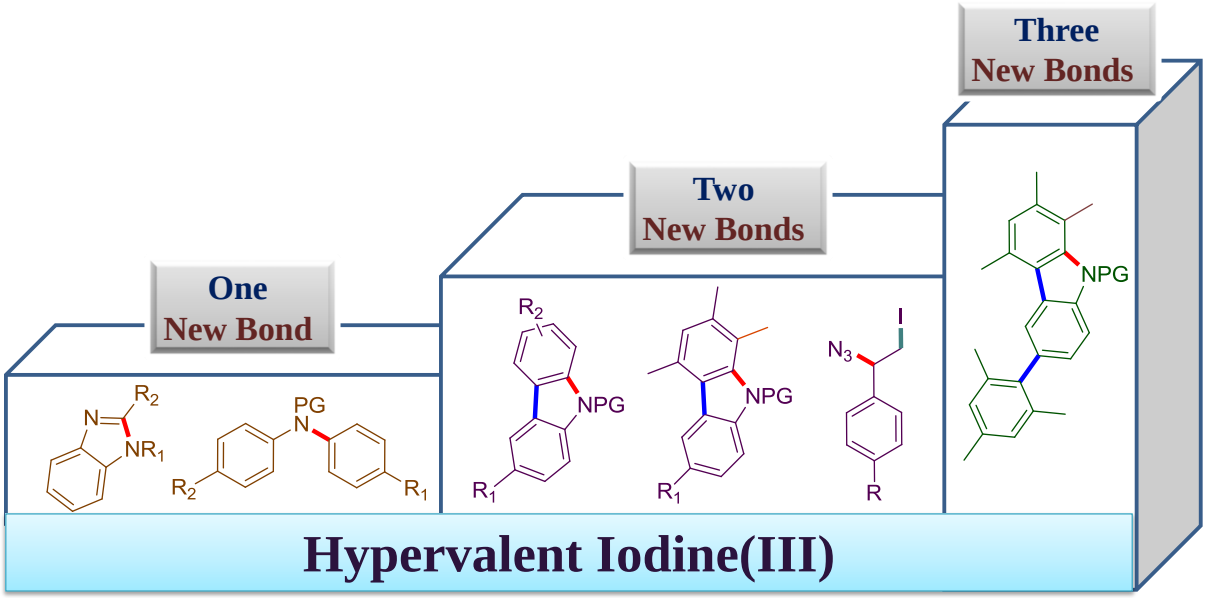


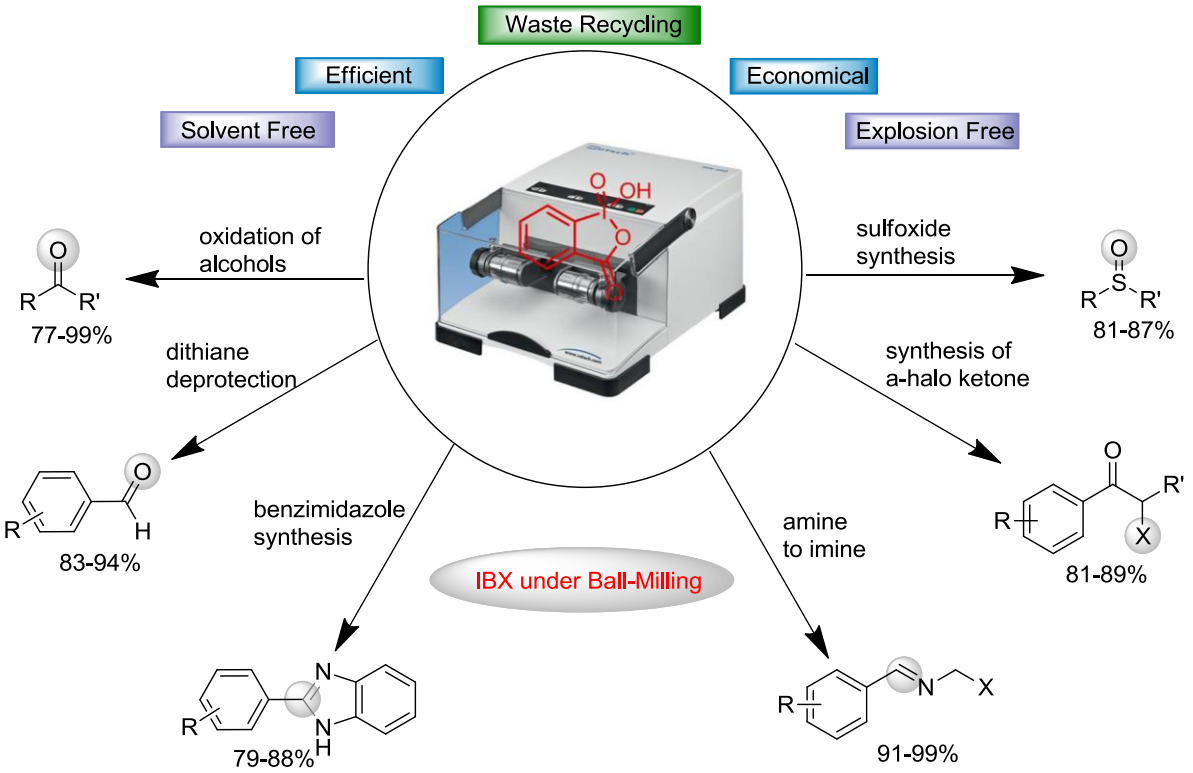
Figure 5.38: ^{13}C NMR spectrum of 1-methyl-3-(*p*-tolyl)isoquinoline (**12**).

SUMMARY


Three
New Bonds
Two
New Bonds
One
New Bond
NPG
NPG
NPG
Hypervalent Iodine(III)

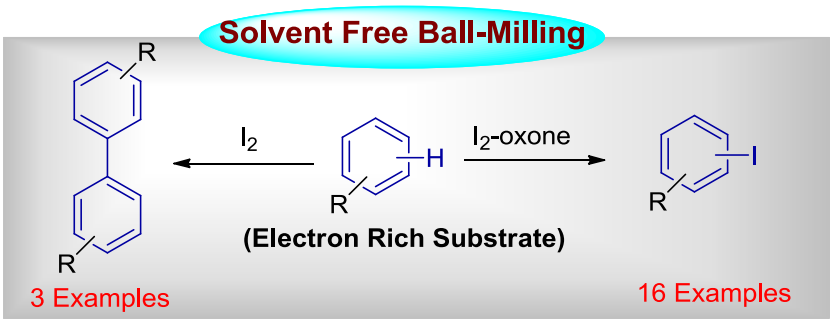
Works are NOT Part of the Thesis

IBX mediated oxidations



T. K. Achar, S. Maiti and P. Mal, *RSC Adv.* **2014**, *4*, 12834-12839.

Aryl-iodination and biarylation



S. Maiti and P. Mal, *Synth. Commun.* **2014**, *44*, 3461-3469.