Synthesis of Nitrogen Based *N*-Heterocycles *via* Metal Free Approach

By

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Contents

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List of Abbreviations Used

Å	Angstrom
Ac	Acetyl
AcOH	Acetic Acid
AcOOH	Peracetic acid
Anhyd	Anhydrous
aq	Aqueous
Bn	benzyl
Bp	Boiling Point
BPO	Benzoyl Peroxide
br	Broad
Bz	Benzoyl
ºC	Degree Celcius
Calcd	Calculated
cm	Centimeter
Conc	Concentrated
Cy	Cyclohexyl
d	Doublet, Days
DCE	1,2-Dichloroethane
DCM	Dichloromethane
dd	Doublet of a Doublet
dil	Dilute
DTBP	Di-tert-butyl peroxide
DMF	*N*,*N*-Dimethyl Formamide
DMP	Dess-Martin Periodinane
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
Hz	Hertz
IBX	2-Iodoxybenzoic acid
IBA	Iodosobenzoic acid
IDB	Iodosylbenzene
IR	Infrared
lit	Liter
m	Multiplet
*m*CPBA	*meta*-chloroperbenzoic acid
*m*CPBA	*meta*-chlorobenzoic acid
NIS	N-iodosuccinimide
M	Molar
MeCN	Acetonitrile
mp	Melting point
Me	Methyl
Min	Minutes
mL	Milliliter
mmol	Millimole
mol	Mole
MS	Mass Spectra, Molecular Sieves
Ms	Methane sulfonyl
M/Z	Mass to charge ratio
nm	Nanometer
NMP	N-Methyl-2-pyrrolidine
NMR	Nuclear Magnetic Resonance
Piv	Pivaloyl
PIDA	Phenyliodine(III) diacetate
PIFA	Phenyliodine bis(trifluoroacetate)
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

Summary

Nitrogen based heterocyclic scaffolds have a pivotal role in medicinal chemistry due to its significant contribution in the development of novel composites. Nature possesses an immense distribution of nitrogen based molecules which includes vitamins, nucleic acids, base pair of DNA and RNA molecule. Nitrogen based molecules have gained prominence at an alarming rate because of its application in agrochemicals, pharmaceuticals and antibiotics.

The electron rich nitrogen containing heterocycles were synthesized by formation of intermediates like nitrenium ion and azidyl radical. Nitrogen intermediates like nitrenium ion, nitrene or azidyl radical are useful in bringing about useful synthetic transformation to produce small organic molecules. The sulfonamide group helps to stabilize the nitrenium ion and this nitrenium ion tautomerizes to form carbenium ion. Nucleophilic attack at the carbenium or the nitrenium ion leads to formation of the desired product. C-H arylation of sulphonamides at the ortho position was successful by formation of carbenium from nitrenium ion. Synthesis of carbazoles was achieved by distal C-H functionalization followed by methyl migration using iodine(III) reagents. The same iodine(III) was generated under *in-situ* conditions using PhI-mCPBA. Terphenyls were synthesized with iodine(III) reagents solely where more facile intramolecular C-N coupling was overcome and intermolecular C-C coupling reaction was established at mild reaction conditions using hypervalent iodine(III) reagents. Using Phosphorus-oxygen interaction, triazoles were synthesided via azidyl radical.

Conclusions

The thesis has been made towards developing of Nitrogen based heterocycles using inexpensive and sustainable reagents. These methodologies are shown to have useful scope to synthesize various small organic molecules with mechanistic details with significant importance. The current thesis contains five chapters and the content of each chapter have been well illustrated with one introduction chapter and four working chapters. The Chapter 1 mainly focuses on a brief introduction of various intermediates like nitrenium , nitrene, azidyl radical for construction of useful synthetic scaffolds. There are two parts in this chapter: (1) Nitrenium ion chemistry in organic synthesis. (2) Azide radical intermediate. In Chapter 2, we have described C-H arylation of sulfonamides using hypervalent iodine(III) reagents. The desired product formation is controlled by the type of nature of the nucleophile available. In t chapter 3, we have successfully demonstrated iodine(III) reagent to functionalize a distal C-H bond in a template free approach for synthesis of carbazoles followed by alkyl migration. Also using iodobenzene and *meta*-perchloroperoxybenzoic acid, iodine(III) was generated under *in-situ* conditions to synthesis carbazoles in good to excellent yields. Chapter 4 deals on synthesis of unsymmetrical 2,6 diarlanilide synthesis. 2 Amidobiphenyls undergo C-H arylation in presence of an oxidant like PIDA where the intramolecular C-N coupling is much more facile. The intramolecular C-N coupling could be successfully controlled by proper choice of substrate and the nucleophilicity of the external nucleophile controls the reaction. The amidobiphenyl substrate was designed in such a way that the arene part of the biarylsulfonamide was made sufficiently electron deficient. This is turn controls the nucleophilicity of the external arene which is superior and intermolecular C-H arylation took place overcoming the intramolecular C-N coupling reaction.Thus, unsymmetrical 2,6 diarylanilide were syntheized under mild and metal free condition. In chapter 5, we have discussed about formation of triazoles in a very mild and efficient manner with good to excellent yield. The phosphorus nitrogen bond energy

is very high which is (617+20) kJ/mole could be broken under mild reaction condition. Such an extremely strong covalent bond activation was assisted by Phosphorus-oxygen interaction. Azidyl radical was confirmed through EPR studies.

Summary

Nitrogen based heterocyclic scaffolds have a pivotal role in medicinal chemistry due to its significant contribution in the development of novel composites. Nature possesses an immense distribution of nitrogen based molecules which includes vitamins, nucleic acids, base pair of DNA and RNA molecule. Nitrogen based molecules have gained prominence at an alarming rate because of its application in agrochemicals, pharmaceuticals and antibiotics.

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CHAPTER 1

Introduction: Synthesis of Nitrogen Based Molecules via Sustainable Approach

1.1 ABSTRACT

This Chapter mainly focuses on the synthesis of *N*-heterocyclic compounds *via* metal free approach. Metal free approaches in particular hypervalent iodine(III) reagents have been extensively used for building *N*-heterocyclic scaffolds *via* important synthetic intermediates like nitrenium , carbenium or nitrene have been discussed elaborately. Various intermediates like nitrenium ion, nitrene radical or azidyl radical which are potentially useful for construction of *N*-heterocyclic scaffolds have been discussed. The nitrogen containing structural motifs have also been extensively used for C-H functionalization reactions, some of which are discussed in this chapter.

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1.2 INTRODUCTION

Synthesis of *N*-Heterocycles has witnessed valiant years in organic chemistry owing to its numerous applications in the development of drug molecules, pharmaceutical and agrochemical industries.[1-3] Natural products which have attracted significant attention due to their bioactive properties involving antimalarial, antifungal, antihypertensive, anti-inflammatory, and trichomonal possess *N*-heterocycle in its backbone.[4] They have sound to be significant intermediates for preparing biologically active compounds. The compounds are also known to act as ligands in coordination chemistry and have a widespread application in homogenous catalysis. They have profound applications in supramolecular chemistry[5], luminescent sensors, and photosensitizers for solar cells and constitute a vital element of the

universe.[6-8] Henceforth, the synthesis of nitrogen based *N*-heterocycles is a demanding subject area in organic chemistry.

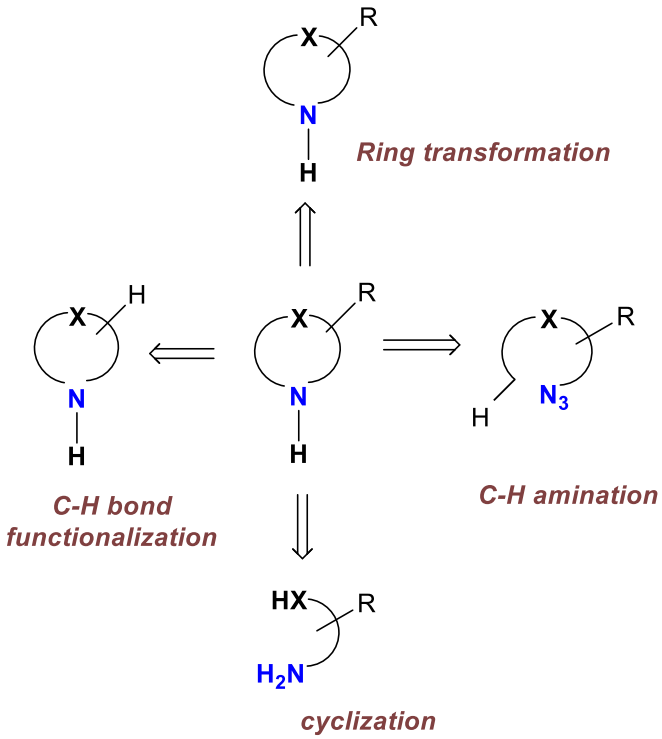


Figure 1.1 Strategies for construction of *N*-heterocyclic scaffolds and its application in organic synthesis.

N-heterocyclic scaffolds are significant due to its extensive application in medicinal chemistry. The need to develop sustainable and greener methods for construction of *N*-heterocyclic moieties has been a growing concern among the synthetic chemists. Metal free synthetic routes which are safer, milder and environment friendly haven always been a better alternative compared to metal mediated synthetic transformations. Among them hypervalent iodine(III) reagents are effectively used to achieve the transformation.[9, 10] Cross Dehydrogenative Coupling[11], C-H amination[12], C-H bond functionalization[13] and transformation of the ring to other forms are some of the approaches involved to construct *N*-heterocyclic scaffolds as displayed in figure 1.1.

1.2 NITRENIUM ION CHEMISTRY

Nitrenium ion can be defined as a di-coordinate species containing a positively charged nitrogen center. These reactive electrophilic intermediates are isoelectronic with carbocations, carbenes and nitrenes possessing six electrons in its valence shell.[14] Nitrenium ions have two non-bonding electron pairs and based on its electronic spin orientation, nitrenium ions exist either in singlet state or triplet state (Figure 1.2).[15] The stability of the nitrenium ion is dependent on its spin state. Generally, it is observed that nitrenium ion in its triplet state is likely more stable. It faces less coulombic repulsion due to favorable exchange interaction between parallel spins, whereas the singlet state of nitrenium ion consists of paired electrons faces more Coulombic repulsion. From a geometric point, the singlet state is expected to have bond angle of (110-130^{o}) whereas triplet state is said to exhibit a large bond angle of (150-160 ^{o}).

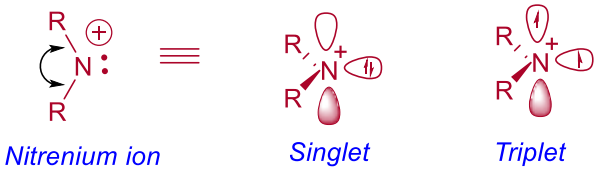


Figure 1.2 Nitrenium ion, its structure and spin state.

The parent nitrenium ion (NH_2^+) was established to stay in a ground triplet state ($^3B_1$) which is separated from the singlet ground state ($^1A_1$) by approximately 30 kcal/mole. Introducing an *N*-alkyl substituent reduced the singlet to triplet (S-T) energy gap, especially when a methyl group is present. It has been found that π donor ligands such as cyanide, halogen, or a

hydroxyl group assist in stabilizing the singlet by donating an electron to vacant $2p_z$ situated on the central atom. With a strongly electron-withdrawing group, nitrenium ion substituted by π donor heteroatom are in lower energy ground singlet state with a high N=X π character. For *N*- hydroxyl *N*-formyl nitrenium ion, the N-O bond has a significant rotational energy barrier to rotation which is approximately (29.7 kcal/mole), as calculated by Glover. This proves the oxygen lone pair has a stabilizing effect as a result of which rotational barrier which exists is extremely low or nil for the nitrogen carbon bond. This fact indicates the role of an acyl substituent plays a minimal for the stability of the alkoxy substituted nitrenium ion. Aryl nitrenium ions exist in a singlet ground state with a short C-N bond and planar geometry, whereas the triplet state exits with a long C-N bond with non-planar geometry, as portrayed in figure 1.3a. Aryl nitrenium ions are stabilized more than parent nitrenium ions. The extra stabilization is due to the vacant p orbital of the nitrogen center with π-lobes of the aromatic ring. The degree of stabilization is also acquired by delocalization of positive charge in the π-orbital of phenyl ring indicated in figure 1.3b. The singlet to triplet splitting in the species varies with the nature of the substituent present on the phenyl ring. Electron donating groups stabilize the singlet state more than the triplet state in general but electron releasing *meta* substituents stabilize the triplet state to such an extent that it becomes its ground state. In such cases, the triplet state possesses an electronic configuration of π, π^* as the electron in the nonbonding lobe of π orbital is shifted to π^* orbital as shown in figure 1.3c.[16]

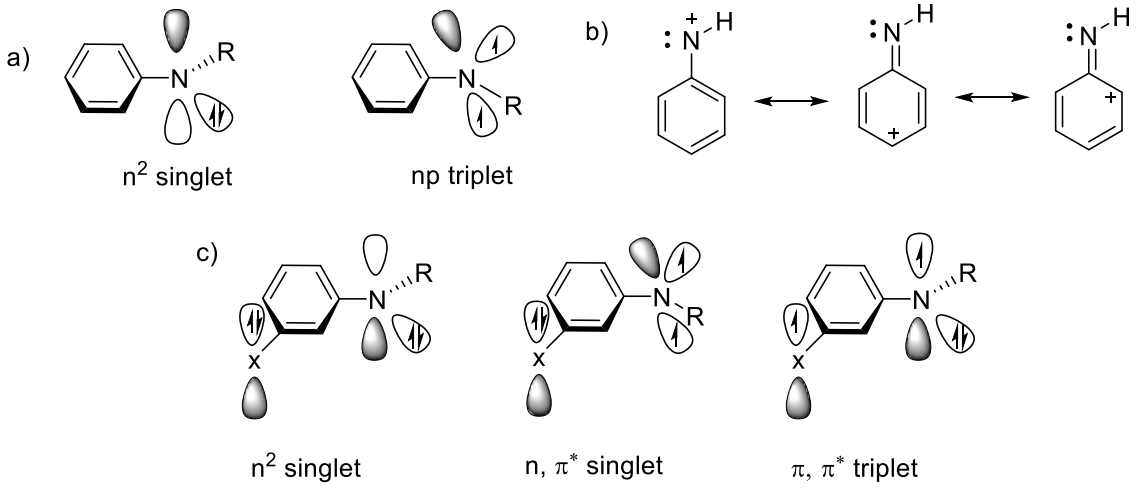


Figure 1.3 a) Spin state of aryl nitrenium ion b) Resonance stabilized π electron cloud of aryl nitrenium ion c) spin state of *meta* substituted π electron donor of aryl nitrenium ion.

1.3 HYPERVALENT IODINE(III) REAGENTS

Hypervalent iodine reagents have risen to prominence in the last few decades. The ease of its availability, high stability, controlled oxidizing ability have made them highly versatile for the construction of critical heterocyclic scaffolds. Commonly used hypervalent iodine reagents for the generation of nitrenium are $PhI(OAc)_2$, $PhI(OCOCF_3)_2$, $PhI(OPiv)_2$, Dess-martin periodinane (DMP), 2-iodoxy benzoic acid (IBX) have been greatly utilized to develop a plethora of organic molecules as displayed in figure 1.4. [10]

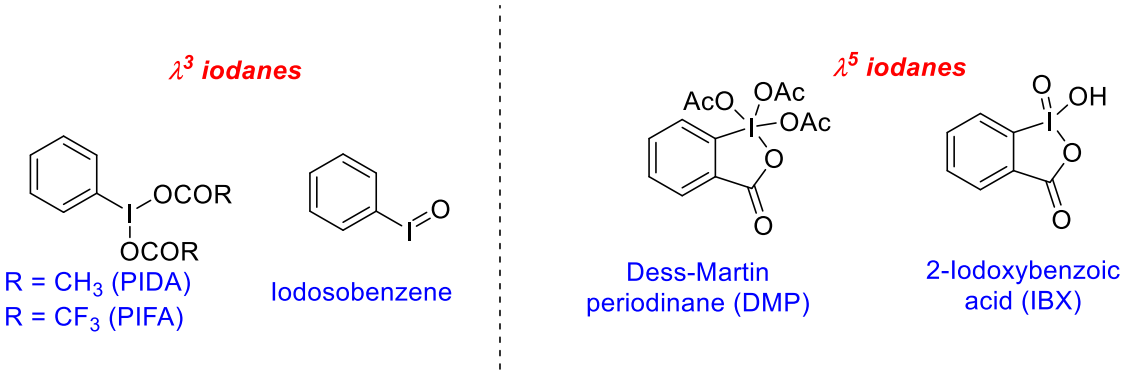
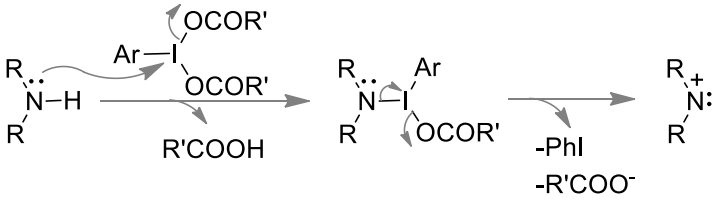


Figure 1.4 Examples of hypervalent iodine reagents.

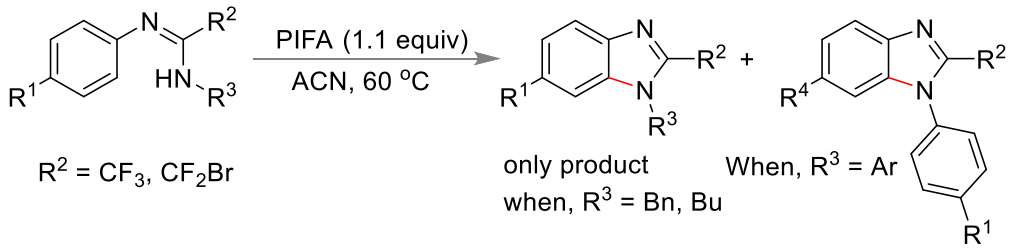
1.4 REACTIVITY

Nitrenium ion can be generated from iodine(III) reagents by employing a secondary amine. The nitrogen lone pair attacks the electrophilic iodine center to form amido-λ^3-iodane (Scheme 1.4). N-I bond heterolysis leads to the formation of nitrenium ions with reductive elimination of iodoarene. Nitrenium ions are electrophilic in nature and are easily prone to nucleophilic attack. Nucleophile present in the reaction system attacks the electrophilic nitrenium ion to produce the desired product.[17]



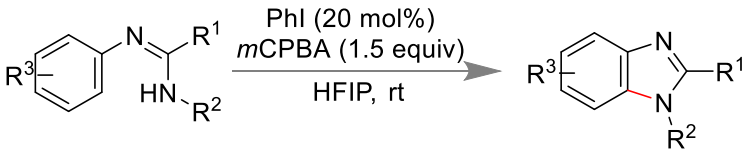
Scheme 1.1 Nitrenium ion formation from iodine(III) reagents.

This concept has been utilized in synthetic methodologies to develop significant structural motifs, especially *N*-heterocyclic scaffolds, some of which is discussed here. Wu and co-workers have synthesized 1,2-disubstituted benzimidazoles by intramolecular cyclization using bistrifluoroacetoxyiodobenzene (Scheme 1.2).[18] N-*aryl* substituted imidamides produce two different products based on the stability of nitrenium ion generated from it. However, only one product formation is formed with aliphatic substituted imidamides are used as precursors. Mechanistic studies revealed that nitrenium ion generated from iodine(III) reagents undergo resonance delocalization and based on the stabilizing ability by adjacent aryl groups, nitrenium ions exhibit in two different resonating states. This resulted in formation of two different products.



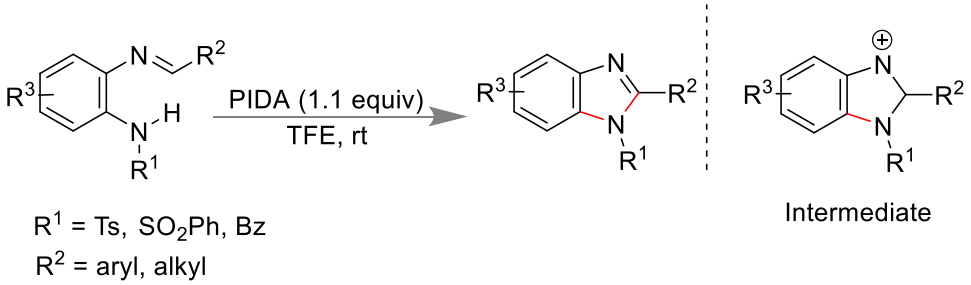
Scheme 1.2 Benzimidazole synthesis mediated by PIFA.

Intramolecular C-H amination was demonstrated by Punniyamurthy group for the preparation of 1,2-disubstitutedbenzimidazoles (Scheme 1.3).[19] Iodobenzene (PhI) combined with oxidant *m*CPBA produced iodine(III) condition under *in-situ* conditions. Sulfonyl protected amines like Ts-, Ms- were effective and produced the desired product whereas amidines were unsuccessful with alkyl substitution or without substitution deliver the desired outcome.



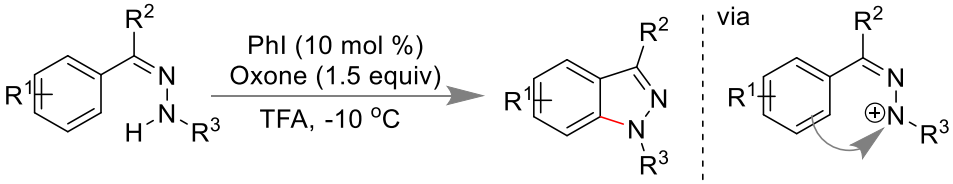
Scheme 1.3 Benzimidazole synthesis mediated by PhI AND *m*CBPA.

Mal and coworkers were successful in establishing an intramolecular C-H amidation using PIDA to synthesize benzimidazole, as shown in scheme 1.4.[20] The methodology was effective to produce the targeted products in excellent yields. The reaction proceeded by the formation of nitrenium ion intermediate. ICP-OES experiments were conducted to check the trace of metal impurity in hypervalent iodine reagents.



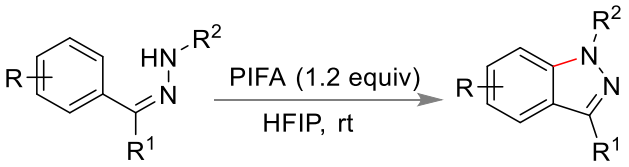
Scheme 1.4. Benzimidazole synthesis *via* intramolecular C-H amidation.

Tanimori and coworkers have established an iodobenzene catalyzed reaction of aryl hydrazones using oxone as oxidant at -10 ^{0}C to synthesize indazole. Here iodine(III) was generated *in situ,* which furnished the nitrenium ion following intramolecular nucleophilic attack producing indazoles.



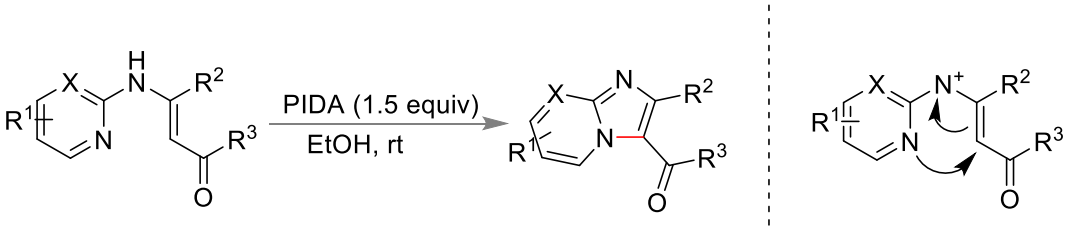
Scheme 1.5 Iodobenzene catalyzed indazole synthesis

Another work where synthesis of 1*H*-indazoles was achieved using hypervalent iodine(III) reagent PIFA at room temperature by intramolecular C-H amination technique. (Scheme 1.6).[21] The mechanistic pathway is quite similar where the reaction proceeded through the generation of nitrenium ion intermediate and further nucleophilic attack taking place from aryl group.



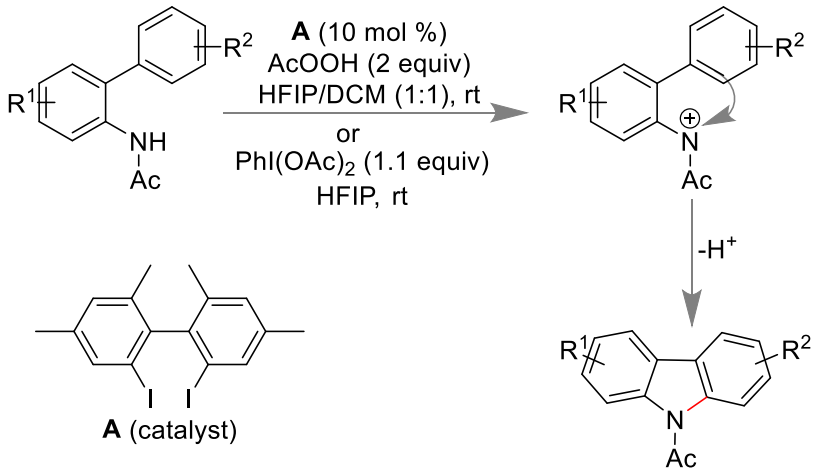
Scheme 1.6 PIFA mediated indazole synthesis.

Imidazopyrimidines are another class of *N*-heterocyclic compounds that have potential applications in medicine. Synthesis of Imidazo[1,2-a]pyrimidines was successfully achieved in acetonitrile and PIDA in ethanol (Scheme 1.7).[22] Nitrenium ion was generated where nucleophilic attack from nitrogen of pyrimidyl/pyridine ring took place on benzene ring following deprotonation to gain aromaticity.



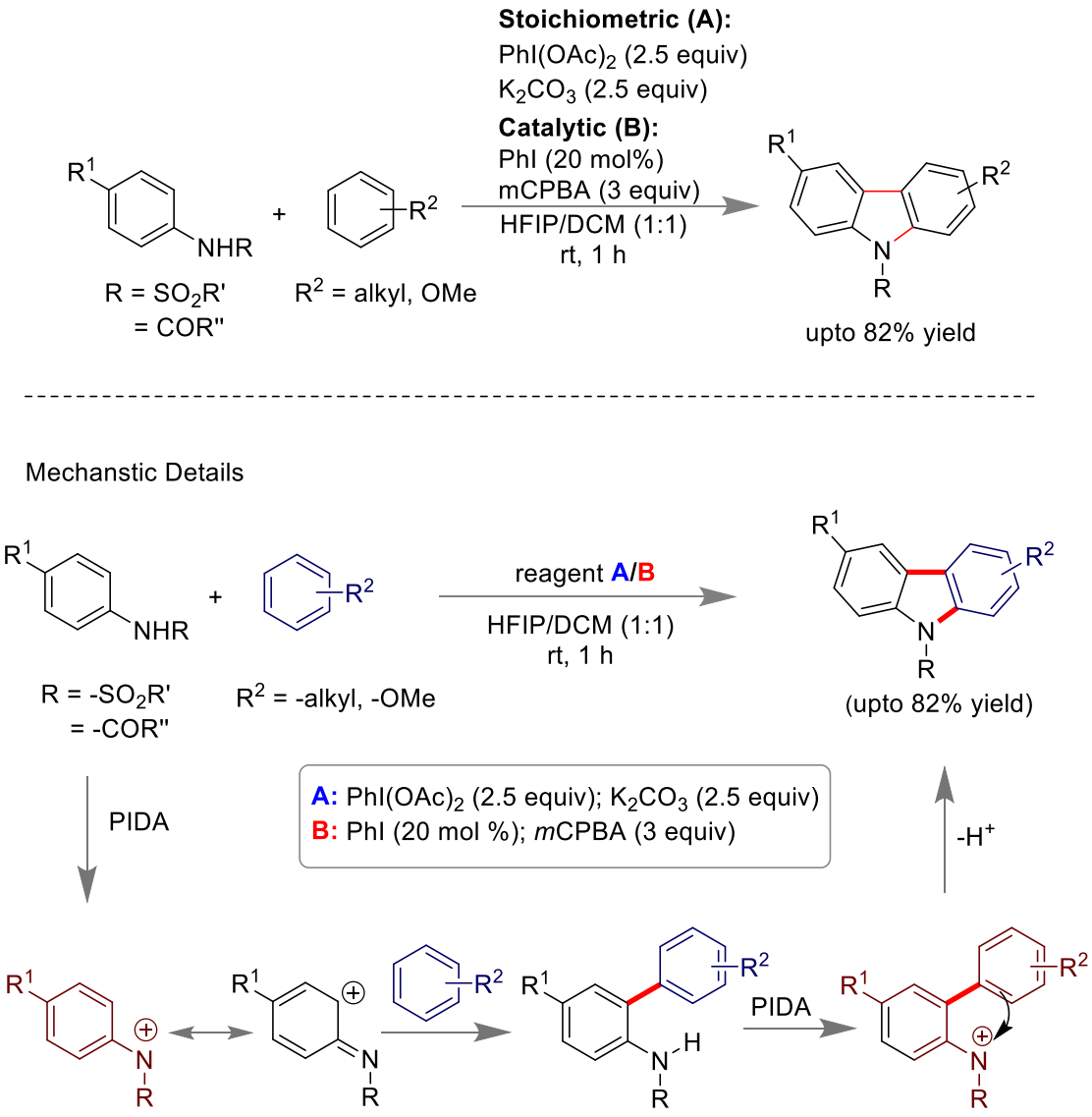
Scheme 1.7 Synthesis of Imidazo[1,2-a]pyrimidines mediated by PIFA.

Carbazole in an important heterocyclic scaffold found in numerous drug molecules. As a result, the synthesis of carbazoles in the mild and metal free condition is highly desirable. 2-acetaminobiaryls were used as precursors to achieve the targeted carbazole using hypervalent iodine(III) reagent PIDA and generating iodine(III) under *in-situ* conditions. (Scheme 1.8).[23] Later, this methodology was extended on 2,6-diarylacetanilides to get 1-arylcarbazoles by electrocyclization using PIDA.[24]



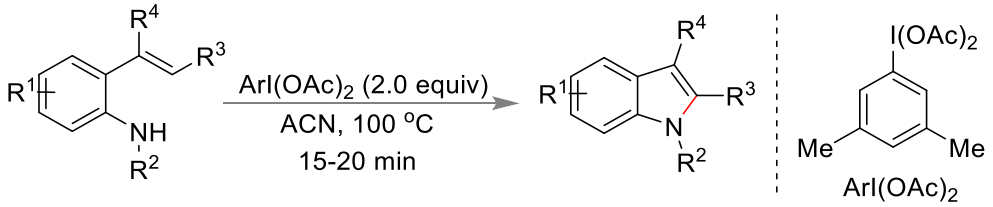
Scheme 1.8 Carbazole synthesis by C-H bond functionalization

Mal and co-workers have used iodine(III) reagent to synthesize carbazoles between nonfunctionalized arenes and anilides. (Scheme 1.9).[25] Iodine (III) was generated under two conditions (i) by use of PhI(OAc)2 in a stoichiometric amount in combination with K2CO3 and (ii) use of the catalytic amount of iodobenzene in the presence of (mCPBA) as an oxidant. Better yields were obtained with a stoichiometric amount of the reagent PIDA. The mechanism proceeded by forming the nitrenium ion followed by carbenium ion to form a C-C bond which further underwent nucleophilic attack from the arene part to form carbazaole as a product.



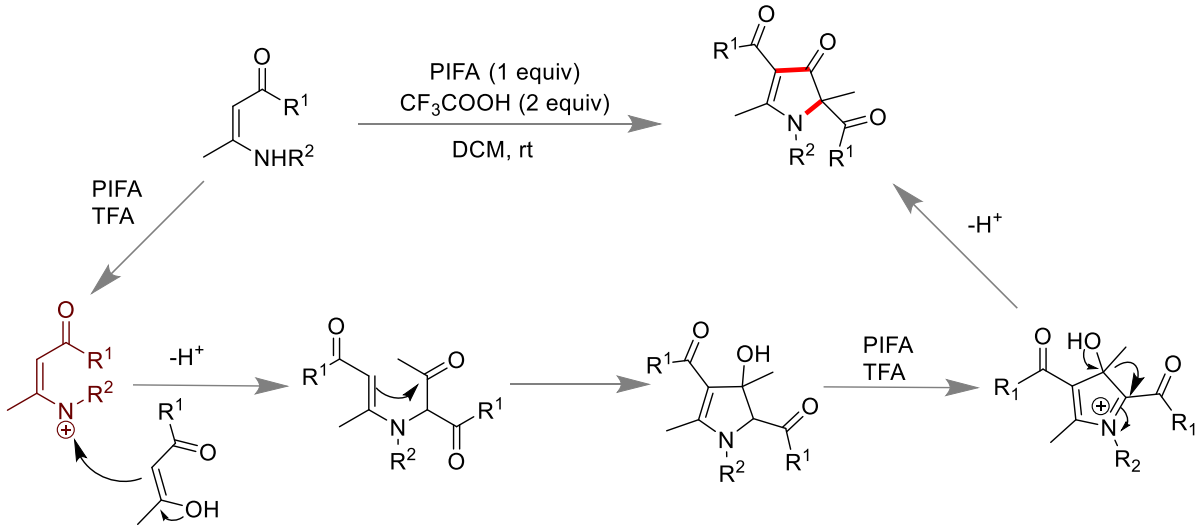
Scheme 1.9 Synthesis of carbazole by cross dehydrogenative coupling.

Indole based scaffolds were synthesized by Su and Mo group, as shown in (Scheme 1.10).[26] 3,5-Dimethylphenyliodine diacetate was the iodine(III) reagent used in acetonitrile solvent to synthesize indoles. The reaction proceeded through nitrenium ion formation along with the incorporation of acetoxy group to produce the desired product.



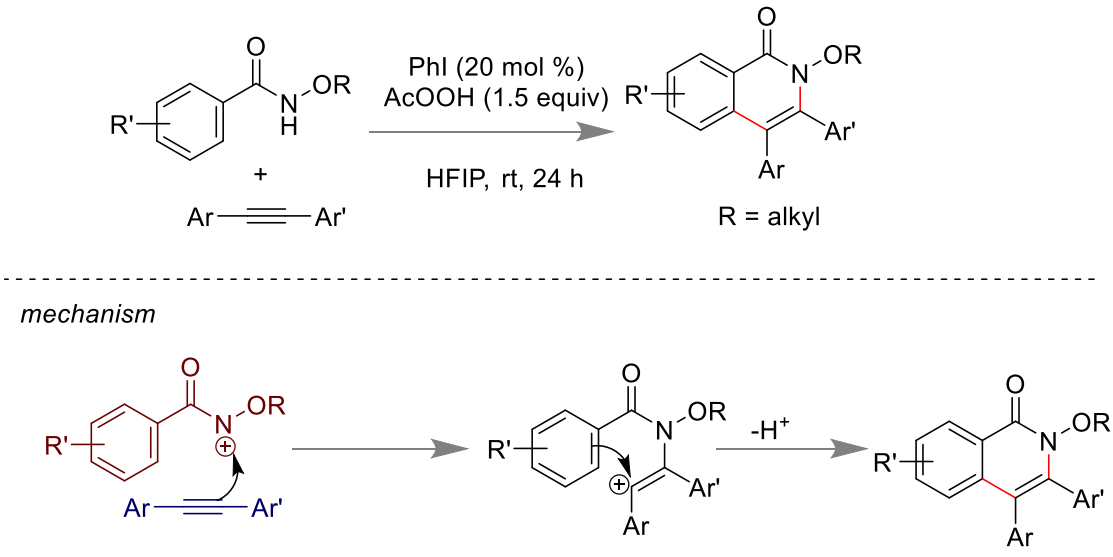
Scheme 1.10 Synthesis of indole synthesis mediated by hypervalent iodine(III) reagent.

Dong and co-workers have synthesized pyrrolinones by using PIFA as an oxidant in a sequential manner by forming Carbon-Carbon and Carbon -Nitrogen bond (Scheme 1.11).[27] Authors have speculated that the reaction mechanism proceeded by forming nitrenium ion intermediate following a benzilic acid type rearrangement.



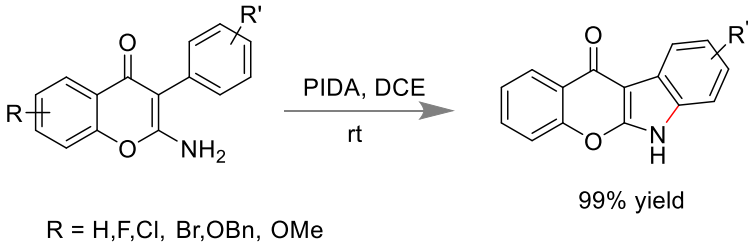
Scheme 1.11 Pyrrolinones synthesis mediated by PIFA.

Antonchick has established a hypervalent iodine(III) condition under in-situ conditions by annulation reaction to synthesize the isoquinoline system at room temperature conditions. (Scheme 1.12).[28] Iodobenzene was used as a catalyst in the presence of an oxidant like peracetic acid (AcOOH).



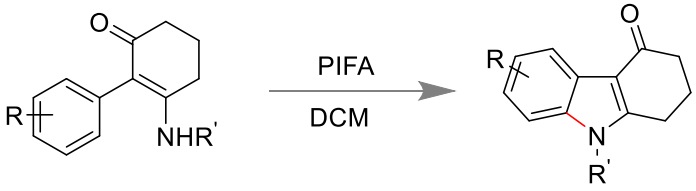
Scheme 1.12 Isoquinolinone synthesis catalyzed by iodobenzene.

The oxidant hypervalent iodine(III) reagent had been used to construct chromeno[2,3-b]indol-11(6H)-ones using pendant free amine *via* intramolecular oxidative C-N coupling. [29] The reaction proceeded via nitrene formation as the intermediate with loss of proton to form indolone derivative as products.



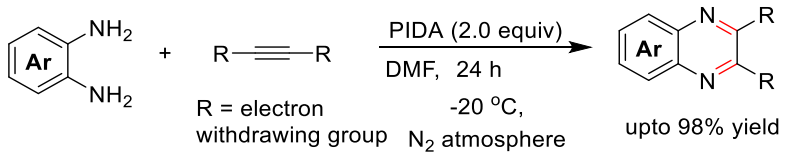
Scheme 1.13 Oxidative C-N coupling mediated by nitrene intermediate.

Kang Zhao and coworkers have illustrated formation of carbazolone via oxidative coupling of C(sp^2)- NH bond from 2-aryl enaminones.[30] Carbazolones are key intermediate for synthesis of alkaloids and drugs. The reaction pathway involved two potential mechanistic pathways to form the desired products. The mechanism involved a concerted process when R was substituted by an alkyl substituent and by the formation of nitrene intermediate when R was replaced by hydrogen.



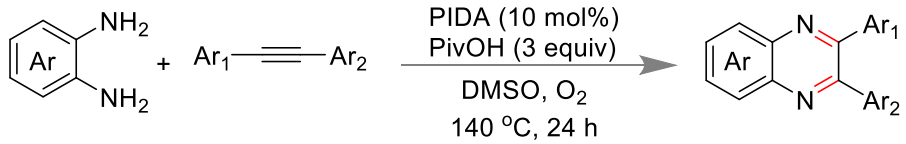
Scheme 1.14 Intramolecular cyclization for synthesis of carbazolones.

Minakata and co-workers have established synthesis of quinoxalines from electron-deficient alkynes and *ortho* phenylenediamines using hypervalent iodine(III) reagents under an inert atmosphere a temperature of -20°C.[31] The methodology proved to be efficiently producing the quinoxalines in excellent yields.



Scheme 1.15 Hyervalent iodine(III) reagent mediated quinoxaline synthesis.

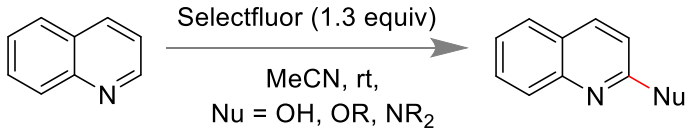
Quinoxalines were synthesized when *ortho*-phenylenediamines were made to react with internal alkynes under *in-situ* in the presence of hypervalent iodine(III) reagent (Scheme 1.16). [32] PIDA was used in catalytic amount along with 3.0 equivalent of pivalic acid as an additive to generate the pivaloyl derivative of hypervalent iodine(III) reagent.[32]. The iodine(III) reagent generated under *in-situ* conditions reacted with diarylacetylene substrate to form a 1,2-dicarbonyl compound as an intermediate which reacted with *ortho* phenylenediamine producing quinoxalines.



Scheme 1.16 Synthesis of quinoxaline from ortho phenylenediamines.

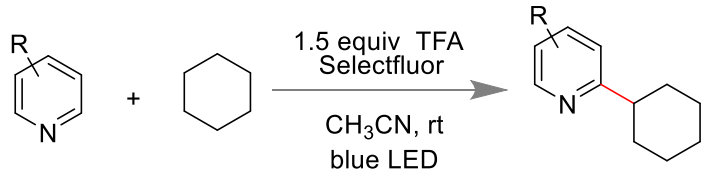
1.5 C-H functionalization of N- heterocycles

N-heterocycles are significantly important functional moieties [33] in natural products and the pharmaceutical industry. C-H functionalization of N-heterocycles had been reported by Hei and co-workers in a mild metal free approach using selectfluor in acetonitrile as solvent.



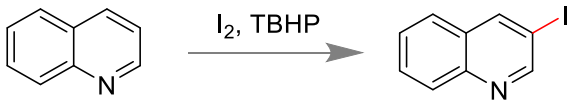
Scheme 1.17 C-H functionalization of quinoline with selectfluor.

Pyridine based *N*-heterocyclic moieties undergo C-H arylation with alkylated heteroarenes to produce a C-H arylation product. Using visible light, oxidative sp^3 C-H arylation occurred at environmentally benign conditions affording C-H functionalization of pyridine.[34]



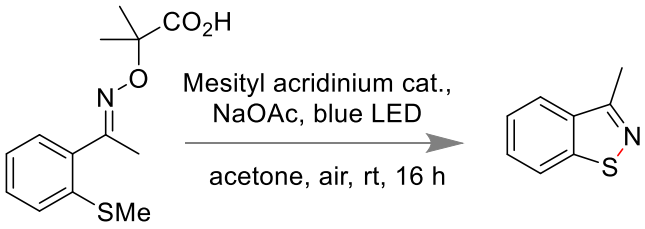
Scheme 1.18 Visible light mediated C-H Arylation with heteroarenes.

Fused N- heterocyclic iodides were synthesized by using TBHP and molecular iodine.[35] Regioselective C-H functionalization *via* molecular iodine activation and using nitrogen based heterocycle generated electrophilic iodine species I^+ and produced $^tBuO\cdot$ as a free radical.



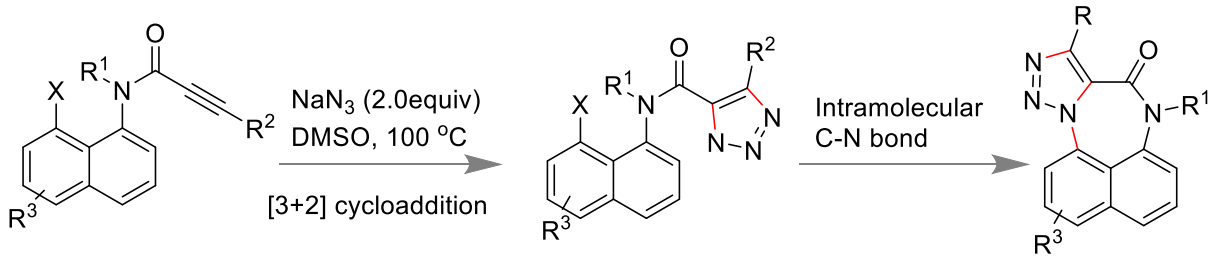
Scheme 1.19 Regioselective iodination of *N*-heterocyclic arenes.

A sustainable approach for the synthesis of α-Amino-oxy acid has been used to construct isothiazoles using visible light photo-redox catalysis.[36] The simple strategy included simple reaction conditions with an array of substrate scope and divergent functional groups.



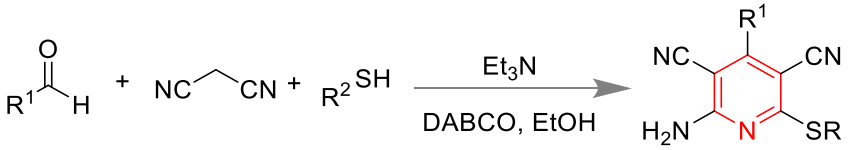
Scheme 1.20 Metal free approaches for synthesis of isothiazoles.

Diazepinone skeletons are significant as they are used in the treatment of the central nervous system. The C-N coupling to synthesize triazole fused diazepinone was achieved *via* triazole formation in the intermediate step involving [3+2] cycloaddition using sodium azide.



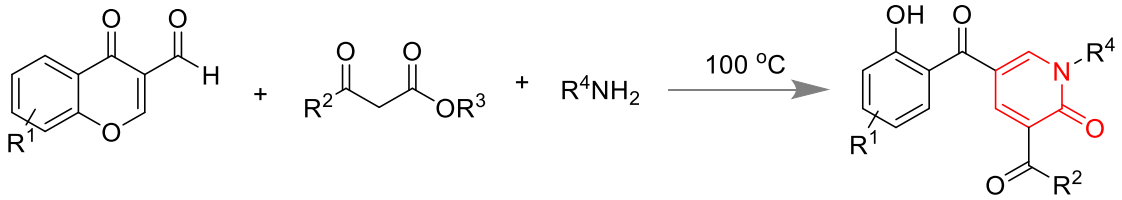
Scheme 1.21 Synthesis of triazole fused diazepinone using sodium azide.

Multicomponent synthesis of functionalized pyridines had been achieved by aldehyde, thiol and malononitrile which under in-situ conditions was accompanied by the formation of enaminonitrile.[37] The reaction was successful with aromatic, heteroaromatic, or heteroaromatic aldehydes to produce the functionalized pyridines in a wide array.



Scheme 1.22 Metal free multicomponent reaction for the synthesis of functionalized pyridine.

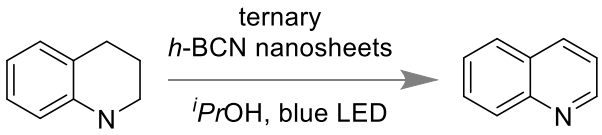
2-pyridones were synthesized by Lee and co-workers using 4-oxo-4H-chromene3-carbaldehyde, 1,3-diketoesters and primary amines without the use of solvent and catalyst.[38] The methodology sustained a broad functional group and produced the desired product with less reactive aromatic amines.



Scheme 1.23 Synthesis of pyridone in the absence of catalyst and solvent.

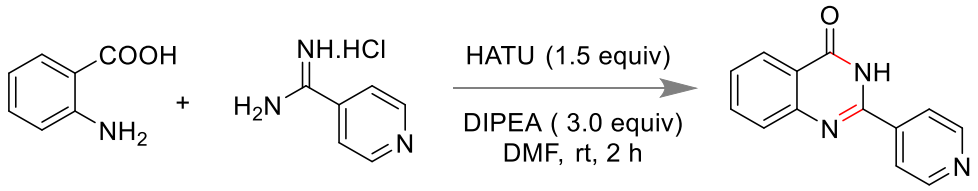
Hexagonal BCN nanosheets have been employed for the dehydrogenation of N-heterocycles using a visible light source. The process involved the evolution of hydrogen gas and hence

does not require any proton acceptor. The method involved h-BCN as the photocatalyst and isopropanol as solvent, forming the unsaturated heterocycle under visible light irradiation.



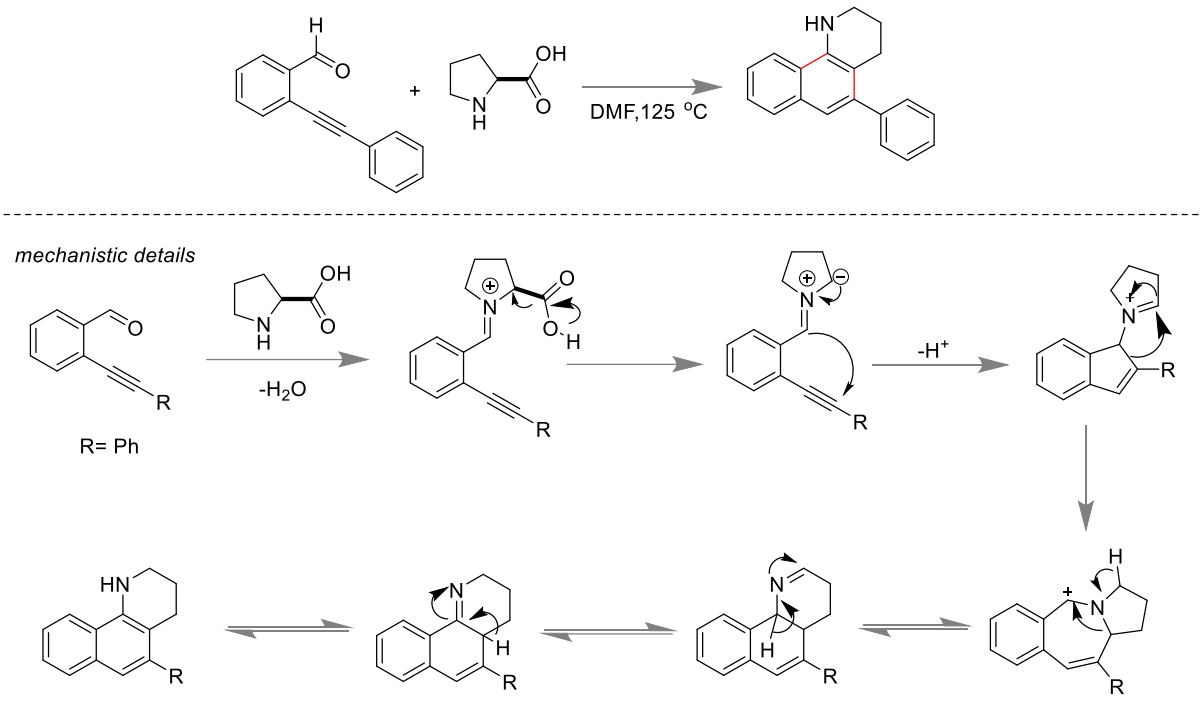
Scheme 1.24 Metal free dehydrogenation of N-heterocycle using visible light.

Synthesis of quinazolinone has been established from 2-amino benzoic acid and 4-amidinopyridine hydrochloride using HATU as a coupling partner and in the presence of a base in solvent DMF.[39] The metal free protocol was applied to synthesize diverse nitrogen-based N-heterocycles, which are significant in the pharmaceutical industry.



Scheme 1.25 Metal free synthesis of quinazolinone using a coupling reagent HATU.

Synthesis of tetrahydroquinolines in one pot has been established by Kundu and co-workers.[40] The key features involved the formation of three bonds simultaneously by metal free decarboxylative cyclization with one carbon ring expansion in one pot. The reaction proceeded by the formation of the imine intermediate by condensation of the aldehyde and amine, which undergoes decarboxylation to form the azomethine intermediate followed by endo dig cyclization and ring expansion to include a benzyl carbocation. Subsequent steps involving rearrangement led to formation of the product tetrahydroquinoline.



Scheme 1.26 Metal free decarboxylative cyclization from amino acids.

1.6 Azides in organic synthesis

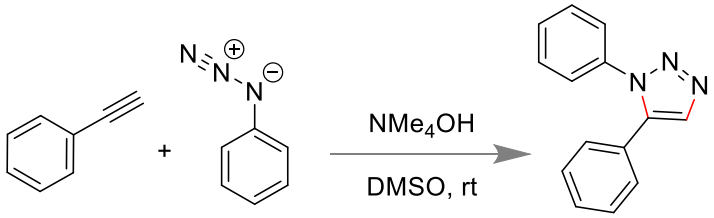
Azides form an essential category of compounds which have numerous applications in a vast array of discipline. The powerful utility of this functional group lies in its versatility and the ability to be transformed into necessary heterocyclic scaffolds. Click chemistry prevalent for a long time results from the potential application of azides in medicine, drug discovery, chemical biology, and material science. The versatile applications of azide have numerous synthetic routes to access significant structural motifs from a plethora of synthons which have expanded the synthetic availability of azide reagents and their application in organic chemistry.

Trimethylsilylazide has been used as an azide source for azidation of alkenes under metal free conditions using visible light photocatalysis. β azidoalcohols that are significant in nitrogen-containing heterocycles have been synthesized from readily available feedstock chemicals

like alkenes. [41] The mechanism was speculated to proceed by forming the azido radical and the alkene radical cation.

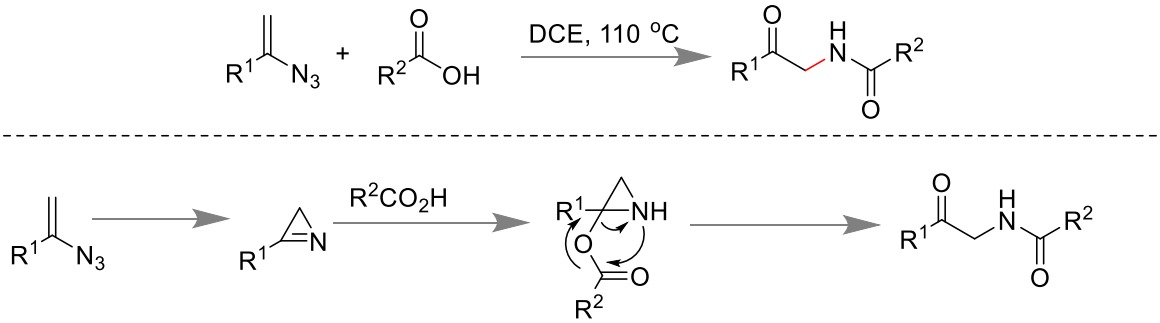
Scheme 1.27 Synthesis of β-azidoalcohol from alkenes using visible light photocatalysis.

1,5-Diarylsubstituted 1,2,3-triazoles have been reported in mild reaction conditions using azide in solvent DMSO and using a catalytic proportion of tetraalkylammonium hydroxide. The solvent DMSO plays an active role in various proton relay events.



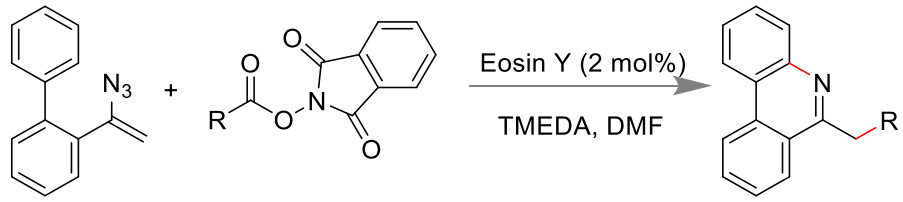
Scheme 1.28 Synthesis of triazoles using terminal akynes and organic azide.

Carboxylic acid and vinyl azides were used to prepare α-amidoketones through cascaded reactions.[42] The protocol showed wide functional group tolerance along with a vast array of substrate scope. The methodology was applied to a number of drug molecules with late stage modifications. The mechanistic studies showed the formation of an azirine as an intermediate step by decomposition of the azide. The azirine underwent a reaction with carboxylic acid to form azidirine followed by a thermal rearrangement to the α-amidoketone as the product.



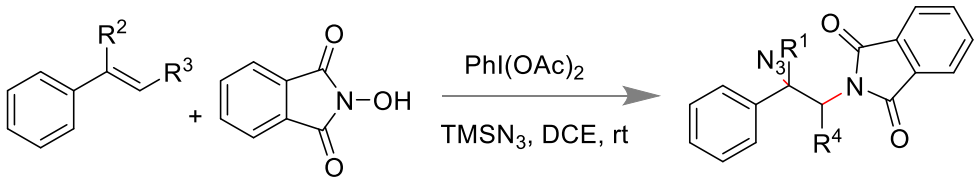
Scheme 1.29 Synthesis of α-amidoketone using terminal alkynyl azide.

Phenanthridines have been constructed using N-acycloxyphthalimides and vinyl azides under visible light irradiation.[43] The reaction proceeded by a radical pathway with decarboxylation followed by cyclization to form substituted phenanthridines.



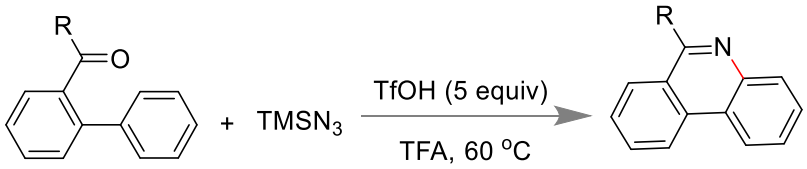
Scheme 1.30 Synthesis of substituted phenanthridines using vinyl azides and N-acycloxylphthalimides.

Xia and co-workers have established oxidation of alkenes under mild conditions using hypervalent iodine(III) reagent to generate the azido radical.[44] Consecutively, C-O and C-N bond was formed simultaneously from easily available precursors. The protocol tolerated a variety of substituted alkenes to afford the desired oxyazidation product.



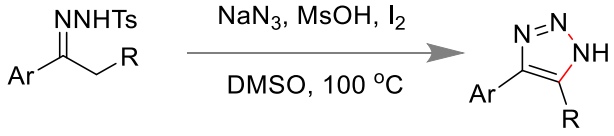
Scheme 1.31 Oxyazidation of alkenes using trimethylsilylazide and PIDA.

Phenanthridines have been synthesized using trimethyl silyl azide, which is the nitrogen source.[45] The method involved nitrogen incorporation using azide as the nitrogen source. The inhibition of the Schmidt reaction led to the elimination of byproduct, which proved the high chemoselectivity of the designed protocol or methodology.



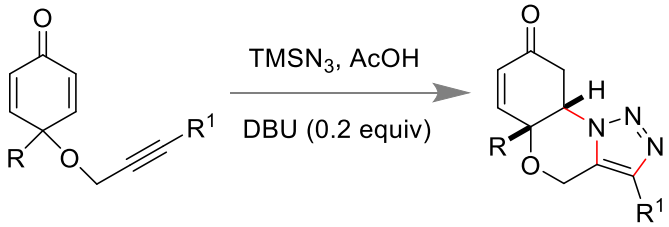
Scheme 1.32 Synthesis of phenanthridines using $TMSN_3$ as nitrogen source.

Shu group have established cyclization of 4-aryl-NH-1,2,3-triazoles from N-tosyl hydrazones and using sodium azide.[46] This mild and metal-free cascaded [4 + 1] cyclization took place by C−N and N−N bond formation, respectively. The investigation of the mechanism revealed that nitrogen N_1 of the triazole was from sodium azide.



Scheme 1.33 Synthesis of triazoles mediated by molecular iodine.

1,2,3-triazole-fused dihydrobenzoxazinone derivatives were synthesized by cascaded β azidation using trimethyl silyl azide as the azide source.[47] The protocol applied to ample substrates, which provided a variable scope and took place efficiently using a variety of alkynylated cyclohexa 2,5-dienones, affording tricyclic scaffolds, which are cis-triazole-fused.



Scheme 1.34 Synthesis of triazole fused tricyclic scaffolds mediated by base.

OBJECTIVE

Thus, this chapter aims to discuss the scope of the thesis. Nitrogen containing scaffolds are significant due to its application in the pharmaceutical industry, in medicinal chemistry, for developing important drug molecules. The development of sustainable strategies involving nitrogenous based molecules will always be a highly demanding research topic in organic synthesis. The present thesis encompasses developing sustainable methods comprising nitrogen based N-heterocycles for its construction or application.

1.7 NOTES AND REFERENCES

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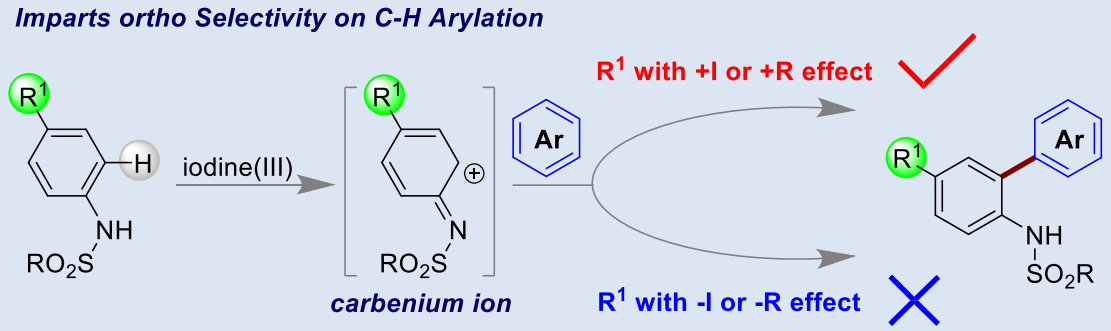
CHAPTER 2

C2-H Arylation Of Sulfonamides By Steric And Electronic Control

2.1 ABSTRACT



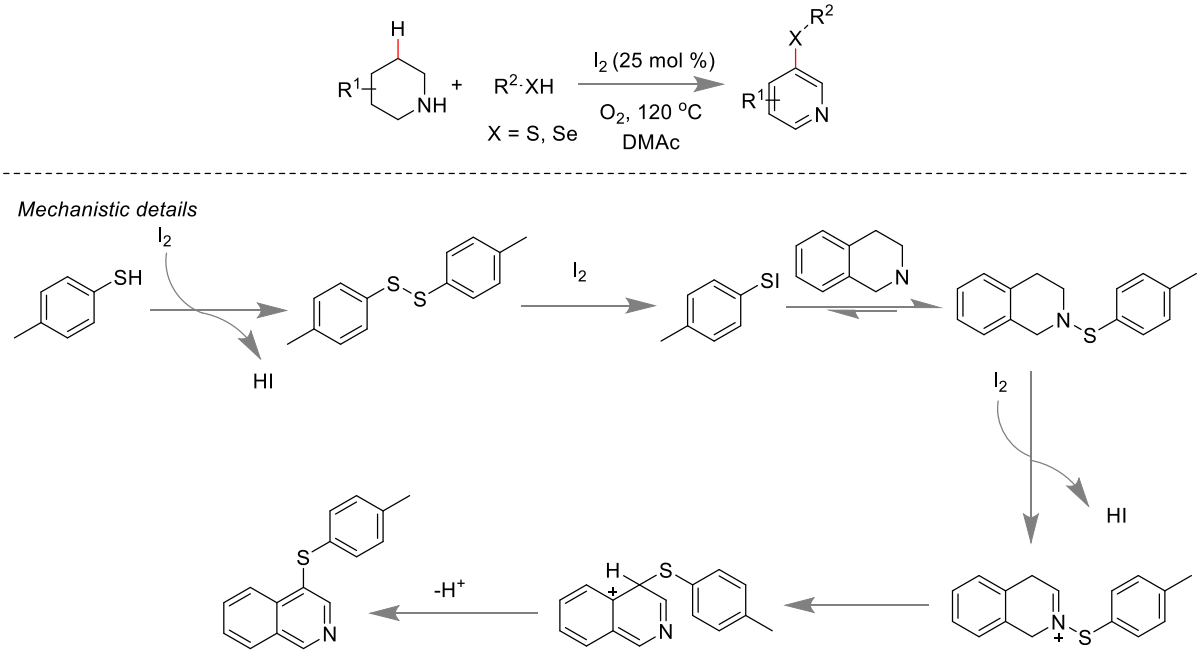
Arylsulfonamides generated electrophilic nitrenium ion, which was readily convertible to the tautomeric carbenium ion *via* resonance on reaction with phenyliodine diacetate. Depending on the nucleophile in the reaction mixture, C-H arylation took place. A scale of substrates where the electronic effect was operative resulted in C-H arylation of the sulfonamides.

2.2 INTRODUCTION

C-H bond functionalization by Dehydrogenative C-C coupling reaction[1-3] has come into prominence as a significant tool for organic chemists.[4-8] Traditional metal-mediated synthetic transformations for the construction of C-C bonds have expanded due to high application in industry.[9-13] Such methods are highly hazardous that produce unwanted toxic side products. Functionalization of aromatic C-H bond by the metal-free approach has been an exciting subject of interest among researchers. In such a perspective, hypervalent iodine(III) in organic synthesis for functionalization of C-H bond to construct significant structural motifs

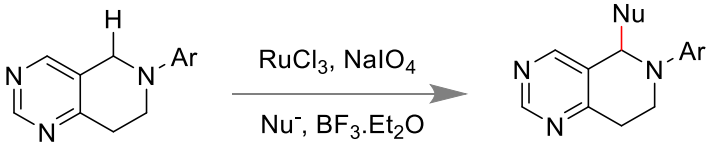
is well known for its ease of availability, stability, and cost-effective nature. C-C coupling reactions in an intermolecular approach have been explored using hypervalent iodine(III) reagents. [14, 15]

Recently C-H bond functionalization by a metal free approach using iodine in catalytic conditions has been developed by the Lei group.[16] Site-selective bond functionalization of piperidine and tetrahydroisoquinoline derivatives at the β-position took place using oxygen as the sole oxidant. Mechanistic studies predict oxidation followed by rearrangement produced the desired product.



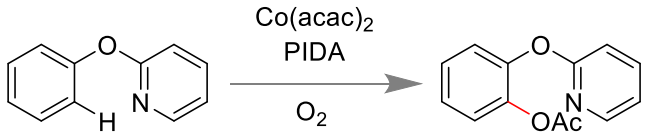
Scheme 2.1 β Selective functionalization of piperidine using a terminal oxidant like oxygen.

Cheng and co-workers has established C-H bond Functionalization in pyrimidine based substrates using metal catalyst in solvent THF and methanol (1:1) by volume. [17] It proceeded by two steps process forming a hemiaminal ether which on reaction with $BF_3.Et_2O$ lead to formation of iminium cation that incorporates the nucleophile to produce the C-H functionalization product.



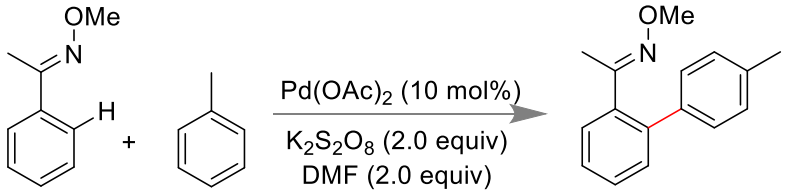
Scheme 2.2 C-H functionalization via two steps process using Ru as a catalyst.

Hypervalent iodine reagents have been widely employed for the functionalization of aromatic C-H bonds. C-H functionalization of aromatic C-H bond was achieved using phenyliodine diacetate (PIDA) and an inexpensive cobalt catalyst under neutral conditions.[18] Acetoxylation of C(sp^2)-H bond took place under mild conditions Mechanistic studies proclaim that the source of the acetoxy group was available from PIDA.



Scheme 2.3 C-H Functionalization using phenyl iodine diacetate (PIDA) as the acetoxy source.

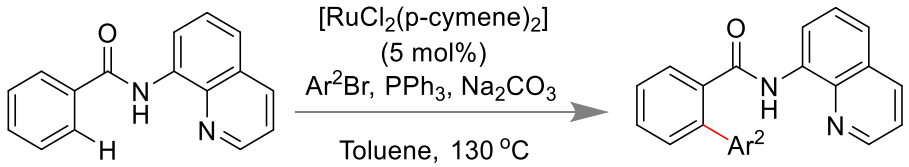
Directing group enabled C-H arylation was developed by using the mechanochemistry approach using ball mill.[19] Electron-rich and electron-deficient oxime acted as an efficient directing group for the C-H arylation forming the biaryls in high selectivity and in a short time of one hour with 600 rpm in 60 stainless steel grinding balls of 2 mm diameter. Initially, cyclopalladation at the oxime center was followed by fast activation of the C-H bond by arene at Pd(IV) center, which might cause its high selectivity.



Scheme 2.4 Intermolecular C-H arylation via mechanochemistry.

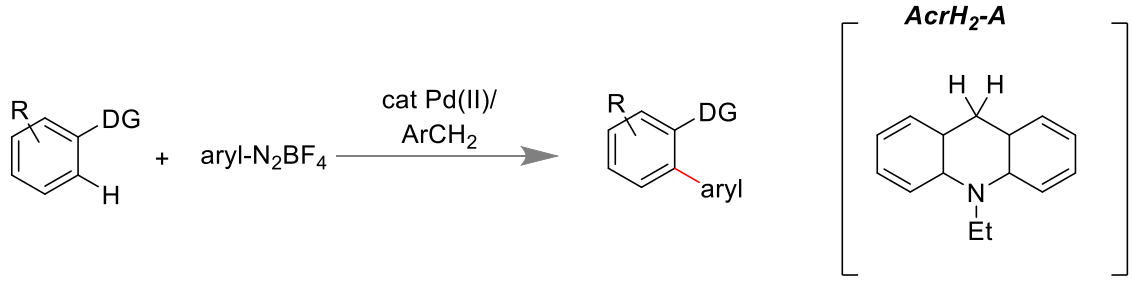
Bidentate directing group enabled C-H functionalization was reported by Chatani group using Ru as catalyst. 8-aminoquinoline was used as a directing group for C-H activation to couple

with aryl bromides.[20] The C-H activation step was facilitated by employing triphenyl phosphine. Authors speculated that presence of a bidentate directing group was necessary for the reaction to be successful.



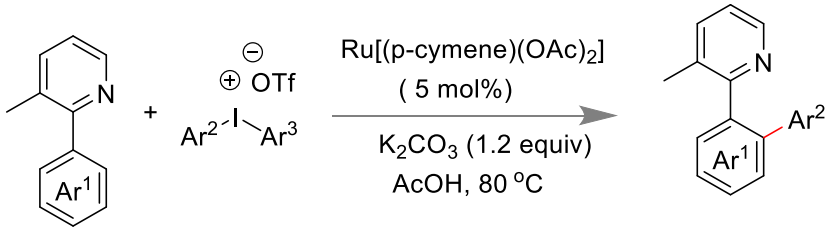
Scheme 2.5 Intermolecular C-H arylation using Ru as catalyst.

Directed C-H Arylation by use of dual Pd and photoredox catalysis of arenes with aryl diazonium salts was achieved with a broad functional group and at mild reaction conditons.[21] Biaryl motifs were synthesized by merging organic photoredox catalysis with palladium metal under irradiation of 36W Blue LED and in solvent MeOH.



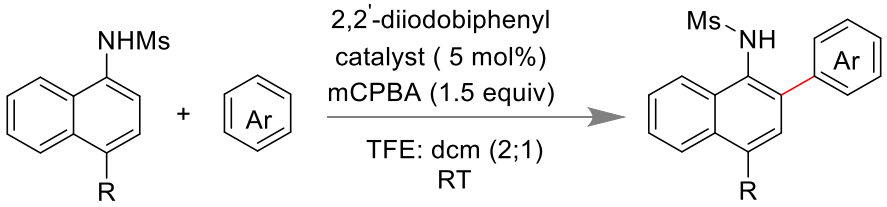
Scheme 2.6 Intermolecular C-H arylation using $AcrH_2$ as photocatalyst.

Diaryl iodonium salts have been broadly used as arylation source inorganic synthesis. Chatani group reported arylation of 2-arylpyridines using ruthenium(II) catalyst.[22] It was observed with mixed aryl group that the more electron-rich and sterically unhindered aromatic group transfer took place with more excellent selectivity.



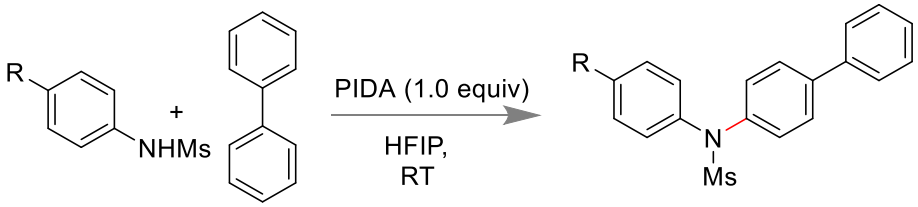
Scheme 2.7 C-H arylation using diaryl iodonium salt as arylation source.

Kita and the group have established C-H arylation of naphthyl anilides with aromatic hydrocarbons.[23] The first organocatalytic oxidative biaryl coupling was established using diiodbiphenyl as catalyst and an oxidant like meta percholorobenzoic acid. Also, stoichiometric amounts of iodine(III) successfully produced the C-H arylation product.



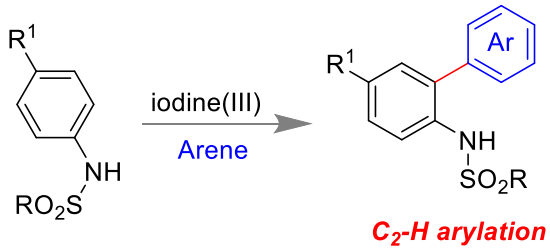
Scheme 2.8 C-H arylation of napthylsulfonamides using di-iodobiphenyl arene in catalytic amount.

Soft-Hard Acid-Base principle was used to demonstrate and preferentially functionalize a C-N bond using hypervalent iodine(III) as the reagent and by choice of appropriate nucleophile.[24] Biphenyl (soft) nucleophile prefers to react with nitrenium (soft) to form the C-N arylated product.



Scheme 2.9 C-H arylation of sulfonamides using HSAB approach.

This work brings into focus C_2-H arylation of sulfonamides involving iodine(III) reagents with proper choice of external nucleophiles. Sterically hindered arenes like mesitylene or triethyl benzene were potential nucleophiles in the reaction system. The reaction was controlled by the nucleophilicity of the arene available in the reaction mixture. The electronic substituent on the *para*- position of the sulfonamide possesses the feasibility and the outcome of the reaction.



Scheme 2.10 Oxidative arylation of sulfonamides using sterically hindered arenes.

Weak interactions[25, 26] or soft force in an organic synthetic reaction control the outcome of a product.[27] We focused on understanding the reactivity of sulfonamides by soft forces.[28] C-H arylation reaction of sulfonamide[23] was achieved by reactivity control of carbenium ion[29, 30] in preference to nitrenium ion.[31-34] Amides and amines react with iodine(III) reagents to produce a nitrenium ion as an electrophilic reactive intermediate. Depending on the nucleophile, the C-H arylation took place. Hypervalent iodine(III) reagent PIDA was used for C_2-H arylation of sulfonamides. Nitrenium ions are isoelectronic[35] with carbenium ions, and its utility in organic synthesis is expanding at a fast pace.[32, 36, 37] Ligand exchange at the electrophilic iodine atom led to formation amido-λ^3-iodane.[38] Heterolysis of nitrogen iodine bond along with reductive elimination led to the formation of nitrenium ion (Figure 2.1a). Nitrenium ions are readily convertible to carbenium ion and correspondingly attacked by the added nucleophile. Sterically hindered nucleophiles[24] led to oxidative coupling with electrophilic carbenium ion.(Figure 2.1b). The stability of the carbenium ion controls the selectivity of the product. Sulfonamides with electron releasing substituents (either by +I or +R effect) at the *para* position generated more stable carbenium ion (Figure 2.1c), which favored coupling with arene nucleophile. Contrastingly, substituted sulfonamide containing electron withdrawing group produced relatively less stable or unstable carbenium ion, to unfavor C-C coupling (Figure 2.1c). Heren in, we focussed on selective C-arylation of sulphonamides using iodine(III) reagent.

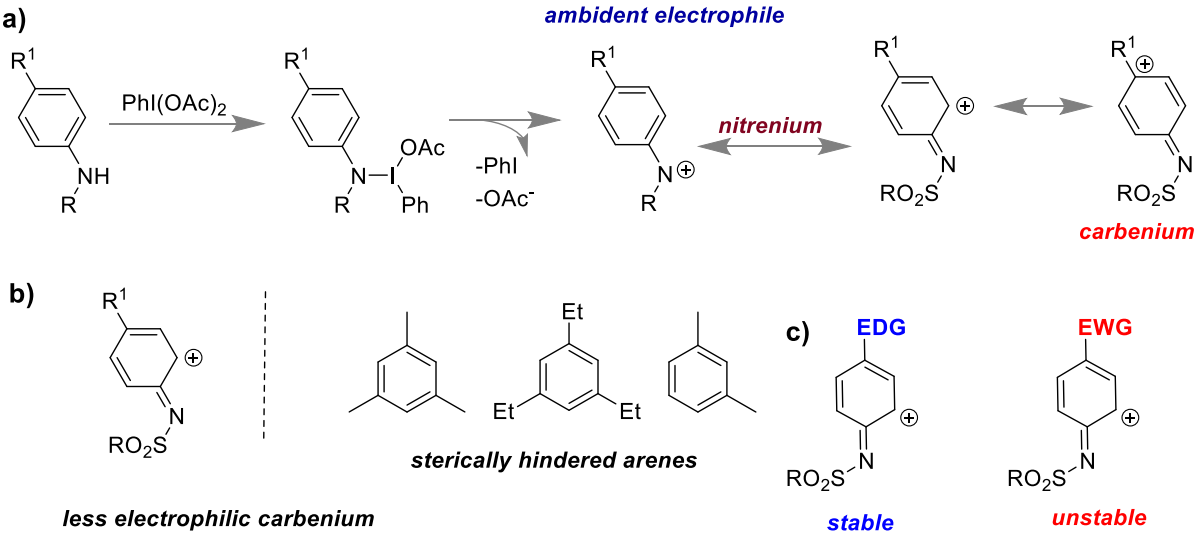
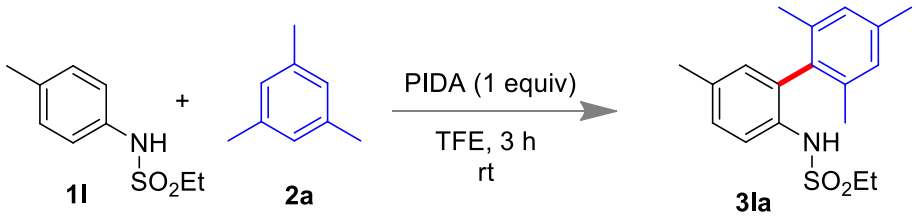


Figure 2.1 a) Mechanistic pathway for generation of nitrenium to carbenium b) sterically hindered arenes that undergo C-H arylation c) electronic effect of sulfonamides on C_2H arlation of sulfonamides.

2.3 RESULTS AND DISCUSSIONS

N-(*p*-tolylethanesulfonamide) **1k** was chosen as the sulfonamide**.** By taking an appropriate nucleophile like mesitylene **2** , C-H arylated product **3ka** produced in good yield when 1.0 equiv of PIDA was used in HFIP (entry 1). A slight excess of the oxidant did not produce appreciable difference in yield. Switching the solvent from HFIP to TFE, led to maximum yield of the C-H arylated product. 96% (entry 3). Iodine (III) was generated by employing iodobenzene in catalytic amount with *meta*-chloroperbenzoic acid (*m*CPBA) as an oxidant to produce a low yield. When 1.0 equiv of iodobenzene was used to generate the iodine (III) species, no substantial change was noticed (entry 5). Hypervalent iodine reagents like PIFA and PhIO were ineffective for oxidative coupling. (entries 6 and 7). Non-fluorinated solvents like DCE, DCM, and acetonitrile failed to produce the targeted product.

Table 2.1 Optimization table.

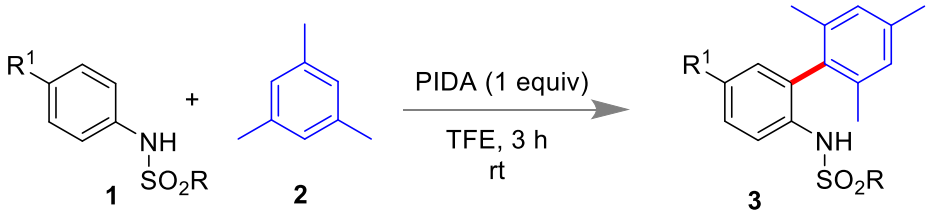


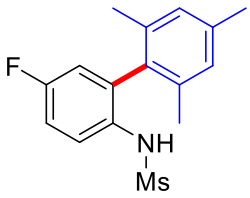
entry	iodine (III) (equiv)	solvent	yield (%)
1	PIDA(1.0)	HFIP	89
2	PIDA(1.5)	HFIP	85
3	PIDA(1.0)	TFE	96
4[a]	PhI (0.2)	TFE	32
5[a]	PhI (1)	TFE	24
6	PhIO	TFE	0
7	PIFA (1.0)	TFE	48
8	PIDA(1.0)	ACN	0
9	PIDA (1.0)	DCM	0
10	PIDA(1.0)	DCE	0

[a]0.2 mmol of **1k**, 0.6 mmol of mesitylene were used; [b]Yields were calculated based on recovery of reactants after column chromatography. Oxidant [c]*m*CPBA utilized in 0.2 mmol

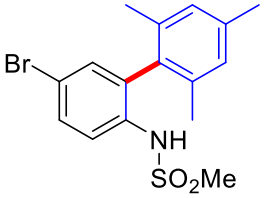
With the optimized reaction condition in hand, a wide array of substrate scope was tested. Sulfonamides were chosen as the anilide source and mesitylene as the coupling partner as indicated in Figure 2.2. Halogen-containing sulfonamides reacted with hypervalent iodine(III) reagent, producing good yield with maximum yield obtained with iodo-substituted anilide (3da). Alkyl substituents like methyl, ethyl, *iso*-propyl, *tert*-butyl tolerated reaction

conditions making good to moderate output. Other protecting groups led to the formation of product in good to excellent yield. (**3ka** and **3la**). If electron-withdrawing groups substitute the para position of the sulfonamide like CN, CF_3 and NO_2, the desired C-H arylation failed to take place due to instability of the generated nitrenium or carbenium ion.

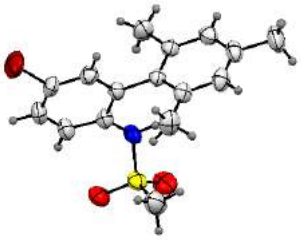


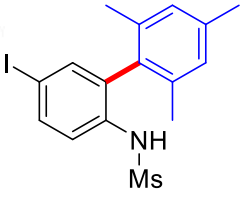


3aa, 66%

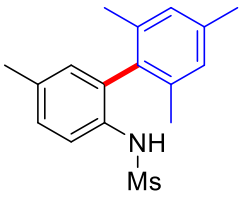


3ba, 67%

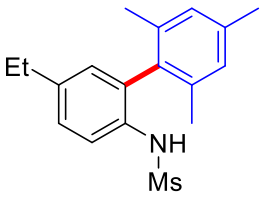




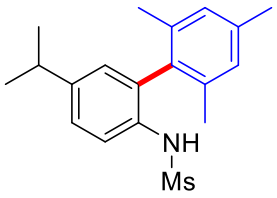
3ca, 77%



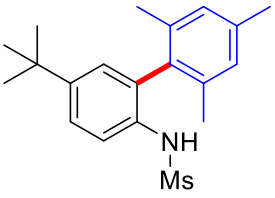
3da, 48%



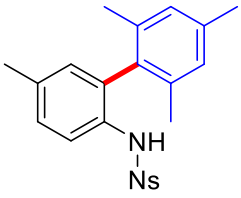
3ea, 58%



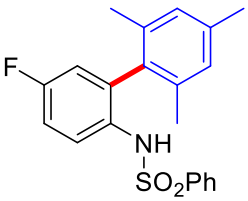
3fa, 68%



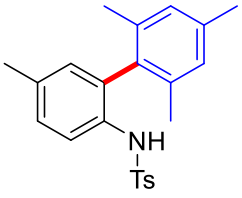
3ga, 53%



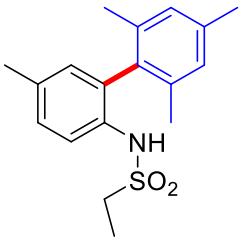
3ha, 50%



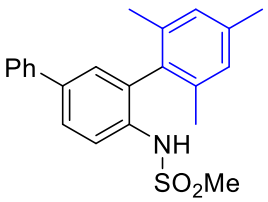
3ia, 51%



3ja, 81%



3ka, 96%



3la, 62%

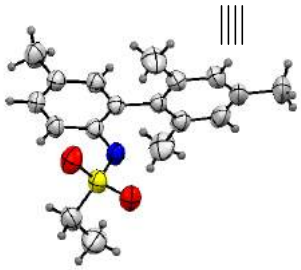


Figure 2.2. Scope of arylation reaction using mesitylene as arene source. Reaction condtions: 1.0 equiv of PIDA in TFE, 3.0 equiv of mesitylene was used at room temperature for 3 h, yield calculated based on recovered reactants.

The electronic factor plays an important role in stabilizing the nitrenium ion, which decides the fate of the reaction. Electron rich arenes like triethyl benzene as the arene source, and several alkyl-substituted sulfonamides were used, and it was found that moderate yield was produced in most of the cases (Figure 2.3). Sulfonamides containing halogen at the *para* position of anilide led to moderate yields of the desired product. (**3bb**, **3cb**, **3db**). Disubsituttion of anilides with EWG like Cl, CF_3 generated an unstable nitrenium ion, and an electron-rich nucleophile like triethyl benzene could not make the reaction successful. (**3pb**, **3rb**, **3sb**, **3tb**).

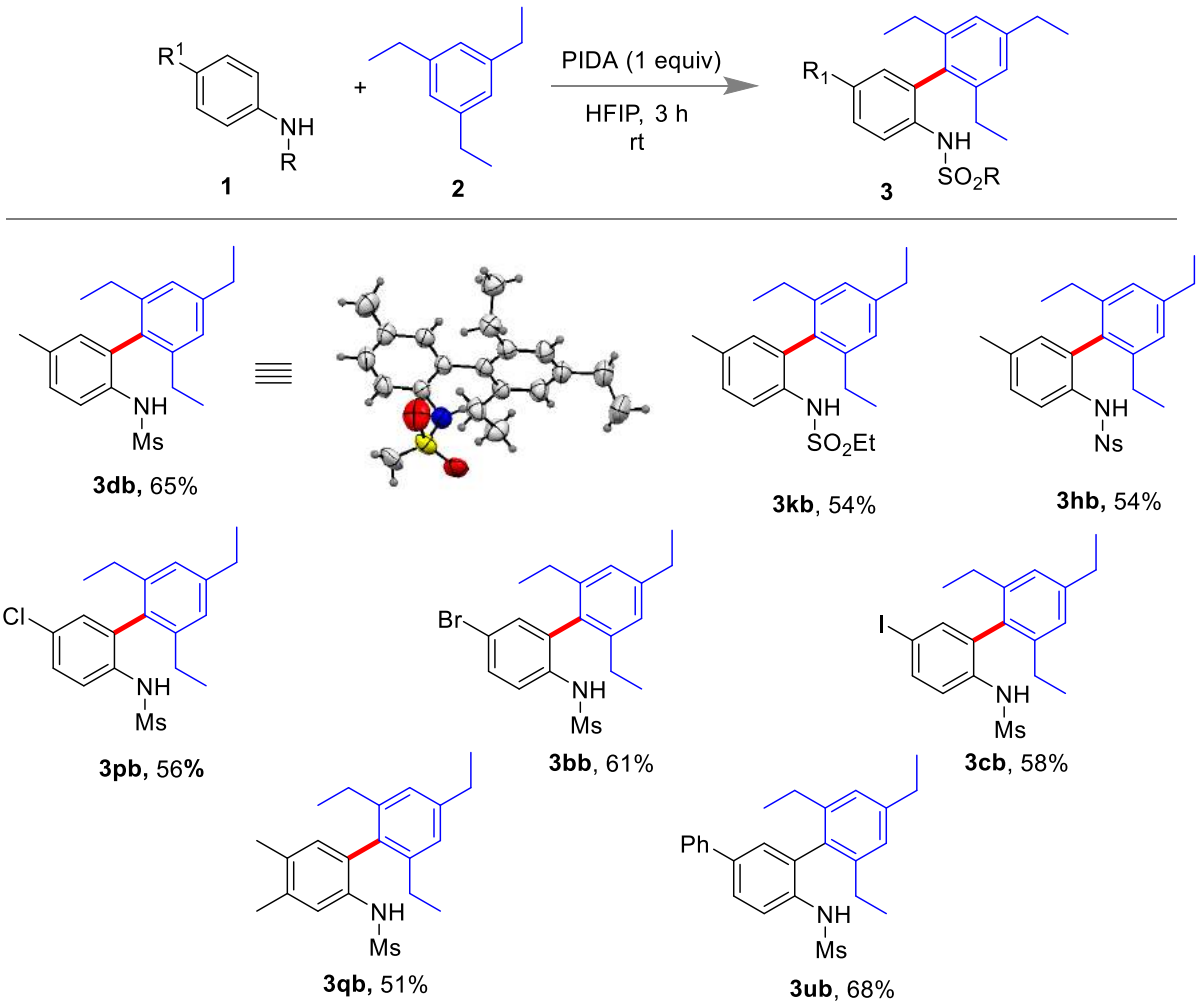


Figure 2.3. Scope of arylation using triethyl benzene as arene source; Reaction conditions: 1.0 equiv of PIDA in TFE, 3.0 equiv of mesitylene was used at room temperature for 3 h, yield calculated based on recovered reactants.

We next targeted to vary the arene source as shown in figure 2.4, and it was seen Bromo or iodo substituted arene gave an appreciable yield of product (**3ec**, **3lc**, **3cc**, **3ee**). Alkyl substituted sulfonamide resulted in relatively poor yield with Bromo substituted mesitylene (**3ec**). When dimethyanisole was used as arene source, two regioselective products were produced in 1:1 ratio (**3eg**). Arenes like trimethoxy benzene, tribromobenzene, tetramethyl benzene did not make the product, which might be due to the steric effect.

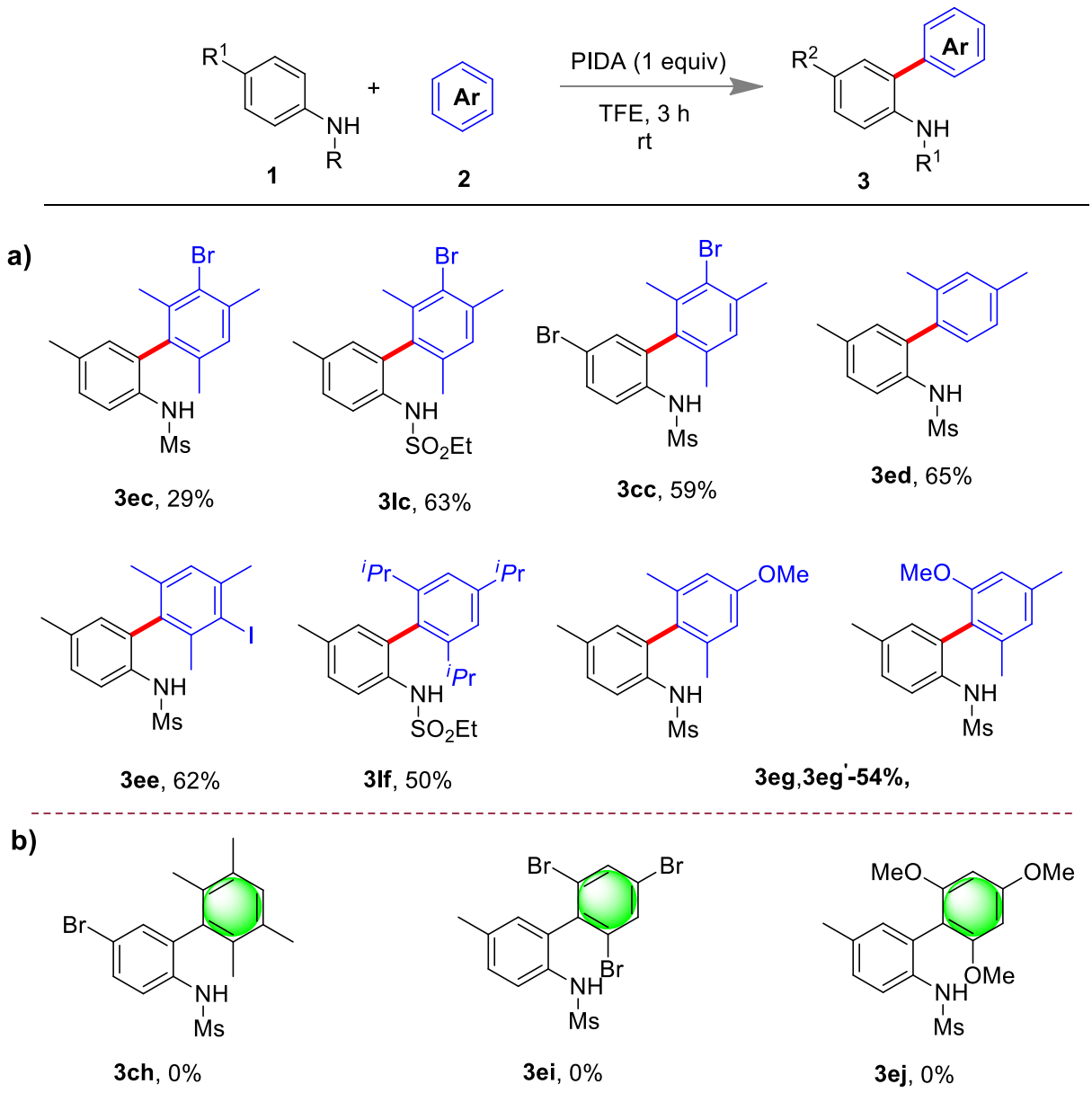
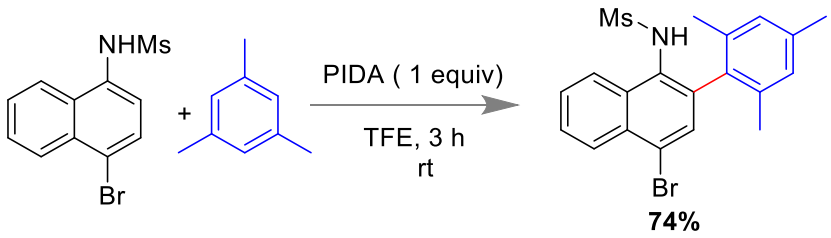


Figure 2.4. Scope of arylation varying the arene source. Reaction condtions: 1.0 equiv of PIDA in TFE, 3.0 equiv of mesitylene was used at room temperature for 3 h, yield calculated based on recovered reactants.

The methodology was extended to naphthalene-based aromatic system, and it was noticed that the arylated product was formed in good yield shown in scheme 2.11.



Scheme 2.11 Scope of arylation for naphthalene based sulfonamide. Reaction condtions: 1.0 equiv of PIDA in TFE, 3.0 equiv of mesitylene was used at room temperature for 3 h, yield calculated based on recovered reactants.

2.4 CONCLUSIONS

The Dehydrogenative C-H Arylation of biarylsulfonamides generated carbenium ion in the presence of iodine(III) reagent. The formation of C-H arylated product over N arylated product showed the key role of the nucleophile or the electronic effect of substituent on the sulfonamide. The C-H arylation was achieved in most of the substrates giving moderate to good yield in a mild reaction control. Overall, the proposed methodology was applied to form C-C bond which has an extensive application in industry and medicine.

2.5 EXPERIMENTAL SECTION

(General Methods) Chromatographic (Column) purifications of the compounds were done using silica gel (mesh 230-400) and hexane-ethyl acetate mixtures as eluent unless otherwise specified. The NMR spectra were recorded on 700 MHz or 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 ppm for ^{13}C). The peak patterns are designated as follows: s: singlet; d: doublet; t: triplet; q: quartet; m: multiplet; dd: doublet of doublets; td: triplet of doublets; brs: broad singlet. The coupling constants (*J*) are reported in hertz (Hz). ESI-TOF (time of flight) mass spectrometer has been used to record high-resolution mass spectra (HR-MS). Infrared (IR) spectral data are reported in wave number (cm^{-1}). FT-IR

spectra were recorded after making thin layer of the compounds on the surface of NaCl crystal using dichloromethane. Melting points (mp) of the compounds were determined with a digital melting point apparatus and are uncorrected. Good quality crystals of the compounds **3ka**, **3ba**, **3db** were obtained after slow evaporation of ethyl acetate solution. The crystals data were collected with Bruker SMART D8 goniometer equipped with an APEX CCD detector and with an INCOATEC micro source (Cu-Kα radiation, λ = 0.71073 Å). SAINT+[39] and SADABS[40] were used to integrate the intensities and to correct the absorption respectively The structure was resolved by direct methods and refined on F^2 with SHELXL-97.[41]

Representative method for preparation of *N*-(5-bromo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide. To a stirred solution of *N*-(4-bromophenyl)methanesulfonamide **1b**, (40 mg, 0.159 mmol) in 2.0 mL of TFE, mesitylene (67 µL, 0.479 mmol) was added. PIDA (51 mg, 0.159 mmol) dissolved in 1.0 mL of TFE was then added dropwise to the reaction containing mixture. The reaction mixture was stirred for 2 h. On complete consumption of substrate, the reaction mixture was evaporated to dryness. Column chromatography had been done to isolate the pure product *N*-(5-bromo-2',4',6'-trimethyl-[1.1'-biphenyl]-2-yl)methanesulfonamide (**3ba**) as white solid in 39 mg (67%) yield using 5% ethylacetate-hexane.

Compound Characterization data

***N*-(5-Fluoro-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3aa):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; yield (37 mg, 57%); mp 164-166 ºC (lit.[42] 164-165 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 8.8, 4.8 Hz, 1H), 7.54 (s, 1H), 7.36 (td, *J* = 8.4, 2.8 Hz, 1H), 7.10 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.19 (s, 1H), 3.20 (s, 3H), 3.20 (s, 4H), 2.61 (s, 3H), 2.25 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6 (d, $^1J_{C\text{-}F}$ = 243 Hz), 139.0,

136.5, 132.6 (d, $^3J_{C\text{-}F}$ = 8 Hz), 131.4, 130.9 (d, $^4J_{C,F}$ = 3 Hz), 129.3, 119.8 (d, $^2J_{C,F}$ = 8 Hz), 117.3 (d, $^2J_{C,F}$ = 22 Hz), 115.5 (d, $^2J_{C,F}$ = 22 Hz), 38.7, 21.1, 20.1.

***N*-(5-Bromo-2',4',6'-trimethyl-[1.1'-biphenyl]-2-yl)methanesulfonamide (3ba):** R_f = 0.4 (hexane:ethyl acetate: 9:1); white solid; yield (34 mg, 67%), (40 mg starting material taken, 5 mg starting material recovered); mp 172-175 °C (lit.[42] 173-175 ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.8 Hz, 1H), 7.49 (dd, *J* = 8.8; 1.0 Hz, 1H), 7.23 (d, *J* = 2.4 Hz, 1H), 6.98 (s, 2H), 5.99 (brs, 1H), 2.97 (s, 3H), 2.33 (s, 3H), 1.97 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.2, 136.7, 134.1, 133.3, 132.2, 131.8, 130.9, 129.4, 119.0, 117.2, 39.9, 21.3, 20.2.

***N*-(5-Iodo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3ca):** R_f = 0.40 (hexane : ethyl acetate 9:1); white solid; yield 41 mg (77%), (40 mg starting material taken, 2mg stating material recovered); mp 176-177 ºC (lit.[42] 176-178 ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (dd, *J* = 8.8; 2.0 Hz, 1H), 7.46 (d, 8.8 Hz, 1H), 7.42 (d, *J* = 2.0 Hz, 1H), 6.97 (s, 2H), 5.99 (brs, 1H), 2.97 (s, 3H), 2.33 (s, 3H), 1.96 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.1, 139.2, 137.8, 136.7, 134.9, 132.3, 130.8, 129.4, 119.2, 87.7, 39.9, 21.3, 20.3.

***N*-(2',4',5,6'-Tetramethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3da):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 17 mg (48%), (40 mg starting material taken, 19 mg starting material recovered); mp 122-124 ºC (lit.[42] 123-124 ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.0 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 1H), 6.97 (s, 2H), 6.89 (s, 1H), 5.92 (s, 1H), 2.93 (s, 3H), 2.34 (s, 6H), 1.97 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 136.8, 134.1, 132.6, 132.2, 131.0, 130.4, 129.4, 129.2, 117.8, 39.7, 21.2, 20.8, 20.3.

***N*-(5-Ethyl-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3ea):** R_f = 0.50 (hexane : ethylacetate 9:1); white solid; 32 mg (68%), (40 mg starting material taken, 8 mg stating material recovered) ; mp 111-113 ºC (lit.[42] 112-114 ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.4 Hz, 1H), 7.20 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.97 (s, 2H), 6.91 (d, *J* = 2.0 Hz, 1H), 5.92 (s, 1H), 2.96 (s, 3H), 2.64 (q, *J* = 7.6 Hz, 2H), 2.33 (s, 3H), 1.96 (s, 6H), 1.24 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.6, 138.4, 136.7, 132.7, 132.4, 130.3, 129.8, 129.1, 128.2, 117.7, 39.8, 28.2, 21.2, 20.3, 15.7.

***N*-(5-Isopropyl-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3fa):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 30 mg (59%), (40 mg starting material taken, 7 mg stating material recovered); mp 142-145 ºC (lit.[42] 143-145 ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.8 Hz, 1H), 7.22 (dd, *J* = 8.4; 2 Hz, 1H), 6.98 (s, 2H), 6.94 (d, *J* = 2 Hz, 1H), 5.93 (s, 1H), 2.94 (s, 3H), 2.91-2.87 (m,1H), 2.34 (s, 3H), 1.96 (s, 6H), 1.3 (s,3H), 1.3 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.3, 138.4, 136.8, 132.9, 132.4, 130.3, 129.1, 128.6, 126.7, 117.7, 39.9, 33.5, 24.1, 21.1, 20.3.

***N*-(5-(*tert*-Butyl)-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3ga):** R_f= 0.50 (hexane : ethyl acetate 9:1); white solid; 28 mg (53%), (40 mg starting material taken, 5 mg stating material recovered); mp 174-175 ºC (lit.[42] 174-175 ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.4 Hz, 1H), 7.37 (dd, *J* = 8.8; 2 Hz, 1H), 7.09 (d, *J* = 2 Hz, 1H), 6.98 (s, 2H), 5.93 (s, 1H), 2.95 (s, 3H), 2.34 (s, 3H), 1.96 (s, 6H), 1.30 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 138.5, 136.8, 133.0, 132.1, 129.7, 129.1, 127.7, 125.4, 117.2, 39.8, 34.5, 31.4, 21.1, 20.3.

4-Nitro-N-(2′,4′,5,6′-tetramethyl-[1,1′-biphenyl]-2-yl)benzenesulfonamide (3ha): R_f = 0.40 (hexane:ethyl acetate 9:1); yellow solid; 24 mg (50%), (40 mg starting material taken, 5 mg stating material recovered); mp 192-194 °C (lit.[42] 193-195 °C); ^{1}H NMR (400 MHz, CDCl3) δ 8.25 (d, *J* = 8.8 Hz, 2H), 7.88 (d, *J* = 8.8 Hz, 2H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.13 (d, *J* = 7.2 Hz, 1H), 6.90 (s, 2H), 6.76 (s, 1H), 6.21 (s, 1H), 2.33 (s, 3H), 2.28 (s, 3H), 1.25 (s, 6H); ^{13}C NMR (100 MHz, CDCl3) δ 150.3, 145.5, 138.7, 136.6, 135.2 132.2, 131.1, 130.8, 129.3, 129.1, 126.1, 128.7, 124.4, 118.8, 21.3, 20.9, 20.0.

***N*-(5-Fluoro-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (3ia):** R_f = 0.40 (hexane : ethyl acetate 9:1); white solid; 24 mg (51%) (40 mg starting material taken, 5 mg stating material recovered); mp 164-167 °C; (lit.[42] 165-167 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 9.2; 4.0 Hz, 1H), 7.72-7.67 (m, 2H), 7.56-7.52 (m, 1H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.04 – 6.99 (m, 1H), 6.90 (s, 2H), 6.68-6.65 (m, 1H), 6.11 (s, 1H), 2.33 (s, 3H), 1.61 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.56 (d, $^1J_{C,F}$ = 243 Hz), 139.5, 138.9, 136.7, 133.3, 132.7 (d, $^3J_{C,F}$ = 8.0 Hz), 131.3, 130.5 (d, $^4J_{C,F}$ = 3 Hz), 129.3, 129.1, 127.3, 120.3 (d, $^3J_{C,F}$ = 8.0 Hz), 117.0 (d, $^2J_{C,F}$ = 22.0 Hz), 115.2 (d, $^2J_{C,F}$ = 22.0 Hz); 21.2, 19.7.

4-Methyl-*N*-(2',4',5,6'-tetramethyl-[1, 1'-biphenyl]-2-yl)benzenesulfonamide (3ja): R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 34 mg (81%), (40 mg starting material taken, 11 mg stating material recovered); mp 151-153 °C (lit.[42] 150-153 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.59 (m, 3H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.09 (dd, *J* = 8.4; 2.0 Hz, 1H), 6.90 (s, 2H), 6.72 (d, *J* = 2 Hz, 1H), 6.09 (s, 1H), 2.37 (s, 3H), 2.33 (s, 3H), 2.26 (s, 3H), 1.64 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 142.9, 138.3, 137, 133.8, 132.5, 131.9, 130.7, 130.3, 129.8, 129.0, 128.9, 127.4, 118.3, 21.6, 21.1, 20.9, 19.9.

***N*-(2',4',5 ,6'-Tetramethyl-[1, 1'-biphenyl]-2-yl)ethanesulfonamide (3ka):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 37 mg (96%), (40 mg starting material taken, 24 mg starting material recovered); mp 119-121 ºC (lit.[42] 120-121 ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.0 Hz, 1H), 7.15 (d, *J* = 8.4 Hz, 1H), 6.97 (s, 2H), 6.87 (s, 1H), 5.86 (s, 1H), 3.07 (q, *J* = 6.8 Hz, 2H), 2.33 (s, 6H), 1.98 (s, 6H), 1.25 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 136.7, 133.8, 132.6, 132.4, 131.0, 130.0, 129.3, 129.1, 117.5, 46.4, 21.2, 20.8, 20.3, 8.2.

***N*-(2'',4'',6''-Trimethyl-[1,1':3',1''-terphenyl]-4'-yl)methanesulfonamide (3la):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 37 mg (62%); mp 172-174 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.4 Hz, 1H), 7.64 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.59 (d, *J* = 7.2 Hz, 2H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.35 (m, 2H), 7.02 (s, 2H), 6.07 (s, 1H), 3.02 (s, 3H), 2.36 (s, 3H), 2.03 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.1, 138.7, 137.4, 136.9, 134.1, 132.3, 130.6, 129.2, 129.0, 128.9, 127.5, 127.4, 126.8, 117.7, 39.9, 21.3, 20.3; IR (KBr) ϑ = 3441, 2061, 1633 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{22}H_{23}NO_2SNa$ 388.1342; Found 388.1327.

***N*-(2',4',6'-Triethyl-5-methyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3db):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 48 mg (65%); mp 139-141 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.0 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 1H), 7.03 (s, 2H), 6.93 (s, 1H), 5.94 (s, 1H), 2.95 (s, 3H), 2.68 (q, *J* = 7.6 Hz, 2H), 2.3 (s, 3H), 2.34-2.15 (m, 4H), 1.30 (t, *J* = 7.6 Hz, 3H), 1.05 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1, 142.8, 133.4, 132.7, 131.7, 131.3, 129.4, 129.3, 126.3, 116.9, 39.8, 28.8, 26.6, 20.8, 15.4; IR (KBr) ϑ = 3441, 2064, 1635, 1161 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{27}NO_2SNa$ 368.1655; Found 368.1672.

***N*-(2',4',6'-Triethyl-5-methyl-[1,1'-biphenyl]-2-yl)ethanesulfonamide (3kb):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 39 mg (54%); mp 99-101 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.4 Hz, 1H), 7.17 – 7.14 (dd, *J* = 8.4, 1.6 Hz , 1H), 7.02 (s, 2H), 6.91 (s, 1H), 5.85 (s, 1H), 3.09 (q, *J* = 7.6 Hz, 2H), 2.68 (q, *J* = 7.6 Hz, 2H), 2.32 (s, 3H), 2.32 – 2.15 (m, 4H), 1.33 – 1.24 (m, 6H), 1.05 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.9, 142.8, 132.9, 132.6, 131.7, 131.4, 129.2, 128.9, 126.1, 116.7, 46.7, 28.8, 28.8, 20.8, 15.3 (×2), 8.2; IR (KBr) ϑ = 3441, 2065, 1635, 533 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{29}NO_2SNa$ 382.1811; Found 382.1836.

4-Nitro-*N*-(2′,4′,6′-triethyl-5-methyl-[1, 1′-biphenyl]-2-yl)benzenesulfonamide (3hb): R_f = 0.50 (hexane:ethyl acetate 9:1); white solid; 35 mg (54%); mp 148-151 °C; (lit.[42] 149-152 ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (^{1}H NMR (400 MHz, CDCl3) δ 8.34−8.22 (m, 2H), 7.96−7.88 (m, 2H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.13 (d, *J* = 8.4 Hz, 1H), 6.97 (s, 2H), 6.83 (s, 1H), 6.23 (s, 1H), 2.68 (q, *J* = 7.6 Hz, 2H), 2.28 (s, 3H), 1.88 (q, *J* = 7.6 Hz, 4H), 1.33-1.29 (m, 3H), 0.92−0.88 (m, 6H); ^{13}C NMR (100 MHz, CDCl3) δ 150.3, 145.5, 145.3, 142.7, 134.3, 131.6, 131.3, 131.0, 129.8, 129.3, 128.7, 126.1, 124.4, 117.5, 28.9, 26.3, 20.1, 15.5, 15.2.

***N*-(5-Chloro-2',4',6'-triethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3pb):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 40 mg (56%); mp 153-157º C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.8 Hz, 1H), 7.36 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.13 (d, *J* = 2.4 Hz, 1H), 7.04 (s, 1H), 6.01 (s, 1H), 2.98 (s, 3H), 2.68 (q, *J* = 7.6 Hz, 2H), 2.33-2.14 (m, 4H), 1.30 (t, *J* = 7.6 Hz, 3H), 1.06 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 142.7, 134.0, 131.0 , 130.9, 129.9, 129.0, 128.8, 126.5, 117.8, 40.1, 28.8, 26.7, 15.4; IR (KBr) ϑ = 3442,

2070, 1635, 1161 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{24}ClNO_2SNa$ 388.1108; Found 388.1118.

***N*-(5-bromo-2',4',6'-triethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3bb):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 40 mg (61%); mp 156-159 ºC (lit.[42] 155-158 ºC); ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.8Hz, 1H), 7.50 (d, *J* = 8.8 Hz, 1H), 7.27 (s, 1H), 7.03 (s, 2H), 6.01 (s, 1H), 2.98 (s, 3H), 2.67 (q, *J* = 7.6 Hz, 2H), 2.33-2.14 (m, 4H), 1.30 (t, *J* = 7.6 Hz, 3H), 1.05 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 142.8, 134.7, 133.9, 131.8, 131.3, 129.9, 126.5, 118.2, 116.6, 40.2, 28.9, 26.7, 15.3.

***N*-(2',4',6'-triethyl-5-iodo-[1,1'-biphenyl]-2-yl)methanesulfonamide (3cb):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 36 mg (58%) (40 mg starting material taken, 5 mg stating material recovered); mp 156-159 ºC (lit.[42] 157-159 ºC); ^1H NMR (400 MHz, $CDCl_3$ δ 7.68 (d, *J* = 8.8 Hz, 1H), 7.47 (s, 1H), 7.45 (s, 1H), 7.03 (s, 2H), 6.02 (s, 1H), 2.99 (s, 3H), 2.67 (q, *J* = 7.6 Hz, 2H), 2.31-2.16 (m, 4H), 1.30 (t, *J* = 7.6 Hz, 3H), 1.05 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.7, 142.7, 139.8, 137.6, 135.3, 131.4, 129.8, 126.5, 118.3, 87.0, 40.0, 28.8, 26.6, 15.4.

***N*-(2',4',6'-Triethyl-4,5-dimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3qb):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 37 mg (51%); mp 143-144 ºC. ^1H NMR (400 MHz, $CDCl_3$) δ 7.09 (s, 1H), 7.00 (s, 2H), 6.87 (s, 1H), 5.44 (s, 1H), 2.65 (q, *J* = 7.6 Hz, 2H), 2.44 (s, 3H), 2.40 – 2.21 (m, 10H), 1.25 (t, *J* = 7.6 Hz, 3H), 1.08 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 144.4, 142.5, 138.2, 137.2, 137.1, 134.9, 131.2, 130.9 ,129.9, 125.3, 41.9, 28.9, 26.7, 21.2, 19.9, 15.9, 15.3; IR (KBr) ῡ = 3441, 2066, 1635 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{29}NO_2SNa$ 382.1815; Found 388.1811.

***N*-(2'',4'',6''-Triethyl-[1,1':3',1''-terphenyl]-4'-yl)methanesulfonamide (3ub):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 45 mg (68%); mp 180-182 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.4 Hz, 1H), 7.64 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.58 (d, *J* = 7.6 Hz, 2H), 7.49 – 7.40 (m, 3H), 7.35 (t, *J* = 7.2 Hz, 1H), 7.07 (s, 2H), 6.08 (s, 1H), 3.04 (s, 3H), 2.70 (q, *J* = 7.6 Hz, 2H), 2.54 – 2.16 (m, 4H), 1.33 (t, *J* = 7.6 Hz, 3H), 1.08 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.4, 142.9, 140.1, 136.6, 134.6, 131.1, 129.8, 129.5, 129.1, 127.4, 127.4, 126.8, 126.4, 116.9, 40.0, 28.8, 26.7, 15.6, 15.5; IR (KBr) ʊ = 3441, 2068, 1637 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{29}NO_2SNa$ 430.1811; Found 430.1788.

***N*-(3'Bromo-2',4',5',6'-tetramethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3dc):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 41 mg (49%); mp 165-166 ºC (lit.[42] 165-167 ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.4 Hz, 1H), 7.39 – 7.37 (m, 1H), 7.04 (s, 1H), 6.09 (s, 1H), 3.11 (s, 3H), 2.62 (s, 3H), 2.53 (s, 3H), 2.29 (s, 3H), 2.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0, 136.8, 135.7, 134.5, 134.4, 132.1, 131.0, 130.6, 130.3, 129.8, 126.4, 39.9, 24.1, 21.7, 20.8, 20.2.

***N*-(3'-Bromo-2',4',5,6'-tetramethyl-[1,1'-biphenyl]-2-yl)ethanesulfonamide (3kc):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 50 mg (63%); mp 162-164 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.4 Hz, 1H), 7.19 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.10 (s, 1H), 6.86 (d, *J* = 1.4 Hz, 1H), 5.83 (s, 1H), 3.10 (q, *J* = 7.6 Hz, 2H), 2.47 (s, 3H), 2.35 (s, 3H), 2.14 (s, 3H), 1.96 (s, 3H), 1.28 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.8, 136.8, 135.7, 134.6, 134.0, 132.2, 130.9, 130.5, 130.1, 129.6, 126.3, 117.8, 46.6, 24.1, 21.7, 20.8,

20.1, 8.2; ῡ = 3441, 2066, 1635 cm^{-1}; HRMS (ESI/QTOF) m/z: [M + Na]+ Calcd for $C_{18}H_{22}BrNO_2SNa$ 418.0447; Found 418.0442.

***N*-(3',5-Dibromo-2',4',6'-trimethyl-[1.1'-biphenyl]-2-yl]methanesulfonamide (3bc):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 47 mg (59%); mp 165-167 ºC (lit.[42] 166-167 ºC); ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.4 Hz, 1H), 7.51 (d, *J* = 8.8 Hz, 1H), 7.20 (s, 1H), 7.08 (s, 1H), 5.92 (s, 1H), 2.98 (s, 3H), 2.45 (s, 3H), 2.11 (s, 3H), 1.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.8, 136.8, 135.5, 134.0, 133.2, 132.8, 132.2, 132.1, 130.8, 126.5, 119.2, 117.3, 40.2, 24.2, 21.7, 20.1.

***N*-(2',4',5'-Trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3dd):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 40 mg (65%) (40 mg starting material taken, 5 mg stating material recovered); mp 112-114 ºC; ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.4 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 1H), 7.14 (s, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 7.6 Hz, 2H), 7.01 (s, 1H), 6.99 (s, 1H), 2.84 (s, 3H), 2.38 (s, 3H), 2.35 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 138.7, 136.4, 134.4, 133.5, 132.5, 132.1, 131.8, 131.3, 129.6, 129.4, 127.5, 119.4, 39.6, 21.3, 20.8, 19.7; ῡ = 3441, 2065, 1635 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{19}NO_2SNa$ 312.1029; Found 312.1010.

***N*-(2',4',6'-triisopropyl-5-methyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3ke):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 40 mg (50%); mp 171-172 ºC (lit.[43] 170-172 ºC); ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.4 Hz, 1H), 7.16 (d, *J* = 8.4 Hz, 1H), 7.10 (s, 2H), 6.91 (s, 1H), 5.95 (s, 1H), 3.17 (q, *J* = 7.2Hz, 2H), 2.94 (sept, *J* = 6.8 Hz 1H), 2.47 (sept, *J* = 6.8 Hz 1H) , 2.32 (s, 3H), 1.36 - 1.30 (m, 9H), 1.17 (d, *J* = 6.8 Hz, 6H), 1.04 (d, *J* = 6.8

Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.8, 147.5, 133.2, 132.4, 131.9, 130.1, 129.0, 128.6, 121.9, 115.6, 47.2, 34.4, 30.6, 25.0, 24.1, 23.8, 20.8, 8.2.

***N*-(4-Bromo-2-mesitylnaphthalen-1-yl)methanesulfonamide (3va):** R_f = 0.80 (hexane : ethyl acetate 9:1); white solid; 36 mg (74%), (40 mg starting material taken, 6 mg stating material recovered); ^1H NMR (400 MHz, $CDCl_3$) δ 8.31-8.28 (m, 2H), 7.67-7.65 (m,3H), 7.01 (s, 2H), 6.34 (s, 1H), 2.35 (s, 3H), 2.34 (s, 3H), 2.07 (s, 6H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 138.2, 137.7, 136.6, 134.7, 133.6, 132.1, 132.0, 129.8, 128.7, 128.2, 127.8, 127.7, 124.2, 123.1, 42.0, 21.1, 20.5; ῡ = 3573, 2065, 1635 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{20}BrNO_2SNa$ 440.0290; Found 440.0273.

2.6 NOTES AND REFERENCES

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NMR Spectra of Selected Compounds

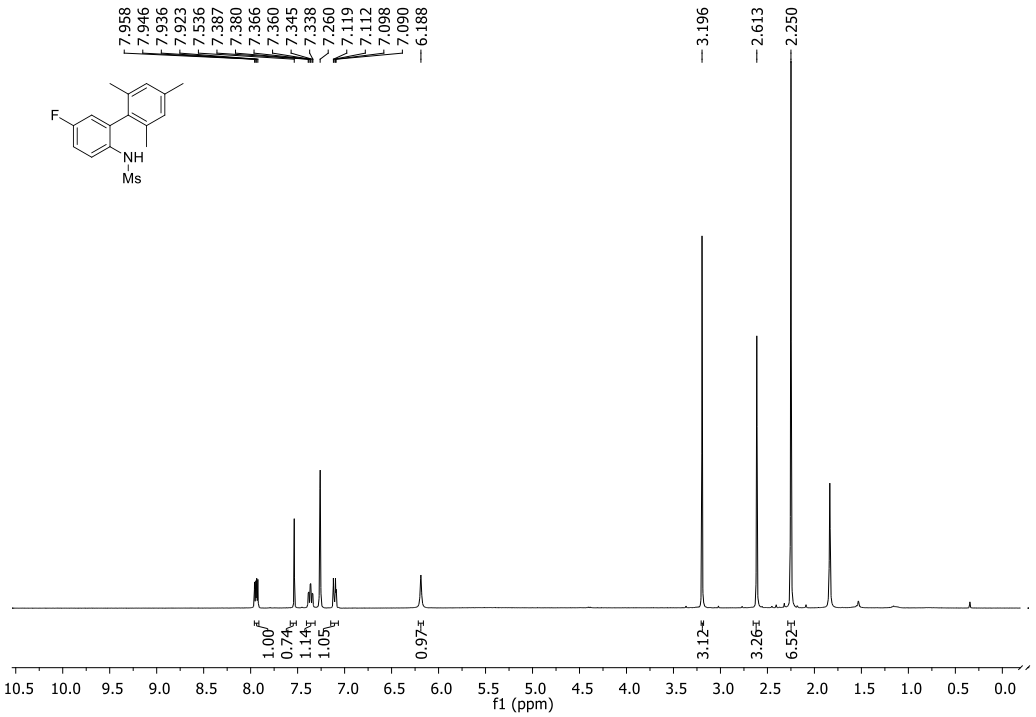


Figure 2.5. [1]H NMR spectrum of *N*-(5-fluoro-2' ,4' ,6'-trimethyl-[1, 1'-biphenyl]-2-yl)methanesulfonamide **(3aa)**

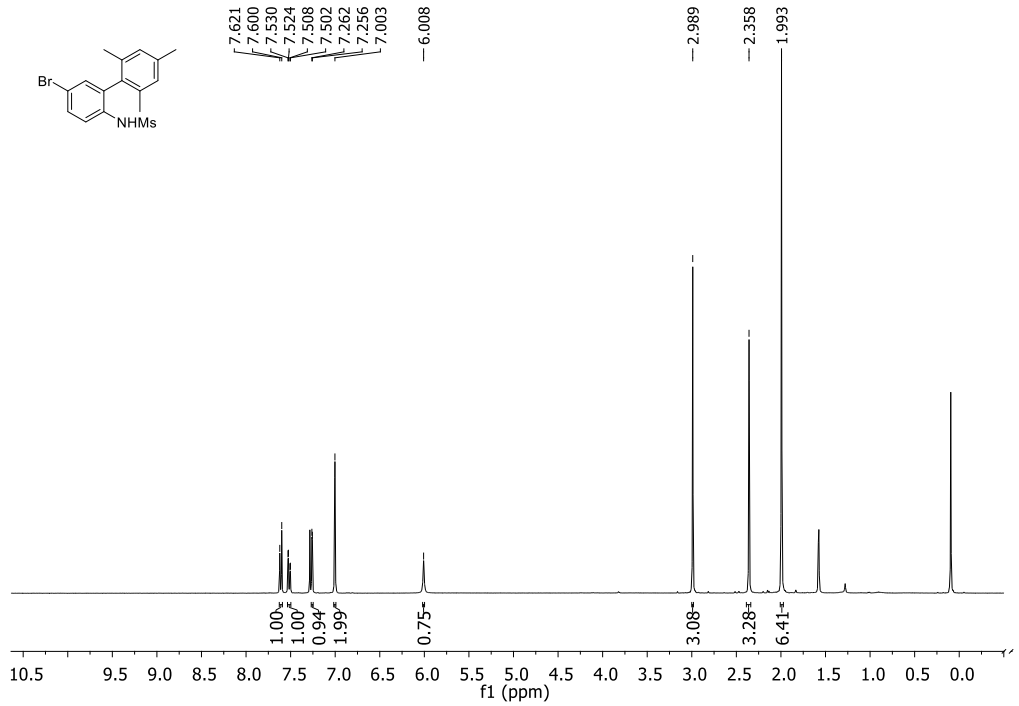


Figure 2.6. [1]H NMR spectrum of *N*-(5-bromo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3ba**)

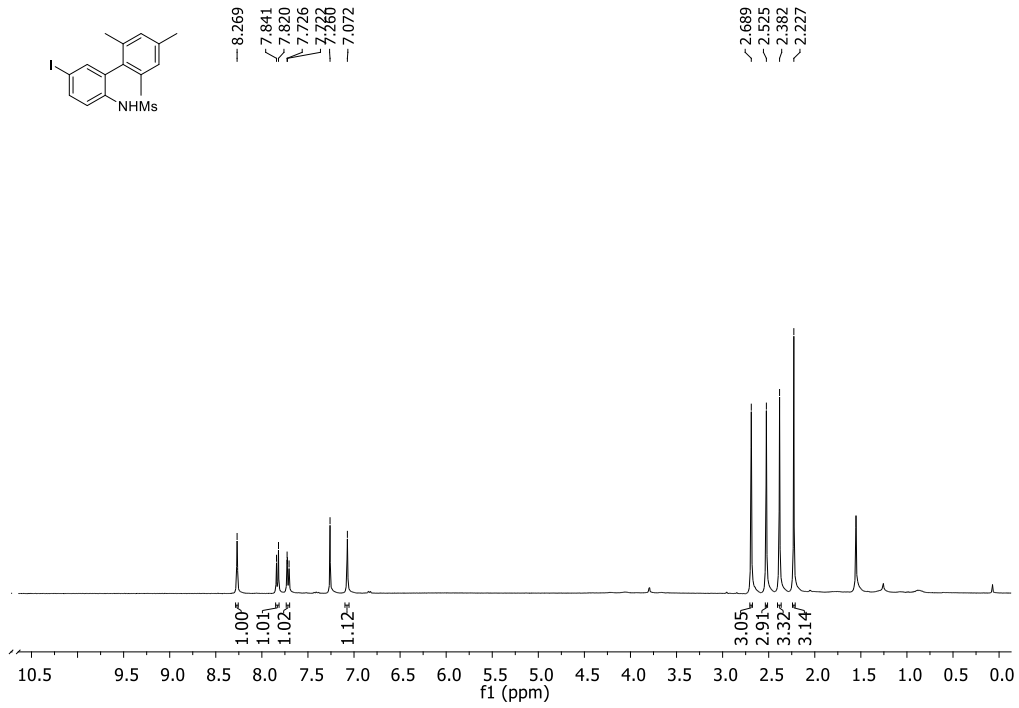


Figure 2.7. ^{1}H NMR spectrum of *N*-(5-iodo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3ca**)

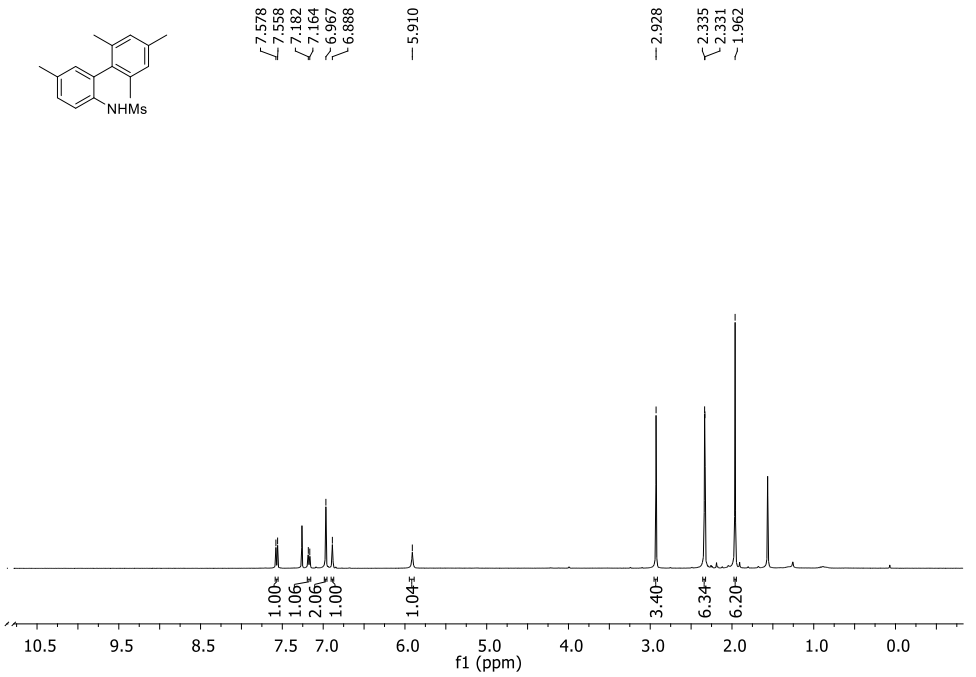


Figure 2.8. ^{1}H NMR spectrum of *N*-(2',4',5, 6'-tetramethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3da**)

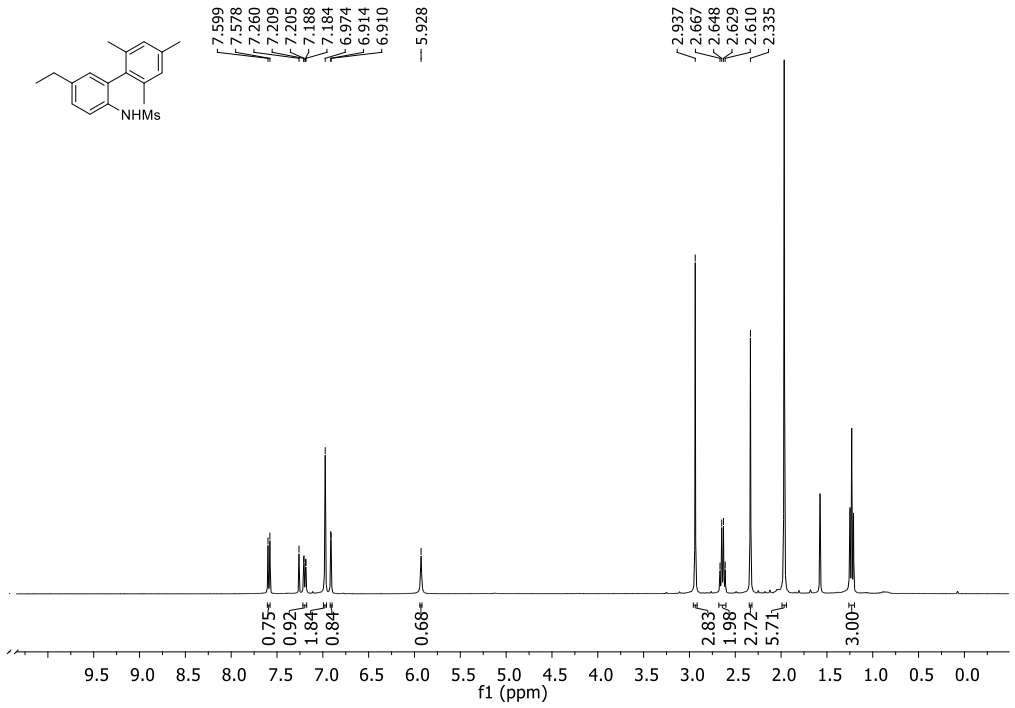


Figure 2.9. [1]H NMR spectrum of *N*-(5-ethyl-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3ea**)

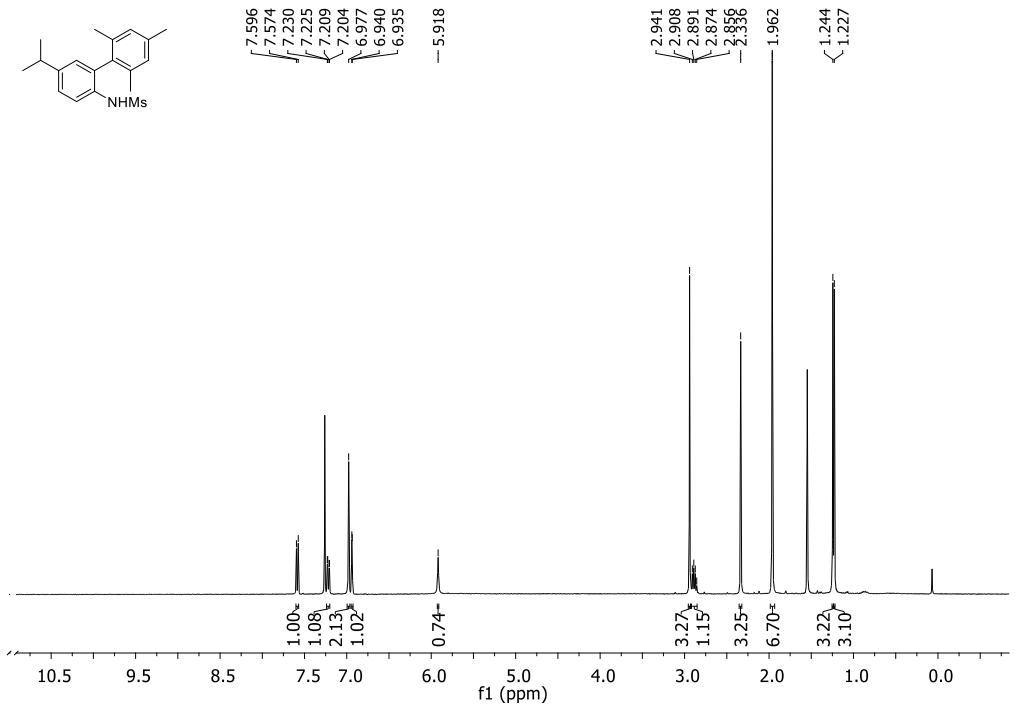


Figure 2.10.. [1]H NMR spectrum of *N*-(5-isopropyl-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3fa)**

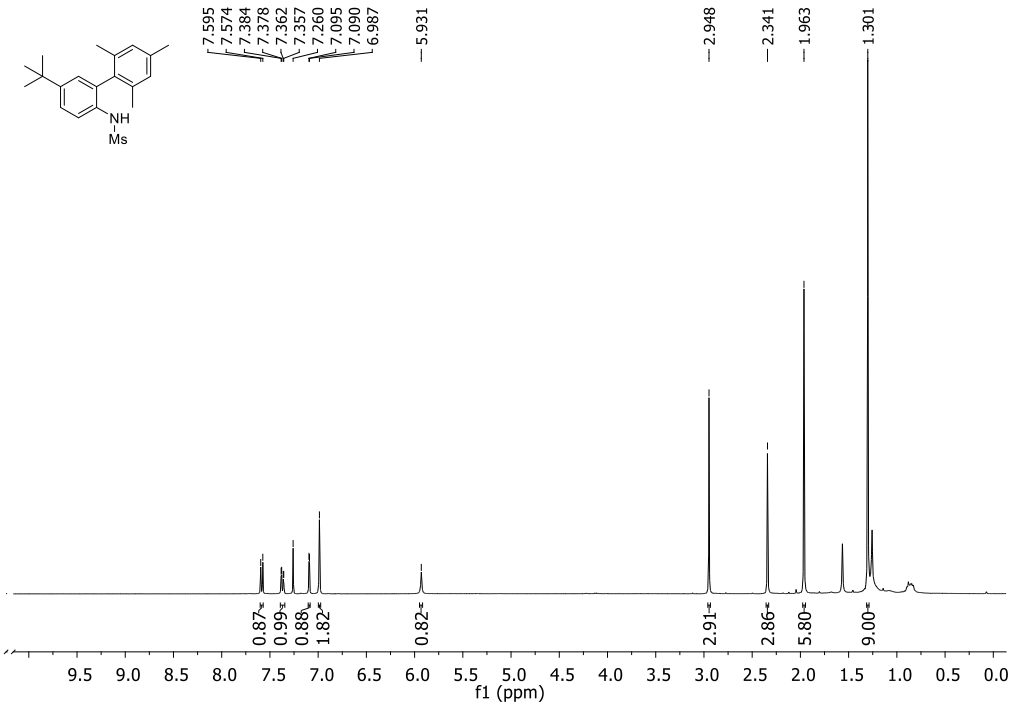


Figure 2.11. ^{1}H NMR spectrum of *N*-(5-(*tert*-butyl)-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3ga**)

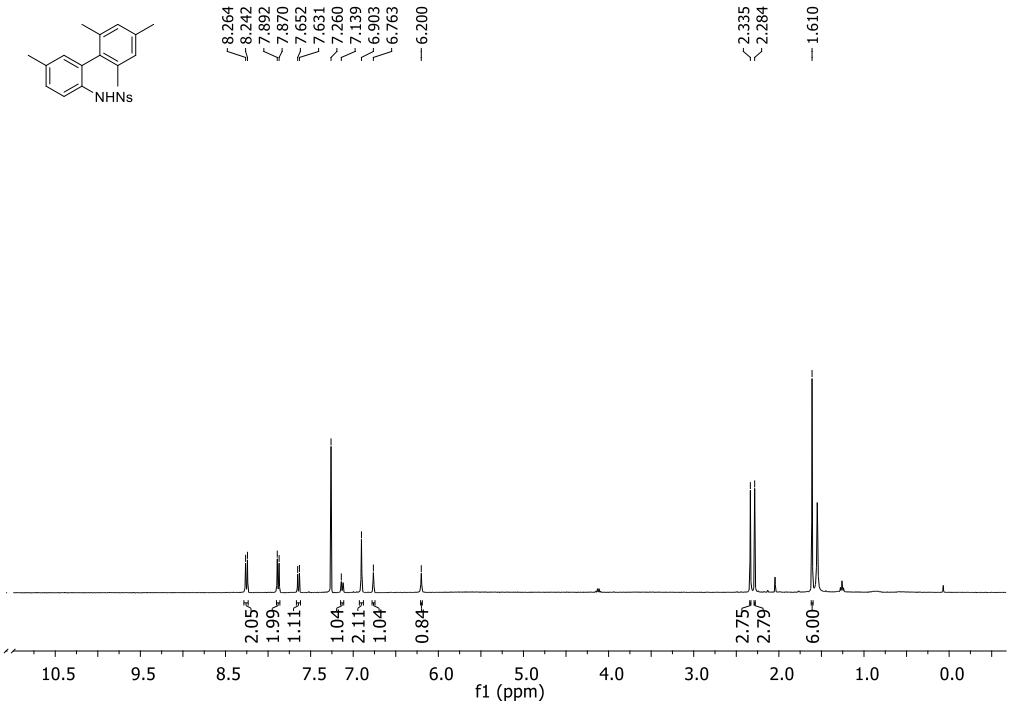


Figure 2.12. ^{1}H NMR spectrum of 4-nitro-*N*-(2',4',5', 6'-tetraimethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide **(3ha)**

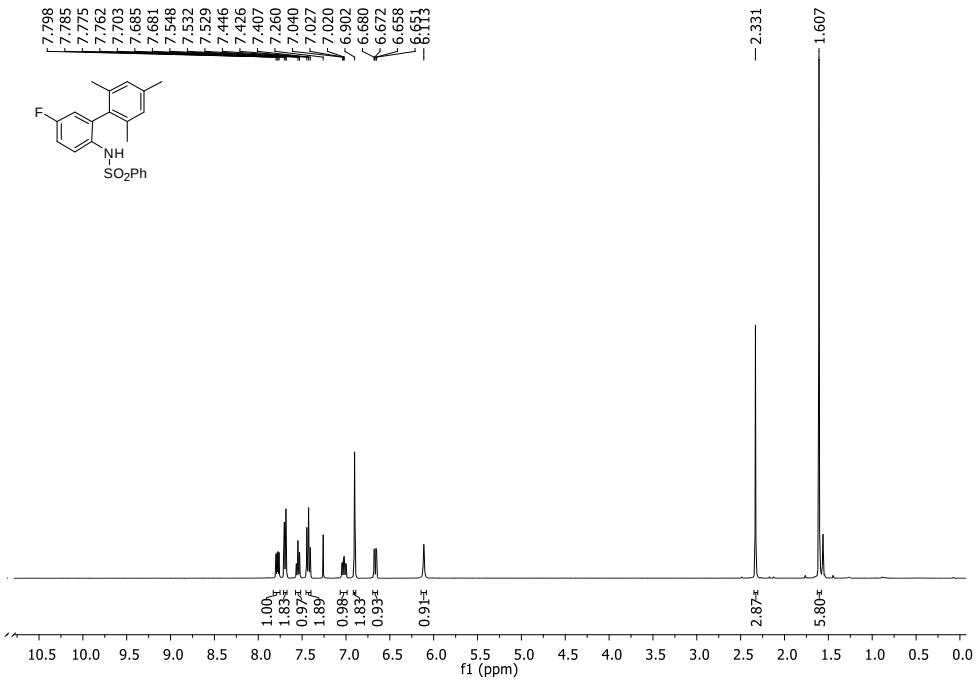


Figure 2.13. ^{1}H NMR spectrum of *N*-(5-fluoro-2',6'-dimethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (**3ia**)

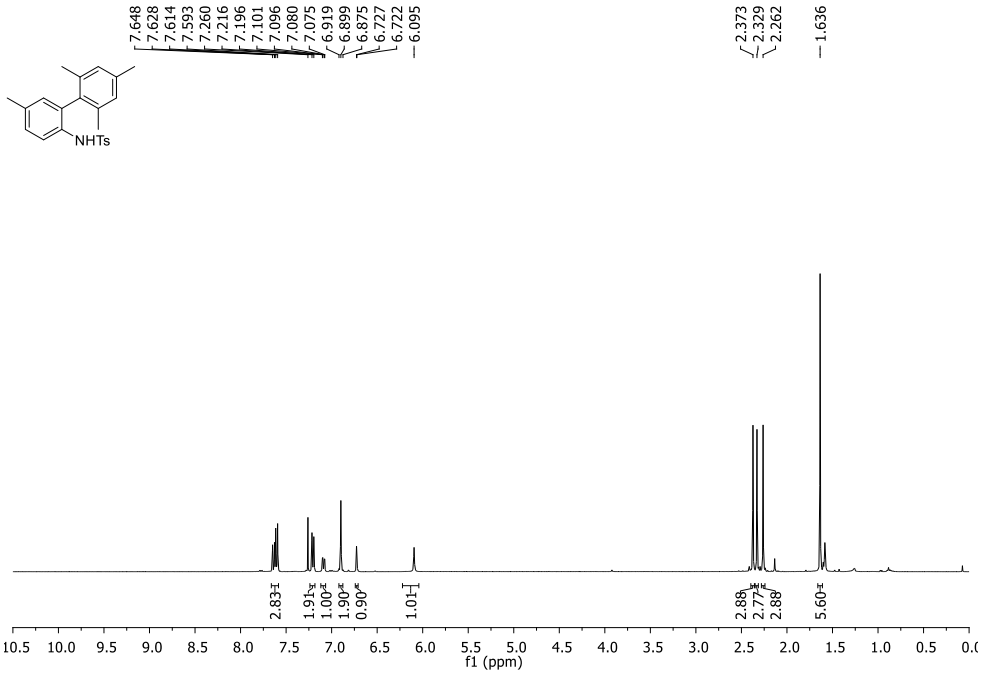


Figure 2.14. ^{1}H NMR spectrum of 4-methyl-*N*-(2',4' ,5' 6'-tetramethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (**3ja**)

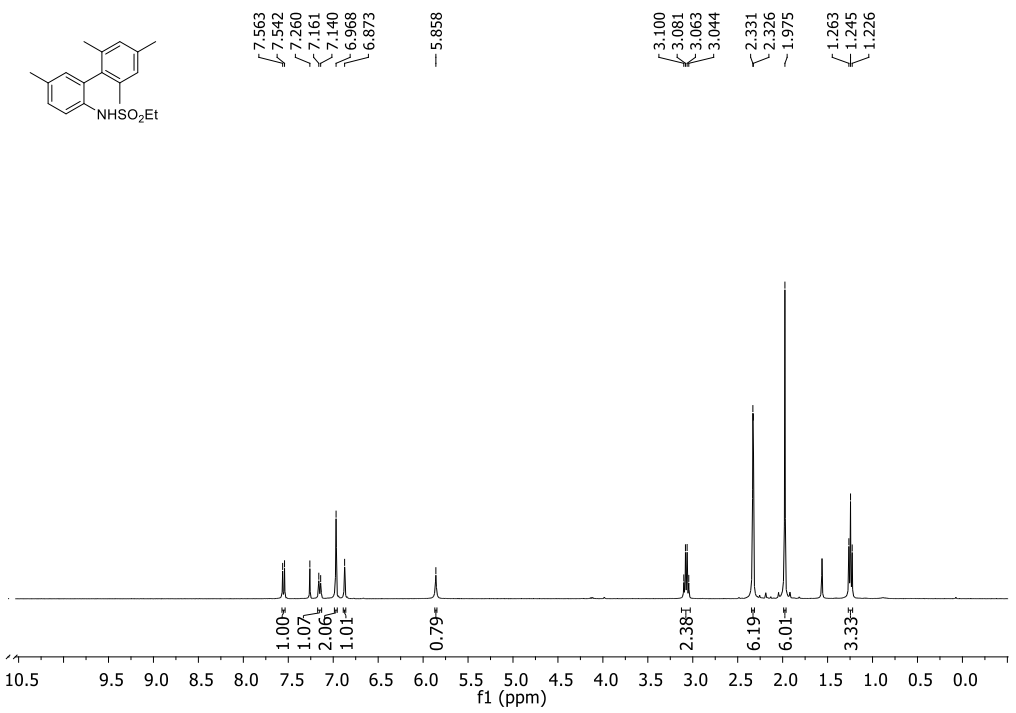


Figure 2.15. ^{1}H NMR spectrum of *N*-(2', 4' ,5' 6'-tetramethyl-[1,1'-biphenyl]-2-yl)ethanesulfonamide (**3ka**)

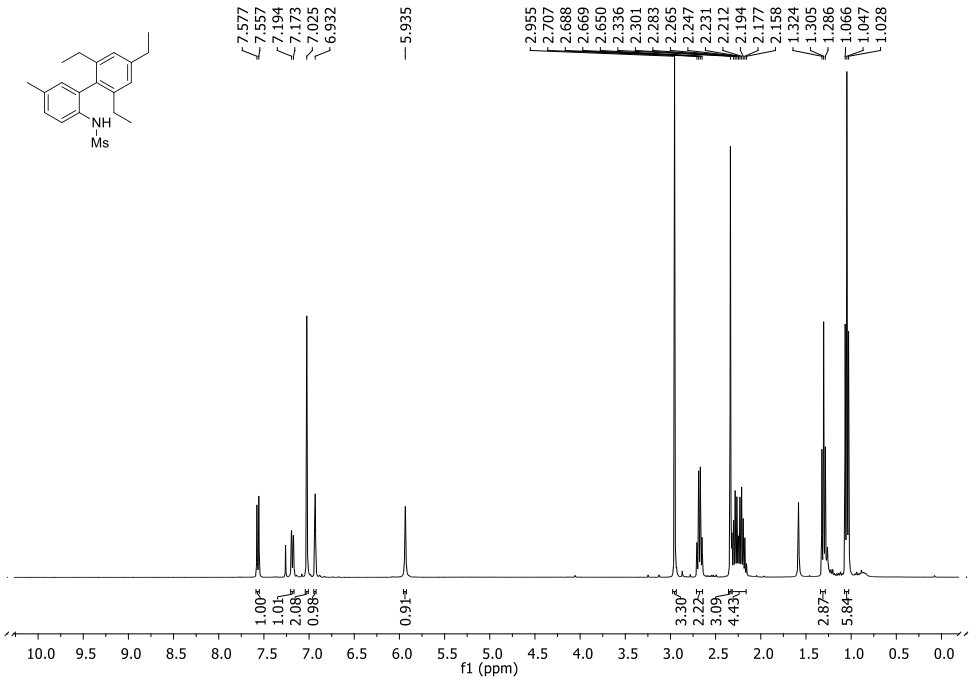


Figure 2.16. ^{1}H NMR spectrum of *N*-(2',4', 6'-triethyl-5-methyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3db**)

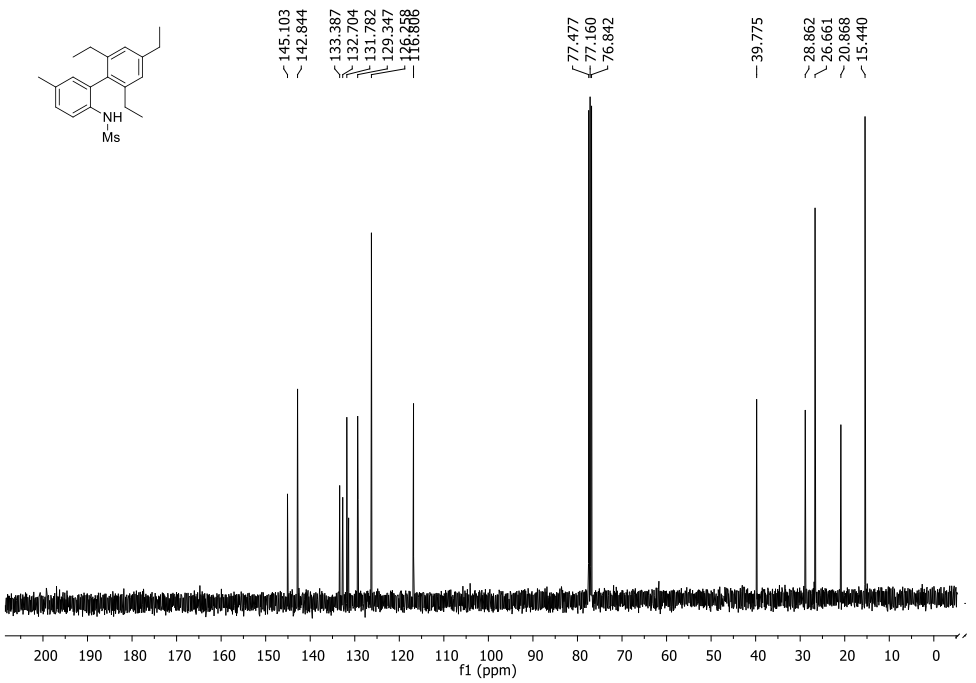


Figure 2.17. ^{13}C NMR spectrum of *N*-(2',4', 6'-triethyl-5-methyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3db**)

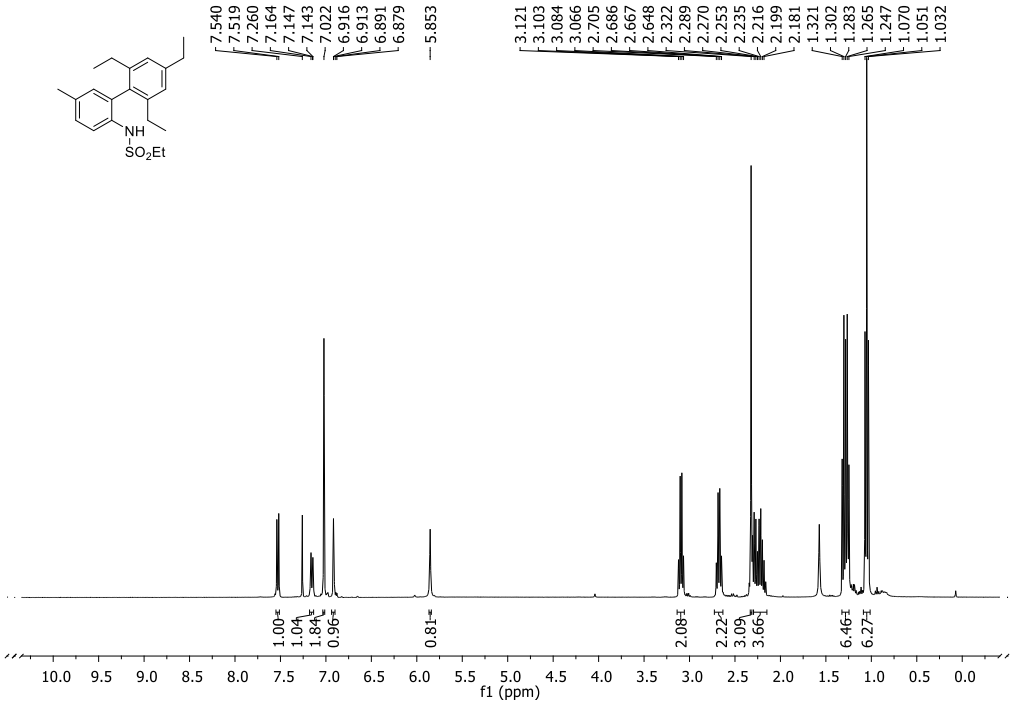


Figure 2.18. ^{1}H NMR spectrum of *N*-(2',4', 6'-triethyl-5-methyl-[1,1'-biphenyl]-2-yl)ethanesulfonamide (**3kb**)

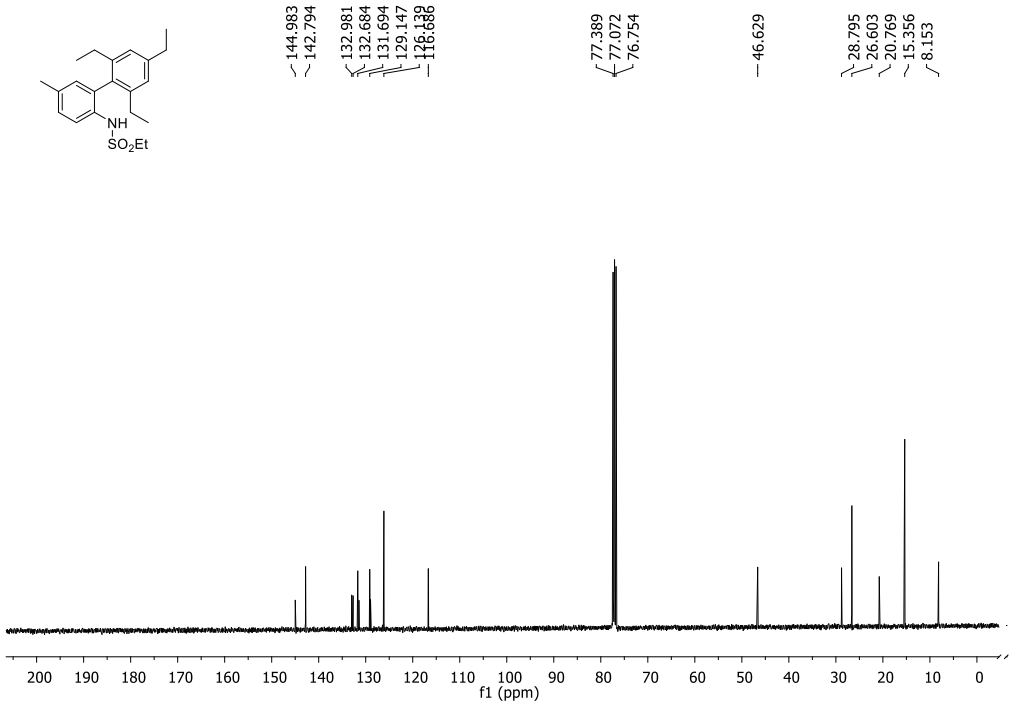


Figure 2.19. ^{13} C NMR spectrum of *N*-(2',4', 6'-triethyl-5-methyl-[1,1'-biphenyl]-2-yl)ethanesulfonamide (**3kb**)

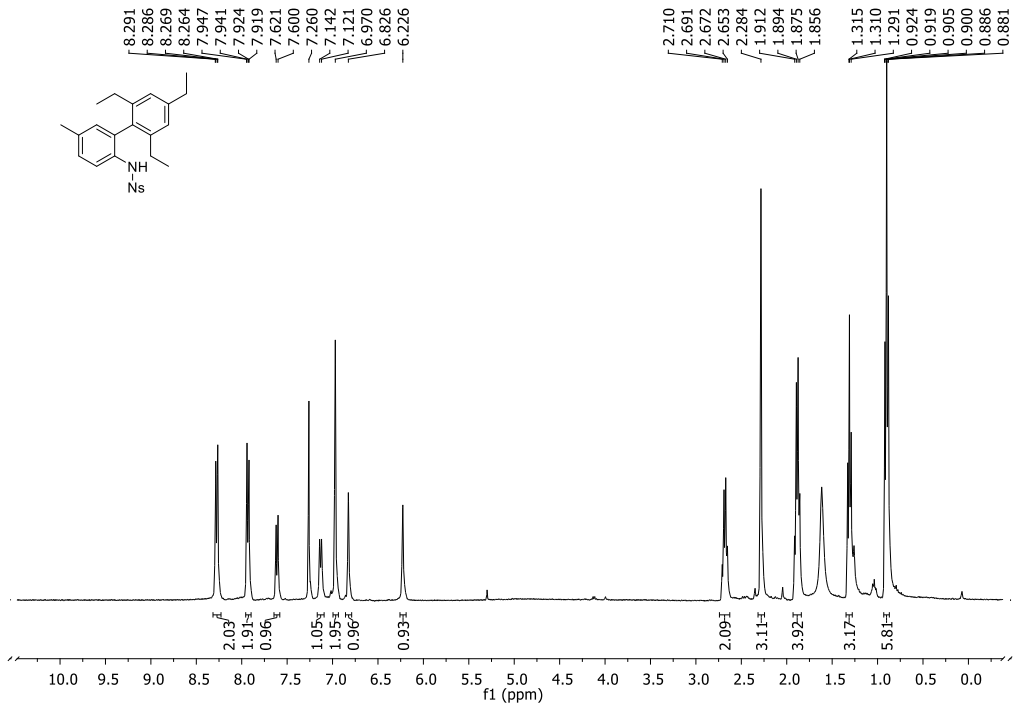


Figure 2.20. ^{1}H NMR spectrum of 4-nitro-*N*-(2',4', 6'-triethyl-5-methyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (**3hb**)

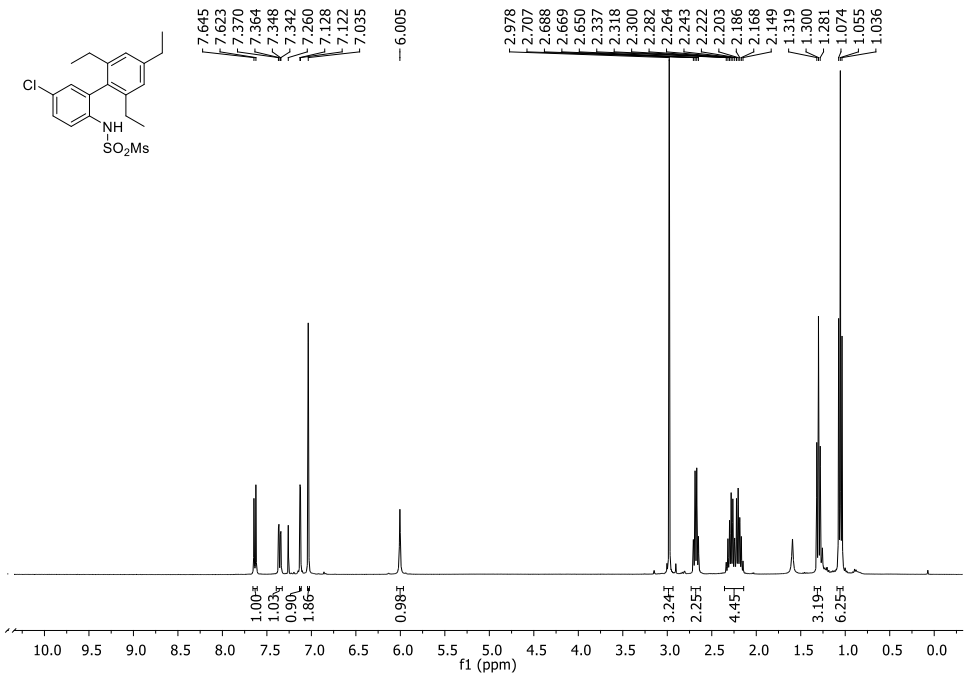


Figure 2.21. ^{1}H NMR spectrum of *N*-(5-chloro-2',4', 6'-triethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3pb**)

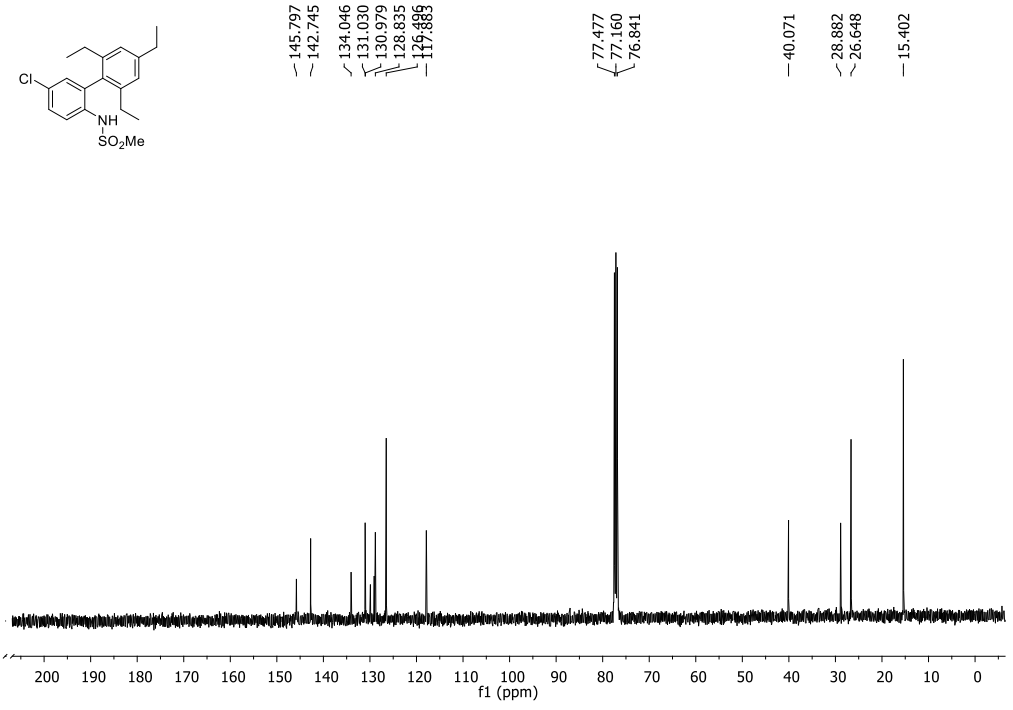


Figure 2.22. ^{13}C NMR spectrum of *N*-(5-chloro-2',4', 6'-triethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3pb**)

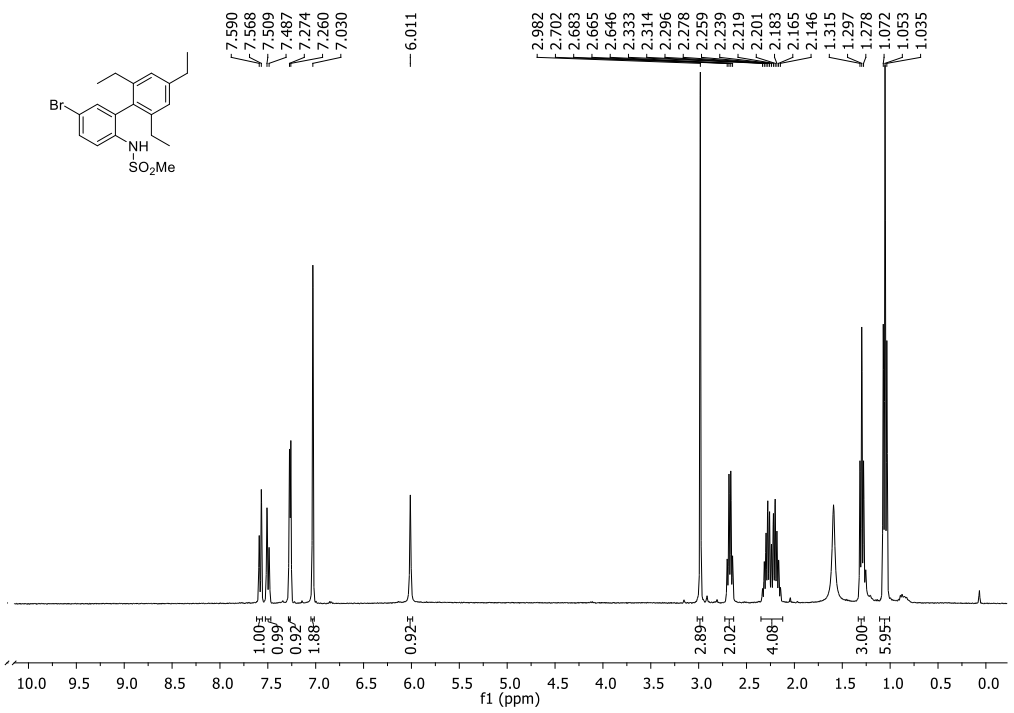


Figure 2.23. ^{1}H NMR spectrum of *N*-(5-bromo-2',4', 6'-triethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3bb**)

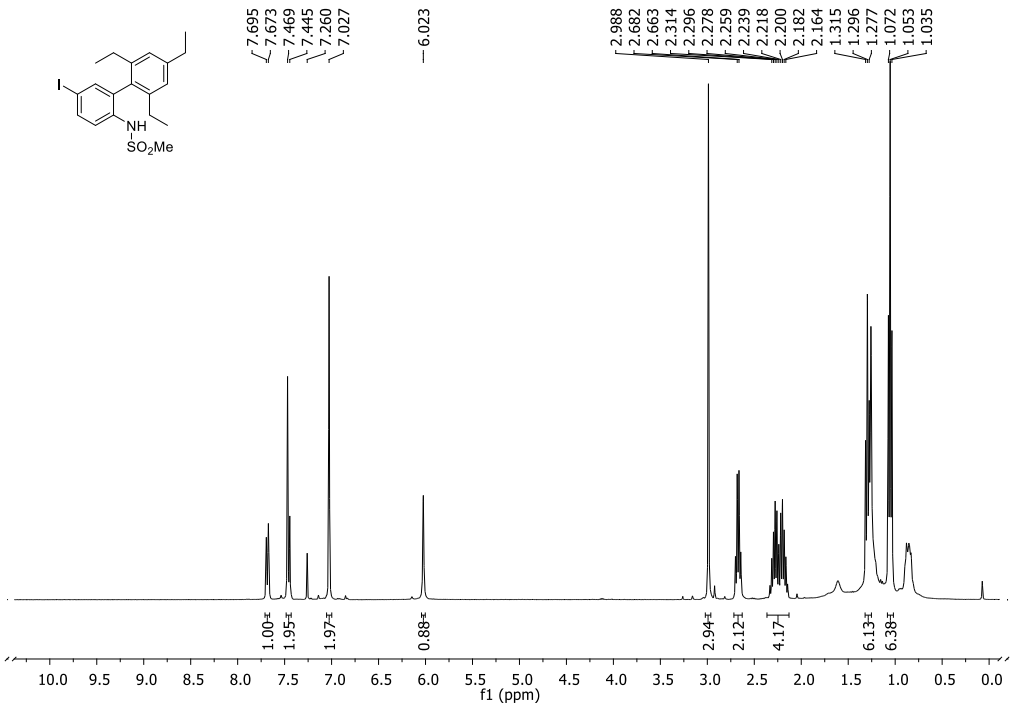


Figure 2.24. ^{1}H NMR spectrum of *N*-(2',4', 6'-triethyl-5-iodo-[1,1'-biphenyl]-2-yl)methanesulfonamide **(3cb**)

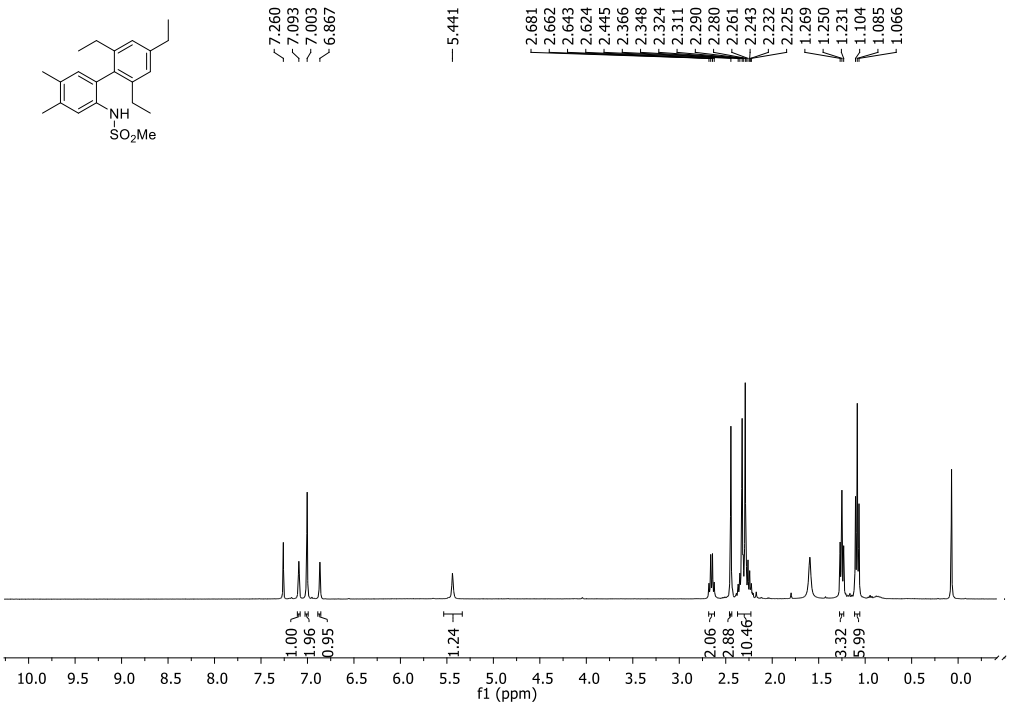


Figure 2.25. ^{1}H NMR spectrum of *N*-(2',4', 6'-triethyl-4,5-dimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3qb**)

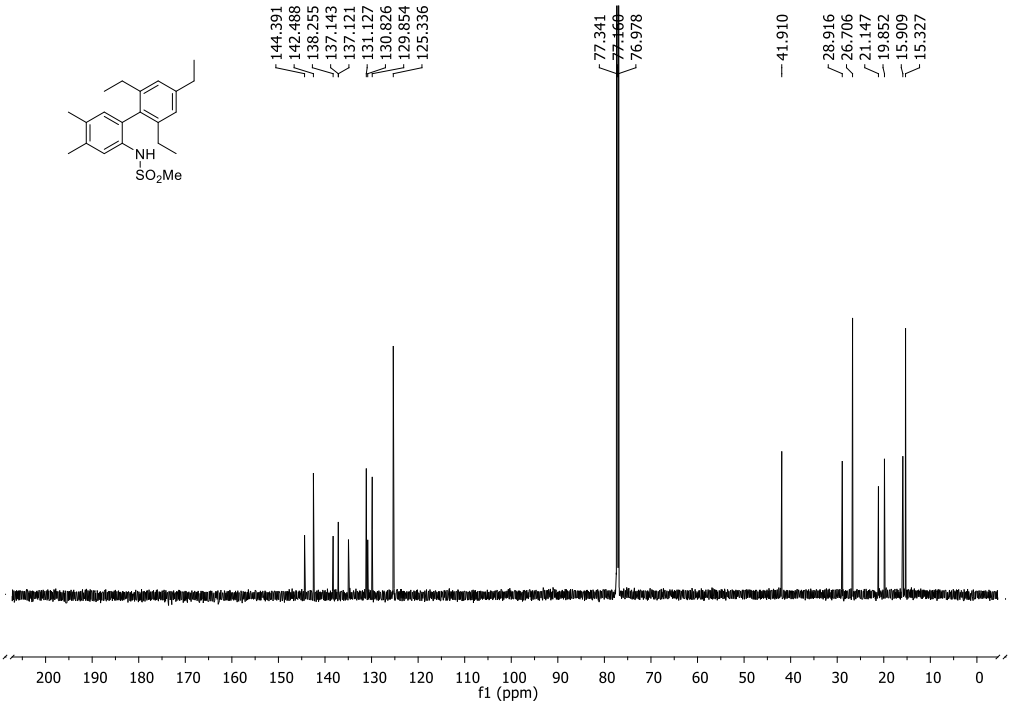


Figure 2.26. ^{13}C NMR spectrum of *N*-(2',4', 6'-triethyl-4,5-dimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3qb**)

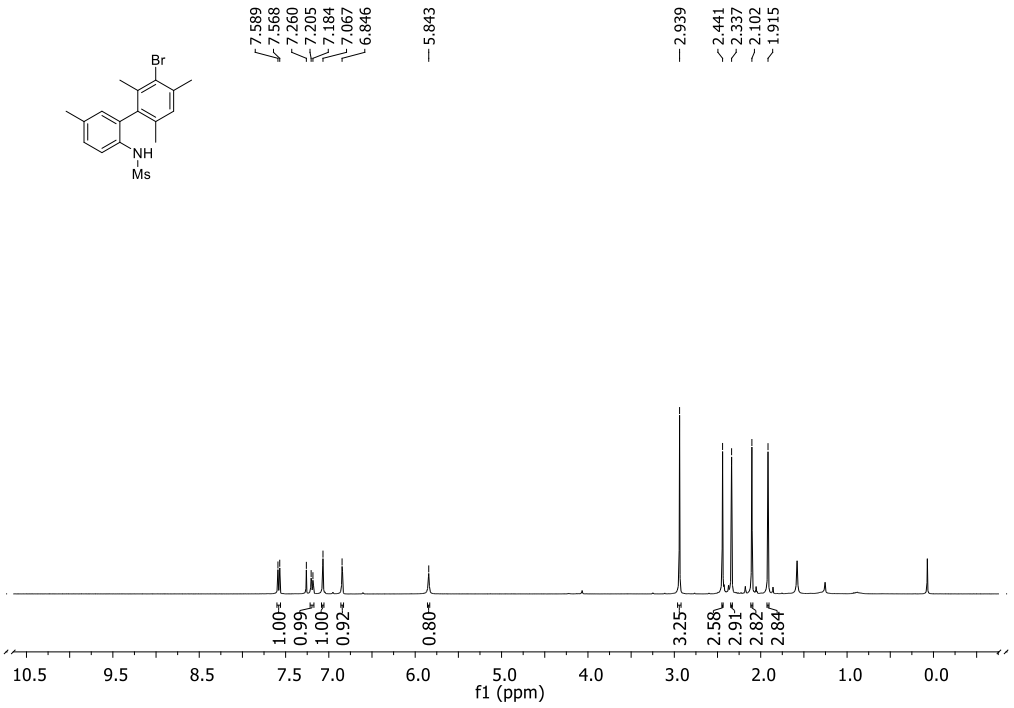


Figure 2.27. [1]H NMR spectrum of *N*-(2',4', 6'-triethyl-4,5-dimethyl-[1,1'-biphenyl]-2yl)methanesulfonamide (**3dc**)

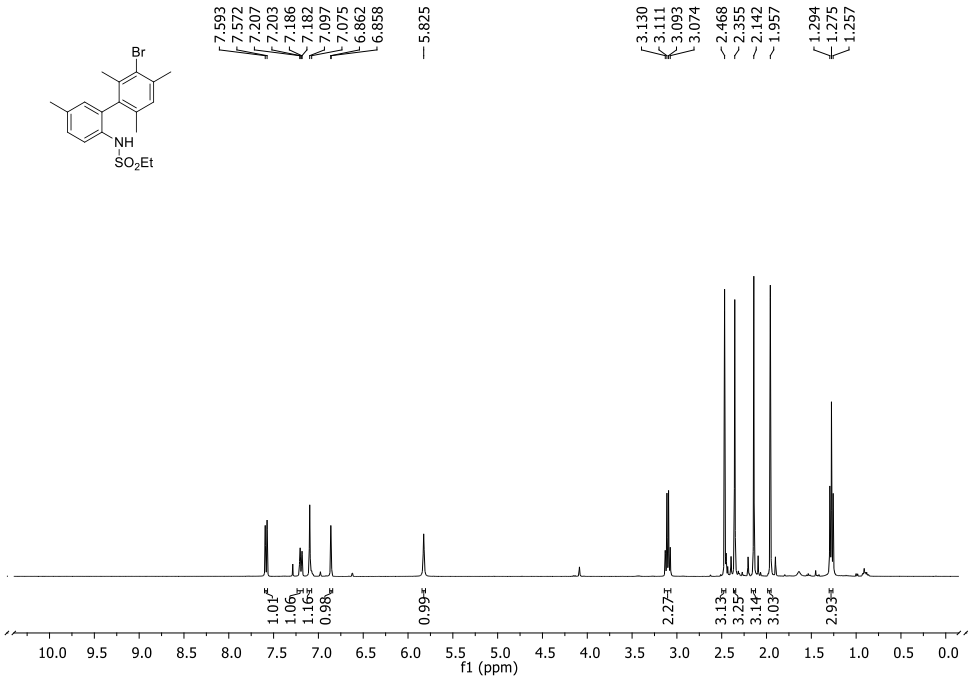


Figure 2.27. [1]H NMR spectrum of *N*-(3'-bromo-2',4',5, 6'-tetramethyl-[1,1'-biphenyl]-2-yl)ethanesulfonamide (**3kc**)

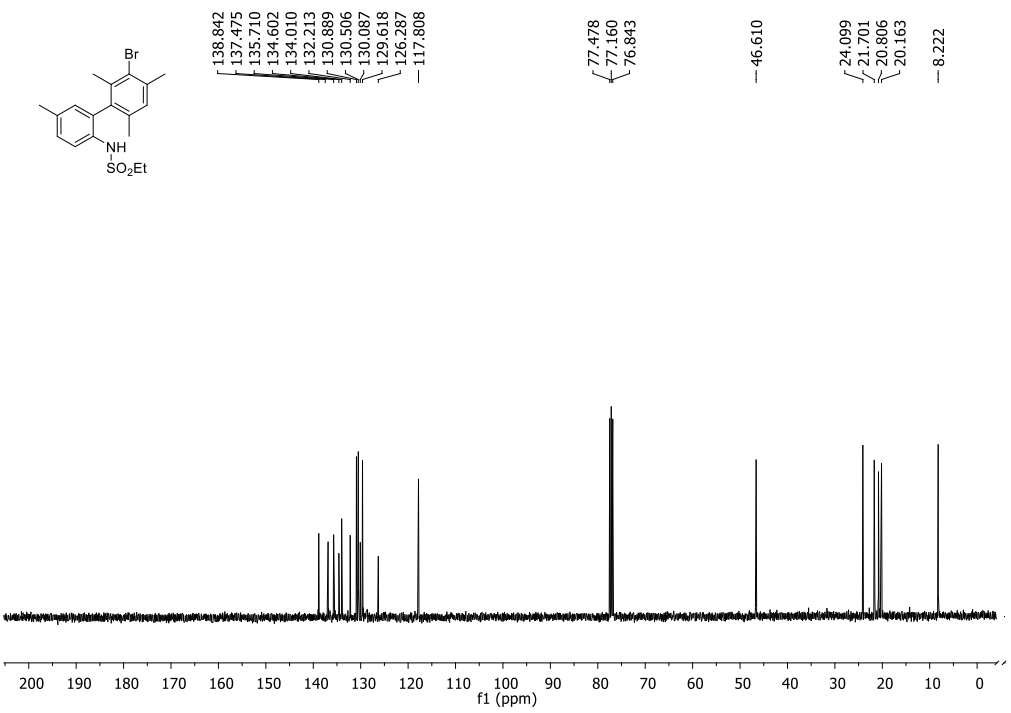


Figure 2.28. ^{13}C NMR spectrum of *N*-(3'-bromo-2',4',5, 6'-tetramethyl-[1,1'-biphenyl]-2-yl)ethanesulfonamide (**3kc**)

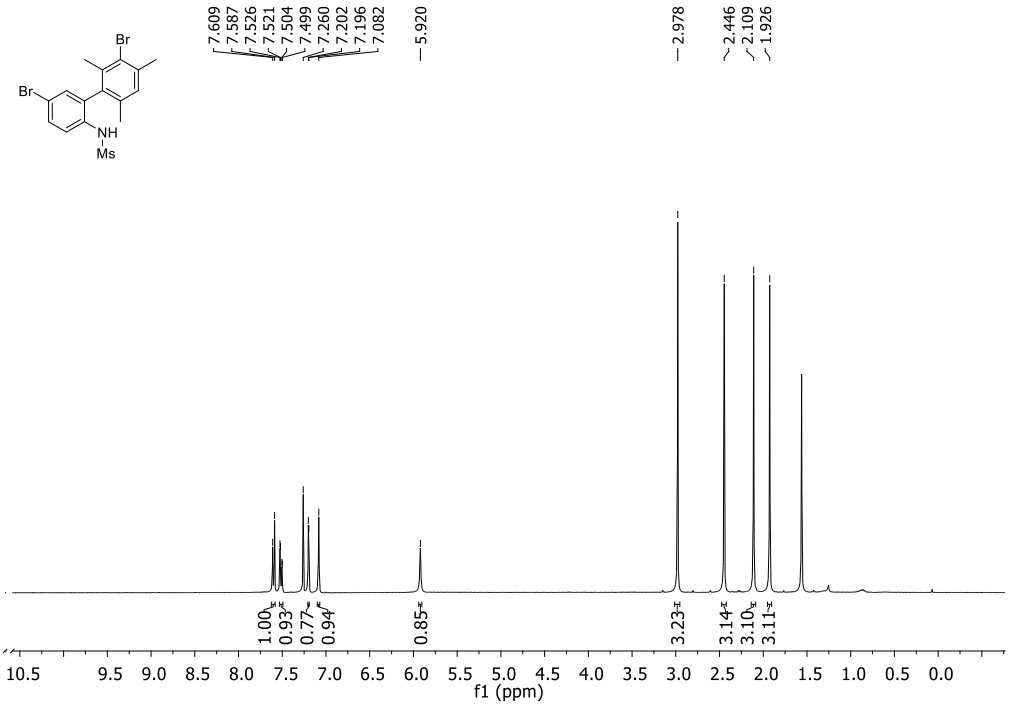


Figure 2.29. ^{1}H NMR spectrum of *N*-(3', 5-dibromo-2',4', 6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3bc**)

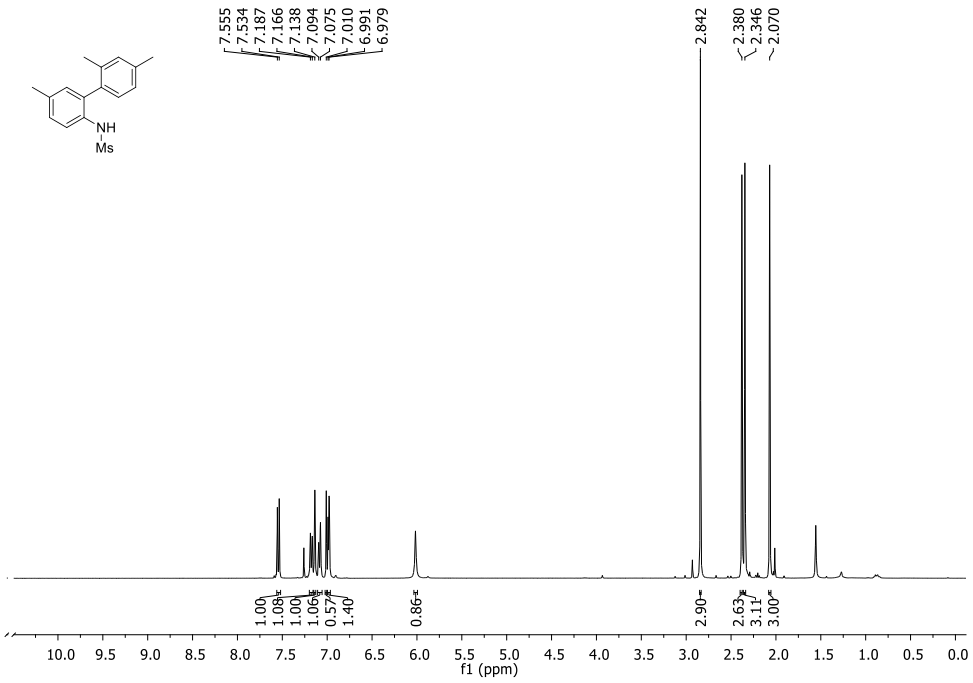


Figure 2.30. ^{1}H NMR spectrum of *N*-(2',4', 5'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3dd**)

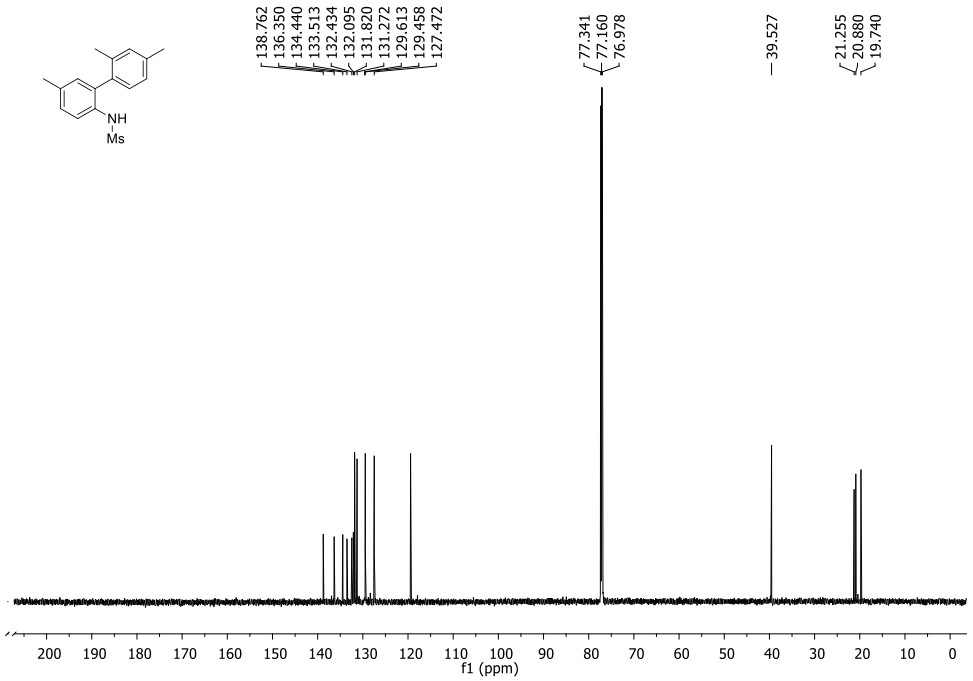


Figure 2.31. ^{13}C NMR spectrum of *N*-(2',4', 5'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3dd**)

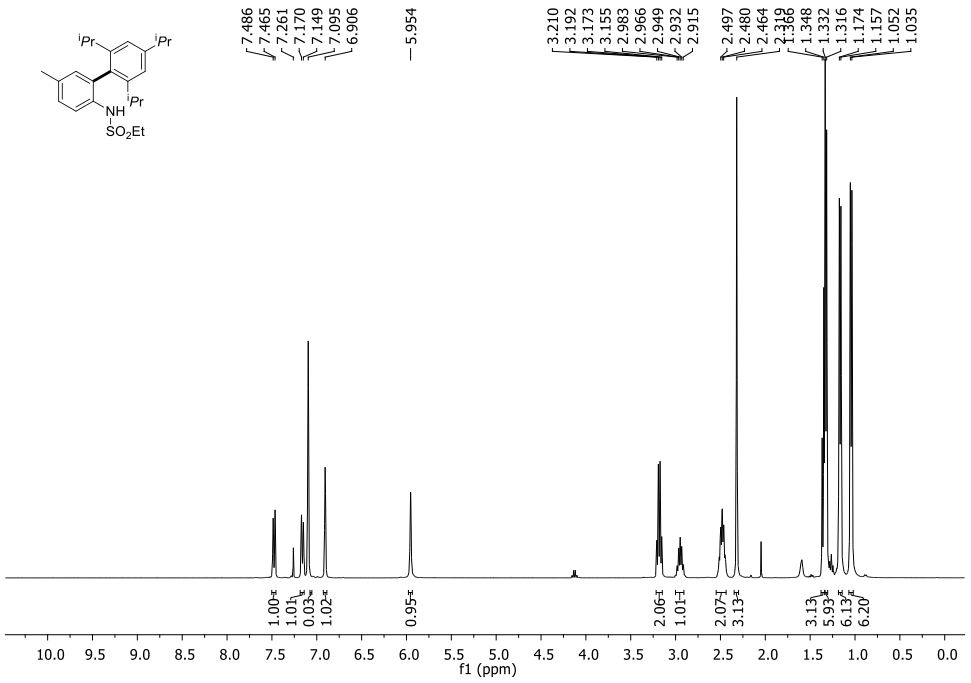


Figure 2.32. [1]H NMR spectrum of *N*-(2',4',6'-triisopropyl-5-methyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3ke**)

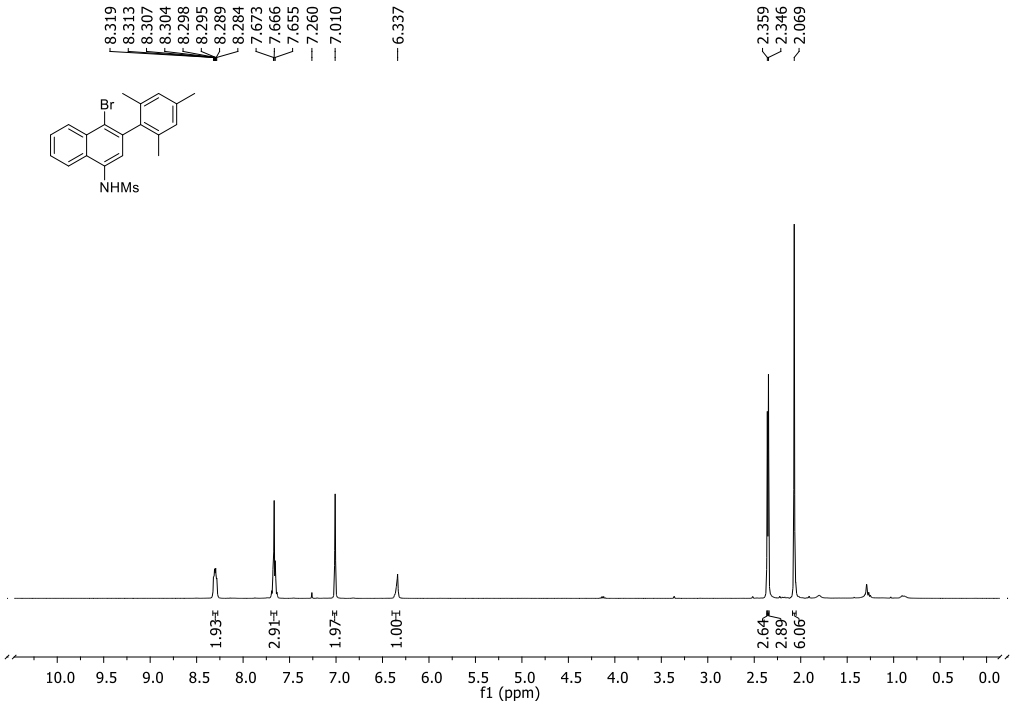


Figure 2.33. [1]H NMR spectrum of *N*-(4-bromo-2-mesitylnaphthalen-1-yl)methanesulfonamide **(3va)**

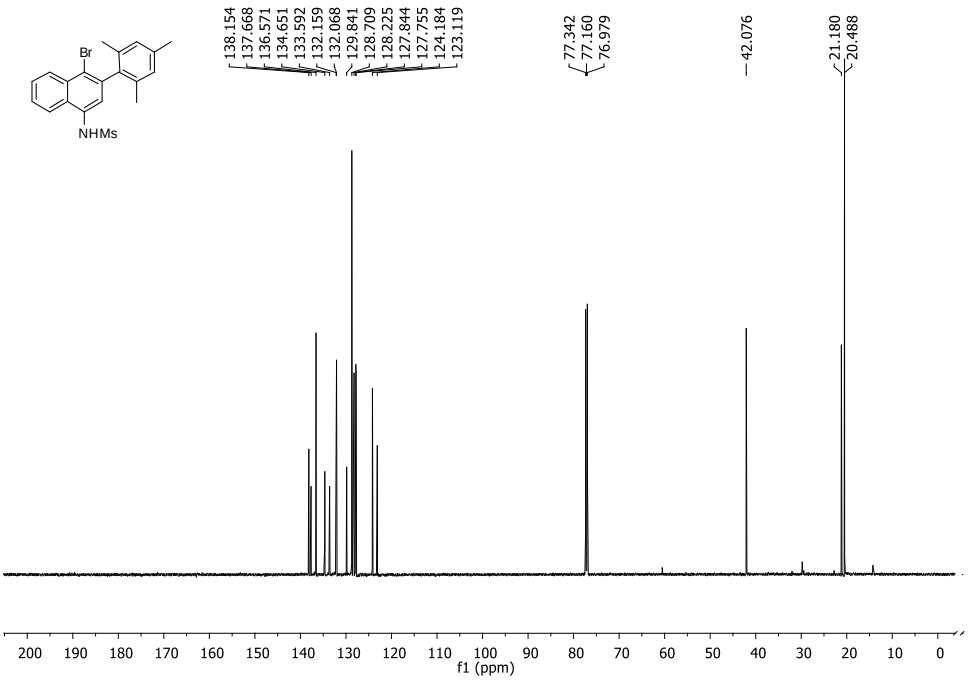
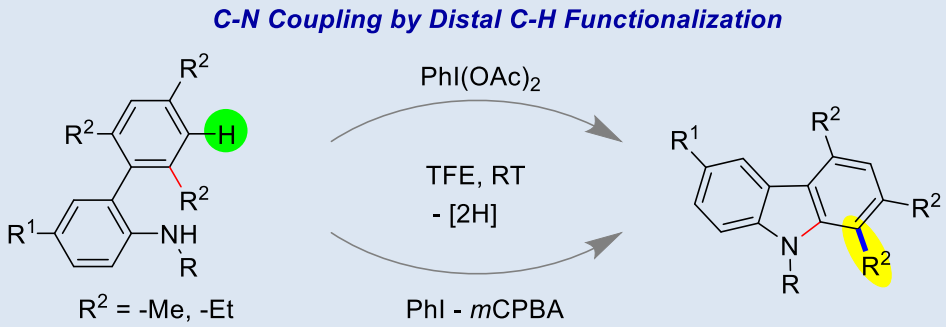


Figure 2.34. ^{13}C NMR spectrum of *N*-(4-bromo-2-mesitylnaphthalen-1-yl)methanesulfonamide **(3va)**

CHAPTER 3

Nitrenium ion in Distal C-H Functionalization for Synthesis of Carbazoles

3.1 ABSTRACT



This chapter focuses on generation of nitrenium ion intermediate from a biarylsulphonamide *via* nitrenium ion followed by migration of alkyl which lead to the synthesis of carbazoles Stoichiometric amount of iodine(III) reagent has been used, or it has been generated under in-situ conditions by using iodobenzene and an oxidant like meta perchlorobenzoic acid. This strategy of C-H amination is highly beneficial for synthesizing 1,2,4-trialkyl substituted carbazoles at ambient temperature and in an open atmosphere.

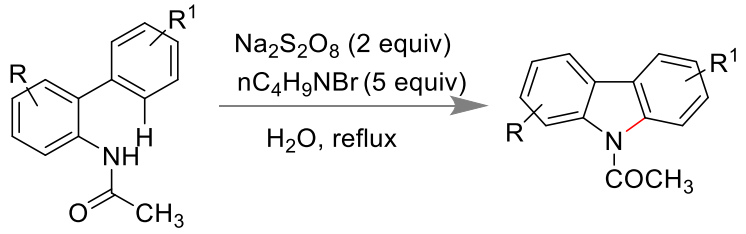
3.2 INTRODUCTION

The synthesis of nitrogenous heterocycles via C-N coupling has gained prominence for ages.[1-3] Metal free approach for C-H amination is more significant and preferable than the conventional approach for metal-mediated C-N bond synthesis methods to construct amines[4, 5, 6]. As a result, metal free techniques involving hypervalent iodine(III) reagents that are less toxic and inexpensive are highly desirable for oxidative C-N bond synthesis[7, 8] and in many

cross-dehydrogenative coupling (CDC) reactions.[9-11] The environmentally benign nature, ease of availability, stability, and controlled oxidizing ability of hypervalent iodine reagents make them highly versatile and valuable for synthetic transformations.[12-17] Amines (or amides) react with hypervalent iodine(III) mediated to produce nitrenium ion, an electrophilic species highly recognized as a potential synthetic intermediate derived in synthetic conversions. Mechanistic studies involve forming nitrenium ions involving ligand exchange of iodine(III) with amines accompanied by reductive elimination of iodoarene. Herein we have exemplified an intramolecular C-N coupling reaction using the concept of distal C-H bond functionalization strategy involving alkyl migration to synthesize carbazoles. The biarylsulfonanilides were made to react with stoichiometric amounts of phenyliodine diacetate (PIDA) or iodine (III) was *in-situ* obtained from iodobenzene(PhI)-*meta*-chloroperbenzoic acid (*m*CPBA) combination in TFE at room temperature. Our focus was to carry out the synthetic transformations from nitrenium ion intermediates using distal C-H functionalization. Previous approaches involving intramolecular C-H amination strategies for constructing carbazole motifs are centered on proximal C-H bond functionalization, some of which have been discussed later.[18] Carbazole motifs are widespread and abundantly found in various pharmaceutical and natural products.[14] This has led to devise an approach for multiple methods to develop carbazoles.

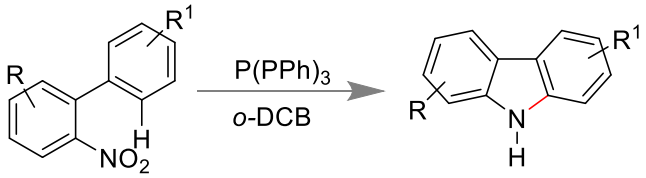
3.3 Proximal C-H Bond Functionalization reactions.

Natarajan group had synthesized N substituted carbazoles using the proximal C-H Bond functionalization approach.[19] Proximal C-H bond functionalization took place position forming carbazoles. Potassium peroxodisulfate and TBABr in combination, generated the N-centered radical followed by an intramolecular attack by the arene, led to the formation of desired product proximal C-H bond functionalization.



Scheme 3.1 Proximal C-H Bond functionalization using potassium peroxodisulfate.

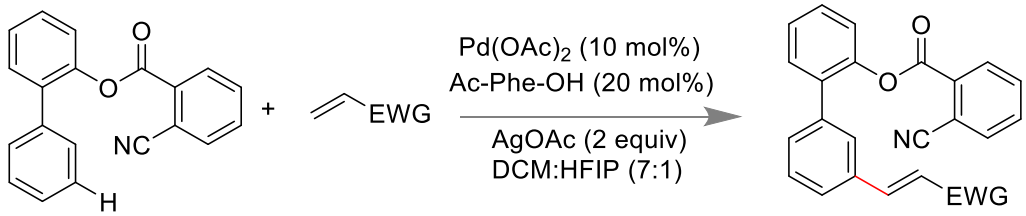
Carbazole synthesis via proximal C-H bond functionalization was achieved using triphenylphosphine in o-dichlorobenzene. Nitrobiphenyl underwent reductive deoxygenation generating N-centered radical. Cyclization took place with functionalization at the proximal C-H bond.



Scheme 3.2 Proximal C-H Bond functionalization using triphenyl phosphine.

3.4 Distal C-H Bond functionalization Reactions.

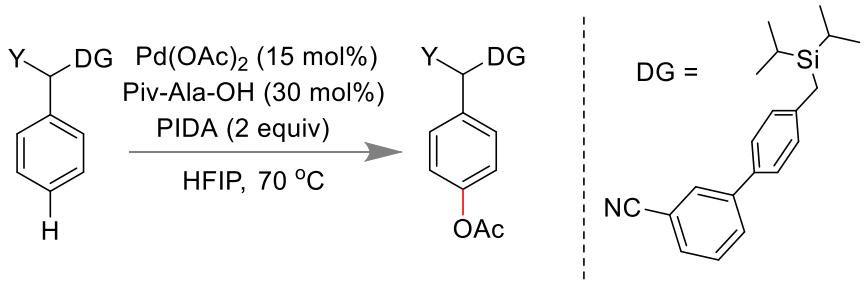
Distal C-H functionalization assisted by nitrile-based template using Palladium catalyst for olefination of a biaryl system has been reported by Maiti and co-workers.[20] The reaction proceeded with excellent regioselectivity and stereoselectivity, producing a good synthetic yield of the functionalized olefin in biaryl motif. The olefination occurred at a distal *meta* position instead of proximal ortho olefination.



Scheme 3.3 Selective distal C–H olefination of biaryl motif catalysed by Pd.

Para selective C-H acetoxylation was reported using silicon containing biaryl template using palladium metal and using phenyl iodine diacetate as the acetoxy source.[21] The distal C-H

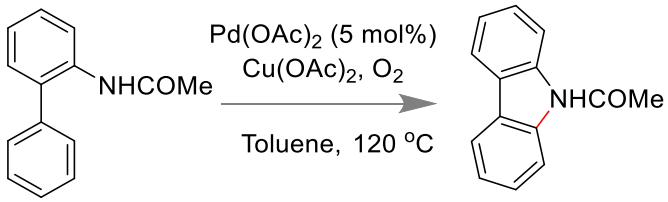
functionalization occurred at site-selective *para* position with help of directing group approach by forming a D-shaped assembly and hence termed as D-shaped template-assisted para C-H functionalization.



Scheme 3.4 D-shaped template assisted *para* C-H functionalization.

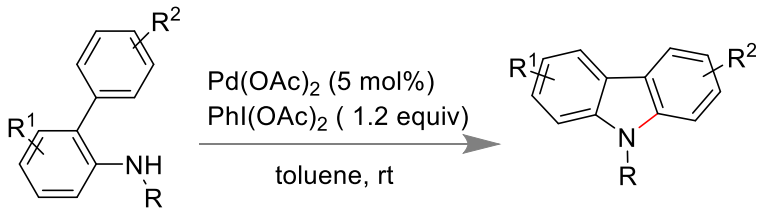
3.5 C-H Amination Methods for Synthesis of Carbazoles.

Methods for developing a C-H amination strategy are a significant target in organic synthesis. Traditional metal-mediated approach for C-H amination employing Palladium (Pd) assisted by copper acetate ($Cu(OAc)_2$) as co-oxidant was developed by Buchwald.[22] The strategy to prepare such heterocyclic scaffold carbazole involved C-H activation by Palladium and copper. Copper acetate was utilized to convert Pd(0) to Pd(II).



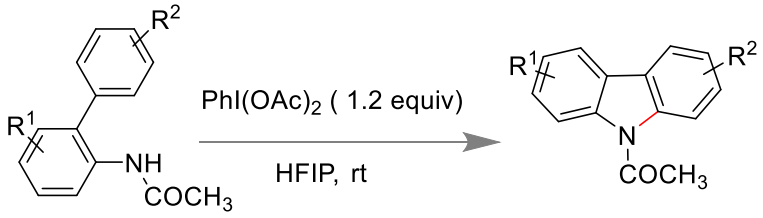
Scheme 3.5 C-H amination for the synthesis of carbazole by bimetallic approach.

A few years later, Gaunt reestablished the oxidative C-N coupling using palladium independently phenyliodine diacetate (PIDA).[23] The reaction took place by Pd(II)/Pd(IV) catalytic cycle followed by reductive elimination from Pd(IV) state, forming desired C-H amination. The role of the oxidant PIDA was to oxidize Pd(II) to Pd(IV) to attain desired carbazole as the product.



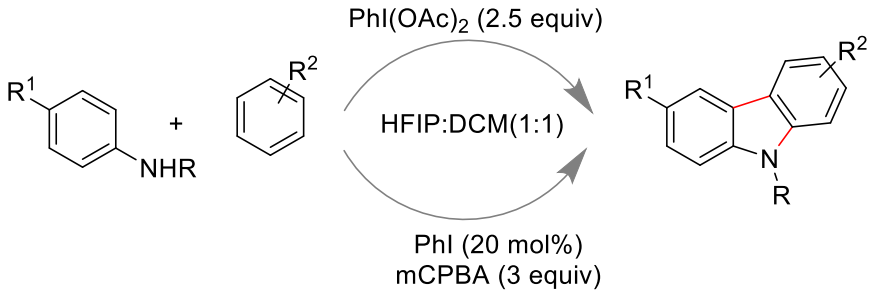
Scheme 3.6 Carbazole synthesis *via* bimetallic approach.

C-H amination by C-N coupling simply by using hypervalent iodine(III) reagent was developed by Antonchick and co-workers.[24] The transformation of 2-acetaminobiphenyl to *N*-acetylcarbazole in the presence of an oxidant like (diacetoxy)iodobenzene at ambient temperature led to the synthesis of triazoles.



Scheme 3.7 Synthesis of carbazole by metal free approach.

Carbazole synthesis by intermolecular annulation processes revolves with iodine(III) condition has been developed by Mal and co- workers.[14, 15] The demerits of the protocol involved use of larger proportions of oxidants like phenyl iodine diacetate (PIDA) and *meta*-perchlorobenzoic acid (*m*CPBA).

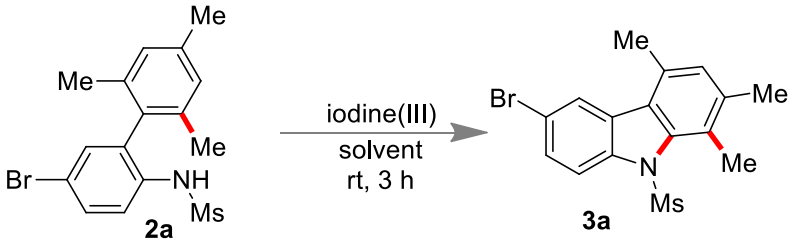


Scheme 3.8 Intermolecular C-H amination for carbazole synthesis.

3.6 RESULTS AND DISCUSSIONS

The reaction was optimized using *N*-(5-bromo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulphonamide (**2a**) and several oxidants and solvents were screened to obtain the desired carbazole. The biaryl sulfonamide (**2a)** was synthesized by taking *N*-(4-bromophenyl) and mesitylene by studying earlier reports. When the biaryl sulfonamide **2a** was made to react with 1.0 equiv of PIDA in 2,2,2-trifluoroethanol (TFE) at room temperature, 6-bromo-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (**3a**) was produced with 90% yield as indicated (Table 3.1, entry 1). The product **3a** showed a rise in yield to (98%) (Table 1, entry 2) using 1.2 equiv of PIDA in solvent 2,2,2-trifluoroethanol. 1,1,1,3,3,3-hexafluoroisopropanol (HFIP), DCE or ACN were some of the solvents which were screened, which were less effective compared to TFE (entry 4-6). The reaction was sluggish, and the desired product was obtained in trace amount (entry 3). Other oxidants like $PhI(OCOCF_3)_2$ (PIFA), which is a comparatively more potent oxidant, resulted in a reduction of yield to about 57% (entry 7). A substantial rise in yield was obtained using PhI(OPiv)2 as an oxidizing agent (entry 8).

Table 3.1. Optimization of Method A



entry	oxidant (equiv)	solvent	yield (%)[a]
1	PIDA (1.0)	TFE	90
2	PIDA(1.2)	TFE	98
3	PIDA(1.2)	DCM	<5%
4	PIDA (1.5)	HFIP	53
5	PIDA (1.5)	DCE	41
6	PIDA (1.5)	ACN	29

7	$PhI(OCOCF_3)_2$ (1.2)	TFE	57
8	$PhI(OPiv)_2$ (1.2)	TFE	69

All reactions were done at room temperature. [a]yields of the isolated product after column chromatography

We targeted to achieve the desired carbazole to generate iodine(III) condition under *in situ* conditions. *N*-(5-bromo-2',4',6'-triethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2l**) chosen as the model substrate which was treated with catalytic amount of iodobenzene (20 mol%) in presence of oxidant 3-chloroperbenzoic acid (*m*CPBA) insolvent TFE . The targeted product 6-Bromo-1,2,4-triethyl-9-methylsulfonyl)-carbazole (**3l**) was formed with 48% yield (Table 3.2, entry 1). When solvent DCM was used in combination with HFIP in 1:1 mixture or TFE-DCM (1:1) by volume, no such improvement in yield was observed (entry 2-4). It was observed that with the increase in the percentage of iodobenzene, an abrupt rise in yield was noted (entry 5).The maximum yield of product **3k** was obtained when 1.0 equivalent of PhI was utilized in combination with an oxidant like mCPBA (1.5 equiv) (entry 6). The results did not improve on substituting electron-withdrawing Cl- or electron-donating Me- on the iodobenzene ring to generate iodine(III) under *in situ* conditions (entry 7-8). The protocol of the C-H amination reaction and the optimized reaction condition of the pathways were applied and extended to an array of substrates that bear electron-donating and electron-withdrawing substrates (Figure 3.1 & 3.2). A stoichiometric amount of PIDA yielded the desired product in good to excellent yields. (Figure 3.1, **3a-3g)**.The decreased yield was observed when an electron withdrawing group was introduced in the aryl group at the C_2-position of anilide (Figure 3.1, **3h-3i**).This concretely proves that the nucleophilic part of the arene must be more electron-rich to attain the formation of carbazoles are formed in a more convenient approach. As a result, it was attempted to make the adjacent arene ring of the anilide more electron-rich by using triethyl substituted arenes. The reaction did not work

proficiently, which lead to the formation of unidentified products which were mostly inseparable. If an electron-withdrawing group is present at the *para* position of the anilide moiety, carbazole formation took place Figure 3.1, (**3j-3l**). When the protecting group was varied, the obtained products were formed in good yield to excellent yields (Figure 3.1, **3m-3r**).

The methodology involving PhI-*m*CPBA for *in-situ* generation of iodine(III) led to carbazole synthesis in relatively lesser yield than the stoichiometric version of PIDA as an oxidant. (Figure 3.2). Literature reports based on the generation of nitrenium helped to understand the mechanistic pathway as described in Figure 3.3. The reaction proceeded *via* iodine(III) reagent, which generated the nitrenium ion intermediate **3** in both cases of the stoichiometric amount of iodine(III) reagent or by an in-situ generation of iodine(III) by using PhI and *m*CPBA**.** This lead to nucleophilic attack from the adjacent arene to produce the carbocation **4** followed by migration of alkyl group in successive steps and deprotonation gave rise to the formation of the desired aromatized carbazole **5**. The role of solvent TFE is vital in determining the yield of the reaction. The reaction was sluggish when DCM was solely used as a solvent. It is observed that the intermediate nitrenium ion formed is stabilized in polar non-nucleophilic solvent TFE, which gave rise to the optimum result. TFE also possesses hydrogen bonding of fluoroalcohol with the iodine(III) reagent described by Compton and co-workers.[25] It was noticed that with an increase in the percentage of TFE in DCM, the yield of product **3a** also rose, and the maximum product was obtained when TFE was solely used as a solvent(Figure 3.4).

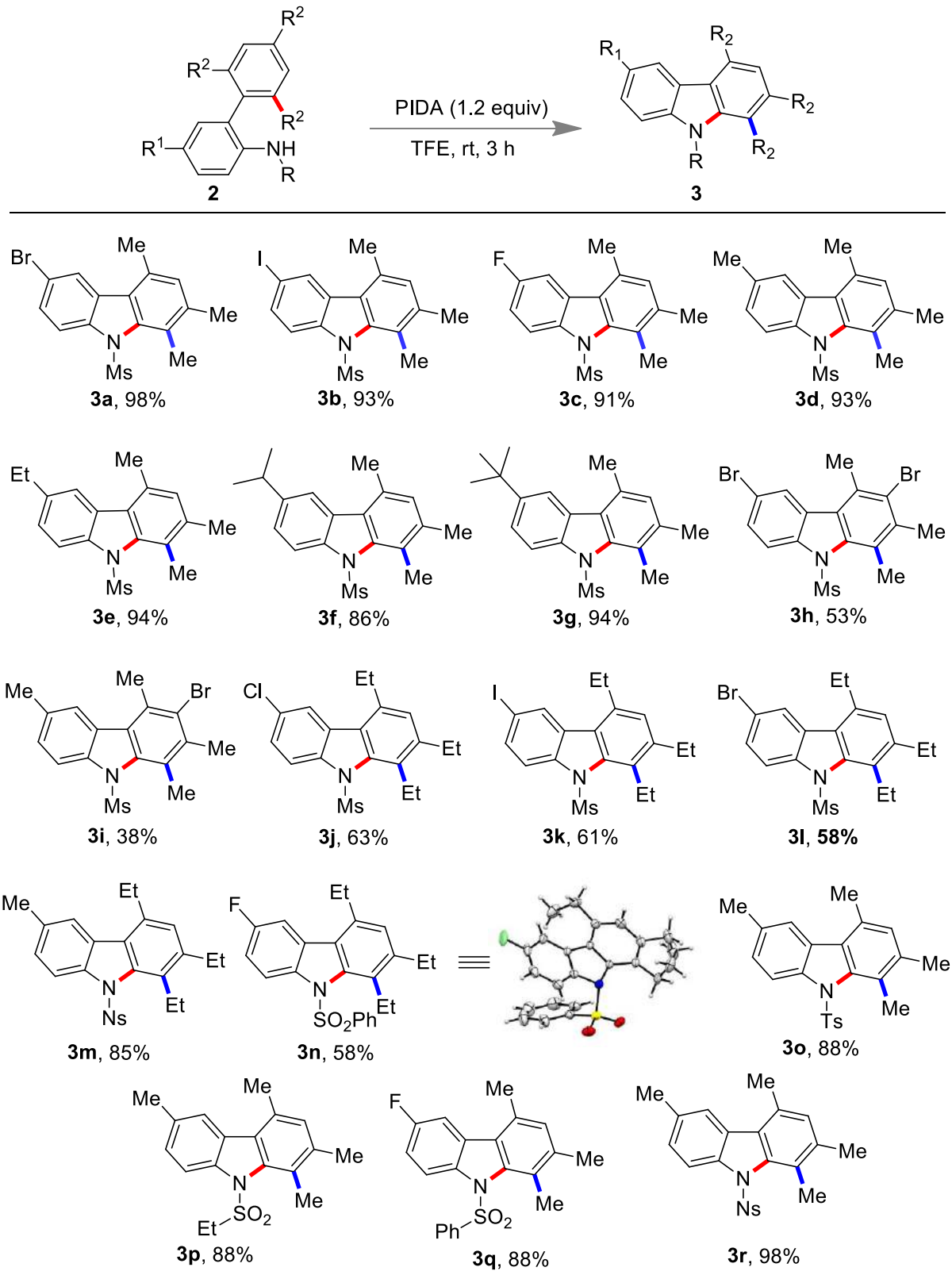
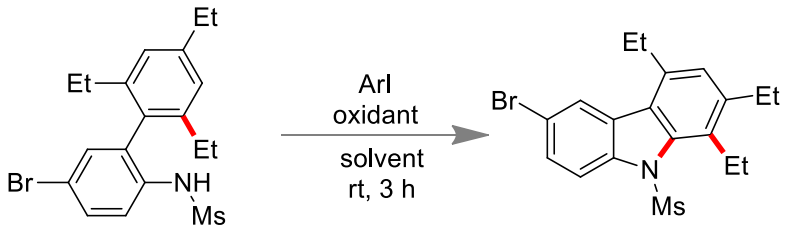


Figure 3.1. Substrate scope of biarylsufonamides using PIDA, Reaction conditions: 0.108 mmol of 2 and 1.2 equiv of PIDA in TFE (0.2 M)

Table 3.2 Optimization of Method B



2l **3l**

entry	ArI (equiv)	oxidant (1.5 equiv)	solvent	yield (%)
1	PhI (0.2)	*m*CPBA	TFE	48
2	PhI (0.2)	*m*CPBA	HFIP	32
3	PhI (0.2)	*m*CPBA	DCM	12
4	PhI (0.2)	*m*CPBA	TFE/DCM (2:1)	48
5	PhI (0.5)	*m*CPBA	TFE	76
6	PhI (1.0)	*m*CPBA	TFE	89
7	Cl-C_6H_4-I (1.0)	*m*CPBA	TFE	64
8	Me-C_6H_4-I (1.0)	*m*CPBA	TFE	67

Reaction conditions: All reactions done at room temperature. Yields of isolated product after column chromatography

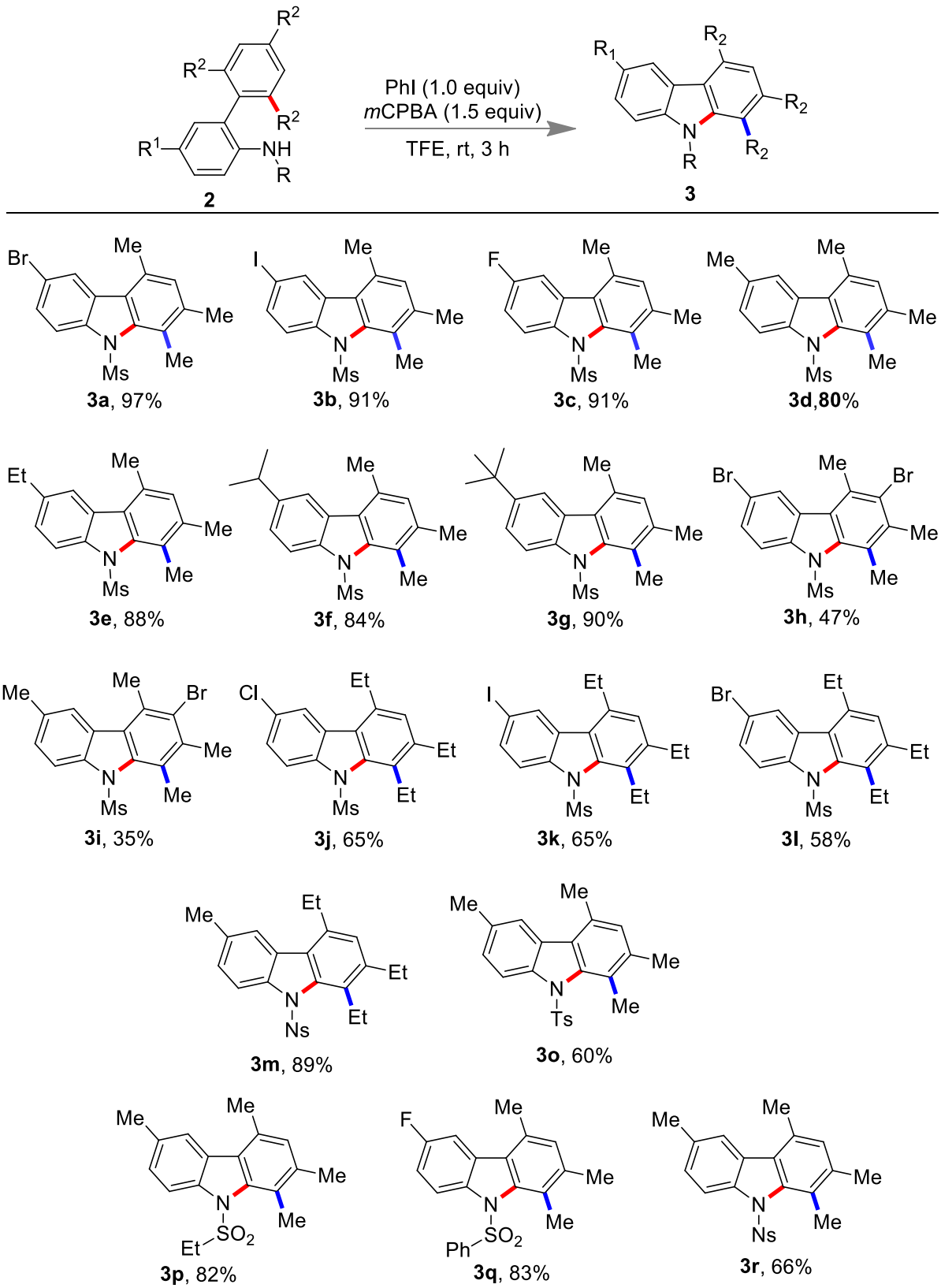


Figure 3.2 Substrate scope of biarylsufonamides using PhI-*m*CPBA, Reaction conditions: 0.108 mmol of 2 and 1.2 equiv of PIDA in TFE (0.2 M)

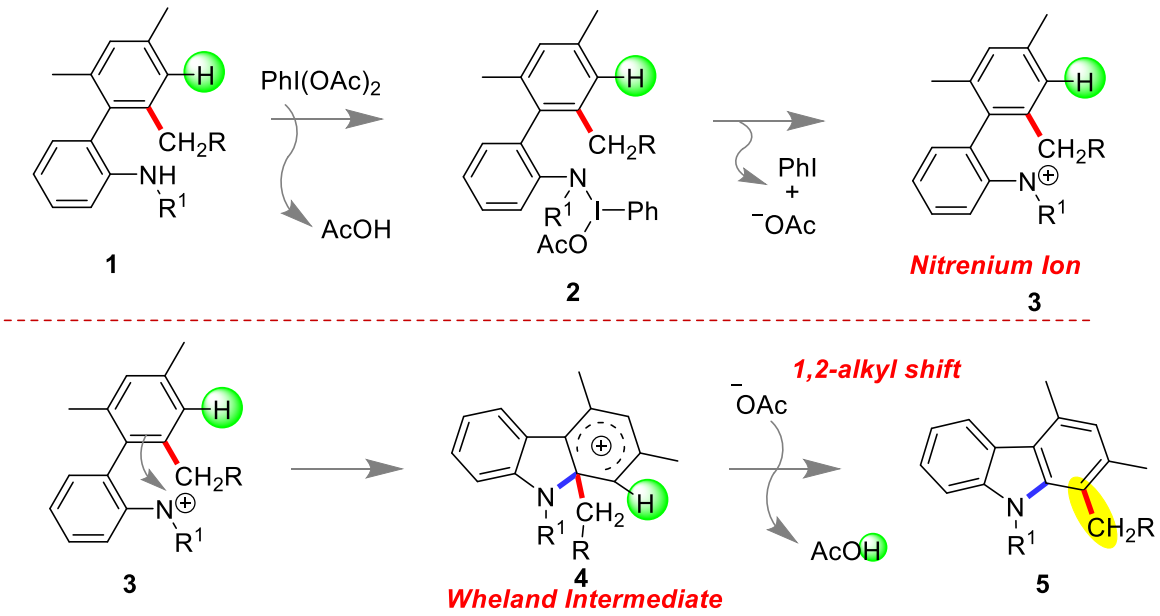


Figure 3.3 Proposed reaction mechanism

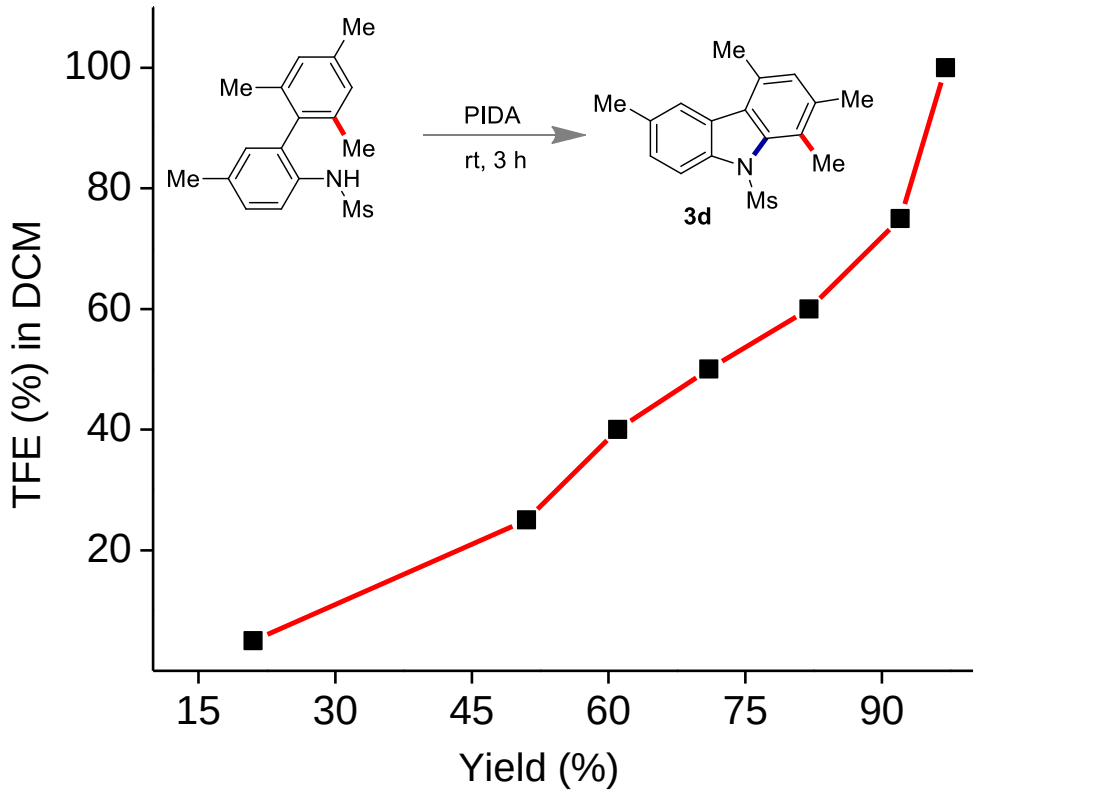
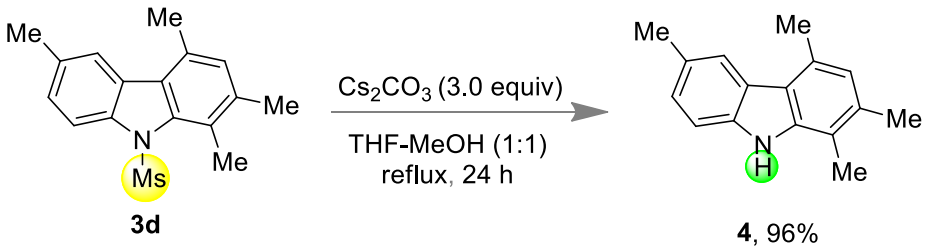


Figure 3.4 Monitoring the role of solvent TFE.



Scheme 3.9 Synthesis of NH carbazole, Reaction conditions: 0.108 mmol of 2 and 1.2 equiv of PIDA in TFE (0.2 M)

Post synthetic applications involve synthesis of 1,2,4,6-tetramethyl-9H-carbazole (**7**) was from **3d** using Cs_2CO_3 by following previous reports (Scheme 3.9).

3.7 CONCLUSIONS

In conclusion, hypervalent iodine mediated nitrenium ion chemistry was utilized for the synthesis of carbazoles. Distal C-H functionalization was successfully achieved along with the migration of the alkyl group. This efficient method for C-H amination yielded carbazoles with excellent yields. The reaction was facile at ambient temperature and in open atmosphere conditions which made the protocol significant. We hope that this intramolecular oxidative C-N amination strategy will have a significant impact on synthesizing complex structural motifs.

3.8 EXPERIMENTAL SECTION

General Methods. Chromatographic (Column) purifications of the compounds were done using silica gel (mesh 230–400) and hexane – ethyl acetate mixtures as eluent unless otherwise specified. NMR spectra were taken on a 400 MHz or 700 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 ppm for ^{13}C). The peak patterns are designated as follows: s: singlet; d: doublet; t: triplet; q: quartet; m: multiplet; dd: doublet of doublets; td: triplet of doublets; brs: broad singlet. The coupling constants (*J*) are reported in

hertz (Hz). High-resolution mass spectra (HR-MS) had been recorded on an ESI-TOF (time of flight) mass spectrometer. Infrared (IR) spectral data are reported in wave number (cm^{-1}). FT-IR spectra were recorded after making thin layer of the compounds on the surface of NaCl crystal using dichloromethane. A digital melting point apparatus was used to determine the melting points (mp) of the compounds. Good quality crystals of the compounds **3n** were obtained after slow evaporation of ethyl acetate solution. The crystals data were collected with Bruker SMART D8 goniometer equipped with an APEX CCD detector and with an INCOATEC micro source (Mo-Kα radiation, λ = 0.71073 Å). SAINT+[26]and SADABS[27] were used to integrate the intensities and to correct the absorption respectively. The structure was resolved by direct methods and refined on F^2 with SHELXL-97.[28]

Representative method for preparation of 6-bromo-1,2,4-trimethyl-9-(methylsufonyl)-carbazole (3a)

Method A. To *N*-5(bromo-2,4.6-trimethyl-[1,1-biphenyl]-2yl)methaneulfonamide (40 mg, 0.108 mmol) in TFE, the hypervalent reagent PIDA (51 mg, 0.325mmol) dissolved in TFE was added slowly to it. The reaction mixture was constantly stirred at room temperature for approximately 2 h. Complete consumption of starting material was observed in TLC. The reaction mixture was evaporated to dryness and the product 6-bromo-1,2,4-trimethyl-9(methylsulfonyl)-carbazole (**3a)** was purified by column chromatography to obtain white solid 38 mg (98%) at 2% hexane-ethyl acetate.

Method B. To *N*-(5-bromo-2,4.6-trimethyl-[1,1-biphenyl]-2yl)methaneulfonamide (40mg,0.108mmol) in TFE, PhI (0.108mmol, 13μL) and *m*CPBA (0.27mmol, 28mg) was added portionwise and it was found that complete conversion of substrate took place in 2 h to give the desired product. The reaction mixture was evaporated to dryness, and the product 6-

bromo-1,2,4-trimethyl-9(methylsulfonyl)-carbazole **(3a)**was obtained as white solid 37mg (97%) using 2% hexane-ethylacetate solvent mixture for silica gel column chromatography.

Representative method for preparation of *N*-(5-bromo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide. To a stirred solution of *N*-(4-bromophenyl)methanesulfonamide **1a**, (40 mg, 0.159 mmol) in TFE, mesitylene (67 µL, 0.479 mmol) was added. PIDA (51 mg, 0.159 mmol) dissolved in TFE was then added drop wise to the reaction vial. The reaction vial was shaken vigorously for 2 h. On complete consumption of substrate, the reaction mixture was evaporated to dryness. Column chromatography has been done to isolate the pure product*N*-(5-bromo-2',4',6'-trimethyl-[1.1'-biphenyl]-2-yl)methanesulfonamide (**2a**) as white solid in 67% yield using 5% ethylacetate-hexane.

Procedure for the synthesis of 4. 1,2,4,6-Tetramethyl-9-(methylsulfonyl)-9*H*-carbazole (**3d**) (40 mg, 0.132 mmol) was dissolved in EtOH and treated with aq NaOH (5M). The resulting solution has been shaken at 60°C up to completion (6 h). Solvent was evaporated under reduced pressure, diluted with dichloromethane (CH_2Cl_2) and neutralized with 1M aq HCl. The aqueous layer was dissolved with additional CH_2Cl_2 and the organic portion was dried over anhydrous Na_2SO_4 and was filtered. The filtrate was kept in vacuum and the compound was isolated using silica gel column chromatography (6% EtOAc in hexane) to get 1,2,4,6-tetramethyl-9*H*-carbazole (**6**) as white solid (28 mg, 0.125 mmol, yield 95%).

Compound Characterization Data

***N*-(5-Bromo-2',4',6'-trimethyl-[1.1'-biphenyl]-2-yl)methanesulfonamide (2a):** R_f = 0.4 (hexane:ethyl acetate: 9:1); white solid; 39 mg (67%); mp 173-175 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.8 Hz, 1H), 7.49 (dd, *J* = 8.8; 1.0Hz, 1H), 7.23 (d, *J* = 2.4 Hz, 1H),

6.98 (s, 2H), 5.99 (brs, 1H), 2.97 (s, 3H), 2.33 (s, 3H), 1.97 (s, 6H);^{13}C NMR (100 MHz, $CDCl_3$) δ 139.2, 136.7, 134.1, 133.3, 132.2, 131.8, 130.9, 129.4, 119.0, 117.2, 39.9, 21.3, 20.2; IR (KBr) ῡ = 3426, 2099, 1643, 1470, 1326, 1168 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{16}H_{18}BrNO_2S$ $[M + Na]^+$: 390.0134, found: 390.0144.

***N*-(5-Iodo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (2b):** R_f= 0.40 (hexane : ethyl acetate 9:1); white solid; 41 mg (77%); mp 176-178 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (dd, *J* = 8.8; 2.0 Hz, 1H), 7.46 (d, 8.8 Hz, 1H), 7.42 (d, *J* = 2.0 Hz, 1H), 6.97 (s, 2H), 5.99 (brs, 1H), 2.97 (s, 3H), 2.33 (s, 3H), 1.96 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.1, 139.2, 137.8, 136.7, 134.9, 132.3, 130.8, 129.4, 119.2, 87.7, 39.9, 21.3, 20.3; IR (KBr) ῡ = 3441, 2359, 2050, 1634, 536 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{16}H_{18}INO_2S$ $[M + Na]^+$: 437.9995, found: 437.9986.

***N*-(5-Fluoro-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (2c):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 37 mg (57%); mp 164-165 °C; ^{1}H NMR (700 MHz, DMSO) δ 8.51 (s, 1H), 7.41 (dd, *J* = 9.1, 5.6 Hz, 1H), 7.2-7.18 (m, 1H), 6.99-6.82 (m, 3H), 2.74 (s, 3H), 2.27 (s, 3H), 1.93 (s, 6H); ^{13}C NMR (100MHz, $CDCl_3$) δ 159.6 (d, $^1J_{C\text{-}F}$ = 243 Hz), 139.0, 136.5, 132.6 (d, $^3J_{C\text{-}F}$ = 8 Hz), 131.4, 130.9 (d, $^4J_{C,F}$= 3 Hz), 129.3, 119.8 (d, $^2J_{C,F}$ = 8 Hz), 117.3 (d, $^2J_{C,F}$ = 22 Hz), 115.5 (d, $^2J_{C,F}$ = 22 Hz), 38.7, 21.1, 20.1; IR (KBr) ῡ = 3431, 2359, 2089, 1867, 1180, 1155 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{16}H_{18}FNO_2S$ $[M + Na]^+$: 330.0934, found: 330.0947

***N*-(2',4',5,6'-Tetramethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (2d):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 11 mg (48%); mp 123-124 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.0 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 1H), 6.97 (s, 2H), 6.89 (s, 1H), 5.92

(s, 1H), 2.93 (s, 3H), 2.34 (s, 6H), 1.97 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 136.8, 134.1, 132.6, 132.2, 131.0, 130.4, 129.4, 129.2, 117.8, 39.7, 21.2, 20.8, 20.3; IR (KBr) ῡ = 3431, 2358, 2341, 2089, 1646 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{17}H_{21}NO_2S$ [M + Na]$^+$: 326.1185, found: 326.1203.

***N*-(5-Ethyl-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (2e):** R_f = 0.50 (hexane : ethylacetate 9:1); white solid; 35 mg (68%); mp 112-114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.4 Hz, 1H), 7.20 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.97 (s, 2H), 6.91 (d, *J*= 2 Hz, 1H), 5.92 (s, 1H), 2.96 (s, 3H), 2.64 (q, *J* = 7.6 Hz, 2H), 2.33 (s, 3H), 1.96 (s, 6H), 1.24 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.6, 138.4, 136.7, 132.7, 132.4, 130.3, 129.8, 129.1, 128.2, 117.7, 39.8, 28.2, 21.2, 20.3, 15.7; IR (KBr) ῡ = 3430, 2925, 2089, 1646, 1171 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{18}H_{23}NO_2S$ [M + Na]$^+$: 340.1342, found: 340.1358.

***N*-(5-Isopropyl-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (2f):** R_f= 0.50 (hexane : ethyl acetate 9:1); white solid; 30mg (59%); mp 143-145 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.8 Hz, 1H), 7.22 (dd, *J* = 8.4; 2 Hz, 1H), 6.98 (s, 2H), 6.94 (d, *J* = 2 Hz, 1H), 5.93 (s, 1H), 2.94 (s, 3H), 2.91-2.87 (m,1H), 2.34 (s, 3H), 1.96 (s, 6H), 1.3 (s,3H), 1.3 (s,3H); ^{13}C NMR (100 MHz, $CDCl_3$)δ 145.3, 138.4, 136.8, 132.9, 132.4, 130.3, 129.1, 128.6, 126.7, 117.7, 39.9, 33.5, 24.1, 21.1, 20.3; IR (KBr) ῡ = 3427, 2089, 1868, 1644, 1160 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{19}H_{25}NO_2S$ [M + Na]$^+$: 354.1498, found: 354.1518.

***N*-(5-(*tert*-Butyl)-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (2g):** R_f= 0.50 (hexane : ethyl acetate 9:1); white solid; 28mg (53%); mp 174-175 °C; ^{1}H NMR (400

MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.4 Hz, 1H), 7.37 (dd, *J* = 8.8; 2 Hz, 1H), 7.09 (d, *J* = 2 Hz, 1H), 6.98 (s, 2H), 5.93 (s, 1H), 2.95 (s, 3H), 2.34 (s, 3H), 1.96 (s, 6H), 1.30 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 138.5, 136.8, 133.0, 132.1, 129.7, 129.1, 127.7, 125.4, 117.2, 39.8, 34.5, 31.4, 21.1, 20.3; IR (KBr)ῡ = 3259, 2965, 1614, 1336, 1503, 1272 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{20}H_{27}NO_2S$ $[M + Na]^+$: 368.1655, found: 368.1633.

***N*-(3',5-Dibromo-2',4',6'-trimethyl-[1.1'-biphenyl]-2-yl]methanesulfonamide (2h):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid;47 mg (59%); mp 166-167 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.4 Hz, 1H), 7.51 (d, *J* = 8.8 Hz, 1H), 7.20 (s, 1H), 7.08 (s, 1H), 5.92 (s, 1H), 2.98 (s, 3H), 2.45 (s, 3H), 2.11 (s, 3H), 1.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.8, 136.8, 135.5, 134.0, 133.2, 132.8, 132.2, 132.1, 130.8, 126.5, 119.2, 117.3, 40.2, 24.2, 21.7, 20.1; IR (KBr) ῡ = 3428, 2089, 1646, 1539, 1339 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{16}H_{17}Br_2NO_2S$ $[M + Na]^+$: 467.9239, found: 467.9217.

***N*-(3'-Bromo-2',4',5,6'-tetramethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (2i):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 41 mg (49%) ; mp 165-167 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.4 Hz, 1H), 7.39-7.37 (m, 1H), 7.26 (s, 1H), 7.04 (s, 1H), 6.09 (s, 1H), 3.11 (s, 3H), 2.62 (s, 3H), 2.53 (s, 3H), 2.29 (s, 3H), 2.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 136.8, 135.7, 134.5, 134.4, 132.1, 131.0, 130.6, 130.3, 129.8, 126.4, 118.0, 39.9, 24.1, 21.7, 20.9, 20.2; IR (KBr) ῡ = 3398, 2089, 1646, 1456, 1160 cm^{-1}; HR-MS(ESI-TOF): m/z calculated for $C_{17}H_{20}BrNO_2S$ $[M + Na]^+$: 404.0290, found: 404.0281.

***N*-(5-Chloro-2',4',6'-triethyl-[1, 1-biphenyl-2-yl)methanesulfonamide (2j):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 40 mg (56%); mp 153-157 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.8 Hz, 1H), 7.36 (dd, *J* = 6.4; 2.4 Hz, 1H), 7.13 (d, *J* = 2.4 Hz, 1H),

7.04 (s, 2H), 6.01 (s, 1H), 2.98 (s, 3H), 2.68 (q, *J* = 7.6 Hz, 2H), 2.37 – 2.11 (m, 4H), 1.30 (t, *J* = 7.6 Hz, 3H), 1.06 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 142.7, 134.1, 131.1, 130.9, 129.9, 129.1, 128.9, 126.5, 117.8, 40.0, 28.8, 26.7, 15.4; IR (KBr) ῡ = 3420, 2962, 1868, 1647, 1159 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{19}H_{24}ClNO_2S$ [M + H]$^+$: 366.1289, found: 366.1297.

***N*-(2',4',6'-Triethyl-5-iodo-[1,1'-biphenyl]-2-yl)methanesulfonamide (2k):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 36 mg (58%); mp 157-159 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.8Hz, 1H), 7.47 (s, 1H), 7.45 (s, 1H), 7.03 (s, 2H), 6.02 (s, 1H), 2.99 (s, 3H), 2.67 (q, *J* = 7.6 Hz, 2H), 2.31-2.16 (m, 4H), 1.30 (t, *J* = 7.6 Hz, 3H), 1.05 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.7, 142.7, 139.8, 137.6, 135.3, 131.4, 129.8, 126.5, 118.3, 87.0, 40.0, 28.8, 26.6, 15.4; IR (KBr) ῡ = 3407, 2948, 1434, 1026 cm^{-1}; HR-MS(ESI-TOF): m/z calculated for $C_{19}H_{24}INO_2S$ [M + Na]$^+$: 480.0465, found: 480.0448.

***N*-(5-Bromo-2',4',6'-triethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (2l):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 40 mg (61%); mp 155-158 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.8Hz, 1H), 7.50 (d, *J* = 8.8 Hz, 1H), 7.27 (s, 1H), 7.03 (s, 2H), 6.01 (s, 1H), 2.98 (s, 3H), 2.67 (q, *J* = 7.6 Hz, 2H), 2.33-2.14 (m, 4H), 1.30 (t, *J* = 7.6 Hz, 3H), 1.05 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 142.8, 134.7, 133.9, 131.8, 131.3, 129.9, 126.5, 118.2, 116.6, 40.2, 28.9, 26.7, 15.3; IR (KBr) ῡ = 3427, 2099, 1646, 1470, 1168 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{19}H_{24}BrNO_2S$ [M + Na]$^+$: 432.0603, found: 432.0574.

4-Nitro-*N*-(2',4',6'-triethyl-5-methyl-[1, 1'-biphenyl]-2-yl)benzenesulfonamide (2m): R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 35 mg (54%); mp 149-152 ℃; ^{1}H NMR (400

MHz, $CDCl_3$) δ 8.34-8.22 (m, 2H), 7.96-7.88 (m, 2H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.13 (d, *J* = 8.4 Hz, 1H), 6.97 (s, 2H), 6.83 (s, 1H), 6.23 (s, 1H), 2.68 (q, *J* = 7.6 Hz, 2H), 2.28 (s, 3H), 1.88 (q, *J* = 7.6Hz, 4H), 1.33-1.29 (m, 3H), 0.92-0.88 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 145.5, 145.3, 142.7, 134.3, 131.6, 131.3, 131.0, 129.8, 129.3, 128.7, 126.1, 124.4, 117.5, 28.9, 26.3, 20.1, 15.5, 15.2; IR (KBr) ῡ = 3420, 2064, 1646, 1539, 1170 cm^{-1}; HR-MS(ESI-TOF): m/z calculated for $C_{25}H_{28}N_2O_4S$ $[M + Na]^+$: 475.1662, found: 475.1679.

***N*-(2',4',6'-Triethyl-5-fluoro-[1, 1'-biphenyl]-2-yl)benzenesulfonamide (2n):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 45 mg (65%); mp 154-156 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78-7.71 (m, 3H), 7.55 (d, *J* = 7.2 Hz, 1H), 7.45 (t, *J* = 7.2 Hz, 2H), 7.02 (t, *J* = 8.6 Hz, 1H), 6.97 (s, 2H), 6.73 (d, *J* = 8.4 Hz, 1H), 6.12 (s, 1H), 2.68 (q, *J* = 7.6 Hz, 2H), 1.92 – 1.83 (m, 4H), 1.31 (t, *J* = 7.6Hz, 3H), 0.91 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 159.0 (d, $^1J_{C,F}$ = 243 Hz), 145.6, 142.7, 139.5, 133.3, 131.5 (d,$^3J_{C,F}$ = 8 Hz), 131.0 (d, $^4J_{C,F}$ = 2.6 Hz), 130.2, 129.2, 127.3, 126.1, 119.1 (d, $^3J_{C,F}$ = 8 Hz), 117.6 (d, $^2J_{C,F}$ = 22.0 Hz), 115.2 (d, $^2J_{C,F}$ = 22.0 Hz), 28.9, 26.2, 15.4, 15.2.; IR (KBr) ῡ = 3426, 2341, 2089, 1843, 1643, 1456, 1338 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{24}H_{26}FNO_2S$ $[M + Na]^+$: 434.1560, found: 434.1585.

4-Methyl-*N*-(2',4',5,6'-tetramethyl-[1, 1'-biphenyl]-2-yl)benzenesulfonamide (2o): R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 34 mg (81%); mp 150-153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.59 (m, 3H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.09 (dd, *J* = 8.4; 2.0 Hz, 1H), 6.90 (s, 2H), 6.72 (d, *J* = 2 Hz, 1H), 6.09 (s, 1H), 2.37 (s, 3H), 2.33 (s, 3H), 2.26 (s, 3H), 1.64 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 142.9, 138.3, 137, 133.8, 132.5, 131.9, 130.7, 130.3, 129.8, 129.0, 128.9, 127.4, 118.3, 21.6, 21.1, 20.9, 19.9; IR (KBr) ῡ = 3419, 2084,

1652, 1392, 1165 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{23}H_{25}NO_2S$ $[M + Na]^+$: 402.1498, found: 402.1493.

***N*-(2',4',5 ,6'-Tetramethyl-[1, 1'-biphenyl]-2-yl)ethanesulfonamide (2p) :** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 37mg (96%); mp 120-121 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.0 Hz, 1H), 7.15 (d, *J* = 8.4 Hz, 1H), 6.97 (s, 2H), 6.87 (s, 1H), 5.86 (s, 1H), 3.07 (q, *J* = 6.8 Hz, 2H), 2.33 (s, 6H), 1.98 (s, 6H), 1.25 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 136.7, 133.8, 132.6, 132.4, 131.0, 130.0, 129.3, 129.1, 117.5, 46.4, 21.2, 20.8, 20.3, 8.2; IR (KBr) ῡ = 3427, 2359, 2089, 1644, 1540, cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{18}H_{23}NO_2S$ $[M + Na]^+$: 340.1342, found: 340.1335.

***N*-(5-Fluoro-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (2q):** R_f = 0.40 (hexane : ethyl acetate 9:1); white solid; 24 mg (51%); mp 165-167 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 9.2; 4.0 Hz, 1H), 7.72 – 7.67 (m, 2H), 7.56 – 7.52 (m, 1H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.04 – 6.99 (m, 1H), 6.90 (s, 2H), 6.68-6.65 (m, 1H), 6.11 (s, 1H), 2.33 (s, 3H), 1.61 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.56 (d, $^1J_{C,F}$ = 243 Hz), 139.5, 138.9, 136.7, 133.3, 132.7 (d, $^3J_{C,F}$ = 8.0 Hz), 131.3, 130.5 (d, $^4J_{C,F}$ = 3 Hz), 129.3, 129.1, 127.3, 120.3 (d, $^3J_{C,F}$ = 8.0 Hz), 117.0 (d, $^2J_{C,F}$ = 22.0 Hz), 115.2 (d, $^2J_{C,F}$ = 22.0 Hz); 21.2, 19.7.; IR (KBr) ῡ = 2077, 1645, 1504, 1386, 1168 cm^{-1}, HR-MS (ESI-TOF): m/z calculated for $C_{21}H_{20}FNO_2S$ $[M + Na]^+$: 392.1091, found: 392.1099.

4-Nitro-N-(2',4',5,6'-tetramethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (2r): R_f = 0.40 (hexane : ethyl acetate 9:1); yellow solid; 24 mg (50%); mp 193-195 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.8 Hz, 2H), 7.88 (d, *J* = 8.8 Hz, 2H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.13 (d, *J* = 7.2 Hz, 1H), 6.90 (s, 2H), 6.76 (s, 1H), 6.21 (s, 1H), 2.33 (s, 3H), 2.28 (s, 3H),

1.25 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 145.5, 138.7, 136.6, 135.2 132.2, 131.1, 130.8, 129.3, 129.1, 126.1, 128.7, 124.4, 118.8, 21.3, 20.9, 20.0; IR (KBr) ῡ = 3429, 2922, 2357, 1685, 1167 cm^{-1} ; HR-MS (ESI-TOF): m/z calculated for $C_{22}H_{22}N_2O_4S$ $[M + Na]^+$: 433.1192, found: 433.1177.

6-Bromo-1,2,4-trimethyl-9(methylsulfonyl)-carbazole (3a):[14] R_f = 0.6 (hexane:ethyl acetate 19:1);white solid; Method A: 38 mg (98%), Method B: 37 mg (97%); mp 82-84 ℃; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.53 (d, *J* = 8.4 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 (175 MHz, $CDCl_3$) δ 141.4, 141.0, 138.8, 132.9, 130.6, 130.2, 129.3, 127.6, 125.9, 125.2, 120.6, 119.6, 34.4, 20.4, 20.2 , 18.6.

6-Iodo-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (3b):[14] R_f= 0.6 (hexane:ethyl acetate 19:1); white solid; Method A: 37 mg (93%), Method B: 36 mg (91%) mp 113-116 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.82 (d , *J* = 8 Hz, 1H), 7.71 (d, *J* = 8 Hz, 1H), 7.07 (s, 1H), 2.69 (s, 3H), 2.52 (s, 3H), 2.38 (s, 3H), 2.23 (s, 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6, 141.19, 138.9, 135.2, 133.3, 131.2, 130.6, 130.1, 127.7, 125.7 , 121.0 , 90.6, 34.5, 20.4, 20.2 , 18.6.

6-Fluoro-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (3c):[14] R_f = 0.6 (hexane:ethyl acetate 19:1); white solid; Method A: 36 mg (91%), Method B: 36 mg (91%); mp 91-93 ℃; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.00 (q, *J* = 4.6 Hz, 1H), 7.63 (dd, *J* = 8.8, 2.4 Hz,1H), 7.12 (dt, *J* = 8.8, 2.4 Hz, 1H), 7.07 (s, 1H), 2.68 (s, 3H), 2.53 (s, 3H), 2.38 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 161.3 (d, $^1J_{C,F}$ = 242 Hz), 142.0, 138.7, 138.12, 132.5 (d, $^3J_{C,F}$

= 10.0 Hz), 130.5, 130.1, 127.9, 126.5 (d, $^{4}J_{C,F}$ = 3.0 Hz), 120.4 (d, $^{3}J_{C,F}$ = 10.0 Hz), 113.6 (d, $^{2}J_{C,F}$ = 24.0 Hz), 109.0 (d, $^{2}J_{C,F}$= 24.0 Hz), 34.0, 20.5, 19.9, 18.5.

1,2,4,6-Tetramethyl-9-(methylsulfonyl-)-carbazole (3d):[14] R_f = 0.6 (hexane : ethyl acetate 19:1); white solid; Method A: 37 mg (93%), Method B: 31 mg (80%); mp 73-75 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.4 Hz, 1H), 7.75 (s, 1H), 7.23 (dd, *J* = 7.0; 1.0 Hz, 1H), 7.05 (s, 1H), 2.71 (s, 3H), 2.53 (s, 3H), 2.50 (s, 3H), 2.37 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 141.4, 140.1, 137.7, 135.8, 131.3, 130.4, 129.8, 127.6, 127.6, 127.2, 122.8, 118.8, 33.8, 21.8, 20.4, 20.3, 18.6.

6-Ethyl-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (3e):[14] R_f = 0.6 (hexane : ethyl acetate 19:1); white solid; Method A: 37 mg (94%), Method B : 35 mg (88%); mp 102-104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8 Hz, 1H), 7.78 (s, 1H), 7.27 (s, 1H), 7.06 (s, 1H), 2.81 (q, *J* = 7.6 Hz, 2H), 2.73 (s, 3H), 2.54 (s, 3H), 2.38 (s, 3H), 2.18 (s, 3H), 1.34 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.4, 141.4, 140.3, 137.6, 131.3, 130.4, 129.8, 127.6, 127.2, 126.4, 121.6, 119 , 34.0, 29.2, 20.3, 20.4,18.6, 16.1.

6-Isopropyl-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (3f):[14] R_f = 0.6 (hexane : ethyl acetate 19:1); white solid; Method A: 34 mg (86%), Method B: 33 (84%); mp 73-76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.8 Hz, 1H), 7.78 (s, 1H), 7.29 (d, *J* = 8.4 Hz, 1H), 7.05 (s, 1H), 3.06 (septet, *J* = 6.8 Hz, 1H), 2.72 (s, 3H), 2.53 (s, 3H), 2.37 (s, 3H), 2.18 (s, 3H), 1.33 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 147.0, 141.4, 140.3, 137.6, 131.2, 130.3, 129.8, 127.6, 127.3, 125.0, 120.2, 119.0, 34.4, 34.0, 24.4, 20.3, 20.3, 18.6.

6-(Tert-butyl)-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (3g):[14] R_f = 0.6 (hexane : ethyl acetate 19:1); white solid; Method A: 37 mg (94%), Method B: 36 mg (91%); mp 132-134 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.96 (d, *J* = 2.4 Hz, 1H), 7.95 (d, *J* = 4.4 Hz, 1H), 7.46 (dd, d, *J* = 7.0; 1.4 Hz, 1H), 7.04 (s, 1H), 2.73 (s, 3H), 2.53 (s, 3H), 2.37 (s, 3H), 2.18 (s, 3H), 1.41 (s, 9H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 149.2, 141.4, 140.0, 137.6, 130.9, 130.4, 129.6, 127.6, 127.4, 124.2, 119.0 , 118.6 , 35.0, 34.0, 31.8, 20.4, 20.2, 18.6.

3,6-Dibromo-1,2,4-trimethyl-9-(methylsulfonyl)-9*H*-carbazole (3h):[14] R_f = 0.6 (hexane : ethyl acetate 19:1); white solid; Method A: 21 mg (53%), Method B: 19 mg (47%); mp 180-184 °C ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.15 (d, *J* = 2.0 Hz, 1H), 7.95 (d, *J* = 8.6 Hz, 1H), 7.57 (dd, *J* = 8.6; 2.0 Hz, 1H), 2.88 (s, 3H), 2.61 (s, 3H), 2.56 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 141.2, 140.4 , 138.6 , 132.3, 130.4 , 130.0, 129.2, 127.7, 126.7, 125.8, 120.6, 119.8, 34.4, 21.8, 21, 20.6.

3-Bromo-1,2,4,6-tetramethyl-9-(methylsulfonyl)-carbazole (3i): R_f = 0.6 (hexane :ethyl acetate 19:1); white solid; Method A: 15 mg (38%), Method B: 14 mg (35%); mp 100-104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (brs, 1H), 7.87 (brs, 1H), 7.26 (brs, 1H), 2.88 (s, 3H), 2.60 (s, 3H), 2.55 (s, 6H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.3, 140.3, 138.1, 135.8, 130.2, 129.8, 129.3, 127.5, 127.2, 124.2, 123.6, 122.9, 34.4, 23.7, 21.8, 21.0, 20.6; IR (KBr) ῡ = 3432, 2064, 1645, 1457,1173 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{17}H_{18}BrNO_2S$ $[M + Na]^+$: 402.0134, found: 402.0130.

6-Chloro-1,2,4-triethyl-9-(methylsulfonyl)-carbazole (3j): R_f = 0.6 (hexane : ethyl acetate 19:1); yellow liquid; Method A: 25 mg (63%), Method B: 26 mg (66%); ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.6 Hz, 1H), 7.89 (d, *J* = 2.0 Hz, 1H), 7.38 (dd, *J* = 8.6; 2.0 Hz,

1H), 7.14 (s, 1H), 3.28 (q, *J* = 7.6 Hz, 2H), 3.08 (q, *J* =7.6 Hz, 2H), 2.82 (q, *J* = 7.6 Hz, 2H), 2.20 (s, 3H), 1.41 (t, *J* = 7.6 Hz, 3H), 1.31 (t, *J* = 7.6 Hz, 3H), 1.14 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (175MHz, $CDCl_3$) δ 144.7, 141.6, 141.0, 136.9, 133.8, 132.4, 132.2, 128.2, 126.6, 125.8, 122.4, 120.8, 34.3, 26.6, 26.5, 23.1, 16.2, 15.0, 14.2; IR (KBr): ῡ = 3428, 1867, 1646, 1456, 1362 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{19}H_{22}ClNO_2S$ $[M + Na]^+$: 386.0952, found: 386.0942.

1,2,4-Triethyl-6-iodo-9-(methylsulfonyl)-carbazole (3k): R_f = 0.6 (hexane:ethyl acetate 19:1); yellow oil; Method A: 24 mg (61%), Method B: 26 mg (65%); ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.24 (d, *J* = 1.6 Hz, 1H), 7.82 (d, *J* = 8.4 Hz, 1H), 7.70 (dd, *J* = 8.6; 1.6 Hz, 1H), 7.13 (s, 1H), 3.27 (q, *J* = 7.6 Hz, 2H), 3.06 (q, *J* = 7.6 Hz, 2H), 2.81 (q, *J* = 7.6 Hz, 2H), 2.20 (s, 3H), 1.40 (t, *J* = 7.6 Hz, 3H), 1.31 (t, *J* = 7.6 Hz, 3H), 1.13 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 144.5, 142.0, 140.9, 136.6, 135.0, 133.4, 133.1, 131.2, 127.9, 125.4, 121.3, 90.8, 34.2, 26.4, 26.3, 23.0, 16.1, 14.8, 14.0; IR (KBr): ῡ = 3428, 2931, 2089, 1868, 1366,1361 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{19}H_{22}INO_2S$ $[M + Na]^+$: 478.0308, found: 478.0317.

6-Bromo-1,2,4-triethyl-9-methylsulfonyl)-carbazole (3l):[14] R_f = 0.6 (hexane : ethyl acetate 19:1); colourless liquid; Method A: 23 mg (58%); ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.93 (d, *J* = 8.6 Hz, 1H), 7.52 (dd, *J* = 8.6; 1.4 Hz, 1H), 7.13 (s, 1H), 3.27 (q, *J* = 7.6 Hz, 2H), 3.07 (q, *J* = 7.6 Hz, 2H), 2.81 (q, *J* = 7.6 Hz, 2H), 2.20 (s, 3H), 1.40 (t, *J* = 7.6 Hz, 3H), 1.31 (t, *J* = 7.6 Hz, 3H), 1.13 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5, 141.3, 141.2, 136.7, 133.6, 132.6, 129.2, 127.9, 125.6, 125.2, 121.0, 119.7, 34.2, 26.4, 26.3, 22.9, 16.1, 14.9, 14.0.

1,2,4-Triethyl-6-methyl-9-(4-nitrophenyl)-carbazole (3m): R_f = 0.6 (hexane : ethyl acetate 19:1); yellow solid; Method A: 33 mg (85%) , Method B: 35 mg (89%); mp 160-164 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 2H) 7.30 (s, 1H), 7.18 (d, *J* = 8.0 Hz, 1H), 7.02 (s, 1H), 6.98 (d, *J* = 8.0 Hz, 2H), 3.41 (q, *J* = 7.6 Hz, 2H), 2.88-2.75 (m, 4H), 2.39 (s, 3H), 1.35 (t, *J* = 7.6 Hz, 3H), 1.18 (t, *J* = 7.6 Hz, 3H), 1.06 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 150.1, 143.7, 141.2, 139.4, 138.9, 136.6, 136.6, 134.0, 131.7, 128.7, 128.5, 127.6, 127.3, 122.4, 122.5, 120.5, 26.5, 26.2, 22.9, 21.8, 16.4, 15.2, 14.3; IR (KBr) ῡ = 3426, 2089, 1868, 1644, 1456, 1174 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{25}H_{26}N_2O_4S$ $[M + Na]^+$: 473.1505, found: 473.1494.

1,2,4-Triethyl-6-fluoro-9-(phenylsulfonyl)-carbazole) (3n): R_f = 0.6 (hexane : ethyl acetate 19:1); white solid; Method B: 26 mg (65%); mp 149-151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 8.8; 2.4 Hz, 1H), 7.26 (t, *J* = 6.8 Hz, 1H) 7.17 (dd, *J* = 6.8; 2.4 Hz, 1H), 7.08-6.93 (m, 4H), 6.82(s, 1H), 6.80(s, 1H), 3.43 (q, *J* = 7.4 Hz, 2H), 2.83 (q, *J* = 7.4 Hz, 2H), 2.76 (q, *J* = 7.4 Hz, 2H), 1.34 (t, *J* = 7.4 Hz, 3H), 1.18 (t, *J* = 7.4 Hz, 3H), 1.06 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3 (d, $^1J_{C,F}$ = 236 Hz), 144.1, 142.4, 138.4, 136.5, 134.1, 133.2 (d,$^3J_{C,F}$ = 9.0 Hz), 133.16 (×2), 128.2, 127.6, 127.4, 127.2 (d, $^4J_{C,F}$ = 3.1 Hz), 121.2 (d,$^3J_{C,F}$ = 9.0 Hz), 112.9 (d, $^2J_{C,F}$ = 25.0 Hz), 108.3 (d, $^2J_{C,F}$ = 25.0 Hz), 26.3, 26.2, 22.9, 16.3, 15.1, 14.3; IR (KBr) ῡ = 3418, 2965, 2089, 1867, 1645, cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{24}H_{24}FNO_2S$ $[M + Na]^+$: 432.1404 found: 432.1419.

1,2,4,6-Tetramethyl-9-tosyl-carbazole (3o):[14] R_f = 0.6 (hexane:ethyl acetate 19:1); white solid; Method A: 35 mg (88%), Method B: 24 mg (60%); mp 98-100 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.7 Hz, 1H), 7.40 (s, 1H), 7.13 (d, *J* = 8.4 Hz, 1H), 6.96 (s, 1H), 6.85 (d, *J* = 8.4 Hz, 2H), 6.79 (d, *J* = 8.4 Hz, 2H), 2.65 (s, 3H), 2.49 (s, 3H), 2.39 (s,3H),

2.38(s, 3H), 2.18 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 143.8, 141.9, 139.9, 137.2, 135.2, 131.9, 131.8, 130.0, 129.3, 128.4, 127.9, 127.6, 127.4, 126.9, 122.2, 119.6, 21.8, 21.5, 20.5, 20.0, 18.6.

9-(Ethylsulfonyl)-1,2,4,6-tetramethyl-carbazole (3p): R_f = 0.6 (hexane:ethyl acetate 19:1); white solid; Method A: 35 mg (88%) , Method B: 32 mg (82%); mp 124-126 ºC; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.4 Hz, 1H), 7.75 (s, 1H), 7.22 (dd, *J* = 7.7; 1.0 Hz, 1H), 7.03 (s, 1H), 2.71 (s, 3H), 2.55 (s, 3H), 2.50 (s, 3H), 2.41 (q, *J* = 7.4 Hz, *2*H), 2.37 (s, 3H), 0.92 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 141.8, 139.8, 137.6, 135.4, 131.0, 130.1, 129.8, 127.5, 127.1, 126.9, 122.7, 118.5, 42.8, 21.8, 20.4, 20.3, 18.7, 7.4; IR (KBr) ῦ = 3445, 2348, 1653, 1456, 1359 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{18}H_{21}NO_2S$ [M + Na]$^+$: 338.1185, found: 338.1197.

6-Fluoro-1,2,4-trimethyl-9-(phenylsulfonyl)-carbazole (3q):[14] R_f = 0.6 (hexane : ethyl acetate 19:1); white solid; Method A: 35 mg (88%), Method B: 33 mg (83%); mp 159-161 °C ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 5.1; 2.8 Hz 1H), 7.28 (t, *J* = 7.7 Hz, 1H), 7.24 (dd, *J* = 9.1; 2.8 Hz, 1H), 7.04-7.01 (m, 2H), 7.00 (d, *J* = 5.0 Hz, 2H), 6.94 (d, *J* = 4.4 Hz, 2H), 2.67 (s, 3H), 2.44 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 161.0 (d, $^1J_{C,F}$ = 241 Hz), 142.5, 138.3, 137.8 (d, $^4J_{C,F}$ = 2.0 Hz), 134.0, 133.3, 133.1 (d, $^3J_{C,F}$ = 9.0 Hz), 130.3, 129.7, 128.0, 127.8, 127.3 (d, $^4J_{C,F}$ = 3.2 Hz), 127.2, 121.1 (d, $^3J_{C,F}$ = 9.0 Hz), 112.94 (d, $^2J_{C,F}$ = 25.0 Hz), 108.38 (d, $^2J_{C,F}$= 25.0 Hz), 20.5, 19.6, 18.5.

1,2,4,6-Tetramethyl-9-(4-nitrophenyl)sulfonyl)-carbazole (3r): R_f = 0.6 (hexane : ethyl acetate 19:1); yellow solid; mp 161-163 °C; Method A: 36 mg (98%) , Method B 26 mg (66%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.4 Hz, 1H), 7.83 (d, *J* = 8.8 Hz, 2H), 7.38

(s, 1H), 7.17 (d, *J* = 8.4 Hz, 1H), 7.11 (d, *J* = 8.8 Hz, 2H), 7.01 (s, 1H), 2.65 (s, 3H), 2.47 (s, 3H), 2.42 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.2, 141.2, 139.7, 139.0, 137.8, 136.3, 131.7, 130.8, 129.9, 128.6, 127.8, 127.7, 127.3, 122.8, 122.5, 119.7, 21.7, 20.4, 19.9, 18.4; IR (KBr) ῡ = 3442, 2390, 2348, 1635, 672, 524 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{22}H_{20}N_2O_4S[M + Na]^+$: 431.1036. found: 431.1045.

1,2,4,6-Tetramethyl-9*H*-carbazole (4): R_f = 0.7 (hexane : ethyl acetate 4:1); white solid; 28 mg (95%); mp 105-108 ºC; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.85 (s, 1H), 7.35 (d, *J* = 7.7 Hz, 1H), 7.23 (d, *J* = 8.4 Hz, 1H), 2.99 (s, 3H), 2.59 (s, 3H), 2.54 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 140.2, 139.1, 137.3, 130.5, 129.0, 128.9, 128.5, 124.7, 123.2, 121.3, 116.5, 115.9, 26.7, 20.4, 20.3, 17.8; IR (KBr) ῡ = 3441, 2395, 1632, 512 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{16}H_{17}N[M\ ]^+$: 223.1356. found: 223.1352.

3.9 NOTES AND REFERNCES

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NMR SPECTRA OF SELECTED COMPOUNDS

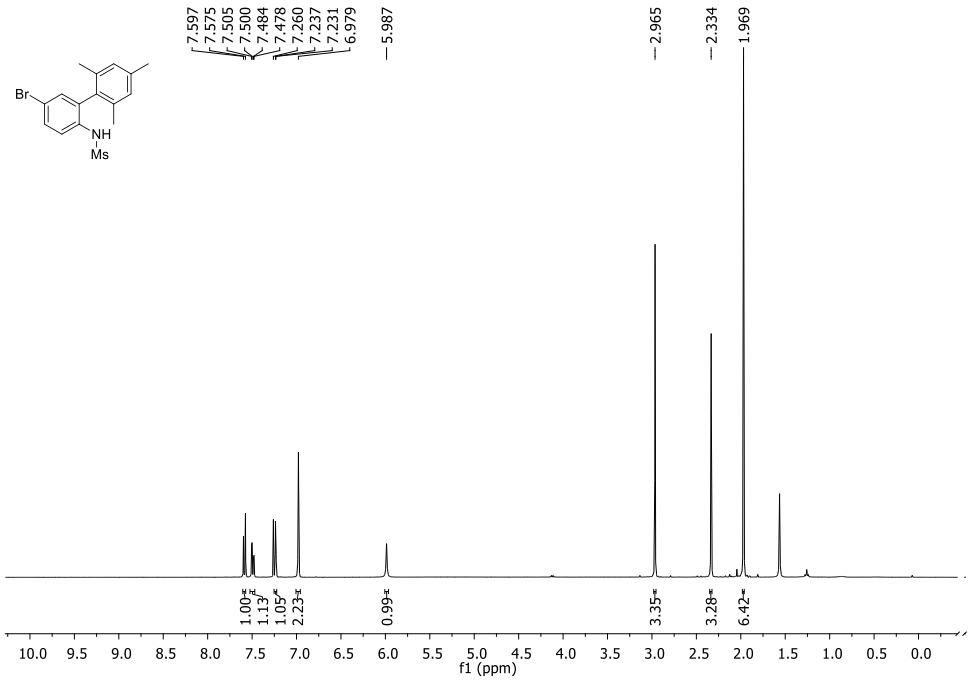


Figure 3.5 ^{1}H NMR spectrum of *N*-(5-Bromo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2a**)

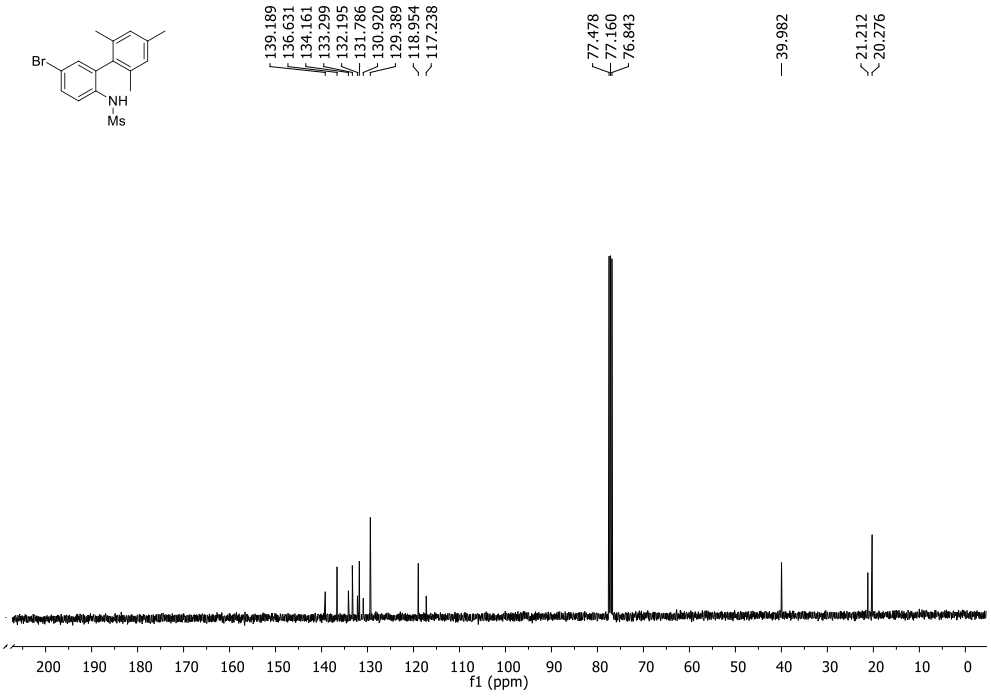


Figure 3.6 ^{13}C NMR spectrum of *N*-(5-Bromo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2a**)

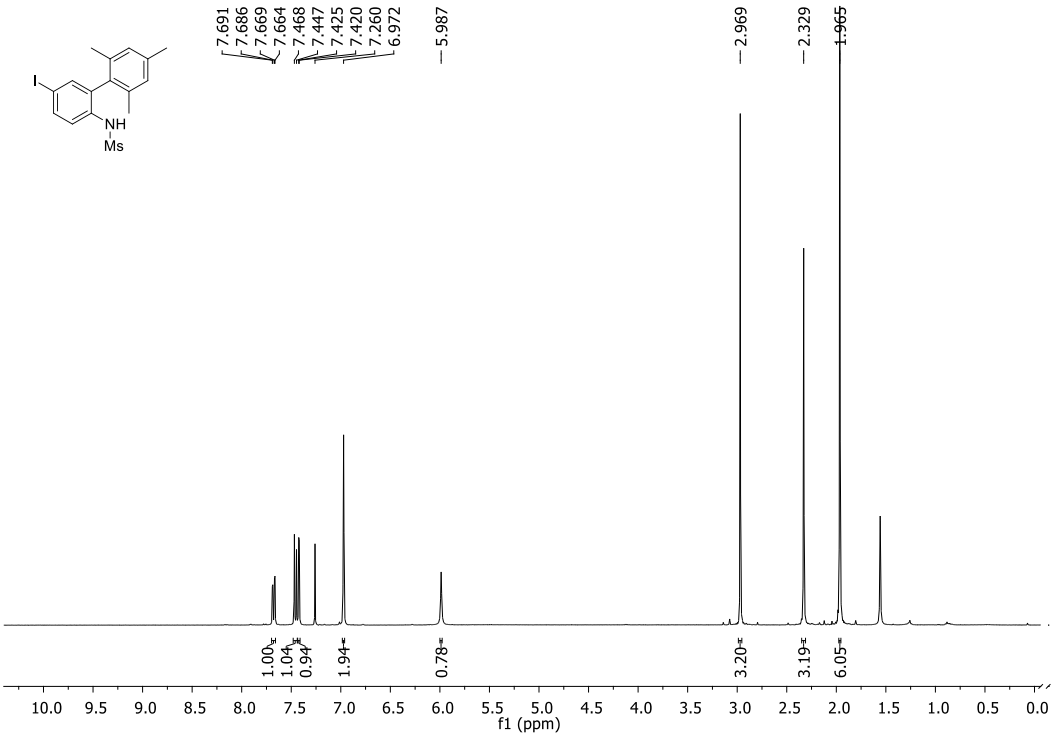


Figure 3.7 ^{1}H NMR spectrum of *N*-(5-Iodo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2b**)

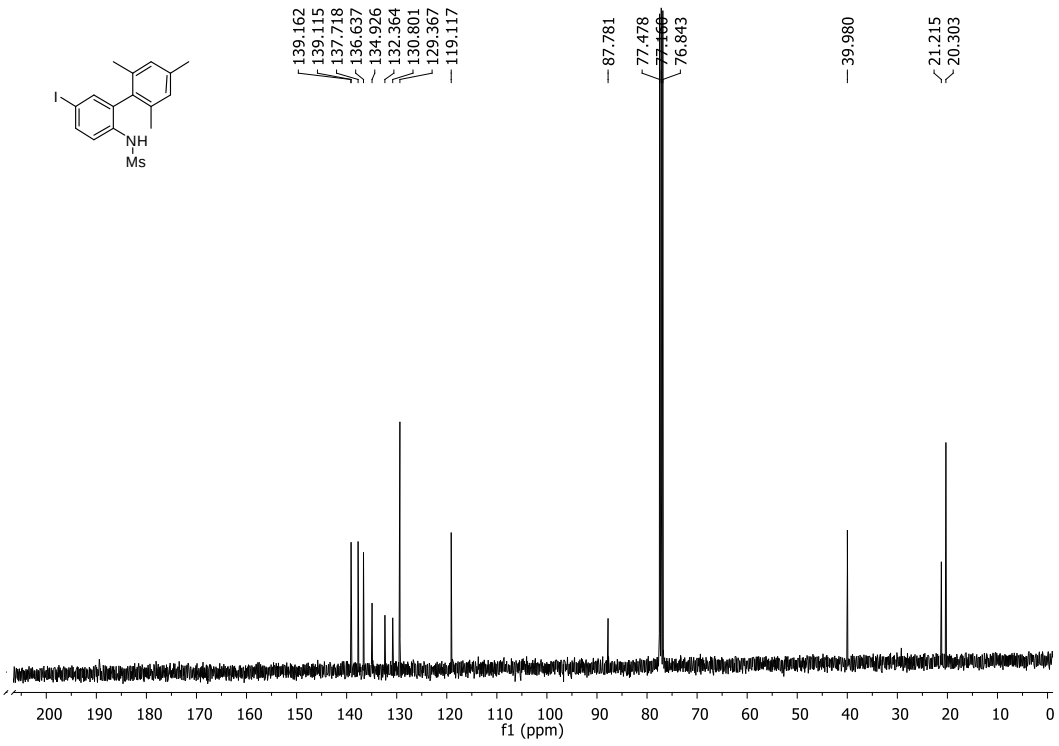


Figure 3.8 ^{13}C NMR spectrum of *N*-(5-Iodo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2b)**

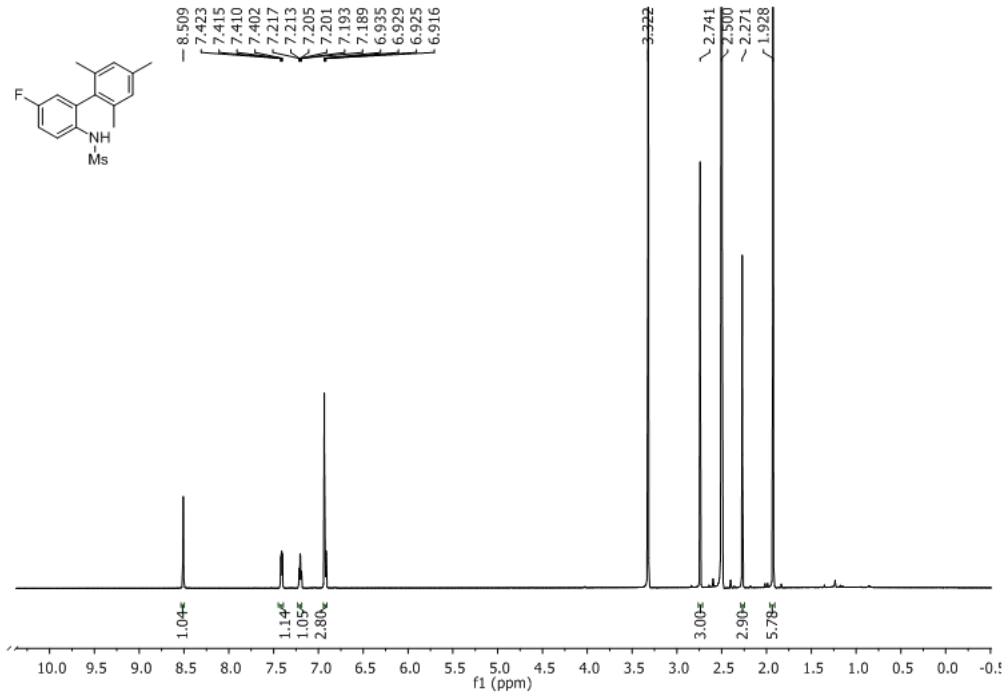


Figure 3.9 ^{1}H NMR spectrum of *N*-(5-Fluoro-2' ,4' ,6'-trimethyl-[1, 1'-biphenyl]-2-yl)methanesulfonamide **(2c)**

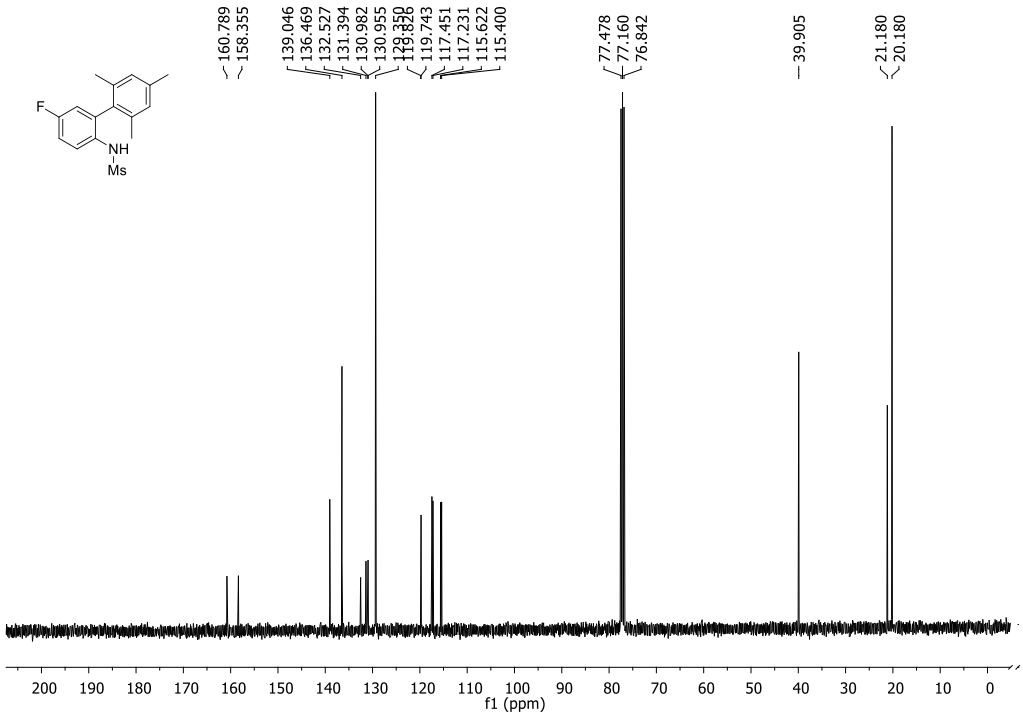


Figure 3.10 ^{13}C NMR spectrum of *N*-(5-Fluoro-2' ,4' ,6'-trimethyl-[1, 1'-biphenyl]-2-yl)methanesulfonamide **(2c)**

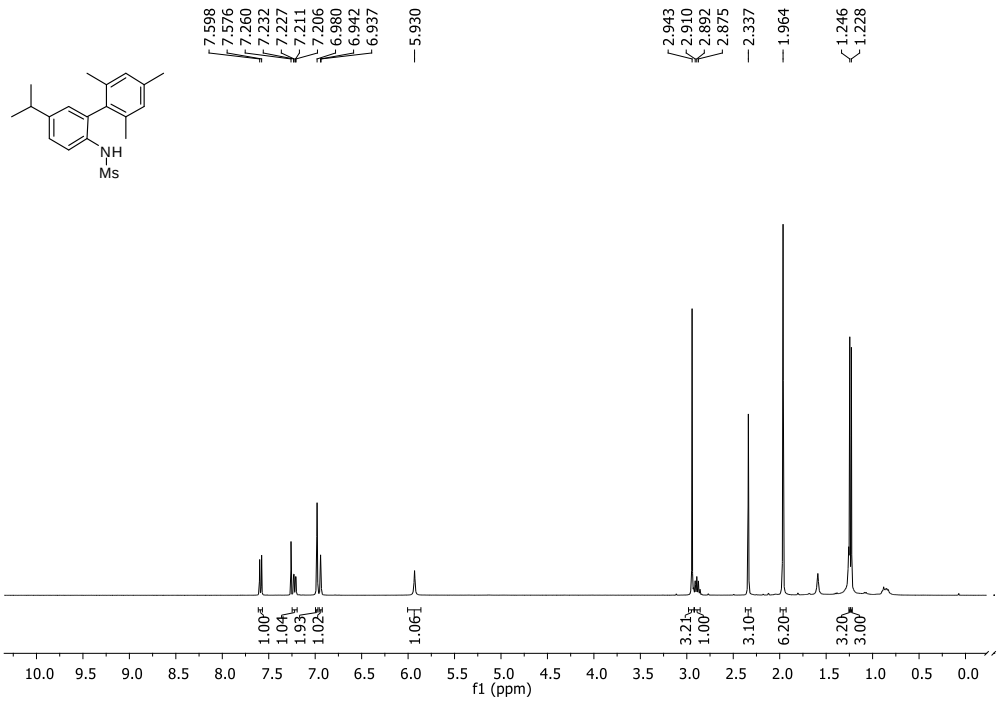


Figure 3.11 [1]H NMR spectrum of *N*-(5-Isopropyl-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2f**)

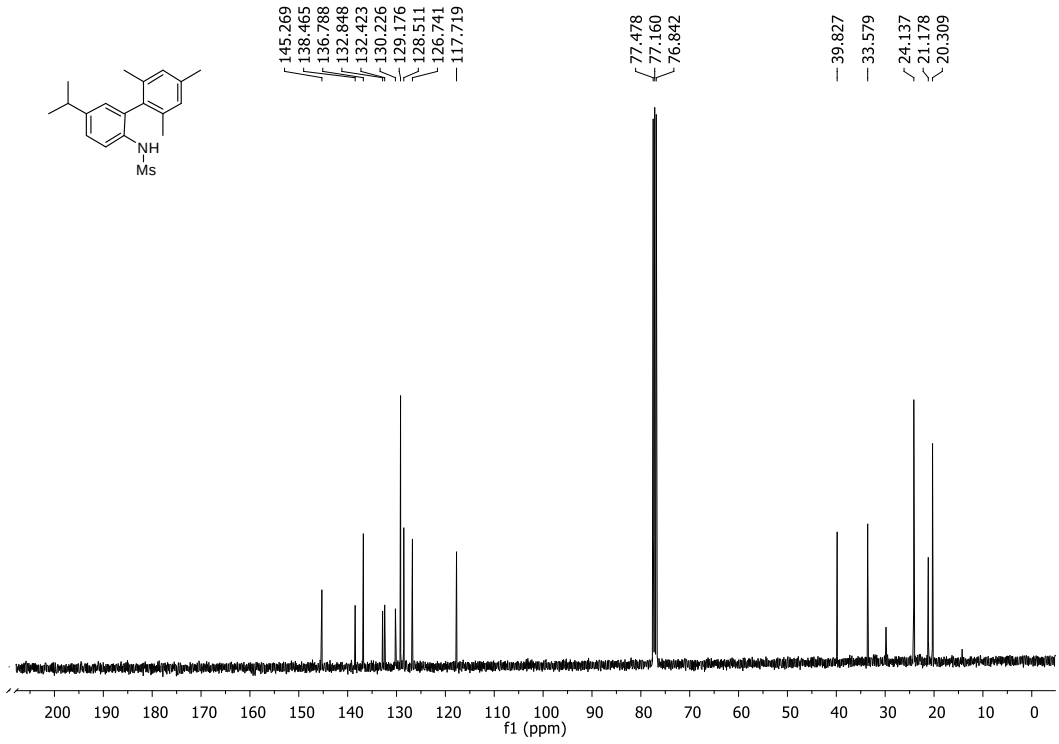


Figure 3.12 [13]CNMR spectrum of *N*-(5-Isopropyl-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2f**)

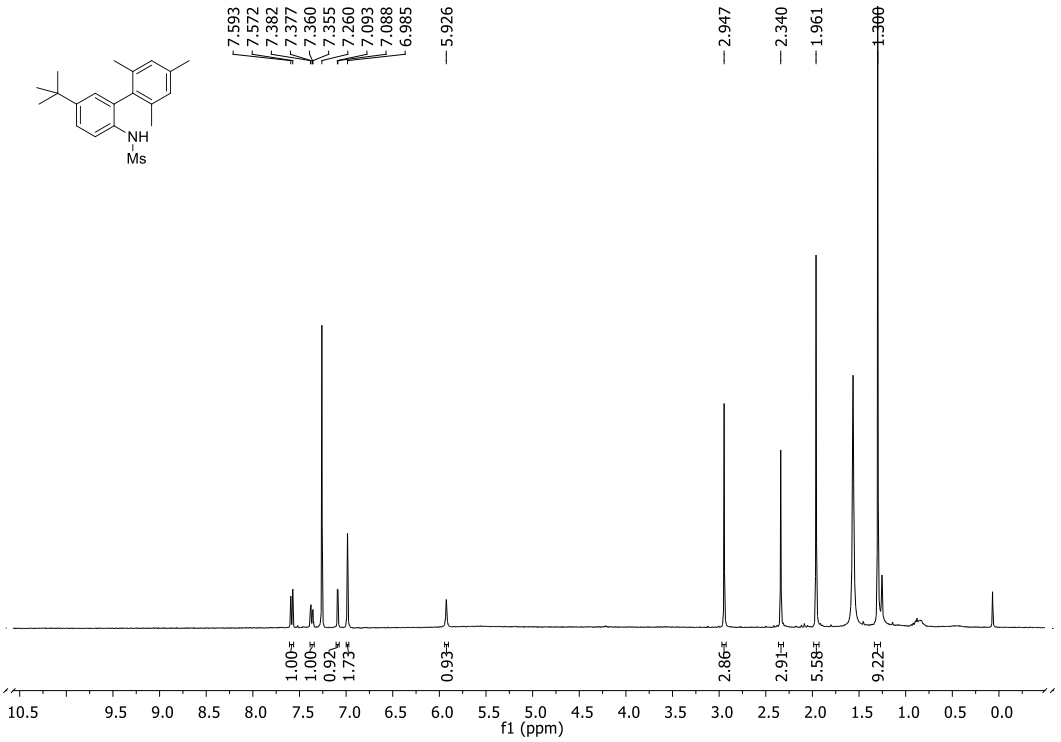


Figure 3.13 ^{1}H NMR spectrum of *N*-(5-(*tert*-Butyl)-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2g**)

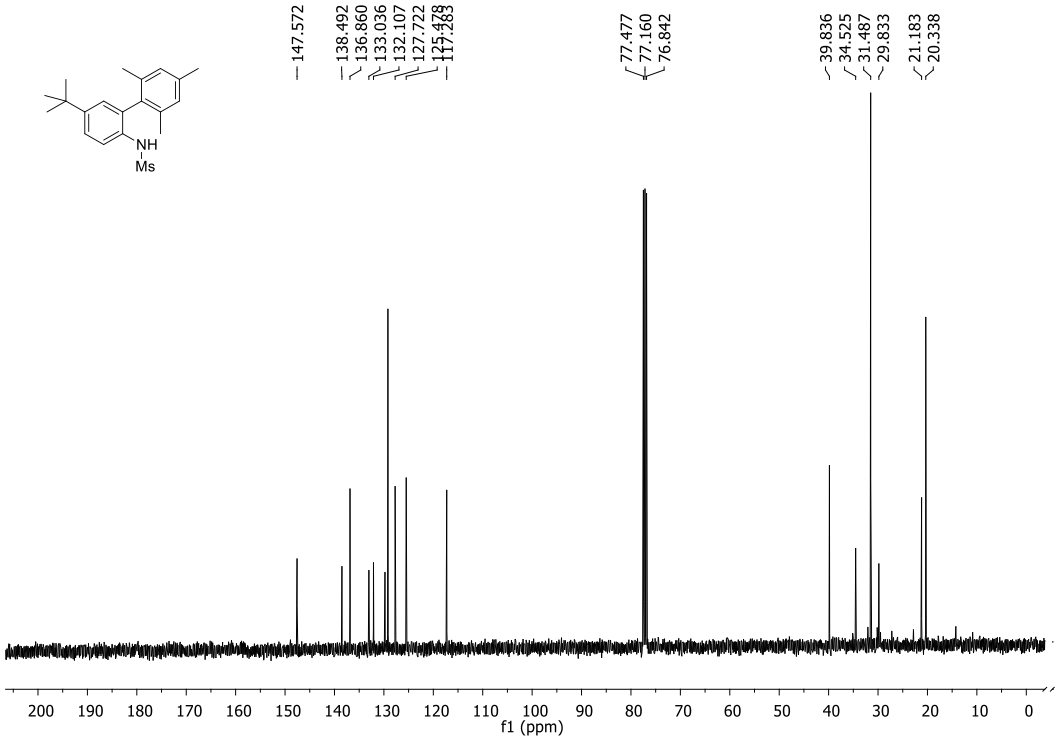


Figure 3.14 ^{13}C NMR spectrum of *N*-(5-(*tert*-Butyl)-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2g**)

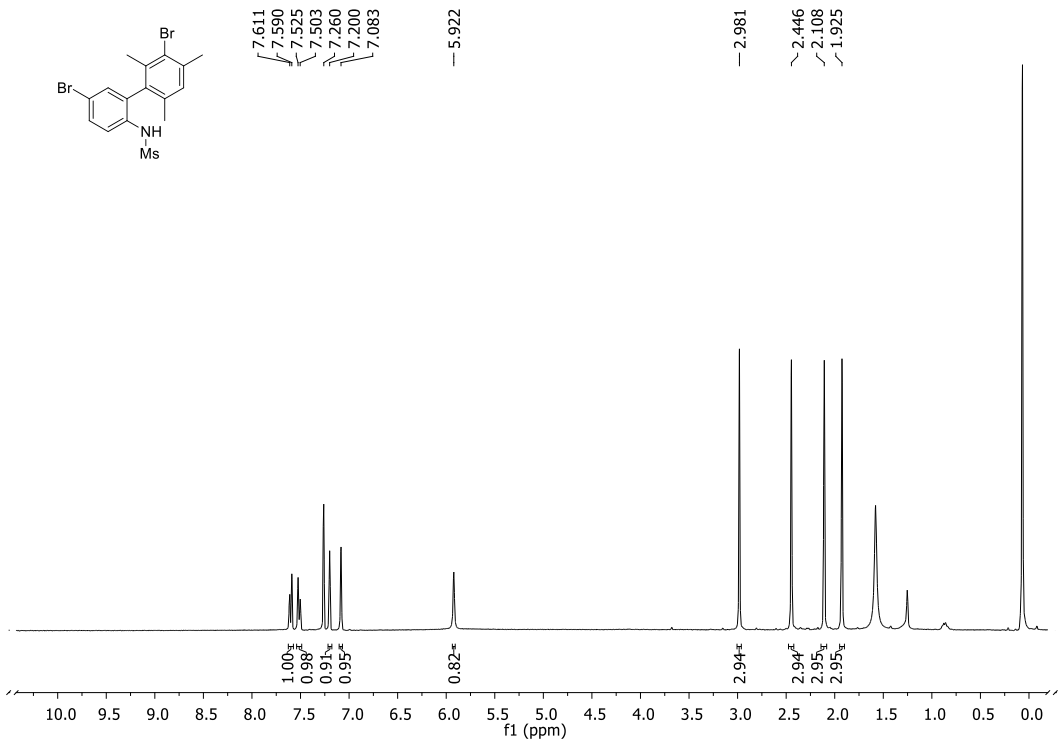


Figure 3.15 ^{1}H NMR spectrum of *N*-(3',5-Dibromo-2',4',6'-trimethyl-[1.1'-biphenyl]-2-yl]methanesulfonamide (**2h)**

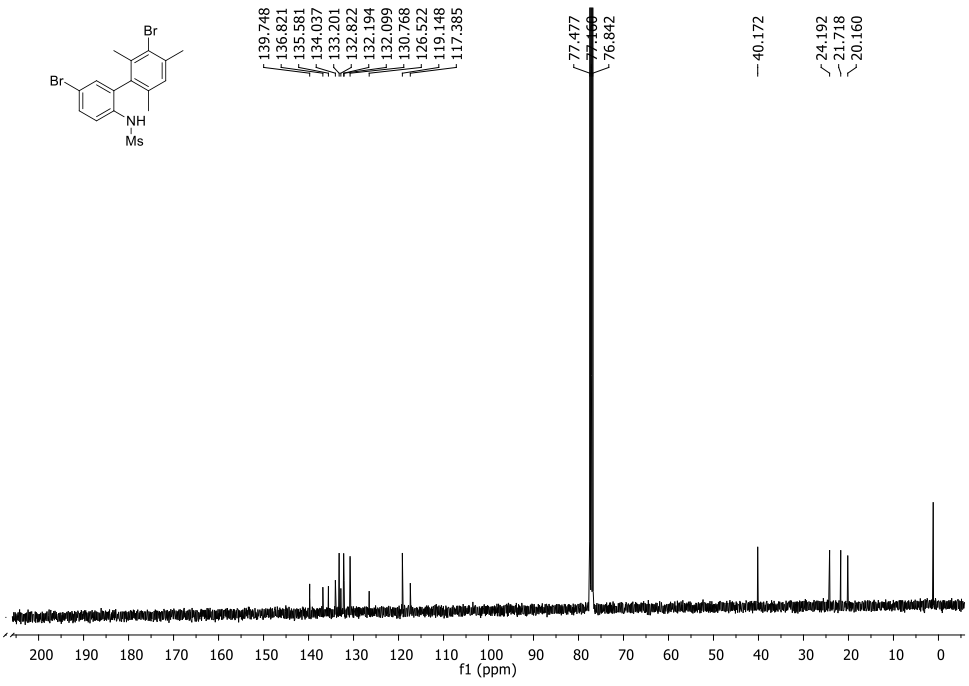


Figure 3.16 ^{13}C NMR spectrum of *N*-(3',5-Dibromo-2',4',6'-trimethyl-[1.1'-biphenyl]-2-yl]methanesulfonamide (**2h**)

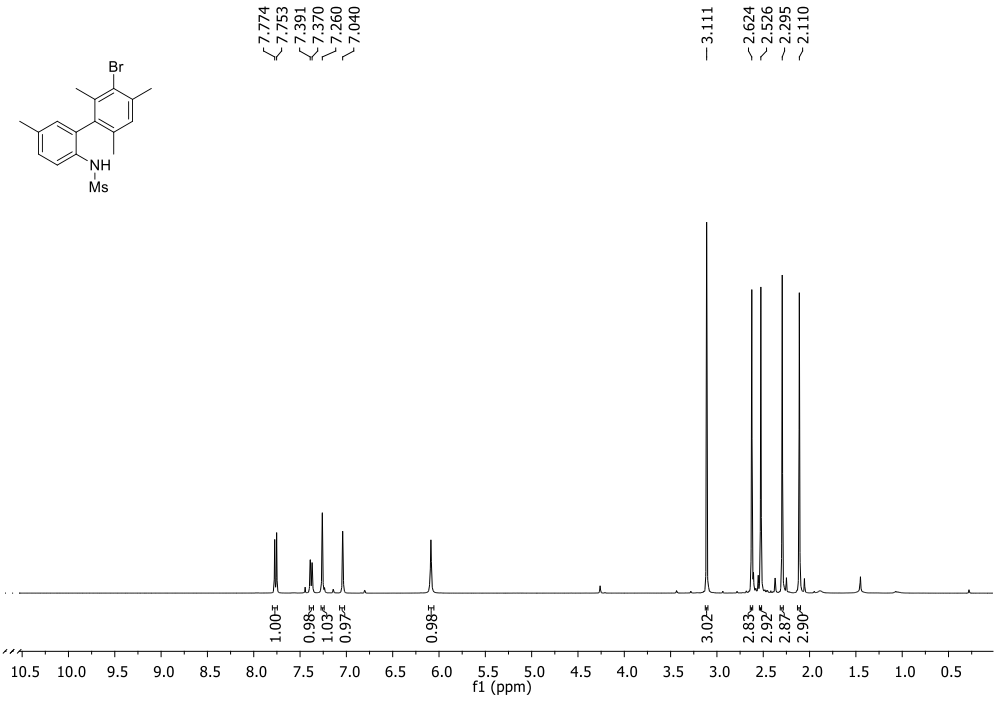


Figure 3.17 ^{1}H NMR spectrum *N*-(3'-Bromo-2',4', 5', 6'-tetramethyl–[1,1'-biphenyl]-2-yl)methanesulfonamide (**2i**)

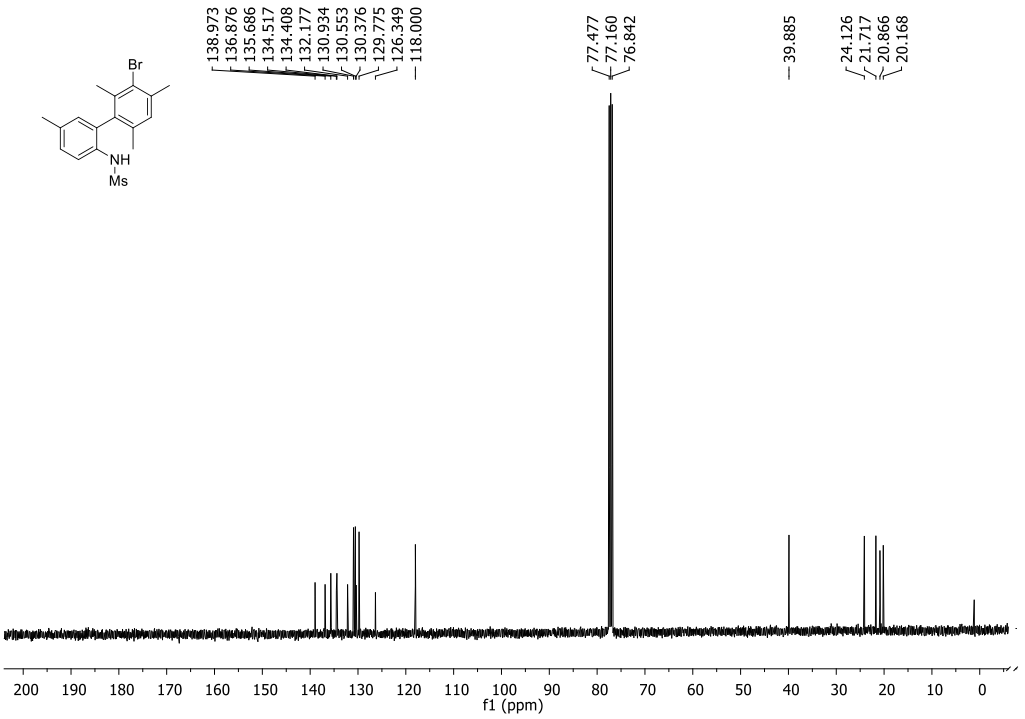


Figure 3.18 ^{13}C NMR spectrum of *N*-(3'-Bromo-2',4', 5', 6'-tetramethyl–[1,1'-biphenyl]-2-yl)methanesulfonamide (**2i**)

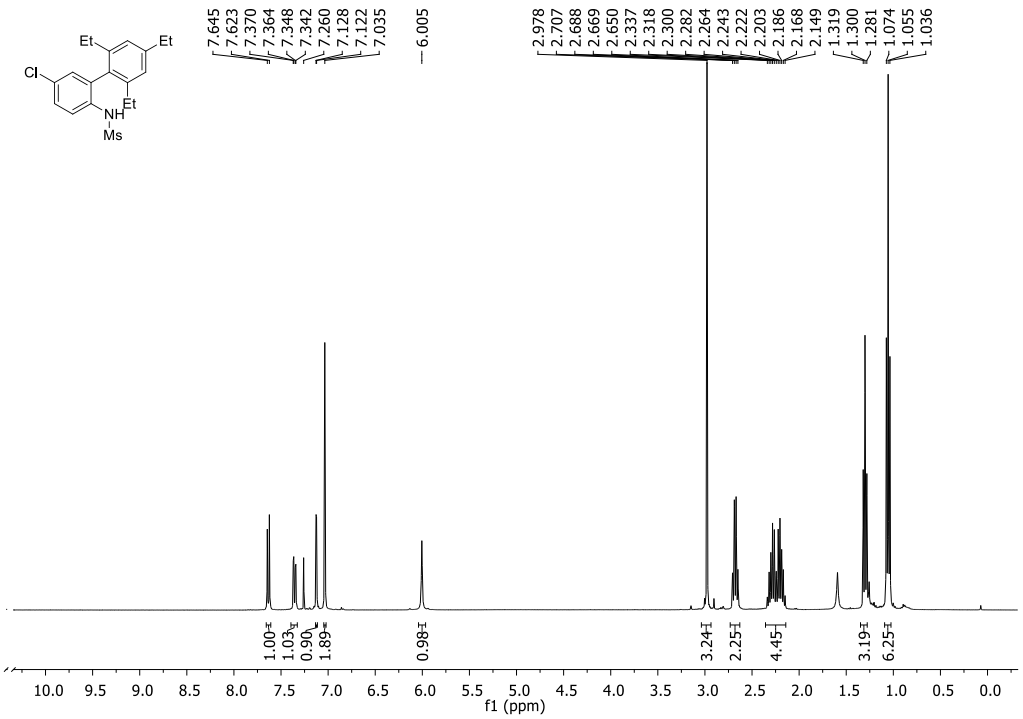


Figure 3.19 ^{1}H NMR spectrum of *N*-(5-Chloro-2',4', 6'-triethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2j**)

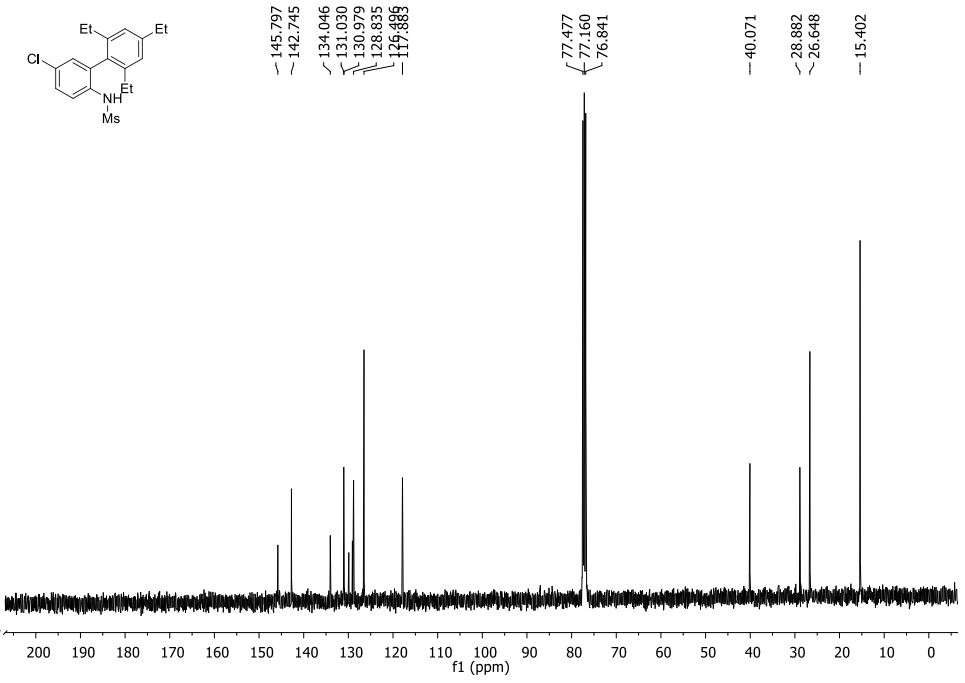


Figure 3.20 ^{13}C NMR spectrum of *N*-(5-Chloro-2',4', 6'-triethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2j**)

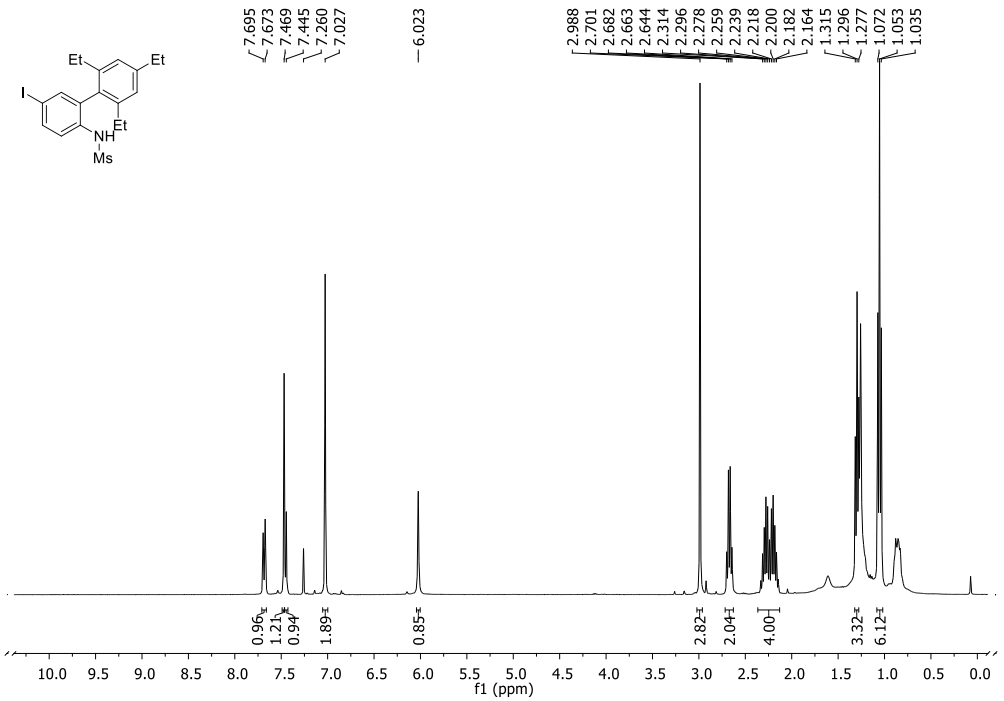


Figure 3.21 [1]H NMR spectrum of *N*-(2',4', 6'-Triethyl-5-iodo-[1,1'-biphenyl]-2-yl)methanesulfonamide **(2k**)

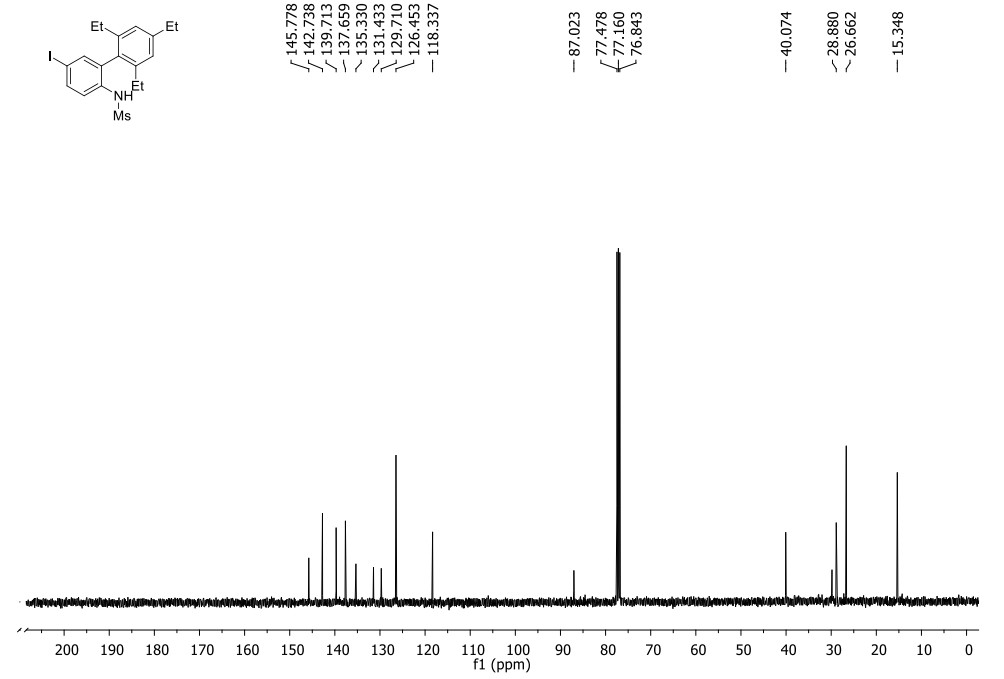


Figure 3.22 [13]C NMR spectrum of *N*-(2',4', 6'-Triethyl-5-iodo-[1,1'-biphenyl]-2-yl)methanesulfonamide **(2k**)

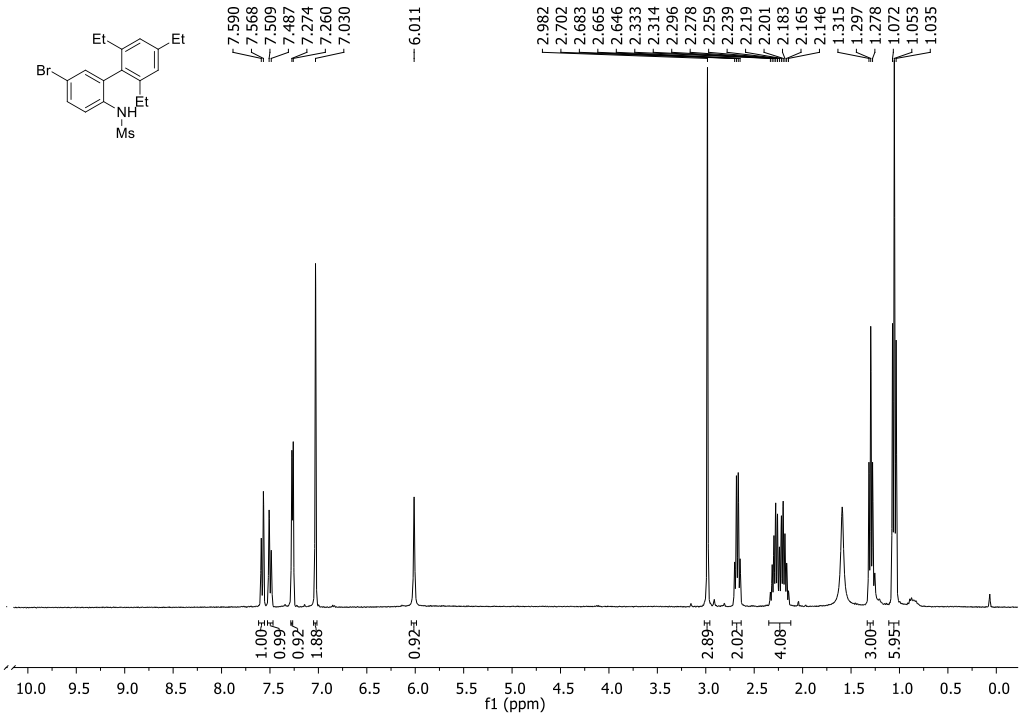


Figure 3.23 ^{1}H NMR spectrum of *N*-(5-Bromo-2',4', 6'-triethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2l**)

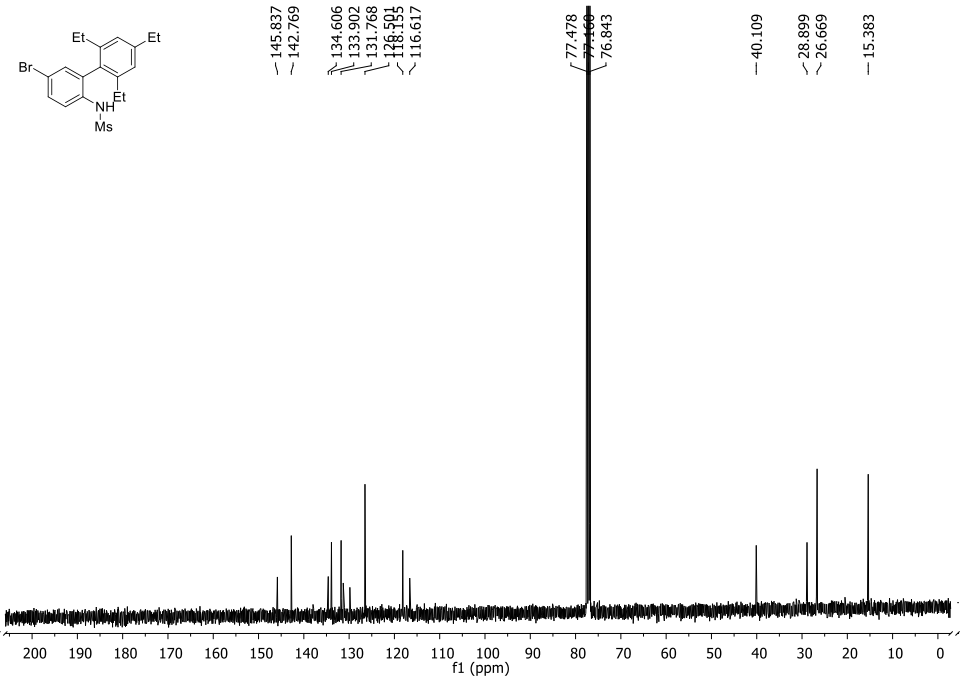


Figure 3.24 ^{13}CNMR spectrum of *N*-(5-Bromo-2',4', 6'-triethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2l**)

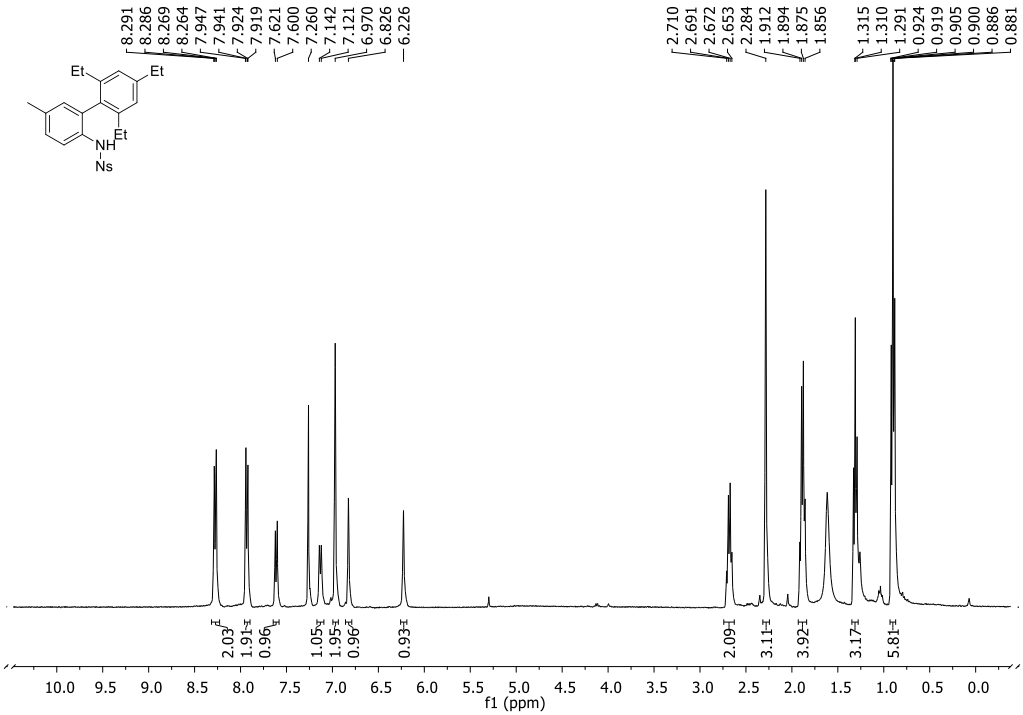


Figure 3.25 ^{1}H NMR spectrum of 4-Nitro-*N*-(2',4', 6'-triethyl-5-methyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (**2m**)

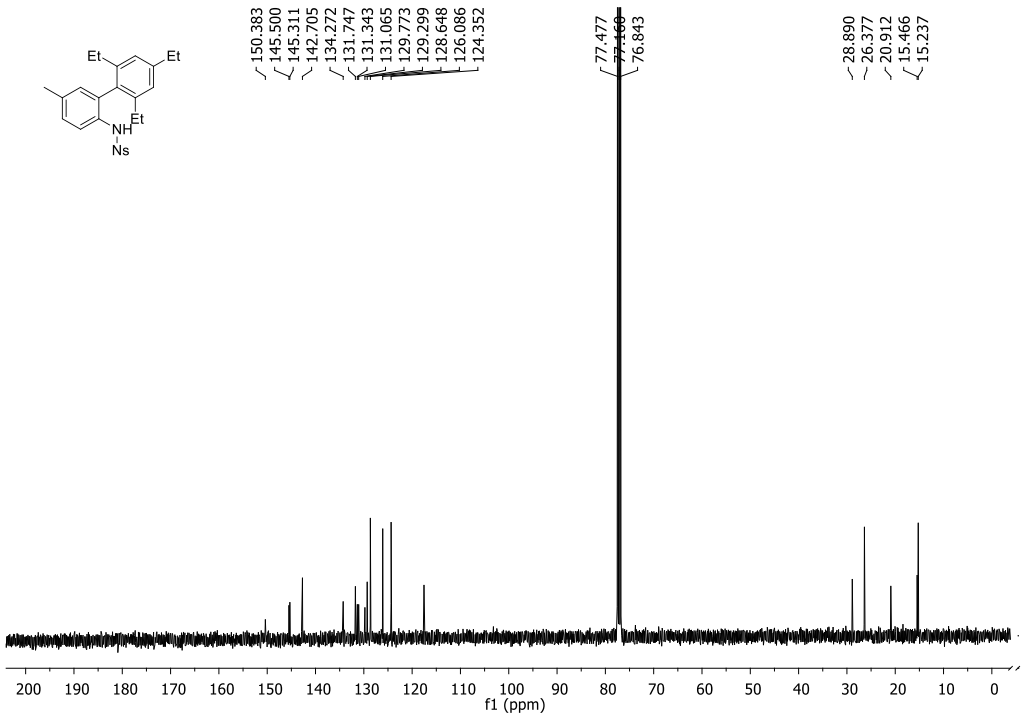


Figure 3.26 ^{13}C NMR spectrum of 4-Nitro-*N*-(2',4', 6'-triethyl-5-methyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (**2m**)

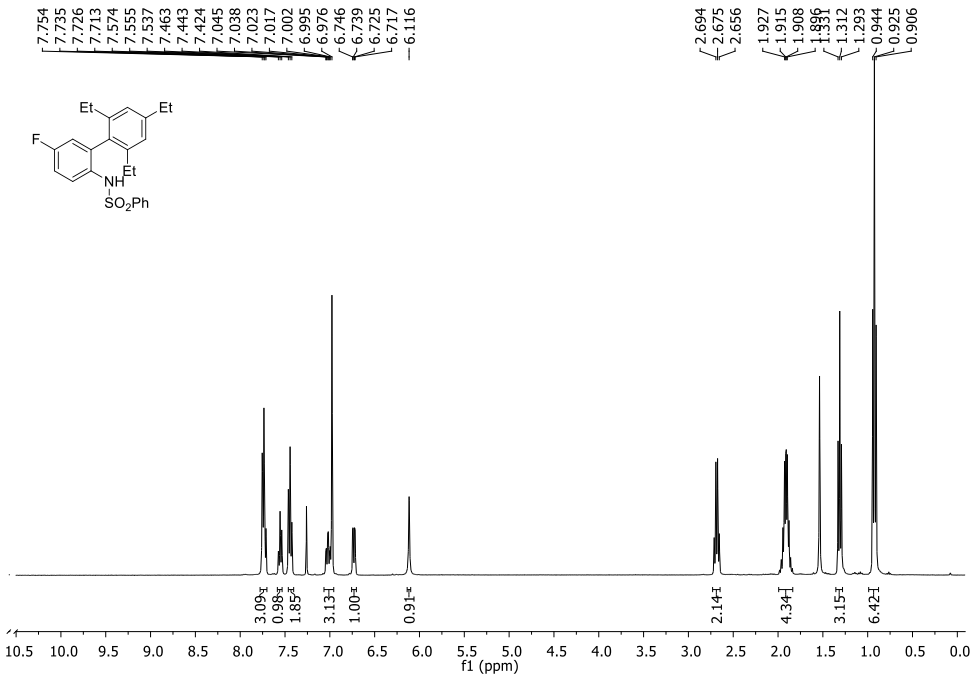


Figure 3.27 ^{1}H NMR spectrum of *N*-(2',4',6'-Triethyl-5-fluoro-[1, 1'-biphenyl]-2-yl)benzenesulfonamide (**2n**)

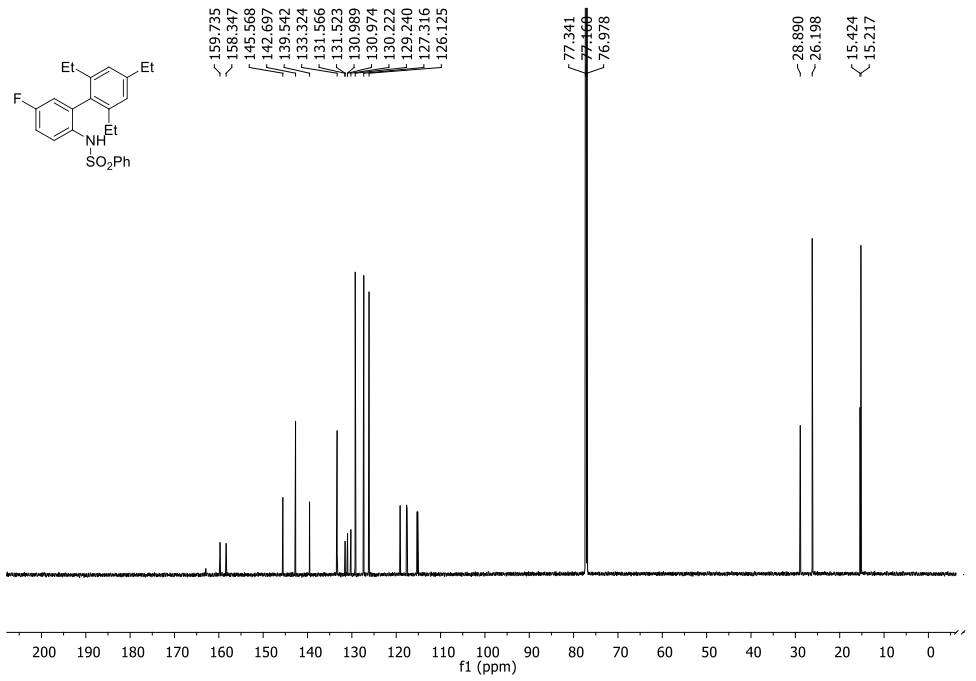
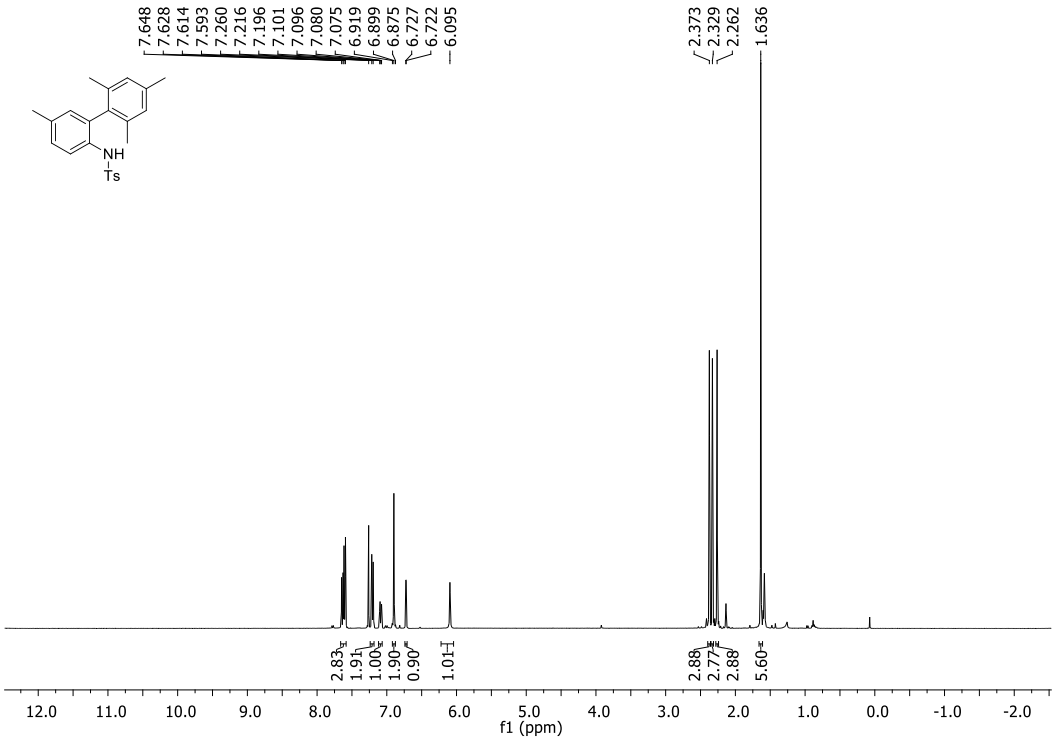


Figure 3.28 ^{13}C NMR spectrum of *N*-(2',4',6'-Triethyl-5-fluoro-[1, 1'-biphenyl]-2-yl)benzenesulfonamide (**2n**)



. **Figure 3.29** [1]H NMR spectrum of 4-Methyl-*N*-(2',4' ,5' 6'-tetramethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (**2o)**

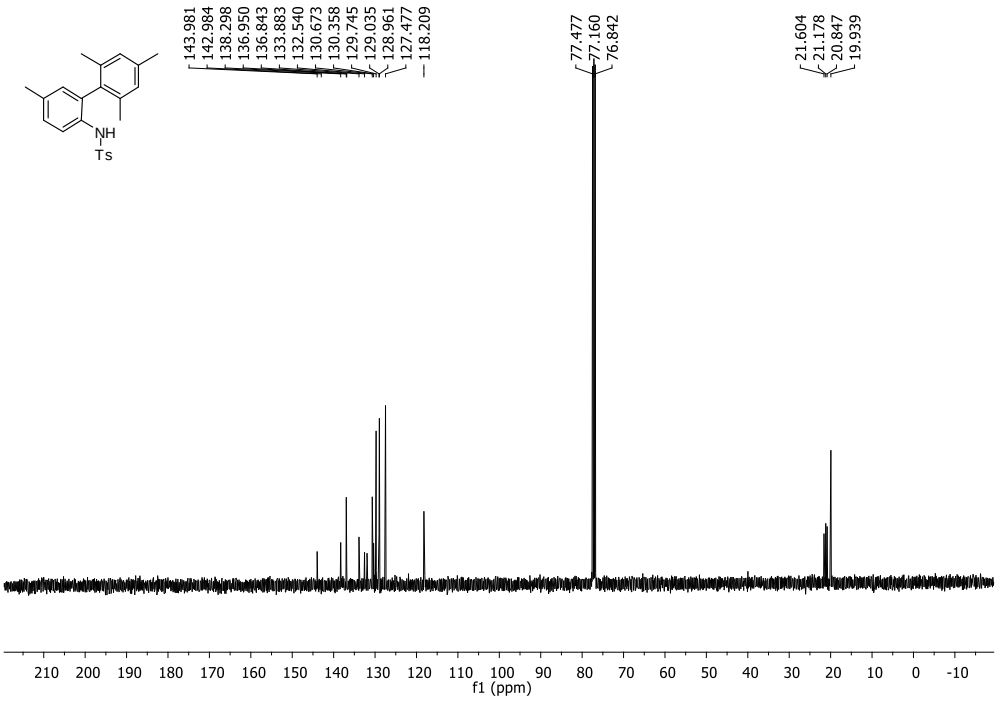


Figure 3.30 [13]C NMR spectrum of 4-Methyl-*N*-(2',4' ,5' 6'-tetramethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (**2o)**

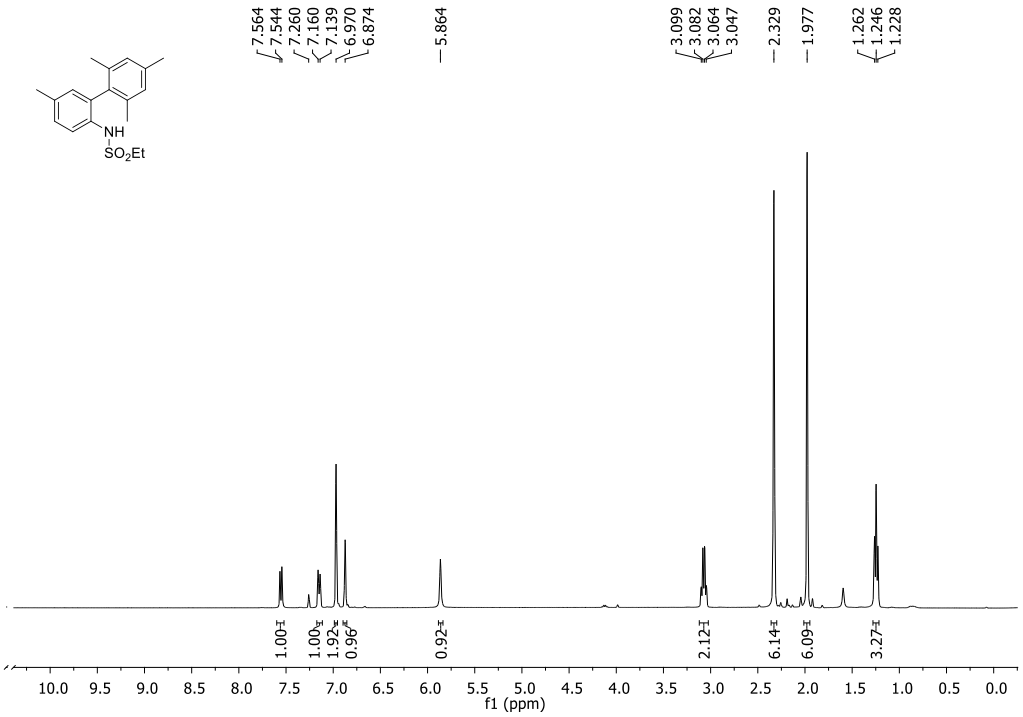


Figure 3.31 ^{1}H NMR spectrum of *N*-(2',4' ,5' 6'-Tetramethyl-[1,1'-biphenyl]-2-yl)ethanesulfonamide (**2p**)

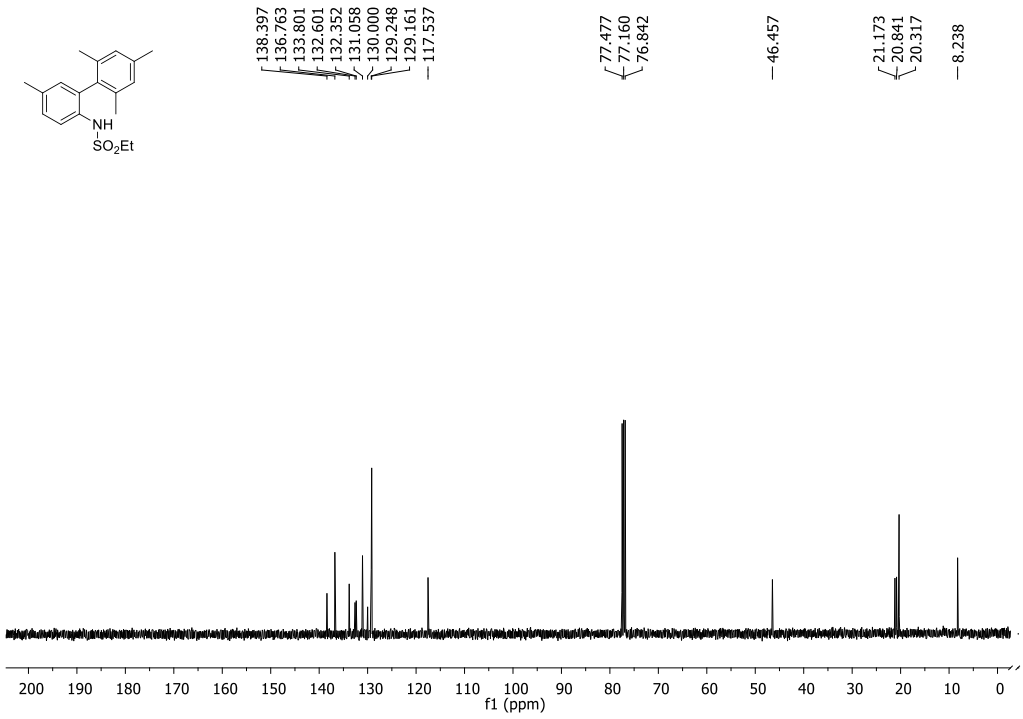


Figure 3.32 ^{13}C NMR spectrum of *N*-(2',4' ,5' 6'-Tetramethyl-[1,1'-biphenyl]-2-yl)ethanesulfonamide (**2p**)

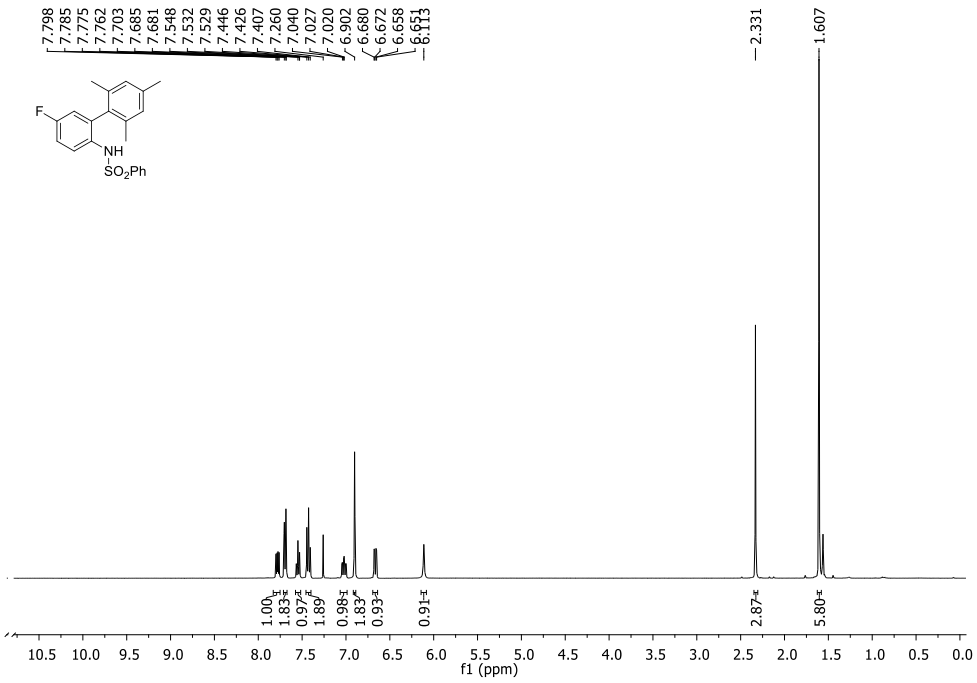


Figure 3.33 ^{1}H NMR spectrum of *N*-(5-Fluoro-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (**2q**)

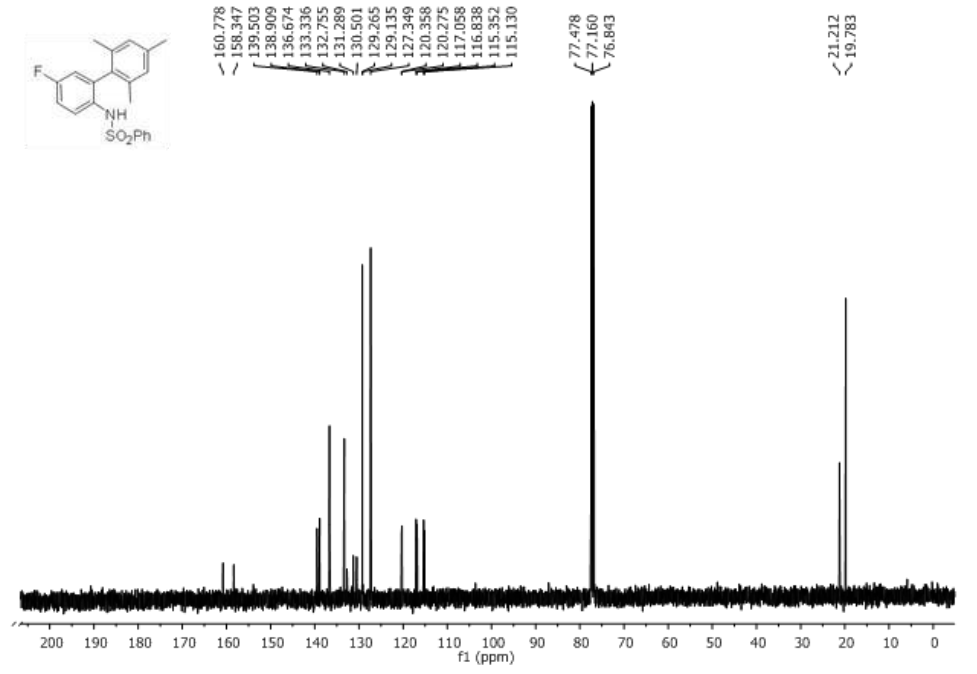


Figure 3.34 ^{13}C NMR spectrum of *N*-(5-Fluoro-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (**2q**)

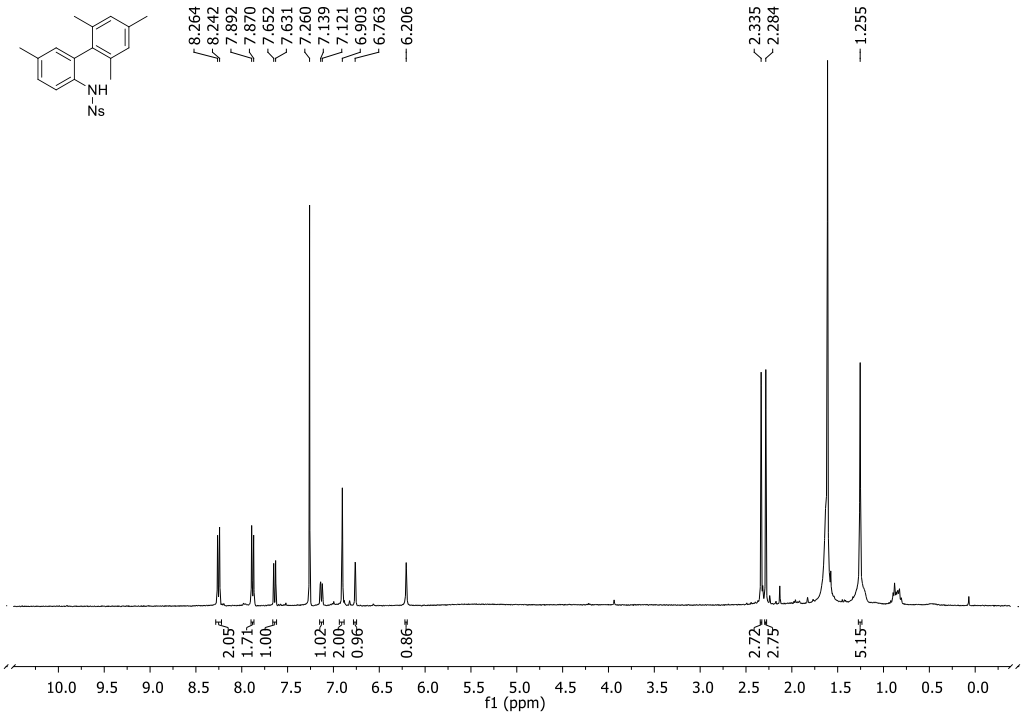


Figure 3.35 ^{1}H NMR spectrum of 4-Nitro-*N*-(2',4',5', 6'-tetramethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide**(2r)**

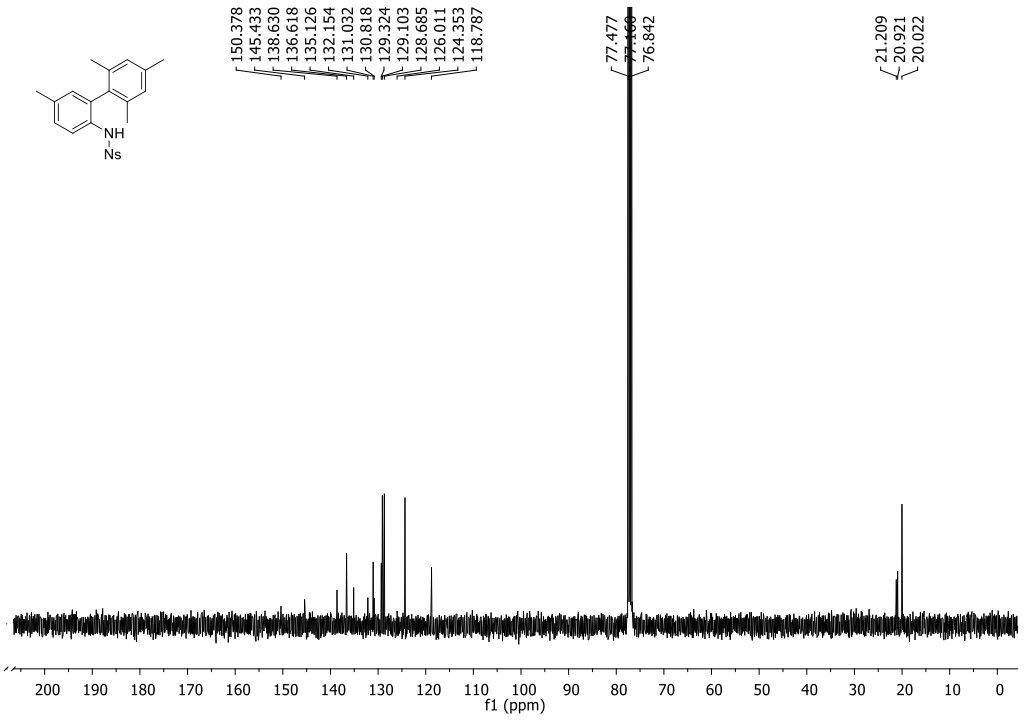


Figure 3.36 ^{13}C NMR spectrum of 4-Nitro-*N*-(2',4',5', 6'-tetramethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide**(2r)**

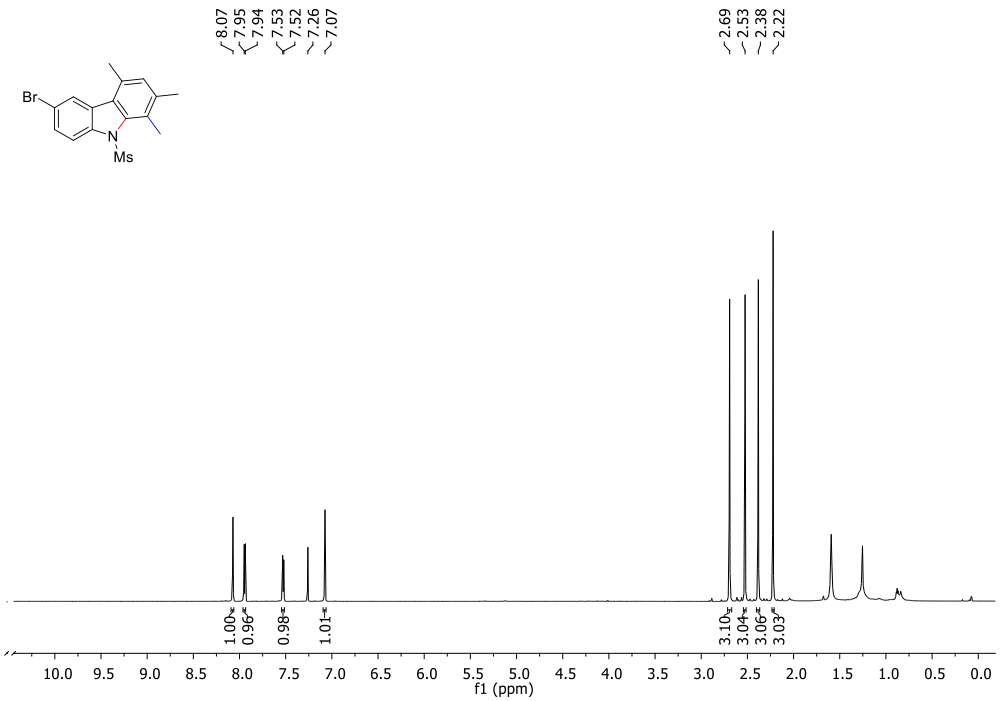


Figure 3.37 ^{1}H NMR spectrumof 6–Bromo-1,2,4-trimethyl-9(methylsulfonyl)-carbazole **(3a)**

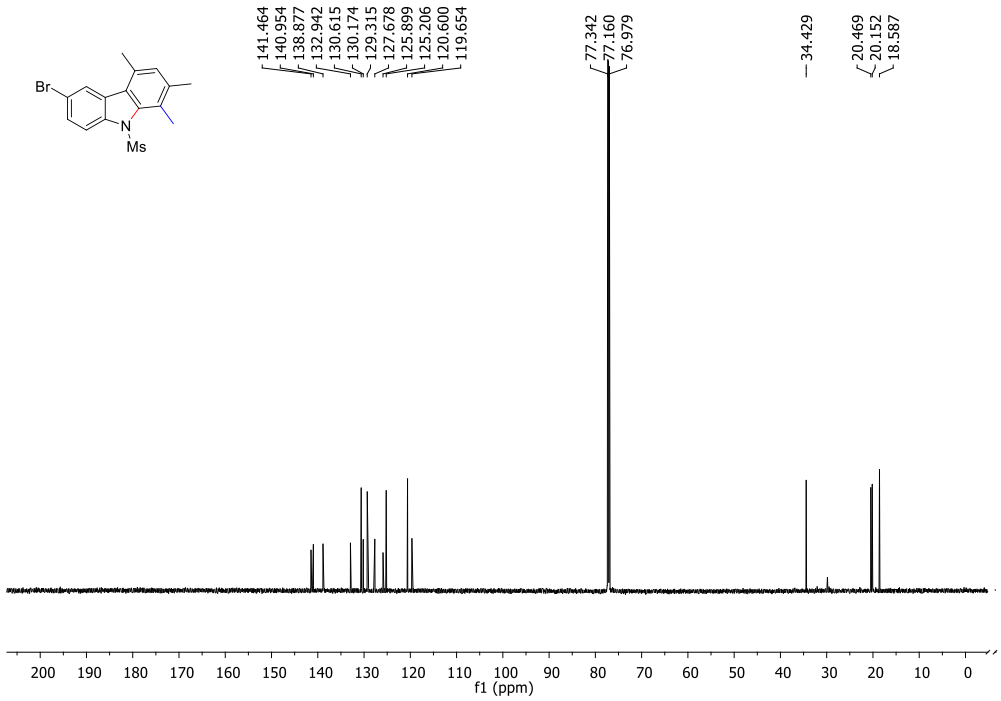


Figure 3.38 ^{13}C NMR spectrum of 6–Bromo-1,2,4-trimethyl-9(methylsulfonyl)-carbazole**(3a)**

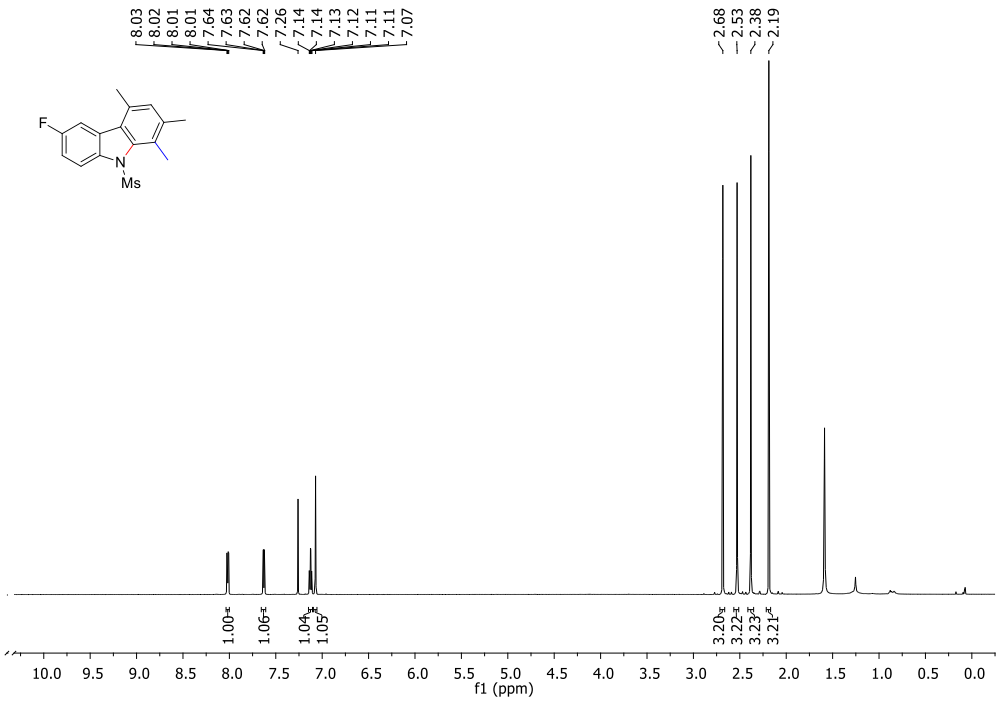


Figure 3.39 ^{1}H NMR spectrum of 6-Fluoro-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole **(3c)**

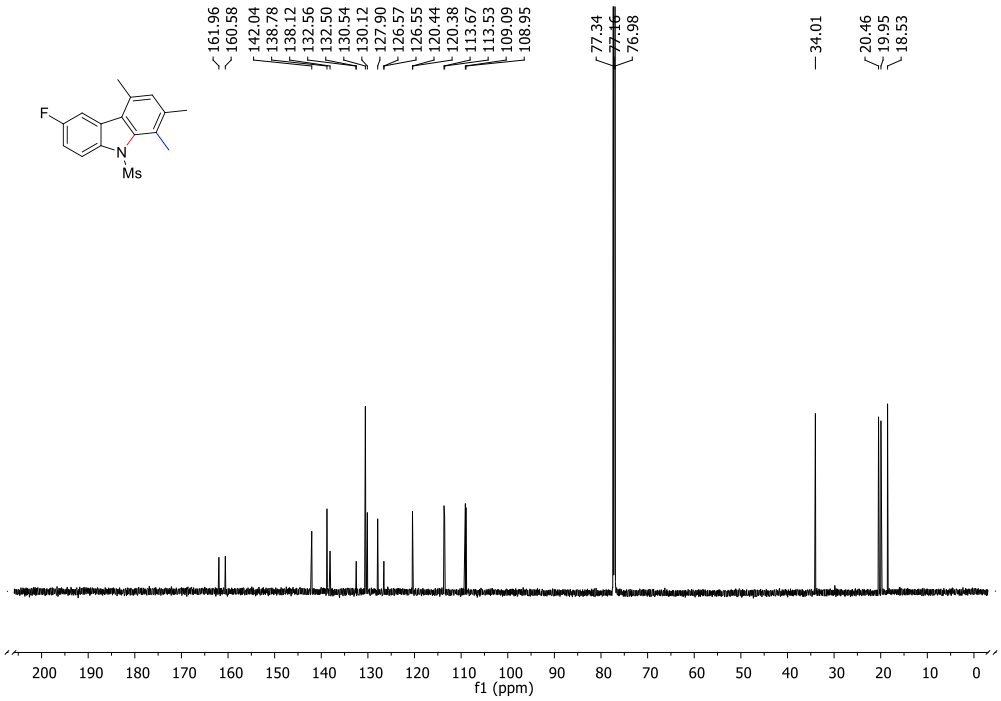


Figure 3.40 ^{13}C NMR spectrum of 6-Fluoro-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole **(3c)**

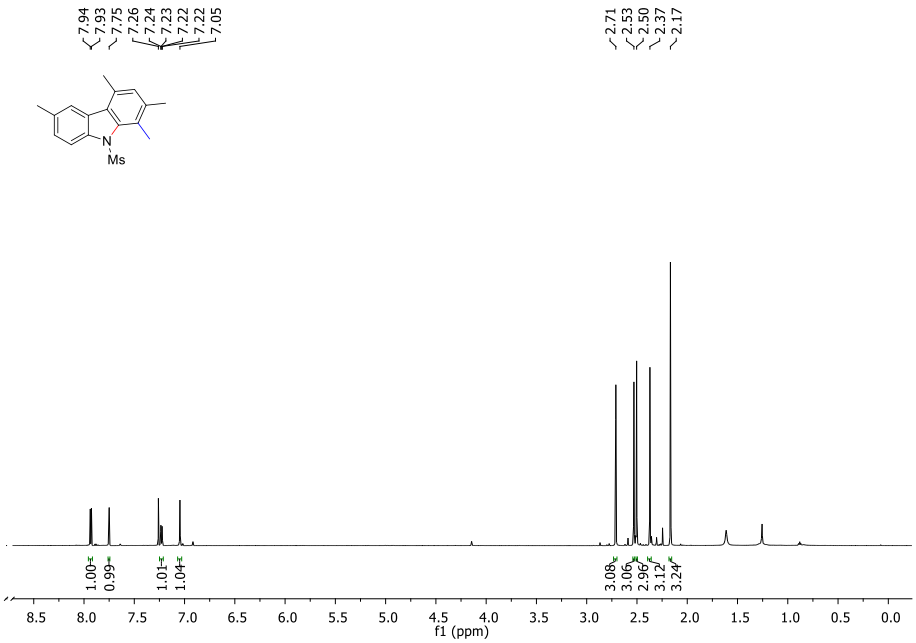


Figure 3.41 ^{1}H NMR spectrum of 1,2,4,6-Tetramethyl-9-(methylsulfonyl-)-carbazole **(3d)**

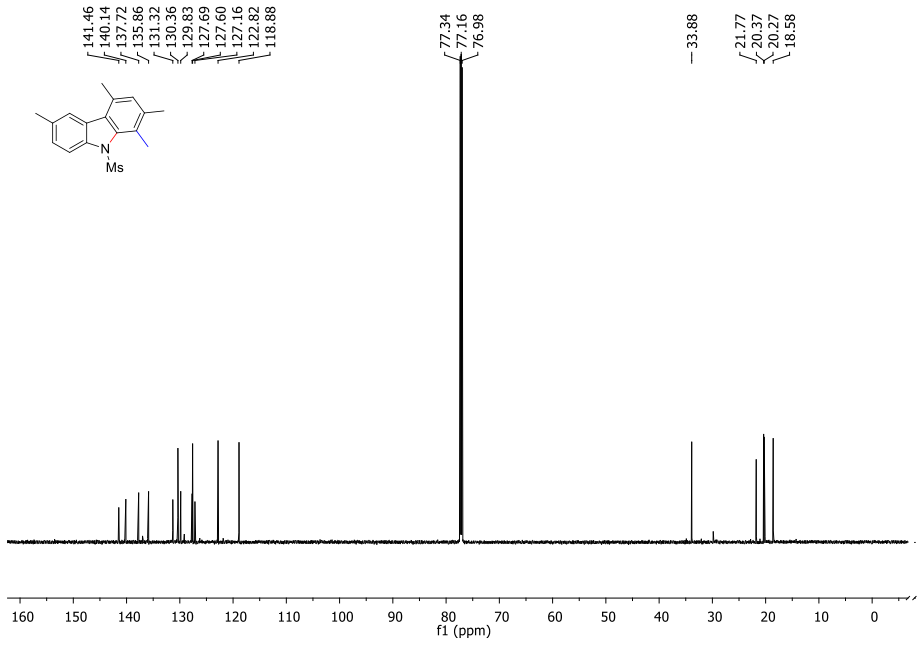


Figure 3.42 ^{13}C NMR spectraof 1,2,4,6-Tetramethyl-9-(methylsulfonyl-)-carbazole **(3d)**

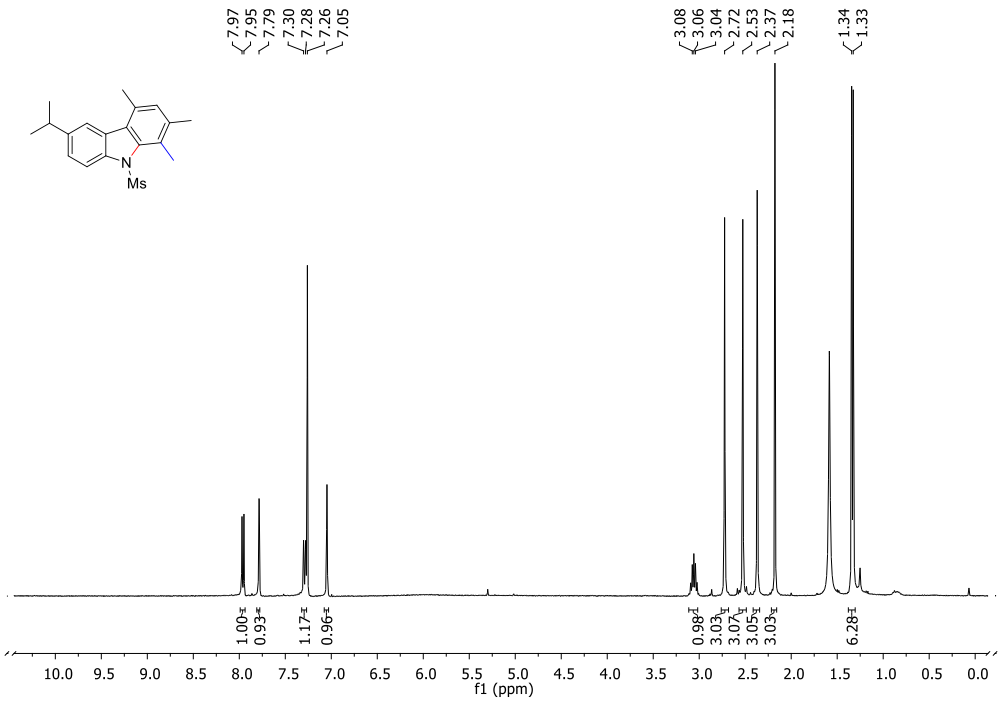


Figure 3.43 [1]H NMR spectrum of 6-Isopropyl-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (**3f**)

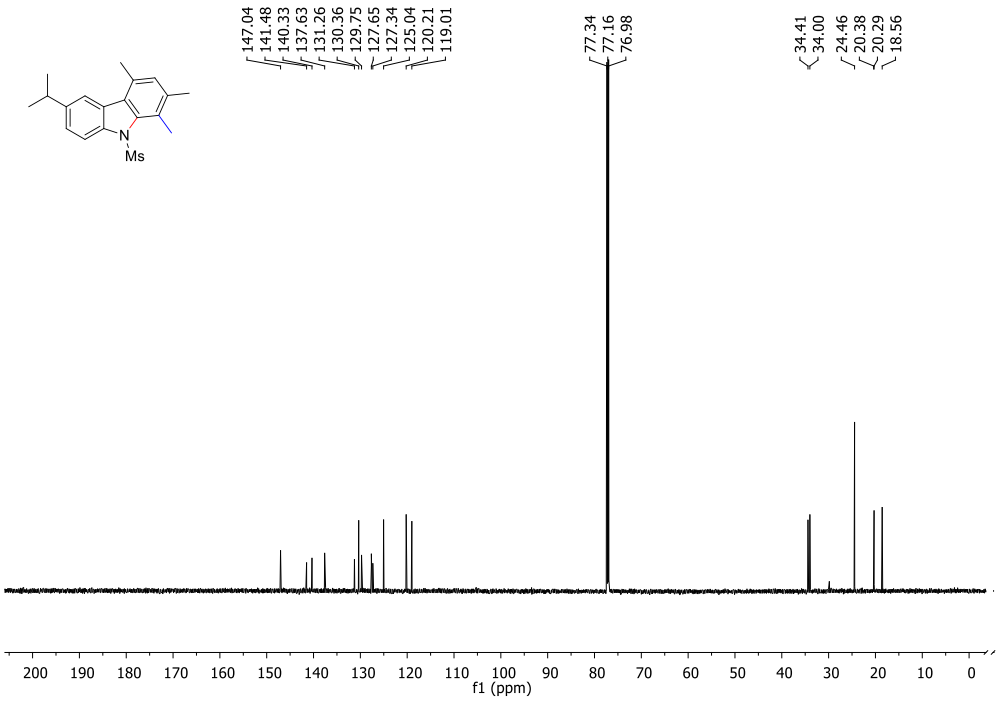


Figure 3.44 [13]C NMR spectrum of 6-Isopropyl-1,2,4-trimethyl-9-(methylsulfonyl)carbazole **(3f)**

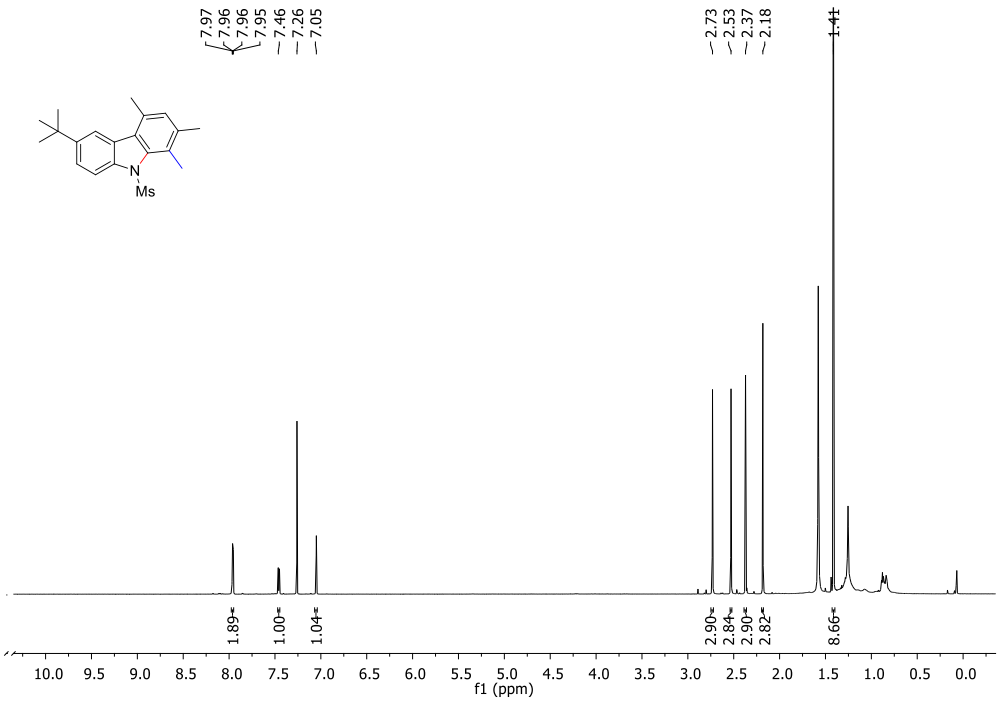


Figure 3.45 ^{1}H NMR spectrum of 6-(*tert*-butyl)-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (**3g)**

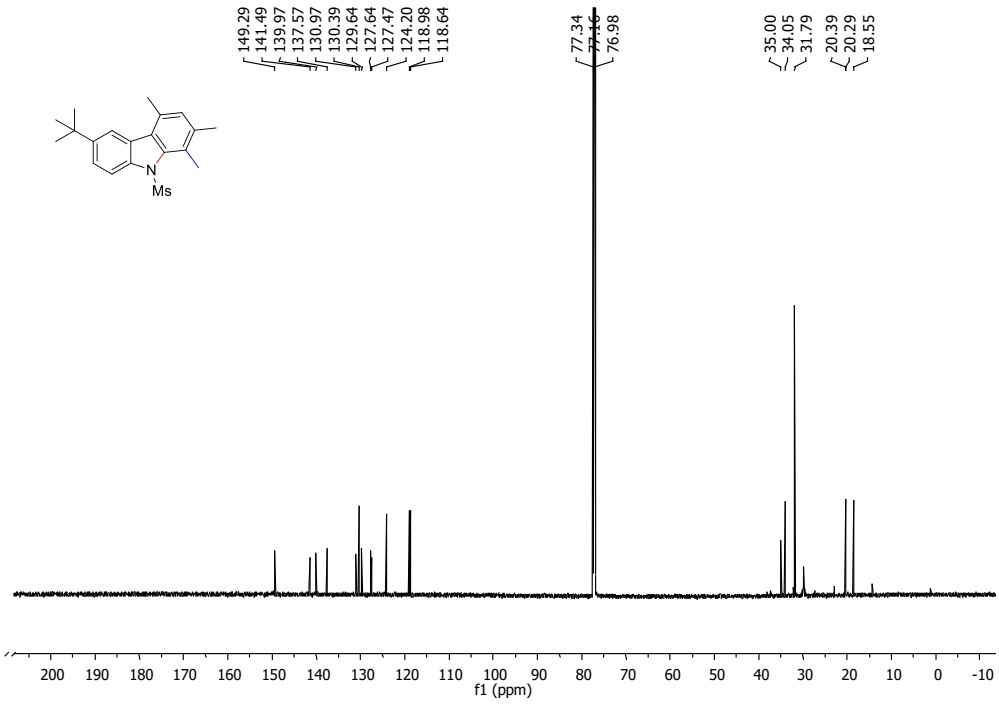


Figure 3.46 ^{13}C NMR spectra of 6-*(tert*-Butyl)-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (**3g)**

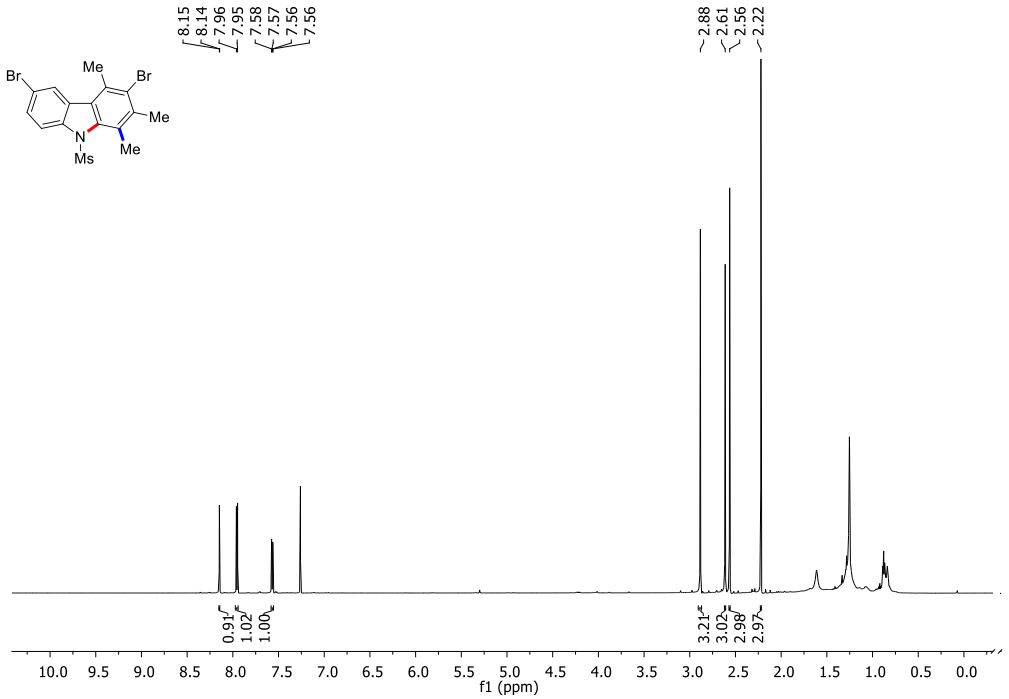


Figure 3.47 [1]H NMR spectrum of3,6-Dibromo-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (**3h)**

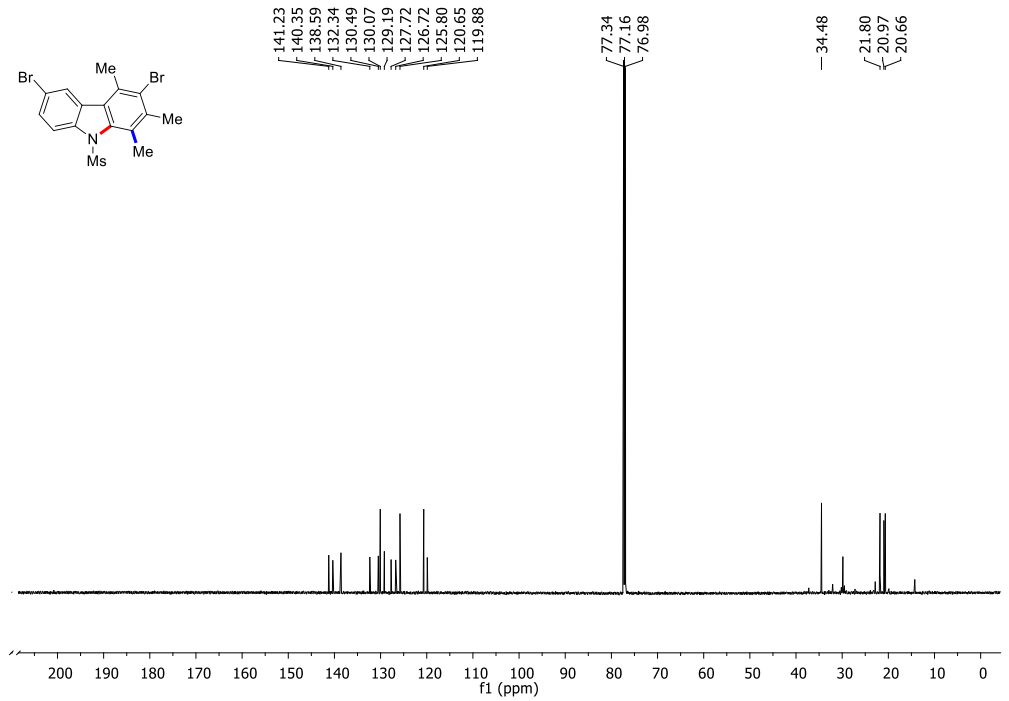


Figure 3.48 [13]CNMR spectrum of3,6-Dibromo-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole **(3h)**

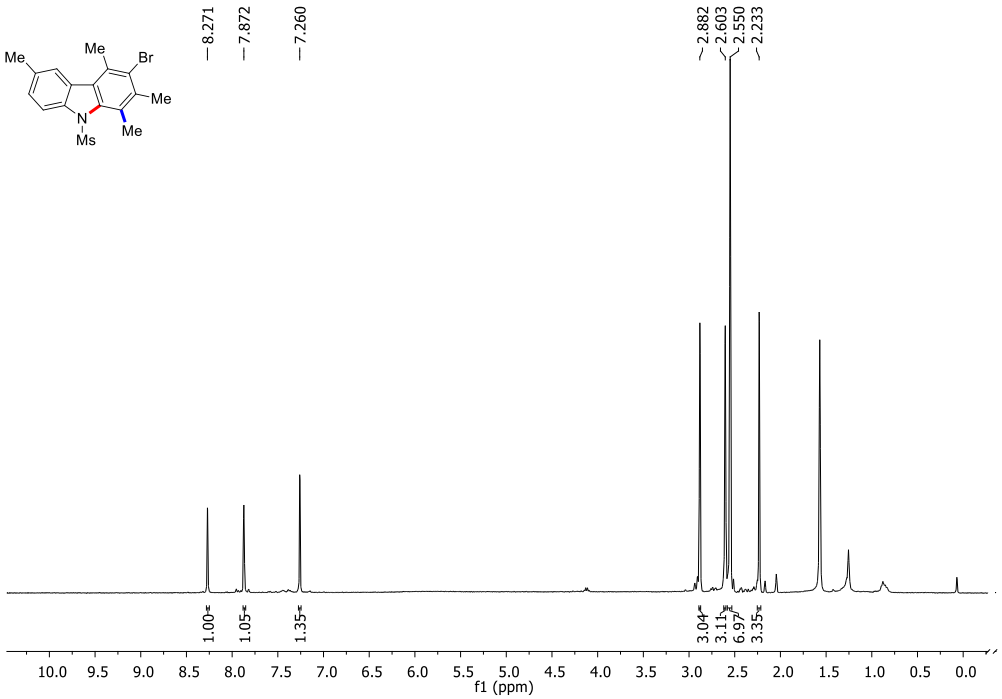


Figure 3.49 ^{1}H NMR spectrum of 3-Bromo-1,2,4,6-tetramethyl-9-(methylsulfonyl)-carbazole **(3i)**

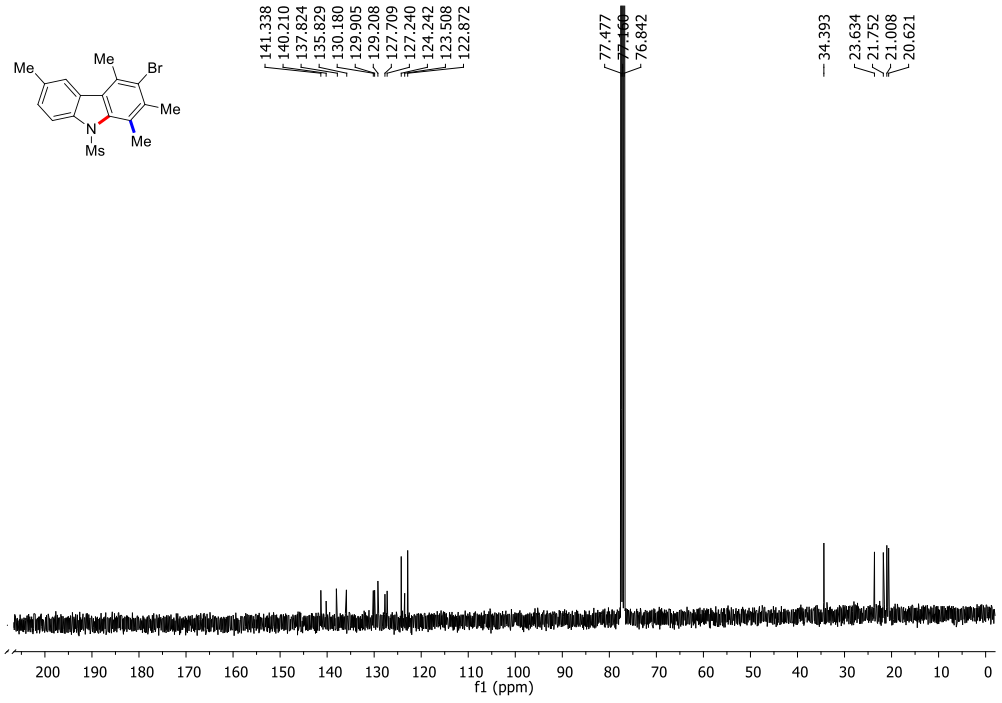


Figure 3.50 ^{13}C NMR spectrum of 3-Bromo-1,2,4,6-tetramethyl-9-(methylsulfonyl)-carbazole**(3i)**

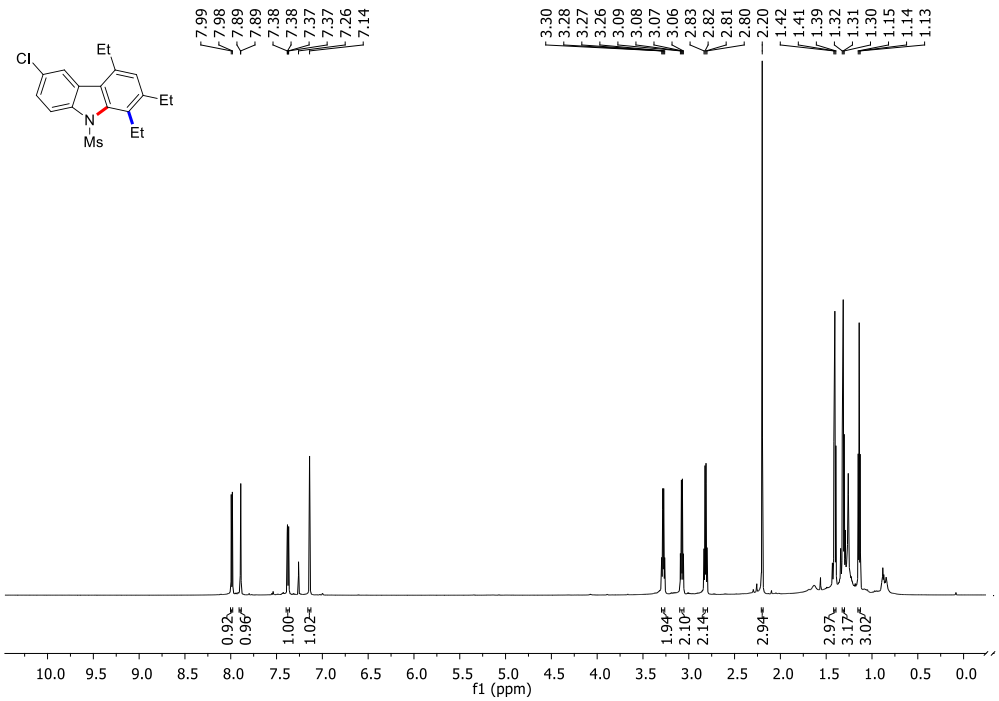


Figure 3.51 [1]H NMR spectrum of 6-Chloro-1,2,4-triethyl-9-(methylsulfonyl)-carbazole **(3j)**

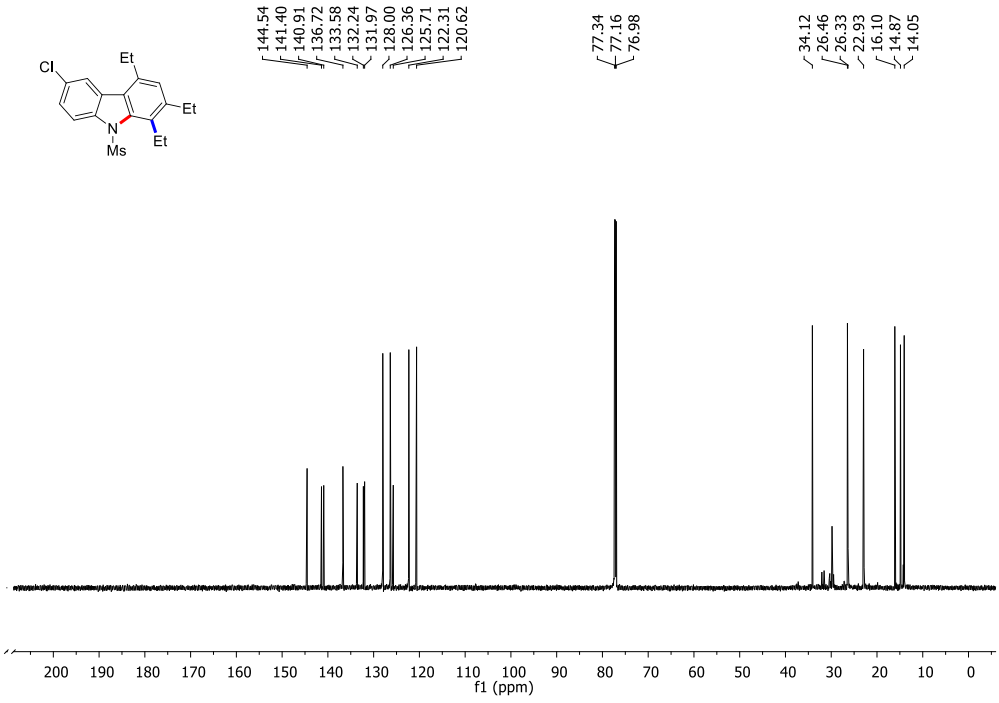


Figure 3.52 [13] C NMR spectrum of 6-Chloro-1,2,4-triethyl-9-(methylsulfonyl)-carbazole **(3j)**

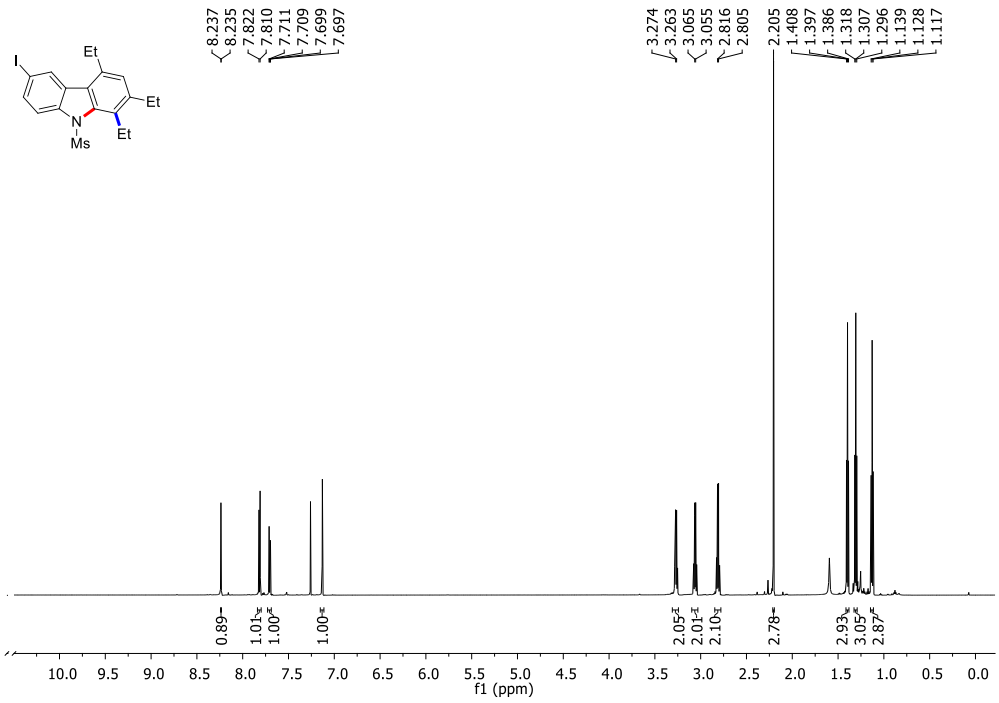


Figure 3.53 ^{1}H NMR spectrum of 1,2,4-Triethyl-6-iodo-9-(methylsulfonyl)carbazole **(3k)**

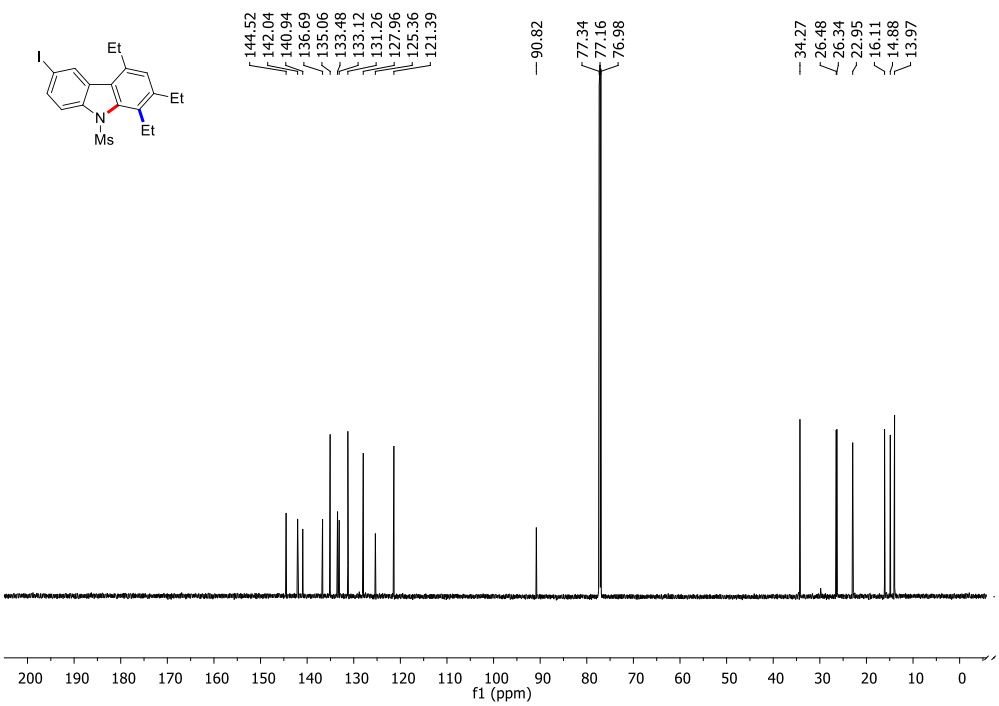


Figure 3.54 ^{13}C NMR spectrum of 1,2,4-Triethyl-6-iodo-9-(methylsulfonyl)-carbazole **(3k)**

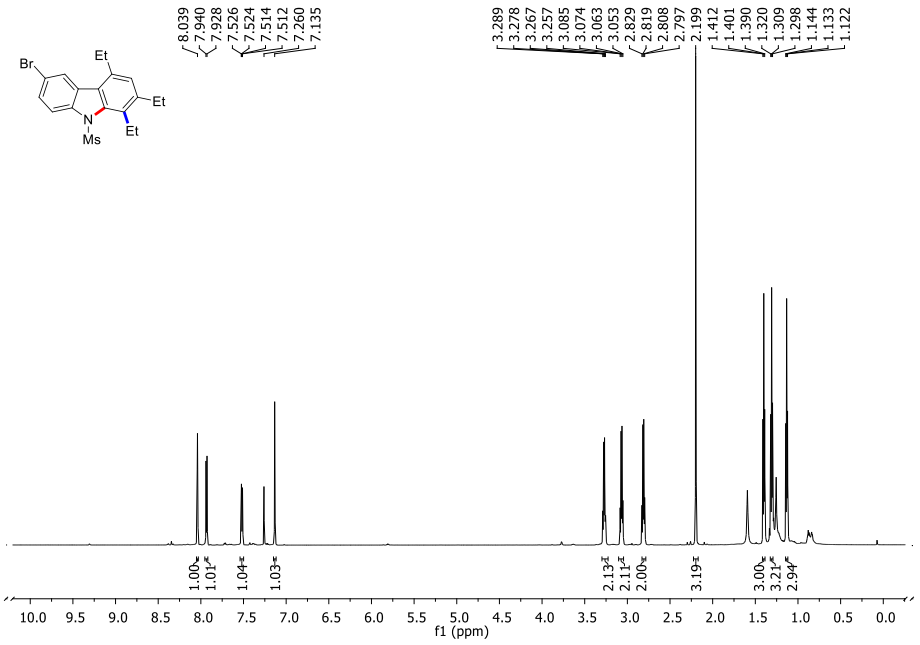


Figure 3.55 ^{1}H NMR spectrum of 6-Bromo-1,2,4-triethyl-9-methylsulfonyl)-carbazole **(3l)**

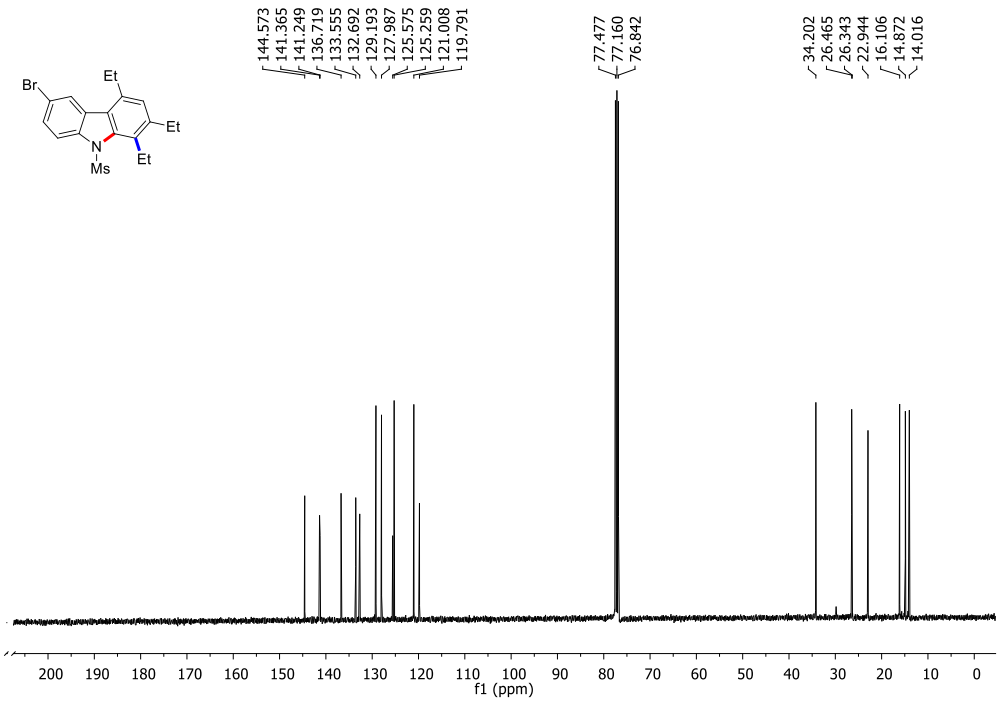


Figure 3.56 ^{13}C NMR spectra of 6-Bromo-1,2,4-triethyl-9-methylsulfonyl)-carbazole (**3l**)

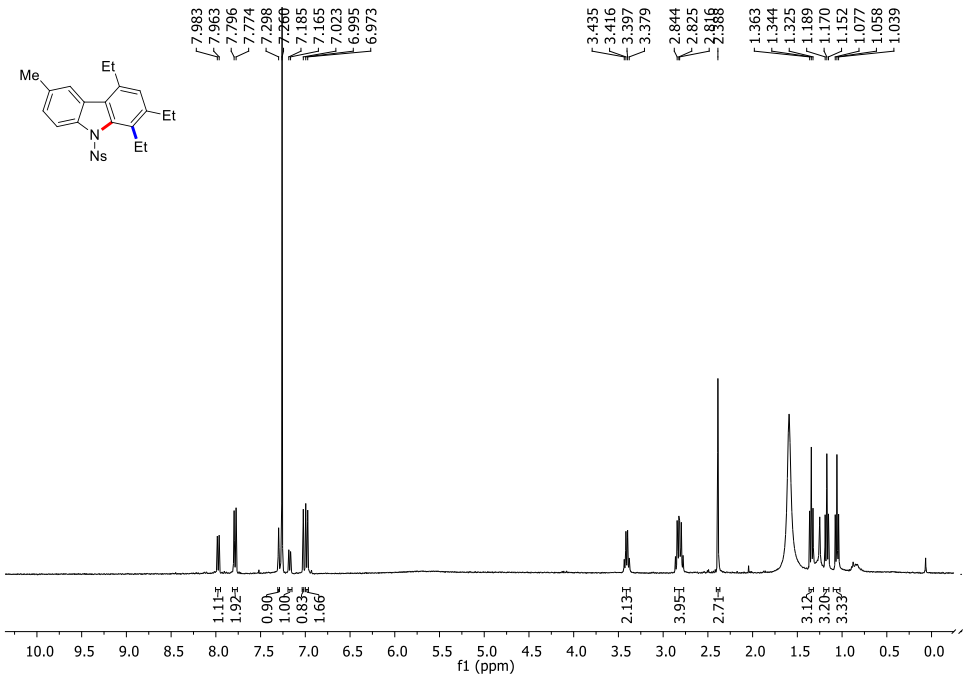


Figure 3.57 [1]H NMR spectrum of 1,2,4-Triethyl-6-methyl-9-(4-nitrophenyl)-carbazole (**3m**)

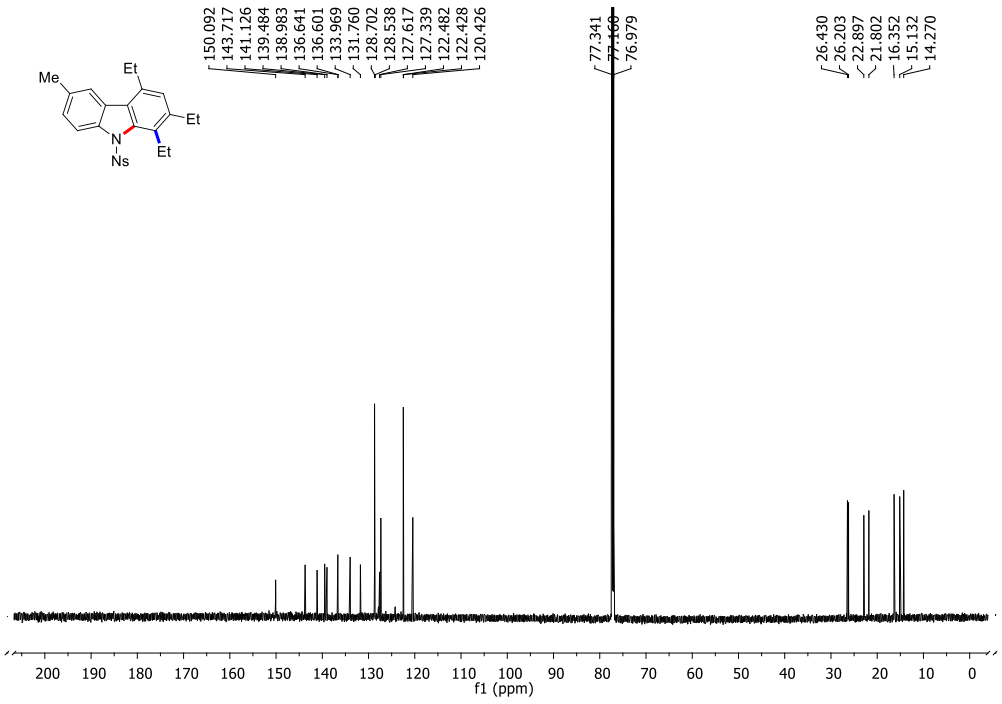


Figure 3.58 [13]C NMR spectrum of 1,2,4-Triethyl-6-methyl-9-(4-nitrophenyl)-carbazole **(3m)**

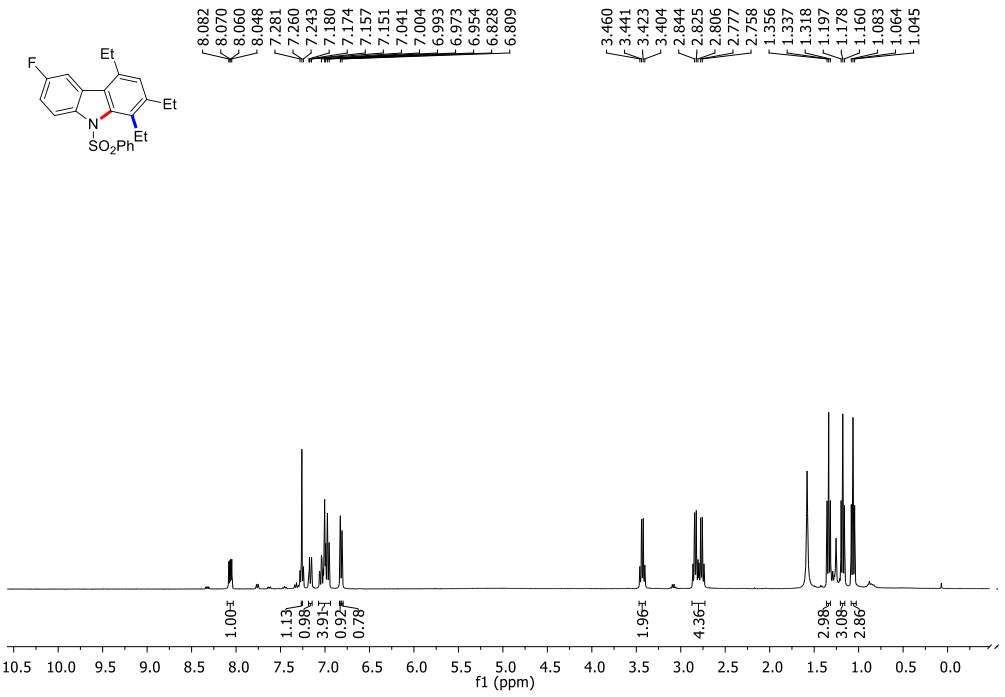


Figure 3.59 ^{1}H NMR spectrum of 1,2,4-Triethyl-6-fluoro-9-(phenylsulfonyl)-carbazole) (**3n**)

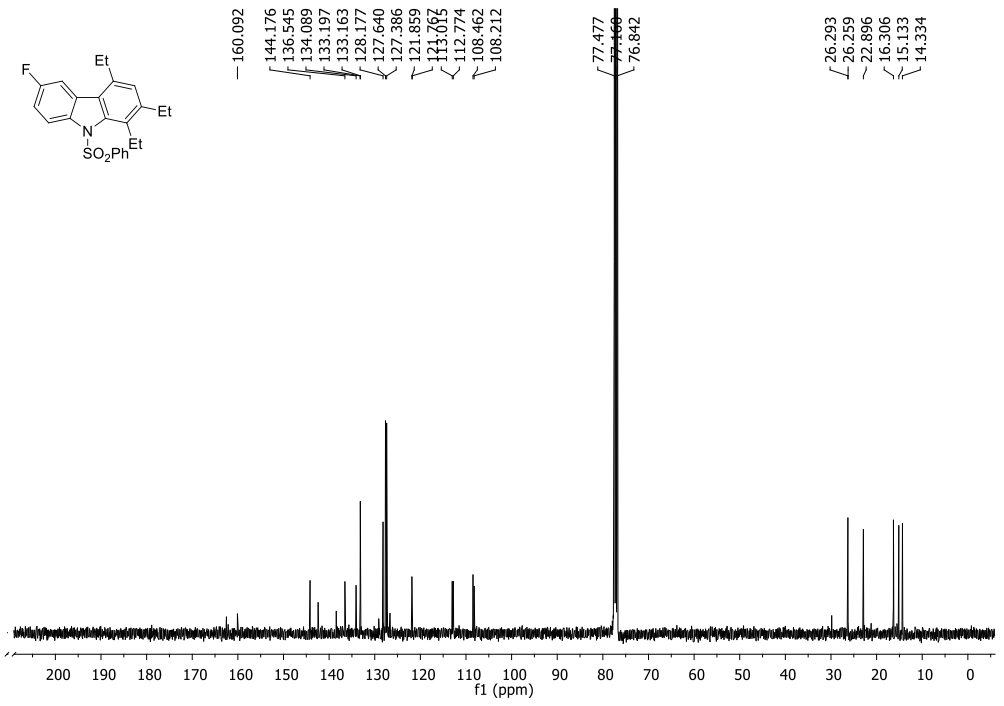


Figure 3.60 ^{13}C NMR spectrum of 1,2,4-Triethyl-6-fluoro-9-(phenylsulfonyl)-carbazole) (**3n**)

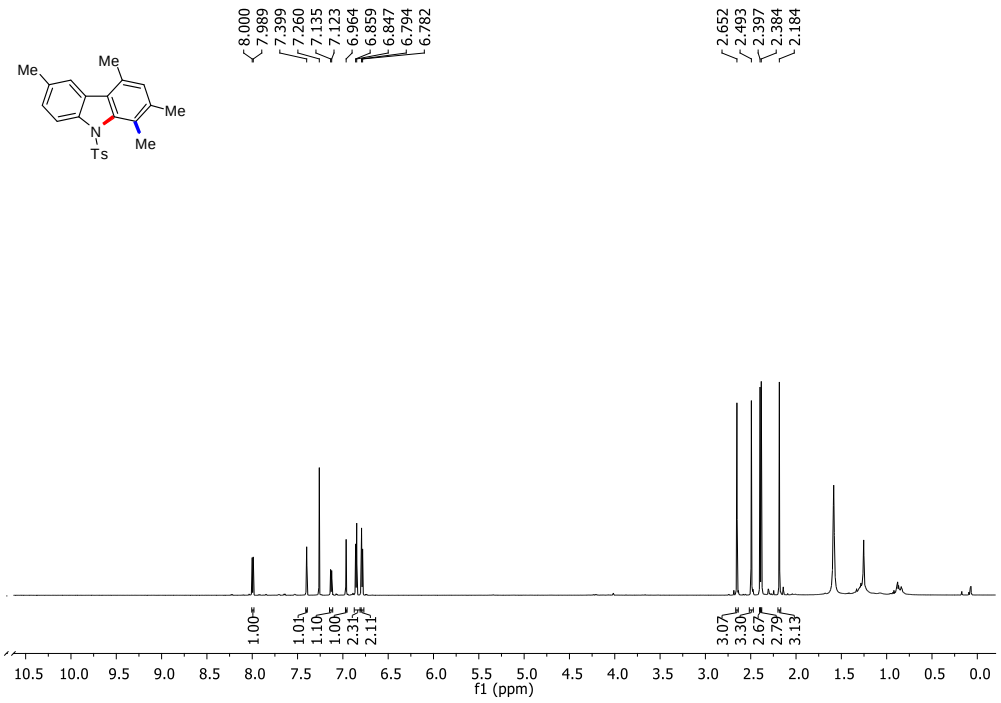


Figure 3.61 ^{1}H NMR spectrum of 1,2,4,6-Tetramethyl-9-tosyl-carbazole (**3o**)

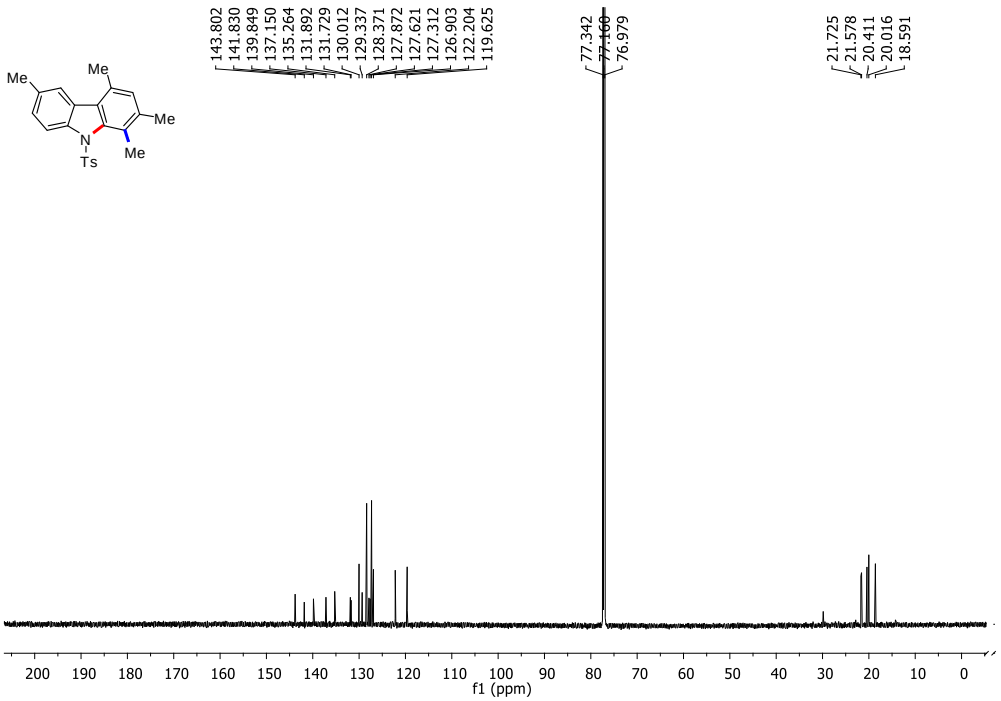


Figure 3.62 ^{13}C NMR spectrum of 1,2,4,6-Tetramethyl-9-tosyl-carbazole (**3o**)

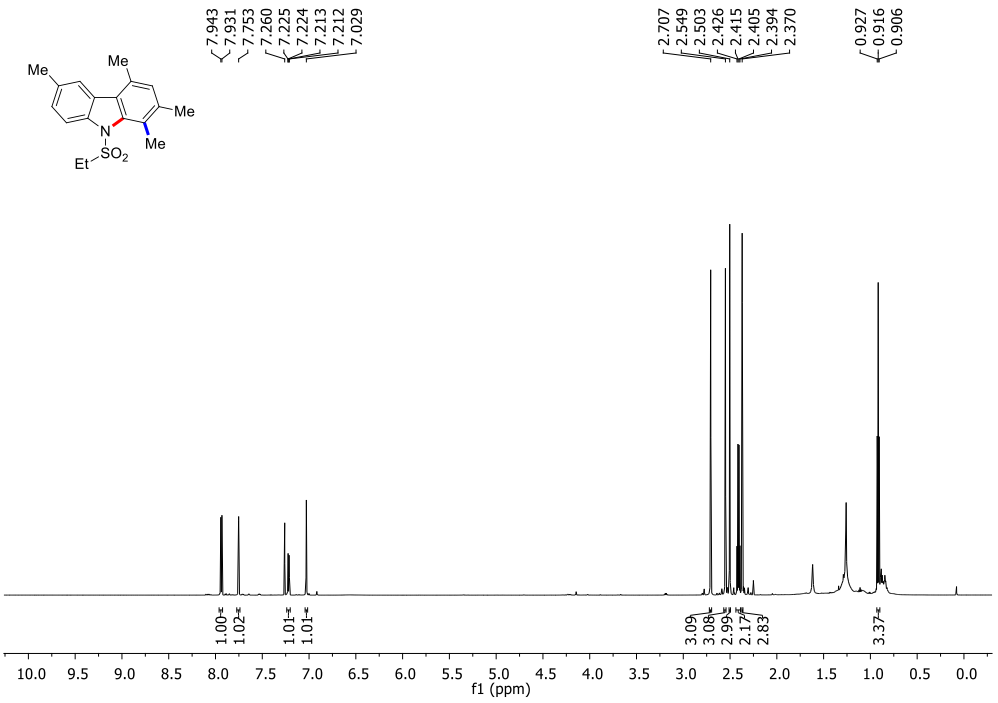


Figure 3.63 ^{1}H NMR spectrum of 9-(Ethylsulfonyl)-1,2,4,6-tetramethyl-carbazole (**3p**)

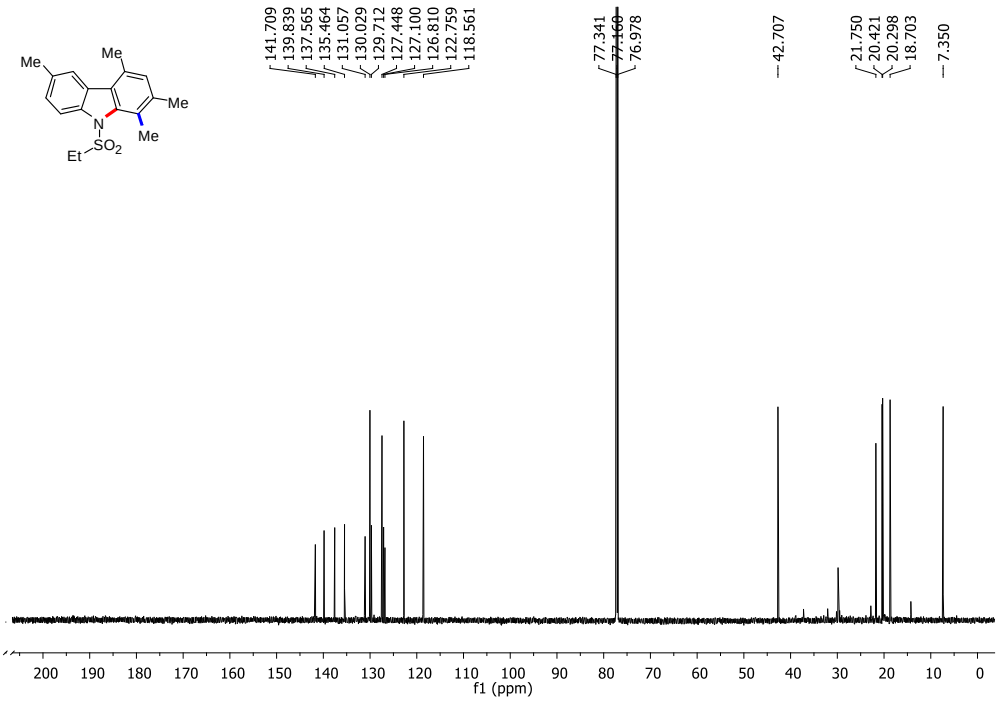


Figure 3.64 ^{13}C NMR spectrum of 9-(Ethylsulfonyl)-1,2,4,6-tetramethyl-carbazole (**3p**)

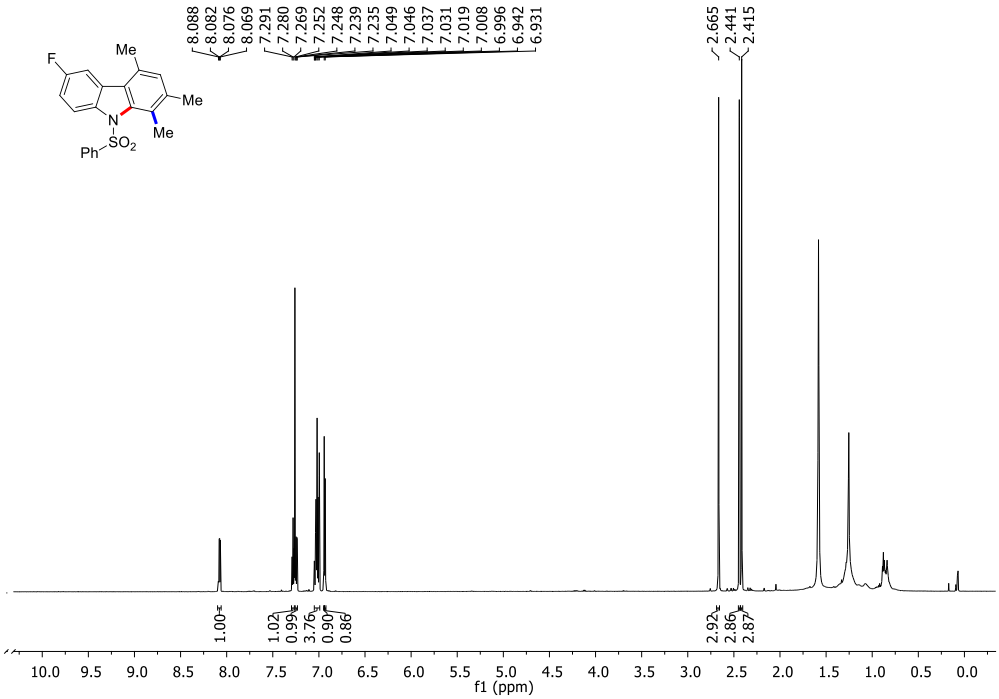


Figure 3.65 ^{1}H NMR spectrum of 6-Fluoro-1,2,4-trimethyl-9-(phenylsulfonyl)-carbazole (**3q**)

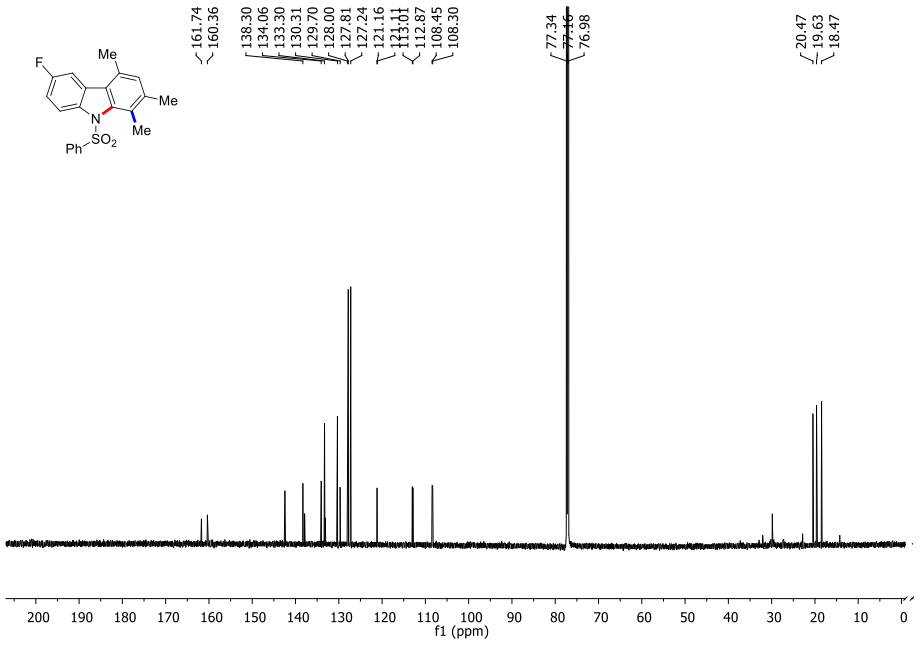


Figure 3.66 ^{13}C NMR spectrum of 6-Fluoro-1,2,4-trimethyl-9-(phenylsulfonyl)-carbazole (**3q**)

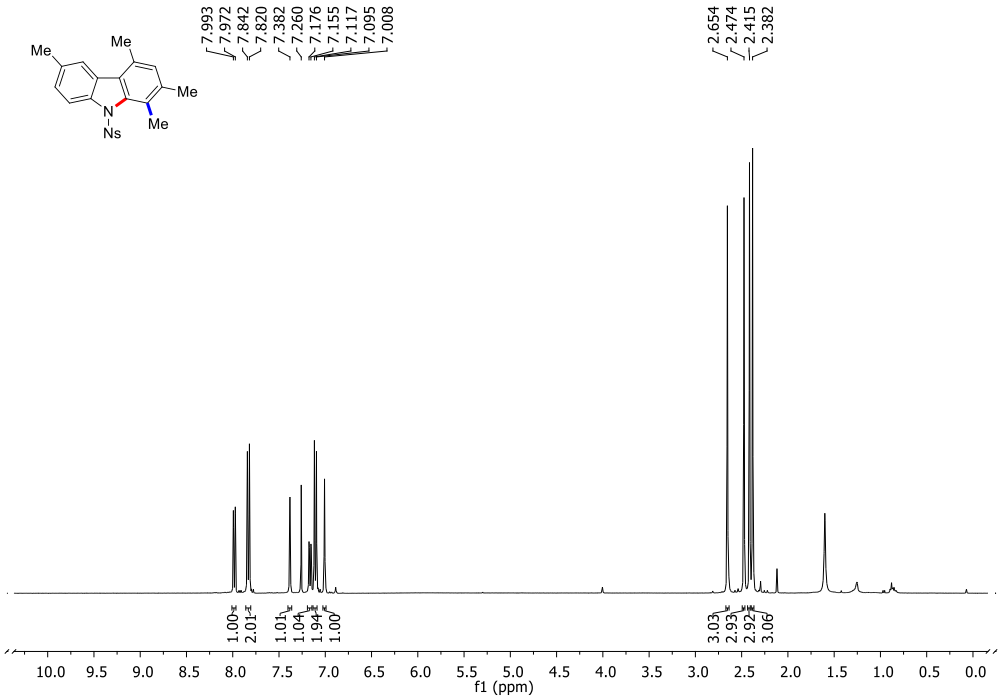


Figure 3.67 ^{1}H NMR spectrum of1,2,4,6-Tetramethyl-9-(4-nitrophenylsulfonyl)-carbazole **(3r)**

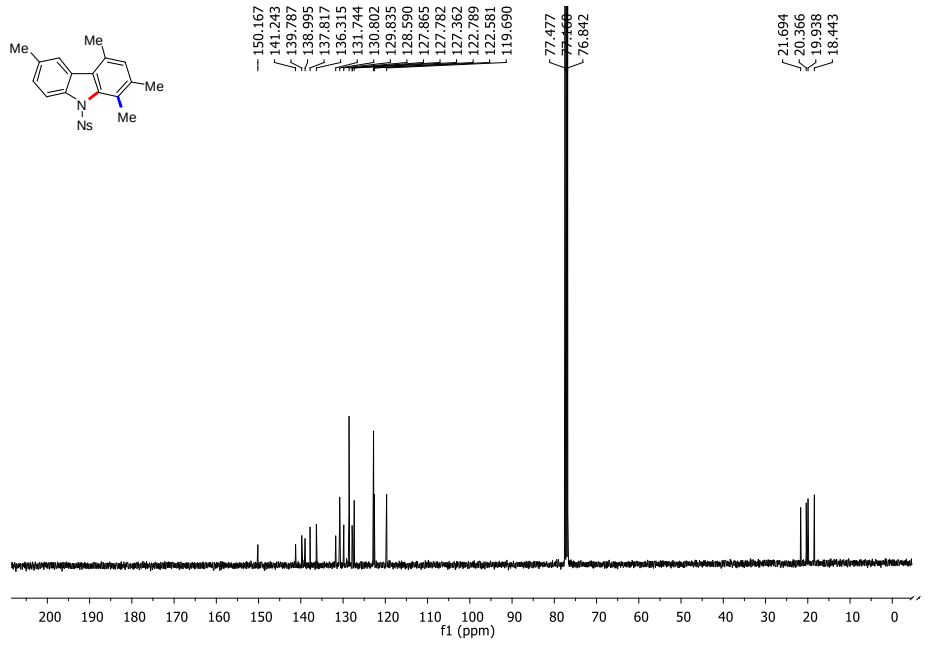


Figure 3.68 ^{13}C NMR spectrum of 1,2,4,6-Tetramethyl-9-(4-nitrophenylsulfonyl)-carbazole **(3r)**

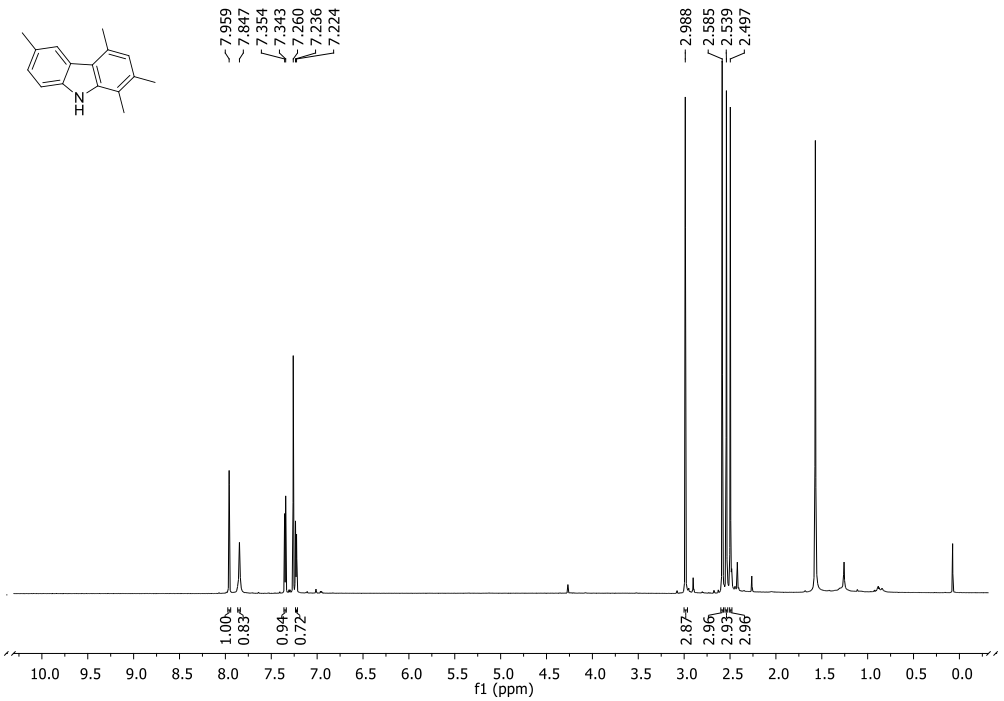


Figure 3.69 ^{1}H NMR spectrum of 1,2,4,6-Tetramethyl-9*H*-carbazole **(4)**

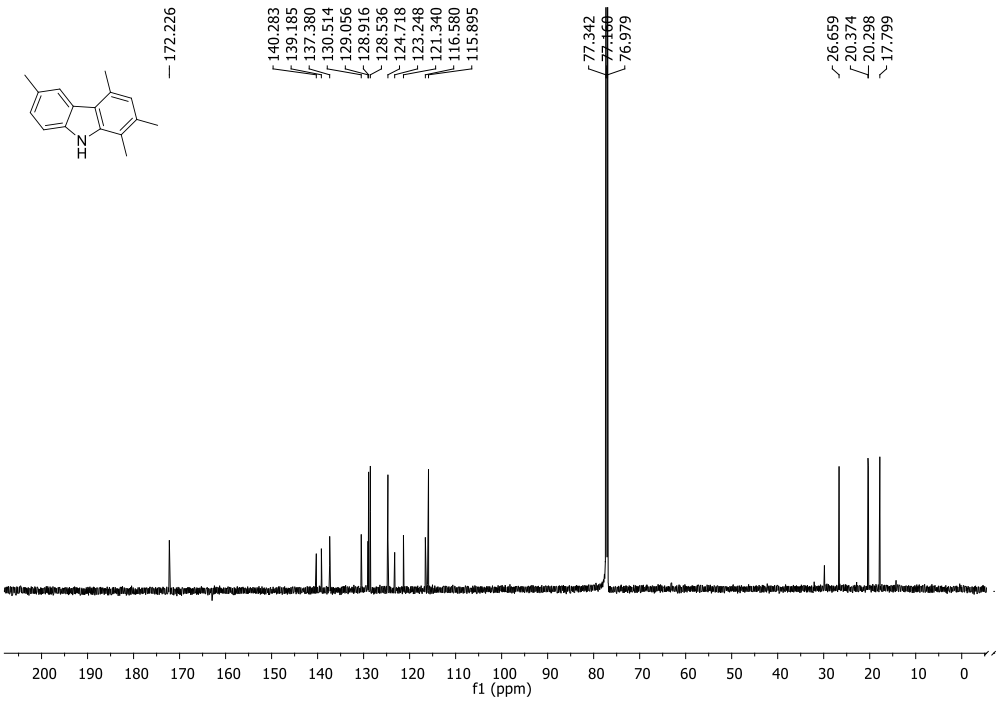
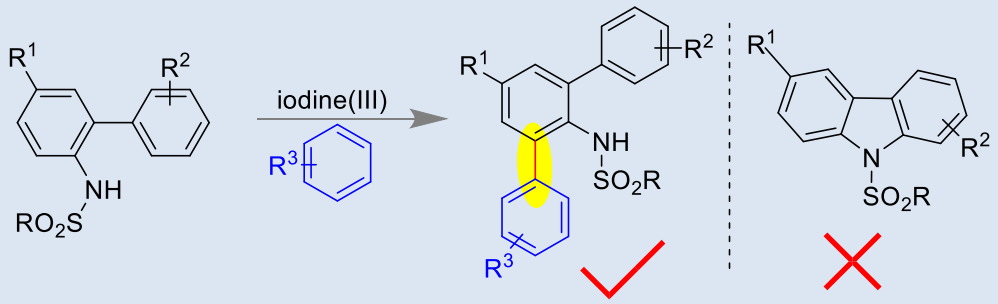


Figure 3.70 ^{13}C NMR spectrum of 1,2,4,6-Tetramethyl-9*H*-carbazole **(4)**

CHAPTER 4

Intermolecular C-C Coupling of 2-Amidobiphenyls using Iodine(III) Reagent

4.1 ABSTRACT



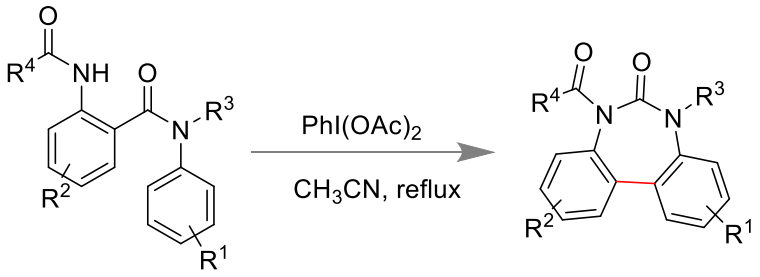
The 2-Amidobiphenyls undergo intramolecular N–H arylation when an oxidant like hypervalent iodine(III) reagent is employed in the reaction system. Treatment of 2-amidobiphenyl and an arene with $PhI(OAc)_2$ as a sole oxidant using mesitylene as nucleophile led to intermolecular C–H arylation by suppressing intramolecular oxidative C-N coupling . A scale of biaryalsulfonamides were designed yielded the targeted triaryl motifs in moderate to good yield.

4.2 INTRODUCTION

The essence of organic synthesis lies in the construction of C-C bond reactions[1-4] as it has given rise to numerous methodologies for effective transformations, which has been highly

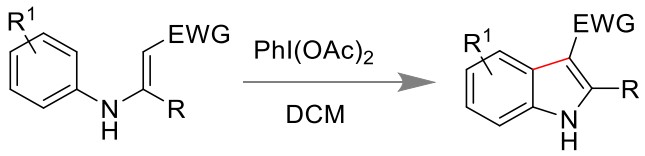
beneficial in the synthetic community. Traditional methods, including conversions assisted by a template, have grown in recent times to functionalize an unactivated aromatic system.[5-7] Several methods are reported with metals for C-H bond functionalization of 2-amidobiphenyl as a precursor.[8-10] Hypervalent iodine(III) reagents that are inexpensive, mild, and can be easily handled at room temperature have been utilized to construct C-C bond.[11, 12] Very few research groups are involved in exploring C-H bond functionalization under metal free condition.[13-15] Hypervalent iodine(III) reagents are employed in various oxidative transformations[16-18] and in achieving various cyclization for the construction of bioactive molecules. The recent decade has witnessed the utilty of hypervalent iodine(III) reagents as metal free reagents working in environmentally benign conditions.[2, 19-21] Buchwald and co-workers have demonstrated the use of iodine(III) reagents to functionalize biaryl acetamide for synthesis of carbazoles.[22] The *N*-protected biarylamine and its oxidative cyclisation has been extensively reported under metal and metal free conditions.[23, 24 25, 26] Oxidative cyclisation of 2-amidobiphenyl moiety to multisubstituted carbazoles is a well-explored reaction system in the presence of an oxidant or light.[27-29]

Carbon carbon bond formation reactions involving iodine(III) reagents which have used been to construct significant structural motifs. Zhao group has developed an intramolecular aryl-aryl coupling by rearranging *N*-phenyl benzamides by employing hypervalent iodine(III) reagents.[30]



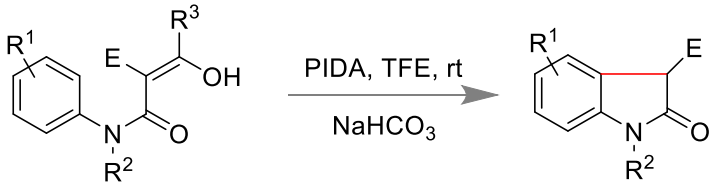
Scheme 4.1 Intramolecular aryl-aryl coupling using hypervalent iodine(III) reagent.

N- aryl enamines were used to construct the C-C bond of the indole based moieties by hypervalent iodine(III) reagents.[11] The proposed methodology involved enormous functional group tolerance under metal free conditions and mild reaction conditions.



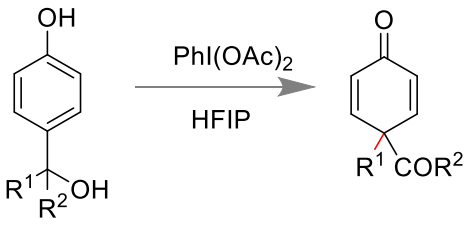
Scheme 4.2 Synthesis of indole based scaffold using hypervalent iodine(III) reagent.

A series of monofunctionalized oxindoles were synthesized by Zhao group using phenyl iodine diacetate (PIDA). C-C bond was formed along with deacylation to give oxoindole as a product which could be easily used to transform to naturally occurring horsfiline.[1]



Scheme 4.3 Synthesis of oxindoles using hypervalent iodine(III) reagent.

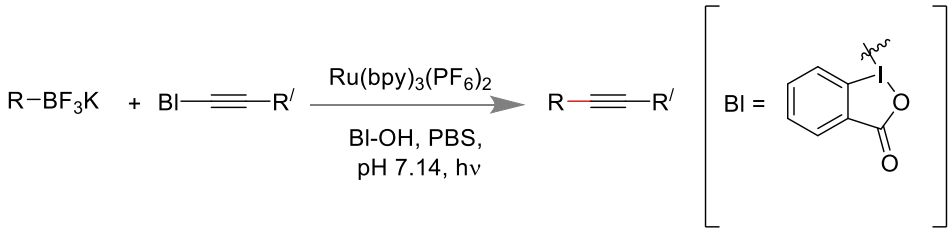
C-C bond formation reactions have been elucidated by Sylvian Canesi where an oxidative Wagner Meerwin rearrangement has been established mediated by iodine(III) reagent.[31] The strategy of aromatic ring umpoloung has been established for the synthesis of highly functionalized moieties.



Scheme 4.4 Oxidative Wagner Meerwin transposition using hypervalent iodine(III) reagent.

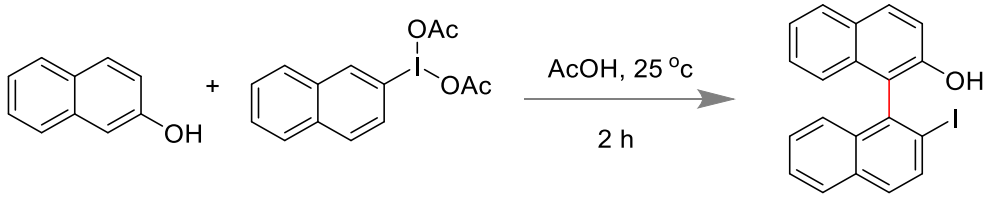
Chen and co-workers have used primary, secondary, and tertiary alkyl trifluoro borates to demonstrate deboronative alkynylation reaction to construct silyl, alkyl and allyl substituted

alkynes.[32] C-C bond formation reaction was developed using cyclic iodine(III) reagents with photoredox catalyst.



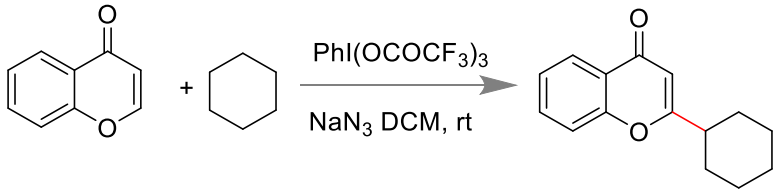
Scheme 4.5 Deboronative alkynylation reaction using hypervalent iodine(III) reagent merged with photoredox catalyst.

Biaryls were synthesized by Yorimitsu and co-workers *via* sigmatropic rearrangement by coupling hypervalent iodine(III) reagents with phenol for dehydrogenative C-C coupling. [33] The reaction underwent ligand exchange at the iodine center, followed by [3,3] sigmatropic rearrangement with regioselectivity to form the product. C-C bond formation reaction using mild hypervalent iodine(III) reagents is convenient to bring about effective transformations in organic synthesis under metal free conditions.



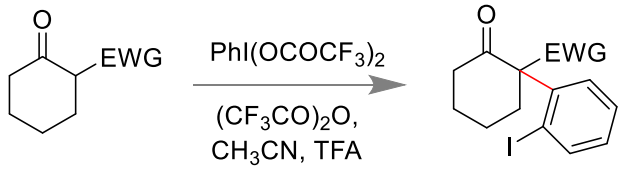
Scheme 4.6 Dehydrogenative biaryl synthesis via 3,3 sigmatropic rearrangement.

Antonchick group has illustrated the functionalization of selective aliphatic C-H bonds of thiochromones and chromones at the C_2 position.[34] Direct oxidative functionalization of chromones mediated by hypervalent iodine(III) reagent under mild conditions took place to produce functionalized chromones which are bioactive products. Cyclohexane is activated by proton abstraction by the azidyl radical generated from $PhI(OCOCF_3)_2$ and NaN_3. The nucleophilic cyclohexyl radical attacks the most electrophilic C_2 position of the chromone followed by oxidation to form the cross coupled product.



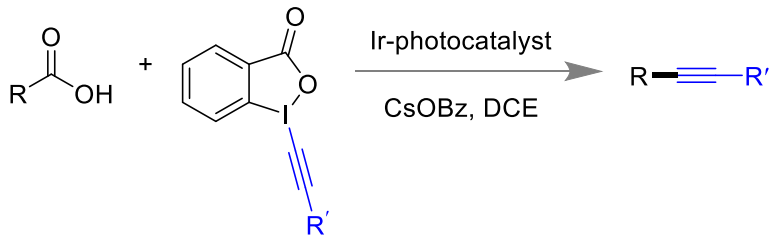
Scheme 4.7 Synthesis of functionalized chromones mediated by hypervalent iodine(III) reagent.

Synthesis of α-(2-iodoaryl)ketones by rearrangement of an iodonium enolate by α arylation of a carbonyl compound without use of base was accomplished using hypervalent iodine reagent ($ArI(O_2CCF_3)_2$) as the source of aryl group.[35] The protocol was extended to activated ketones, like α-cyanoketones and substituted aryliodanes. C-H functionalization of the keto compound proceeded *via* [3,3] rearrangement of an iodonium enolate.



Scheme 4.8 Synthesis of α-(2-iodoaryl)ketones mediated by $PhI(OCOCF_3)_2$ (PIFA).

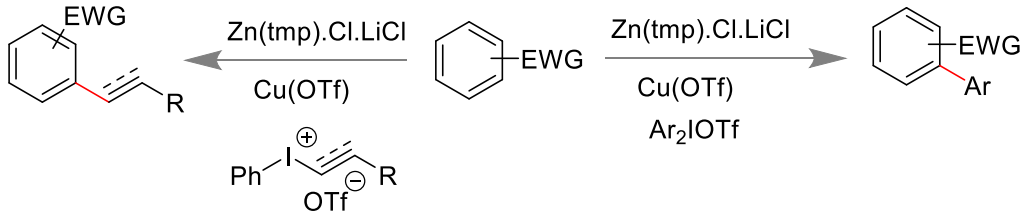
Waser group had reported decarboxylative alkynylation with EBX as the source of alkyne using Ir as protocatalyst under visible light irradiation.[36] Authors speculated that sunlight and blue LED was sutiable enough to produce the desired C-C bond.



Scheme 4.9 Decarboxylative alkynylation using photoredox catalysis and EBX reagent.

Diverse heteroaryl compound synthesis by formation of carbon-carbon bond was illustrated by Wang and co-workers by C-H zincation followed by coupling of iodonium salts with Cu

metal.[37] Various arylation, alkynylation, and vinylation were possible to attain under mild conditions to give acesss to wide scope of heterobiaryls.



Scheme 4.10. Arylation and alkenylation using iodonium salt.

The previous approaches for construction of C-C bond involve usage of iodine based reagents. Our approach was to use the hypervalent iodine(III) reagents for construction of terphenyls. The synthetic utility of carbenium ion intermediate over the nitrenium ion which is formed by reacting biaryl sulfonamides with iodine(III) reagents is a rare phenomena due to superior reactivity of nitrenium ion. In order to address this fundamental challenge, we targeted to develop an intermolecular coupling reaction by controlling the possibility of intramolecular coupling. 2-aminobiphenyl was chosen as the substrate which can undergo both intramolecular coupling in a more facile way. It was our assumption that a suitable nucleophile of choice controls the outcome of the reaction. The potential nucleophilicilty of the external nucleophile suppressed the intramolecular C-N coupling and intermolecular C-C coupling was successfully achieved employing hypervalent iodine(III) reagents that are potentially strong oxidants. C-H arylation took place intermolecularly and preceded oxidative C-N coupling. Unsymmetrical 2,6-diaryl anilides were synthesized using PIDA as the sole oxidant for the transformation to take place at room temperature open atmosphere condition under metal-free conditions. The arylsulfonyl groups controlled the reactivity of nitrenium ion to react with the external arene in an intermolecular fashion

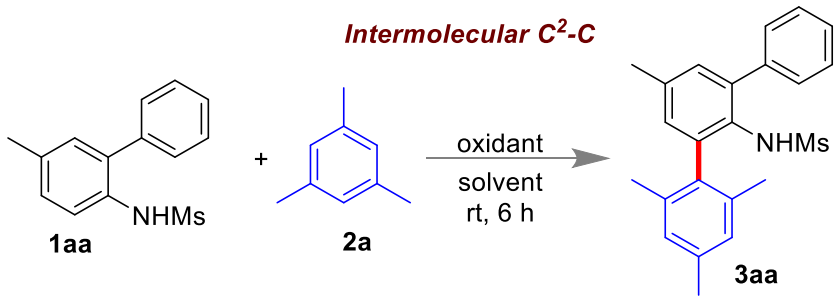
suppressing the route oxidative C-N coupling. 2,6-Diaryl aniline derivatives are useful synthetic intermediates effective in various synthetic transformations.[38, 39] Literature studies show that symmetrical 2,6-diarylanilide derivatives were constructed from Pd-catalyzed arylation acetanilide.[40] Unsymmetrical 2,6-diarylanilides were synthesized under metal free conditions, which have not been reported so far. Site-selective intermolecular C-C or C-N coupling reactions were also applicable *via* orthogonal reaction modulation strategy[41] by the stereoelectronic control on the generated nitrenium ions. [42, 43] Recent reports on orthogonal strategies[41] have been applied in various research areas like organic synthesis,[44, 45] organometallic chemistry,[46] supramolecular chemistry[47] mechanochemistry,[48] etc. 2-amidobiphenyls undergo intramolecular N-H arylation in the presence of hypervalent iodine(III) reagents followed by cyclization through C-N coupling reaction.[28, 49] This work shows an unusual intermolecular C-C coupling reaction of 2-amidobiphenyl by electronic control involving a carbenium ion over a nitrenium ion. An array of substrates were designed, which afforded the targeted *C*-arylated product in moderate to good yield furnishing terphenyls. The electronic factor played a significant role in controlling the formation of the product. As a result, we could successfully show that the substrate and the nucleophile control the selectivity for intermolecular arylation preferred over intramolecular arylation.

4.3 RESULTS AND DISCUSSION

We established the intermolecular C^2-H arylation by employing the arene of the biaryl sulfonamides possessing various electron-deficient groups or the nucleophilicity of the external nucleophile. The reaction was optimized taking *N*-(5-methyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**1a**) and mesitylene (**2a**) in (Table 4.1) for synthesis of *N*-

(2,4,5',6-tetramethyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (**3aa**) by involving 1.0 equiv of PIDA, in 1,1,1,3,3,3 hexafluoroisopropanal (HFIP), yield of C^2-H arylated product (**3aa**) was obtained with 64% yield (entry 1). However on increasing the proportion of PIDA to 1.2 equiv, the yield was further reduced to 60%, (entry 2). Increasing the portion of PIDA to 1.5 equiv further resulted in drastic reduction of 34% (entry 3). Other Iodine(III) oxidants were taken into account, but it was found to be ineffective with PIFA where yield got reduced to 5% (entry 4), whereas $PhI(OPiv)_2$ produced an appreciable good yield of 62%. (entry 6). Solvents like 2,2,2-trifluoroethanol (TFE) were afforded to produce the desired product in good yield, but the reaction did not proceed in DCM and DCE solvent. This indicates that a fluorinated solvent is desirable for the stabilization of the generated nitrenium ion intermediate.

Table 4.1. Optimization for the intermolecular C^2-C reaction.[a]



entry	oxidant (equiv)	solvent	yield (%)[b]
1	PIDA (1.0)	HFIP	64
2	PIDA (1.2)	HFIP	60
3	PIDA (1.5)	HFIP	34
4	PIFA (1.0)	HFIP	5
5	PIDA (1.0)	TFE	60
6	$PhI(OCOPiv)_2$ (1.0)	HFIP	62

7	PIDA (1.0)	DCM	0
8	PIDA (1.0)	DCE	0

[a]Reaction conditions: 1.0 equiv (0.153 mmol) of **1a**, 10 equiv of mesitylene (1.53 mmol) of (**2a**); Yield of isolated products after column chromatography.

C^2-C arylation products were obtained when biaryl sulfonamides with unsubstitution in phenyl ring with various alkyl-substituted aryl based arenes (Figure 4.1a). It was observed that mesitylene, anisole and *m*-xylene produced good yield of products with methyl and isopropyl group substituted biarylsulfonamide (**3aa-bc**). *tert*-Butyl substituted amidobiphenyl reacted with electron-rich arenes like mesitylene, 1,3,5-triethyl benzene and anisole to lead to the formation of the desired product in sufficient quantity (**3ca-cb**). Substrates containing various other protecting groups like ethanesulfonyl, produced the product in appreciable yield. (**3da-dd)**. The electronic effect of 2-amidobiphenyls were monitored with para-substituted electron withdrawing fluorine group on the arene moiety. Also, arene part of the biphenyl system was made electron deficient, so that same C^2-C arylation was achieved under standard reaction conditions. (Figure 4.1b). Arenes like mesitylene and 1,3,5-triethybenzene were used as arenes to generate the desired product in sufficiently good yield (**3ea-fd**). Amidobiphenyls substituted by mesyl group gave rise to moderate yield of products with halogen-substituted group in other part of arene (**3ga-gd**). When acetyl group was introduced in the other part of arene in the 2-amidobiphenyl moiety, it was found that reaction was successfully achieved to form the C-H arylated product in appreciable (71%, **3hd**) yields. A nitro group at arene of biphenyl unit also made the

reaction turn fruitful with electron-rich arenes like *m*-xylene and 1,3,5-triethyl benzene producing the desired products in sufficient yields(**3ic-id**). An array of substrate scopes was prepared to portray how the electronic factor resulted in the formation C^2-C arylation product overcoming the more facile intramolecular C-N coupling.

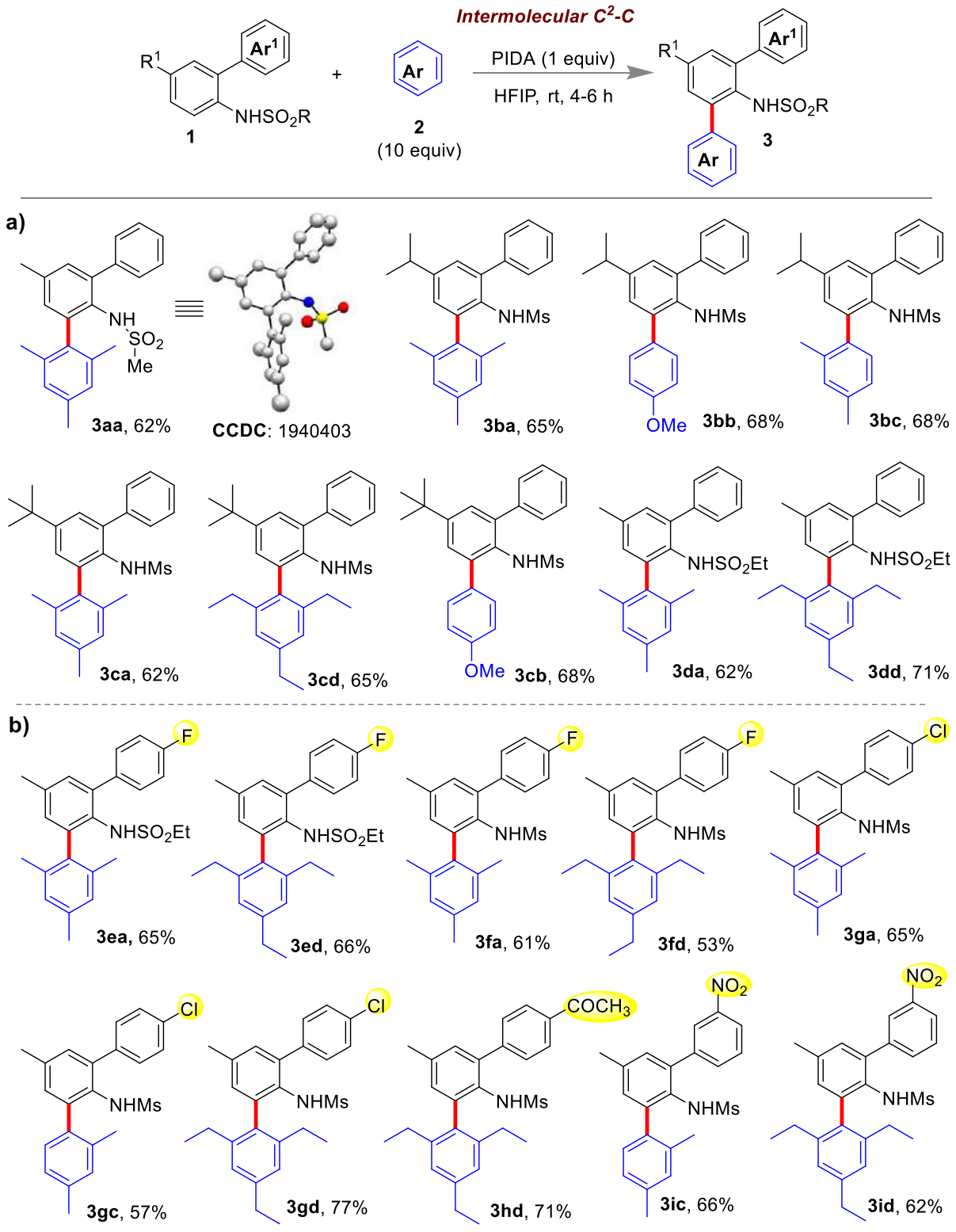


Figure 4.1. Substrate scope of biaryl sulfonamides with hypervalent iodine reagent PIDA and arenes. a) varying nucleophiles b) varying arene part of the biaryl sulfonamides with electron deficient group. Reaction conditions: 1.0 equiv of **1**, 10.0 equiv of arene **2** and 1.0 equiv of PIDA in HFIP.

Under similar reaction conditions, *para*-unsubstituted aminobiphenyl produced arylation at C^4-position. We thereby anticipated that the reaction was sterically controlled *via* carbenium ion intermediate.[42] The more stable carbenium was formed at the *para* position, which reacted with the nucleophile 1,3,5-triethyl benzene to undergo intermolecular arylation in a facile approach. This methodology was previously well-established in the literature.[50] So, we did not investigate it further, and as a representative example, the synthesis of **4jd** has been shown in Figure 4.2.

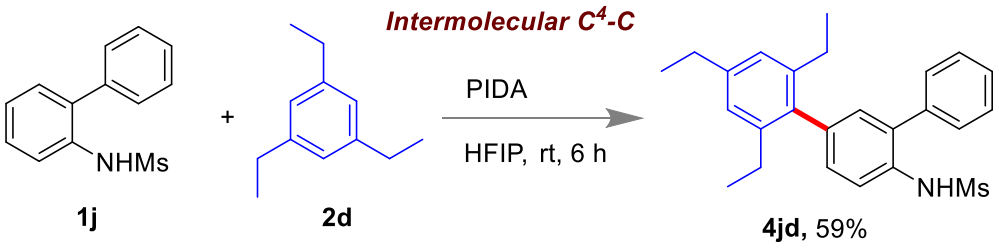


Figure 4.2. Scope for biphenyl methanesulfonamide. Reaction conditions: 1.0 equiv of **1j**, 10 equiv of triethyl benzene and 1.0 equiv of PIDA in HFIP.

Further we went on to establish the stereoelectronic controlled intermolecular C-N bond formation reaction. The steric effect of the sulfonyl group was investigated by employing a tosyl protected biaryl amine or a benzene sulfonyl protecting group with different arenes which formed the *N*-arylated product in 1.0 equiv of PIDA and solvent HFIP **5kd-la** (Figure 4.3). As described by Canesi, the σ donation effect of the mesyl group[51] to stabilize the positively charged aromatic ring is one of the probable reasons for forming an intermolecular

N- arylated product. The steric effect hindered the formation of carbenium ion where nucleophilicity of the arene ring in amidobiphenyl moiety was reduced because of the presence of the fluoride group. Rapid attack at the nitrenium ion took place by the external arene nucleophile, which formed *N*-arylation product.

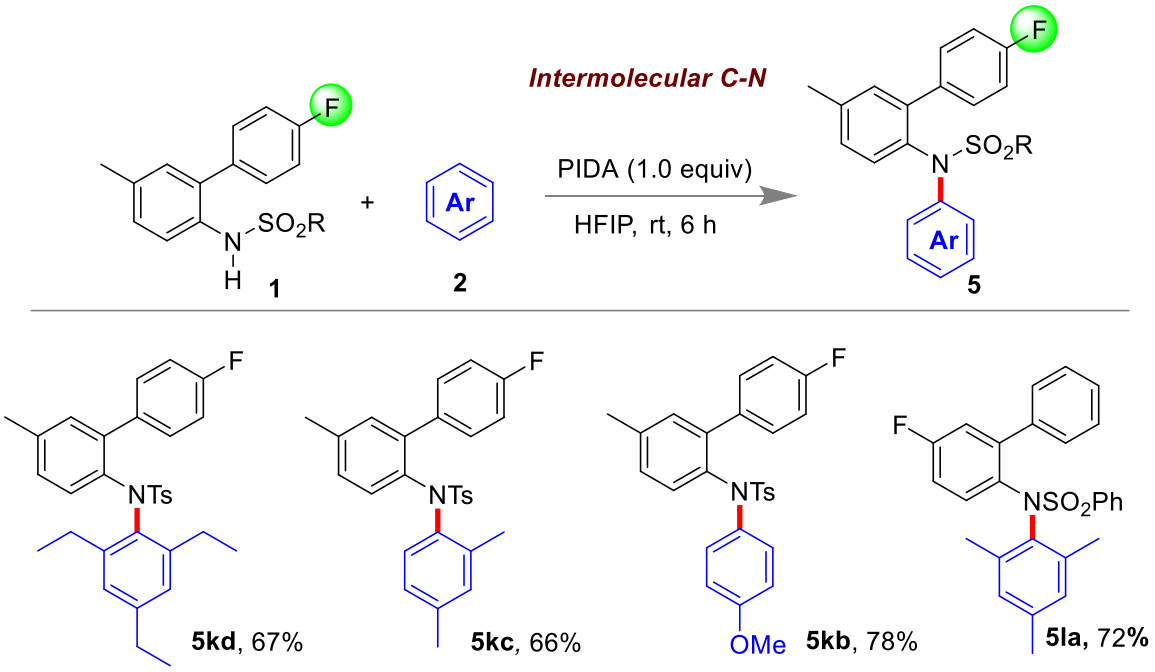


Figure 4.3. Scope for intermolecular C-N bond formation with biarylsulfonamides. Reaction conditions: 1.0 equiv of **1**, 10 equiv of arene **2** and 1.0 equiv of PIDA in HFIP.

The controlling factor which promotes intermolecular C-C coupling reaction was found to be more feasible than intramolecular C-N coupling. Out of curiosity, we investigated the reaction outcome by making the arene part of the biarylsulfonamide electron-rich by introducing a substituent with electron-donating methyl or methoxy group. C_2-H functionalization was hindered, and intramolecular C-N bond formation produced carbazole as a product. The use of mesitylene was the arene source that led to the synthesis of carbazoles (**6a-d**) which were isolated in good to moderate yield. On taking toluene as an external nucleophile, carbazole formation predominantly took place to obtain the products in good yields (**6e-f**), as displayed in figure 4.4.

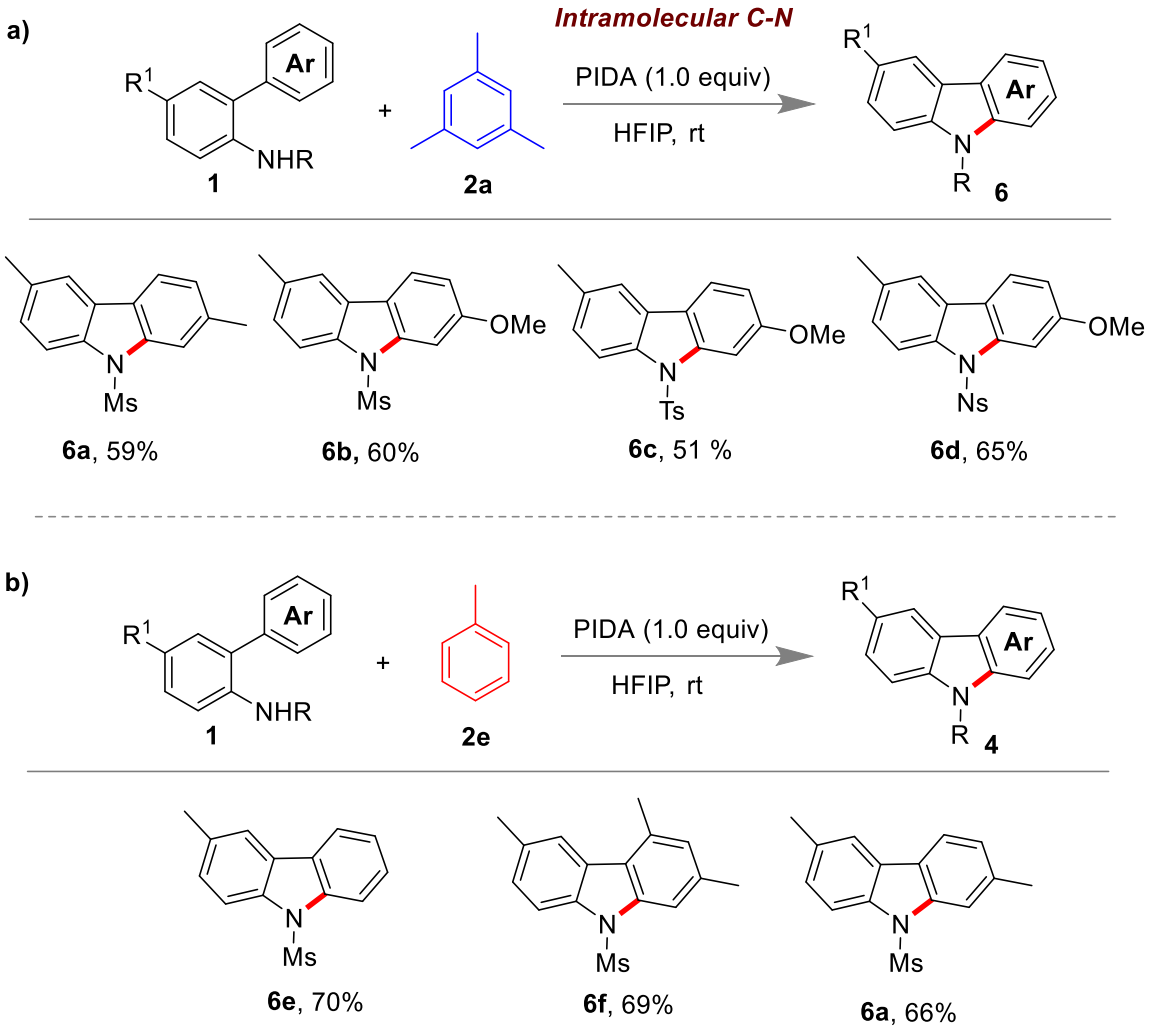


Figure 4.4 Scope for intramolecular C-N coupling for a) and b)nuclephiles. Reaction conditions: 1.0 equiv of **1**, 10.0 equiv of arene **2** and 1.0 equiv of PIDA in HFIP.

Gram scale synthesis of the established methodology was done with 3.82 mmol of amidobiphenyl **1a** and mesitylene **2a**, in the same reaction condition which formed that C^2-C arylated product in good yield (Figure 4.5).

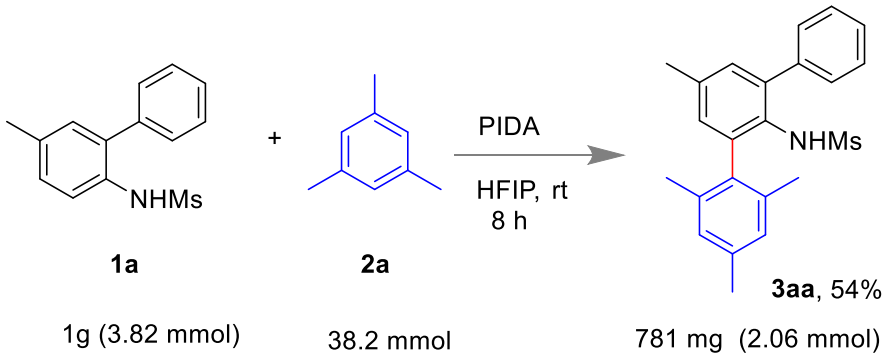


Figure 4.5. Large scale synthesis of **3aa**. Reaction conditions: 1.0 equiv of **1**, 10 equiv of arene **2a** and 1.0 equiv of PIDA in HFIP.

4.4 CONCLUSIONS

In short, we have achieved to produce an intermolecular C^2-H arylation product overcoming the more facile intramolecular C-N coupling product in the presence of an oxidant. The stereoelectronic factor plays a significant role in controlling the outcome for the formation of either of four possible C-C or C-N coupling reaction products. Intermolecular C^4-C, intermolecular C^2-C, intermolecular C-N, or intramolecular C-N bond formation reactions were formed in a particular condition which reestablished orthogonal reactivity modulation approach.[45] In most of the cases, the major products were isolated. Trace amount of minor products was formed but could not be separated. Other arenes were used, which showed that the nucleophilicity of the arene along with steric and electronic environment are the major ruling factors on the fate of a reaction. We anticipated that this methodology would be useful to understand the reactivity control of reaction intermediates which would thereby provide a new opportunity to

organic chemists for constructing expedient methods for the synthesis of terphenyl motifs under mild metal-free conditions.

4.5 EXPERIMENTAL SECTION

General methods. Chromatographic (Column) purifications of the compounds were done using silica gel (mesh 230–400) and hexane – ethyl acetate mixtures as eluent unless otherwise specified. NMR spectra had been recorded 700 MHz or 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 ppm for ^{13}C). The peak patterns are designated as follows: s: singlet; d: doublet; t: triplet; q: quartet; m: multiplet; dd: doublet of doublets; td: triplet of doublets; brs: broad singlet. The coupling constants (*J*) were reported in hertz (Hz). High-resolution mass spectra (HR-MS) were recorded on an ESI-TOF (time of flight) mass spectrometer. Infrared (IR) spectral data are reported in wave number (cm^{-1}). FT-IR spectra were recorded after making thin layer of the compounds on the surface of NaCl crystal using dichloromethane. Good quality crystals of the compounds **3aa** were obtained after slow evaporation of ethyl acetate solution. The crystals data were collected with Bruker SMART D8 goniometer equipped with an APEX CCD detector and with an INCOATEC micro source (Cu-Kα radiation, λ = 0.71073 Å). SAINT+[52] and SADABS[53] were used to integrate the intensities and to correct the absorption respectively The structure was resolved by direct methods and refined on F^2 with SHELXL-97.[54]

Representative method for preparation of *N*-(2,4,5',6-tetramethyl-[1,1' : 3', 1''-terphenyl]-2'-yl) methanesulfonamide (**3aa**)

To *N*-(5-methyl-[1,1'-biphenyl]-2-yl)methanesulfonamide **(1a)** (40 mg, 0.153 mmol) in 2 ml HFIP, mesitylene as the arene source (213 µl, 1.530 mmol) was added followed by addition of the hypervalent iodine reagent PIDA (50 mg, 0.153 mmol) dissolved in 1 ml HFIP . The reaction mixture was shaken for 6 h at room temperature. Following, the reaction mixture was evaporated to complete dryness to afford the product *N*-(2,4,5',6-tetramethyl-[1,1' : 3', 1"- terphenyl]-2'-yl) methanesulfonamide (**3aa**) which was isolated by column chromatography to obtain white solid 39 mg (62%) at 5% ethyl acetate hexane.

Representative method for preparation of *N*-(5-methyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (1aa).

To a solution of *p*-toluidine (500 mg, 4.67 mmol) in acetonitrile solvent kept at 0 °C, N-bromosuccinimide (935 mg, 5.60 mmol) was added portionwise to the stirred solution. The reaction mixture was shaken for 2 h.When the reaction mixture was evaporated to dryness and redissolved in dichloromethane. Aqueous work up was done to remove the succinimide byproduct. The volatile portion was then removed in vacuum and brown oily liquid was obtained as prouct. In many substrates, starting material was left in reaction mixture which required isolation by column chromatography isolated using 8% ethyl acetate hexane.[55]

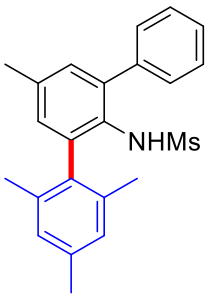
In a dry sealed tube, phenyl boronic acid (1.5 equiv), K_2CO_3 (4 equiv) and $Pd(PPh_3)_4$ were dissolved in a mixture of toluene: ethanol: water in ratio 3:2:1. 2 Bromoaniline was poured to the resulting solution and the reaction mixture was heated at 80 ^{0}C for 24 h. After cooling to room temperature, the biphasic reaction mixture was diluted with ammonium chloride and CH_2Cl_2.The combined organic phase was extracted twice with DCM (50 ml X 2) and the organic phase was dried over Na_2SO_4 and filtered. The filtrate was concentrated and isolated by column chromatography on silica gel afforded the product (yield 50-70%)[56].

The biphenyl amine was protected using mesyl chloride (1.5 equiv) by its slow addition in a solution of substrate and pyridine (1.2 equiv) dissolved in

dichoromethane at 0 ^{0}C. The reaction mixture was stirred at room temperature for 2 h to afford the desired product. The reaction mixture was quenched with NH_4Cl and the resuting solution was extracted with DCM twice (50 ml *2) and the organic phase was dried over Na_2SO_4 and filtered. White solid (**1aa**) was obtained when the filtrate was evaporated which was redissolved in ethanol to obtain recrystallised product with 70% yield.

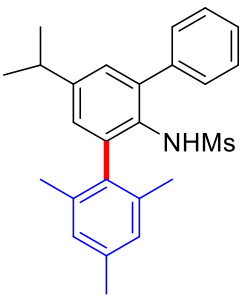
Compound Characterization Data

***N*-(2,4,5',6-tetramethyl-[1,1' : 3', 1''- terphenyl]-2'-yl) methanesulfonamide** (**3aa**): R_f =



0.4 (hexane : ethyl acetate 9:1); white solid; 38 mg (62%); mp 204-206 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.43 (m, 4H), 7.38 – 7.35 (m, 1H), (d, *J* = 6.8 Hz, 1H), 7.13 (d, *J* = 1.6 Hz, 1H), 6.97 (s, 3H), 5.58 (s, 1H), 2.38 (s, 3H), 2.32 (s, 3H), 2.09 (s, 6H), 1.91 (s, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.7, 139.2, 137.7, 137.6, 137.0, 136.6, 135.3, 130.9, 130.8, 130.4, 130.2, 128.7, 128.6, 127.7, 41.9, 21.2, 21.1, 20.6; IR (KBr) $\tilde{\nu}$ = 3438, 1635, 1317, 1146 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{23}H_{25}NO_2SNa$ 402.1498; found 402.1517.

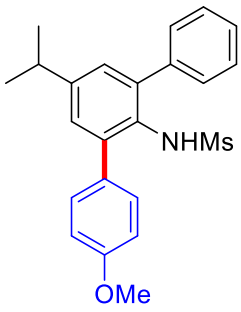
***N*-(5'-isopropyl-2,4,6- trimethyl- [1,1': 3', 1''-terphenyl]-2'-yl)methanesulfonamide**



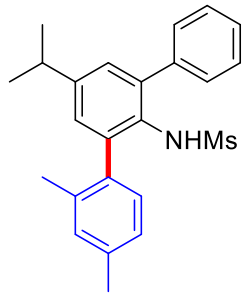
(3ba): R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 37 mg (65%); mp 210 −212 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.44 (m, 4H), 7.39 – 7.36 (m, 1H), 7.15 (d, *J* = 1.6 Hz, 1H), 7.02 (d, *J* = 2.0 Hz, 1H), 6.98 (s, 2H), 5.62 (s, 1H), 2.94 (*sept*, *J* = 6.8 Hz, 1H), 2.33 (s, 3H), 2.09 (s, 6H), 1.92 (s, 3H), 1.28 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (175 MHz,

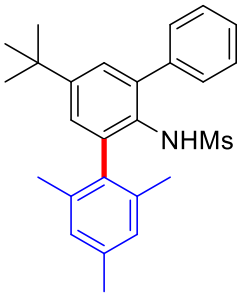
$CDCl_3$) δ 147.6, 140.0, 139.2, 137.7, 137.5, 137.1, 135.7, 130.5, 130.2, 128.7, 128.6, 128.4, 128.2, 127.7, 42.0, 33.7, 24.1, 21.2, 20.6; IR (KBr) $\tilde{\nu}$ = 3438, 1643, 1556, 1503 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{25}H_{29}NO_2SNa$ 430.1811; found 430.1810.

***N*-(5'-isopropyl-4-methoxy-[1,1': 3',1''- terphenyl]-2'-yl)methanesulfonamide) (3bb) :** R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 37 mg (68%); mp 205 − 207 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.50 (m, 4H), 7.45 – 7.40 (m, 3H), 7.19 (s, 2H), 7.03 (dd, *J* = 6.8, 2.0 Hz, 2H), 5.84 (s, 1H), 3.88 (s, 3H), 2.97 (*sept*, *J* = 6.8 Hz, 1H), 2.03 (s, 3H), 1.32 (s, 3H), 1.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 148.0, 140.4, 140.2, 140.1, 132.1, 131.2, 130.2, 129.3, 128.8, 128.6, 128.4, 127.7, 114.2, 55.4, 42.1, 33.8, 24.0; IR (KBr) $\tilde{\nu}$ = 3445, 2959, 1733, 1635, 1318, 1146 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{23}H_{25}NO_3SNa$ 418.1447; found 418.1446.



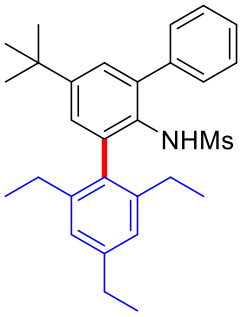
***N*-(5'-isopropyl-2,4-dimethyl-[1,1': 3',1''-terphenyl]-2'-yl)methanesulfonamide (3bc):** R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 37 mg (68%); mp 128 − 130 °C; **¹**H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.44 (m, 4H), 7.42 – 7.38 (m, 1H), 7.20 (d, *J* = 7.6 Hz, 1H), 7.16 (d, *J* = 2.0 Hz, 1H), 7.12 (s, 1H), 7.10 (s, 1H), 7.08 (d, *J* = 1.8 Hz, 1H), 5.67 (s, 1H), 2.94 (*sept*, *J* = 7.2 Hz, 1H), 2.36 (s, 3H), 2.17 (s, 3H), 1.94 (s, 3H), 1.28 (s, 3H), 1.27 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 147.5, 139.8, 139.5, 139.2, 137.9, 136.6, 136.4, 131.2, 130.6, 130.2, 130.0, 128.7, 128.6, 128.4, 127.8, 126.7, 41.9, 33.8, 24.1, 23.9, 21.3, 20.1; IR (KBr) $\tilde{\nu}$ = 3438, 2089, 1644, 1644, 1456, 1318, 1147 cm^{-1};HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{24}H_{27}NO_2SNa$ 416.1655; found 416.1672.



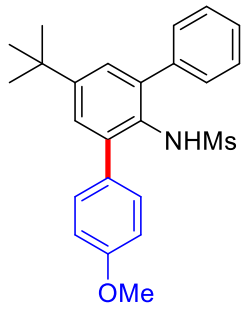


***N*-(5'-(tert-butyl)-2,4,6-trimethyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (3ca):** R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 35 mg (62%); mp 245 – 247 °C ; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.51 – 7.49 (m, 2H), 7.47 (t, *J* = 8.4 Hz, 2H), 7.39 (t, *J* = 7.0 Hz, 1H), 7.29 (d, *J* = 2.1 Hz, 1H), 7.17 (d, *J* = 2.1 Hz, 1H), 6.99 (s, 2H), 5.62 (s, 1H), 2.33 (s, 3H), 2.10 (s, 6H), 1.92 (s, 3H), 1.33 (s, 9H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 149.2, 140.1, 138.8, 137.7, 137.2, 137.1, 136.0, 130.2, 130.2, 128.6, 128.5, 127.7, 127.7, 127.0, 41.9, 34.7, 31.5, 21.2, 20.6; IR (KBr) $\tilde{\nu}$ = 3438, 2089, 1644, 1456, 1318, 1147 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{26}H_{31}NO_2SNa$ 444.1968; found 444.1976.

***N*-(5'-(tert-butyl)-2,4,6-triethyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (3cd):** R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 40 mg (65%); mp 237 – 239 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.50 (m, 2H), 7.47 – 7.43 (t, *J* = 7.2 Hz, 2H), 7.37 (t, *J* = 7.2 Hz, 1H), 7.29 (d, *J* = 2.4 Hz, 1H), 7.23 (d, *J* = 2.4 Hz, 1H), 7.05 (s, 2H), 5.56 (s, 1H), 2.68 (q, *J* = 7.2 Hz, 2H), 2.42 – 2.32 (m, 4H), 1.88 (s, 3H), 1.33 (s, 9H), 1.28 (t, *J* = 7.6 Hz, 3H), 1.11 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.1, 144.6, 143.2, 140.6, 138.5, 136.4, 134.5, 130.5, 130.3, 128.5, 128.2, 127.7, 127.1, 125.7, 42.1, 34.6, 31.4, 28.9, 26.8, 15.6, 15.5; IR (KBr) $\tilde{\nu}$ = 3438, 2085, 1635, 1456, 1318, 1146 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{29}H_{37}NO_2SNa$ 486.2437; found 486.2451.

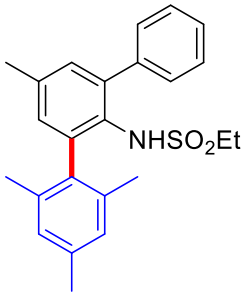


***N*-(5'-(*tert*-butyl)-4-methoxy-[1,1': 3',1''-terphenyl]-2'-yl)methaneslfonamide (3cb):** R_f =



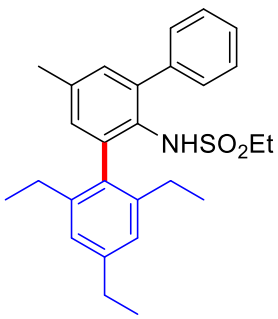
0.4 (hexane : ethyl acetate 9:1); white solid; 37 mg (68%); mp 159 – 161 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.44 (m, 4H), 7.41 (t, *J* = 8.4 Hz, 3H), 7.31 (s, 2H), 7.00 (d, *J* = 8.4 Hz, 2H), 5.78 (s, 1H), 3.86 (s, 3H), 2.01 (s, 3H), 1.35 (s, 9H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 150.3, 140.4, 139.9, 139.6, 132.3, 131.2, 130.1, 129.1, 128.6, 127.8, 127.8, 127.5, 114.1, 55.4, 42.0, 34.8, 31.4; IR (KBr) $\tilde{\nu}$ = 3438, 2963, 1656, 1632, 1311, 1146 cm^{-1};HR-MS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{24}H_{27}NO_3SNa$ 432.1604; found 432.1587.

***N*-(2,4,5',6-tetramethyl-[1, 1':3', 1''-terphenyl]-2'-yl)ethanesulfonamide (3da):** R_f = 0.4



(hexane : ethyl acetate 9:1); white solid; 36 mg (62%); mp 119 – 121 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.0 Hz, 2H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.37 (t, *J* = 7.0 Hz, 1H), 7.12 (s, 1H), 6.96 (s, 3H), 5.38 (s, 1H), 2.38 (s, 3H), 2.32 (s, 3H), 2.09 (s, 6H), 1.74 (q, *J* = 7.7 Hz, 2H), 0.91 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 139.8, 139.5, 137.7, 137.6, 137.0, 136.5, 135.5, 131.0, 130.8, 130.6, 130.1, 128.7, 128.5, 127.8, 48.4, 21.2, 21.0, 20.6, 8.5; IR (KBr) $\tilde{\nu}$ = 3438, 2084, 1641, 1322, 1144 cm^{-1};HR-MS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{24}H_{27}NO_2SNa$ 416.1655; found 416.1674.

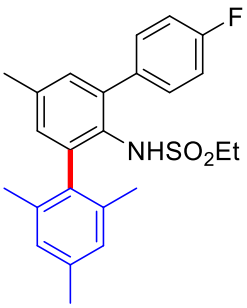
***N*-(2,4,6-triethyl-5'-methyl-[1,1':3',1''- terphenyl]-2'-yl)ethanesulfonamide (3dd) :** R_f =



0.4 (hexane : ethyl acetate 9:1); white solid; 45 mg (71%); mp 128 – 130 °C**;** R_f = 0.4 (hexane:ethyl acetate: 9:1); white solid; 39 mg (62%); mp 173−175; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.41 (m,

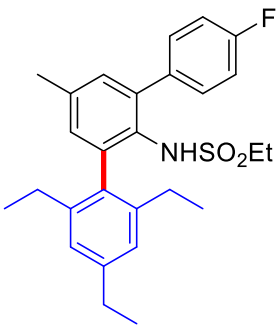
4H), 7.37 – 7.34 (m, 1H), 7.12 (s, 1H), 7.03 (s, 2H), 7.01 (s, 1H), 5.33 (s, 1H), 2.67 (dd, *J* = 15.2, 7.6 Hz, 2H), 2.43 – 2.33 (m, 7H), 1.67 (dd, *J* = 14.8, 7.6 Hz, 2H), 1.26 (t, *J* = 7.6 Hz, 3H), 1.11 (t, *J* = 7.6 Hz, 6H), 0.88 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 142.9, 142.3, 140.2 , 139.2, 137.0, 135.9, 134.2, 131.3, 130.9, 130.2 , 128.4, 127.7, 125.5, 48.3, 28.9, 26.8, 21.1, 15.9, 15.3, 8.5; IR (KBr) $\tilde{\nu}$ = 3373, 2092, 1643, 1322,1140 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{27}H_{33}NO_2SNa$ 458.2124; found 458.2148.

***N*-(4''- Fluoro-2, 4, 5', 6 – tetramethyl-[1, 1': 3', 1''-terphenyl]-2'-yl)ethanesulfonamide**



(**3ea**): R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 37 mg (65%); mp 168 – 170 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.46 – 7.44 (m, 2H), 7.14 (t, *J* = 8.4 Hz, 2H), 7.09 (s, 1H), 6.96 (s, 3H), 5.33 (s, 1H), 2.37 (s, 3H), 2.32 (s, 3H), 2.08 (s, 6H), 1.80 (q, *J* = 7.7 Hz, 2H), 0.93 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 162.5 (d, $^1J_{C\text{-}F}$ = 246 Hz), 138.6, 137.8, 137.7, 137.1 , 136.8 , 135.6 (d, $^4J_{C\text{-}F}$ = 3.5 Hz), 135.5, 131.8 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 131.19 , 130.9, 130.6, 128.7, 115.51 (d, $^2J_{C\text{-}F}$ = 21.4 Hz), 48.4, 21.2, 21.1 , 20.6 , 8.6 ; IR (KBr) $\tilde{\nu}$ = 3442, 1634, 1633, 1322, 1140 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{24}H_{26}FNO_2SNa$ 434.1560; found 434.1573.

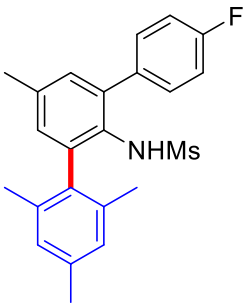
***N*-(2, 4, 6-triethyl- 4''- fluoro-5'-methyl-[1,1': 3', 1''- terphenyl]-2'-yl)ethanesulfonamide**



(3ed): R_f = 0.4 (hexane : ethyl acetate: 9:1); white solid; 41 mg (66%); mp 155 – 157 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.43 (m, 2H), 7.13 (t, *J* = 8.8 Hz, 2H), 7.09 (s, 1H), 7.03 (s, 2H), 7.02 (s, 1H), 5.30 (s, 1H), 2.67 (q, *J* = 7.2 Hz, 2H), 2.44 – 2.30 (m, 7H), 1.74 (q, *J* = 7.6 Hz, 2H), 1.27 (t, *J* = 7.6 Hz, 3H), 1.11 (t, *J* = 7.6 Hz, 6H), 0.91 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4 (d, $^1J_{C\text{-}F}$ = 256 Hz), 144.6,

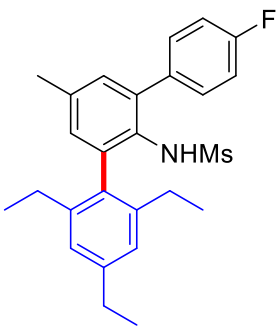
142.9, 138.3, 137.2, 136.1, 135.9, 134.2, 131.9 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz), 131.6, 131.0, 130.9, 125.5, 115.44 (d, $^{2}J_{C\text{-}F}$ = 21.2 Hz), 48.4, 28.9, 26.7, 21.1, 15.9, 15.2, 8.5; IR (KBr) $\tilde{\nu}$ = 3438, 2092, 1635, 1329, 1150 cm^{-1};HR-MS (ESI-TOF) m/z $[M + Na]^{+}$ calcd for $C_{27}H_{32}FNO_2SNa$ 476.2030; found 476.2040.

***N*-(4''- Fluoro- 2, 4, 5', 6- tetramethyl-[1,1':3',1''-terphenyl]-2'-yl]methanesulfonamide**



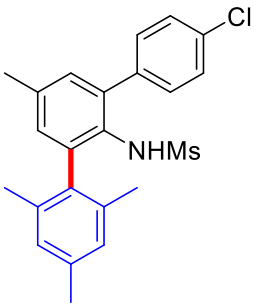
(3fa): R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 35 mg (61%); mp 207 – 209 °C **;** R_f = 0.4 (hexane:ethyl acetate: 9:1); white solid; 39 mg (62%); ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.45 (dd, *J* = 8.4, 5.6 Hz, 2H), 7.14 (t, *J* = 8.4 Hz, 2H), 7.09 (s, 1H), 6.97 (s, 3H), 5.53 (s, 1H), 2.38 (s, 3H), 2.31 (s, 3H), 2.08 (s, 6H), 1.97 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 162.53 (d, $^{1}J_{C\text{-}F}$ = 246.0 Hz), 138.4, 137.8 (*2), 137.0, 136.8, 135.6 (d, $^{4}J_{C\text{-}F}$ = 3.4 Hz), 135.3, 131.9 (d, $^{3}J_{C\text{-}F}$ = 8.1 Hz), 131.1, 130.9, 130.5, 128.7,115.6 (d, $^{2}J_{C\text{-}F}$ = 21.0 Hz), 42.1, 21.2, 21.1, 20.6 ; IR (KBr) $\tilde{\nu}$ = 3421, 2359, 2339, 1652 cm^{-1};HR-MS (ESI-TOF) m/z $[M + H]^{+}$ calcd for $C_{23}H_{25}FNO_2S$ 398.1585; found 398.1573.

***N*-(2,4,6-triethyl-4''-fluoro-5'-methyl-[1,1': 3', 1''-terphenyl]-2'-yl)methanesulfonamide**



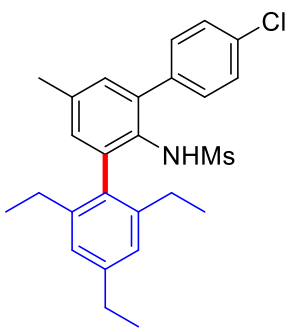
(3fd): R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 34 mg (53%); mp 193 – 195 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.46 – 7.44 (m, 2H), 7.14 (t, *J* = 8.4 Hz, 2H), 7.10 (s, 1H), 7.03 (s, 2H), 7.01 (s, 1H), 5.49 (s, 1H), 2.66 (q, *J* = 7.7 Hz, 2H), 2.41 –2.30 (m, 7H), 1.93 (s, 3H), 1.26 (t, *J* = 7.7 Hz, 3H), 1.11 (t, *J* = 7.7 Hz, 6H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 162.5 (d, $^{1}J_{C\text{-}F}$ = 246.0 Hz), 144.7, 143.0, 138.1, 137.1, 136.3, 136.1 (d, $^{4}J_{C\text{-}F}$ = 3.2 Hz), 133.9, 131.93 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz), 131.5, 131.06, 130.7, 125.5, 115.5 (d, $^{2}J_{C\text{-}F}$ =

21.2 Hz), 42.2, 28.9, 26.7, 21.1, 15.7, 15.3; IR (KBr) $\tilde{\nu}$ = 3422, 1635, 1511, 1314, 1143 cm^{-1};HR-MS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{26}H_{31}FNO_2S$ 440.2054; found 440.2036.



***N*-(4''-chloro-2, 4, 5',6-tetramethyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (3ga):** R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 37 mg (65%); mp 191 – 193 °C**;** ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.43 (s, 4H), 7.09 (s, 1H), 6.98 (s, 1H), 6.97 (s, 2H), 5.55 (s, 1H), 2.38 (s, 3H), 2.32 (s, 3H), 2.08 (s, 6H), 1.98 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 138.3, 138.2, 138.0, 137.9, 137.1, 136.9, 135.3, 133.9, 131.5, 131.3, 130.8, 130.3, 128.8, 128.7, 42.1, 21.2, 21.1, 20.6; IR (KBr) $\tilde{\nu}$ = 3441, 2390, 2049, 1633, 1142 cm^{-1};HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{23}H_{24}ClNO_2SNa$ 436.1108; found 436.1133.

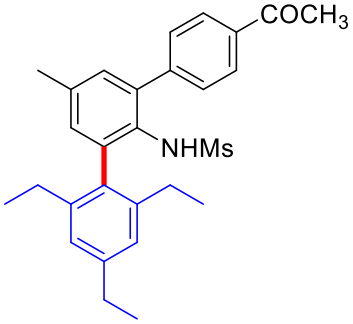
***N*-(4''-chloro-2,4,5'-trimethyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (3gc):** R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 31 mg (57%); mp 171 – 173 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (s, 4H), 7.16 (d, *J* = 7.6 Hz, 1H), 7.11– 7.05 (m, 4H), 5.63 (s, 1H), 2.38 (s, 3H), 2.36 (s, 3H), 2.16 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.4, 138.5, 138.1, 137.9, 136.9, 136.5, 136.0, 134.0, 131.6, 131.4, 131.1, 130.8, 130.6, 129.8, 128.8, 126.8, 42.0, 21.2, 21.0, 20.0; IR (KBr) $\tilde{\nu}$ = 3438, 2098, 2049, 1720, 1492, 1316, 1146 cm^{-1};HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{22}H_{22}ClNO_2SNa$ 422.0952; found 422.0935.



***N*-(4''-chloro-2,4,6-triethyl-5'-methyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (3gd):** R_f = 0.4 (hexane : ethyl acetate:

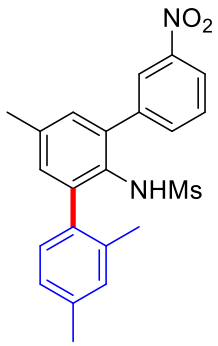
9:1); white solid; 48 mg (77%); mp 154 – 156 °C**;** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (s, 4H), 7.09 (s, 1H), 7.03 (s, 3H), 5.48 (s, 1H), 2.66 (q, *J* = 7.6 Hz, 2H), 2.45 – 2.27 (m, 7H), 1.95 (s, 3H), 1.26 (t, *J* = 7.6 Hz, 3H), 1.11 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 142.9, 138.6, 137.9, 137.3, 136.3, 133.9 , 133.8, 131.7, 131.6, 130.9, 130.5, 128.7, 125.6, 42.2, 28.9, 26.7, 21.1, 15.7, 15.4 ; IR (KBr) $\tilde{\nu}$ = 3503, 2092, 1736, 1641, 1317, 1148 cm^{-1};HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{26}H_{30}ClNO_2SNa$ 478.1578; found 478.1573.

***N*-(4''-acetyl-2,4,6-triethyl-5'-methyl-[1,1':3',1''-terphenyl]-2'-yl)methanesufonamide**



(3hd): R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 43 mg (71%); mp 163 – 165 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.4 Hz, 2H), 7.60 (d, *J* = 7.7 Hz, 2H), 7.12 (s, 1H), 7.05 (s, 1H), 7.03 (s, 2H), 5.51 (s, 1H), 2.67 (q, *J* = 7.7 Hz, 2H), 2.64 (s, 3H), 2.43 – 2.39 (m, 5H), 2.35 – 2.30 (*sept*, *J* = 7.7 Hz , 2H), 1.92 (s, 3H), 1.27 (t, *J* = 7.7 Hz, 3H), 1.12 (t, *J* = 7.7 Hz, 6H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 197.8, 145.1, 144.8, 142.9, 138.1, 137.6, 136.5, 136.1, 133.7, 131.9, 130.8, 130.5, 130.4, 128.5, 125.6, 42.2, 28.9, 26.9, 26.8 , 21.1, 15.7, 15.3; IR (KBr) $\tilde{\nu}$ = 3438, 1720, 1641, 1530, 1449 cm^{-1};HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{28}H_{33}NO_3SNa$ 486.2073; found 486.2067.

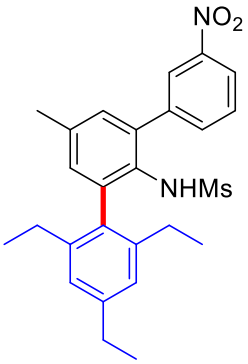
***N*-(2,4, 5'-trimethyl-3''-nitro-[1,1':3',1''-terphenyl]-2'yl)methanesulfonamide (3ic):** R_f =



0.4 (hexane : ethyl acetate 9:1); white solid; 36 mg (66%); mp 164 – 166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (t, *J* = 2.0 Hz, 1H), 8.24 – 8.21 (m, 1H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.63 (t, *J* = 8.0 Hz, 1H), 7.16 (s, 1H), 7.15 – 7.09 (m, 4H), 5.69 (s, 1H), 2.41 (s, 3H), 2.37 (s, 3H), 2.17 (s, 3H), 2.02 (s,

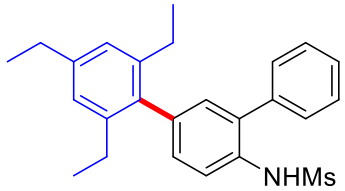
3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.5, 139.9, 138.4, 138.0, 137.6, 136.4, 136.3, 135.5, 132.2, 131.3, 130.9, 130.4, 129.4, 126.9, 124.8, 122.6, 41.8, 21.3, 21.1, 20.1; IR (KBr) $\tilde{\nu}$ = 3438, 2092, 1641, 1555, 1449 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{22}H_{22}N_2O_4SNa$ 433.1192; found 433.120

***N*-(2,4,6-triethyl-5'-methyl-3''-nitro-[1,1':3',1''-terphenyl]-2'yl]methanesulfonamide**

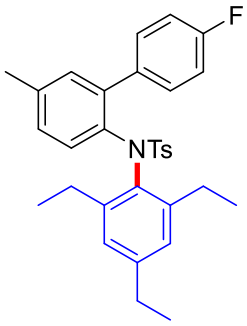


(3id): R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 31 mg (62%); mp 203 – 205 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.64 (t, *J* = 8.0 Hz, 1H), 7.16 (s,1H), 7.10 (s, 1H), 7.05 (s, 2H), 5.49 (s, 1H), 2.67 (q, *J* = 7.2 Hz, 2H), 2.46 – 2.27 (m, 7H), 1.98 (s, 3H), 1.27 (t, *J* = 7.6 Hz, 3H), 1.13 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 144.9, 142.8, 141.9, 137.9, 137.3, 136.9, 136.5, 133.6, 132.4, 130.9, 130.2, 129.4, 125.6, 125.0, 122.5, 42.1, 28.9, 26.8, 21.1, 15.7, 15.4; IR (KBr) $\tilde{\nu}$ = 3438, 2092, 1643, 1350, 1148 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{26}H_{30}N_2O_4SNa$ 489.1818; found 489.1800.

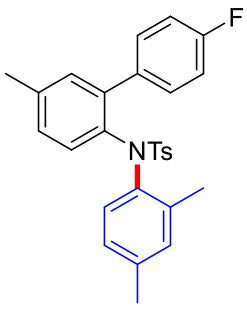
***N*-([1, 1'- biphenyl]-2-yl)-*N*-(2,4,6-triethylphenyl)methanesulfonamide (3jd)**: R_f = 0.4



(hexane : ethyl acetate 9:1); white solid; 39 mg (59%); mp 157 – 159 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.0 Hz, 1H), 7.49 (t, *J* = 7.2 Hz, 2H), 7.42 (t, *J* = 7.2 Hz, 1H), 7.36 (d, *J* = 7.6 Hz, 2H), 7.21 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.12 (s, 1H), 6.98 (s, 2H), 6.57 (s, 1H), 2.95 (s, 3H), 2.66 (q, *J* = 7.6 Hz, 2H), 2.36 (q, *J* = 7.2 Hz, 4H), 1.28 (t, *J* = 7.6 Hz, 3H), 1.05 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.8, 142.3, 137.6, 137.4, 137.0, 132.9, 132.6, 132.4, 132.3, 130.5, 129.7, 129.2, 128.6, 125.5, 40.0, 28.9, 27.1, 15.8, 15.6; IR (KBr) $\tilde{\nu}$ = 3437, 2965, 2092, 1641, 1332, 1168 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{25}H_{29}NO_2SNa$ 430.1811; found 430.1810.



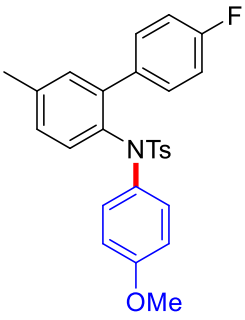
***N*-(4'-fluoro-5-methyl-[1,1'-biphenyl]-2-yl)-4-methyl-*N*-(2, 4, 6 – triethylphenyl)benzenesulfonamide (3fd'):** R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 39 mg (67%); mp 140 – 142 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.25 (s, 2H), 7.08 (dd, *J* = 8.4, 1.4 Hz, 1H), 6.70 (s, 2H), 6.68 (t, *J* = 8.4 Hz, 2H), 6.56 (s, 1H), 6.33 – 6.31 (m, 2H), 2.56 (q, *J* = 7.7 Hz, 2H), 2.47 – 2.40 (m, 5H), 2.23 (s, 3H), 1.78 –1.75 (m, 2H), 1.22 (t, *J* = 7.7 Hz, 3H), 0.85 (t, *J* = 7.7 Hz, 6H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 161.92 (d, $^1J_{C\text{-}F}$ = 244 Hz), 144.9, 144.5, 143.4, 138.2, 138.1, 137.4, 136.4 (d, $^4J_{C\text{-}F}$ = 4 Hz) , 135.3, 135.2, 134.0, 130.9 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 129.3, 128.2, 128.2, 127.2, 126.4, 114.00 (d, $^2J_{C\text{-}F}$ = 21.0 Hz), 28.5, 24.8, 21.6, 20.5 , 15.8, 14.3; IR (KBr) $\tilde{\nu}$ = 3438, 2089, 1644, 1142 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{32}H_{35}FNO_2S$ 516.2367; found 516.2385.



***N*-(2,4-dimethylphenyl)-N-(4'-fluoro-5-methyl-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide (3fc'):** R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 34 mg (66%); mp 139-141 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 1H), 7.25 (s, 3H), 7.12 (s, 1H), 7.09 (dd, *J* = 7.7, 1.4 Hz, 1H), 6.98 (t, *J* = 8.4 Hz, 2H), 6.94 (s, 1H), 6.74 (s, 1H), 6.60 (d, *J* = 8.4 Hz, 1H), 6.41 (d, *J* = 6.3 Hz, 1H), 2.44 (s, 3H), 2.30 (s, 3H), 2.17 (s, 3H), 1.54 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 162.57 (d, $^1J_{C\text{-}F}$ = 244.0 Hz), 143.6, 141.5, 138.1, 137.7, 137.6, 136.8, 136.4, 136.1(d, $^4J_{C\text{-}F}$ = 3.0 Hz), 132.9, 132.1, 131.4 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 130.7, 129.7, 129.5, 128.4, 128.3, 126.4, 114.93

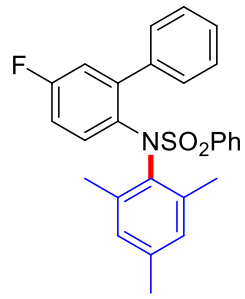
(d, $^{2}J_{C\text{-}F}$ = 21.0 Hz), 21.7, 21.0, 20.9, 18.6; IR (KBr) $\tilde{\nu}$ = 3441, 2084, 1641 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + H]^{+}$ calcd for $C_{28}H_{27}FNO_2S$ 460.1741; found 460.1713.

***N*-(4'-fluoro-5-methyl-[1,1'-biphenyl]-2-yl)-4-methyl-*N*-(4-methoxyphenyl)-4-**



methylbenzenesulfonamide (3fb'): R_f = 0.4 (hexane:ethyl acetate: 9:1); white solid; 41 mg (78%); mp 150-152 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.49 (d, *J* = 7.7 Hz, 2H), 7.34 (dd, *J* = 8.4, 5.5 Hz, 2H), 7.25 (d, *J* = 8.4 Hz, 2H), 7.11 (s, 2H), 7.08 – 7.06 (m, 3H), 6.61 – 6.58 (m, 4H), 3.71 (s, 3H), 2.44 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4 (d, $^{1}J_{C\text{-}F}$ = 244.0 Hz), 158.4, 143.6, 141.4, 138.3, 137.8, 137.3, 135.3 (d, $^{4}J_{C\text{-}F}$ = 3.0 Hz), 133.4, 132.4, 131.4 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz), 129.8, 129.5, 129.0, 128.1, 127.8, 114.8 (d, $^{2}J_{C\text{-}F}$ = 21.0 Hz), 113.7, 55.4, 21.7, 21.2; IR (KBr) $\tilde{\nu}$ = 3438, 1644, 1506, 1163, 1033 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^{+}$ calcd for $C_{27}H_{24}FNO_3SNa$ 484.1353; found 484.1360.

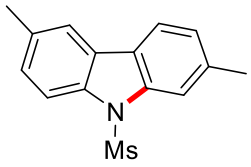
***N*-(5-fluoro-[1,1'-biphenyl]-2-yl)-*N*-mesitylbenzenesulfonamide (3fa'):** R_f = 0.4



(hexane:ethyl acetate: 9:1); colourless sticky liquid; 40 mg (72 %); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (dd, *J* = 9.2, 5.2 Hz, 1H), 7.77 – 7.75 (m, 2H), 7.61 – 7.57 (m, 1H), 7.47 (t, *J* = 8.0 Hz, 2H), 7. 61 – 7.57 (m, 1H), 7.05 – 7.00 (m, 3H), 6.63(s, 2H), 6.59 (dd, *J* = 8.8, 3.2 Hz, 1H), 6.63 – 6.35 (m, 2H), 2.22 (s, 3H), 1.73 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.88 (d, $^{1}J_{C\text{-}F}$ = 248.0 Hz), 143.24 (d, $^{3}J_{C\text{-}F}$= 8.0 Hz), 140.4, 139.7, 138.9, 137.9, 136.1, 134.49 (d, $^{4}J_{C\text{-}F}$ = 3.2 Hz), 133.1, 131.1 (d, $^{3}J_{C\text{-}F}$ = 8.5 Hz), 130.1, 129.2, 128.9, 128.5, 127.7, 127.6, 119.6 (d, $^{2}J_{C\text{-}F}$ = 21.7 Hz), 113.7 (d, $^{2}J_{C\text{-}F}$ = 21.7 Hz), 20.9, 20.4*2; IR (KBr) $\tilde{\nu}$

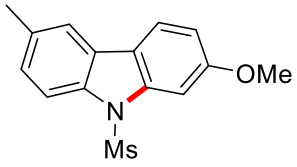
= 3517, 1641, 1165 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{27}H_{24}FNO_2SNa$ 468.1404; found 468.1332.

2, 6-dimethyl-9-(methylsulfonyl)-9*H*-carbazole (4a): R_f = 0.4 (hexane:ethyl acetate: 9:1);



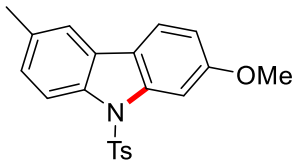
white solid; 22 mg (59%); mp 92– 94 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.4 Hz, 1H), 7.96 (s, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.74 (s, 1H), 7.28 (d, *J* = 1.6 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 1H), 2.93 (s, 3H), 2.54 (s, 3H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.2, 138.1, 138.0, 134.0, 128.3, 126.7, 125.5, 124.1, 120.1, 119.9, 115.1, 114.6, 38.3, 22.3, 21.4; IR (KBr) $\tilde{\nu}$ = 3423, 2089, 1641, 1362, 1162 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{15}H_{16}NO_2S$ 274.0896; found 274.0888.

2-methoxy-6-methyl-9-(methylsulfonyl)-9*H*-carbazole (4b): R_f = 0.4 (hexane:ethyl



acetate: 9:1); white solid; 24 mg (60%); mp 157 – 159 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.4 Hz, 1H), 7.82 (d, *J* = 8.4 Hz, 1H), 7.70(s, 1H), 7.69(s, 1H), 7.22 (dd, *J* = 8.4, 1.1 Hz, 1H), 7.00 (dd, *J* = 8.4, 2.4 Hz, 1H), 3.92 (s, 3H), 2.93 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 140.1, 136.6, 134.1, 127.5, 126.7, 120.8, 119.8, 119.6, 114.5, 112.5, 99.5, 55.9, 38.3, 21.4; IR (KBr) $\tilde{\nu}$ = 3439, 2925, 1352, 1337, 1232, cm^{-1}; HR-MS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{15}H_{16}NO_3S$ 290.0845; found 290.0835.

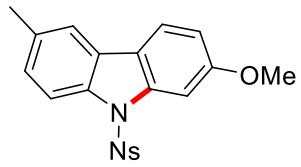
2-methoxy-6-methyl-9-tosyl-9*H*-carbazole (4c): R_f = 0.4 (hexane:ethyl acetate: 9:1); white



solid; 20 mg (51%); mp 141 – 143 °C; ^{1}H NMR (400 MHz, δ 8.14 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 2.2 Hz, 1H), 7.71 – 7.66 (m,

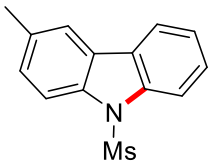
3H), 7.56 (s, 1H), 7.20 (d, *J* = 8.4 Hz, 1H), 7.08 (d, *J* = 8.0 Hz, 2H), 6.93 (dd, *J* = 8.4, 2.4 Hz, 1H), 3.95 (s, 3H), 2.45 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 144.9, 140.1, 136.6, 135.1, 133.7, 129.7, 127.3, 126.6, 125.4, 120.6, 120.0, 119.4, 114.9, 112.2, 100.1, 55.9, 21.6, 21.4; IR (KBr) $\tilde{\nu}$ = 3441, 2359, 2341, 1640, 1367, 1170, 1150 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{21}H_{20}NO_3S$ 366.1158; found 366.1144.

2-methoxy-6-methyl-9-((4-nitrophenyl)sulfonyl)-9*H*-carbazole (4d): R_f = 0.4



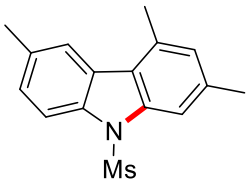
(hexane:ethyl acetate: 9:1); white solid; 26 mg (65%); mp 164 – 166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (t, *J* = 8.8 Hz, 3H), 7.90 (d, *J* = 8.8 Hz, 2H), 7.82 (d, *J* = 2.4 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.55 (s, 1H), 7.23 (d, *J* = 7.6 Hz, 1H), 6.96 (dd, *J* = 8.4, 2.4 Hz, 1H), 3.95 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 150.7, 142.8, 139.7, 136.1, 134.8, 127.8, 127.7, 127.2, 124.3, 120.9, 120.4, 119.8, 115.0, 112.7, 100.5, 56.0, 22.4; IR (KBr) $\tilde{\nu}$ = 3441, 2064, 1625, 1377, 1175, 1041 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{20}H_{16}N_2O_5SNa$ 419.0672; found 419.0659.

3-methyl-9-(methylsulfonyl)-9*H*-carbazole (4e)[23]: R_f = 0.4 (hexane:ethyl acetate: 9:1);



white solid; 28 mg (70%); mp 84 – 86°C (lit. 85 – 88°C)[23]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.4 Hz, 1H), 8.03 (d, *J* = 8.4 Hz, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.80 (s, 1H), 7.50 – 7.46 (m, 1H), 7.41 (td, *J* = 7.6, 0.8 Hz, 1H), 7.31 (dd, *J* = 8.8, 1.2 Hz, 1H), 2.94 (s, 3H), 2.53 (s, 3H).

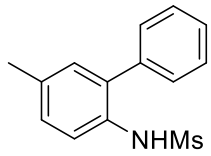
2,4,6-trimethyl-9-(methylsulfonyl)-9*H*-carbazole (4f)[43]: R_f = 0.5 (hexane:ethyl acetate:



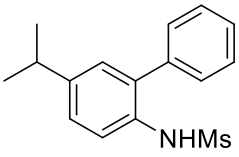
19:1); white solid; 27 mg (69%); mp 105 – 107°C (lit. 106-107 °C)[43] ; ^{1}H NMR (400 MHz, $CDCl_3$) 8.07 (d, *J* = 8.4 Hz, 1H), 7.85 (s, 2H),

7.28 (s, 1H), 7.01 (s, 1H), 2.91 (s, 3H), 2.77 (s, 3H), 2.53 (s, 3H), 2.50 (s, 3H).

***N*-(5-methyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (1a)[28] :** R_f = 0.6 (hexane : ethyl acetate 9:1); white solid; 859 mg (62%); mp 66 – 66°C (lit. 65 – 66°C)[28]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.4 Hz, 1H), 7.50 – 7.46 (m, 2H), 7.44 – 7.40 (m, 1H), 7.32 – 7.30 (m, 2H), 7.20 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.40 (s, 1H), 2.80 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 135.2, 133.9, 131.5, 131.4, 129.7, 129.5, 129.1, 128.5, 121.8, 39.6, 20.9.



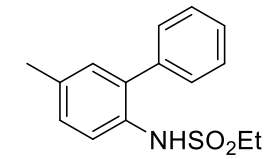
***N*-(5-isopropyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (1b):** R_f = 0.6 (hexane : ethyl acetate 9:1); white solid; 989 mg (73%); mp 91 – 93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.4 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.44 – 7.41 (m, 1H), 7.34 – 7.32 (m, 2H), 7.24 (d, *J* = 2.1 Hz, 1H), 7.13 (d, *J* = 2.0 Hz, 1H), 6.43 (s, 1H), 2.92 (sept, 1H), 2.81 (s, 3H), 1.27 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.1, 138.7, 133.9, 131.5, 129.5, 129.2, 128.9, 128.4, 127.1, 121.1, 39.7, 33.6, 24.7; IR (KBr) $\tilde{\nu}$ = 3437, 2092, 1641, 1327, 1156 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{16}H_{19}NO_2SNa$ 312.1029; found 312.1005.



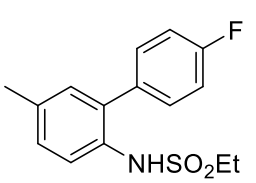
***N*-(5-*tert*-butyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (1c):** R_f = 0.6 (hexane : ethyl acetate 9:1); white solid; 995 mg (75%); mp 90 – 92 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.4 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.45 – 7.39 (m, 2H), 7.35 – 7.33 (m, 2H), 7.17 (d, *J* = 7.6 Hz, 1H), 6.43 (s, 1H), 2.83 (s, 3H), 1.33 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 138.2, 133.4, 131.3,

129.5, 129.2, 128.4, 127.8, 126.1, 120.6, 39.8, 34.6, 31.5; IR (KBr) $\tilde{\nu}$ = 3421, 2961, 1645, 1328, 1159 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{17}H_{21}NO_2SNa$ 326.1185; found 326.1193.

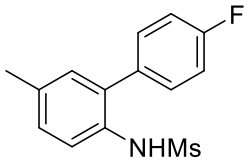
***N*-(5-methyl-[1,1'-biphenyl]-2-yl)ethanesulfonamide (1d) :** R_f = 0.6 (hexane : ethyl acetate 9:1); yellow sticky liquid, 865 mg (63%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.4 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.43 (t, *J* = 7.2 Hz, 1H), 7.33 – 7.31 (m, 2H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.08 (s, 1H), 6.39 (s, 1H), 2.94 (q, *J* = 7.2 Hz, 2H), 2.35 (s, 3H), 1.11 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9, 134.7, 133.5, 131.5, 131.4, 129.6, 129.5, 129.1, 128.4, 120.6, 46.1, 20.8, 8.0; IR (KBr) $\tilde{\nu}$ = 3438, 2089, 1645, 1328, 1150 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{15}H_{17}NO_2SNa$ 298.0872; found 298.0878.



***N*-(4'-fluoro-5-methyl-[1,1'-biphenyl]-2-yl)ethanesulfonamide (1e):** R_f = 0.6 (hexane : ethyl acetate: 9:1); white solid; 977 mg (66%); mp 133 – 135 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.4 Hz, 1H), 7.32 – 7.29 (m, 2H), 7.20 – 7.15 (m, 3H), 7.04 (s, 1H), 6.22 (s, 1H), 2.98 (q, *J* = 7.2 Hz, 2H), 2.35 (s, 3H), 1.16 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8 (d, $^1J_{C\text{-}F}$ = 248.0 Hz), 134.8, 133.8 (d, $^4J_{C\text{-}F}$ = 3.4Hz) , 132.5, 131.6 , 131.5, 131.0 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 129.8, 120.6, 116.5 (d, $^2J_{C\text{-}F}$ = 21.5 Hz), 46.4, 20.9, 8.1; IR (KBr) $\tilde{\nu}$ = 3438, 1651, 1495, 1150 cm^{-1} ; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{15}H_{16}FNO_2SNa$ 316.0778; found 316.0783.

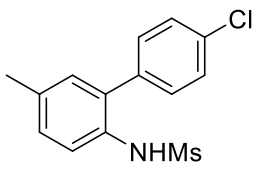


***N*-(4'-fluoro-5-methyl-[1,1'- biphenyl]-2-yl)benzenesulfonamide (1f) :** R_f = 0.6 (hexane : ethyl acetate 9:1); white solid; 980 mg (65%); mp 92 – 94 °C**;** ^1H

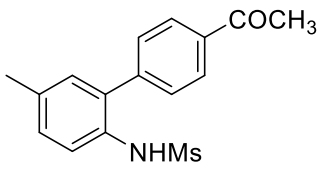


NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.4 Hz, 1H), 7.32 – 7.28 (m, 2H), 7.20 – 7.15 (m, 3H), 7.07 (s, 1H), 6.36 (s, 1H), 2.82 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.67 (d, $^1J_{C-F}$ = 248.0 Hz), 135.3, 133.8, 133.2, 131.5, 131.4, 131.0 (d, $^3J_{C-F}$ = 8.1 Hz), 129.8, 121.6, 116.39 (d, $^2J_{C-F}$ = 21.4 Hz), 39.9, 20.8; IR (KBr) $\tilde{\nu}$ = 3373, 2092, 1643, 1322, 1155, 1089 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{14}H_{14}FNO_2SNa$ 302.0621; found 302.0624.

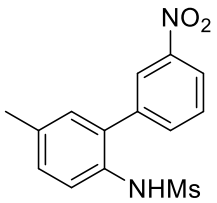
***N*-(4'-chloro-5-methyl-[1,1'- biphenyl]-2-yl)methanesulfonamide (1g) :** R_f = 0.6 (hexane : ethyl acetate 9:1); white solid; 985 mg (61%); mp 95 – 97 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.4 Hz, 1H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.28 (s, 2H), 7.20 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.06 (s, 1H), 6.27 (s, 1H), 2.84 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.3, 135.4, 134.6, 132.9, 131.4, 131.3, 130.6, 130.0, 129.7, 121.5, 40.0, 20.9; IR (KBr) $\tilde{\nu}$ = 3373, 2092, 1643, 1389, 1322, 1155cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{14}H_{14}ClNO_2SNa$ 318.0326; found 318.0306.

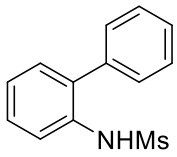


***N*-(4'-acetyl-5-methyl-[1,1'- biphenyl]-2-yl)methanesulfonamide (1h) :** R_f = 0.6 (hexane : ethyl acetate 9:1); yellow sticky liquid; 1.1g (67%); ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.0 Hz, 2H), 7.55 (d, *J* = 8.4 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 1H), 7.12 (s, 1H), 6.32 (s, 1H), 2.86 (s, 3H), 2.68 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.5, 142.8, 136.8, 135.5, 131.2, 131.2, 133.2, 130.3, 129.5, 129.4, 121.7, 40.1, 26.8, 20.9 ; IR (KBr) $\tilde{\nu}$ = 3441, 2390, 2049, 1633, 1142 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{16}H_{18}NO_3SNa$ 304.1002; found 304.1028.



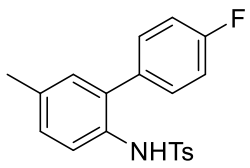
***N*-(5-methyl-3'-nitro-[1,1'- biphenyl]-2-yl)methanesulfonamide (1i) :** R_f = 0.7 (hexane : ethyl acetate 9:1); white solid; 996 mg (60%); mp 160 – 162 °C**;** ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.4 Hz, 1H), 8.22 (s, 1H), 7.73 (d, *J* = 7.2 Hz, 1H), 7.67 (t, *J* = 8.0 Hz, 1H), 7.50 (d, *J* = 8.4 Hz, 1H), 7.28(s, 1H), 7.12 (s, 1H), 6.22 (s, 1H), 2.89 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 139.9, 136.3, 135.5, 132.9, 131.6, 131.1, 130.7, 130.2, 124.4, 123.1, 122.9, 40.3, 20.9; IR (KBr) $\tilde{\nu}$ = 3438, 2092, 1529, 1351, 1154 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{14}H_{14}N_2O_4SNa$ 329.0566; found 329.0566.





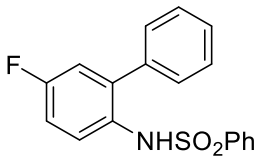
N-([1,1'-biphenyl]-2-yl)methanesulfonamide (1j)[23]: R_f = 0.6 (hexane : ethyl acetate 9:1); white solid; 888 mg (61%); mp 65 – 67 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.4 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.45 – 7.43 (m, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.34 (d, *J* = 7.0 Hz, 2H), 7.29 – 7.27 (m, 1H), 7.23 (t, *J* = 7.2 Hz, 1H), 6.56 (s, 1H), 2.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.5, 133.9, 133.4, 130.8, 129.5, 129.0, 129.0, 128.5, 125.0, 120.3, 39.8.

4-methyl-*N*-(5-methyl-1,1' biphenyl]-2-yl)benzenesulfonamide (1k) : R_f = 0.6 (hexane : ethyl acetate 9:1); white solid; 811 mg (60%); mp 131–133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.4 Hz, 1H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 7.14 (d, *J* = 8.4 Hz, 1H), 6.99 (t, *J* = 8.4 Hz, 2H), 6.88 (s, 1H), 6.79 – 6.75 (m, 2H), 6.34 (s, 1H), 2.41 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162 (d, $^1J_{C\text{-}F}$ = 248.0 Hz), 144.0, 136.4, 135.2, 133.5, 131.2, 131.1, 130.8, 130.7, 129.7, 129.6, 127.3, 122.6, 116.0 (d, $^2J_{C\text{-}F}$ = 21.4 Hz), 21.7, 20.9. IR

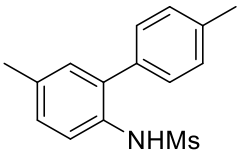


(KBr) $\tilde{\nu}$ = 3438, 2092, 1641, 1495, 1333, 1163, 1091 cm^{-1}; HR-MS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{20}H_{18}FNO_2SNa$ 378.0934; found 378.0912.

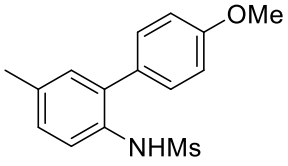
***N*-(5-fluoro-[1,1'-biphenyl]-2-yl) benzenesulfonamide (1l)[23]:** R_f = 0.6 (hexane : ethyl acetate 9:1); white solid; 800 mg (61%); mp 72 – 74 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 8.8, 5.6 Hz, 1H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.48 (d, *J* = 7.2 Hz, 2H), 7.40 – 7.28 (m, 5H), 7.07 (td, *J* = 8.4, 2.8 Hz, 1H), 6.82 (dd, *J* = 8.8, 3.2 Hz, 1H), 6.72 (d, *J* = 7.2 Hz, 2H), 6.49 (d, *J* = 5.6 Hz, 1H).



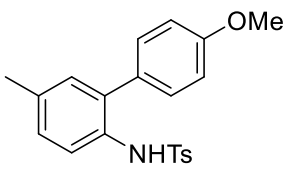
***N*-(4',5-dimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (1m)**: R_f = 0.4 (hexane:ethyl acetate: 9:1); white solid; 923 mg (65%); mp 74 – 76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.0 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.19 – 7. 16 (m, 3H), 7.08 (s, 1H), 6.43 (s, 1H), 2.79 (s, 3H), 2.42 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 135.1, 134.7, 133.8, 133.2, 131.4, 130.2, 129.5, 128.9, 120.9, 39.5, 21.3, 20.9; IR (KBr) $\tilde{\nu}$ = 3440, 2924, 1641, 1330,1157, 971cm^{-1}; HR-MS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{15}H_{17}NO_2SNa$ 298.0872; found 298.0879.



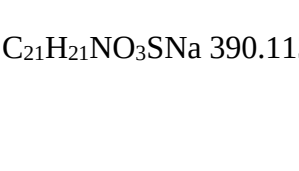
***N*-(4'-methoxy-5-methyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (1n)**: R_f = 0.4 (hexane:ethyl acetate: 9:1); white solid; 1123 mg (71%); mp 72 – 74 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.4 Hz, 1H), 7.24 – 7.21 (m, 2H), 7.17 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.07 (d, *J* = 1.6 Hz, 1H), 7.01 – 6.99 (m, 2H), 6.42 (s, 1H), 3.87 (s, 3H), 2.81 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 135.0, 133.6, 133.3, 131.6, 130.3, 129.8, 129.4, 120.9, 114.9, 55.5, 39.6, 20.9; IR (KBr) $\tilde{\nu}$ = 3422, 2080, 1640, 1325, 1246, 1154, cm^{-1}; HR-MS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{15}H_{17}NO_3SNa$ 314.0821; found 314.0826.



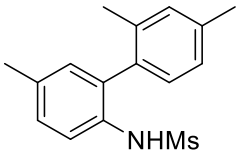
***N*-(4'-methoxy-5-methyl-[1,1'-biphenyl]-2yl)-4-methylbenzenesulfonamide) (1o)**: R_f = 0.5 (hexane:ethyl acetate: 19:1); white solid; 985 mg (70%), mp 131 – 133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.4 Hz, 1H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 6.8 Hz, 1H), 6.88 – 6.83 (m, 3H), 6.74 (d, *J* = 8.4 Hz, 2H), 6.47 (s, 1H), 3.85 (s, 3H), 2.40 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 143.7, 136.4, 134.7, 133.8, 131.5, 131.2, 130.1, 129.7, 129.6, 129.1, 127.3, 121.7, 114.9, 55.9, 21.7, 20.9; IR (KBr) $\tilde{\nu}$ = 3422, 2080, 1640, 1493, 1334, 1246, 1163 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{21}H_{21}NO_3SNa$ 390.1134; found 390.1129.



***N*-(4'-methoxy-5-methyl-[1,1'-biphenyl]-2yl)- 4-nitrobenzenesulfonamide (1p)**: R_f = 0.5 (hexane:ethyl acetate: 19:1); white solid; 1129 mg (83%), mp 170 – 172 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.8 Hz, 2H), 7.63 (d, *J* = 8.8 Hz, 2H), 7.56 (d, *J* = 8.4 Hz, 1H), 7.16 (d, *J* = 8.4 Hz, 1H), 6.91 (s, 1H), 6.82 – 6.80 (m, 2H), 6.71 – 6.69 (m, 3H), 3.84 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 136.7, 135.2, 131.4, 130.5, 129.8, 129.4, 128.5, 127.4, 124.1, 123.9, 123.7, 114.8, 114.6, 55.5, 21.0; IR (KBr) $\tilde{\nu}$ = 3423, 2359,1640, 1529, 1347, 1167 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{20}H_{18}N_2O_5SNa$ 421.0829; found 421.0825.



***N*-(2',4',5-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (1q)[57]**: R_f = 0.4 (hexane:ethyl acetate: 9:1); white solid; 891 mg (60%); mp 110 – 112



(lit. 112 – 114 °C)[57] °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.4 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 1H), 7.13 (s, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 7.03 – 6.97 (m, 2H), 6.01 (s, 1H), 2.84 (s, 3H), 2.38 (s, 3H), 2.34 (s, 3H), 2.06 (s, 3H)

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NMR Spectra of Selected Compounds

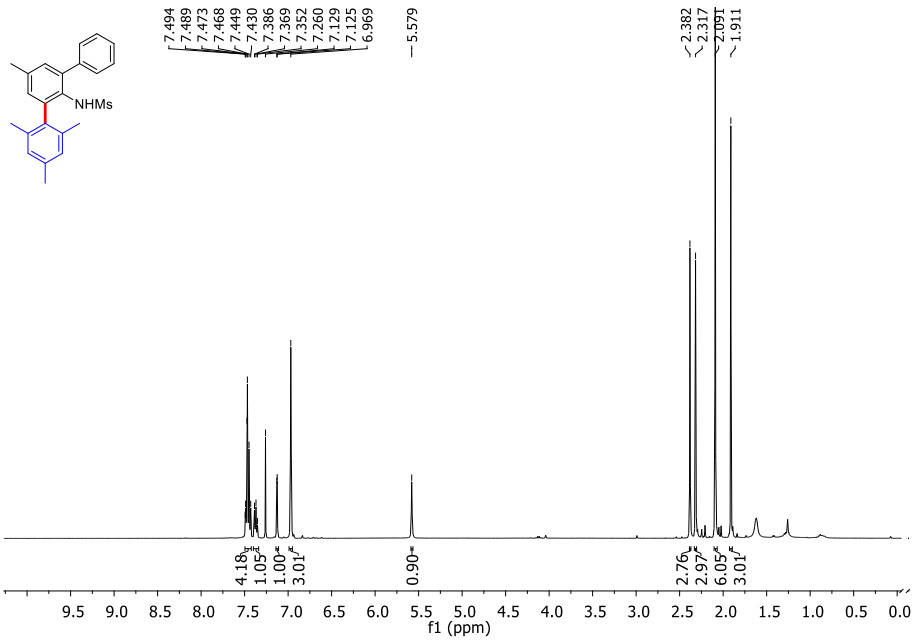


Figure 4.6. [1] H NMR spectrum of *N*-(2,4,5',6-tetramethyl-[1,1' : 3', 1"- terphenyl]-2'-yl) methanesulfonamide (**3aa**)

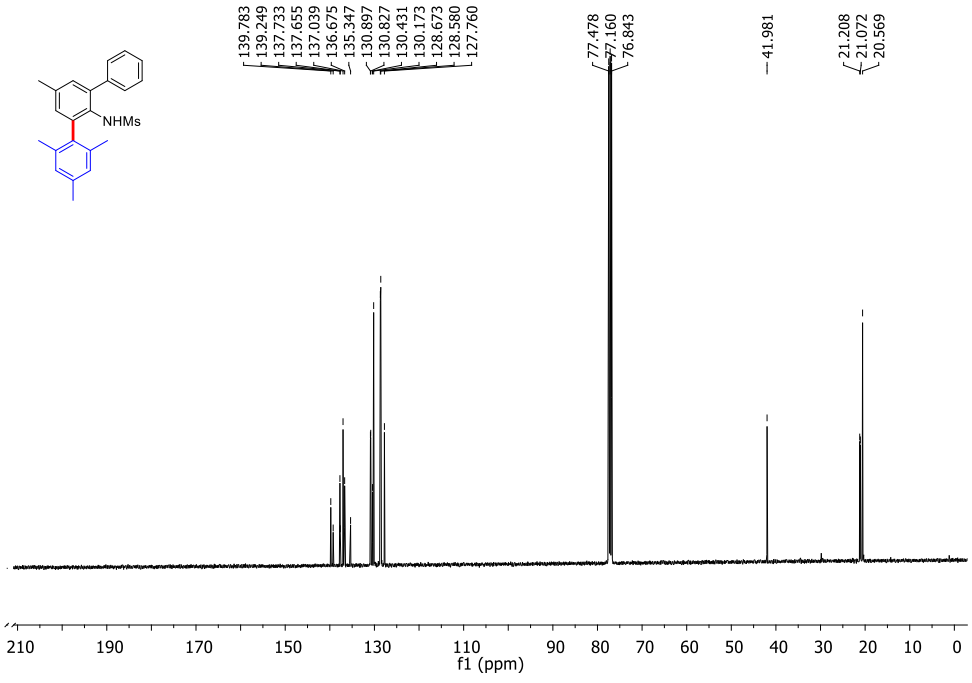


Figure 4.7. [13]C NMR spectrum of *N*-(2,4,5',6-tetramethyl-[1,1' : 3', 1"- terphenyl]-2'-yl) methanesulfonamide (**3aa**)

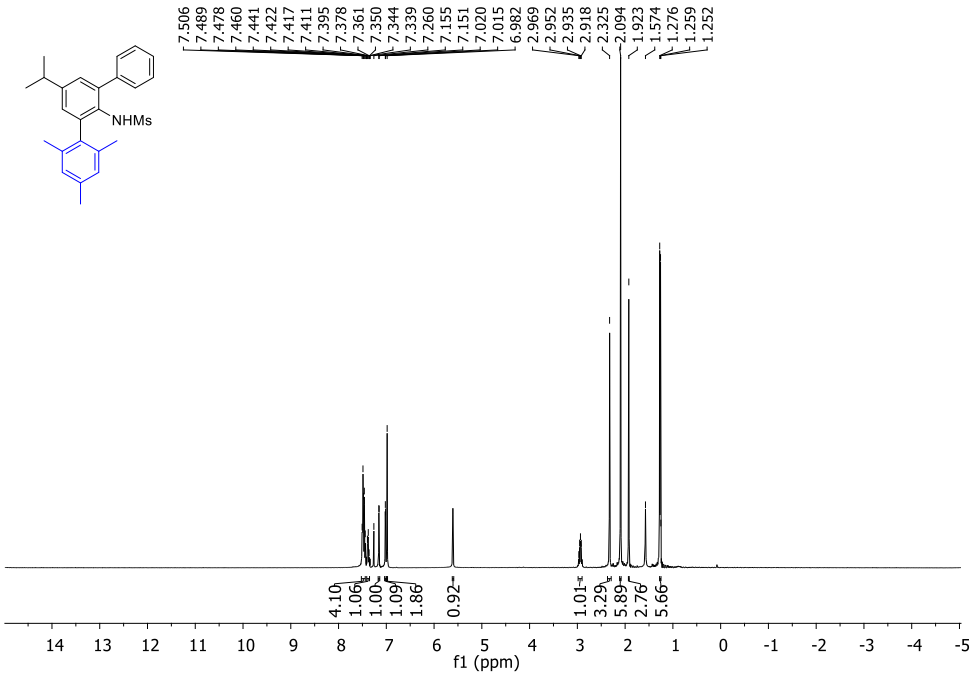


Figure 4.8. [1] H NMR spectrum of *N*-(5'-isopropyl-2,4,6- trimethyl- [1,1': 3', 1"-terphenyl]-2'-yl)methanesulfonamide (**3ba**)

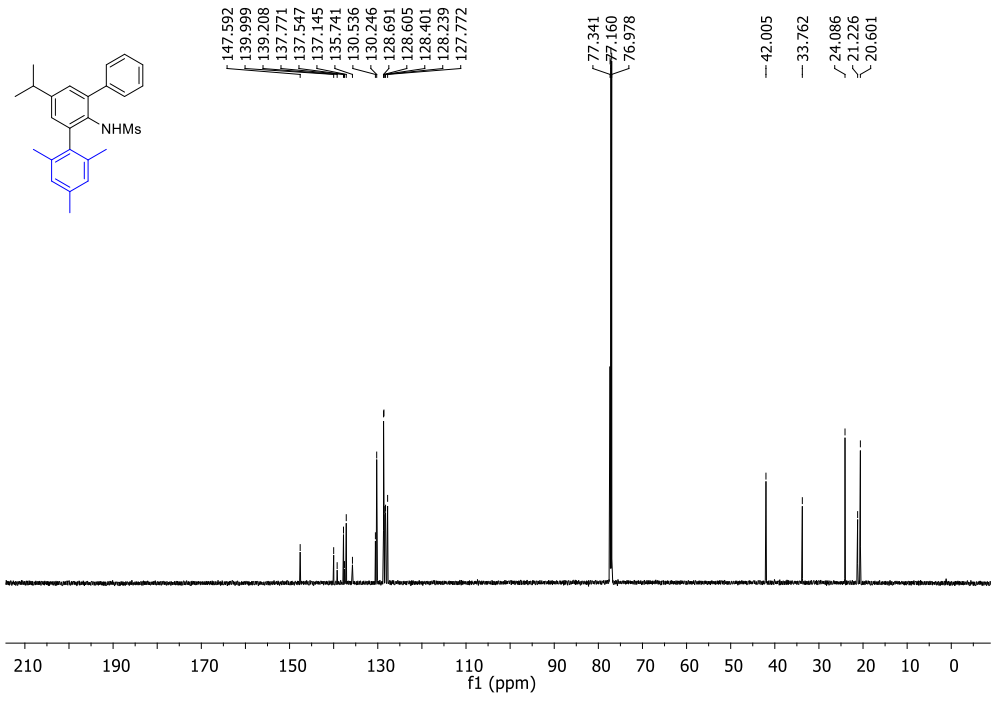


Figure 4.9. [13]C NMR spectrum of *N*-(5'-isopropyl-2,4,6- trimethyl- [1,1': 3', 1"-terphenyl]-2'-yl)methanesulfonamide (**3ba**)

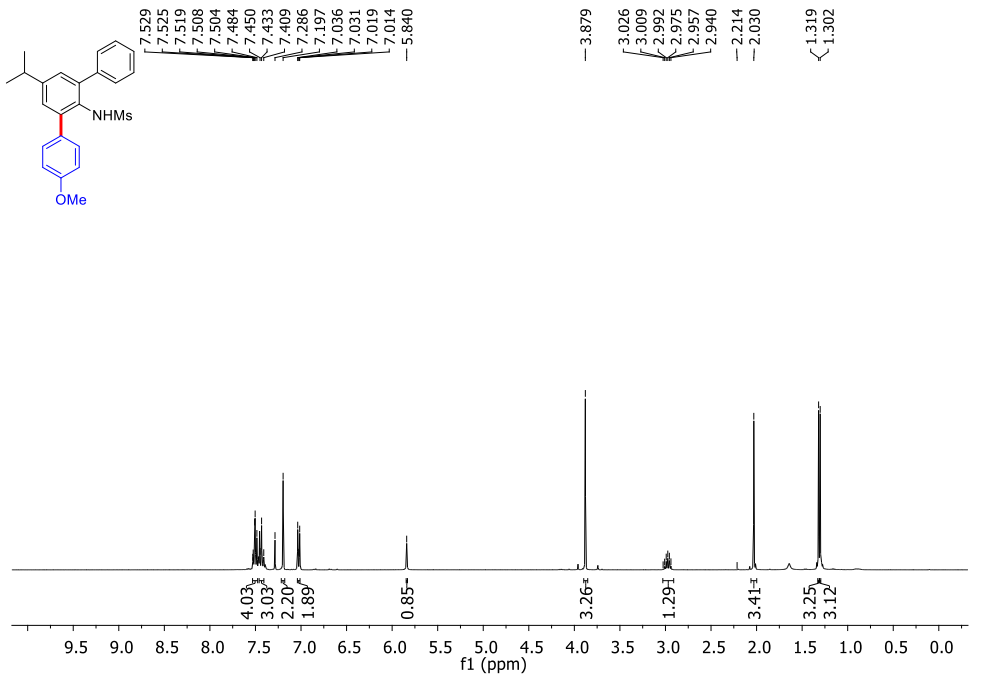


Figure 4.10. [1] H NMR spectrum of *N*-(5'-isopropyl-4-methoxy-[1,1' : 3',1''- terphenyl]-2'-yl)methanesulfonamide (**3bb**)

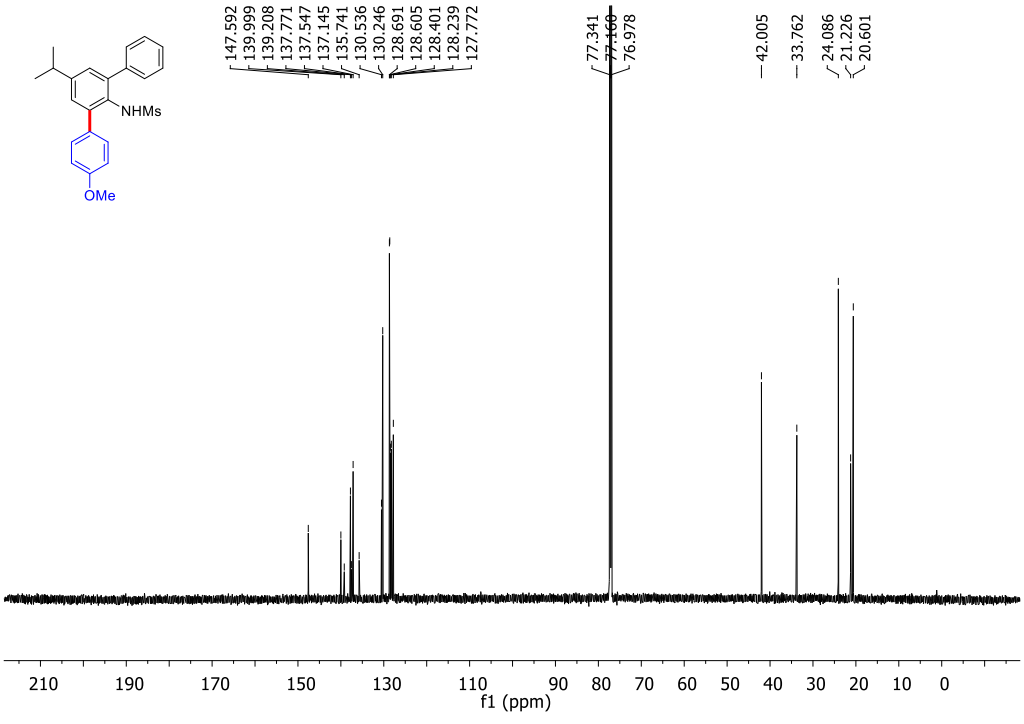


Figure 4.11. [13] C NMR spectrum of *N*-(5'-isopropyl-4-methoxy-[1,1' : 3',1''- terphenyl]-2'-yl)methanesulfonamide (**3bb**)

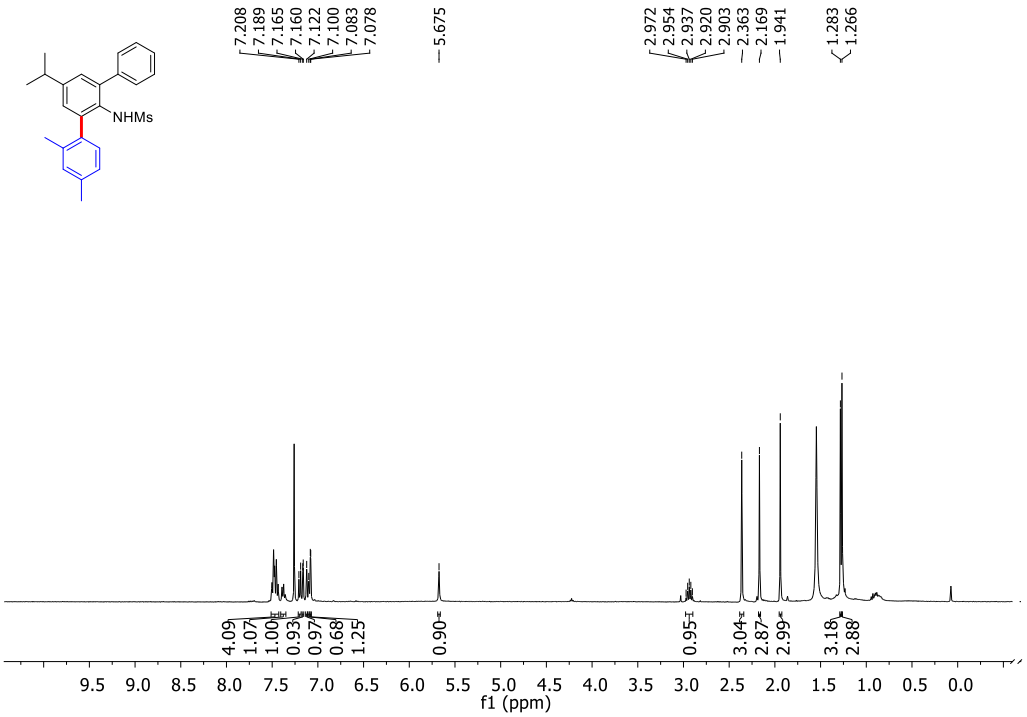


Figure 4.12. [1] H NMR spectrum of *N*-(5'-isopropyl-2,4-dimethyl-[1,1': 3',1"-terphenyl]-2'-yl)methanesulfonamide (**3bc**)

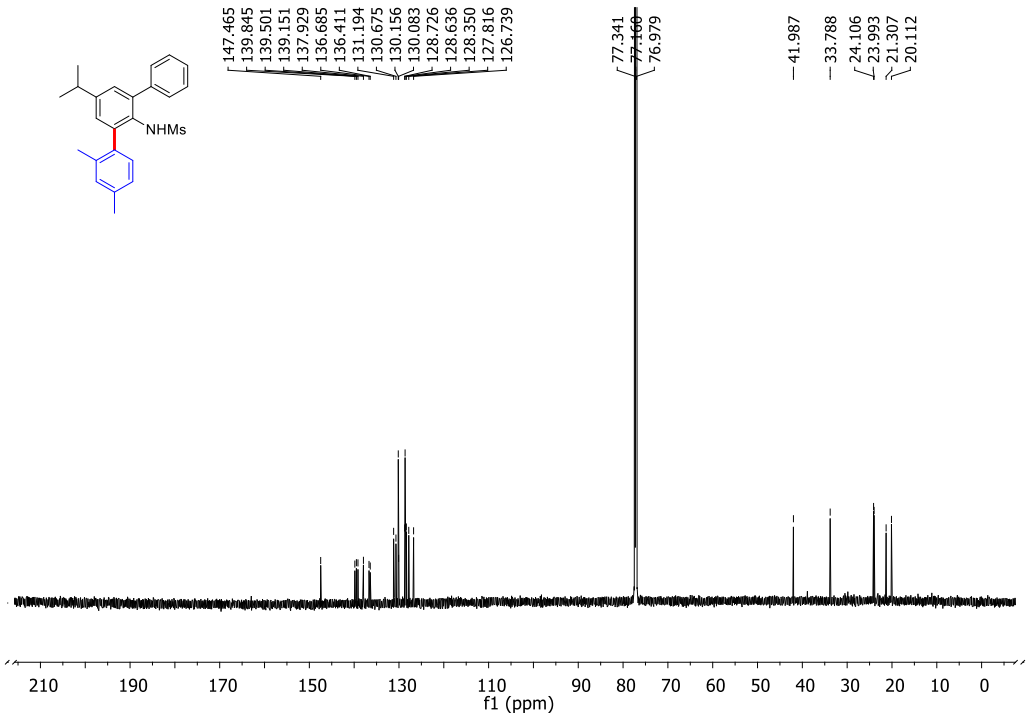


Figure 4.13. [13]C NMR spectrum of *N*-(5'-isopropyl-2,4-dimethyl-[1,1': 3',1"-terphenyl]-2'-yl)methanesulfonamide (**3bc**)

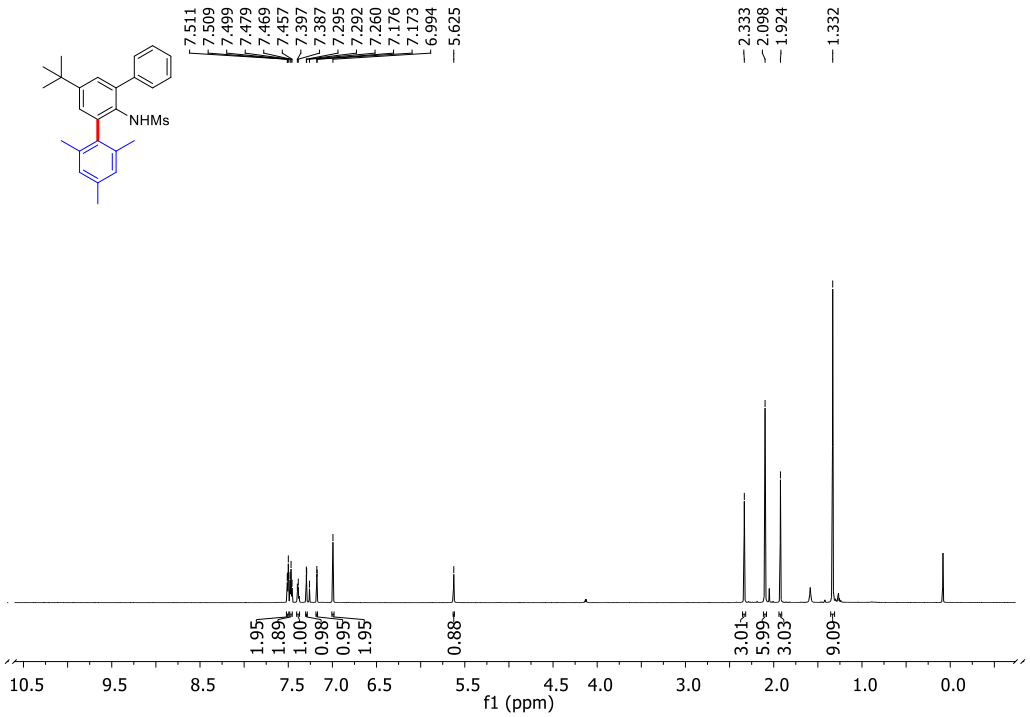


Figure 4.14. [1] H NMR spectrum of *N*-(5'-(tert-butyl)-2,4,6-trimethyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (**3ca**)

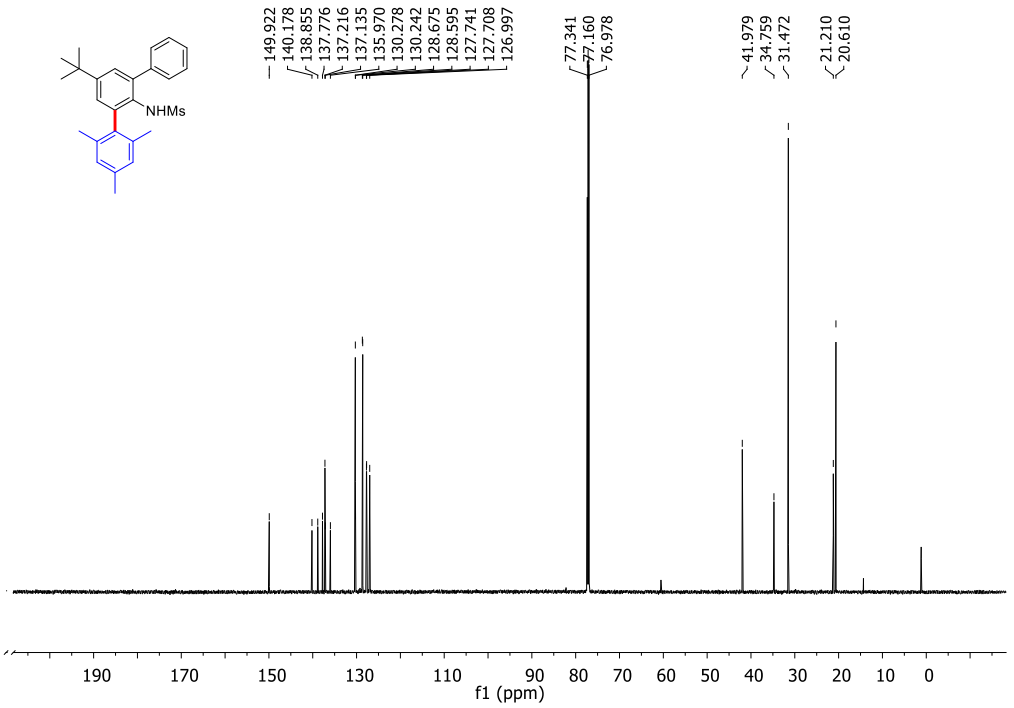


Figure 4.15. [13]C NMR spectrum of *N*-(5'-(tert-butyl)-2,4,6-trimethyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (**3ca**)

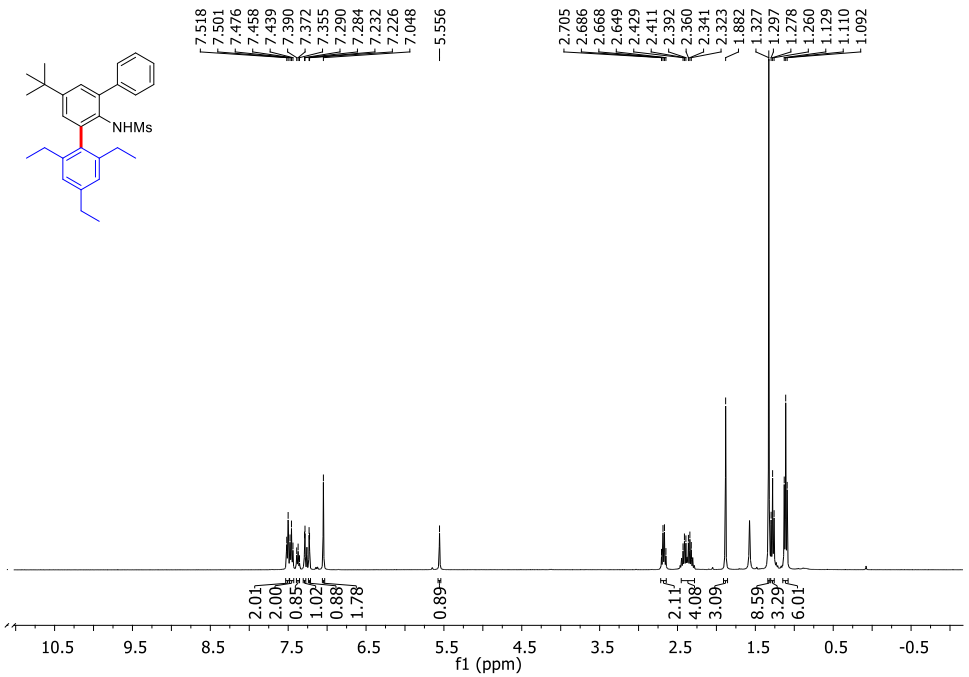


Figure 4.16. ^{1}H NMR spectrum of *N*-(5'-(tert-butyl)-2,4,6-triethyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (**3cd**)

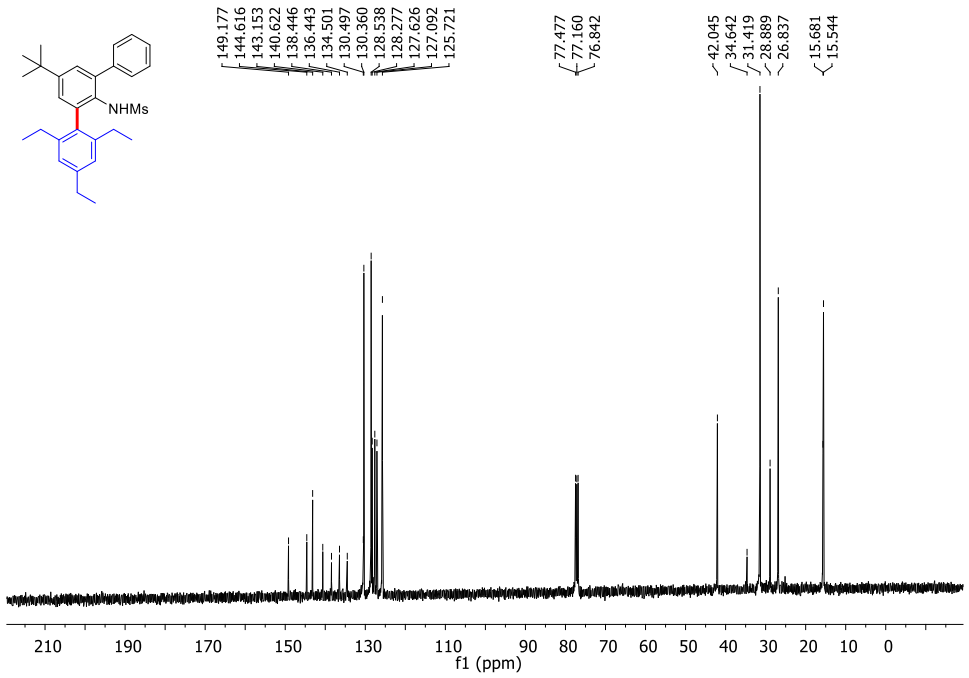


Figure 4.17. ^{13}C NMR spectrum of *N*-(5'-(tert-butyl)-2,4,6-triethyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (**3cd**)

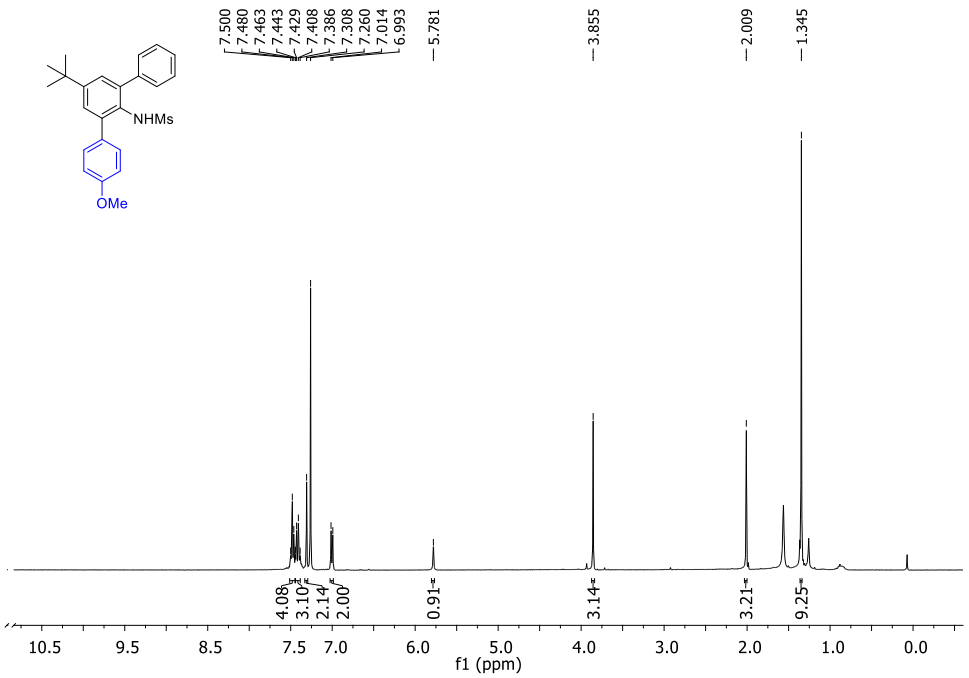


Figure 4.18. ^{1}H NMR spectrum of *N*-(5'-(*tert*-butyl)-4-methoxy-[1,1': 3',1"-terphenyl]-2'-yl)methaneslfonamide (**3cb**)

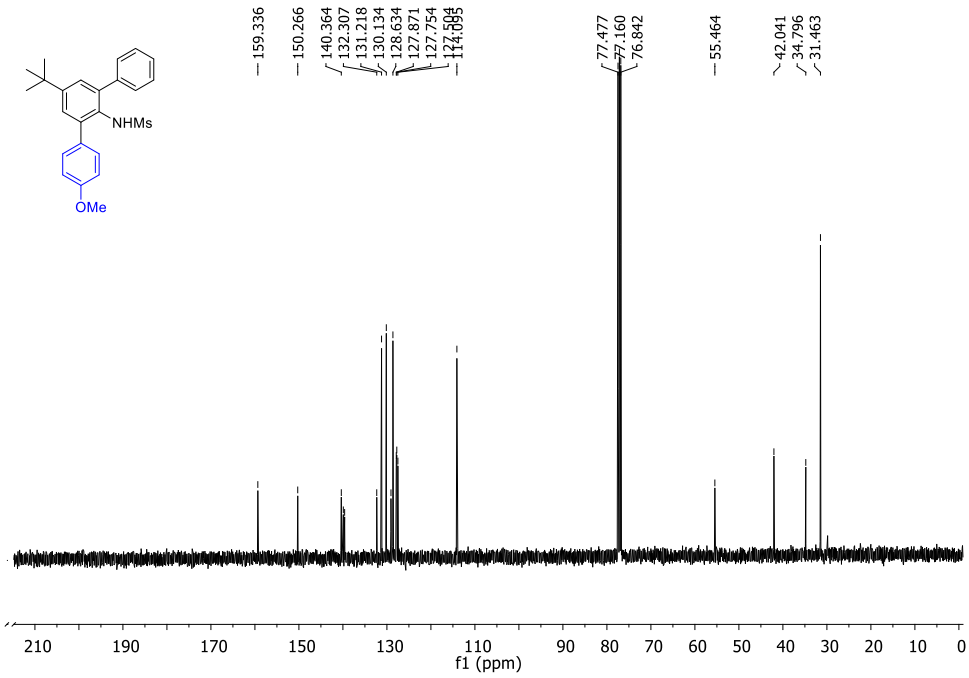


Figure 4.19. ^{13}C NMR spectrum of *N*-(5'-(*tert*-butyl)-4-methoxy-[1,1': 3',1"-terphenyl]-2'-yl)methaneslfonamide (**3cb**)

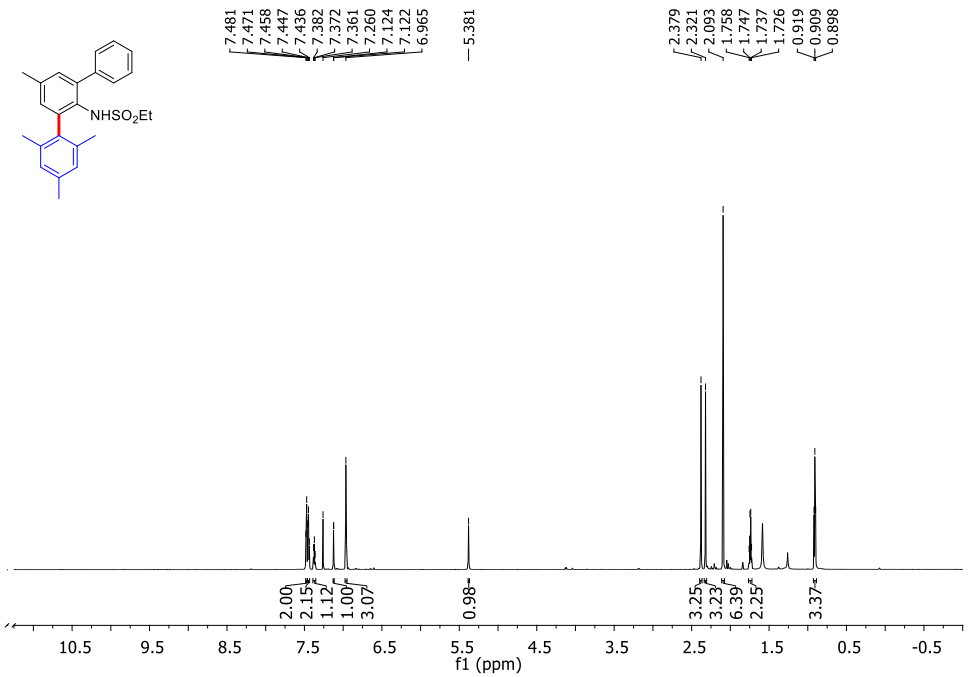


Figure 4.20. ^{1}H NMR spectrum of *N*-(2,4,5',6-tetramethyl-[1, 1':3', 1"-terphenyl]-2'-yl)ethanesulfonamide (**3da**)

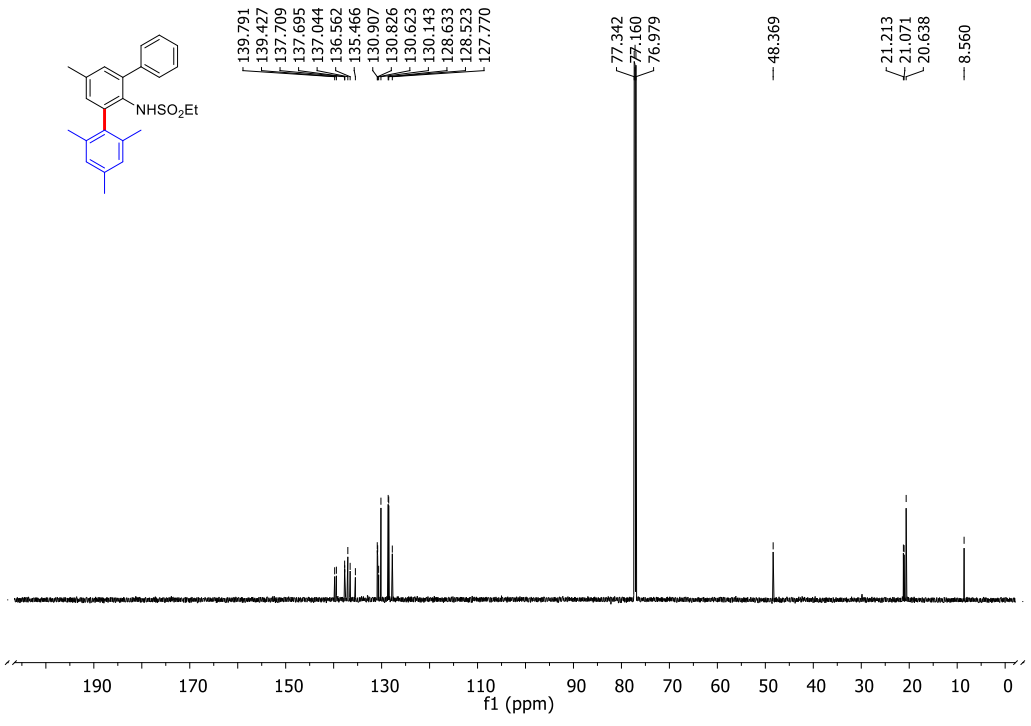


Figure 4.21. ^{1}H NMR spectrum of *N*-(2,4,5',6-tetramethyl-[1, 1':3', 1"-terphenyl]-2'-yl)ethanesulfonamide (**3da**)

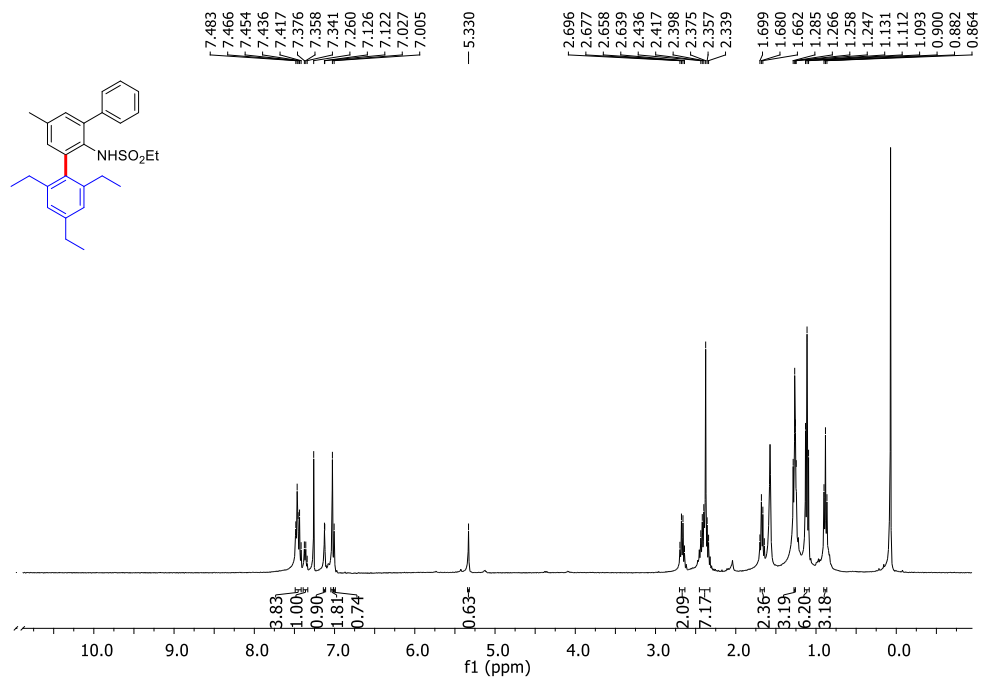


Figure 4.22. ^{1}H NMR spectrum of *N*-(2,4,6-triethyl-5'-methyl-[1,1':3',1"- terphenyl]-2'-yl)ethanesulfonamide (**3dd**)

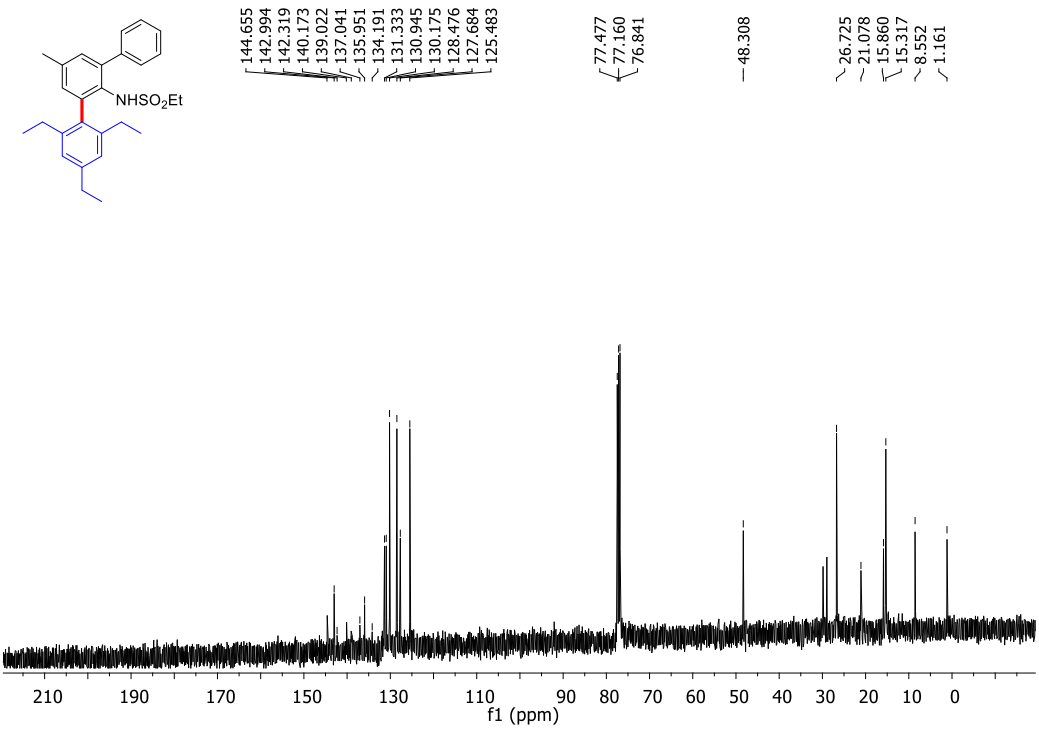


Figure 4.23. ^{13}C NMR spectrum of *N*-(2,4,6-triethyl-5'-methyl-[1,1':3',1"- terphenyl]-2'-yl)ethanesulfonamide (**3dd**)

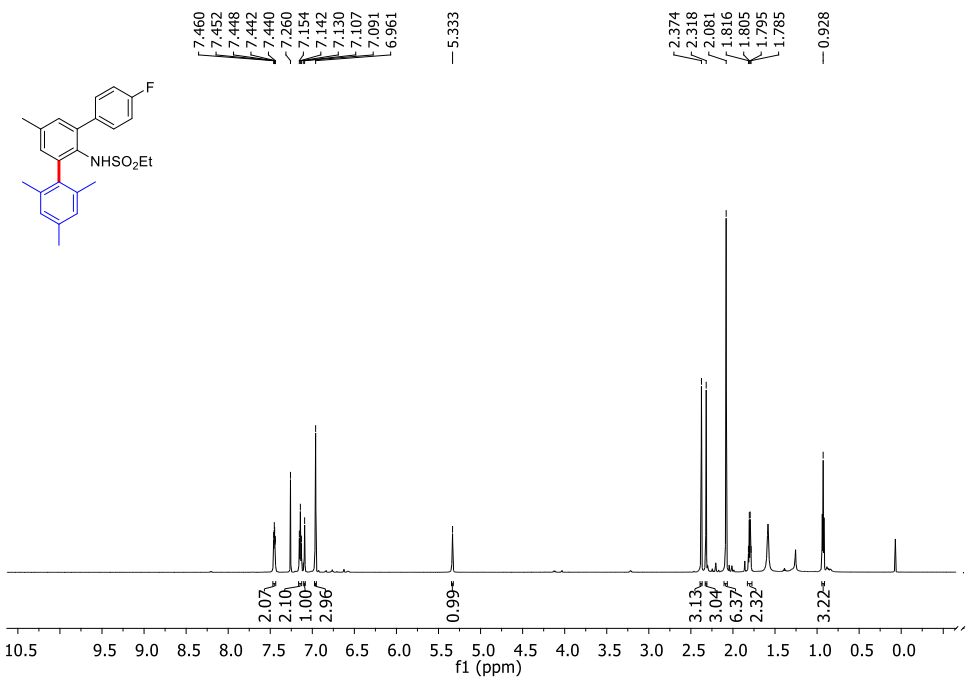


Figure 4.24. ^{1}H NMR spectrum of *N*-(4"- Fluoro-2, 4, 5', 6-tetramethyl-[1, 1': 3', 1"-terphenyl]-2'-yl)ethanesulfonamide (**3ea**)

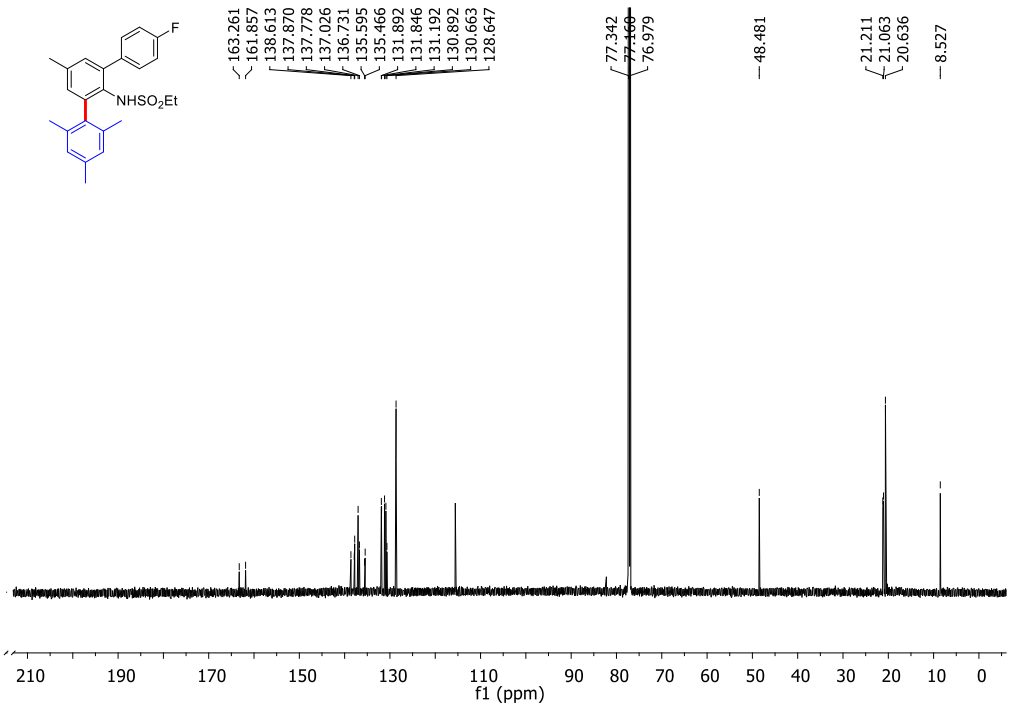


Figure 4.25. ^{13}C NMR spectrum of *N*-(4"- Fluoro-2, 4, 5', 6-tetramethyl-[1, 1': 3', 1"-terphenyl]-2'-yl)ethanesulfonamide (**3ea**)

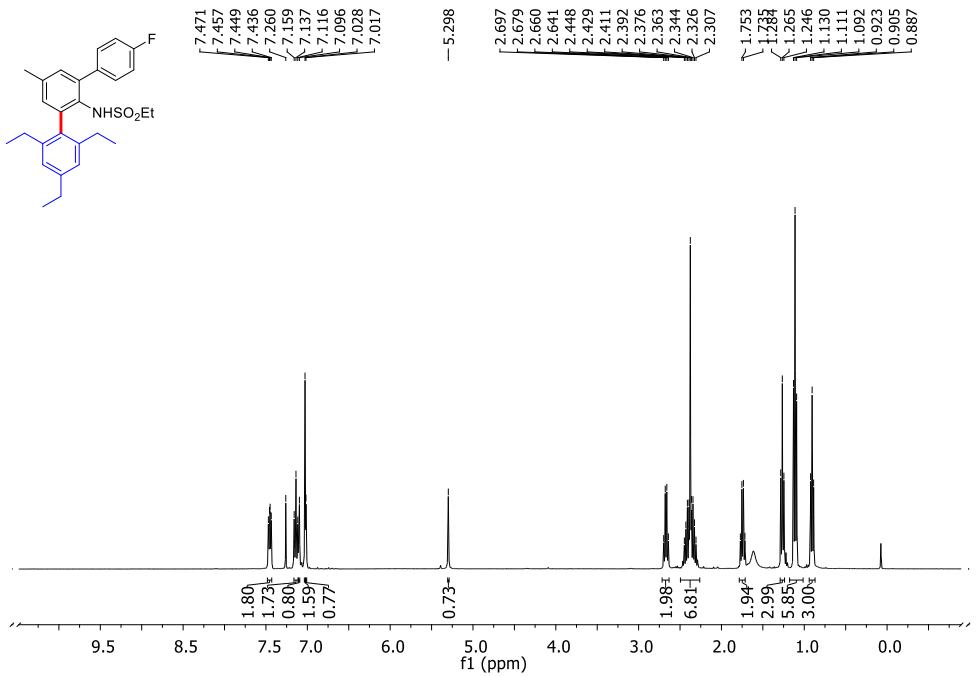


Figure 4.26. ^{1}H NMR spectrum of *N*-(2, 4, 6-triethyl- 4''- fluoro-5'-methyl-[1,1': 3', 1''-terphenyl]-2'-yl)ethanesulfonamide (**3ed**)

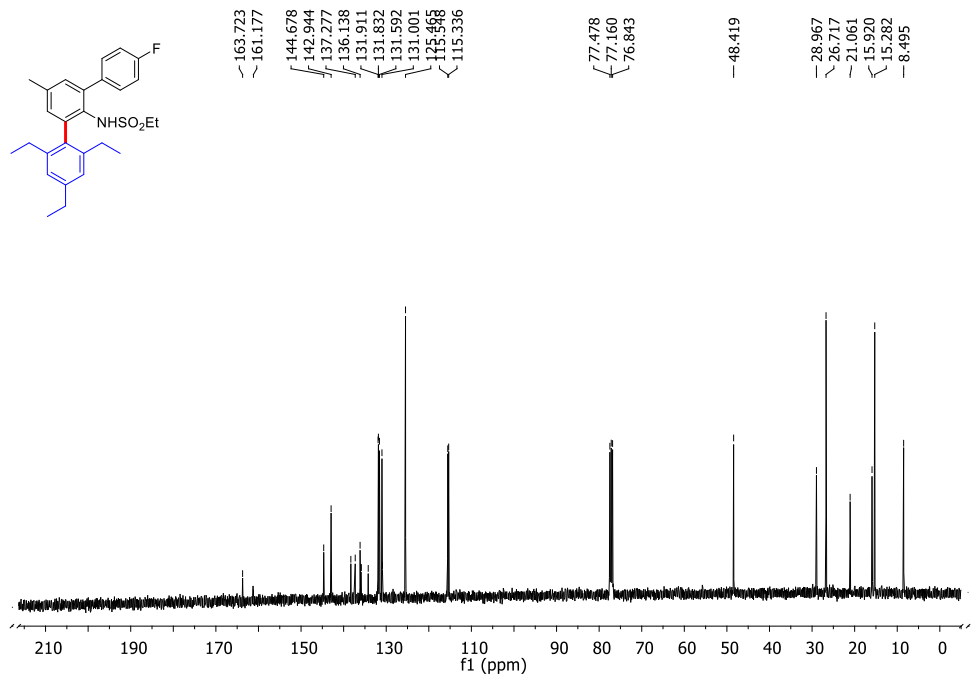


Figure 4.27. ^{13}C NMR spectrum of *N*-(2, 4, 6-triethyl- 4''- fluoro-5'-methyl-[1,1': 3', 1''-terphenyl]-2'-yl)ethanesulfonamide (**3ed**)

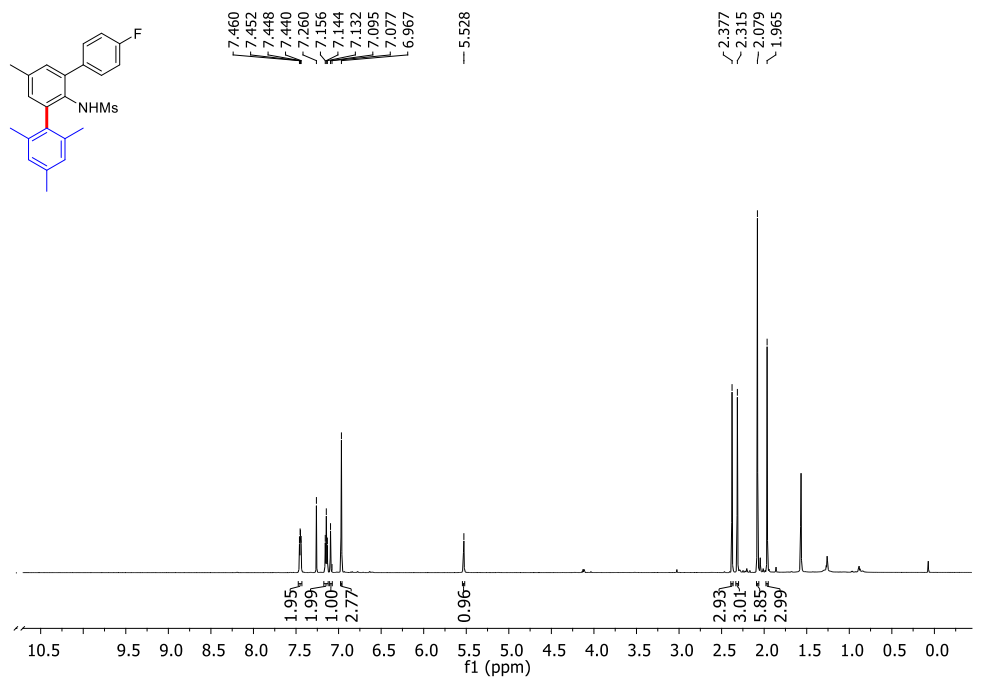


Figure 4.28. ^{1}H NMR spectrum of *N*-(4''- Fluoro- 2, 4, 5', 6- tetramethyl-[1,1':3',1''-terphenyl]-2'-yl]methanesulfonamide (**3fa**)

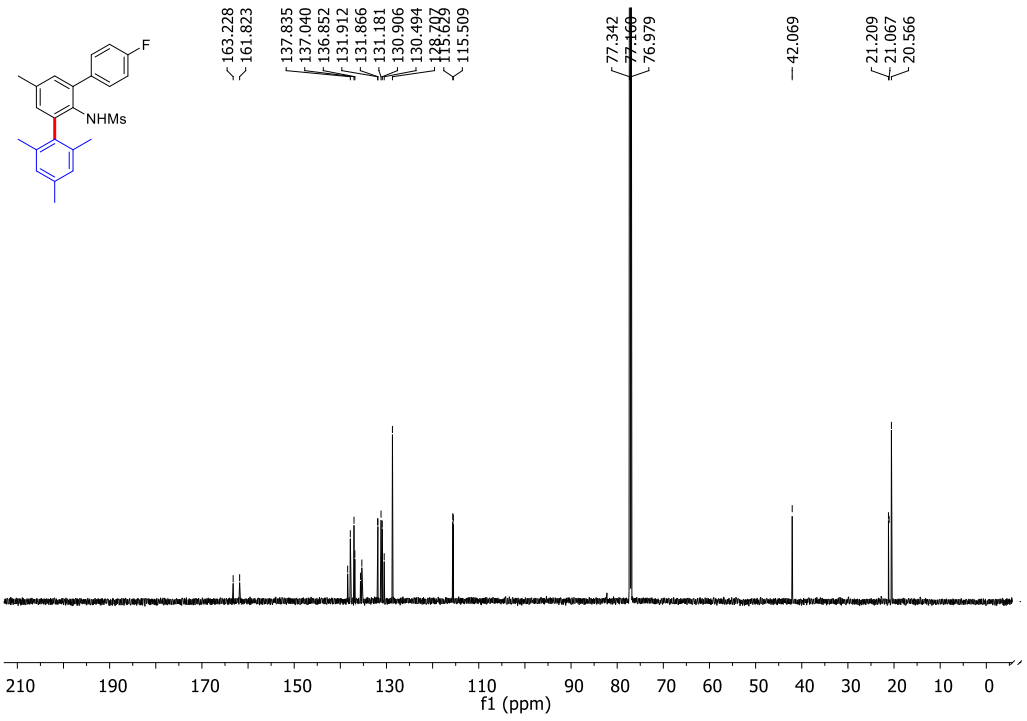


Figure 4.29. ^{13}C NMR spectrum of *N*-(4''- Fluoro- 2, 4, 5', 6- tetramethyl-[1,1':3',1''-terphenyl]-2'-yl]methanesulfonamide (**3fa**)

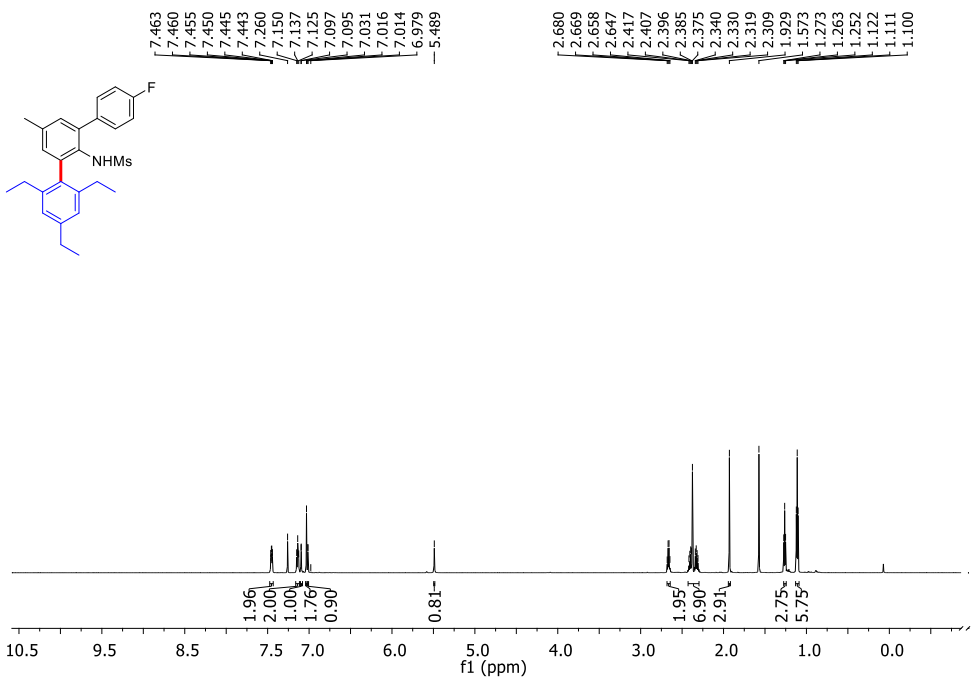


Figure 4.30. ^{1}H NMR spectrum of *N*-(2,4,6-triethyl-4"-fluoro-5'-methyl-[1,1': 3', 1"-terphenyl]-2'-yl)methanesulfonamide (**3fd**)

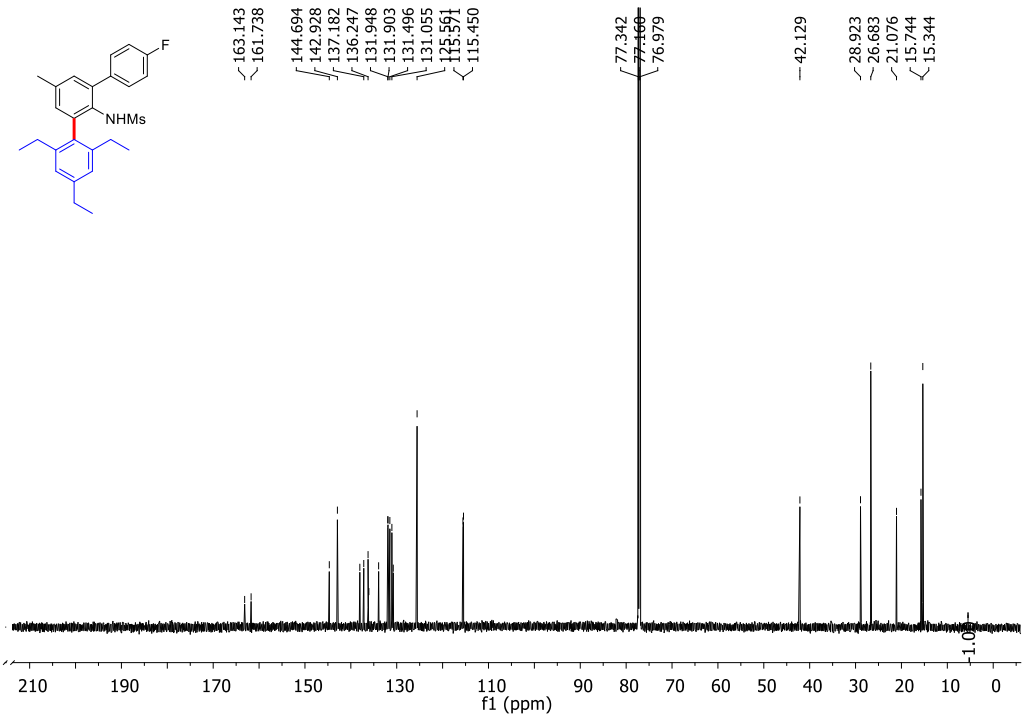


Figure 4.31. ^{13}C NMR spectrum of *N*-(2,4,6-triethyl-4"-fluoro-5'-methyl-[1,1': 3', 1"-terphenyl]-2'-yl)methanesulfonamide (**3fd**)

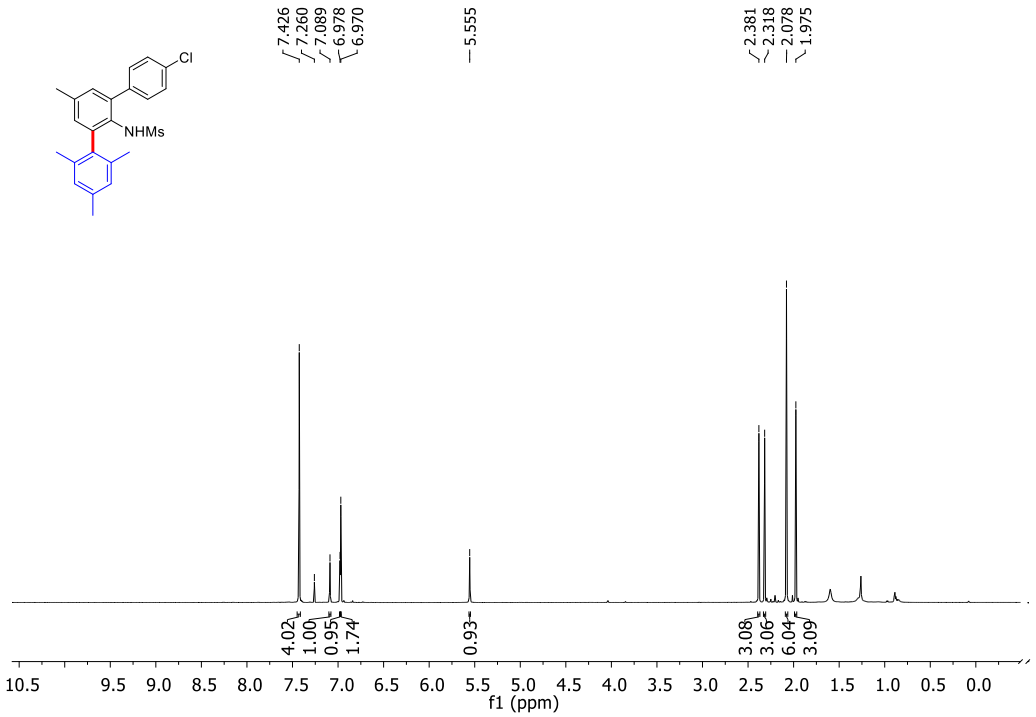


Figure 4.32. ^{1}H NMR spectrum of *N*-(4''-chloro-2, 4, 5',6-tetramethyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (**3ga**)

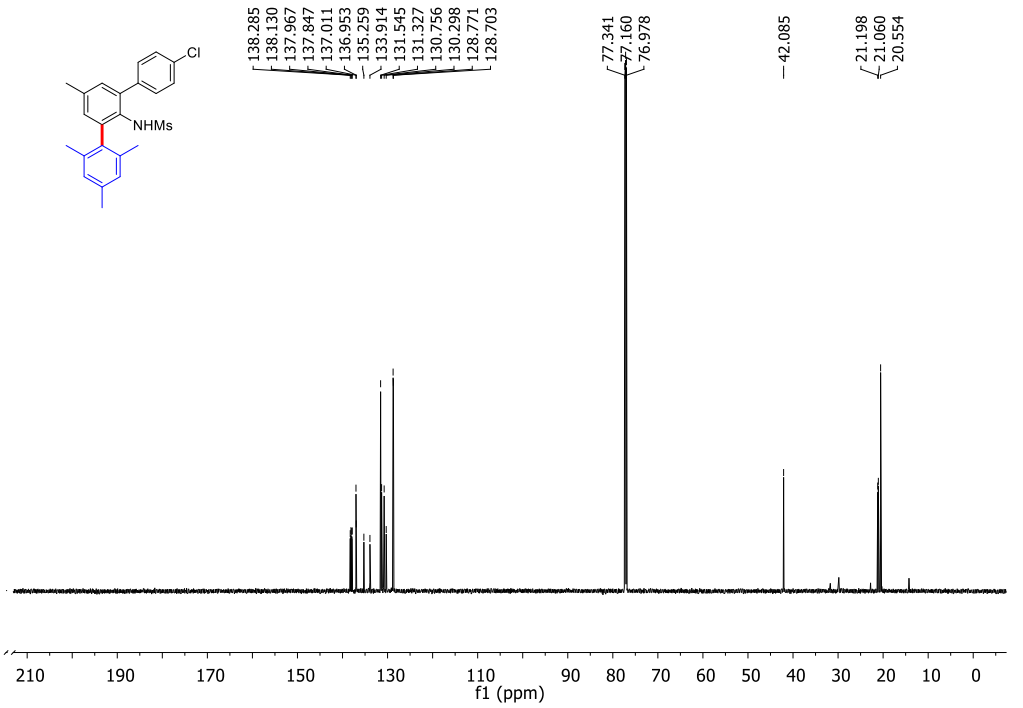


Figure 4.33. ^{13}C NMR spectrum of *N*-(4''-chloro-2, 4, 5',6-tetramethyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (**3ga**)

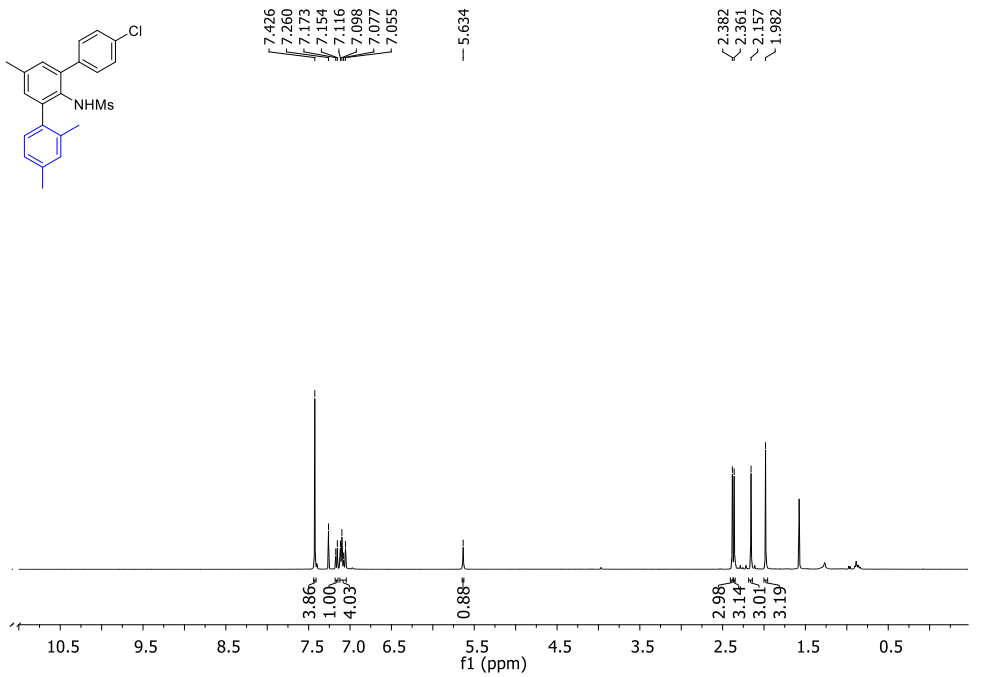


Figure 4.34. ^{1}H NMR spectrum of *N*-(4"-chloro-2,4,5'-trimethyl-[1,1':3',1"-terphenyl]-2'-yl)methanesulfonamide (**3gc**)

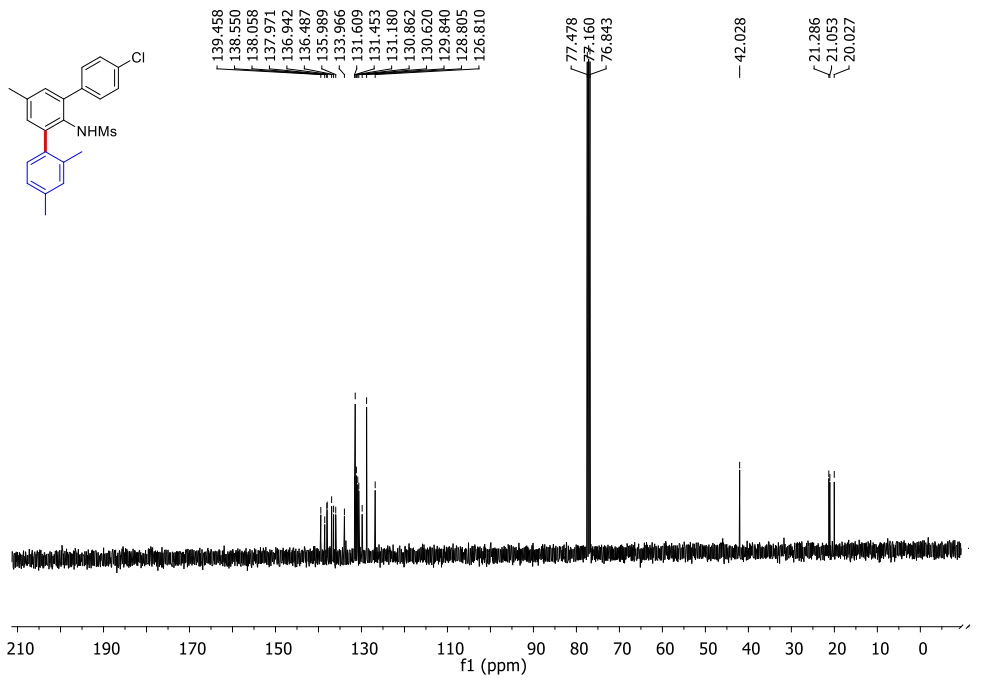


Figure 4.35. ^{13}C NMR spectrum of *N*-(4"-chloro-2,4,5'-trimethyl-[1,1':3',1"-terphenyl]-2'-yl)methanesulfonamide (**3gc**)

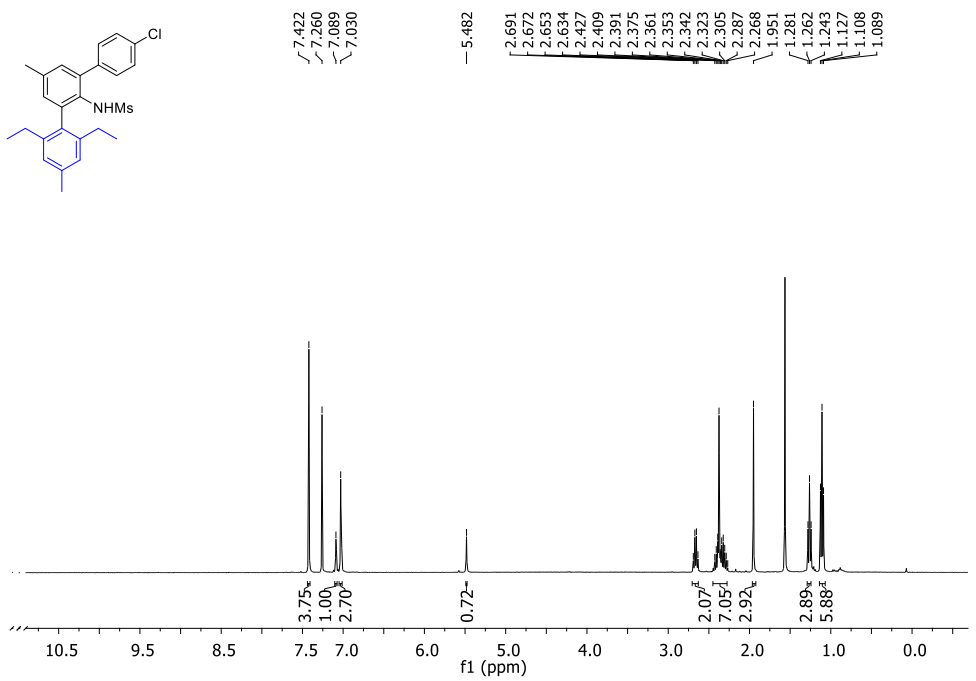


Figure 4.36. ^{1}H NMR spectrum of *N*-(4"-chloro-2,4,6-triethyl-5'-methyl-[1,1':3',1"-terphenyl]-2'-yl)methanesulfonamide (**3gd**)

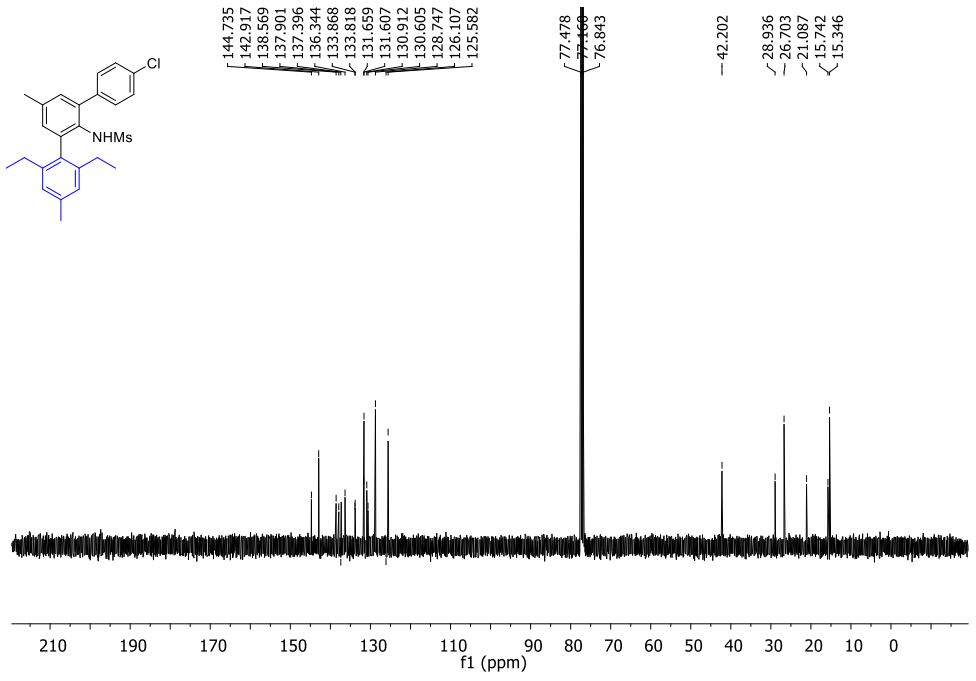


Figure 4.37. ^{13}C NMR spectrum of *N*-(4"-chloro-2,4,6-triethyl-5'-methyl-[1,1':3',1"-terphenyl]-2'-yl)methanesulfonamide (**3gd**)

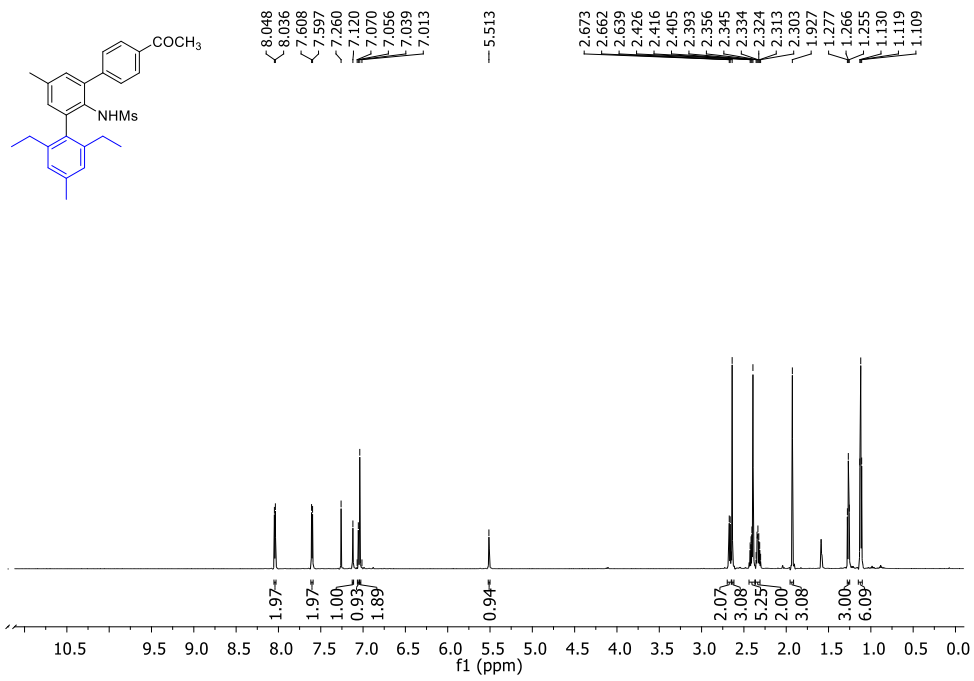


Figure 4.38. ^{1}H NMR spectrum of *N*-(4''-acetyl-2,4,6-triethyl-5'-methyl-[1,1':3',1''-terphenyl]-2'-yl)methanesufonamide (**3hd)**

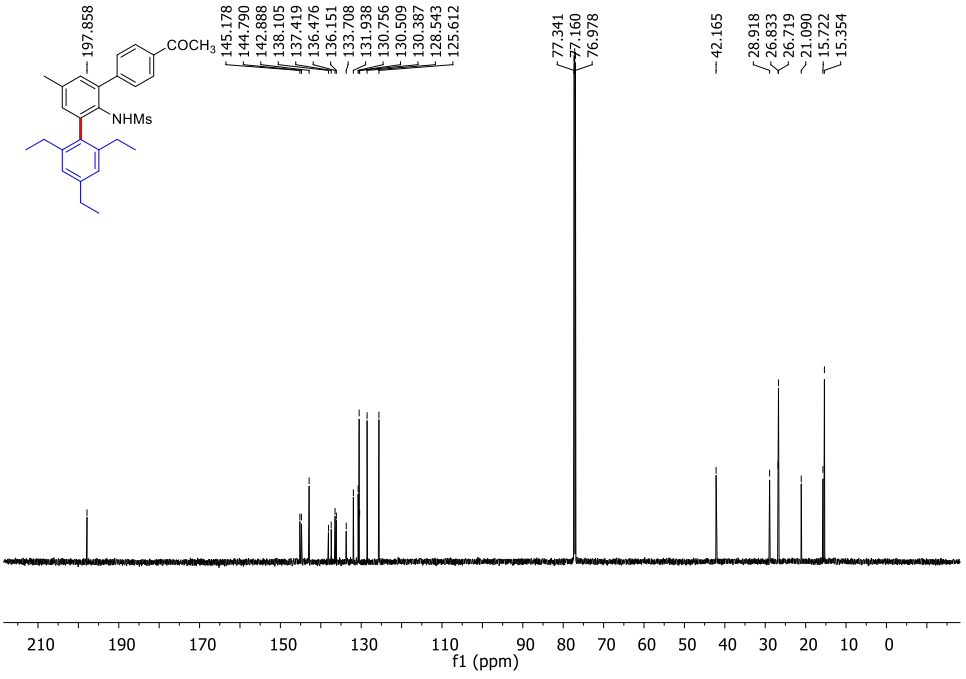


Figure 4.39. ^{13}C NMR spectrum of *N*-(4''-acetyl-2,4,6-triethyl-5'-methyl-[1,1':3',1''-terphenyl]-2'-yl)methanesufonamide (**3hd**)

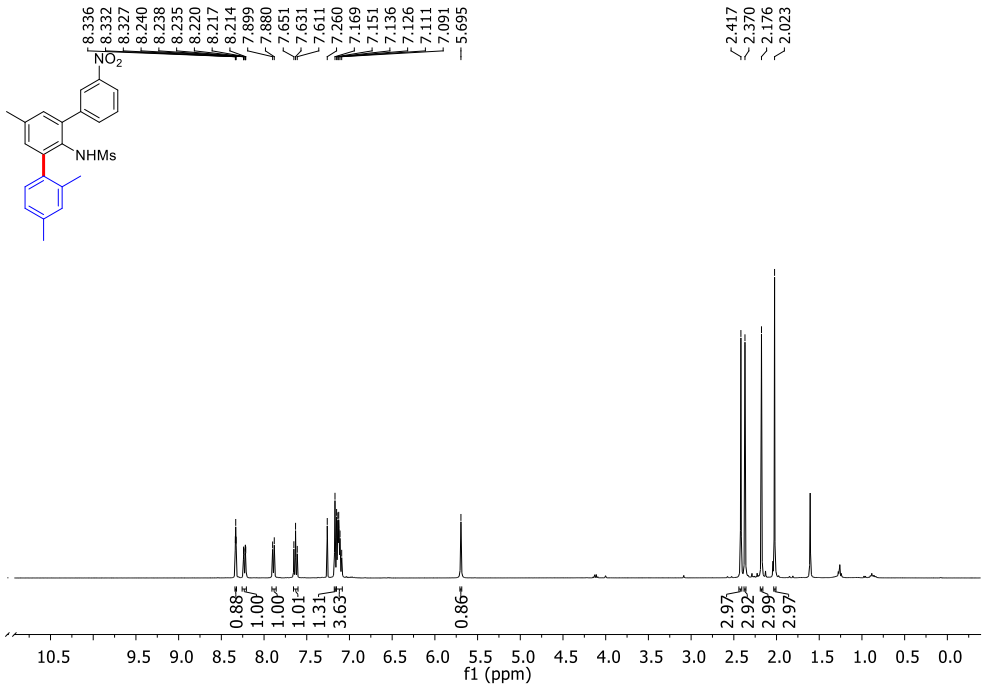


Figure 4.40. ^{1}H NMR spectrum of *N*-(2,4, 5'-trimethyl-3"-nitro-[1,1':3',1"-terphenyl]-2'yl)methanesulfonamide (**3ic**)

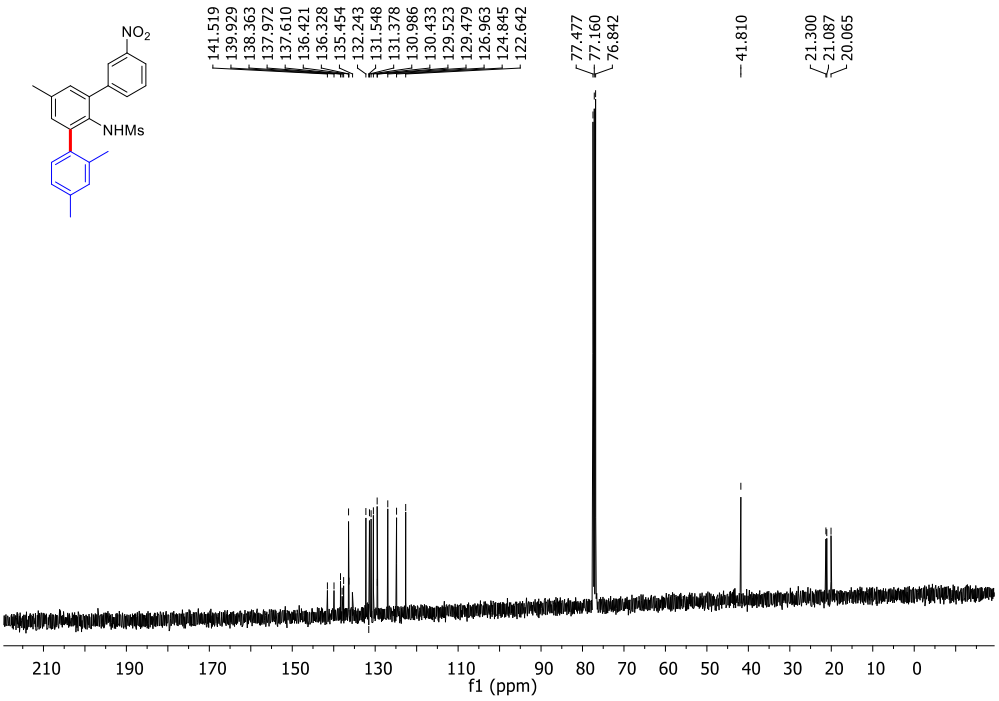


Figure 4.41. ^{13}C NMR spectrum of *N*-(2,4, 5'-trimethyl-3"-nitro-[1,1':3',1"-terphenyl]-2'yl)methanesulfonamide (**3ic**)

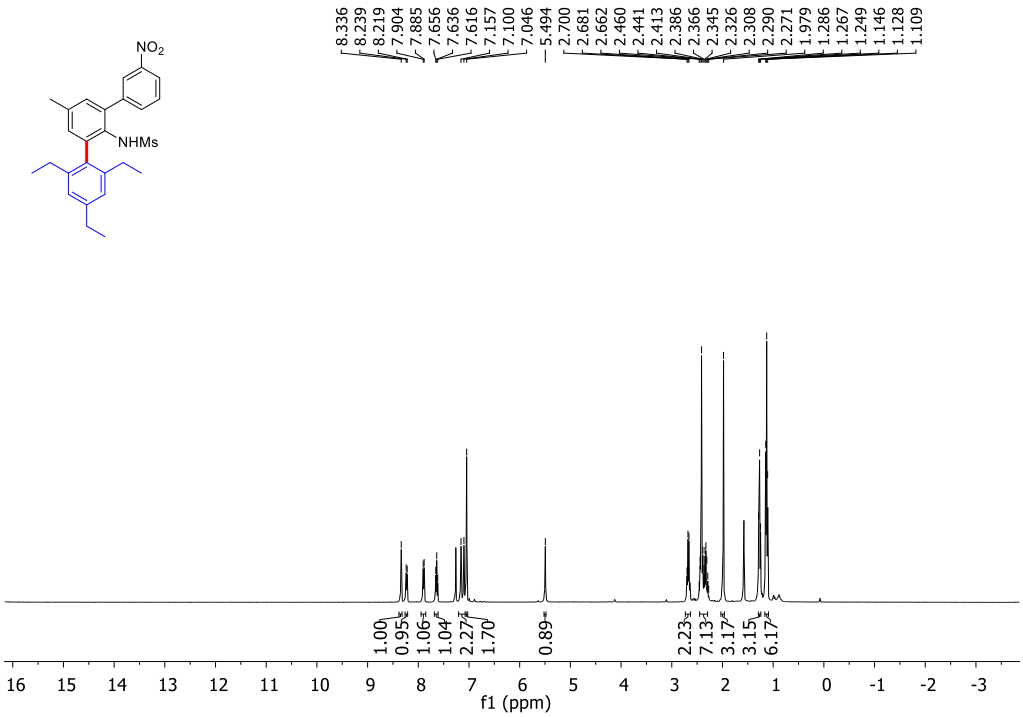


Figure 4.42. ^{1}H NMR spectrum of *N*-(2,4,6-triethyl-5'-methyl-3"-nitro-[1,1':3',1"-terphenyl]-2'yl]methanesulfonamide **(3id)**

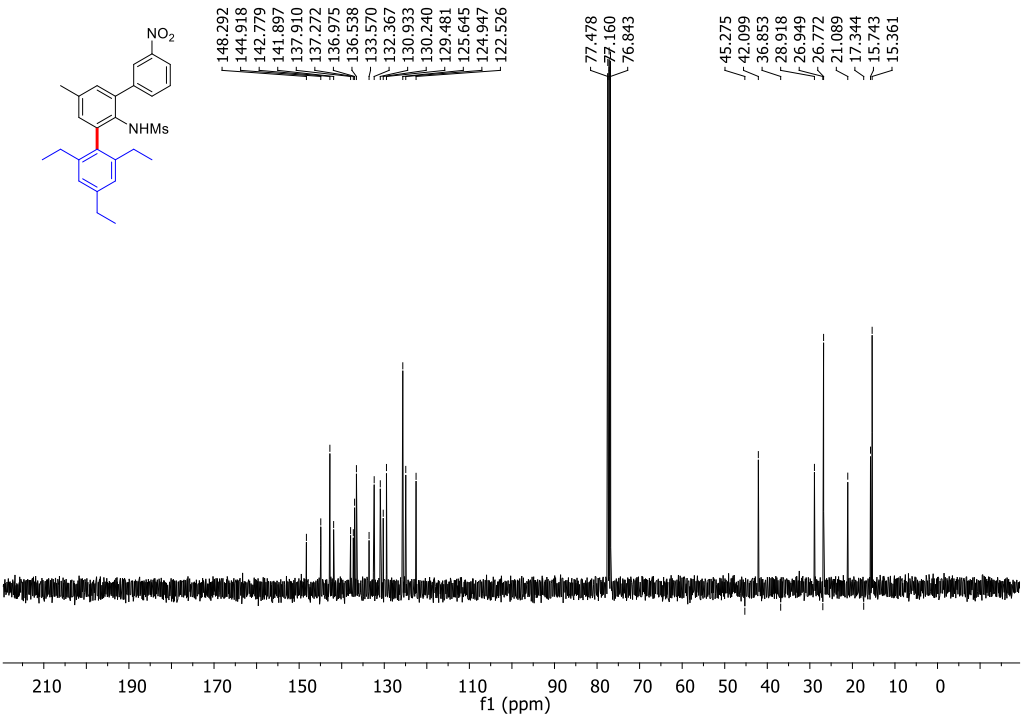


Figure 4.43. ^{13}C NMR spectrum of *N*-(2,4,6-triethyl-5'-methyl-3"-nitro-[1,1':3',1"-terphenyl]-2'yl]methanesulfonamide **(3id)**

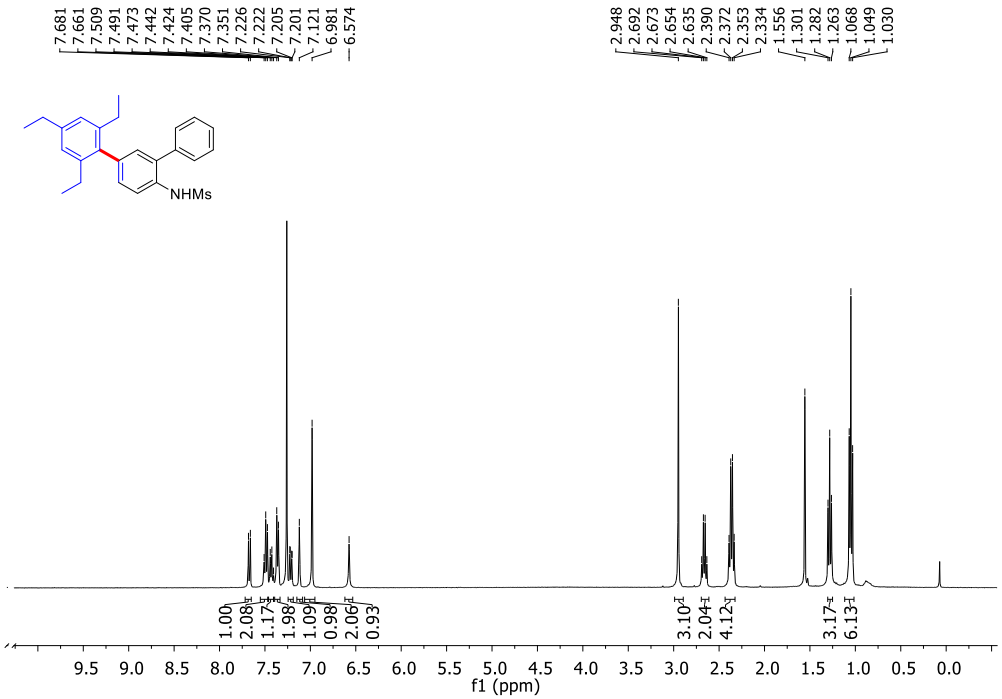


Figure 4.44. ^{1}H NMR spectrum of *N*-([1, 1'- biphenyl]-2-yl)-*N*-(2,4,6-triethylphenyl)methanesulfonamide (**4jd**)

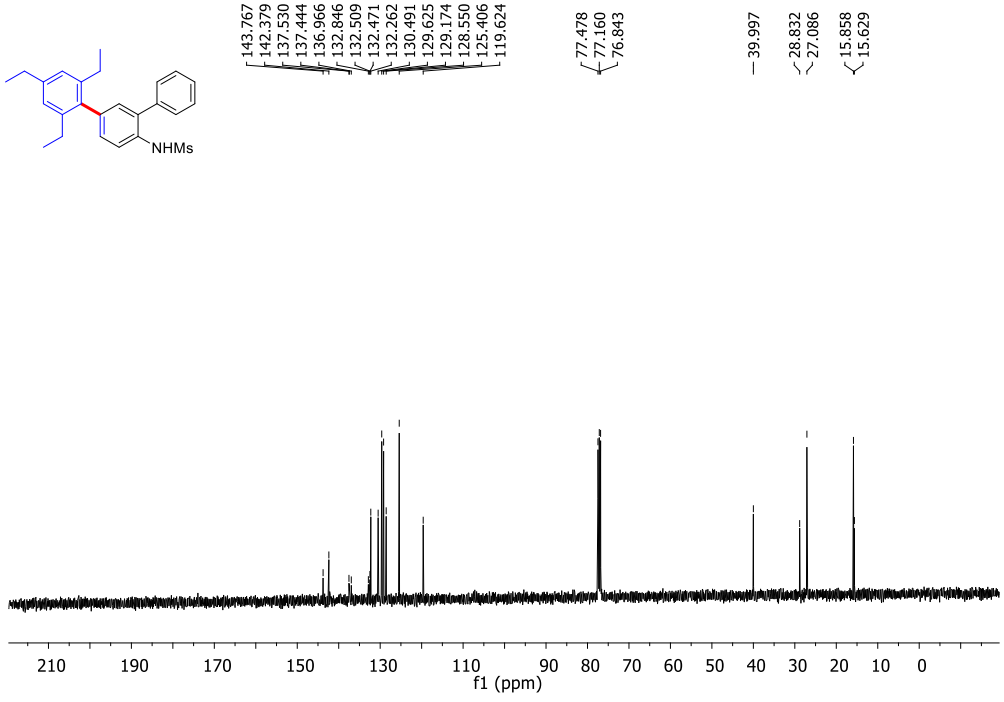


Figure 4.45. ^{13}C NMR spectrum of *N*-([1, 1'- biphenyl]-2-yl)-*N*-(2,4,6-triethylphenyl)methanesulfonamide (**4jd**)

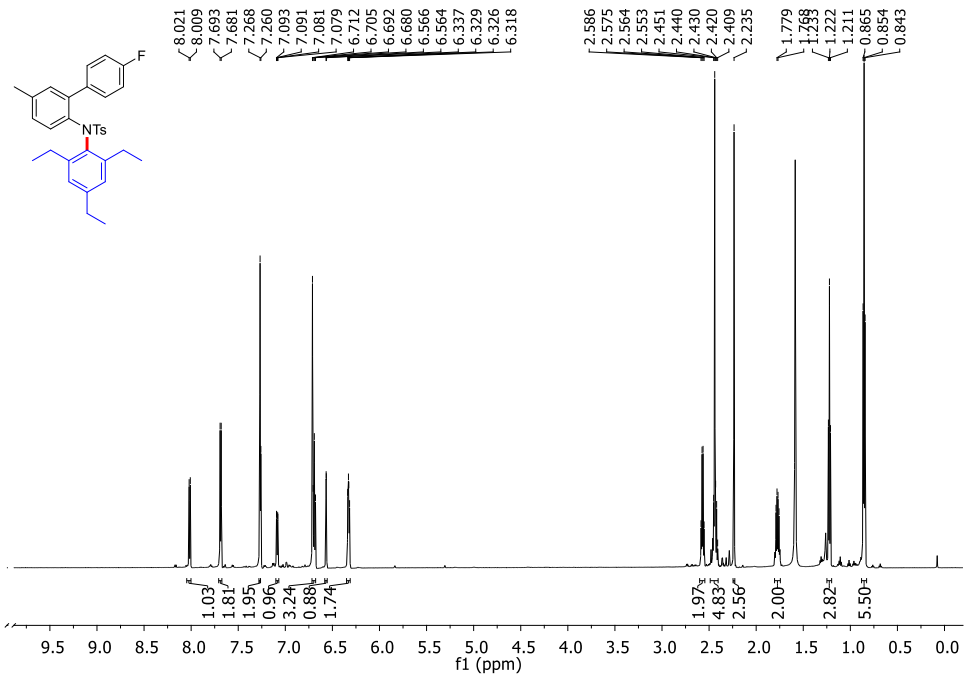


Figure 4.46. ^{1}H NMR spectrum of N-(4'-fluoro-5-methyl-[1,1'-biphenyl]-2-yl)-4-methyl-N-(2, 4,6 –triethylphenyl)benzenesulfonamide (**5kd**)

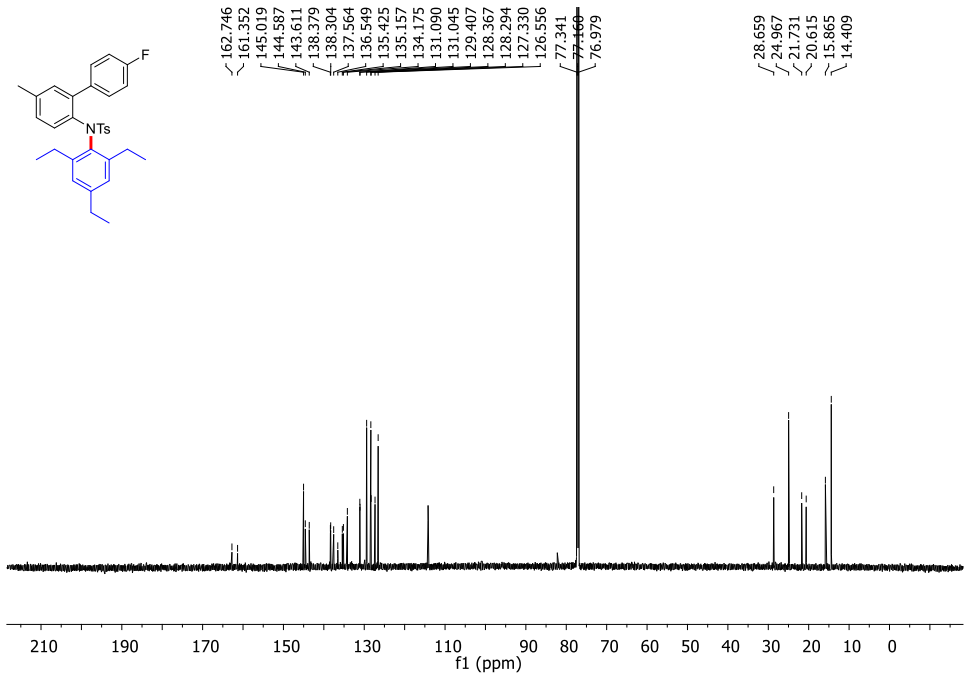


Figure 4.47. ^{13}C NMR spectrum of N-(4'-fluoro-5-methyl-[1,1'-biphenyl]-2-yl)-4-methyl-N-(2, 4,6 –triethylphenyl)benzenesulfonamide (**5kd**)

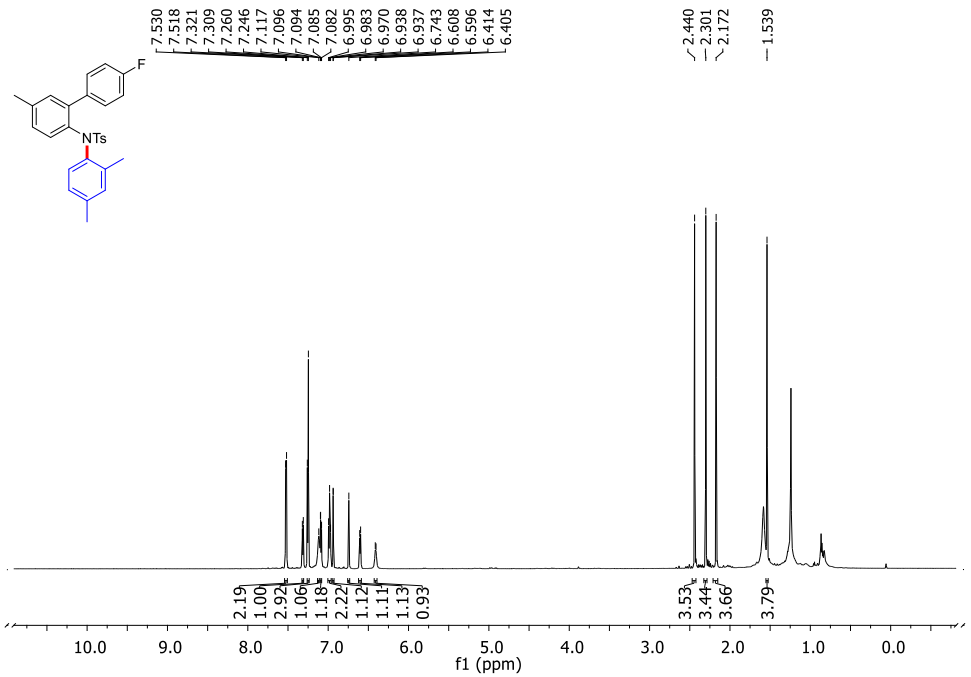


Figure 4.48. ^{1}H NMR spectrum of *N*-(2,4-dimethylphenyl)-N-(4'-fluoro-5-methyl-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide (**5kc**)

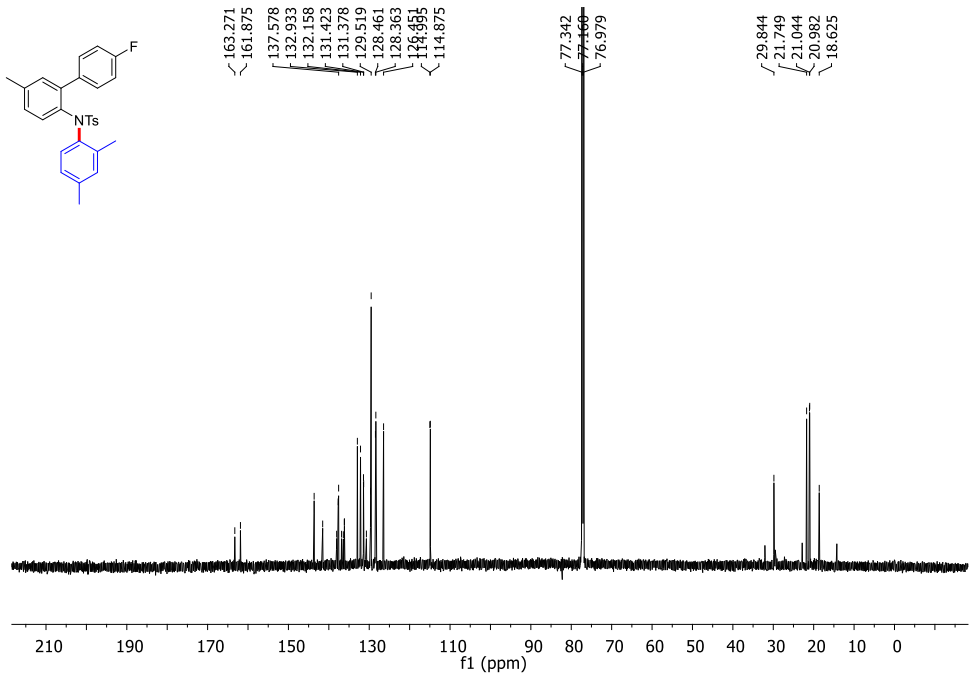


Figure S48. ^{13}C NMR spectrum of *N*-(2,4-dimethylphenyl)-N-(4'-fluoro-5-methyl-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide (**5kc**)

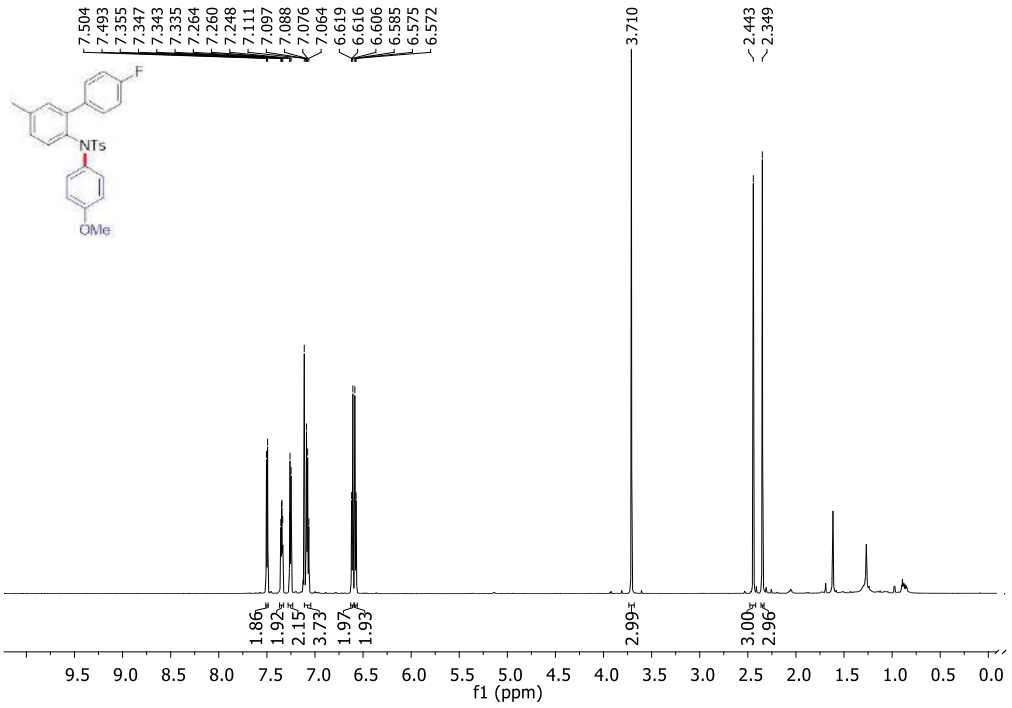


Figure 4.49. ^{1}H NMR spectrum of *N*-(4'-fluoro-5-methyl-[1,1'-biphenyl]-2-yl)-4-methyl-*N*-(4-methoxyphenyl)-4-methylbenzenesulfonamide (**5kb**)

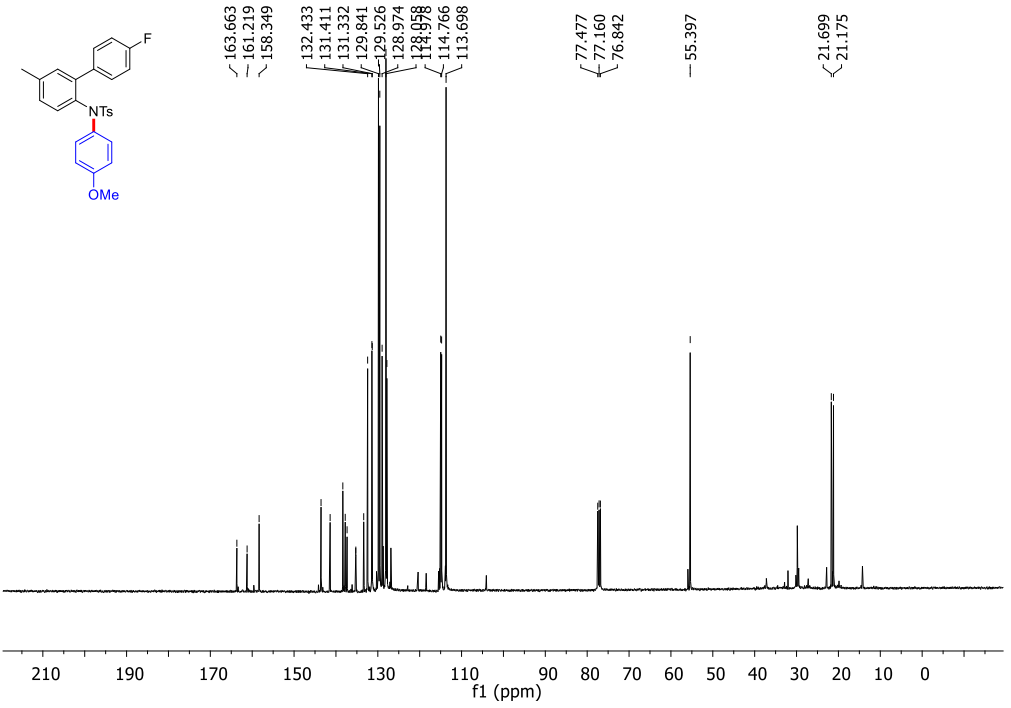


Figure 4.50. ^{13}C NMR spectrum of *N*-(4'-fluoro-5-methyl-[1,1'-biphenyl]-2-yl)-4-methyl-*N*-(4-methoxyphenyl)-4-methylbenzenesulfonamide (**5kb**)

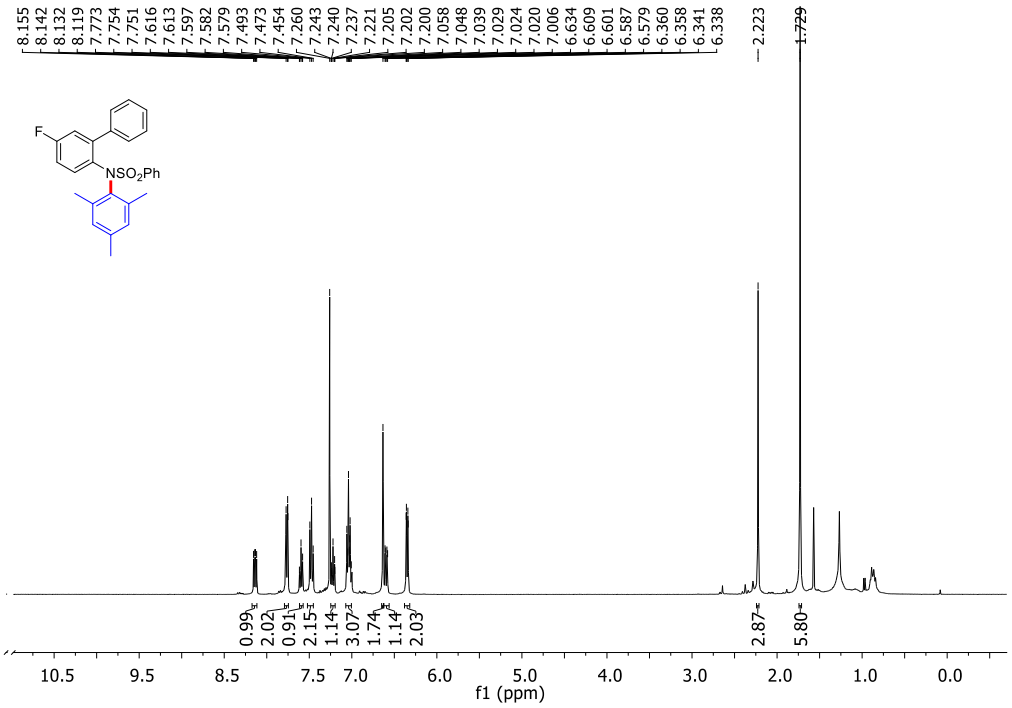


Figure 4.51. ^{1}H NMR spectrum of *N*-(5-fluoro-[1,1'-biphenyl]-2-yl)-*N*-mesitylbenzenesulfonamide (**5la**)

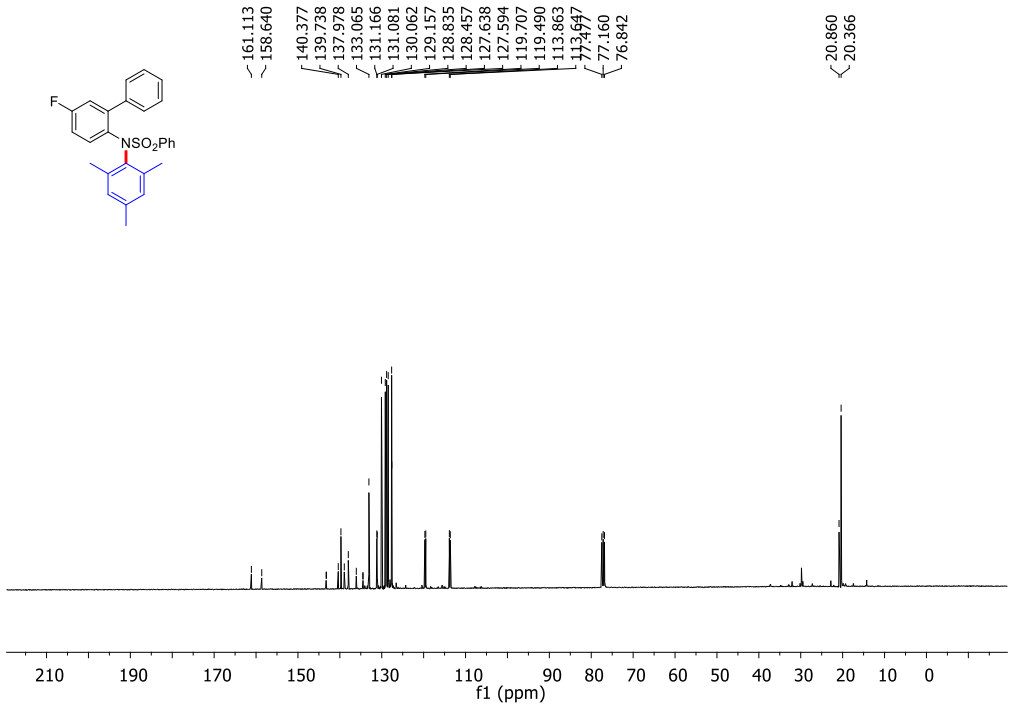
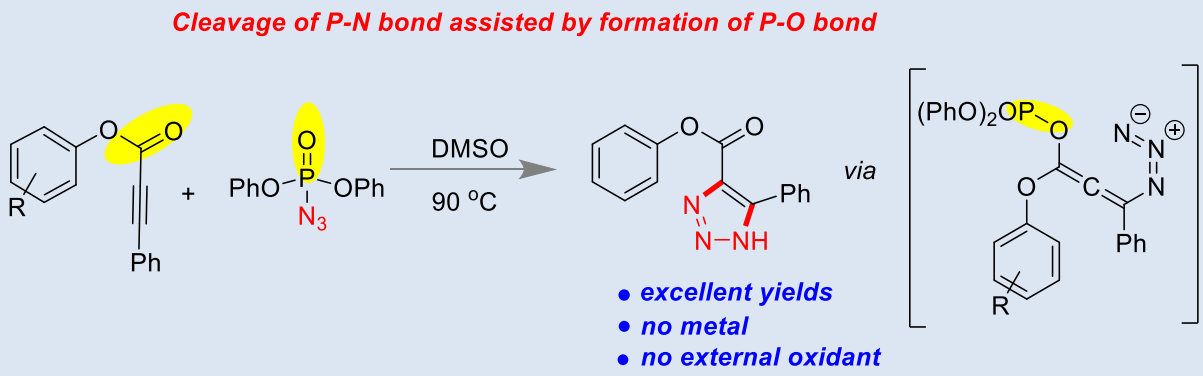


Figure 4.52. ^{13}C NMR spectrum of *N*-(5-fluoro-[1,1'-biphenyl]-2-yl)-*N*-mesitylbenzenesulfonamide (**5la**)

CHAPTER 5

Expedient Synthesis of Triazoles Directed by Phosphorus Oxygen Interaction

5.1 ABSTRACT



Phosphoryl azide, is still in obscurity and is less explored as an azide source employed in azide-alkyne cycloaddition. Herein, we report the synthesis of N_1-H triazoles using phosphoryl azide in solvent DMSO. Mechanistic investigations conclude the formation of an azidyl radical in the presence of a keto-containing compound. The probable reason for the product formation is phosphorus oxygen interaction, which cleaves the phosphorus nitrogen bond. Good to the excellent yield of N_1-H triazole scaffolds were synthesized following the protocol.

5.2 INTRODUCTION

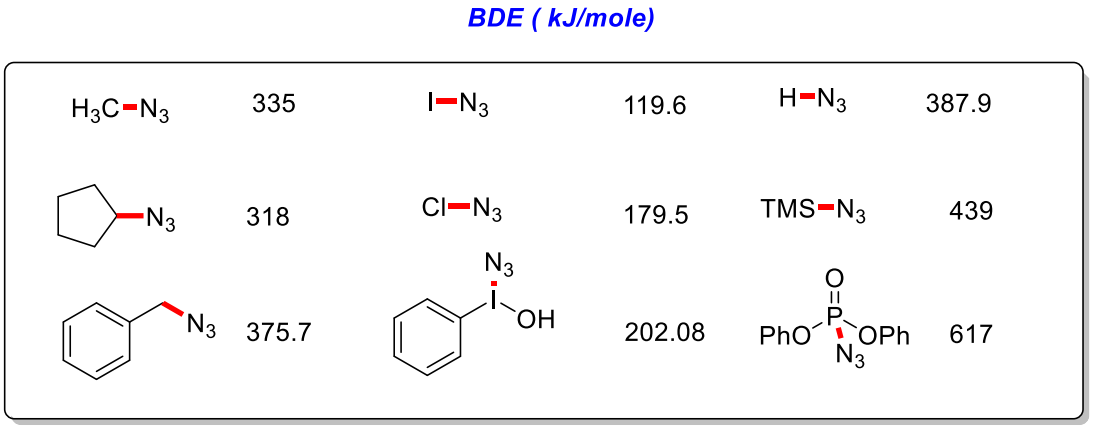
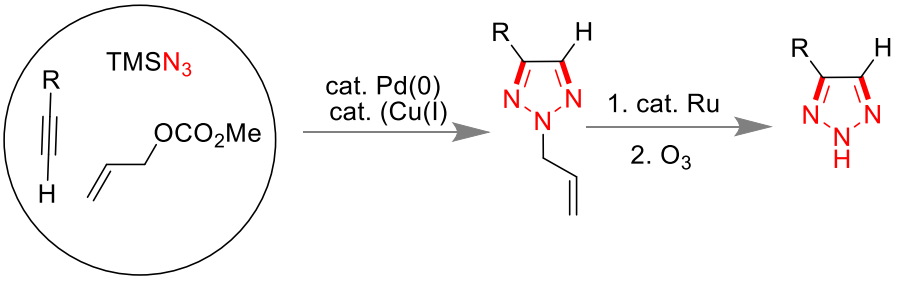


Figure 5.1 Binding energy for the commonly used azides in azide alkyne cycloaddition.

The triazole unit is a vital pharmacophore and has diverse applications in pharmaceutical and agrochemical industries exhibiting biological activity.[1-3] Its inbuilt structure infuses high aromatic stability, dipole-dipole and π –π stacking interactions, hydrogen bonding ability which necessitates its demand in biomedical research and supramolecular chemistry.[4-7] Triazoles have a widespread application in dyes and as corrosion inhibitors. Huisgen's [3+2] cycloaddition reaction between mono substituted acetylene and azide for the construction of triazole framework requires extremely harsh reaction conditions with poor regioselectivity, low yield, and difficulty in purification.[8-10] Common [11] azides employed for azide-alkyne cycloaddition with their binding energy have been displayed in figure 5.1. Diphenyl phosphoryl azide is a relatively less explored azide reagent in organic synthesis due to its high bond dissociation energy. The use of internal alkyne for azide-alkyne cycloaddition is rugged, and hence very few reports are noted in the literature.[12-14] The need to develop sustainable methodologies to synthesize triazoles with internal alkynes urges its significance in its synthesis. The traditional methods involving catalysts like Cu, Ru, Rh, or Ir have been

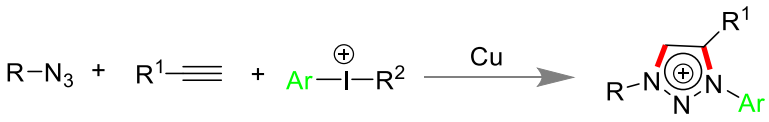
employed for the regiospecific synthesis of triazoles.[12, 15-21]. However, these methodologies utilize toxic metals, which hinders its utility in biomolecules and the field of chemical biology.[22, 23] Due to several detrimental effects in involving toxic metal for synthesis of triazoles, the need to develop metal free methodologies have been a growing concern and valued matter of subject for synthetic chemists.[24] *N*-substituted triazoles are synthesized in abundance, but methods to access *N-H* triazoles in a single step are scarcely known.[13, 14, 25-27] N-H triazoles are important, valuable synthetic intermediates in transformation and are known to have potential application in pharmaceuticals, and materials.[4] Synthesis of *N-H* triazole involves multiple-step process involving deprotection of *N*-substituted 1, 2, 3-triazoles in most of the cases.[28-30] Herein, we have developed a direct method to access N_1–H triazole carboxylate using phophorylazide as the azide source in solvent DMSO where the carbonyl group of propiolate assisted to cleave the P-N bond in phophorylazide to generate the azide radicals.

Yamamoto group has developed [3+2] cycloaddition reaction for the synthesis of N-H triazoles in a two-step process involving Pd (0)-Cu (I) metals using trimethyl silyl azide triazoles to give rise to N-H triazole.[30] The reaction proceeded via formation of π-allylpalladium azide complex with the extrusion of carbondioxide.



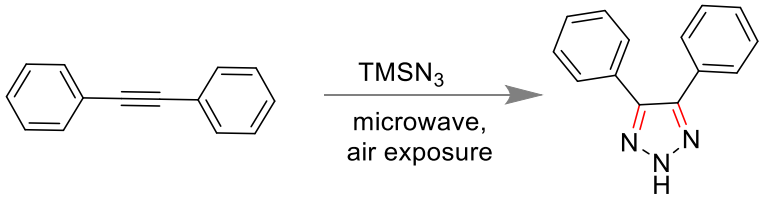
Scheme 5.1 Multistep process for the synthesis of N-H triazoles using the bimetallic approach.

1,2,3,4 triaolium salts have been synthesized using terminal alkyne and aryl iodonium salt with copper catalyst under neat conditions in one pot.[25] The reaction scope tolerated a variety of functional groups, and hence the protocol was helpful for access to precursors of pyridyl-mesoionic carbene ligands.



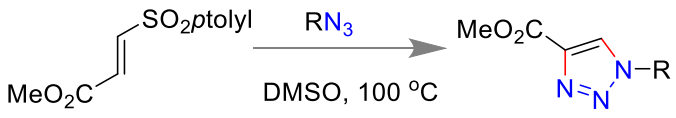
Scheme 5.2 Multistep process for synthesis of triazolium salt using copper.

The microwave-assisted solvent-free synthesis of 1,2,3 triazoles was accomplished by Prakash and co-workers by [3+2] cycloaddition reaction of alkyne and trimethylsilyl azide.[13] The mild reaction condition resulted in triazoles forming in good to excellent yields on a practical scale.



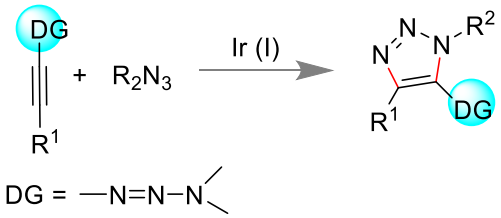
Scheme 5.3 Microwave-assisted triazole synthesis using trimethyl silyl azide.

Pathak and co-workers developed a metal free synthetic route for the regioselective synthesis of 1,2,3 triazoles from vinyl sulfones.[24] The protocol tolerated a wide range of functional groups and marked the synthesis of 1,4 disubstituted triazole synthesis for the first time.



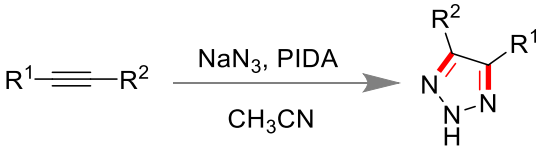
Scheme 5.4 Synthesis of 1,2,3-triazole using vinyl sulfone.

Ciu group have developed [3+2] cycloaddition mediated by iridium catalyst.[31] Synthesis of functionalized triazoles was achieved by directing groups like triazene, which was further transformed to amino, amide, halogen, and other heterocyclic substituents in a mild efficient approach.



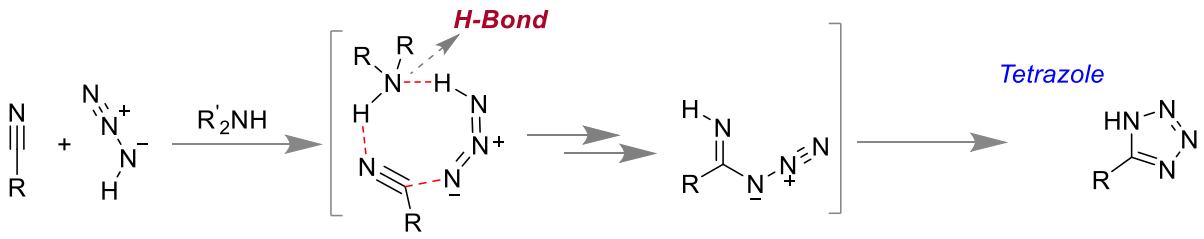
Scheme 5.5 Synthesis of functionalized triazole assisted by directing group.

Hypervalent iodine(III) reagents have proved to be effective in generating azide radicals from PIDA.[14] Synthesis of N-H triazoles was successfully achieved in a single step followed by a cascaded type reaction mechanism.



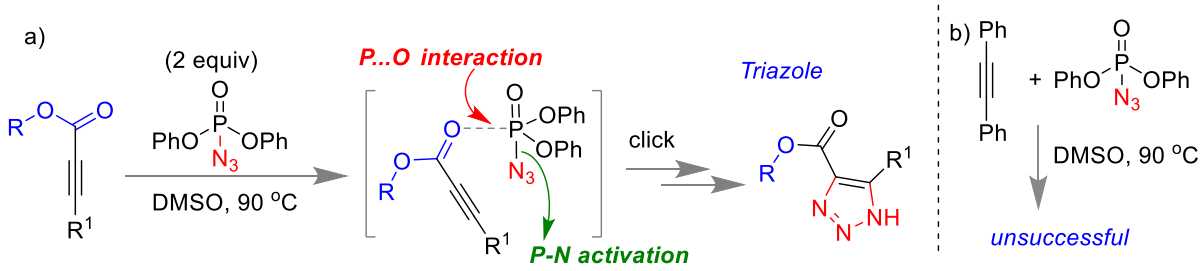
Scheme 5.6 Synthesis of N-H triazoles by the formation of azidyl radical.

Weak interactions often take up a signifying character in controlling product selectivity. Hydrogen bonding interactions control the formation of tetrazoles. The mechanistic pathway has been supported with DFT calculations to validate the hypothesis.[32]



Scheme 5.7 Synthesis of tetrazoles enabled by weak interactions.

Our approach was to utilize the directing nature of carbonyl group of the propiolate ester and the interaction of oxygen with phosphorus which controlled the reaction and favored synthesis of triazoles (Scheme 5.8b). We desired to achieve click reaction using internal alkynes like diphenyl acetylene and other electron withdrawing substituted alkyne, but it failed to deliver the product (Figure 5.8c). The targeted reaction was successful without the use of an external oxidant or metal. Simply by modifying the substrate by introducing a carbonyl group, P-N bond cleavage took place. Our targeted N-H triazoles were synthesized in a gentle and efficient approach with excellent yield. To the best of our knowledge, we were able to successfully activate P-N bond with the help of P…O interaction for the first time.



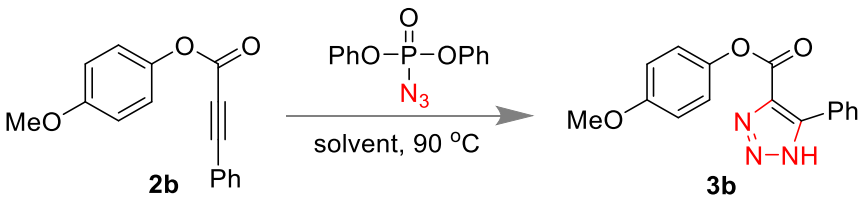
Scheme 5.8 Synthesis of triazoles enabled by weak interactions.

5.3 RESULTS AND DISCUSSION

Initially, diphenyl acetylene was chosen to undergo reaction with diphenyl phosphoryl azide (DPPA), but it failed to deliver the product. We modified the substrate and introduced a carbonyl group into it. We hypothesized that 4-methoxyphenyl 3-phenylpropiolate will undergo reaction with DPPA due to interaction between phosphorus and oxygen. 4-methoxyphenyl 3-phenylpropiolate (1.0 equiv)) (**2b**) and phosphoryl azidate (1.0 equiv) were taken and the [3+2] cycloaddition reaction was successfully established forming 4-

methoxyphenyl-5-phenyl-1*H*-1,2,3-triazole-4- carboxylate (**3b**) in tetrahydrofuran (THF) with 17% yield. Switching the solvent tetrahydrofuran (THF) to dimethyl sulfoxide (DMSO) resulted in rise of yield to 45% (entry 2). Further, increasing the equivalency of phosphoryl azidate to 1.5, an abrupt rise in yield to 69% was noticed (entry 3). Change in the equivalency of DPPA to 2.0, further rise in yield to 86% was noticed (entry 4). Other solvents were screened, and it was found that 1,2-dichloroethane (DCE) and acetonitrile (ACN) failed to deliver the desired product (entries 4 and 5). However, when dimethyl formamide (DMF) was used as a solvent, 60% yield of desired product was obtained (entry 7). Sodium azide was used as the azide source, the yield was decreased to 20% (entry 8).

Table 5. 1 Optimization of the reaction condition.[a]



entry	azide source (equiv)	solvent	yield (%)[b]
1	$PO(OPh)_2N_3$ (1.0)	THF	17
2	$PO(OPh)_2N_3$ (1.0)	DMSO	45
3	$PO(OPh)_2N_3$ (1.5)	DMSO	69
4	$PO(OPh)_2N_3$ (2.0)	DMSO	86
5	$PO(OPh)_2N_3$ (2.0)	CH_3CN	N.R
6	$PO(OPh)_2N_3$ (2.0)	DCE	N.R
7	$PO(OPh)_2N_3$ (2.0)	DMF	60
8	NaN_3(1.0)	DMSO	20

[a]Reaction condition: All reactions were done at 90 °C using 1.0 equiv of **2a**. [b]Yield of isolated products after column chromatography.

A scale of substrates were prepared (Figure 5.2) with the optimized condition, and it was noted that when phenyl group was used as the substituent –R, product was formed in good yield (**3a**, 81%). When *para* position of phenyl ring was substituted with an alkyl group and varied, good yield of the product were produced in both cases (**3b**-**c**). Replacing with other halogen groups, good to excellent yields of the product were observed in most cases (**3d**-**g**), with the highest yield when fluoro substituted propiolate derivative was used. With phenyl group as *para* substituent on the phenyl ring of the ester molecule, sufficiently good yield of the product was noted.(**3h**, 82%). Changing the substitution position from *para*- to *meta*- or *ortho*-, no appreciable difference was noted, and good to excellent yields of the product were observed mostly (**3i**-**l**). Substituents with electron-donating or electron-withdrawing group substituent at para position of phenyl ring did not produce a substantial difference in yield of product which incurred that electronic effect is not operative in the methodology. Di-substitution with two alkyl groups in the phenyl ring resulted in a good yield of product (**3m**, 76%). Naphthalene based substrates tolerated the reaction condition and resulted in good yields of product (**3n** and **3o**). Sterically hindered substrates reduced the yield of the product (**3q** and **3r**). Dimethylacetylene dicarboxylate and diethylacetylene dicarboxylate showed a reduction in yields of the product (3s and 3t), as the presence of two carbonyl groups hinders the directional nature of carbonyl substituent. When aliphatic methyl and ethyl were used as substituents, yield reduced abruptly as the intermediate generated in the reaction mixture might have stabilized by the aromatic ring (**3u** and **3v**). Bromophenyl or chlorophenyl substituted ester furnished the desired products **3w** and **3x** in moderate yield.

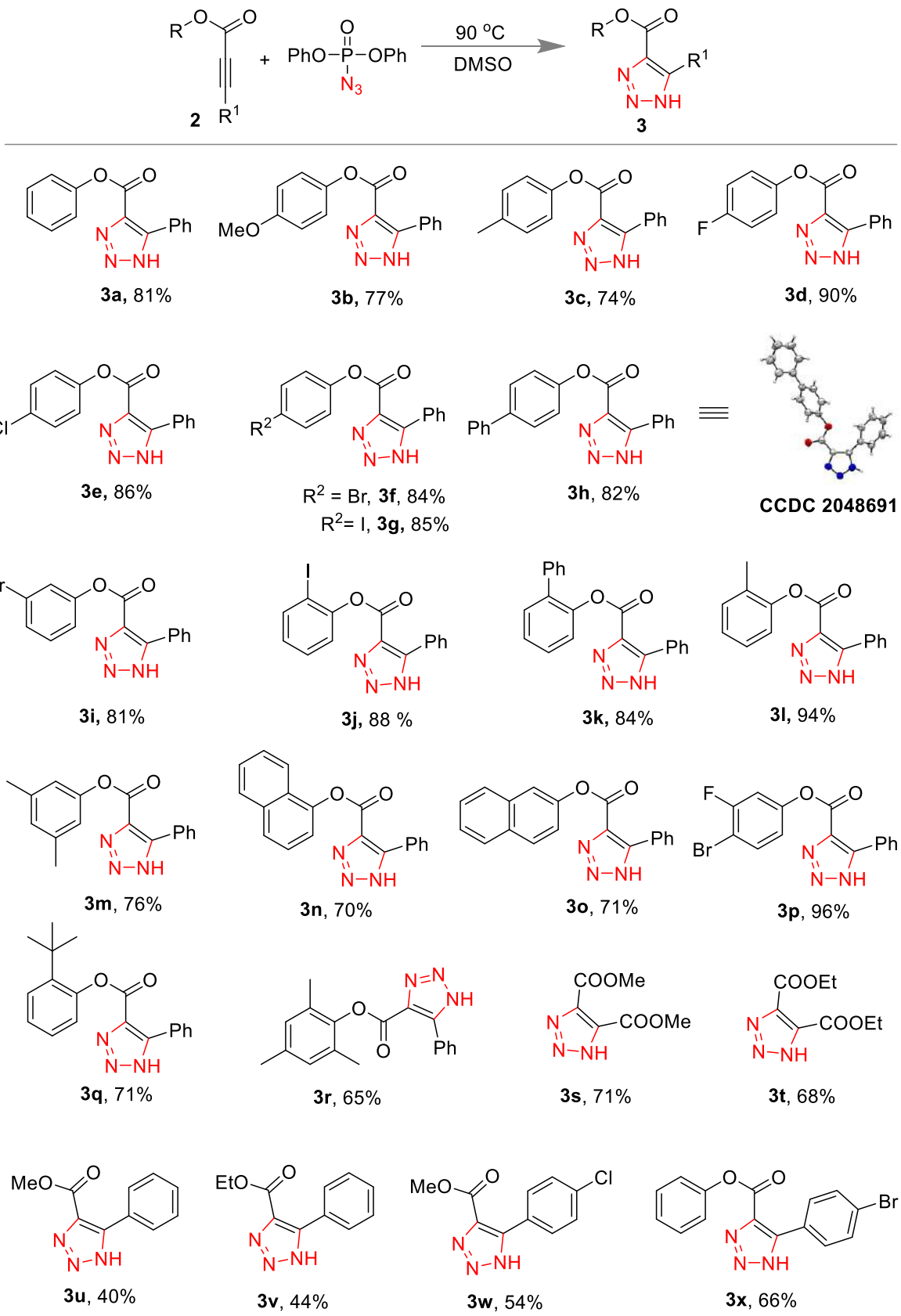


Figure 5.2. Scope for synthesis of N-H triazoles. Reaction conditions: 1.0 equiv of **2** and 2.0 equiv of the azide; all reactions were done at 90 °C for 7 h. Yield of isolated products after

column chromatography are shown. X-Ray structure of the compound **3h** (CCDC 2048691) has been shown.

To understand the mechanistic pathway, control experiments were done (Figure 5.3). The reaction pathway was monitored to understand whether the reaction proceeded *via* a radical or ionic pathway. Following standard reaction conditions, when a radical scavenger butylated hydroxytoluene (BHT) was employed in the reaction, a mixture of products was observed, which was not conclusive. When the reaction was treated using (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl radical (TEMPO, 3.0 equiv) under standard reaction condition, the yield of compound **3f** was reduced to a great extent (42%) as indicated in Figure 5.3a. To confirm the proton source in triazole, various other control experiments were conducted. Bromo substituted propiolate (**2f**) was treated with standard reaction condition using $PO(OPh)_2N_3$ (2 equiv) in DMSO for 7 h, product (**3f**) was formed along with by-product $PO(OPh)_2OH$ confirmed from ESI-MS. It was assumed that as P-O bond cleaved, followed by triazole ring taking up proton from the water present in DMSO and the hydroxyl part $(OH)^-$ combines with $PO(OPh)_2^+$ to form $PO(OPh)_2OH$ (251.0465) confirmed from ESI-MS analysis (*vide infra*). Further, when iodo-substituted propiolate (**2g**) was made to react with DPPA (2 equiv) under normal standard conditions in DMSO-d_6 for 7 h, deuterium incorporation was not found and product (**3g**, MW 391.987) was confirmed from ESI-MS analysis, which concluded that DMSO proton was not participating in the reaction mixture (Figure 5.3b). This confirmed that the DMSO proton was not involved in the formation of N-H triazole. Further, to confirm the source of proton in triazole, the starting material **2e** underwent reaction under standard conditions using $PO(OPh)_2N_3$ (2 equiv) in dry DMSO and D_2O for 7 h. Further, ESI-MS was recorded for the reaction mixture, and it was observed that a peak was obtained at 301.127, which led us to conclude that incorporation of deuterium

occurred forming N-D triazole (**3e'**) (Figure 3c).This proves that the water present in DMSO is the source of proton in triazole. When benzoyl substituted alkyne (**2y**) was used as a precursor instead of the propiolate, the reaction was successful to produce phenyl(5-phenyl-1H-1,2,3-triazol-4-yl)methanone (**4y**) in 81% yield (Figure 5.3d). On the other hand, when diphenyl acetylene was used, the reaction failed (Scheme 5.8b). Based on this observation, precursor (**2z**) was slightly modified by introducing a methylene group instead of carbonyl group to note the result. It was noted that the reaction failed to proceed, which implied that the carbonyl group had a prime role in the reaction (Figure 5.3d). When highly electron deficient alkynes 1-(phenylethynyl)-3,5-bis(trifluoromethyl)benzene (**3z**) and 1,3- difluoro-5-(phenylethynyl)benzene) (**4z**) were treated with diphenylphosphoryl azide (DPPA), triazole was not observed. This evidenced that essential role of carbonyl group as shown in (Figure 5.3e).

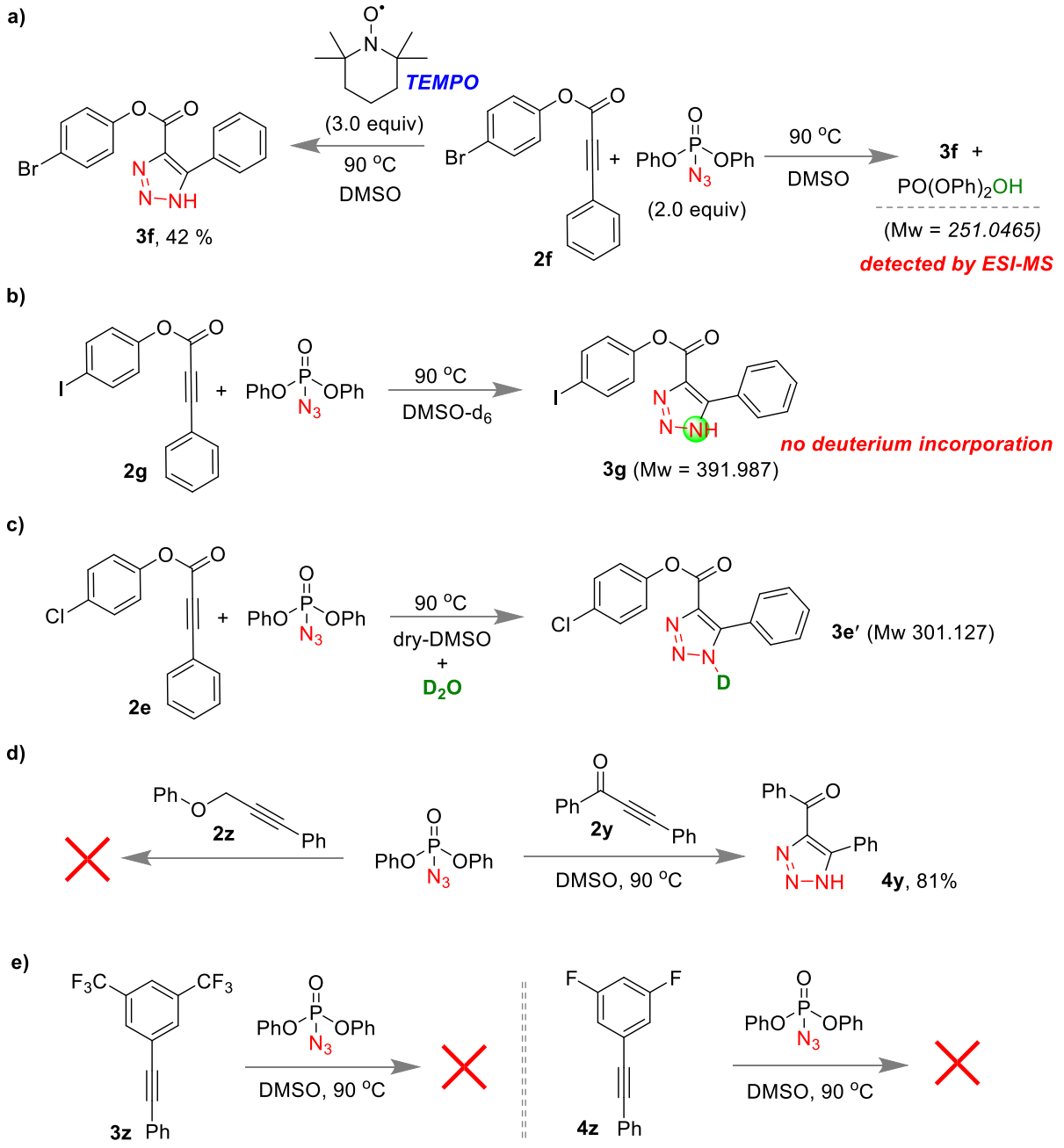


Figure 5.3. Control experiments to understand the mechanistic pathway of the azide-alkyne cycloaddition. Standard reaction conditions: 1.0 equiv of **2** and 2.0 equiv of the azide; all reactions were done at 90 °C for 7 h and yield of isolated products after column chromatography are shown. a) Reactions of **2f** in the presence and in absence of TEMPO. b) and c) Deuterium incorporation experiments. d) Reactivities of internal alkynes. e) with electron-withdrawing alkynes.

EPR experiments were conducted as shown in Figure 5.4 which helped to establish the radical mechanism.[33] When phenyl propiolate derivative (**2f**), phosphoryl azidate in DMSO (1 mL) was heated for 2 h at 90 °C in the presence of 0.5 mL of a spin trapping agent 5,5-dimethyl-1-pyrroline-*N*-oxide (DMPO), a new signal was noticed (Figure 5.4a). This indicated that azidyl radical might have formed and trapped by DMPO which creates a stable DMPO-N_3 radical. The azidyl radical was generated only when the substrate has been introduced in the reaction medium. This proved that the P…O interaction helped to cleave the phosphorus nitrogen bond. The above mentioned hypothesis was further strengthened, when phosphoryl azidate was solely heated in a solvent at 90 °C for 4 h when no new signal was observed (Figure 5.4b).

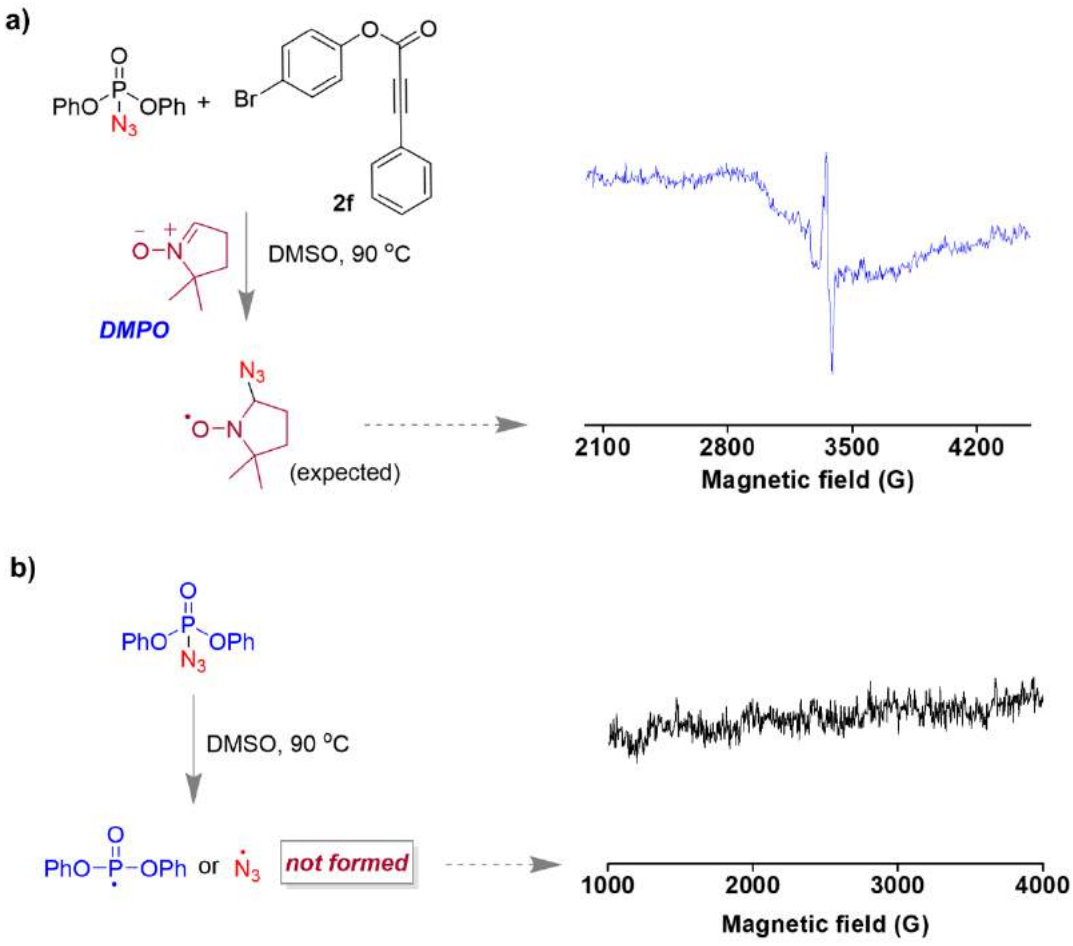


Figure 5.4 a) Scheme of the EPR experiment employing DMPO under standard condition and corresponding spectra. b) No radical formation was observed when phosphoryl azidate was heated alone.

Based on the control experiments and literature reports,[14] a plausible mechanistic pathway was proposed in Figure 5.5a. It was assumed that the proximity between the molecules led to phosphorus oxygen interaction in ***a,*** or it may proceed through transition state ***b***. DPPA solely cannot generate the phosphorus radical and azidyl radical species until the substrate phenyl propiolate was introduced in the reaction. The interaction of phosphorus with oxygen helped to form the azidyl radical, which was confirmed through EPR. The azidyl radical attacks the alkyne, and its counterpart attack the oxygen simultaneously to form a stable phosphorus oxygen bond forming intermediate ***c***. The bond dissociation energy of P-N bond is extremely high (617 kJ/mole) which was cleaved due to the interaction of phosphorus oxygen bond. Successive steps led to the formation of triazole ring by constructing the intermediate ***d*** by ring closure. Finally water molecule in DMSO attacked the ring forming **3** by cleavage of P-O bond. Table 5.1 (entry 8) showed that sodium azide did not prove effective for the reaction because sodium lacks any vacant d orbital. Hence, there was no scope for back bonding, unlike phosphorus. Thus, it is anticipated that P…O interaction was vital for the reaction to proceed to completion.

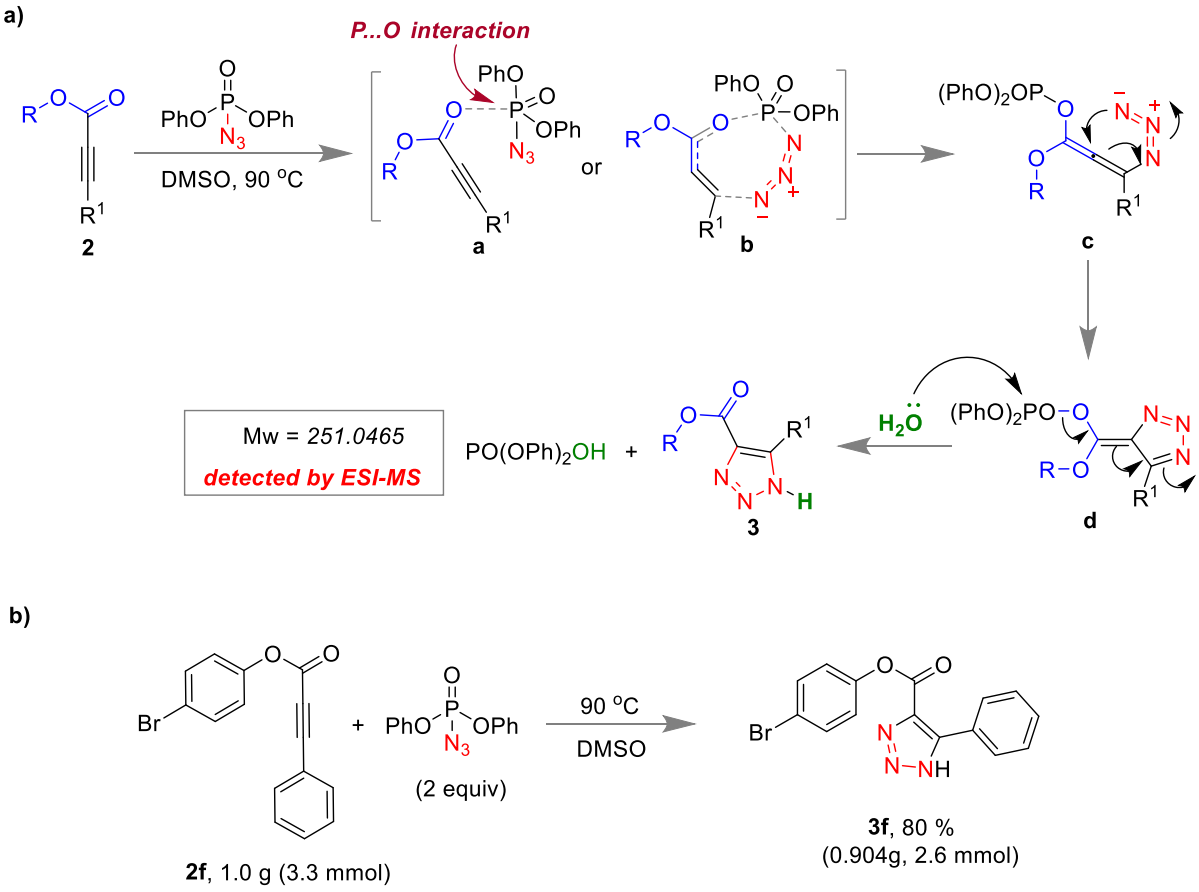


Figure 5.5 a) Plausible mechanistic pathway for formation of triazole ring. b) Gram scale reaction for triazole synthesis; Reaction conditions: 1.0 equiv of **2** and 2.0 equiv of the azide; reaction was done at 90 °C for 7 h. Yield of isolated product after column chromatography.

Further, the reaction was carried on a gram scale leading to the formation of the desired product by taking 1g (3.3 mmol) of bromophenyl propiolate and treating it with standard reaction conditions. A sufficient yield of product (**3f**, 80%) was obtained, claiming that methodology is scalable and can have ample application in medicine and industry. (figure 5.5 b).

5.4 CONCLUSIONS

In conclusion, a mild metal free direct method was developed to synthesize N-H triazoles by utilizing the phosphorus oxygen interaction, which is the key step for the synthesis of

triazoles. The carbonyl group is essential for the interaction of lone pair of oxygen with vacant d orbital of phosphorus, which is nothing but P…O interaction. The dissociation of the phosphorus nitrogen bond could also take place without the involvement of any external oxidant or metal. The formation of azidyl radical has been explained with the help of EPR studies. The optimization studies and the control experiments clearly prove the activation of phosphorus nitrogen bond *via* P…O interaction. Thus, the close proximity between the molecules leads to the phosphorus oxygen interaction that enables synthesize triazoles which will be of ample use to the scientific community for the synthesis of triazoles which are useful in medicinal chemistry. Also, it will help to bridge the gap between supramolecular and organic chemistry and unfold the utility of multiple co-operative interactions in organic synthesis.

5.5 EXPERIMENTAL SECTION

General Methods: Chromatographic (column) purifications of the compounds were done using silica gel (mesh 230-400) and hexane-ethyl acetate mixtures as eluent unless otherwise specified. Infrared (IR) spectral data are reported in wave number (cm^{-1}). FT-IR spectra were recorded after making thin layer of the compounds on the surface of NaCl crystal using dichloromethane.

Representative method for preparation of phenyl-3-phenylpropiolate (2a). To a solution containing 3-phenylpropiolic acid (0.5 g, 1.0 equiv) in 5 mL dichloromethane (CH_2Cl_2), phenol (321 mg, 1.0 equiv in CH_2Cl_2 (5 mL) was added at 0 °C. Then a mixture of DCC (0.7 g, 1.0 equiv) and DMAP dissolved (0.41 mg, 0.1 equiv) in CH_2Cl_2 (10 mL) was added in a drop wise manner to the reaction mixture. The mixture was shaken at 0 °C for 1 h, and then at room temperature for 12 h. The resulting reaction mixture was extracted by EtOAc (3 × 10 mL) and dried over anhydrous Na_2SO_4. The organic layer was removed under vacuum and

crude products were isolated by column chromatography (eluent: hexane/EtOAc = 95/5) and 0.49 g of white solid was isolated as phenyl-3-phenylproiolate. The other starting derivatives were prepared by following the similar procedure.

Representative method for preparation of phenyl 5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3a). In a sealed tube phenyl-3-phenylpropiolate **2a** (60 mg, 0.267 mmol) in 1 mL DMSO was taken and to it the azide reagent phosphoryl azidate (98 µL, 0.534 mmol) was added to the solution and heated to 90 ℃ for 7 h until full consumption of starting materials. The reaction mixture was removed from heating and was cooled for several minutes. Aqueous work up was followed by chromatographic column separation to isolate pure product phenyl 5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3a**) as white solid in 57 mg (81%) yield using 18% ethylacetate-hexane as eluent.

EPR spectra was recorded at 298 K using EPR spectrometer derived at 9.4335 GHz. Typical spectrometer parameters are shown as follows, scan range: 100 G; center field set: 3480.00 G; time constant: 0.16 ms; scan time: 122.88 s; modulation amplitude: 20.0 G; modulation frequency: 100 kHz; receiver gain: 2.00×102 ; microwave power: 7.14e-001 mW.

Spin-trapping experiment in presence DMPO.1 A mixture of 4-Bromophenyl 3-phenylpropiolate (0.19 mmol), phosphoryl azidate (75 µL), in solvent DMSO was heated for 5 hr at 9 0℃and DMPO (20 µL) were stirred in 1.0 mL of DMSO and heated in oil bath for 10 min. Afterwards, 20 µL solution was quickly transferred into EPR tube and 200 µL DMSO was added to analyze EPR. Similar experiment was performed without the propiolate

Good quality crystals of the compounds **3h** were obtained after slow evaporation of ethyl acetate solution. The crystals data were collected with Bruker SMART D8 goniometer equipped with an APEX CCD detector and with an INCOATEC micro source (Cu-Kα radiation, λ = 0.71073 Å). SAINT+[34] and SADABS[35] were used to integrate the intensities and to correct the absorption respectively The structure was resolved by direct methods and

refined on F^2 with SHELXL-97.[34] ORTEP drawing of the compound **3**shows ellipsoid contour at the 50% probability level

Compound Characterization Data

Phenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3a). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 57 mg (81%); mp 152–154 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.81 (s, 2H), 7.49 – 7.47 (m, 3H), 7.45 (d, *J* = 7.6 Hz, 2H), 7.31 (d, *J* = 7.2 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR ([(100 MHz $CDCl_3$-DMSO-d_6 (20 : 1)]) δ 160.1, 146.4, 150.3, 133.5, 129.8, 129.5, 129.4, 128.4, 127.6, 126.1, 121.7; ῡ = 3418, 2258, 2130, 1651 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{11}N_3O_2Na$ 288.0743; Found 288.0767.

4-Methoxyphenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3b). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 54 mg (77%); mp 171–173 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.82 (d, *J* = 5.2 Hz, 2H), 7.52-7.44 (m, 3H), 7.18 (d, *J* = 8.8 Hz, 2H), 6.98 (d, *J* = 8.8 Hz, 2H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.8, 157.1, 143.4, 130.1, 129.6, 129.3, 128.4, 123.6, 122.7, 122.5, 114.6, 55.5; ῡ = 3421, 2923, 2853, 1639 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{14}N_3O_3$ 296.1030; Found 296.1039.

***p*-Tolyl-5-phenyl-1H-1,2,3-triazole-4-carboxylate (3c).** R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 52 mg (74%); mp 132-134 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.81 – 7.80 (m, 2H), 7.50 – 7.47 (m, 3H), 7.24 (d, *J* = 8.4 Hz, 2H), 7.13 (d, *J* = 8.4 Hz, 2H), 2.31 (s, 3H); ^{13}C NMR [(100 MHz $CDCl_3$-DMSO-d_6 (20 : 1)] δ 159.9, 147.9, 135.3, 129.5(×2), 129.2, 128.9(×2), 127.9, 120.9(×2), 20.5; ῡ = 3421, 2923, 2853, 1467 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{13}N_3O_2Na$ 302.0900; Found 302.0914.

4-Fluorophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3d). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 64 mg (90%); mp 199–201°C ; ^{1}H NMR (NMR [(400 MHz $CDCl_3$-DMSO-d_6 (20 : 1)]) δ 7.76 (s, 2H), 7.55 (s, 1H), 7.37 (d, *J* = 3.2 Hz, 3H), 7.12 – 7.09 (m, 2H), 7.03 – 6.99 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 160.5 (d, $^1J_{C\text{-}F}$ = 253 Hz), 146.4 (d, $^4J_{C\text{-}F}$ = 2.4 Hz), 129.8, 129.4 (×3), 128.4 (×2), 123.3 (d, $^3J_{C\text{-}F}$ = 8.6 Hz), 116.16 (d, $^2J_{C\text{-}F}$ = 23.5 Hz); ῡ = 3437, 1643, 1173 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{10}FN_3O_2Na$ 306.0649; Found 306.0641.

4-Chlorophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3e). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 60 mg (86%); mp 236–238 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.80 – 7.78 (m, 2H), 7.65 – 7.61 (m, 2H), 7.50 – 7.47 (m, 3H), 7.27 – 7.23 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.5, 149.5, 142.4, 132.7, 129.9, 129.4, 128.6, 125.5, 124.5, 118.7 (×2); ῡ = 3420, 2098, 1652, 1476 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{11}ClN_3O_2$ 300.0534; Found 300.0528.

4-Bromophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3f). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 58 mg (84%); mp 235–237 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.83 – 7.80 (m, 2H), 7.65 – 7.64 (m, 2H), 7.50 – 7.48 (m, 3H), 7.29 – 7.26 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.5, 149.5, 132.8, 132.4, 130.1, 129.5 (×2), 128.7, 124.6, 118.8, 117.8; ῡ = 3410, 2257, 2130, 1653 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{10}BrN_3O_2Na$ 365.9849; Found 365.9858.

4-Iodophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3g). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 57 mg (84%); mp 238–240 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.70 (d, *J* = 7.6 Hz, 4H), 7.39 (d, *J* = 4.8 Hz, 3H), 7.02 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR [(100

MHz $CDCl_3$-DMSO-d_6 (20 : 1)] δ 159.3, 149.8, 138.0, 132.8, 129.3, 128.9, 127.9, 127.3, 123.6, 113.5, 89.7; ῡ = 3437, 2358, 2093, 1639 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{11}IN_3O_2$ 391.9890; Found 391.9916.

[1,1'-Biphenyl]-4-yl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3h). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 56 mg (82%); mp 197-199 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 7.85 (d, *J* = 5.2 Hz, 2H), 7.75 – 7.73 (m, 2H), 7.70 – 7.67 (m, 2H), 7.53 – 7.46 (m, 5H), 7.40 – 7.36 (m, 3H); ^{13}C NMR [(100 MHz $CDCl_3$-DMSO-d_6 (20 : 1)] δ 159.7, 149.3, 139.7, 138.6, 129.2(×2), 128.9, 128.4, 127.9, 127.7, 127.0(×2), 126.6, 121.6; ῡ = 3421, 2923, 2358, 1645 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{16}N_3O_2$ 342.1237; Found 342.1240.

3-Bromophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3i). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 55 mg (81%); mp 148–150 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.81–7.79 (m, 2H), 7.44 – 7.35 (m, 5H), 7.24 – 7.21 (m, 1H), 7.12 (dd, *J* = 8.4, 1.2 Hz, 1H), 6.85 (brs, 1H); ^{13}C NMR δ ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 150.6, 147.2, 133.6, 130.7, 130.4, 129.6, 129.4, 128.7, 127.0, 125.2, 122.6, 120.6; ῡ = 3438, 2359, 2097, 1644 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{11}BrN_3O_2$ 344.0029; Found 344.0037.

2-Iodophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3j). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 59 mg (88%); mp 157–159 °C; ^1H NMR [(400 MHz $CDCl_3$-DMSO-d_6 (20 : 1)] δ 7.92 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.83 (d, *J* = 3.6 Hz, 2H), 7.51 – 7.46 (m, 4H), 7.38 (d, *J* = 6.8 Hz, 1H), 7.11 (td, *J* = 7.6, 1.6 Hz, 1H); ^{13}C NMR [(100 MHz $CDCl_3$-DMSO-d_6 (20 : 1)] δ 159.4, 151.0, 139.6, 133.2, 129.7, 129.5, 129.4, 128.4, 127.9, 123.3, 121.8,

118.8, 90.6; ῡ = 3438, 2359, 2078, 1644, 1461 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{11}IN_3O_2$ 391.9890; Found 391.9897.

[1,1'-Biphenyl]-2-yl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3k). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 57 mg (84%); mp 194–196 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 7.51– 7.44 (m, 5H), 7.42 – 7.36 (m, 5H), 7.33 – 7.28 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 151.7, 147.0, 136.8, 134.3, 133.3, 130.9, 130.7, 129.2, 129.1, 128.9, 128.6, 128.5, 128.3, 127.7, 126.9, 123.3, 116; ῡ = 3441, 2065, 1635 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{16}N_3O_2$ 342.1237; Found 342.1229.

***o*-Tolyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3l).** R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 64 mg (94%); mp 131–133 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.81– 7.78 (m, 2H), 7.41 – 7.33 (m, 3H), 7.22 – 7.12 (m, 3H), 7.06 (dd, *J* = 8.0, 1.6 Hz, 1H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 148.8, 133.4, 131.4, 130.3, 130.1, 129.4, 128.5, 127.1, 126.5, 121.9, 120.6, 115.1, 16.3; ῡ = 3437, 2358, 2339, 1644 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{14}N_3O_2$ 280.1081; Found 280.1082.

3,5-Dimethylphenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3m). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 53 mg (76%); mp 138–140 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 7.82 – 7.79 (m, 2H), 7.51 – 7.47 (m, 3H), 6.92 (s, 1H), 6.85 (s, 2H), 2.27 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.6, 150.0, 145.5, 139.0, 129.6, 129.3, 128.4, 127.8, 127.5, 119.3, 113.0, 20.8; ῡ = 3413, 2359, 2255, 1651 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{15}N_3O_2Na$ 316.1056; Found 316.1043.

Naphthalen-1-yl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3n). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 48 mg (70%); mp 131–133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 – 7.81 (m, 4H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.49 – 7.35 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 146.3, 134.8, 130.2, 129.4, 128.7, 128.1, 127.4, 126.8, 126.8, 126.7, 126.6, 125.5, 121.4, 118.3; ῡ = 3437, 2094, 1644, 1461 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{14}N_3O_2$ 316.1081; Found 316.1069.

Naphthalen-2-yl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3o). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 49 mg (71%); mp 177–179 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.02 – 7.92 (m, 3H), 7.86 – 7.82 (m, 3H), 7.58 – 7.44 (m, 6H); ^{13}C NMR [(100 MHz, $CDCl_3$-DMSO-d_6 (20 : 1)]) δ 159.8, 147.5, 133.2, 131.1, 129.2, 129.0, 128.9, 127.9, 127.3, 127.2, 126.2(×2), 125.4, 120.7, 118.3; ῡ = 3421, 2955, 2924, 1639 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{14}N_3O_2$ 316.1081; Found 316.1101.

4-Bromo-3-fluorophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3p). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 66 mg (96%); mp 220–222 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.83 – 7.78 (m, 3H), 7.53 – 7.48 (m, 4H), 7.17 – 7.15 (m, 1H); ^{13}C NMR ([(100 MHz, $CDCl_3$-DMSO-d_6 (20 : 1)]) δ 158.8, 158.5 ($^1J_{C\text{-}F}$ = 246 Hz), 150.03 (d, $^3J_{C\text{-}F}$ = 9.8 Hz), 133.4, 129.4, 129.1, 128.9, 128.1, 127.8, 119.3 (d, $^4J_{C\text{-}F}$ = 3.5 Hz), 111.4 (d, $^2J_{C\text{-}F}$ = 25.4 Hz), 105.2 (d, $^3J_{C\text{-}F}$ = 21 Hz), 104.0 (d, $^2J_{C\text{-}F}$ = 30.6 Hz); ῡ = 3437, 2358, 2089, 1652 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_9BrFN_3O_2Na$ 383.9754; Found 383.9736.

2-(*tert*-Butyl)phenyl 5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3q). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 49 mg (71%); mp 200–202 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.82 (m, 2H), 7.42 – 7.41 (m, 4H), 7.24 – 7.19 (m, 2H), 7.11 (d, *J* = 7.6 Hz, 1H), 1.30

(s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2, 148.7, 134.3, 141.6, 130.1, 129.4(×2), 128.6(×2), 127.6, 127.1, 126.3, 124.1, 34.7, 30.3; ῡ = 3585, 2258, 2130, 1651 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{19}N_3O_2Na$ 344.1369; Found 344.1389.

Mesityl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3r). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 45 mg (65%); mp 197–199 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.82 (m, 2H), 7.40 – 7.38 (m, 3H), 6.86 (s, 2H), 2.26 (s, 3H), 2.11 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 145.5, 135.8, 130.0, 129.9, 129.43, 129.36, 128.5, 127.9, 120.5, 114.1, 20.9, 16.4; ῡ = 3422, 1639, 1468 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{18}N_3O_2$ 308.1394; Found 308.1396.

Dimethyl-1*H*-1,2,3-triazole-4, 5-dicarboxylate (3s). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 56 mg (71%); mp 177–179 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.00 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 138.7, 53.3; ῡ = 3437, 2253, 2127, 1658 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_6H_8N_3O_4$ 186.0509; Found 186.0527.

Diethyl-1*H*-1,2,3-triazole-4,5-dicarboxylate (3t). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 51 mg (68%); mp 180–182 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.46 (q, J = 7.2 Hz, 4H), 1.40 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2, 138.6, 62.8, 14.2; ῡ = 3437, 2358, 2097, 1641 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_8H_{11}N_3O_4Na$ 236.0642; Found 236.0659.

Methyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3u). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 25 mg (40%) ; mp 113–115 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.79 (m, 2H), 7.46 – 7.42 (m, 3H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 146.6,

134.1, 129.9, 129.3, 128.5, 127.8, 52.6; ῡ = 3441, 2358, 2089, 1644 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{10}H_9N_3O_2Na$ 226.0587; Found 226.0584.

Ethyl-5-phenyl-1H-1,2,3- triazole-4-carboxylate (3v). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 33 mg (44%) mp 122–124 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (m, 2H), 7.45 (m, 3H), 4.42 – 4.39 (m, 2H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 146.9, 129.8, 129.4 (×2), 128.5, 128.2, 61.8 14.1; ῡ = 3422, 2359, 1652, 1456 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{11}H_{11}N_3O_2Na$ 240.0743; Found 260.0733.

Methyl–5–(4-chlorophenyl–1*H*-1,2,3-triazole-4-carboxylate (3w). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 34 mg (54%); mp 144 –146 ℃; ^1H NMR ([(400 MHz $CDCl_3$-DMSO-d_6 (20 : 1)]) δ 7.42 (d, *J* = 7.6 Hz, 2H), 7.02 (d, *J* = 8.0 Hz, 2H), 3.50 (s, 3H); ^{13}C NMR ([(100 MHz $CDCl_3$-DMSO-d_6 (20 : 1)]) δ 161.4, 134.6(×2), 130.38(×2),128.1(×2), 51.8; ῡ = 3421, 2359, 2339, 1739, 1644 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{10}H_8N_3O_2ClNa$ 260.0197; Found 260.0173.

Phenyl 5-(4-bromophenyl)-1*H*-1,2,3-triazole-4-carboxylate (3x). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 45 mg (66%); mp 145 –147 ℃; ^1H NMR (400 MHz, DMSO-d_6) δ 7.72 (d, *J* = 8.4 Hz, 2H), 7.48 – 7.46 (m, 2H), 7.35 – 7.31 (m, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.12 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR ([(100 MHz $CDCl_3$-DMSO-d_6 (20 : 1)]) δ 159.7, 149.9, 131.1, 130.7, 129.8, 129.2, 127.4, 125.9, 123.5, 121.5, 113.6; ῡ = 3437, 2085, 1644 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{11}N_3BrO_2$ 344.0029; Found . 344.0008

Phenyl-(5-phenyl-1H-1,2,3-triazol-4-yl)methanone (4y).[36] R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 65 mg (81%); mp 86–88 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 7.6 Hz, 2H), 7.71 – 7.69 (m, 2H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.45 – 7.41(m, 2H), 7.37 –

7.35 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.3, 146.4, 141.3, 137.1, 133.6, 130.6, 129.8, 128.9, 128.7, 128.5, 127.9.

Phenyl-3-phenylpropiolate (2a).[37] R_f = 0.8 (hexane : ethyl acetate 20:1); white solid; 0.49 g (65%); mp 38-40 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.62 (m, 2H), 7.51 – 7.47 (m, 1H), 7.44 – 7.38 (m, 4H), 7.30 – 7.28 (m, 1H), 7.21 – 7.18 (m, 2H).

4-Methoxyphenyl-3-phenylpropiolate (2b).[37] R_f = 0.80 (hexane : ethyl acetate 20:1); white solid; .44g (51%); mp 67– 69 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.2 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.11 (d, *J* = 9.0 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 2H), 3.81 (s, 3H).

***p*-Tolyl-3-phenylpropiolate (2c).**[37] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; .50g (62%); mp 56–58 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.2Hz, 2H), 7.49 (t, *J* = 8.8 Hz, 1H), 7.41 (t, *J* = 8.0 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 7.08 (d, *J* = 8.4 Hz, 2H), 2.37 (s, 3H).

4-Fluorophenyl-3-phenylpropiolate (2d).[38] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.41g (51%); mp 78–80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.0 Hz, 2H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.17 (m, 2H), 7.10 (t, *J* = 8.0 Hz, 2H).

4-Chlorophenyl-3-phenylpropiolate (2e).[38] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.47g (55%); mp 73–75 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.62 (m, 2H), 7.52 – 7.48 (m, 1H), 7.43 – 7.37 (m, 4H), 7.16 – 7.13 (m, 2H).

4-Bromophenyl-3-phenylpropiolate (2f).[37] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.59g (58%); mp 62–64 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 7.6 Hz, 2H), 7.54 – 7.48 (m, 3H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.10 (d, *J* = 8.8 Hz, 2H).

4-Iodophenyl-3-phenylpropiolate (2g).[39] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.71g (60%); mp 58-60 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.4 Hz, 2H), 7.63 (d, *J* = 7.6 Hz, 2H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 6.97 (d, *J* = 8.4 Hz, 2H).

[1,1'-biphenyl]-4-yl-3-phenylpropiolate (2h).[39] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.62 g (61%); mp 133–135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.62 (m, 4H), 7.59 – 7.57 (m, 2H), 7.52 – 7.35 (m, 6H), 7.28 – 7.26 (m, 2H).

3-Bromophenyl-3-phenylpropiolate (2i).[39] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.68 g (67%); mp 99–101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 – 8.32 (m, 2H), 7.69 – 7.67 (m, 2H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.47 – 7.41 (m, 4H).

2-Iodophenyl-3-phenylpropiolate (2j).[40] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.78 g (66%); mp 77–79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 8.0, 1.2 Hz,

1H), 7.66 – 7.64 (m, 2H), 7.52 – 7.48 (m, 1H), 7.43 – 7.38 (m, 3H), 7.20 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.05 – 6.99 (m, 1H).

[1,1'-biphenyl]-2-yl-3-phenylpropiolate (2k).[41] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.58 g (58%); mp 85–87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.53 (m, 2H), 7.48 – 7.35 (m, 11H), 7.25 – 7.23 (m, 1H).

***o*-Tolyl-3-phenylpropiolate (2l).**[37] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.50 g (63%); mp 60–62; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.62 (m, 2H), 7.51 – 7.47 (m, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.28 – 7.27 (m, 1H), 7.24 – 7.17 (m, 2H), 7.12 – 7.09 (m, 1H), 2.27(s, 3H).

3,5-Dimethylphenyl-3-phenylpropiolate (2m).[42] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.45 g (54%); mp 68–70 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.61 (m, 2H), 7.51 – 7.46 (m, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 6.90 (s, 1H), 6.83 (s, 2H), 2.33 (s, 6H).

Naphthalen-1-yl-3-phenylpropiolate (2n).[37] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.66 g (71%); mp 55–57 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 – 8.00 (m, 1H), 7.91 – 7.89 (m, 1H), 7.80 (d, *J* = 8.4 Hz, 1H), 7.67 – 7.64 (m, 2H), 7.58 – 7.48 (m, 4H), 7.43 (t, *J* = 8.0 Hz, 2H), 7.37 (d, *J* = 7.6 Hz, 1H).

Naphthalen-2-yl-3-phenylpropiolate (2o).[37] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.64 g (69%); mp 89–91 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.83 (m, 3H), 7.68 – 7.64 (m, 3H), 7.54 – 7.48 (m, 3H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.34 (dd, *J* = 8.8, 2.0 Hz, 1H).

4-Bromo-3-fluorophenyl-3-phenylpropiolate (2p). R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.70 g (64%); mp 82–84 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 – 7.63 (m, 2H), 7.61 – 7.57 (m, 1H), 7.53 – 7.49 (m, 1H), 7.42 (t, *J* = 8.0 Hz, 2H), 7. 07 (dd, *J* = 8.8, 2.4, 1H), 6.95– 6.93 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 157.8, 151.5, 150.0 ($^3J_{C\text{-}F}$ = 9.4 Hz) , 133.9, 133.4, 131.5, 128.9, 119.1, 118.7 ($^4J_{C\text{-}F}$ = 3.7 Hz) 110.9 (d, $^2J_{C\text{-}F}$ = 25.4 Hz), 89.8, 79.9 ; ϑ = 3437, 2359, 2339, 2225, 1644, 1481; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_8BrFO_2Na$ 340.9584; Found 340.9571

2-(*tert*-Butyl)phenyl-3-phenylpropiolate (2q).[43] R_f = 0.3 (hexane : ethyl acetate 7:3); white solid; 0.67 g (67%); mp 62 – 64 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.62 (m, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.45 – 7.39 (m, 2H), 7.28 (s, 1H), 7.24 – 7.21 (m, 1H), 7.11 – 7.05 (m, 1H), 6.88 (t, *J* = 7.2 Hz, 1H), 6.67 (d, *J* = 8.0 Hz, 1H), 1.42 (s, 9H).

Mesityl-3-phenylpropiolate (2r). R_f = 0.30 (hexane : ethyl acetate 7:3); colourless liquid ; 0.45 g (51%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.2 Hz, 2H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 6.91 (s, 2H), 6.80 (s, 2H), 2.29 (s, 3H), 2.22 (s, 6H), 2.20 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 150.0, 145.5, 136.1, 133.4, 131.1, 129.9, 129.5, 129.4, 129.2, 128.8, 122.9, 119.5, 88.4, 80.2, 20.9, 20.5, 16.4, 16.0. (minor amount of the other isomer); ϑ = 3427, 2923, 2852, 2359, 1606 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{17}O_2$ 265.1223; Found 265.1212.

Phenyl-3-(4-bromophenyl)propiolate (2x). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 0.44 g (66%); mp 98–100 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.54 (m, 2H), 7.49 – 7.47 (m, 2H), 7.44 – 7.40 (m, 2H), 7.30 – 7.28 (m, 1H), 7.20 – 7.18 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 150.2, 134.6, 132.2, 129.8, 126.6, 126.1, 121.5, 118.3, 87.5,

81.3; ῡ = 3437, 2923, 2092, 1643, 1278 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{10}BrO_2$ 300.9859; Found 300.9844.

(3-Phenoxyprop-1-yn-1yl)benzene (2z).[44] R_f = 0.10 (hexane : ethyl acetate 20:1); brown liquid; 0.60 g (69%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.43 (m, 2H), 7.32 – 7.30 (m, 5H), 7.05 – 7.00 (m, 3H), 4.92 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9, 132.0, 129.6, 128.8, 128.4, 122.4, 121.6, 115.1, 87.4, 84.2, 56.9.

1-(Phenylethynyl)-3,5-bis(trifluoromethyl)benzene(3z).[45] R_f = 0.70 (hexane); colorless liquid; .57 mg (74%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (s, 2H), 7.82 (s, 1H), 7.59 – 7.54 (m, 2H), 7.40 – 7.39 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.9 (q, $^2J_{C-F}$ = 33.6Hz), 131.8, 131.4, 129.3, 128.6, 125.7, 124.3, 121.9, 121.6 (q, $^4J_{C-F}$ = 4.0 Hz), 92.8, 86.3.

1,3-Difluoro-5-(phenylethynyl)benzene (4z)[46] R_f = 0.70 (hexane); colorless liquid; .57 mg (74%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.52 (m, 2H), 7.38 – 7.36 (m, 3H), 7.05 (d, *J* = 6.0 Hz, 2H), 6.81 (t, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1 (dd, $^1J_{C-F}$ = 247, $^3J_{C-F}$ =13.5 Hz), 131.9, 129.1, 128.6, 126.13 (t, $^3J_{C-F}$ = 11.7 Hz), 122.4, 114.8 – 114.4 (m), 104.53 (t, $^2J_{C-F}$ = 25.2 Hz), 91.4, 87.2(t, $^4J_{C-F}$ = 4.0 Hz).

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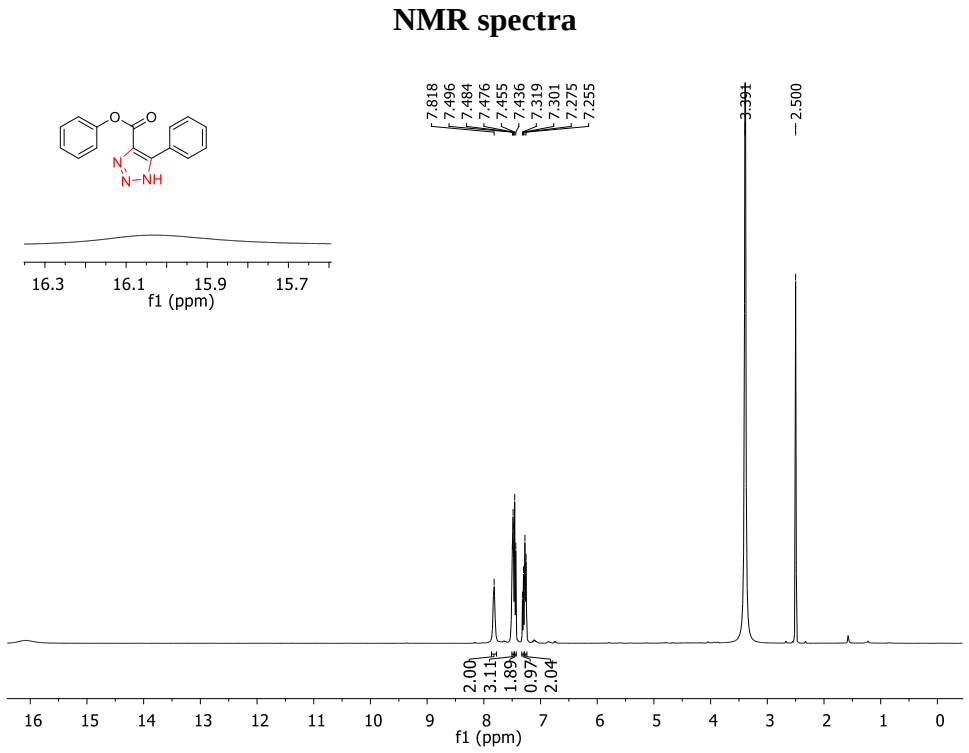

Figure 5.6. ^{1}H NMR spectrum of phenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3a**) in DMSO-d_6

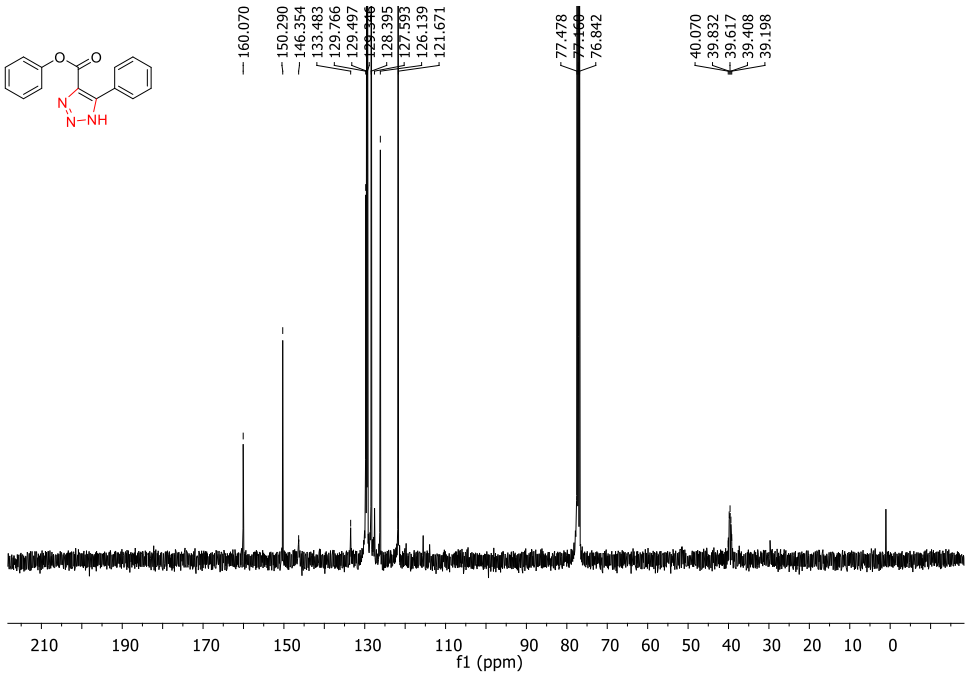

Figure 5.7. ^{13}C NMR spectrum of phenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3a**) in $CDCl_3$:DMSO-d_6.

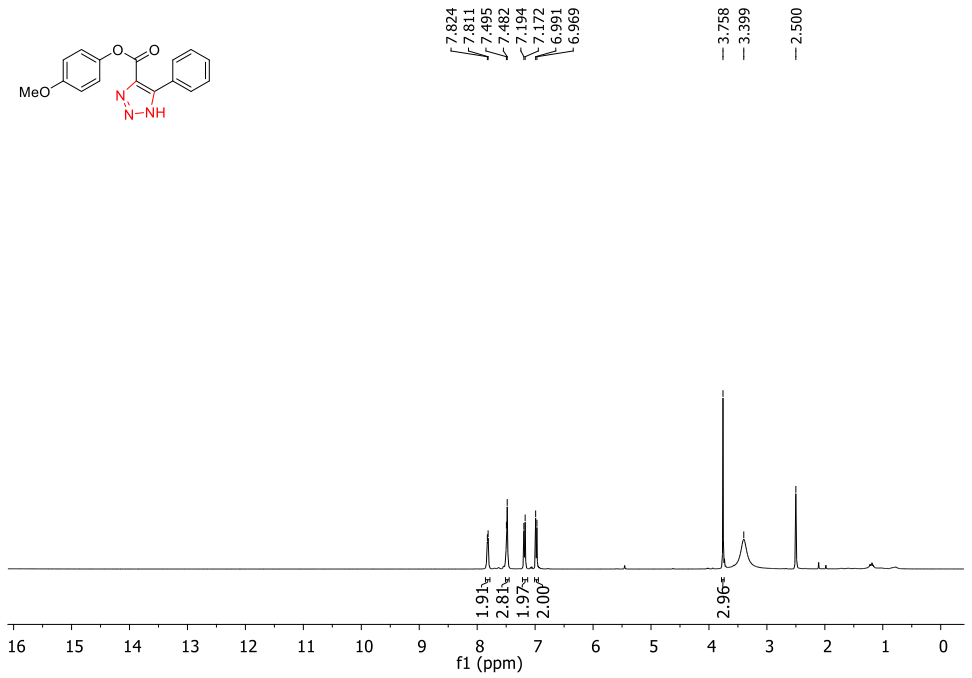

Figure 5.8. ^{1}H NMR spectrum of 4-methoxyphenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3b**) in DMSO-d_6.

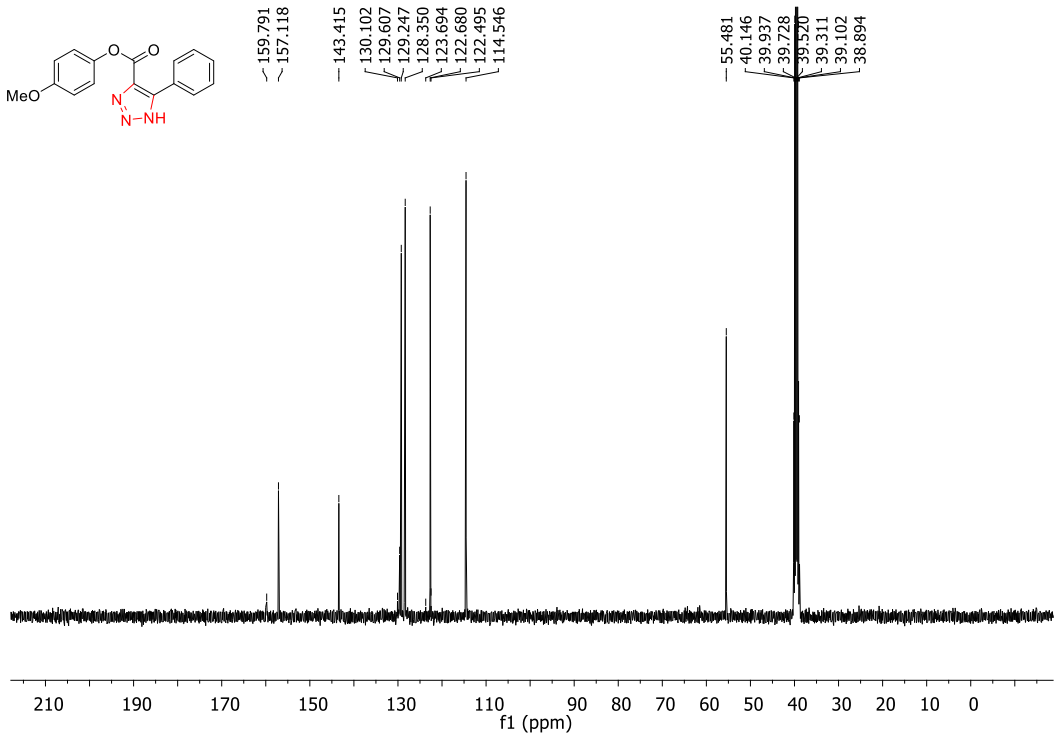

Figure 5.9. ^{13}C NMR spectrum of 4-methoxyphenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3b**) in DMSO-d$_6$.

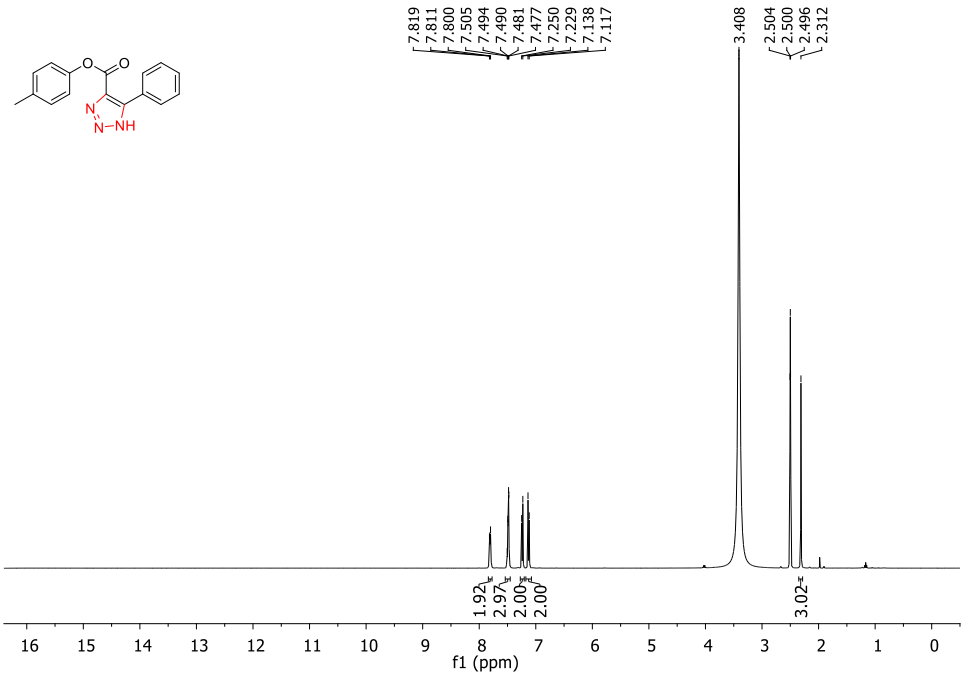

Figure 5.10. ^{1}H NMR spectrum of *p*-tolyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3c**) in DMSO-d$_6$.

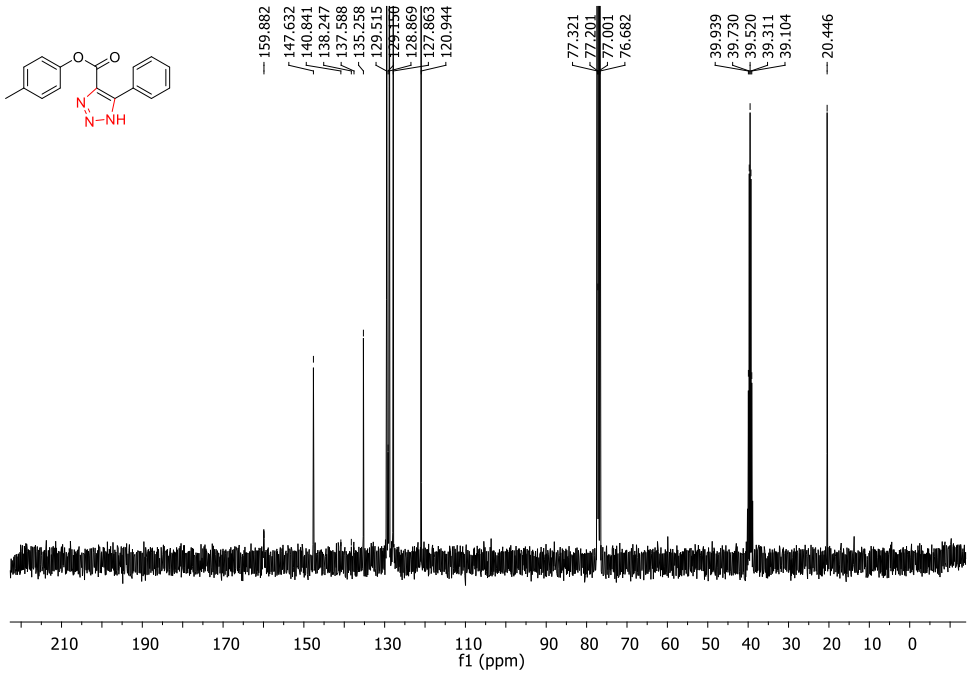

Figure 5.11. ^{13}C NMR spectrum of *p*-tolyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3c**) $CDCl_3$:DMSO-d_6

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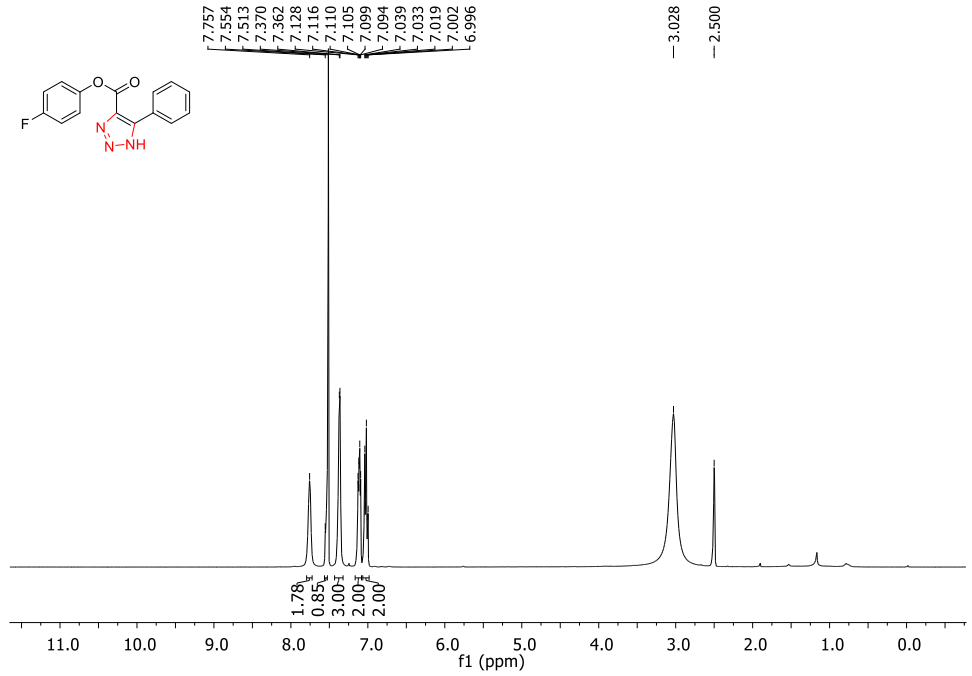

Figure 5.12. ^{1}H NMR spectrum of 4-fluorophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3d**) in $CDCl_3$: DMSO-d_6.

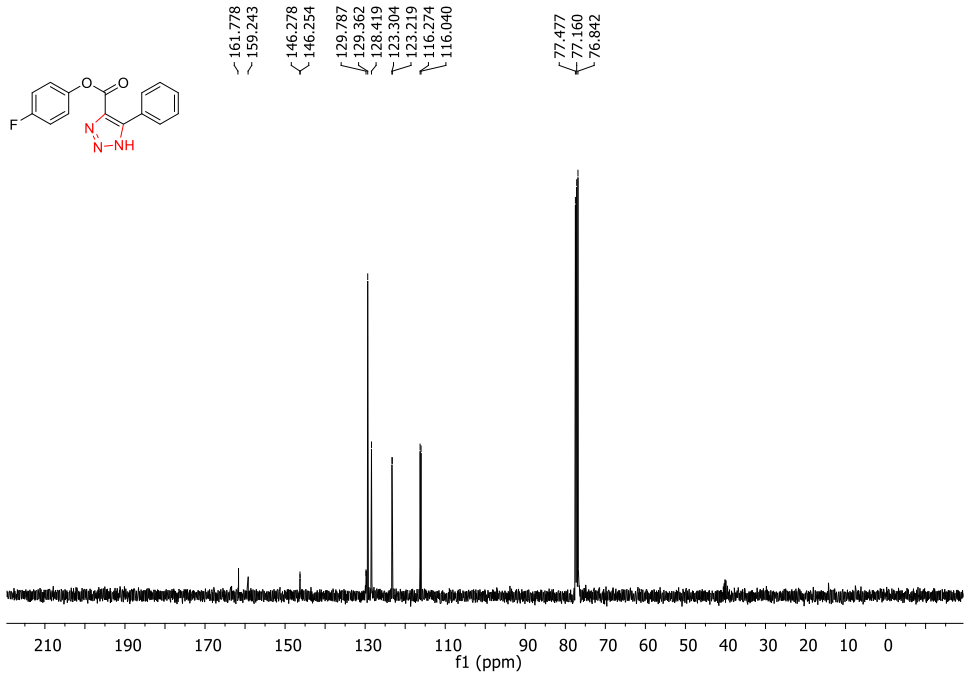

Figure 5.13. ^{13}C NMR spectrum of 4-fluorophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3d**) in $CDCl_3$.

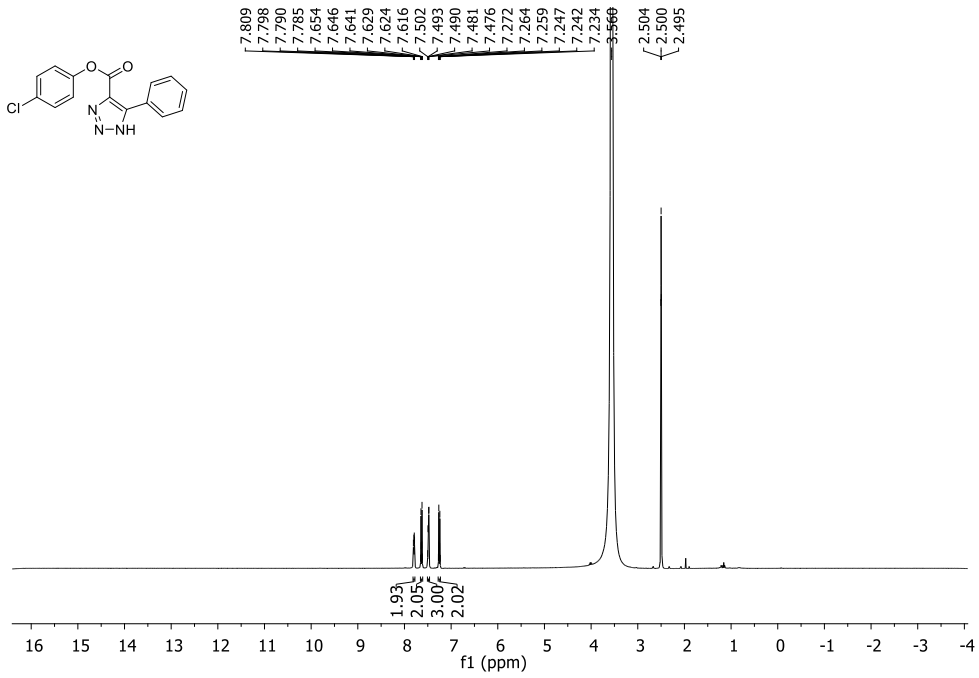

Figure 5.14. ^{1}H NMR spectrum of 4-chlorophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3e**) in DMSO-d_6

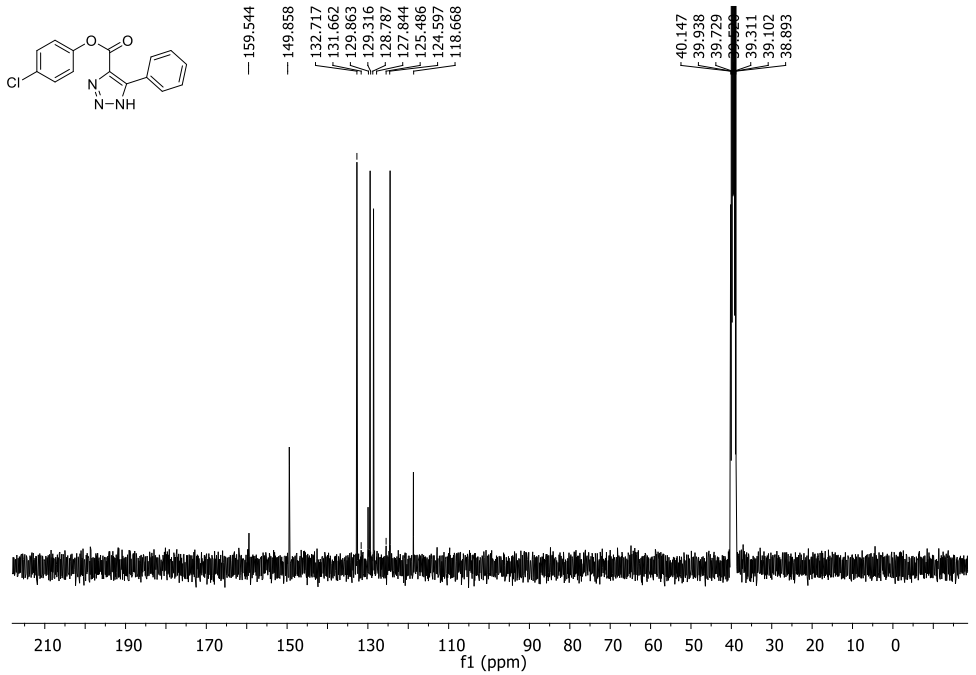

Figure 5.15. ^{13}C NMR spectrum of 4-chlorophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3e**) in DMSO-d$_6$.

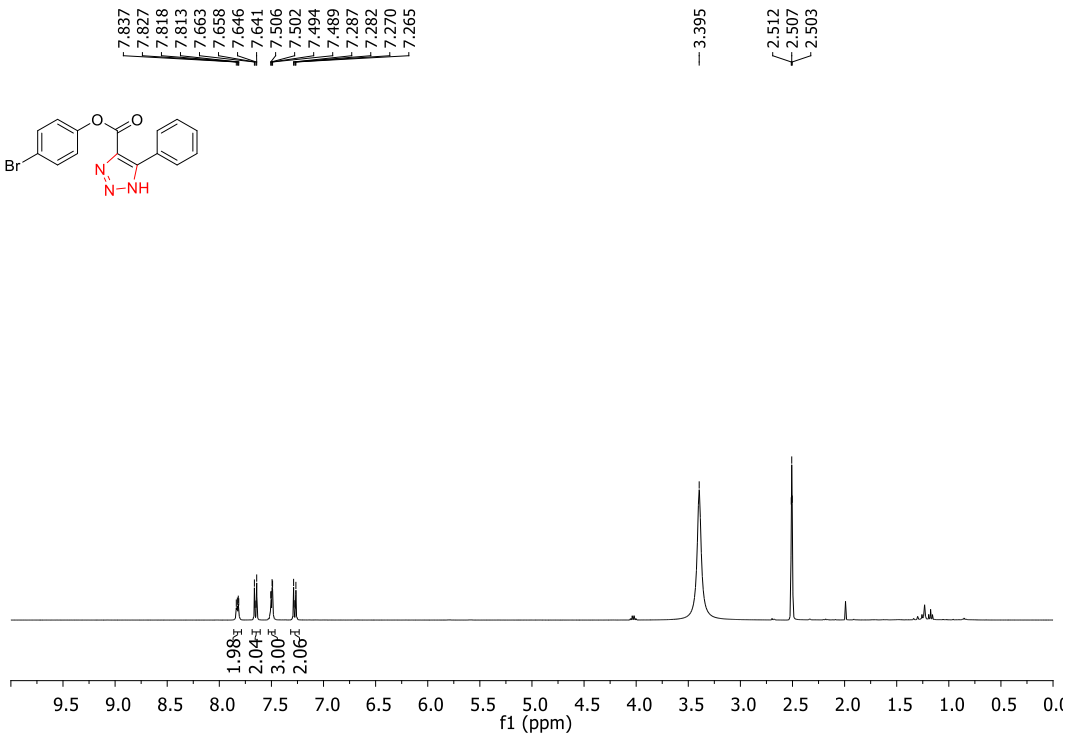

Figure 5.16. ^{1}H NMR spectrum of 4-bromophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3f**) in DMSO-d$_6$.

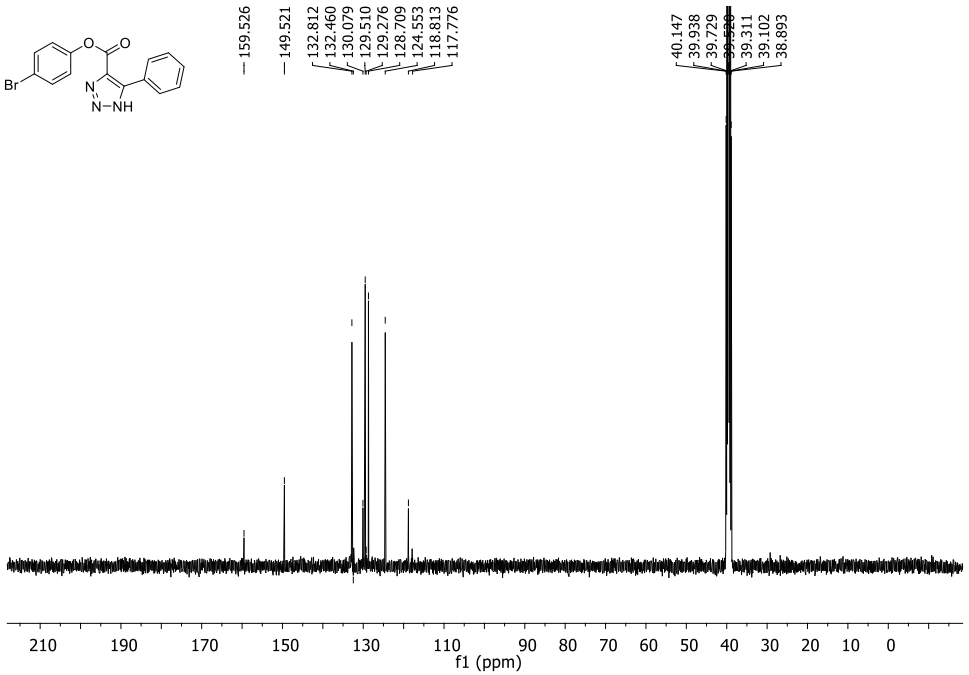

Figure 5.17. ^{13}C NMR spectrum of 4-bromophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3f**) in DMSO-d$_6$.

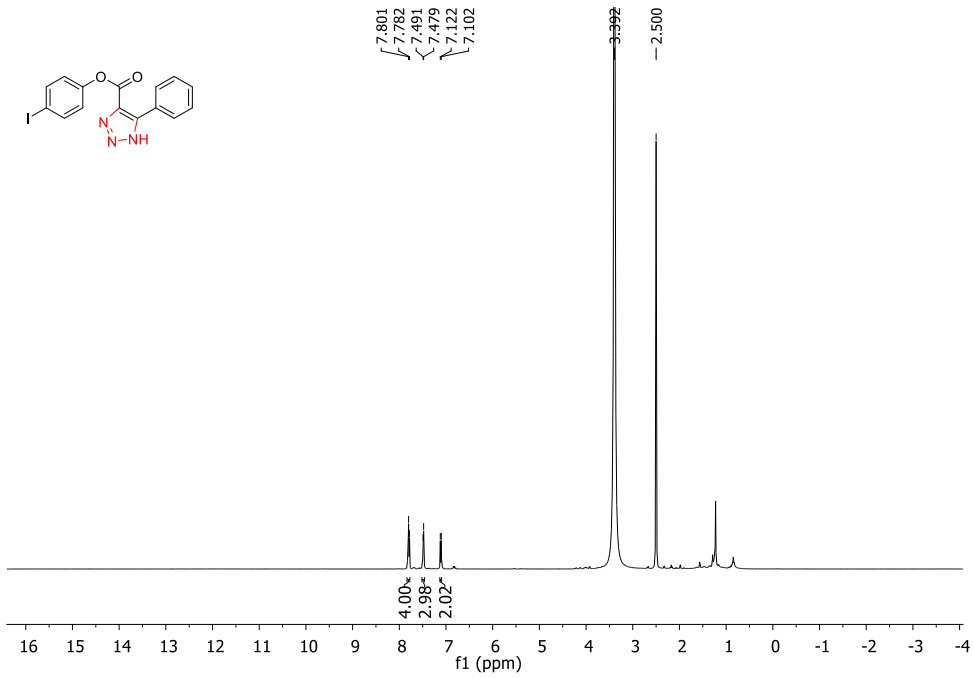

Figure 5.18. ^{1}H NMR spectrum of 4-iodophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3g**) in DMSO-d$_6$.

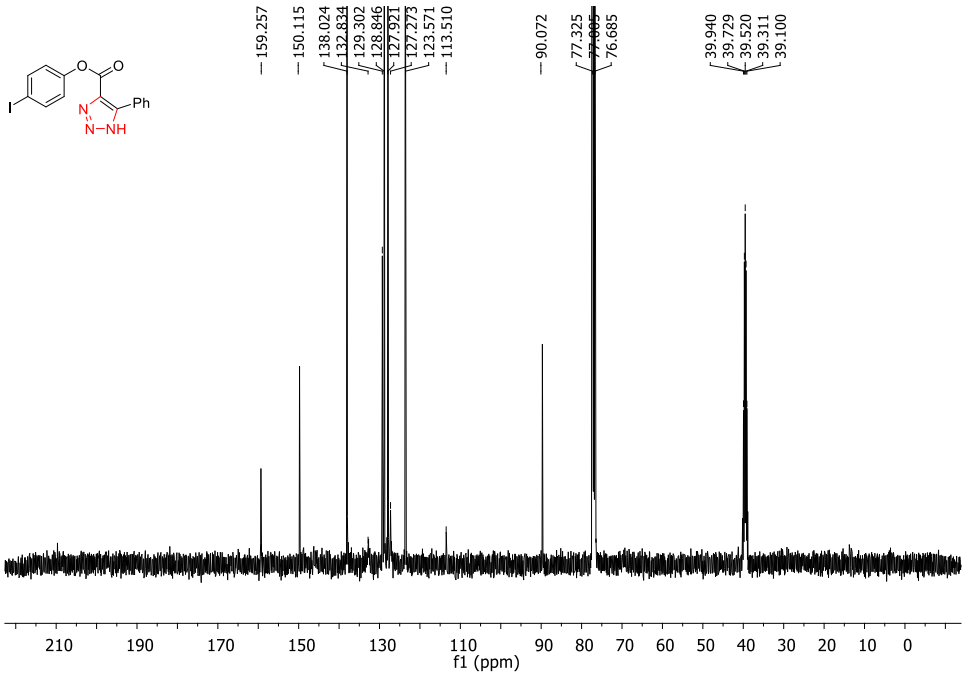

Figure 5.19. ^{13}C NMR spectrum of 4-iodophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3g**) in $CDCl_3$:DMSO-d_6.

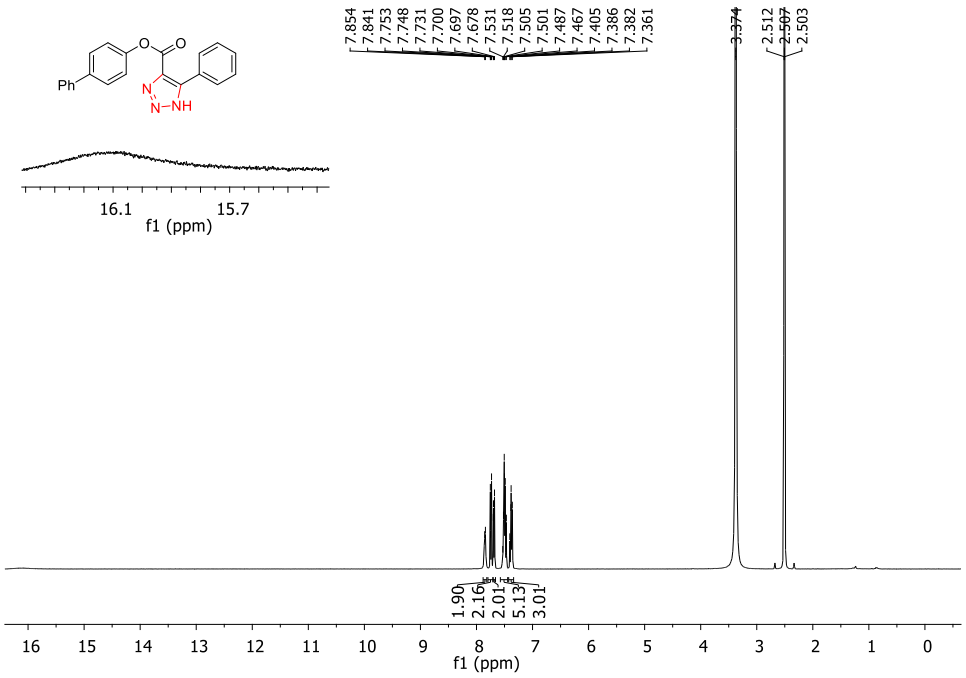

Figure 5.20. ^{1}H NMR spectrum of [1,1'-biphenyl]-4-yl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3h**) in DMSO-d_6.

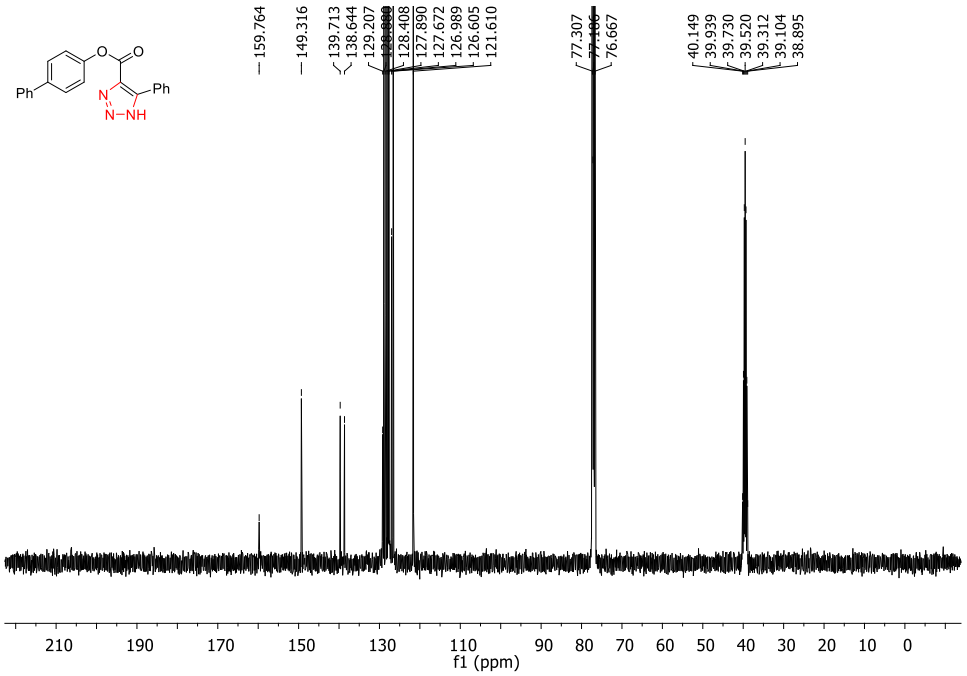

Figure 5.21. ^{13}C NMR spectrum of [1,1'-biphenyl]-4-yl 5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3h**) in $CDCl_3$: DMSO-d6.

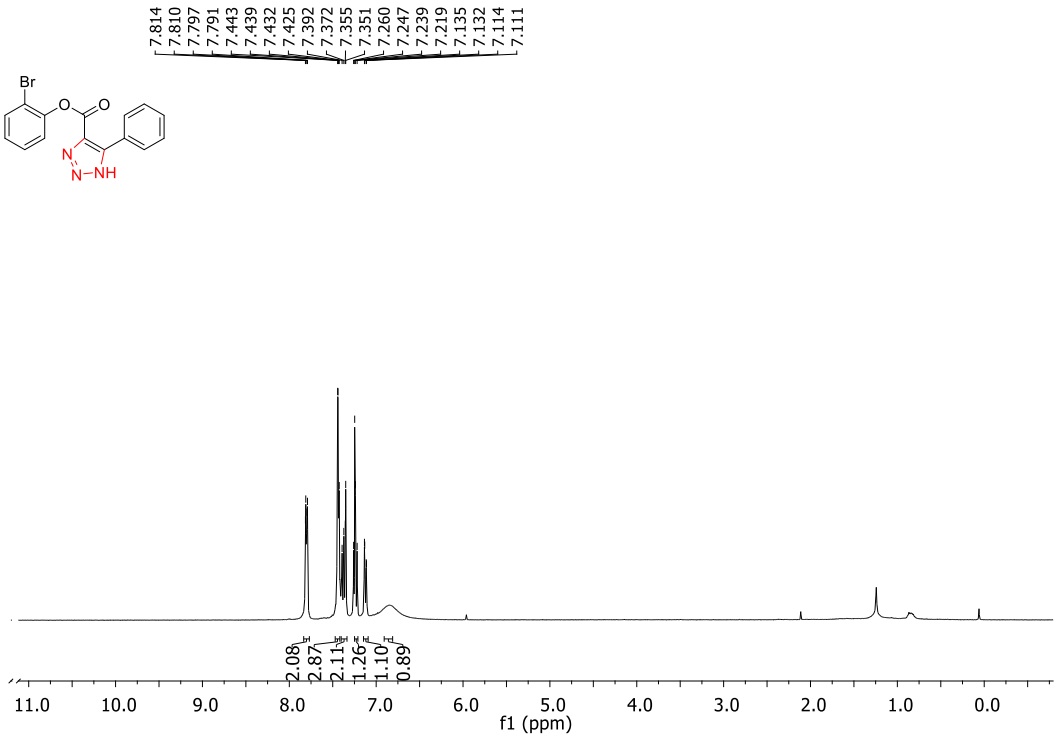

Figure 5.22. ^{1}H NMR spectrum of 3-bromophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3i**) in $CDCl_3$.

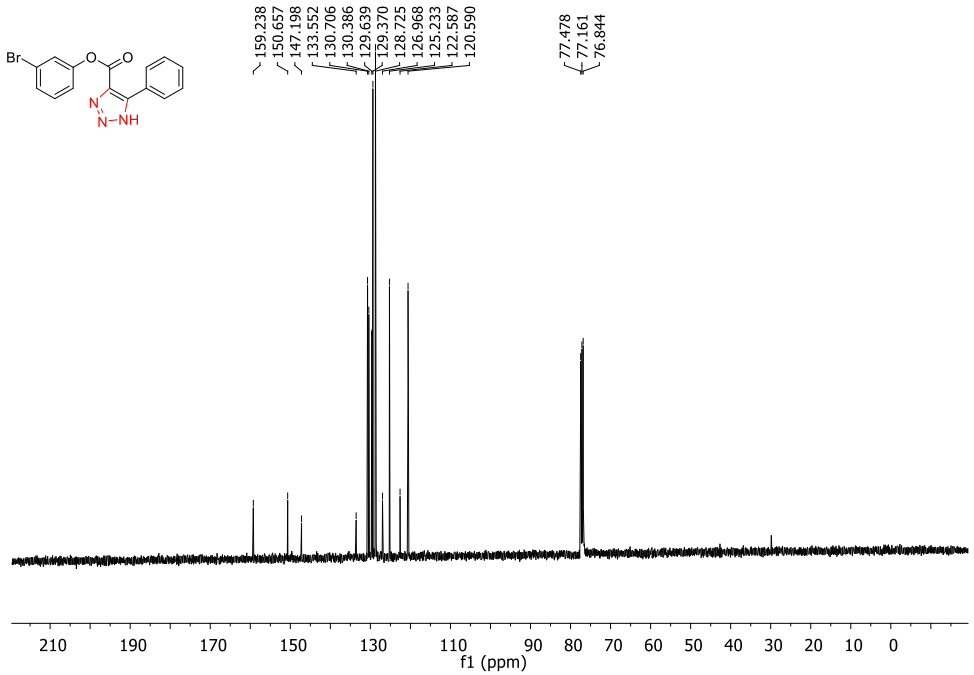

Figure 5.23. ^{13}C NMR spectrum of 3-bromophenyl 5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3i**) in $CDCl_3$.

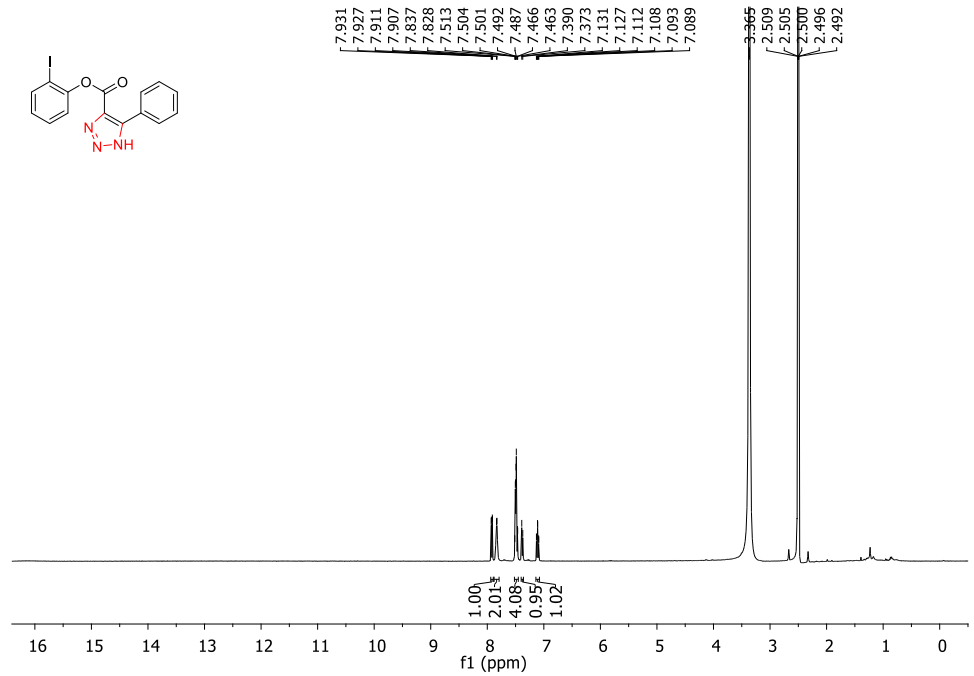

Figure 5.24. ^{1}H NMR spectrum of 2-iodophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3j**) in $CDCl_3$:DMSO-d_6.

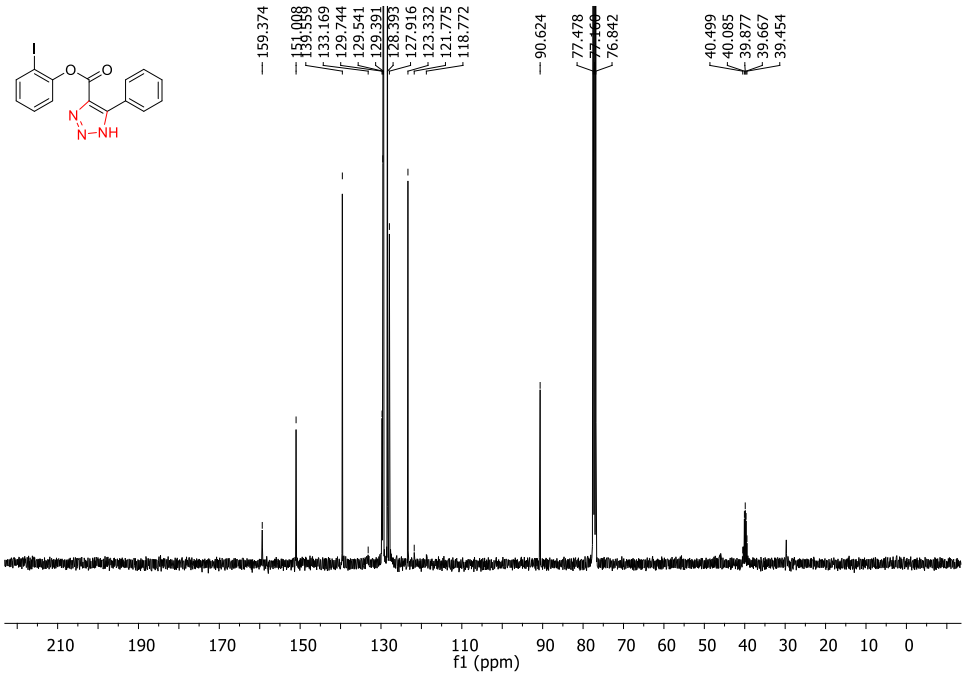

Figure 5.25. ^{13}C NMR spectrum of 2-iodophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3j**) in CDCl3: DMSO-d$_6$.

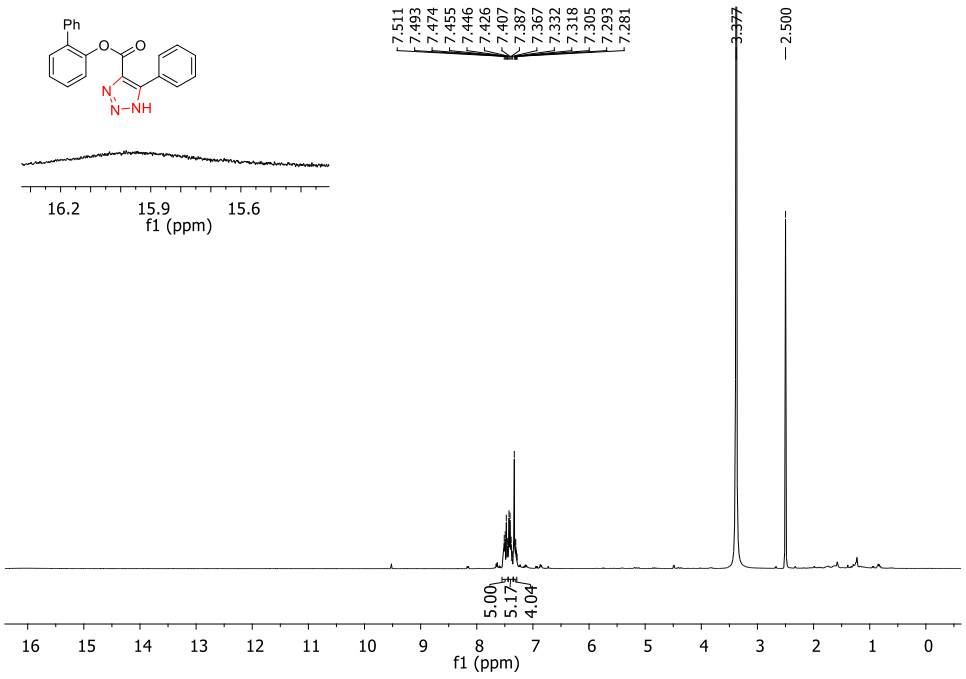

Figure 5.26. ^{1}H NMR spectrum of [1,1'-biphenyl]-2-yl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3k**) in DMSO-d$_6$.

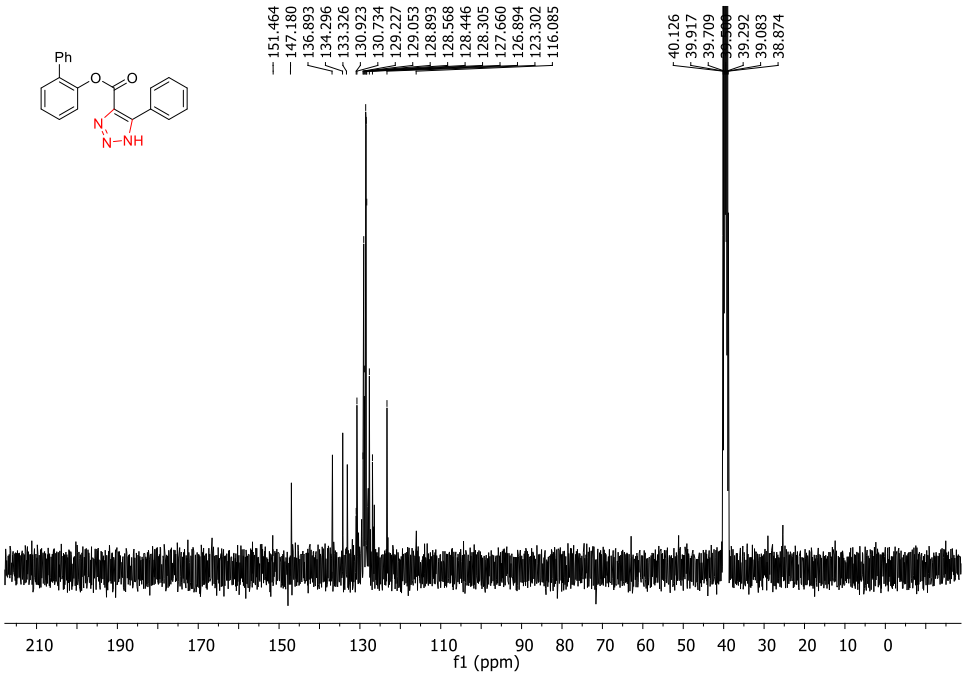

Figure 5.27. ^{13}C NMR spectrum of [1,1'-biphenyl]-2-yl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3k**) in DMSO-d_6.

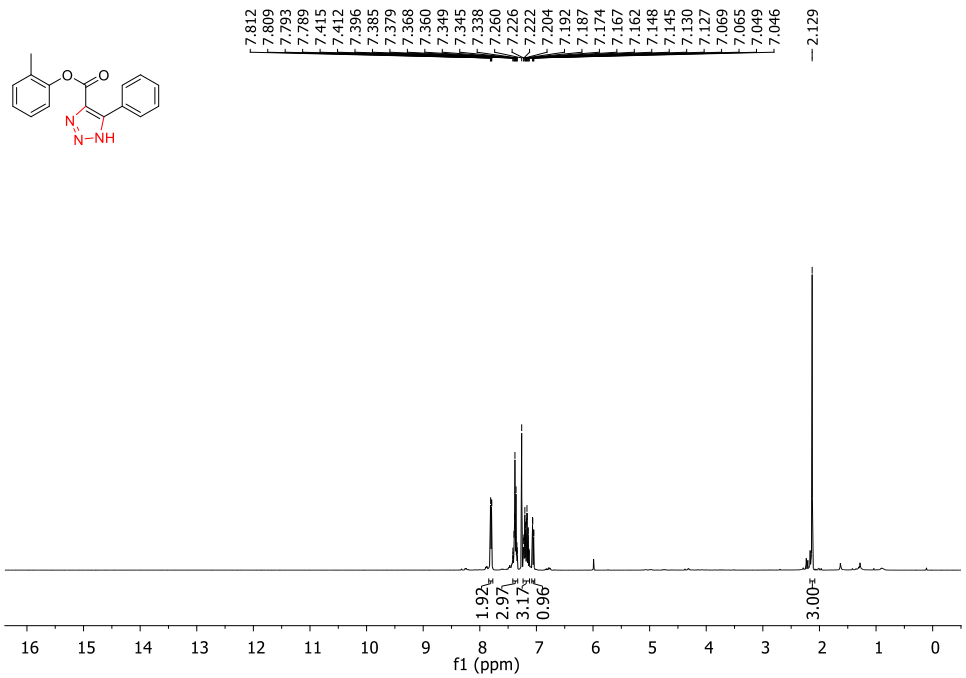

Figure 5.28. ^{1}H NMR spectrum of *o*-tolyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3l**) in $CDCl_3$.

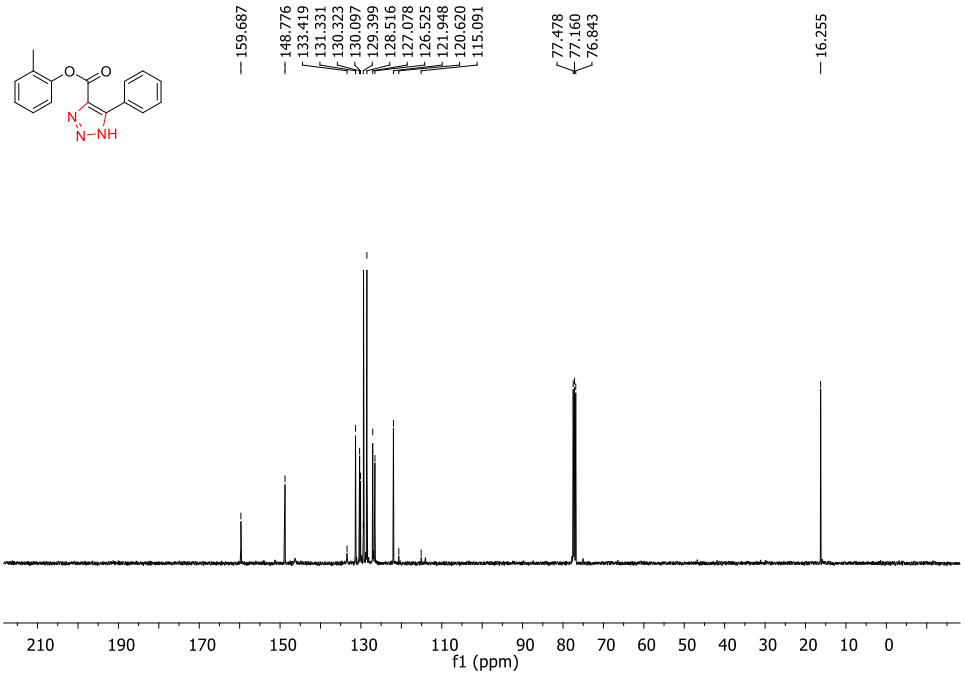

Figure 5.29. ^{13}C NMR spectrum of *o*-tolyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3l**) in $CDCl_3$.

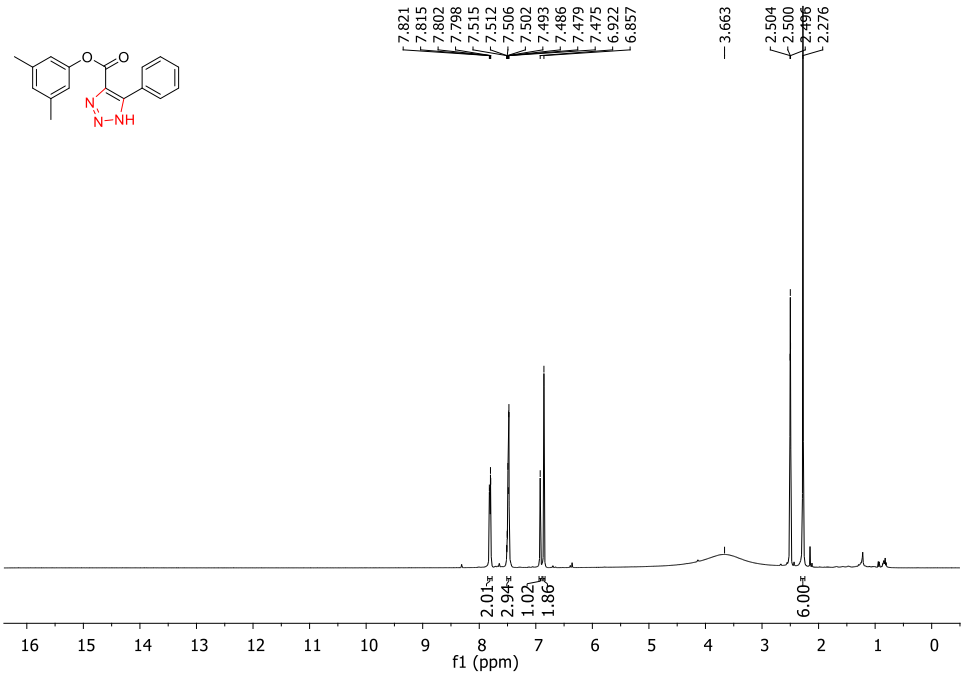

Figure 5.30. ^{1}H NMR spectrum of 3,5-dimethylphenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3m**) in DMSO-d_6.

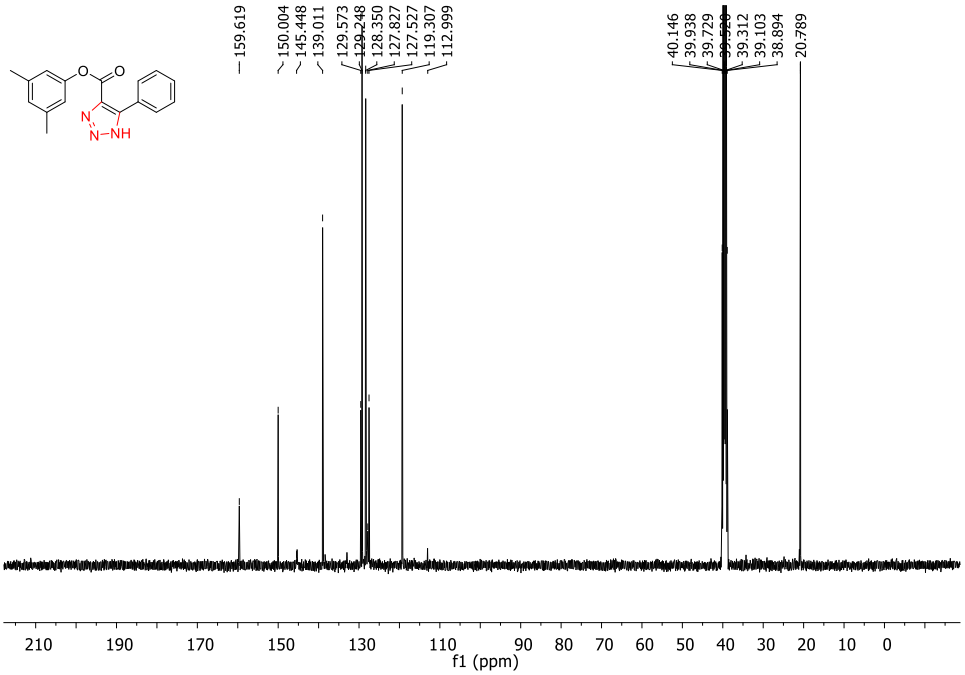

Figure 5.31. ^{13}C NMR spectrum of 3,5-dimethylphenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3m**) in DMSO-d_6.

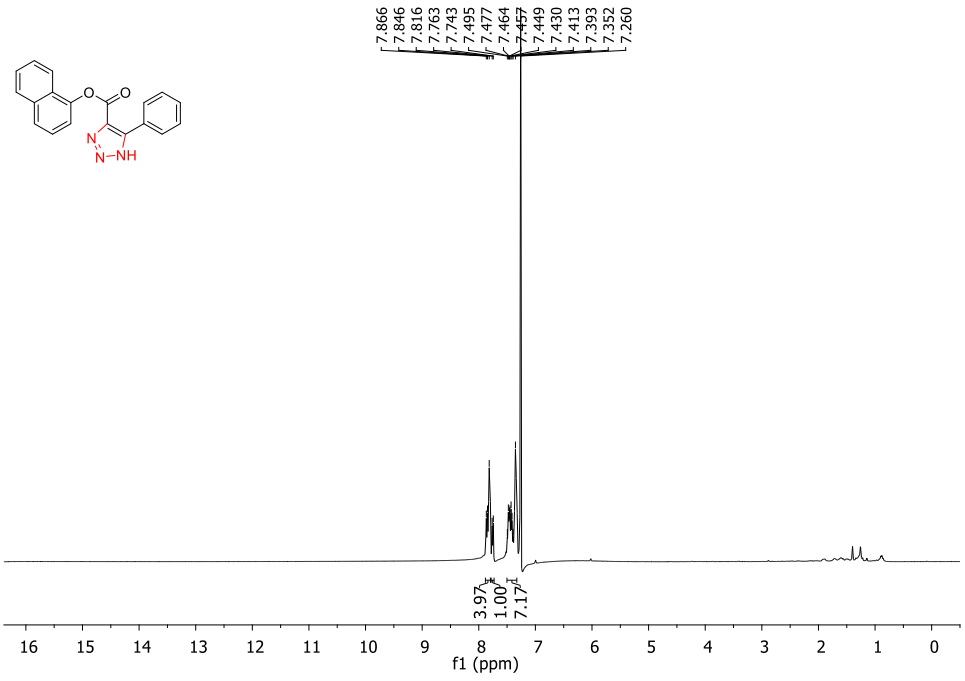

Figure 5.32. ^{1}H NMR spectrum of naphthalen-1-yl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3n**) in $CDCl_3$.

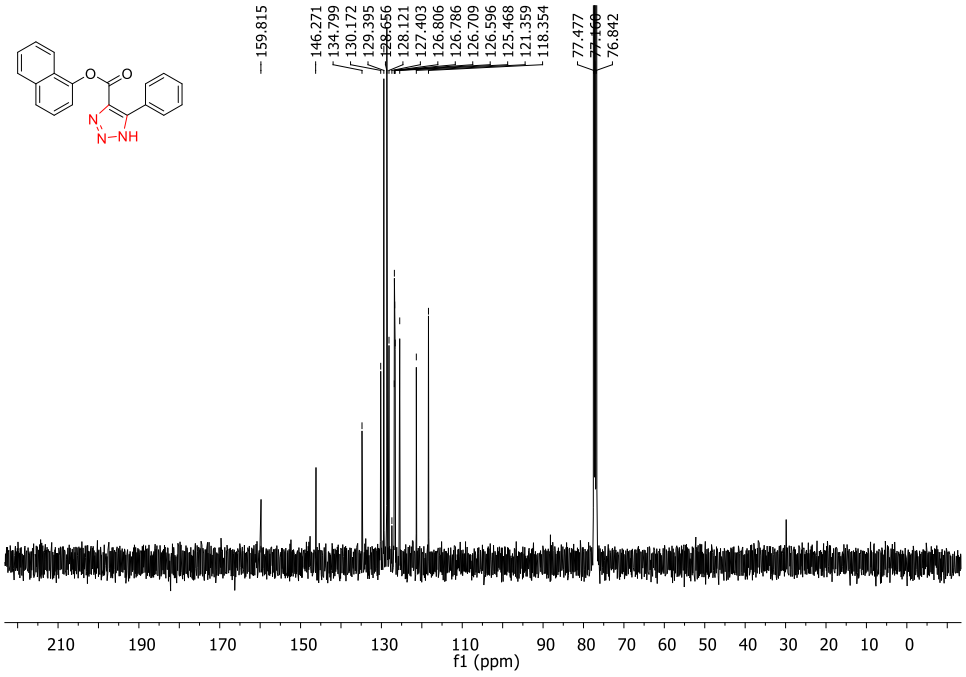

Figure 5.33. ^{13}C NMR spectrum of naphthalen-1-yl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3n**) in $CDCl_3$.

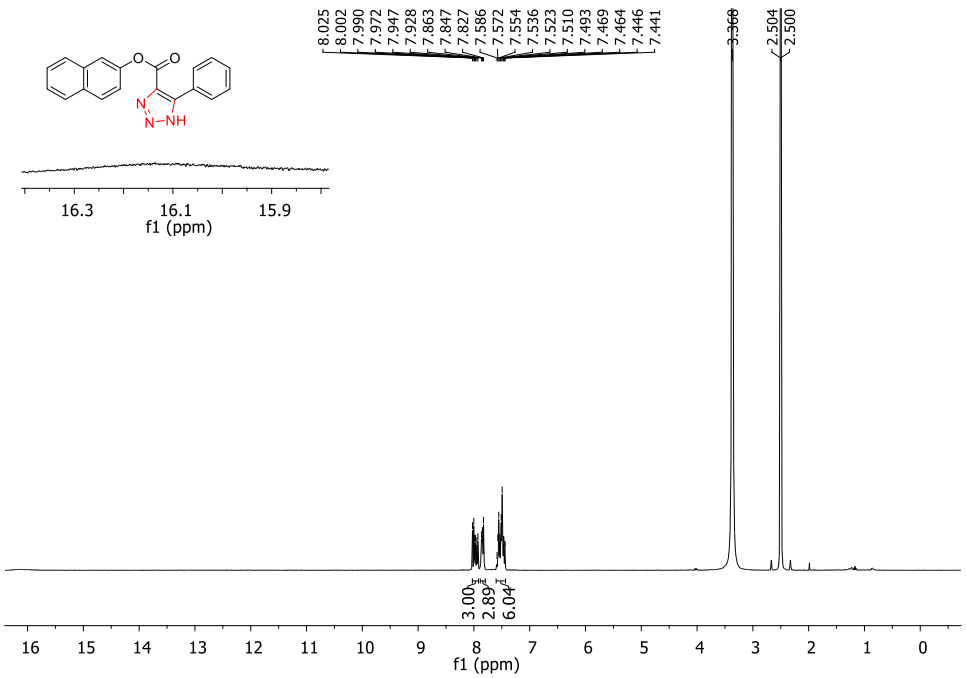

Figure 5.34. ^{1}H NMR spectrum of naphthalen-2-yl 5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3o**) in DMSO-d_6.

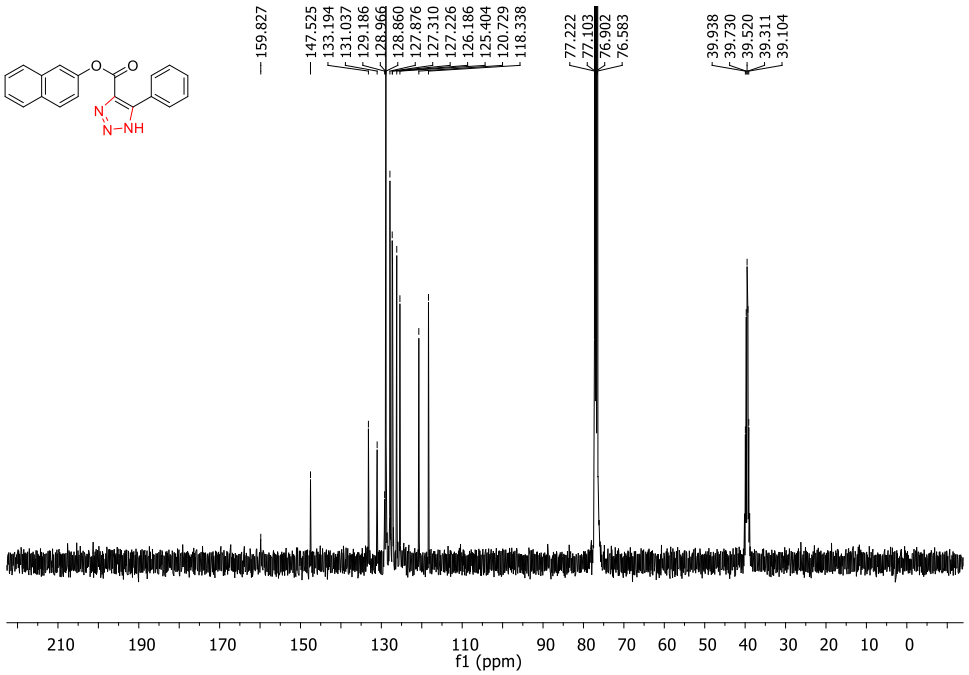

Figure 5.35. ^{13}C NMR spectrum of naphthalen-2-yl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3o**) in $CDCl_3$: DMSO-d_6.

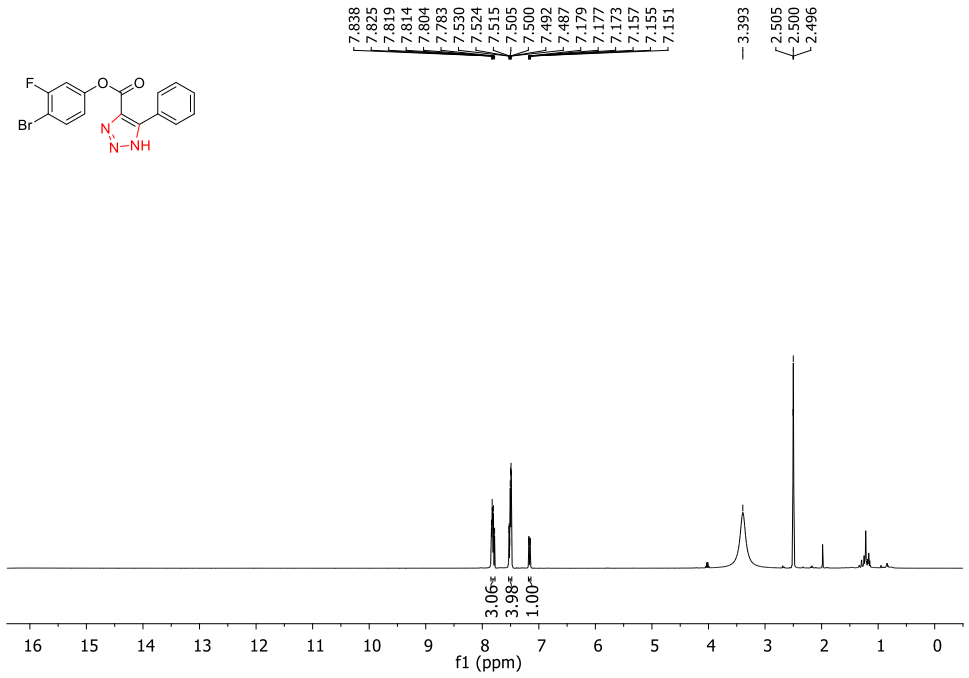

Figure 5.36. ^{1}H NMR spectrum of 4-bromo-3-fluorophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3p**) in DMSO-d_6.

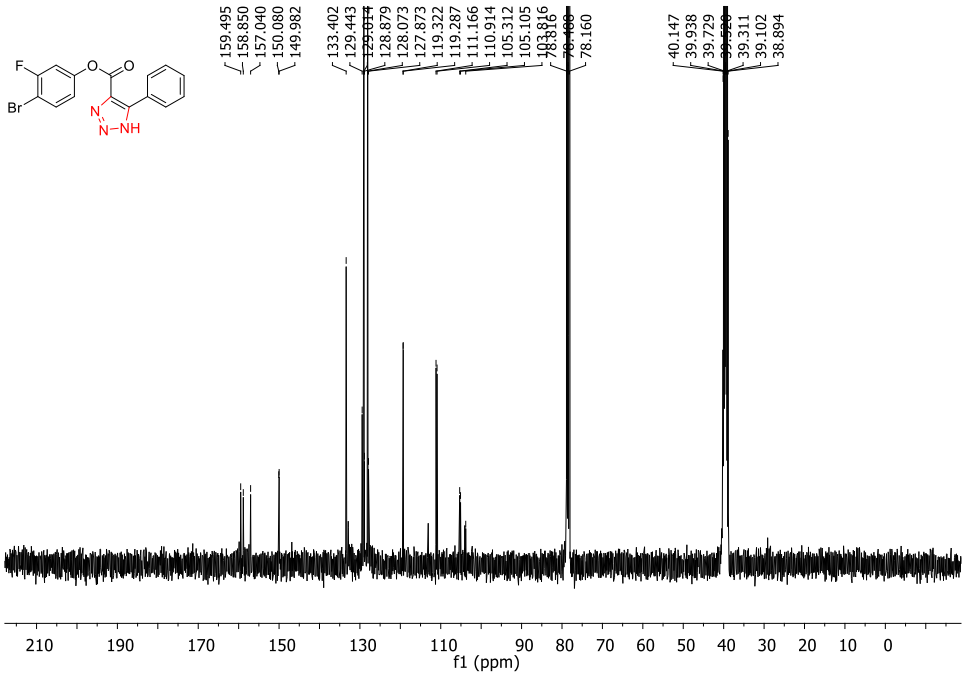

Figure 5.37. ^{13}C NMR spectrum of 4-bromo-3-fluorophenyl 5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3p**) in $CDCl_3$: DMSO-d_6.

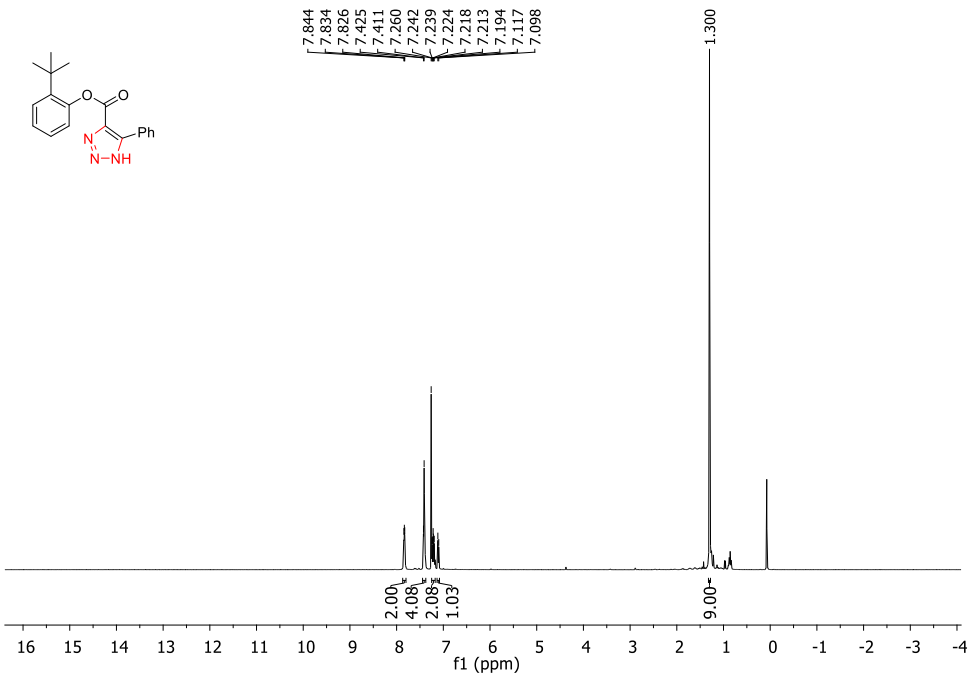

Figure 5.38. ^{1}H NMR spectrum of 2-(*tert*-butyl)phenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3q**) in $CDCl_3$.

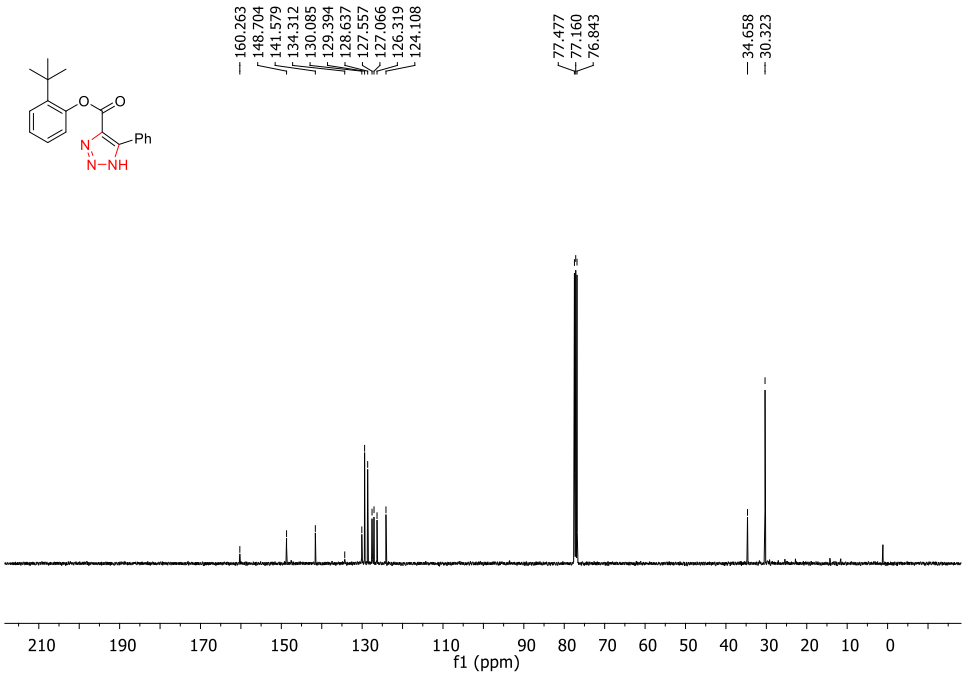

Figure 5.39. ^{13}C NMR spectrum of 2-(*tert*-butyl)phenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3q**) in $CDCl_3$.

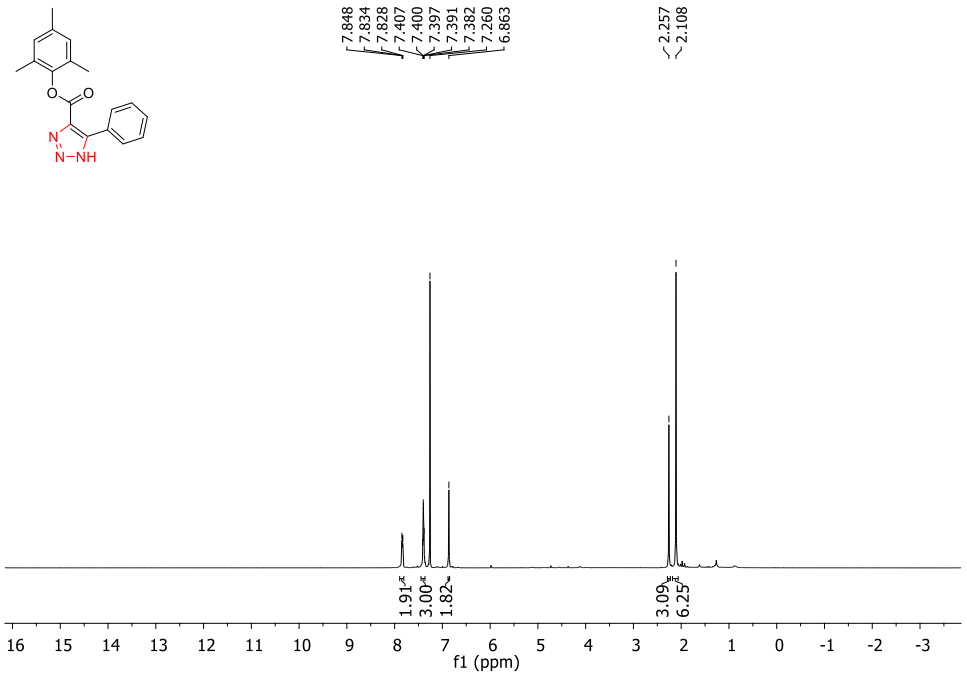

Figure 5.40. ^{1}H NMR spectrum of mesityl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3r**) in $CDCl_3$.

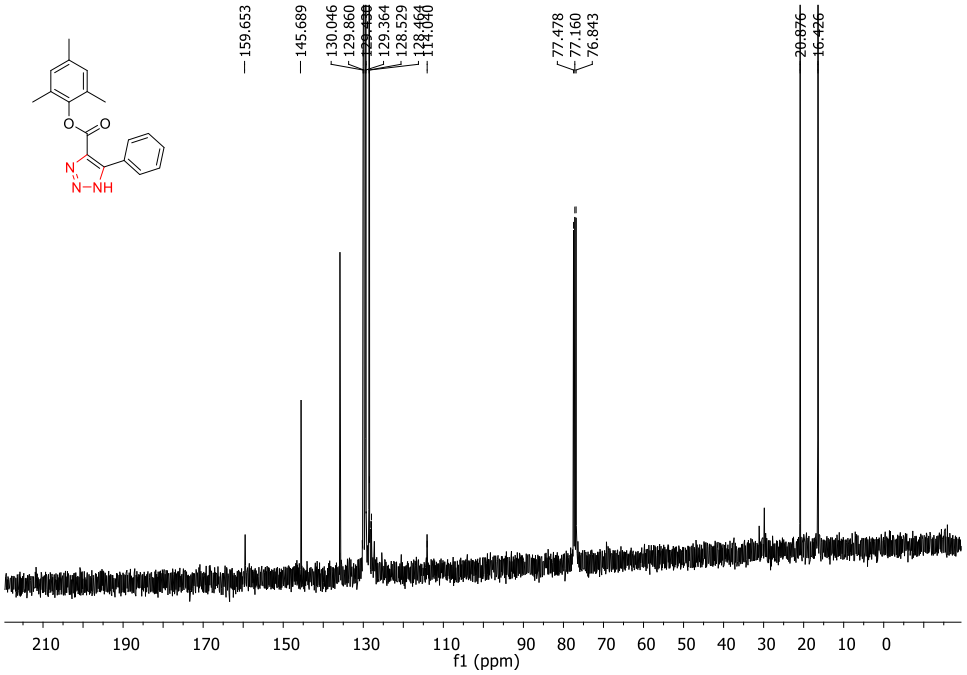

Figure 5.41. ^{13}C NMR spectrum of mesityl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3r**) in $CDCl_3$.

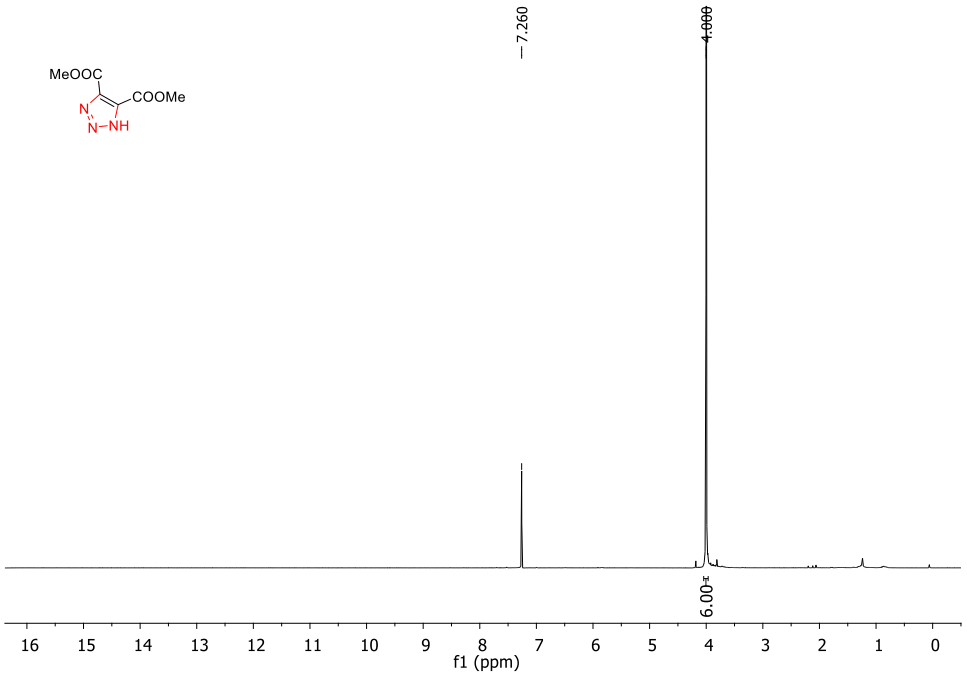

Figure 5.42. ^{1}H NMR spectrum of dimethyl-1 *H*-1,2,3-triazole-4,5-dicarboxylate (**3s**) in $CDCl_3$.

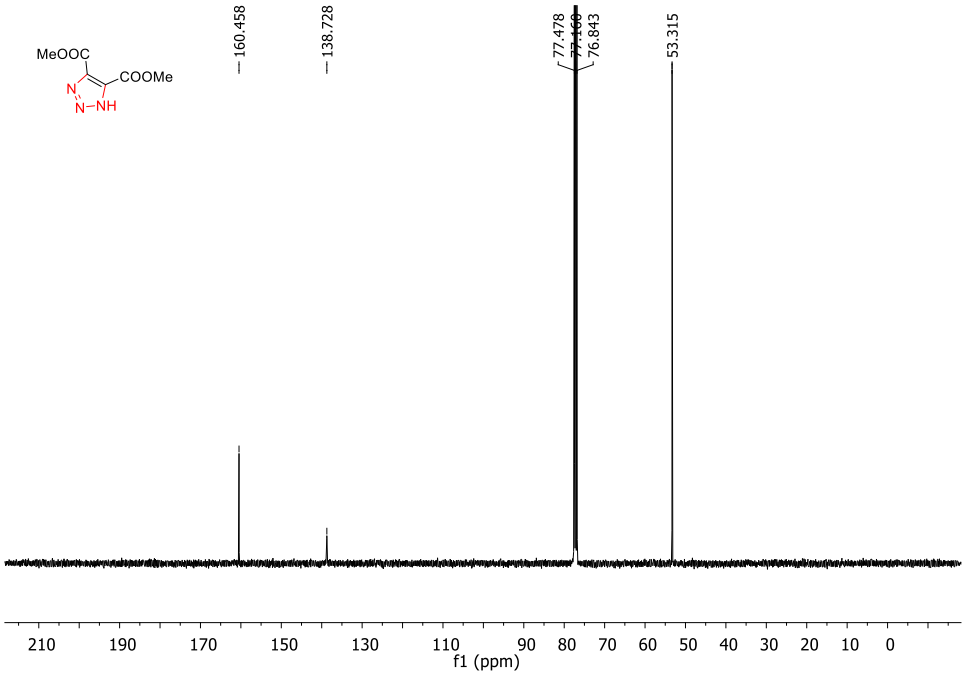

Figure 5.43. ^{13}C NMR spectrum of dimethyl-1 *H*-1,2,-3-triazole-4,-5-dicarboxylate (**3s**) in $CDCl_3$.

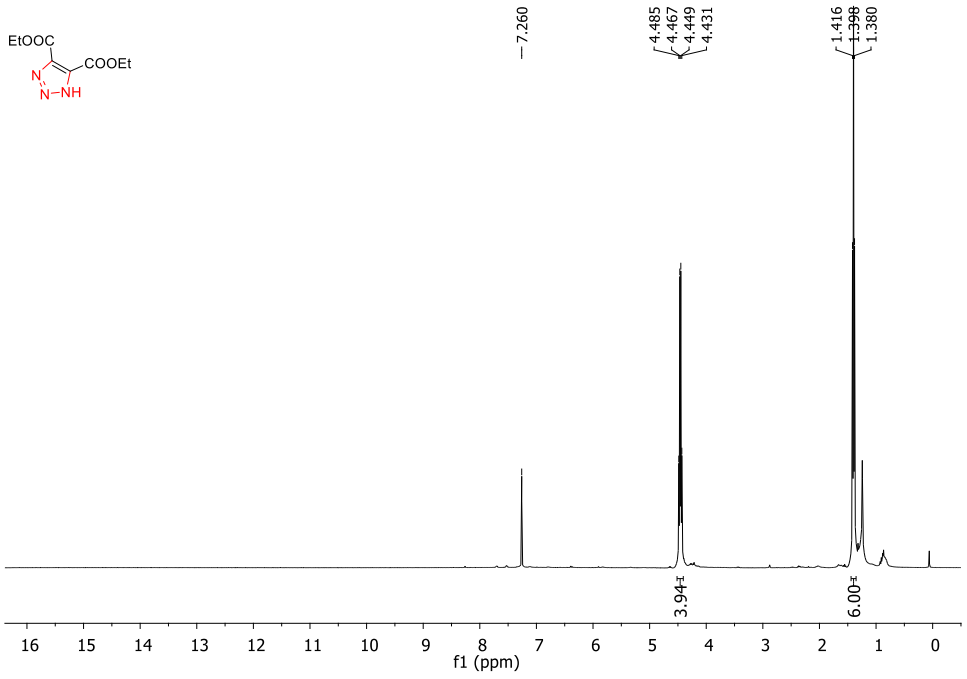

Figure 5.44. ^{1}H NMR spectrum of diethyl-1*H*-1,2,3-triazole-4,5-dicarboxylate (**3t**) in $CDCl_3$.

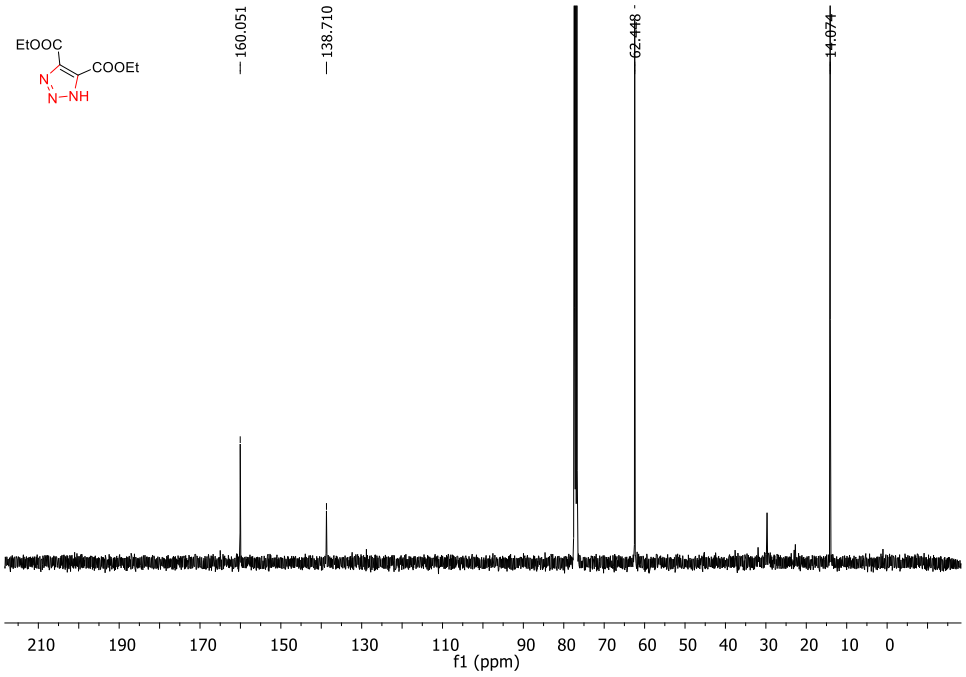

Figure 5.45. ^{13}C NMR spectrum of diethyl-1*H*-1,2,3-triazole-4,5-dicarboxylate (**3t**) in $CDCl_3$.

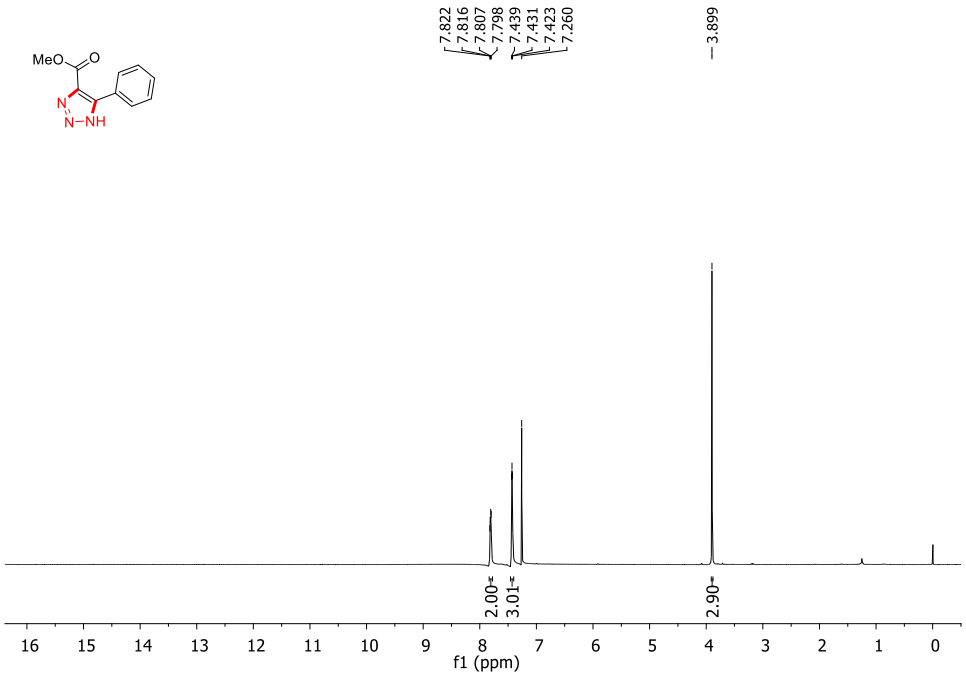

Figure 5.46. ^{1}H NMR spectrum of methyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3u**) in $CDCl_3$.

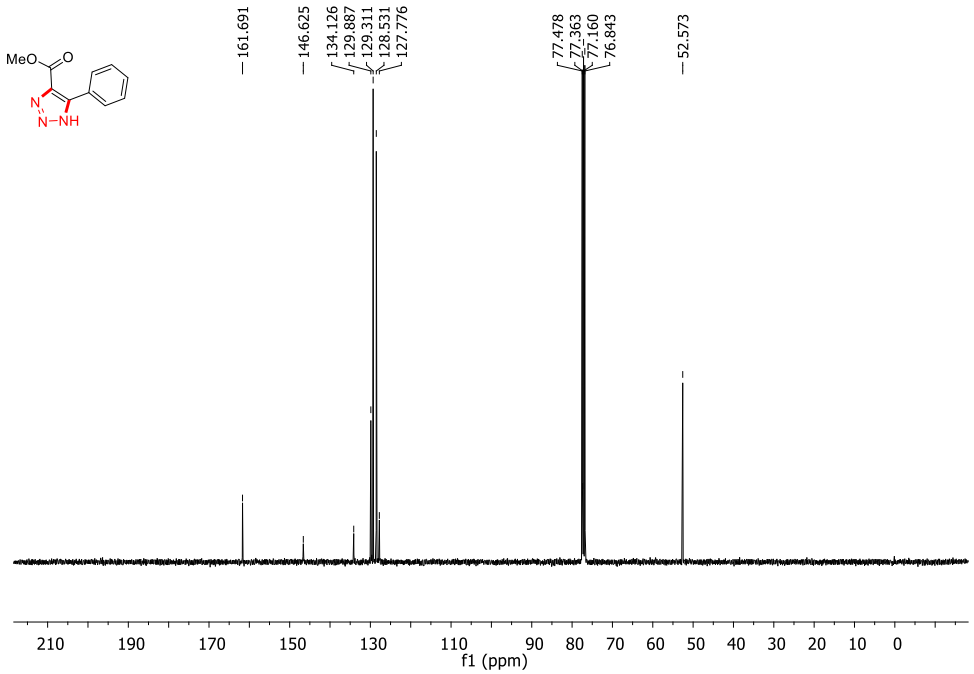

Figure 5.47. ^{13}C NMR spectrum of methyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3u**) in $CDCl_3$.

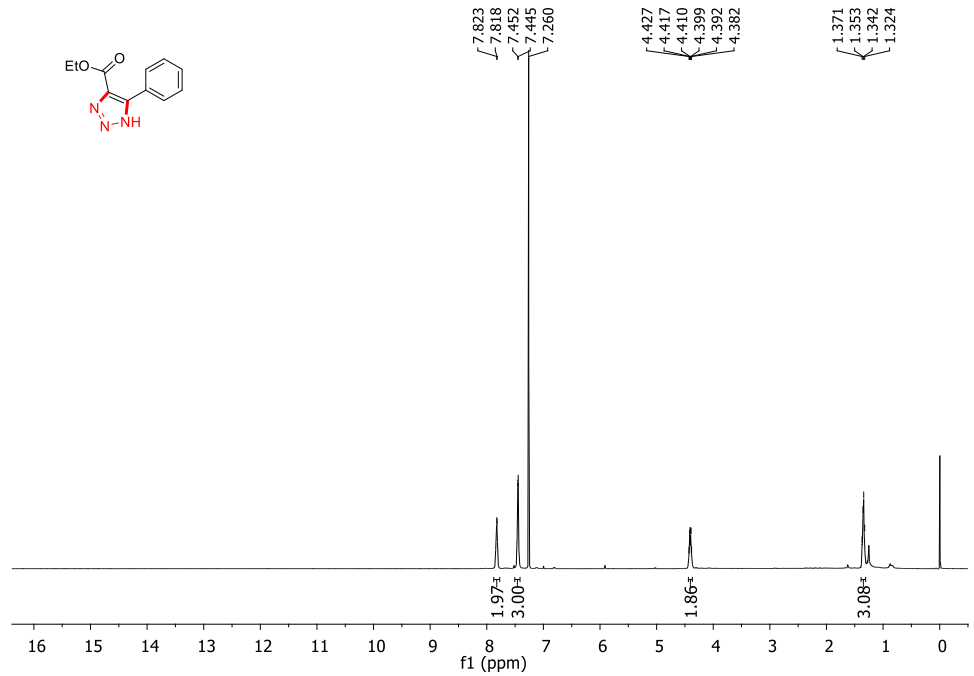

Figure 5.48. ^{1}H NMR spectrum of ethyl-5-phenyl-1H-1,2,3-triazole-4-carboxylate (**3v**) in $CDCl_3$

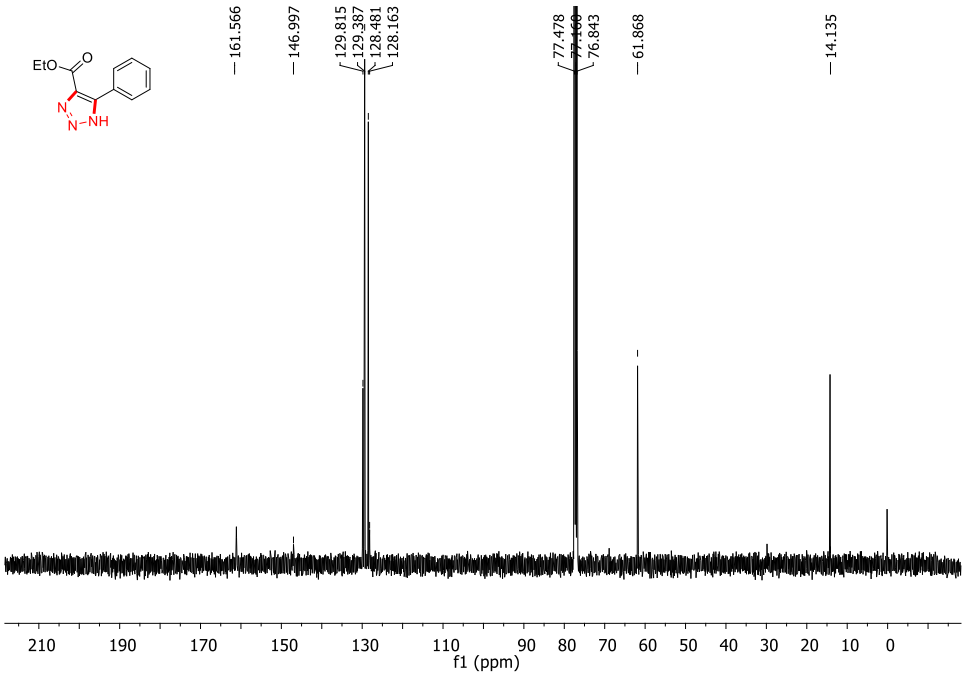

Figure 5.49. ^{13}C NMR spectrum of ethyl-5-phenyl-1H-1,2,3-triazole-4-carboxylate (**3v**) in $CDCl_3$.

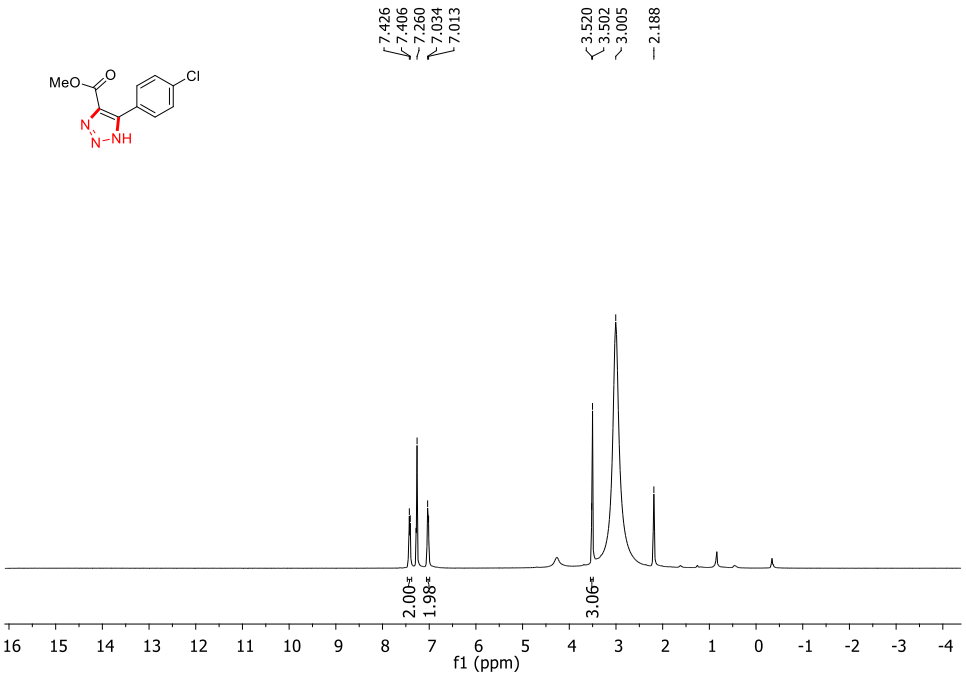

Figure 5.50. ^{1}H NMR spectrum of methyl-5-(4-chlorophenyl-1*H*-1,2,3-triazole-4-carboxylate (**3w**) in $CDCl_3$:DMSO-d_6.

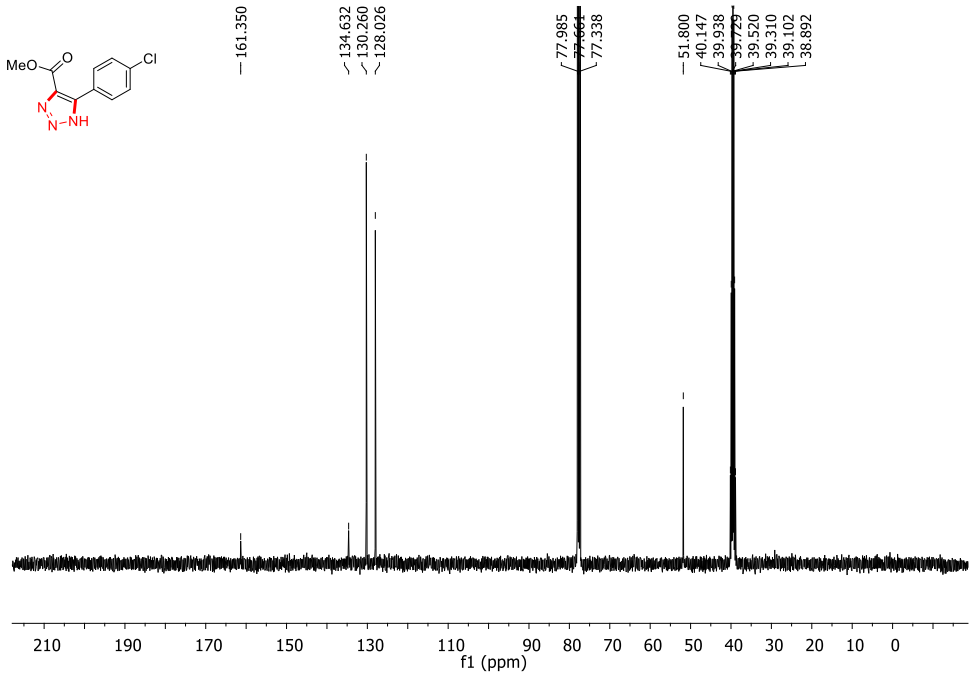

Figure 5.51. ^{13}C NMR spectrum of methyl-5-(4-chlorophenyl-1*H*-1,2,3-triazole-4-carboxylate (**3w**) in $CDCl_3$:DMSO-d_6.

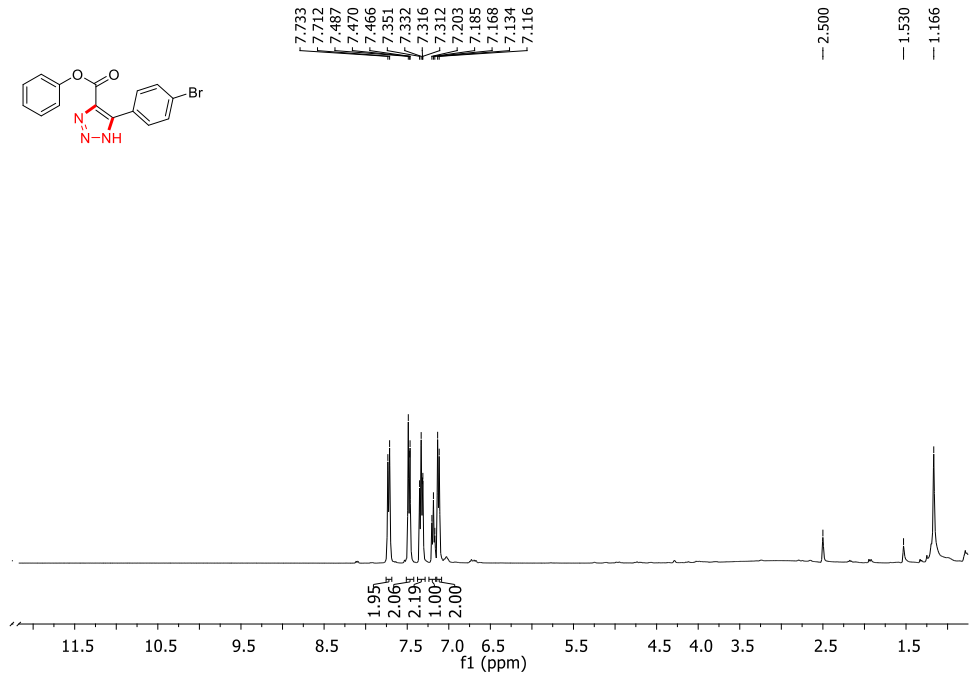

Figure 5.52. ^{1}H NMR spectrum of phenyl 5-(4-bromophenyl)-1*H*-1,2,3-triazole-4-carboxylate (**3x**) in DMSO-d_6.

.

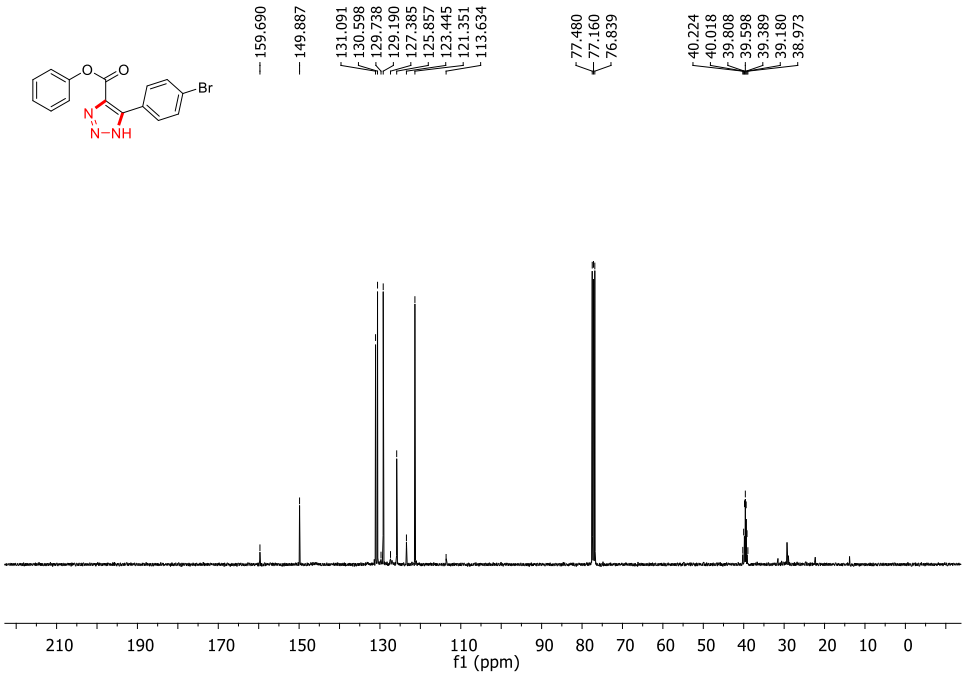

Figure 5.53. ^{13}C NMR spectrum of phenyl-5-(4-bromophenyl)-1*H*-1,2,3-triazole-4-carboxylate (**3x**) in $CDCl_3$:DMSO-d_6.

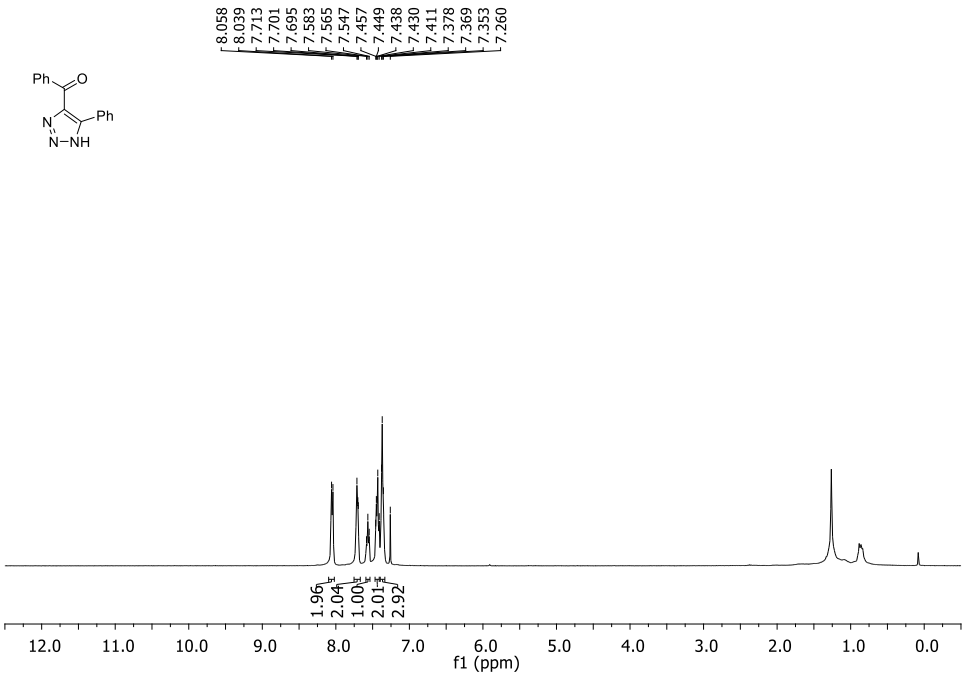

Figure 5.54. ^{1}H NMR spectrum of phenyl (5-phenyl-1H-1,2,3triazol-4-yl)methanone (**4y**) in $CDCl_3$.

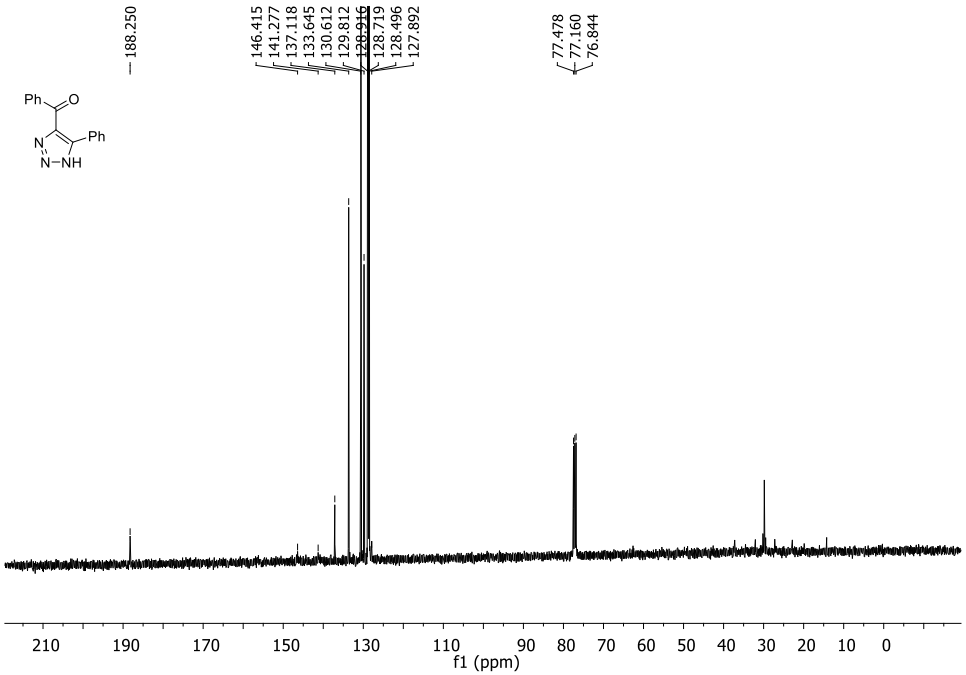

Figure 5.55. ^{13}C NMR spectrum of phenyl (5-phenyl-1H-1,2,3triazol-4-yl)methanone (**4y**) in $CDCl_3$.

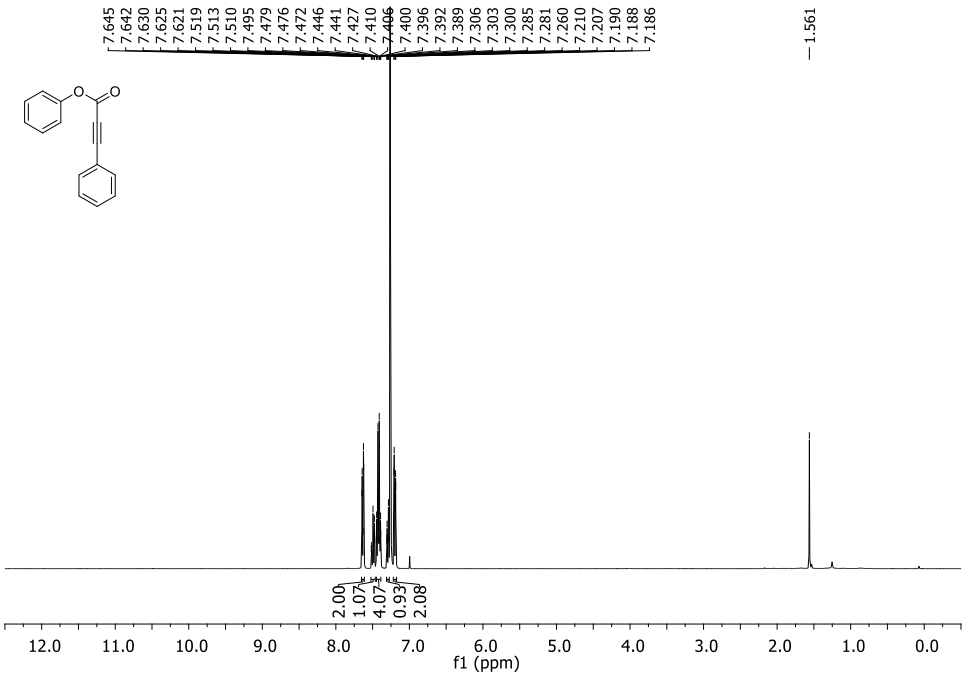

Figure 5.56. ^{1}H NMR spectrum of phenyl-3-phenylpropiolate (**2a**) in $CDCl_3$.

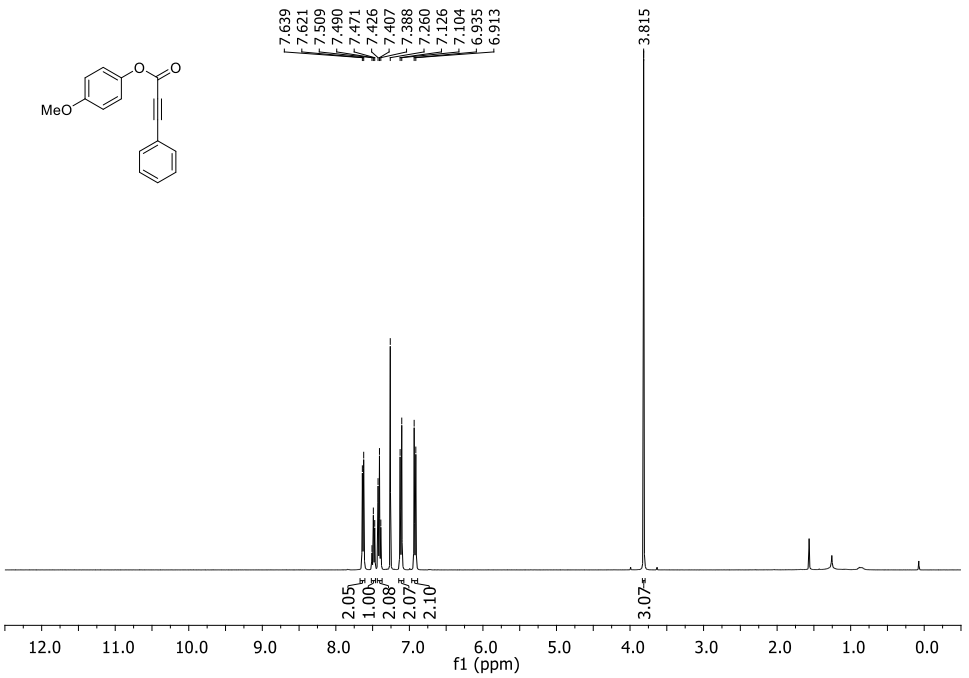

Figure 5.57. ^{1}H NMR spectrum of 4-methoxyphenyl-3-phenylpropiolate in $CDCl_3$ (**2b**).

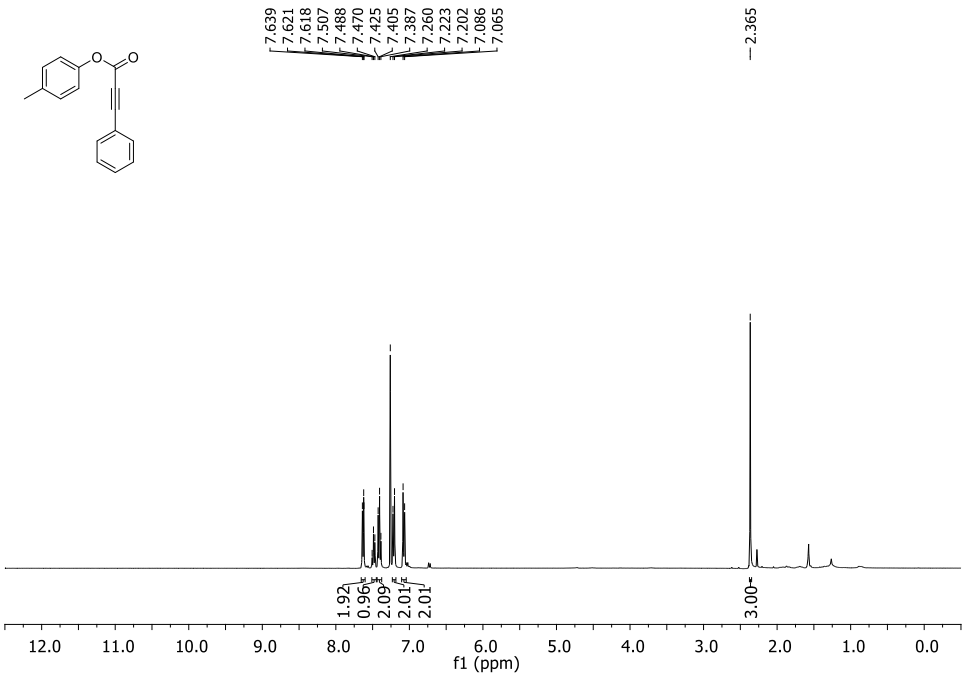

Figure 5.58. ^{1}H NMR spectrum of *p*-tolyl-3-phenylpropiolate (**2c**) in $CDCl_3$.

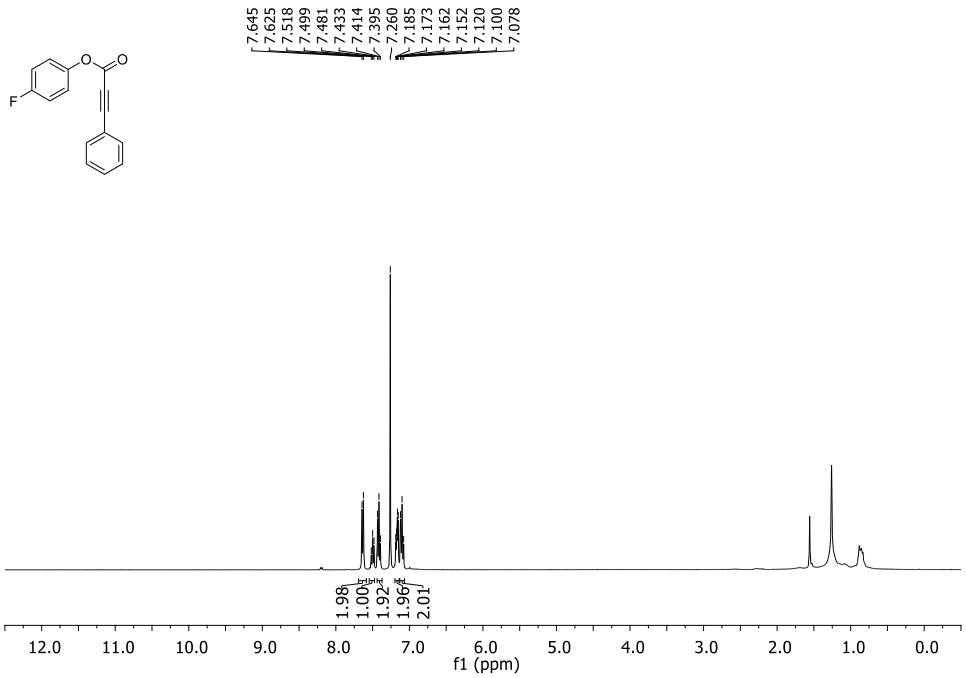

Figure 5.59. ^{1}H NMR spectrum of 4-fluorophenyl-3-phenylpropiolate (**2d**) in $CDCl_3$.

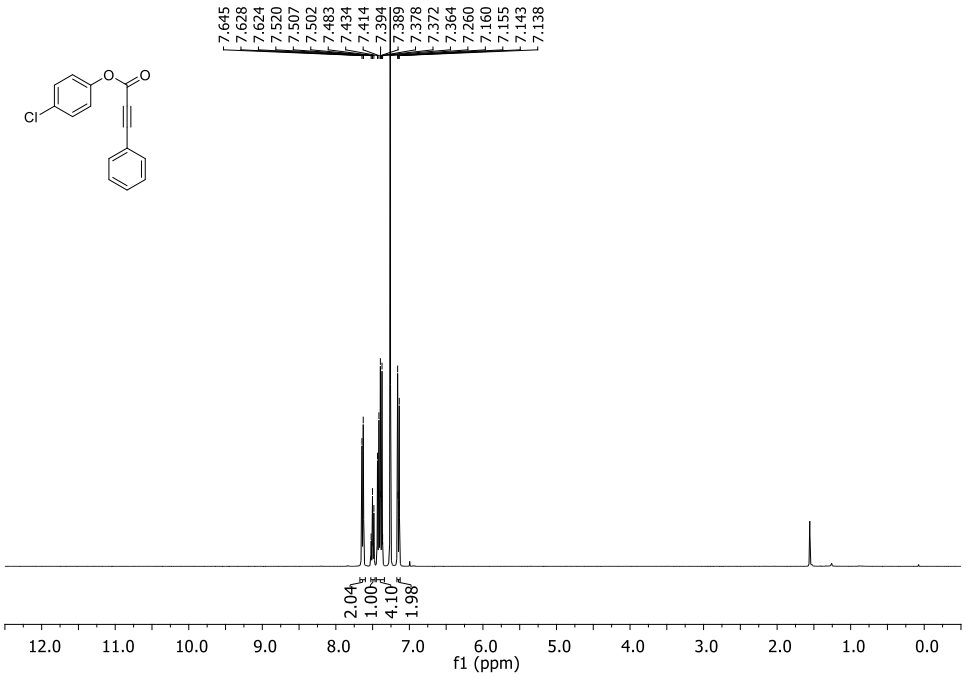

Figure 5.60. ^{1}H NMR spectrum of 4-chlorophenyl-3-phenylpropiolate (**2e**) in $CDCl_3$.

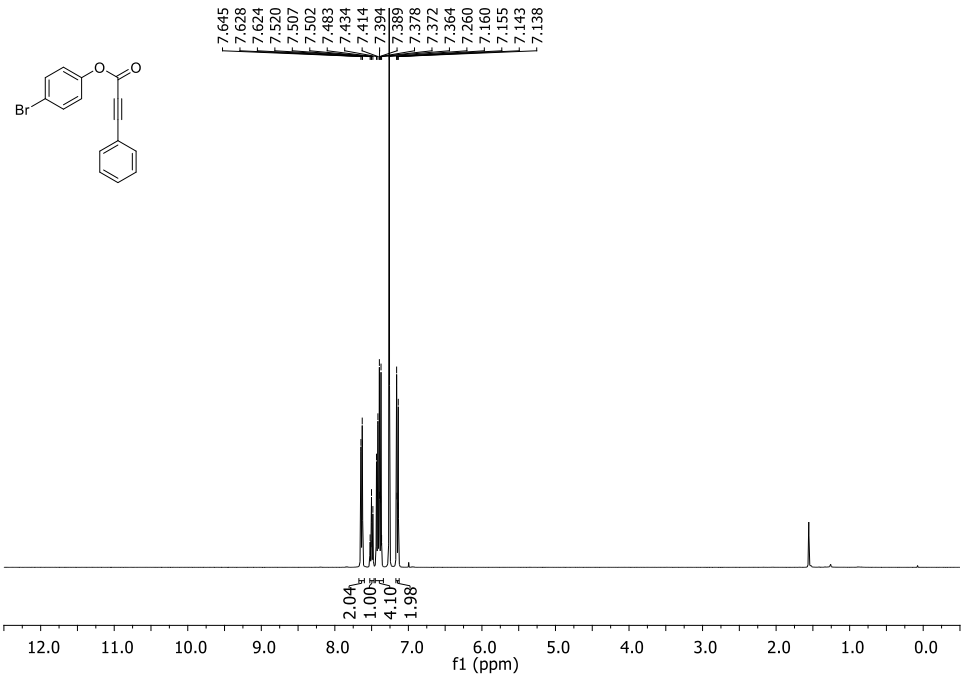

Figure 5.61. ^{1}H NMR spectrum of 4-bromophenyl-3-phenylpropiolate (**2f**) in $CDCl_3$.

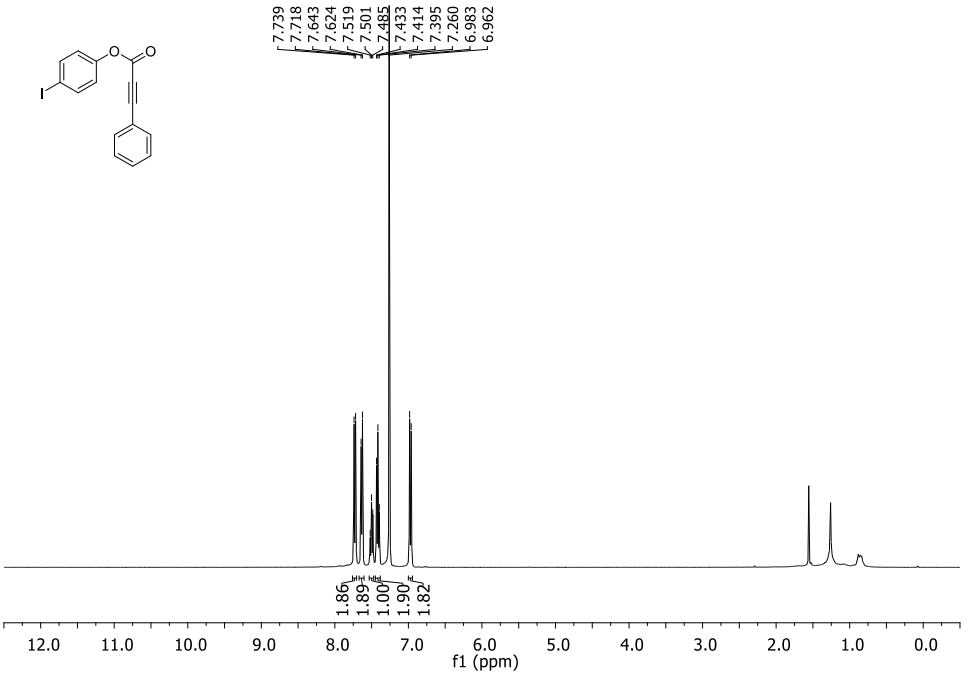

Figure 5.62. ^{1}H NMR spectrum of 4-iodophenyl-3-phenylpropiolate (**2g**) in $CDCl_3$.

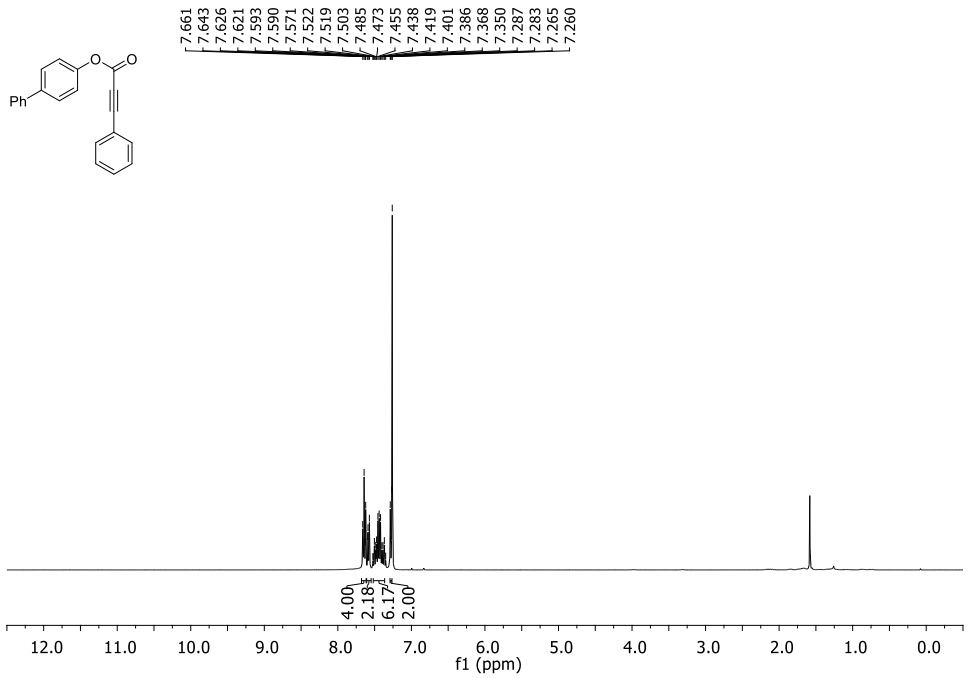

Figure 5.63. ^{1}H NMR spectrum of [1,1'-biphenyl]-4-yl-3-phenylpropiolate (**2h**) in $CDCl_3$.

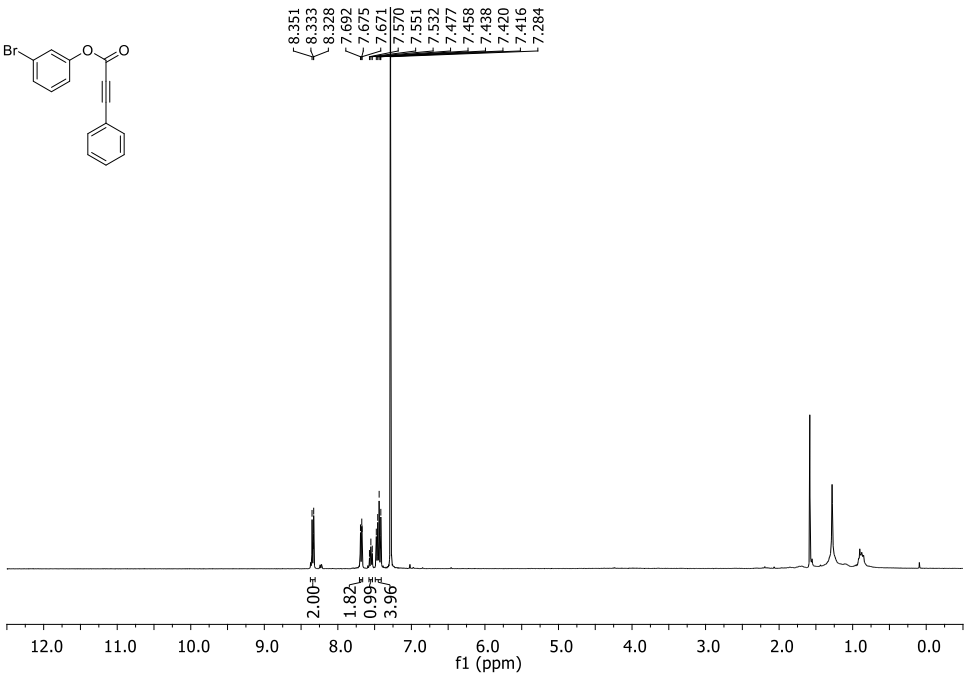

Figure 5.64. ^{1}H NMR spectrum of 3-bromophenyl-3-phenylpropiolate (**2i**) in $CDCl_3$.

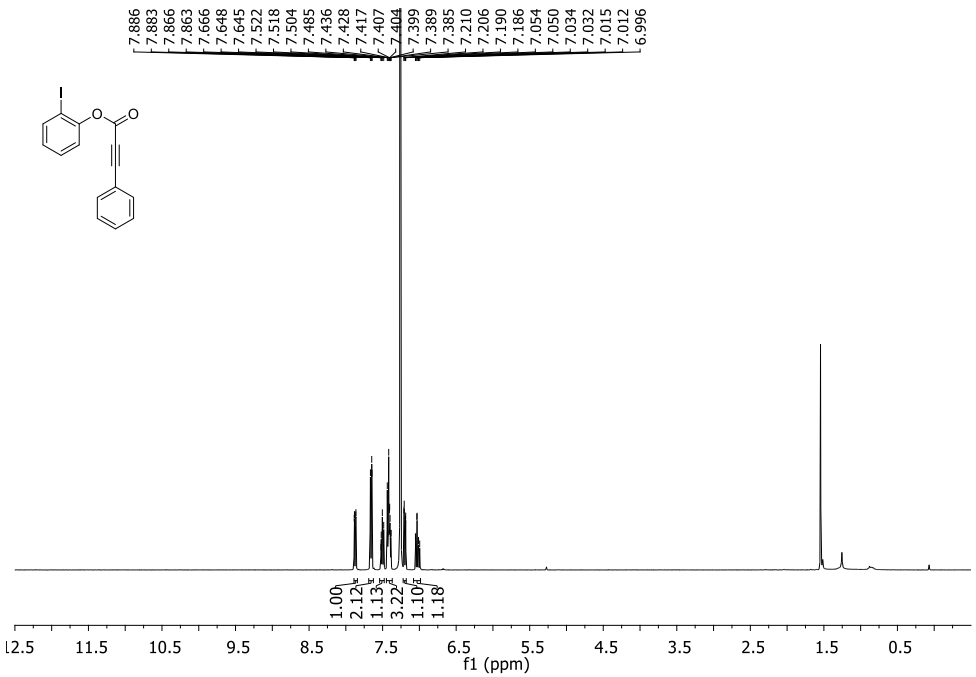

Figure 5.65. ^{1}H NMR spectrum of 2-iodophenyl-3-phenylpropiolate (**2j**) in $CDCl_3$.

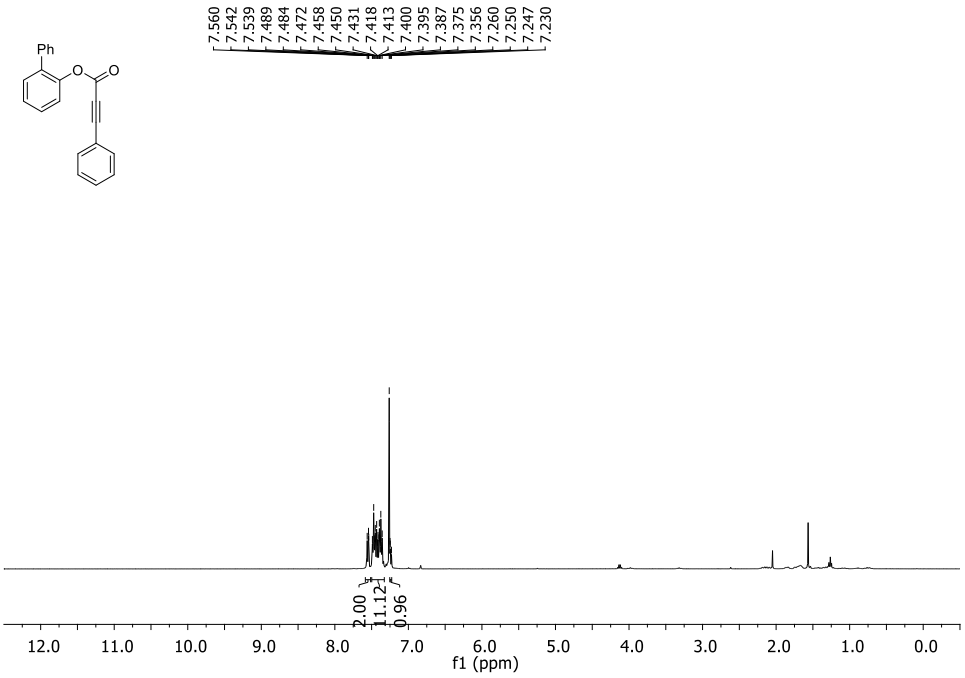

Figure 5.63. ^{1}H NMR spectrum of [1,1'-biphenyl]-2-yl-3-phenylpropiolate (**2k**) in $CDCl_3$.

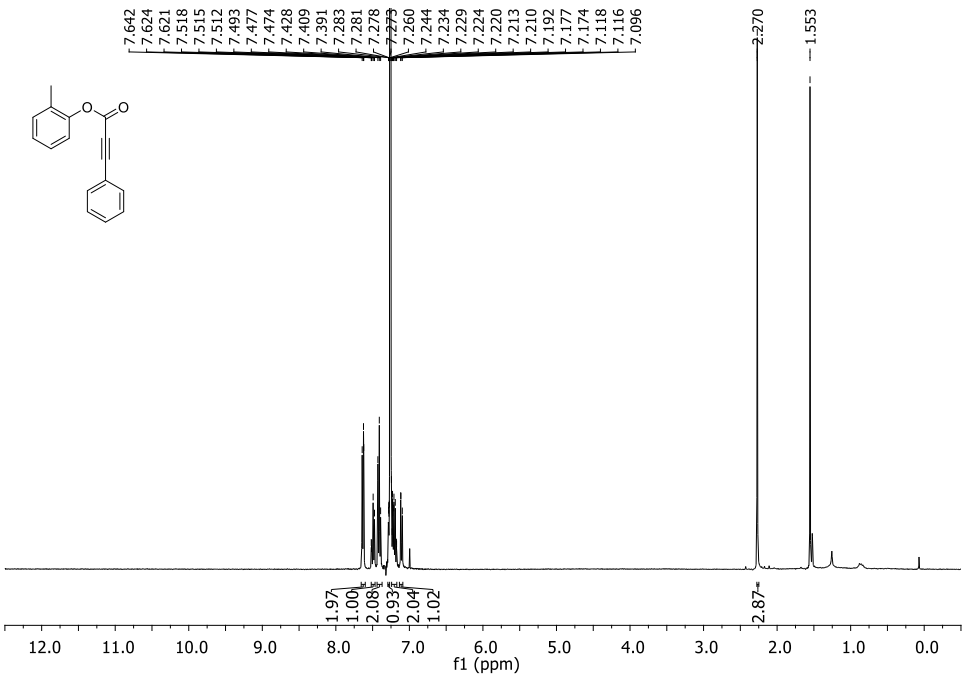

Figure 5.64. ^{1}H NMR spectrum of *o*-tolyl-3-phenylpropiolate (**2l**) in $CDCl_3$.

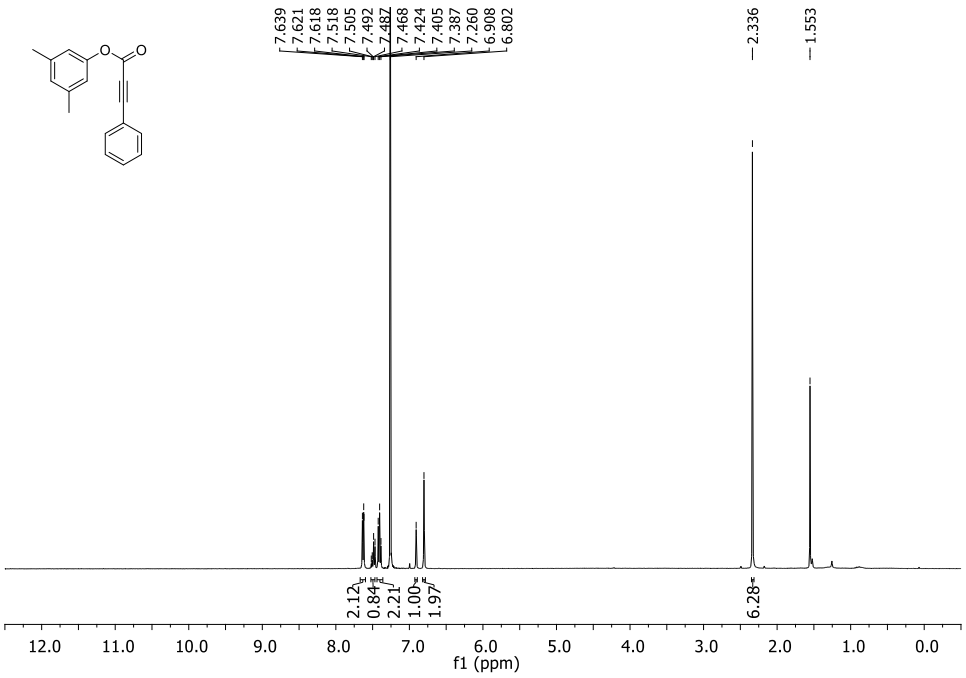

Figure 5.65. ^{1}H NMR spectrum of 3,5-dimethylphenyl-3-phenylpropiolate (**2m**) in $CDCl_3$.

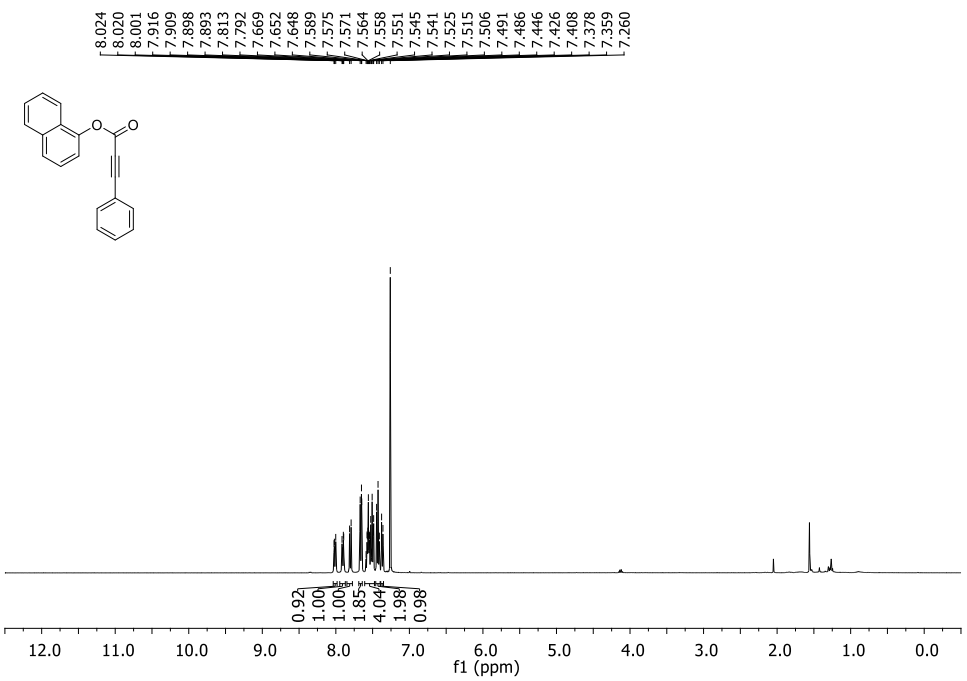

Figure 5.66. ^{1}H NMR spectrum of naphthalen-1-yl 3-phenylpropiolate (**2n**) in $CDCl_3$.

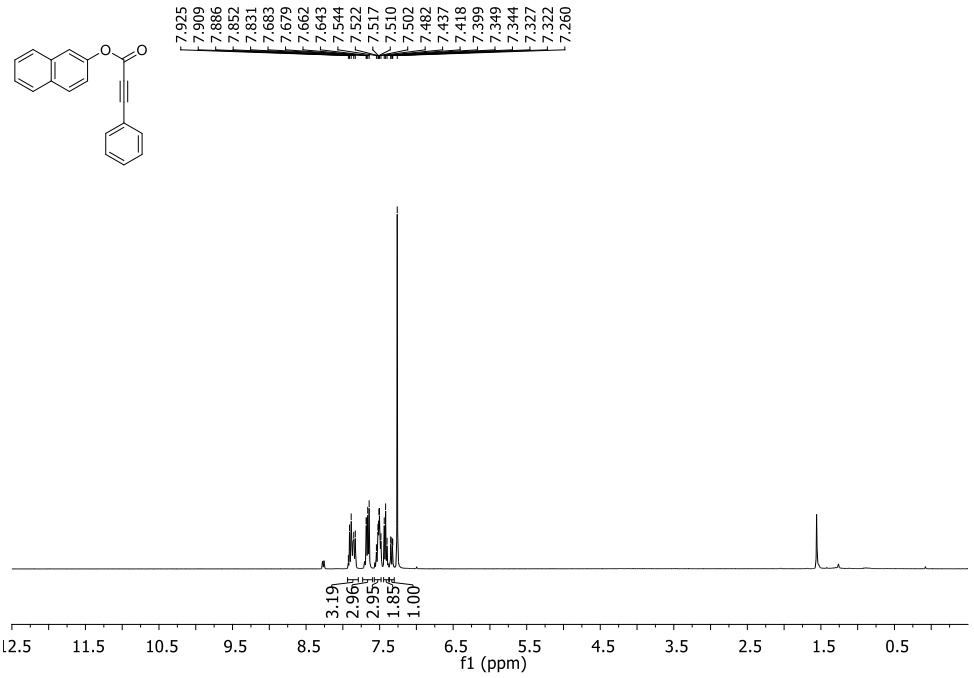

Figure 5.67. ^{1}H NMR spectrum of naphthalen-2-yl-3-phenylpropiolate (**2o**) in $CDCl_3$.

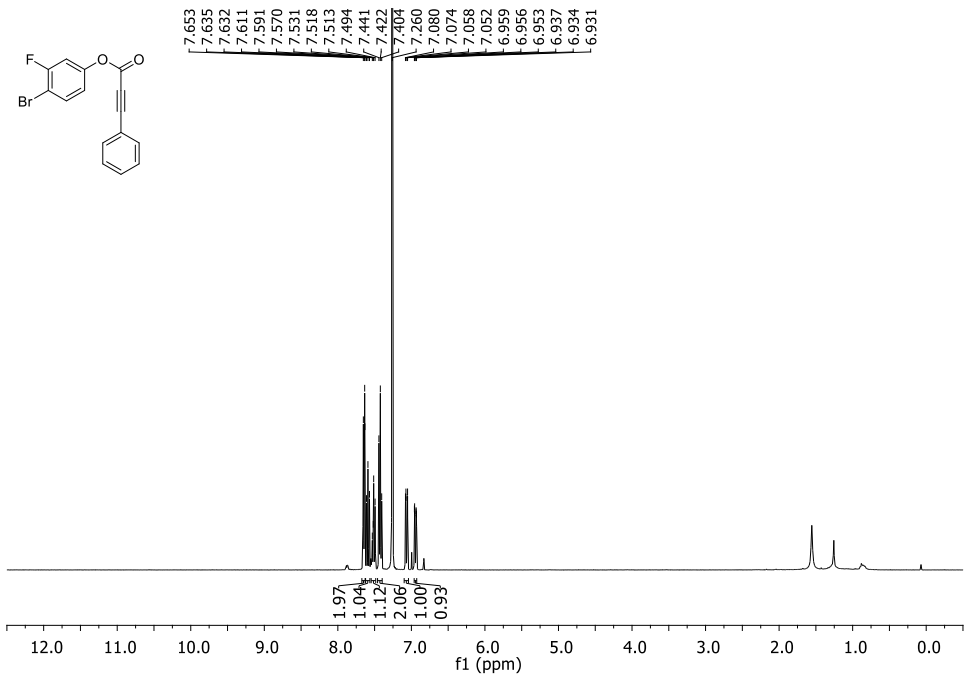

Figure 5.68. ^{1}H NMR spectrum of 4-bromo-3-fluorophenyl-3-phenylpropiolate (**2p**) in $CDCl_3$.

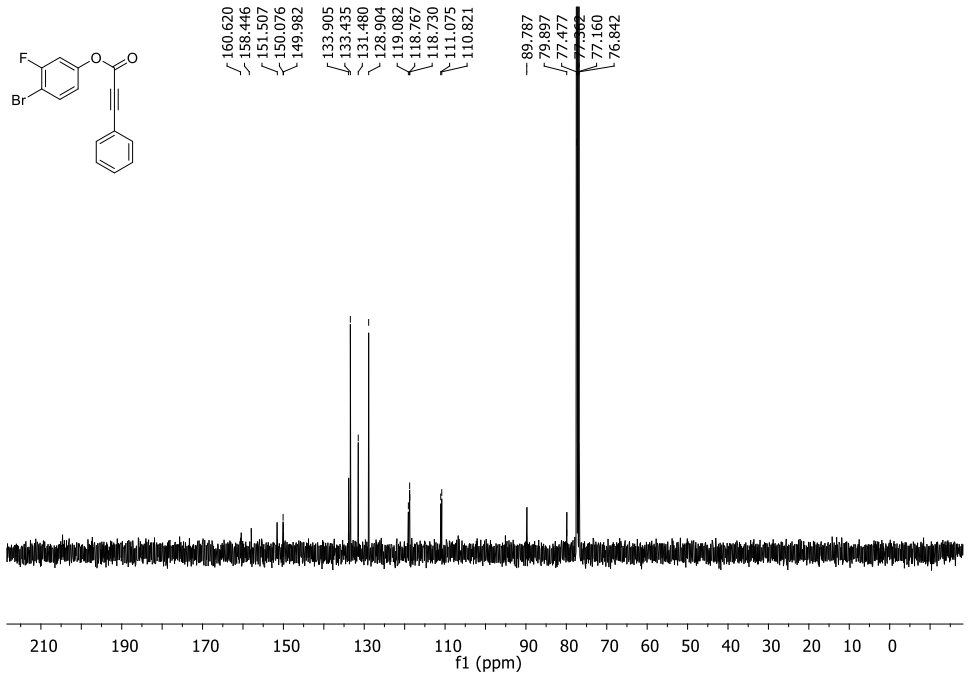

Figure 5.69 ^{13}C NMR spectrum of 4-bromo-3-fluorophenyl-3-phenylpropiolate (**2p**) in $CDCl_3$.

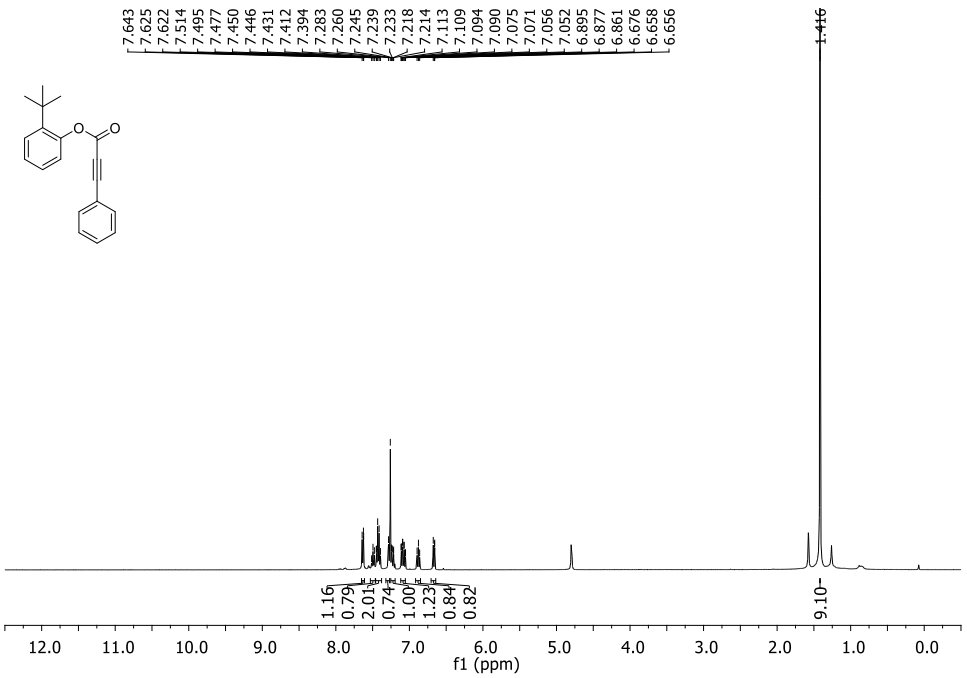

Figure 5.70. ^{1}H NMR spectrum of 2-(*tert*-butyl)phenyl 3-phenylpropiolate (**2q**) in $CDCl_3$.

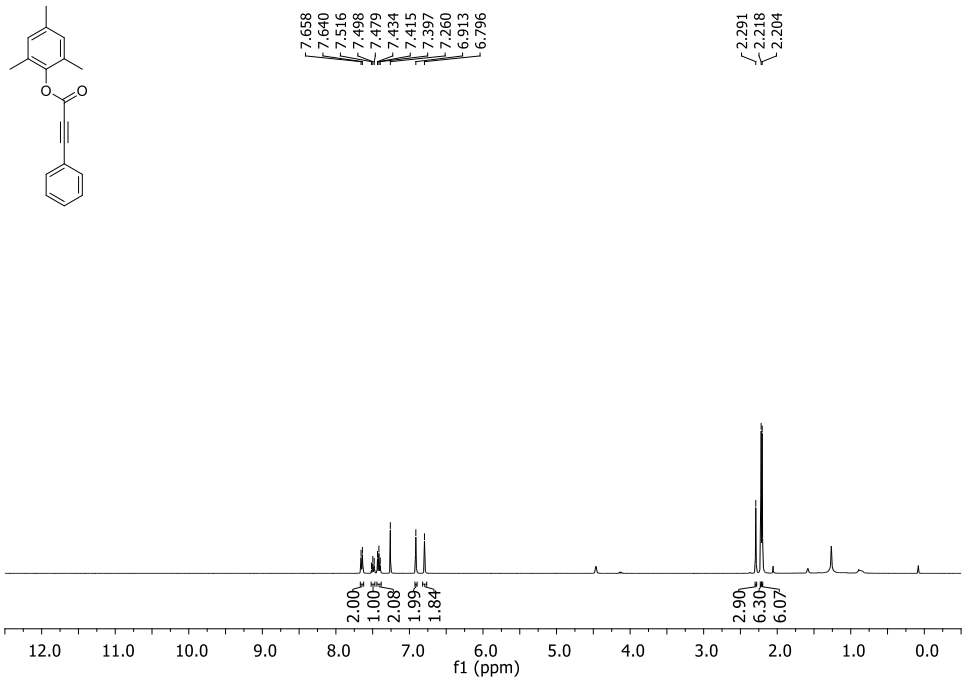

Figure 5.71. ^{1}H NMR spectrum of mesityl-3-phenylpropiolate (**2r**) in $CDCl_3$.

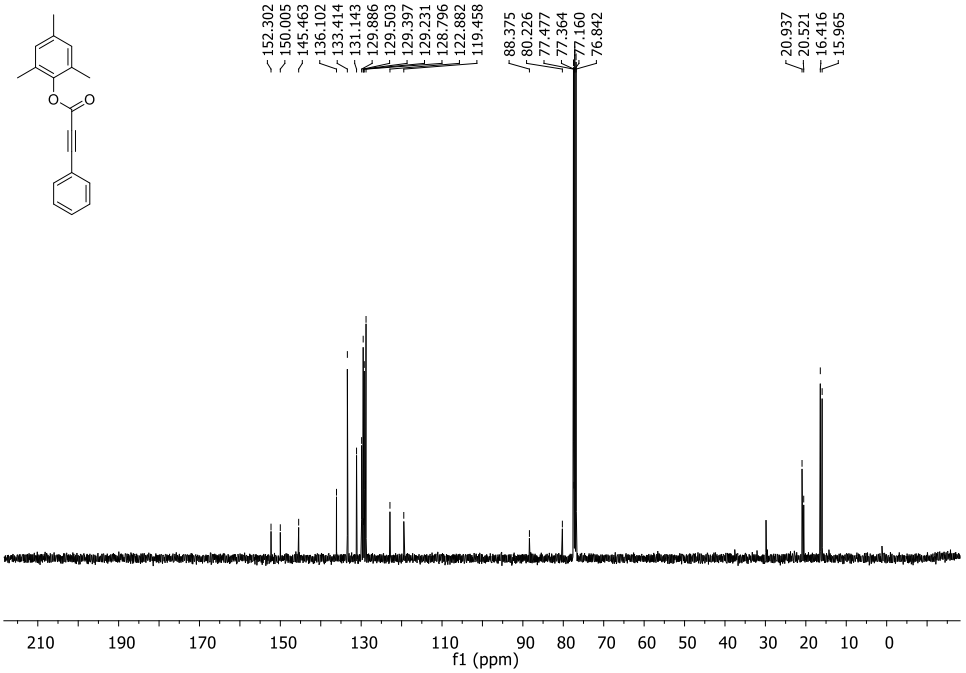

Figure 5.72. ^{13}C NMR spectrum of mesityl-3-phenylpropiolate (**2r**) in $CDCl_3$.

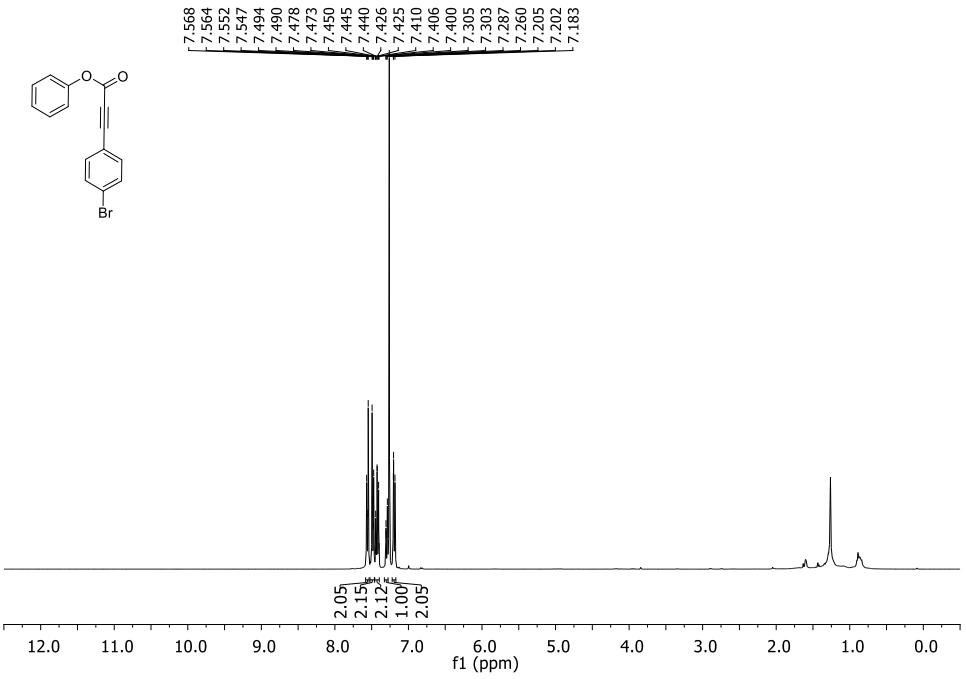

Figure 5.73. ^{1}H NMR spectrum of phenyl 3-(4-bromophenyl)propiolate (**2x**) in $CDCl_3$.

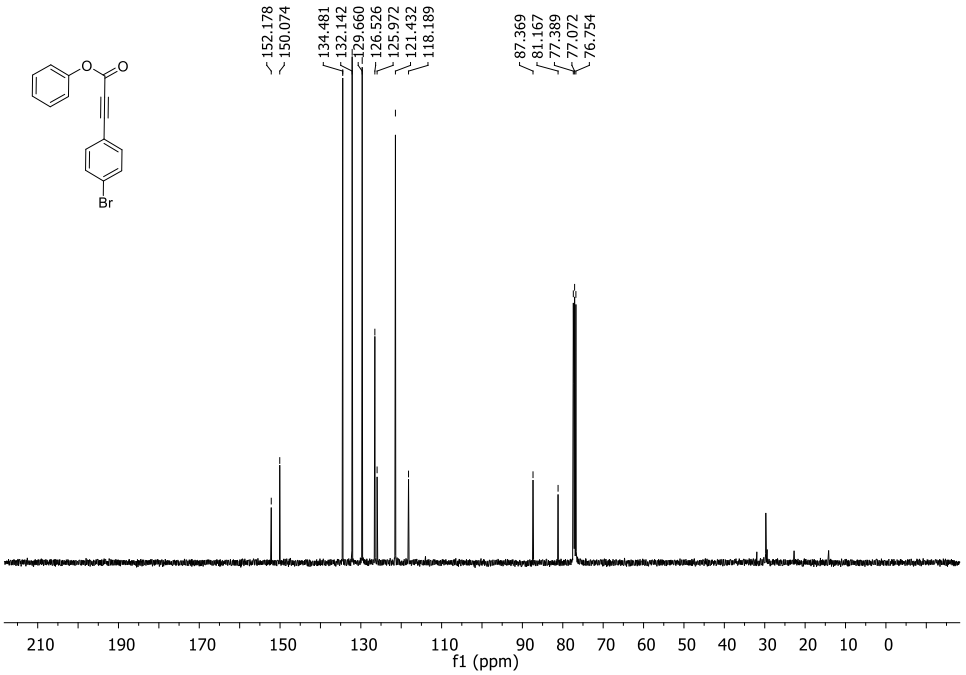

Figure 5.74. ^{13}C NMR spectrum of phenyl 3-(4-bromophenyl)propiolate (**2x**) in $CDCl_3$.

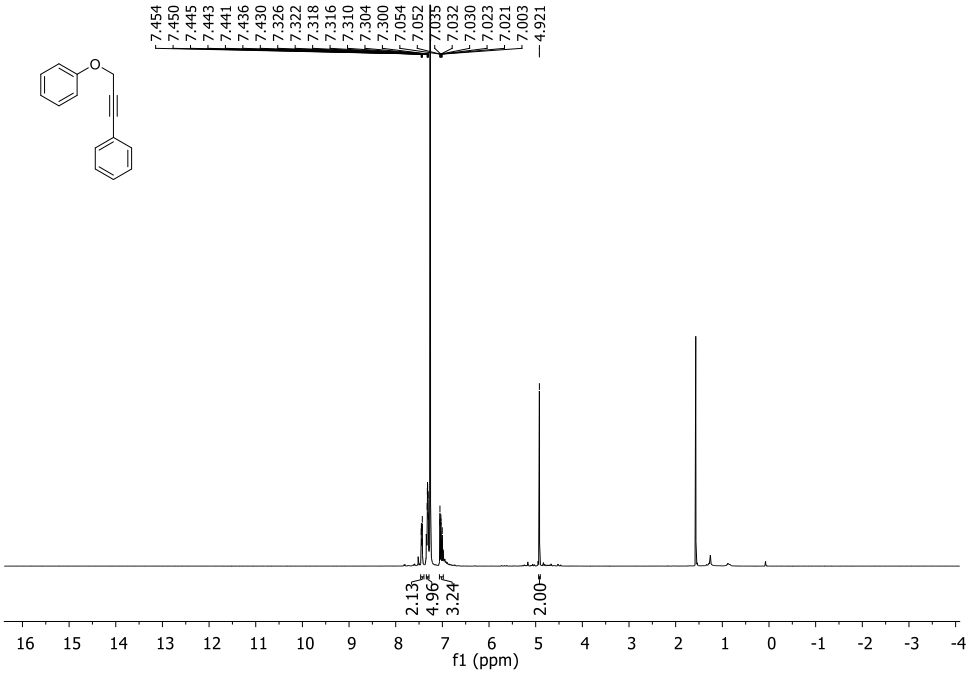

Figure 5.75. ^{1}H NMR spectrum of (3-phenoxyprop-1-yn-1yl)benzene (**2z**) in $CDCl_3$.

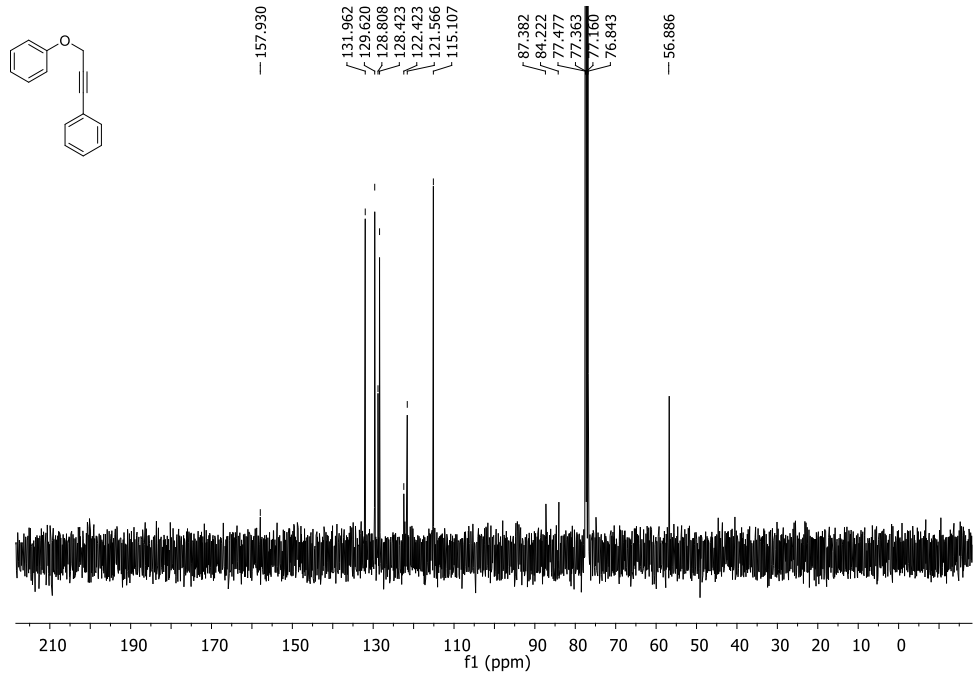

Figure 5.76. ^{13}C NMR spectrum of (3-phenoxyprop-1-yn-1yl)benzene (**2z**) in $CDCl_3$.

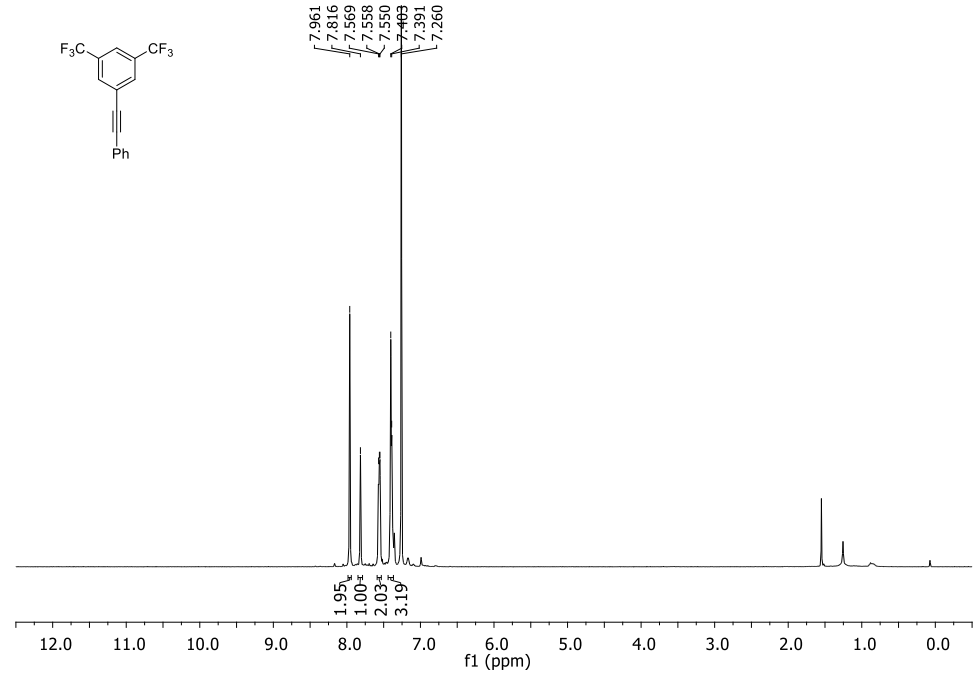

Figure 5.77. ^{1}H NMR spectrum of 1-(phenylethynyl)-3,5-bis(trifluoromethyl)benzene **(3z)** in $CDCl_3$.

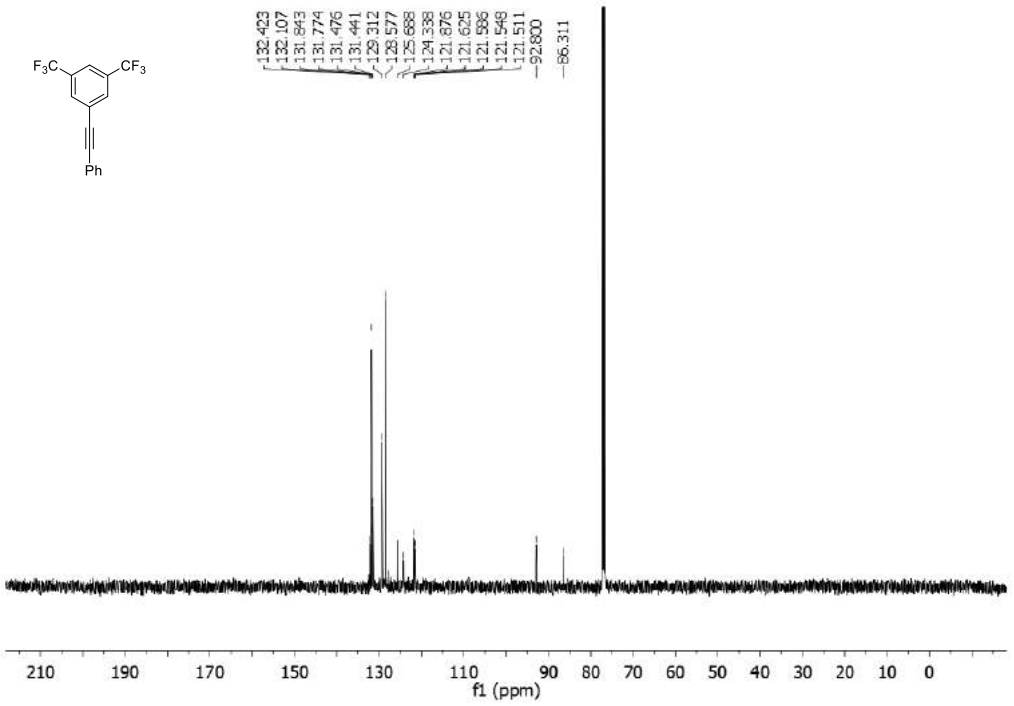

Figure 5.78. ^{13}C NMR spectrum of 1-(phenylethynyl)-3,5-bis(trifluoromethyl)benzene **(3z)** in $CDCl_3$.

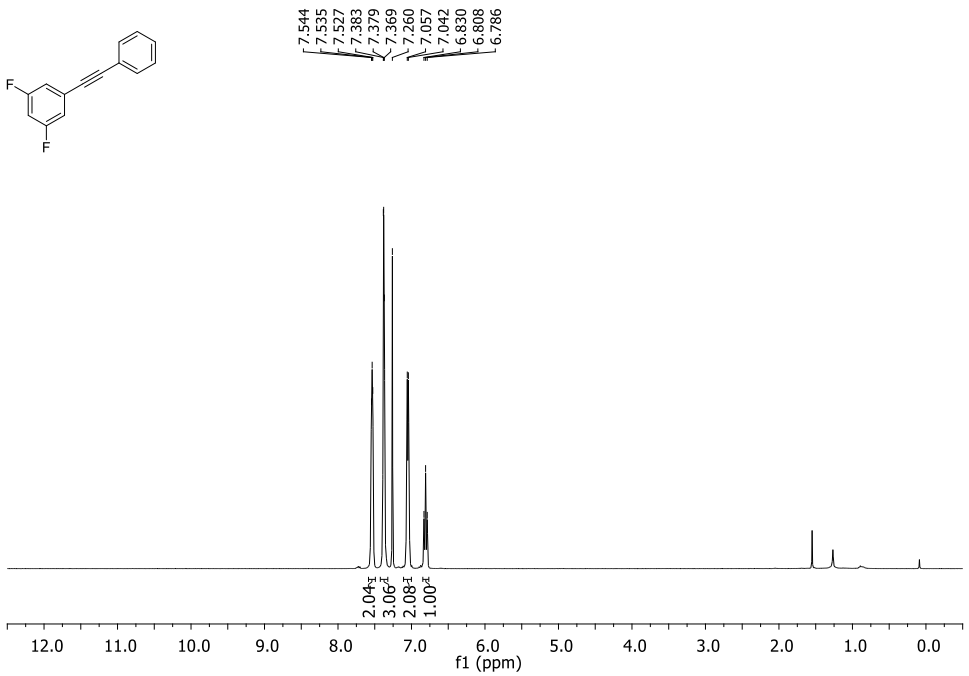

Figure 5.79. ^{1}H NMR spectrum of 1,3-difluoro-5-(phenylethynyl)benzene**(4z)** in $CDCl_3$.

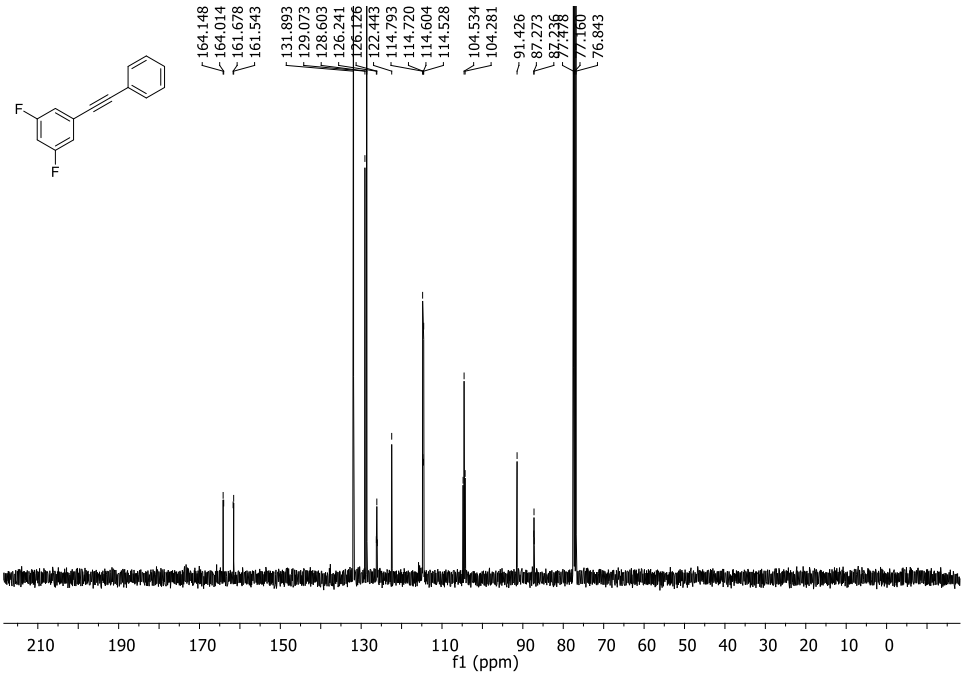

Figure 5.80. ^{13}C NMR spectrum of 1,3-difluoro-5-(phenylethynyl)benzene **(4z)** in $CDCl_3$.

Synthesis of Nitrogen Based *N*-Heterocycles *via* Metal Free Approach

By

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of

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Homi Bhabha National Institute[1]

Recommendations of the Viva Voce Committee

As members of the Viva Voce Committee, we certify that we have read the dissertation prepared by <ANKITA BAL> entitled < "SYNTHESIS OF NITROGEN BASED N-HETEROCYCLES VIA METAL FREE APPROACH" > and recommend that it may be accepted as fulfilling the thesis requirement for the award of Degree of Doctor of Philosophy.

Chairman - Name & Signature with date PROF. A. SRINIVASAN	Prof 09.07.2021
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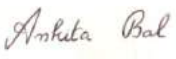

Ankita Bal

DECLARATION

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.

Ankita Bal.

Ankita Bal

List of Publications arising from the thesis

Journals published

- 1. **Bal, A**.; Maiti, S.; Mal, P. Iodine(III)-Enabled Distal C–H Functionalization of Biarylsulfonanilides

  J. Org. Chem. **2018**, *83*, 11278-11287.

- 2. **Bal, A**.; Maiti, S.; Mal, P. Steric and Electronic Effect on C2-H Arylation of Sulfonamides

  ChemistrySelect.**2019**, *4*, 7010-7014.

- 3. **Bal, A**.; Maiti, S.; Mal, P. Intermolecular C-Arylation of 2-Amidobiphenyls Overcoming Intramolecular N-Arylation

  Asian J. Org. Chem. **2020**, *9*, 1783-1786.

- 4. **Bal, A**.; Maiti, S.; Mal, P. Strategies to Control Hypervalent Iodine – Primary Amine Reactions

  Chemistry An Asian Journal. **2019**, *15*, 624-635.

- 5. Maiti, S.; Alam, M. T.; **Bal, A**.; Mal, P. Nitrenium Ions from Amine-Iodine(III) Combinations

  Adv. Synth. Catal. **2019**, *361*, 4401-4422.

Communicated

- 1. **Bal, A**.; Mal, P. Phosphorus-Oxygen Interaction Controlled Phosphorus-Nitrogen Bond Activation in a Click Reaction.

Under Preparation

- **Bal, A**.; Dinda, T.; Mal, P. NIS mediated synthesis of oxazoline via Mechanochemistry.

CONFERENCE AND PRESENTATIONS

1. **Oral Presentation:** 27th International Society of Heterocyclic Chemistry Congress (ISHC) at Kyoto, Japan on (1-6)th September 2019.

2. **Poster Presentation:** The Present and Future of Excellence in Organic Synthesis, Tejpur University, on (7-8)th January 2021.

3. **Poster Presentation:** International Conference on Chemistry for Human Development (ICCHD-2020) on (9-11th) January, 2020.

4. **Poster Presentation:** Frontier in Chemical Science (FICS-2018) at IIT Guwahati on (6-8)th December 2018

5. **Poster Presentation:** National Bioorganic Chemistry Conference (NBCC-2018) at NISER Bhubaneswar, on (22-24)th December 2018.

6. **Workshop:** RSC publishing workshop at NISER Bhubaneswar, 23rd September 2016

7. **Workshop:** ACS on campus at NISER Bhubaneswar on 23rd July 2018.

Ankita Bal

Dedicated to

My Parents

&

My Brother

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…… Ankita Bal

Contents

SUMMARY

Nitrogen based heterocyclic scaffolds have a pivotal role in medicinal chemistry due to their significant contribution to developing novel composites. Nature possesses an immense distribution of nitrogen-based molecules, including vitamins, nucleic acids, base pair of DNA, and RNA molecule. Nitrogen-based molecules have gained prominence at an alarming rate because of its application in agrochemicals, pharmaceuticals and antibiotics.

The electron rich nitrogen containing heterocycles were synthesized by the formation of intermediates like nitrenium ion and azidyl radical. Nitrogen intermediates like nitrenium ion, nitrene or azidyl radical are useful in bringing about beneficial synthetic transformation to produce small organic molecules. Nitrenium ion could be successfully generated by treating sulfonamide with hypervalent iodine(III) reagent PIDA. The sulfonamide group helps to stabilize the nitrenium ion and this nitrenium ion tautomerizes to form carbenium ion. Nucleophilic attack at the carbenium or the nitrenium ion leads to the formation of the desired product. C-H arylation of sulphonamides at the ortho position was achieved by the formation of carbenium from nitrenium ion. Synthesis of carbazoles was achieved by distal C-H functionalization followed by methyl migration using iodine(III) reagents. The same iodine(III) was generated under *in-situ* conditions using PhI-mCPBA. Terphenyls were synthesized with iodine(III) reagents solely where more facile intramolecular C-N coupling was overcome and intermolecular C-C coupling reaction was established at mild reaction conditions using hypervalent iodine(III) reagents. Using Phosphorus- oxygen interaction, triazoles were synthesized via azidyl radical. The high phosphorus nitrogen bond energy of approximately 617kJ/mole is cleaved due to weak phosphorus-oxygen interaction. The weak interaction controls the selectivity of the product and triazoles have been synthesized in excellent yield without the use of metal or any external oxidant. Achieving a click reaction for an internal alkyne without metal involvement is a challenging task that we could

successfully overcome using non-covalent interaction. Phosphorus oxygen interaction is a special kind of pnicogen type of interaction classified as group 15. Phosphorus nitrogen bond activation controlled by phosphorus oxygen interaction yield triazoles in good to excellent yields.

List of Schemes

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List of Abbreviations Used

Å	Angstrom
Ac	Acetyl
AcOH	Acetic Acid
AcOOH	Peracetic acid
Anhyd	Anhydrous
aq	Aqueous
Bn	benzyl
Bp	Boiling Point
BPO	Benzoyl Peroxide
br	Broad
Bz	Benzoyl
^{o}C	Degree Celcius
Calcd	Calculated
cm	Centimeter
Conc	Concentrated
Cy	Cyclohexyl
d	Doublet, Days
DCE	1,2-Dichloroethane
DCM	Dichloromethane
dd	Doublet of a Doublet
dil	Dilute
DTBP	Di-tert-butyl peroxide
DMF	*N*,*N*-Dimethyl Formamide
DMP	Dess-Martin Periodinane
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
Hz	Hertz
IBX	2-Iodoxybenzoic acid
IBA	Iodosobenzoic acid
IDB	Iodosylbenzene
IR	Infrared
lit	Liter
m	Multiplet
*m*CPBA	*meta*-chloroperbenzoic acid
*m*CPBA	*meta*-chlorobenzoic acid
NIS	N-iodosuccinimide
M	Molar
MeCN	Acetonitrile
mp	Melting point
Me	Methyl
Min	Minutes
mL	Milliliter
mmol	Millimole
mol	Mole
MS	Mass Spectra, Molecular Sieves
Ms	Methane sulfonyl
M/Z	Mass to charge ratio
nm	Nanometer
NMP	N-Methyl-2-pyrrolidine
NMR	Nuclear Magnetic Resonance
Piv	Pivaloyl
PIDA	Phenyliodine(III) diacetate
PIFA	Phenyliodine bis(trifluoroacetate)
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

CHAPTER 1

Introduction: Synthesis of Nitrogen Based Molecules via Sustainable Approach

1.1 ABSTRACT

This Chapter mainly focuses on the synthesis of *N*-heterocyclic compounds *via* metal free approach. Metal free approaches in particular hypervalent iodine(III) reagents have been extensively used for building *N*-heterocyclic scaffolds *via* important synthetic intermediates like nitrenium , carbenium or nitrene have been discussed elaborately. Various intermediates like nitrenium ion, nitrene radical or azidyl radical which are potentially useful for construction of *N*-heterocyclic scaffolds have been discussed. The nitrogen containing structural motifs have also been extensively used for C-H functionalization reactions, some of which are discussed in this chapter.

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1.2 INTRODUCTION

Synthesis of *N*-Heterocycles has witnessed valiant years in organic chemistry owing to its numerous applications in the development of drug molecules, pharmaceutical and agrochemical industries.[1-3] Natural products which have attracted significant attention due to their bioactive properties involving antimalarial, antifungal, antihypertensive, anti-inflammatory, and trichomonal possess *N*-heterocycle in its backbone.[4] They have sound to be significant intermediates for preparing biologically active compounds. The compounds are also known to act as ligands in coordination chemistry and have a widespread application in homogenous catalysis. They have profound applications in supramolecular chemistry[5], luminescent sensors, and photosensitizers for solar cells and constitute a vital element of the

universe.[6-8] Henceforth, the synthesis of nitrogen based *N*-heterocycles is a demanding subject area in organic chemistry.

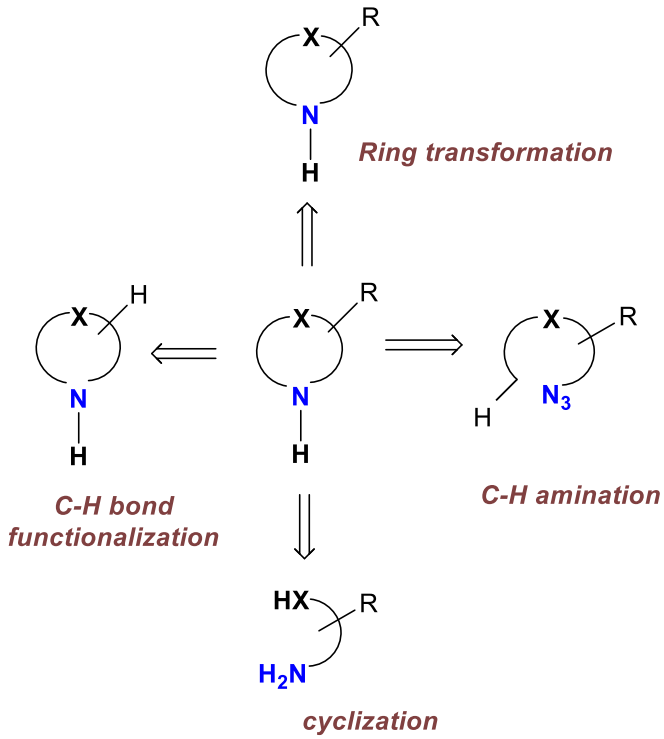


Figure 1.1 Strategies for construction of *N*-heterocyclic scaffolds and its application in organic synthesis.

N-heterocyclic scaffolds are significant due to its extensive application in medicinal chemistry. The need to develop sustainable and greener methods for construction of *N*-heterocyclic moieties has been a growing concern among the synthetic chemists. Metal free synthetic routes which are safer, milder and environment friendly haven always been a better alternative compared to metal mediated synthetic transformations. Among them hypervalent iodine(III) reagents are effectively used to achieve the transformation.[9, 10] Cross Dehydrogenative Coupling[11], C-H amination[12], C-H bond functionalization[13] and transformation of the ring to other forms are some of the approaches involved to construct *N*-heterocyclic scaffolds as displayed in figure 1.1.

1.2 NITRENIUM ION CHEMISTRY

Nitrenium ion can be defined as a di-coordinate species containing a positively charged nitrogen center. These reactive electrophilic intermediates are isoelectronic with carbocations, carbenes and nitrenes possessing six electrons in its valence shell.[14] Nitrenium ions have two non-bonding electron pairs and based on its electronic spin orientation, nitrenium ions exist either in singlet state or triplet state (Figure 1.2).[15] The stability of the nitrenium ion is dependent on its spin state. Generally, it is observed that nitrenium ion in its triplet state is likely more stable. It faces less coulombic repulsion due to favorable exchange interaction between parallel spins, whereas the singlet state of nitrenium ion consists of paired electrons faces more Coulombic repulsion. From a geometric point, the singlet state is expected to have bond angle of (110-130^{o}) whereas triplet state is said to exhibit a large bond angle of (150-160 ^{o}).

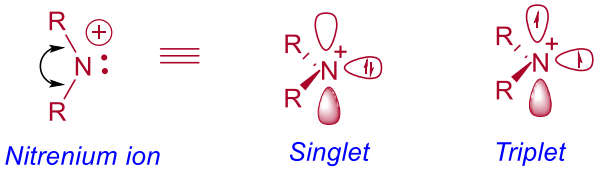


Figure 1.2 Nitrenium ion, its structure and spin state.

The parent nitrenium ion (NH_2^+) was established to stay in a ground triplet state ($^3B_1$) which is separated from the singlet ground state ($^1A_1$) by approximately 30 kcal/mole. Introducing an *N*-alkyl substituent reduced the singlet to triplet (S-T) energy gap, especially when a methyl group is present. It has been found that π donor ligands such as cyanide, halogen, or a

hydroxyl group assist in stabilizing the singlet by donating an electron to vacant $2p_z$ situated on the central atom. With a strongly electron-withdrawing group, nitrenium ion substituted by π donor heteroatom are in lower energy ground singlet state with a high N=X π character. For *N*- hydroxyl *N*-formyl nitrenium ion, the N-O bond has a significant rotational energy barrier to rotation which is approximately (29.7 kcal/mole), as calculated by Glover. This proves the oxygen lone pair has a stabilizing effect as a result of which rotational barrier which exists is extremely low or nil for the nitrogen carbon bond. This fact indicates the role of an acyl substituent plays a minimal for the stability of the alkoxy substituted nitrenium ion. Aryl nitrenium ions exist in a singlet ground state with a short C-N bond and planar geometry, whereas the triplet state exits with a long C-N bond with non-planar geometry, as portrayed in figure 1.3a. Aryl nitrenium ions are stabilized more than parent nitrenium ions. The extra stabilization is due to the vacant p orbital of the nitrogen center with π-lobes of the aromatic ring. The degree of stabilization is also acquired by delocalization of positive charge in the π-orbital of phenyl ring indicated in figure 1.3b. The singlet to triplet splitting in the species varies with the nature of the substituent present on the phenyl ring. Electron donating groups stabilize the singlet state more than the triplet state in general but electron releasing *meta* substituents stabilize the triplet state to such an extent that it becomes its ground state. In such cases, the triplet state possesses an electronic configuration of π, π^* as the electron in the nonbonding lobe of π orbital is shifted to π^* orbital as shown in figure 1.3c.[16]

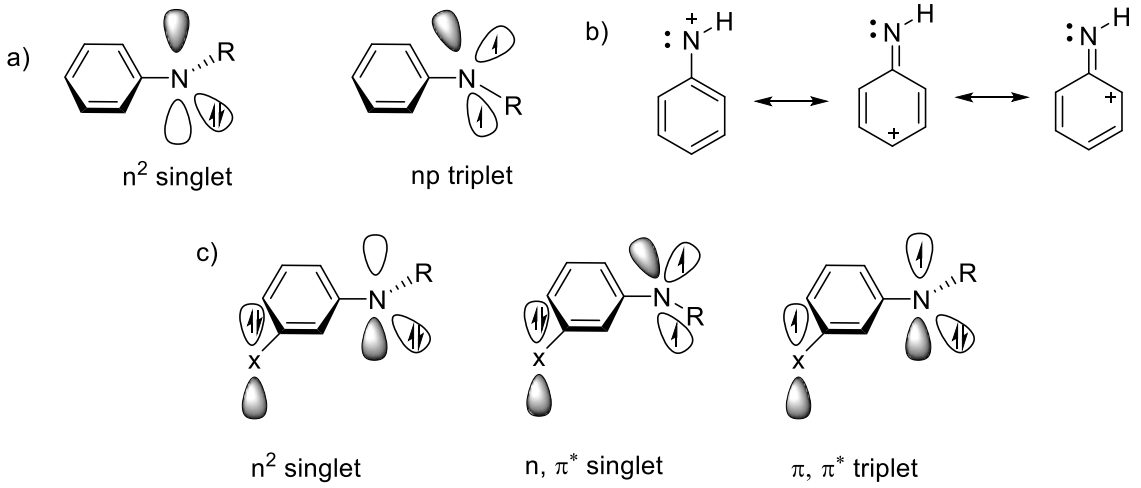


Figure 1.3 a) Spin state of aryl nitrenium ion b) Resonance stabilized π electron cloud of aryl nitrenium ion c) spin state of *meta* substituted π electron donor of aryl nitrenium ion.

1.3 HYPERVALENT IODINE(III) REAGENTS

Hypervalent iodine reagents have risen to prominence in the last few decades. The ease of its availability, high stability, controlled oxidizing ability have made them highly versatile for the construction of critical heterocyclic scaffolds. Commonly used hypervalent iodine reagents for the generation of nitrenium are $PhI(OAc)_2$, $PhI(OCOCF_3)_2$, $PhI(OPiv)_2$, Dess-martin periodinane (DMP), 2-iodoxy benzoic acid (IBX) have been greatly utilized to develop a plethora of organic molecules as displayed in figure 1.4. [10]

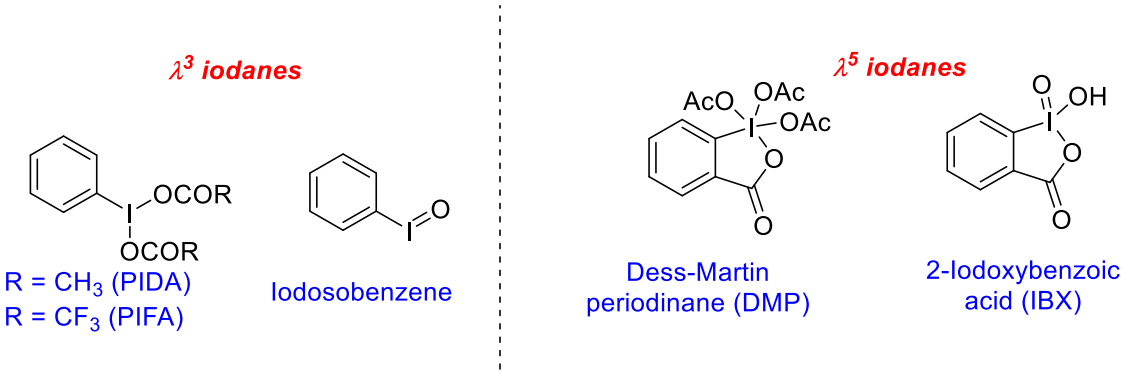
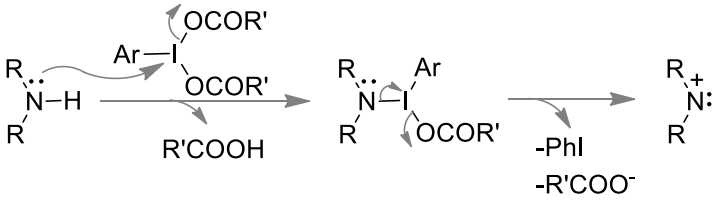


Figure 1.4 Examples of hypervalent iodine reagents.

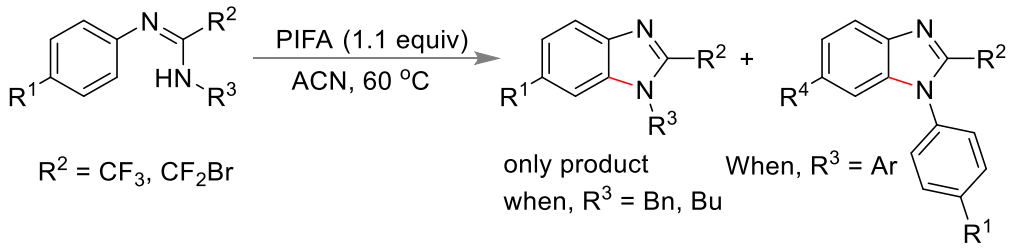
1.4 REACTIVITY

Nitrenium ion can be generated from iodine(III) reagents by employing a secondary amine. The nitrogen lone pair attacks the electrophilic iodine center to form amido-λ^3-iodane (Scheme 1.4). N-I bond heterolysis leads to the formation of nitrenium ions with reductive elimination of iodoarene. Nitrenium ions are electrophilic in nature and are easily prone to nucleophilic attack. Nucleophile present in the reaction system attacks the electrophilic nitrenium ion to produce the desired product.[17]



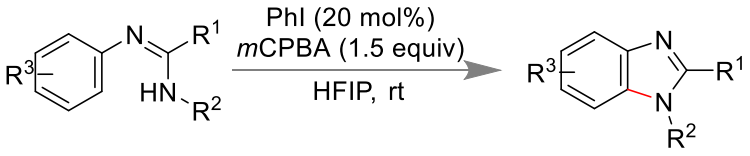
Scheme 1.1 Nitrenium ion formation from iodine(III) reagents.

This concept has been utilized in synthetic methodologies to develop significant structural motifs, especially *N*-heterocyclic scaffolds, some of which is discussed here. Wu and co-workers have synthesized 1,2-disubstituted benzimidazoles by intramolecular cyclization using bistrifluoroacetoxyiodobenzene (Scheme 1.2).[18] N-*aryl* substituted imidamides produce two different products based on the stability of nitrenium ion generated from it. However, only one product formation is formed with aliphatic substituted imidamides are used as precursors. Mechanistic studies revealed that nitrenium ion generated from iodine(III) reagents undergo resonance delocalization and based on the stabilizing ability by adjacent aryl groups, nitrenium ions exhibit in two different resonating states. This resulted in formation of two different products.



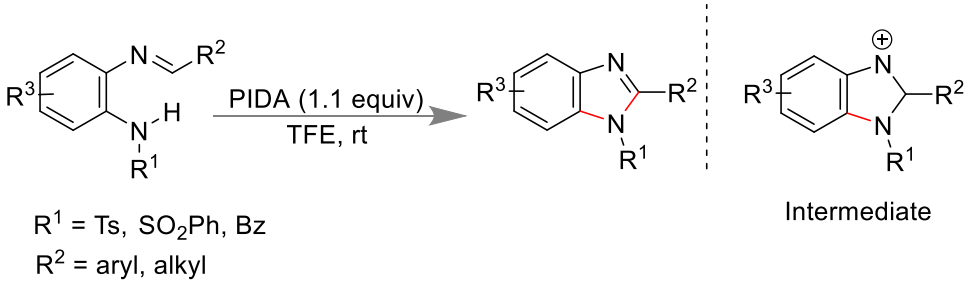
Scheme 1.2 Benzimidazole synthesis mediated by PIFA.

Intramolecular C-H amination was demonstrated by Punniyamurthy group for the preparation of 1,2-disubstitutedbenzimidazoles (Scheme 1.3).[19] Iodobenzene (PhI) combined with oxidant *m*CPBA produced iodine(III) condition under *in-situ* conditions. Sulfonyl protected amines like Ts-, Ms- were effective and produced the desired product whereas amidines were unsuccessful with alkyl substitution or without substitution deliver the desired outcome.



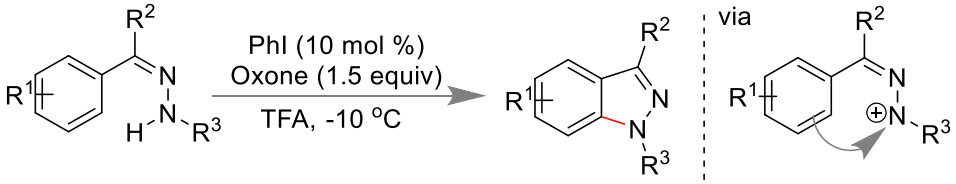
Scheme 1.3 Benzimidazole synthesis mediated by PhI AND *m*CBPA.

Mal and coworkers were successful in establishing an intramolecular C-H amidation using PIDA to synthesize benzimidazole, as shown in scheme 1.4.[20] The methodology was effective to produce the targeted products in excellent yields. The reaction proceeded by the formation of nitrenium ion intermediate. ICP-OES experiments were conducted to check the trace of metal impurity in hypervalent iodine reagents.



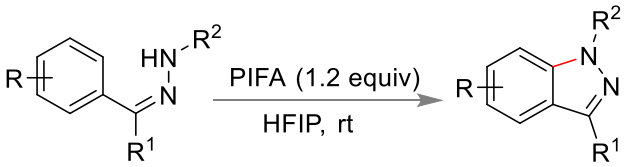
Scheme 1.4. Benzimidazole synthesis *via* intramolecular C-H amidation.

Tanimori and coworkers have established an iodobenzene catalyzed reaction of aryl hydrazones using oxone as oxidant at -10 ^{0}C to synthesize indazole. Here iodine(III) was generated *in situ,* which furnished the nitrenium ion following intramolecular nucleophilic attack producing indazoles.



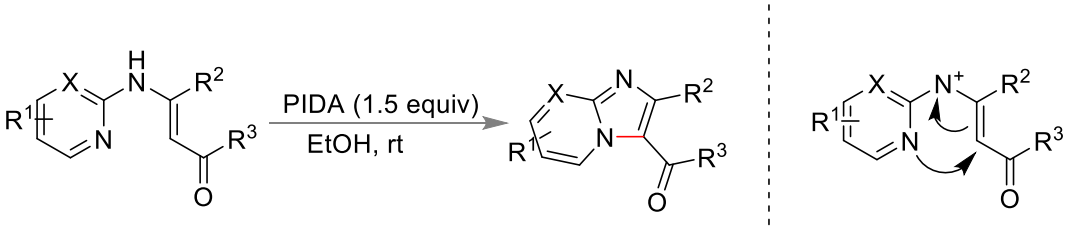
Scheme 1.5 Iodobenzene catalyzed indazole synthesis

Another work where synthesis of 1*H*-indazoles was achieved using hypervalent iodine(III) reagent PIFA at room temperature by intramolecular C-H amination technique. (Scheme 1.6).[21] The mechanistic pathway is quite similar where the reaction proceeded through the generation of nitrenium ion intermediate and further nucleophilic attack taking place from aryl group.



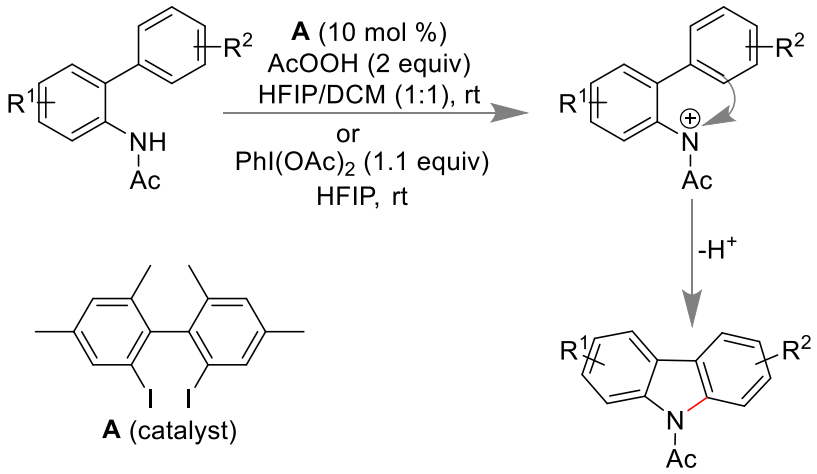
Scheme 1.6 PIFA mediated indazole synthesis.

Imidazopyrimidines are another class of *N*-heterocyclic compounds that have potential applications in medicine. Synthesis of Imidazo[1,2-a]pyrimidines was successfully achieved in acetonitrile and PIDA in ethanol (Scheme 1.7).[22] Nitrenium ion was generated where nucleophilic attack from nitrogen of pyrimidyl/pyridine ring took place on benzene ring following deprotonation to gain aromaticity.



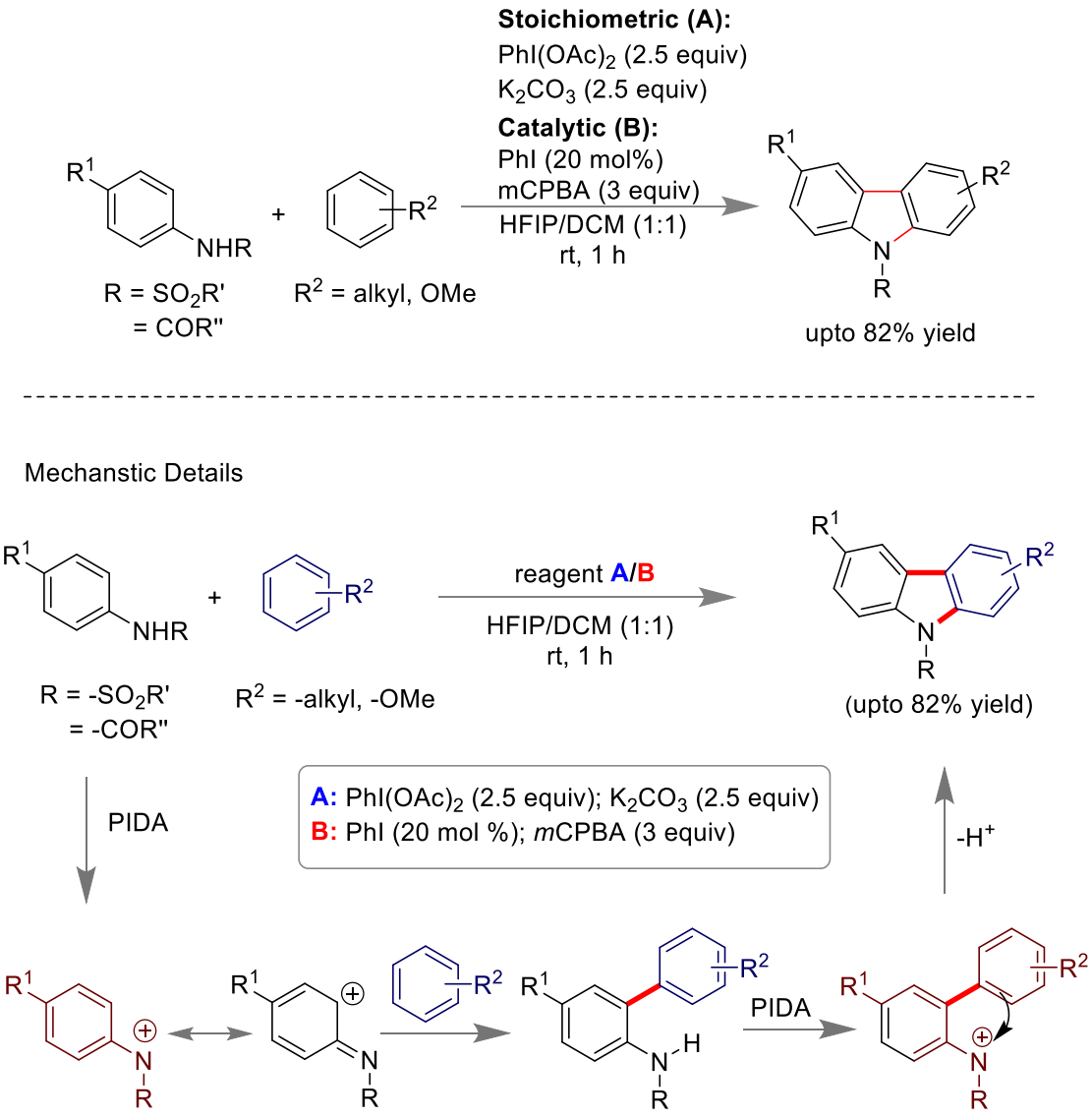
Scheme 1.7 Synthesis of Imidazo[1,2-a]pyrimidines mediated by PIFA.

Carbazole in an important heterocyclic scaffold found in numerous drug molecules. As a result, the synthesis of carbazoles in the mild and metal free condition is highly desirable. 2-acetaminobiaryls were used as precursors to achieve the targeted carbazole using hypervalent iodine(III) reagent PIDA and generating iodine(III) under *in-situ* conditions. (Scheme 1.8).[23] Later, this methodology was extended on 2,6-diarylacetanilides to get 1-arylcarbazoles by electrocyclization using PIDA.[24]



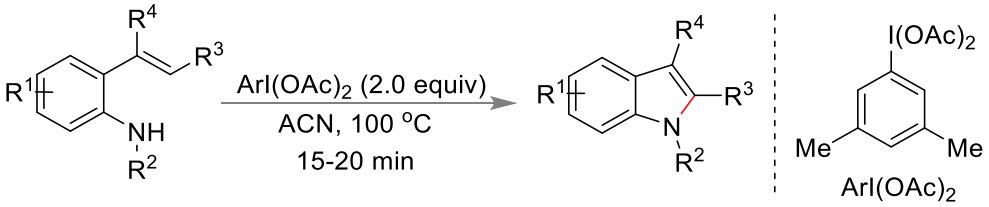
Scheme 1.8 Carbazole synthesis by C-H bond functionalization

Mal and co-workers have used iodine(III) reagent to synthesize carbazoles between nonfunctionalized arenes and anilides. (Scheme 1.9).[25] Iodine (III) was generated under two conditions (i) by use of PhI(OAc)2 in a stoichiometric amount in combination with K2CO3 and (ii) use of the catalytic amount of iodobenzene in the presence of (mCPBA) as an oxidant. Better yields were obtained with a stoichiometric amount of the reagent PIDA. The mechanism proceeded by forming the nitrenium ion followed by carbenium ion to form a C-C bond which further underwent nucleophilic attack from the arene part to form carbazaole as a product.



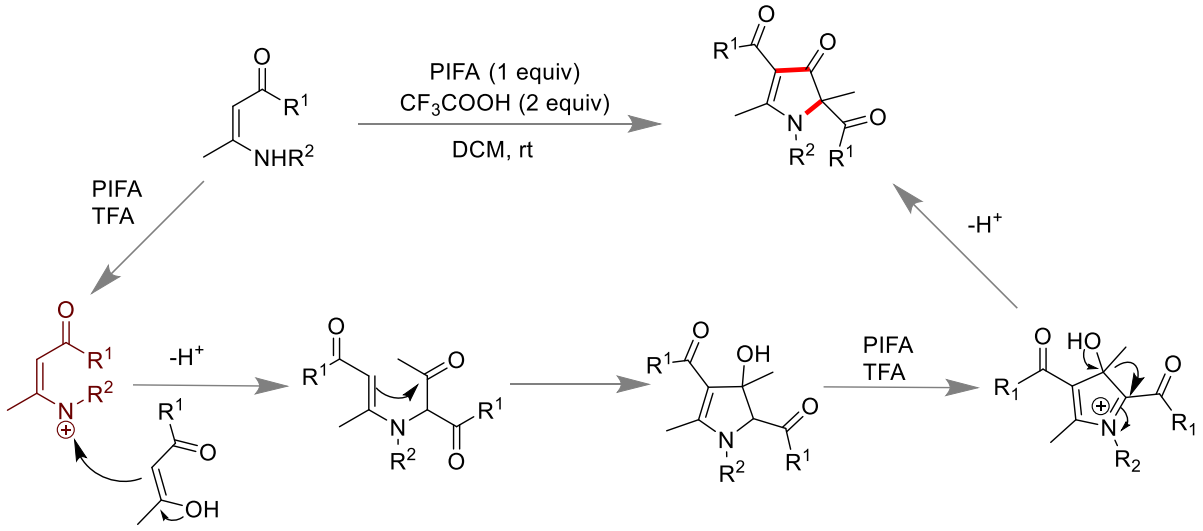
Scheme 1.9 Synthesis of carbazole by cross dehydrogenative coupling.

Indole based scaffolds were synthesized by Su and Mo group, as shown in (Scheme 1.10).[26] 3,5-Dimethylphenyliodine diacetate was the iodine(III) reagent used in acetonitrile solvent to synthesize indoles. The reaction proceeded through nitrenium ion formation along with the incorporation of acetoxy group to produce the desired product.



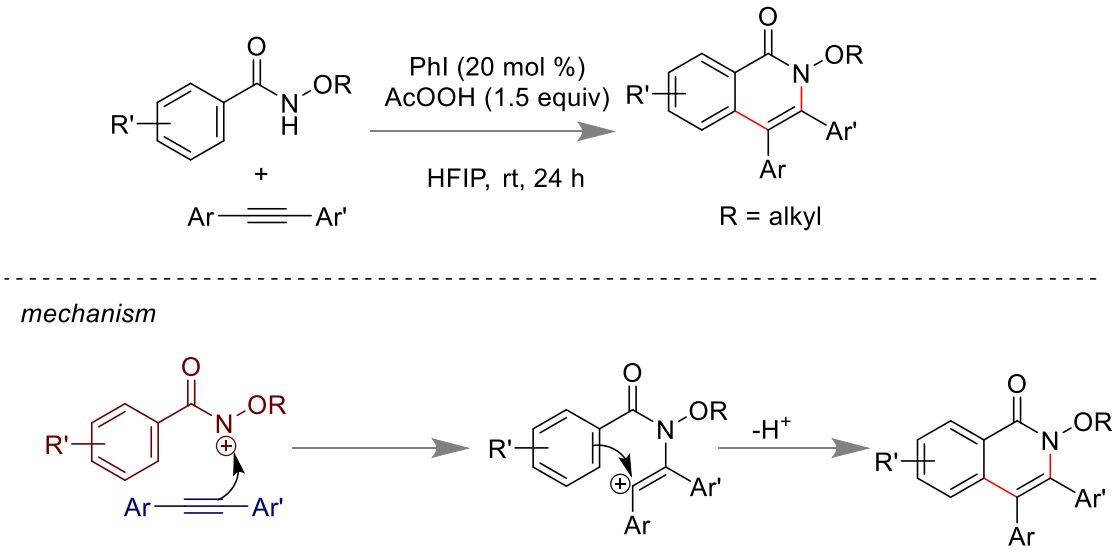
Scheme 1.10 Synthesis of indole synthesis mediated by hypervalent iodine(III) reagent.

Dong and co-workers have synthesized pyrrolinones by using PIFA as an oxidant in a sequential manner by forming Carbon-Carbon and Carbon -Nitrogen bond (Scheme 1.11).[27] Authors have speculated that the reaction mechanism proceeded by forming nitrenium ion intermediate following a benzilic acid type rearrangement.



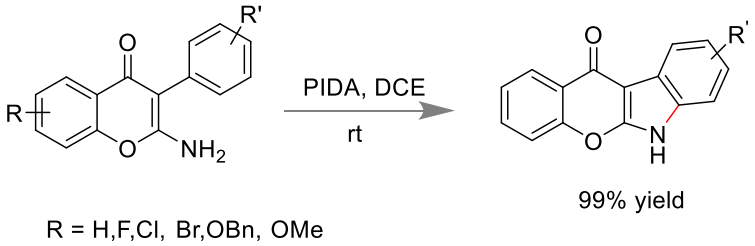
Scheme 1.11 Pyrrolinones synthesis mediated by PIFA.

Antonchick has established a hypervalent iodine(III) condition under in-situ conditions by annulation reaction to synthesize the isoquinoline system at room temperature conditions. (Scheme 1.12).[28] Iodobenzene was used as a catalyst in the presence of an oxidant like peracetic acid (AcOOH).



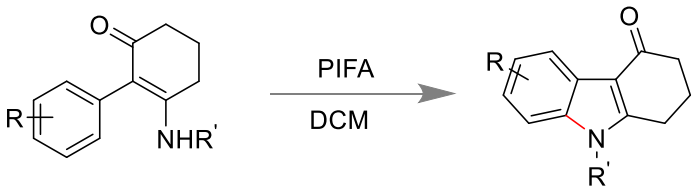
Scheme 1.12 Isoquinolinone synthesis catalyzed by iodobenzene.

The oxidant hypervalent iodine(III) reagent had been used to construct chromeno[2,3-b]indol-11(6H)-ones using pendant free amine *via* intramolecular oxidative C-N coupling. [29] The reaction proceeded via nitrene formation as the intermediate with loss of proton to form indolone derivative as products.



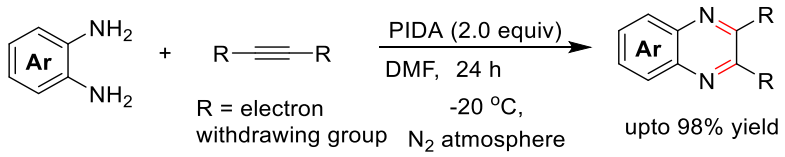
Scheme 1.13 Oxidative C-N coupling mediated by nitrene intermediate.

Kang Zhao and coworkers have illustrated formation of carbazolone via oxidative coupling of C(sp^2)- NH bond from 2-aryl enaminones.[30] Carbazolones are key intermediate for synthesis of alkaloids and drugs. The reaction pathway involved two potential mechanistic pathways to form the desired products. The mechanism involved a concerted process when R was substituted by an alkyl substituent and by the formation of nitrene intermediate when R was replaced by hydrogen.



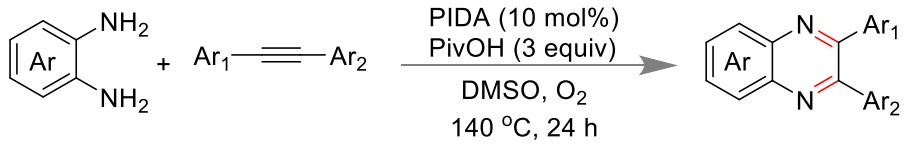
Scheme 1.14 Intramolecular cyclization for synthesis of carbazolones.

Minakata and co-workers have established synthesis of quinoxalines from electron-deficient alkynes and *ortho* phenylenediamines using hypervalent iodine(III) reagents under an inert atmosphere a temperature of -20°C.[31] The methodology proved to be efficiently producing the quinoxalines in excellent yields.



Scheme 1.15 Hyervalent iodine(III) reagent mediated quinoxaline synthesis.

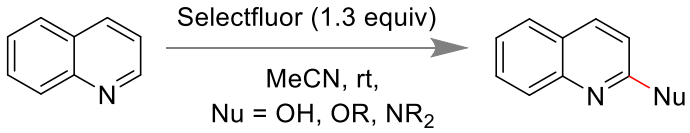
Quinoxalines were synthesized when *ortho*-phenylenediamines were made to react with internal alkynes under *in-situ* in the presence of hypervalent iodine(III) reagent (Scheme 1.16). [32] PIDA was used in catalytic amount along with 3.0 equivalent of pivalic acid as an additive to generate the pivaloyl derivative of hypervalent iodine(III) reagent.[32]. The iodine(III) reagent generated under *in-situ* conditions reacted with diarylacetylene substrate to form a 1,2-dicarbonyl compound as an intermediate which reacted with *ortho* phenylenediamine producing quinoxalines.



Scheme 1.16 Synthesis of quinoxaline from ortho phenylenediamines.

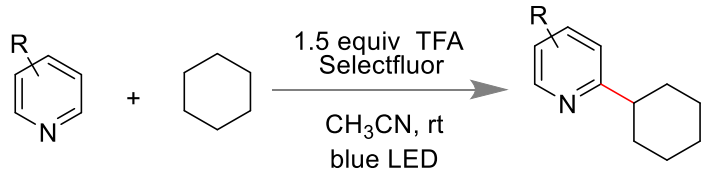
1.5 C-H functionalization of N- heterocycles

N-heterocycles are significantly important functional moieties [33] in natural products and the pharmaceutical industry. C-H functionalization of N-heterocycles had been reported by Hei and co-workers in a mild metal free approach using selectfluor in acetonitrile as solvent.



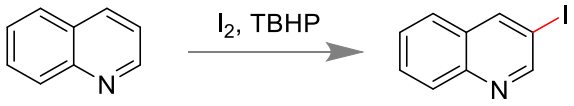
Scheme 1.17 C-H functionalization of quinoline with selectfluor.

Pyridine based *N*-heterocyclic moieties undergo C-H arylation with alkylated heteroarenes to produce a C-H arylation product. Using visible light, oxidative sp^3 C-H arylation occurred at environmentally benign conditions affording C-H functionalization of pyridine.[34]



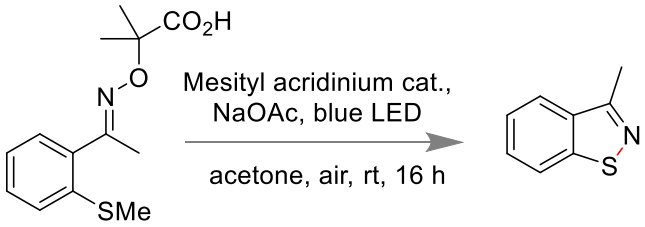
Scheme 1.18 Visible light mediated C-H Arylation with heteroarenes.

Fused N- heterocyclic iodides were synthesized by using TBHP and molecular iodine.[35] Regioselective C-H functionalization *via* molecular iodine activation and using nitrogen based heterocycle generated electrophilic iodine species I^+ and produced $^tBuO\cdot$ as a free radical.



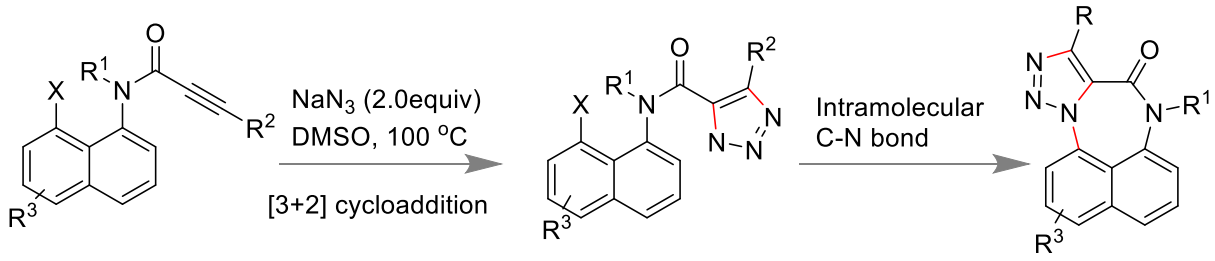
Scheme 1.19 Regioselective iodination of *N*-heterocyclic arenes.

A sustainable approach for the synthesis of α-Amino-oxy acid has been used to construct isothiazoles using visible light photo-redox catalysis.[36] The simple strategy included simple reaction conditions with an array of substrate scope and divergent functional groups.



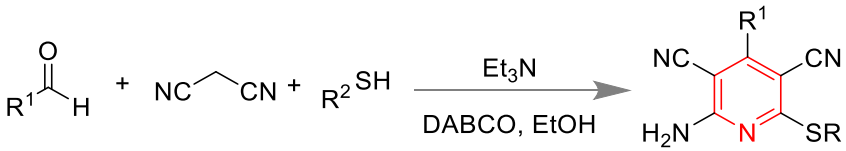
Scheme 1.20 Metal free approaches for synthesis of isothiazoles.

Diazepinone skeletons are significant as they are used in the treatment of the central nervous system. The C-N coupling to synthesize triazole fused diazepinone was achieved *via* triazole formation in the intermediate step involving [3+2] cycloaddition using sodium azide.



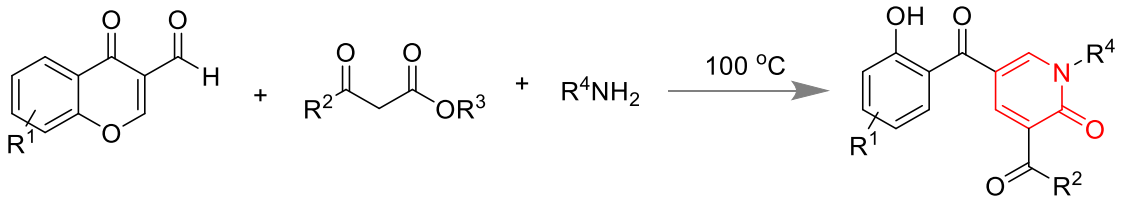
Scheme 1.21 Synthesis of triazole fused diazepinone using sodium azide.

Multicomponent synthesis of functionalized pyridines had been achieved by aldehyde, thiol and malononitrile which under in-situ conditions was accompanied by the formation of enaminonitrile.[37] The reaction was successful with aromatic, heteroaromatic, or heteroaromatic aldehydes to produce the functionalized pyridines in a wide array.



Scheme 1.22 Metal free multicomponent reaction for the synthesis of functionalized pyridine.

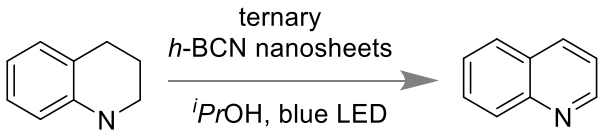
2-pyridones were synthesized by Lee and co-workers using 4-oxo-4H-chromene3-carbaldehyde, 1,3-diketoesters and primary amines without the use of solvent and catalyst.[38] The methodology sustained a broad functional group and produced the desired product with less reactive aromatic amines.



Scheme 1.23 Synthesis of pyridone in the absence of catalyst and solvent.

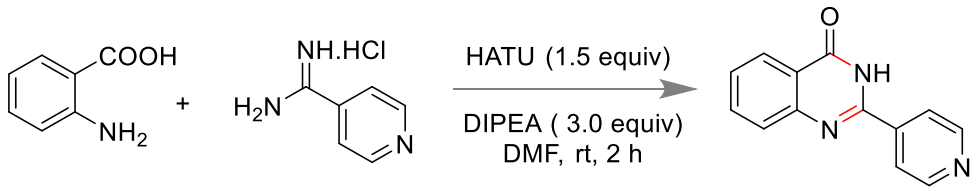
Hexagonal BCN nanosheets have been employed for the dehydrogenation of N-heterocycles using a visible light source. The process involved the evolution of hydrogen gas and hence

does not require any proton acceptor. The method involved h-BCN as the photocatalyst and isopropanol as solvent, forming the unsaturated heterocycle under visible light irradiation.



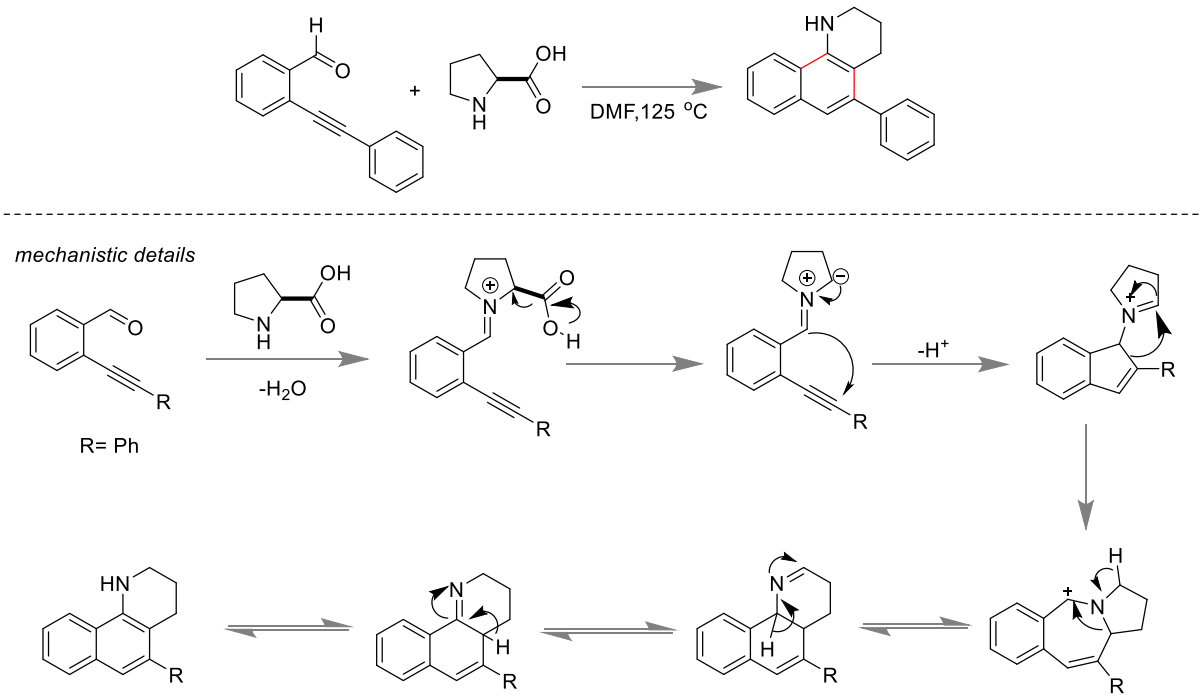
Scheme 1.24 Metal free dehydrogenation of N-heterocycle using visible light.

Synthesis of quinazolinone has been established from 2-amino benzoic acid and 4-amidinopyridine hydrochloride using HATU as a coupling partner and in the presence of a base in solvent DMF.[39] The metal free protocol was applied to synthesize diverse nitrogen-based N-heterocycles, which are significant in the pharmaceutical industry.



Scheme 1.25 Metal free synthesis of quinazolinone using a coupling reagent HATU.

Synthesis of tetrahydroquinolines in one pot has been established by Kundu and co-workers.[40] The key features involved the formation of three bonds simultaneously by metal free decarboxylative cyclization with one carbon ring expansion in one pot. The reaction proceeded by the formation of the imine intermediate by condensation of the aldehyde and amine, which undergoes decarboxylation to form the azomethine intermediate followed by endo dig cyclization and ring expansion to include a benzyl carbocation. Subsequent steps involving rearrangement led to formation of the product tetrahydroquinoline.



Scheme 1.26 Metal free decarboxylative cyclization from amino acids.

1.6 Azides in organic synthesis

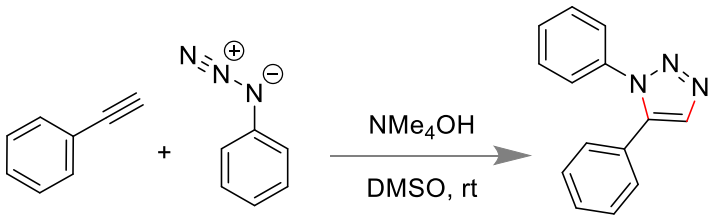
Azides form an essential category of compounds which have numerous applications in a vast array of discipline. The powerful utility of this functional group lies in its versatility and the ability to be transformed into necessary heterocyclic scaffolds. Click chemistry prevalent for a long time results from the potential application of azides in medicine, drug discovery, chemical biology, and material science. The versatile applications of azide have numerous synthetic routes to access significant structural motifs from a plethora of synthons which have expanded the synthetic availability of azide reagents and their application in organic chemistry.

Trimethylsilylazide has been used as an azide source for azidation of alkenes under metal free conditions using visible light photocatalysis. β azidoalcohols that are significant in nitrogen-containing heterocycles have been synthesized from readily available feedstock chemicals

like alkenes. [41] The mechanism was speculated to proceed by forming the azido radical and the alkene radical cation.

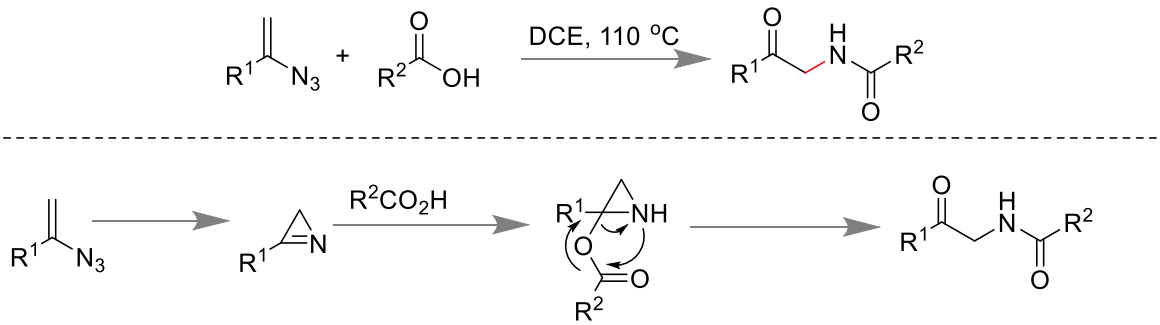
Scheme 1.27 Synthesis of β-azidoalcohol from alkenes using visible light photocatalysis.

1,5-Diarylsubstituted 1,2,3-triazoles have been reported in mild reaction conditions using azide in solvent DMSO and using a catalytic proportion of tetraalkylammonium hydroxide. The solvent DMSO plays an active role in various proton relay events.



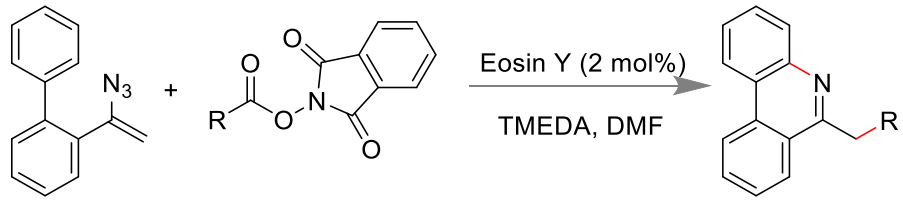
Scheme 1.28 Synthesis of triazoles using terminal akynes and organic azide.

Carboxylic acid and vinyl azides were used to prepare α-amidoketones through cascaded reactions.[42] The protocol showed wide functional group tolerance along with a vast array of substrate scope. The methodology was applied to a number of drug molecules with late stage modifications. The mechanistic studies showed the formation of an azirine as an intermediate step by decomposition of the azide. The azirine underwent a reaction with carboxylic acid to form azidirine followed by a thermal rearrangement to the α-amidoketone as the product.



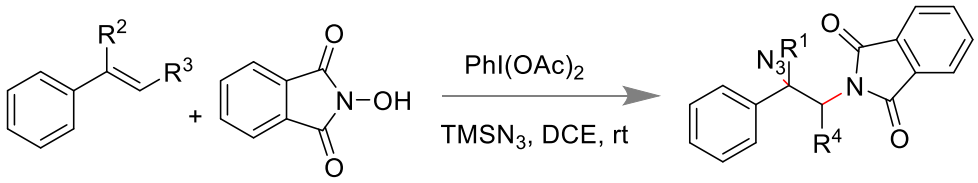
Scheme 1.29 Synthesis of α-amidoketone using terminal alkynyl azide.

Phenanthridines have been constructed using N-acycloxyphthalimides and vinyl azides under visible light irradiation.[43] The reaction proceeded by a radical pathway with decarboxylation followed by cyclization to form substituted phenanthridines.



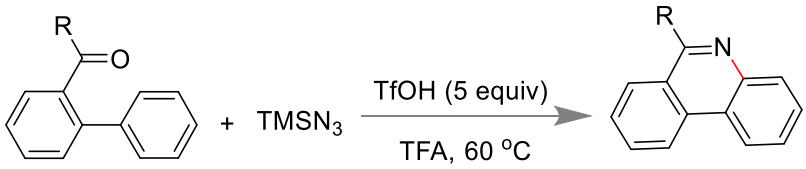
Scheme 1.30 Synthesis of substituted phenanthridines using vinyl azides and N-acycloxylphthalimides.

Xia and co-workers have established oxidation of alkenes under mild conditions using hypervalent iodine(III) reagent to generate the azido radical.[44] Consecutively, C-O and C-N bond was formed simultaneously from easily available precursors. The protocol tolerated a variety of substituted alkenes to afford the desired oxyazidation product.



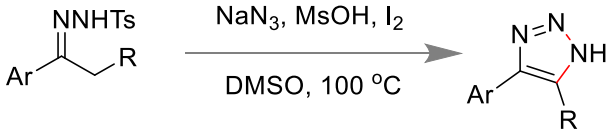
Scheme 1.31 Oxyazidation of alkenes using trimethylsilylazide and PIDA.

Phenanthridines have been synthesized using trimethyl silyl azide, which is the nitrogen source.[45] The method involved nitrogen incorporation using azide as the nitrogen source. The inhibition of the Schmidt reaction led to the elimination of byproduct, which proved the high chemoselectivity of the designed protocol or methodology.



Scheme 1.32 Synthesis of phenanthridines using $TMSN_3$ as nitrogen source.

Shu group have established cyclization of 4-aryl-NH-1,2,3-triazoles from N-tosyl hydrazones and using sodium azide.[46] This mild and metal-free cascaded [4 + 1] cyclization took place by C−N and N−N bond formation, respectively. The investigation of the mechanism revealed that nitrogen N_1 of the triazole was from sodium azide.



Scheme 1.33 Synthesis of triazoles mediated by molecular iodine.

1,2,3-triazole-fused dihydrobenzoxazinone derivatives were synthesized by cascaded β azidation using trimethyl silyl azide as the azide source.[47] The protocol applied to ample substrates, which provided a variable scope and took place efficiently using a variety of alkynylated cyclohexa 2,5-dienones, affording tricyclic scaffolds, which are cis-triazole-fused.

Scheme 1.34 Synthesis of triazole fused tricyclic scaffolds mediated by base.

OBJECTIVE

Thus, this chapter aims to discuss the scope of the thesis. Nitrogen containing scaffolds are significant due to its application in the pharmaceutical industry, in medicinal chemistry, for developing important drug molecules. The development of sustainable strategies involving nitrogenous based molecules will always be a highly demanding research topic in organic synthesis. The present thesis encompasses developing sustainable methods comprising nitrogen based N-heterocycles for its construction or application.

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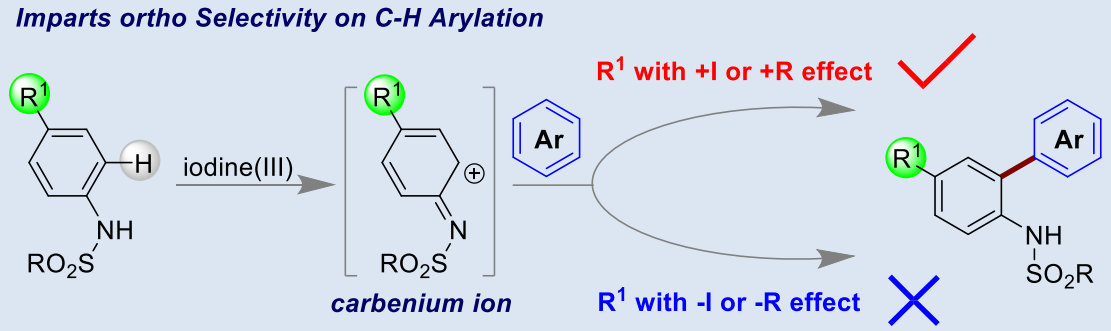
CHAPTER 2

C2-H Arylation Of Sulfonamides By Steric And Electronic Control

2.1 ABSTRACT



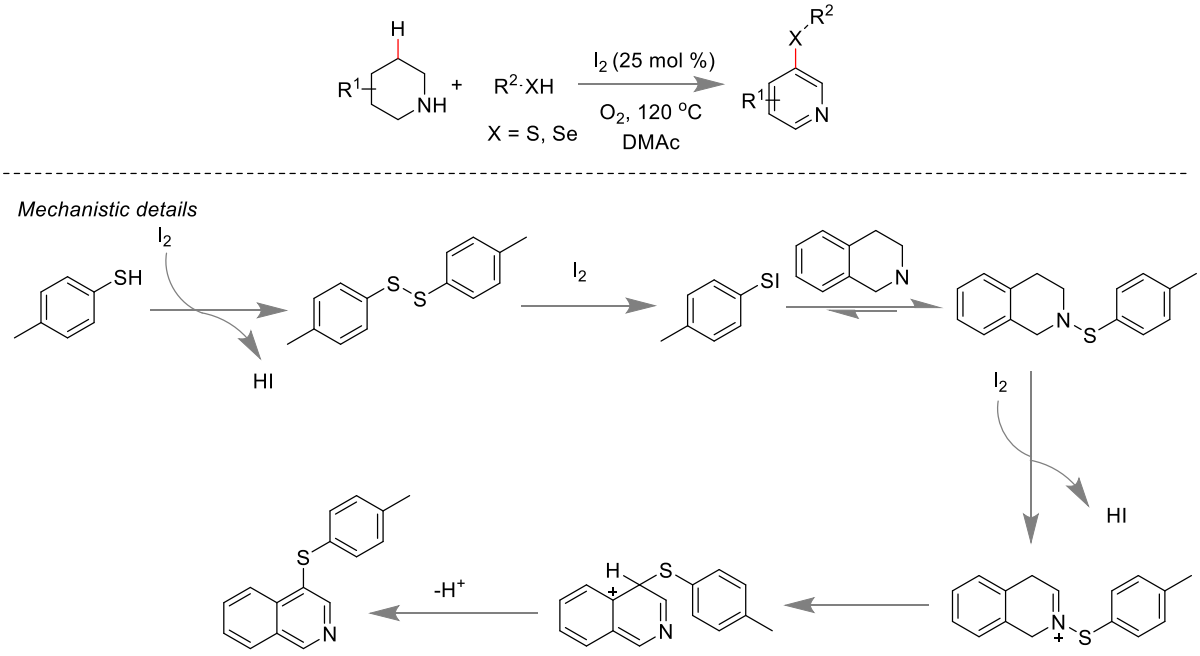
Arylsulfonamides generated electrophilic nitrenium ion, which was readily convertible to the tautomeric carbenium ion *via* resonance on reaction with phenyliodine diacetate. Depending on the nucleophile in the reaction mixture, C-H arylation took place. A scale of substrates where the electronic effect was operative resulted in C-H arylation of the sulfonamides.

2.2 INTRODUCTION

C-H bond functionalization by Dehydrogenative C-C coupling reaction[1-3] has come into prominence as a significant tool for organic chemists.[4-8] Traditional metal-mediated synthetic transformations for the construction of C-C bonds have expanded due to high application in industry.[9-13] Such methods are highly hazardous that produce unwanted toxic side products. Functionalization of aromatic C-H bond by the metal-free approach has been an exciting subject of interest among researchers. In such a perspective, hypervalent iodine(III) in organic synthesis for functionalization of C-H bond to construct significant structural motifs

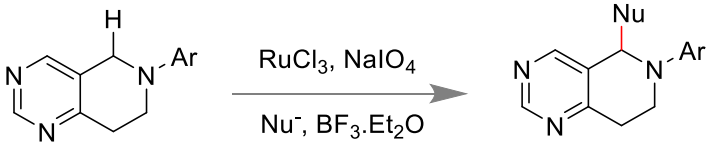
is well known for its ease of availability, stability, and cost-effective nature. C-C coupling reactions in an intermolecular approach have been explored using hypervalent iodine(III) reagents. [14, 15]

Recently C-H bond functionalization by a metal free approach using iodine in catalytic conditions has been developed by the Lei group.[16] Site-selective bond functionalization of piperidine and tetrahydroisoquinoline derivatives at the β-position took place using oxygen as the sole oxidant. Mechanistic studies predict oxidation followed by rearrangement produced the desired product.



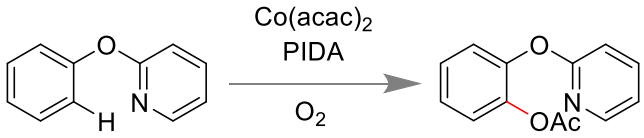
Scheme 2.1 β Selective functionalization of piperidine using a terminal oxidant like oxygen.

Cheng and co-workers has established C-H bond Functionalization in pyrimidine based substrates using metal catalyst in solvent THF and methanol (1:1) by volume. [17] It proceeded by two steps process forming a hemiaminal ether which on reaction with $BF_3.Et_2O$ lead to formation of iminium cation that incorporates the nucleophile to produce the C-H functionalization product.



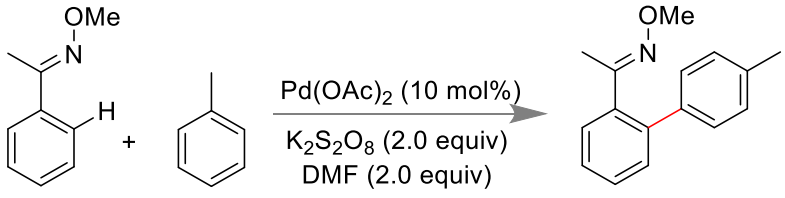
Scheme 2.2 C-H functionalization via two steps process using Ru as a catalyst.

Hypervalent iodine reagents have been widely employed for the functionalization of aromatic C-H bonds. C-H functionalization of aromatic C-H bond was achieved using phenyliodine diacetate (PIDA) and an inexpensive cobalt catalyst under neutral conditions.[18] Acetoxylation of C(sp^2)-H bond took place under mild conditions Mechanistic studies proclaim that the source of the acetoxy group was available from PIDA.



Scheme 2.3 C-H Functionalization using phenyl iodine diacetate (PIDA) as the acetoxy source.

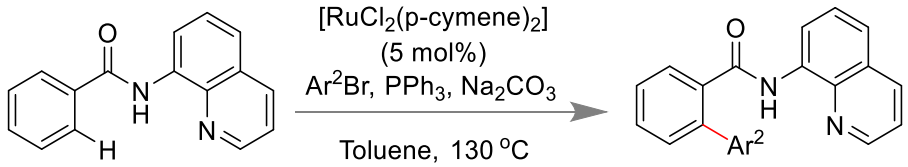
Directing group enabled C-H arylation was developed by using the mechanochemistry approach using ball mill.[19] Electron-rich and electron-deficient oxime acted as an efficient directing group for the C-H arylation forming the biaryls in high selectivity and in a short time of one hour with 600 rpm in 60 stainless steel grinding balls of 2 mm diameter. Initially, cyclopalladation at the oxime center was followed by fast activation of the C-H bond by arene at Pd(IV) center, which might cause its high selectivity.



Scheme 2.4 Intermolecular C-H arylation via mechanochemistry.

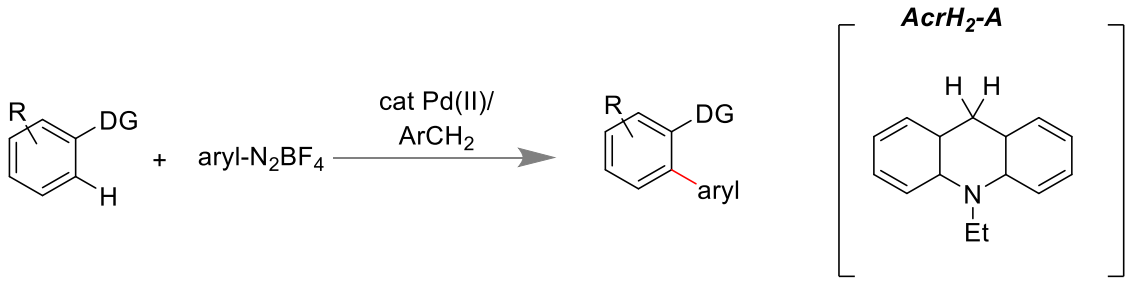
Bidentate directing group enabled C-H functionalization was reported by Chatani group using Ru as catalyst. 8-aminoquinoline was used as a directing group for C-H activation to couple

with aryl bromides.[20] The C-H activation step was facilitated by employing triphenyl phosphine. Authors speculated that presence of a bidentate directing group was necessary for the reaction to be successful.



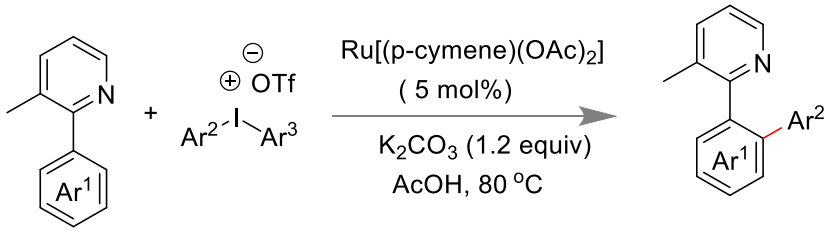
Scheme 2.5 Intermolecular C-H arylation using Ru as catalyst.

Directed C-H Arylation by use of dual Pd and photoredox catalysis of arenes with aryl diazonium salts was achieved with a broad functional group and at mild reaction conditons.[21] Biaryl motifs were synthesized by merging organic photoredox catalysis with palladium metal under irradiation of 36W Blue LED and in solvent MeOH.



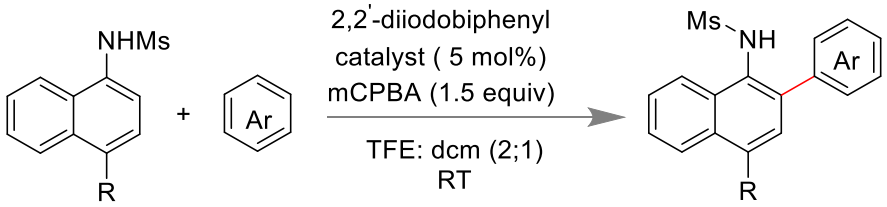
Scheme 2.6 Intermolecular C-H arylation using $AcrH_2$ as photocatalyst.

Diaryl iodonium salts have been broadly used as arylation source inorganic synthesis. Chatani group reported arylation of 2-arylpyridines using ruthenium(II) catalyst.[22] It was observed with mixed aryl group that the more electron-rich and sterically unhindered aromatic group transfer took place with more excellent selectivity.



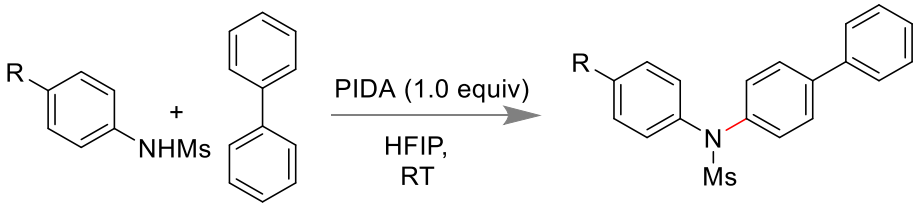
Scheme 2.7 C-H arylation using diaryl iodonium salt as arylation source.

Kita and the group have established C-H arylation of naphthyl anilides with aromatic hydrocarbons.[23] The first organocatalytic oxidative biaryl coupling was established using diiodbiphenyl as catalyst and an oxidant like meta percholorobenzoic acid. Also, stoichiometric amounts of iodine(III) successfully produced the C-H arylation product.



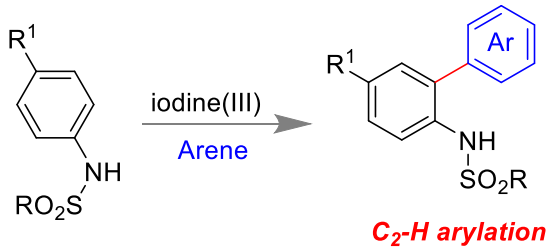
Scheme 2.8 C-H arylation of napthylsulfonamides using di-iodobiphenyl arene in catalytic amount.

Soft-Hard Acid-Base principle was used to demonstrate and preferentially functionalize a C-N bond using hypervalent iodine(III) as the reagent and by choice of appropriate nucleophile.[24] Biphenyl (soft) nucleophile prefers to react with nitrenium (soft) to form the C-N arylated product.



Scheme 2.9 C-H arylation of sulfonamides using HSAB approach.

This work brings into focus C_2-H arylation of sulfonamides involving iodine(III) reagents with proper choice of external nucleophiles. Sterically hindered arenes like mesitylene or triethyl benzene were potential nucleophiles in the reaction system. The reaction was controlled by the nucleophilicity of the arene available in the reaction mixture. The electronic substituent on the *para*- position of the sulfonamide possesses the feasibility and the outcome of the reaction.



Scheme 2.10 Oxidative arylation of sulfonamides using sterically hindered arenes.

Weak interactions[25, 26] or soft force in an organic synthetic reaction control the outcome of a product.[27] We focused on understanding the reactivity of sulfonamides by soft forces.[28] C-H arylation reaction of sulfonamide[23] was achieved by reactivity control of carbenium ion[29, 30] in preference to nitrenium ion.[31-34] Amides and amines react with iodine(III) reagents to produce a nitrenium ion as an electrophilic reactive intermediate. Depending on the nucleophile, the C-H arylation took place. Hypervalent iodine(III) reagent PIDA was used for C_2-H arylation of sulfonamides. Nitrenium ions are isoelectronic[35] with carbenium ions, and its utility in organic synthesis is expanding at a fast pace.[32, 36, 37] Ligand exchange at the electrophilic iodine atom led to formation amido-λ^3-iodane.[38] Heterolysis of nitrogen iodine bond along with reductive elimination led to the formation of nitrenium ion (Figure 2.1a). Nitrenium ions are readily convertible to carbenium ion and correspondingly attacked by the added nucleophile. Sterically hindered nucleophiles[24] led to oxidative coupling with electrophilic carbenium ion.(Figure 2.1b). The stability of the carbenium ion controls the selectivity of the product. Sulfonamides with electron releasing substituents (either by +I or +R effect) at the *para* position generated more stable carbenium ion (Figure 2.1c), which favored coupling with arene nucleophile. Contrastingly, substituted sulfonamide containing electron withdrawing group produced relatively less stable or unstable carbenium ion, to unfavor C-C coupling (Figure 2.1c). Heren in, we focussed on selective C-arylation of sulphonamides using iodine(III) reagent.

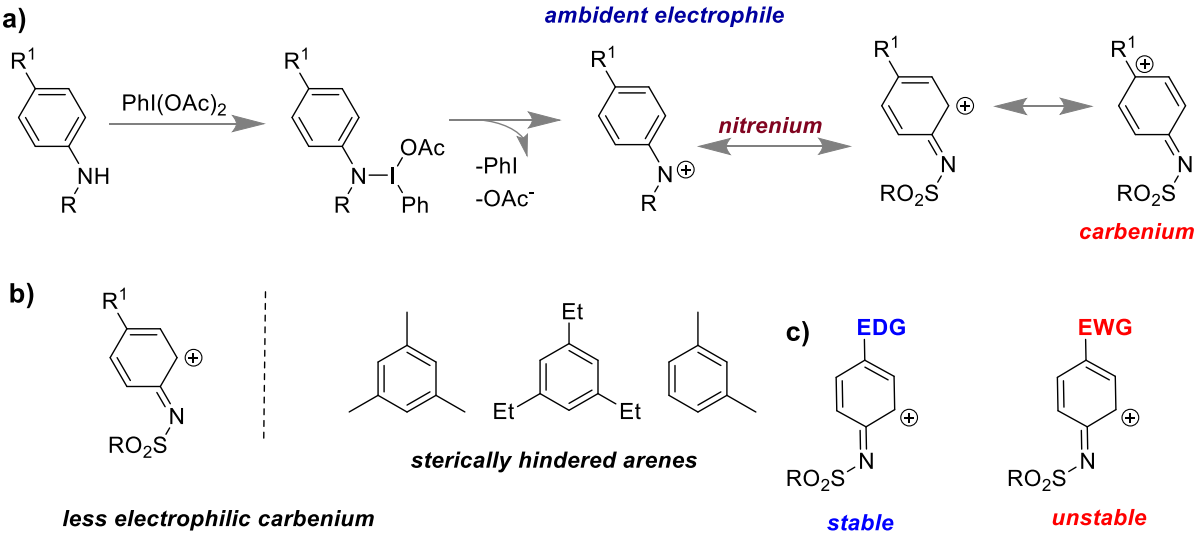
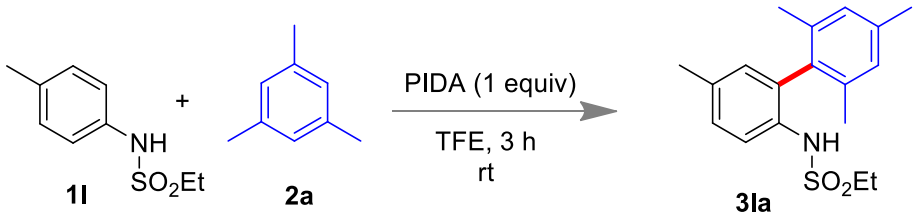


Figure 2.1 a) Mechanistic pathway for generation of nitrenium to carbenium b) sterically hindered arenes that undergo C-H arylation c) electronic effect of sulfonamides on C_2H arlation of sulfonamides.

2.3 RESULTS AND DISCUSSIONS

N-(*p*-tolylethanesulfonamide) **1k** was chosen as the sulfonamide**.** By taking an appropriate nucleophile like mesitylene **2** , C-H arylated product **3ka** produced in good yield when 1.0 equiv of PIDA was used in HFIP (entry 1). A slight excess of the oxidant did not produce appreciable difference in yield. Switching the solvent from HFIP to TFE, led to maximum yield of the C-H arylated product. 96% (entry 3). Iodine (III) was generated by employing iodobenzene in catalytic amount with *meta*-chloroperbenzoic acid (*m*CPBA) as an oxidant to produce a low yield. When 1.0 equiv of iodobenzene was used to generate the iodine (III) species, no substantial change was noticed (entry 5). Hypervalent iodine reagents like PIFA and PhIO were ineffective for oxidative coupling. (entries 6 and 7). Non-fluorinated solvents like DCE, DCM, and acetonitrile failed to produce the targeted product.

Table 2.1 Optimization table.

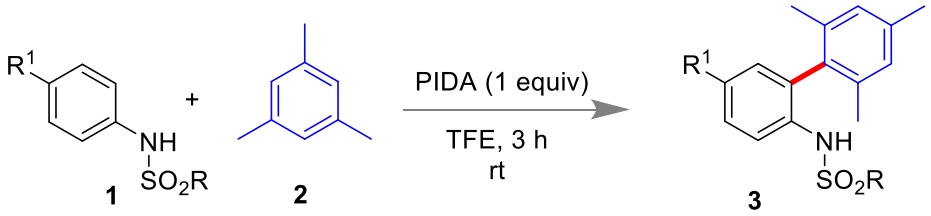


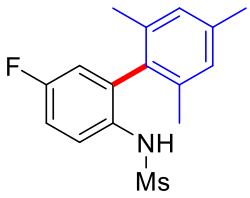
entry	iodine (III) (equiv)	solvent	yield (%)
1	PIDA(1.0)	HFIP	89
2	PIDA(1.5)	HFIP	85
3	PIDA(1.0)	TFE	96
4[a]	PhI (0.2)	TFE	32
5[a]	PhI (1)	TFE	24
6	PhIO	TFE	0
7	PIFA (1.0)	TFE	48
8	PIDA(1.0)	ACN	0
9	PIDA (1.0)	DCM	0
10	PIDA(1.0)	DCE	0

[a]0.2 mmol of **1k**, 0.6 mmol of mesitylene were used; [b]Yields were calculated based on recovery of reactants after column chromatography. Oxidant [c]*m*CPBA utilized in 0.2 mmol

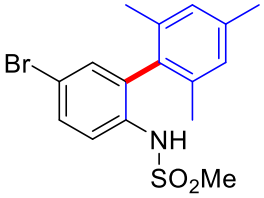
With the optimized reaction condition in hand, a wide array of substrate scope was tested. Sulfonamides were chosen as the anilide source and mesitylene as the coupling partner as indicated in Figure 2.2. Halogen-containing sulfonamides reacted with hypervalent iodine(III) reagent, producing good yield with maximum yield obtained with iodo-substituted anilide (3da). Alkyl substituents like methyl, ethyl, *iso*-propyl, *tert*-butyl tolerated reaction

conditions making good to moderate output. Other protecting groups led to the formation of product in good to excellent yield. (**3ka** and **3la**). If electron-withdrawing groups substitute the para position of the sulfonamide like CN, CF_3 and NO_2, the desired C-H arylation failed to take place due to instability of the generated nitrenium or carbenium ion.

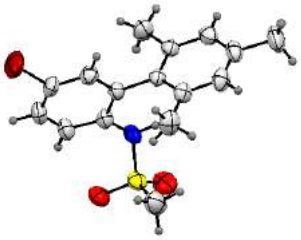


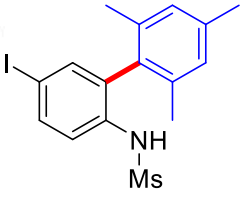


3aa, 66%

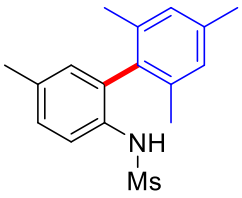


3ba, 67%

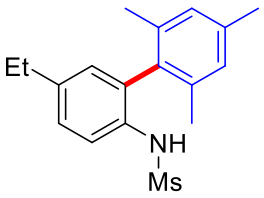




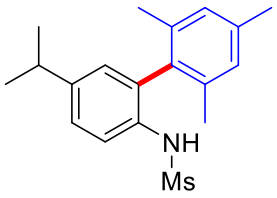
3ca, 77%



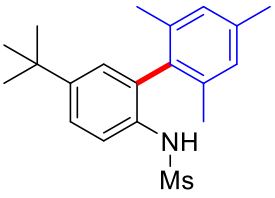
3da, 48%



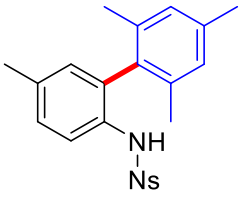
3ea, 58%



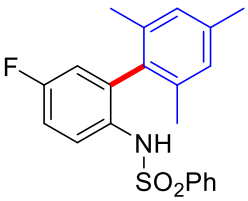
3fa, 68%



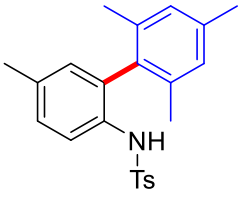
3ga, 53%



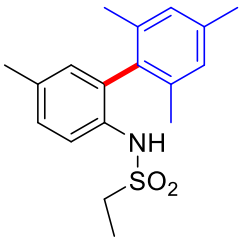
3ha, 50%



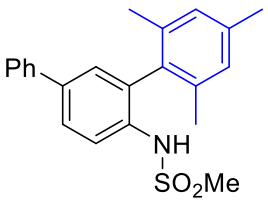
3ia, 51%



3ja, 81%



3ka, 96%



3la, 62%

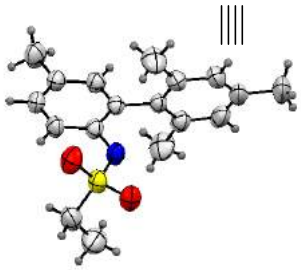


Figure 2.2. Scope of arylation reaction using mesitylene as arene source. Reaction condtions: 1.0 equiv of PIDA in TFE, 3.0 equiv of mesitylene was used at room temperature for 3 h, yield calculated based on recovered reactants.

The electronic factor plays an important role in stabilizing the nitrenium ion, which decides the fate of the reaction. Electron rich arenes like triethyl benzene as the arene source, and several alkyl-substituted sulfonamides were used, and it was found that moderate yield was produced in most of the cases (Figure 2.3). Sulfonamides containing halogen at the *para* position of anilide led to moderate yields of the desired product. (**3bb**, **3cb**, **3db**). Disubsituttion of anilides with EWG like Cl, CF_3 generated an unstable nitrenium ion, and an electron-rich nucleophile like triethyl benzene could not make the reaction successful. (**3pb**, **3rb**, **3sb**, **3tb**).

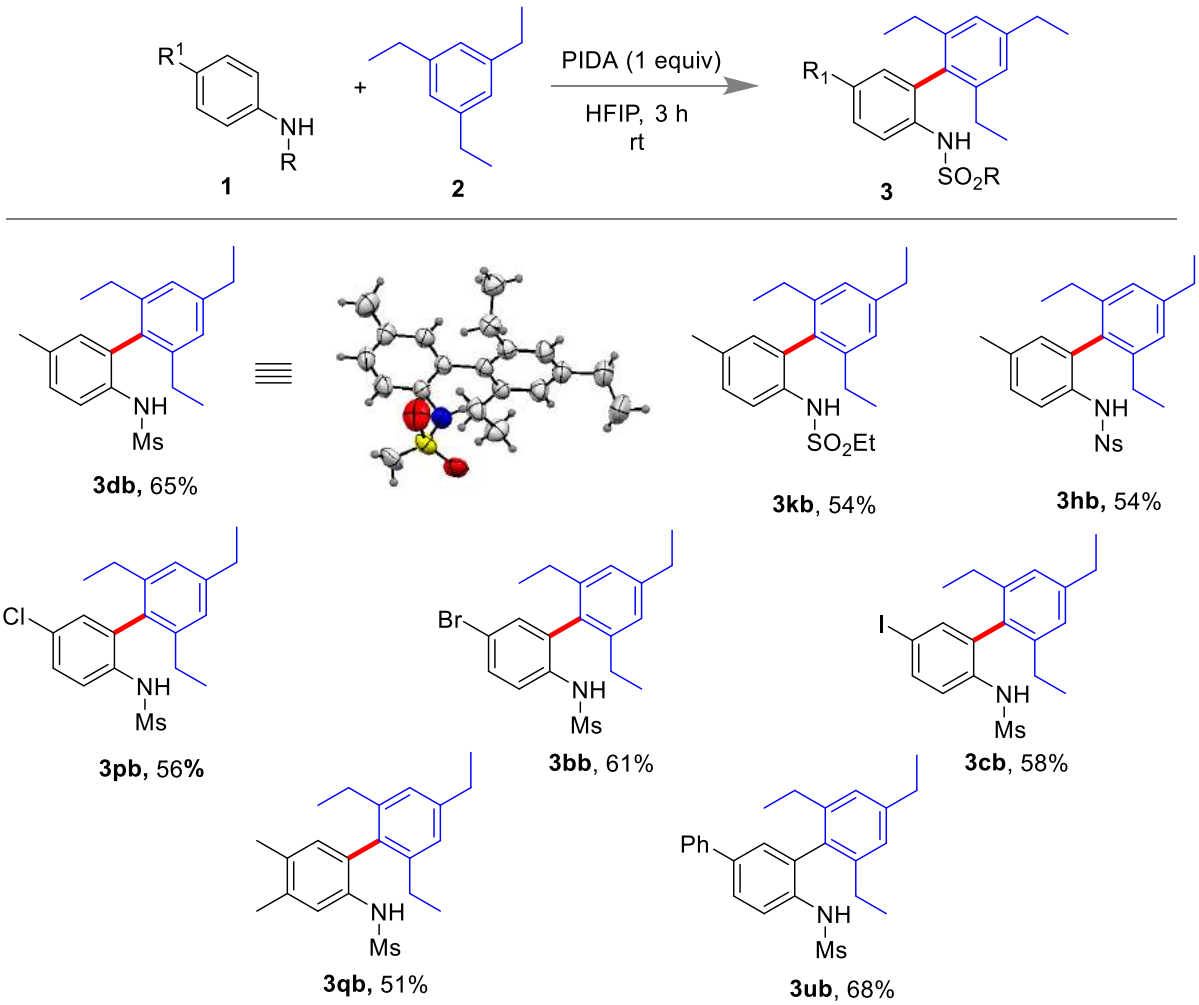


Figure 2.3. Scope of arylation using triethyl benzene as arene source; Reaction conditions: 1.0 equiv of PIDA in TFE, 3.0 equiv of mesitylene was used at room temperature for 3 h, yield calculated based on recovered reactants.

We next targeted to vary the arene source as shown in figure 2.4, and it was seen Bromo or iodo substituted arene gave an appreciable yield of product (**3ec**, **3lc**, **3cc**, **3ee**). Alkyl substituted sulfonamide resulted in relatively poor yield with Bromo substituted mesitylene (**3ec**). When dimethyanisole was used as arene source, two regioselective products were produced in 1:1 ratio (**3eg**). Arenes like trimethoxy benzene, tribromobenzene, tetramethyl benzene did not make the product, which might be due to the steric effect.

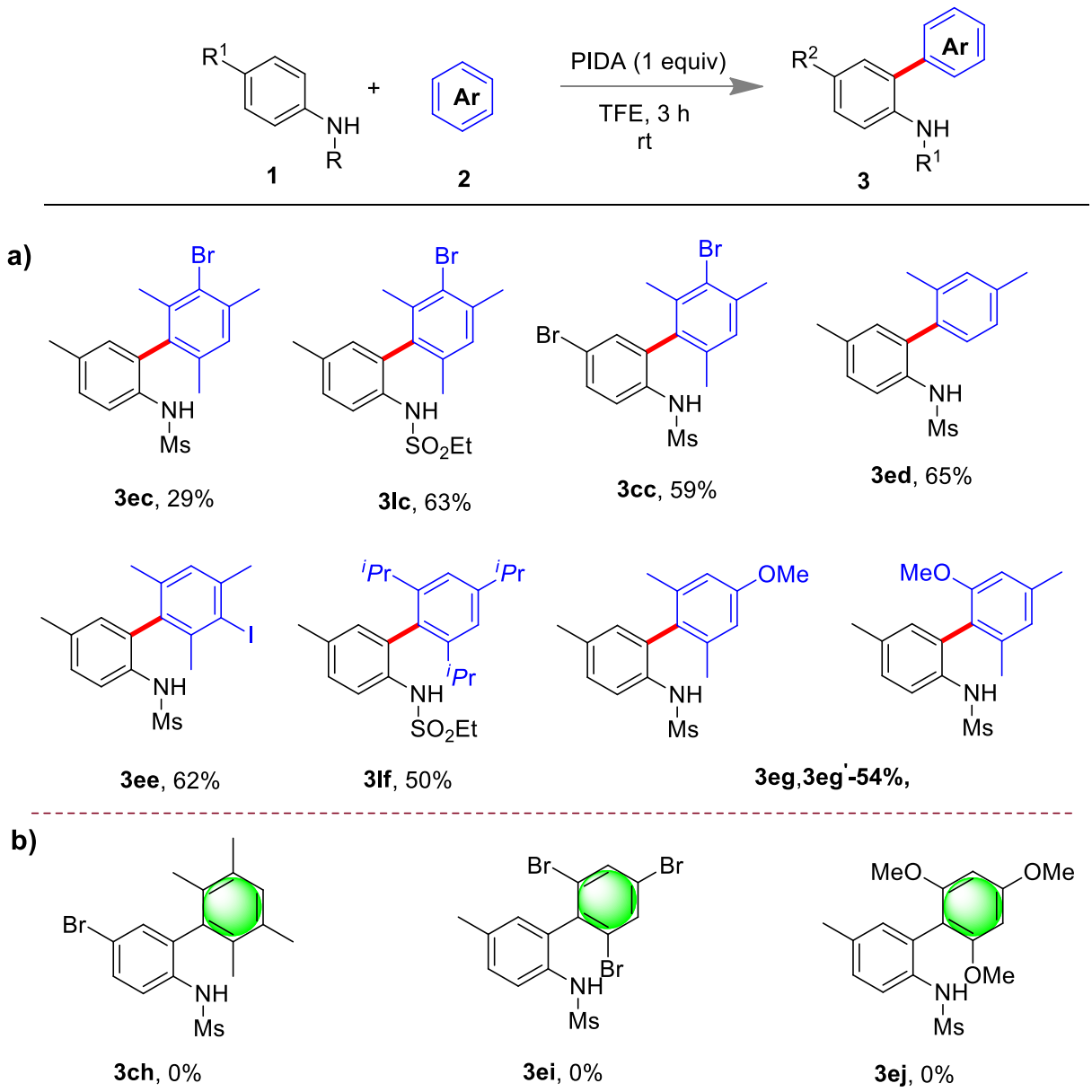
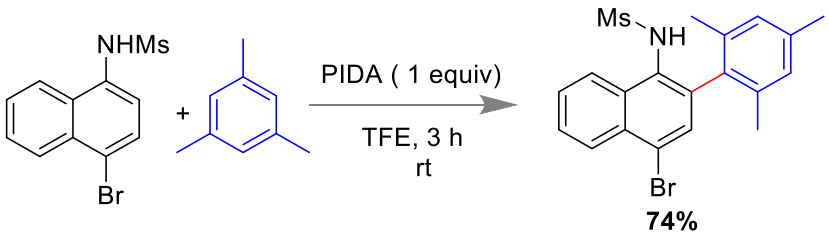


Figure 2.4. Scope of arylation varying the arene source. Reaction condtions: 1.0 equiv of PIDA in TFE, 3.0 equiv of mesitylene was used at room temperature for 3 h, yield calculated based on recovered reactants.

The methodology was extended to naphthalene-based aromatic system, and it was noticed that the arylated product was formed in good yield shown in scheme 2.11.



Scheme 2.11 Scope of arylation for naphthalene based sulfonamide. Reaction condtions: 1.0 equiv of PIDA in TFE, 3.0 equiv of mesitylene was used at room temperature for 3 h, yield calculated based on recovered reactants.

2.4 CONCLUSIONS

The Dehydrogenative C-H Arylation of biarylsulfonamides generated carbenium ion in the presence of iodine(III) reagent. The formation of C-H arylated product over N arylated product showed the key role of the nucleophile or the electronic effect of substituent on the sulfonamide. The C-H arylation was achieved in most of the substrates giving moderate to good yield in a mild reaction control. Overall, the proposed methodology was applied to form C-C bond which has an extensive application in industry and medicine.

2.5 EXPERIMENTAL SECTION

(General Methods) Chromatographic (Column) purifications of the compounds were done using silica gel (mesh 230-400) and hexane-ethyl acetate mixtures as eluent unless otherwise specified. The NMR spectra were recorded on 700 MHz or 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 ppm for ^{13}C). The peak patterns are designated as follows: s: singlet; d: doublet; t: triplet; q: quartet; m: multiplet; dd: doublet of doublets; td: triplet of doublets; brs: broad singlet. The coupling constants (*J*) are reported in hertz (Hz). ESI-TOF (time of flight) mass spectrometer has been used to record high-resolution mass spectra (HR-MS). Infrared (IR) spectral data are reported in wave number (cm^{-1}). FT-IR

spectra were recorded after making thin layer of the compounds on the surface of NaCl crystal using dichloromethane. Melting points (mp) of the compounds were determined with a digital melting point apparatus and are uncorrected. Good quality crystals of the compounds **3ka**, **3ba**, **3db** were obtained after slow evaporation of ethyl acetate solution. The crystals data were collected with Bruker SMART D8 goniometer equipped with an APEX CCD detector and with an INCOATEC micro source (Cu-Kα radiation, λ = 0.71073 Å). SAINT+[39] and SADABS[40] were used to integrate the intensities and to correct the absorption respectively The structure was resolved by direct methods and refined on F^2 with SHELXL-97.[41]

Representative method for preparation of *N*-(5-bromo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide. To a stirred solution of *N*-(4-bromophenyl)methanesulfonamide **1b**, (40 mg, 0.159 mmol) in 2.0 mL of TFE, mesitylene (67 µL, 0.479 mmol) was added. PIDA (51 mg, 0.159 mmol) dissolved in 1.0 mL of TFE was then added dropwise to the reaction containing mixture. The reaction mixture was stirred for 2 h. On complete consumption of substrate, the reaction mixture was evaporated to dryness. Column chromatography had been done to isolate the pure product *N*-(5-bromo-2',4',6'-trimethyl-[1.1'-biphenyl]-2-yl)methanesulfonamide (**3ba**) as white solid in 39 mg (67%) yield using 5% ethylacetate-hexane.

Compound Characterization data

***N*-(5-Fluoro-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3aa):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; yield (37 mg, 57%); mp 164-166 ºC (lit.[42] 164-165 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 8.8, 4.8 Hz, 1H), 7.54 (s, 1H), 7.36 (td, *J* = 8.4, 2.8 Hz, 1H), 7.10 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.19 (s, 1H), 3.20 (s, 3H), 3.20 (s, 4H), 2.61 (s, 3H), 2.25 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6 (d, $^1J_{C\text{-}F}$ = 243 Hz), 139.0,

136.5, 132.6 (d, $^3J_{C\text{-}F}$ = 8 Hz), 131.4, 130.9 (d, $^4J_{C,F}$ = 3 Hz), 129.3, 119.8 (d, $^2J_{C,F}$ = 8 Hz), 117.3 (d, $^2J_{C,F}$ = 22 Hz), 115.5 (d, $^2J_{C,F}$ = 22 Hz), 38.7, 21.1, 20.1.

***N*-(5-Bromo-2',4',6'-trimethyl-[1.1'-biphenyl]-2-yl)methanesulfonamide (3ba):** R_f = 0.4 (hexane:ethyl acetate: 9:1); white solid; yield (34 mg, 67%), (40 mg starting material taken, 5 mg starting material recovered); mp 172-175 °C (lit.[42] 173-175 ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.8 Hz, 1H), 7.49 (dd, *J* = 8.8; 1.0 Hz, 1H), 7.23 (d, *J* = 2.4 Hz, 1H), 6.98 (s, 2H), 5.99 (brs, 1H), 2.97 (s, 3H), 2.33 (s, 3H), 1.97 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.2, 136.7, 134.1, 133.3, 132.2, 131.8, 130.9, 129.4, 119.0, 117.2, 39.9, 21.3, 20.2.

***N*-(5-Iodo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3ca):** R_f = 0.40 (hexane : ethyl acetate 9:1); white solid; yield 41 mg (77%), (40 mg starting material taken, 2mg stating material recovered); mp 176-177 ºC (lit.[42] 176-178 ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (dd, *J* = 8.8; 2.0 Hz, 1H), 7.46 (d, 8.8 Hz, 1H), 7.42 (d, *J* = 2.0 Hz, 1H), 6.97 (s, 2H), 5.99 (brs, 1H), 2.97 (s, 3H), 2.33 (s, 3H), 1.96 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.1, 139.2, 137.8, 136.7, 134.9, 132.3, 130.8, 129.4, 119.2, 87.7, 39.9, 21.3, 20.3.

***N*-(2',4',5,6'-Tetramethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3da):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 17 mg (48%), (40 mg starting material taken, 19 mg starting material recovered); mp 122-124 ºC (lit.[42] 123-124 ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.0 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 1H), 6.97 (s, 2H), 6.89 (s, 1H), 5.92 (s, 1H), 2.93 (s, 3H), 2.34 (s, 6H), 1.97 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 136.8, 134.1, 132.6, 132.2, 131.0, 130.4, 129.4, 129.2, 117.8, 39.7, 21.2, 20.8, 20.3.

***N*-(5-Ethyl-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3ea):** R_f = 0.50 (hexane : ethylacetate 9:1); white solid; 32 mg (68%), (40 mg starting material taken, 8 mg stating material recovered) ; mp 111-113 ºC (lit.[42] 112-114 ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.4 Hz, 1H), 7.20 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.97 (s, 2H), 6.91 (d, *J* = 2.0 Hz, 1H), 5.92 (s, 1H), 2.96 (s, 3H), 2.64 (q, *J* = 7.6 Hz, 2H), 2.33 (s, 3H), 1.96 (s, 6H), 1.24 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.6, 138.4, 136.7, 132.7, 132.4, 130.3, 129.8, 129.1, 128.2, 117.7, 39.8, 28.2, 21.2, 20.3, 15.7.

***N*-(5-Isopropyl-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3fa):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 30 mg (59%), (40 mg starting material taken, 7 mg stating material recovered); mp 142-145 ºC (lit.[42] 143-145 ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.8 Hz, 1H), 7.22 (dd, *J* = 8.4; 2 Hz, 1H), 6.98 (s, 2H), 6.94 (d, *J* = 2 Hz, 1H), 5.93 (s, 1H), 2.94 (s, 3H), 2.91-2.87 (m,1H), 2.34 (s, 3H), 1.96 (s, 6H), 1.3 (s,3H), 1.3 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.3, 138.4, 136.8, 132.9, 132.4, 130.3, 129.1, 128.6, 126.7, 117.7, 39.9, 33.5, 24.1, 21.1, 20.3.

***N*-(5-(*tert*-Butyl)-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3ga):** R_f= 0.50 (hexane : ethyl acetate 9:1); white solid; 28 mg (53%), (40 mg starting material taken, 5 mg stating material recovered); mp 174-175 ºC (lit.[42] 174-175 ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.4 Hz, 1H), 7.37 (dd, *J* = 8.8; 2 Hz, 1H), 7.09 (d, *J* = 2 Hz, 1H), 6.98 (s, 2H), 5.93 (s, 1H), 2.95 (s, 3H), 2.34 (s, 3H), 1.96 (s, 6H), 1.30 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 138.5, 136.8, 133.0, 132.1, 129.7, 129.1, 127.7, 125.4, 117.2, 39.8, 34.5, 31.4, 21.1, 20.3.

4-Nitro-N-(2′,4′,5,6′-tetramethyl-[1,1′-biphenyl]-2-yl)benzenesulfonamide (3ha): R_f = 0.40 (hexane:ethyl acetate 9:1); yellow solid; 24 mg (50%), (40 mg starting material taken, 5 mg stating material recovered); mp 192-194 °C (lit.[42] 193-195 °C); ^{1}H NMR (400 MHz, CDCl3) δ 8.25 (d, *J* = 8.8 Hz, 2H), 7.88 (d, *J* = 8.8 Hz, 2H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.13 (d, *J* = 7.2 Hz, 1H), 6.90 (s, 2H), 6.76 (s, 1H), 6.21 (s, 1H), 2.33 (s, 3H), 2.28 (s, 3H), 1.25 (s, 6H); ^{13}C NMR (100 MHz, CDCl3) δ 150.3, 145.5, 138.7, 136.6, 135.2 132.2, 131.1, 130.8, 129.3, 129.1, 126.1, 128.7, 124.4, 118.8, 21.3, 20.9, 20.0.

***N*-(5-Fluoro-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (3ia):** R_f = 0.40 (hexane : ethyl acetate 9:1); white solid; 24 mg (51%) (40 mg starting material taken, 5 mg stating material recovered); mp 164-167 °C; (lit.[42] 165-167 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 9.2; 4.0 Hz, 1H), 7.72-7.67 (m, 2H), 7.56-7.52 (m, 1H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.04 – 6.99 (m, 1H), 6.90 (s, 2H), 6.68-6.65 (m, 1H), 6.11 (s, 1H), 2.33 (s, 3H), 1.61 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.56 (d, $^1J_{C,F}$ = 243 Hz), 139.5, 138.9, 136.7, 133.3, 132.7 (d, $^3J_{C,F}$ = 8.0 Hz), 131.3, 130.5 (d, $^4J_{C,F}$ = 3 Hz), 129.3, 129.1, 127.3, 120.3 (d, $^3J_{C,F}$ = 8.0 Hz), 117.0 (d, $^2J_{C,F}$ = 22.0 Hz), 115.2 (d, $^2J_{C,F}$ = 22.0 Hz); 21.2, 19.7.

4-Methyl-*N*-(2',4',5,6'-tetramethyl-[1, 1'-biphenyl]-2-yl)benzenesulfonamide (3ja): R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 34 mg (81%), (40 mg starting material taken, 11 mg stating material recovered); mp 151-153 °C (lit.[42] 150-153 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.59 (m, 3H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.09 (dd, *J* = 8.4; 2.0 Hz, 1H), 6.90 (s, 2H), 6.72 (d, *J* = 2 Hz, 1H), 6.09 (s, 1H), 2.37 (s, 3H), 2.33 (s, 3H), 2.26 (s, 3H), 1.64 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 142.9, 138.3, 137, 133.8, 132.5, 131.9, 130.7, 130.3, 129.8, 129.0, 128.9, 127.4, 118.3, 21.6, 21.1, 20.9, 19.9.

***N*-(2',4',5 ,6'-Tetramethyl-[1, 1'-biphenyl]-2-yl)ethanesulfonamide (3ka):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 37 mg (96%), (40 mg starting material taken, 24 mg starting material recovered); mp 119-121 ºC (lit.[42] 120-121 ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.0 Hz, 1H), 7.15 (d, *J* = 8.4 Hz, 1H), 6.97 (s, 2H), 6.87 (s, 1H), 5.86 (s, 1H), 3.07 (q, *J* = 6.8 Hz, 2H), 2.33 (s, 6H), 1.98 (s, 6H), 1.25 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 136.7, 133.8, 132.6, 132.4, 131.0, 130.0, 129.3, 129.1, 117.5, 46.4, 21.2, 20.8, 20.3, 8.2.

***N*-(2'',4'',6''-Trimethyl-[1,1':3',1''-terphenyl]-4'-yl)methanesulfonamide (3la):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 37 mg (62%); mp 172-174 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.4 Hz, 1H), 7.64 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.59 (d, *J* = 7.2 Hz, 2H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.35 (m, 2H), 7.02 (s, 2H), 6.07 (s, 1H), 3.02 (s, 3H), 2.36 (s, 3H), 2.03 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.1, 138.7, 137.4, 136.9, 134.1, 132.3, 130.6, 129.2, 129.0, 128.9, 127.5, 127.4, 126.8, 117.7, 39.9, 21.3, 20.3; IR (KBr) ϑ = 3441, 2061, 1633 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{22}H_{23}NO_2SNa$ 388.1342; Found 388.1327.

***N*-(2',4',6'-Triethyl-5-methyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3db):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 48 mg (65%); mp 139-141 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.0 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 1H), 7.03 (s, 2H), 6.93 (s, 1H), 5.94 (s, 1H), 2.95 (s, 3H), 2.68 (q, *J* = 7.6 Hz, 2H), 2.3 (s, 3H), 2.34-2.15 (m, 4H), 1.30 (t, *J* = 7.6 Hz, 3H), 1.05 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1, 142.8, 133.4, 132.7, 131.7, 131.3, 129.4, 129.3, 126.3, 116.9, 39.8, 28.8, 26.6, 20.8, 15.4; IR (KBr) ϑ = 3441, 2064, 1635, 1161 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{27}NO_2SNa$ 368.1655; Found 368.1672.

***N*-(2',4',6'-Triethyl-5-methyl-[1,1'-biphenyl]-2-yl)ethanesulfonamide (3kb):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 39 mg (54%); mp 99-101 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.4 Hz, 1H), 7.17 – 7.14 (dd, *J* = 8.4, 1.6 Hz , 1H), 7.02 (s, 2H), 6.91 (s, 1H), 5.85 (s, 1H), 3.09 (q, *J* = 7.6 Hz, 2H), 2.68 (q, *J* = 7.6 Hz, 2H), 2.32 (s, 3H), 2.32 – 2.15 (m, 4H), 1.33 – 1.24 (m, 6H), 1.05 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.9, 142.8, 132.9, 132.6, 131.7, 131.4, 129.2, 128.9, 126.1, 116.7, 46.7, 28.8, 28.8, 20.8, 15.3 (×2), 8.2; IR (KBr) ϑ = 3441, 2065, 1635, 533 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{29}NO_2SNa$ 382.1811; Found 382.1836.

4-Nitro-*N*-(2′,4′,6′-triethyl-5-methyl-[1, 1′-biphenyl]-2-yl)benzenesulfonamide (3hb): R_f = 0.50 (hexane:ethyl acetate 9:1); white solid; 35 mg (54%); mp 148-151 °C; (lit.[42] 149-152 ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (^{1}H NMR (400 MHz, CDCl3) δ 8.34−8.22 (m, 2H), 7.96−7.88 (m, 2H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.13 (d, *J* = 8.4 Hz, 1H), 6.97 (s, 2H), 6.83 (s, 1H), 6.23 (s, 1H), 2.68 (q, *J* = 7.6 Hz, 2H), 2.28 (s, 3H), 1.88 (q, *J* = 7.6 Hz, 4H), 1.33-1.29 (m, 3H), 0.92−0.88 (m, 6H); ^{13}C NMR (100 MHz, CDCl3) δ 150.3, 145.5, 145.3, 142.7, 134.3, 131.6, 131.3, 131.0, 129.8, 129.3, 128.7, 126.1, 124.4, 117.5, 28.9, 26.3, 20.1, 15.5, 15.2.

***N*-(5-Chloro-2',4',6'-triethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3pb):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 40 mg (56%); mp 153-157º C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.8 Hz, 1H), 7.36 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.13 (d, *J* = 2.4 Hz, 1H), 7.04 (s, 1H), 6.01 (s, 1H), 2.98 (s, 3H), 2.68 (q, *J* = 7.6 Hz, 2H), 2.33-2.14 (m, 4H), 1.30 (t, *J* = 7.6 Hz, 3H), 1.06 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 142.7, 134.0, 131.0 , 130.9, 129.9, 129.0, 128.8, 126.5, 117.8, 40.1, 28.8, 26.7, 15.4; IR (KBr) ϑ = 3442,

2070, 1635, 1161 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{24}ClNO_2SNa$ 388.1108; Found 388.1118.

***N*-(5-bromo-2',4',6'-triethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3bb):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 40 mg (61%); mp 156-159 ºC (lit.[42] 155-158 ºC); ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.8Hz, 1H), 7.50 (d, *J* = 8.8 Hz, 1H), 7.27 (s, 1H), 7.03 (s, 2H), 6.01 (s, 1H), 2.98 (s, 3H), 2.67 (q, *J* = 7.6 Hz, 2H), 2.33-2.14 (m, 4H), 1.30 (t, *J* = 7.6 Hz, 3H), 1.05 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 142.8, 134.7, 133.9, 131.8, 131.3, 129.9, 126.5, 118.2, 116.6, 40.2, 28.9, 26.7, 15.3.

***N*-(2',4',6'-triethyl-5-iodo-[1,1'-biphenyl]-2-yl)methanesulfonamide (3cb):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 36 mg (58%) (40 mg starting material taken, 5 mg stating material recovered); mp 156-159 ºC (lit.[42] 157-159 ºC); ^1H NMR (400 MHz, $CDCl_3$ δ 7.68 (d, *J* = 8.8 Hz, 1H), 7.47 (s, 1H), 7.45 (s, 1H), 7.03 (s, 2H), 6.02 (s, 1H), 2.99 (s, 3H), 2.67 (q, *J* = 7.6 Hz, 2H), 2.31-2.16 (m, 4H), 1.30 (t, *J* = 7.6 Hz, 3H), 1.05 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.7, 142.7, 139.8, 137.6, 135.3, 131.4, 129.8, 126.5, 118.3, 87.0, 40.0, 28.8, 26.6, 15.4.

***N*-(2',4',6'-Triethyl-4,5-dimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3qb):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 37 mg (51%); mp 143-144 ºC. ^1H NMR (400 MHz, $CDCl_3$) δ 7.09 (s, 1H), 7.00 (s, 2H), 6.87 (s, 1H), 5.44 (s, 1H), 2.65 (q, *J* = 7.6 Hz, 2H), 2.44 (s, 3H), 2.40 – 2.21 (m, 10H), 1.25 (t, *J* = 7.6 Hz, 3H), 1.08 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 144.4, 142.5, 138.2, 137.2, 137.1, 134.9, 131.2, 130.9 ,129.9, 125.3, 41.9, 28.9, 26.7, 21.2, 19.9, 15.9, 15.3; IR (KBr) ῡ = 3441, 2066, 1635 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{29}NO_2SNa$ 382.1815; Found 388.1811.

***N*-(2'',4'',6''-Triethyl-[1,1':3',1''-terphenyl]-4'-yl)methanesulfonamide (3ub):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 45 mg (68%); mp 180-182 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.4 Hz, 1H), 7.64 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.58 (d, *J* = 7.6 Hz, 2H), 7.49 – 7.40 (m, 3H), 7.35 (t, *J* = 7.2 Hz, 1H), 7.07 (s, 2H), 6.08 (s, 1H), 3.04 (s, 3H), 2.70 (q, *J* = 7.6 Hz, 2H), 2.54 – 2.16 (m, 4H), 1.33 (t, *J* = 7.6 Hz, 3H), 1.08 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.4, 142.9, 140.1, 136.6, 134.6, 131.1, 129.8, 129.5, 129.1, 127.4, 127.4, 126.8, 126.4, 116.9, 40.0, 28.8, 26.7, 15.6, 15.5; IR (KBr) ʊ = 3441, 2068, 1637 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{29}NO_2SNa$ 430.1811; Found 430.1788.

***N*-(3'Bromo-2',4',5',6'-tetramethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3dc):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 41 mg (49%); mp 165-166 ºC (lit.[42] 165-167 ºC); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.4 Hz, 1H), 7.39 – 7.37 (m, 1H), 7.04 (s, 1H), 6.09 (s, 1H), 3.11 (s, 3H), 2.62 (s, 3H), 2.53 (s, 3H), 2.29 (s, 3H), 2.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0, 136.8, 135.7, 134.5, 134.4, 132.1, 131.0, 130.6, 130.3, 129.8, 126.4, 39.9, 24.1, 21.7, 20.8, 20.2.

***N*-(3'-Bromo-2',4',5,6'-tetramethyl-[1,1'-biphenyl]-2-yl)ethanesulfonamide (3kc):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 50 mg (63%); mp 162-164 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.4 Hz, 1H), 7.19 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.10 (s, 1H), 6.86 (d, *J* = 1.4 Hz, 1H), 5.83 (s, 1H), 3.10 (q, *J* = 7.6 Hz, 2H), 2.47 (s, 3H), 2.35 (s, 3H), 2.14 (s, 3H), 1.96 (s, 3H), 1.28 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.8, 136.8, 135.7, 134.6, 134.0, 132.2, 130.9, 130.5, 130.1, 129.6, 126.3, 117.8, 46.6, 24.1, 21.7, 20.8,

20.1, 8.2; ῡ = 3441, 2066, 1635 cm^{-1}; HRMS (ESI/QTOF) m/z: [M + Na]+ Calcd for $C_{18}H_{22}BrNO_2SNa$ 418.0447; Found 418.0442.

***N*-(3',5-Dibromo-2',4',6'-trimethyl-[1.1'-biphenyl]-2-yl]methanesulfonamide (3bc):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 47 mg (59%); mp 165-167 ºC (lit.[42] 166-167 ºC); ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.4 Hz, 1H), 7.51 (d, *J* = 8.8 Hz, 1H), 7.20 (s, 1H), 7.08 (s, 1H), 5.92 (s, 1H), 2.98 (s, 3H), 2.45 (s, 3H), 2.11 (s, 3H), 1.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.8, 136.8, 135.5, 134.0, 133.2, 132.8, 132.2, 132.1, 130.8, 126.5, 119.2, 117.3, 40.2, 24.2, 21.7, 20.1.

***N*-(2',4',5'-Trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3dd):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 40 mg (65%) (40 mg starting material taken, 5 mg stating material recovered); mp 112-114 ºC; ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.4 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 1H), 7.14 (s, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 7.6 Hz, 2H), 7.01 (s, 1H), 6.99 (s, 1H), 2.84 (s, 3H), 2.38 (s, 3H), 2.35 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 138.7, 136.4, 134.4, 133.5, 132.5, 132.1, 131.8, 131.3, 129.6, 129.4, 127.5, 119.4, 39.6, 21.3, 20.8, 19.7; ῡ = 3441, 2065, 1635 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{19}NO_2SNa$ 312.1029; Found 312.1010.

***N*-(2',4',6'-triisopropyl-5-methyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (3ke):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 40 mg (50%); mp 171-172 ºC (lit.[43] 170-172 ºC); ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.4 Hz, 1H), 7.16 (d, *J* = 8.4 Hz, 1H), 7.10 (s, 2H), 6.91 (s, 1H), 5.95 (s, 1H), 3.17 (q, *J* = 7.2Hz, 2H), 2.94 (sept, *J* = 6.8 Hz 1H), 2.47 (sept, *J* = 6.8 Hz 1H) , 2.32 (s, 3H), 1.36 - 1.30 (m, 9H), 1.17 (d, *J* = 6.8 Hz, 6H), 1.04 (d, *J* = 6.8

Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.8, 147.5, 133.2, 132.4, 131.9, 130.1, 129.0, 128.6, 121.9, 115.6, 47.2, 34.4, 30.6, 25.0, 24.1, 23.8, 20.8, 8.2.

***N*-(4-Bromo-2-mesitylnaphthalen-1-yl)methanesulfonamide (3va):** R_f = 0.80 (hexane : ethyl acetate 9:1); white solid; 36 mg (74%), (40 mg starting material taken, 6 mg stating material recovered); ^1H NMR (400 MHz, $CDCl_3$) δ 8.31-8.28 (m, 2H), 7.67-7.65 (m,3H), 7.01 (s, 2H), 6.34 (s, 1H), 2.35 (s, 3H), 2.34 (s, 3H), 2.07 (s, 6H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 138.2, 137.7, 136.6, 134.7, 133.6, 132.1, 132.0, 129.8, 128.7, 128.2, 127.8, 127.7, 124.2, 123.1, 42.0, 21.1, 20.5; ῡ = 3573, 2065, 1635 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{20}BrNO_2SNa$ 440.0290; Found 440.0273.

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NMR Spectra of Selected Compounds

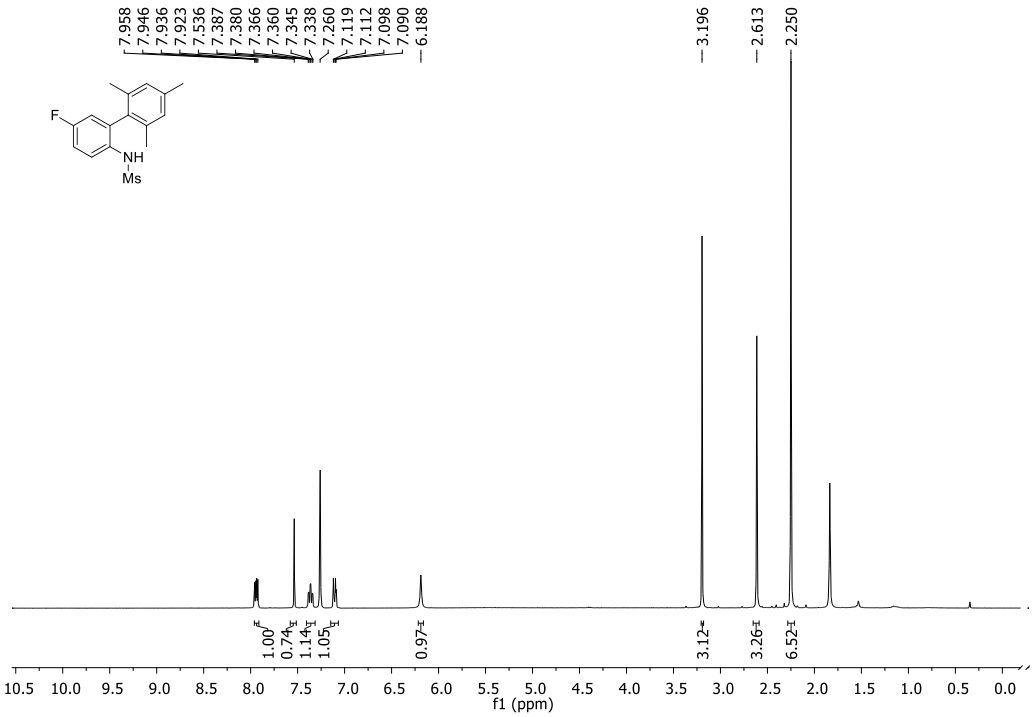


Figure 2.5. [1]H NMR spectrum of *N*-(5-fluoro-2' ,4' ,6'-trimethyl-[1, 1'-biphenyl]-2-yl)methanesulfonamide **(3aa)**

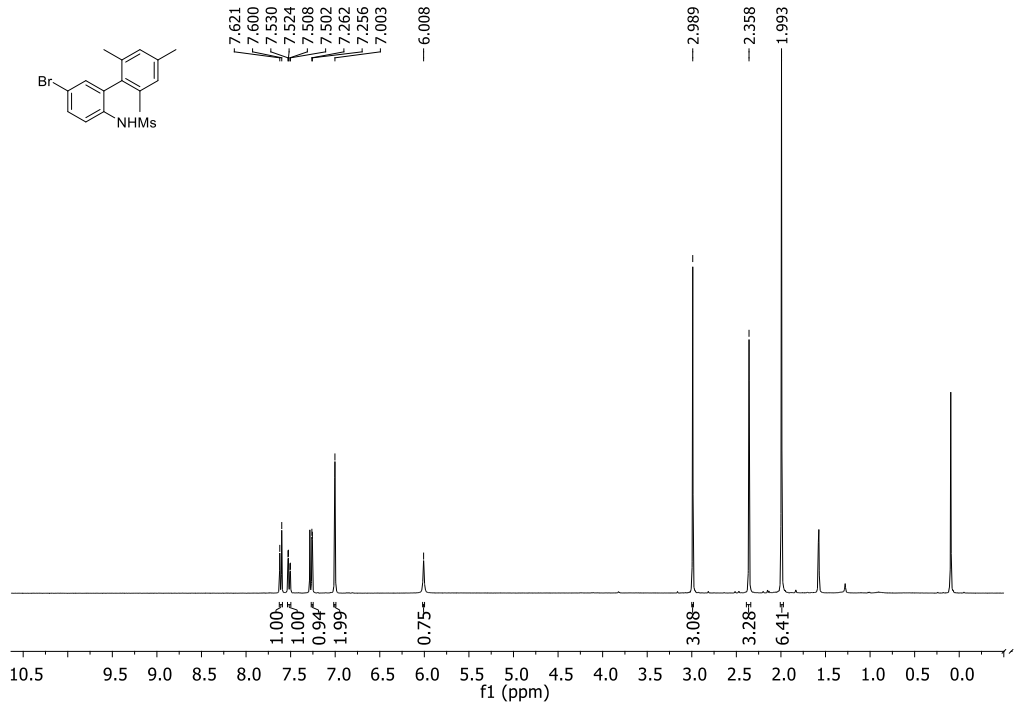


Figure 2.6. [1]H NMR spectrum of *N*-(5-bromo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3ba**)

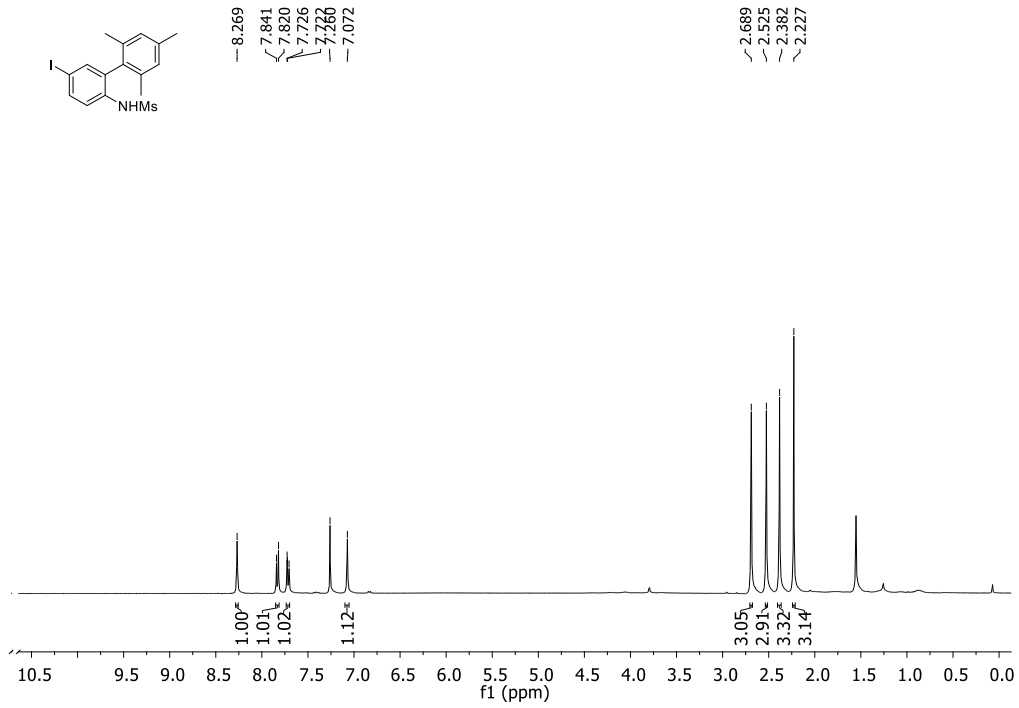


Figure 2.7. ^{1}H NMR spectrum of *N*-(5-iodo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3ca**)

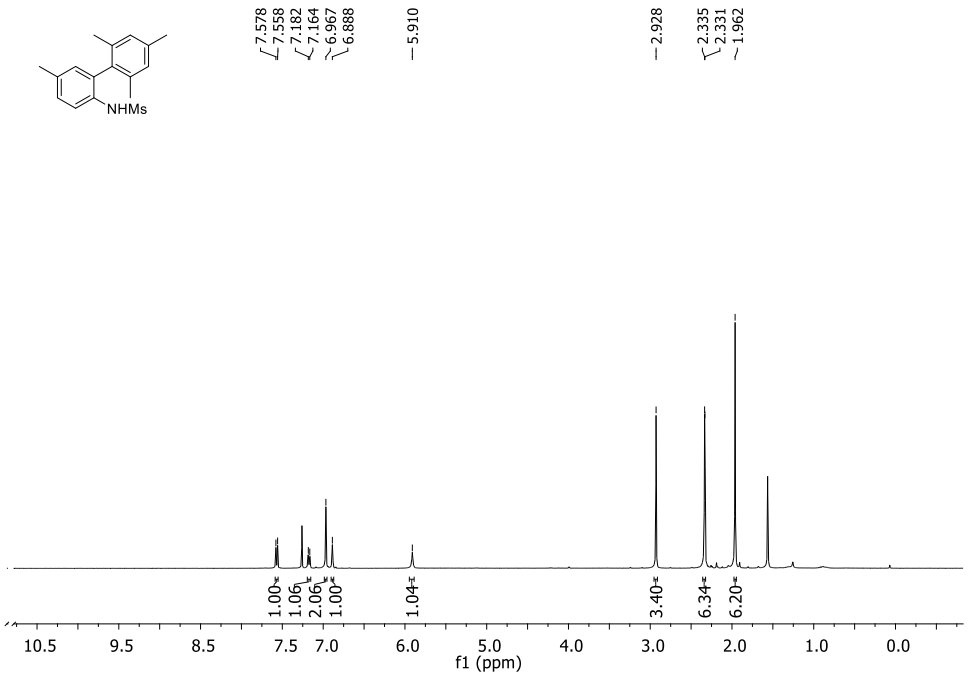


Figure 2.8. ^{1}H NMR spectrum of *N*-(2',4',5, 6'-tetramethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3da**)

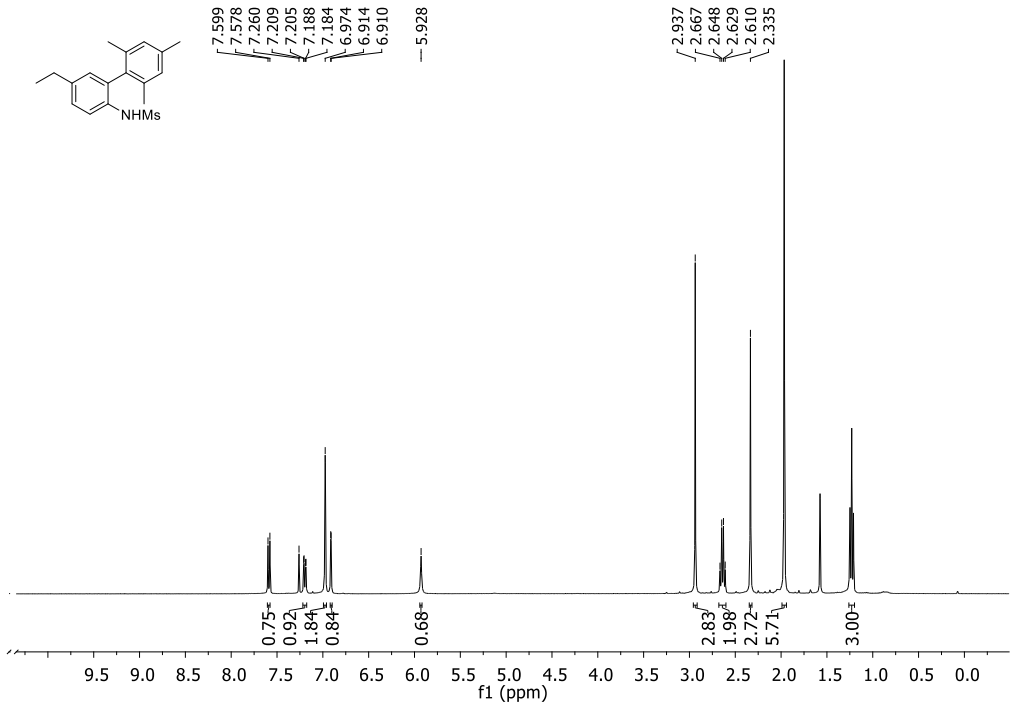


Figure 2.9. [1]H NMR spectrum of *N*-(5-ethyl-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3ea**)

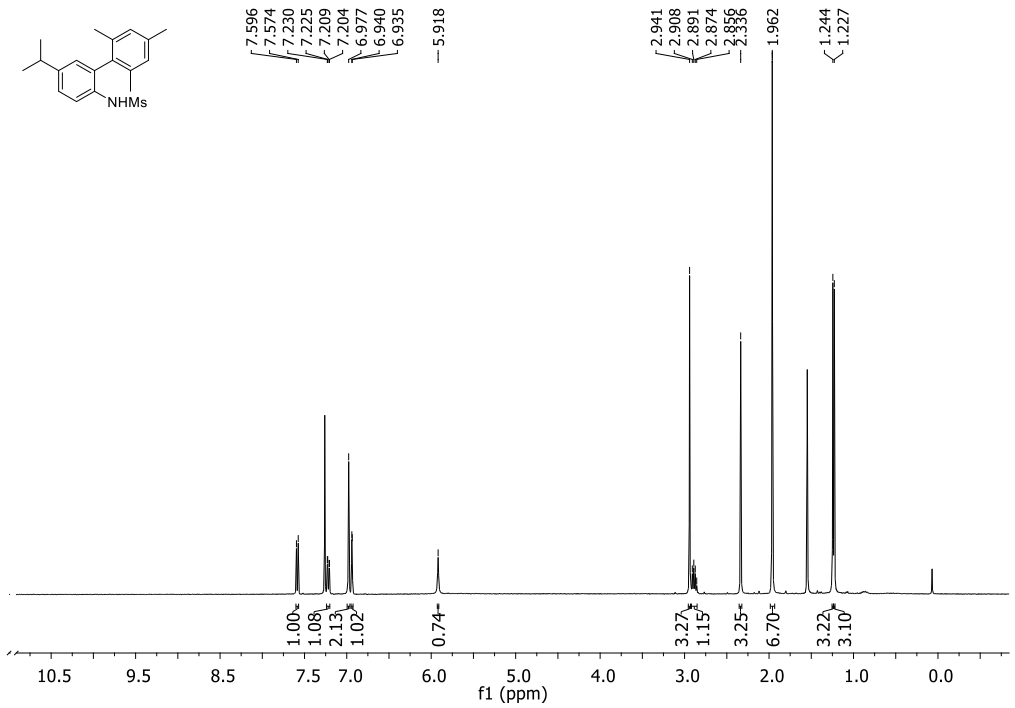


Figure 2.10.. [1]H NMR spectrum of *N*-(5-isopropyl-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3fa)**

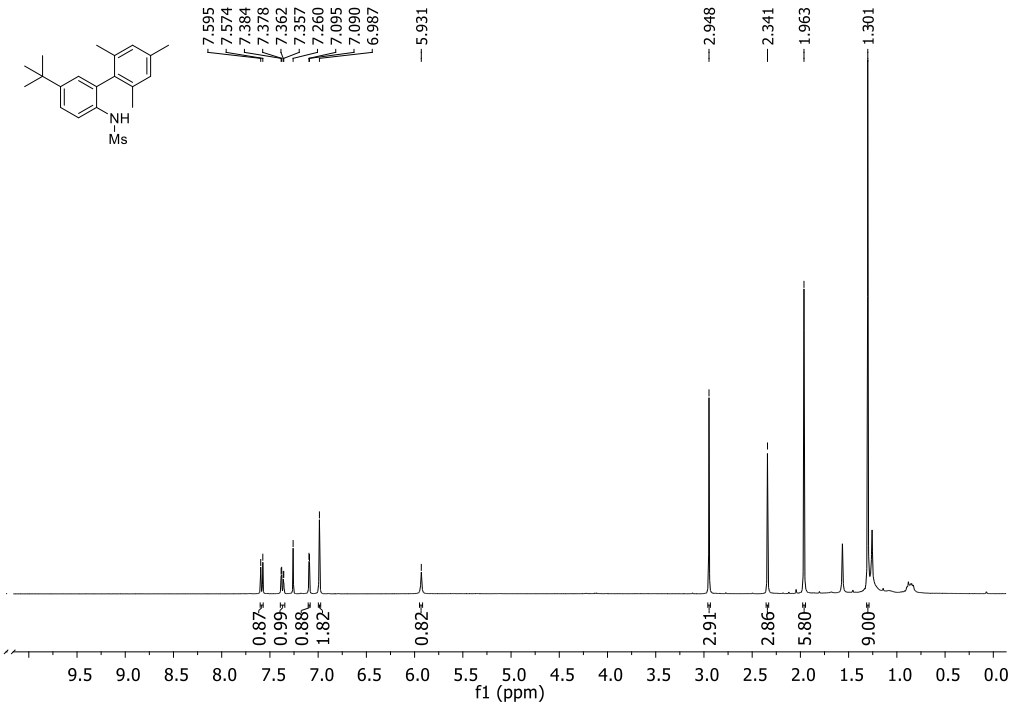


Figure 2.11. ^{1}H NMR spectrum of *N*-(5-(*tert*-butyl)-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3ga**)

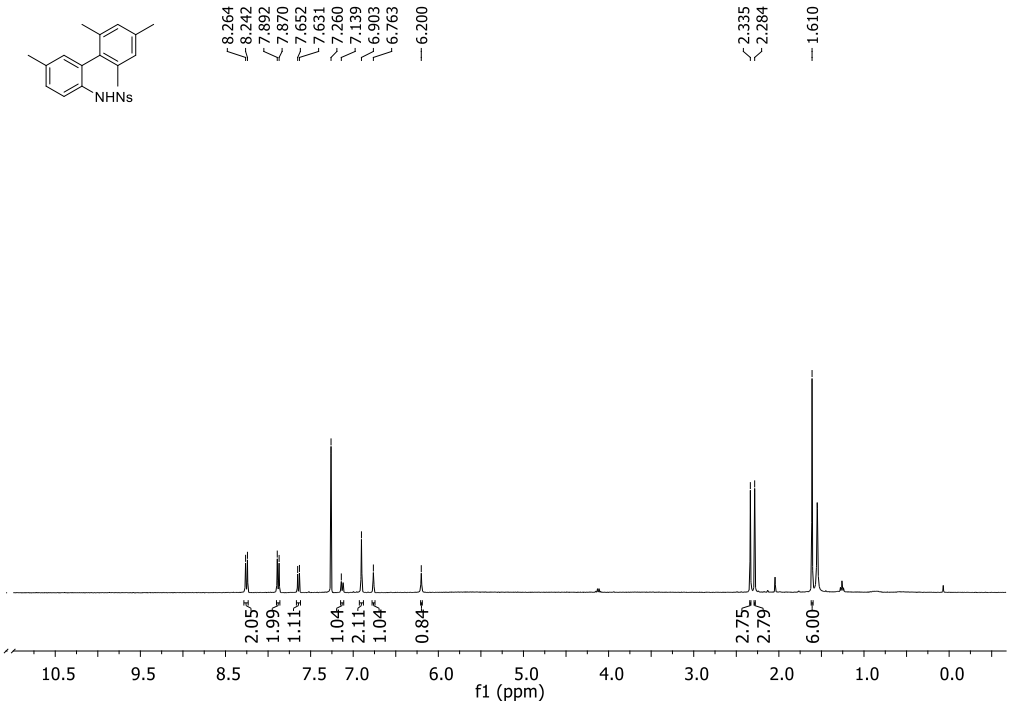


Figure 2.12. ^{1}H NMR spectrum of 4-nitro-*N*-(2',4',5', 6'-tetraimethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide **(3ha)**

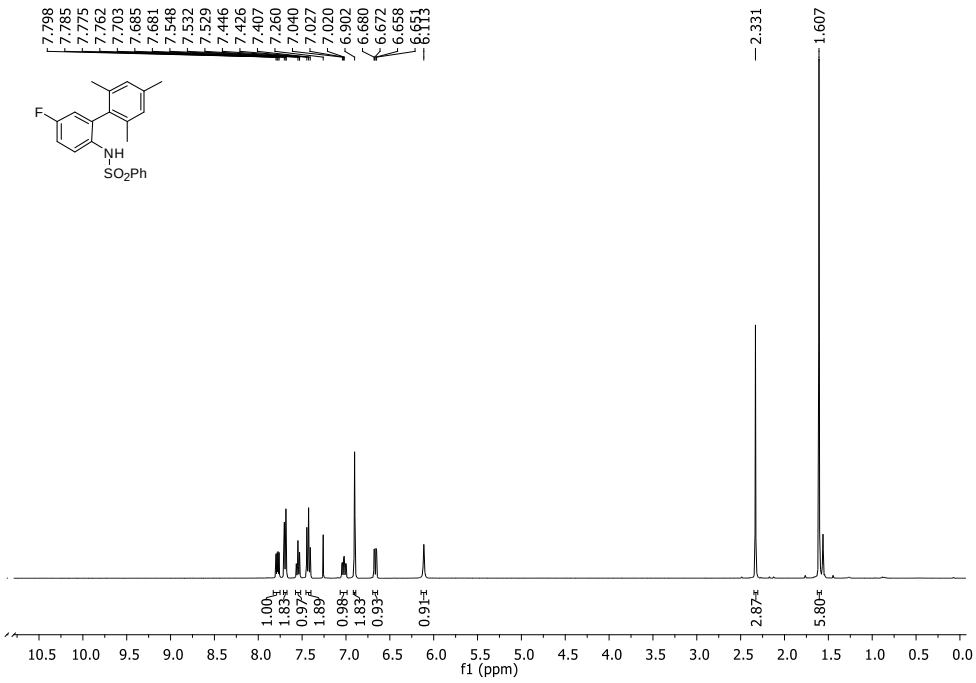


Figure 2.13. ^{1}H NMR spectrum of *N*-(5-fluoro-2',6'-dimethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (**3ia**)

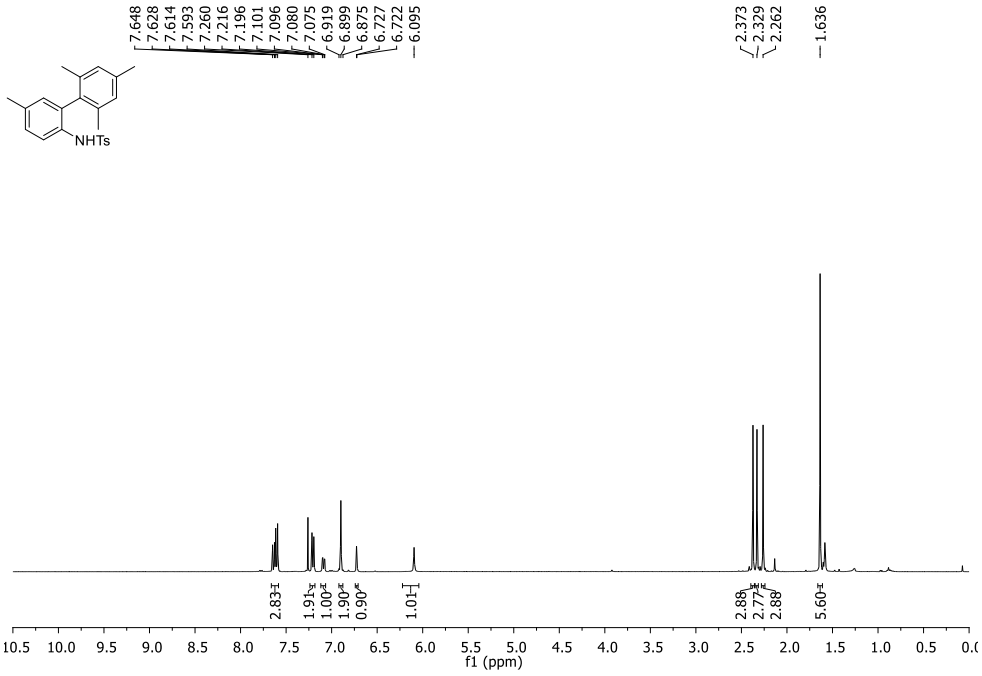


Figure 2.14. ^{1}H NMR spectrum of 4-methyl-*N*-(2',4' ,5' 6'-tetramethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (**3ja**)

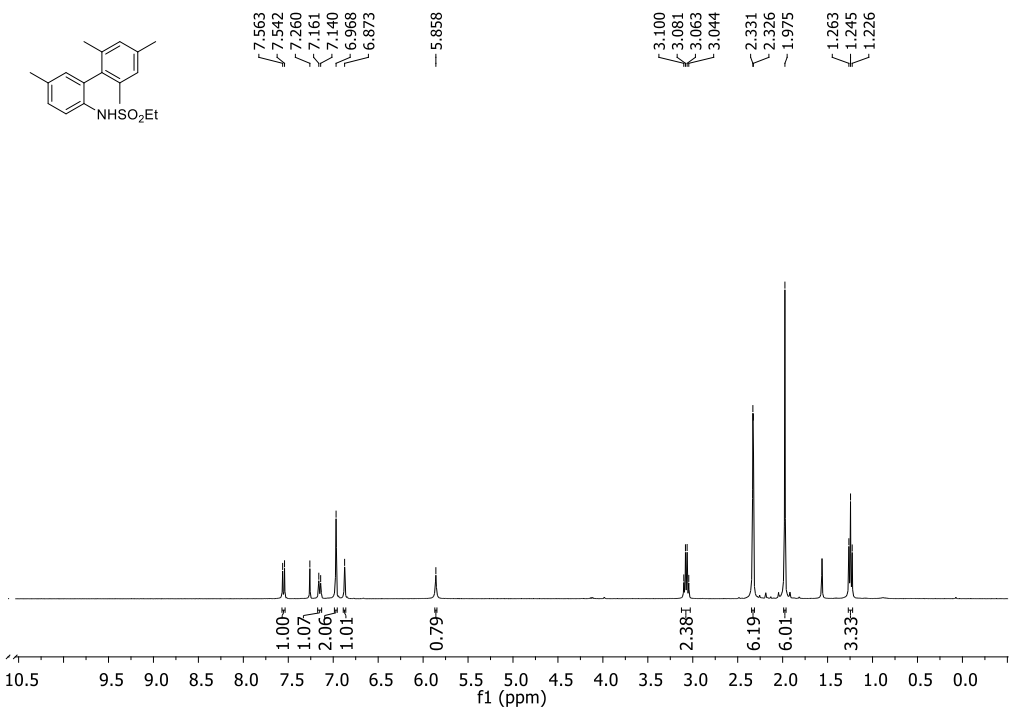


Figure 2.15. ^{1}H NMR spectrum of *N*-(2', 4' ,5' 6'-tetramethyl-[1,1'-biphenyl]-2-yl)ethanesulfonamide (**3ka**)

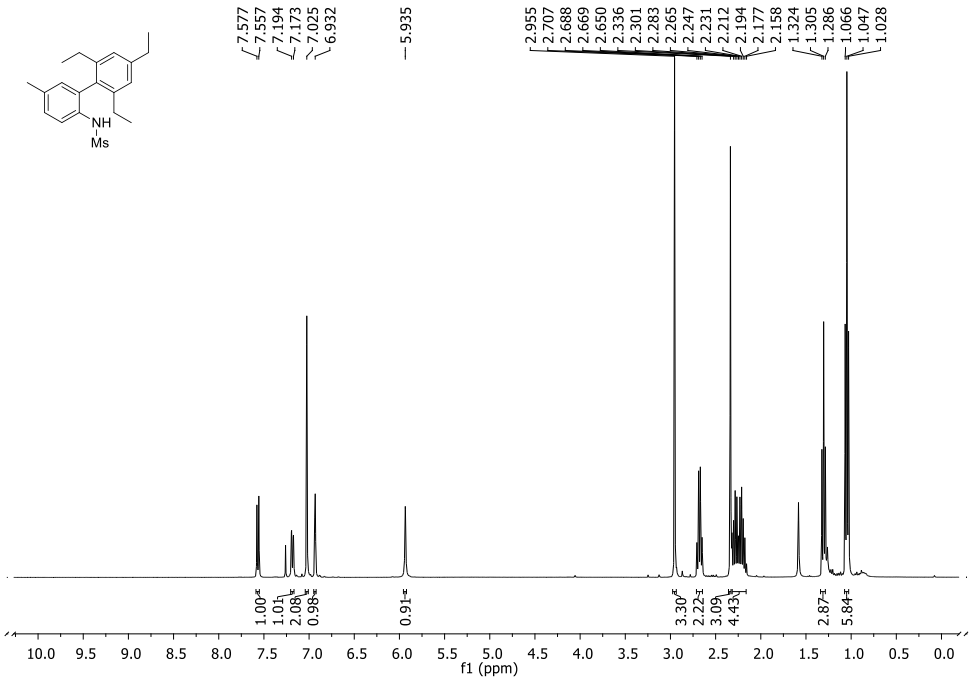


Figure 2.16. ^{1}H NMR spectrum of *N*-(2',4', 6'-triethyl-5-methyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3db**)

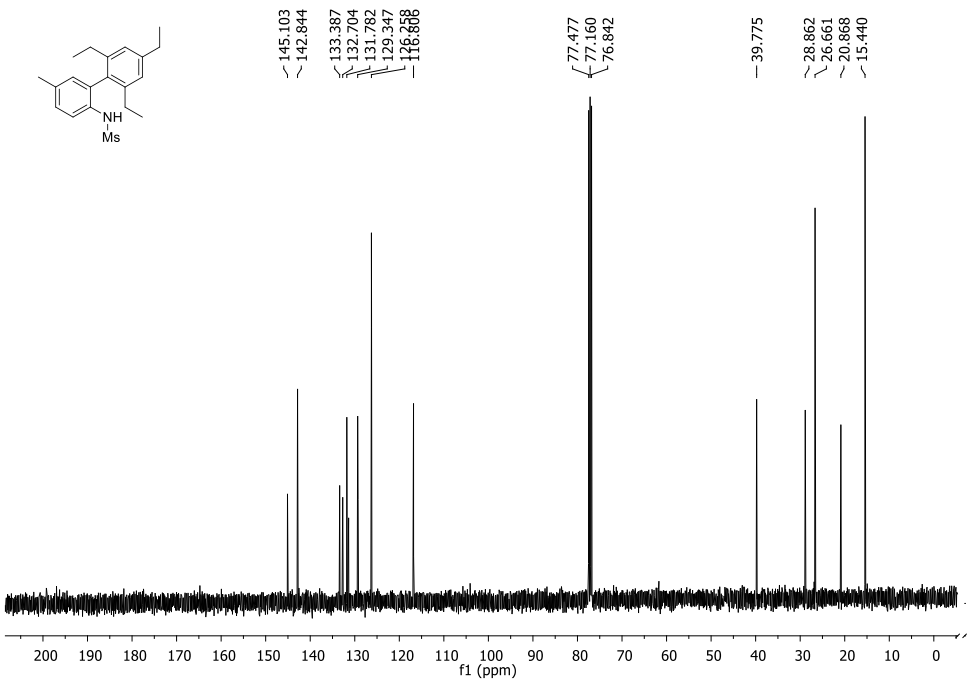


Figure 2.17. ^{13}C NMR spectrum of *N*-(2',4', 6'-triethyl-5-methyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3db**)

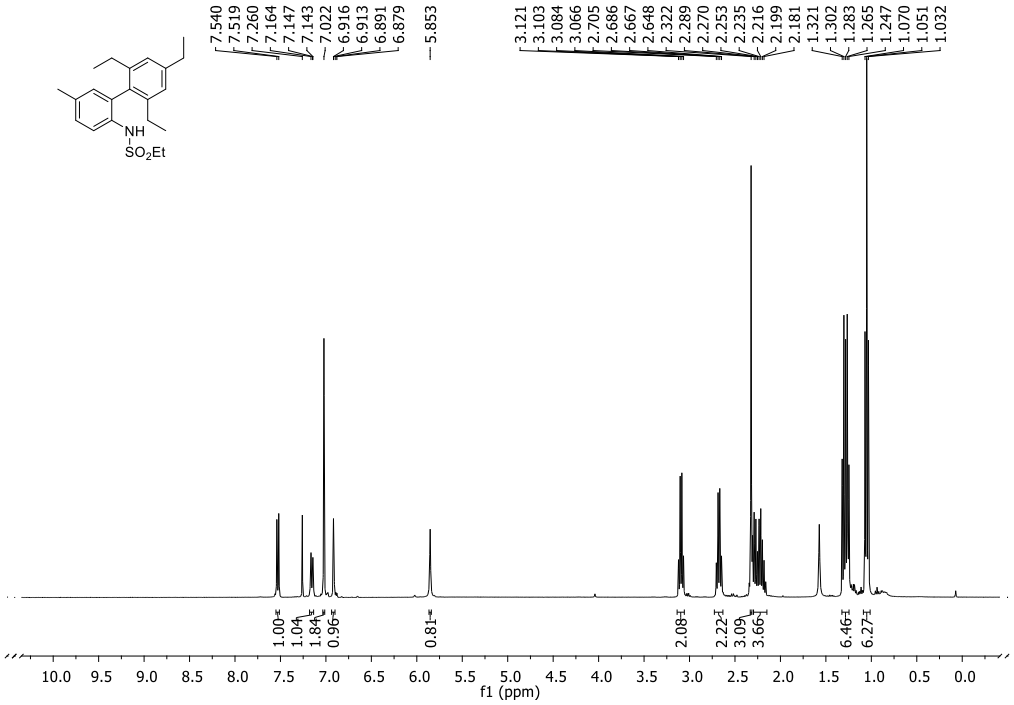


Figure 2.18. ^{1}H NMR spectrum of *N*-(2',4', 6'-triethyl-5-methyl-[1,1'-biphenyl]-2-yl)ethanesulfonamide (**3kb**)

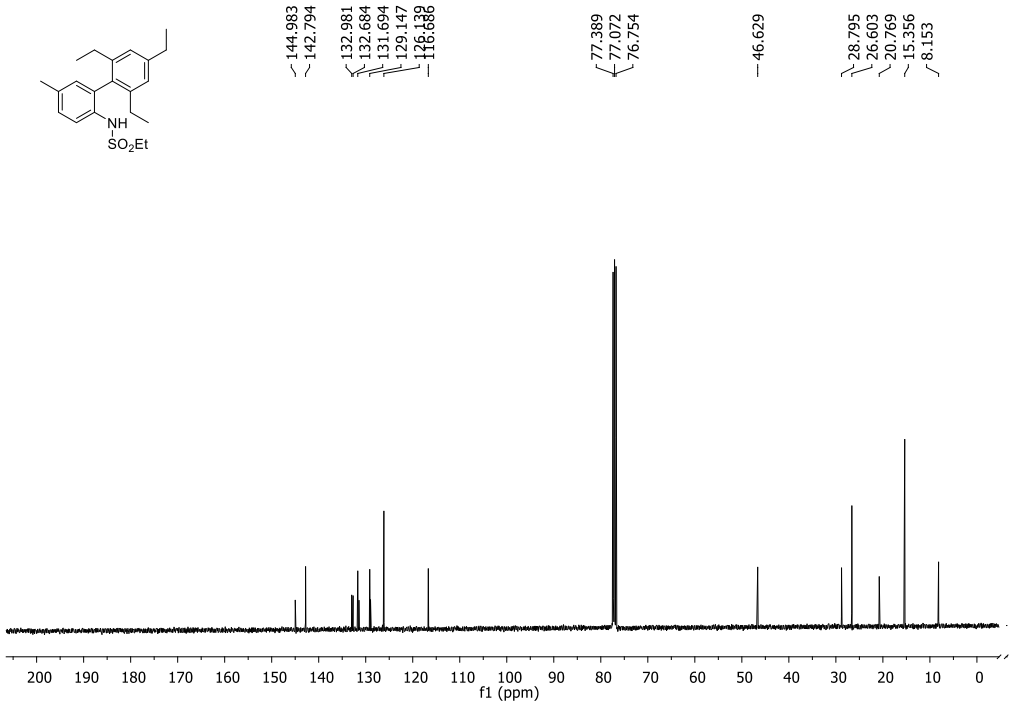


Figure 2.19. ^{13} C NMR spectrum of *N*-(2',4', 6'-triethyl-5-methyl-[1,1'-biphenyl]-2-yl)ethanesulfonamide (**3kb**)

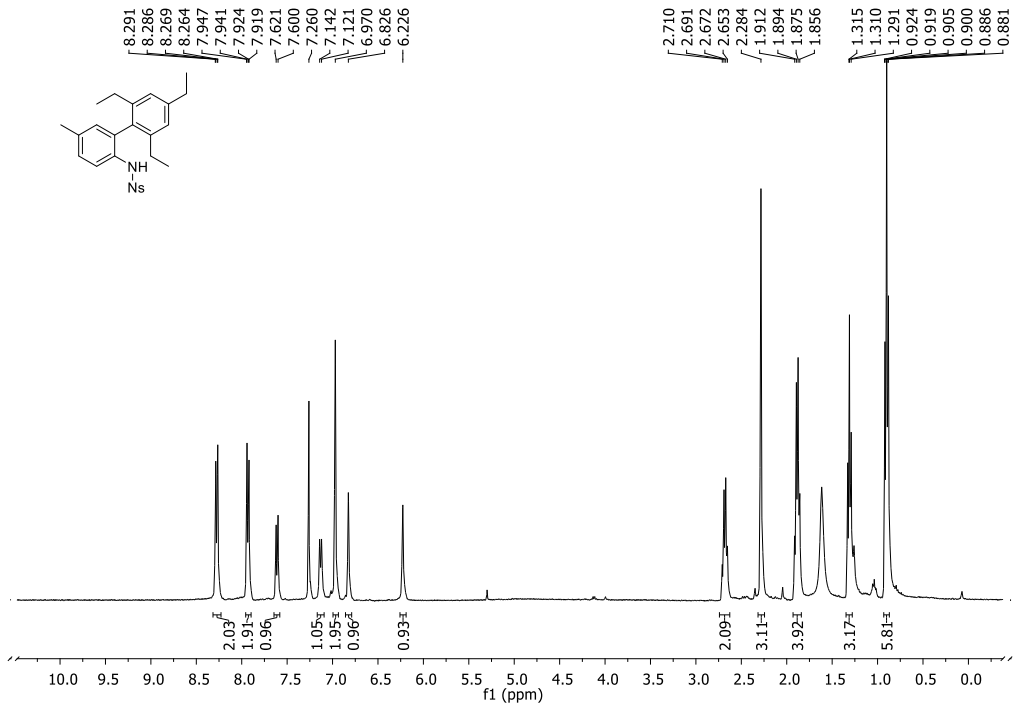


Figure 2.20. ^{1}H NMR spectrum of 4-nitro-*N*-(2',4', 6'-triethyl-5-methyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (**3hb**)

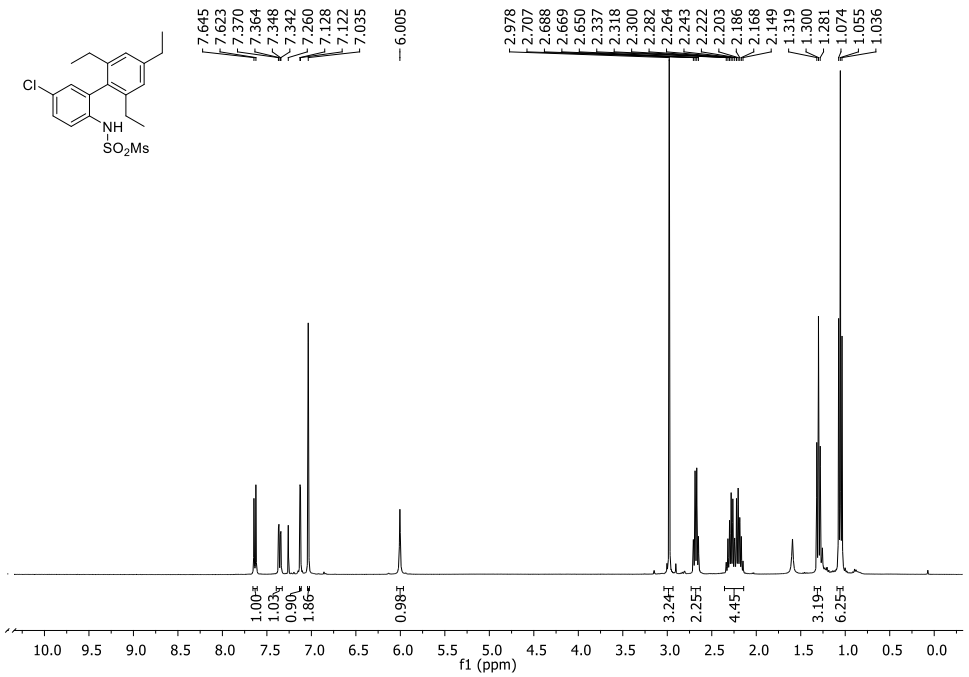


Figure 2.21. ^{1}H NMR spectrum of *N*-(5-chloro-2',4', 6'-triethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3pb**)

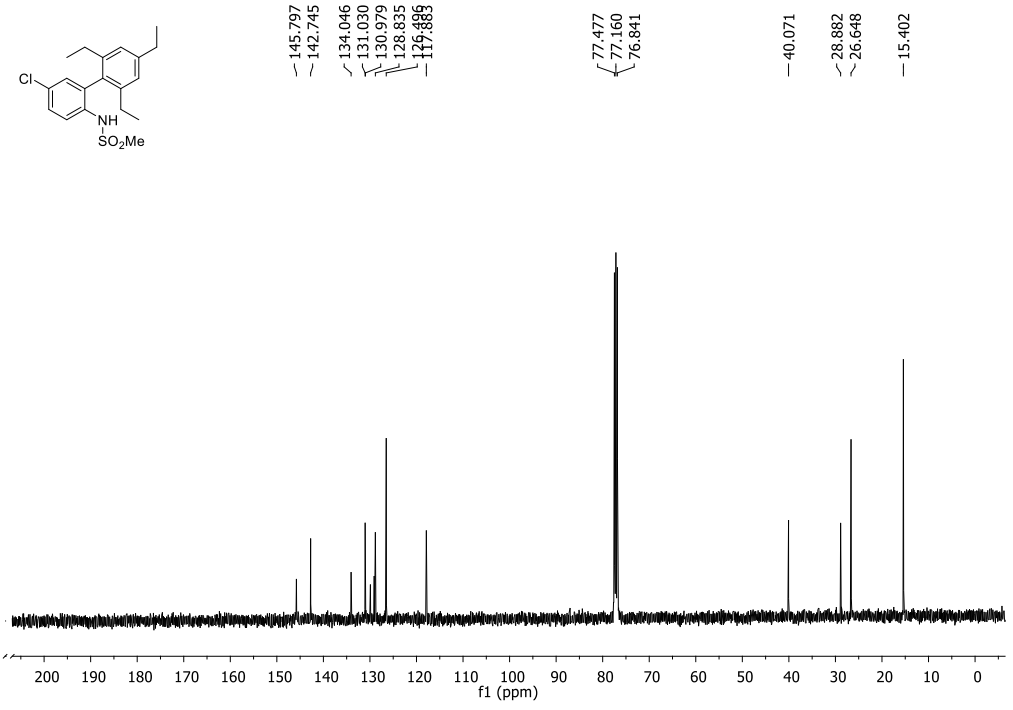


Figure 2.22. ^{13}C NMR spectrum of *N*-(5-chloro-2',4', 6'-triethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3pb**)

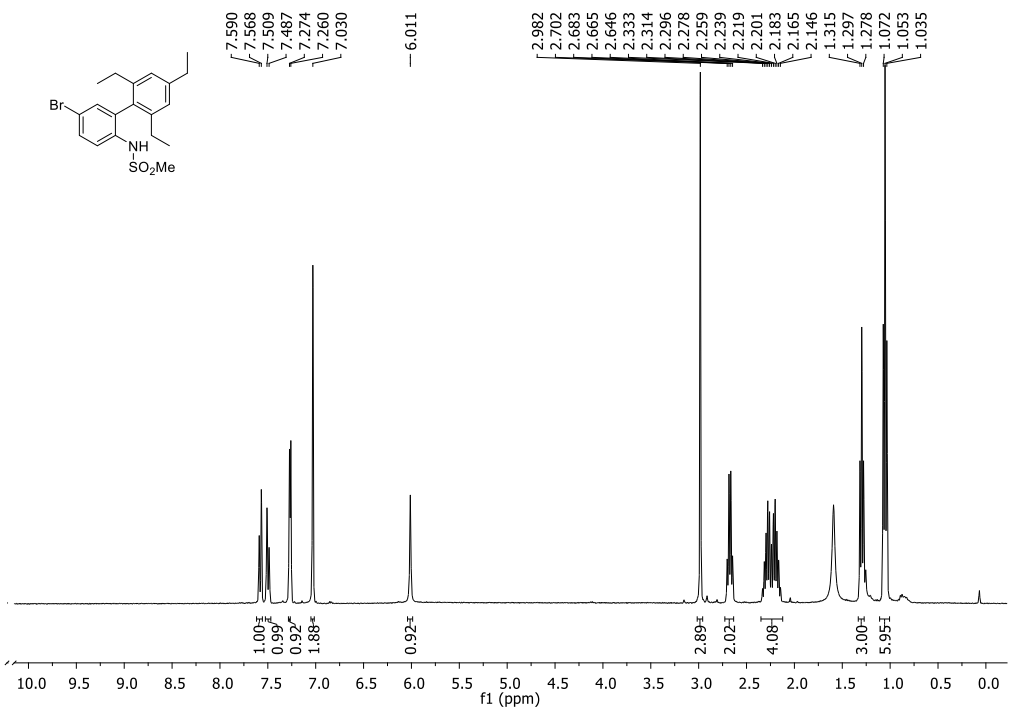


Figure 2.23. ^{1}H NMR spectrum of *N*-(5-bromo-2',4', 6'-triethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3bb**)

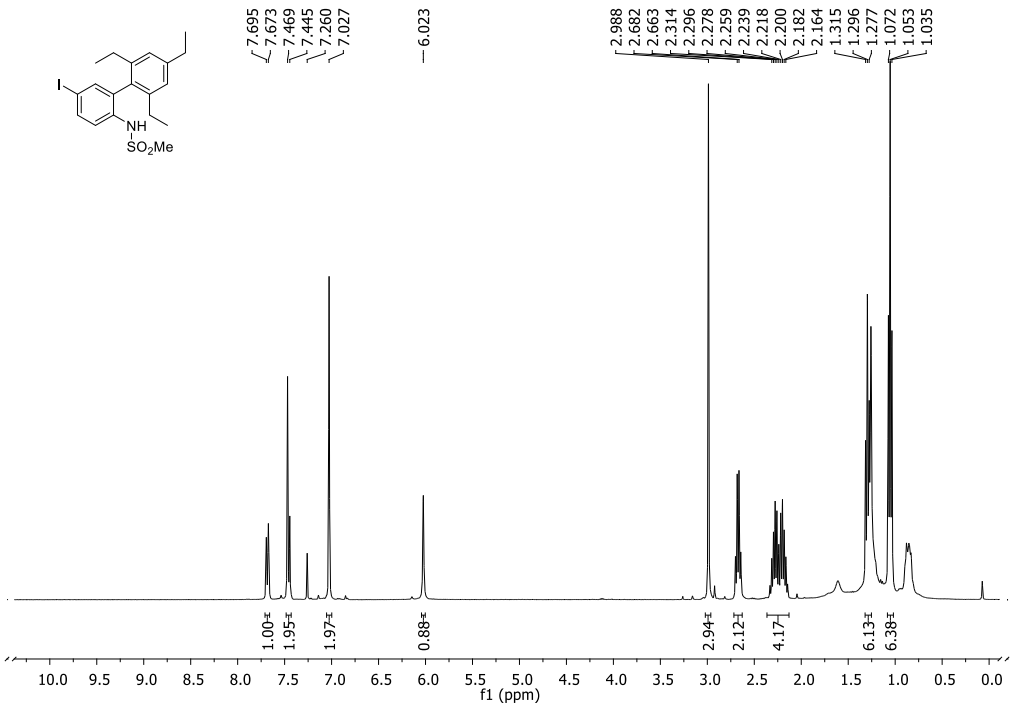


Figure 2.24. ^{1}H NMR spectrum of *N*-(2',4', 6'-triethyl-5-iodo-[1,1'-biphenyl]-2-yl)methanesulfonamide **(3cb**)

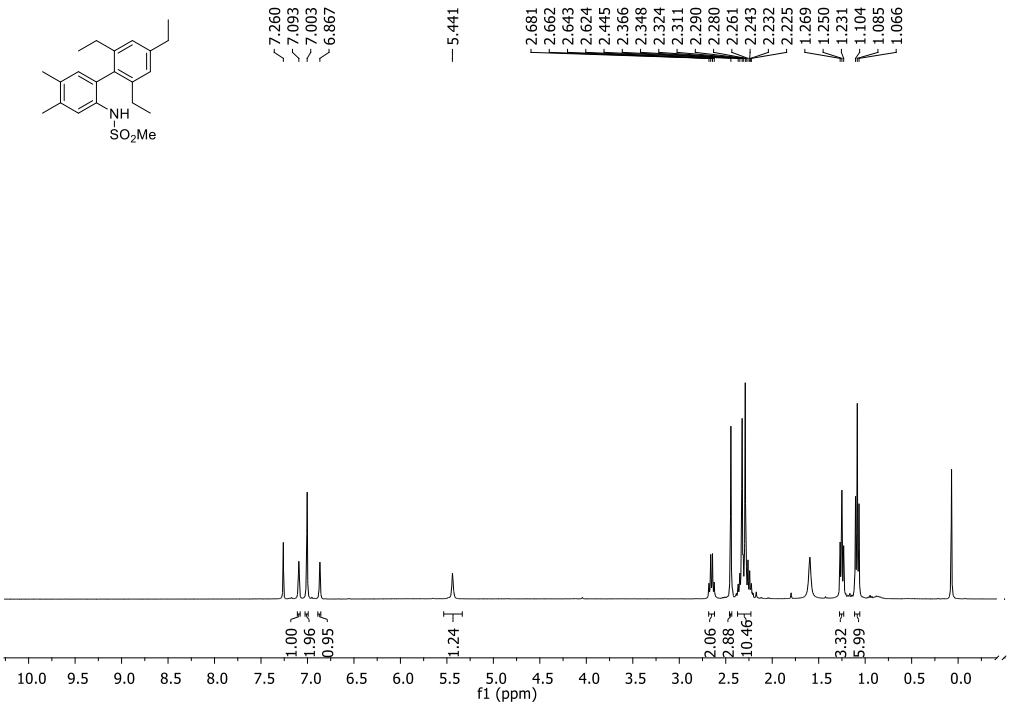


Figure 2.25. ^{1}H NMR spectrum of *N*-(2',4', 6'-triethyl-4,5-dimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3qb**)

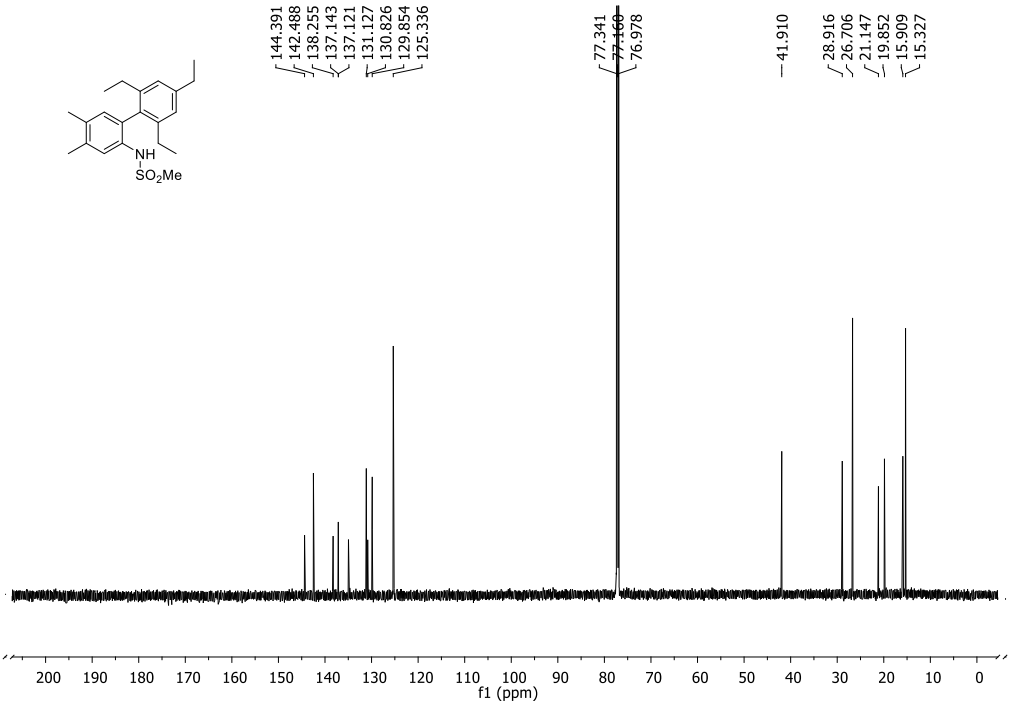


Figure 2.26. ^{13}C NMR spectrum of *N*-(2',4', 6'-triethyl-4,5-dimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3qb**)

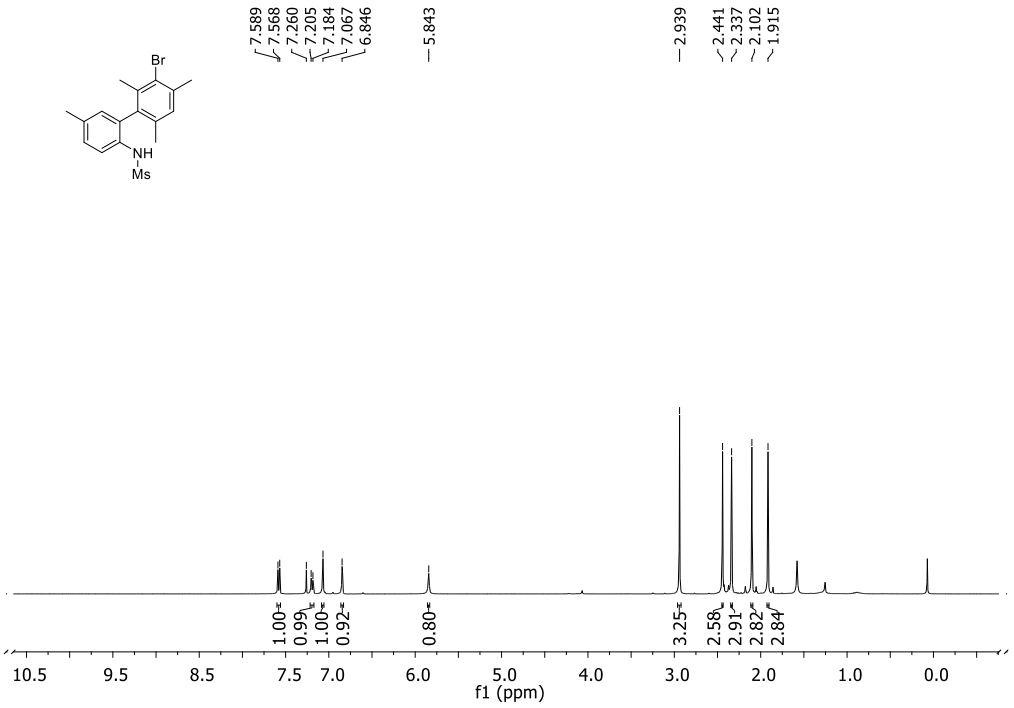


Figure 2.27. [1]H NMR spectrum of *N*-(2',4', 6'-triethyl-4,5-dimethyl-[1,1'-biphenyl]-2yl)methanesulfonamide (**3dc**)

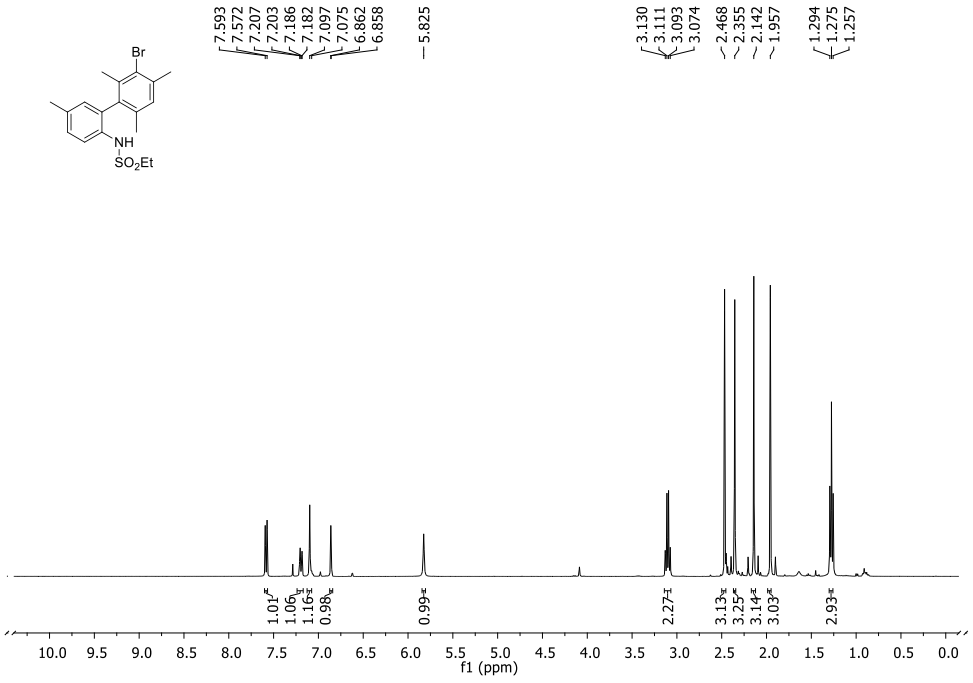


Figure 2.27. [1]H NMR spectrum of *N*-(3'-bromo-2',4',5, 6'-tetramethyl-[1,1'-biphenyl]-2-yl)ethanesulfonamide (**3kc**)

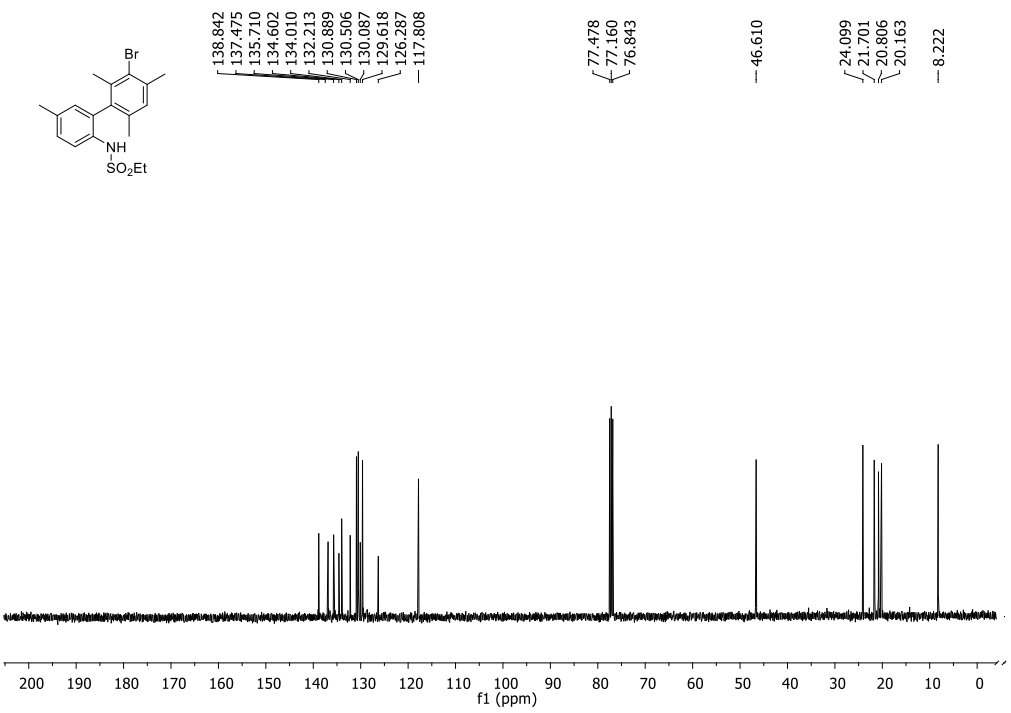


Figure 2.28. ^{13}C NMR spectrum of *N*-(3'-bromo-2',4',5, 6'-tetramethyl-[1,1'-biphenyl]-2-yl)ethanesulfonamide (**3kc**)

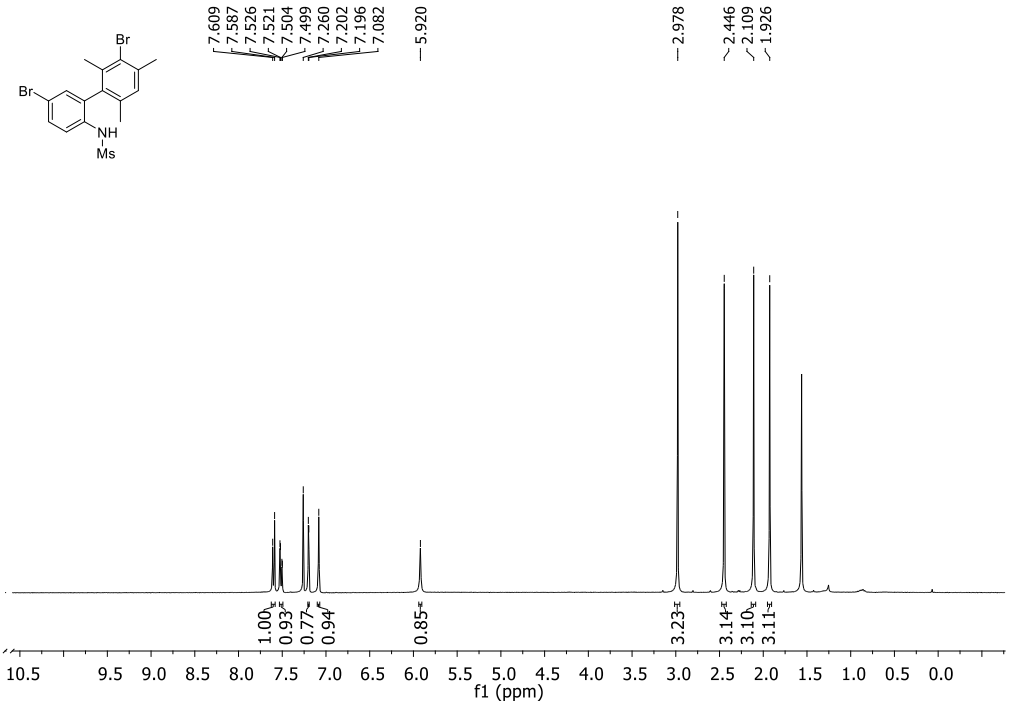


Figure 2.29. ^{1}H NMR spectrum of *N*-(3', 5-dibromo-2',4', 6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3bc**)

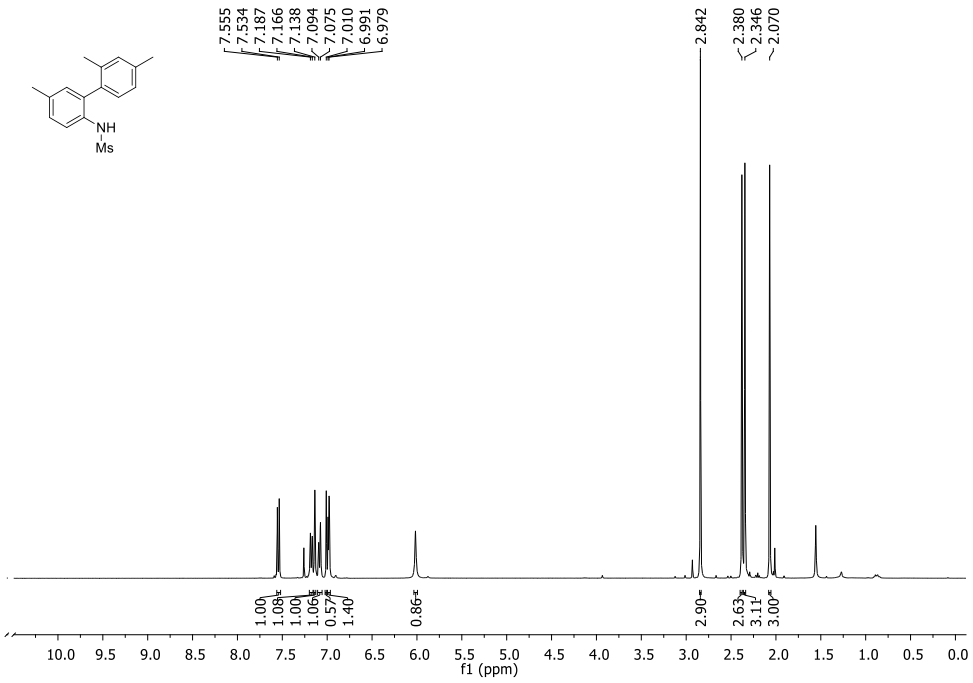


Figure 2.30. ^{1}H NMR spectrum of *N*-(2',4', 5'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3dd**)

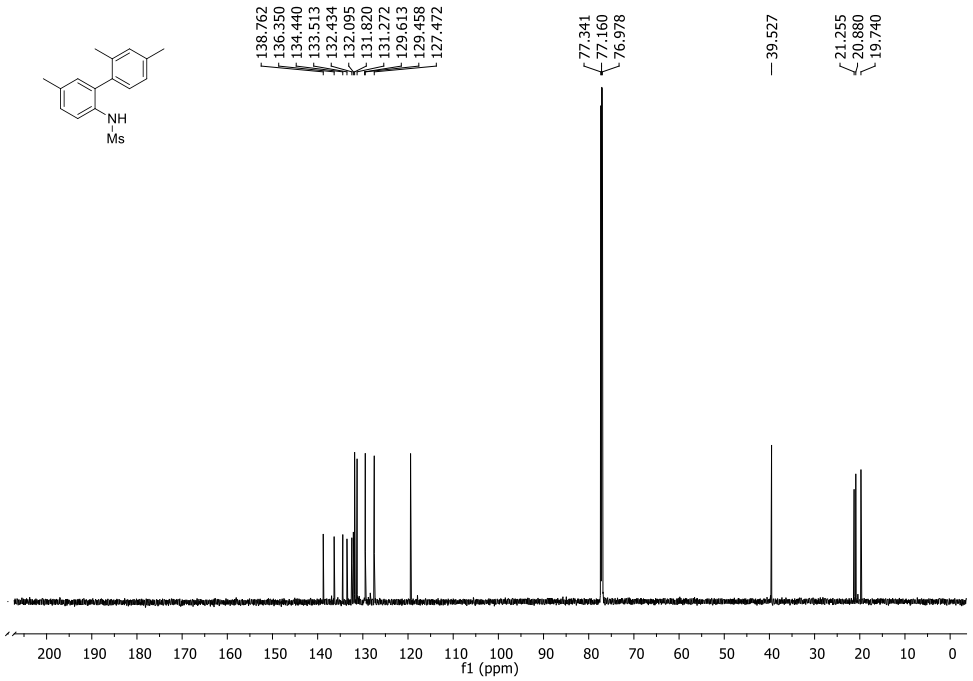


Figure 2.31. ^{13}C NMR spectrum of *N*-(2',4', 5'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3dd**)

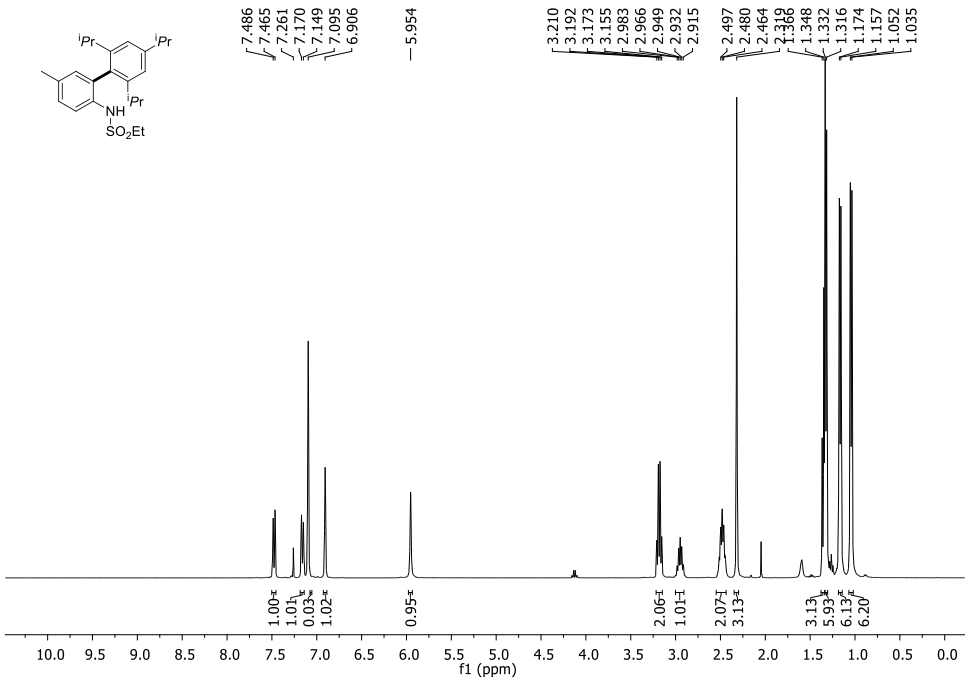


Figure 2.32. [1]H NMR spectrum of *N*-(2',4',6'-triisopropyl-5-methyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**3ke**)

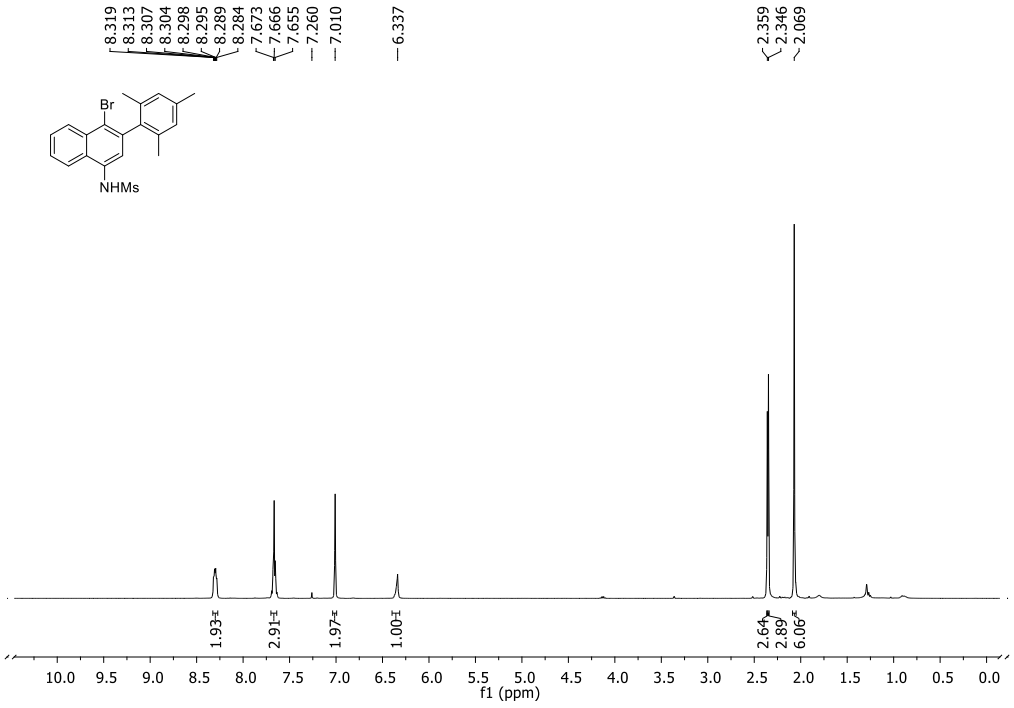


Figure 2.33. [1]H NMR spectrum of *N*-(4-bromo-2-mesitylnaphthalen-1-yl)methanesulfonamide **(3va)**

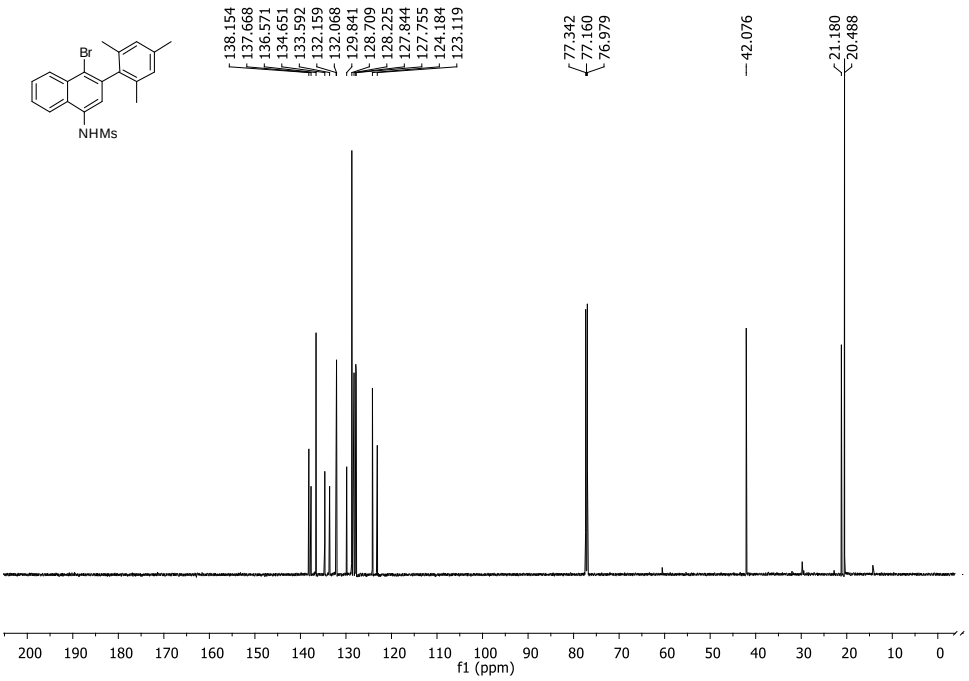
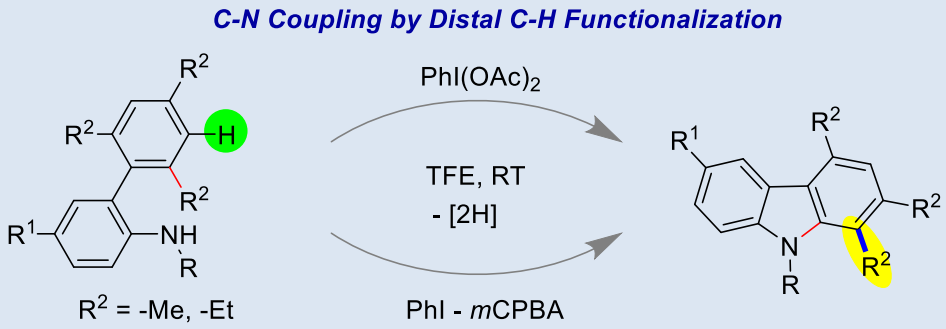


Figure 2.34. ^{13}C NMR spectrum of *N*-(4-bromo-2-mesitylnaphthalen-1-yl)methanesulfonamide **(3va)**

CHAPTER 3

Nitrenium ion in Distal C-H Functionalization for Synthesis of Carbazoles

3.1 ABSTRACT



This chapter focuses on generation of nitrenium ion intermediate from a biarylsulphonamide *via* nitrenium ion followed by migration of alkyl which lead to the synthesis of carbazoles Stoichiometric amount of iodine(III) reagent has been used, or it has been generated under in-situ conditions by using iodobenzene and an oxidant like meta perchlorobenzoic acid. This strategy of C-H amination is highly beneficial for synthesizing 1,2,4-trialkyl substituted carbazoles at ambient temperature and in an open atmosphere.

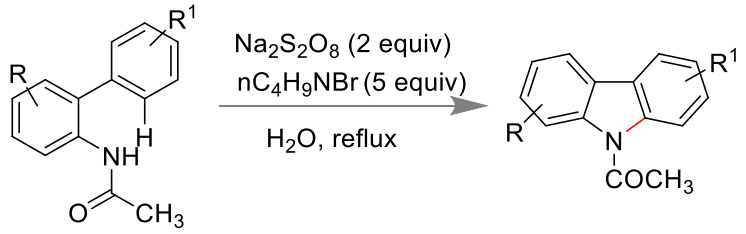
3.2 INTRODUCTION

The synthesis of nitrogenous heterocycles via C-N coupling has gained prominence for ages.[1-3] Metal free approach for C-H amination is more significant and preferable than the conventional approach for metal-mediated C-N bond synthesis methods to construct amines[4, 5, 6]. As a result, metal free techniques involving hypervalent iodine(III) reagents that are less toxic and inexpensive are highly desirable for oxidative C-N bond synthesis[7, 8] and in many

cross-dehydrogenative coupling (CDC) reactions.[9-11] The environmentally benign nature, ease of availability, stability, and controlled oxidizing ability of hypervalent iodine reagents make them highly versatile and valuable for synthetic transformations.[12-17] Amines (or amides) react with hypervalent iodine(III) mediated to produce nitrenium ion, an electrophilic species highly recognized as a potential synthetic intermediate derived in synthetic conversions. Mechanistic studies involve forming nitrenium ions involving ligand exchange of iodine(III) with amines accompanied by reductive elimination of iodoarene. Herein we have exemplified an intramolecular C-N coupling reaction using the concept of distal C-H bond functionalization strategy involving alkyl migration to synthesize carbazoles. The biarylsulfonanilides were made to react with stoichiometric amounts of phenyliodine diacetate (PIDA) or iodine (III) was *in-situ* obtained from iodobenzene(PhI)-*meta*-chloroperbenzoic acid (*m*CPBA) combination in TFE at room temperature. Our focus was to carry out the synthetic transformations from nitrenium ion intermediates using distal C-H functionalization. Previous approaches involving intramolecular C-H amination strategies for constructing carbazole motifs are centered on proximal C-H bond functionalization, some of which have been discussed later.[18] Carbazole motifs are widespread and abundantly found in various pharmaceutical and natural products.[14] This has led to devise an approach for multiple methods to develop carbazoles.

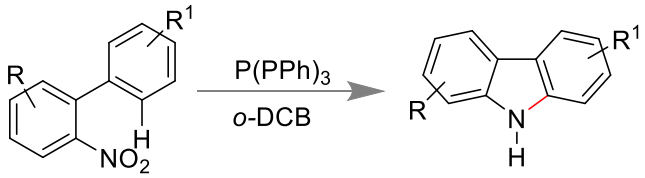
3.3 Proximal C-H Bond Functionalization reactions.

Natarajan group had synthesized N substituted carbazoles using the proximal C-H Bond functionalization approach.[19] Proximal C-H bond functionalization took place position forming carbazoles. Potassium peroxodisulfate and TBABr in combination, generated the N-centered radical followed by an intramolecular attack by the arene, led to the formation of desired product proximal C-H bond functionalization.



Scheme 3.1 Proximal C-H Bond functionalization using potassium peroxodisulfate.

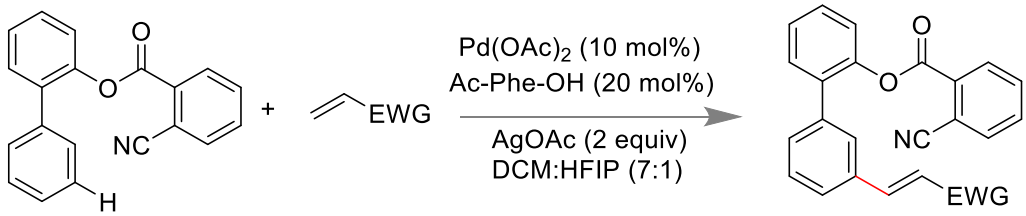
Carbazole synthesis via proximal C-H bond functionalization was achieved using triphenylphosphine in o-dichlorobenzene. Nitrobiphenyl underwent reductive deoxygenation generating N-centered radical. Cyclization took place with functionalization at the proximal C-H bond.



Scheme 3.2 Proximal C-H Bond functionalization using triphenyl phosphine.

3.4 Distal C-H Bond functionalization Reactions.

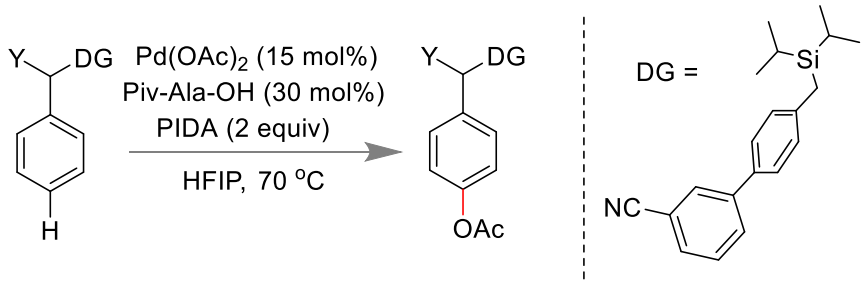
Distal C-H functionalization assisted by nitrile-based template using Palladium catalyst for olefination of a biaryl system has been reported by Maiti and co-workers.[20] The reaction proceeded with excellent regioselectivity and stereoselectivity, producing a good synthetic yield of the functionalized olefin in biaryl motif. The olefination occurred at a distal *meta* position instead of proximal ortho olefination.



Scheme 3.3 Selective distal C–H olefination of biaryl motif catalysed by Pd.

Para selective C-H acetoxylation was reported using silicon containing biaryl template using palladium metal and using phenyl iodine diacetate as the acetoxy source.[21] The distal C-H

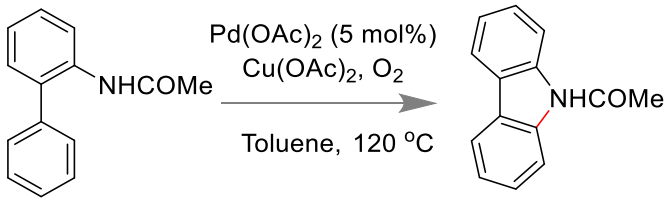
functionalization occurred at site-selective *para* position with help of directing group approach by forming a D-shaped assembly and hence termed as D-shaped template-assisted para C-H functionalization.



Scheme 3.4 D-shaped template assisted *para* C-H functionalization.

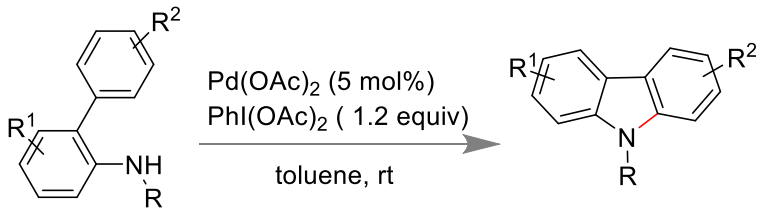
3.5 C-H Amination Methods for Synthesis of Carbazoles.

Methods for developing a C-H amination strategy are a significant target in organic synthesis. Traditional metal-mediated approach for C-H amination employing Palladium (Pd) assisted by copper acetate ($Cu(OAc)_2$) as co-oxidant was developed by Buchwald.[22] The strategy to prepare such heterocyclic scaffold carbazole involved C-H activation by Palladium and copper. Copper acetate was utilized to convert Pd(0) to Pd(II).



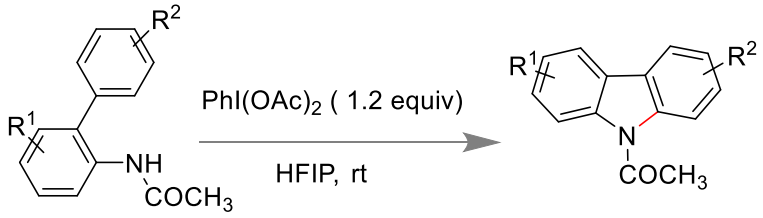
Scheme 3.5 C-H amination for the synthesis of carbazole by bimetallic approach.

A few years later, Gaunt reestablished the oxidative C-N coupling using palladium independently phenyliodine diacetate (PIDA).[23] The reaction took place by Pd(II)/Pd(IV) catalytic cycle followed by reductive elimination from Pd(IV) state, forming desired C-H amination. The role of the oxidant PIDA was to oxidize Pd(II) to Pd(IV) to attain desired carbazole as the product.



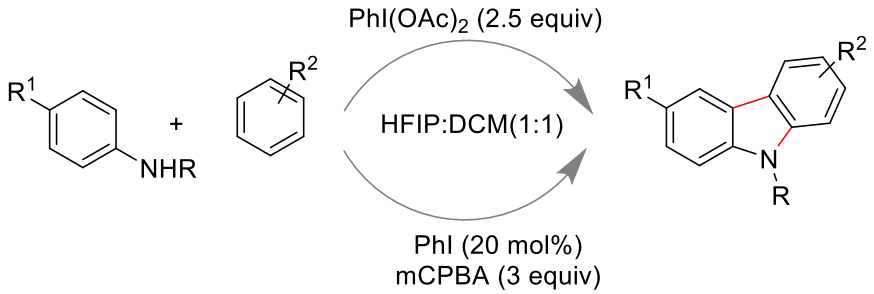
Scheme 3.6 Carbazole synthesis *via* bimetallic approach.

C-H amination by C-N coupling simply by using hypervalent iodine(III) reagent was developed by Antonchick and co-workers.[24] The transformation of 2-acetaminobiphenyl to *N*-acetylcarbazole in the presence of an oxidant like (diacetoxy)iodobenzene at ambient temperature led to the synthesis of triazoles.



Scheme 3.7 Synthesis of carbazole by metal free approach.

Carbazole synthesis by intermolecular annulation processes revolves with iodine(III) condition has been developed by Mal and co- workers.[14, 15] The demerits of the protocol involved use of larger proportions of oxidants like phenyl iodine diacetate (PIDA) and *meta*-perchlorobenzoic acid (*m*CPBA).

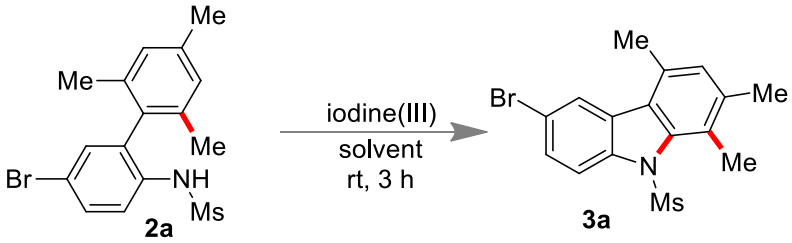


Scheme 3.8 Intermolecular C-H amination for carbazole synthesis.

3.6 RESULTS AND DISCUSSIONS

The reaction was optimized using *N*-(5-bromo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulphonamide (**2a**) and several oxidants and solvents were screened to obtain the desired carbazole. The biaryl sulfonamide (**2a)** was synthesized by taking *N*-(4-bromophenyl) and mesitylene by studying earlier reports. When the biaryl sulfonamide **2a** was made to react with 1.0 equiv of PIDA in 2,2,2-trifluoroethanol (TFE) at room temperature, 6-bromo-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (**3a**) was produced with 90% yield as indicated (Table 3.1, entry 1). The product **3a** showed a rise in yield to (98%) (Table 1, entry 2) using 1.2 equiv of PIDA in solvent 2,2,2-trifluoroethanol. 1,1,1,3,3,3-hexafluoroisopropanol (HFIP), DCE or ACN were some of the solvents which were screened, which were less effective compared to TFE (entry 4-6). The reaction was sluggish, and the desired product was obtained in trace amount (entry 3). Other oxidants like $PhI(OCOCF_3)_2$ (PIFA), which is a comparatively more potent oxidant, resulted in a reduction of yield to about 57% (entry 7). A substantial rise in yield was obtained using PhI(OPiv)2 as an oxidizing agent (entry 8).

Table 3.1. Optimization of Method A



entry	oxidant (equiv)	solvent	yield (%)[a]
1	PIDA (1.0)	TFE	90
2	PIDA(1.2)	TFE	98
3	PIDA(1.2)	DCM	<5%
4	PIDA (1.5)	HFIP	53
5	PIDA (1.5)	DCE	41
6	PIDA (1.5)	ACN	29

7	$PhI(OCOCF_3)_2$ (1.2)	TFE	57
8	$PhI(OPiv)_2$ (1.2)	TFE	69

All reactions were done at room temperature. [a]yields of the isolated product after column chromatography

We targeted to achieve the desired carbazole to generate iodine(III) condition under *in situ* conditions. *N*-(5-bromo-2',4',6'-triethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2l**) chosen as the model substrate which was treated with catalytic amount of iodobenzene (20 mol%) in presence of oxidant 3-chloroperbenzoic acid (*m*CPBA) insolvent TFE . The targeted product 6-Bromo-1,2,4-triethyl-9-methylsulfonyl)-carbazole (**3l**) was formed with 48% yield (Table 3.2, entry 1). When solvent DCM was used in combination with HFIP in 1:1 mixture or TFE-DCM (1:1) by volume, no such improvement in yield was observed (entry 2-4). It was observed that with the increase in the percentage of iodobenzene, an abrupt rise in yield was noted (entry 5).The maximum yield of product **3k** was obtained when 1.0 equivalent of PhI was utilized in combination with an oxidant like mCPBA (1.5 equiv) (entry 6). The results did not improve on substituting electron-withdrawing Cl- or electron-donating Me- on the iodobenzene ring to generate iodine(III) under *in situ* conditions (entry 7-8). The protocol of the C-H amination reaction and the optimized reaction condition of the pathways were applied and extended to an array of substrates that bear electron-donating and electron-withdrawing substrates (Figure 3.1 & 3.2). A stoichiometric amount of PIDA yielded the desired product in good to excellent yields. (Figure 3.1, **3a-3g)**.The decreased yield was observed when an electron withdrawing group was introduced in the aryl group at the C_2-position of anilide (Figure 3.1, **3h-3i**).This concretely proves that the nucleophilic part of the arene must be more electron-rich to attain the formation of carbazoles are formed in a more convenient approach. As a result, it was attempted to make the adjacent arene ring of the anilide more electron-rich by using triethyl substituted arenes. The reaction did not work

proficiently, which lead to the formation of unidentified products which were mostly inseparable. If an electron-withdrawing group is present at the *para* position of the anilide moiety, carbazole formation took place Figure 3.1, (**3j-3l**). When the protecting group was varied, the obtained products were formed in good yield to excellent yields (Figure 3.1, **3m-3r**).

The methodology involving PhI-*m*CPBA for *in-situ* generation of iodine(III) led to carbazole synthesis in relatively lesser yield than the stoichiometric version of PIDA as an oxidant. (Figure 3.2). Literature reports based on the generation of nitrenium helped to understand the mechanistic pathway as described in Figure 3.3. The reaction proceeded *via* iodine(III) reagent, which generated the nitrenium ion intermediate **3** in both cases of the stoichiometric amount of iodine(III) reagent or by an in-situ generation of iodine(III) by using PhI and *m*CPBA**.** This lead to nucleophilic attack from the adjacent arene to produce the carbocation **4** followed by migration of alkyl group in successive steps and deprotonation gave rise to the formation of the desired aromatized carbazole **5**. The role of solvent TFE is vital in determining the yield of the reaction. The reaction was sluggish when DCM was solely used as a solvent. It is observed that the intermediate nitrenium ion formed is stabilized in polar non-nucleophilic solvent TFE, which gave rise to the optimum result. TFE also possesses hydrogen bonding of fluoroalcohol with the iodine(III) reagent described by Compton and co-workers.[25] It was noticed that with an increase in the percentage of TFE in DCM, the yield of product **3a** also rose, and the maximum product was obtained when TFE was solely used as a solvent(Figure 3.4).

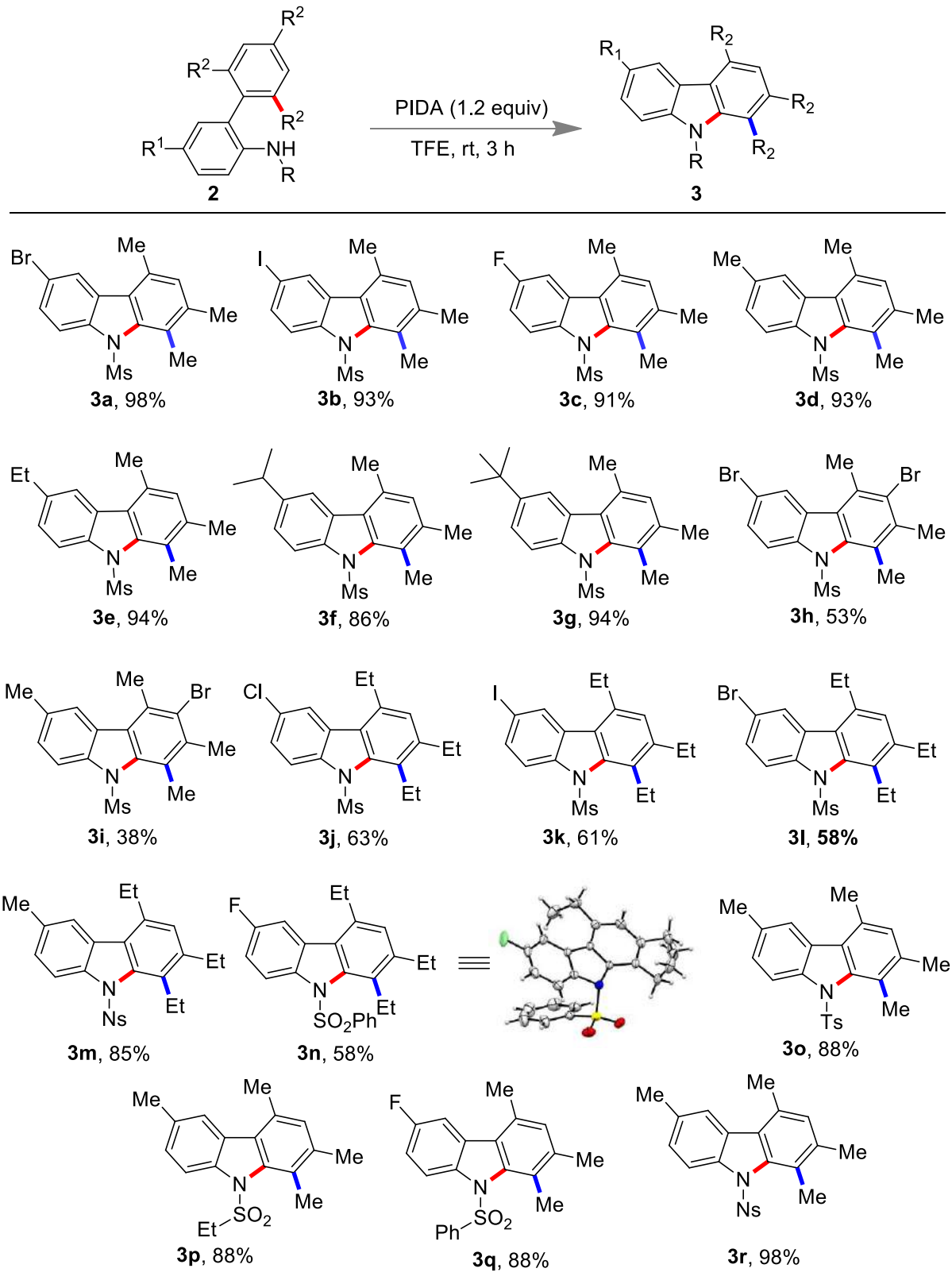
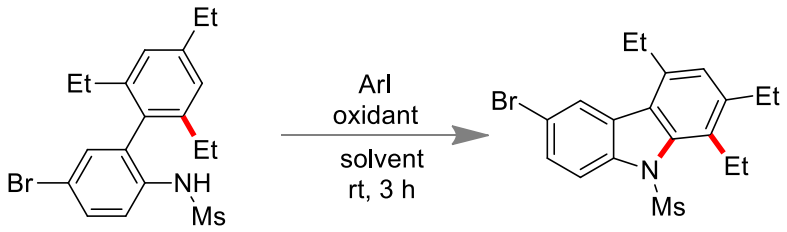


Figure 3.1. Substrate scope of biarylsufonamides using PIDA, Reaction conditions: 0.108 mmol of 2 and 1.2 equiv of PIDA in TFE (0.2 M)

Table 3.2 Optimization of Method B



2l **3l**

entry	ArI (equiv)	oxidant (1.5 equiv)	solvent	yield (%)
1	PhI (0.2)	*m*CPBA	TFE	48
2	PhI (0.2)	*m*CPBA	HFIP	32
3	PhI (0.2)	*m*CPBA	DCM	12
4	PhI (0.2)	*m*CPBA	TFE/DCM (2:1)	48
5	PhI (0.5)	*m*CPBA	TFE	76
6	PhI (1.0)	*m*CPBA	TFE	89
7	Cl-C_6H_4-I (1.0)	*m*CPBA	TFE	64
8	Me-C_6H_4-I (1.0)	*m*CPBA	TFE	67

Reaction conditions: All reactions done at room temperature. Yields of isolated product after column chromatography

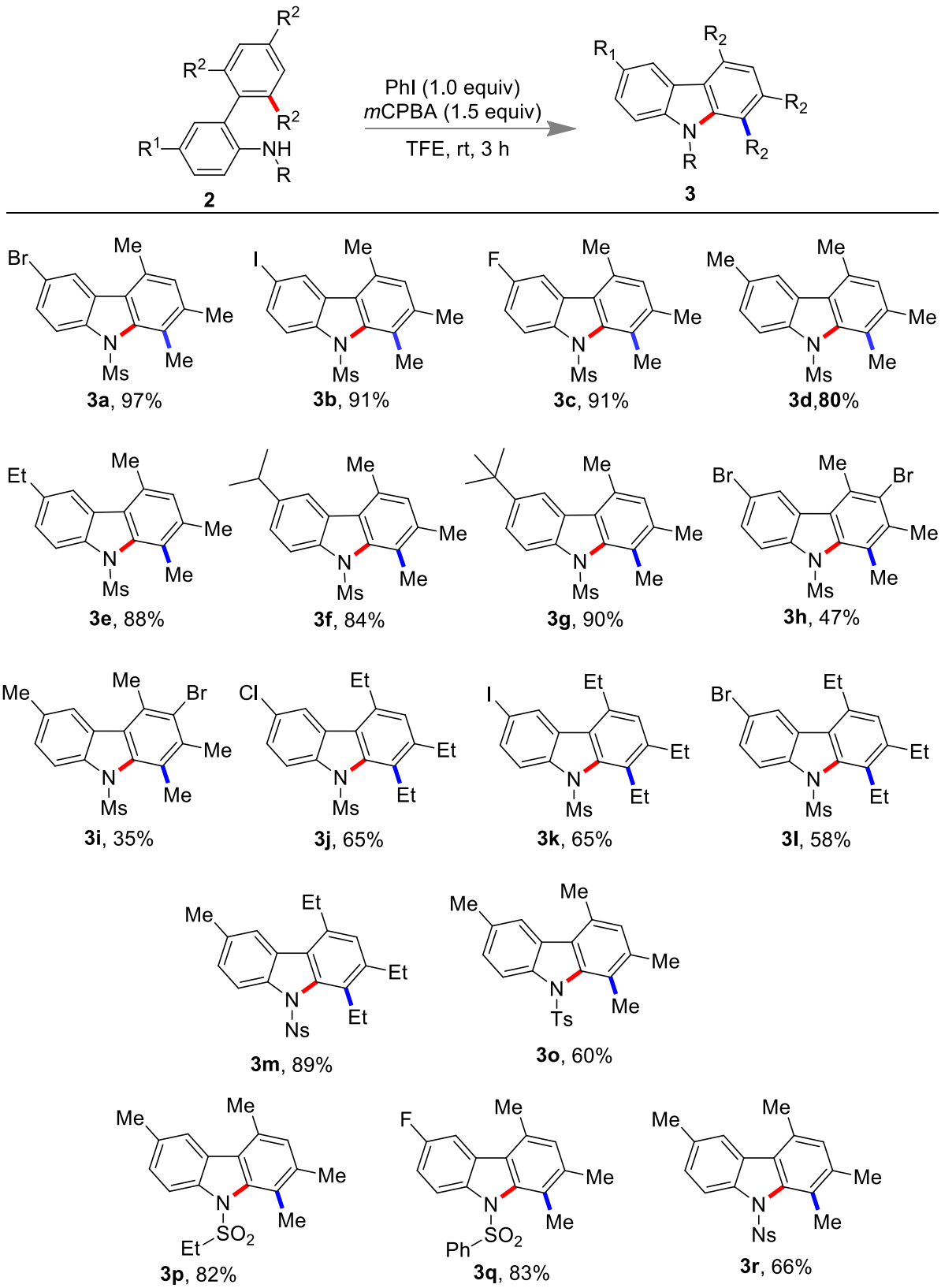


Figure 3.2 Substrate scope of biarylsufonamides using PhI-*m*CPBA, Reaction conditions: 0.108 mmol of 2 and 1.2 equiv of PIDA in TFE (0.2 M)

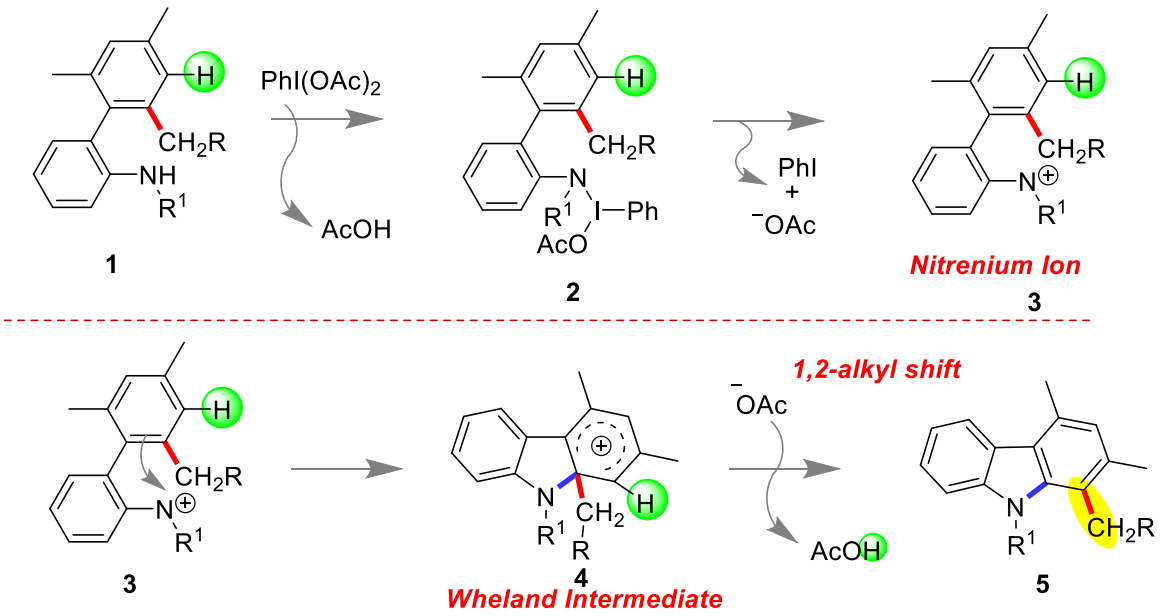


Figure 3.3 Proposed reaction mechanism

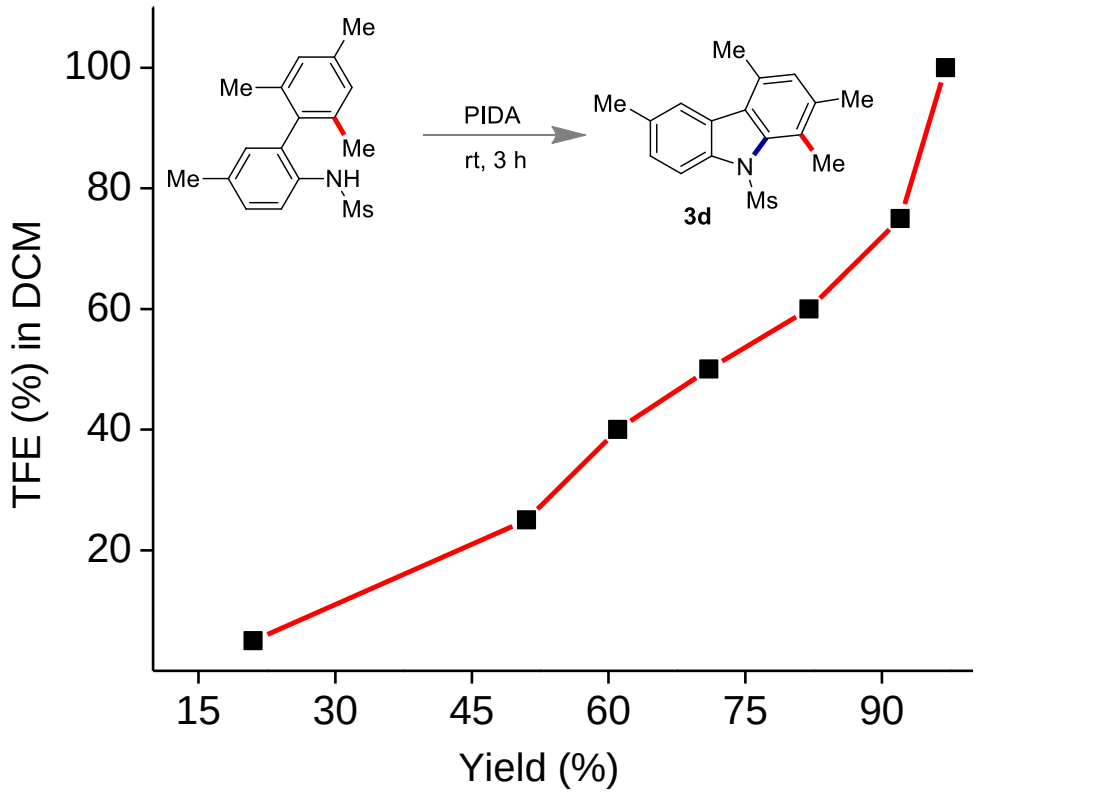
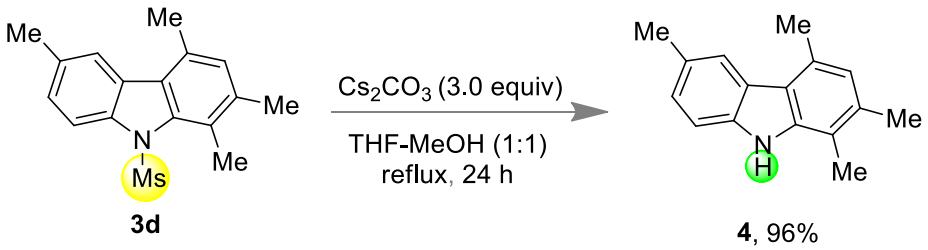


Figure 3.4 Monitoring the role of solvent TFE.



Scheme 3.9 Synthesis of NH carbazole, Reaction conditions: 0.108 mmol of 2 and 1.2 equiv of PIDA in TFE (0.2 M)

Post synthetic applications involve synthesis of 1,2,4,6-tetramethyl-9H-carbazole (**7**) was from **3d** using Cs_2CO_3 by following previous reports (Scheme 3.9).

3.7 CONCLUSIONS

In conclusion, hypervalent iodine mediated nitrenium ion chemistry was utilized for the synthesis of carbazoles. Distal C-H functionalization was successfully achieved along with the migration of the alkyl group. This efficient method for C-H amination yielded carbazoles with excellent yields. The reaction was facile at ambient temperature and in open atmosphere conditions which made the protocol significant. We hope that this intramolecular oxidative C-N amination strategy will have a significant impact on synthesizing complex structural motifs.

3.8 EXPERIMENTAL SECTION

General Methods. Chromatographic (Column) purifications of the compounds were done using silica gel (mesh 230–400) and hexane – ethyl acetate mixtures as eluent unless otherwise specified. NMR spectra were taken on a 400 MHz or 700 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 ppm for ^{13}C). The peak patterns are designated as follows: s: singlet; d: doublet; t: triplet; q: quartet; m: multiplet; dd: doublet of doublets; td: triplet of doublets; brs: broad singlet. The coupling constants (*J*) are reported in

hertz (Hz). High-resolution mass spectra (HR-MS) had been recorded on an ESI-TOF (time of flight) mass spectrometer. Infrared (IR) spectral data are reported in wave number (cm^{-1}). FT-IR spectra were recorded after making thin layer of the compounds on the surface of NaCl crystal using dichloromethane. A digital melting point apparatus was used to determine the melting points (mp) of the compounds. Good quality crystals of the compounds **3n** were obtained after slow evaporation of ethyl acetate solution. The crystals data were collected with Bruker SMART D8 goniometer equipped with an APEX CCD detector and with an INCOATEC micro source (Mo-Kα radiation, λ = 0.71073 Å). SAINT+[26]and SADABS[27] were used to integrate the intensities and to correct the absorption respectively. The structure was resolved by direct methods and refined on F^2 with SHELXL-97.[28]

Representative method for preparation of 6-bromo-1,2,4-trimethyl-9-(methylsufonyl)-carbazole (3a)

Method A. To *N*-5(bromo-2,4.6-trimethyl-[1,1-biphenyl]-2yl)methaneulfonamide (40 mg, 0.108 mmol) in TFE, the hypervalent reagent PIDA (51 mg, 0.325mmol) dissolved in TFE was added slowly to it. The reaction mixture was constantly stirred at room temperature for approximately 2 h. Complete consumption of starting material was observed in TLC. The reaction mixture was evaporated to dryness and the product 6-bromo-1,2,4-trimethyl-9(methylsulfonyl)-carbazole (**3a)** was purified by column chromatography to obtain white solid 38 mg (98%) at 2% hexane-ethyl acetate.

Method B. To *N*-(5-bromo-2,4.6-trimethyl-[1,1-biphenyl]-2yl)methaneulfonamide (40mg,0.108mmol) in TFE, PhI (0.108mmol, 13μL) and *m*CPBA (0.27mmol, 28mg) was added portionwise and it was found that complete conversion of substrate took place in 2 h to give the desired product. The reaction mixture was evaporated to dryness, and the product 6-

bromo-1,2,4-trimethyl-9(methylsulfonyl)-carbazole **(3a)**was obtained as white solid 37mg (97%) using 2% hexane-ethylacetate solvent mixture for silica gel column chromatography.

Representative method for preparation of *N*-(5-bromo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide. To a stirred solution of *N*-(4-bromophenyl)methanesulfonamide **1a**, (40 mg, 0.159 mmol) in TFE, mesitylene (67 µL, 0.479 mmol) was added. PIDA (51 mg, 0.159 mmol) dissolved in TFE was then added drop wise to the reaction vial. The reaction vial was shaken vigorously for 2 h. On complete consumption of substrate, the reaction mixture was evaporated to dryness. Column chromatography has been done to isolate the pure product*N*-(5-bromo-2',4',6'-trimethyl-[1.1'-biphenyl]-2-yl)methanesulfonamide (**2a**) as white solid in 67% yield using 5% ethylacetate-hexane.

Procedure for the synthesis of 4. 1,2,4,6-Tetramethyl-9-(methylsulfonyl)-9*H*-carbazole (**3d**) (40 mg, 0.132 mmol) was dissolved in EtOH and treated with aq NaOH (5M). The resulting solution has been shaken at 60°C up to completion (6 h). Solvent was evaporated under reduced pressure, diluted with dichloromethane (CH_2Cl_2) and neutralized with 1M aq HCl. The aqueous layer was dissolved with additional CH_2Cl_2 and the organic portion was dried over anhydrous Na_2SO_4 and was filtered. The filtrate was kept in vacuum and the compound was isolated using silica gel column chromatography (6% EtOAc in hexane) to get 1,2,4,6-tetramethyl-9*H*-carbazole (**6**) as white solid (28 mg, 0.125 mmol, yield 95%).

Compound Characterization Data

***N*-(5-Bromo-2',4',6'-trimethyl-[1.1'-biphenyl]-2-yl)methanesulfonamide (2a):** R_f = 0.4 (hexane:ethyl acetate: 9:1); white solid; 39 mg (67%); mp 173-175 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.8 Hz, 1H), 7.49 (dd, *J* = 8.8; 1.0Hz, 1H), 7.23 (d, *J* = 2.4 Hz, 1H),

6.98 (s, 2H), 5.99 (brs, 1H), 2.97 (s, 3H), 2.33 (s, 3H), 1.97 (s, 6H);^{13}C NMR (100 MHz, $CDCl_3$) δ 139.2, 136.7, 134.1, 133.3, 132.2, 131.8, 130.9, 129.4, 119.0, 117.2, 39.9, 21.3, 20.2; IR (KBr) ῡ = 3426, 2099, 1643, 1470, 1326, 1168 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{16}H_{18}BrNO_2S$ $[M + Na]^+$: 390.0134, found: 390.0144.

***N*-(5-Iodo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (2b):** R_f= 0.40 (hexane : ethyl acetate 9:1); white solid; 41 mg (77%); mp 176-178 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (dd, *J* = 8.8; 2.0 Hz, 1H), 7.46 (d, 8.8 Hz, 1H), 7.42 (d, *J* = 2.0 Hz, 1H), 6.97 (s, 2H), 5.99 (brs, 1H), 2.97 (s, 3H), 2.33 (s, 3H), 1.96 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.1, 139.2, 137.8, 136.7, 134.9, 132.3, 130.8, 129.4, 119.2, 87.7, 39.9, 21.3, 20.3; IR (KBr) ῡ = 3441, 2359, 2050, 1634, 536 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{16}H_{18}INO_2S$ $[M + Na]^+$: 437.9995, found: 437.9986.

***N*-(5-Fluoro-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (2c):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 37 mg (57%); mp 164-165 °C; ^{1}H NMR (700 MHz, DMSO) δ 8.51 (s, 1H), 7.41 (dd, *J* = 9.1, 5.6 Hz, 1H), 7.2-7.18 (m, 1H), 6.99-6.82 (m, 3H), 2.74 (s, 3H), 2.27 (s, 3H), 1.93 (s, 6H); ^{13}C NMR (100MHz, $CDCl_3$) δ 159.6 (d, $^1J_{C\text{-}F}$ = 243 Hz), 139.0, 136.5, 132.6 (d, $^3J_{C\text{-}F}$ = 8 Hz), 131.4, 130.9 (d, $^4J_{C,F}$= 3 Hz), 129.3, 119.8 (d, $^2J_{C,F}$ = 8 Hz), 117.3 (d, $^2J_{C,F}$ = 22 Hz), 115.5 (d, $^2J_{C,F}$ = 22 Hz), 38.7, 21.1, 20.1; IR (KBr) ῡ = 3431, 2359, 2089, 1867, 1180, 1155 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{16}H_{18}FNO_2S$ $[M + Na]^+$: 330.0934, found: 330.0947

***N*-(2',4',5,6'-Tetramethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (2d):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 11 mg (48%); mp 123-124 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.0 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 1H), 6.97 (s, 2H), 6.89 (s, 1H), 5.92

(s, 1H), 2.93 (s, 3H), 2.34 (s, 6H), 1.97 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 136.8, 134.1, 132.6, 132.2, 131.0, 130.4, 129.4, 129.2, 117.8, 39.7, 21.2, 20.8, 20.3; IR (KBr) ῡ = 3431, 2358, 2341, 2089, 1646 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{17}H_{21}NO_2S$ [M + Na]$^+$: 326.1185, found: 326.1203.

***N*-(5-Ethyl-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (2e):** R_f = 0.50 (hexane : ethylacetate 9:1); white solid; 35 mg (68%); mp 112-114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.4 Hz, 1H), 7.20 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.97 (s, 2H), 6.91 (d, *J*= 2 Hz, 1H), 5.92 (s, 1H), 2.96 (s, 3H), 2.64 (q, *J* = 7.6 Hz, 2H), 2.33 (s, 3H), 1.96 (s, 6H), 1.24 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.6, 138.4, 136.7, 132.7, 132.4, 130.3, 129.8, 129.1, 128.2, 117.7, 39.8, 28.2, 21.2, 20.3, 15.7; IR (KBr) ῡ = 3430, 2925, 2089, 1646, 1171 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{18}H_{23}NO_2S$ [M + Na]$^+$: 340.1342, found: 340.1358.

***N*-(5-Isopropyl-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (2f):** R_f= 0.50 (hexane : ethyl acetate 9:1); white solid; 30mg (59%); mp 143-145 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.8 Hz, 1H), 7.22 (dd, *J* = 8.4; 2 Hz, 1H), 6.98 (s, 2H), 6.94 (d, *J* = 2 Hz, 1H), 5.93 (s, 1H), 2.94 (s, 3H), 2.91-2.87 (m,1H), 2.34 (s, 3H), 1.96 (s, 6H), 1.3 (s,3H), 1.3 (s,3H); ^{13}C NMR (100 MHz, $CDCl_3$)δ 145.3, 138.4, 136.8, 132.9, 132.4, 130.3, 129.1, 128.6, 126.7, 117.7, 39.9, 33.5, 24.1, 21.1, 20.3; IR (KBr) ῡ = 3427, 2089, 1868, 1644, 1160 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{19}H_{25}NO_2S$ [M + Na]$^+$: 354.1498, found: 354.1518.

***N*-(5-(*tert*-Butyl)-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (2g):** R_f= 0.50 (hexane : ethyl acetate 9:1); white solid; 28mg (53%); mp 174-175 °C; ^{1}H NMR (400

MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.4 Hz, 1H), 7.37 (dd, *J* = 8.8; 2 Hz, 1H), 7.09 (d, *J* = 2 Hz, 1H), 6.98 (s, 2H), 5.93 (s, 1H), 2.95 (s, 3H), 2.34 (s, 3H), 1.96 (s, 6H), 1.30 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 138.5, 136.8, 133.0, 132.1, 129.7, 129.1, 127.7, 125.4, 117.2, 39.8, 34.5, 31.4, 21.1, 20.3; IR (KBr)ῡ = 3259, 2965, 1614, 1336, 1503, 1272 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{20}H_{27}NO_2S$ $[M + Na]^+$: 368.1655, found: 368.1633.

***N*-(3',5-Dibromo-2',4',6'-trimethyl-[1.1'-biphenyl]-2-yl]methanesulfonamide (2h):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid;47 mg (59%); mp 166-167 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.4 Hz, 1H), 7.51 (d, *J* = 8.8 Hz, 1H), 7.20 (s, 1H), 7.08 (s, 1H), 5.92 (s, 1H), 2.98 (s, 3H), 2.45 (s, 3H), 2.11 (s, 3H), 1.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.8, 136.8, 135.5, 134.0, 133.2, 132.8, 132.2, 132.1, 130.8, 126.5, 119.2, 117.3, 40.2, 24.2, 21.7, 20.1; IR (KBr) ῡ = 3428, 2089, 1646, 1539, 1339 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{16}H_{17}Br_2NO_2S$ $[M + Na]^+$: 467.9239, found: 467.9217.

***N*-(3'-Bromo-2',4',5,6'-tetramethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (2i):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 41 mg (49%) ; mp 165-167 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.4 Hz, 1H), 7.39-7.37 (m, 1H), 7.26 (s, 1H), 7.04 (s, 1H), 6.09 (s, 1H), 3.11 (s, 3H), 2.62 (s, 3H), 2.53 (s, 3H), 2.29 (s, 3H), 2.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 136.8, 135.7, 134.5, 134.4, 132.1, 131.0, 130.6, 130.3, 129.8, 126.4, 118.0, 39.9, 24.1, 21.7, 20.9, 20.2; IR (KBr) ῡ = 3398, 2089, 1646, 1456, 1160 cm^{-1}; HR-MS(ESI-TOF): m/z calculated for $C_{17}H_{20}BrNO_2S$ $[M + Na]^+$: 404.0290, found: 404.0281.

***N*-(5-Chloro-2',4',6'-triethyl-[1, 1-biphenyl-2-yl)methanesulfonamide (2j):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 40 mg (56%); mp 153-157 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.8 Hz, 1H), 7.36 (dd, *J* = 6.4; 2.4 Hz, 1H), 7.13 (d, *J* = 2.4 Hz, 1H),

7.04 (s, 2H), 6.01 (s, 1H), 2.98 (s, 3H), 2.68 (q, *J* = 7.6 Hz, 2H), 2.37 – 2.11 (m, 4H), 1.30 (t, *J* = 7.6 Hz, 3H), 1.06 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 142.7, 134.1, 131.1, 130.9, 129.9, 129.1, 128.9, 126.5, 117.8, 40.0, 28.8, 26.7, 15.4; IR (KBr) ῡ = 3420, 2962, 1868, 1647, 1159 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{19}H_{24}ClNO_2S$ [M + H]$^+$: 366.1289, found: 366.1297.

***N*-(2',4',6'-Triethyl-5-iodo-[1,1'-biphenyl]-2-yl)methanesulfonamide (2k):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 36 mg (58%); mp 157-159 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.8Hz, 1H), 7.47 (s, 1H), 7.45 (s, 1H), 7.03 (s, 2H), 6.02 (s, 1H), 2.99 (s, 3H), 2.67 (q, *J* = 7.6 Hz, 2H), 2.31-2.16 (m, 4H), 1.30 (t, *J* = 7.6 Hz, 3H), 1.05 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.7, 142.7, 139.8, 137.6, 135.3, 131.4, 129.8, 126.5, 118.3, 87.0, 40.0, 28.8, 26.6, 15.4; IR (KBr) ῡ = 3407, 2948, 1434, 1026 cm^{-1}; HR-MS(ESI-TOF): m/z calculated for $C_{19}H_{24}INO_2S$ [M + Na]$^+$: 480.0465, found: 480.0448.

***N*-(5-Bromo-2',4',6'-triethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (2l):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 40 mg (61%); mp 155-158 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.8Hz, 1H), 7.50 (d, *J* = 8.8 Hz, 1H), 7.27 (s, 1H), 7.03 (s, 2H), 6.01 (s, 1H), 2.98 (s, 3H), 2.67 (q, *J* = 7.6 Hz, 2H), 2.33-2.14 (m, 4H), 1.30 (t, *J* = 7.6 Hz, 3H), 1.05 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 142.8, 134.7, 133.9, 131.8, 131.3, 129.9, 126.5, 118.2, 116.6, 40.2, 28.9, 26.7, 15.3; IR (KBr) ῡ = 3427, 2099, 1646, 1470, 1168 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{19}H_{24}BrNO_2S$ [M + Na]$^+$: 432.0603, found: 432.0574.

4-Nitro-*N*-(2',4',6'-triethyl-5-methyl-[1, 1'-biphenyl]-2-yl)benzenesulfonamide (2m): R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 35 mg (54%); mp 149-152 ℃; ^{1}H NMR (400

MHz, $CDCl_3$) δ 8.34-8.22 (m, 2H), 7.96-7.88 (m, 2H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.13 (d, *J* = 8.4 Hz, 1H), 6.97 (s, 2H), 6.83 (s, 1H), 6.23 (s, 1H), 2.68 (q, *J* = 7.6 Hz, 2H), 2.28 (s, 3H), 1.88 (q, *J* = 7.6Hz, 4H), 1.33-1.29 (m, 3H), 0.92-0.88 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 145.5, 145.3, 142.7, 134.3, 131.6, 131.3, 131.0, 129.8, 129.3, 128.7, 126.1, 124.4, 117.5, 28.9, 26.3, 20.1, 15.5, 15.2; IR (KBr) ῡ = 3420, 2064, 1646, 1539, 1170 cm^{-1}; HR-MS(ESI-TOF): m/z calculated for $C_{25}H_{28}N_2O_4S$ $[M + Na]^+$: 475.1662, found: 475.1679.

***N*-(2',4',6'-Triethyl-5-fluoro-[1, 1'-biphenyl]-2-yl)benzenesulfonamide (2n):** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 45 mg (65%); mp 154-156 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78-7.71 (m, 3H), 7.55 (d, *J* = 7.2 Hz, 1H), 7.45 (t, *J* = 7.2 Hz, 2H), 7.02 (t, *J* = 8.6 Hz, 1H), 6.97 (s, 2H), 6.73 (d, *J* = 8.4 Hz, 1H), 6.12 (s, 1H), 2.68 (q, *J* = 7.6 Hz, 2H), 1.92 – 1.83 (m, 4H), 1.31 (t, *J* = 7.6Hz, 3H), 0.91 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 159.0 (d, $^1J_{C,F}$ = 243 Hz), 145.6, 142.7, 139.5, 133.3, 131.5 (d,$^3J_{C,F}$ = 8 Hz), 131.0 (d, $^4J_{C,F}$ = 2.6 Hz), 130.2, 129.2, 127.3, 126.1, 119.1 (d, $^3J_{C,F}$ = 8 Hz), 117.6 (d, $^2J_{C,F}$ = 22.0 Hz), 115.2 (d, $^2J_{C,F}$ = 22.0 Hz), 28.9, 26.2, 15.4, 15.2.; IR (KBr) ῡ = 3426, 2341, 2089, 1843, 1643, 1456, 1338 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{24}H_{26}FNO_2S$ $[M + Na]^+$: 434.1560, found: 434.1585.

4-Methyl-*N*-(2',4',5,6'-tetramethyl-[1, 1'-biphenyl]-2-yl)benzenesulfonamide (2o): R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 34 mg (81%); mp 150-153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.59 (m, 3H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.09 (dd, *J* = 8.4; 2.0 Hz, 1H), 6.90 (s, 2H), 6.72 (d, *J* = 2 Hz, 1H), 6.09 (s, 1H), 2.37 (s, 3H), 2.33 (s, 3H), 2.26 (s, 3H), 1.64 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 142.9, 138.3, 137, 133.8, 132.5, 131.9, 130.7, 130.3, 129.8, 129.0, 128.9, 127.4, 118.3, 21.6, 21.1, 20.9, 19.9; IR (KBr) ῡ = 3419, 2084,

1652, 1392, 1165 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{23}H_{25}NO_2S$ $[M + Na]^+$: 402.1498, found: 402.1493.

***N*-(2',4',5 ,6'-Tetramethyl-[1, 1'-biphenyl]-2-yl)ethanesulfonamide (2p) :** R_f = 0.50 (hexane : ethyl acetate 9:1); white solid; 37mg (96%); mp 120-121 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.0 Hz, 1H), 7.15 (d, *J* = 8.4 Hz, 1H), 6.97 (s, 2H), 6.87 (s, 1H), 5.86 (s, 1H), 3.07 (q, *J* = 6.8 Hz, 2H), 2.33 (s, 6H), 1.98 (s, 6H), 1.25 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 136.7, 133.8, 132.6, 132.4, 131.0, 130.0, 129.3, 129.1, 117.5, 46.4, 21.2, 20.8, 20.3, 8.2; IR (KBr) ῡ = 3427, 2359, 2089, 1644, 1540, cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{18}H_{23}NO_2S$ $[M + Na]^+$: 340.1342, found: 340.1335.

***N*-(5-Fluoro-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (2q):** R_f = 0.40 (hexane : ethyl acetate 9:1); white solid; 24 mg (51%); mp 165-167 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 9.2; 4.0 Hz, 1H), 7.72 – 7.67 (m, 2H), 7.56 – 7.52 (m, 1H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.04 – 6.99 (m, 1H), 6.90 (s, 2H), 6.68-6.65 (m, 1H), 6.11 (s, 1H), 2.33 (s, 3H), 1.61 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.56 (d, $^1J_{C,F}$ = 243 Hz), 139.5, 138.9, 136.7, 133.3, 132.7 (d, $^3J_{C,F}$ = 8.0 Hz), 131.3, 130.5 (d, $^4J_{C,F}$ = 3 Hz), 129.3, 129.1, 127.3, 120.3 (d, $^3J_{C,F}$ = 8.0 Hz), 117.0 (d, $^2J_{C,F}$ = 22.0 Hz), 115.2 (d, $^2J_{C,F}$ = 22.0 Hz); 21.2, 19.7.; IR (KBr) ῡ = 2077, 1645, 1504, 1386, 1168 cm^{-1}, HR-MS (ESI-TOF): m/z calculated for $C_{21}H_{20}FNO_2S$ $[M + Na]^+$: 392.1091, found: 392.1099.

4-Nitro-N-(2',4',5,6'-tetramethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (2r): R_f = 0.40 (hexane : ethyl acetate 9:1); yellow solid; 24 mg (50%); mp 193-195 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.8 Hz, 2H), 7.88 (d, *J* = 8.8 Hz, 2H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.13 (d, *J* = 7.2 Hz, 1H), 6.90 (s, 2H), 6.76 (s, 1H), 6.21 (s, 1H), 2.33 (s, 3H), 2.28 (s, 3H),

1.25 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 145.5, 138.7, 136.6, 135.2 132.2, 131.1, 130.8, 129.3, 129.1, 126.1, 128.7, 124.4, 118.8, 21.3, 20.9, 20.0; IR (KBr) ῡ = 3429, 2922, 2357, 1685, 1167 cm^{-1} ; HR-MS (ESI-TOF): m/z calculated for $C_{22}H_{22}N_2O_4S$ $[M + Na]^+$: 433.1192, found: 433.1177.

6-Bromo-1,2,4-trimethyl-9(methylsulfonyl)-carbazole (3a):[14] R_f = 0.6 (hexane:ethyl acetate 19:1);white solid; Method A: 38 mg (98%), Method B: 37 mg (97%); mp 82-84 ℃; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.53 (d, *J* = 8.4 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 (175 MHz, $CDCl_3$) δ 141.4, 141.0, 138.8, 132.9, 130.6, 130.2, 129.3, 127.6, 125.9, 125.2, 120.6, 119.6, 34.4, 20.4, 20.2 , 18.6.

6-Iodo-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (3b):[14] R_f= 0.6 (hexane:ethyl acetate 19:1); white solid; Method A: 37 mg (93%), Method B: 36 mg (91%) mp 113-116 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.82 (d , *J* = 8 Hz, 1H), 7.71 (d, *J* = 8 Hz, 1H), 7.07 (s, 1H), 2.69 (s, 3H), 2.52 (s, 3H), 2.38 (s, 3H), 2.23 (s, 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6, 141.19, 138.9, 135.2, 133.3, 131.2, 130.6, 130.1, 127.7, 125.7 , 121.0 , 90.6, 34.5, 20.4, 20.2 , 18.6.

6-Fluoro-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (3c):[14] R_f = 0.6 (hexane:ethyl acetate 19:1); white solid; Method A: 36 mg (91%), Method B: 36 mg (91%); mp 91-93 ℃; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.00 (q, *J* = 4.6 Hz, 1H), 7.63 (dd, *J* = 8.8, 2.4 Hz,1H), 7.12 (dt, *J* = 8.8, 2.4 Hz, 1H), 7.07 (s, 1H), 2.68 (s, 3H), 2.53 (s, 3H), 2.38 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 161.3 (d, $^1J_{C,F}$ = 242 Hz), 142.0, 138.7, 138.12, 132.5 (d, $^3J_{C,F}$

= 10.0 Hz), 130.5, 130.1, 127.9, 126.5 (d, $^{4}J_{C,F}$ = 3.0 Hz), 120.4 (d, $^{3}J_{C,F}$ = 10.0 Hz), 113.6 (d, $^{2}J_{C,F}$ = 24.0 Hz), 109.0 (d, $^{2}J_{C,F}$= 24.0 Hz), 34.0, 20.5, 19.9, 18.5.

1,2,4,6-Tetramethyl-9-(methylsulfonyl-)-carbazole (3d):[14] R_f = 0.6 (hexane : ethyl acetate 19:1); white solid; Method A: 37 mg (93%), Method B: 31 mg (80%); mp 73-75 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.4 Hz, 1H), 7.75 (s, 1H), 7.23 (dd, *J* = 7.0; 1.0 Hz, 1H), 7.05 (s, 1H), 2.71 (s, 3H), 2.53 (s, 3H), 2.50 (s, 3H), 2.37 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 141.4, 140.1, 137.7, 135.8, 131.3, 130.4, 129.8, 127.6, 127.6, 127.2, 122.8, 118.8, 33.8, 21.8, 20.4, 20.3, 18.6.

6-Ethyl-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (3e):[14] R_f = 0.6 (hexane : ethyl acetate 19:1); white solid; Method A: 37 mg (94%), Method B : 35 mg (88%); mp 102-104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8 Hz, 1H), 7.78 (s, 1H), 7.27 (s, 1H), 7.06 (s, 1H), 2.81 (q, *J* = 7.6 Hz, 2H), 2.73 (s, 3H), 2.54 (s, 3H), 2.38 (s, 3H), 2.18 (s, 3H), 1.34 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.4, 141.4, 140.3, 137.6, 131.3, 130.4, 129.8, 127.6, 127.2, 126.4, 121.6, 119 , 34.0, 29.2, 20.3, 20.4,18.6, 16.1.

6-Isopropyl-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (3f):[14] R_f = 0.6 (hexane : ethyl acetate 19:1); white solid; Method A: 34 mg (86%), Method B: 33 (84%); mp 73-76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.8 Hz, 1H), 7.78 (s, 1H), 7.29 (d, *J* = 8.4 Hz, 1H), 7.05 (s, 1H), 3.06 (septet, *J* = 6.8 Hz, 1H), 2.72 (s, 3H), 2.53 (s, 3H), 2.37 (s, 3H), 2.18 (s, 3H), 1.33 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 147.0, 141.4, 140.3, 137.6, 131.2, 130.3, 129.8, 127.6, 127.3, 125.0, 120.2, 119.0, 34.4, 34.0, 24.4, 20.3, 20.3, 18.6.

6-(Tert-butyl)-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (3g):[14] R_f = 0.6 (hexane : ethyl acetate 19:1); white solid; Method A: 37 mg (94%), Method B: 36 mg (91%); mp 132-134 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.96 (d, *J* = 2.4 Hz, 1H), 7.95 (d, *J* = 4.4 Hz, 1H), 7.46 (dd, d, *J* = 7.0; 1.4 Hz, 1H), 7.04 (s, 1H), 2.73 (s, 3H), 2.53 (s, 3H), 2.37 (s, 3H), 2.18 (s, 3H), 1.41 (s, 9H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 149.2, 141.4, 140.0, 137.6, 130.9, 130.4, 129.6, 127.6, 127.4, 124.2, 119.0 , 118.6 , 35.0, 34.0, 31.8, 20.4, 20.2, 18.6.

3,6-Dibromo-1,2,4-trimethyl-9-(methylsulfonyl)-9*H*-carbazole (3h):[14] R_f = 0.6 (hexane : ethyl acetate 19:1); white solid; Method A: 21 mg (53%), Method B: 19 mg (47%); mp 180-184 °C ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.15 (d, *J* = 2.0 Hz, 1H), 7.95 (d, *J* = 8.6 Hz, 1H), 7.57 (dd, *J* = 8.6; 2.0 Hz, 1H), 2.88 (s, 3H), 2.61 (s, 3H), 2.56 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 141.2, 140.4 , 138.6 , 132.3, 130.4 , 130.0, 129.2, 127.7, 126.7, 125.8, 120.6, 119.8, 34.4, 21.8, 21, 20.6.

3-Bromo-1,2,4,6-tetramethyl-9-(methylsulfonyl)-carbazole (3i): R_f = 0.6 (hexane :ethyl acetate 19:1); white solid; Method A: 15 mg (38%), Method B: 14 mg (35%); mp 100-104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (brs, 1H), 7.87 (brs, 1H), 7.26 (brs, 1H), 2.88 (s, 3H), 2.60 (s, 3H), 2.55 (s, 6H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.3, 140.3, 138.1, 135.8, 130.2, 129.8, 129.3, 127.5, 127.2, 124.2, 123.6, 122.9, 34.4, 23.7, 21.8, 21.0, 20.6; IR (KBr) ῡ = 3432, 2064, 1645, 1457,1173 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{17}H_{18}BrNO_2S$ $[M + Na]^+$: 402.0134, found: 402.0130.

6-Chloro-1,2,4-triethyl-9-(methylsulfonyl)-carbazole (3j): R_f = 0.6 (hexane : ethyl acetate 19:1); yellow liquid; Method A: 25 mg (63%), Method B: 26 mg (66%); ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.6 Hz, 1H), 7.89 (d, *J* = 2.0 Hz, 1H), 7.38 (dd, *J* = 8.6; 2.0 Hz,

1H), 7.14 (s, 1H), 3.28 (q, *J* = 7.6 Hz, 2H), 3.08 (q, *J* =7.6 Hz, 2H), 2.82 (q, *J* = 7.6 Hz, 2H), 2.20 (s, 3H), 1.41 (t, *J* = 7.6 Hz, 3H), 1.31 (t, *J* = 7.6 Hz, 3H), 1.14 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (175MHz, $CDCl_3$) δ 144.7, 141.6, 141.0, 136.9, 133.8, 132.4, 132.2, 128.2, 126.6, 125.8, 122.4, 120.8, 34.3, 26.6, 26.5, 23.1, 16.2, 15.0, 14.2; IR (KBr): ῡ = 3428, 1867, 1646, 1456, 1362 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{19}H_{22}ClNO_2S$ $[M + Na]^+$: 386.0952, found: 386.0942.

1,2,4-Triethyl-6-iodo-9-(methylsulfonyl)-carbazole (3k): R_f = 0.6 (hexane:ethyl acetate 19:1); yellow oil; Method A: 24 mg (61%), Method B: 26 mg (65%); ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.24 (d, *J* = 1.6 Hz, 1H), 7.82 (d, *J* = 8.4 Hz, 1H), 7.70 (dd, *J* = 8.6; 1.6 Hz, 1H), 7.13 (s, 1H), 3.27 (q, *J* = 7.6 Hz, 2H), 3.06 (q, *J* = 7.6 Hz, 2H), 2.81 (q, *J* = 7.6 Hz, 2H), 2.20 (s, 3H), 1.40 (t, *J* = 7.6 Hz, 3H), 1.31 (t, *J* = 7.6 Hz, 3H), 1.13 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 144.5, 142.0, 140.9, 136.6, 135.0, 133.4, 133.1, 131.2, 127.9, 125.4, 121.3, 90.8, 34.2, 26.4, 26.3, 23.0, 16.1, 14.8, 14.0; IR (KBr): ῡ = 3428, 2931, 2089, 1868, 1366,1361 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{19}H_{22}INO_2S$ $[M + Na]^+$: 478.0308, found: 478.0317.

6-Bromo-1,2,4-triethyl-9-methylsulfonyl)-carbazole (3l):[14] R_f = 0.6 (hexane : ethyl acetate 19:1); colourless liquid; Method A: 23 mg (58%); ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.93 (d, *J* = 8.6 Hz, 1H), 7.52 (dd, *J* = 8.6; 1.4 Hz, 1H), 7.13 (s, 1H), 3.27 (q, *J* = 7.6 Hz, 2H), 3.07 (q, *J* = 7.6 Hz, 2H), 2.81 (q, *J* = 7.6 Hz, 2H), 2.20 (s, 3H), 1.40 (t, *J* = 7.6 Hz, 3H), 1.31 (t, *J* = 7.6 Hz, 3H), 1.13 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5, 141.3, 141.2, 136.7, 133.6, 132.6, 129.2, 127.9, 125.6, 125.2, 121.0, 119.7, 34.2, 26.4, 26.3, 22.9, 16.1, 14.9, 14.0.

1,2,4-Triethyl-6-methyl-9-(4-nitrophenyl)-carbazole (3m): R_f = 0.6 (hexane : ethyl acetate 19:1); yellow solid; Method A: 33 mg (85%) , Method B: 35 mg (89%); mp 160-164 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 2H) 7.30 (s, 1H), 7.18 (d, *J* = 8.0 Hz, 1H), 7.02 (s, 1H), 6.98 (d, *J* = 8.0 Hz, 2H), 3.41 (q, *J* = 7.6 Hz, 2H), 2.88-2.75 (m, 4H), 2.39 (s, 3H), 1.35 (t, *J* = 7.6 Hz, 3H), 1.18 (t, *J* = 7.6 Hz, 3H), 1.06 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 150.1, 143.7, 141.2, 139.4, 138.9, 136.6, 136.6, 134.0, 131.7, 128.7, 128.5, 127.6, 127.3, 122.4, 122.5, 120.5, 26.5, 26.2, 22.9, 21.8, 16.4, 15.2, 14.3; IR (KBr) ῡ = 3426, 2089, 1868, 1644, 1456, 1174 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{25}H_{26}N_2O_4S$ $[M + Na]^+$: 473.1505, found: 473.1494.

1,2,4-Triethyl-6-fluoro-9-(phenylsulfonyl)-carbazole) (3n): R_f = 0.6 (hexane : ethyl acetate 19:1); white solid; Method B: 26 mg (65%); mp 149-151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 8.8; 2.4 Hz, 1H), 7.26 (t, *J* = 6.8 Hz, 1H) 7.17 (dd, *J* = 6.8; 2.4 Hz, 1H), 7.08-6.93 (m, 4H), 6.82(s, 1H), 6.80(s, 1H), 3.43 (q, *J* = 7.4 Hz, 2H), 2.83 (q, *J* = 7.4 Hz, 2H), 2.76 (q, *J* = 7.4 Hz, 2H), 1.34 (t, *J* = 7.4 Hz, 3H), 1.18 (t, *J* = 7.4 Hz, 3H), 1.06 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3 (d, $^1J_{C,F}$ = 236 Hz), 144.1, 142.4, 138.4, 136.5, 134.1, 133.2 (d,$^3J_{C,F}$ = 9.0 Hz), 133.16 (×2), 128.2, 127.6, 127.4, 127.2 (d, $^4J_{C,F}$ = 3.1 Hz), 121.2 (d,$^3J_{C,F}$ = 9.0 Hz), 112.9 (d, $^2J_{C,F}$ = 25.0 Hz), 108.3 (d, $^2J_{C,F}$ = 25.0 Hz), 26.3, 26.2, 22.9, 16.3, 15.1, 14.3; IR (KBr) ῡ = 3418, 2965, 2089, 1867, 1645, cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{24}H_{24}FNO_2S$ $[M + Na]^+$: 432.1404 found: 432.1419.

1,2,4,6-Tetramethyl-9-tosyl-carbazole (3o):[14] R_f = 0.6 (hexane:ethyl acetate 19:1); white solid; Method A: 35 mg (88%), Method B: 24 mg (60%); mp 98-100 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.7 Hz, 1H), 7.40 (s, 1H), 7.13 (d, *J* = 8.4 Hz, 1H), 6.96 (s, 1H), 6.85 (d, *J* = 8.4 Hz, 2H), 6.79 (d, *J* = 8.4 Hz, 2H), 2.65 (s, 3H), 2.49 (s, 3H), 2.39 (s,3H),

2.38(s, 3H), 2.18 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 143.8, 141.9, 139.9, 137.2, 135.2, 131.9, 131.8, 130.0, 129.3, 128.4, 127.9, 127.6, 127.4, 126.9, 122.2, 119.6, 21.8, 21.5, 20.5, 20.0, 18.6.

9-(Ethylsulfonyl)-1,2,4,6-tetramethyl-carbazole (3p): R_f = 0.6 (hexane:ethyl acetate 19:1); white solid; Method A: 35 mg (88%) , Method B: 32 mg (82%); mp 124-126 ºC; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.4 Hz, 1H), 7.75 (s, 1H), 7.22 (dd, *J* = 7.7; 1.0 Hz, 1H), 7.03 (s, 1H), 2.71 (s, 3H), 2.55 (s, 3H), 2.50 (s, 3H), 2.41 (q, *J* = 7.4 Hz, *2*H), 2.37 (s, 3H), 0.92 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 141.8, 139.8, 137.6, 135.4, 131.0, 130.1, 129.8, 127.5, 127.1, 126.9, 122.7, 118.5, 42.8, 21.8, 20.4, 20.3, 18.7, 7.4; IR (KBr) ῦ = 3445, 2348, 1653, 1456, 1359 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{18}H_{21}NO_2S$ [M + Na]$^+$: 338.1185, found: 338.1197.

6-Fluoro-1,2,4-trimethyl-9-(phenylsulfonyl)-carbazole (3q):[14] R_f = 0.6 (hexane : ethyl acetate 19:1); white solid; Method A: 35 mg (88%), Method B: 33 mg (83%); mp 159-161 °C ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 5.1; 2.8 Hz 1H), 7.28 (t, *J* = 7.7 Hz, 1H), 7.24 (dd, *J* = 9.1; 2.8 Hz, 1H), 7.04-7.01 (m, 2H), 7.00 (d, *J* = 5.0 Hz, 2H), 6.94 (d, *J* = 4.4 Hz, 2H), 2.67 (s, 3H), 2.44 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 161.0 (d, $^1J_{C,F}$ = 241 Hz), 142.5, 138.3, 137.8 (d, $^4J_{C,F}$ = 2.0 Hz), 134.0, 133.3, 133.1 (d, $^3J_{C,F}$ = 9.0 Hz), 130.3, 129.7, 128.0, 127.8, 127.3 (d, $^4J_{C,F}$ = 3.2 Hz), 127.2, 121.1 (d, $^3J_{C,F}$ = 9.0 Hz), 112.94 (d, $^2J_{C,F}$ = 25.0 Hz), 108.38 (d, $^2J_{C,F}$= 25.0 Hz), 20.5, 19.6, 18.5.

1,2,4,6-Tetramethyl-9-(4-nitrophenyl)sulfonyl)-carbazole (3r): R_f = 0.6 (hexane : ethyl acetate 19:1); yellow solid; mp 161-163 °C; Method A: 36 mg (98%) , Method B 26 mg (66%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.4 Hz, 1H), 7.83 (d, *J* = 8.8 Hz, 2H), 7.38

(s, 1H), 7.17 (d, *J* = 8.4 Hz, 1H), 7.11 (d, *J* = 8.8 Hz, 2H), 7.01 (s, 1H), 2.65 (s, 3H), 2.47 (s, 3H), 2.42 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.2, 141.2, 139.7, 139.0, 137.8, 136.3, 131.7, 130.8, 129.9, 128.6, 127.8, 127.7, 127.3, 122.8, 122.5, 119.7, 21.7, 20.4, 19.9, 18.4; IR (KBr) ῡ = 3442, 2390, 2348, 1635, 672, 524 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{22}H_{20}N_2O_4S[M + Na]^+$: 431.1036. found: 431.1045.

1,2,4,6-Tetramethyl-9*H*-carbazole (4): R_f = 0.7 (hexane : ethyl acetate 4:1); white solid; 28 mg (95%); mp 105-108 ºC; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.85 (s, 1H), 7.35 (d, *J* = 7.7 Hz, 1H), 7.23 (d, *J* = 8.4 Hz, 1H), 2.99 (s, 3H), 2.59 (s, 3H), 2.54 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 140.2, 139.1, 137.3, 130.5, 129.0, 128.9, 128.5, 124.7, 123.2, 121.3, 116.5, 115.9, 26.7, 20.4, 20.3, 17.8; IR (KBr) ῡ = 3441, 2395, 1632, 512 cm^{-1}; HR-MS (ESI-TOF): m/z calculated for $C_{16}H_{17}N[M\ ]^+$: 223.1356. found: 223.1352.

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NMR SPECTRA OF SELECTED COMPOUNDS

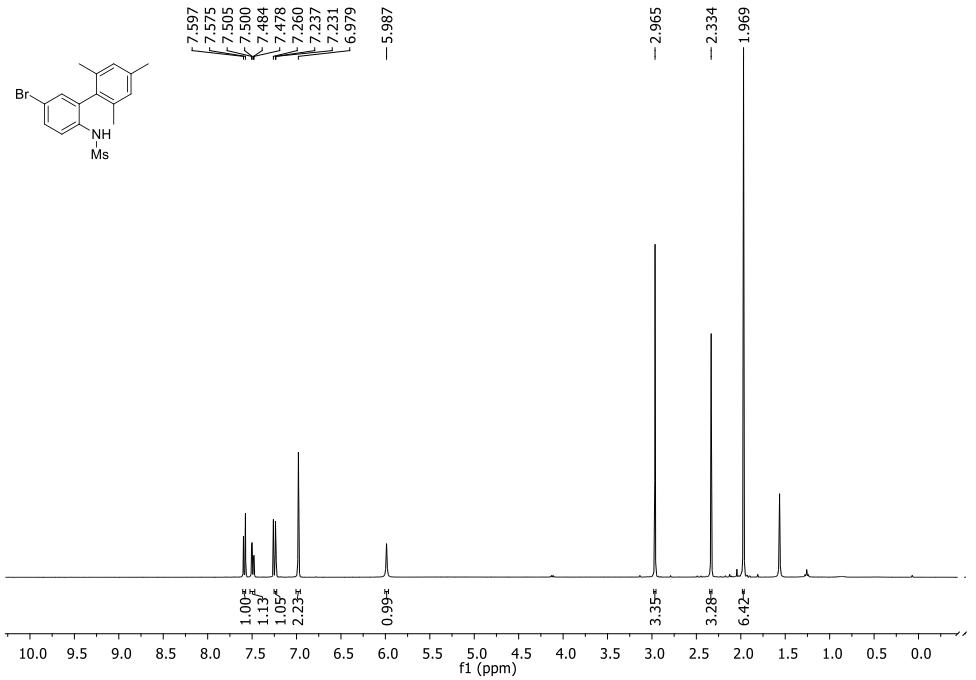


Figure 3.5 ^{1}H NMR spectrum of *N*-(5-Bromo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2a**)

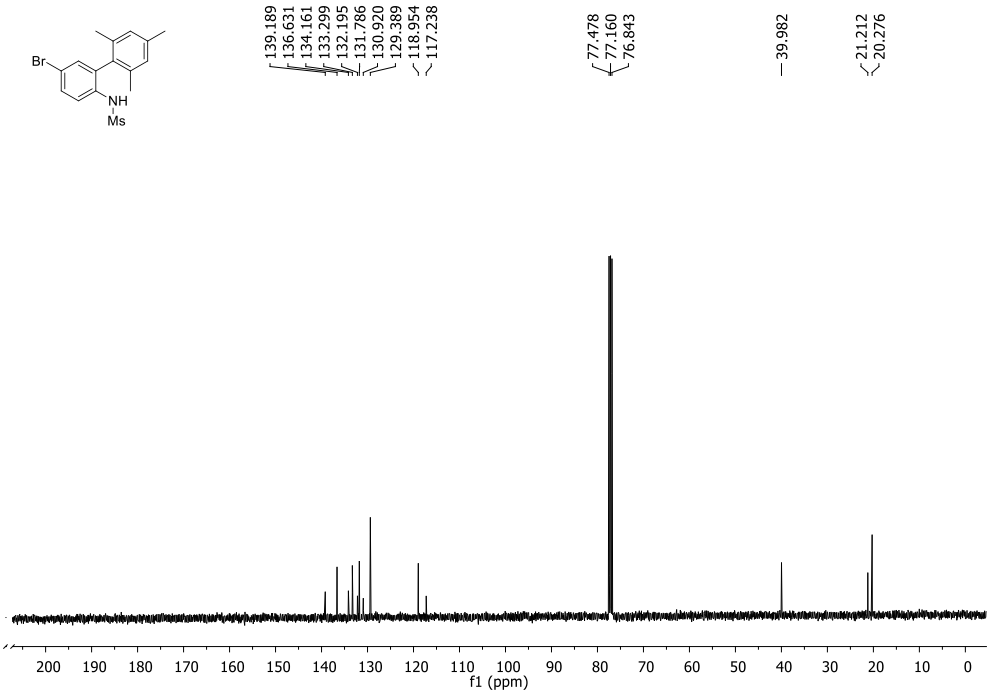


Figure 3.6 ^{13}C NMR spectrum of *N*-(5-Bromo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2a**)

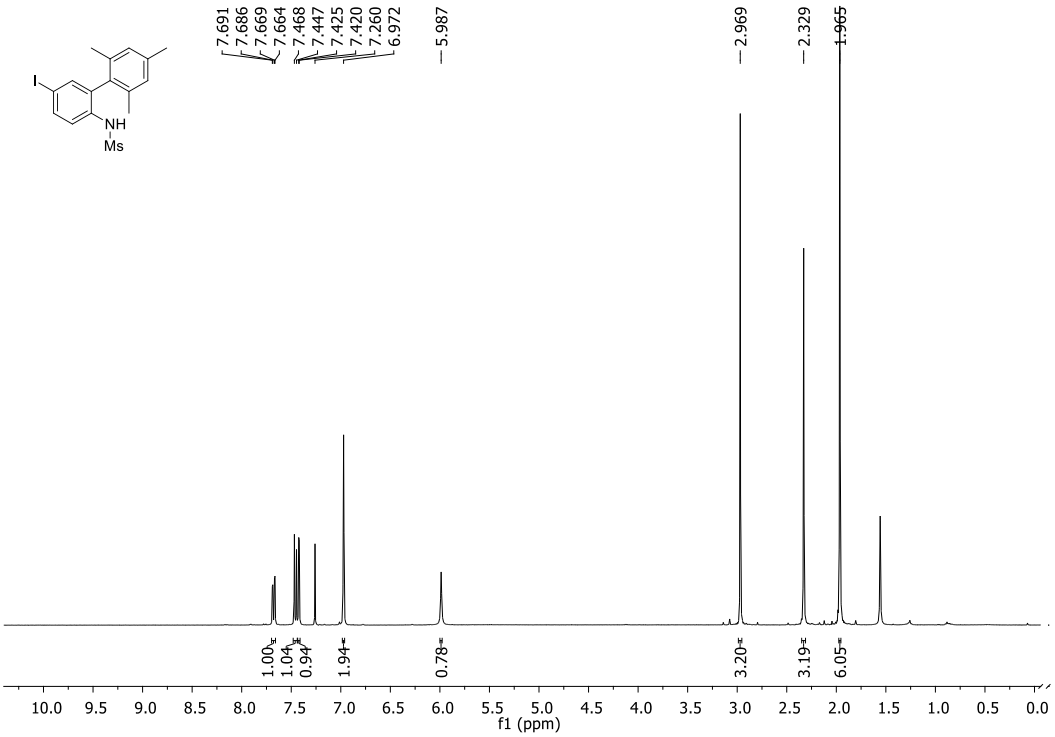


Figure 3.7 ^{1}H NMR spectrum of *N*-(5-Iodo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2b**)

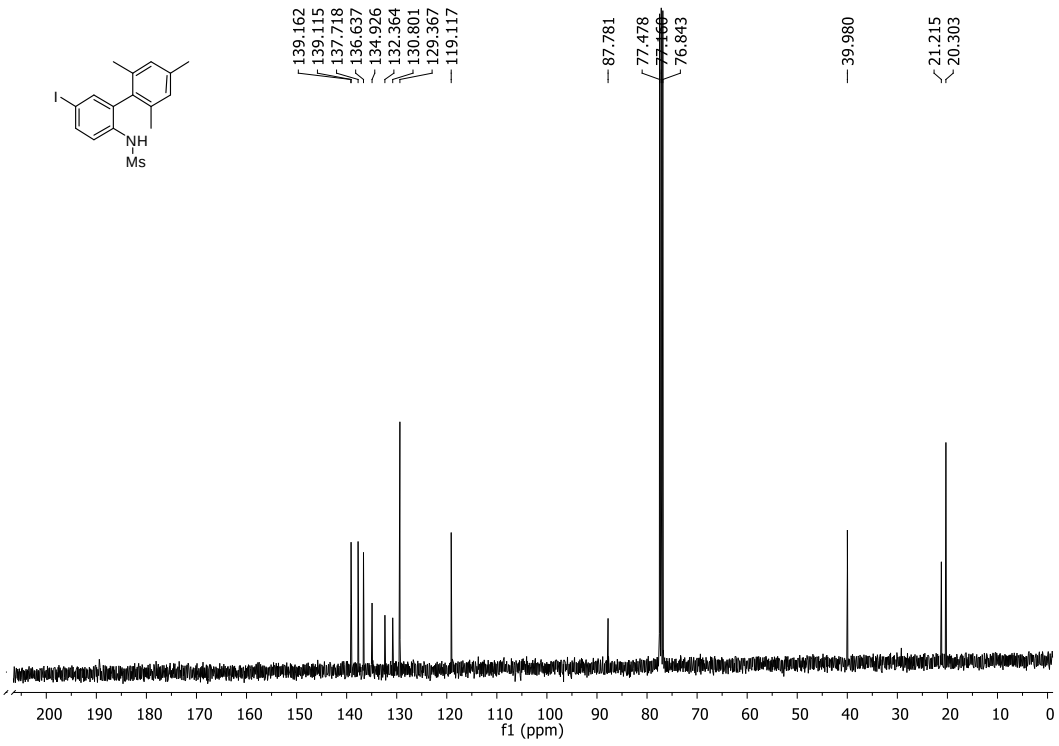


Figure 3.8 ^{13}C NMR spectrum of *N*-(5-Iodo-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2b)**

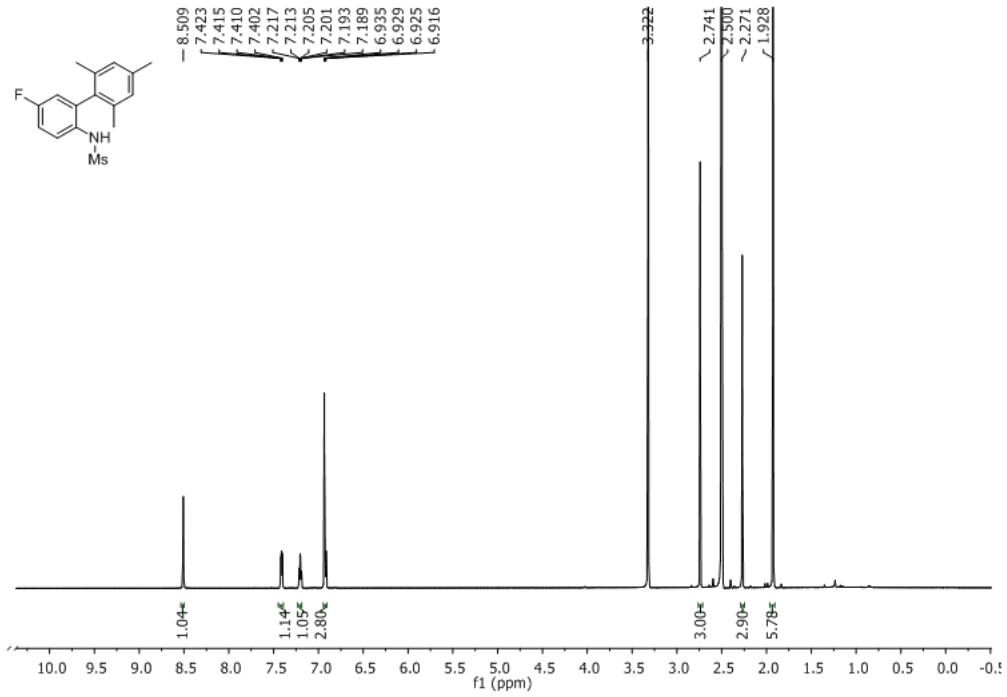


Figure 3.9 ^{1}H NMR spectrum of *N*-(5-Fluoro-2' ,4' ,6'-trimethyl-[1, 1'-biphenyl]-2-yl)methanesulfonamide **(2c)**

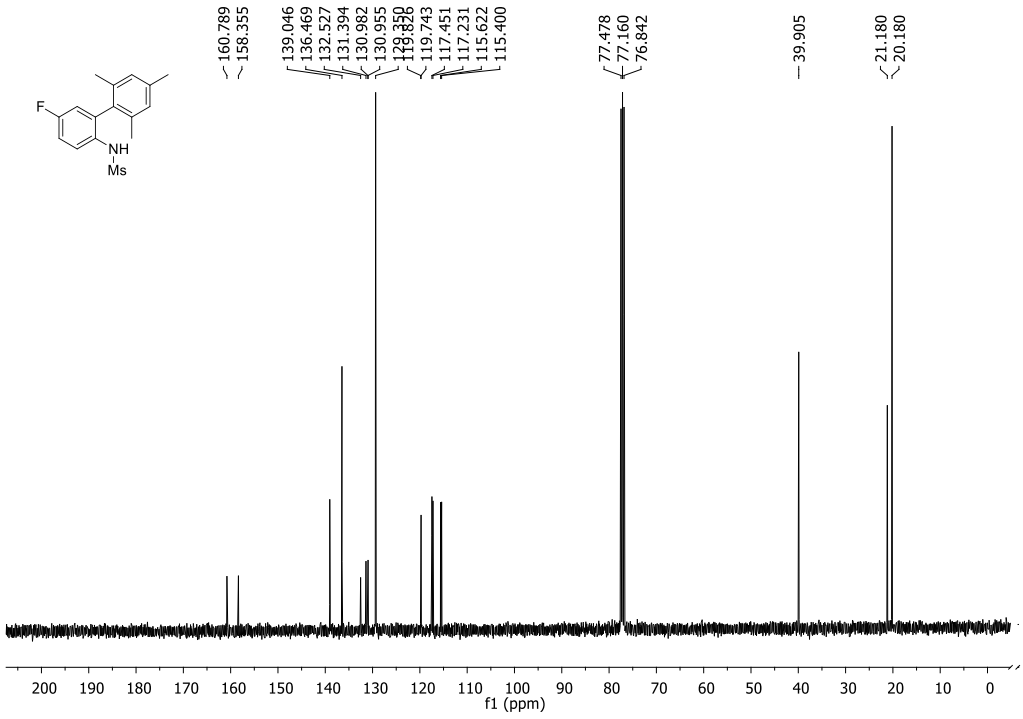


Figure 3.10 ^{13}C NMR spectrum of *N*-(5-Fluoro-2' ,4' ,6'-trimethyl-[1, 1'-biphenyl]-2-yl)methanesulfonamide **(2c)**

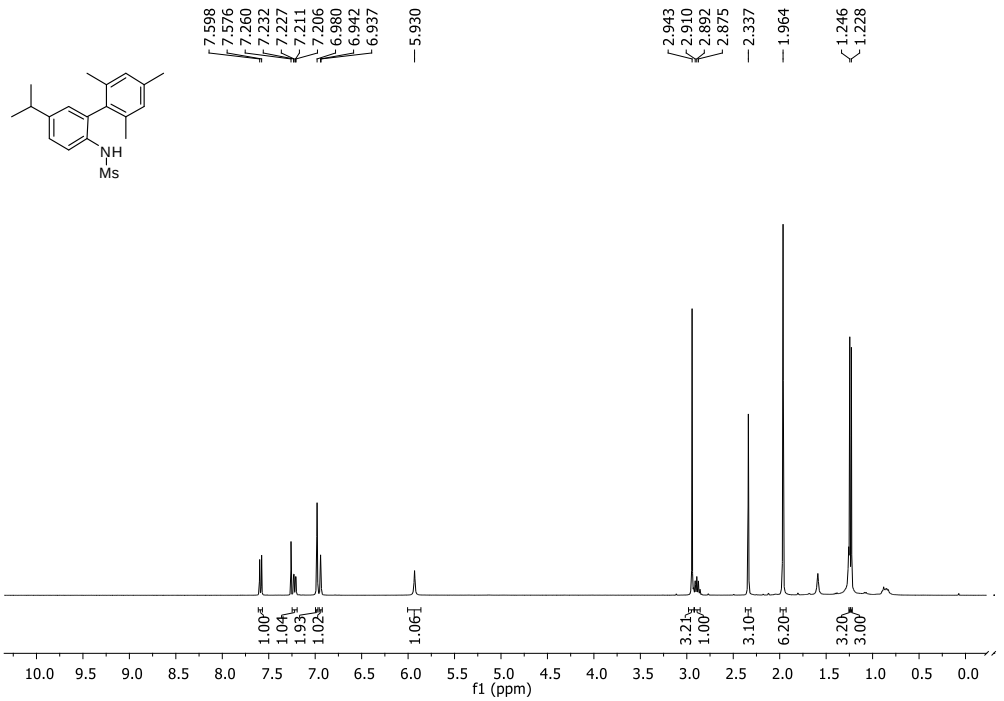


Figure 3.11 [1]H NMR spectrum of *N*-(5-Isopropyl-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2f**)

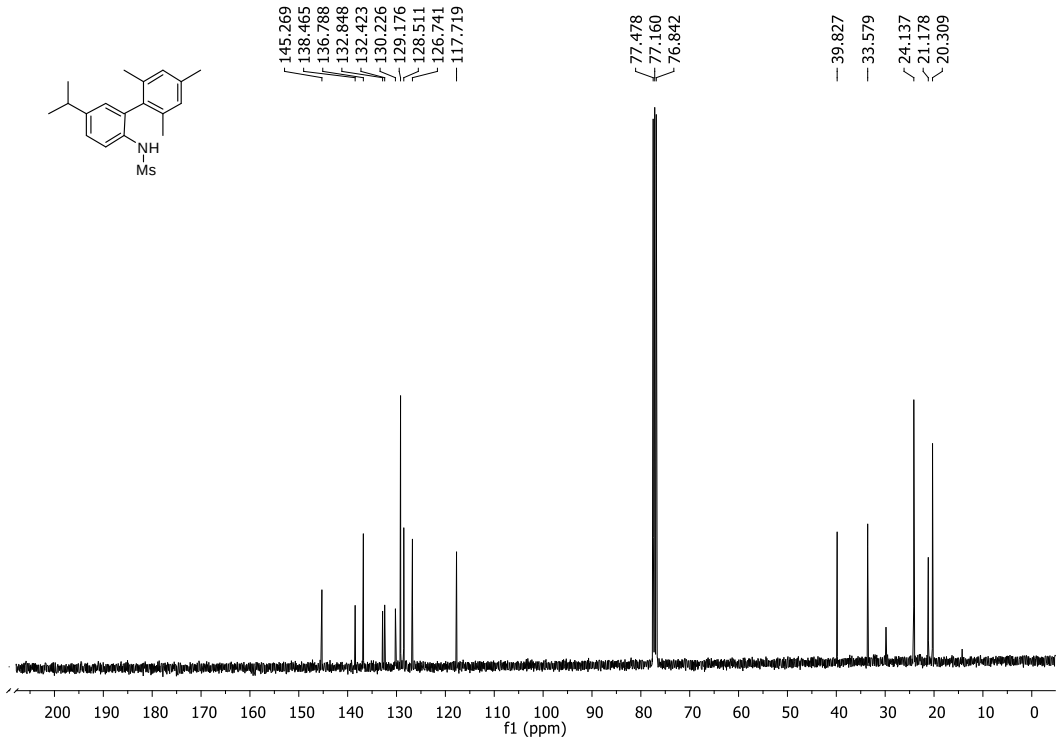


Figure 3.12 [13]CNMR spectrum of *N*-(5-Isopropyl-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2f**)

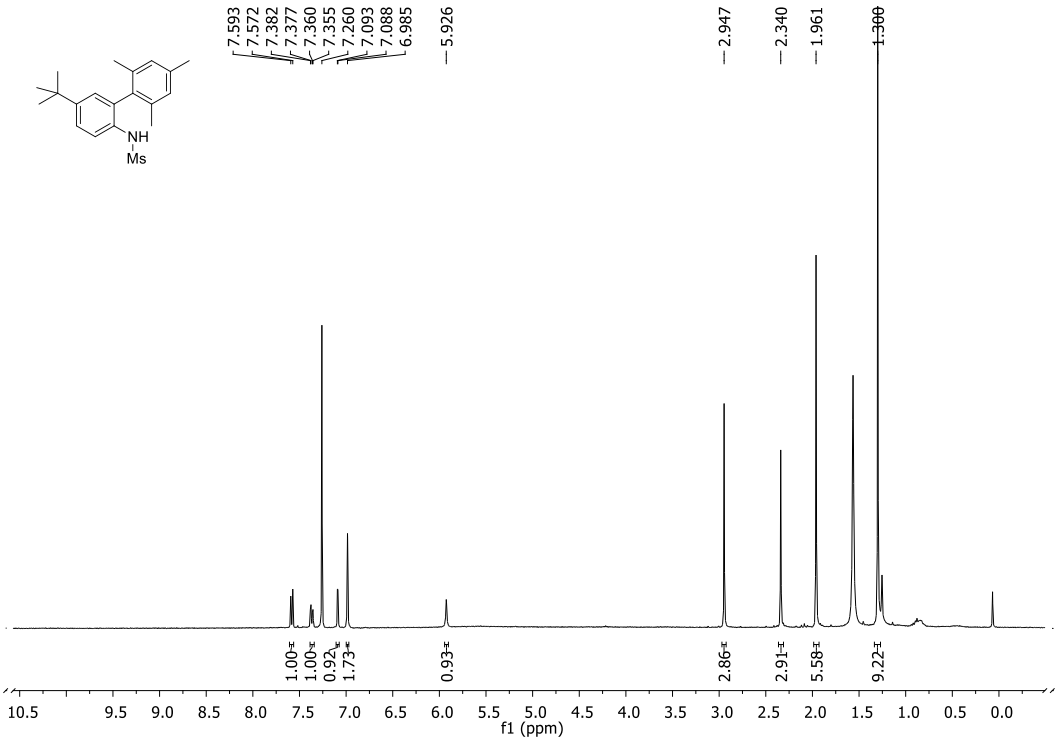


Figure 3.13 ^{1}H NMR spectrum of *N*-(5-(*tert*-Butyl)-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2g**)

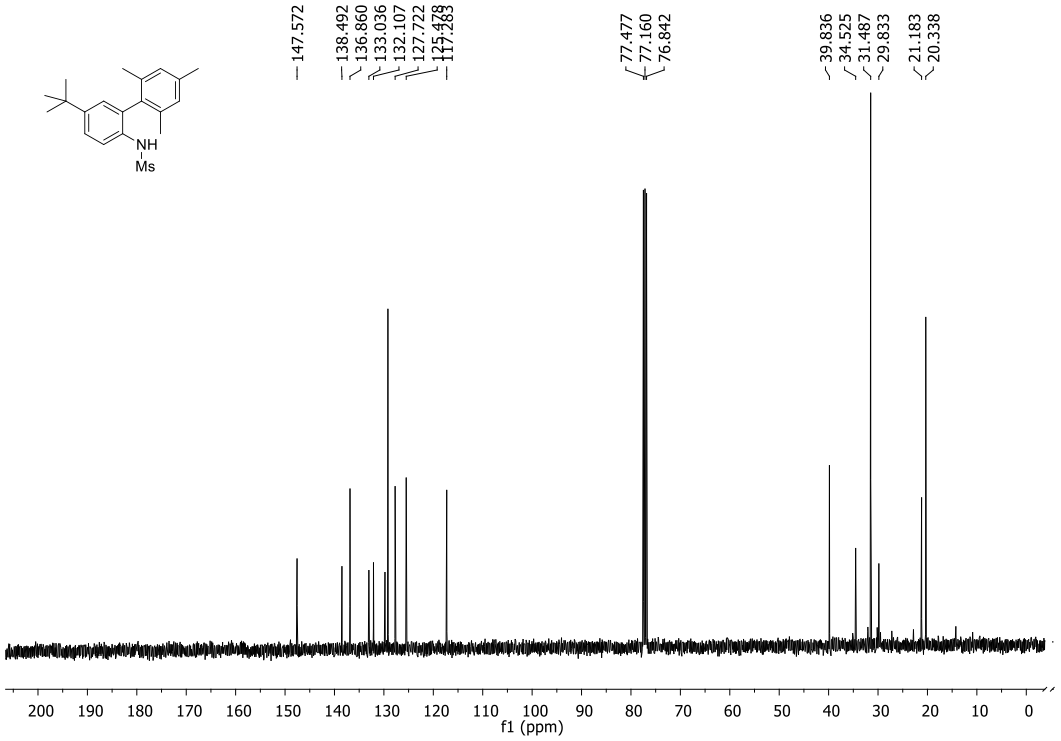


Figure 3.14 ^{13}C NMR spectrum of *N*-(5-(*tert*-Butyl)-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2g**)

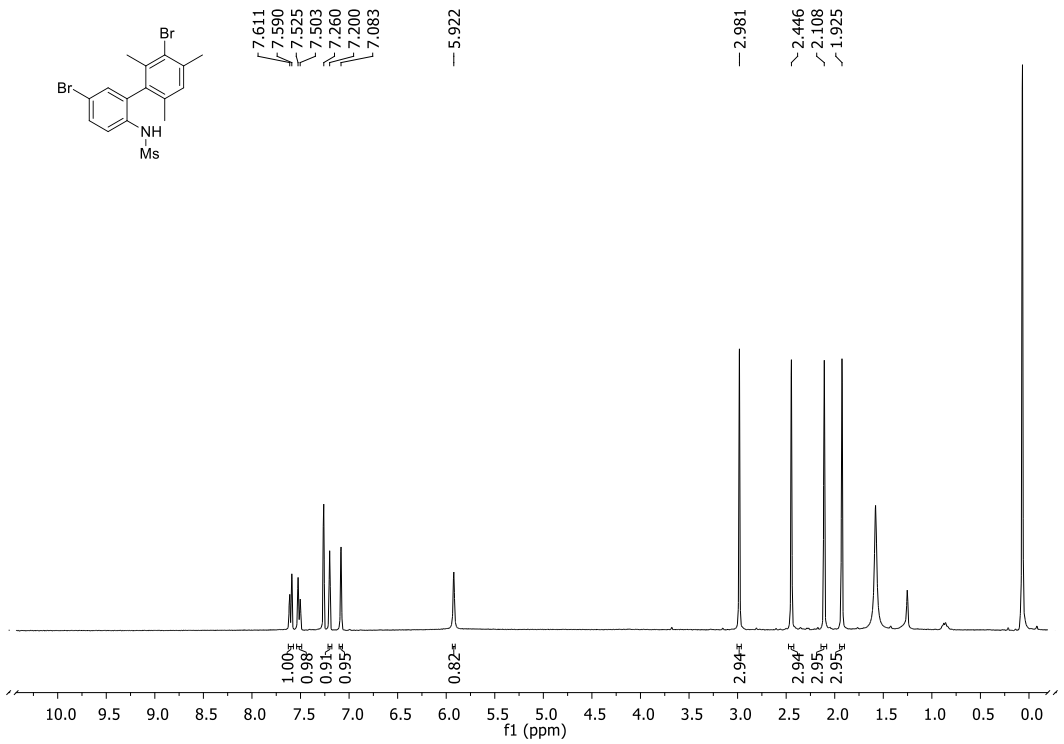


Figure 3.15 ^{1}H NMR spectrum of *N*-(3',5-Dibromo-2',4',6'-trimethyl-[1.1'-biphenyl]-2-yl]methanesulfonamide (**2h)**

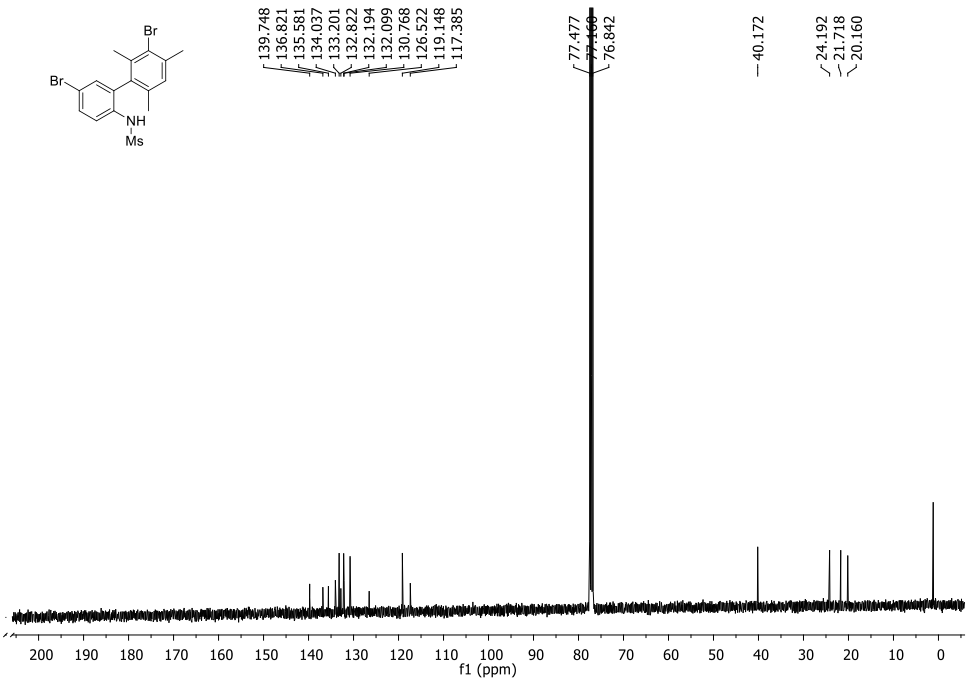


Figure 3.16 ^{13}C NMR spectrum of *N*-(3',5-Dibromo-2',4',6'-trimethyl-[1.1'-biphenyl]-2-yl]methanesulfonamide (**2h**)

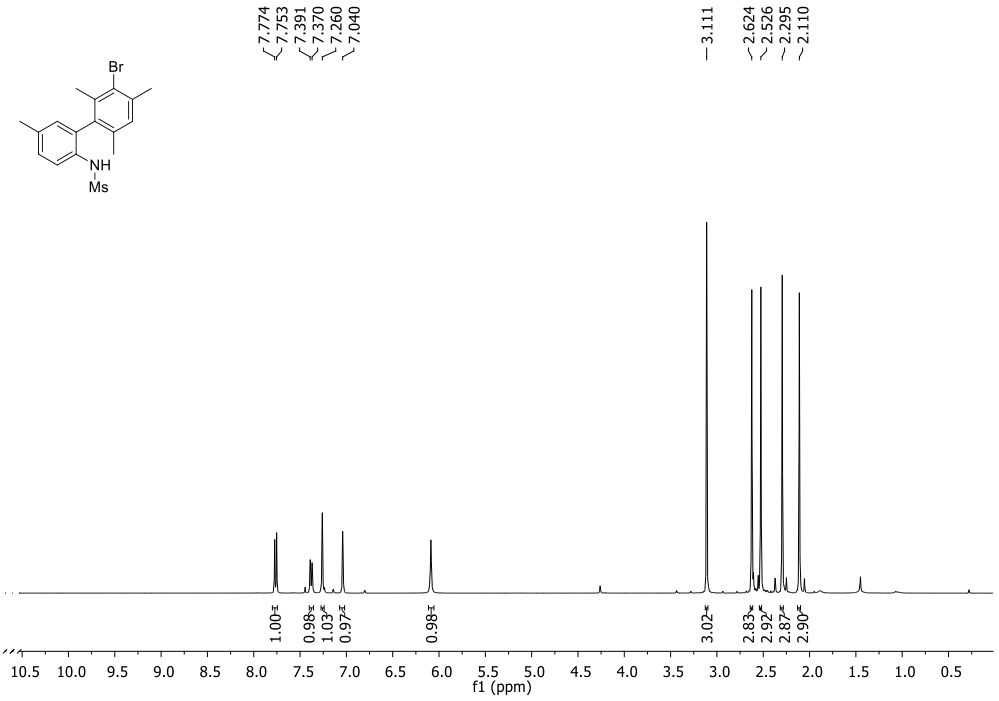


Figure 3.17 ^{1}H NMR spectrum *N*-(3'-Bromo-2',4', 5', 6'-tetramethyl–[1,1'-biphenyl]-2-yl)methanesulfonamide (**2i**)

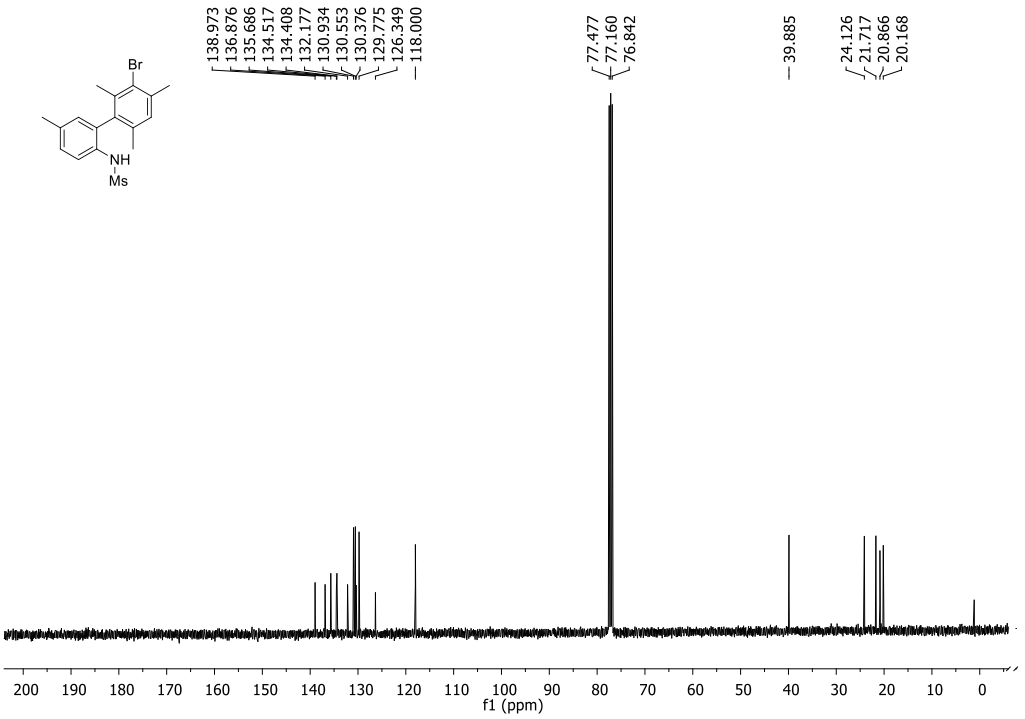


Figure 3.18 ^{13}C NMR spectrum of *N*-(3'-Bromo-2',4', 5', 6'-tetramethyl–[1,1'-biphenyl]-2-yl)methanesulfonamide (**2i**)

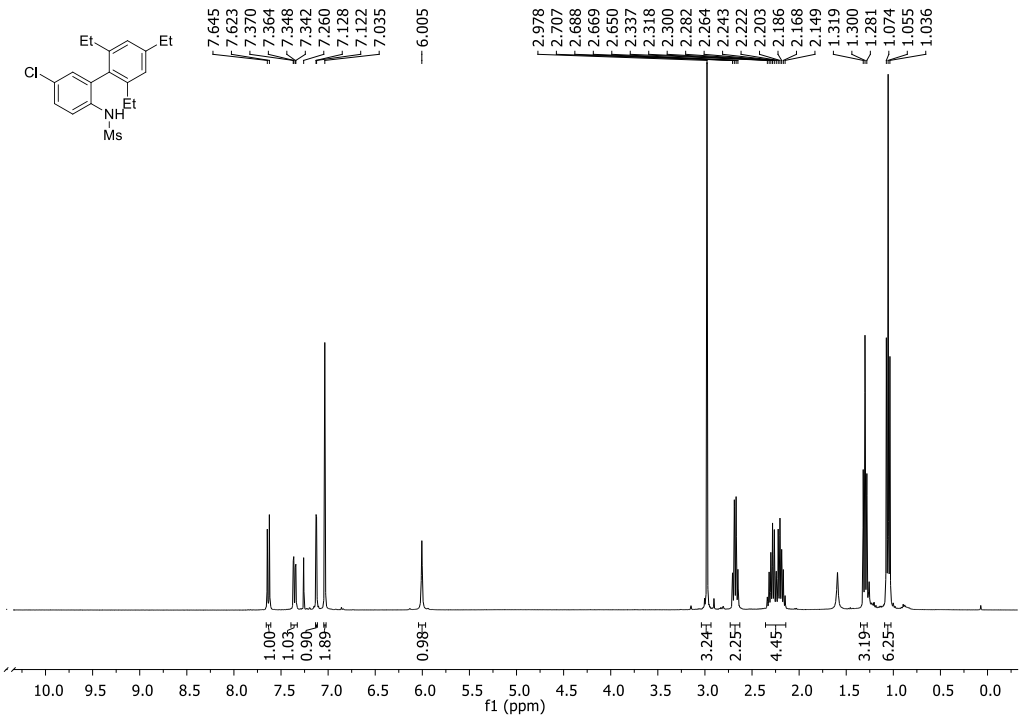


Figure 3.19 ^{1}H NMR spectrum of *N*-(5-Chloro-2',4', 6'-triethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2j**)

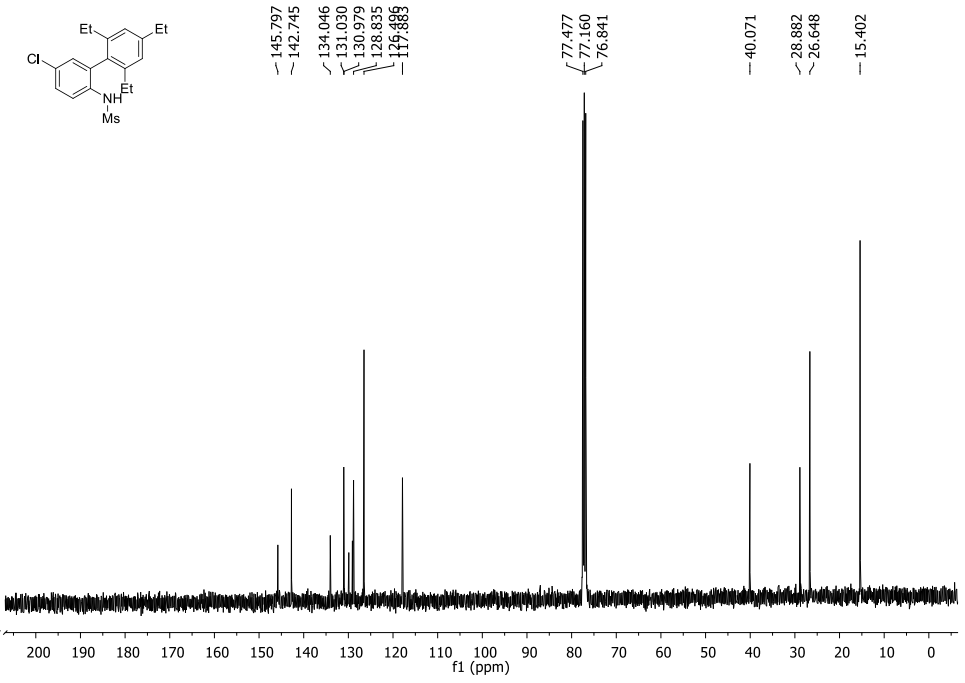


Figure 3.20 ^{13}C NMR spectrum of *N*-(5-Chloro-2',4', 6'-triethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2j**)

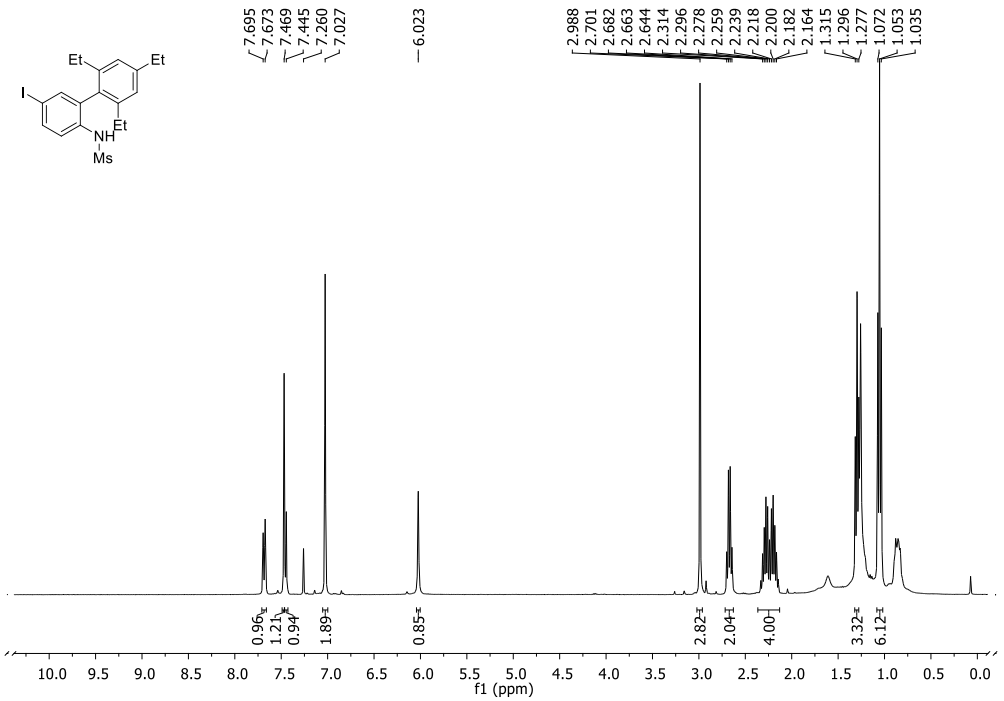


Figure 3.21 [1]H NMR spectrum of *N*-(2',4', 6'-Triethyl-5-iodo-[1,1'-biphenyl]-2-yl)methanesulfonamide **(2k**)

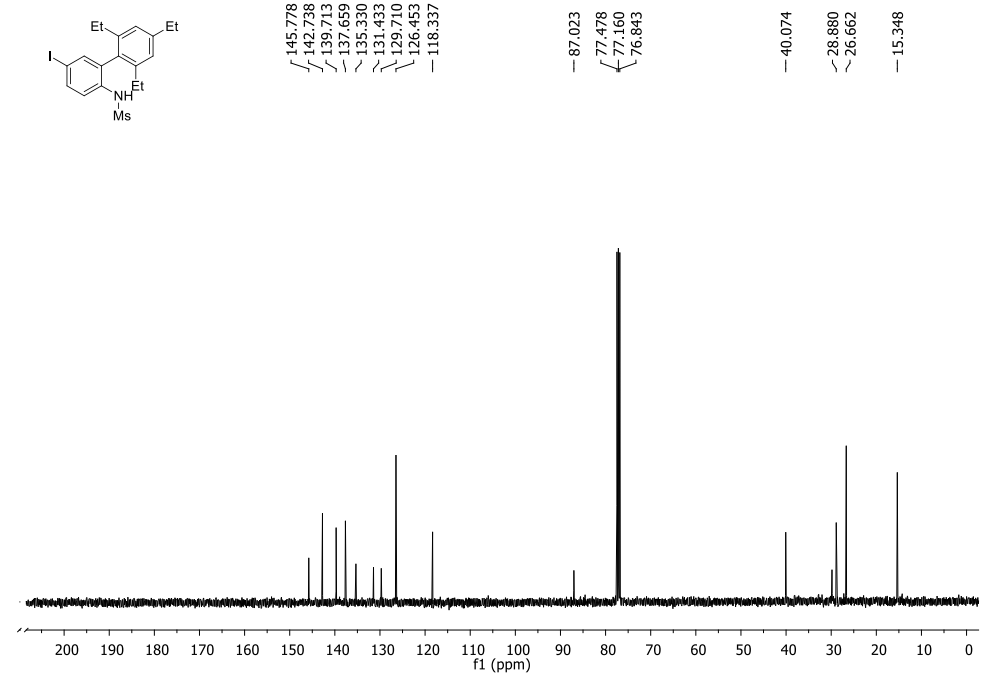


Figure 3.22 [13]C NMR spectrum of *N*-(2',4', 6'-Triethyl-5-iodo-[1,1'-biphenyl]-2-yl)methanesulfonamide **(2k**)

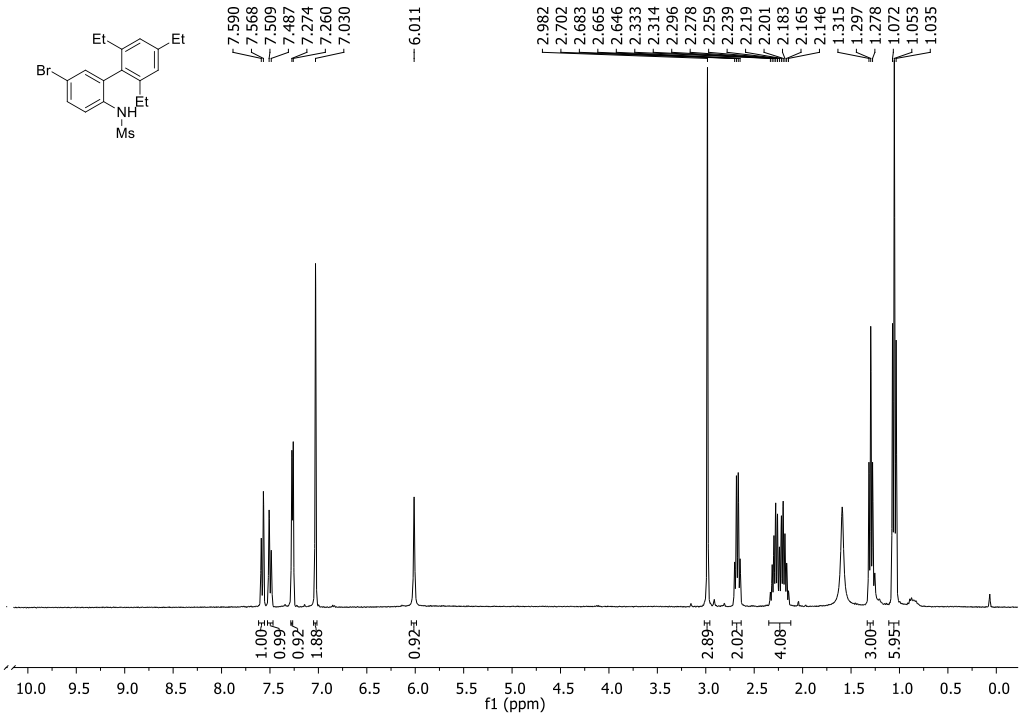


Figure 3.23 ^{1}H NMR spectrum of *N*-(5-Bromo-2',4', 6'-triethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2l**)

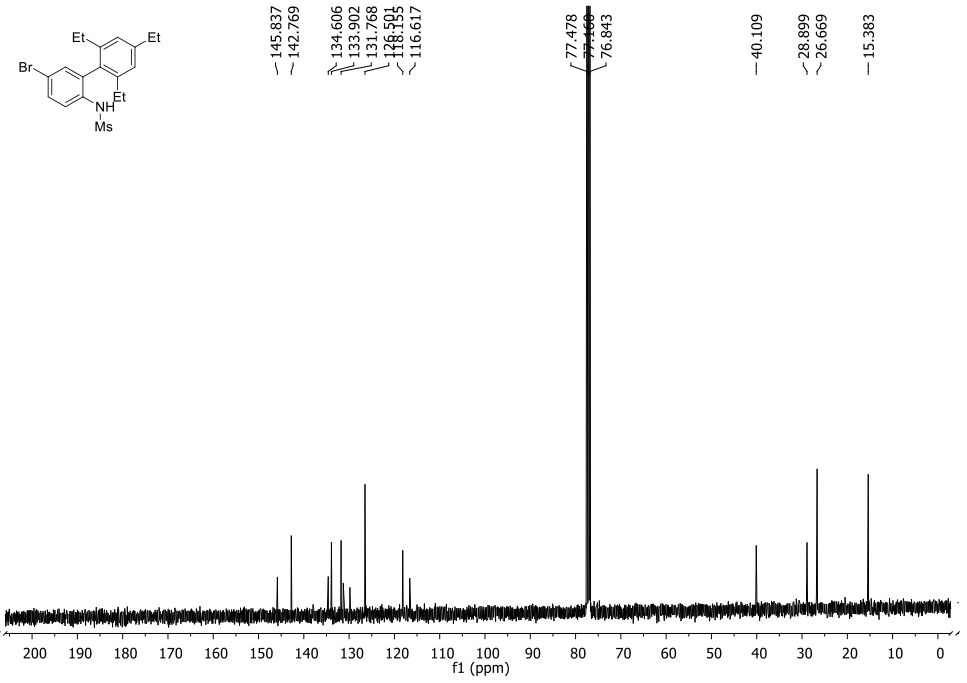


Figure 3.24 ^{13}CNMR spectrum of *N*-(5-Bromo-2',4', 6'-triethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**2l**)

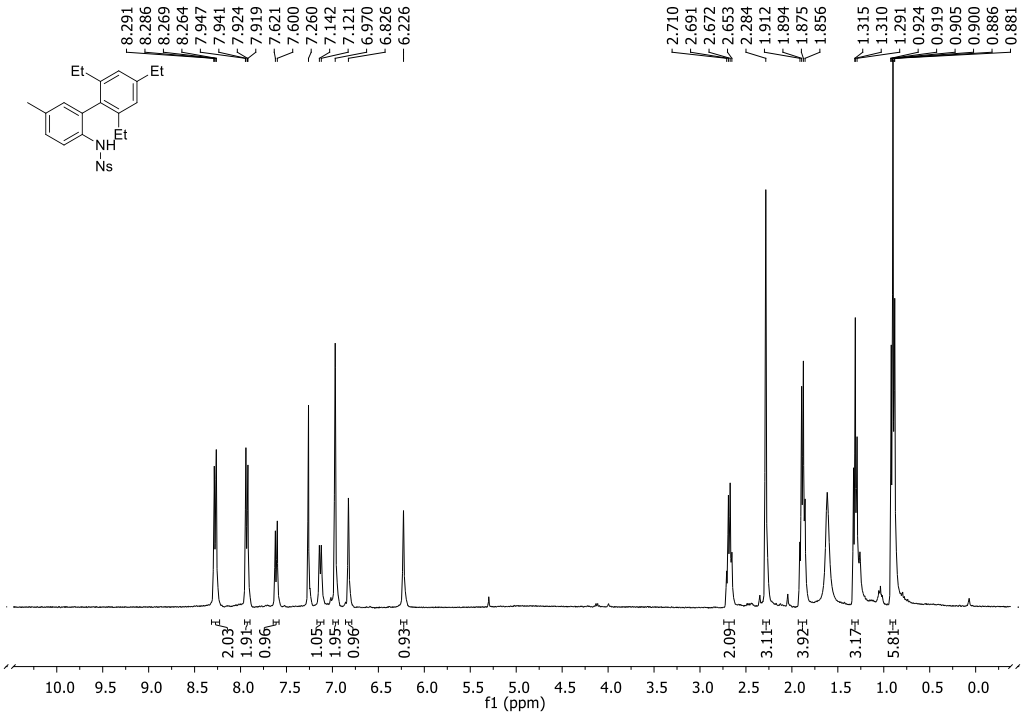


Figure 3.25 ^{1}H NMR spectrum of 4-Nitro-*N*-(2',4', 6'-triethyl-5-methyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (**2m**)

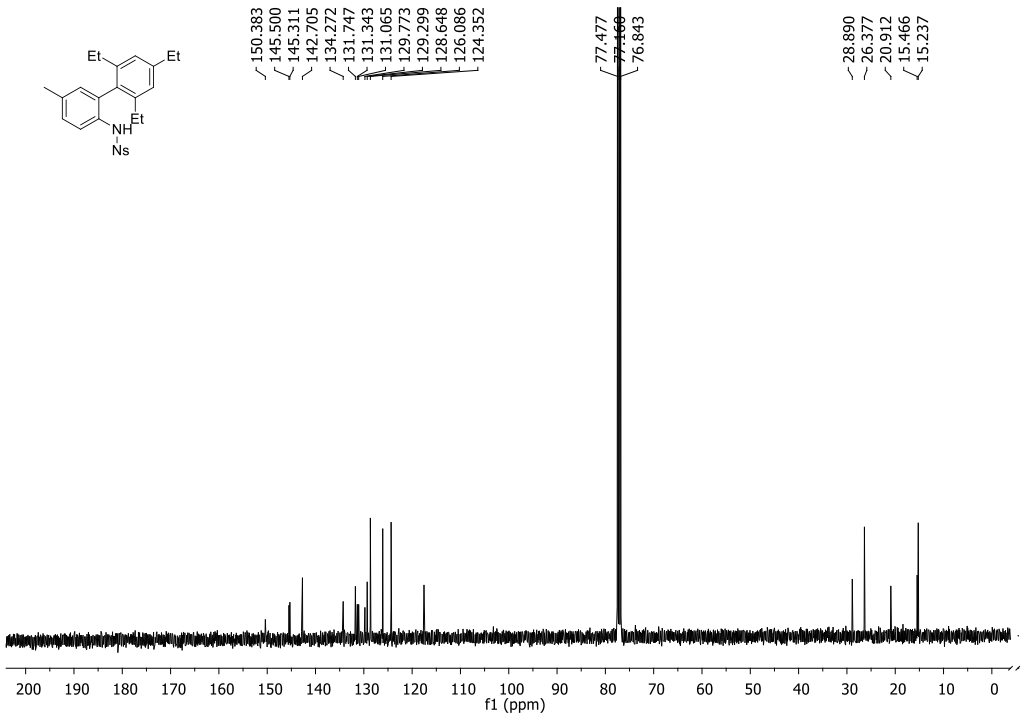


Figure 3.26 ^{13}C NMR spectrum of 4-Nitro-*N*-(2',4', 6'-triethyl-5-methyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (**2m**)

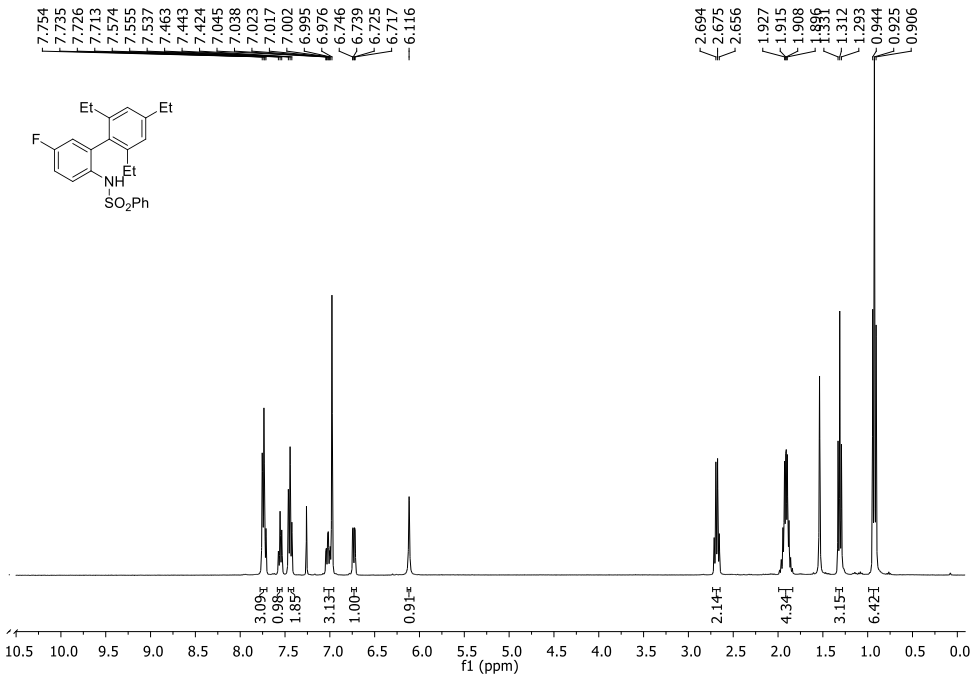


Figure 3.27 ^{1}H NMR spectrum of *N*-(2',4',6'-Triethyl-5-fluoro-[1, 1'-biphenyl]-2-yl)benzenesulfonamide (**2n**)

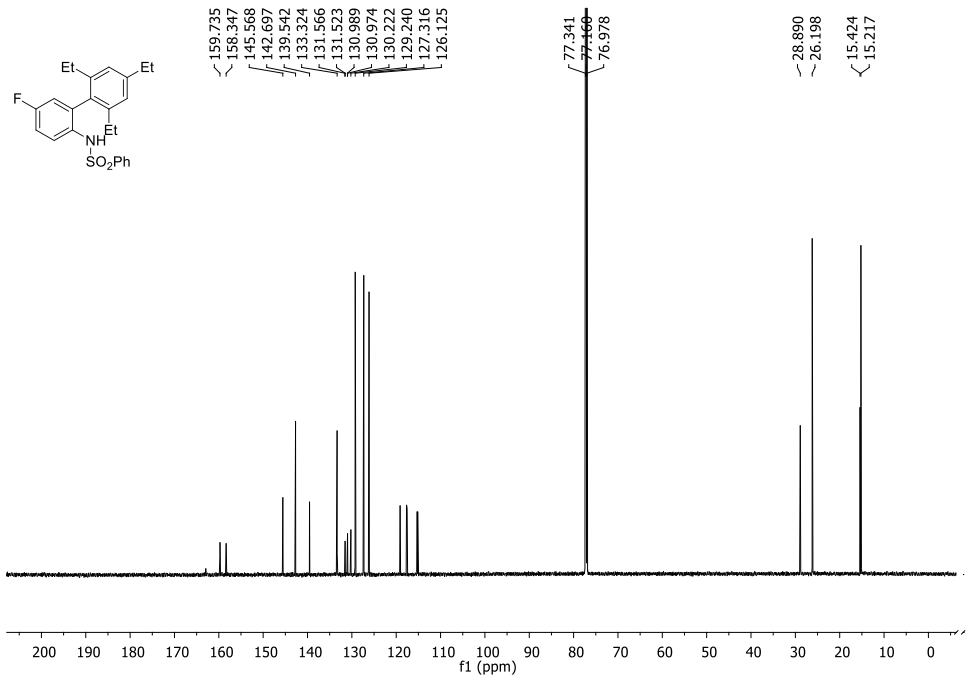
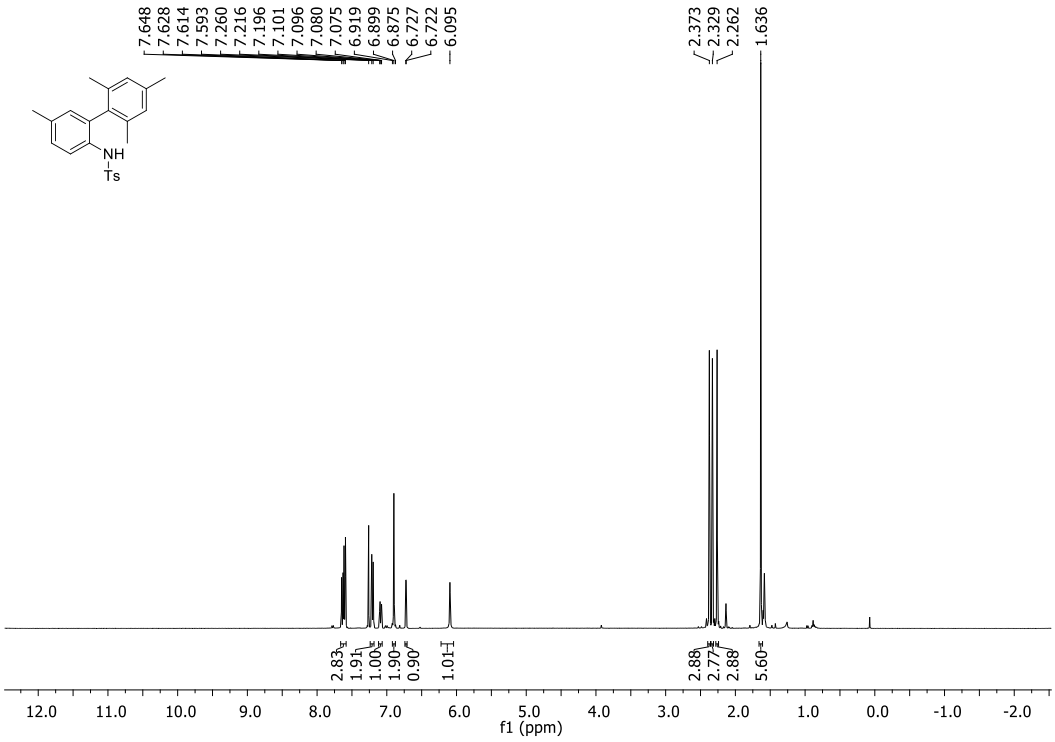


Figure 3.28 ^{13}C NMR spectrum of *N*-(2',4',6'-Triethyl-5-fluoro-[1, 1'-biphenyl]-2-yl)benzenesulfonamide (**2n**)



. **Figure 3.29** [1]H NMR spectrum of 4-Methyl-*N*-(2',4' ,5' 6'-tetramethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (**2o)**

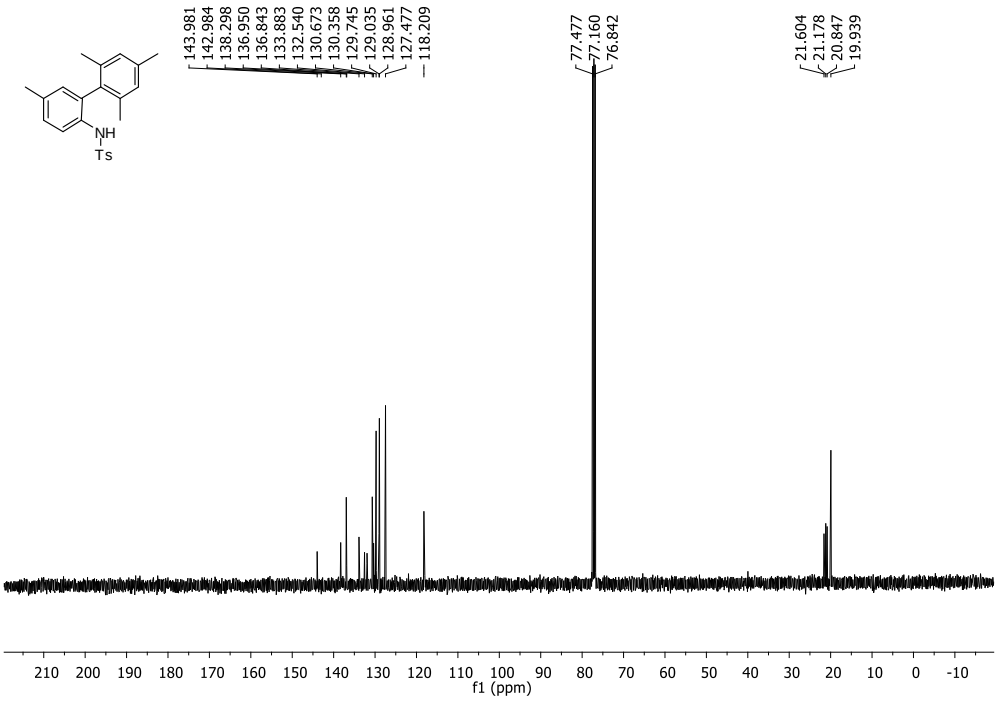


Figure 3.30 [13]C NMR spectrum of 4-Methyl-*N*-(2',4' ,5' 6'-tetramethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (**2o)**

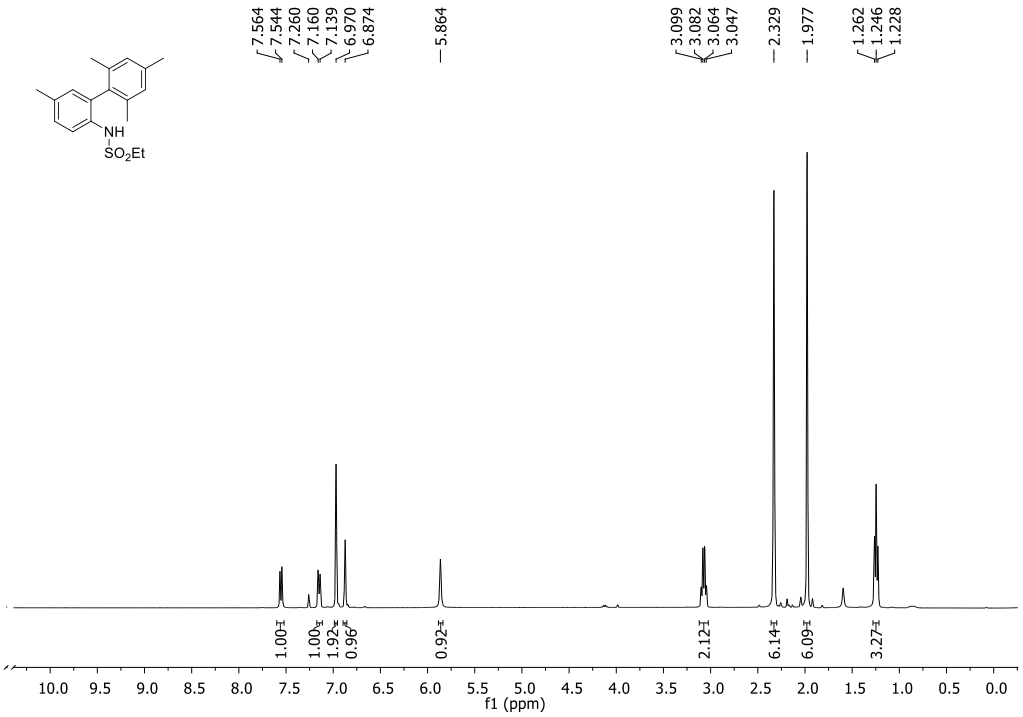


Figure 3.31 ^{1}H NMR spectrum of *N*-(2',4' ,5' 6'-Tetramethyl-[1,1'-biphenyl]-2-yl)ethanesulfonamide (**2p**)

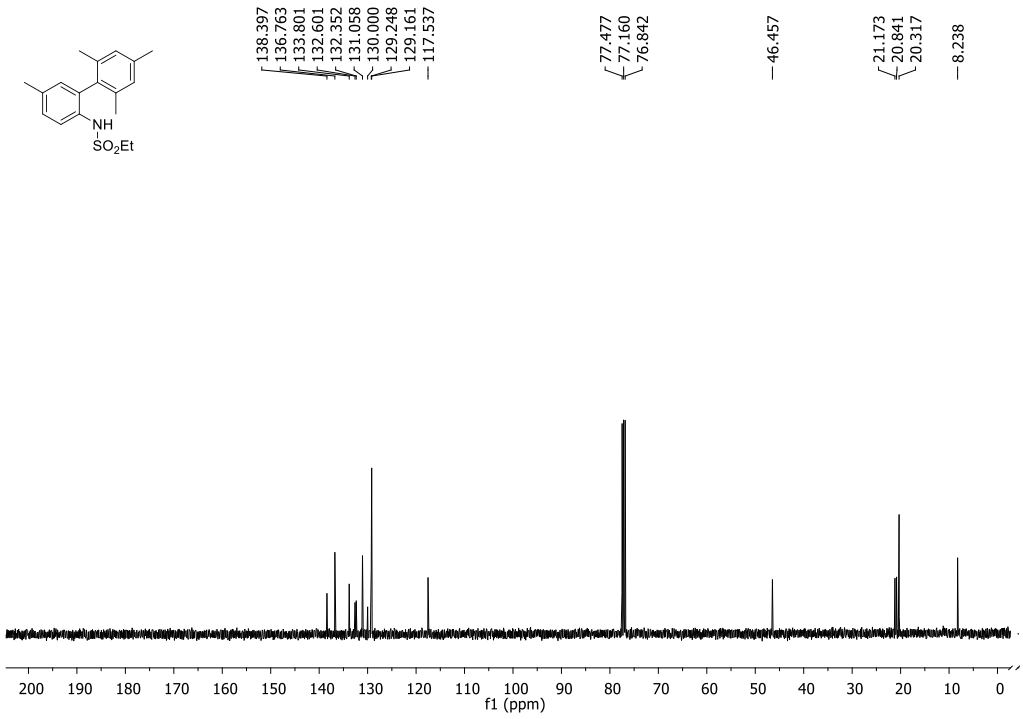


Figure 3.32 ^{13}C NMR spectrum of *N*-(2',4' ,5' 6'-Tetramethyl-[1,1'-biphenyl]-2-yl)ethanesulfonamide (**2p**)

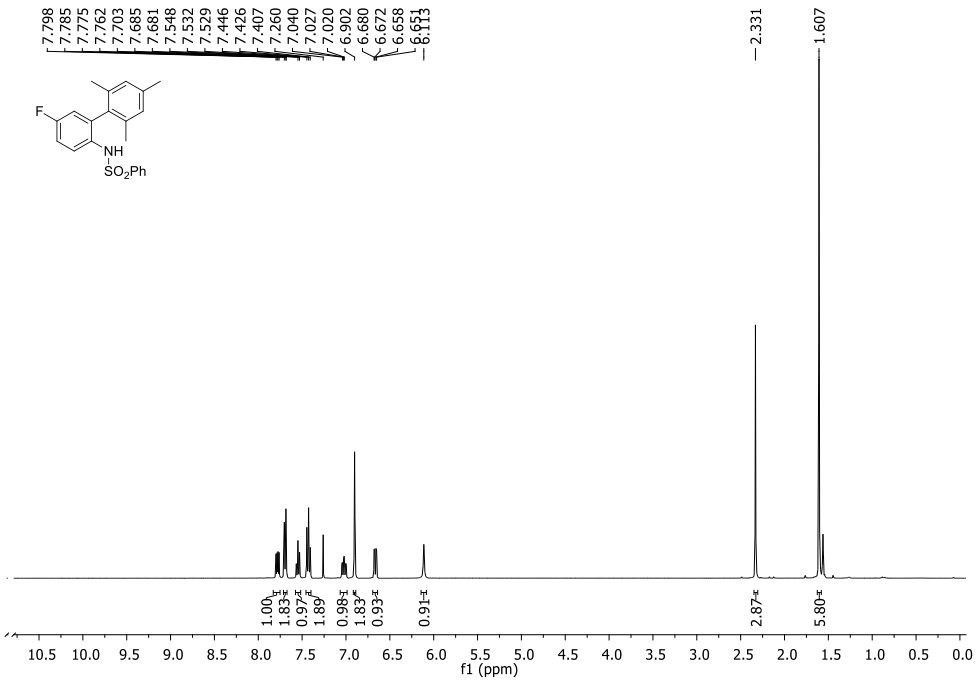


Figure 3.33 ^{1}H NMR spectrum of *N*-(5-Fluoro-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (**2q**)

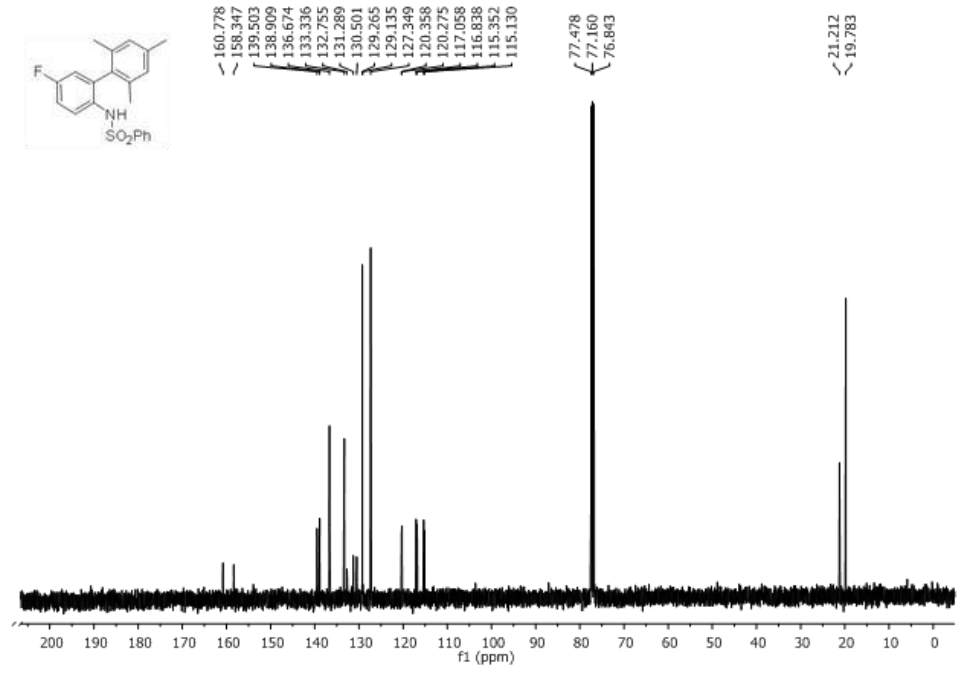


Figure 3.34 ^{13}C NMR spectrum of *N*-(5-Fluoro-2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide (**2q**)

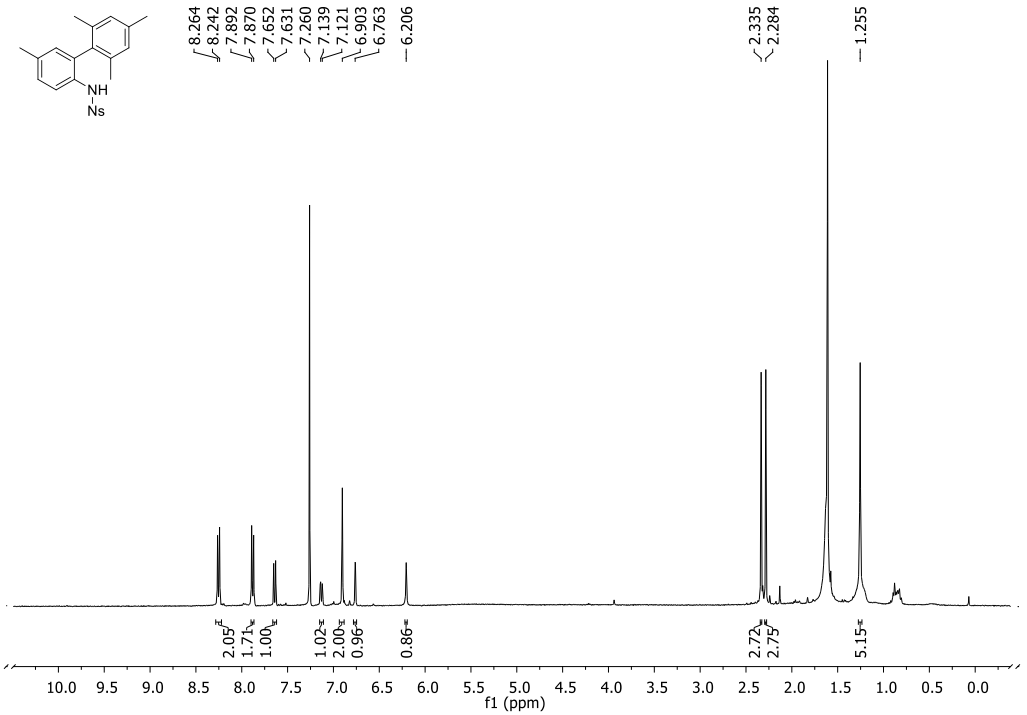


Figure 3.35 ^{1}H NMR spectrum of 4-Nitro-*N*-(2',4',5', 6'-tetramethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide**(2r)**

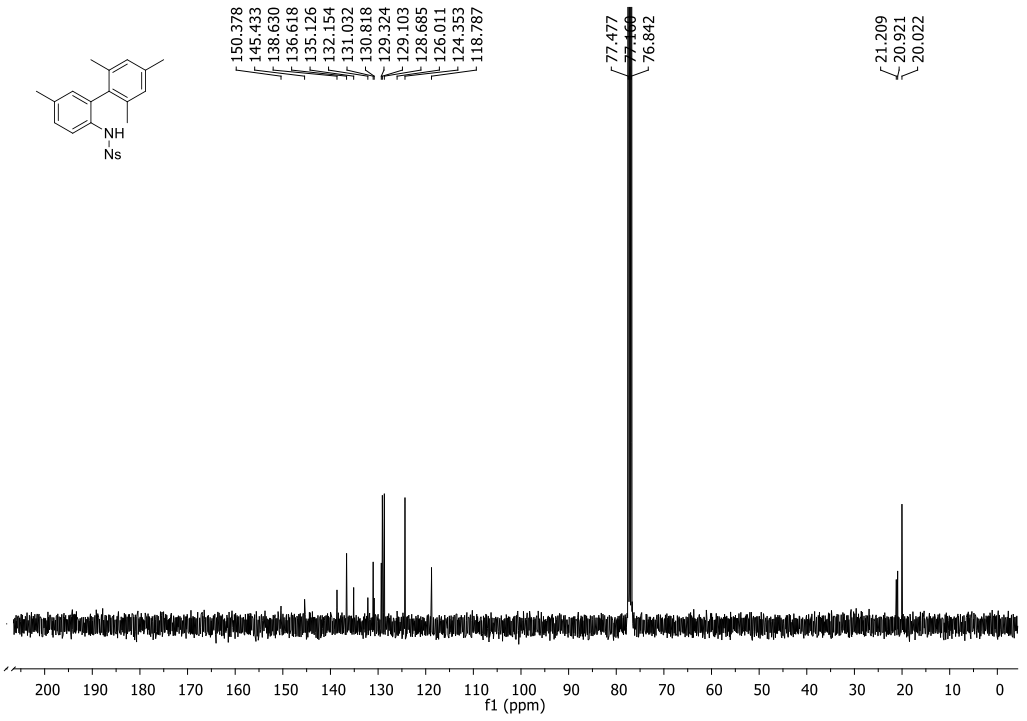


Figure 3.36 ^{13}C NMR spectrum of 4-Nitro-*N*-(2',4',5', 6'-tetramethyl-[1,1'-biphenyl]-2-yl)benzenesulfonamide**(2r)**

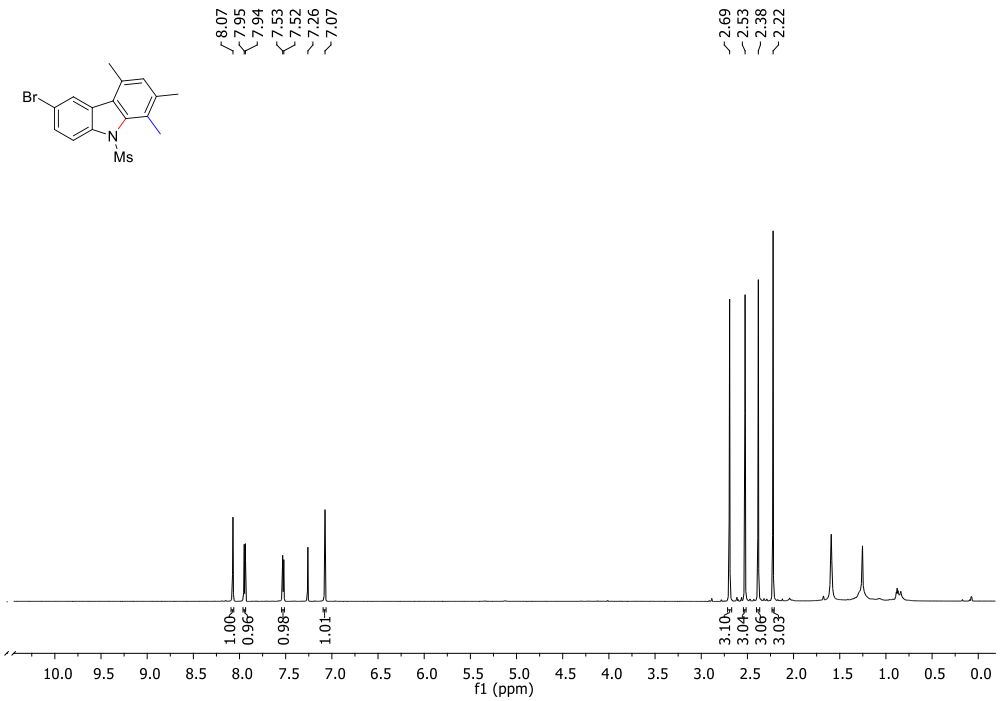


Figure 3.37 ^{1}H NMR spectrumof 6–Bromo-1,2,4-trimethyl-9(methylsulfonyl)-carbazole **(3a)**

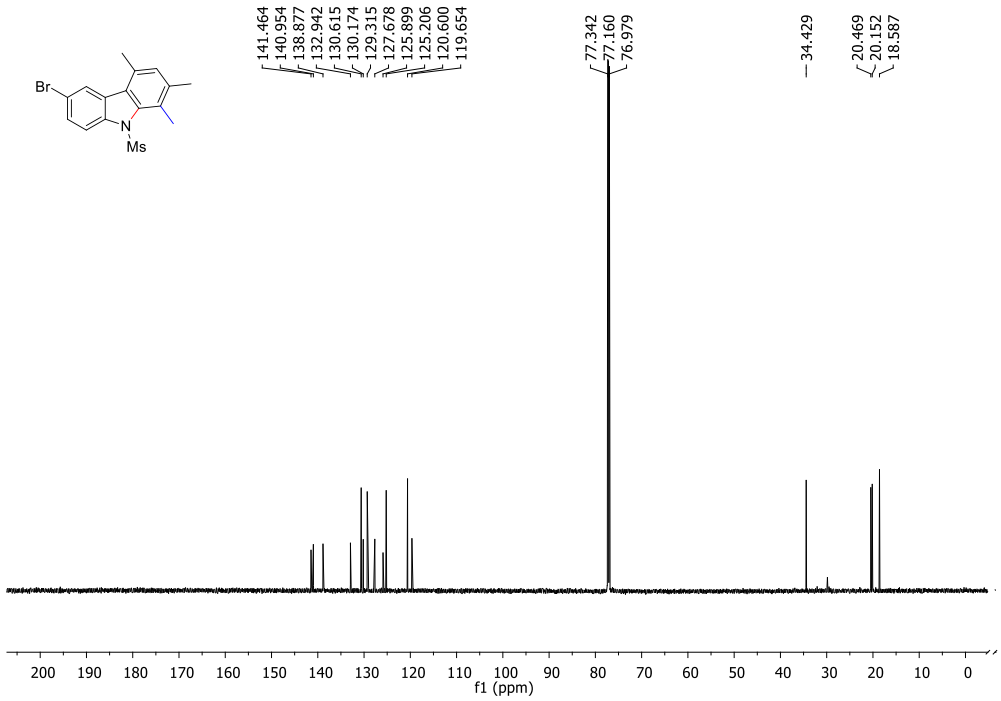


Figure 3.38 ^{13}C NMR spectrum of 6–Bromo-1,2,4-trimethyl-9(methylsulfonyl)-carbazole**(3a)**

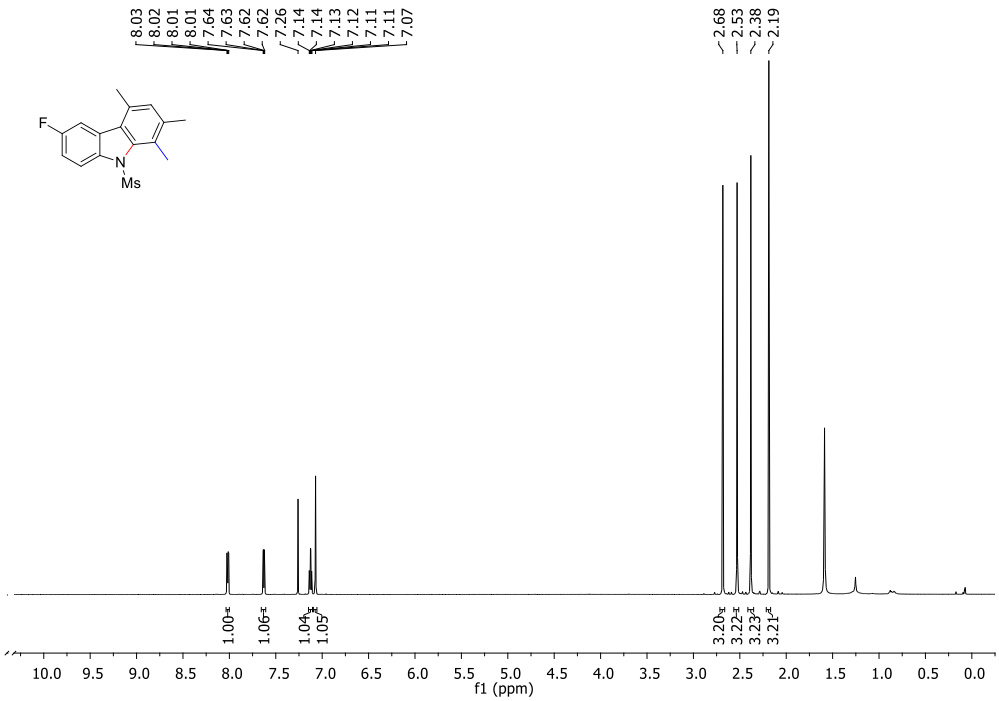


Figure 3.39 ^{1}H NMR spectrum of 6-Fluoro-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole **(3c)**

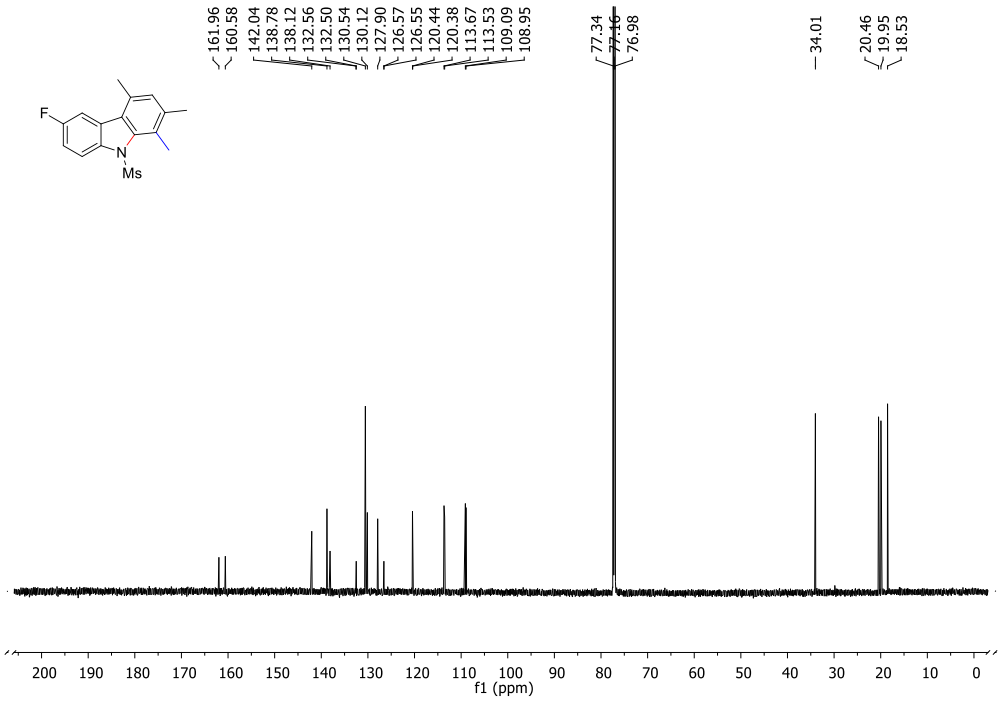


Figure 3.40 ^{13}C NMR spectrum of 6-Fluoro-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole **(3c)**

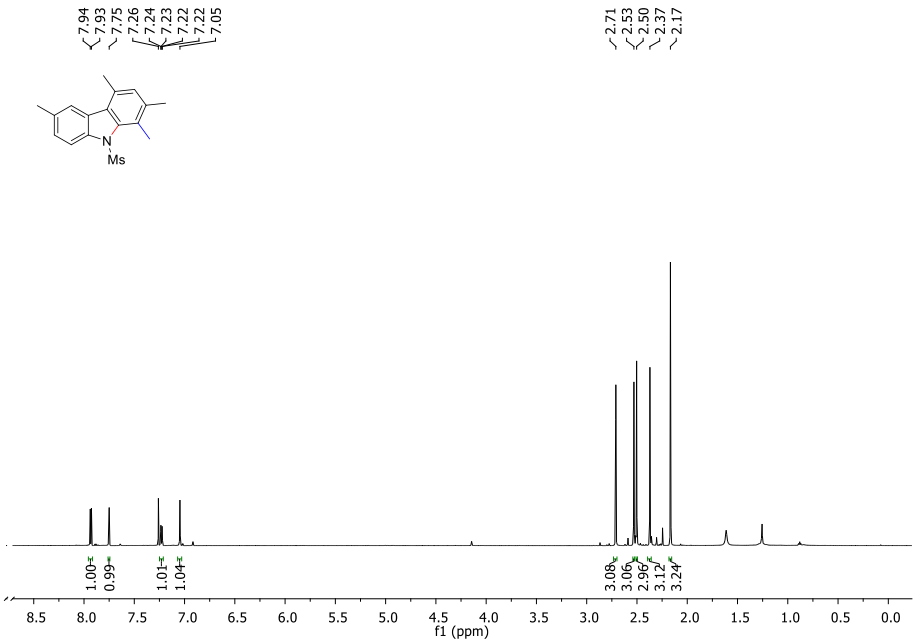


Figure 3.41 ^{1}H NMR spectrum of 1,2,4,6-Tetramethyl-9-(methylsulfonyl-)-carbazole **(3d)**

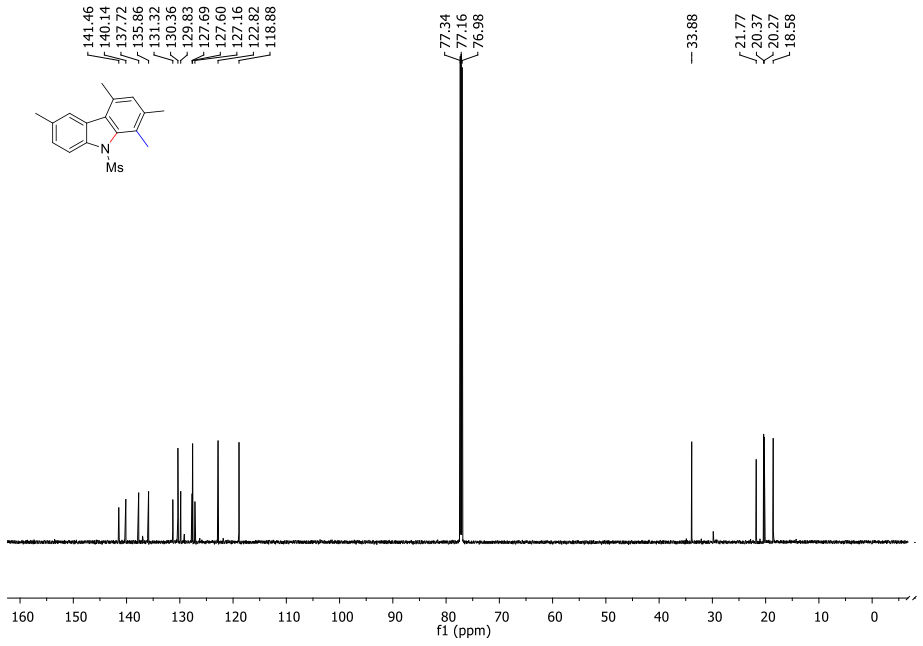


Figure 3.42 ^{13}C NMR spectraof 1,2,4,6-Tetramethyl-9-(methylsulfonyl-)-carbazole **(3d)**

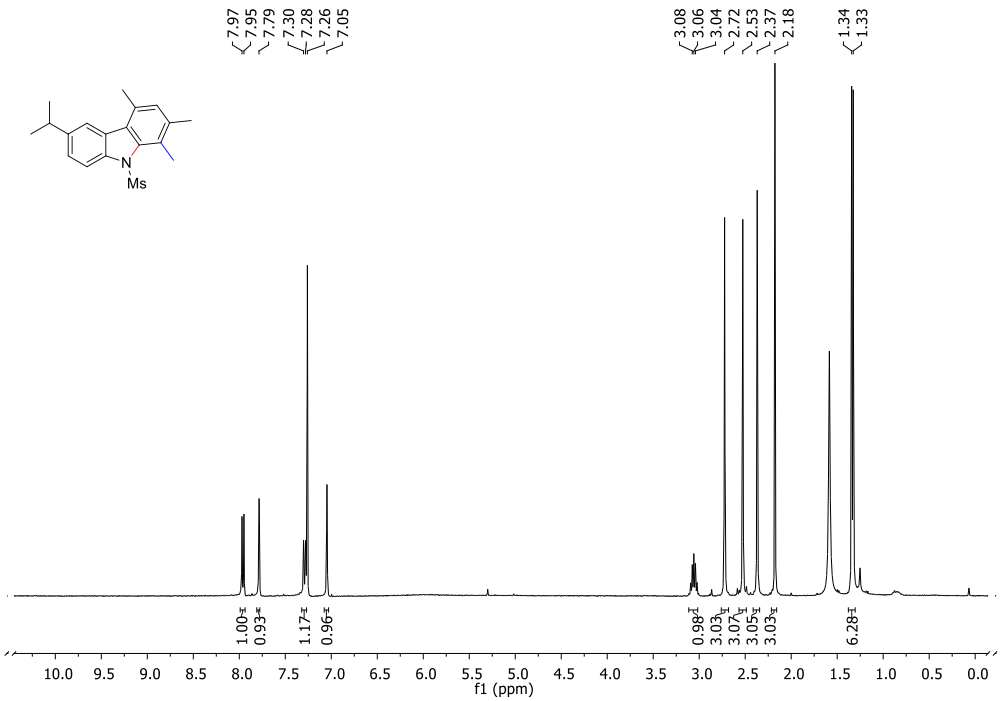


Figure 3.43 [1]H NMR spectrum of 6-Isopropyl-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (**3f**)

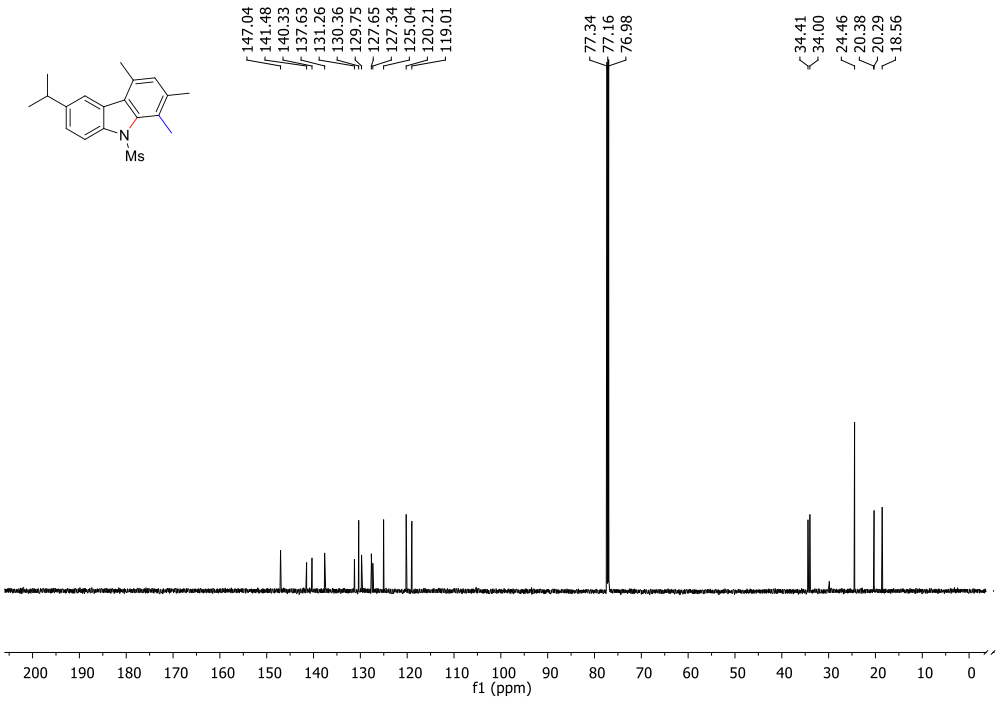


Figure 3.44 [13]C NMR spectrum of 6-Isopropyl-1,2,4-trimethyl-9-(methylsulfonyl)carbazole **(3f)**

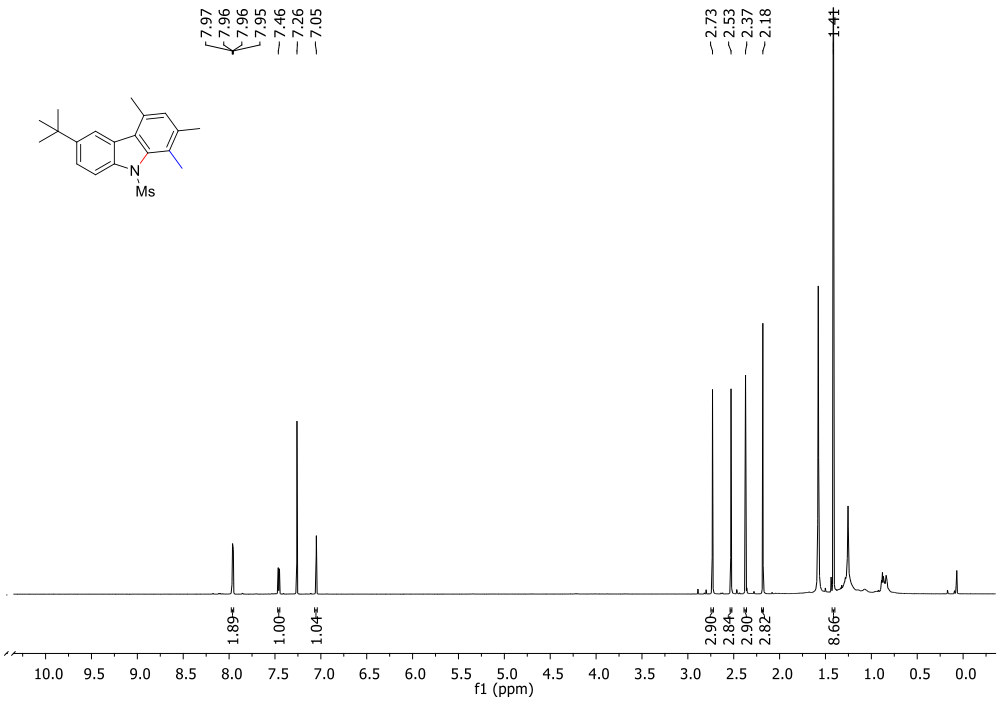


Figure 3.45 ^{1}H NMR spectrum of 6-(*tert*-butyl)-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (**3g)**

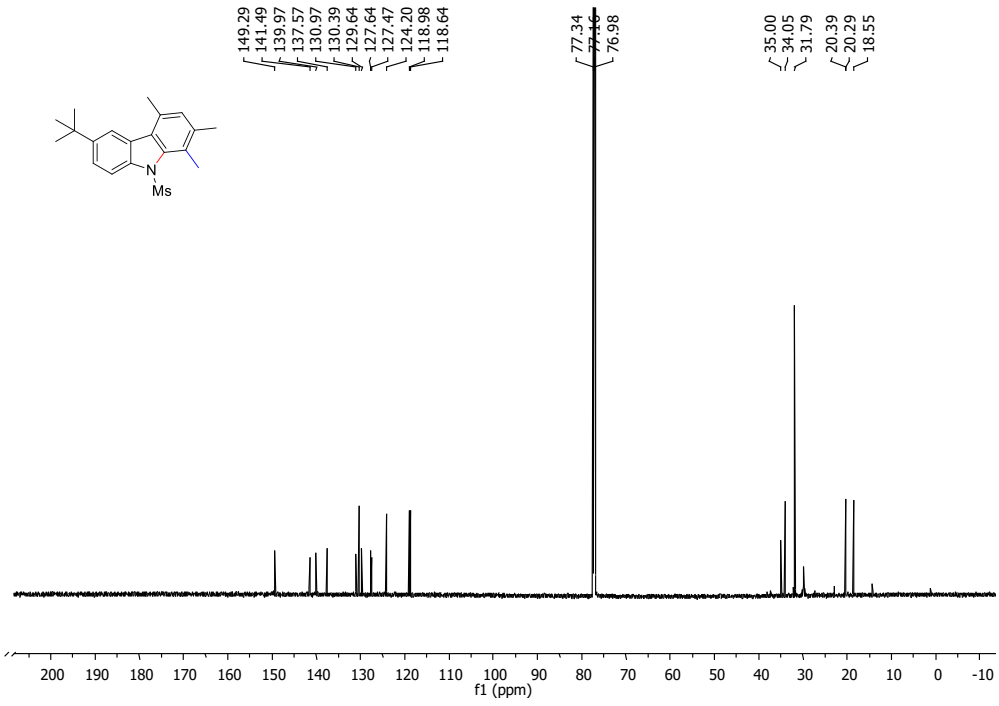


Figure 3.46 ^{13}C NMR spectra of 6-*(tert*-Butyl)-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (**3g)**

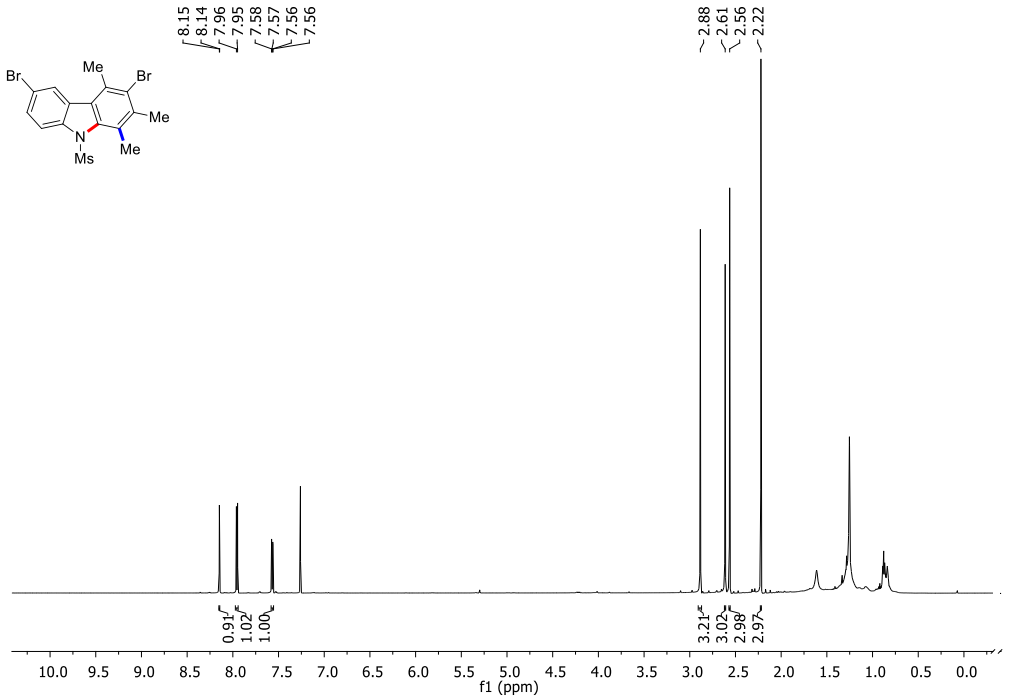


Figure 3.47 [1]H NMR spectrum of3,6-Dibromo-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole (**3h)**

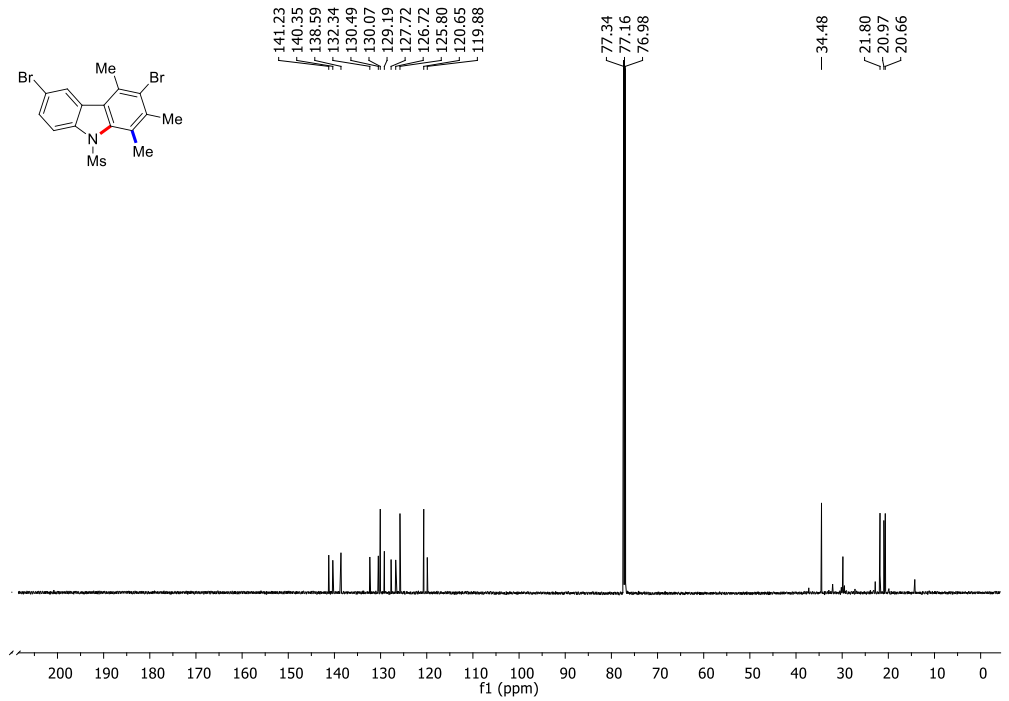


Figure 3.48 [13]CNMR spectrum of3,6-Dibromo-1,2,4-trimethyl-9-(methylsulfonyl)-carbazole **(3h)**

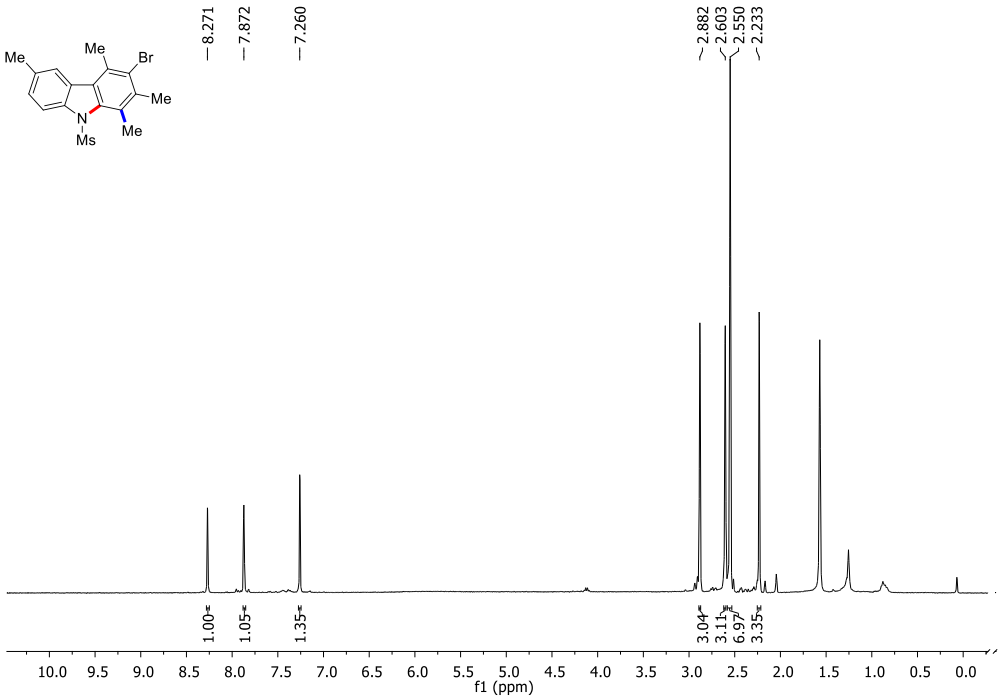


Figure 3.49 ^{1}H NMR spectrum of 3-Bromo-1,2,4,6-tetramethyl-9-(methylsulfonyl)-carbazole **(3i)**

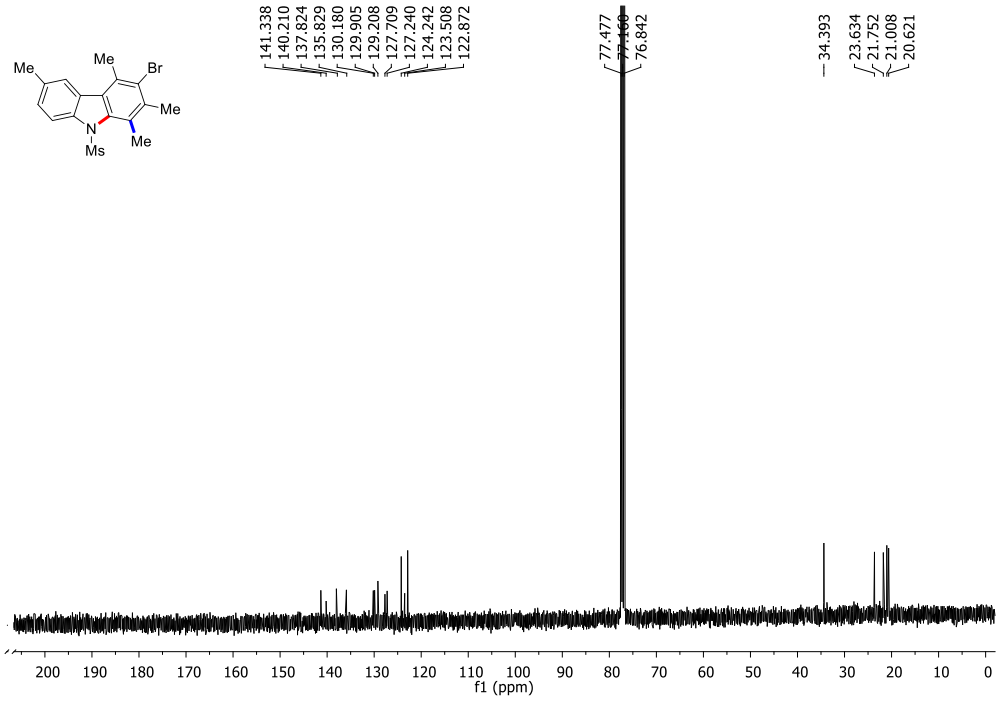


Figure 3.50 ^{13}C NMR spectrum of 3-Bromo-1,2,4,6-tetramethyl-9-(methylsulfonyl)-carbazole**(3i)**

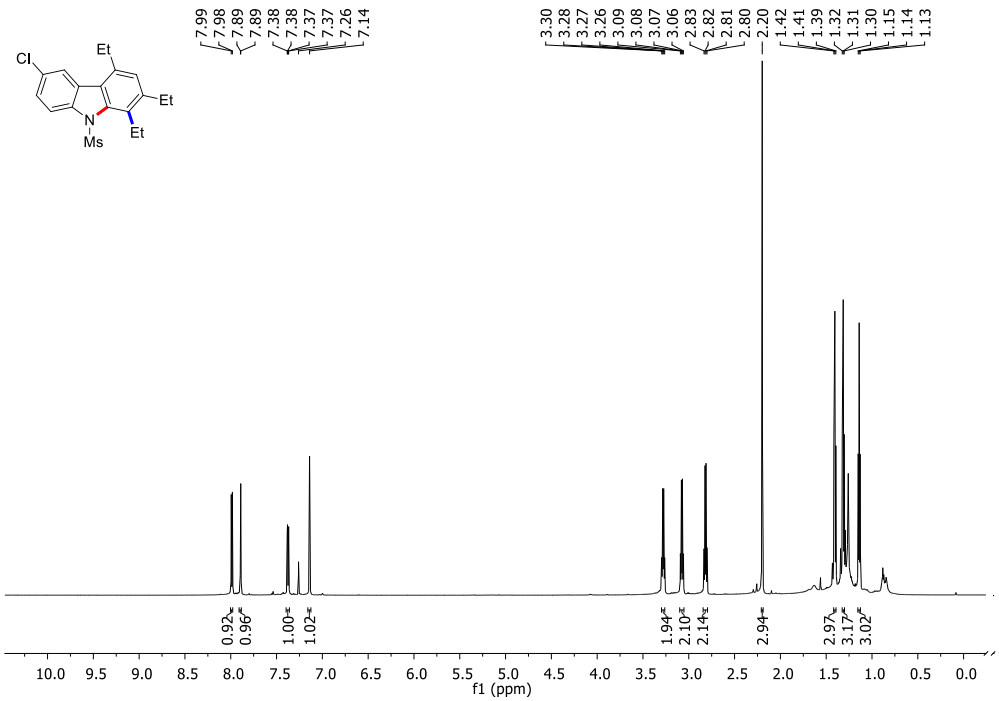


Figure 3.51 [1]H NMR spectrum of 6-Chloro-1,2,4-triethyl-9-(methylsulfonyl)-carbazole **(3j)**

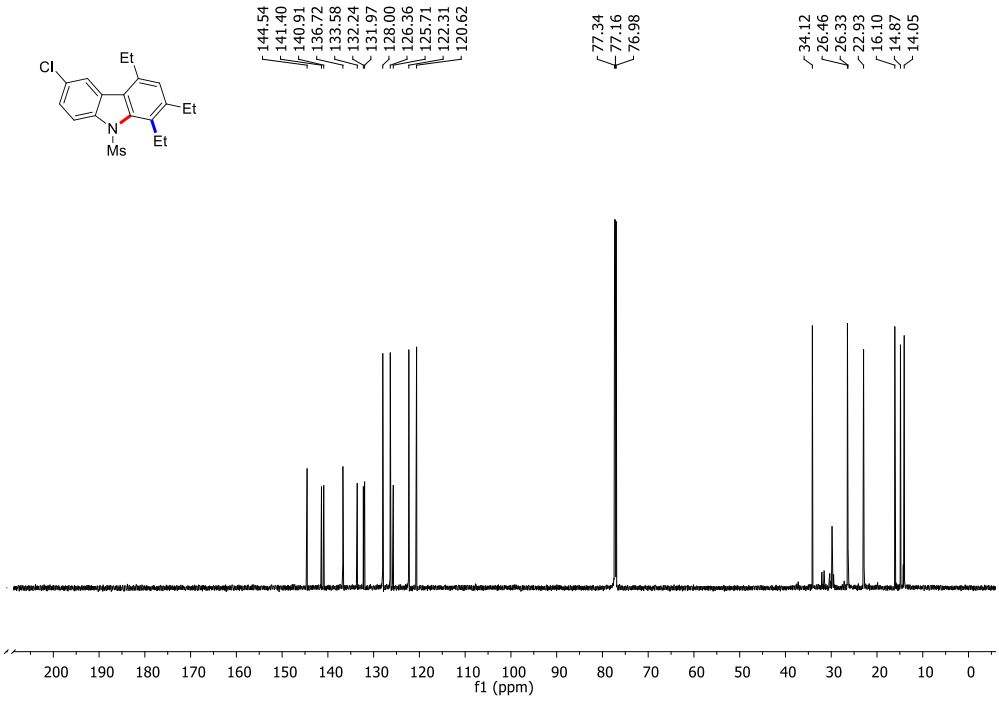


Figure 3.52 [13] C NMR spectrum of 6-Chloro-1,2,4-triethyl-9-(methylsulfonyl)-carbazole **(3j)**

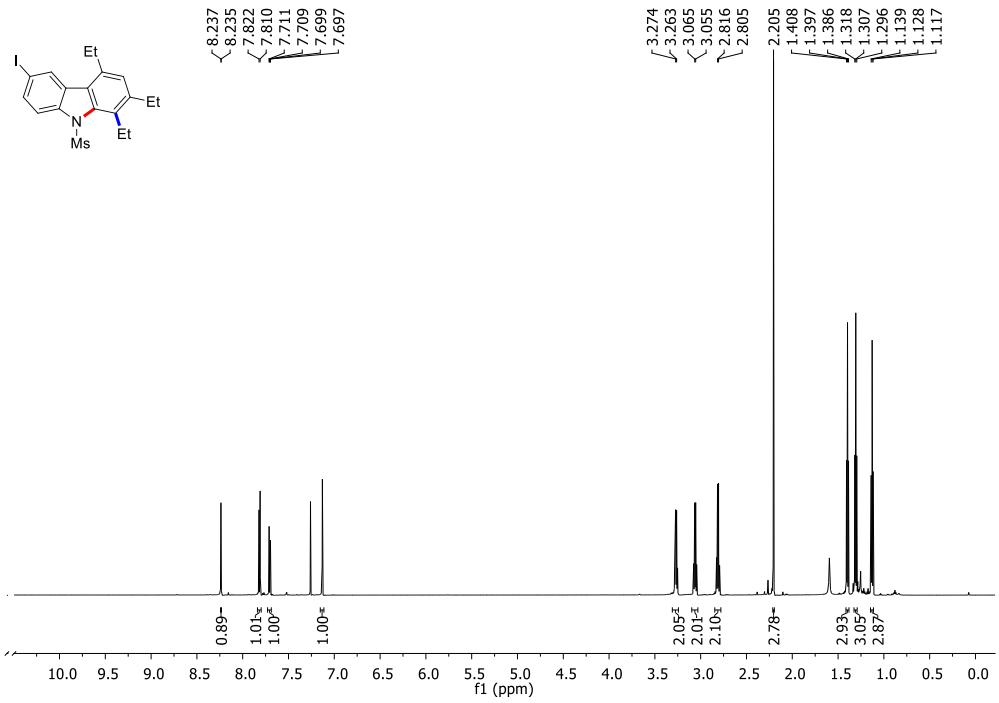


Figure 3.53 ^{1}H NMR spectrum of 1,2,4-Triethyl-6-iodo-9-(methylsulfonyl)carbazole **(3k)**

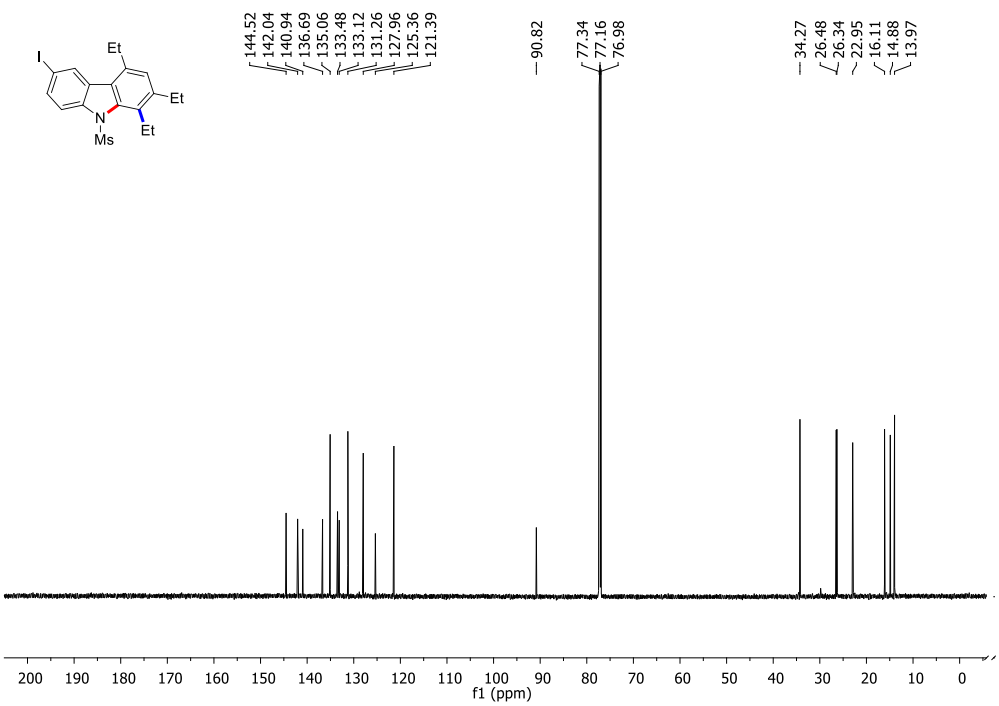


Figure 3.54 ^{13}C NMR spectrum of 1,2,4-Triethyl-6-iodo-9-(methylsulfonyl)-carbazole **(3k)**

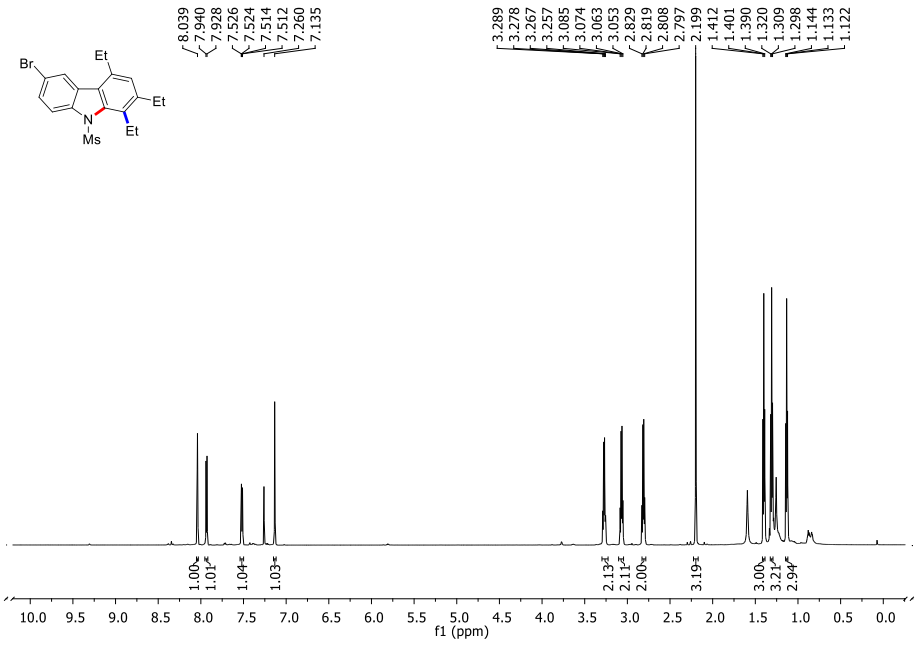


Figure 3.55 ^{1}H NMR spectrum of 6-Bromo-1,2,4-triethyl-9-methylsulfonyl)-carbazole **(3l)**

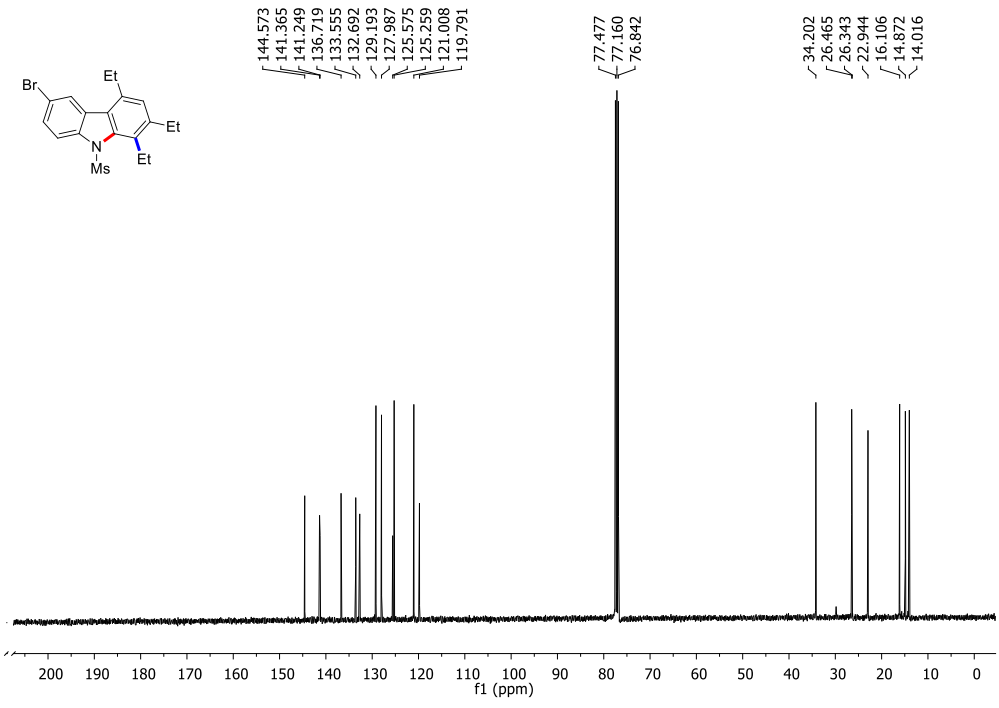


Figure 3.56 ^{13}C NMR spectra of 6-Bromo-1,2,4-triethyl-9-methylsulfonyl)-carbazole (**3l**)

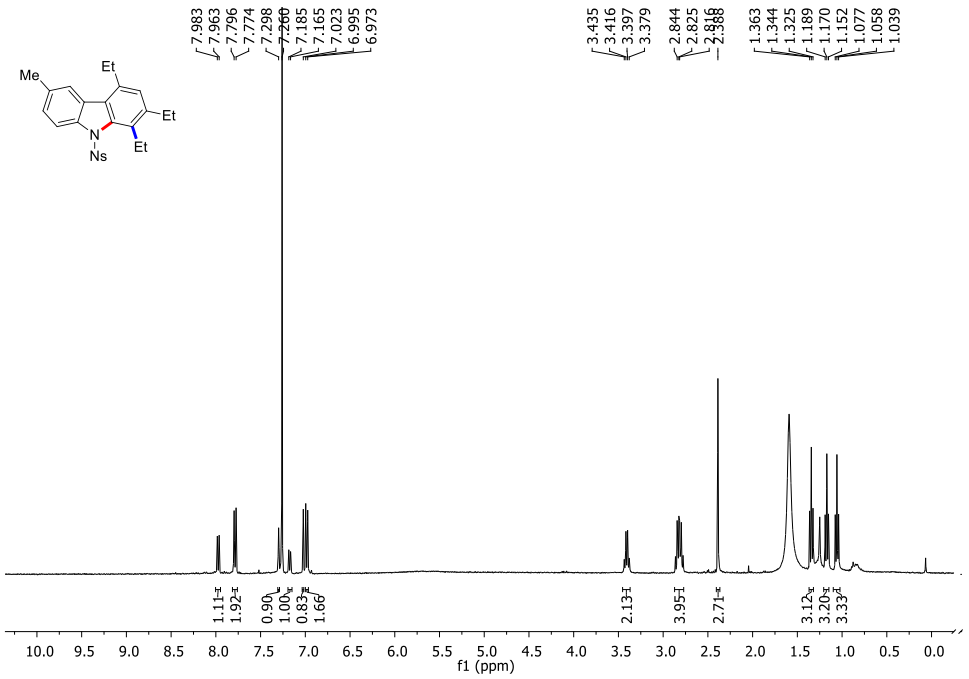


Figure 3.57 [1]H NMR spectrum of 1,2,4-Triethyl-6-methyl-9-(4-nitrophenyl)-carbazole (**3m**)

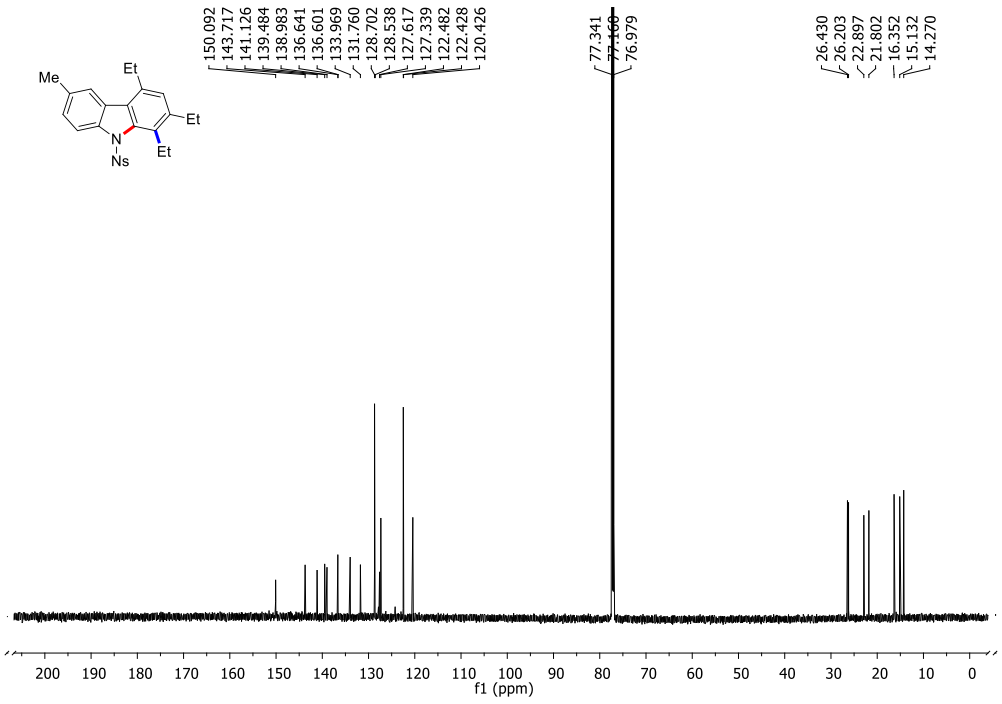


Figure 3.58 [13]C NMR spectrum of 1,2,4-Triethyl-6-methyl-9-(4-nitrophenyl)-carbazole **(3m)**

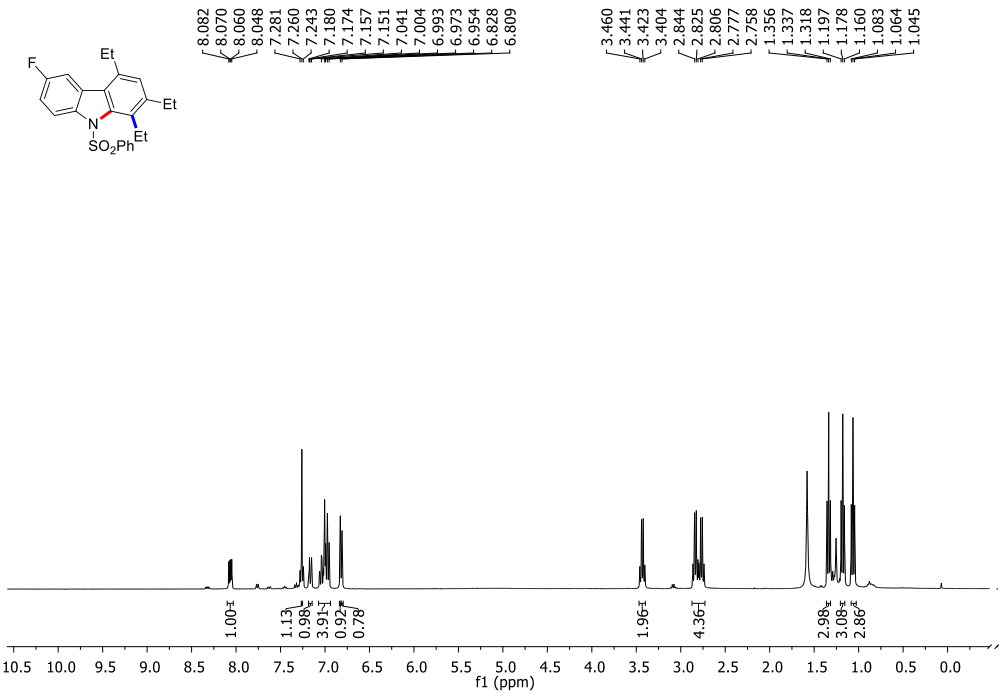


Figure 3.59 ^{1}H NMR spectrum of 1,2,4-Triethyl-6-fluoro-9-(phenylsulfonyl)-carbazole) (**3n**)

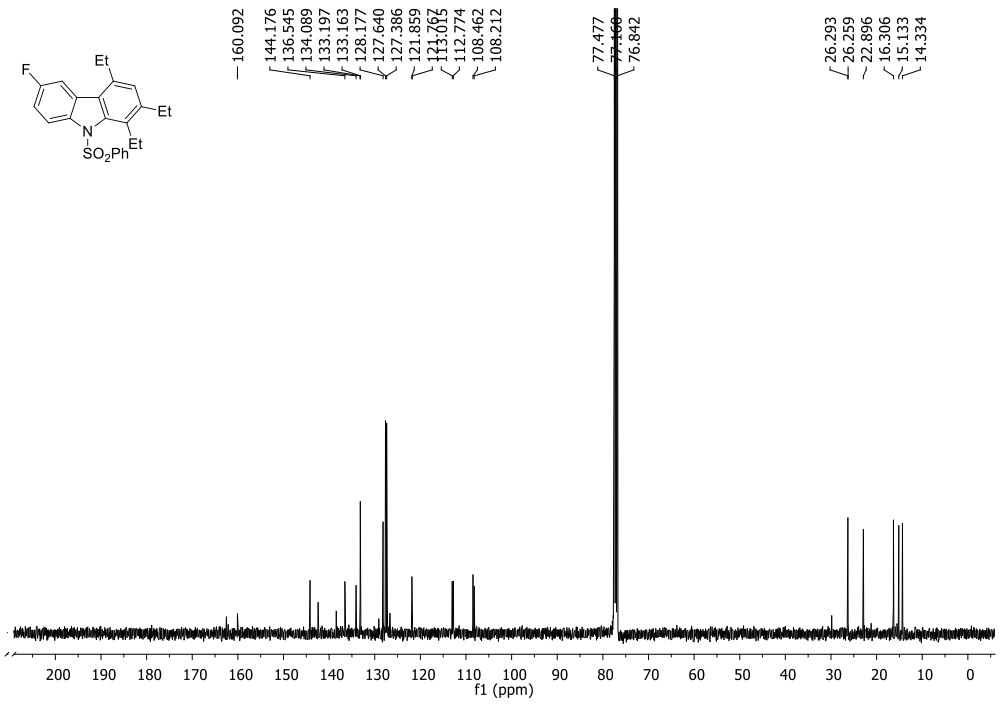


Figure 3.60 ^{13}C NMR spectrum of 1,2,4-Triethyl-6-fluoro-9-(phenylsulfonyl)-carbazole) (**3n**)

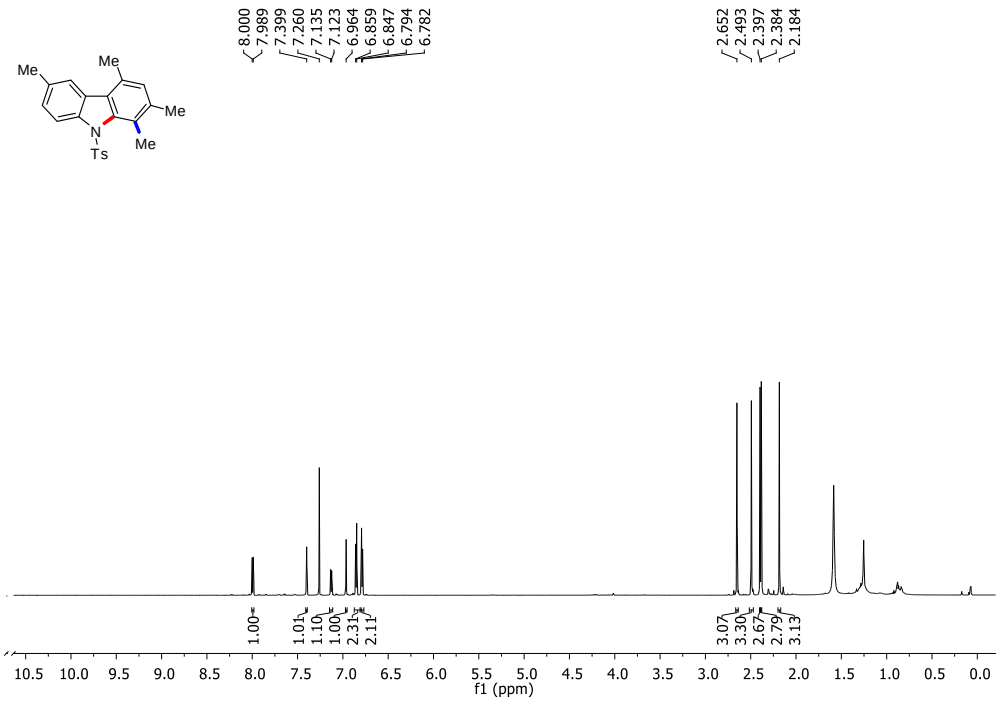


Figure 3.61 ^{1}H NMR spectrum of 1,2,4,6-Tetramethyl-9-tosyl-carbazole (**3o**)

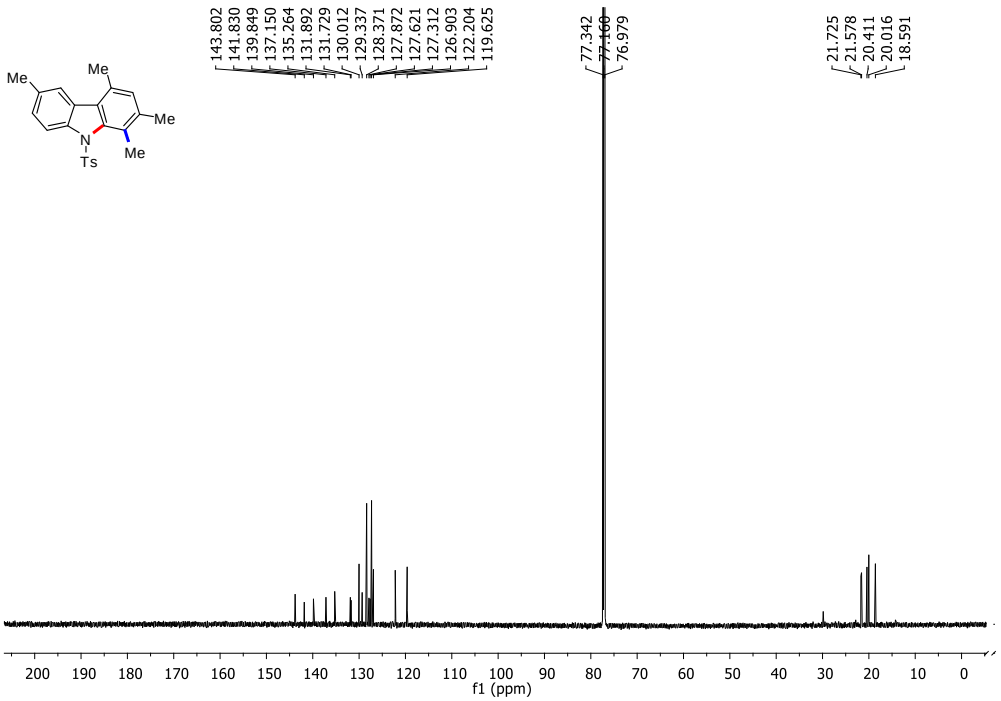


Figure 3.62 ^{13}C NMR spectrum of 1,2,4,6-Tetramethyl-9-tosyl-carbazole (**3o**)

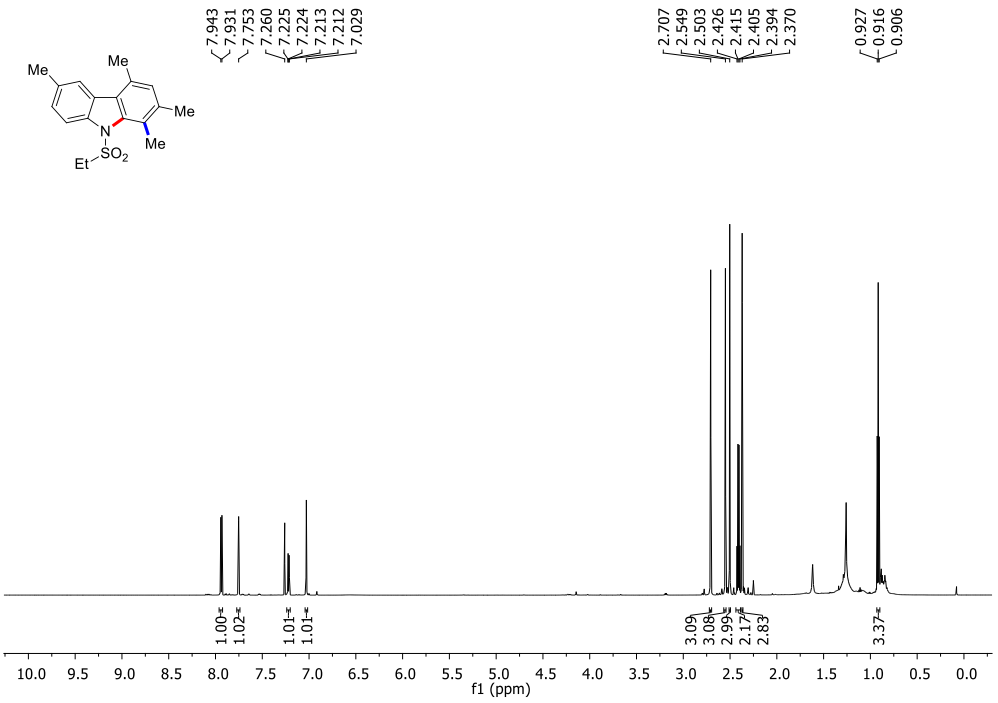


Figure 3.63 ^{1}H NMR spectrum of 9-(Ethylsulfonyl)-1,2,4,6-tetramethyl-carbazole (**3p**)

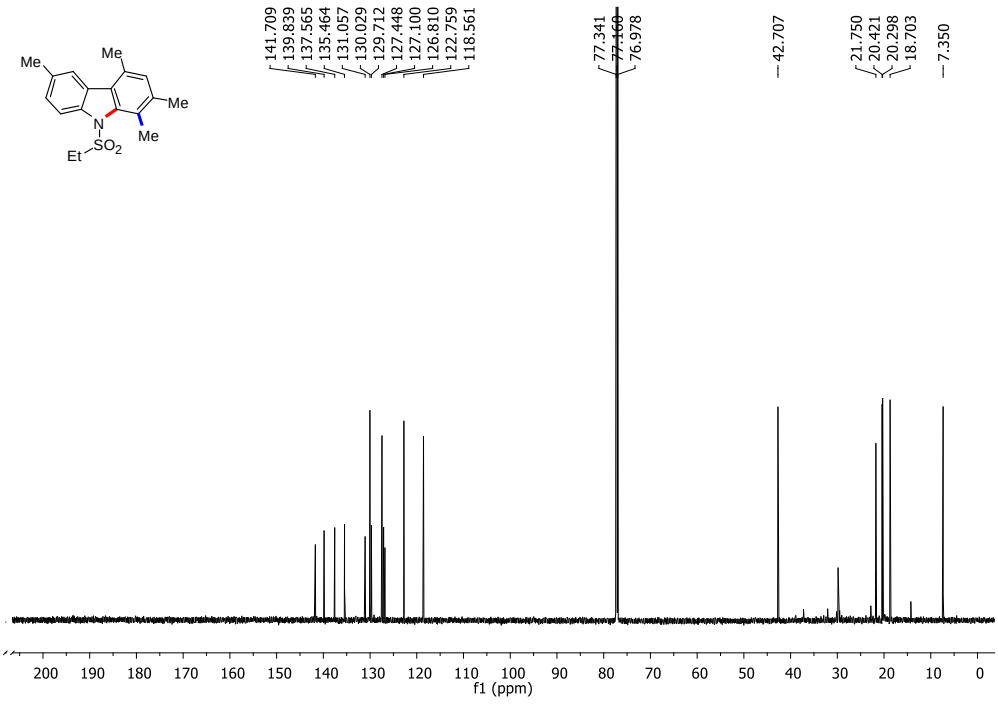


Figure 3.64 ^{13}C NMR spectrum of 9-(Ethylsulfonyl)-1,2,4,6-tetramethyl-carbazole (**3p**)

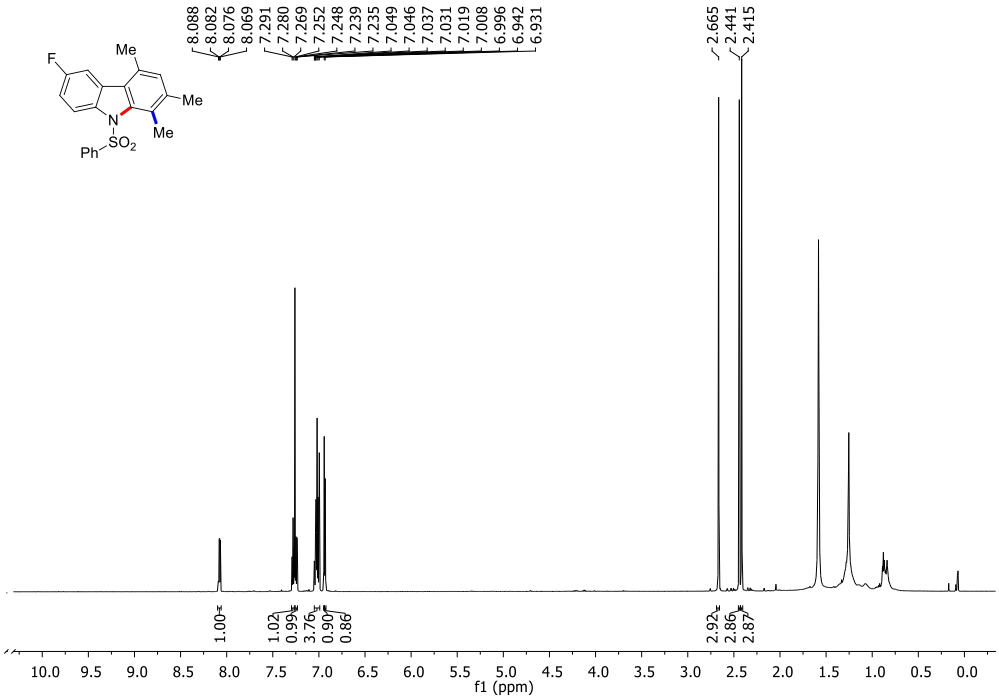


Figure 3.65 ^{1}H NMR spectrum of 6-Fluoro-1,2,4-trimethyl-9-(phenylsulfonyl)-carbazole (**3q**)

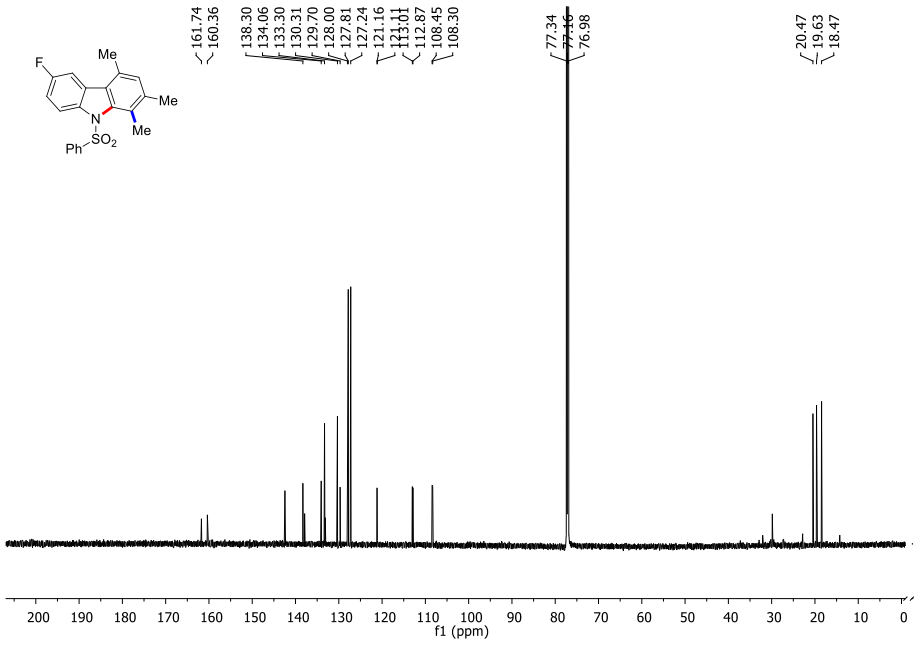


Figure 3.66 ^{13}C NMR spectrum of 6-Fluoro-1,2,4-trimethyl-9-(phenylsulfonyl)-carbazole (**3q**)

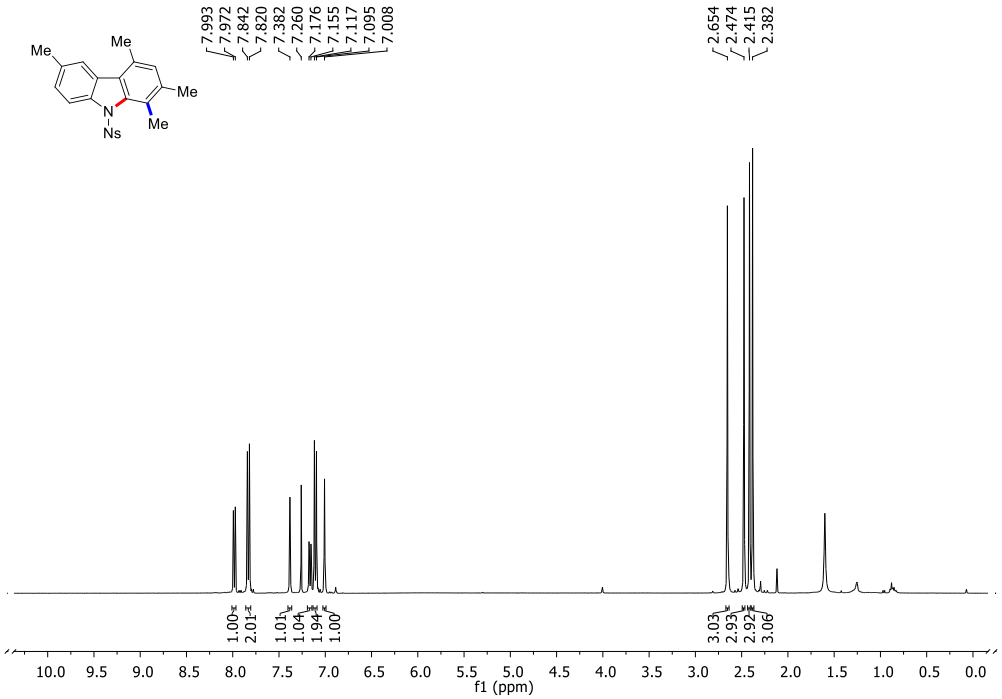


Figure 3.67 ^{1}H NMR spectrum of1,2,4,6-Tetramethyl-9-(4-nitrophenylsulfonyl)-carbazole **(3r)**

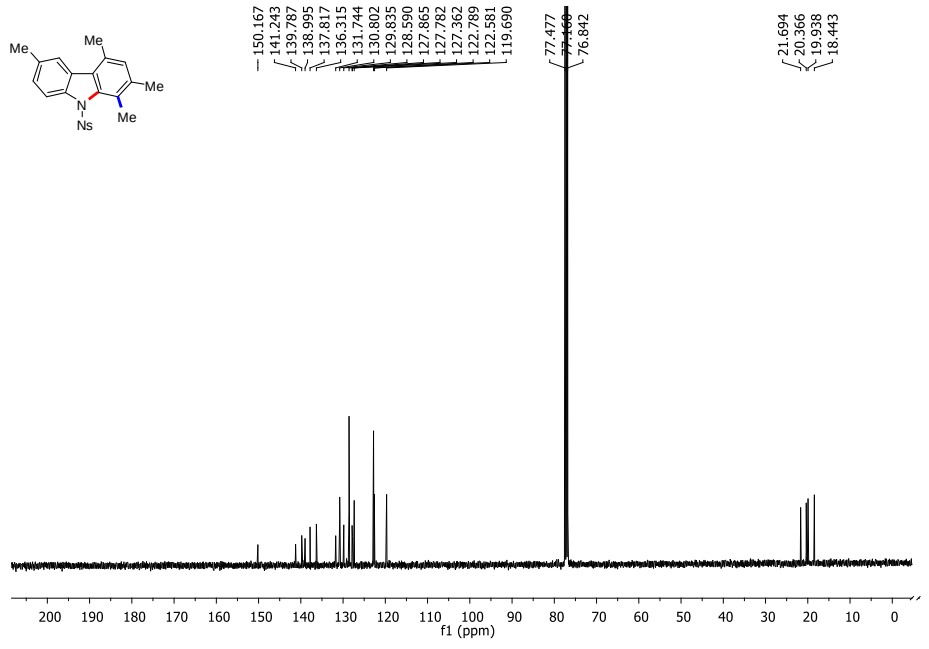


Figure 3.68 ^{13}C NMR spectrum of 1,2,4,6-Tetramethyl-9-(4-nitrophenylsulfonyl)-carbazole **(3r)**

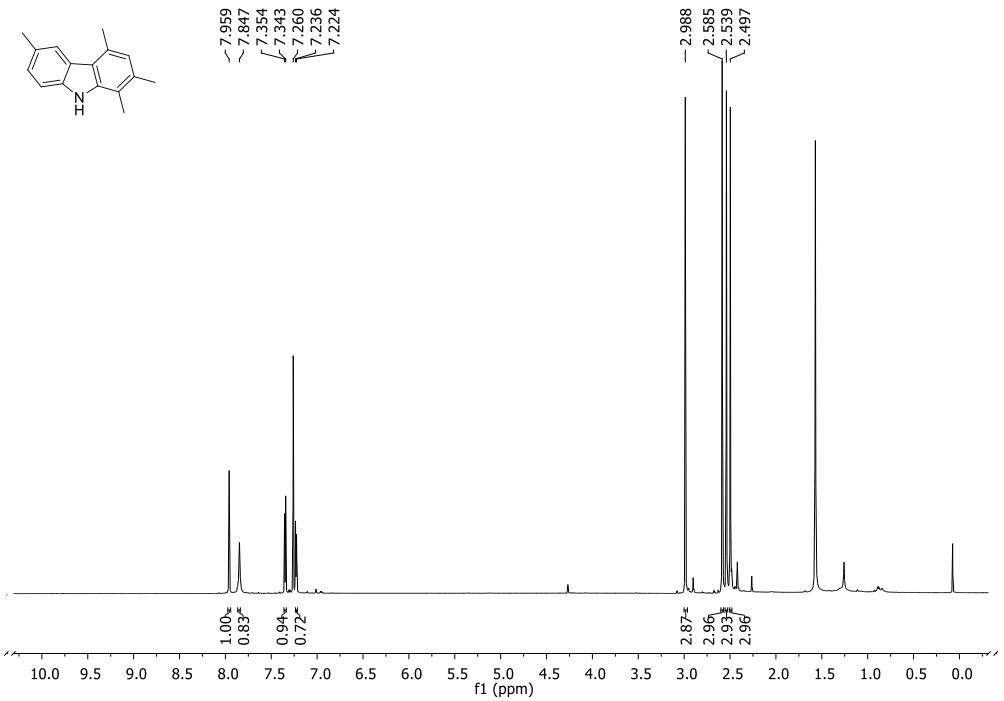


Figure 3.69 ^{1}H NMR spectrum of 1,2,4,6-Tetramethyl-9*H*-carbazole **(4)**

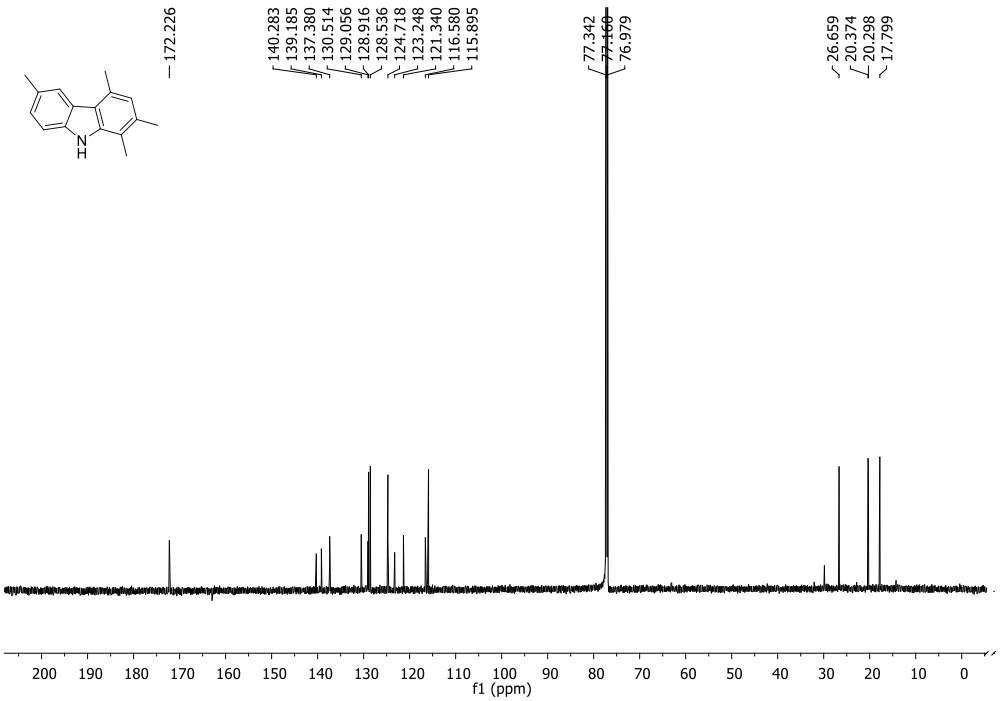
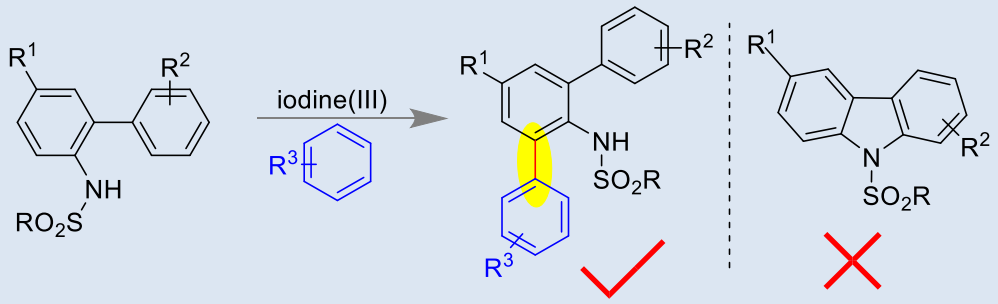


Figure 3.70 ^{13}C NMR spectrum of 1,2,4,6-Tetramethyl-9*H*-carbazole **(4)**

CHAPTER 4

Intermolecular C-C Coupling of 2-Amidobiphenyls using Iodine(III) Reagent

4.1 ABSTRACT



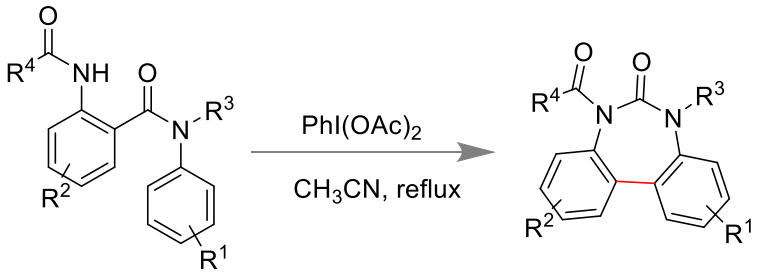
The 2-Amidobiphenyls undergo intramolecular N–H arylation when an oxidant like hypervalent iodine(III) reagent is employed in the reaction system. Treatment of 2-amidobiphenyl and an arene with $PhI(OAc)_2$ as a sole oxidant using mesitylene as nucleophile led to intermolecular C–H arylation by suppressing intramolecular oxidative C-N coupling . A scale of biaryalsulfonamides were designed yielded the targeted triaryl motifs in moderate to good yield.

4.2 INTRODUCTION

The essence of organic synthesis lies in the construction of C-C bond reactions[1-4] as it has given rise to numerous methodologies for effective transformations, which has been highly

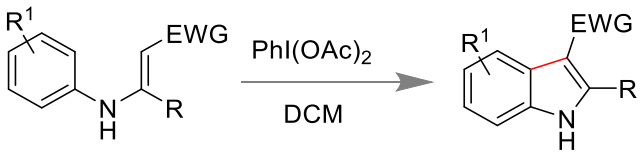
beneficial in the synthetic community. Traditional methods, including conversions assisted by a template, have grown in recent times to functionalize an unactivated aromatic system.[5-7] Several methods are reported with metals for C-H bond functionalization of 2-amidobiphenyl as a precursor.[8-10] Hypervalent iodine(III) reagents that are inexpensive, mild, and can be easily handled at room temperature have been utilized to construct C-C bond.[11, 12] Very few research groups are involved in exploring C-H bond functionalization under metal free condition.[13-15] Hypervalent iodine(III) reagents are employed in various oxidative transformations[16-18] and in achieving various cyclization for the construction of bioactive molecules. The recent decade has witnessed the utilty of hypervalent iodine(III) reagents as metal free reagents working in environmentally benign conditions.[2, 19-21] Buchwald and co-workers have demonstrated the use of iodine(III) reagents to functionalize biaryl acetamide for synthesis of carbazoles.[22] The *N*-protected biarylamine and its oxidative cyclisation has been extensively reported under metal and metal free conditions.[23, 24 25, 26] Oxidative cyclisation of 2-amidobiphenyl moiety to multisubstituted carbazoles is a well-explored reaction system in the presence of an oxidant or light.[27-29]

Carbon carbon bond formation reactions involving iodine(III) reagents which have used been to construct significant structural motifs. Zhao group has developed an intramolecular aryl-aryl coupling by rearranging *N*-phenyl benzamides by employing hypervalent iodine(III) reagents.[30]



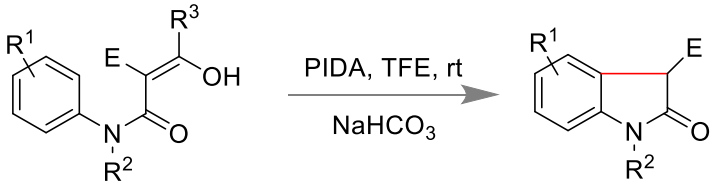
Scheme 4.1 Intramolecular aryl-aryl coupling using hypervalent iodine(III) reagent.

N- aryl enamines were used to construct the C-C bond of the indole based moieties by hypervalent iodine(III) reagents.[11] The proposed methodology involved enormous functional group tolerance under metal free conditions and mild reaction conditions.



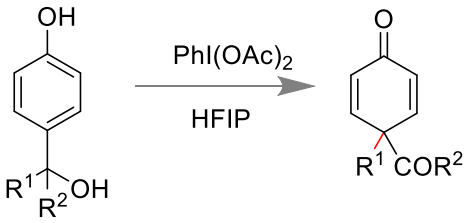
Scheme 4.2 Synthesis of indole based scaffold using hypervalent iodine(III) reagent.

A series of monofunctionalized oxindoles were synthesized by Zhao group using phenyl iodine diacetate (PIDA). C-C bond was formed along with deacylation to give oxoindole as a product which could be easily used to transform to naturally occurring horsfiline.[1]



Scheme 4.3 Synthesis of oxindoles using hypervalent iodine(III) reagent.

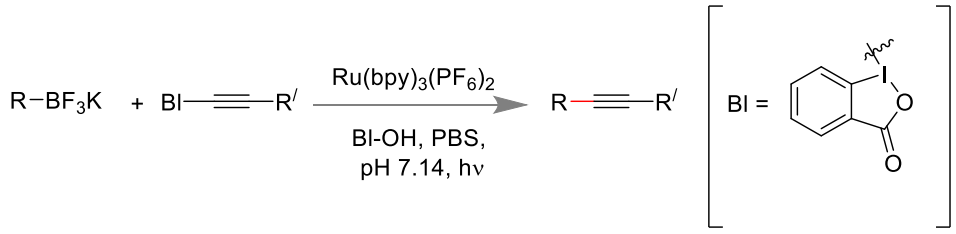
C-C bond formation reactions have been elucidated by Sylvian Canesi where an oxidative Wagner Meerwin rearrangement has been established mediated by iodine(III) reagent.[31] The strategy of aromatic ring umpoloung has been established for the synthesis of highly functionalized moieties.



Scheme 4.4 Oxidative Wagner Meerwin transposition using hypervalent iodine(III) reagent.

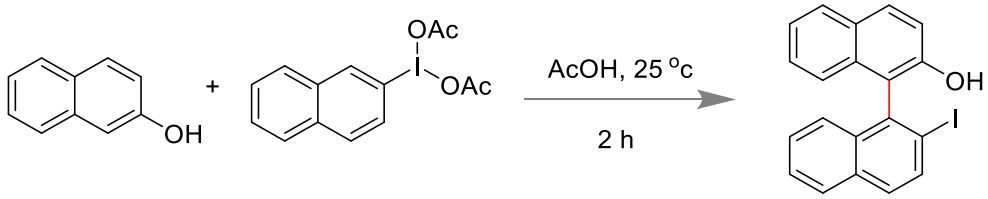
Chen and co-workers have used primary, secondary, and tertiary alkyl trifluoro borates to demonstrate deboronative alkynylation reaction to construct silyl, alkyl and allyl substituted

alkynes.[32] C-C bond formation reaction was developed using cyclic iodine(III) reagents with photoredox catalyst.



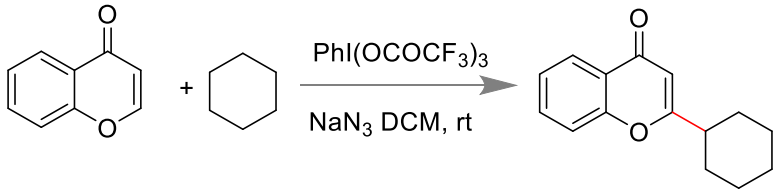
Scheme 4.5 Deboronative alkynylation reaction using hypervalent iodine(III) reagent merged with photoredox catalyst.

Biaryls were synthesized by Yorimitsu and co-workers *via* sigmatropic rearrangement by coupling hypervalent iodine(III) reagents with phenol for dehydrogenative C-C coupling. [33] The reaction underwent ligand exchange at the iodine center, followed by [3,3] sigmatropic rearrangement with regioselectivity to form the product. C-C bond formation reaction using mild hypervalent iodine(III) reagents is convenient to bring about effective transformations in organic synthesis under metal free conditions.



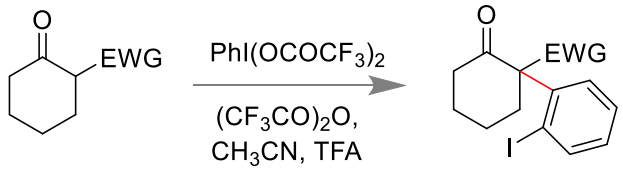
Scheme 4.6 Dehydrogenative biaryl synthesis via 3,3 sigmatropic rearrangement.

Antonchick group has illustrated the functionalization of selective aliphatic C-H bonds of thiochromones and chromones at the C_2 position.[34] Direct oxidative functionalization of chromones mediated by hypervalent iodine(III) reagent under mild conditions took place to produce functionalized chromones which are bioactive products. Cyclohexane is activated by proton abstraction by the azidyl radical generated from $PhI(OCOCF_3)_2$ and NaN_3. The nucleophilic cyclohexyl radical attacks the most electrophilic C_2 position of the chromone followed by oxidation to form the cross coupled product.



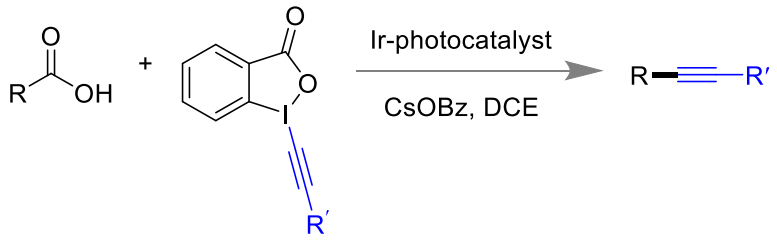
Scheme 4.7 Synthesis of functionalized chromones mediated by hypervalent iodine(III) reagent.

Synthesis of α-(2-iodoaryl)ketones by rearrangement of an iodonium enolate by α arylation of a carbonyl compound without use of base was accomplished using hypervalent iodine reagent ($ArI(O_2CCF_3)_2$) as the source of aryl group.[35] The protocol was extended to activated ketones, like α-cyanoketones and substituted aryliodanes. C-H functionalization of the keto compound proceeded *via* [3,3] rearrangement of an iodonium enolate.



Scheme 4.8 Synthesis of α-(2-iodoaryl)ketones mediated by $PhI(OCOCF_3)_2$ (PIFA).

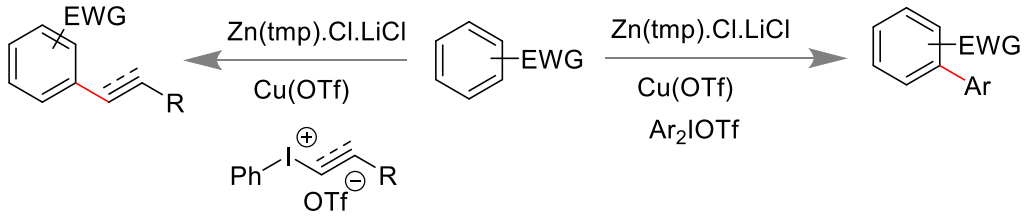
Waser group had reported decarboxylative alkynylation with EBX as the source of alkyne using Ir as protocatalyst under visible light irradiation.[36] Authors speculated that sunlight and blue LED was sutiable enough to produce the desired C-C bond.



Scheme 4.9 Decarboxylative alkynylation using photoredox catalysis and EBX reagent.

Diverse heteroaryl compound synthesis by formation of carbon-carbon bond was illustrated by Wang and co-workers by C-H zincation followed by coupling of iodonium salts with Cu

metal.[37] Various arylation, alkynylation, and vinylation were possible to attain under mild conditions to give acesss to wide scope of heterobiaryls.



Scheme 4.10. Arylation and alkenylation using iodonium salt.

The previous approaches for construction of C-C bond involve usage of iodine based reagents. Our approach was to use the hypervalent iodine(III) reagents for construction of terphenyls. The synthetic utility of carbenium ion intermediate over the nitrenium ion which is formed by reacting biaryl sulfonamides with iodine(III) reagents is a rare phenomena due to superior reactivity of nitrenium ion. In order to address this fundamental challenge, we targeted to develop an intermolecular coupling reaction by controlling the possibility of intramolecular coupling. 2-aminobiphenyl was chosen as the substrate which can undergo both intramolecular coupling in a more facile way. It was our assumption that a suitable nucleophile of choice controls the outcome of the reaction. The potential nucleophilicilty of the external nucleophile suppressed the intramolecular C-N coupling and intermolecular C-C coupling was successfully achieved employing hypervalent iodine(III) reagents that are potentially strong oxidants. C-H arylation took place intermolecularly and preceded oxidative C-N coupling. Unsymmetrical 2,6-diaryl anilides were synthesized using PIDA as the sole oxidant for the transformation to take place at room temperature open atmosphere condition under metal-free conditions. The arylsulfonyl groups controlled the reactivity of nitrenium ion to react with the external arene in an intermolecular fashion

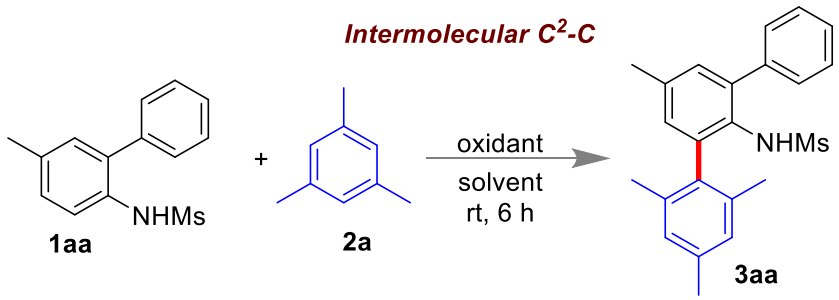
suppressing the route oxidative C-N coupling. 2,6-Diaryl aniline derivatives are useful synthetic intermediates effective in various synthetic transformations.[38, 39] Literature studies show that symmetrical 2,6-diarylanilide derivatives were constructed from Pd-catalyzed arylation acetanilide.[40] Unsymmetrical 2,6-diarylanilides were synthesized under metal free conditions, which have not been reported so far. Site-selective intermolecular C-C or C-N coupling reactions were also applicable *via* orthogonal reaction modulation strategy[41] by the stereoelectronic control on the generated nitrenium ions. [42, 43] Recent reports on orthogonal strategies[41] have been applied in various research areas like organic synthesis,[44, 45] organometallic chemistry,[46] supramolecular chemistry[47] mechanochemistry,[48] etc. 2-amidobiphenyls undergo intramolecular N-H arylation in the presence of hypervalent iodine(III) reagents followed by cyclization through C-N coupling reaction.[28, 49] This work shows an unusual intermolecular C-C coupling reaction of 2-amidobiphenyl by electronic control involving a carbenium ion over a nitrenium ion. An array of substrates were designed, which afforded the targeted *C*-arylated product in moderate to good yield furnishing terphenyls. The electronic factor played a significant role in controlling the formation of the product. As a result, we could successfully show that the substrate and the nucleophile control the selectivity for intermolecular arylation preferred over intramolecular arylation.

4.3 RESULTS AND DISCUSSION

We established the intermolecular C^2-H arylation by employing the arene of the biaryl sulfonamides possessing various electron-deficient groups or the nucleophilicity of the external nucleophile. The reaction was optimized taking *N*-(5-methyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (**1a**) and mesitylene (**2a**) in (Table 4.1) for synthesis of *N*-

(2,4,5',6-tetramethyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (**3aa**) by involving 1.0 equiv of PIDA, in 1,1,1,3,3,3 hexafluoroisopropanal (HFIP), yield of C^2-H arylated product (**3aa**) was obtained with 64% yield (entry 1). However on increasing the proportion of PIDA to 1.2 equiv, the yield was further reduced to 60%, (entry 2). Increasing the portion of PIDA to 1.5 equiv further resulted in drastic reduction of 34% (entry 3). Other Iodine(III) oxidants were taken into account, but it was found to be ineffective with PIFA where yield got reduced to 5% (entry 4), whereas $PhI(OPiv)_2$ produced an appreciable good yield of 62%. (entry 6). Solvents like 2,2,2-trifluoroethanol (TFE) were afforded to produce the desired product in good yield, but the reaction did not proceed in DCM and DCE solvent. This indicates that a fluorinated solvent is desirable for the stabilization of the generated nitrenium ion intermediate.

Table 4.1. Optimization for the intermolecular C^2-C reaction.[a]



entry	oxidant (equiv)	solvent	yield (%)[b]
1	PIDA (1.0)	HFIP	64
2	PIDA (1.2)	HFIP	60
3	PIDA (1.5)	HFIP	34
4	PIFA (1.0)	HFIP	5
5	PIDA (1.0)	TFE	60
6	$PhI(OCOPiv)_2$ (1.0)	HFIP	62

7	PIDA (1.0)	DCM	0
8	PIDA (1.0)	DCE	0

[a]Reaction conditions: 1.0 equiv (0.153 mmol) of **1a**, 10 equiv of mesitylene (1.53 mmol) of (**2a**); Yield of isolated products after column chromatography.

C^2-C arylation products were obtained when biaryl sulfonamides with unsubstitution in phenyl ring with various alkyl-substituted aryl based arenes (Figure 4.1a). It was observed that mesitylene, anisole and *m*-xylene produced good yield of products with methyl and isopropyl group substituted biarylsulfonamide (**3aa-bc**). *tert*-Butyl substituted amidobiphenyl reacted with electron-rich arenes like mesitylene, 1,3,5-triethyl benzene and anisole to lead to the formation of the desired product in sufficient quantity (**3ca-cb**). Substrates containing various other protecting groups like ethanesulfonyl, produced the product in appreciable yield. (**3da-dd)**. The electronic effect of 2-amidobiphenyls were monitored with para-substituted electron withdrawing fluorine group on the arene moiety. Also, arene part of the biphenyl system was made electron deficient, so that same C^2-C arylation was achieved under standard reaction conditions. (Figure 4.1b). Arenes like mesitylene and 1,3,5-triethybenzene were used as arenes to generate the desired product in sufficiently good yield (**3ea-fd**). Amidobiphenyls substituted by mesyl group gave rise to moderate yield of products with halogen-substituted group in other part of arene (**3ga-gd**). When acetyl group was introduced in the other part of arene in the 2-amidobiphenyl moiety, it was found that reaction was successfully achieved to form the C-H arylated product in appreciable (71%, **3hd**) yields. A nitro group at arene of biphenyl unit also made the

reaction turn fruitful with electron-rich arenes like *m*-xylene and 1,3,5-triethyl benzene producing the desired products in sufficient yields(**3ic-id**). An array of substrate scopes was prepared to portray how the electronic factor resulted in the formation C^2-C arylation product overcoming the more facile intramolecular C-N coupling.

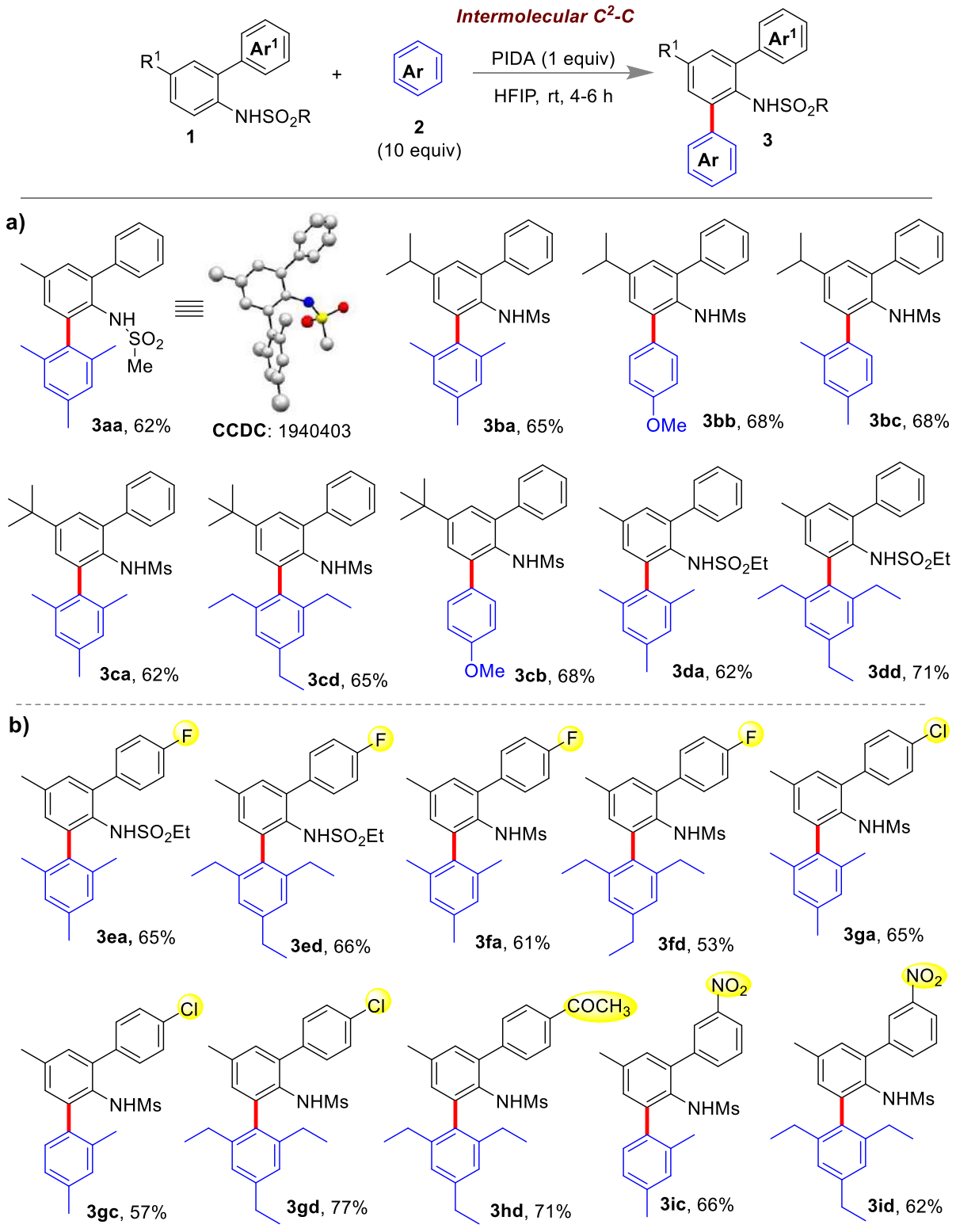


Figure 4.1. Substrate scope of biaryl sulfonamides with hypervalent iodine reagent PIDA and arenes. a) varying nucleophiles b) varying arene part of the biaryl sulfonamides with electron deficient group. Reaction conditions: 1.0 equiv of **1**, 10.0 equiv of arene **2** and 1.0 equiv of PIDA in HFIP.

Under similar reaction conditions, *para*-unsubstituted aminobiphenyl produced arylation at C^4-position. We thereby anticipated that the reaction was sterically controlled *via* carbenium ion intermediate.[42] The more stable carbenium was formed at the *para* position, which reacted with the nucleophile 1,3,5-triethyl benzene to undergo intermolecular arylation in a facile approach. This methodology was previously well-established in the literature.[50] So, we did not investigate it further, and as a representative example, the synthesis of **4jd** has been shown in Figure 4.2.

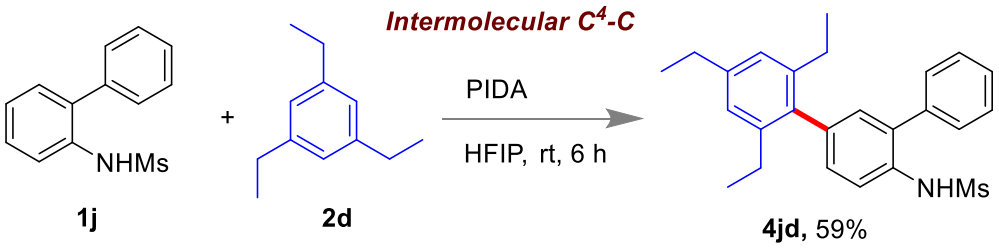


Figure 4.2. Scope for biphenyl methanesulfonamide. Reaction conditions: 1.0 equiv of **1j**, 10 equiv of triethyl benzene and 1.0 equiv of PIDA in HFIP.

Further we went on to establish the stereoelectronic controlled intermolecular C-N bond formation reaction. The steric effect of the sulfonyl group was investigated by employing a tosyl protected biaryl amine or a benzene sulfonyl protecting group with different arenes which formed the *N*-arylated product in 1.0 equiv of PIDA and solvent HFIP **5kd-la** (Figure 4.3). As described by Canesi, the σ donation effect of the mesyl group[51] to stabilize the positively charged aromatic ring is one of the probable reasons for forming an intermolecular

N- arylated product. The steric effect hindered the formation of carbenium ion where nucleophilicity of the arene ring in amidobiphenyl moiety was reduced because of the presence of the fluoride group. Rapid attack at the nitrenium ion took place by the external arene nucleophile, which formed *N*-arylation product.

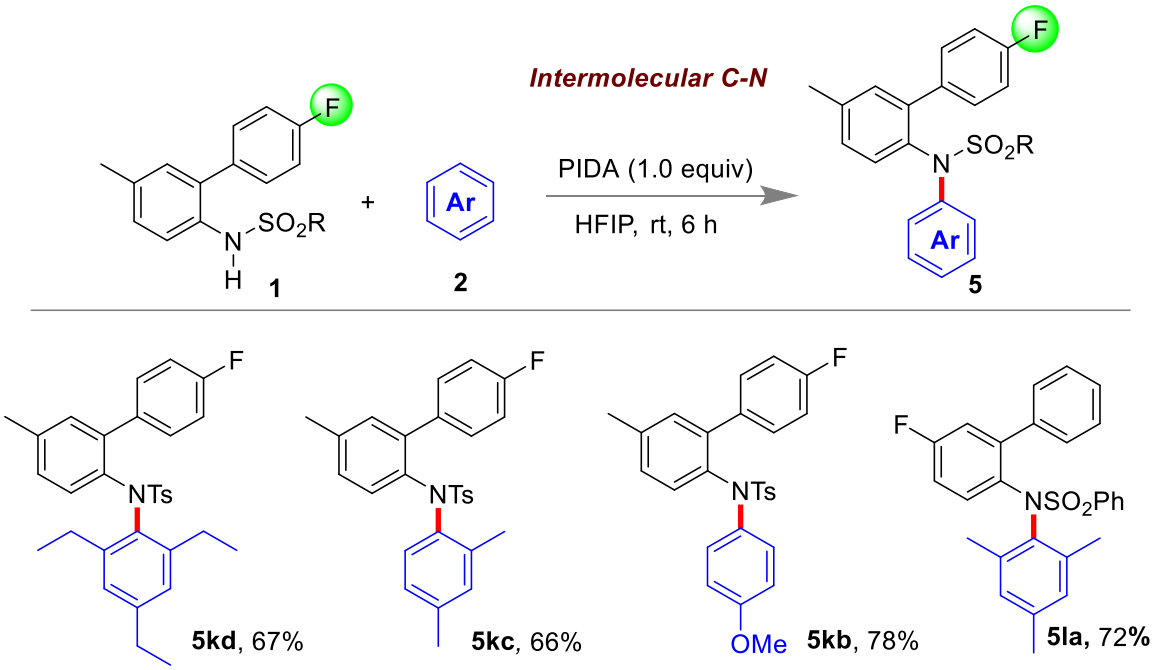


Figure 4.3. Scope for intermolecular C-N bond formation with biarylsulfonamides. Reaction conditions: 1.0 equiv of **1**, 10 equiv of arene **2** and 1.0 equiv of PIDA in HFIP.

The controlling factor which promotes intermolecular C-C coupling reaction was found to be more feasible than intramolecular C-N coupling. Out of curiosity, we investigated the reaction outcome by making the arene part of the biarylsulfonamide electron-rich by introducing a substituent with electron-donating methyl or methoxy group. C_2-H functionalization was hindered, and intramolecular C-N bond formation produced carbazole as a product. The use of mesitylene was the arene source that led to the synthesis of carbazoles (**6a-d**) which were isolated in good to moderate yield. On taking toluene as an external nucleophile, carbazole formation predominantly took place to obtain the products in good yields (**6e-f**), as displayed in figure 4.4.

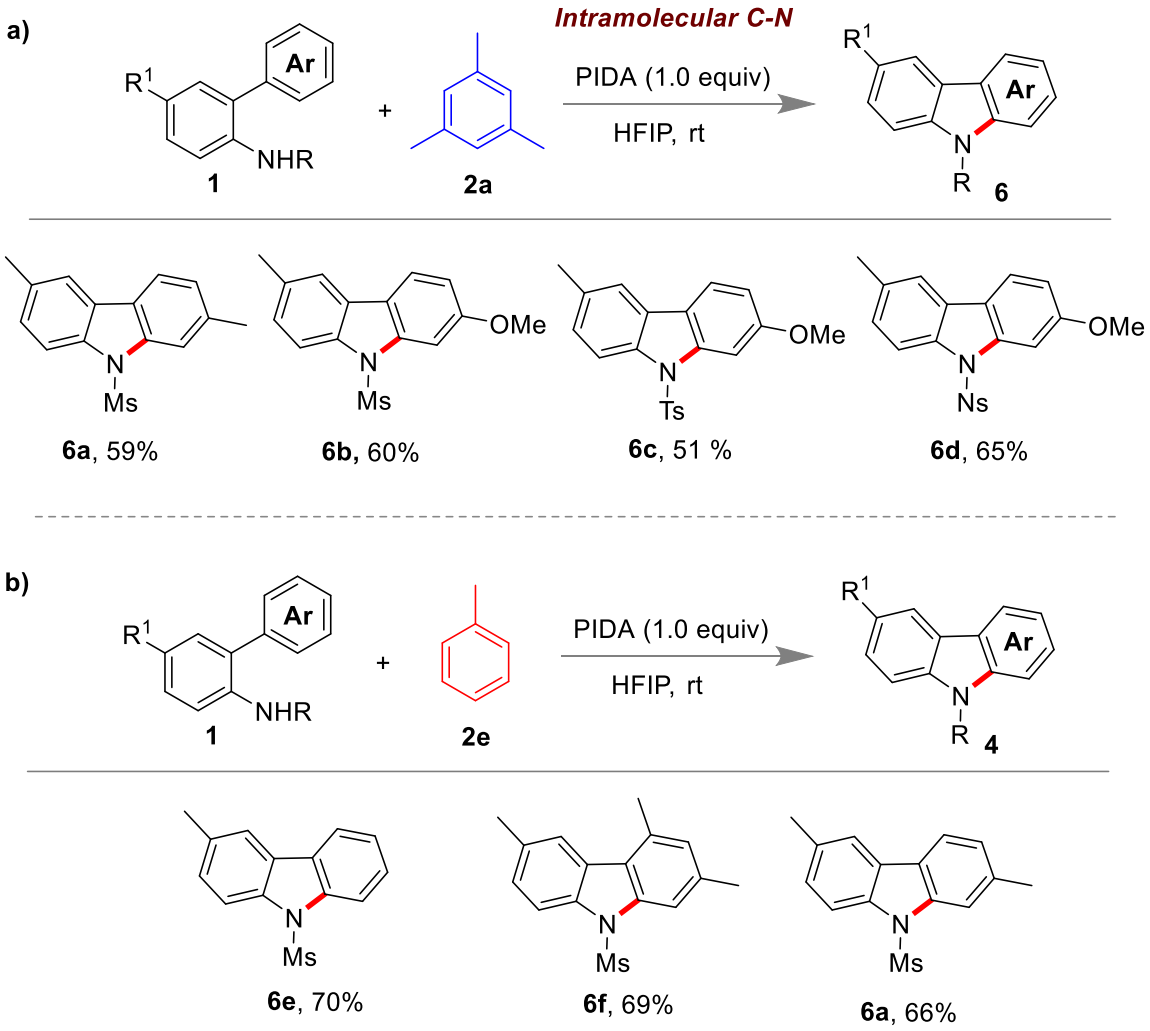


Figure 4.4 Scope for intramolecular C-N coupling for a) and b)nuclephiles. Reaction conditions: 1.0 equiv of **1**, 10.0 equiv of arene **2** and 1.0 equiv of PIDA in HFIP.

Gram scale synthesis of the established methodology was done with 3.82 mmol of amidobiphenyl **1a** and mesitylene **2a**, in the same reaction condition which formed that C^2-C arylated product in good yield (Figure 4.5).

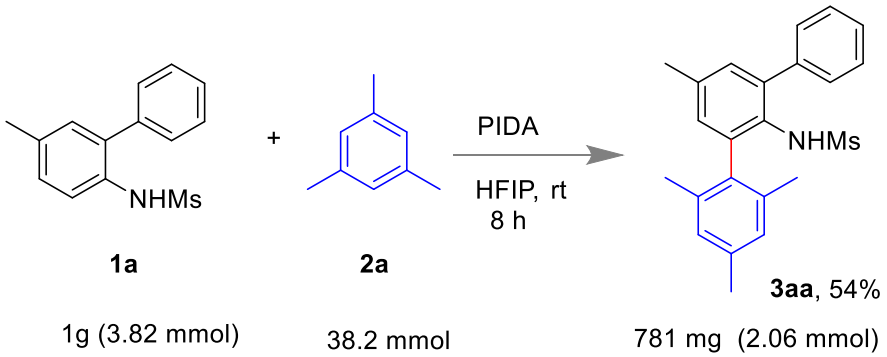


Figure 4.5. Large scale synthesis of **3aa**. Reaction conditions: 1.0 equiv of **1**, 10 equiv of arene **2a** and 1.0 equiv of PIDA in HFIP.

4.4 CONCLUSIONS

In short, we have achieved to produce an intermolecular C^2-H arylation product overcoming the more facile intramolecular C-N coupling product in the presence of an oxidant. The stereoelectronic factor plays a significant role in controlling the outcome for the formation of either of four possible C-C or C-N coupling reaction products. Intermolecular C^4-C, intermolecular C^2-C, intermolecular C-N, or intramolecular C-N bond formation reactions were formed in a particular condition which reestablished orthogonal reactivity modulation approach.[45] In most of the cases, the major products were isolated. Trace amount of minor products was formed but could not be separated. Other arenes were used, which showed that the nucleophilicity of the arene along with steric and electronic environment are the major ruling factors on the fate of a reaction. We anticipated that this methodology would be useful to understand the reactivity control of reaction intermediates which would thereby provide a new opportunity to

organic chemists for constructing expedient methods for the synthesis of terphenyl motifs under mild metal-free conditions.

4.5 EXPERIMENTAL SECTION

General methods. Chromatographic (Column) purifications of the compounds were done using silica gel (mesh 230–400) and hexane – ethyl acetate mixtures as eluent unless otherwise specified. NMR spectra had been recorded 700 MHz or 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 ppm for ^{13}C). The peak patterns are designated as follows: s: singlet; d: doublet; t: triplet; q: quartet; m: multiplet; dd: doublet of doublets; td: triplet of doublets; brs: broad singlet. The coupling constants (*J*) were reported in hertz (Hz). High-resolution mass spectra (HR-MS) were recorded on an ESI-TOF (time of flight) mass spectrometer. Infrared (IR) spectral data are reported in wave number (cm^{-1}). FT-IR spectra were recorded after making thin layer of the compounds on the surface of NaCl crystal using dichloromethane. Good quality crystals of the compounds **3aa** were obtained after slow evaporation of ethyl acetate solution. The crystals data were collected with Bruker SMART D8 goniometer equipped with an APEX CCD detector and with an INCOATEC micro source (Cu-Kα radiation, λ = 0.71073 Å). SAINT+[52] and SADABS[53] were used to integrate the intensities and to correct the absorption respectively The structure was resolved by direct methods and refined on F^2 with SHELXL-97.[54]

Representative method for preparation of *N*-(2,4,5',6-tetramethyl-[1,1' : 3', 1''-terphenyl]-2'-yl) methanesulfonamide (**3aa**)

To *N*-(5-methyl-[1,1'-biphenyl]-2-yl)methanesulfonamide **(1a)** (40 mg, 0.153 mmol) in 2 ml HFIP, mesitylene as the arene source (213 µl, 1.530 mmol) was added followed by addition of the hypervalent iodine reagent PIDA (50 mg, 0.153 mmol) dissolved in 1 ml HFIP . The reaction mixture was shaken for 6 h at room temperature. Following, the reaction mixture was evaporated to complete dryness to afford the product *N*-(2,4,5',6-tetramethyl-[1,1' : 3', 1"- terphenyl]-2'-yl) methanesulfonamide (**3aa**) which was isolated by column chromatography to obtain white solid 39 mg (62%) at 5% ethyl acetate hexane.

Representative method for preparation of *N*-(5-methyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (1aa).

To a solution of *p*-toluidine (500 mg, 4.67 mmol) in acetonitrile solvent kept at 0 °C, N-bromosuccinimide (935 mg, 5.60 mmol) was added portionwise to the stirred solution. The reaction mixture was shaken for 2 h.When the reaction mixture was evaporated to dryness and redissolved in dichloromethane. Aqueous work up was done to remove the succinimide byproduct. The volatile portion was then removed in vacuum and brown oily liquid was obtained as prouct. In many substrates, starting material was left in reaction mixture which required isolation by column chromatography isolated using 8% ethyl acetate hexane.[55]

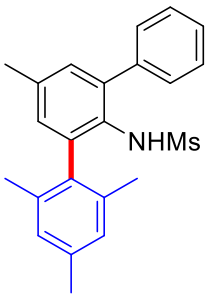
In a dry sealed tube, phenyl boronic acid (1.5 equiv), K_2CO_3 (4 equiv) and $Pd(PPh_3)_4$ were dissolved in a mixture of toluene: ethanol: water in ratio 3:2:1. 2 Bromoaniline was poured to the resulting solution and the reaction mixture was heated at 80 ^{0}C for 24 h. After cooling to room temperature, the biphasic reaction mixture was diluted with ammonium chloride and CH_2Cl_2.The combined organic phase was extracted twice with DCM (50 ml X 2) and the organic phase was dried over Na_2SO_4 and filtered. The filtrate was concentrated and isolated by column chromatography on silica gel afforded the product (yield 50-70%)[56].

The biphenyl amine was protected using mesyl chloride (1.5 equiv) by its slow addition in a solution of substrate and pyridine (1.2 equiv) dissolved in

dichoromethane at 0 ^{0}C. The reaction mixture was stirred at room temperature for 2 h to afford the desired product. The reaction mixture was quenched with NH_4Cl and the resuting solution was extracted with DCM twice (50 ml *2) and the organic phase was dried over Na_2SO_4 and filtered. White solid (**1aa**) was obtained when the filtrate was evaporated which was redissolved in ethanol to obtain recrystallised product with 70% yield.

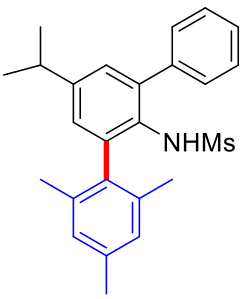
Compound Characterization Data

***N*-(2,4,5',6-tetramethyl-[1,1' : 3', 1''- terphenyl]-2'-yl) methanesulfonamide** (**3aa**): R_f =



0.4 (hexane : ethyl acetate 9:1); white solid; 38 mg (62%); mp 204-206 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.43 (m, 4H), 7.38 – 7.35 (m, 1H), (d, *J* = 6.8 Hz, 1H), 7.13 (d, *J* = 1.6 Hz, 1H), 6.97 (s, 3H), 5.58 (s, 1H), 2.38 (s, 3H), 2.32 (s, 3H), 2.09 (s, 6H), 1.91 (s, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.7, 139.2, 137.7, 137.6, 137.0, 136.6, 135.3, 130.9, 130.8, 130.4, 130.2, 128.7, 128.6, 127.7, 41.9, 21.2, 21.1, 20.6; IR (KBr) $\tilde{\nu}$ = 3438, 1635, 1317, 1146 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{23}H_{25}NO_2SNa$ 402.1498; found 402.1517.

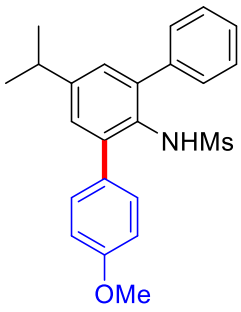
***N*-(5'-isopropyl-2,4,6- trimethyl- [1,1': 3', 1''-terphenyl]-2'-yl)methanesulfonamide**



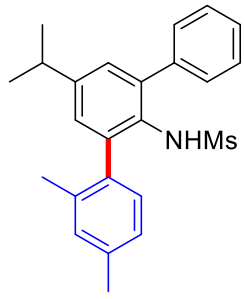
(3ba): R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 37 mg (65%); mp 210 −212 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.44 (m, 4H), 7.39 – 7.36 (m, 1H), 7.15 (d, *J* = 1.6 Hz, 1H), 7.02 (d, *J* = 2.0 Hz, 1H), 6.98 (s, 2H), 5.62 (s, 1H), 2.94 (*sept*, *J* = 6.8 Hz, 1H), 2.33 (s, 3H), 2.09 (s, 6H), 1.92 (s, 3H), 1.28 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (175 MHz,

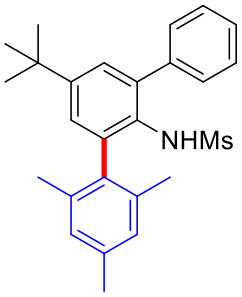
$CDCl_3$) δ 147.6, 140.0, 139.2, 137.7, 137.5, 137.1, 135.7, 130.5, 130.2, 128.7, 128.6, 128.4, 128.2, 127.7, 42.0, 33.7, 24.1, 21.2, 20.6; IR (KBr) $\tilde{\nu}$ = 3438, 1643, 1556, 1503 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{25}H_{29}NO_2SNa$ 430.1811; found 430.1810.

***N*-(5'-isopropyl-4-methoxy-[1,1': 3',1''- terphenyl]-2'-yl)methanesulfonamide) (3bb) :** R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 37 mg (68%); mp 205 − 207 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.50 (m, 4H), 7.45 – 7.40 (m, 3H), 7.19 (s, 2H), 7.03 (dd, *J* = 6.8, 2.0 Hz, 2H), 5.84 (s, 1H), 3.88 (s, 3H), 2.97 (*sept*, *J* = 6.8 Hz, 1H), 2.03 (s, 3H), 1.32 (s, 3H), 1.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 148.0, 140.4, 140.2, 140.1, 132.1, 131.2, 130.2, 129.3, 128.8, 128.6, 128.4, 127.7, 114.2, 55.4, 42.1, 33.8, 24.0; IR (KBr) $\tilde{\nu}$ = 3445, 2959, 1733, 1635, 1318, 1146 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{23}H_{25}NO_3SNa$ 418.1447; found 418.1446.



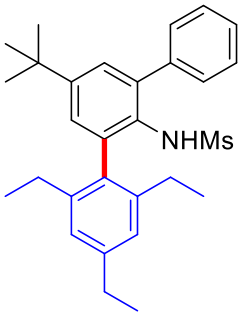
***N*-(5'-isopropyl-2,4-dimethyl-[1,1': 3',1''-terphenyl]-2'-yl)methanesulfonamide (3bc):** R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 37 mg (68%); mp 128 − 130 °C; **¹**H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.44 (m, 4H), 7.42 – 7.38 (m, 1H), 7.20 (d, *J* = 7.6 Hz, 1H), 7.16 (d, *J* = 2.0 Hz, 1H), 7.12 (s, 1H), 7.10 (s, 1H), 7.08 (d, *J* = 1.8 Hz, 1H), 5.67 (s, 1H), 2.94 (*sept*, *J* = 7.2 Hz, 1H), 2.36 (s, 3H), 2.17 (s, 3H), 1.94 (s, 3H), 1.28 (s, 3H), 1.27 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 147.5, 139.8, 139.5, 139.2, 137.9, 136.6, 136.4, 131.2, 130.6, 130.2, 130.0, 128.7, 128.6, 128.4, 127.8, 126.7, 41.9, 33.8, 24.1, 23.9, 21.3, 20.1; IR (KBr) $\tilde{\nu}$ = 3438, 2089, 1644, 1644, 1456, 1318, 1147 cm^{-1};HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{24}H_{27}NO_2SNa$ 416.1655; found 416.1672.



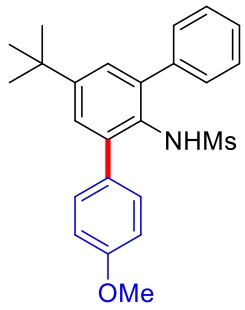


***N*-(5'-(tert-butyl)-2,4,6-trimethyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (3ca):** R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 35 mg (62%); mp 245 – 247 °C ; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.51 – 7.49 (m, 2H), 7.47 (t, *J* = 8.4 Hz, 2H), 7.39 (t, *J* = 7.0 Hz, 1H), 7.29 (d, *J* = 2.1 Hz, 1H), 7.17 (d, *J* = 2.1 Hz, 1H), 6.99 (s, 2H), 5.62 (s, 1H), 2.33 (s, 3H), 2.10 (s, 6H), 1.92 (s, 3H), 1.33 (s, 9H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 149.2, 140.1, 138.8, 137.7, 137.2, 137.1, 136.0, 130.2, 130.2, 128.6, 128.5, 127.7, 127.7, 127.0, 41.9, 34.7, 31.5, 21.2, 20.6; IR (KBr) $\tilde{\nu}$ = 3438, 2089, 1644, 1456, 1318, 1147 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{26}H_{31}NO_2SNa$ 444.1968; found 444.1976.

***N*-(5'-(tert-butyl)-2,4,6-triethyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (3cd):** R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 40 mg (65%); mp 237 – 239 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.50 (m, 2H), 7.47 – 7.43 (t, *J* = 7.2 Hz, 2H), 7.37 (t, *J* = 7.2 Hz, 1H), 7.29 (d, *J* = 2.4 Hz, 1H), 7.23 (d, *J* = 2.4 Hz, 1H), 7.05 (s, 2H), 5.56 (s, 1H), 2.68 (q, *J* = 7.2 Hz, 2H), 2.42 – 2.32 (m, 4H), 1.88 (s, 3H), 1.33 (s, 9H), 1.28 (t, *J* = 7.6 Hz, 3H), 1.11 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.1, 144.6, 143.2, 140.6, 138.5, 136.4, 134.5, 130.5, 130.3, 128.5, 128.2, 127.7, 127.1, 125.7, 42.1, 34.6, 31.4, 28.9, 26.8, 15.6, 15.5; IR (KBr) $\tilde{\nu}$ = 3438, 2085, 1635, 1456, 1318, 1146 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{29}H_{37}NO_2SNa$ 486.2437; found 486.2451.

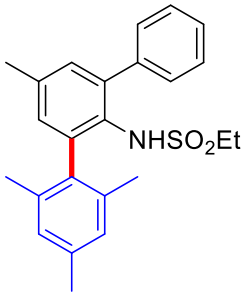


***N*-(5'-(*tert*-butyl)-4-methoxy-[1,1': 3',1''-terphenyl]-2'-yl)methaneslfonamide (3cb):** R_f =



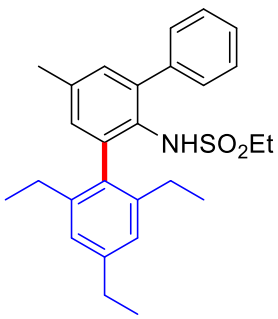
0.4 (hexane : ethyl acetate 9:1); white solid; 37 mg (68%); mp 159 – 161 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.44 (m, 4H), 7.41 (t, *J* = 8.4 Hz, 3H), 7.31 (s, 2H), 7.00 (d, *J* = 8.4 Hz, 2H), 5.78 (s, 1H), 3.86 (s, 3H), 2.01 (s, 3H), 1.35 (s, 9H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 150.3, 140.4, 139.9, 139.6, 132.3, 131.2, 130.1, 129.1, 128.6, 127.8, 127.8, 127.5, 114.1, 55.4, 42.0, 34.8, 31.4; IR (KBr) $\tilde{\nu}$ = 3438, 2963, 1656, 1632, 1311, 1146 cm^{-1};HR-MS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{24}H_{27}NO_3SNa$ 432.1604; found 432.1587.

***N*-(2,4,5',6-tetramethyl-[1, 1':3', 1''-terphenyl]-2'-yl)ethanesulfonamide (3da):** R_f = 0.4



(hexane : ethyl acetate 9:1); white solid; 36 mg (62%); mp 119 – 121 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.0 Hz, 2H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.37 (t, *J* = 7.0 Hz, 1H), 7.12 (s, 1H), 6.96 (s, 3H), 5.38 (s, 1H), 2.38 (s, 3H), 2.32 (s, 3H), 2.09 (s, 6H), 1.74 (q, *J* = 7.7 Hz, 2H), 0.91 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 139.8, 139.5, 137.7, 137.6, 137.0, 136.5, 135.5, 131.0, 130.8, 130.6, 130.1, 128.7, 128.5, 127.8, 48.4, 21.2, 21.0, 20.6, 8.5; IR (KBr) $\tilde{\nu}$ = 3438, 2084, 1641, 1322, 1144 cm^{-1};HR-MS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{24}H_{27}NO_2SNa$ 416.1655; found 416.1674.

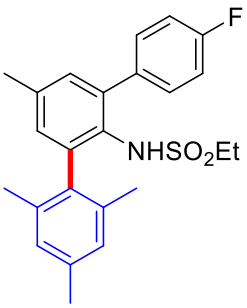
***N*-(2,4,6-triethyl-5'-methyl-[1,1':3',1''- terphenyl]-2'-yl)ethanesulfonamide (3dd) :** R_f =



0.4 (hexane : ethyl acetate 9:1); white solid; 45 mg (71%); mp 128 – 130 °C**;** R_f = 0.4 (hexane:ethyl acetate: 9:1); white solid; 39 mg (62%); mp 173−175; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.41 (m,

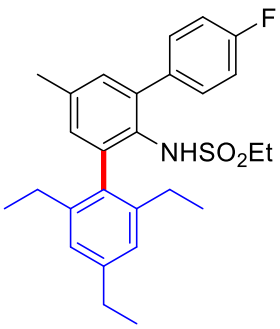
4H), 7.37 – 7.34 (m, 1H), 7.12 (s, 1H), 7.03 (s, 2H), 7.01 (s, 1H), 5.33 (s, 1H), 2.67 (dd, *J* = 15.2, 7.6 Hz, 2H), 2.43 – 2.33 (m, 7H), 1.67 (dd, *J* = 14.8, 7.6 Hz, 2H), 1.26 (t, *J* = 7.6 Hz, 3H), 1.11 (t, *J* = 7.6 Hz, 6H), 0.88 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 142.9, 142.3, 140.2 , 139.2, 137.0, 135.9, 134.2, 131.3, 130.9, 130.2 , 128.4, 127.7, 125.5, 48.3, 28.9, 26.8, 21.1, 15.9, 15.3, 8.5; IR (KBr) $\tilde{\nu}$ = 3373, 2092, 1643, 1322,1140 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{27}H_{33}NO_2SNa$ 458.2124; found 458.2148.

***N*-(4''- Fluoro-2, 4, 5', 6 – tetramethyl-[1, 1': 3', 1''-terphenyl]-2'-yl)ethanesulfonamide**



(**3ea**): R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 37 mg (65%); mp 168 – 170 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.46 – 7.44 (m, 2H), 7.14 (t, *J* = 8.4 Hz, 2H), 7.09 (s, 1H), 6.96 (s, 3H), 5.33 (s, 1H), 2.37 (s, 3H), 2.32 (s, 3H), 2.08 (s, 6H), 1.80 (q, *J* = 7.7 Hz, 2H), 0.93 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 162.5 (d, $^1J_{C\text{-}F}$ = 246 Hz), 138.6, 137.8, 137.7, 137.1 , 136.8 , 135.6 (d, $^4J_{C\text{-}F}$ = 3.5 Hz), 135.5, 131.8 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 131.19 , 130.9, 130.6, 128.7, 115.51 (d, $^2J_{C\text{-}F}$ = 21.4 Hz), 48.4, 21.2, 21.1 , 20.6 , 8.6 ; IR (KBr) $\tilde{\nu}$ = 3442, 1634, 1633, 1322, 1140 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{24}H_{26}FNO_2SNa$ 434.1560; found 434.1573.

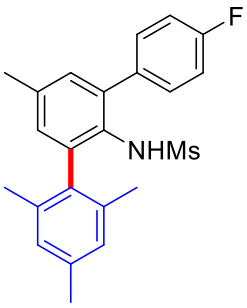
***N*-(2, 4, 6-triethyl- 4''- fluoro-5'-methyl-[1,1': 3', 1''- terphenyl]-2'-yl)ethanesulfonamide**



(3ed): R_f = 0.4 (hexane : ethyl acetate: 9:1); white solid; 41 mg (66%); mp 155 – 157 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.43 (m, 2H), 7.13 (t, *J* = 8.8 Hz, 2H), 7.09 (s, 1H), 7.03 (s, 2H), 7.02 (s, 1H), 5.30 (s, 1H), 2.67 (q, *J* = 7.2 Hz, 2H), 2.44 – 2.30 (m, 7H), 1.74 (q, *J* = 7.6 Hz, 2H), 1.27 (t, *J* = 7.6 Hz, 3H), 1.11 (t, *J* = 7.6 Hz, 6H), 0.91 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4 (d, $^1J_{C\text{-}F}$ = 256 Hz), 144.6,

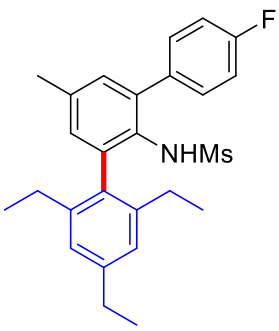
142.9, 138.3, 137.2, 136.1, 135.9, 134.2, 131.9 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz), 131.6, 131.0, 130.9, 125.5, 115.44 (d, $^{2}J_{C\text{-}F}$ = 21.2 Hz), 48.4, 28.9, 26.7, 21.1, 15.9, 15.2, 8.5; IR (KBr) $\tilde{\nu}$ = 3438, 2092, 1635, 1329, 1150 cm^{-1};HR-MS (ESI-TOF) m/z $[M + Na]^{+}$ calcd for $C_{27}H_{32}FNO_2SNa$ 476.2030; found 476.2040.

***N*-(4''- Fluoro- 2, 4, 5', 6- tetramethyl-[1,1':3',1''-terphenyl]-2'-yl]methanesulfonamide**



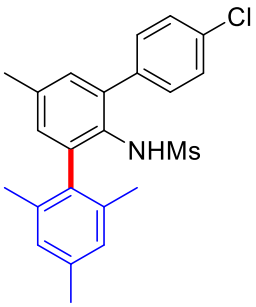
(3fa): R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 35 mg (61%); mp 207 – 209 °C **;** R_f = 0.4 (hexane:ethyl acetate: 9:1); white solid; 39 mg (62%); ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.45 (dd, *J* = 8.4, 5.6 Hz, 2H), 7.14 (t, *J* = 8.4 Hz, 2H), 7.09 (s, 1H), 6.97 (s, 3H), 5.53 (s, 1H), 2.38 (s, 3H), 2.31 (s, 3H), 2.08 (s, 6H), 1.97 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 162.53 (d, $^{1}J_{C\text{-}F}$ = 246.0 Hz), 138.4, 137.8 (*2), 137.0, 136.8, 135.6 (d, $^{4}J_{C\text{-}F}$ = 3.4 Hz), 135.3, 131.9 (d, $^{3}J_{C\text{-}F}$ = 8.1 Hz), 131.1, 130.9, 130.5, 128.7,115.6 (d, $^{2}J_{C\text{-}F}$ = 21.0 Hz), 42.1, 21.2, 21.1, 20.6 ; IR (KBr) $\tilde{\nu}$ = 3421, 2359, 2339, 1652 cm^{-1};HR-MS (ESI-TOF) m/z $[M + H]^{+}$ calcd for $C_{23}H_{25}FNO_2S$ 398.1585; found 398.1573.

***N*-(2,4,6-triethyl-4''-fluoro-5'-methyl-[1,1': 3', 1''-terphenyl]-2'-yl)methanesulfonamide**



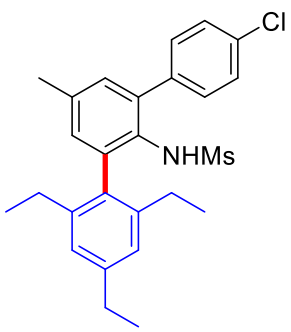
(3fd): R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 34 mg (53%); mp 193 – 195 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.46 – 7.44 (m, 2H), 7.14 (t, *J* = 8.4 Hz, 2H), 7.10 (s, 1H), 7.03 (s, 2H), 7.01 (s, 1H), 5.49 (s, 1H), 2.66 (q, *J* = 7.7 Hz, 2H), 2.41 –2.30 (m, 7H), 1.93 (s, 3H), 1.26 (t, *J* = 7.7 Hz, 3H), 1.11 (t, *J* = 7.7 Hz, 6H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 162.5 (d, $^{1}J_{C\text{-}F}$ = 246.0 Hz), 144.7, 143.0, 138.1, 137.1, 136.3, 136.1 (d, $^{4}J_{C\text{-}F}$ = 3.2 Hz), 133.9, 131.93 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz), 131.5, 131.06, 130.7, 125.5, 115.5 (d, $^{2}J_{C\text{-}F}$ =

21.2 Hz), 42.2, 28.9, 26.7, 21.1, 15.7, 15.3; IR (KBr) $\tilde{\nu}$ = 3422, 1635, 1511, 1314, 1143 cm^{-1};HR-MS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{26}H_{31}FNO_2S$ 440.2054; found 440.2036.



***N*-(4''-chloro-2, 4, 5',6-tetramethyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (3ga):** R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 37 mg (65%); mp 191 – 193 °C**;** ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.43 (s, 4H), 7.09 (s, 1H), 6.98 (s, 1H), 6.97 (s, 2H), 5.55 (s, 1H), 2.38 (s, 3H), 2.32 (s, 3H), 2.08 (s, 6H), 1.98 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 138.3, 138.2, 138.0, 137.9, 137.1, 136.9, 135.3, 133.9, 131.5, 131.3, 130.8, 130.3, 128.8, 128.7, 42.1, 21.2, 21.1, 20.6; IR (KBr) $\tilde{\nu}$ = 3441, 2390, 2049, 1633, 1142 cm^{-1};HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{23}H_{24}ClNO_2SNa$ 436.1108; found 436.1133.

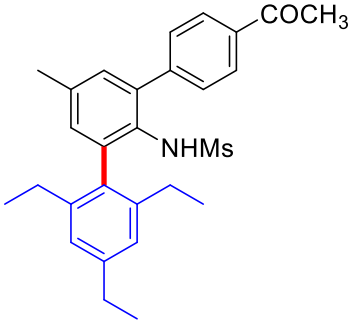
***N*-(4''-chloro-2,4,5'-trimethyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (3gc):** R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 31 mg (57%); mp 171 – 173 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (s, 4H), 7.16 (d, *J* = 7.6 Hz, 1H), 7.11– 7.05 (m, 4H), 5.63 (s, 1H), 2.38 (s, 3H), 2.36 (s, 3H), 2.16 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.4, 138.5, 138.1, 137.9, 136.9, 136.5, 136.0, 134.0, 131.6, 131.4, 131.1, 130.8, 130.6, 129.8, 128.8, 126.8, 42.0, 21.2, 21.0, 20.0; IR (KBr) $\tilde{\nu}$ = 3438, 2098, 2049, 1720, 1492, 1316, 1146 cm^{-1};HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{22}H_{22}ClNO_2SNa$ 422.0952; found 422.0935.



***N*-(4''-chloro-2,4,6-triethyl-5'-methyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (3gd):** R_f = 0.4 (hexane : ethyl acetate:

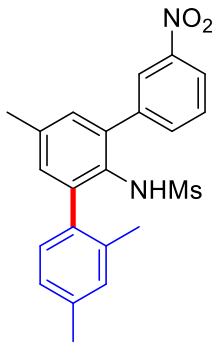
9:1); white solid; 48 mg (77%); mp 154 – 156 °C**;** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (s, 4H), 7.09 (s, 1H), 7.03 (s, 3H), 5.48 (s, 1H), 2.66 (q, *J* = 7.6 Hz, 2H), 2.45 – 2.27 (m, 7H), 1.95 (s, 3H), 1.26 (t, *J* = 7.6 Hz, 3H), 1.11 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 142.9, 138.6, 137.9, 137.3, 136.3, 133.9 , 133.8, 131.7, 131.6, 130.9, 130.5, 128.7, 125.6, 42.2, 28.9, 26.7, 21.1, 15.7, 15.4 ; IR (KBr) $\tilde{\nu}$ = 3503, 2092, 1736, 1641, 1317, 1148 cm^{-1};HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{26}H_{30}ClNO_2SNa$ 478.1578; found 478.1573.

***N*-(4''-acetyl-2,4,6-triethyl-5'-methyl-[1,1':3',1''-terphenyl]-2'-yl)methanesufonamide**



(3hd): R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 43 mg (71%); mp 163 – 165 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.4 Hz, 2H), 7.60 (d, *J* = 7.7 Hz, 2H), 7.12 (s, 1H), 7.05 (s, 1H), 7.03 (s, 2H), 5.51 (s, 1H), 2.67 (q, *J* = 7.7 Hz, 2H), 2.64 (s, 3H), 2.43 – 2.39 (m, 5H), 2.35 – 2.30 (*sept*, *J* = 7.7 Hz , 2H), 1.92 (s, 3H), 1.27 (t, *J* = 7.7 Hz, 3H), 1.12 (t, *J* = 7.7 Hz, 6H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 197.8, 145.1, 144.8, 142.9, 138.1, 137.6, 136.5, 136.1, 133.7, 131.9, 130.8, 130.5, 130.4, 128.5, 125.6, 42.2, 28.9, 26.9, 26.8 , 21.1, 15.7, 15.3; IR (KBr) $\tilde{\nu}$ = 3438, 1720, 1641, 1530, 1449 cm^{-1};HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{28}H_{33}NO_3SNa$ 486.2073; found 486.2067.

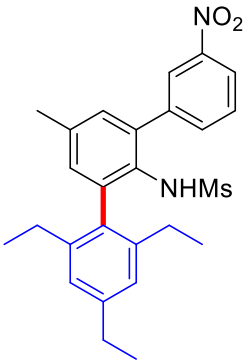
***N*-(2,4, 5'-trimethyl-3''-nitro-[1,1':3',1''-terphenyl]-2'yl)methanesulfonamide (3ic):** R_f =



0.4 (hexane : ethyl acetate 9:1); white solid; 36 mg (66%); mp 164 – 166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (t, *J* = 2.0 Hz, 1H), 8.24 – 8.21 (m, 1H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.63 (t, *J* = 8.0 Hz, 1H), 7.16 (s, 1H), 7.15 – 7.09 (m, 4H), 5.69 (s, 1H), 2.41 (s, 3H), 2.37 (s, 3H), 2.17 (s, 3H), 2.02 (s,

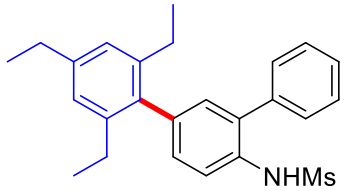
3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.5, 139.9, 138.4, 138.0, 137.6, 136.4, 136.3, 135.5, 132.2, 131.3, 130.9, 130.4, 129.4, 126.9, 124.8, 122.6, 41.8, 21.3, 21.1, 20.1; IR (KBr) $\tilde{\nu}$ = 3438, 2092, 1641, 1555, 1449 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{22}H_{22}N_2O_4SNa$ 433.1192; found 433.120

***N*-(2,4,6-triethyl-5'-methyl-3''-nitro-[1,1':3',1''-terphenyl]-2'yl]methanesulfonamide**

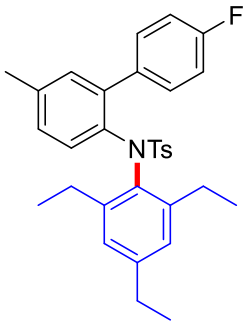


(3id): R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 31 mg (62%); mp 203 – 205 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.64 (t, *J* = 8.0 Hz, 1H), 7.16 (s,1H), 7.10 (s, 1H), 7.05 (s, 2H), 5.49 (s, 1H), 2.67 (q, *J* = 7.2 Hz, 2H), 2.46 – 2.27 (m, 7H), 1.98 (s, 3H), 1.27 (t, *J* = 7.6 Hz, 3H), 1.13 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 144.9, 142.8, 141.9, 137.9, 137.3, 136.9, 136.5, 133.6, 132.4, 130.9, 130.2, 129.4, 125.6, 125.0, 122.5, 42.1, 28.9, 26.8, 21.1, 15.7, 15.4; IR (KBr) $\tilde{\nu}$ = 3438, 2092, 1643, 1350, 1148 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{26}H_{30}N_2O_4SNa$ 489.1818; found 489.1800.

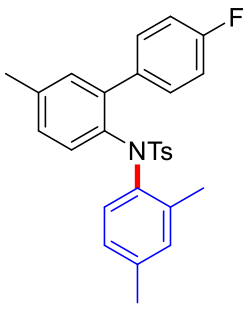
***N*-([1, 1'- biphenyl]-2-yl)-*N*-(2,4,6-triethylphenyl)methanesulfonamide (3jd)**: R_f = 0.4



(hexane : ethyl acetate 9:1); white solid; 39 mg (59%); mp 157 – 159 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.0 Hz, 1H), 7.49 (t, *J* = 7.2 Hz, 2H), 7.42 (t, *J* = 7.2 Hz, 1H), 7.36 (d, *J* = 7.6 Hz, 2H), 7.21 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.12 (s, 1H), 6.98 (s, 2H), 6.57 (s, 1H), 2.95 (s, 3H), 2.66 (q, *J* = 7.6 Hz, 2H), 2.36 (q, *J* = 7.2 Hz, 4H), 1.28 (t, *J* = 7.6 Hz, 3H), 1.05 (t, *J* = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.8, 142.3, 137.6, 137.4, 137.0, 132.9, 132.6, 132.4, 132.3, 130.5, 129.7, 129.2, 128.6, 125.5, 40.0, 28.9, 27.1, 15.8, 15.6; IR (KBr) $\tilde{\nu}$ = 3437, 2965, 2092, 1641, 1332, 1168 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{25}H_{29}NO_2SNa$ 430.1811; found 430.1810.



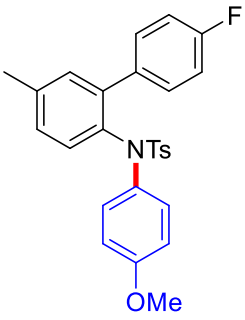
***N*-(4'-fluoro-5-methyl-[1,1'-biphenyl]-2-yl)-4-methyl-*N*-(2, 4, 6 – triethylphenyl)benzenesulfonamide (3fd'):** R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 39 mg (67%); mp 140 – 142 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.25 (s, 2H), 7.08 (dd, *J* = 8.4, 1.4 Hz, 1H), 6.70 (s, 2H), 6.68 (t, *J* = 8.4 Hz, 2H), 6.56 (s, 1H), 6.33 – 6.31 (m, 2H), 2.56 (q, *J* = 7.7 Hz, 2H), 2.47 – 2.40 (m, 5H), 2.23 (s, 3H), 1.78 –1.75 (m, 2H), 1.22 (t, *J* = 7.7 Hz, 3H), 0.85 (t, *J* = 7.7 Hz, 6H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 161.92 (d, $^1J_{C\text{-}F}$ = 244 Hz), 144.9, 144.5, 143.4, 138.2, 138.1, 137.4, 136.4 (d, $^4J_{C\text{-}F}$ = 4 Hz) , 135.3, 135.2, 134.0, 130.9 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 129.3, 128.2, 128.2, 127.2, 126.4, 114.00 (d, $^2J_{C\text{-}F}$ = 21.0 Hz), 28.5, 24.8, 21.6, 20.5 , 15.8, 14.3; IR (KBr) $\tilde{\nu}$ = 3438, 2089, 1644, 1142 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{32}H_{35}FNO_2S$ 516.2367; found 516.2385.



***N*-(2,4-dimethylphenyl)-N-(4'-fluoro-5-methyl-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide (3fc'):** R_f = 0.4 (hexane : ethyl acetate 9:1); white solid; 34 mg (66%); mp 139-141 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 1H), 7.25 (s, 3H), 7.12 (s, 1H), 7.09 (dd, *J* = 7.7, 1.4 Hz, 1H), 6.98 (t, *J* = 8.4 Hz, 2H), 6.94 (s, 1H), 6.74 (s, 1H), 6.60 (d, *J* = 8.4 Hz, 1H), 6.41 (d, *J* = 6.3 Hz, 1H), 2.44 (s, 3H), 2.30 (s, 3H), 2.17 (s, 3H), 1.54 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 162.57 (d, $^1J_{C\text{-}F}$ = 244.0 Hz), 143.6, 141.5, 138.1, 137.7, 137.6, 136.8, 136.4, 136.1(d, $^4J_{C\text{-}F}$ = 3.0 Hz), 132.9, 132.1, 131.4 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 130.7, 129.7, 129.5, 128.4, 128.3, 126.4, 114.93

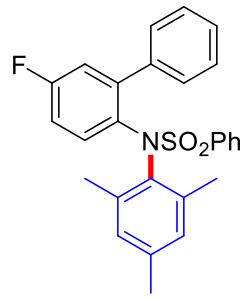
(d, $^{2}J_{C\text{-}F}$ = 21.0 Hz), 21.7, 21.0, 20.9, 18.6; IR (KBr) $\tilde{\nu}$ = 3441, 2084, 1641 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + H]^{+}$ calcd for $C_{28}H_{27}FNO_2S$ 460.1741; found 460.1713.

***N*-(4'-fluoro-5-methyl-[1,1'-biphenyl]-2-yl)-4-methyl-*N*-(4-methoxyphenyl)-4-**



methylbenzenesulfonamide (3fb'): R_f = 0.4 (hexane:ethyl acetate: 9:1); white solid; 41 mg (78%); mp 150-152 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.49 (d, *J* = 7.7 Hz, 2H), 7.34 (dd, *J* = 8.4, 5.5 Hz, 2H), 7.25 (d, *J* = 8.4 Hz, 2H), 7.11 (s, 2H), 7.08 – 7.06 (m, 3H), 6.61 – 6.58 (m, 4H), 3.71 (s, 3H), 2.44 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4 (d, $^{1}J_{C\text{-}F}$ = 244.0 Hz), 158.4, 143.6, 141.4, 138.3, 137.8, 137.3, 135.3 (d, $^{4}J_{C\text{-}F}$ = 3.0 Hz), 133.4, 132.4, 131.4 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz), 129.8, 129.5, 129.0, 128.1, 127.8, 114.8 (d, $^{2}J_{C\text{-}F}$ = 21.0 Hz), 113.7, 55.4, 21.7, 21.2; IR (KBr) $\tilde{\nu}$ = 3438, 1644, 1506, 1163, 1033 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^{+}$ calcd for $C_{27}H_{24}FNO_3SNa$ 484.1353; found 484.1360.

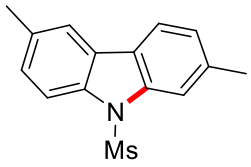
***N*-(5-fluoro-[1,1'-biphenyl]-2-yl)-*N*-mesitylbenzenesulfonamide (3fa'):** R_f = 0.4



(hexane:ethyl acetate: 9:1); colourless sticky liquid; 40 mg (72 %); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (dd, *J* = 9.2, 5.2 Hz, 1H), 7.77 – 7.75 (m, 2H), 7.61 – 7.57 (m, 1H), 7.47 (t, *J* = 8.0 Hz, 2H), 7. 61 – 7.57 (m, 1H), 7.05 – 7.00 (m, 3H), 6.63(s, 2H), 6.59 (dd, *J* = 8.8, 3.2 Hz, 1H), 6.63 – 6.35 (m, 2H), 2.22 (s, 3H), 1.73 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.88 (d, $^{1}J_{C\text{-}F}$ = 248.0 Hz), 143.24 (d, $^{3}J_{C\text{-}F}$= 8.0 Hz), 140.4, 139.7, 138.9, 137.9, 136.1, 134.49 (d, $^{4}J_{C\text{-}F}$ = 3.2 Hz), 133.1, 131.1 (d, $^{3}J_{C\text{-}F}$ = 8.5 Hz), 130.1, 129.2, 128.9, 128.5, 127.7, 127.6, 119.6 (d, $^{2}J_{C\text{-}F}$ = 21.7 Hz), 113.7 (d, $^{2}J_{C\text{-}F}$ = 21.7 Hz), 20.9, 20.4*2; IR (KBr) $\tilde{\nu}$

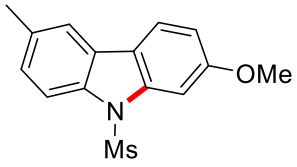
= 3517, 1641, 1165 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{27}H_{24}FNO_2SNa$ 468.1404; found 468.1332.

2, 6-dimethyl-9-(methylsulfonyl)-9*H*-carbazole (4a): R_f = 0.4 (hexane:ethyl acetate: 9:1);



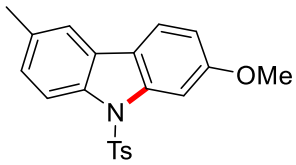
white solid; 22 mg (59%); mp 92– 94 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.4 Hz, 1H), 7.96 (s, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.74 (s, 1H), 7.28 (d, *J* = 1.6 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 1H), 2.93 (s, 3H), 2.54 (s, 3H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.2, 138.1, 138.0, 134.0, 128.3, 126.7, 125.5, 124.1, 120.1, 119.9, 115.1, 114.6, 38.3, 22.3, 21.4; IR (KBr) $\tilde{\nu}$ = 3423, 2089, 1641, 1362, 1162 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{15}H_{16}NO_2S$ 274.0896; found 274.0888.

2-methoxy-6-methyl-9-(methylsulfonyl)-9*H*-carbazole (4b): R_f = 0.4 (hexane:ethyl



acetate: 9:1); white solid; 24 mg (60%); mp 157 – 159 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.4 Hz, 1H), 7.82 (d, *J* = 8.4 Hz, 1H), 7.70(s, 1H), 7.69(s, 1H), 7.22 (dd, *J* = 8.4, 1.1 Hz, 1H), 7.00 (dd, *J* = 8.4, 2.4 Hz, 1H), 3.92 (s, 3H), 2.93 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 140.1, 136.6, 134.1, 127.5, 126.7, 120.8, 119.8, 119.6, 114.5, 112.5, 99.5, 55.9, 38.3, 21.4; IR (KBr) $\tilde{\nu}$ = 3439, 2925, 1352, 1337, 1232, cm^{-1}; HR-MS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{15}H_{16}NO_3S$ 290.0845; found 290.0835.

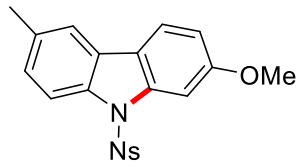
2-methoxy-6-methyl-9-tosyl-9*H*-carbazole (4c): R_f = 0.4 (hexane:ethyl acetate: 9:1); white



solid; 20 mg (51%); mp 141 – 143 °C; ^{1}H NMR (400 MHz, δ 8.14 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 2.2 Hz, 1H), 7.71 – 7.66 (m,

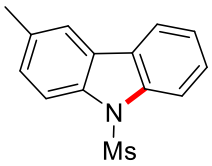
3H), 7.56 (s, 1H), 7.20 (d, *J* = 8.4 Hz, 1H), 7.08 (d, *J* = 8.0 Hz, 2H), 6.93 (dd, *J* = 8.4, 2.4 Hz, 1H), 3.95 (s, 3H), 2.45 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 144.9, 140.1, 136.6, 135.1, 133.7, 129.7, 127.3, 126.6, 125.4, 120.6, 120.0, 119.4, 114.9, 112.2, 100.1, 55.9, 21.6, 21.4; IR (KBr) $\tilde{\nu}$ = 3441, 2359, 2341, 1640, 1367, 1170, 1150 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{21}H_{20}NO_3S$ 366.1158; found 366.1144.

2-methoxy-6-methyl-9-((4-nitrophenyl)sulfonyl)-9*H*-carbazole (4d): R_f = 0.4



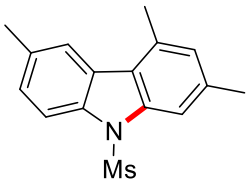
(hexane:ethyl acetate: 9:1); white solid; 26 mg (65%); mp 164 – 166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (t, *J* = 8.8 Hz, 3H), 7.90 (d, *J* = 8.8 Hz, 2H), 7.82 (d, *J* = 2.4 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.55 (s, 1H), 7.23 (d, *J* = 7.6 Hz, 1H), 6.96 (dd, *J* = 8.4, 2.4 Hz, 1H), 3.95 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 150.7, 142.8, 139.7, 136.1, 134.8, 127.8, 127.7, 127.2, 124.3, 120.9, 120.4, 119.8, 115.0, 112.7, 100.5, 56.0, 22.4; IR (KBr) $\tilde{\nu}$ = 3441, 2064, 1625, 1377, 1175, 1041 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{20}H_{16}N_2O_5SNa$ 419.0672; found 419.0659.

3-methyl-9-(methylsulfonyl)-9*H*-carbazole (4e)[23]: R_f = 0.4 (hexane:ethyl acetate: 9:1);



white solid; 28 mg (70%); mp 84 – 86°C (lit. 85 – 88°C)[23]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.4 Hz, 1H), 8.03 (d, *J* = 8.4 Hz, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.80 (s, 1H), 7.50 – 7.46 (m, 1H), 7.41 (td, *J* = 7.6, 0.8 Hz, 1H), 7.31 (dd, *J* = 8.8, 1.2 Hz, 1H), 2.94 (s, 3H), 2.53 (s, 3H).

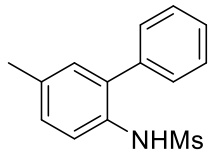
2,4,6-trimethyl-9-(methylsulfonyl)-9*H*-carbazole (4f)[43]: R_f = 0.5 (hexane:ethyl acetate:



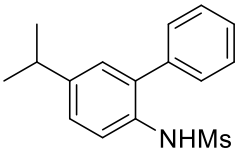
19:1); white solid; 27 mg (69%); mp 105 – 107°C (lit. 106-107 °C)[43] ; ^{1}H NMR (400 MHz, $CDCl_3$) 8.07 (d, *J* = 8.4 Hz, 1H), 7.85 (s, 2H),

7.28 (s, 1H), 7.01 (s, 1H), 2.91 (s, 3H), 2.77 (s, 3H), 2.53 (s, 3H), 2.50 (s, 3H).

***N*-(5-methyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (1a)[28] :** R_f = 0.6 (hexane : ethyl acetate 9:1); white solid; 859 mg (62%); mp 66 – 66°C (lit. 65 – 66°C)[28]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.4 Hz, 1H), 7.50 – 7.46 (m, 2H), 7.44 – 7.40 (m, 1H), 7.32 – 7.30 (m, 2H), 7.20 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.40 (s, 1H), 2.80 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 135.2, 133.9, 131.5, 131.4, 129.7, 129.5, 129.1, 128.5, 121.8, 39.6, 20.9.



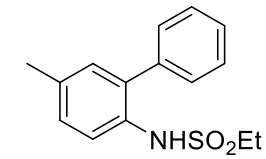
***N*-(5-isopropyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (1b):** R_f = 0.6 (hexane : ethyl acetate 9:1); white solid; 989 mg (73%); mp 91 – 93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.4 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.44 – 7.41 (m, 1H), 7.34 – 7.32 (m, 2H), 7.24 (d, *J* = 2.1 Hz, 1H), 7.13 (d, *J* = 2.0 Hz, 1H), 6.43 (s, 1H), 2.92 (sept, 1H), 2.81 (s, 3H), 1.27 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.1, 138.7, 133.9, 131.5, 129.5, 129.2, 128.9, 128.4, 127.1, 121.1, 39.7, 33.6, 24.7; IR (KBr) $\tilde{\nu}$ = 3437, 2092, 1641, 1327, 1156 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{16}H_{19}NO_2SNa$ 312.1029; found 312.1005.



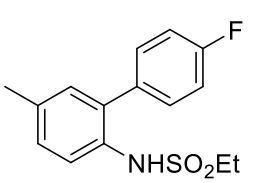
***N*-(5-*tert*-butyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (1c):** R_f = 0.6 (hexane : ethyl acetate 9:1); white solid; 995 mg (75%); mp 90 – 92 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.4 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.45 – 7.39 (m, 2H), 7.35 – 7.33 (m, 2H), 7.17 (d, *J* = 7.6 Hz, 1H), 6.43 (s, 1H), 2.83 (s, 3H), 1.33 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 138.2, 133.4, 131.3,

129.5, 129.2, 128.4, 127.8, 126.1, 120.6, 39.8, 34.6, 31.5; IR (KBr) $\tilde{\nu}$ = 3421, 2961, 1645, 1328, 1159 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{17}H_{21}NO_2SNa$ 326.1185; found 326.1193.

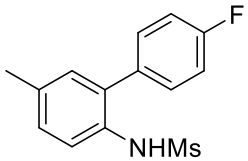
***N*-(5-methyl-[1,1'-biphenyl]-2-yl)ethanesulfonamide (1d) :** R_f = 0.6 (hexane : ethyl acetate 9:1); yellow sticky liquid, 865 mg (63%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.4 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.43 (t, *J* = 7.2 Hz, 1H), 7.33 – 7.31 (m, 2H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.08 (s, 1H), 6.39 (s, 1H), 2.94 (q, *J* = 7.2 Hz, 2H), 2.35 (s, 3H), 1.11 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9, 134.7, 133.5, 131.5, 131.4, 129.6, 129.5, 129.1, 128.4, 120.6, 46.1, 20.8, 8.0; IR (KBr) $\tilde{\nu}$ = 3438, 2089, 1645, 1328, 1150 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{15}H_{17}NO_2SNa$ 298.0872; found 298.0878.



***N*-(4'-fluoro-5-methyl-[1,1'-biphenyl]-2-yl)ethanesulfonamide (1e):** R_f = 0.6 (hexane : ethyl acetate: 9:1); white solid; 977 mg (66%); mp 133 – 135 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.4 Hz, 1H), 7.32 – 7.29 (m, 2H), 7.20 – 7.15 (m, 3H), 7.04 (s, 1H), 6.22 (s, 1H), 2.98 (q, *J* = 7.2 Hz, 2H), 2.35 (s, 3H), 1.16 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8 (d, $^1J_{C\text{-}F}$ = 248.0 Hz), 134.8, 133.8 (d, $^4J_{C\text{-}F}$ = 3.4Hz) , 132.5, 131.6 , 131.5, 131.0 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 129.8, 120.6, 116.5 (d, $^2J_{C\text{-}F}$ = 21.5 Hz), 46.4, 20.9, 8.1; IR (KBr) $\tilde{\nu}$ = 3438, 1651, 1495, 1150 cm^{-1} ; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{15}H_{16}FNO_2SNa$ 316.0778; found 316.0783.

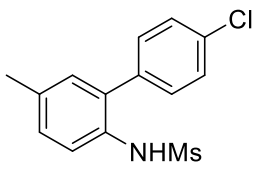


***N*-(4'-fluoro-5-methyl-[1,1'- biphenyl]-2-yl)benzenesulfonamide (1f) :** R_f = 0.6 (hexane : ethyl acetate 9:1); white solid; 980 mg (65%); mp 92 – 94 °C**;** ^1H

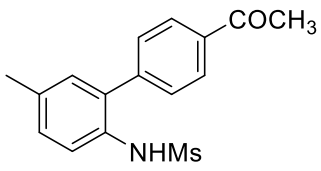


NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.4 Hz, 1H), 7.32 – 7.28 (m, 2H), 7.20 – 7.15 (m, 3H), 7.07 (s, 1H), 6.36 (s, 1H), 2.82 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.67 (d, $^1J_{C-F}$ = 248.0 Hz), 135.3, 133.8, 133.2, 131.5, 131.4, 131.0 (d, $^3J_{C-F}$ = 8.1 Hz), 129.8, 121.6, 116.39 (d, $^2J_{C-F}$ = 21.4 Hz), 39.9, 20.8; IR (KBr) $\tilde{\nu}$ = 3373, 2092, 1643, 1322, 1155, 1089 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{14}H_{14}FNO_2SNa$ 302.0621; found 302.0624.

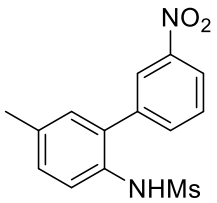
***N*-(4'-chloro-5-methyl-[1,1'- biphenyl]-2-yl)methanesulfonamide (1g) :** R_f = 0.6 (hexane : ethyl acetate 9:1); white solid; 985 mg (61%); mp 95 – 97 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.4 Hz, 1H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.28 (s, 2H), 7.20 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.06 (s, 1H), 6.27 (s, 1H), 2.84 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.3, 135.4, 134.6, 132.9, 131.4, 131.3, 130.6, 130.0, 129.7, 121.5, 40.0, 20.9; IR (KBr) $\tilde{\nu}$ = 3373, 2092, 1643, 1389, 1322, 1155cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{14}H_{14}ClNO_2SNa$ 318.0326; found 318.0306.

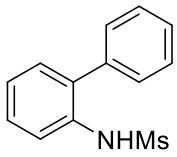


***N*-(4'-acetyl-5-methyl-[1,1'- biphenyl]-2-yl)methanesulfonamide (1h) :** R_f = 0.6 (hexane : ethyl acetate 9:1); yellow sticky liquid; 1.1g (67%); ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.0 Hz, 2H), 7.55 (d, *J* = 8.4 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 1H), 7.12 (s, 1H), 6.32 (s, 1H), 2.86 (s, 3H), 2.68 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.5, 142.8, 136.8, 135.5, 131.2, 131.2, 133.2, 130.3, 129.5, 129.4, 121.7, 40.1, 26.8, 20.9 ; IR (KBr) $\tilde{\nu}$ = 3441, 2390, 2049, 1633, 1142 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{16}H_{18}NO_3SNa$ 304.1002; found 304.1028.



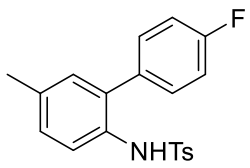
***N*-(5-methyl-3'-nitro-[1,1'- biphenyl]-2-yl)methanesulfonamide (1i) :** R_f = 0.7 (hexane : ethyl acetate 9:1); white solid; 996 mg (60%); mp 160 – 162 °C**;** ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.4 Hz, 1H), 8.22 (s, 1H), 7.73 (d, *J* = 7.2 Hz, 1H), 7.67 (t, *J* = 8.0 Hz, 1H), 7.50 (d, *J* = 8.4 Hz, 1H), 7.28(s, 1H), 7.12 (s, 1H), 6.22 (s, 1H), 2.89 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 139.9, 136.3, 135.5, 132.9, 131.6, 131.1, 130.7, 130.2, 124.4, 123.1, 122.9, 40.3, 20.9; IR (KBr) $\tilde{\nu}$ = 3438, 2092, 1529, 1351, 1154 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{14}H_{14}N_2O_4SNa$ 329.0566; found 329.0566.





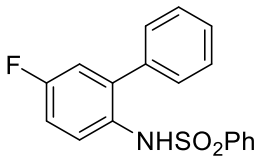
N-([1,1'-biphenyl]-2-yl)methanesulfonamide (1j)[23]: R_f = 0.6 (hexane : ethyl acetate 9:1); white solid; 888 mg (61%); mp 65 – 67 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.4 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.45 – 7.43 (m, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.34 (d, *J* = 7.0 Hz, 2H), 7.29 – 7.27 (m, 1H), 7.23 (t, *J* = 7.2 Hz, 1H), 6.56 (s, 1H), 2.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.5, 133.9, 133.4, 130.8, 129.5, 129.0, 129.0, 128.5, 125.0, 120.3, 39.8.

4-methyl-*N*-(5-methyl-1,1' biphenyl]-2-yl)benzenesulfonamide (1k) : R_f = 0.6 (hexane : ethyl acetate 9:1); white solid; 811 mg (60%); mp 131–133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.4 Hz, 1H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 7.14 (d, *J* = 8.4 Hz, 1H), 6.99 (t, *J* = 8.4 Hz, 2H), 6.88 (s, 1H), 6.79 – 6.75 (m, 2H), 6.34 (s, 1H), 2.41 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162 (d, $^1J_{C\text{-}F}$ = 248.0 Hz), 144.0, 136.4, 135.2, 133.5, 131.2, 131.1, 130.8, 130.7, 129.7, 129.6, 127.3, 122.6, 116.0 (d, $^2J_{C\text{-}F}$ = 21.4 Hz), 21.7, 20.9. IR

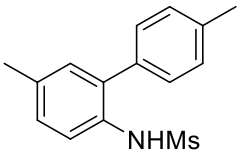


(KBr) $\tilde{\nu}$ = 3438, 2092, 1641, 1495, 1333, 1163, 1091 cm^{-1}; HR-MS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{20}H_{18}FNO_2SNa$ 378.0934; found 378.0912.

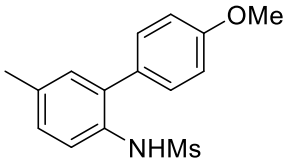
***N*-(5-fluoro-[1,1'-biphenyl]-2-yl) benzenesulfonamide (1l)[23]:** R_f = 0.6 (hexane : ethyl acetate 9:1); white solid; 800 mg (61%); mp 72 – 74 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 8.8, 5.6 Hz, 1H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.48 (d, *J* = 7.2 Hz, 2H), 7.40 – 7.28 (m, 5H), 7.07 (td, *J* = 8.4, 2.8 Hz, 1H), 6.82 (dd, *J* = 8.8, 3.2 Hz, 1H), 6.72 (d, *J* = 7.2 Hz, 2H), 6.49 (d, *J* = 5.6 Hz, 1H).



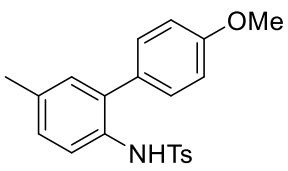
***N*-(4',5-dimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (1m)**: R_f = 0.4 (hexane:ethyl acetate: 9:1); white solid; 923 mg (65%); mp 74 – 76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.0 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.19 – 7. 16 (m, 3H), 7.08 (s, 1H), 6.43 (s, 1H), 2.79 (s, 3H), 2.42 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 135.1, 134.7, 133.8, 133.2, 131.4, 130.2, 129.5, 128.9, 120.9, 39.5, 21.3, 20.9; IR (KBr) $\tilde{\nu}$ = 3440, 2924, 1641, 1330,1157, 971cm^{-1}; HR-MS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{15}H_{17}NO_2SNa$ 298.0872; found 298.0879.



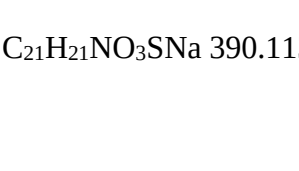
***N*-(4'-methoxy-5-methyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (1n)**: R_f = 0.4 (hexane:ethyl acetate: 9:1); white solid; 1123 mg (71%); mp 72 – 74 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.4 Hz, 1H), 7.24 – 7.21 (m, 2H), 7.17 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.07 (d, *J* = 1.6 Hz, 1H), 7.01 – 6.99 (m, 2H), 6.42 (s, 1H), 3.87 (s, 3H), 2.81 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 135.0, 133.6, 133.3, 131.6, 130.3, 129.8, 129.4, 120.9, 114.9, 55.5, 39.6, 20.9; IR (KBr) $\tilde{\nu}$ = 3422, 2080, 1640, 1325, 1246, 1154, cm^{-1}; HR-MS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{15}H_{17}NO_3SNa$ 314.0821; found 314.0826.



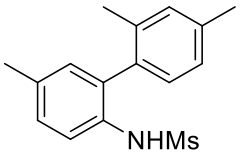
***N*-(4'-methoxy-5-methyl-[1,1'-biphenyl]-2yl)-4-methylbenzenesulfonamide) (1o)**: R_f = 0.5 (hexane:ethyl acetate: 19:1); white solid; 985 mg (70%), mp 131 – 133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.4 Hz, 1H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 6.8 Hz, 1H), 6.88 – 6.83 (m, 3H), 6.74 (d, *J* = 8.4 Hz, 2H), 6.47 (s, 1H), 3.85 (s, 3H), 2.40 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 143.7, 136.4, 134.7, 133.8, 131.5, 131.2, 130.1, 129.7, 129.6, 129.1, 127.3, 121.7, 114.9, 55.9, 21.7, 20.9; IR (KBr) $\tilde{\nu}$ = 3422, 2080, 1640, 1493, 1334, 1246, 1163 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{21}H_{21}NO_3SNa$ 390.1134; found 390.1129.



***N*-(4'-methoxy-5-methyl-[1,1'-biphenyl]-2yl)- 4-nitrobenzenesulfonamide (1p)**: R_f = 0.5 (hexane:ethyl acetate: 19:1); white solid; 1129 mg (83%), mp 170 – 172 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.8 Hz, 2H), 7.63 (d, *J* = 8.8 Hz, 2H), 7.56 (d, *J* = 8.4 Hz, 1H), 7.16 (d, *J* = 8.4 Hz, 1H), 6.91 (s, 1H), 6.82 – 6.80 (m, 2H), 6.71 – 6.69 (m, 3H), 3.84 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 136.7, 135.2, 131.4, 130.5, 129.8, 129.4, 128.5, 127.4, 124.1, 123.9, 123.7, 114.8, 114.6, 55.5, 21.0; IR (KBr) $\tilde{\nu}$ = 3423, 2359,1640, 1529, 1347, 1167 cm^{-1}; HR-MS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{20}H_{18}N_2O_5SNa$ 421.0829; found 421.0825.



***N*-(2',4',5-trimethyl-[1,1'-biphenyl]-2-yl)methanesulfonamide (1q)[57]**: R_f = 0.4 (hexane:ethyl acetate: 9:1); white solid; 891 mg (60%); mp 110 – 112



(lit. 112 – 114 °C)[57] °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.4 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 1H), 7.13 (s, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 7.03 – 6.97 (m, 2H), 6.01 (s, 1H), 2.84 (s, 3H), 2.38 (s, 3H), 2.34 (s, 3H), 2.06 (s, 3H)

4.6 NOTES AND REFERENCES

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NMR Spectra of Selected Compounds

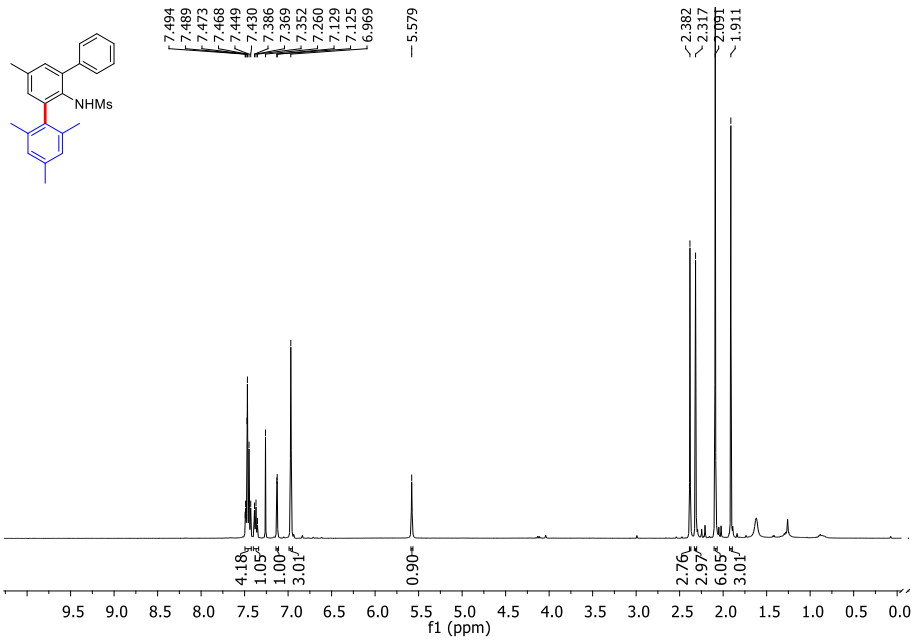


Figure 4.6. [1] H NMR spectrum of *N*-(2,4,5',6-tetramethyl-[1,1' : 3', 1"- terphenyl]-2'-yl) methanesulfonamide (**3aa**)

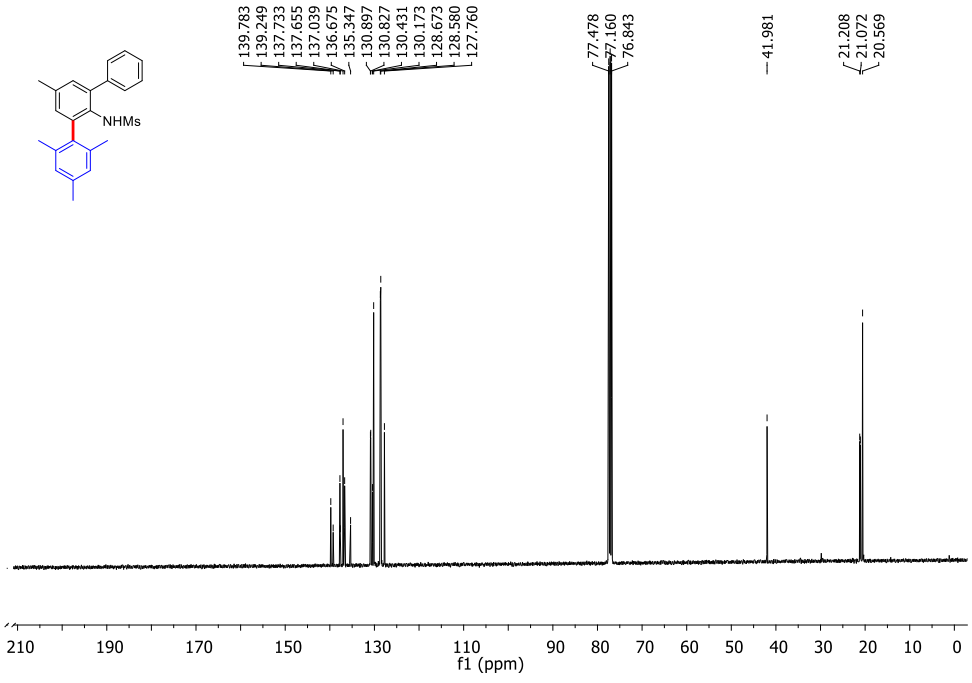


Figure 4.7. [13]C NMR spectrum of *N*-(2,4,5',6-tetramethyl-[1,1' : 3', 1"- terphenyl]-2'-yl) methanesulfonamide (**3aa**)

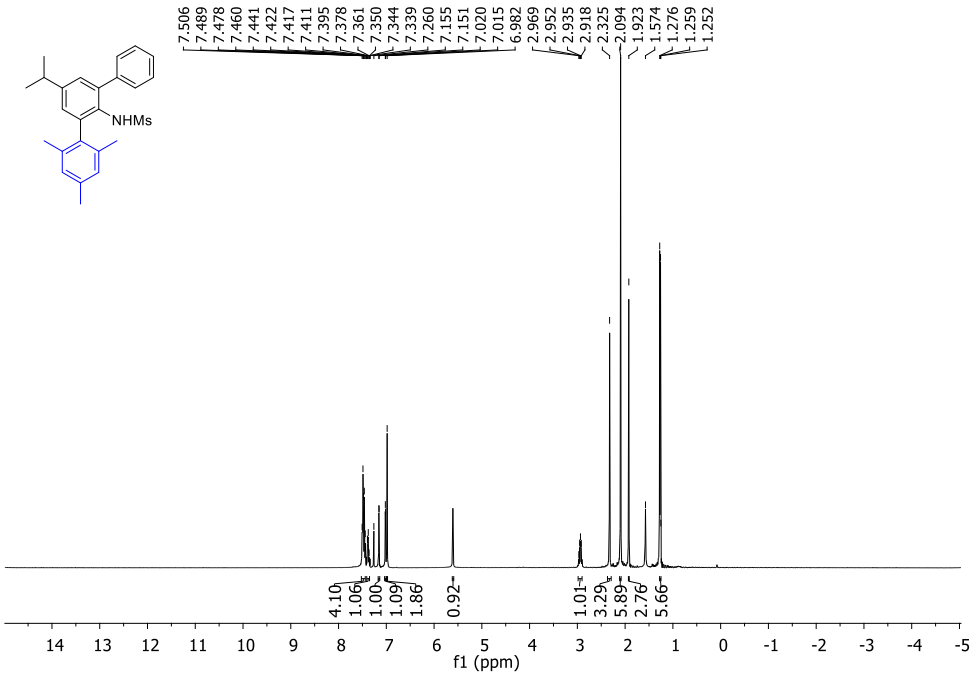


Figure 4.8. [1] H NMR spectrum of *N*-(5'-isopropyl-2,4,6- trimethyl- [1,1': 3', 1"-terphenyl]-2'-yl)methanesulfonamide (**3ba**)

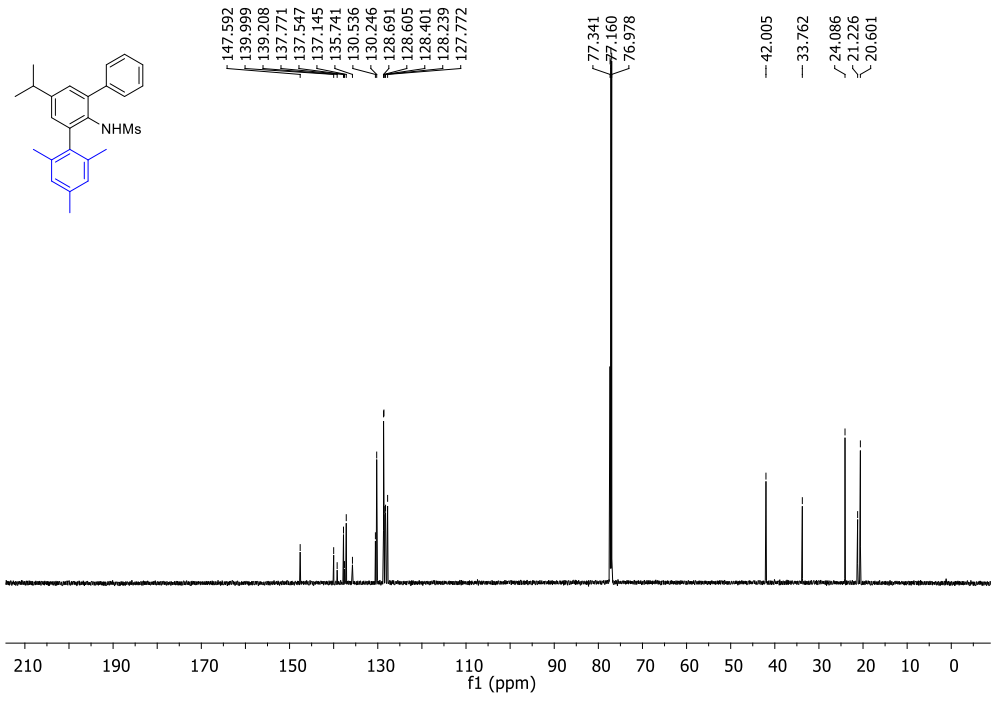


Figure 4.9. [13]C NMR spectrum of *N*-(5'-isopropyl-2,4,6- trimethyl- [1,1': 3', 1"-terphenyl]-2'-yl)methanesulfonamide (**3ba**)

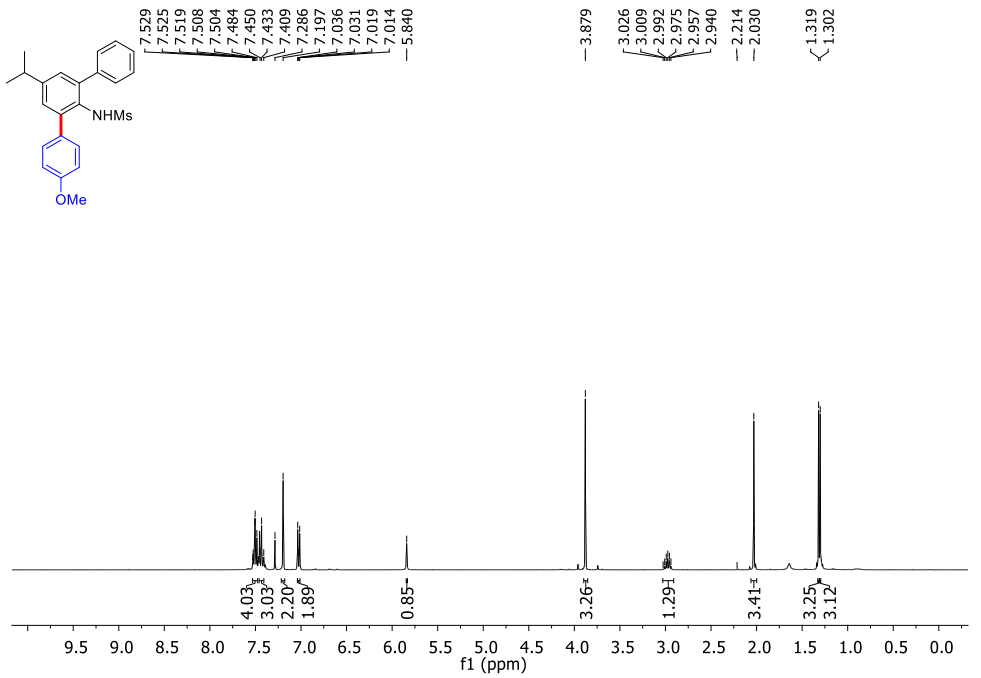


Figure 4.10. [1] H NMR spectrum of *N*-(5'-isopropyl-4-methoxy-[1,1' : 3',1''- terphenyl]-2'-yl)methanesulfonamide (**3bb**)

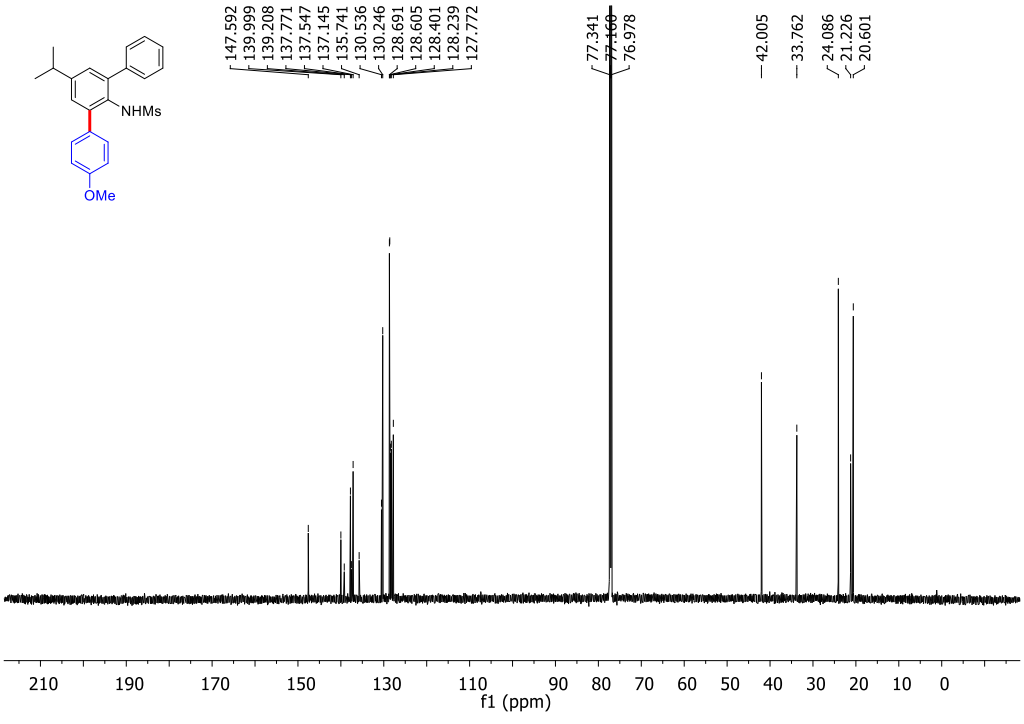


Figure 4.11. [13] C NMR spectrum of *N*-(5'-isopropyl-4-methoxy-[1,1' : 3',1''- terphenyl]-2'-yl)methanesulfonamide (**3bb**)

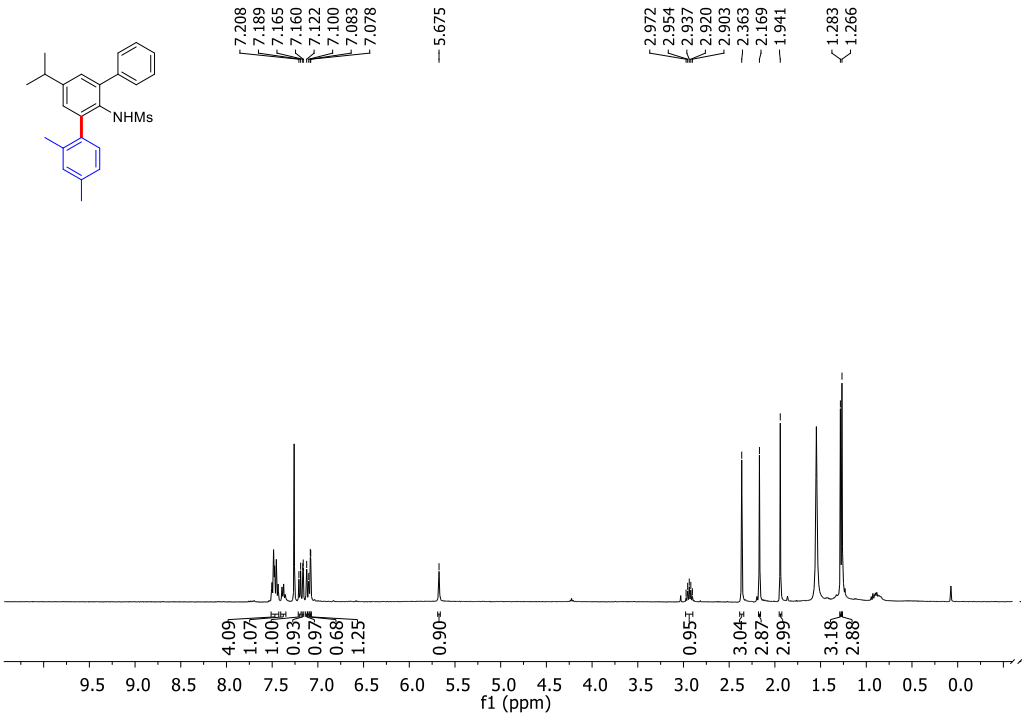


Figure 4.12. [1] H NMR spectrum of *N*-(5'-isopropyl-2,4-dimethyl-[1,1': 3',1"-terphenyl]-2'-yl)methanesulfonamide (**3bc**)

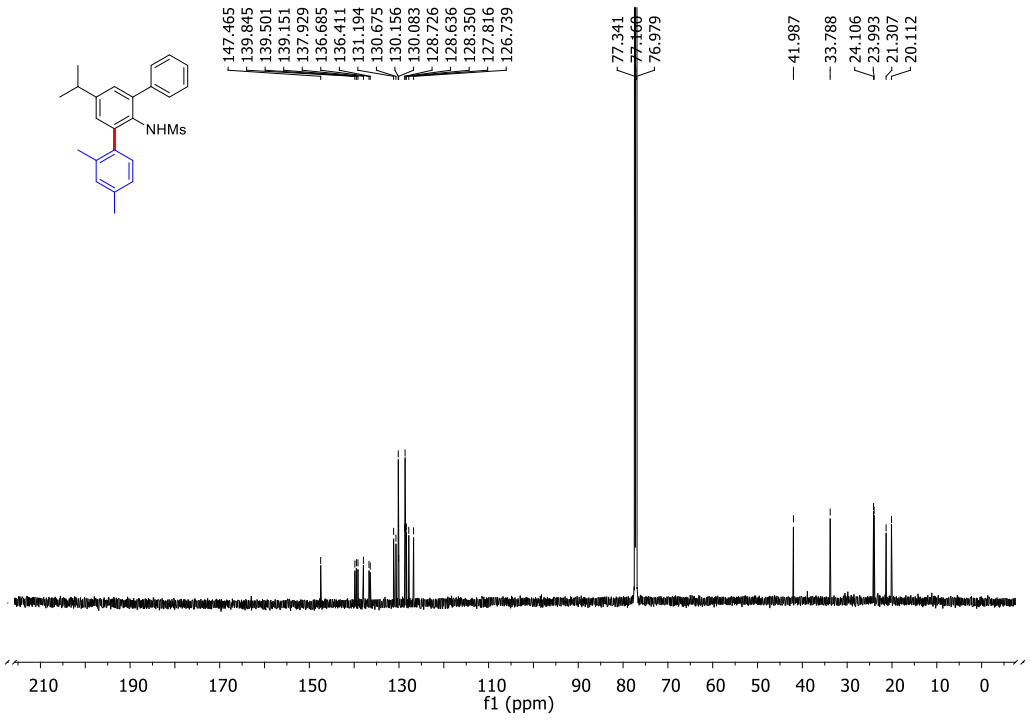


Figure 4.13. [13]C NMR spectrum of *N*-(5'-isopropyl-2,4-dimethyl-[1,1': 3',1"-terphenyl]-2'-yl)methanesulfonamide (**3bc**)

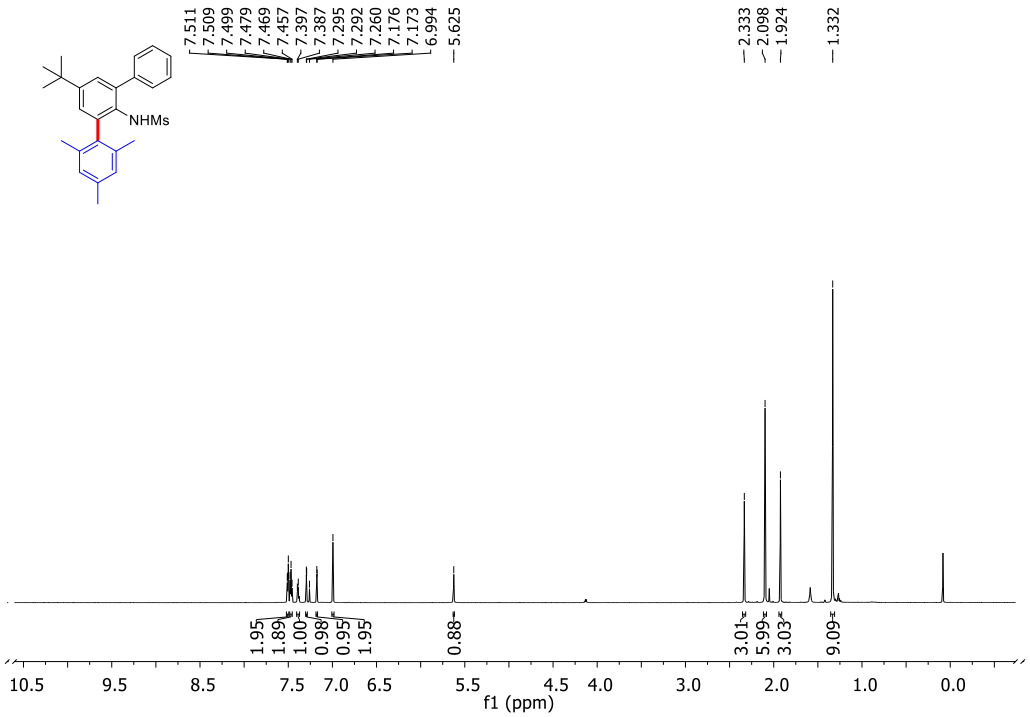


Figure 4.14. [1] H NMR spectrum of *N*-(5'-(tert-butyl)-2,4,6-trimethyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (**3ca**)

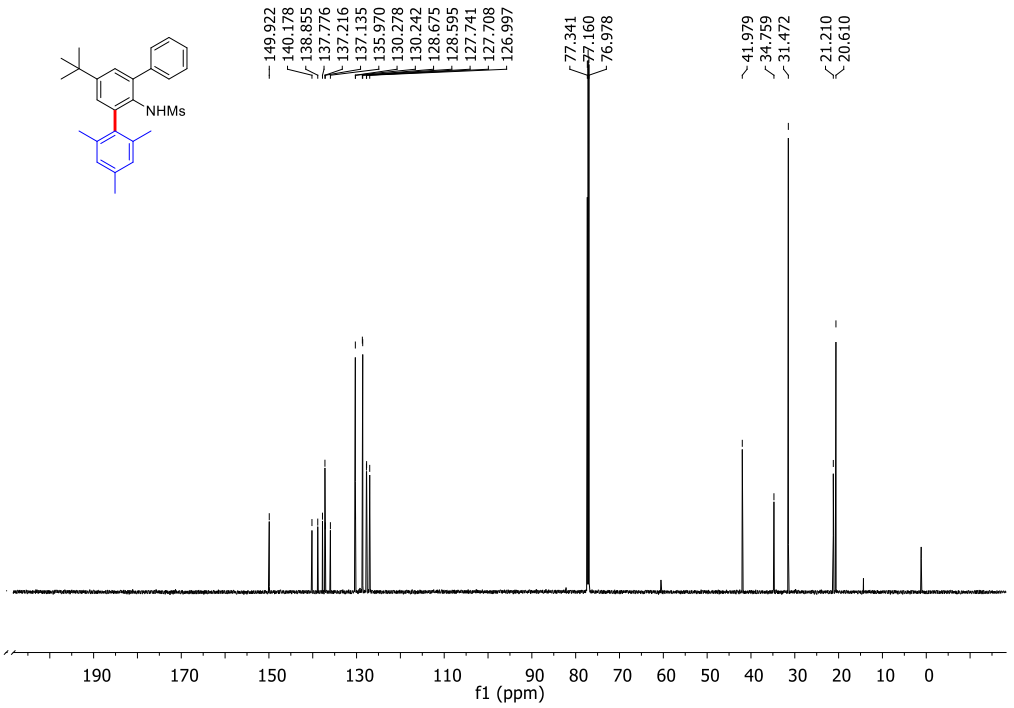


Figure 4.15. [13]C NMR spectrum of *N*-(5'-(tert-butyl)-2,4,6-trimethyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (**3ca**)

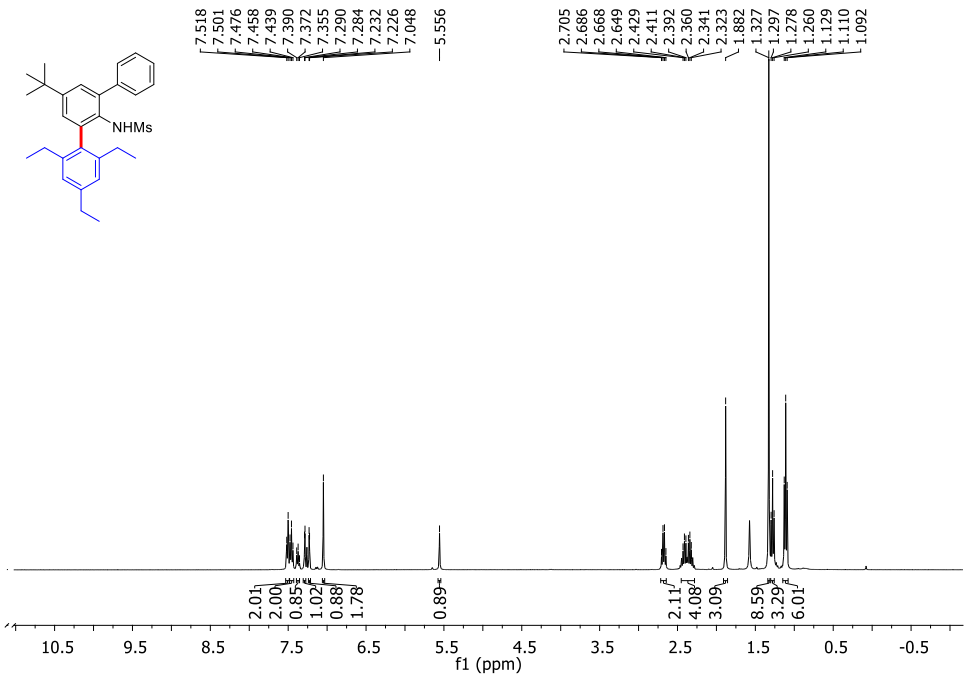


Figure 4.16. ^{1}H NMR spectrum of *N*-(5'-(tert-butyl)-2,4,6-triethyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (**3cd**)

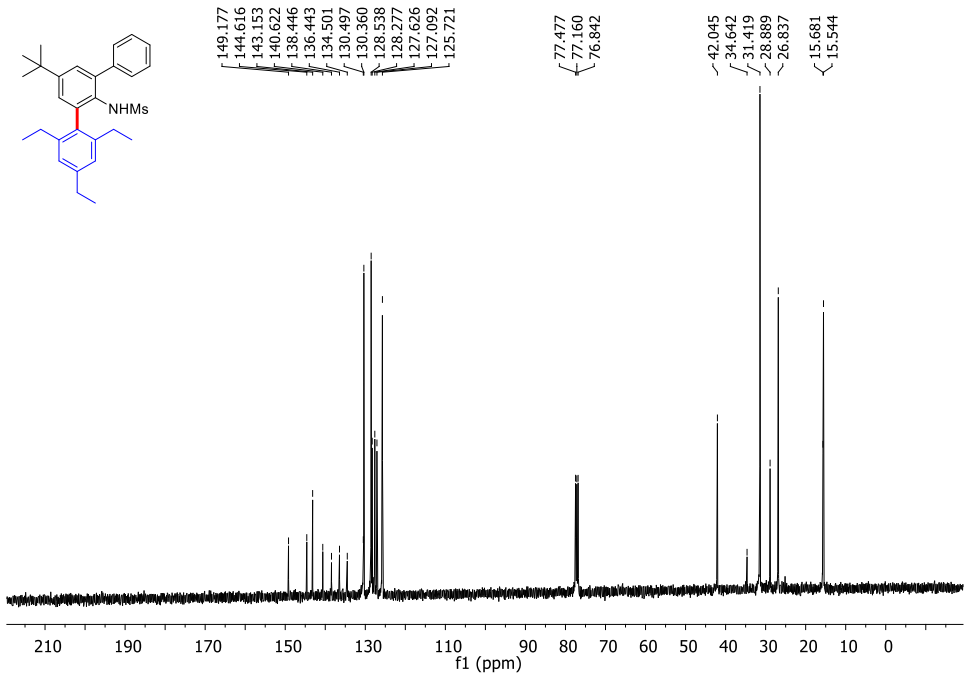


Figure 4.17. ^{13}C NMR spectrum of *N*-(5'-(tert-butyl)-2,4,6-triethyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (**3cd**)

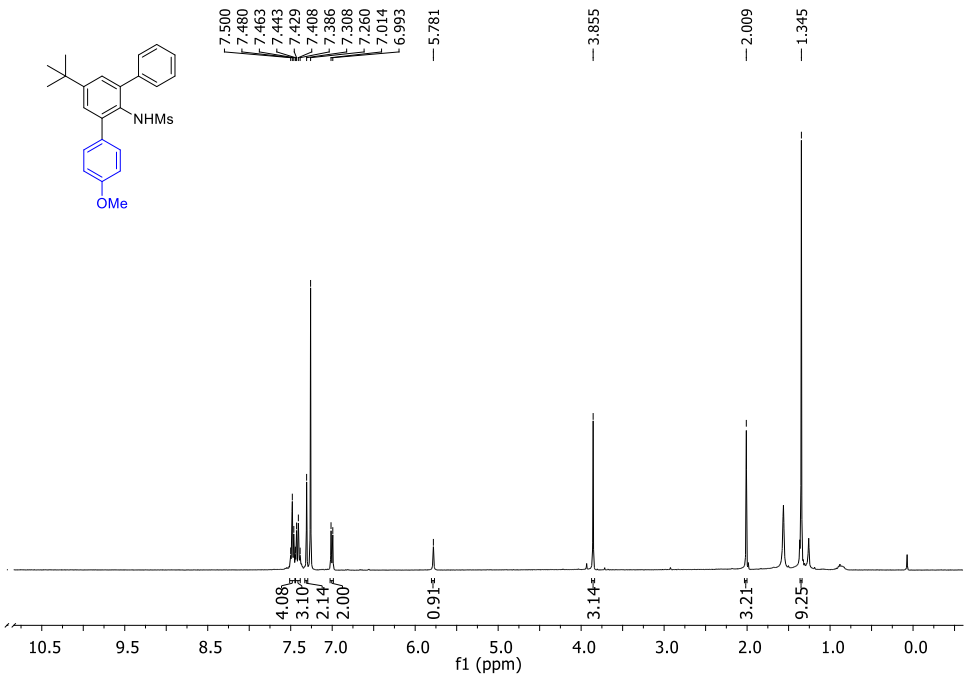


Figure 4.18. ^{1}H NMR spectrum of *N*-(5'-(*tert*-butyl)-4-methoxy-[1,1': 3',1"-terphenyl]-2'-yl)methaneslfonamide (**3cb**)

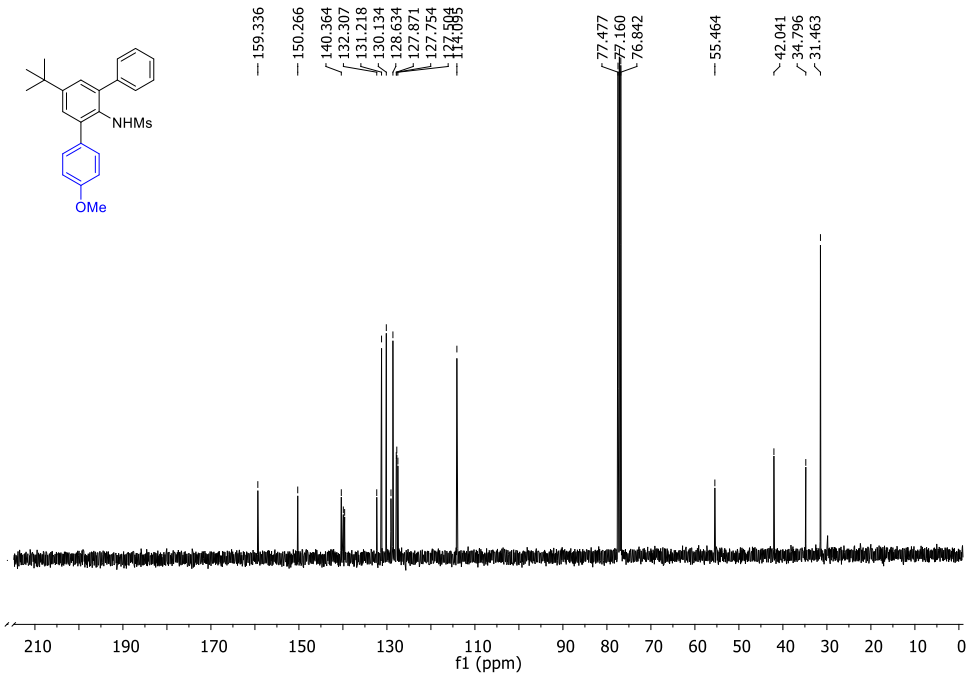


Figure 4.19. ^{13}C NMR spectrum of *N*-(5'-(*tert*-butyl)-4-methoxy-[1,1': 3',1"-terphenyl]-2'-yl)methaneslfonamide (**3cb**)

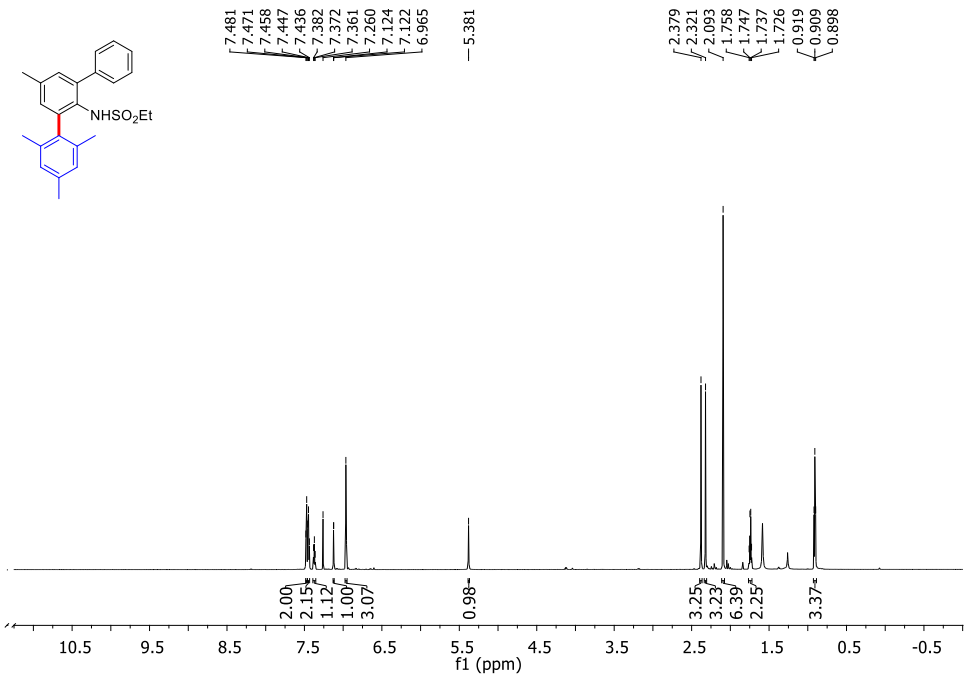


Figure 4.20. ^{1}H NMR spectrum of *N*-(2,4,5',6-tetramethyl-[1, 1':3', 1"-terphenyl]-2'-yl)ethanesulfonamide (**3da**)

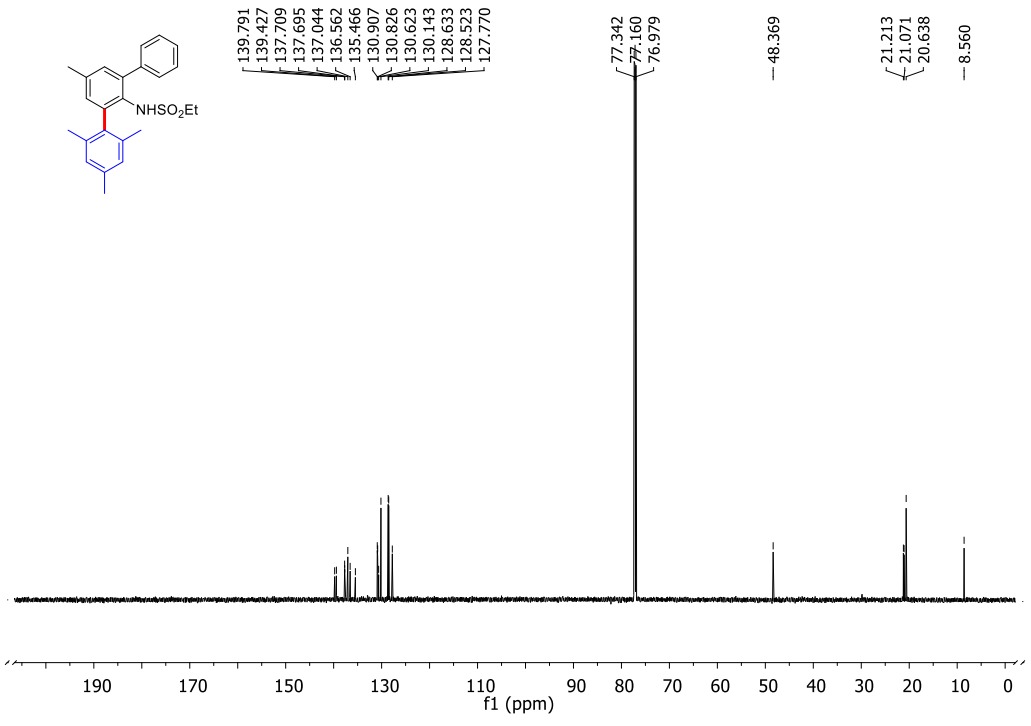


Figure 4.21. ^{1}H NMR spectrum of *N*-(2,4,5',6-tetramethyl-[1, 1':3', 1"-terphenyl]-2'-yl)ethanesulfonamide (**3da**)

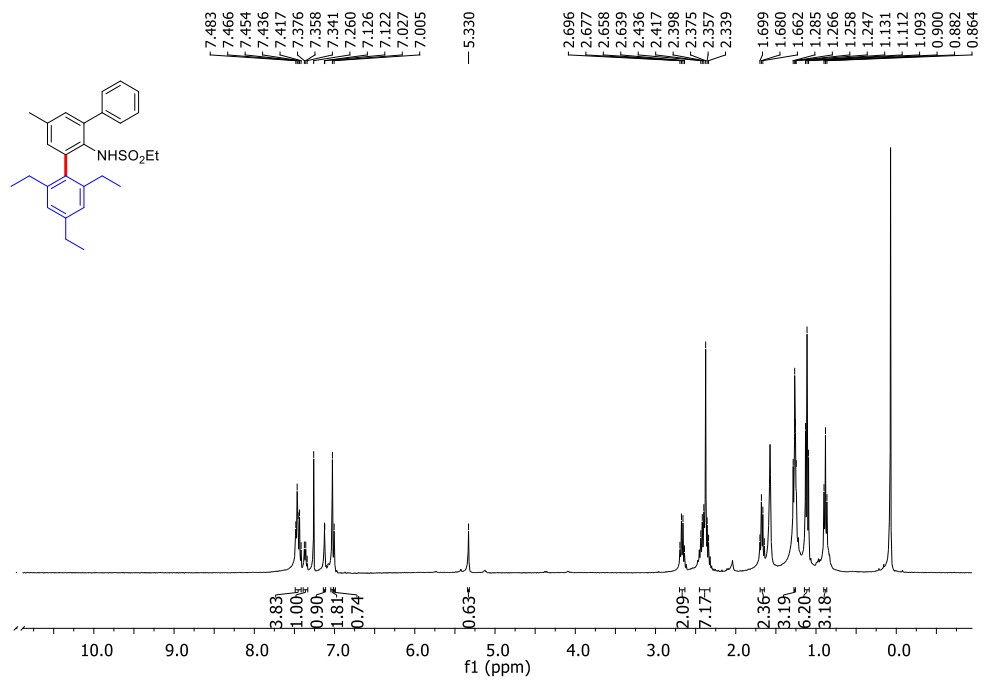


Figure 4.22. ^{1}H NMR spectrum of *N*-(2,4,6-triethyl-5'-methyl-[1,1':3',1"- terphenyl]-2'-yl)ethanesulfonamide (**3dd**)

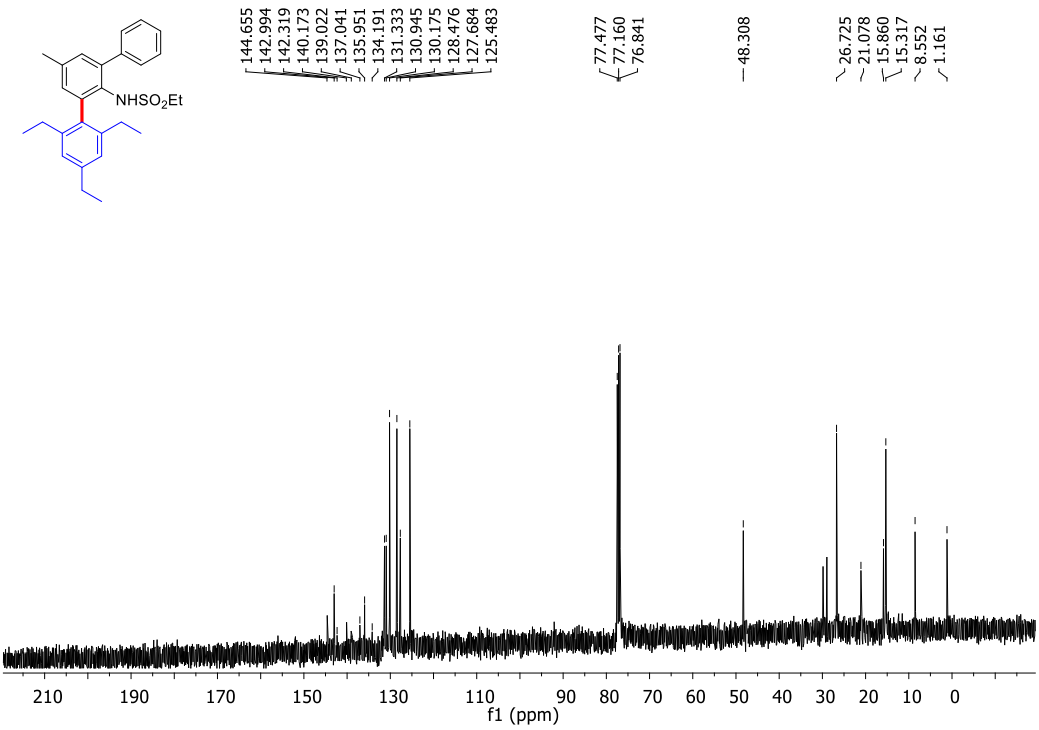


Figure 4.23. ^{13}C NMR spectrum of *N*-(2,4,6-triethyl-5'-methyl-[1,1':3',1"- terphenyl]-2'-yl)ethanesulfonamide (**3dd**)

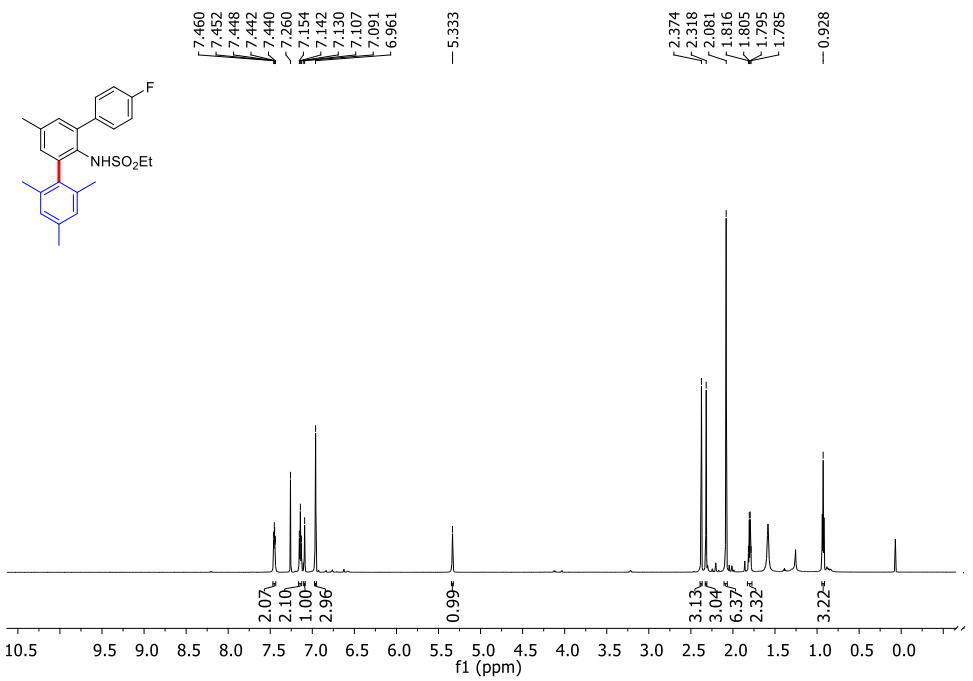


Figure 4.24. ^{1}H NMR spectrum of *N*-(4"- Fluoro-2, 4, 5', 6-tetramethyl-[1, 1': 3', 1"-terphenyl]-2'-yl)ethanesulfonamide (**3ea**)

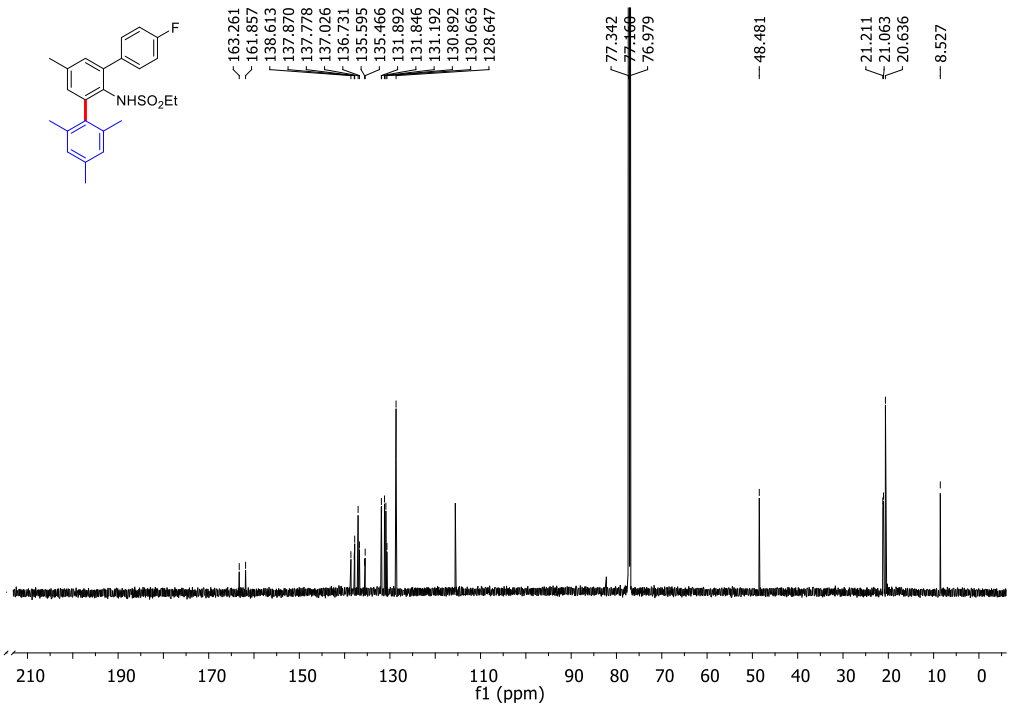


Figure 4.25. ^{13}C NMR spectrum of *N*-(4"- Fluoro-2, 4, 5', 6-tetramethyl-[1, 1': 3', 1"-terphenyl]-2'-yl)ethanesulfonamide (**3ea**)

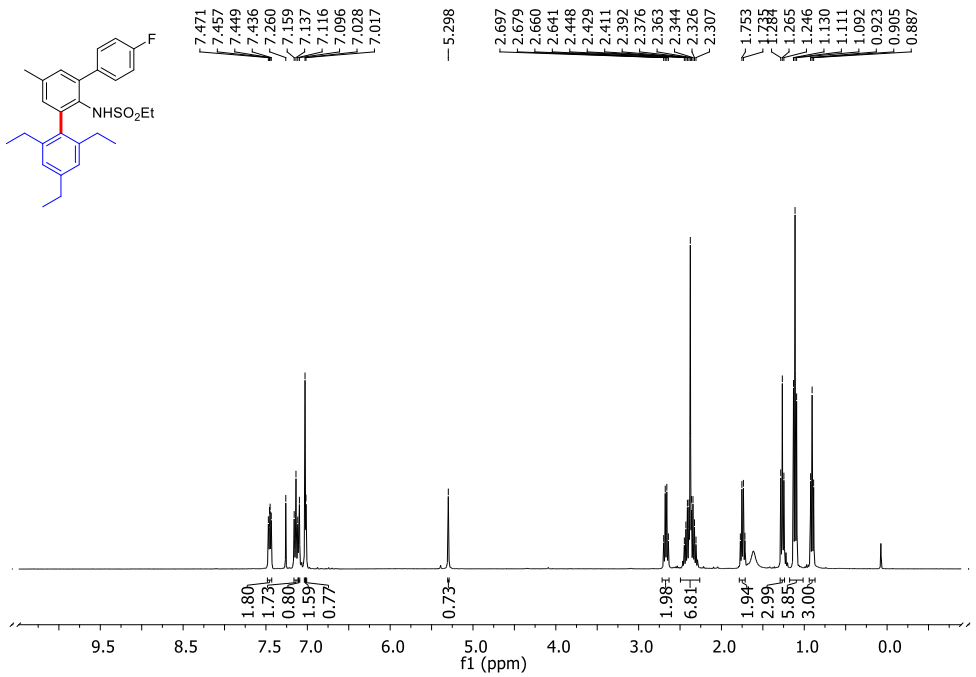


Figure 4.26. ^{1}H NMR spectrum of *N*-(2, 4, 6-triethyl- 4''- fluoro-5'-methyl-[1,1': 3', 1''-terphenyl]-2'-yl)ethanesulfonamide (**3ed**)

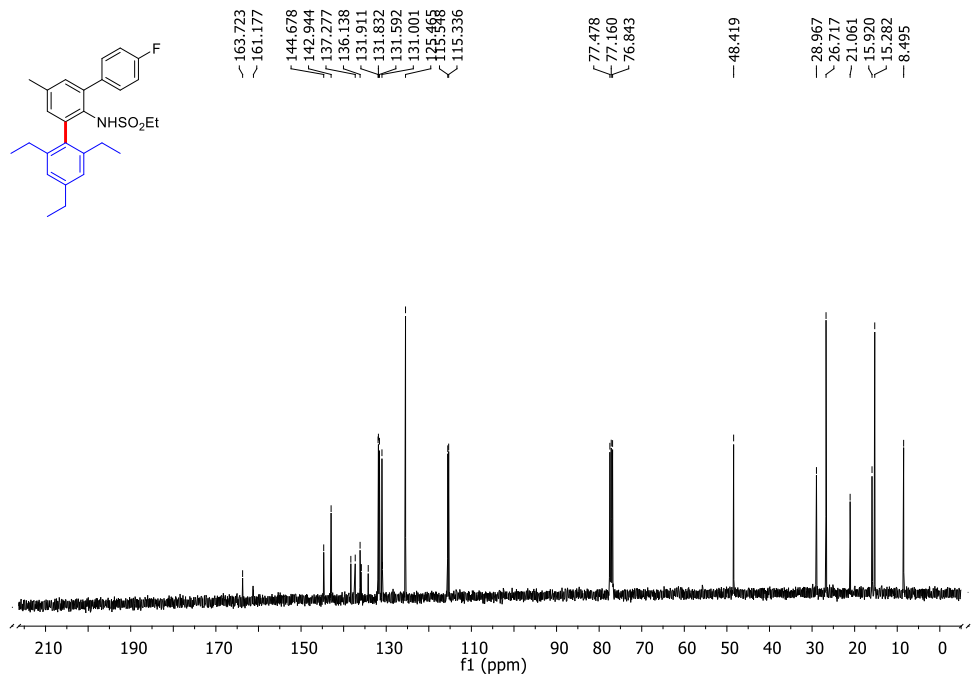


Figure 4.27. ^{13}C NMR spectrum of *N*-(2, 4, 6-triethyl- 4''- fluoro-5'-methyl-[1,1': 3', 1''-terphenyl]-2'-yl)ethanesulfonamide (**3ed**)

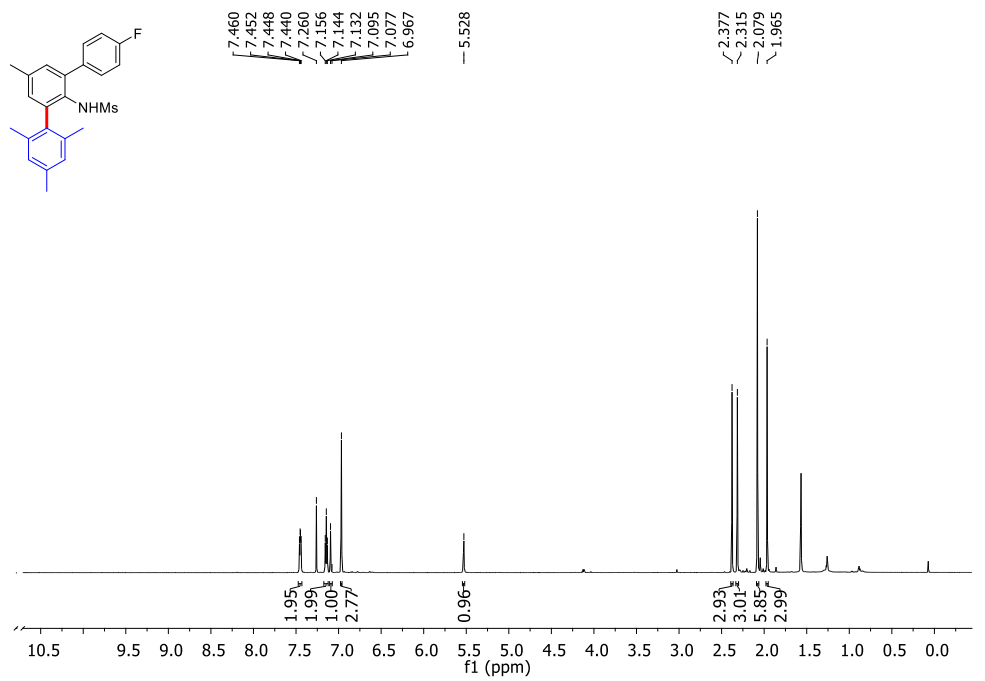


Figure 4.28. ^{1}H NMR spectrum of *N*-(4''- Fluoro- 2, 4, 5', 6- tetramethyl-[1,1':3',1''-terphenyl]-2'-yl]methanesulfonamide (**3fa**)

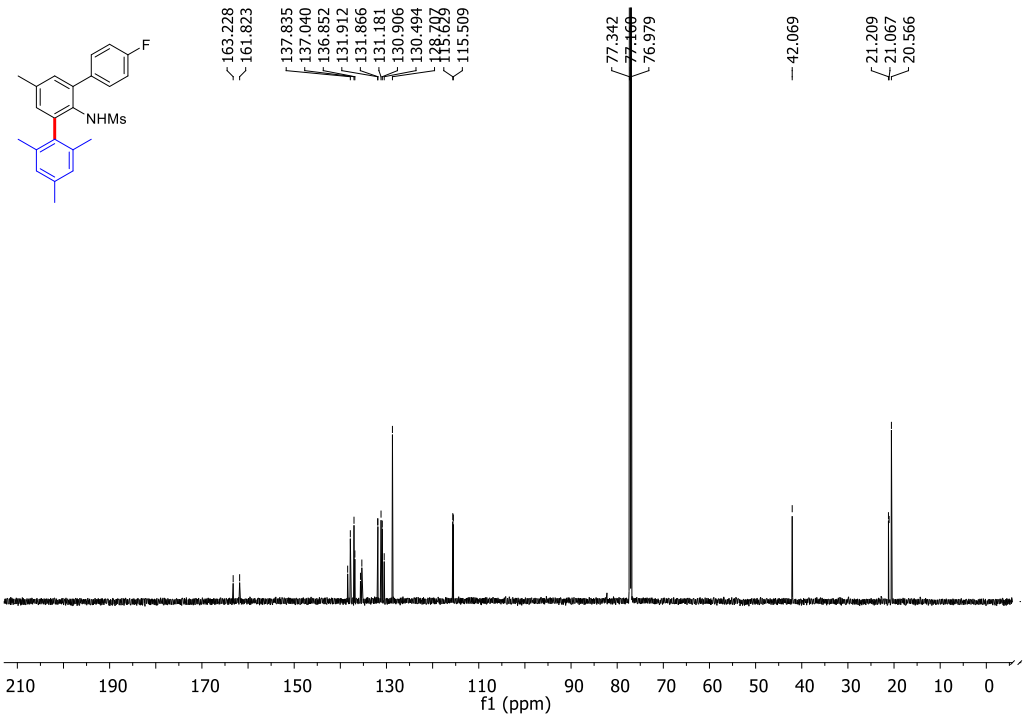


Figure 4.29. ^{13}C NMR spectrum of *N*-(4''- Fluoro- 2, 4, 5', 6- tetramethyl-[1,1':3',1''-terphenyl]-2'-yl]methanesulfonamide (**3fa**)

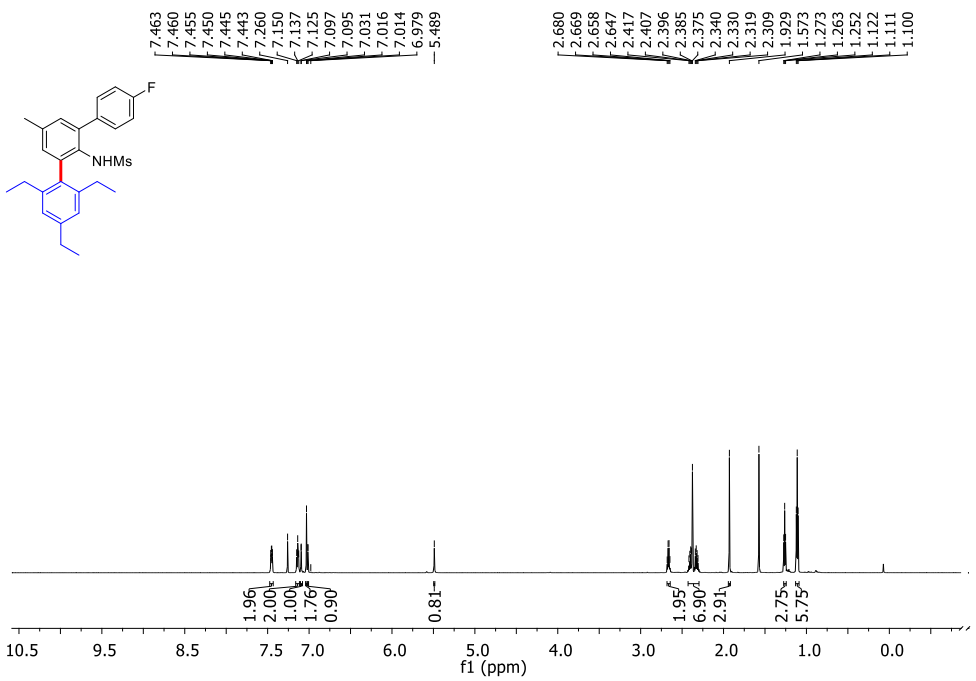


Figure 4.30. ^{1}H NMR spectrum of *N*-(2,4,6-triethyl-4"-fluoro-5'-methyl-[1,1': 3', 1"-terphenyl]-2'-yl)methanesulfonamide (**3fd**)

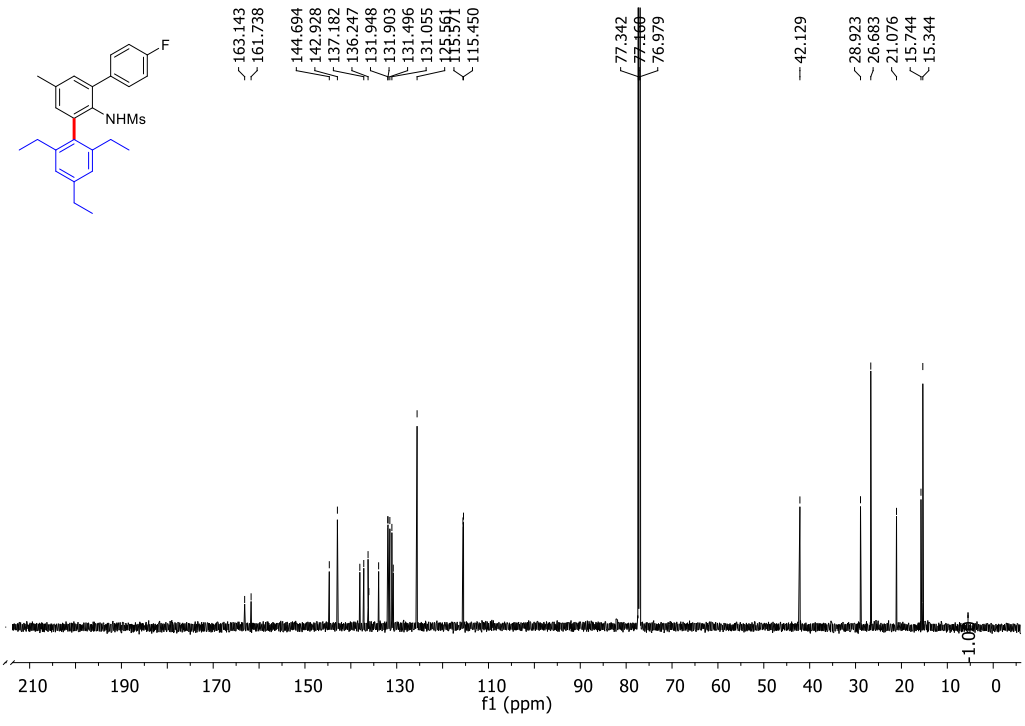


Figure 4.31. ^{13}C NMR spectrum of *N*-(2,4,6-triethyl-4"-fluoro-5'-methyl-[1,1': 3', 1"-terphenyl]-2'-yl)methanesulfonamide (**3fd**)

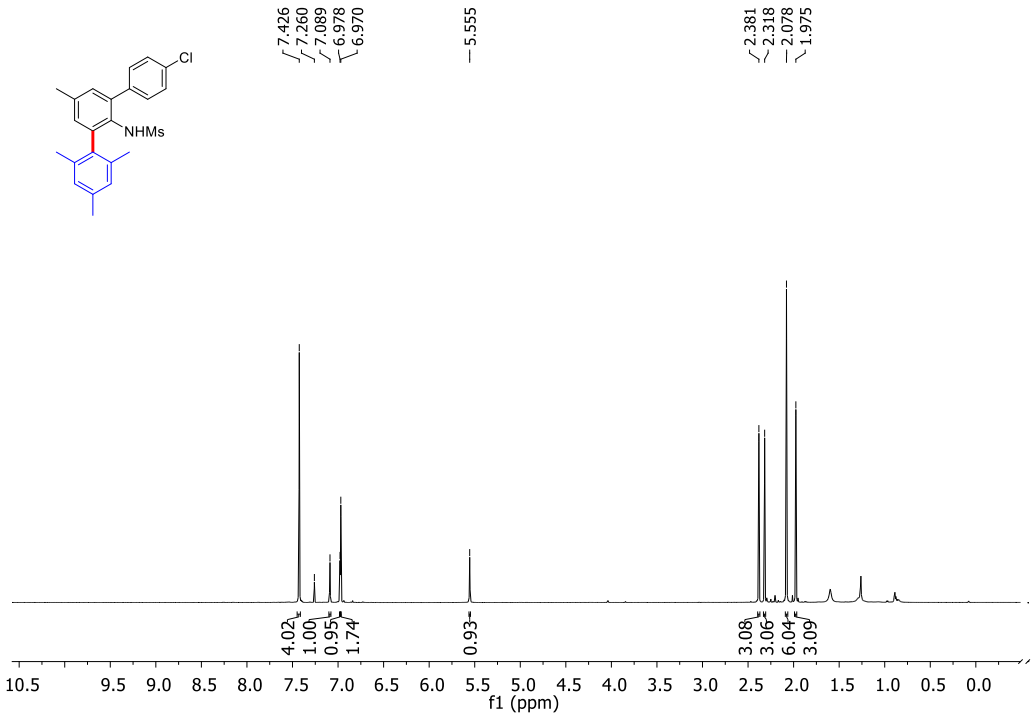


Figure 4.32. ^{1}H NMR spectrum of *N*-(4''-chloro-2, 4, 5',6-tetramethyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (**3ga**)

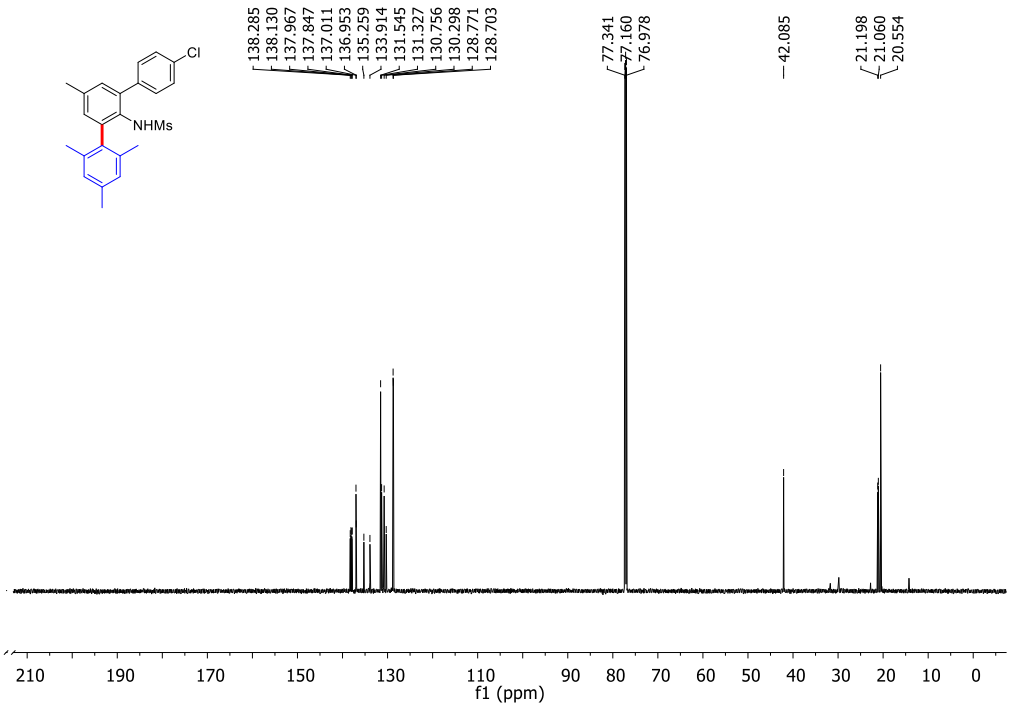


Figure 4.33. ^{13}C NMR spectrum of *N*-(4''-chloro-2, 4, 5',6-tetramethyl-[1,1':3',1''-terphenyl]-2'-yl)methanesulfonamide (**3ga**)

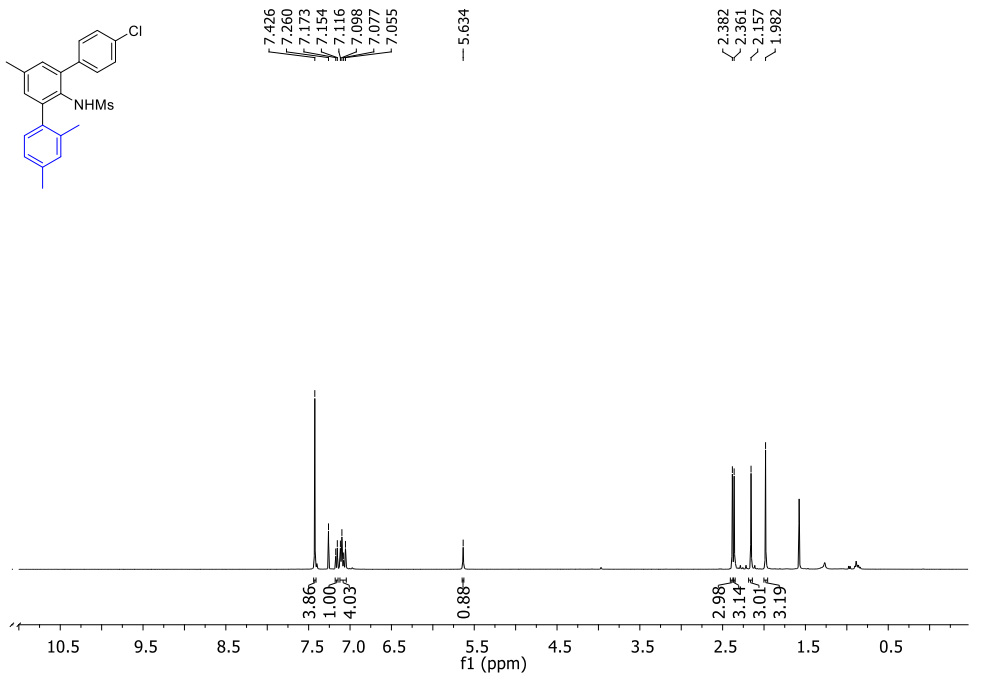


Figure 4.34. ^{1}H NMR spectrum of *N*-(4"-chloro-2,4,5'-trimethyl-[1,1':3',1"-terphenyl]-2'-yl)methanesulfonamide (**3gc**)

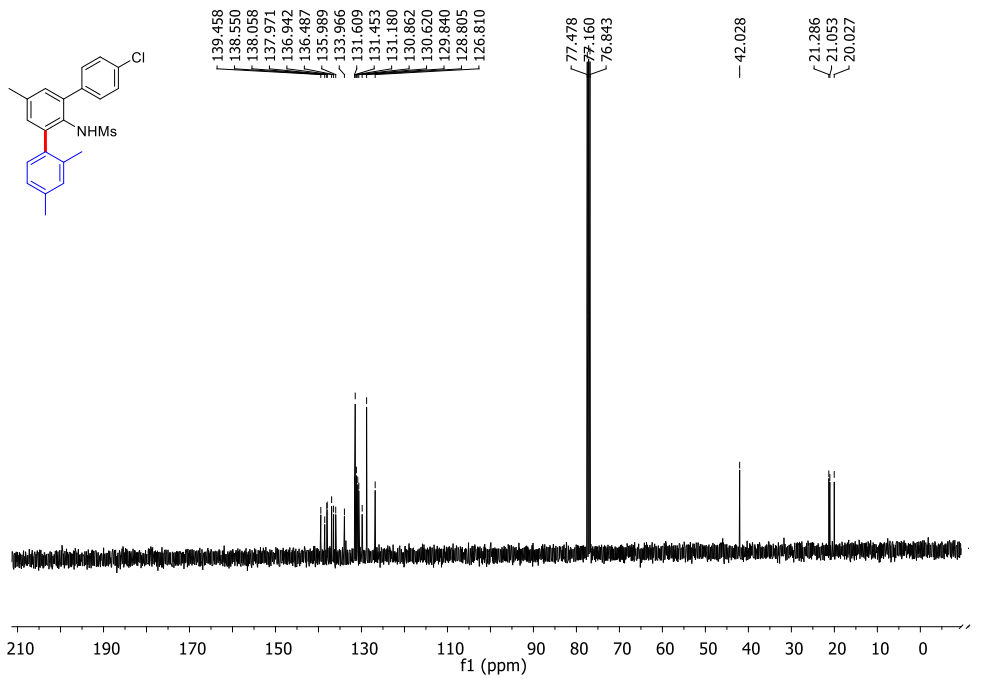


Figure 4.35. ^{13}C NMR spectrum of *N*-(4"-chloro-2,4,5'-trimethyl-[1,1':3',1"-terphenyl]-2'-yl)methanesulfonamide (**3gc**)

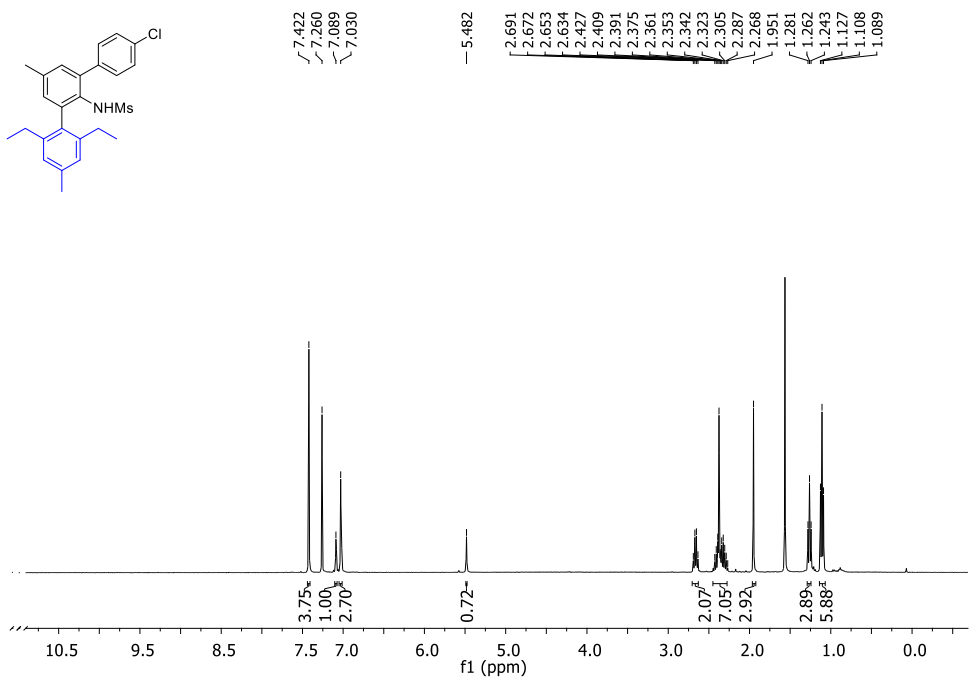


Figure 4.36. ^{1}H NMR spectrum of *N*-(4"-chloro-2,4,6-triethyl-5'-methyl-[1,1':3',1"-terphenyl]-2'-yl)methanesulfonamide (**3gd**)

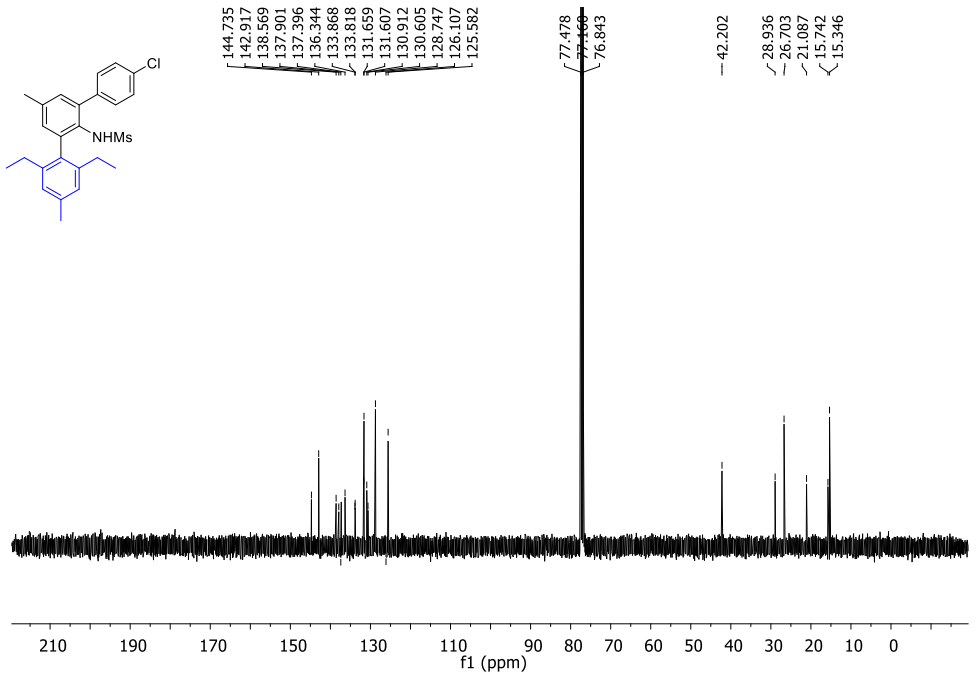


Figure 4.37. ^{13}C NMR spectrum of *N*-(4"-chloro-2,4,6-triethyl-5'-methyl-[1,1':3',1"-terphenyl]-2'-yl)methanesulfonamide (**3gd**)

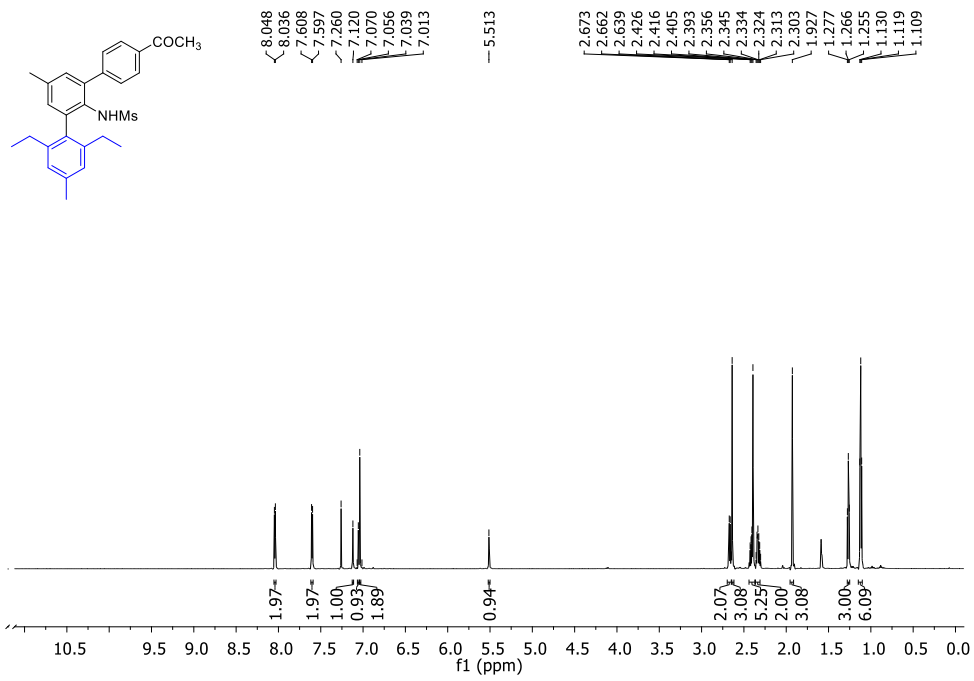


Figure 4.38. ^{1}H NMR spectrum of *N*-(4''-acetyl-2,4,6-triethyl-5'-methyl-[1,1':3',1''-terphenyl]-2'-yl)methanesufonamide (**3hd)**

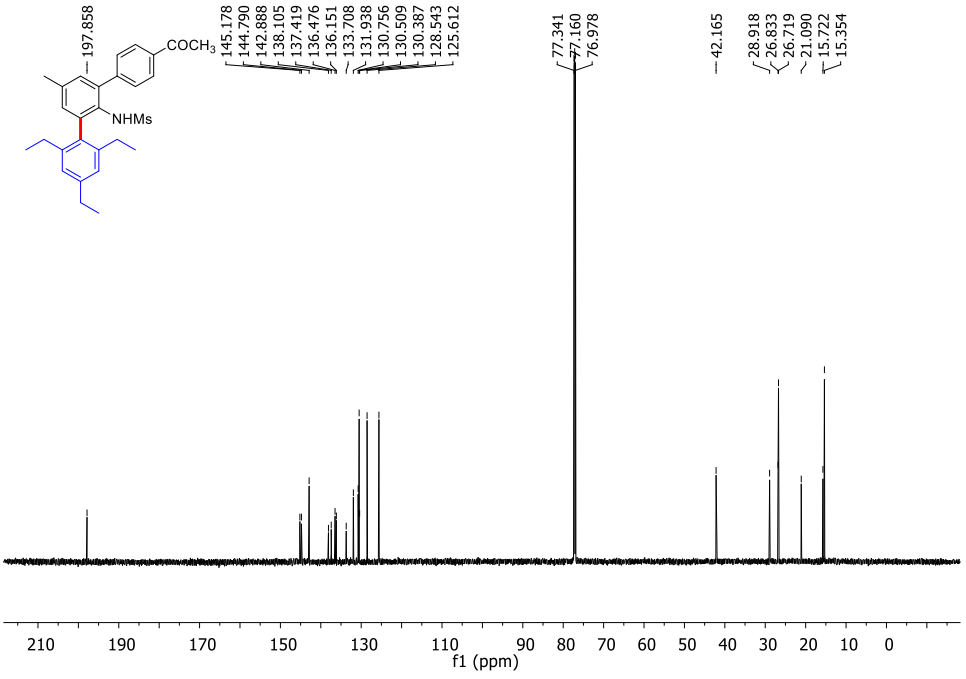


Figure 4.39. ^{13}C NMR spectrum of *N*-(4''-acetyl-2,4,6-triethyl-5'-methyl-[1,1':3',1''-terphenyl]-2'-yl)methanesufonamide (**3hd**)

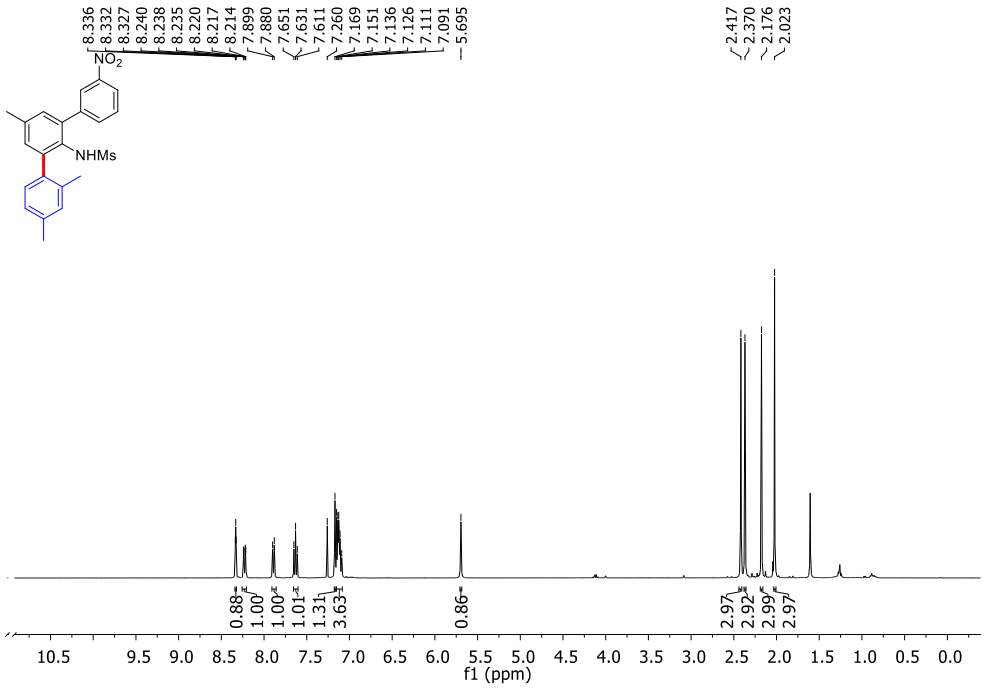


Figure 4.40. ^{1}H NMR spectrum of *N*-(2,4, 5'-trimethyl-3"-nitro-[1,1':3',1"-terphenyl]-2'yl)methanesulfonamide (**3ic**)

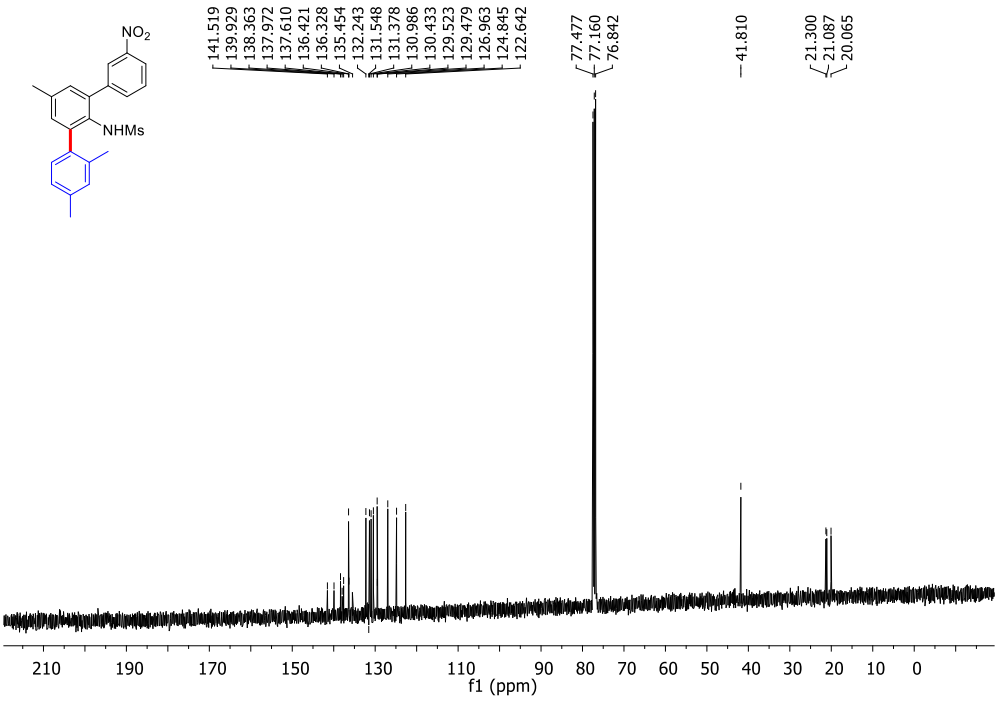


Figure 4.41. ^{13}C NMR spectrum of *N*-(2,4, 5'-trimethyl-3"-nitro-[1,1':3',1"-terphenyl]-2'yl)methanesulfonamide (**3ic**)

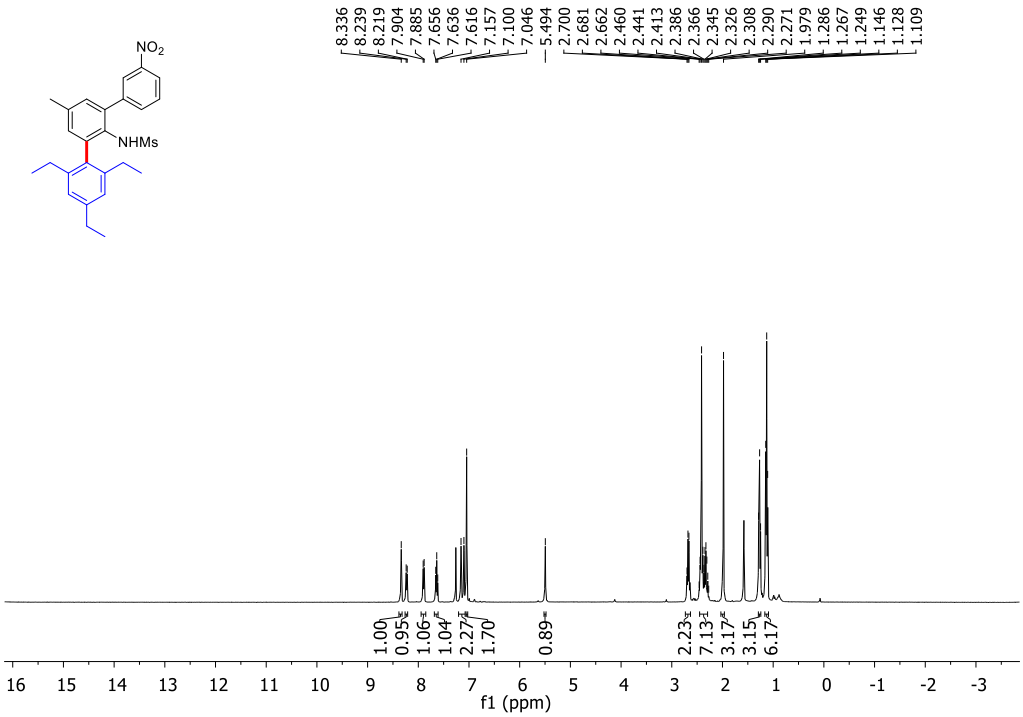


Figure 4.42. ^{1}H NMR spectrum of *N*-(2,4,6-triethyl-5'-methyl-3"-nitro-[1,1':3',1"-terphenyl]-2'yl]methanesulfonamide **(3id)**

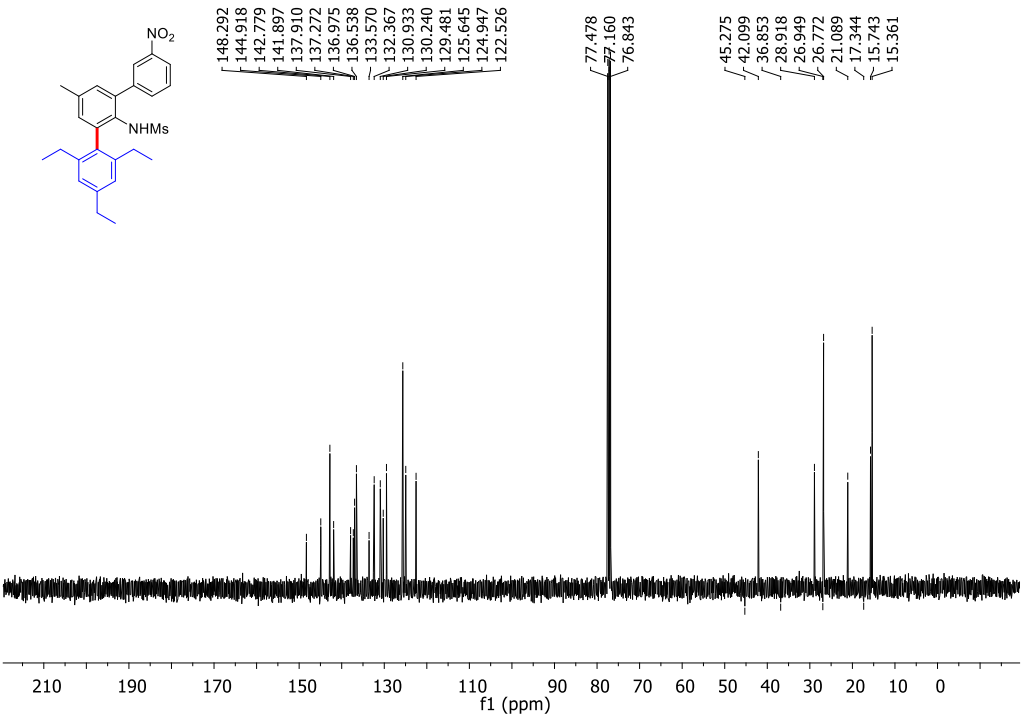


Figure 4.43. ^{13}C NMR spectrum of *N*-(2,4,6-triethyl-5'-methyl-3"-nitro-[1,1':3',1"-terphenyl]-2'yl]methanesulfonamide **(3id)**

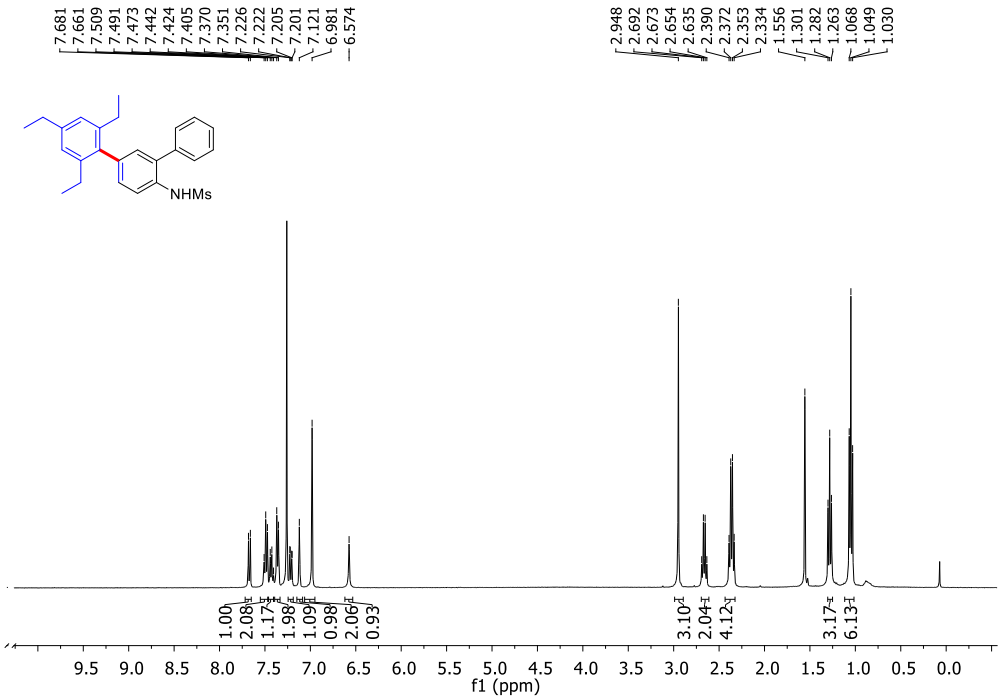


Figure 4.44. ^{1}H NMR spectrum of *N*-([1, 1'- biphenyl]-2-yl)-*N*-(2,4,6-triethylphenyl)methanesulfonamide (**4jd**)

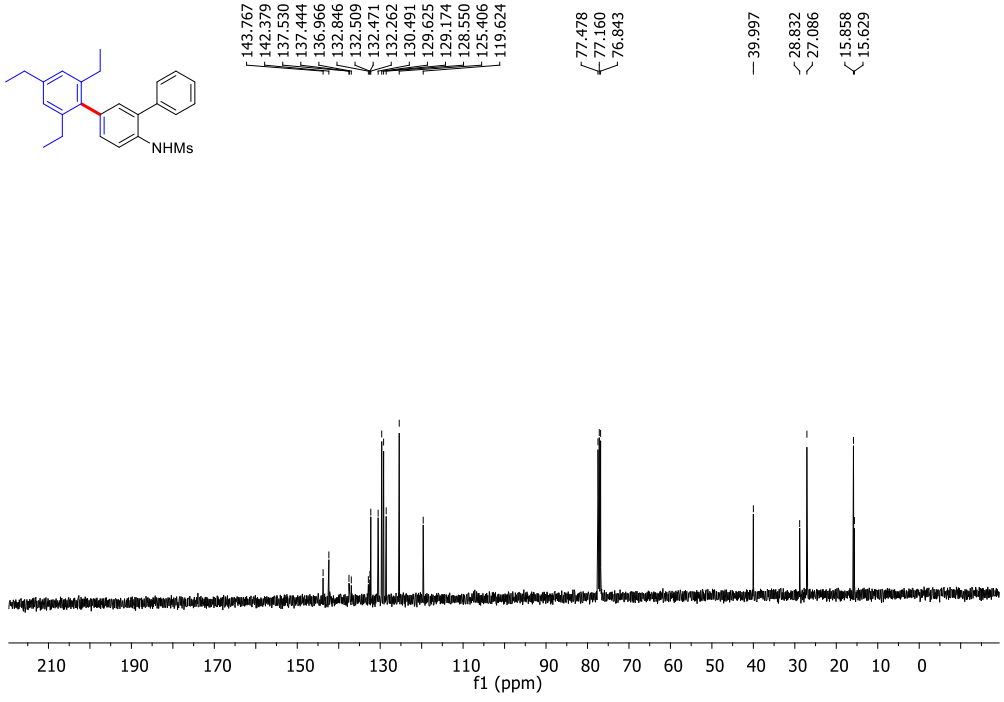


Figure 4.45. ^{13}C NMR spectrum of *N*-([1, 1'- biphenyl]-2-yl)-*N*-(2,4,6-triethylphenyl)methanesulfonamide (**4jd**)

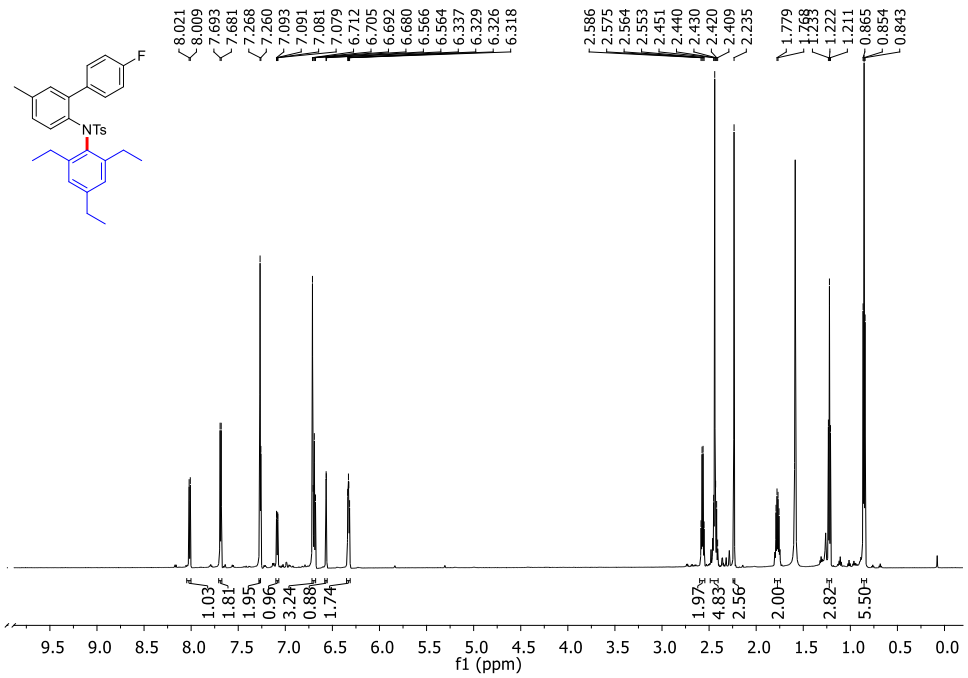


Figure 4.46. ^{1}H NMR spectrum of N-(4'-fluoro-5-methyl-[1,1'-biphenyl]-2-yl)-4-methyl-N-(2, 4,6 –triethylphenyl)benzenesulfonamide (**5kd**)

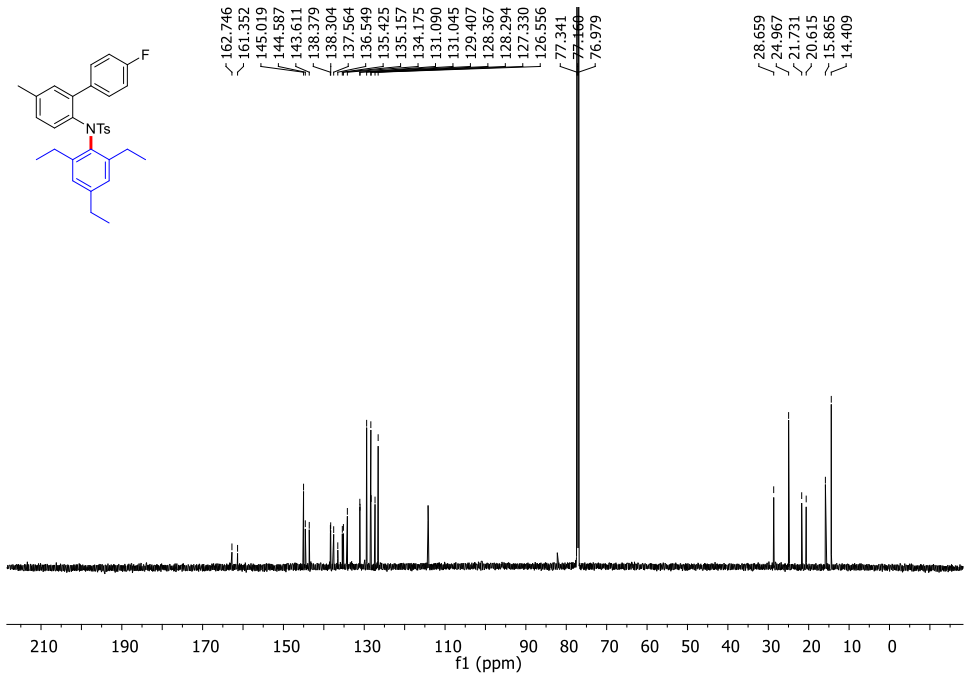


Figure 4.47. ^{13}C NMR spectrum of N-(4'-fluoro-5-methyl-[1,1'-biphenyl]-2-yl)-4-methyl-N-(2, 4,6 –triethylphenyl)benzenesulfonamide (**5kd**)

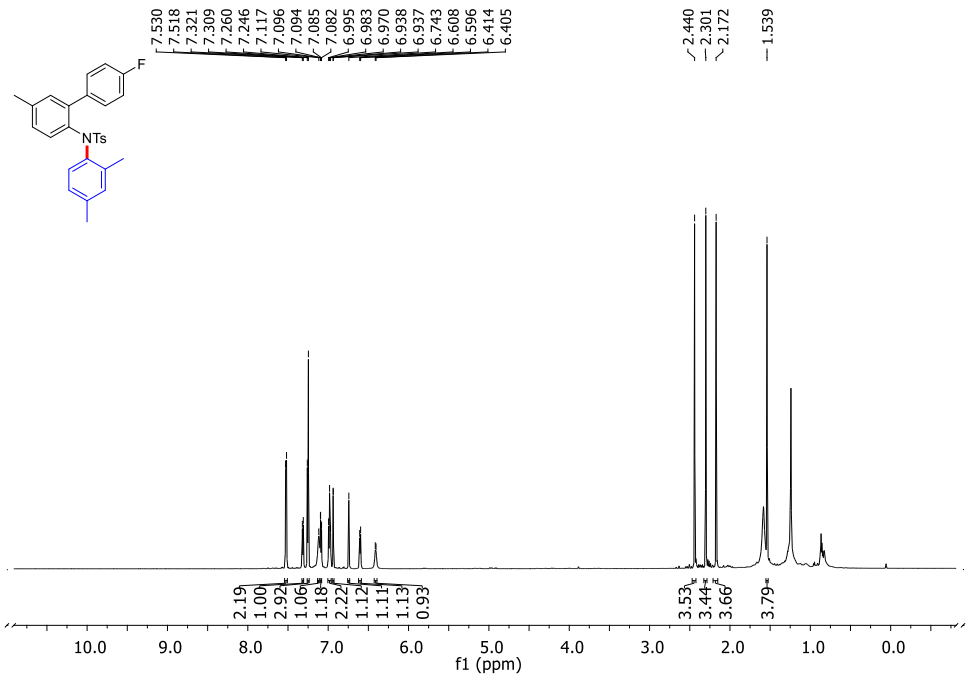


Figure 4.48. ^{1}H NMR spectrum of *N*-(2,4-dimethylphenyl)-N-(4'-fluoro-5-methyl-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide (**5kc**)

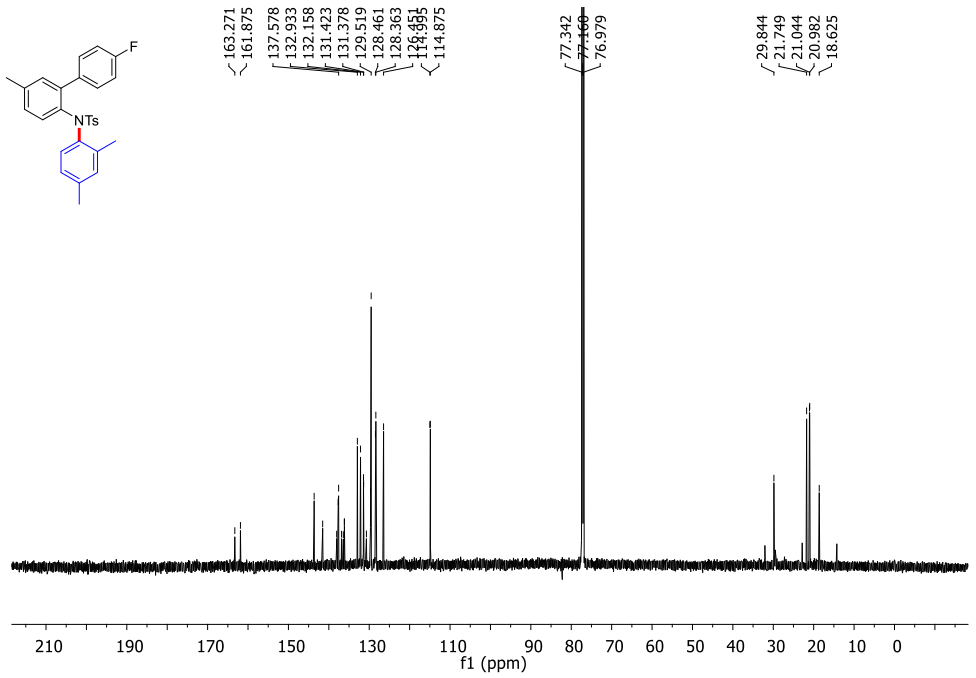


Figure S48. ^{13}C NMR spectrum of *N*-(2,4-dimethylphenyl)-N-(4'-fluoro-5-methyl-[1,1'-biphenyl]-2-yl)-4-methylbenzenesulfonamide (**5kc**)

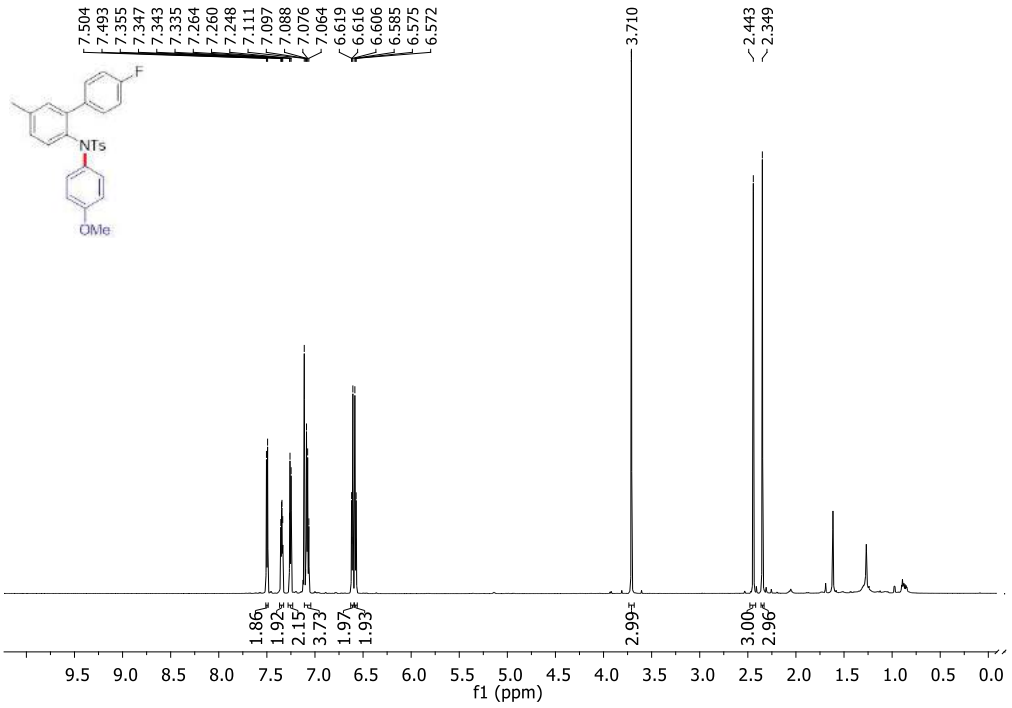


Figure 4.49. ^{1}H NMR spectrum of *N*-(4'-fluoro-5-methyl-[1,1'-biphenyl]-2-yl)-4-methyl-*N*-(4-methoxyphenyl)-4-methylbenzenesulfonamide (**5kb**)

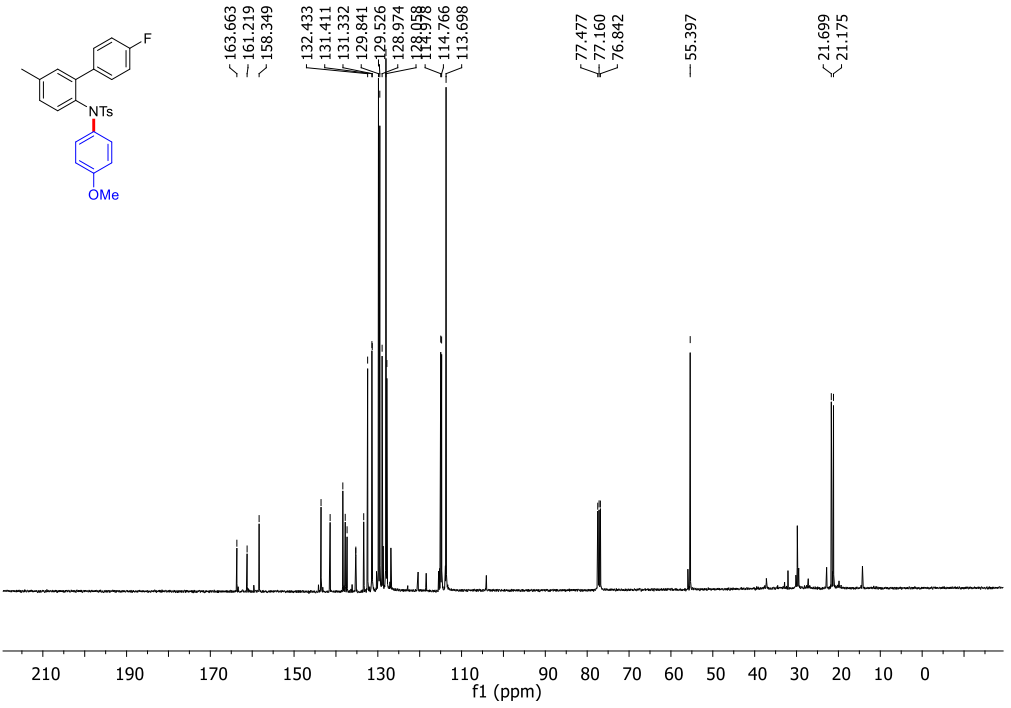


Figure 4.50. ^{13}C NMR spectrum of *N*-(4'-fluoro-5-methyl-[1,1'-biphenyl]-2-yl)-4-methyl-*N*-(4-methoxyphenyl)-4-methylbenzenesulfonamide (**5kb**)

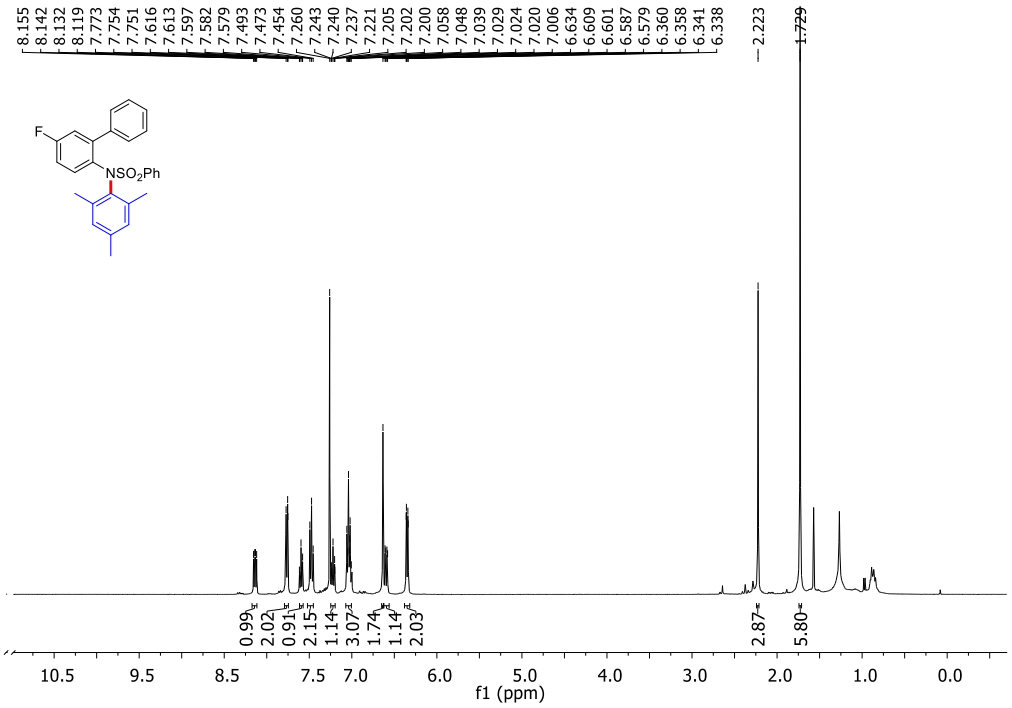


Figure 4.51. ^{1}H NMR spectrum of *N*-(5-fluoro-[1,1'-biphenyl]-2-yl)-*N*-mesitylbenzenesulfonamide (**5la**)

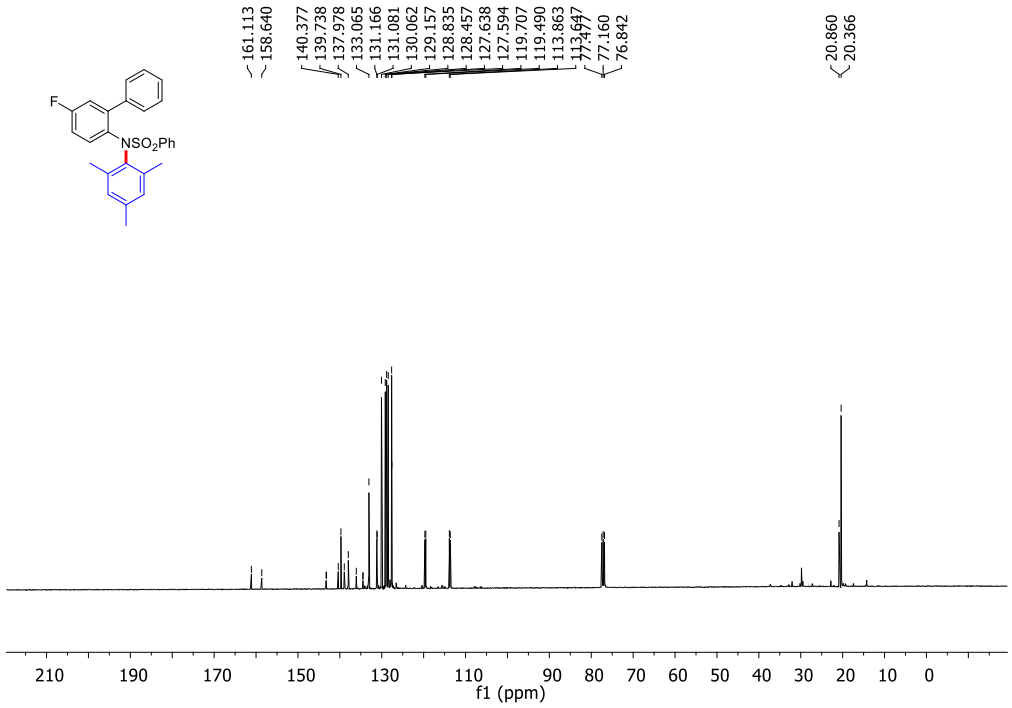
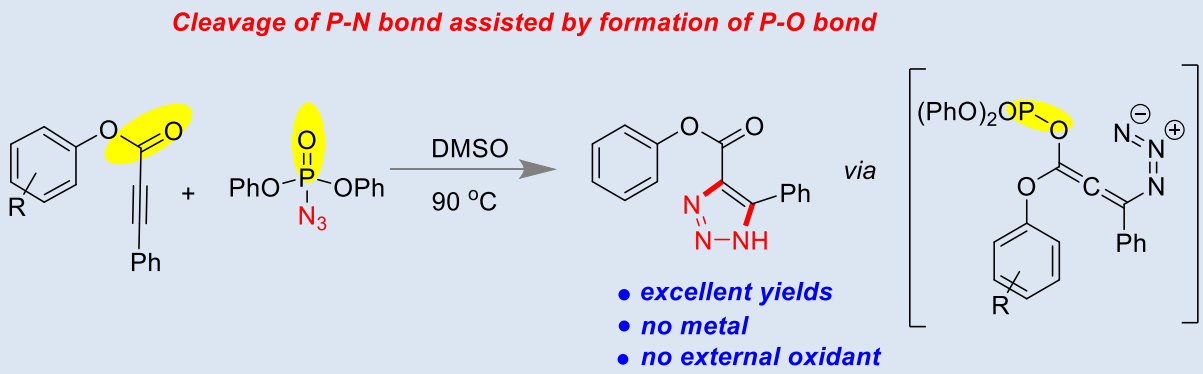


Figure 4.52. ^{13}C NMR spectrum of *N*-(5-fluoro-[1,1'-biphenyl]-2-yl)-*N*-mesitylbenzenesulfonamide (**5la**)

CHAPTER 5

Expedient Synthesis of Triazoles Directed by Phosphorus Oxygen Interaction

5.1 ABSTRACT



Phosphoryl azide, is still in obscurity and is less explored as an azide source employed in azide-alkyne cycloaddition. Herein, we report the synthesis of N_1-H triazoles using phosphoryl azide in solvent DMSO. Mechanistic investigations conclude the formation of an azidyl radical in the presence of a keto-containing compound. The probable reason for the product formation is phosphorus oxygen interaction, which cleaves the phosphorus nitrogen bond. Good to the excellent yield of N_1-H triazole scaffolds were synthesized following the protocol.

5.2 INTRODUCTION

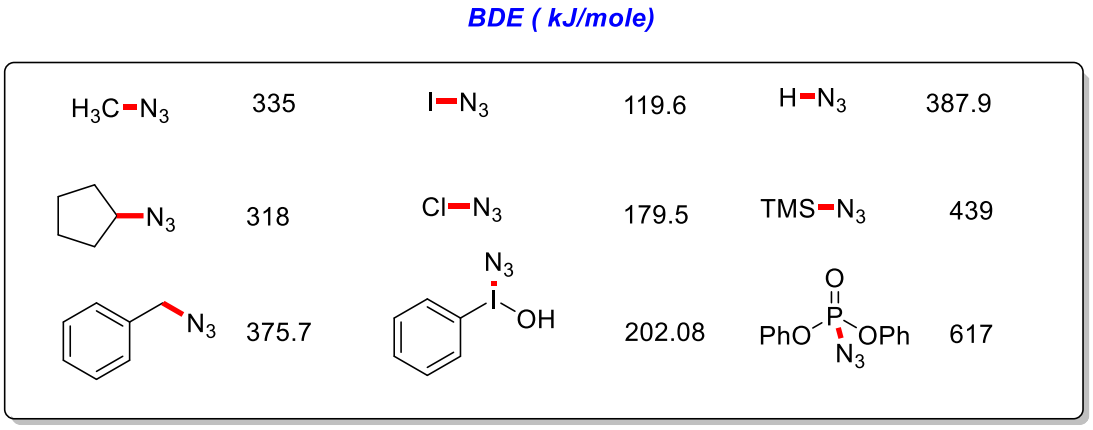
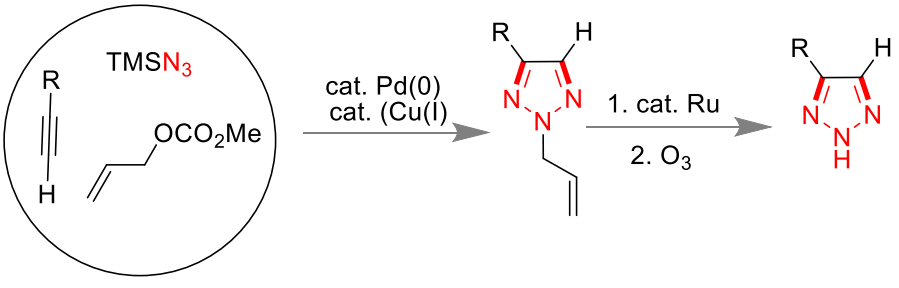


Figure 5.1 Binding energy for the commonly used azides in azide alkyne cycloaddition.

The triazole unit is a vital pharmacophore and has diverse applications in pharmaceutical and agrochemical industries exhibiting biological activity.[1-3] Its inbuilt structure infuses high aromatic stability, dipole-dipole and π –π stacking interactions, hydrogen bonding ability which necessitates its demand in biomedical research and supramolecular chemistry.[4-7] Triazoles have a widespread application in dyes and as corrosion inhibitors. Huisgen's [3+2] cycloaddition reaction between mono substituted acetylene and azide for the construction of triazole framework requires extremely harsh reaction conditions with poor regioselectivity, low yield, and difficulty in purification.[8-10] Common [11] azides employed for azide-alkyne cycloaddition with their binding energy have been displayed in figure 5.1. Diphenyl phosphoryl azide is a relatively less explored azide reagent in organic synthesis due to its high bond dissociation energy. The use of internal alkyne for azide-alkyne cycloaddition is rugged, and hence very few reports are noted in the literature.[12-14] The need to develop sustainable methodologies to synthesize triazoles with internal alkynes urges its significance in its synthesis. The traditional methods involving catalysts like Cu, Ru, Rh, or Ir have been

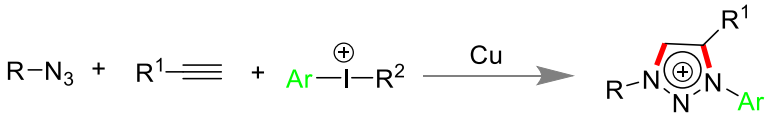
employed for the regiospecific synthesis of triazoles.[12, 15-21]. However, these methodologies utilize toxic metals, which hinders its utility in biomolecules and the field of chemical biology.[22, 23] Due to several detrimental effects in involving toxic metal for synthesis of triazoles, the need to develop metal free methodologies have been a growing concern and valued matter of subject for synthetic chemists.[24] *N*-substituted triazoles are synthesized in abundance, but methods to access *N-H* triazoles in a single step are scarcely known.[13, 14, 25-27] N-H triazoles are important, valuable synthetic intermediates in transformation and are known to have potential application in pharmaceuticals, and materials.[4] Synthesis of *N-H* triazole involves multiple-step process involving deprotection of *N*-substituted 1, 2, 3-triazoles in most of the cases.[28-30] Herein, we have developed a direct method to access N_1–H triazole carboxylate using phophorylazide as the azide source in solvent DMSO where the carbonyl group of propiolate assisted to cleave the P-N bond in phophorylazide to generate the azide radicals.

Yamamoto group has developed [3+2] cycloaddition reaction for the synthesis of N-H triazoles in a two-step process involving Pd (0)-Cu (I) metals using trimethyl silyl azide triazoles to give rise to N-H triazole.[30] The reaction proceeded via formation of π-allylpalladium azide complex with the extrusion of carbondioxide.



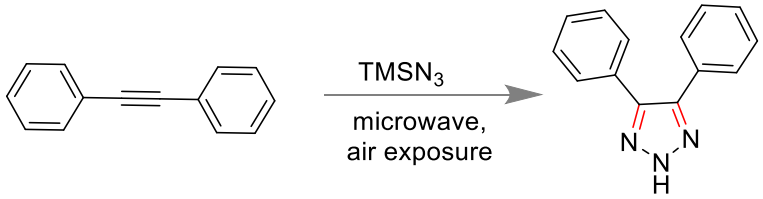
Scheme 5.1 Multistep process for the synthesis of N-H triazoles using the bimetallic approach.

1,2,3,4 triaolium salts have been synthesized using terminal alkyne and aryl iodonium salt with copper catalyst under neat conditions in one pot.[25] The reaction scope tolerated a variety of functional groups, and hence the protocol was helpful for access to precursors of pyridyl-mesoionic carbene ligands.



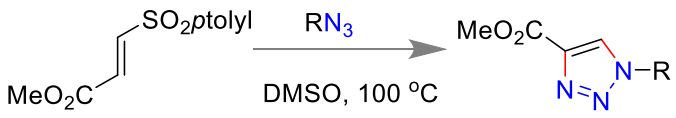
Scheme 5.2 Multistep process for synthesis of triazolium salt using copper.

The microwave-assisted solvent-free synthesis of 1,2,3 triazoles was accomplished by Prakash and co-workers by [3+2] cycloaddition reaction of alkyne and trimethylsilyl azide.[13] The mild reaction condition resulted in triazoles forming in good to excellent yields on a practical scale.



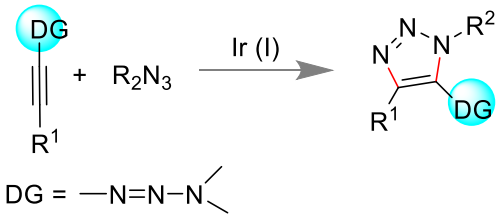
Scheme 5.3 Microwave-assisted triazole synthesis using trimethyl silyl azide.

Pathak and co-workers developed a metal free synthetic route for the regioselective synthesis of 1,2,3 triazoles from vinyl sulfones.[24] The protocol tolerated a wide range of functional groups and marked the synthesis of 1,4 disubstituted triazole synthesis for the first time.



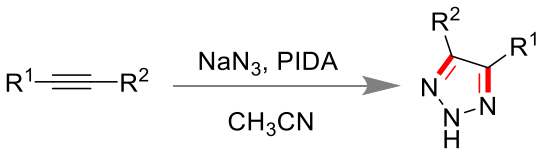
Scheme 5.4 Synthesis of 1,2,3-triazole using vinyl sulfone.

Ciu group have developed [3+2] cycloaddition mediated by iridium catalyst.[31] Synthesis of functionalized triazoles was achieved by directing groups like triazene, which was further transformed to amino, amide, halogen, and other heterocyclic substituents in a mild efficient approach.



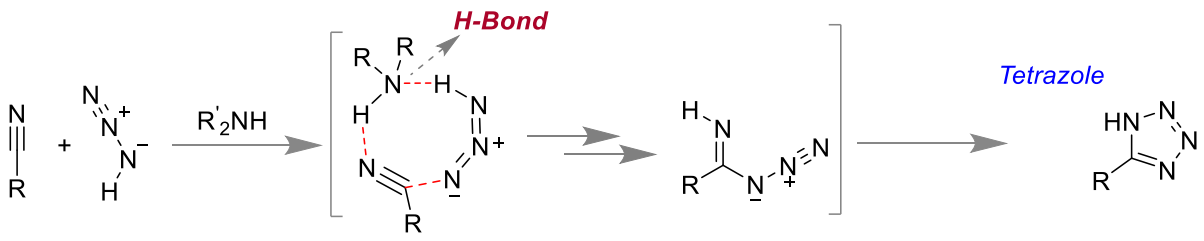
Scheme 5.5 Synthesis of functionalized triazole assisted by directing group.

Hypervalent iodine(III) reagents have proved to be effective in generating azide radicals from PIDA.[14] Synthesis of N-H triazoles was successfully achieved in a single step followed by a cascaded type reaction mechanism.



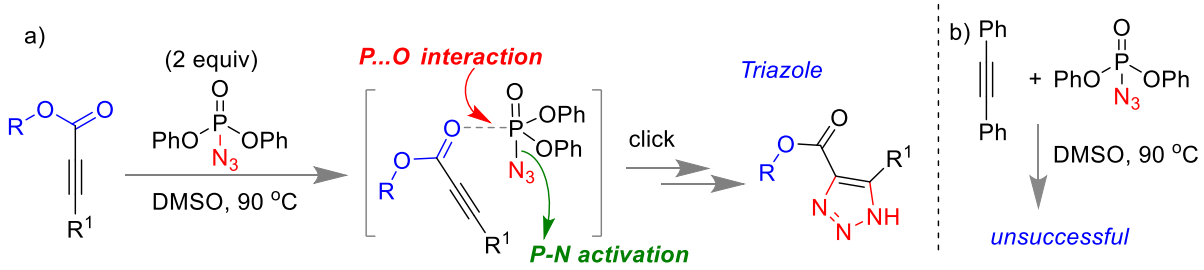
Scheme 5.6 Synthesis of N-H triazoles by the formation of azidyl radical.

Weak interactions often take up a signifying character in controlling product selectivity. Hydrogen bonding interactions control the formation of tetrazoles. The mechanistic pathway has been supported with DFT calculations to validate the hypothesis.[32]



Scheme 5.7 Synthesis of tetrazoles enabled by weak interactions.

Our approach was to utilize the directing nature of carbonyl group of the propiolate ester and the interaction of oxygen with phosphorus which controlled the reaction and favored synthesis of triazoles (Scheme 5.8b). We desired to achieve click reaction using internal alkynes like diphenyl acetylene and other electron withdrawing substituted alkyne, but it failed to deliver the product (Figure 5.8c). The targeted reaction was successful without the use of an external oxidant or metal. Simply by modifying the substrate by introducing a carbonyl group, P-N bond cleavage took place. Our targeted N-H triazoles were synthesized in a gentle and efficient approach with excellent yield. To the best of our knowledge, we were able to successfully activate P-N bond with the help of P…O interaction for the first time.



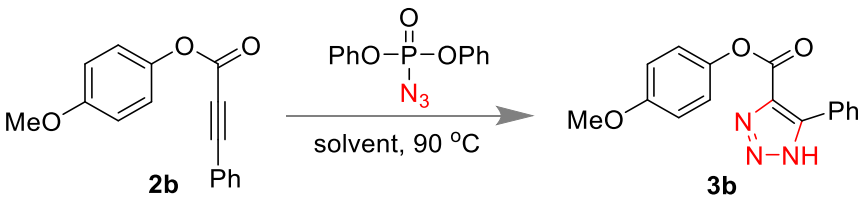
Scheme 5.8 Synthesis of triazoles enabled by weak interactions.

5.3 RESULTS AND DISCUSSION

Initially, diphenyl acetylene was chosen to undergo reaction with diphenyl phosphoryl azide (DPPA), but it failed to deliver the product. We modified the substrate and introduced a carbonyl group into it. We hypothesized that 4-methoxyphenyl 3-phenylpropiolate will undergo reaction with DPPA due to interaction between phosphorus and oxygen. 4-methoxyphenyl 3-phenylpropiolate (1.0 equiv)) (**2b**) and phosphoryl azidate (1.0 equiv) were taken and the [3+2] cycloaddition reaction was successfully established forming 4-

methoxyphenyl-5-phenyl-1*H*-1,2,3-triazole-4- carboxylate (**3b**) in tetrahydrofuran (THF) with 17% yield. Switching the solvent tetrahydrofuran (THF) to dimethyl sulfoxide (DMSO) resulted in rise of yield to 45% (entry 2). Further, increasing the equivalency of phosphoryl azidate to 1.5, an abrupt rise in yield to 69% was noticed (entry 3). Change in the equivalency of DPPA to 2.0, further rise in yield to 86% was noticed (entry 4). Other solvents were screened, and it was found that 1,2-dichloroethane (DCE) and acetonitrile (ACN) failed to deliver the desired product (entries 4 and 5). However, when dimethyl formamide (DMF) was used as a solvent, 60% yield of desired product was obtained (entry 7). Sodium azide was used as the azide source, the yield was decreased to 20% (entry 8).

Table 5. 1 Optimization of the reaction condition.[a]



entry	azide source (equiv)	solvent	yield (%)[b]
1	$PO(OPh)_2N_3$ (1.0)	THF	17
2	$PO(OPh)_2N_3$ (1.0)	DMSO	45
3	$PO(OPh)_2N_3$ (1.5)	DMSO	69
4	$PO(OPh)_2N_3$ (2.0)	DMSO	86
5	$PO(OPh)_2N_3$ (2.0)	CH_3CN	N.R
6	$PO(OPh)_2N_3$ (2.0)	DCE	N.R
7	$PO(OPh)_2N_3$ (2.0)	DMF	60
8	NaN_3(1.0)	DMSO	20

[a]Reaction condition: All reactions were done at 90 °C using 1.0 equiv of **2a**. [b]Yield of isolated products after column chromatography.

A scale of substrates were prepared (Figure 5.2) with the optimized condition, and it was noted that when phenyl group was used as the substituent –R, product was formed in good yield (**3a**, 81%). When *para* position of phenyl ring was substituted with an alkyl group and varied, good yield of the product were produced in both cases (**3b**-**c**). Replacing with other halogen groups, good to excellent yields of the product were observed in most cases (**3d**-**g**), with the highest yield when fluoro substituted propiolate derivative was used. With phenyl group as *para* substituent on the phenyl ring of the ester molecule, sufficiently good yield of the product was noted.(**3h**, 82%). Changing the substitution position from *para*- to *meta*- or *ortho*-, no appreciable difference was noted, and good to excellent yields of the product were observed mostly (**3i**-**l**). Substituents with electron-donating or electron-withdrawing group substituent at para position of phenyl ring did not produce a substantial difference in yield of product which incurred that electronic effect is not operative in the methodology. Di-substitution with two alkyl groups in the phenyl ring resulted in a good yield of product (**3m**, 76%). Naphthalene based substrates tolerated the reaction condition and resulted in good yields of product (**3n** and **3o**). Sterically hindered substrates reduced the yield of the product (**3q** and **3r**). Dimethylacetylene dicarboxylate and diethylacetylene dicarboxylate showed a reduction in yields of the product (3s and 3t), as the presence of two carbonyl groups hinders the directional nature of carbonyl substituent. When aliphatic methyl and ethyl were used as substituents, yield reduced abruptly as the intermediate generated in the reaction mixture might have stabilized by the aromatic ring (**3u** and **3v**). Bromophenyl or chlorophenyl substituted ester furnished the desired products **3w** and **3x** in moderate yield.

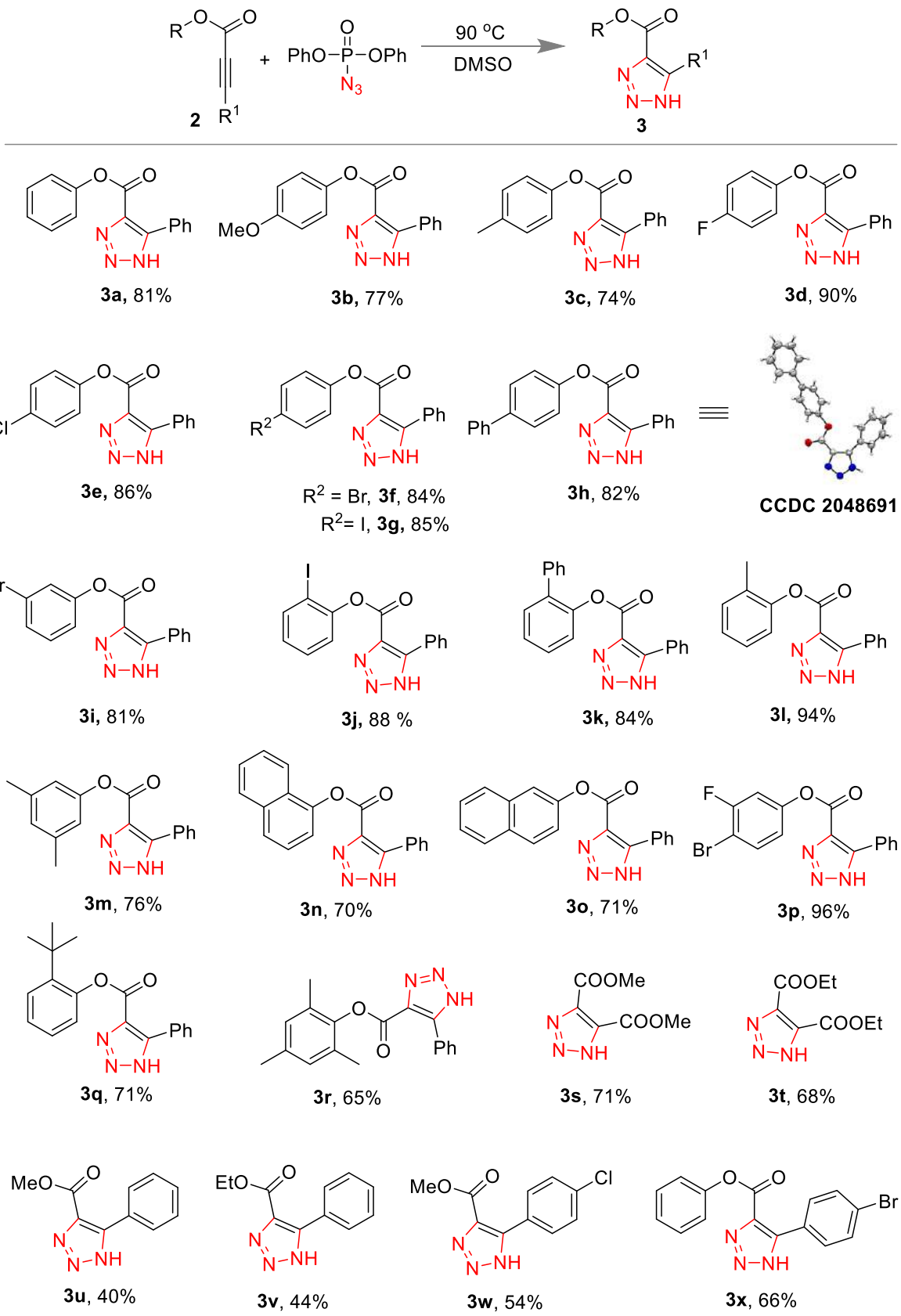


Figure 5.2. Scope for synthesis of N-H triazoles. Reaction conditions: 1.0 equiv of **2** and 2.0 equiv of the azide; all reactions were done at 90 °C for 7 h. Yield of isolated products after

column chromatography are shown. X-Ray structure of the compound **3h** (CCDC 2048691) has been shown.

To understand the mechanistic pathway, control experiments were done (Figure 5.3). The reaction pathway was monitored to understand whether the reaction proceeded *via* a radical or ionic pathway. Following standard reaction conditions, when a radical scavenger butylated hydroxytoluene (BHT) was employed in the reaction, a mixture of products was observed, which was not conclusive. When the reaction was treated using (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl radical (TEMPO, 3.0 equiv) under standard reaction condition, the yield of compound **3f** was reduced to a great extent (42%) as indicated in Figure 5.3a. To confirm the proton source in triazole, various other control experiments were conducted. Bromo substituted propiolate (**2f**) was treated with standard reaction condition using $PO(OPh)_2N_3$ (2 equiv) in DMSO for 7 h, product (**3f**) was formed along with by-product $PO(OPh)_2OH$ confirmed from ESI-MS. It was assumed that as P-O bond cleaved, followed by triazole ring taking up proton from the water present in DMSO and the hydroxyl part $(OH)^-$ combines with $PO(OPh)_2^+$ to form $PO(OPh)_2OH$ (251.0465) confirmed from ESI-MS analysis (*vide infra*). Further, when iodo-substituted propiolate (**2g**) was made to react with DPPA (2 equiv) under normal standard conditions in DMSO-d_6 for 7 h, deuterium incorporation was not found and product (**3g**, MW 391.987) was confirmed from ESI-MS analysis, which concluded that DMSO proton was not participating in the reaction mixture (Figure 5.3b). This confirmed that the DMSO proton was not involved in the formation of N-H triazole. Further, to confirm the source of proton in triazole, the starting material **2e** underwent reaction under standard conditions using $PO(OPh)_2N_3$ (2 equiv) in dry DMSO and D_2O for 7 h. Further, ESI-MS was recorded for the reaction mixture, and it was observed that a peak was obtained at 301.127, which led us to conclude that incorporation of deuterium

occurred forming N-D triazole (**3e'**) (Figure 3c).This proves that the water present in DMSO is the source of proton in triazole. When benzoyl substituted alkyne (**2y**) was used as a precursor instead of the propiolate, the reaction was successful to produce phenyl(5-phenyl-1H-1,2,3-triazol-4-yl)methanone (**4y**) in 81% yield (Figure 5.3d). On the other hand, when diphenyl acetylene was used, the reaction failed (Scheme 5.8b). Based on this observation, precursor (**2z**) was slightly modified by introducing a methylene group instead of carbonyl group to note the result. It was noted that the reaction failed to proceed, which implied that the carbonyl group had a prime role in the reaction (Figure 5.3d). When highly electron deficient alkynes 1-(phenylethynyl)-3,5-bis(trifluoromethyl)benzene (**3z**) and 1,3- difluoro-5-(phenylethynyl)benzene) (**4z**) were treated with diphenylphosphoryl azide (DPPA), triazole was not observed. This evidenced that essential role of carbonyl group as shown in (Figure 5.3e).

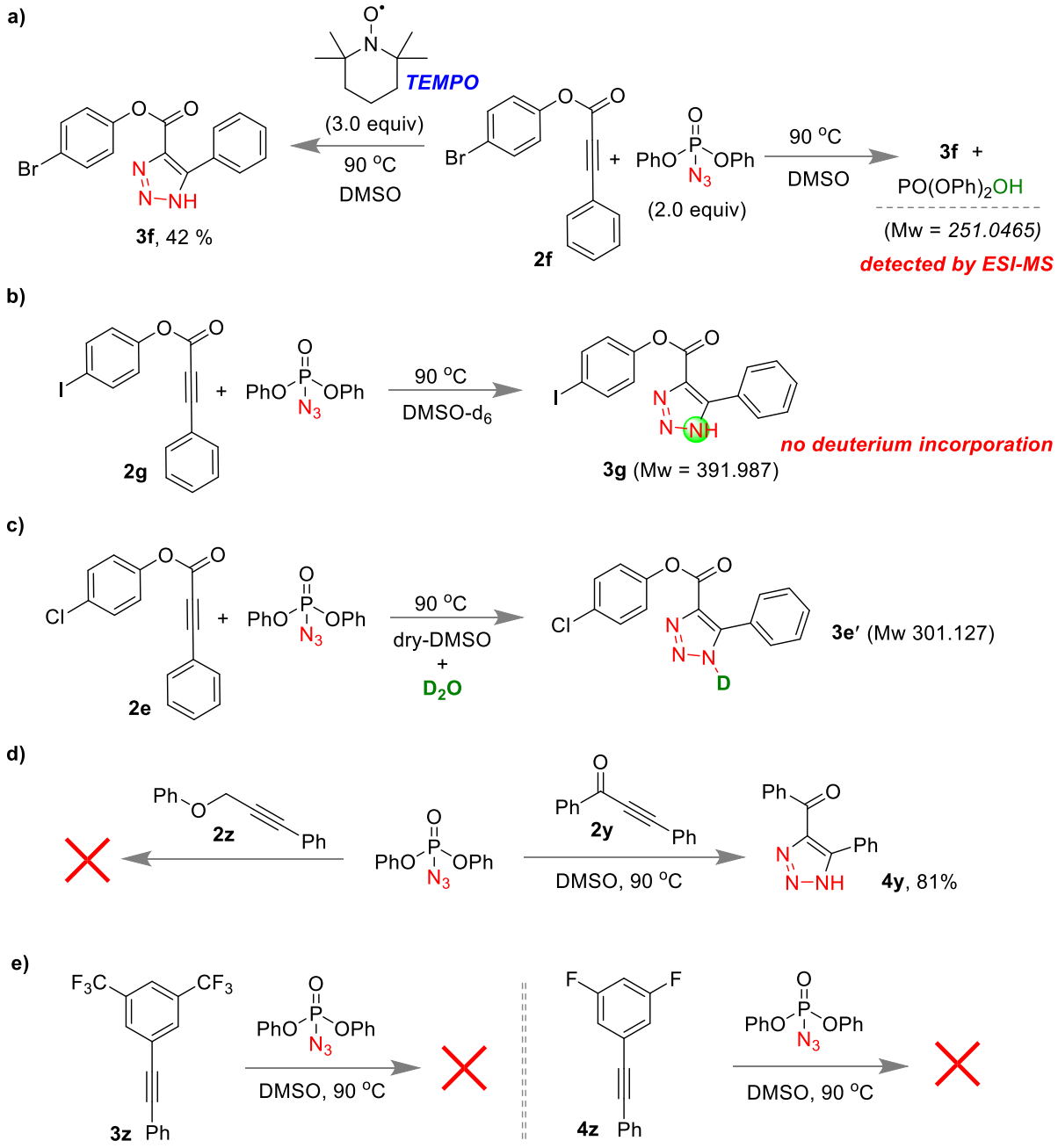


Figure 5.3. Control experiments to understand the mechanistic pathway of the azide-alkyne cycloaddition. Standard reaction conditions: 1.0 equiv of **2** and 2.0 equiv of the azide; all reactions were done at 90 °C for 7 h and yield of isolated products after column chromatography are shown. a) Reactions of **2f** in the presence and in absence of TEMPO. b) and c) Deuterium incorporation experiments. d) Reactivities of internal alkynes. e) with electron-withdrawing alkynes.

EPR experiments were conducted as shown in Figure 5.4 which helped to establish the radical mechanism.[33] When phenyl propiolate derivative (**2f**), phosphoryl azidate in DMSO (1 mL) was heated for 2 h at 90 °C in the presence of 0.5 mL of a spin trapping agent 5,5-dimethyl-1-pyrroline-*N*-oxide (DMPO), a new signal was noticed (Figure 5.4a). This indicated that azidyl radical might have formed and trapped by DMPO which creates a stable DMPO-N_3 radical. The azidyl radical was generated only when the substrate has been introduced in the reaction medium. This proved that the P…O interaction helped to cleave the phosphorus nitrogen bond. The above mentioned hypothesis was further strengthened, when phosphoryl azidate was solely heated in a solvent at 90 °C for 4 h when no new signal was observed (Figure 5.4b).

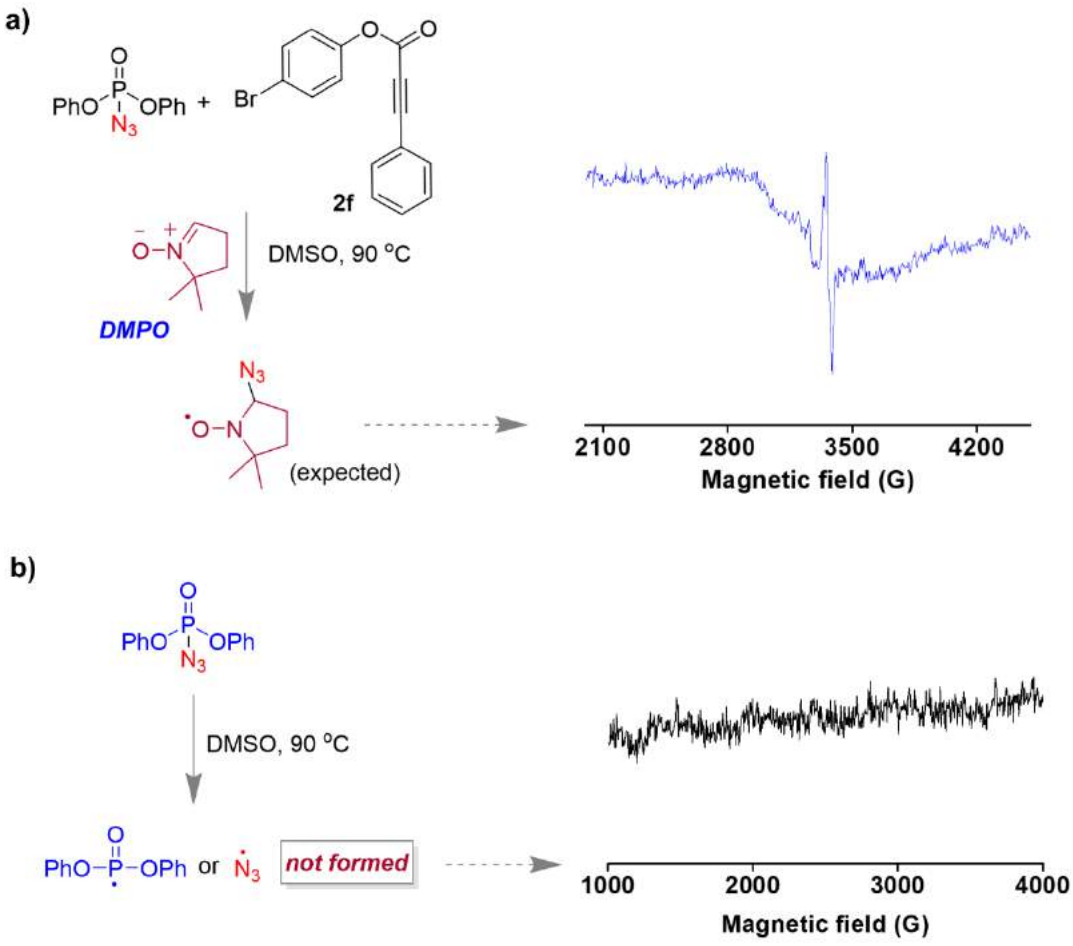


Figure 5.4 a) Scheme of the EPR experiment employing DMPO under standard condition and corresponding spectra. b) No radical formation was observed when phosphoryl azidate was heated alone.

Based on the control experiments and literature reports,[14] a plausible mechanistic pathway was proposed in Figure 5.5a. It was assumed that the proximity between the molecules led to phosphorus oxygen interaction in ***a,*** or it may proceed through transition state ***b***. DPPA solely cannot generate the phosphorus radical and azidyl radical species until the substrate phenyl propiolate was introduced in the reaction. The interaction of phosphorus with oxygen helped to form the azidyl radical, which was confirmed through EPR. The azidyl radical attacks the alkyne, and its counterpart attack the oxygen simultaneously to form a stable phosphorus oxygen bond forming intermediate ***c***. The bond dissociation energy of P-N bond is extremely high (617 kJ/mole) which was cleaved due to the interaction of phosphorus oxygen bond. Successive steps led to the formation of triazole ring by constructing the intermediate ***d*** by ring closure. Finally water molecule in DMSO attacked the ring forming **3** by cleavage of P-O bond. Table 5.1 (entry 8) showed that sodium azide did not prove effective for the reaction because sodium lacks any vacant d orbital. Hence, there was no scope for back bonding, unlike phosphorus. Thus, it is anticipated that P…O interaction was vital for the reaction to proceed to completion.

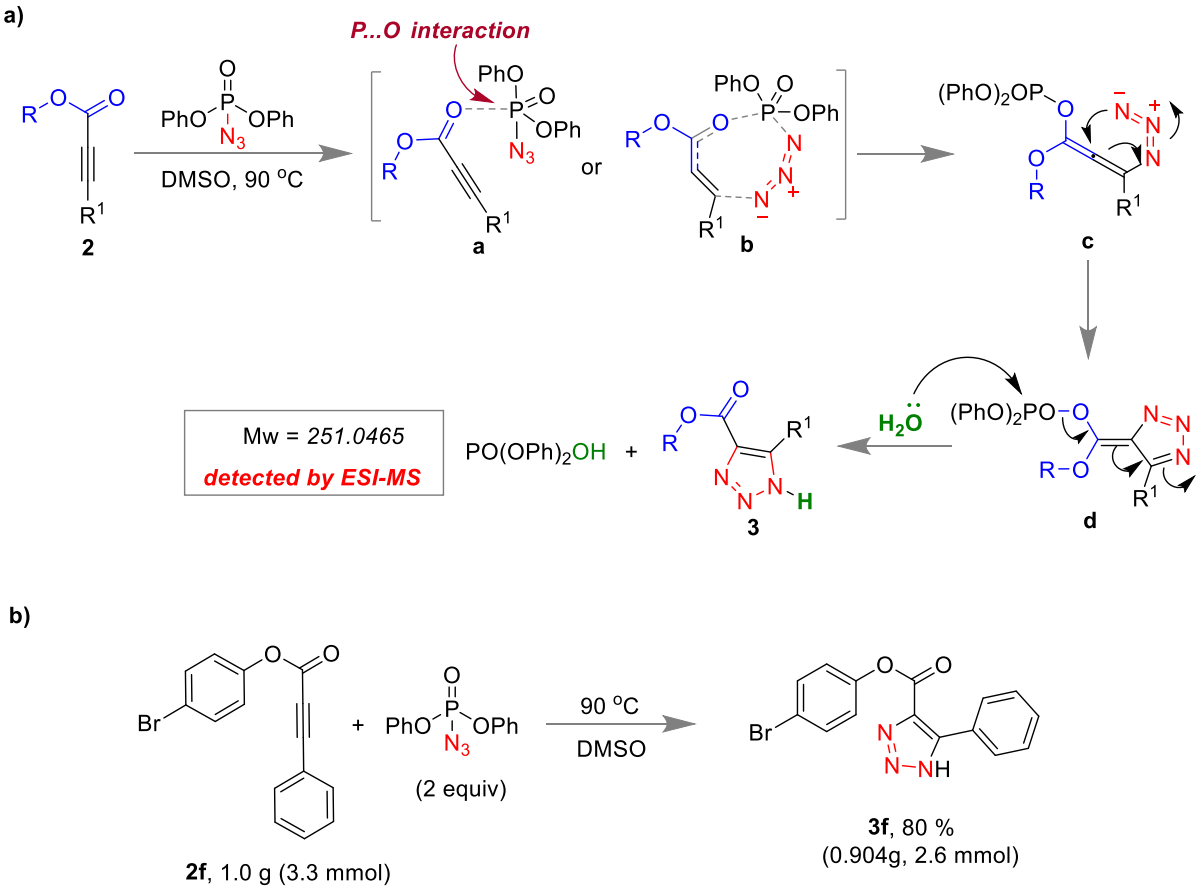


Figure 5.5 a) Plausible mechanistic pathway for formation of triazole ring. b) Gram scale reaction for triazole synthesis; Reaction conditions: 1.0 equiv of **2** and 2.0 equiv of the azide; reaction was done at 90 °C for 7 h. Yield of isolated product after column chromatography.

Further, the reaction was carried on a gram scale leading to the formation of the desired product by taking 1g (3.3 mmol) of bromophenyl propiolate and treating it with standard reaction conditions. A sufficient yield of product (**3f**, 80%) was obtained, claiming that methodology is scalable and can have ample application in medicine and industry. (figure 5.5 b).

5.4 CONCLUSIONS

In conclusion, a mild metal free direct method was developed to synthesize N-H triazoles by utilizing the phosphorus oxygen interaction, which is the key step for the synthesis of

triazoles. The carbonyl group is essential for the interaction of lone pair of oxygen with vacant d orbital of phosphorus, which is nothing but P…O interaction. The dissociation of the phosphorus nitrogen bond could also take place without the involvement of any external oxidant or metal. The formation of azidyl radical has been explained with the help of EPR studies. The optimization studies and the control experiments clearly prove the activation of phosphorus nitrogen bond *via* P…O interaction. Thus, the close proximity between the molecules leads to the phosphorus oxygen interaction that enables synthesize triazoles which will be of ample use to the scientific community for the synthesis of triazoles which are useful in medicinal chemistry. Also, it will help to bridge the gap between supramolecular and organic chemistry and unfold the utility of multiple co-operative interactions in organic synthesis.

5.5 EXPERIMENTAL SECTION

General Methods: Chromatographic (column) purifications of the compounds were done using silica gel (mesh 230-400) and hexane-ethyl acetate mixtures as eluent unless otherwise specified. Infrared (IR) spectral data are reported in wave number (cm^{-1}). FT-IR spectra were recorded after making thin layer of the compounds on the surface of NaCl crystal using dichloromethane.

Representative method for preparation of phenyl-3-phenylpropiolate (2a). To a solution containing 3-phenylpropiolic acid (0.5 g, 1.0 equiv) in 5 mL dichloromethane (CH_2Cl_2), phenol (321 mg, 1.0 equiv in CH_2Cl_2 (5 mL) was added at 0 °C. Then a mixture of DCC (0.7 g, 1.0 equiv) and DMAP dissolved (0.41 mg, 0.1 equiv) in CH_2Cl_2 (10 mL) was added in a drop wise manner to the reaction mixture. The mixture was shaken at 0 °C for 1 h, and then at room temperature for 12 h. The resulting reaction mixture was extracted by EtOAc (3 × 10 mL) and dried over anhydrous Na_2SO_4. The organic layer was removed under vacuum and

crude products were isolated by column chromatography (eluent: hexane/EtOAc = 95/5) and 0.49 g of white solid was isolated as phenyl-3-phenylproiolate. The other starting derivatives were prepared by following the similar procedure.

Representative method for preparation of phenyl 5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3a). In a sealed tube phenyl-3-phenylpropiolate **2a** (60 mg, 0.267 mmol) in 1 mL DMSO was taken and to it the azide reagent phosphoryl azidate (98 µL, 0.534 mmol) was added to the solution and heated to 90 ℃ for 7 h until full consumption of starting materials. The reaction mixture was removed from heating and was cooled for several minutes. Aqueous work up was followed by chromatographic column separation to isolate pure product phenyl 5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3a**) as white solid in 57 mg (81%) yield using 18% ethylacetate-hexane as eluent.

EPR spectra was recorded at 298 K using EPR spectrometer derived at 9.4335 GHz. Typical spectrometer parameters are shown as follows, scan range: 100 G; center field set: 3480.00 G; time constant: 0.16 ms; scan time: 122.88 s; modulation amplitude: 20.0 G; modulation frequency: 100 kHz; receiver gain: 2.00×102 ; microwave power: 7.14e-001 mW.

Spin-trapping experiment in presence DMPO.1 A mixture of 4-Bromophenyl 3-phenylpropiolate (0.19 mmol), phosphoryl azidate (75 µL), in solvent DMSO was heated for 5 hr at 9 0℃and DMPO (20 µL) were stirred in 1.0 mL of DMSO and heated in oil bath for 10 min. Afterwards, 20 µL solution was quickly transferred into EPR tube and 200 µL DMSO was added to analyze EPR. Similar experiment was performed without the propiolate

Good quality crystals of the compounds **3h** were obtained after slow evaporation of ethyl acetate solution. The crystals data were collected with Bruker SMART D8 goniometer equipped with an APEX CCD detector and with an INCOATEC micro source (Cu-Kα radiation, λ = 0.71073 Å). SAINT+[34] and SADABS[35] were used to integrate the intensities and to correct the absorption respectively The structure was resolved by direct methods and

refined on F^2 with SHELXL-97.[34] ORTEP drawing of the compound **3**shows ellipsoid contour at the 50% probability level

Compound Characterization Data

Phenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3a). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 57 mg (81%); mp 152–154 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.81 (s, 2H), 7.49 – 7.47 (m, 3H), 7.45 (d, *J* = 7.6 Hz, 2H), 7.31 (d, *J* = 7.2 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR ([(100 MHz $CDCl_3$-DMSO-d_6 (20 : 1)]) δ 160.1, 146.4, 150.3, 133.5, 129.8, 129.5, 129.4, 128.4, 127.6, 126.1, 121.7; ῡ = 3418, 2258, 2130, 1651 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{11}N_3O_2Na$ 288.0743; Found 288.0767.

4-Methoxyphenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3b). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 54 mg (77%); mp 171–173 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.82 (d, *J* = 5.2 Hz, 2H), 7.52-7.44 (m, 3H), 7.18 (d, *J* = 8.8 Hz, 2H), 6.98 (d, *J* = 8.8 Hz, 2H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.8, 157.1, 143.4, 130.1, 129.6, 129.3, 128.4, 123.6, 122.7, 122.5, 114.6, 55.5; ῡ = 3421, 2923, 2853, 1639 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{14}N_3O_3$ 296.1030; Found 296.1039.

***p*-Tolyl-5-phenyl-1H-1,2,3-triazole-4-carboxylate (3c).** R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 52 mg (74%); mp 132-134 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.81 – 7.80 (m, 2H), 7.50 – 7.47 (m, 3H), 7.24 (d, *J* = 8.4 Hz, 2H), 7.13 (d, *J* = 8.4 Hz, 2H), 2.31 (s, 3H); ^{13}C NMR [(100 MHz $CDCl_3$-DMSO-d_6 (20 : 1)] δ 159.9, 147.9, 135.3, 129.5(×2), 129.2, 128.9(×2), 127.9, 120.9(×2), 20.5; ῡ = 3421, 2923, 2853, 1467 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{13}N_3O_2Na$ 302.0900; Found 302.0914.

4-Fluorophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3d). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 64 mg (90%); mp 199–201°C ; ^{1}H NMR (NMR [(400 MHz $CDCl_3$-DMSO-d_6 (20 : 1)]) δ 7.76 (s, 2H), 7.55 (s, 1H), 7.37 (d, *J* = 3.2 Hz, 3H), 7.12 – 7.09 (m, 2H), 7.03 – 6.99 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 160.5 (d, $^1J_{C\text{-}F}$ = 253 Hz), 146.4 (d, $^4J_{C\text{-}F}$ = 2.4 Hz), 129.8, 129.4 (×3), 128.4 (×2), 123.3 (d, $^3J_{C\text{-}F}$ = 8.6 Hz), 116.16 (d, $^2J_{C\text{-}F}$ = 23.5 Hz); ῡ = 3437, 1643, 1173 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{10}FN_3O_2Na$ 306.0649; Found 306.0641.

4-Chlorophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3e). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 60 mg (86%); mp 236–238 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.80 – 7.78 (m, 2H), 7.65 – 7.61 (m, 2H), 7.50 – 7.47 (m, 3H), 7.27 – 7.23 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.5, 149.5, 142.4, 132.7, 129.9, 129.4, 128.6, 125.5, 124.5, 118.7 (×2); ῡ = 3420, 2098, 1652, 1476 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{11}ClN_3O_2$ 300.0534; Found 300.0528.

4-Bromophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3f). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 58 mg (84%); mp 235–237 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.83 – 7.80 (m, 2H), 7.65 – 7.64 (m, 2H), 7.50 – 7.48 (m, 3H), 7.29 – 7.26 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.5, 149.5, 132.8, 132.4, 130.1, 129.5 (×2), 128.7, 124.6, 118.8, 117.8; ῡ = 3410, 2257, 2130, 1653 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{10}BrN_3O_2Na$ 365.9849; Found 365.9858.

4-Iodophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3g). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 57 mg (84%); mp 238–240 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.70 (d, *J* = 7.6 Hz, 4H), 7.39 (d, *J* = 4.8 Hz, 3H), 7.02 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR [(100

MHz $CDCl_3$-DMSO-d_6 (20 : 1)] δ 159.3, 149.8, 138.0, 132.8, 129.3, 128.9, 127.9, 127.3, 123.6, 113.5, 89.7; ῡ = 3437, 2358, 2093, 1639 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{11}IN_3O_2$ 391.9890; Found 391.9916.

[1,1'-Biphenyl]-4-yl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3h). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 56 mg (82%); mp 197-199 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 7.85 (d, *J* = 5.2 Hz, 2H), 7.75 – 7.73 (m, 2H), 7.70 – 7.67 (m, 2H), 7.53 – 7.46 (m, 5H), 7.40 – 7.36 (m, 3H); ^{13}C NMR [(100 MHz $CDCl_3$-DMSO-d_6 (20 : 1)] δ 159.7, 149.3, 139.7, 138.6, 129.2(×2), 128.9, 128.4, 127.9, 127.7, 127.0(×2), 126.6, 121.6; ῡ = 3421, 2923, 2358, 1645 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{16}N_3O_2$ 342.1237; Found 342.1240.

3-Bromophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3i). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 55 mg (81%); mp 148–150 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.81–7.79 (m, 2H), 7.44 – 7.35 (m, 5H), 7.24 – 7.21 (m, 1H), 7.12 (dd, *J* = 8.4, 1.2 Hz, 1H), 6.85 (brs, 1H); ^{13}C NMR δ ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 150.6, 147.2, 133.6, 130.7, 130.4, 129.6, 129.4, 128.7, 127.0, 125.2, 122.6, 120.6; ῡ = 3438, 2359, 2097, 1644 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{11}BrN_3O_2$ 344.0029; Found 344.0037.

2-Iodophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3j). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 59 mg (88%); mp 157–159 °C; ^1H NMR [(400 MHz $CDCl_3$-DMSO-d_6 (20 : 1)] δ 7.92 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.83 (d, *J* = 3.6 Hz, 2H), 7.51 – 7.46 (m, 4H), 7.38 (d, *J* = 6.8 Hz, 1H), 7.11 (td, *J* = 7.6, 1.6 Hz, 1H); ^{13}C NMR [(100 MHz $CDCl_3$-DMSO-d_6 (20 : 1)] δ 159.4, 151.0, 139.6, 133.2, 129.7, 129.5, 129.4, 128.4, 127.9, 123.3, 121.8,

118.8, 90.6; ῡ = 3438, 2359, 2078, 1644, 1461 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{11}IN_3O_2$ 391.9890; Found 391.9897.

[1,1'-Biphenyl]-2-yl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3k). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 57 mg (84%); mp 194–196 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 7.51– 7.44 (m, 5H), 7.42 – 7.36 (m, 5H), 7.33 – 7.28 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 151.7, 147.0, 136.8, 134.3, 133.3, 130.9, 130.7, 129.2, 129.1, 128.9, 128.6, 128.5, 128.3, 127.7, 126.9, 123.3, 116; ῡ = 3441, 2065, 1635 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{16}N_3O_2$ 342.1237; Found 342.1229.

***o*-Tolyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3l).** R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 64 mg (94%); mp 131–133 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.81– 7.78 (m, 2H), 7.41 – 7.33 (m, 3H), 7.22 – 7.12 (m, 3H), 7.06 (dd, *J* = 8.0, 1.6 Hz, 1H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 148.8, 133.4, 131.4, 130.3, 130.1, 129.4, 128.5, 127.1, 126.5, 121.9, 120.6, 115.1, 16.3; ῡ = 3437, 2358, 2339, 1644 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{14}N_3O_2$ 280.1081; Found 280.1082.

3,5-Dimethylphenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3m). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 53 mg (76%); mp 138–140 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 7.82 – 7.79 (m, 2H), 7.51 – 7.47 (m, 3H), 6.92 (s, 1H), 6.85 (s, 2H), 2.27 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.6, 150.0, 145.5, 139.0, 129.6, 129.3, 128.4, 127.8, 127.5, 119.3, 113.0, 20.8; ῡ = 3413, 2359, 2255, 1651 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{15}N_3O_2Na$ 316.1056; Found 316.1043.

Naphthalen-1-yl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3n). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 48 mg (70%); mp 131–133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 – 7.81 (m, 4H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.49 – 7.35 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 146.3, 134.8, 130.2, 129.4, 128.7, 128.1, 127.4, 126.8, 126.8, 126.7, 126.6, 125.5, 121.4, 118.3; ῡ = 3437, 2094, 1644, 1461 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{14}N_3O_2$ 316.1081; Found 316.1069.

Naphthalen-2-yl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3o). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 49 mg (71%); mp 177–179 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.02 – 7.92 (m, 3H), 7.86 – 7.82 (m, 3H), 7.58 – 7.44 (m, 6H); ^{13}C NMR [(100 MHz, $CDCl_3$-DMSO-d_6 (20 : 1)]) δ 159.8, 147.5, 133.2, 131.1, 129.2, 129.0, 128.9, 127.9, 127.3, 127.2, 126.2(×2), 125.4, 120.7, 118.3; ῡ = 3421, 2955, 2924, 1639 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{14}N_3O_2$ 316.1081; Found 316.1101.

4-Bromo-3-fluorophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3p). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 66 mg (96%); mp 220–222 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.83 – 7.78 (m, 3H), 7.53 – 7.48 (m, 4H), 7.17 – 7.15 (m, 1H); ^{13}C NMR ([(100 MHz, $CDCl_3$-DMSO-d_6 (20 : 1)]) δ 158.8, 158.5 ($^1J_{C\text{-}F}$ = 246 Hz), 150.03 (d, $^3J_{C\text{-}F}$ = 9.8 Hz), 133.4, 129.4, 129.1, 128.9, 128.1, 127.8, 119.3 (d, $^4J_{C\text{-}F}$ = 3.5 Hz), 111.4 (d, $^2J_{C\text{-}F}$ = 25.4 Hz), 105.2 (d, $^3J_{C\text{-}F}$ = 21 Hz), 104.0 (d, $^2J_{C\text{-}F}$ = 30.6 Hz); ῡ = 3437, 2358, 2089, 1652 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_9BrFN_3O_2Na$ 383.9754; Found 383.9736.

2-(*tert*-Butyl)phenyl 5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3q). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 49 mg (71%); mp 200–202 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.82 (m, 2H), 7.42 – 7.41 (m, 4H), 7.24 – 7.19 (m, 2H), 7.11 (d, *J* = 7.6 Hz, 1H), 1.30

(s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2, 148.7, 134.3, 141.6, 130.1, 129.4(×2), 128.6(×2), 127.6, 127.1, 126.3, 124.1, 34.7, 30.3; ῡ = 3585, 2258, 2130, 1651 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{19}N_3O_2Na$ 344.1369; Found 344.1389.

Mesityl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3r). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 45 mg (65%); mp 197–199 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.82 (m, 2H), 7.40 – 7.38 (m, 3H), 6.86 (s, 2H), 2.26 (s, 3H), 2.11 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 145.5, 135.8, 130.0, 129.9, 129.43, 129.36, 128.5, 127.9, 120.5, 114.1, 20.9, 16.4; ῡ = 3422, 1639, 1468 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{18}N_3O_2$ 308.1394; Found 308.1396.

Dimethyl-1*H*-1,2,3-triazole-4, 5-dicarboxylate (3s). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 56 mg (71%); mp 177–179 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.00 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 138.7, 53.3; ῡ = 3437, 2253, 2127, 1658 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_6H_8N_3O_4$ 186.0509; Found 186.0527.

Diethyl-1*H*-1,2,3-triazole-4,5-dicarboxylate (3t). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 51 mg (68%); mp 180–182 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.46 (q, J = 7.2 Hz, 4H), 1.40 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2, 138.6, 62.8, 14.2; ῡ = 3437, 2358, 2097, 1641 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_8H_{11}N_3O_4Na$ 236.0642; Found 236.0659.

Methyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (3u). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 25 mg (40%) ; mp 113–115 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.79 (m, 2H), 7.46 – 7.42 (m, 3H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 146.6,

134.1, 129.9, 129.3, 128.5, 127.8, 52.6; ῡ = 3441, 2358, 2089, 1644 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{10}H_9N_3O_2Na$ 226.0587; Found 226.0584.

Ethyl-5-phenyl-1H-1,2,3- triazole-4-carboxylate (3v). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 33 mg (44%) mp 122–124 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (m, 2H), 7.45 (m, 3H), 4.42 – 4.39 (m, 2H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 146.9, 129.8, 129.4 (×2), 128.5, 128.2, 61.8 14.1; ῡ = 3422, 2359, 1652, 1456 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{11}H_{11}N_3O_2Na$ 240.0743; Found 260.0733.

Methyl–5–(4-chlorophenyl–1*H*-1,2,3-triazole-4-carboxylate (3w). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 34 mg (54%); mp 144 –146 ℃; ^1H NMR ([(400 MHz $CDCl_3$-DMSO-d_6 (20 : 1)]) δ 7.42 (d, *J* = 7.6 Hz, 2H), 7.02 (d, *J* = 8.0 Hz, 2H), 3.50 (s, 3H); ^{13}C NMR ([(100 MHz $CDCl_3$-DMSO-d_6 (20 : 1)]) δ 161.4, 134.6(×2), 130.38(×2),128.1(×2), 51.8; ῡ = 3421, 2359, 2339, 1739, 1644 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{10}H_8N_3O_2ClNa$ 260.0197; Found 260.0173.

Phenyl 5-(4-bromophenyl)-1*H*-1,2,3-triazole-4-carboxylate (3x). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 45 mg (66%); mp 145 –147 ℃; ^1H NMR (400 MHz, DMSO-d_6) δ 7.72 (d, *J* = 8.4 Hz, 2H), 7.48 – 7.46 (m, 2H), 7.35 – 7.31 (m, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.12 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR ([(100 MHz $CDCl_3$-DMSO-d_6 (20 : 1)]) δ 159.7, 149.9, 131.1, 130.7, 129.8, 129.2, 127.4, 125.9, 123.5, 121.5, 113.6; ῡ = 3437, 2085, 1644 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{11}N_3BrO_2$ 344.0029; Found . 344.0008

Phenyl-(5-phenyl-1H-1,2,3-triazol-4-yl)methanone (4y).[36] R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 65 mg (81%); mp 86–88 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 7.6 Hz, 2H), 7.71 – 7.69 (m, 2H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.45 – 7.41(m, 2H), 7.37 –

7.35 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.3, 146.4, 141.3, 137.1, 133.6, 130.6, 129.8, 128.9, 128.7, 128.5, 127.9.

Phenyl-3-phenylpropiolate (2a).[37] R_f = 0.8 (hexane : ethyl acetate 20:1); white solid; 0.49 g (65%); mp 38-40 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.62 (m, 2H), 7.51 – 7.47 (m, 1H), 7.44 – 7.38 (m, 4H), 7.30 – 7.28 (m, 1H), 7.21 – 7.18 (m, 2H).

4-Methoxyphenyl-3-phenylpropiolate (2b).[37] R_f = 0.80 (hexane : ethyl acetate 20:1); white solid; .44g (51%); mp 67– 69 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.2 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.11 (d, *J* = 9.0 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 2H), 3.81 (s, 3H).

***p*-Tolyl-3-phenylpropiolate (2c).**[37] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; .50g (62%); mp 56–58 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.2Hz, 2H), 7.49 (t, *J* = 8.8 Hz, 1H), 7.41 (t, *J* = 8.0 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 7.08 (d, *J* = 8.4 Hz, 2H), 2.37 (s, 3H).

4-Fluorophenyl-3-phenylpropiolate (2d).[38] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.41g (51%); mp 78–80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.0 Hz, 2H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.17 (m, 2H), 7.10 (t, *J* = 8.0 Hz, 2H).

4-Chlorophenyl-3-phenylpropiolate (2e).[38] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.47g (55%); mp 73–75 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.62 (m, 2H), 7.52 – 7.48 (m, 1H), 7.43 – 7.37 (m, 4H), 7.16 – 7.13 (m, 2H).

4-Bromophenyl-3-phenylpropiolate (2f).[37] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.59g (58%); mp 62–64 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 7.6 Hz, 2H), 7.54 – 7.48 (m, 3H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.10 (d, *J* = 8.8 Hz, 2H).

4-Iodophenyl-3-phenylpropiolate (2g).[39] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.71g (60%); mp 58-60 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.4 Hz, 2H), 7.63 (d, *J* = 7.6 Hz, 2H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 6.97 (d, *J* = 8.4 Hz, 2H).

[1,1'-biphenyl]-4-yl-3-phenylpropiolate (2h).[39] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.62 g (61%); mp 133–135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.62 (m, 4H), 7.59 – 7.57 (m, 2H), 7.52 – 7.35 (m, 6H), 7.28 – 7.26 (m, 2H).

3-Bromophenyl-3-phenylpropiolate (2i).[39] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.68 g (67%); mp 99–101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 – 8.32 (m, 2H), 7.69 – 7.67 (m, 2H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.47 – 7.41 (m, 4H).

2-Iodophenyl-3-phenylpropiolate (2j).[40] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.78 g (66%); mp 77–79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 8.0, 1.2 Hz,

1H), 7.66 – 7.64 (m, 2H), 7.52 – 7.48 (m, 1H), 7.43 – 7.38 (m, 3H), 7.20 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.05 – 6.99 (m, 1H).

[1,1'-biphenyl]-2-yl-3-phenylpropiolate (2k).[41] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.58 g (58%); mp 85–87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.53 (m, 2H), 7.48 – 7.35 (m, 11H), 7.25 – 7.23 (m, 1H).

***o*-Tolyl-3-phenylpropiolate (2l).**[37] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.50 g (63%); mp 60–62; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.62 (m, 2H), 7.51 – 7.47 (m, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.28 – 7.27 (m, 1H), 7.24 – 7.17 (m, 2H), 7.12 – 7.09 (m, 1H), 2.27(s, 3H).

3,5-Dimethylphenyl-3-phenylpropiolate (2m).[42] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.45 g (54%); mp 68–70 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.61 (m, 2H), 7.51 – 7.46 (m, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 6.90 (s, 1H), 6.83 (s, 2H), 2.33 (s, 6H).

Naphthalen-1-yl-3-phenylpropiolate (2n).[37] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.66 g (71%); mp 55–57 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 – 8.00 (m, 1H), 7.91 – 7.89 (m, 1H), 7.80 (d, *J* = 8.4 Hz, 1H), 7.67 – 7.64 (m, 2H), 7.58 – 7.48 (m, 4H), 7.43 (t, *J* = 8.0 Hz, 2H), 7.37 (d, *J* = 7.6 Hz, 1H).

Naphthalen-2-yl-3-phenylpropiolate (2o).[37] R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.64 g (69%); mp 89–91 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.83 (m, 3H), 7.68 – 7.64 (m, 3H), 7.54 – 7.48 (m, 3H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.34 (dd, *J* = 8.8, 2.0 Hz, 1H).

4-Bromo-3-fluorophenyl-3-phenylpropiolate (2p). R_f = 0.10 (hexane : ethyl acetate 20:1); white solid; 0.70 g (64%); mp 82–84 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 – 7.63 (m, 2H), 7.61 – 7.57 (m, 1H), 7.53 – 7.49 (m, 1H), 7.42 (t, *J* = 8.0 Hz, 2H), 7. 07 (dd, *J* = 8.8, 2.4, 1H), 6.95– 6.93 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 157.8, 151.5, 150.0 ($^3J_{C\text{-}F}$ = 9.4 Hz) , 133.9, 133.4, 131.5, 128.9, 119.1, 118.7 ($^4J_{C\text{-}F}$ = 3.7 Hz) 110.9 (d, $^2J_{C\text{-}F}$ = 25.4 Hz), 89.8, 79.9 ; ϑ = 3437, 2359, 2339, 2225, 1644, 1481; HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_8BrFO_2Na$ 340.9584; Found 340.9571

2-(*tert*-Butyl)phenyl-3-phenylpropiolate (2q).[43] R_f = 0.3 (hexane : ethyl acetate 7:3); white solid; 0.67 g (67%); mp 62 – 64 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.62 (m, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.45 – 7.39 (m, 2H), 7.28 (s, 1H), 7.24 – 7.21 (m, 1H), 7.11 – 7.05 (m, 1H), 6.88 (t, *J* = 7.2 Hz, 1H), 6.67 (d, *J* = 8.0 Hz, 1H), 1.42 (s, 9H).

Mesityl-3-phenylpropiolate (2r). R_f = 0.30 (hexane : ethyl acetate 7:3); colourless liquid ; 0.45 g (51%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.2 Hz, 2H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 6.91 (s, 2H), 6.80 (s, 2H), 2.29 (s, 3H), 2.22 (s, 6H), 2.20 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 150.0, 145.5, 136.1, 133.4, 131.1, 129.9, 129.5, 129.4, 129.2, 128.8, 122.9, 119.5, 88.4, 80.2, 20.9, 20.5, 16.4, 16.0. (minor amount of the other isomer); ϑ = 3427, 2923, 2852, 2359, 1606 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{17}O_2$ 265.1223; Found 265.1212.

Phenyl-3-(4-bromophenyl)propiolate (2x). R_f = 0.30 (hexane : ethyl acetate 7:3); white solid; 0.44 g (66%); mp 98–100 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.54 (m, 2H), 7.49 – 7.47 (m, 2H), 7.44 – 7.40 (m, 2H), 7.30 – 7.28 (m, 1H), 7.20 – 7.18 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 150.2, 134.6, 132.2, 129.8, 126.6, 126.1, 121.5, 118.3, 87.5,

81.3; ῡ = 3437, 2923, 2092, 1643, 1278 cm^{-1}; HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{10}BrO_2$ 300.9859; Found 300.9844.

(3-Phenoxyprop-1-yn-1yl)benzene (2z).[44] R_f = 0.10 (hexane : ethyl acetate 20:1); brown liquid; 0.60 g (69%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.43 (m, 2H), 7.32 – 7.30 (m, 5H), 7.05 – 7.00 (m, 3H), 4.92 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9, 132.0, 129.6, 128.8, 128.4, 122.4, 121.6, 115.1, 87.4, 84.2, 56.9.

1-(Phenylethynyl)-3,5-bis(trifluoromethyl)benzene(3z).[45] R_f = 0.70 (hexane); colorless liquid; .57 mg (74%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (s, 2H), 7.82 (s, 1H), 7.59 – 7.54 (m, 2H), 7.40 – 7.39 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.9 (q, $^2J_{C-F}$ = 33.6Hz), 131.8, 131.4, 129.3, 128.6, 125.7, 124.3, 121.9, 121.6 (q, $^4J_{C-F}$ = 4.0 Hz), 92.8, 86.3.

1,3-Difluoro-5-(phenylethynyl)benzene (4z)[46] R_f = 0.70 (hexane); colorless liquid; .57 mg (74%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.52 (m, 2H), 7.38 – 7.36 (m, 3H), 7.05 (d, *J* = 6.0 Hz, 2H), 6.81 (t, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1 (dd, $^1J_{C-F}$ = 247, $^3J_{C-F}$ =13.5 Hz), 131.9, 129.1, 128.6, 126.13 (t, $^3J_{C-F}$ = 11.7 Hz), 122.4, 114.8 – 114.4 (m), 104.53 (t, $^2J_{C-F}$ = 25.2 Hz), 91.4, 87.2(t, $^4J_{C-F}$ = 4.0 Hz).

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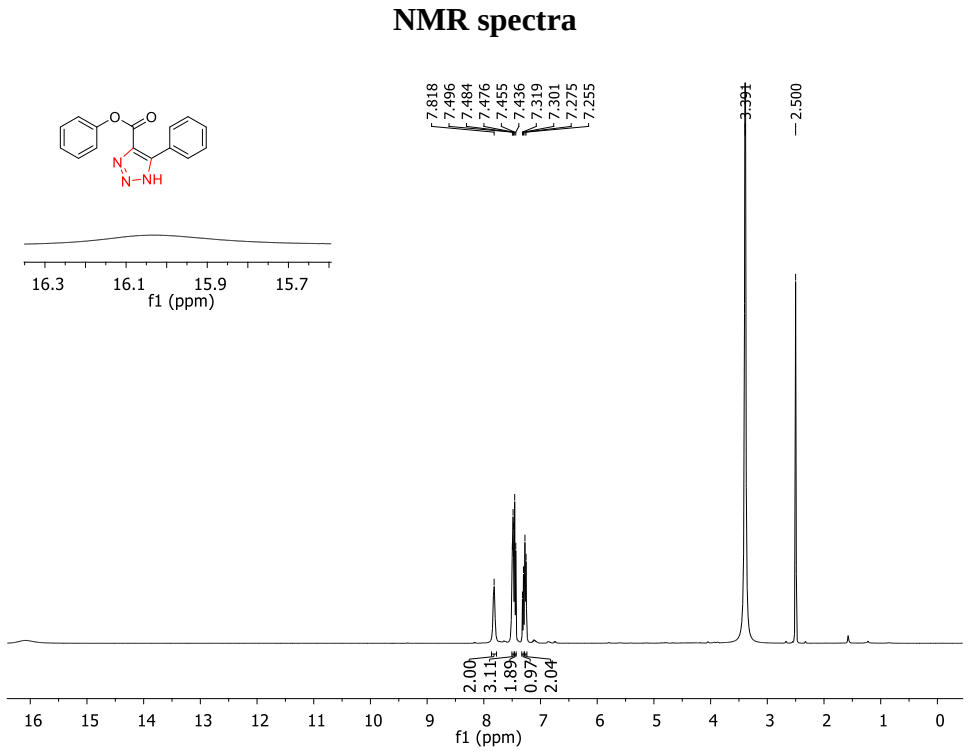

Figure 5.6. ^{1}H NMR spectrum of phenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3a**) in DMSO-d_6

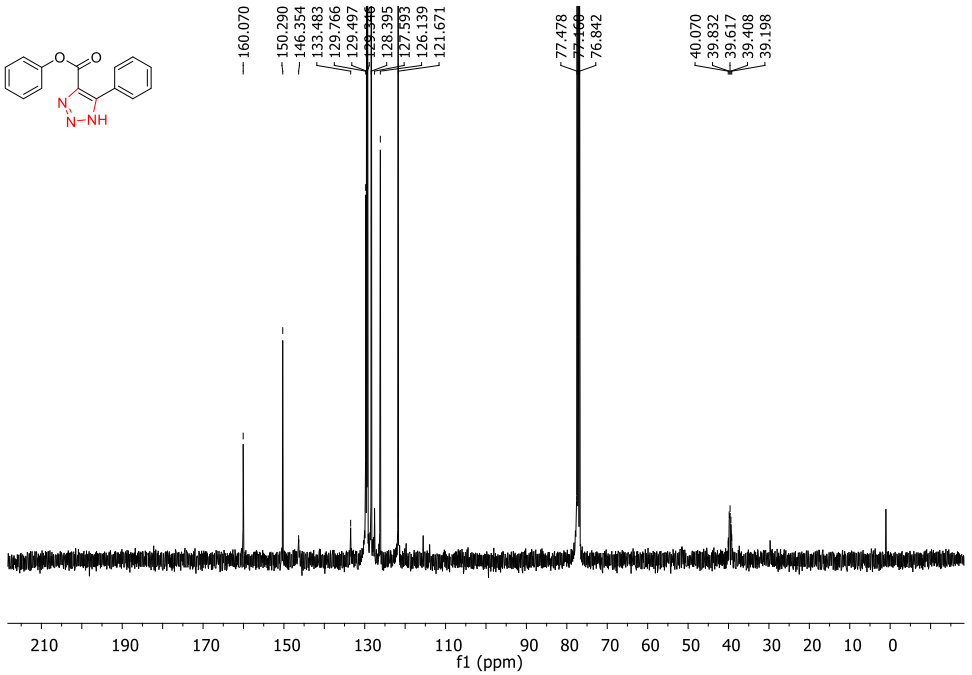

Figure 5.7. ^{13}C NMR spectrum of phenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3a**) in $CDCl_3$:DMSO-d_6.

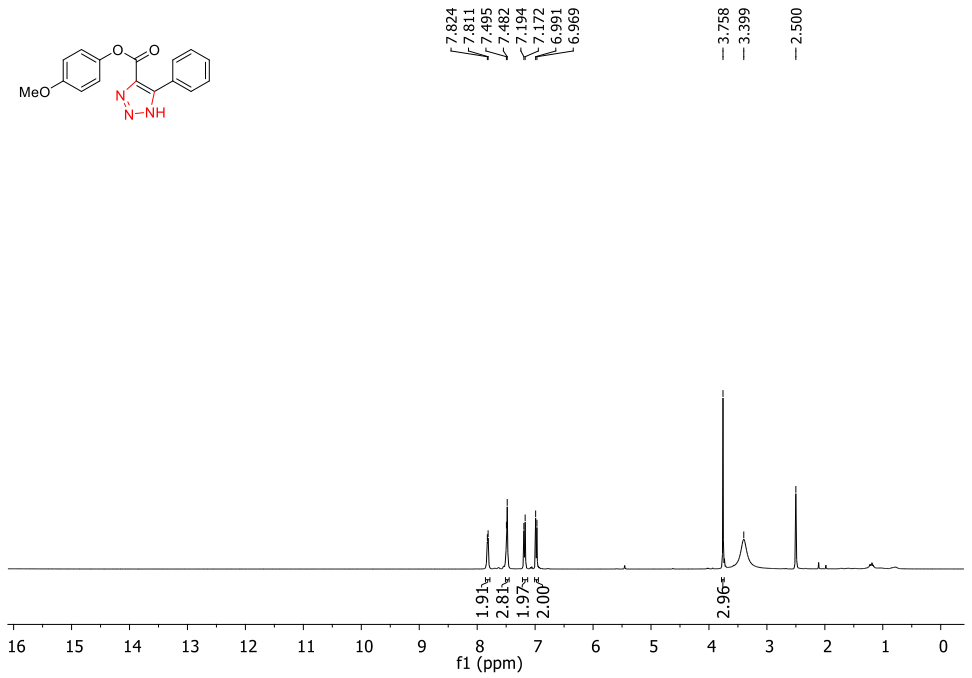

Figure 5.8. ^{1}H NMR spectrum of 4-methoxyphenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3b**) in DMSO-d_6.

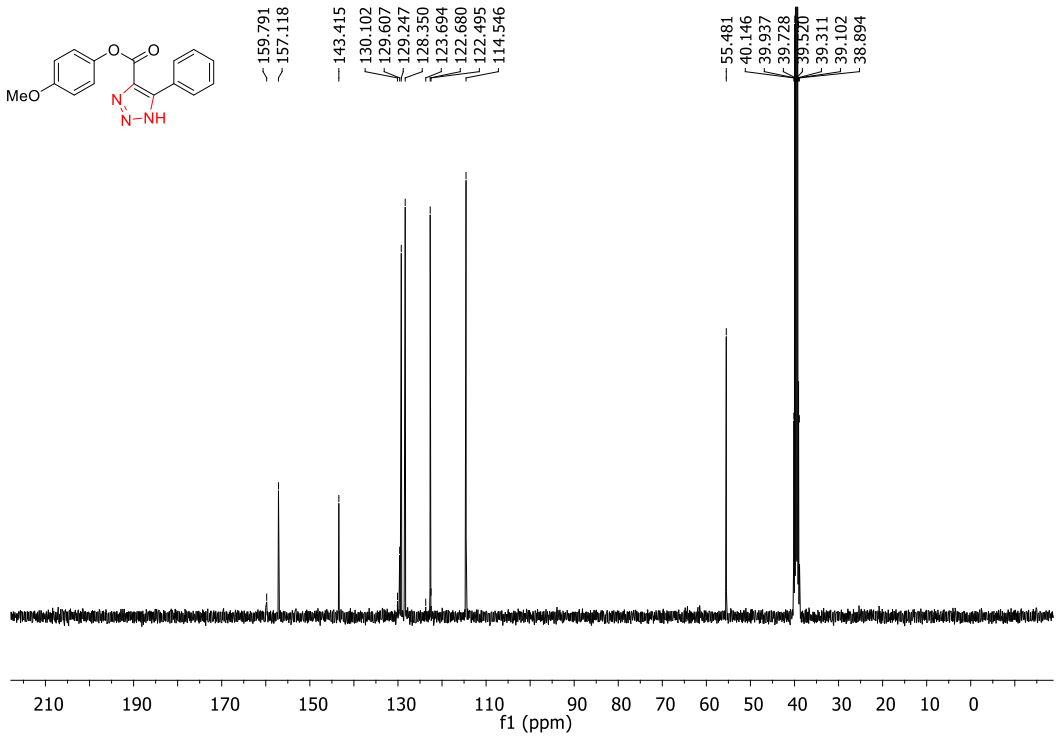

Figure 5.9. ^{13}C NMR spectrum of 4-methoxyphenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3b**) in DMSO-d$_6$.

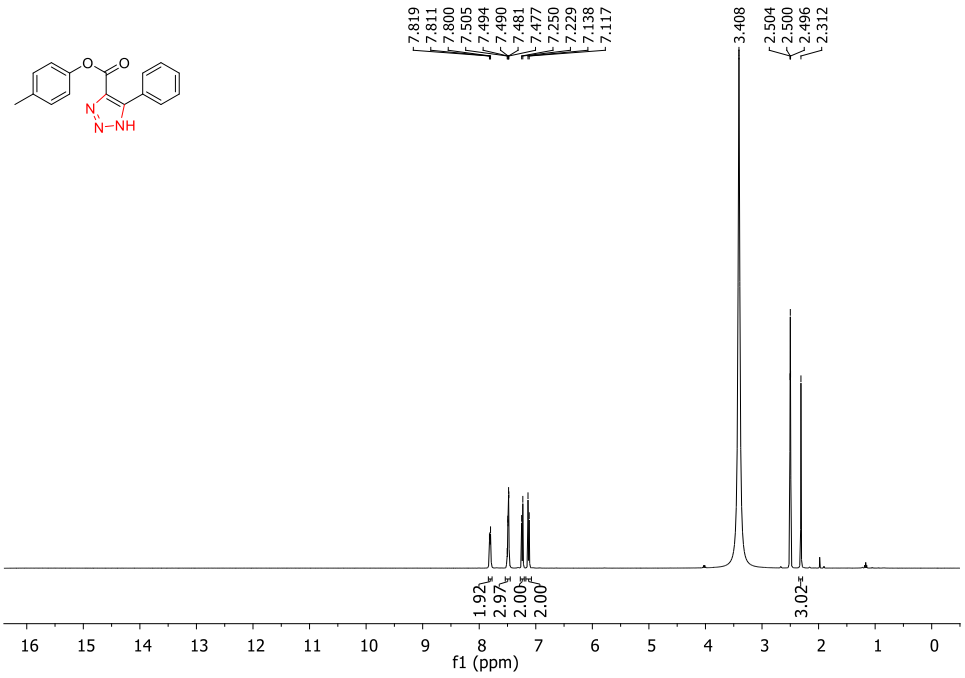

Figure 5.10. ^{1}H NMR spectrum of *p*-tolyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3c**) in DMSO-d$_6$.

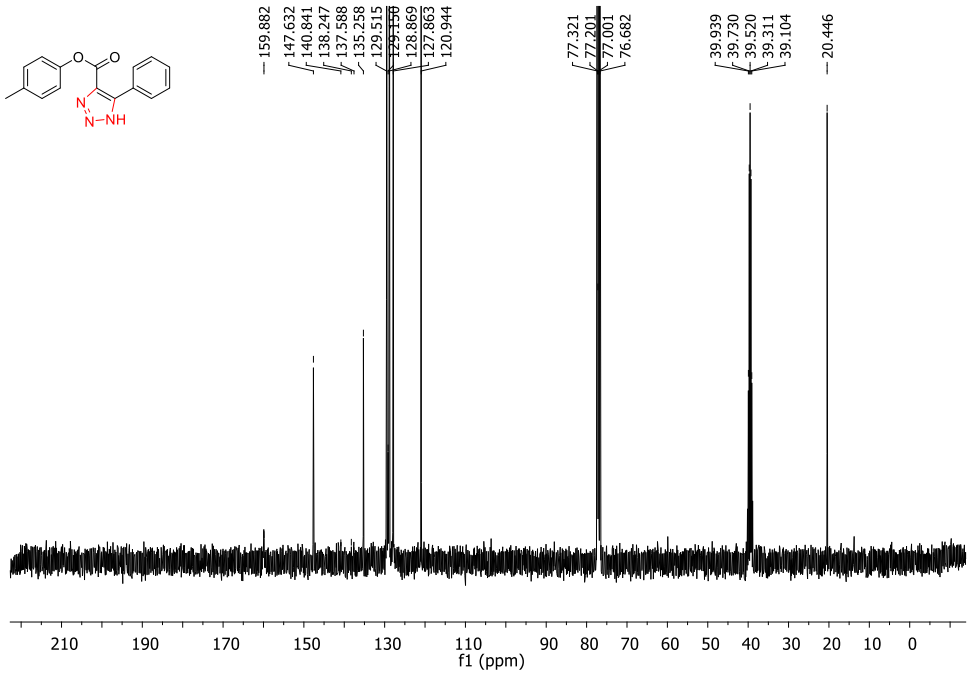

Figure 5.11. ^{13}C NMR spectrum of *p*-tolyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3c**) $CDCl_3$:DMSO-d_6

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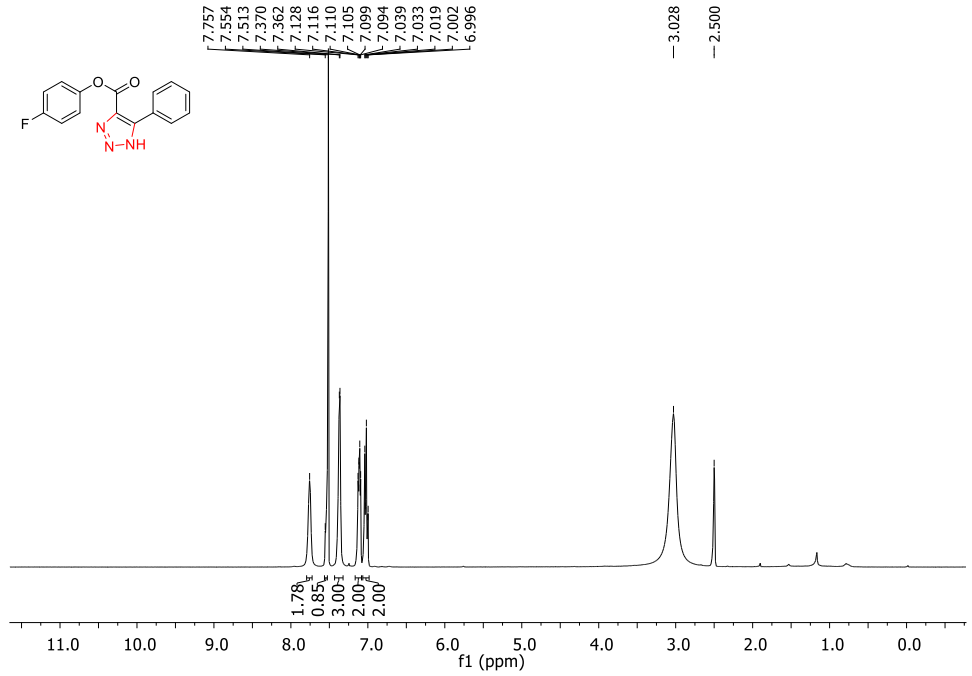


Figure 5.12. ^{1}H NMR spectrum of 4-fluorophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3d**) in $CDCl_3$: DMSO-d_6.

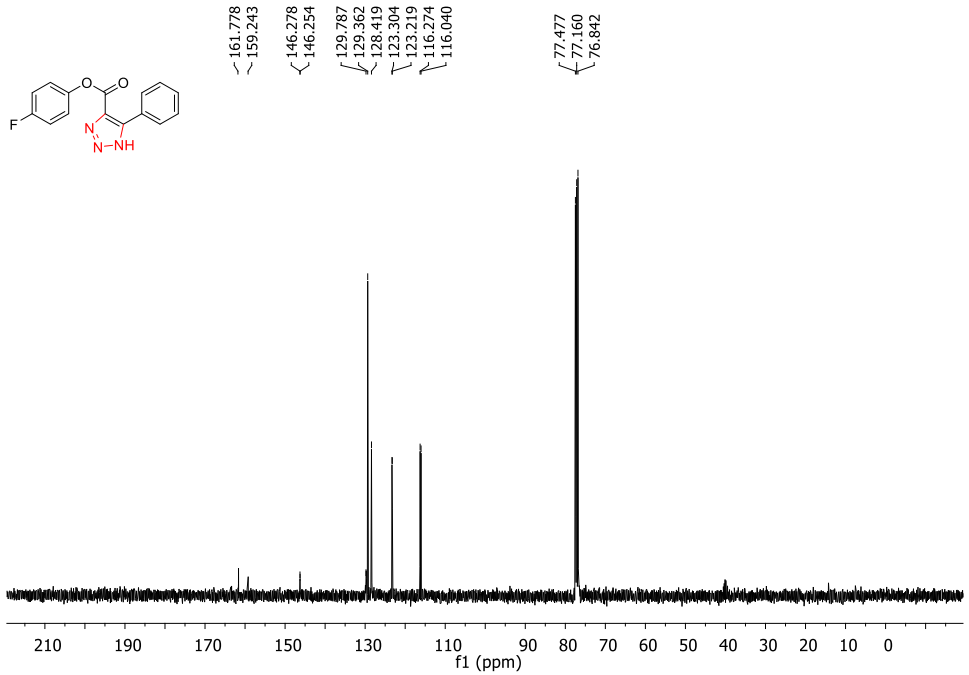


Figure 5.13. ^{13}C NMR spectrum of 4-fluorophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3d**) in $CDCl_3$.

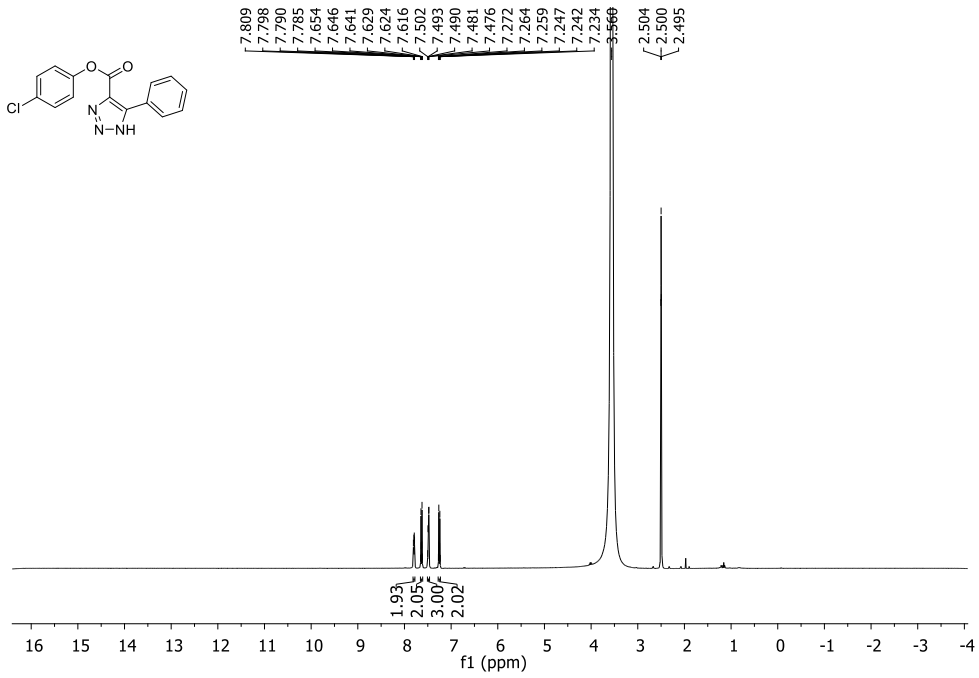


Figure 5.14. ^{1}H NMR spectrum of 4-chlorophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3e**) in DMSO-d_6

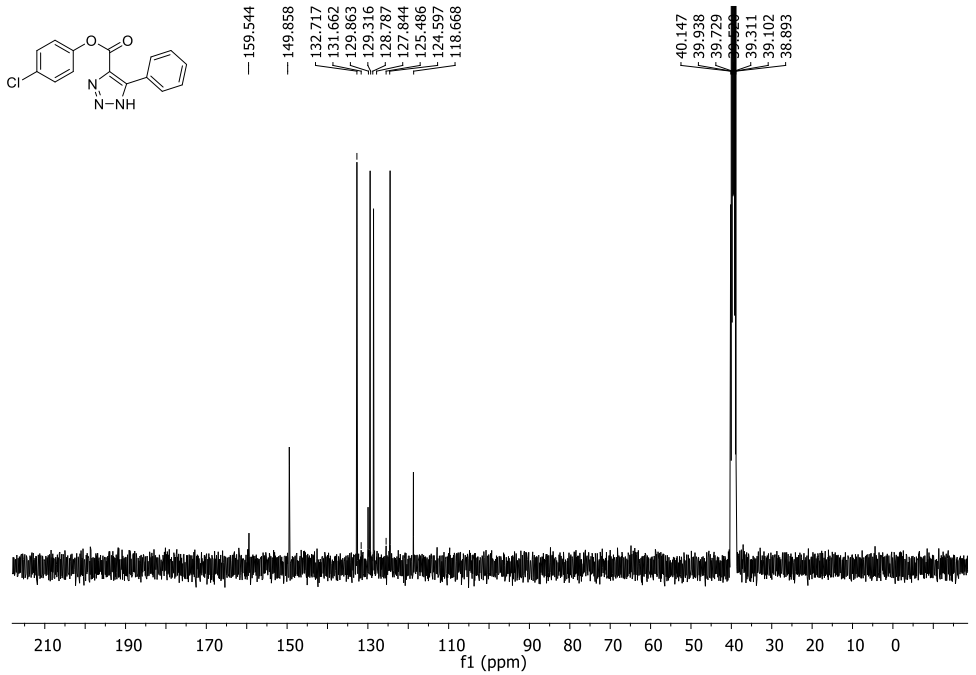


Figure 5.15. ^{13}C NMR spectrum of 4-chlorophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3e**) in DMSO-d$_6$.

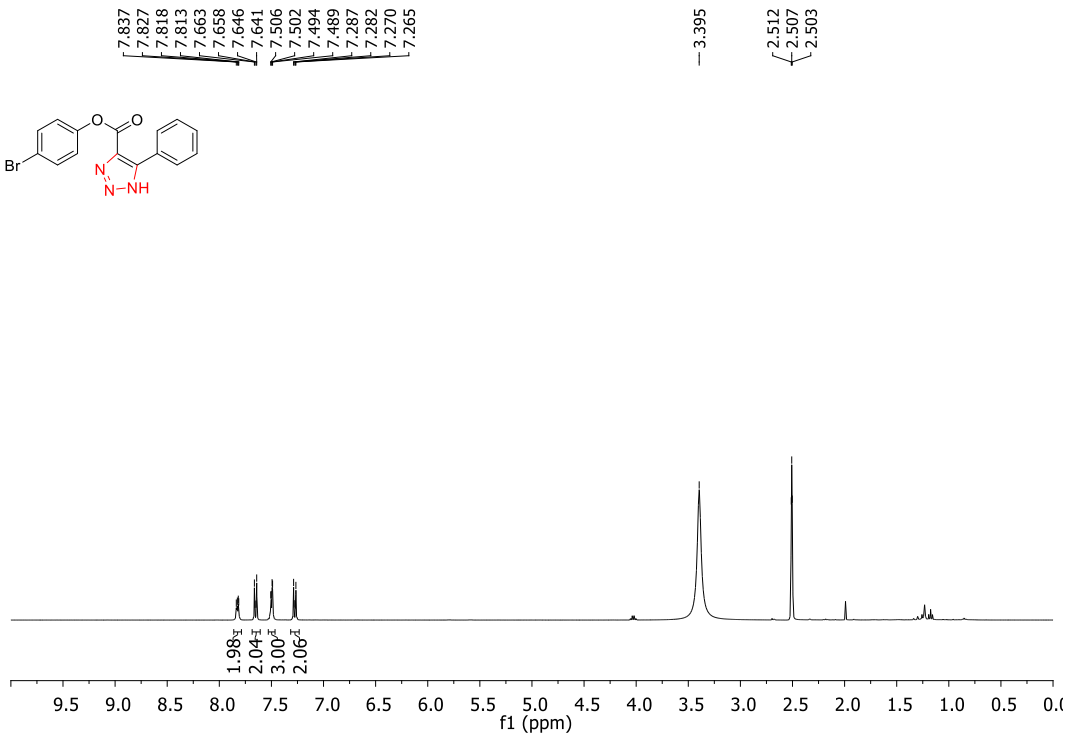


Figure 5.16. ^{1}H NMR spectrum of 4-bromophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3f**) in DMSO-d$_6$.

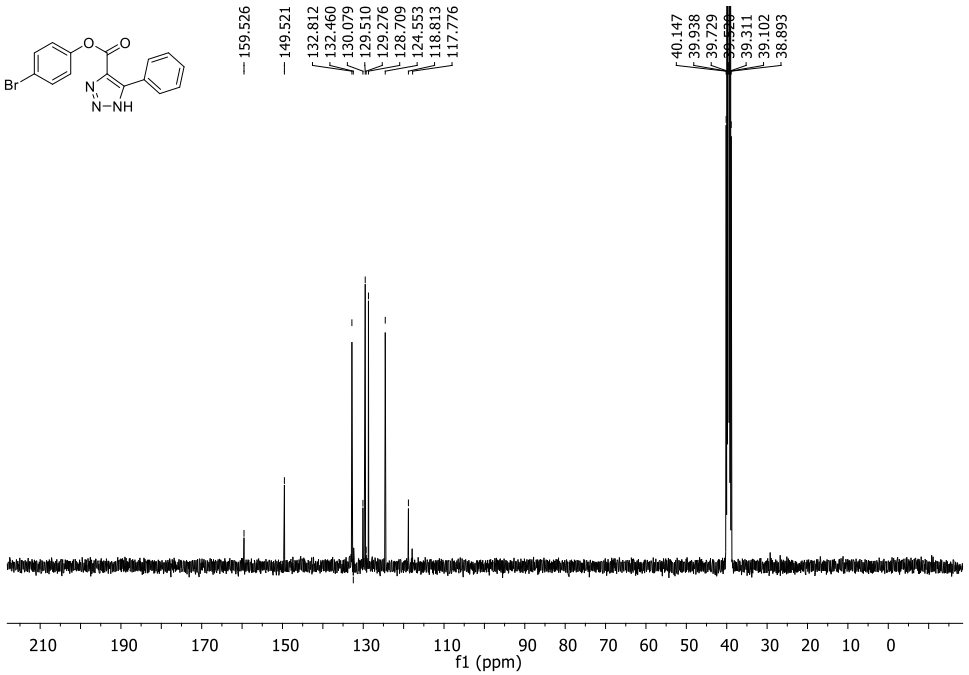


Figure 5.17. ^{13}C NMR spectrum of 4-bromophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3f**) in DMSO-d$_6$.

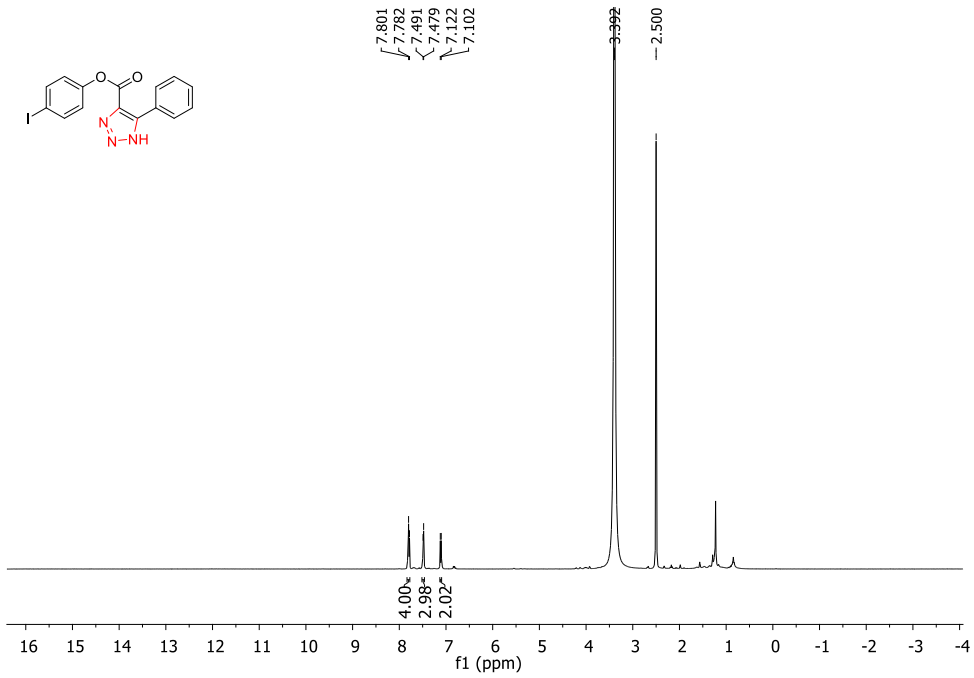


Figure 5.18. ^{1}H NMR spectrum of 4-iodophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3g**) in DMSO-d$_6$.

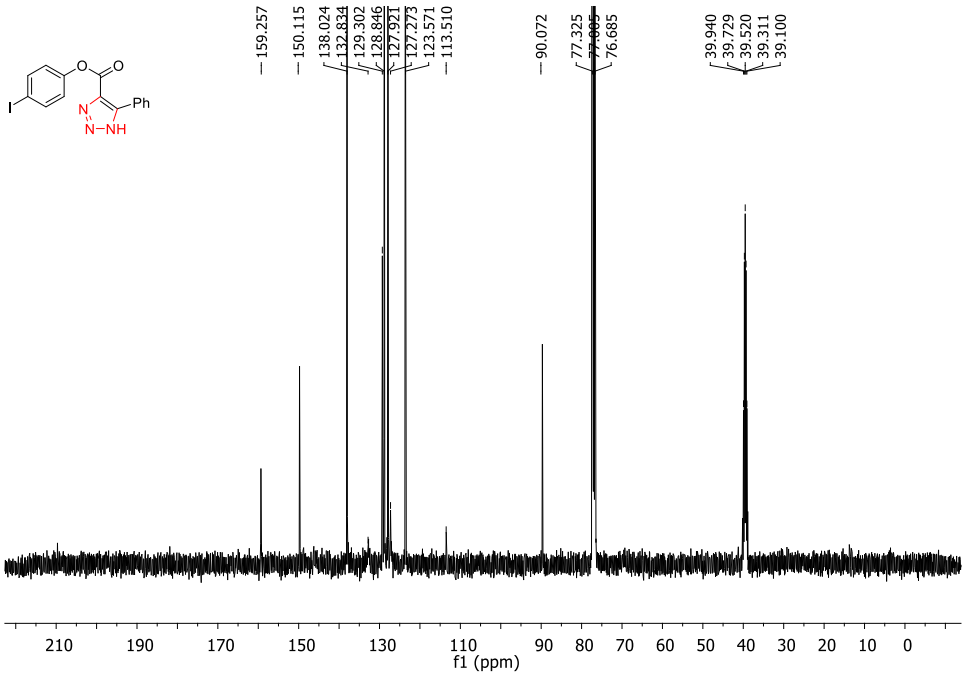


Figure 5.19. ^{13}C NMR spectrum of 4-iodophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3g**) in $CDCl_3$:DMSO-d_6.

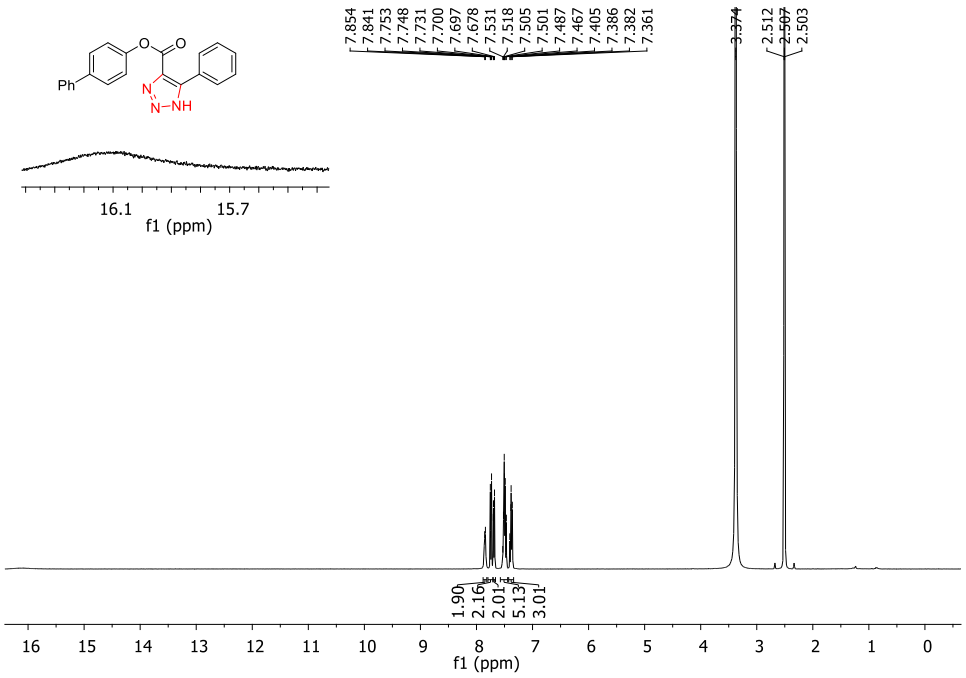


Figure 5.20. ^{1}H NMR spectrum of [1,1'-biphenyl]-4-yl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3h**) in DMSO-d_6.

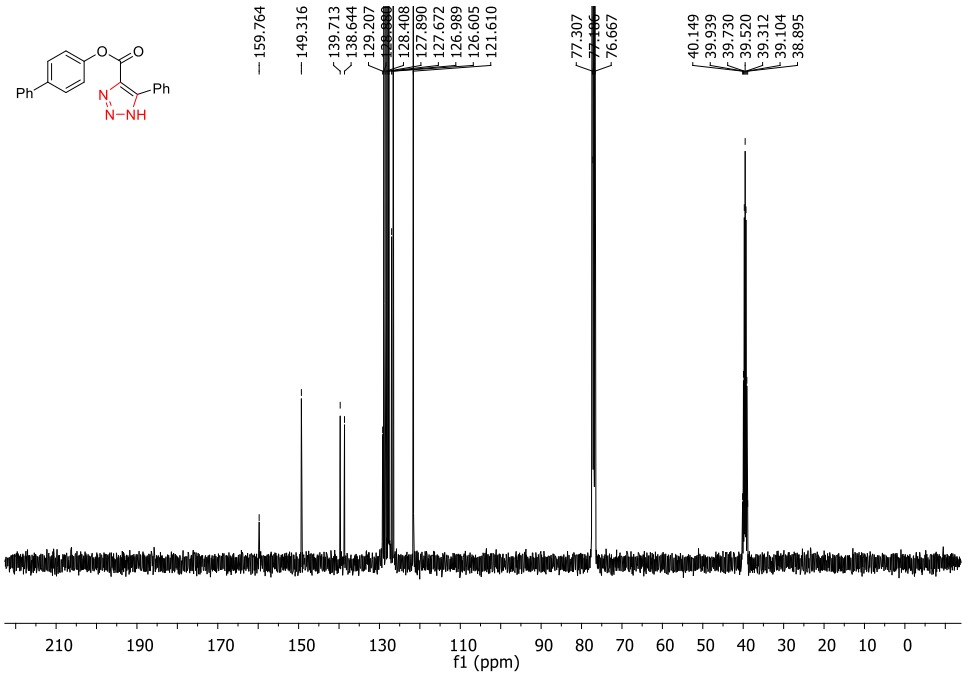


Figure 5.21. ^{13}C NMR spectrum of [1,1'-biphenyl]-4-yl 5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3h**) in $CDCl_3$: DMSO-d6.

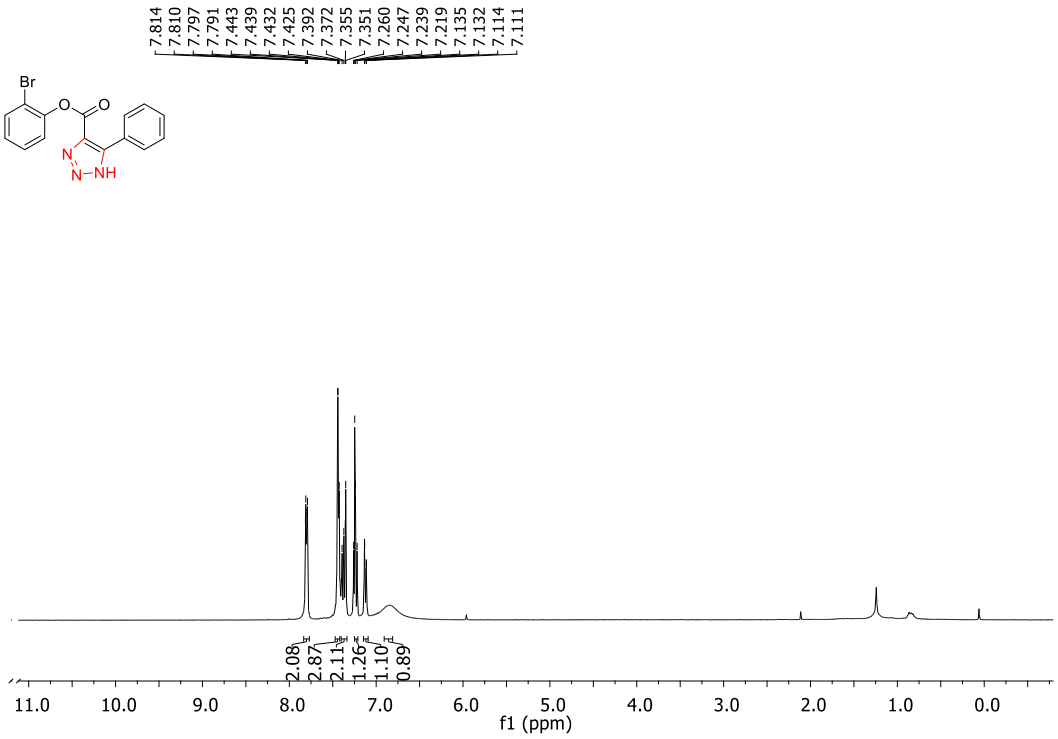


Figure 5.22. ^{1}H NMR spectrum of 3-bromophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3i**) in $CDCl_3$.

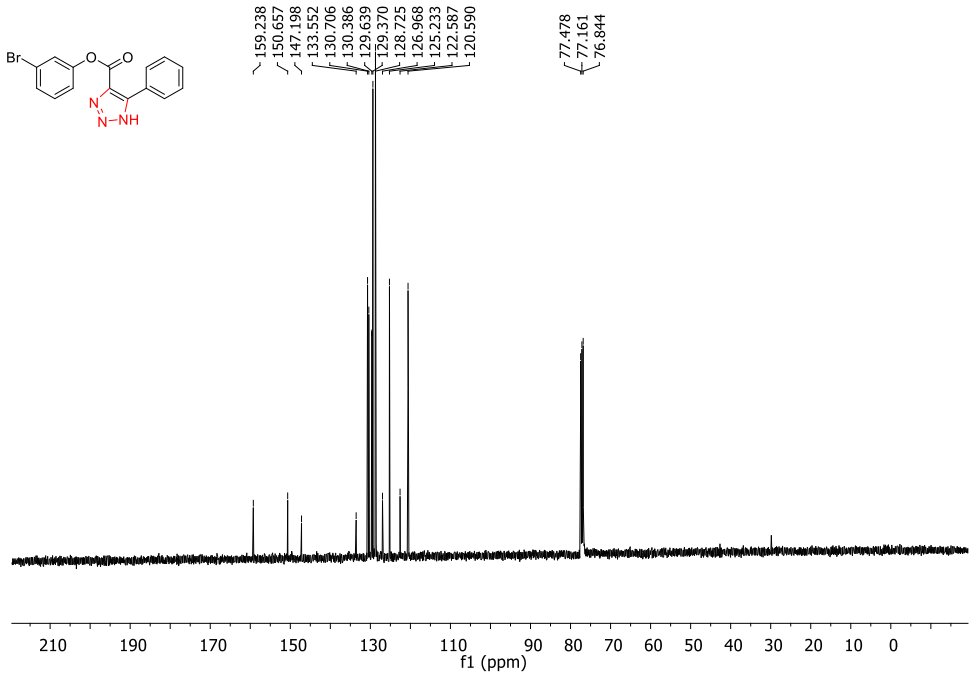


Figure 5.23. ^{13}C NMR spectrum of 3-bromophenyl 5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3i**) in $CDCl_3$.

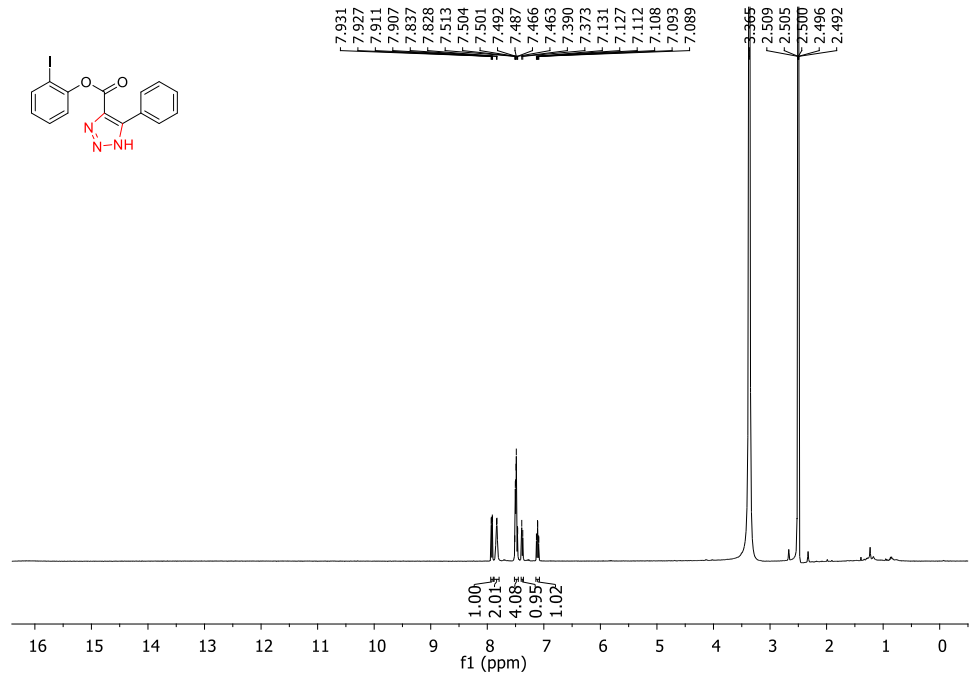


Figure 5.24. ^{1}H NMR spectrum of 2-iodophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3j**) in $CDCl_3$:DMSO-d_6.

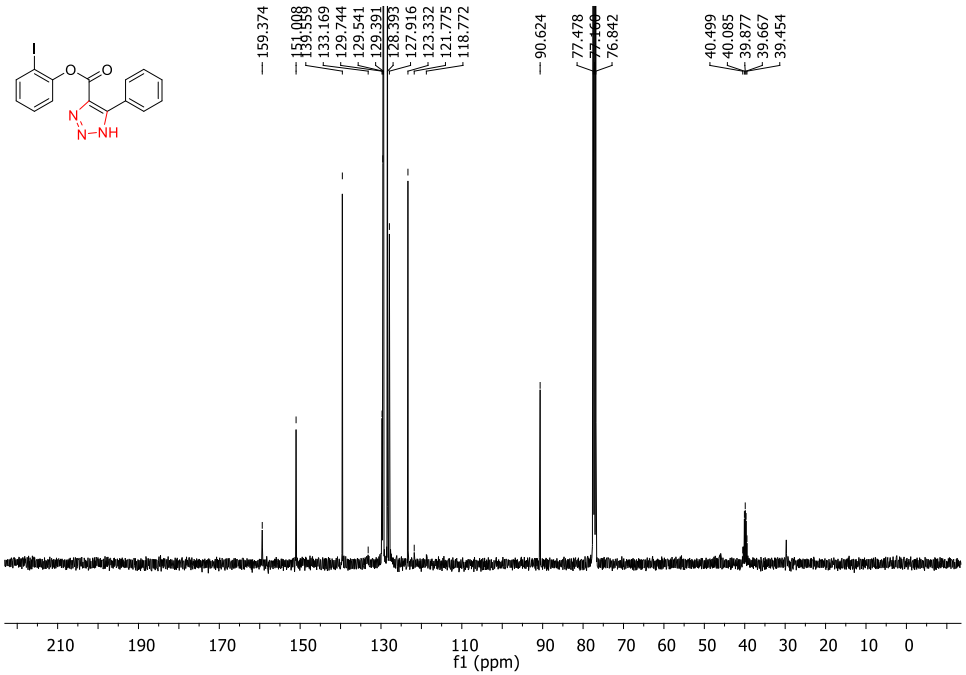


Figure 5.25. ^{13}C NMR spectrum of 2-iodophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3j**) in CDCl3: DMSO-d$_6$.

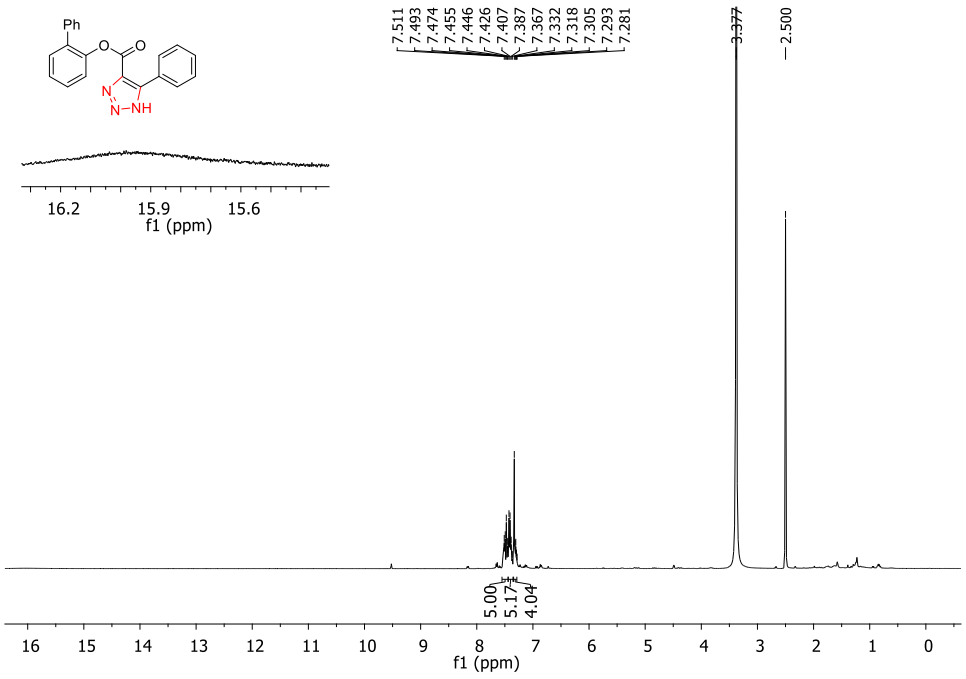


Figure 5.26. ^{1}H NMR spectrum of [1,1'-biphenyl]-2-yl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3k**) in DMSO-d$_6$.

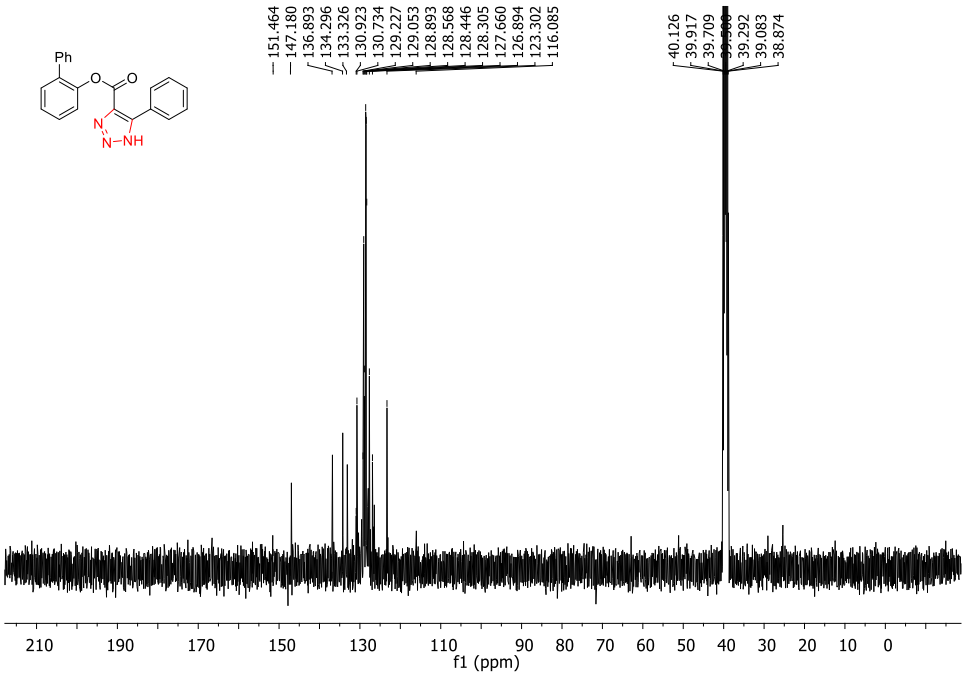


Figure 5.27. ^{13}C NMR spectrum of [1,1'-biphenyl]-2-yl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3k**) in DMSO-d_6.

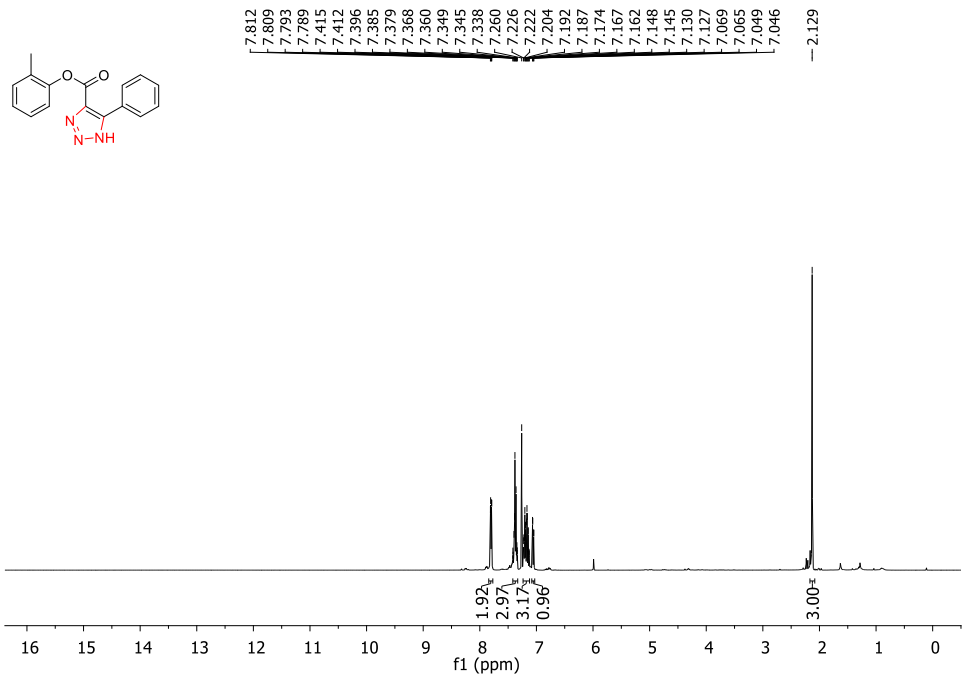


Figure 5.28. ^{1}H NMR spectrum of *o*-tolyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3l**) in $CDCl_3$.

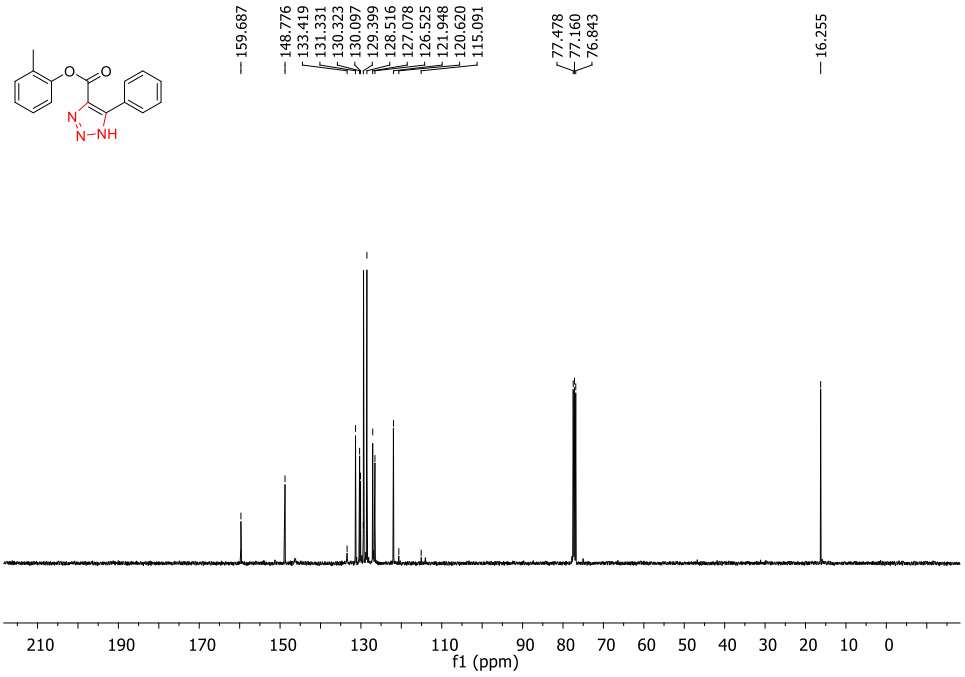


Figure 5.29. ^{13}C NMR spectrum of *o*-tolyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3l**) in $CDCl_3$.

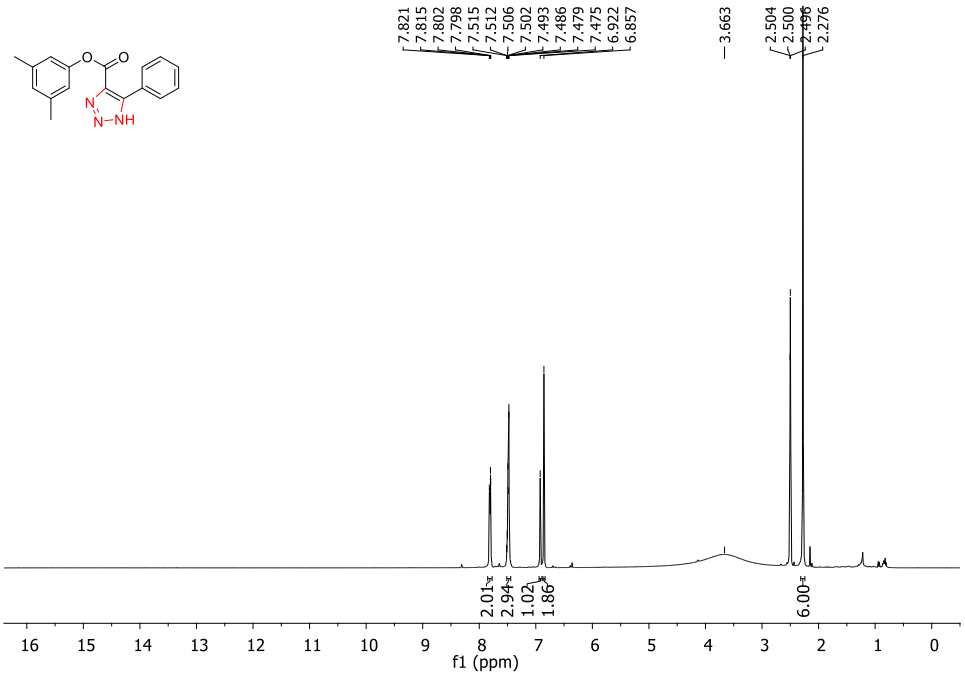


Figure 5.30. ^{1}H NMR spectrum of 3,5-dimethylphenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3m**) in DMSO-d_6.

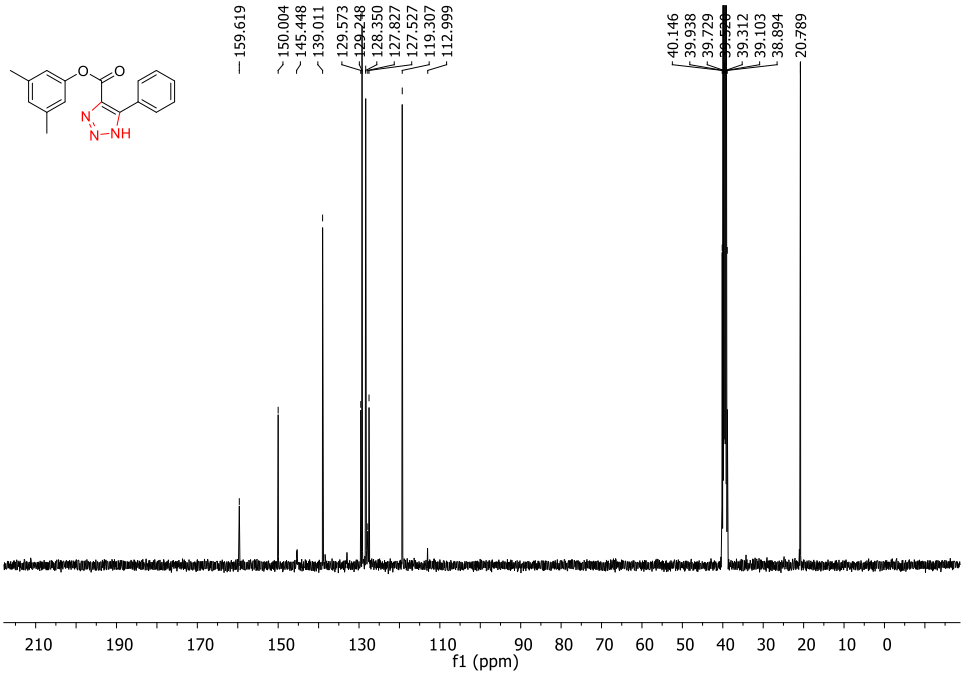


Figure 5.31. ^{13}C NMR spectrum of 3,5-dimethylphenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3m**) in DMSO-d_6.

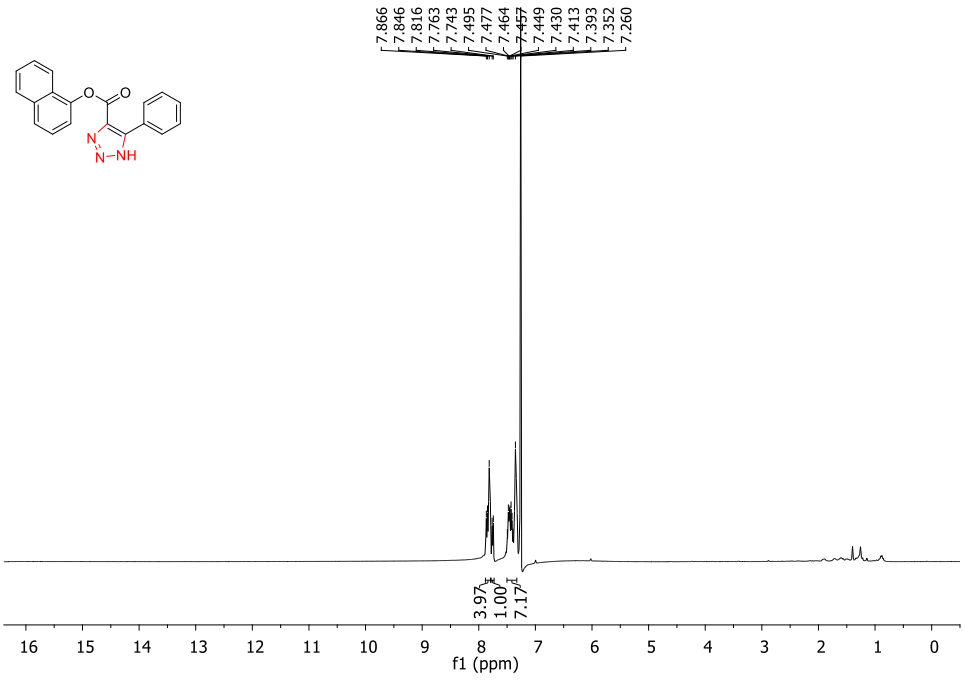


Figure 5.32. ^{1}H NMR spectrum of naphthalen-1-yl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3n**) in $CDCl_3$.

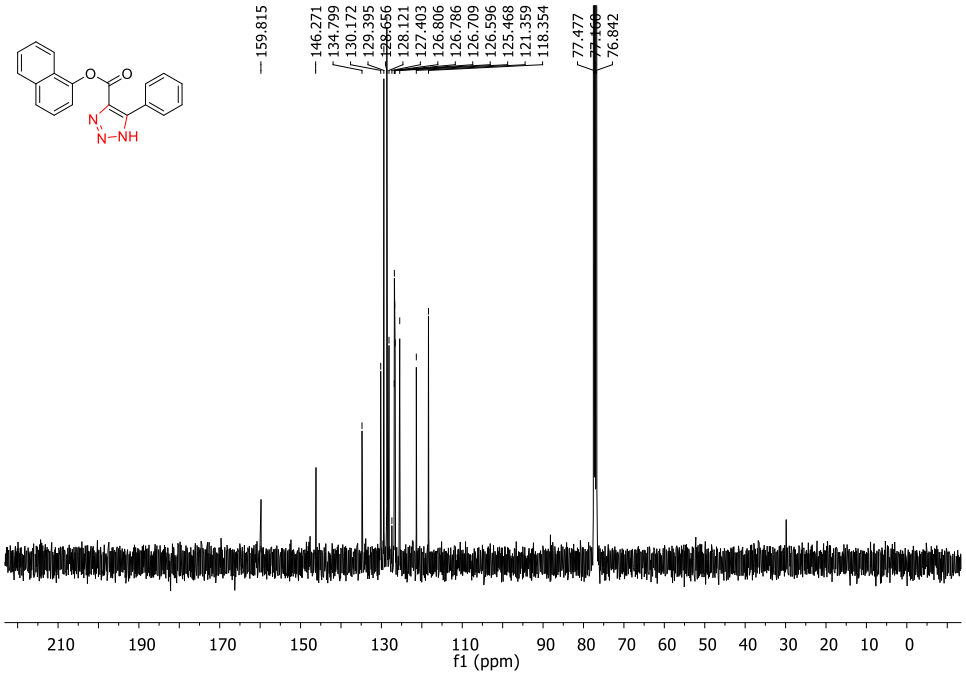


Figure 5.33. ^{13}C NMR spectrum of naphthalen-1-yl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3n**) in $CDCl_3$.

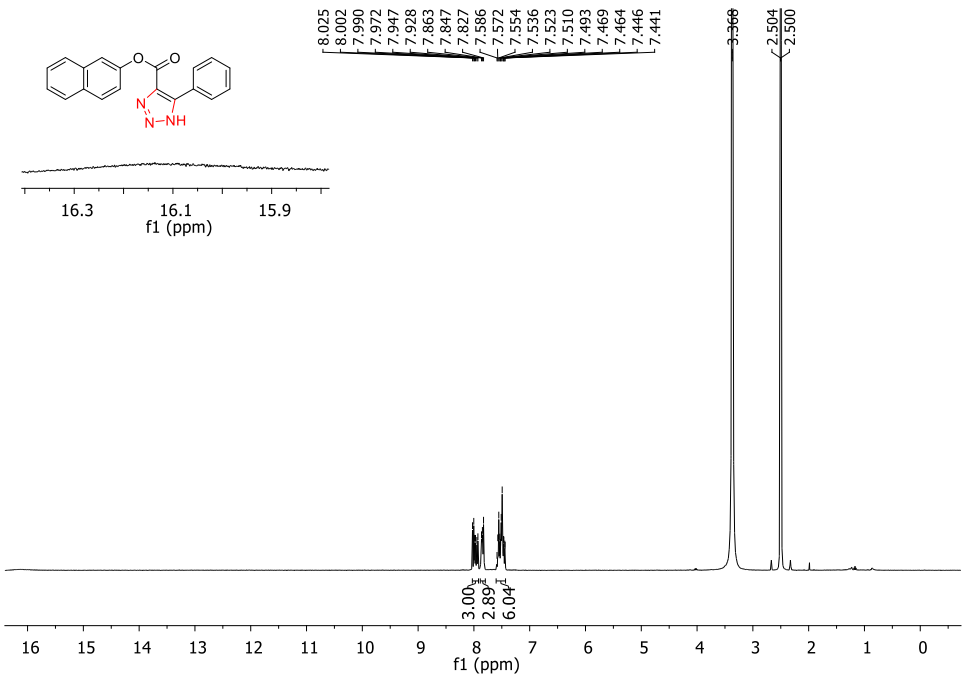


Figure 5.34. ^{1}H NMR spectrum of naphthalen-2-yl 5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3o**) in DMSO-d_6.

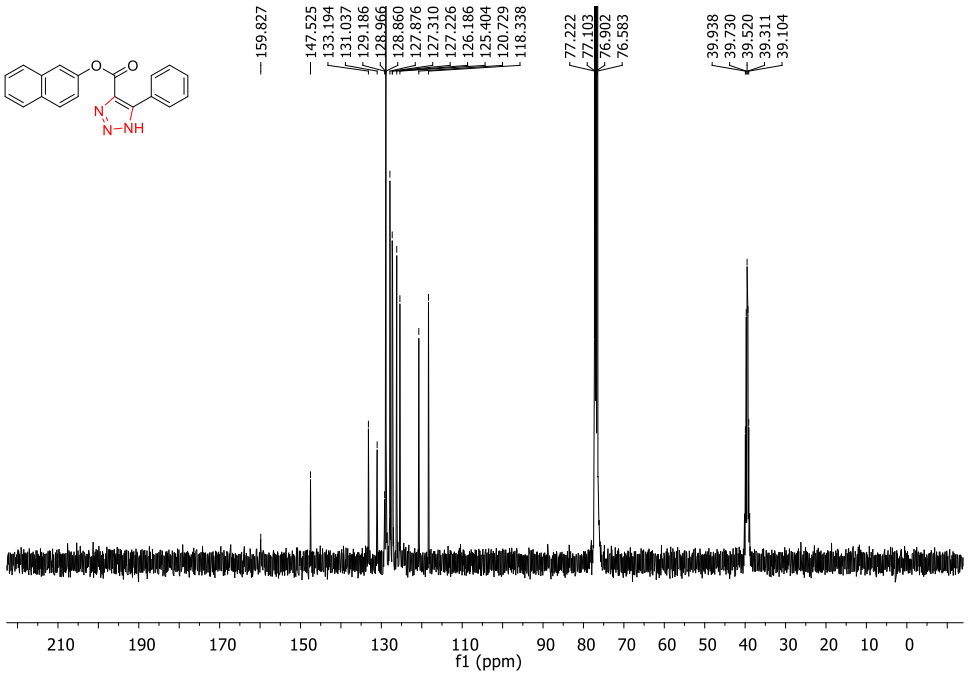


Figure 5.35. ^{13}C NMR spectrum of naphthalen-2-yl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3o**) in $CDCl_3$: DMSO-d_6.

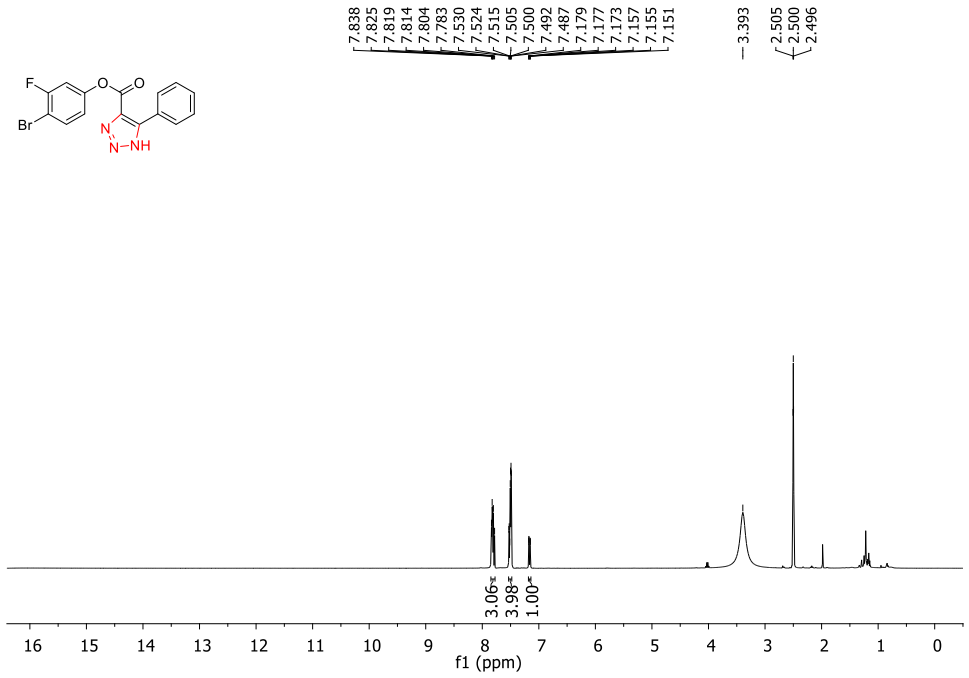


Figure 5.36. ^{1}H NMR spectrum of 4-bromo-3-fluorophenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3p**) in DMSO-d_6.

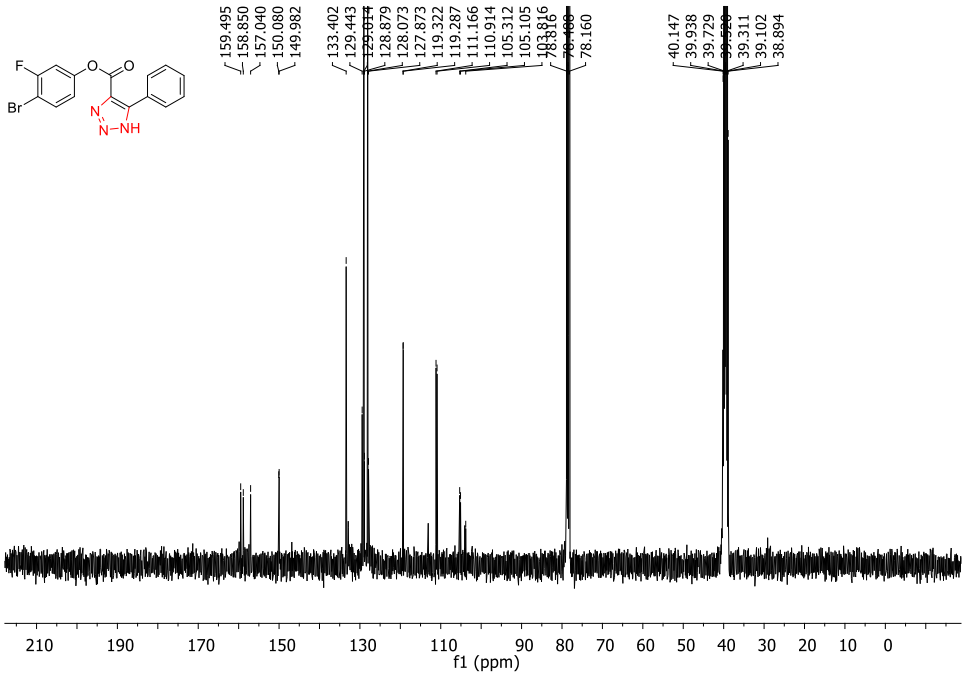


Figure 5.37. ^{13}C NMR spectrum of 4-bromo-3-fluorophenyl 5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3p**) in $CDCl_3$: DMSO-d_6.

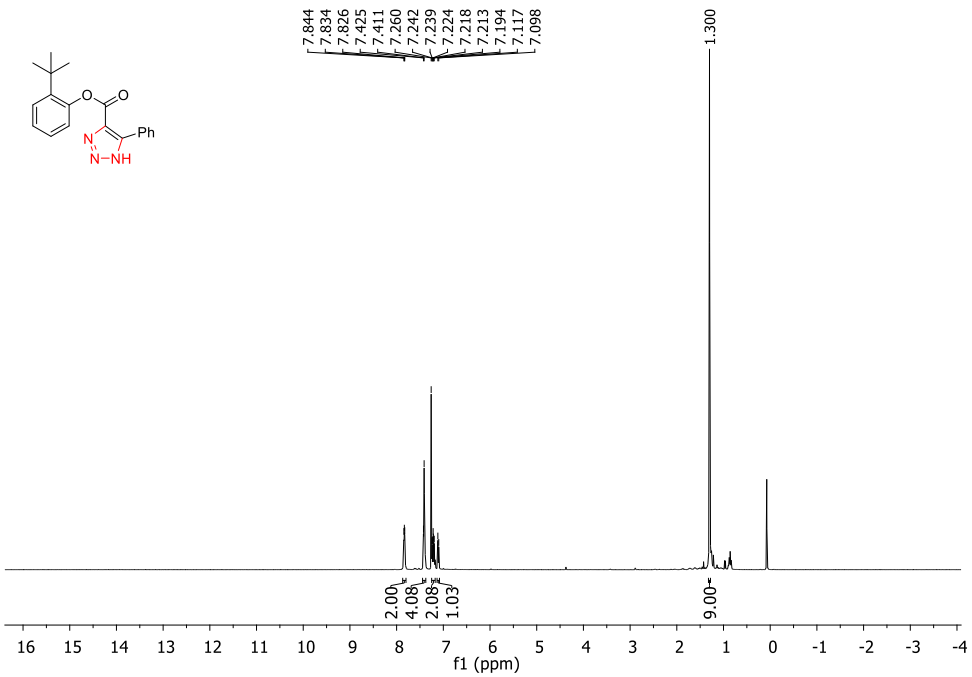


Figure 5.38. ^{1}H NMR spectrum of 2-(*tert*-butyl)phenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3q**) in $CDCl_3$.

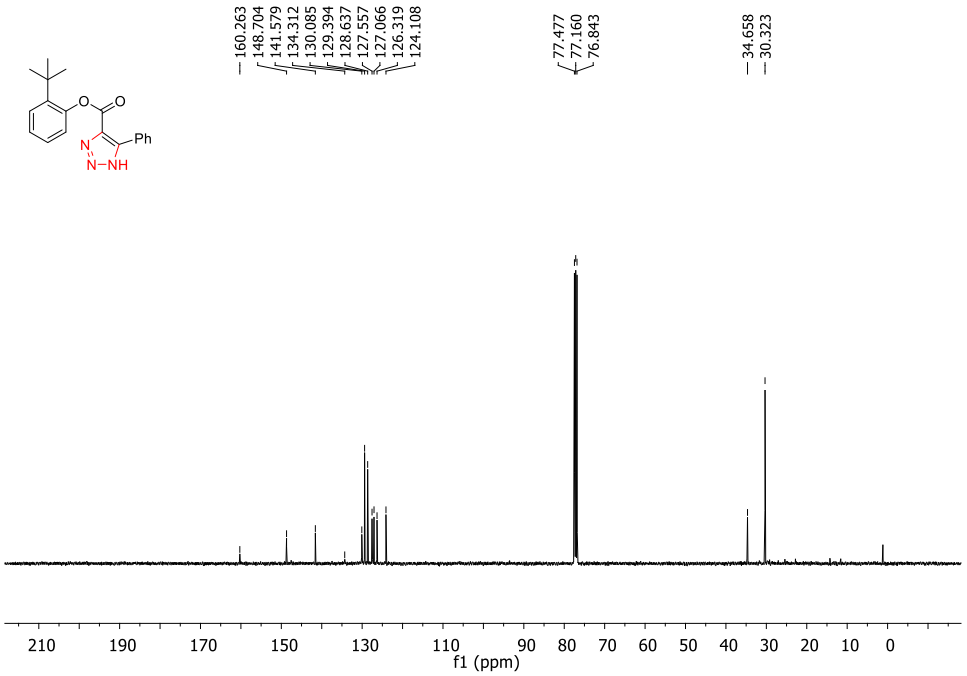


Figure 5.39. ^{13}C NMR spectrum of 2-(*tert*-butyl)phenyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3q**) in $CDCl_3$.

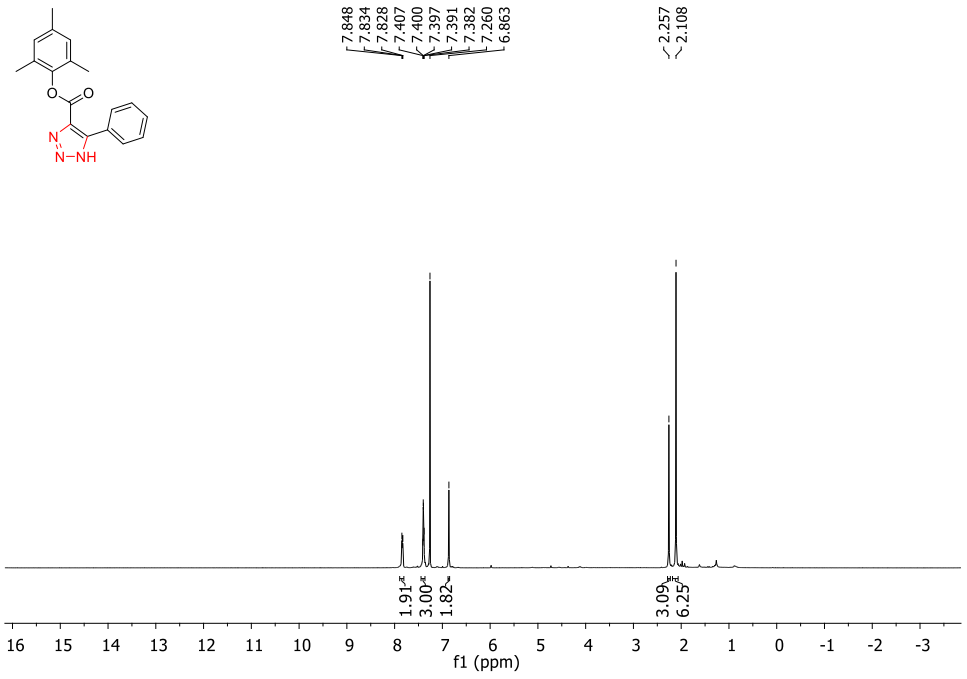


Figure 5.40. ^{1}H NMR spectrum of mesityl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3r**) in $CDCl_3$.

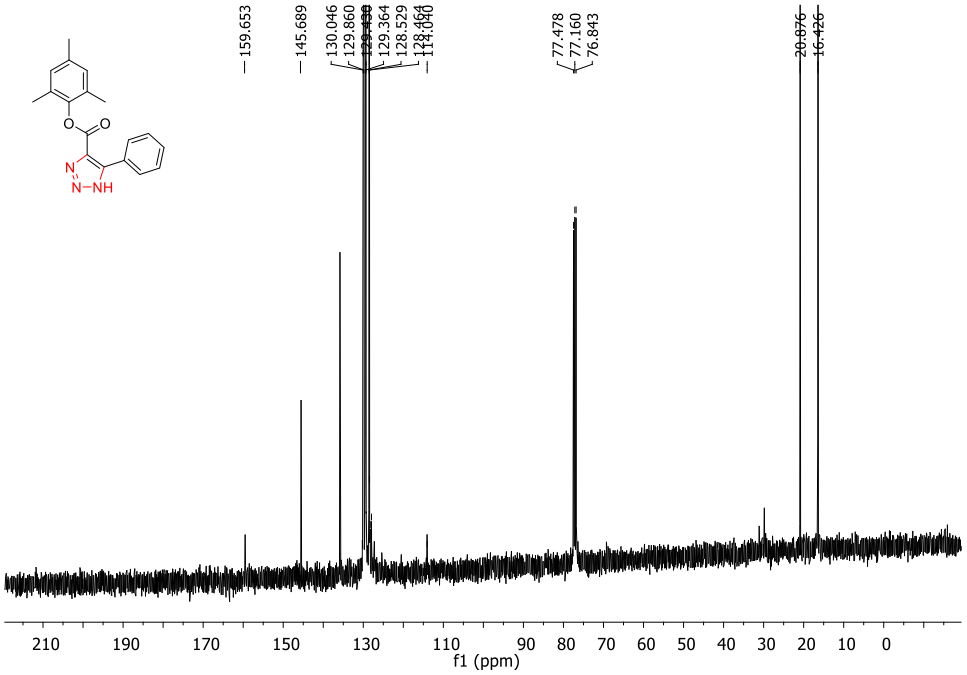


Figure 5.41. ^{13}C NMR spectrum of mesityl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3r**) in $CDCl_3$.

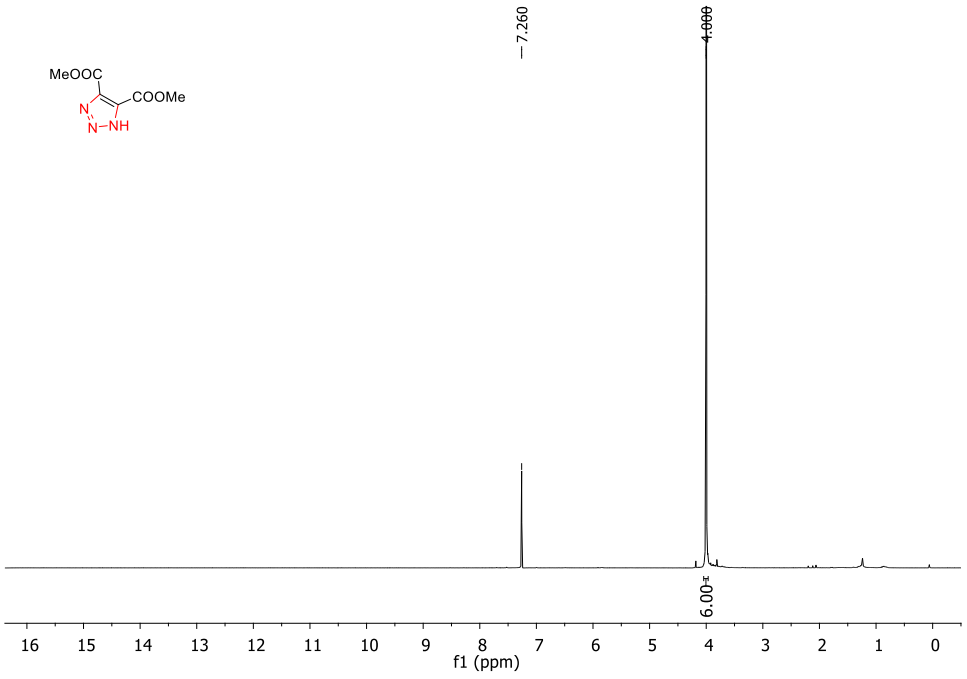


Figure 5.42. ^{1}H NMR spectrum of dimethyl-1 *H*-1,2,3-triazole-4,5-dicarboxylate (**3s**) in $CDCl_3$.

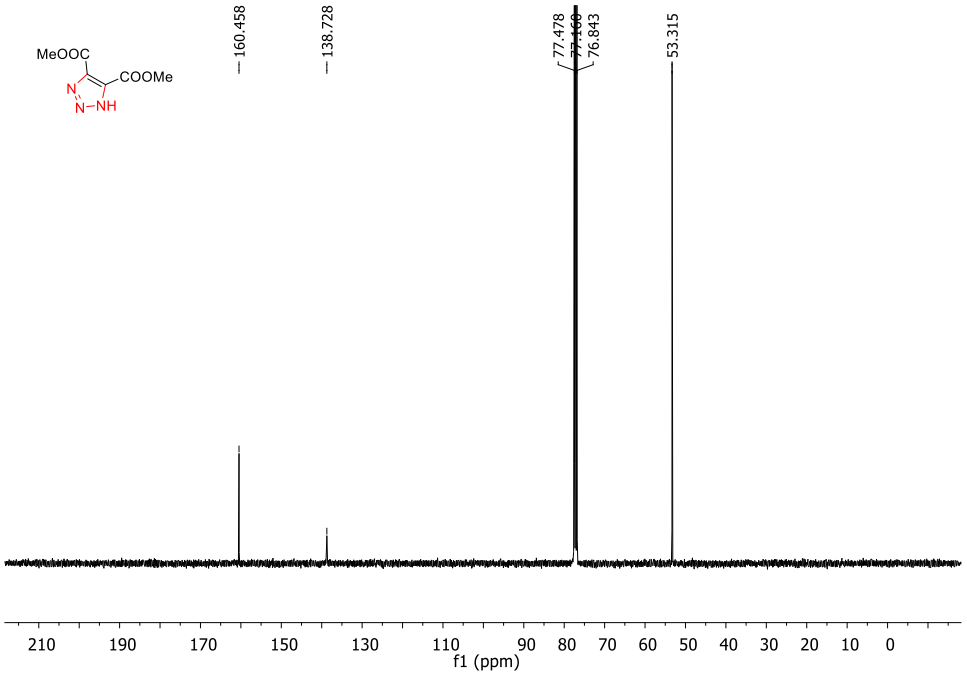


Figure 5.43. ^{13}C NMR spectrum of dimethyl-1 *H*-1,2,-3-triazole-4,-5-dicarboxylate (**3s**) in $CDCl_3$.

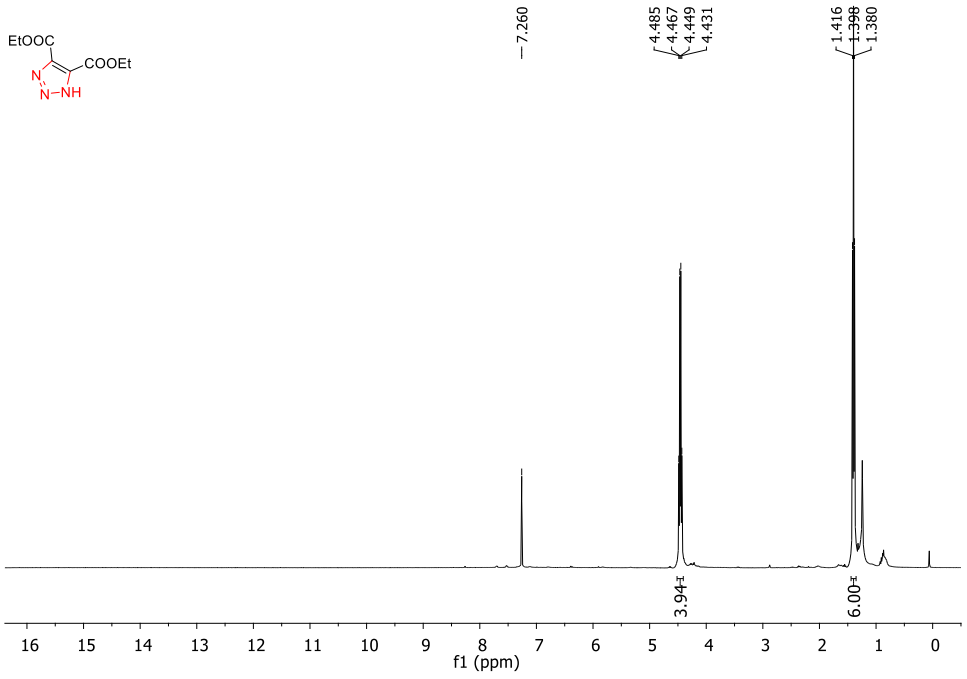


Figure 5.44. ^{1}H NMR spectrum of diethyl-1*H*-1,2,3-triazole-4,5-dicarboxylate (**3t**) in $CDCl_3$.

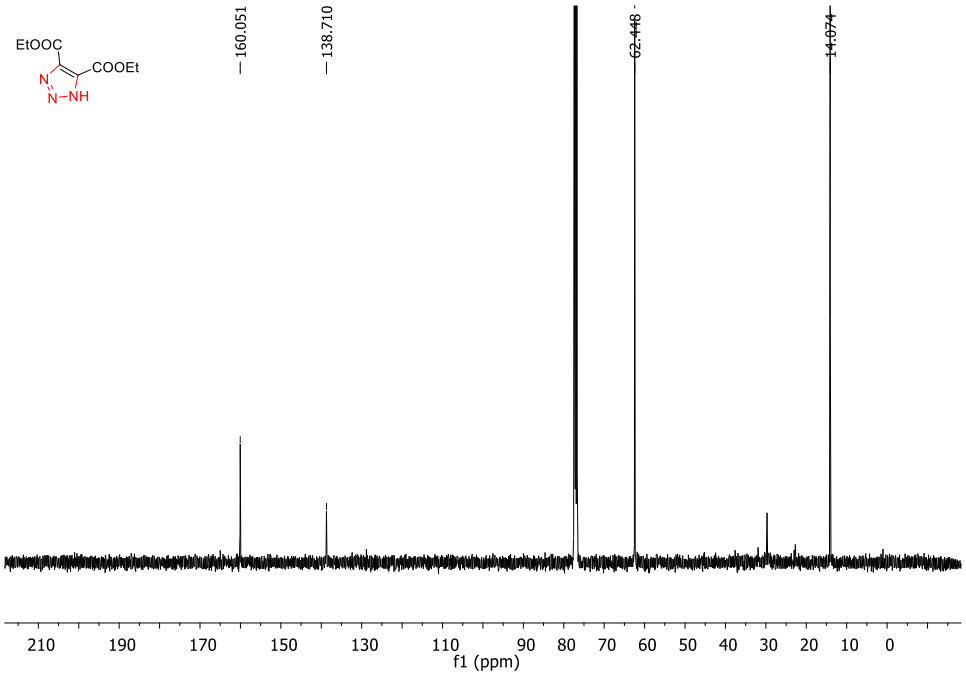


Figure 5.45. ^{13}C NMR spectrum of diethyl-1*H*-1,2,3-triazole-4,5-dicarboxylate (**3t**) in $CDCl_3$.

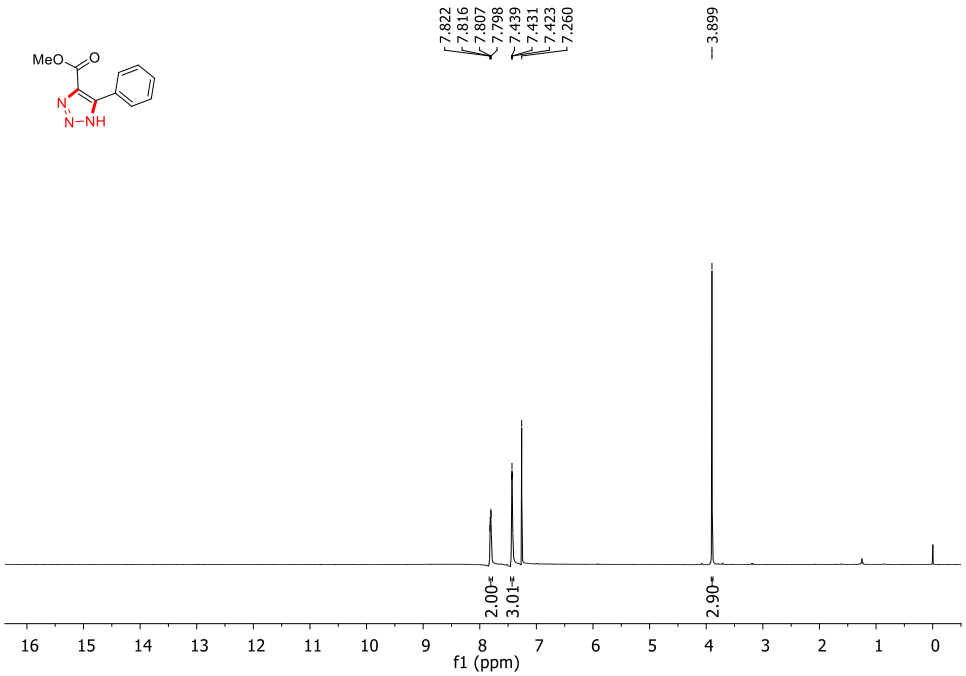


Figure 5.46. ^{1}H NMR spectrum of methyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3u**) in $CDCl_3$.

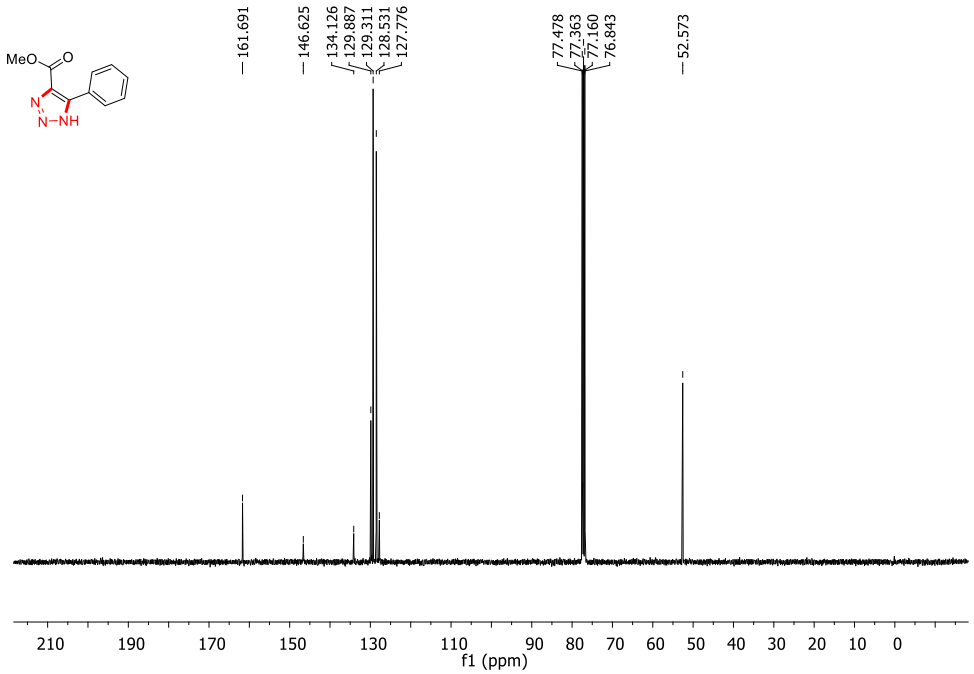


Figure 5.47. ^{13}C NMR spectrum of methyl-5-phenyl-1*H*-1,2,3-triazole-4-carboxylate (**3u**) in $CDCl_3$.

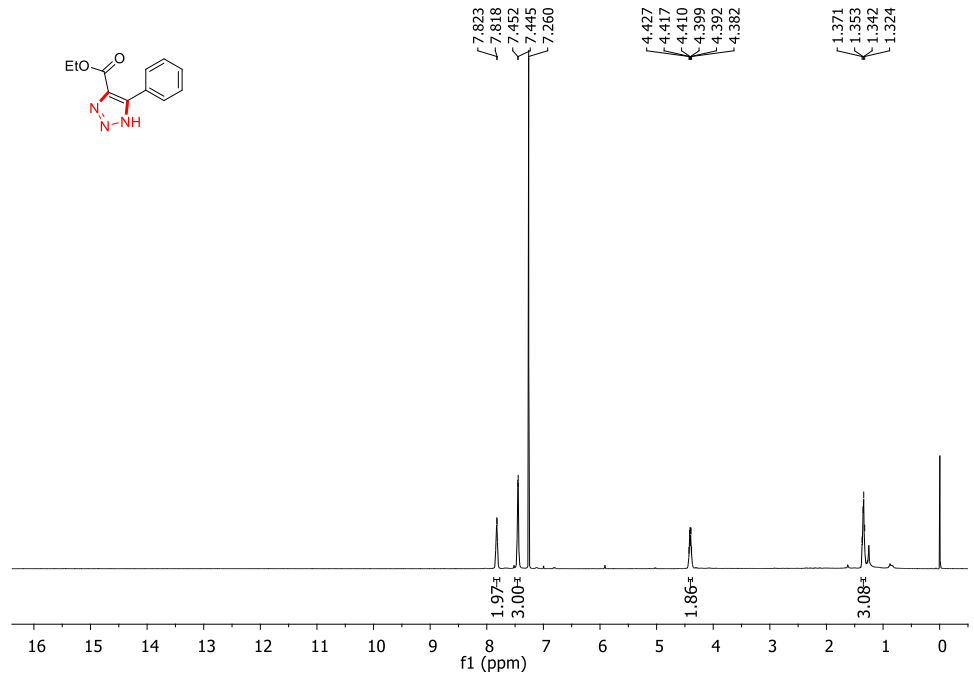


Figure 5.48. ^{1}H NMR spectrum of ethyl-5-phenyl-1H-1,2,3-triazole-4-carboxylate (**3v**) in $CDCl_3$

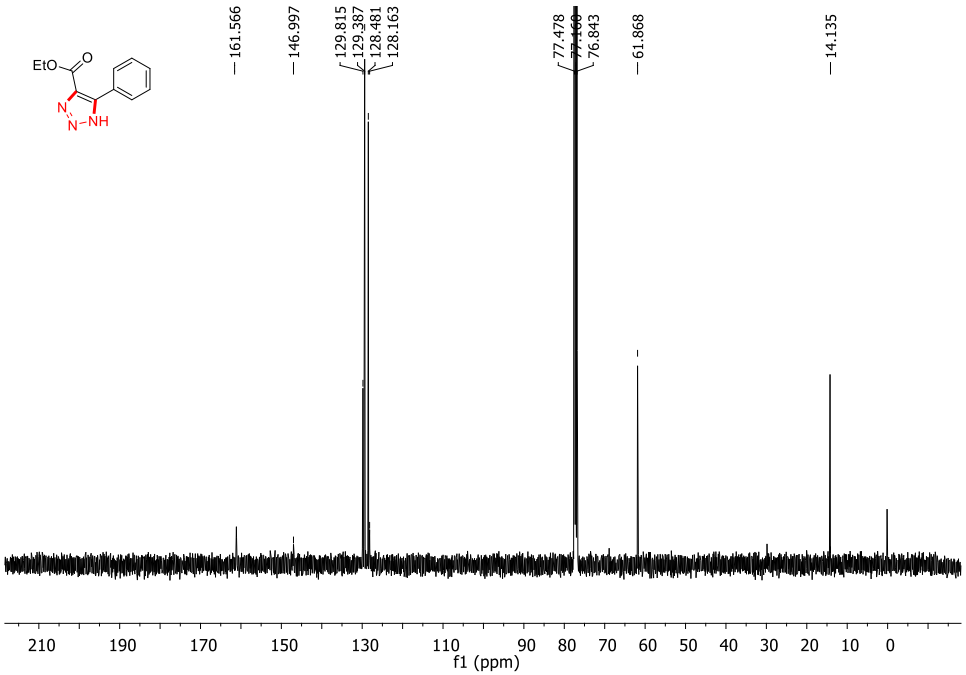


Figure 5.49. ^{13}C NMR spectrum of ethyl-5-phenyl-1H-1,2,3-triazole-4-carboxylate (**3v**) in $CDCl_3$.

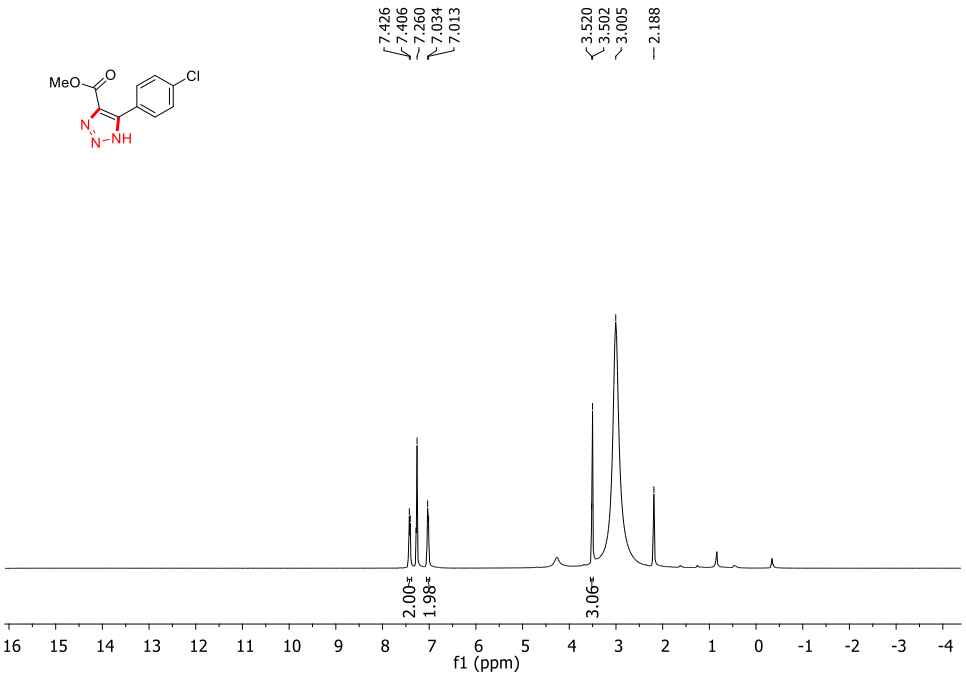


Figure 5.50. ^{1}H NMR spectrum of methyl-5-(4-chlorophenyl-1*H*-1,2,3-triazole-4-carboxylate (**3w**) in $CDCl_3$:DMSO-d_6.

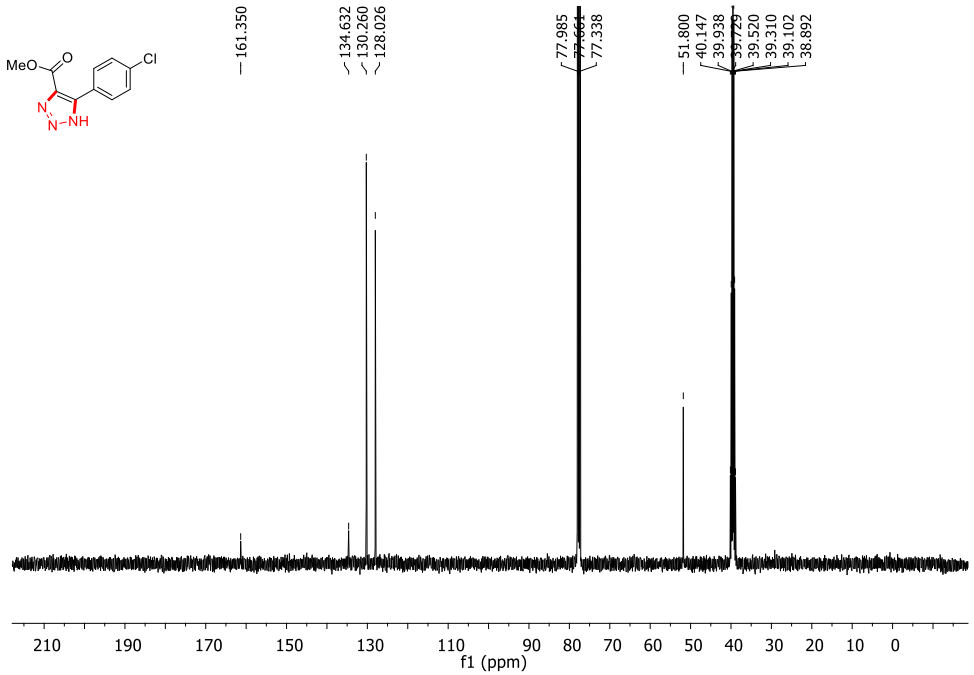


Figure 5.51. ^{13}C NMR spectrum of methyl-5-(4-chlorophenyl-1*H*-1,2,3-triazole-4-carboxylate (**3w**) in $CDCl_3$:DMSO-d_6.

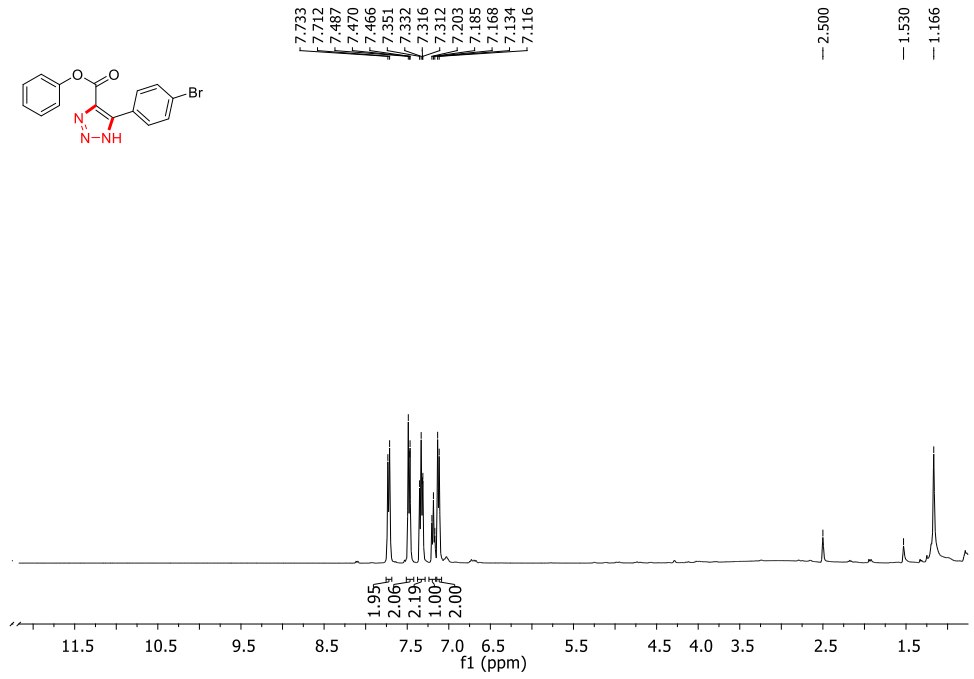


Figure 5.52. ^{1}H NMR spectrum of phenyl 5-(4-bromophenyl)-1*H*-1,2,3-triazole-4-carboxylate (**3x**) in DMSO-d_6.

.

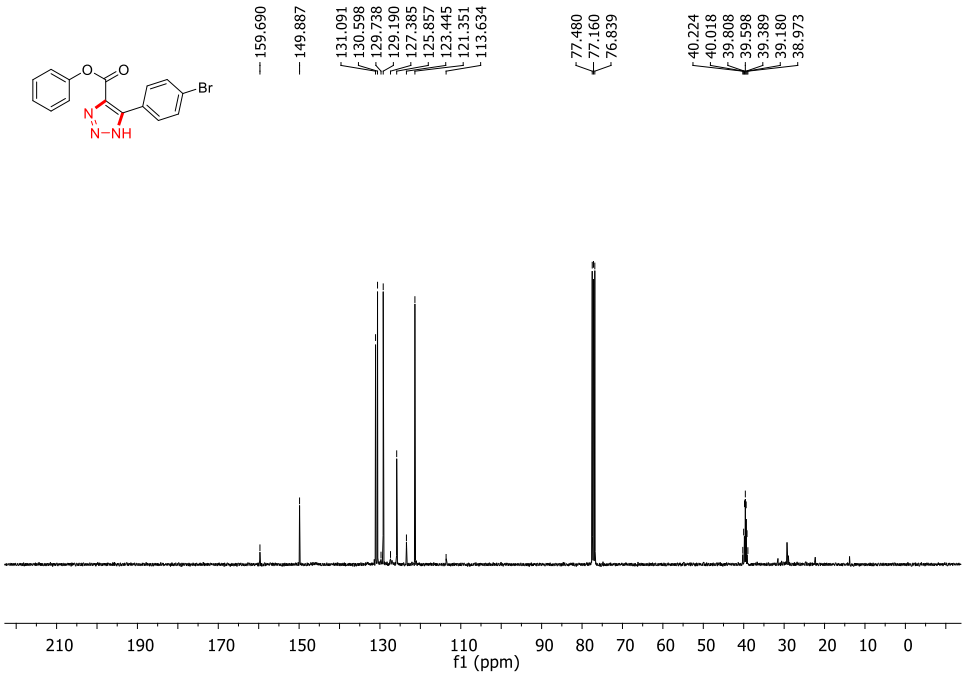


Figure 5.53. ^{13}C NMR spectrum of phenyl-5-(4-bromophenyl)-1*H*-1,2,3-triazole-4-carboxylate (**3x**) in $CDCl_3$:DMSO-d_6.

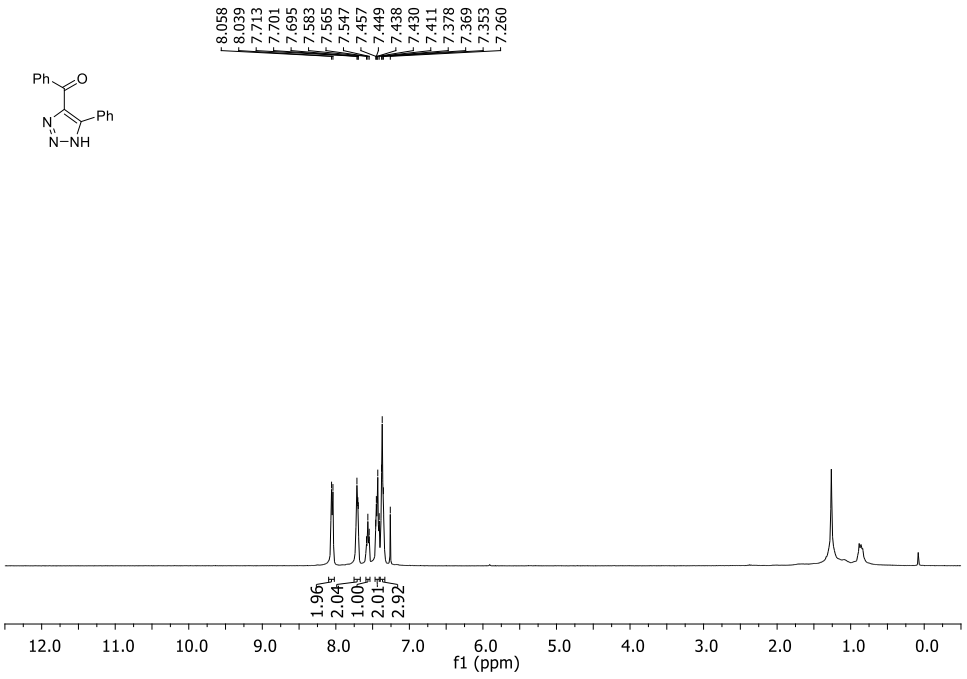


Figure 5.54. ^{1}H NMR spectrum of phenyl (5-phenyl-1H-1,2,3triazol-4-yl)methanone (**4y**) in $CDCl_3$.

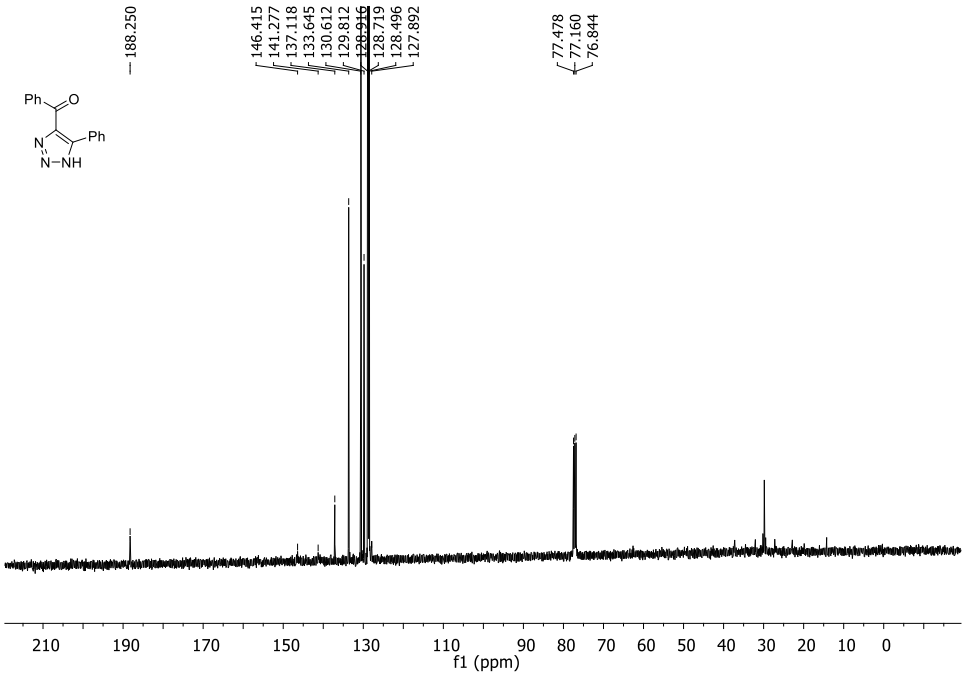


Figure 5.55. ^{13}C NMR spectrum of phenyl (5-phenyl-1H-1,2,3triazol-4-yl)methanone (**4y**) in $CDCl_3$.

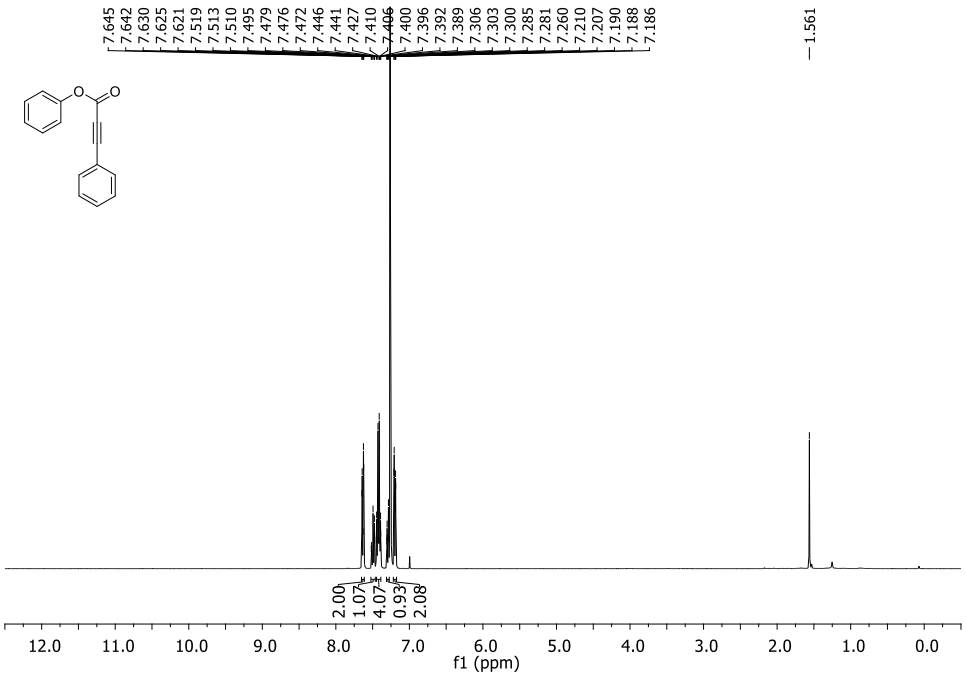


Figure 5.56. ^{1}H NMR spectrum of phenyl-3-phenylpropiolate (**2a**) in $CDCl_3$.

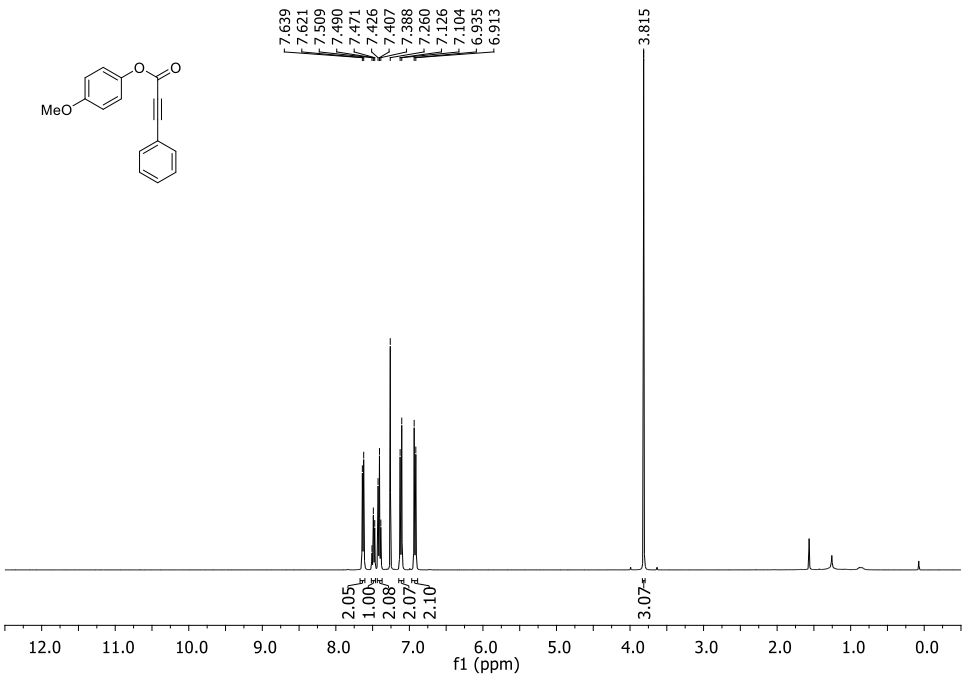


Figure 5.57. ^{1}H NMR spectrum of 4-methoxyphenyl-3-phenylpropiolate in $CDCl_3$ (**2b**).

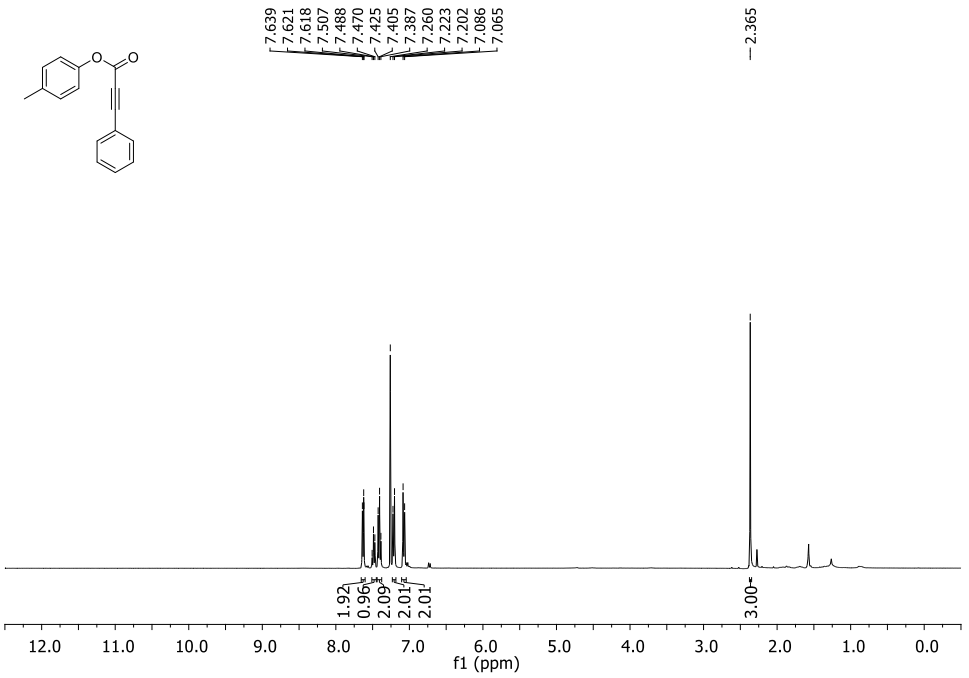


Figure 5.58. ^{1}H NMR spectrum of *p*-tolyl-3-phenylpropiolate (**2c**) in $CDCl_3$.

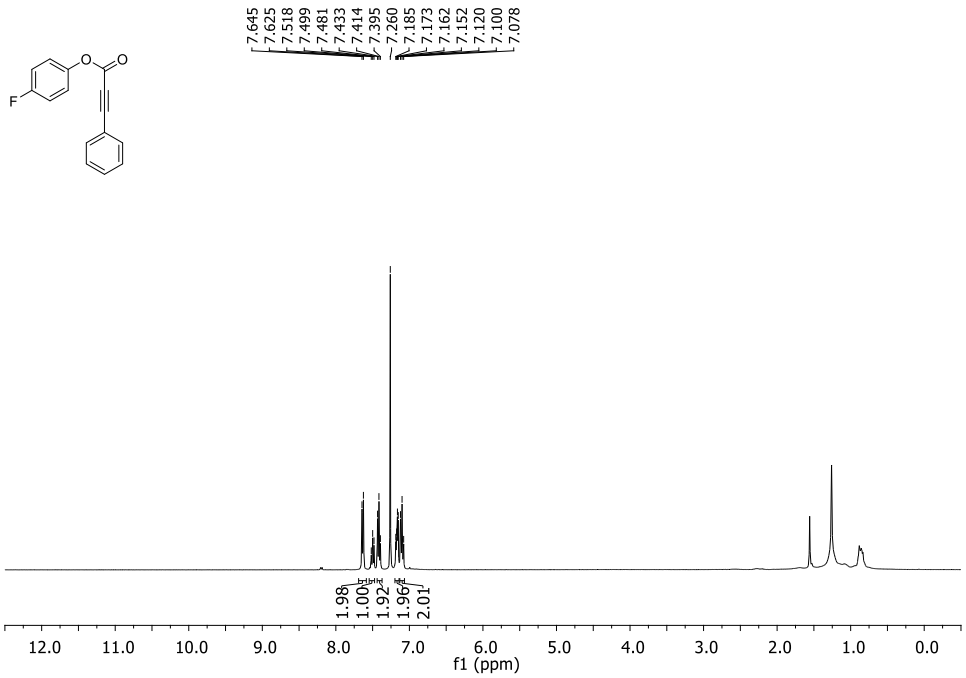


Figure 5.59. ^{1}H NMR spectrum of 4-fluorophenyl-3-phenylpropiolate (**2d**) in $CDCl_3$.

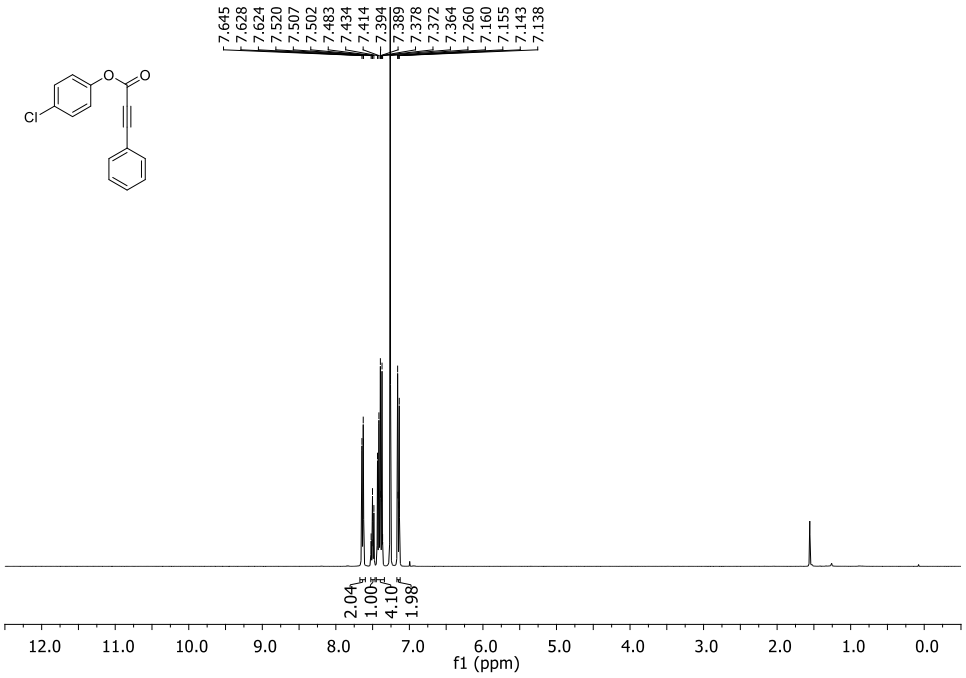


Figure 5.60. ^{1}H NMR spectrum of 4-chlorophenyl-3-phenylpropiolate (**2e**) in $CDCl_3$.

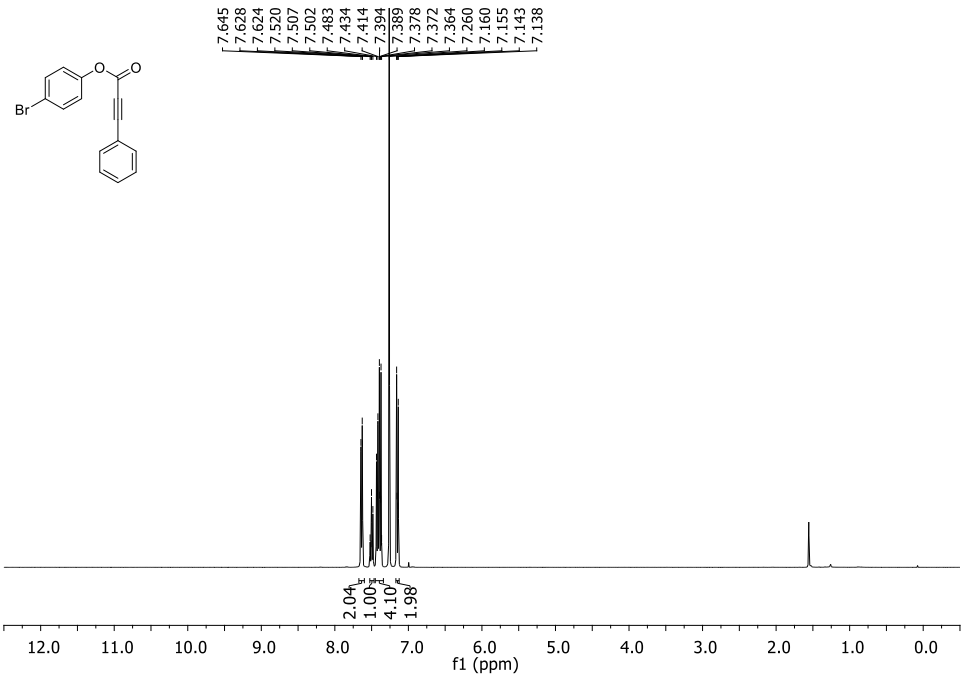


Figure 5.61. ^{1}H NMR spectrum of 4-bromophenyl-3-phenylpropiolate (**2f**) in $CDCl_3$.

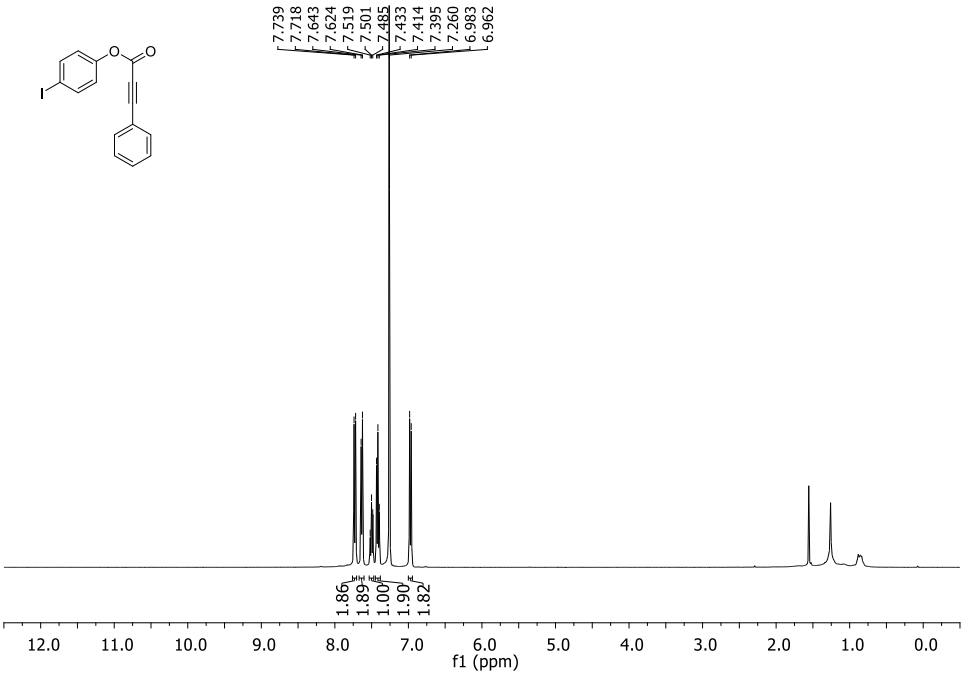


Figure 5.62. ^{1}H NMR spectrum of 4-iodophenyl-3-phenylpropiolate (**2g**) in $CDCl_3$.

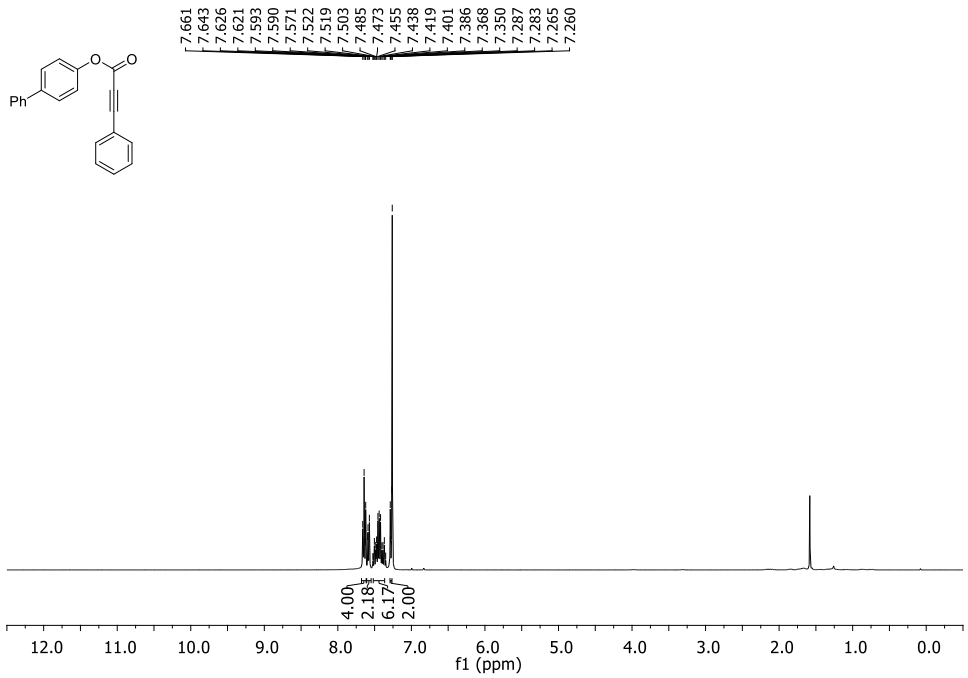


Figure 5.63. ^{1}H NMR spectrum of [1,1'-biphenyl]-4-yl-3-phenylpropiolate (**2h**) in $CDCl_3$.

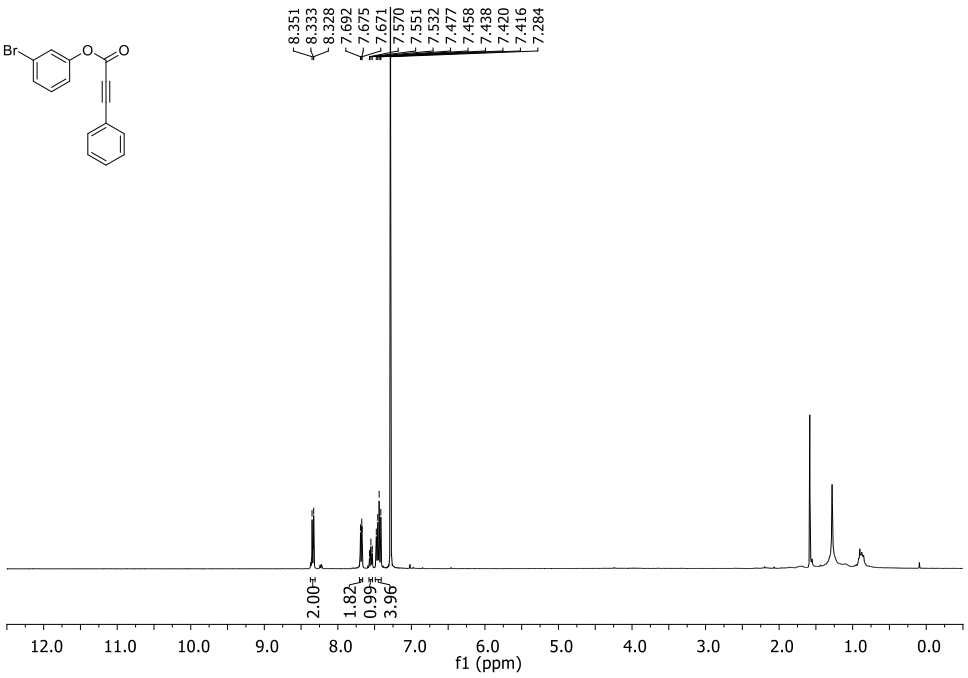


Figure 5.64. ^{1}H NMR spectrum of 3-bromophenyl-3-phenylpropiolate (**2i**) in $CDCl_3$.

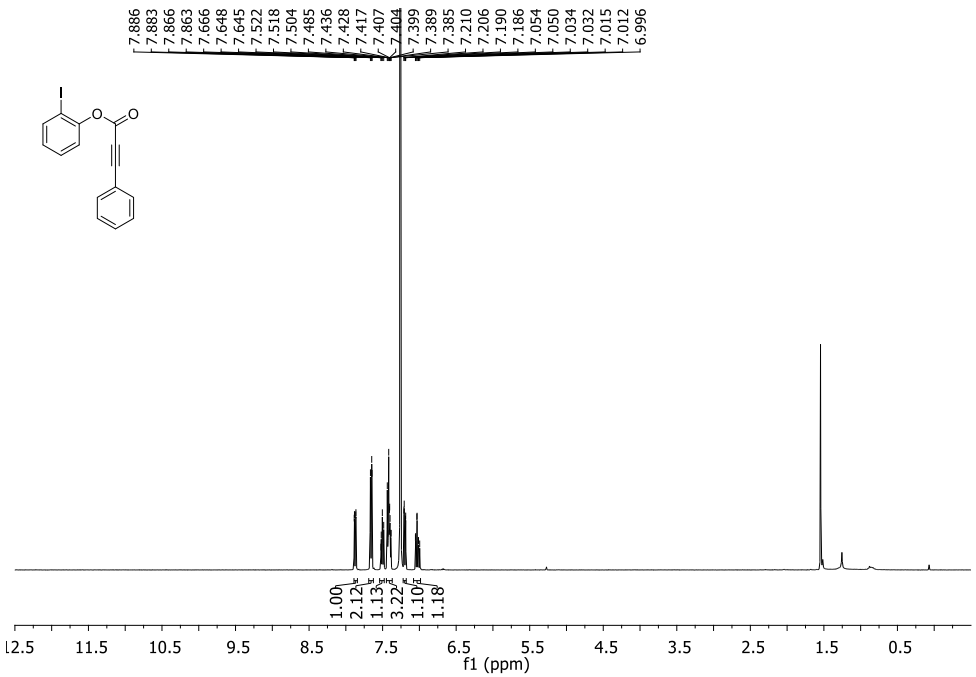


Figure 5.65. ^{1}H NMR spectrum of 2-iodophenyl-3-phenylpropiolate (**2j**) in $CDCl_3$.

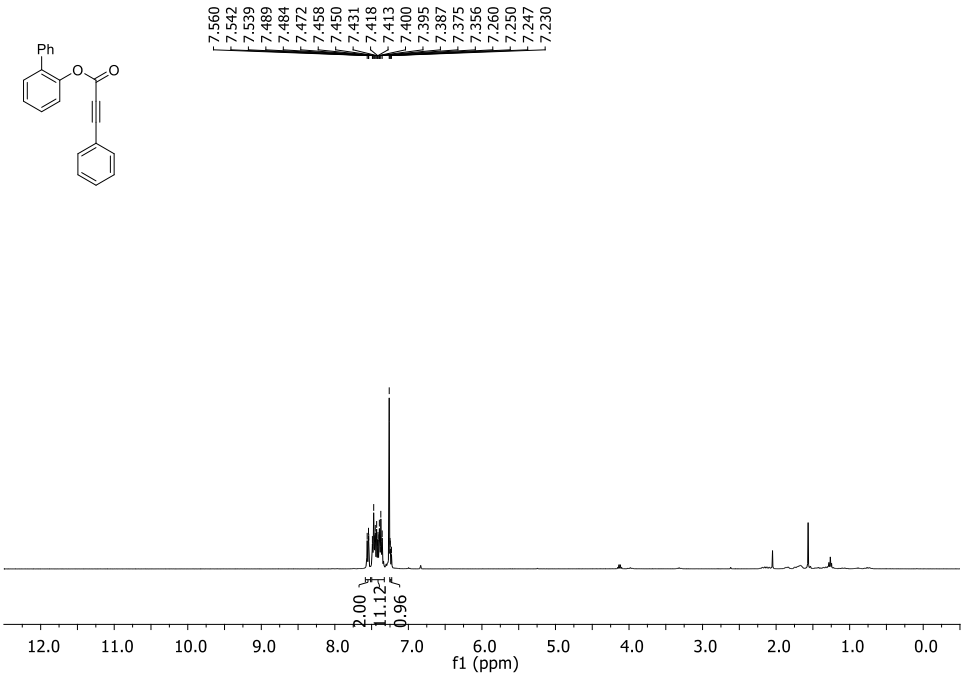


Figure 5.63. ^{1}H NMR spectrum of [1,1'-biphenyl]-2-yl-3-phenylpropiolate (**2k**) in $CDCl_3$.

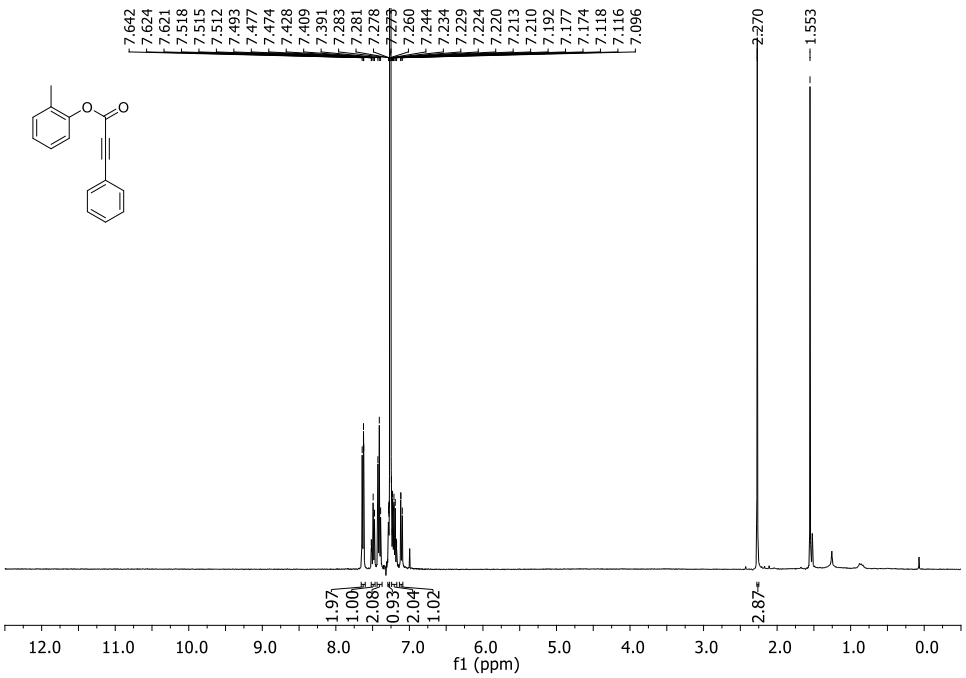


Figure 5.64. ^{1}H NMR spectrum of *o*-tolyl-3-phenylpropiolate (**2l**) in $CDCl_3$.

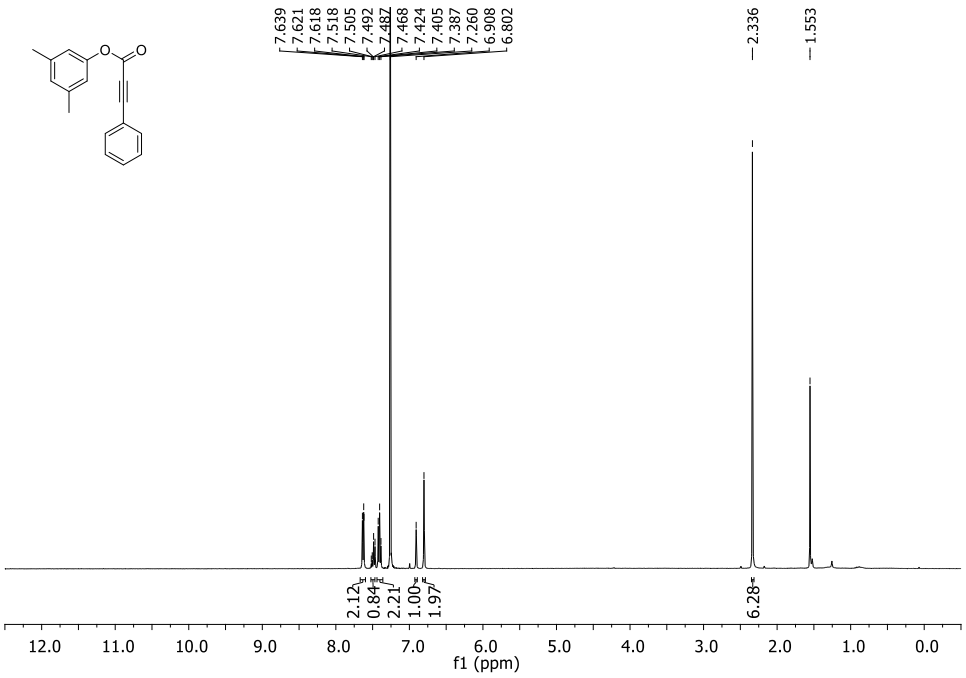


Figure 5.65. ^{1}H NMR spectrum of 3,5-dimethylphenyl-3-phenylpropiolate (**2m**) in $CDCl_3$.

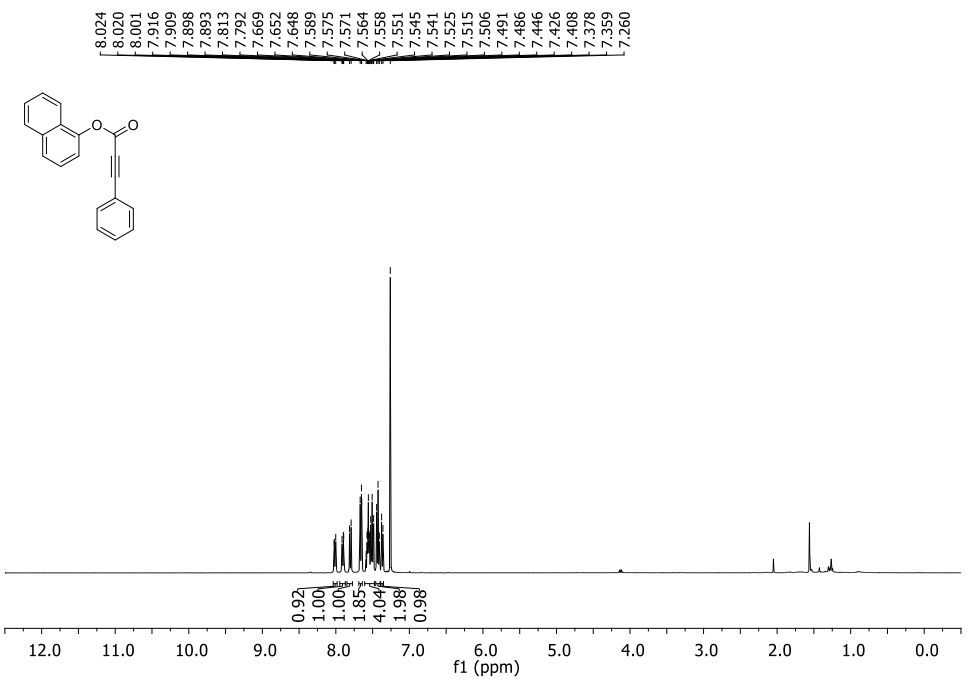


Figure 5.66. ^{1}H NMR spectrum of naphthalen-1-yl 3-phenylpropiolate (**2n**) in $CDCl_3$.

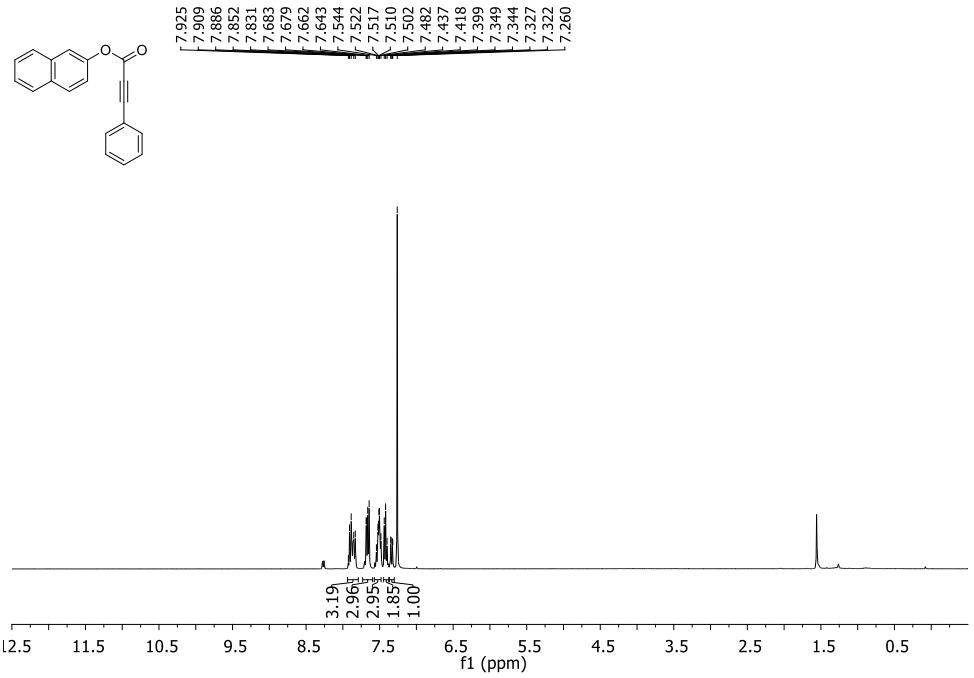


Figure 5.67. ^{1}H NMR spectrum of naphthalen-2-yl-3-phenylpropiolate (**2o**) in $CDCl_3$.

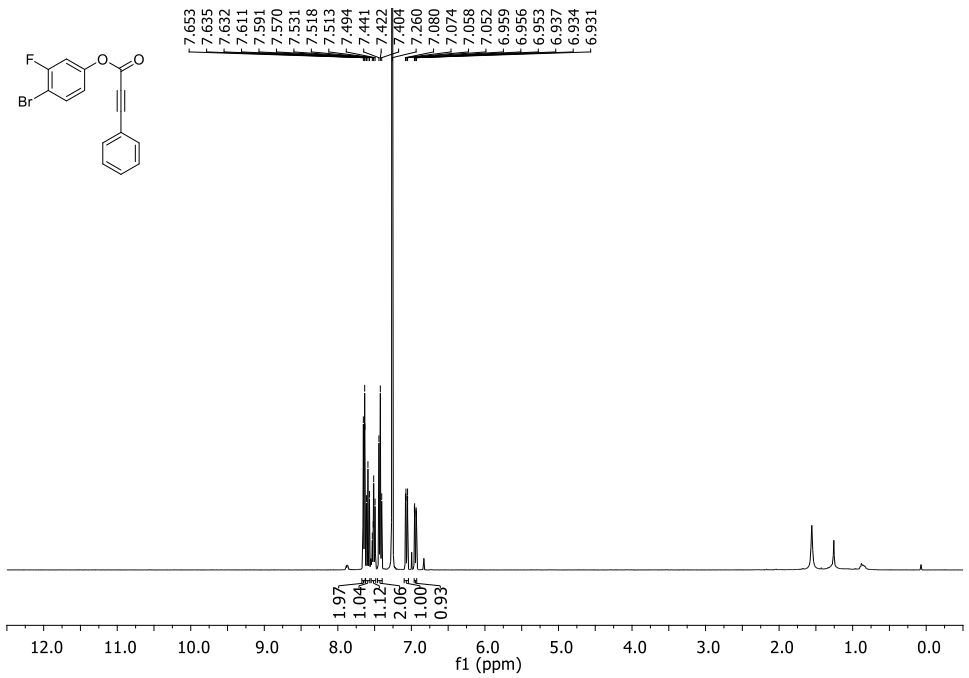


Figure 5.68. ^{1}H NMR spectrum of 4-bromo-3-fluorophenyl-3-phenylpropiolate (**2p**) in $CDCl_3$.

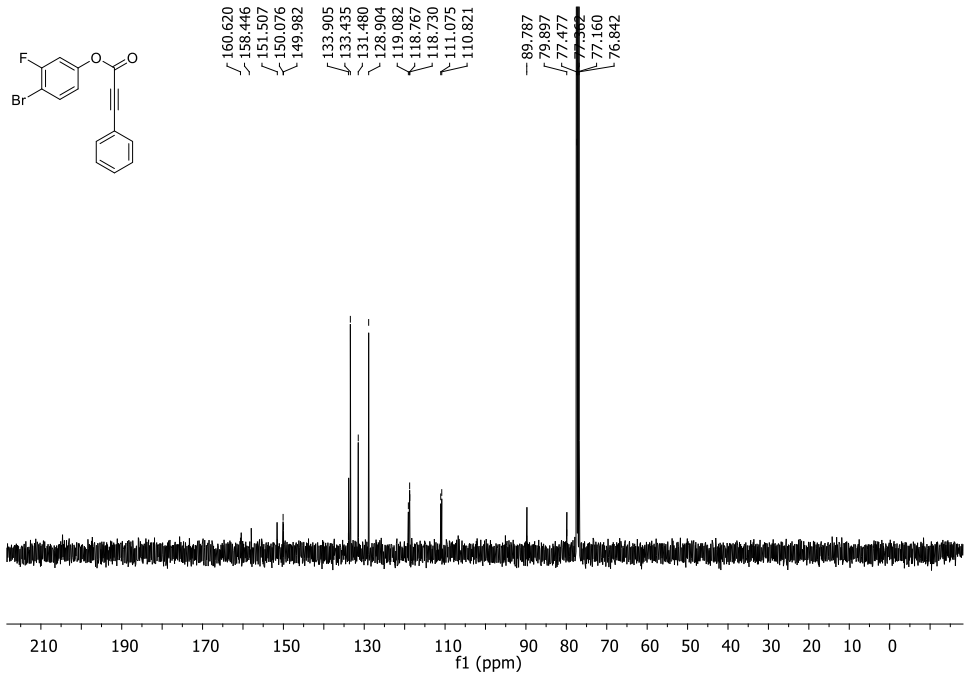


Figure 5.69 ^{13}C NMR spectrum of 4-bromo-3-fluorophenyl-3-phenylpropiolate (**2p**) in $CDCl_3$.

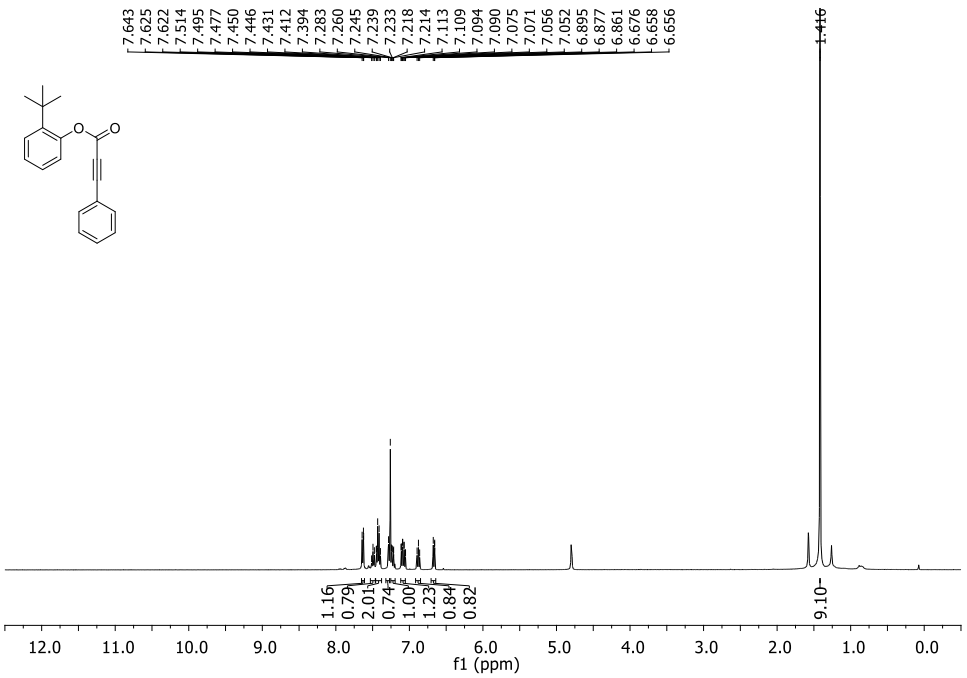


Figure 5.70. ^{1}H NMR spectrum of 2-(*tert*-butyl)phenyl 3-phenylpropiolate (**2q**) in $CDCl_3$.

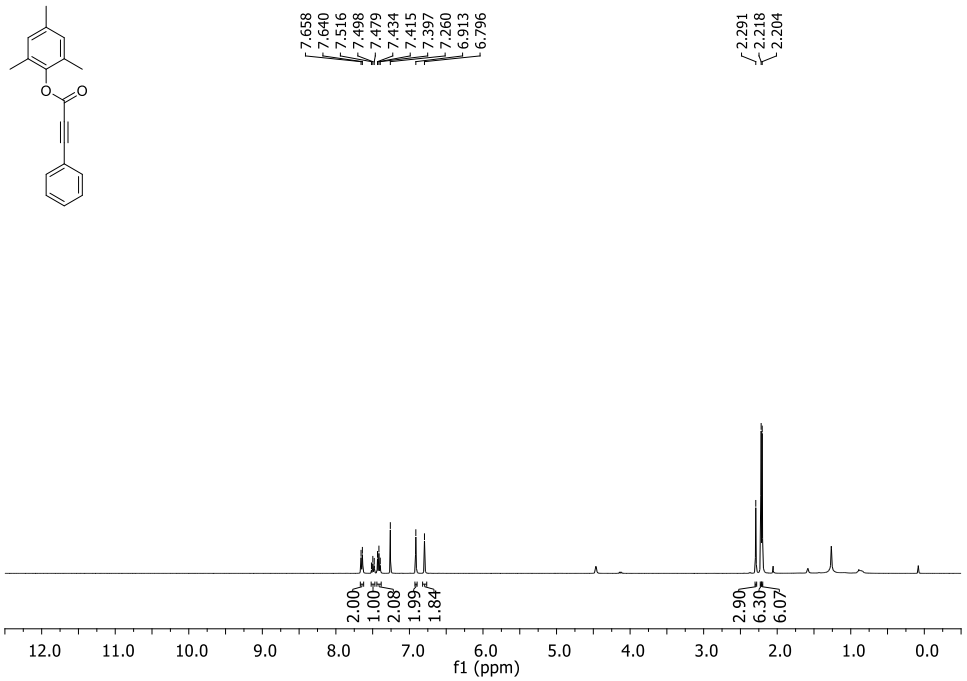


Figure 5.71. ^{1}H NMR spectrum of mesityl-3-phenylpropiolate (**2r**) in $CDCl_3$.

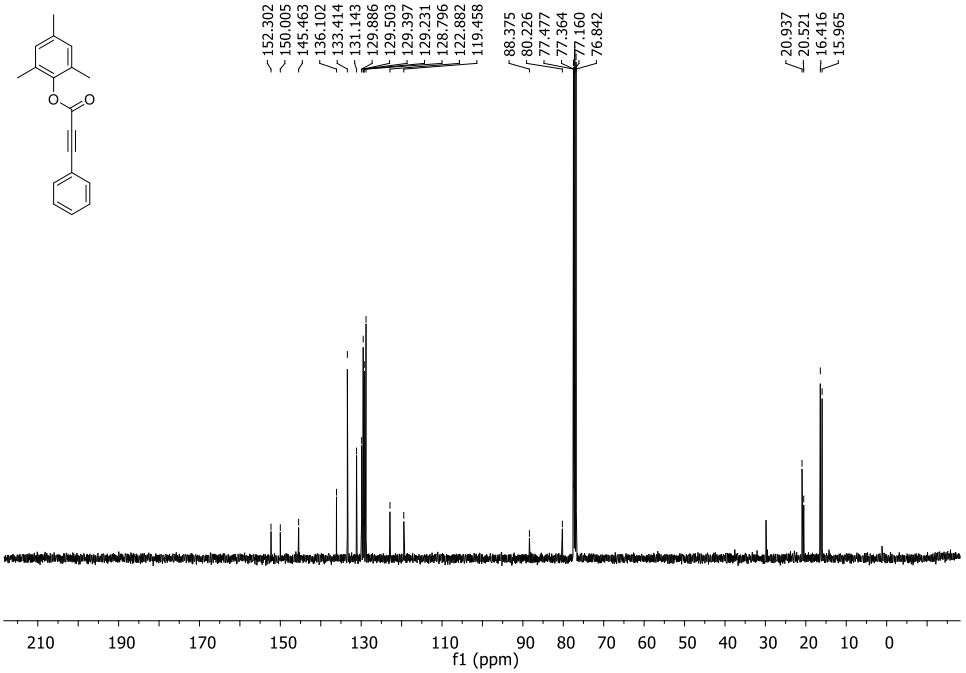


Figure 5.72. ^{13}C NMR spectrum of mesityl-3-phenylpropiolate (**2r**) in $CDCl_3$.

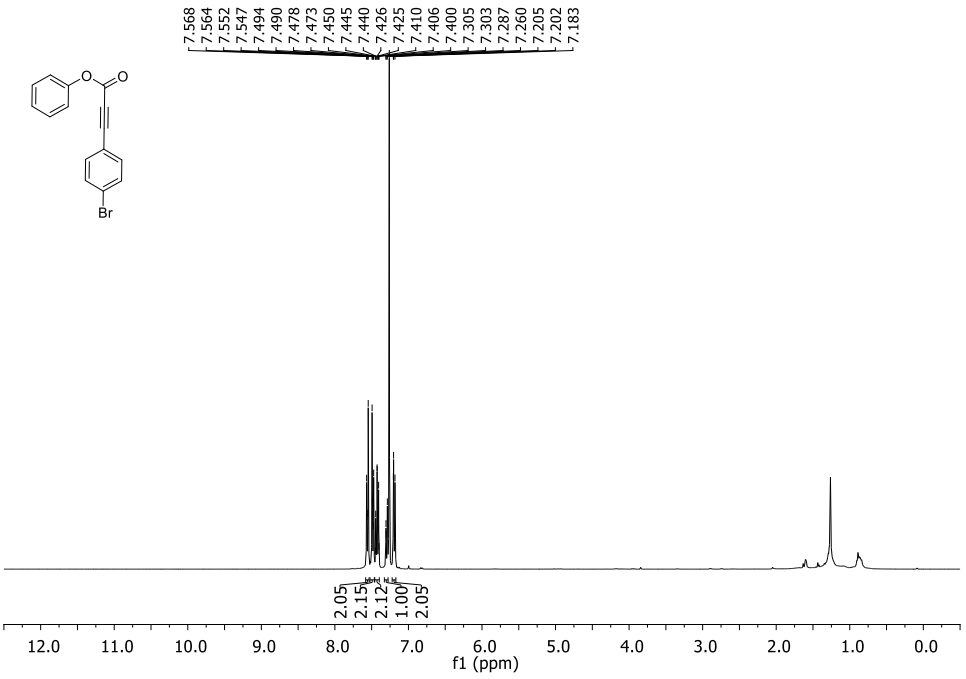


Figure 5.73. ^{1}H NMR spectrum of phenyl 3-(4-bromophenyl)propiolate (**2x**) in $CDCl_3$.

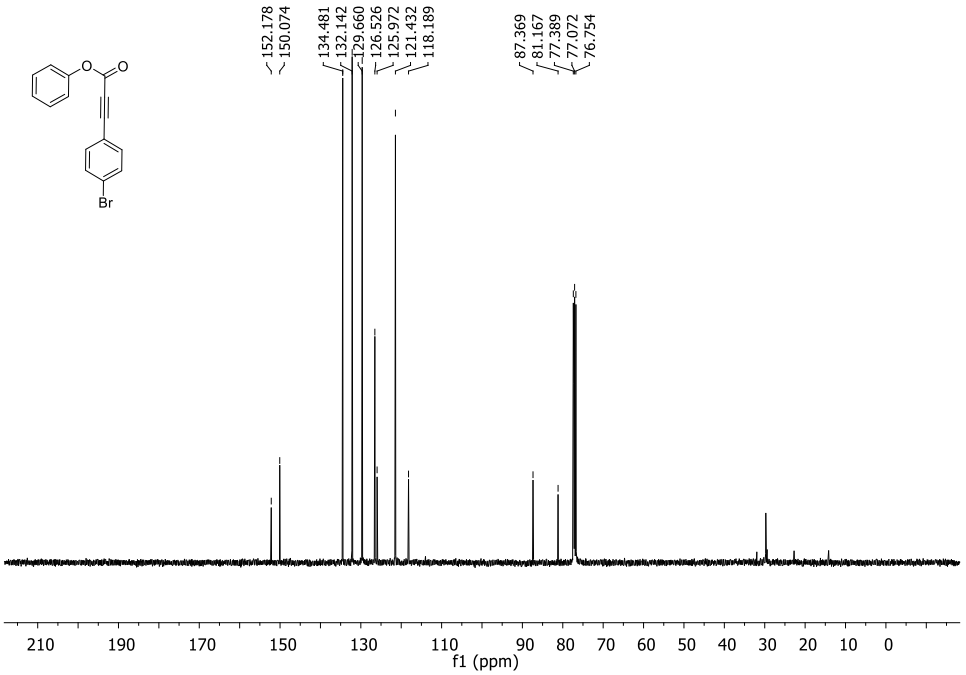


Figure 5.74. ^{13}C NMR spectrum of phenyl 3-(4-bromophenyl)propiolate (**2x**) in $CDCl_3$.

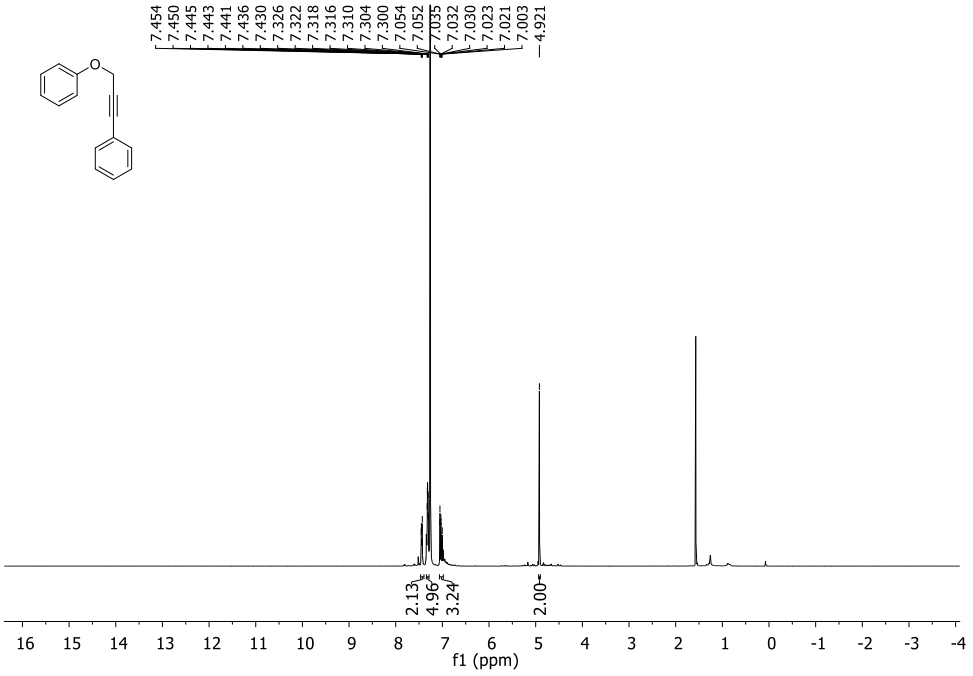


Figure 5.75. ^{1}H NMR spectrum of (3-phenoxyprop-1-yn-1yl)benzene (**2z**) in $CDCl_3$.

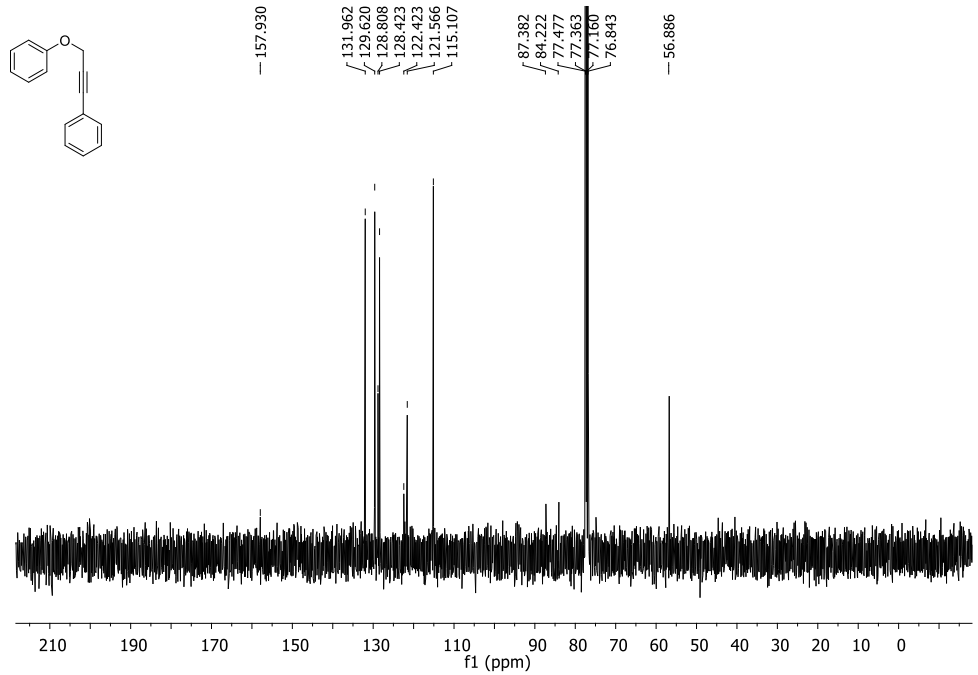


Figure 5.76. ^{13}C NMR spectrum of (3-phenoxyprop-1-yn-1yl)benzene (**2z**) in $CDCl_3$.

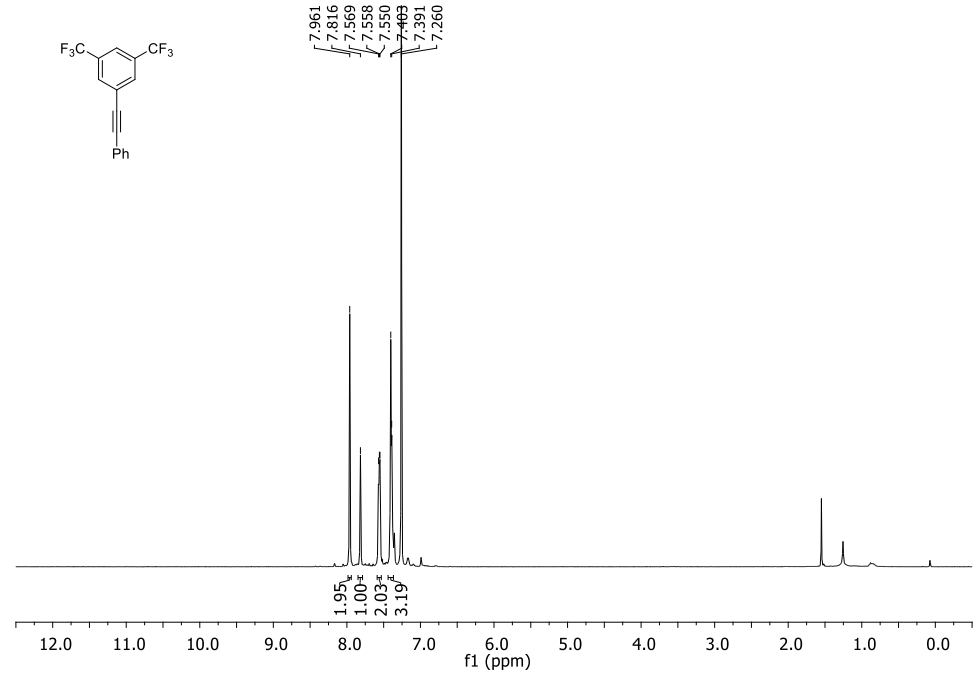


Figure 5.77. ^{1}H NMR spectrum of 1-(phenylethynyl)-3,5-bis(trifluoromethyl)benzene **(3z)** in $CDCl_3$.

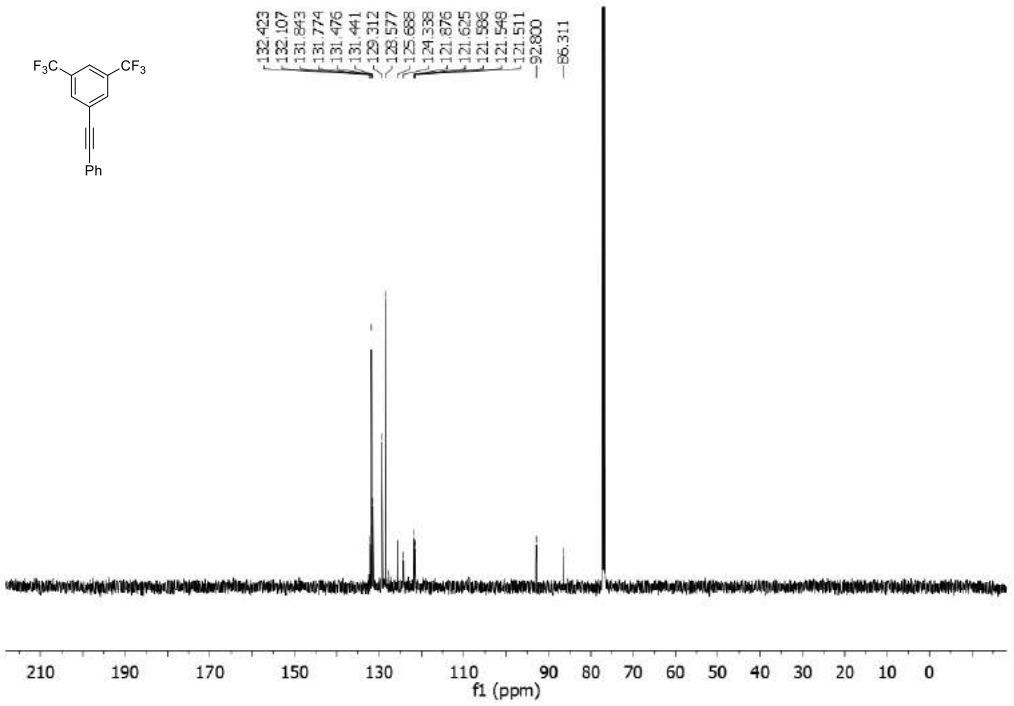


Figure 5.78. ^{13}C NMR spectrum of 1-(phenylethynyl)-3,5-bis(trifluoromethyl)benzene **(3z)** in $CDCl_3$.

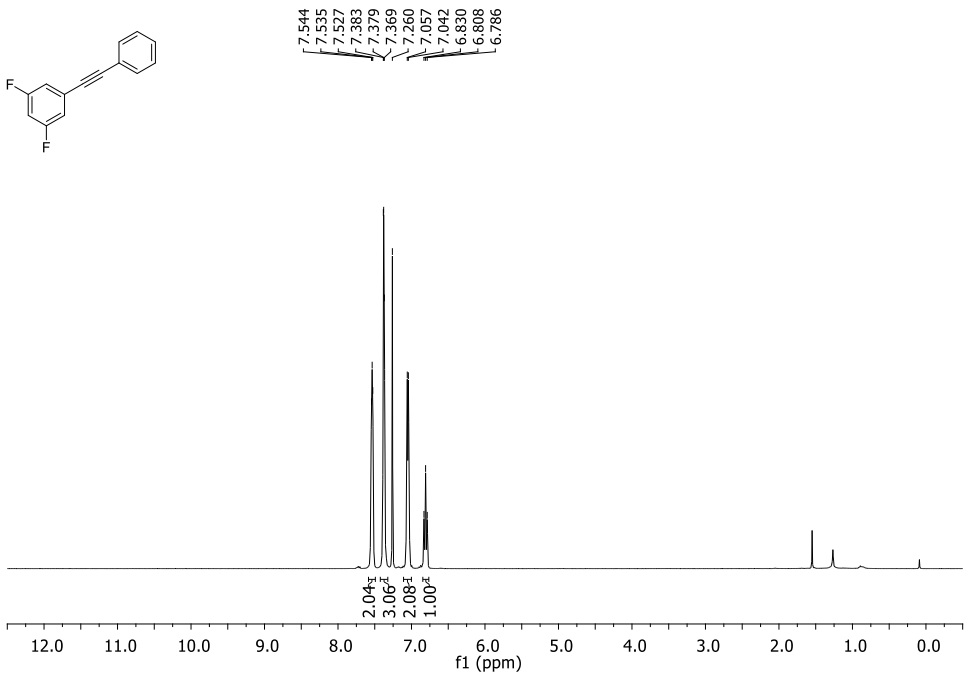


Figure 5.79. ^{1}H NMR spectrum of 1,3-difluoro-5-(phenylethynyl)benzene**(4z)** in $CDCl_3$.

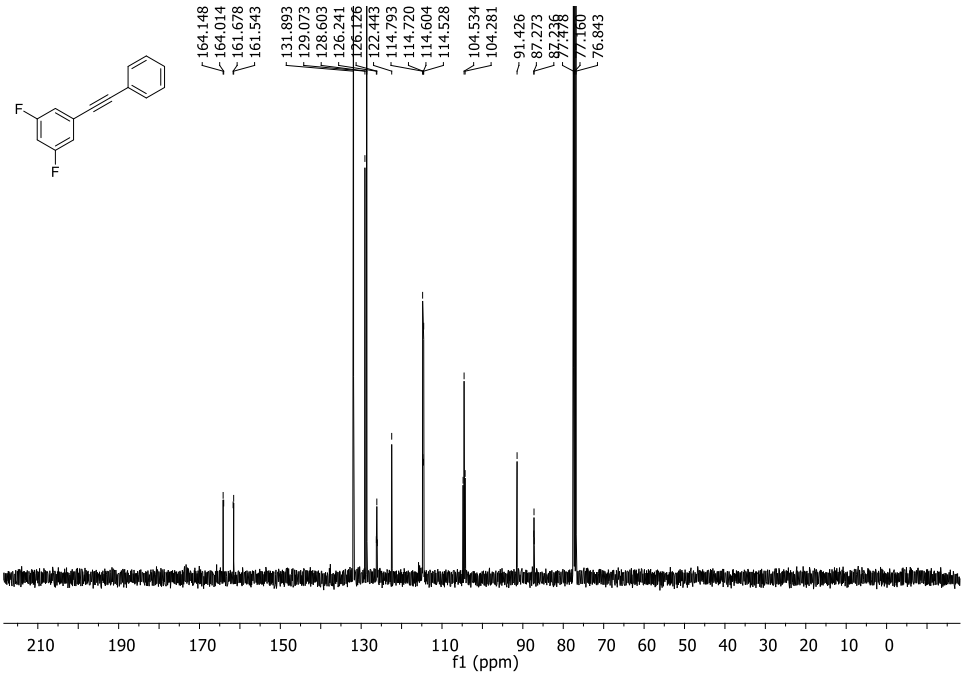
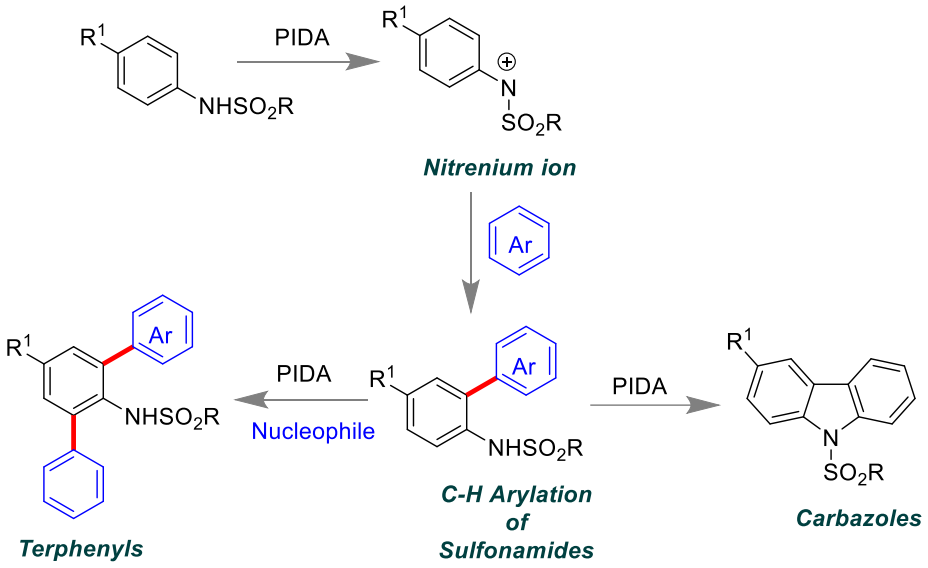
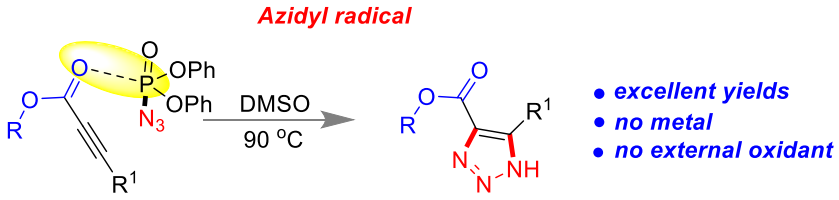


Figure 5.80. ^{13}C NMR spectrum of 1,3-difluoro-5-(phenylethynyl)benzene **(4z)** in $CDCl_3$.

CONCLUSIONS





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Iodine(III)-Enabled Distal C−H Functionalization of Biarylsulfonanilides

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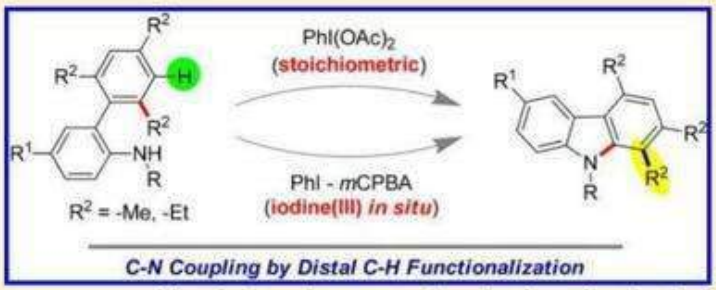
Supporting Information



ABSTRACT: Here we report a metal-free C−N coupling reaction for carbazole synthesis by distal (*-meta*) C−H bond functionalization. Nitrenium ion, a potential synthetic intermediate, was generated in situ from reactions of iodine(III) reagents and biarylsulfonanilides. Following, nitrenium ions were used for intramolecular dehydrogenative C−N coupling reactions via 1,2-alkyl (methyl or ethyl) migration by the expense of C−H bond functionalization at the distal position toward synthesis of 1,2,4-trialkyl-substituted carbazoles. The iodine(III) condition was either maintained by using a stoichiometric amount of phenyliodine diacetate (PIDA) or in-situ generated from iodobenzene (PhI)−*meta*-chloroperbenzoic acid (*m*CPBA) combination.

INTRODUCTION

The environmentally benign and economical methods[1−3] for C−N coupling reactions have gained significance interest in the synthesis of nitrogenous heterocycles.[4−6] Metal-free protocols are more advantageous for C−H amination reactions to synthesize amines[7,8] than traditional metal-mediated C−N bond synthesis.[9] In this aspect, toxic-waste-free and inexpensive iodine(III)-based reagents are highly popular for construction of oxidative C−N bonds[10,11] and cross-dehydrogenative coupling (CDC) reactions.[12−14] Easy availability, high stability, controlled oxidizing ability, and environmentally benign nature of iodine(III) reagents make them widespread in developing new synthetic transformations for the construction of numerous organic scaffolds by C−H and N−H bond functionalization.[15−19]

Divalent nitrogen species with six electrons in its valence shell containing a positive charge on nitrogen is recognized as nitrenium ion.[20−23] They are nitrogen analogues of carbenium ions which act as electrophiles for aromatic electrophilic substitution reactions.[24,25] Nitrenium ions have been known in the literature for a long time;[26,27] however, their use in organic synthesis is relatively less explored.[28−30] Nitrenium ions can be derived from amines (or amides) in hypervalent iodine(III)-mediated organic transformations.[21] Electrochemical anodic oxidation techniques have also been used to generate nitrenium ions using iodine(III) reagent for preparation of valuable structural compounds.[31−33] Recently, we have developed sustainable methods for C−N bond synthesis by using iodine(III) reagents via nitrenium ions.[34−37] Mechanistically, generation of nitrenium ions includes two steps: ligand exchange of iodine(III) with amines and reductive elimination of iodoarene (Figure 1a). The formation of nitrenium ion from sulfonamide has been explored by our group earlier in several reports which follows a similar mechanistic pathway.[34−38] In general, distal C−H bond functionalization reactions are mostly attained through template-assisted transition metal catalysis.[39,40] However, we have shown here the use of nitrenium ion toward metal-free and template-free distal (*-meta*) C−H functionalization (Figure 1b) with alkyl migration via Wheland intermediate (*σ*-complex).

RESULTS AND DISCUSSION

In this work we demonstrate an intramolecular C−N coupling by distal C−H bond functionalization and alkyl migration from biarylsulfonanilides for carbazole synthesis using iodine(III) reagents both stoichiometrically and by in-situ generation of iodine(III) (Figure 2a). The current work is encompassed toward organic transformations involving nitrenium ion

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Steric and Electronic Effect on C_2-H Arylation of Sulfonamides

Ankita Bal, Saikat Maiti, and Prasenjit Mal*[a]

The ambident nature of the electrophile generated in a reaction system controls the outcome of a reaction. Electrophilic nitrenium ion which is convertible to carbenium ion *via* resonance was *in situ* generated by the reactions of iodine(III)-reagent $PhI(OAc)_2$ and arylsulfonamides. The nucleophile added in the reaction controls the reaction for the regiospecific *ortho* C–H arylation or C_2-H arylation. The electron rich arenes react with carbenium ion (electrophiles) to undergo C–H arylation. Electron donating effect (+I or +R effect) of the substituents on sulfonamide stabilizes the carbenium ion to favor oxidative coupling reaction with nucleophiles. Overall, the feasibility of C_2-H arylation of the sulfonamides has been demonstrated by steric and electronic factor that facilitates C–H arylation of sulfonamides.

Introduction

Dehydrogenative C–C coupling reaction[1] by C–H bond functionalization has evolved as a powerful tool in synthetic community due to its high atom economy.[2] Transformations involving metals for construction of C–C bond has developed since decades to synthesize valuable hetercyclic scaffolds.[3] These methods have several disadvantages as it involves the use of hazardous reaction condition, costly metals and their toxic residues. However, metal free approach for functionalization of aromatic C–H bond has fascinated organic chemists in modern era. Among them, hypervalent iodine(III) reagents have been well explored by several researchers for synthesis of significant functional moieties as they are mild, less toxic and can be easily handled at room temperature.[4] Metal free conditions and use of inexpensive iodine(III) reagents have been well explored for intermolecular C–C coupling reactions.[4a,k]

Sulfonamides are significant in organic synthesis because of their potential use as synthetic scaffolds in several important transformations.[5] Our group have earlier investigated *N*-arylation of sulfonamides by choosing an appropriate nucleophile.

Recently, we have reported intermolecular dehydrogenative annulation between sulfonamide and arene for carbazole synthesis, where C–H arylation of sulfonamide was demonstrated as an intermediate step.[6] In this work, we have also taken sulfonamides and varied the nucleophiles to get different product selectivity (C-selective). The nucleophile added in the reaction system is sterically hindered to accesss the more electrophilic nitrogen centre. A range of sulfonamides have been screened with different bulky arenes to understand the reactivity of the sulfonamides with hypervalent iodine(III) reagent.

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Supporting information for this article is available on the WWW under https://doi.org/10.1002/slct.201900944

Results and Discussion

The nature of the chemical reactions can be controlled by the influence of weak interactions[7] or soft force.[8] Therefore, many reactions are designed[9] by exploring cooperative multiple non-covalent interactions like hydrogen bonding,[10] halogen bonding,[11] hydrophobic effect,[12] cation-π,[13] anion-π,[14] etc.[15,16] Our research goal is encircled in understanding the reactivity of non-prefunctionalized substrates by weak or non-covalent interactions.[17] As a result, we have presented C–H arylation reaction of sulfonamide[18] by controlling the reactivity of carbenium ion[6] over nitrenium ion.[19] Amine and amides react with iodine(III) oxidants in some specific way to provide divalent electrophilic ionic intermediate, known as nitrenium ion. The nature and stability of the nitrenium ion leads to numerous oxidative transformations for synthesis of valuable functional molecules by C–H or C–C bond functionalization reactions.[6]

The competitive reactivity of carbenium over ntrenium ion has been demonstrated in (Figure 1) for the oxidative C_2-H arylation of sulfonamide differentiating it from our previous work where the added nucleophile was the biphenyl system which is considered to be less hindered to attack the more electrophilic nitrenium ion to give rise to *N*-arylated product.[20] The reactivity of iodine(III) reagents with sulfonamide for selective *N*-arylation *vs* C_2-H arylation is portrayed in Figure 1. Phenyliodine diacetate (PIDA) is used as a sole reagent for C_2-H arylation to control the reactivity of the ambident electrophilic intermediate.

The nitrenium ions are isoelectronic[21] with carbenium ions and their use in organic synthesis have expanded recently.[19b,22] The nitrenium ions can be generated using iodine(III) oxidant *via* ligand exchange at the iodine center to form an

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COMMUNICATION

Intermolecular C-Arylation of 2-Amidobiphenyls Overcoming Intramolecular N-Arylation

Ankita Bal,[b] Saikat Maiti[a] and Prasenjit Mal*[a]

Dedication ((optional))

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Supporting information for this article is given via a link at the end of the document. Contains crystallographic information (3aa: CCDC 1940403), crystallographic information file (CIF), and NMR spectra.

Abstract: 2-Amidobiphenyls are known to undergo intramolecular N–H arylation in presence of hypervalent iodine(III) reagents which lead to C–N coupling reaction. Herein, an unprecedented intermolecular C–C coupling reaction *via* carbenium ion over a nitrenium ion has been reported using sole oxidant $PhI(OAc)_2$ suppressing the more facile intramolecular C-N coupling.

The prominent reactions in organic synthesis involves C-C bond formation reactions[1] as it has unraveled numerous methodologies for bringing about organic transformations which have diverse applications in industry and academic research. The C-C bond formation involving C-H bond functionalization has opened a new paradigm towards development of better alternatives for synthesis of complex structural motifs as such methods which devoid use of prefunctionalized substrates.[2] Directing group assisted or template assisted metal catalyzed synthetic transformations for functionalization of unactivated aromatic system have expanded at a fast pace recently.[3] Metal free hypervalent iodine(III) reagents are also on the stand for construction of C-C bond by C–H bond functionalization.[4] The current work focuses on intermolecular C^2-H arylation overcoming the more facile intramolecular C-N coupling in presence of an oxidant PIDA.

2-Amidobiphenyl moiety is one of the frequently used precursor for intramolecular oxidative C-N coupling either in metal-free or metal catalyzed reaction conditions. Antonchick and co-workers have established an intramolecular oxidative C-N coupling reaction of 2-acetaminobiphenyls using $PhI(OAc)_2$ (PIDA), involving a nitrenium ion.[5] The reaction proceeded through nitrenium ion formation followed by intramolecular arylation attack (as shown in Figure 1a). Nitrenium ion is a divalent electron deficient species which could be generated from anilides under hypervalent iodine(III) conditions.[4c, 6] Nitrenium ion could also undergo electronic delocalization to build carbenium ion intermediate which are mostly favored in case of sulfonyl protected amines. Kita[4a] and Canesi[4g] have demonstrated intermolecular C^2-arylation of sulfonyl anilide by using iodine(III) reagents. As described by them, the σ-donation effect of the sulfonyl group is operative to stabilize the positively charged carbenium ion.[4g] Intermolecular *N*-arylation using hypervalent iodine reagents have been explored to a large extent.[7] Olofsson[8] and Stuart[9] have reported intermolecular *N*-arylation using diaryliodonium salts.[10]

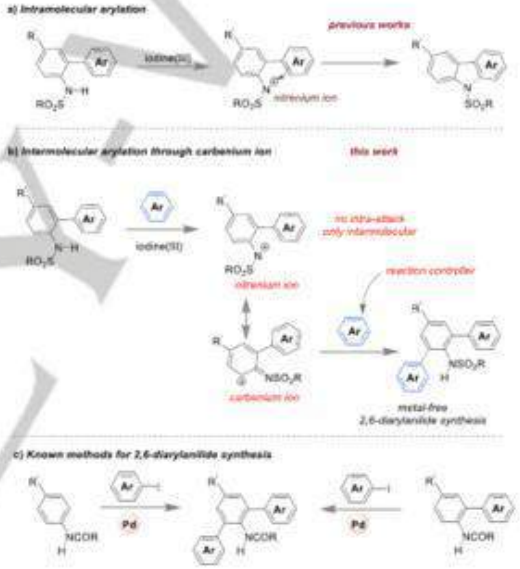

Figure 1. a) Intramolecular C-N coupling. b) Our approach on intermolecular arylation for 2,6-diarylanilide synthesis (*this work*). c) Metal catalyzed C-H arylation of 2-amidobiphenyl system.

However, intermolecular arylation for amidobiphenyl system overcoming intramolecular arylation has not been reported so far in literature. To address this fundamental challenge, we aimed to utilize the carbenium ion over the nitrenium ion for the intermolecular arylation reaction. We hypothesized that use of any suitable external nucleophile might be a potential reaction controller by virtue of its electronic and steric effect. By selecting an appropriate arene with superior nucleophilicity, the intramolecular coupling was inhibited in the same reaction condition. This resulted in intermolecular C-H arylation preceding over intramolecular N-H arylation. Hypervalent iodine(III) reagent phenyliodine diacetate (PIDA) was used as the sole oxidant for the transformation at room temperature open atmosphere condition to furnish unsymmetrical 2,6-diaryl anilides under metal-

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REVIEW

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Nitrenium Ions from Amine-Iodine(III) Combinations

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Abstract. Hypervalent iodine compounds are known for its extensive use as a potential oxidant in organic synthesis. In spite of similar reactivity with transition metals, hypervalent iodine reagents are more preferred because of their environmental sustainability. Among several types of hypervalent iodine reagents, trivalent organo iodine(III) reagents are highly popular due to their easy accessibility, stability and controlled oxidizing reactivity. Also, iodine(III) reagents are commercially available and inexpensive. Amines and amides react with iodine(III) oxidants in some specific way to provide a divalent electrophilic ionic species to produce a nitrenium ion. Depending on the nature and stability of nitrenium ion, numerous oxidative transformations are reported to generate valuable functional molecules. This review encompasses discussions about hypervalent organo iodine(III) enabled organic transformations with the involvement of nitrenium ion as an intermediate.

Keywords: Amine-Iodine(III) Combinations; Carbenium ion; Hypervalent Iodine; Iodine(III); Nitrenium ion

1 Introduction

The chemistry of nitrenium ion has always been a subject of interest among the chemists since its infancy. The combinations of amine or amide with iodine(III) reagents to form nitrenium ion has developed since decades. Divalent nitrogen species with six electrons in its valence shell bearing a positive charge on nitrogen is acknowledged as nitrenium ion **2**.[1] The nitrogen analogues of carbenium ions **1** are electrophilic reactive intermediates, isoelectronic with carbenes.[2] Nitrenium ions have two non-bonding electrons and depending on their electronic spin orientation, nitrenium ions can exist in two different forms *i. e.* singlet state and triplet state (Figure 1).[3]

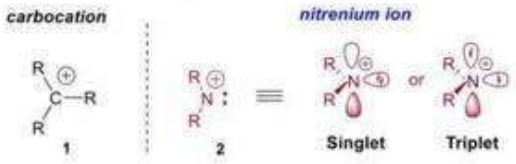

Figure 1. Ionic electrophilic species with 6 valance electrons.

Aryl nitrenium ions get stabilization by π–conjugation with phenyl ring. Aryl nitrenium ions are convertible to carbenium ions by charge delocalization to *ortho*- (**3**) and *para*- position (**4**) of the phenyl ring (Figure 2).[4]

Figure 2. Resonance structures from aryl nitrenium ions and *N*-acyl nitrenium ion.

Nitrenium ions get the stabilization mostly by the interaction of vacant *p* orbital at the nitrogen center with the filled non-bonding orbital of an adjacent heteroatom such as oxygen or nitrogen.[5] On the other hand, *N*-acyl-*N*-alkoxy nitrenium ions **5** are easily accessible, relatively more stable and singlet in nature.[3] *N*-Acylnitrenium ions react solely at the nitrogen center, whereas aryl nitrenium ions are ambiphilic electrophiles which undergo reaction at one of three possible sites (Figure 2). Nitrenium ions must be sufficiently stabilized by the electron-

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CHEMISTRY AN ASIAN JOURNAL Minireview

Strategies to Control Hypervalent Iodine – Primary Amine Reactions

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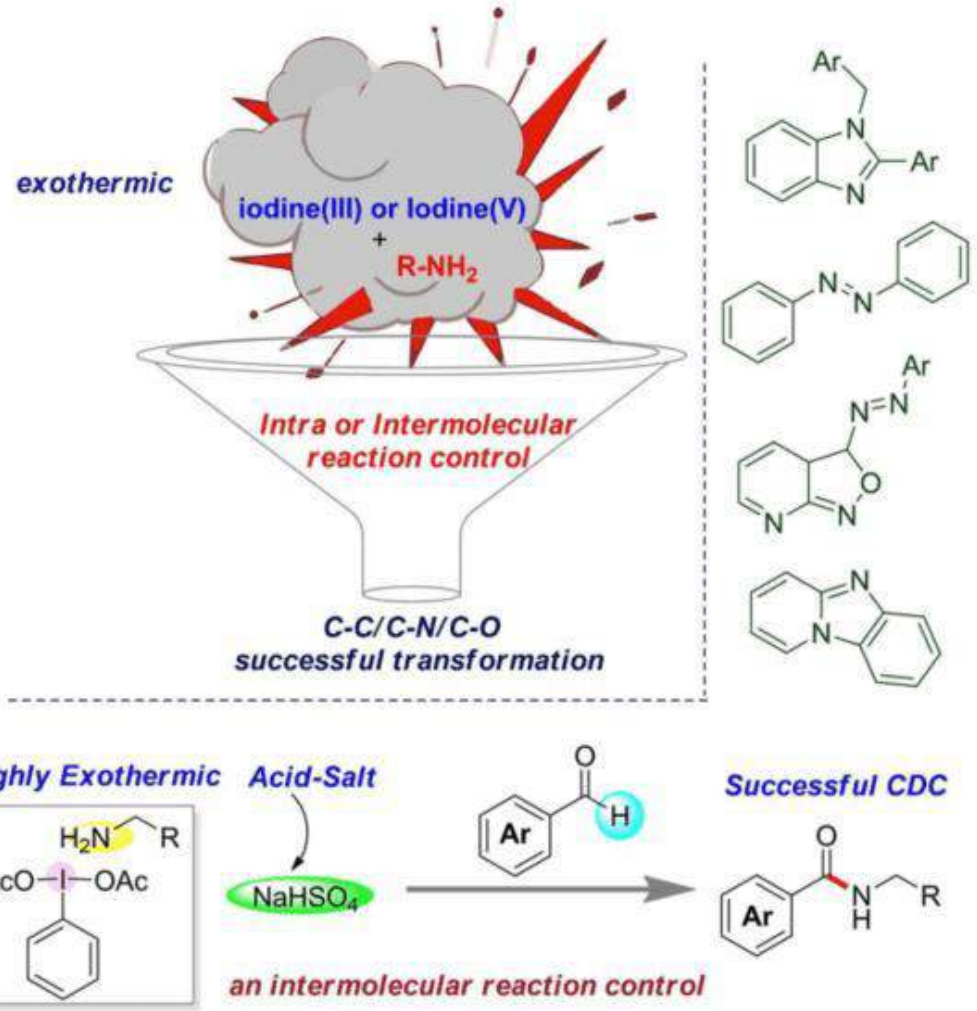

Special Acknowledgement

I end the long PhD journey with a heavy heart as I have lost a loved member of my family just before my defense. I would especially like to acknowledge Lt. Ms. Anita Dutta, my bummi (aunty) who left us for the heavenly abode on 27th of June, 2021, just at 52 years. She was a pure-hearted, innocent soul who loved all the children of our family unconditionally. In the six years of my Ph.D. journey, I could not manage much time with her, which will always remain a big regret in my life. Although she is no more with us, her memories will always be there throughout our life. I would always remain grateful to her for her contribution to my life and pray to God that her departed soul rests in peace in heaven.

Thesis Highlight

Name of the Student: Ankita Bal
Name of the CI/OCC: NISER **NISER Enrolment No.: CHEM11201504010**
Thesis Title: Synthesis of Nitrogen Based N-Heterocycles via Metal Free Approach
Discipline: Chemical Science **Sub-Area of Discipline: Organic Chemistry**

Date of viva voce: 09.07.2021.

Nature possesses an immense distribution of nitrogen-based molecules, including vitamins, nucleic acids, base pair of DNA, and RNA molecule. Nitrogen-based molecules have gained prominence at an alarming rate because of its application in agrochemicals, pharmaceuticals and antibiotics. The electron rich nitrogen containing heterocycles were synthesized by the formation of intermediates like nitrenium ion and azidyl radical. Nitrogen intermediates like nitrenium ion, nitrene or azidyl radical are useful in bringing about beneficial synthetic transformation to produce small organic molecules. Nitrenium ion could be successfully generated by treating sulfonamide with hypervalent iodine(III) reagent PIDA. The sulfonamide group helps to stabilize the nitrenium ion and this nitrenium ion tautomerizes to form carbenium ion. Synthesis of carbazoles was achieved by distal C-H functionalization followed by methyl migration using iodine(III) reagents. The same iodine(III) was generated under *in-situ* conditions using PhI-mCPBA. Terphenyls were synthesized with iodine(III) reagents solely where more facile intramolecular C-N coupling was overcome and intermolecular C-C coupling reaction was established at mild reaction conditions using hypervalent iodine(III) reagents. Using Phosphorus- oxygen interaction, triazoles were synthesized via azidyl radical. Using Phosphorus- oxygen interaction, triazoles were synthesized via azidyl radical. The high phosphorus nitrogen bond energy of approximately 617kJ/mole is cleaved due to weak phosphorus-oxygen interaction. Achieving a click reaction for an internal alkyne without metal involvement is a challenging task that we could successfully overcome using non-covalent interaction. Phosphorus nitrogen bond activation controlled by phosphorus oxygen interaction yielded triazoles in good to excellent yields.

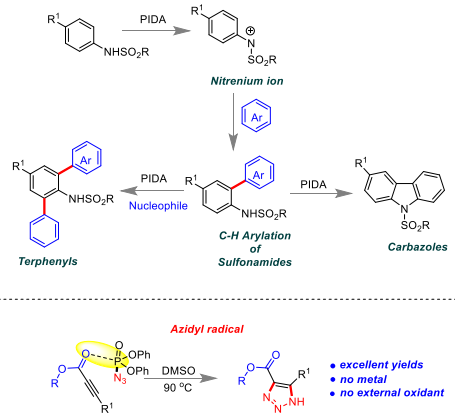

Figure 1a) Nitrenium mediated synthesis of carbazoles and terphenyls. 1b) Triazole synthesis enabled by P-O interaction.