Development of Transition-Metal-Catalyzed Transformations of Triazoles

BY

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THESIS

Submitted as partial fulfillment of the requirements
for the degree of Doctor of Philosophy of Chemistry
in the Graduate College of the
University of Illinois at Chicago, 2017

Chicago, Illinois

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ACKNOWLEDGMENTS

I would like to express my gratitude to my advisor, Professor Vladimir Gevorgyan, for his guidance, and support throughout the years of my study. I am endlessly thankful for teaching me professional disciplines and skills, including presentation, writing, and leadership.

I would also like to thank the members of my thesis committee: Professor Daesung Lee, Professor Duncan Wardrop, Professor Justin T. Mohr and Professor Chad Eichman for their help, criticism, and constructive suggestions.

I would like to thank my former advisors, Professor Jianbo Wang and Professor Yan Zhang at Peking University, who introduced me to research and inspired me to pursue a career in organic chemistry.

I would like to thank all current and former members of Professor Gevorgyan's research group for their friendship and support. It was my pleasure to work with these talented scientists in a multicultural environment. In particular, I thank Dr. Anton V. Gulevich with whom I collaborate on the N-H insertion project.

I would like to express my greatest gratitude to my family for their endless love, as well as unconditional trust and support, throughout these years. I thank my friends, for their company and encouragement during my study.

I would like to thank the entire staff of the Chemistry Department for their help, especially Ms. Rhonda Staudohar, Ms. Silvia Solis, Ms. Patricia Ratajczyk, Dr. Randall Puchalski, Dr. Dan McElheny and Mr. Yonilo Lim.

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LIST OF ABBREVIATIONS

Ac	acetyl
Alk	alkyl
aq	aqueous
Ar	aryl
atm	atmosphere
Bn	benzyl
Boc	*tert*-butoxycarbonyl
Bz	benzoyl
n-Bu	butyl
t-Bu	*tert*-butyl
Calcd	calculated
cat.	catalytic amount
COD	1,5-cyclooctadiene
δ	chemical shifts in parts per million downfield from tetramethylsilane (NMR)
2D	two-dimensional (NMR)
d	doublet
dba	dibenzylidene acetone
DCM	dichloromethane
DCE	1,2-dichloroethane
DCE	1,2-dichloroethane
DEPT	Distortionless Enhancement by Polarization Transfer

LIST OF ABBREVIATIONS (continued)

DFT	Density Functional Theory
DMA	dimethylacetamide
DMB	2,4-dimethoxybenzyl
DMF	dimethylformamide
DMSO	dimethylsulfoxide
EDG	electron-donating group
EE	ethoxyethyl
EI	electron impact ionization (in mass spectrometry)
Et	ethyl
eq	equation
equiv	molar equivalent
EWG	electron-withdrawing group
G	group, Gibbs free energy
g	gram
GC	gas chromatography
h, hrs	hour(s)
HMBC	Heteronuclear Multiple-bond Correlation Spectroscopy (NMR)
HMQC	Heteronuclear Multiple-quantum Coherence Spectroscopy (NMR)
HR	High Resolution (mass spectrometry)
Hz	Hertz
IPr	1,3-bis(2,6-diisopropylphenyl)imidazole-2-ylidene
J	spin-spin coupling constant (NMR)

L	ligand

LIST OF ABBREVIATIONS (continued)

LDA	lithium diisopropylamide
m	multiplet (NMR)
mp	melting point
μ	micro
[M]	metal
M	molar
MS	mass spectrometry
MS	molecular sieves
Me	methyl
Mes	mesityl
MIDA	*N*-methyliminodiacetic acid
mg	milligram
min	minute
mL, ml	milliliter
mm	millimeter
mmol	millimole
mol	mole
MHz	megahertz
m/z	mass to charge ratio
NHC	*N*-heterocyclic carbene
NMR	Nuclear Magnetic Resonance

Ph	phenyl

LIST OF ABBREVIATIONS (continued)

Piv	pivalyl, trimethylacetyl
PMB	*p*-methoxybenzyl
ppm	parts per million
Pr	propyl
i-Pr	isopropyl
n-Pr	propyl
q	quartet (NMR)
quint	quintet (NMR)
rt	room temperature
s	singlet (NMR)
sept	septet (NMR)
t	triplet (NMR)
TBS	*tert*-butyldimethylsilyl
Tf	trifluoromethanesulfonyl
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
Tol, tol	toluenesulfonyl
Ts	*p*-toluenesulfonyl
TDMPP	tris (2,5-dimethoxyphenyl) phosphine

SUMMARY

This thesis describes the development of transition-metal-catalyzed transformations of monocyclic *N*-sulfonyl-1,2,3-triazoles, as well as fused pyridotriazoles, which allows efficient synthesis of various valuable nitrogen-containing compounds.

In Part I, a rhodium-catalyzed intramolecular transunnulation reaction of *N*-sulfonyl-1,2,3-triazoles is disclosed. The introductory section of Part I briefly discusses the ring-chain tautomerism of 1,2,3-triazoles. Then, it describes the recently developed copper-catalyzed azide-alkyne cycloaddition reaction (CuAAC), which offers a general, practical, and robust protocol for synthesis of sulfonyl triazoles. An overview of the developed methodologies employing *N*-sulfonyl-1,2,3-triazoles in transannulation reactions is provided next. Chapter 2 is devoted to the development of a intramolecular transannulation reaction of alkynyl *N*-sulfonyl-1,2,3-triazoles. It is shown that this method provides expeditious access to various 5,5-fused pyrroles from easily available starting materials. Moreover, it can also be used to efficiently construct spiro systems, as well as fused tetrahydropyrrolo-pyrrole cores. In contrast to previously reported methods where ylides are key intermediates, preliminary mechanistic study reveals that a Rh-carbene-alkyne metathesis step is involved in this transformation.

In Part II, a transition-metal-catalyzed transformations of pyridotriazoles is disclosed. Analogously to Part I, the ring-chain tautomerism of pyridotriazoles, and their synthesis as well as reactivity are discussed in the introductory section. One major focus of Part II lies in subsequent section describing the development of a general and efficient rhodium-catalyzed reaction of pyridotriazoles with amides and amines, allowing facile

synthesis of valuable picolylamine derivatives, providing expeditious access to various disubstituted imidazopyridines in a one-pot manner via the subsequent cyclization. Moreover, the imidazopyridines obtained with this protocol are not accessible by previously reported transannulation reaction of pyridotriazoles with nitriles. Another focus of Part II is the discovery of copper-catalyzed intramolecular transannulation reaction of pyridotriazoles with internal alkynes, offering efficient construction of various tri-, tetra-, and pentacyclic fused indolizines, including C6-substituted fused indolizines that cannot be synthesized selectively via known cycloaddition methods. It is not only the first intramolecular transannulation reaction of pyridotriazoles, but also for the first time it is shown that this reaction could also be triggered by Lewis acids.

CONTRIBUTION OF AUTHORS

Several parts of this thesis are reproduced from previously published research articles co-authored with collaborators, who contributed significantly to the present work.

The first part of this thesis (2.1. to 2.5.) is written based on the previously published article ("Intramolecular Transannulation of Alkynyl Triazoles via Alkyne–Carbene Metathesis Step: Access to Fused Pyrroles." Shi, Y.; Gevorgyan, V. *Org. Lett.* **2013**, *15*, 5394). This work was accomplished by myself under supervision of Professor Gevorgyan.

The second part of this thesis (5.1.1. to 5.1.4.) is written based on the previously published article ("Rhodium-Catalyzed NH Insertion of Pyridyl Carbenes Derived from Pyridotriazoles: A General and Efficient Approach to 2-Picolylamines and Imidazo[1,5-a]pyridines." Shi, Y.; Gulevich, A. V.; Gevorgyan, V. *Angew. Chem., Int. Ed*. **2014**, *53*, 14191). This work was accomplished by myself and Dr. Gulevich under supervision of Professor Gevorgyan. The initial result employing 7-Cl-substituted triazole **7-5-a** was obtained by Dr. Gulevich; the further development was performed by myself.

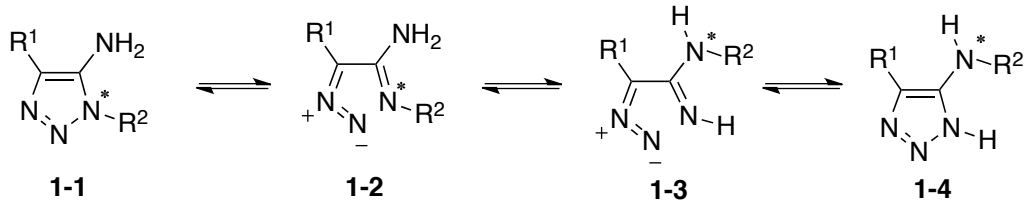
The third part of this thesis (5.2.1. to 5.2.4.) is written based on the previously published article ("Cu-Catalyzed Transannulation Reaction of Pyridotriazoles: General Access to Fused Polycyclic Indolizines," Shi, Y.; Gevorgyan, V. *Chem. Commun*. **2015**, *51*, 17166). This work was accomplished by myself under supervision of Professor Gevorgyan.

PART I. RHODIUM-CATALYZED INTRAMOLECULAR TRANSANNULATION OF *N*-SULFONYL-1,2,3-TRIAZOLES

1. INTRODUCTION

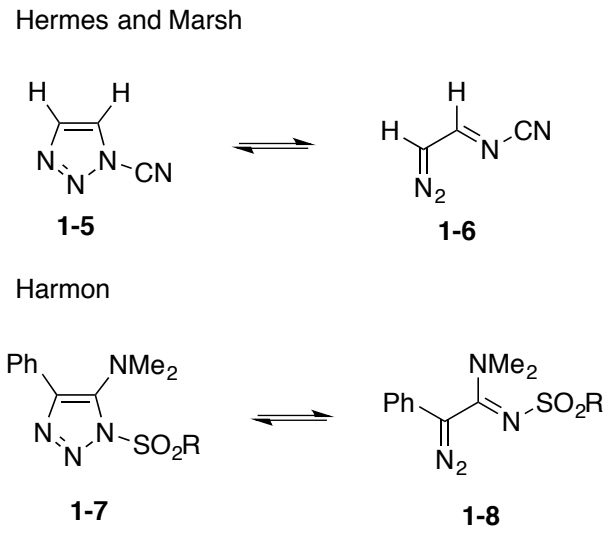
1.1. Ring-chain tautomerism of 1,2,3-triazoles

Known as the Dimroth rearrangement,[1] 1,2,3-triazoles **1-1**, which bear exocyclic amines, could undergo a ring-opening reaction, forming iminodiazo intermediates **1-2**. The latter, upon ring-closure with the different amino group (**1-3**), would produce the isomeric triazoles **1-4** (Scheme 1-1). The reversibility of this tautomerism is governed by various factors, including but not limited to, the nature of the ring substituents, temperature and the reaction medium.



Scheme 1-1

It was found that a strong electron-withdrawing group at the N-1 position of 1,2,3-triazoles would drive the equilibrium towards the ring-opened iminodiazo form. Thus, in 1967, Hermes and Marsh reported that 1-cyano-1,2,3-triazole at slightly elevated temperature existed as a 1 : 1 isomeric mixture of its closed (**1-5)** and open (**1-6)** isomer.[2] Shortly after, Harmon found that *N*-sulfonyl-1,2,3-triazoles processing an amino group at the C-5 position (**1-7**), also existed as an isomeric mixture (**1-7** and **1-8**, Scheme 1-2).[3]



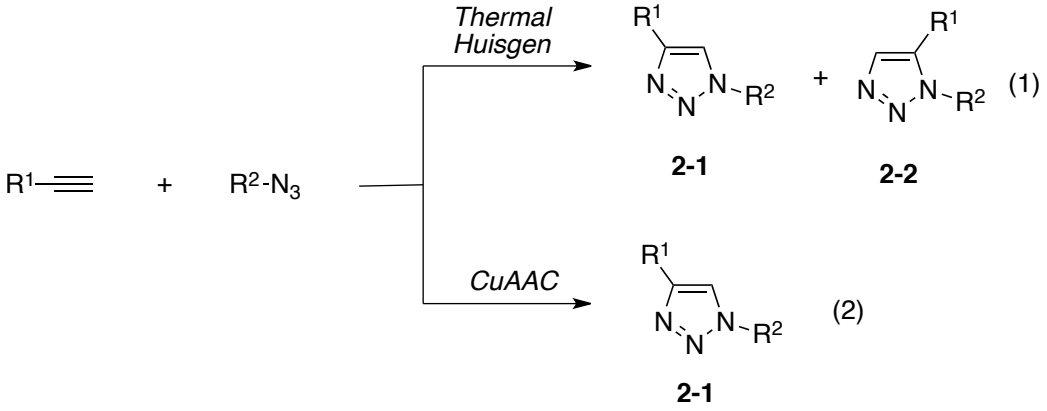
Scheme 1-2

1.2. Synthesis and functionalization of 1,2,3-triazoles

1.1.1. Azide-alkyne Huisgen cycloaddition and CuAAC

Due to importance of 1,2,3-triazoles,[4] great effort has been put into the efficient preparation of these compounds.[5] Traditionally, a classical Huisgen cyclaoaddition reaction[6] has been condidered as the most general method for synthesis of 1,2,3-triazoles. However, this method suffers from harsh conditions as well as poor regioselectivity, as illustrated in Scheme 2-1, eq 1. In 2002, Meldal,[7] Fokin and Sharpless[8] independently investigated the possibility to render cyclaoaddition reaction catalytic. As a result, they developed the copper-catalyzed azide-alkyne cycloaddition reaction (CuAAC), a "click reaction"[9] as a practical, efficient and robust method for synthesis of 1,4-disubstituted-1,2,3-triazoles **2-1** (Scheme 2-1, eq 2). In the presence of a Cu(I) catalyst, an azide is reacted with an alkyne in a [3+2] cycloaddition manner, to form a 5-membered heterocyclic core. The employment of Cu(I) catalytic system is crucial because it not only

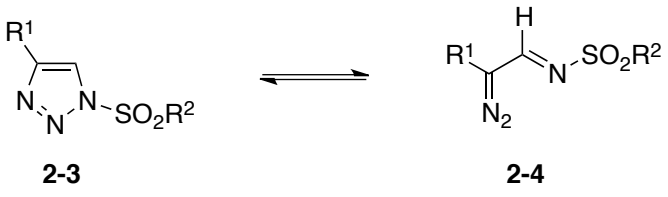
produces a single regioisomer (**2-1** vs **2-2**), but also accelerates the reaction, thus allowing it to proceed at room temperature (versus heating in thermal Huisgen cycloaddition reactions). Therefore, due to the reliability of CuAAC, it has become the most prominent way to access 1,4-disubstituted 1,2,3-triazoles. After its discovery, numerous modified conditions have been reported to improve the originally developed method.[5,10]



Scheme 2-1

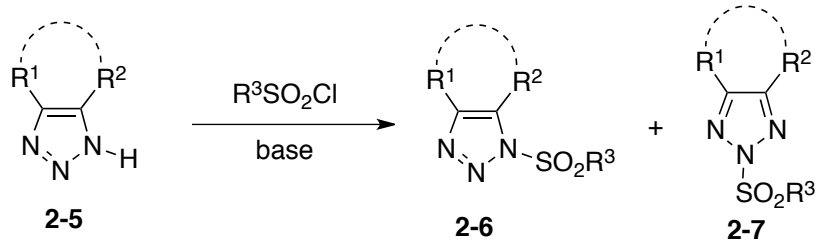
1.1.2. Synthesis of *N*-sulfonyl-1,2,3-triazoles

N-sulfonyl-1,2,3-triazoles **2-3** possess a weakened N1-N2 bond, and, thus, can undergo a facile ring-chain isomerism to generate higher concentration of ring opened isomer, iminodiazo species **2-4**, which is a promising new synthon for diverse transformations (Scheme 2-2).[11]



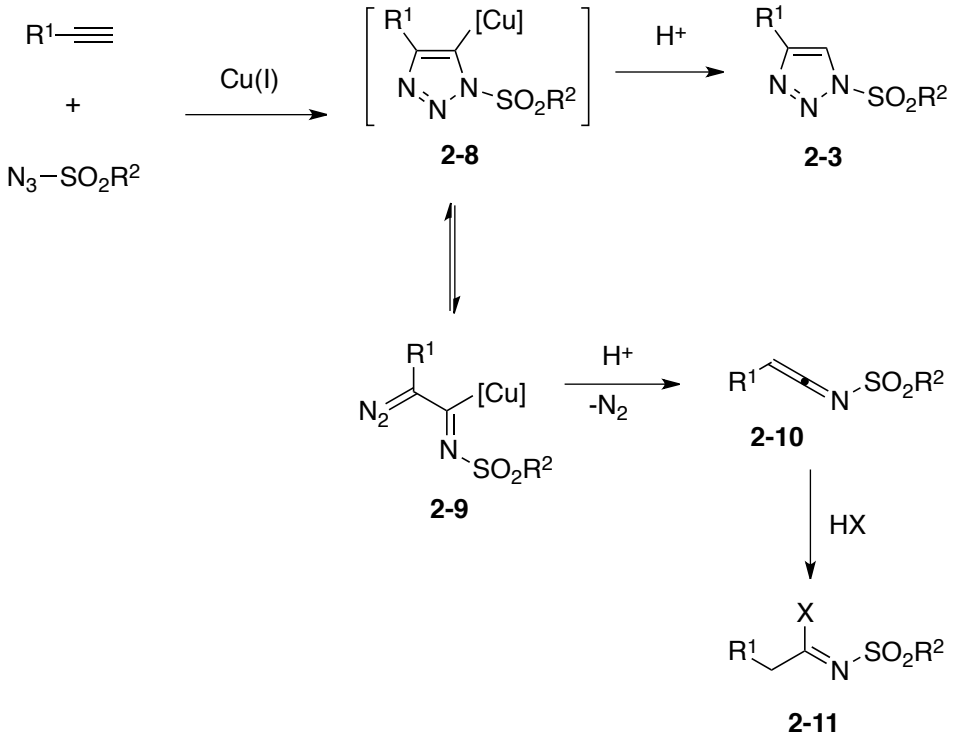
Scheme 2-2

The traditional method for synthesis of *N*-sulfonyl triazoles involves treatment of NH-triazoles with sulfonyl chlorides in the presence of base.[12] However, this method produces a mixture of N1 (**2-6**)- and N2 (**2-7**)-sulfonylated triazoles, where the ratio of the regioisomers depends on the nature of both the triazole ring and the sulfonyl chlorides used (Scheme 2-3). Clearly, this method is not practical because only the N1 isomer (**2-6**) can undergo a ring-chain isomerization to form the desired diazoimine intermediate **2-4**.



Scheme 2-3

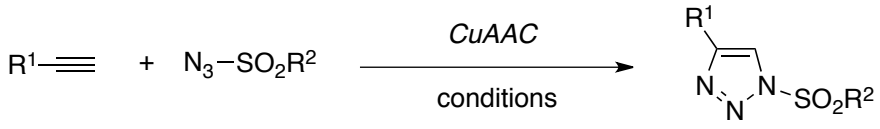
Although, the CuAAC serves as a good method for preparation of *N*-aryl- or alkyl-1,2,3-triazoles, attempts on employment of this strategy for synthesis of *N*-sulfonyl-1,2,3-triazoles were not successful. In this case, the initially formed intermediate **2-8** does not undergo protonation reaction to afford the desired product **2-3**. Instead, upon losing N_2 gas from the ring-opened diazo compound **2-9,** a ketenimine species **2-10** is generated. The latter then react with amines, alcohols, or water, to form amidines, imidates, or amides (**2-11**), respectively (Scheme 2-4).[13]



Scheme 2-4

Fokin, Chang and Sharpless first developed a preparative procedure for synthesis of *N*-sulfonyl-1,2,3-triazoles.[14] They found that this important heterocycle could be obtained regioselectively in good to excellent yields by performing the reactions at low temperature in the presence of 2,6-lutidine and catalytic amounts of CuI (Scheme 2-5, conditions A). Since then, various modified conditions have been reported by several research groups (Scheme 2-5).[14-15] Among them, the method developed by Fokin[15c] constitutes a most practical, simple, and robust protocol for synthesis of sulfonyl triazoles. By employing copper(I) thiophene-2-carboxylate (Liebeskind's reagent), a convenient, bench-stable catalyst, *N*-sulfonyl-1,2,3-triazoles could be formed effectively at ambient temperatures both under anhydrous conditions and in heterogeneous suspension with water. The procedure is quite simple and broad in scope, allowing rapid and efficient access to diverse *N*-sulfonyl-1,2,3-triazoles. Thus, not surprisingly, this method has

become the "standard conditions" for preparation of various *N*-sulfonyl-1,2,3-triazoles Scheme 2-5, conditions B).



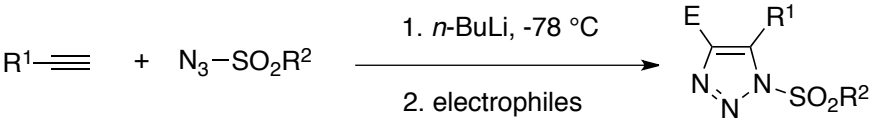
2-3

conditions: A. CuI, 2,6-lutidine, $CHCl_3$, 0°C
B. CuTc, toluene or H_2O, rt
C. $Cu(OAc)_2$ H_2O, 2-aminophenol, MeCN, rt
D. Cu_2O, H_2O, rt
E. CuBr, PhSMe, H_2O, rt
F. $[Tpm^{*,Br}Cu(NCMe)]BF_4$, $CHCl_3$, 40 °C

$Tpm^{*,Br}$ = tris(3,5- dimethyl-4-bromopyrazolyl)methane

Scheme 2-5

Later, Croatt reported a selective synthesis of 4,5-substituted *N*-sulfonyl triazoles (Scheme 2-6).[16] By treating acetylides with sulfonyl azides, 5-substituted *N*-sulfonyl triazole anions were produced, which could be trapped with various electrophiles to form the 4,5-substituted *N*-sulfonyl triazole products **2-12**.



2-12

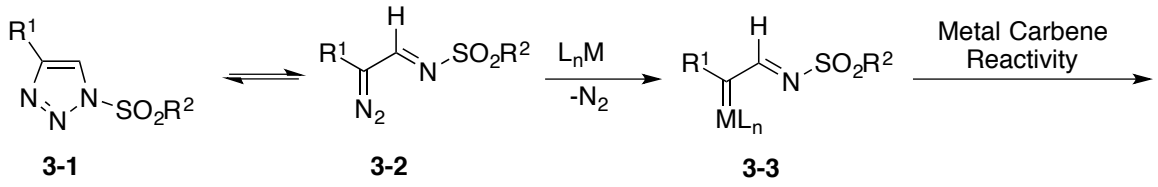
E = Cl, Br, NO_2, CHO, etc.

Scheme 2-6

1.3. Reactions of *N*-sulfonyl-1,2,3-triazoles

As discussed above, *N*-sulfonyl-1,2,3-triazole is an important heterocyclic unit, which can be easily synthesized by the copper-catalyzed azide-alkyne cycloaddition

reaction. Equilibrium exists between ring-closed triazole form **3-1** and ring-opened diazo form **3-2**. The latter, upon treating with transition metals, could be converted into α-imino metallocarbene intermediates (**3-3**), which are highly electrophilic and would undergo a variety of useful transformations (Scheme 3-1). As known, the reactivity profile of metallocarbenes[17] depends on the their structures, giving rise to acceptor **3-4**, acceptor/acceptor **3-5**, and donor/acceptor **3-6** carbenes (Figure 3-1). Therefore, the employment of *N*-sulfonyl-1,2,3-triazoles as precursors offers an entry to new types of transition-metal stabilized donor/acceptor and acceptor carbenes, which could broaden the range of synthetic transformations available for carbene intermediates.



Scheme 3-1

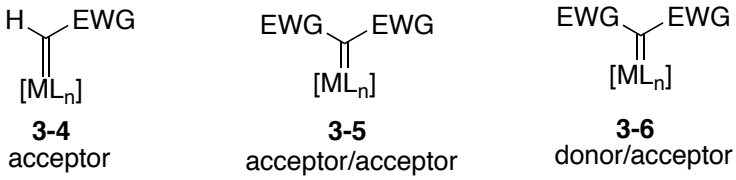
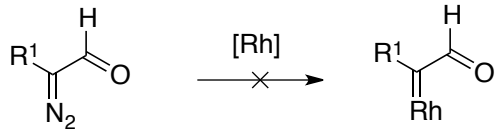


Figure 3-1

To date, only $Rh_2(CO_2R)_4$, $Ni(cod)_2$/ligand, $Ag(CO_2CF_3)$, and Rh(III)/Ag have been shown to efficiently catalyze the transformation of *N*-sulfonyl-1,2,3-triazoles,[11] and of these catalysts, rhodium(II) tetracarboxylates have proven to be the most versatile. It is well known that rhodium carbenes exhibit the wealth of reactivity,[18] and this method of generating the diazo progenitors is particularly attractive considering that sulfonyl triazoles effectively become synthetic equivalents of α-diazo aldehydes **3-7**, which due to

a facile competing Wolff rearrangement,[19] cannot be converted into the attractive corresponding rhodium carbenes **3-8**. In addition, another distinctive feature of using *N*-sulfonyl-1,2,3-triazoles is the generation of metallocarbenes with a pendant sulfonyl imine group. The nitrogen atom exhibits a higher nucleophilicity than the oxygen atom in the related α-oxo metallocarbene (e.g. **3-3** vs **3-8**). Due to this increased nucleophilicity, the α-imino group has the ability to participate in reactions involving zwitterionic intermediates, which can then cyclize into various heterocycles.



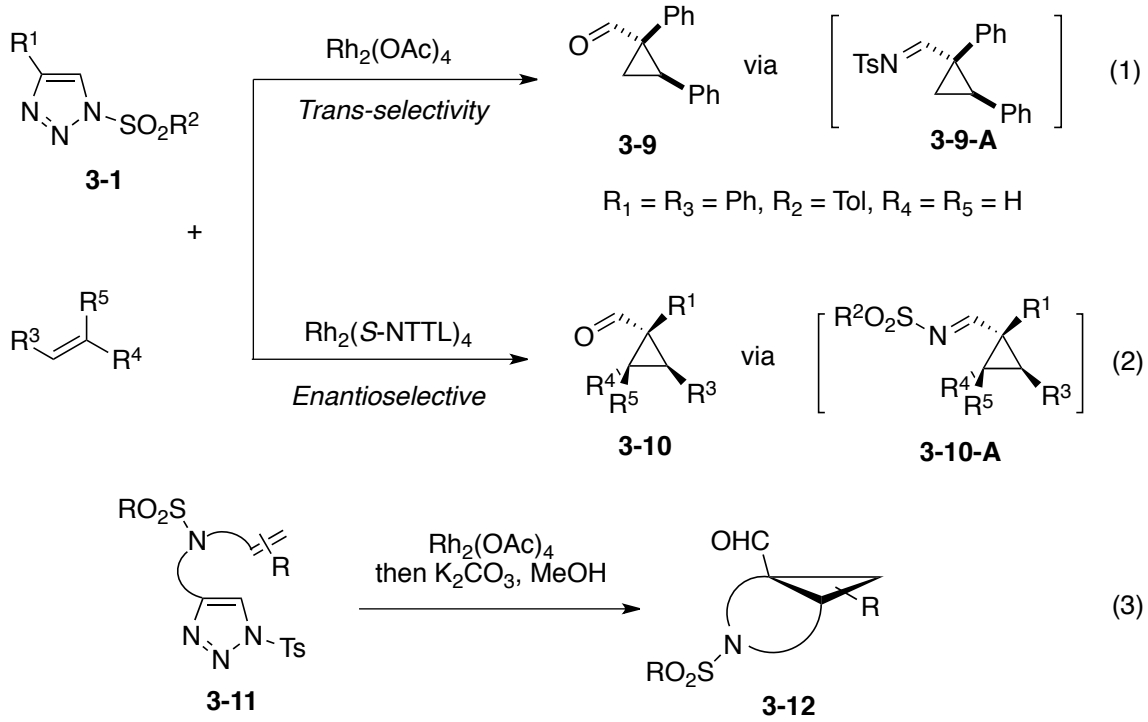
3-7 **3-8**

Scheme 3-2

1.3.1. [2+1] cycloaddition reactions

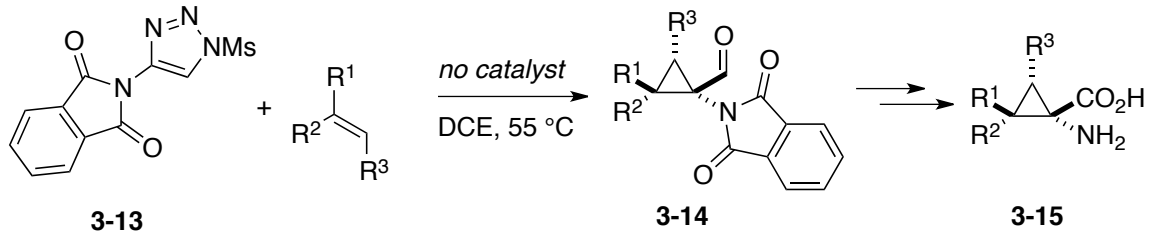
Employment of *N*-sulfonyl-1,2,3-triazoles to generate Rh-iminocarbene intermediates was first introduced by our and Fokin's group.[20] In this work, it was demonstrated that in the presence of 1mol% $Rh_2(OAc)_4$ catalyst, *N*-tosyl-triazole **3-1** (R^1 = Ph, R^2 = Tol) smoothly underwent [2+1] cycloaddition with styrene to quantitatively produce the *trans*-cyclopropane carboxaldehydes **3-9** after a hydrolysis work up (Scheme 3-3, eq 1). Later, a highly enantioselective version of this process was developed by Fokin's group by employing chiral Rh_2(*S*-NTTL)$_4$ catalyst (Scheme 3-3, eq 2).[21]

Recently, an intramolecular [2+1] cyclopropanation reaction was reported by Pan, Xu and co-workers, where a *N*-tethered alkenyl tosyl-triazole **3-11** was used for the efficient construction of azabicyclo[4.1.0]/[5.1.0] system **3-12** (Scheme 3-3, eq 3).[22]



Scheme 3-3

As discussed in section 1.1, *N*-sulfonyl-1,2,3-triazole processing an amino group at the C-5 position (**1-7**), also exists as mixture of a ring-closed triazole form (**1-7**) and a ring-opened diazo form (**1-8**, Scheme 1-2). By taking advantage of this equilibrium, Davies has developed a highly diastereoselective cyclopropanation reaction of 4-phthalimido-*N*-mesyl-1,2,3-triazoles (**3-13**) with alkenes under metal free conditions, which offers an efficient access to cyclopropane α-amino acids **3-15** (Scheme 3-4).[23]

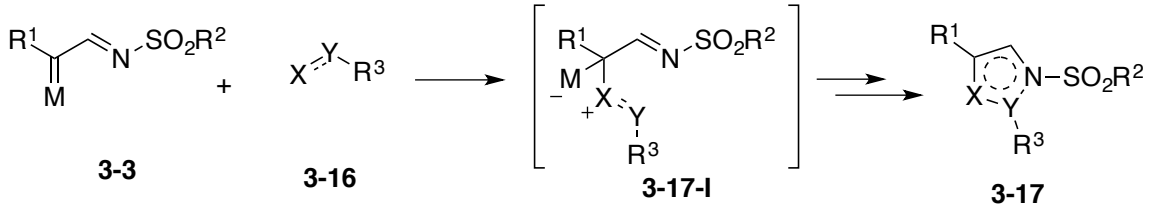


3-13 **3-14** **3-15**

Scheme 3-4

1.3.2. [3+2] cycloaddition reactions

One of the advantages of employing iminocarbenes (**3-3**) derived from *N*-sulfonyl-1,2,3-triazoles (**3-1**) is their ability to react with various dipolarophiles **3-16** to form zwitterion intermediates (e.g. **3-17-I**), which upon cyclization produces various heterocyclic systems **3-17** (Scheme 3-5). This cascade transformation, involving ring opening, N_2 elimination, and a formal [3+2] cycloaddition, was named "transannulation reaction."[24]



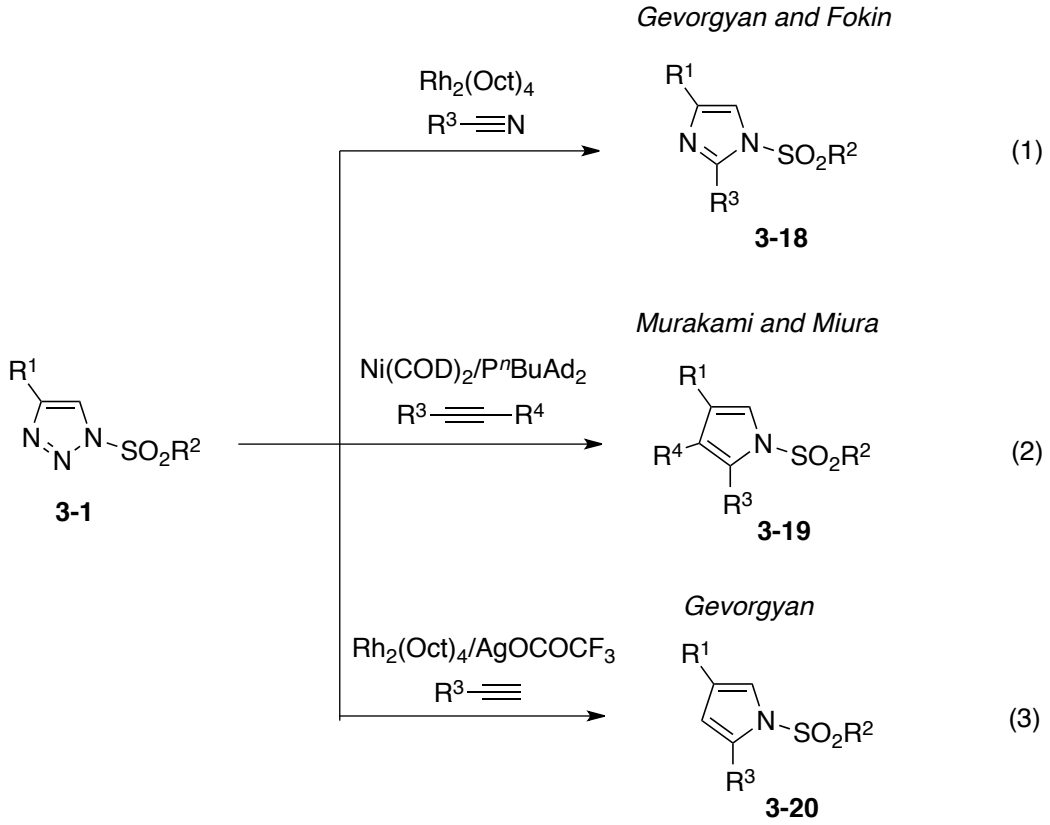
3-3 **3-16** **3-17-I** **3-17**

Scheme 3-5

1.3.2.1. Cycloaddition reactions with nitriles and alkynes

Our and Fokin's group reported that, in the presence of a rhodium(II) catalyst, triazoles **3-1** smoothly react with nitriles, producing imidazoles **3-18** (Scheme 3-6, eq 1).[20] Two different experimental protocols were established, namely, microwave-assisted and a conventional heating method. This work opened a new direction in triazole chemistry, as numerous novel methodologies have been developed since this initial

discovery. Thus, shortly after the first report,[20] the transannulaiton of triazoles with internal (Scheme 3-6, eq 2)[25] and terminal alkynes (Scheme 3-6, eq 3)[26] was accomplished by Murakami's group and our group employing Ni (0)/L_n (for internal alkynes) or Rh/Ag (for terminal alkynes) catalytic systems, respectively. Using this method, polysubstituted pyrroles **3-19** or **3-20** could be obtained in good yields from easily available *N*-sulfonyl-1,2,3-triazoles **3-1**.



Scheme 3-6

1.3.2.2. Cycloaddition reactions with alkenes

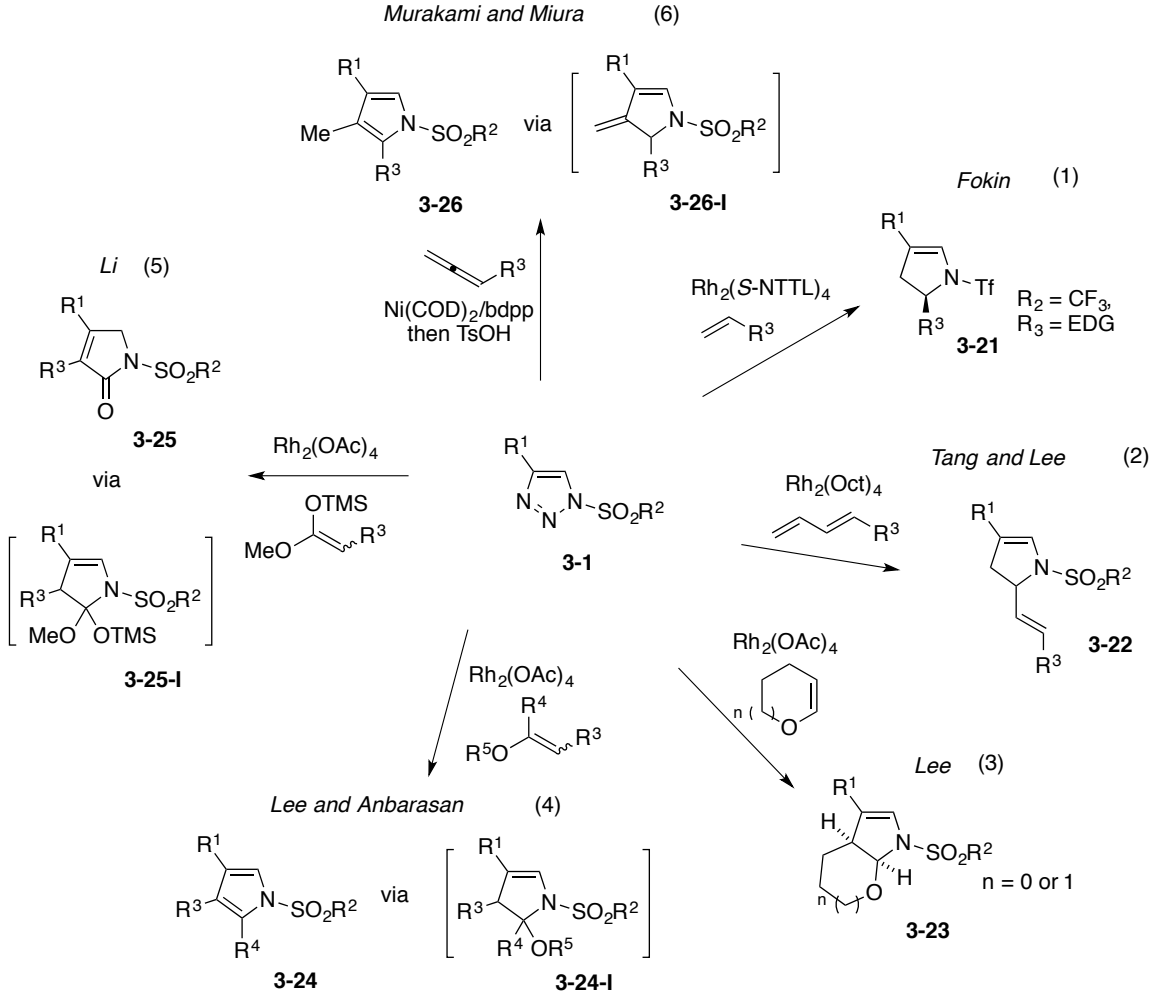
The reactions of olefins with *N*-sulfonyl-1,2,3-triazoles in a [2+1] cycloaddition manner to afford cyclopropane products has been discussed in section 1.3.1. On the other hand, if the iminocarbene intermediate **3-3** serves as an aza-[3C] synthon, a formal [3+2]

cycloaddition reaction could occur to generate useful heterocycle products as illustrated in Scheme 3-7. It was found by Fokin group that, electron-rich methoxystyrenes are capable to undergo transannulation reaction with *N*-sulfonyl-1,2,3-triazoles to produce 2,3-dihydropyrroles **3-21** in excellent yield and moderate enantioselectivity. This transformation proceeds via initial [2+1] cycloaddition with formation of cyclopropane intermediate, which upon rearrangement produces **3-21** (Scheme 3-7, eq 1).[27].

Later, Tang[28] and Lee[29] independently reported formation of alkenyl dihydropyrroles **3-22** upon reacting of **3-1** with 1,3-dienes in a formal [3+2] manner (eq 2). Not surprisingly, alkenyl alkyl ethers, which are highly electron-rich alkenes, are also capable to undergo transannulation reaction with *N*-sulfonyl-1,2,3-triazoles **3-1**, producing various pyrrole derivatives (**3-23** to **3-25**). Lee group reported synthesis of fused dihydropyrroles **3-23** by employing cyclic alkenyl alkyl ether dihydropyrans (eq 3).[30] Lee[31] and Anbarasan[32] group independently reported the reaction of acyclic alkenyl alkyl ethers with triazoles **3-1**. Upon a formal [3+2] cycloaddition reaction to form intermediate **3-24-I**, the latter would undergo elimination to afford final pyrrole products **3-24** in good yields (eq 4). In addition, alkenyl alkyl ethers possessing a –OTMS group also smoothly reacted with **3-1**, leading to [3+2] cycloaddition product **3-25-I**. A subsequent elimination of MeOTMS, followed by the C=C bond isomerization affords 3-pyrrolin-2-one (instead of **3-24**) as a final product **3-25 (**eq 5).[33]

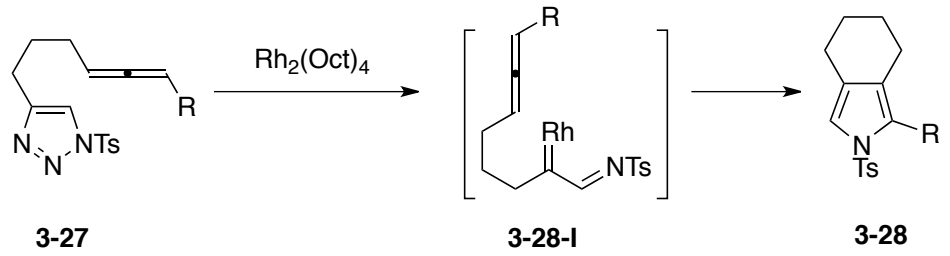
Besides the most popular Rh(II) catalytic system, Ni(0) could also efficiently catalyze the transannulaiton reaction of *N*-sulfonyl-1,2,3-triazoles. It was shown by Murakami and Miura that in the presence of $Ni(COD)_2$ and bdpp ligand (2,4-bis(diphenylphosphine)pentane), transannulation between triazoles **3-1** and allenes

proceed smoothly, providing practical and efficient access to polysubstituted pyrroles **3-26** with all substituents differentiated (eq 6).[34]



Scheme 3-7

In addition to the above discussed intermolecular transannulaiton reactions of *N*-sulfonyl-1,2,3-triazoles with alkenes, an intramolecular version of this chemistry was reported by Sarpong group. In this study, an allene motif was tethered to the triazole core through a three-carbon chain, which reacted with the Rh-carbene species intramolecularly to afford the 3,4-fused pyrroles **3-28** (Scheme 3-8).[35]

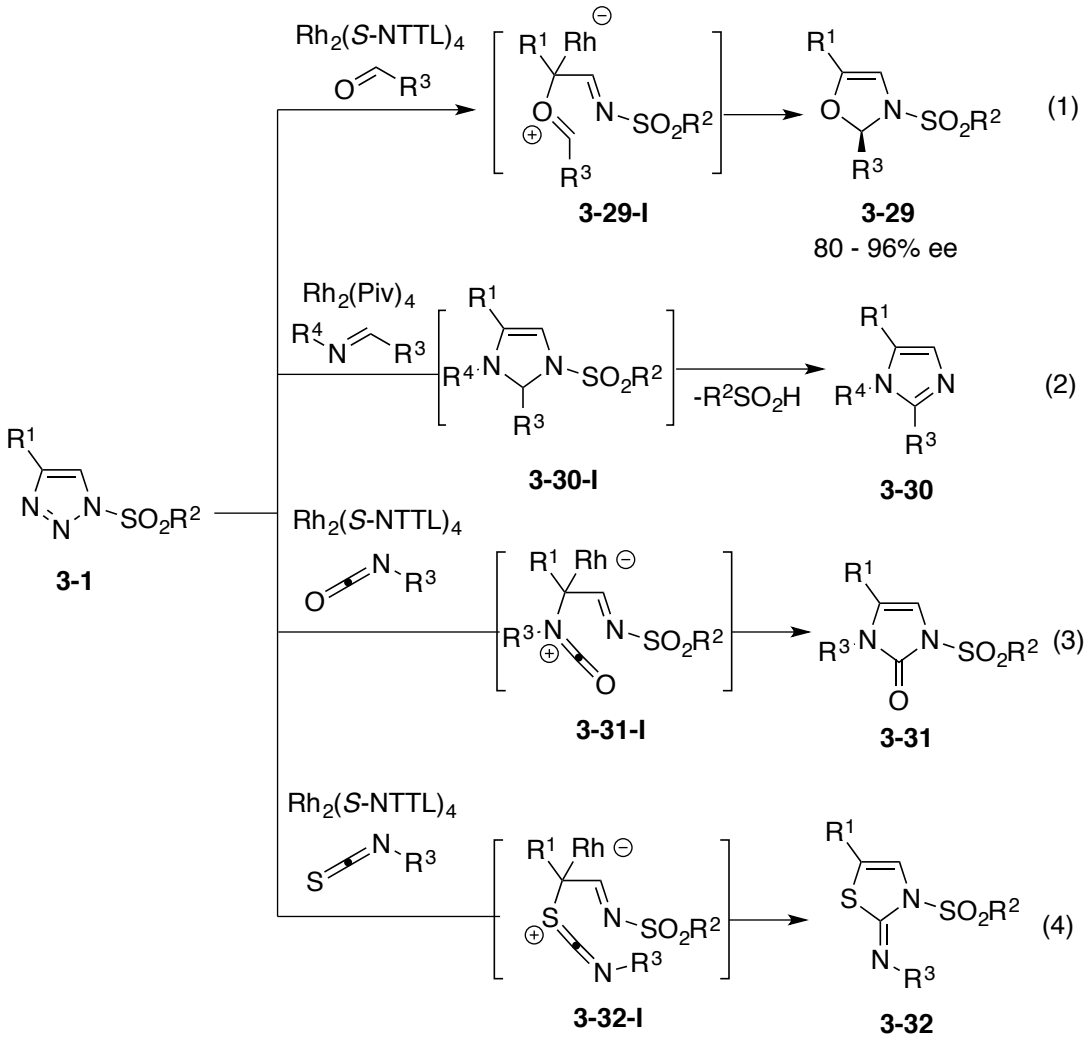


3-27 **3-28-I** **3-28**

Scheme 3-8

1.3.2.3. Cycloaddition reactions with C=X bonds

Besides C=C bonds, highly polarized C=X double bonds are also capable partners for this formal [3+2] cycloaddition reactions of *N*-sulfonyl-1,2,3-triazoles. In this case, the heteroatom would attack the carbenoid carbon to produce an ylide intermediate, followed by cyclization to afford the final heterocyclic product (Scheme 3-9). Fokin investigated a series of C=X bond containing substrates, and reported the transanulaiton reaction of *N*-sulfonyl triazoles with aldehydes. Using this method, 3-sulfonyl-4-oxazolines **3-29** were produced in excellent yields and high levels of enantioselectivity (eq 1). Similarly, by employing aldimine, which bears C=N bond motif, 1,2,5-trisubstituted imidazoles **3-30** could be formed after elimination of sulfinic acids (eq 2).[36] Moreover, the same group has also disclosed transannulation of triazoles **3-1** with heterocumulenes. Thus, imidazolones **3-31** (eq 3) and thiazoles **3-32** (eq 4) could efficiently be synthesized from easily available starting materials.[37] In this method, the regioselectivity was controlled by nucleophilicity of heterocumulene substrates. In the case of isocyanates, the more nucleophilic nitrogen atom would attack the carbenoid carbon to generate ammonium ylide intermediate (**3-31-I**); whereas in the case of isothiocyanates, a sulfonium ylid intermediate **3-32-I** would be produced first.



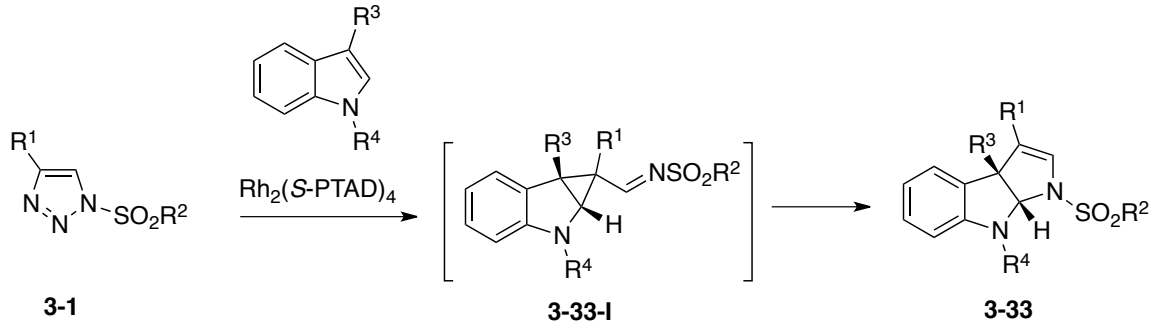
Scheme 3-9

1.3.2.4. Cycloaddition reactions with aromatics

Furthermore, the formal [3+2] cycloaddition of *N*-sulfonyl-1,2,3-triazoles could also proceed with aromatics, giving access to diverse fused systems.

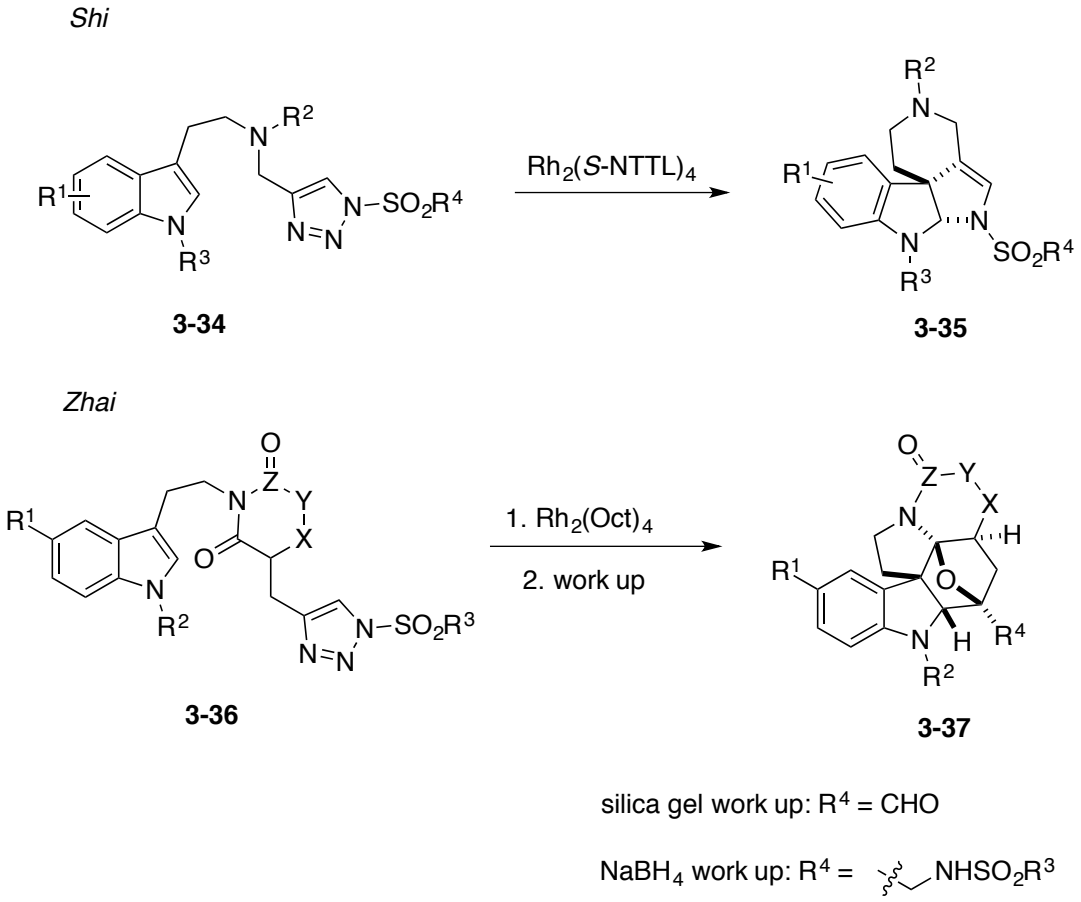
Thus, Davies and co-workers demonstrated an interesting transannulation of triazoles with indoles toward asymmetric synthesis of pyrroloindoline **3-33** (Scheme 3-10).[38] Like the formal [3+2] cycloaddition reaction with alkenes, this transformaiton is initiated by a cyclopropanation reaction, leading to a strained cyclopropylindoline

intermediate **3-33-I**, which then undergoes rearrangement into pyrroloindoline products **3-33**.



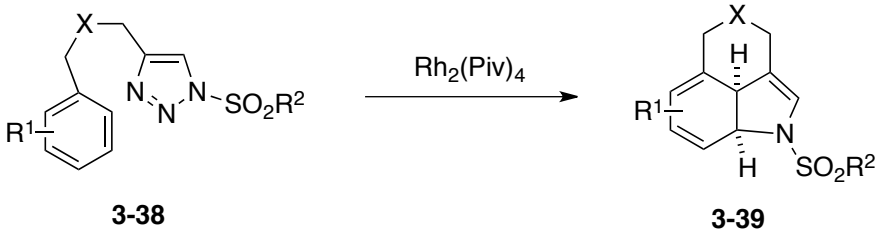
Scheme 3-10

The intramolecular version of this reaction was then explored by Shi[39] and Zhai,[40] as illustrated in Scheme 3-11. By tethering indole motif to the triazole core, various polycyclic systems could be constructed in a single step (e.g. **3-35** and **3-37**), providing an efficient method for rapid synthesis of diverse indole alkaloids.



Scheme 3-11

Murakami and Miura disclosed an interesting dearomatization of simple arenes proceeding through intramolecular transannulation reaction with *N*-sulfonyl-1,2,3-triazoles. In this method, a tricyclic 3,4-fused indole **3-39** could be formed with high efficiency from readily available materials (Scheme 3-12).[41]



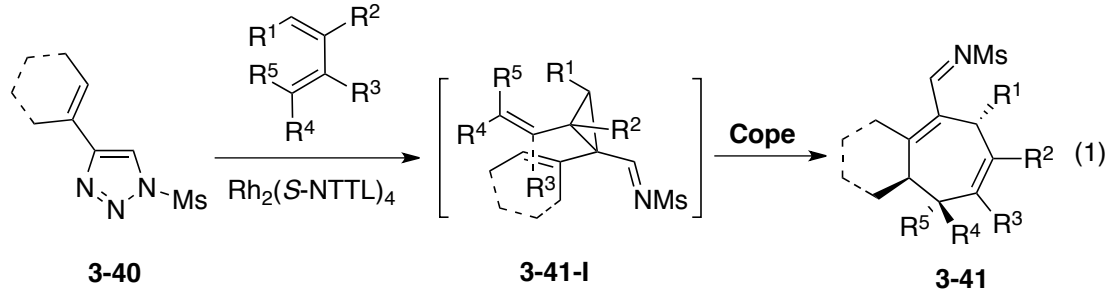
Scheme 3-12

1.3.3. [3+4] cycloaddition reactions

As illustrated above, the reaction between *N*-sulfonyl-1,2,3-triazoles and 1,3-dienes proceeded smoothly to give alkenyl dihydropyrroles **3-22** (Scheme 3-7, eq 2). In this case, only one C-C double bond was involved in the reaction. Alternatively, the 1,3-dienes could also serve as a [4C] synthon, producing 7-membered ring via a formal [3+4] cycloaddition process.

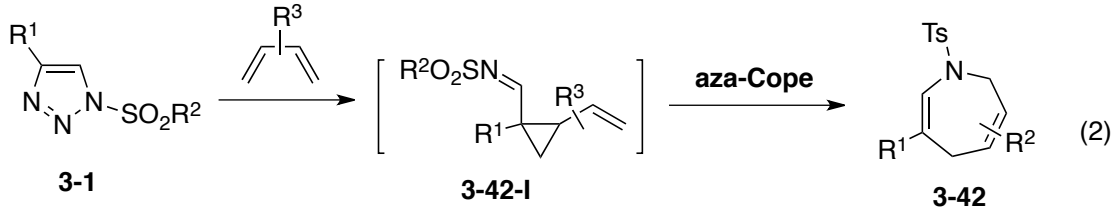
The possibility of this reaction manifold was first deomstrated by Davies using 4-alkenyl-1,2,3-triazoles. Upon reacting with 1,3-dienes, 7-membered carbocycles **3-41** were obtained with high degree of enantioselectivity. This transformation proceeded through a tandem cyclopropanation/Cope rearrangement mechanism with formation of cyclopropane intermediate **3-41-I** (Scheme 3-13, eq 1).[42] In this a formal [3+4] cycloaddition reaction, the alkenyl iminocarbene intermediates served as [3C] synthon, not as an aza-[3C] unit, Later, Tang[28] and Lee[29] independently investigated the aza-variant of this formal [3+4] cycloaddition. Upon reacting triazoles **3-1** with 1,3-dieneds, a similar intermediate **3-42-I** could be formed, which then underwent an aza-Cope rearrangement to afford 7-membered heterocycle – dihydroazepine **3-42** in good yield (Scheme 3-13, eq 2).

Davies



3-40 **3-41-I** **3-41**

Tang and Lee



3-1 **3-42-I** **3-42**

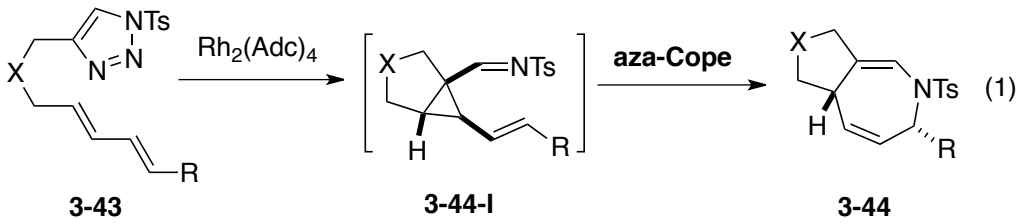
Tang: $Rh_2(Oct)_4$, 4A MS

Lee: Rh_2(*S*-PTAD)$_4$

Scheme 3-13

As a complementary method to the previously discussed intermolecular formal [3+4] cycloaddition of *N*-sulfonyl-1,2,3-triazoles, the intramolecular version was developed by Sarpong group employing allenyl triazoles **3-43** (Scheme 3-14, eq 1).[43] Similarly, this transformation was initiated by an intramolecular [2+1] cycloaddition to form intermediate **3-44-I**, followed by a subsequent aza-Cope rearrangement occurred to produce five-membered ring fused dihydroazepines **3-44**. Later, Shen[44] and Tang[45] further explored this method, expanding its scope to other tetheried patterns (eq 2).

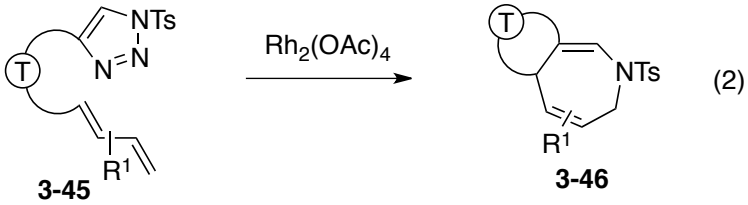
Sarpong



3-43 **3-44-I** **3-44**

X = NTs, O, CR_2

Shen and Tang



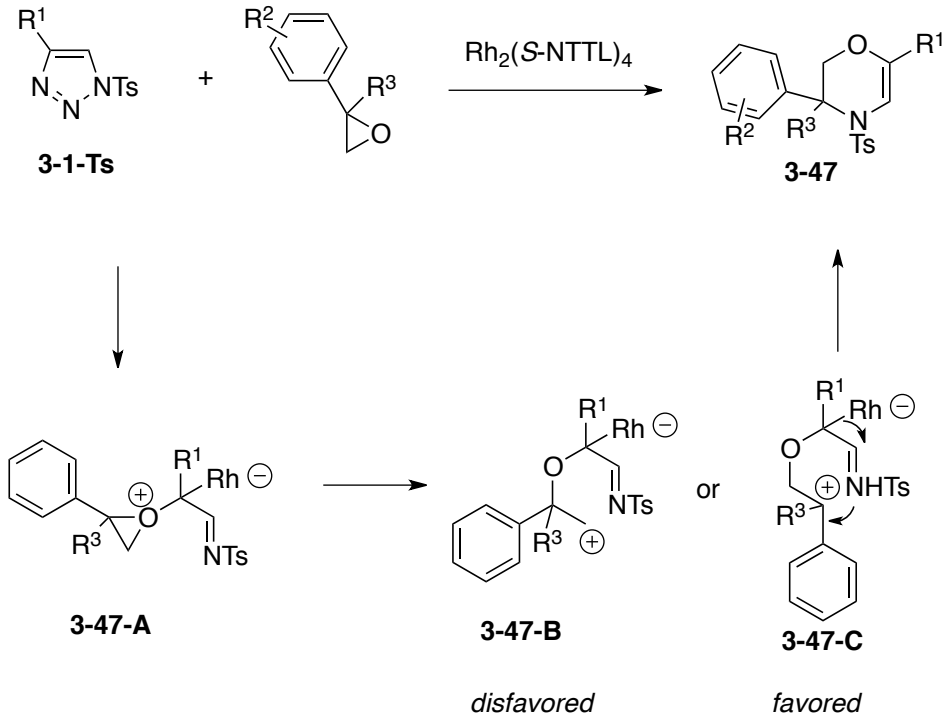
3-45 **3-46**

Scheme 3-14

1.3.4. Transannulation reactions with cyclic compounds

Comparing to the numerous reports on using unsaturated compounds in transannulaiton reactions with *N*-sulfonyl-1,2,3-triazoles, the employment of saturated molecules in this type of reactions is relative rare.

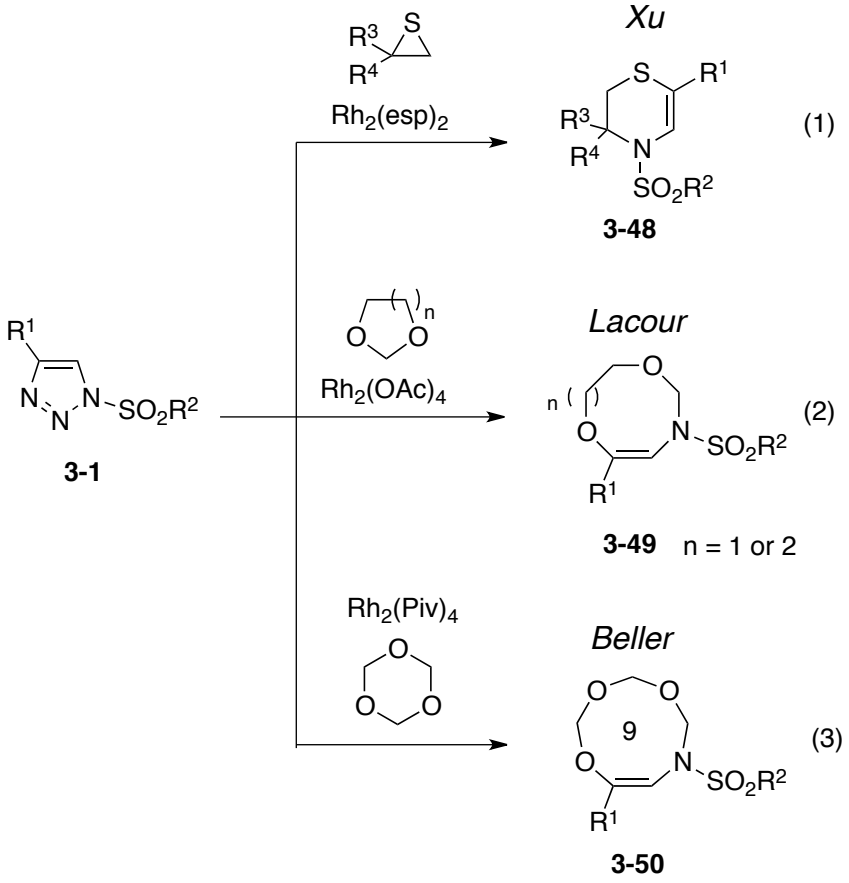
The Chen group by taking advantage of the nucleophilic oxygen in epoxides, developed a formal [3+3] reaction for the synthesis of 3,4-dihydro-2*H*-1,4-dioxazines **3-47** (Scheme 3-15).[46] Driven by the electrophilic activation and a ring strain, the initially formed oxonium ylide intermediates **3-47-A** underwent the C-O bond cleavage to produce carbocationic intermediate **3-47-C**, which upon a subsequent nucleophilic attack by the imino N-atom at carbenium center cyclizes into product **3-47**. The regioselectivity of the ring opening step is controlled by the stability of carbocation intermediates (**3-47-B** vs **3-47-C**).



Scheme 3-15

Later, Xu extended this formal [3+3] cycloaddition method by replacing O atom with S-atom (thiirane), providing a general access to 3,4-dihydro-2*H*-1,4-thiazine derivatives **3-48** (Scheme 3-16, eq 1).[47]

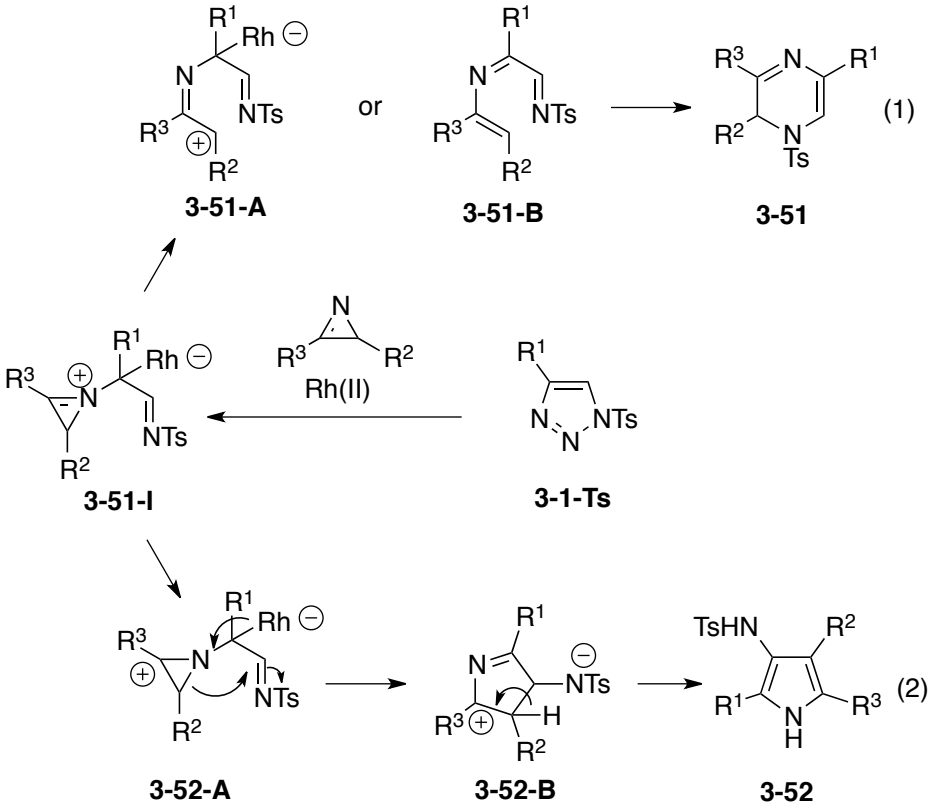
Likewise, multi-oxygen-containing medium-sized rings (1,3-dioxolane, 1,3-dioxane and 1,3,5-trioxane) are also capable partners for this type of transannulation reactions with *N*-sulfonyl-1,2,3-triazoles. Thus, a formal [3+5] or [3+6] cycloaddition reaction proceeded smoothly, giving raise to nitrogen-containing 8- and 9-membered ring systems (**3-49** and **3-50**) in one step in moderate to good yields (eq 2 and eq 3).[48]



Scheme 3-16

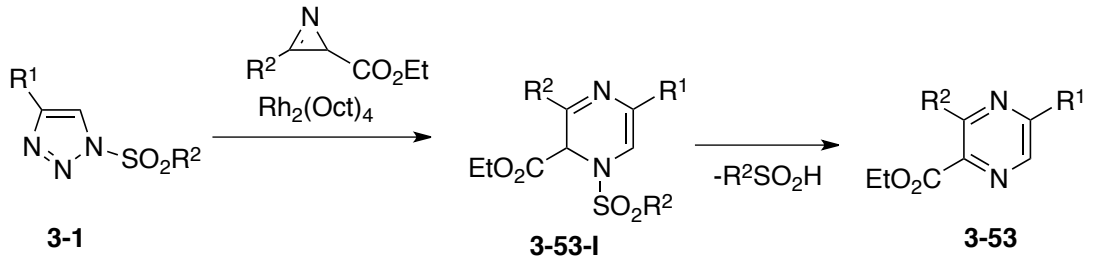
In addition, 2*H*-Azirines, a class of highly strained three-membered cyclic compound, have also been demonstrated to be capable reaction partners in transannulaiton reaction with triazoles **3-1**. Thus, Tang group revealed that in the presence of Rh(II) catalyst, azirines could react smoothly with *N*-sulfonyl-1,2,3-triazoles, producing azirinium ylide intermediates **3-51-I**. The latter, then would undergo ring-opening/ring-closure sequence to afford 1,2-dihydropyrazines **3-51** (Scheme 3-17, eq 1).[49] In this reaction passway, both 2*H*-Azirines and Rh-iminocarbenes served as aza-[3C] synthons. Alternatively, a [2+3] cycloaddition reaction was also developed by the same group, where the Rh-iminocarbene species served as [2C] synthon. Thus, the imino carbon was attacked (**3-52-A**), giving rise to a five-membered zwitterion intermediate **3-**

52-B, which then produced substituted 3-aminopyrroles **3-52** as final products (eq 2). With two competing passways, the outcome of this transformation depended on the nature of substrates, as well as on the reaction conditions.



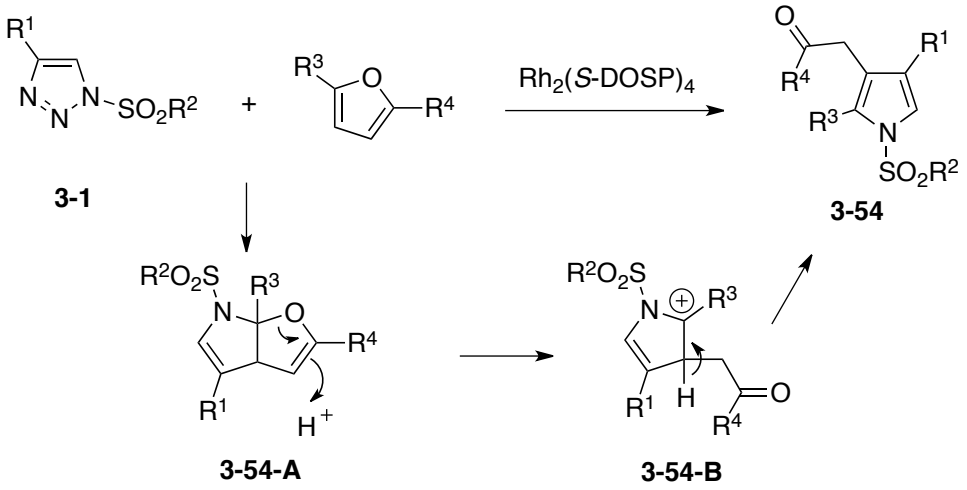
Scheme 3-17

Around the same time, Lee's group reported a similar transannulaiton reaction of **3-1** with ester-substituted 2*H*-Azirines (Scheme 3-18).[50] With the help of an electron-withdrawing ester group, a formal [3+3] product could be formed initially, which then underwent elimination of arylsulfinic acid to afford the substitute pyrazines **3-53** as final products.



Scheme 3-18

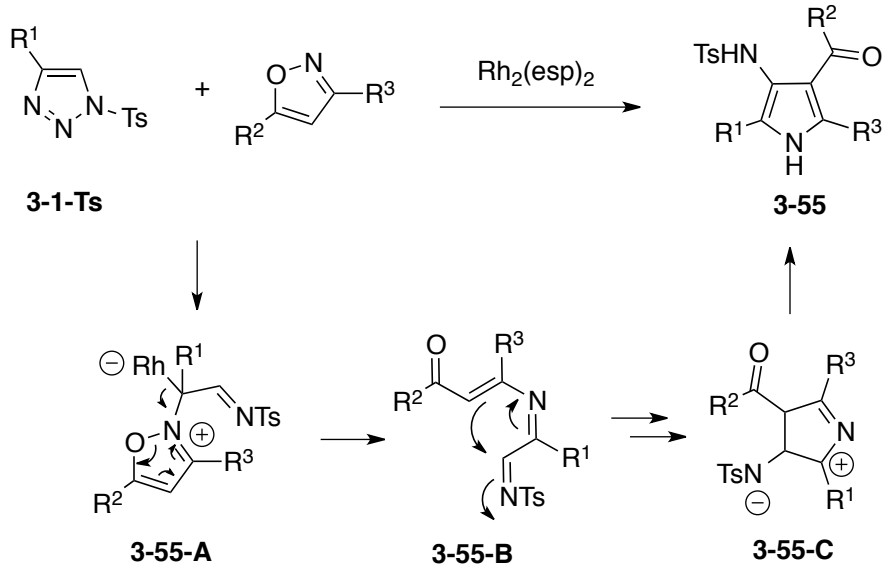
Davies described synthesis of trisubstituted pyrroles via another approach (Scheme 3-19).[51] In this case, the electron-rich 2,5-disubstituted furans smoothly reacted with triazole **3-1** at the C-3 position, generating a formal [3+2] cycloaddition intermediates **3-54-A**. A subsequent ring opening (**3-54-A** to **3-54-B)** followed by proton loss led to formation of pyrrole products **3-54**. However, when unsymmetrically substituted furans ($R^3 \neq R^4$) were submitted to the reaction, mixture of regioisomers was observed.



Scheme 3-19

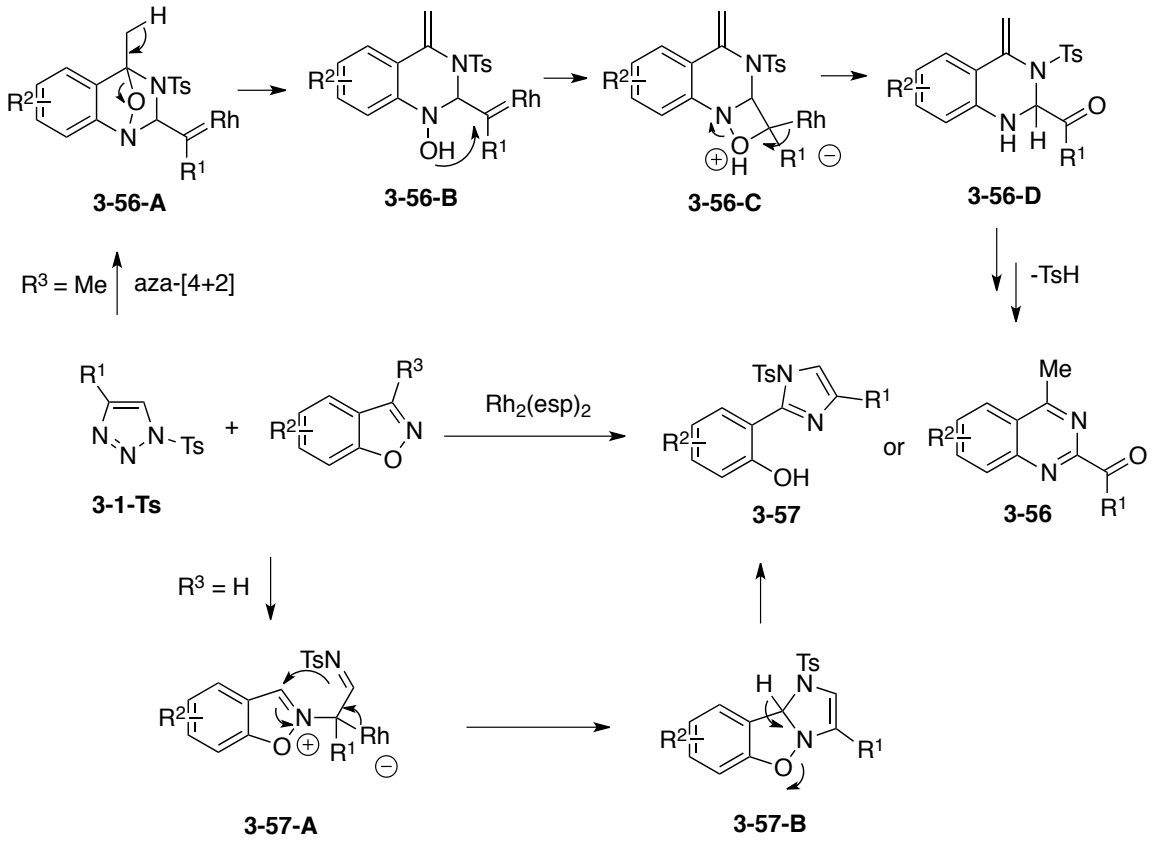
Following this ring-opening concept, Tang group by utilizing relatively labile N-O bond, developed a series of transannulaiton reactions of *N*-sulfonyl-1,2,3-triazoles with isoxazoles or benzisoxazoles. It was found that isoxazoles could participate in

transannulation reaction under Rh-catalyzed conditions as an aza-[3C] component, by reacting with the [2C] Rh-iminocarbene synthon to produce 3-minopyrroles **3-55** (Scheme 3-20).[52]



Scheme 3-20

In continuation of this study, the same group examined the reactivity of 2,1-benzisoxazoles towards transannulation reactions, proving an efficient method for synthesis of quinazoline derivatives **3-56** (Scheme 3-21, top).[53] Different from all other reported works where the *N*-sulfonyl-1,2,3-triazole commonly served as [1C]-, [2C]-, or aza-[3C]-component, it formally served here as an aza-[2C]-component, further enriching the versatile reactivity of Rh-iminocarbenes. Moreover, a formal [3+2] cycloaddition with the C-N double bond of 1,2-benzisoxazole was also reported, offering the rapid construction of diverse imidazole derivatives **3-57** (Scheme 3-21).



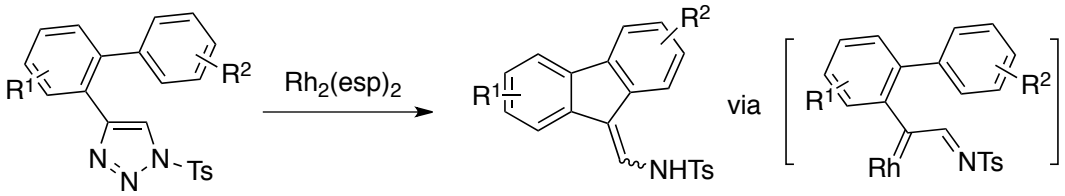
Scheme 3-21

1.3.5. Transannulation reactions via intramolecular C-H insertion

Like Rh-carbenes derived from diazo compounds, Rh-iminocarbenes, which are generated from *N*-sulfonyl-1,2,3-triazoles in the presence of Rh(II) catalyst, could also undergo various insertion reactions into diverse X–H bonds.[54] By employing this strategy, a series of cyclic compounds were produced via intramolecular C-H insertion reactions employing various tethers.

Lee group utilized *N*-sulfonyl-4-biaryl-1,2,3-triazole **3-58** as starting material for an intramolecular sp^2 CH insertion reaction of the generated Rh-iminocarbene intermediate **3-59-I**, thus, proving an efficient method for synthesis of fluorene

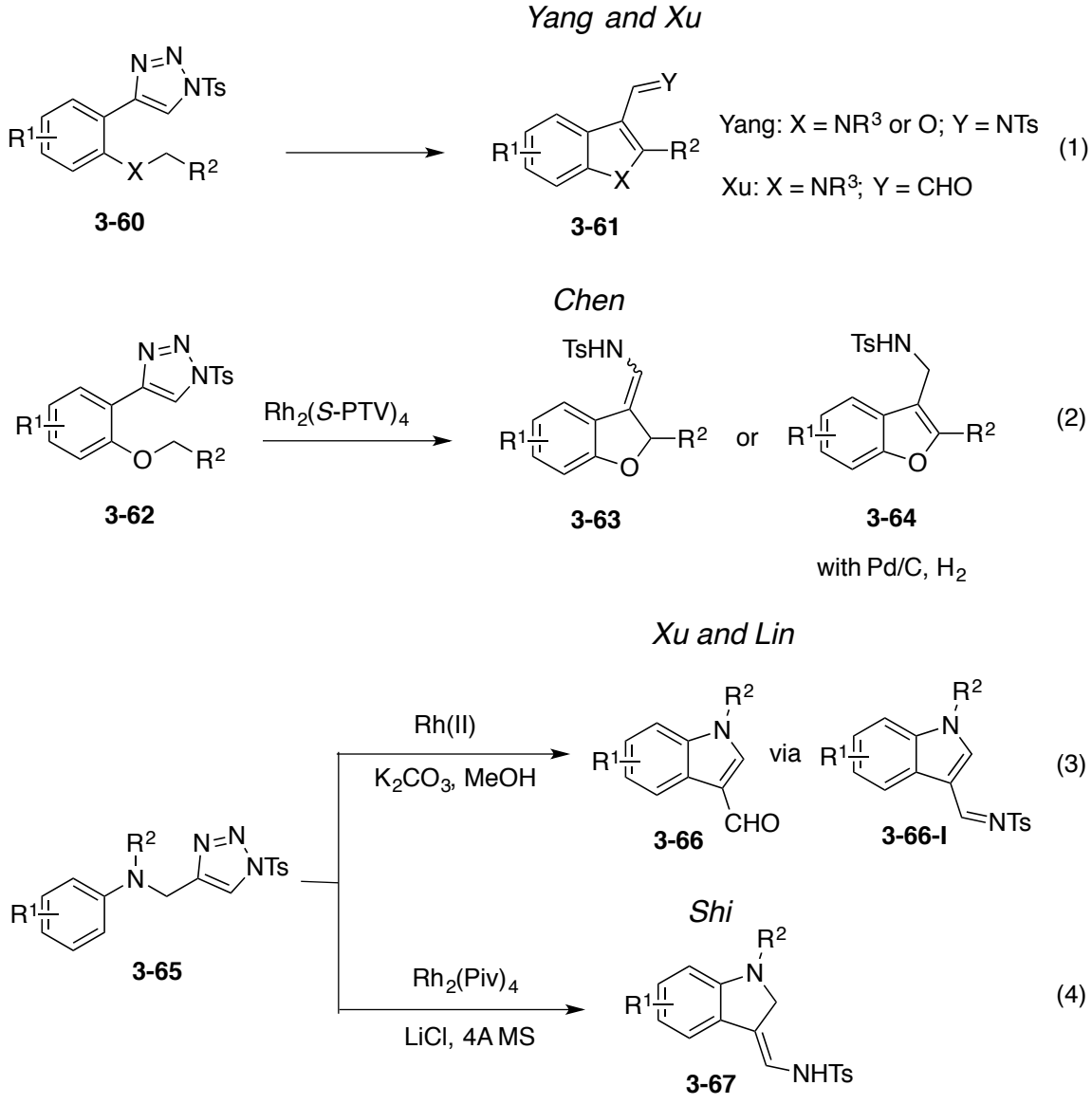
derivatives **3-59** possessing enamine moiety at the C-9 methylene bridge (Scheme 3-22).[55]



3-58 **3-59** **3-59-I**

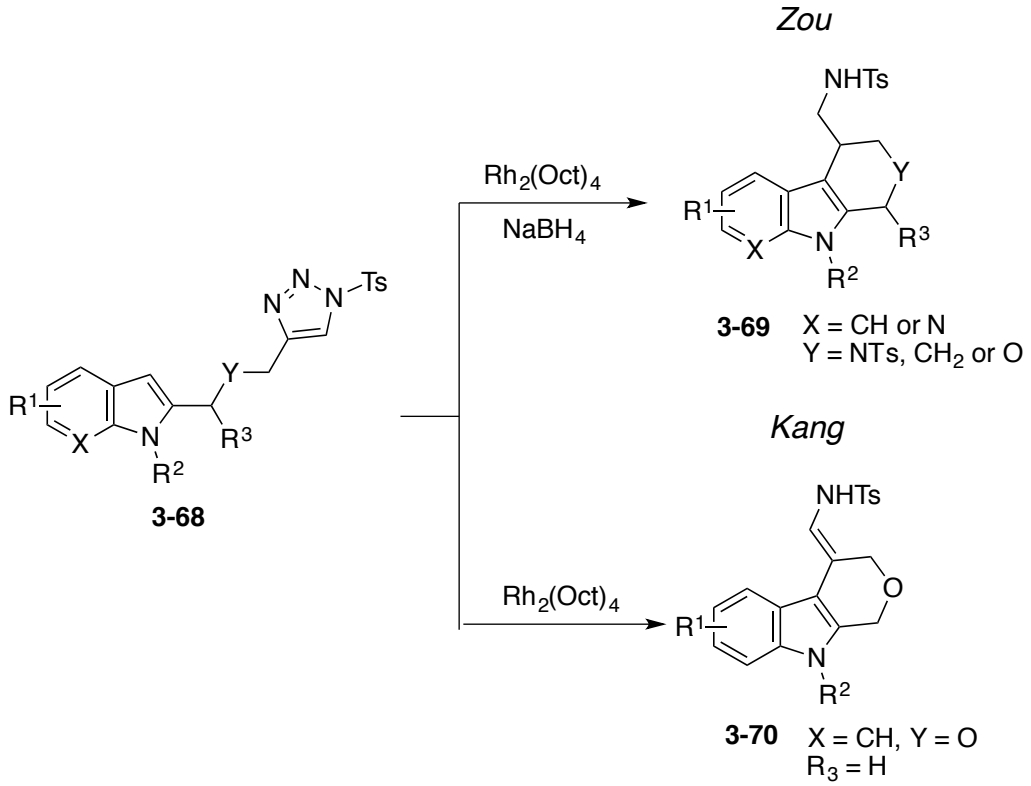
Scheme 3-22

Similarly, a series of indole and benzofuran derivatives were obtained from CH insertion reactions by installing N/O-atom and phenyl groups onto the tether of triazole substrates (Scheme 3-23).[56]



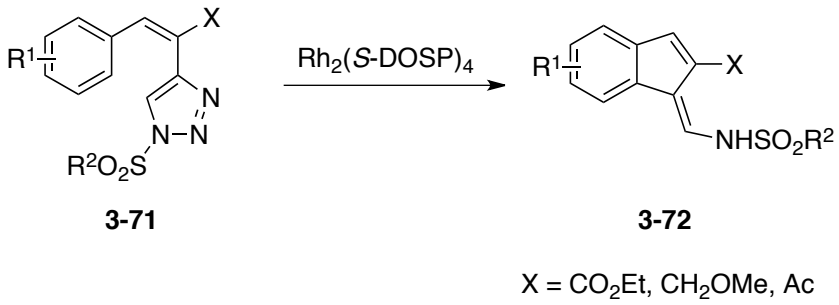
Scheme 3-23

Likewise, the employment of indole as tethering group has enabled rapid construction of polyheterocyclic systems, as illustrated in Scheme 3-24.[57]



Scheme 3-24

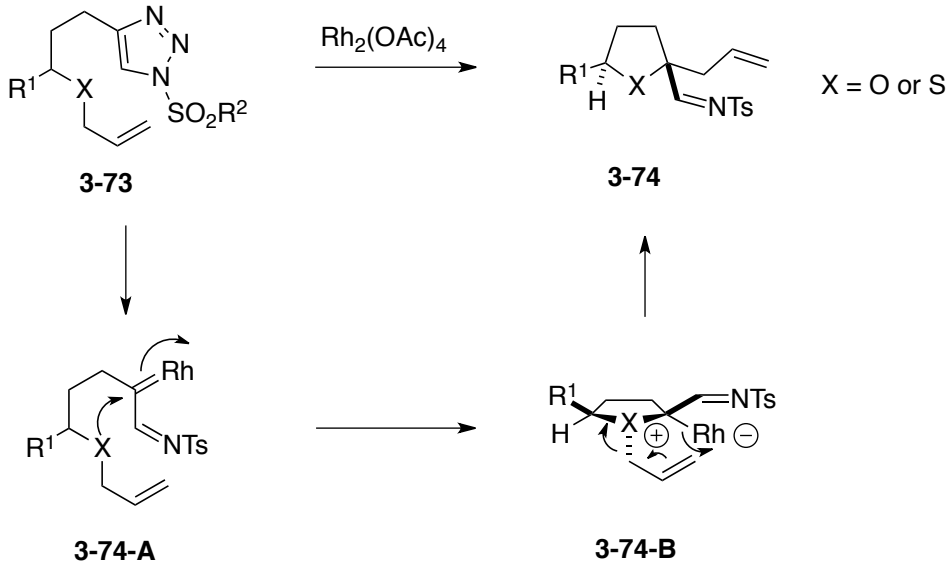
In addition, alkene motif could also serve as a tether, leading to a wide range of functionalized benzofulvenes **3-72** (Scheme 3-25).[58]



Scheme 3-25

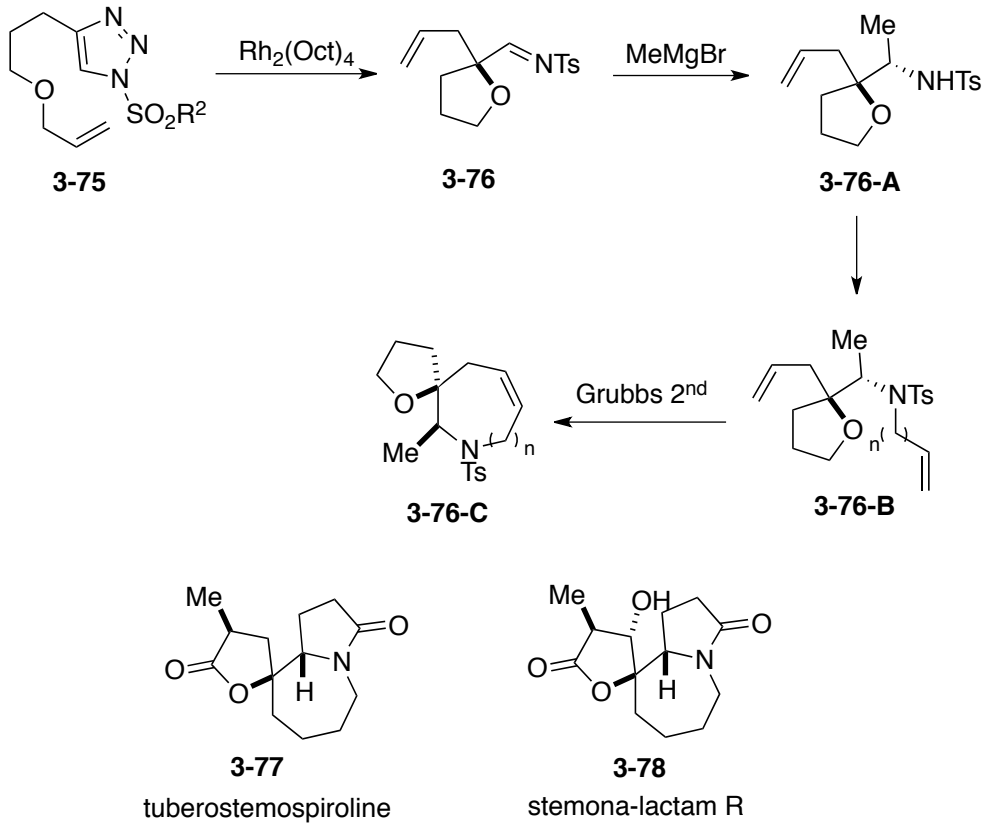
1.3.6. Transannulation reactions via intramolecular generation of ylide intermediates

As shown in previous sections, ylides are important intermediates in the transformations of *N*-sulfonyl-1,2,3-triazoles. The Boyer group demonstrated that with a γ-allyloxy group at the 4-position of *N*-sulfonyl-1,2,3-triazoles (**3-73**), the formed oxonium/sulfonium ylide species **3-74-B** could undergo a [2,3]-sigmatropic rearrangement to deliver the product **3-74** (Scheme 3-26).[59] This method has enabled diastereoselective synthesis of tetrahydrofurans and tetrahydrothiophenes from easily available triazole starting materials.



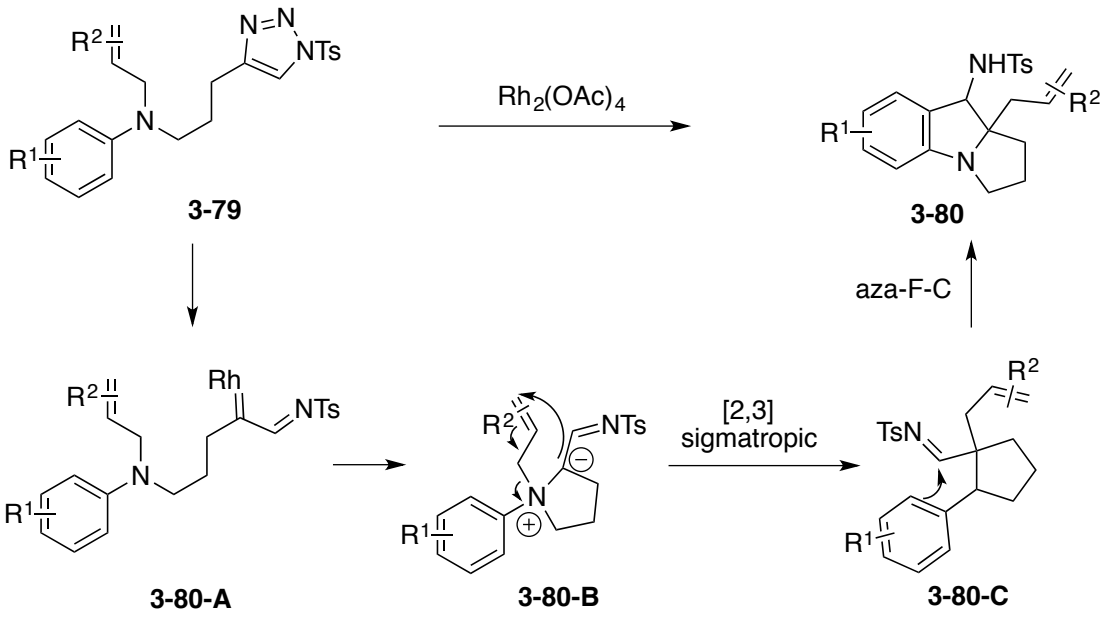
Scheme 3-26

At the same time, Yang group independently disclosed the same method and its application in the total synthesis of (±)-tuberostemospiroline **3-77** and (±)-stemona-lactam R **3-78** as a key step (Scheme 3-27).[60]



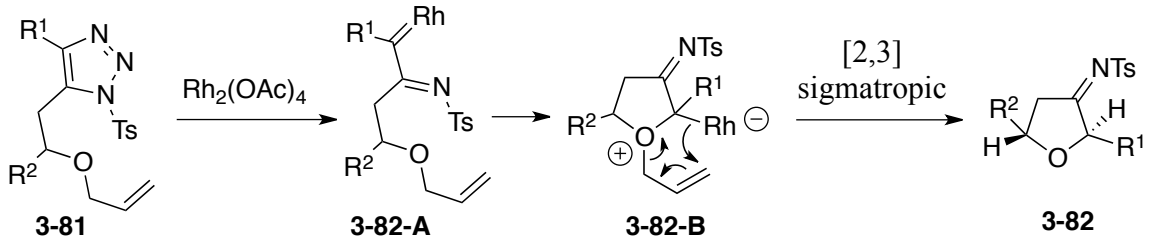
Scheme 3-27

Along this line, Shen group reported that, by replacing O/S atom with an aryl amine motif, the formed ammonium yield **3-80-B** could also undergo a [2,3]-sigmatropic rearrangement to produce a pyrrodinyl sulfonyl imine intermediate **3-80-C**. The latter, upon an aza-Friedel−Crafts reaction with a competent vicinal aromatic ring, would deliver a tricyclic nitrogen-containing scaffold **3-80** (Scheme 3-28).[61] The developed cascade transformation has offered an efficient one-pot protocol for synthesis of functionalized benzopyrrolizidines.



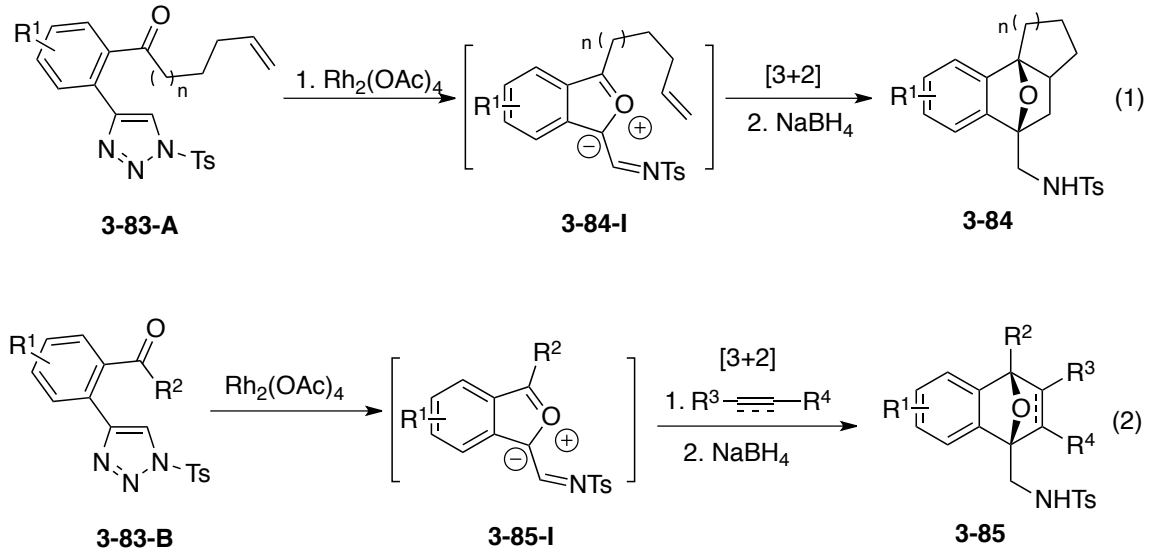
Scheme 3-28

As shown above, the employment of 1,4-substituted *N*-sulfonyl-1,2,3-triazoles has offered a great opportunity for new methodology development. However, reports on employment of *N*-sulfonyl-1,2,3-triazoles possessing a substituent at C5 position are rare.[62] Boyer group first investigated the reactivity of such substrates, reported a unique cascade transformation from **3-81** (Scheme 3-29).[63] Like 1,4-triazoles, in the presence of Rh(II) catalyst, the 1,4,5-substituted *N*-sulfonyl-1,2,3-triazole **3-81** could also participate well in the reaction, producing Rh-iminocarbene species **3-82-A**. Next, upon a similar nucleophilic attack of the O-atom at the carbenoid carbon affords aza-oxonium ylide **3-82-B**, which then underwent [2,3]-sigmatropic rearrangement to deliver *trans*-dihydrofuran-3-imines **3-82** with excellent diastereoselectivity.



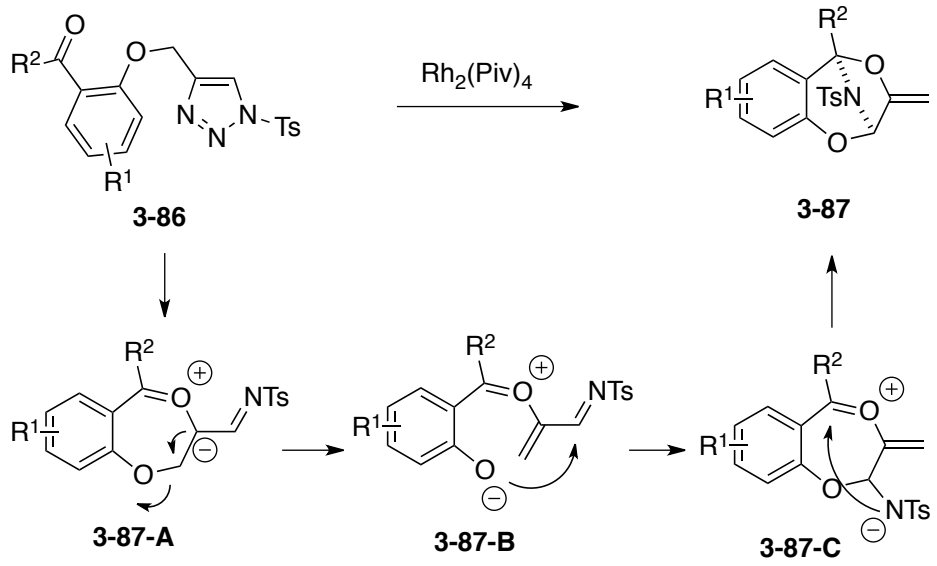
Scheme 3-29

In addition to rearrangement reactions, if the newly formed ylide intermediate could be trapped by another unsaturated motif, it would provide a practical method for rapid construction of polycyclic or bridged systems. With this concept, Yang developed a novel synthetic strategy for efficient synthesis of structurally diverse oxabicyclo[2.2.1]heptenes in a diastereoselective manner (Scheme 3-30).[64] In this transformation, upon reacting carbonyl group with the Rh-iminocarbene, oxonium ylide intermediate (**3-84-I** or **3-85-I**) was formed. Then, a subsequent [3+2] cycloadditon reaction proceeded intra- (eq 1) and intermolecularly (eq 2) to produce oxabicyclo[2.2.1]heptane core **3-84** and **3-85**. Employing this method, two oxygenated quaternary centers, two new carbon−carbon bonds, and one carbon−oxygen bond were formed in a single step.



Scheme 3-30

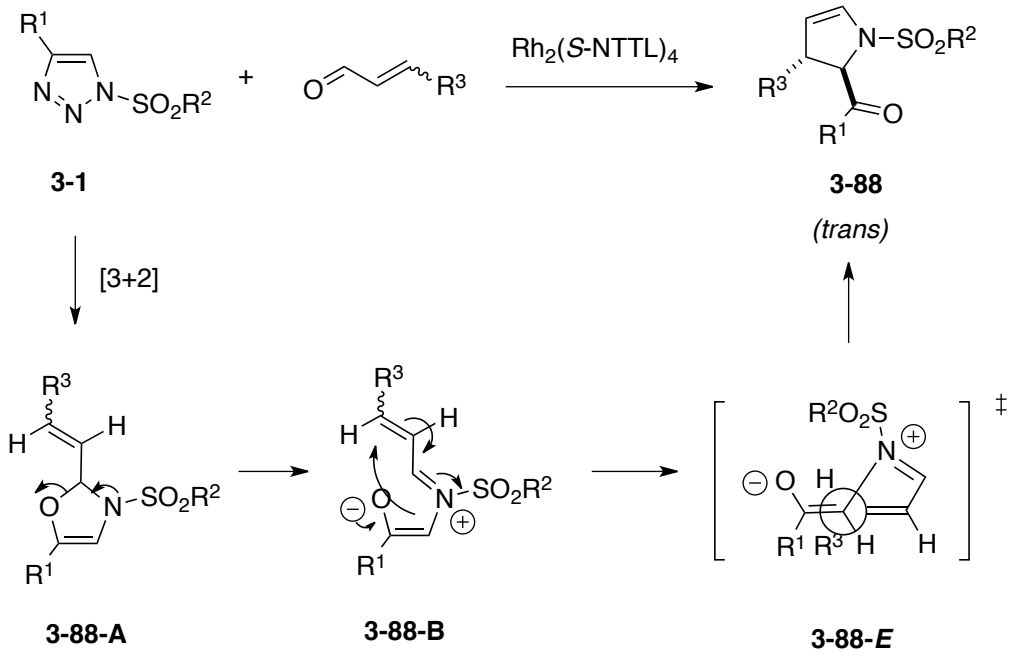
The Shi group reported an unprecedented cascade transformation of triazole **3-86**, which was initiated with an intramolecular reaction between carbonyls and Rh-carbenes.[65]. As shown in Scheme 3-31, after the generation of oxonium ylide **3-87-A**, a C-O bond cleavage occurred resulting in a new zwitterion **3-87-B**, which then recyclized with the imino motif to afford a 7-membered ring (**3-87-C**). Finally, a nucleophilic attack of the nitrogen atom at the oxonium moiety yielded the final product **3-87**. Thus, an aza-bridged benzodioxepine derivative was constructed efficiently via a formal 1,3-rearrangement (**3-87-A** to **3-87-C**)/[4+2] cycloaddition (**3-87-B** to **3-87**) sequence.



Scheme 3-31

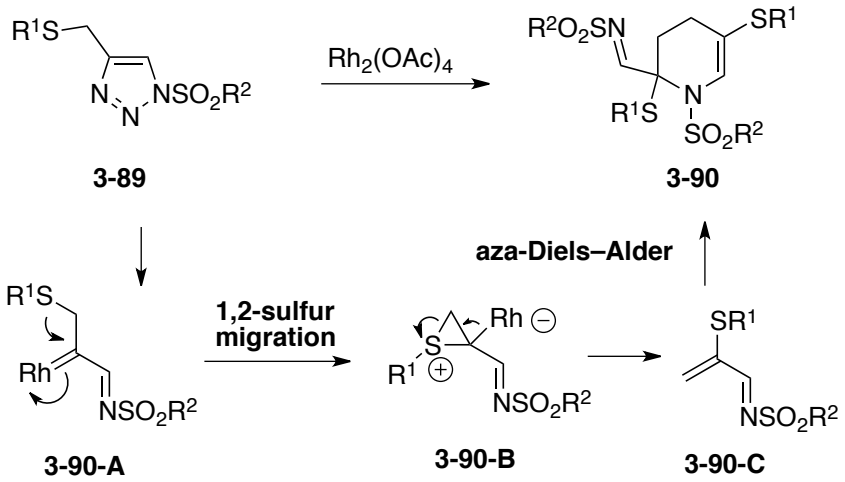
1.3.7. Miscellaneous transformations

Murakami and Miura disclosed a stereoselective synthesis of *trans*-2,3-dihydropyrroles **3-88**, which also employed a ring opening process of the heterocyclic intermediate (Scheme 3-32).[66] In this method, a [3+2] cycloadditon product (**3-88-A**) from *N*-sulfonyl-1,2,3-triazoles and α,β-unsaturated aldehydes was formed first, which upon cleavage of a weak aminal bond under reaction conditions produced intermediate **3-88-A**. The latter then recyclized into dihydropyrroles (**3-88**) via transition state **3-88-*E***.



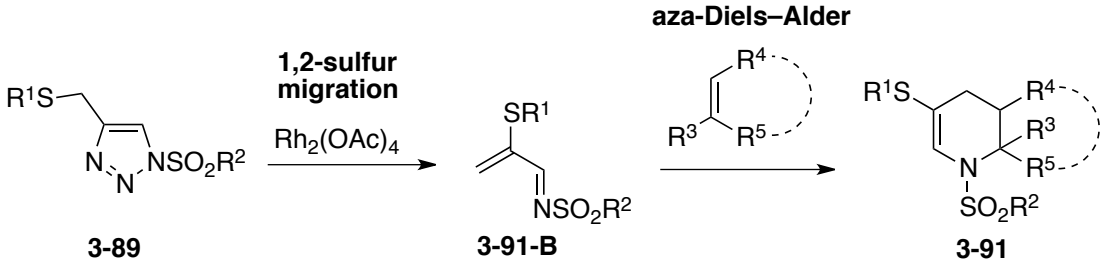
Scheme 3-32

The Shi group by combineing migratory process of the *in situ* generated ylide with cycloadditon reaction, developed a novel and efficient protocol toward S-containing tetrahydropyridine derivatives **3-90** (Scheme 3-33).[67] In this transformation, the initially formed Rh-iminocarbene intermediate **3-90-A** underwent 1,2-sulfur migration, offering an α,β-unsaturated imine **3-90-C**. The latter then served as both aza-diene and dienophile in a subsequent intermolecular aza-Diels–Alder reaction to procude the corresponding heterocycle **3-90**.



Scheme 3-33

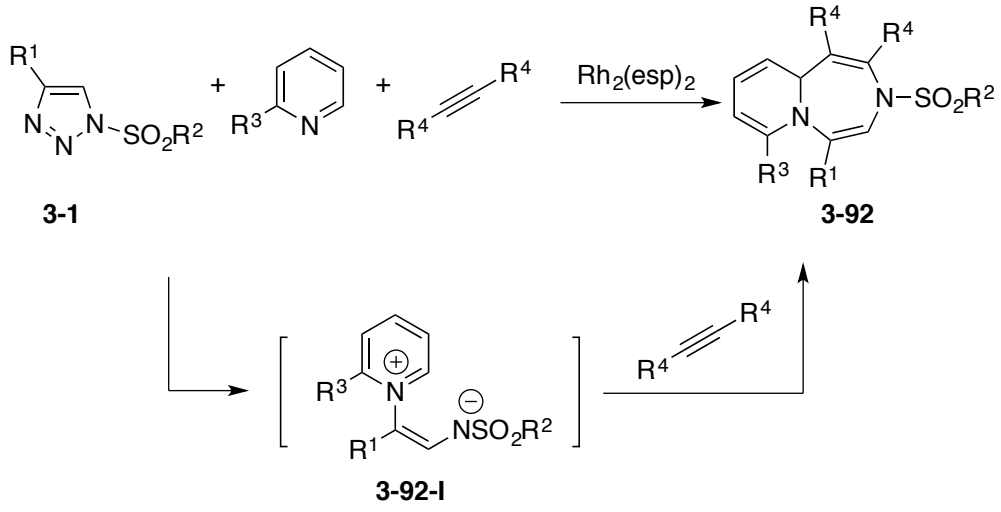
Shortly after, this strategy was further developed by Anbarasan group, where an exogenous alkene dienophile was introduced to the reaction mixture. Thus, through the same α,β-unsaturated imine intermediate **3-91-B**, various sulfur-substituted (fused) tetrahydropyridines (**3-91**) could be obtained in moderate to excellent yields (Scheme 3-34).[68]



Scheme 3-34

As discussed above, formal [m+n] cycloaddition reactions have been established as a general and practical reaction pattern for *N*-sulfonyl-1,2,3-triazoles, which allowed efficient synthesis of diverse range of heterocyclos from simple starting materials. Meanwhile, in contrast to catalytic [3+2]/[4+2] cycloadditions toward construction of five- and six- membered heterocyclic rings, synthetic strategies using a [5+2]

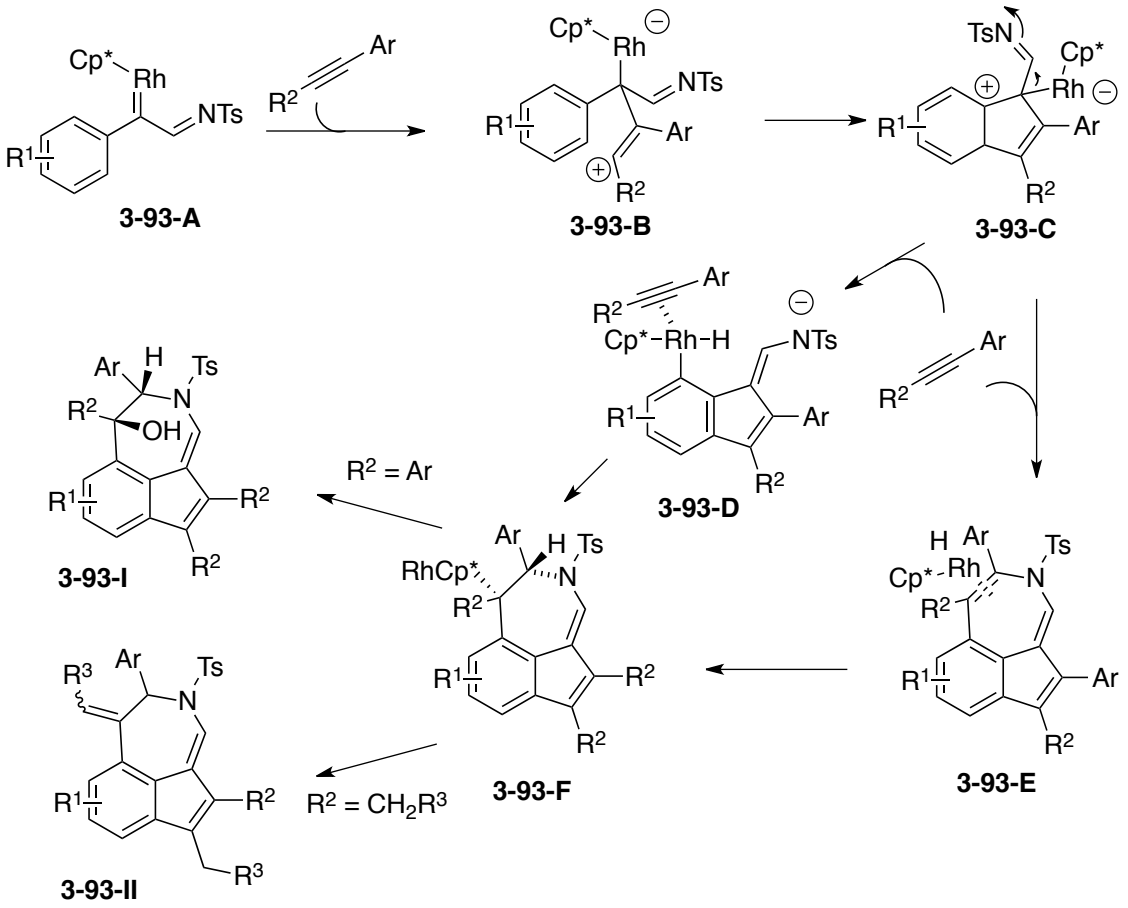
cycloaddition[69] for the construction of seven-membered heterocycles employing triazoles as starting materials are less explored. Recently, the Yoo group first developed a three-component [5+2] cycloaddition reaction of *N*-sulfonyl-1,2,3-triazoles, pyridines, and activated alkynes, offering a novel strategy for synthesis of biologically active 1,4-diazepines **3-92** (Scheme 3-35).[70] Initially, a rhodium carbene derived from, triazole **3-1** reacted with 2-substituted pyridines producing an isolable azomethine ylide intermediate **3-92-I**. Then, this 1,5-dipole was trapped by activated alkynes to afford the 7-membered product **3-92** in a [5+2] cycloaddition manner.



Scheme 3-35

Recently, the Li group reported a unique rhodium(III)-catalyzed [3+2]/[5+2] annulation of 4-aryl-*N*-tosyl-1,2,3-triazoles with internal alkynes (Scheme 3-36).[71] Different from the previously mentioned transannulaiton reactions with alkynes (Scheme 3-6, eq 2 and eq 3), this method provided a straightforward access to fused indeno[1,7-cd]azepine architectures (**3-93**) under the Rh(III)/Ag(I) catalytic system. Similarly, this transformation started with the generation of rhodium-iminocarbene species (**3-93-A**), followed by its tapping with alkynes to form ylide **3-93-B**. However, instead of

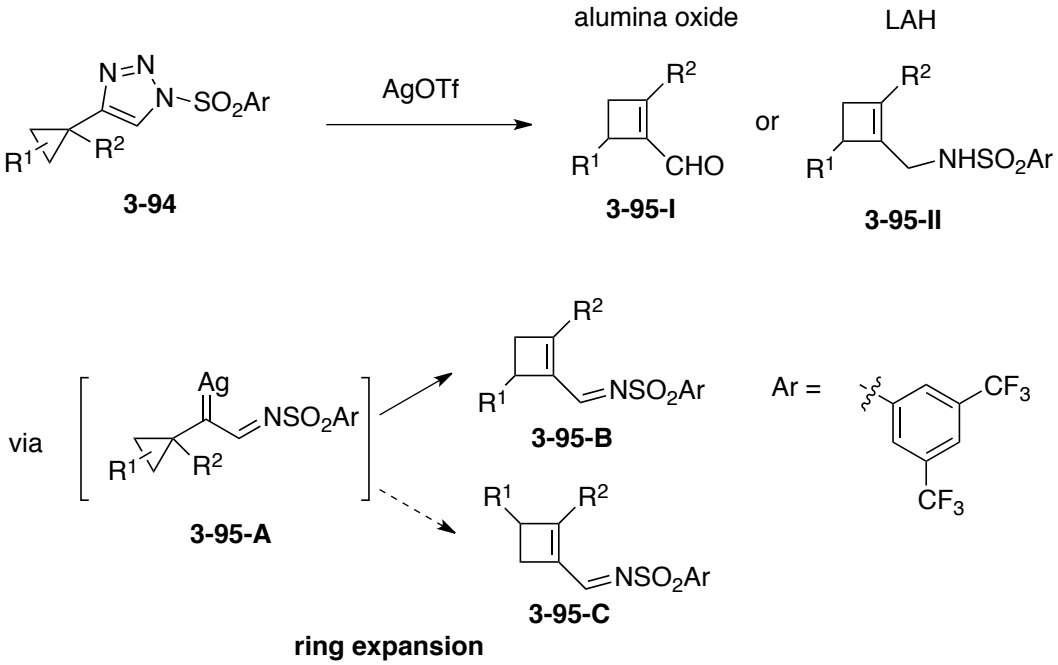
cyclization with the imino group, the intermediate **3-93-B** underwent electrophilic cyclization with the phenyl group to give **3-93-C**. Then, a second annulation with internal alkyne occurred, leading to the product **3-93-I** upon hydroxylation, or to **3-93-II** via β-H elimination.



Scheme 3-36

In addition to the numerous Rh-catalyzed transformations, the only example on silver (I) catalyzed ring opening of *N*-sulfonyl-1,2,3-triazoles was disclosed by Tang (Scheme 3-37).[72] In this reaction, a regioselective ring expansion of cyclopropyl carbene intermediate **3-95-A** was the key step, leading to the formation of imino-cyclobutenes **3-95-B** (favored regioisomer), which then upon hydrolysis afforded an aldehyde **3-95-I**, or upon reduction produced sulfonamide **3-95-II**. It is worthy to mention that, besides the

optimized AgOTf catalyst, $Cu(MeCN)_4PF_6$, as well as the classical $Rh_2(Oct)_4$, could also catalyzed this transformation, albeit with lower yields (for Cu) or regioselectivity (poor selectivity between **3-95-B** and **3-95-C**, for Rh).



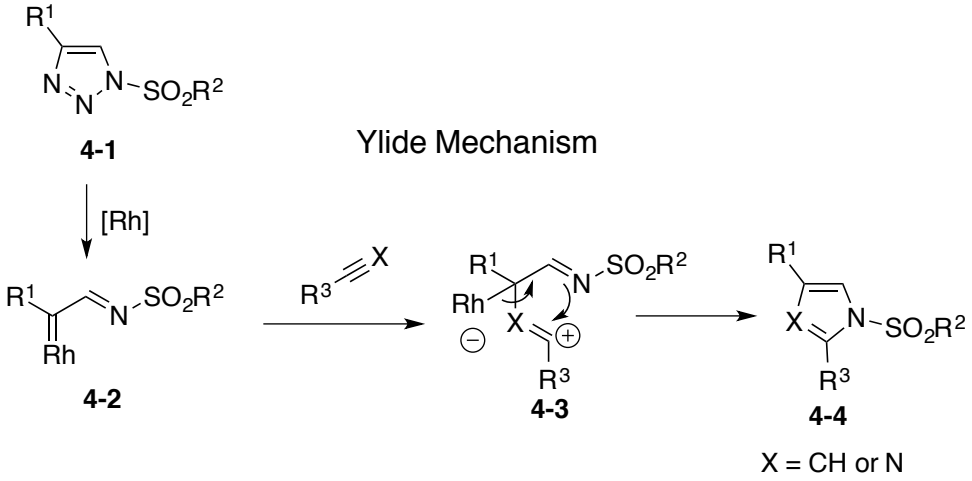
Scheme 3-37

2. TRANSANNULATION OF *N*-TOSYL ALKYNYL TRIAZOLES: ACCESS TO FUSED PRROLES

Previously published as "Intramolecular Transannulation of Alkynyl Triazoles via Alkyne–Carbene Metathesis Step: Access to Fused Pyrroles." Shi, Y.; Gevorgyan, V. *Org. Lett.* **2013**, *15*, 5394.

2.1. Development of an intramolecular transannulation reaction via an alkyne-carbene metathesis step

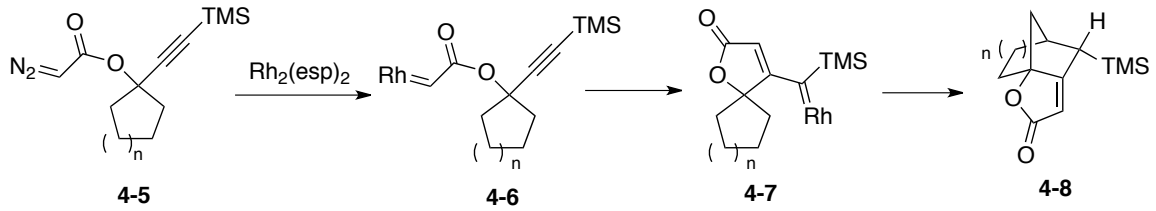
As discussed above, upon treatment of *N*-sulfonyl-1,2,3-triazoles **4-1** with Rh(II) complexes, rhodium-imino carbene species **4-2** could be generated efficiently. These electrophilic carbene intermediates offer wide opportunities for the construction of diverse heterocycles. By employing nitriles and terminal alkynes, our group reported the synthesis of imidazoles (**4-4**, X = N)[20] and substituted pyrroles (**4-4**, X = CH)[26] proceeding via an ylide mechanism (Scheme 4-1).



Scheme 4-1

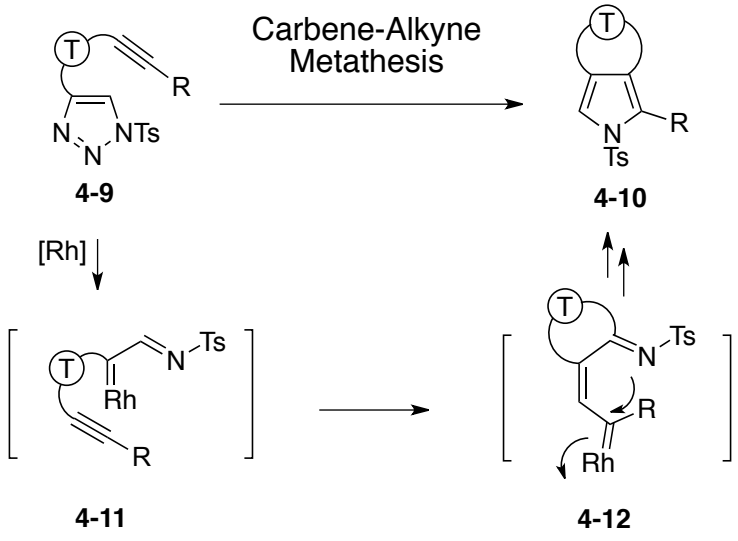
Recently, May has developed an interesting cascade transformation of tethered diazo compounds (**4-5**). This reaction, which relied on carbene-alkyne metathesis[73] step

(**4-6** to **4-7**), allowed for construction of bridged polycyclic ring systems **4-8** with high efficiency (Scheme 4-2).



Scheme 4-2

We hypothesized that this carbene-alkyne metathesis strategy could potentially be adopted to the triazole chemistry. Thus, after the generation of Rh-iminocarbene **4-11**, it would undergo a carbene-alkyne metathesis to form a new Rh-carbene **4-12**. The latter then upon a subsequent nucleophilic attack of the imino N atom at the carbenoid carbon, followed by tautomerization, would produce the fused pyrrole **4-10** (Scheme 4-3).



Scheme 4-3

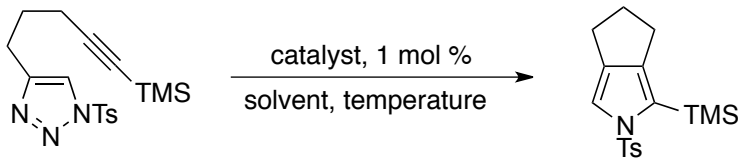
In order to test the above hypothesis, alkynyl triazole **4-9-a**, which was synthesized through the CuAAC reaction from the corresbonding 1,6-diyne and a tosyl

azide,[15c] was subjected to the reaction with rhodium octanoate. To our delight, the desired 5,5-fused pyrrole[74] **4-10-a** was formed in 60% yield (Table 4-1, entry 1).

2.2. Optimization of the reaction conditions

With the initial positive result in hand, we performed the optimization of this transannulation reaction. The effect of different solvent was examinated first. It was found that $CHCl_3$ gave the best result among all the solvent tested (entry 2-5). Next, we screened a series of rhodium (II) catalysts (entry 6-8). Although $Rh_2(Oct)_4$ and $Rh_2(esp)_2$ were nearly equally efficient in the transannulation reaction of **4-9-a**, $Rh_2(esp)_2$ appeared to be a more general catalyst with respect to the substrate scope (Table 4-2). In contrast, $Rh_2(Oct)_4$ was not efficient for substrates bearing aryl substituted alkynes. However, desilylation of the obtained pyrroles during the reaction diminished the yield of this transformation (entry 7). This problem was solved by reducing reaction time under elevated temperature (entry 9), or using a milder condition (entry 11). Thus, the fused pyrrole **4-10-a** could be isolated in 78% yield.

Table 4-1. Optimization of Transannulation Reaction of **4-9-a**[a]



4-9-a **4-10-a**

Entry	Catalyst	Solvent	*t*/°C	Yield/%[b]
1	$Rh_2(Oct)_4$	DCE	80	62[d](60[c])
2	$Rh_2(Oct)_4$	$CHCl_3$	80	63[d]
3	$Rh_2(Oct)_4$	dioxane	80	19
4	$Rh_2(Oct)_4$	THF	80	trace
5	$Rh_2(Oct)_4$	Toluene	80	0
6	Rh_2(*S*-NTTL)$_4$	$CHCl_3$	80	41[d]
7	$Rh_2(esp)_2$	$CHCl_3$	80	63[d]
8	Rh_2(*S*-DOSP)$_4$	$CHCl_3$	80	46[d]
9	$Rh_2(esp)_2$	$CHCl_3$	90	78[e]
10	$Rh_2(esp)_2$	$CHCl_3$	70	76[d,f]
11	$Rh_2(esp)_2$	$CHCl_3$	60	78(78[c,f])
12	$Rh_2(esp)_2$	$CHCl_3$	50	59[g]

[a]**4-9-a** (0.1 mmol) and Rh(II) (1 mol %) were dissolved in the respective solvent (1.0 mL) and heated at the indicated temperature for 12 h. [b]GC yield. [c]Isolated yield. [d]Desilylation of product was observed. [e]Heated for 2 h. [f]Heated for 15 h. [g]Heated for 42 h.

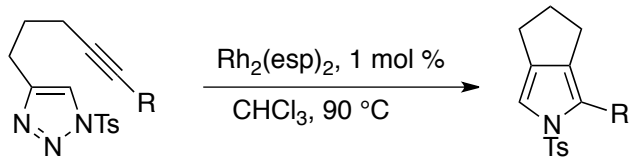
2.3. Reaction scope

After developing an efficient method for synthesis of fused pyrroles, the scope of this intramolecular transformation reaction was examined. First, we tested a series of aryl substituents at the alkyne moiety (Table 4-2, entry 1-12). It was found that a variety of

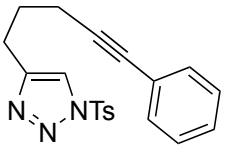
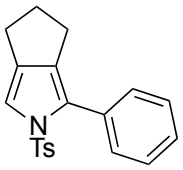
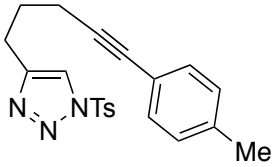
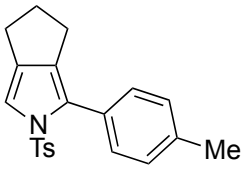
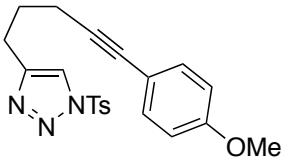
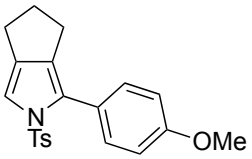
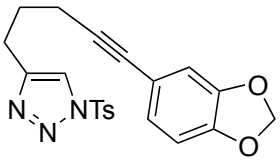
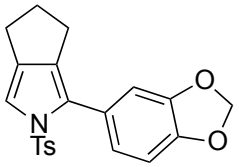
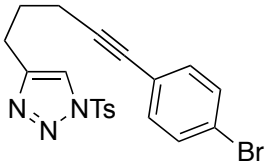
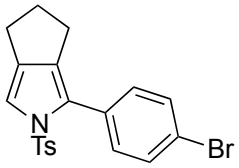
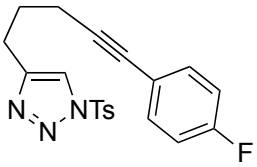
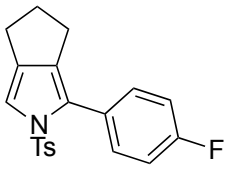
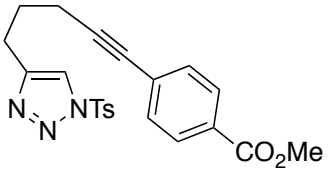
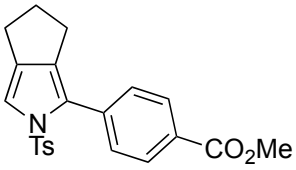
groups, including OMe (**d**, **j**), F (**g**), Br (**f**), CO_2Me (**h**), CF_3 (**i**), and protected diol (**e**), were perfectly tolerated under these reaction conditions to produce the corresponding fused pyrroles (**4-10-d** to **4-10-m**) in reasonable to excellent yields. Likewise, naphthalene- (**4-10-l**) and heterocycle-substituted pyrroles (**4-10-m**) were obtained in good yields. It was also found that triazoles, bearing *ortho*- or *meta*-substituted aryl groups, could also participate in this transannulation reaction to give fused pyrroles **4-10-j** and **4-10-k**.

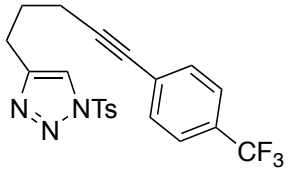
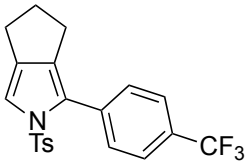
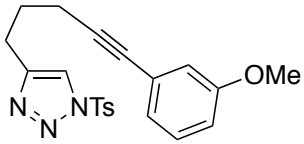
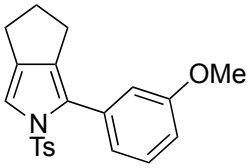
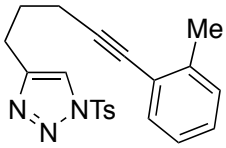
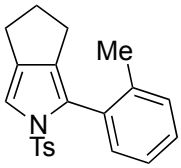
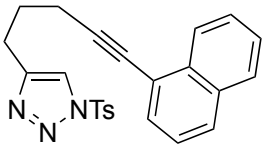
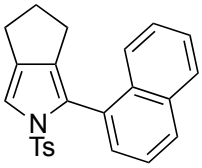
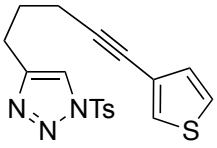
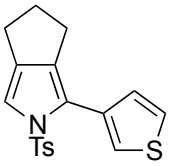
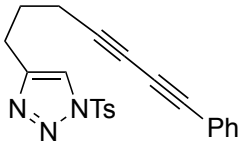
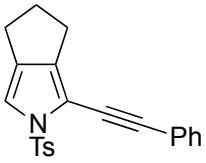
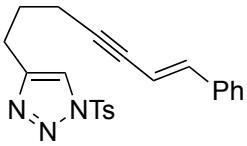
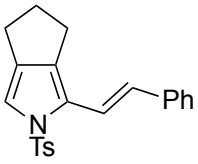
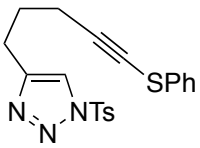
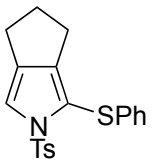
Further investigation indicated that this reaction is not limited to aryl alkynes. Thus, we found that alkynyl (**n**) or alkenyl (**o**) groups can also be efficiently utilized in this transformation to produce the corresponding pyrroles possessing an unsaturated unit at the C-2 position. Notably, the reaction of alkynyl triazole bearing a phenylthio group proceeded smoothly to afford thiopyrrole **4-10-p** in excellent yield. Moreover, TMS (**4-10-a**) and Br (**4-10-q**) groups were compatible with these reaction conditions, thus providing opportunities for further functionalization of the obtained pyrroles.[75]

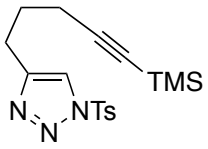
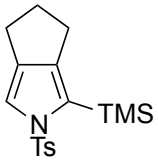
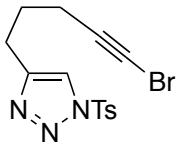
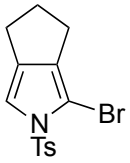
Table 4-2. Transannulation of alkynyl triazoles: R substituent variations.



4-9 **4-10**

Entry	Substrate		Product		Yield/%[a,b]
1		**4-9-b**		**4-10-b**	50
2		**4-9-c**		**4-10-c**	58
3		**4-9-d**		**4-10-d**	88
4		**4-9-e**		**4-10-e**	91
5		**4-9-f**		**4-10-f**	63
6		**4-9-g**		**4-10-g**	42
7		**4-9-h**		**4-10-h**	66

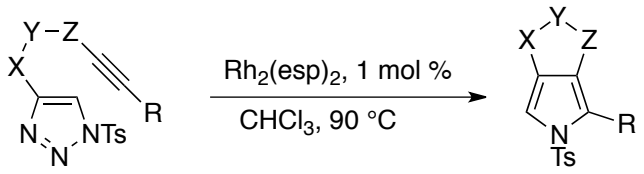
Entry	Substrate		Product		Yield/%[a,b]
8		**4-9-i**		**4-10-i**	65
9		**4-9-j**		**4-10-j**	52
10		**4-9-k**		**4-10-k**	62
11		**4-9-l**		**4-10-l**	83
12		**4-9-m**		**4-10-m**	78
13		**4-9-n**		**4-10-n**	81
14		**4-9-o**		**4-10-o**	87
15		**4-9-p**		**4-10-p**	93

Entry	Substrate		Product		Yield/%[a,b]
16		**4-9-a**		**4-10-a**	78[c]
17		**4-9-q**		**4-10-q**	65

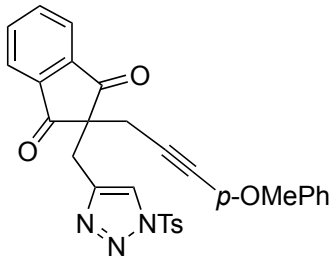
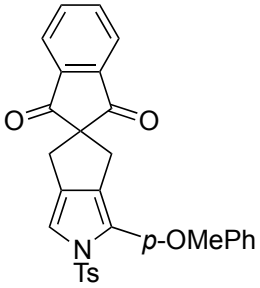
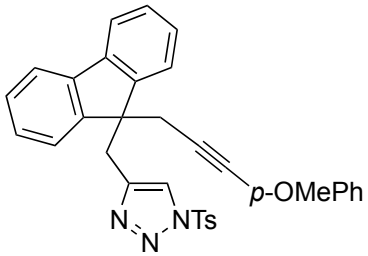
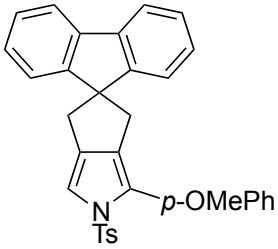
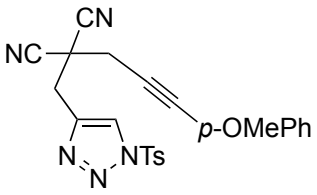
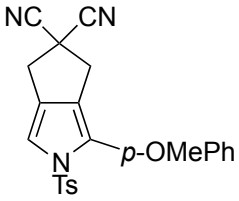
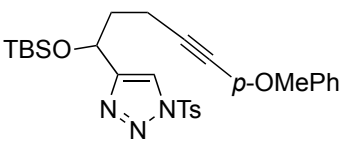
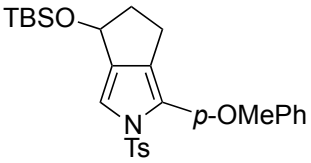
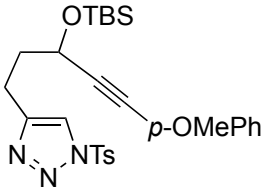
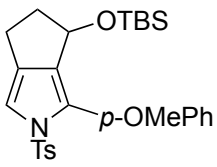
[a]**4-9** (0.2 mmol) and $Rh_2(esp)_2$ (1 mol %) were dissolved in $CHCl_3$ (3.0 mL) and heated at 90 °C for 2 h. [b]Isolated yields. [c]Heated at 60 °C for 15 h.

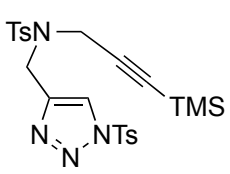
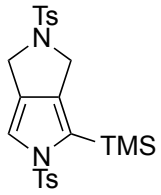
We also investigated the scope of the reaction with respect to a triazole-alkyne tether (Table 4-3). It was found that substrates possessing a C-3 tether reacted well, including those possessing ketone (**4-10-r**), nitrile (**4-10-t**), and protected alcohol (**4-10-u**, **4-10-v**) functional groups to produce the corresponding fused pyrroles in good yields. Notably, this method also allows an efficient access to polycyclic spiro systems **4-10-r**, **4-10-s**. Furthermore, a substrate with a nitrogen tether underwent a smooth transannulation reaction to give a bicyclic tetrahydropyrrolo-pyrrole skeleton **4-10-w**.

Table 4-3. Transannulation of alkynyl triazoles: tether variations.



4-9 **4-10**

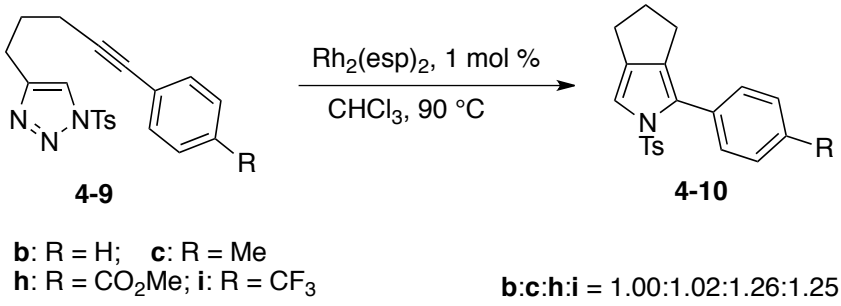
Entry	Substrate		Product		Yield/%[a,b]
1		**4-9-r**		**4-10-r**	70
2		**4-9-s**		**4-10-s**	68
3		**4-9-t**		**4-10-t**	81[c]
4		**4-9-u**		**4-10-u**	64
5		**4-9-v**		**4-10-v**	57

Entry	Substrate	Product	Yield/%[a,b]
6	 **4-9-w**	 **4-10-w**	70[d]

[a]**4-9** (0.2 mmol) and $Rh_2(esp)_2$ (1 mol %) were dissolved in $CHCl_3$ (3.0 mL) and heated at 90 °C for 2 h. [b]Isolated yields. [c]Heated at 90 °C for 15 h. [d]Heated at 60 °C for 15 h.

2.4. Mechanistic considerations

Naturally, we were interested in the investigation of the mechanisms of herein described intramolecular transunnation reaction of alkynyl triazoles **4-9** into fused pyrroles **4-10**. The relative rate comparison indicated that the triazoles bearing an electron-deficient aryl group (**4-9-h** and **4-9-i**) reacted faster than those having electron-neutral (**4-9-b**) or electron-rich (**4-9-c**) aryl groups (Scheme 4-4). This result does not support an ylide mechanism, which strongly favors electron-rich alkynes. Based on this, we believed that the initially hypothesized carbene-alkyne metathesis step was involved in this transformation (Scheme 4-3).



Scheme 4-4

2.5. Summary

This part is written based on the previously published article ("Intramolecular Transannulation of Alkynyl Triazoles via Alkyne–Carbene Metathesis Step: Access to Fused Pyrroles." Shi, Y.; Gevorgyan, V. *Org. Lett.* **2013**, *15*, 5394). This work was accomplished by myself under supervision of Professor Gevorgyan.

An efficient rhodium-catalyzed intramolecular transannulation reaction of alkynyl *N*-tosyltriazoles was developed, which involves a Rh-carbene-alkyne metathesis step. This new method provides expeditious access to various 5,5-fused pyrroles from easily available starting materials. Moreover, it can also be used to efficiently construct spiro systems, as well as fused tetrahydropyrrolo-pyrrole cores.

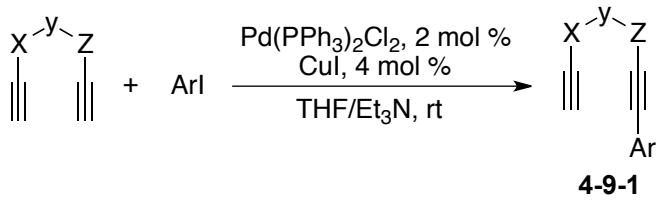
3. EXPERIMENTAL SECTION

3.1. General information

GC/MS analysis was performed on a Hewlett Packard Model 6890 GC interfaced to a Hewlett Packard Model 5973 mass selective detector (15 m x 0.25 mm capillary column, HP-5MS). NMR spectra were recorded on Bruker Avance DRX-500 (500 MHz) or DPX-400 (400 MHz) instrument. ^{1}H and ^{13}C NMR chemical shifts (δ) are reported in parts per million (ppm). LRMS and HRMS analyses were performed on Micromass 70 VSE mass spectrometer. Column chromatography was carried out employing Silicycle Silica-P flash silica gel (40-63 μm). Precoated silica gel plates F-254 were used for thin-layer analytical chromatography. All manipulations with transition metal catalysts were conducted in oven-dried glassware under inert atmosphere using a combination of glovebox and standard Schlenk techniques unless otherwise noted. Chloroform (99.9%, extra dry) was purchased from Acros Organics and was used without further purification. Anhydrous dichloromethane, toluene, and THF (BHT-free) was purchased from Aldrich, degassed with argon, and dried by passage through activated alumina on an Innovative Technology PureSolv system. All starting materials were purchased from Strem Chemicals, Aldrich, Gelest Inc., TCI America, or Alfa Aesar, or synthesized via known literature procedures. All manipulations with transition metal catalysts were conducted in oven-dried glassware under inert atmosphere using a combination of glovebox and standard Schlenk techniques.

3.2. Preparation of triazoles

Preparation of monosubstituted 1,6-heptadiynes – sonogashira coupling: General Procedure A



4-9-1

Scheme 4-5

A 50 mL round bottle containing $Pd(PPh_3)_2Cl_2$ (2 mol%) and CuI (4 mol%) was evacuated and purged with Ar 3 times. To this flask, THF (15 mL) and triethylamine (5 mL) were added via syringe. Then ArI (1.0 equiv, or dissolve in 5 mL THF if solid) and 1,6-heptadiyne (1.2 equiv, or dissolve in 5 mL THF if solid) were added. The reaction mixture was allowed to stir at room temperature overnight and then filtered through a short path of silica gel. The filtrate was concentrated under reduced pressure. Flash chromatography on silica gel to afford crude mono-substituted 1,6-heptadiynes (**4-9-1**), which can be used in next step (Scheme 4-5).

Preparation of alkynyl triazoles via CuAAC reaction: General Procedure B

4-9

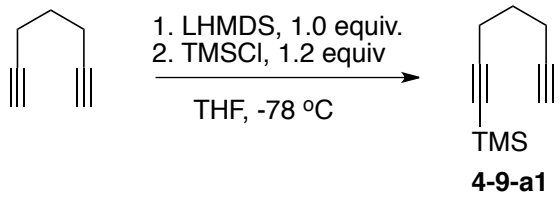
Scheme 4-6

To a stirring solution of 1,6-haptadiyne (1.0 equiv) and CuTc (10 mol%) in Toluene (0.2 M) was added tosyl azide (~1.2 equiv) dropwise. The reaction mixture was

allowed to stir at room temperature until 1,6-haptadiyne was consumed. The solvent was then removed under reduced pressure and the crude product was subjected to column chromatography to afford desired triazole (Scheme 4-6).

Detailed procedure for preparation of individual substrate：

1-tosyl-4-(5-(trimethylsilyl)pent-4-yn-1-yl)-1H-1,2,3-triazole (4-9-a):

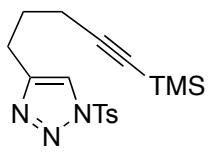


4-9-a1

Scheme 4-7

Under Ar protection, a solution of 1,6-heptadiyne (3.0 mmol) in THF (15 mL) was cooled to -78 °C. Then LHMDS (1.0 M solution in THF, 3.0 mL) was added. After stirring for 45 min, TMSCl (3.6 mmol) was added at -78 °C and the reaction mixture was allowed to stir for 3 h at the same temperature. Saturated ammonium chloride was then added and then warmed to room temperature. The mixture was extracted with ether, dried over Na_2SO_4, and the solvent was removed in vacuo. The crude product **4-9-a1** was then submitted to next step without further purification (Scheme 4-7).

Compound **4-9-a** was prepared according to **General Procedure B**. **4-9-a1** (~2.3 mmol) and tosyl azide (2.5 mmol) were used. 63% yield over 2 steps.

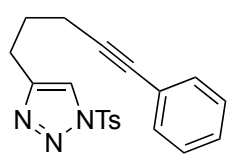


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.18 Hz, 2 H), 7.87 (s, 1 H), 7.37 (d, *J* = 8.18 Hz, 2 H), 2.82 (t, *J* = 7.60 Hz, 2 H), 2.44 (s, 3 H), 2.26 (t, *J* = 7.02 Hz, 2 H), 1.87 (quin, *J* = 7.31 Hz, 2 H), -0.14 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.13, 133.22, 130.37, 128.57, 120.55, 105.96, 85.54,

77.32, 27.47, 24.19, 21.77, 19.18, 0.09. HRMS (ESI) calculated for $C_{17}H_{24}N_3O_2SSi$ $[M+H]^+$: 362.1358, found: 362.1355.

4-(5-phenylpent-4-yn-1-yl)-1-tosyl-1H-1,2,3-triazole (4-9-b):

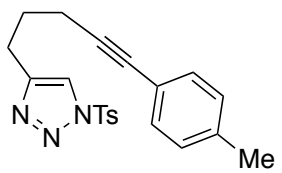
Compounds **4-9-b** was prepared according to **General Procedure A** followed by **General Procedure B**. 1,6-heptadiyne (3.0 mmol), iodobenzene (2.5 mmol), and tosyl azide (1.6 mmol) were used. 40% yield over 2 steps.



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.44 Hz, 2 H), 7.91(s, 1 H), 7.40 – 7.37 (m, 4 H), 2.91 (t, *J* = 7.52 Hz, 2 H), 2.48 – 2.45 (m, 5 H), 1.98 (quin, *J* = 7.24 Hz, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.22, 147.16, 133.24, 131.55, 130.41, 128.58, 128.24, 127.73, 123.67, 120.63, 88.87, 81.53, 27.72, 24.38, 21.81, 18.82. HRMS (ESI) calculated for $C_{20}H_{20}N_3O_2S$ $[M+H]^+$: 366.1276, found: 366.1266.

4-(5-(p-tolyl)pent-4-yn-1-yl)-1-tosyl-1H-1,2,3-triazole (4-9-c):

Compounds **4-9-c** was prepared according to **General Procedure A** followed by **General Procedure B**. 1,6-heptadiyne (3.0 mmol), 1-iodo-4-methylbenzene (2.5 mmol), and tosyl azide (2.2 mmol)were used. 48% yield over 2 steps.

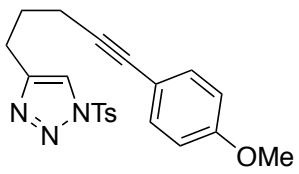


^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.44 Hz, 2 H), 7.90 (s, 1 H), 7.38 (d, *J* = 8.07 Hz, 2 H), 7.28 (d, *J* = 8.07 Hz, 2 H), 7.09 (d, *J* = 7.70 Hz, 2 H), 2.90 (t, *J* = 7.52 Hz, 2 H), 2.46 – 2.44 (m, 5 H), 2.34 (s, 3 H), 1.97 (quin, *J* = 7.24 Hz, 10 H). ^{13}C NMR (126 MHz, acetone-*d*6) δ 147.44, 137.61, 133.57, 131.26, 130.57, 128.98, 128.30, 121.49, 120.91, 88.28, 81.05,

27.84, 24.10, 20.75, 20.41, 18.29. HRMS (ESI) calculated for $C_{21}H_{22}N_3O_2S$ $[M+H]^+$: 380.1433, found: 380.1423.

4-(5-(4-methoxyphenyl)pent-4-yn-1-yl)-1-tosyl-1H-1,2,3-triazole (4-9-d):

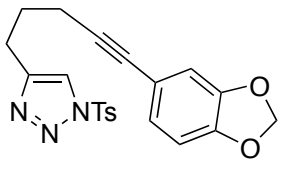
Compounds **4-9-d** was prepared according to **General Procedure A** followed by **General Procedure B**. 1,6-heptadiyne (3.0 mmol), 1-iodo-4-methoxybenzene (2.5 mmol), and tosyl azide (2.4 mmol) were used. 57% yield over 2 steps.



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.44 Hz, 2 H), 7.90 (s, 1 H), 7.38 (d, *J* = 8.07 Hz, 2 H), 7.32 (d, *J* = 8.80 Hz, 2 H), 6.82 (d, *J* = 8.80 Hz, 2 H), 3.80 (s, 3 H), 2.90 (t, *J* = 7.52 Hz, 2 H), 2.46 - 2.43 (m, 5 H), 1.96 (quin, *J* = 7.24 Hz, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.16, 147.28, 147.11, 133.26, 132.88, 130.39, 128.60, 120.58, 115.80, 113.85, 87.21, 81.27, 55.25, 27.81, 24.40, 21.81, 18.81. HRMS (ESI) calculated for $C_{21}H_{22}N_3O_3S$ $[M+H]^+$: 396.1382, found: 396.1386.

4-(5-(benzo[d][1,3]dioxol-5-yl)pent-4-yn-1-yl)-1-tosyl-1H-1,2,3-triazole (4-9-e):

Compounds **4-9-e** was prepared according to **General Procedure A** followed by **General Procedure B**. 1,6-heptadiyne (3.0 mmol), 5-iodobenzo[1,3]dioxole (2.5 mmol), and tosyl azide (2.4 mmol were used. 56% yield over 2 steps.

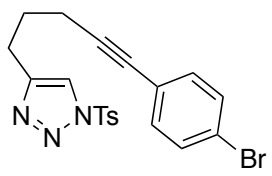


^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.07 Hz, 2 H), 7.90 (s, 1 H), 7.37 (d, *J* = 8.07 Hz, 2 H), 6.90 (d, *J* = 7.70 Hz, 1 H), 6.83 (s, 1 H), 6.72 (d, *J* = 8.07 Hz, 1 H), 5.95, (s, 2 H), 2.89 (t, *J* = 7.52 Hz,21 H), 2.44 - 2.41 (m, 5 H), 1.95 (quin, *J* = 7.24 Hz, 2 H). ^{13}C NMR (126 MHz,

$CDCl_3$) δ 147.39, 147.32, 147.2, 147.13, 133.24, 130.39, 128.60, 125.91, 120.58, 116.93, 111.61, 108.33, 101.18, 87.05, 81.27, 27.75, 24.38, 21.82, 18.76. HRMS (ESI) calculated for $C_{21}H_{20}N_3O_4S$ $[M+H]^+$: 410.1175, found: 410.1183.

4-(5-(4-bromophenyl)pent-4-yn-1-yl)-1-tosyl-1H-1,2,3-triazole (4-9-f):

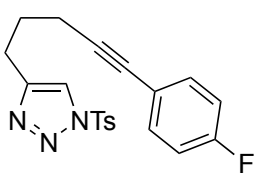
Compounds **4-9-f** was prepared according to **General Procedure A** followed by **General Procedure B**. 1,6-heptadiyne (3.0 mmol), 1-bromo-4-iodobenzene (2.5 mmol), and tosyl azide (2.2 mmol) were used. 50% yield over 2 steps.



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.48 Hz, 2 H), 7.90 (s, 1 H), 7.41 (d, *J* = 8.48 Hz, 2 H), 7.37 (d, *J* = 8.18 Hz, 2 H), 7.23 (d, *J* = 8.48 Hz, 2 H), 2.89 (t, *J* = 7.60 Hz, 2 H), 2.46 – 2.43 (m, 5 H), 1.97 (quin, *J* = 7.23 Hz, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.17, 147.08, 133. 22, 133.02, 131.45, 130.39, 128.61, 122. 63, 121.82, 120.57, 90.15, 80.53, 27.60, 24.41, 21.82, 18.85. HRMS (ESI) calculated for $C_{20}H_{19}BrN_3O_2S$ $[M+H]^+$: 444.0381, found: 444.0379.

4-(5-(4-fluorophenyl)pent-4-yn-1-yl)-1-tosyl-1H-1,2,3-triazole (4-9-g):

Compounds **4-9-g** was prepared according to **General Procedure A** followed by **General Procedure B**. 1,6-heptadiyne (3.0 mmol), 1-fluoro-4-iodobenzene (2.5 mmol), and tosyl azide (2.0 mmol) were used. 48% yield over 2 steps.

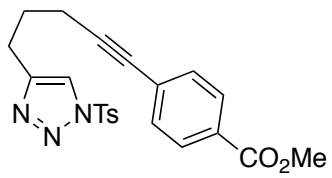


^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 – 7.90 (m, 2 H), 7.67 (s, 1 H), 7.37 – 7.31 (m, 4 H), 6.98 – 6.94 (m, 2 H), 2.88 (t, *J* = 7.52 Hz, 2 H), 2.43 – 2.40 (m, 5 H), 1.95 (quin, *J* = 7.24 Hz, 2 H). ^{13}C NMR

(126 MHz, $CDCl_3$) δ 162.15 (d, J = 249.48 Hz), 152.36, 146.51, 138.02, 133.36, 133.29, 130.39, 130.13, 128.61, 115.45 (d, J = 22.68), 88.24, 80.56, 27.32, 24.69, 21.76, 18.79. HRMS (ESI) calculated for $C_{20}H_{19}FN_3O_2S$ $[M+H]^+$: 384.1182, found: 384.1172.

methyl 4-(5-(1-tosyl-1H-1,2,3-triazol-4-yl)pent-1-yn-1-yl)benzoate (4-9-h):

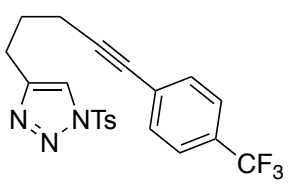
Compounds **4-9-h** was prepared according to **General Procedure A** followed by **General Procedure B**. 1,6-heptadiyne (3.0 mmol), methyl 4-iodobenzoate (2.5 mmol), and tosyl azide (2.2 mmol) were used. 48% yield over 2 steps.



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 8.44 Hz, 2 H), 7.95 (d, J = 8.44 Hz, 2 H), 7.91 (s, 1 H), 7.43 (d, J = 8.44 Hz, 2 H), 7.37 (d, J = 8.07 Hz, 2 H), 3.91 (s, 3 H), 2.90 (t, J = 7.70 Hz, 2 H), 2.49 (t, J = 6.97 Hz, 2 H), 2.44 (s, 3 H), 1.99 (quin, J = 7.24 Hz, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.59, 147.17, 147.04, 133.20, 131.48, 130.41, 129.42, 129.05, 128.61, 128.45, 120.60, 92.30, 81.00, 52.16, 27.57, 24.41, 21.82, 18.93. HRMS (ESI) calculated for $C_{22}H_{22}N_3O_4S$ $[M+H]^+$: 424.1331, found: 424.1322.

1-tosyl-4-(5-(4-(trifluoromethyl)phenyl)pent-4-yn-1-yl)-1H-1,2,3-triazole (4-9-i):

Compounds **4-9-i** was prepared according to **General Procedure A** followed by **General Procedure B**. 1,6-heptadiyne (3.0 mmol),1-iodo-4-(trifluoromethyl)benzene (2.5 mmol), and tosyl azide (2.2 mmol) were used. 54% yield over 2 steps.

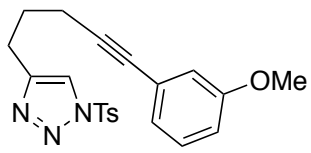


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 8.48 Hz, 2 H), 7.91 (s, 1 H), 7.53, (d, J = 8.28 Hz, 2 H), 7.47 (d, J = 8.40 Hz, 2 H), 7.37 (d, J = 8.18 Hz, 2 H), 2.90 (t, J = 7.60 Hz, 2 H), 2.48 (t, J

= 7.02 Hz, 2 H), 2.44 (s, 3 H), 1.99 (quin, *J* = 7.12 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.20, 147.02, 133.21, 131.78, 130.41, 129.29, 128.60, 128.60, 128.57 (q, *J* = 220 Hz), 126.16, 125.10 (d, *J* = 3.0 Hz), 120.59, 91.72, 80.38, 27.56, 24.42, 21.80, 18.85. HRMS (ESI) calculated for $C_{21}H_{19}F_3N_3O_2S$ $[M+H]^+$: 434.1150, found: 434.1145.

4-(5-(3-methoxyphenyl)pent-4-yn-1-yl)-1-tosyl-1H-1,2,3-triazole (4-9-j):

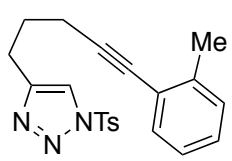
Compounds **4-9-j** was prepared according to **General Procedure A** followed by **General Procedure B**. 1,6-heptadiyne (3.0 mmol), 1-iodo-3-methoxybenzene (2.5 mmol), and tosyl azide (2.2 mmol) were used. 52% yield over 2 steps.



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.18 Hz, 2 H), 7.90 (s, 1 H), 7.37 (d, *J* = 8.48 Hz, 2 H), 7.21 – 7.17 (m, 1 H), 6.98 (d, *J* = 7.60 Hz, 1 H), 6.92 (s, 1 H), 6.84 (dd, *J* = 8.33, 2.48 Hz, 1 H), 3.79 (s, 1 H), 2.90 (t, *J* = 7.60 Hz, 2 H), 2.47 – 2.44 (m, 5 H), 1.98 (quin, *J* = 7.23 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.29, 147.18, 147.14, 133.25, 130.39, 129.28, 128.60, 124.66, 124.09, 120.60, 116.41, 114.33, 88.72, 81.47, 55.25, 27.69, 24.39, 21.81, 18.80. HRMS (ESI) calculated for $C_{21}H_{22}N_3O_3S$ $[M+H]^+$: 396.1382, found: 396.1384.

4-(5-(o-tolyl)pent-4-yn-1-yl)-1-tosyl-1H-1,2,3-triazole (4-9-k):

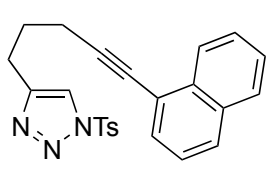
Compounds **4-9-k** was prepared according to **General Procedure A** followed by **General Procedure B**. 1,6-heptadiyne (3.0 mmol), 1-iodo-2-methylbenzene (2.5 mmol), and tosyl azide (2.2 mmol) were used. 50% yield over 2 steps.



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.18 Hz, 2 H), 7.92 (s, 1 H), 7.35 (d, *J* = 7.89 Hz, 2 H), 7.17 – 7.16 (m, 2 H), 7.13 – 7.08 (m, 1 H), 2.92 (t, *J* = 7.45 Hz, 2 H), 2.50 (t, *J* = 6.87 Hz, 2 H), 2.42 (s, 3 H), 2.41 (s, 3 H), 1.99 (quin, *J* = 7.23 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.24, 147.18, 139.89, 133.23, 131.84, 130.42, 129.35, 128.56, 127.71, 125.48, 123.46, 120.66, 92.87, 80.41, 27.92, 24.41, 21.80, 20.77, 18.99. HRMS (ESI) calculated for $C_{21}H_{22}N_3O_2S$ $[M+H]^+$: 380.1433, found: 380.1434.

4-(5-(naphthalen-1-yl)pent-4-yn-1-yl)-1-tosyl-1H-1,2,3-triazole (4-9-l):

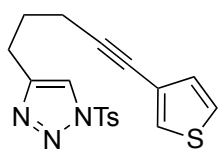
Compounds **4-9-l** was prepared according to **General Procedure A** followed by **General Procedure B**. 1,6-heptadiyne (3.0 mmol), 1-iodonaphthalene (2.5 mmol), and tosyl azide (2.0 mmol) were used. 45% yield over 2 steps.



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.18 Hz, 1 H), 7.98 (d, *J* = 8.18 Hz, 2 H), 7.84 (d, *J* = 7.89 Hz, 1 H), 7.79 (d, *J* = 8.18 Hz, 1 H), 7.62 (d, *J* = 7.02 Hz, 1 H), 7.58 – 7.49 (m, 2 H), 7.42 – 7.35 (m, 3 H), 2.99 (t, *J* = 7.60 Hz, 2 H), 2.63 (t, *J* = 6.87 Hz, 2 H), (2.43 s, 3 H), 2.09 (quin, *J* = 7.23 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.17, 147.13, 133.43, 133.18, 130.88, 130.39, 130.14, 128.60, 128.25,128.15, 126.61, 126.29, 126.13, 125.22, 121.25, 120.65, 93.89, 79.56, 27.92, 24.51, 21.81, 19.16. HRMS (ESI) calculated for $C_{24}H_{22}N_3O_2S$ $[M+H]^+$: 416.1433, found: 416.1425.

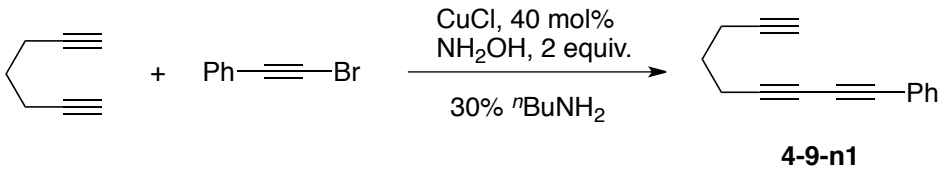
4-(5-(thiophen-3-yl)pent-4-yn-1-yl)-1-tosyl-1H-1,2,3-triazole (4-9-m):

Compounds **4-9-m** was prepared according to **General Procedure A** followed by **General Procedure B**. 1,6-heptadiyne (3.0 mmol), 3-iodothiophene (2.5 mmol), and tosyl azide (2.2 mmol) were used. 51% yield over 2 steps.



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.44 Hz, 2 H), 7.90 (s, 1 H), 7.38 (d, *J* = 8.44 Hz, 2 H), 7.35 – 7.34 (m, 1 H), 7.24 -7.23 (m, 1 H), 7.06 (d, *J* = 4.77 Hz, 1 H), 2.89 (t, *J* = 7.70 Hz, 2 H), 2.45 – 2.43 (m, 5 H), 1.96 (quin, *J* = 7.15 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.75, 147.15, 133.23, 130.39, 129.92, 128.60, 127.81, 125.12, 120.60, 125.57, 88.35, 76.56, 27.69, 24.39, 21.83, 18.80. HRMS (ESI) calculated for $C_{18}H_{18}N_3O_2S_2$ $[M+H]^+$: 372.0840, found: 372.0838.

4-(7-phenylhepta-4,6-diyn-1-yl)-1-tosyl-1H-1,2,3-triazole (4-9-n):

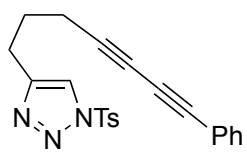


4-9-n1

Scheme 4-8

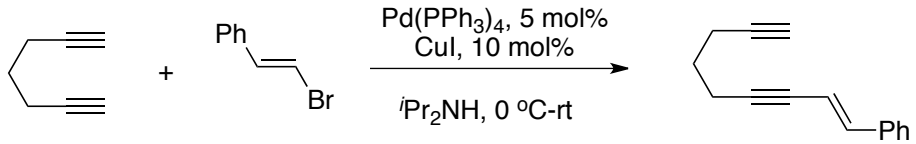
To a solution of 1,6-heptadiyne (6 mmol) in 30% aqueous ^{n}BuNH$_2$ (2 mL) at room temperature was added CuCl (2.4 mmol) and NH_2OH•HCl (2 equiv) under Ar protection. Alkynyl bromide (3 mmol, in 3 mL THF) was added dropwise to the reaction. The mixture was allowed to stir at room temperature for 4 hours. The reaction was quenched with H_2O and extracted with ether. The organic layer was washed with brine and dried with Na_2SO_4. Remove the solvent to afford crude **4-9-n1**, which can be used in next step directly (Scheme 4-8).

Compound **4-9-n** was prepared according to **General Procedure B**. **4-9-n1** (~1.0 mmol) and tosyl azide (1.2 mmol) were used. 23% yield over 2 steps.



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 8.07 Hz, 2 H), 7.91 (s, 1 H), 7.47 (d, J = 6.60 Hz, 2 H), 7.38 – 7.29 (m, 5 H), 2.87 (t, J = 7.70 Hz, 2 H), 2.43 (s, 3 H), 2.41 (t, J = 6.79 Hz, 2 H), 1.95 (quin, J = 7.15 Hz, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.19, 146.81, 133.20, 132.51, 130.42, 128.97, 128.60, 128.38, 121.88, 120.71, 83.23, 75.18, 74.12, 66.06, 27.26, 24.25, 21.82, 18.96. HRMS (ESI) calculated for $C_{22}H_{20}N_3O_2S$ $[M+H]^+$: 390.1276, found: 390.1275.

(E)-4-(7-phenylhept-6-en-4-yn-1-yl)-1-tosyl-1H-1,2,3-triazole (4-9-o):

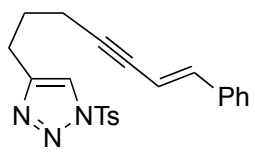


4-9-o1

Scheme 4-9

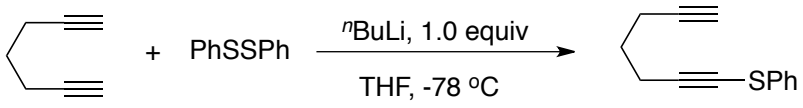
Under Ar protection, diisopropylamine (15 mL) was added to a round bottle containing $Pd(PPh_3)_4$ (5 mol%) and CuI (10 mol%). After cooling to 0 ^{o}C, alkenyl bromide (2.5 mmol) and 1,6-heptadiyne (3.0 mmol) were added. The reaction mixture was allowed to warm to room temperature gradually. After stirring for 12 h, the reaction mixture was filtered through silica gel and the filtrate was concentrated under reduced pressure. Flash chromatography on silica gel to afford crude **4-9-o1**, which can be used in next step (Scheme 4-9).

Compound **4-9-o** was prepared according to **General Procedure B**. **4-9-o1** (~1.8 mmol) and tosyl azide (2.2 mmol) were used. 49% yield over 2 steps.



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 8.48 Hz, 2 H), 7.91 (s, 1 H), 7.39 – 7.28 (m, 7 H), 6.87 (d, J = 16.37 Hz, 1 H), 6.14 (d, J = 16.08 Hz, 1 H), 2.88 (t, J = 7.60 Hz, 2 H), 2.45 – 2.41 (m, 5 H), 1.94 (quin, J = 7.23 Hz, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.22, 147.17, 140.42, 136.41, 133.23, 130.42, 128.69, 128.58, 128.36, 126.08, 120.66, 108.52, 91.42, 80.71, 27.75, 24.40, 21.82, 19.06. HRMS (ESI) calculated for $C_{22}H_{22}N_3O_2S$ $[M+H]^+$: 392.1433, found: 392.1437.

4-(5-(phenylthio)pent-4-yn-1-yl)-1-tosyl-1H-1,2,3-triazole (4-9-p):



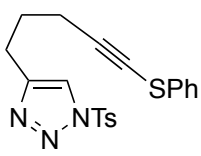
4-9-p1

Scheme 4-10

1,6-heptadiyne (3 mmol) was dissolved in THF (15 mL) under nitrogen. The solution was cooled to -78 ºC. A 2.5 M solution of ^{n}BuLi was slowly added to the reaction flask and the mixture was stirred at -78ºC for 30 minutes. A solution of the disulfide (3 mmol) in THF (5 mL) was then added dropwise to the reaction via syringe. The resulting solution was warmed to 25ºC and subsequently stirred for 2 h. After cooling the reaction mixture to -40ºC, a solution of *p*-nitrobenzyl bromide (3 mmol) in THF (5 mL) was added dropwise via syringe. Upon warming to 25ºC, the mixture was stirred for another 2 h or until complete as monitored by TLC. The reaction was then quenched with saturated NH_4Cl and the aqueous layer was extracted three times with diethyl ether. The organic layers were combined, dried over Na_2SO_4, filtered, and

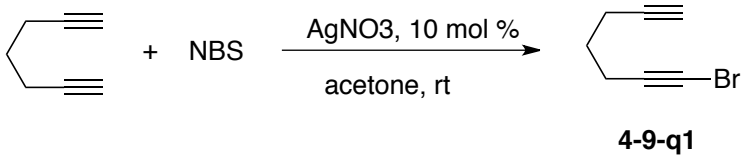
concentrated using rotary evaporation. The resulting product **4-9-p1** was purified using flash chromatography and submitted to next step (Scheme 4-10).

Compound **4-9-p** was prepared according to **General Procedure B**. **4-9-p1** (~2.3 mmol) and tosyl azide (2.8 mmol) were used. 59% yield over 2 steps.



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.48 Hz, 2 H), 7.89 (s, 1 H), 7.41 – 7.30 (m, 6 H), 7.22 – 7.18 (m, 1 H), 2.88 (t, *J* = 7.45 Hz, 2 H), 2.50 (t, *J* = 6.87 Hz, 2 H), 2.44 (s, 3 H), 1.97 (quin, *J*=7.23 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.15, 146.95, 133.35, 133.22, 130.41, 129.15, 128.60, 126.27, 125.92, 120.62, 98.39, 66.08, 27.67, 24.33, 21.81, 19.70. HRMS (ESI) calculated for $C_{20}H_{20}N_3O_2S_2$ $[M+H]^+$: 398.0997, found: 398.0995.

4-(5-bromopent-4-yn-1-yl)-1-tosyl-1H-1,2,3-triazole (4-9-q):

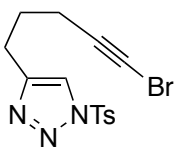


4-9-q1

Scheme 4-11

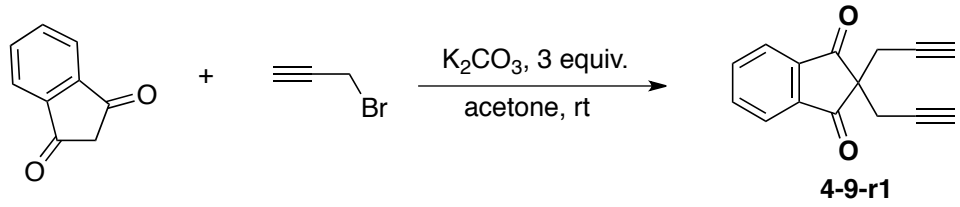
To a solution of 1,6- heptadiyne (3.0 mmol) in acetone (15 mL) was added NBS (6 mmol) and $AgNO_3$ (0.3 mmol) at room temperature with magnetic stirring. After 2-3 hours, the reaction mixture was diluted with hexanes (30 mL) and filtered off the crystals formed. The filtrate was concentrated under reduced pressure and passed through a pad of silica gel using hexane as an eluent. The filtrate was collected and evaporated under reduced pressure to afford crude **4-9-q1**, which was used in next step without further purification (Scheme 4-11).

Compound **4-9-q** was prepared according to **General Procedure B. 4-9-q1** (~1.5 mmol) and tosyl azide (1.8 mmol) were used. 31% yield over 2 steps.



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.48 Hz, 2 H), 7.88 (s, 1 H), 7.37 (d, *J* = 7.89 Hz, 2 H), 2.82 (t, *J* = 7.60 Hz, 2H), 2.25 (t, *J* = 6.87 Hz, 2 H), 2.44 (s, 3 H), 1.88 (quin, *J* = 7.23 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.18, 133.21, 130.41, 128.59, 120.63, 79.14, 38.87, 27.28, 24.22, 21.83, 19.07. HRMS (ESI) calculated for $C_{14}H_{15}BrN_3O_2S$ $[M+H]^+$: 368.0068, found: 368.0075.

2-(3-(4-methoxyphenyl)prop-2-yn-1-yl)-2-((1-tosyl-1H-1,2,3-triazol-4-yl)methyl)-1H-indene-1,3(2H)-dione (4-9-r):

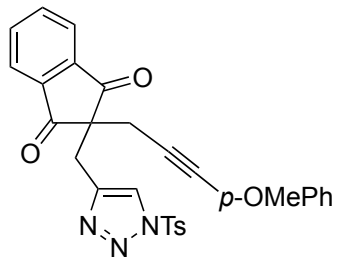


4-9-r1

Scheme 4-12

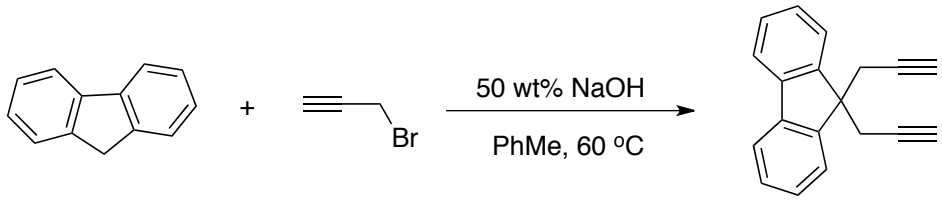
Indene-1,3-dione (3 mmol) was dissolved in acetone (30 mL). To this solution 3 equiv of K_2CO_3 and propargyl bromide (80% in toluene) were added. The mixture was stirred at room temperature for 16 h. The solvent was removed in vacuo. The residual solid was dissolved in water and DCM was added. The layers were separated and the aqueous layer was extracted with DCM. The combined organic layers were dried over sodium sulfate and filtered. Evaporation of the solvent delivered the pure corresponding 1,6-heptadiyne **4-9-r1**, which can be used in next step (Scheme 4-12).

Compound **4-9-r** was prepared from **4-9-r1** according to **General Procedure A** followed by **General Procedure B**. 1,6-heptadiyne (2.8 mmol), 1-iodo-4-methoxybenzene (2.5 mmol) and tosyl azide (2.1 mmol) were used. 46% yield over 3 steps.



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 – 7.77 (m, 7 H), 7.31 (d, *J* = 8.07 Hz, 2 H), 6.81 (d, *J* = 8.07 Hz, 2 H), 6.64 (d, *J* = 8.07 Hz, 2 H), 3.72 (s, 3 H), 3.31 (s, 2 H), 2.91 (s, 2 H), 2.42 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.25, 159.34, 147.16, 142.36, 141.89, 135.66, 132.97, 132.66, 130.25, 128.52, 123.23, 121.94, 114.57, 113.60, 84.70, 81.70, 56.40, 55.18, 28.38, 25.81, 21.81. HRMS (ESI) calculated for $C_{29}H_{24}N_3O_5S$ $[M+H]^+$: 526.1437, found: 526.1421.

4-((9-(3-(4-methoxyphenyl)prop-2-yn-1-yl)-9H-fluoren-9-yl)methyl)-1-tosyl-1H-1,2,3-triazole (4-9-s):



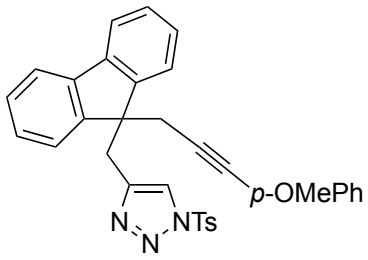
4-9-s1

Scheme 4-13

To a solution of fluororene (5 mmol) in PhMe (10 mL) were added propargyl bromide (3.0 equiv, 80% in toluene), 50 wt% aqueous NaOH solution (5 mL), and tetrabutylammonium bromide (0.5 mmol). The mixture was stirred at 60 °C until complete conversion. The resulting mixture was poured into water until all salt dissolved.

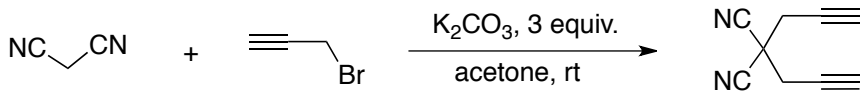
The aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over sodium sulfate. The solvent was removed in vacuo to obtain crude product **4-9-s1** in 71% yield, which can be used in next step (Scheme 4-13).

Compound **4-9-s** was prepared from **4-9-s1** according to **General Procedure A** followed by **General Procedure B**. 1,6-heptadiyne (3.5 mmol), 1-iodo-4-methoxybenzene (2.9 mmol) and tosyl azide (2.4 mmol) were used. 48% yield over last 2 steps.



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 – 7.59 (m, 4 H), 7.51 (d, *J* = 7.34 Hz, 2 H), 7.36 – 7.28 (m, 8 H), 6.85 (d, *J* = 8.44 Hz, 2 H), 6.64 (s, 1 H), 3.82 (s, 3 H), 3.74 (s, 2 H), 2.92 (s, 2 H), 2.46 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.39, 147.82, 146.58, 143.88, 140.23, 133.33, 132.98, 130.13, 128.05, 127.97, 127.48, 123.91, 120.96, 119.70, 115.51, 113.95, 84.99, 83.31, 55.30, 52.46, 33.41, 30.41, 21.79. HRMS (ESI) calculated for $C_{33}H_{28}N_3O_3S$ $[M+H]^+$: 546.1851, found: 546.1849.

2-(3-(4-methoxyphenyl)prop-2-yn-1-yl)-2-((1-tosyl-1H-1,2,3-triazol-4-yl)methyl)malononitrile (4-9-t):



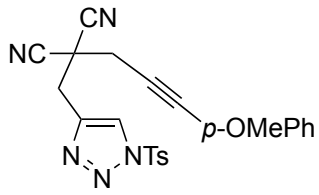
4-9-t1

Scheme 4-14

The malononitrile (5 mmol) was dissolved in acetone (30 mL). To this solution 3 equiv of K_2CO_3 and propargyl bromide (80% in toluene) were added. The mixture was

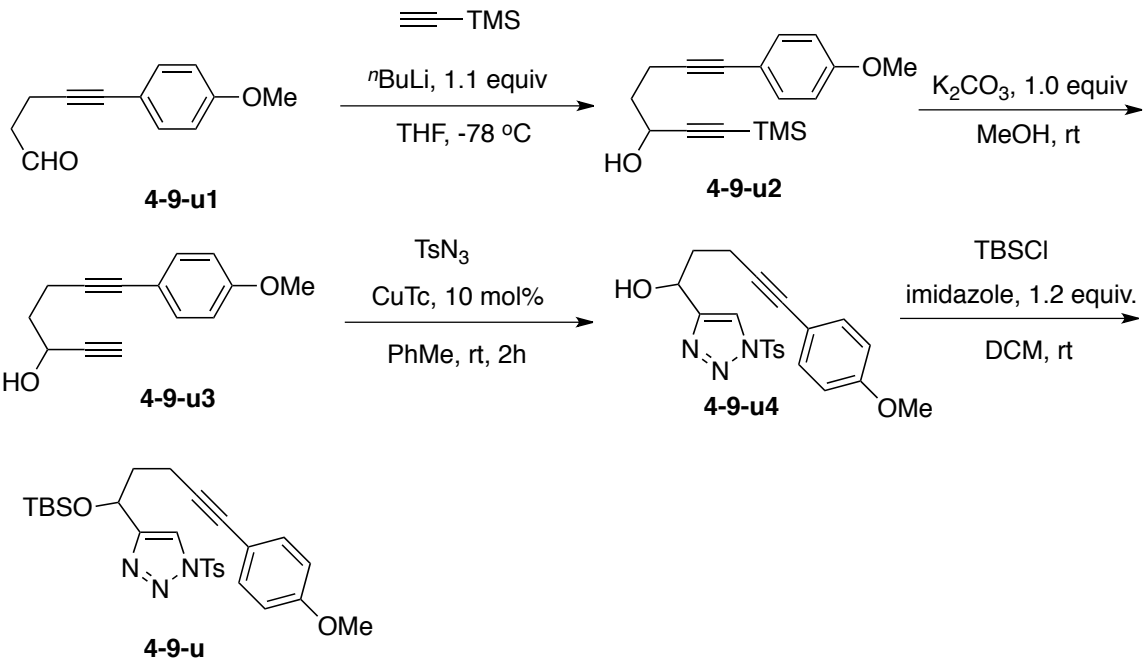
stirred at room temperature for 16 h and then solvent was removed in vacuo. Flash column chromatography to achieve crude **4-9-t1** in 44% yield (Scheme 4-14).

Compound **4-9-t** was prepared from **4-9-t1** according to **General Procedure A** followed by **General Procedure B**. 1,6-heptadiyne (2.2 mmol), 1-iodo-4-methoxybenzene (1.8 mmol) and tosyl azide (1.6 mmol) were used. 47% yield over last 2 steps.



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1 H), 8.00 (d, J = 8.18 Hz, 2 H), 7.41 – 7.39 (m, 4 H), 6.84 (d, J = 8.77 Hz, 2 H), 3.81 (s, 3 H), 3.59 (s, 2 H), 3.20 (s, 2 H), 2.45 (s, 3 H). ^{13}C NMR (126 MHz, acetone-*d*6) δ 160.31, 148.06, 140.19, 133.26, 132.92, 130.74, 128.57, 124.49, 114.61, 114.15, 113.89, 85.95, 79.49, 54.84, 37.94, 31.71, 20.82. HRMS (ESI) calculated for $C_{23}H_{20}N_5O_3S$ $[M+H]^+$: 446.1287, found: 446.1271.

4-(1-((tert-butyldimethylsilyl)oxy)-5-(4-methoxyphenyl)pent-4-yn-1-yl)-1-tosyl-1H-1,2,3-triazole (4-9-u):

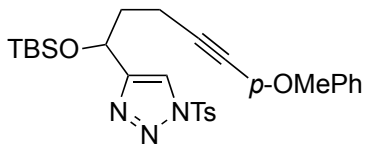


Scheme 4-15

Under Ar protection, to a solution of ethynyltrimethylsilane (3.0 mmol) in THF (25 mL) cooled to -78 °C was added ^{n}BuLi (2.5 M solution in hexane). After stirring for 45 min, aldehyde **4-9-u1** (3.2 mmol) was added at -78 °C. The reaction mixture was allowed to stir for 1 h at -78 °C and then warmed to room temperature gradually. Saturated ammonium chloride was then added. The mixture was extracted with EtOAc, dried over Na_2SO_4, and the solvent was removed in vacuo to afford crude **4-9-u2**. The residual was dissolved in MeOH (10 mL) and K_2CO_3 was then added. The mixture was stirred at room temperature for 2 h. Then the solvent was removed in vacuo. Flash chromatography afforded crude **4-9-u3**.

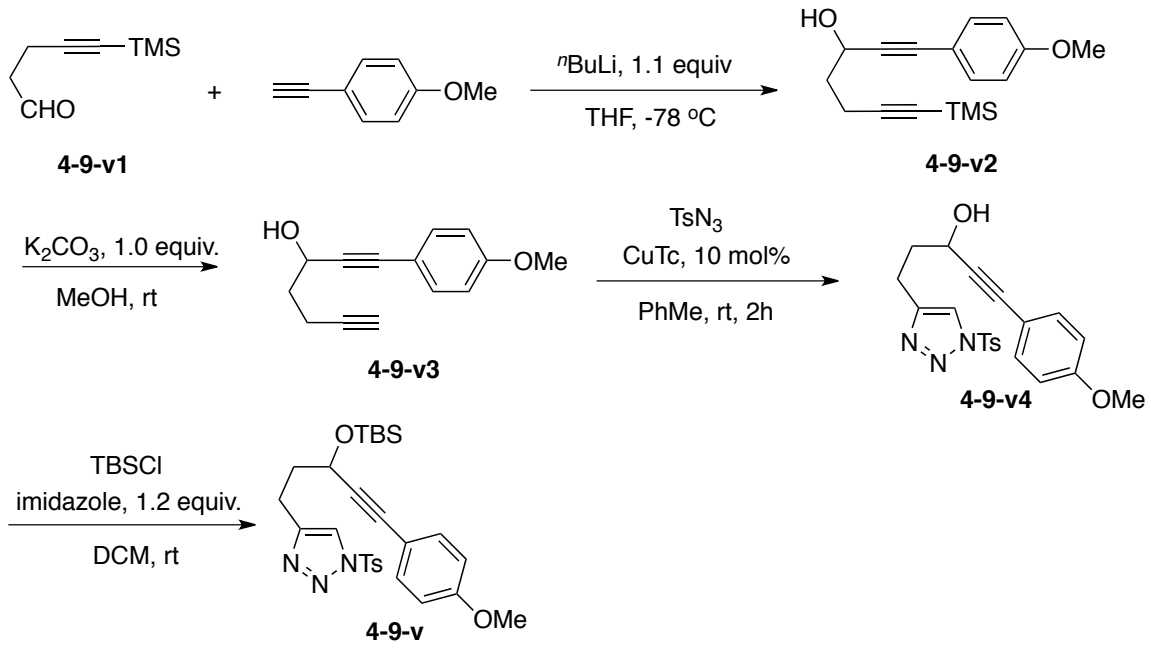
Compound **4-9-u4** was prepared according to **General Procedure B**. **4-9-u3** (~2.2 mmol) and tosyl azide (2.6 mmol) were used. 65% yield from aldehyde **4-9-u1.**

To a solution of imidazole (1.2 equiv) and TBSCl (1.2 equiv) was added triazole **4-9-u4** (~1.7 mmol, in 3 mL DCM) at room temperature. The mixture was stirred under Ar for 3h, and the solvent was removed in vacuo. Chromatography afforded **4-9-u** in 40% yield.



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 4.77 Hz, 2 H), 7.96 (s, 1 H), 7.37 (d, *J* = 8.44 Hz, 2 H), 7.29 (d, *J* = 8.80 Hz, 2 H), 6.80 (d, *J* = 8.80 Hz, 2 H), 5.14 – 5.12 (m, 1 H), 3.79 (s, 3 H), 2.56 – 2.49 (m, 1 H), 2.46 – 2.41 (m, 4 H), 2.07 – 2.01 (m, 2 H), 0.88 (s, 9 H), 0.11 (s, 3 H), 0.09 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.09, 152.11, 147.22, 133.17, 132.85, 130.41, 128.57, 120.80, 115.89, 113.82, 87.34, 81.00, 66.49, 55.24, 37.40, 25.76, 21.82, 18.07, 15.20, -4.74, -4.96. HRMS (ESI) calculated for $C_{27}H_{36}N_3O_4SSi$ $[M+H]^+$: 526.2196, found: 526.2203.

4-(3-((tert-butyldimethylsilyl)oxy)-5-(4-methoxyphenyl)pent-4-yn-1-yl)-1-tosyl-1H-1,2,3- triazole (4-9-v):

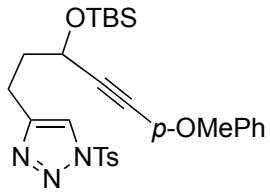


Scheme 4-16

Under Ar protection, to a solution of 1-ethynyl-4-methoxybenzene (3.0 mmol) in THF (25 mL) cooled to -78 °C was added ^{n}BuLi (2.5 M solution in Hexane). After stirring for 45 min, aldehyde **4-9-v1** (3.2 mmol) was added at -78 °C. The reaction mixture was allowed to stir for 1 h at -78 °C and then warmed to room temperature gradually. Saturated ammonium chloride was then added. The mixture was extracted with EtOAc, dried over Na_2SO_4, and the solvent was removed in vacuo to afford crude **4-9-v2**. The residual was dissolved in MeOH (10 mL) and K_2CO_3 was then added. The mixture was stirred at room temperature for 2 h. Then the solvent was removed in vacuo. Flash chromatography afforded crude **4-9-v3.**

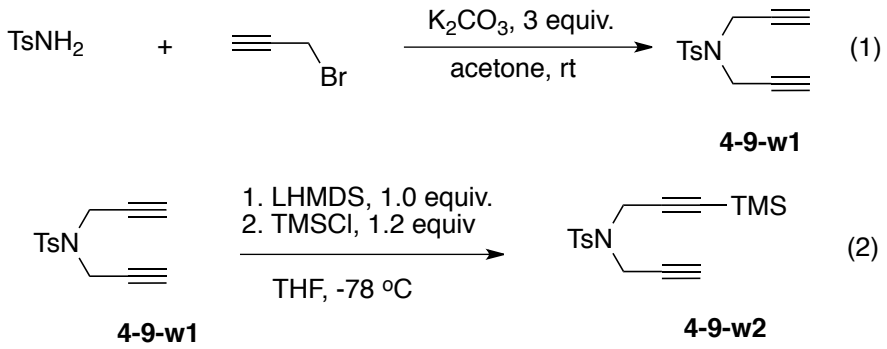
Compound **4-9-v4** was prepared according to **General Procedure B**. **4-9-v3** (~2.1 mmol) and tosyl azide (2.5 mmol) were used. 63% yield from **4-9-v1**.

To a solution of imidazole (1.2 equiv) and TBSCl (1.2 equiv) was added triazole **4-9-v4** (~1.7 mmol, in 3 mL DCM) at room temperature. The mixture was stirred under Ar for 3h, and the solvent was removed in vacuo. Chromatography afforded **4-9-v** in 67% yield.



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.48 Hz, 2 H), 7.89 (s, 1 H), 7.37 (d, *J* = 7.89 Hz, 2 H), 7.33 (d, *J* = 9.06 Hz, 2 H), 6.83 (d, *J* = 8.77 Hz, 2 H), 4.62 (t, *J* = 5.99 Hz, 1 H), 3.80 (s, 3 H), 2.95 – 2.91 (m, 2 H), 2.44 (s, 3 H), 2.14 – 2.09 (m, 2 H), 0.91 (s, 9 H), 0.16 (s, 3 H), 0.12 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.60, 147.07, 132.93, 130.38, 130.22, 128.58, 127.05, 114.90, 113.91, 88.65, 84.69, 62.53, 55.28, 37.46, 25.83, 21.80, 21.24, 18.24, -4.37, -4.96. HRMS (ESI) calculated for $C_{27}H_{36}N_3O_4SSi$ $[M+H]^+$: 526.2196, found: 526.2201.

4-methyl-N-((1-tosyl-1H-1,2,3-triazol-4-yl)methyl)-N-(3-(trimethylsilyl)prop-2-yn-1-yl)benzenesulfonamide (4-9-w):



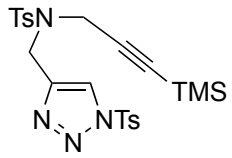
Scheme 4-17

Tosyl amine (3 mmol) was dissolved in 30 mL acetone. To this solution 3 equiv of K_2CO_3 and propargyl bromide (80% in toluene) were added. The mixture was stirred

at room temperature for 16 h. The solvent was removed in vacuo. The residual solid was dissolved in water and DCM was added. The layers were separated and the aqueous layer was extracted with DCM. The combined organic layers were dried over sodium sulfate and filtered. Evaporation of the solvent delivered the pure corresponding 1,6-heptadiyne **4-9-w1**, which can be used in next step without further purification.

Under Ar protection, to a solution of 1,6-heptadiyne **4-9-w1** (~3.0 mmol) in THF (25 mL) cooled to -78 ^{o}C was added LHMDS (1.0 M solution in THF, 3.0 mL). After stirring for 45 min, TMSCl (3.6 mmol)was added at -78 ^{o}C and the reaction mixture was allowed to stir for 3 h at the same temperature. Saturated ammonium chloride was then added and the mixture was warmed to room temperature. The mixture was extracted with ether, dried over Na_2SO_4, and the solvent was removed in vacuo. The crude **4-9-w2** was then submitted to next step without further purification.

Compound **4-9-w** was prepared from **4-9-w2** according to **General Procedure B**. **4-9-w2** (~2.1 mmol) and tosyl azide (2.5 mmol) were used. 47% yield over 3 steps.

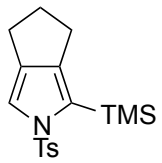


^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13, (s, 1 H), 8.00 (d, J = 8.19 Hz, 2 H), 7.74 (d, J = 8.48 Hz, 2 H), 7.40 (d, J = 8.48 Hz, 2 H), 7.30 (d, J = 8.18 Hz, 2 H), 4.51 (s, 2 H), 4.10 (s, 2 H), 2.46 (s, 2 H), 2.43 (s, 2 H), 0.00 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.46, 143.93, 143.68, 135.70, 132.90, 130.51, 129.70, 128.79, 127.71, 122.86, 97.48, 91.62, 41.65, 38.15, 21.86, 21.55, 0.46. HRMS (ESI) calculated for $C_{23}H_{29}N_4O_4S_2Si$ $[M+H]^+$: 517.1399, found: 517.1393.

3.3. Synthesis of fused pyrroles via Rh-Catalyzed intramolecular transannulation reactions

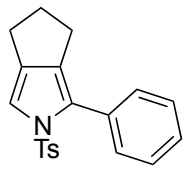
General procedure: An oven-dried 3.0 mL V-vial equipped with a stirring bar was charged with $Rh_2(esp)_2$ (1.5 mg, 1 mol %), triazole **4-9** (0.2 mmol), and chloroform (3 mL) under N_2 atmosphere. The reaction vessel was capped with Mininert syringe valve and the reaction mixture was stirred at 90 °C for 2 hours. Upon completion the reaction mixture was cooled to room temperature, concentrated under reduced pressure, and the crude product was purified by column chromatography to afford fused pyrrole **4-10**.

2-tosyl-1-(trimethylsilyl)-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrole (4-10-a): Heated at 60 ^{o}C for 15 h. 78%



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.77 Hz, 2 H), 7.23 (d, *J* = 8.18 Hz, 2 H), 7.04 (s, 1 H), 2.67 (t, *J* = 7.02 Hz, 2 H), 2.67 – 2.53 (m, 2 H), 2.38 (s, 3 H), 2.23 (quin, *J* = 7.31 Hz, 2 H), -0.28 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.88, 143.83, 137.98, 135.81, 129.60, 126.52, 125.97, 118.38, 30.69, 27.51, 23.94, 21.54, -1.09. HRMS (ESI) calculated for $C_{17}H_{23}NO_2SSi$ $[M+H]^+$: 333.1219, found: 333.12109.

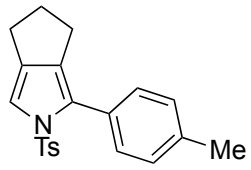
1-phenyl-2-tosyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrole (4-10-b): 50%



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.32 (m, 3 H), 7.28 – 7.26 (m, 4 H), 7.10 (d, *J* = 8.07 Hz, 2 H), 7.02 (s, 1 H), 2.59 (t, *J* = 6.60 Hz, 2 H), 2.45 (t, *J* = 7.50 Hz, 2 H), 2.36 (s, 3 H), 2.22 (quin, *J* = 7.06 Hz, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.05, 138.22, 135.85, 135.04, 131.70, 130.45, 129.19,

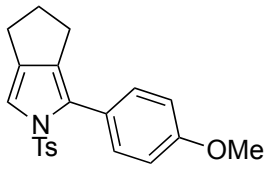
127.54, 127.38, 127.22, 126.98, 115.11, 30.81, 24.82, 24.73, 21.57. HRMS (ESI) calculated for $C_{20}H_{20}NO_2S$ $[M+H]^+$: 338.1215, found: 338.1221.

1-(p-tolyl)-2-tosyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrole (4-10-c): 58%



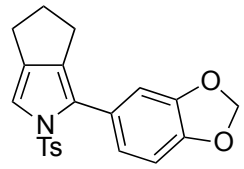
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.07 Hz, 2H), 7.19 – 7.14 (m, 4 H), 7.11 (d, *J* = 8.07 Hz, 2 H), 7.00 (s, 1 H), 2.59 (t, *J* = 7.15 Hz, 2 H), 2.44 (t, *J* = 7.50 Hz, 2 H), 2.40 (s, 3 H), 2.36 (s, 3 H), 2.22 (quin, *J* = 7.24 Hz, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.01, 137.92, 137.33, 135.92, 135.13, 130.32, 129.19, 128.80, 128.16, 127.35, 126.99, 114.89, 30.81, 24.81, 24.75, 21.57, 21.37. HRMS (ESI) calculated for $C_{21}H_{22}NO_2S$ $[M+H]^+$: 352.1371, found: 352.1369.

1-(4-methoxyphenyl)-2-tosyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrole (4-10-d): 88%



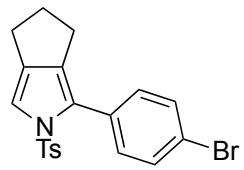
^{1}H NMR (500 MHz, benzene-*d*6) δ 7.27 (d, *J* = 8.44 Hz, 2 H), 7.20 – 7.18 (m, 2 H), 7.11 (d, *J* = 7.70 Hz, 2 H), 7.00 (s, 1 H), 6.89 – 6.86 (m, 2 H), 3.85 (s, 3 H), 2.60 – 2.57 (m, 2 H), 2.43 (d, *J* = 7.35 Hz, 2 H), 2.35 (s, 3 H), 2.21 (quin, *J* = 7.24 Hz, 2 H). ^{13}C NMR (126 MHz, benzene-*d*6) δ 159.53, 143.60, 137.52, 136.79, 134.73, 132.07, 129.07, 127.19, 124.48, 115.14, 113.17, 54.53, 30.74, 24.79, 24.68, 20.76. HRMS (ESI) calculated for $C_{21}H_{22}NO_3S$ $[M+H]^+$: 368.1320, found: 368.1327.

1-(benzo[*d*][1,3]dioxol-5-yl)-2-tosyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrole (4-10-e): 91%



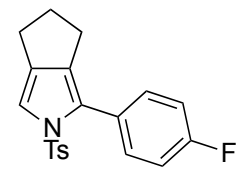
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (d, J = 8.44 Hz, 2 H), 7.13 (d, J = 8.44 Hz, 2 H), 6.98 (s, 1 H), 6.77 – 6.76 (m, 2 H), 6.69 – 6.67 (m, 1 H), 5.99 (s, 2 H), 2.58 (t, J = 7.34 Hz, 2 H), 2.42 (t, J = 7.25, 2 H), 2.36 (s, 3 H), 2.21 (quin, J = 7.43 Hz, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.14, 146.76, 144.13, 137.83, 135.89, 134.91, 129.22, 127.02, 126.79, 125.38, 124.23, 114.77, 111.15, 107.40, 101.08, 30.76, 24.78, 24.73, 21.57. HRMS (ESI) calculated for $C_{21}H_{20}NO_4S$ $[M+H]^+$: 382.1113, found: 382.1108.

1-(4-bromophenyl)-2-tosyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrole (4-10-f): 63%



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, J = 8.07 Hz, 2 H), 7.28 (d, J = 8.44 Hz, 2 H), 7.16 – 7.12 (4 H), 7.02 (s, 1 H), 2.59 (t, J = 7.15 Hz, 2 H), 2.42 (t, J = 7.20 Hz, 2 H), 2.22 (quin, J = 7.15 Hz, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.30, 138.82, 135.66, 135.35, 131.88, 130.67, 130.63, 129.30, 126.89, 125.99, 121.76, 115.60, 30.78, 24.82, 24.69, 21.59. HRMS (ESI) calculated for $C_{20}H_{19}BrNO_2S$ $[M+H]^+$: 416.0320, found: 416.0325.

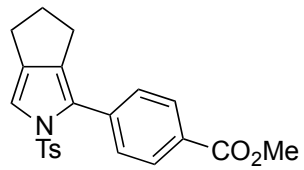
1-(4-fluorophenyl)-2-tosyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrole (4-10-g): 42%



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 – 7.21 (m, 4 H), 7.12 (d, J = 8.07 Hz, 2 H), 7.03 – 7.00 (m, 2 H), 2.61 – 2.58 (m, 2 H), 2.42 (d, J = 7.20, 2 H), 2.36 (s, 3 H), 2.23 (quin, J = 7.24 Hz, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.31 (d, J = 245.7 Hz), 144.23, 138.20, 135.80, 134.92, 132.21

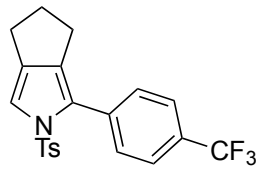
(d, J = 8.82 Hz), 129.27, 127.68 (d, J = 3.78 Hz), 126.92, 125.99, 115.08, 114.42 (d, J = 22.68 Hz), 30.79, 24.72, 21.57. HRMS (ESI) calculated for $C_{20}H_{19}FNO_2S$ $[M+H]^+$: 356.1121, found: 356.1112.

methyl 4-(2-tosyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-yl)benzoate (4-10-h): 66%



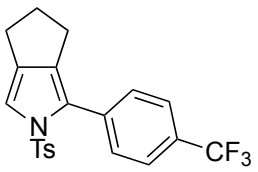
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.18 Hz, 2 H), 7.37 (d, J = 8.48 Hz, 2 H), 7.26 (d, J = 8.40 Hz, 2 H), 7.11 (d, J = 8.18 Hz, 2 H), 7.04 (s, 1 H), 3.94 (s, 3 H), 2.59 (t, J = 7.16 Hz, 2 H), 2.46 (t, J = 7.20 Hz, 2 H), 2.35 (s, 3 H), 2.23 (quin, J = 7.16 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.01, 144.36, 139.84, 136.40, 135.70, 135.54, 130.04, 129.31, 128.72, 126.86, 126.41, 116.35, 109.56, 52.12, 30.78, 25.01, 24.67, 21.58. HRMS (ESI) calculated for $C_{22}H_{22}NO_4S$ $[M+H]^+$: 396.1270, found: 396.1260.

2-tosyl-1-(4-(trifluoromethyl)phenyl)-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrole (4-10-i): 65%



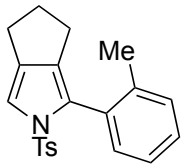
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, J = 8.07 Hz, 2 H), 7.41 (d, J = 8.07 Hz, 2 H), 7.27 (d, J = 8.44 Hz, 2 H), 7.12 (d, J = 8.07 Hz, 2 H), 7.05 (s, 1 H), 2.60 (td, J = 7.24, 1.28 Hz, 2 H), 2.46 (t, J = 7.15 Hz, 2 H), 2.36 (s, 3 H), 2. 24 (quin, J = 7.15 Hz, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.42, 139.80, 135.52, 135.39, 131.82, 130.38, 128.57, 129.35, 126.39 (q, J = 272.2 Hz), 126.85, 125.83, 124.38 (q, J = 3.78 Hz), 123.16, 116.23, 30.78, 24.91, 24.68, 21.57. HRMS (ESI) calculated for $C_{21}H_{19}F_3NO_2S$ $[M+H]^+$: 406.1089, found: 406.1095.

2-tosyl-1-(4-(trifluoromethyl)phenyl)-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrole (4-10-j): 52%



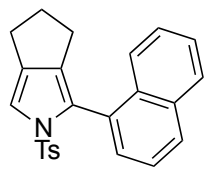
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.07 Hz, 2 H), 7.24 – 7.21 (m, 1 H), 7.11 (d, *J* = 8.07 Hz, 2 H), 7.02 (s, 1 H), 6.88 – 6.83 (m, 3 H), 3.81 (s, 3 H), 2.59 (t, *J* = 6.79 Hz, 2 H), 2.46 (t, *J* = 7.40 Hz, 2 H), 2.36 (s, 3 H), 2.22 (quin, *J* = 7.24 Hz, 2 H). ^{13}C NMR (100 MHz, acetone-d6) δ 158.89, 144.65, 138.14, 136.03, 134.93, 132.99, 129.41, 128.36, 126.85, 122.58, 115.74, 115.30, 113.45, 109.56, 54.61, 30.52, 24.54, 24.26, 20.54. HRMS (ESI) calculated for $C_{21}H_{22}NO_3S$ $[M+H]^+$: 368.1320, found: 368.1310.

1-(o-tolyl)-2-tosyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrole (4-10-k): 62%



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.24 (m, 3 H), 7.16 – 7.09 (m, 5 H), 7.02 – 6.99 (m, 1 H), 2.64 (t, *J* = 7.60 Hz, 2 H), 2.38 (s, 3 H), 2.33 – 2.21 (m, 4 H), 1.89 (s, 3 H). ^{13}C NMR (126 MHz, acetone-*d*6) δ 144.70, 138.88, 137.04, 136.39, 133.64, 131.92, 131.07, 129.49, 129.30, 128.38, 127.05, 125.19, 124.54, 113.82, 30.59, 29.69, 24.34, 20.56, 19.09. HRMS (ESI) calculated for $C_{21}H_{22}NO_2S$ $[M+H]^+$: 352.1371, found: 352.1363.

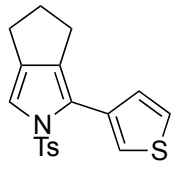
1-(naphthalen-1-yl)-2-tosyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrole (4-10-l): 83%



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.07 Hz, 1 H), 7.82 (d, *J* = 8.44 Hz, 1 H), 7.50 – 7.37 (m, 3 H), 7.21 – 7.18 (m, 3 H), 7.07 (d, *J* = 8.44 Hz, 2 H), 6.83 (d, *J* = 8.07 Hz, 2H), 2.71 – 2.69 (m, 2 H), 2.28 – 2.25 (m, 4 H), 2.22 (s, 3 H). ^{13}C NMR (100 MHz, acetone-*d*6) δ 144.49, 138.41, 135.90,

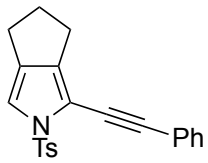
133.73, 133.38, 132.93, 130.11, 129.28, 128.74, 128.02, 126.89, 125.88, 125.64, 125.42, 124.57, 123.75, 114.45, 109.56, 30.53, 24.44, 20.47. HRMS (ESI) calculated for $C_{24}H_{22}NO_2S$ $[M+H]^+$: 388.1371, found: 388.1374.

1-(thiophen-3-yl)-2-tosyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrole (4-10-m): 78%



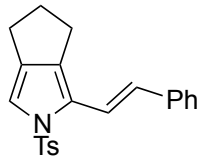
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.44 Hz, 2 H), 7.26 – 7.25 (m, 1 H), 7.15 – 7.09 (m, 4 H), 7.03 (s, 1 H), 2.60 (t, J = 7.50 Hz, 2 H), 2.47 (t, *J* = 7.35 Hz, 2 H), 2.35 (s, 3 H), 2.23 (quin, *J* = 7.24 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.11, 137.86, 135.88, 134.32, 131.57, 129.95, 129.27, 126.98, 124.92, 123.80, 114.68, 30.75, 25.04, 24.76, 21.57. HRMS (ESI) calculated for $C_{18}H_{18}NO_2S_2$ $[M+H]^+$: 344.0779, found: 344.0776.

1-(phenylethynyl)-2-tosyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrole (4-10-n):81%



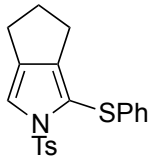
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.44 Hz, 2 H), 7.54 – 7.52 (m, 2 H), 7.39 – 7.34 (m, 3 H), 7.26 – 7.25 (m, 2 H), 7.04 (s, 1 H), 2.64 (t, *J* = 7.15 Hz, 2 H), 2.60 (t, *J* = 6.79 Hz, 2 H), 2.38 (s, 3 H), 2.26 (quin, *J* = 7.24 Hz, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.67, 143.70, 136.01, 133.85, 131.16, 129.69, 128.38, 128.23, 127.58, 123.23, 114.95, 107.52, 95.51, 80.06, 30.50, 25.25, 24.90, 21.63. HRMS (ESI) calculated for $C_{22}H_{20}NO_2S$ $[M+H]^+$: 362.1215, found: 362.1211.

(*E*)-1-styryl-2-tosyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrole (4-10-o): 87%



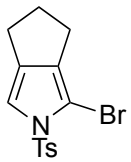
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 – 7.65 (m, 3 H), 7.46 – 7.44 (m, 2 H), 7.36 – 7.33 (m, 2 H), 7.26 – 7.23 (m, 3 H), 6.99 (s, 1 H), 6.61 (d, *J*=16.14 Hz, 1 H), 2.74 (t, *J* = 7.15 Hz, 2 H), 2.59 (t, *J* = 7.34 Hz, 2 H), 2.36 – 2.30 (m, 5 H). ^{13}C NMR (100 MHz, acetone-*d*6) δ 145.13, 137.62, 136.52, 136.05, 135.17, 130.04, 129.15, 128.74, 127.42, 126.74, 126.01, 124.96, 117.44, 114.17, 30.55, 26.49, 23.92, 20.52. HRMS (ESI) calculated for $C_{22}H_{22}NO_2S$ $[M+H]^+$: 364.1371, found: 364.1369.

1-(phenylthio)-2-tosyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrole (4-10-p): 93%



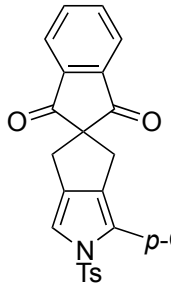
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.44 Hz, 2 H), 7.31 (s, 1 H), 7.08 – 7.01 (m, 5 H), 6.79 – 6.77 (m, 2 H), 2.67 (t, *J* = 7.50 Hz, 2 H), 2.47 (t, *J* = 7.85 Hz, 2 H), 2.29 – 2.22 (m, 5 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.72, 144.39, 137.54, 135.76, 133.23, 129.41, 128.58, 127.79, 125.82, 125.08, 117.89, 110.77, 30.29, 25.26, 25.23, 21.51. HRMS (ESI) calculated for $C_{20}H_{20}NO_2S_2$ $[M+H]^+$: 370.0935, found: 370.0939.

1-bromo-2-tosyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrole (4-10-q): 65%



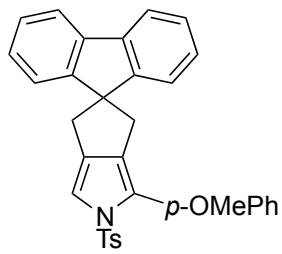
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.48 Hz, 2 H), 7.29 (d, *J* = 7.89 Hz, 2 H), 7.11 (s, 1 H), 2.62 (td, *J* = 7.23, 1.32 Hz, 2 H), 2.44 (t, *J* = 7.44 Hz), 2.41 (s, 3 H), 2.22 (quin, *J* = 7.23 Hz, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.88, 138.76135.72, 134.39, 129.76, 127.64, 115.93, 30.06, 25.41, 25.01, 21.66. HRMS (ESI) calculated for $C_{14}H_{15}BrNO_2S$ $[M+H]^+$: 340.0007, found: 340.0012.

1-(4-methoxyphenyl)-2-tosyl-4,6-dihydro-2*H*-spiro[cyclopenta[*c*]pyrrole-5,2'-indene]-1',3'-dione (4-10-r): 70%



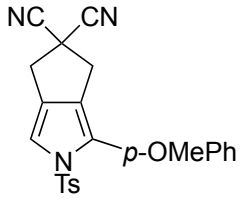
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 – 7.96 (m, 2 H), 7.86 – 7.84 (m, 2 H), 7.28 - 7.26(m, 2 H), 7.16 – 7.14 (m, 4 H), 7.09 (s, 1 H), 6.81 (d, *J* = 8.80 Hz, 2 H), 3.82 (s, 3 H), 3.03 (s, 2 H), 2.83 (s, 2 H), 2.39 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.99, 159.37, 144.41, 141.17, 136.02, 135.91, 133.54, 131.97, 129.39, 127.19, 126.98, 123.71, 123.11, 114.80, 112.89, 64.31, 55.24, 33.02, 32.52, 21.60. HRMS (ESI) calculated for $C_{29}H_{23}NO_5S$ $[M]^+$: 497.1297, found: 497.13013.

1-(4-methoxyphenyl)-2-tosyl-4,6-dihydro-2*H*-spiro[cyclopenta[*c*]pyrrole-5,9'-fluorene] (4-10-s): 68%



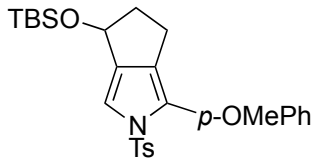
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.70 Hz, 2 H), 7.41 (d, *J* = 8.07 Hz, 2 H), 7.34 – 7.31 (m, 2 H), 2.25 – 2.22 (m, 4 H), 7.17 (s, 1 H), 7.13 – 7.10 (m, 2 H), 7.00 (d, *J* = 7.70 Hz, 2 H), 6.85 (d, *J* = 8.80 Hz, 2 H), 3.83 (s, 3 H), 3.01 (s, 2 H), 2.90 (s, 2 H), 2.48 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.31, 151.25, 144.26, 139.42, 136.13, 135.63, 134.33, 131.58, 129.24, 129.13, 127.47, 127.23, 123.60, 122.33, 119.82, 116.35, 113.01, 62.44, 55.24, 37.35, 37.43, 21.73. HRMS (ESI) calculated for $C_{33}H_{27}NO_3S$ $[M]^+$: 517.17117, found: 517.17054.

1-(4-methoxyphenyl)-2-tosyl-4,6-dihydrocyclopenta[*c*]pyrrole-5,5(2*H*)-dicarbonitrile (4-10-t): Heated at 90 ^{o}C for 15 h. 81%



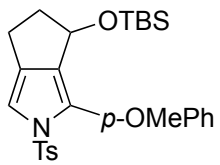
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 – 7.22 (m, 3 H), 7.13 (d, *J* = 8.44 Hz, 2 H), 7.08 (d, *J* = 8.80 Hz, 2 H), 6.86 (d, *J* = 8.44 Hz, 2 H), 3.86 (s, 3 H), 3.50 (s, 2 H), 3.29 (s, 2 H), 2.37 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.04, 145.11, 135.23, 132.08, 129.57, 128.80, 127.98, 127.17, 125.30, 121.57, 115.95, 115.88, 113.26, 55.34, 38.34, 38.24, 38.10, 21.63. HRMS (ESI) calculated for $C_{23}H_{19}N_3O_3S$ $[M]^+$: 417.1147, found: 417.11406.

4-((tert-butyldimethylsilyl)oxy)-1-(4-methoxyphenyl)-2-tosyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrole (4-10-u): 64%



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.24 (m, 2 H), 7.16 – 7.09 (m, 5 H), 6.85 – 6.83 (m, 2 H), 5.15 – 5.12 (m, 1 H), 3.85 (s, 3 H), 2.63 – 2.55 (m, 1 H), 2.59 – 2.47 (m, 1 H), 2.35– 2.27 (m, 4 H), 2.18 – 2.12 (m, 1 H), 0.93 (s, 9 H), 0.13 (s, 3 H), 0.12 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.25, 144.26, 136.92, 135.29, 132.04, 129.26, 127.14, 126.70, 123.49, 115.38, 112.88, 70.50, 55.24, 41.62, 25.91, 22.56, 21.57, 18.32, -4.59. HRMS (ESI) calculated for $C_{27}H_{36}NO_4SSi$ $[M+H]^+$: 498.2134, found: 498.2134.

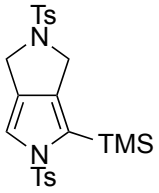
6-((tert-butyldimethylsilyl)oxy)-1-(4-methoxyphenyl)-2-tosyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrole (4-10-v): 57%



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.24 (m, 2 H), 7.15 – 7.09 (m, 4 H), 7.02 (s, 1 H), 6.82 – 6.80 (m, 2 H), 4.94 – 4.92 (m, 1 H), 3.84 (s, 3 H), 2.82 – 2.73 (m, 1 H), 2.54 – 2.42 (m, 2 H), 2.36 (s, 3 H), 2.16 – 2.09 (m, 1 H), -0.71 (s, 9 H), -0.20 (s, 3 H), -0.28 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ

159.58, 144.21, 137.89, 136.11, 132.90, 132.38, 129.23, 128.19, 127.20, 123.04, 113.76, 112.65, 55.31, 41.77, 25.68, 22.37, 21.56, 17.99, -5.06, -5.19. HRMS (ESI) calculated for $C_{27}H_{36}NO_4SSi$ $[M+H]^+$: 498.2134, found: 498.2121.

2,5-ditosyl-4-(trimethylsilyl)-1,2,3,5-tetrahydropyrrolo[3,4-*c*]pyrrole (4-10-w):70%



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.07 Hz, 2 H), 7.49 (d, *J* = 8.44 Hz, 2 H), 7.33 (d, *J* = 8.07 Hz, 2 H), 7.26 (d, *J* = 6.75 Hz, 2 H), 7.08 (s, 1 H), 4.36 (s, 2 H), 4.30 (s, 2 H), 2.42 (s, 3 H), 2.40 (s, 3 H), 0.25 (s, 9 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.70, 143.70, 139.42, 137.07, 134.04, 129.86, 127.74, 127.49, 127.20, 126.11, 117.86, 49.02, 46.62, 21.59, 21.53, 0.60. HRMS (ESI) calculated for $C_{23}H_{28}N_2O_4S_2Si$ $[M+H]^+$: 488.1260, found: 488.12543.

3.4. Relative rate comparison study

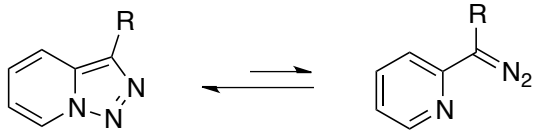
The relative rate study was performed in separate vials. An oven-dried 3.0 mL V-vial equipped with a stirring bar was charged with $Rh_2(esp)_2$ (1 mol %), triazole **4-9** (0.1 mmol), and $CDCl_3$ (2 mL) under N_2 atmosphere. The reaction vessel was capped with Mininert syringe valve and the reaction mixture was stirred at 90 °C for about 7 min (20%-30% conversion). Then it was cooled to room temperature and analyzed by NMR.

PART II TRANSITION-METAL-CATALYZED TRANSFORMATIONS OF PYRIDOTRIAZOLES

4. INTRODUCTION

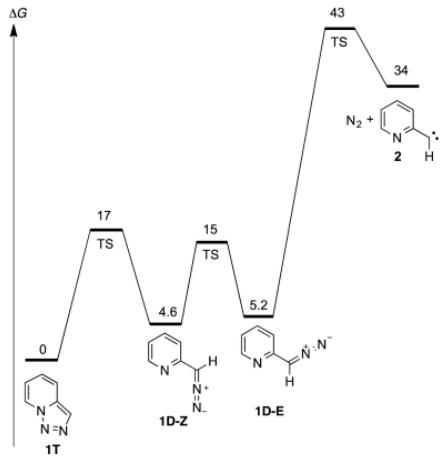
4.1. Ring-chain tautomerism of pyridotriazoles

Similar to *N*-sulfonyl-1,2,3-triazoles, the triazoloazine-diazomethylazine valence tautomerism also exist in pyridotriazole derivatives **5-1** ([1,2,3]triazolo[1,5-*a*]pyridines).[76] As illustrated in Figure 5-1, the calculation indicates an enthalpy difference of 6−10 kcal/mol between the ring-closed triazole form (**5-1**) and the ring-opening diazo form (**5-2**), with triazoles at the lowest enthalpy and an activation barrier around 20 kcal/mol for the ring opening process.[76b] Thus, it is difficult to observe the minor ring-opened diazo form in solution directly.



5-1 **5-2**

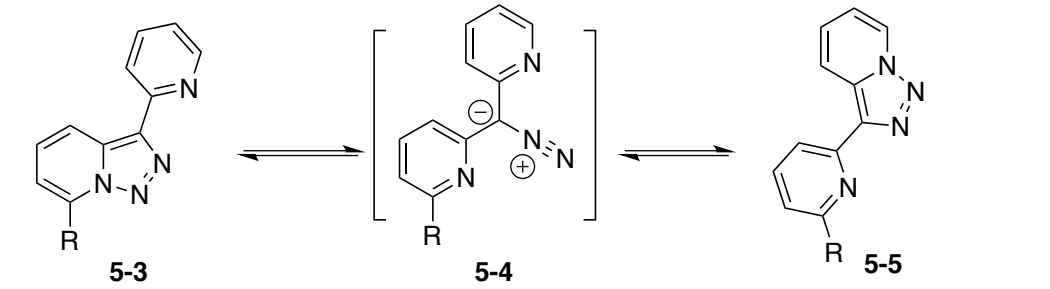
Scheme 5-1



Free energy diagram (relative values of ΔG in kcal/mol) for triazolo/diazomethylpyridine **1T** and **1D** and their dissociation to 2-pyridylcarbene **2** and N_2 and the transition states connecting them at the B3LYP/6-31G* level. The corresponding values of ΔH are 0, 17.5, 6.7, 16, 7.3, 48, and 47 kcal/mol.

Figure 5-1

Abarca group studied the ring–chain tautomerism of pyridotriazoles by both DFT and experimental method.[76f] During the preparation of pyridotriazole derivatives, they observed an isomerization reaction from **5-3** to **5-5** (Scheme 5-2). It was hypothesized that the ring-opened diazo compound **5-4** was the key to this transformation, and the ratio of two isomers (**5-3** and **5-5**) could depend on some characteristics of the R substituents. The DFT calculation revealed that electronic properties of the R group indeed affected this equilibrium. Therefore, pyridotriazoles possessing electron-donating substituents (R = TMS, $B(OR)_2$) favoured the **5-3** form, whereas pyridotriazoles with electron-withdrawing substituents (R = $CH_3C(O)$, Br, Cl, I, *p*-C_6H_4OMe) favored the **5-5** form. In the case of R = Me, both forms were present (75% of **5-3**, 25% of **5-5**). This calculation study was also supported by their further experimental data.



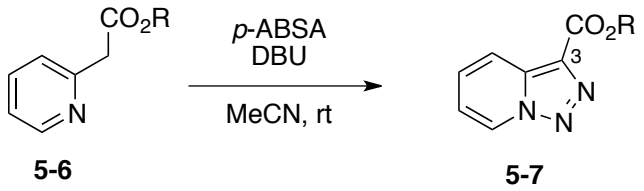
Scheme 5-2

4.2. Synthesis and functionalization of pyridotriazoles

4.2.1. Synthesis of pyridotriazoles

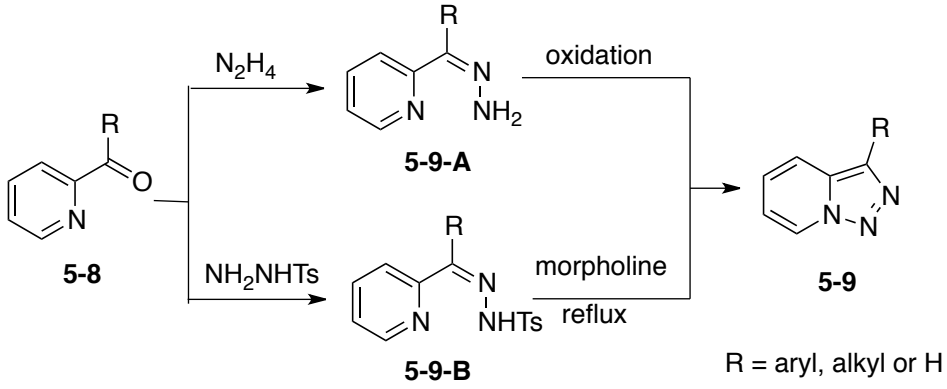
Pyridotriazoles, considered as the ring-closed form of heteroaryl-diazo compounds, could be easily synthesized via classical methods for the preparation of normal diazo species.

As illustrated in Scheme 5-3, pyridotriazoles possessing an ester substituent at the C3 position (**5-7**) was obtained from the corresponding pyridylacetates **5-6** by a diazo transfer reaction using *p*-acetamidobenzenesulfonyl azide (*p*-ABSA) and DBU in acetonitrile at room temperature.[77]



Scheme 5-3

On the other hand, pyridotriazoles bearing aryl, alkyl substituents or H atom (**5-8**), could easily be synthesized from the corresponding carbonyl compounds **5-8**. Two synthetic routes via hydrozones presume either oxidation reactions of hydronzon **5-9-A**, or elimination reactions of Ts-hydrozone **5-9-B** under basic conditions (Scheme 5-4).[78]

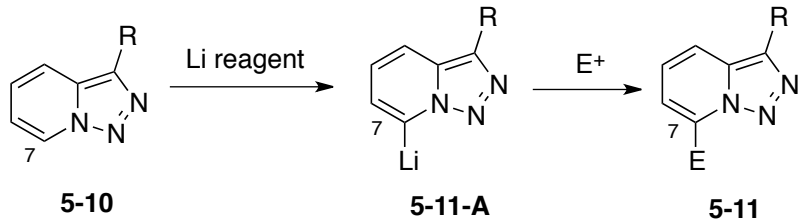


Scheme 5-4

4.2.2. Functionalization of the pyridotriazole core

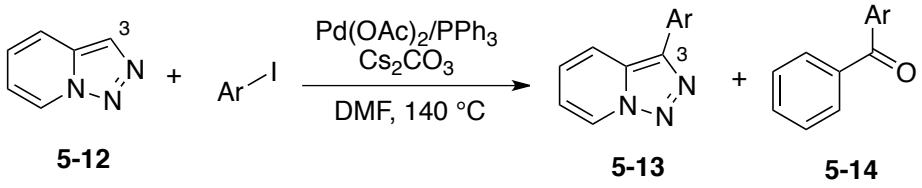
Traditionally, the functionalization of pyridotriazole core on its most acidic C7-position could be easily accomplished via lithiation strategy (Scheme 5-5).[79] The directing effect of *peri*-nitrogen atom would lead to the formation of 7-lithiated

intermediate **5-11-A** selectively, which then upon reacting with diverse electrophiles affords various 7-substituted pyridotriazoles **5-11**.



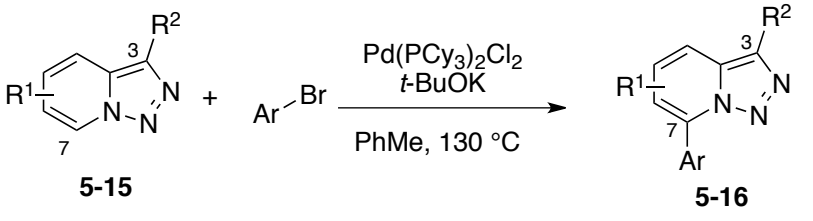
Scheme 5-5

Nowadays, the palladium-catalyzed C-H activation strategy has been extensively explored and widely used for the preparation of functionalized aromatics.[80] Employing this concept, the direct C3 arylation of pyridotriazoles has been investigated using palladium catalysis. However, the desired products **5-13** were obtained in low yields along with the formation of denitrogenative ring-opening byproducts **5-14** (Scheme 5-6).[81]



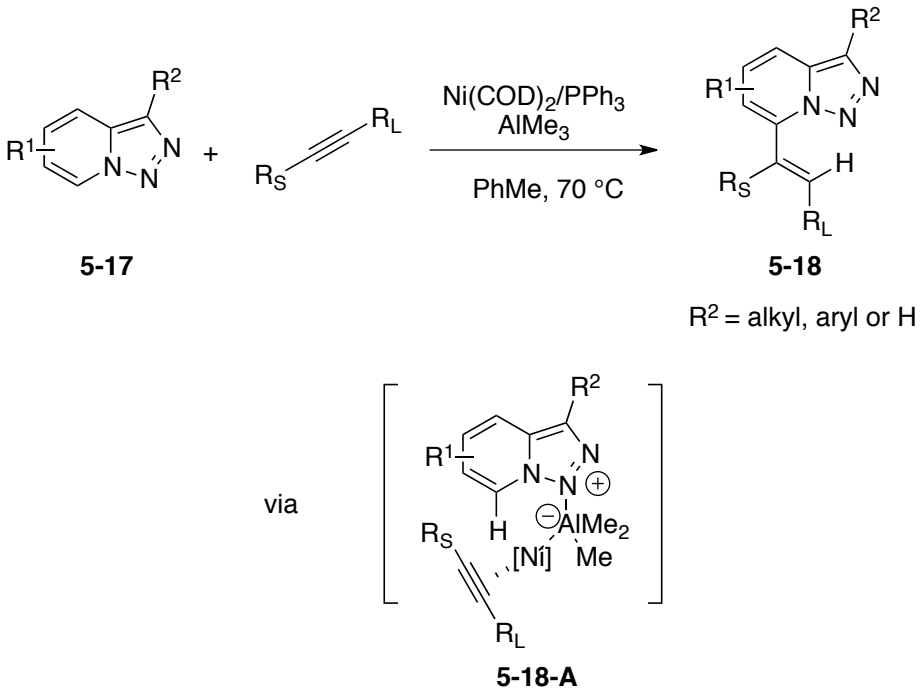
Scheme 5-6

In contrast to the lower efficient palladium-catalyzed C3 arylation of pyridotriazles, the C7 arylation was recently reported by Hong group (Scheme 5-7).[82] Employing C3 substituted triazoles **5-15**, arylation reaction proceeded smoothly in the presence of palladium catalyst and *t*-BuOK, producing C7-arylated **5-16** in good yields (Scheme 5-7).[82]



Scheme 5-7

The C7 alkenylation of pyridotriazoles was accomplished by employment of nickel catalysis (Scheme 5-8).[83] Different from the arylation strategy, pyridotriazoles possessing H atom at the C3 position were tolerated under these conditions (R^2 = H). The Lewis acid $AlMe_3$ was found to be crucial for this transformation, which delivers the nickel catalyst to the C7 via coordination with both triazole N atom and the catalyst (**5-18-A**).



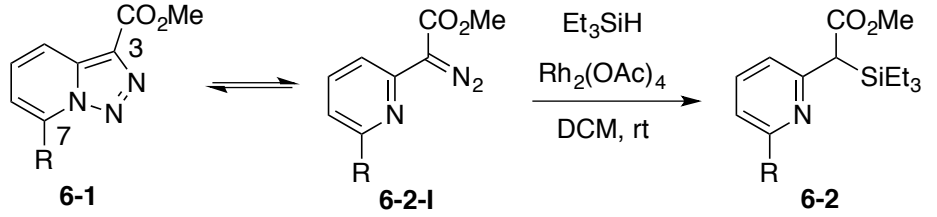
Scheme 5-8

4.3. Reactions of pyridotriazoles

Compared to the extensive investigation on *N*-sulfonyl-1,2,3-triazoles, the pyridotriazoles are much less developed.

4.3.1. Transannulation reactions of pyridotriazoles

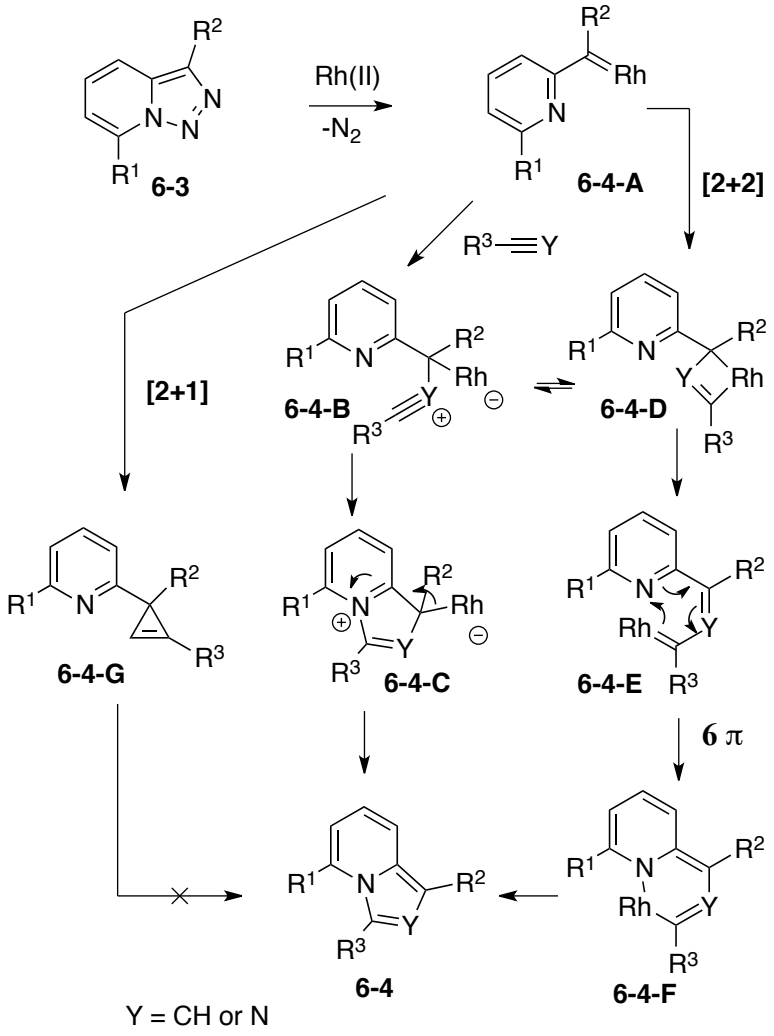
As discussed above, the tautomerism of pyridotriazole makes it a good candidate to serve as a carbene precursor. Different from the monocyclic *N*-sulfonyl-1,2,3-triazoles, the adjacent pyridine ring offers a great opportunity for construction of diverse fused *N*-heterocycles. Our group tested this hypothesis by performing Si-H insertion reaction, a method developed by Doyle and coworkers for the efficient trapping of Rh carbenes,[84] to efficiently produce the insertion product **6-2** (Scheme 6-1).[24] In this early work, an activating group (R) at C7 position, as well as an electron withdrawing group at C3 position, was crucial to drive the equilibrium towards the formation of reactive ring-opened pyridyl diazo compounds.



Scheme 6-1

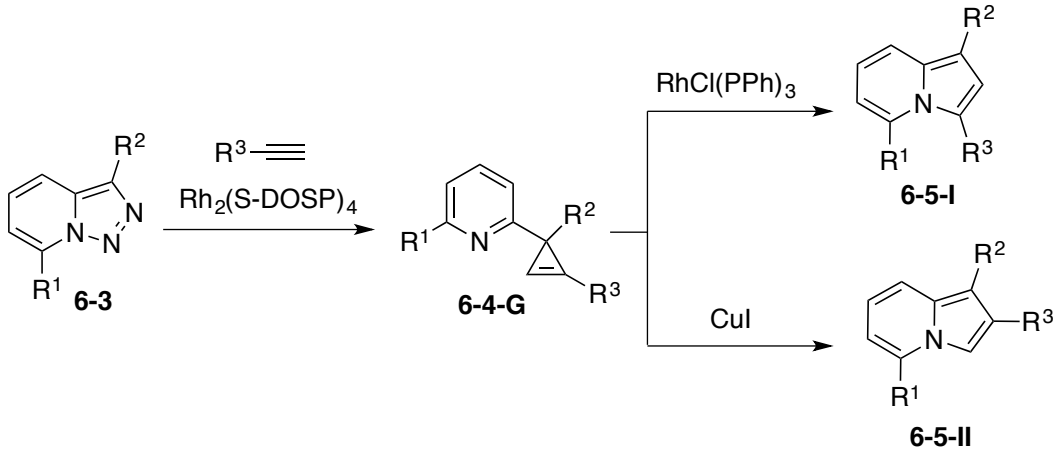
Based on this, a transannulation reaction of pyridotriazoles **6-3** with alkynes and nitriles toward indolizines and imidazopyridines **6-4** was developed (Scheme 6-2).[24] In the presence of Rh(II) catalyst, an electrophilic rhodium carbene intermediate could be produced. Then, a direct nucleophilic attack of alkyne or nitrile on *in situ* generated **6-4-**

A afforded ylide species **6-4-B**, which could cyclize to give a final reaction product **6-4**. Alternatively, a [2+2] cycloaddition of Rh-carbene **6-4-A** with C-C or C-N triple bond could result in a metallacyclobutene **6-4-D**, which can also be formed from ylide **6-4-B**. Then, metathesis followed by 6 π-cyclization and subsequent reductive elimination furnished final product **6-4**. The [2+1] cycloaddition/rearrangement mechanism was ruled out for formation of indolizines (**6-4**, Y = CH), since independently prepared intermediate **6-4-G** failed to be transferred into the corresponding heterocycle under these reaction conditions.



Scheme 6-2

Later, our group found that by employing $RhCl(PPh)_3$ or CuI catalyst, the above-mentioned rearrangement reaction from cyclopropene intermediates (**6-4-G**) towards indolozines (**6-5**) could occur with excellent regioselectivity, offering efficient regiodivergent synthesis of 1,3- and 1,2-disubstituted indolizine derivatives (Scheme 6-3).[85]

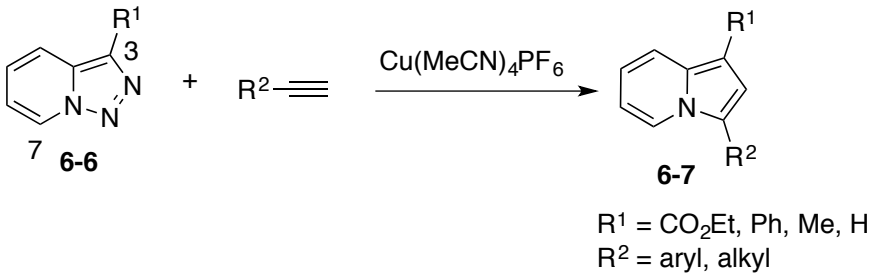


Scheme 6-3

Although the Rh-catalyzed denitrogenative transannulation reaction is a powerful method for synthesis of nitrogen-containing heterocycles, the requisite activating group at C7 (**6-3**, R^1 = Cl, Br, or OMe) and an EWG at C3 (**6-3**, R^2 = ester or Ar) limit this method to be widely utilized in organic synthesis. Our group broke these limitations by developing a series of methodologies, aiming at the employment of simple, unactivated pyridotriazoles as metal-carbene precursors in various transformations.[86]

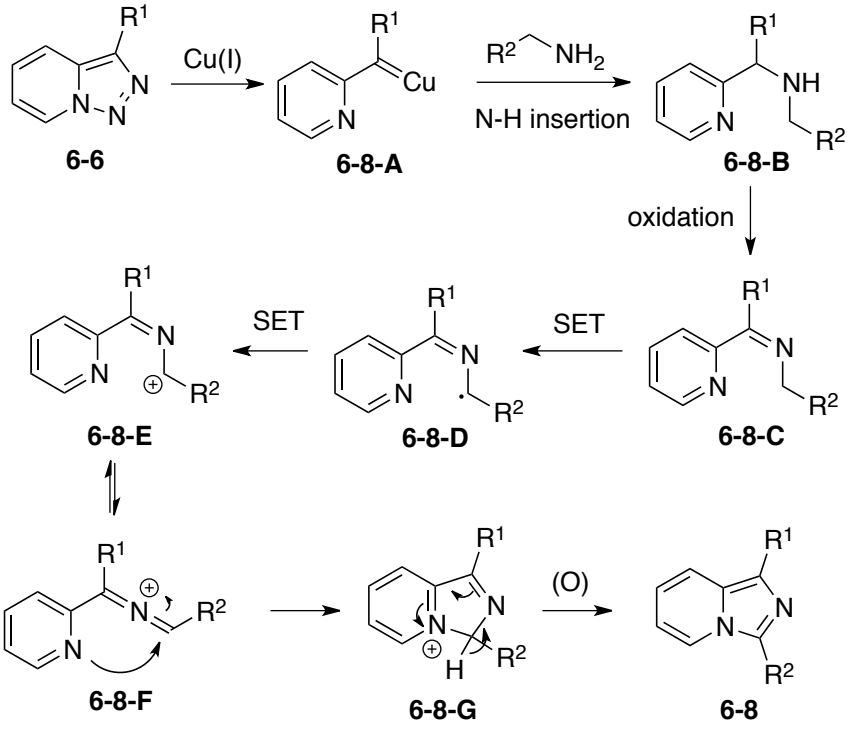
In order to employ cheaper catalysts, our group developed copper catalyzed transannulation reactions of pyridotriazole **6-6** with terminal alkynes (Scheme 6-4).[86a] Compared to the previously reported rhodium conditions (Scheme 6-2 and 6-3), this method features not only the use of cheap catalyst and easily handled aerobic conditions, but also a broader scope of both employed pyridotriazoles (no activating group at C7, no

EWG required at C3) and terminal alkynes (no aromatic group required), thus substantially broadening the scope of inolizines (**6-7**) accessible via this approach .



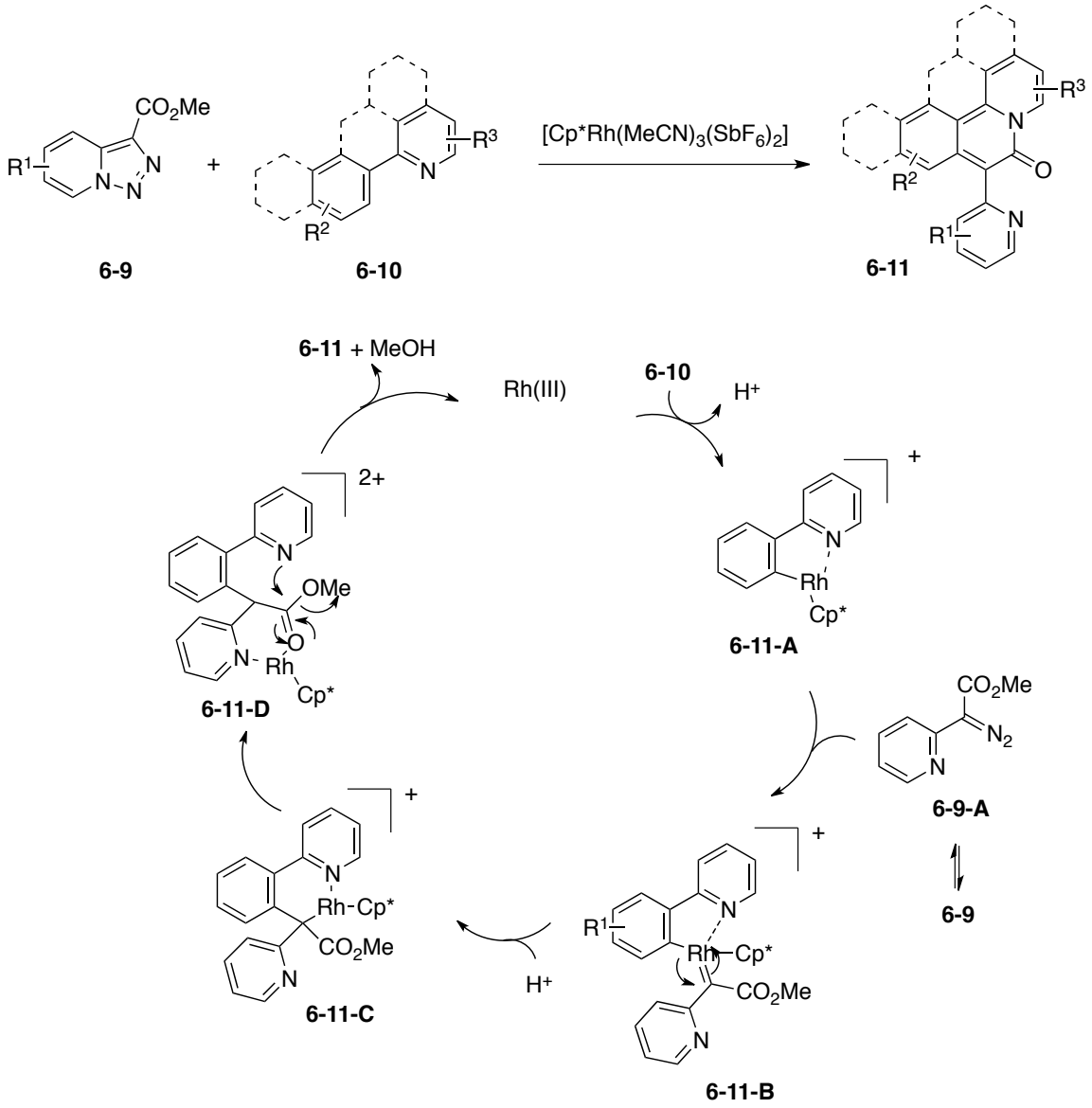
Scheme 6-4

Later, the Adimurthy group extended this copper-catalyzed strategy to transannulation of pyridotriazoles with benzylamines and amino acids (upon decarboxylation) (Scheme 6-5).[87] Similarly, a copper carbene **6-8-A** was generated from pyridotriazole, which would undergo N-H insertion reaction with amines followed by oxidation to afford imine intermediate **6-8-C**. Then, upon electron transfer (SET) and a subsequent intramolecular cyclization, the desired imidazo[1,5-*a*]pyridine products **6-8** could be obtained.



Scheme 6-5

Besides rhodium (II) and copper catalysts, Rh(III) complexes are also capable to react with pyridotriaozles, to produce metallocarbene species. The advantage of using this new catalytic system on pyridotriazoles is the ability to combine this chemistry with transition-metal catalyzed directed C-H activation strategy.[88] Recently, the Glorius group first realized this concept by developing a direct access to novel fluorescent scaffolds (Scheme 6-6).[89] This transformation was initiated by a directed C-H activation step, producing a cationic rhodacycle **6-11-A**. Then, upon reacting with the *in situ* generated diazo compound and N_2 loss, the Rh(III) carbene intermediate **6-11-B** was formed, which underwent a migratory insertion (**6-11-B** to **6-11-C**) and protodemetalation (**6-11-C** to **6-11-D**) to afford **6-11-D**. Finally, nucleophilic substitution at the activated ester carbonyl led to fluorophore products **6-11**. The unique part of **6-11** is their pyridine and carbonyl moieties, which make them bidentate luminophores with sensing capabilities (Figure 6-1).



Scheme 6-6

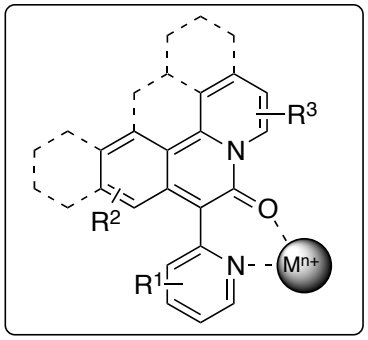
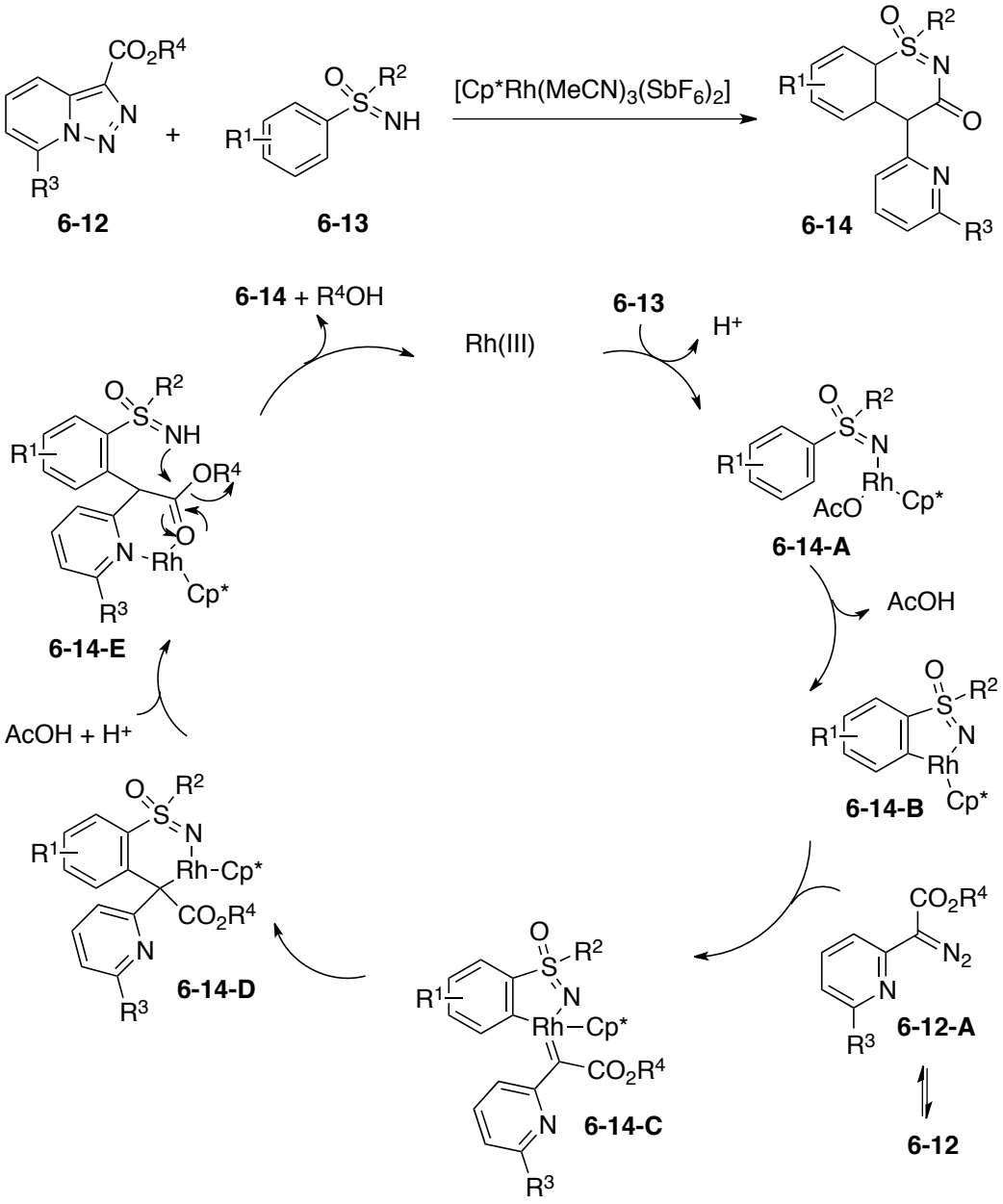


Figure 6-1

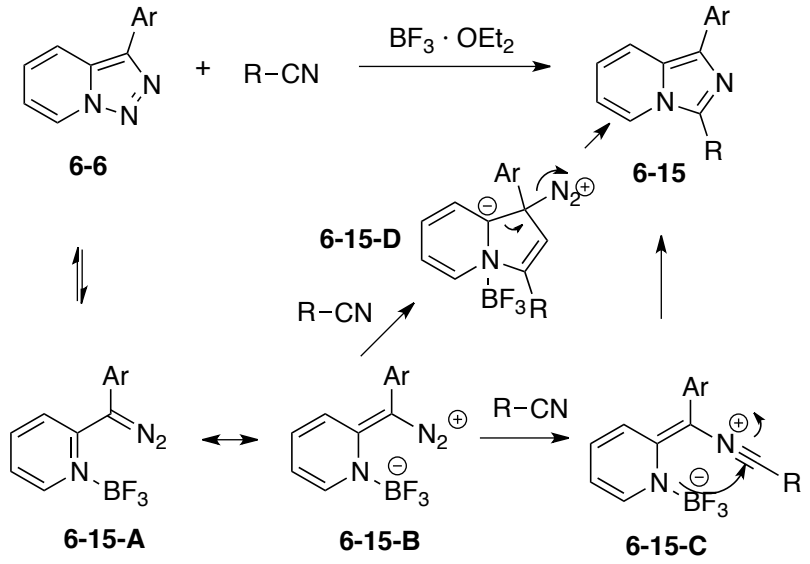
In continuation of this Rh(III) catalysis strategy, Lee group disclosed an efficient method for synthesis of a wide range of 1,2-benzothiazines (Scheme 6-7).[90] Analogously to Glorius' report, first, a five-membered rhodacycle **6-14-B** was formed via a directed C-H activation, which then reacted with the *in situ* generated diazo **6-12-A** to afford metal carbene **6-14-C**. Then, a subsequent migratory insertion (**6-14-C** to **6-14-D**), followed by elimination of alcohol produced the final product **6-14**. However, this novel domino process was limited to pyridotriazoles possessing activating groups at C7 position (R^3 = Cl or Br).



Scheme 6-7

In addition to the transition-metal catalyzed reactions, Adimurthy group recently reported a Lewis acid-catalyzed transannulation of pyridotriazoles with nitriles in a combined solvent system (Scheme 6-8).[91] In this method, the authors utilized coordination between $BF_3 \cdot Et_2O$ and the pyridine nitrogen atom to facilitate the ring opening process of pyridotriazoles (**6-15-A** and **6-15-B**). Next, a subsequent nucleophilic

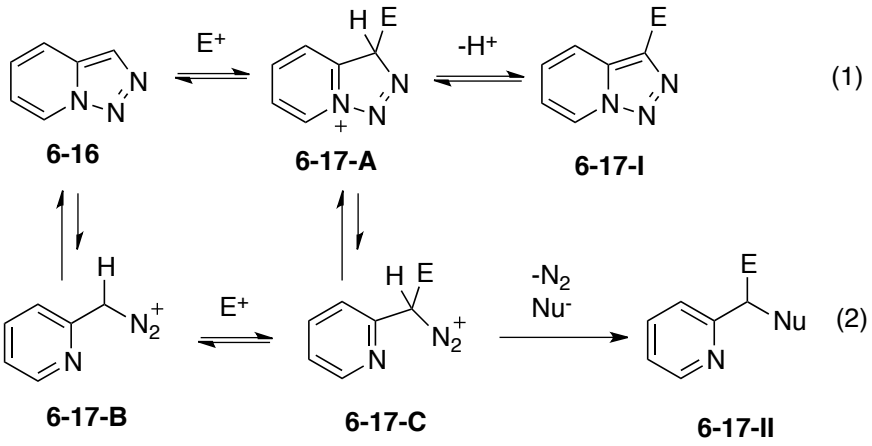
attack of nitriles to diazo intermediate **6-15-B**, followed by N_2 loss and ring closure afforded the reaction product [1,5-*a*]pyridines **6-15**.



Scheme 6-8

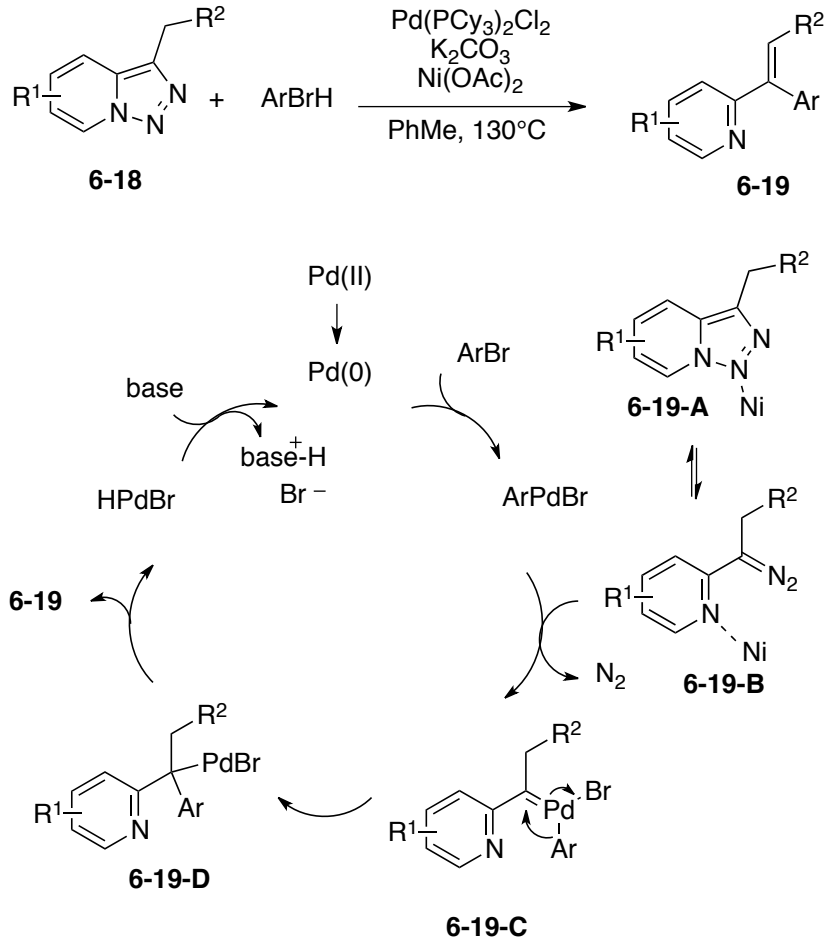
4.3.2. Other denitrogenative transformations of pyridotriazoles

Back in 1981, the ring opening reactions of [1,2,3]triazolo[1,5-*a*]pyridines were observed upon treatment with electrophiles, which led to the formation of various pyridine derivatives (Scheme 6-9).[92] This process could be attributed to the tautomerization between **6-16** and **6-17-B**, or, more likely, to the tautomerization of the electrophilic addition intermediate **6-17-A** to **6-17-C**. The outcome of this reaction was determined by the stability of intermediate **6-17-A**. If the electrophile E^+ was an electron-withdrawing in nature, the intermediate **6-17-A** would be longer-lived, and deprotonation of the cyclic form competed successfully with the loss of nitrogen, thus substitution product **6-17-I** was obtained (eq 1). If the electrophile E^+ was only weakly stabilizing of the diazonium intermediate, a nucleophilic attack with loss of nitrogen would be favored, producing the ring-opening product **6-17-II** (eq 2).



Scheme 6-9

As mentioned above, the Hong group reported a palladium-catalyzed direct C7 arylation reaction of pyridotriazoles (Scheme 5-5).[82] In the paper, the authors also described a denitrogenative arylation reaction at C3 position of **6-18**. Upon switching base form ^{t}BuOK to K_2CO_3, and employment of $Ni(OAc)_2$ as an additive, a Pd-carbene species was generated after the loss of N_2 (**6-19-C**), which underwent a migratory insertion to form intermediate **6-19-D**. The latter upon β-H elimination, produced alkene product **6-19** (Scheme 6-10).[82]


R2
R1
N
N
+
ArBrH
Pd(PCy3)2Cl2
K2CO3
Ni(OAc)2
PhMe, 130°C
Ar
6-18
6-19
Pd(II)
Pd(0)
base
base+-H
Br −
HPdBr
ArBr
ArPdBr
6-19-A
Ni
N2
6-19-B
6-19
PdBr
6-19-D
Br
Pd
6-19-C

Scheme 6-10

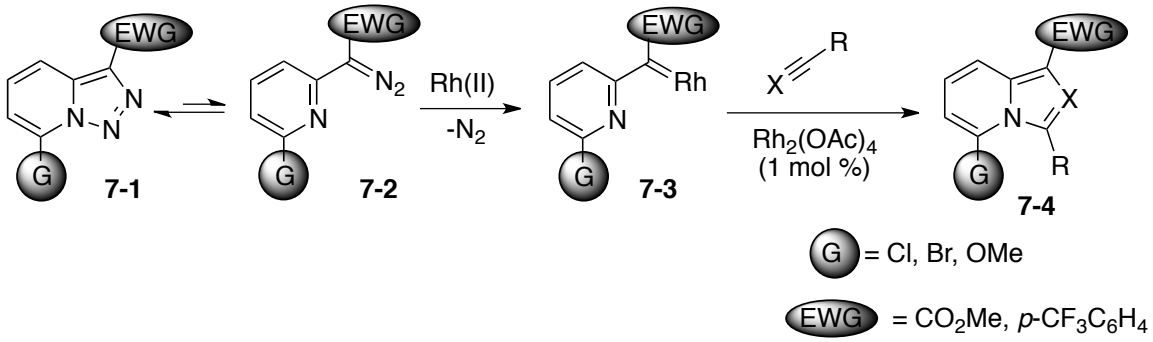
5. TRANSITION-METAL CATALYZED TRANSFORMATIONS OF PYRIDOTRIAZOLES

5.1. Intermolecular NH insertion of pyridyl carbenes derived from pyridotriazoles : a general and efficient approach to 2-picolylamines and imidazo[1,5-a]pyridines

Previously published as "Rhodium-Catalyzed NH Insertion of Pyridyl Carbenes Derived from Pyridotriazoles: A General and Efficient Approach to 2-Picolylamines and Imidazo[1,5-a]pyridines." Shi, Y.; Gulevich, A. V.; Gevorgyan, V. *Angew. Chem., Int. Ed*. **2014**, *53*, 14191.

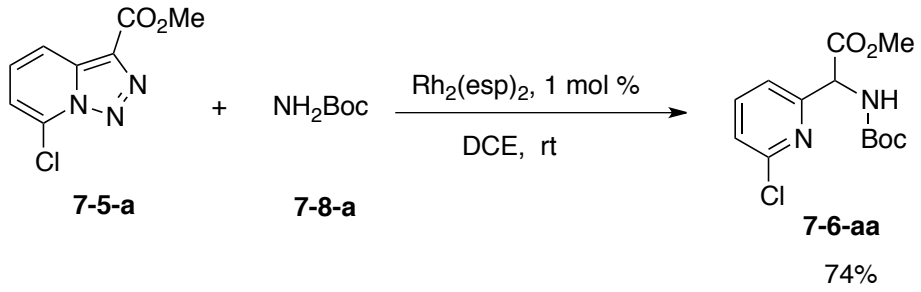
5.1.1. Development of the intermolecular NH insertion of pyridyl carbenes

As discussed above, transition-metal-catalyzed denitrogenative transannulation of pyridotriazoles has become a powerful method for synthesis of nitrogen-containing heterocycles. In 2007, our group reported the first transannulation reaction of pyridotriazoles based on the reaction of **7-1**with nitriles (X = N) and alkynes (X = CH, Scheme 7-1).[24] However, the requirement of an activating group at C7, as well as an electron-withdrawing groups at C3, limited its application. Naturally, we were interested in expanding the scope of this methodology by breaking the current substrate limitations.

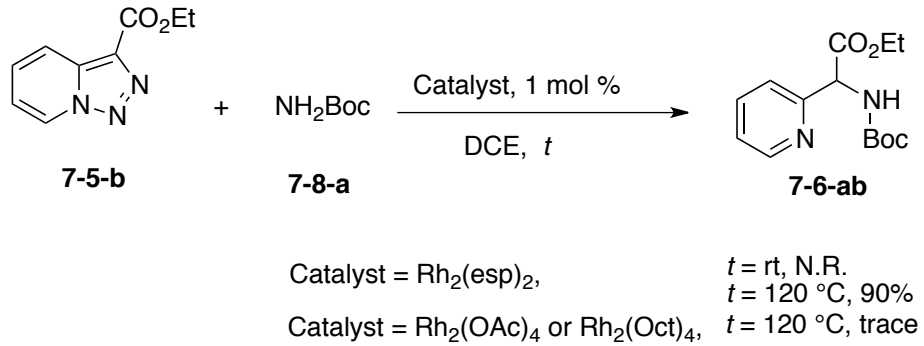


Scheme 7-1

We first investigated the rhodium-catalyzed NH insertion reaction[54f] with carbamate **7-8-a** using 7-Cl-substituted triazole **7-5-a**, which proved to be an effective carbene precursor[24, 85] (Scheme 7-2). Indeed, the reaction proceeded smoothly, producing the desired piclolyl amine[93] **7-6-aa** in 74% yield in the presence of a [$Rh_2(esp)_2$] catalyst at room temperature. However, attempts to employ the 7-unsubstituted pyridotriazole **7-5-b** under these reaction conditions failed. To our delight, upon raising temperature to 120 °C, the N-H insertion reaction carried out smoothly, furnishing picolylamine **7-6-ab** in 90% yield (Scheme 7-3).



Scheme 7-2

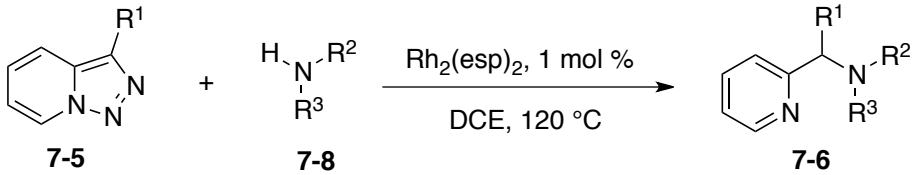


Scheme 7-3

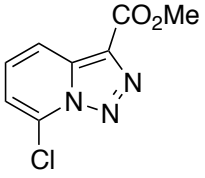
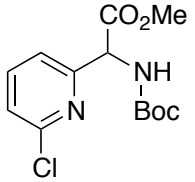
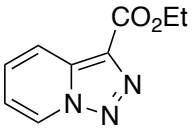
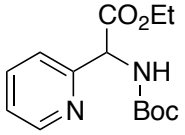
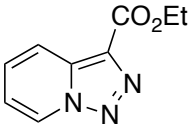
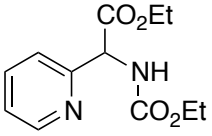
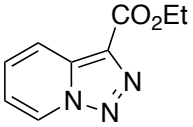
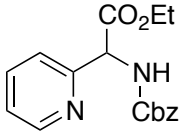
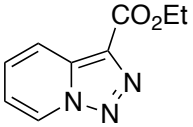
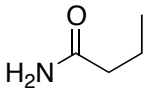
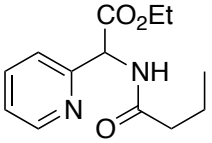
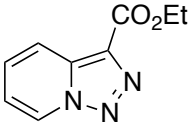
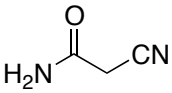
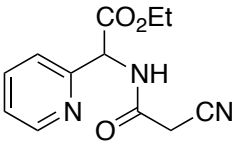
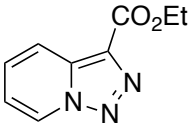
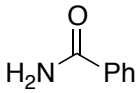
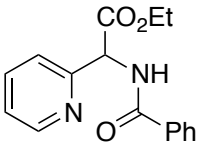
5.1.2. Reaction scope

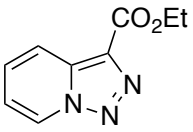
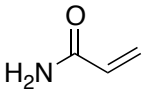
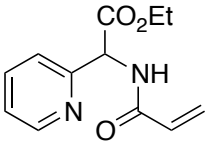
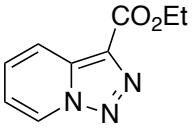
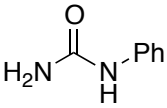
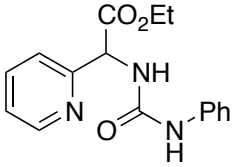
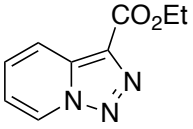
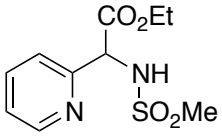
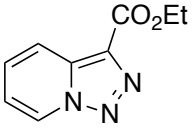
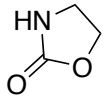
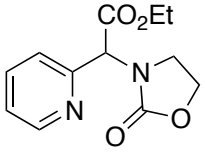
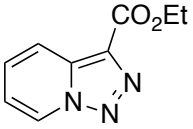
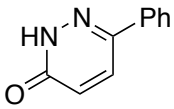
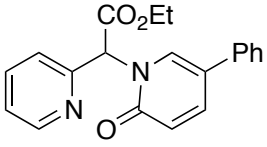
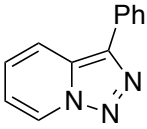
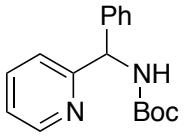
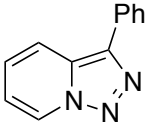
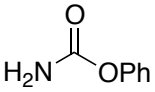
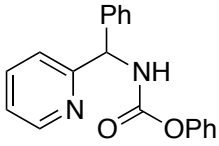
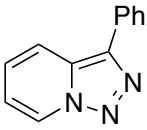
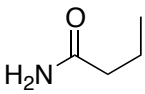
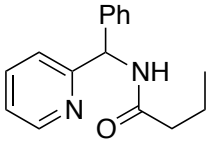
With these efficient catalytic conditions in hand, we examined the scope of the NH insertion reaction without further optimization. It was shown that, alkyl carbamates, such as ^{t}BuOCONH$_2$, EtOCONH$_2$, and BnOCONH$_2$ produced the picolyl amines **7-6-ab** to **7-6-ad** in high yields (Table 7-1, entries 2–4). The reaction also worked efficiently with alkyl and aryl amides (entries 5–7), as well as with alkenyl amide (entry 8). Notably, a cyano group and alkenyl moiety, which normally react with metal carbenes, stayed intact under these reaction conditions (entries 6 and 8). Moreover, we found that phenyl urea and sulfonamide could also participate in this transformation to produce the insertion products **7-6-ai** and **7-6-aj** (entries 9 and 10). Secondary amides, such as oxazolidin-2-one (entry 11) and 3(2-*H*)-pyridazinone (entry 12), were also competent reaction partners. Notably, the reaction also efficiently proceeded with pyridotriazoles containing different substituents at the C3 poisition. Thus, 3-aryl pyridotriazoles (entries 13–16) and even 3-methyl pyridotriazole (entry 17) reacted smoothly to produce the desired NH insertion products. In addition, 4-methyl pyridotriazole (entry 18), *N*-fused quinolinotriazole (entry 19), and benzoxazolotriazole (entry 20) also underwent an efficient NH insertion reaction to afford the corresponding amides.

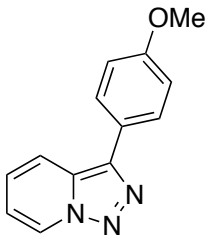
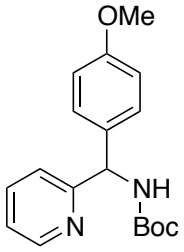
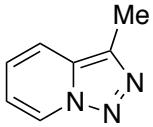
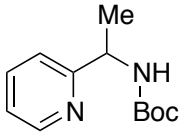
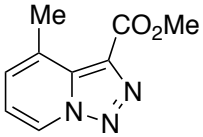
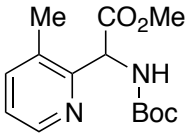
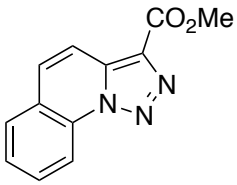
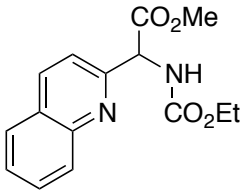
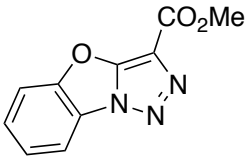
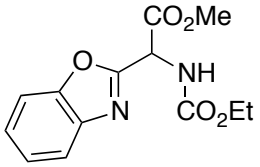
Table 7-1. Substrate scope for the rhodium(II)-catalyzed reaction of pyridotriazoles with amides.



7-5 **7-8** **7-6**

Entry	Substrate		Substrate		Product		Yield/ %[a,b]
1		**7-5-a**	NH_2Boc	**7-8-a**		**7-6-aa**	74[c]
2		**7-5-b**	NH_2Boc	**7-8-a**		**7-6-ab**	90
3		**7-5-b**	NH_2CO_2Et	**7-8-b**		**7-6-ac**	91
4		**7-5-b**	NH_2Cbz	**7-8-c**		**7-6-ad**	65
5		**7-5-b**		**7-8-d**		**7-6-ae**	85
6		**7-5-b**		**7-8-e**		**7-6-af**	87
7		**7-5-b**		**7-8-f**		**7-6-ag**	76

Entry	Substrate		Substrate		Product		Yield/ %[a,b]
8		**7-5-b**		**7-8-g**		**7-6-ah**	85
9		**7-5-b**		**7-8-h**		**7-6-ai**	75
10		**7-5-b**	NH_2SO_2Me	**7-8-i**		**7-6-aj**	68[d]
11		**7-5-b**		**7-8-j**		**7-6-ak**	66
12		**7-5-b**		**7-8-k**		**7-6-al**	75
13		**7-5-c**	NH_2Boc	**7-8-a**		**7-6-am**	89
14		**7-5-c**		**7-8-l**		**7-6-an**	75
15		**7-5-c**		**7-8-d**		**7-6-ao**	81

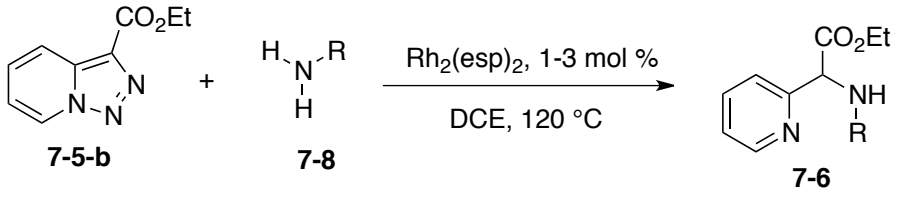
Entry	Substrate		Substrate		Product		Yield/ %[a,b]
16		**7-5-d**	NH_2Boc	**7-8-a**		**7-6-ap**	77
17		**7-5-e**	NH_2Boc	**7-8-a**		**7-6-aq**	88
18		**7-5-f**	NH_2Boc	**7-8-a**		**7-6-ar**	66
19		**7-5-g**	NH_2CO_2Et	**7-8-b**		**7-6-as**	63
20		**7-5-h**	NH_2CO_2Et	**7-8-b**		**7-6-at**	91

[a]The triazole **7-5** (0.20 mmol), NH compounds **7-8** (1.5 equiv), and $[Rh_2(esp)_2]$ (1.0 mol%) were heated in 2 mL of anhydrous DCE at 120 °C until completion. [b]Isolated yield. [c]Performed at room temperature. [d]3.0 mol% $Rh_2(esp)_2$.

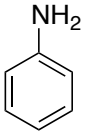
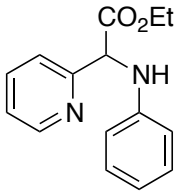
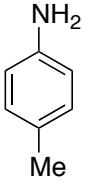
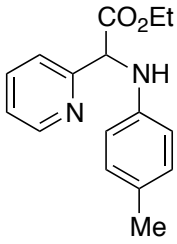
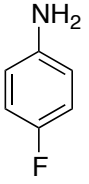
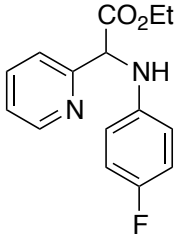
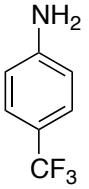
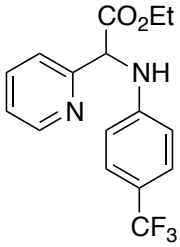
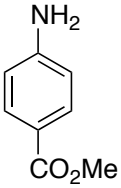
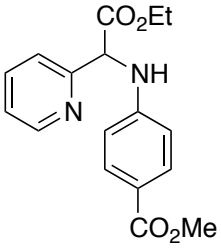
After developing the NH insertion reaction with various amides, we turned our attention to more challenging aromatic and aliphatic amines, which, as a result of their high basicity, may potentially deactivate the rhodium(II) catalyst. To our delight, reasonable to good yields in the reaction of **7-5-b** with anilines were achieved upon

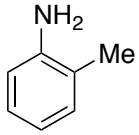
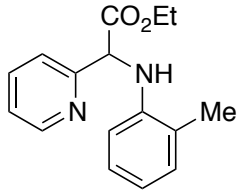
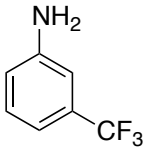
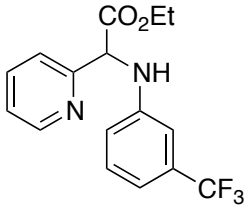
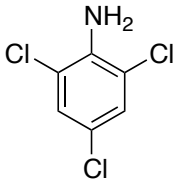
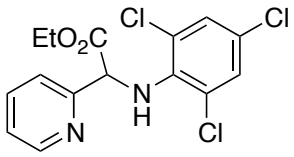
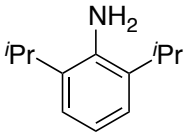
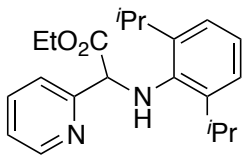
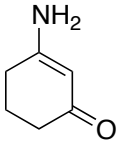
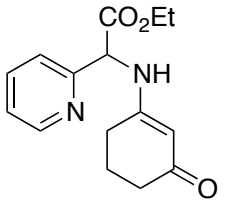
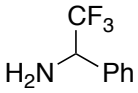
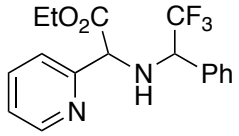
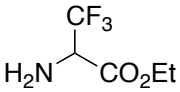
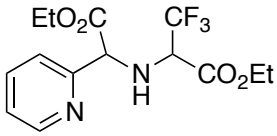
raising the catalyst loading to 3 mol% (Table 7-2, entries 1–9). Thus, anilines bearing functional groups, such as halogens (entries 3 and 8), CF_3 (entries 4 and 7), and CO_2Me (entry 5), efficiently underwent the reaction with **7-5-b** to produce the insertion products. Moreover, sterically hindered 2,6-dichloro, and 2,6-diisopropylaniline reacted smoothly to give the corresponding insertion products in reasonable yield (entries 8 and 9). In addition, an enamine also underwent the NH insertion reaction to form the corresponding product **7-6-bj** (entry 10). Among aliphatic amines, a-CF_3-substituted alkyl amines could undergo an NH insertion reaction, which was demonstrated by the reactions of **7-5-b** with 2,2,2-trifluoro-1-phenylethane-1-amine (entry 11). Notably, the successful NH insertion reaction with CF_3-amino acid (entry 12) opens access to fluorinated opine derivatives (**7-6-bl**).[94]

Table 7-2. Substrate scope for the rhodium(II)-catalyzed reaction of pyridotriazoles with anilines and aliphatic amines.



7-5-b **7-8** **7-6**

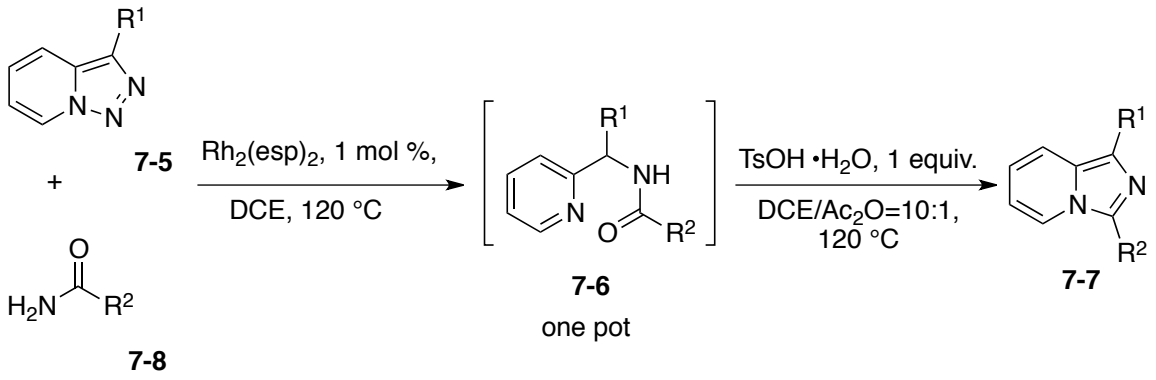
Entry	Substrate		Product		Yield/%[a,b]
1		**7-8-m**		**7-6-ba**	88
2		**7-8n**		**7-6-bb**	63
3		**7-8-o**		**7-6-bc**	80
4		**7-8-p**		**7-6-bd**	86
5		**7-8-q**		**7-6-be**	72

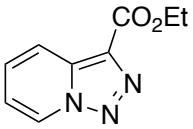
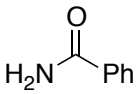
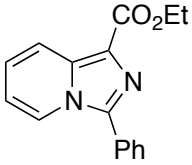
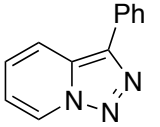
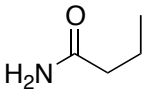
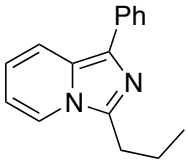
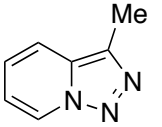
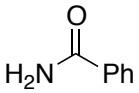
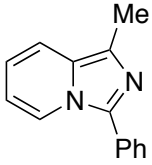
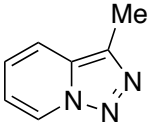
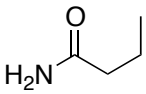
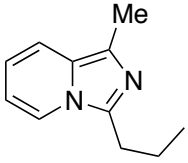
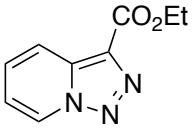
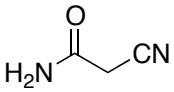
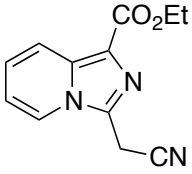
Entry	Substrate	Product		Yield/%[a,b]
6		**7-8-r**		**7-6-bf**	76
7		**7-8-s**		**7-6-bg**	71
8		**7-8-t**		**7-6-bh**	90
9		**7-8-u**		**7-6-bi**	47
10		**7-8-v**		**7-6-bj**	91[c]
11		**7-8-w**		**7-6-bk**	87
12		**7-8-x**		**7-6-bl**	82

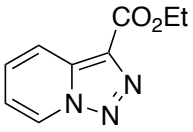
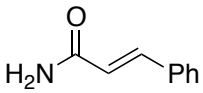
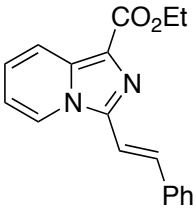
[a]The triazole **7-5-b** (0.20 mmol), NH compounds **7-8** (1.5 equiv), and [$Rh_2(esp)_2$] (3.0 mol%) were heated in 2 mL of anhydrous DCE at 120 °C until completion. [b]Isolated yield. [c]1.0 mol% $Rh_2(esp)_2$.

Along the lines of our studies on the development of new transformations toward heterocyclic molecules, we envisioned that the obtained picolylamides **7-6** could be cyclized into the imidazopyridines[95] **7-7** by a nucleophilic attack of the pyridine nitrogen atom at a suitably activated amide group (Table 7-3).[96] Accordingly, we developed a formal one-pot transannulation reaction of pyridotriazoles with primary amides which proceeds by the rhodium-catalyzed NH insertion reaction and subsequent cyclization into imidazo[1,5-a]pyridines. Notably, this transannulation reaction of **7-5** with amides has a much broader scope compared to that of the previously developed transannulation reaction with nitriles (Scheme 7-1). Thus, the AG is not necessary for the successful reaction, and the substituent at C3 is not limited to an electron-withdrawing group. Generally, the developed transannulation reaction allows an efficient synthesis of imidazo[1,5-*a*]pyridines containing aryl, alkenyl and alkyl substituents (Table 7-3, entries 1–6).

Table 7-3. One-pot synthesis of imidazo[1,5-a]pyridines by NH insertion/cyclization process.



Entry	Substrate		Substrate		Product		Yield/%[a,b]
1		**7-5-b**		**7-8-f**		**7-7-a**	70
2		**7-5-c**		**7-8-d**		**7-7-b**	77
3		**7-5-e**		**7-8-f**		**7-7-c**	73
4		**7-5-e**		**7-8-d**		**7-7-d**	81
5		**7-5-b**		**7-8-e**		**7-7-e**	58

Entry	Substrate	Substrate	Product	Yield/%[a,b]
6	 **7-5-b**	 **7-8-y**	 **7-7-f**	78

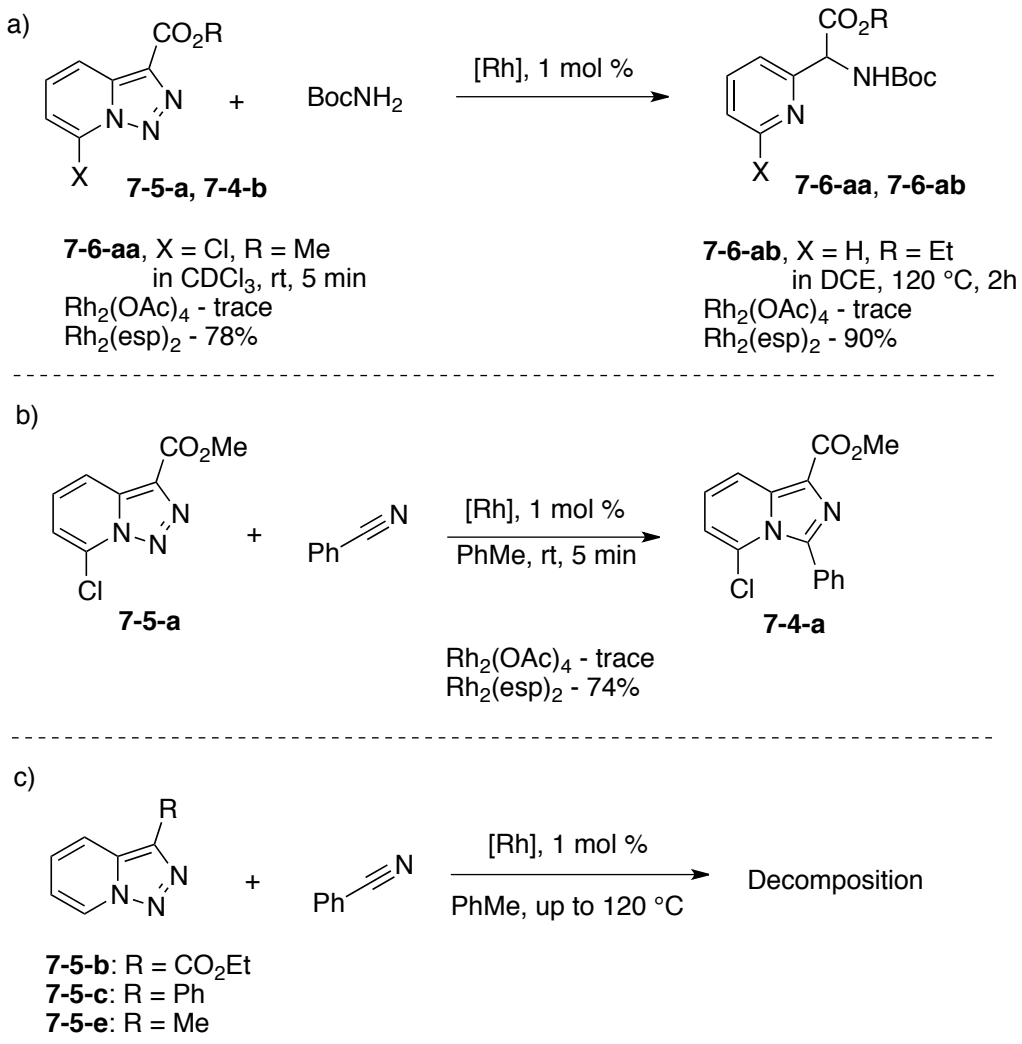
[a] The triazole **7-5** (0.20 mmol), amides **7-8** (1.5 equiv), and $Rh_2(esp)_2$ (1.0 mol%) were heated in 2 mL of anhydrous DCE at 120 °C until completion. Then $TsOH \cdot H_2O$ (1.0 equiv) and Ac_2O (0.2 mL) were added and the reaction mixture was heated at 120 °C.

[b] Isolated yield.

5.1.3. Reactivity comparison

To understand the superior efficiency of the newly developed reaction of pyridotriazoles with amines over the previously reported reaction with nitriles, we performed reactions of the pyridotriazoles **7-5-a**, **7-5-b** with $BocNH_2$ and PhCN in the presence of different rhodium catalysts (Scheme 7-4). Thus, it was found that $[Rh_2(esp)_2]$, indeed, is a superior catalyst over the previously used $Rh_2(OAc)_4$ for reactions of pyridotriazole, both with amides and nitriles (Scheme 7-4a, 7-4b). It was also verified that amides showed higher reactivity towards rhodium(II)/pyridocarbene (i.e. B, Scheme 7-4) over nitriles, since even $[Rh_2(esp)_2]$ catalyst was not efficient for transannulation of unactivated pyridotriazoles **29b**,**c**,**e** with nitriles (Scheme 7-4c). It is believed that the NH insertion reaction of pyridotriazoles, analogously to that of phenyldiazoacetates, proceeds by an ylide mechanism.[97] However, it requires higher temperatures to produce sufficient amounts of a reactive diazo form (i.e. B, Scheme 7-4). Overall, we believe that a superior

efficiency of the newly developed reaction of pyridotriazoles with amines and amides over the previously reported reaction with nitriles can be attributed to a combination of an increased potency of the rhodium catalyst and a higher reactivity of amines and amides over that of nitriles.



Scheme 7-4

5.1.4. Summary

This part is written based on the previously published article ("Rhodium-Catalyzed NH Insertion of Pyridyl Carbenes Derived from Pyridotriazoles: A General and Efficient Approach to 2-Picolylamines and Imidazo[1,5-a]pyridines." Shi, Y.; Gulevich, A. V.; Gevorgyan, V. *Angew. Chem., Int. Ed*. **2014**, *53*, 14191). This work was accomplished by myself and Dr. Gulevich under supervision of Professor Gevorgyan. The initial result employing 7-Cl-substituted triazole **7-5-a** was obtained by Dr. Gulevich; the further development was performed by myself.

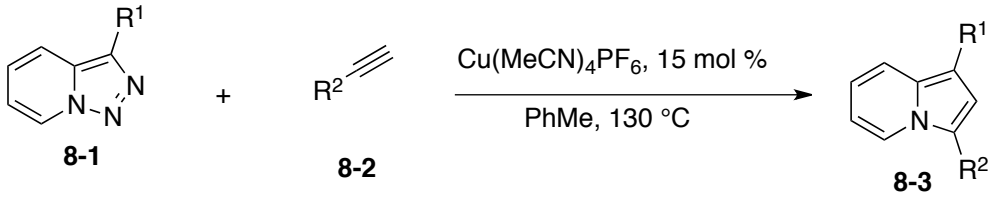
In conclusion, we have developed a general and efficient rhodium-catalyzed reaction of pyridotriazoles with amides and amines to produce valuable picolylamine derivatives. The subsequent cyclization provides expeditious access to various disubstituted imidazopyridines in a one-pot manner. The developed protocol allowed the synthesis of polysubstituted imidazopyridines, which were not accessible by previously reported transannulation reaction of pyridotriazoles with nitriles.

5.2. Cu-catalyzed transannulation reaction of pyridotriazoles: general access to fused polycyclic indolizines

Previously published as "Cu-Catalyzed Transannulation Reaction of Pyridotriazoles: General Access to Fused Polycyclic Indolizines," Shi, Y.; Gevorgyan, V. *Chem. Commun*. **2015**, *51*, 17166.

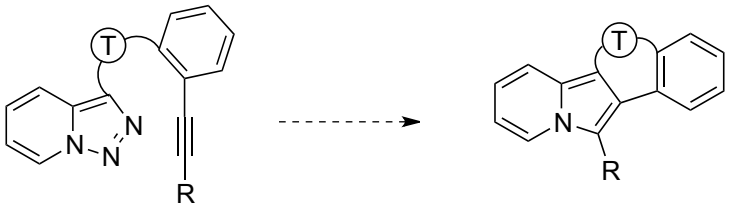
5.2.1. Development of the intramolecular transannulation reaction of pyridotriazoles

In part I, the intramolecular transannulaiton reaction of alkynyl tethered *N*-sulfonyl-1,2,3-triazoles was discussed. Meanwhile, the intermolecular reaction between pyridotriazoles and terminal alkynes, which provided efficient synthesis of indolizine derivatives, was also reported by our group.[24, 85-86] Despite a much broader reaction scope and employment of cheap copper catalyst in this newly developed method (Scheme 8-1), it was still limited to terminal alkynes, which precluded the possibility of an intramolecular transannulation reaction toward valuable polycyclic fused *N*-heterocycles.



Scheme 8-1

Aiming at the development of new methodology, which could offer rapid construction of polyheterocycles, we hypothesized that, by tethering an alkynyl motif to the pyridotriazole core (**8-4**), fused indolizine product **8-5** could be formed via intramolecular transannulation reaction (Scheme 8-2).[98]



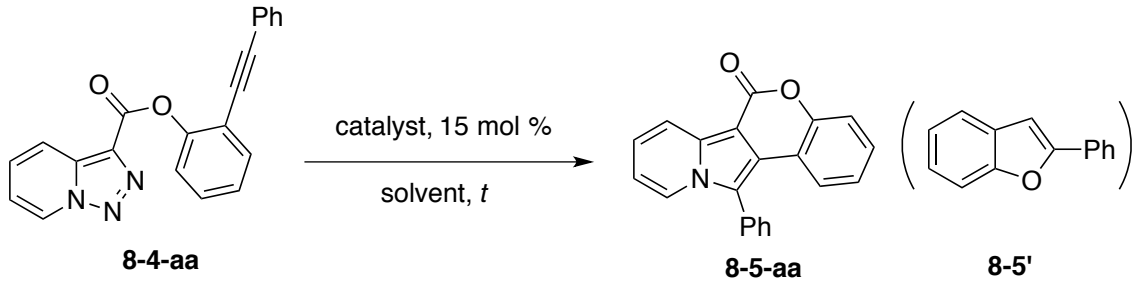
8-4 **8-5**

Scheme 8-2.

5.2.2. Optimization of the reaction conditions

To test this hypothesis, we synthesized an ester-tethered substrate **8-4-aa** and examined its reactivity under various conditions. It was found that this reaction could be accomplished in the presence of a Cu-catalyst (Table 8-1). The formation of the benzofuran byproduct **8-5'** via cleavage of the ester C-O bond was observed when employing cationic copper catalysts (Table 8-1, Entry 1-3). Fortunately, upon switching to electrophilic copper catalysts, the amount of **8-5'** was dramatically reduced (Entry 4-6). It was shown that the use of Cu(II) catalyst was less efficient compared to Cu(I) (entry 7). Further screening of solvent revealed that DCE was the best among all the solvent tested. Thus, pyridotriazole **23aa** was converted efficiently to the desired tetracyclic δ-valerolactone-fused indolizine product by employing 15 mol% of CuBr•SMe catalyst in dichloroethane under higher temperature (entry 6). Formation of the indolizine product was observed when using other Lewis acid catalyst, but with very low efficiency (entry 14). In the absence of any catalyst, no desired product was formed under thermal conditions.

Table 8-1. Optimization of Transannulation Reaction of **8-4-aa**



8-4-aa **8-5-aa** **8-5'**

Entry	Catalyst	Loading	Solvent	Temperature/°C	GC Yield/%[a]
1	$Cu(MeCN)_4PF_6$	15 mol %	DCE	140	48
2	$[Cu(OTf)]_2$ Bz	15 mol %	DCE	140	26
3	CuOAc	15 mol %	DCE	140	56
4	CuCl	15 mol %	DCE	140	73
5	CuBr	15 mol %	DCE	140	67
6	**CuBr•SMe_2**	**15 mol %**	**DCE**	**140**	**85**
7	$CuBr_2$	15 mol %	DCE	140	43
8	CuBr SMe_2	15 mol %	PhCl	140	75
9	CuBr SMe_2	15 mol %	$PhCF_3$	140	74
10	CuBr SMe_2	15 mol %	PhMe	140	63
11	CuBr SMe_2	15 mol %	DCE	130	81
12	CuBr SMe_2	15 mol %	DCE	150	86
13	CuBr SMe_2	10 mol %	DCE	140	78
14	$In(OTf)_3$	15 mol %	DCE	140	10
15	none	--	DCE	140	0

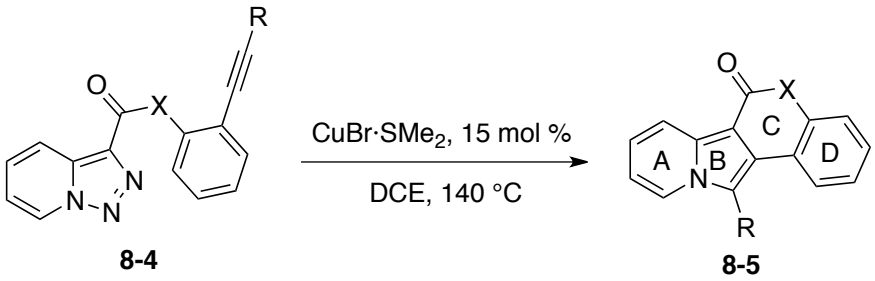
[a] (0.05 mmol) and catalyst (15 mol %) were dissolved in solvent (0.5 mL) and heated at the indicated temperature.

5.2.3. Reaction scope

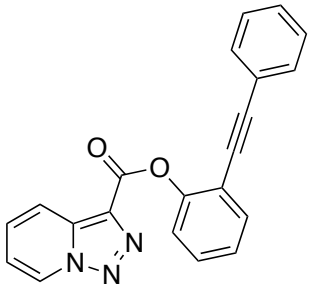
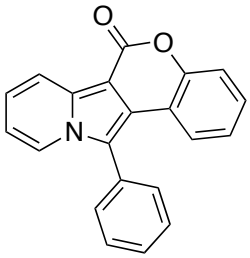
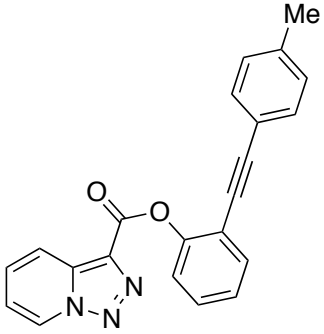
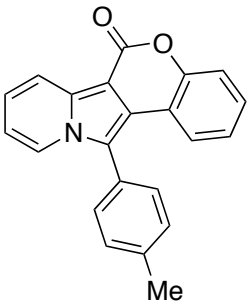
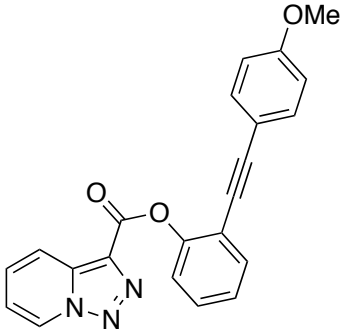
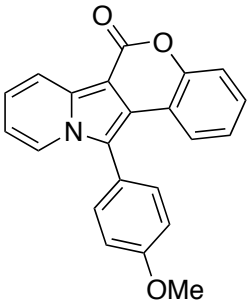
With the optimized condition in hand, we next tested the scope of this copper catalyzed transannulation reaction. It appeared to be quite general with respect to the arylalkyne moiety (Table 8-2, entries 1–10). Thus, a variety of tethered internal arylalkynes bearing electron-neutral, electron-withdrawing, and electron-donating substituents at the *ortho*-, *meta*- and *para*-positions participated well in this transannulation reaction toward fused indolizine **8-5**. It was also found that this reaction is not limited to aryl alkynes. Thus, alkenyl (**ak**), as well as alkyl (**al**) alkynes could also be utilized in this transformation to produce the corresponding indolizines. Moreover, an electron-deficient alkyne **8-4-am** was also found to be a competent substrate. Notably, the reaction of alkynyl pyridotriazole bearing a silyl substituent proceeded smoothly to afford 3-TBS-indolizine **8-5-an** in good yield, which upon desilylation offered access to the C3-nonsubstituted indolizine.

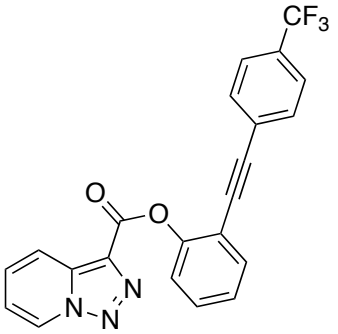
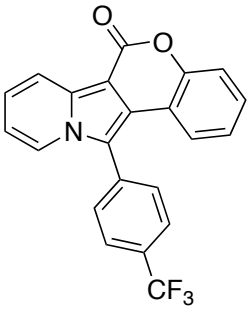
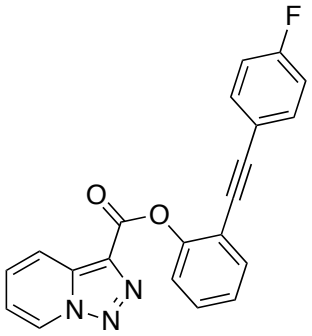
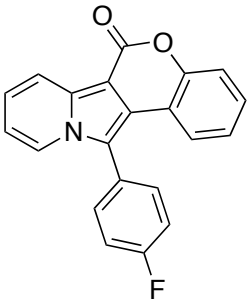
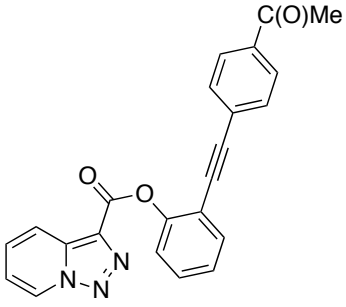
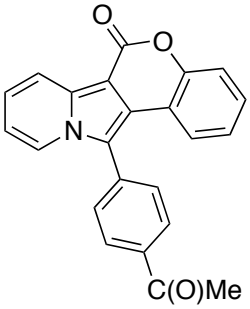
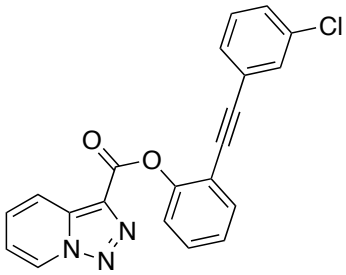
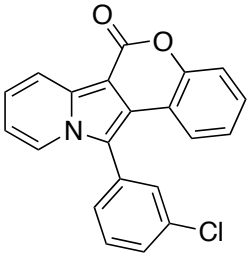
Next, the scope of rings A and D was examined (Table 8-2, entries 15–19). It was found that variuous substituents at the ring A (**8-4-ao**, **8-4-ap**) were tolerated under these reaction conditions, which for the first time, enabled synthesis of the C6-substituted indolizines in a selective manner.[99] Notably, the reaction proceeded smoothly to construct pentacyclic fused systems **8-5-aq** and **8-5-ar**. In addition, a tetracyclic indolizine with a non-aromatic ring D (**24as**) could also be produced in good yield. Moreover, pyridotriazole possessing an amide tether underwent transannulation reaction to afford the corresponding lactam-fused product **8-5-at**, albeit in a moderate yield.

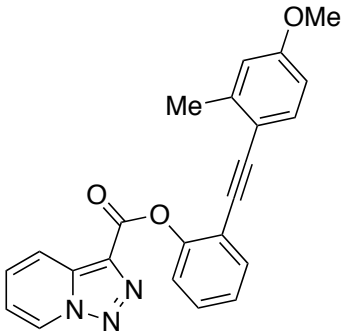
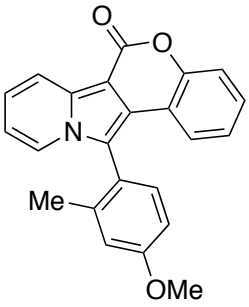
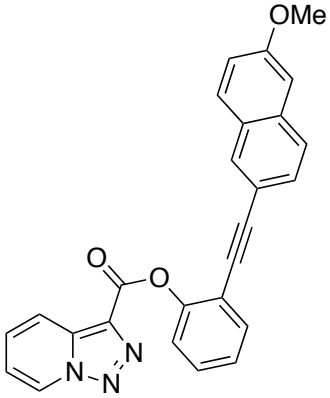
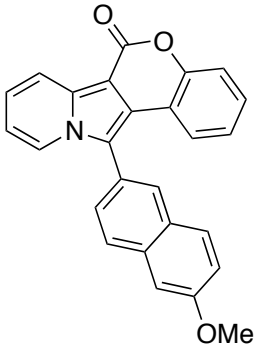
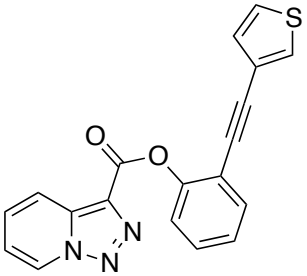
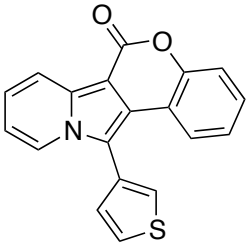
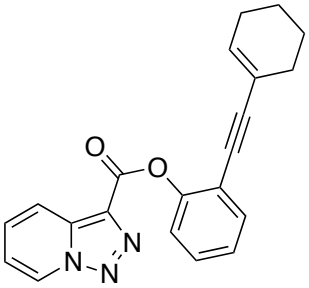
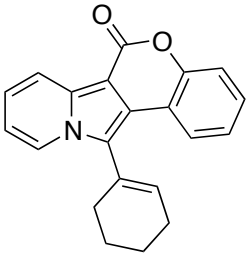
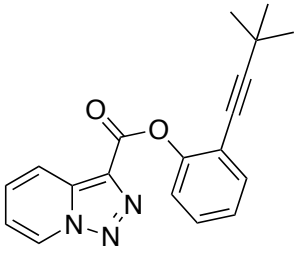
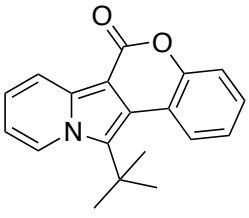
Table 8-2. Scope of copper catalyzed transannulation reaction of pyridotriazoles

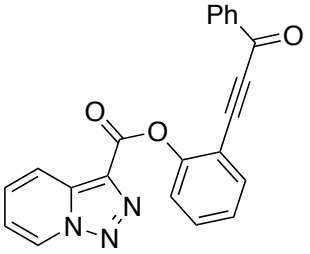
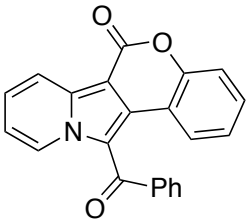
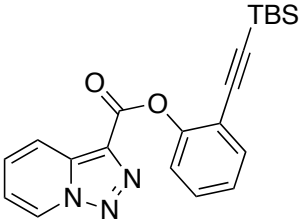
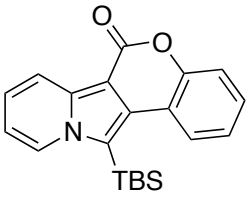
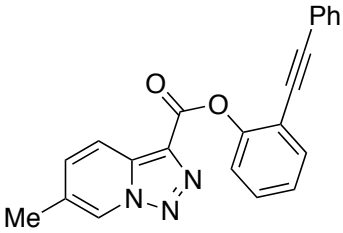
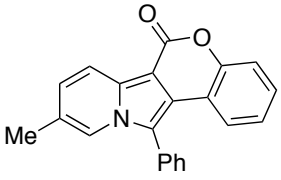
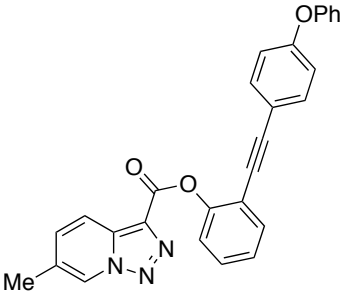
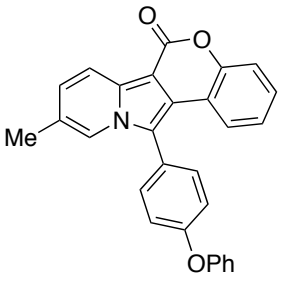
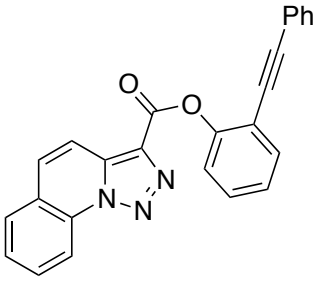
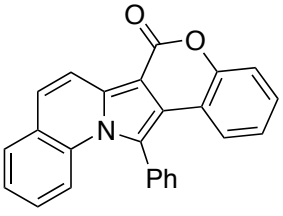


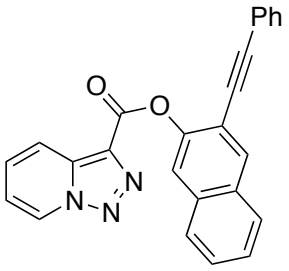
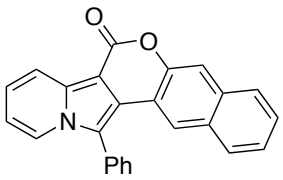
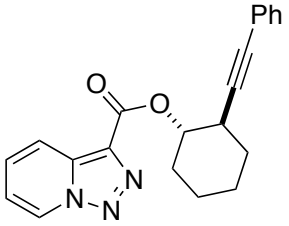
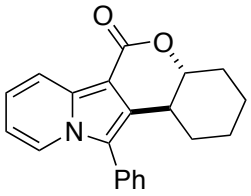
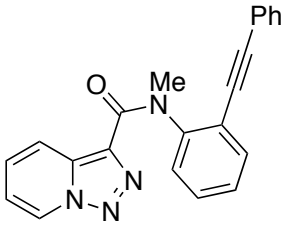
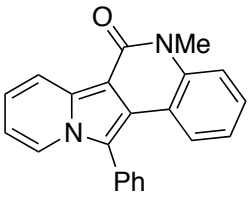
8-4 **8-5**

Entry	Substrate		Product		Yield/%[a,b]
1		**8-4-aa**		**8-5-aa**	83
2		**8-4-ab**		**8-5-ab**	75
3		**8-4-ac**		**8-5-ac**	85[c]

Entry	Substrate		Product		Yield/%[a,b]
4		**8-4-ad**		**8-5-ad**	80
5		**8-4-ae**		**8-5-ae**	73
6		**8-4-af**		**8-5-af**	78
7		**8-4-ag**		**8-5-ag**	58

Entry	Substrate		Product		Yield/%[a,b]
8		**8-4-ah**		**8-5-ah**	76
9		**8-4-ai**		**8-5-ai**	81
10		**8-4-aj**		**8-5-aj**	64
11		**8-4-ak**		**8-5-ak**	47
12		**8-4-al**		**8-5-al**	41

Entry	Substrate		Product		Yield/%[a,b]
13		**8-4-am**		**8-5-am**	50
14		**8-4-an**		**8-5-an**	67[c]
15		**8-4-ao**		**8-5-ao**	78
16		**8-4-ap**		**8-5-ap**	71
17		**8-4-aq**		**8-5-aq**	60[d]

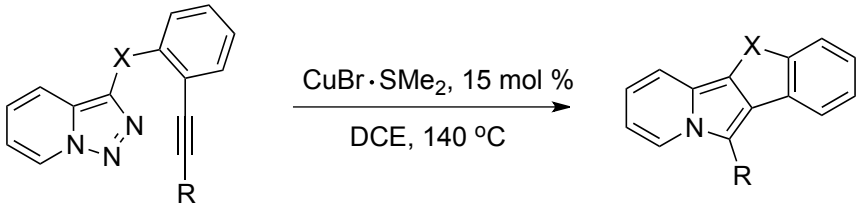
Entry	Substrate	Product	Yield/%[a,b]
18	 **8-4-ar**	 **8-5-ar**	68
19	 **8-4-as**	 **8-5-as**	60
20	 **8-4-at**	 **8-5-at**	52

[a]Pyridotriazole **8-4** (0.20 mmol) and CuBr•SMe_2 (15 mol%) were heated in 2 mL of dry DCE at 140 °C until completion (in general, 24 h for entries 1-20, 27; 2 h for entries 21-26, 28). [b]Isolated yields. [c]5 mol% $[Rh^*CpCl_2]_2$ in 2 mL of dry mesitylene at 140 °C. [d]Performed at 180 °C in PhCl.

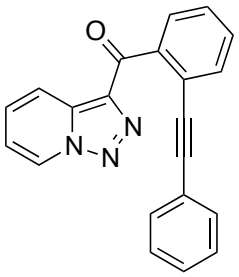
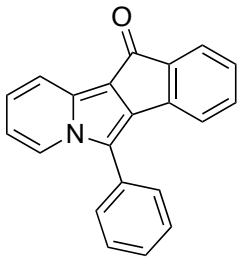
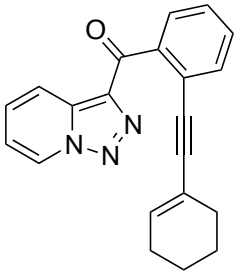
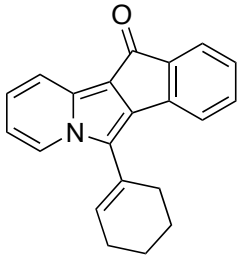
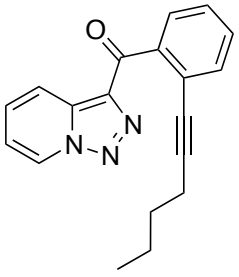
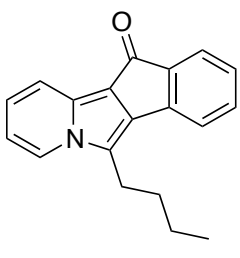
After developing the transannulation reaction to form a 6-membered C ring, we turned our attention to the construction of a 5-membered ring (Table 8-3). We were pleased to find that, aryl (**8-4-ba**), alkenyl (**8-4-bb**), alkyl (**8-4-bc**) and silyl (**8-4-bd**) groups at the alkyne moiety were all perfectly compatible under these reaction conditions to efficiently afford the corresponding indanone-fused indolizines. Surprisingly, terminal alkynes could also be utilized to produce **8-5-be**, although in a low yield. Remarkably, 1,3-strained C3,5-disubstituted fused indolizines **8-5-bf**, **8-5-bg**[100] were efficiently

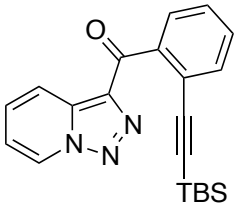
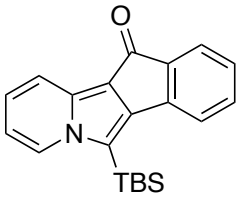
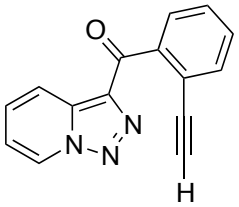
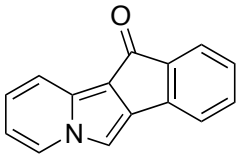
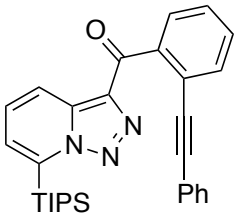
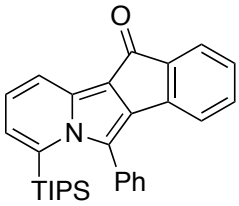
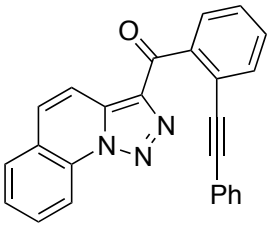
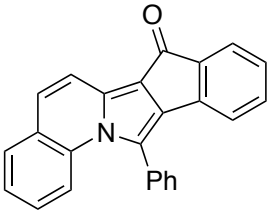
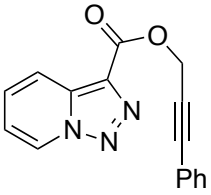
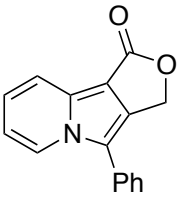
constructed by this method. In addition to the above mentioned indanone-fused indolizines, a tricyclic γ-butyrolactonefused indolizine **8-5-bh** could also be obtained albeit in diminished yield.

Table 8-3. Scope of copper catalyzed transannulation reaction of pyridotriazoles



8-4 **8-5**

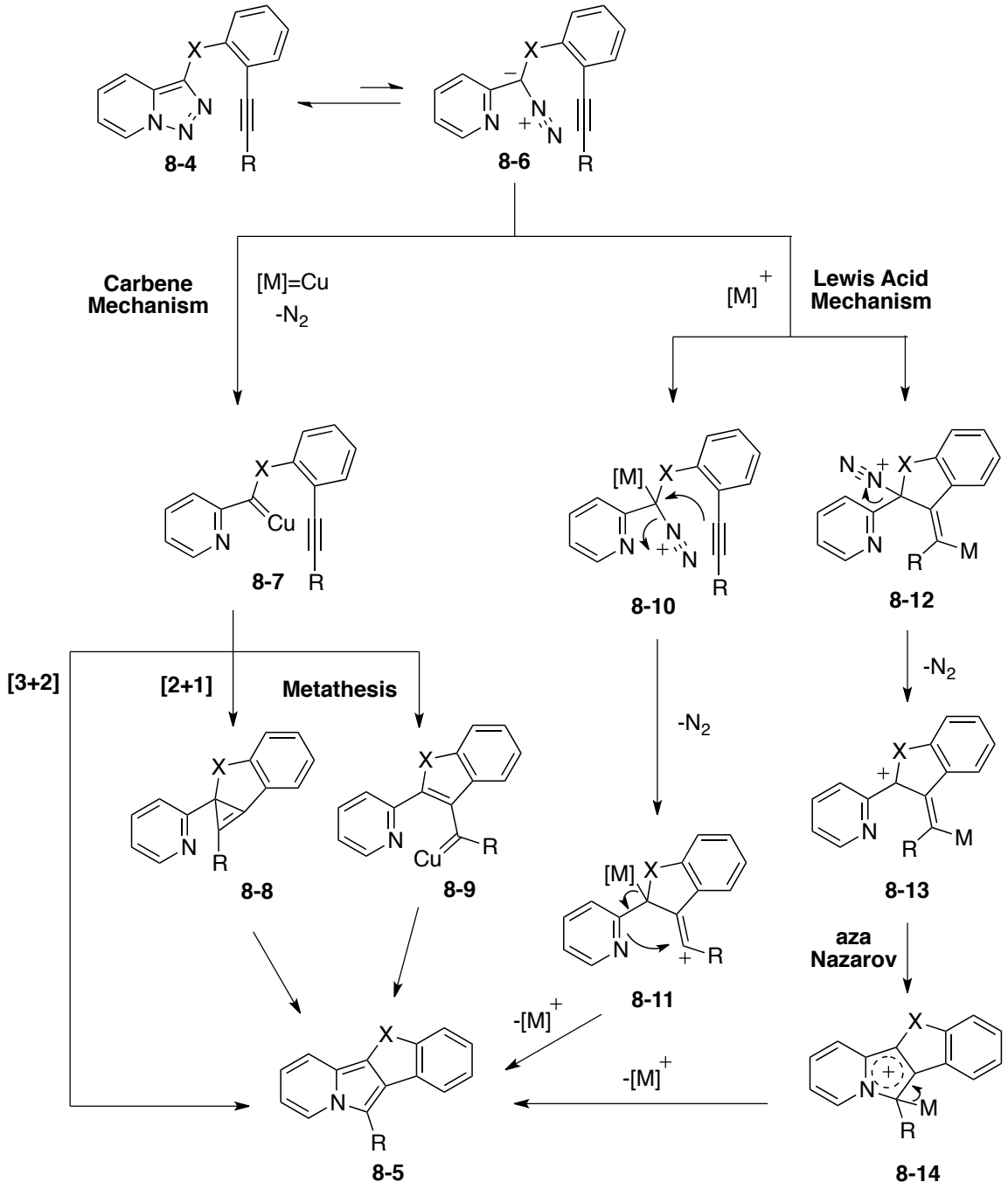
Entry	Substrate		Product		Yield/%[a,b]
1		**8-4-ba**		**8-5-ba**	91
2		**8-4-bb**		**8-5-bb**	87
3		**8-4-bc**		**8-5-bc**	73

Entry	Substrate		Product		Yield/%[a,b]
4		**8-4-bd**		**8-5-bd**	90
5		**8-4-be**		**8-5-be**	23
6		**8-4-bf**		**8-5-bf**	95
7		**8-4-bg**		**8-5-bg**	85
8		**8-4-bh**		**8-5-bh**	40(84[c])

[a] Pyridotriazole **8-4** (0.20 mmol) and CuBr•SMe_2 (15 mol%) were heated in 2 mL of dry DCE at 140 °C until completion (in general, 24 h for entries 1–20, 27; 2 h for entries 21–26, 28). [b]Isolated yields. [c]1.0 mol% $Rh_2(esp)_2$ in 2 mL of dry Toluene at 120 °C.

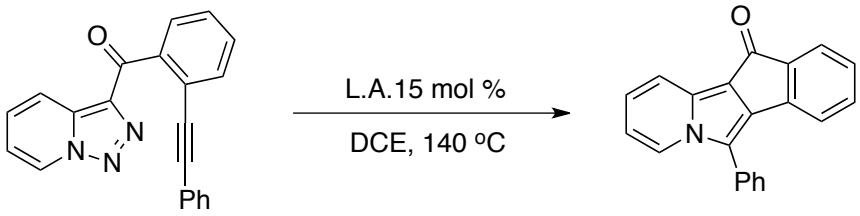
5.2.4. Mechanistic considerations

Naturally, after establishing the scope of this intramolecular transannulation reaction, we were eager to clarify the reaction pathway (Scheme 8-3). Apparently, pyridotriazole **8-4** exists in equilibrium with the diazo form **8-6**, which can react with the copper catalyst to generate a copper carbene intermediate **8-7**.[101] Next, a direct [3+2] cyclization would lead to the indolizine product **8-5**.[24] Alternatively, a [2+1] cycloaddition would produce a cyclopropene intermediate **8-8**, which would then isomerize into indolizine **8-5**.[85] Also, one cannot exclude the carbene–alkyne metathesis pathway involving a newly formed copper carbene intermediate **8-9**.[98] During optimization (Table 8-4), we unexpectedly found that Lewis acids, such as $In(OTf)_3$ or TIPSOTf, could also catalyze this transformation (Table 8-4, entry1 and 7, Scheme 8-4). Based on this observation, we envisioned an alternative Lewis acid activation pathway, according to which, the diazo form **8-6** can be metallated to produced intermediate **8-10**, which would then undergo a denitrogenative cyclization to form a cationic intermediate **8-11**. A subsequent cyclization and a metal loss of the latter would result in the formation of the fused indolizine product **8-5**. Also, the reaction could be triggered by a nucleophilic attack of the diazo carbon at the Lewis acid-activated triple bond to form intermediate **8-12**. The latter, upon exclusion of dinitrogen, aza-Nazarov cyclization, and a metal loss, would be converted into indolizine **8-5**.[102]


8-4
8-6
Carbene Mechanism
[M]=Cu
-N2
[M]+
Lewis Acid Mechanism
8-7
8-10
8-12
[3+2]
[2+1]
Metathesis
-N2
-N2
8-8
8-9
8-13
aza Nazarov
8-11
-[M]+
-[M]+
8-5
8-14

Scheme 8-3

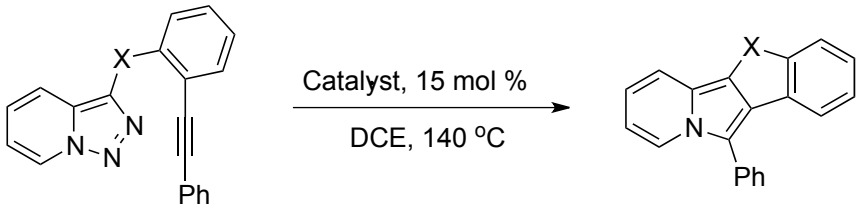
Table 8-4



8-4-ba **8-5-ba**

Entry	Catalyst/15 mol %	GC Yield/%[a]
1	**TIPSOTf**	**30**
2	$AlCl_3$	decompose
3	$HfCl_4$	decompose
4	$ZnCl_2$	<10, decompose
5	BF_3 Et_2O	decompose
6	$Eu(OTf)_3$	48
7	**$In(OTf)_3$**	**64**
8	$Sm(OTf)_3$	57
9	$La(OTf)_3$	39
10	$Y(OTf)_3$	<20
11	$Sc(OTf)_3$	decompose
12	$Yb(OTf)_3$	20
13	$Zn(OTf)_2$	<20

[a]Pyridotriazole **8-4** (0.20 mmol) and catalyst (15 mol%) were heated in 2 mL of dry DCE at 140 °C until completion.



8-4 **8-5**

Cat. $In(OTf)_3$: X = C(O), **8-5-ba**, 64%
X = C(O)O, **8-5-aa**, 10%

Cat. TIPSOTf: X = C(O), **8-5-ba**, 30%

Scheme 8-4

5.2.5. Summary

This part is written based on the previously published article ("Cu-Catalyzed Transannulation Reaction of Pyridotriazoles: General Access to Fused Polycyclic Indolizines," Shi, Y.; Gevorgyan, V. *Chem. Commun*. **2015**, *51*, 17166). This work was accomplished by myself under supervision of Professor Gevorgyan.

In summary, we developed an efficient copper-catalyzed intramolecular transannulation reaction of pyridotriazoles with internal alkynes. This first intramolecular transannulation reaction of pyridotriazoles provides expeditious and general access to various tri-, tetra-, and pentacyclic fused indolizines, including C6-substituted fused indolizines that cannot be synthesized selectively via known cycloaddition methods. For the first time it was shown that this reaction could also be triggered by Lewis acids.

6. EXPERIMENTAL SECTION

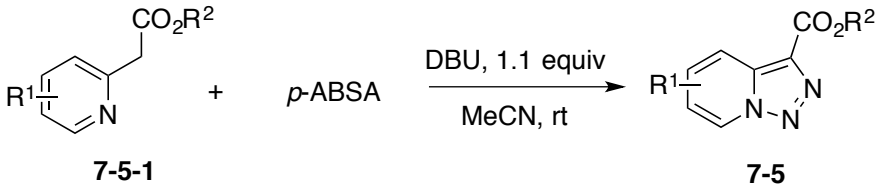
6.1. Rhodium-Catalyzed N-H Insertion of Pyridyl Carbenes Derived from Pyridotriazoles

6.1.1. General information

GC/MS analysis was performed on a Hewlett Packard Model 6890 GC interfaced to a Hewlett Packard Model 5973 mass selective detector (15 m x 0.25 mm capillary column, HP-5MS). NMR spectra were recorded on Bruker Avance DRX-500 (500 MHz) or DPX-400 (400 MHz) instrument. ^{1}H and ^{13}C NMR chemical shifts (δ) are reported in parts per million (ppm). LRMS and HRMS analyses were performed on Micromass 70 VSE mass spectrometer. Column chromatography was carried out employing Silicycle Silica-P flash silica gel (40-63 μm). Precoated silica gel plates F-254 were used for thin-layer analytical chromatography. All manipulations with transition metal catalysts were conducted in oven-dried glassware under inert atmosphere using a combination of glovebox and standard Schlenk techniques unless otherwise noted. Anhydrous dichloromethane, toluene, and THF (BHT-free) was purchased from Aldrich, degassed with argon, and dried by passage through activated alumina on an Innovative Technology PureSolv system. All starting materials were purchased from Strem Chemicals, Aldrich, Gelest Inc., TCI America, or Alfa Aesar, or synthesized via known literature procedures. All manipulations with transition metal catalysts were conducted in oven-dried glassware under inert atmosphere using a combination of glovebox and standard Schlenk techniques.

6.1.2. Preparation of Pyridoriazoles

General Procedure A

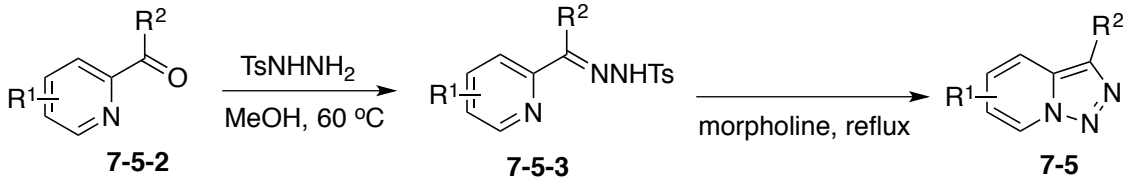


7-5-1 **7-5**

Scheme 9-1

Pyridotriazoles (**7-5-a**, **7-5-b**, **7-5-f** to **7-5-h**) were prepared via the diazotransfer reaction of 2-(pyridin-2-yl) acetate (**7-5-1**). To a stirred solution of 2-(pyridin-2-yl) acetate (1.0 equiv) and DBU (1.1 equiv) in dry acetonitrile, 4-acetamidobenzenesulfonyl azide (*p*-ABSA, 1.0 equiv) was added at room temperature in small portions over a 5 min period. The resulting yellow solution was stirred overnight. After removal of solvent, the residue was taken up into 150 mL of dichloromethane, washed with water and brine, and dried over sodium sulfate. Silica chromatography gave the product (**7-5**) as white or yellowish solid.

General Procedure B



7-5-2 **7-5-3** **7-5**

Scheme 9-2

Pyridotriazoles (**7-5-c** to **7-5-e**) were prepared from the 2-pyridylketone (**7-5-2**). A mixture of *p*-toluenesulfonylhydrazide (1.05 equiv) and methanol (1 mL/mmol) was heated at 60 °C until dissolve. To this solution, 2-pyridylketone was added (dissolve in

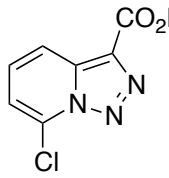
MeOH if it is solid). The reaction was heated at 60 °C until complete, then cooled in ice bath. The tosylhydrazone began to crystallize (sometimes the hydrazone may start crystallize during heating). The product (**7-5-3**) was collected by filtration and used directly in next step.

The hydrazone obtained from last step was dissolved in morpholine (1.8 mL/g) and heated at 90 °C. After 1-4 h, the excess morpholine was removed in vacuo. The resulting yellow solid was suspended in diethyl ether, and filtered to remove morpholine toluenesulphinate. The filtrate was concentrated in vacuo, and the resulting solid residue was purified using silica gel chromatography to provide pyridotriazole **7-5**.

Detailed procedure for preparation of individual substrate：

methyl 7-chloro-[1,2,3]triazolo[1,5-a]pyridine-3-carboxylate (7-5-a):

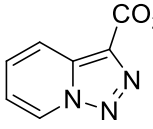
Compound **7-5-a** is known compound and was prepared follow literature.[24]



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1 H), 7.53 (t, *J*=7.89 Hz, 1 H), 7.22 (s, 1 H), 4.03 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.34, 136.64, 129.81, 128.40, 117.46, 116.37, 52.09.

Ethyl [1,2,3]triazolo[1,5-a]pyridine-3-carboxylate (7-5-b):

Compound **7-5-b** was prepared according to **General Procedure A.** 10 mmol scale, 91%yield.

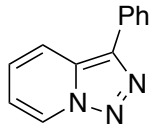


^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (dt, *J*=7.02, 0.88 Hz, 1 H), 8.25 (d, *J*=8.77 Hz, 1 H), 7.54 (ddd, *J*=8.77, 6.72, 0.88 Hz, 1 H), 7.15 (td, *J*=6.87, 1.17 Hz, 1 H), 4.50 (q, *J*=7.21 Hz, 2 H), 1.46 (t, *J*=7.16 Hz, 3 H). ^{13}C NMR (100

MHz, $CDCl_3$) δ 161.36, 135.05, 129.46, 129.08, 125.87, 119.32, 116.31, 61.07, 14.39. HRMS (ESI) calculated for $C_9H_{10}N_3O_2$ $[M+H]^+$: 192.0773, found: 192.0775.

3-phenyl-[1,2,3]triazolo[1,5-a]pyridine (7-5-c):

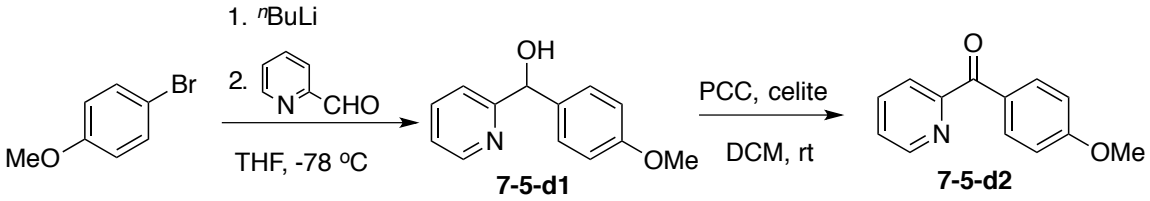
Compound **7-5-c** is known compound and was prepared follow literature.[83]



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, *J*=7.02 Hz, 1 H), 7.99 – 7.94 (m, 3 H), 7.50 (t, *J*=7.45 Hz, 2 H), 7.39 – 7.36 (m, 1 H), 7.30 – 7.26 (m, 1 H), 6.98 (t, *J*=6.72 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 137.84, 131.36, 130.34, 128.92, 127.79, 126.54, 125.53, 125.49, 118.29, 115.21.

3-(4-methoxyphenyl)-[1,2,3]triazolo[1,5-a]pyridine (7-5-d):

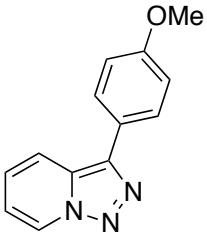


Scheme 9-3

A solution of 1-bromo-4-methoxybenzene (5 mmol) in THF (8 mL) was treated with *n*-BuLi (1.4 equiv, 1.6 M solution in hexane) at -78°C dropwise. After stirring at the same temperature for 1 h, 2-pyridinecarboxaldehyde (1.4 equiv) was added and the temperature was kept stable for more 80 min before warming to room temperature. The solution was then stirred overnight and quenched by addition of water. The mixture was then extracted with ethyl acetate, dried over Na_2SO_4. After removal of solvent, the crude alcohol **7-5-d1** was purified using flash silica gel chromatography.

Pyridinium chlorochromate (3.7 mmol) was dissolved in CH_2Cl_2 (600 mL), and 0.6 g of Celite was added with stirring. The alcohol (**7-5-d1**, ~3.5 mmol) was then added and the slurry was stirred at room temperature for 20 min. Upon completion, the solution was concentrated, and crude ketone product (**7-5-d2**) was purified by flash chromatography.

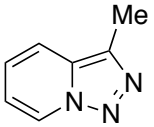
Compound **7-5-d** was prepared according to **General Procedure B.** 37% yield over 4 steps.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.73 (d, *J*=6.97 Hz, 1 H), 7.95 (d, *J*=9.17 Hz, 1 H), 7.88 (d, *J*=8.80 Hz, 2 H), 7.27 (dd, *J*=8.99, 6.79 Hz, 1 H), 7.05 (d, *J*=8.80 Hz, 2 H), 6.99 (t, *J*=6.60 Hz, 1 H), 3.87 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.32, 137.89, 129.99, 127.90, 125.46, 125.14, 123.95, 118.39, 115.21, 114.07, 55.32. HRMS (ESI) calculated for $C_{13}H_{12}N_3O$ $[M+H]^+$: 226.0980, found: 226.0979.

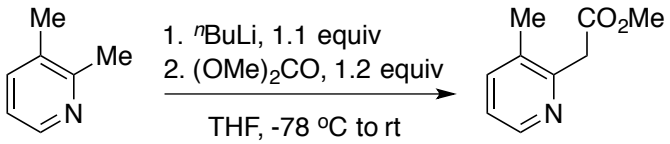
3-methyl-[1,2,3]triazolo[1,5-a]pyridine (7-5-e):

Compound **7-5-e** is known and was prepared follow literature.[83]



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, *J*=7.31 Hz, 1 H), 7.57 (d, *J*=9.06 Hz, 1 H), 7.13 (dd, *J*=8.77, 6.72 Hz, 1 H), 6.89 (t, *J*=6.87 Hz, 1 H), 2.58 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.22, 131.48, 124.94, 123.54, 117.38, 114.83, 10.23.

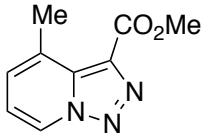
methyl 4-methyl-[1,2,3]triazolo[1,5-a]pyridine-3-carboxylate (7-5-f):



7-5-f1

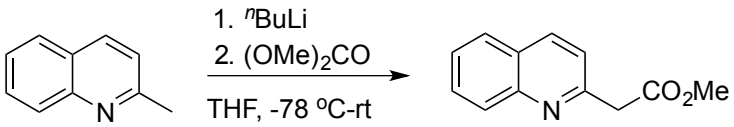
Scheme 9-4

Under Ar protection, a solution of 2,3-lutidie (5.0 mmol) in THF (20 mL) was cooled to -78 ^{o}C. To this solution was added ^{n}BuLi (1.6 M solution in THF, 3.4 mL). After stirring for 1 h, $CO(OMe)_2$ (6 mmol) was added via syringe. The resulting mixture was allowed to react for 3 h at this temperature and then warm to rt. When complete, the reaction was quenched with saturated ammonium chloride solution. Then the mixture was extracted with ethyl acetate, dried over Na_2SO_4, After removal of solvent, the crude pyridinyl acetate (7-5-f1) was purified using flash silica gel chromatography. 64% yield. Compound **7-5-f** was prepared according to **General Procedure A.** 55% yield over 2 steps.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (d, *J*=6.97 Hz, 1 H), 7.25 (d, *J*=7.70 Hz, 1 H), 7.03 (t, *J*=6.79 Hz, 1 H), 4.02 (s, 3 H), 2.87 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.9, 135.03, 130.73, 130.11, 129.23, 123.71, 116.39, 52.20, 21.07. HRMS (ESI) calculated for $C_9H_{10}N_3O_2$ $[M+H]^+$: 192.0773, found: 192.0777.

methyl [1,2,3]triazolo[1,5-a]quinoline-3-carboxylate (7-5-g):

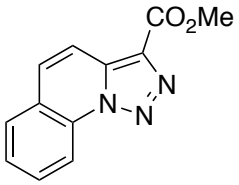


7-5-g1

Scheme 9-5

Under Ar protection, a solution of 2-methylquinoline (5.0 mmol) in THF (20 mL) was cooled to -78 °C. To this solution was added ^{n}BuLi (1.6 M solution in THF, 3.4 mL). After stirring for 1 h, $CO(OMe)_2$ (6 mmol) was added via syringe. The resulting mixture was allowed to react for 3 h at this temperature and then warm to room temperature. When reaction is complete, saturated ammonium chloride was added. The mixture was extracted with ethyl acetate, dried over Na_2SO_4, and the solvent was removed in vacuo. The crude quinolinyl acetate **7-5-g1** was purified using flash silica gel chromatography. 43% yield.

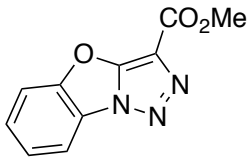
Compound **7-5-g** was prepared according to **General Procedure A.** 38% yield over 2 steps.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.84 (d, *J*=8.44 Hz, 1 H), 8.09 (d, *J*=9.17 Hz, 1 H), 7.92 (d, *J*=8.07 Hz, 1 H), 7.85 – 7.78 (m, 2 H), 7.69 – 7.66 (m, 1 H), 4.07 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.98, 133.67, 131.57, 131.08, 130.92, 130.42, 128.72, 127.80, 124.01, 116.55, 115.41, 52.16. HRMS (ESI) calculated for $C_{12}H_{10}N_3O_2$ $[M+H]^+$: 228.0773, found: 228.0772.

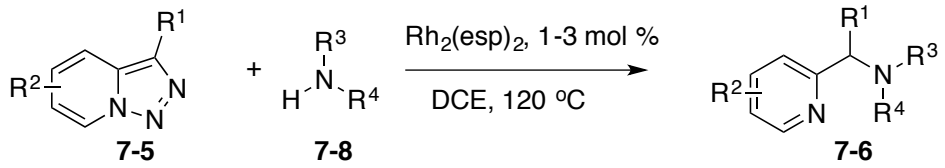
methyl benzo[4,5]oxazolo[3,2-c][1,2,3]triazole-3-carboxylate (7-5-h):

Compound **7-5-h** was prepared follow literature.[77]



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J*=7.70 Hz, 1 H), 7.51 (d, *J*=7.70 Hz, 1 H), 7.32 – 7.25 (m, 2 H), 3.95 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.80, 153.93, 150.54, 141.71, 124.65, 124.17, 119.00, 110.25, 52.87. HRMS (ESI) calculated for $C_{10}H_7N_3NaO_3$ $[M+Na]^+$: 240.0385, found: 240.0386.

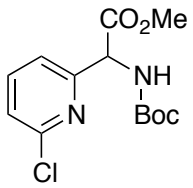
6.1.3. Rh(II) Catalyzed N-H Insertions



Scheme 9-6

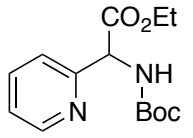
General Procedure: An oven-dried 3.0 mL V-vial equipped with a stirring bar was charged with $Rh_2(esp)_2$ (1-3 mol %), pyridotriazole **7-5** (0.2 mmol), amine or amide **7-8** and DCE (2 mL) under N_2 atmosphere. The reaction vessel was capped with Mininert syringe valve and the reaction mixture was stirred at 120 °C. Upon completion the reaction mixture was cooled to room temperature, concentrated under reduced pressure, and the crude product was purified by column chromatography to afford the corresponding N-H insertion products **7-6**.

methyl 2-((tert-butoxycarbonyl)amino)-2-(6-chloropyridin-2-yl)acetate (7-6-aa): 74%. 1 mol% $Rh_2(esp)_2$ was used.



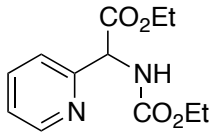
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (t, *J*=7.70 Hz, 1 H), 7.39 (d, *J*=7.70 Hz, 1 H), 7.28 (d, *J*=7.70 Hz, 1 H), 6.11 (d, *J*=6.97 Hz, 1 H), 5.42 (d, *J*=7.70 Hz, 1 H), 3.74 (s, 3 H), 1.45 (s, 9 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.97, 155.44, 155.17, 151.17, 139.50, 124.04, 121.56, 80.32, 58.23, 52.91, 28.28. HRMS (ESI) calculated for $C_{13}H_{18}ClN_2O_4$ $[M+H]^+$: 301.0955, found: 301.0957.

ethyl 2-((tert-butoxycarbonyl)amino)-2-(pyridin-2-yl)acetate (7-6-ab): 90%. 1 mol% $Rh_2(esp)_2$ was used.



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, *J*=4.09 Hz, 1 H), 7.69 (td, *J*=7.67, 1.32 Hz, 1 H), 7.46 (d, *J*=7.89 Hz, 1 H), 7.25 – 7.22 (m, 1 H), 6.27 (d, *J*=7.31 Hz, 1 H), 5.40 (d, *J*=7.60 Hz, 1 H), 4.17 (q, *J*=7.21 Hz, 2 H), 1.43 (s, 9 H), 1.19 (t, *J*=7.16 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.06, 155.25, 54.47, 149.06, 137.09, 123.22, 123.04, 109.50, 79.93, 61.73, 58.58, 28.24, 13.96. HRMS (ESI) calculated for $C_{14}H_{21}N_2O_4$ $[M+H]^+$: 281.1501, found: 281.1495.

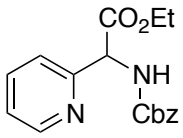
ethyl 2-((ethoxycarbonyl)amino)-2-(pyridin-2-yl)acetate (7-6-ac): 91%. 1 mol% $Rh_2(esp)_2$ was used.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (d, *J*=4.03 Hz, 1 H), 7.73 – 7.69 (m, 1 H), 7.48 (d, *J*=7.70 Hz, 1 H), 7.25 – 7.25 (m, 1 H), 6.41 (br, 1 H), 5.46 (d, *J*=7.34 Hz, 1 H), 4.21 – 4.12 (m, 4 H), 1.26 – 1.19 (m, 6 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.95, 156.04, 154.39, 149.32, 136.95, 123.25,

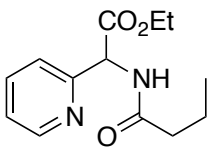
122.99, 61.82, 61.19, 58.79, 14.49, 13.98. HRMS (ESI) calculated for $C_{12}H_{17}N_2O_4$ $[M+H]^+$: 253.1188, found: 253.1181.

ethyl 2-(((benzyloxy)carbonyl)amino)-2-(pyridin-2-yl)acetate (7-6-ad): 65%. 1 mol% $Rh_2(esp)_2$ was used.



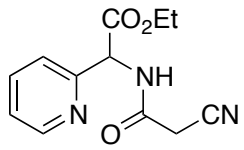
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (d, *J*=4.09 Hz, 1 H), 7.77 – 7.73 (m, 1 H), 7.51 (d, *J*=7.89 Hz, 1 H), 7.36 – 7.29 (m, 6 H), 6.62 (d, *J*=7.02 Hz, 1 H), 5.51 (d, *J*=7.60 Hz, 1 H), 5.14 (s, 1 H), 5.13 (s, 1 H), 4.25 – 4.15 (m, 2 H), 1.21 (t, *J*=7.16 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.55, 155.80, 154.00, 148.76, 137.56, 136.23, 128.45, 128.08, 128.02, 123.49, 123.32, 67.04, 62.02, 58.70, 13.98. HRMS (ESI) calculated for $C_{17}H_{19}N_2O_4$ $[M+H]^+$: 315.1345, found: 315.1335.

ethyl 2-butyramido-2-(pyridin-2-yl)acetate (7-6-ae): 85%. 1 mol% $Rh_2(esp)_2$ was used.



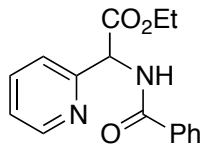
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (d, *J*=4.40 Hz, 1 H), 7.70 (t, *J*=7.70 Hz, 1 H), 7.49 (d, *J*=7.70 Hz, 1 H), 7.29 – 7.23 (m, 2 H), 5.64 (d, *J*=6.97 Hz, 1 H), 4.19 – 4.13 (m, 2 H), 2.29 – 2.26 (m, 2 H), 1.70 – 1.66 (m, 2 H), 1.19 (t, *J*=7.15 Hz, 3 H), 0.93 (t, *J*=7.34 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.71, 169.72, 154.03, 149.12, 137.05, 123.24, 61.76, 57.15, 38.13, 18.89, 13.92, 13.61. HRMS (ESI) calculated for $C_{13}H_{19}N_2O_3$ $[M+H]^+$: 251.1396, found: 251.1391.

ethyl 2-(2-cyanoacetamido)-2-(pyridin-2-yl)acetate (7-6-af): 87%. 1 mol% $Rh_2(esp)_2$ was used.



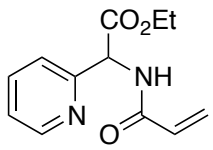
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J*=4.68 Hz, 1 H), 8.09 (d, *J*=6.14 Hz, 1 H), 7.74 (td, *J*=7.67, 1.61 Hz, 1 H), 7.51 (d, *J*=7.60 Hz, 1 H), 7.30 – 7.27 (m, 1 H), 5.61 (d, *J*=7.02 Hz, 1 H), 4.21 – 4.14 (m, 2 H), 3.52 (s, 2 H), 1.20 (t, *J*=7.16 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.74, 161.14, 152.54, 149.11, 137.43, 123.73, 123.26, 114.10, 62.24, 57.58, 25.77, 13.92. HRMS (ESI) calculated for $C_{12}H_{14}N_3O_3$ $[M+H]^+$: 248.1035, found: 248.1033.

ethyl 2-benzamido-2-(pyridin-2-yl)acetate (7-6-ag): 76%. 1 mol% $Rh_2(esp)_2$ was used.



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, *J*=4.09 Hz, 1 H), 8.13 – 8.11 (br, 1 H), 7.92 – 7.90 (m, 2 H), 7.77 (td, *J*=7.67, 1.61 Hz, 1 H), 7.61 (d, *J*=7.60 Hz, 1 H), 7.53 – 7.43 (m, 3 H), 7.32 – 7.29 (m, 1 H), 5.87 (d, *J*=7.02 Hz, 1 H), 4.26 – 4.19 (m, 2 H), 1.24 (t, *J*=7.02 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.55, 166.87, 153.84, 148.80, 137.60, 133.60, 131.77, 128.51, 127.27, 123.58, 123.54, 62.05, 57.48, 14.02. HRMS (ESI) calculated for $C_{16}H_{17}N_2O_3$ $[M+H]^+$: 285.1239, found: 285.1231.

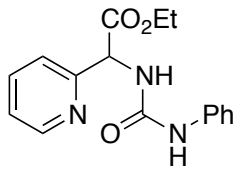
ethyl 2-acrylamido-2-(pyridin-2-yl)acetate (7-6-ah): 85%. 1 mol% $Rh_2(esp)_2$ was used.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, *J*=4.77 Hz, 1 H), 7.70 (td, *J*=7.70, 1.47 Hz, 1 H), 7.51 (d, *J*=8.07 Hz, 1 H), 7.44 – 7.43 (br, 1 H), 7.26 – 7.24 (m, 1 H), 6.34 – 6.22 (m, 2 H), 5.73 (d, *J*=6.97 Hz, 1 H), 5.67 (dd, *J*=9.90, 1.83 Hz, 1 H), 4.21 – 4.15 (m, 2 H), 1.20 (t, *J*=6.97 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.48, 164.99, 154.01, 149.11, 137.17, 130.30, 127.08, 123.36,

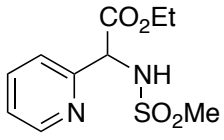
123.33, 61.91, 57.31, 13.95. HRMS (ESI) calculated for $C_{12}H_{15}N_2O_3$ $[M+H]^+$: 235.1083, found: 235.1082.

ethyl 2-(3-phenylureido)-2-(pyridin-2-yl)acetate (7-6-ai): 75%. 3 mol% $Rh_2(esp)_2$ was used.



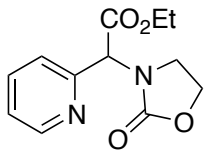
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, *J*=4.38 Hz, 1 H), 7.79 (s, 1 H), 7.71 (td, *J*=7.75, 1.75 Hz, 1 H), 7.57 (d, *J*=7.89 Hz, 1 H), 7.32 (d, *J*=7.60 Hz, 2 H), 7.24 – 7.17 (m, 4 H), 7.01 – 6.97 (m, 1 H), 5.78 (d, *J*=7.31 Hz, 1 H), 4.19 – 4.10 (m, 2 H), 1.17 (t, *J*=7.16 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.75, 155.23, 155.11, 148.83, 138.86, 137.55, 128.92, 123.73, 123.36, 123.01, 119.92, 62.01, 58.27, 13.92. HRMS (ESI) calculated for $C_{16}H_{18}N_3O_3$ $[M+H]^+$: 300.1348, found: 300.1345.

ethyl 2-(methylsulfonamido)-2-(pyridin-2-yl)acetate (7-6-aj): 68%. 3 mol% $Rh_2(esp)_2$ was used.



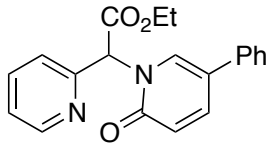
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (d, *J*=4.40 Hz, 1 H), 7.75 (td, *J*=7.70, 1.47 Hz, 1 H), 7.48 (d, *J*=8.07 Hz, 1 H), 7.30 (dd, *J*=6.97, 5.14 Hz, 1 H), 6.25 (d, *J*=7.70 Hz, 1 H), 5.36 (d, *J*=8.07 Hz, 1 H), 4.24 – 4.18 (m, 2 H), 2.95 (s, 3 H), 1.22 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.36, 153.67, 149.32, 137.46, 123.74, 123.14, 62.40, 60.26, 42.10, 13.98. HRMS (ESI) calculated for $C_{10}H_{15}N_2O_4S$ $[M+H]^+$: 259.0753, found: 259.0750.

ethyl 2-(2-oxooxazolidin-3-yl)-2-(pyridin-2-yl)acetate (7-6-ak): 66%. 3 mol% $Rh_2(esp)_2$ was used.



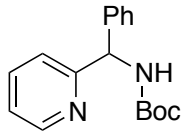
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (d, *J*=4.40 Hz, 1 H), 7.74 (td, *J*=7.70, 1.83 Hz, 1 H), 7.39 (d, *J*=8.07 Hz, 1 H), 7.29 (dd, *J*=6.79, 4.95 Hz, 1 H), 5.80 (s, 1 H), 4.42 – 4.38 (m, 1 H), 4.26 – 4.23 (m, 2 H), 4.12 (td, *J*=8.80, 6.97 Hz, 1 H), 3.33 (td, *J*=8.80, 6.97 Hz, 1 H), 1.22 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.86, 158.40, 154.07, 149.40, 137.37, 124.20, 123.46, 62.78, 61.65, 61.95, 42.13, 14.01. HRMS (ESI) calculated for $C_{12}H_{15}N_2O_4$ $[M+H]^+$: 251.1032, found: 251.1026.

ethyl 2-(2-oxo-5-phenylpyridin-1(2H)-yl)-2-(pyridin-2-yl)acetate (7-6-al): 75%. 3 mol% $Rh_2(esp)_2$ was used.



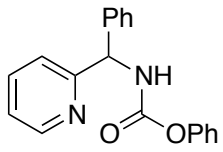
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (d, *J*=4.77 Hz, 1 H), 7.98 (d, *J*=6.97 Hz, 2 H), 7.83 (d, *J*=9.17 Hz, 1 H), 7.78 (td, *J*=7.61, 1.65 Hz, 1 H), 7.66 (d, *J*=7.70 Hz, 1 H), 7.50 – 7.44 (m, 3 H), 7.32 (dd, *J*=6.97, 5.50 Hz, 1 H), 7.26 (d, *J*=9.17 Hz, 1 H), 6.73 (s, 1 H), 4.26 (q, *J*=6.97 Hz, 2 H), 1.22 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.35, 162.80, 156.14, 154.23, 149.79, 137.05, 135.99, 129.52, 128.87, 127.67, 126.67, 123.86, 123.24, 117.90, 77.50, 61.81, 13.99. HRMS (ESI) calculated for $C_{19}H_{18}N_3O_3$ $[M+H]^+$: 336.1348, found: 336.1343.

tert-butyl (phenyl(pyridin-2-yl)methyl)carbamate (7-6-am): 89%. 1 mol% $Rh_2(esp)_2$ was used.



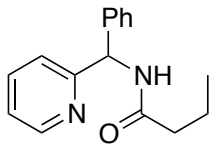
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (d, *J*=4.68 Hz, 1 H), 7.61 (t, *J*=7.60 Hz, 1 H), 7.35 – 7.16 (m, 7 H), 6.53 (br, 1 H), 5.87 (d, *J*=6.72 Hz, 1 H), 1.43 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.28, 155.19, 148.83, 142.29, 136.78, 128.56, 127.33, 127.10, 122.41, 122.25, 79.43, 58.86, 28.35. HRMS (ESI) calculated for $C_{17}H_{21}N_2O_2$ $[M+H]^+$: 285.1603, found: 285.1593.

phenyl (phenyl(pyridin-2-yl)methyl)carbamate (7-6-an): 75%. 1 mol% $Rh_2(esp)_2$ was used.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (d, *J*=4.03 Hz, 1 H), 7.65 (td, *J*=7.61, 1.65 Hz, 1 H), 7.41-7.39 (m, 2 H), 7.34 – 7.31 (m, 4 H), 7.28-7.13 (m, 7 H), 5.97 (d, *J*=6.97 Hz, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.38, 153.93, 151.08, 148.80, 141.68, 136.93, 129.14, 128.68, 127.67, 127.37, 125.12, 122.53, 122.53, 121.58, 59.15. HRMS (ESI) calculated for $C_{19}H_{17}N_2O_2$ $[M+H]^+$: 305.1290, found: 305.1283.

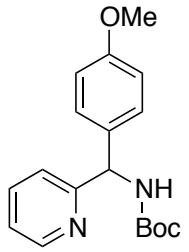
N-(phenyl(pyridin-2-yl)methyl)butyramide (7-6-ao): 81%. 1 mol% $Rh_2(esp)_2$ was used.



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, *J*=4.09 Hz, 1 H), 7.64 – 7.58 (m, 2 H), 7.33 – 7.19 (m, 7 H), 6.17 (d, *J*=7.31 Hz, 1 H), 2.27 (t, *J*=9.50 Hz, 2 H), 1.73 – 1.64 (m, 2 H), 0.93 (t, *J*=7.45 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.11, 158.85, 148.81, 142.07, 136.87, 128.55, 127.33,

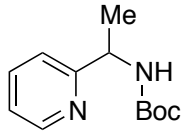
127.24, 122.79, 122.39, 57.13, 38.64, 19.05, 13.73. HRMS (ESI) calculated for $C_{16}H_{19}N_2O$ $[M+H]^+$: 255.1497, found: 255.1493.

tert-butyl ((4-methoxyphenyl)(pyridin-2-yl)methyl)carbamate (7-6-ap): 77%. 1 mol% $Rh_2(esp)_2$ was used.



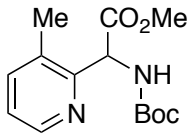
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (d, *J*=4.40 Hz, 1 H), 7.61 (t, *J*=7.34 Hz, 1 H), 7.26 – 7.15 (m, 4 H), 6.82 (d, *J*=8.44 Hz, 2 H), 6.49 (d, *J*=6.24 Hz, 1 H), 5.81 (d, *J*=6.97 Hz, 1 H), 3.76 (s, 3 H), 1.43 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.58, 158.73, 155.16, 14.84, 136.67, 134.59, 128.29, 122.26, 122.13, 113.90, 58.24, 55.14, 28.34, 28.16. HRMS (ESI) calculated for $C_{18}H_{23}N_2O_3$ $[M+H]^+$: 315.1709, found: 315.1702.

tert-butyl (1-(pyridin-2-yl)ethyl)carbamate (7-6-aq) 88%. 1 mol% $Rh_2(esp)_2$ was used.



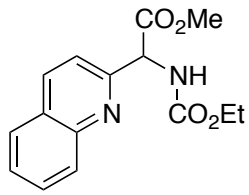
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 – 8.52 (m, 1 H), 7.64 (td, *J*=7.67, 1.90 Hz, 1 H), 7.24 (d, *J*=7.89 Hz, 1 H), 7.17 (ddd, *J*=7.45, 4.97, 1.02 Hz, 1 H), 5.73 (br, 1 H), 4.86 – 4.82 (m, 1 H), 1.46 – 1.42 (m, 12 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.65, 155.24, 148.90, 136.87, 122.17, 121.19, 79.22, 51.06, 28.39, 22.71. HRMS (ESI) calculated for $C_{12}H_{19}N_2O_2$ $[M+H]^+$: 223.1447, found: 223.1440.

methyl 2-((tert-butoxycarbonyl)amino)-2-(3-methylpyridin-2-yl)acetate (7-6-ar): 66%. 1 mol% $Rh_2(esp)_2$ was used.



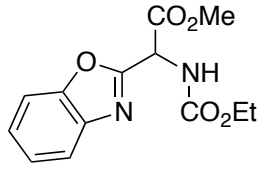
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39 (d, *J*=4.40 Hz, 1 H), 7.51 (d, *J*=7.34 Hz, 5 H), 7.15 (dd, *J*=7.70, 4.77 Hz, 1 H), 6.18 (d, *J*=8.07 Hz, 1 H), 5.66 (d, *J*=8.44 Hz, 1 H), 3.70 (s, 3 H), 2.50 (s, 3 H), 1.45 (s, 9 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.91, 155.49, 153.32, 146.84, 138.68, 123.20, 79.96, 55.09, 52.56, 28.30, 18.48. HRMS (ESI) calculated for $C_{14}H_{21}N_2O_4$ $[M+H]^+$: 281.1501, found: 281.1500.

methyl 2-((ethoxycarbonyl)amino)-2-(quinolin-2-yl)acetate (7-6-as): 63%. 1 mol% $Rh_2(esp)_2$ was used.



^{1}H NMR (500 MHz, acetone-*d*6) δ 8.39 (d, *J*=8.44 Hz, 1 H), 8.05 (d, *J*=8.44 Hz, 1 H), 7.98 (d, *J*=8.07 Hz, 1 H), 7.79 (t, *J*=7.52 Hz, 1 H), 7.70 (d, *J*=8.44 Hz, 1 H), 7.64 – 7.61 (m, 1 H), 7.08 (br, 1 H), 5.66 (d, *J*=7.34 Hz, 1 H), 4.13 – 4.09 (m, 2 H), 3.71 (s, 3 H), 1.23 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, acetone-*d*6) δ 170.12, 155.82, 154.69, 147.16, 137.30, 129.95, 129.01, 127.83. 127.77, 126.96, 120.51, 60.58, 59.52, 51.93, 14.04. HRMS (ESI) calculated for $C_{15}H_{17}N_2O_4$ $[M+H]^+$: 289.1188, found: 289.1187.

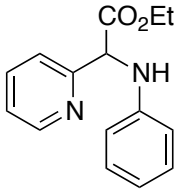
methyl 2-(benzo[d]oxazol-2-yl)-2-((ethoxycarbonyl)amino)acetate (7-6-at): 91%. 1 mol% $Rh_2(esp)_2$ was used.



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, *J*=6.97 Hz, 1 H), 7.55 (d, *J*=7.34 Hz, 1 H), 7.37 (quin, *J*=7.06 Hz, 2 H), 6.01 (d, *J*=6.24 Hz, 1 H), 5.83 (d, *J*=8.07 Hz, 1 H), 4.19 – 4.15 (m, 2 H), 3.83 (s, 3 H),

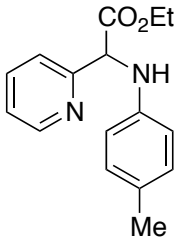
1.27 (t, J=7.00 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.36, 160.30, 155.61, 150.90, 140.58, 125.75, 124.80, 120.55, 110.97, 61.87, 53.62, 52.73, 14.44. HRMS (ESI) calculated for $C_{13}H_{15}N_2O_5$ $[M+H]^+$: 279.0981, found: 279.0977.

ethyl 2-(phenylamino)-2-(pyridin-2-yl)acetate (7-6-ba): 88%. 3 mol% $Rh_2(esp)_2$ was used.



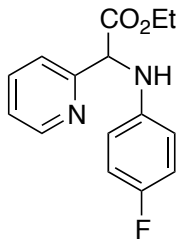
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (d, *J*=4.40 Hz, 1 H), 7.72 – 7.69(m, 1 H), 7.51 (d, *J*=7.70 Hz, 1 H), 7.27 – 7.25 (m, 1 H), 7.17- 7.13 (m, 2 H), 6.74 – 6.71 (m, 1 H), 6.66 (d, *J*=8.44 Hz, 2 H), 5.72 (br, 1 H), 5.30 (s, 1 H), 4.24 – 4.17 (m, 2 H), 1.19 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.01, 156.27, 149.02, 145.98, 137.39, 129.24, 123.22, 122.14, 118.28, 113.56, 62.13, 61.91, 14.01. HRMS (ESI) calculated for $C_{15}H_{17}N_2O_2$ $[M+H]^+$: 257.1290, found: 257.1286.

ethyl 2-(pyridin-2-yl)-2-(p-tolylamino)acetate (7-6-bb): 63%. 3 mol% $Rh_2(esp)_2$ was used.



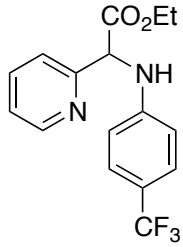
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 – 8.62 (m, 1 H), 7.69 (td, *J*=7.70, 1.83 Hz, 1 H), 7.50 (d, *J*=7.70 Hz, 1 H), 7.25 (ddd, *J*=7.52, 4.95, 1.10 Hz, 1 H), 6.96 (d, *J*=8.07 Hz, 2 H), 6.58 (d, *J*=8.44 Hz, 2 H), 5.26 (s, 1 H), 4.24 – 4.16 (m, 2 H), 2.21 (s, 3 H), 1.19 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.21, 156.49, 149.23, 143.68, 137.18, 129.74, 127.45, 123.12, 122.06, 113.67, 62.53, 61.84, 20.36, 14.05. HRMS (ESI) calculated for $C_{16}H_{19}N_2O_2$ $[M+H]^+$: 271.1447, found: 271.1445.

ethyl 2-((4-fluorophenyl)amino)-2-(pyridin-2-yl)acetate (7-6-bc): 80%. 3 mol% $Rh_2(esp)_2$ was used.



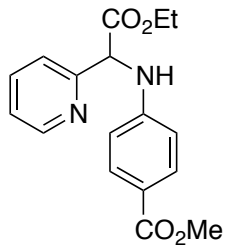
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (d, *J*=4.40 Hz, 1 H), 7.71 (td, *J*=7.70, 1.47 Hz, 1 H), 7.49 (d, *J*=7.70 Hz, 1 H), 7.28 – 7.25 (m, 1 H), 6.88 – 6.83 (m, 2 H), 6.62 – 6.58 (m, 2 H), 5.22 (s, 1 H), 4.22 – 4.16 (m, 2 H), 1.18 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.01, 156.23 (d, *J*=236.9 Hz), 156.01, 149.23, 142.34, 137.30, 123.28, 122.15, 115.73(d, *J*=21.4 Hz), 114.47 (d, *J*=8.82 Hz), 62.70, 61.95, 14.04. HRMS (ESI) calculated for $C_{15}H_{16}FN_2O_2$ $[M+H]^+$: 275.1196, found: 275.1184.

ethyl 2-(pyridin-2-yl)-2-((4-(trifluoromethyl)phenyl)amino)acetate (7-6-bd): 86%. 3 mol% $Rh_2(esp)_2$ was used.



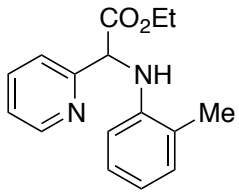
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (d, *J*=4.03 Hz, 1 H), 7.74 (t, *J*=7.52 Hz, 1 H), 7.51 (d, *J*=8.07 Hz, 1 H), 7.39 (d, *J*=8.44 Hz, 2 H), 7.31 – 7.29 (m, 1 H), 6.67 (d, *J*=8.44 Hz, 2 H), 5.89 (br, 1 H), 5.32 (s, 1 H), 4.25 – 4.16 (m, 2 H), 1.20 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.42, 155.19, 149.06, 148.41, 37.69, 126.65 (q, *J*=3.78 Hz), 124.79 (q, *J*=270.9 Hz), 123.57, 122.20, 119.76 (d, *J*=11.3 Hz), 112.71, 62.27, 61.37, 14.03. HRMS (ESI) calculated for $C_{16}H_{16}F_3N_2O_2$ $[M+H]^+$: 325.1164, found: 325.1156.

methyl 4-((2-ethoxy-2-oxo-1-(pyridin-2-yl)ethyl)amino)benzoate (7-6-be): 72%. 3 mol% $Rh_2(esp)_2$ was used.



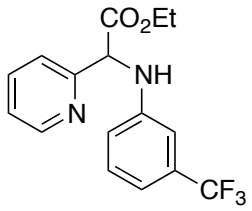
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, *J*=4.38 Hz, 1 H), 7.85 – 7.82 (m, 2 H), 7.71 (td, *J*=7.60, 1.75 Hz, 1 H), 7.48 (d, *J*=7.89 Hz, 1 H), 7.29 – 7.25 (m, 1 H), 6.62 (d, *J*=8.48 Hz, 2 H), 6.00 (br, 1 H), 5.31 (s, 1 H), 4.19 (qq, *J*=10.75, 7.08 Hz, 2 H), 1.18 (t, *J*=7.16 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.46, 167.09, 155.07, 149.69, 149.21, 137.40, 131.46, 123.45, 122.10, 119.41, 112.36, 62.16, 61.31, 51.52, 14.01. HRMS (ESI) calculated for $C_{17}H_{19}N_2O_4$ $[M+H]^+$: 315.1345, found: 315.1335.

ethyl 2-(pyridin-2-yl)-2-(o-tolylamino)acetate (7-6-bf): 76%. 3 mol% $Rh_2(esp)_2$ was used.



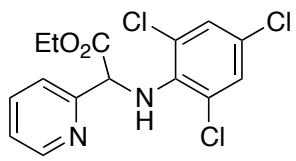
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, *J*=4.97 Hz, 1 H), 7.71 (td, *J*=7.67, 1.61 Hz, 1 H), 7.52 (d, *J*=7.89 Hz, 1 H), 7.29 – 7.27 (m, 1 H), 7.09 – 7.01 (m, 2 H), 6.67 (t, *J*=7.31 Hz, 1 H), 6.47 (d, *J*=8.18 Hz, 1 H), 5.34 (s, 1 H), 4.24 – 4.16 (m, 2 H), 2.32 (s, 3 H), 1.20 (t, *J*=7.16 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.35, 156.49, 149.39, 144.14, 137.02, 130.21, 126.96, 123.08, 122.77, 121.84, 117.80, 110.64, 62.35, 61.85, 17.51, 14.01. HRMS (ESI) calculated for $C_{16}H_{19}N_2O_2$ $[M+H]^+$: 271.1447, found: 271.1444.

ethyl 2-(pyridin-2-yl)-2-((3-(trifluoromethyl)phenyl)amino)acetate (7-6-bg): 71%. 3 mol% $Rh_2(esp)_2$ was used.



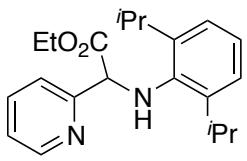
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (d, *J*=4.04 Hz, 1 H), 7.75 (td, *J*=7.61, 1.65 Hz, 1 H), 7.52 (d, *J*=7.70 Hz, 1 H), 7.32 – 7.22 (m, 2 H), 6.95 (d, *J*=7.70 Hz, 1 H), 6.88 (s, 1 H), 6.80 (dd, *J*=8.25, 1.65 Hz, 1 H), 5.78 (br, 1 H), 5.32 (s, 1 H), 4.26 – 4.17 (m, 2 H), 1.19 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.51, 155.14, 148.93, 146.14, 137.71, 131.55 (d, *J*=31.5 Hz), 129.73, 124.16 (q, *J*=272.2 Hz), 123.55, 122.33, 116.37, 114.68 (q, *J*=3.78 Hz), 109.85 (q, J=3.78Hz). HRMS (ESI) calculated for $C_{16}H_{16}F_3N_2O_2$ $[M+H]^+$: 325.1164, found: 325.1152.

ethyl 2-(pyridin-2-yl)-2-((2,4,6-trichlorophenyl)amino)acetate (7-6-bh): 90%. 3 mol% $Rh_2(esp)_2$ was used.



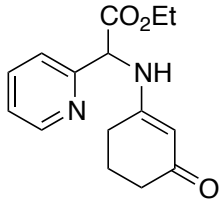
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (d, *J*=4.03 Hz, 1 H), 7.69 (t, *J*=7.52 Hz, 1 H), 7.46 (d, *J*=7.70 Hz, 1 H), 7.25 – 7.23 (m, 1 H), 7.20 (s, 2 H), 6.10 (br, 1 H), 5.84 (s, 1 H), 4.18 – 4.12 (m, 2 H), 1.16 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.63, 155.36, 149.23, 139.65, 137.06, 128.53, 125.80, 125.50, 123.27, 122.77, 63.13, 61.87, 13.95. HRMS (ESI) calculated for $C_{15}H_{14}C_{l3}N_2O_2$ $[M+H]^+$: 359.0121, found: 359.0113.

ethyl 2-((2,6-diisopropylphenyl)amino)-2-(pyridin-2-yl)acetate (7-6-bi): 47%. 3 mol% $Rh_2(esp)_2$ was used.



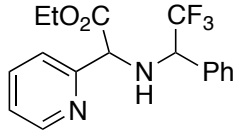
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (d, *J*=4.40 Hz, 1 H), 7.65 (t, *J*=7.34 Hz, 1 H), 7.31 (d, *J*=7.70 Hz, 1 H), 7.25 – 7.23 (m, 1 H), 7.06 – 7.01 (m, 3 H), 4.90 (s, 1 H), 4.17 (qd, *J*=7.09, 2.57 Hz, 2 H), 3.28 – 3.20 (m, 2 H), 1.21 (d, *J*=6.60 Hz, 6 H), 1.16 (t, *J*=7.15 Hz, 3 H), 1.09 (d, *J*=6.60 Hz, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.83, 157.27, 149.26, 141.96, 140.89, 136.92, 123.61, 123.56, 122.95, 122.61, 67.90, 61.45, 27.66, 24.08, 14.02. HRMS (ESI) calculated for $C_{21}H_{29}N_2O_2$ $[M+H]^+$: 341.2229, found: 341.2220.

ethyl 2-((3-oxocyclohex-1-en-1-yl)amino)-2-(pyridin-2-yl)acetate (7-6-bj): 91%. 1 mol% $Rh_2(esp)_2$ was used.



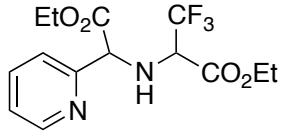
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (d, *J*=4.09 Hz, 1 H), 7.72 (td, *J*=7.67, 1.61 Hz, 1 H), 7.45 (d, *J*=7.89 Hz, 1 H), 7.27 (dd, *J*=4.68, 2.05 Hz, 1 H), 6.37 (d, *J*=5.85 Hz, 1 H), 5.12 (d, *J*=6.72 Hz, 1 H), 5.03 (s, 1 H), 4.21 – 4.13 (m, 2 H), 2.52 – 2.41 (m, 2 H), 2.31 – 2.27 (m, 2 H), 2.01 – 1.93 (m, 2 H), 1.19 (t, *J*=7.02 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.51, 169.17, 162.49, 153.03, 149.33, 137.31, 123.64, 122.67, 98.67, 62.35, 59.81, 36.32, 29.54, 21.77, 13.93. HRMS (ESI) calculated for $C_{15}H_{19}N_2O_3$ $[M+H]^+$: 275.1396, found: 275.1394.

ethyl 2-(pyridin-2-yl)-2-((2,2,2-trifluoro-1-phenylethyl)amino)acetate (7-6-bk): 87%, dr = 1:1. 3 mol% $Rh_2(esp)_2$ was used.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (d, *J*=4.40 Hz, 1 H), 8.55 (d, *J*=4.40 Hz, 1 H), 7.69 (t, *J*=7.70 Hz, 1 H), 7.65 (td, *J*=7.70, 1.10 Hz, 1 H), 7.44-7.21 (m, 14 H), 4.54 (s, 1 H), 4.42-4.38 (m, 2 H), 4.20-4.03 (m, 5 H), 3.34 (br, 2 H), 1.17 (t, *J*=7.15 Hz, 3 H), 1.13 (t, *J*=6.97 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.23, 171.00, 156.32, 149.57, 149.51, 137.05, 136.95, 133.54, 133.10, 129.35, 129.26, 129.16, 128.80, 128.77, 128.74, 125.30 (d, *J*=278.8 Hz), 125.19 (d, *J*=278.8 Hz), 123.21, 123.13, 123.08, 122.88, 64.12, 63.36, 62.49 (q, *J*=28.75 Hz), 62.17 (q, *J*=28.75 Hz), 61.64, 61.46, 14.10, 13.98. HRMS (ESI) calculated for $C_{17}H_{18}F_3N_2O_2$ $[M+H]^+$: 339.1320, found: 339.1308.

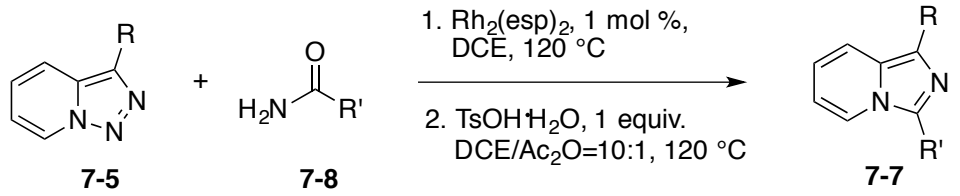
ethyl 2-((2-ethoxy-2-oxo-1-(pyridin-2-yl)ethyl)amino)-3,3,3-trifluoropropanoate (7-6-bl): 82%, dr = 1:0.6. 3 mol% $Rh_2(esp)_2$ was used.



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56-8.55 (m, 1.6 H), 7.70 (qd, *J*=7.60, 1.46 Hz, 1.6 H), 7.46 (d, *J*=7.60 Hz, 1 H), 7.40 (d, *J*=7.89 Hz, 0.6 H), 7.22-7.25 (m, 1.6 H), 4.76 (s, 0.6 H), 4.66 (s, 1 H), 4.34-4.25 (m, 2 H), 4.23-4.13 (m, 4.4 H), 3.95 (q, *J*=7.31 Hz, 0.6 H), 3.85 (q, *J*=7.50 Hz, 1 H), 3.56 (br, 1.6 H), 1.31 (t, *J*=7.16 Hz, 3 H), 1.26-1.15 (m, 6.6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.01, 170.73, 166.54, 156.21, 149.39, 149.18, 137.14, 136.99, 124.79 (d, *J*=5.04 Hz), 123.24, 122.83, 122.72, 122.04 (d, *J*=6.30 Hz), 65.60, 64.85, 62.60, 62.35, 61.72, 61.57, 61.27 (d, *J*=36.54 Hz), 60.12 (*J*=37.80 Hz), 13.96,

13.92, 13.85. HRMS (ESI) calculated for $C_{14}H_{18}F_3N_2O_4$ $[M+H]^+$: 335.1219, found: 335.1217.

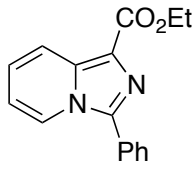
6.1.4. Synthesis of Imidazo[1,2-a]pyridines



Scheme 9-7

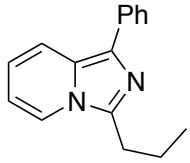
General Procedure: An oven-dried 3.0 mL V-vial equipped with a stirring bar was charged with $Rh_2(esp)_2$ (1 mol %), pyridotriazole **7-5** (0.3 mmol), amide **7-8** and DCE (2 mL) under N_2 atmosphere. The reaction vessel was capped with Mininert syringe valve and the reaction mixture was stirred at 120 °C until complete. Then it was cooled down to room temperature and $TsOH \cdot H_2O$ (0.3 mol), Ac_2O (0.2 mL) were added under air. The reaction was allowed to heat again at 120 ^oC until the N-H insertion product was consumed. Upon completion the mixture was cooled to room temperature, diluted with ethyl acetate and washed with aqueous $NaHCO_3$. Then the organic phase was dried over Na_2SO_4, concentrated under reduced pressure, purified by column chromatography to afford the corresponding imidazopyridine product **7-7**.

ethyl 3-phenylimidazo[1,5-a]pyridine-1-carboxylate (7-7-a): 70%.



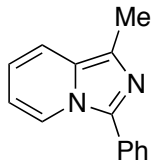
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, *J*=7.34 Hz, 1 H), 8.26 (d, *J*=9.17 Hz, 1 H), 7.79 (d, *J*=7.34 Hz, 2 H), 7.55-7.49 (m, 3 H), 7.13 (dd, *J*=8.99, 6.42 Hz, 1 H), 6.78 (t, *J*=6.79 Hz, 1 H), 4.50 (q, *J*=6.97 Hz, 2 H), 1.47 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.58, 139.12, 135.42, 129.53, 129.09, 128.96, 128.81, 124.15, 122.49, 121.80, 120.11, 114.37, 60.40, 14.66. HRMS (ESI) calculated for $[M+H]^+$: 267.1134, found: 267.1131.

1-phenyl-3-propylimidazo[1,5-a]pyridine (7-7-b): 77%.



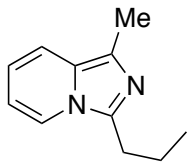
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J*=7.34 Hz, 2 H), 7.76 (d, *J*=9.17 Hz, 1 H), 7.72 (d, *J*=6.97 Hz, 1 H), 7.44 (t, *J*=7.70 Hz, 2 H), 7.28-7.25 (m, 1 H), 6.70 (dd, *J*=8.99, 6.42 Hz, 1 H), 6.54 (t, *J*=6.60 Hz, 1 H), 3.01 (t, *J*=7.70 Hz, 2 H), 1.90 (sxt, *J*=7.56 Hz, 2H), 1.07 (t, *J*=7.34 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.87, 135.23, 129.96, 128.62, 126.46, 126.34, 126.06, 120.96, 119.02, 118.52, 112.31, 28.63, 20.66, 14.01. HRMS (ESI) calculated for $[M+H]^+$: 237.1392, found: 237.1393.

1-methyl-3-phenylimidazo[1,5-a]pyridine (7-7-c): 73%.



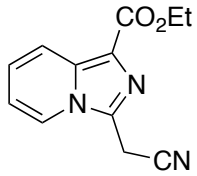
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, *J*=7.34 Hz, 1 H), 7.78 (d, *J*=7.70 Hz, 2 H), 7.50 (t, *J*=7.70 Hz, 2 H), 7.42-7.38 (m, 2 H), 6.62 (dd, *J*=8.99, 6.42 Hz, 1 H), 6.49 (t, *J*=6.79 Hz, 1 H), 2.58 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.27, 129.95, 128.92, 128.49, 127.87, 127.74, 121.08, 118.33, 117.21, 113.06, 12.35. HRMS (ESI) calculated for $[M+H]^+$: 209.1079, found: 209.1078.

1-methyl-3-propylimidazo[1,5-a]pyridine (7-7-d): 81%.



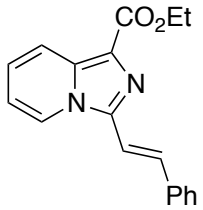
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J*=7.02 Hz, 1 H), 7.29 (d, *J*=9.06 Hz, 1 H), 6.53 (dd, *J*=8.92, 6.28 Hz, 1 H), 6.47-6.43 (m, 1 H), 2.92 (t, *J*=7.6 Hz, 2 H), 2.49 (s, 3 H), 1.84 (sxt, *J*=7.48 Hz, 2 H), 1.00 (t, *J*=7.45 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.02, 126.28, 125.96, 120.27, 118.17, 115.93, 112.11, 28.31, 20.63, 13.95, 12.18. HRMS (ESI) calculated for $[M+H]^+$: 175.1235, found: 175.1227.

ethyl 3-(cyanomethyl)imidazo[1,5-a]pyridine-1-carboxylate (7-7-e): 58%.



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J*=9.35 Hz, 1 H), 8.04 (d, *J*=7.02 Hz, 1 H), 7.22 (dd, *J*=9.06, 6.72 Hz, 1H), 6.97 (t, *J*=6.87 Hz, 1 H), 4.46 (q, *J*=7.21 Hz, 2 H), 2.16 (s, 2 H), 1.45 (t, *J*=7.16 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.79, 135.48, 127.17, 124.56, 121.28, 120.20, 115.36, 113.47, 60.63, 17.08, 14.53. HRMS (ESI) calculated for $[M+H]^+$: 230.0930, found: 230.0932.

(*E*)-ethyl 3-styrylimidazo[1,5-a]pyridine-1-carboxylate (7-7-f): 78%.



^{1}H NMR (500 MHz, acetone-*d*6) δ 8.78 (d, *J*=6.97 Hz, 1 H), 8.17 (d, *J*=9.17 Hz, 1 H), 7.77-7.68 (m, 4 H), 7.41 (t, *J*=7.70 Hz, 2 H), 7.34-7.31 (m, 1 H), 7.25 (dd, *J*=8.99, 6.42 Hz, 1 H), 7.02-6.99 (m, 1 H), 4.40 (q, *J*=7.09 Hz, 2 H), 1.41 (t, *J*=7.15 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.30, 137.37, 136.09, 134.92, 133.95, 128.70, 128.50, 126.78, 124.03, 121.64, 120.05, 114.49, 110.91, 109.47, 60.42, 14.52. HRMS (ESI) calculated for $[M+H]^+$: 293.1290, found: 293.1280.

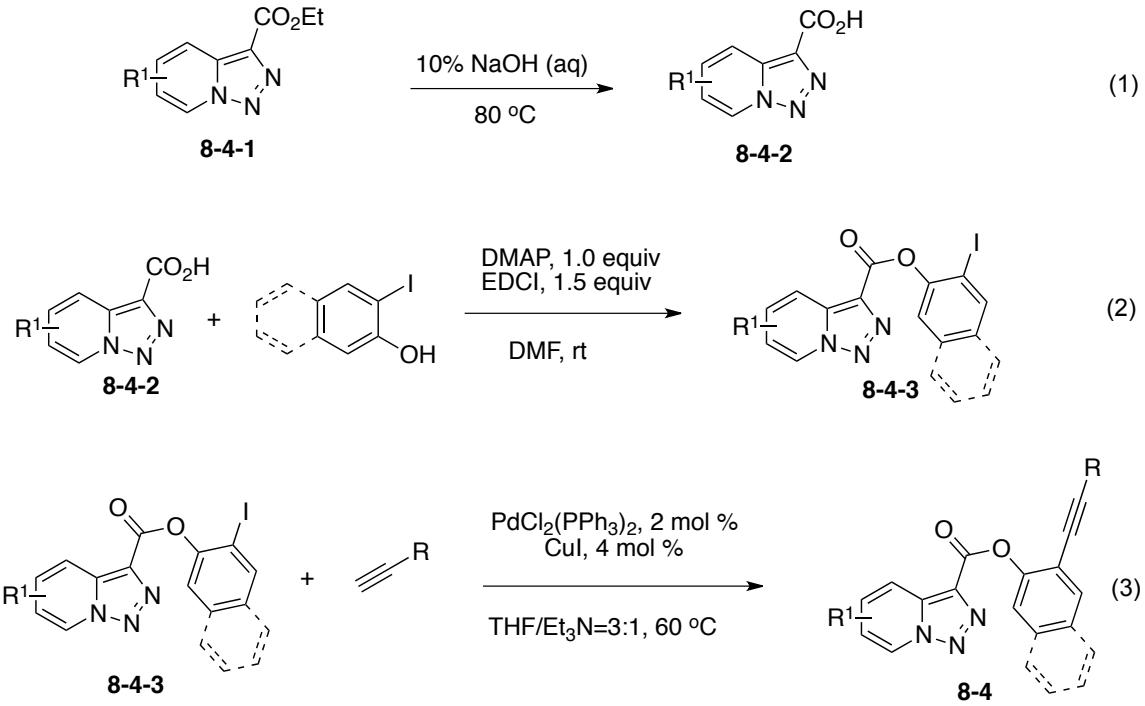
6.2. Cu-catalyzed transannulation reaction of pyridotriazoles: general access to fused polycyclic indolizines

6.2.1. General information

GC/MS analysis was performed on a Hewlett Packard Model 6890 GC interfaced to a Hewlett Packard Model 5973 mass selective detector (15 m x 0.25 mm capillary column, HP-5MS). NMR spectra were recorded on Bruker Avance DRX-500 (500 MHz) or DPX-400 (400 MHz) instrument. LRMS and HRMS analyses were performed on Micromass 70 VSE mass spectrometer. Column chromatography was carried out employing Silicycle Silica-P flash silica gel (40-63 μm). Precoated silica gel plates F-254 were used for thin-layer analytical chromatography. All manipulations with transition metal catalysts were conducted in oven-dried glassware under inert atmosphere using a combination of glovebox and standard Schlenk techniques unless otherwise noted. Anhydrous dichloromethane, toluene, and THF (BHT-free) was purchased from Aldrich, degassed with argon, and dried by passage through activated alumina on an Innovative Technology PureSolv system. All starting materials were purchased from Strem Chemicals, Aldrich, Gelest Inc., TCI America, or Alfa Aesar, or synthesized via known literature procedures. All manipulations with transition metal catalysts were conducted in oven-dried glassware under inert atmosphere using a combination of glovebox and standard Schlenk techniques.

6.2.2. Preparation of Pyridoriazoles

Synthesis of ester/amide tethered pyridotriazoles: General Procedure A.



Scheme 10-1

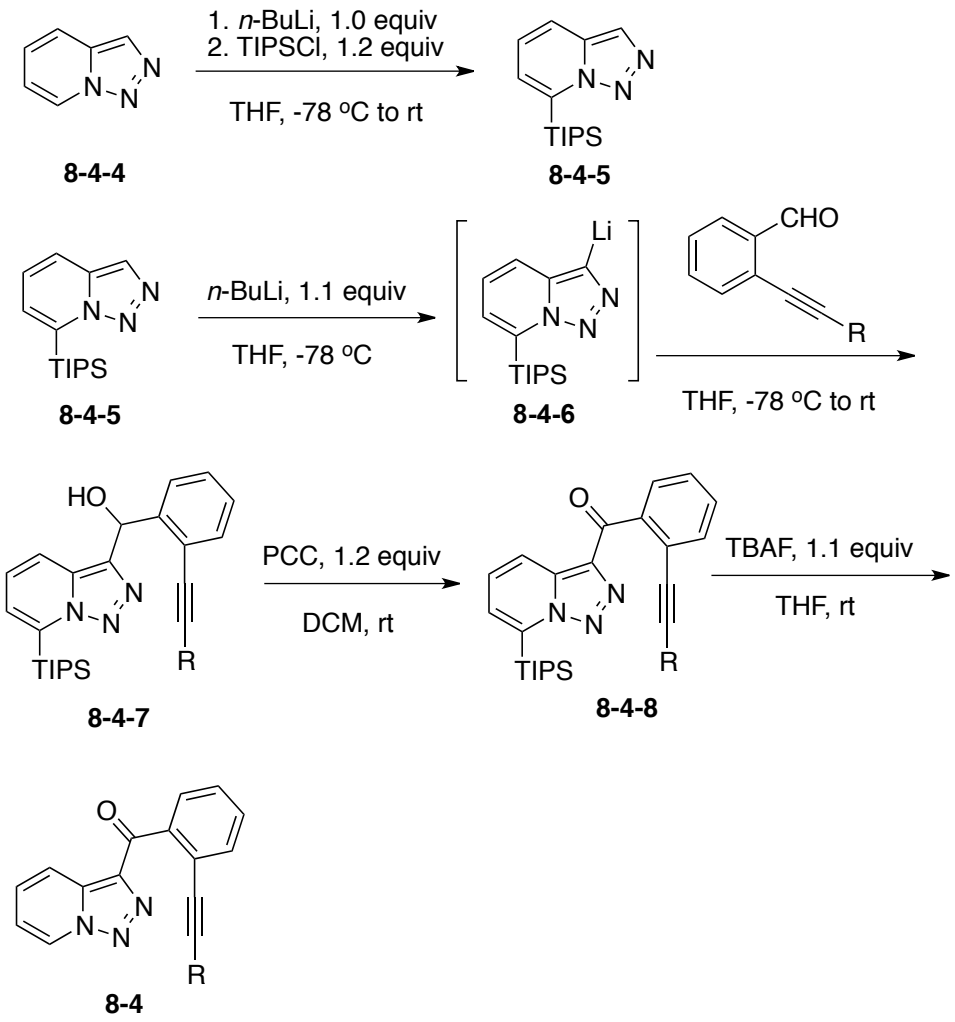
Carboxylic acid **8-4-2** was prepared via hydrolysis of ester **8-4-1** under basic conditions. A suspension of pyridotriazole **8-4-1** (20 mmol) in 10% NaOH aqueous solution (20 mL) was heated at 80 ^{o}C until a clear solution is formed (about 1 h). Then, the reaction mixture was allowed to cool down to room temperature, and 2 M HCl was added to pH = 2. White precipitate (carboxylic acid **8-4-2**) formed during acidification and was collected by filtration. It can be used directly in the next step without purification (Scheme 10-1, eq 1)).

To a stirred suspension of compound **8-4-2** (10 mmol, 1.0 equiv), 2-iodophenol (12 mmol, 1.2 equiv), and 4-(dimethylamino)pyridine (DMAP, 10 mmol, 1.0 equiv) in DMF was added 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDCI,

15 mmol, 1.5 equiv). The mixture was stirred at room temperature for 2 h (until a clear solution is formed). Then water was added. The mixture was extracted with ethyl acetate twice, and the combined organic layers were washed with 1 M HCl, water, saturated aqueous Na_2CO_3, brine, and dried over anhydrous Na_2SO_4. Evaporation of solvent afforded yellow solid (**8-4-3**), which can be used directly in the next step without purification (Scheme 10-1, eq 2).

Alkynyl pyridotriazole **8-4** was prepared from compound **8-4-3** and terminal alkyne via Sonogashira cross-coupling reaction. A round-bottom flask equipped with a stirring bar was charged with $PdCl_2(PPh_3)_2$ (2 mol %), CuI (4 mol %), compound **8-4-3** (0.5 mmol, 1.0 equiv), terminal alkyne (0.75 mmol, 1.5 equiv), and solvent (THF/Et_3N=3:1) under N_2 atmosphere. The reaction mixture was stirred at 60 °C. Upon completion (about 4 h), the reaction mixture was cooled to room temperature, filtered through a short path of silica gel, concentrated under reduced pressure, and the crude product was purified by column chromatography to afford the corresponding alkynyl pyridotriazole substrate **8-4** (Scheme 10-1, eq 3).

Synthesis of ketone tethered pyridotriazoles: General Procedure B.



Scheme 10-2

To a stirred solution of compound **8-4-4** (20 mmol, 1.0 equiv) in THF was added dropwise *n*-BuLi (2.5 M, 8 mL, 1.0 equiv) at -78 °C under argon. After addition, the solution was allowed to stir for 30 min at the same temperature. Then, TIPSCl (24 mmol, 1.2 equiv) was added dropwise and the solution was allowed to warm to room temperature. After stirring for 1 h, the reaction was quenched with saturated aqueous NH_4Cl and the aqueous layer was extracted with EtOAc three times. The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under

reduced pressure. The residue was purified by column chromatography on silica gel to afford compound **8-4-5**.

To a stirred solution of compound **8-4-5** (1.0 mmol, 1.0 equiv) in THF was added dropwise *n*-BuLi (2.5 M, 0.44 mL, 1.1 equiv) at -78 °C under argon. After addition, the solution was allowed to stir for 1 h at the same temperature. Then, 2-(alkynyl)benzaldehyde (1.2 mmol, 1.2 equiv) was added dropwise and the solution was allowed to warm to room temperature then stirred for 1 h. The reaction was quenched with saturated aqueous NH_4Cl and the aqueous layer was extracted with EtOAc three times. The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford compound **8-4-7**.

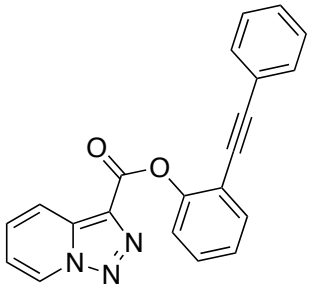
To a DCM solution of compound **8-4-7** was added pyridinium chlorochromate (PCC, 1.2 equiv). The resulting mixture was allowed to react for 1 h at room temperature. Upon completion, the reaction mixture was filtered through a short path of silica gel, concentrated under reduced pressure, and purified by column chromatography to afford compound **8-4-8**.

To a THF solution of compound **8-4-8** was added TBAF (1.1 equiv, 1M solution in THF), and the reaction mixture was stirred at room temperature for 1 h. Upon completion, the mixture was concentrated under reduced pressure, and the crude product was purified by column chromatography to afford the corresponding alkynyl pyridotriazole substrate **8-4**.

Detailed procedure for preparation of individual substrate：

2-(phenylethynyl)phenyl [1,2,3]triazolo[1,5-a]pyridine-3-carboxylate (8-4-aa):

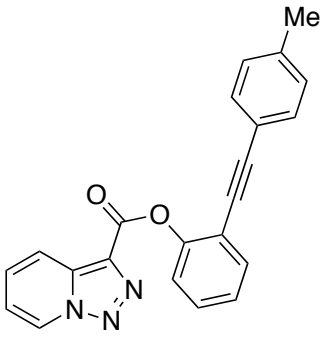
Compound **8-4-aa** was prepared according to the **General Procedure A.**



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.88 (d, *J*=6.97 Hz, 1 H), 8.41 (d, *J*=8.80 Hz, 1 H), 7.64 (d, *J*=7.34 Hz, 1 H), 7.53 - 7.50 (m, 1 H), 7.45 - 7.40 (m, 2 H), 7.30 (t, *J*=7.34 Hz, 1 H), 7.23 – 7.14, (m, 6 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.10, 151.14, 132.98, 131.40, 129.81, 129.46, 128.33, 128.11, 126.11, 122.71, 122.55, 119.49, 117.40, 116.59, 94.58, 84.40. HRMS (ESI) calculated for $C_{21}H_{14}N_3O_2$ $[M+H]^+$: 340.1086, found: 340.1080. Overlapping signals in ^{13}C spectrum due to highly aromatic structure.

2-(p-tolylethynyl)phenyl [1,2,3]triazolo[1,5-a]pyridine-3-carboxylate (8-4-ab):

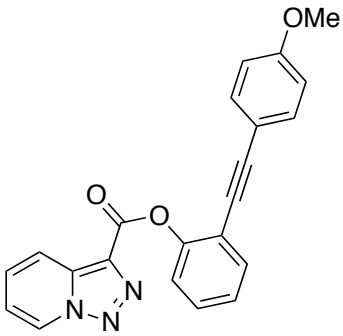
Compound **8-4-ab** was prepared according to the **General Procedure A.**



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (d, *J*=6.72 Hz, 1 H), 8.39 (d, *J*=9.06 Hz, 1 H), 7.62 (d, *J*=7.60 Hz, 1 H), 7.53 – 7.49 (m, 1 H), 7.41 – 7.38 (m, 2 H), 7.29 – 7.28 (m, 1 H), 7.18 (t, *J*=6.72 Hz, 1 H), 7.10 (d, *J*=7.89 Hz, 2H), 6.95 (d, *J*=7.89 Hz, 2 H), 2.25 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.98, 150.97, 138.50, 135.38, 132.84, 131.22, 129.81, 129.22, 128.83, 128.48, 126.06, 126.00, 122.44, 119.52, 117.50, 116.59, 94.76, 83.68, 21.35. HRMS (ESI) calculated for $C_{22}H_{16}N_3O_2$ $[M+H]^+$: 354.1243, found: 354.1238.

2-((4-methoxyphenyl)ethynyl)phenyl [1,2,3]triazolo[1,5-a]pyridine-3-carboxylate (8-4-ac):

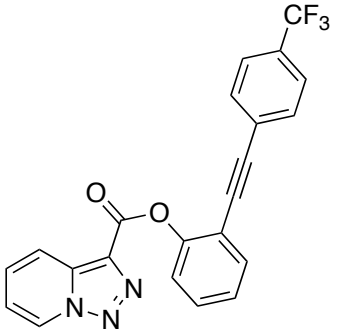
Compound **8-4-ac** was prepared according to the **General Procedure A.**



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (d, *J*=6.72 Hz, 1 H), 8.40 (d, *J*=8.77 Hz, 1 H), 7.61 (d, *J*=7.60 Hz, 1 H), 7.52 (t, *J*=7.89 Hz, 1 H), 7.40 – 7.39 (m, 2 H), 7.30 – 7.28 (m, 1 H), 7.20 – 7.13 (m, 3 H), 6.67 (d, *J*=8.48 Hz, 2 H), 3.72 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.57, 159.01, 150.92, 135.42, 132.84, 132.74, 129.79, 129.06, 128.55, 126.06, 126.01, 122.44, 119.41, 117.66, 116.61, 114.73, 113.72, 94.67, 83.10, 55.17. HRMS (ESI) calculated for $C_{22}H_{16}N_3O_3$ $[M+H]^+$: 370.1192, found: 370.1183.

2-((4-(trifluoromethyl)phenyl)ethynyl)phenyl [1,2,3]triazolo[1,5-a]pyridine-3-carboxylate (8-4-ad):

Compound **8-4-ad** was prepared according to the **General Procedure A.**

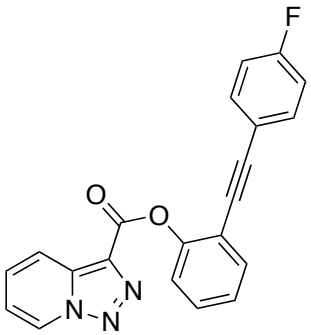


^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (d, *J*=6.72 Hz, 1 H), 8.37 (d, *J*=8.77 Hz, 1 H), 7.65 (d, *J*=7.60 Hz, 1 H), 7.58 – 7.54 (m, 1 H), 7.49 – 7.39 (m, 4 H), 7.33 – 7.30 (m, 3 H), 7.21 (t, *J*=6.58 Hz, 1 H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.03, 151.25, 135.54, 133.00, 131.57, 130.09, 129.97, 129.69, 127.39 (q, *J*=183 Hz), 126.23, 126.15, 125.03 (q, *J*=5 Hz), 122.64, 122.34, 119.22, 116.75, 116.71, 92.99, 86.67. HRMS (ESI) calculated for $C_{22}H_{13}F_3N_3O_2$ $[M+H]^+$:

408.0960, found: 408.0960. Overlapping signals in ^{13}C spectrum due to highly aromatic structure.

2-((4-fluorophenyl)ethynyl)phenyl [1,2,3]triazolo[1,5-a]pyridine-3-carboxylate (8-4-ae):

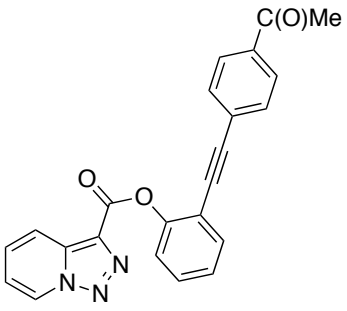
Compound **8-4-ae** was prepared according to the **General Procedure A.**



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (d, *J*=7.02 Hz, 1 H), 8.38 (d, *J*=8.77 Hz, 1 H), 7.61 (d, *J*=7.02 Hz, 1 H), 7.56 – 7.52 (m, 1 H), 7.45 – 7.37 (m, 2 H), 7.29 (t, *J*=7.45 Hz, 1 H), 7.21 – 7.18 (m, 3 H), 6.85 (t, *J*=8.62 Hz, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.42 (d, *J*=250.7 Hz), 159.01, 151.12, 135.49, 133.29 (d, *J*=6.3 Hz), 132.84, 129.83, 129.50, 128.46, 126.12, 126.09, 122.55, 119.30, 118.80 (d, *J*=3.8 Hz), 117.25, 116.62, 115.42 (d, *J*=21.4 Hz), 93.47, 84.09. HRMS (ESI) calculated for $C_{21}H_{13}FN_3O_2$ $[M+H]^+$: 358.0992, found: 358.0982.

2-((4-acetylphenyl)ethynyl)phenyl [1,2,3]triazolo[1,5-a]pyridine-3-carboxylate (8-4-af):

Compound **8-4-af** was prepared according to the **General Procedure A.**

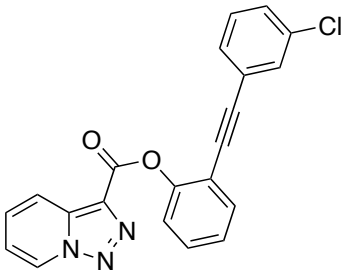


^{1}H NMR (500 MHz, $CDCl_3$) δ 8.90 (d, *J*=6.24 Hz, 1 H), 8.38 (d, *J*=8.44 Hz, 1 H), 7.75 (d, *J*=7.70 Hz, 2 H), 7.65 (d, *J*=7.34 Hz, 1 H), 7.56 (t, *J*=7.52 Hz, 1 H), 7.48 -7.46 (m, 1 H), 7.41 – 7.40 (m, 1 H), 7.33 – 7.29 (m, 3 H), 7.22 – 7.20 (m, 1 H), 2.53 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ

197.23, 159.03, 151.26, 136.15, 135.55, 133.05, 131.49, 130.09, 129.96, 128.37, 128.04, 127.55, 126.23, 126.18, 122.67, 119.30, 116.89, 116.69, 93.66, 87.62, 26.56. HRMS (ESI) calculated for $C_{23}H_{16}N_3O_3$ $[M+H]^+$: 382.1192, found: 382.1189.

2-((3-chlorophenyl)ethynyl)phenyl [1,2,3]triazolo[1,5-a]pyridine-3-carboxylate (8-4-ag):

Compound **8-4-ag** was prepared according to the **General Procedure A.**

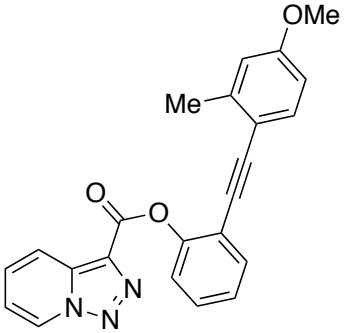


^{1}H NMR (500 MHz, $CDCl_3$) δ 8.90 (d, *J*=5.87 Hz, 1 H), 8.39 (d, *J*=8.07 Hz, 1 H), 7.62 (d, *J*=6.60 Hz, 1 H), 7.57 – 7.54 (m, 1 H), 7.45 – 7.39 (m, 2 H), 7.31 – 7.30 (m, 1 H), 7.20 – 7.16 (m, 2 H), 7.10 – 7.08 (m, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.01, 151.33, 147.11, 135.53, 133.86, 132.92, 131.15, 129.96, 129.86, 129.45, 129.37, 128.53, 128.40, 126.17, 124.39, 122.64, 119.27, 116.93, 116.64, 93.06, 85.63. HRMS (ESI) calculated for $C_{21}H_{13}ClN_3O_2$ $[M+H]^+$: 374.0696, found: 374.0689.

2-((4-methoxy-2-methylphenyl)ethynyl)phenyl [1,2,3]triazolo[1,5-a]pyridine-3-carboxylate (8-4-ah):

Compound **8-4-ah** was prepared according to the **General Procedure A.**

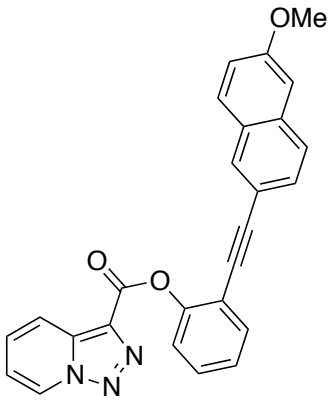
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (d, *J*=7.02 Hz, 1 H), 8.38 (d, *J*=9.06 Hz, 1 H), 7.64 – 7.62 (m, 1 H), 7.54 – 7.51 (m, 1 H), 7.42 – 7.35 (m, 2 H), 7.31 – 7.27 (m, 1 H), 7.20 – 7.13 (m, 2 H), 6.59 – 6.58 (m, 1 H), 6.53 (dd, *J*=8.48, 2.34 Hz, 1 H), 3.72 (s, 3 H), 2.17



(s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.60, 159.10, 150.67, 141.88, 135.52, 133.19, 132.97, 129.74, 128.99, 126.13, 126.04, 122.53, 119.43, 118.15, 116.56, 114.83, 111.07, 93.57, 86.82, 55.12, 20.66. HRMS (ESI) calculated for $C_{23}H_{18}N_3O_3$ $[M+H]^+$: 384.1348, found: 384.1343. Overlapping signals in ^{13}C spectrum due to highly aromatic structure.

2-((6-methoxynaphthalen-2-yl)ethynyl)phenyl [1,2,3]triazolo[1,5-a]pyridine-3-carboxylate (8-4-ai):

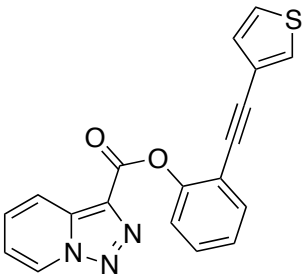
Compound **8-4-ai** was prepared according to the **General Procedure A.**



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.83 (d, *J*=6.97 Hz, 1 H), 8.38 (d, *J*=8.80 Hz, 1 H), 7.65 (d, *J*=7.34 Hz, 1 H), 7.58 (s, 1 H), 7.48 – 7.41 (m, 5 H), 7.31 – 7.29 (m, 1 H), 7.20 (dd, *J*=8.44, 1.47 Hz, 1 H), 7.11 (td, *J*=6.88, 1.28 Hz, 1 H), 7.05 (dd, *J*=8.99, 2.38 Hz, 1 H), 6.97 (d, *J*=2.20 Hz, 1 H), 3.84 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.01, 158.23, 151.17, 135.39, 133.98, 132.74, 131.15, 129.77, 129.24, 129.06, 128.52, 128.46, 128.05, 126.52, 126.08, 125.93, 122.47, 119.28, 119.24, 117.50, 117.43, 116.53, 105.59, 95.30, 84.07, 55.19. HRMS (ESI) calculated for $C_{26}H_{18}N_3O_3$ $[M+H]^+$: 420.1348, found: 420.1340.

2-(thiophen-3-ylethynyl)phenyl [1,2,3]triazolo[1,5-a]pyridine-3-carboxylate (8-4-aj):

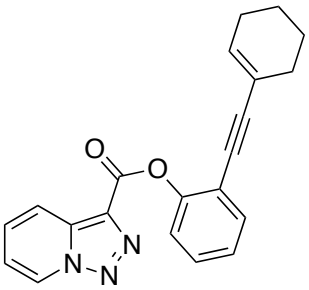
Compound **8-4-aj** was prepared according to the **General Procedure A.**



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.87 (d, *J*=5.87 Hz, 1 H), 8.38 (d, *J*=8.44 Hz, 1 H), 7.60 (d, *J*=6.97 Hz, 1 H), 7.53 – 7.50 (m, 1 H), 7.42 – 7.39 (m, 2 H), 7.28 – 7.11 (m, 4 H), 6.85 (s, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.96, 151.05, 135.40, 132.76, 129.81, 129.49, 129.33, 128.81, 128.49, 126.05, 125.18, 122.49, 121.71, 119.31, 117.30, 116.62, 89.74, 83.91. HRMS (ESI) calculated for $C_{19}H_{12}N_3O_2S$ $[M+H]^+$: 346.0650, found: 346.0645. Overlapping signals in ^{13}C spectrum due to highly aromatic structure.

2-(cyclohex-1-en-1-ylethynyl)phenyl [1,2,3]triazolo[1,5-a]pyridine-3-carboxylate (8-4-ak):

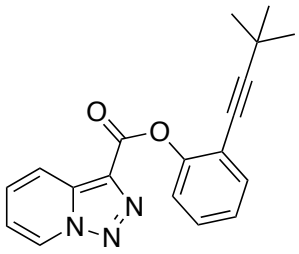
Compound **8-4-ak** was prepared according to the **General Procedure A.**



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.87 (d, *J*=6.60 Hz, 1 H), 8.37 (d, *J*=8.44 Hz, 1 H), 7.57 (t, *J*=7.70 Hz, 1 H), 7.48 (d, *J*=7.34 Hz, 1 H), 7.35 – 7.30 (m, 2 H), 7.21 – 7.19 (m, 2 H), 5.86 (m, 1 H), 1.90 – 1.83 (m, 4 H), 1.43 – 1.36 (m, 4 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.86, 150.83, 135.52, 135.30, 132.65, 129.68, 128.75, 128.55, 125.98, 125.92, 122.28, 120.24, 119.39, 117.83, 116.58, 96.59, 81.65, 28.57, 25.45, 21.92, 21.13. HRMS (ESI) calculated for $C_{21}H_{18}N_3O_2$ $[M+H]^+$: 344.1399, found: 344.1389.

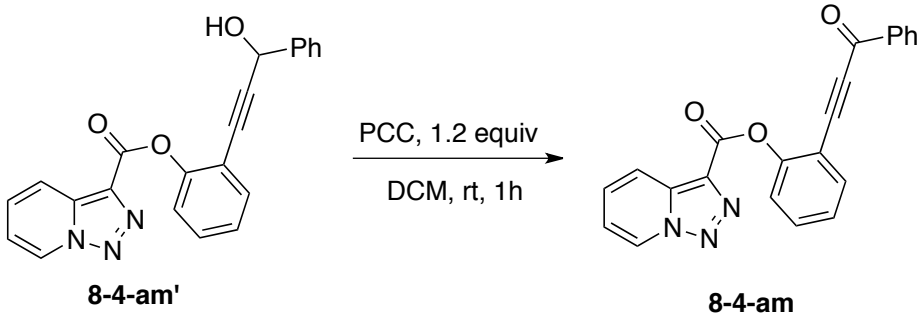
2-(3,3-dimethylbut-1-yn-1-yl)phenyl [1,2,3]triazolo[1,5-a]pyridine-3-carboxylate (8-4-al):

Compound **8-4-al** was prepared according to the **General Procedure A.**



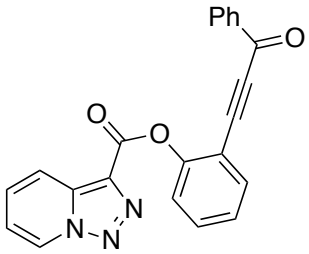
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (d, *J*=7.02 Hz, 1 H), 8.38 (d, *J*=8.77 Hz, 1 H), 7.60 (dd, *J*=8.33, 7.16 Hz, 1 H), 7.48 (dd, *J*=7.75, 1.32 Hz, 1 H), 7.36 – 7.32 (m, 1 H), 7.28 – 7.26 (m, 1 H), 7.23 – 7.20 (m, 2 H), 0.98 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.92, 151.16, 135.36, 132.77, 129.72, 128.67, 128.59, 126.09, 125.97, 122.20, 119.41, 118.15, 116.59, 104.01, 73.92, 30.46, 27.82. HRMS (ESI) calculated for $C_{19}H_{18}N_3O_2$ $[M+H]^+$: 320.1399, found: 320.1397.

2-(3-oxo-3-phenylprop-1-yn-1-yl)phenyl [1,2,3]triazolo[1,5-a]pyridine-3-carboxylate (8-4-am):



8-4-am' **8-4-am**

Scheme 10-3



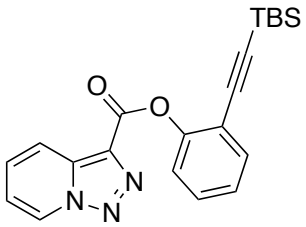
Compound **8-4-am'** was prepared according to the **General Procedure A**, followed by oxidation using PCC to afford compound **8-4-am**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (d, *J*=7.02 Hz, 1 H), 8.35 (d, *J*=9.06 Hz, 1 H), 8.03 (d, *J*=7.60 Hz, 2 H), 7.80 (d, *J*=6.72 Hz, 1 H), 7.61 – 7.55 (m, 2 H), 7.48 – 7.35 (m, 3 H), 7.24 – 7.17 (m, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.58, 158.85, 152.26, 136.42, 135.70, 134.84, 133.91, 132.14, 130.18, 129.40, 128.29, 126.40,

126.06, 123.00, 119.30, 116.75, 114.57, 91.24, 87.64. HRMS (ESI) calculated for $C_{22}H_{14}N_3O_3$ $[M+H]^+$: 368.1035, found: 368.1030.

2-((tert-butyldimethylsilyl)ethynyl)phenyl [1,2,3]triazolo[1,5-a]pyridine-3-carboxylate (8-4-an):

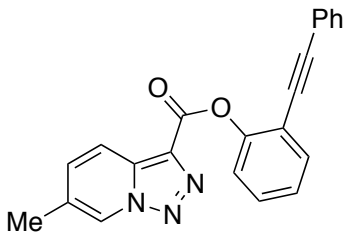
Compound **8-4-an** was prepared according to the **General Procedure A.**



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.90 (d, *J*=6.97 Hz, 1 H), 8.37 (d, *J*=8.80 Hz, 1 H), 7.61 – 7.57 (m, 2 H), 7.42 – 7.39 (m, 1 H), 7.30 – 7.20 (m, 3 H), 0.67 (s, 9 H), -0.12 (s, 6 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.93, 151.58, 141.62, 135.56, 133.48, 129.67, 128.64, 126.06, 122.49, 119.56, 117.67, 116.52, 100.13, 98.38. 25.70, 16.26, -5.04. HRMS (ESI) calculated for $C_{21}H_{24}N_3O_2Si$ $[M+H]^+$: 378.1638, found: 378.1632.

2-(phenylethynyl)phenyl 6-methyl-[1,2,3]triazolo[1,5-a]pyridine-3-carboxylate (8-4-ao):

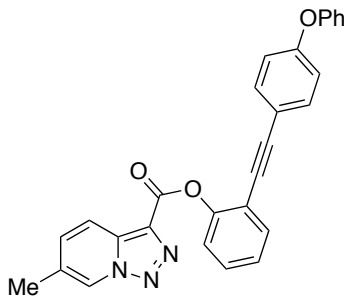
Compound **8-4-ao** was prepared according to the **General Procedure A.**



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 (s, 1 H), 8.26 (d, *J*=9.17 Hz, 1 H), 7.63 (dd, *J*=7.89, 1.28 Hz, 1 H), 7.44 – 7.34 (m, 3 H), 7.30 – 7.27 (m, 1 H), 7.22 – 7.19 (m, 3 H), 7.17 – 7.14 (m, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.13, 151.23, 134.23, 132.98, 132.95, 131.45, 129.48, 128.33, 128.13, 127.23, 126.10, 123.77, 122.80, 122.61, 118.48, 117.49, 94.59, 84.48, 18.22. HRMS (ESI) calculated for $C_{22}H_{16}N_3O_2$ $[M+H]^+$: 354.1243, found: 354.1239.

2-((4-phenoxyphenyl)ethynyl)phenyl 6-methyl-[1,2,3]triazolo[1,5-a]pyridine-3-carboxylate (8-4-ap):

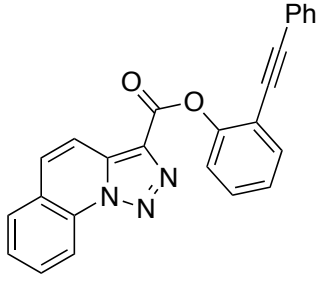
Compound **8-4-ap** was prepared according to the **General Procedure A.**



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 (s, 1 H), 8.27 (d, *J*=8.80 Hz, 1 H), 7.62 (d, *J*=7.34 Hz, 1 H), 7.43 – 7.26 (m, 6 H), 7.17 (d, *J*=8.44 Hz, 2 H), 7.11 (t, *J*=7.15 Hz, 1 H), 6.95 (d, *J*=7.70 Hz, 2 H), 6.77 (d, *J*=8.44 Hz, 2 H), 2.46 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.16, 157.66, 156.26, 151.16, 134.26, 133.08, 132.95, 132.85, 129.85, 129.32, 128.33, 127.24, 126.11, 123.88, 123.80, 122.60, 119.39, 118.48, 118.11, 117.61, 117.33, 94.26, 83.89, 18.23. HRMS (ESI) calculated for $C_{28}H_{20}N_3O_3$ $[M+H]^+$: 446.1505, found: 446.1495.

2-(phenylethynyl)phenyl [1,2,3]triazolo[1,5-a]quinoline-3-carboxylate (8-4-aq):

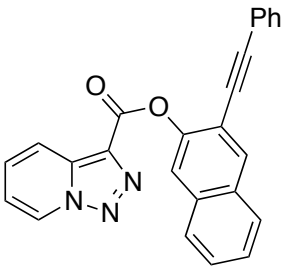
Compound **8-4-aq** was prepared according to the **General Procedure A.**



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.88 (d, *J*=8.07 Hz, 1 H), 8.21 (d, *J*=9.54 Hz, 1 H), 7.91 (d, *J*=8.07 Hz, 1 H), 7.85 (t, *J*=7.70 Hz, 1 H), 7.75 (d, *J*=9.17 Hz, 1 H), 7.70 – 7.64 (m, 2 H), 7.46 – 7.41 (m, 2 H), 7.32 – 7.29 (m, 1 H), 7.25 – 7.24 (m, 2 H), 7.18 – 7.10 (m, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.21, 151.14, 139.52, 134.06, 132.98, 131.40, 131.02, 130.90, 130.40, 129.45, 128.73, 128.28, 128.08, 127.87, 126.12, 123.96, 122.70, 122.56, 117.43, 116.50, 115.40, 94.63, 84.40. HRMS (ESI) calculated for $C_{25}H_{16}N_3O_2$ $[M+H]^+$: 390.1243, found: 390.1233.

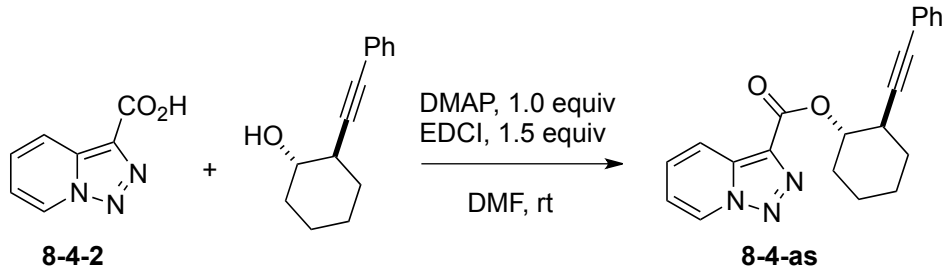
3-(phenylethynyl)naphthalen-2-yl [1,2,3]triazolo[1,5-a]pyridine-3-carboxylate (8-4-ar):

Compound **8-4-ar** was prepared according to the **General Procedure A.**



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.86 (d, *J*=6.97 Hz, 1 H), 8.40 (d, *J*=8.80 Hz, 1 H), 8.15 (s, 1 H), 7.84 – 7.81 (m, 3 H), 7.53 – 7.47 (m, 3 H), 7.23 – 7.13 (m, 6 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.36, 147.67, 135.48, 133.20, 131.37, 131.21, 129.80, 128.55, 128.33, 128.09, 127.61, 127.58, 127.34, 128.45, 126.00, 122.68, 119.86, 119.36, 116.56, 116.39, 94.33, 84.90. HRMS (ESI) calculated for $C_{25}H_{16}N_3O_2$ $[M+H]^+$: 390.1243, found: 390.1234.

2-(phenylethynyl)cyclohexyl [1,2,3]triazolo[1,5-a]pyridine-3-carboxylate (8-4-as):

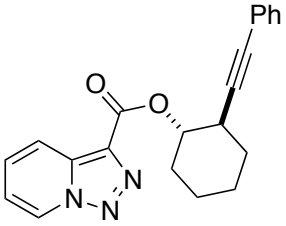


8-4-2 **8-4-as**

Scheme 10-4

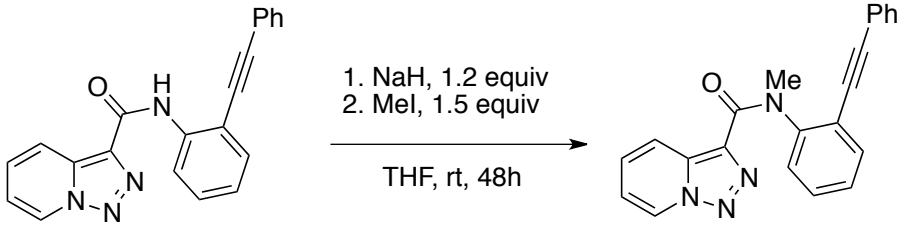
To a stirred suspension of carboxylic acid **8-4-2** (1.0 equiv), 2-(phenylethynyl)cyclohexan-1-ol (1.2 equiv) and 4-(dimethylamino)pyridine (DMAP, 1.0 equiv) in DMF was added 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDCI, 1.5 equiv). The mixture was stirred at room temperature for 2 h (until a clear solution is formed). After water was added, the mixture was extracted with ethyl acetate, and the organic layer was washed with 1 M HCl, water, saturated aqueous Na_2CO_3, and

brine, and dried over anhydrous Na_2SO_4. The solution was concentrated under reduced pressure and the crude product was purified by column chromatography to afford compound **8-4-as**.



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J*=6.72 Hz, 1 H), 8.25 (d, *J*=9.06 Hz, 1 H), 7.47 (dd, *J*=8.33, 7.16 Hz, 1 H), 7.24 – 7.21 (m, 2 H), 7.14 – 7.07 (m, 4 H), 5.24 (td, *J*=9.06, 3.80 Hz, 1 H), 2.95 (td, *J*=9.35, 4.09 Hz, 1 H), 2.26 – 2.13 (m, 2 H), 1.83 – 1.75 (m, 2 H), 1.70 – 1.58 (m, 2 H), 1.53 – 1.45 (m, 1 H), 1.40 – 1.31 (m, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.49, 134.78, 131.30, 129.38, 128.99, 127.86, 127.48, 125.71, 123.23, 119.16, 116.18, 90.03, 82.08, 75.17, 35.20, 30.48, 30.39, 23.84, 23.34. HRMS (ESI) calculated for $C_{21}H_{20}N_3O_2$ $[M+H]^+$: 346.1556, found: 346.1553.

N-methyl-N-(2-(phenylethynyl)phenyl)-[1,2,3]triazolo[1,5-a]pyridine-3-carboxamide (8-4-at):



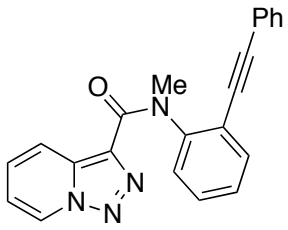
8-4-at' **8-4-at**

Scheme 10-5

Compound **8-4-at'** was prepared according to the **General Procedure A,** followed by methylation to form compound **8-4-at**.

To a THF solution of **8-4-at'** (1.0 equiv) was added NaH (95%, 1.2 equiv) under argon atmosphere at room temperature. After 2 h, MeI (1.5 equiv) was added and the

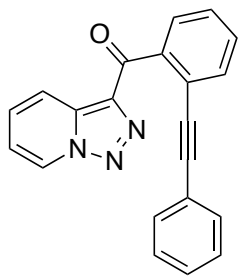
reaction mixture was allowed to react until completion. Then, the mixture was concentrated under reduced pressure and the crude product was purified by column chromatography to afford compound **8-4-at**.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, *J*=6.24 Hz, 1 H), 8.23 (d, *J*=8.44 Hz, 1 H), 7.49 – 7.40 (m, 5 H), 7.28 – 7.22 (m, 5 H), 6.92 (t, *J*=6.05 Hz, 1 H), 3.57 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.68, 146.30, 135.15, 132.84, 132.34, 131.43, 129.42, 128.46, 128.36, 128.17, 127.45, 127.34, 125.05, 122.72, 122.06, 119.87, 115.78, 93.63, 85.84, 37.54. HRMS (ESI) calculated for $C_{22}H_{17}N_4O$ $[M+H]^+$: 353.1402, found: 353.1396.

[1,2,3]triazolo[1,5-a]pyridin-3-yl(2-(phenylethynyl)phenyl)methanone (8-4-ba):

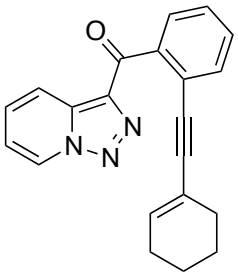
Compound **8-4-ba** was prepared according to the **General Procedure B**.



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (d, *J*=7.02 Hz, 1 H), 8.52 (d, *J*=8.77 Hz, 1 H), 7.92 – 7.90 (m, 1 H), 7.69 (dd, *J*=7.60, 0.88 Hz, 1 H), 7.61 (dd, *J*=8.48, 7.31 Hz, 1 H), 7.54 – 7.46 (m, 2 H), 7.25 – 7.16 (m, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.16, 140.64, 135.19, 133.16, 131.35, 130.62, 130.22, 129.55, 128.17, 128.05, 127.82, 125.72, 122.97, 122.19, 120.12, 116.89, 109.46, 93.47, 87.89. HRMS (ESI) calculated for $C_{21}H_{14}N_3O$ $[M+H]^+$: 324.1137, found: 324.1133.

[1,2,3]triazolo[1,5-a]pyridin-3-yl(2-(cyclohex-1-en-1-ylethynyl)phenyl)methanone (8-4-bb):

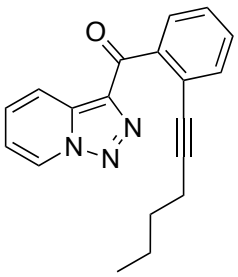
Compound **8-4-bb** was prepared according to the **General Procedure B**.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.85 (d, *J*=6.97 Hz, 1 H), 8.49 (d, *J*=8.80 Hz, 1 H), 7.82 (d, *J*=7.34 Hz, 1 H), 7.62 – 7.55 (m, 2 H), 7.47 – 7.39 (m, 2 H), 7.19 (t, *J*=6.79 Hz, 1 H), 5.90 (br, 1 H), 1.98 (br, 2 H), 1.87 (br, 2 H), 1.49 - 1.48 (m, 4 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 188.44, 140.48, 137.26, 135.33, 135.14, 132.95, 130.52, 130.03, 129.33, 127.28, 125.68, 122.77, 120.50, 120.18, 116.80, 95.65, 85.29, 28.52, 25.58, 22.08, 21.29. HRMS (ESI) calculated for $C_{21}H_{18}N_3O$ $[M+H]^+$: 328.1450, found: 328.1447.

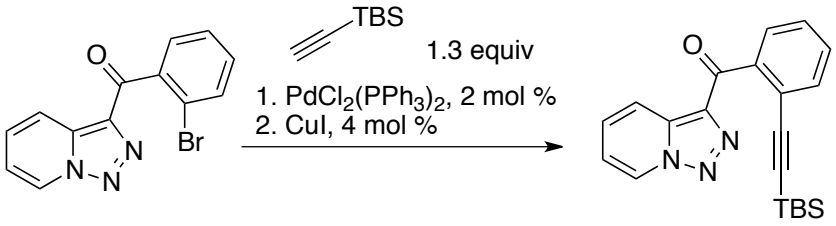
[1,2,3]triazolo[1,5-a]pyridin-3-yl(2-(hex-1-yn-1-yl)phenyl)methanone (8-4-bc):

Compound **8-4-bc** was prepared according to the **General Procedure B**.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.86 (d, *J*=6.60 Hz, 1 H), 8.51 (d, *J*=8.44 Hz, 1 H), 7.75 (d, *J*=6.97 Hz, 1 H), 7.62 (t, *J*=7.52 Hz, 1 H), 7.54 (d, *J*=7.34 Hz, 1 H), 7.46 – 7.40 (m, 2 H), 7.20 (t, *J*=6.60 Hz, 1 H), 2.21 (t, *J*=6.60 Hz, 2 H), 1.27 – 1.16 (m, 4 H), 0.72 (t, *J*=6.97 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 188.91, 140.84, 137.26, 135.14, 133.23, 130.37, 130.06, 128.92, 127.08, 125.74, 122.89, 120.24, 116.81, 95.05, 78.88, 30.33, 21.63, 19.10, 13.45. HRMS (ESI) calculated for $C_{19}H_{18}N_3O$ $[M+H]^+$: 304.1450, found: 304.1450.

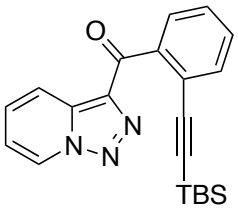
[1,2,3]triazolo[1,5-a]pyridin-3-yl(2-((tert-butyldimethylsilyl) ethynyl) phenyl) methanone (8-4-bd):



8-4-bd' **8-4-bd**

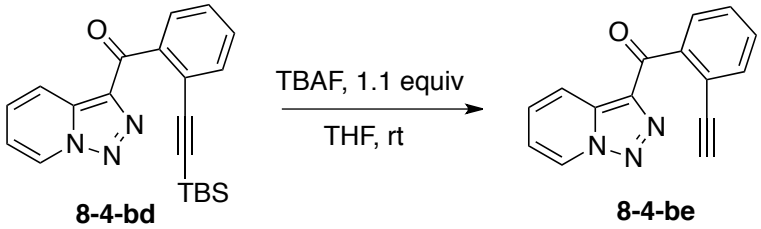
Scheme 10-6

Compound **8-4-bd'** was prepared according to the **General Procedure B**, followed by Sonogashira cross-coupling reaction to form **8-4-bd.**



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.83 (d, *J*=6.97 Hz, 1 H), 8.45 (d, *J*=8.80 Hz, 1 H), 7.72 – 7.70 (m, 1 H), 7.62 – 7.59 (m, 2 H), 7.45 – 7.43 (m, 2 H), 7.18 (t, *J*=6.60 Hz, 1 H), 0.67 (s, 9 H), -0.12 (s, 6 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 188.83, 141.80, 137.17, 134.89, 133.24, 130.17, 128.27, 128.15, 125.68, 121.78, 119.97, 116.86, 103.41, 97.50, 25.66, 16.26, -5.14. HRMS (ESI) calculated for $C_{12}H_{24}N_3OSi$ $[M+H]^+$: 362.1689, found: 362.1681.

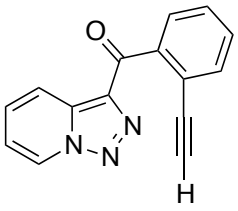
[1,2,3]triazolo[1,5-a]pyridin-3-yl(2-ethynylphenyl)methanone (8-4-be):



8-4-bd **8-4-be**

Scheme 10-7

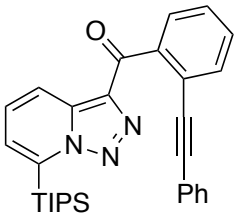
To a THF solution of compound **8-4-bd** was added TBAF (1.1 equiv, 1M solution in THF), and the reaction mixture was stirred at room temperature for 1 h. Upon completion, the mixture was concentrated under reduced pressure, and the crude product was purified by column chromatography to afford compound **8-4-be**.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.87 (d, *J*=6.60 Hz, 1 H), 8.56 (d, *J*=8.80 Hz, 1 H), 7.94 – 7.92 (m, 1 H), 7.69 – 7.62 (m, 2 H), 7.51 – 7.49 (m, 2 H), 7.22 (t, *J*=6.79 Hz, 1 H), 3.14 (s, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 187.75, 140.92, 136.93, 135.49, 134.27, 130.65, 130.39, 129.89, 128.27, 125.83, 121.06, 120.39, 117.03, 81.81, 81.24. HRMS (ESI) calculated for $C_{15}H_{10}N_3O$ $[M+H]^+$: 248.0824, found: 248.0818.

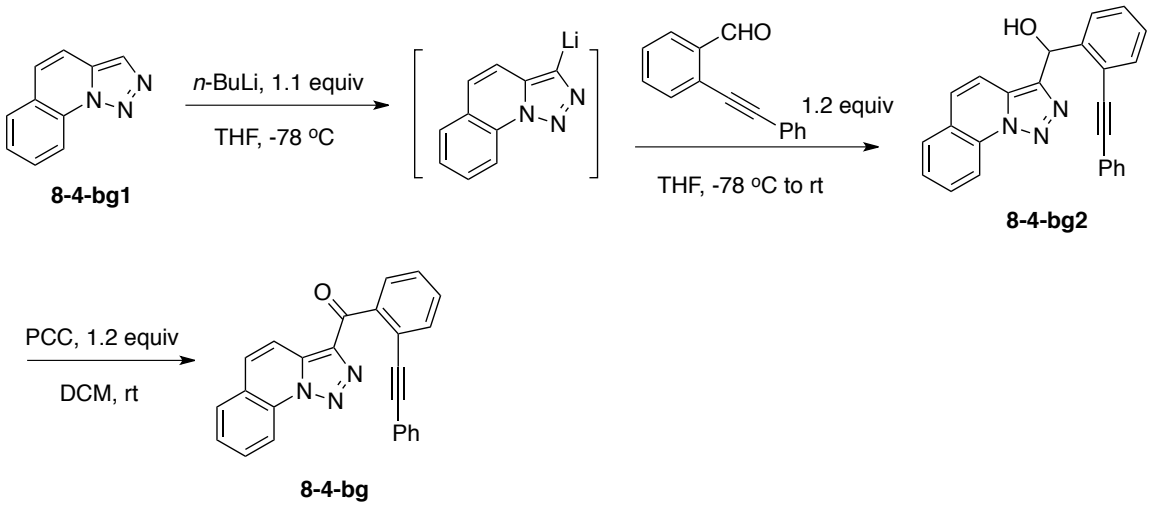
(2-(phenylethynyl)phenyl)(7-(triisopropylsilyl)-[1,2,3]triazolo[1,5-a]pyridin-3-yl)methanone (8-4-bf):

Compound **8-4-bf** was prepared according to the **General Procedure B**.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (d, *J*=8.44 Hz, 1 H), 7.91 (d, *J*=7.34 Hz, 1 H), 7.68 (d, *J*=7.34 Hz, 1 H), 7.58 (t, *J*=7.70 Hz, 1 H), 7.53 – 7.47 (m, 2 H), 7.32 (d, *J*=6.60 Hz, 1 H), 7.20 – 7.16 (m, 5 H), 1.77 (quin, *J*=7.43 Hz, 3 H), 1.09 (d, *J*=7.70 Hz, 18 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 188.58, 141.12, 139.99, 136.65, 135.20, 133.03, 131.39, 130.40, 129.40, 129.03, 128.09, 128.02, 127.89, 125.73, 123.08, 122.22, 120.21, 93.52, 88.06, 18.60, 11.48. HRMS (ESI) calculated for $C_{30}H_{34}N_3OSi$ $[M+H]^+$: 480.2471, found: 480.2467.

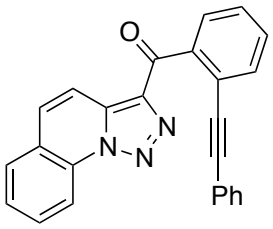
[1,2,3]triazolo[1,5-a]quinolin-3-yl(2-(phenylethynyl)phenyl)methanone (8-4-bg):



8-4-bg1 **8-4-bg2** **8-4-bg**

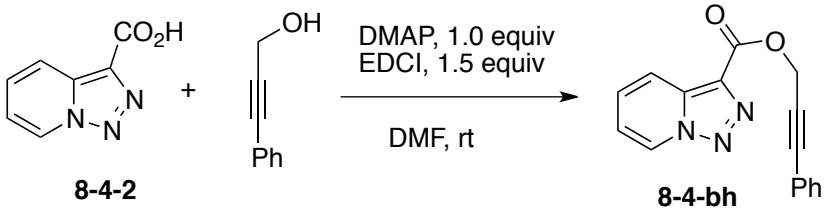
Scheme 10-8

Compound **8-4-bg** was prepared according to the **General Procedure B**.



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, *J*=8.48 Hz, 1 H), 8.30 (d, *J*=9.06 Hz, 1 H), 7.97 (d, *J*=7.02 Hz, 1 H), 7.89 (d, *J*=8.18 Hz, 1 H), 7.84 – 7.78 (m, 2 H), 7.71 (d, *J*=7.31 Hz, 1 H), 7.66 – 7.62 (m, 1 H), 7.56 – 7.48 (m, 2 H), 7.26 – 7.25 (m, 2 H), 7.18 – 7.13 (m, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.49, 140.59, 138.72, 133.68, 133.21, 131.35, 131.20, 131.14, 130.88, 130.72, 129.75, 128.56, 128.12, 127.99, 127.79, 127.70, 124.21, 122.94, 122.31, 116.37, 116.11, 93.57, 87.96. HRMS (ESI) calculated for $C_{25}H_{16}N_3O$ $[M+H]^+$: 374.1293, found: 374.1287.

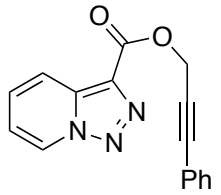
3-phenylprop-2-yn-1-yl [1,2,3]triazolo[1,5-a]pyridine-3-carboxylate (8-4-bh):



8-4-2 **8-4-bh**

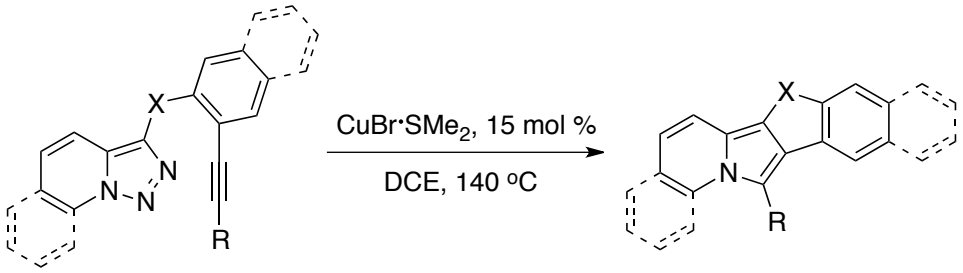
Scheme 10-9

Compound **8-4-bh** was prepared according to the **General Procedure A**.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.83 (d, *J*=6.60 Hz, 1 H), 8.28 (d, *J*=8.44 Hz, 1 H), 7.56 (t, *J*=7.52 Hz, 1 H), 7.44 (d, *J*=5.87 Hz, 2 H), 7.29 – 7.28 (m, 3 H), 7.16 (t, *J*=6.42 Hz, 1 H), 5.27 (s, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.49, 135.15, 131.80, 129.49, 128.68, 128.18, 125.92, 122.00, 119.20, 116.46, 86.75, 82.69, 53.17. HRMS (ESI) calculated for $C_{16}H_{12}N_3O_2$ $[M+H]^+$: 278.0930, found: 278.0929.

6.2.3. Cu-catalyzed intramolecular transannulation reaction



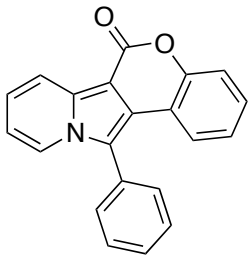
8-4 **8-5**

Scheme 10-10

General Procedure: An oven-dried 3.0 mL V-vial equipped with a stirring bar was charged with CuBr•SMe_2 (15 mol %), alkynylpyridotriazole **8-4** (0.2 mmol) and DCE (2 mL) under N_2 atmosphere. The reaction vessel was capped with Mininert syringe valve and the reaction mixture was stirred at 140 °C. Upon completion the reaction mixture was cooled to room temperature, concentrated under reduced pressure, and the crude product was purified by column chromatography to afford the corresponding transannulation product **8-5**.

12-phenyl-6H-chromeno[3,4-a]indolizin-6-one (8-5-aa):

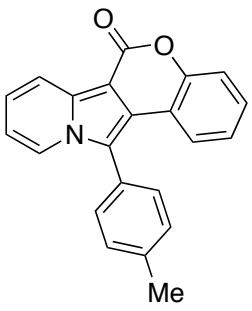
Was prepared according to the **General Procedure** in 83% yield.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37 (d, *J*=8.80 Hz, 1 H), 7.94 (d, *J*=6.60 Hz, 1 H), 7.66 – 7.60 (m, 3 H), 7.57 – 7.56 (m, 2 H), 7.36 – 7.34 (m, 2 H), 7.31 – 7.28 (m, 1 H), 7.21 (t, *J*=7.70 Hz, 1 H), 6.98 (t, *J*=7.52 Hz, 1 H), 6.87 (t, *J*=6.79 Hz, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.92, 152.43, 134.40, 131.45, 130.06, 129.89, 129.77, 128.58, 123.74, 123.46, 123.31, 122.52, 119.46, 118.95, 117.62, 116.67, 114.64, 96.85. HRMS (ESI) calculated for $C_{21}H_{13}NO_2$ $[M+H]^+$: 312.1025, found: 312.1016. Overlapping signals in ^{13}C spectrum due to highly aromatic structure.

12-(p-tolyl)-6H-chromeno[3,4-a]indolizin-6-one (8-5-ab):

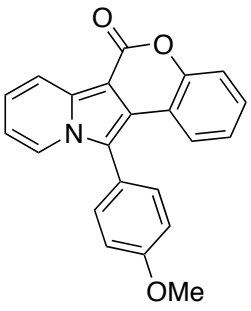
Was prepared according to the **General Procedure** in 75% yield.



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J*=8.77 Hz, 1 H), 7.95 (d, *J*=7.02 Hz, 1 H), 7.46 - 7.27 (m, 7 H), 7.23 - 7.19 (m, 1 H), 6.99 (t, *J*=7.31 Hz, 1 H), 6.86 (t, *J*=6.72 Hz, 1 H), 2.52 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.00, 152.39, 139.82, 134.35, 131.23, 130.60, 128.49, 126.89, 123.79, 123.42, 123.38, 122.41, 119.42, 119.07, 117.59, 116.78, 114.54, 96.72, 21.52. HRMS (ESI) calculated for $C_{22}H_{15}NO_2$ $[M+H]^+$: 326.1181, found: 326.1174.

12-(4-methoxyphenyl)-6H-chromeno[3,4-a]indolizin-6-one (8-5-ac):

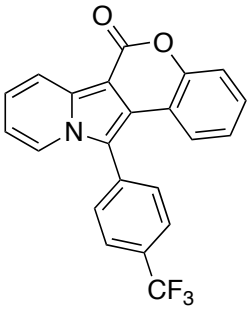
Was prepared according to the **General Procedure** in 85% yield.



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J*=8.77 Hz, 1 H), 7.93 (d, *J*=7.02 Hz, 1 H), 7.47 – 7.44 (m, 2 H), 7.38 – 7.27 (m, 3 H), 7.22 – 7.14 (m, 3 H), 7.01 – 6.97 (m, 1 H), 6.86 (td, *J*=6.87, 1.17 Hz, 1 H), 3.94 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.55, 158.97, 152.39, 134.28, 132.75, 128.46, 123.74, 123.36, 123.33, 122.51, 121.78, 119.38, 118.82, 117.57, 116.81, 115.30, 114.53, 96.63, 55.39. HRMS (ESI) calculated for $C_{22}H_{15}NO_3$ $[M+H]^+$: 342.1130, found: 342.1124.

12-(4-(trifluoromethyl)phenyl)-6H-chromeno[3,4-a]indolizin-6-one (8-5-ad):

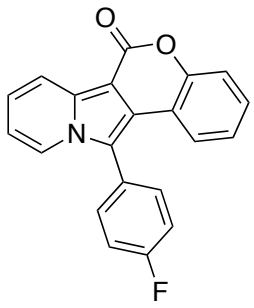
Was prepared according to the **General Procedure** in 80% yield.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 (d, *J*=8.44 Hz, 1 H), 7.96 – 7.88 (m, 3 H), 7.77 – 7.76 (m, 2 H), 7.33 – 7.29 (m, 3 H), 7.24 – 7.21 (m, 1 H), 7.04 – 6.98 (m, 1 H), 6.93 – 6.87 (m, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.64, 152.46, 134.77, 134.11, 132.09, 131.76 (q, *J*=34.0 Hz), 129.00, 126.89 (q, *J*=3.78 Hz), 123.90, 123.82 (d, *J*=272.2 Hz), 123.62, 123.14, 122.97, 119.64, 117.84, 117.03, 116.19, 115.06, 97.24. HRMS (ESI) calculated for $C_{22}H_{12}F_3NO_2$ $[M+H]^+$: 380.0898, found: 380.0893. Overlapping signals in ^{13}C spectrum due to highly aromatic structure.

12-(4-fluorophenyl)-6H-chromeno[3,4-a]indolizin-6-one (8-5-ae):

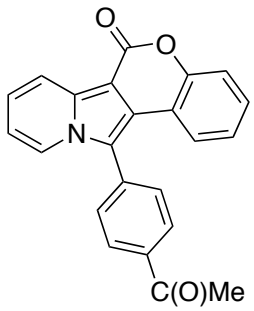
Was prepared according to the **General Procedure** in 73% yield.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 (d, *J*=8.80 Hz, 1 H), 7.90 (d, *J*=6.97 Hz, 1 H), 7.58 – 7.55 (m, 2 H), 7.37 – 7.28 (m, 5 H), 7.21 (t, *J*=7.70 Hz, 1 H), 7.00 (t, *J*=7.15 Hz, 1 H), 6.88 (t, *J*=6.60 Hz, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.47 (d, *J*=249.5 Hz), 158.79, 152.43, 134.45, 133.62, 133.55, 128.73, 126.04 (d, *J*=3.78 Hz), 123.68, 123.50, 123.15, 122.86, 119.49, 117.71, 117.62, 117.20 (d, *J*=21.4 Hz), 116.50, 114.80, 96.85. HRMS (ESI) calculated for $C_{21}H_{12}FNO_2$ $[M+H]^+$: 330.0930, found: 330.0929.

2-(4-acetylphenyl)-6H-chromeno[3,4-a]indolizin-6-one (8-5-af):

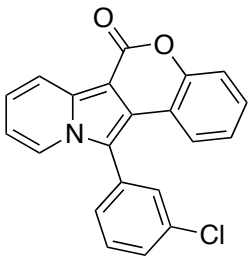
Was prepared according to the **General Procedure** in 78% yield.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (d, *J*=8.80 Hz, 1 H), 8.23 (d, *J*=8.07 Hz, 2 H), 7.97 (d, *J*=6.97 Hz, 1 H), 7.73 (d, *J*=8.07 Hz, 2 H), 7.35 – 7.31 (m, 3 H), 7.27 – 7.24 (m, 1 H), 6.99 (t, *J*=7.52 Hz, 1 H), 6.91 (t, *J*=6.79 Hz, 1 H), 2.74 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.35, 158.71, 152.49, 137.84, 135.02, 134.83, 131.80, 129.70, 128.98, 123.92, 123.59, 123.06, 119.70, 117.84, 117.55, 116.30, 115.03, 97.33, 26.76. HRMS (ESI) calculated for $C_{23}H_{15}NO_3$ $[M+H]^+$: 354.1130, found: 354.1126.

12-(3-chlorophenyl)-6H-chromeno[3,4-a]indolizin-6-one (8-5-ag):

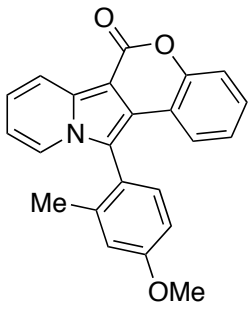
Was prepared according to the **General Procedure** in 58% yield.



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, *J*=8.48 Hz, 1 H), 7.94 (d, *J*=6.72 Hz, 1 H), 7.60 – 7.59 (m, 3 H), 7.49 (br, 1 H), 7.38 – 7.33 (m, 3 H), 7.28 – 7.24 (m, 1 H), 7.03 (t, *J*=6.87 Hz, 1 H), 6.92 (t, *J*=6.72 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.79, 152.46, 135.71, 134.60, 131.95, 131.48, 131.25, 130.06, 129.82, 128.89, 123.82, 123.64, 123.61, 123.17, 122.97, 119.60, 117.79, 117.16, 116.30, 114.97, 97.03. HRMS (ESI) calculated for $C_{21}H_{12}ClNO_2$ $[M+H]^+$: 346.0635, found: 346.0630.

12-(4-methoxy-2-methylphenyl)-6H-chromeno[3,4-a]indolizin-6-one (8-5-ah):

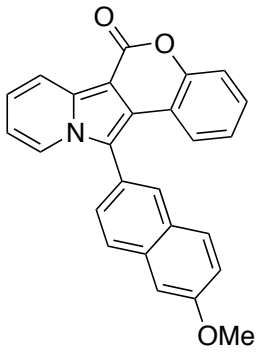
Was prepared according to the **General Procedure** in 76% yield.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (d, *J*=8.80 Hz, 1 H), 7.71 (d, *J*=6.60 Hz, 1 H), 7.38 – 7.36 (m, 1 H), 7.32 – 7.29 (m, 2 H), 7.27 – 7.24 (m, 1 H), 7.19 (d, *J*=7.70 Hz, 1 H), 7.03 – 6.96 (m, 3 H), 6.89 (t, *J*=6.60 Hz, 1 H), 3.93 (s, 3 H), 2.00 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.90, 159.05, 152.45, 141.26, 134.37, 133.20, 128.46, 123.67, 123.55, 123.33, 123.27, 122.84, 121.11, 119.49, 118.09, 117.52, 116.97, 116.47, 114.64, 112.59, 96.60, 55.31, 19.49. HRMS (ESI) calculated for $C_{23}H_{17}NO_3$ $[M+H]^+$: 356.1287, found: 356.1279.

12-(6-methoxynaphthalen-2-yl)-6H-chromeno[3,4-a]indolizin-6-one (8-5-ai):

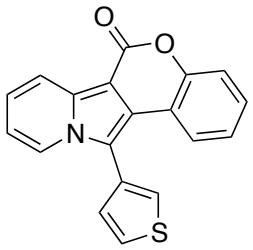
Was prepared according to the **General Procedure** in 81% yield.



^{1}H NMR (500 MHz, DMSO-*d*6) δ 8.25 (d, *J*=8.44 Hz, 1 H), 8.18 – 8.16 (m, 2 H), 8.12 (d, *J*=8.44 Hz, 1 H), 7.94 (d, *J*=8.80 Hz, 1 H), 7.64 (d, *J*=8.07 Hz, 1 H), 7.51 (s, 1 H), 7.45 (t, *J*=7.52 Hz, 1 H), 7.38 – 7.35 (m, 2 H), 7.28 – 7.26 (m, 2 H), 7.09 (t, *J*=6.42 Hz, 1 H), 7.01 (t, *J*=6.60 Hz, 1 H), 3.94 (s, 3 H). ^{13}C NMR (126 MHz, DMSO-*d*6) δ 158.91, 158.04, 152.36, 135.27, 134.25, 131.41, 130.36, 129.49, 129.35, 129.07, 129.01, 125.35, 124.88, 124.54, 124.32, 123.74, 122.02, 119.96, 119.74, 118.70, 117.88, 116.76, 115.95, 106.62, 96.07, 55.90. HRMS (ESI) calculated for $C_{26}H_{17}NO_3$ $[M+H]^+$: 392.1287, found: 292.1277.

12-(thiophen-3-yl)-6H-chromeno[3,4-a]indolizin-6-one (8-5-aj):

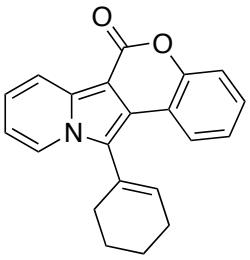
Was prepared according to the **General Procedure** in 64% yield.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 (d, *J*=8.44 Hz, 1 H), 7.98 (d, *J*=5.87 Hz, 1 H), 7.67 (br, 2 H), 7.43 (d, *J*=6.97 Hz, 1 H), 7.33 – 7.29 (m, 3 H), 7.21 – 7.19 (m, 1 H), 7.05 – 7.02 (m, 1 H), 6.90 – 6.87 (m, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.86, 152.45, 134.64, 129.81, 129.18, 128.70, 128.15, 127.89, 123.77, 123.67, 123.58, 123.55, 123.40, 119.43, 117.64, 116.65, 114.71, 113.58, 96.85. HRMS (ESI) calculated for $C_{19}H_{11}NO_2S$ $[M+H]^+$: 318.0589, found: 318.0584.

12-(cyclohex-1-en-1-yl)-6H-chromeno[3,4-a]indolizin-6-one (8-5-ak):

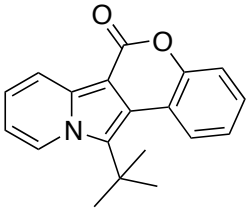
Was prepared according to the **General Procedure** in 47% yield.



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, *J*=8.77 Hz, 1 H), 8.08 (d, *J*=7.02 Hz, 1 H), 7.95 (d, *J*=7.60 Hz, 1 H), 7.37 – 7.35 (m, 2 H), 7.24 – 7.18 (m, 2 H), 6.94 (td, *J*=6.87, 0.88 Hz, 1 H), 6.21 – 6.19 (m, 1 H), 2.38 – 2.37 (m, 2 H), 2.29 -2.28 (m, 2 H), 1.95 – 1.85 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.03, 152.33, 135.71, 133.94, 128.27, 128.20, 123.83, 123.67, 123.29, 122.91, 121.13, 120.96, 119.49, 117.60, 117.08, 114.42, 96.25, 27.96, 25.85, 22.86, 21.85. HRMS (ESI) calculated for $C_{21}H_{17}NO_2$ $[M+H]^+$: 316.1338, found: 316.1330.

12-(tert-butyl)-6H-chromeno[3,4-a]indolizin-6-one (8-5-al):

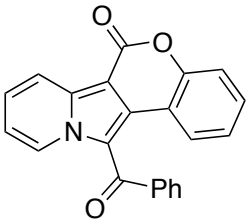
Was prepared according to the **General Procedure** in 41% yield.



^{1}H NMR (500 MHz, acetone-*d*6) δ 8.97 (d, *J*=7.34 Hz, 1 H), 8.37 (d, *J*=8.80 Hz, 1 H), 8.19 – 8.17 (m, 1 H), 7.44 – 7.41 (m, 1 H), 7.34 – 7.30 (m, 3 H), 7.06 – 7.03 (m, 1 H), 1.83 (s, 9 H). ^{13}C NMR (126 MHz, acetone-*d*6) δ 157.84, 152.28, 135.05, 129.63, 128.66, 128.23, 127.86, 125.74, 124.55, 122.82, 119.02, 117.74, 117.45, 113.76, 97.95, 34.07, 28.94. HRMS (ESI) calculated for $C_{19}H_{17}NO_2$ $[M+H]^+$: 292.1338, found: 292.1338.

12-benzoyl-6H-chromeno[3,4-a]indolizin-6-one (8-5-am):

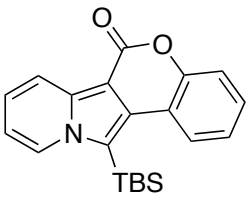
Was prepared according to the **General Procedure** in 50% yield.



^{1}H NMR (500 MHz, $CDCl_3$) δ 9.25 (d, *J*=6.97 Hz, 1 H), 8.56 (d, *J*=8.80 Hz, 1 H), 7.85 (d, *J*=7.70 Hz, 2 H), 7.59 – 7.56 (m, 1 H), 7.52 (t, *J*=7.70 Hz, 1 H), 7.44 – 7.41 (m, 2 H), 7.35 – 7.33 (m, 1 H), 7.30 – 7.28 (m, 1 H), 7.13 (t, *J*=6.79 Hz, 1 H), 6.97 (d, *J*=8.07 Hz, 1 H), 6.75 (t, *J*=7.52 Hz, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 187.69, 158.23, 153.11, 139.06, 137.30, 133.48, 130.40, 129.87, 129.83, 129.17, 127.92, 127.70, 127.56, 123.14, 119.50, 117.72, 117.36, 116.53, 114.89, 96.06. HRMS (ESI) calculated for $C_{22}H_{13}NO_3$ $[M+H]^+$: 340.0974, found: 340.0970.

12-(tert-butyldimethylsilyl)-6H-chromeno[3,4-a]indolizin-6-one (8-5-an):

An oven-dried 3.0 mL V-vial equipped with a stirring bar was charged with $[Rh^*CpCl_2]_2$ (5 mol %), alkynylpyridotriazole **8-4-an** (0.2 mmol) and mesitylene (2 mL) under N_2 atmosphere. The reaction vessel was capped with Mininert syringe valve and the reaction mixture was stirred at 140 °C. Upon completion the reaction mixture was cooled to room temperature, concentrated under reduced pressure, and the crude product was purified by column chromatography to afford the transannulation products in 67% yield.

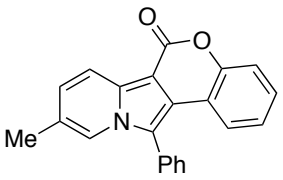


^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, *J*=6.97 Hz, 1 H), 8.49 (d, *J*=8.80 Hz, 1 H), 8.11 (d, *J*=8.07 Hz, 1 H), 7.41 (d, *J*=3.67 Hz, 2 H), 7.33 – 7.30 (m, 1 H), 7.25 – 7.22 (m, 1 H), 6.95 (t, *J*=6.79 Hz, 1 H), 1.20 (s, 9 H), 0.55 (s, 6 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.93, 152.39, 139.11, 136.30, 128.93, 128.59, 126.89, 124.27, 122.46, 119.90, 117.81, 117.37, 117.15, 114.14,

99.96, 27.58, 20.35, -1.37. HRMS (ESI) calculated for $C_{21}H_{23}NO_2Si$ $[M+H]^+$: 350.1576, found: 350.1570.

9-methyl-12-phenyl-6H-chromeno[3,4-a]indolizin-6-one (8-5-ao):

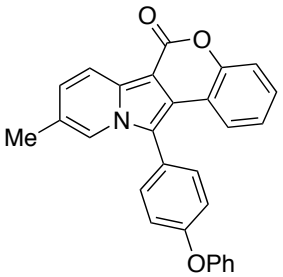
Was prepared according to the **General Procedure** in 78% yield.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (d, *J*=9.17 Hz, 1 H), 7.71 (s, 1 H), 7.68 – 7.61 (m, 3 H), 7.56 (d, *J*=6.24 Hz, 2 H), 7.36 – 7.27 (m, 3 H), 7.08 (d, *J*=9.17 Hz, 1 H), 6.97 (t, *J*=7.52 Hz, 1 H), 2.28 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.03, 152.45, 133.19, 131.57, 130.36, 129.92, 129.73, 128.42, 126.61, 124.67, 123.70, 123.44, 121.21, 118.88, 118.63, 117.67, 116.91, 109.58, 96.61, 18.63. HRMS (ESI) calculated for $C_{22}H_{16}NO_2$ $[M+H]^+$: 326.1181, found: 326.1177.

9-methyl-12-(4-phenoxyphenyl)-6H-chromeno[3,4-a]indolizin-6-one (8-5-ap):

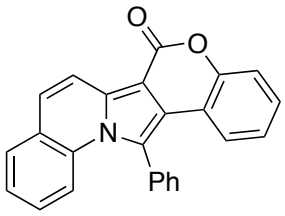
Was prepared according to the **General Procedure** in 71% yield.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, *J*=9.17 Hz, 1 H), 7.73 (s, 1 H), 7.50 (d, *J*=8.44 Hz, 2 H), 7.47 – 7.44 (m, 2 H), 7.38 – 7.28 (m, 3 H), 7.25 – 7.20 (m, 5 H), 7.06 – 7.00 (m, 2 H), 2.29 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.00, 155.91, 152.44, 133.16, 133.11, 130.08, 128.42, 126.58, 124.66, 124.41, 124.30, 123.66, 123.46, 122.57, 121.20, 120.07, 119.10, 118.83, 118.04, 117.68, 116.95, 96.52, 18.66. HRMS (ESI) calculated for $C_{28}H_{20}NO_3$ $[M+H]^+$: 418.1443, found: 418.1441.

14-phenyl-6H-chromeno[3',4':3,4]pyrrolo[1,2-a]quinolin-6-one (8-5-aq):

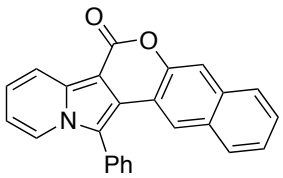
PhCl was used as solvent and heated at 180 ^{o}C to afford the product in 60% yield.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.45 (d, *J*=9.17 Hz, 1 H), 7.79 (d, *J*=7.70 Hz, 1 H), 7.71 – 7.69 (m, 3 H), 7.63 – 7.62 (m, 2 H), 7.54 (d, *J*=9.17 Hz, 1 H), 7.39 – 7.35 (m, 3 H), 7.28 – 7.27 (m, 1 H), 7.19 (t, *J*=7.70 Hz, 1 H), 6.92 – 6.92 (m, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.21, 152.23, 134.37, 134.08, 133.80, 131.58, 130.18, 130.08, 129.33, 128.24, 128.06, 126.05, 125.21, 124.98, 123.61, 123.43, 122.00, 117.92, 117.68, 117.62, 116.99, 99.56. HRMS (ESI) calculated for $C_{25}H_{15}NO_2$ $[M+H]^+$: 362.1181, found: 362.1181.

13-phenyl-7H-benzo[6,7]chromeno[3,4-a]indolizin-7-one (8-5-ar):

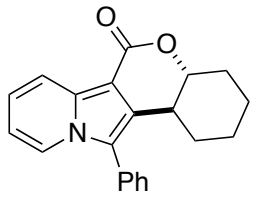
Was prepared according to the **General Procedure** in 68% yield.



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, *J*=9.06 Hz, 1 H), 7.98 (d, *J*=7.02 Hz, 1 H), 7.82 (s, 1 H), 7.77 (d, *J*=8.18 Hz, 1 H), 7.73 – 7.68 (m, 4 H), 7.65 – 7.63 (m, 2 H), 7.50 (d, *J*=8.18 Hz, 1 H), 7.43 – 7.40 (m, 1 H), 7.33 – 7.30 (m, 1 H), 7.25 – 7.21 (m, 1 H), 6.88 (td, *J*=6.87, 1.17 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.91, 150.46, 134.78, 133.05, 131.49, 130.07, 130.00, 129.96, 129.71, 127.87, 127.14, 126.60, 124.97, 123.70, 123.39, 123.02, 122.22, 119.61, 119.52, 117.00, 114.67, 113.30, 96.88. HRMS (ESI) calculated for $C_{25}H_{15}NO_2$ $[M+H]^+$: 362.1181, found: 362.1168.

12-phenyl-1,2,3,4,4a,12b-hexahydro-6H-chromeno[3,4-a]indolizin-6-one (8-5-as):

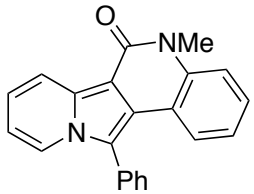
Was prepared according to the **General Procedure** in 60% yield.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (d, *J*=8.80 Hz, 1 H), 7.76 (d, *J*=6.97 Hz, 1 H), 7.52 – 7.48 (m, 3 H), 7.38 (br, 2 H), 7.12 – 7.09 (m, 1 H), 6.67 (t, *J*=6.60 Hz, 1 H), 4.13 (td, *J*=11.19, 4.03 Hz, 1 H), 2.99 (td, *J*=11.46, 3.48 Hz, 1 H), 1.71 (qd, *J*=12.29, 3.85 Hz, 1 H), 1.58 – 1.56 (m, 1 H), 1.36 – 1.18 (m, 2 H), 1.00 (qd, *J*=12.78, 3.12 Hz, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.23, 135.11, 131.31, 130.55, 129.52, 129.00, 123.43, 123.24, 120.53, 119.02, 113.02, 99.38, 83.32, 38.66, 31.67, 27.86, 25.17, 24.30. HRMS (ESI) calculated for $C_{21}H_{19}NO_2$ $[M+H]^+$: 318.1494, found: 318.1489.

5-methyl-12-phenylindolizino[1,2-c]quinolin-6(5H)-one (8-5-at):

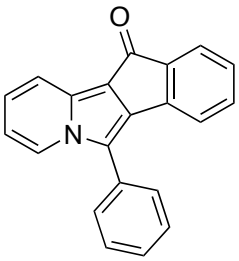
Was prepared according to the **General Procedure** in 52% yield.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (d, *J*=8.80 Hz, 1 H), 7.91 (d, *J*=6.97 Hz, 1 H), 7.66 – 7.55 (m, 6 H), 7.39 – 7.39 (m, 2 H), 7.17 – 7.14 (m, 1 H), 6.95 (dt, *J*=7.89, 4.13 Hz, 1 H), 6.82 (t, *J*=6.42 Hz, 1 H), 3.81 (s, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.27, 139.01, 132.23, 131.73, 131.51, 129.87, 129.37, 127.78, 124.40, 122.40, 122.30, 121.30, 120.97, 120.05, 117.77, 117.61, 115.06, 114.03, 102.72, 28.67. HRMS (ESI) calculated for $C_{22}H_{16}N_2O$ $[M+H]^+$: 325.1341, found: 325.1332.

6-phenyl-11H-indeno[2,1-a]indolizin-11-one (8-5-ba):

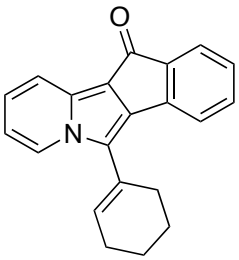
Was prepared according to the **General Procedure** in 91% yield.



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J*=6.97 Hz, 1 H), 7.70 (d, *J*=8.80 Hz, 1 H), 7.62 – 7.48 (m, 6 H), 7.18 – 7.15 (m, 3 H), 7.04 (t, *J*=7.52 Hz, 1 H), 6.56 (t, *J*=6.60 Hz, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.16, 142.48, 138.76, 135.48, 132.43, 132.21, 129.59, 129.42, 129.36, 128.92, 128.03, 125.55, 124.93, 123.49, 120.65, 120.50, 118.96, 113.56, 112.83. HRMS (ESI) calculated for $C_{21}H_{13}NO$ $[M+H]^+$: 296.1075, found: 296.1074.

6-(cyclohex-1-en-1-yl)-11H-indeno[2,1-a]indolizin-11-one (8-5-bb):

Was prepared according to the **General Procedure** in 87% yield.

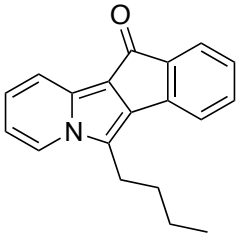


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J*=7.02 Hz, 1 H), 7.64 (d, *J*=8.77 Hz, 1 H), 7.53 (d, *J*=7.31 Hz, 1 H), 7.29 – 7.22 (m, 2 H), 7.16 – 7.13 (m, 1 H), 7.01 – 6.97 (m, 1 H), 6.57 (t, *J*=6.43 Hz, 1 H), 6.14 (br, 1 H), 2.34 – 2.32 (m, 4 H), 1,91 – 1.80 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.04, 142.66, 139.11, 133.96, 133.36, 132.08, 132.01, 127.61, 127.42, 125.68, 124.97, 123.39, 122.98, 120.93, 118.85, 112.84, 112.40, 28.03, 25.63, 22.73, 21.96. HRMS (ESI) calculated for $C_{21}H_{17}NO$ $[M+H]^+$: 300.1388, found: 300.1386.

6-butyl-11H-indeno[2,1-a]indolizin-11-one (8-5-bc):

Was prepared according to the **General Procedure** in 73% yield.

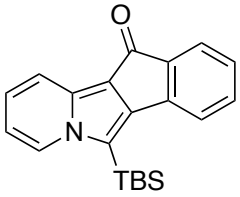
^{1}H NMR (500 MHz, acetone-*d*6) δ 8.12 (d, *J*=6.97 Hz, 1 H), 7.56 (d, *J*=8.80 Hz, 1 H), 7.48 (d, *J*=7.34 Hz, 1 H), 7.43 (d, *J*=7.34 Hz, 1 H), 7.36 (t, *J*=7.34 Hz, 1 H), 7.19 (t,



J=7.52 Hz, 1 H), 7.15 – 7.12 (m, 1 H), 6.77 (t, *J*=6.42 Hz, 1 H), 3.11 (t, *J*=7.52 Hz, 2 H), 1.73 – 1.67 (m, 2 H), 1.50 – 1.42 (m, 2 H), 0.94 (t, *J*=7.34 Hz, 3 H). ^{13}C NMR (126 MHz, acetone-*d*6) δ 183.62, 142.61, 139.38, 133.91, 132.30, 131.72, 127.44, 125.61, 124.96, 122.82, 121.17, 117.98, 112.65, 29.63, 24.19, 22.16, 13.26. HRMS (ESI) calculated for $C_{19}H_{17}NO$ $[M+H]^+$: 276.1388, found: 276.1391.

6-(tert-butyldimethylsilyl)-11H-indeno[2,1-a]indolizin-11-one (8-5-bd):

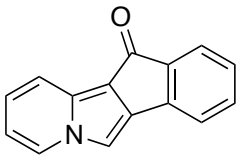
Was prepared according to the **General Procedure** in 90% yield.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, *J*=7.34 Hz, 1 H), 7.72 (d, *J*=8.44 Hz, 1 H), 7.55 (d, *J*=7.34 Hz, 1 H), 7.48 (d, *J*=7.70 Hz, 1 H), 7.30 – 7.27 (m, 1 H), 7.17 (t, *J*=7.34 Hz, 1 H), 7.05 (t, *J*=7.52 Hz, 1 H), 6.57 (t, *J*=6.60 Hz, 1 H), 1.03 (s, 9 H), 0.57 (s, 6 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.07, 148.57, 142.70, 139.74, 135.28, 132.03, 129.36, 127.80, 125.68, 123.25, 122.89, 119.59, 118.72, 115.86, 112.50, 26.50, 19.45, -2.63. HRMS (ESI) calculated for $C_{21}H_{23}NOSi$ $[M+H]^+$: 334.1627, found: 334.1624.

11H-indeno[2,1-a]indolizin-11-one (8-5-be):

Was prepared according to the **General Procedure** in 23% yield.

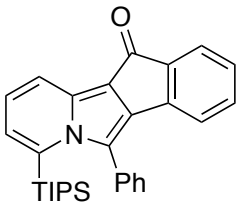


^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, *J*=6.97 Hz, 1 H), 7.67 (d, *J*=9.17 Hz, 1 H), 7.54 (d, *J*=7.34 Hz, 1 H), 7.32 – 7.27 (m, 2 H), 7.18 (t, *J*=7.34 Hz, 1 H), 7.09 (s, 1 H), 7.05 – 7.01 (m, 1 H), 6.60 (t, *J*=6.79 Hz, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.14, 142.43, 138.49, 137.86, 132.37,

128.11, 127.62, 125.48, 123.52, 121.22, 118.93, 113.93, 112.89, 107.22. HRMS (ESI) calculated for $C_{15}H_9NO$ $[M+H]^+$: 220.0762, found: 220.0765.

6-phenyl-4-(triisopropylsilyl)-11H-indeno[2,1-a]indolizin-11-one (8-5-bf):

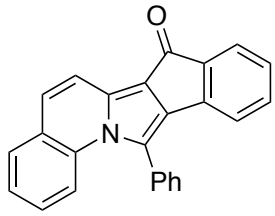
Was prepared according to the **General Procedure** in 95% yield.



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, *J*=8.07 Hz, 1 H), 7.53 – 7.47 (m, 6 H), 7.11 – 7.09 (m, 2 H), 7.01 – 6.98 (m, 2 H), 6.84 – 6.83 (m, 1 H), 0.96 (d, *J*=7.34 Hz, 18 H), 0.76 (dt, *J*=14.76, 7.47 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.48, 142.39, 141.12, 139.14, 137.81, 135.14, 132.58, 132.17, 130.81, 129.03, 128.59, 127.84, 126.92, 125.05, 123.43, 123.30, 120.00, 119.87, 114.37, 19.30, 13.16. HRMS (ESI) calculated for $C_{30}H_{33}NOSi$ $[M+H]^+$: 452.2410, found: 452.2400.

12-phenyl-7H-indeno[2',1':3,4]pyrrolo[1,2-a]quinolin-7-one (8-5-bg):

Was prepared according to the **General Procedure** in 85% yield.

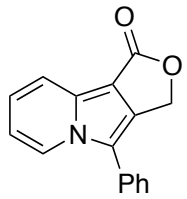


^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, *J*=9.17 Hz, 1 H), 7.66 – 7.57 (m, 7 H), 7.37 (d, *J*=9.17 Hz, 1 H), 7.32 (d, *J*=8.80 Hz, 1 H), 7.28 – 7.26 (m, 1 H), 7.18 – 7.12 (m, 3 H), 6.90 (d, *J*=6.97 Hz, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.43, 142.00, 139.36, 135.25, 134.83, 133.47, 132.72, 131.36, 130.05, 129.20, 129.11, 128.38, 127.74, 126.80, 125.39, 124.24, 124.21, 123.77, 120.43, 117.67, 117.33, 116.24. HRMS (ESI) calculated for $C_{25}H_{15}NO$ $[M+H]^+$: 346.1232, found: 346.1228.

4-phenyl-1H,3H-furo[3,4-a]indolizin-1-one (8-5-bh):

Was prepared according to the general procedure in 40% yield.

Rh(II) conditions: An oven-dried 3.0 mL V-vial equipped with a stirring bar was charged with $Rh(esp)_2$ (1.0 mol %), alkynylpyridotriazole **8-4-bh** (0.2 mmol) and PhMe (2 mL) under N_2 atmosphere. The reaction vessel was capped with Mininert syringe valve and the reaction mixture was stirred at 120 °C. Upon completion the reaction mixture was cooled to room temperature, concentrated under reduced pressure, and the crude product was purified by column chromatography to afford **8-5-bh** in 84% yield.



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (d, *J*=6.97 Hz, 1 H), 7.87 (d, *J*=8.80 Hz, 1 H), 7.54 – 7.48 (m, 4 H), 7.42 – 7.40 (m, 1 H), 7.15 – 7.12 (m, 1 H), 6.84 (t, *J*=6.60 Hz, 1 H), 5.35 (s, 2 H). ^{13}C NMR (126 MHz, DMSO-*d6*) δ 166.50, 138.50, 129.88, 129.82, 129.44, 128.38, 127.98, 125.14, 123.85, 117.93, 116.66, 114.79, 103.57, 66.25. HRMS (ESI) calculated for $C_{16}H_{11}NO_2$ $[M+H]^+$: 250.0868, found: 250.0871.

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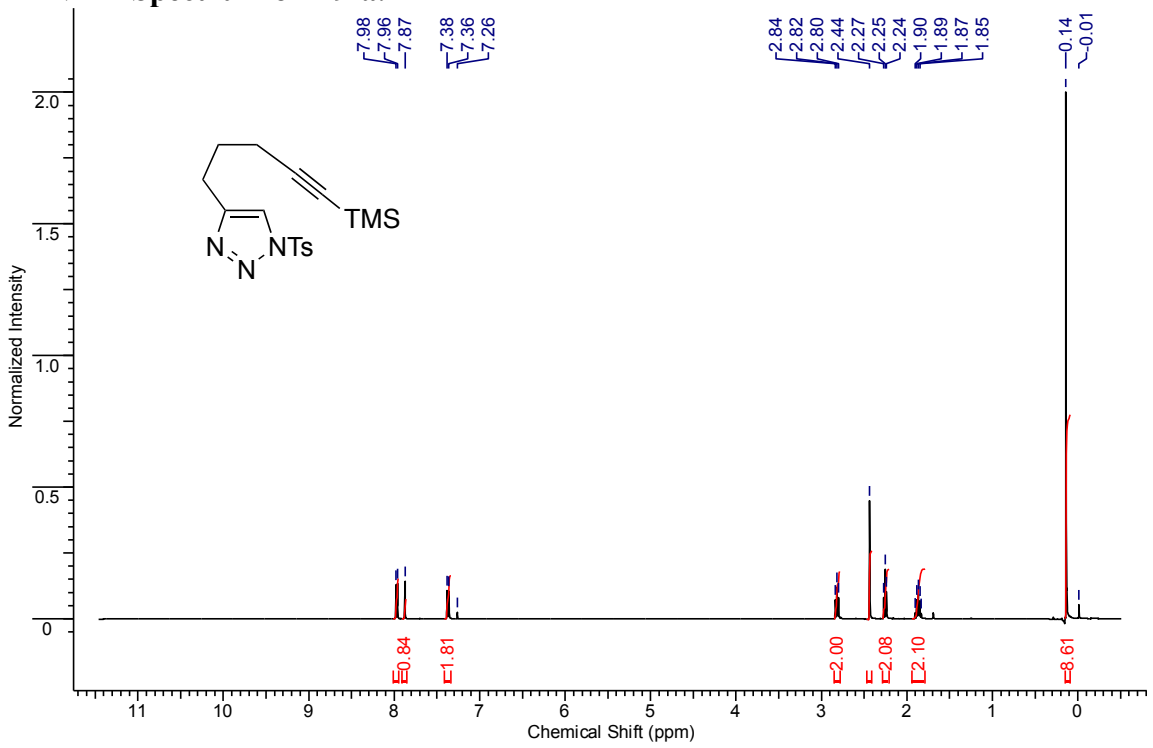
8. APPENDICES

^{1}H NMR Spectrum of 4-9-a:



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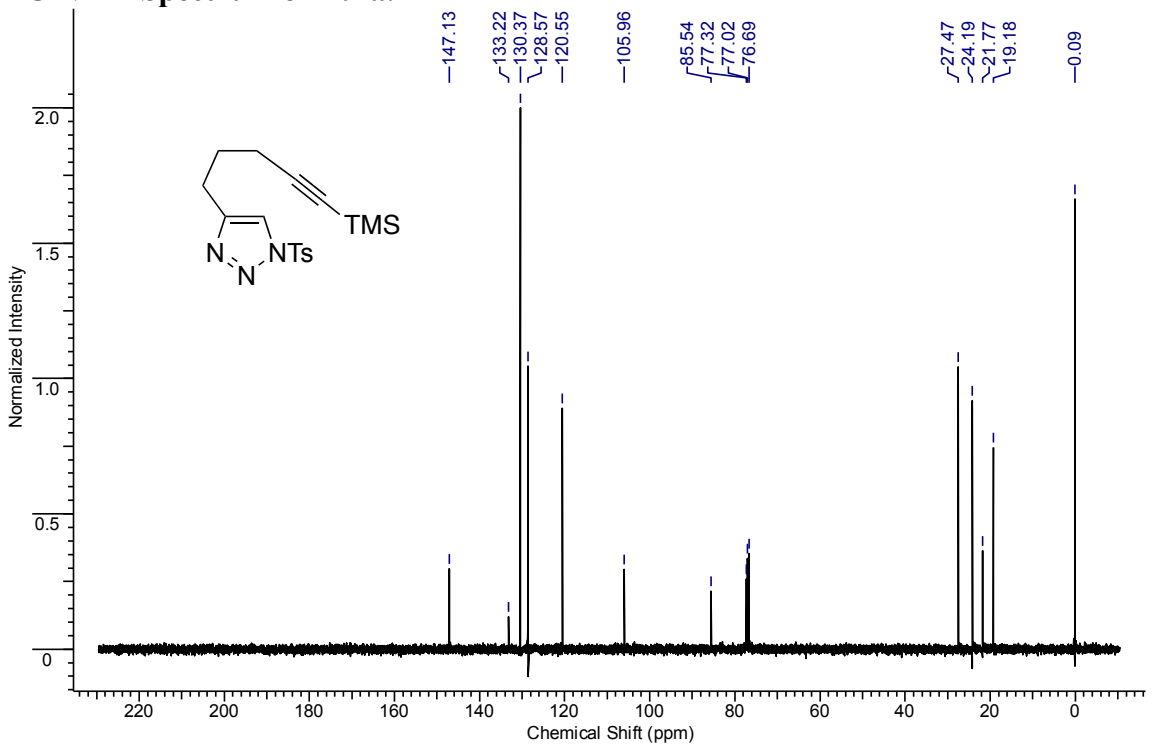

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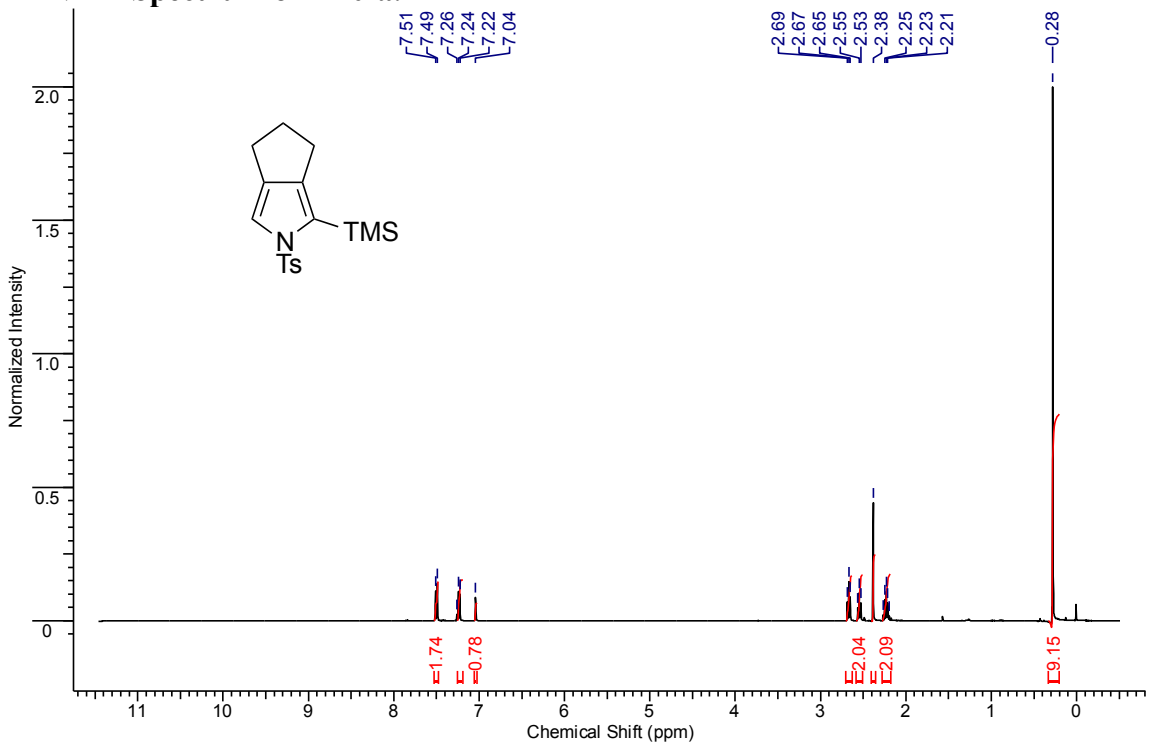

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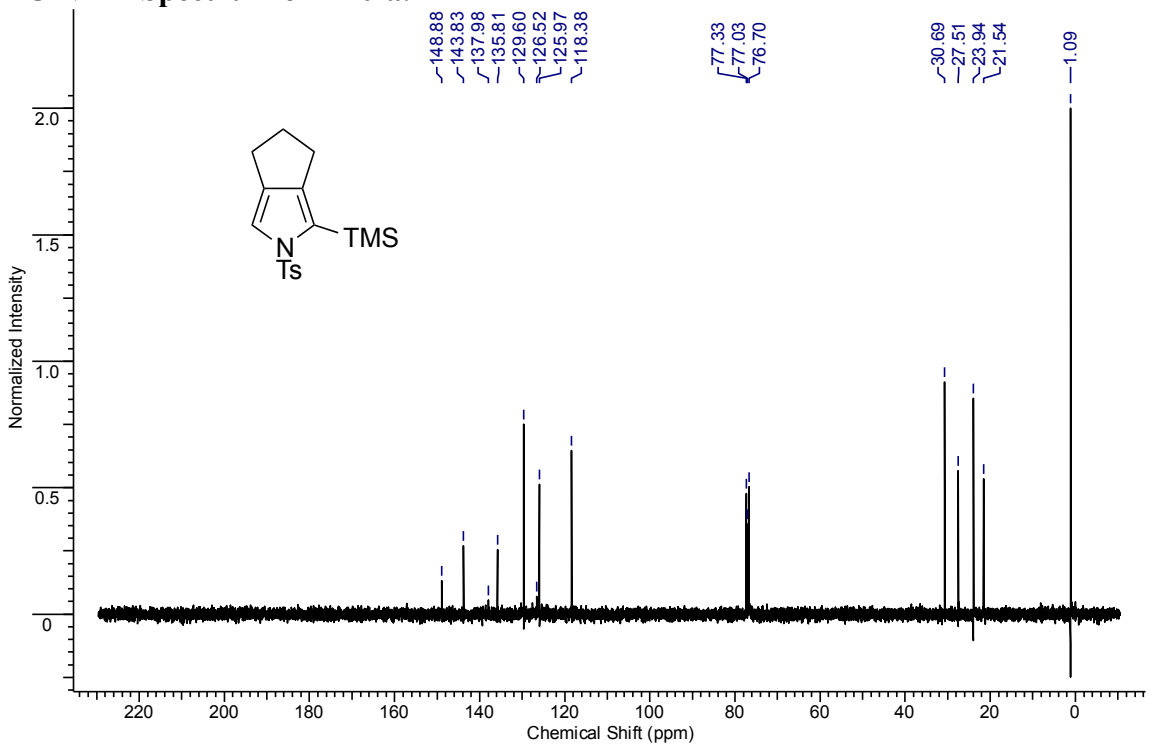

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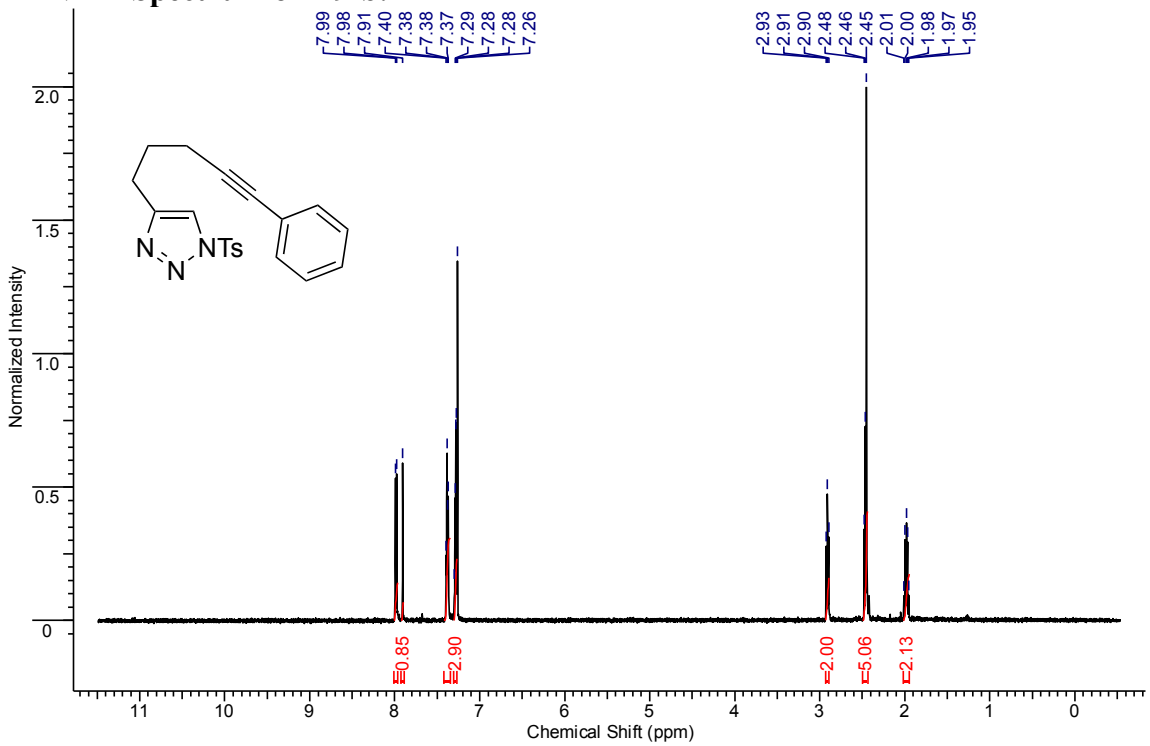

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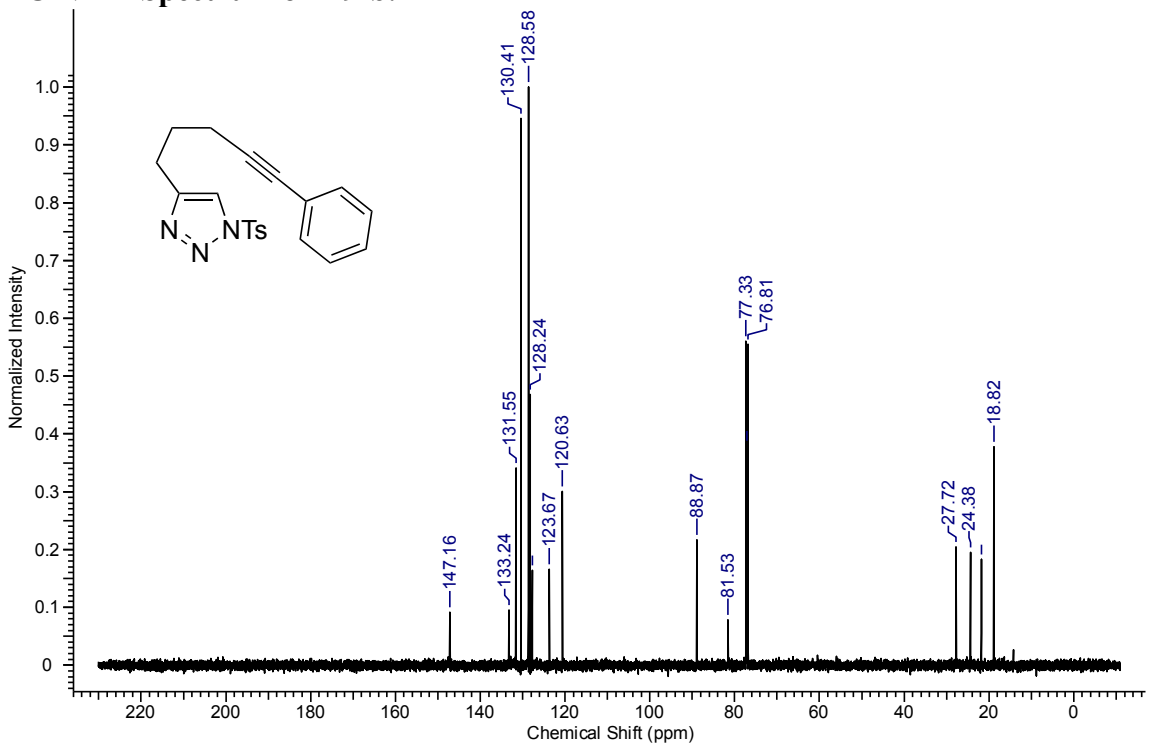

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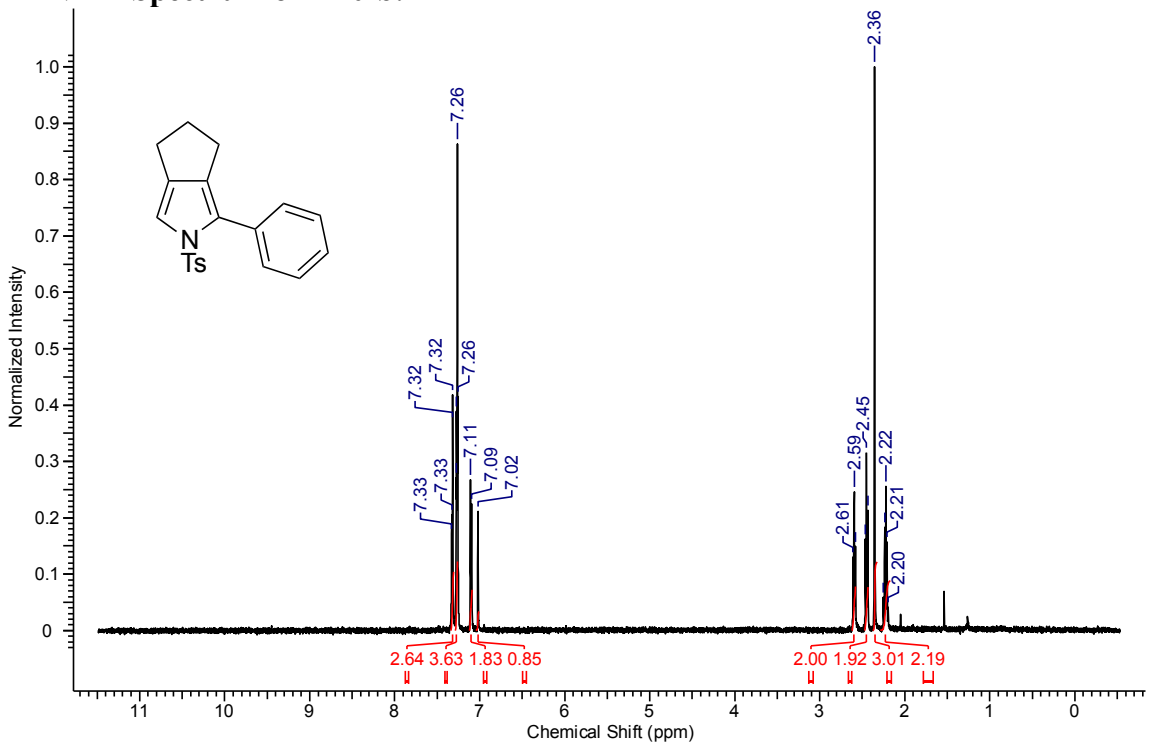

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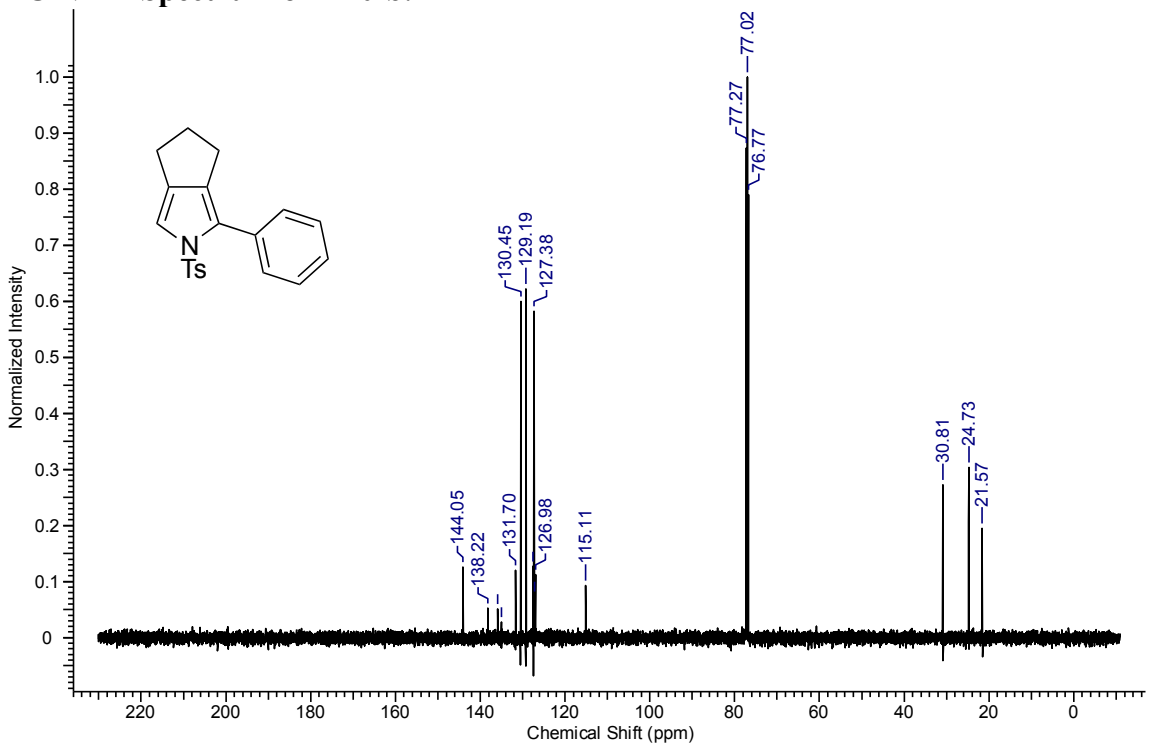

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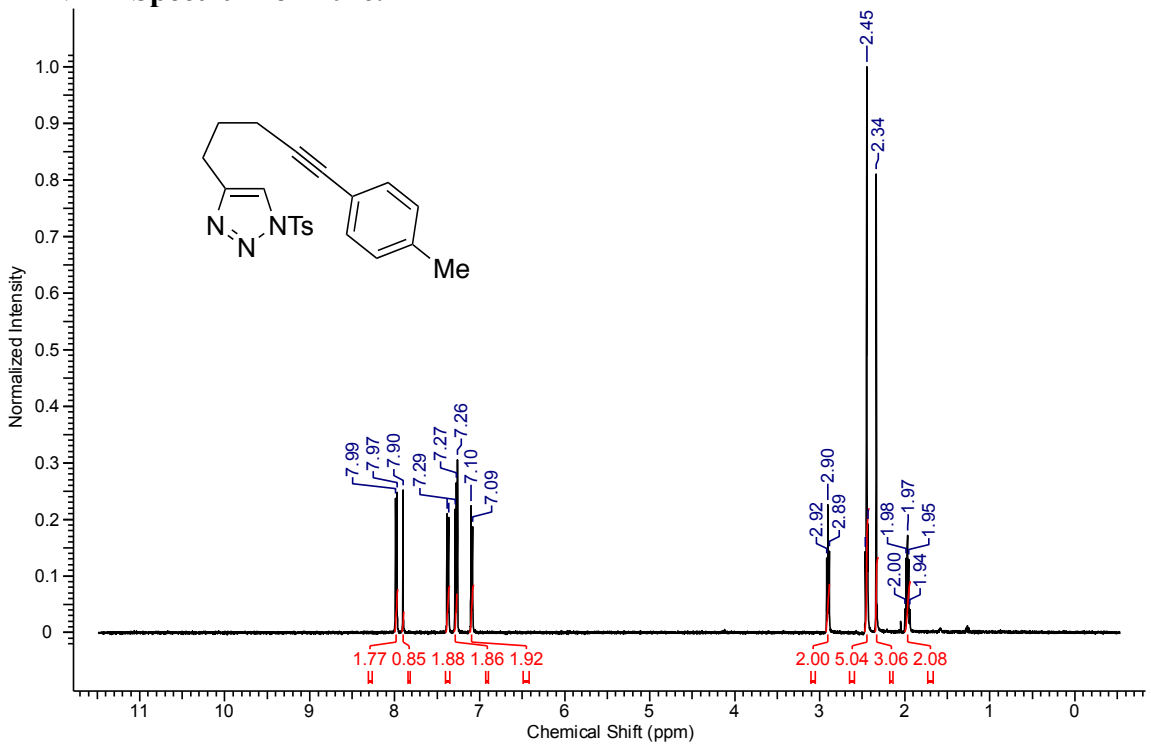

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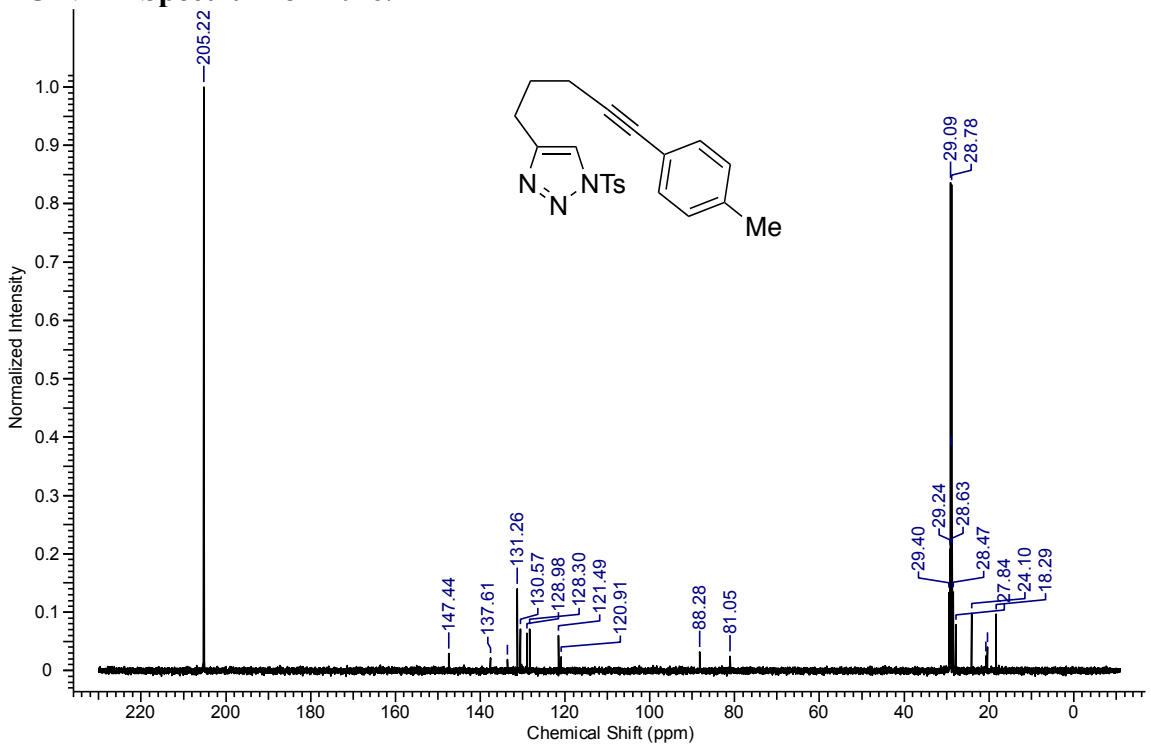

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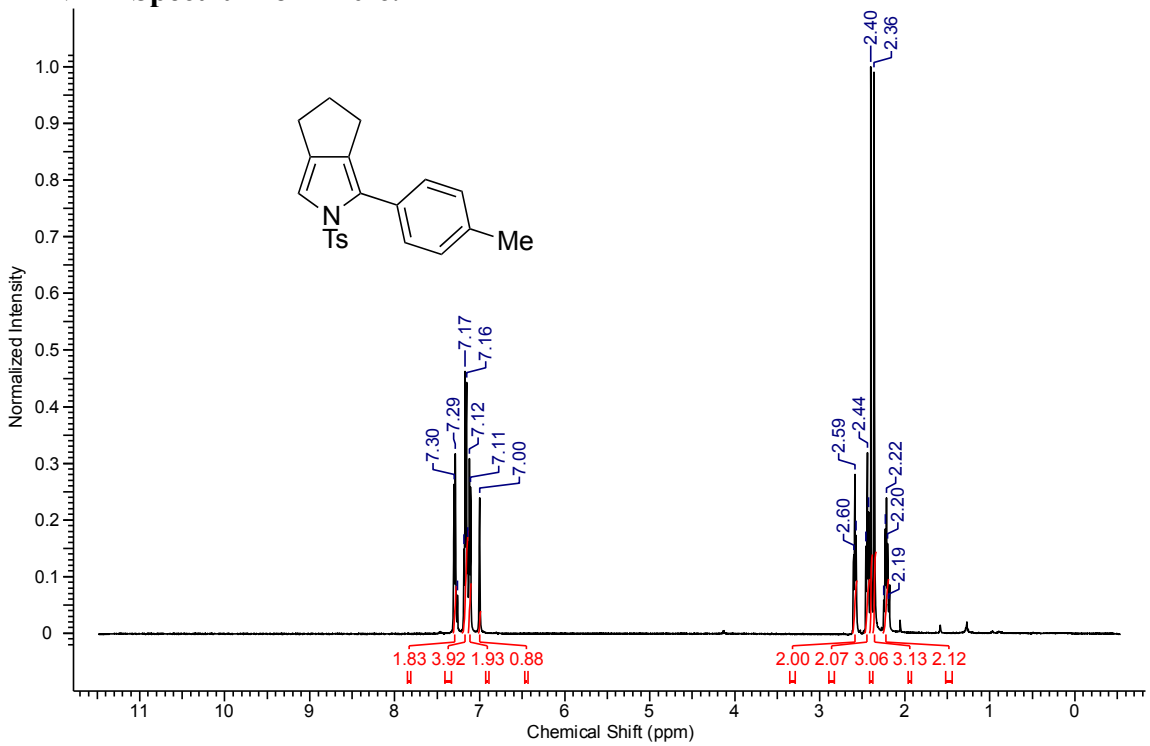

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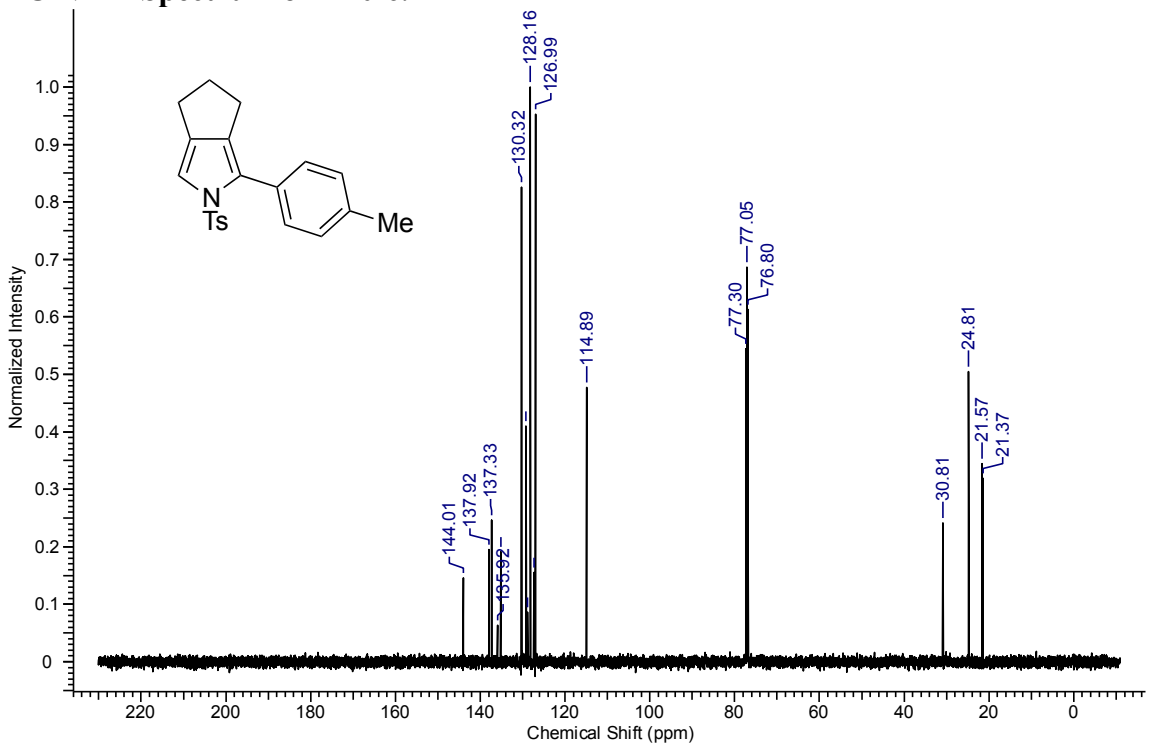

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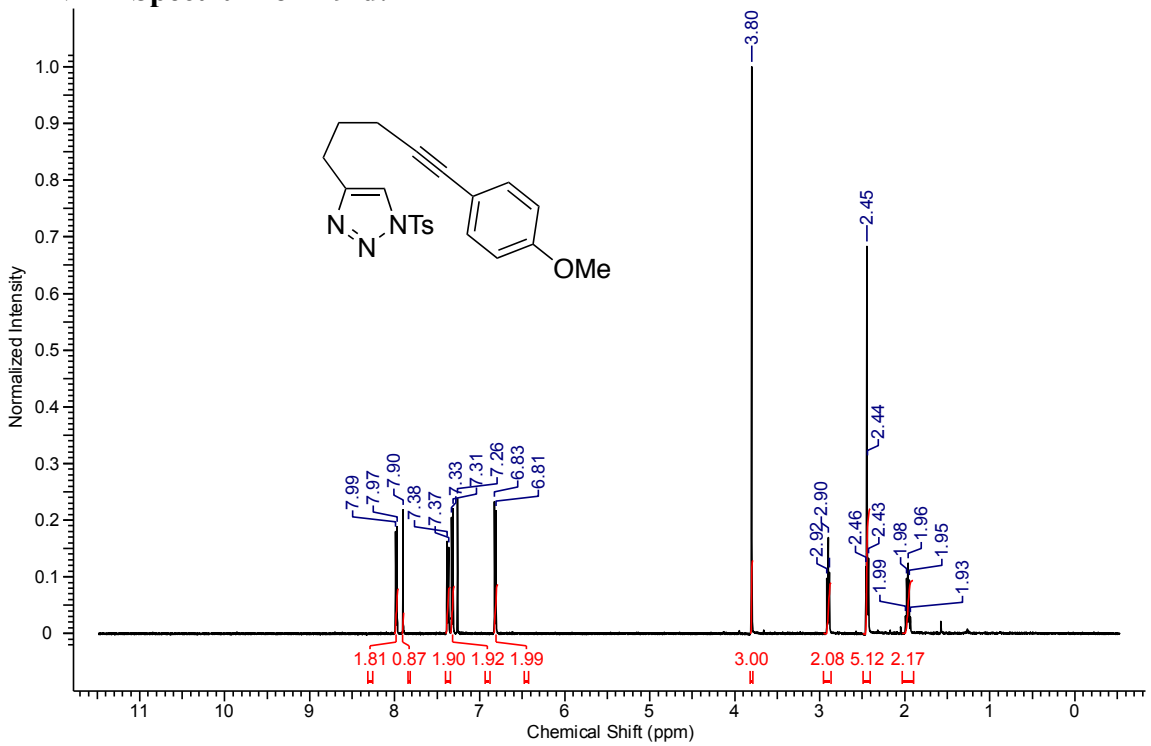

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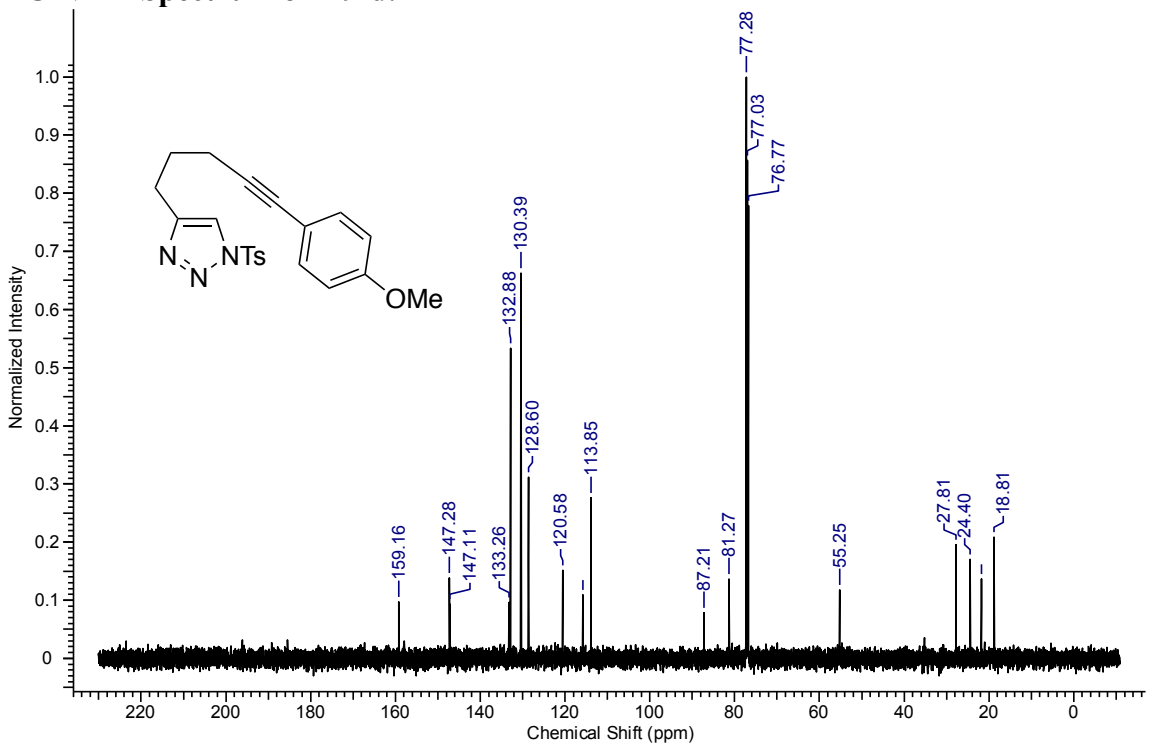

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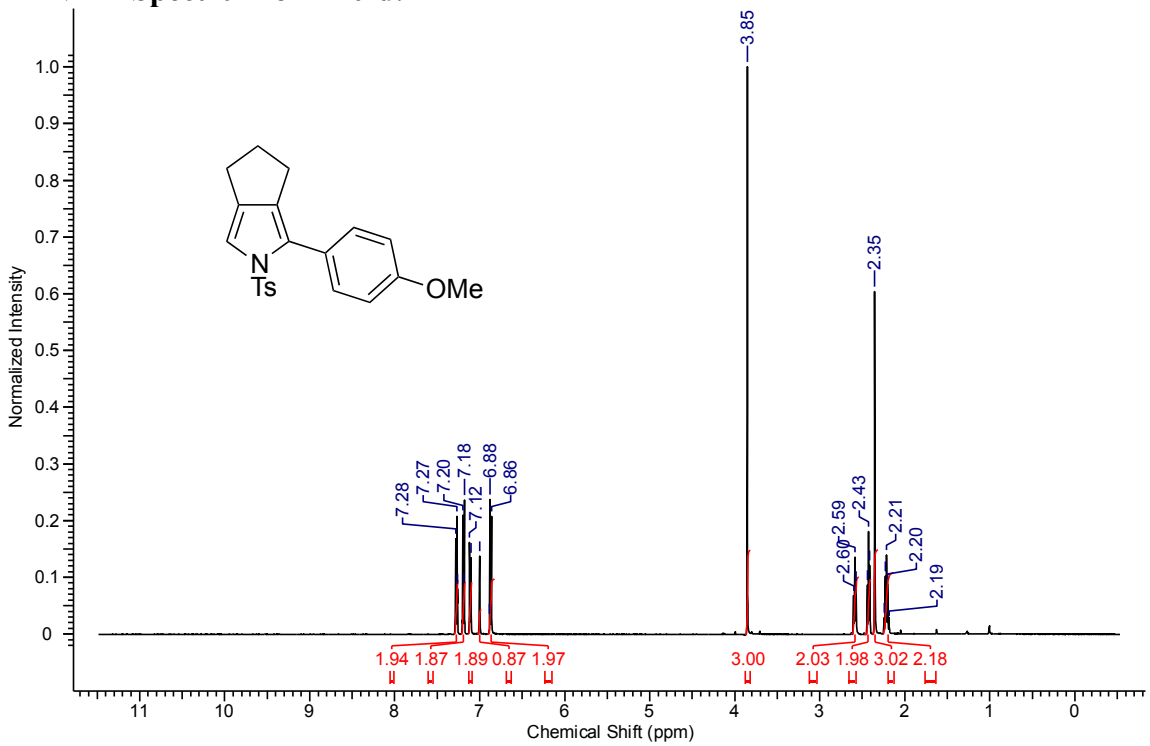

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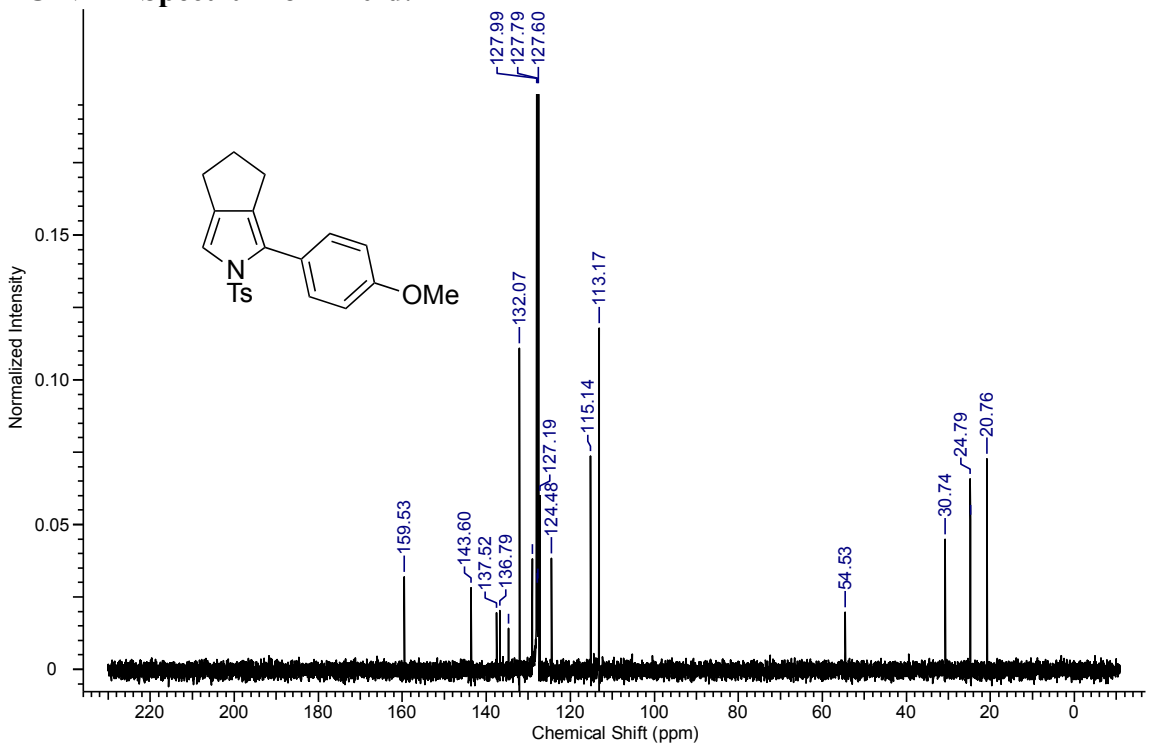

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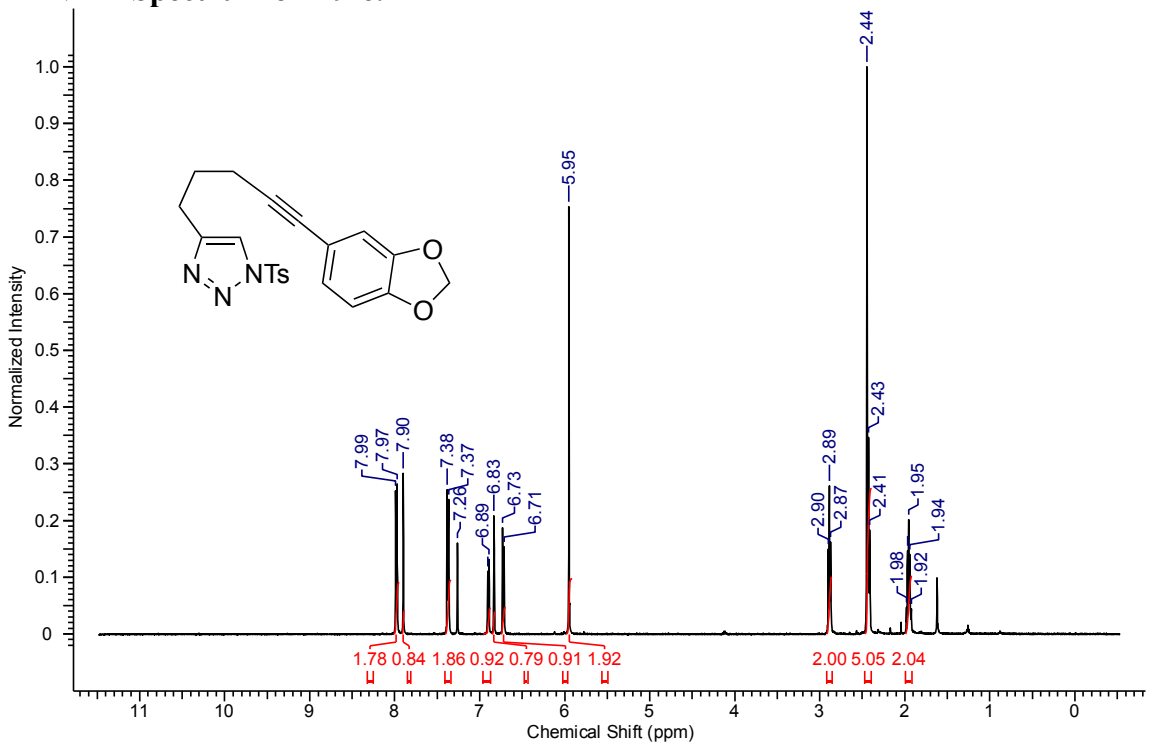

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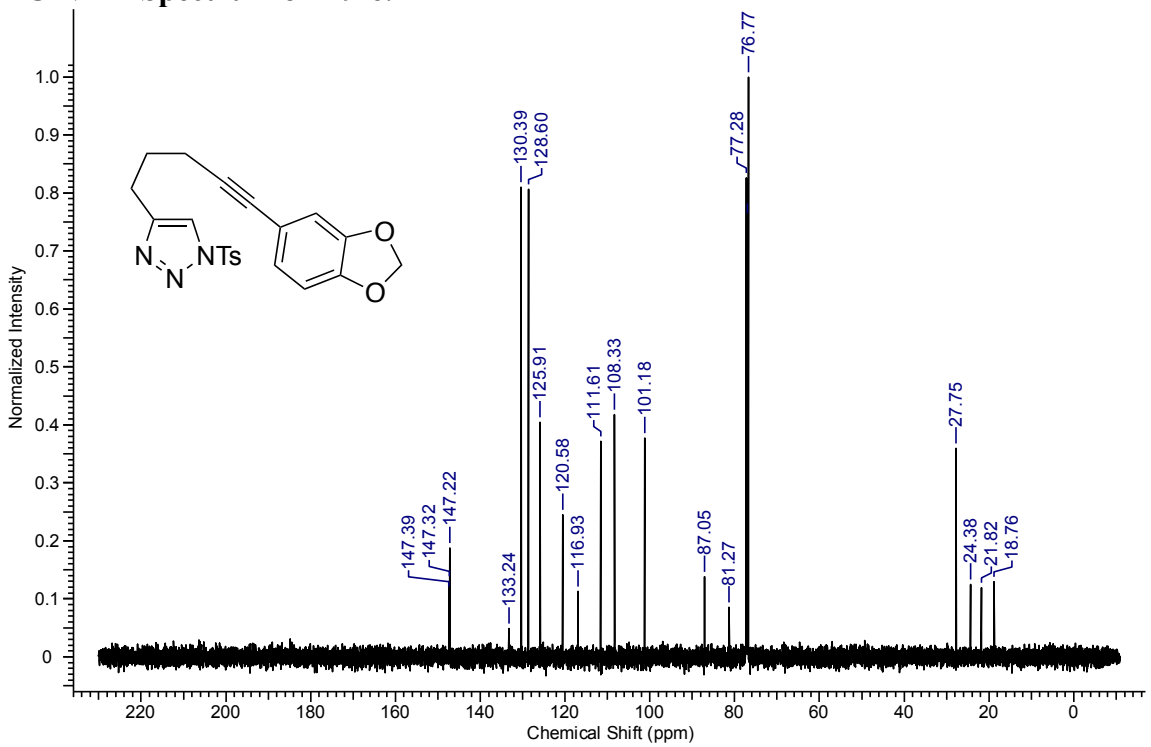

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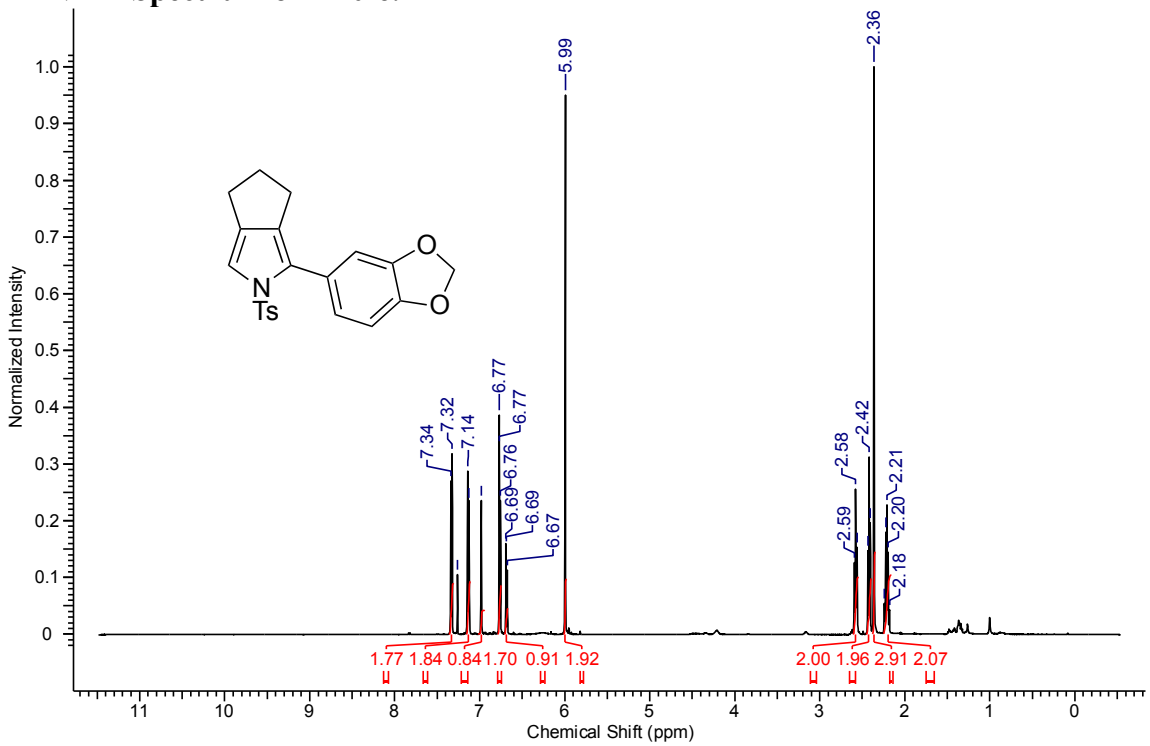

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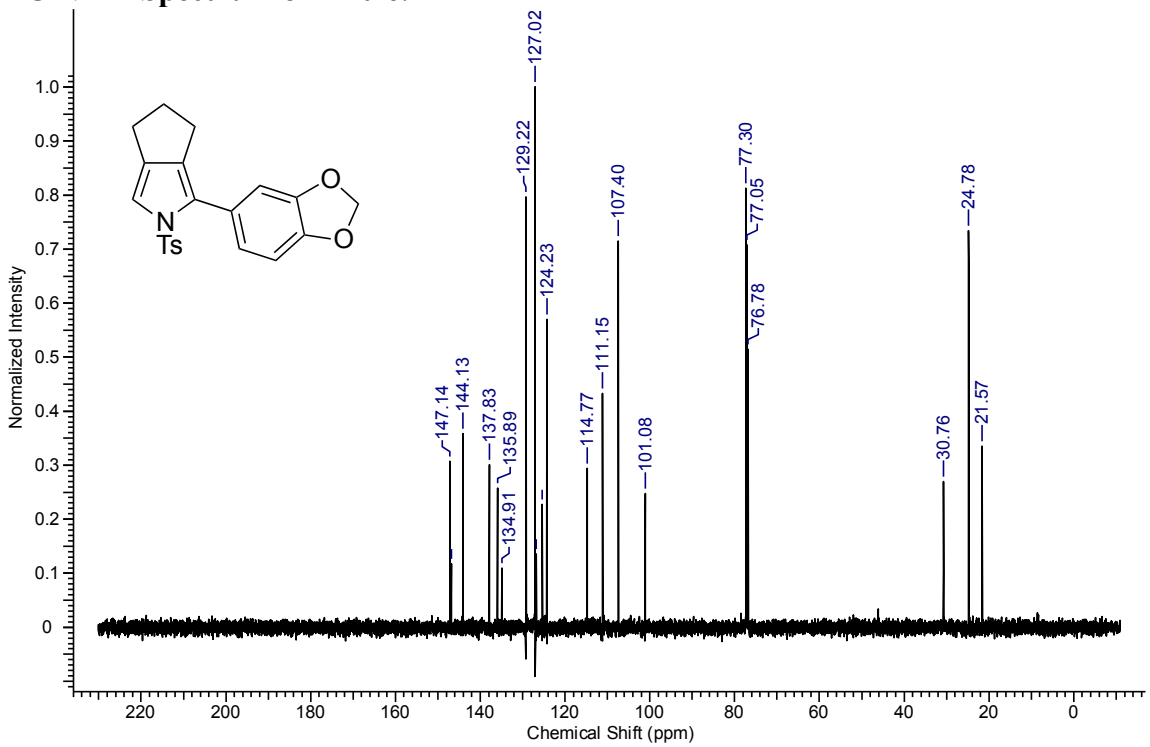

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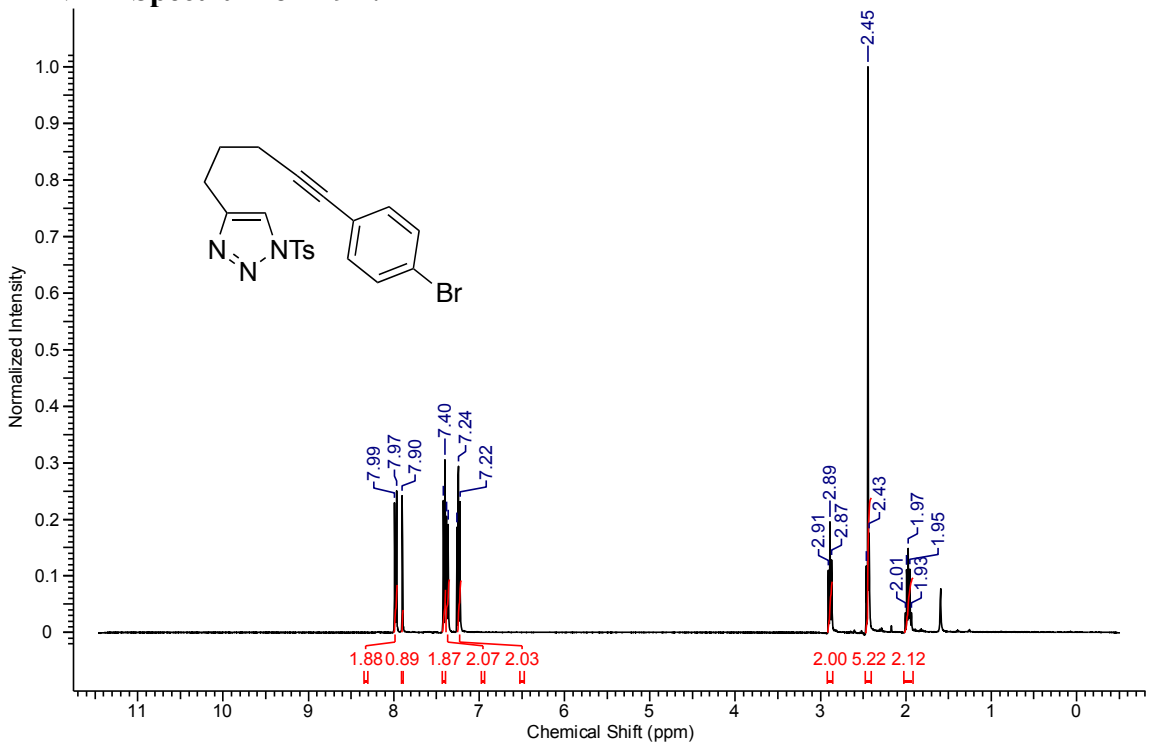

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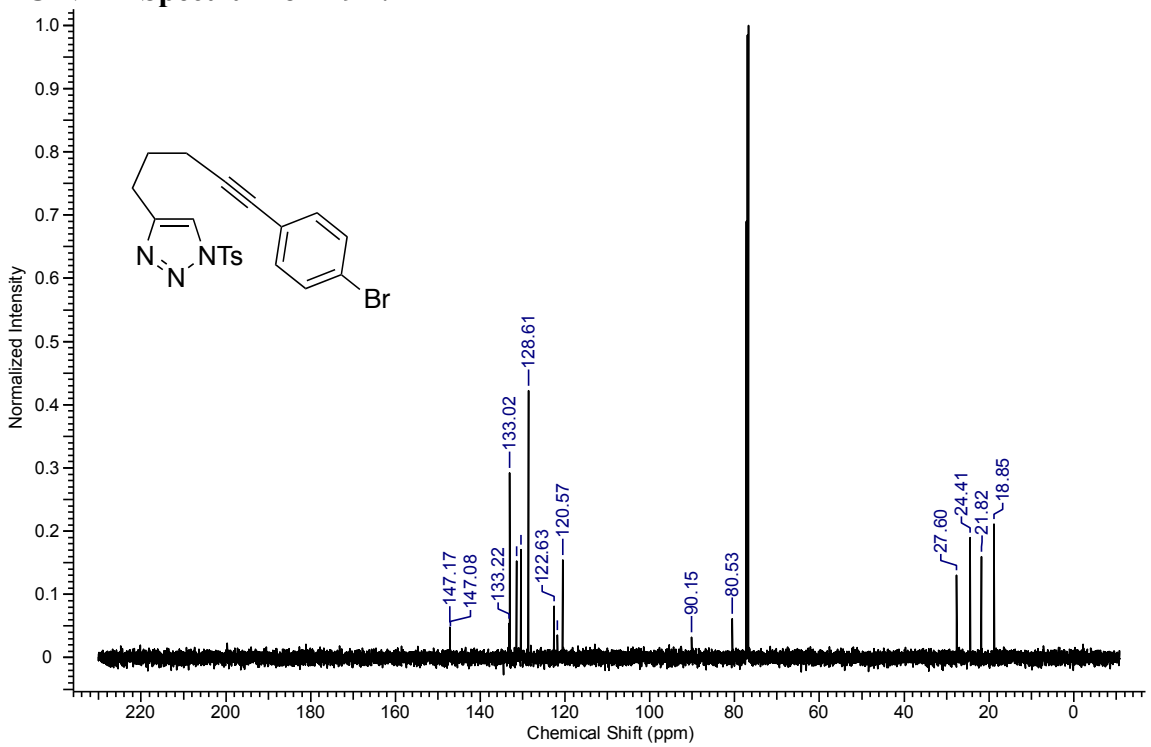

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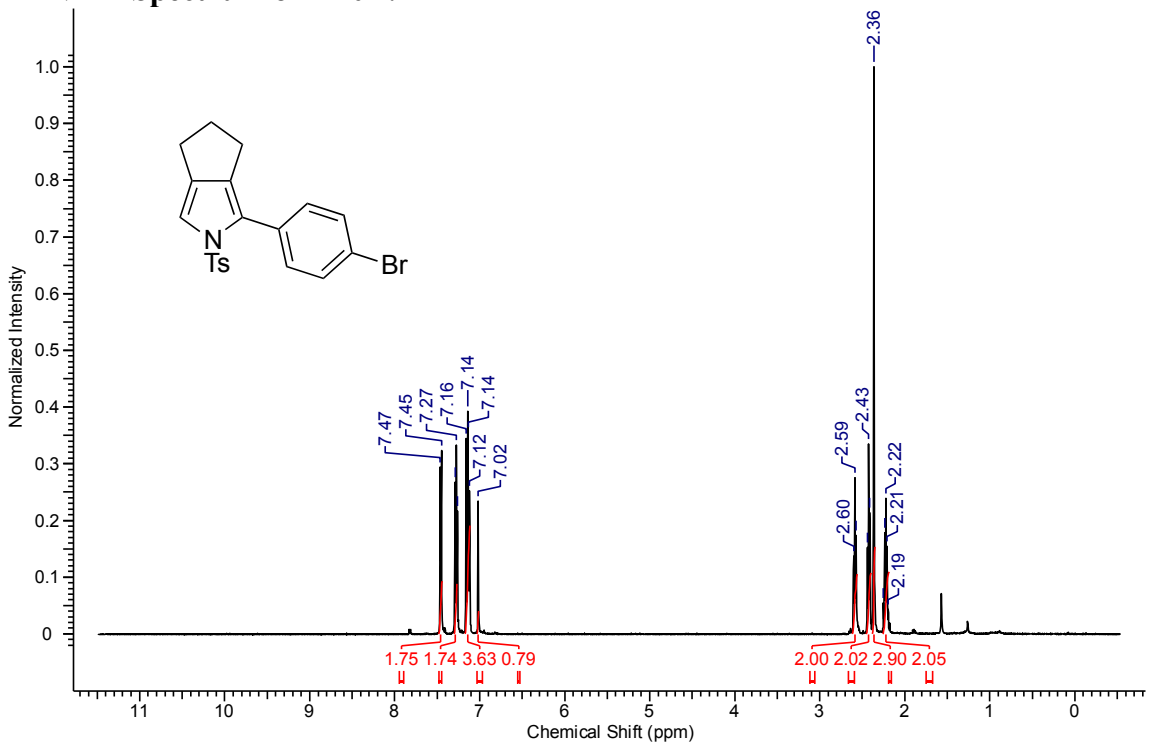

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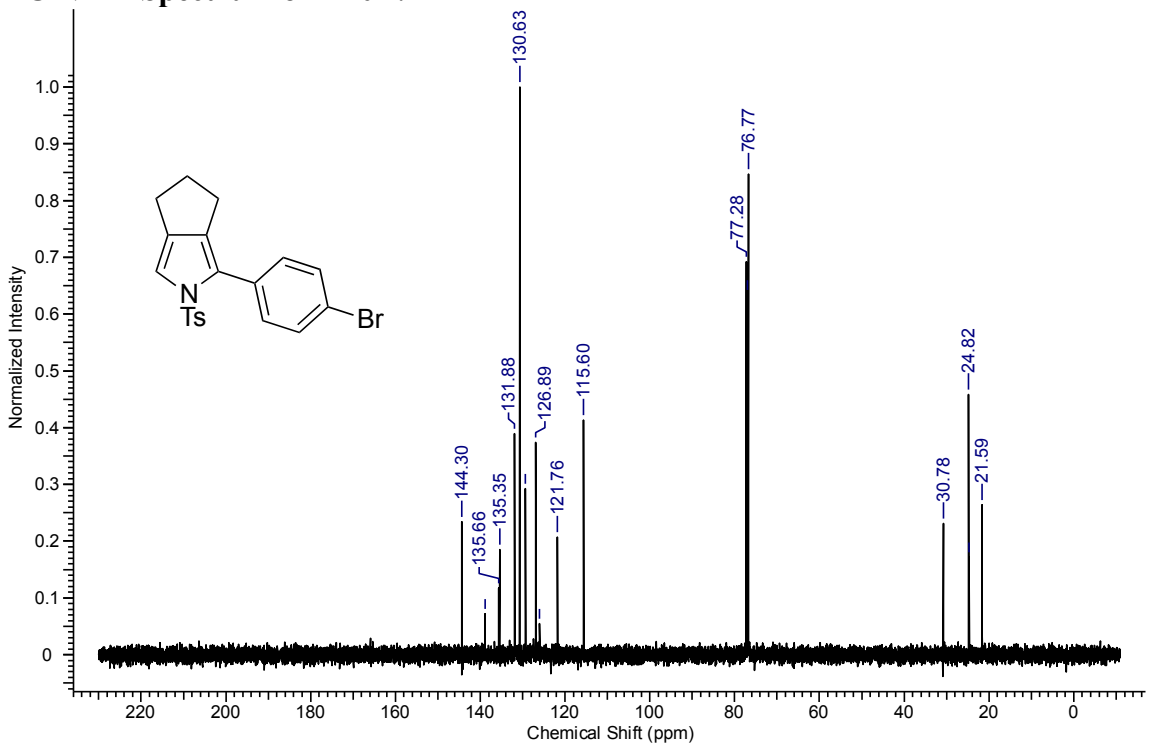

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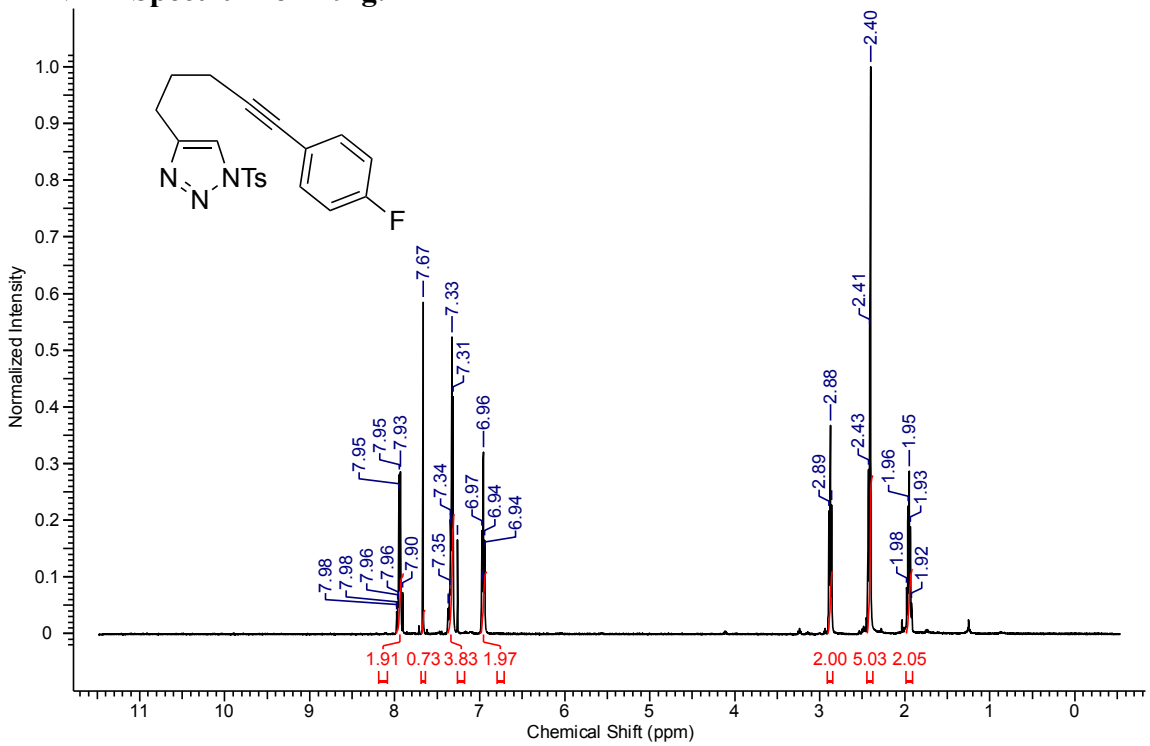

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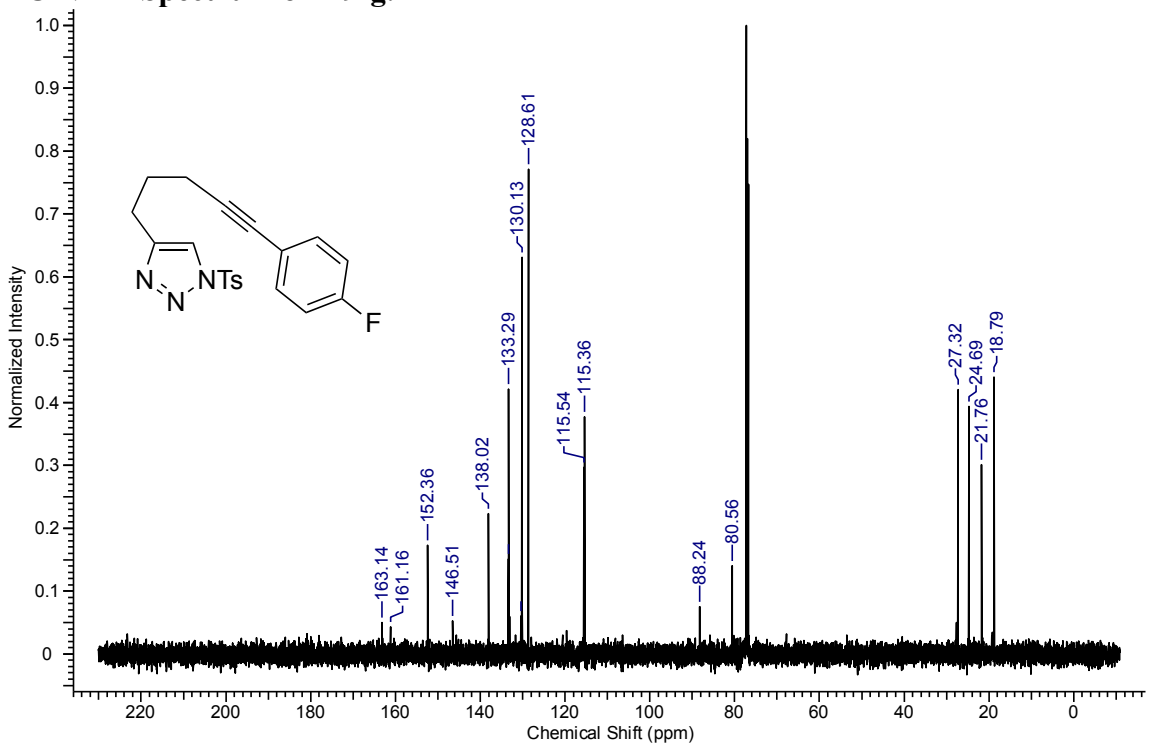

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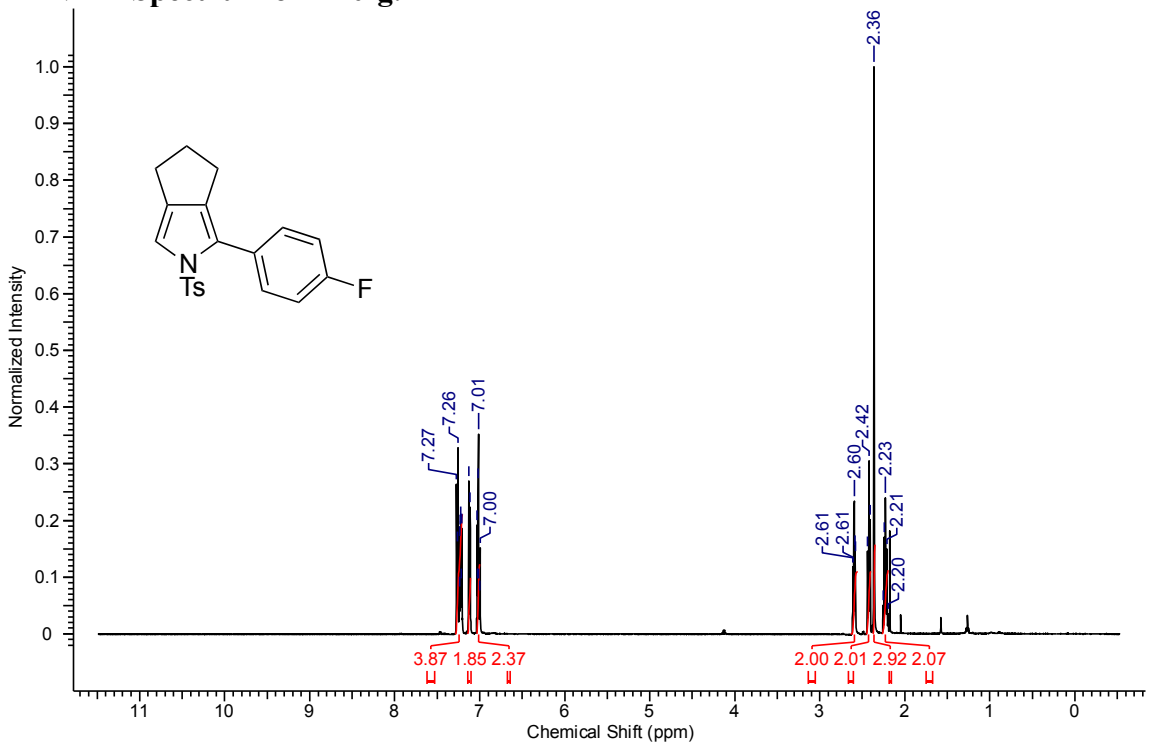

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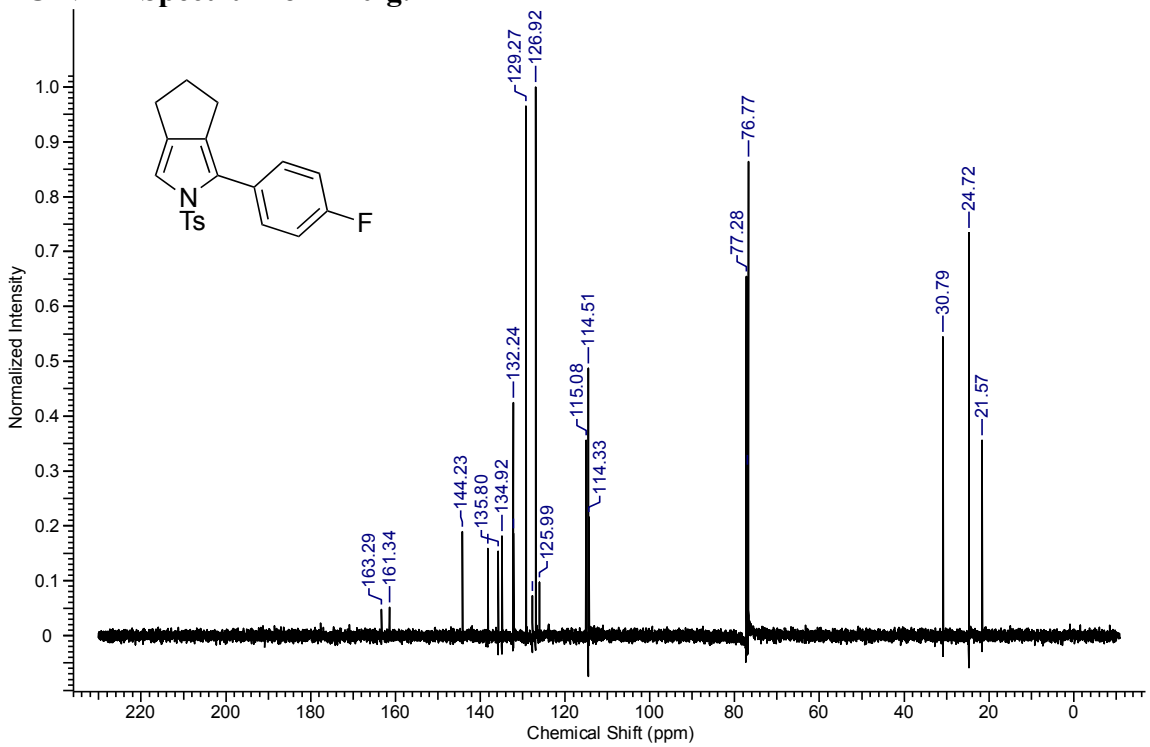

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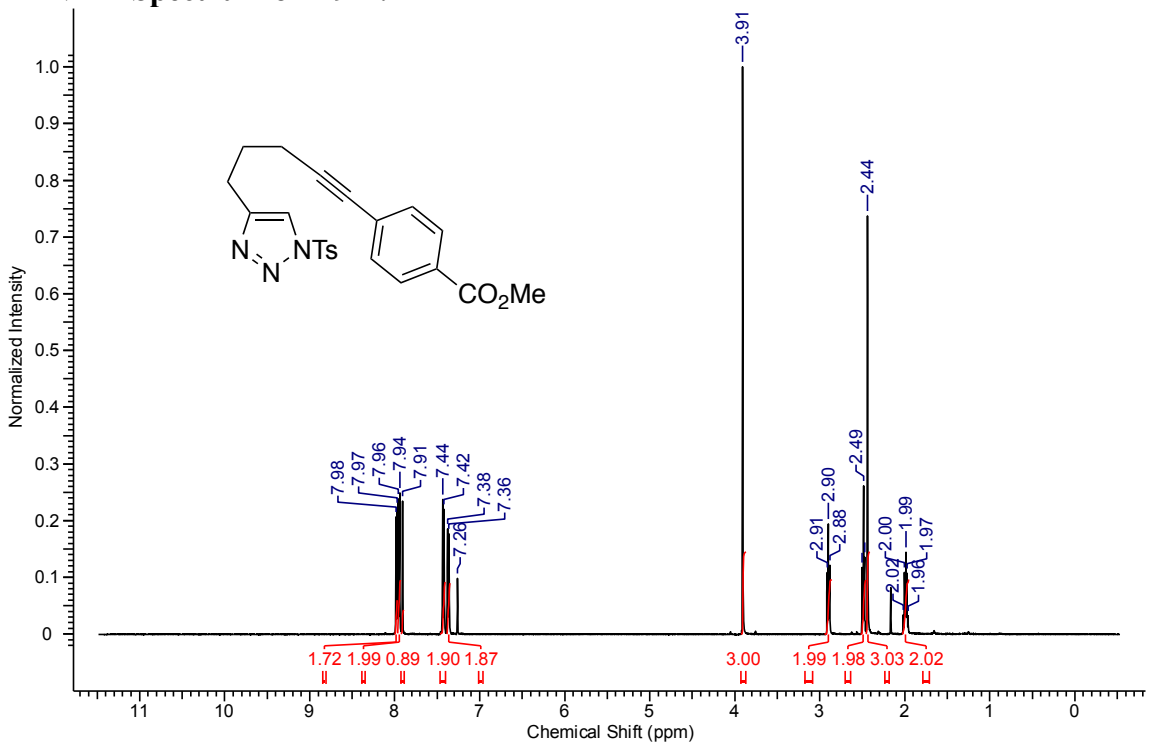

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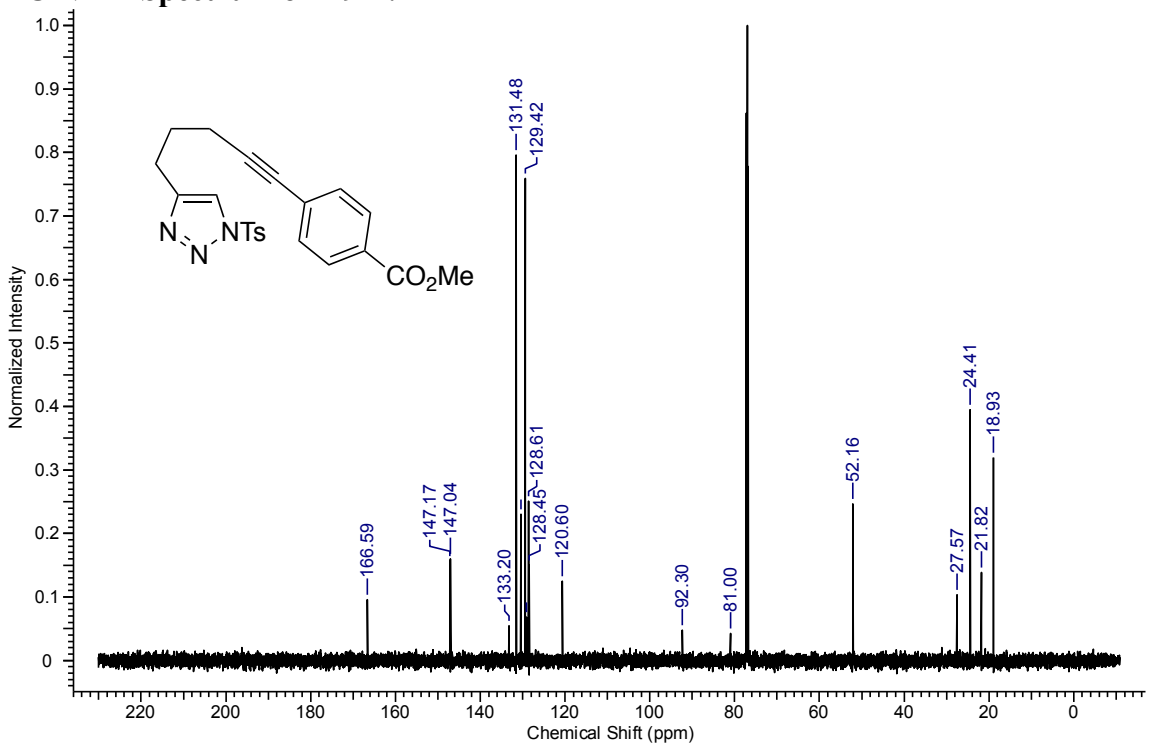

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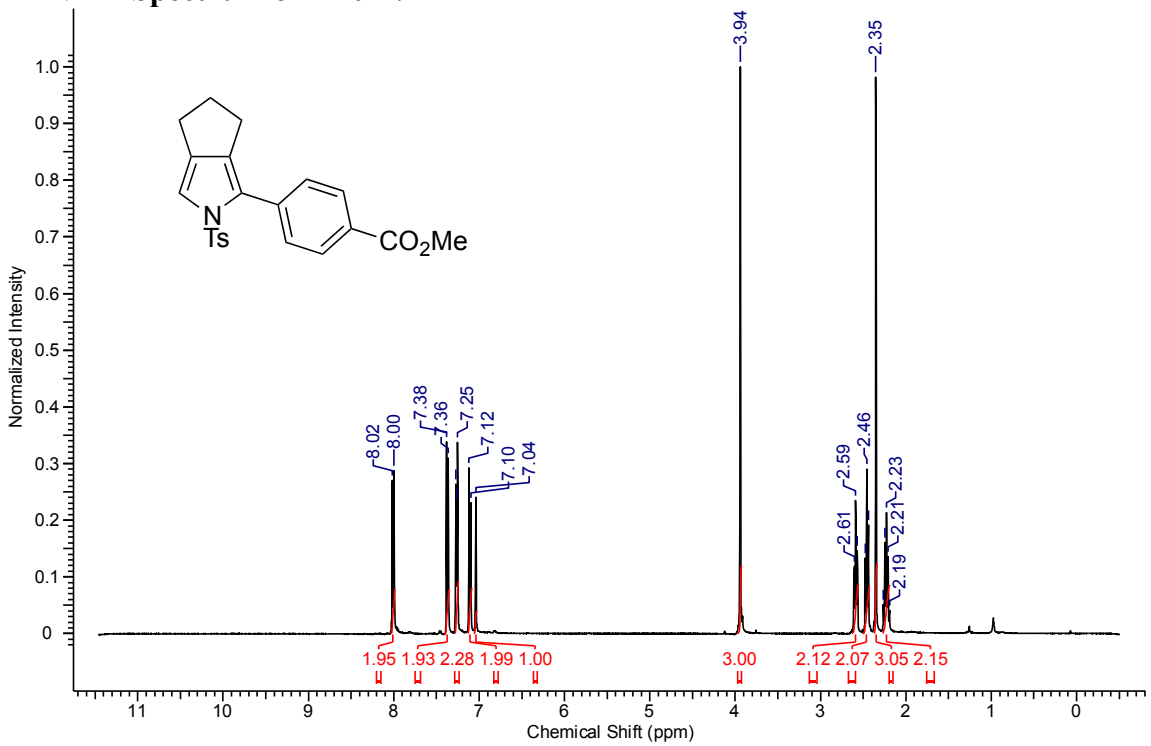

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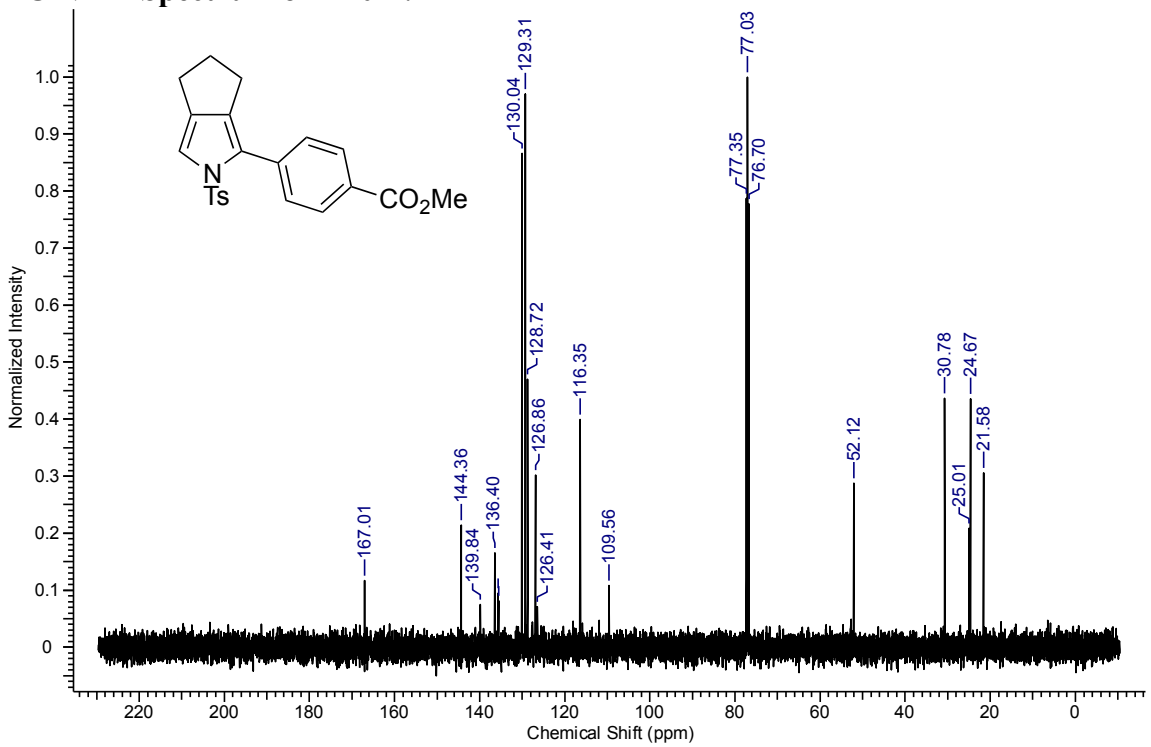
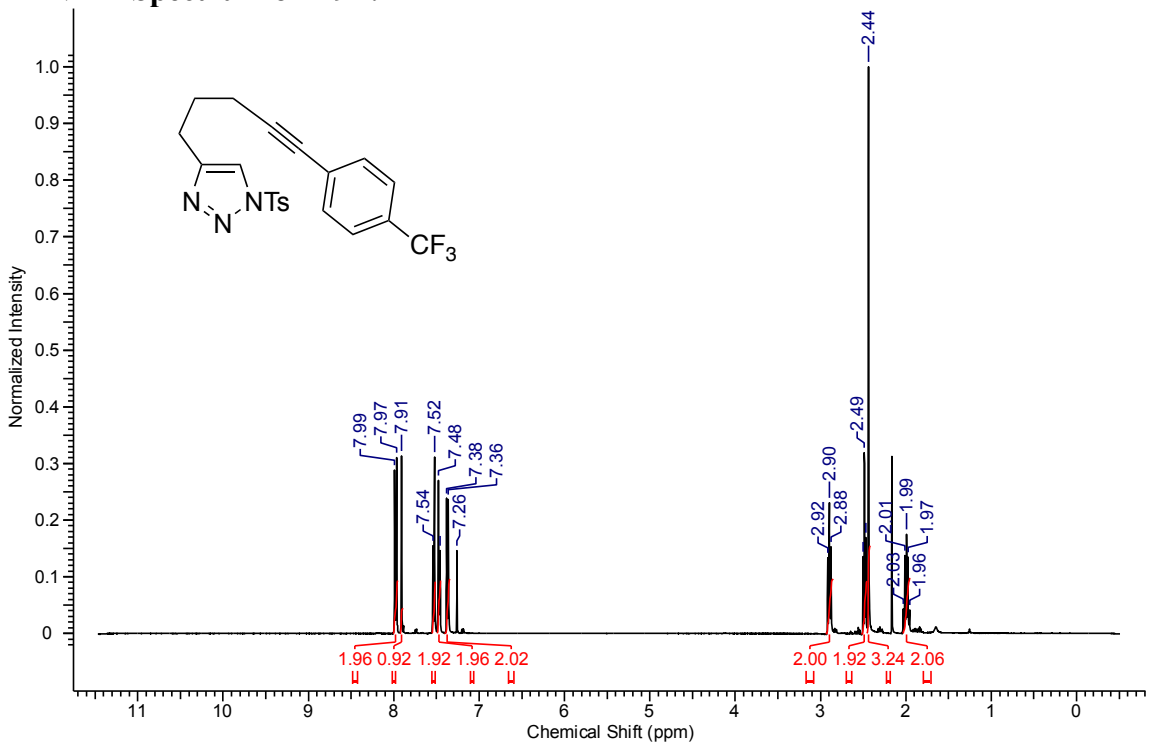
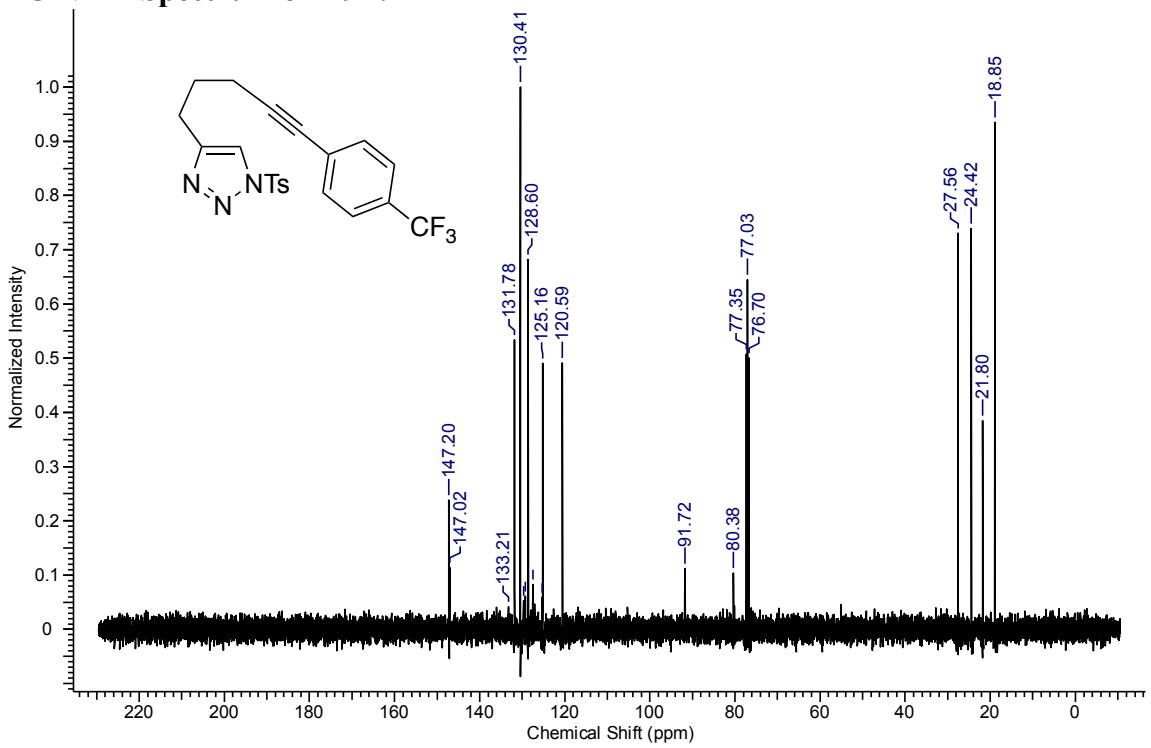


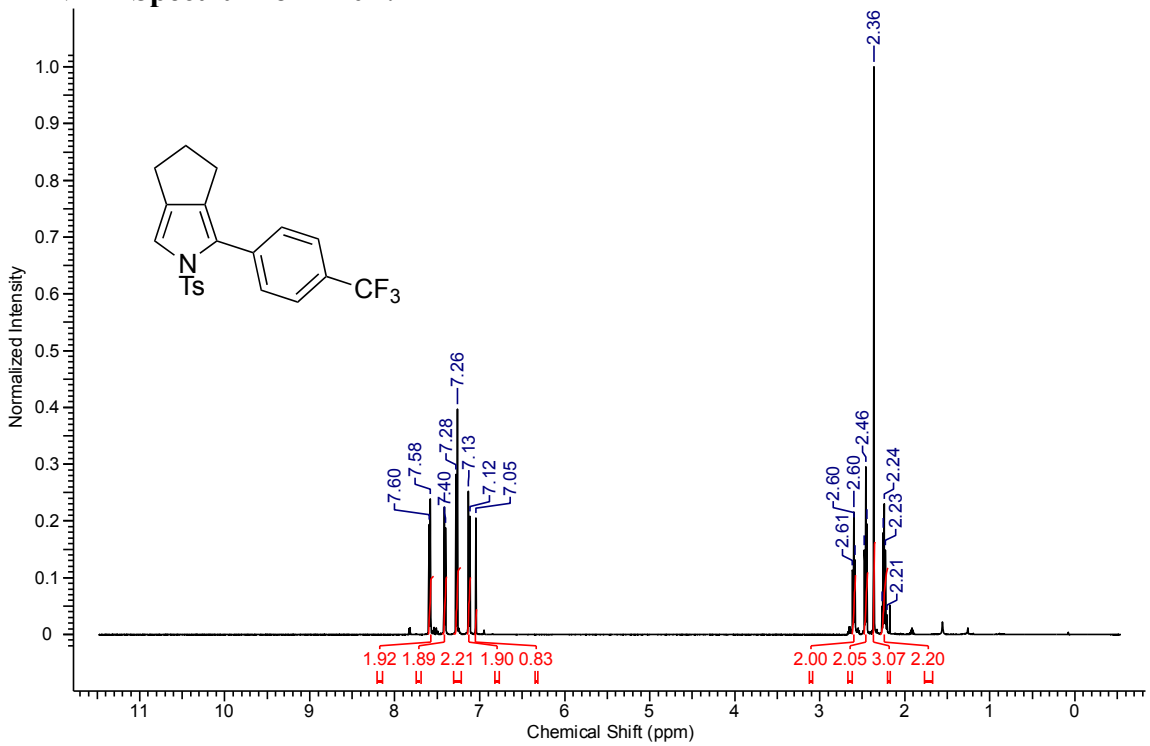
^{1}H NMR Spectrum of 4-9-i:



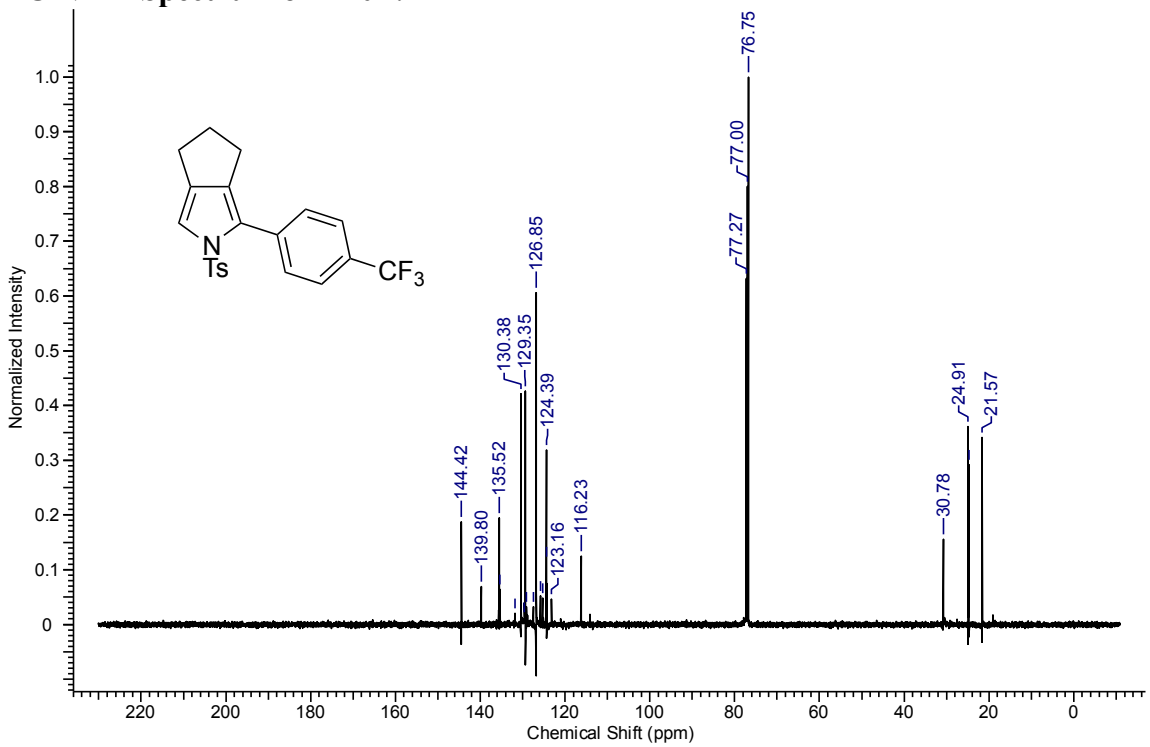
^{13}C NMR Spectrum of 4-9-i:



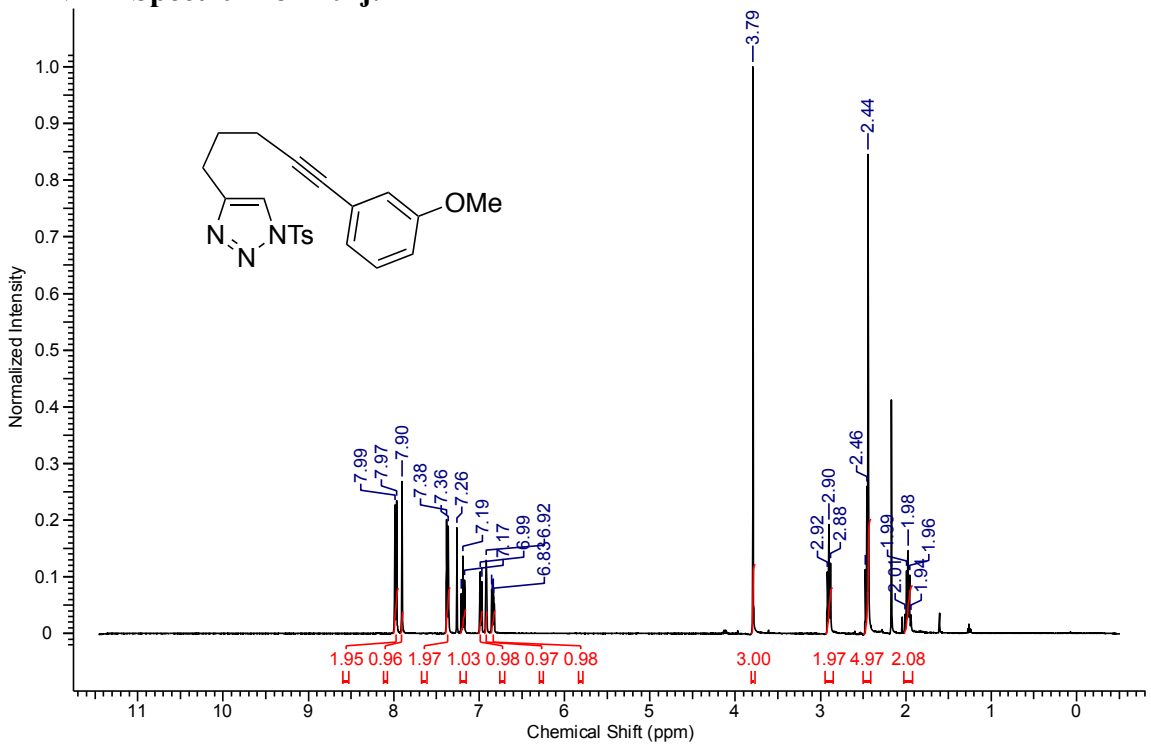
^{1}H NMR Spectrum of 4-10-i:



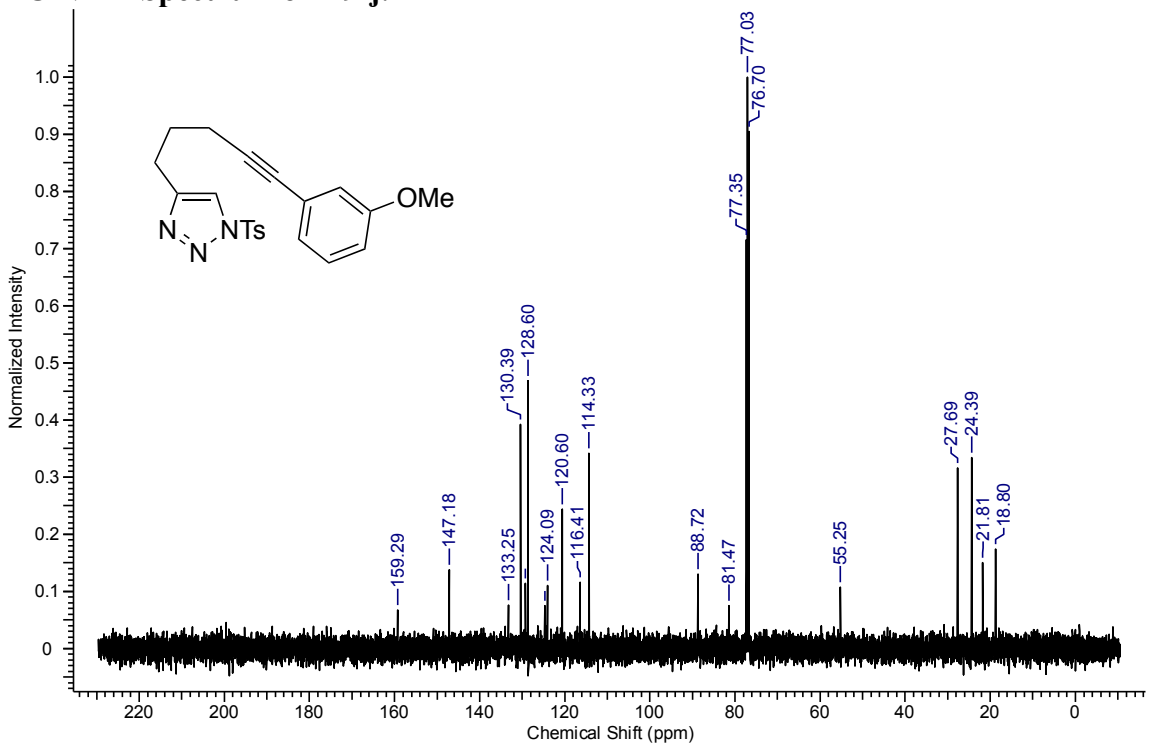
^{13}C NMR Spectrum of 4-10-i:



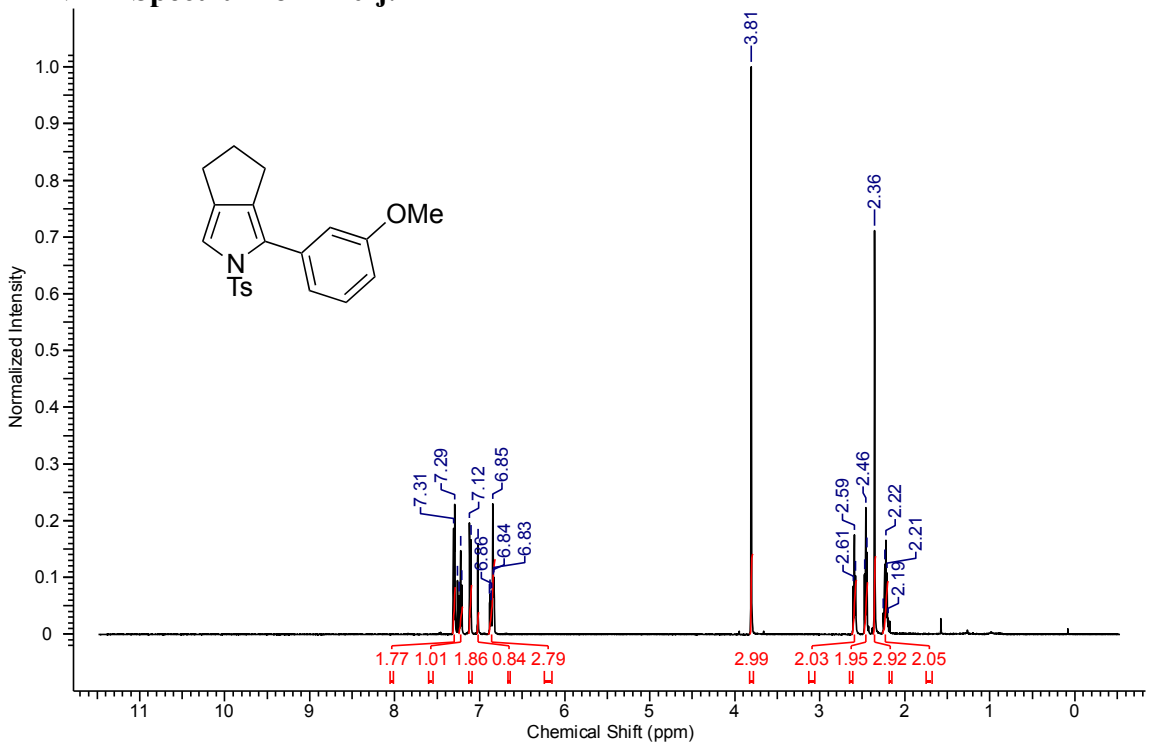
^{1}H NMR Spectrum of 4-9-j:



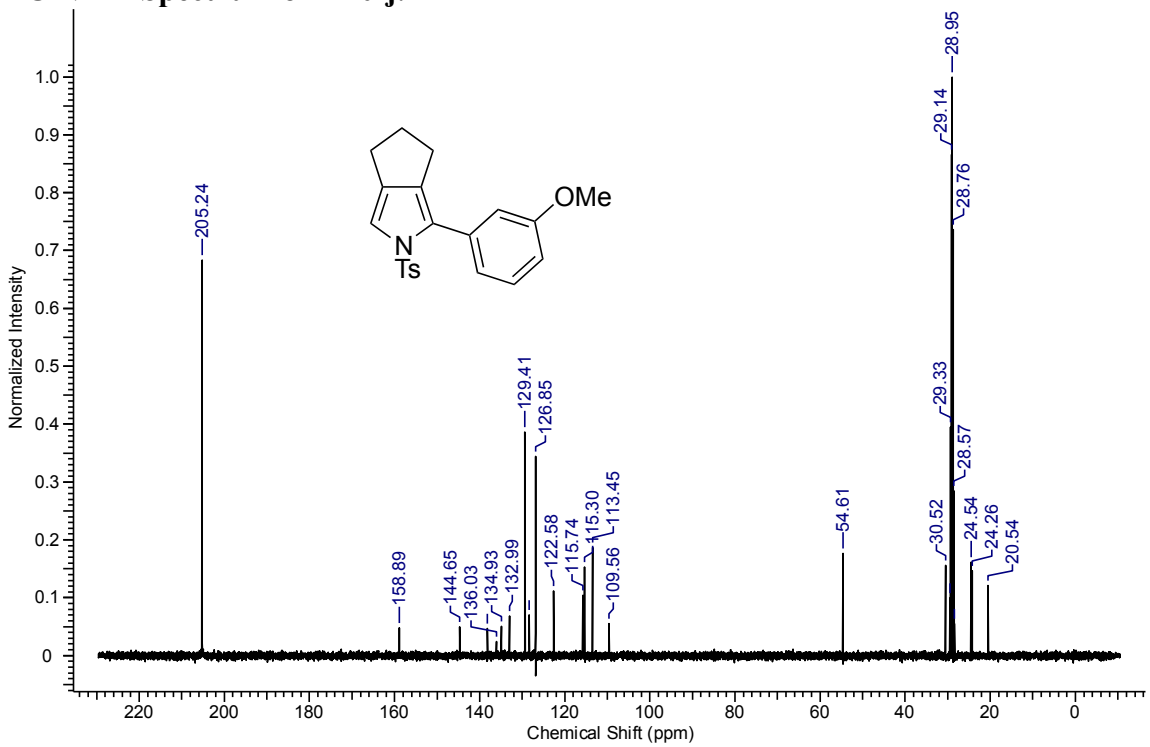
^{13}C NMR Spectrum of 4-9-j:



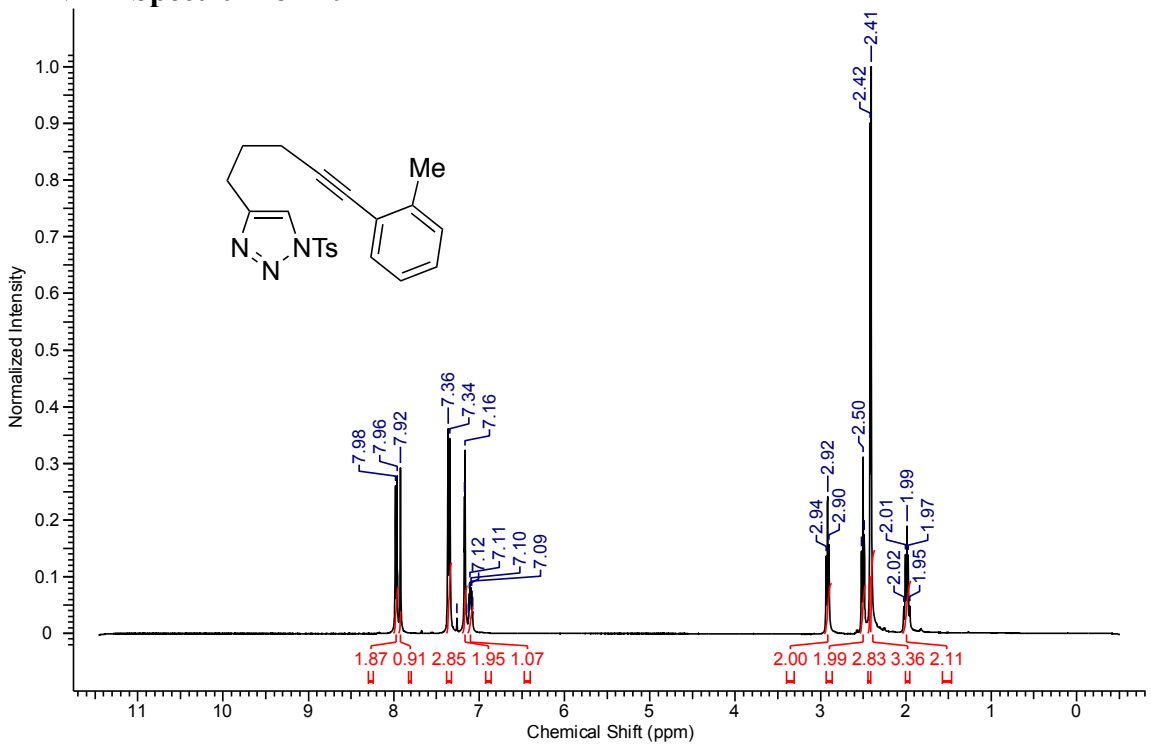
^{1}H NMR Spectrum of 4-10-j:



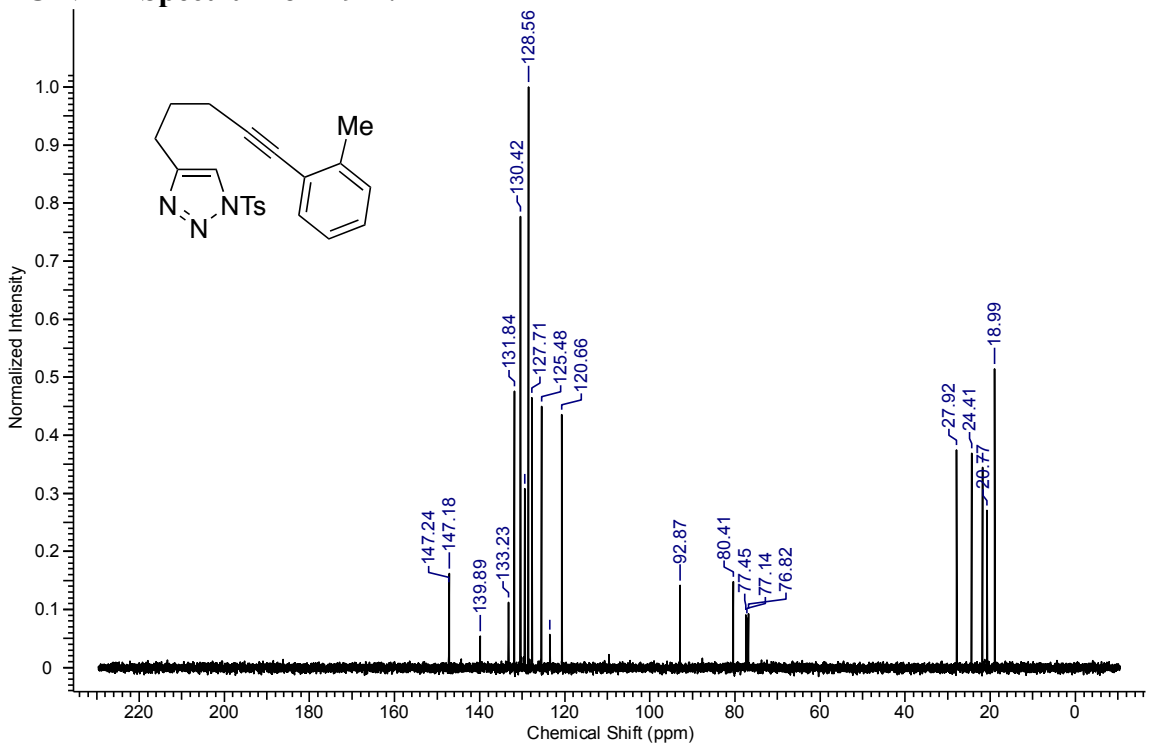
^{13}C NMR Spectrum of 4-10-j:



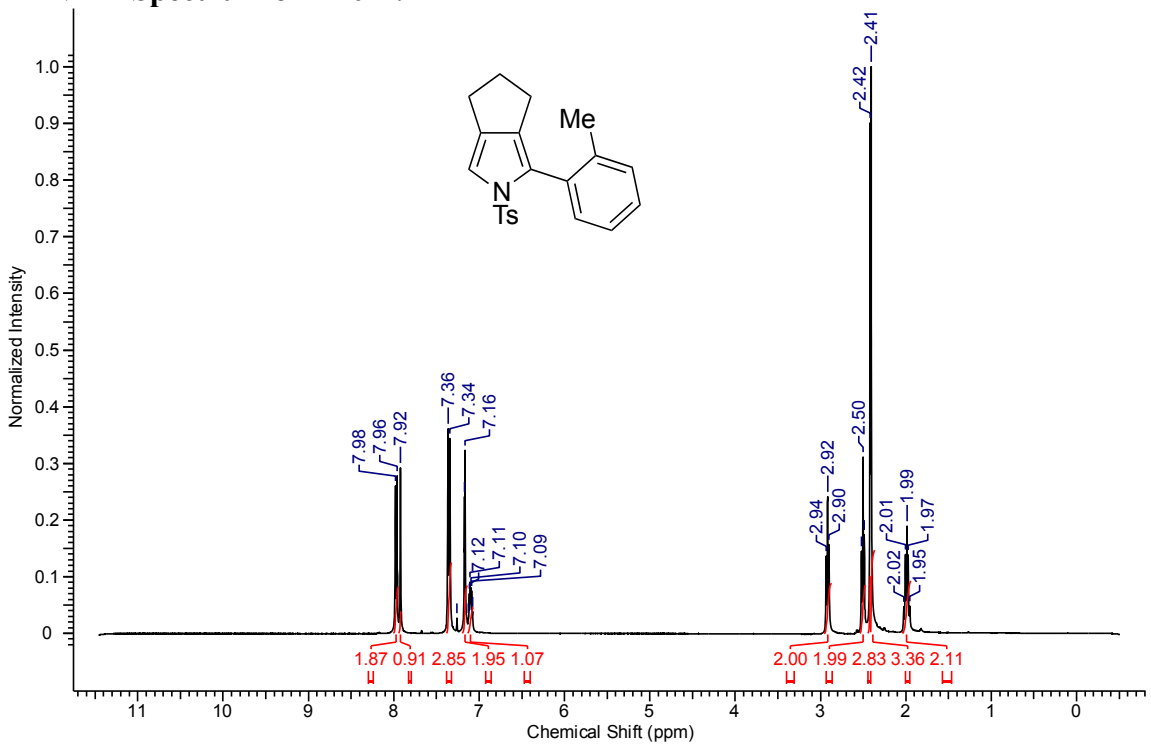
^{1}H NMR Spectrum of 4-9-k



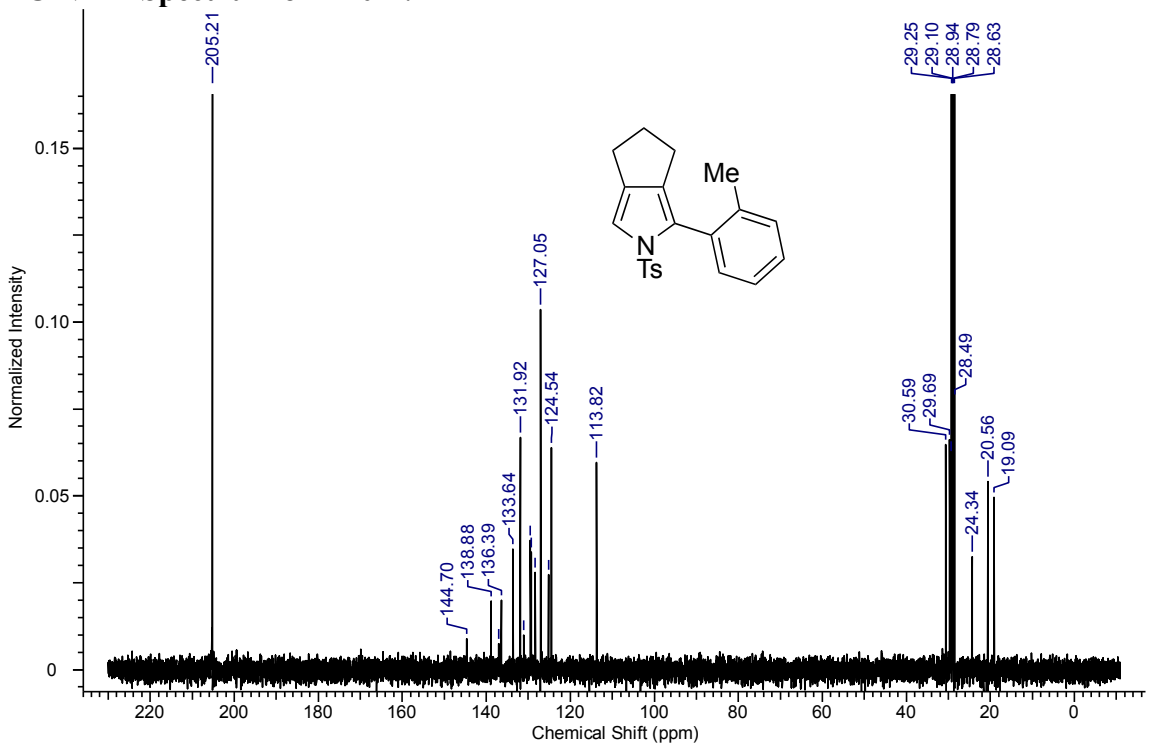
^{13}C NMR Spectrum of 4-9-k:



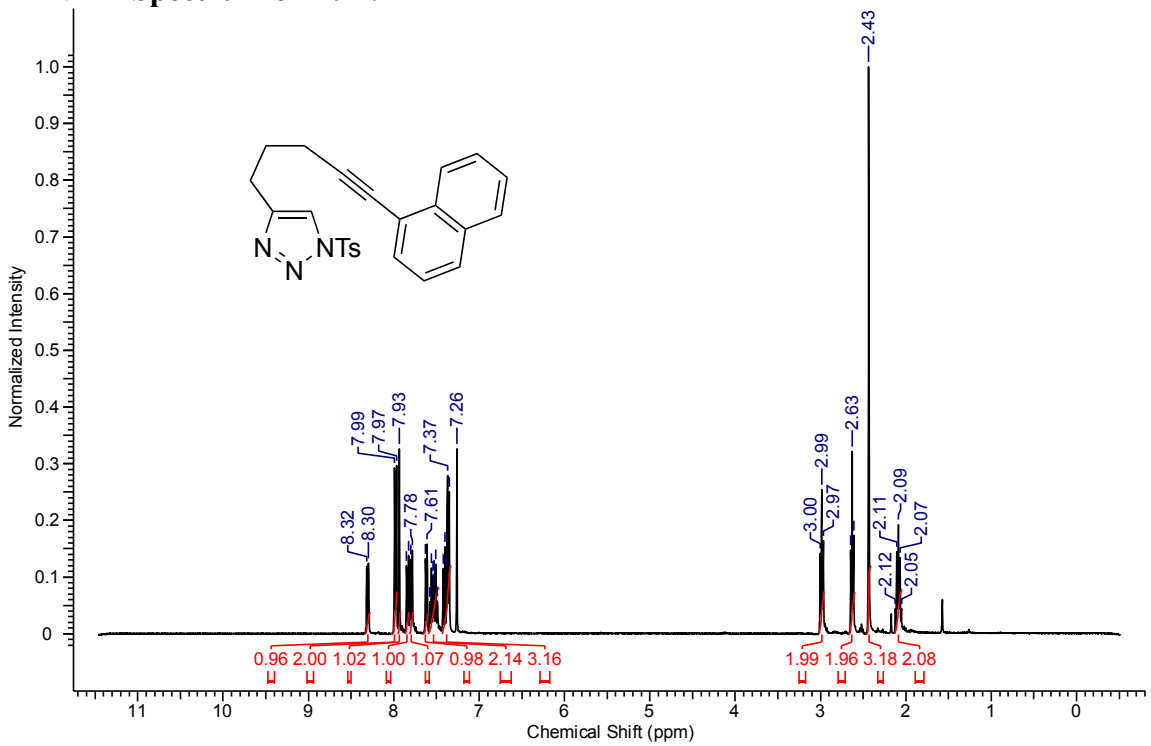
^{1}H NMR Spectrum of 4-10-k:



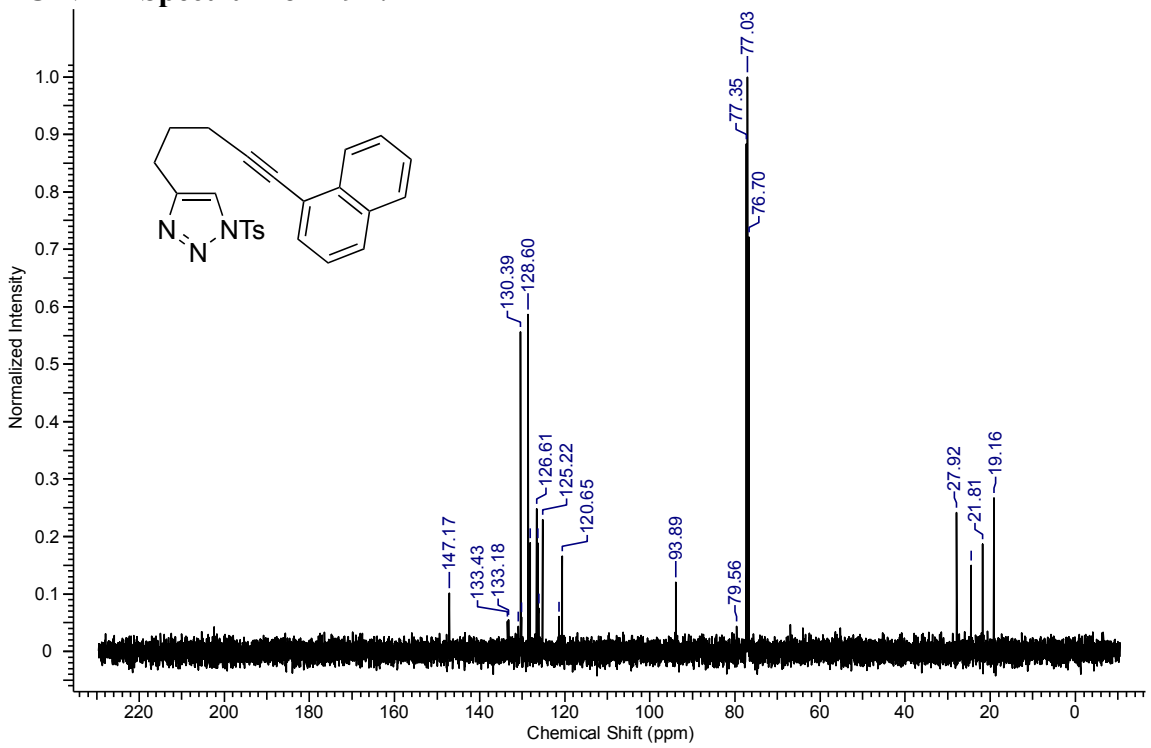
^{13}C NMR Spectrum of 4-10-k:



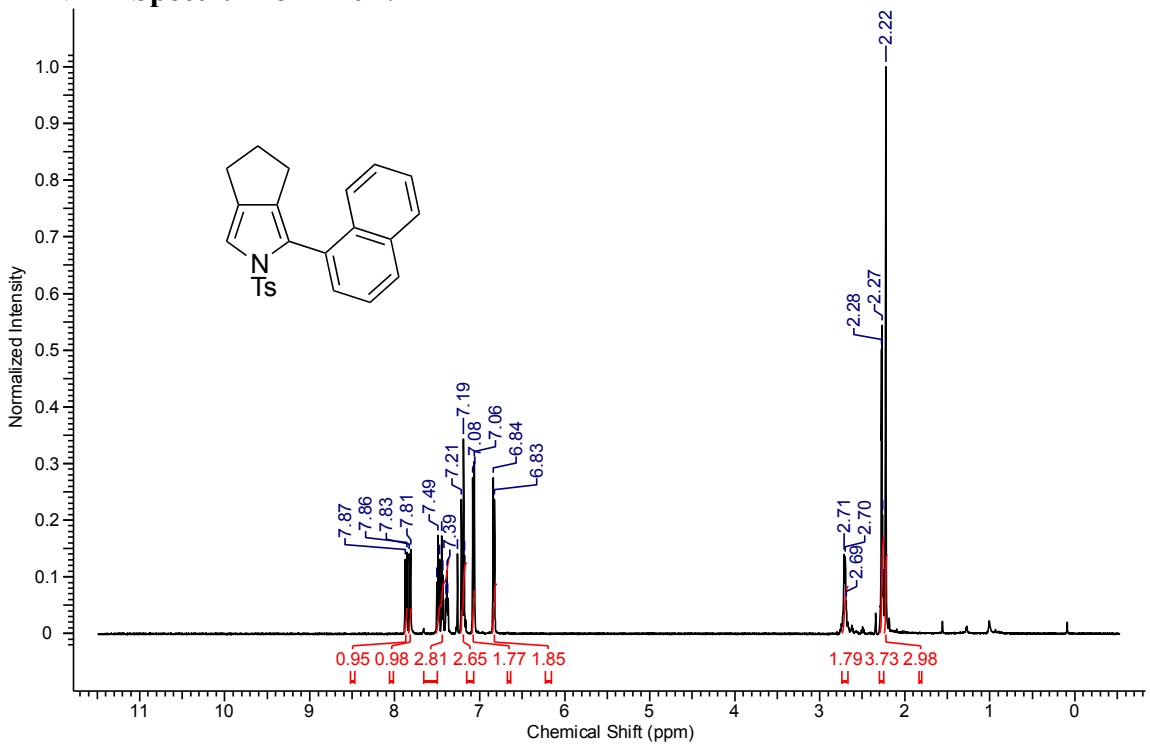
^{1}H NMR Spectrum of 4-9-l:



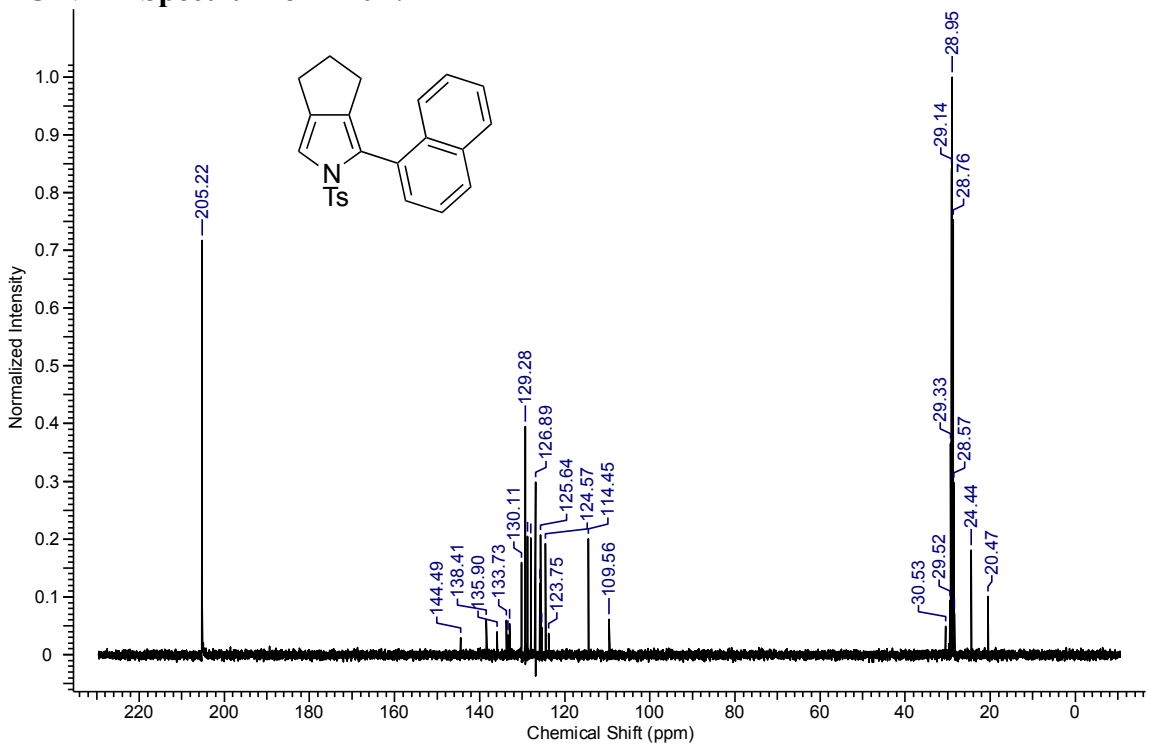
^{13}C NMR Spectrum of 4-9-l:



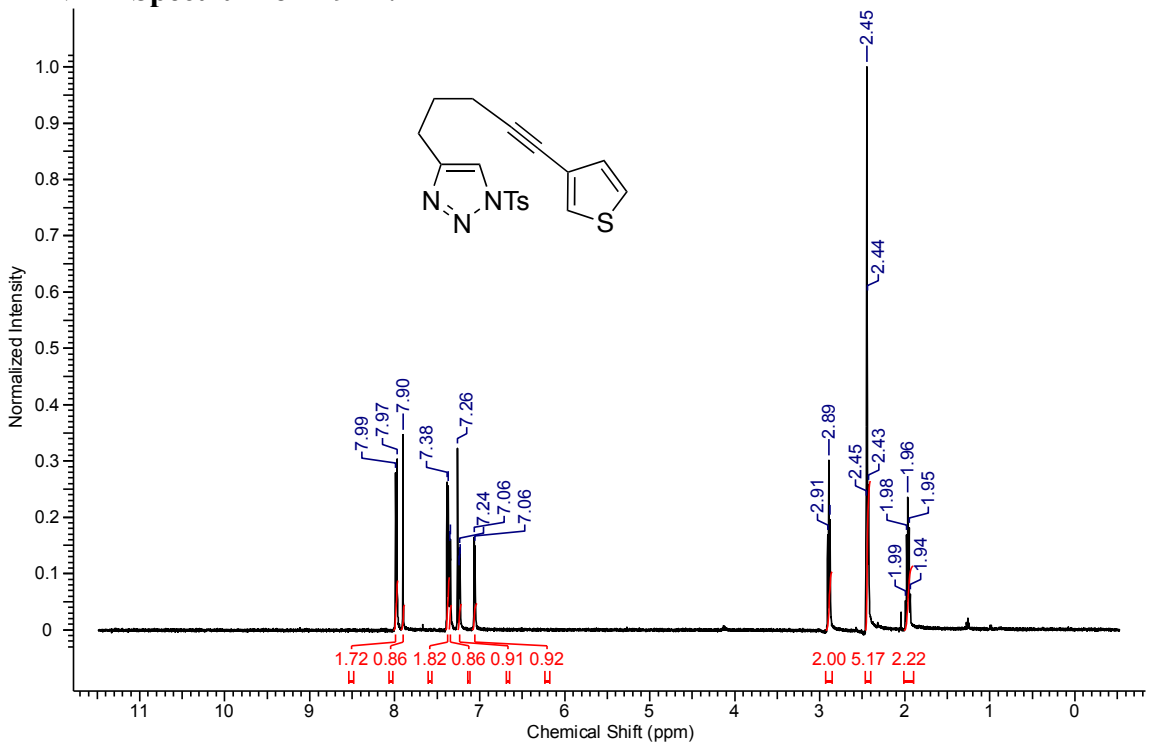
^{1}H NMR Spectrum of 4-10-l:



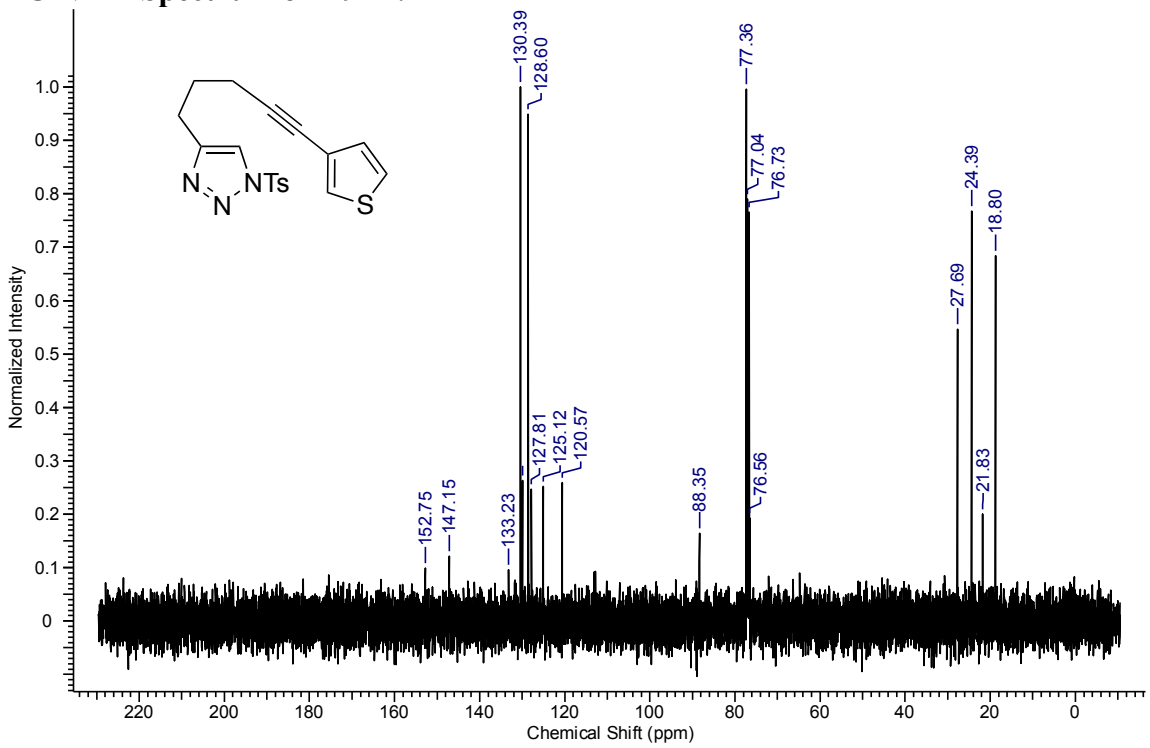
^{13}C NMR Spectrum of 4-10-l:



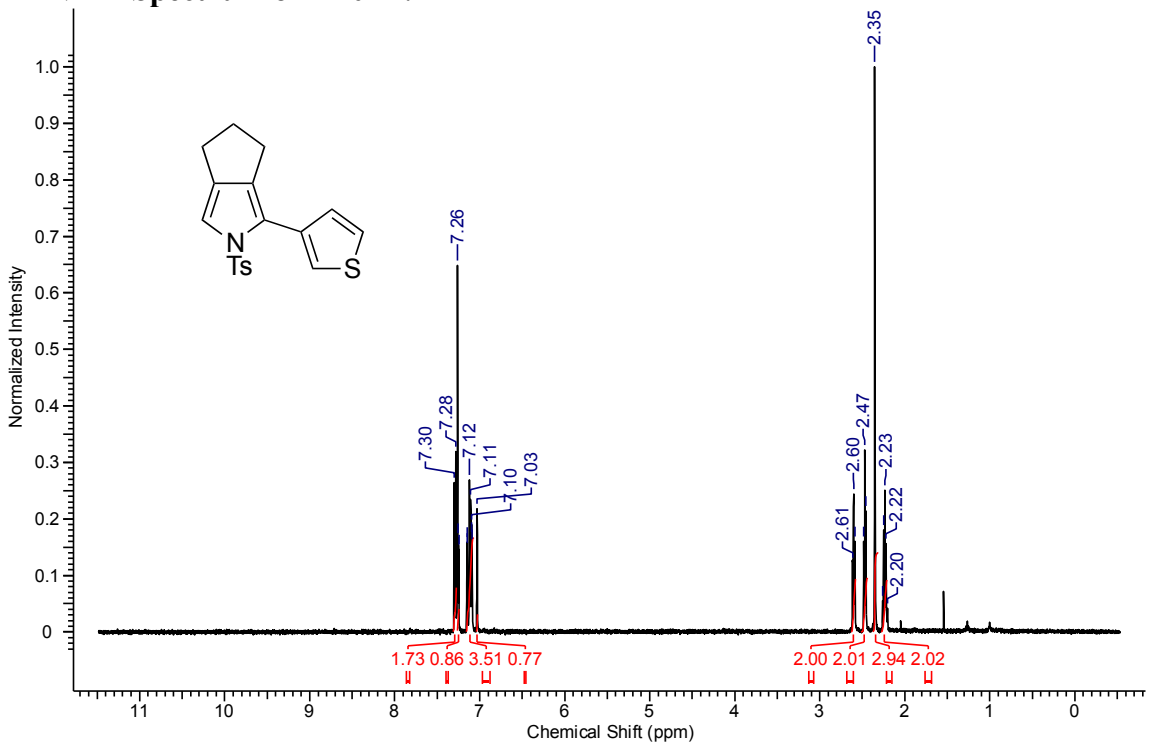
^{1}H NMR Spectrum of 4-9-m:



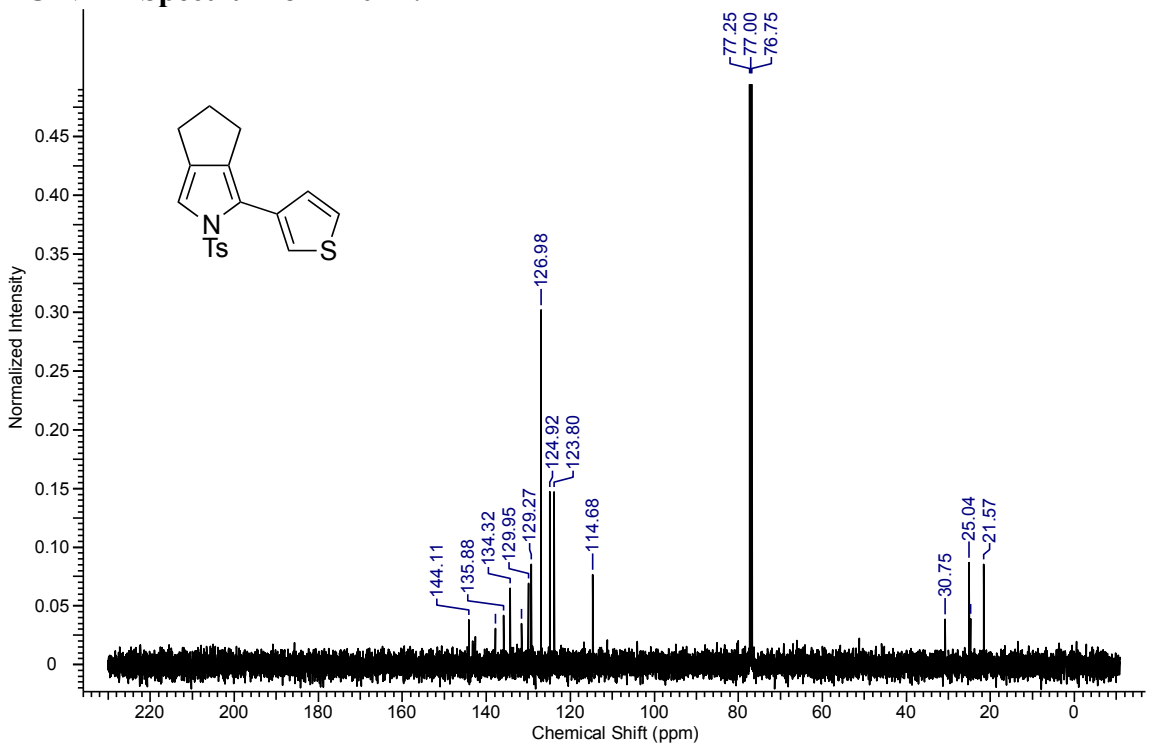
^{13}C NMR Spectrum of 4-9-m:



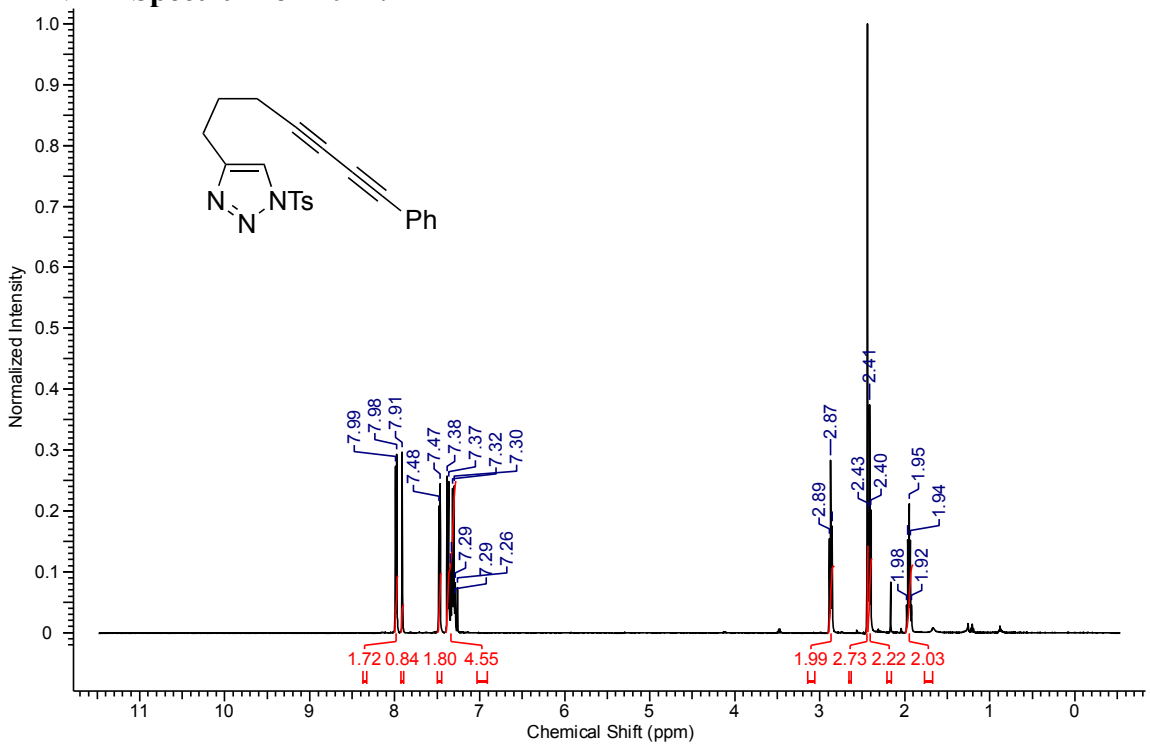
^{1}H NMR Spectrum of 4-10-m:



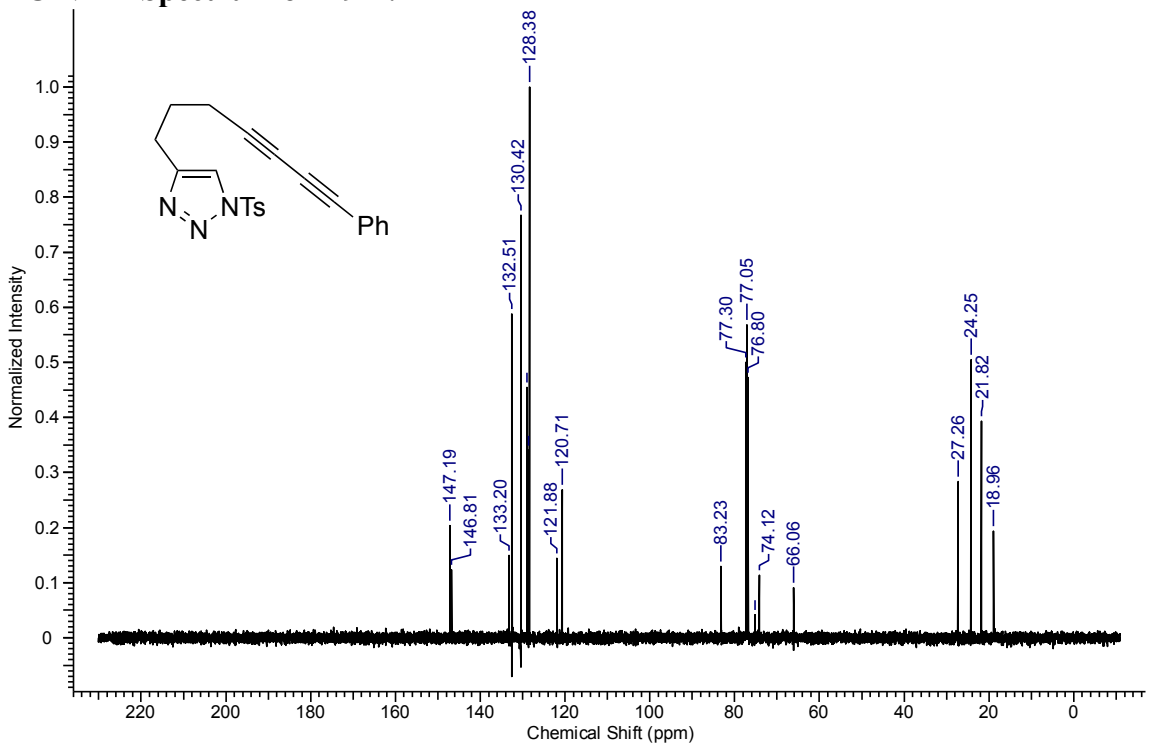
^{13}C NMR Spectrum of 4-10-m:



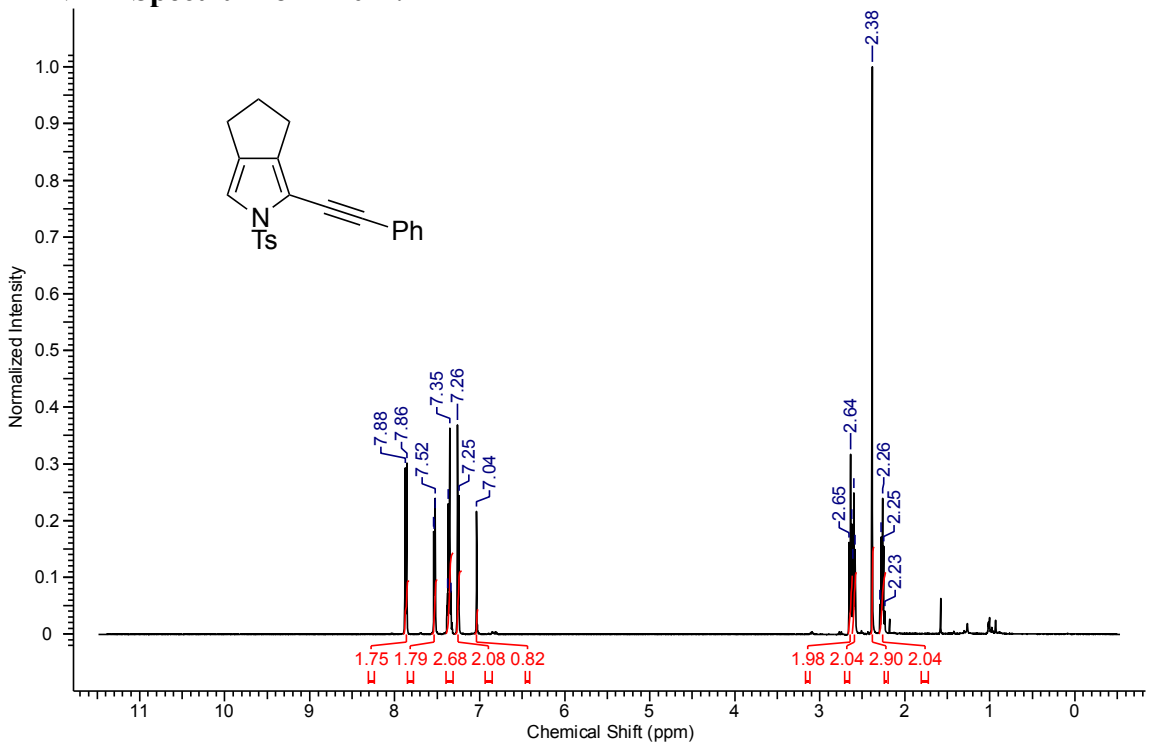
^{1}H NMR Spectrum of 4-9-n:



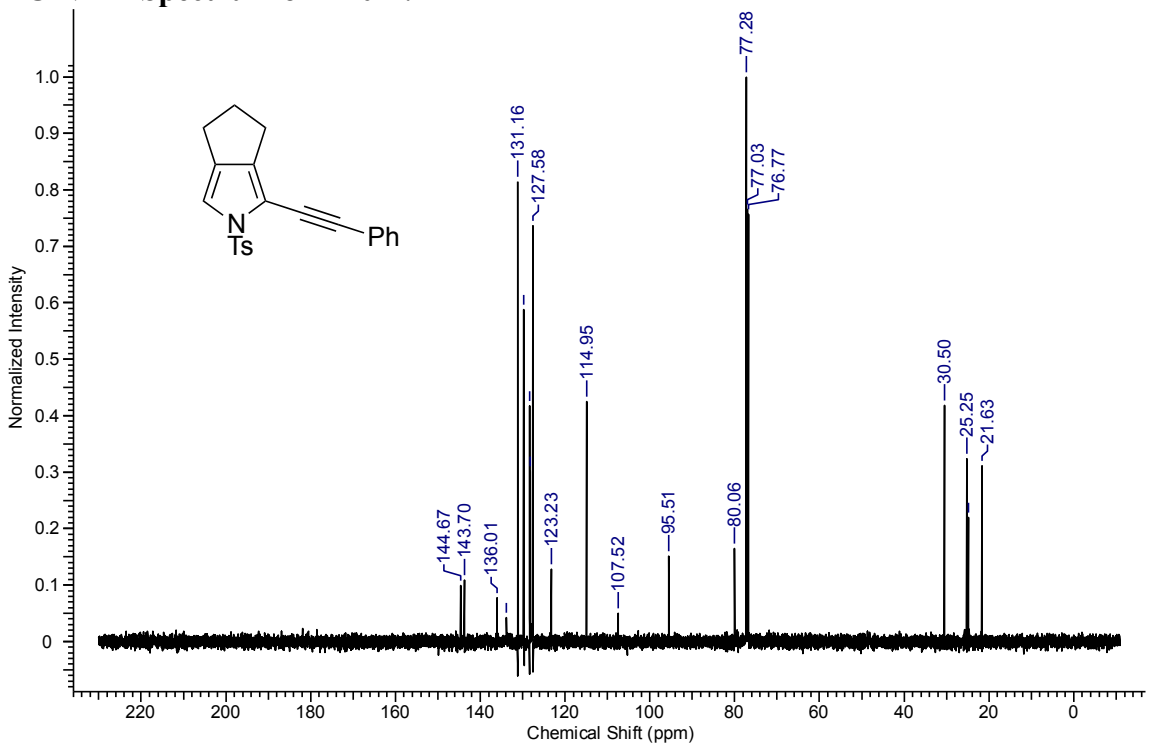
^{13}C NMR Spectrum of 4-9-n:



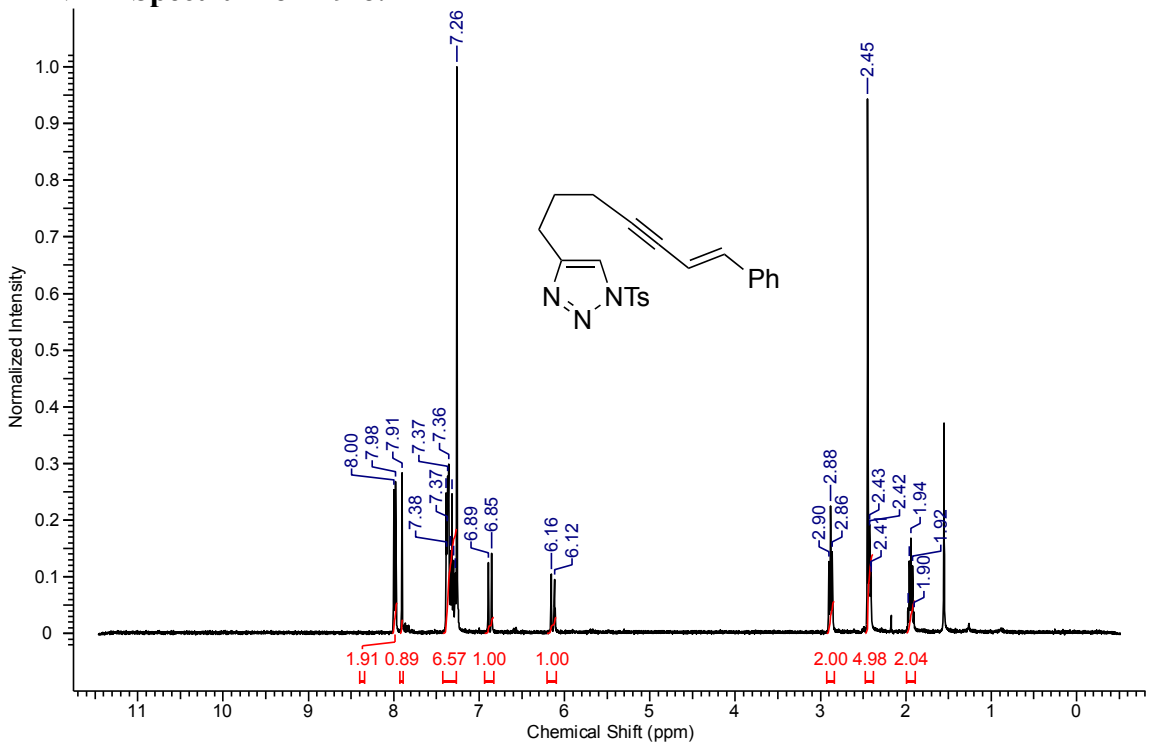
^{1}H NMR Spectrum of 4-10-n:



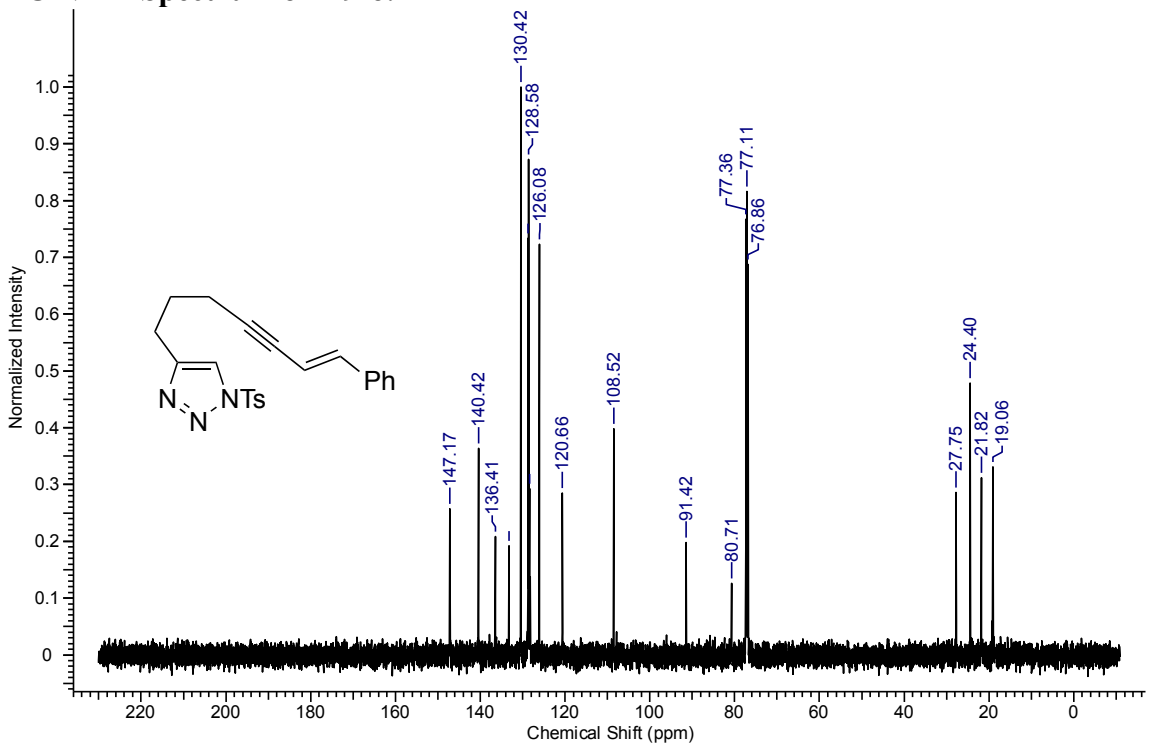
^{13}C NMR Spectrum of 4-10-n:



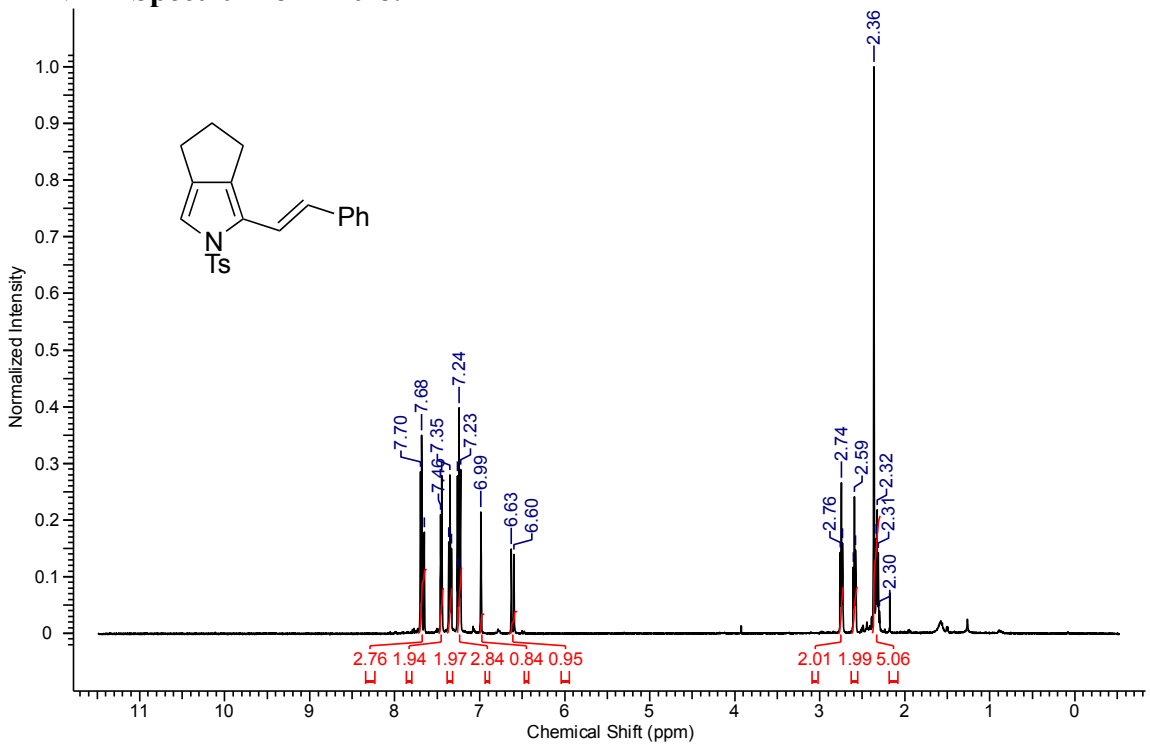
^{1}H NMR Spectrum of 4-9-o:



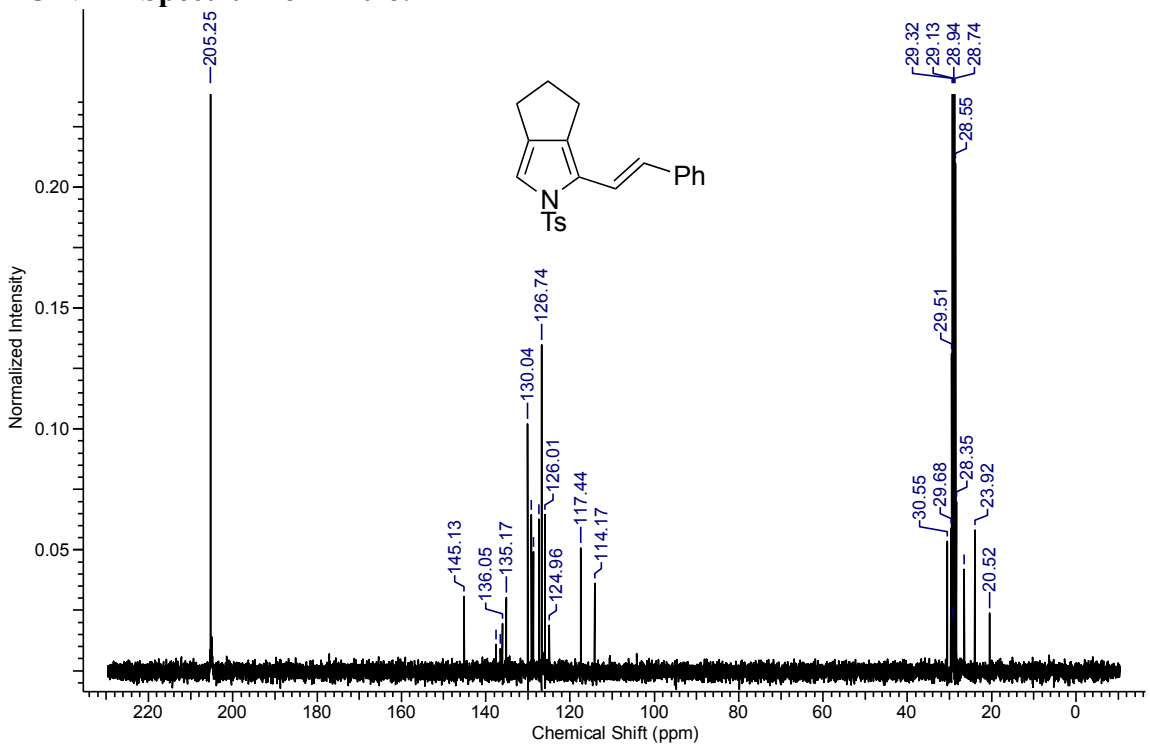
^{13}C NMR Spectrum of 4-9-o:



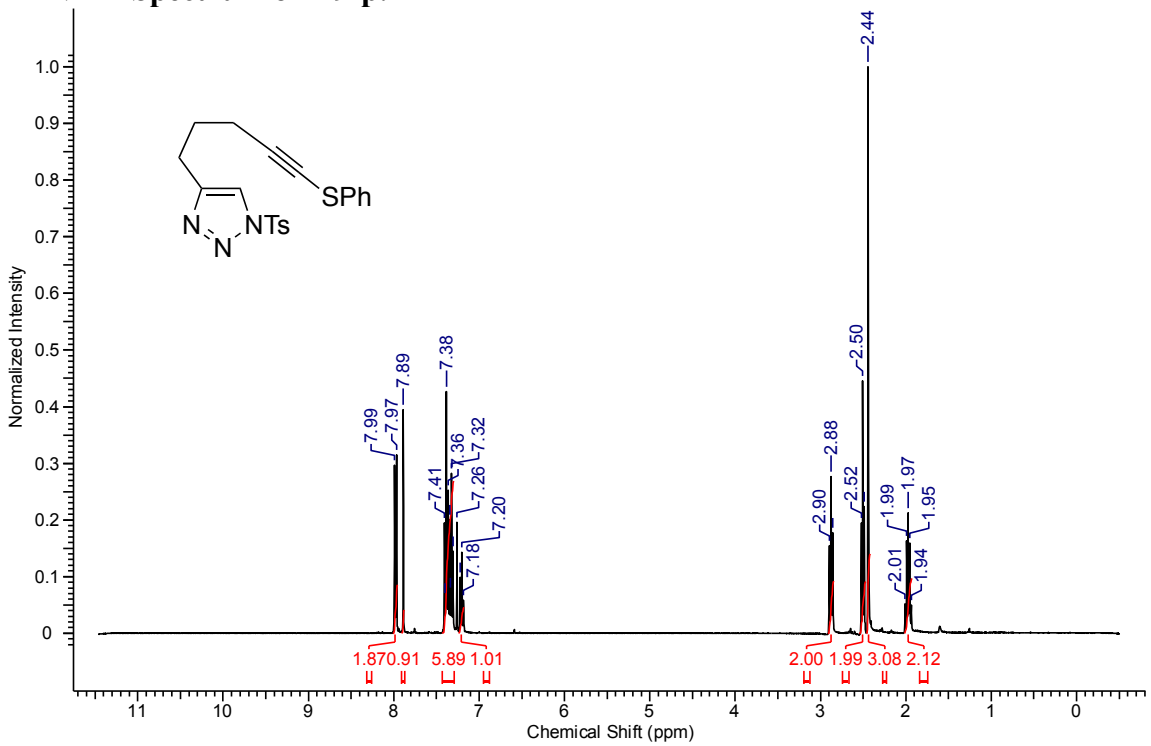
^{1}H NMR Spectrum of 4-10-o:



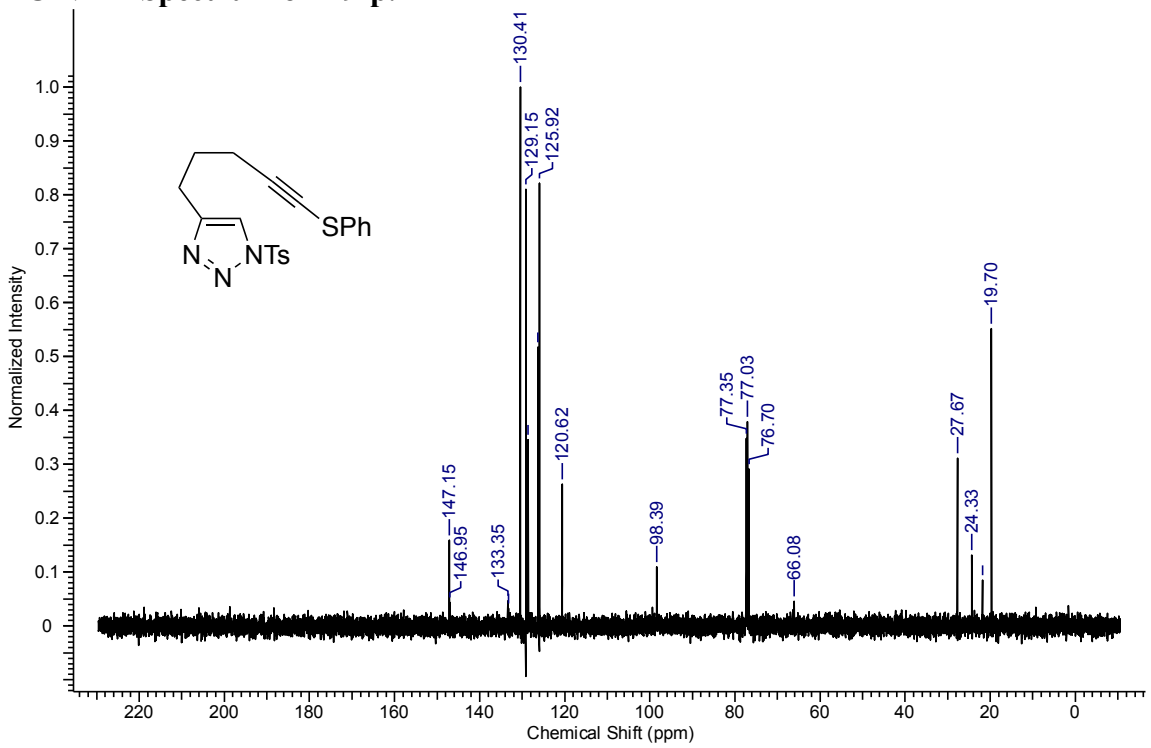
^{13}C NMR Spectrum of 4-10-o:



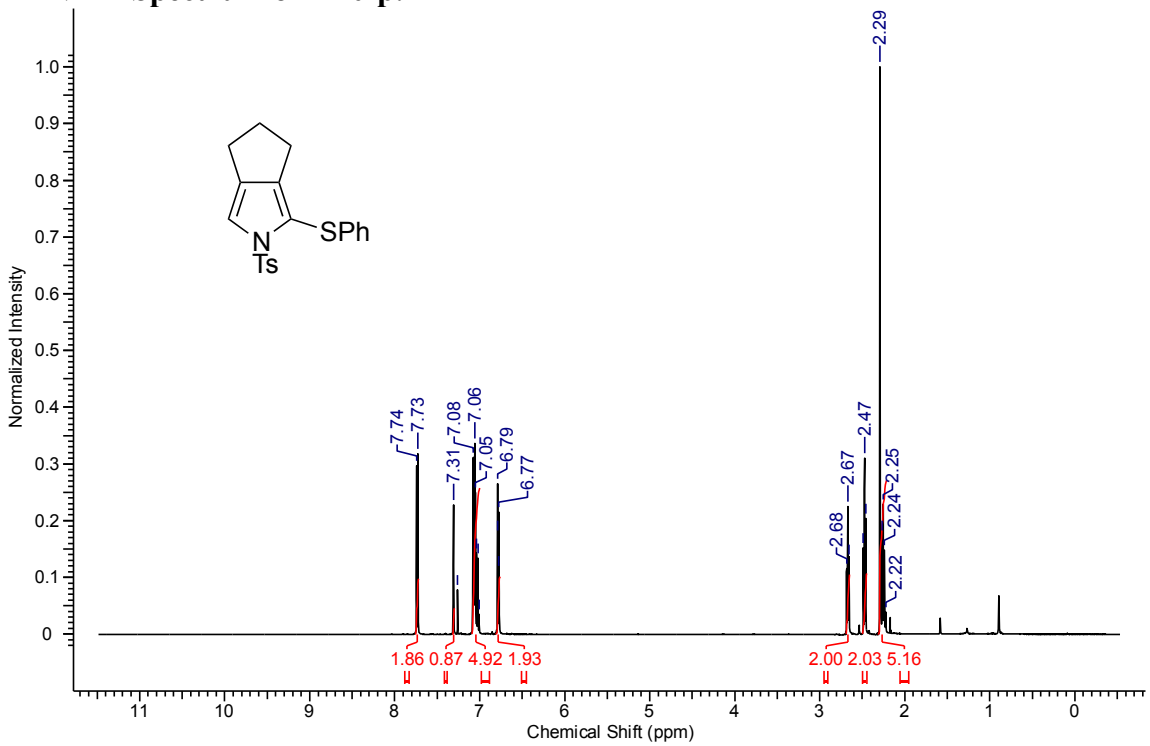
^{1}H NMR Spectrum of 4-9-p:



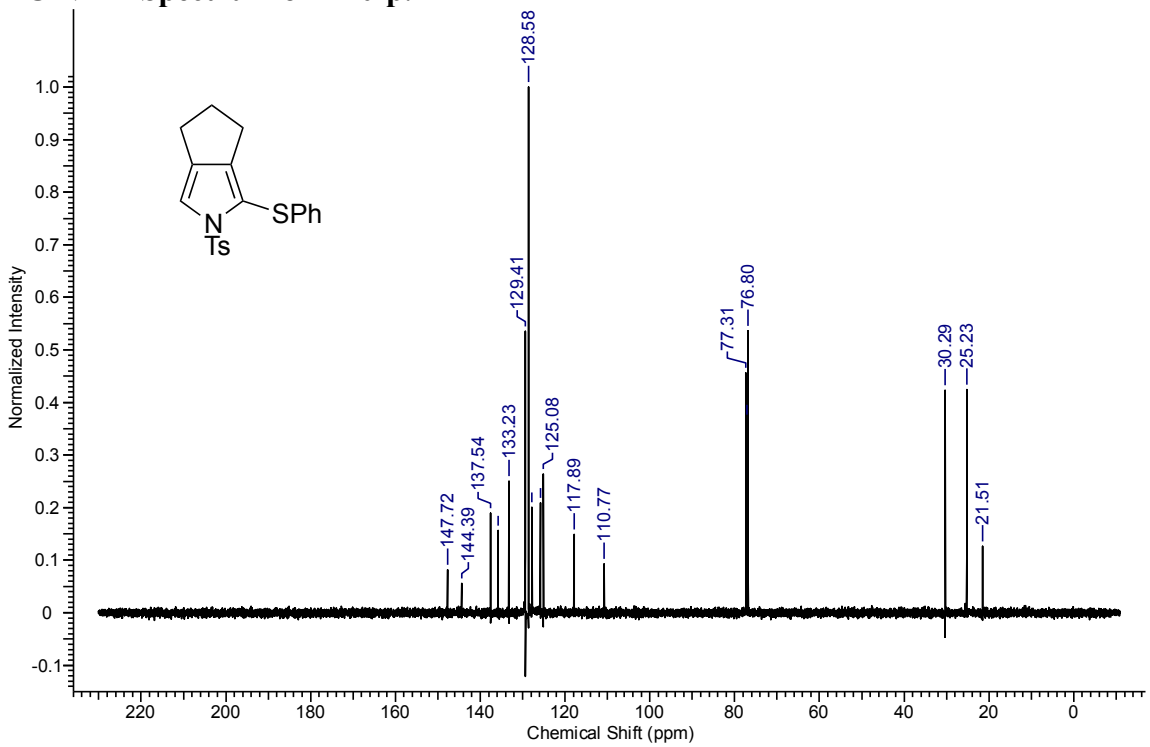
^{13}C NMR Spectrum of 4-9-p:



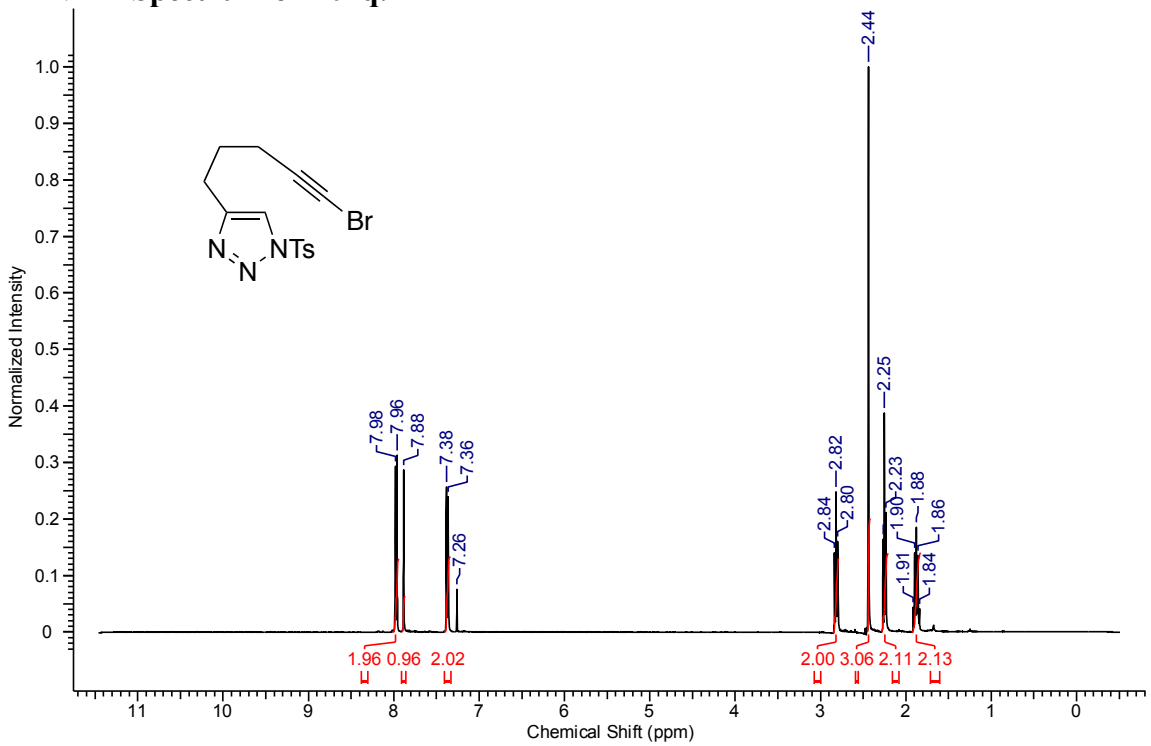
^{1}H NMR Spectrum of 4-10-p:



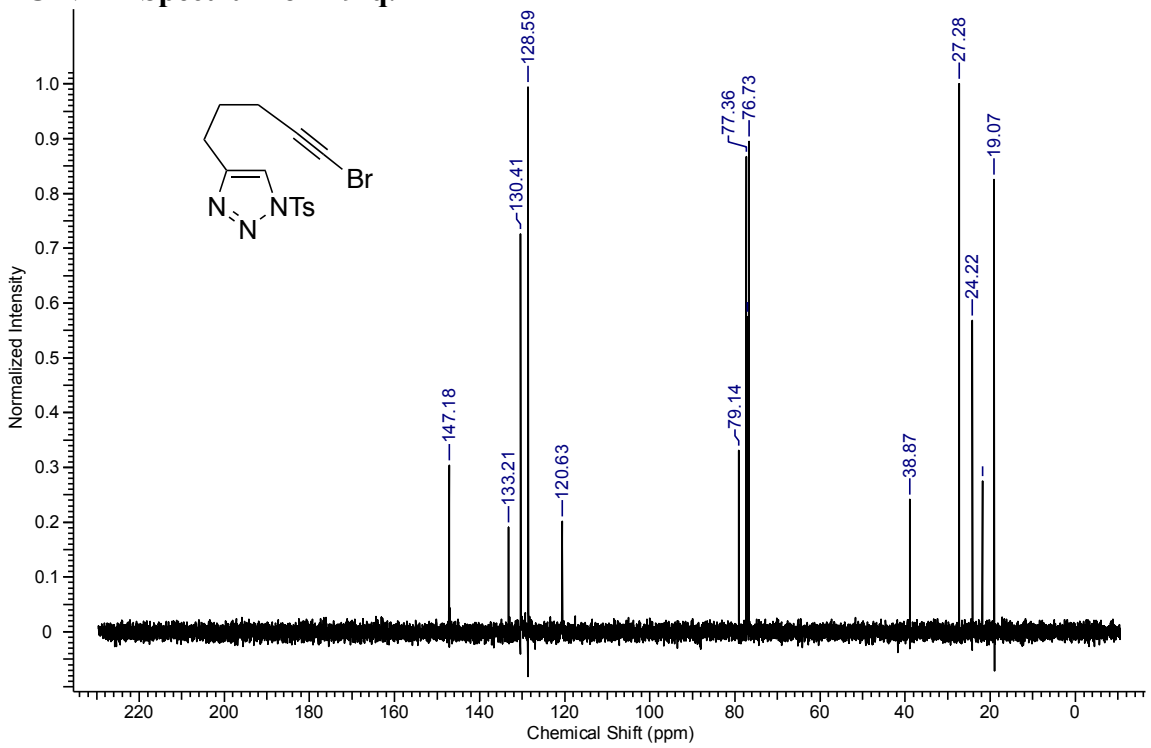
^{13}C NMR Spectrum of 4-10-p:



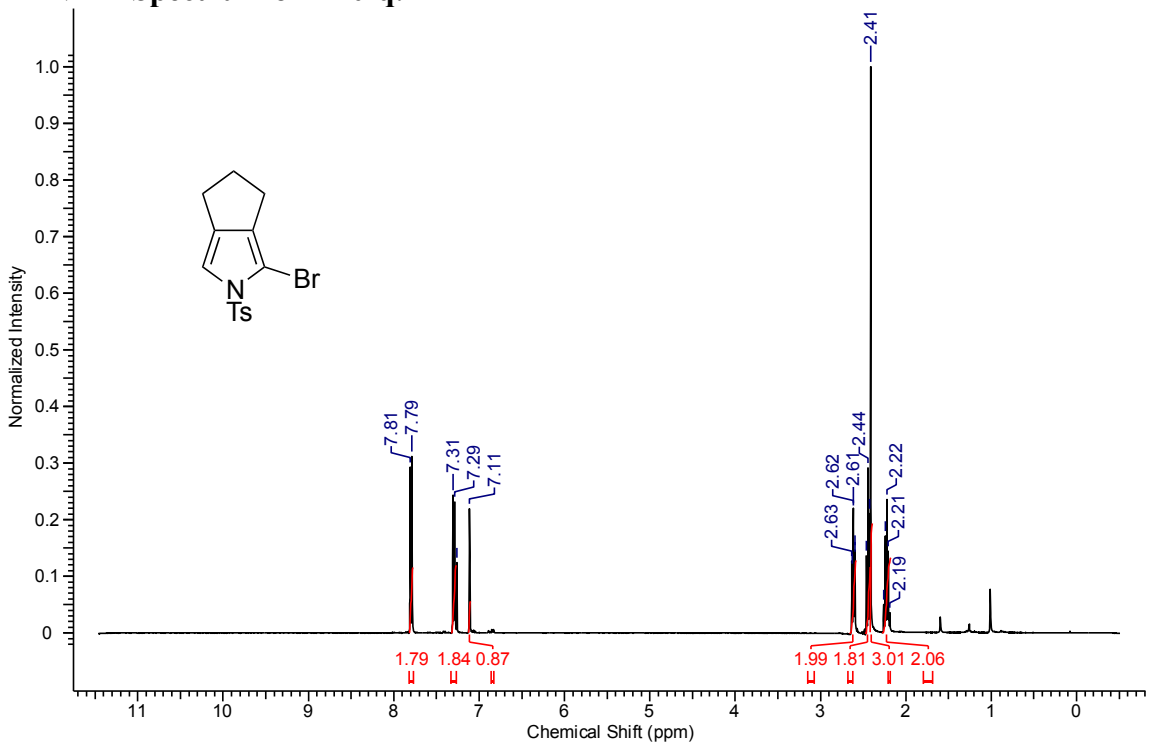
^{1}H NMR Spectrum of 4-9-q:



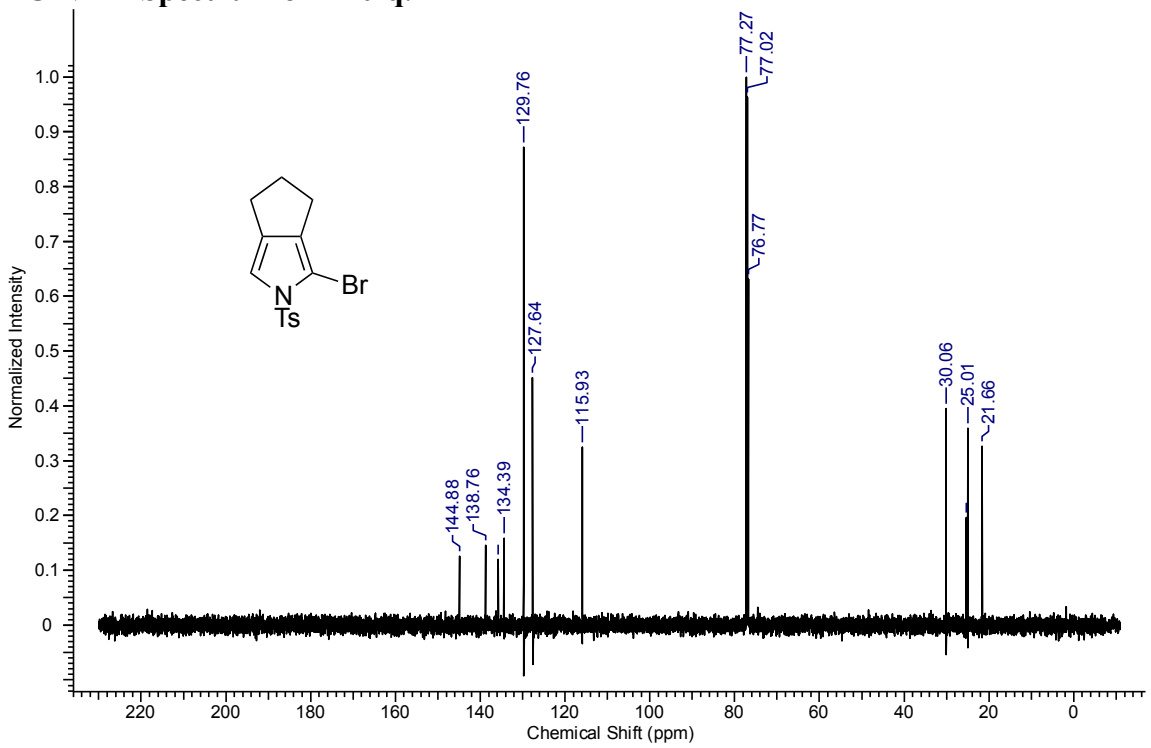
^{13}C NMR Spectrum of 4-9-q:



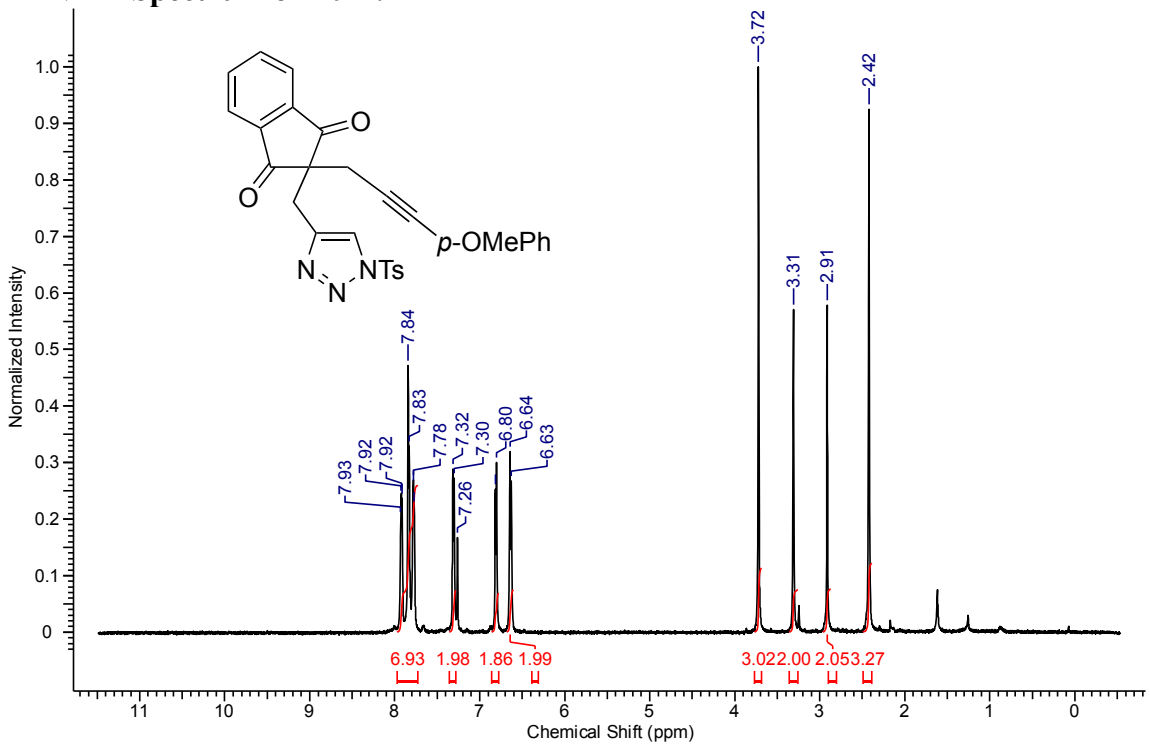
^{1}H NMR Spectrum of 4-10-q:



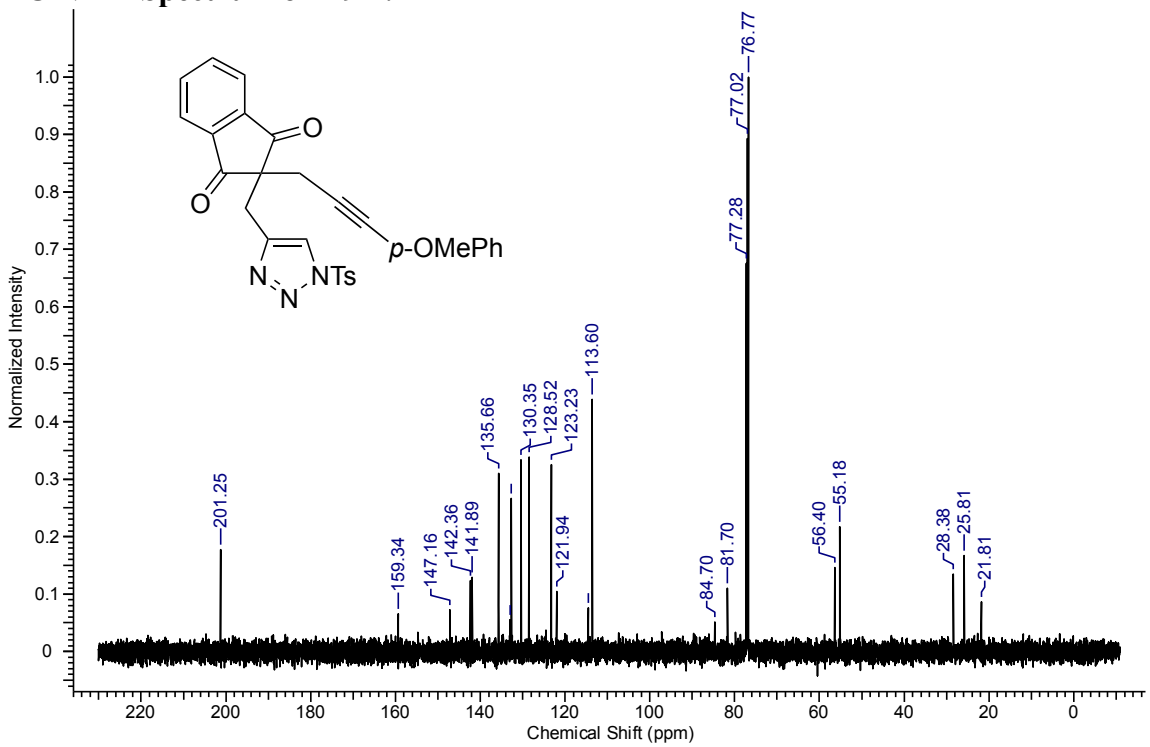
^{13}C NMR Spectrum of 4-10-q:



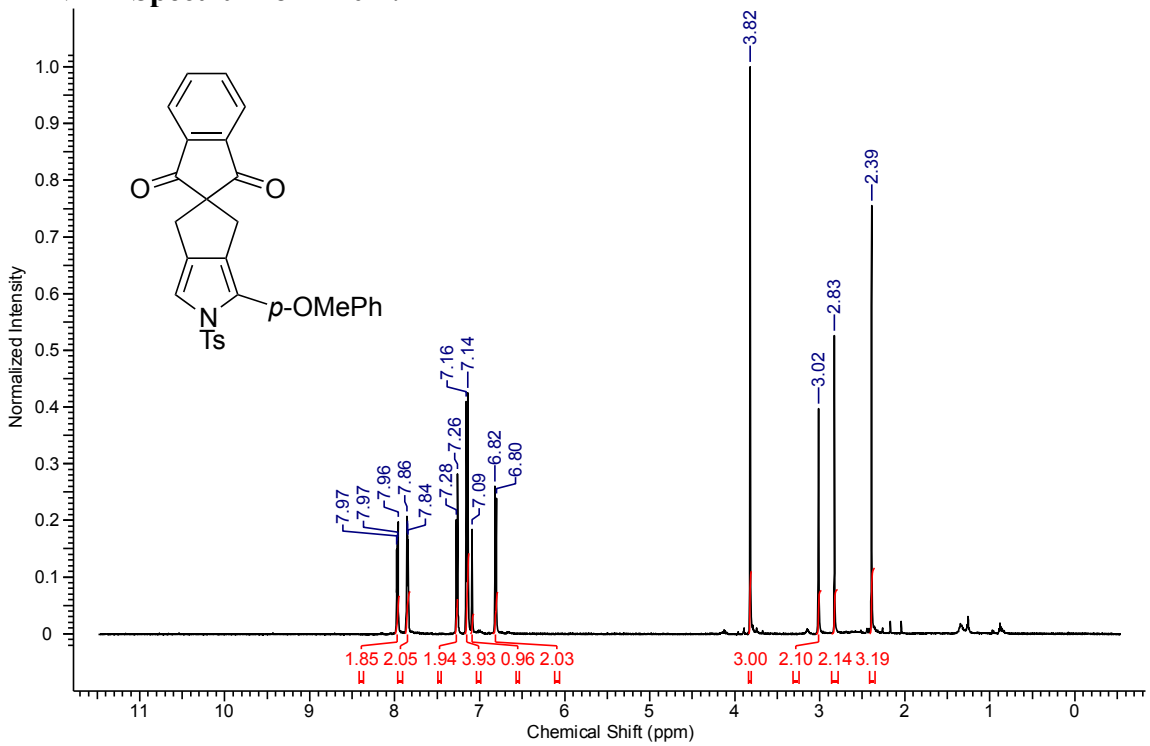
^{1}H NMR Spectrum of 4-9-r:



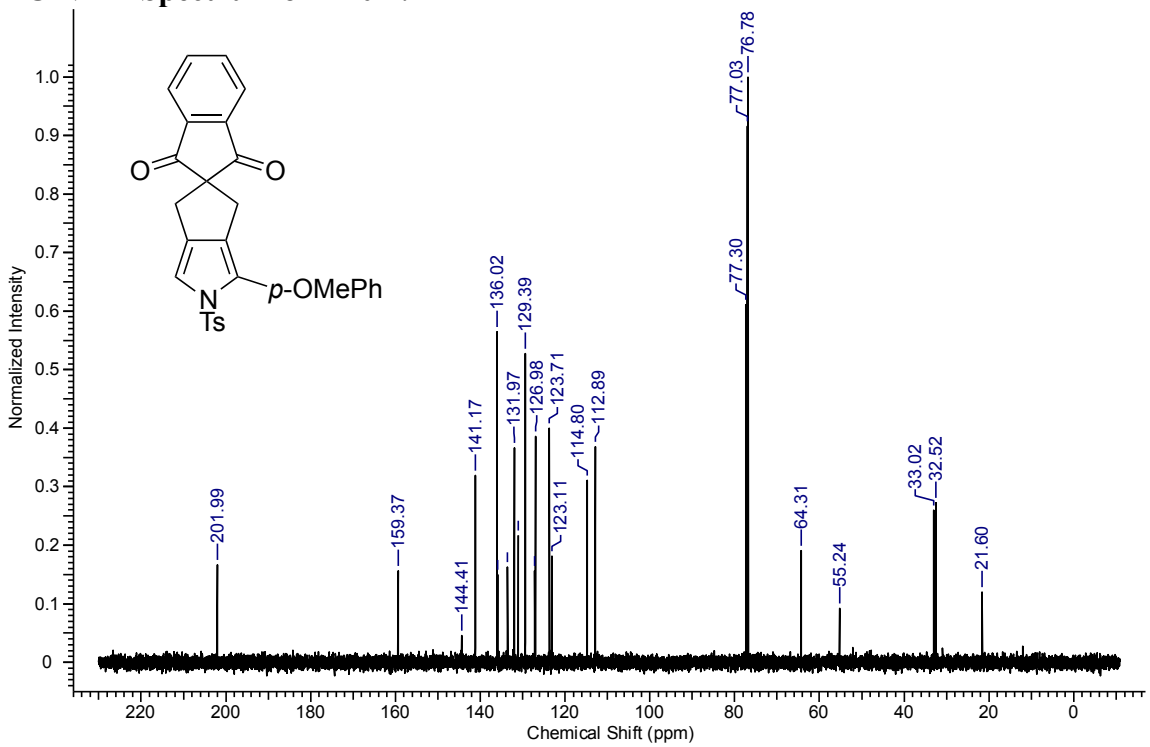
^{13}C NMR Spectrum of 4-9-r:



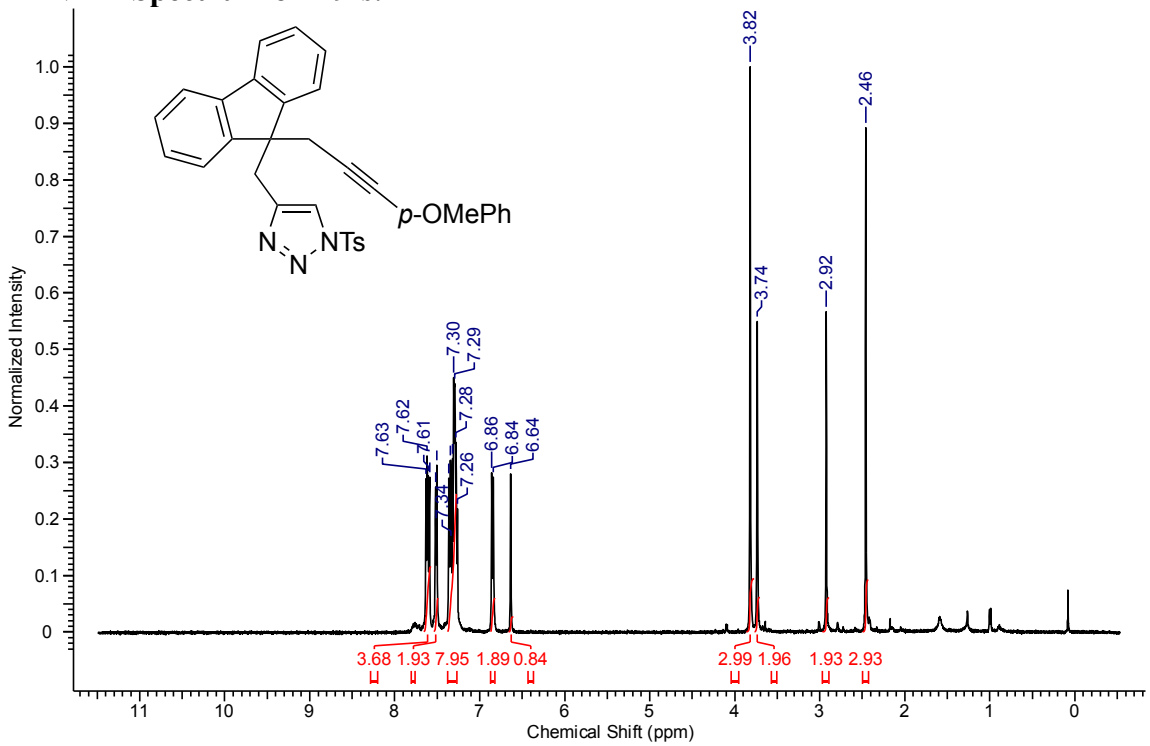
^{1}H NMR Spectrum of 4-10-r:



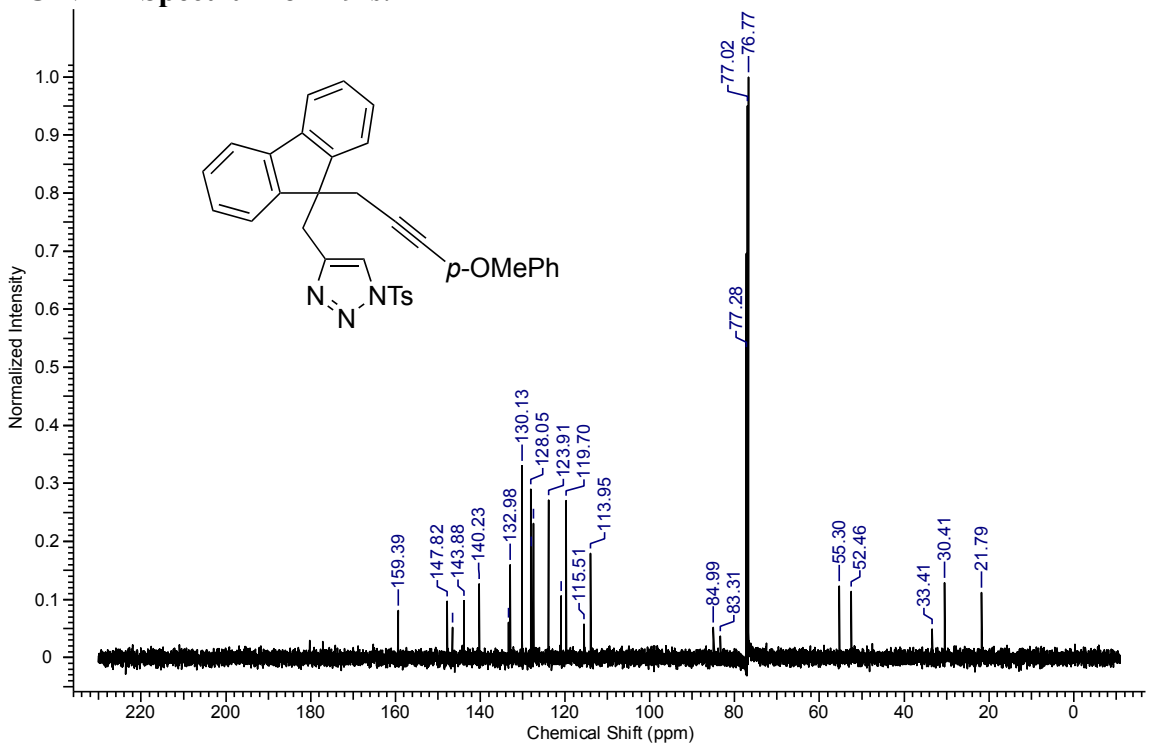
^{13}C NMR Spectrum of 4-10-r:



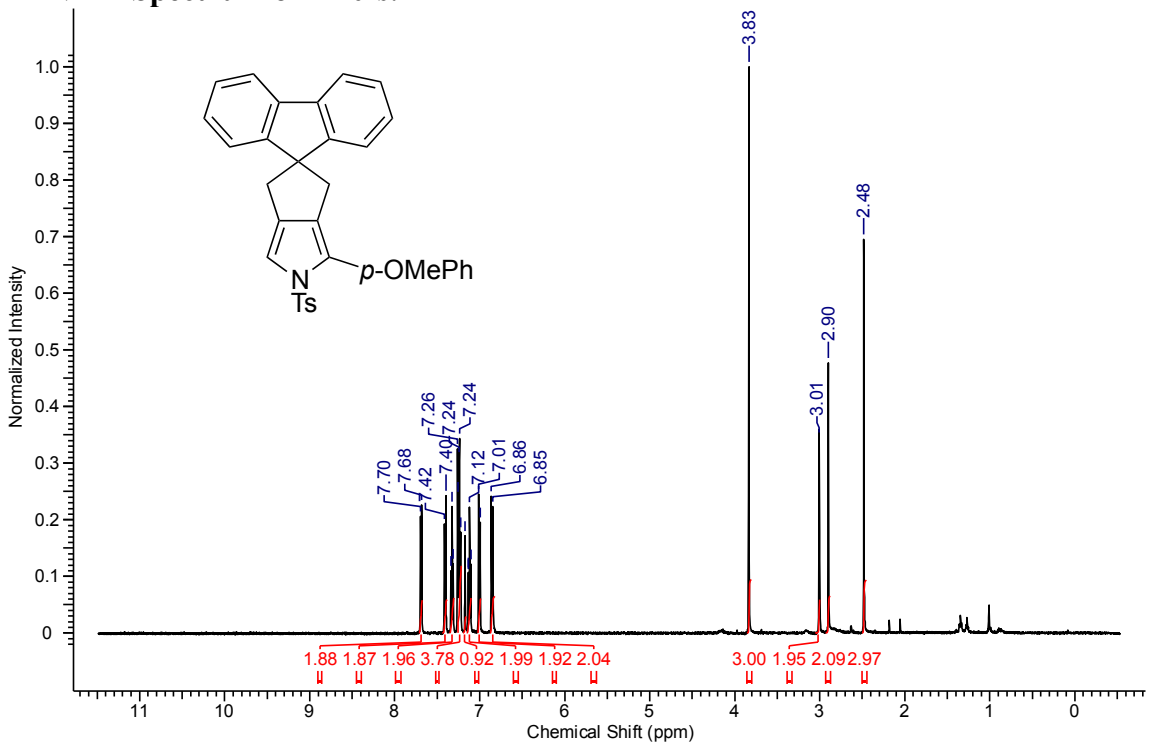
^{1}H NMR Spectrum of 4-9-s:



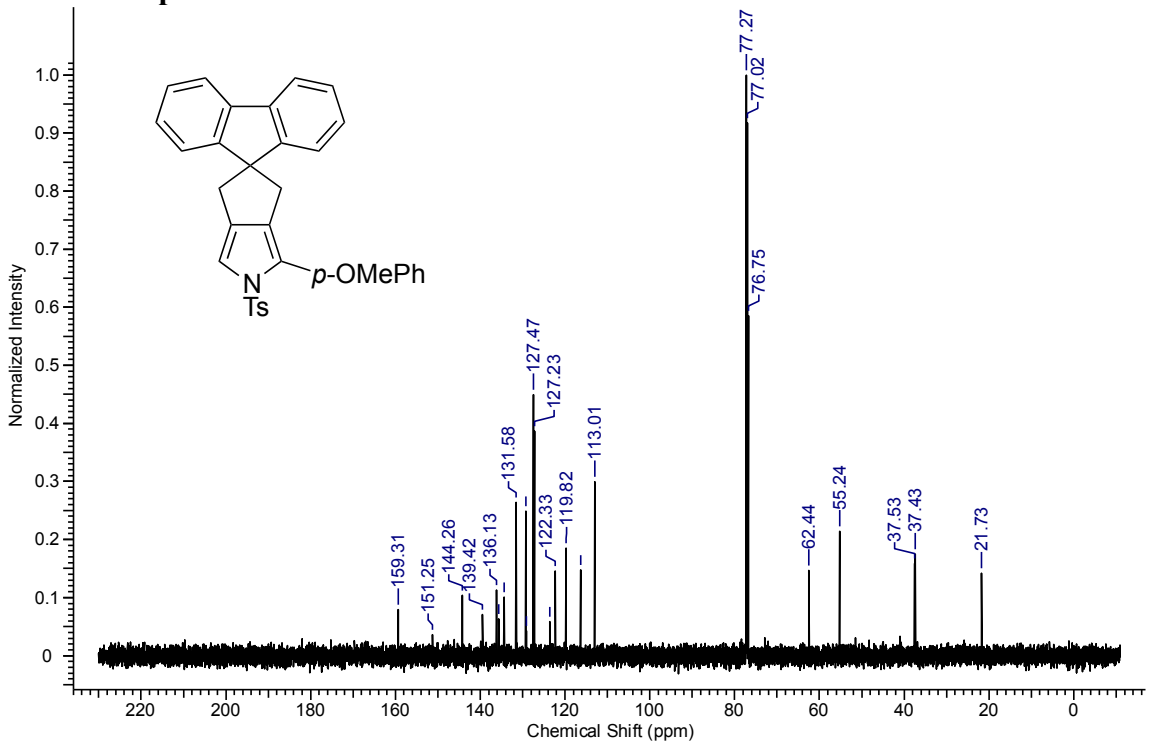
^{13}C NMR Spectrum of 4-9-s:



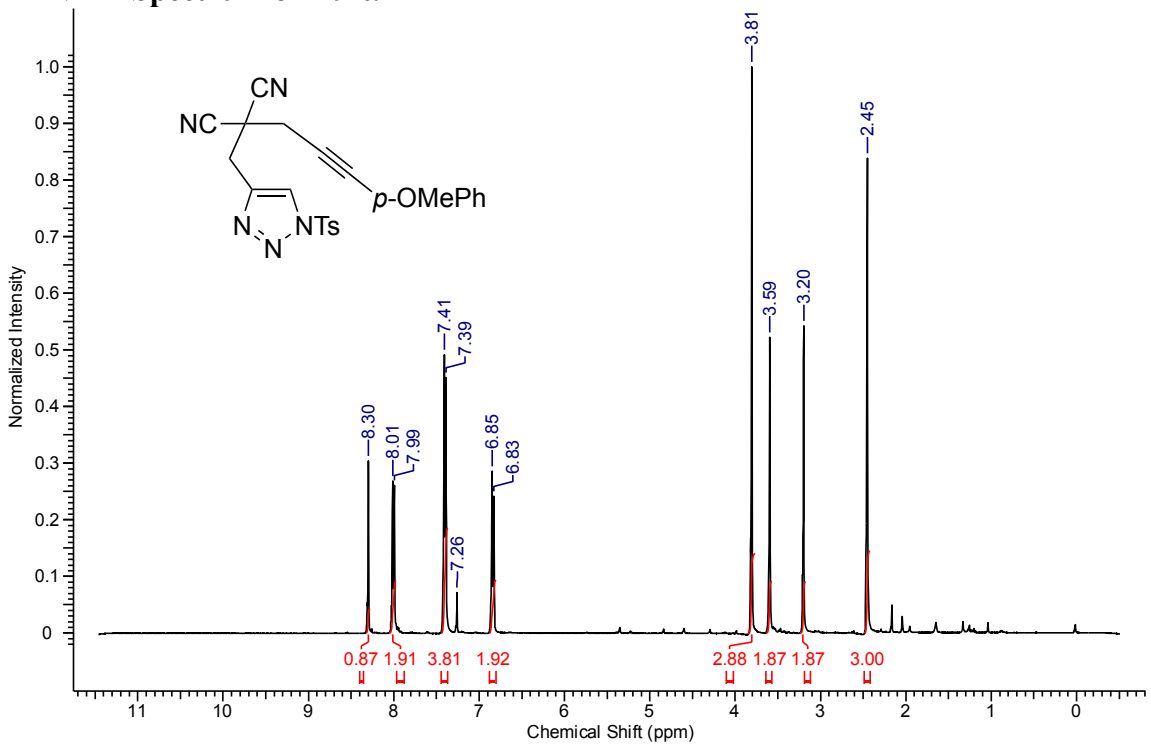
^{1}H NMR Spectrum of 4-10-s:



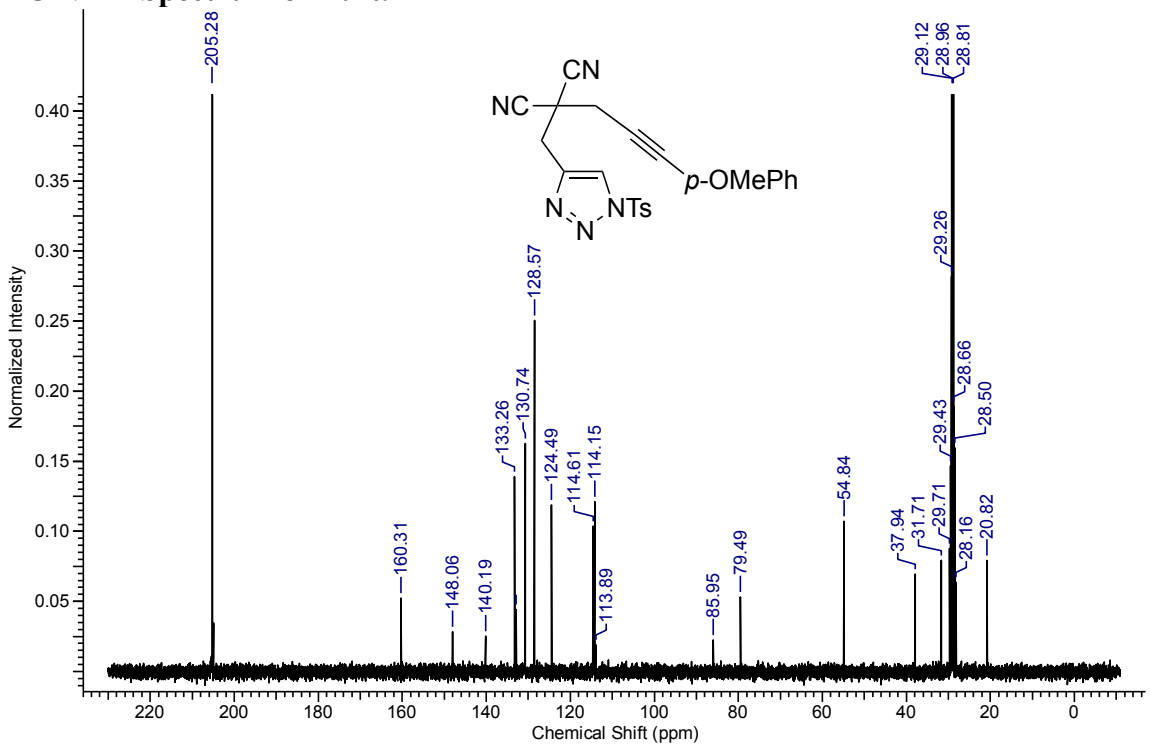
^{13}C NMR Spectrum of 4-10-s:



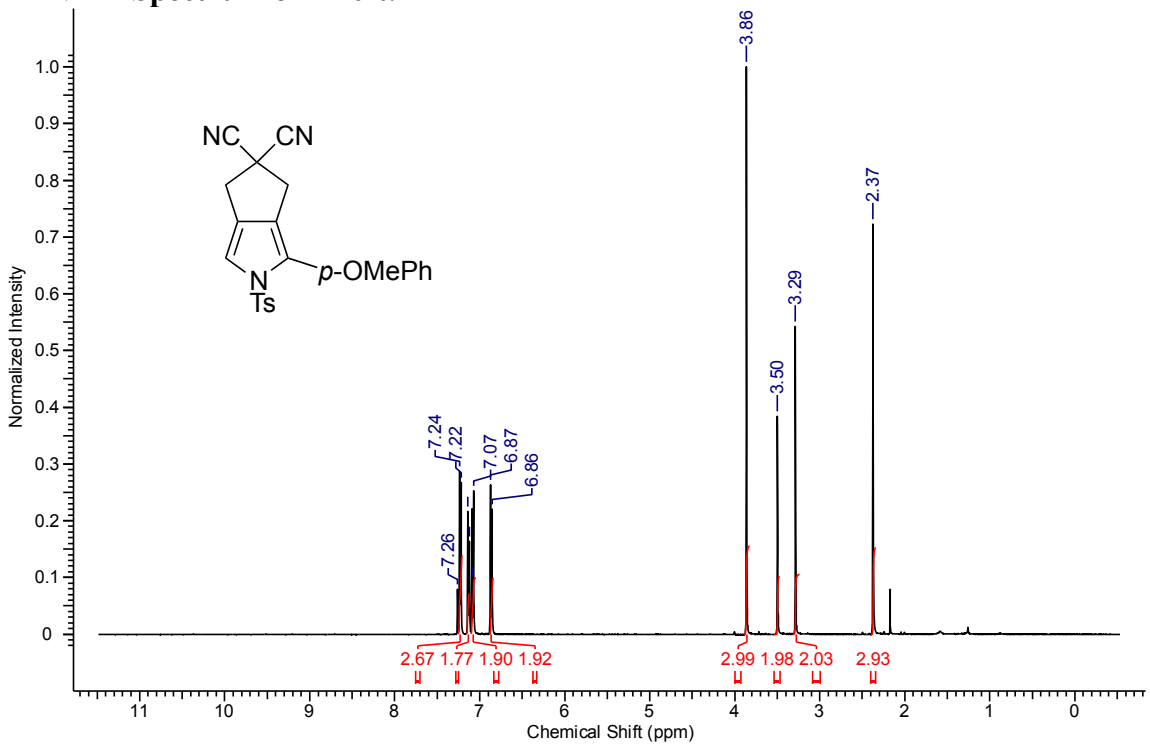
^{1}H NMR Spectrum of 4-9-t:



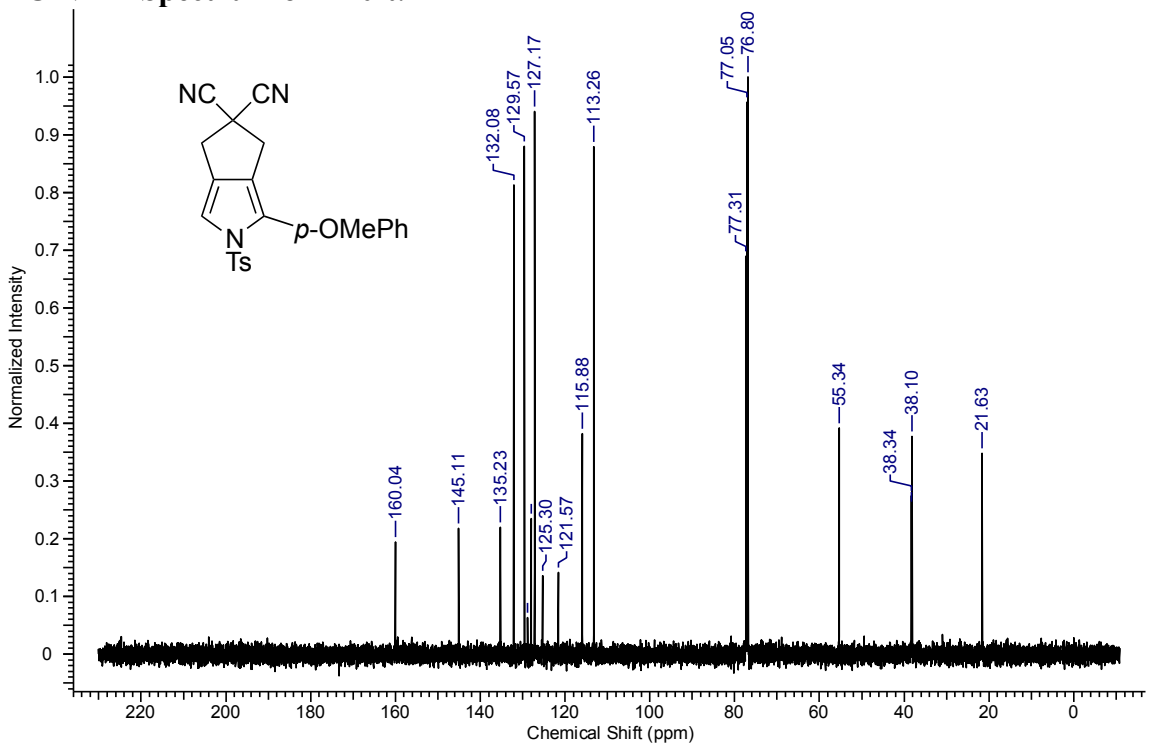
^{13}C NMR Spectrum of 4-9-t:



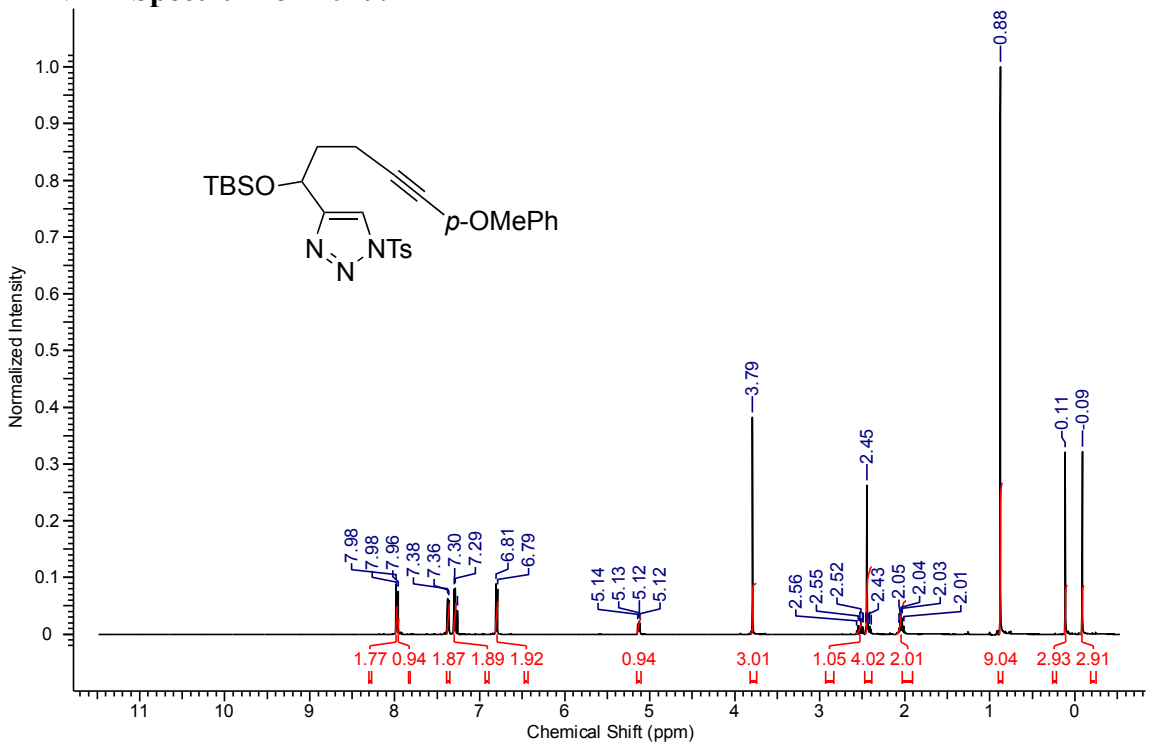
^{1}H NMR Spectrum of 4-10-t:



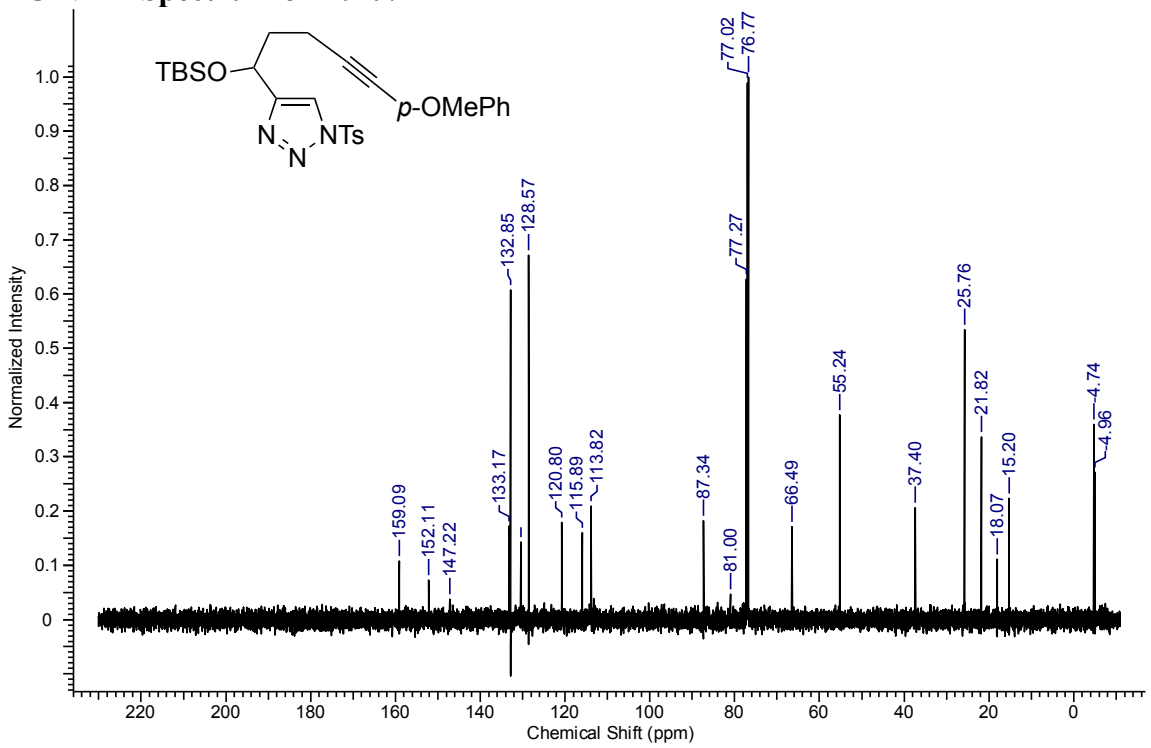
^{13}C NMR Spectrum of 4-10-t:



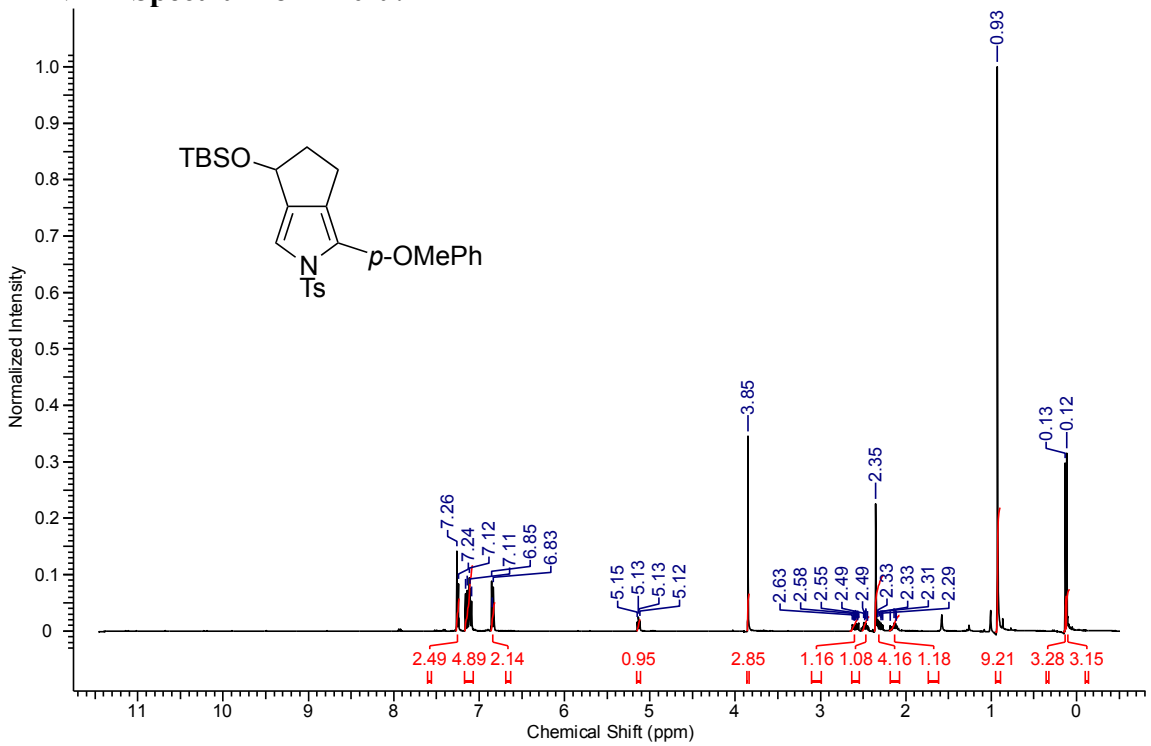
^{1}H NMR Spectrum of 4-9-u:



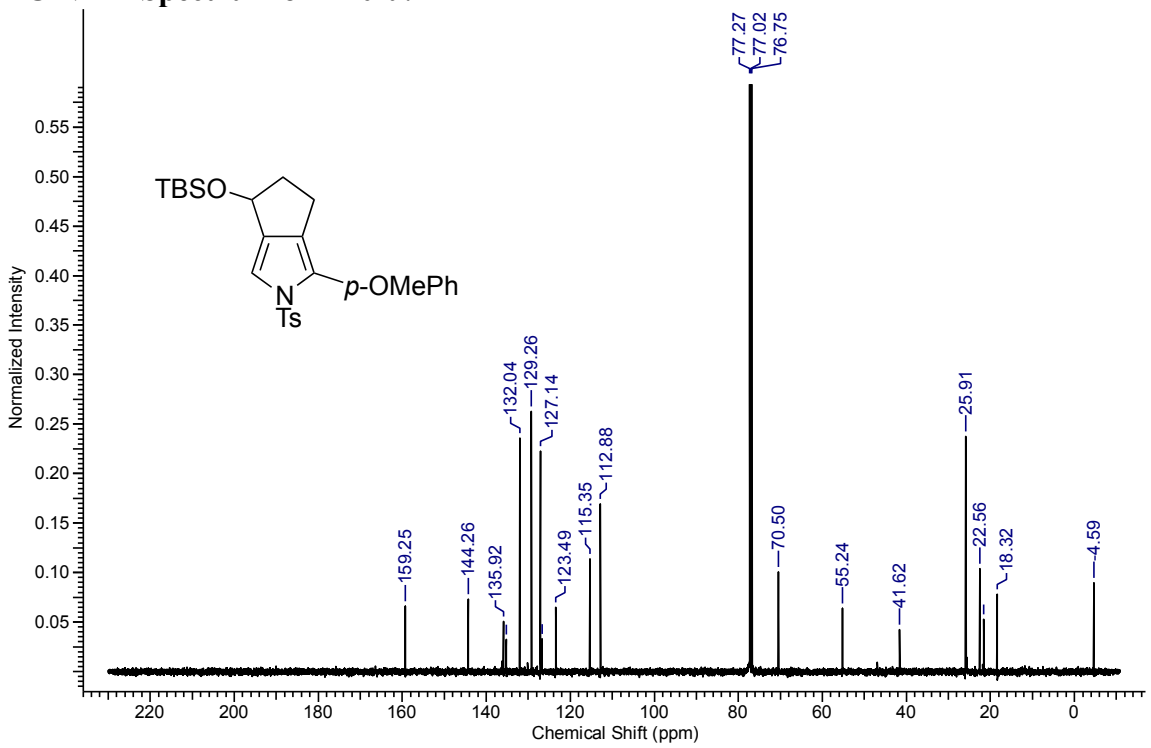
^{13}C NMR Spectrum of 4-9-u:



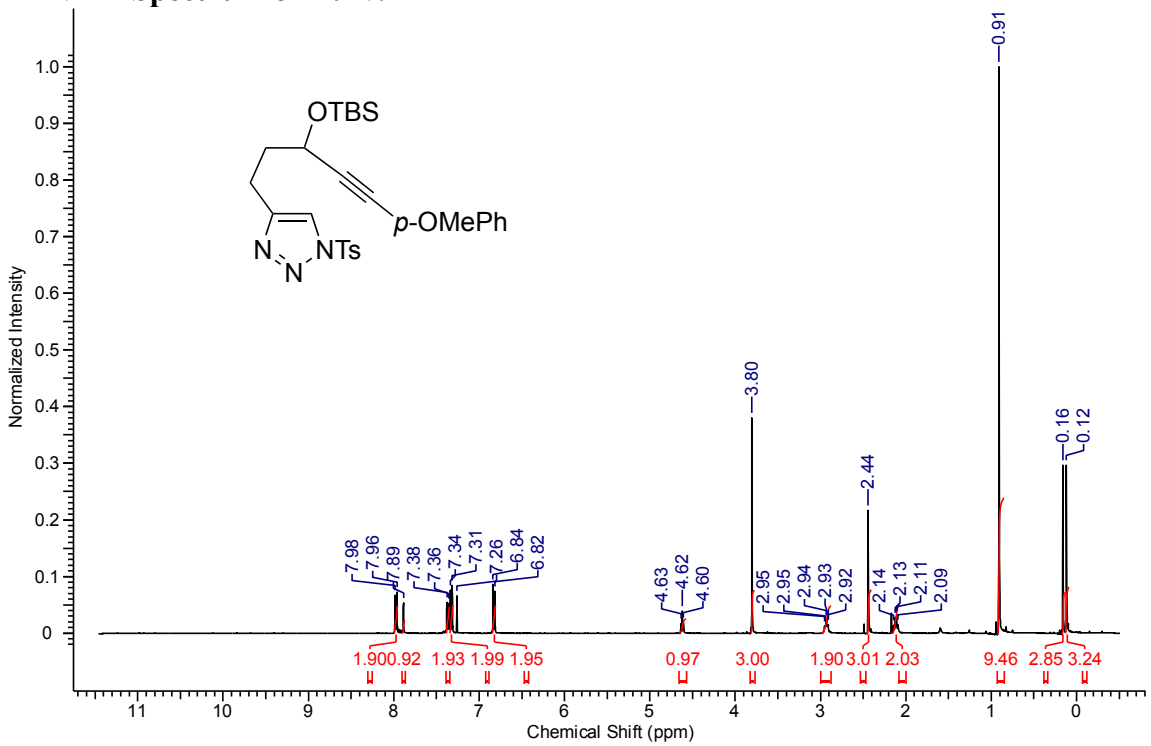
^{1}H NMR Spectrum of 4-10-u:



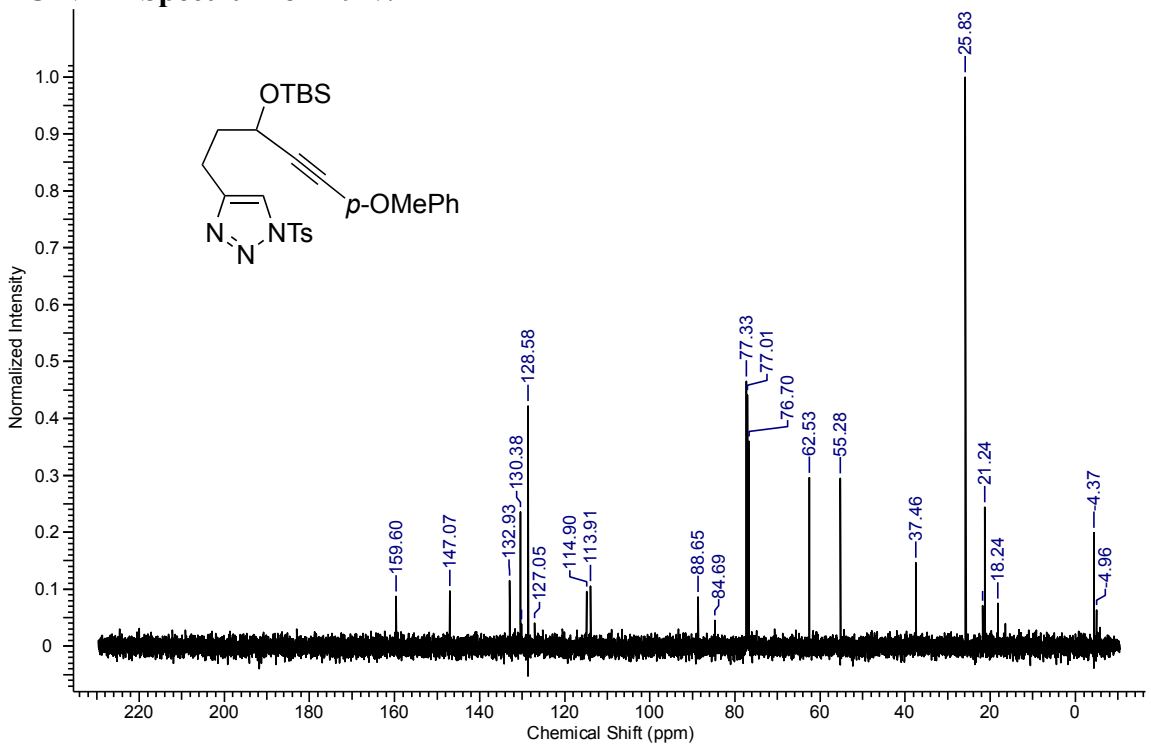
^{13}C NMR Spectrum of 4-10-u:



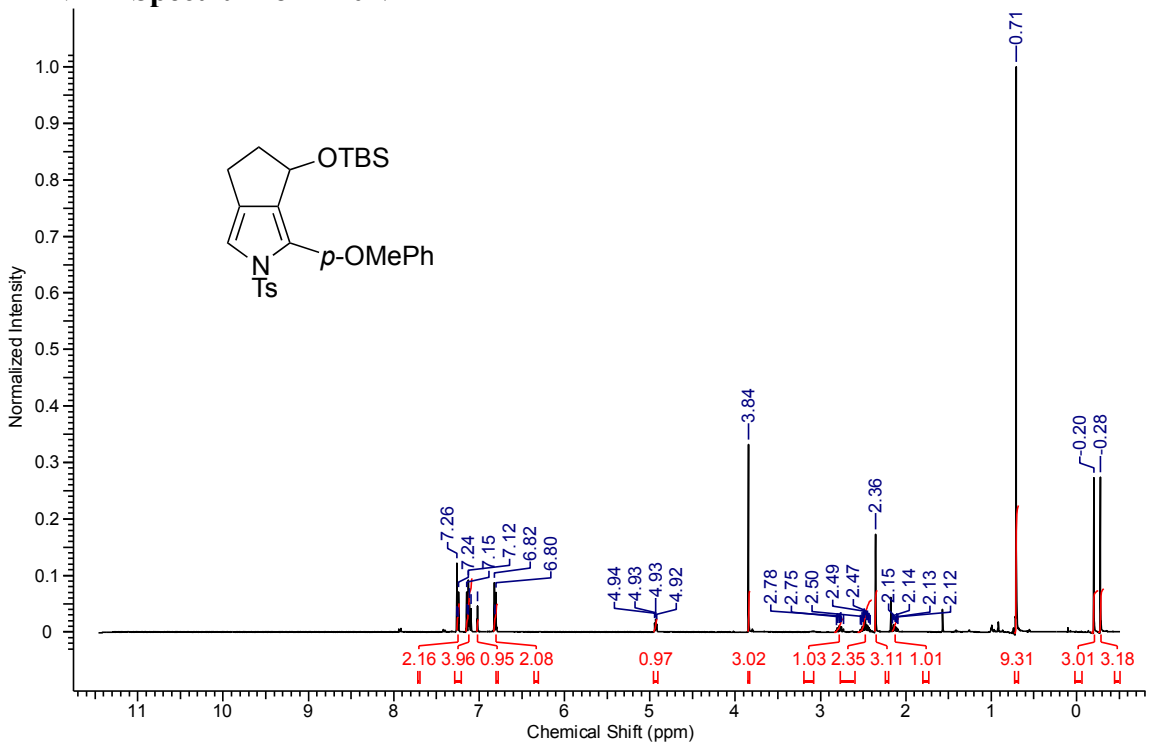
^{1}H NMR Spectrum of 4-9-v:



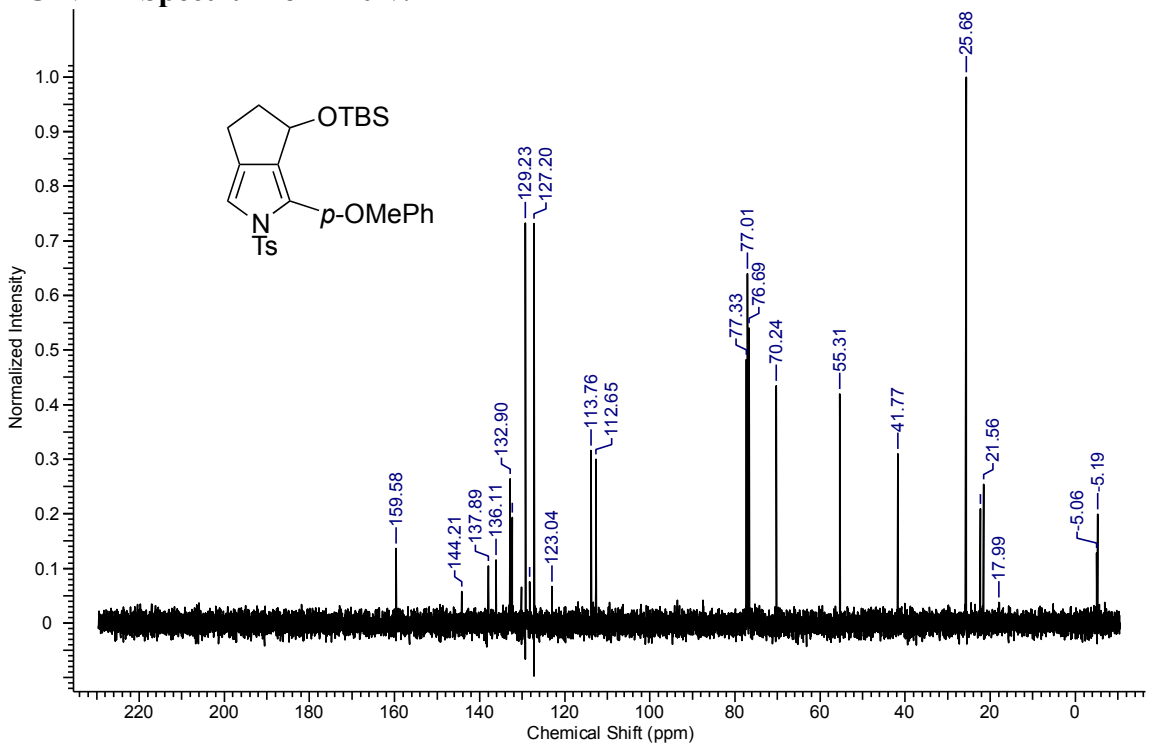
^{13}C NMR Spectrum of 4-9-v:



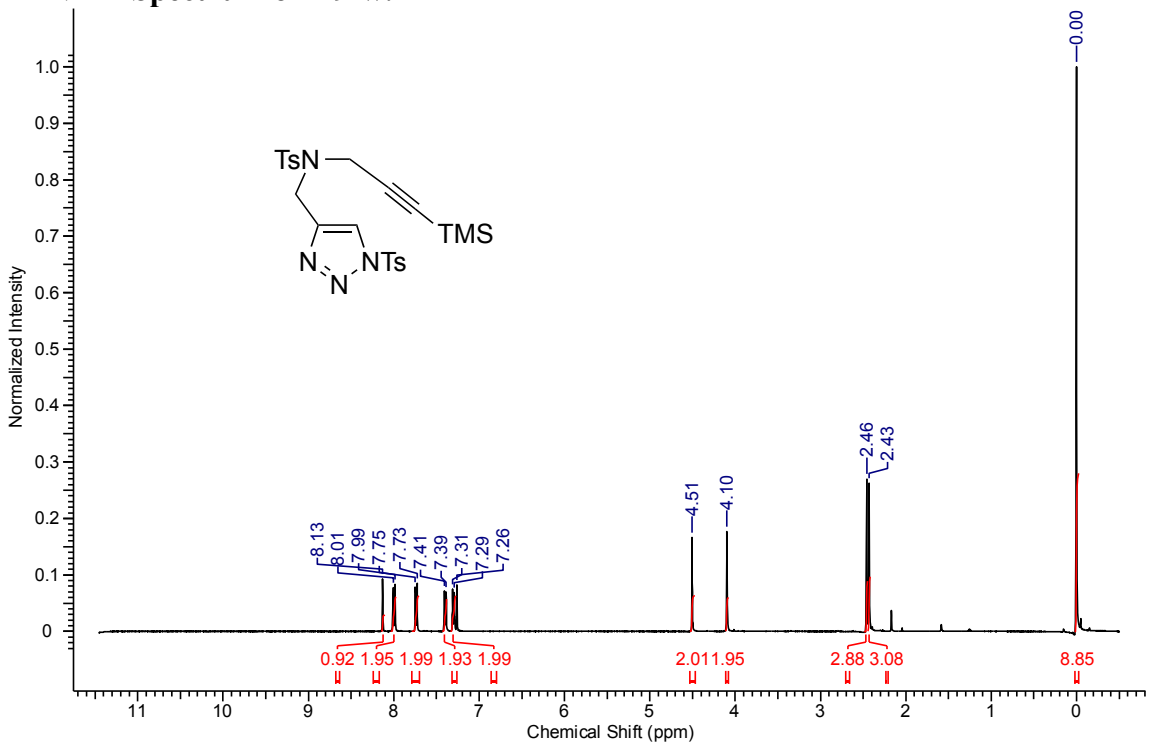
^{1}H NMR Spectrum of 4-10-v



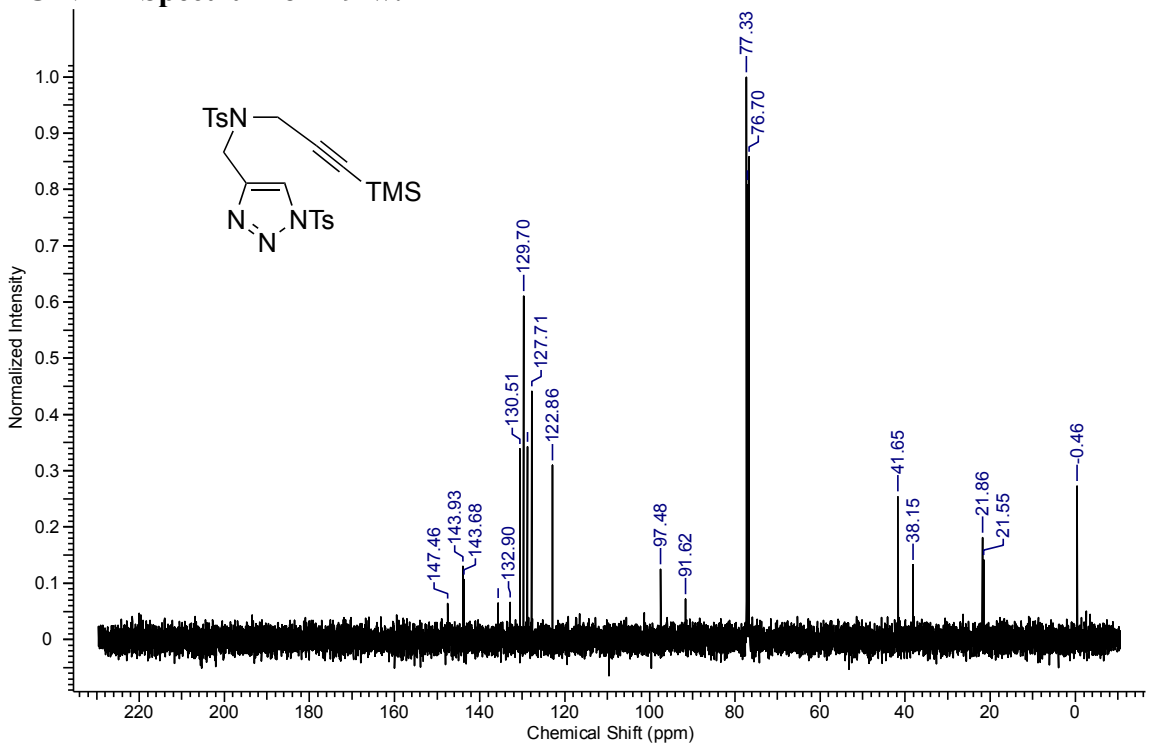
^{13}C NMR Spectrum of 4-10-v:



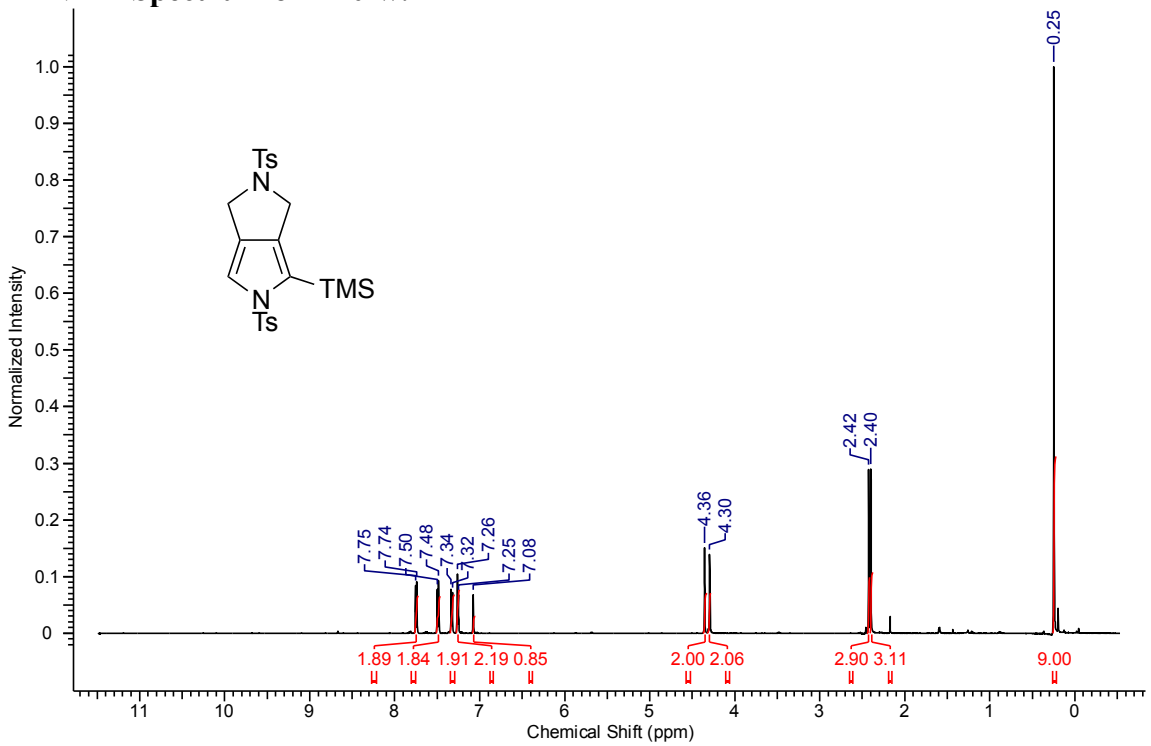
^{1}H NMR Spectrum of 4-9-w:



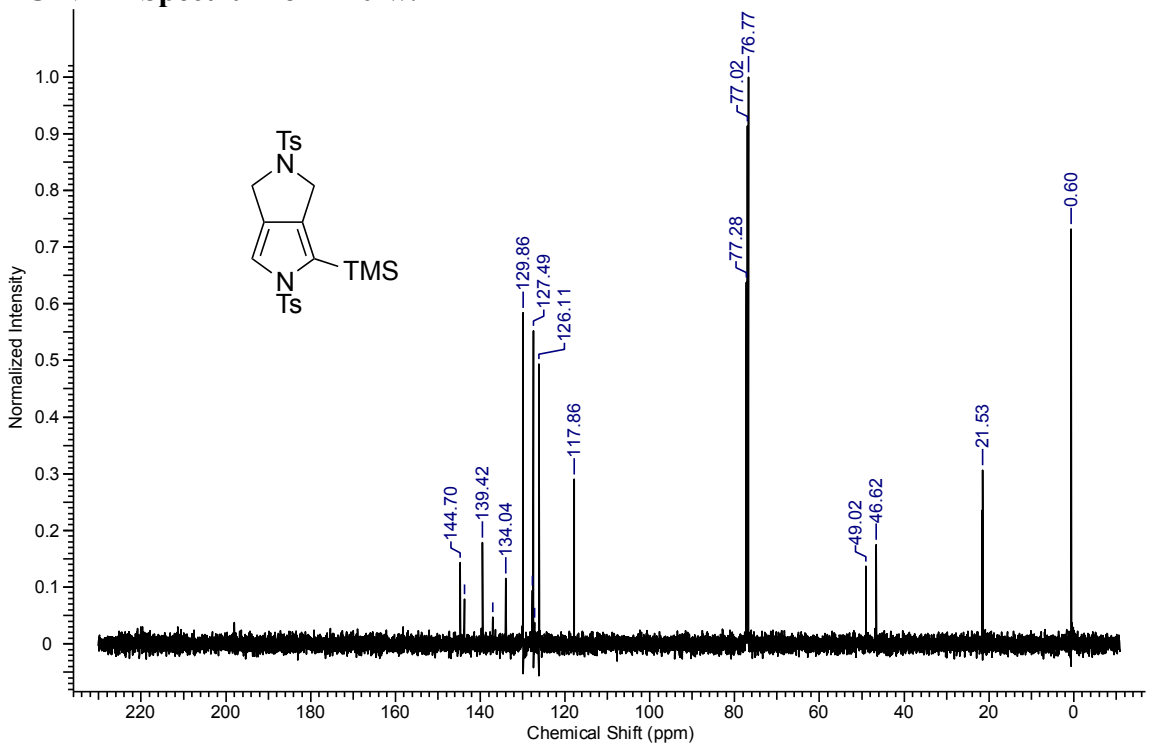
^{13}C NMR Spectrum of 4-9-w:



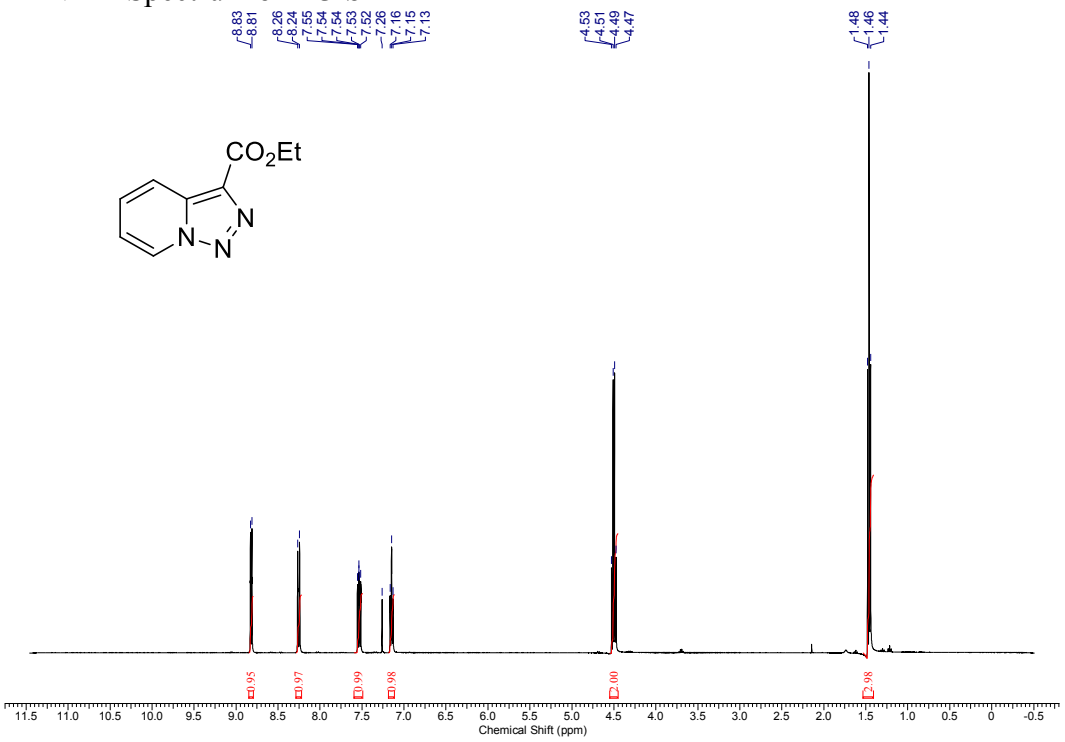
^{1}H NMR Spectrum of 4-10-w:



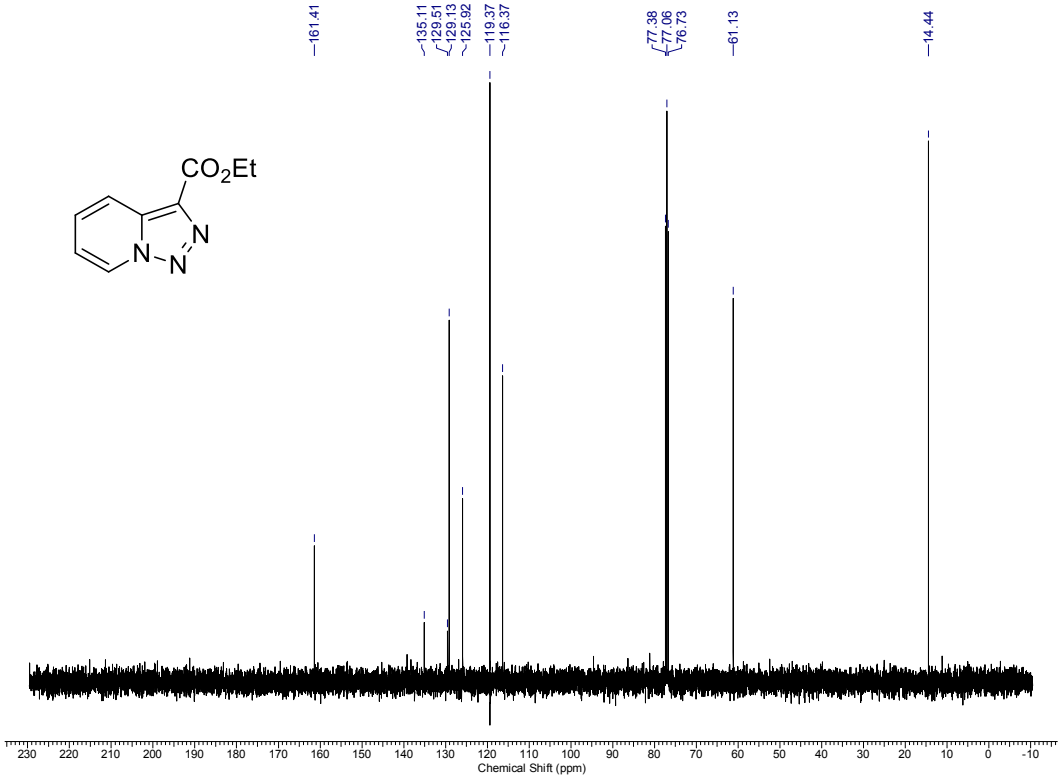
^{13}C NMR Spectrum of 4-10-w:



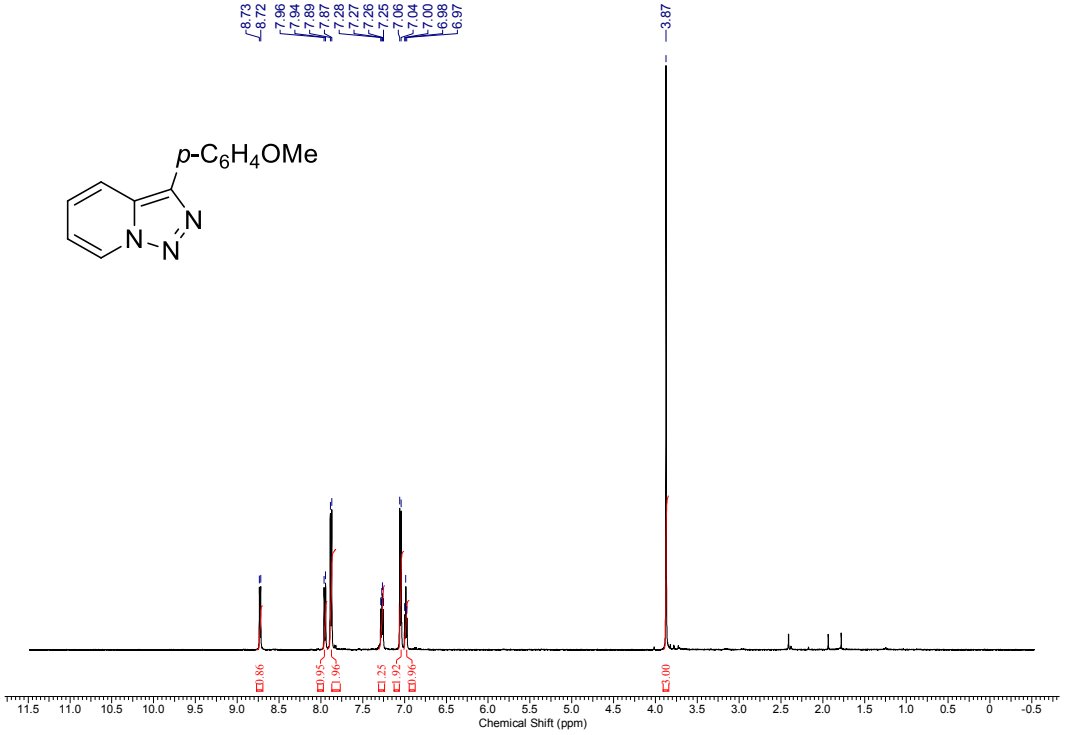
^{1}H NMR Spectrum of **7-5-b**



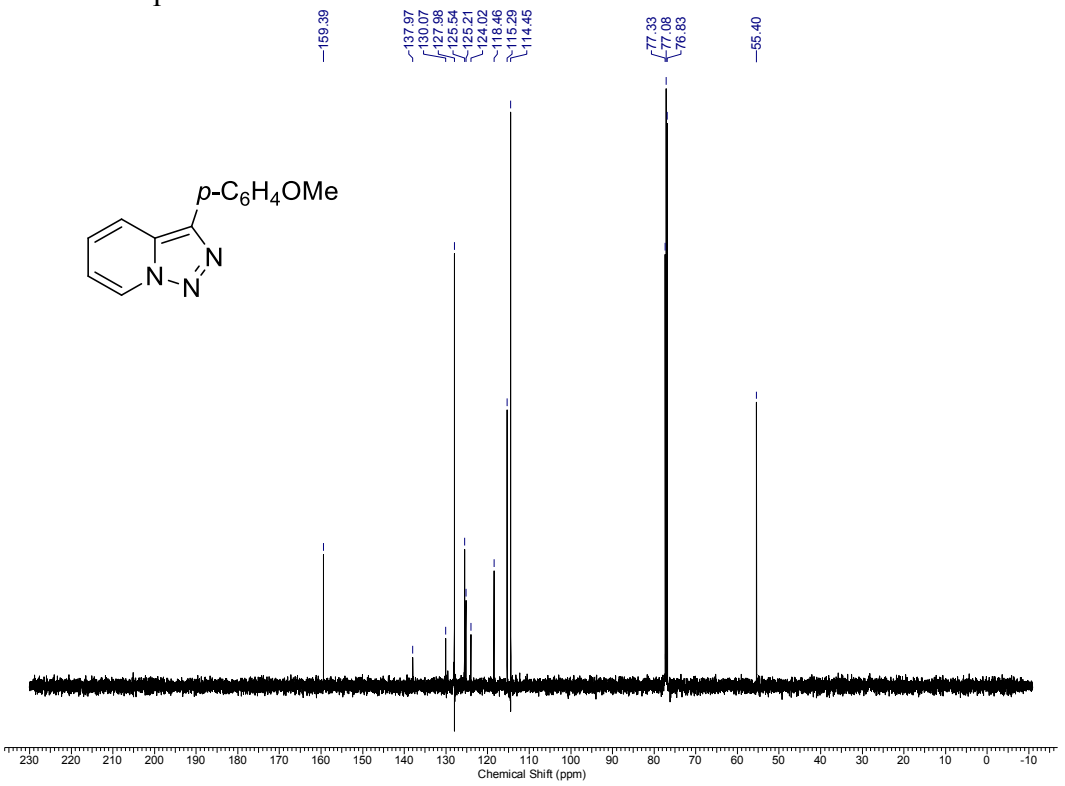
^{13}C NMR Spectrum of **7-5-b**



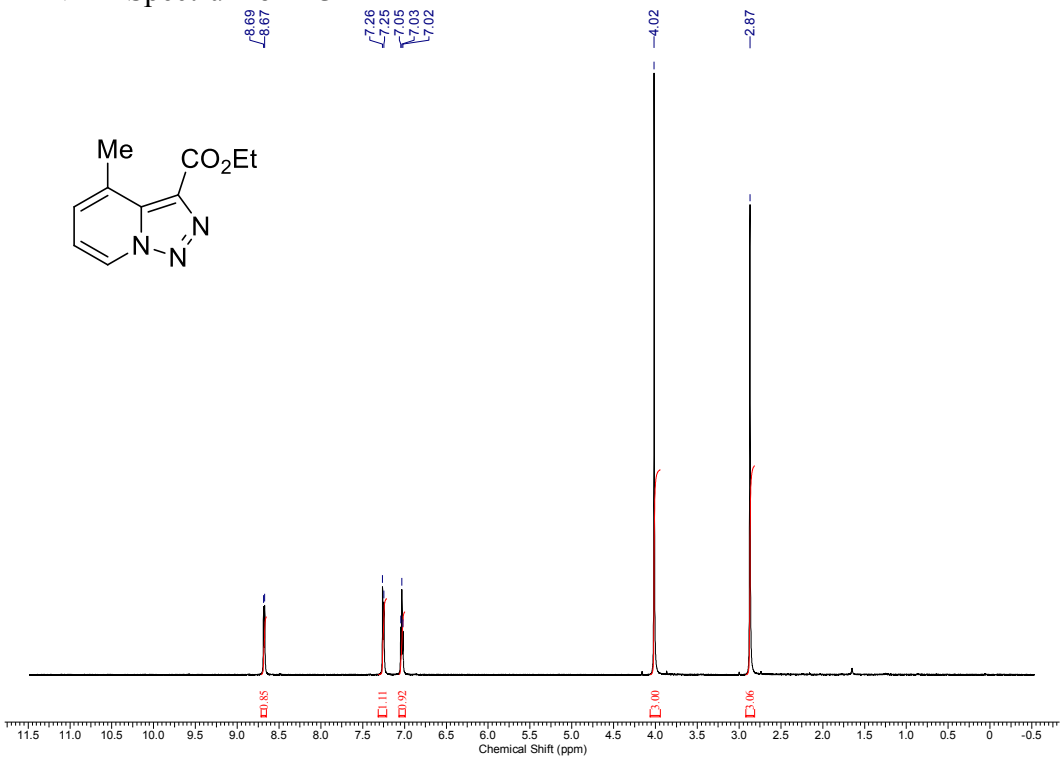
^{1}H NMR Spectrum of **7-5-d**



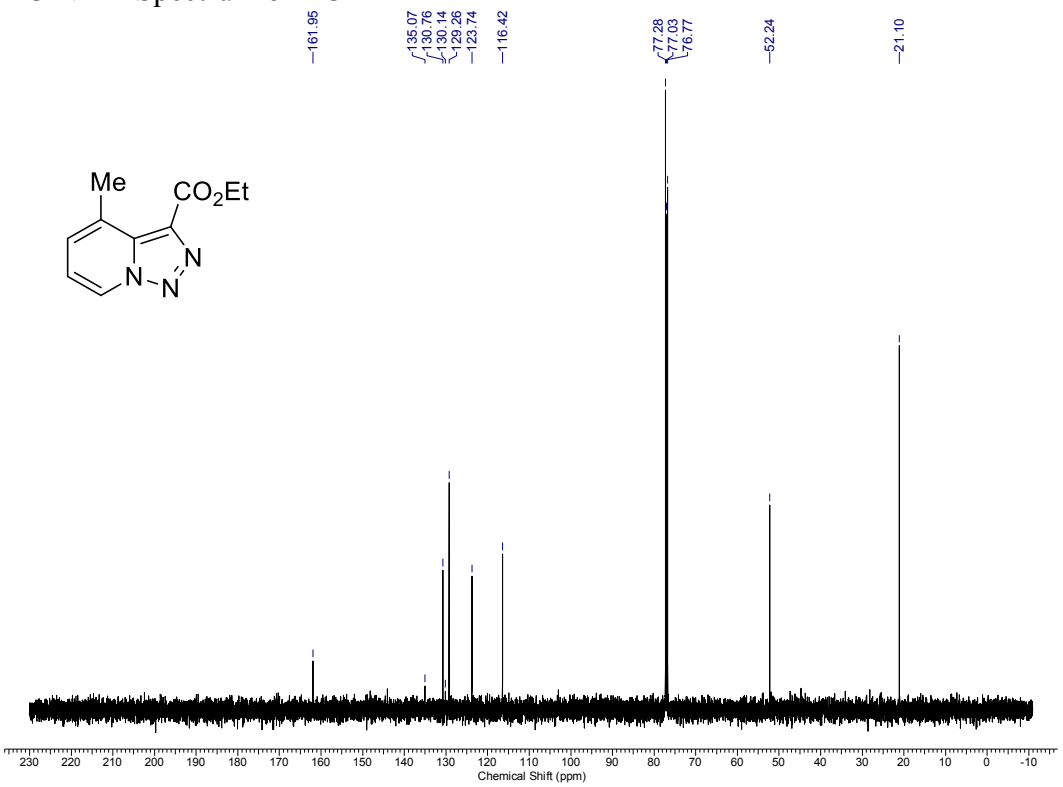
^{13}C NMR Spectrum of **7-5-d**



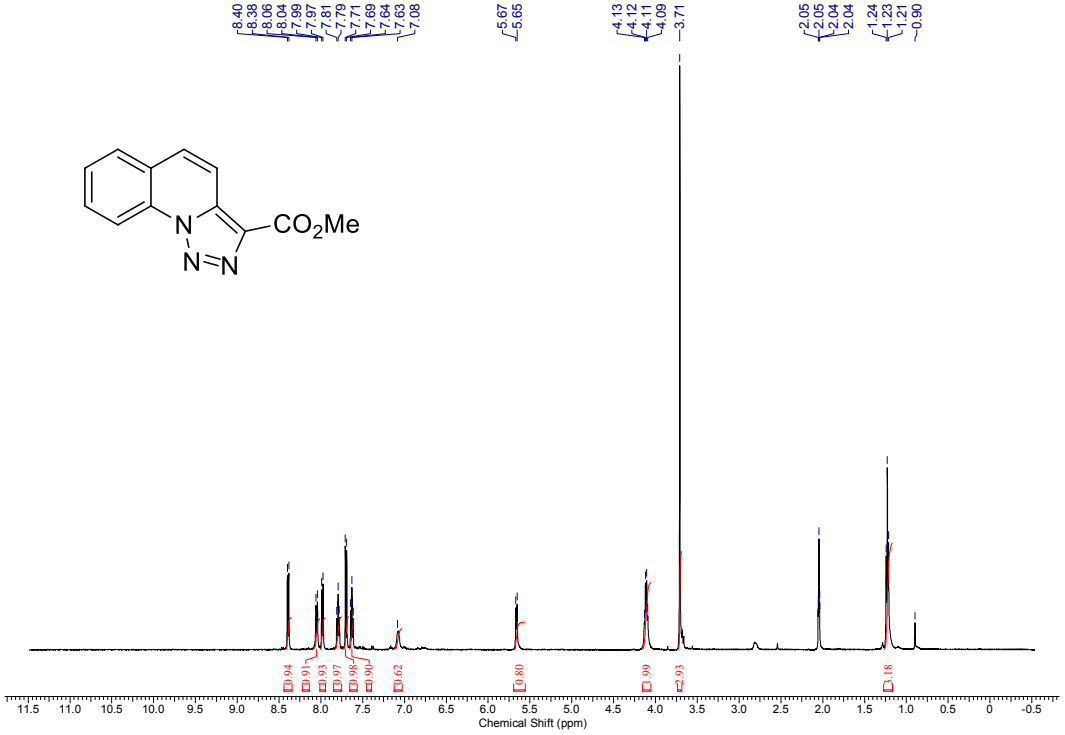
^{1}H NMR Spectrum of **7-5-f**



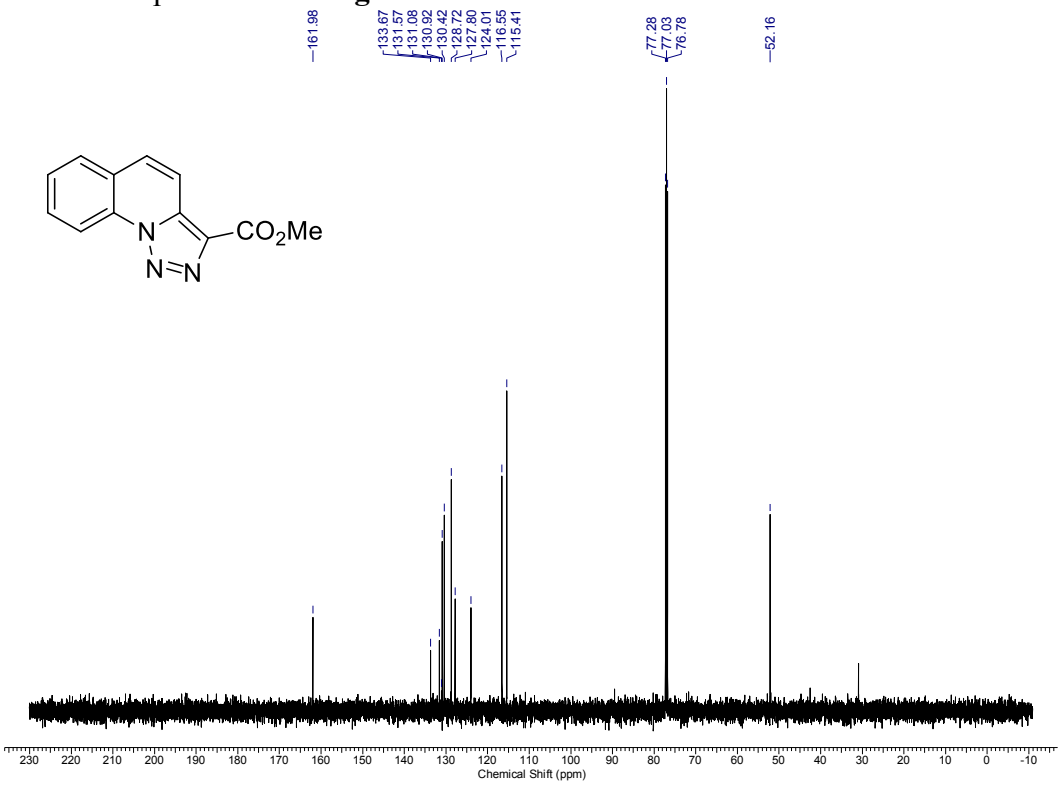
^{13}C NMR Spectrum of **7-5-f**



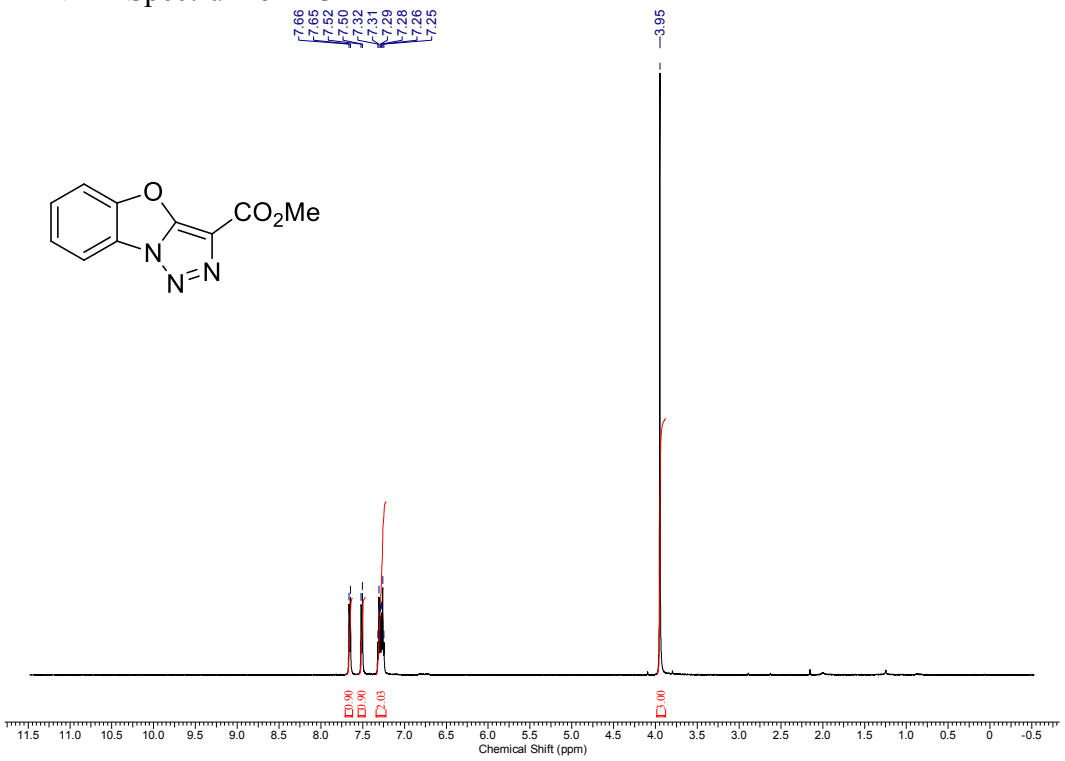
^{1}H NMR Spectrum of **7-5-g**



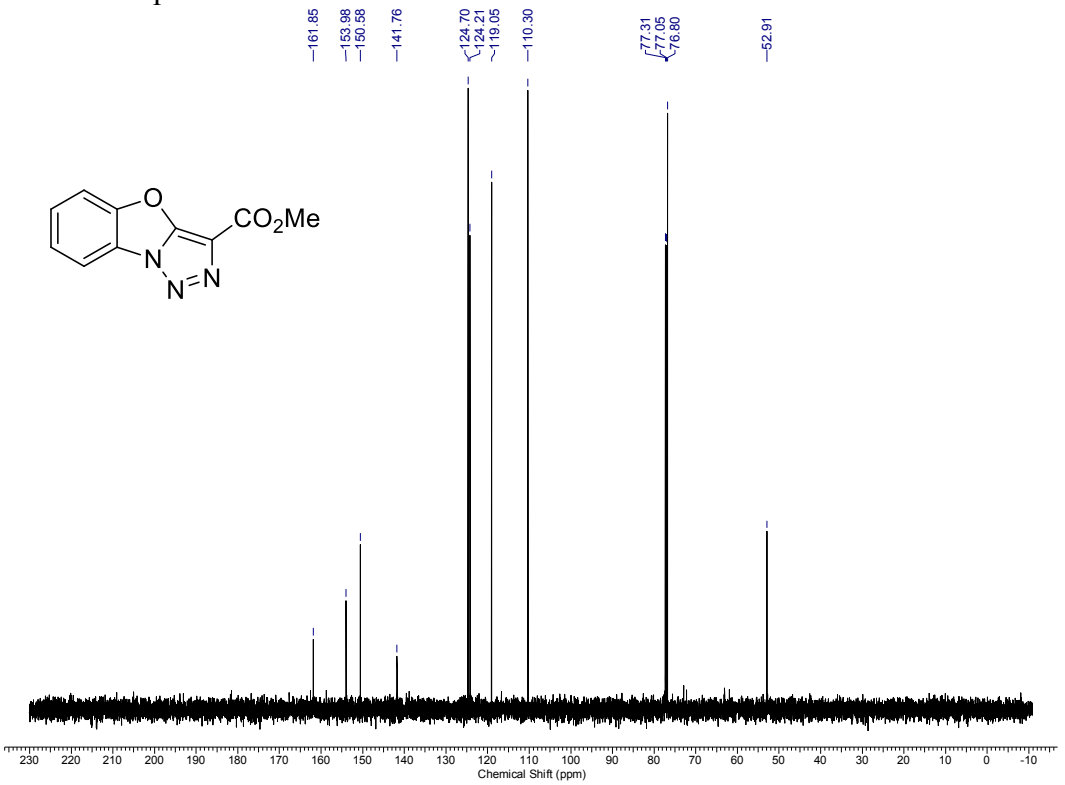
^{13}C NMR Spectrum of **7-5-g**



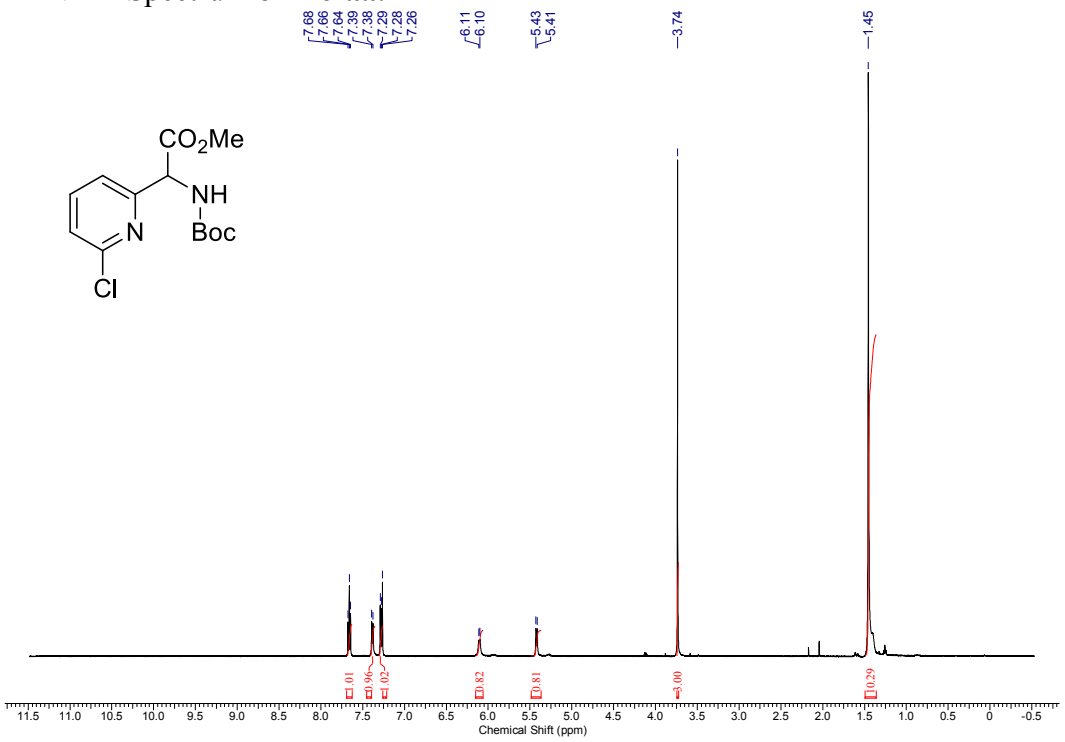
^{1}H NMR Spectrum of **7-5-h**



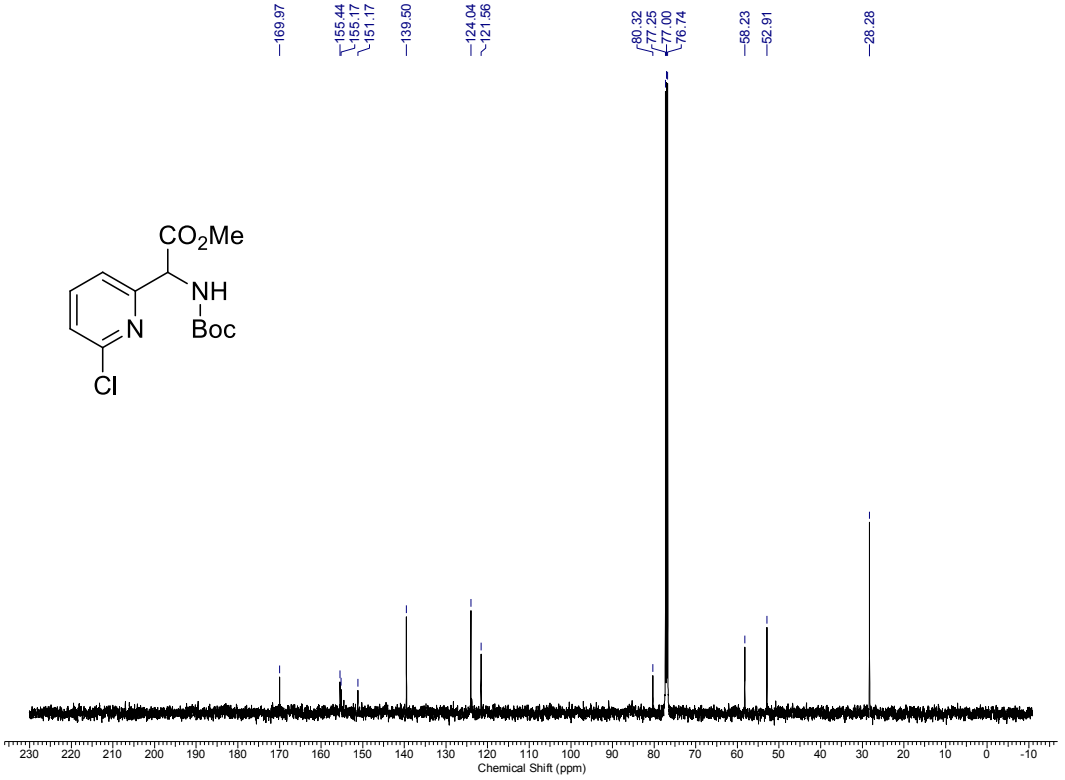
^{13}C NMR Spectrum of **7-5-h**



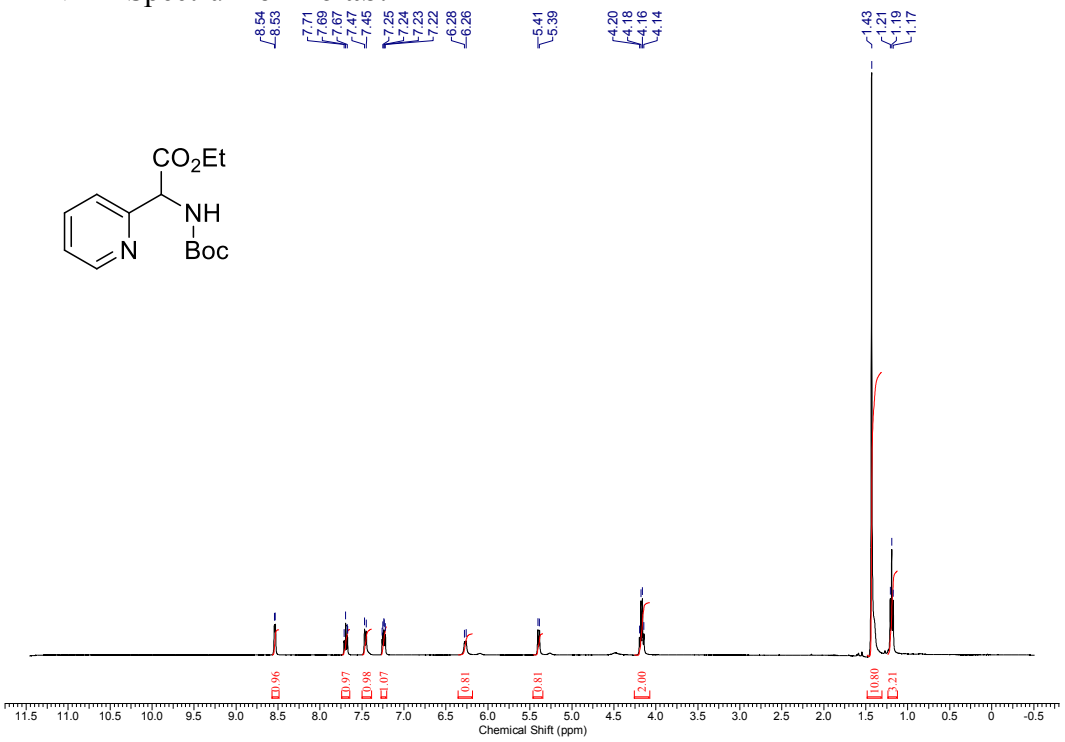
^{1}H NMR Spectrum of **7-6-aa**:



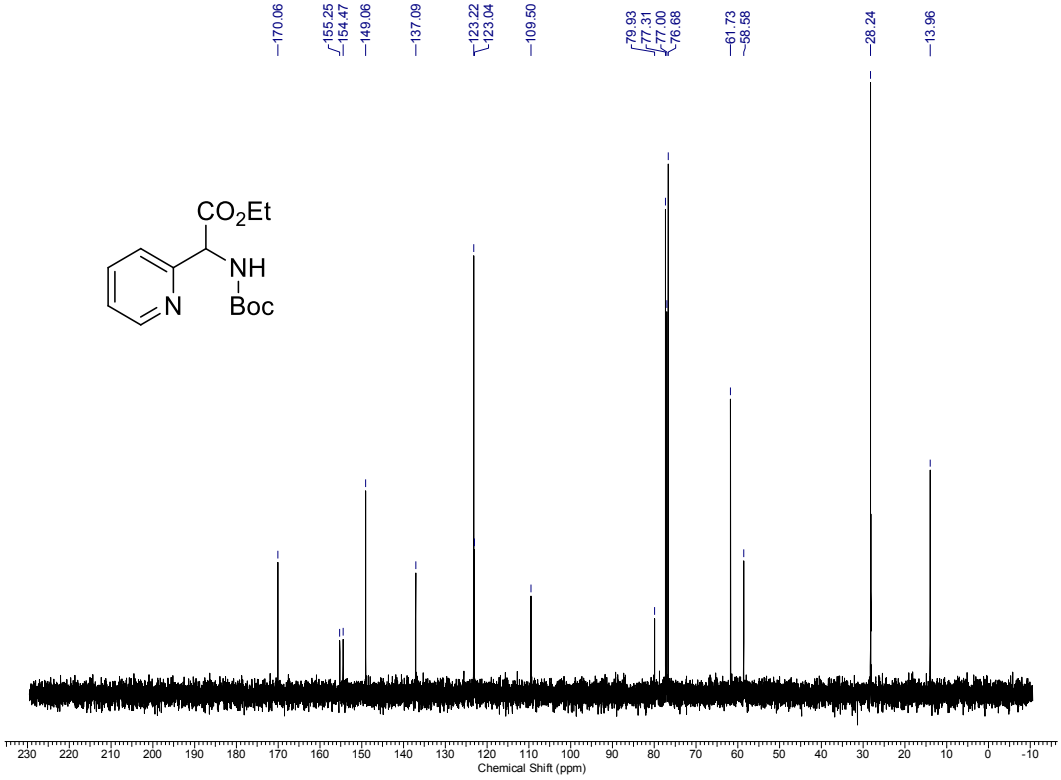
^{13}C NMR Spectrum of **7-6-aa**:



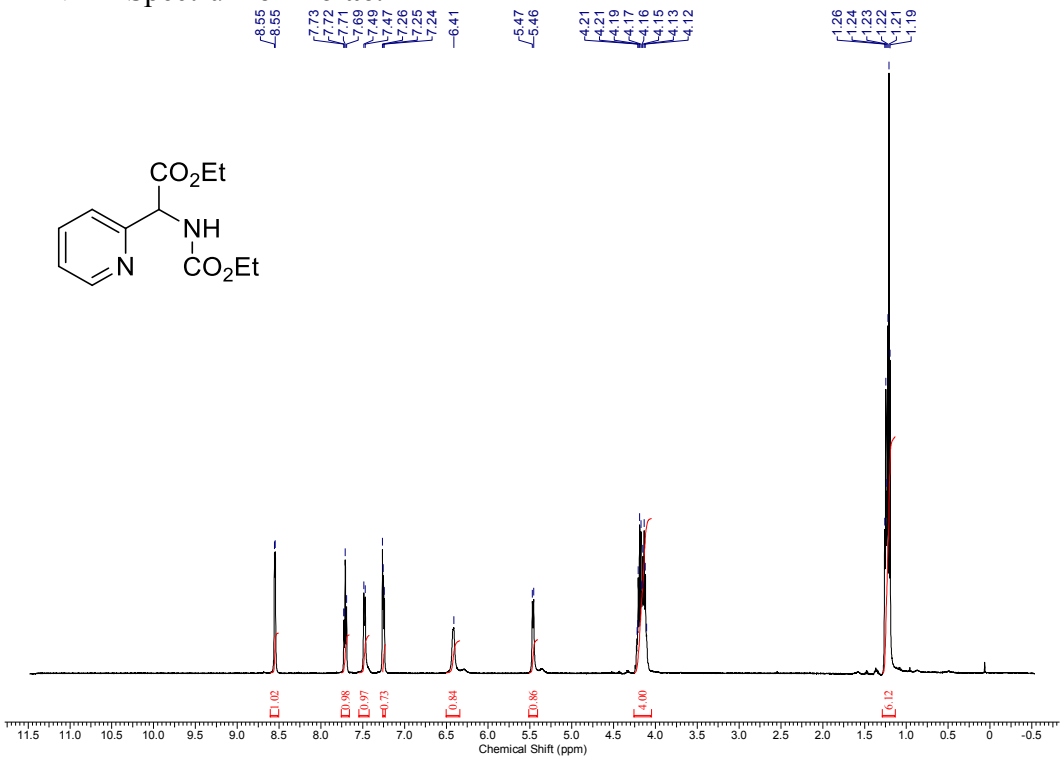
^{1}H NMR Spectrum of **7-6-ab**:



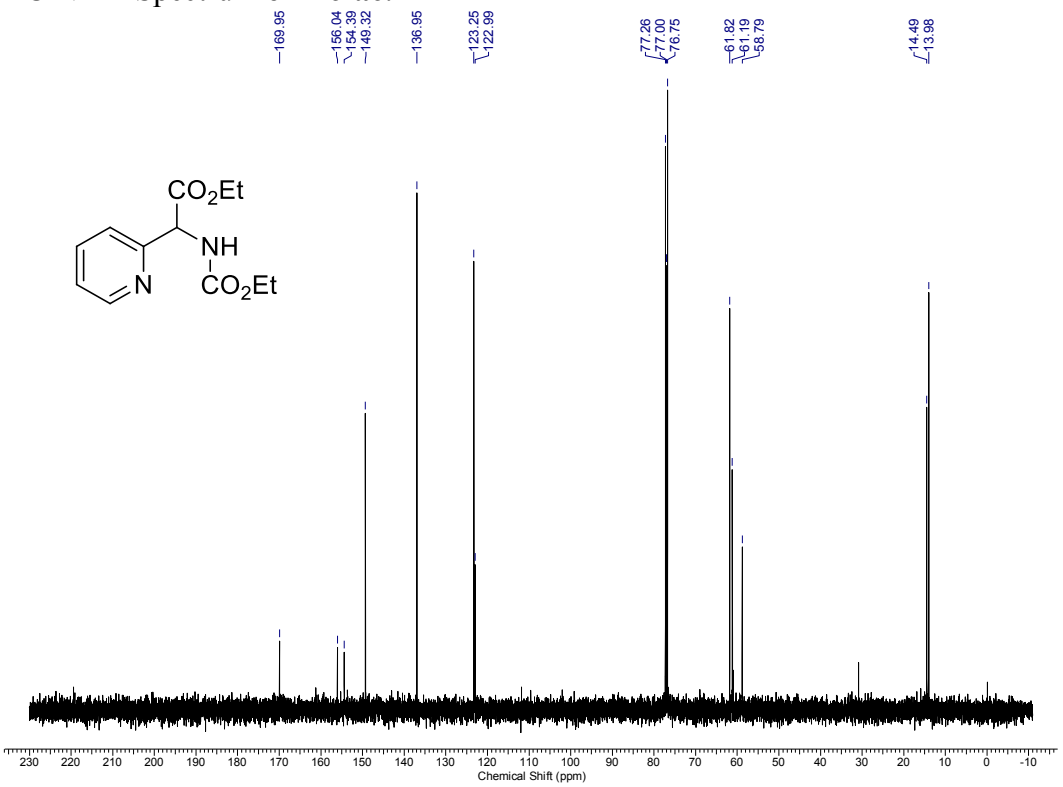
^{13}C NMR Spectrum of **7-6-ab**:



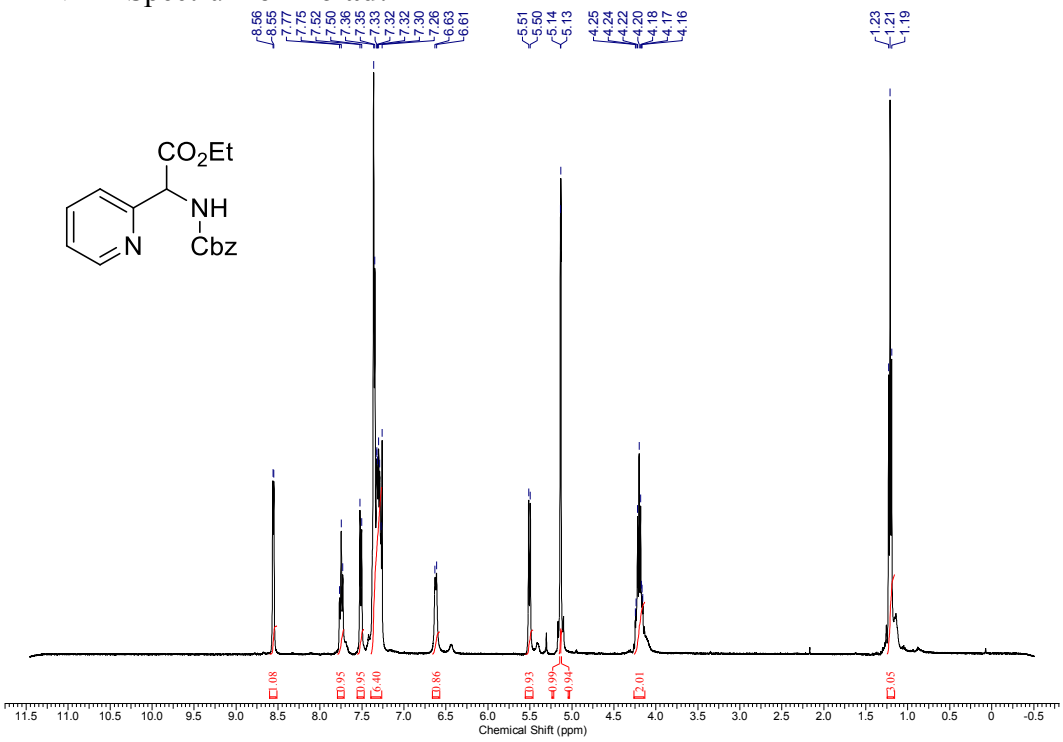
^{1}H NMR Spectrum of **7-6-ac**:



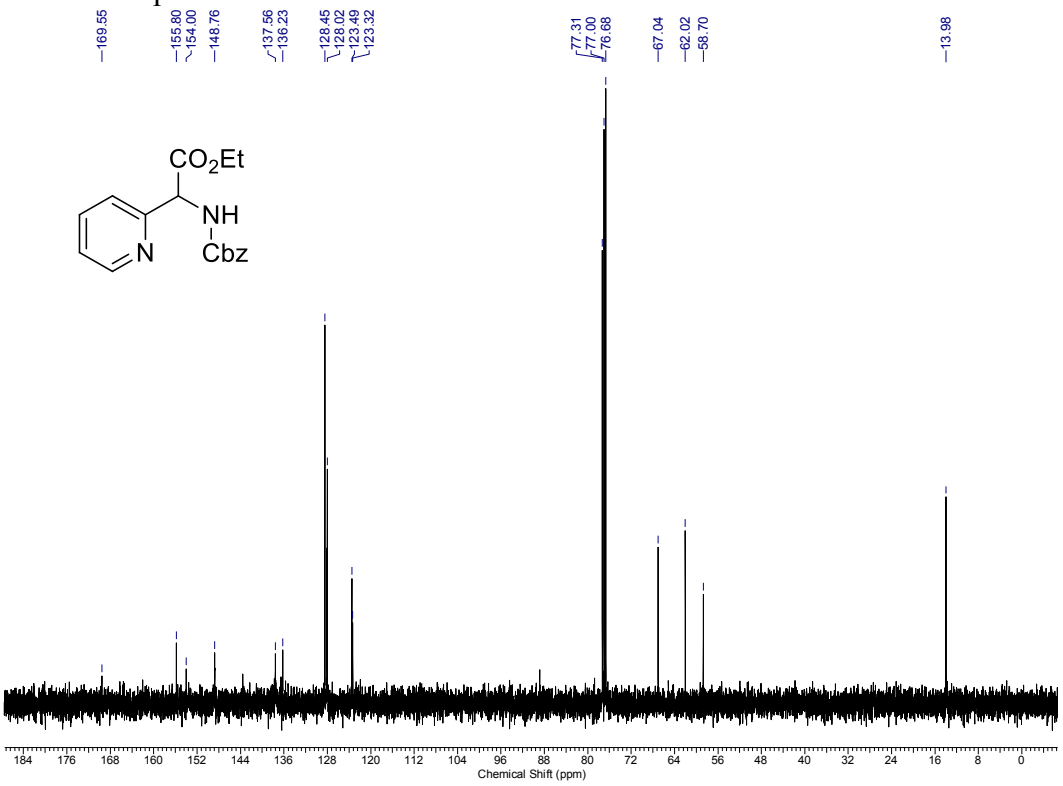
^{13}C NMR Spectrum of **7-6-ac**:



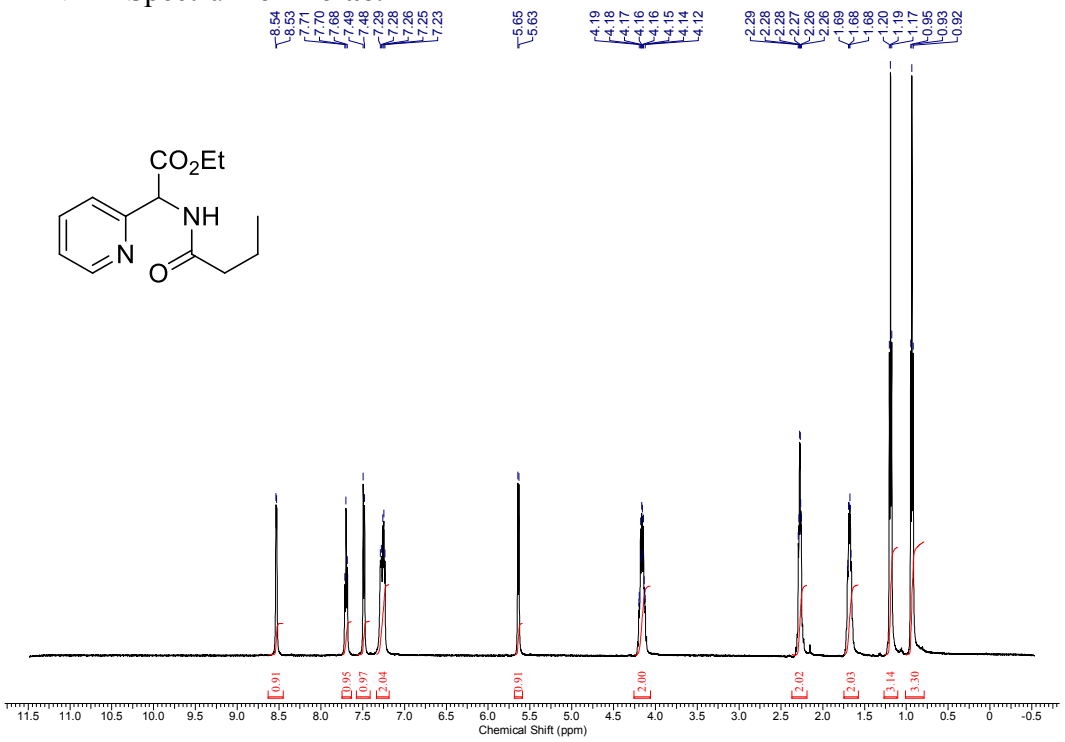
^{1}H NMR Spectrum of **7-6-ad**:



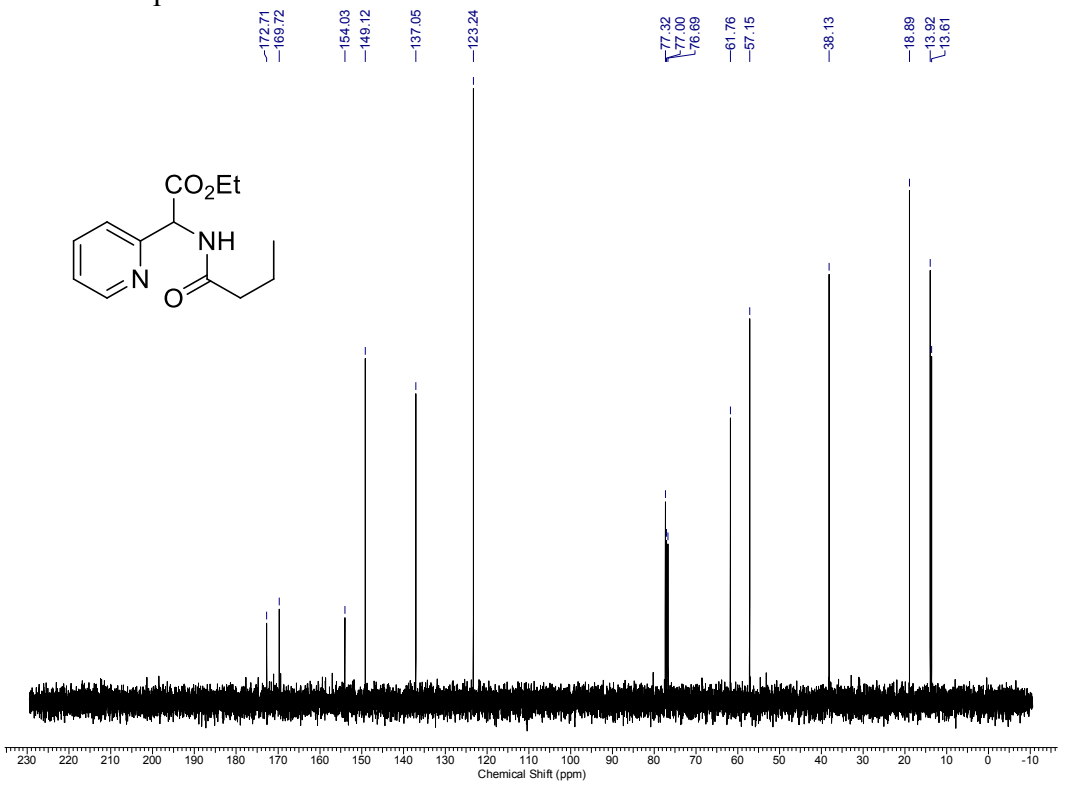
^{13}C NMR Spectrum of **7-6-ad**:



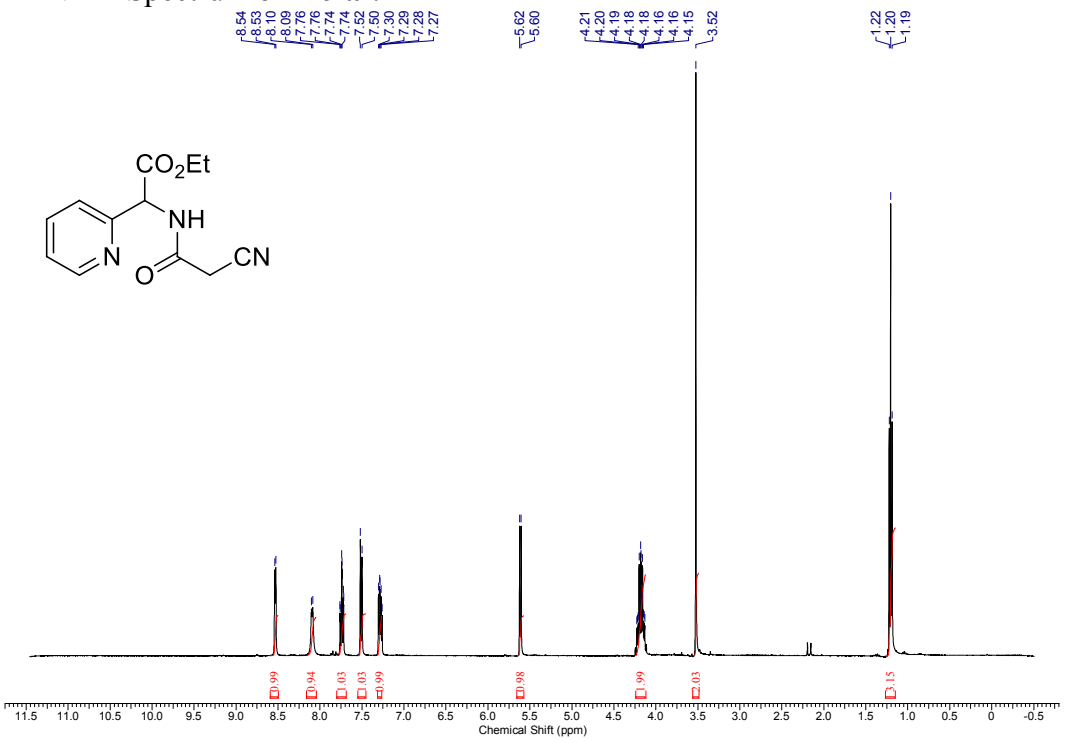
^{1}H NMR Spectrum of **7-6-ae**:



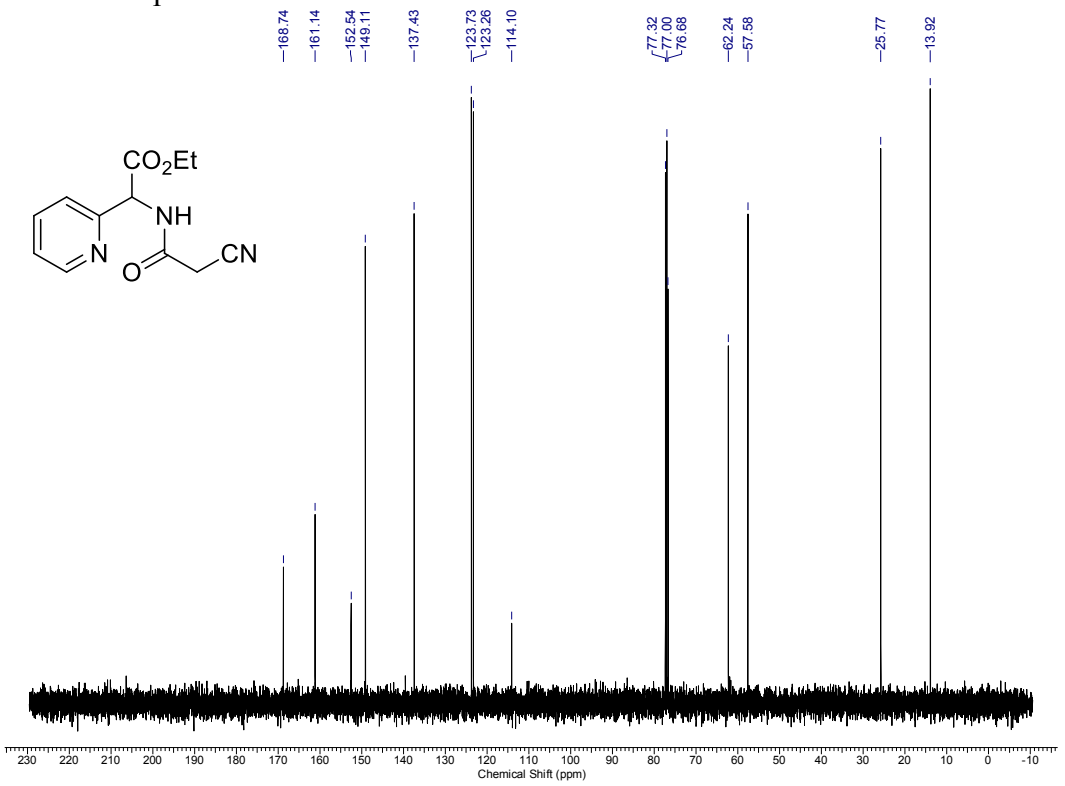
^{13}C NMR Spectrum of **7-6-ae**:



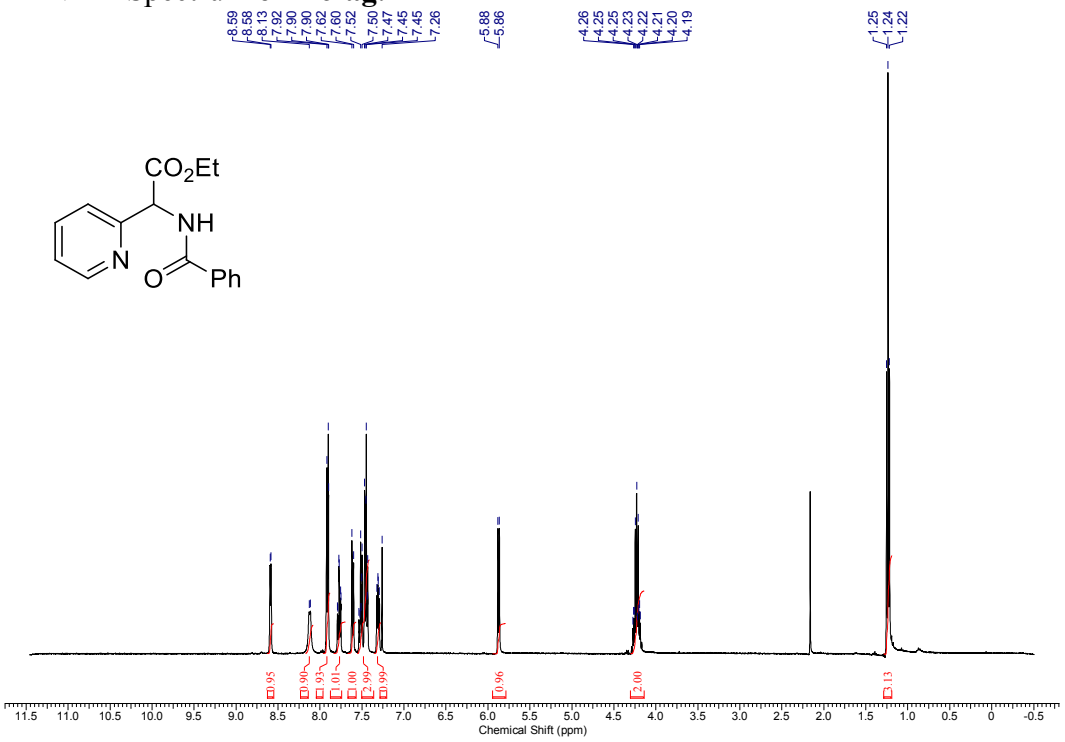
^{1}H NMR Spectrum of **7-6-af**:



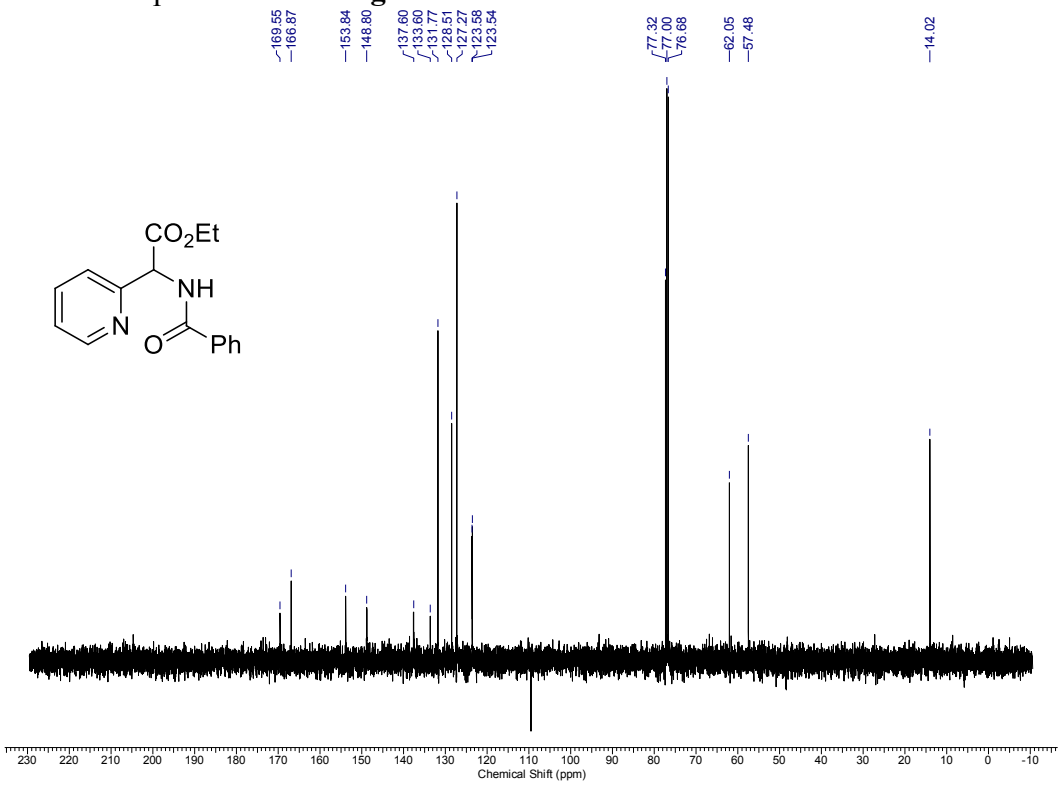
^{13}C NMR Spectrum of **7-6-af**:



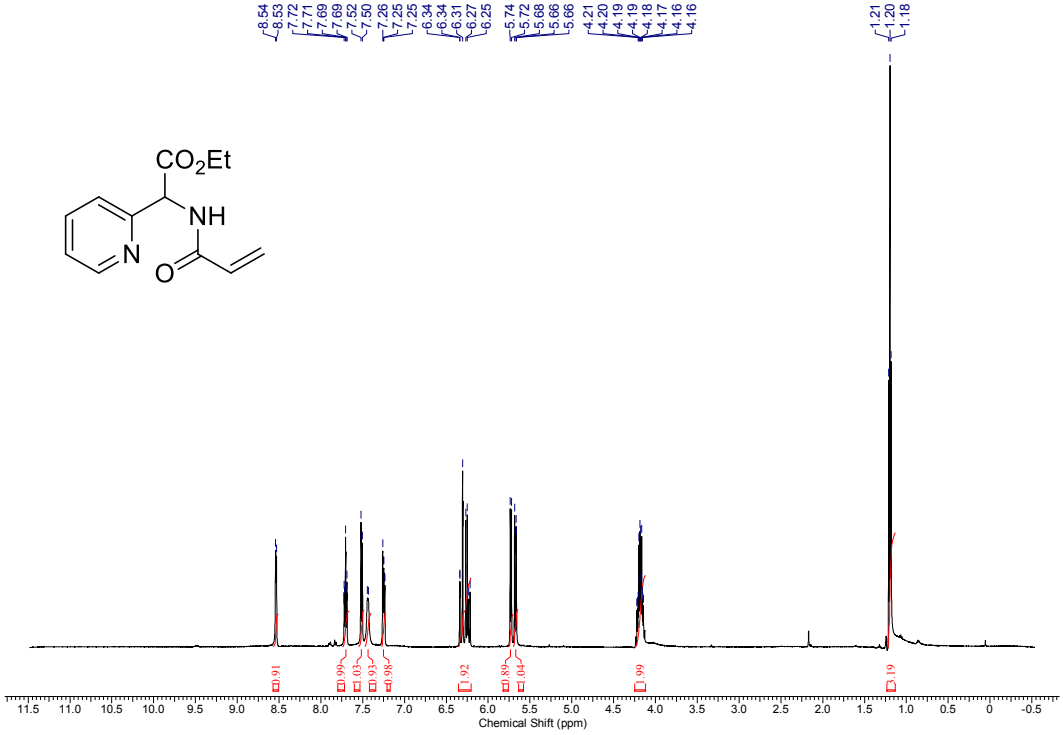
^{1}H NMR Spectrum of **7-6-ag**:



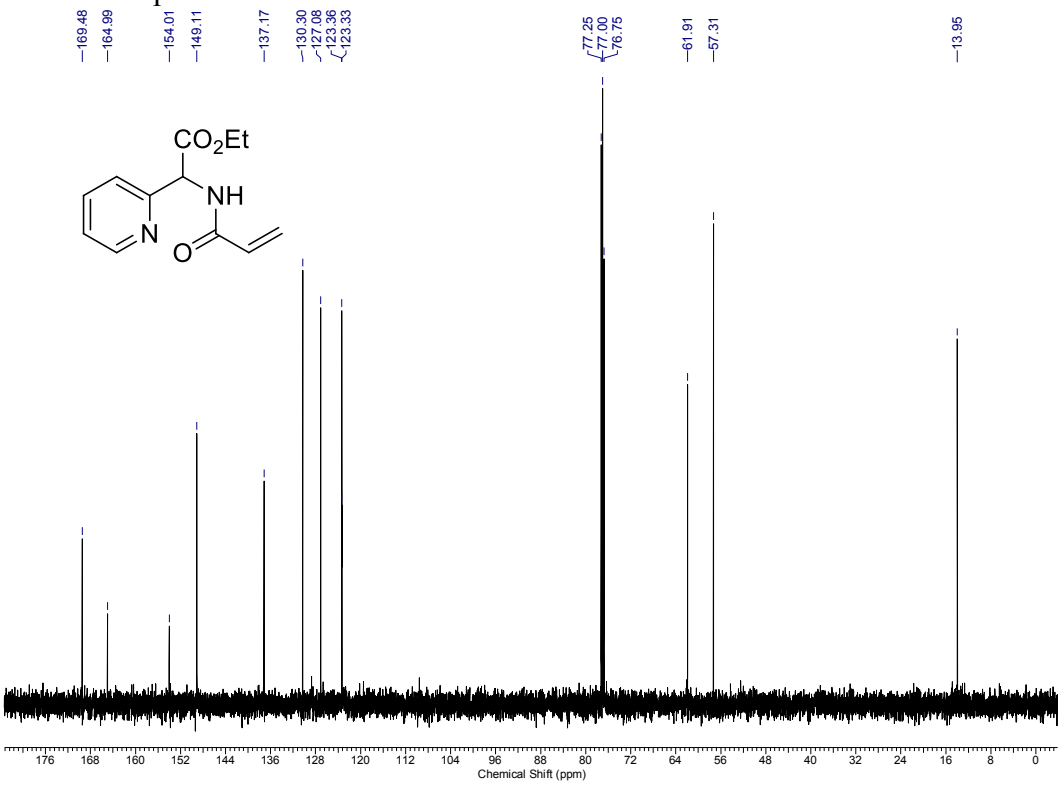
^{13}C NMR Spectrum of **7-6-ag**:



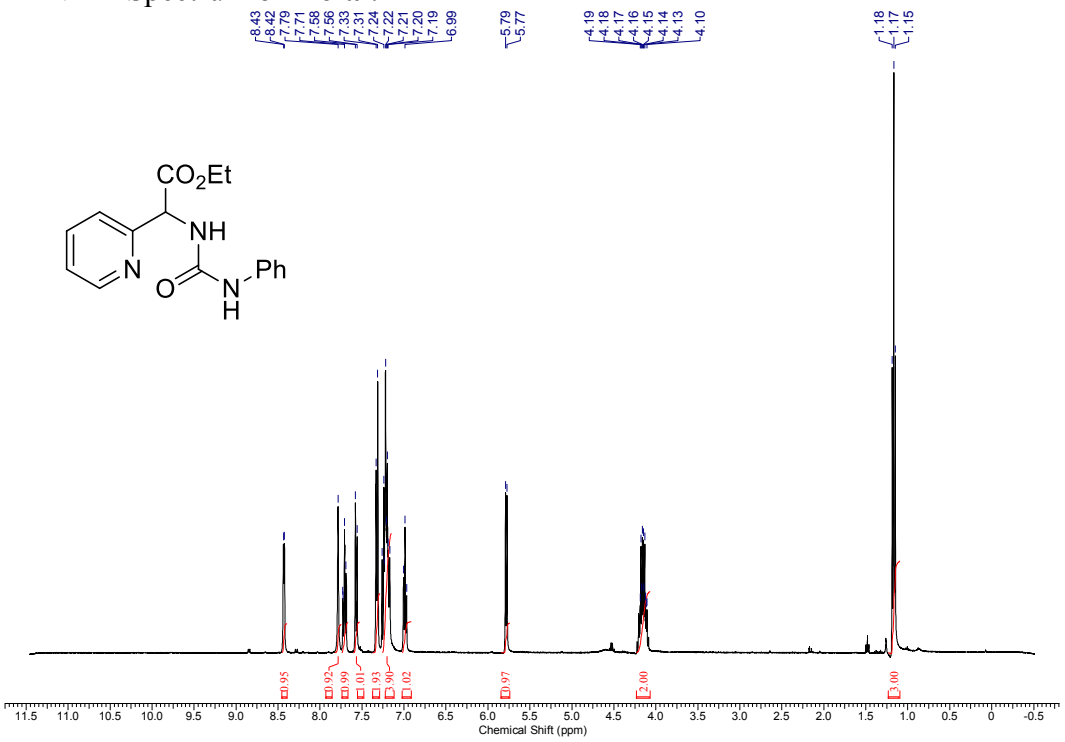
^{1}H NMR Spectrum of **7-6-ah**:



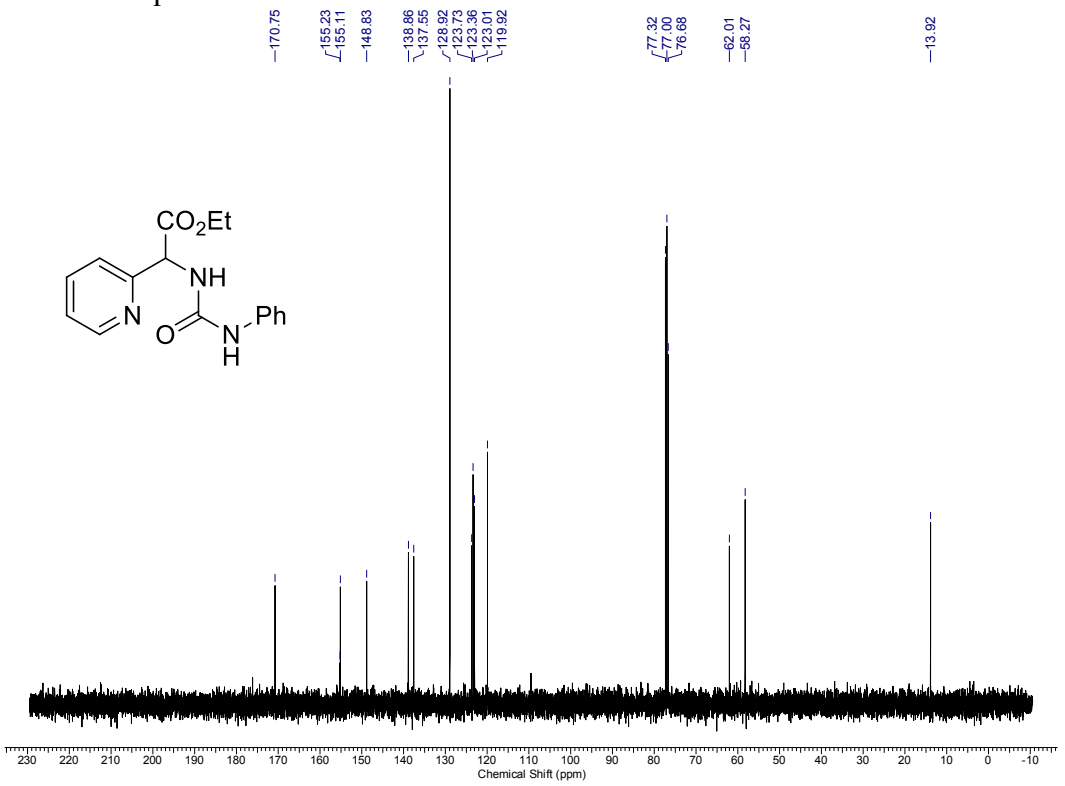
^{13}C NMR Spectrum of **7-6-ah**:



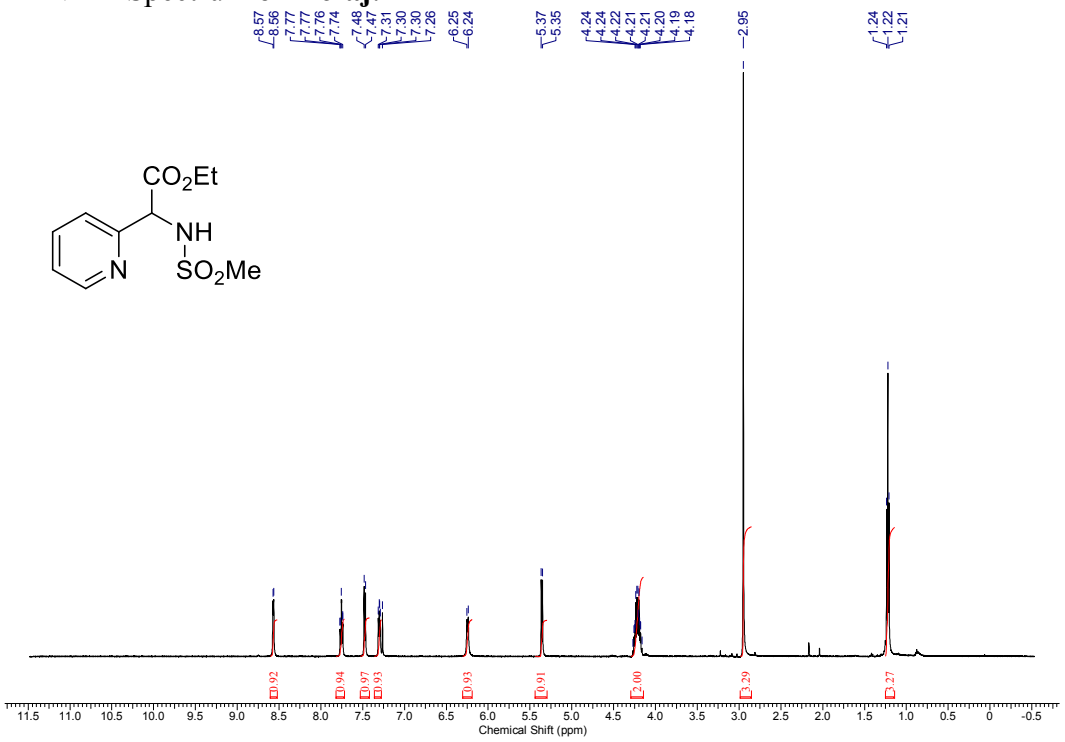
^{1}H NMR Spectrum of **7-6-ai**:



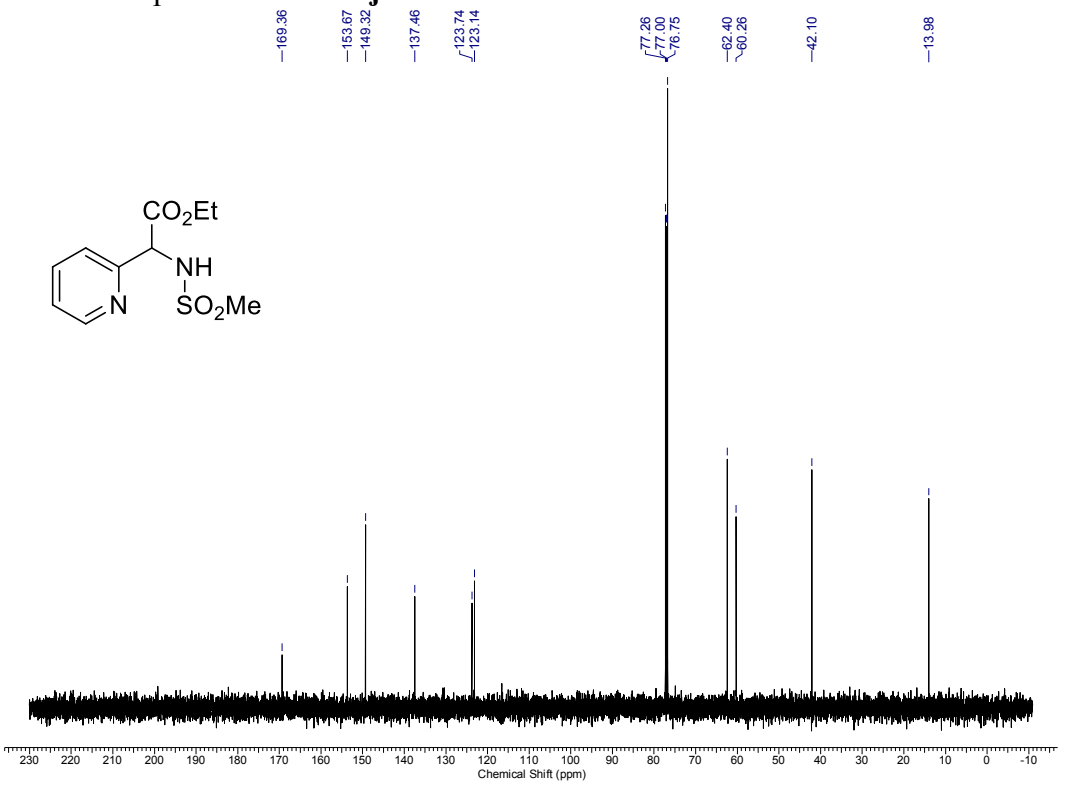
^{13}C NMR Spectrum of **7-6-ai**:



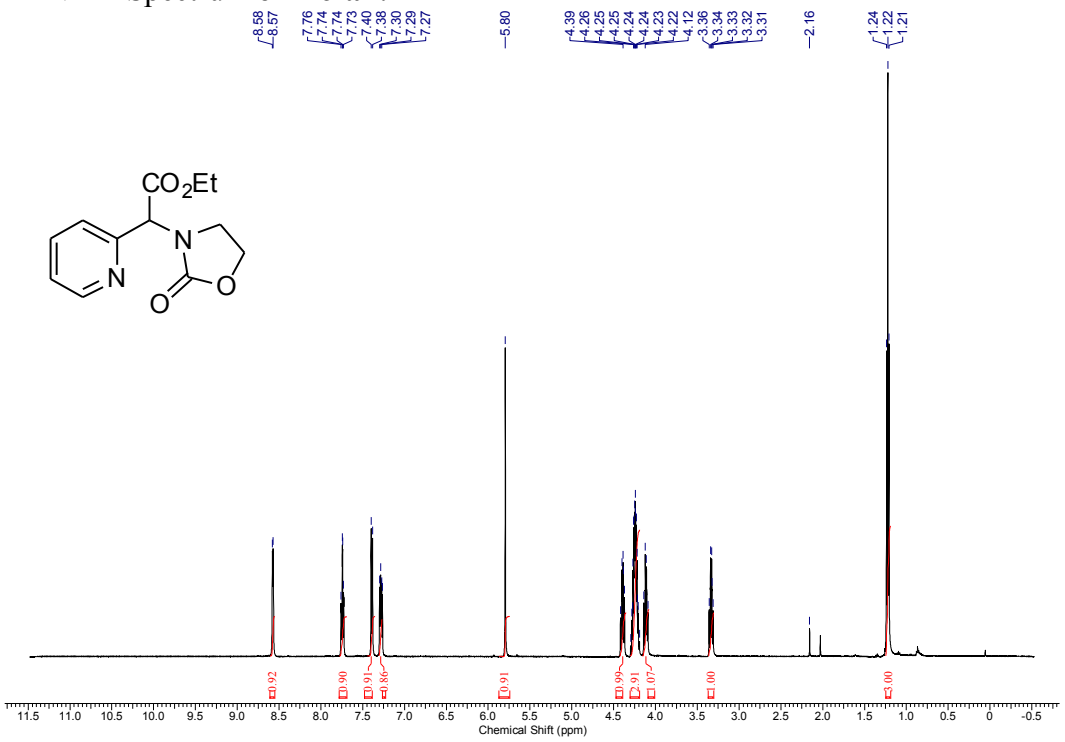
^{1}H NMR Spectrum of **7-6-aj**:



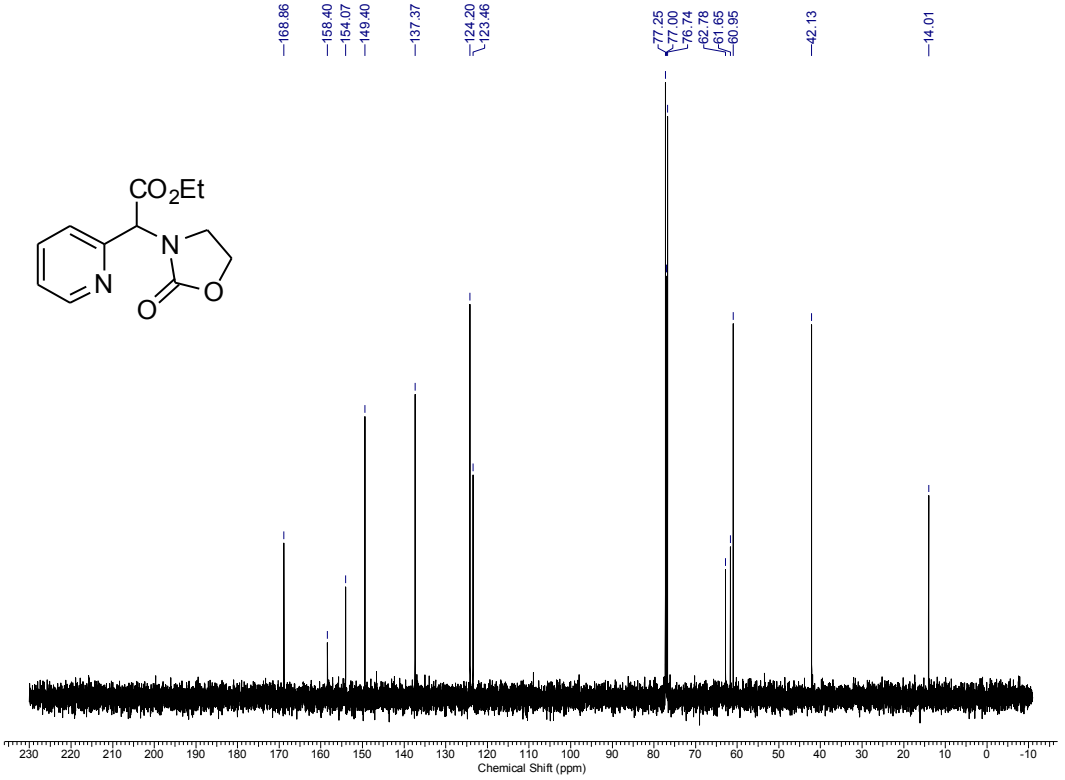
^{13}C NMR Spectrum of **7-6-aj**:



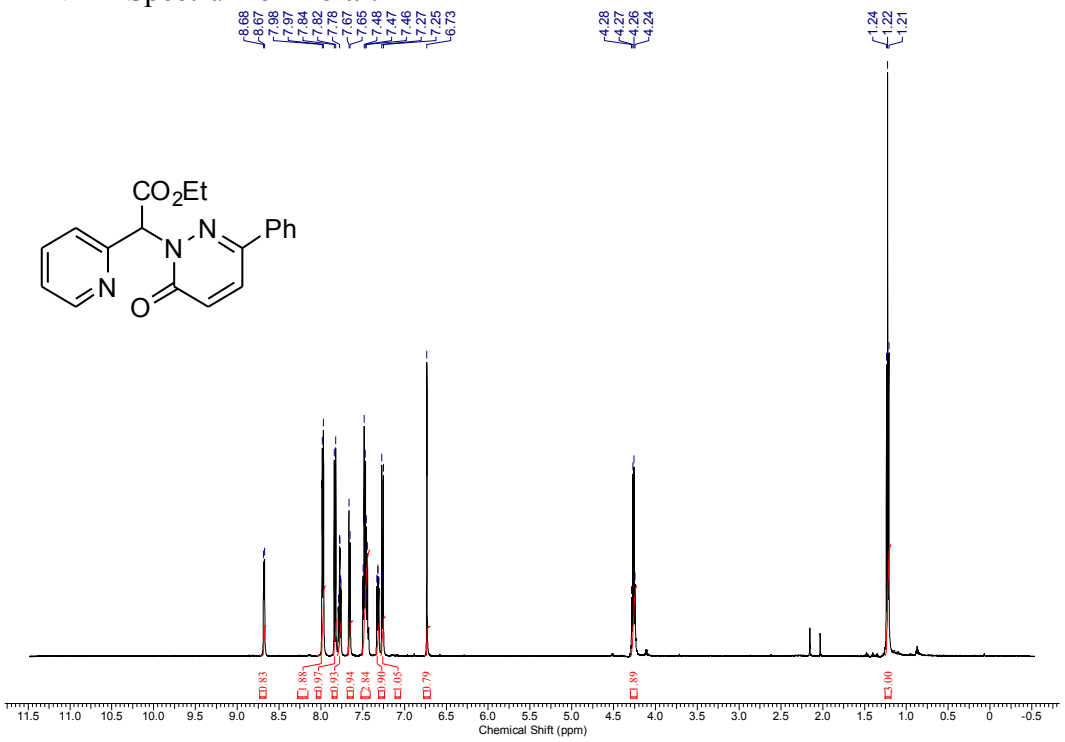
^{1}H NMR Spectrum of **7-6-ak**:



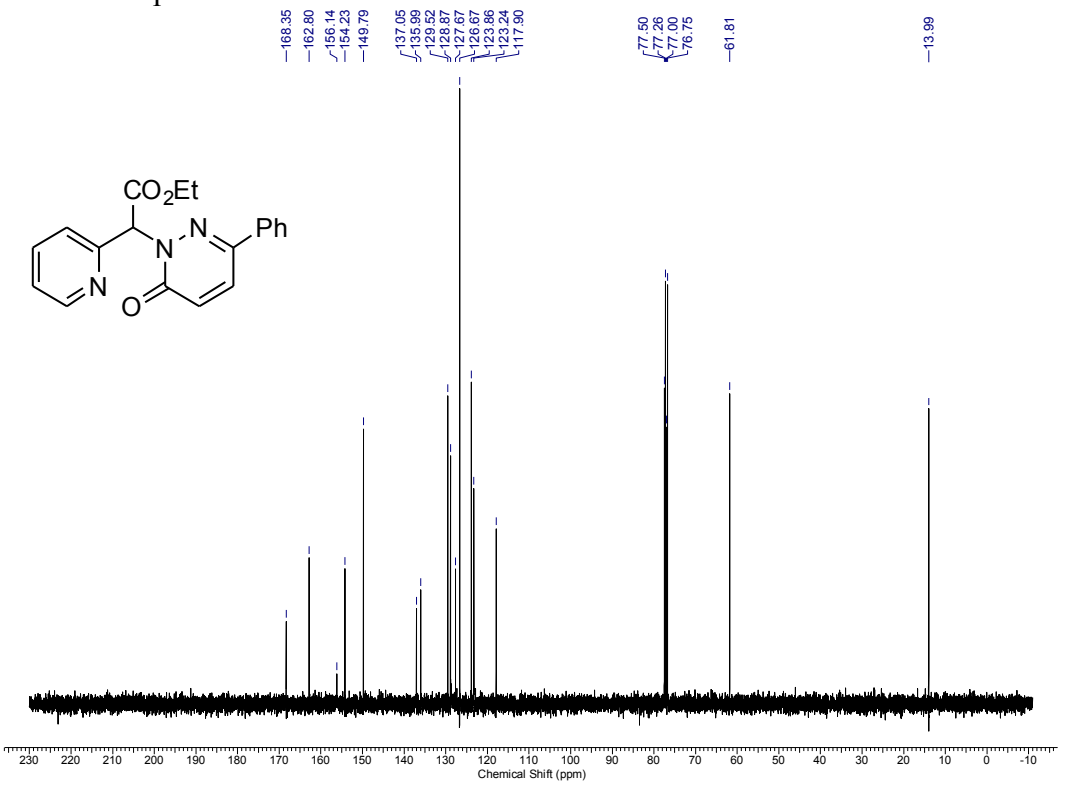
^{13}C NMR Spectrum of **7-6-ak**:



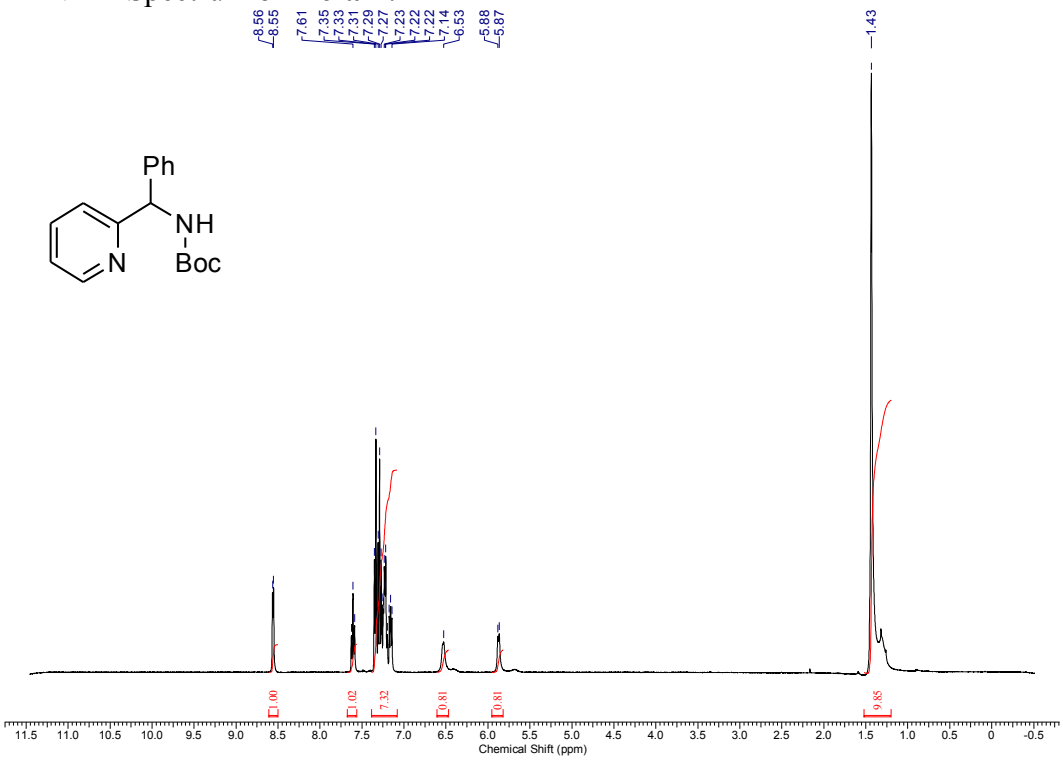
^{1}H NMR Spectrum of **7-6-al**:



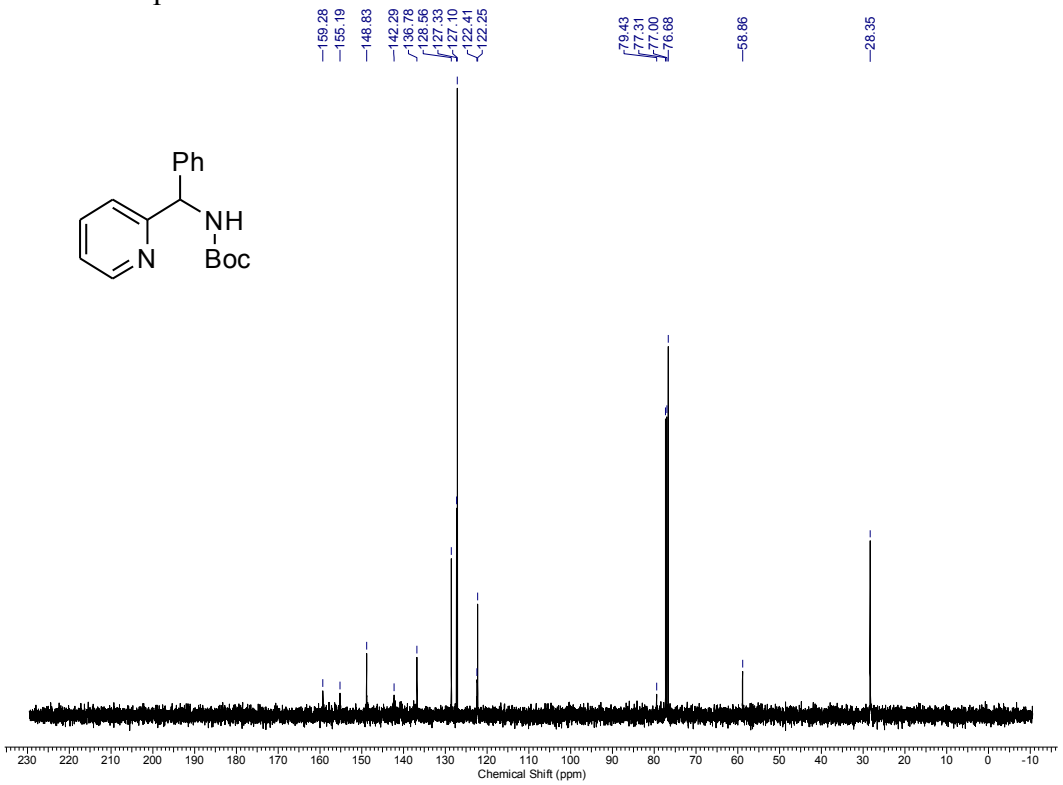
^{13}C NMR Spectrum of **7-6-al**:



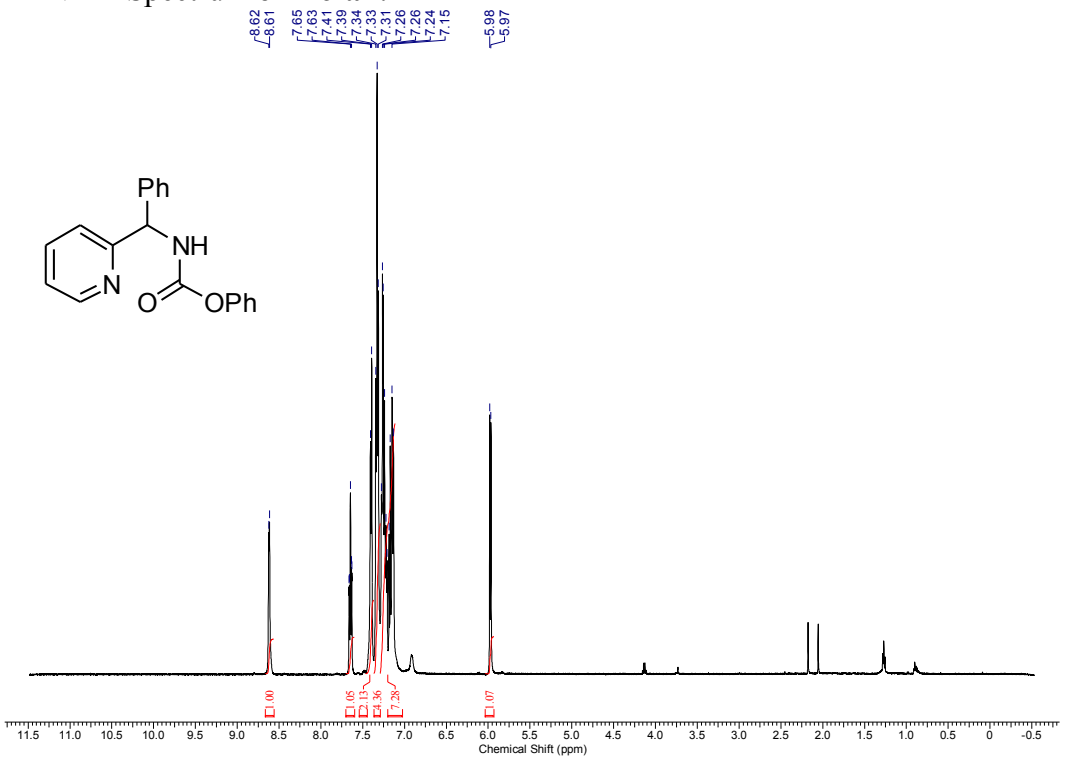
^{1}H NMR Spectrum of **7-6-am**:



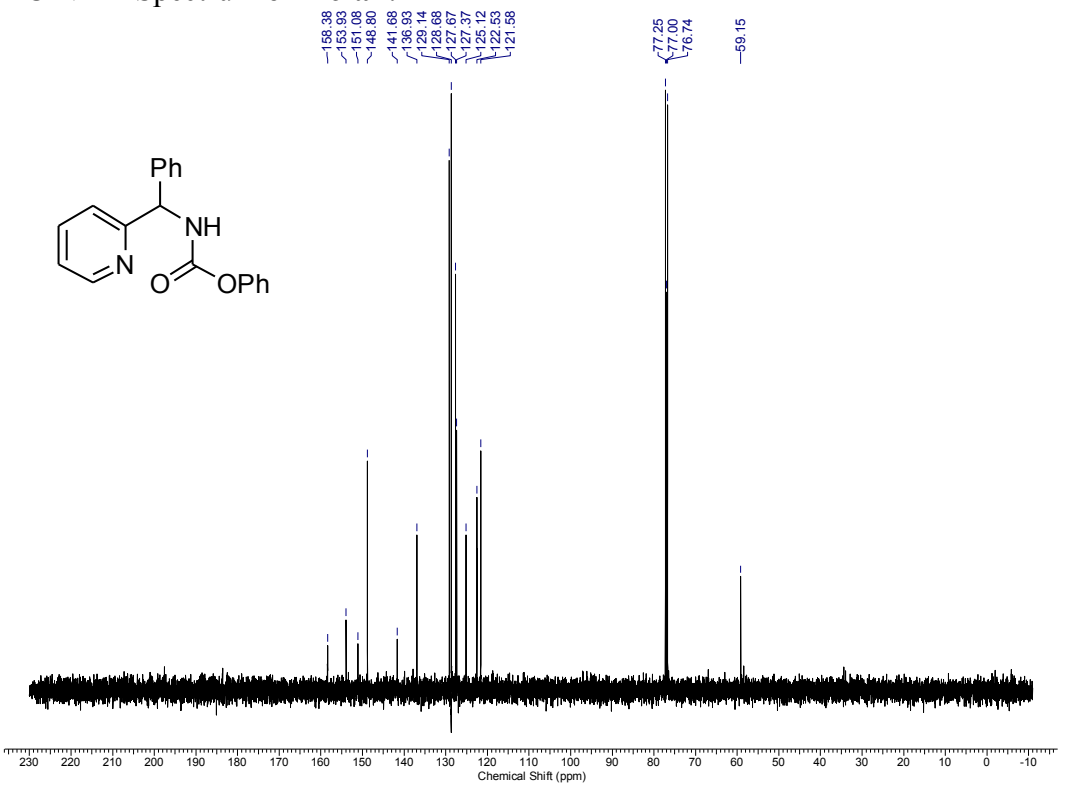
^{13}C NMR Spectrum of **7-6-am**:



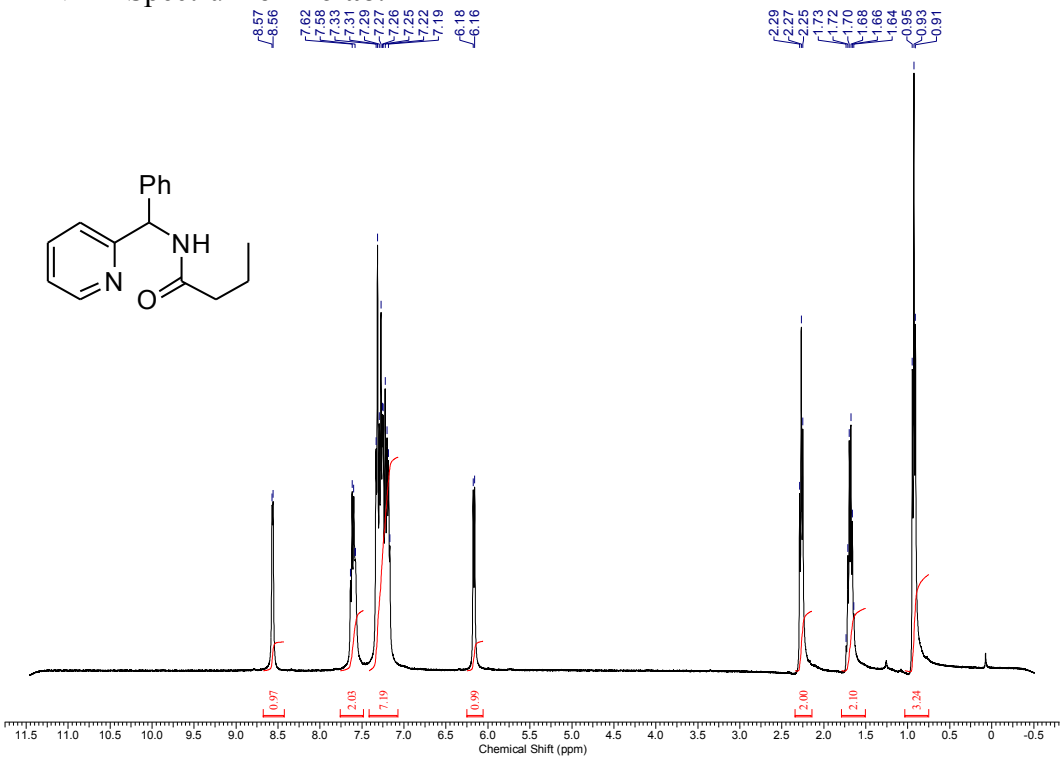
^{1}H NMR Spectrum of **7-6-an**:



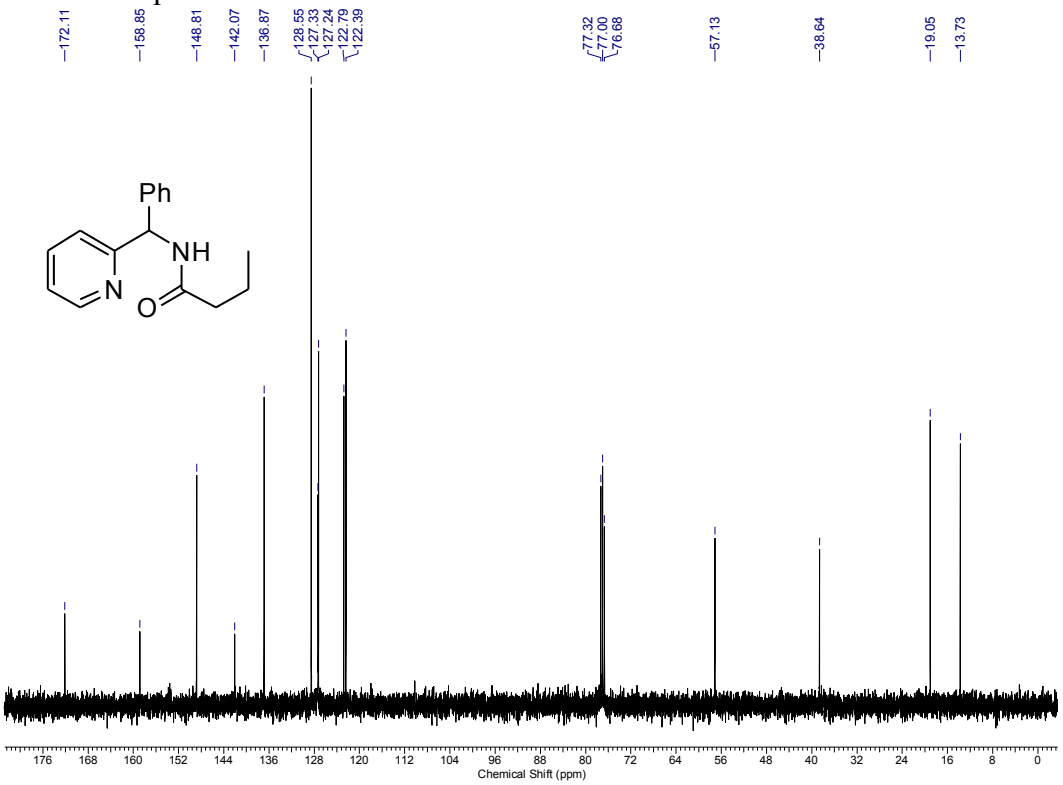
^{13}C NMR Spectrum of **7-6-an**:



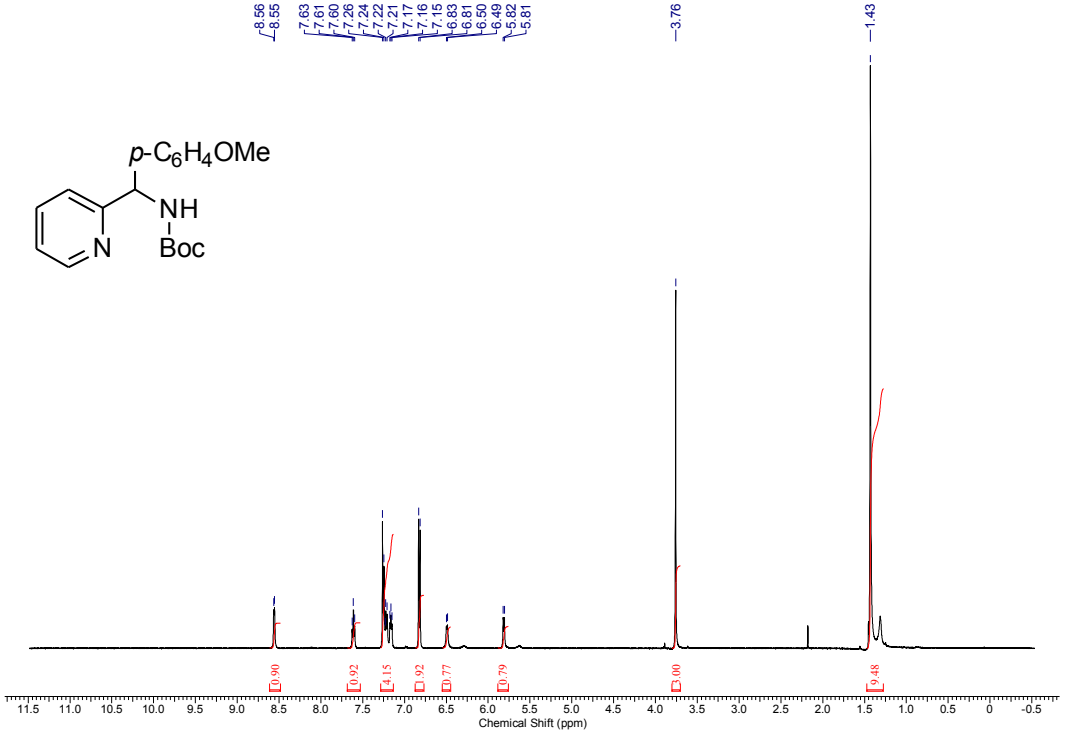
^{1}H NMR Spectrum of **7-6-ao**:



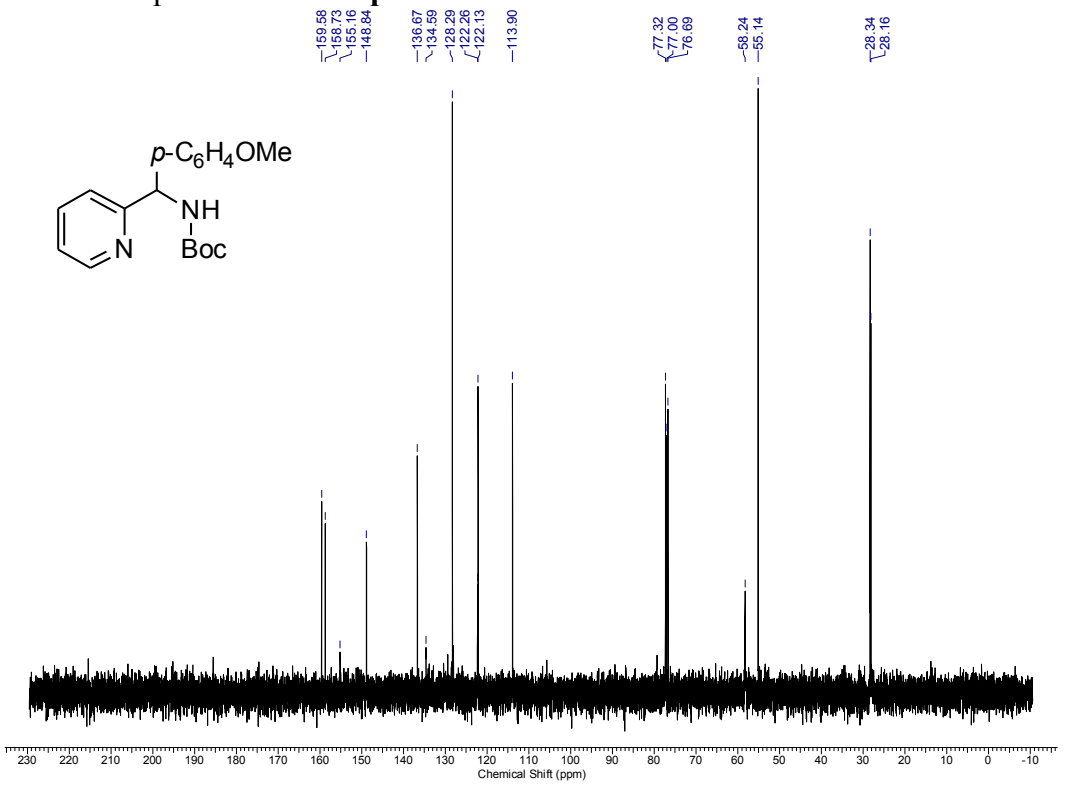
^{13}C NMR Spectrum of **7-6-ao**:



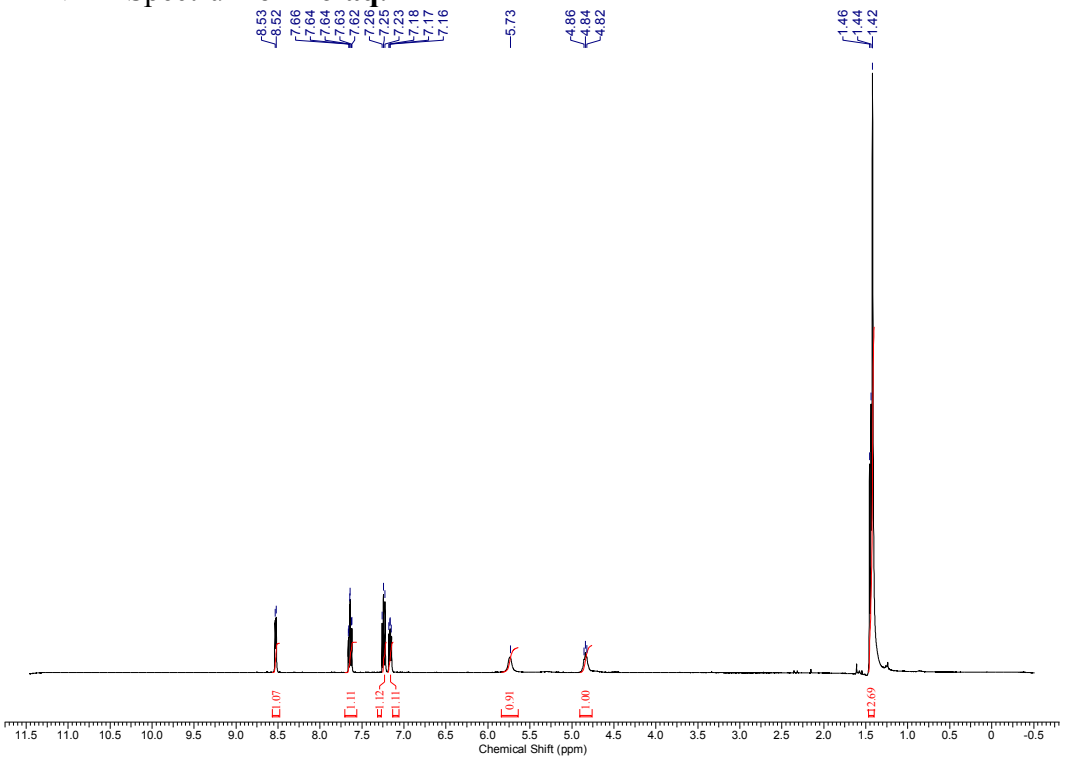
^{1}H NMR Spectrum of **7-6-ap**:



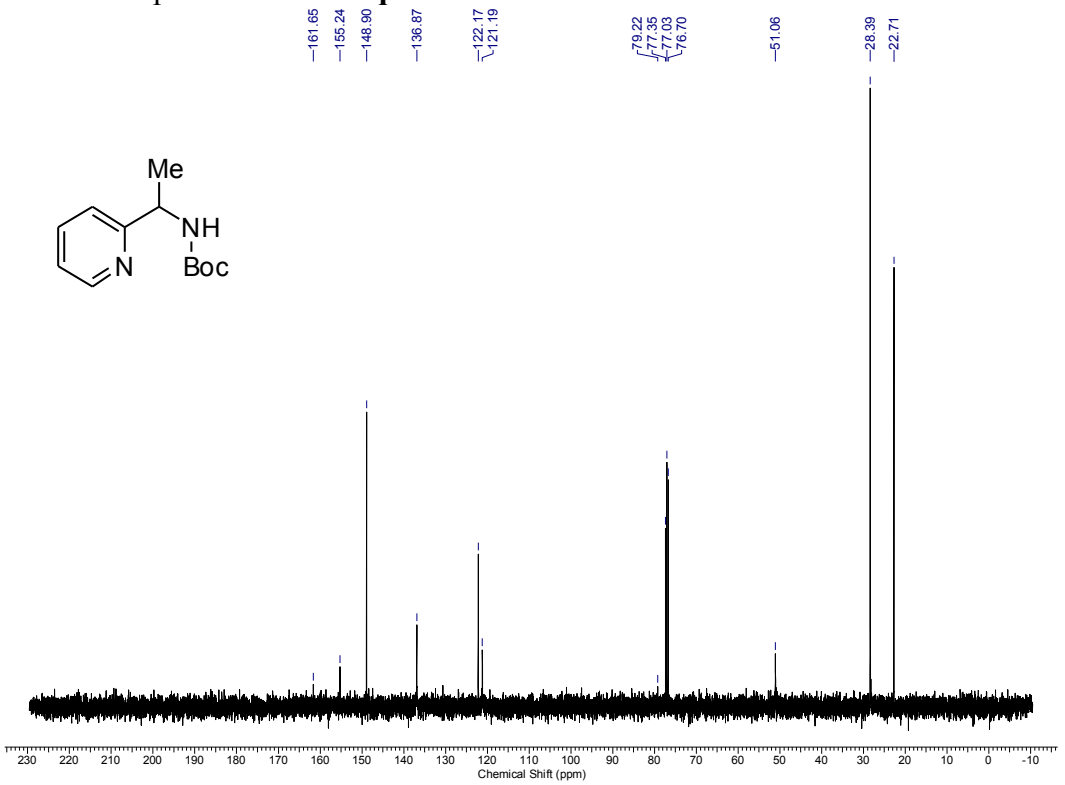
^{13}C NMR Spectrum of **7-6-ap**:



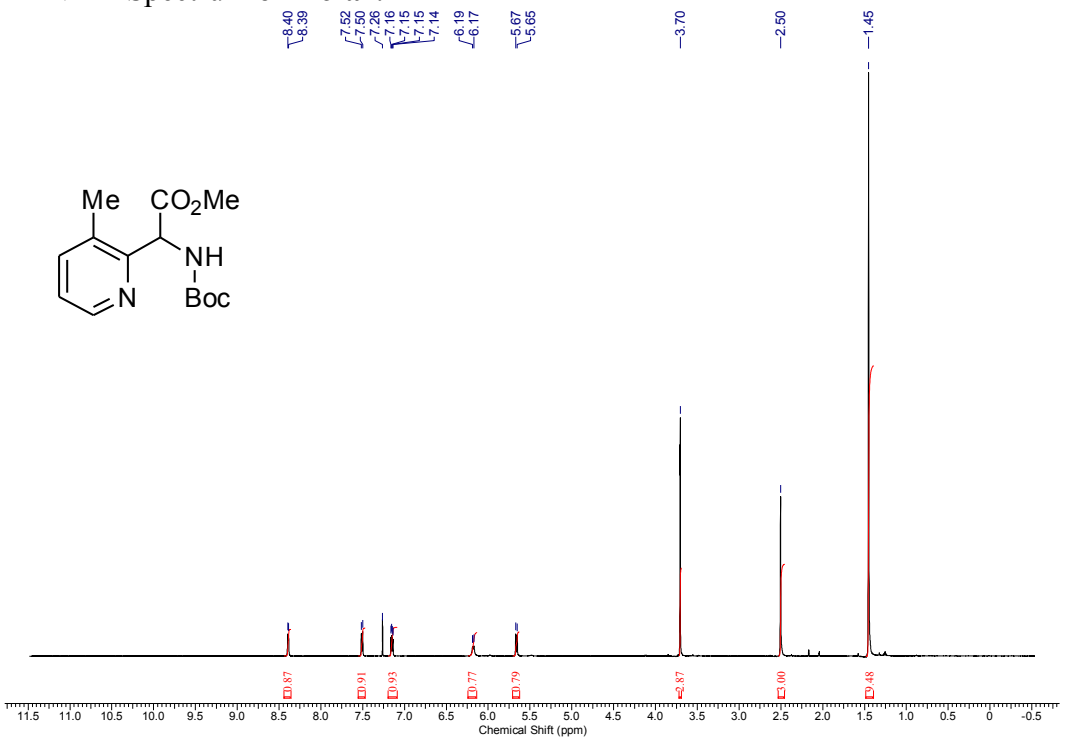
^{1}H NMR Spectrum of **7-6-aq**:



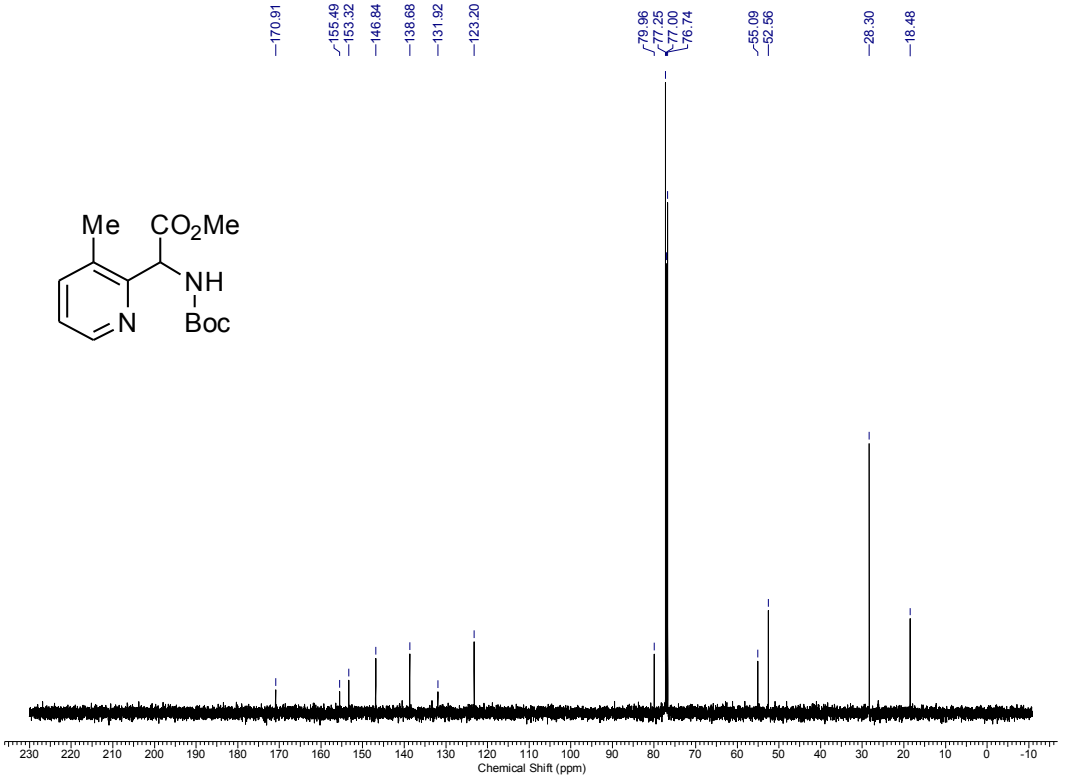
^{13}C NMR Spectrum of **7-6-aq**:



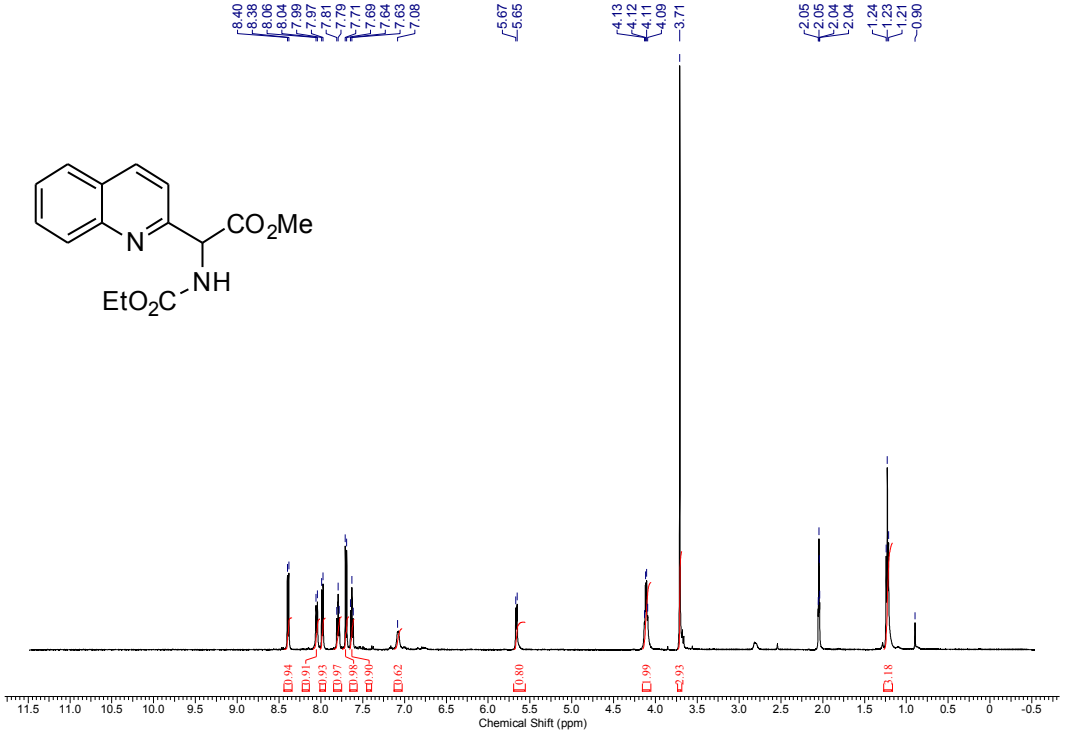
^{1}H NMR Spectrum of **7-6-ar**:



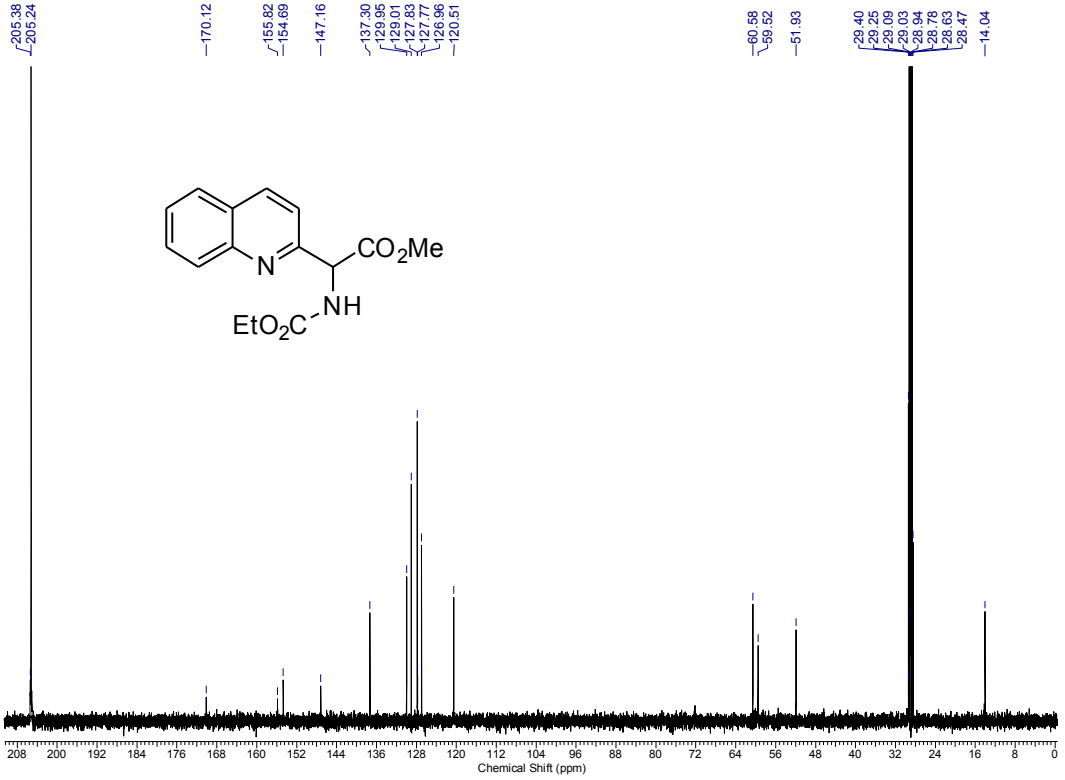
^{13}C NMR Spectrum of **7-6-ar**:



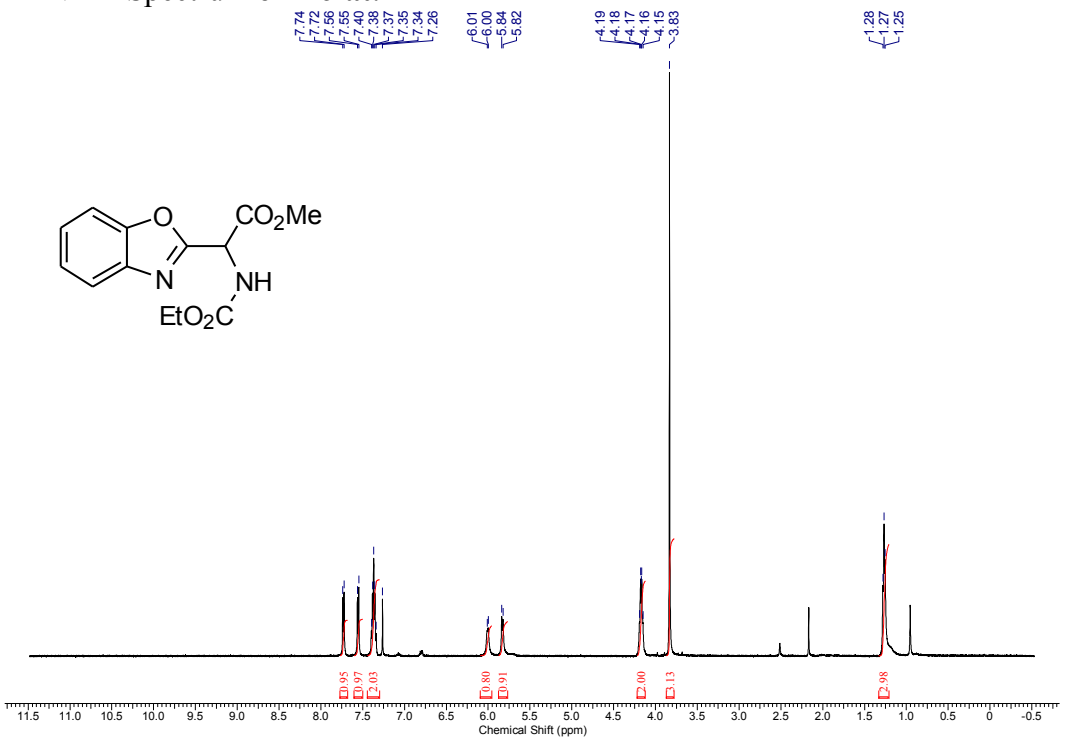
^{1}H NMR Spectrum of **7-6-as**:



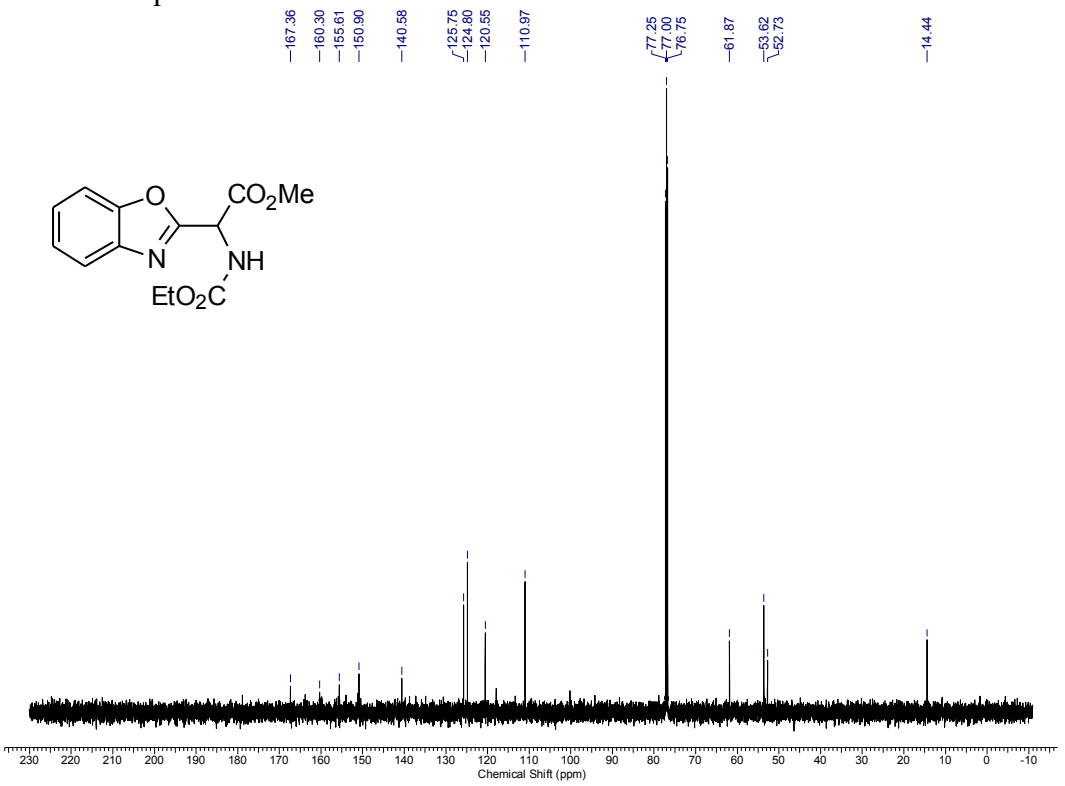
^{13}C NMR Spectrum of **7-6-as**:



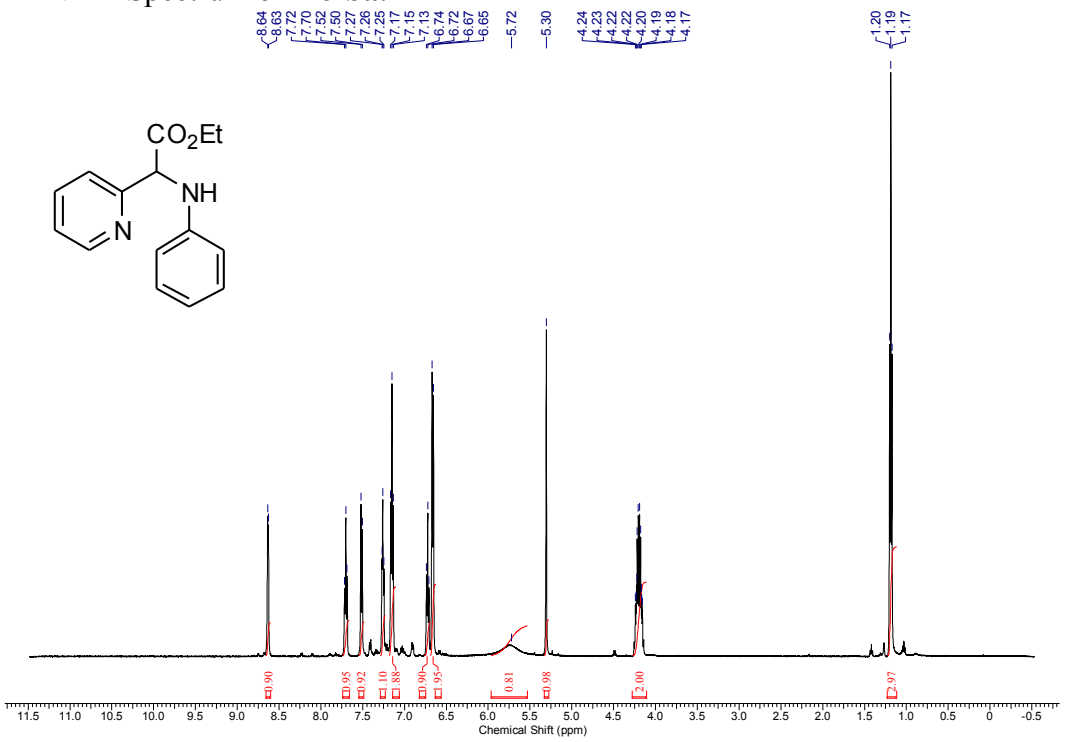
^{1}H NMR Spectrum of **7-6-at**:



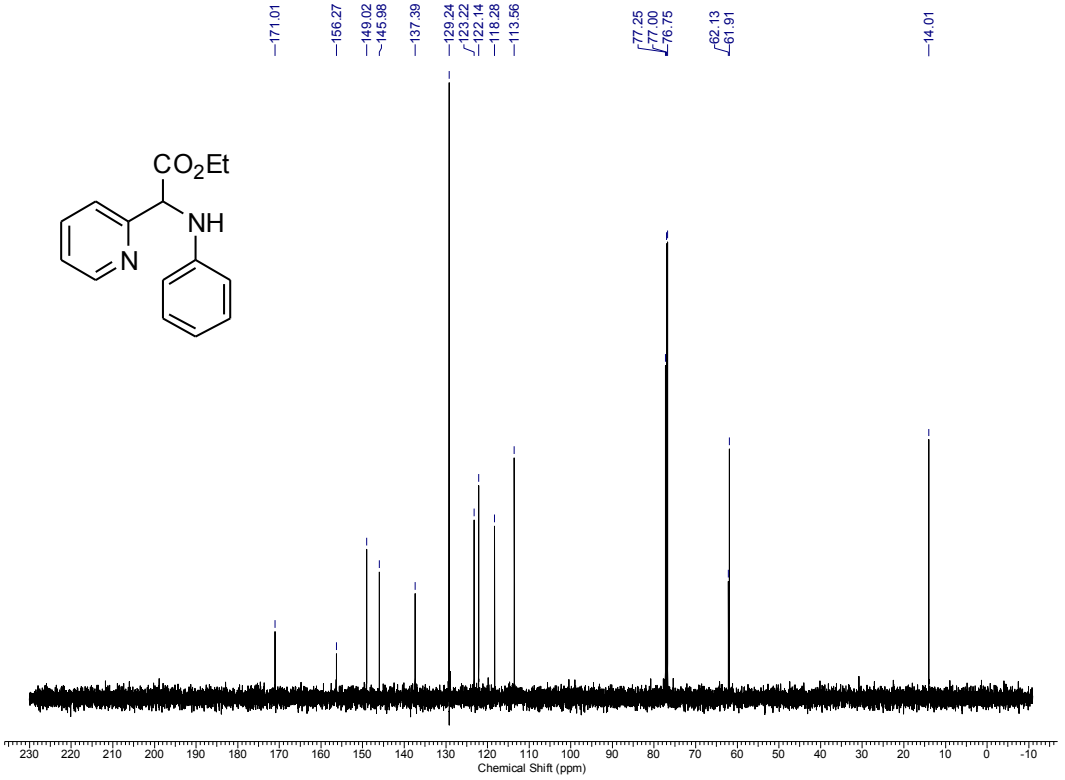
^{13}C NMR Spectrum of **7-6-at**:



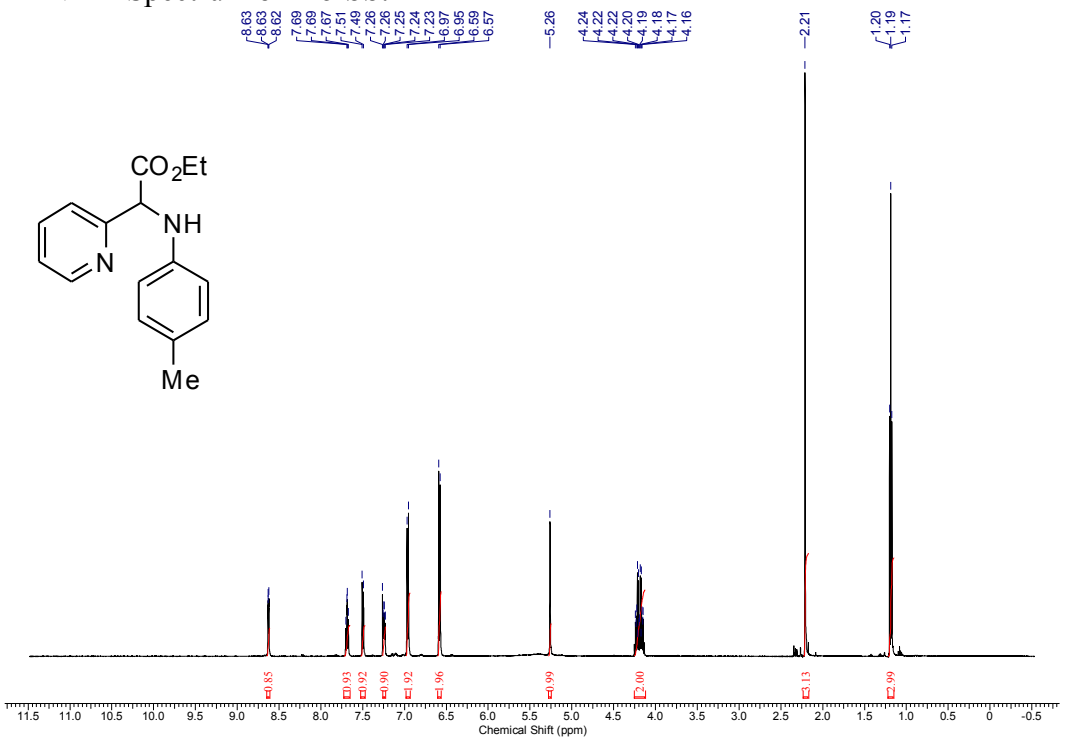
^{1}H NMR Spectrum of **7-6-ba**:



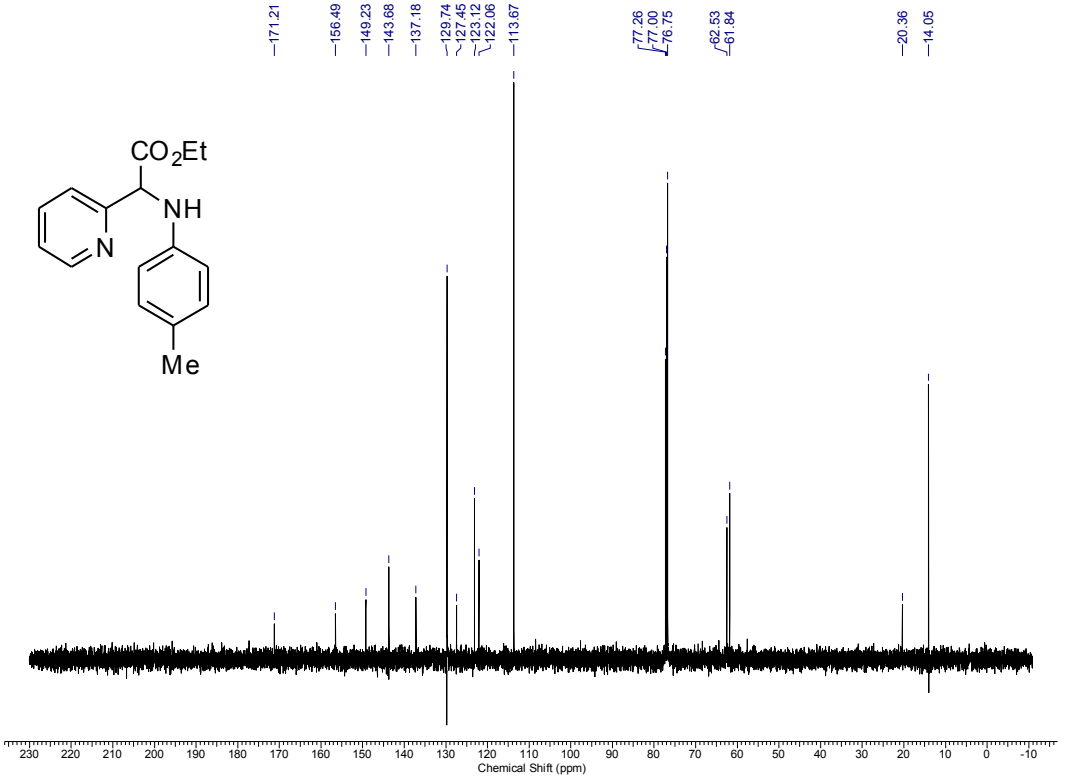
^{13}C NMR Spectrum of **7-6-ba**:



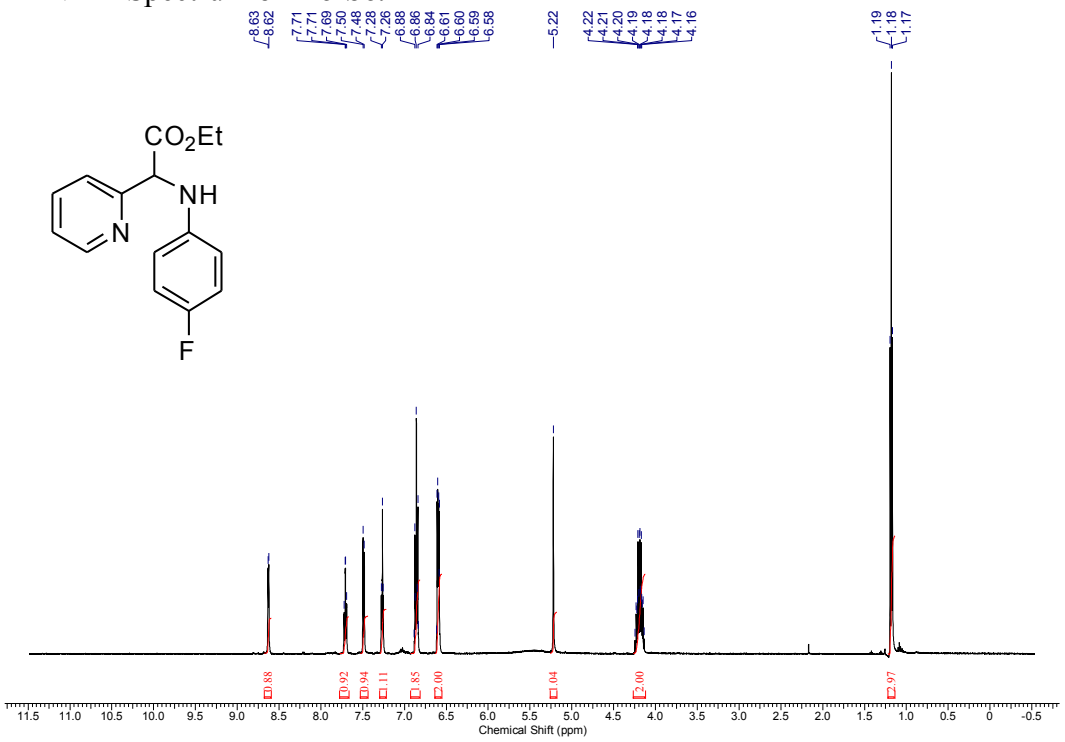
^{1}H NMR Spectrum of **7-6-bb**:



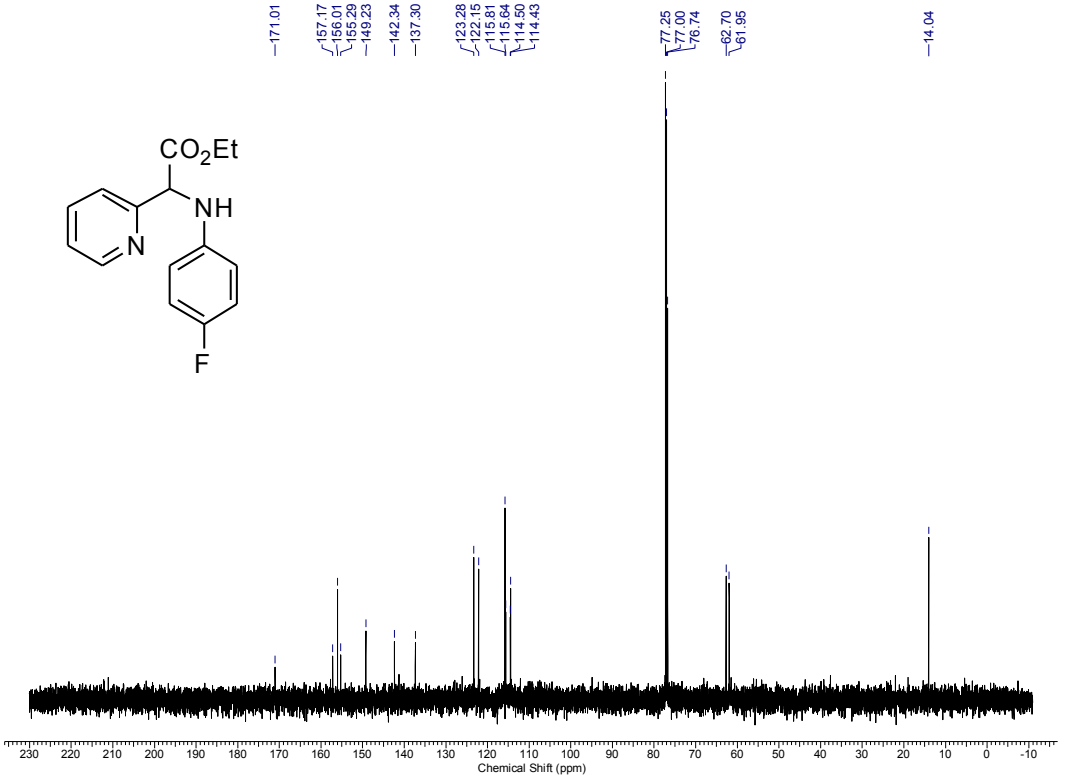
^{13}C NMR Spectrum of **7-6-bb**:



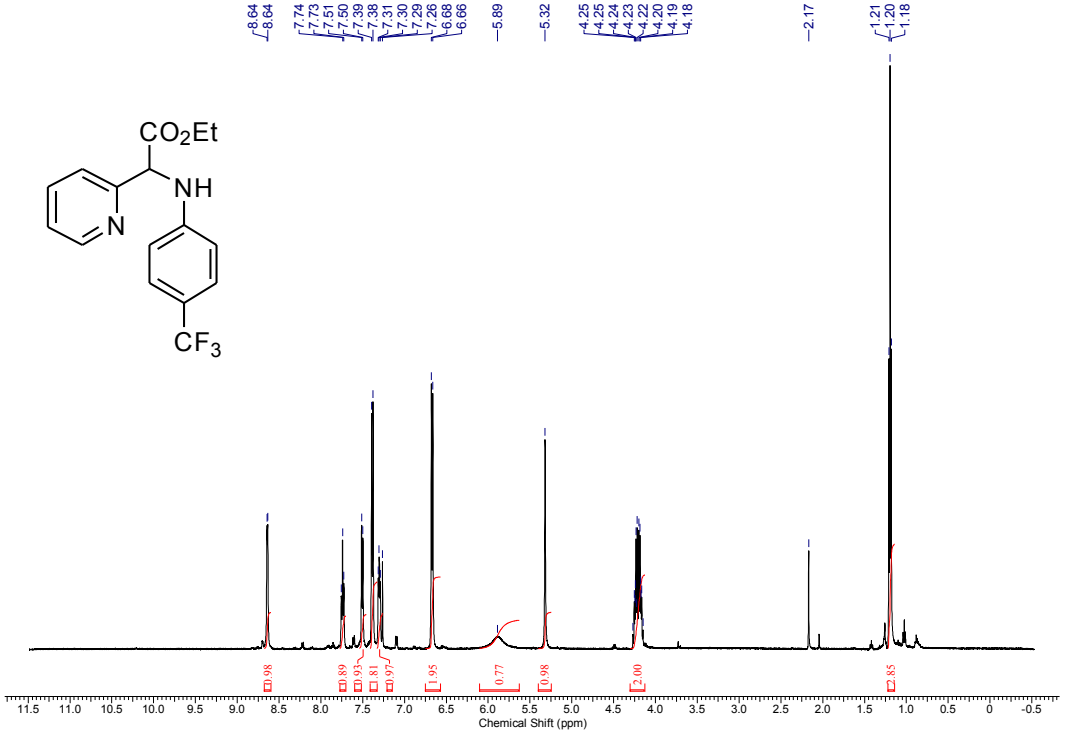
^{1}H NMR Spectrum of **7-6-bc**:



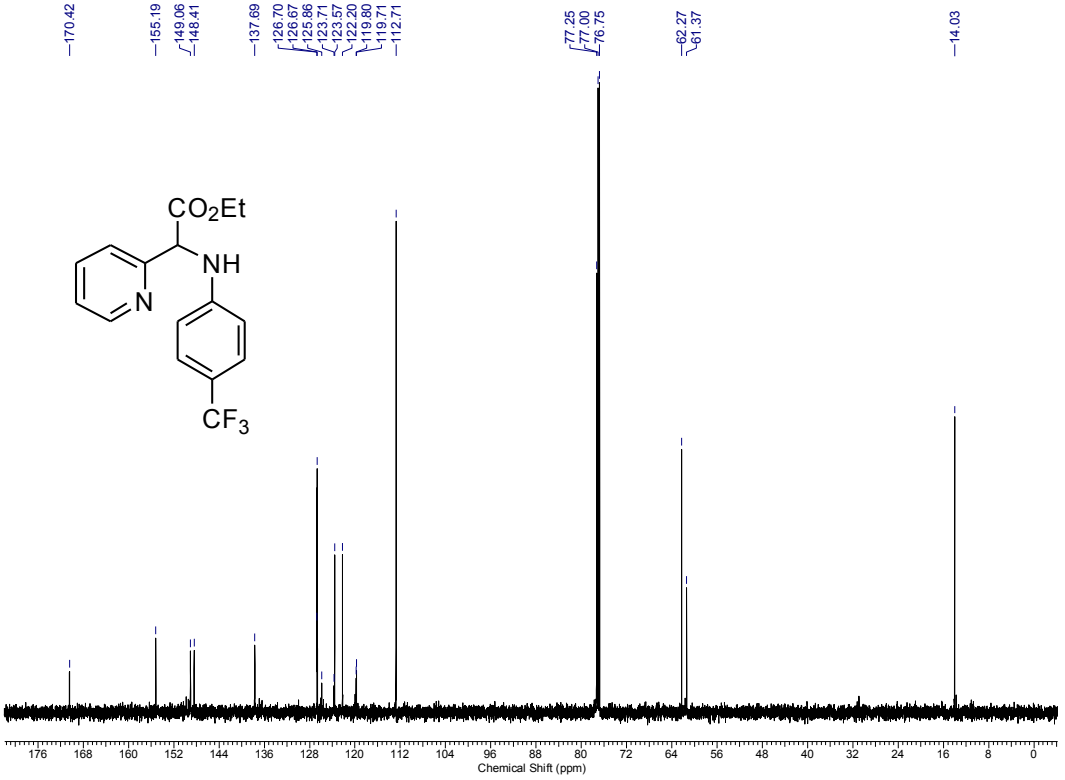
^{13}C NMR Spectrum of **7-6-bc**:



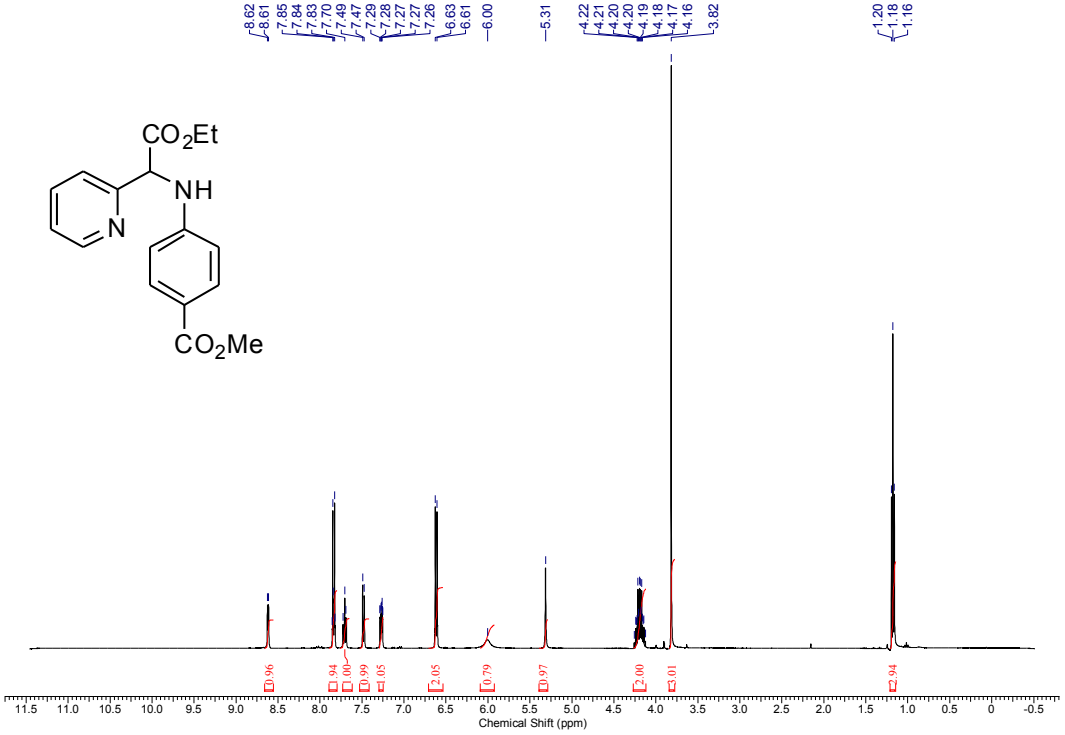
^{1}H NMR Spectrum of **7-6-bd**:



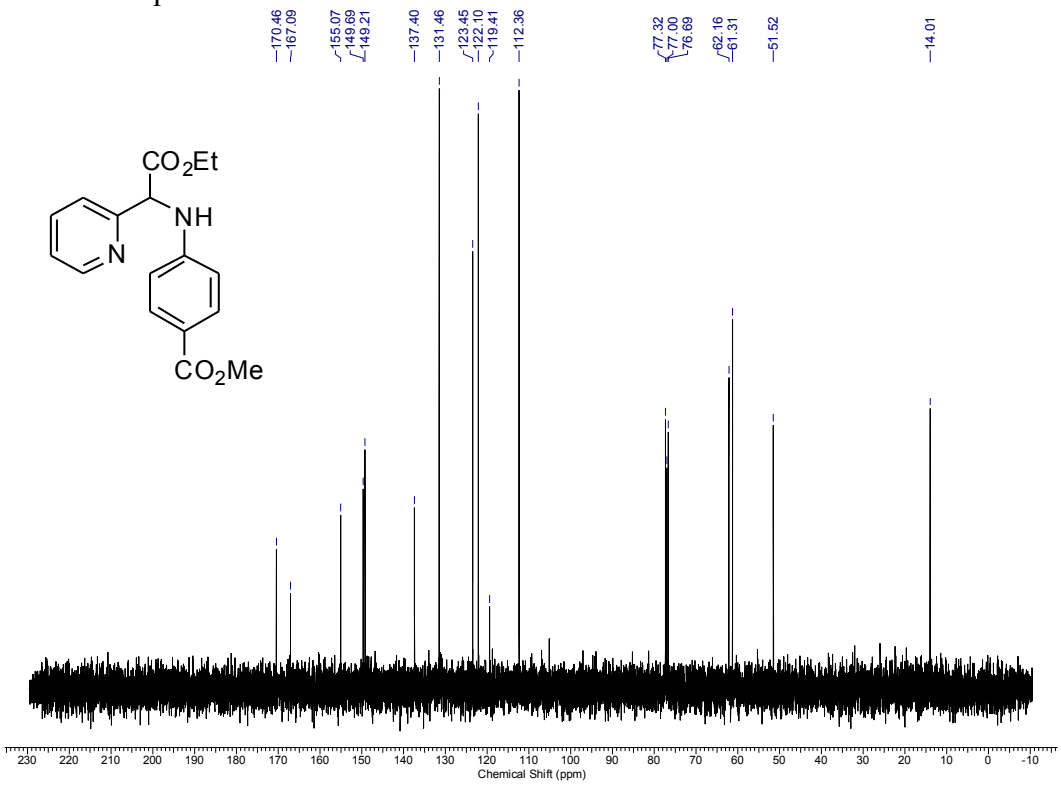
^{13}C NMR Spectrum of **7-6-bd**:



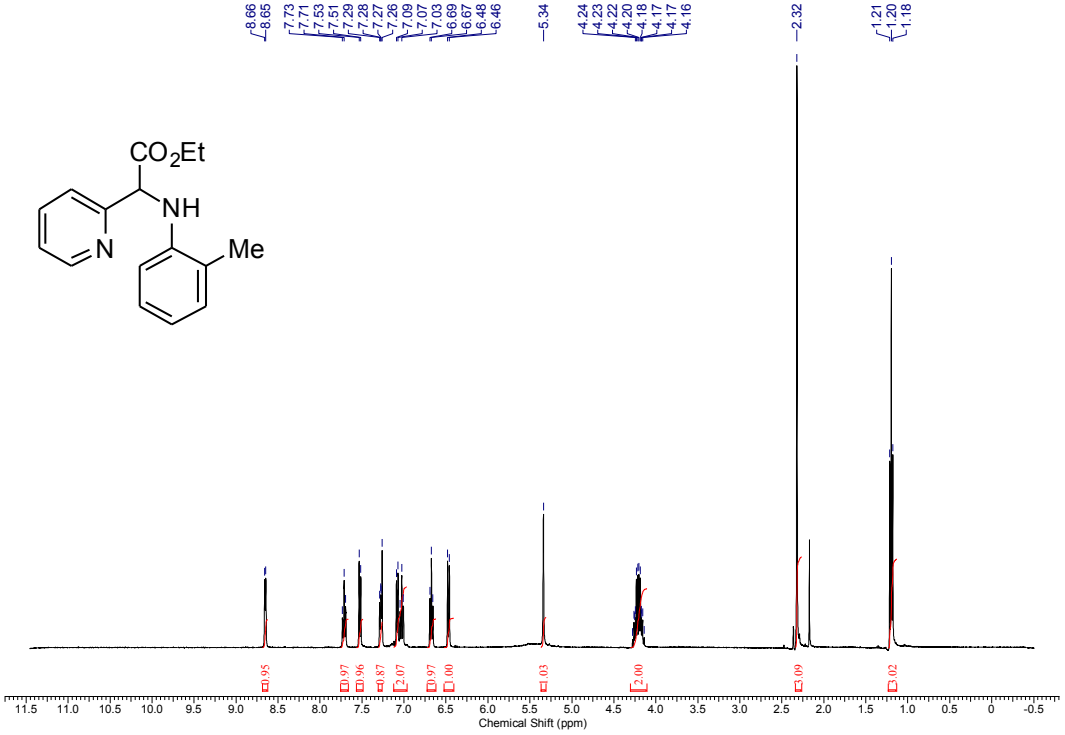
^{1}H NMR Spectrum of **7-6-be**:



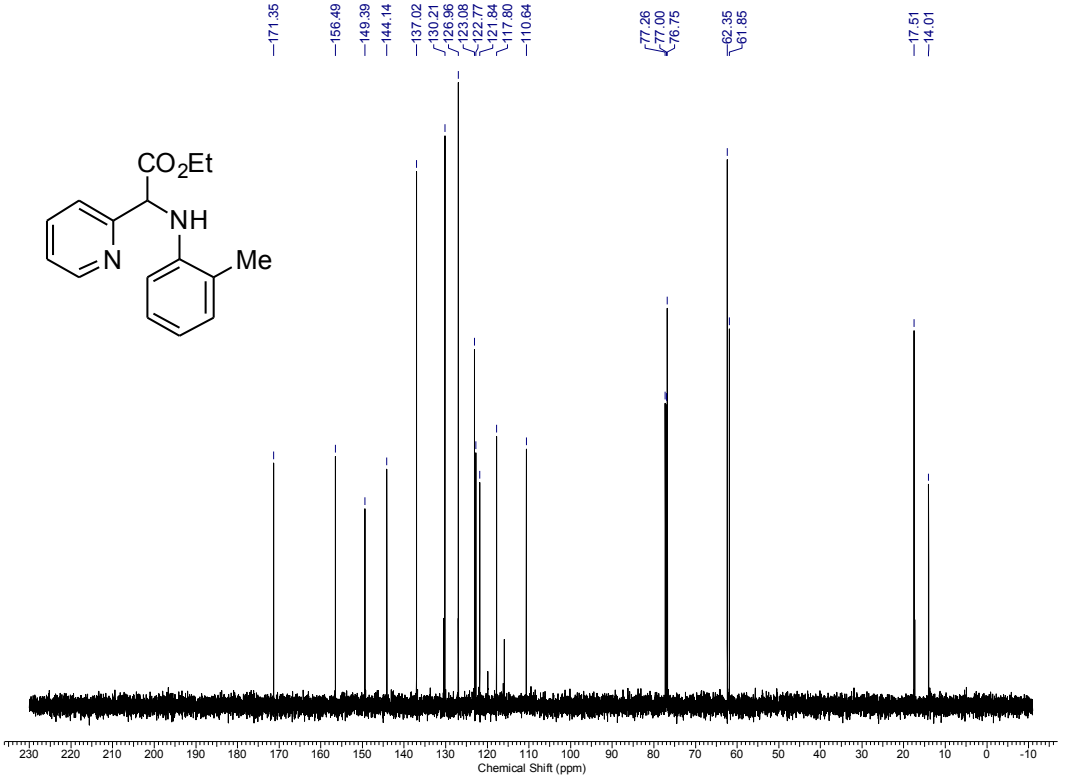
^{13}C NMR Spectrum of **7-6-be**:



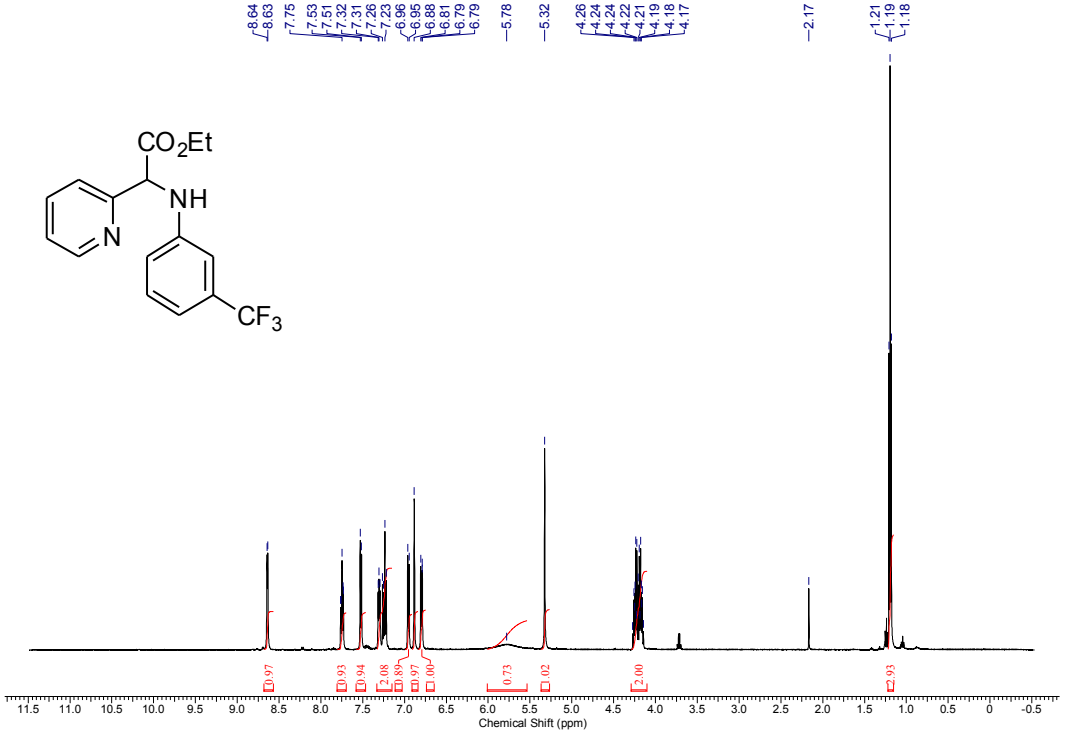
^{1}H NMR Spectrum of **7-6-bf**:



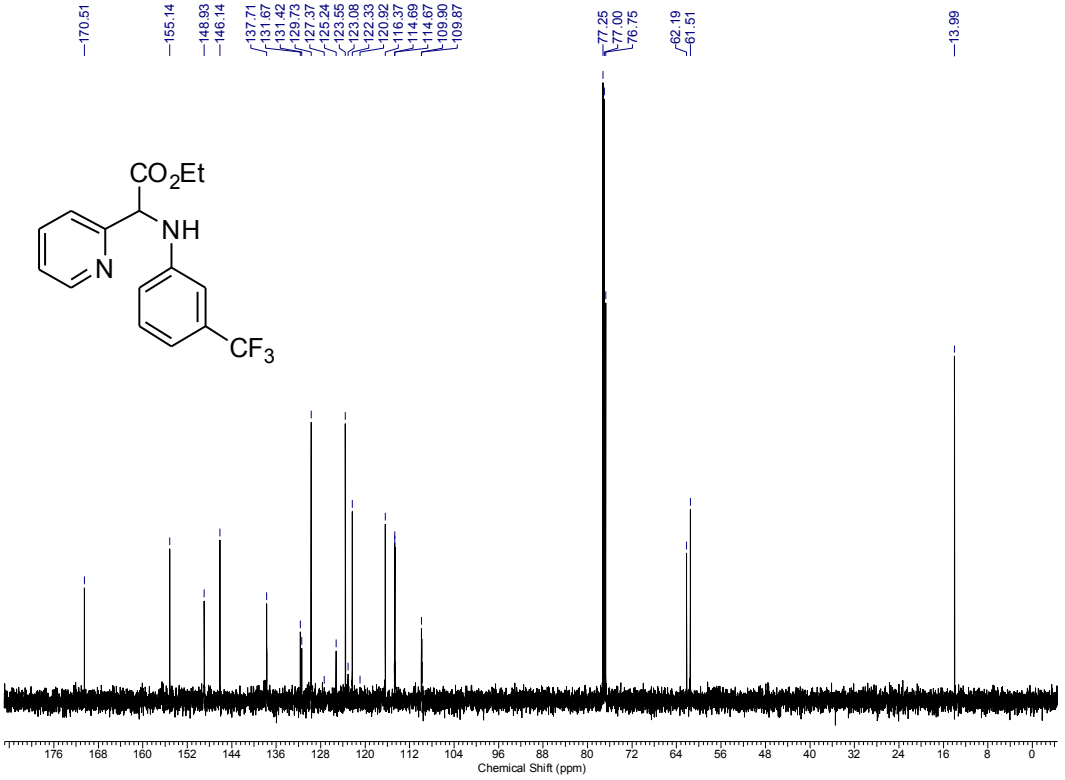
^{13}C NMR Spectrum of **7-6-bf**:



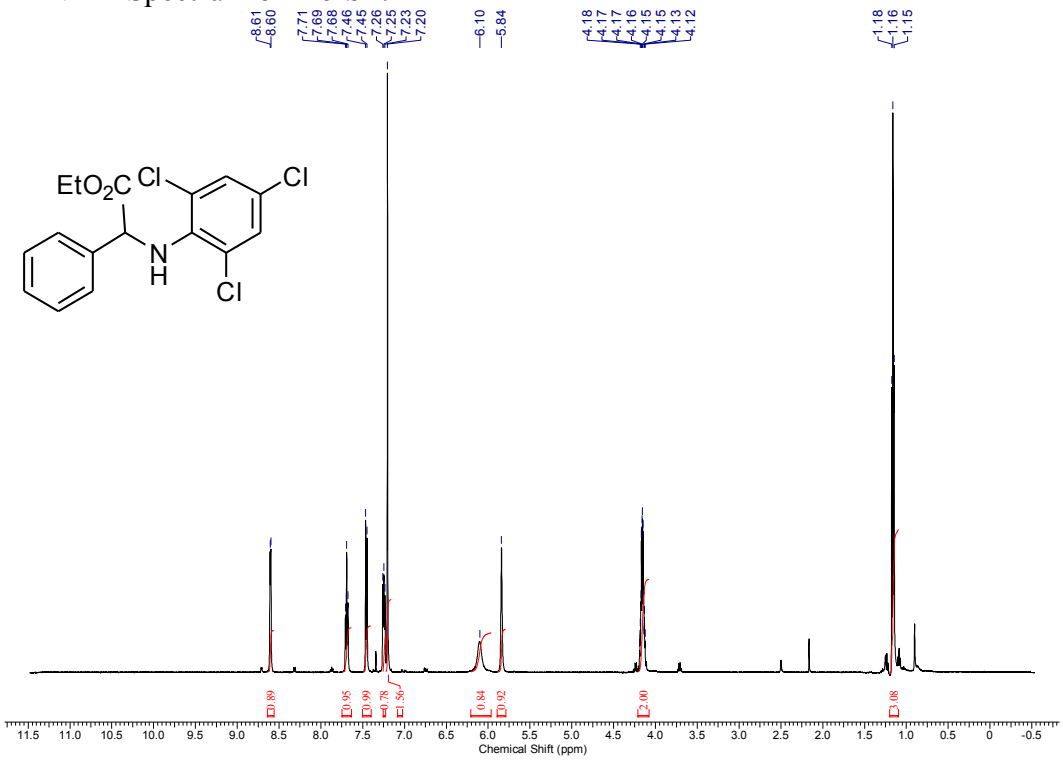
^{1}H NMR Spectrum of **7-6-bg**:



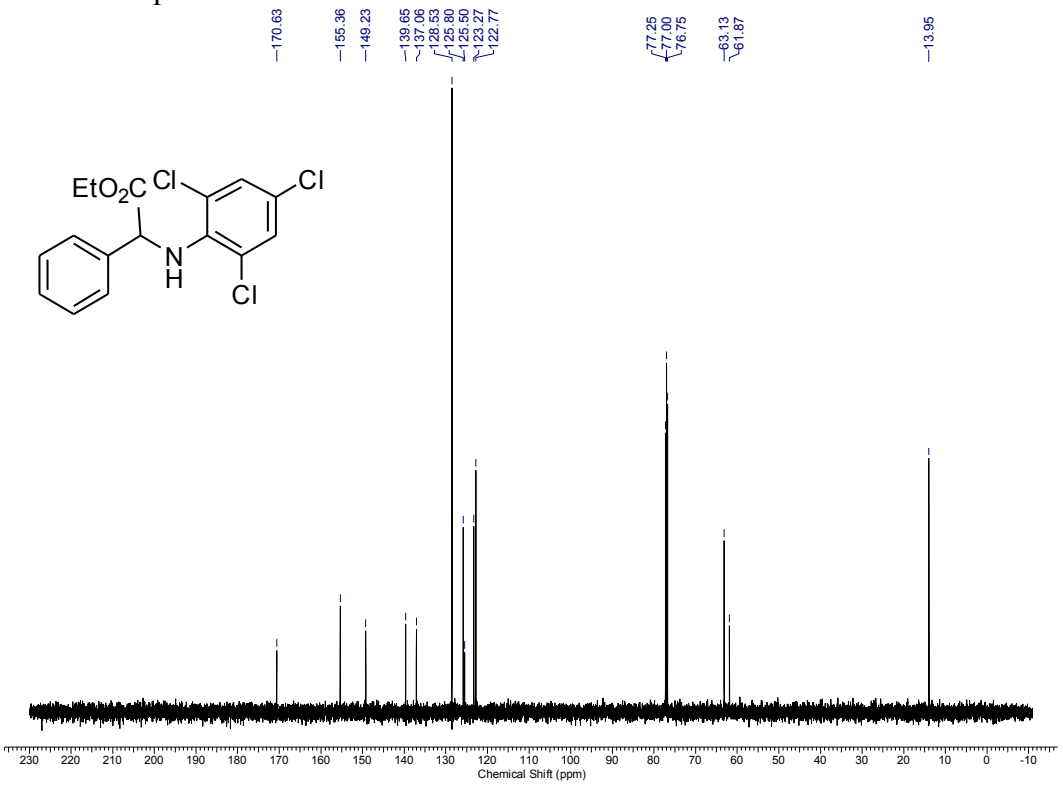
^{13}C NMR Spectrum of **7-6-bg**:



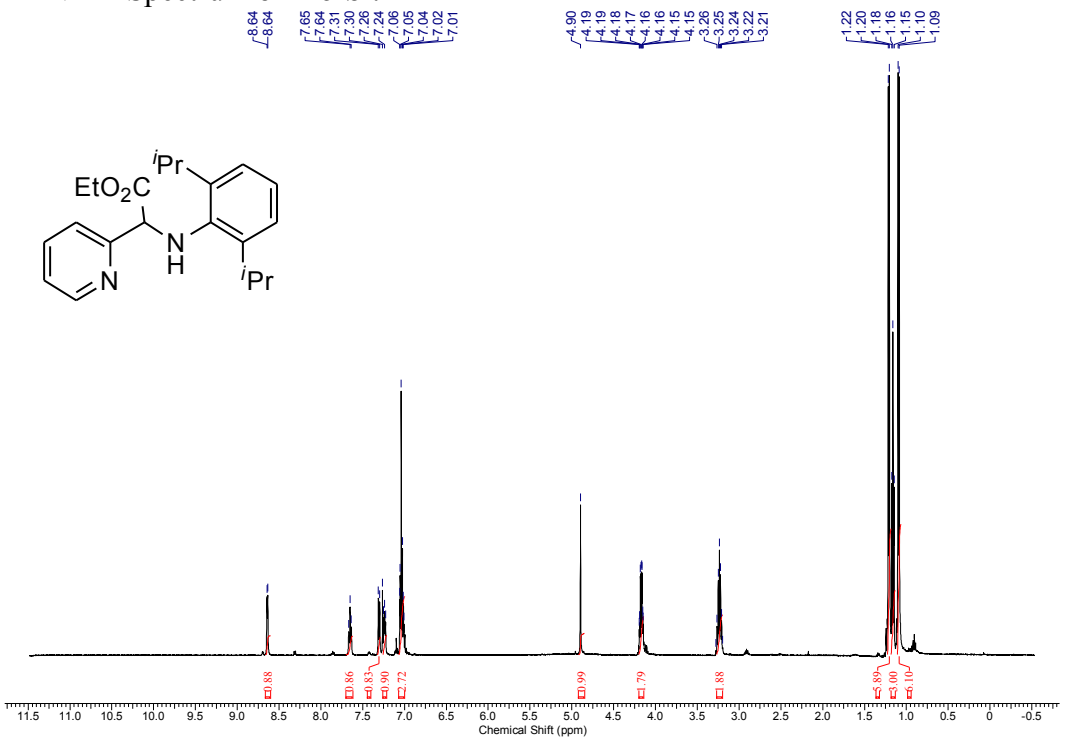
^{1}H NMR Spectrum of **7-6-bh**:



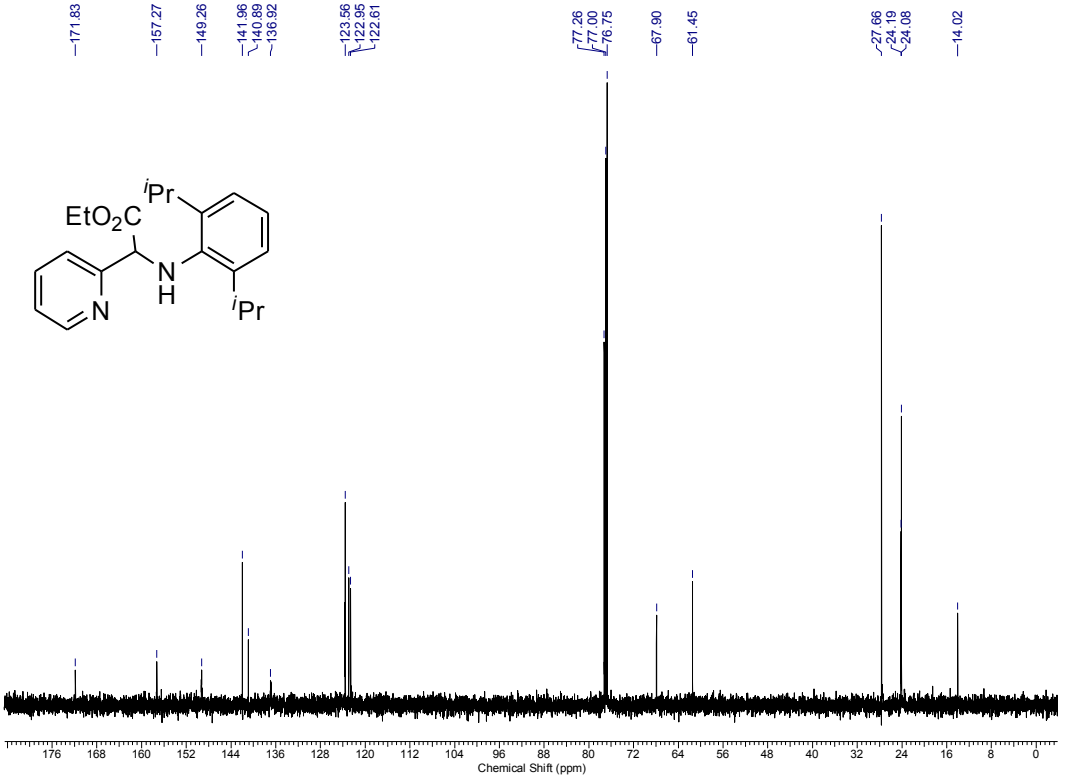
^{13}C NMR Spectrum of **7-6-bh**:



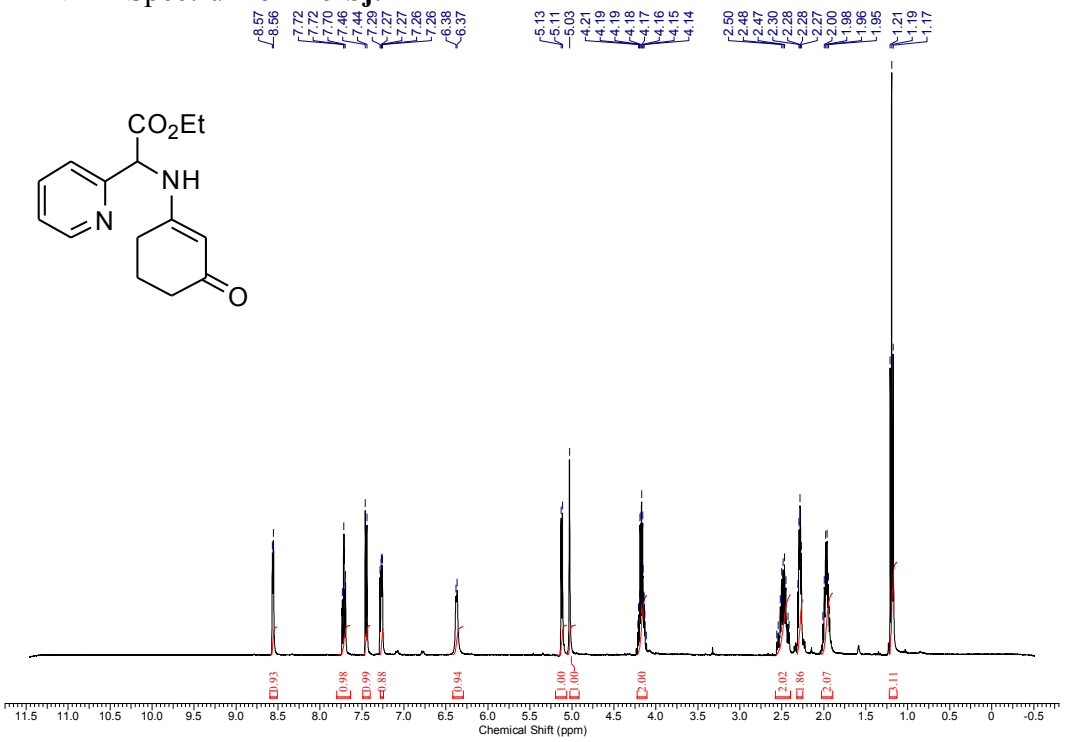
^{1}H NMR Spectrum of **7-6-bi**:



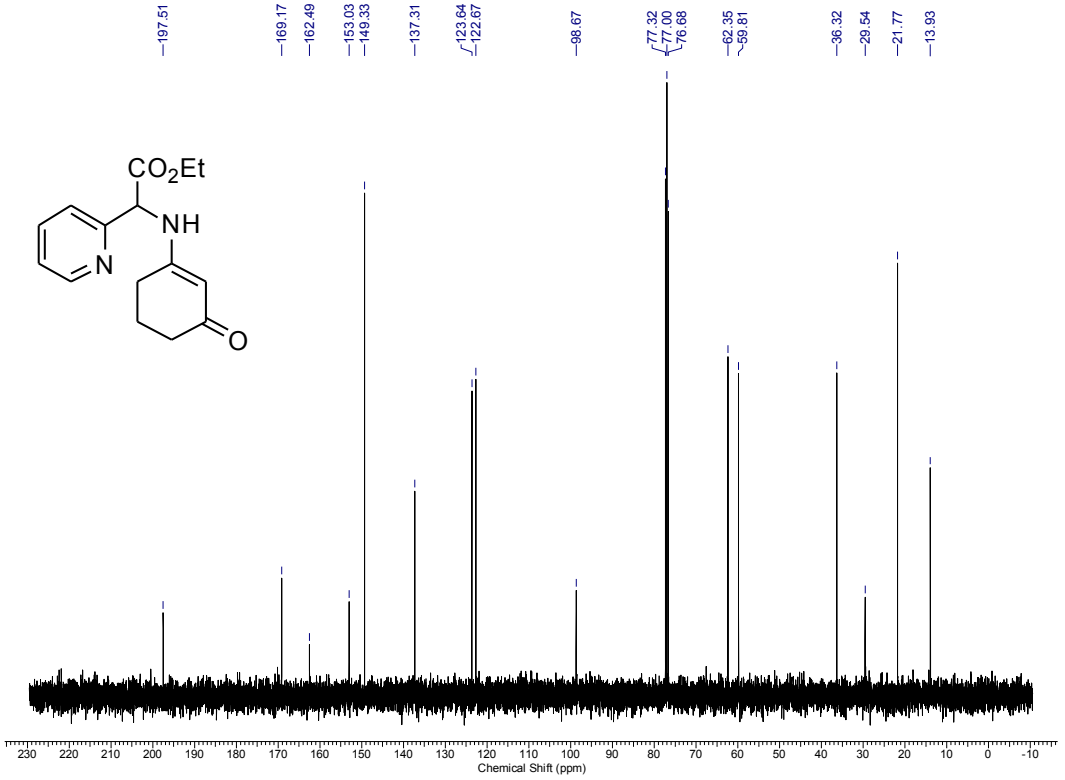
^{13}C NMR Spectrum of **7-6-bi**:



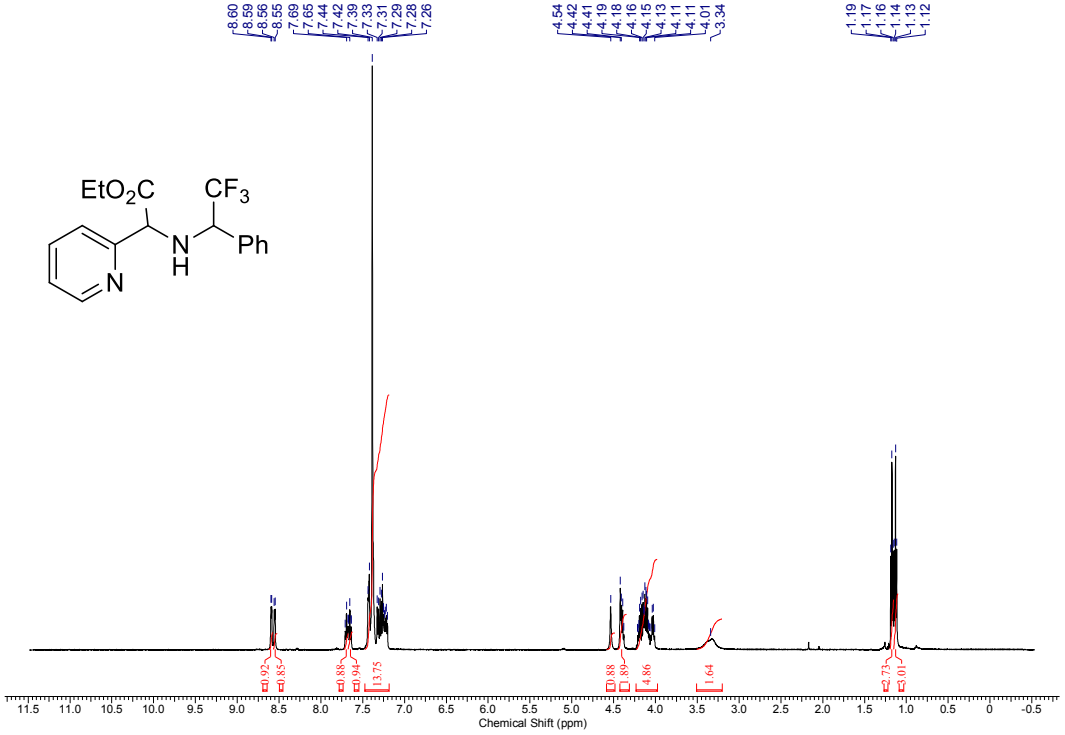
^{1}H NMR Spectrum of **7-6-bj**:



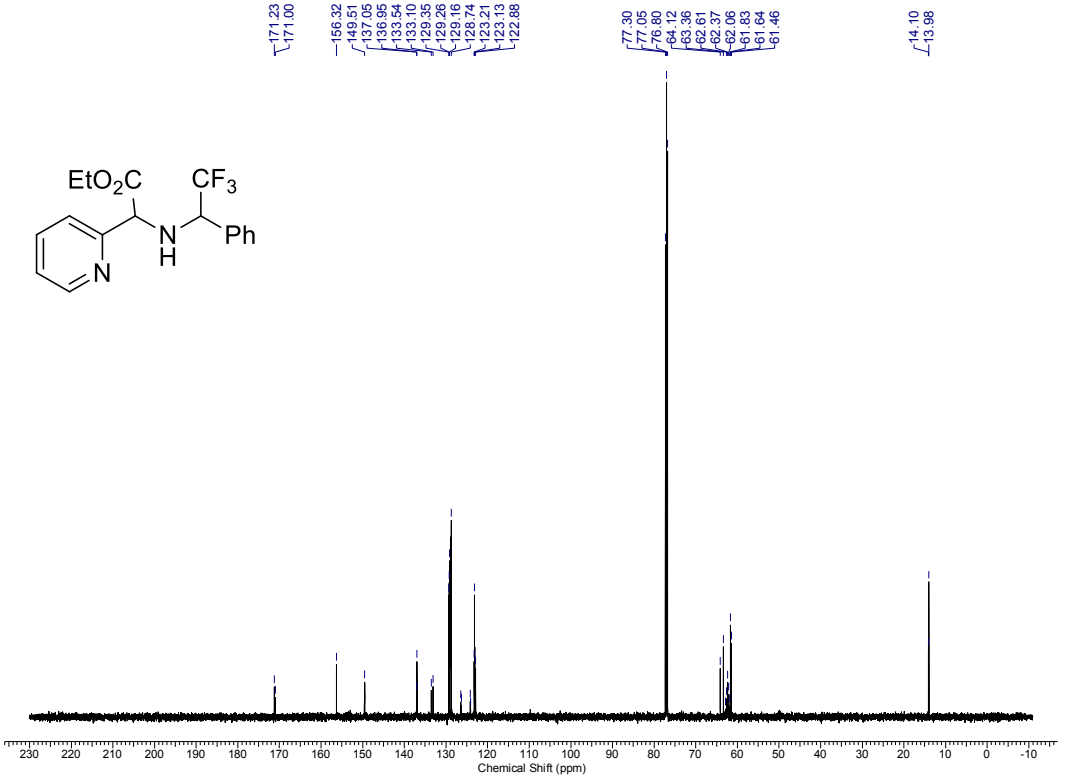
^{13}C NMR Spectrum of **7-6-bj**:



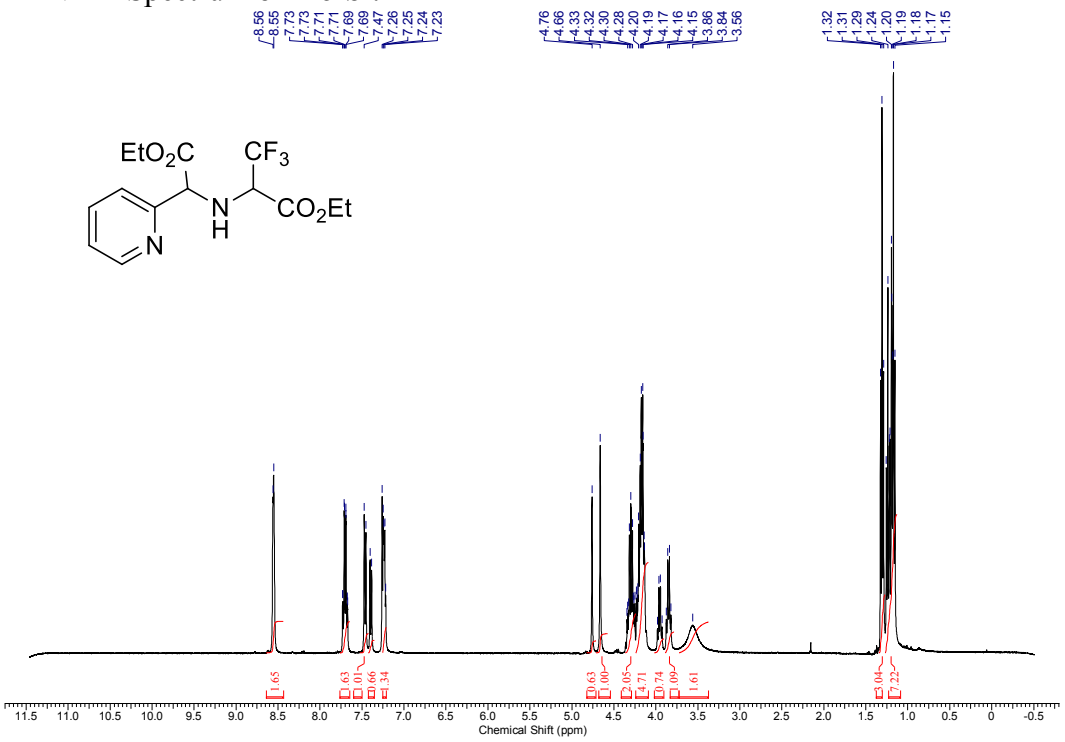
^{1}H NMR Spectrum of **7-6-bk**:



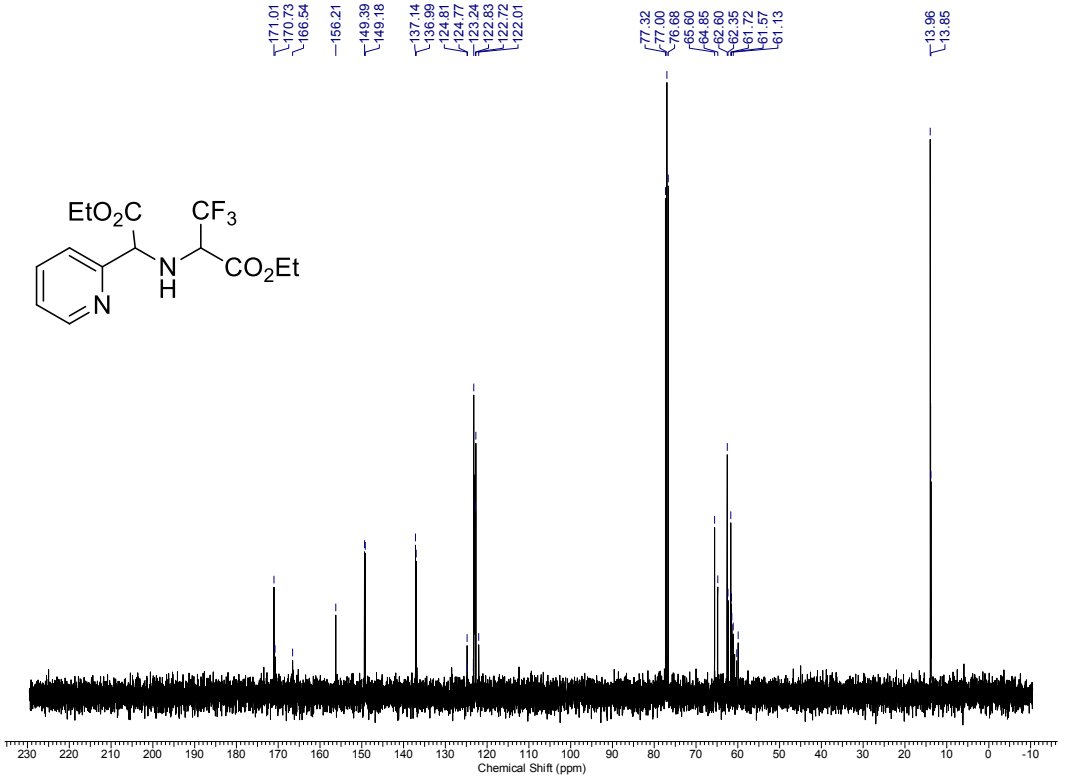
^{13}C NMR Spectrum of **7-6-bk**:



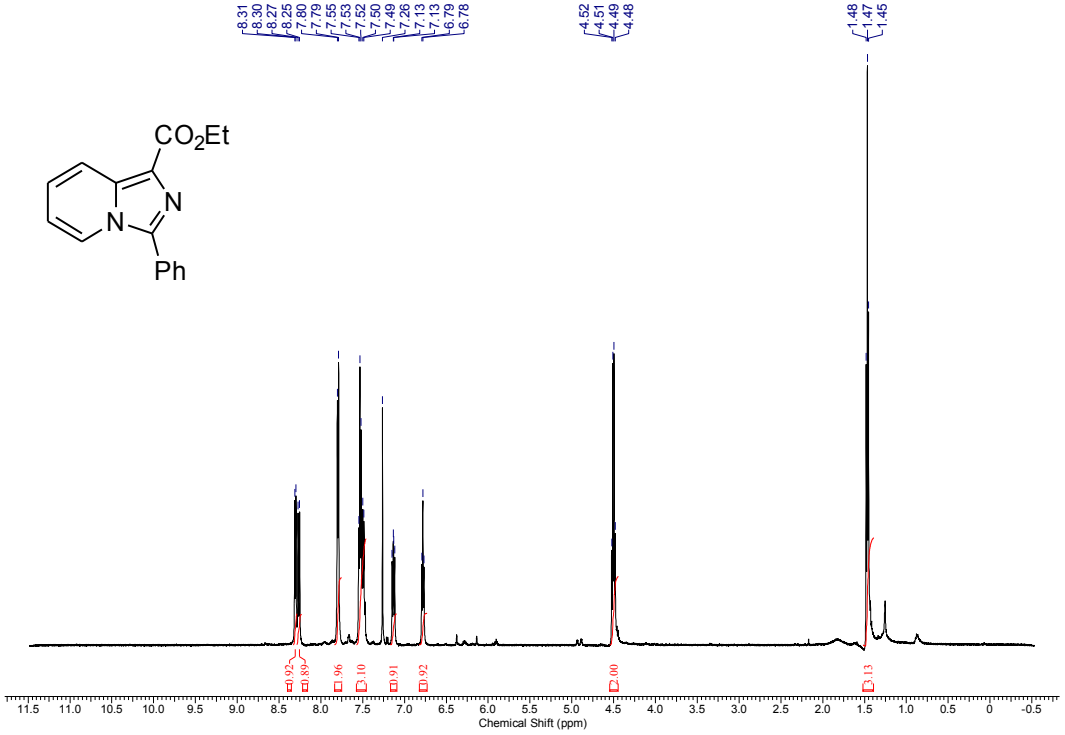
^{1}H NMR Spectrum of **7-6-bl**:



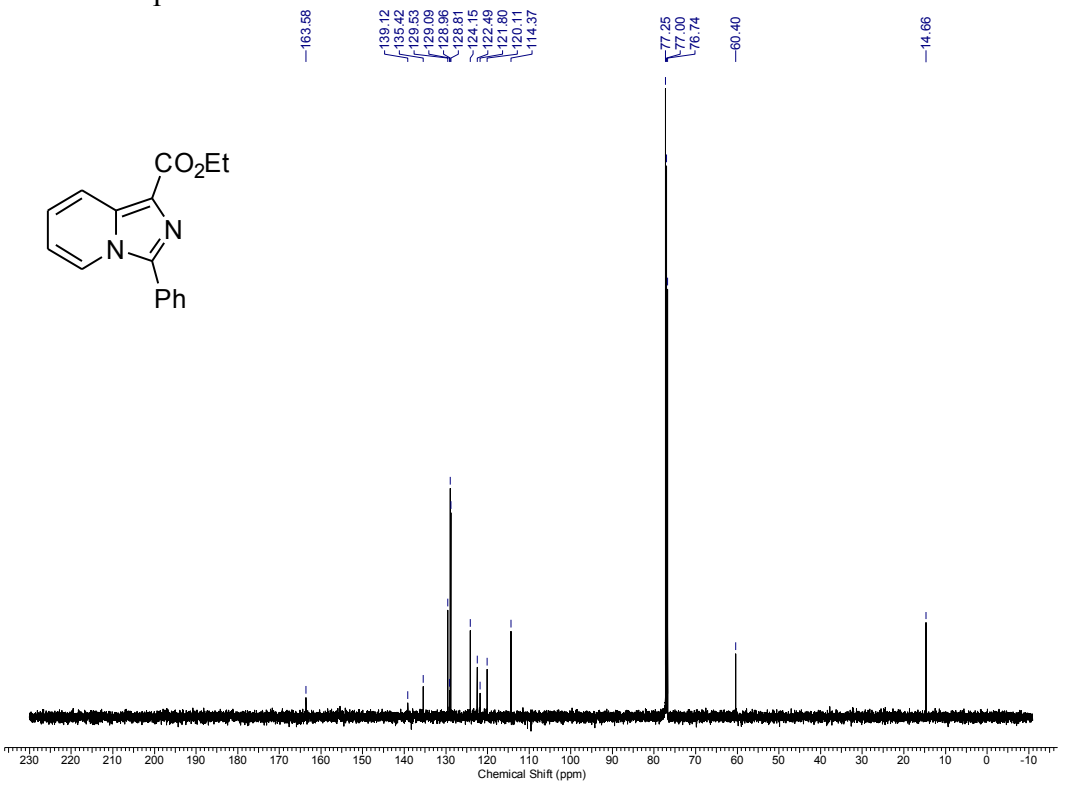
^{13}C NMR Spectrum of **7-6-bl**:



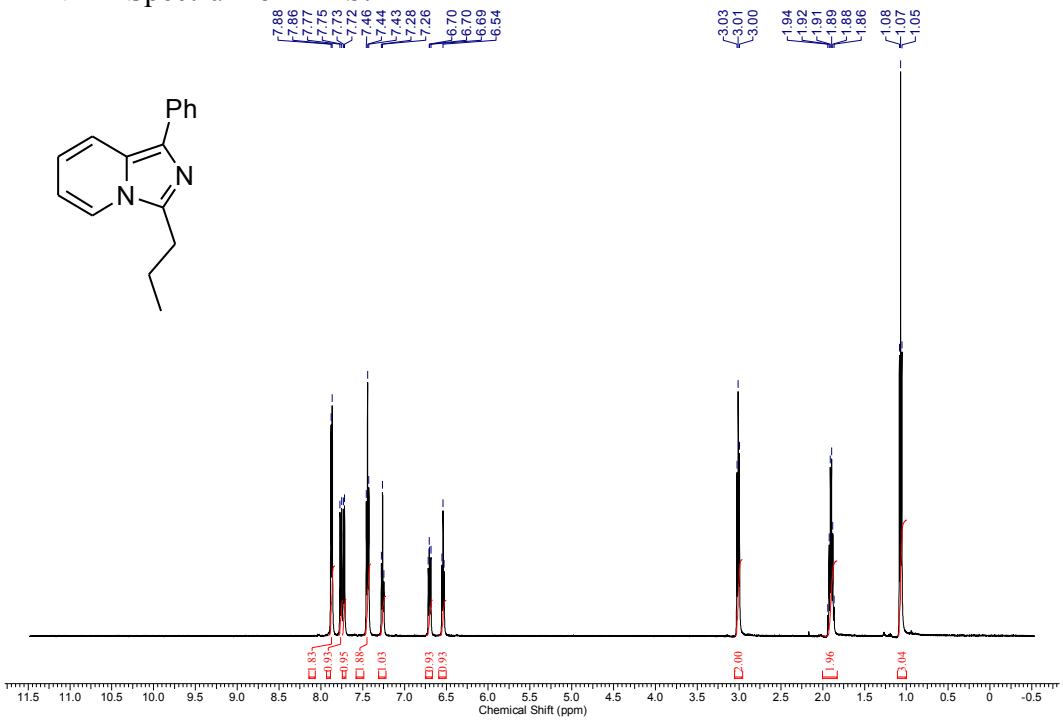
^{1}H NMR Spectrum of **7-7-a**:



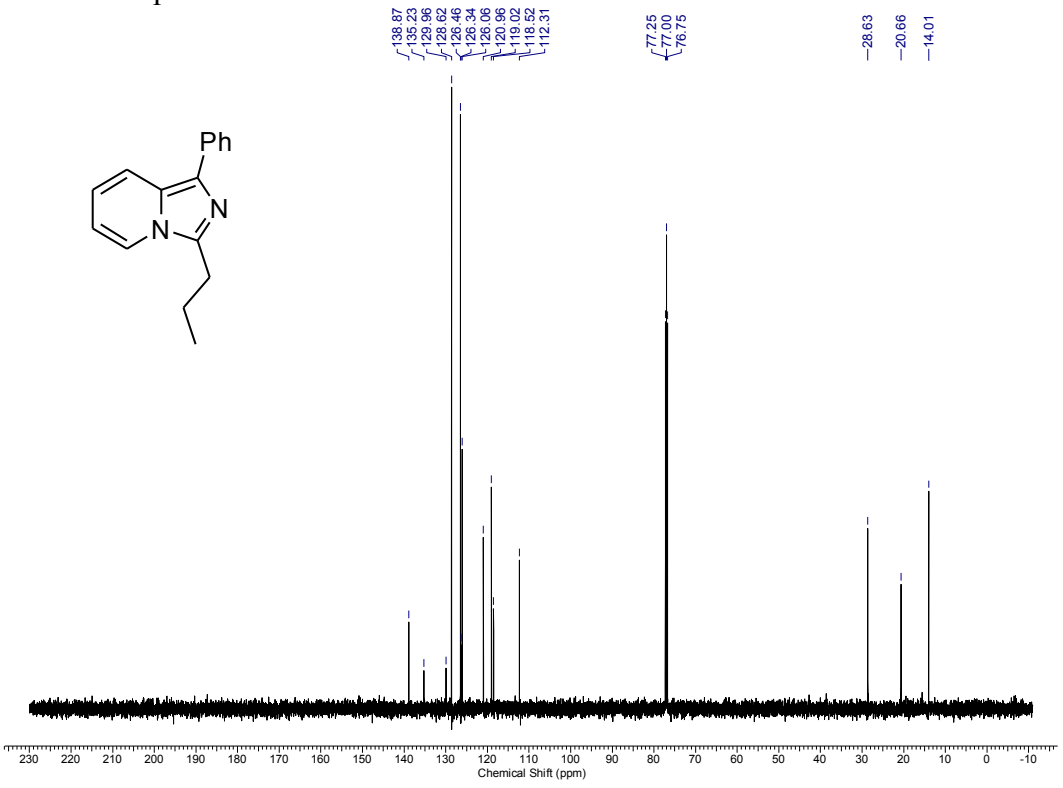
^{13}C NMR Spectrum of **7-7-a**:



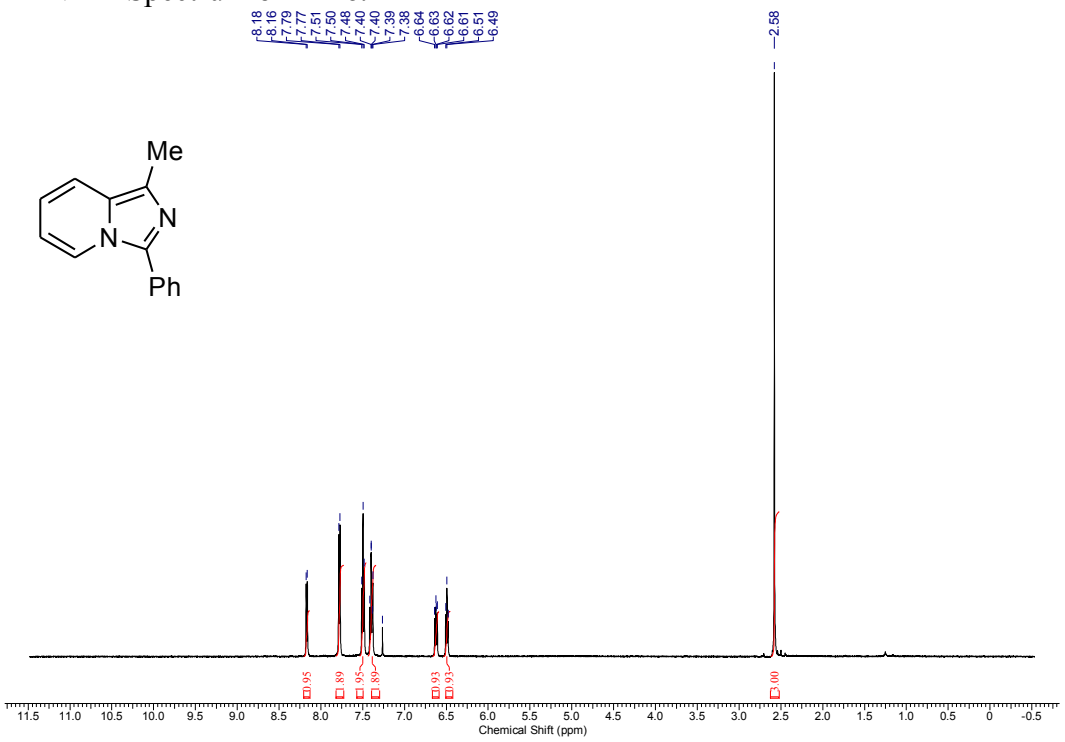
^{1}H NMR Spectrum of **7-7-b**:



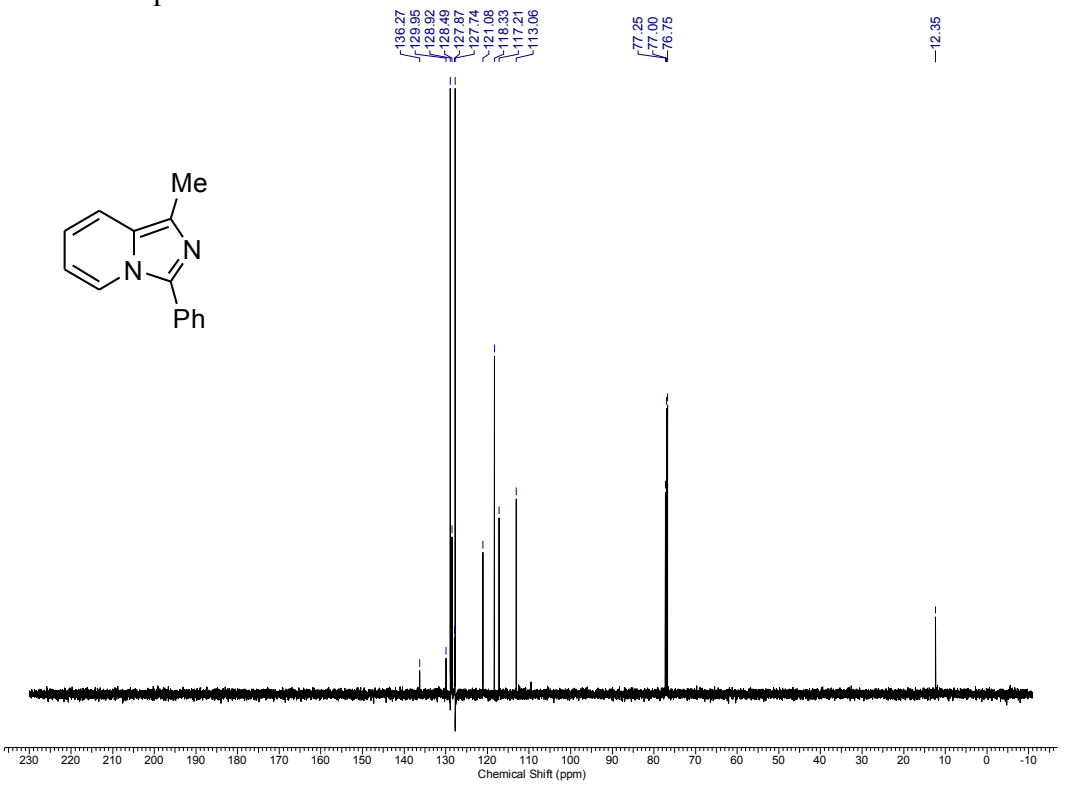
^{13}C NMR Spectrum of **7-7-b**:



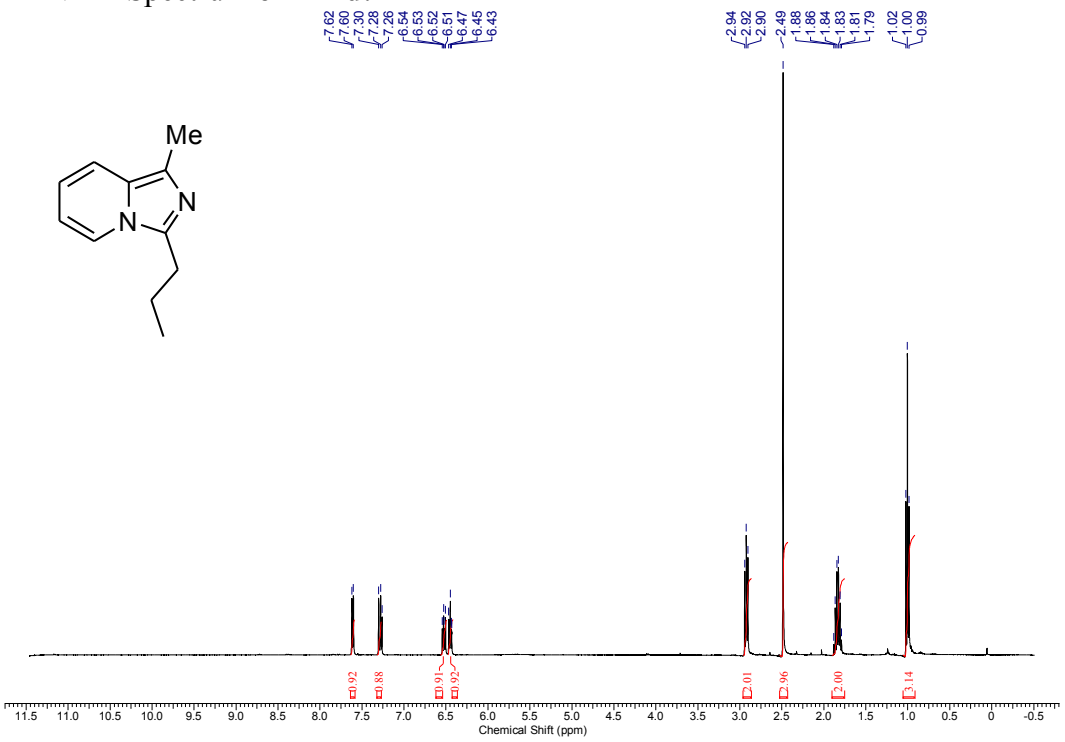
^{1}H NMR Spectrum of **7-7-c**:



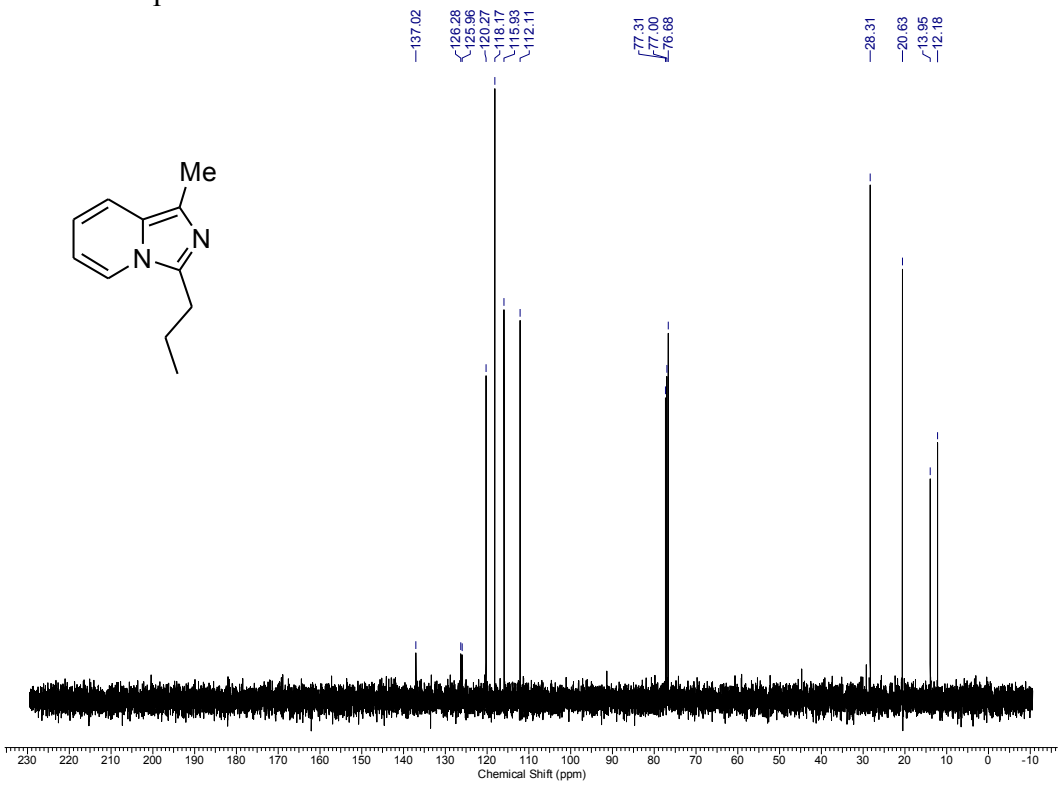
^{13}C NMR Spectrum of **7-7-c**:



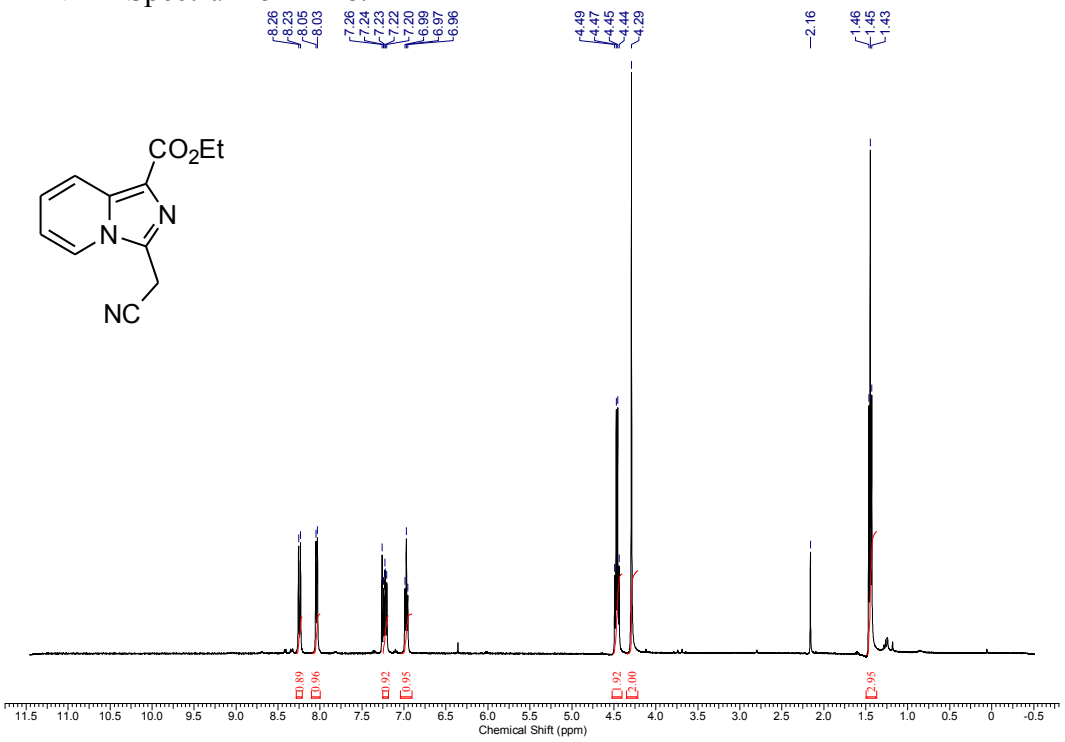
^{1}H NMR Spectrum of **7-7-d**:



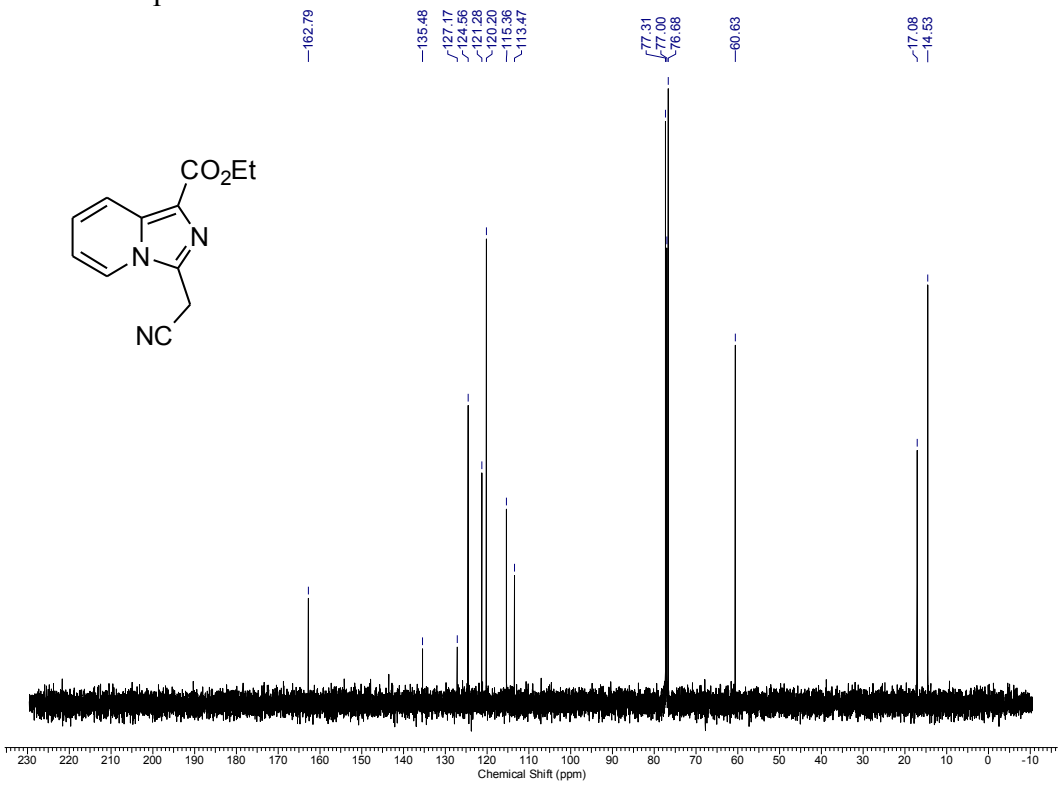
^{13}C NMR Spectrum of **7-7-d**:



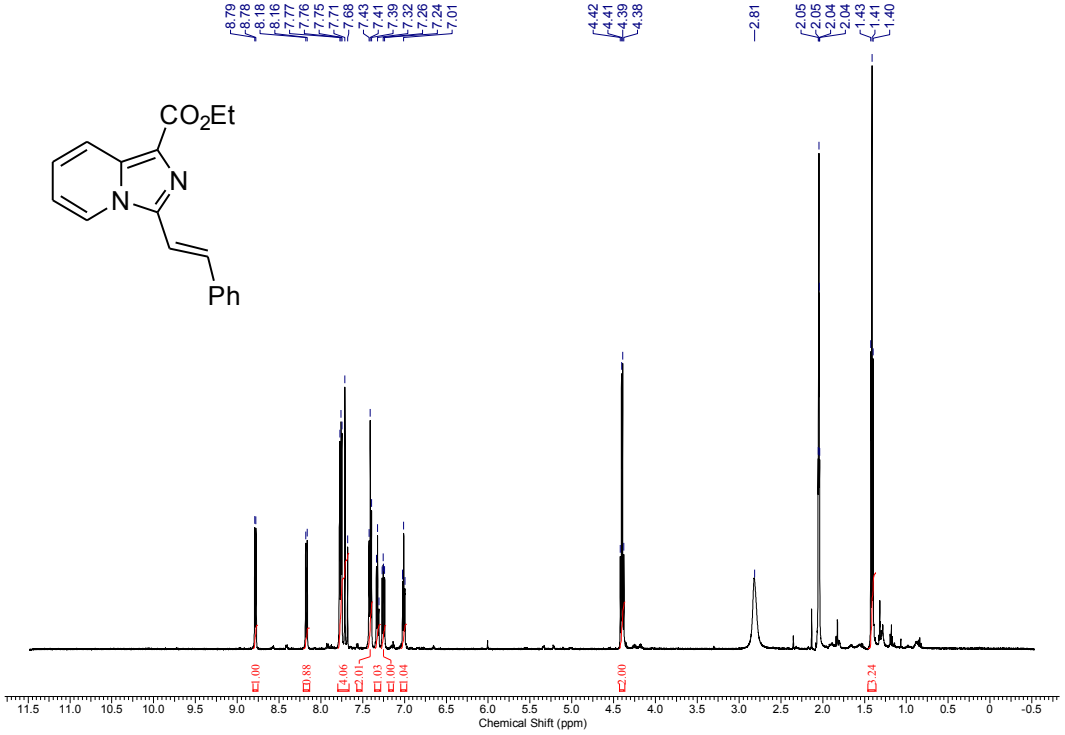
^{1}H NMR Spectrum of **7-7-e**:



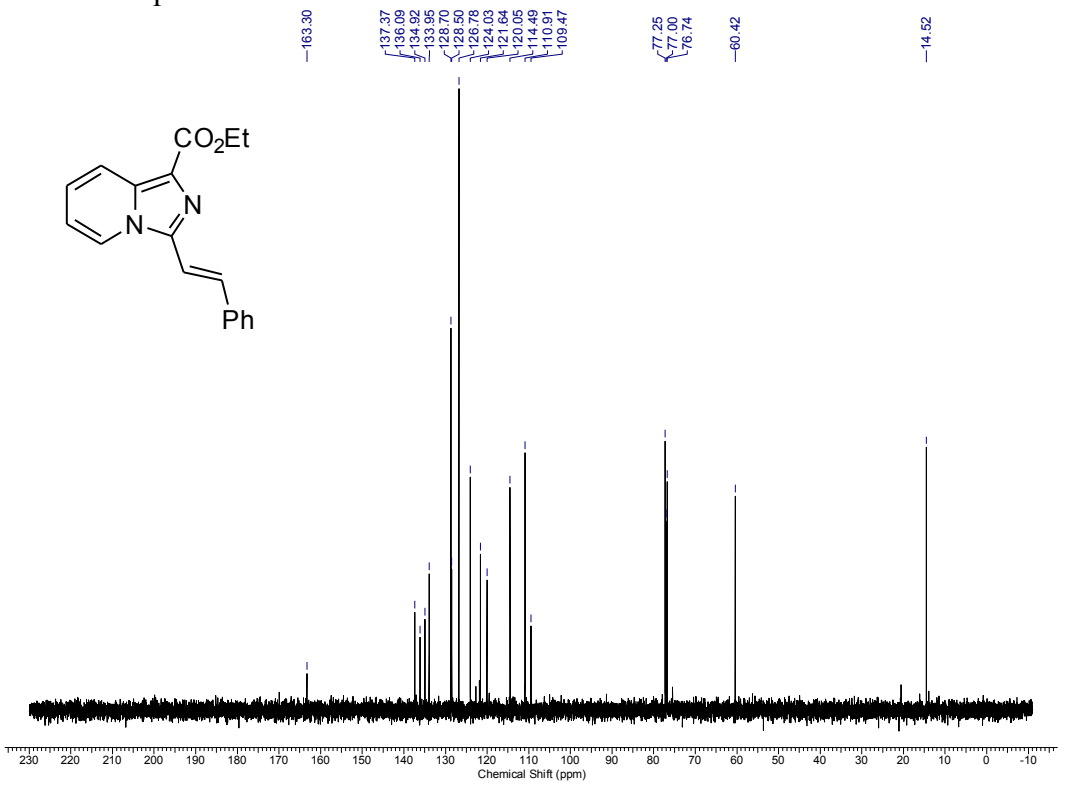
^{13}C NMR Spectrum of **7-7-e**:



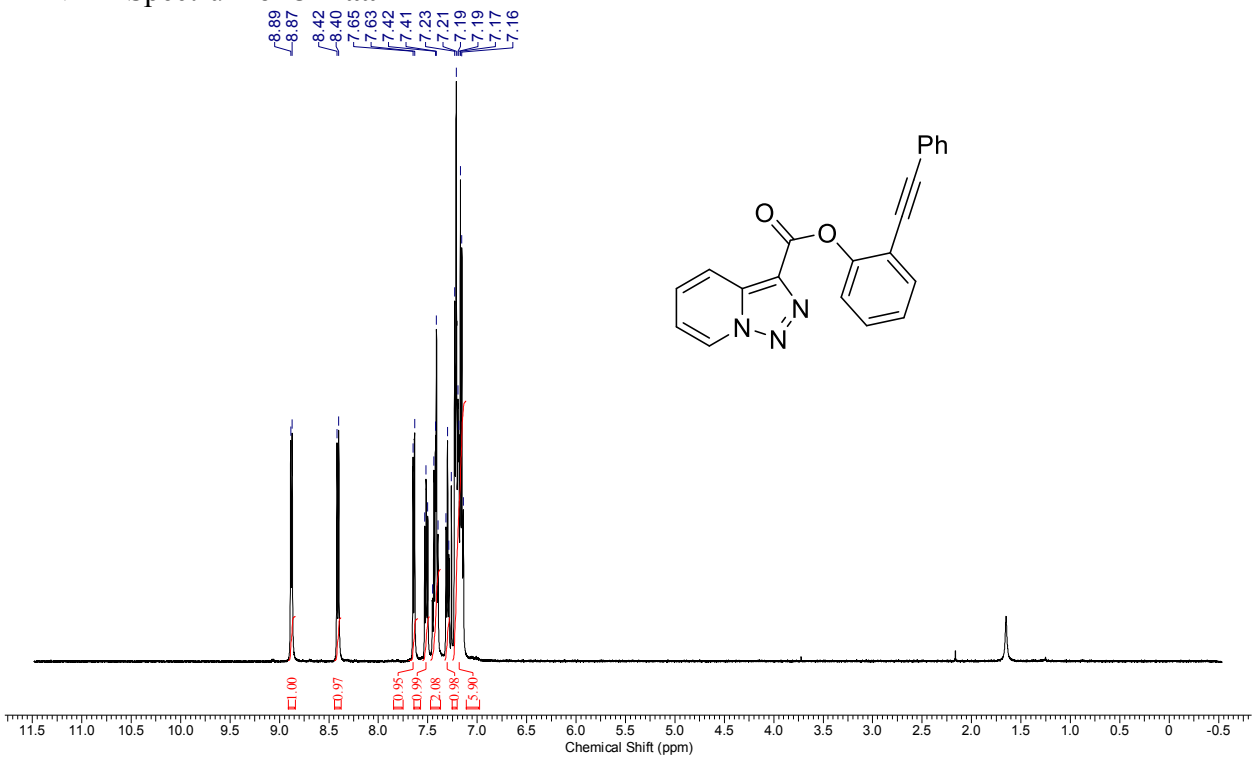
^{1}H NMR Spectrum of **7-7-f:**



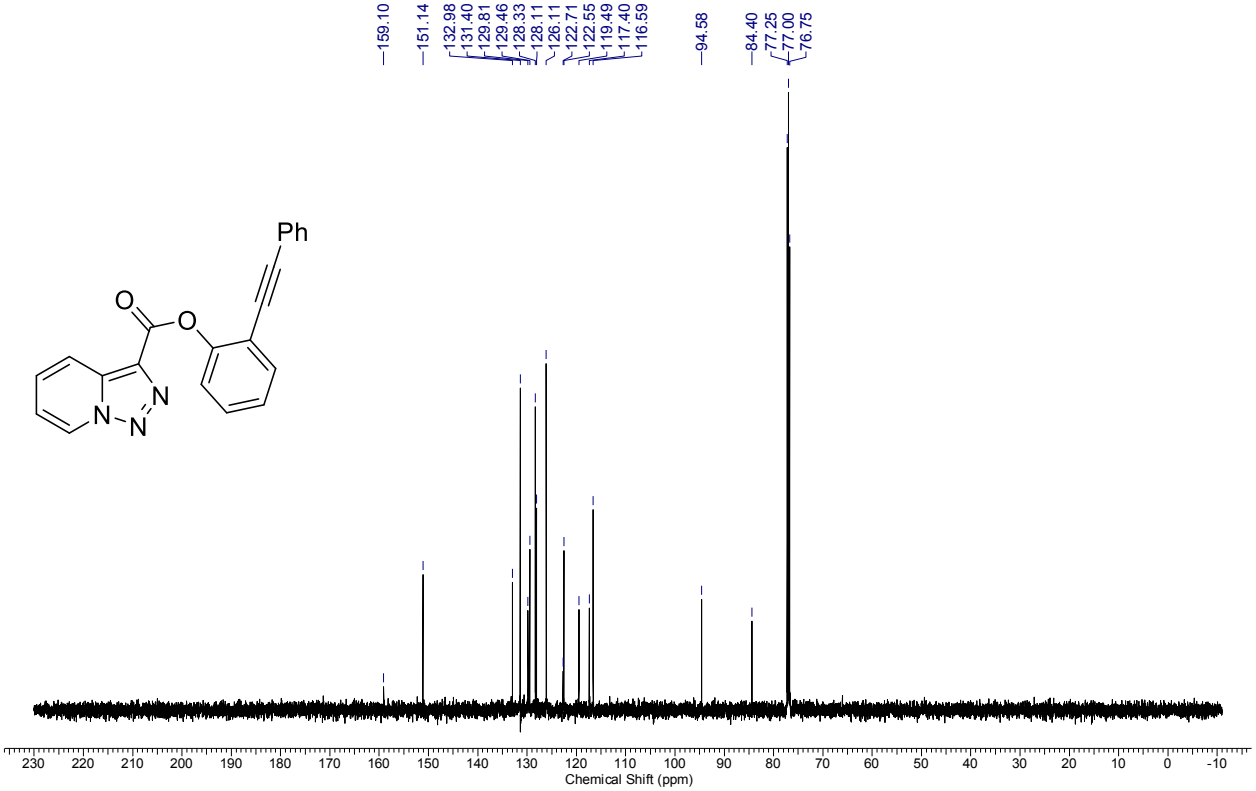
^{13}C NMR Spectrum of **7-7-f**:



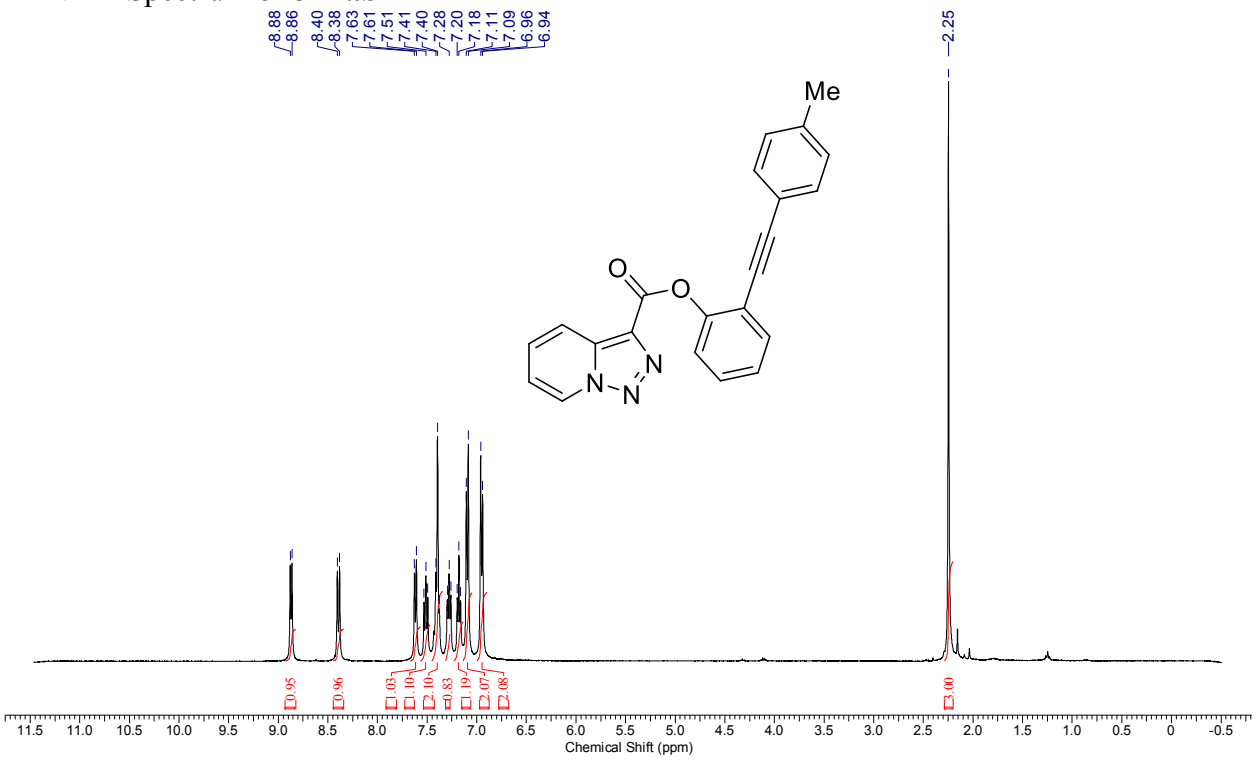
^{1}H NMR Spectrum of **8-4-aa**



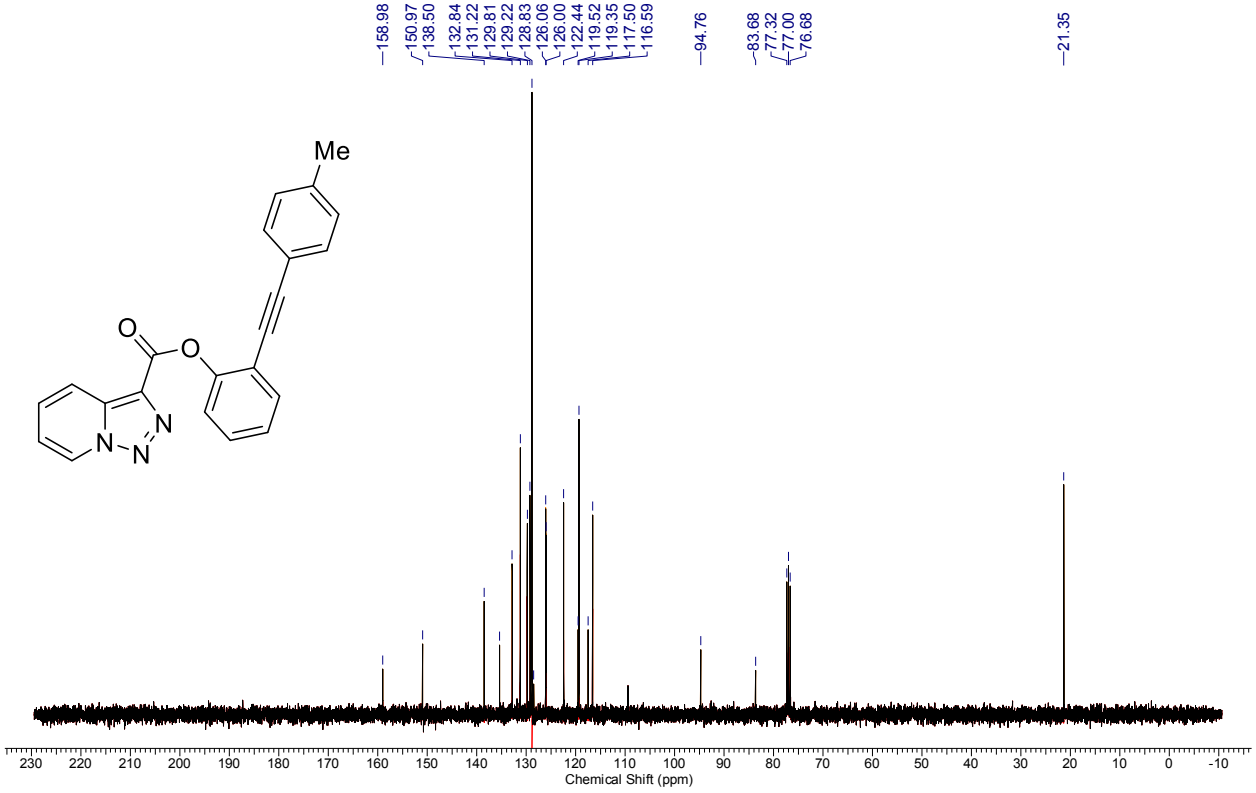
^{13} NMR Spectrum of **8-4-aa**



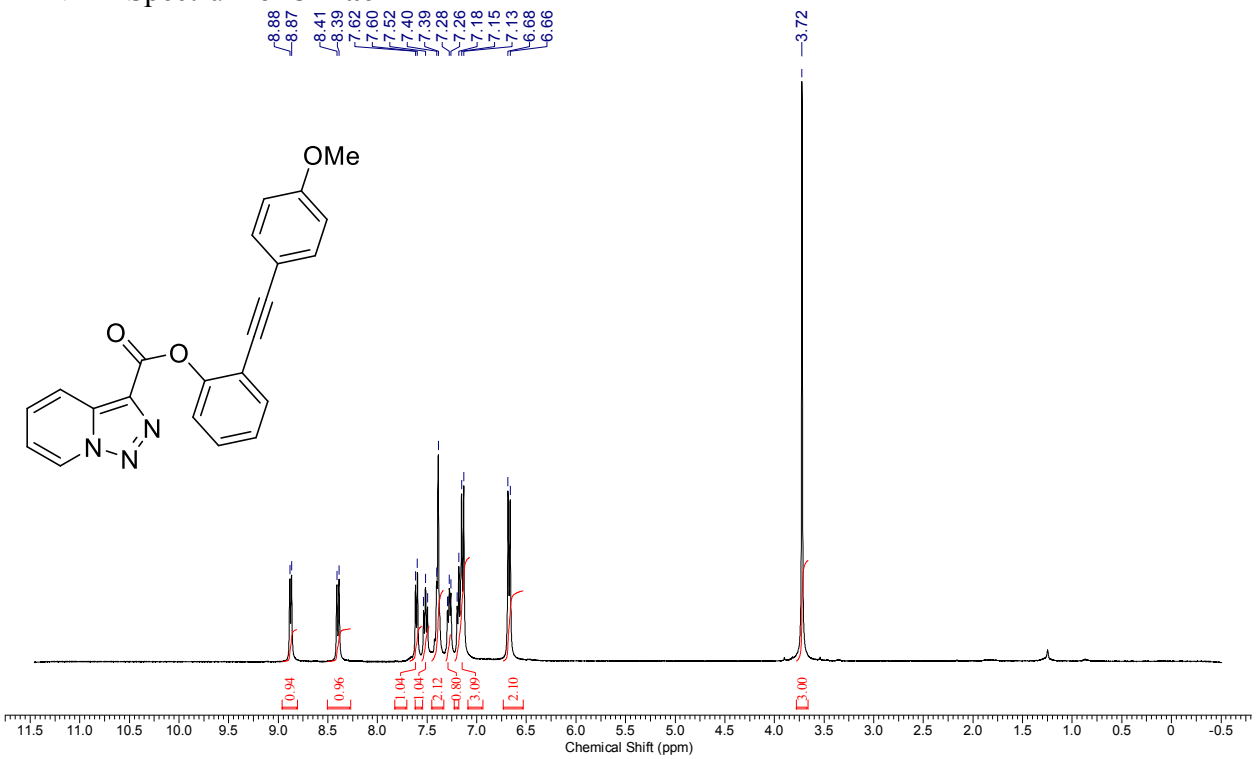
^{1}H NMR Spectrum of **8-4-ab**



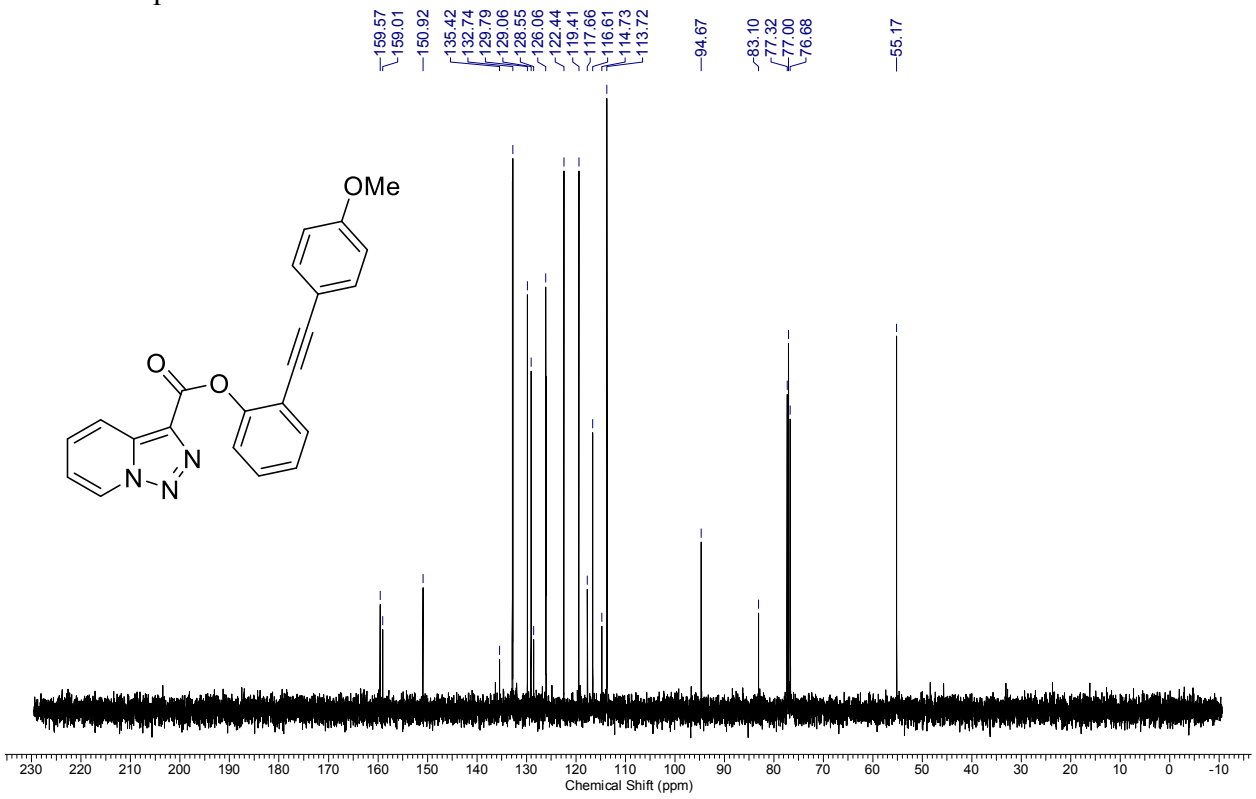
^{13}C NMR Spectrum of **8-4-ab**



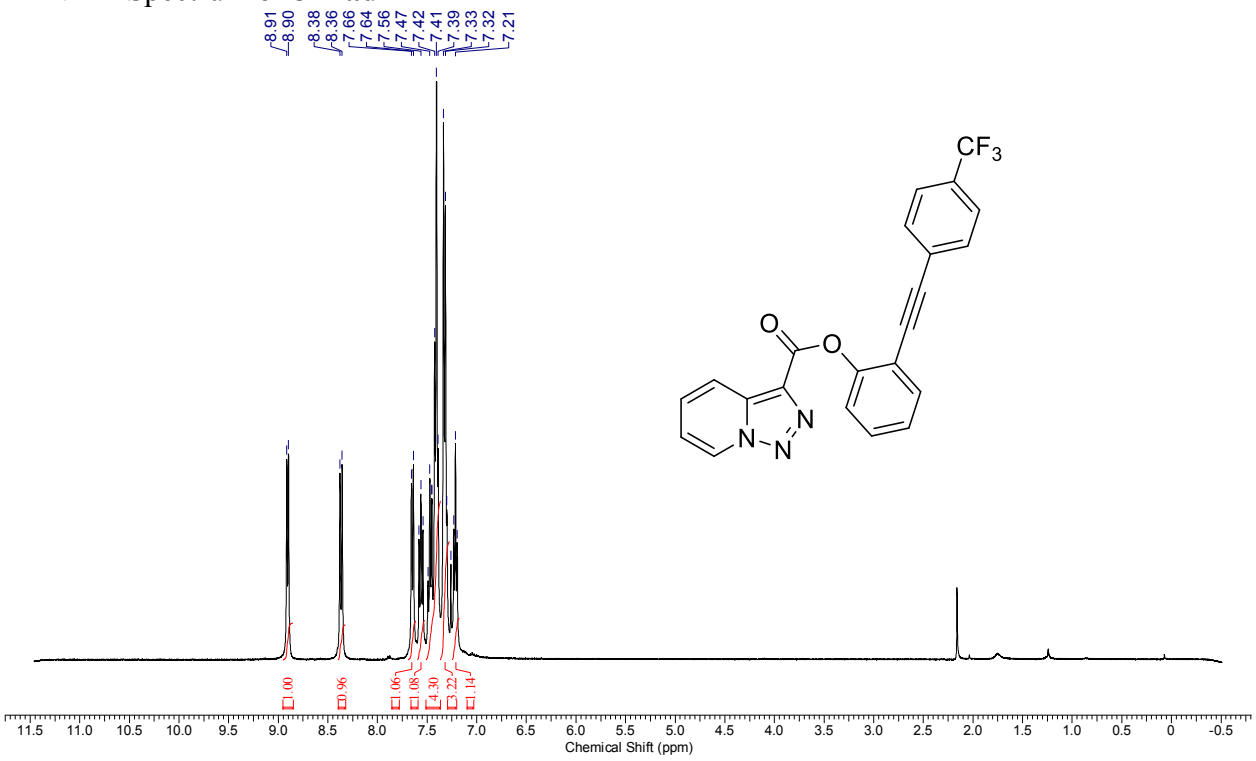
^{1}H NMR Spectrum of **8-4-ac**



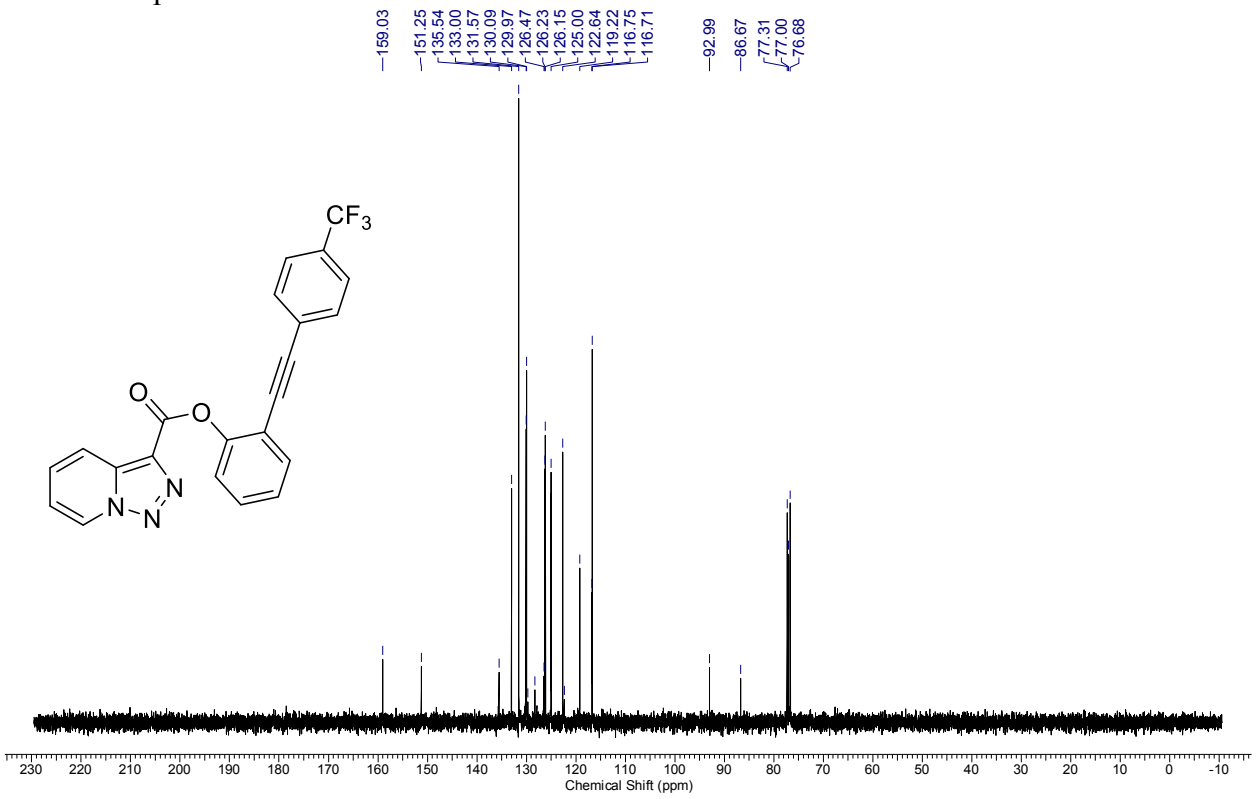
^{13}C NMR Spectrum of **8-4-ac**



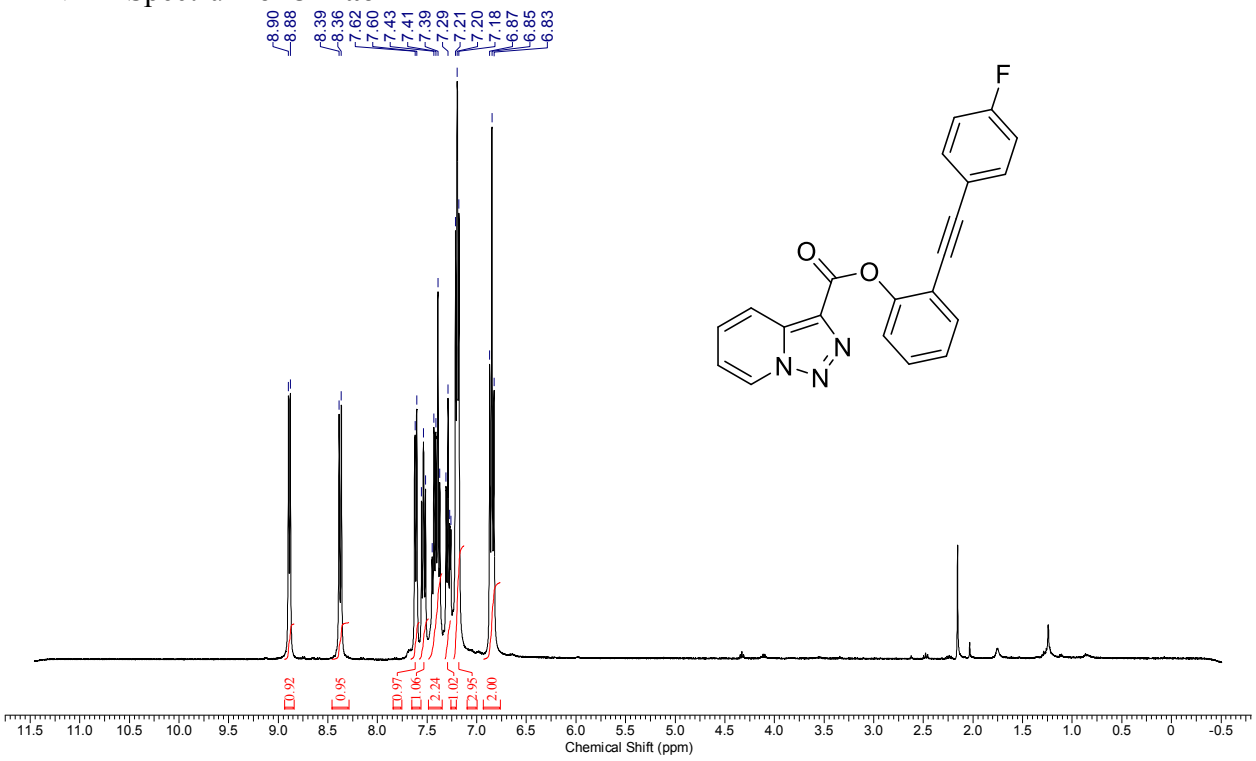
^{1}H NMR Spectrum of **8-4-ad**



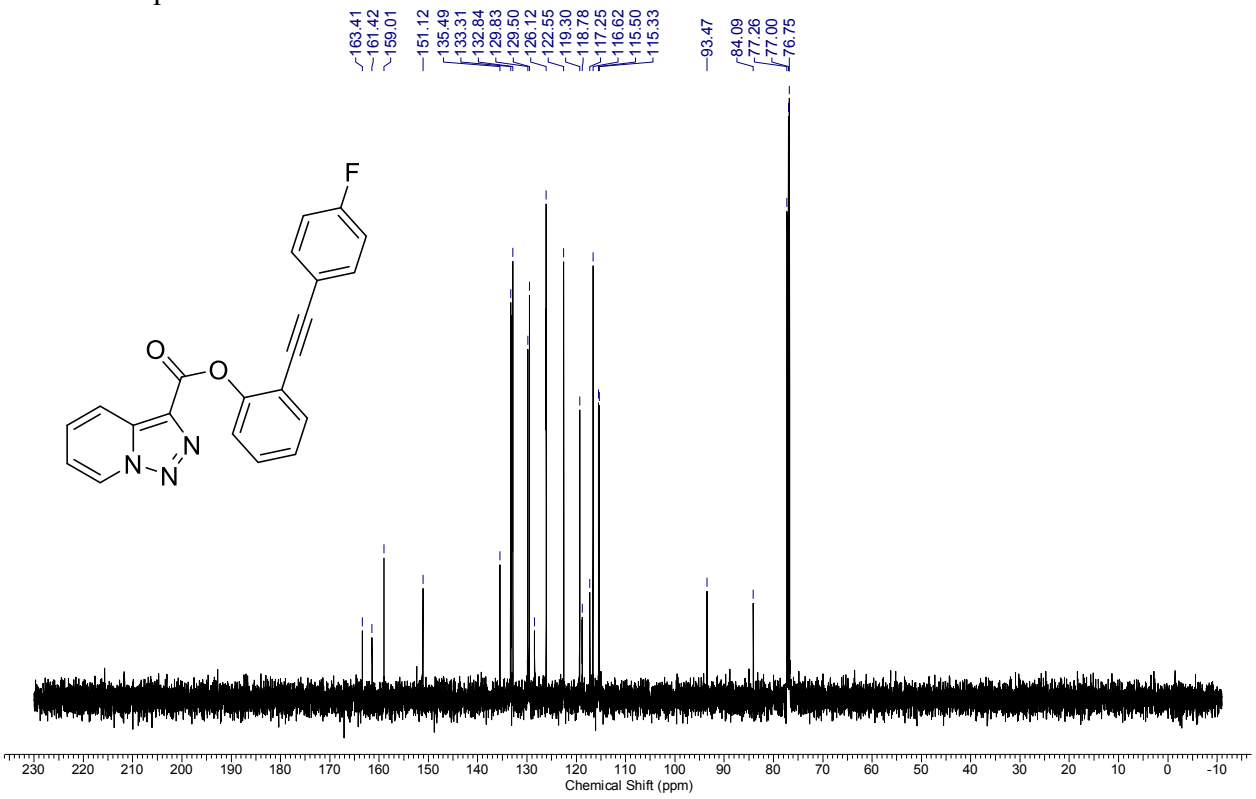
^{13}C NMR Spectrum of **8-4-ad**



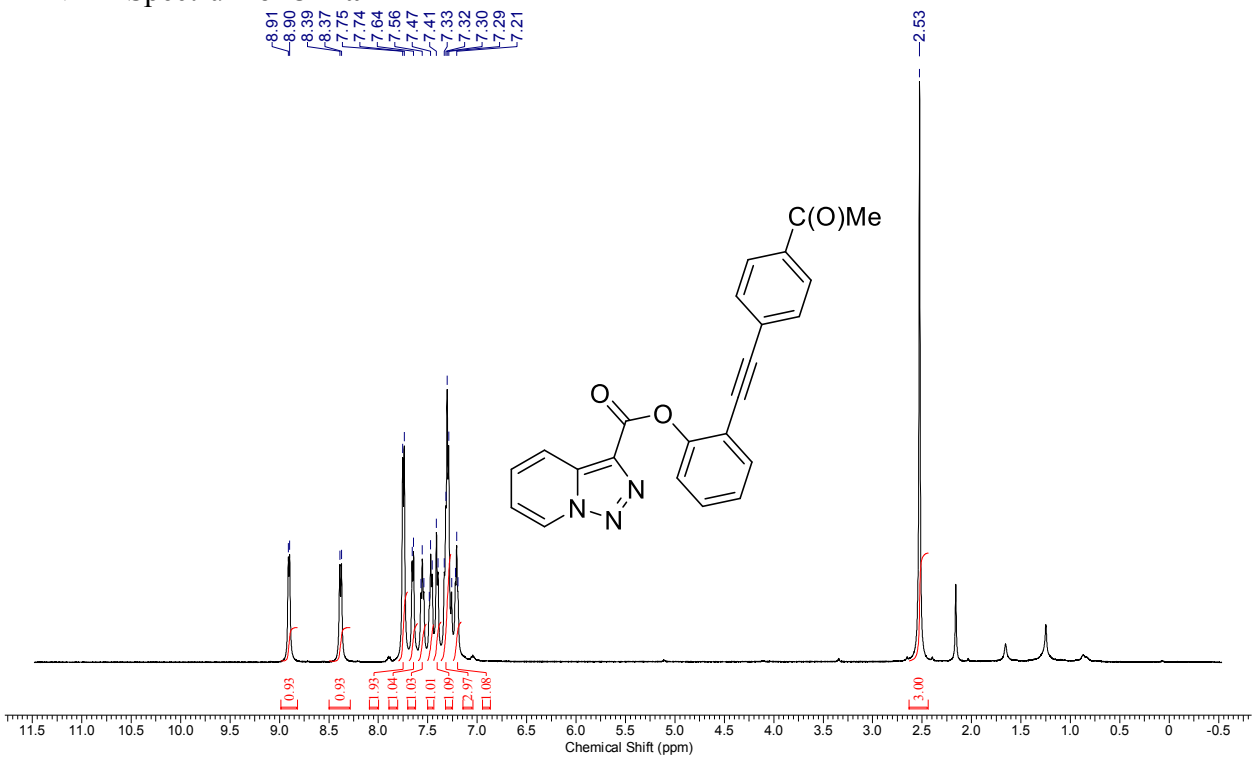
^{1}H NMR Spectrum of **8-4-ae**



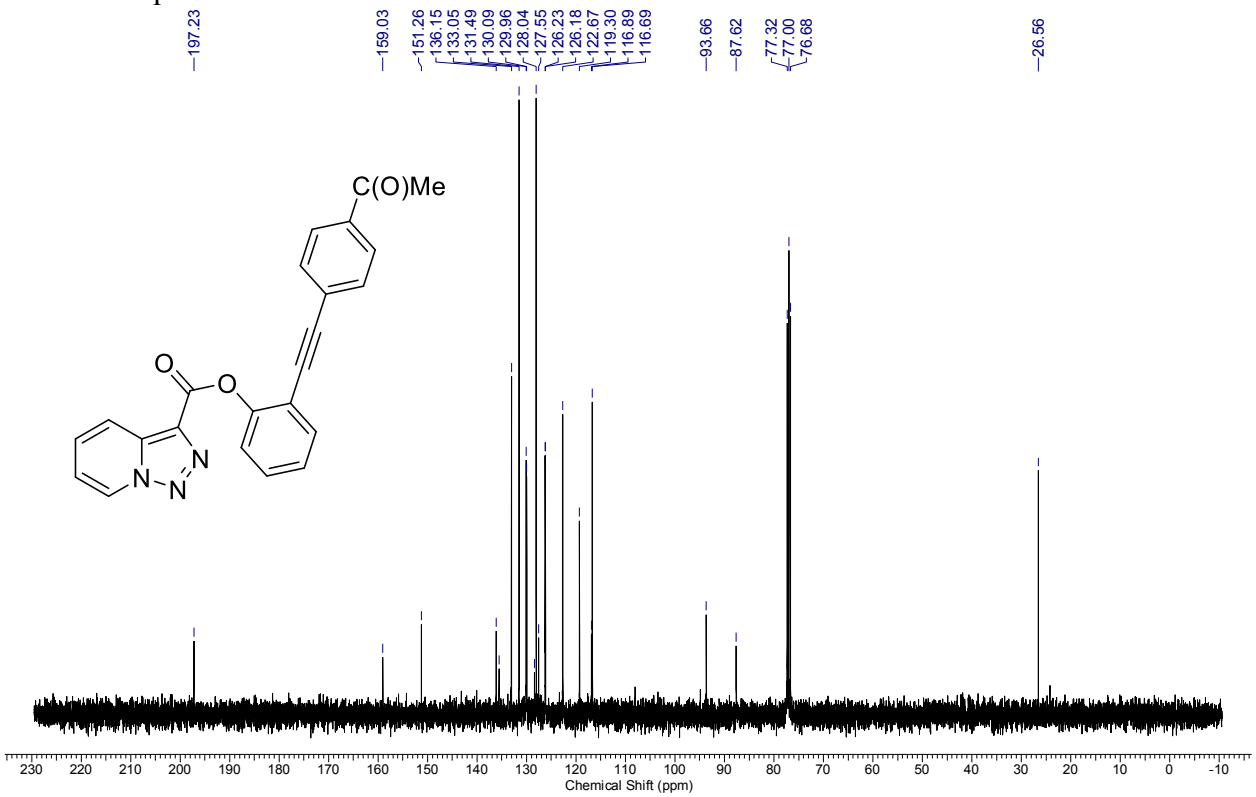
^{13}C NMR Spectrum of **8-4-ae**



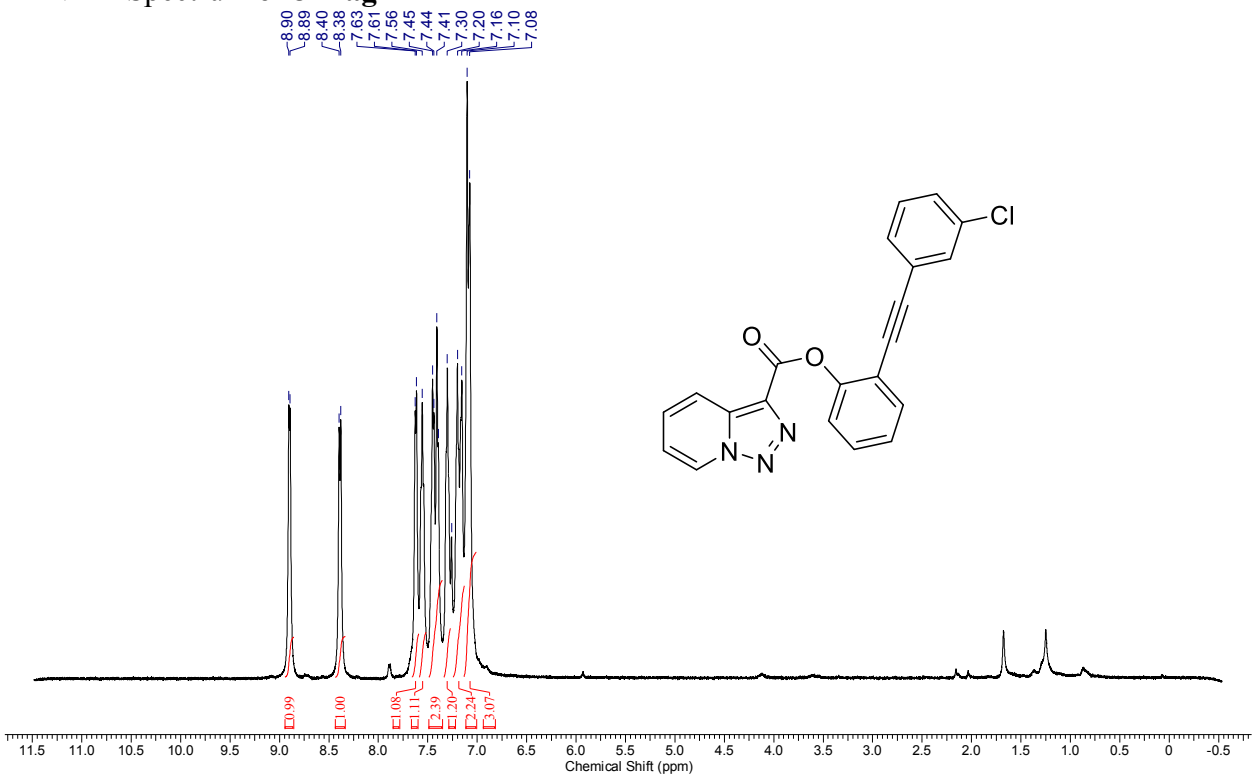
^{1}H NMR Spectrum of **8-4-af**



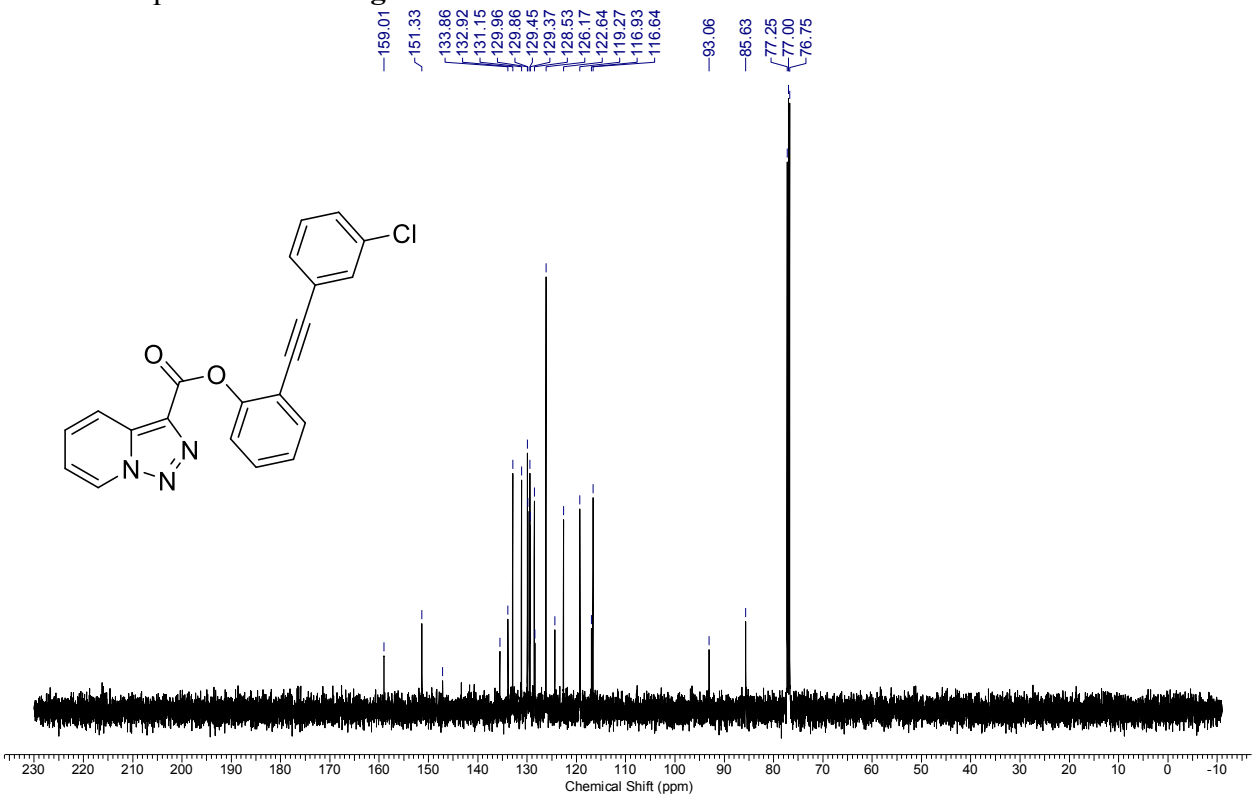
^{13}C NMR Spectrum of **8-4-af**



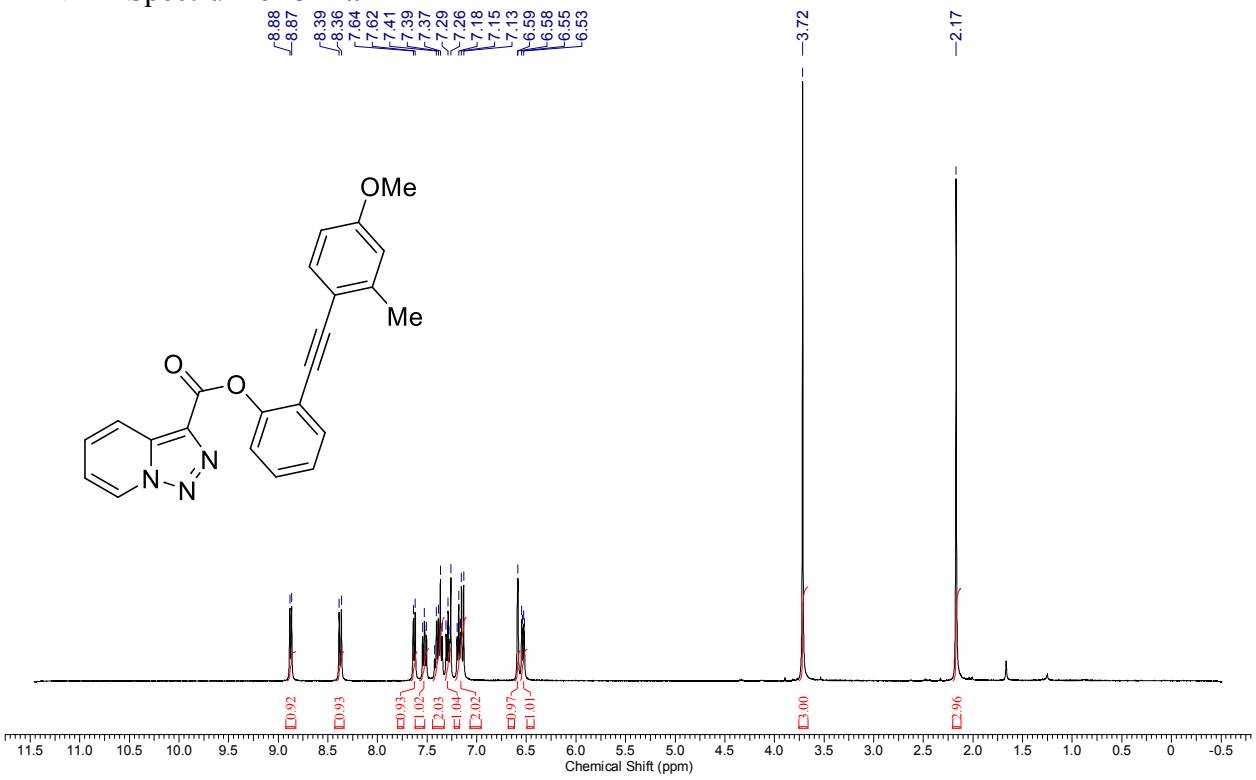
^{1}H NMR Spectrum of **8-4-ag**



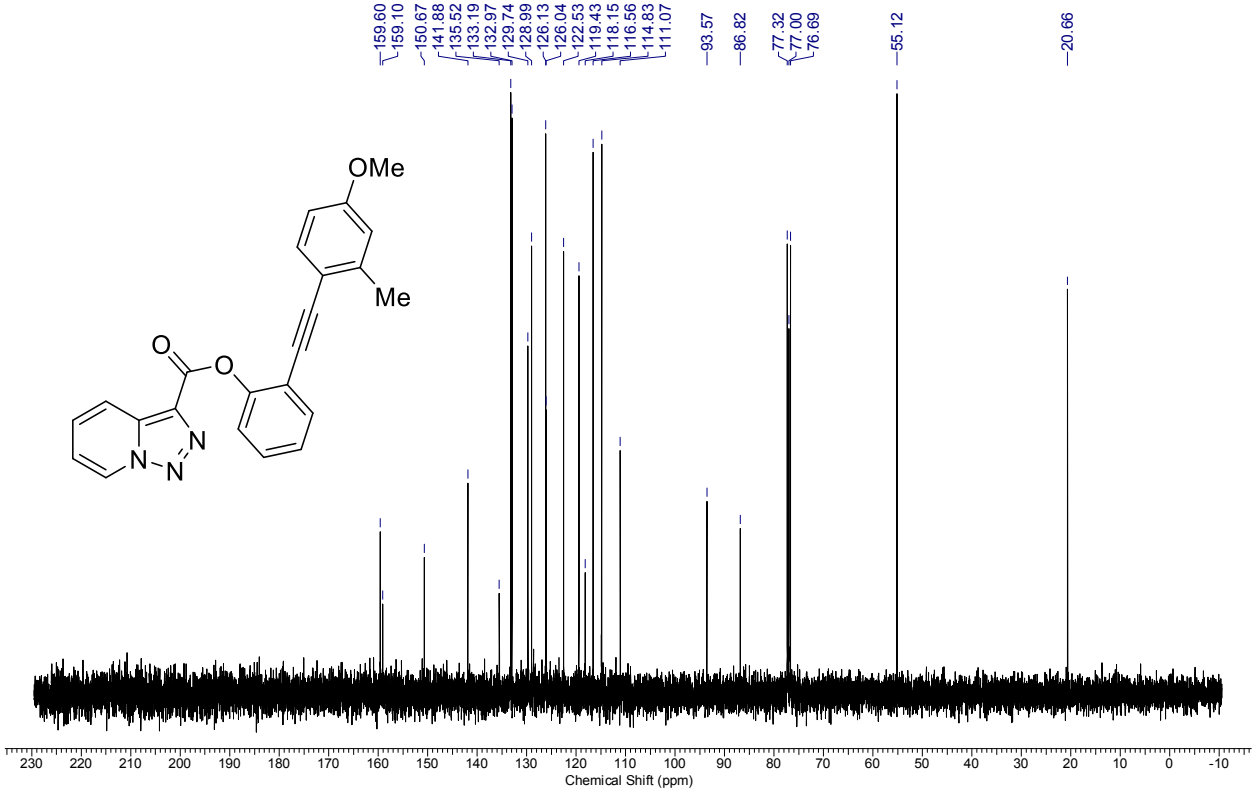
^{13}C NMR Spectrum of **8-4-ag**



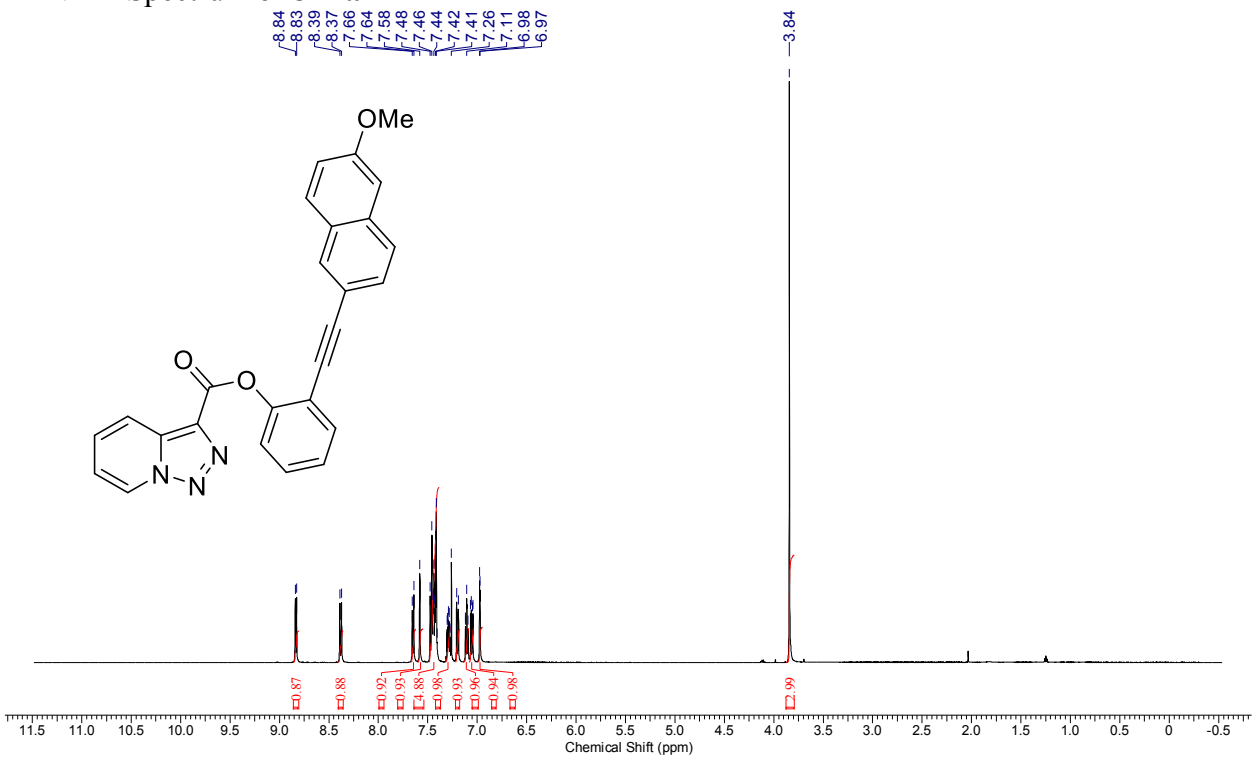
^{1}H NMR Spectrum of **8-4-ah**



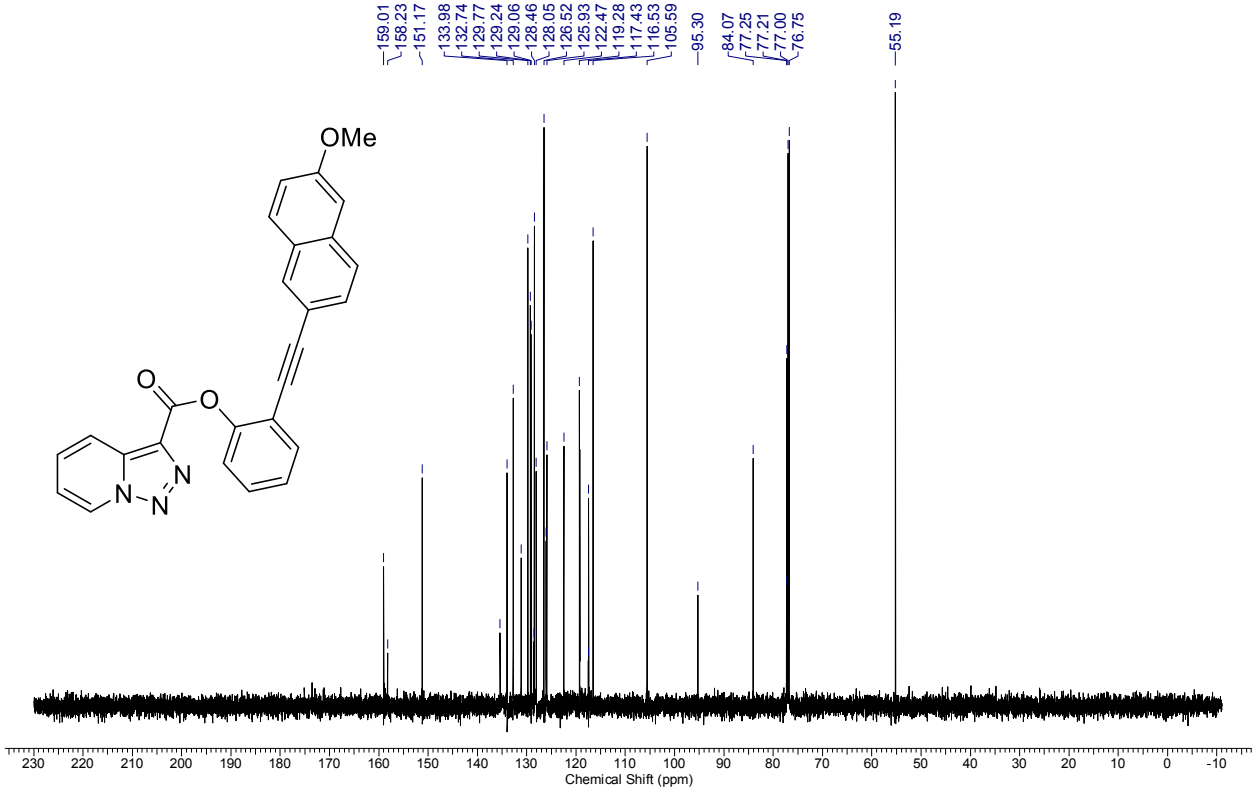
^{13}C NMR Spectrum of **8-4-ah**



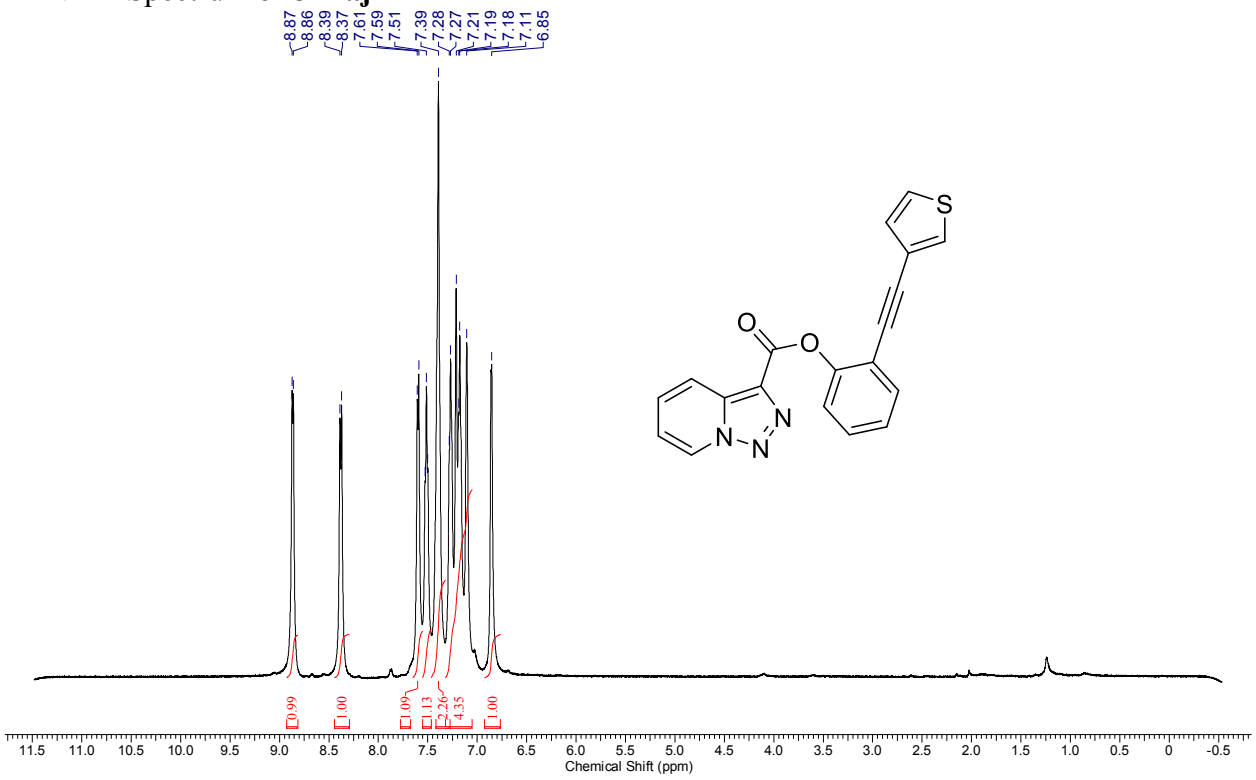
^{1}H NMR Spectrum of **8-4-ai**



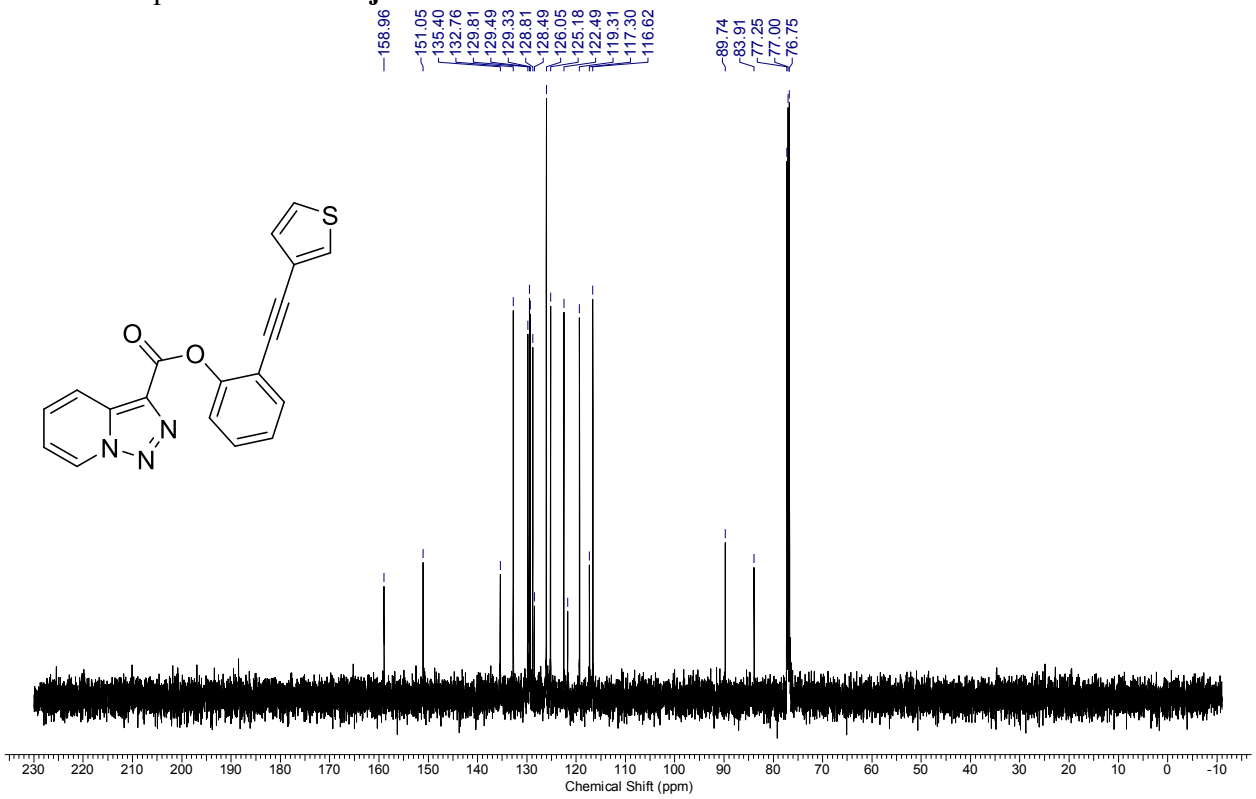
^{13}C NMR Spectrum of **8-4-ai**



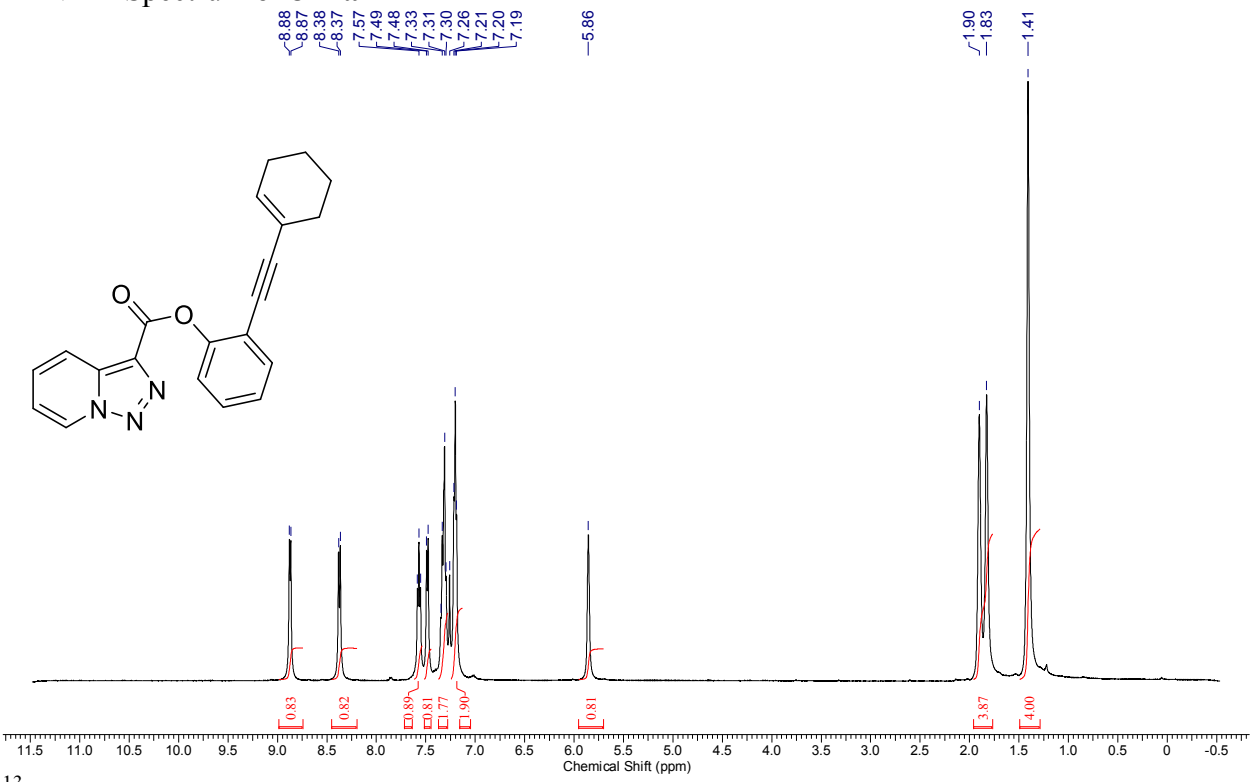
^{1}H NMR Spectrum of **8-4-aj**



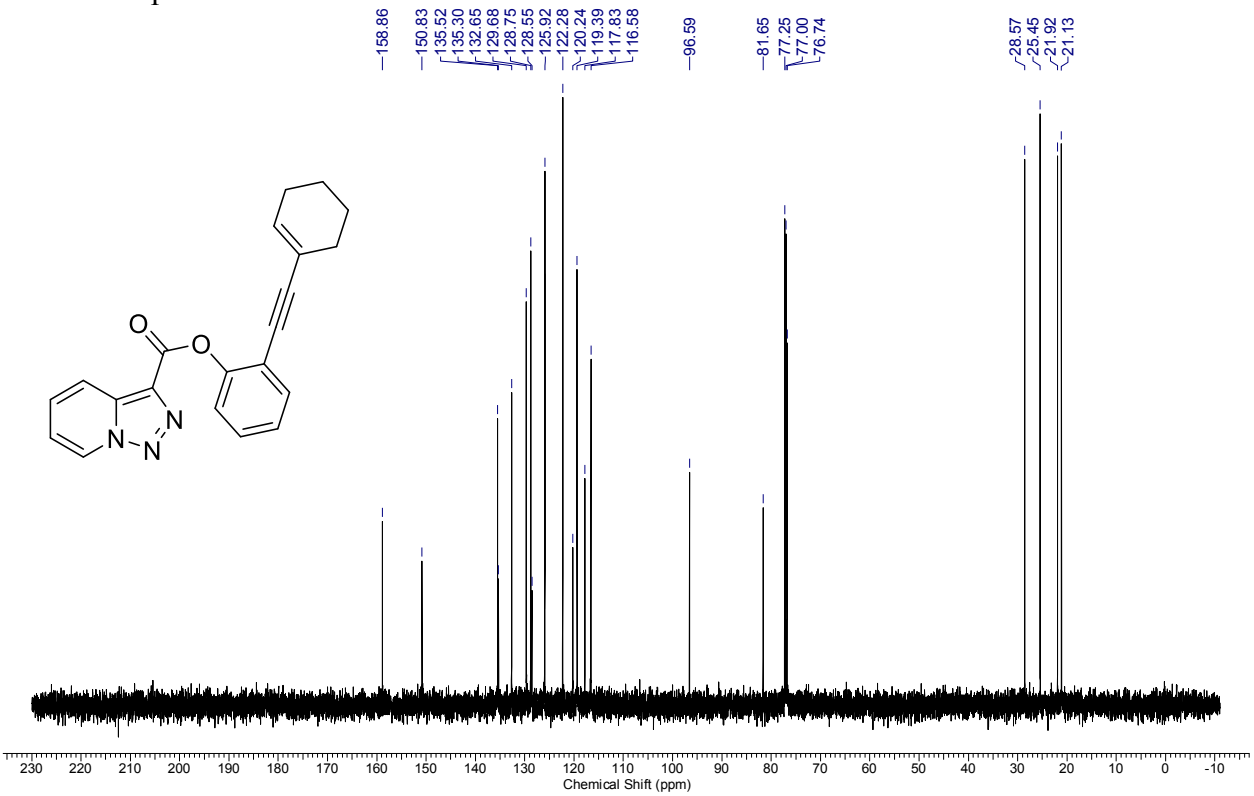
^{13}C NMR Spectrum of **8-4-aj**



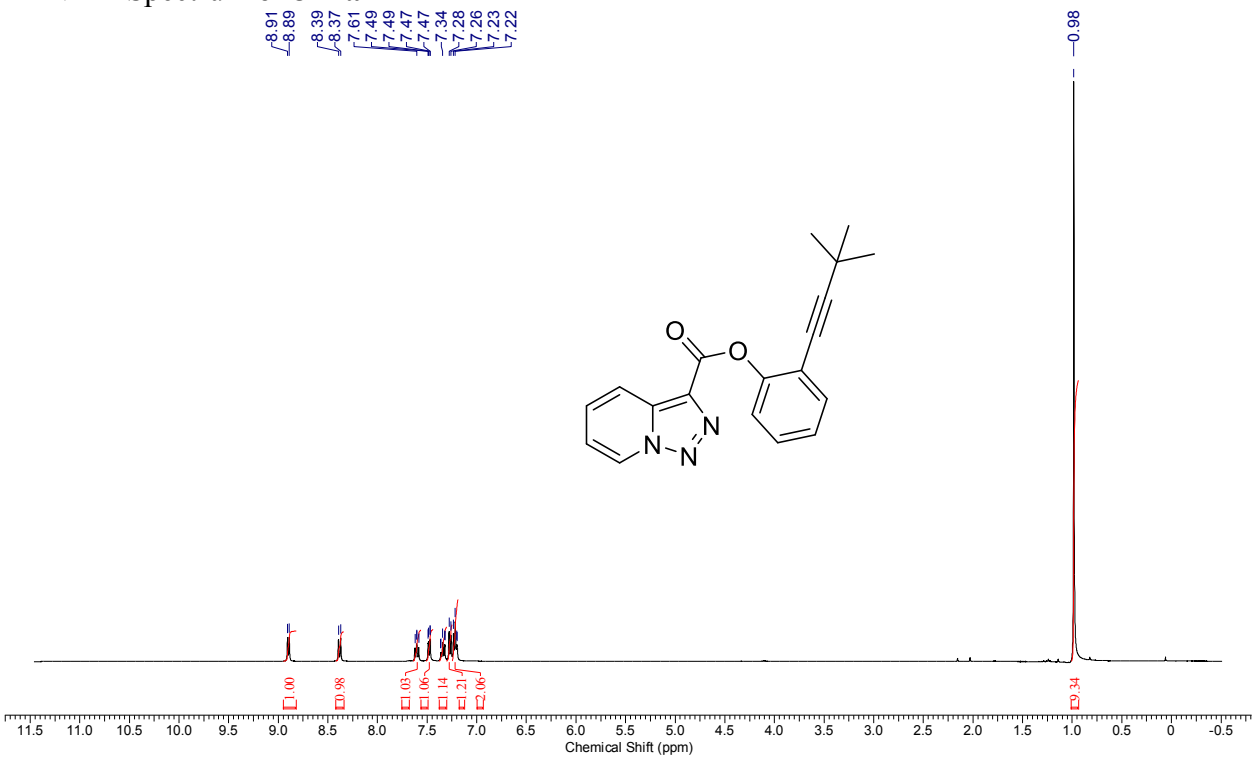
^{1}H NMR Spectrum of **8-4-ak**



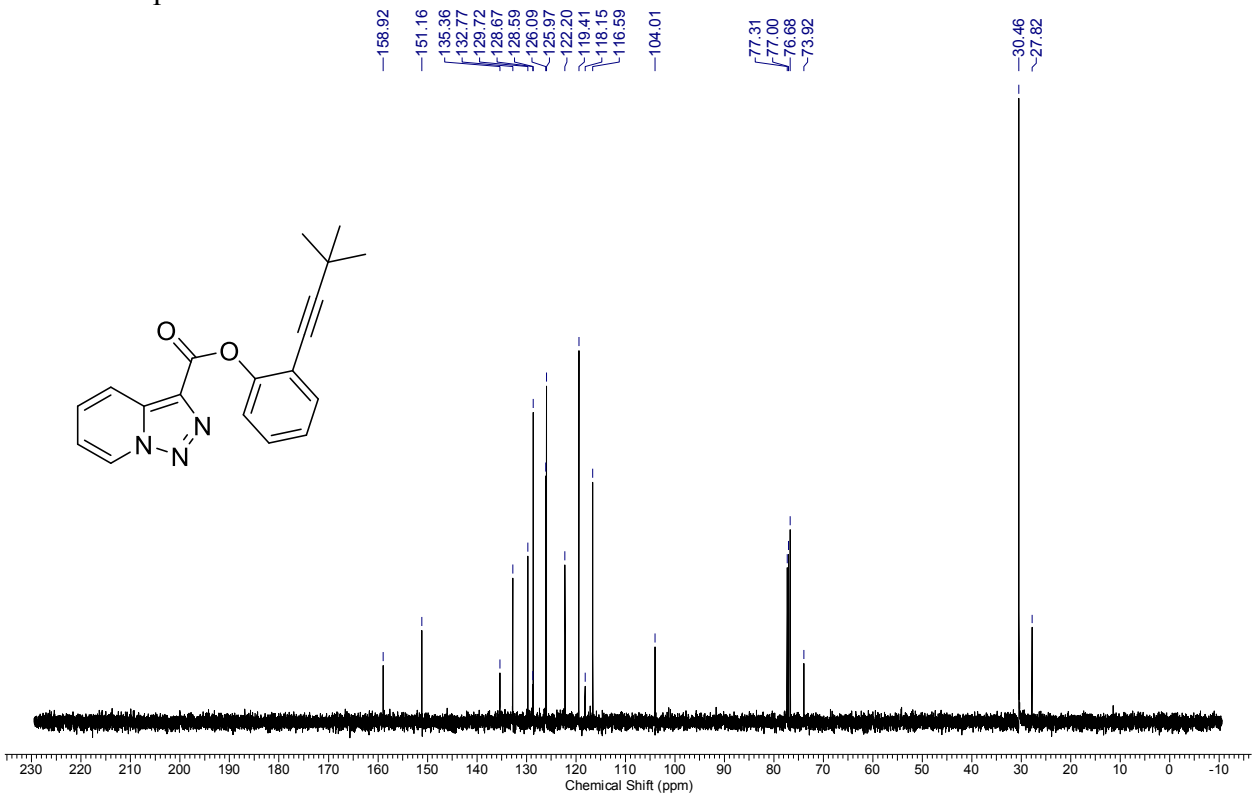
^{13}C NMR Spectrum of **8-4-ak**



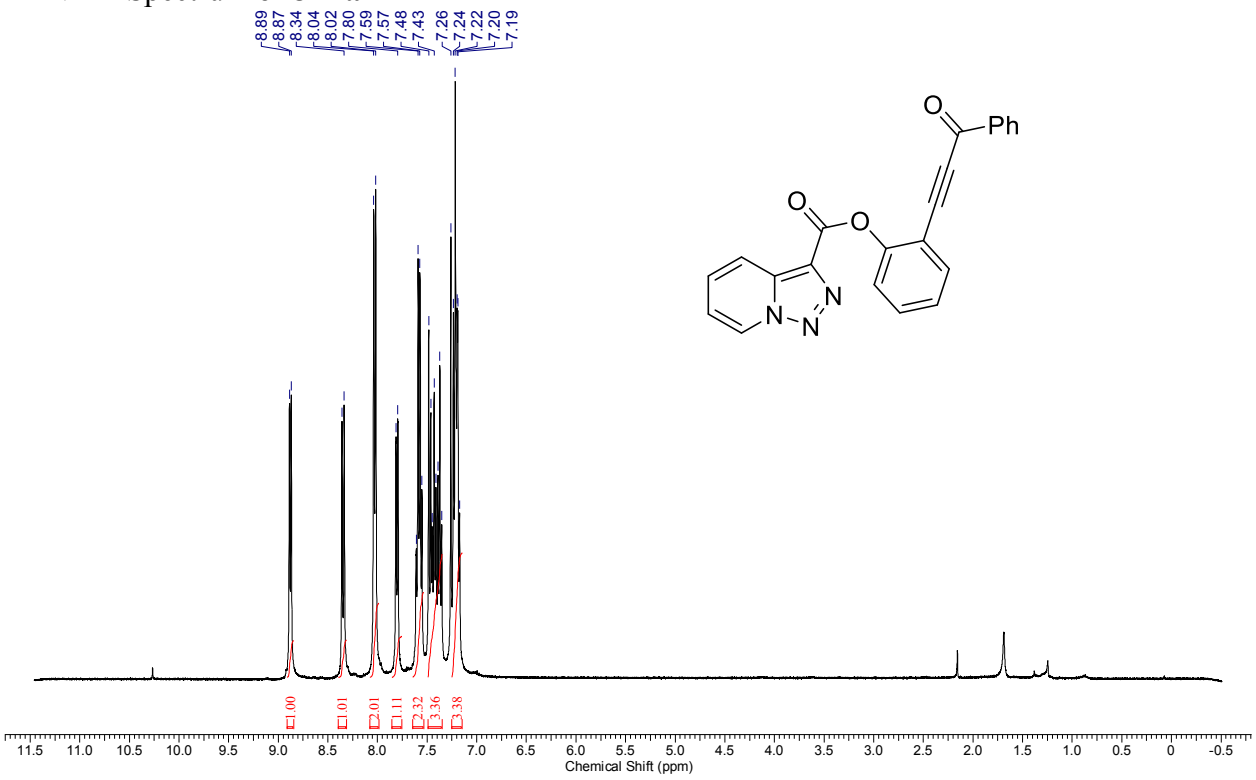
^{1}H NMR Spectrum of **8-4-al**



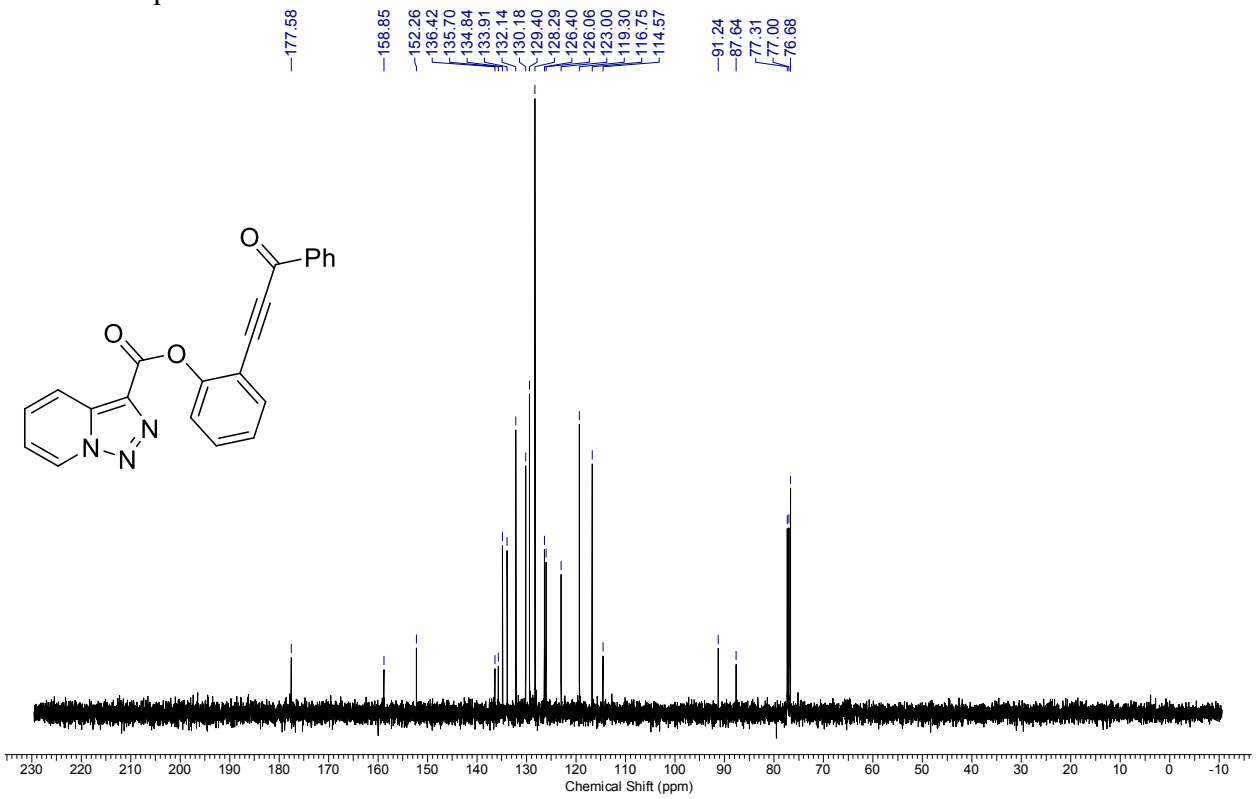
^{13}C NMR Spectrum of **8-4-al**



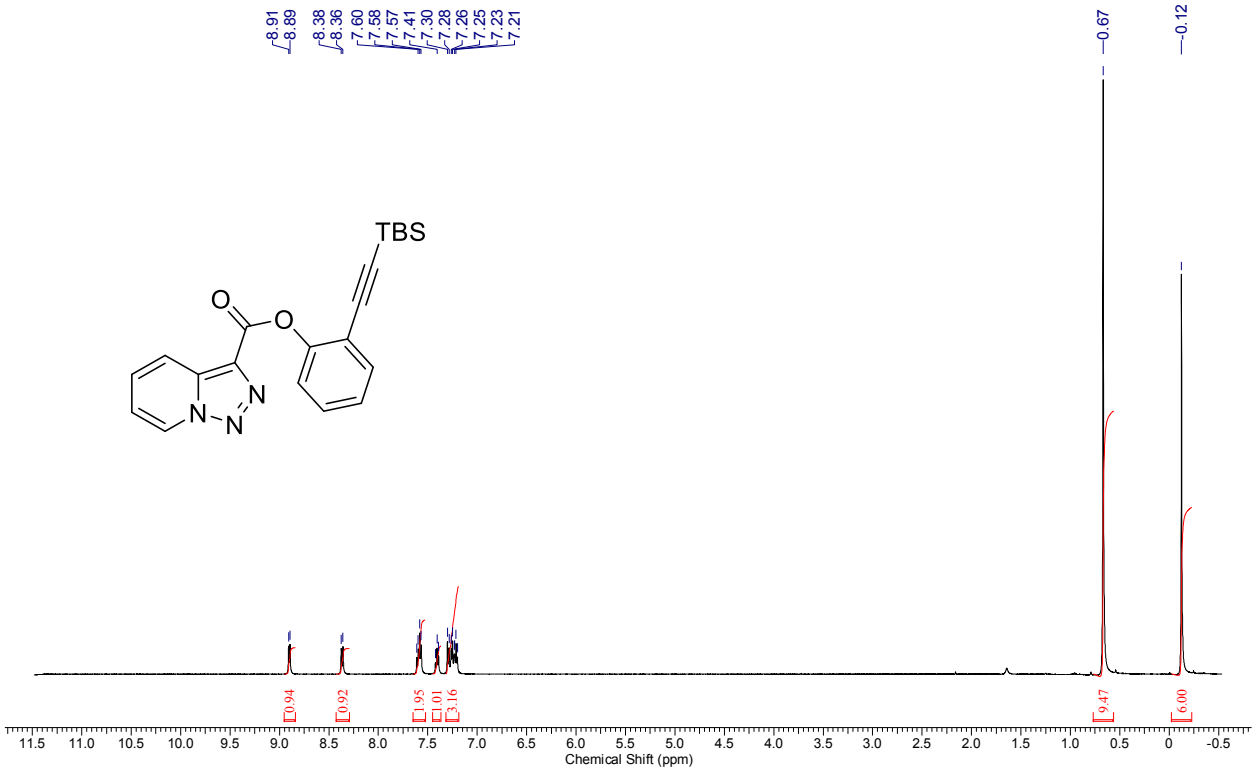
^{1}H NMR Spectrum of **8-4-am**



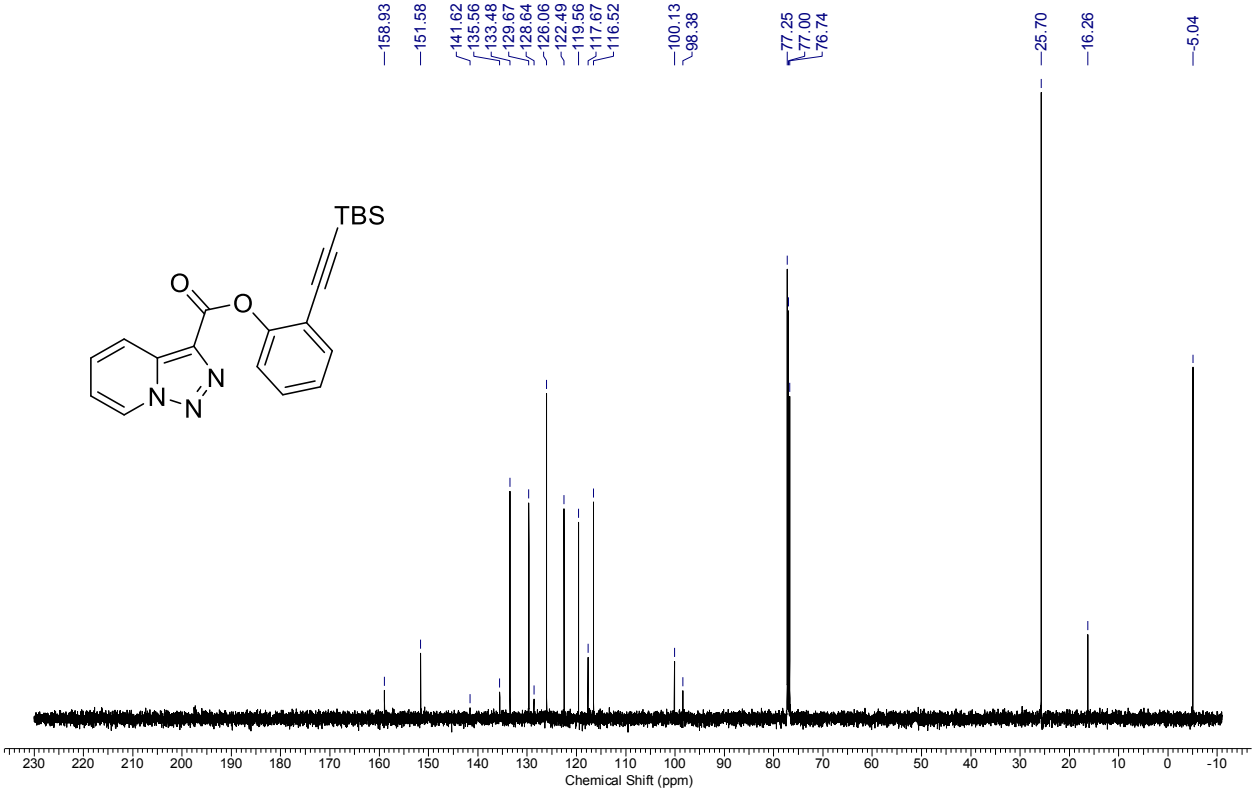
^{13}C NMR Spectrum of **8-4-am**



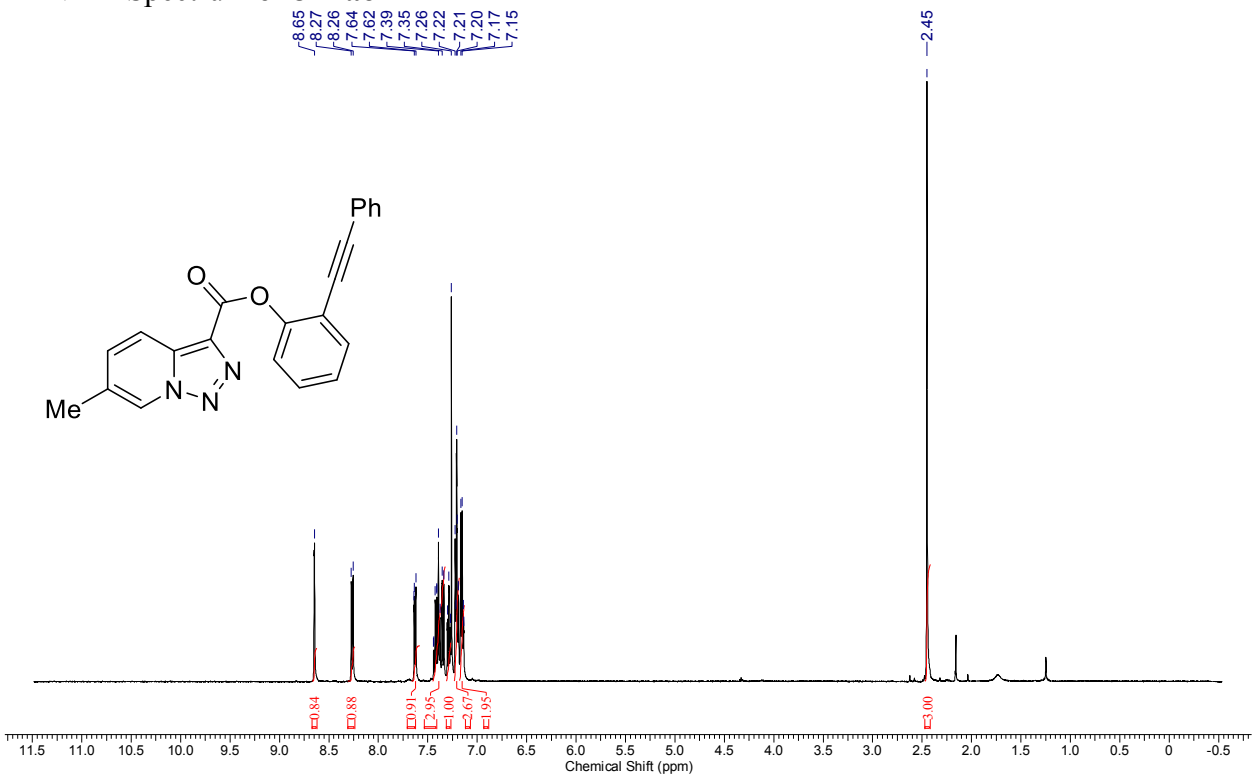
^{1}H NMR Spectrum of **8-4-an**



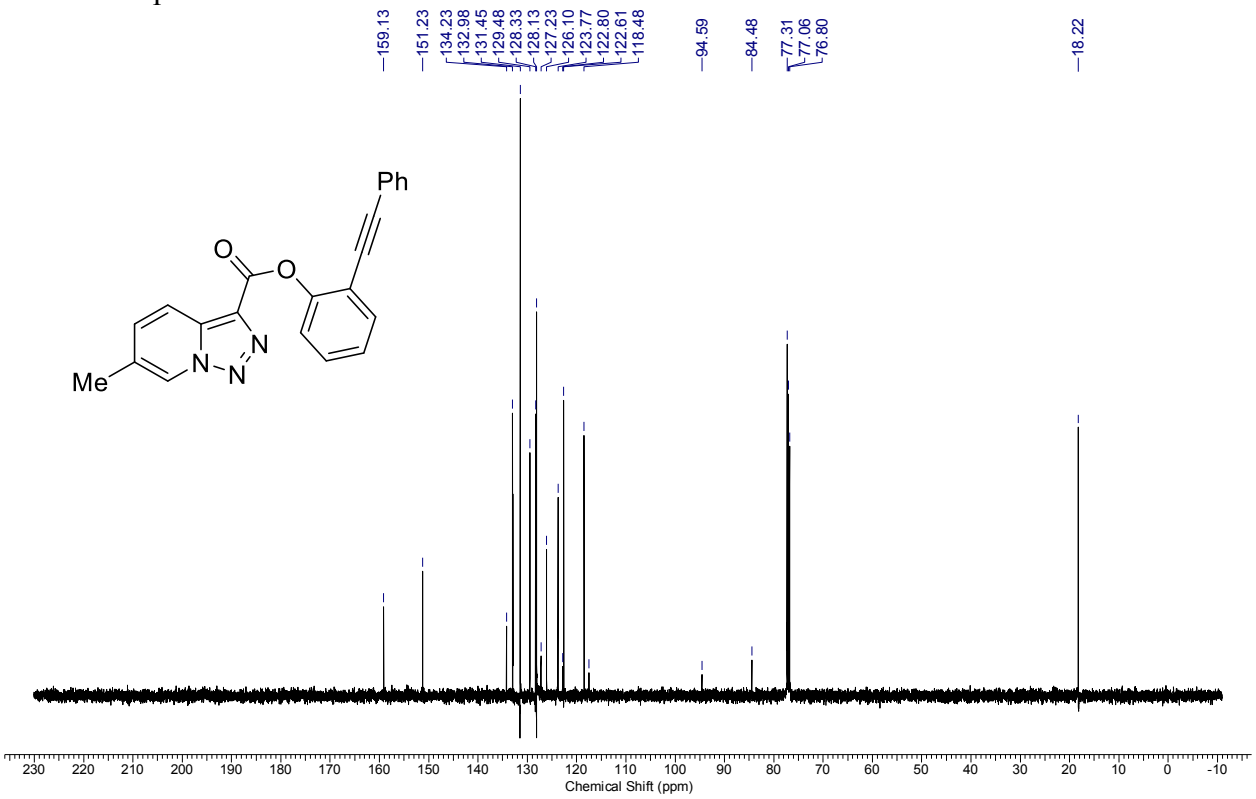
^{13}C NMR Spectrum of **8-4-an**



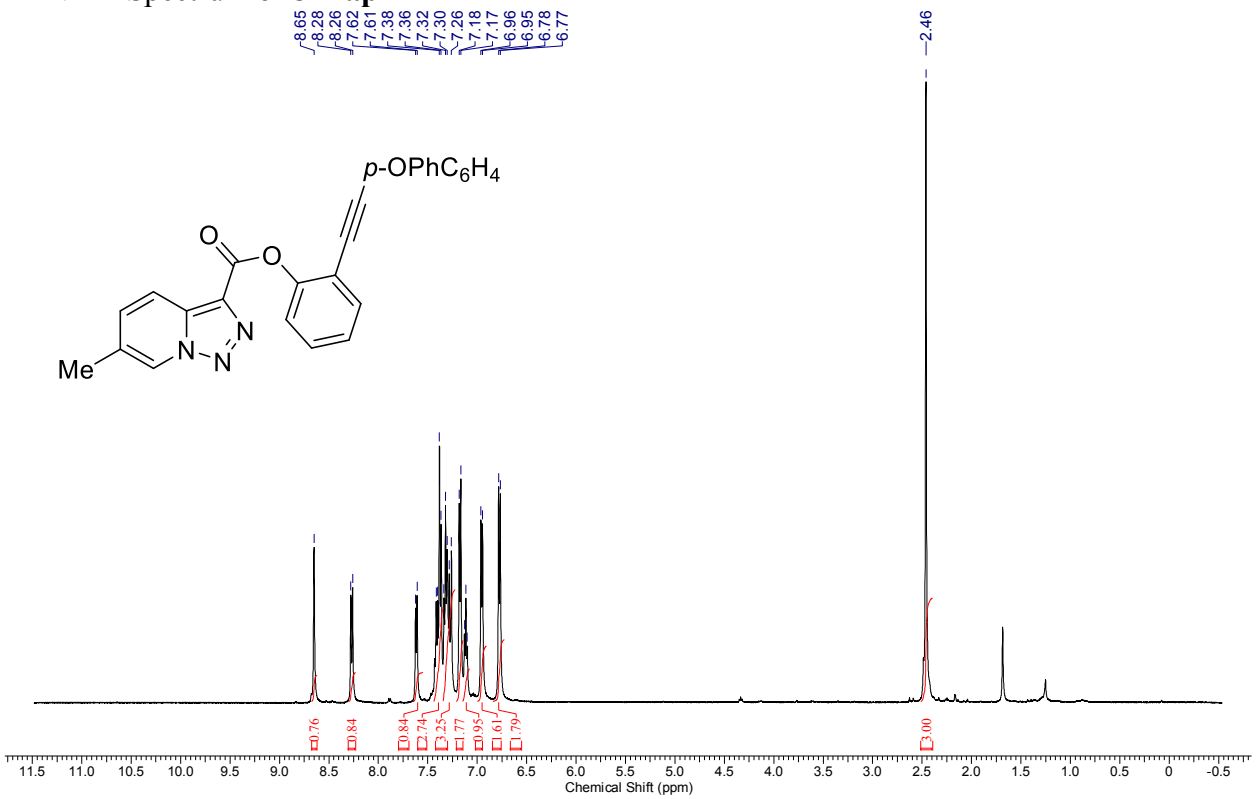
^{1}H NMR Spectrum of **8-4-ao**



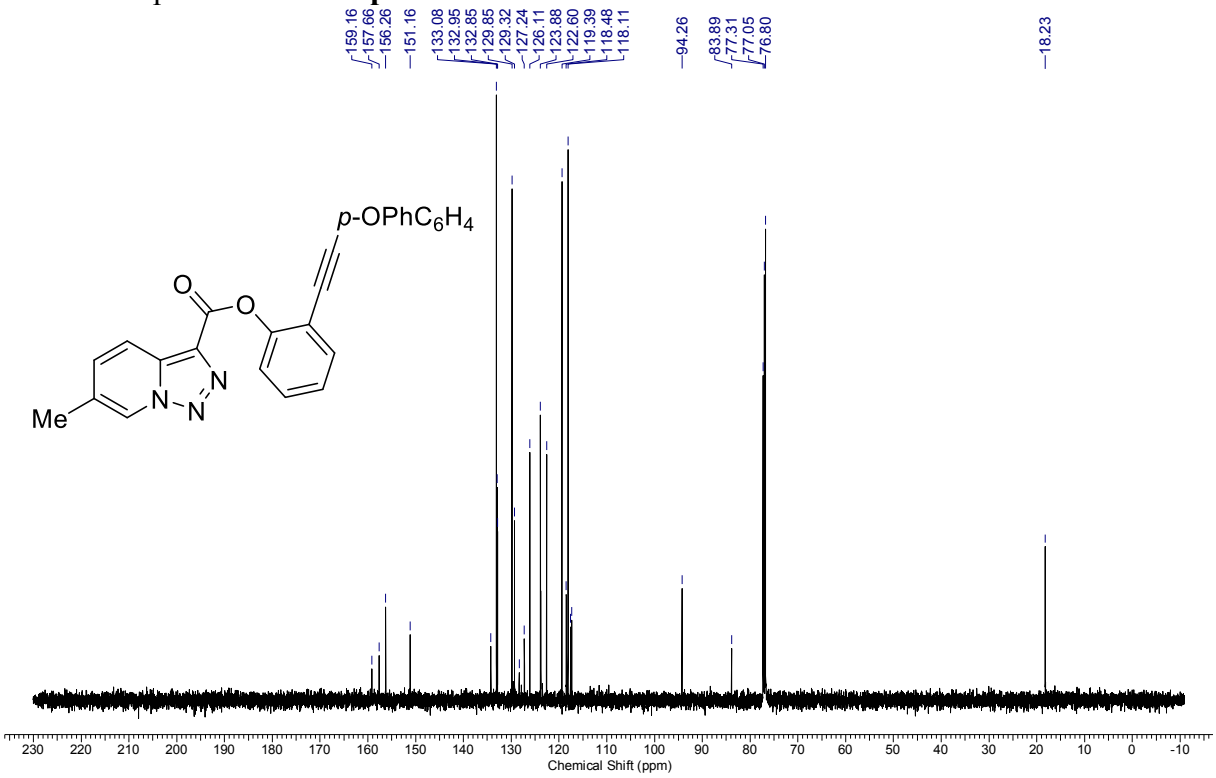
^{13}C NMR Spectrum of **8-4-ao**



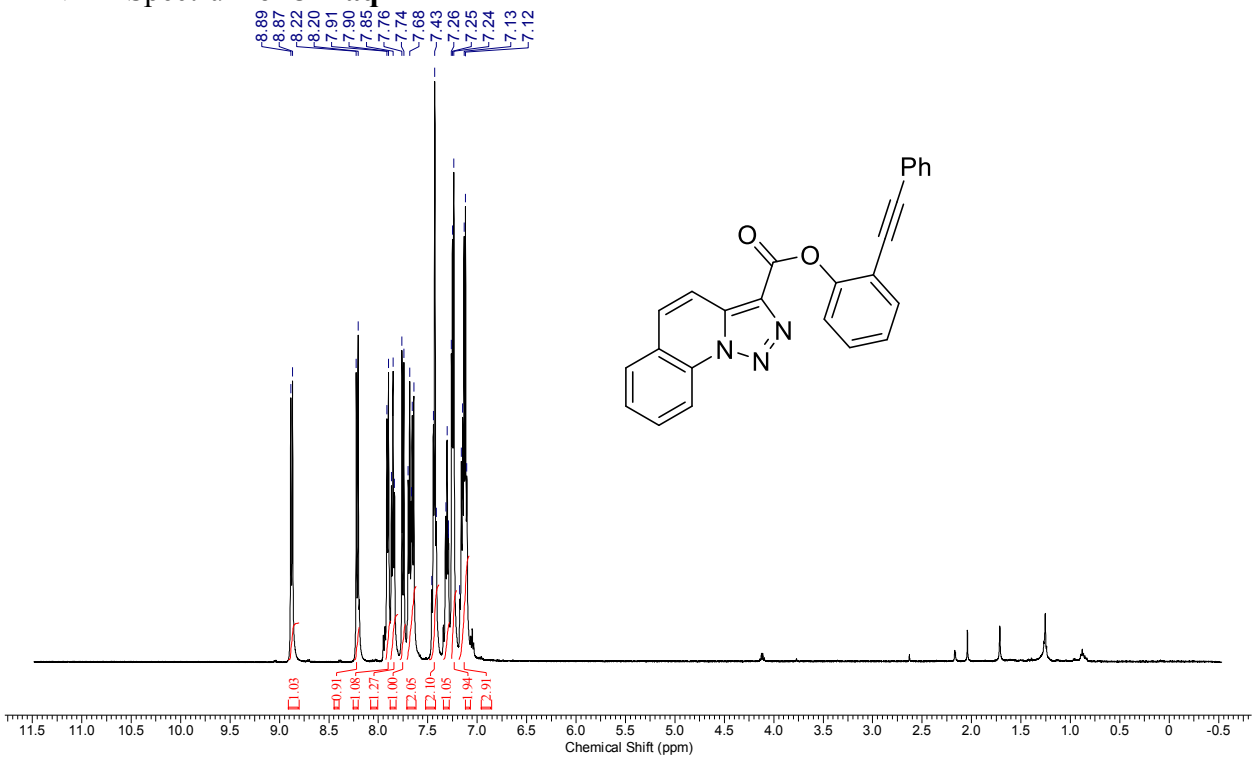
^{1}H NMR Spectrum of **8-4-ap**



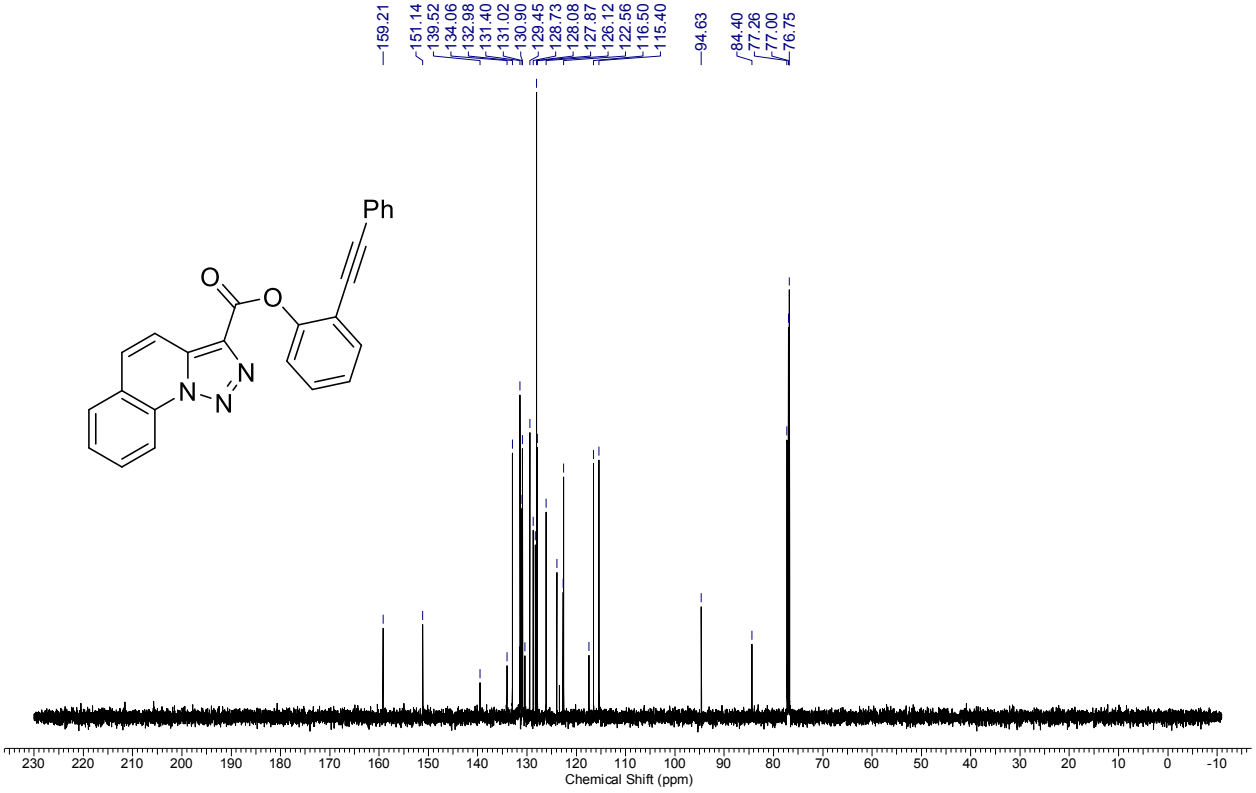
^{13}C NMR Spectrum of **8-4-ap**



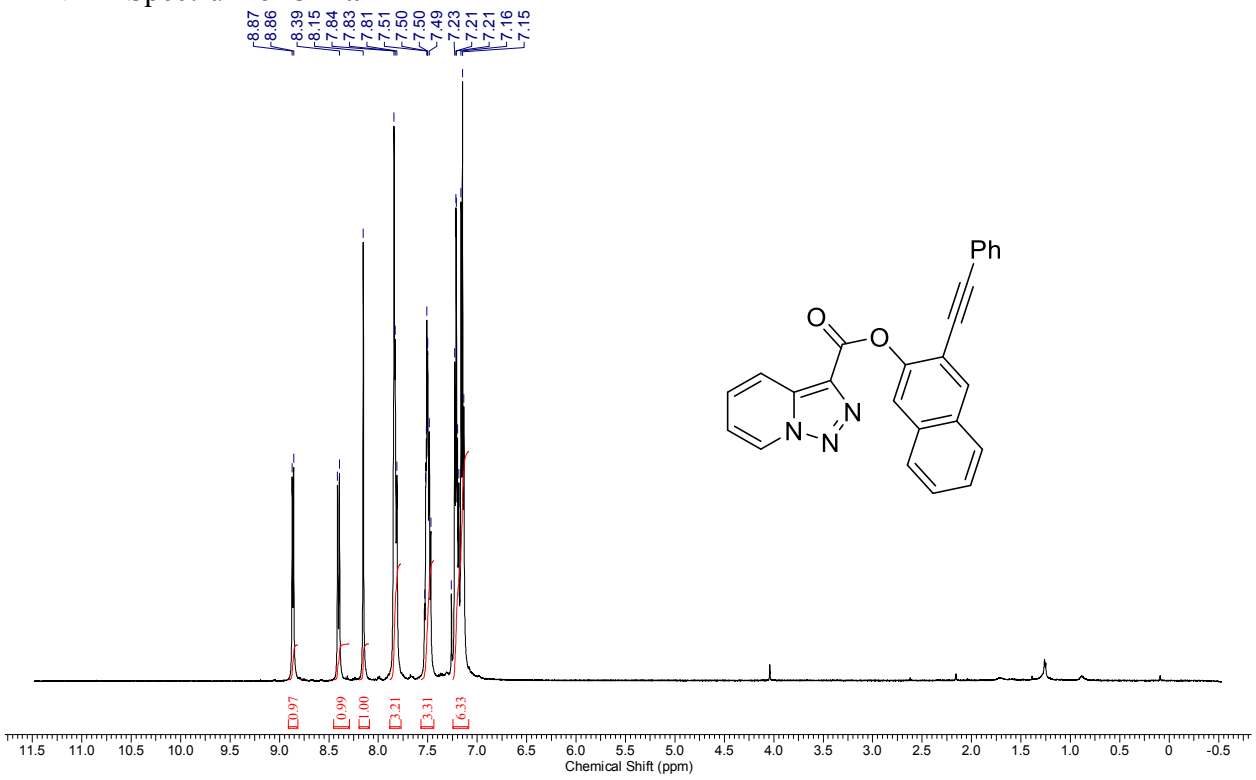
^{1}H NMR Spectrum of **8-4-aq**



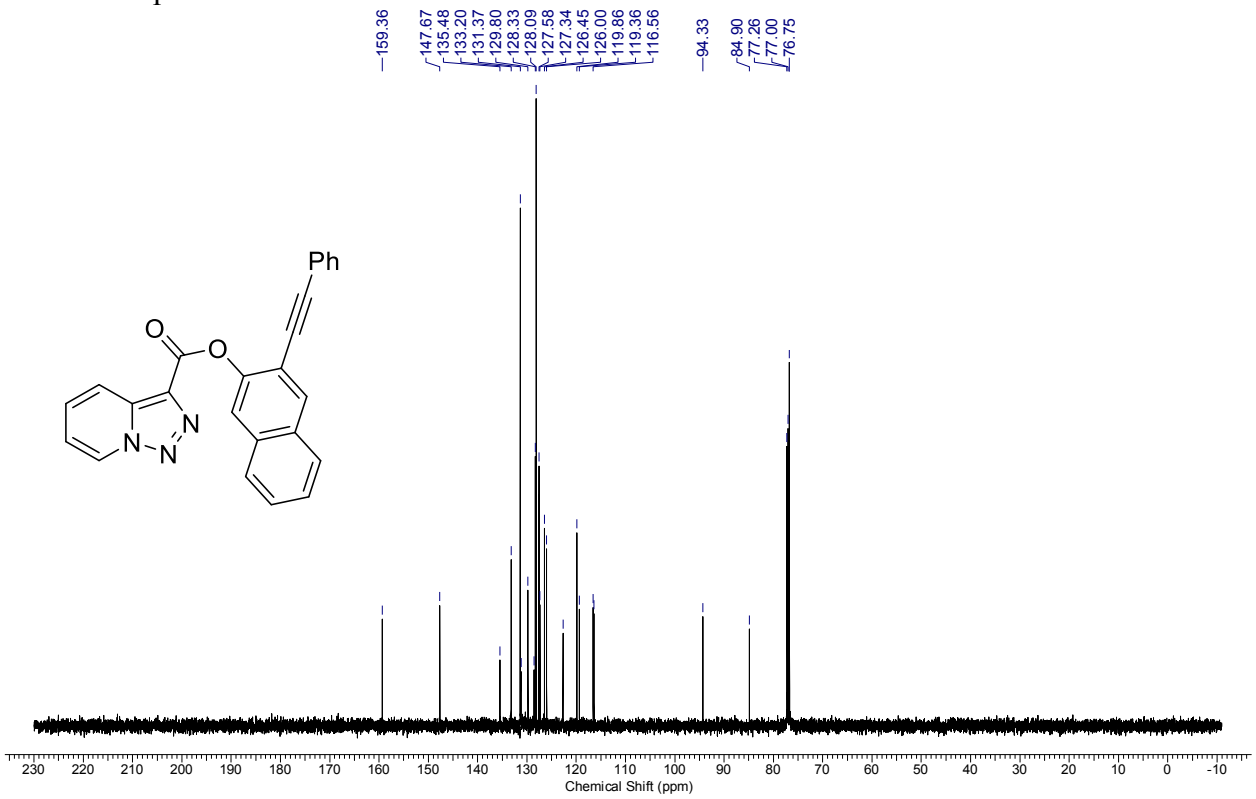
^{13}C NMR Spectrum of **8-4-aq**



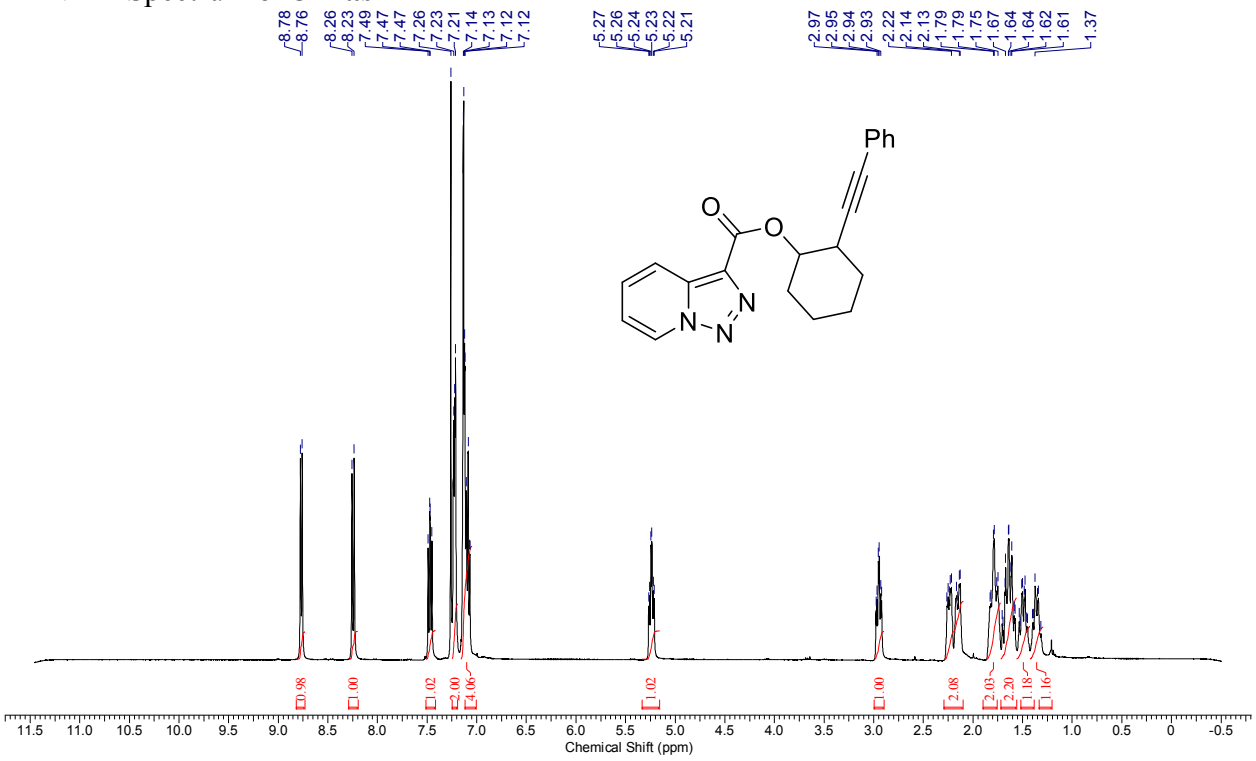
^{1}H NMR Spectrum of **8-4-ar**



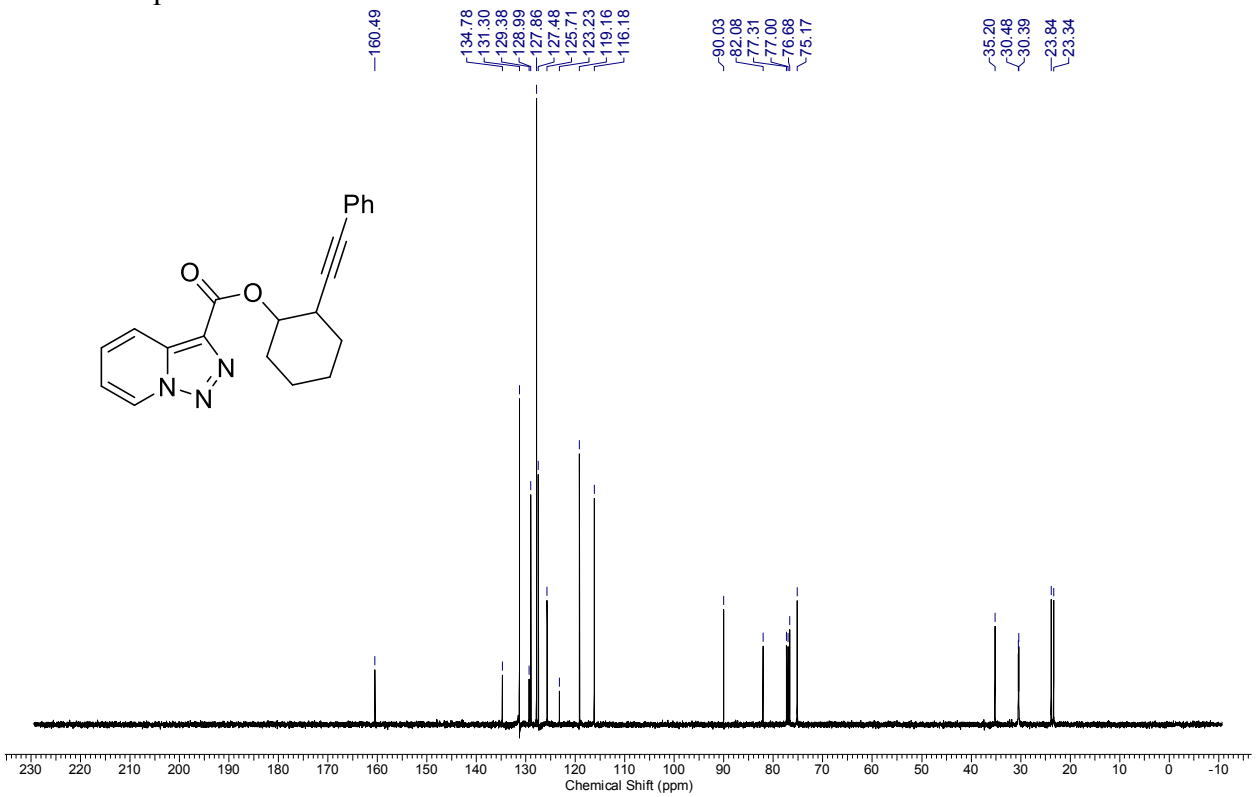
^{13}C NMR Spectrum of **8-4-ar**



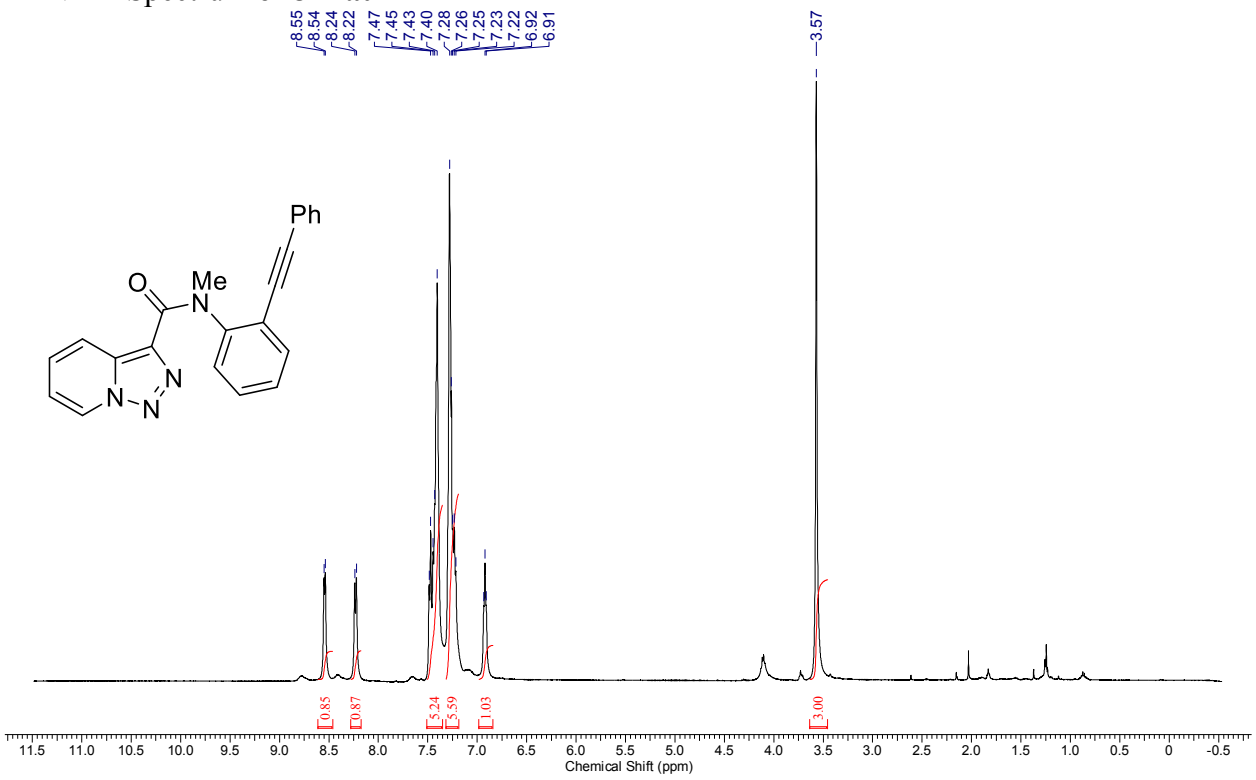
^{1}H NMR Spectrum of **8-4-as**



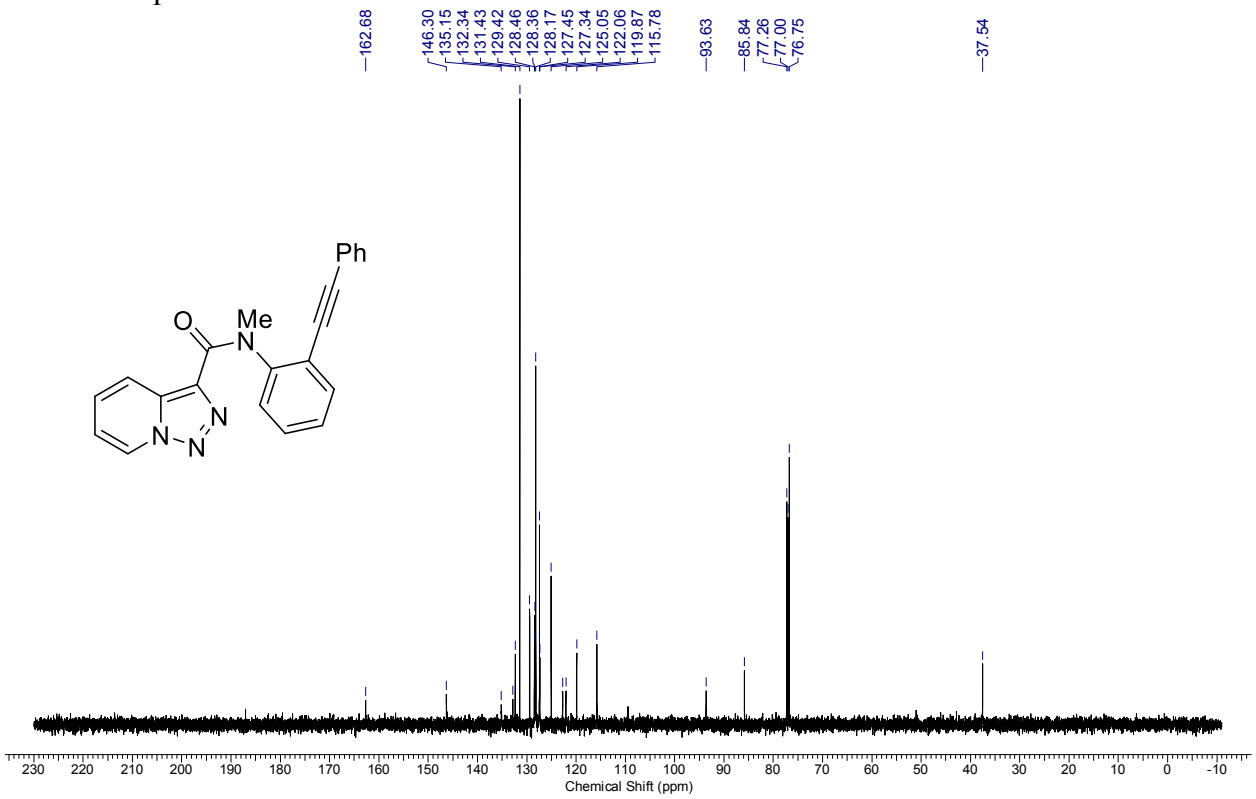
^{13}C NMR Spectrum of **8-4-as**



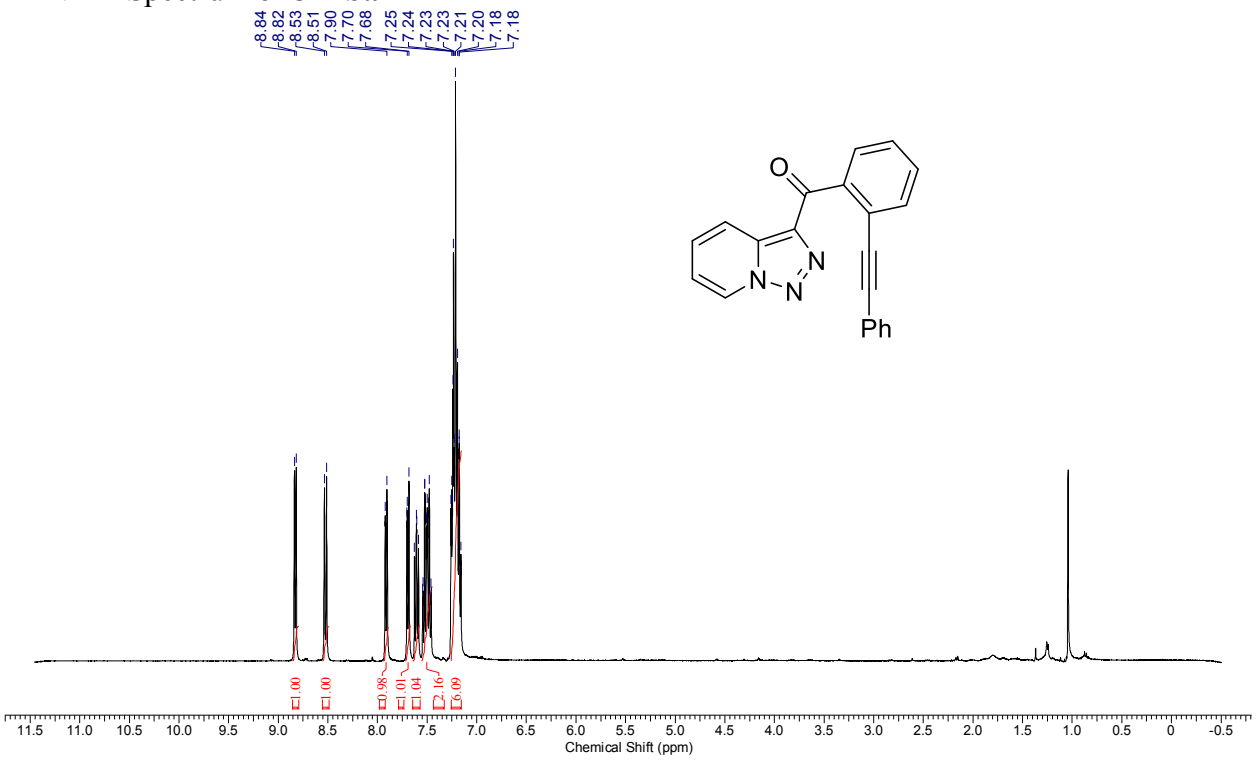
^{1}H NMR Spectrum of **8-4-at**



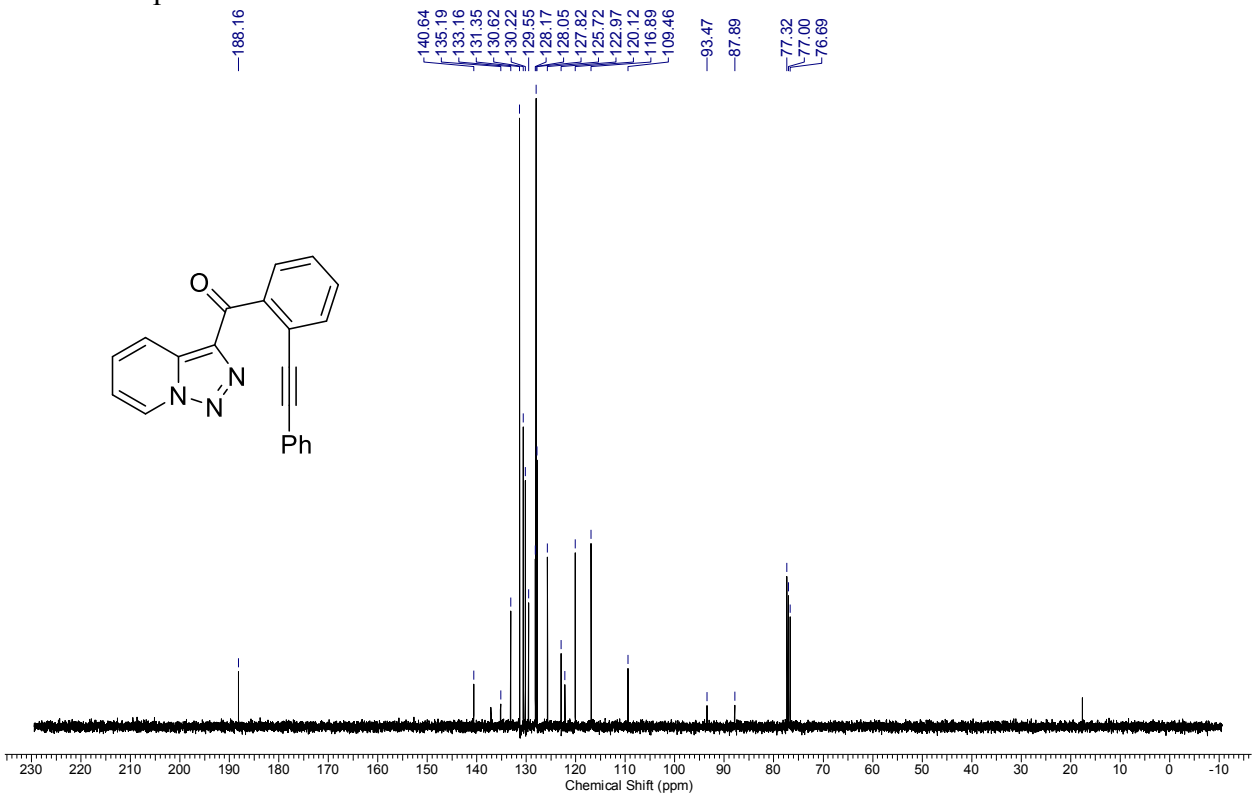
^{13}C NMR Spectrum of **8-4-at**



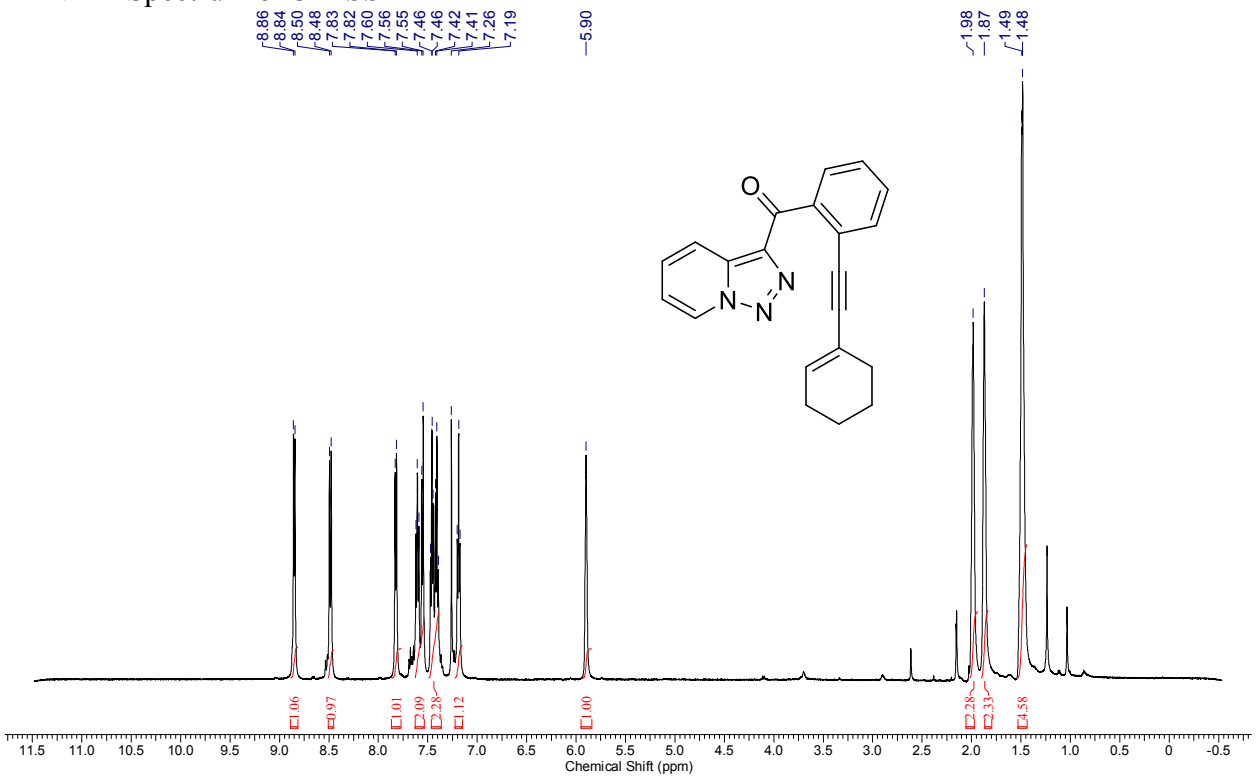
^{1}H NMR Spectrum of **8-4-ba**



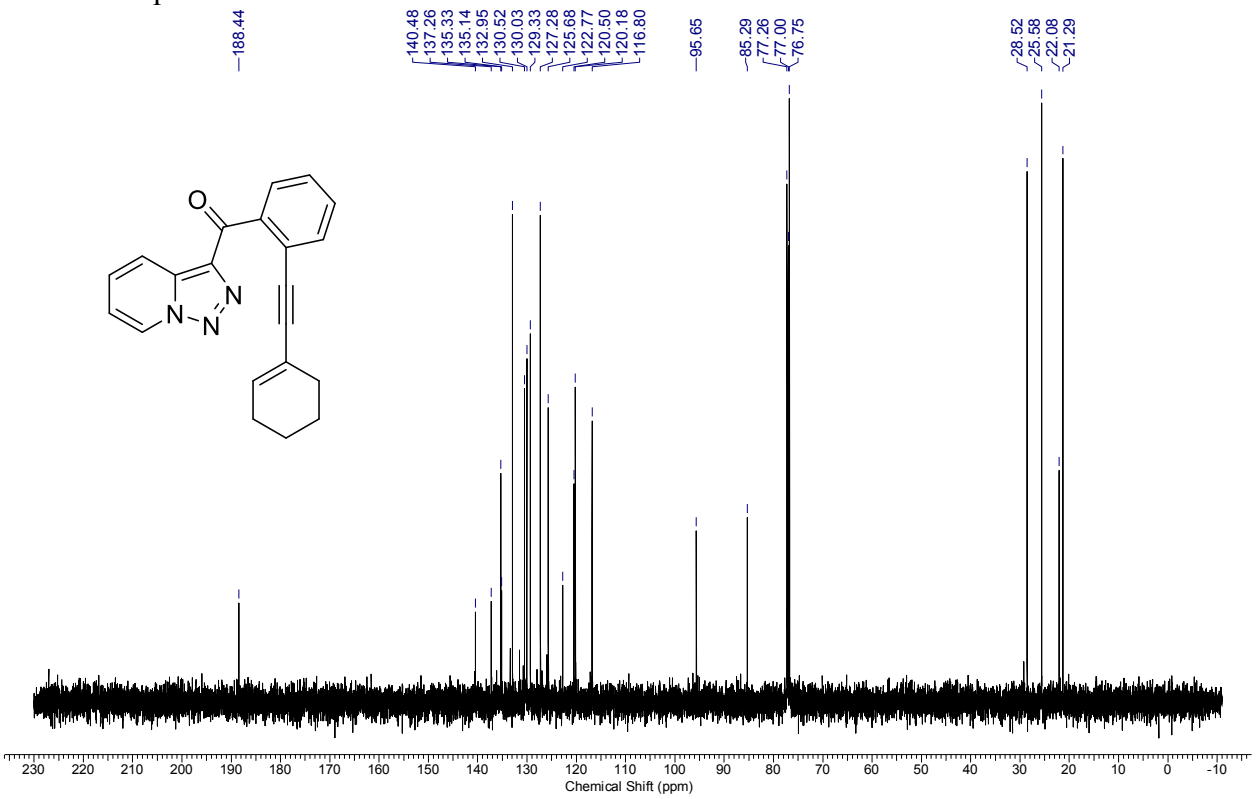
^{13}C NMR Spectrum of **8-4-ba**



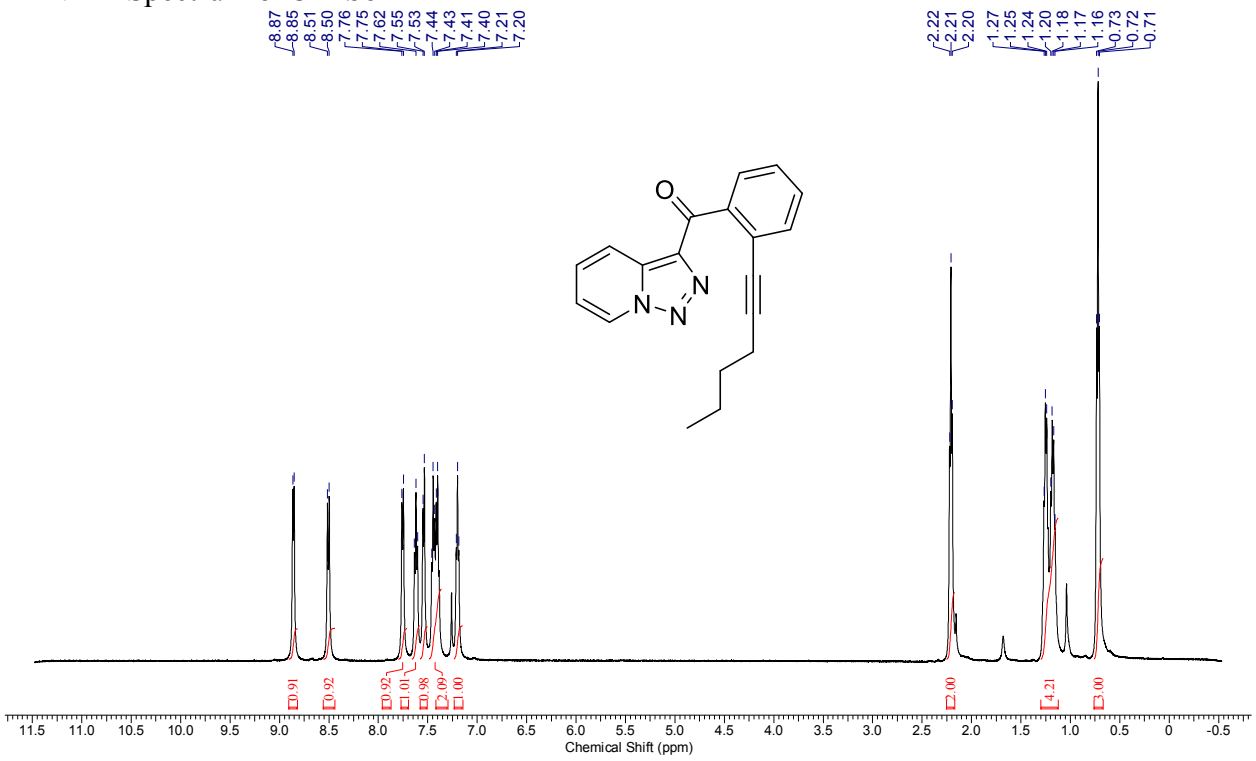
^{1}H NMR Spectrum of **8-4-bb**



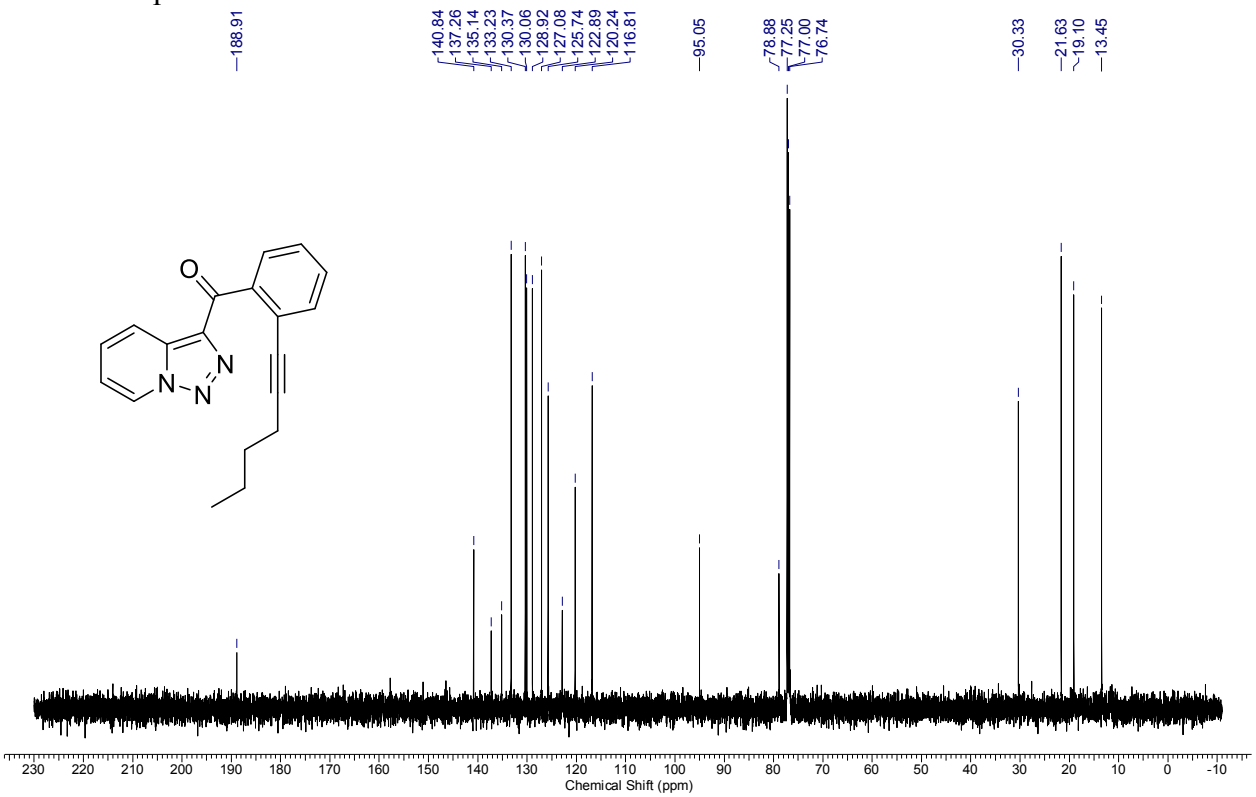
^{13}C NMR Spectrum of **8-4-bb**



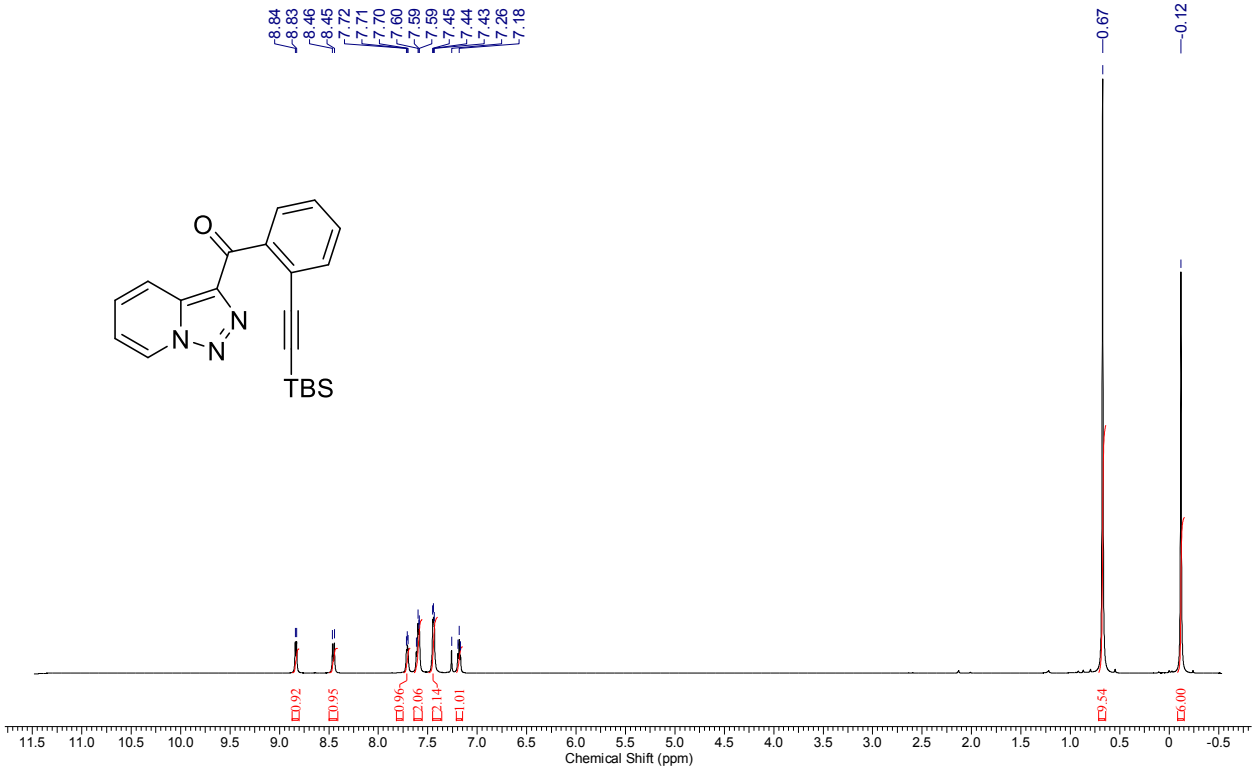
^{1}H NMR Spectrum of **8-4-bc**



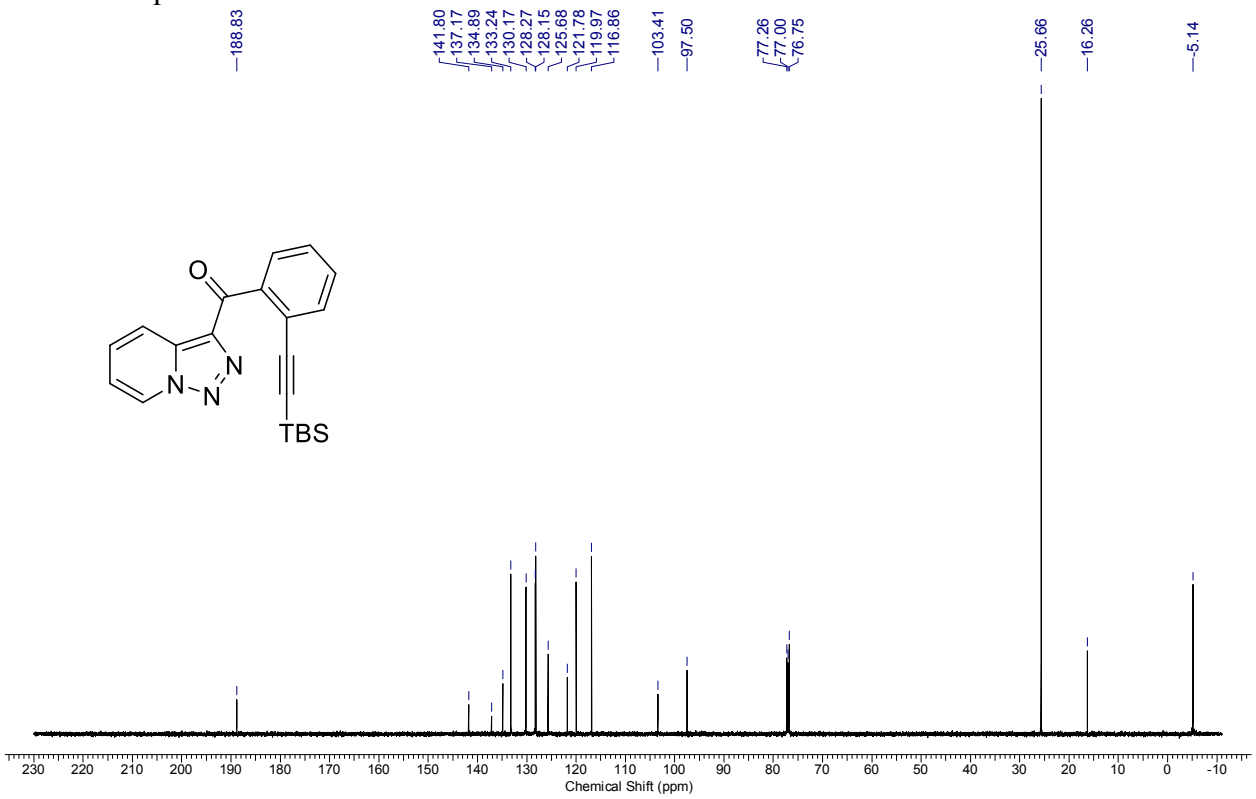
^{13}C NMR Spectrum of **8-4-bc**



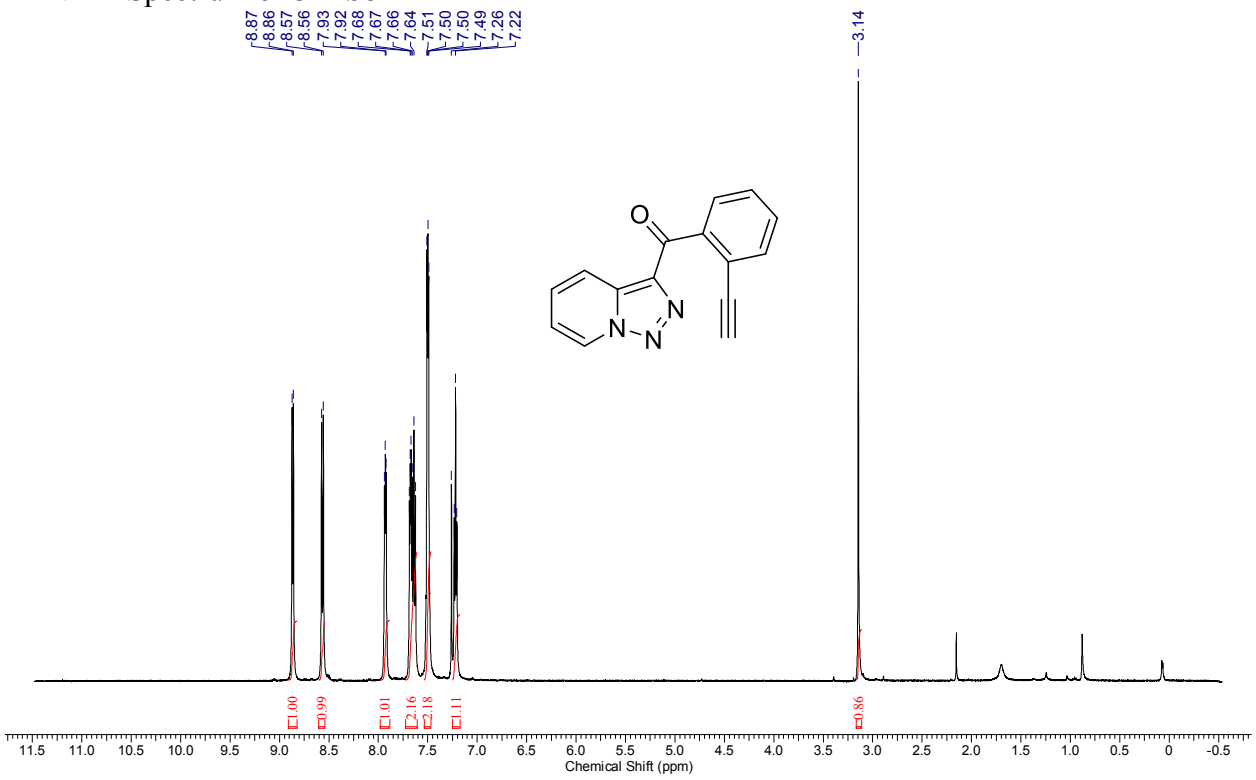
^{1}H NMR Spectrum of **8-4-bd**



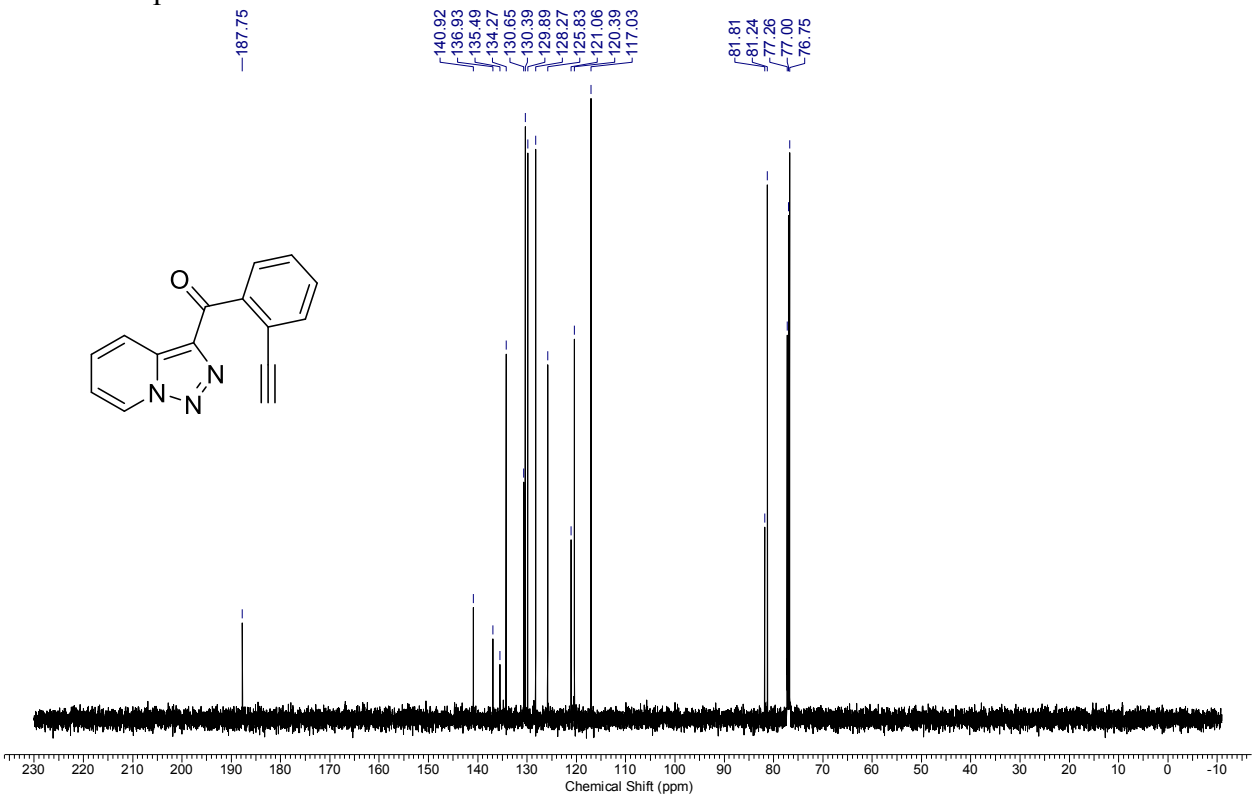
^{13}C NMR Spectrum of **8-4-bd**



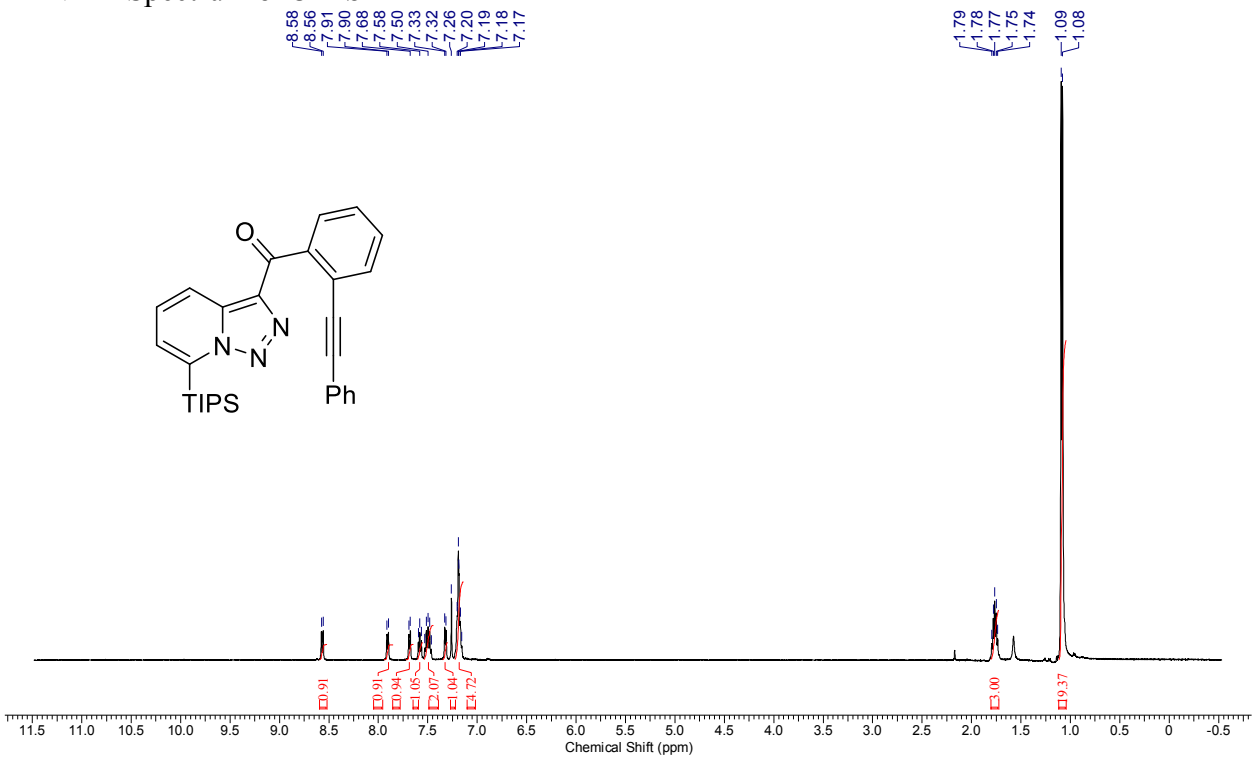
^{1}H NMR Spectrum of **8-4-be**



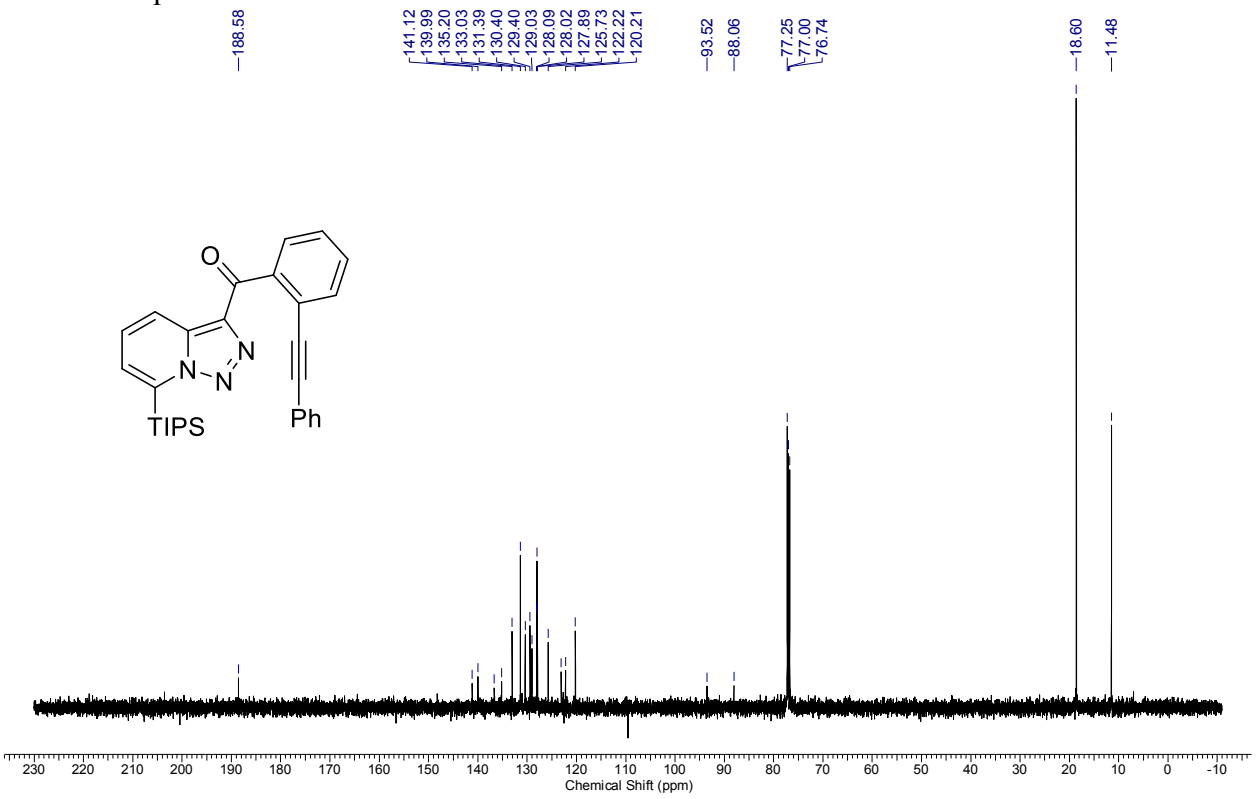
^{13}C NMR Spectrum of **8-4-be**



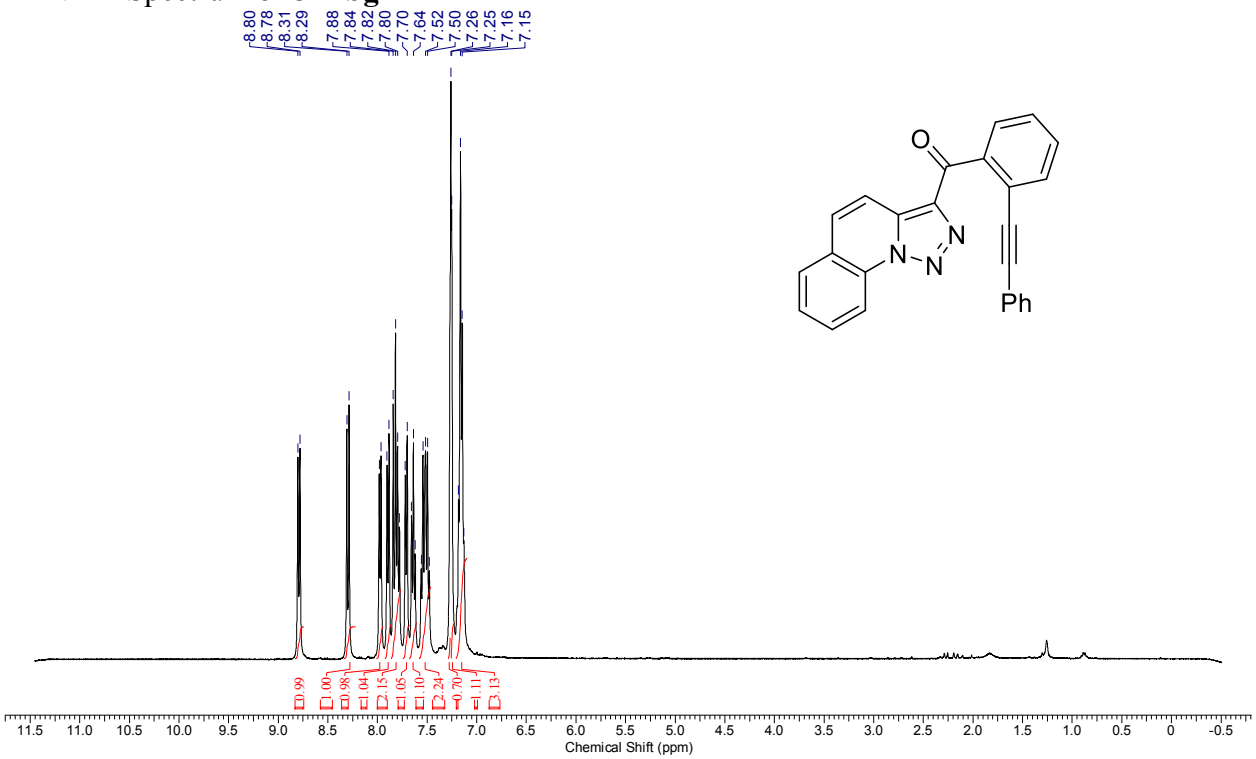
^{1}H NMR Spectrum of **8-4-bf**



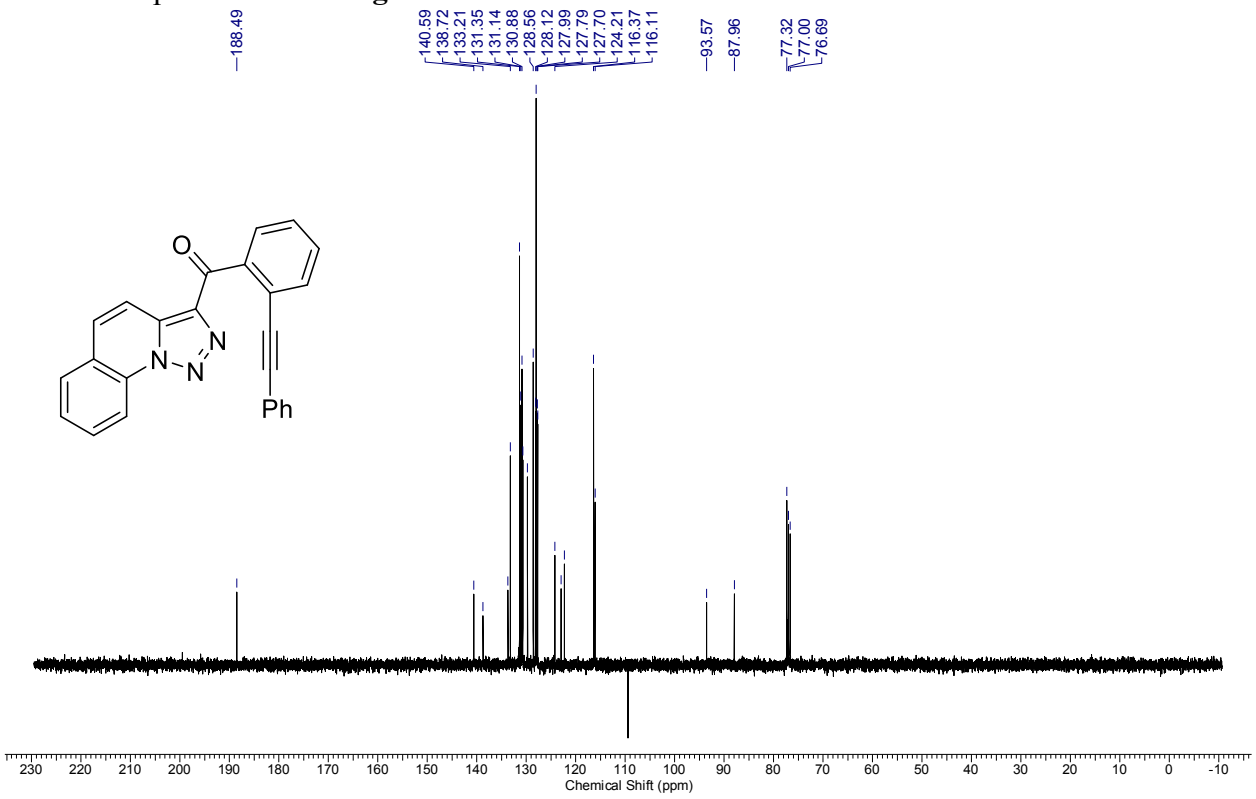
^{13}C NMR Spectrum of **8-4-bf**



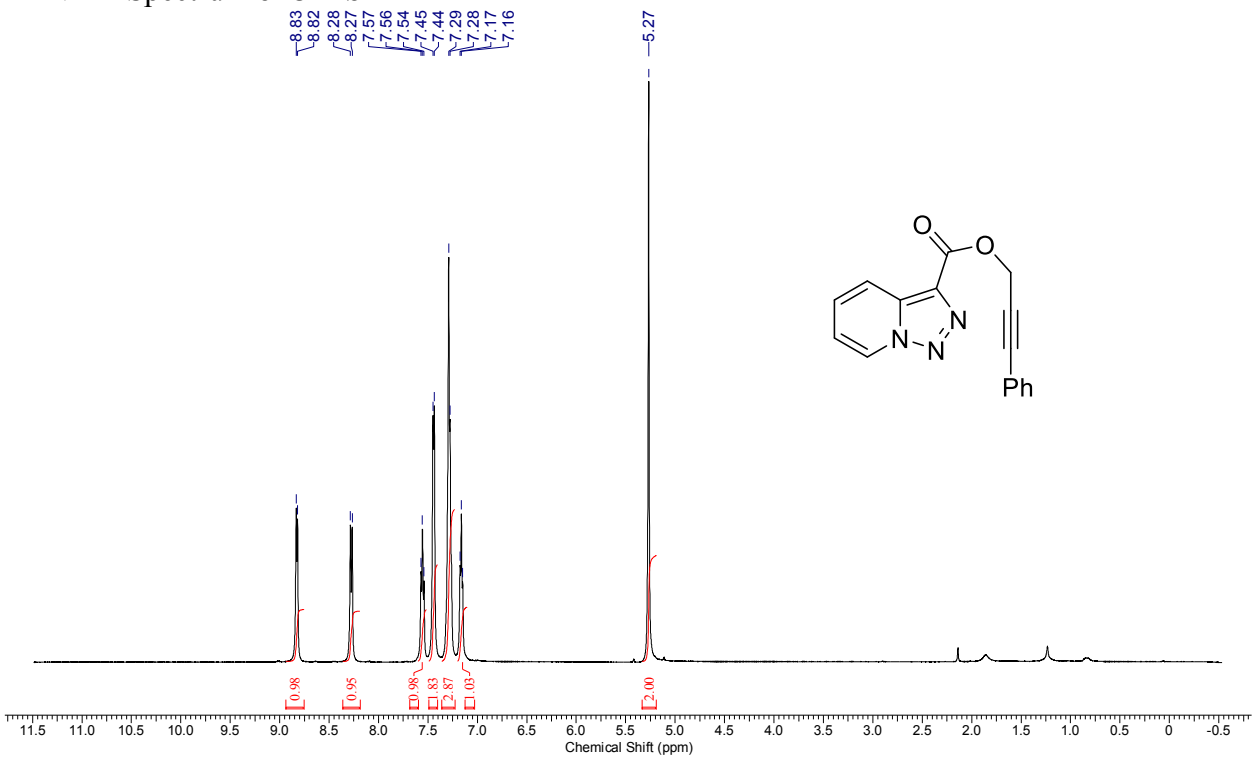
^{1}H NMR Spectrum of **8-4-bg**



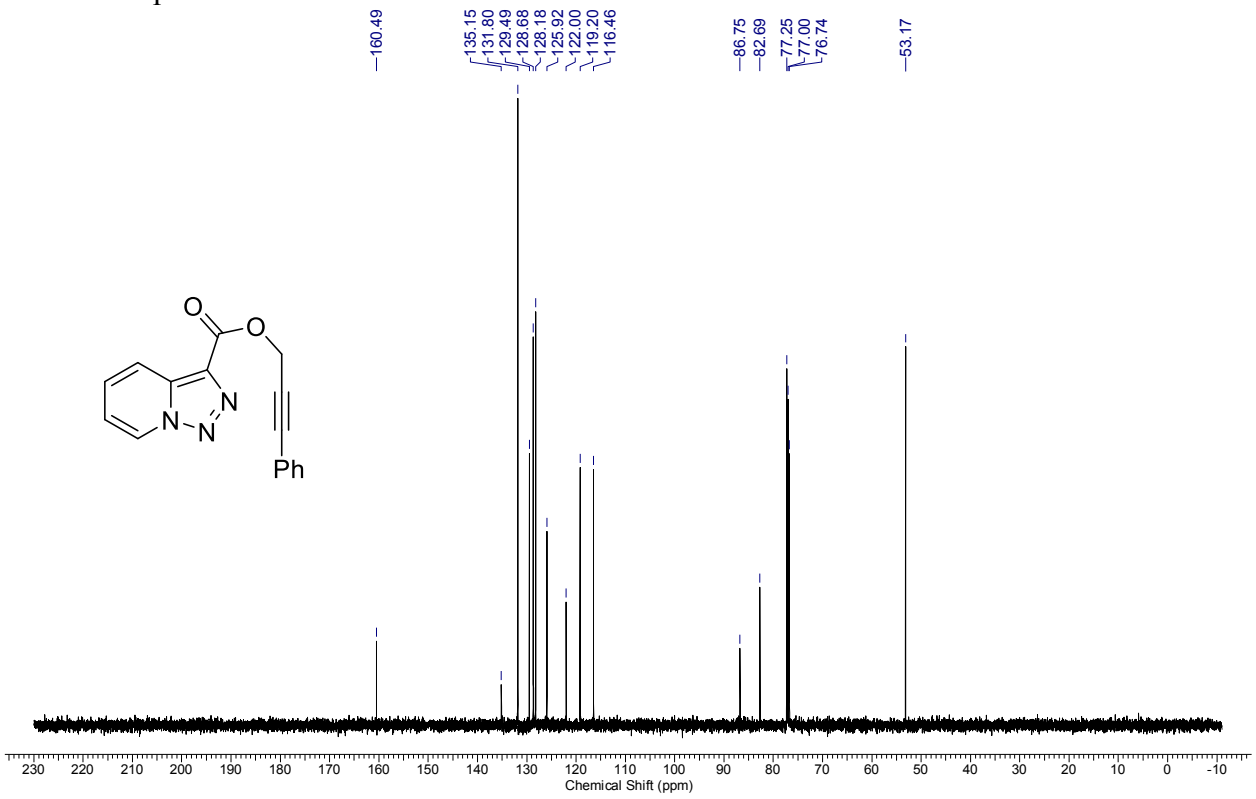
^{13}C NMR Spectrum of **8-4-bg**



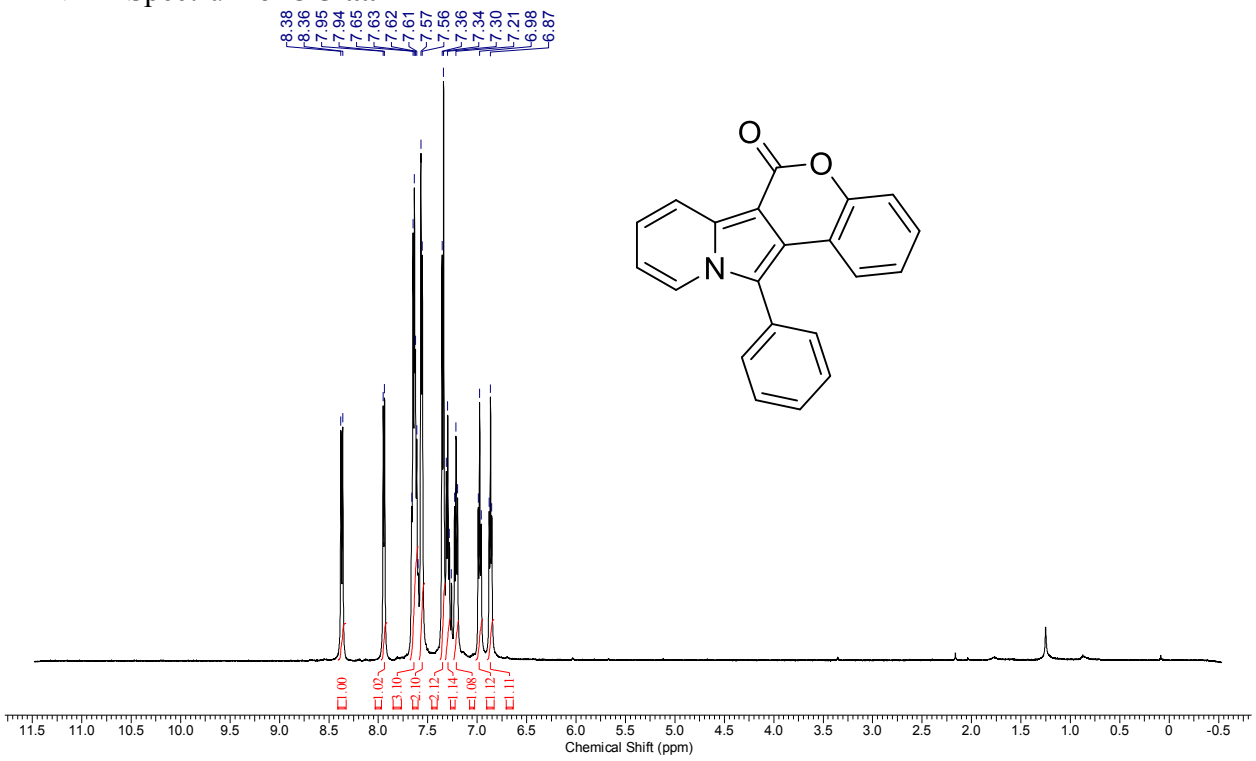
^{1}H NMR Spectrum of **8-4-bh**



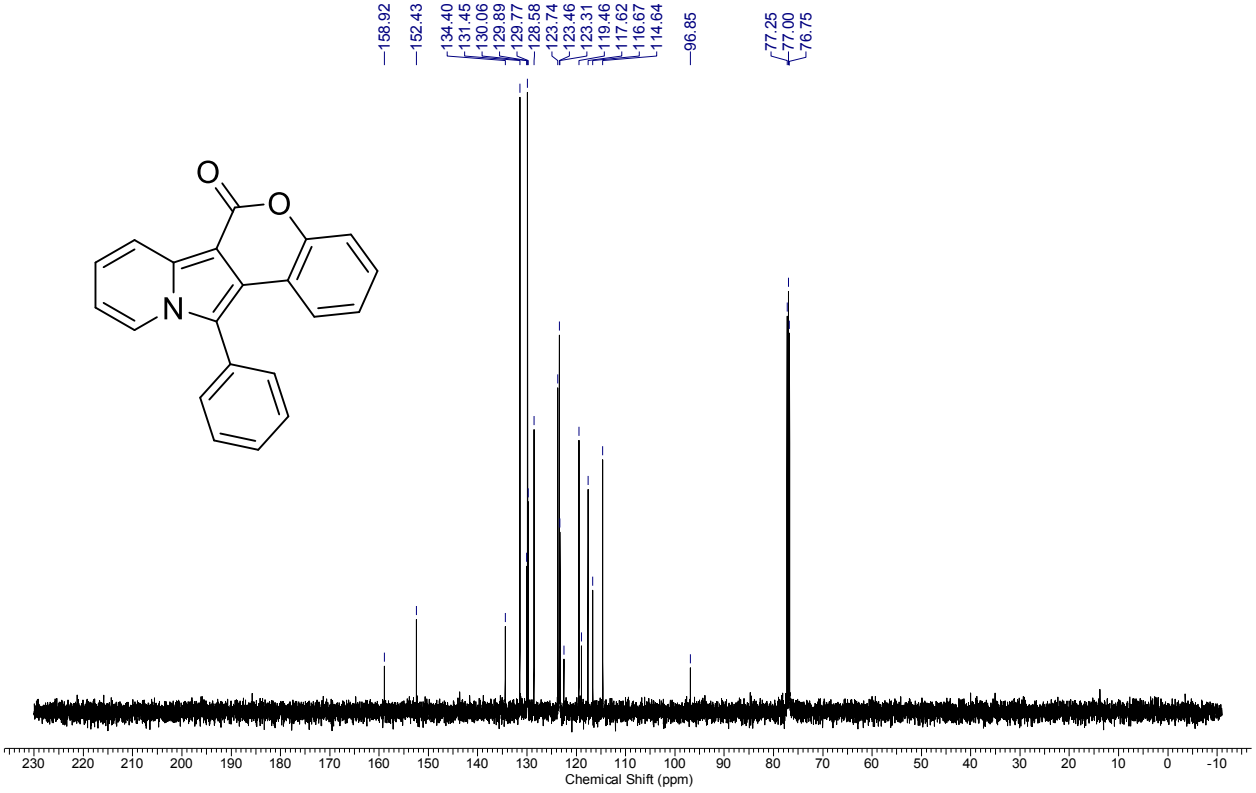
^{13}C NMR Spectrum of **8-4-bh**



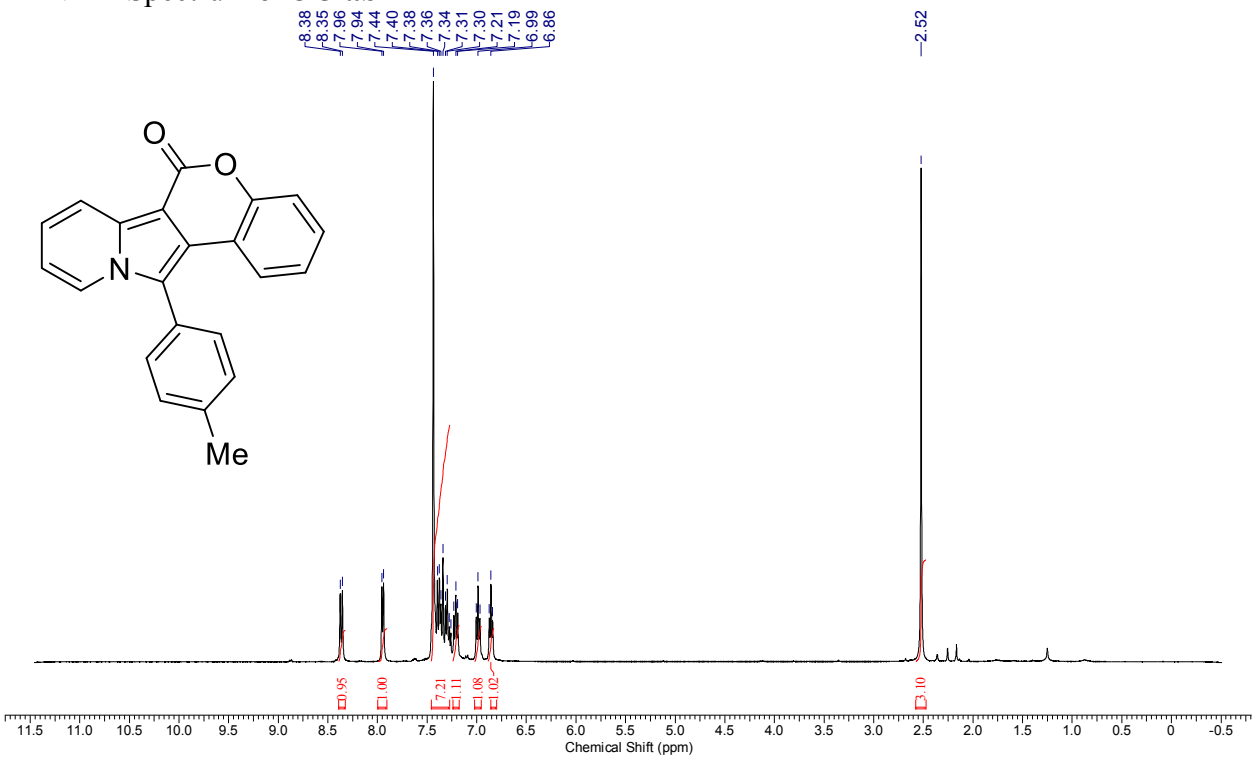
^{1}H NMR Spectrum of **8-5-aa**



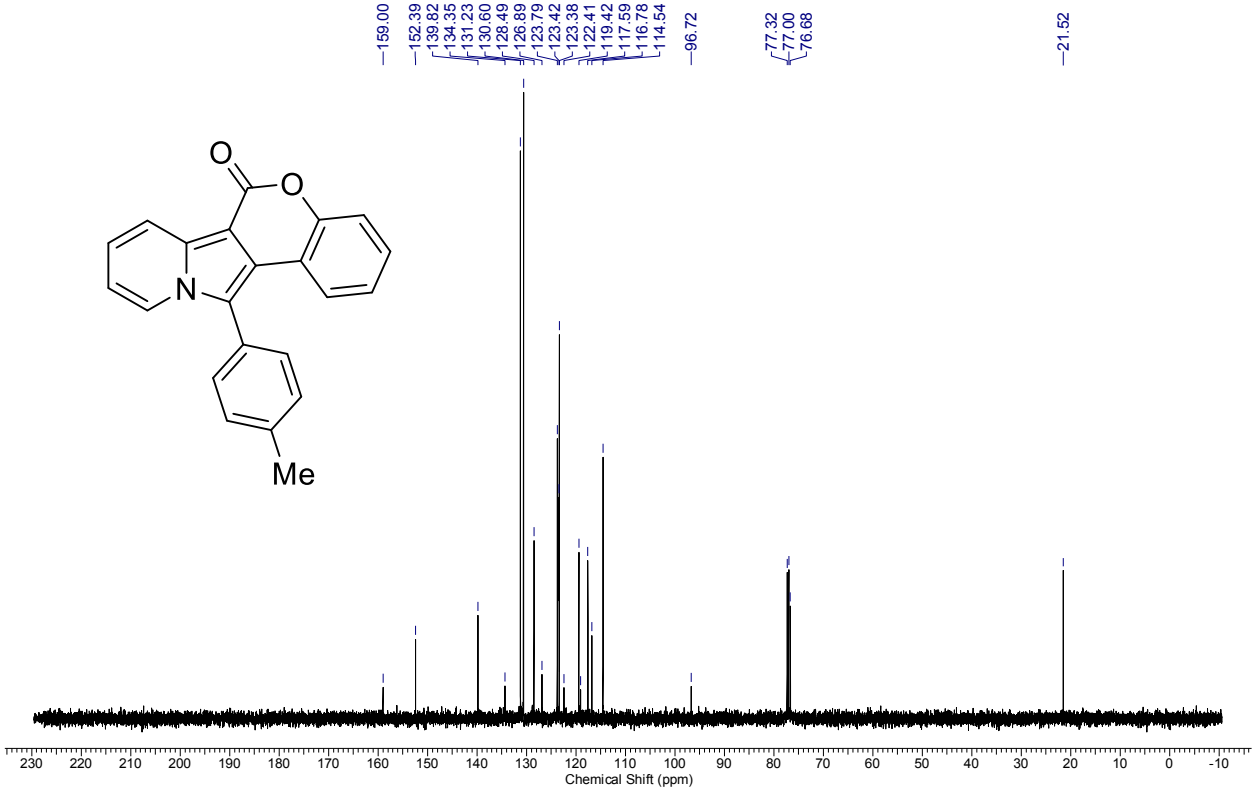
^{13}C NMR Spectrum of **8-5-aa**



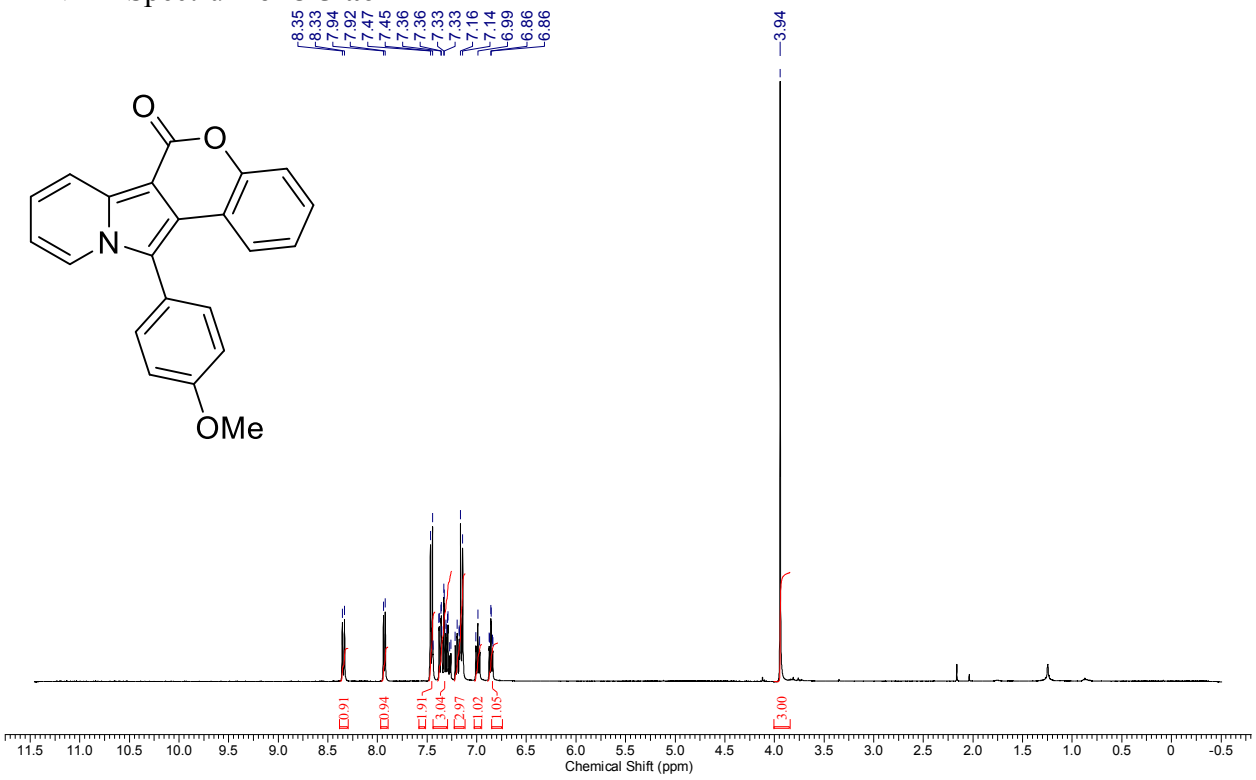
^{1}H NMR Spectrum of **8-5-ab**



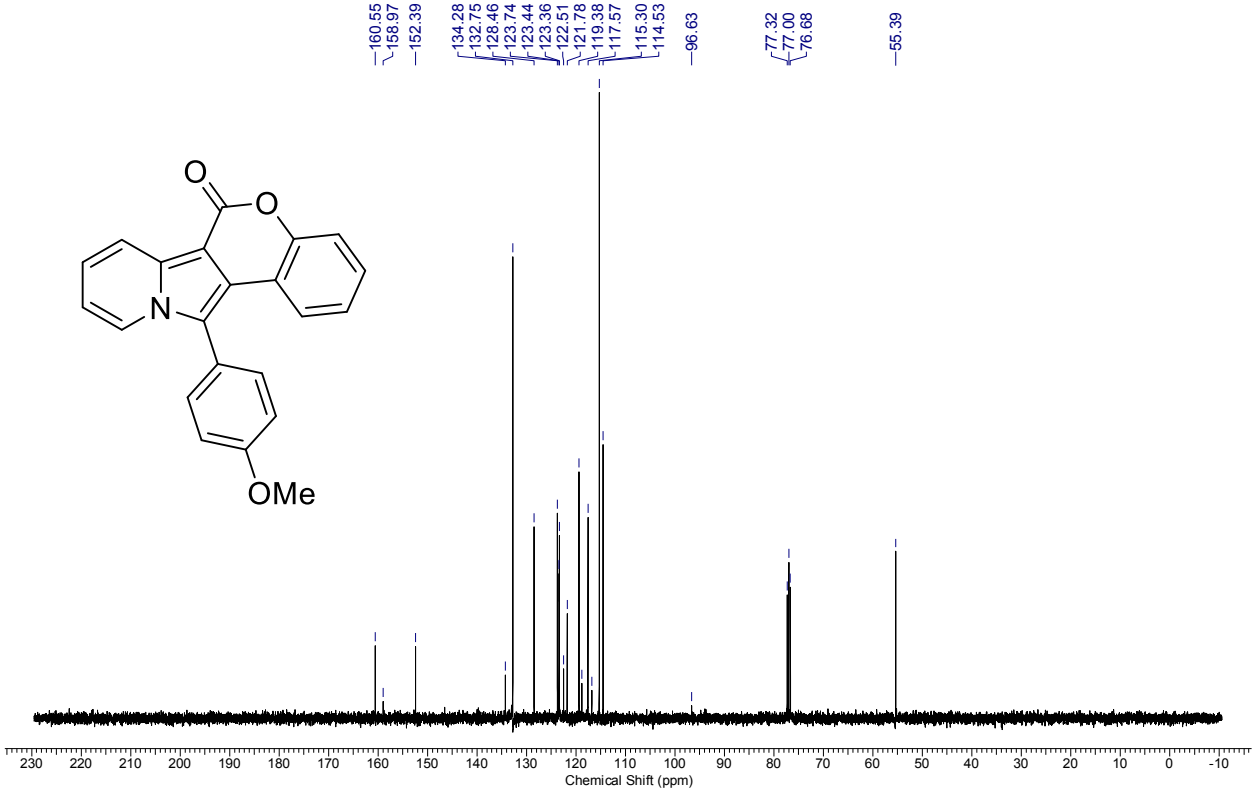
^{13}C NMR Spectrum of **8-5-ab**



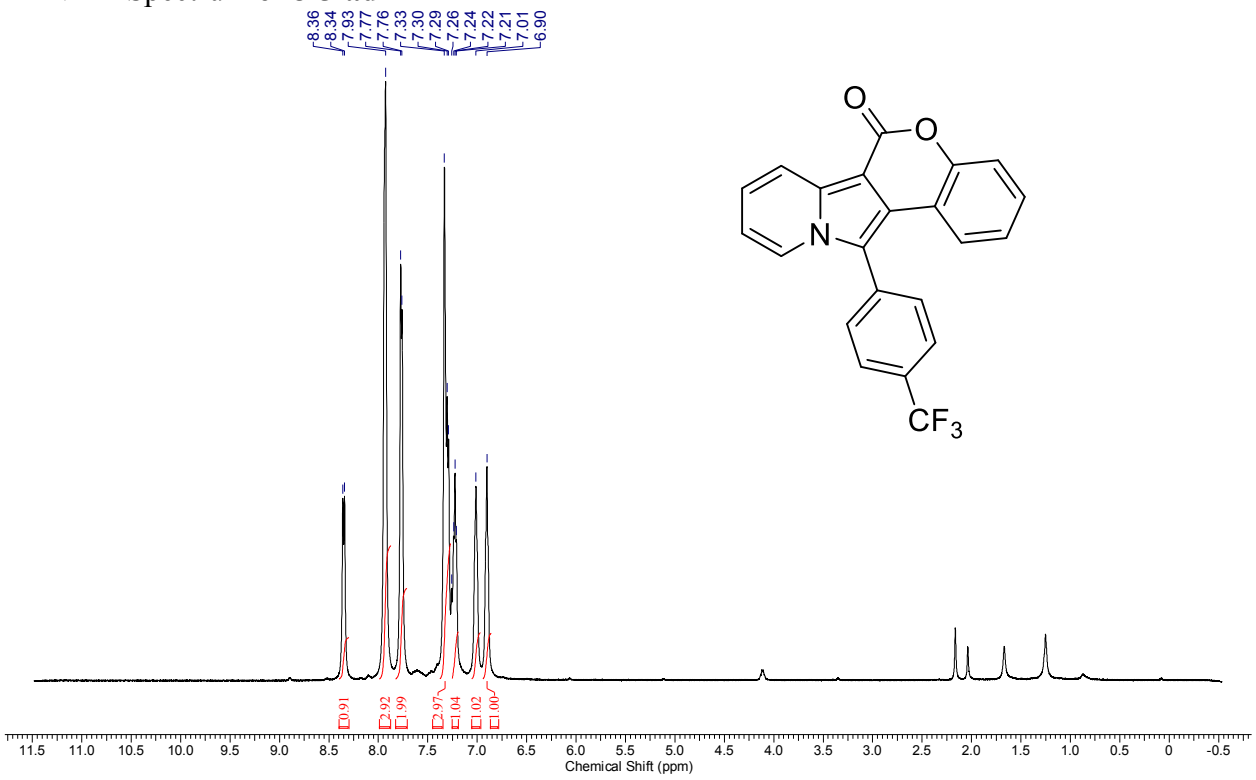
^{1}H NMR Spectrum of **8-5-ac**



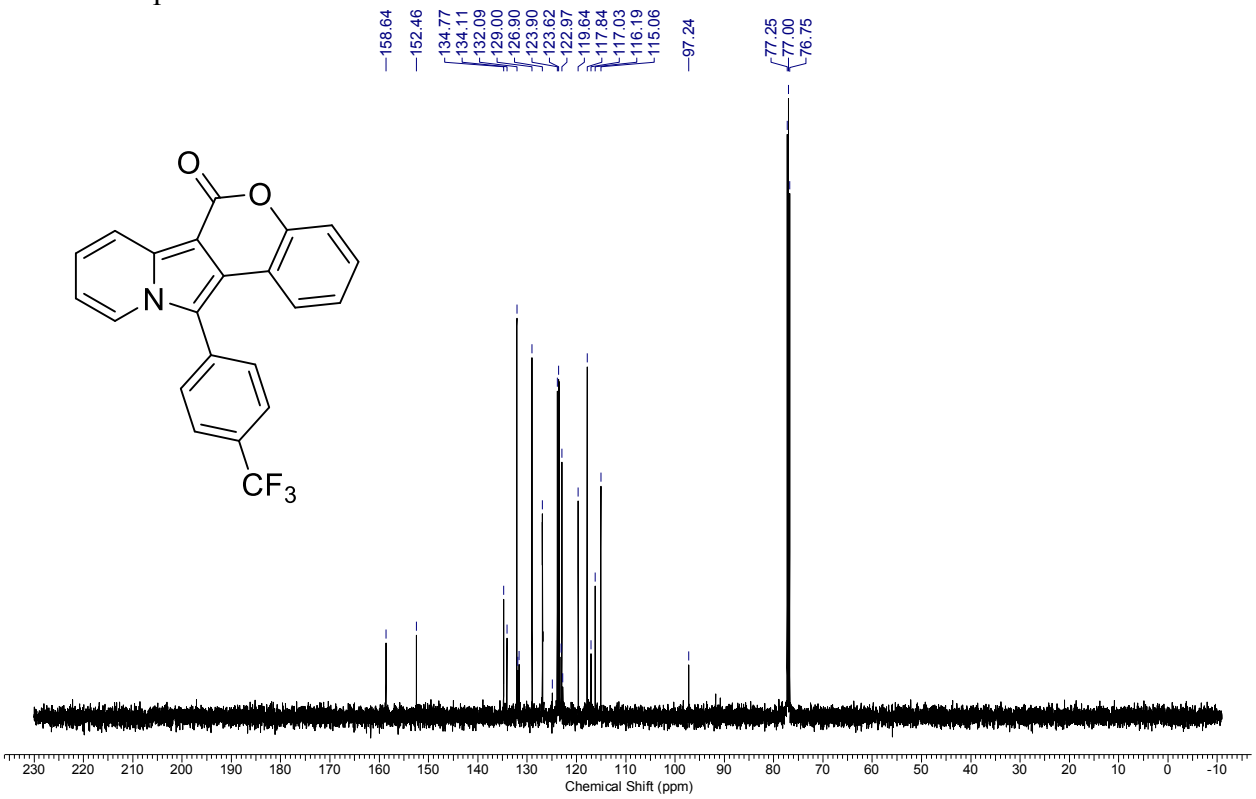
^{13}C NMR Spectrum of **8-5-ac**



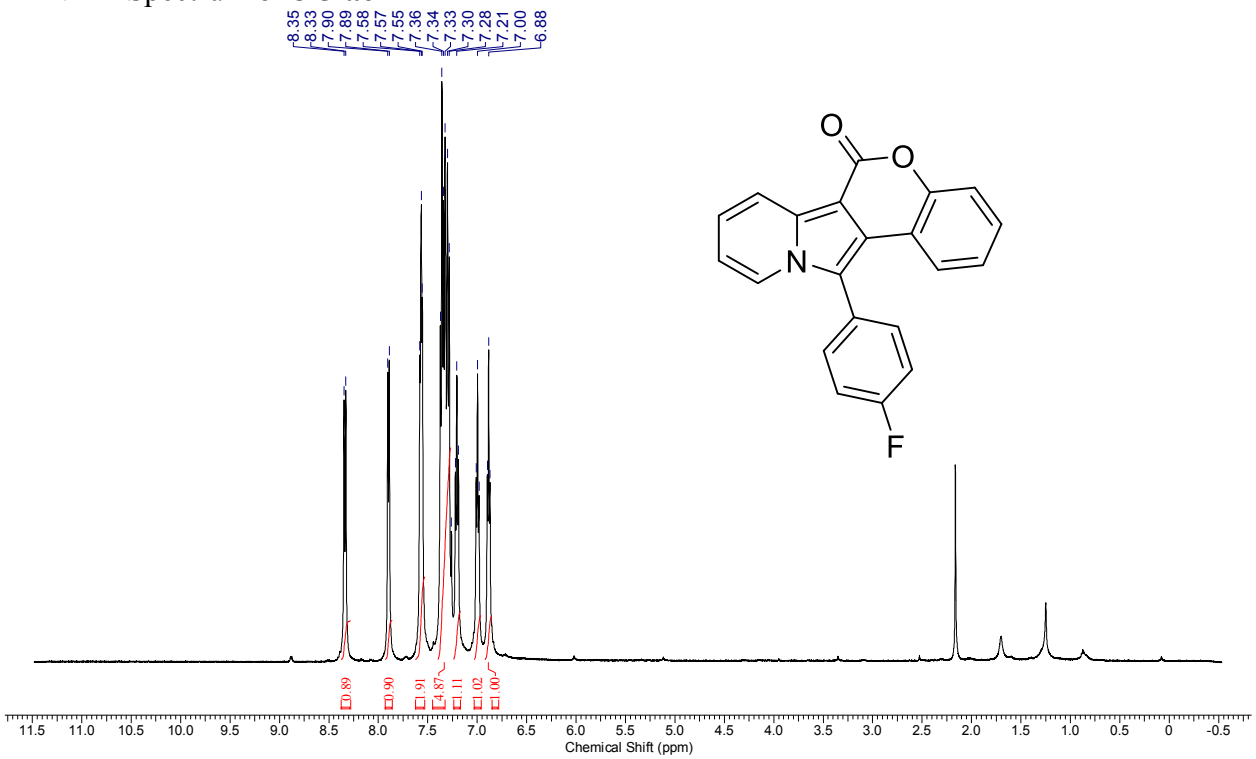
^{1}H NMR Spectrum of **8-5-ad**



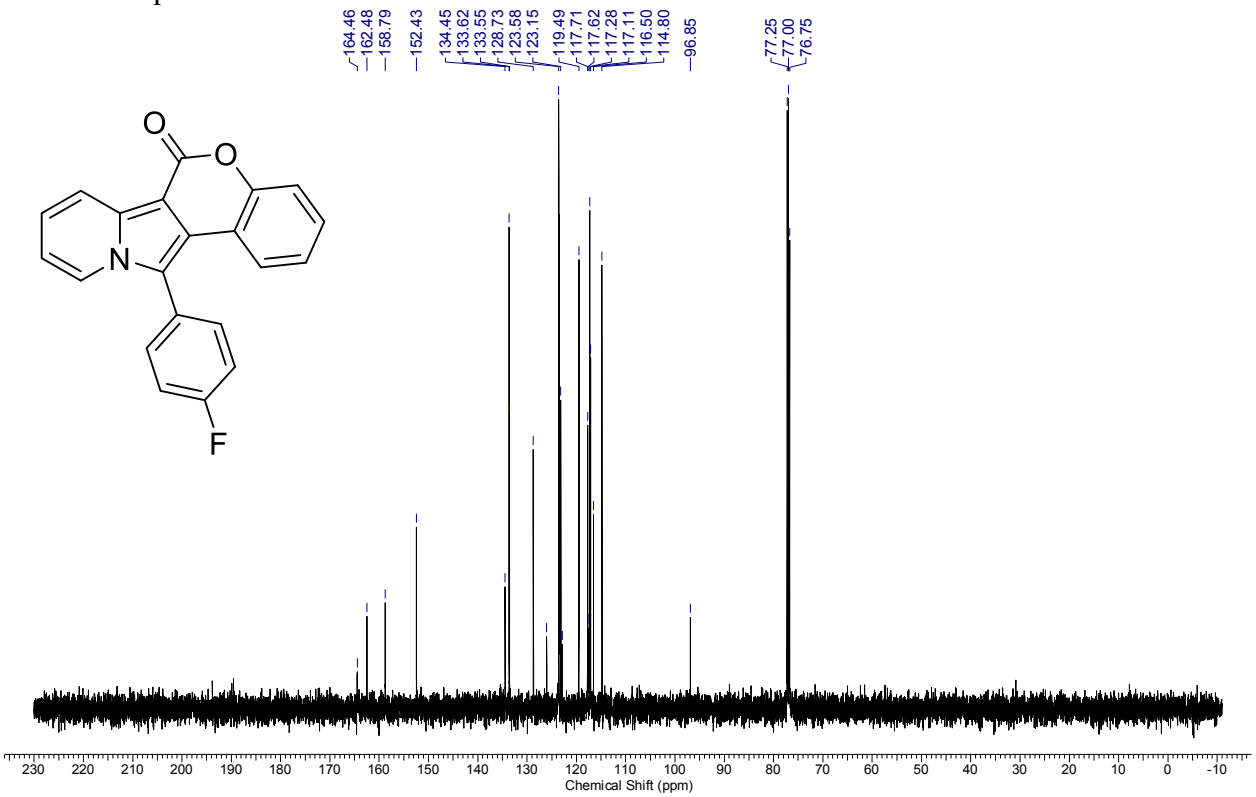
^{13}C NMR Spectrum of **8-5-ad**



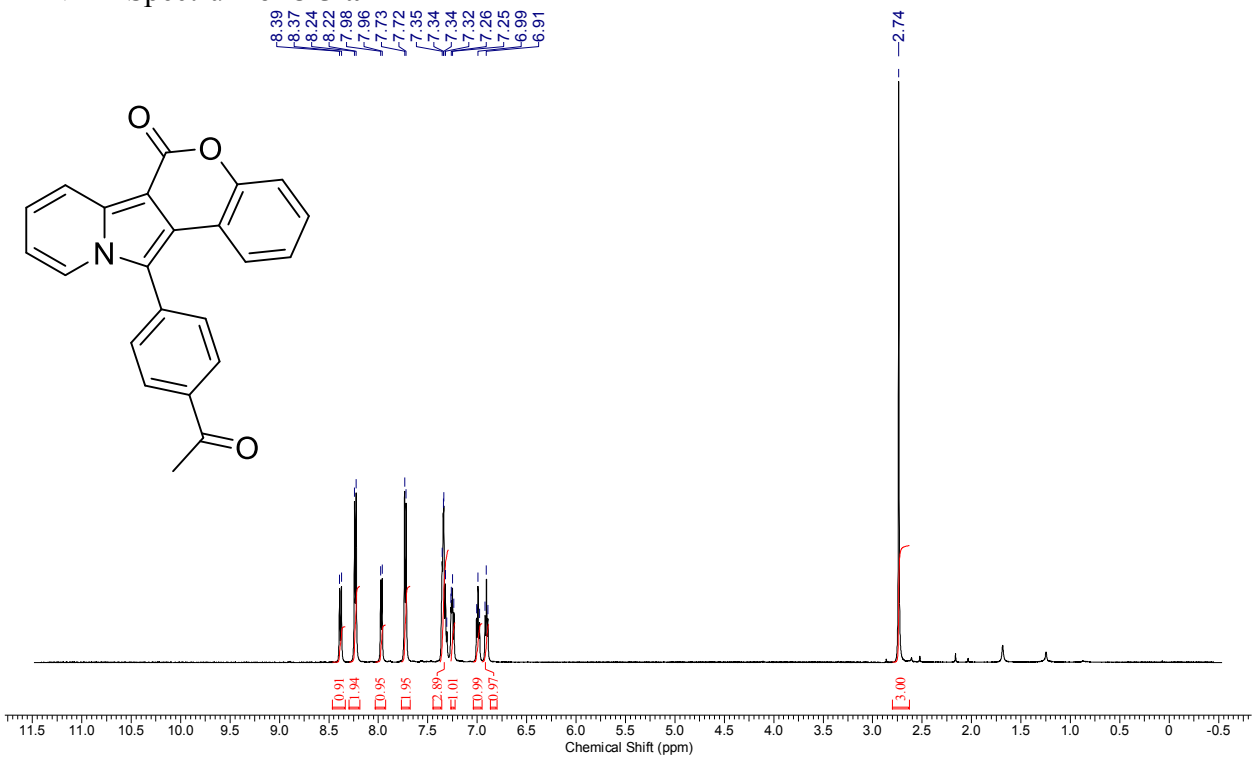
^{1}H NMR Spectrum of **8-5-ae**



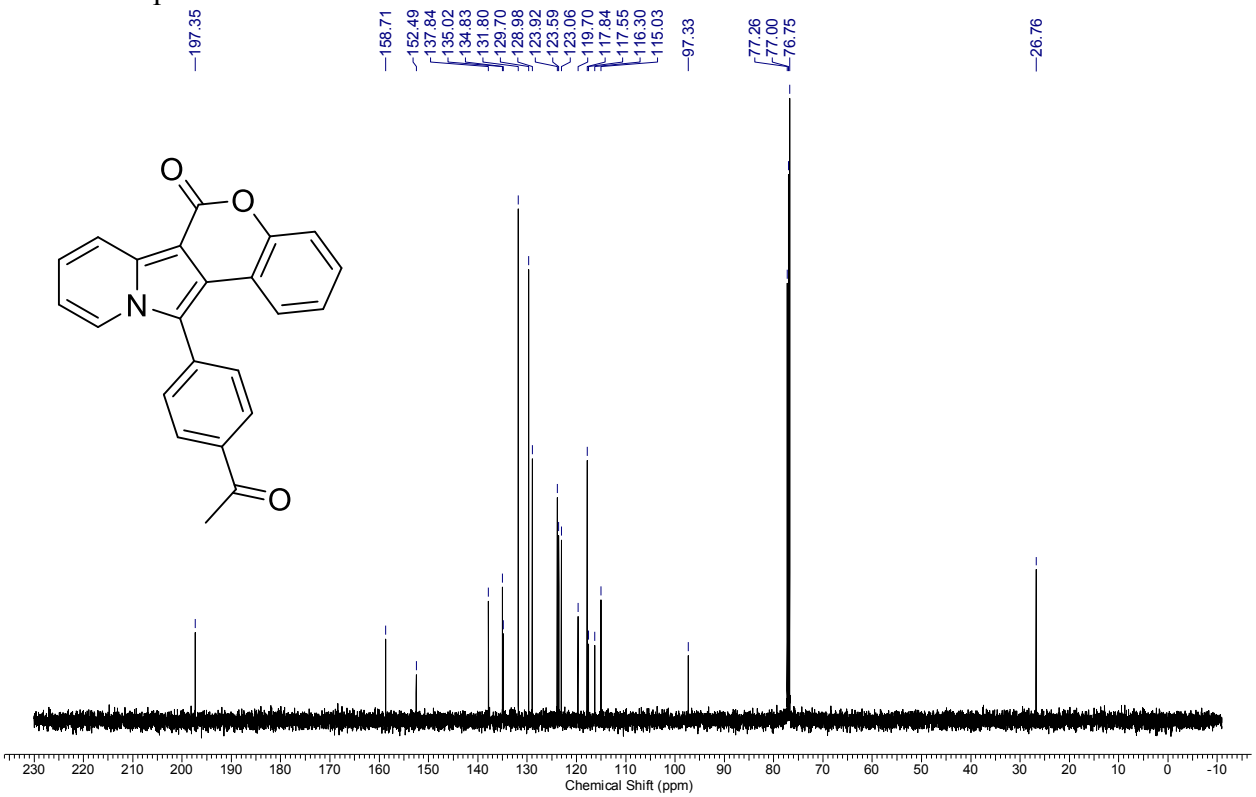
^{13}C NMR Spectrum of **8-5-ae**



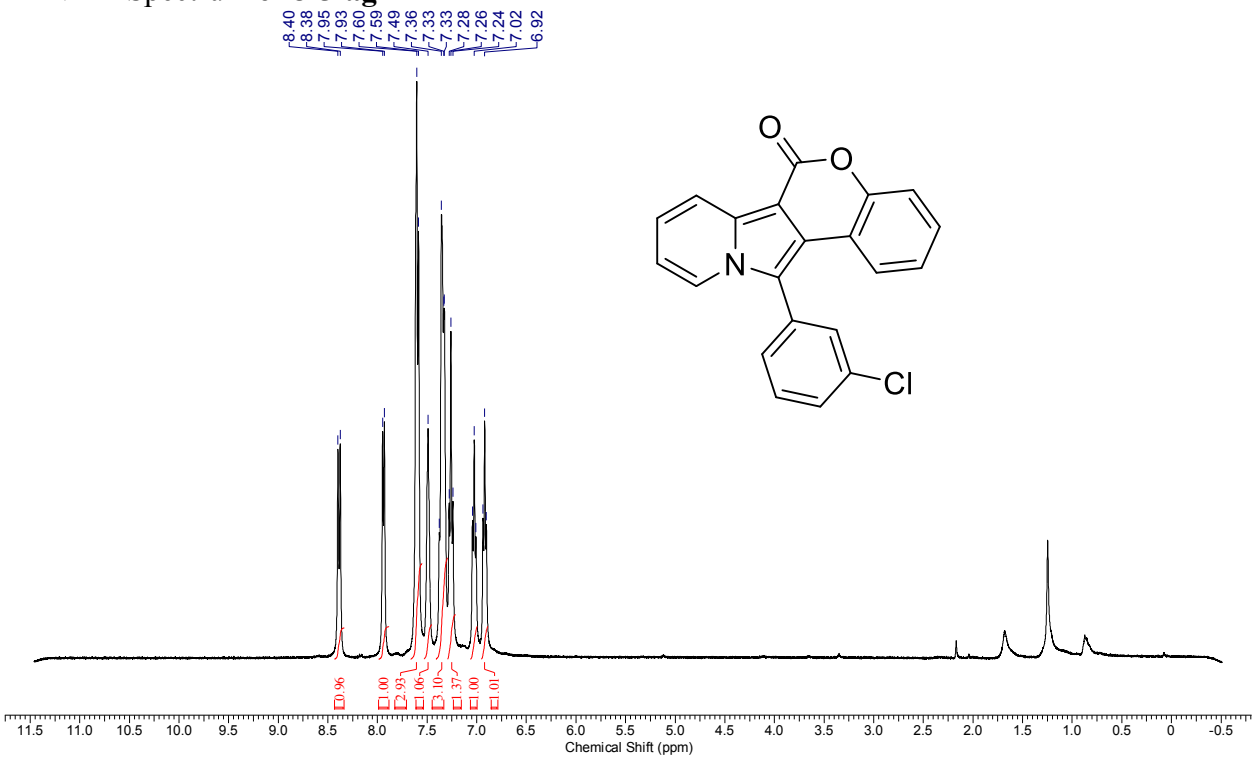
^{1}H NMR Spectrum of **8-5-af**



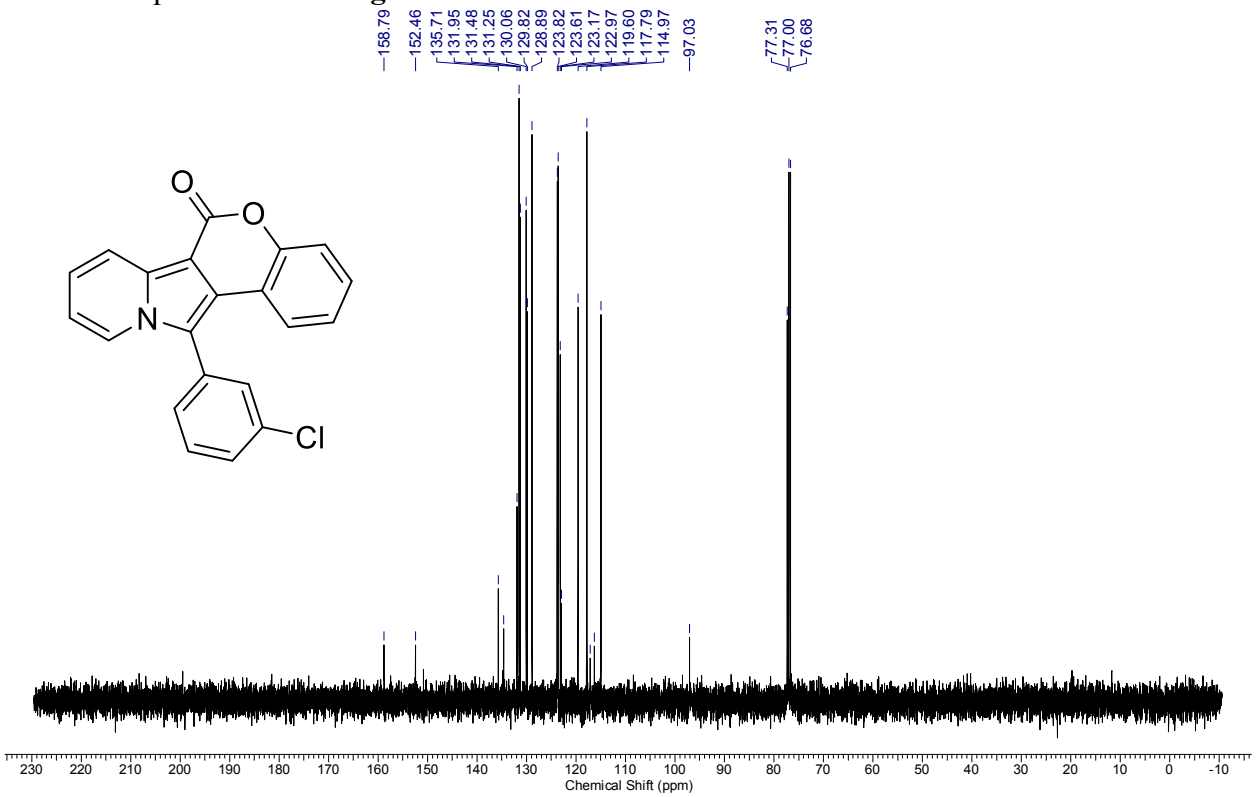
^{13}C NMR Spectrum of **8-5-af**



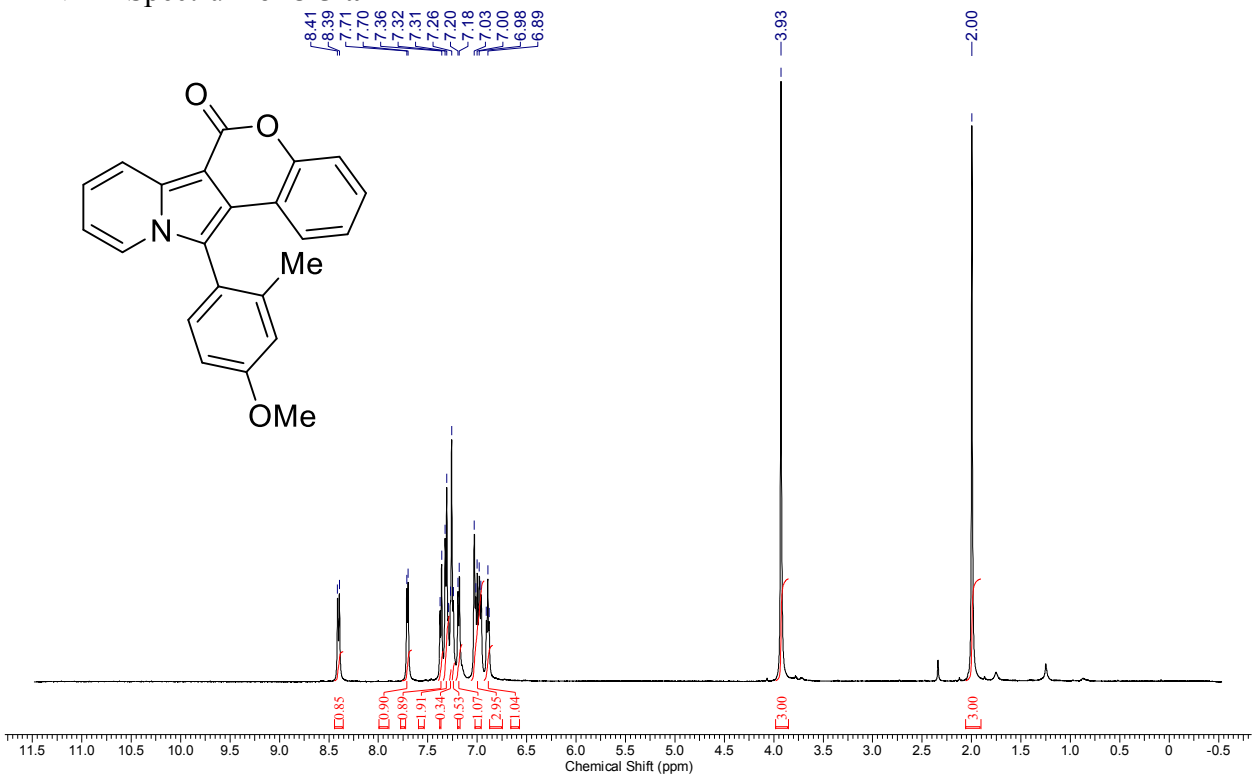
^{1}H NMR Spectrum of **8-5-ag**



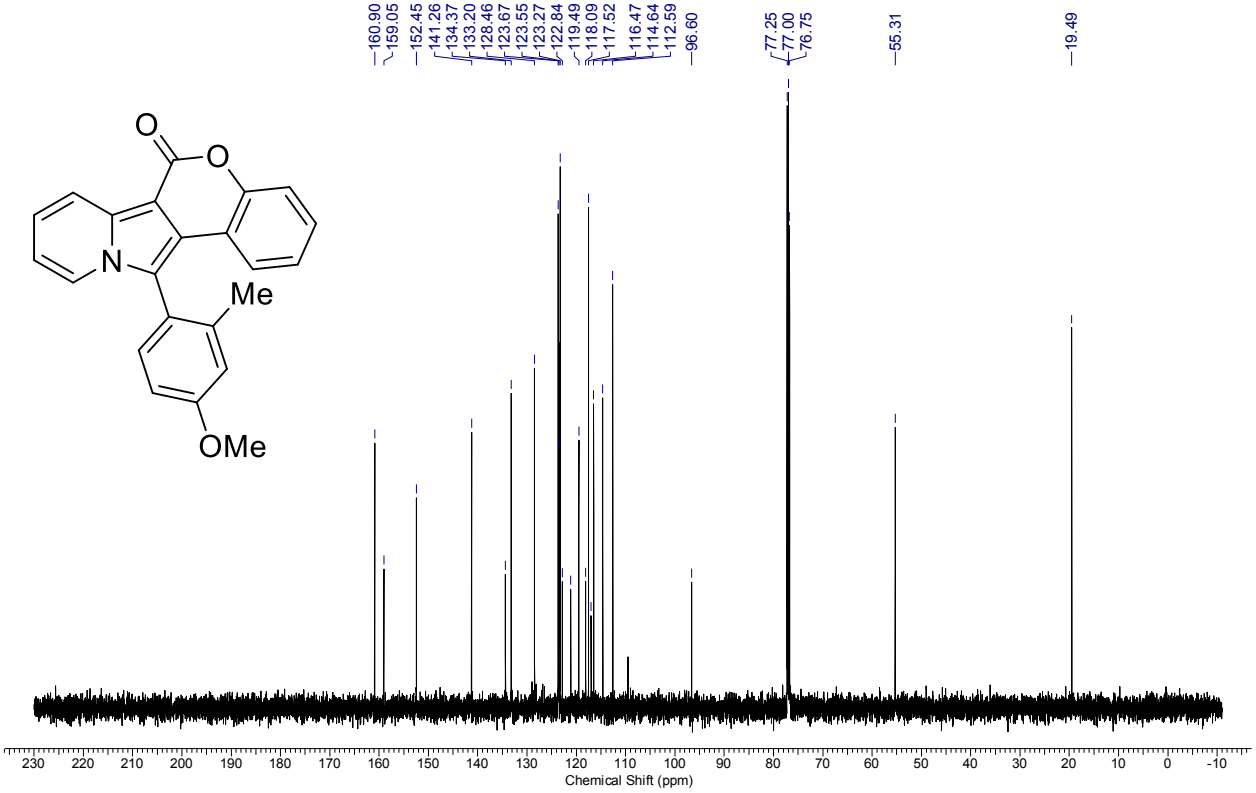
^{13}C NMR Spectrum of **8-5-ag**



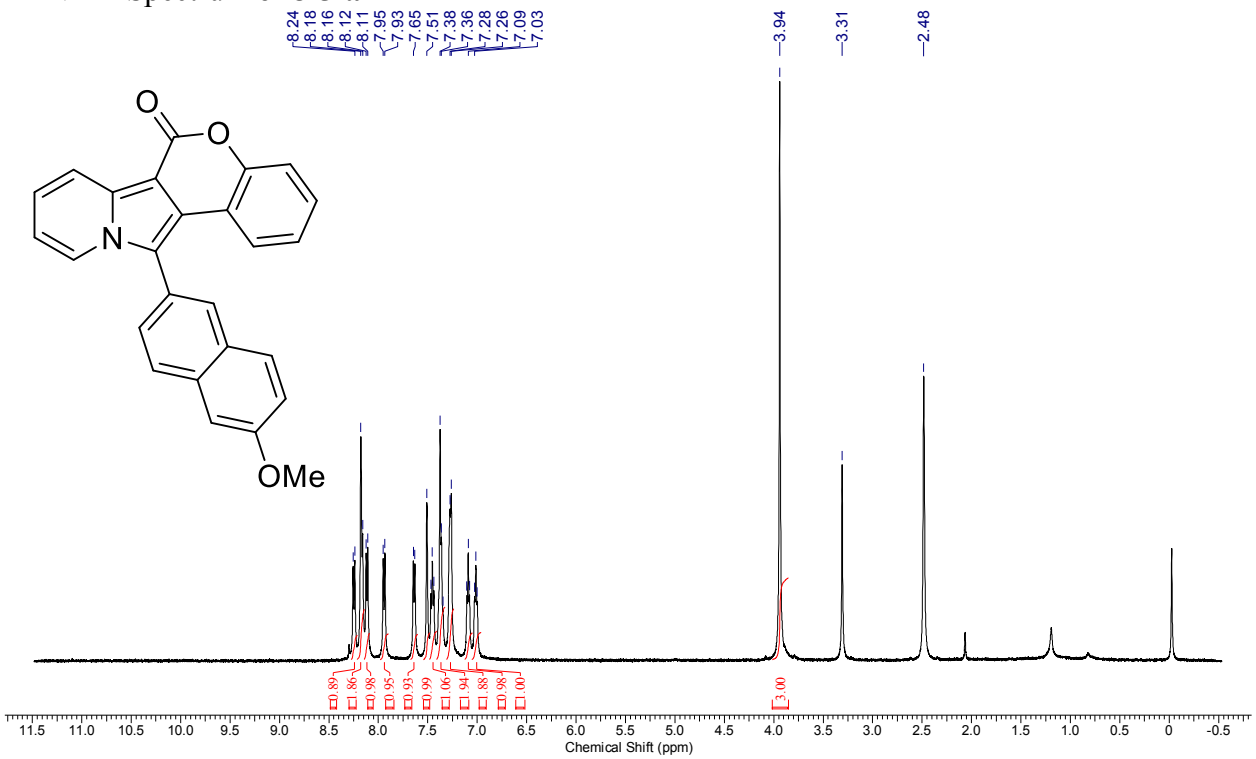
^{1}H NMR Spectrum of **8-5-ah**



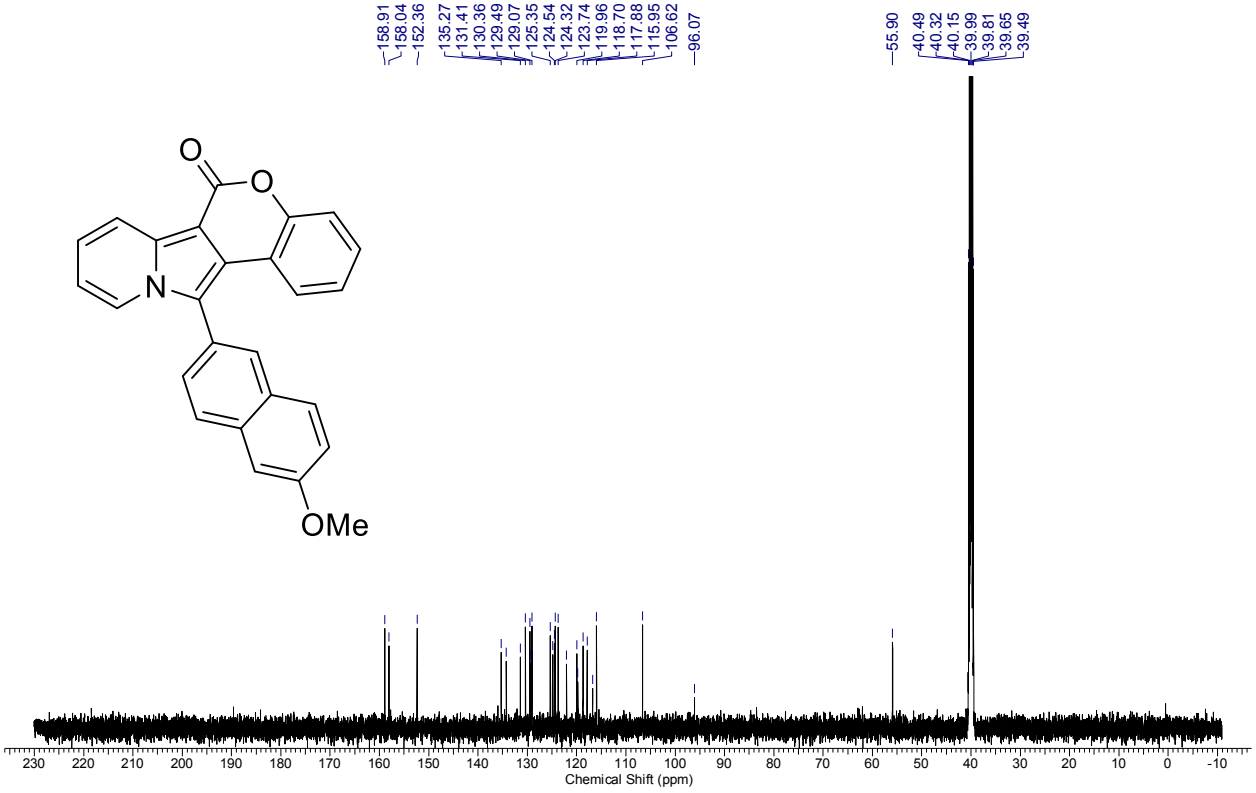
^{13}C NMR Spectrum of **8-5-ah**



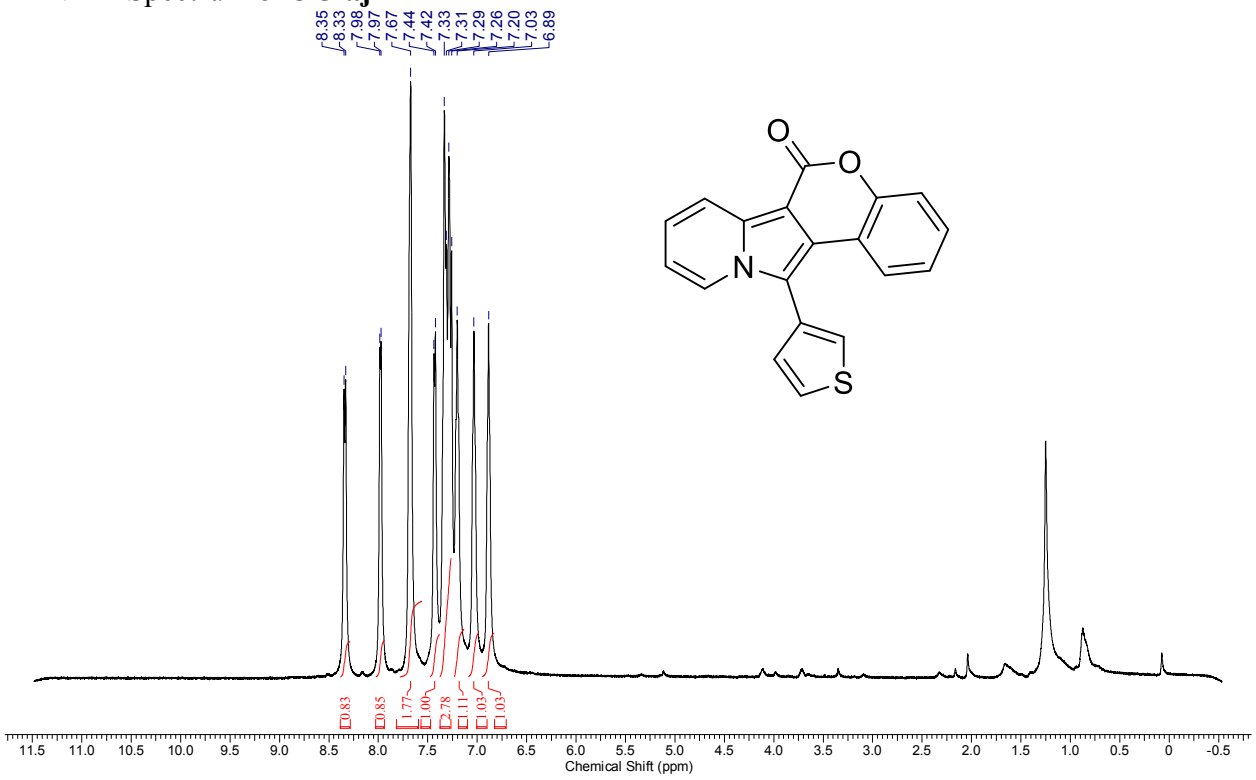
^{1}H NMR Spectrum of **8-5-ai**



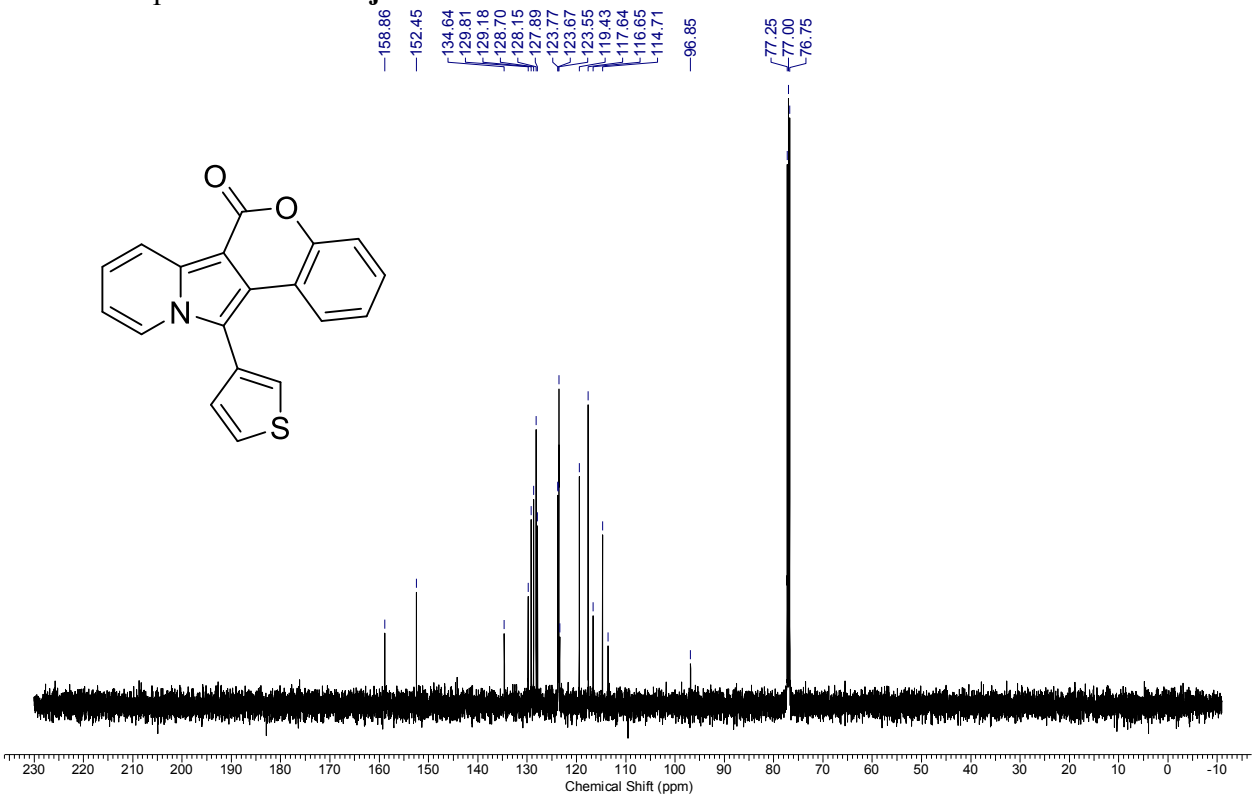
^{13}C NMR Spectrum of **8-5-ai**



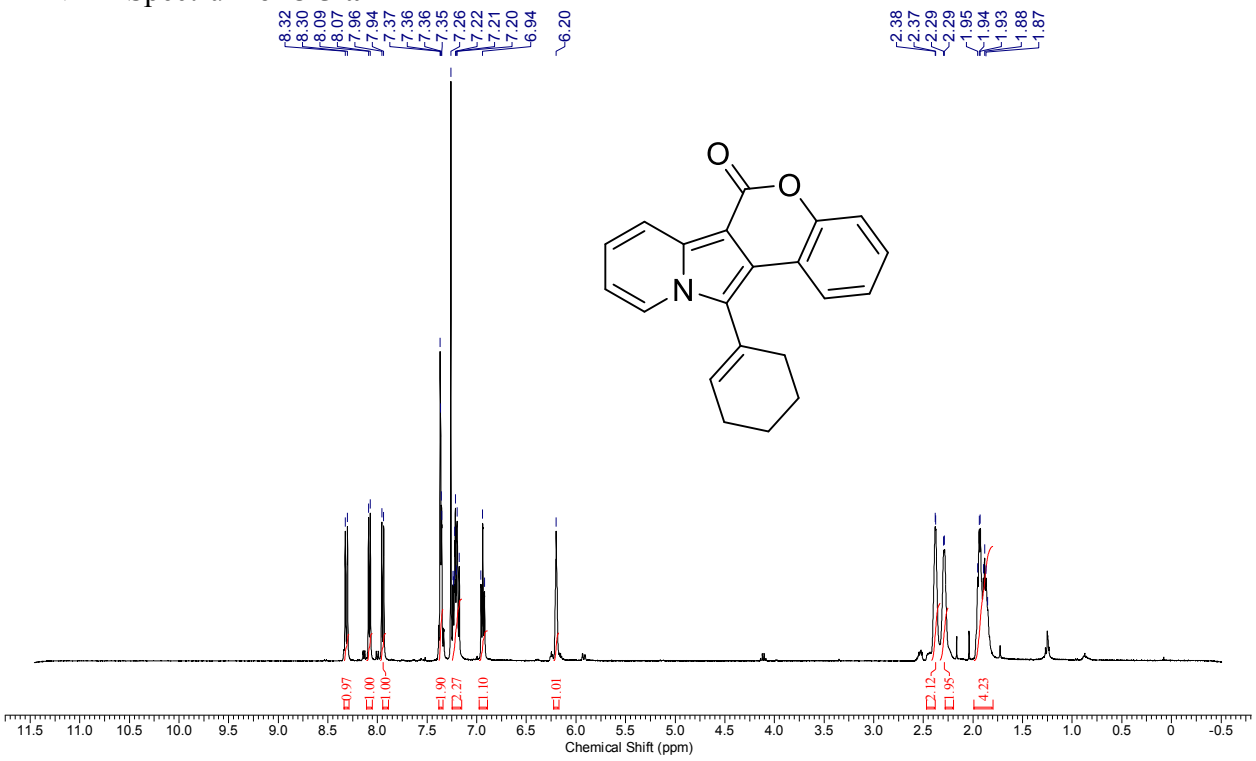
^{1}H NMR Spectrum of **8-5-aj**



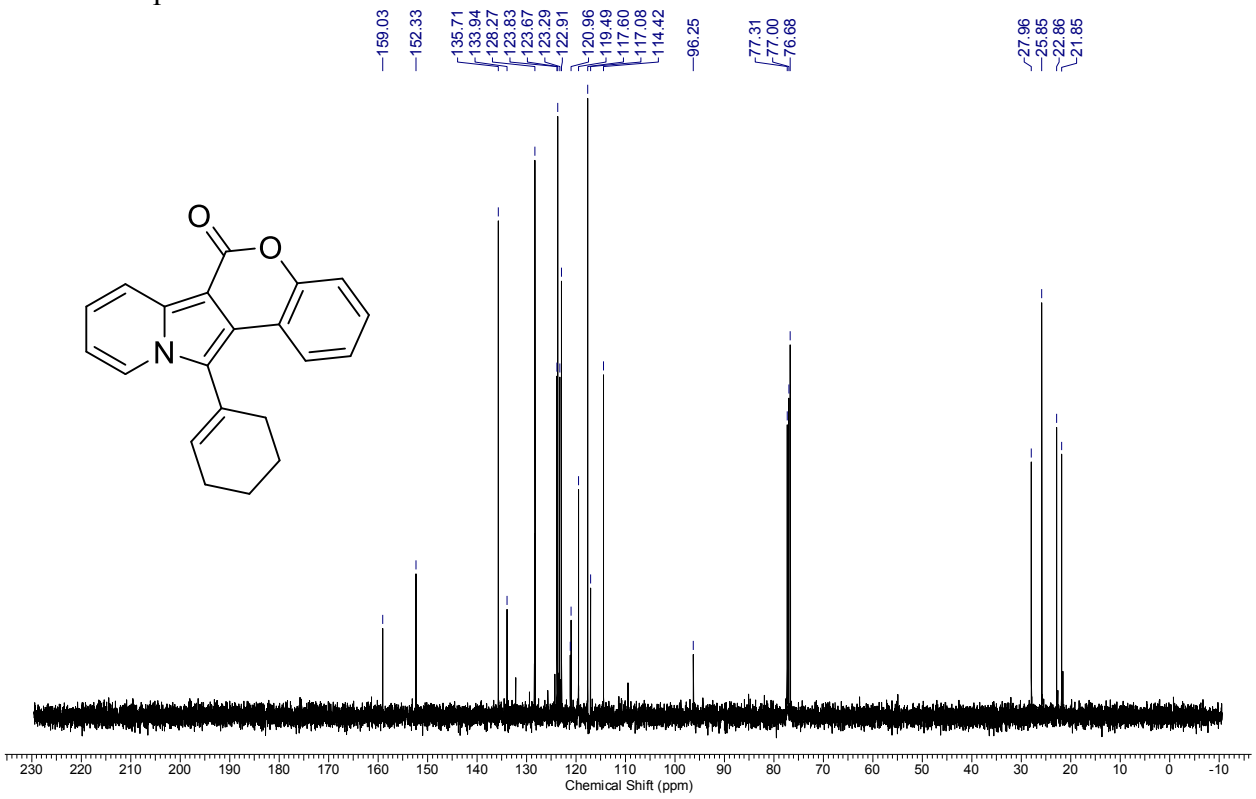
^{13}C NMR Spectrum of **8-5-aj**



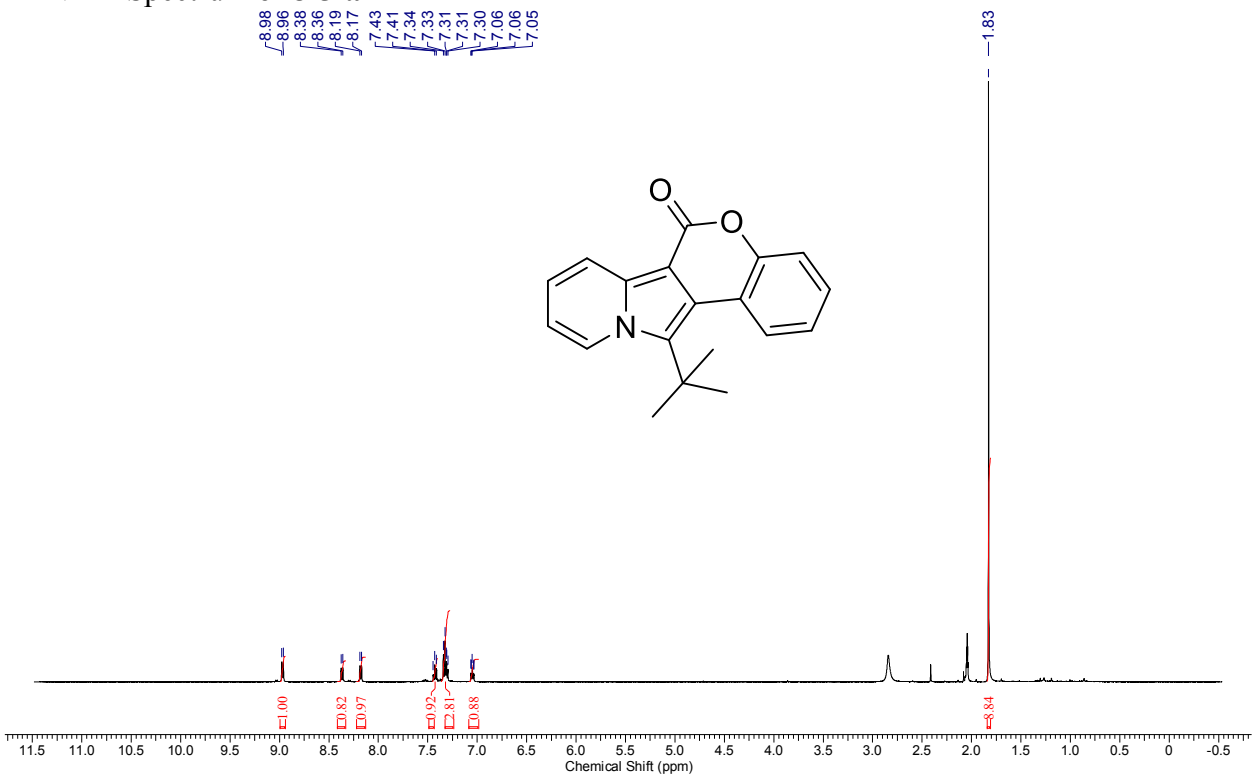
^{1}H NMR Spectrum of **8-5-ak**



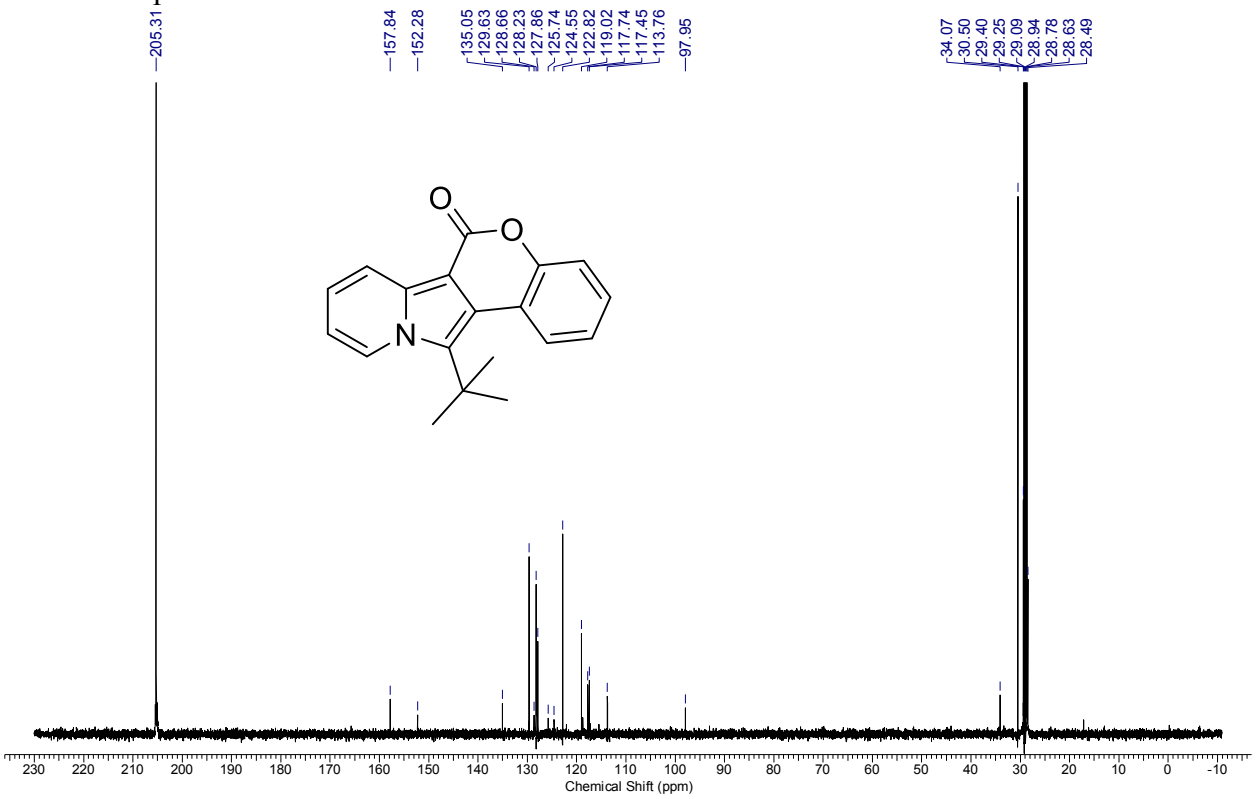
^{13}C NMR Spectrum of **8-5-ak**



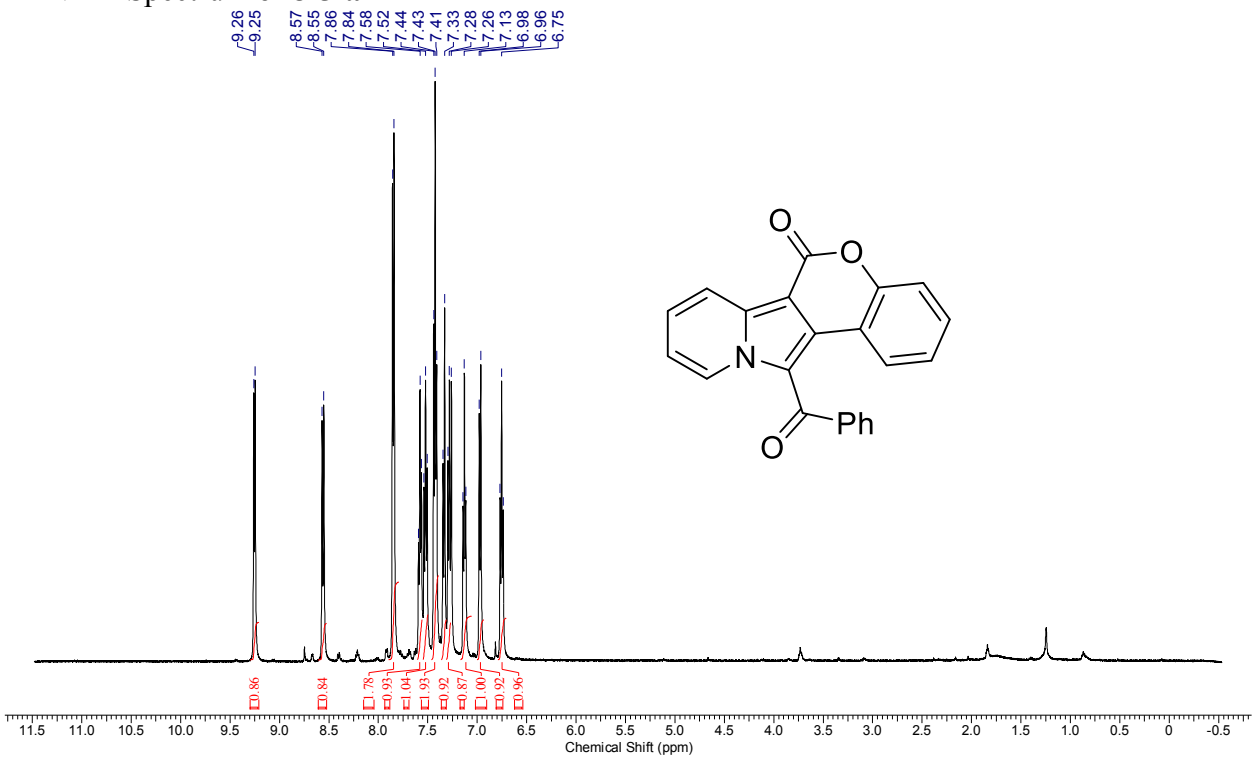
^{1}H NMR Spectrum of **8-5-al**



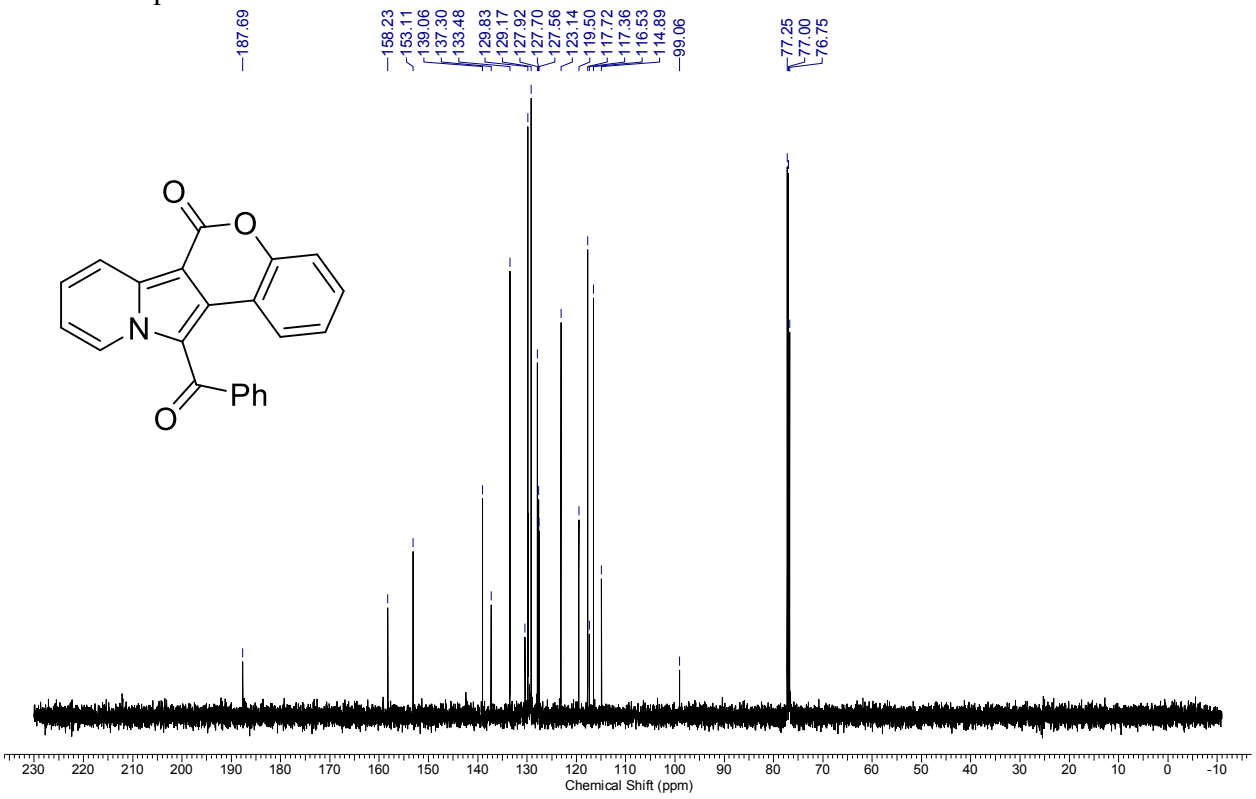
^{13}C NMR Spectrum of **8-5-al**



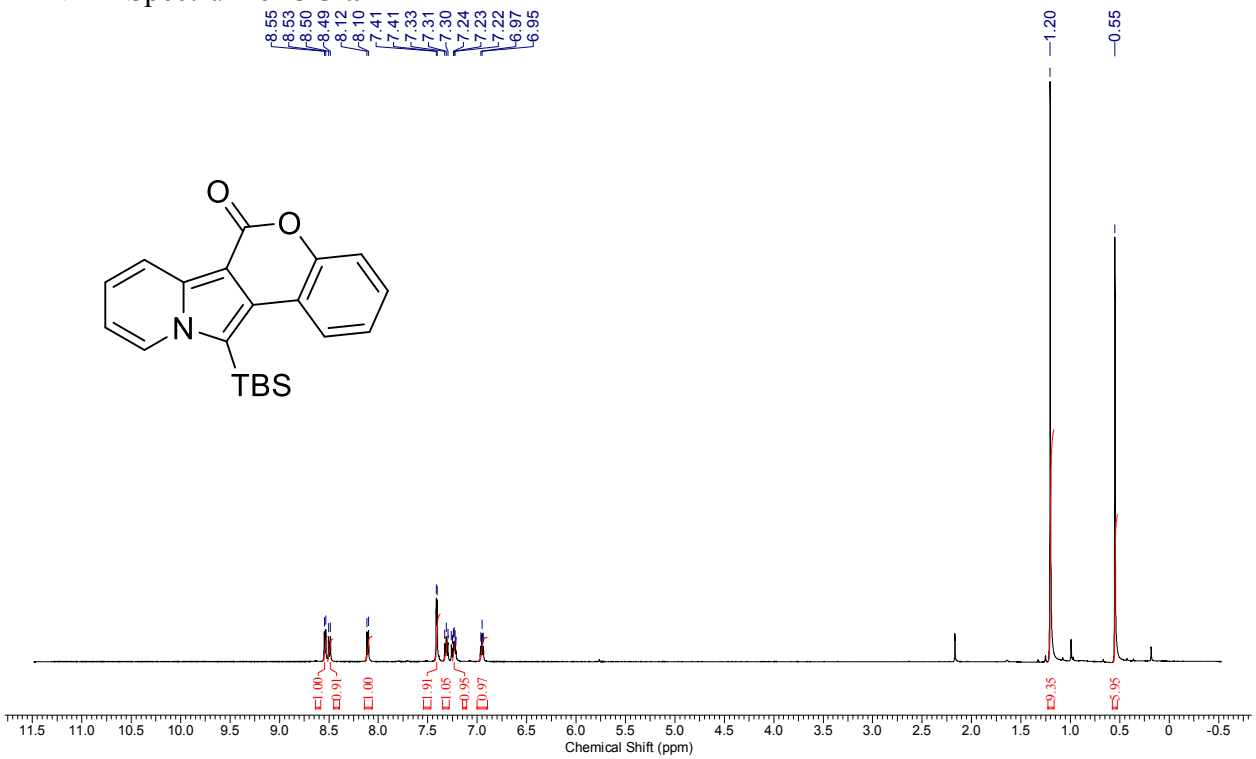
^{1}H NMR Spectrum of **8-5-am**



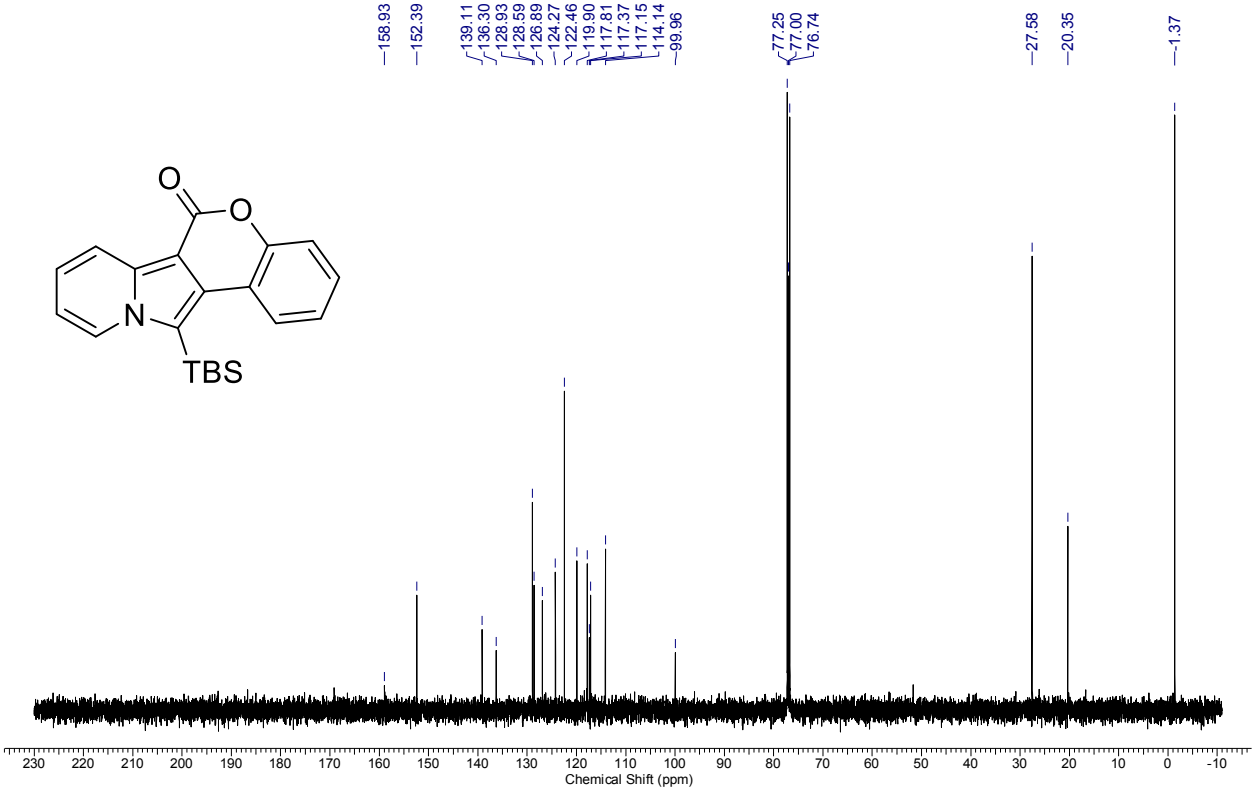
^{13}C NMR Spectrum of **8-5-am**



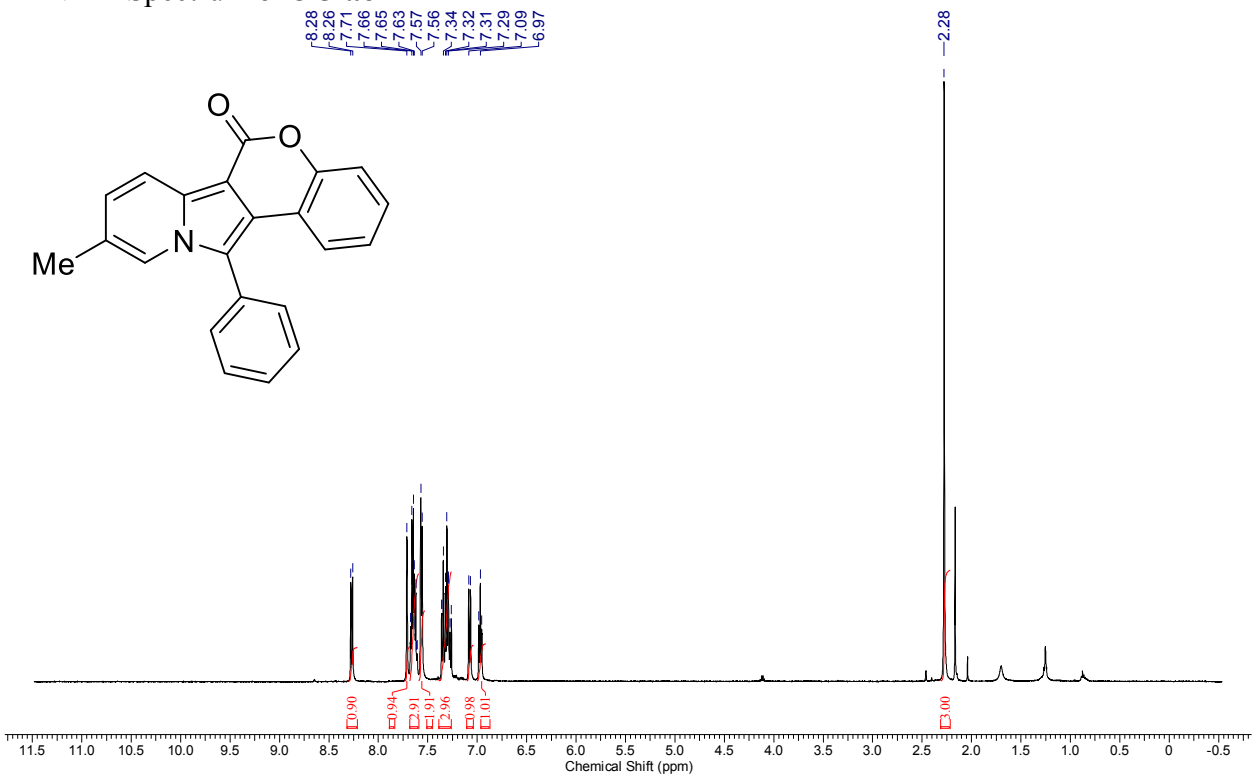
^{1}H NMR Spectrum of **8-5-an**



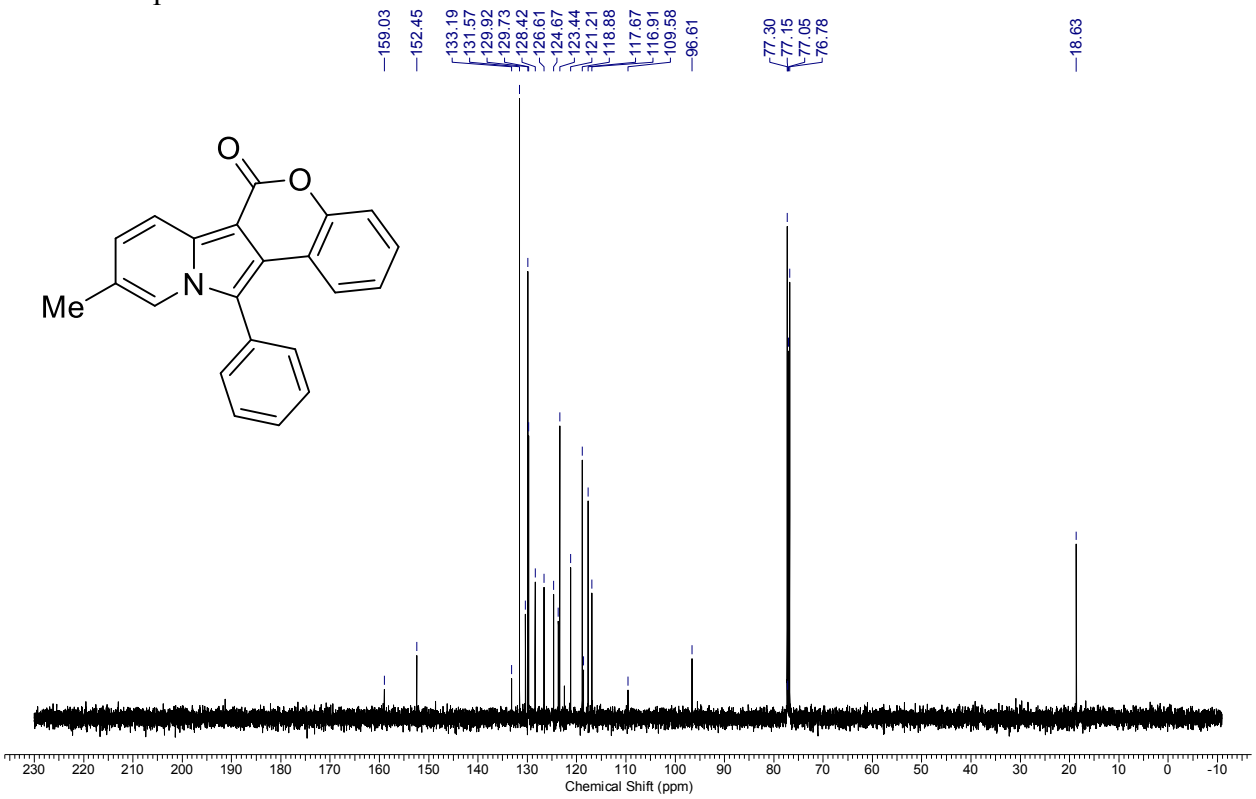
^{13}C NMR Spectrum of **8-5-an**



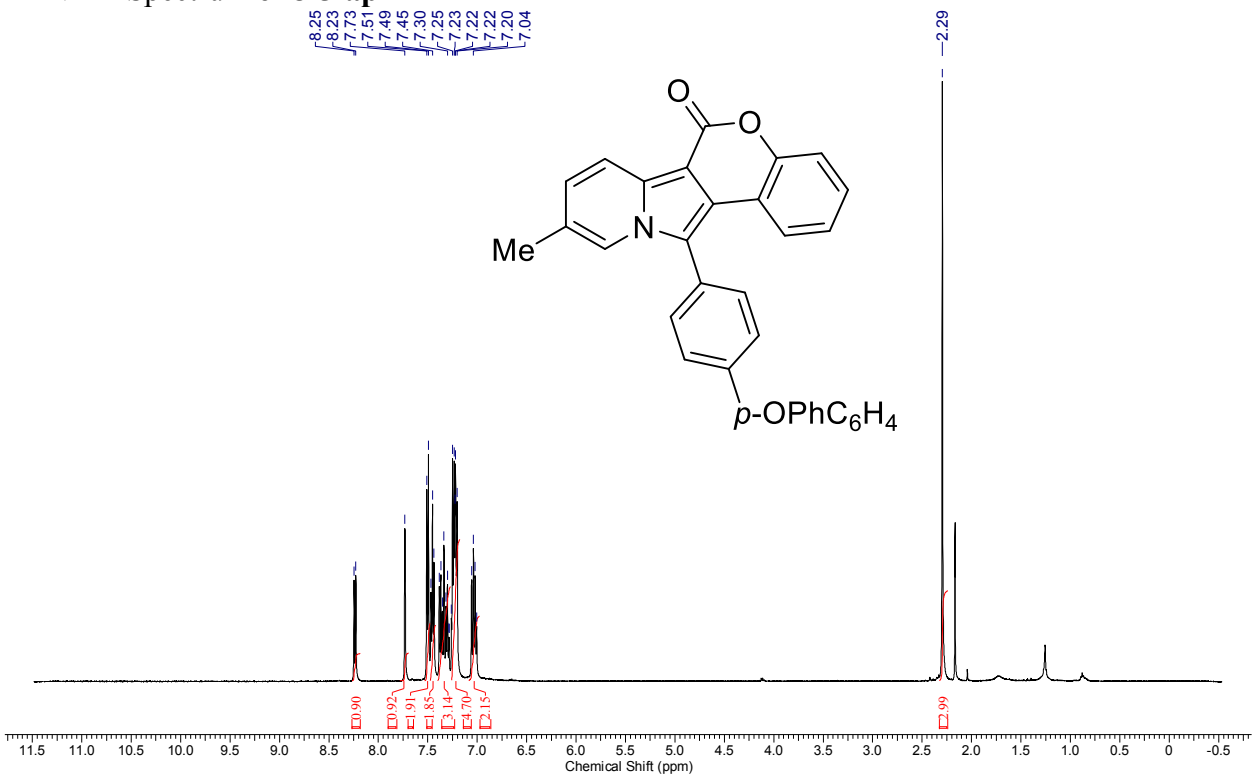
^{1}H NMR Spectrum of **8-5-ao**



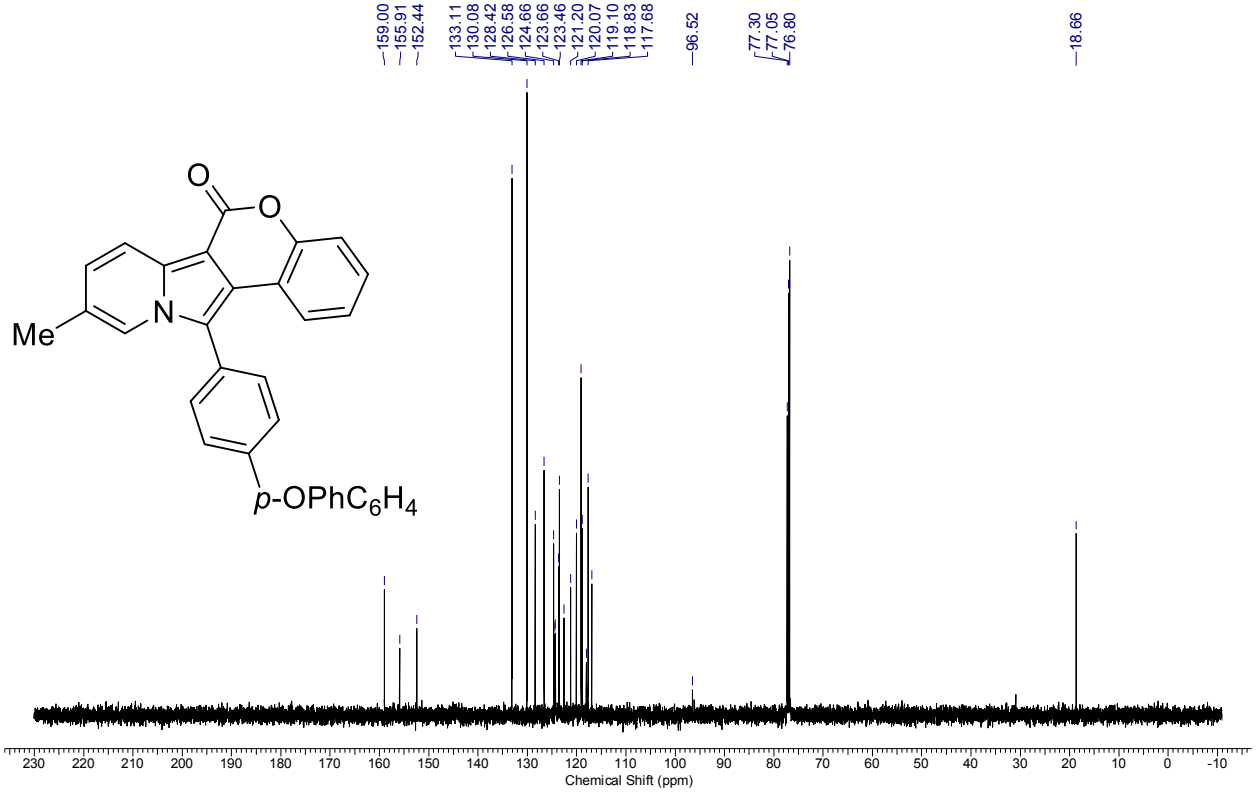
^{13}C NMR Spectrum of **8-5-ao**



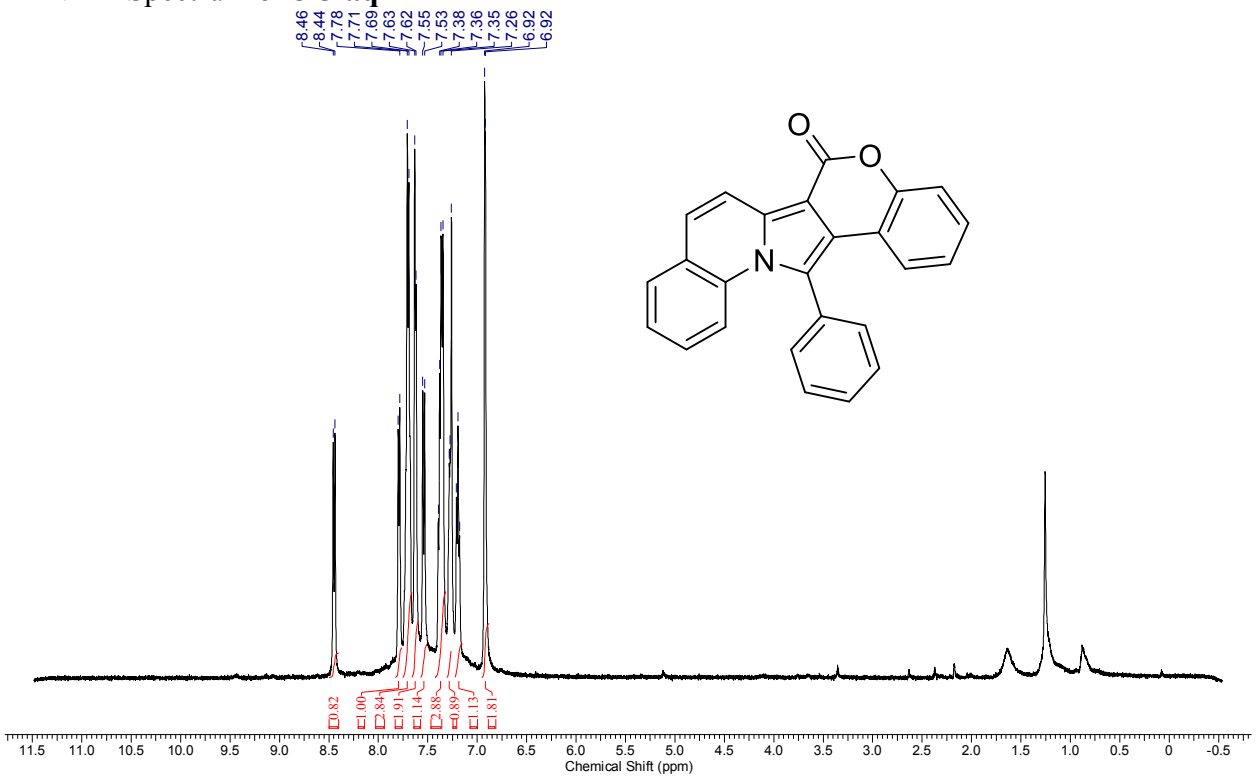
^{1}H NMR Spectrum of **8-5-ap**



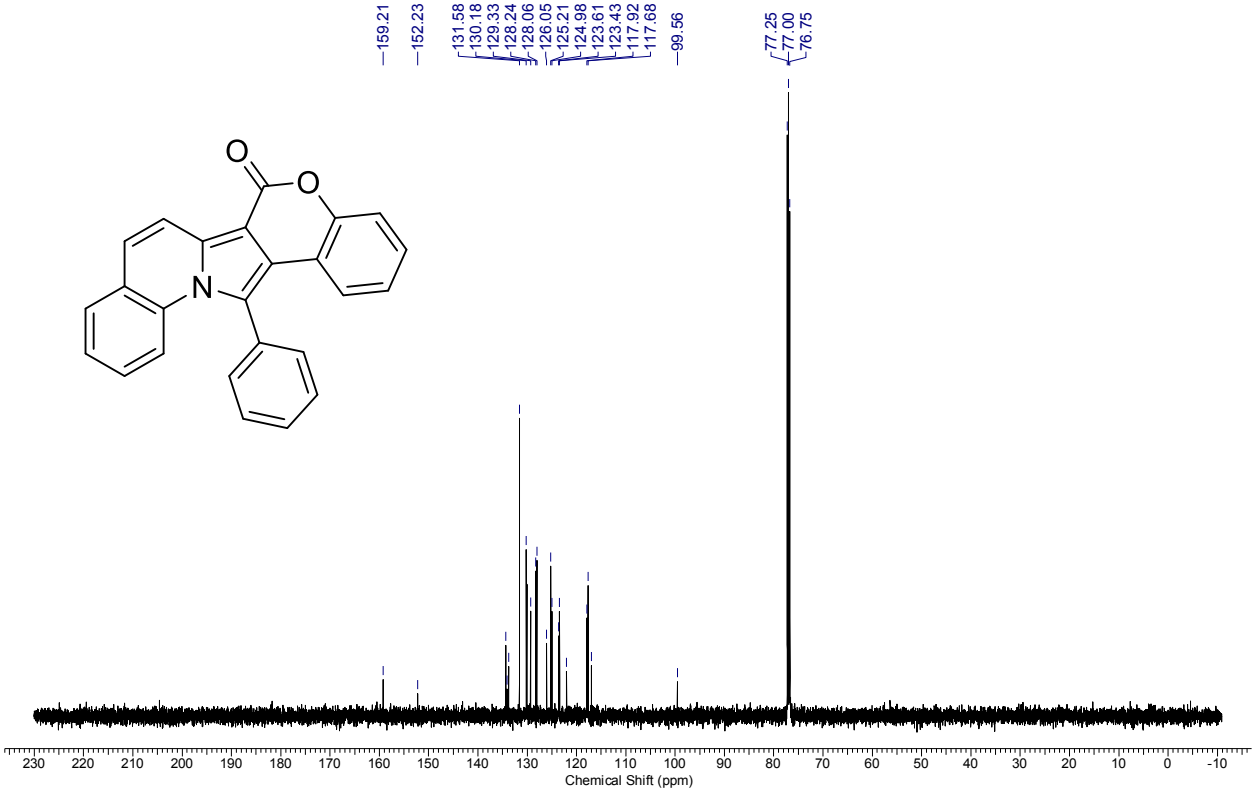
^{13}C NMR Spectrum of **8-5-ap**



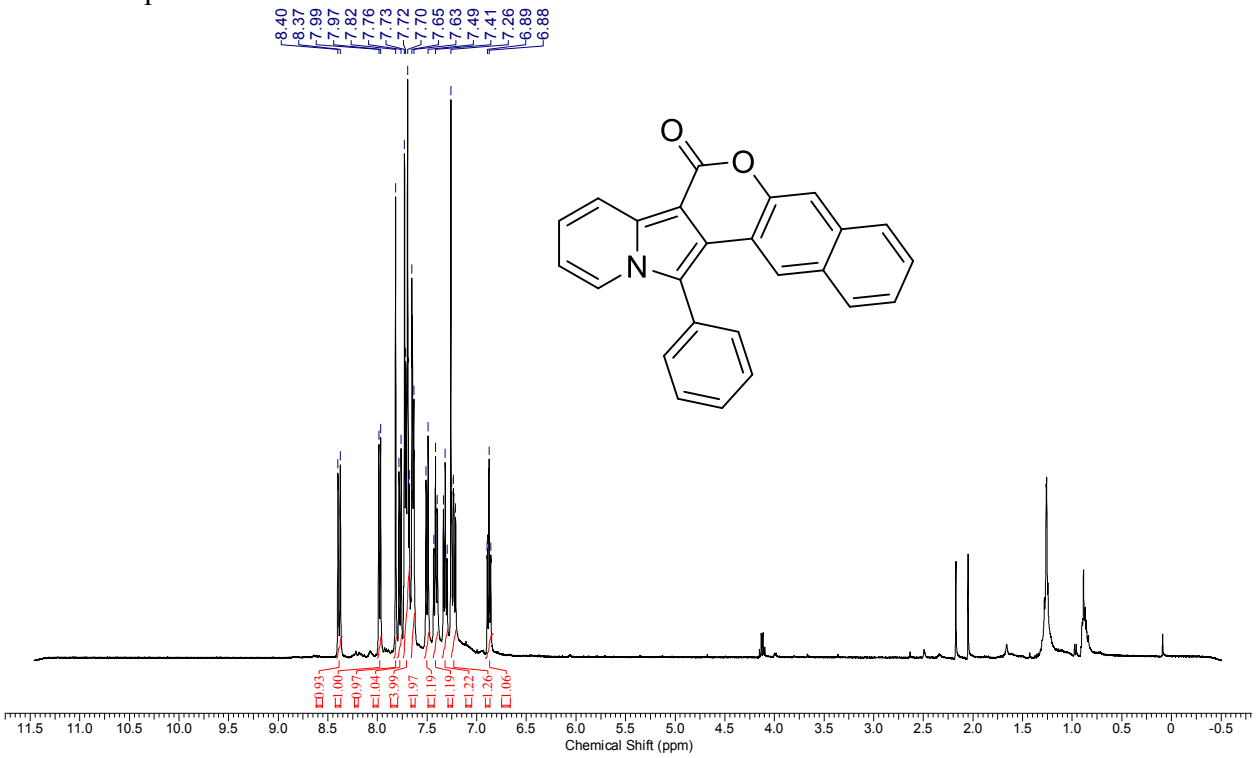
^{1}H NMR Spectrum of **8-5-aq**



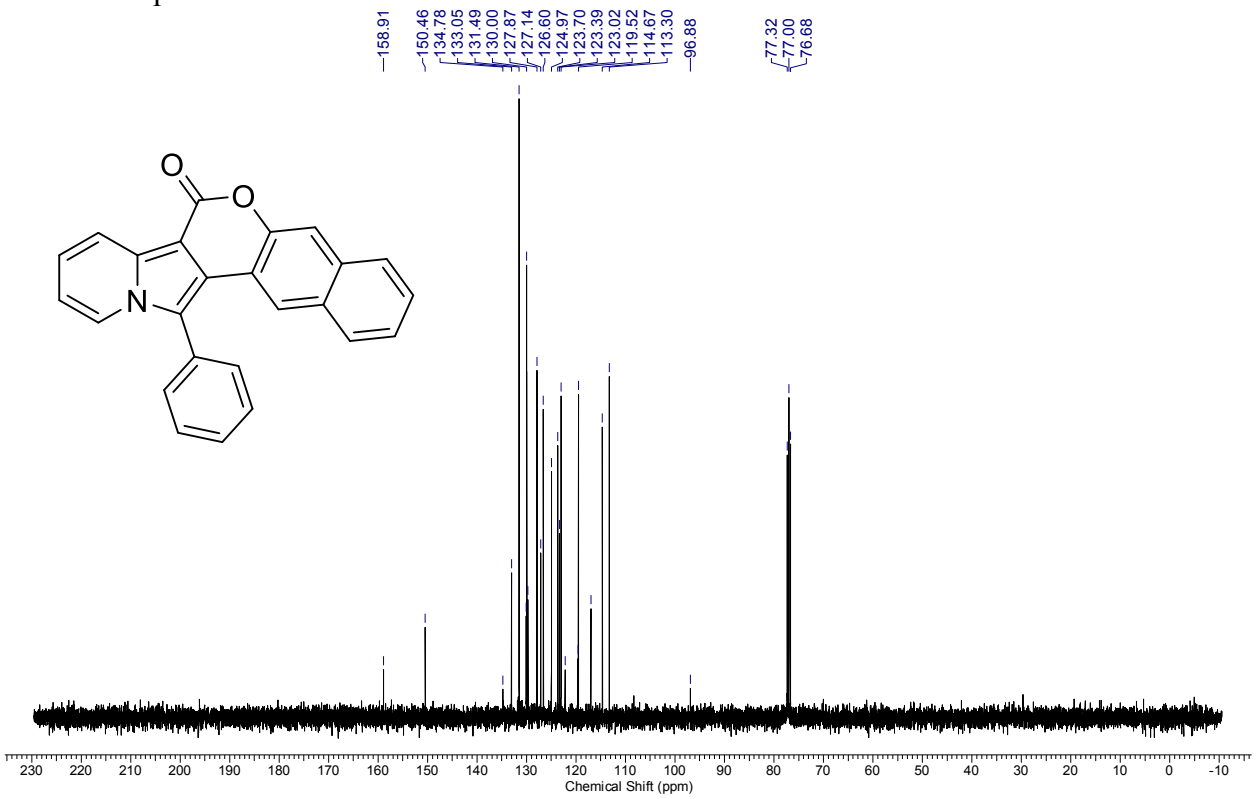
^{13}C NMR Spectrum of **8-5-aq**



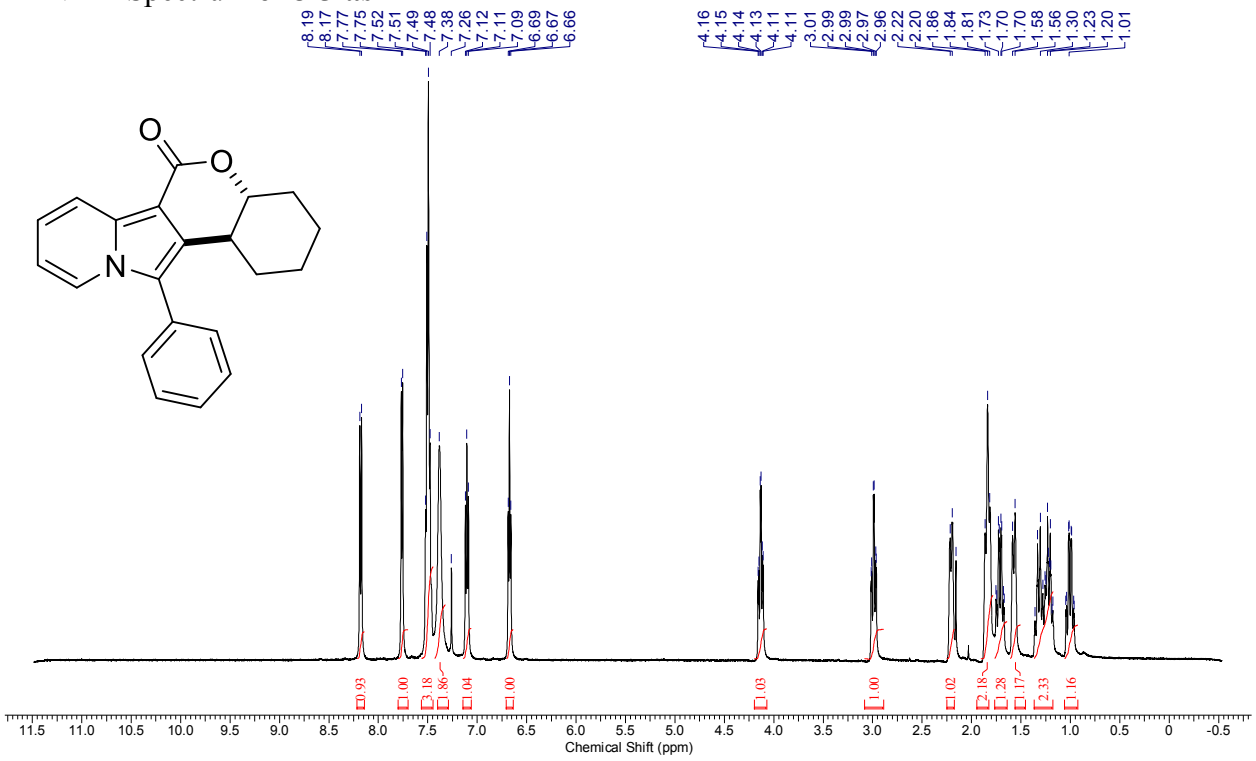
^{1}H NMR Spectrum of **8-5-ar**



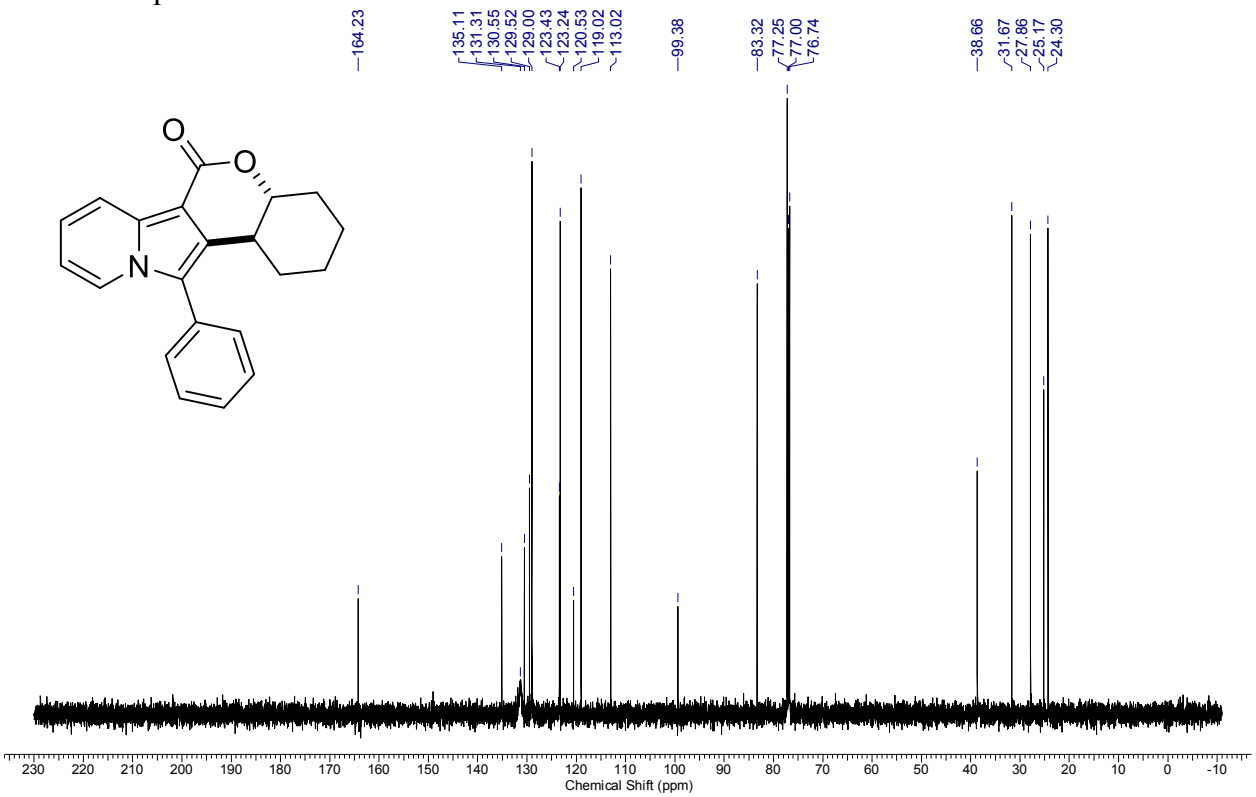
^{13}C NMR Spectrum of **8-5-ar**



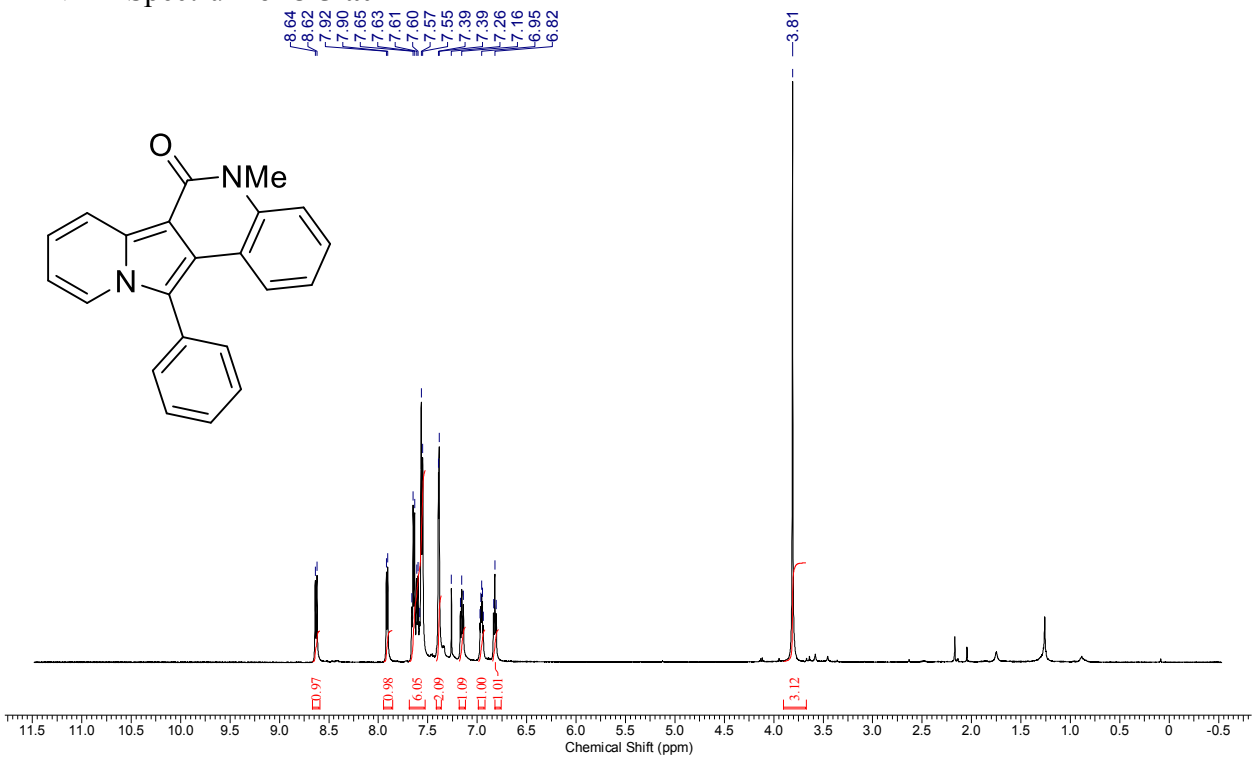
^{1}H NMR Spectrum of **8-5-as**



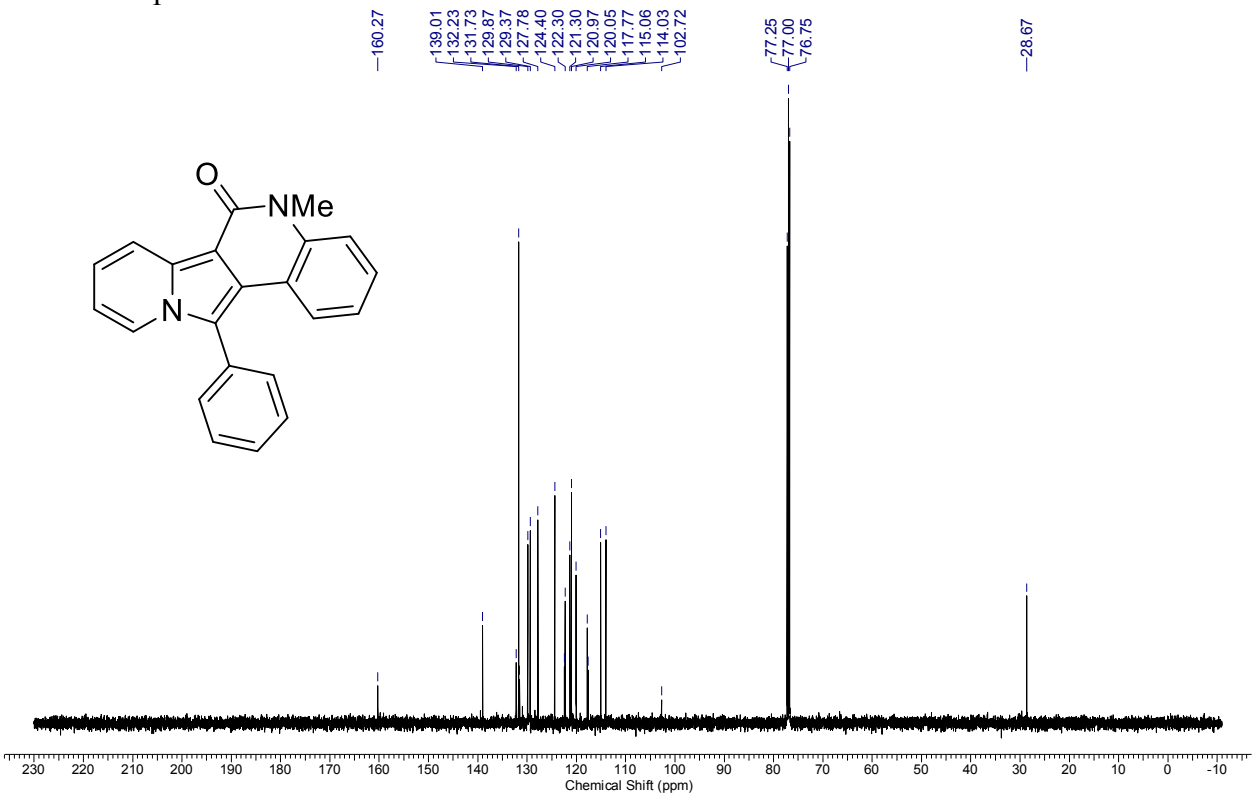
^{13}C NMR Spectrum of **8-5-as**



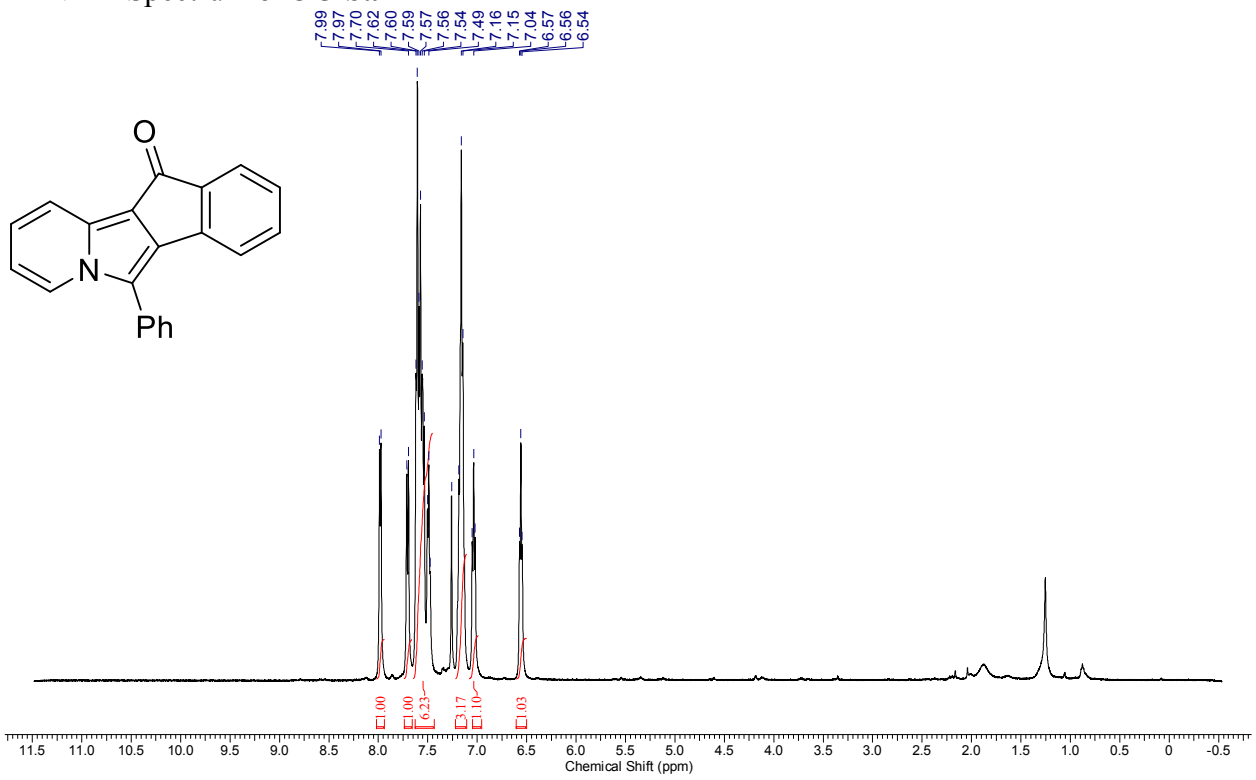
^{1}H NMR Spectrum of **8-5-at**



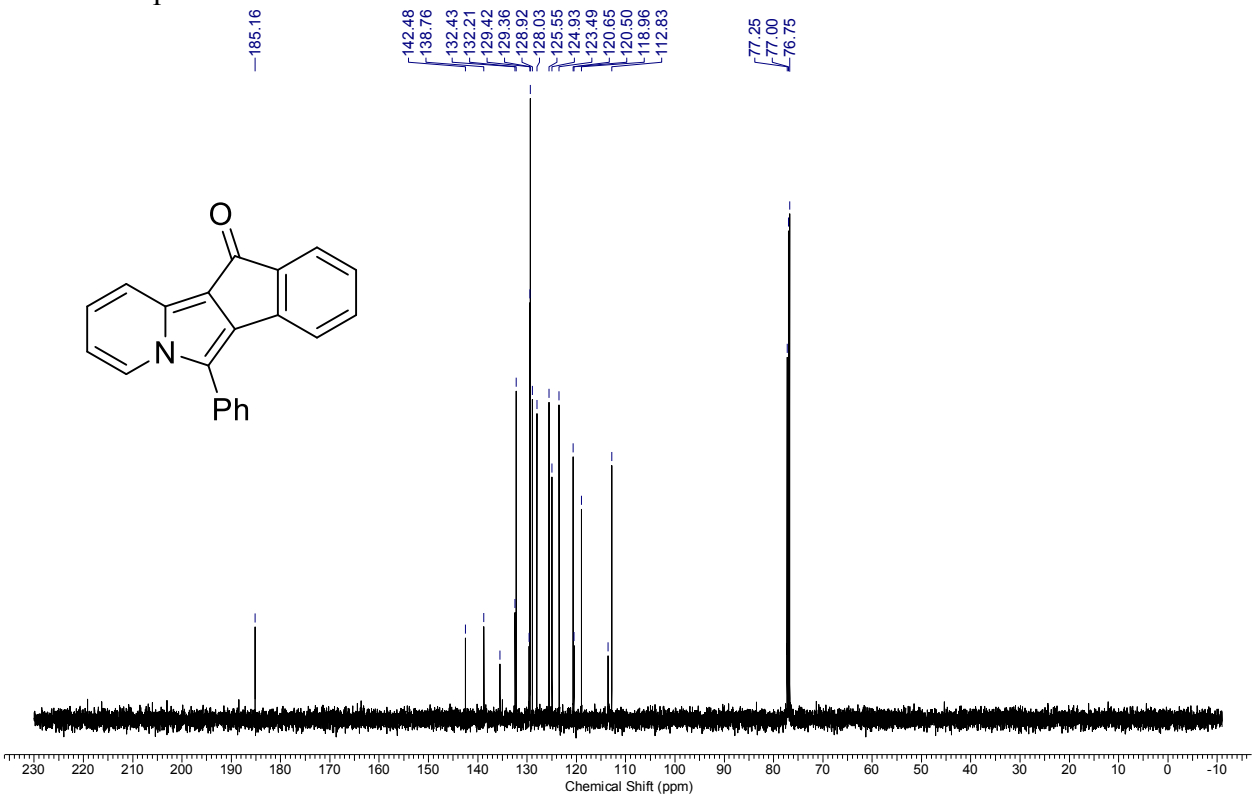
^{13}C NMR Spectrum of **8-5-at**



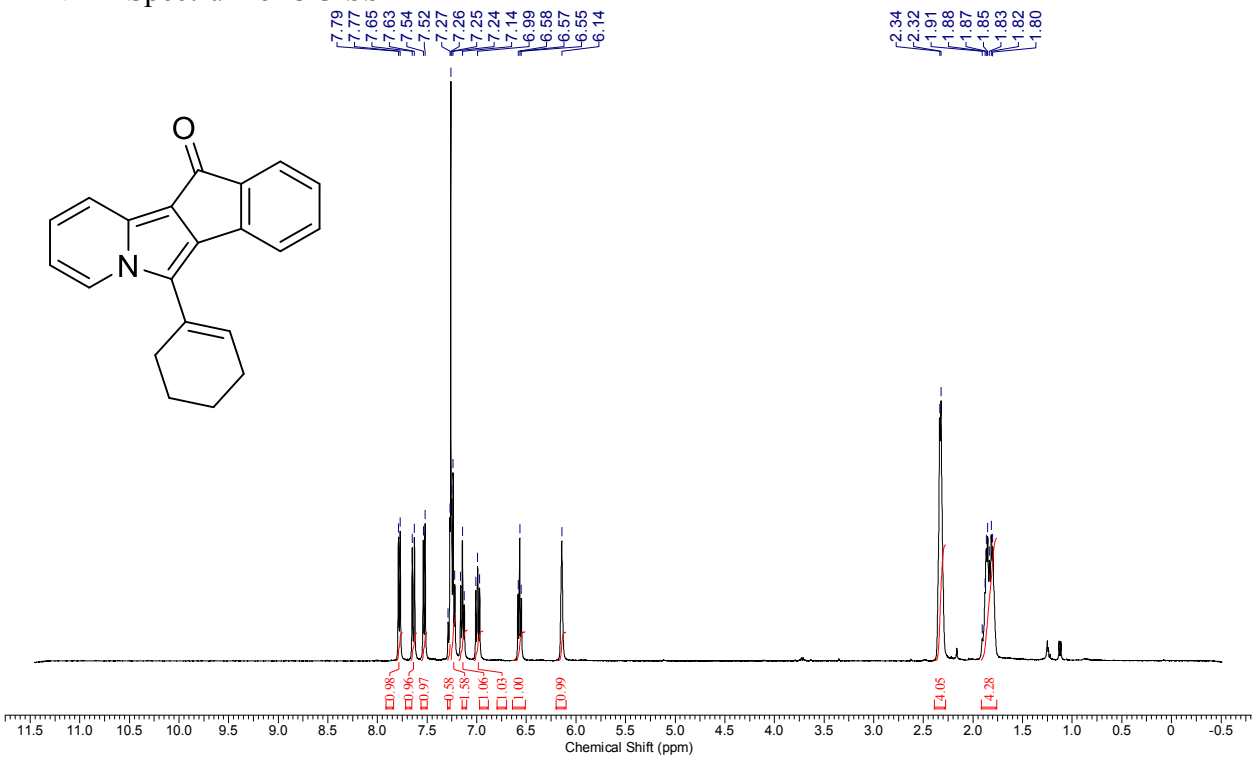
^{1}H NMR Spectrum of **8-5-ba**



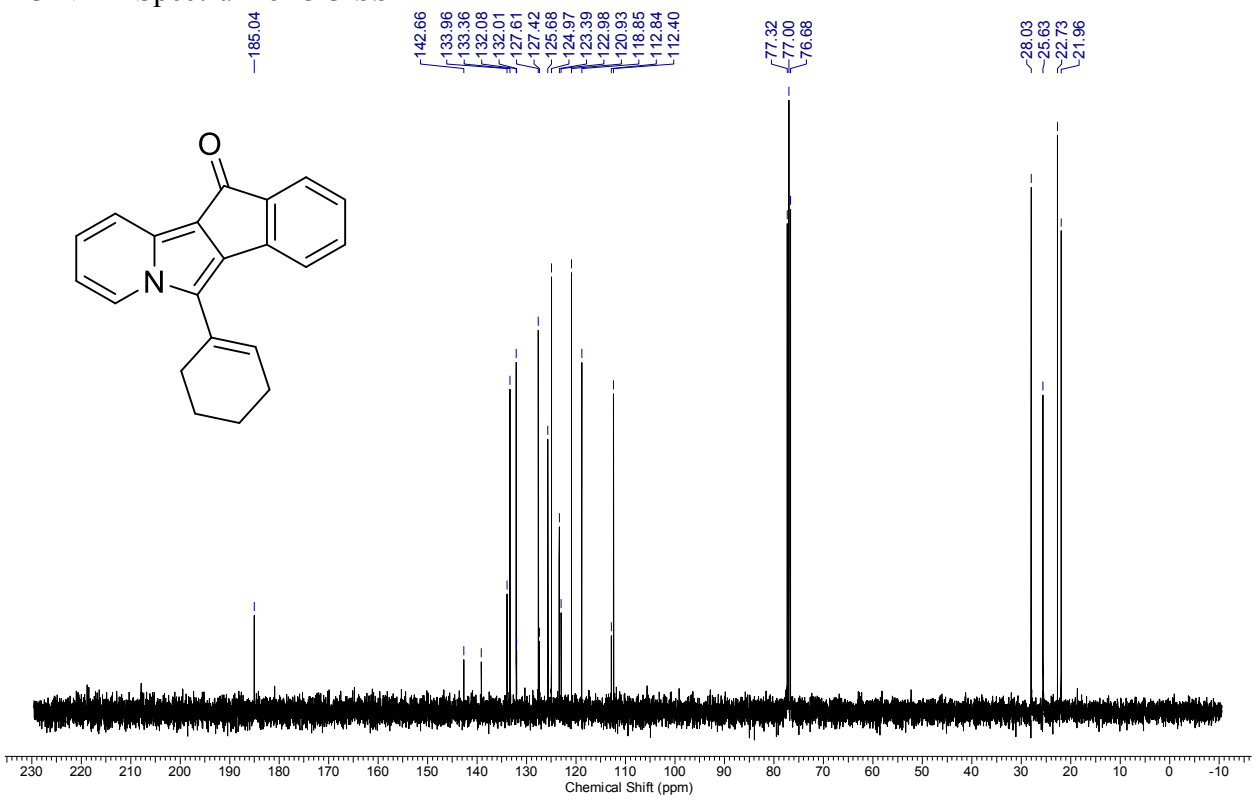
^{13}C NMR Spectrum of **8-5-ba**



^{1}H NMR Spectrum of **8-5-bb**



^{13}C NMR Spectrum of **8-5-bb**



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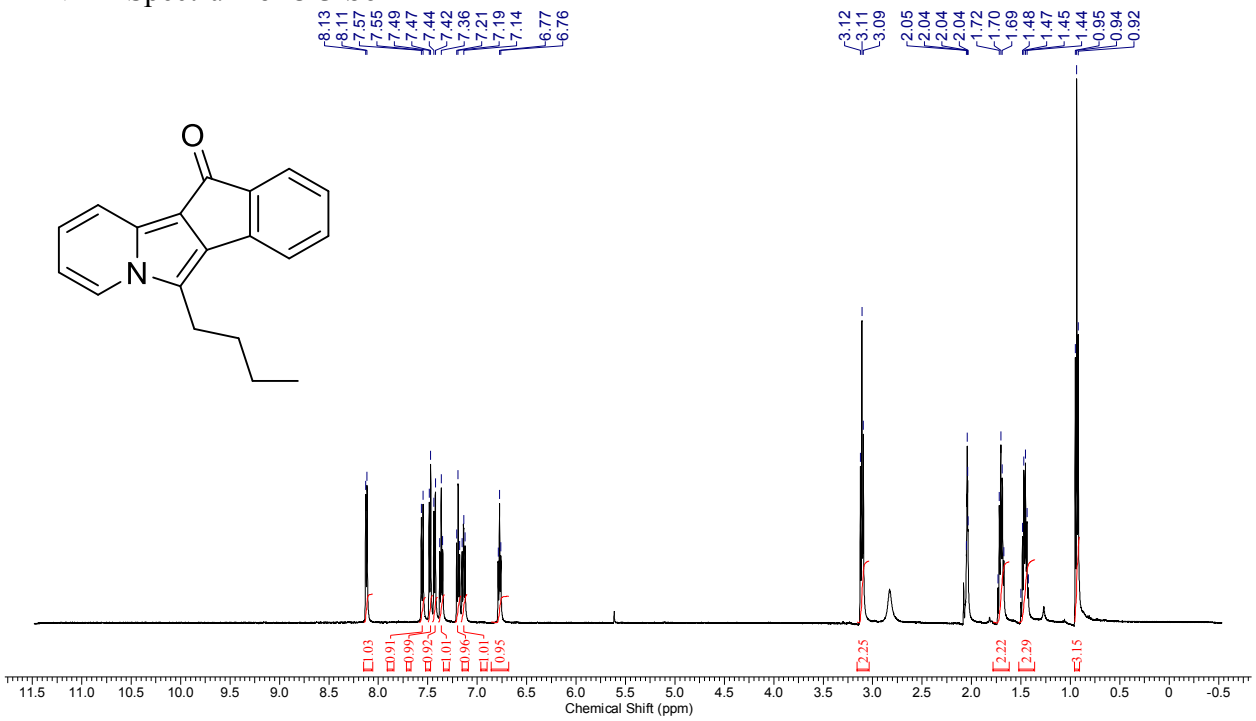

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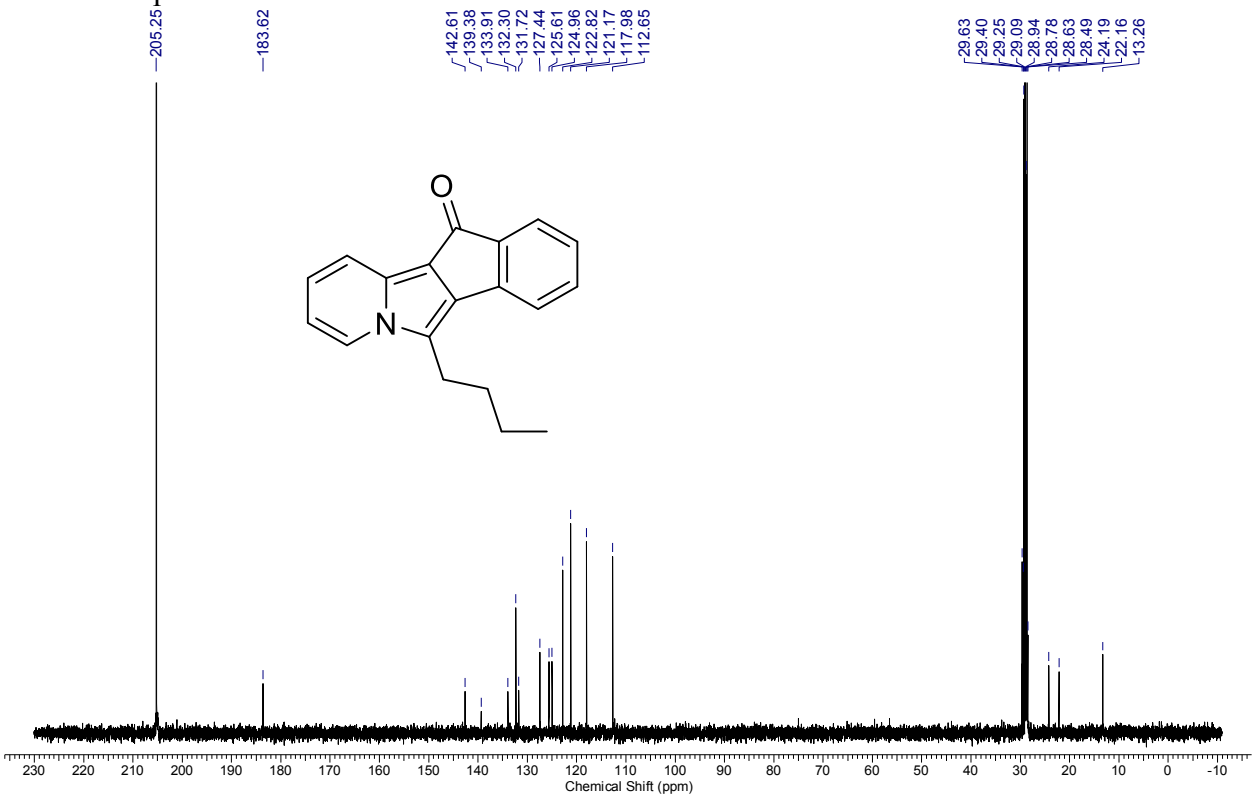

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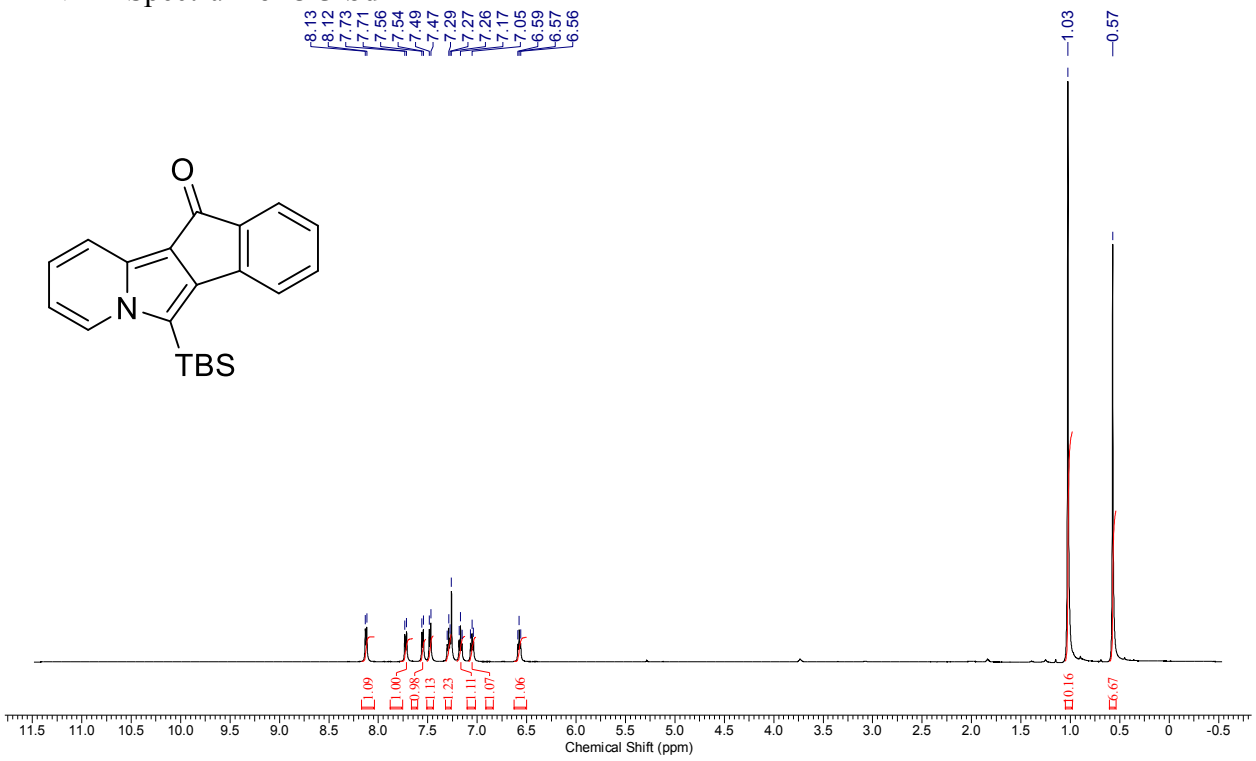

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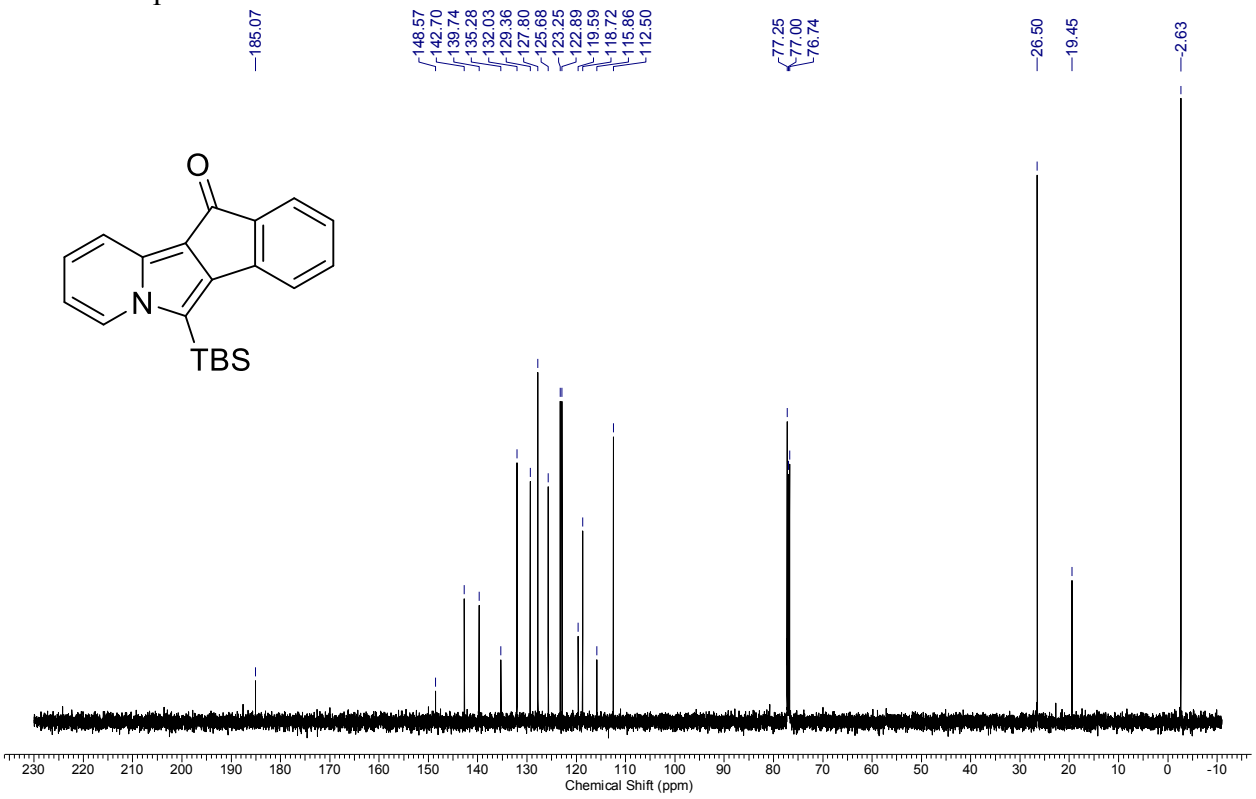

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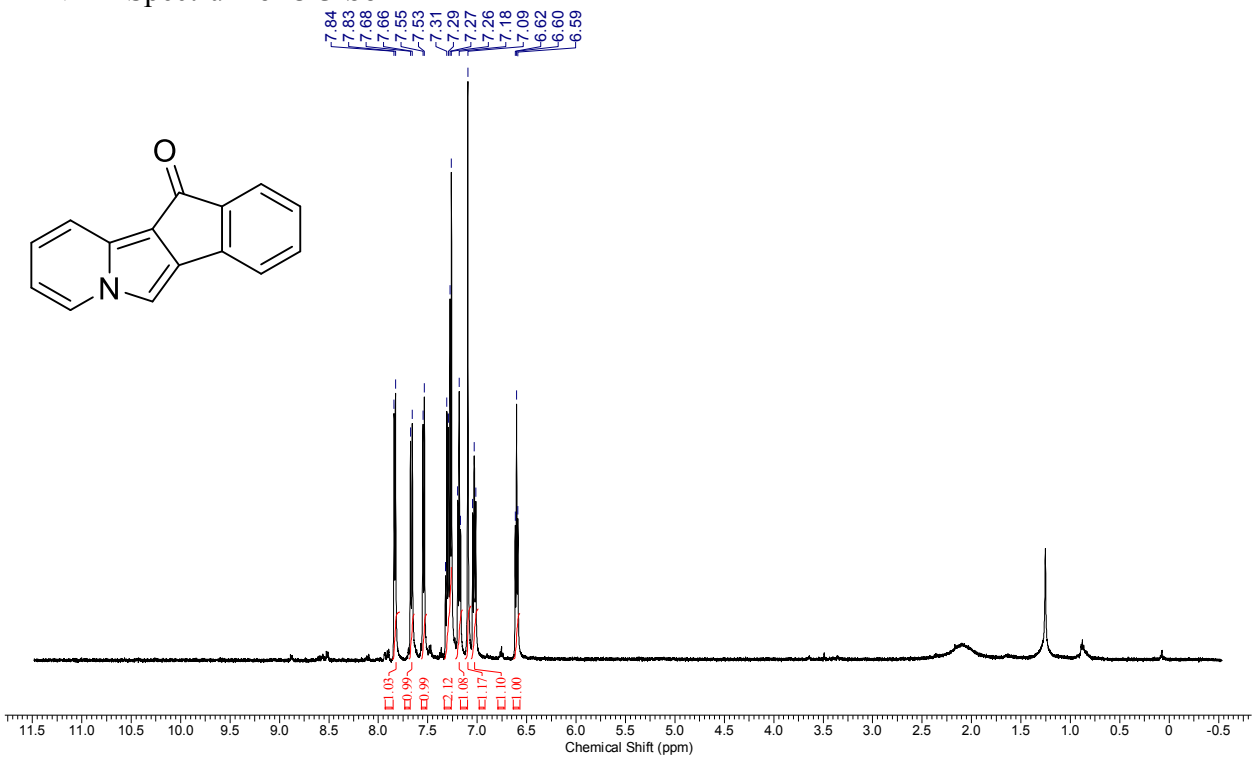

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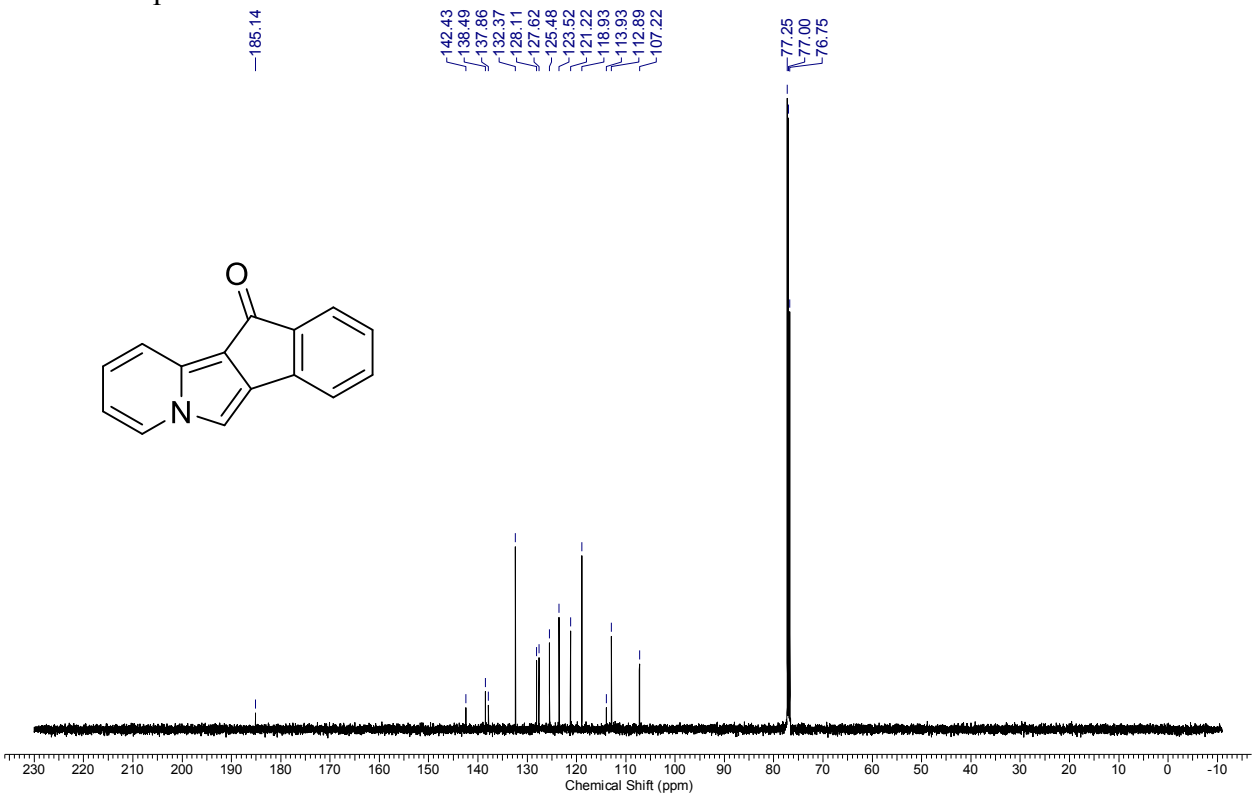

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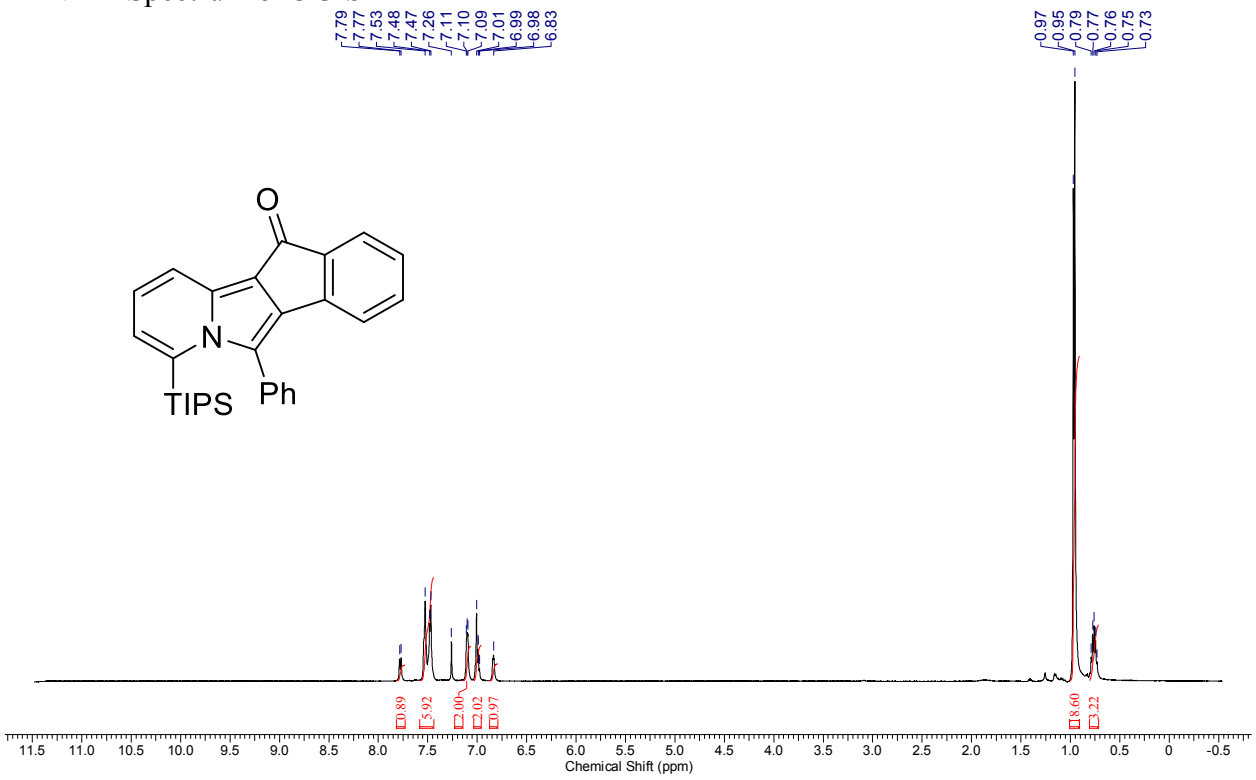

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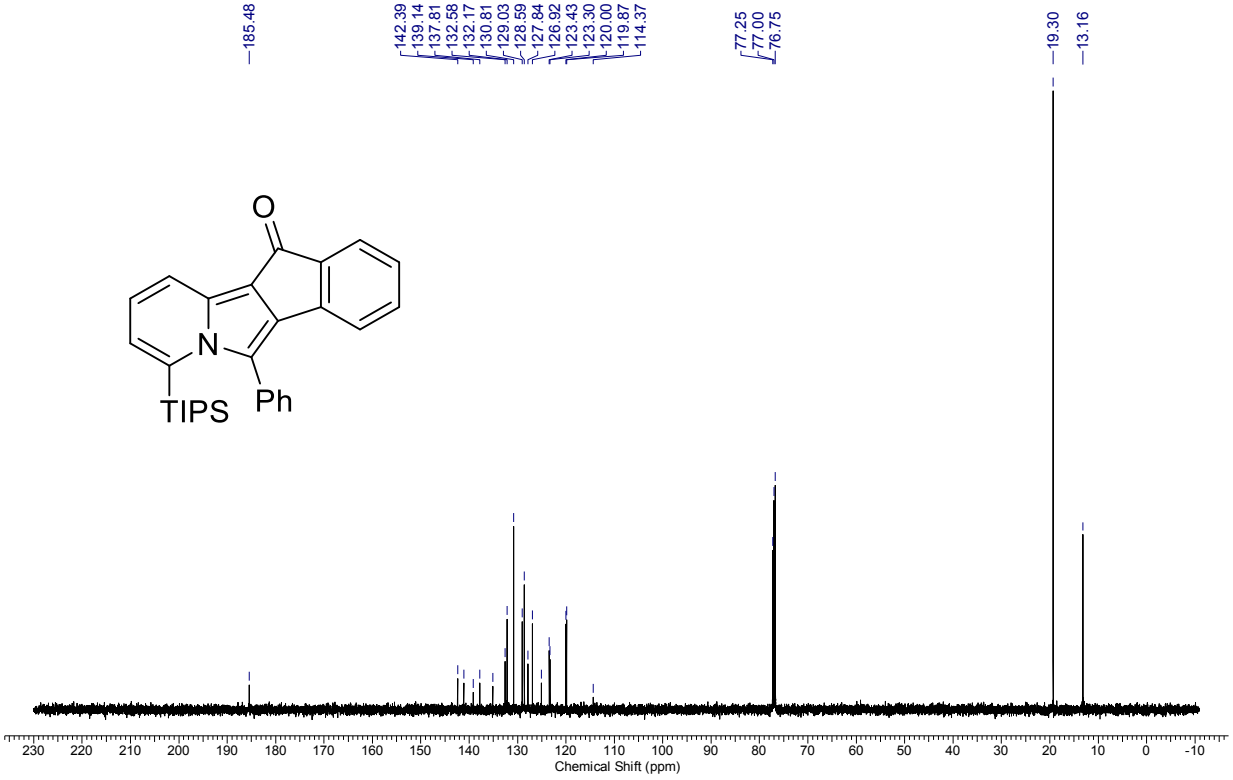

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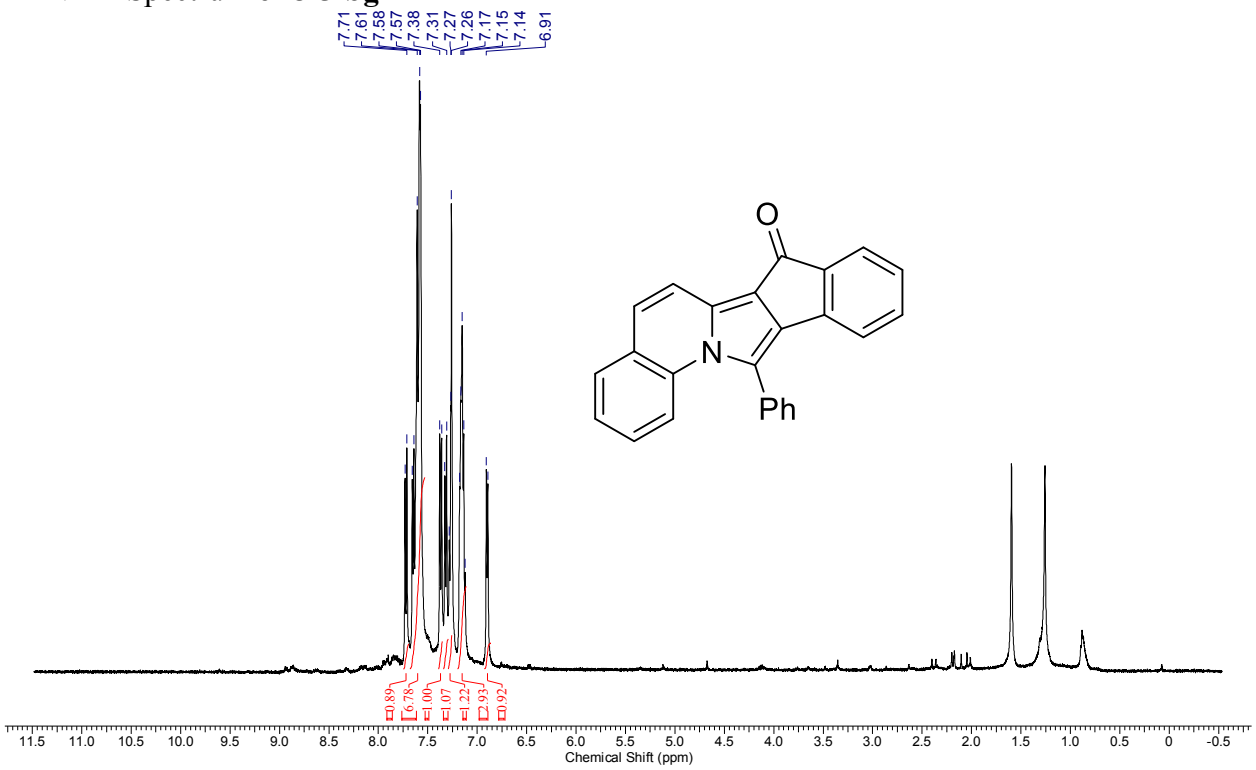

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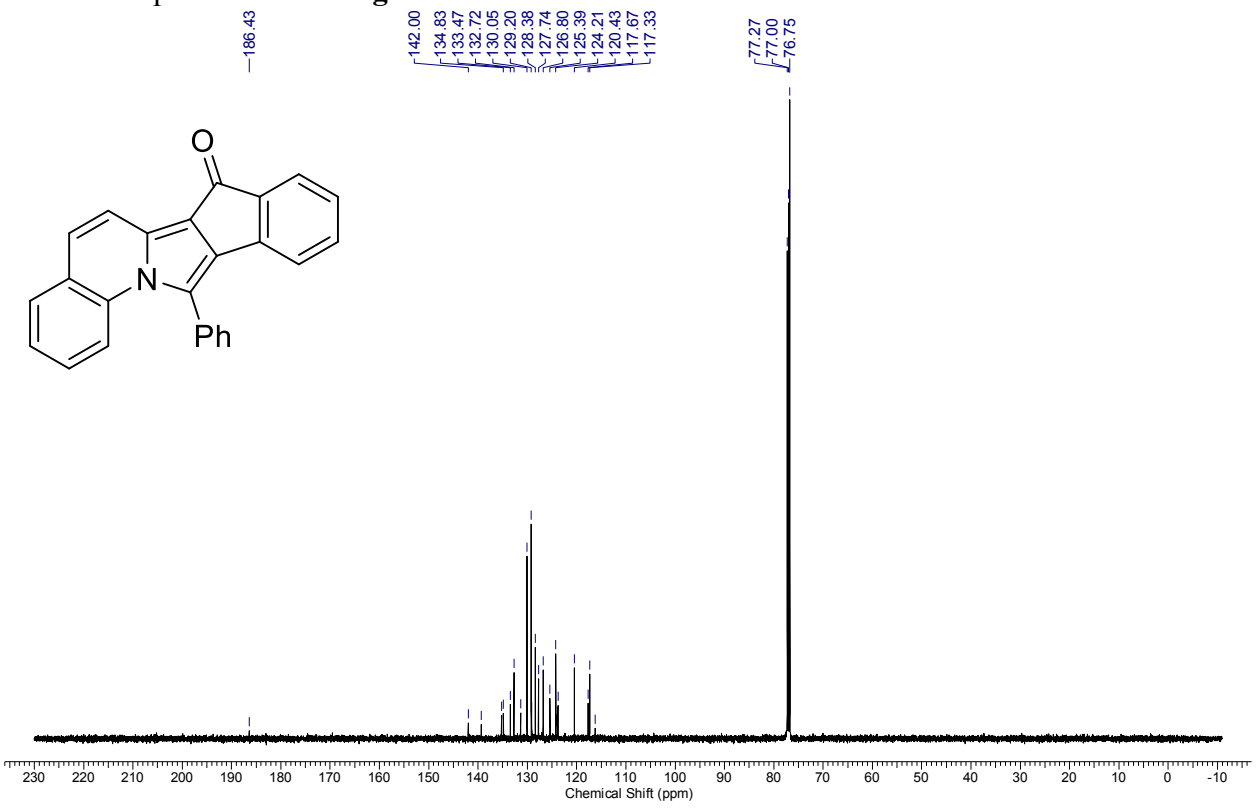

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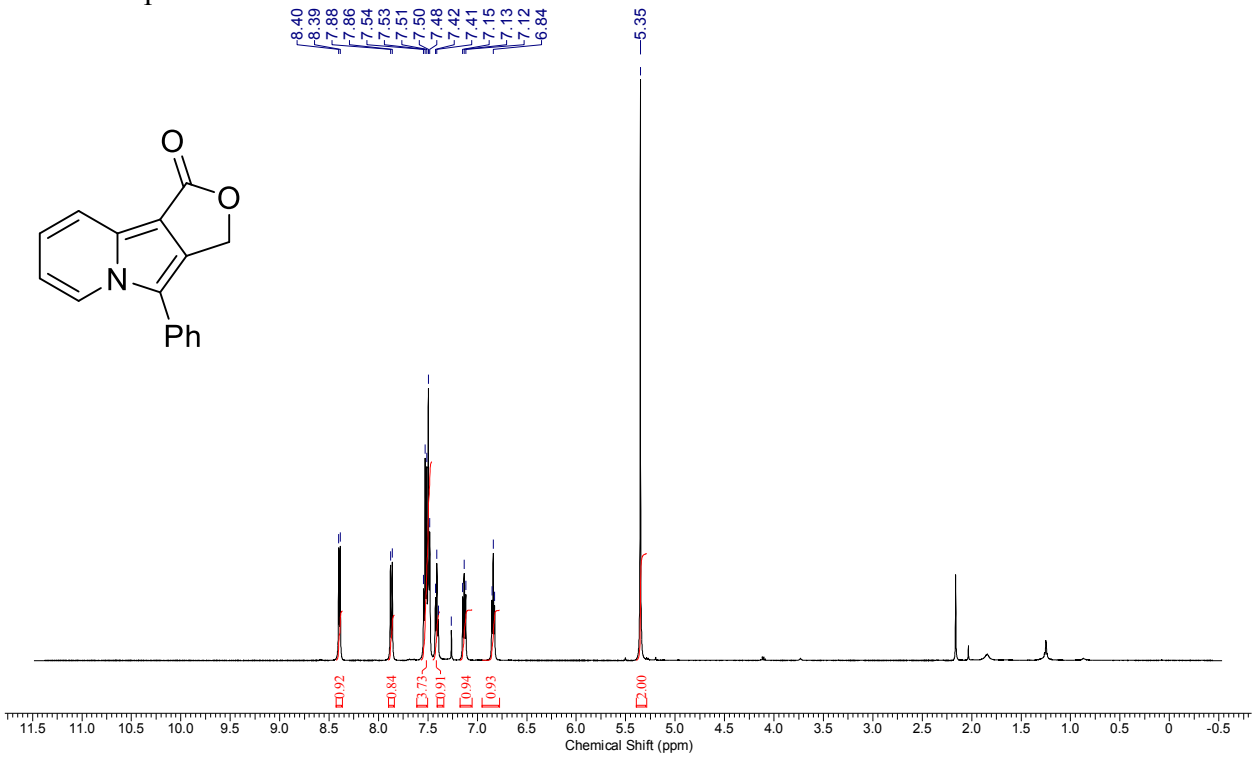

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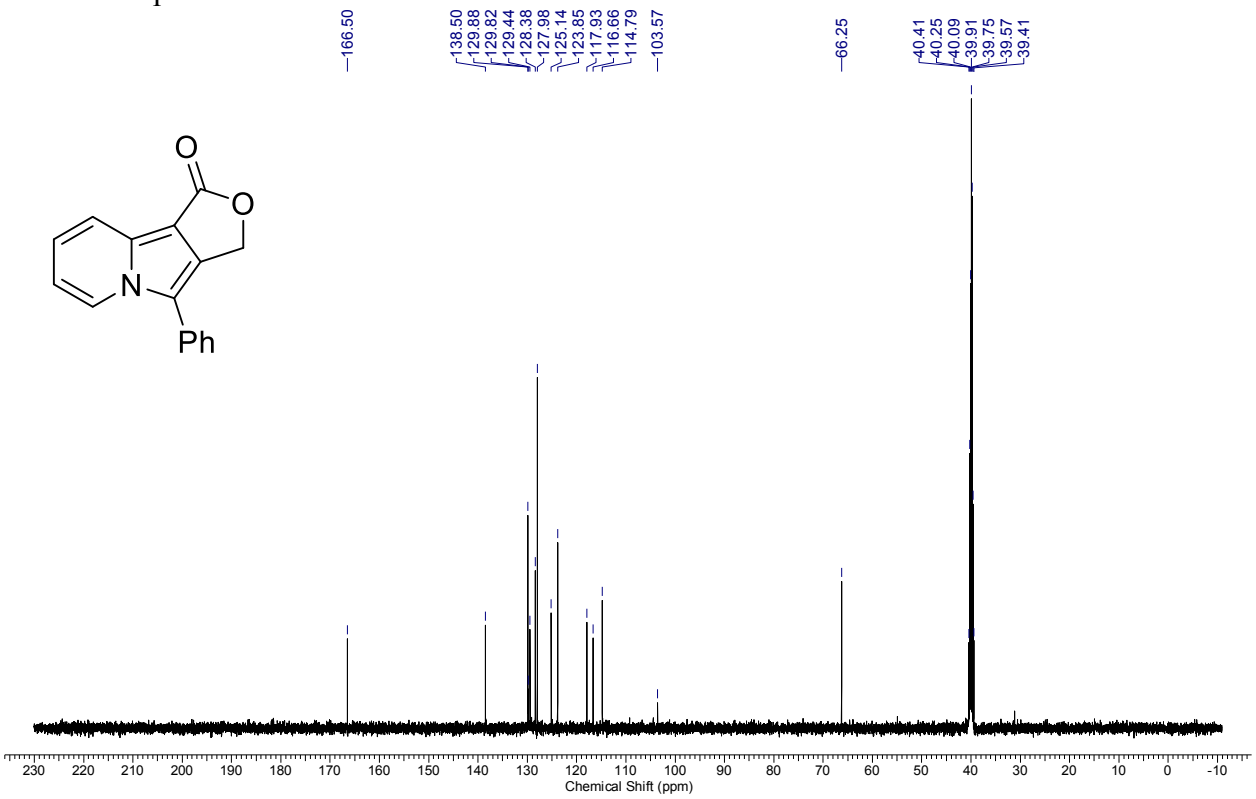

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3. Shi, Y.; Gevorgyan, V. "Cu-Catalyzed Transannulation Reaction of Pyridotriazoles: General Access to Fused Polycyclic Indolizines," *Chem. Commun*. **2015**, *51*, 17166.

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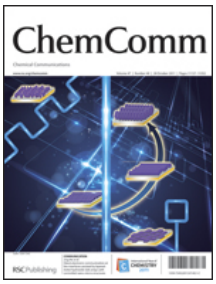

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Author: Yi Shi,Vladimir Gevorgyan

Publication: Chemical Communications (Cambridge)

Publisher: Royal Society of Chemistry

Date: Oct 1, 2015

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Shi, Y.; Gevorgyan, V. "Cu-Catalyzed Transannulation Reaction of Pyridotriazoles: General Access to Fused Polycyclic Indolizines," *Chem. Commun*. **2015**, *51*, 17166-17169.

PRESENTATIONS: Shi, Y.; Gevorgyan, V. “Intramolecular Transannulation of Alkynyl Triazoles via Alkyne–Carbene Metathesis Step: Access to Fused Pyrroles,” the 7th Negishi-Brown Lectures, Purdue University, West Lafayette, IN, October 6-7, 2014

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Shi, Y.; Gevorgyan, V. “Transition-Metal-Catalyzed Transformations of Triazoles: Efficient Access to (Poly)Cyclic Heterocycles,” Gordon Research Conferences, Salve Regina University, Newport, RI, July 24-29, 2016 (poster).