FACILE SYNTHESIS OF (4-NITROPHENYL)THIO-SUBSTITUTED 1-PYRROLINES

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FACILE SYNTHESIS OF (4-NITROPHENYL)THIO-SUBSTITUTED 1-PYRROLINES

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ABSTRACT

FACILE SYNTHESIS OF (4-NITROPHENYL)THIO-SUBSTITUTED 1-PYRROLINES

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The importance of heterocyclic compounds is enormous in synthetic organic chemistry due to their presence in bioactive molecules. Five-membered 1-pyrrolines are one of the most important classes of them. They have recently drawn great attention from synthetic chemists since they have a prominent role for the synthesis of a great number of pharmaceutical molecules. Therefore, there is intense research on their synthesis.

In this project, we concentrated on the synthesis of (4-nitrophenyl)thio-substituted 1-pyrrolines. We have synthesized a variety of (4-nitrophenyl)thio-substituted 1-pyrroline derivatives with one-pot two-steps reactions by using two different bases.

Firstly, the synthesis of α,β-alkynic ketone derivatives was achieved from aryl chlorides and terminal alkynes by using Pd-catalyzed coupling reaction. Secondly, 21 diverse derivatives of N-propargylic β-enaminones were synthesized with conjugate addition of propargylamine to α,β-alkynic ketones.

In the last step of this project, we investigated the addition of 4-nitrobenzenesulfenyl chloride to N-propargylic β-enaminones and the cyclization of resulting intermediate compound. After we treated N-propargylic β-enaminones with 4-nitrobenzenesulfenyl

chloride, NaH or Cs_2CO_3 was added into reaction medium for the cyclization of intermediate product in ACN at reflux condition. Each derivative was synthesized by using both bases and their yields were compared. Consequently, one-pot two-steps reactions were performed and 21 novel derivatives of (4-nitrophenyl)thio-substituted 1-pyrrolines were obtained in good yields.

Keywords: Heterocyclic compounds, five-membered rings, N-propargylic β-enaminones, (4-nitrophenyl)thio-substituted 1-pyrrolines.

ÖZ

SÜLFENİL SÜBSTİTÜYE 1-PİROLİN TÜREVLERİNİN SENTEZİ

Korkmaz, Esra
Yüksek Lisans, Kimya
Tez Danışmanı: Prof. Dr. Metin Zora

Temmuz 2019, 148 sayfa

Sentetik organik kimyada heterosiklik bileşiklerin önemi biyoaktif moleküllerde bulunmaları nedeniyle büyüktür. Beş üyeli 1-pirolinler bunların en önemli sınıflarından biridir. Son zamanlarda, bu bileşikler birçok farmasötik molekülün sentezi için önemli bir role sahip olduklarından sentetik kimyacıların büyük dikkatini çekmişlerdir. Bu nedenle, bunların sentezleri konusunda yoğun araştırma vardır.

Bu projede, biz (4-nitrofenil)tiyo-sübstitüye 1-pirolinlerin sentezi üzerinde yoğunlaştık. İki farklı baz kullanarak tek potlu iki aşamalı reaksiyonlarla çeşitli (4-nitrofenil)tiyo-sübstitüye 1-pirolin türevlerini sentezledik.

İlk olarak, α,β-alkinik keton bileşikleri, aril klorürlerden ve terminal alkinlerden Pd-katalizli kenetlenme tepkimeleri ile elde edildi. İkinci olarak, 21 farklı N-proparjilik β-enaminon türevi, proparjilaminin α,β-alkinik ketonlara konjuge katılma reaksiyonları ile sentezlendi.

Bu projenin son aşamasında, 4-nitrobenzensülfenil klorürün N-proparjilik β-enaminon bileşiğine ilave edilmesini ve daha sonra elde edilen ara bileşiğin halkalaşmasını araştırdık. N-Proparjilik β-enaminon bileşiğini 4-nitrobenzensülfenil klorür ile kaynattıktan sonra, NaH veya Cs_2CO_3 bazı asetonitril çözücüsü içerisinde geri soğutucu altında reaksiyon ortamına eklenmiştir. Her türev iki bazda kullanılarak

sentezlenmiş ve onların verimleri kıyaslanmıştır. Sonuç olarak, tek potlu iki aşamalı reaksiyonlar gerçekleştirilmiş ve 21 yeni (4-nitrofenil)tiyo-sübstitüye 1-pirolin türevleri iyi verimlerde elde edilmiştir.

Anahtar Kelimeler: Heterohalkalı bileşikler, beş üyeli halkalar, N-proparjilik β-enaminonlar, (4-nitrofenil)tiyo-sübstitüye 1-pirolinler.

To My Dear Devoted Family

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TABLE OF CONTENTS

LIST OF TABLES

TABLES

LIST OF FIGURES

FIGURES

LIST OF SCHEMES

SCHEMES

LIST OF ABBREVIATIONS

ACN	acetonitrile
br	broad (spectral)
Cs_2CO_3	cesium carbonate
d	doublet (spectral)
DCM	dichloromethane
dd	doublet of doublets (spectral)
DMF	dimethylformamide
DMSO	dimethyl sulfoxide
dt	doublet of triplets (spectral)
FT	fourier transform
Hz	Hertz
J	coupling constant
m	multiplet (spectral)
min	minute(s)
NaH	sodium hydride
NOESY	nuclear overhauser effect spectroscopy
ppm	parts per million (in NMR)
q	quartet (spectral)
r.t.	room temperature
s	singlet (spectral)

t	triplet (spectral)
THF	tetrahydrofuran
TLC	thin layer chromatography
td	triplet of doublets (spectral)
tdd	triplet of doublet of doublets (spectral)
TMS	trimethylsilane
tt	triplet of triplets (spectral)
δ	chemical shift in parts per million downfield from tetramethylenesilane (TMS)

CHAPTER 1

INTRODUCTION

Organic chemistry is defined as the chemistry of compounds comprising of carbon element. Carbon forms the foundation of life on earth. Therefore, it has a different status in the science of chemistry. Carbon containing compounds include a variety of organic compounds, in which carbon atom forms strong covalent bonds with other carbon atoms.[1,2]

Organic compounds are present in many areas of our lives. All living beings include them in their construction. For instance, proteins that are the building blocks of our body and DNA that plays a role in inheritance are made up of organic compounds. Besides this, molecules like carbohydrates and fats which are the source of food for us are organic substances. In addition, the importance of organic molecules in the pharmaceutical industry cannot be ignored. All of medicines that fight severe diseases and cure us consist of organic matters. Therefore, the interest in organic chemistry has increased enormously day by day.[2]

Organic compounds can contain other atoms as well, such as oxygen, nitrogen, phosphorous and sulphur in addition to carbon. In fact, many of them are composed of ring systems.[2] These organic compounds that include rings constituted from carbon and at least one heteroatom are called as heterocyclic compounds.[3] Some examples of heterocyclic compunds are given in Figure 1.

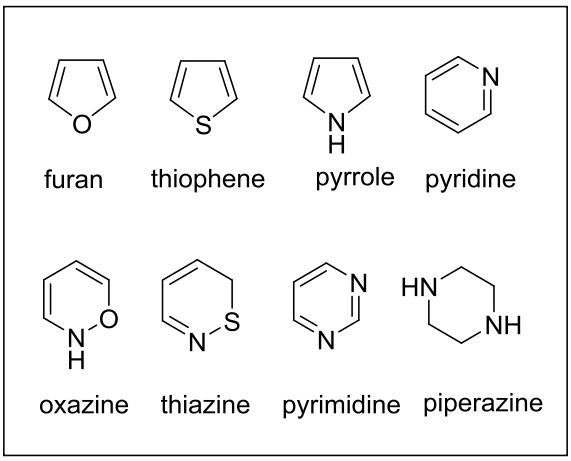


Figure 1. Some examples of heterocyclic compounds.

1.1 Heterocyclic Compounds

The majority of organic chemistry consists of heterocyclic compounds. Although there are many heterocyclic compounds, their numbers continue to rise daily because of their presence in many areas of science.[4] They are separated into two groups as aliphatic and aromatic. Those containing amines, esters and amides are exemplified as aliphatic heterocycles. On the other hand, aromatic heterocyclic compounds possess a heteroatom in their unsaturated ring, similar to benzene in terms of certain features.[5,6] Their physicochemical properties are influenced by the type and size of the ring structures as well as the groups attached to them.[3]

Heterocyclic compounds may consist of naturally. Some of them are produced by animals and plants. In particular, many alkaloids, chemical compounds in the amine structure produced naturally by plants, consist of heterocyclic rings. Camphothecin, for example, is of great importance as an anticancer agent (Figure 2).[7]

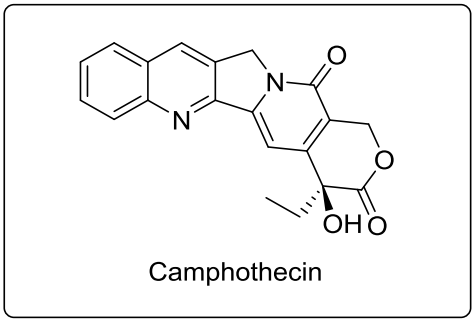


Figure 2. Structure of Camphothecin.

1.1.1. Importance of Heterocyclic Compounds

Heterocyclic compounds which form a major research field in organic chemistry have great importance in terms of biology and industry. Most of the drugs and biologically active agrochemicals, as well as some dyes, pesticide and herbicides, are composed of heterocyclic ring structures.[8,9] A vast number of heterocyclic compounds are required for life. For instance, a variety of compounds including amino acids, such as histidine and tryptophan, vitamins and coenzymes like riboflavin and pyridoxine, and genetic material DNA formed from purine and pyrimidine derivatives, are made up by heterocyclic ring systems (Figure 3).[10,11]

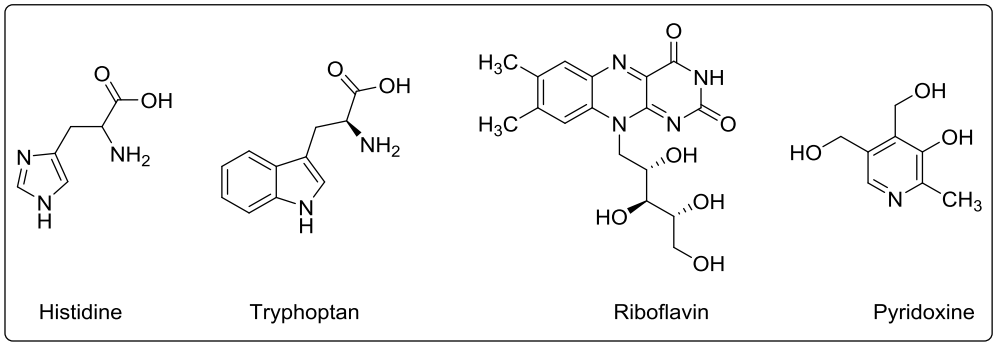


Figure 3. Structures of some amino acids, vitamins and coenzymes.

In addition, heterocyclic compounds appear in a wide range of fields. For instance, they are present in the structures of many natural drugs. Some representative examples of natural drugs are given in Figure 4. Additionally, all biological events such as energy supply, conduction of nerve impulses and transduction of genetic data, are chemical in nature and occur by the inclusion of a lot of heterocyclic compounds like vitamins, enzymes and coenzymes. All these play a significant role in chemical processes of the human body.[8]

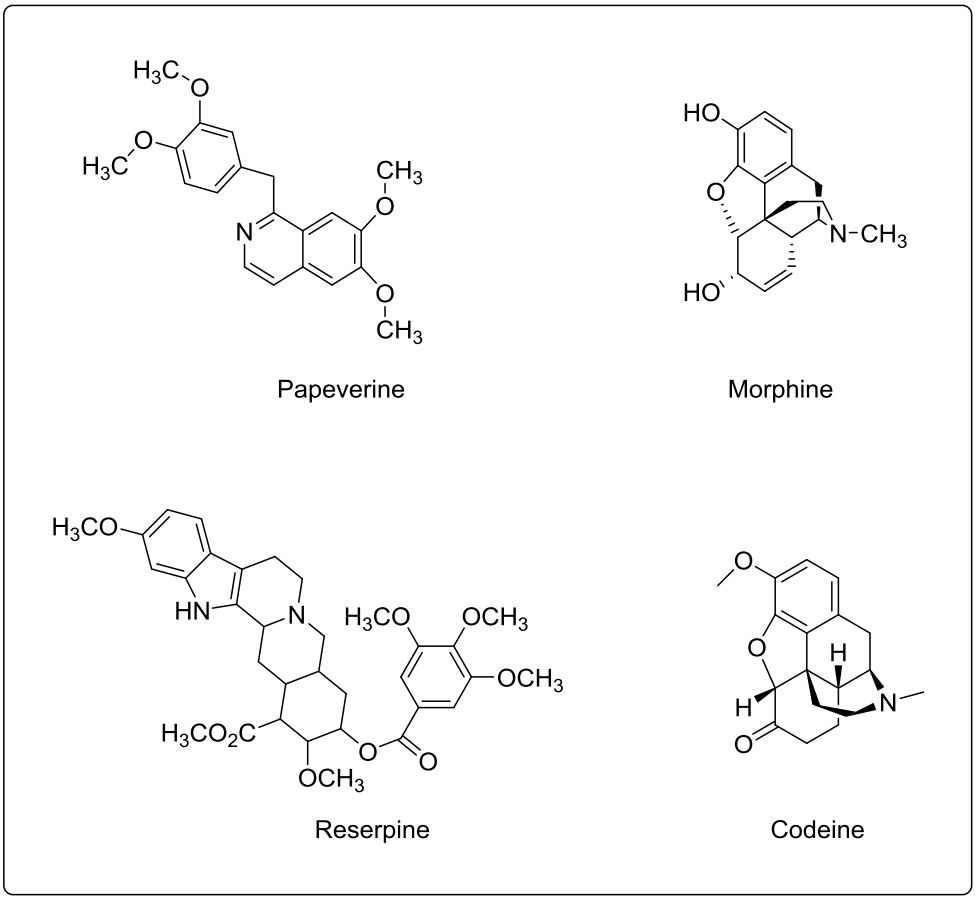


Figure 4. Structures of some natural drugs.

1.2. Pyrrolines

The significance of heterocyclic molecules in organic synthesis is undeniable, but the most important of them is undoubtedly nitrogen-containing heterocyclic compounds because of their presence in the structure of drugs and natural products. Among them, pyrrolines, possessing structural formula of C_4H_7N, have recently attracted much notice.[12] They, also referred to as dihydropyrroles, are mostly obtained by hydrogenation from aromatic pyrroles. They have three different isomers, which results from the position of the double bond. Accordingly, they are called 1-pyrroline (3,4-dihydro-2*H*-pyrroles), 2-pyrroline (2,3-dihydro-1*H*-pyrroles) and 3-pyrroline (2,5-dihydro-1*H*-pyrroles) (Figure 5).[13,14]

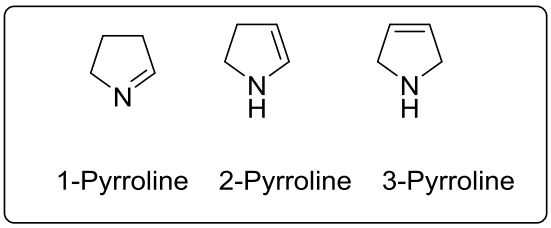


Figure 5. Structures of pyrroline isomers.

Although all pyrrolines are employed as building blocks in the synthesis of biologically active compounds, 1-pyrrolines are the most notable among them because of their presence in biologically active compounds such as hemes, chlorophylls and alkaloids.[15]

1.2.1. 1-Pyrrolines

1-Pyrroline, possessing a characteristic odour, is a naturally volatilizable compound. Living beings can take advantage of this smell for chemical signals and other aims. Insects and plants can release 1-pyrroline to the medium as an ingredient of sex pheromone or for objectives of signalling and smell imitation.[16] For instance, male mediterranean fruit flies generate 1-pyrroline as an attractive pheromone ingredient due to its odour because the imine (—N=CH —) functionality found in 1-pyrroline structure can give it an important molecular character in the smell process.[17]

Studies have shown that 1-pyrroline is present as monomer and trimer in liquid solution (Figure 6). In fact, there is a balance between its monomer and trimer states. However, trimer is more stable than monomer at room temperature whereas it exists in monomer state in the gas phase.[16,18]

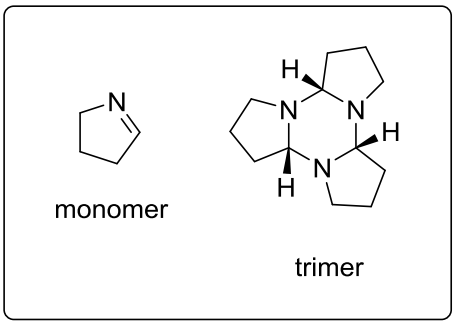


Figure 6. Monomer and trimer states of 1-pyrroline.

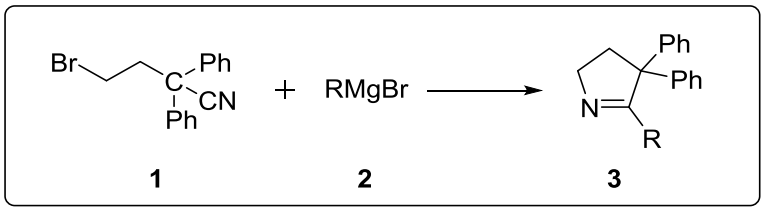
1-Pyrroline has some reaction centers such as C=N bond, nitrogen atom, methylene group and alkenyl carbon in its structure. For example, addition reactions can be carried out via C=N bond. The trimer shown in Figure 6 consists of three 1-pyrroline molecules as a result of the cycloaddition reaction of C=N bonds in pyrroline

molecules. Moreover, the other reactions may occur by the cleavage of C=N bond as a consequence of the pyrroline ring opening.[19]

1.2.2. Synthesis of 1-Pyrrolines

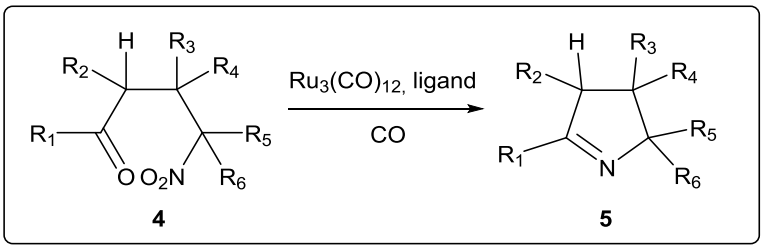
It has been shown that 1-pyrrolines can be used as intermediates in the synthesis of different molecules having a great variety of pharmaceutical activities. For this reason, there has been intense research on this subject through the last decades.[20] Various methods have been developed for synthesis of 1-pyrrolines by using acyclic, alicyclic and heterocyclic compounds.[13] Some of them are summarised below.

In 1959, Demoen and Janssen synthesized substituted 1-pyrrolines in moderate yields as illustrated in Scheme 1.[13] In this study, γ-bromonitrile **1** was reacted with aryl Grignard reagents **2** to afford 2-aryl-3,3-diphenyl-1-pyrroline derivatives **3**.



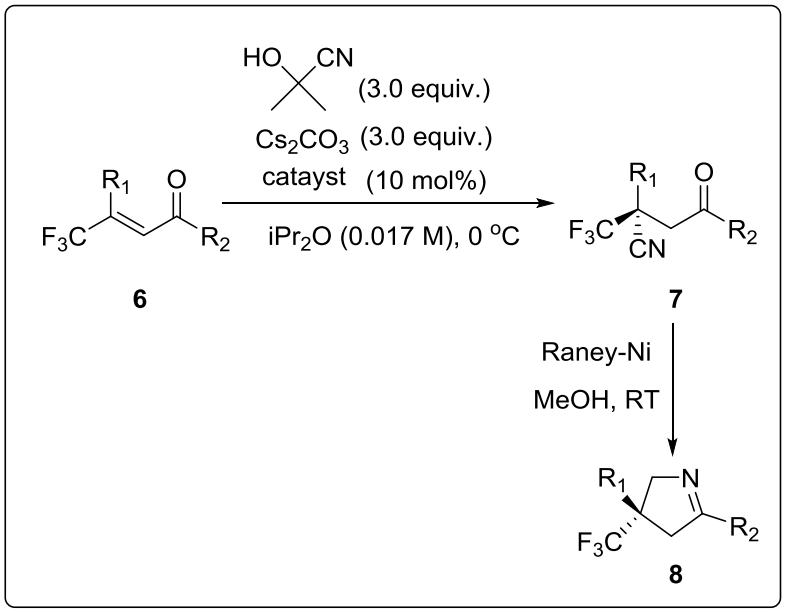
Scheme 1. Synthesis of 2-aryl-3,3-diphenyl-1-pyrroline derivatives.

In 1995, Watanabe and co-workers developed a method to synthesize 1-pyrroline derivatives from catalytic cyclocondensation of γ-nitrocarbonyl compounds **4** as depicted in Scheme 2.[21] Herein, reaction was carried out in the presence of ruthenium catalyst and some ligands under CO atmosphere. This reaction was the first example to achieve 1-pyrroline derivatives **5** by using the transition metal catalyst.



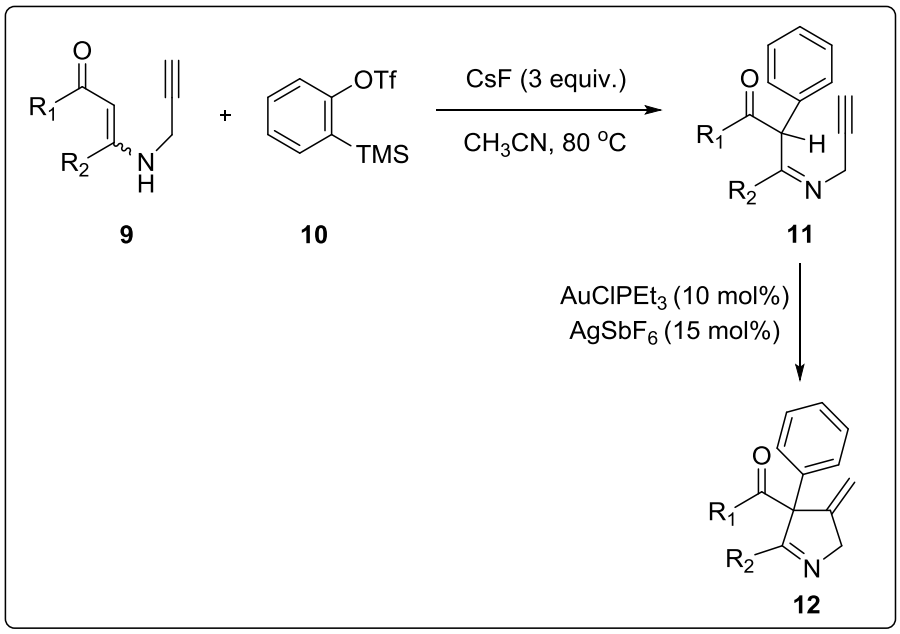
Scheme 2. Synthesis of 1-pyrrolines from γ-nitrocarbonyl compounds.

Recently, Shibata research group reported an enantioselective synthesis of trifluoromethyl-substituted 1-pyrrolines as shown in Scheme 3.[22] Firstly, the conjugate cyanation of β-aryl-β-trifluoromethyl-substituted enones **6** was occurred in the presence of acetone cyanohydrin and catalyst (*N*-2,5-bis(trifluoromethylbenzyl) *O*-methyl quinidinium bromide). Then, the resulting conjugate addition products **7** were reacted with Raney nickel in MeOH to afford β-trifluoromethyl-substituted 3,5-diarylpyrrolines **8**.



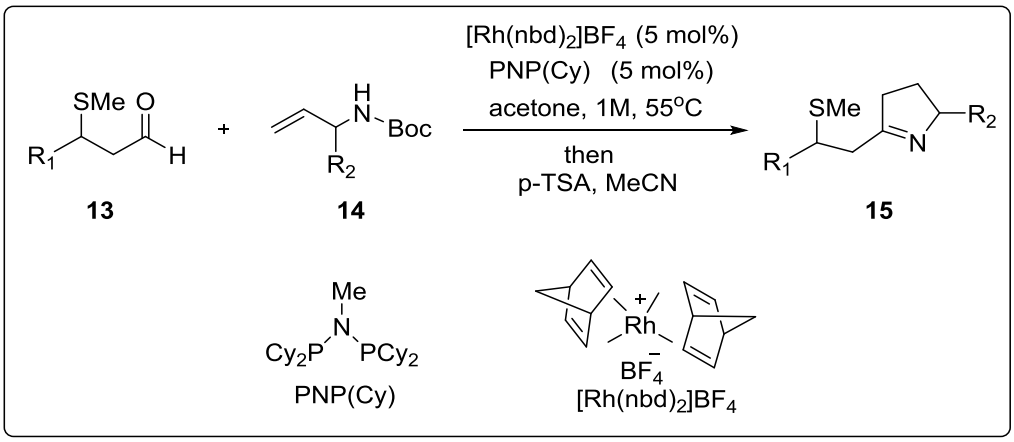
Scheme 3. Synthesis of β-trifluoromethyl-substituted 3,5-diarylpyrrolines.

In 2014, Karunakar and co-workers have developed a novel approach to synthesize 1-pyrroline derivatives by means of one-pot gold(I) catalyzed reaction as given in Scheme 4.[23] In this study, N-propargylic β-enaminone **9** was reacted with benzyne formed *in situ* from the reaction of 2-(trimethylsilyl)phenyl trifluoromethanesulfonate **10** and CsF in acetonitrile solvent. Then, 4-methylene-1-pyrroline derivatives **12** were obtained in satisfactory yields via the cyclization of substituted N-propargylic β-enaminone **11** with $AuCl_3/AgSbF_6$.



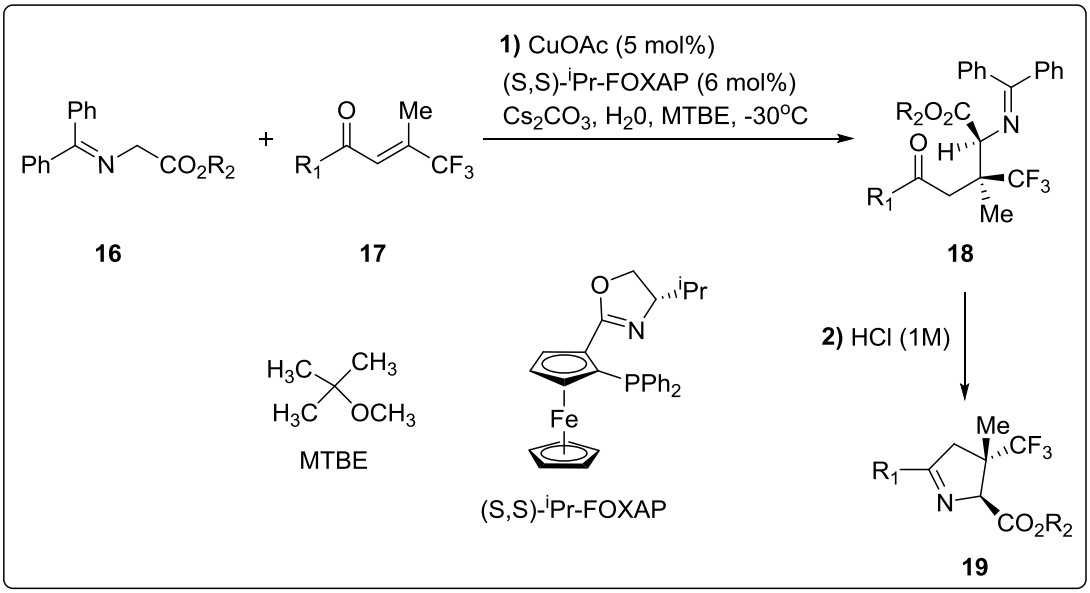
Scheme 4. Synthesis of 4-methylene-1-pyrroline derivatives.

In 2016, Willis research group reported the synthesis of 1-pyrrolines through linear selective hydroacylation reaction (Scheme 5).[24] First, hydroacylative coupling of S-chelating aldehydes **13** with allylic amines **14** was carried out in the presence of PNP(Cy)-derived catalyst. Then, the treatment of resulting product with p-toluenesulfonic acid (p-TSA) led to cyclization, which resulted in the cleavage of Boc-group, to give 1-pyrroline derivatives **15** in high yields.



Scheme 5. Synthesis of 1-pyrrolines with linear selective hydroacylation reaction.

One year later, in 2017, Zhang and co-workers described a methodology to synthesize multisubstituted 1-pyrroline derivatives, possessing two adjacent stereogenic centers, via one-pot copper-catalyzed asymmetric Michael addition of ketiminoesters **16** to β-trifluoromethyl-substituted enones **17** as shown in Scheme 6.[25] Herein, after the Michael addition product **18** was obtained, hydrolytic cyclization afforded desired 1-pyrroline derivatives **19** in high yields.



Scheme 6. Synthesis of substituted 1-pyrrolines.

1.2.3. Importance of 1-Pyrrolines

1-Pyrrolines possess significant roles in several fields of science, [26] since they can be employed as synthetic building blocks as well as owning a variety of biological activities.[27] For instance, they are involved in the synthesis of many bioactive natural products as given in Figure 7. They are also used as intermediates in the synthesis of various pyrrolidine alkaloids and catalysts.[28]

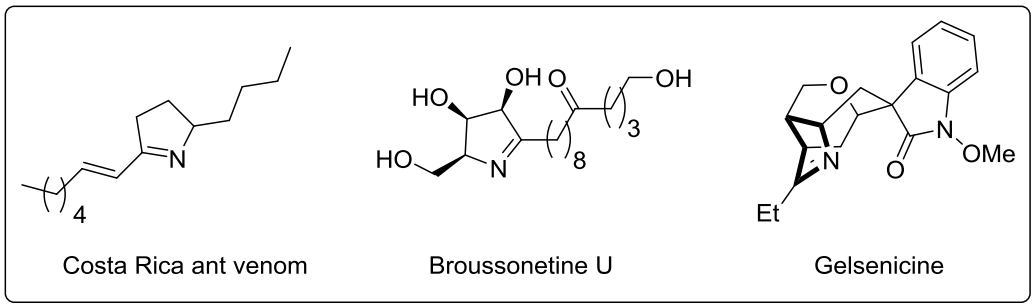


Figure 7. Representative 1-pyrroline containing natural products.

Notably, 1-pyrrolines exhibit some functions like semiochemicals, flavouring material for diverse nourishment products, high affinity radioligands and therapeutic complexes, some examples of which are given in Figure 8.[23]

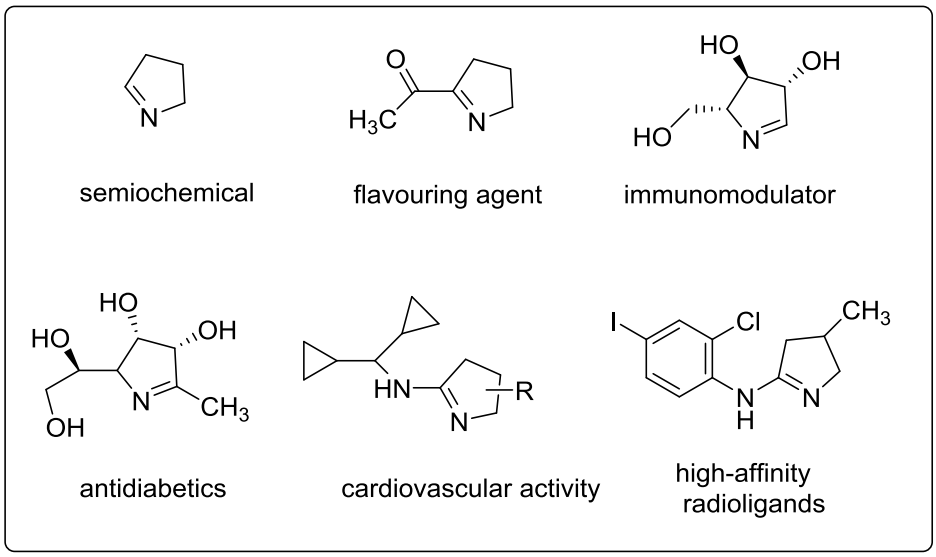


Figure 8. Some examples of the important 1-pyrroline derivatives.

In addition, they are employed as intermediates in the synthesis of various pharmaceutically active compounds. For instance, β-lactam derivatives, diaryl pyrrolizine acetic acid derivatives and fluoroquinolones can be given as examples for such 1-pyrroline derivatives, which are shown in Figure 9.[23]

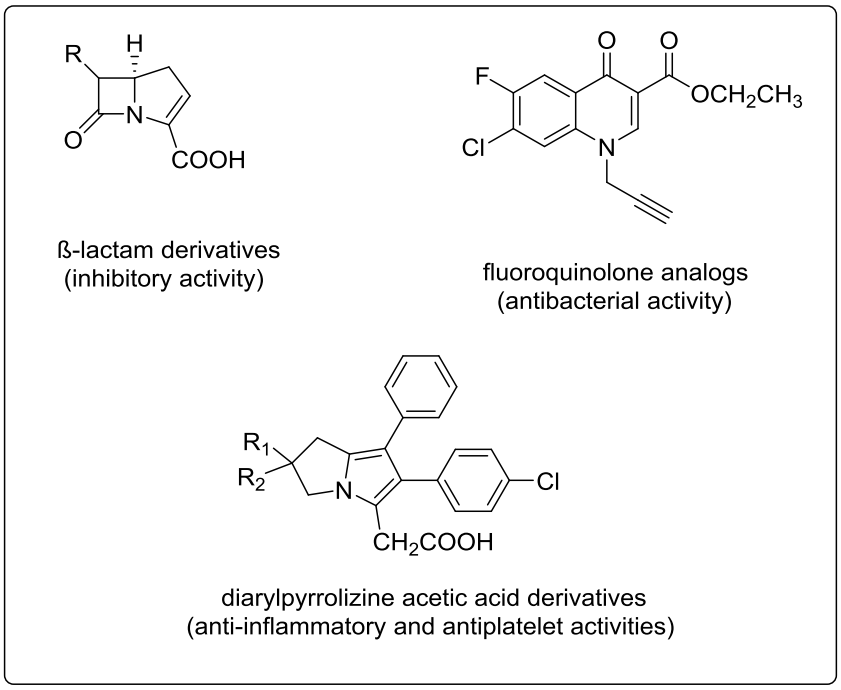


Figure 9. Some examples of pharmaceutically active compounds synthesized from 1-pyrroline derivatives.

1.3. N-propargylic β-enaminones

β-Enaminones are used as important intermediates in a great number of syntheses in organic chemistry due to the reactivity obtained from their conjugated systems, O=C-C=C-N.[29] Moreover, they display both nucleophilic and electrophilic characters due to the presence of enamine and enone functional groups in their structures.[30,31] For this reason, they have drawn attention in the synthesis of heterocyclic compounds.[31]

In particular, N-propargylic β-enaminones **20** have recently attracted great interest since they play an important role as building blocks in organic synthesis.[32] Due to their distinctive functional groups like alkene, alkyne, enone, enamine, and enaminone, they have been accepted as remarkable substrates as depicted in Figure 10.[33]

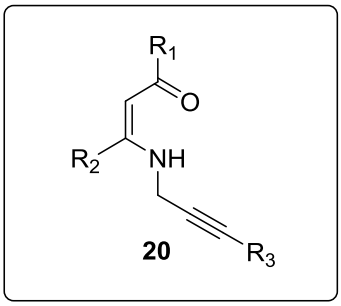
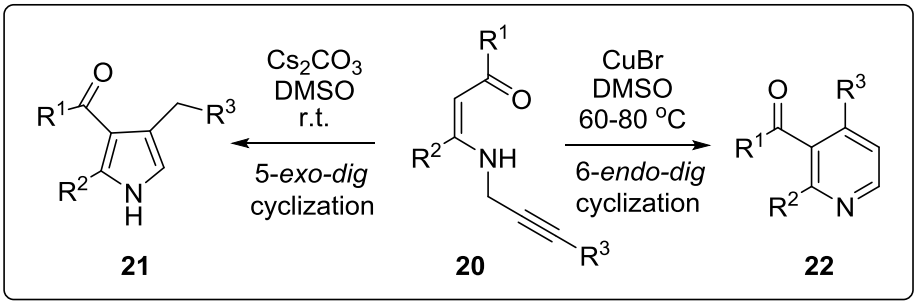


Figure 10. Structure of N-propargylic β-enaminones.

1.3.1. Reactions of N-propargylic β-enaminones

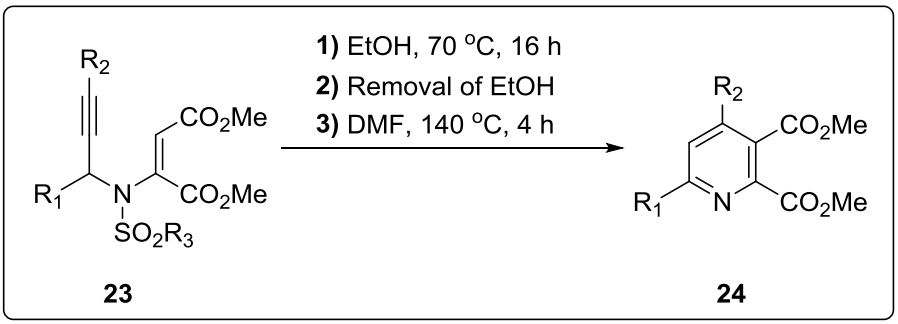
N-Propargylic β-enaminones **20** serve as valuable intermediates for the synthesis of heterocyclic compounds such as pyrroles, dihydropyrroles and pyrrolidinones. Therefore, in literature, there are many studies containing their conversion to the corresponding heterocyclic molecules.[33]

In 2008, Cacchi research group reported the synthesis of polysubstituted pyrroles and pyridines by the cyclization of N-propargylic β-enaminones. When treated with Cs_2CO_3 in DMSO, N-propargylic β-enaminones **20** afforded pyrrole derivatives **21** via 5-*exo-dig* cyclization (Scheme 7).[34] On the other hand, the cyclization of N-propargylic β-enaminones **20** with CuBr yielded pyridine derivatives **22** through 6-*endo-dig* cyclization.[34]



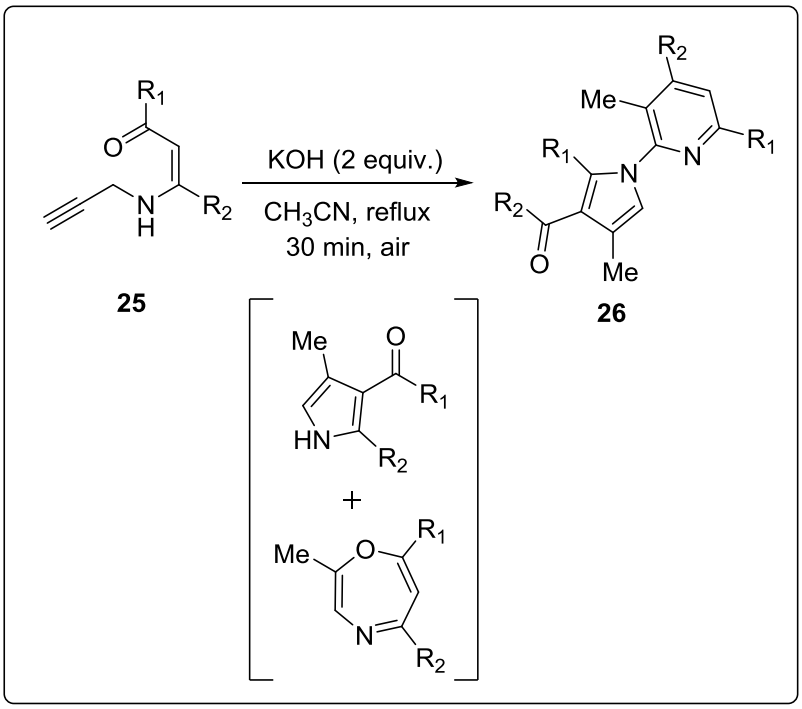
Scheme 7. Synthesis of polysubstituted pyrroles and pyridines.

Later, Wan and co-workers synthesized the substituted pyridines from N-sulfonyl, N-propargylic β-enaminone via one-pot three-step reaction. After an aza-Claisen rearrangement of N-sulfonyl, N-propargylic β-enaminones **23** happened, substituted pyridine derivatives **24** were obtained by electrocyclization and elimination, respectively (Scheme 8).[35]



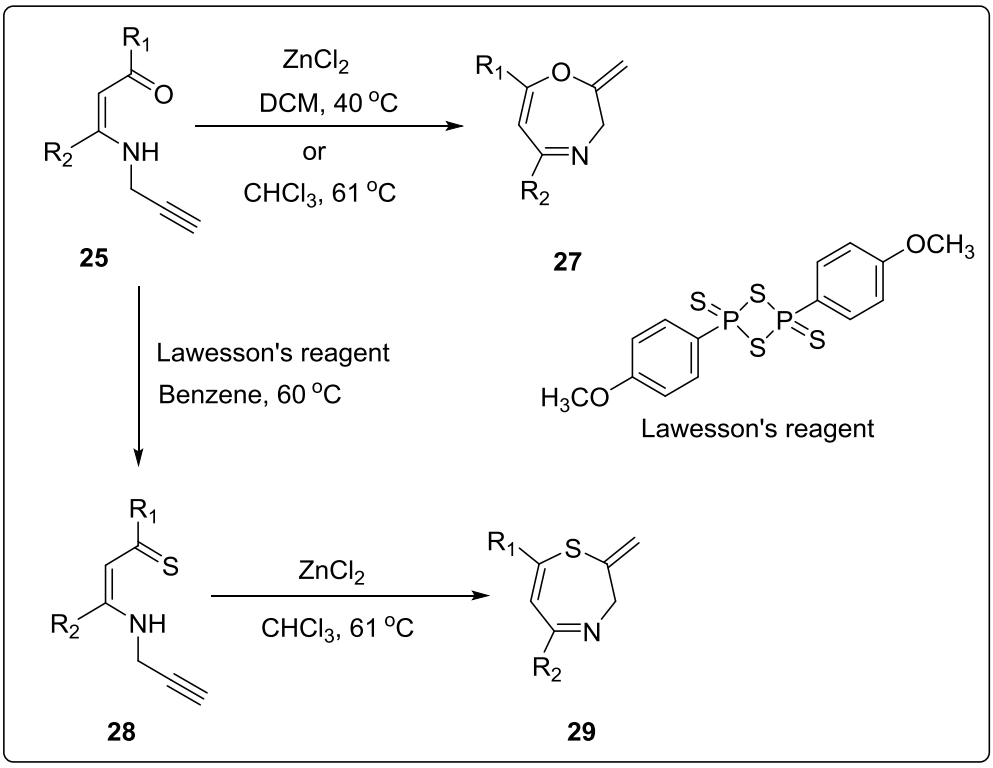
Scheme 8. Synthesis of substituted pyridine derivatives.

In 2016, Cui research group developed a method to synthesize the substituted pyrrole compounds. This procedure allowed the regiospecific synthesis of N-(2-pyridyl)pyrroles **26** from N-propargylic β-enaminones **25** under basic medium after the pyrrole and 1,4-oxazepine compounds occured *in situ* as shown in Scheme 9.[36]



Scheme 9. Synthesis of N-(2-pyridyl)pyrrole compounds.

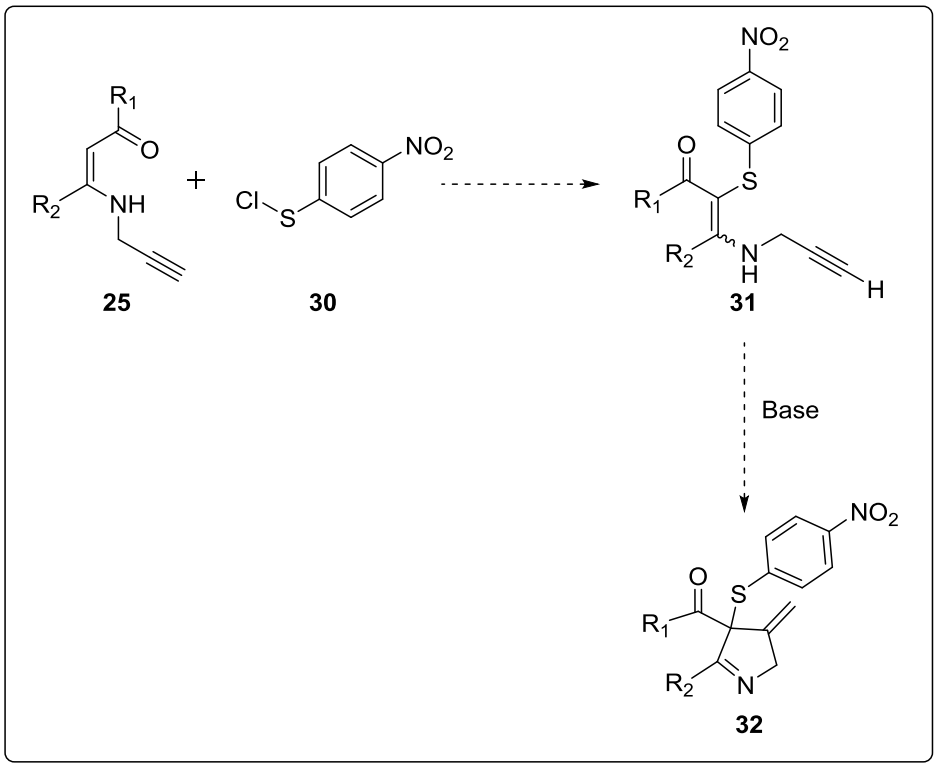
In 2017, Zora and co-workers described a methodology to synthesize 1,4-oxazepines. N-propargylic β-enaminones **25** was converted 2-methylene-2,3-dihydro-1,4-oxazepines **27** via 7-*exo-dig* cyclization in the presence of $ZnCl_2$ by using DCM or $CHCl_3$ solvent (Scheme 10).[37] One year later, they showed that when reacted with $ZnCl_2$ at reflux condition in chloroform, N-propargylic β-enaminothiones **28**, obtained by the thionation of β-enaminones **25** with Lawesson's reagent,[38] produced the corresponding 2-methylene-2,3-dihydro-1,4-thiazepines **29** (Scheme 10).[39]



Scheme 10. Synthesis of 2-methylene-2,3-dihydro-1,4-oxazepines and 2-methylene-2,3-dihydro-1,4-thiazepines.

1.4. Aim of the Thesis

In this project, our aim was to synthesize the five-membered 1-pyrroline derivatives **32** starting from N-propargylic β-enaminones **25** according to the strategy as shown in Scheme 11. We first intended to synthesize 4-nitrobenzenesulfenyl-substituted N-propargylic β-enaminones **31**. Then, we planned to convert them into 1-pyrroline derivatives **32** in basic medium.



Scheme 11. Strategy for the synthesis of (4-nitrophenyl)thio-substituted 1-pyrrolines.

Initially, we synthesized N-propargylic β-enaminones **25** as the starting materials. We expected that, in the first step, the reaction of N-propargylic β-enaminones **25** with 4-nitrobenzenesulfenyl chloride **30** would provide sulfenyl-substituted N-propargylic β-enaminones **31**. Then, in the second step, the cyclization of β-enaminones **31** in the presence of base could afford 4-methylene-1-pyrroline derivatives **32** (Scheme 11). Subsequently, we optimized the reaction conditions for the higher yields of 1-pyrroline derivatives **32** and explored their substrate scope.

Briefly, in this thesis, the scope, limitations and proposed mechanism for the formation of 4-methylene-1-pyrrolines **32** from N-propargylic β-enaminones **25** will be discussed in detail.

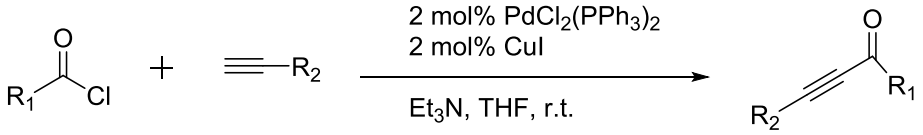
CHAPTER 2

RESULTS AND DISCUSSION

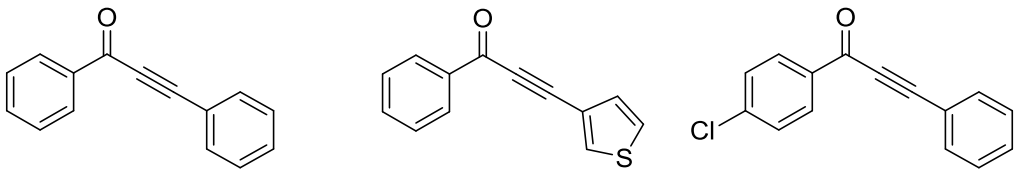
2.1. Synthesis of α,β-Alkynic Ketones

In the first part of our project, we synthesized α,β-alkynic ketones **35** from aryl chlorides **33** and terminal alkynes **34** by using Pd and Cu catalysts via Sonogashira cross-coupling reaction (Table 1).[37,40,41] In this reaction, NEt_3 and THF were used as the base and solvent, respectively. Reactions were conducted at room temperature under argon atmosphere. As shown in Table 1, we have obtained 21 derivatives of α,β-alkynic ketones **35** containing various electron-withdrawing and electron-donating groups in different yields changing from 46 to 98% .

Table 1. Synthesis of α,β-alkynic ketone derivatives **35**.[a]



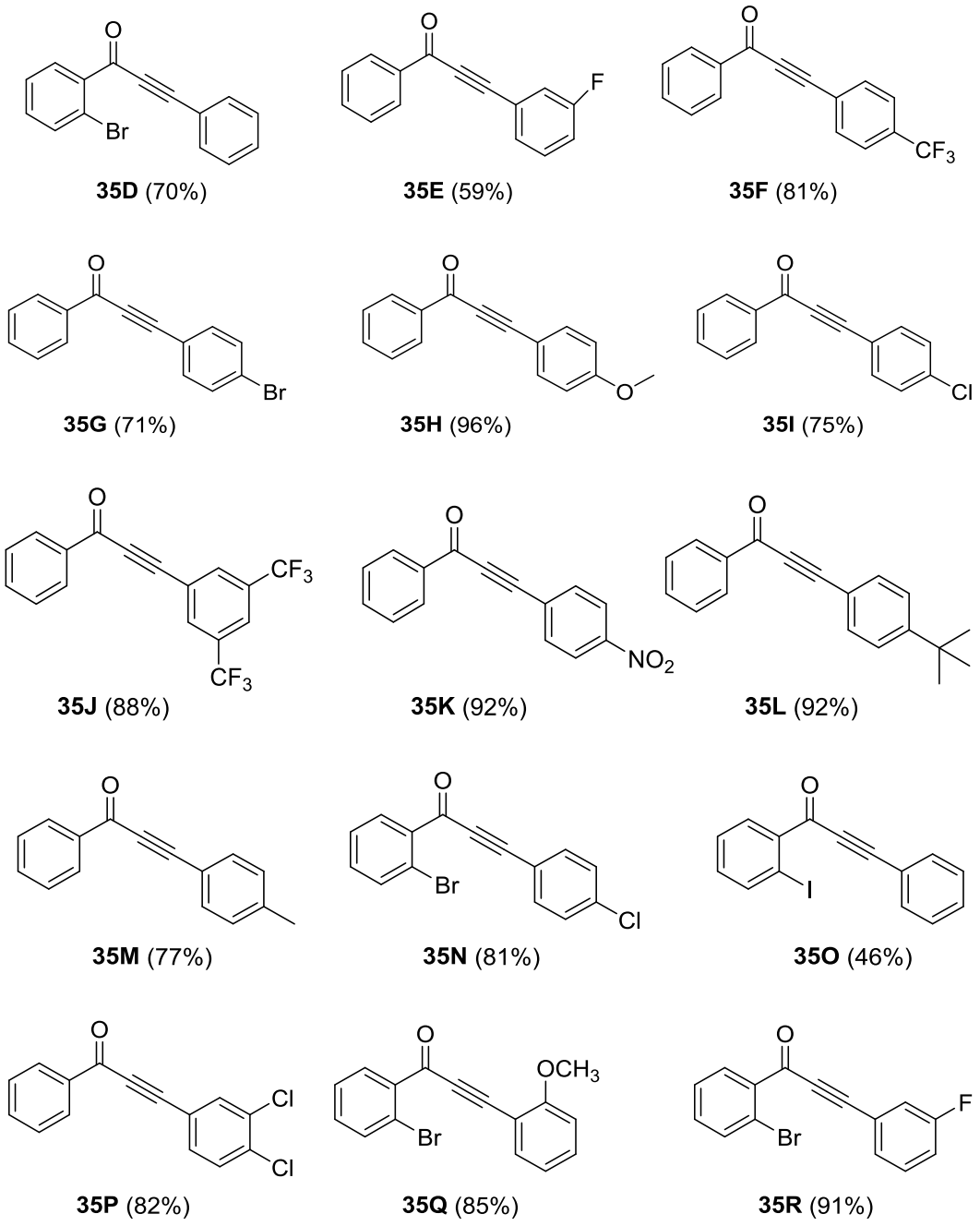
33 **34** **35**



35A (90) **35B** (93%) **35C** (98%)

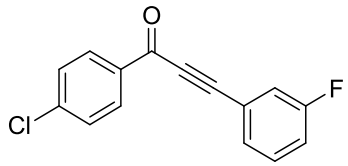
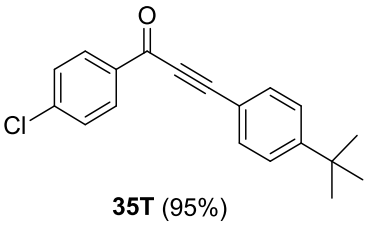
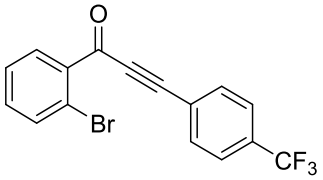
[a]Yields of the isolated products.

Table 1. Continued.



[a]Yields of the isolated products.

Table 1. Continued.

 **35S** (93%)	 **35T** (95%)	 **35U** (88%)

[a]Yields of the isolated products.

The structures of α,β-alkynic ketones **35** were identified by their ^{1}H and ^{13}C NMR spectra. As an example, ^{1}H and ^{13}C NMR spectra of 1,3-diphenylprop-2-yn-1-one (**35A**) are given in Figures 11 and 12. In the ^{1}H NMR spectrum, the resonation of aromatic ten hydrogens for two phenyl groups is seen between 7.33-8.28 ppm, as indicated in Figure 11. In the ^{13}C NMR spectrum (Figure 12), aromatic eight carbons for two phenyl groups resonate between 119.0-137.0 ppm. The peak of carbonyl carbon appears at 177.8 ppm while the peaks of two alkynic carbons are seen in 86.9 and 93.0 ppm (Figure 12).

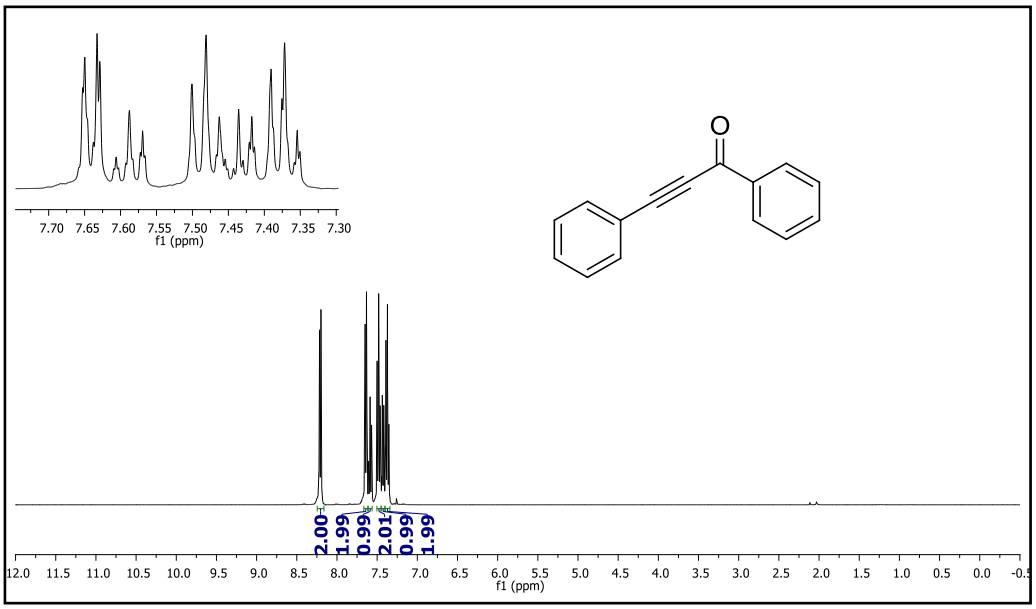


Figure 11. ^{1}H NMR spectrum of 1,3-diphenylprop-2-yn-1-one (**35A**).

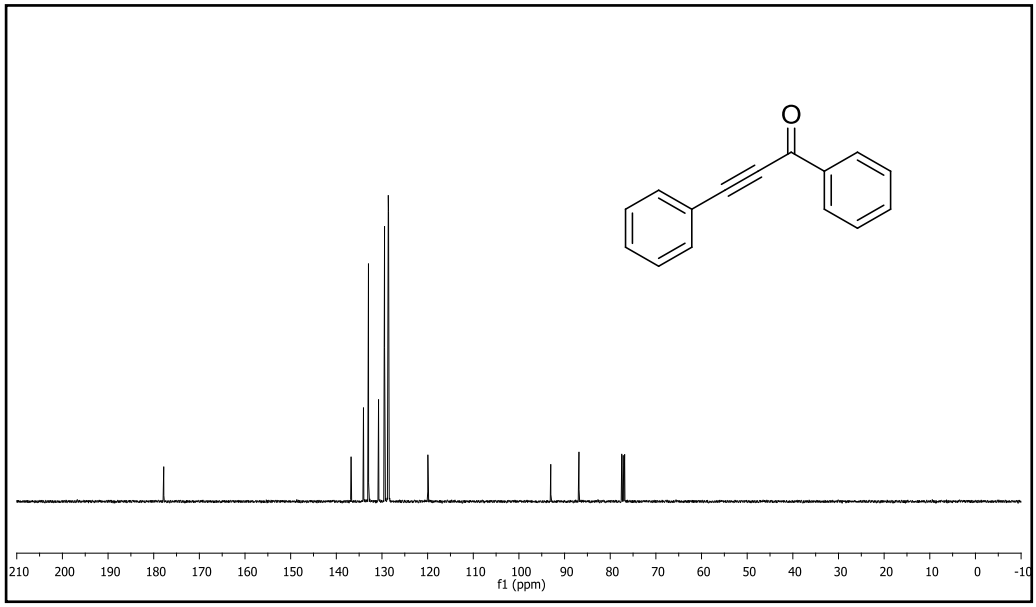
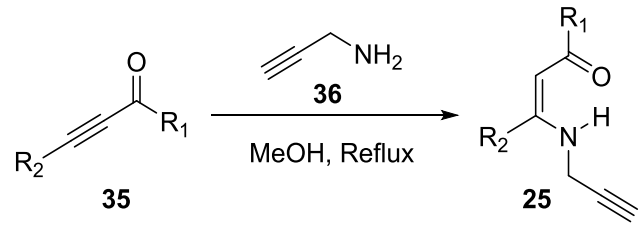


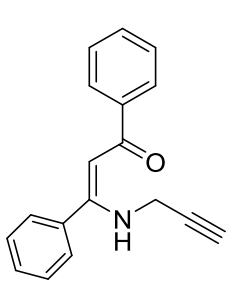
Figure 12. ^{13}C NMR spectrum of 1,3-diphenylprop-2-yn-1-one (**35A**).

2.2. Synthesis of N-Propargylic β-Enaminones

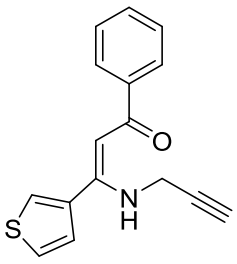
In the second part of our project, 1,4-conjugate addition of propargylamine (**36**) to α,β-alkynic ketones **35** was conducted in methanol at reflux conditions to synthesize N-propargylic β-enaminones **25** (Table 2).[34] This reaction is known as an example of Michael addition reaction. By employing this reaction, 21 different derivatives of N-propargylic β-enaminones **25** were achieved in a good yield from 71 to 98% (Table 2). These compounds have proven to possess *Z* stereochemistry as indicated by NOESY experiments because there is an intramolecular hydrogen bond among amine hydrogen and carbonyl oxygen, which stabilizes β-enaminone derivatives **25**.[34]

Table 2. Synthesis of N-propargylic β-enaminone derivatives **25**.[a]

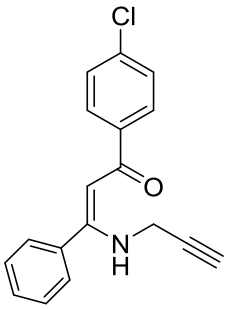




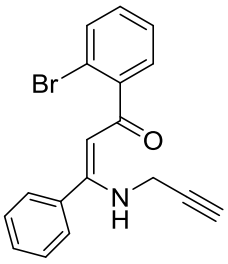
25A (95%)



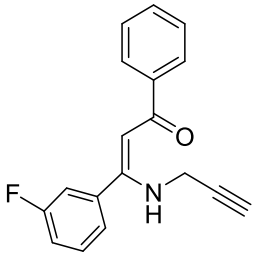
25B (92%)



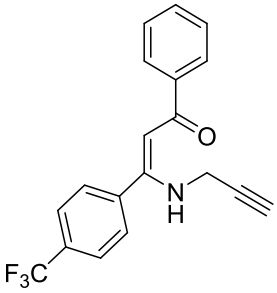
25C (91%)



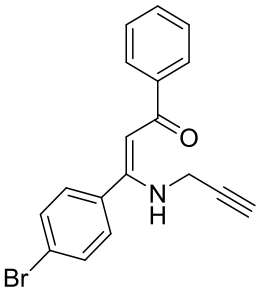
25D (94%)



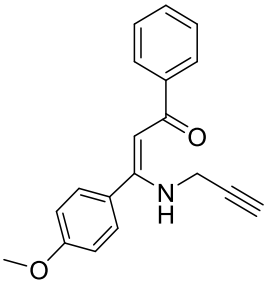
25E (86%)



25F (89%)



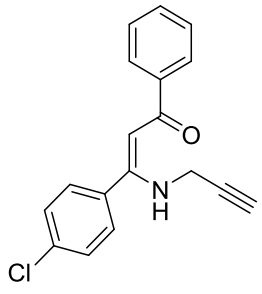
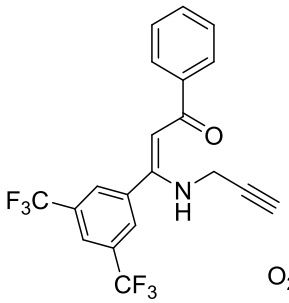
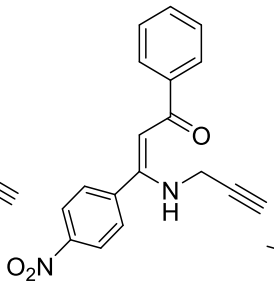
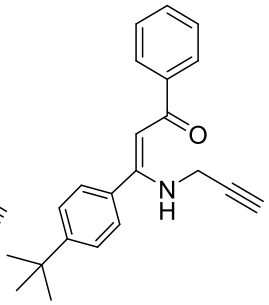
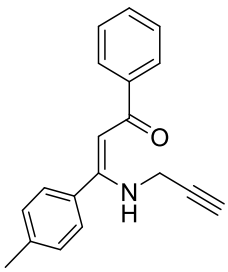
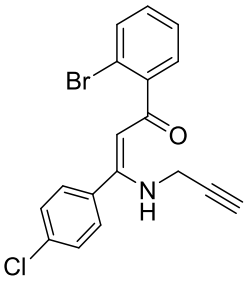
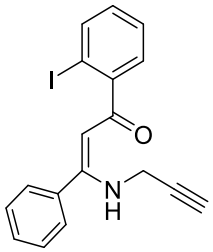
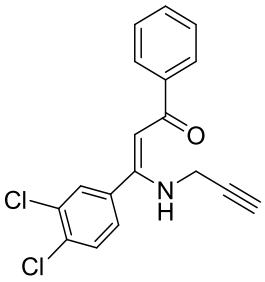
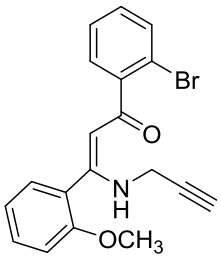
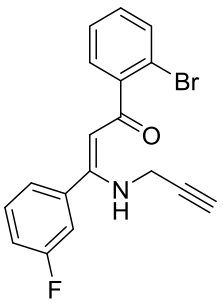
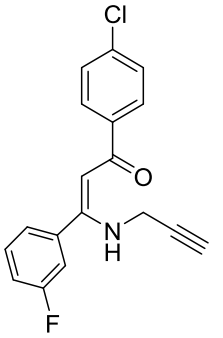
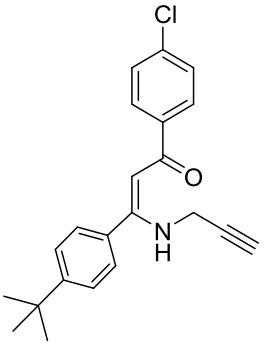
25G (81%)



25H (91%)

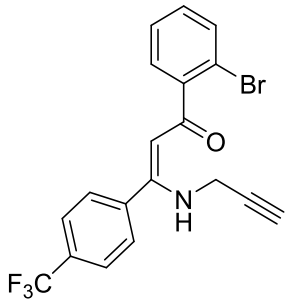
[a]Yields of the isolated products.

Table 2. Continued.

			
25I (92%)	**25J** (71%)	**25K** (72%)	**25L** (88%)
			
25M (88%)	**25N** (96%)	**25O** (73%)	**25P** (90%)
			
25Q (88%)	**25R (**84%)	**25S** (87%)	**25T** (98%)

[a]Yields of the isolated products.

Table 2. Continued.



25U (95%)

[a]Yields of the isolated products.

^{1}H and ^{13}C NMR spectra provided the identification of the structures for these compounds. ^{1}H and ^{13}C NMR spectra of (*Z*)-1,3-diphenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**25A**) are given in Figures 13 and 14 as an example.

In the ^{1}H NMR spectrum (Figure 13), the resonation of aromatic ten hydrogens for two phenyl groups is seen between 7.28-7.90 ppm. Acetylenic hydrogen gives a triplet at 2.32 ppm. However, the vinylic α-hydrogen appears as a singlet at 5.82 ppm. In addition, two methylene hydrogens (CH_2) resonate at 3.86 ppm as a doublet of doublets and amine hydrogen is seen as a triplet at 11.39 ppm (Figure 13).

In the ^{13}C NMR spectrum (Figure 14), carbonyl carbon appears at 188.6 ppm. The resonation of aromatic eight carbons for two phenyl groups is seen between 126.0-140.0 ppm. Methylene carbon (CH_2) peak shows at 33.9 ppm whereas two alkynic carbons resonate at 72.4 and 79.6 ppm. Finally, one (CH) of double bond carbon peaks comes at 94.3 ppm but the other carbon (C) peak appears at 165.5 ppm (Figure 14).

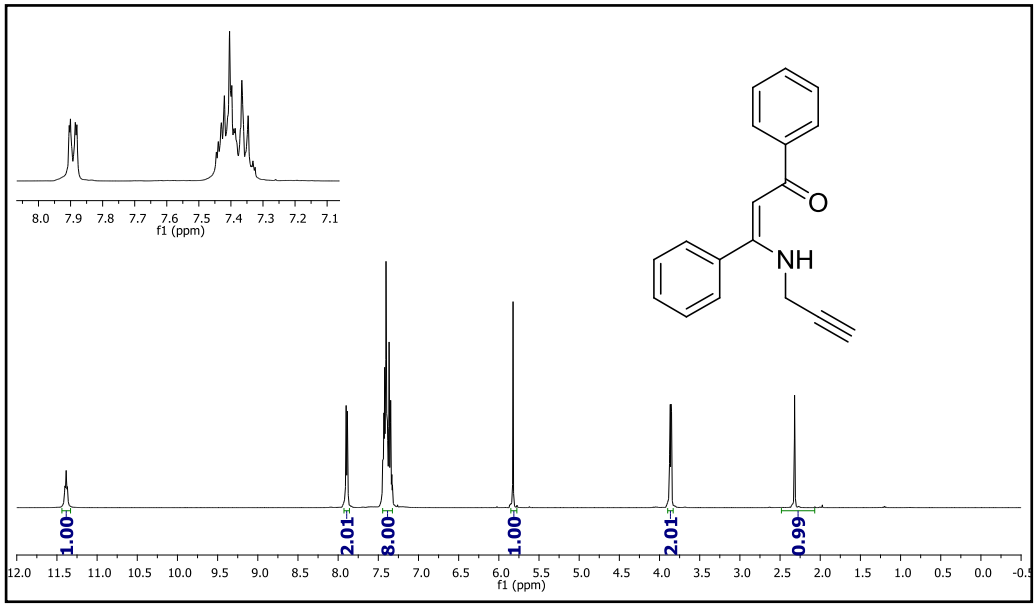


Figure 13. ^{1}H NMR spectrum of (Z)-1,3-diphenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**25A**).

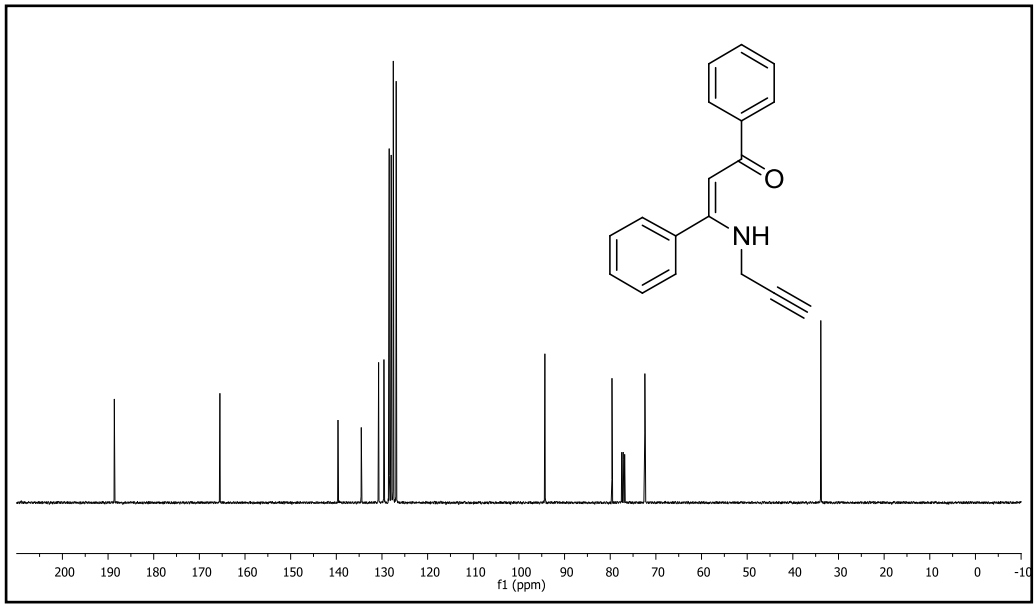


Figure 14. ^{13}C NMR spectrum of (Z)-1,3-diphenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**25A**).

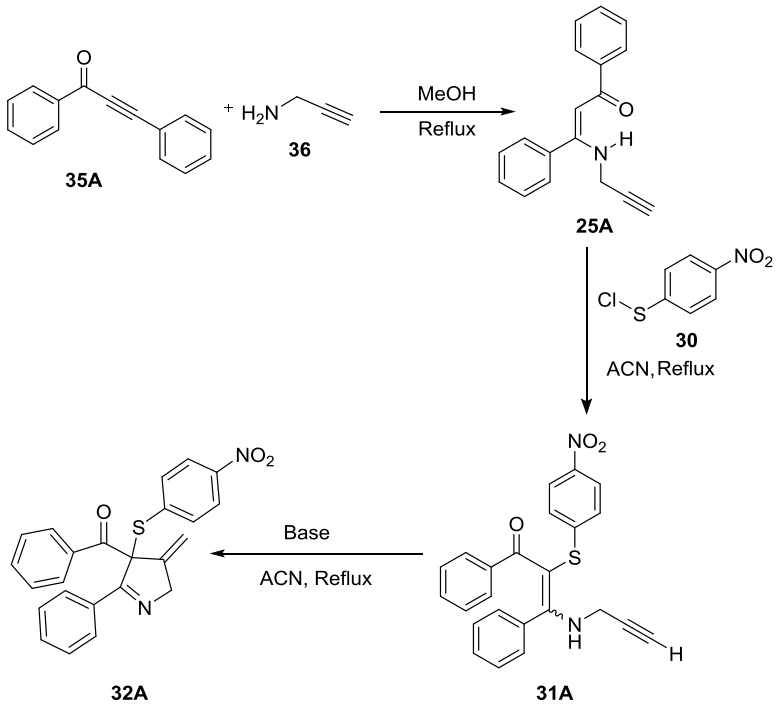
2.3. Synthesis of (4-Nitrophenyl)thio-substituted 1-Pyrrolines

After the synthesis of N-propargylic β-enaminone **25**, we explored their reactions with 4-nitrobenzenesulfenyl chloride **30** to test the formation of (4-nitrophenyl)thio-substituted 1-pyrrolines **32**. Moreover, optimization reactions were carried out in order to obtain higher yields of the products.

First of all, one-pot three-steps reactions were performed (Table 3). In this respect, all reactions were carried out in tandem three steps without making column chromatography for the resulting intermediate compounds. In the first step, 1.0 equiv. of α,β-alkynic ketone **35A** was reacted with 1.2 equiv. of propargylamine **36** in methanol at reflux condition. After the formation of N-propargylic β-enaminone **25A**, as indicated by the TLC analysis, reaction was terminated and methanol was removed. In the second step, the resulting product **25A** was treated with 4-nitrobenzenesulfenyl chloride **30** in ACN at reflux condition. After the *in situ* formation of intermediate product **31A**, as concluded by the TLC analysis, in the third step, base was added into reaction medium to initiate the cyclization of intermediate product **31A**. Finally, target cyclized product **32A** was obtained and purified by column chromatography, as depicted in Table 3.

When 1.5 equiv. of 4-nitrobenzenesulfenyl chloride **30** and 1.0 equiv. NaH were used, these reactions did not produce the expected product **32A** in good yields (7-9%), (Table 3, entries 1 and 2). However, when we decreased the amount of 4-nitrobenzenesulfenyl chloride **30** from 1.5 to 1.2 equiv., a higher yield (49%) was obtained (Table 3, entry 3). When the reaction time was increased under same conditions, the lower yield (27%) was obtained (Table 3, entry 4). Then, reaction was tried by using 1.0 equiv. Cs_2CO_3, which gave the desired product **32A** in 30% yield (Table 3, entry 5). However, when 2.0 equiv. Cs_2CO_3 were employed by shortening the reaction time, a higher yield (49%) was obtained (Table 3, entry 6).

Table 3. Optimization studies for synthesis of (4-nitrophenyl)thio-substituted 1-pyrroline **32A** via one-pot three-steps reactions.



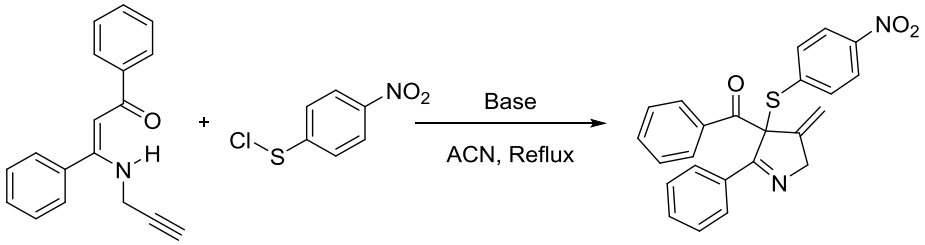
Entry	Sulfenyl Chloride (equiv.)	Base (equiv.)	Time (h)	Yield(%)[a]
1	1.5	NaH (1.0)	11	7
2	1.5	NaH (1.0)	17	9
3	**1.2**	**NaH (1.0)**	**9.5**	**49**
4	1.2	NaH (1.0)	15	27
5	1.2	Cs_2CO_3 (1.0)	17.5	30
6	**1.2**	**Cs_2CO_3 (2.0)**	**9.5**	**49**

[a] Yield of the isolated products.

Secondly, one-pot reactions were performed (Table 4). In this regard, all reactions were carried out in one step in which 1.0 equiv. of N-propargylic β-enaminone **25A**, 1.2 equiv. of 4-nitrobenzenesulfenyl chloride **30** and base were reacted with each other in ACN at reflux condition to form (4-nitrophenyl)thio-substituted 1-pyrroline compound **32A** (Table 4). At the end, the desired product **32A** was purified by column chromatography.

In these reactions, the equivalents of bases were changed. When we used 1.0 equiv. NaH, the target product **32A** was obtained in 37% yield (Table 4, entry 1). Then, the reaction was tried by using 1.5 equiv. NaH, but no significant change in the yield (42%) was observed (Table 4, entry 2). In addition, Cs_2CO_3 was used as a base under same conditions. When 1.0 equiv. of it was used, a better yield (53%) was obtained as compared to NaH (Table 4, entry 3). However, when the amount of Cs_2CO_3 was increased from 1.0 to 1.5 equiv., the desired product **32A** was resulted in 35% yield (Table 4, entry 4).

Table 4. Optimization studies for synthesis of (4-nitrophenyl)thio-substituted 1-pyrroline **32A** via one-pot reactions.



25A **30** **32A**

Entry	Base (equiv.)	Time (h)	Yield(%)[a]
1	NaH (1.0)	4.5	37
2	NaH (1.5)	3.5	42
3	**Cs_2CO_3 (1.0)**	**4.0**	**53**
4	Cs_2CO_3 (1.5)	3.5	35

[a]Yield of the isolated products.

Thirdly, one-pot two-steps reactions were performed (Table 5). In this respect, 1.0 equiv. of N-propargylic β-enaminone **25A** was treated with 1.2 equiv. of 4-nitrobenzenesulfenyl chloride **30** in ACN at reflux condition. Then, base was added for the cyclization after the intermediate product **31A** formed as indicated by the TLC analysis, as shown in Table 5. Finally, the desired product **32A** was obtained and purified by column chromatography.

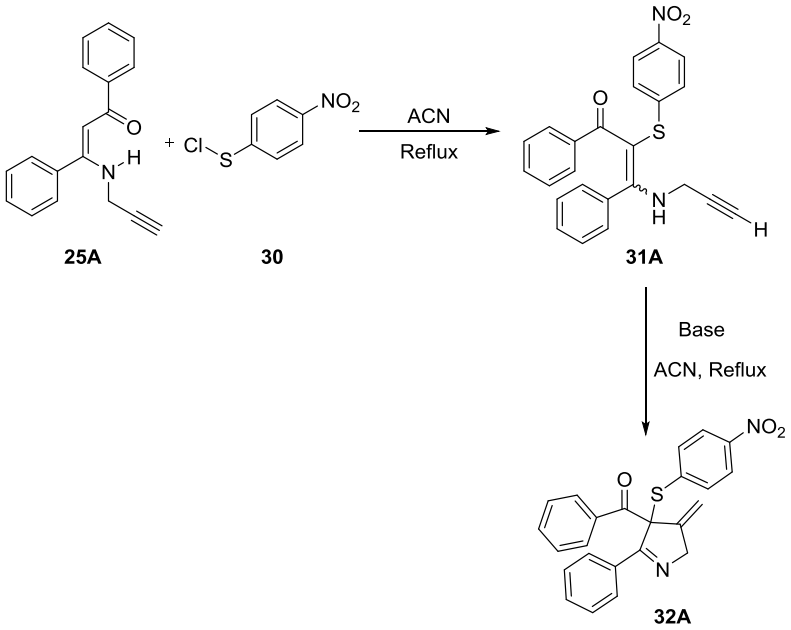
Reactions were carried out by using different equivalents of NaH and Cs_2CO_3. Firstly, 2.0 equiv. of NaH was employed in the reaction, but the target product **32A** was obtained in a low yield **(**11%) (Table 5, entry 1). When the reaction was repeated in longer reaction time under the same conditions, the yield of **32A** (13%) did not change much (Table 5, entry 2). However, the amount of NaH was reduced from 2.0 to 1.5

equiv., the yield of **32A** (29%) was improved slightly (Table 5, entry 3). When we decreased the amount of NaH to 1.0 equiv., the highest yield (71%) of **32A** was achieved (Table 5, entry 4). The same reaction was also tried by increasing the reaction time, but the relatively lower yields (64 and 60%) were obtained (Table 5, entries 5 and 6, respectively). Moreover, we carried out the reaction by using Cs_2CO_3 as a base. When 2.0 equiv. of it was employed, we did not get satisfactory result (21%) (Table 5, entry 7). When the amount of Cs_2CO_3 was decreased from 2.0 to 1.5 equiv., the yield of **32A** improved a little (35%) (Table 5, entry 8). When 1.0 equiv. of Cs_2CO_3 was used, a good yield of **32A** (68%) was achieved (Table 5, entry 9).

In the optimization studies, 71 and 68% yields of **32A** were obtained in the presence of 1.0 equiv. NaH and Cs_2CO_3, respectively (Table 5). These yields were the highest and close to each other. Therefore, we have synthesized the derivatives of (4-nitrophenyl)thio-substituted 1-pyrrolines **32** according to one-pot two-steps reaction method by employing both NaH and Cs_2CO_3.

By using optimized conditions (Table 5, entries 4 and 9), we synthesized 21 different derivatives of (4-nitrophenyl)thio-substituted 1-pyrrolines **32** with electron-withdrawing and electron-donating groups, as shown in Table 6. When we evaluate the yields of 1-pyrrolines **32** for NaH base, the highest yield (87%) was obtained for *p*-chloro-substituted 1-pyrroline derivative **32C**. On the other hand, *p*-nitrobenzene-substituted 1-pyrroline derivative **32K** was resulted in the lowest yield (42%). Halogen containing derivatives was achieved in good yields, higher than (50%) (Table 6). In the case of Cs_2CO_3 base, the highest yield (81%) was obtained from thiophene-containing derivative **32B**. However, *p*-nitrobenzene-substituted 1-pyrroline derivative **32K** formed in the lowest yield (32%). Other derivatives containing halogen groups formed in good yields (Table 6).

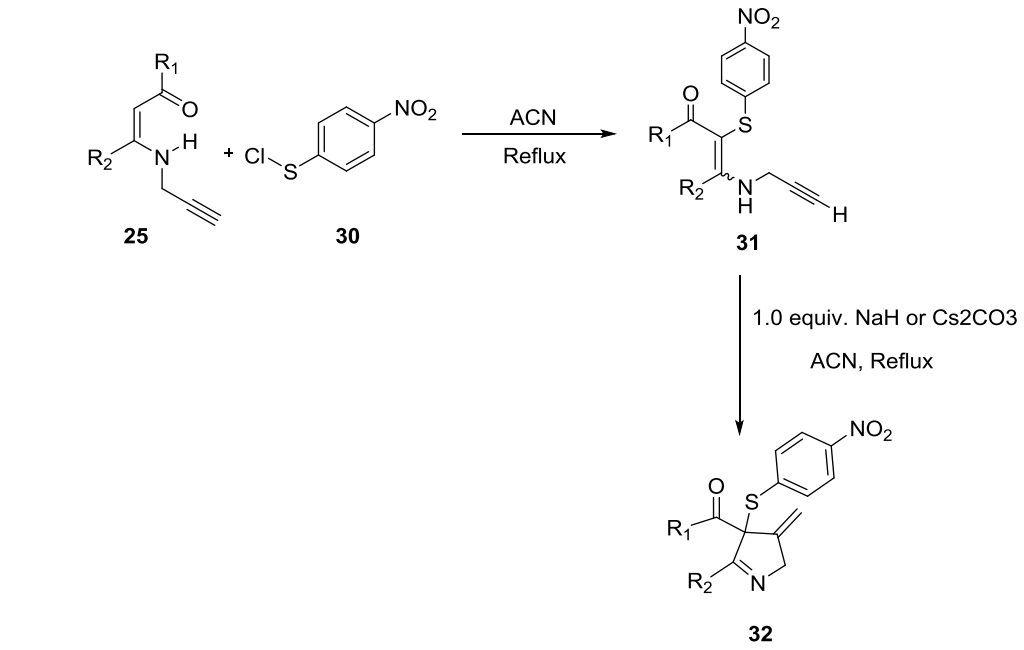
Table 5. Optimization studies for synthesis of (4-nitrophenyl)thio-substituted 1-pyrroline **32A** via one-pot two-steps reactions.



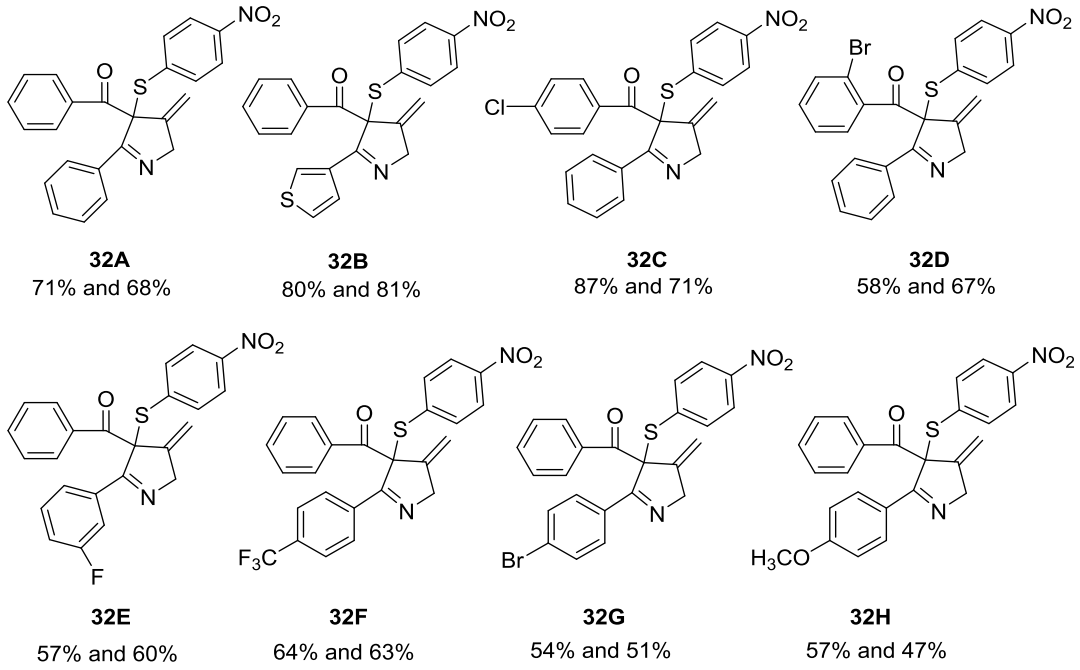
Entry	Base (equiv.)	Time (h)	Yield(%)[a]
1	NaH (2.0)	6.5	11
2	NaH (2.0)	8.5	13
3	NaH (1.5)	5.5	29
4	**NaH (1.0)**	**7.0**	**71**
5	NaH (1.0)	8.0	64
6	NaH (1.0)	10	60
7	Cs_2CO_3 (2.0)	6.0	21
8	Cs_2CO_3 (1.5)	5.0	35
9	**Cs_2CO_3 (1.0)**	**6.5**	**68**

[a]Yield of the isolated products.

Table 6. Synthesis of (4-nitrophenyl)thio-substituted 1-pyrroline derivatives **32**.[a,b]



25 30 31 32



32A 71% and 68%

32B 80% and 81%

32C 87% and 71%

32D 58% and 67%

32E 57% and 60%

32F 64% and 63%

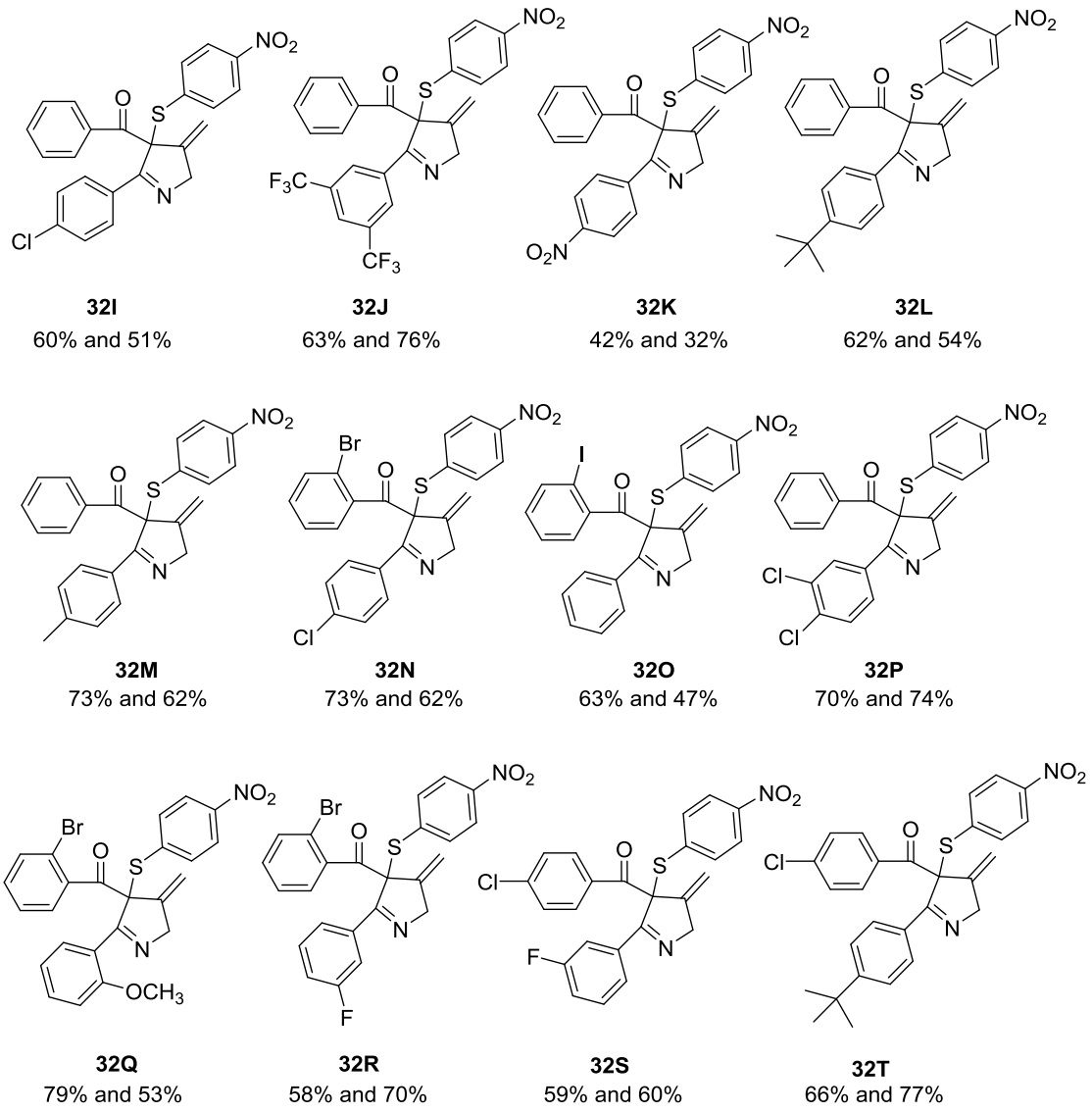
32G 54% and 51%

32H 57% and 47%

[a]Yields of the isolated products.

[b]First yields show those obtained with NaH while second ones display those obtained with Cs_2CO_3.

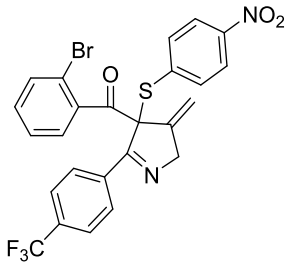
Table 6. Continued.



[a]Yields of the isolated products.

[b]First yields show those obtained with NaH while second ones display those obtained with Cs_2CO_3.

Table 6. Continued.



32U
63% and 68%

[a]Yields of the isolated products.

[b]First yields show those obtained with NaH while second ones display those obtained with Cs_2CO_3.

As a representative example, ^{1}H and ^{13}C NMR spectra of 1-pyrroline **32A** are given in Figures 15 and 16. In the ^{1}H NMR spectrum (Figure 15), the resonation of aromatic ten hydrogens for two phenyl groups occurs between 6.75-7.22 ppm. Hydrogen peaks of the phenyl group with NO_2 group appear as two doublets at 7.48 and 7.86 ppm. In addition, two methylene hydrogens appear at 4.49 ppm as a singlet. Finally, exo vinylic hydrogens resonate at 4.93 and 5.16 ppm as singlets (Figure 15).

In the ^{13}C NMR spectrum (Figure 16), carbonyl carbon appears at 194.4 ppm. The resonation of aromatic twelve carbons for three phenyl groups occurs between 122-143 ppm. In addition, methylene carbon peak appears at 56.8 ppm. One of exo double bond carbons ($=CH_2$) resonates at 109.0 ppm while the other carbon peak (=C) comes at 147.6 ppm. Finally, sulfur-bonded carbon peak (C-S) appears at 120.0 ppm, but nitrogen bonded carbon (C=N) peak comes at 150.9 ppm (Figure 16).

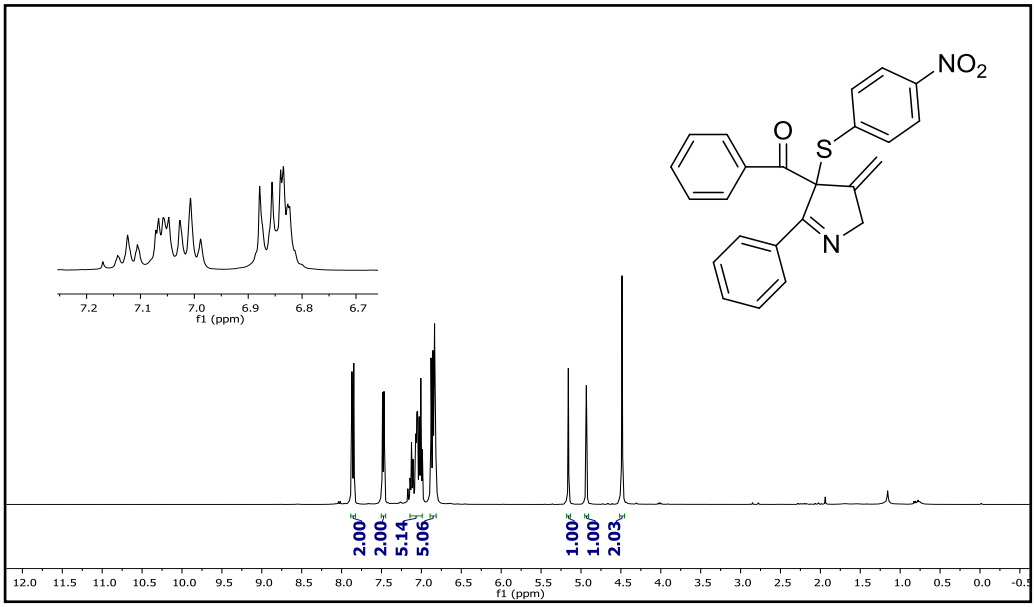


Figure 15. ^{1}H NMR spectrum of (3-methylene-4-((4-nitrophenyl)thio)-5-phenyl-3,4-dihydro-2H-pyrrol-4-yl)(phenyl)methanone (**32A**).

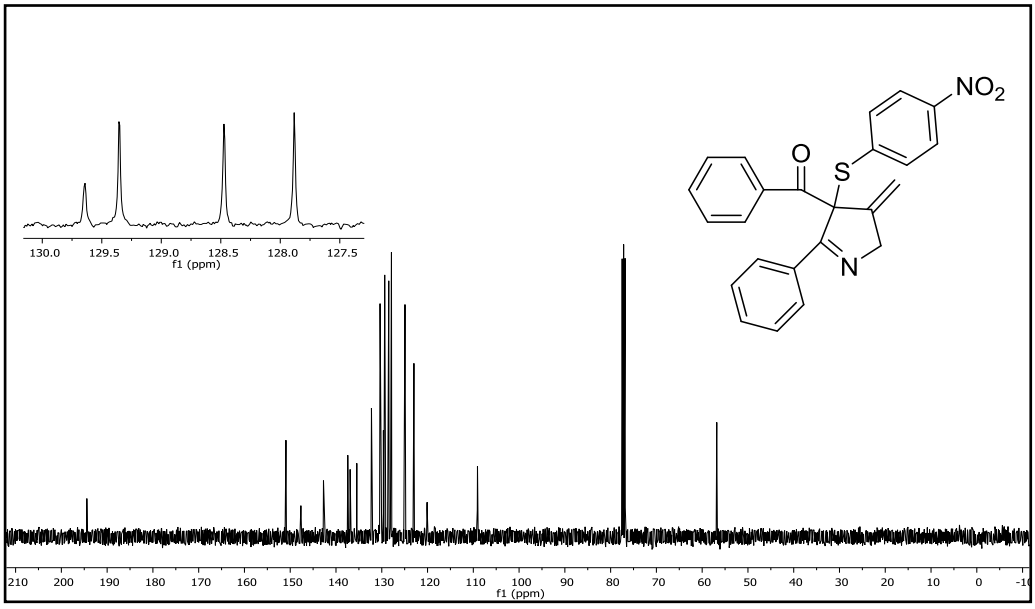
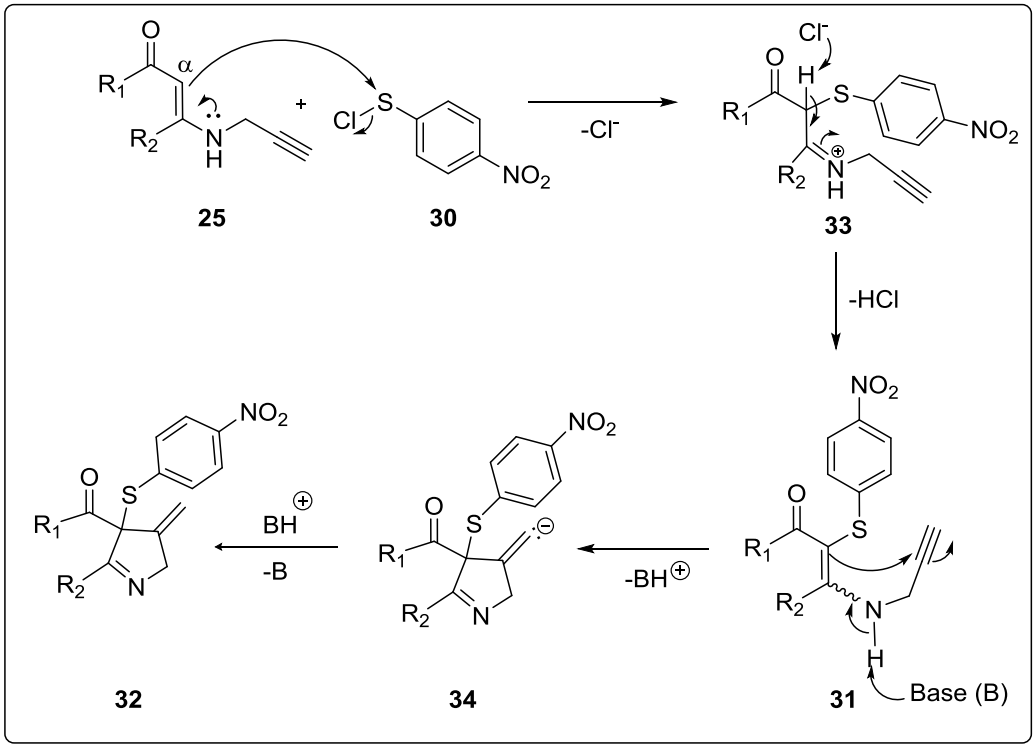


Figure 16. ^{13}C NMR spectrum of (3-methylene-4-((4-nitrophenyl)thio)-5-phenyl-3,4-dihydro-2H-pyrrol-4-yl)(phenyl)methanone (**32A**).

Proposed mechanism for the synthesis of (4-nitrophenyl)thio-substituted 1-pyrrolines **32** is shown in Scheme 12. First, α-carbon of N-propargylic β-enaminone **25** attacks sulphur atom of 4-nitrobenzenesulfenyl chloride **30** as a result of resonance interaction. Then, chloride ion abstracts the hydrogen atom on α-carbon of the intermediate **33** to produce thio-substituted N-propargylic β-enaminone compound **31**. Subsequently, base abstracts the amine hydrogen, which initiates the cyclization to give nitrogen containing five-membered vinyl anion **34**. Upon protonation, 4-methylene-1-pyrroline derivative **32** is obtained (Scheme 12).



Scheme 12. Proposed mechanism for the synthesis of (4-nitrophenyl)thio-substituted 1-pyrrolines **32**.

CHAPTER 3

CONCLUSION

To sum up, we synthesized 21 different derivatives of (4-nitrophenyl)thio-substituted 1-pyrrolines **32** in good yields via one-pot two-steps reaction method by using both NaH and Cs_2CO_3 bases for the same reactions.

In the first part of our project, α,β-alkynic ketone derivatives **35** as the starting compounds were synthesized in 46-98% yields by Sonogashira cross-coupling reaction in which the coupling reaction of aryl chlorides **33** with terminal alkynes **34** was performed under palladium and copper-catalyzed conditions.

In the second part of our study, conjugate addition of propargylamine (**36**) to α,β-alkynic ketones **35** was carried out in methanol at reflux condition to produce N-propargylic β-enaminone derivatives **25**. Overall, 21 different derivatives of N-propargylic β-enaminones **25** were synthesized in high yields, changing from 71 to 98%.

In the last part of our project, the reaction of N-propargylic β-enaminone derivatives **25** with 4-nitrobenzenesulfenyl chloride **30** was performed to obtain (4-nitrophenyl)thio-substituted 1-pyrroline derivatives **32**. To achieve the high yields, we carried out optimization reactions by one-pot three-steps, one-pot and one-pot two-steps reactions, using two different bases. For this reason, the amount of bases and 4-nitrobenzenesulfenyl chloride **30** and the reaction time were changed during the course of the optimization reactions. The highest yields (71 and 68%) with 1.0 equiv. of NaH and Cs_2CO_3, respectively, were obtained by one-pot two-steps reaction method.

Synthesis of (4-nitrophenyl)thio-substituted 1-pyrroline derivatives **32** were carried out with respect to this reaction method. We prepared 21 novel thio-substituted 1-pyrroline derivatives **32** containing electron-withdrawing and electron-donating

groups by using both NaH and Cs_2CO_3 bases. Athough, in many cases, the obtained yields are comparable, NaH generally gave better yields than Cs_2CO_3.

CHAPTER 4

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were recorded at 400 and 100 MHz by using Bruker Spectrospin Avance DPX400 Ultrashield spectrometer. The chemical shift are reported as parts per million (ppm) downfield in TMS (trimethylsilane) reference. Coupling constants (*J*) are yielded in hertz (Hz) and spin multiplicities are given as broad (br), singlet (s), doublet (d), doublet of doublets (dd), triplet (t), triplet of triplets (tt), quartet (q), m (multiplet), doublet of triplets (dt), triplet of triplets (tt), triplet of doublets (td) and triplet of doublet of doublets (tdd). Flash chromatography with using silica gel (Merck 230-400) provided the purification of samples after reactions were finished. TLC (thin layer chromatography) was applied by using 0.25 mm commercially available silica gel plates to observe the reactions and visualization was achieved with short wavelength UV lamp (254 nm). Different hexane-ethyl acetate solvent mixtures were used as eluent for flash chromatography and their volume:volume ratio were modified according to their employments. These solvents were distilled to get rid of impurity. Attenuated total reflection (ATR) was used to record the infrared spectra (IR). Band positions are given as reciprocal centimeters (cm^{-1}). Argon gas (ca. 0.1 psi) supplied inert atmosphere. All glassware and other equipments were carefully cleaned down and dried in oven.

4.1. General Procedure 1. Synthesis of α,β-Alkynic Ketone Derivatives 35

The corresponding benzoyl chloride derivative **33** (1.2 mmol) was dissolved in THF (5.0 mL) in a round-bottomed flask. Then, $PdCl_2(PPh_3)_2$ (0.02 mmol) and Et_3N (1.2 mmol) were added and stirred for 10 min at room temperature under argon. Then, CuI (0.02 mmol) was added and the reaction mixture was stirred for another 10 min. Subsequently, terminal alkyne **34** (1.0 mmol) was added slowly to the reaction medium and the resulting mixture was stirred until the end of the reaction, as monitored by the TLC analysis (19:1 hexane/ethyl acetate). When the reaction finished, extraction was performed with ethyl acetate (50 mL), saturated aqueous NH_4Cl (50 mL) and 0.1 N HCl solution. The combined organic phases were dried with $MgSO_4$. Finally, flash chromatography was performed by using hexane as the eluent to purify the crude product.

4.1.1. Synthesis of 1,3-Diphenylprop-2-yn-1-one (35A)

General Procedure **1** was followed by using benzoyl chloride (1.23 g, 8.72 mmol), $PdCl_2(PPh_3)_2$ (102,07 mg, 0.15 mmol), Et_3N (888,97 mg, 8.72 mmol), CuI (27.63 mg, 0.15 mmol) and phenylacetylene (742,56 mg, 7.27 mmol), which afforded 1.34 g (89%) of the indicated product **35A** as yellow oil (R_f = 0.54 in 4:1 hexane/ethyl acetate).

35A: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27–8.16 (m, 2H), 7.64 (dt, *J* = 8.4, 1.8 Hz, 2H), 7.61–7.55 (m, 1H), 7.52–7.45 (m, 2H), 7.43 (dt, *J* = 2.8, 2.1 Hz, 1H), 7.40–7.34 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.8 (CO), 136.8 (C), 134.1 (CH), 132.9 (CH), 130.8 (CH), 129.4 (CH), 128.6 (CH), 128.6 (CH), 119.9 (C), 93.0 (C), 86.9 (C); IR (neat): 3059, 3032, 2195, 1638, 1597, 1579, 1488, 1448, 1314, 1284, 1239, 1208, 1171, 1096, 1069, 1031, 1011, 995, 920, 846, 814, 794, 757, 696 cm^{-1}. The spectral data were in agreement with those reported previously for this compound.[41]

4.1.2. Synthesis of 1-Phenyl-3-(thiophen-3-yl)prop-2-yn-1-one (35B)

General Procedure **1** was followed by using benzoyl chloride (795 mg, 5.65 mmol) $PdCl_2(PPh_3)_2$ (66 mg, 0.09 mmol), Et_3N (576 mg, 5.65 mmol), CuI (17 mg, 0.09 mmol) and 3-ethynylthiophene (509 mg, 4.71 mmol), which afforded 925 mg (93%) of the indicated product **35B** as orange-brown oil (R_f = 0.67 in 4:1 hexane/ethyl acetate).

35B: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23–8.14 (m, 2H), 7.98–7.72 (m, 1H), 7.64–7.58 (m, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.43–7.33 (m, 1H), 7.32–7.27 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.0 (CO), 136.8 (C), 134.2 (CH), 134.0 (CH), 130.3 (CH), 129.6 (CH), 128.7 (CH), 126.4 (CH), 119.4 (C), 88.6 (C), 87.2 (C); IR (neat): 3105, 3063, 2148, 1631, 1596, 1546, 1514, 1487, 1448, 1409, 1359, 1312, 1266, 1217, 1167, 1080, 1032, 1014, 924, 872, 827, 784, 695 cm^{-1}. The spectral data were in agreement with those reported previously for this compound.[40]

4.1.3. Synthesis of 1-(4-Chlorophenyl)-3-phenylprop-2-yn-1-one (35C)

General Procedure **1** was followed by using 4-chlorobenzoyl chloride (871.55 mg, 4.98 mmol), $PdCl_2(PPh_3)_2$ (58.27 mg, 0.08 mmol), Et_3N (507.46 mg, 4.98 mmol), CuI (15.77 mg, 0.08 mmol) and phenylacetylene (423.88 mg, 4.15 mmol), which afforded 950 mg (95%) of the indicated product **35C** as a yellow solid (R_f = 0.68 in 4:1 hexane/ethyl acetate).

35C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.6 Hz, 2H), 7.73–7.59 (m, 2H), 7.55–7.34 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6 (CO), 140.7 (C), 135.3 (C), 133.1 (CH), 131.0 (C), 130.9 (CH), 129.0 (CH), 128.8 (CH), 119.9 (CH), 93.7 (C), 86.6 (C); IR (neat): 3262, 3085, 3061, 3032, 3032, 2472, 2197, 1953, 1649, 1582, 1480, 1445, 1398, 1301, 1276, 1205, 1168, 1108, 1089, 1029, 1007, 994, 913, 847, 812, 749, 738, 680 cm^{-1}. The spectral data were in agreement with those reported previously for this compound.[40]

4.1.4. Synthesis of 1-(2-Bromophenyl)-3-phenylprop-2-yn-1-one (35D*)*

General Procedure **1** was followed by using 2-bromobenzoyl chloride (924 mg, 4.21 mmol) $PdCl_2(PPh_3)_2$ (49 mg, 0.07 mmol), Et_3N (428 mg, 4.20 mmol), CuI (13 mg, 0.07 mmol) and phenylacetylene (359 mg, 3.51 mmol), which afforded 459 mg (46%) of the indicated product **35D** as yellow oil (R_f = 0.3 in 4:1 hexane/ethyl acetate).
35D: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.69 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.66–7.60 (m, 2H), 7.54–7.30 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.5 (CO), 137.5 (C), 134.9 (CH), 133.5 (CH), 133.2 (CH), 132.8 (CH), 131.1 (CH), 128.8 (CH), 127.5 (CH), 121.3 (C), 119.9 (C), 94.3 (C), 87.9 (C); IR (neat): 3059, 2192, 1733, 1648, 1584, 1562, 1488, 1464, 1443, 1431, 1372, 1297, 1201, 1128, 1062, 1026, 1007, 994, 814, 757, 736, 688 cm^{-1}. The spectral data were in agreement with those reported previously for this compound.[42]

4.1.5. Synthesis of 3-(3-Fluorophenyl)-1-phenylprop-2-yn-1-one (35E)

General Procedure **1** was followed by using benzoyl chloride (753 mg, 5.35 mmol) $PdCl_2(PPh_3)_2$ (63 mg, 0.09 mmol), Et_3N (545 mg, 5.35 mmol), CuI (17 mg, 0.09 mmol) and 1-ethynyl-3-fluorobenzene (536 mg, 4.46 mmol), which afforded 503 mg (50.3 %) of the indicated product **35E** as a yellow solid (R_f = 0.68 in 4:1 hexane/ethyl acetate); mp 60.1–61.0 °C.
35E: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28–8.05 (m, 2H), 7.64–7.55 (m, 1H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.41 (d, *J* = 7.7 Hz, 1H), 7.37–7.27 (m, 2H), 7.17–7.09 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.5 (CO), 162.22 (d, ^1J = 248.3 Hz, CF), 136.6 (CH), 134.3 (CH), 130.4 (d, ^3J = 8.4 Hz, CH), 129.5 (CH), 128.9 (d, ^4J = 3.0 Hz, CH), 128.7 (C), 121.9 (d, ^3J = 9.3 Hz, C), 119.6 (d, ^2J = 23.3 Hz, CH), 118.2 (d, ^2J = 21.1 Hz, CH), 90.9 (d, ^4J = 3.3 Hz, C), 87.1 (C); IR (neat): 3259, 3000, 2458, 2201, 1649, 1597, 1579, 1485, 1468, 1446, 1426, 1338, 1314, 1299, 1267, 1251, 1228, 1169, 1144, 1077, 1029, 1015, 998, 923, 867, 781, 765, 691 cm^{-1}. The spectral data were in agreement with those reported previously for this compound.[43]

4.1.6. Synthesis of 1-Phenyl-3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-one (35F)

General Procedure **1** was followed by using benzoyl chloride (616 mg, 4.38 mmol), $PdCl_2(PPh_3)_2$ (51 mg, 0.07 mmol), Et_3N (446 mg, 4.38 mmol), CuI (14 mg, 0.07 mmol) and 4-ethynyl-α,α,α-trifluorotoluene (621 mg, 3.65 mmol), which afforded 808 mg (81%) of the indicated product **35F** as a brown solid (R_f = 0.75 in 4:1 hexane/ethyl acetate); mp 82.9–83.7ºC.

35F: ^{1}H NMR (400 MHz, $CDCI_3$) δ 8.21 (d, J = 7.3 Hz, 2H), 7.78 (d, J = 8.2 Hz, 2H), 7.70–7.62 (m, 3H), 7.53 (t, J = 7.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2 (CO), 136.5 (C), 134.5 (CH), 133.2 (CH), 132.2 (q, ^2J = 32.4 Hz, C), 129.6 (CH), 128.7 (CH), 125.6 (q, ^3J = 3.6 Hz, CH), 123.9 (C), 123.6 (q, ^1J = 272.6 Hz, CF_3), 90.2 (C), 88.1 (C); IR (neat): 3052, 2205, 1638, 1596, 1578, 1449, 1405, 1314, 1290, 1212, 1165, 1105, 1066, 1028, 1008, 938, 844, 792, 760, 695, 632, 597, 526 cm^{-1}. MS (ESI, m/z): 275.06 $[M+H]^+$; HRMS (ESI) calcd. for $C_{16}H_{10}F_3O$: 275.06783 $[M+H]^+$, found: 275.06850.

4.1.7. Synthesis of 3-(4-Bromophenyl)-1-phenylprop-2-yn-1-one (35G)

General Procedure **1** was followed by using benzoyl chloride (592 mg, 4.20 mmol), $PdCl_2(PPh_3)_2$ (49 mg, 0.07 mmol), Et_3N (428 mg, 4.20 mmol), CuI (13 mg, 0.07 mmol) and 1-bromo-4-ethynyl benzene (635 mg, 3.51 mmol), which afforded 710 mg (71%) of the indicated product **35G** as a brownish-yellow solid (R_f = 0.67 in 4:1 hexane/ethyl acetate); mp 114.1–115.7 ºC.

35G: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13–8.10 (m, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.49–7.44 (m, 4H), 7.42 (d, J = 7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.78 (CO), 136.76 (C), 134.39 (CH), 134.31 (CH), 132.14 (CH), 129.61 (CH), 128.73 (CH), 125.66 (C), 119.08 (C), 91.67 (C), 87.76 (C); IR (neat): 3053, 2195, 1629, 1577, 1473, 1447, 1393, 1325, 1292, 1205, 1170, 1062, 1029, 1007, 817, 791, 692, 639, 628, 528, 438 cm^{-1}. MS (ESI, m/z): 284.99 $[M+H]^+$; HRMS (ESI) calcd. for $C_{15}H_9BrO$: 284.99095 $[M+H]^+$, found: 284.99160.

4.1.8. Synthesis of 3-(4-Methoxyphenyl)-1-phenylprop-2-yn-1-one (35H)

General Procedure **1** was followed by using benzoyl chloride (358 mg, 2.50 mmol) $PdCl_2(PPh_3)_2$ (30 mg, 0.04 mmol), Et_3N (259 mg, 2.54 mmol), CuI (8 mg, 0.04 mmol) and 4-ethynylanisole (280 mg, 2.12 mmol), which afforded 225 mg (45%) of the indicated product **35H** as a yellow solid (R_f = 0.41 in 4:1 hexane/ethyl acetate).
35H: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27–8.14 (m, 2H), 7.68–7.56 (m, 3H), 7.53–7.47 (m, 2H), 6.91 (tt, *J* = 9.3, 2.3 Hz, 2H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.0 (CO), 161.8 (C), 137.1 (C), 135.2 (CH), 133.9 (CH), 129.5 (CH), 128.6 (CH), 114.5 (CH), 111.9 (C), 94.4 (C), 86.9 (C), 55.5 (CH_3); IR (neat): 3198, 3096, 3077, 3052, 3014, 2978, 2941, 2842, 2594, 2555, 2424, 2325, 2185, 2083, 2068, 1979, 1911, 1825, 1783, 1730, 1659, 1622, 1597, 1568, 1510, 1459, 1441, 1315, 1293, 1253, 1210, 1189, 1168, 1113, 1009, 833, 793, 695 cm^{-1}. The spectral data were in agreement with those reported previously for this compound.[40]

4.1.9. Synthesis of 3-(4-Chlorophenyl)-1-phenylprop-2-yn-1-one (35I)

General Procedure **1** was followed by using benzoyl chloride (351 mg, 2.50 mmol) $PdCl_2(PPh_3)_2$ (29 mg, 0.04 mmol), Et_3N (255 mg, 2.50 mmol), CuI (8 mg, 0.04 mmol) and 1-chloro-4-ethynylbenzene (284 mg, 2.08 mmol), which afforded 376 mg (75%) of the indicated product **35I** as a yellow solid (R_f = 0.63 in 4:1 hexane/ethyl acetate).
35I: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.2 Hz, 2H), 7.54–7.39 (m, 3H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.5 (CO), 137.1 (C), 136.6 (C), 134.2 (CH), 129.4 (CH), 129.0 (CH), 128.6 (CH), 118.5 (C), 91.5 (C), 87.5 (C). (Note that two CH peaks overlap on each other); IR (neat): 3408, 3251,3211, 3157, 3083, 3054, 3031, 3002, 2504, 2433, 2327, 2309, 2196, 2116, 2032, 1966, 1915, 1825, 1786, 1733, 1697, 1659, 1629, 1598, 1578, 1489, 1478, 1447, 1399, 1316, 1294, 1205, 1170, 1085, 1030, 1008, 939, 821, 791, 722, 692 cm^{-1}. The spectral data were in agreement with those reported previously for this compound.[40]

4.1.10. Synthesis of 3-(3,5-Bis(trifluoromethyl)phenyl)-1-phenylprop-2-yn-1-one (35J)

General Procedure **1** was followed by using benzoyl chloride (246 mg, 1.75 mmol), $PdCl_2(PPh_3)_2$ (21 mg, 0.03 mmol), Et_3N (179 mg, 1.75 mmol), CuI (6 mg, 0.03 mmol) and 1-ethynyl-3,5-bis(trifluoromethyl)benzene (348 mg, 1.46 mmol), which afforded 439 mg (88%) of the indicated product **35J** as a brown solid (R_f = 0.81 in 4:1 hexane/ethyl acetate); mp 65.1–66.5ºC.

35J: ^{1}H NMR (400 MHz, $CDCI_3$) δ 8.20 (dd, J = 8.3, 1.1 Hz, 2H), 8.10 (s, 2H), 7.97 (s, 1H), 7.67 (tt, J = 7.0, 1.2 Hz, 1H), 7.59-7.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2 (CO), 136.4 (C), 134.8 (CH), 132.81 (CH), 132.65 (q, ^2J = 34.1 Hz, C-CF_3), 129.7 (CH), 128.9 (CH), 124.1 (q, ^3J = 6.2 Hz, CH), 122.82 (C), 122.79 (q, ^1J = 272.9 Hz, CF_3), 88.67 (C), 88.05 (C); IR (neat): 3097, 2211, 1638, 1597, 1580, 1451, 1378, 1316, 1275, 1204, 1126, 1034, 1017, 896, 846, 795, 703, 681, 629, 542, 428, 410 cm^{-1}. MS (ESI, m/z): 343.05 $[M+H]^+$; HRMS (ESI) calcd. for $C_{17}H_9F_6O$: 343.05521 $[M+H]^+$, found: 343.05441.

4.1.11. Synthesis of 3-(4-Nitrophenyl)-1-phenylprop-2-yn-1-one (35K)

General Procedure **1** was followed by using benzoyl chloride (336 mg, 2.39 mmol), $PdCl_2(PPh_3)_2$ (28 mg, 0.04 mmol), Et_3N (243 mg, 2.39 mmol), CuI (8 mg, 0.04 mmol) and 1-ethynyl-4-nitrobenzene (293mg, 1.99 mmol), which afforded 185 mg (45%) of the indicated product **35K** as a bright yellow solid (R_f = 0.50 in 4:1 hexane/ethyl acetate).

35K: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (dt, J = 8.9, 1.9 2H), 8.23–8.17 (m, 2H), 7.84 (dt, J = 8.9, 1.9 2H), 7.67 (tt, J = 2.4, 1.2 Hz, 1H), 7.57–7.52 (dd, J = 10.7, 4.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.5 (CO), 148.7 (C), 136.5 (C), 134.8 (CH), 133.8 (C), 129.8 (CH), 128.9 (CH), 126.9 (CH), 123.9 (CH), 89.9 (C), 89.3 (C); IR (neat): 3104, 3067, 2934, 2844, 2696, 2444, 2322, 2289, 2205, 2145, 1980, 1935, 1811, 1782, 1733, 1685, 1633, 1592, 1519, 1449, 1402, 1370, 1341, 1312, 1287, 1211,

1169, 1102, 1027, 1007, 855, 804, 751, 711, 681, 642, 525, 426 cm^{-1}. The spectral data were in agreement with those reported previously for this compound.[40]

4.1.12. Synthesis of 3-(4-(Tert-butyl)phenyl)-1-phenylprop-2-yn-1-one (35L)

General Procedure **1** was followed by using benzoyl chloride (323 mg, 2.30 mmol), $PdCl_2(PPh_3)_2$ (27 mg, 0.04 mmol), Et_3N (234 mg, 2.30 mmol), CuI (7 mg, 0.04 mmol) and 4-tert-butylphenylacetylene (302 mg, 1.91 mmol), which afforded 460 mg (92%) of the indicated product **35L** as yellow oil (R_f = 0.54 in 4:1 hexane/ethyl acetate).
35L: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 5,2, 3,3 Hz, 2H), 7.43–7.37 (m, 3H), 7.31 (d, *J* = 7,8 Hz, 2H), 7.21 (d, *J* = 8,6 Hz, 2H), 1.11 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.83 (CO), 154.31 (C), 137.01 (C), 134.05 (CH), 133.04 (CH), 129.52 (CH), 128.65 (CH), 125.79 (CH), 117.02 (C), 93.75 (C), 86.87 (C), 34.15 (C), 30.57 (CH_3); IR (neat): 3065, 2961, 2904, 2867, 2192, 1637, 1597, 1578, 1504, 1448, 1394, 1363, 1313, 1288, 1212, 1171, 1107, 1029, 1008, 834, 792, 697, 650, 563, 524, 414 cm^{-1}. MS (ESI, m/z): 263,14 $[M+H]^+$; HRMS (ESI) calcd. for $C_{19}H_{19}O$: 263,14304 $[M+H]^+$, found: 263,14298.

4.1.13. Synthesis of 1-Phenyl-3-(p-tolyl)prop-2-yn-1-one (35M)

General Procedure **1** was followed by using benzoyl chloride (382 mg, 2.72 mmol), $PdCl_2(PPh_3)_2$ (32 mg, 0.05 mmol), Et_3N (277 mg, 2.72 mmol), CuI (9 mg, 0.05 mmol) and p-tolyacetylene (264 mg, 2.27 mmol), which afforded 384 mg (77%) of the indicated product **35M** as a brownish-orange solid (R_f = 0.56 in 4:1 hexane/ethyl acetate); mp 58.3–59.6 ºC.
35M: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (dd, *J* = 8.0, 1.0 Hz, 2H), 7.59–7.28 (m, 5H), 7.06 (d, *J* = 7.9 Hz, 2H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.4 (CO), 141.2 (C), 136.6 (C), 133.7 (CH), 132.8 (CH), 129.2 (CH), 129.1 (CH), 128.3 (CH), 116.6 (C), 93.4 (C), 86.6 (C), 21.3 (CH_3); IR (neat): 3066, 3025, 2915, 2854, 2442, 2325, 2303, 2193, 2125, 1969, 1916, 1826, 1731, 1671, 1626, 1596, 1577, 1507, 1488,

1448, 1409, 1375, 1314, 1293, 1245, 1206, 1168, 1119, 1106, 1072, 1029, 1007, 958, 939, 855, 814, 793, 765, 696 cm^{-1}. The spectral data were in agreement with those reported previously for this compound.[40]

4.1.14. Synthesis of 1-(2-Bromophenyl)-3-(4-chlorophenyl)prop-2-yn-1-one (35N)

General Procedure **1** was followed by using 2-bromobenzoyl chloride (392 mg, 1.79 mmol), $PdCl_2(PPh_3)_2$ (21 mg, 0.03mmol), Et_3N (182 mg, 1.79 mmol), CuI (6 mg, 0.03 mmol) and 1-chloro-4-ethynylbenzene (204 mg, 1.49 mmol), which afforded 405 mg (81%) of the indicated product **35N** as a light brown solid (R_f = 0.65 in 4:1 hexane/ethyl acetate); mp 95.8–97 ^oC.

35N: ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.2 Hz, 1H), 7.64 (d, *J* = 7.7 Hz, 1H), 7.51 (d, *J* = 8.2 Hz, 2H), 7.45–7.37 (m, 2H), 7.33 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1 (CO), 137.4 (C), 137.1 (C), 135.0 (CH), 134.3 (CH), 133.6 (CH), 132.8 (CH), 129.1 (CH), 127.5 (CH), 121.3 (C), 118.4 (C), 92.7 (C), 88.6 (C); IR (neat): 3081, 2349, 2196, 2155, 2063, 1968, 1646, 1582, 1480, 1427, 1298, 1200, 1085, 1059, 1035, 1011, 999, 829, 775, 728, 666, 634, 533, 480, 456, 423, 412 cm^{-1}. MS (ESI, m/z): 318.95 $[M+H]^+$; HRMS (ESI) calcd. for $C_{15}H_9BrClO$: 318.95198, $[M+H]^+$, found: 318.95318.

4.1.15. Synthesis of 1-(2-Iodophenyl)-3-phenylprop-2-yn-1-one (35O)

General Procedure **1** was followed by using 2-iodobenzoyl chloride (483 mg, 1.81 mmol), $PdCl_2(PPh_3)_2$ (21 mg, 0.03mmol), Et_3N (185 mg, 1.81 mmol), CuI (6 mg, 0.03 mmol) and phenylacetylene (154 mg, 1.51 mmol), which afforded 230 mg (46%) of the indicated product **35O** as yellow oil (R_f = 0.67 in 4:1 hexane/ethyl acetate).

35O: ^1H NMR (400 MHz, $CDCl_3$) δ 8.14 (dd, *J* = 7.8, 1.6 Hz, 1H), 8.06 (dd, *J* = 7.9, 0.9 Hz, 1H), 7.65 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.54–7.37 (m, 4H), 7.21 (td, *J* = 7.7, 1.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.2 (CO), 142.2 (CH), 139.6 (C), 133.54 (CH), 133.23 (CH), 133.13 (CH), 131.1 (CH), 128.83 (CH), 128.21 (CH), 120.1 (C),

94.5 (C), 92.9 (C), 87.3 (C); IR (neat): 3056, 2507, 2190, 1724, 1642, 1577, 1487, 1460, 1443, 1427, 1290, 1199, 1123, 1055, 1026, 1004, 991, 812, 780, 755, 731, 645, 618, 534, 463 cm^{-1}. MS (ESI, m/z): 332.97 $[M+H]^+$; HRMS (ESI) calcd. for $C_{15}H_{10}IO$: 332.97708 $[M+H]^+$, found: 332.97818.

4.1.16. Synthesis of 3-(3,4-Dichlorophenyl)-1-phenylprop-2-yn-1-one (35P)

General Procedure **1** was followed by using benzoyl chloride (307 mg, 2.18 mmol), $PdCl_2(PPh_3)_2$ (26 mg, 0.04mmol), Et_3N (223 mg, 2.18 mmol), CuI (7 mg, 0.04 mmol) and 3,4-dichlorophenylacetylene (311 mg, 1.82 mmol), which afforded 407 mg (82%) of the indicated product **35P** as a light yellow solid (R_f = 0.65 in 4:1 hexane/ethyl acetate); mp 111.5–112.8 ºC.

35P: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 7.4 Hz, 2H), 7.65 (s, 1H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.48–7.38 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2 (CO), 136.3 (C), 135.3 (C), 134.18 (CH), 134.16 (CH), 132.9 (C), 131.7 (CH), 130.6 (CH), 129.3 (CH), 128.5 (CH), 119.8 (C), 89.4 (C), 87.7 (C); IR (neat): 3734, 2196, 2022, 1632, 1595, 1577, 1448, 1374, 1313, 1295, 1250, 1208, 1170, 1124, 1028, 1013, 823, 788, 688, 647, 583, 531, 417 cm^{-1}. MS (ESI, m/z): 275.00 $[M+H]^+$; HRMS (ESI) calcd. for $C_{15}H_9Cl_2O$: 275.0025 $[M+H]^+$, found: 275.00198.

4.1.17. Synthesis of 1-(2-Bromophenyl)-3-(2-methoxyphenyl)prop-2-yn-1-one (35Q)

General Procedure **1** was followed by using 2-bromobenzoyl chloride (417 mg, 1.90 mmol), $PdCl_2(PPh_3)_2$ (22 mg, 0.03 mmol), Et_3N (194 mg, 1.90 mmol), CuI (6 mg, 0.03 mmol) and 1-ethynyl-2-methoxybenzene (210 mg, 1.59 mmol), which afforded 426 mg (85%) of the indicated product **35Q** as a light yellow solid (R_f = 0.38 in 4:1 hexane/ethyl acetate); mp 47.1–48.5ºC.

35Q: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.66 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.54 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.46-7.38 (m, 2H), 7.34 (td, *J* = 7.7, 1.8 Hz, 1H), 6.93 (td, *J* = 7.6, 0.8 Hz, 1H), 6.90 (d, *J* = 8.5 Hz, 1H), 3.88 (s, 3H); ^{13}C

NMR (100 MHz, $CDCl_3$) δ 177.2 (CO), 161.9 (C), 137.2 (C), 134.96 (CH), 134.92 (CH), 133.6 (CH), 133.3 (CH), 132.9 (CH), 127.3 (CH), 121.2 (C), 120.7 (CH), 110.9 (CH), 109.1 (C), 92.1(C), 91.4 (C), 55.9 (OCH_3). The spectral data were in agreement with those reported previously for this compound.[44]

4.1.18. Synthesis of 1-(2-Bromophenyl)-3-(3-fluorophenyl)prop-2-yn-1-one (35R)

General Procedure **1** was followed by using 2-bromobenzoyl chloride (435 mg, 1.98 mmol), $PdCl_2(PPh_3)_2$ (23 mg, 0.03 mmol), Et_3N (202 mg, 1.98 mmol), CuI (6 mg, 0.03 mmol) and 1-ethynyl-3-fluorobenzene (198 mg, 1.65 mmol), which afforded 457 mg (91%) of the indicated product **35R** as an orange solid (R_f = 0.58 in 4:1 hexane/ethyl acetate); mp 61.5–62.5 ^oC.

35R: ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (dd, J = 7.7, 1.5 Hz, 1H), 7.64–7.53 (m, 1H), 7.43–7.35 (m, 1H), 7.33–7.25 (m, 3H), 7.23–7.17 (m, 1H), 7.13–7.05 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6 (CO), 161.9 (d, ^1J = 248.2 Hz, CF), 136.5 (C), 134.8 (CH), 133.4 (CH), 132.8 (CH), 130.3 (d, ^3J = 8.4 Hz, CH), 128.7 (d, ^4J = 3.0 Hz, CH), 127.3 (CH), 121.4 (d, ^3J = 9.4 Hz, C), 120.9 (C), 119.3 (d, ^2J = 23.1 Hz, CH), 118.2 (d, ^2J = 21.1 Hz, CH), 91.7 (d, ^4J = 3.4 Hz, C), 87.8 (C); IR (neat): 3069, 2195, 1648, 1579, 1520, 1484, 1429, 1336, 1301, 1263, 1222, 1167, 1149, 1079, 1059, 1011, 922, 872, 785, 736, 697 cm^{-1}; MS (ESI, m/z): 302.98 $[M+H]^+$; HRMS (ESI) calcd. for $C_{15}H_9BrFO$: 302.9815$[M+H]^+$, found: 302.9823.

4.1.19. Synthesis of 1-(4-Chlorophenyl)-3-(3-fluorophenyl)prop-2-yn-1-one (35S)

General Procedure **1** was followed by using 4-chlorobenzoyl chloride (403 mg, 2.30 mmol), $PdCl_2(PPh_3)_2$ (28 mg, 0.04mmol), Et_3N (234 mg, 2.30 mmol), CuI (8 mg, 0.04mmol) and 1-ethynyl-3-fluorobenzene (232 mg, 1.93 mmol), which afforded 464

mg (93%) of the indicated product **35S** as a pale orange solid (R_f = 0.70 in 4:1 hexane/ethyl acetate); mp 125.7–126.3 ºC.

35S: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.5 Hz, 2H), 7.52–7.44 (m, 3H), 7.44–7.33 (m, 2H), 7.24–7.14 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.5 (CO), 162.4 (d, ^1J = 248.6 Hz, CF), 141.1 (C), 135.2 (C), 131.0 (CH), 130.6 (d, ^3J = 8.6 Hz, CH), 129.2 (CH), 129.1 (d, ^4J = 3.0 Hz, CH), 121.8 (d, ^3J = 9.2 Hz, C), 119.8 (d, ^2J = 23.4 Hz, CH), 118.6 (d, ^2J = 21.2 Hz, CH), 91.7 (d, ^4J = 3.2 Hz, C), 86.9 (C); IR (neat): 3251, 3090, 3078, 3059, 3040, 2454, 2324, 2202, 1941, 1923, 1867, 1788, 1722, 1682, 1633, 1607, 1582, 1481, 1428, 1398, 1304, 1268, 1223, 1168, 1154, 1108, 1087, 1030, 1008, 922, 889, 842, 783, 738, 718, 671 cm^{-1}; MS (ESI, m/z): 259.03 $[M+H]^+$; HRMS (ESI) calcd. for $C_{15}H_9ClFO$: 259.0320 $[M+H]^+$, found: 259.0319.

4.1.20. Synthesis of 3-(4-(Tert-butyl)phenyl)-1-(4-chlorophenyl)prop-2-yn-1-one (35T)

General Procedure **1** was followed by using 4-chlorobenzoyl chloride (354 mg, 2.02 mmol), $PdCl_2(PPh_3)_2$ (21 mg, 0.03mmol), Et_3N (206 mg, 2.02 mmol), CuI (6 mg, 0.03mmol) and 1-(tert-butyl)-4-ethynylbenzene (266 mg, 1.68 mmol), which afforded 474 mg (95%) of the indicated product **35T** as a yellow solid (R_f = 0.80 in 4:1 hexane/ethyl acetate); mp 104.3–105.9 ºC.

35T: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.7 Hz, 2H), 7.52 (d, *J* = 8.5 Hz, 2H), 7.39–7.32 (m, 4H), 1.23 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9 (CO), 155.0 (C), 140.8 (C), 135.7 (C), 133.3 (CH), 131.1 (CH), 129.2 (CH), 126.1 (CH), 117.1 (C), 94.6 (C), 86.8 (C), 35.4 (C), 31.3 (CH_3); IR (neat): 3848, 2963, 2194, 2144, 2049, 2020, 1630, 1585, 1572, 1484, 1400, 1300, 1085, 1285, 1265, 1215, 1161, 1108, 1090, 1025, 1006, 838, 746, 675, 627, 597, 533, 488, 424, 410 cm^{-1}. MS (ESI, m/z): 297.10 $[M+H]^+$; HRMS (ESI) calcd. for $C_{19}H_{18}ClO$: 297.10407, $[M+H]^+$, found: 297.10463.

4.1.21. Synthesis of 1-(2-Bromophenyl)-3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-one (35U)

General Procedure **1** was followed by using 2-bromobenzoyl chloride (374 mg, 1.70 mmol), $PdCl_2(PPh_3)_2$ (20 mg, 0.03 mmol), Et_3N (174 mg, 1.70 mmol), CuI (5 mg, 0.03 mmol) 1-ethynyl-4-(trifluoromethyl)benzene (242 mg, 1.42 mmol), which afforded 439 mg (88%) of the indicated product **35U** as a yellow solid (R_f = 0.65 in 4:1 hexane/ethyl acetate); mp 69.8–71.4ºC.

35U: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.75 (d, *J* = 8.1 Hz, 2H), 7.71 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.47 (td, *J* = 7.5, 1.2 Hz, 1H), 7.40 (td, *J* = 7.6, 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2 (CO), 137.2 (C), 135.2 (CH), 133.8 (CH), 133.3 (CH), 133.0 (CH), 132.5 (q, ^2J = 32.9 Hz, C), 127.6 (CH), 125.7 (q, ^3J = 3.8 Hz, CH), 123.9 (C), 123.6 (q, ^1J = 272.8 Hz, CF_3), 121.5 (C), 91.6 (C), 89.1 (C); IR (neat): 3058, 2200, 1648, 1611, 1583, 1562, 1462, 1432, 1402, 1318, 1296, 1275, 1203, 1172, 1119, 1105, 1067, 1055, 1014, 999, 849, 780 cm^{-1}. MS (ESI, m/z): 352.978 $[M+H]^+$; HRMS (ESI) calcd. for $C_{16}H_9BrF_3O$: 352.97834 $[M+H]^+$, found: 352.97833.

4.2. General Procedure 2. Synthesis of N-Propargylic β-Enaminones 25

In a round-bottomed flask, α,β-alkynic ketones **35** (1.0 mmol) and propargylamine (**36**) (1.2 mmol) were heated in methanol (5 mL) at reflux condition for about 2 h. Reaction was monitored by the TLC analysis (4:1 hexane/ethyl acetate). After reaction was over, methanol was removed by using rotary evaporator. Then, the obtained crude product was purified via flash chromatography by using 7:1 hexane/ethyl acetate as the eluent.

4.2.1. Synthesis of (*Z*)-1,3-Diphenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (25A)

General Procedure **2** was followed by using 1,3-diphenylprop-2-yn-1-one (**35A**) (326.7 mg, 1.58 mmol) and propargylamine (104.4 mg, 1.90 mmol) were employed to afford 384 mg (93%) of the indicated product **25A** as a yellow solid (R_f = 0.44 in 4:1 hexane/ethyl acetate).

25A: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.39 (t, *J* = 6.0 Hz, 1H), 7.89 (dd, *J* = 7.7, 1.7 Hz, 2H), 7.50–7.29 (m, 8H), 5.82 (s, 1H), 3.86 (dd, *J* = 6.3, 2.5 Hz, 2H), 2.32 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.6 (CO), 165.5 (C), 139.6 (C), 134.5 (C), 130.7 (CH), 129.6 (CH), 128.4 (CH), 127.9 (CH), 127.5 (CH), 126.9 (CH), 94.3 (CH), 79.6 (C), 72.4 (CH), 33.9 (CH_2); IR (neat): 3224, 3055, 3022, 2113, 1596, 1585, 1547, 1478, 1443, 1429, 1346, 1324, 1294, 1266, 1242, 1219, 1139, 1053, 1026, 924, 803, 775, 763, 729, 703, 676 cm^{-1}. The spectral data were in agreement with those reported previously for this compound.[34]

4.2.2. Synthesis of (*Z*)-1-Phenyl-3-(prop-2-yn-1-ylamino)-3-(thiophen-3-yl)prop-2-en-1-one (25B)

General Procedure **2** was followed by using 1-phenyl-3-(thiophen-3-yl)prop-2-yn-1-one (**35B**) (689 mg, 3.24 mmol) and propargylamine (214 mg, 3.89 mmol) were employed to afford 796 mg (92%) of the indicated product **25B** as a yellow solid (R_f = 0.5 in 4:1 hexane/ethyl acetate); mp 77.4–78.3 °C.

25B: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.42 (br s, 1H), 7.98–7.85 (m, 2H), 7.63 (dd, *J* = 3.0, 1.2 Hz, 1H), 7.47–7.37 (m, 4H), 7.27 (dd, *J* = 5.0, 1.3 Hz, 1H), 5.94 (s, 1H), 4.02 (dd, *J* = 6.4, 2.5 Hz, 2H), 2.38 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.9 (CO), 160.5 (C), 139.9 (C), 135.4 (C), 130.9 (CH), 128.2 (CH), 127.2 (CH), 127.0 (CH), 126.6 (CH), 126.2 (CH), 94.2 (CH), 79.9 (C), 72.6 (CH), 34.1 (CH_2); IR (neat): 3249, 3102, 2921, 2119, 2064, 1985, 1953, 1896, 1769, 1576, 1553, 1497, 1425, 1393, 1371, 1314, 1289, 1248, 1227, 1131, 1079, 1057, 1021, 924, 894, 864,

823, 799, 784, 754, 713, 695 cm^{-1}. The spectral data were in agreement with those reported previously for this compound.[40]

4.2.3. Synthesis of (*Z*)-1-(4-Chlorophenyl)-3-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (25C)

General Procedure **2** was followed by using 1-(4-chlorophenyl)-3-phenylprop-2-yn-1-one (**35C**) (1.01 g, 4.21 mmol) and propargylamine (278.2 mg, 5.05 mmol) were employed to afford 1.134 g (91%) of the indicated product **25C** as a yellow solid (R_f = 0.45 in 4:1 hexane/ethyl acetate).

25C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.34 (br s, 1H), 7.82 (d, *J* = 8.5 Hz, 2H), 7.46 (s, 5H), 7.35 (d, *J* = 8.5 Hz, 2H), 5.77 (s, 1H), 3.93 (dd, *J* = 6.3, 2.4 Hz, 2H), 2.32 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.5 (CO), 166.2 (C), 138.3 (C), 137.1 (C), 134.7 (C), 129.9 (CH), 128.8 (CH), 128.6 (CH), 128.5 (CH), 127.8 (CH), 94.3 (CH), 79.7 (C), 72.7 (CH), 34.3 (CH_2); IR (neat): 3229, 3065, 3027, 2184, 2164, 2114, 2026, 1983, 1895, 1593, 1561, 1543, 1518, 1477, 1431, 1395, 1352, 1327, 1295, 1267, 1144, 1091, 1074, 1015, 927, 838, 801, 774, 753, 698 cm^{-1}. The spectral data were in agreement with those reported previously for this compound.[34]

4.2.4. Synthesis of (*Z*)-1-(2-Bromophenyl)-3-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (25D)

General Procedure **2** was followed by using 1-(2-bromophenyl)-3-phenylprop-2-yn-1-one (**35D**) (197.3 mg, 0.69 mmol) and propargylamine (46 mg, 0.83 mmol) were employed to afford 219 mg (94%) of the indicated product **25D** as reddish-orange oil (R_f = 0.31 in 4:1 hexane/ethyl acetate).

25D: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.11 (br s, 1H), 7.56 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.50–7.40 (m, 6H), 7.30 (td, *J* = 7.5, 1.0 Hz, 1H), 7.18 (td, *J* = 7.7, 1.7 Hz, 1H), 5.47 (s, 1H), 3.96 (dd, *J* = 6.4, 2.5 Hz, 2H), 2.35 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.9 (CO), 165.7 (C), 142.9 (C), 134.3 (C), 133.3

(CH), 130.2 (CH), 129.9 (CH), 129.1 (CH), 128.6 (CH), 127.8 (CH), 127.1 (CH), 119.3 (C), 98.3 (CH), 79.5 (C), 72.7 (CH), 34.3 (CH_2); IR (neat): 3288, 3055, 2119, 1732, 1588, 1560, 1484, 1461, 1427, 1359, 1319, 1269, 1218, 1182, 1146, 1123, 1084, 1025, 1000, 949, 927, 873, 755, 701, 669 cm-1; MS (ESI, m/z): 340.03 $[M+H]^+$; HRMS (ESI) calcd. for $C_{18}H_{15}BrNO$: 340.0332 $[M+H]^+$, found: 340.0333.

4.2.5. Synthesis of (*Z*)-3-(3-Fluorophenyl)-1-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (25E)

General Procedure **2** was followed by using 3-(3-fluorophenyl)-1-phenylprop-2-yn-1-one (**35E**) (425 mg, 1.90 mmol) and propargylamine (126 mg, 2.28 mmol) were employed to afford 458 mg (86%) of the indicated product **25E** as a pale yellow solid (R_f = 0.5 in 4:1 hexane/ethyl acetate); mp 93.8–94.8 ºC.

25E: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.28 (br s, 1H), 8.06–7.80 (m, 2H), 7.52–7.36 (m, 4H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.23 (dt, *J* = 9.0, 2.1 Hz, 1H), 7.17 (td, *J* = 8.4, 2.3 Hz, 1H), 5.85 (s, 1H), 3.92 (dd, *J* = 6.3, 2.4 Hz, 2H), 2.35 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.3 (CO), 164.1 (C), 162.5 (d, ^1J = 248.3 Hz, CF), 139.7 (C), 136.9 (d, ^3J = 7.5 Hz, C), 131.1 (CH), 130.5 (d, ^3J = 8.3 Hz, CH), 128.2 (CH), 127.2 (CH), 123.6 (d, ^4J = 3.0 Hz, CH), 116.8 (d, ^2J = 21.0 Hz, CH), 115.1 (d, ^2J = 22.7 Hz, CH), 94.7 (CH), 79.6 (C), 72.7 (CH), 34.1 (CH_2); IR (neat): 3222, 3055, 2939, 2111, 1974, 1939, 1875, 1804, 1747, 1599, 1548, 1519, 1474, 1431, 1348, 1323, 1299, 1284, 1265, 1250, 1227, 1203, 1179, 1158, 1123, 1054, 1026, 999, 965, 929, 888, 877, 788, 736, 707, 675 cm^{-1}; MS (ESI, m/z): 280.11 $[M+H]^+$; HRMS (ESI) calcd. for $C_{18}H_{15}FNO$: 280.1132 $[M+H]^+$, found: 280.1134.

4.2.6. Synthesis of (*Z*)-1-Phenyl-3-(prop-2-yn-1-ylamino)-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (25F)

General Procedure **2** was followed by using 1-Phenyl-3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-one (**35F**) (730 mg, 2.66 mmol) and propargylamine (176 mg, 3.19 mmol) were employed to afford 776 mg (89%) of the indicated product **25F** as a light brown solid (R_f = 0.69 in 4:1 hexane/ethyl acetate); mp 99.1–99.8ºC.

25F: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.23 (t, *J* = 6.7 Hz, 1H), 7.89 (dd, *J* = 8.2, 1.4 Hz, 2H), 7.75 (d, *J* = 8.1 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.50–7.37 (m, 3H), 5.83 (s, 1H), 3.90 (dd, *J* = 6.4, 2.5 Hz, 2H), 2.32 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.4 (CO), 164.0 (C), 139.6 (C), 138.4 (C), 131.8 (q, ^{2}J = 33.0 Hz, C-CF_3), 131.3 (CH), 128.4 (CH), 128.3 (CH), 127.2 (CH), 125.7 (q, ^{3}J = 3.6 Hz, CH), 123.8 (q, ^{1}J = 271.0 Hz, CF_3), 94.9 (CH), 79.5 (C), 72.8 (CH), 34.2 (CH_2); IR (neat): 3286, 2930, 1597, 1580, 1541, 1323, 1293, 1226, 1193, 1122, 1105, 1072, 1053, 1017, 921, 848, 759, 747, 707, 682, 647, 631, 599, 554, 489, 469, 421. MS (ESI, m/z): 330.11 $[M+H]^+$; HRMS (ESI) calcd. for $C_{19}H_{15}F_3NO$: 330.11003 $[M+H]^+$, found: 330.11120.

4.2.7. Synthesis of (*Z*)-3-(4-Bromophenyl)-1-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (25G)

General Procedure **2** was followed by using 3-(4-bromophenyl)-1-phenylprop-2-yn-1-one (**35G**) (118 mg, 0.41 mmol) and propargylamine (27 mg, 0.49 mmol) were employed to afford 113 mg (81%) of the indicated product **25G** as a light brown solid (R_f = 0.58 in 4:1 hexane/ethyl acetate); mp 92.6–93.8 ºC.

25G: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.28 (t, *J* = 6.4 Hz, 1H), 7.91 (d, *J* = 7.0 Hz, 2H), 7.62 (d, *J* = 8.5 Hz, 2H), 7.49–7.36 (m, 5H), 5.83 (s, 1H), 3.92 (dd, *J* = 6.5, 2.5 Hz, 2H), 2.34 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.3 (CO), 164.5 (C), 139.8 (C), 133.8 (C), 132.0 (CH), 131.2 (CH), 129.6 (CH), 128.2 (CH), 127.2 (CH), 124.3 (C), 94.8 (CH), 79.7 (C), 72.7 (CH), 34.2 (CH_2); IR (neat): 3226, 2990,

2937, 2349, 1594, 1577, 1546, 1473, 1321, 1295, 1239, 1220, 1176, 1138, 1073, 1050, 1021, 1008, 944, 926, 831, 789, 692, 678, 623, 560, 472, 460 cm^{-1}. MS (ESI, m/z): 338.01 $[M-H]^-$; HRMS (ESI) calcd. for $C_{18}H_{13}BrNO$: 338.01860 $[M-H]^-$, found: 338.01729 .

4.2.8. Synthesis of (*Z*)-3-(4-Methoxyphenyl)-1-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (25H)

General Procedure **2** was followed by using 3-(4-methoxyphenyl)-1-phenylprop-2-yn-1-one (**35H**) (211 mg, 0.90 mmol) and propargylamine (59.5 mg, 1.08 mmol) were employed to afford 238 mg (91%) of the indicated product **25H** as reddish- orange oil (R_f = 0.29 in 4:1 hexane/ethyl acetate).

25H: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.37 (bs, 1H), 7.90 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.49–7.35 (m, 5H), 7.00–6.95 (m, 2H), 5.84 (s, 1H), 3.97 (dd, *J* = 6.3, 2.5 Hz, 2H), 3.84 (s, 3H), 2.32 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.9 (CO), 165.9 (C), 160.9 (C), 140.1 (C), 130.9 (C), 129.5 (CH), 128.3 (CH), 127.2 (CH), 114.1 (CH), 94.6 (CH), 80.0 (C), 72.5 (CH), 55.4 (CH_3), 34.3 (CH_2), (Note that two CH peaks overlap on each other); IR (neat): 3285, 3057, 3020, 3003, 2959, 2933, 2907, 2837, 2167, 2120, 2104, 1909, 1731, 1668, 1583, 1559, 1497, 1328, 1293, 1247, 1174, 1142, 1056, 1023, 836, 808, 757, 689, 653, 555, 418 cm^{-1}. The spectral data were in agreement with those reported previously for this compound.[40]

4.2.9. Synthesis of (*Z*)-3-(4-Chlorophenyl)-1-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (25I)

General Procedure **2** was followed by using 3-(4-chlorophenyl)-1-phenylprop-2-yn-1-one (**35I**) (362 mg, 1.50 mmol) and propargylamine (99 mg, 1.80 mmol) were employed to afford 408 mg (92%) of the indicated product **25I** as a pale yellow solid (R_f = 0.50 in 4:1 hexane/ethyl acetate); mp 91.9–93.1 ^{o}C.

25I: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.27 (br s, 1H), 7.95–7.83 (m, 2H), 7.51–7.34 (m, 7H), 5.81 (s, 1H), 3.91 (dd, *J* = 6.3, 2.3 Hz, 2H), 2.32 (t, *J* = 2.4 Hz, 1H); ^{13}C

NMR (100 MHz, $CDCl_3$) δ 189.3 (CO), 164.6 (C), 139.8 (C), 136.1 (C), 133.3 (C), 131.3 (CH), 129.4 (CH), 129.1 (CH), 128.4 (CH), 127.2 (CH), 94.8 (CH), 79.7 (C), 72.7 (CH), 34.3 (CH_2); IR (neat): 3229, 3065, 3027, 2184, 2164, 2114, 2026, 1983, 1895, 1593, 1561, 1543, 1518, 1477, 1431, 1395, 1352, 1327, 1295, 1267, 1144, 1091, 1074, 1015, 927, 838, 801, 774, 753, 698 cm^{-1}; MS (ESI, m/z): 296.08 $[M+H]^+$; HRMS (ESI) calcd. for $C_{18}H_{15}ClNO$: 296.0837 $[M+H]^+$, found: 296.0848.

4.2.10. Synthesis of (*Z*)-3-(3,5-Bis(trifluoromethyl)phenyl)-1-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (25J)

General Procedure **2** was followed by using 3-(3,5-bis(trifluoromethyl)phenyl)-1-phenylprop-2-yn-1-one (**35J**) (423 mg, 1.24 mmol) and propargylamine (82 mg, 1.49 mmol) were employed to afford 350 mg (71%) of the indicated product **25J** as a light brown solid (R_f = 0.65 in 4:1 hexane/ethyl acetate); mp 111.6–112.3°C.

25J: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.17 (t, *J* = 6.1 Hz, 1H), 8.02 (s, 3H), 7.90 (d, *J* = 7.0 Hz, 2H), 7.55–7.34 (m, 3H), 5.85 (s, 1H), 3.86 (dd, *J* = 6.6, 2.5 Hz, 2H), 2.35 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.7 (CO), 161.7 (C), 139.0 (C), 136.8 (C), 132.1 (q, ^2J = 33.8 Hz, C-CF_3), 131.4 (CH), 128.24 (CH), 128.16 (CH), 127.1 (CH), 123.3 (q, ^3J = 4.6 Hz, CH), 122.7 (q, ^1J = 273.2 Hz, CF_3), 95.4 (CH), 79.0 (C), 72.8 (CH), 34.0 (CH_2); IR (neat): 3281, 2927, 2168, 1597, 1577, 1535, 1462, 1378, 1278, 1245, 1226, 1173, 1123, 1054, 1023, 903, 846, 752, 692, 673, 638, 603, 546, 523, 471, 444 cm^{-1}. MS (ESI, m/z): 398.09 $[M+H]^+$; HRMS (ESI) calcd. for $C_{20}H_{14}F_6NO$: 398.09741 $[M+H]^+$, found: 398.09854.

4.2.11. Synthesis of (*Z*)-3-(4-Nitrophenyl)-1-phenyl-3-(prop-2-yn-1-ylamino) prop-2-en-1-one (25K)

General Procedure **2** was followed by using 3-(4-nitrophenyl)-1-phenylprop-2-yn-1-one (**35K**) (452 mg, 1.80 mmol) and propargylamine (119 mg, 2.16 mmol) were

employed to afford 396 mg (72%) of the indicated product **25K** as a bright yellow solid (R_f = 0.25 in 4:1 hexane/ethyl acetate); mp 125.4–126.5 °C.

25K: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.17 (br s, 1H), 8.33 (tt, *J* = 8.9, 1.9 Hz, 2H), 7.90–7.86 (m, 2H), 7.69 (tt, *J* = 8.8, 1.9 Hz, 2H), 7.50–7.37 (m, 3H), 5.83 (s, 1H), 3.88 (dd, *J* = 6.5, 2.5 Hz, 2H), 2.33 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.8 (CO), 162.9 (C), 148.7 (C), 141.2 (C), 139.5 (C), 131.6 (CH), 129.2 (CH), 128.5 (CH), 127.3 (CH), 124.1 (CH), 95.3 (CH), 79.5 (C), 73.1 (CH), 34.3 (CH_2); IR (neat): 3243, 3109, 3076, 3052, 3036, 3019, 2974, 2943, 2848, 2448, 2116, 1808, 1730, 1684, 1608, 1595, 1572, 1551, 1511, 1492, 1477, 1444, 1427, 1345, 1319, 1296, 1242, 1225, 1179, 1141, 1107, 1073, 1051, 1022, 926, 855, 803, 762, 743, 690 cm^{-1}; MS (ESI, m/z): 307.11 $[M+H]^+$; HRMS (ESI) calcd. for $C_{18}H_{15}N_2O_3$: 307.1077 $[M+H]^+$, found: 307.1088.

4.2.12. Synthesis of (*Z*)-3-(4-(Tert-butyl)phenyl)-1-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (25L)

General Procedure **2** was followed by using 3-(4-(tert-butyl)phenyl)-1-phenylprop-2-yn-1-one (**35L**) (409 mg, 1.56 mmol) and propargylamine (103 mg, 1.87 mmol) were employed to afford 437 mg (88%) of the indicated product **25L** as a yellow solid (R_f = 0.63 in 4:1 hexane/ethyl acetate); mp 108.8–109.8 °C.

25L: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.39 (br s, 1H), 7.91 (dd, *J* = 7.8, 1.5 Hz, 2H), 7.59–7.28 (m, 7H), 5.86 (s, 1H), 3.96 (dd, *J* = 6.3, 2.5 Hz, 2H), 2.32 (t, *J* = 2.4 Hz, 1H), 1.36 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.62 (CO), 165.77 (C), 152.91 (C), 139.84 (C), 131.74 (C), 130.66 (CH), 127.97 (CH), 127.43 (CH), 126.92 (CH), 125.38 (CH), 94.32 (CH), 79.74 (C), 72.29 (CH), 34.57 (CH_2), 34.05 (C), 31.01 (CH_3); IR (neat): 3287, 3252, 2953, 2863, 1578, 1547, 1497, 1353, 1326, 1290, 1266, 1221, 1147, 1107, 1054, 1022, 930, 840, 806, 756, 742, 706, 687, 636, 592, 559, 489, 458, 420 cm^{-1}. MS (ESI, m/z): 318.18 $[M+H]^+$; HRMS (ESI) calcd. for $C_{22}H_{24}NO$: 318.18524 $[M+H]^+$, found: 318.18594.

4.2.13. Synthesis of (*Z*)-1-Phenyl-3-(prop-2-yn-1-ylamino)-3-(p-tolyl)prop-2-en-1-one (25M)

General Procedure **2** was followed by using 1-phenyl-3-(p-tolyl)prop-2-yn-1-one (**35M**) (345 mg, 1.57 mmol) and propargylamine (104 mg, 1.88 mmol) were employed to afford 381 mg (88%) of the indicated product **25M** as reddish-orange oil (*Rf* = 0.50 in 4:1 hexane/ethyl acetate).

25M: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.38 (br s, 1H), 7.93 (dd, *J* = 8.0, 1.5 Hz, 2H), 7.50–7.38 (m, 5H), 7.29 (d, *J* = 7.7 Hz, 2H), 5.87 (s, 1H), 3.98 (dd, *J* = 6.3, 2.4 Hz, 2H), 2.44 (s, 3H), 2.34 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.0 (CO), 166.2 (C), 140.1 (C), 132.1 (C), 130.9 (C), 129.4 (CH), 128.3 (CH), 127.8 (CH), 127.2 (CH), 94.6 (CH), 79.9 (C), 72.5 (CH), 34.3 (CH_2), 21.4 (CH_3) (Note that two CH peaks overlap on each other); IR (neat): 3287, 3056, 3026, 2919, 2861, 1666, 1579, 1555, 1499, 1482, 1446, 1356, 1327, 1289, 1266, 1248, 1181, 1142, 1055, 1022, 1001, 972, 926, 872, 825, 755, 689 cm-1. The spectral data were in agreement with those reported previously for this compound.[40]

4.2.14. Synthesis of (*Z*)-1-(2-Bromophenyl)-3-(4-chlorophenyl)-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (25N)

General Procedure **2** was followed by using 1-(2-bromophenyl)-3-(4-chlorophenyl)prop-2-yn-1-one (**35N**) (396 mg, 1.18 mmol) and propargylamine (78 mg, 1.42 mmol) were employed to afford 426 mg (96%) of the indicated product **25N** as a brown solid (R_f = 0.45 in 4:1 hexane/ethyl acetate); mp 82.3–83.6 ºC.

25N: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.02 (t, *J* = 6.6 Hz, 1H), 7.56 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.46–7.40 (m, 5H), 7.30 (td, *J* = 7.5, 1.2 Hz, 1H), 7.19 (td, *J* = 7.7, 1.8 Hz, 1H), 5.44 (s, 1H), 3.94 (dd, *J* = 6.5, 2.5 Hz, 2H), 2.34 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.2 (CO), 164.4 (C), 142.8 (C), 136.2 (C), 133.4 (CH), 132.7 (C), 130.4 (CH), 129.3 (CH), 129.2 (CH), 129.0 (CH), 127.2 (CH), 119.4 (C), 98.5 (CH), 79.5 (C), 72.9 (CH), 34.3 (CH_2); IR (neat): 3297, 3053, 2930, 2349, 1589, 1554, 1478, 1420, 1364, 1320, 1260, 1216, 1145, 1084, 1015, 923, 871, 831, 778, 753, 738,

656, 638, 624, 562, 522, 471, 415 cm^{-1}. MS (ESI, m/z): 371.97 $[M-H]^-$; HRMS (ESI) calcd. for $C_{18}H_{12}BrClNO$: 371.97963 $[M-H]^-$, found: 371.97983.

4.2.15. Synthesis of (*Z*)-1-(2-Iodophenyl)-3-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (25O)

General Procedure **2** was followed by using 1-(2-iodophenyl)-3-phenylprop-2-yn-1-one (**35O**) (202 mg, 0.61 mmol) and propargylamine (40 mg, 0.73 mmol) were employed to afford 173 mg (73%) of the indicated product **25O** as light brown oil (R_f = 0.50 in 4:1 hexane/ethyl acetate).

25O: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.07 (br s, 1H), 7.85 (d, *J* = 7.9 Hz, 1H), 7.52–7.37 (m, 6H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.00 (td, *J* = 7.7, 1.7 Hz, 1H), 5.41 (s, 1H), 3.96 (dd, *J* = 6.4, 2.4 Hz, 2H), 2.33 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.4 (CO), 165.8 (CH), 146.4 (C), 139.9 (CH), 134.3 (C), 130.34 (CH), 130.04 (CH), 128.71 (CH), 128.35 (CH), 127.8 (CH), 97.7 (CH), 92.6 (C), 79.6 (C), 72.7 (CH), 34.3 (CH_2). (Note that two CH peaks overlap on each other); IR (neat): 3286, 3054, 2918, 2853, 2120, 1557, 1481, 1358, 1315, 1144, 1075, 1032, 1010, 925, 870, 749, 698, 638, 563, 496, 439 cm^{-1}. MS (ESI, m/z): 388.01 $[M+H]^+$; HRMS (ESI) calcd. for $C_{18}H_{15}INO$: 388.01928 $[M+H]^+$, found: 388.01906.

4.2.16. Synthesis of (*Z*)-3-(3,4-Dichlorophenyl)-1-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (25P)

General Procedure **2** was followed by using 3-(3,4-dichlorophenyl)-1-phenylprop-2-yn-1-one (**35P**) (311 mg, 1.13 mmol) and propargylamine (75 mg, 1.36 mmol) were employed to afford 335 mg (90%) of the indicated product **25P** as a light yellow solid (R_f = 0.59 in 4:1 hexane/ethyl acetate); mp 97.7–98.2 ^oC.

25P: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.17 (t, *J* = 6.5 Hz, 1H), 7.89 (dd, *J* = 8.2, 1.4 Hz, 2H), 7.62 (d, *J* = 2.0 Hz, 1H), 7.55 (d, *J* = 8.2 Hz, 1H), 7.49–7.39 (m, 3H), 7.35 (dd, *J* = 8.2, 2.0 Hz, 1H), 5.81 (s, 1H), 3.90 (dd, *J* = 6.4, 2.5 Hz, 2H), 2.33 (t, *J* = 2.5

Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.6 (CO), 163.0 (C), 139.6 (C), 134.86 (C), 134.39 (C), 133.3 (C), 131.4 (CH), 130.90 (CH), 130.01 (CH), 128.4 (CH), 127.3 (CH), 95.1 (CH), 79.6 (C), 72.9 (CH), 34.3 (CH_2). (Note that two CH peaks overlap on each other); IR (neat): 3244, 2968, 2349, 2185, 1575, 1541, 1460, 1321, 1297, 1241, 1224, 1149, 1074, 1052, 1024, 926, 897, 828, 801, 779, 740, 710, 682, 638, 551, 521, 460, 425 cm^{-1}. MS (ESI, m/z): 328.03 $[M-H]^-$; HRMS (ESI) calcd. for $C_{18}H_{12}Cl_2NO$: 328.03014 $[M-H]^-$, found: 328.03126.

4.2.17. Synthesis of (*Z*)-1-(2-Bromophenyl)-3-(2-methoxyphenyl)-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (25Q)

General Procedure **2** was followed by using 1-(2-bromophenyl)-3-(2-methoxyphenyl)prop-2-yn-1-one (**35Q**) (307 mg, 0.97 mmol) and propargylamine (64 mg, 1.16 mmol) were employed to afford 316 mg (88%) of the indicated product **25Q** as a light brown solid (R_f = 0.30 in 4:1 hexane/ethyl acetate); mp 118.5–120^{o}C.

25Q: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.22 (t, *J* = 6.2 Hz, 1H), 7.58 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.50 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.44 (ddd, *J* = 8.7, 7.5, 1.8 Hz, 1H), 7.36–7.28 (m, 2H), 7.20 (td, *J* = 7.7, 1.8 Hz, 1H), 7.04 (td, *J* = 7.5, 1.0 Hz, 1H), 6.98 (dd, *J* = 8.5, 0.9 Hz, 1H), 5.41 (s, 1H), 3.89 (s, 5H), 2.28 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.5 (CO), 163.1 (C), 155.8 (C), 142.9 (C), 133.1 (CH), 131.2 (CH), 129.9 (CH), 129.7 (CH), 129.1 (CH), 126.8 (CH), 123.1 (C), 120.7 (C), 119.3 (CH), 110.6 (CH), 97.7 (CH), 79.0 (C), 72.0 (CH), 55.4 (OCH_3), 33.8 (CH_2); IR (neat): 3247, 2190, 1587, 1536, 1485, 1461, 1328, 1237, 1163, 1084, 1065, 1023, 796, 753 cm^{-1}; MS (ESI, m/z): 370.04 $[M+H]^+$; HRMS (ESI) calcd. for $C_{19}H_{17}BrNO_2$: 370.0437 $[M+H]^+$, found: 370.0440.

4.2.18. Synthesis of (*Z*)-1-(2-Bromophenyl)-3-(3-fluorophenyl)-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (25R)

General Procedure **2** was followed by using 1-(2-bromophenyl)-3-(3-fluorophenyl)prop-2-yn-1-one (**35R**) (346 mg, 1.14 mmol) and propargylamine (75 mg, 1.37 mmol) were employed to afford 342 mg (84%) of the indicated product **25R** as a dark orange solid (R_f = 0.5 in 4:1 hexane/ethyl acetate); mp 45.0–46.8 °C.
25R: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.01 (br s, 1H), 7.56 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.47–7.39 (m, 2H), 7.33–7.26 (m, 2H), 7.24–7.12 (m, 3H), 5.47 (s, 1H), 3.95 (dd, *J* = 6.4, 2.5 Hz, 2H), 2.35 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.1 (CO), 163.9 (C), 162.3 (d, ^{1}J = 248.3 Hz, CF), 142.6 (C), 136.1 (d, ^{3}J = 7.6 Hz, C), 133.2 (CH), 130.4 (d, ^{3}J = 8.3 Hz, CH), 130.4 (CH), 129.0 (CH), 127.1 (CH), 123.6 (d, ^{4}J = 3.1 Hz, CH), 119.2 (C), 116.9 (d, ^{2}J = 21.0 Hz, CH), 114.9 (d, ^{2}J = 22.8 Hz, CH), 98.2 (CH), 79.3 (C), 72.9 (CH), 34.2 (CH_2); IR (neat): 3311, 3296, 3263, 3178, 3066, 2986, 2928, 2906, 2115, 1935, 1885, 1818, 1735, 1591, 1549, 1477, 1462, 1422, 1365, 1322, 1289, 1247, 1225, 1195, 1131, 1080, 1024, 927, 884, 867, 791, 759, 745, 705, 684 cm^{-1}; MS (ESI, m/z): 358.02 $[M+H]^+$; HRMS (ESI) calcd. for $C_{18}H_{14}BrFNO$: 358.0237 $[M+H]^+$, found: 358.0239.

4.2.19. Synthesis of (*Z*)-1-(4-Chlorophenyl)-3-(3-fluorophenyl)-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (25S)

General Procedure **2** was followed by using 1-(4-chlorophenyl)-3-(3-fluorophenyl)prop-2-yn-1-one (**35S**) (359 mg, 1.39 mmol) and propargylamine (92 mg, 1.67 mmol) were employed to afford 377 mg (87%) of the indicated product **25S** as a pale yellow solid (*Rf* = 0.48 in 4:1 hexane/ethyl acetate); mp 132.8–133.6 °C.
25S: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.28 (br s, 1H), 7.85 (d, *J* = 8.4 Hz, 2H), 7.52–7.43 (m, 1H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 7.2 Hz, 1H), 7.26–7.16 (m, 2H), 5.79 (s, 1H), 3.95 (dd, *J* = 6.3, 2.2 Hz, 2H), 2.35 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.9 (CO), 164.7 (C), 162.7 (d, ^{1}J = 248.6 Hz, CF), 138.1 (C), 137.4 (C), 136.8 (d, ^{3}J = 8.2 Hz, C), 130.7 (d, ^{3}J = 8.3 Hz, CH), 128.7 (CH), 128.6 (CH), 123.7 (d, ^{4}J = 3.1

Hz, CH), 117.1 (d, ^2J = 20.9 Hz, CH), 115.2 (d, ^2J = 22.8 Hz, CH), 94.4 (CH), 79.5 (C), 72.9 (CH), 34.3 (CH_2); IR (neat): 3231, 3063, 2115, 2038, 1598, 1544, 1470, 1433, 1351, 1325, 1281, 1252, 1230, 1201, 1169, 1129, 1092, 1063, 1014, 931, 891, 871, 837, 793, 764, 736, 704, 684 cm-1; MS (ESI, m/z): 314.07 $[M+H]^+$; HRMS (ESI) calcd. for $C_{18}H_{14}ClFNO$: 314.0743 $[M+H]^+$, found: 314.0746.

4.2.20. Synthesis of (*Z*)-3-(4-(Tert-butyl)phenyl)-1-(4-chlorophenyl)-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (25T)

General Procedure **2** was followed by using 3-(4-(tert-butyl)phenyl)-1-(4-chlorophenyl)prop-2-yn-1-one (**35T**) (423 mg, 1.42 mmol) and propargylamine (94 mg, 1.70 mmol) were employed to afford 492 mg (98%) of the indicated product **25T** as a reddish-orange solid (R_f = 0.71 in 4:1 hexane/ethyl acetate); mp 72.3–72.9 ºC.
25T: ^{1}H NMR (400 MHz,$CDCl_3$) δ 11.36 (s, 1H), 7.83 (d, *J* = 8.6 Hz, 2H), 7.49 (d, *J* = 8.5 Hz, 2H), 7.42 (d, *J* = 8.5 Hz, 2H), 7.36 (d, *J* = 8.6 Hz, 2H), 5.78 (s, 1H), 3.99 (dd, *J* = 6.3, 2.5 Hz, 2H), 2.33 (t, *J* = 2.5 Hz, 1H), 1.36 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.2 (CO), 166.2 (C), 153.1 (C), 138.2 (C), 136.8 (C), 131.5 (C), 128.38 (CH), 128.24 (CH), 127.4 (CH), 125.4 (CH), 94.0 (CH), 79.5 (C), 72.3 (CH), 34.68 (CH_2), 34.17 (C), 31.0 (CH_3); IR (neat): 3283, 2903, 2342, 2215, 1582, 1539, 1501, 1478, 1397, 1327, 1295, 1267, 1221, 1146, 1107, 1089, 1063, 1009, 930, 874, 839, 773, 699, 672, 627, 566, 477, 409 cm^{-1}. MS (ESI, m/z): 352.14 $[M+H]^+$; HRMS (ESI) calcd. for $C_{22}H_{23}ClNO$: 352.14627 $[M+H]^+$, found: 352.14759.

4.2.21. Synthesis of (*Z*)-1-(2-Bromophenyl)-3-(prop-2-yn-1-ylamino)-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (25U)

General Procedure **2** was followed by using 1-(2-bromophenyl)-3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-one (**35U**) (362 mg, 1.02 mmol) and propargylamine (67 mg, 1.22 mmol) were employed to afford 397 mg (95%) of the indicated product **25U** as reddish-orange oil (R_f = 0.43 in 4:1 hexane/ethyl acetate).

25U: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.02 (br t, *J* = 5.8 Hz, 1H), 7.71 (d, *J* = 8.3 Hz, 2H), 7.62 (d, *J* = 8.2 Hz, 2H), 7.55 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.45 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.30 (td, *J* = 7.5, 1.0 Hz, 1H), 7.18 (td, *J* = 7.7, 1.7 Hz, 1H), 5.46 (s, 1H), 3.91 (dd, *J* = 6.5, 2.5 Hz, 2H), 2.35 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.3 (CO), 163.8 (C), 142.6 (C), 137.9 (C), 133.4 (CH), 131 .9 (q, ^{2}J = 32.8 Hz, C), 130.5 (CH), 129.2 (CH), 128.4 (CH), 127.2 (CH), 125.7 (q, ^{3}J = 3.7 Hz, CH), 123.7 (q, ^{1}J = 272.4 Hz, CF_3), 119.3 (C), 98.6 (CH), 79.3 (C), 73.0 (CH), 34.3 (CH_2); IR (neat): 3297, 1587, 1561, 1319, 1167, 1125, 1063, 1018, 849, 740 cm^{-1}; MS (ESI, m/z): 408.02 $[M+H]^+$; HRMS (ESI) calcd. for $C_{19}H_{14}BrF_3NO$: 408.0205 $[M+H]^+$, found: 408.0206.

4.3. General Procedure 3. Synthesis of (4-Nitrophenyl)thio-Substituted 1-Pyrroline Derivatives 32

One-pot two-steps reactions were performed by using two different bases, NaH and Cs_2CO_3. First, in a round-bottomed flask, the corresponding N-propargylic β-enaminone derivative **25** (1.0 mmol) and 4-nitrobenzenesulfenyl chloride **30** (1.2 mmol) were heated in acetonitrile (5 mL) at reflux condition under argon. Then, base (NaH or Cs_2CO_3) was added into reaction medium for the formation of the intermediate compound **31**, as concluded by the TLC analysis (4:1 hexane/ethyl acetate). Subsequently, extraction was performed by using ethyl acetate (50 mL) and saturated aqueous NH_4Cl solution (50 mL). The combined organic phases were dried with $MgSO_4$. Finally, purification of the crude was performed by flash chromatography by using 4:1 hexane/ethyl acetate as the eluent.

4.3.1. Synthesis of (3-Methylene-4-((4-nitrophenyl)thio)-5-phenyl-3,4-dihydro-2H-pyrrol-4-yl)(phenyl)methanone (32A)

General Procedure **3** was followed by using (*Z*)-1,3-diphenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**25A**) (94 mg, 0.36 mmol) and 4-nitrobenzenesulfenyl chloride (86 mg, 0.43 mmol) to afford 95 mg (64%) and 99.9 mg (67%) of the indicated product **32A** for NaH and Cs_2CO_3, respectively as an orange-brown solid (R_f = 0.38 in 4:1 hexane/ethyl acetate); mp 124.1-125 ^oC.

32A: ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 9.1 Hz, 2H), 7.48 (d, *J* = 7.2 Hz, 2H), 7.21–6.95 (m, 5H), 6.92–6.76 (m, 5H), 5.16 (s, 1H), 4.93 (s, 1H), 4.49 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.4 (CO), 150.9 (C), 147.6 (C), 142.7 (C), 137.4 (C), 136.9 (C), 135.4 (C), 132.2 (CH), 130.3 (CH), 129.64 (CH), 129.35 (CH), 128.4 (CH), 127.8 (CH), 124.9 (CH), 122.9 (CH), 120.0 (C), 109.0 (=CH_2), 56.8 (CH_2); IR (neat): 3066, 2919, 2848, 2170, 1606, 1527, 1505, 1485, 1445, 1335, 1311, 1269, 1235, 1166, 1096, 1071, 1037, 925, 884, 855, 783, 755, 715, 692, 649, 637, 577, 534, 510, 417 cm^{-1}. MS (ESI, m/z): 415.11 $[M+H]^+$; HRMS (ESI) calcd. for $C_{24}H_{19}N_2O_3S$: 415.11109 $[M+H]^+$, found: 415.11119.

4.3.2. Synthesis of (3-Methylene-4-((4-nitrophenyl)thio)-5-(thiophen-3-yl)-3,4-dihydro-2H-pyrrol-4-yl)(phenyl)methanone (32B)

General Procedure **3** was followed by using (*Z*)-1-phenyl-3-(prop-2-yn-1-ylamino)-3-(thiophen-3-yl)prop-2-en-1-one (**25B**) (97 mg, 0.36 mmol) and 4-nitrobenzenesulfenyl chloride (87 mg, 0.43 mmol) to afford 121 mg (80%) and 123 mg (81%) of the indicated product **32B** for NaH and Cs_2CO_3, respectively as a reddish-orange solid (R_f = 0.40 in 4:1 hexane/ethyl acetate); mp 76.1-77.5 ^oC.

32B: ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 9.1 Hz, 2H), 7.57 (d, *J* = 7.4 Hz, 2H), 7.30–7.20 (m, 2H), 7.14 (t, *J* = 7.6 Hz, 2H), 6.94 (d, *J* = 9.1 Hz, 2H), 6.81 (dd, *J* = 5.1, 3.0 Hz, 1H), 6.63 (dd, *J* = 5.1, 1.3 Hz, 1H), 5.23 (s, 1H), 4.98 (s, 1H), 4.50 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.8 (CO), 150.7 (C), 142.7 (C), 141.8 (C),

137.2 (C), 136.86 (C), 136.39 (C), 132.0 (CH), 128.98 (CH), 128.92 (CH), 127.79 (CH), 127.29 (CH), 126.3 (CH), 124.7 (CH), 122.4 (CH), 118.9 (C), 109.0 (=CH_2), 56.5 (CH_2); IR (neat): 3102, 2958, 2917, 2849, 2356, 1590, 1494, 1446, 1307, 1279, 1237, 1174, 1108, 837, 798, 749, 692, 640, 582, 525, 450, 415 cm^{-1}. MS (ESI, m/z): 421.06 $[M+H]^+$; HRMS (ESI) calcd. for $C_{22}H_{17}N_2O_3S_2$: 421.06751 $[M+H]^+$, found: 421.06810.

4.3.3. Synthesis of (4-Chlorophenyl)(3-methylene-4-((4-nitrophenyl)thio)-5-phenyl-3,4-dihydro-2H-pyrrol-4-yl)methanone (32C)

General Procedure **3** was followed by using (*Z*)-1-(4-chlorophenyl)-3-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**25C**) (96 mg, 0.33 mmol) and 4-nitrobenzenesulfenyl chloride (80 mg, 0.40 mmol) to afford 129 mg (87%) and 105 mg (71%) of the indicated product **32C** for NaH and Cs_2C0_3, respectively as a reddish-orange solid (R_f = 0.53 in 4:1 hexane/ethyl acetate); mp 84.3-85.7 ºC.

32C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 9.0 Hz, 2H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.15–6.92 (m, 10H), 5.28 (s, 1H), 5.02 (s, 1H), 4.55 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.7 (CO), 150.6 (C), 145.3 (C), 142.7 (C), 138.0 (C), 136.3 (C), 135.69 (C), 135.10 (C), 130.36 (CH), 130.19 (CH), 129.6 (CH), 128.3 (CH), 127.8 (CH), 124.6 (CH), 123.0 (CH), 119.3 (C), 109.0 (=CH_2), 56.8 (CH_2); IR (neat): 3078, 2919, 2850, 2337, 1638, 1587, 1495, 1311, 1239, 1171, 1087, 1011, 911, 853, 767, 739, 696, 645, 613, 578, 554, 476, 446, 415 cm^{-1}. MS (ESI, m/z): 449.07 $[M+H]^+$; HRMS (ESI) calcd. for $C_{24}H_{18}ClN_2O_3S$: 449.07212 $[M+H]^+$, found: 449.07340.

4.3.4. Synthesis of (2-Bromophenyl)(3-methylene-4-((4-nitrophenyl)thio)-5-phenyl-3,4-dihydro-2H-pyrrol-4-yl)methanone (32D)

General Procedure **3** was followed by using (*Z*)-1-(2-bromophenyl)-3-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**25D**) (93 mg, 0.27 mmol) and 4-nitrobenzenesulfenyl chloride (64 mg, 0.32 mmol) to afford 77 mg (58%) and 90.3

mg (67%) of the indicated product **32D** for NaH and Cs_2CO_3, respectively as an orange solid (R_f = 0.21 in 4:1 hexane/ethyl acetate); mp 149.7-150.2°C.

32D: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (dd, *J* = 9.4, 2.7 Hz, 2H), 7.19–7.11 (m, 4H), 6.99–6.89 (m, 6H), 6.85 (td, *J* = 7.7, 1.9 Hz, 1H), 5.30 (s, 1H), 4.97 (s, 1H), 4.54 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.5 (CO), 152.7 (C), 151.0 (C), 143.6 (C), 140.6 (C), 137.2 (C), 135.0 (C), 133.1 (CH), 131.1 (CH), 130.99 (CH), 130.92 (CH), 130.14 (CH), 128.2 (CH), 126.4 (CH), 124.9 (CH), 124.7 (CH), 120.6 (C), 119.7 (C), 109.2 (=CH_2), 57.6 (CH_2); IR (neat): 3057, 2908, 2172, 2044, 1980, 1961, 1907, 1631, 1587, 1509, 1490, 1426, 1336, 1307, 1288, 1236, 1173, 1103, 1025, 895, 850, 773, 739, 691, 631, 569, 552, 512, 473, 457 cm^{-1}. MS (ESI, m/z): 493.02 $[M+H]^+$; HRMS (ESI) calcd. for $C_{24}H_{18}BrN_2O_3S$: 493.02160 $[M+H]^+$, found: 493.02257.

4.3.5. Synthesis of (5-(3-Fluorophenyl)-3-methylene-4-((4-nitrophenyl)thio)-3,4-dihydro-2H-pyrrol-4-yl)(phenyl)methanone (32E)

General Procedure **3** was followed by using (*Z*)-3-(3-fluorophenyl)-1-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**25E**) (96 mg, 0.34 mmol) and 4-nitrobenzenesulfenyl chloride (82 mg, 0.41 mmol) to afford 83 mg (57%) and 88 mg (60%) of the indicated product **32E** for NaH and Cs_2CO_3, respectively as a reddish-orange solid (R_f = 0.21 in 4:1 hexane/ethyl acetate); mp 92.8-93.5 °C.

32E: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 9.1 Hz, 2H), 7.52 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.08 (t, *J* = 7.7 Hz, 2H), 6.92–6.75 (m, 5H), 6.56 (tdd, *J* = 8.3, 2.7, 1.1 Hz, 1H), 5.19 (d, *J* = 1.0 Hz, 1H), 4.95 (s, 1H), 4.47 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.8 (CO), 162.1 (d, ^1J = 248.0 Hz, CF), 150.4 (C), 144.9 (d, ^4J = 3.5 Hz, C), 142.7 (C), 137.4 (d, ^3J = 7.4 Hz, C), 136.9 (C), 136.0 (C), 132.3 (CH), 129.8 (d, ^3J = 8.2 Hz, CH), 129.0 (CH), 127.7 (CH), 125.9 (d, ^4J = 3.1 Hz, CH), 124.7 (CH), 122.5 (CH), 121.2 (C), 116.4 (d, ^2J = 16.2 Hz, CH), 116.2 (d, ^2J = 14.7 Hz, CH), 109.3 (=CH_2), 56.4 (CH_2); IR (neat): 3067, 2165, 2040, 1738, 1613, 1591, 1538, 1494, 1426, 1369, 1337, 1310, 1265, 1239, 1215, 1174, 1138, 1096, 1035, 928, 870, 848, 815, 788, 753, 705, 686, 668, 640, 590, 520, 508, 415 cm^{-1}. MS (ESI, m/z):

433.10 $[M+H]^+$; HRMS (ESI) calcd. for $C_{24}H_{18}FN_2O_3S$: 433.10167 $[M+H]^+$, found: 433.10230.

4.3.6. Synthesis of (3-Methylene-4-((4-nitrophenyl)thio)-5-(4-(trifluoromethyl)phenyl)-3,4-dihydro-2H-pyrrol-4-yl)(phenyl)methanone (32F)

General Procedure **3** was followed by using (*Z*)-1-phenyl-3-(prop-2-yn-1-ylamino)-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (**25F**) (97 mg, 0.29 mmol) and 4-nitrobenzenesulfenyl chloride (70 mg, 0.35 mmol) to afford 89 mg (64%) and 88 mg (63%) of the indicated product **32F** for NaH and Cs_2CO_3, respectively as a yellow solid (R_f = 0.22 in 4:1 hexane/ethyl acetate); mp 148.8-150.1 ºC.

32F: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 9.1 Hz, 2H), 7.50 (d, *J* = 7.1 Hz, 2H), 7.25–7.17 (m, 3H), 7.15–7.03 (m, 4H), 6.88 (d, *J* = 9.1 Hz, 2H), 5.21 (d, *J* = 1.0 Hz, 1H), 4.97 (s, 1H), 4.48 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.6 (CO), 150.3 (C), 144.4 (C), 142.8 (C), 138.7 (C), 136.7 (C), 135.6 (C), 132.5 (CH), 130.8 (q, ^2J = 32.6 Hz, C-CF_3), 130.0 (CH), 129.1 (CH), 127.9 (CH), 125.1 (q, ^3J = 8.1 Hz, CH), 124.9 (CH), 123.4 (q, ^1J = 270.6 Hz, CF_3), 122.6 (CH), 119.0 (C), 109.7 (=CH_2), 56.5 (CH_2); IR (neat): 2927, 2330, 2177, 1976, 1593, 1525, 1495, 1339, 1320, 1285, 1231, 1167, 1124, 1109, 1064, 1034, 1014, 887, 851, 833, 743, 718, 690, 633, 598, 511, 439, 411 cm^{-1}. MS (ESI, m/z): 483.09 $[M+H]^+$; HRMS (ESI) calcd. for $C_{25}H_{18}F_3N_2O_3S$: 483.09847 $[M+H]^+$, found: 483.09849.

4.3.7. Synthesis of (5-(4-Bromophenyl)-3-methylene-4-((4-nitrophenyl)thio)-3,4-dihydro-2H-pyrrol-4-yl)(phenyl)methanone (32G)

General Procedure **3** was followed by using (*Z*)-3-(4-bromophenyl)-1-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**25G**) (90 mg, 0.26 mmol) and 4-nitrobenzenesulfenyl chloride (62 mg, 0.31 mmol) to afford 69 mg (54%) and 66.6 mg (51%) of the indicated product **32G** for NaH and Cs_2CO_3, respectively as light orange oil (R_f = 0.25 in 4:1 hexane/ethyl acetate).

32G: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 9.1 Hz, 2H), 7.57 (d, *J* = 7.1 Hz, 2H), 7.30 (t, *J* = 7.4 Hz, 1H), 7.16 (t, *J* = 7.7 Hz, 2H), 7.09–6.99 (m, 4H), 6.94 (d, *J* = 9.2 Hz, 2H), 5.26 (s, 1H), 5.02 (s, 1H), 4.54 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.7 (CO), 150.4 (C), 145.5 (C), 142.7 (C), 136.9 (C), 136.1 (C), 134.1 (C), 132.3 (CH), 131.5 (CH), 131.2 (CH), 129.1 (CH), 127.8 (CH), 124.8 (CH), 123.7 (C), 122.7 (CH), 120.7 (C), 109.3 (=CH_2), 56.6 (CH_2); IR (neat): 3061, 2923, 2848, 2114, 1998, 1906, 1730, 1590, 1528, 1475, 1446, 1393, 1333, 1313, 1286, 1236, 1174, 1100, 1069, 1027, 1008, 927, 887, 855, 821, 728, 715, 693, 649, 500, 481, 428, 416 cm^{-1}. MS (ESI, m/z): 493.02 $[M+H]^+$; HRMS (ESI) calcd. for $C_{24}H_{18}BrN_2O_3S$: 493.02160 $[M+H]^+$, found: 493.02162.

4.3.8. Synthesis of (5-(4-Methoxyphenyl)-3-methylene-4-((4-nitrophenyl)thio)-3,4-dihydro-2H-pyrrol-4-yl)(phenyl)methanone (32H)

General Procedure **3** was followed by using (*Z*)-3-(4-methoxyphenyl)-1-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**25H**) (86 mg, 0.29 mmol) and 4-nitrobenzenesulfenyl chloride (70 mg, 0.35 mmol) to afford 73 mg (57%) and 61.6 mg (47%) of the indicated product **32H** for NaH and Cs_2CO_3, respectively as an orange solid (R_f = 0.21 in 4:1 hexane/ethyl acetate); mp 88.7-89.2 ºC.

32H: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 9.1 Hz, 2H), 7.54 (d, *J* = 7.1 Hz, 2H), 7.22 (t, *J* = 7.4 Hz, 1H), 7.10 (t, *J* = 7.6 Hz, 2H), 7.04 (d, *J* = 8.8 Hz, 2H), 6.95 (d, *J* = 9.2 Hz, 2H), 6.43 (d, *J* = 8.8 Hz, 2H), 5.23 (s, 1H), 4.99 (s, 1H), 4.55 (s, 2H), 3.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.2 (CO), 160.2 (C), 150.9 (C), 148.1 (C), 142.5 (C), 137.4 (C), 137.1 (C), 131.76 (CH), 131.69 (CH), 129.0 (CH), 127.69 (C), 127.59 (CH), 124.6 (CH), 122.9 (CH), 118.2 (C), 113.6 (CH), 108.4 (=CH_2), 56.8 (CH_2), 54.9 (CH_3); IR (neat): 3377, 2836, 2254, 2190, 2160, 2044, 2005, 1968, 1684, 1591, 1576, 1559, 1497, 1446, 1331,1313, 1286, 1237, 1171, 1108, 1025, 848, 752, 709, 671, 558, 521, 420 cm^{-1}. MS (ESI, m/z): 445.12 $[M+H]^+$; HRMS (ESI) calcd. for $C_{25}H_{21}N_2O_4S$: 445.12165 $[M+H]^+$, found: 445.12193.

4.3.9. Synthesis of (5-(4-Chlorophenyl)-3-methylene-4-((4-nitrophenyl)thio)-3,4-dihydro-2H-pyrrol-4-yl)(phenyl)methanone (32I)

General Procedure **3** was followed by using (*Z*)-3-(4-chlorophenyl)-1-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**25I**) (93 mg, 0.31 mmol) and 4-nitrobenzenesulfenyl chloride (74 mg, 0.37 mmol) to afford 84 mg (60%) and 71.9 mg (51%) of the indicated product **32I** for NaH and Cs_2CO_3, respectively as an orange solid (R_f = 0.22 in 4:1 hexane/ethyl acetate); mp; 104.5-105.5 ^oC.

32I: ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 9.1 Hz, 2H), 7.57 (d, *J* = 7.1 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 1H), 7.15 (t, *J* = 7.7 Hz, 2H), 7.09 (d, *J* = 8.5 Hz, 2H), 6.97–6.87 (m, 4H), 5.26 (s, 1H), 5.02 (s, 1H), 4.54 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.1 (CO) 150.7 (C), 145.8 (C), 143.0 (C), 137.2 (C), 136.4 (C), 135.6 (C), 134.0 (C), 132.6 (CH), 131.3 (CH), 129.4 (CH), 128.80 (CH), 128.12 (CH), 125.0 (CH), 123.0 (CH), 120.9 (C), 109.5 (=CH_2), 56.8 (CH_2); IR (neat): 3007, 2851, 2142, 2046, 2010, 1590, 1486, 1446, 1331, 1313, 1286, 1234, 1174, 1089, 1011, 857, 753, 736, 717, 694, 512, 470 cm^{-1}. MS (ESI, m/z): 449.07 $[M+H]^+$; HRMS (ESI) calcd. for $C_{24}H_{18}ClN_2O_3S$: 449.07212 $[M+H]^+$, found: 449.07145.

4.3.10. Synthesis of (5-(3,5-Bis(trifluoromethyl)phenyl)-3-methylene-4-((4-nitrophenyl)thio)-3,4-dihydro-2H-pyrrol-4-yl)(phenyl)methanone (32J)

General Procedure **3** was followed by using (*Z*)-3-(3,5-bis(trifluoromethyl)phenyl)-1-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**25J**) (99 mg, 0.25 mmol) and 4-nitrobenzenesulfenyl chloride (60 mg, 0.30 mmol) to afford 87 mg (63%) and 104.2 mg (76%) of the indicated product **32J** for NaH and Cs_2CO_3, respectively as a brownish-yellow solid (R_f = 0.44 in 4:1 hexane/ethyl acetate); mp 205.8-206.5^oC.

32J: ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 9.1 Hz, 2H), 7.50 (s, 2H), 7.43 (d, *J* = 7.1 Hz, 2H), 7.33 (s, 1H), 7.22–7.14 (m, 1H), 7.05 (t, *J* = 7.7 Hz, 2H), 6.92 (d, *J* = 9.1 Hz, 2H), 5.29 (s, 1H), 5.00 (s, 1H), 4.49 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.3 (CO), 150.0 (C), 143.3 (q, ^2J = 29.2 Hz, C-CF_3), 137.6 (C), 136.7 (C), 134.9

(C), 132.7 (CH), 131.79 (C), 131.45 (C), 129.56 (q, ^{3}J = 8.3 Hz, CH), 129.01 (CH), 127.9 (CH), 125.0 (CH), 123.4 (CH), 122.92 (q, ^{1}J = 272.9 Hz, CF_3), 122.46 (q, ^{3}J = 7.2 Hz, CH), 120.9 (C), 110.5 (=CH_2), 57.0 (CH_2); IR (neat): 2349, 2136, 1974, 1957, 1608, 1545, 1517, 1381, 1342, 1278, 1222, 1172, 1122, 1029, 860, 845, 716, 699, 677, 646, 534, 411 cm^{-1}. MS (ESI, m/z): 551.08 $[M+H]^+$; HRMS (ESI) calcd. for $C_{26}H_{17}F_6N_2O_3S$: 551.08586 $[M+H]^+$, found: 551.08601.

4.3.11. Synthesis of (3-Methylene-5-(4-nitrophenyl)-4-((4-nitrophenyl)thio)-3,4-dihydro-2H-pyrrol-4-yl)(phenyl)methanone (32K)

General Procedure **3** was followed by using (*Z*)-3-(4-nitrophenyl)-1-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**25K**) (98 mg, 0.32 mmol) and 4-nitrobenzenesulfenyl chloride (76 mg, 0.38 mmol) to afford 62 mg (42%) and 47 mg (32%) of the indicated product **32K** for NaH and Cs_2CO_3, respectively as reddish orange oil (R_f = 0.10 in 4:1 hexane/ethyl acetate).

32K: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 9.1 Hz, 2H), 7.83 (d, *J* = 8.9 Hz, 2H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.38–7.34 (m, 3H), 7.21 (t, *J* = 7.7 Hz, 2H), 6.95 (d, *J* = 9.2 Hz, 2H), 5.34 (d, *J* = 1.1 Hz, 1H), 5.08 (d, *J* = 1.0 Hz, 1H), 4.55 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.2 (CO), 150.1 (C), 147.3 (C), 143.0 (C), 142.5 (C), 141.4 (C), 136.4 (C), 135.0 (CH), 133.1 (C), 130.2 (CH), 129.3 (CH), 128.1 (CH), 125.0 (CH), 124.0 (C), 123.4 (CH), 122.6 (CH), 110.4 (=CH_2), 56.4 (CH_2); IR (neat): 2915, 2848, 2360, 2236, 2197, 2179, 2011, 1942, 1613, 1589, 1492, 1337, 1307, 1282, 1232, 1103, 1035, 895, 866, 847, 727, 717, 693, 651, 526, 501, 474, 448, 418 cm^{-1}. MS (ESI, m/z): 460.096 $[M+H]^+$; HRMS (ESI) calcd. for $C_{24}H_{18}N_3O_5S$: 460.09617 $[M+H]^+$, found: 460.09654.

4.3.12. Synthesis of (5-(4-(Tert-butyl)phenyl)-3-methylene-4-((4-nitrophenyl)thio)-3,4-dihydro-2H-pyrrol-4-yl)(phenyl)methanone (32L)

General Procedure **3** was followed by using (*Z*)-3-(4-(tert-butyl)phenyl)-1-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**25L**) (95 mg, 0.30 mmol) and 4-nitrobenzenesulfenyl chloride (72 mg, 0.36 mmol) to afford 88 mg (62%) and 76.1 mg (54%) of the indicated product **32L** for NaH and Cs_2CO_3, respectively as an orange solid (R_f = 0.41 in 4:1 hexane/ethyl acetate); mp 190.7-191.5 ^oC.

32L: ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 9.1 Hz, 2H), 7.46 (d, *J* = 7.1 Hz, 2H), 7.13 (t, *J* = 7.4 Hz, 1H), 7.06–6.99 (m, 4H), 6.97 (d, *J* = 9.2 Hz, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 5.24 (s, 1H), 5.00 (s, 1H), 4.56 (s, 2H), 1.03 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.2 (CO), 152.7 (C), 150.7 (C), 148.5 (C), 142.4 (C), 137.5 (C), 137.0 (C), 132.1 (C), 131.3 (CH), 130.0 (CH), 128.8 (CH), 127.3 (CH), 124.9 (CH), 124.6 (CH), 122.8 (CH), 119.2 (C), 108.4 ($=CH_2$), 56.6 (CH_2), 34.2 (C), 30.4 (CH_3); IR (neat): 3035, 2946, 1603, 1511, 1489, 1437, 1367, 1332, 1310, 1291, 1264, 1225, 1162, 1097, 1027, 978, 888, 858, 786, 745, 716, 696, 656, 639, 627, 565, 533, 514, 412 cm^{-1}. MS (ESI, m/z): 471.17 $[M+H]^+$; HRMS (ESI) calcd. for $C_{28}H_{27}N_2O_3S$: 471.17369 $[M+H]^+$, found: 471.17459.

4.3.13. Synthesis of (3-Methylene-4-((4-nitrophenyl)thio)-5-(p-tolyl)-3,4-dihydro-2H-pyrrol-4-yl)(phenyl)methanone (32M)

General Procedure **3** was followed by using (*Z*)-1-phenyl-3-(prop-2-yn-1-ylamino)-3-(p-tolyl)prop-2-en-1-one (**25M**) (101 mg, 0.37 mmol) and 4-nitrobenzenesulfenyl chloride (88 mg, 0.44 mmol) to afford 115 mg (73%) and 97.5 mg (62%) of the indicated product **32M** for NaH and Cs_2CO_3, respectively as an orange-brown solid (R_f = 0.31 in 4:1 hexane/ethyl acetate); mp 164.7-165.5^oC.

32M: ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 9.1 Hz, 2H), 7.56 (d, *J* = 7.2 Hz, 2H), 7.21 (t, *J* = 7.4 Hz, 1H), 7.09 (t, *J* = 7.7 Hz, 2H), 7.02 (d, *J* = 8.1 Hz, 2H), 6.95 (d, *J* = 9.1 Hz, 2H), 6.70 (d, *J* = 8.0 Hz, 2H), 5.22 (s, 1H), 5.00 (s, 1H), 4.56 (s, 2H),

2.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.1 (CO), 150.7 (C), 147.8 (C), 142.3 (C), 139.5 (C), 137.2 (C), 136.9 (C), 132.2 (C), 131.6 (CH), 130.0 (CH), 129.0 (CH), 128.8 (CH), 127.4 (CH), 124.5 (CH), 122.6 (CH), 118.9 (C), 108.4 (=CH_2), 56.4 (CH_2), 20.7 (CH_3); IR (neat): 2349, 2155, 2051, 1993, 1974, 1733, 1612, 1591, 1531, 1494, 1342, 1313, 1289, 1239, 1180, 1163, 1100, 1037, 847, 818, 789, 711, 665, 636, 530, 418 cm^{-1}. MS (ESI, m/z): 429.12 $[M+H]^+$; HRMS (ESI) calcd. for $C_{25}H_{21}N_2O_3S$: 429.12674 $[M+H]^+$, found: 429.12707.

4.3.14. Synthesis of (2-Bromophenyl)(5-(4-chlorophenyl)-3-methylene-4-((4-nitrophenyl)thio)-3,4-dihydro-2H-pyrrol-4-yl)methanone (32N)

General Procedure **3** was followed by using (*Z*)-1-(2-bromophenyl)-3-(4-chlorophenyl)-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**25N**) (100 mg, 0.27 mmol) and 4-nitrobenzenesulfenyl chloride (64 mg, 0.32 mmol) to afford 104 mg (73%) and 87.3 mg (62%) of the indicated product **32N** for NaH and Cs_2CO_3, respectively as a yellowish-brown solid (R_f = 0.19 in 4:1 hexane/ethyl acetate); mp 97.7-99.2 ^{o}C.

32N: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 9.0 Hz, 2H), 7.17 (td, *J* = 8.5, 7.7, 1.6 Hz, 2H), 7.08 (d, *J* = 8.4 Hz, 2H), 7.03–6.93 (m, 4H), 6.87 (d, *J* = 8.4 Hz, 2H), 5.30 (s, 1H), 4.97 (s, 1H), 4.51 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.8 (CO), 150.7 (C), 150.4 (C), 143.4 (C), 140.2 (C), 136.5 (C), 135.8 (C), 133.2 (C), 132.8 (CH), 131.8 (CH), 130.76 (CH), 130.70 (CH), 128.1 (CH), 126.3 (CH), 124.7 (CH), 124.5 (CH), 120.3 (C), 120.0 (C), 109.2 (=CH_2), 57.2 (CH_2); IR (neat): 2024, 1589, 1514, 1482, 1426, 1334, 1307, 1289, 1232, 1174, 1105, 1089, 1027, 1012, 853, 819, 787, 736, 648, 631, 515, 465, 408 cm^{-1}. MS (ESI, m/z): 526.98 $[M+H]^+$; HRMS (ESI) calcd. for $C_{24}H_{17}BrClN_2O_3S$: 526.98263 $[M+H]^+$, found: 526.98157.

4.3.15. Synthesis of (2-Iodophenyl)(3-methylene-4-((4-nitrophenyl)thio)-5-phenyl-3,4-dihydro-2H-pyrrol-4-yl)methanone (32O)

General Procedure **3** was followed by using (*Z*)-1-(2-iodophenyl)-3-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**25O**) (72 mg, 0.19 mmol) and 4-nitrobenzenesulfenyl chloride (46 mg, 0.23 mmol) to afford 65 mg (63%) and 47.2 mg (47 %) of the indicated product **32O** for NaH and Cs_2CO_3, respectively as an orange-brown solid (R_f = 0.38 in 4:1 hexane/ethyl acetate); mp 97.7-99.2^oC.

32O: ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 9.1 Hz, 2H), 7.48 (d, *J* = 7.9 Hz, 1H), 7.18–7.14 (m, 3H), 6.99–6.90 (m, 6H), 6.68 (td, *J* = 7.6, 1.7 Hz, 1H), 5.32 (s, 1H), 4.97 (s, 1H), 4.57 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.4 (CO), 152.3 (C), 150.7 (C), 143.39 (C), 143.32 (C), 139.6 (CH), 136.8 (C), 134.9 (C), 130.94 (CH), 130.56 (CH), 130.35 (CH), 129.8 (CH), 128.0 (CH), 126.8 (CH), 124.74 (CH), 124.50 (CH), 118.8 (C), 109.0 (=CH_2), 94.4 (C), 57.3 (CH_2); IR (neat): 2349, 2241, 2204, 2097, 2016, 1975, 1591, 1513, 1334, 1308, 1286, 1233, 1108, 1013, 853, 772, 736, 697, 667, 631, 579, 568, 499, 447, 418 cm^{-1}. MS (ESI, m/z): 541.00 $[M+H]^+$; HRMS (ESI) calcd. for $C_{24}H_{18}IN_2O_3S$: 541.00773 $[M+H]^+$, found: 541.00810.

4.3.16. Synthesis of (5-(3,4-Dichlorophenyl)-3-methylene-4-((4-nitrophenyl)thio)-3,4-dihydro-2H-pyrrol-4-yl)(phenyl)methanone (32P)

General Procedure **3** was followed by using (*Z*)-3-(3,4-dichlorophenyl)-1-phenyl-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**25P**) (89 mg, 0.27 mmol) and 4-nitrobenzenesulfenyl chloride (64 mg, 0.32 mmol) to afford 91 mg (70%) and 96.4 mg (74%) of the indicated product **32P** for NaH base and Cs_2CO_3, respectively as a yellowish-brown solid (R_f = 0.29 in 4:1 hexane/ethyl acetate); mp 87.7-89.3 ^oC.

32P: ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 9.1 Hz, 2H), 7.56 (d, *J* = 7.1 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 1H), 7.25 (d, *J* = 9.9 Hz, 2H), 7.18 (t, *J* = 7.7 Hz, 2H), 7.00– 6.95 (m, 3H), 5.28 (d, *J* = 0.7 Hz, 1H), 5.03 (s, 1H), 4.52 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.6 (CO), 150.2 (C), 144.0 (C), 142.9 (C), 136.9 (C), 135.64 (C), 135.14

(C), 133.3 (C), 132.53 (C), 132.44 (CH), 131.4 (CH), 130.1 (CH), 128.88 (CH), 128.59 (CH), 127.8 (CH), 124.9 (CH), 122.8 (CH), 121.9 (C), 109.7 (=CH_2), 56.6 (CH_2); IR (neat): 3061, 2832, 1729, 1590, 1555, 1493, 1462, 1377, 1331, 1312, 1288, 1232, 1165, 1129, 1107, 1027, 886, 849, 783, 749, 700, 653, 637, 511, 415 cm^{-1}. MS (ESI, m/z): 483.033 $[M+H]^+$; HRMS (ESI) calcd. for $C_{24}H_{17}Cl_2N_2O_3S$: 483.03314 $[M+H]^+$, found: 483.03315.

4.3.17. Synthesis of (2-Bromophenyl)(5-(2-methoxyphenyl)-3-methylene-4-((4-nitrophenyl)thio)-3,4-dihydro-2H-pyrrol-4-yl)methanone (32Q)

General Procedure **3** was followed by using (*Z*)-1-(2-bromophenyl)-3-(2-methoxyphenyl)-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**25Q**) (99 mg, 0.27 mmol) and 4-nitrobenzenesulfenyl chloride (64 mg, 0.32 mmol) to afford 111 mg (79%) and 74.2 mg (53%) of the indicated product **32Q** for NaH and Cs_2CO_3, respectively as a dark brown solid (R_f = 0.19 in 4:1 hexane/ethyl acetate); mp 123.8-125.2 ^oC.

32Q: ^1H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 9.1 Hz, 2H), 7.23 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.13 (dd, *J* = 7.7, 2.1 Hz, 2H), 6.95 (d, *J* = 9.1 Hz, 2H), 6.92–6.83 (m, 3H), 6.63 (t, *J* = 7.5 Hz, 1H), 6.15 (d, *J* = 8.3 Hz, 1H), 5.30 (s, 1H), 5.00 (s, 1H), 4.49 (s, 2H), 3.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.8 (CO), 155.7 (C), 150.1 (C), 149.7 (C), 143.2 (C), 140.9 (C), 137.8 (C), 132.8 (CH), 132.4 (CH), 131.7 (CH), 130.1 (CH), 129.2 (CH), 125.6 (CH), 124.1 (CH), 123.8 (CH), 123.5 (C), 120.14 (CH), 120.05 (C), 117.5 (C), 109.6 (=CH_2), 108.1 (CH), 56.0 (CH_2), 54.7 (CH_3); IR (neat): 2832, 2158, 2030, 2015, 1996, 1732, 1582, 1506, 1485, 1459, 1335, 1292, 1240, 1179, 1131, 1101, 1025, 851, 797, 746, 731, 703, 685, 668, 630, 585, 557, 507, 490, 473 cm^{-1}. MS (ESI, m/z): 523.03 $[M+H]^+$; HRMS (ESI) calcd. for $C_{25}H_{20}BrN_2O_4S$: 523.03217 $[M+H]^+$, found: 523.03322.

4.3.18. Synthesis of (2-Bromophenyl)(5-(3-fluorophenyl)-3-methylene-4-((4-nitrophenyl)thio)-3,4-dihydro-2H-pyrrol-4-yl)methanone (32R)

General Procedure **3** was followed by using (*Z*)-1-(2-bromophenyl)-3-(3-fluorophenyl)-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**25R**) (107 mg, 0.30 mmol) and 4-nitrobenzenesulfenyl chloride (72 mg, 0.36 mmol) to afford 89 mg (58%) and 106.9 mg (70%) of the indicated product **32R** for NaH and Cs_2CO_3, respectively as a brown solid (R_f = 0.29 in 4:1 hexane/ethyl acetate); mp 132.8-133.9 ºC.

32R: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 9.0 Hz, 2H), 7.20 (d, *J* = 7.7 Hz, 2H), 7.03–6.88 (m, 6H), 6.84 (dt, *J* = 9.0, 2.1 Hz, 1H), 6.61 (td, *J* = 8.2, 2.6 Hz, 1H), 5.31 (s, 1H), 4.98 (s, 1H), 4.52 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.3 (CO), 161.9 (d, ^1J = 248.7 Hz, CF), 150.7 (C), 150.36 (d, ^4J = 2.5 Hz, C), 143.8 (C), 140.4 (C), 137.2 (d, ^3J = 7.7 Hz, C), 136.7 (C), 133.2 (CH), 131.2 (CH), 131.0 (CH), 129.8 (d, ^3J = 8.5 Hz, CH), 127.18 (d, ^4J = 3.0 Hz, CH), 126.6 (CH), 124.8 (2CH), 120.79 (C), 120.54 (C), 117.54 (d, ^2J = 22.2 Hz, CH), 117.09 (d, ^2J = 21.1 Hz, CH), 109.6 (=CH_2), 57.4 (CH_2). (Note that two CH peaks overlap on each other); IR (neat): 2086, 2002, 1982, 1956, 1917, 1584, 1509, 1490, 1428, 1336, 1308, 1290, 1236, 1174, 1138, 1102, 1037, 931, 873, 850, 812, 779, 744, 706, 629, 583, 566, 507, 457, 426 cm^{-1}. MS (ESI, m/z): 511.01 $[M+H]^+$; HRMS (ESI) calcd. for $C_{24}H_{17}BrFN_2O_3S$: 511.01218 $[M+H]^+$, found: 511.01369.

4.3.19. Synthesis of (4-Chlorophenyl)(5-(3-fluorophenyl)-3-methylene-4-((4-nitrophenyl)thio)-3,4-dihydro-2H-pyrrol-4-yl)methanone (32S)

General Procedure **3** was followed by using (*Z*)-1-(4-chlorophenyl)-3-(3-fluorophenyl)-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**25S**) (94 mg, 0.30 mmol) and 4-nitrobenzenesulfenyl chloride (72 mg, 0.36 mmol) to afford 83 mg (59%) and 84 mg (60%) of the indicated product **32S** for NaH and Cs_2CO_3, respectively as an orange solid (R_f = 0.42 in 4:1 hexane/ethyl acetate); mp 87.7-89.2 ºC.

32S: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 9.1 Hz, 2H), 7.51 (d, *J* = 8.6 Hz, 2H), 7.11 (d, *J* = 8.5 Hz, 2H), 6.98–6.90 (m, 4H), 6.85 (dt, *J* = 9.6, 1.8 Hz, 1H), 6.70 (ddt,

J = 7.2, 4.7, 2.6 Hz, 1H), 5.28 (s, 1H), 5.03 (s, 1H), 4.53 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.4 (CO), 162.1 (d, ^1J = 248.7 Hz, CF), 150.3 (C), 145.4 (C), 142.8 (C), 138.5 (C), 137.2 (d, ^3J = 7.3 Hz, C), 135.71 (C), 135.38 (C), 130.26 (CH), 130.0 (d, ^3J = 8.2 Hz, CH), 128.0 (CH), 125.9 (d, ^4J = 1.9 Hz, CH), 124.7 (CH), 122.9 (CH), 120.5 (C), 116.5 (d, ^2J = 22.1 Hz, 2CH), 109.5 (=CH_2), 56.6 (CH_2). (Note that two CH peaks overlap on each other); IR (neat): 2909, 2145, 2079, 1737, 1584, 1484, 1433, 1331, 1310, 1290, 1234, 1216, 1170, 1136, 1086, 1011, 867, 850, 806, 781, 744, 708, 690, 667, 587, 544, 506, 480, 413 cm^{-1}. MS (ESI, m/z): 467.06 $[M+H]^+$; HRMS (ESI) calcd. for $C_{24}H_{17}ClFN_2O_3S$: 467.0627 $[M+H]^+$, found: 467.06392.

4.3.20. Synthesis of (5-(4-(Tert-butyl)phenyl)-3-methylene-4-((4-nitrophenyl)thio)-3,4-dihydro-2H-pyrrol-4-yl)(4-chlorophenyl)methanone (32T)

General Procedure **3** was followed by using (*Z*)-3-(4-(tert-butyl)phenyl)-1-(4-chlorophenyl)-3-(prop-2-yn-1-ylamino)prop-2-en-1-one (**25T**) (90 mg, 0.26 mmol) and 4-nitrobenzenesulfenyl chloride (62 mg, 0.31 mmol) to afford 87 mg (66%) and 99.5 mg (77%) of the indicated product **32T** for NaH and Cs_2CO_3, respectively as a brownish-yellow solid (R_f = 0.50 in 4:1 hexane/ethyl acetate); mp: 194.8-195.4 ^oC.

32T: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 9.1 Hz, 2H), 7.34 (d, *J* = 8.5 Hz, 2H), 7.04–6.93 (m, 6H), 6.90 (d, *J* = 8.4 Hz, 2H), 5.26 (s, 1H), 5.00 (s, 1H), 4.54 (s, 2H), 1.06 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.2 (CO), 153.6 (C), 151.0 (C), 149.8 (C), 143.0 (C), 137.53 (C), 137.05 (C), 136.5 (C), 132.4 (C), 130.6 (CH), 130.5 (CH), 127.7 (CH), 125.4 (CH), 124.9 (CH), 123.6 (CH), 119.0 (C), 109.0 (=CH_2), 57.3 (CH_2), 34.6 (C), 30.8 (CH_3); IR (neat): 2960, 2349, 2182, 2128, 1956, 1587, 1511, 1492, 1334, 1309, 1235, 1169, 1087, 1011, 895, 863, 838, 787, 742, 694, 670, 651, 624, 565, 480, 445, 415 cm^{-1}. MS (ESI, m/z): 505.13 $[M+H]^+$; HRMS (ESI) calcd. for $C_{28}H_{26}ClN_2O_3S$: 505.13472 $[M+H]^+$, found: 505.13575.

4.3.21. Synthesis of (2-Bromophenyl)(3-methylene-4-((4-nitrophenyl)thio)-5-(4-(trifluoromethyl)phenyl)-3,4-dihydro-2H-pyrrol-4-yl)methanone (32U)

General Procedure **3** was followed by using (*Z*)-1-(2-bromophenyl)-3-(prop-2-yn-1-ylamino)-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (**25U**) (87 mg, 0.21 mmol) and 4-nitrobenzenesulfenyl chloride (49 mg, 0.25 mmol) to afford 75 mg (63%) and 81.4 mg (68%) of the indicated product **32U** for NaH and Cs_2CO_3, respectively as reddish-orange oil (R_f = 0.24 in 4:1 hexane/ethyl acetate).

32U: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 9.0 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.20–7.11 (m, 4H), 7.00–6.95 (m, 3H), 6.89 (td, *J* = 7.7, 1.7 Hz, 1H), 5.34 (s, 1H), 5.00 (s, 1H), 4.53 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.0 (CO), 150.4 (C), 149.8 (C), 143.9 (C), 140.2 (C), 138.4 (C), 136.3 (C), 133.1 (CH), 131.56 (C), 131.29 (CH), 131.23 (CH), 131.01 (CH), 126.6 (CH), 124.96 (CH), 124.92 (CH), 124.90 (CH), 123.04 (q, ^1J= 272.6 Hz, CF_3), 121.7 (C), 120.5 (C), 109.9 (=CH_2), 57.4 (CH_2); IR (neat): 1966, 1942, 1731, 1590, 1492, 1427, 1321, 1287, 1231, 1163, 1106, 1064, 1015, 852, 734, 707, 630, 594, 512, 461, 420 cm^{-1}. MS (ESI, m/z): 561.0 $[M+H]^+$; HRMS (ESI) calcd. for $C_{25}H_{17}BrF_3N_2O_3S$: 561.00899 $[M+H]^+$, found: 561.01040.

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APPENDICES A

NMR DATA

Bruker Spectrospin Avance DPX400 Ultrashield spectrometer was made use of getting ^{1}H and ^{13}C NMR spectrums.

^{1}H and ^{13}C NMR spectrums for each compound are demonstrated down there.

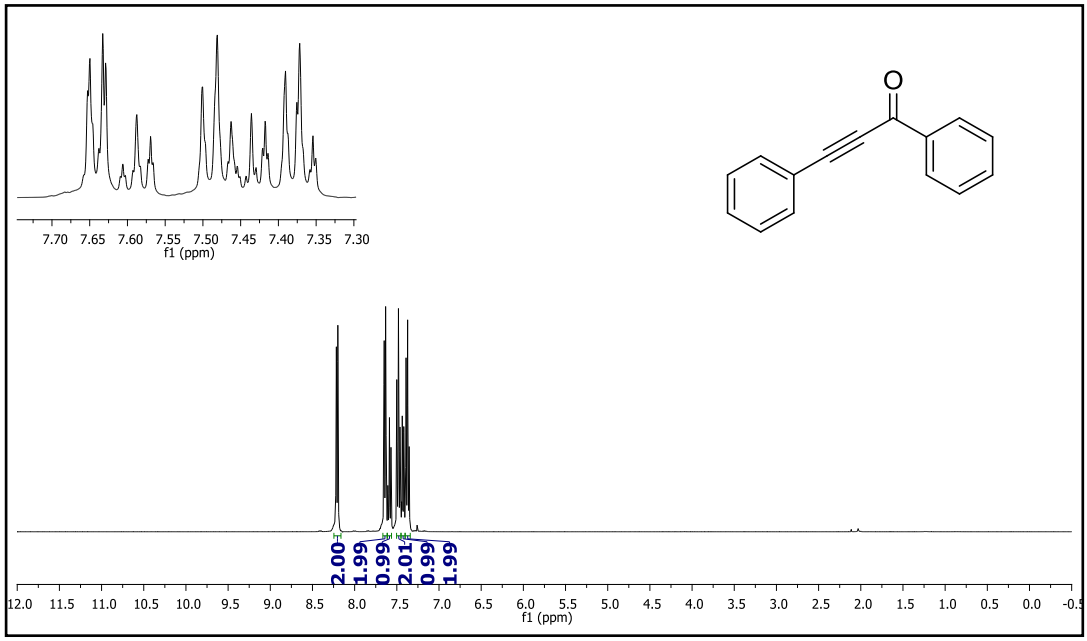

Figure 17. ^{1}H NMR spectrum of compound **35A**.

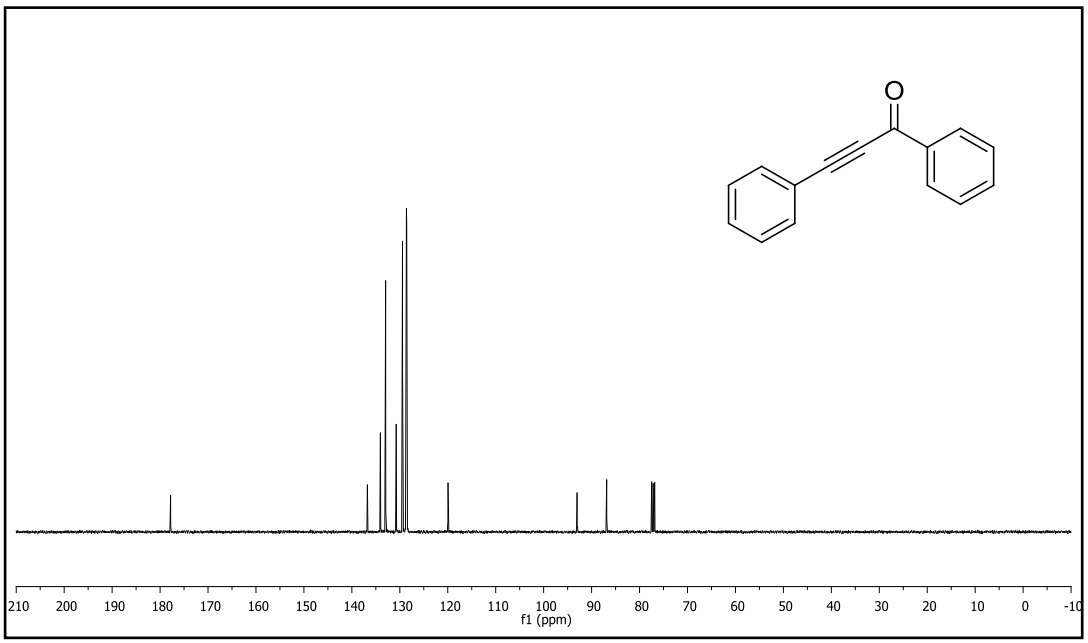

Figure 18. ^{13}C NMR spectrum of compound **35A**.

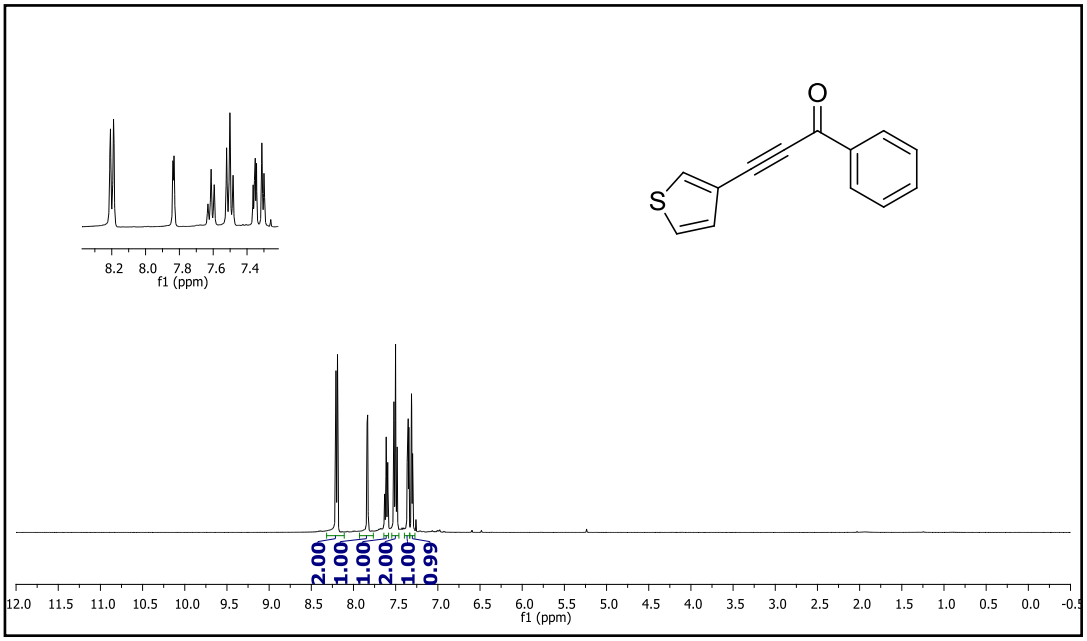

Figure 19. ^{1}H NMR spectrum of compound **35B**.

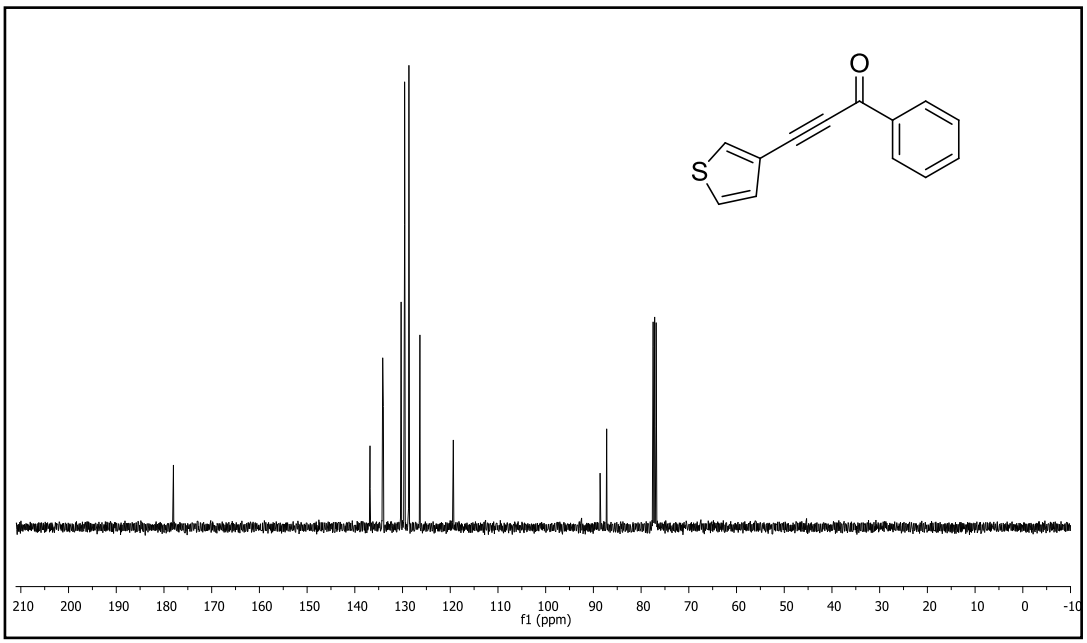

Figure 20. ^{13}C NMR spectrum of compound **35B**.

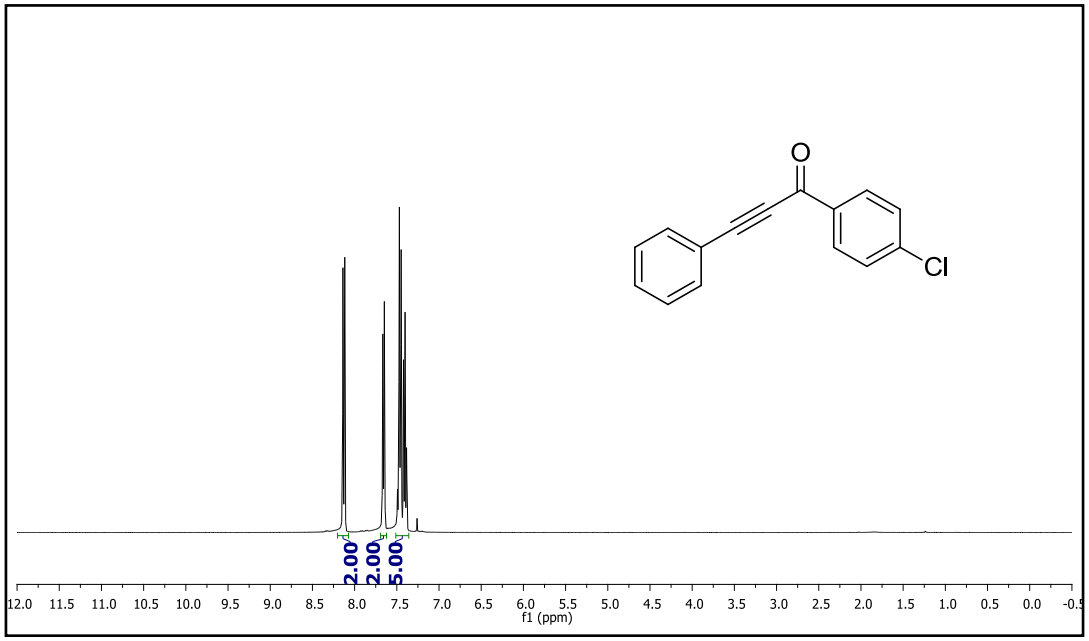

Figure 21. ^{1}H NMR spectrum of compound **35C**.

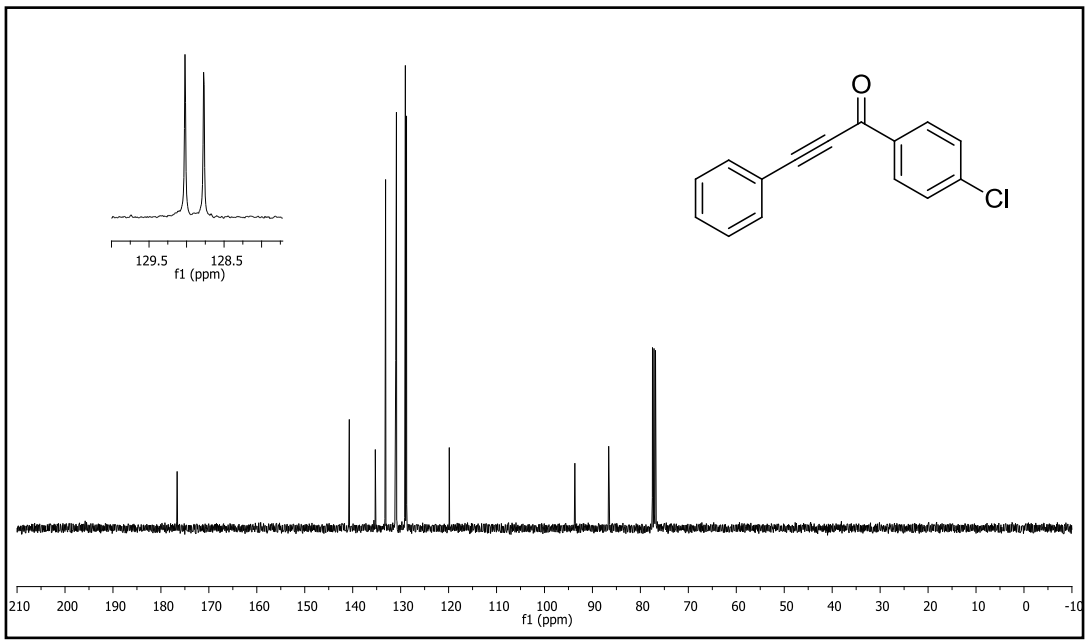

Figure 22. ^{13}C NMR spectrum of compound **35C**.

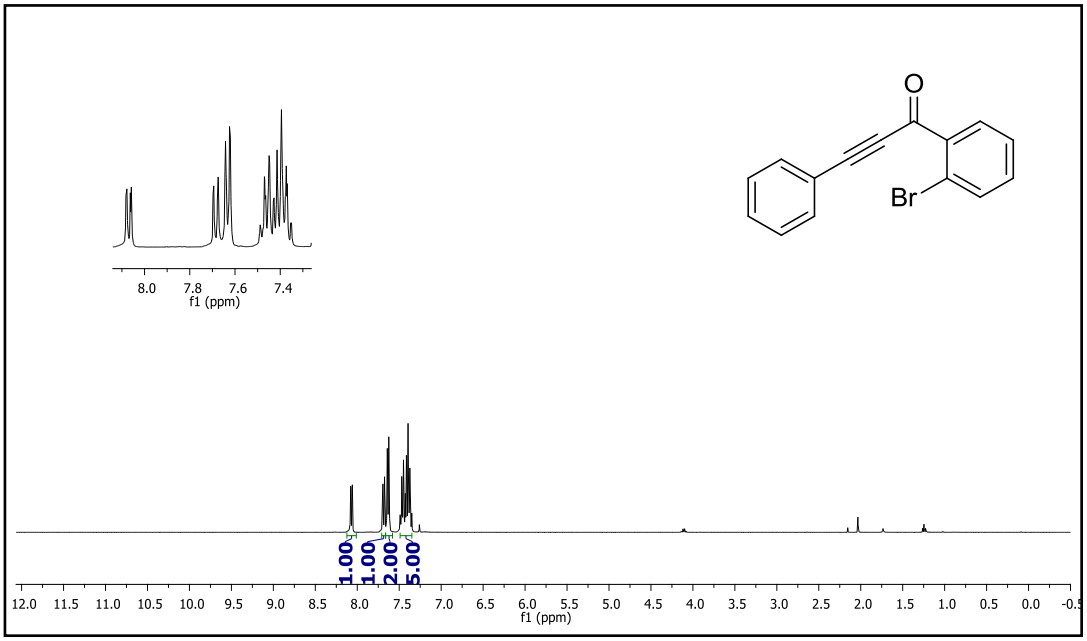

Figure 23. ^{1}H NMR spectrum of compound **35D**.

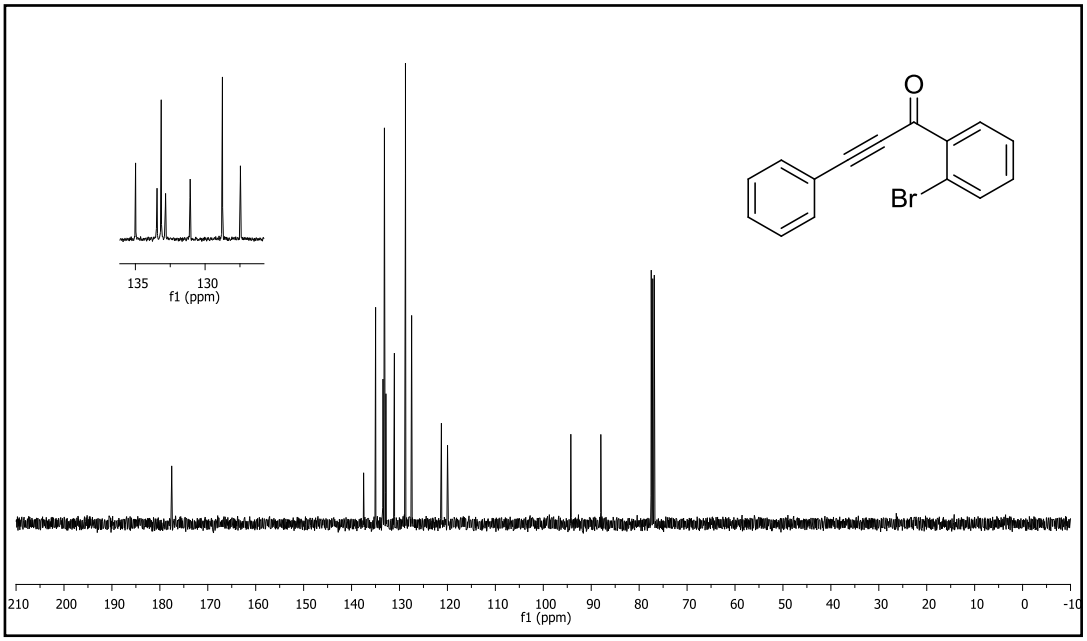

Figure 24. ^{13}C NMR spectrum of compound **35D**.

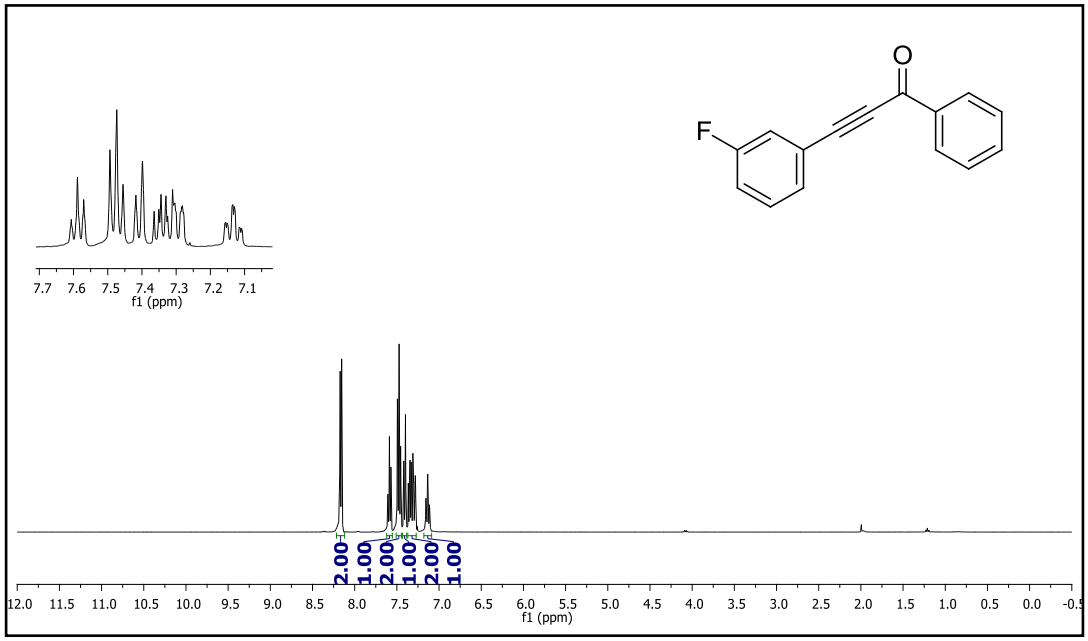

Figure 25. ^{1}H NMR spectrum of compound **35E**.

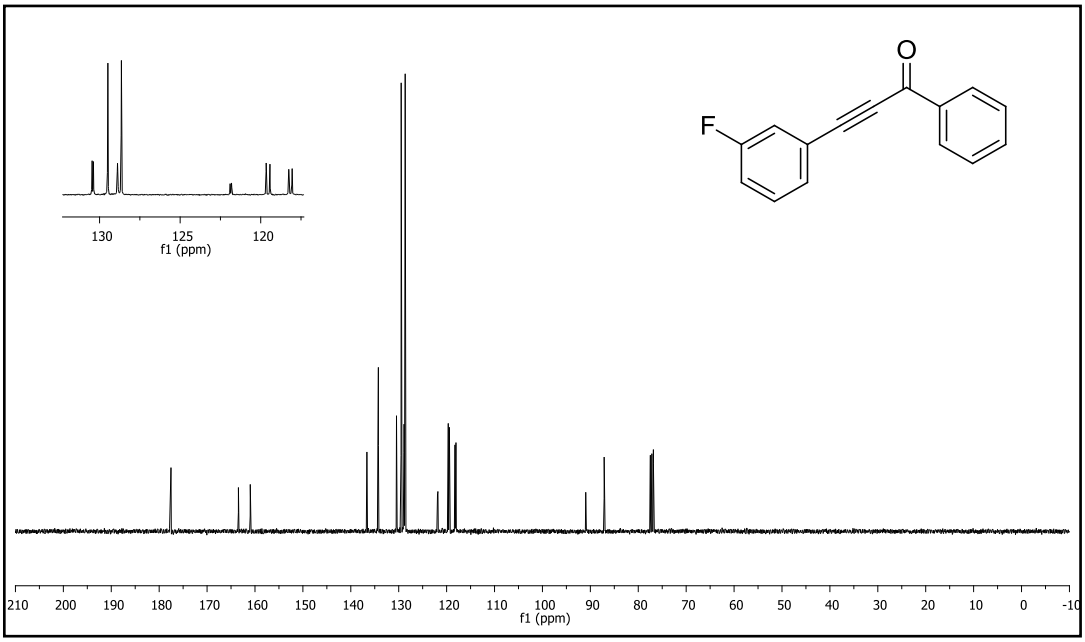

Figure 26. ^{13}C NMR spectrum of compound **35E**.

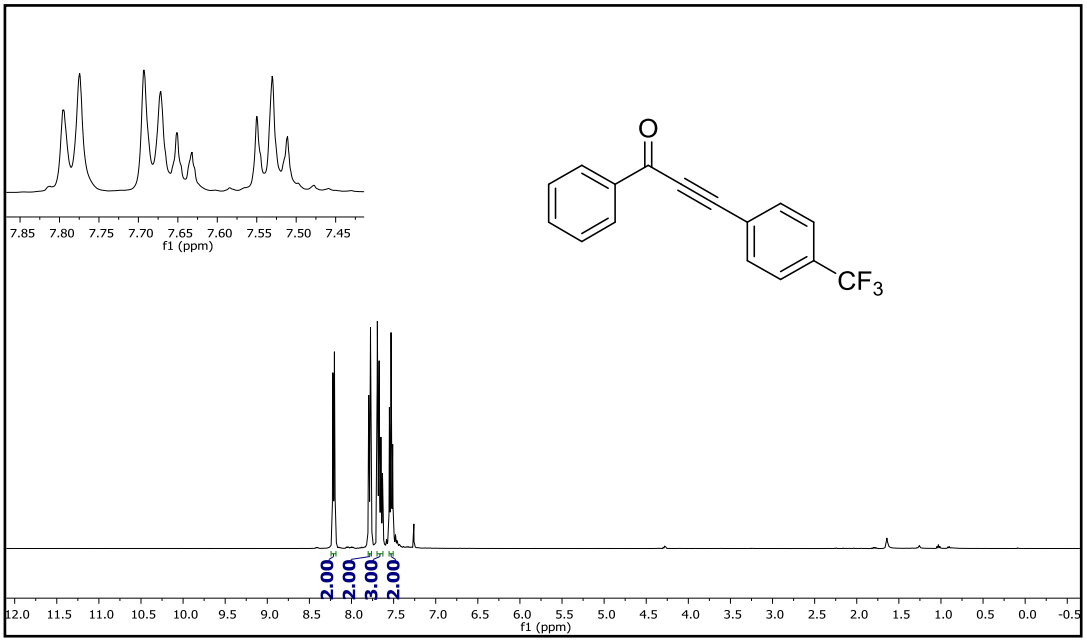

Figure 27. ^{1}H NMR spectrum of compound **35F**.

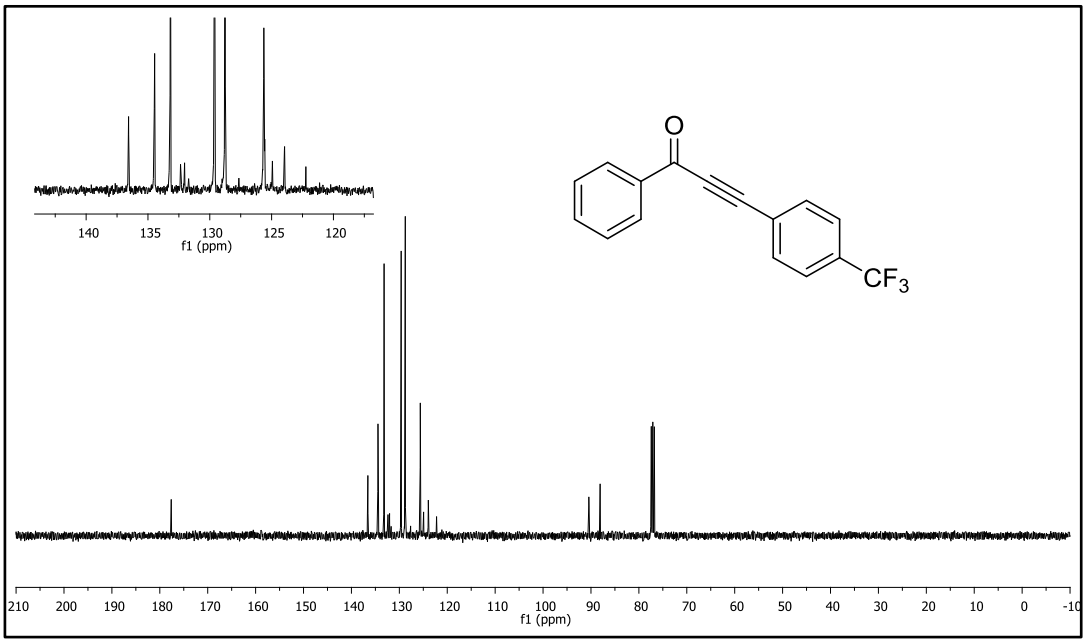

Figure 28. ^{13}C NMR spectrum of compound **35F**.

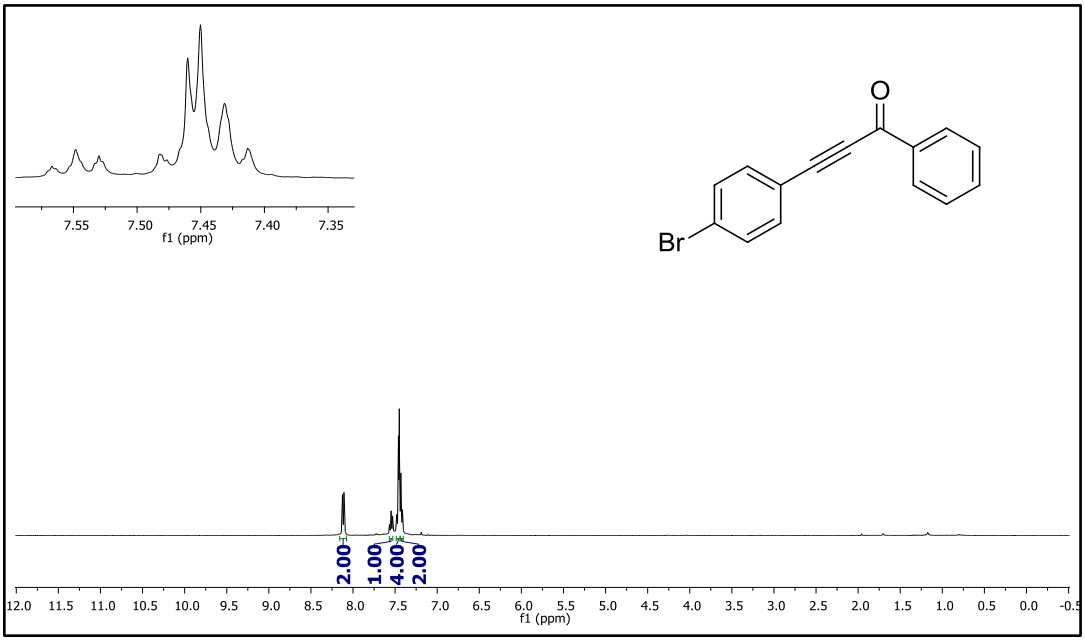

Figure 29. ^{1}H NMR spectrum of compound **35G**.

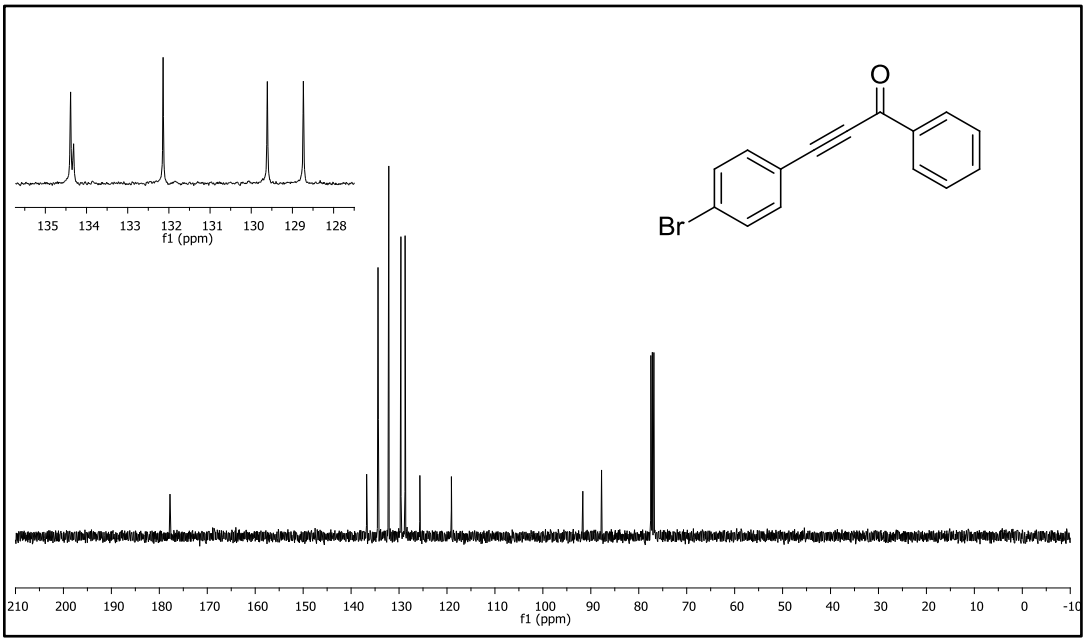

Figure 30. ^{13}C NMR spectrum of compound **35G**.

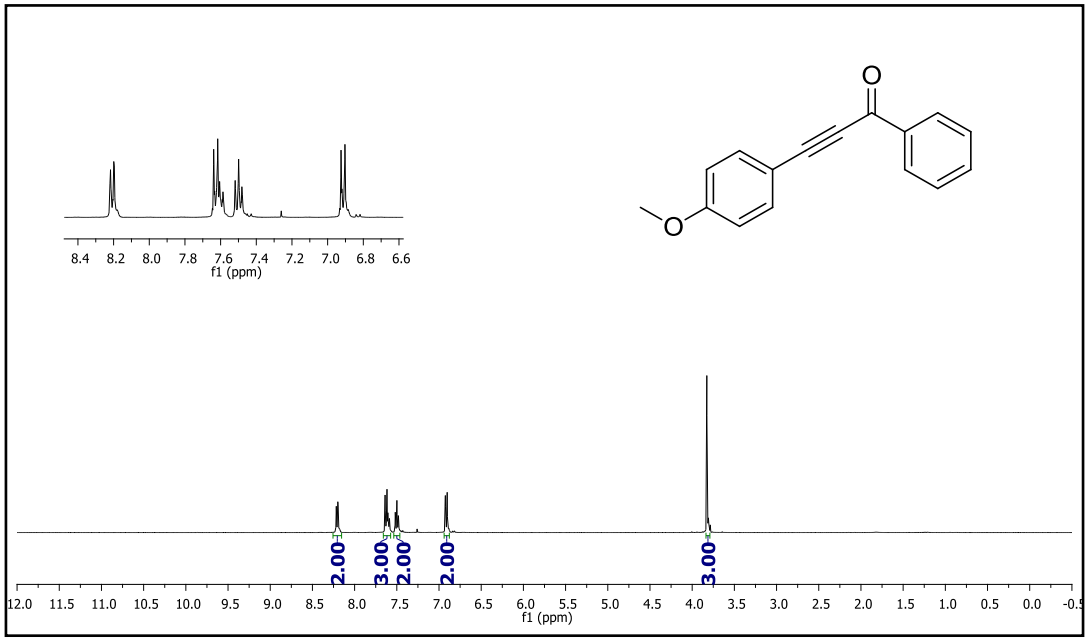

Figure 31. ^{1}H NMR spectrum of compound **35H**.

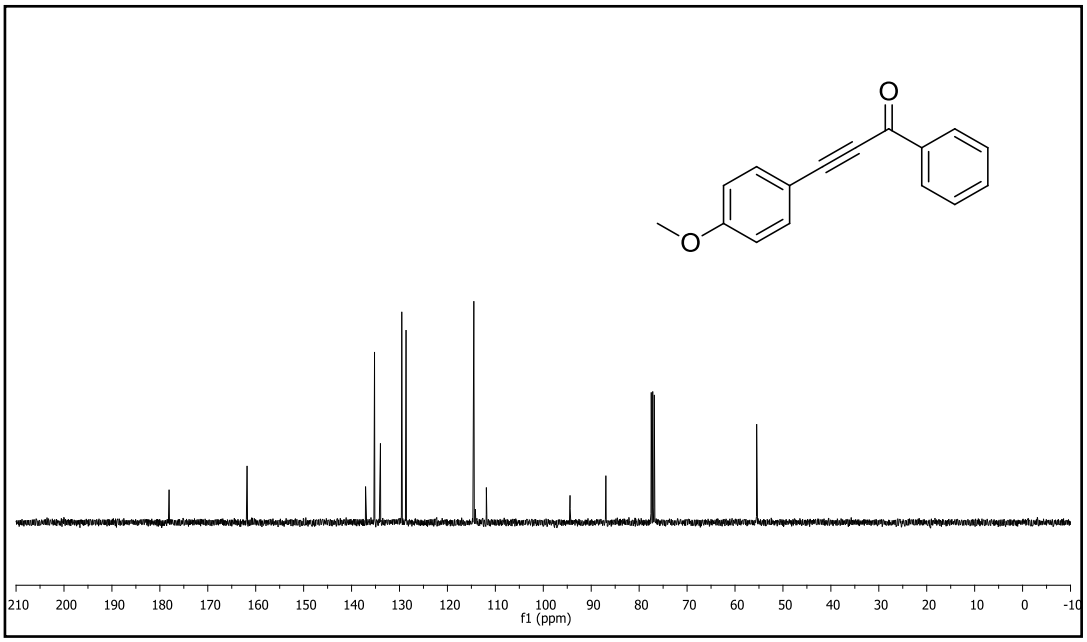

Figure 32. ^{13}C NMR spectrum of compound **35H**.

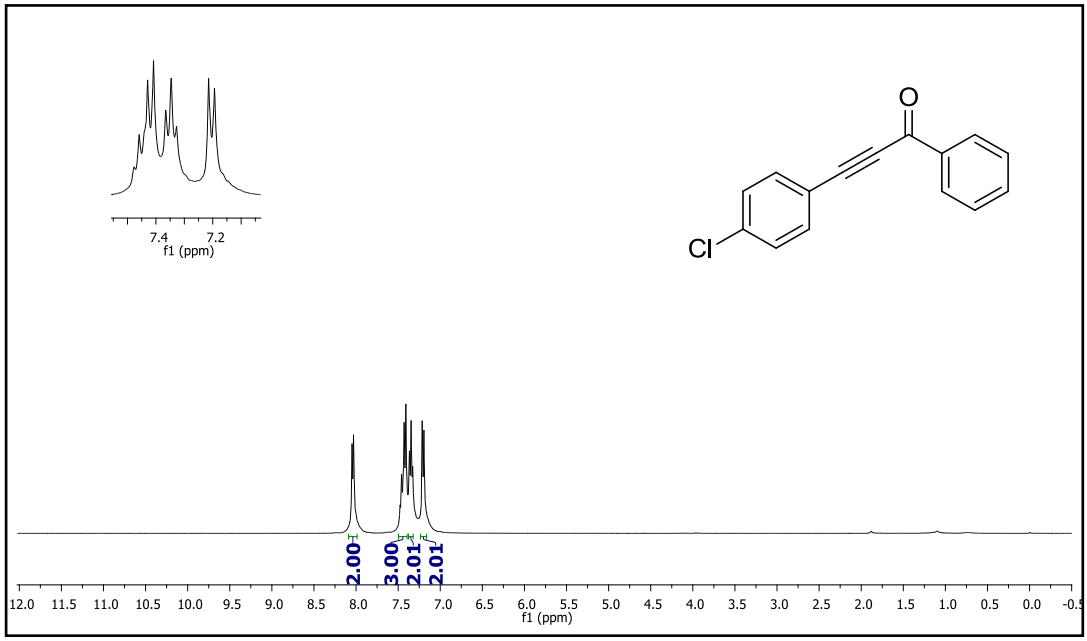

Figure 33. ^{1}H NMR spectrum of compound **35I**.

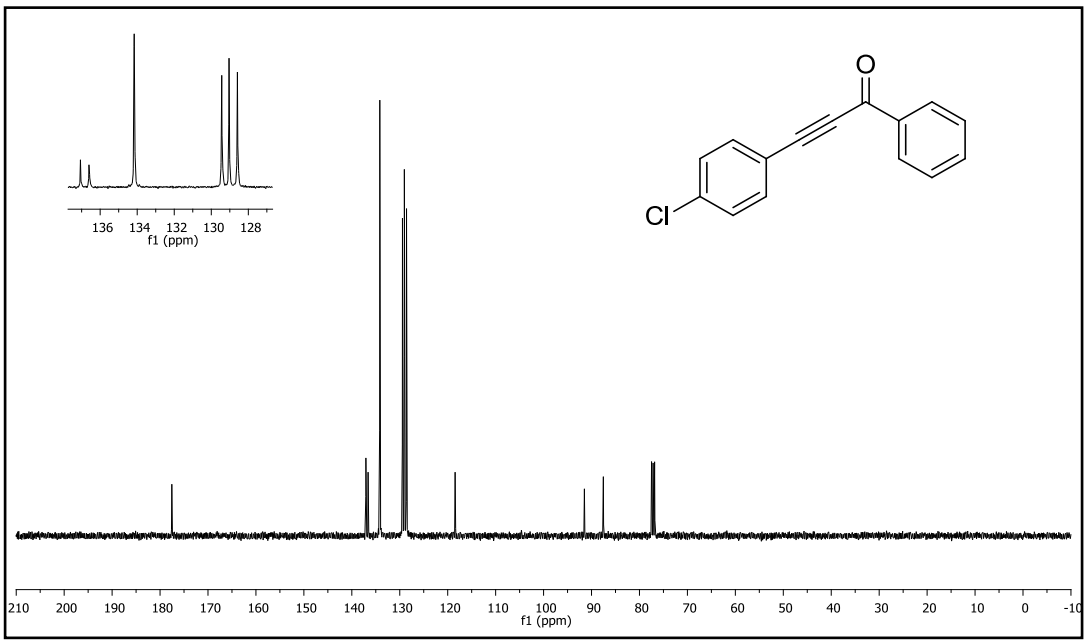

Figure 34. ^{13}C NMR spectrum of compound **35I**.

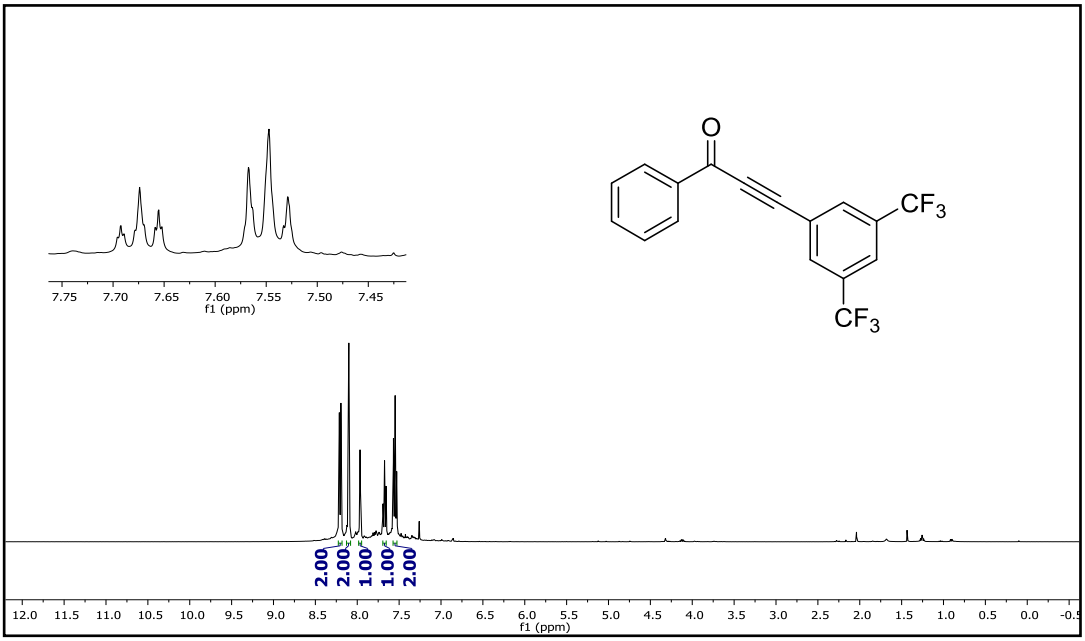

Figure 35. ^{1}H NMR spectrum of compound **35J**.

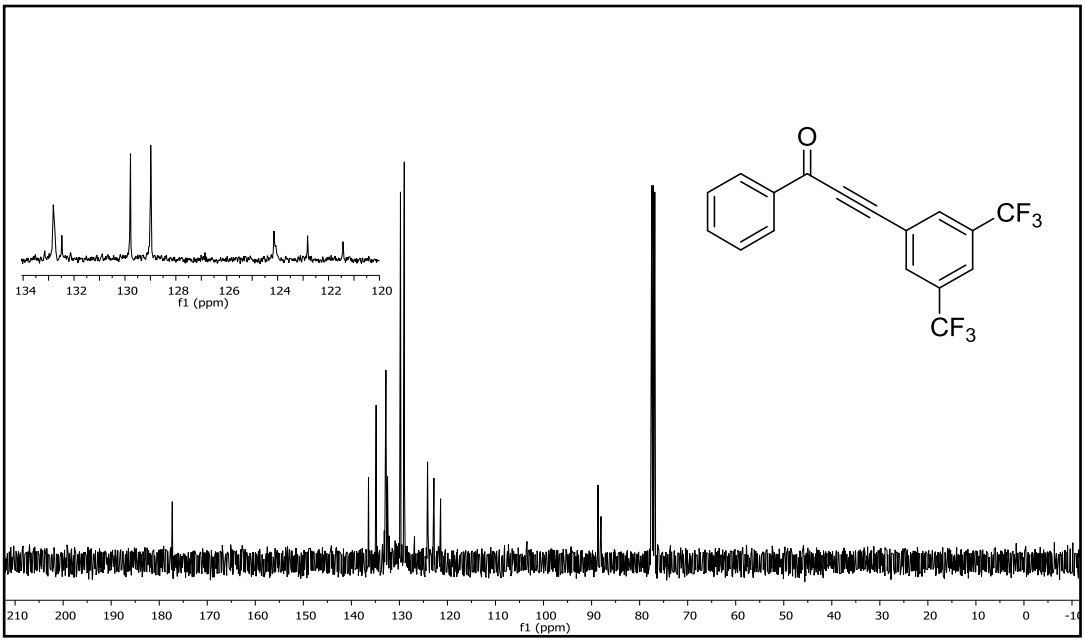

Figure 36. ^{13}C NMR spectrum of compound **35J**.

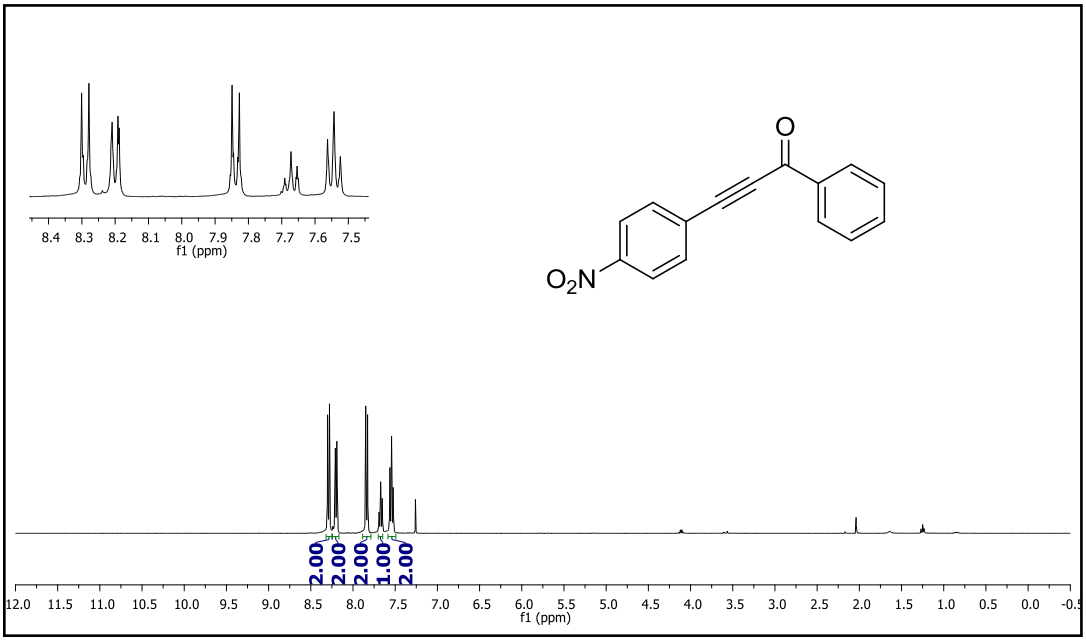

Figure 37. ^{1}H NMR spectrum of compound **35K**.

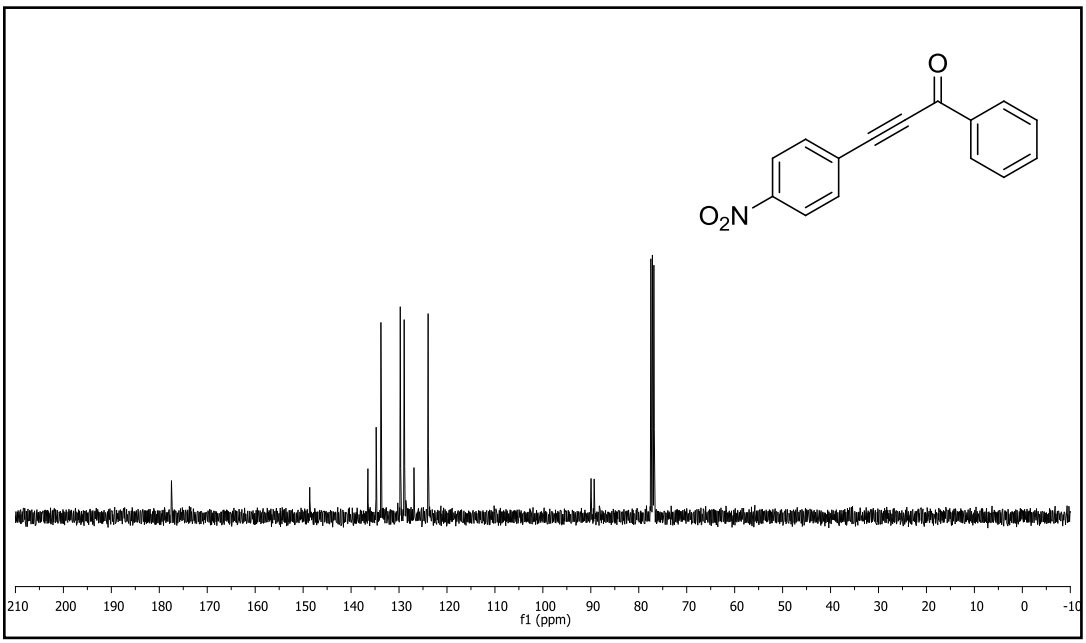

Figure 38. ^{13}C NMR spectrum of compound **35K**.

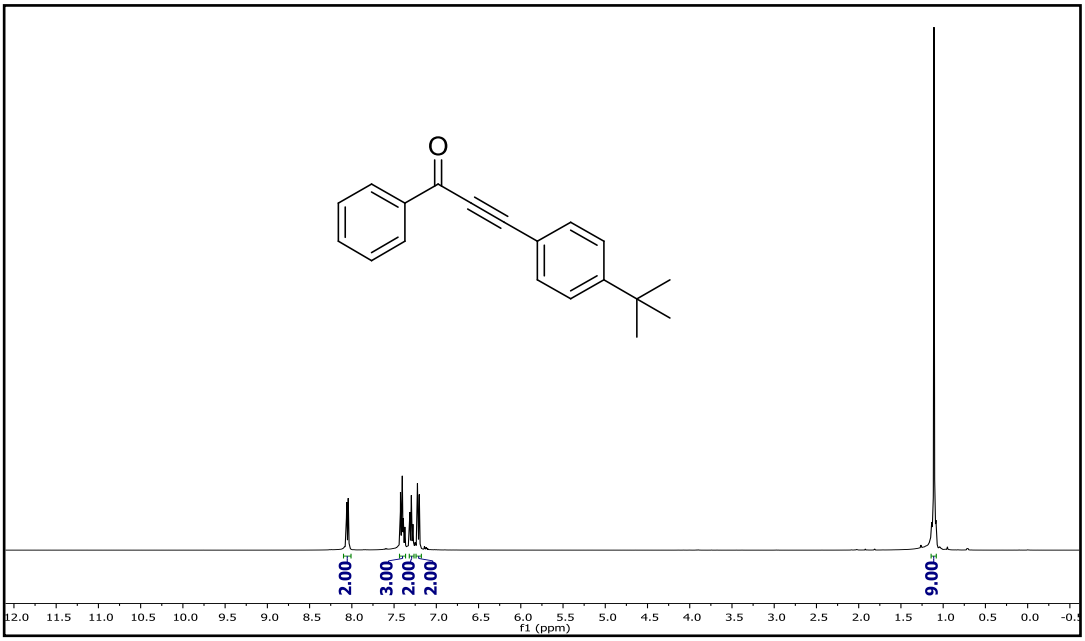

Figure 39. ^{1}H NMR spectrum of compound **35L**.

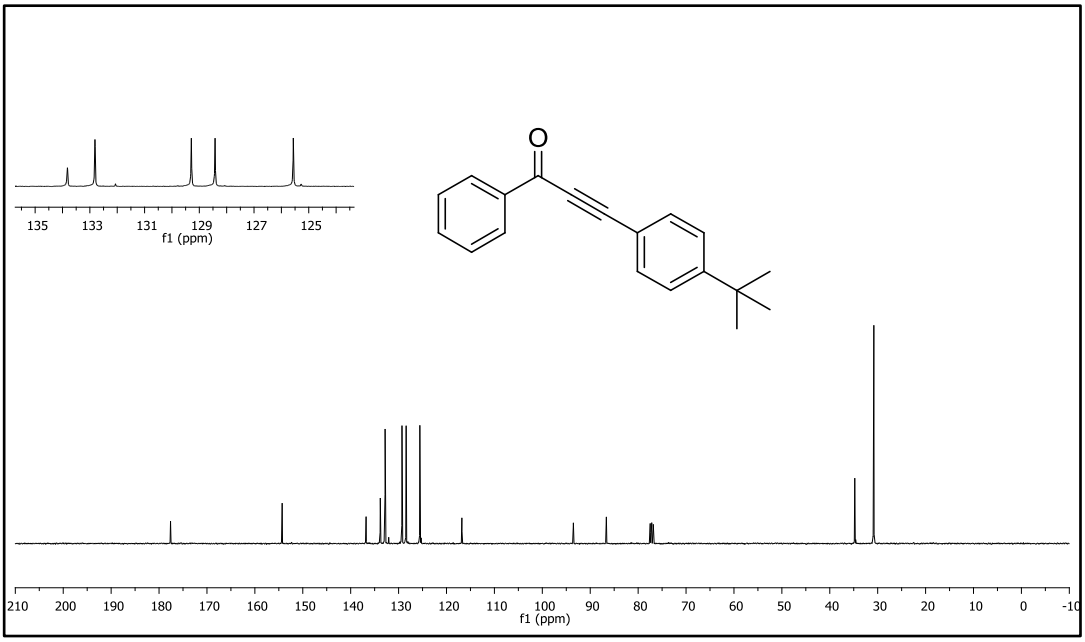

Figure 40. ^{13}C NMR spectrum of compound **35L**.

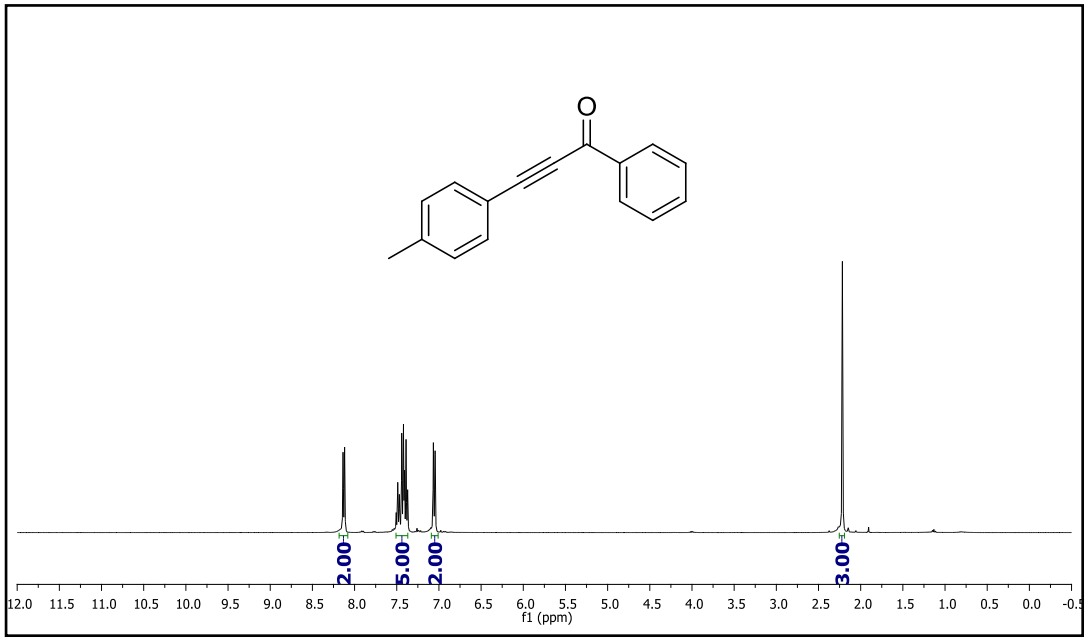

Figure 41. ^{1}H NMR spectrum of compound **35M**.

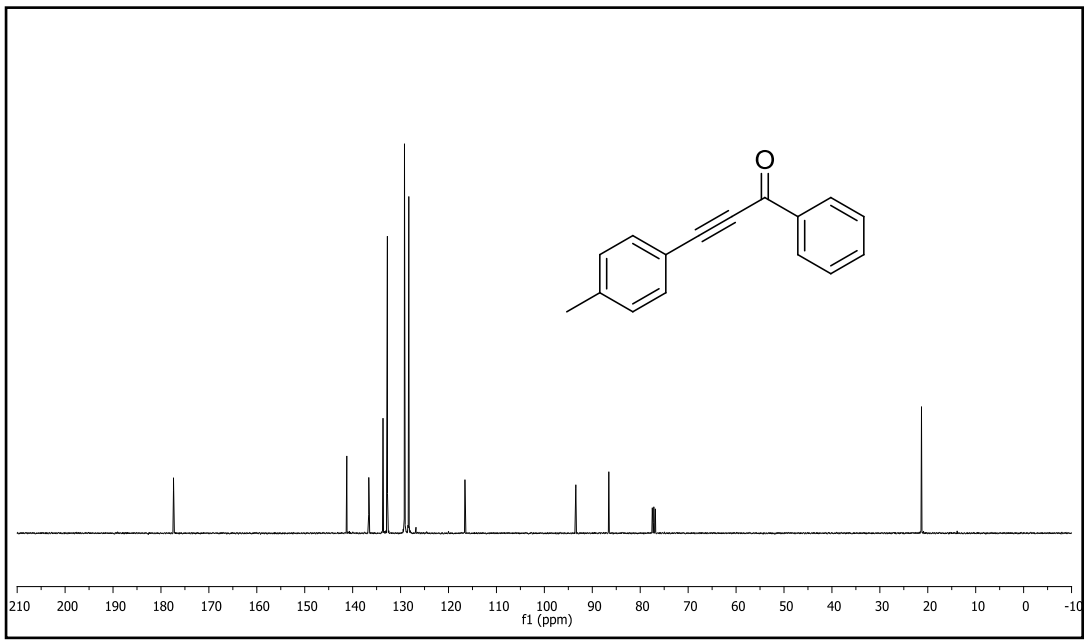

Figure 42. ^{13}C NMR spectrum of compound **35M**.

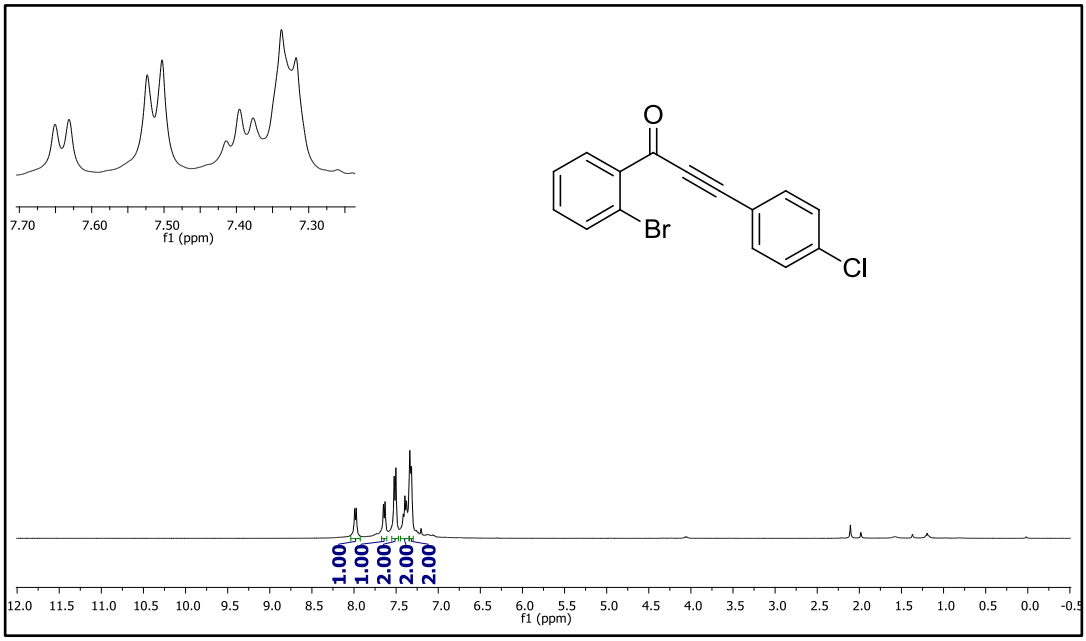

Figure 43. ^{1}H NMR spectrum of compound **35N**.

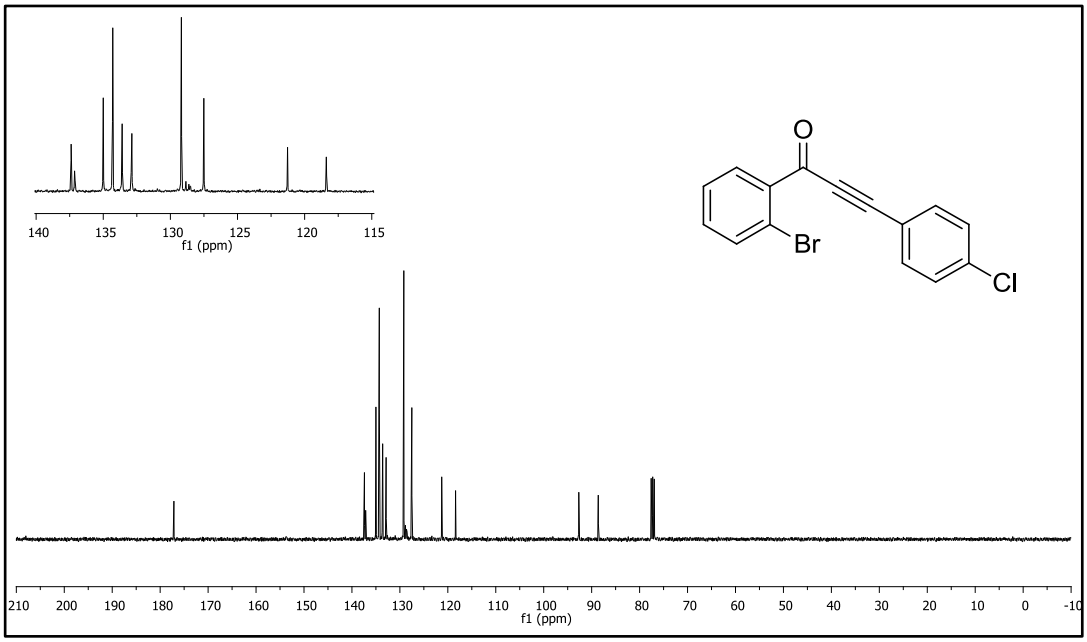

Figure 44. ^{13}C NMR spectrum of compound **35N**.

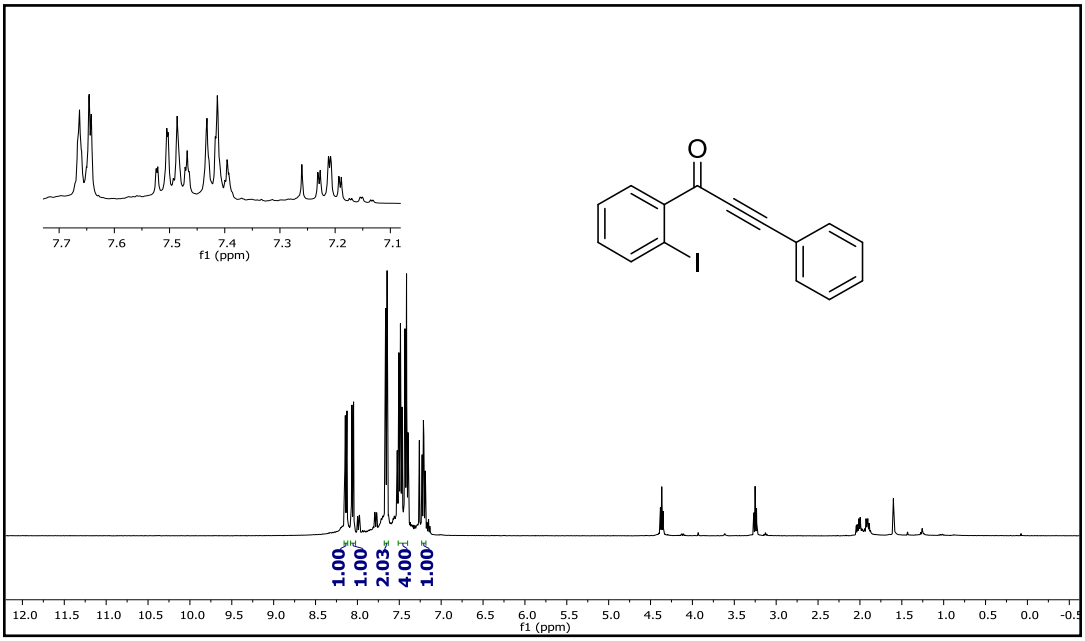

Figure 45. ^{1}H NMR spectrum of compound **35O**.

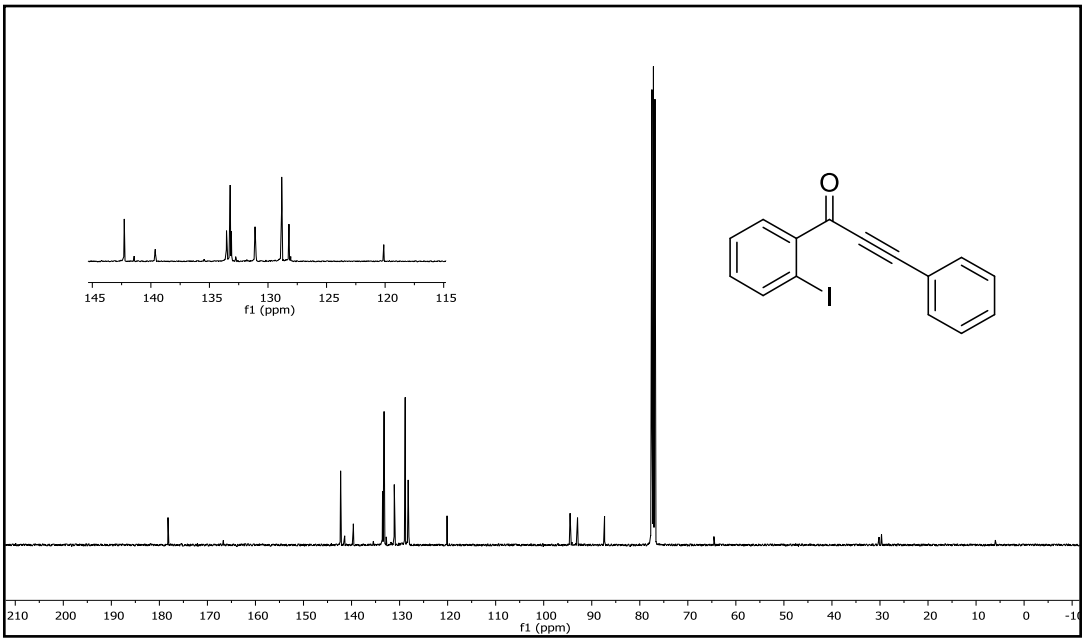

Figure 46. ^{13}C NMR spectrum of compound **35O**.

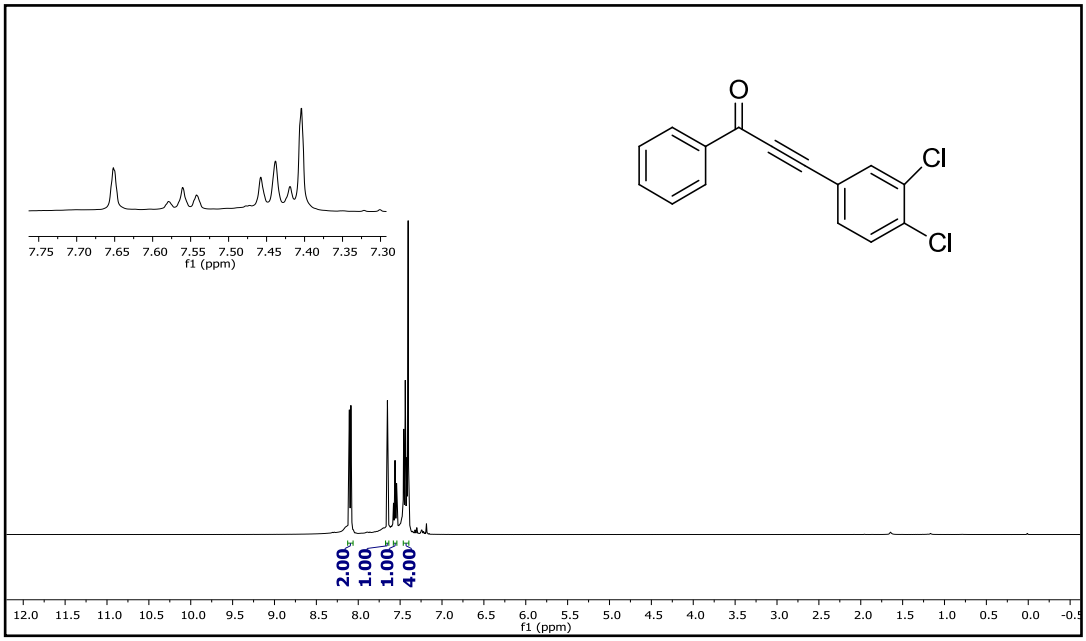

Figure 47. ^{1}H NMR spectrum of compound **35P**.

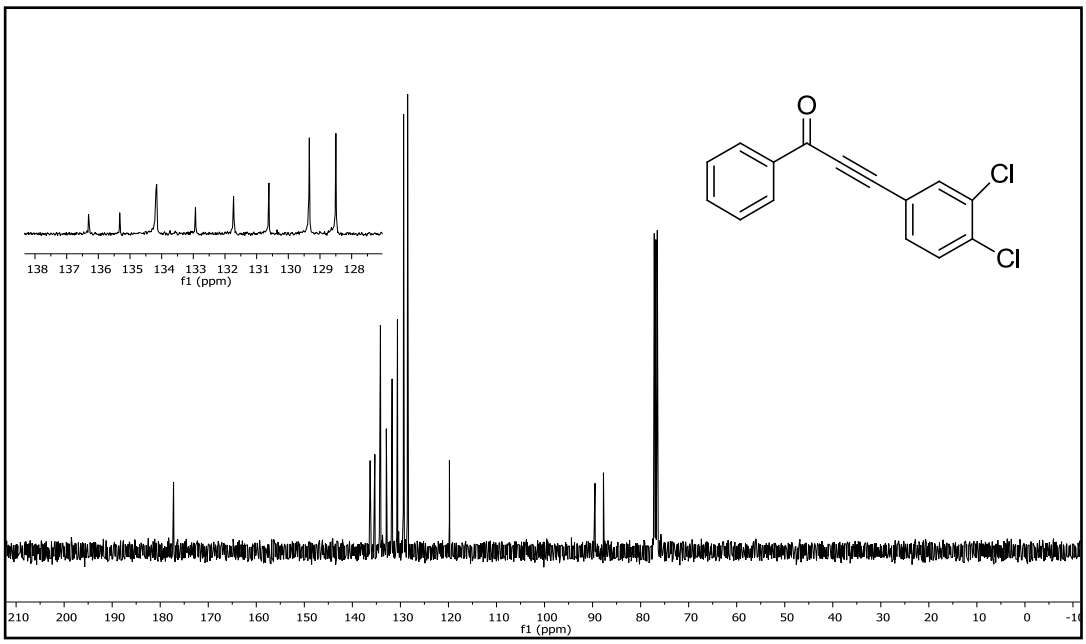

Figure 48. ^{13}C NMR spectrum of compound **35P**.

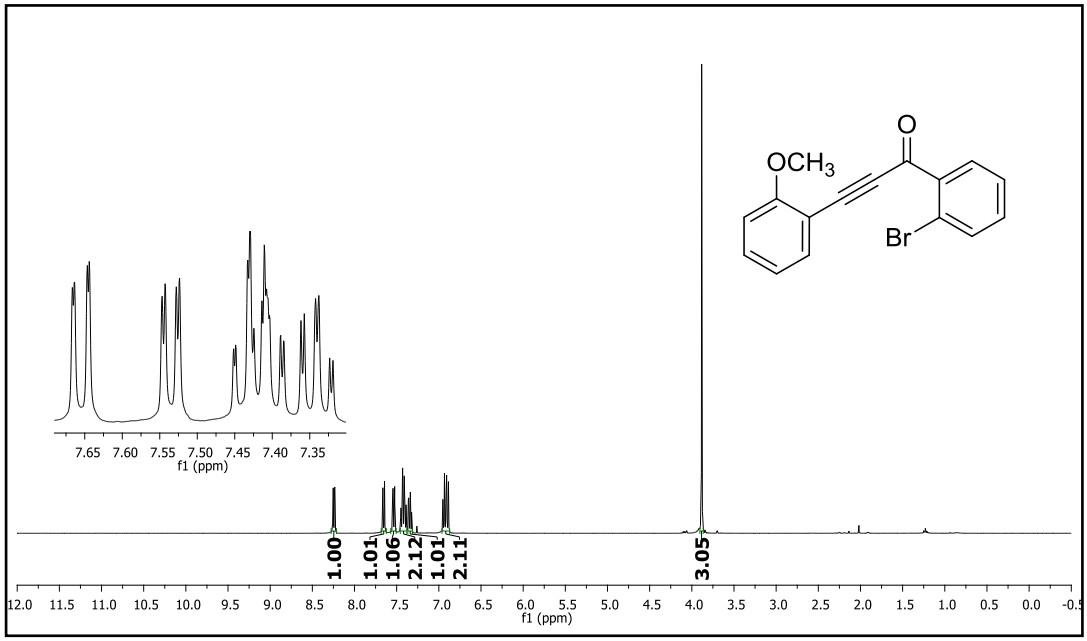

Figure 49. ^{1}H NMR spectrum of compound **35Q**.

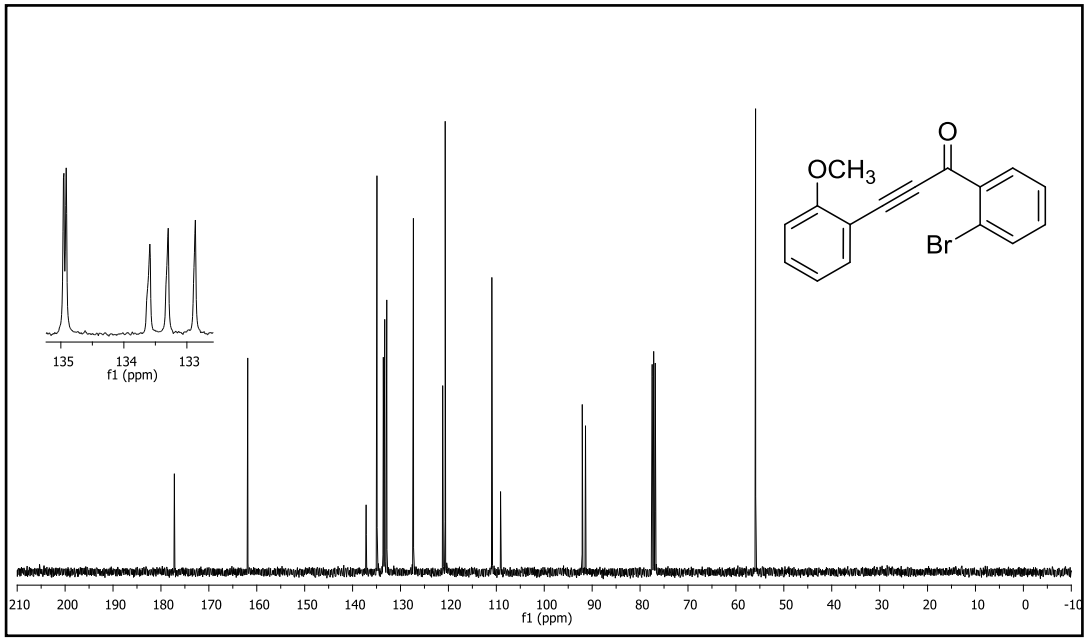

Figure 50. ^{13}C NMR spectrum of compound **35Q**.

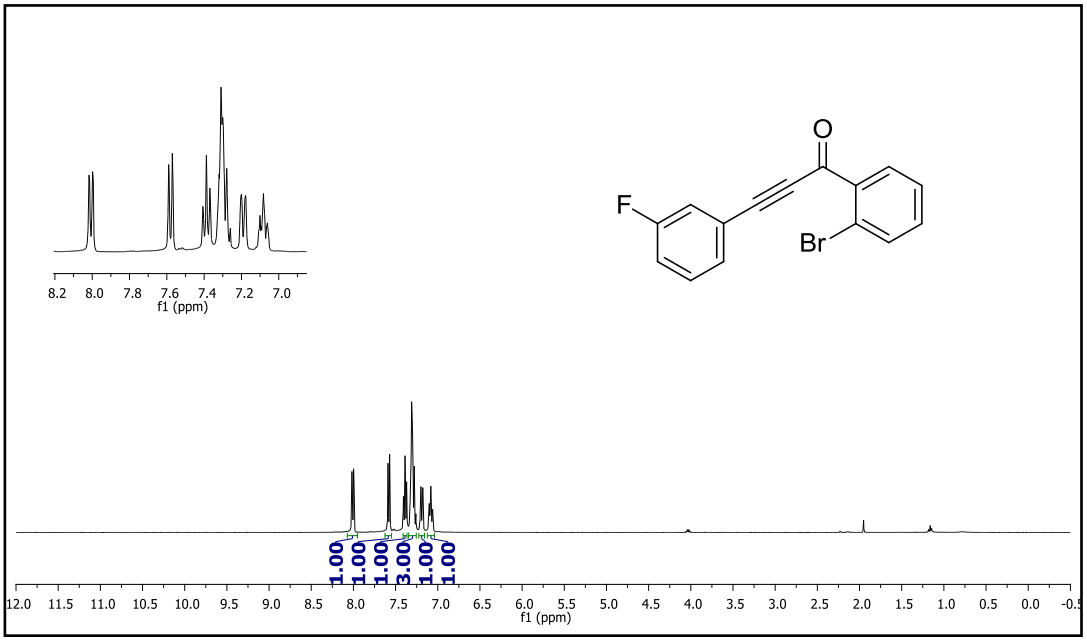

Figure 51. ^{1}H NMR spectrum of compound **35R**.

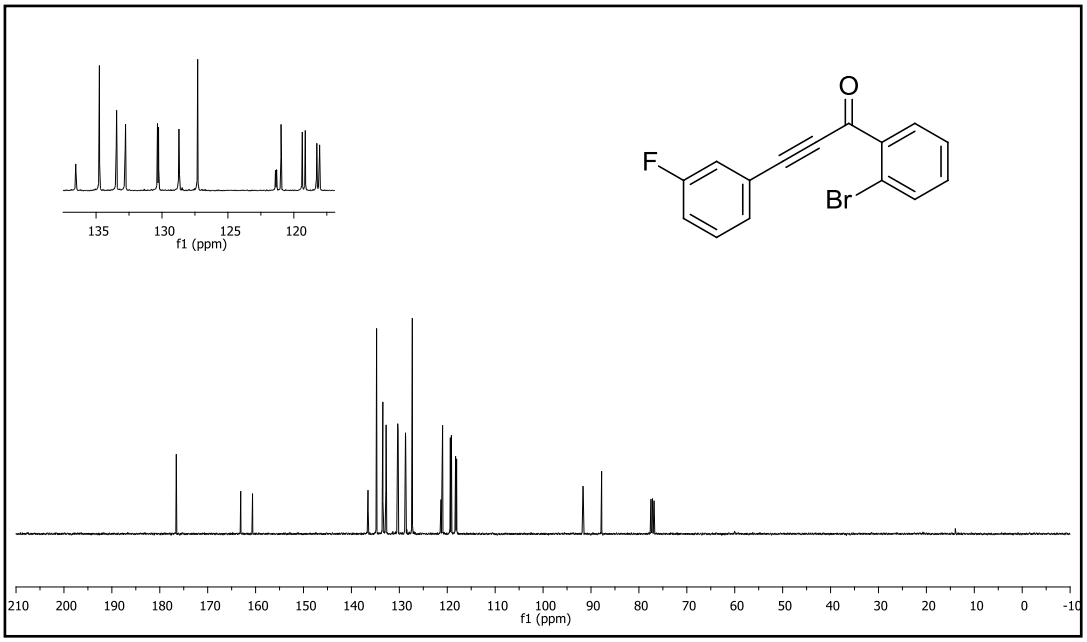

Figure 52. ^{13}C NMR spectrum of compound **35R**.

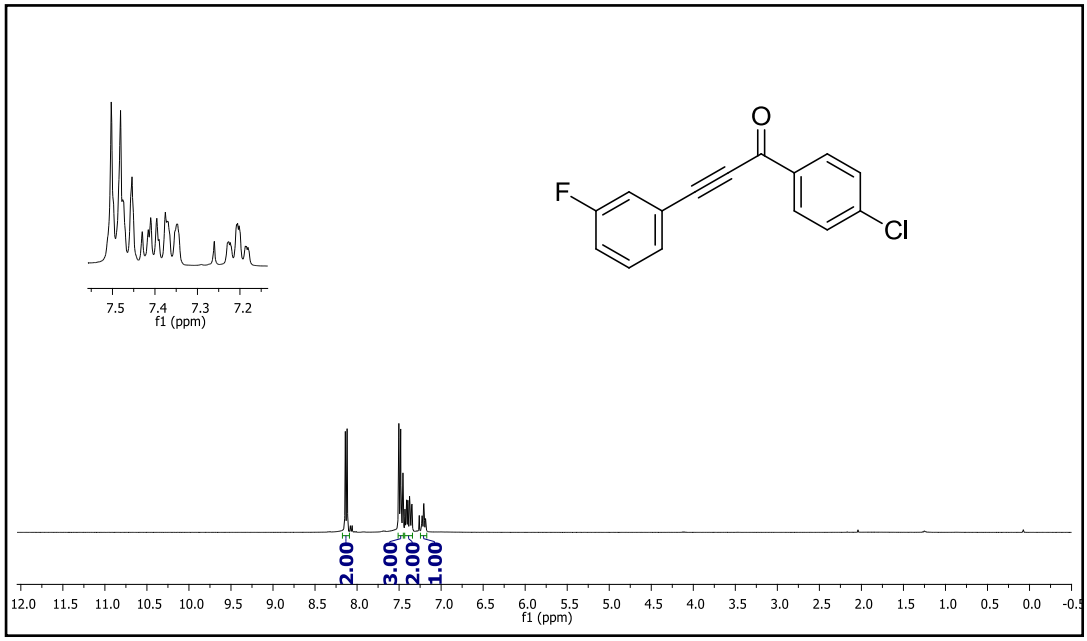

Figure 53. ^{1}H NMR spectrum of compound **35S**.

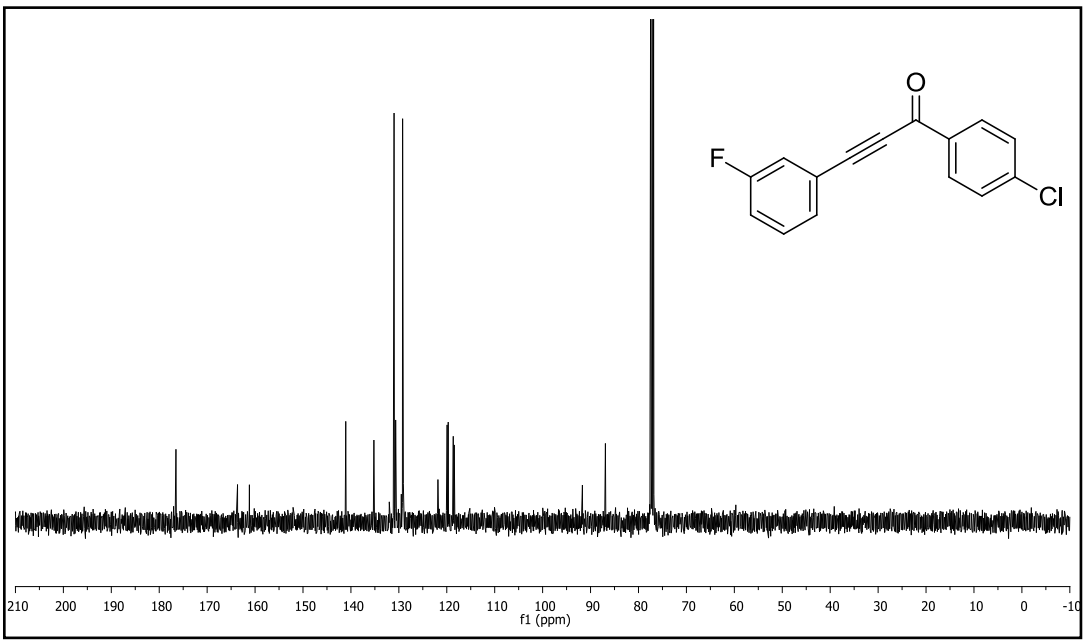

Figure 54. ^{13}C NMR spectrum of compound **35S**.

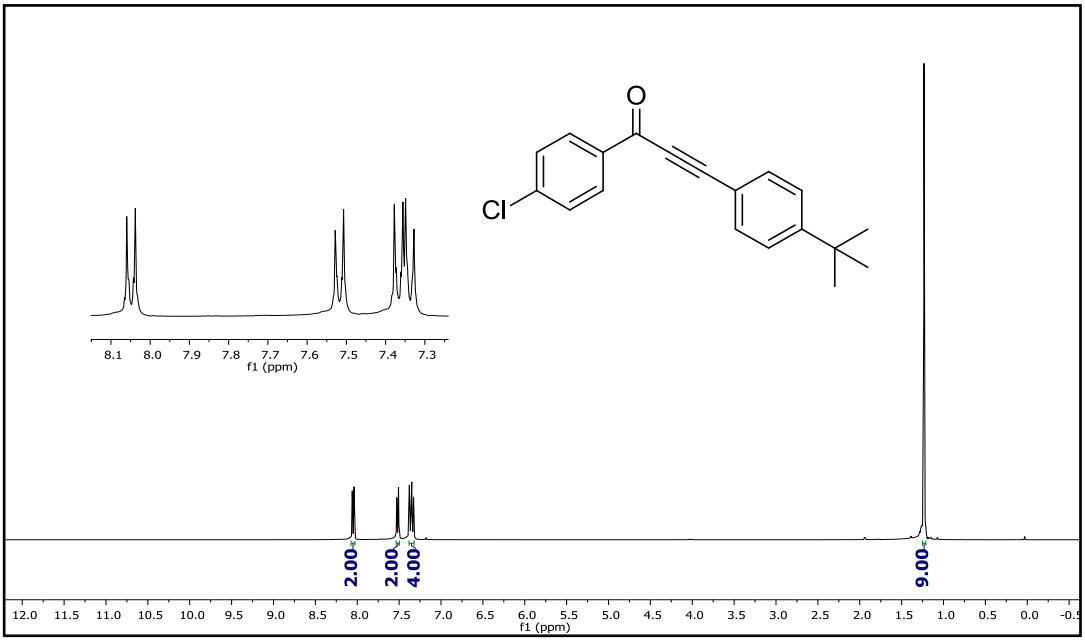

Figure 55. ^{1}H NMR spectrum of compound **35T**.

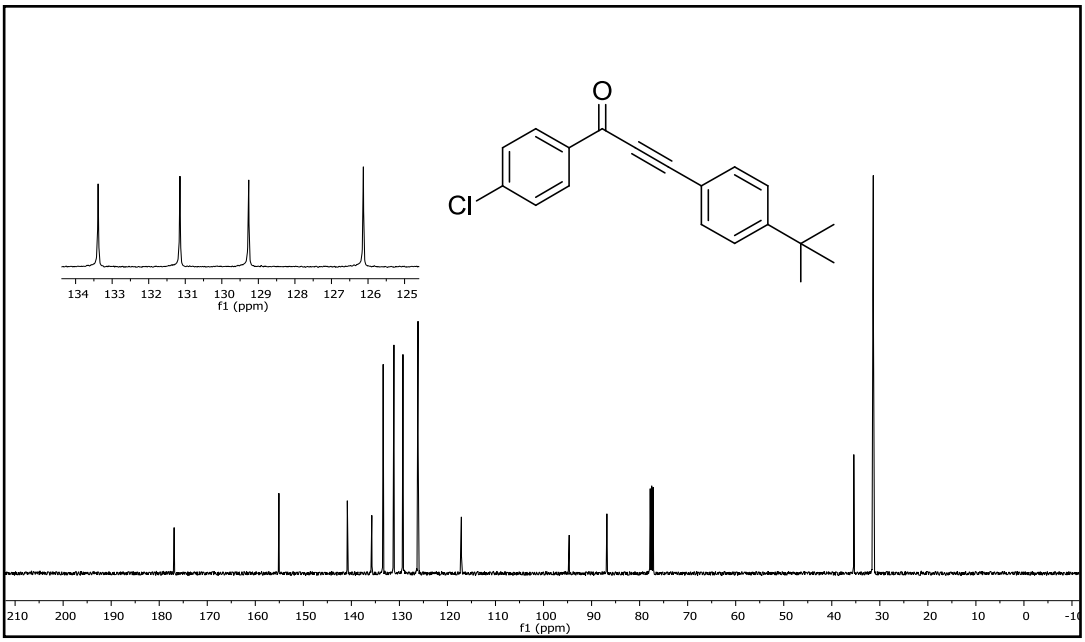

Figure 56. ^{13}C NMR spectrum of compound **35T**.

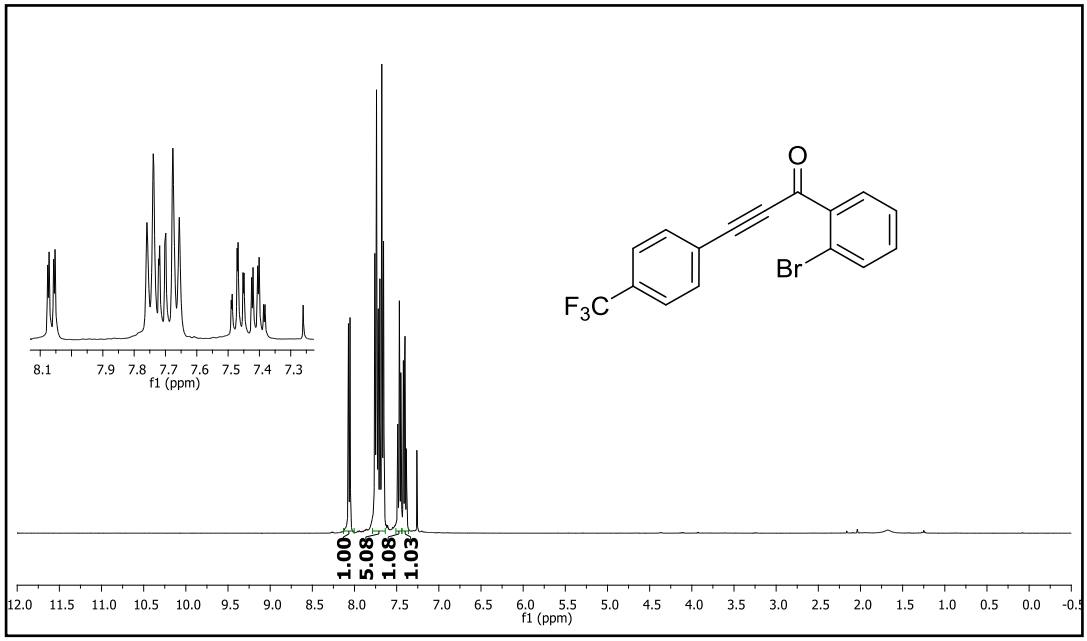

Figure 57. ^{1}H NMR spectrum of compound **35U**.

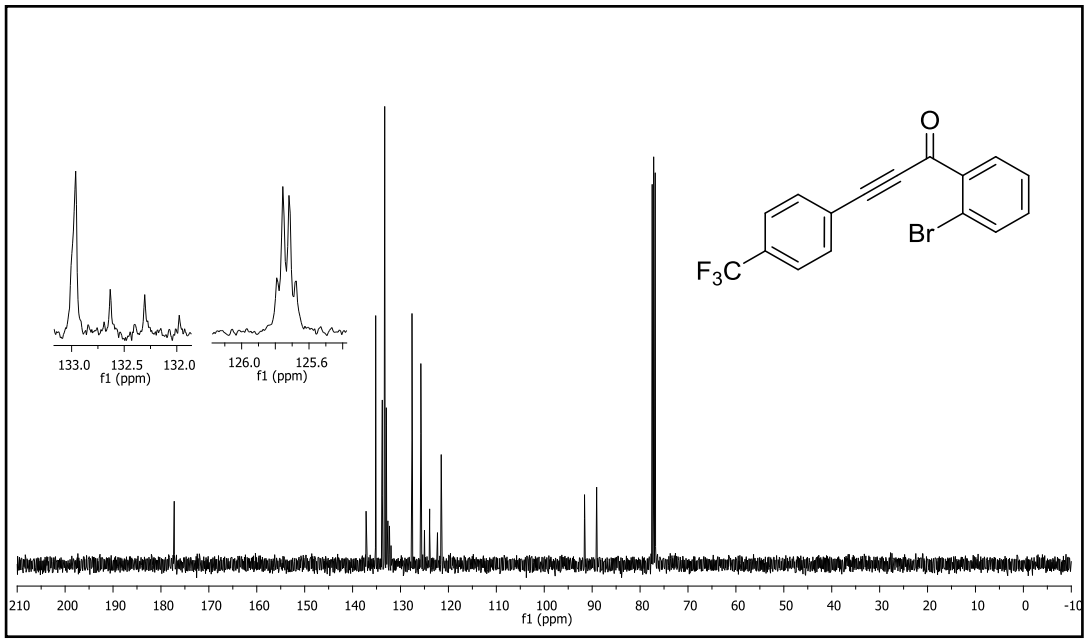

Figure 58. ^{13}C NMR spectrum of compound **35U**.

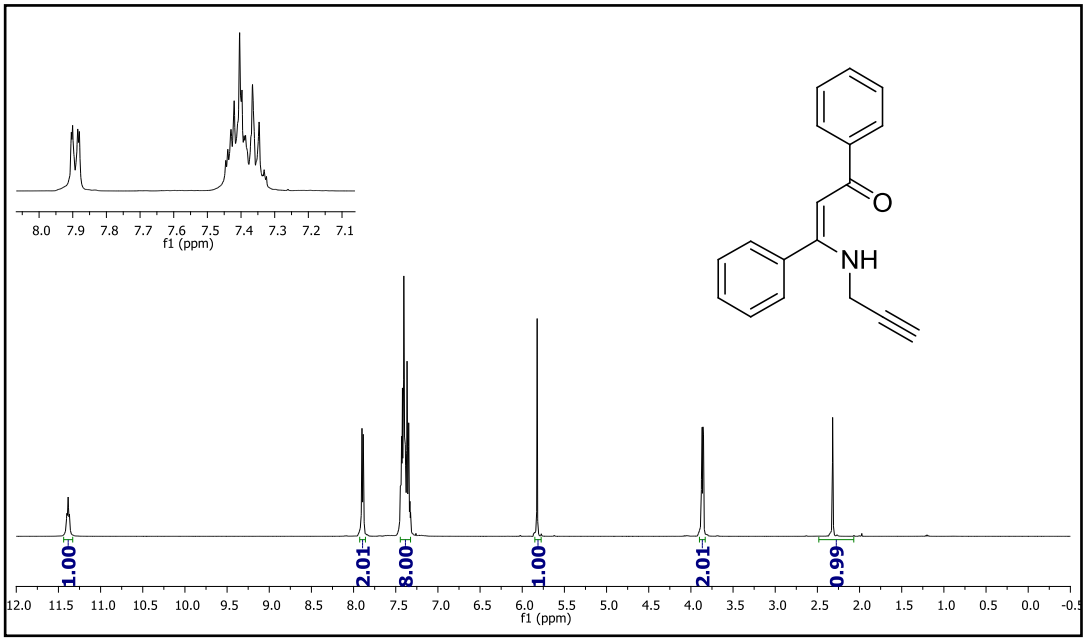

Figure 59. ^{1}H NMR spectrum of compound **25A**.

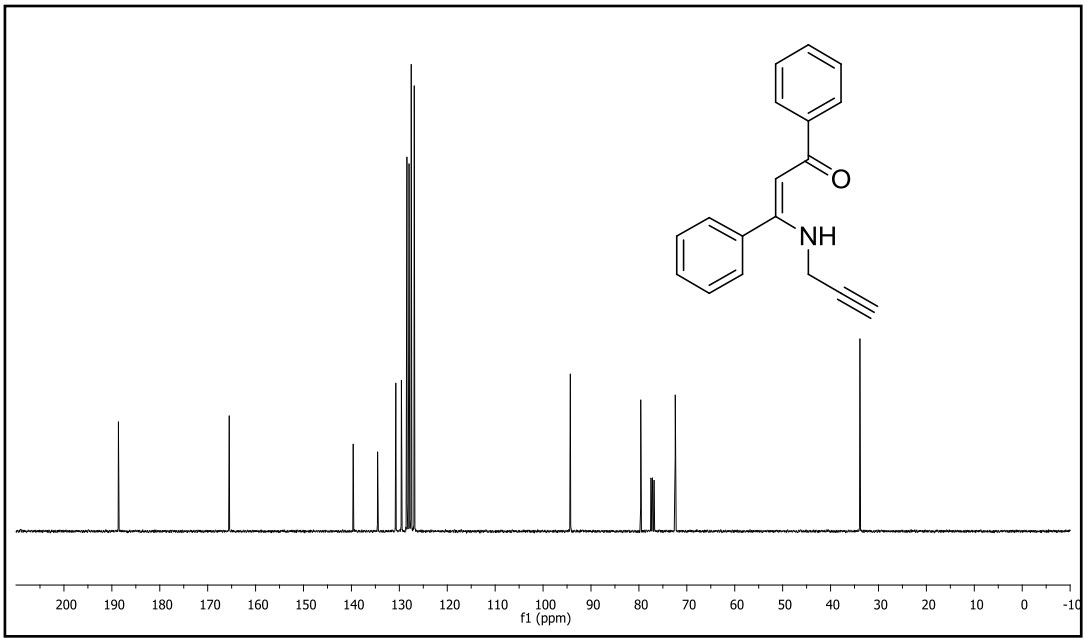

Figure 60. ^{13}C NMR spectrum of compound **25A**.

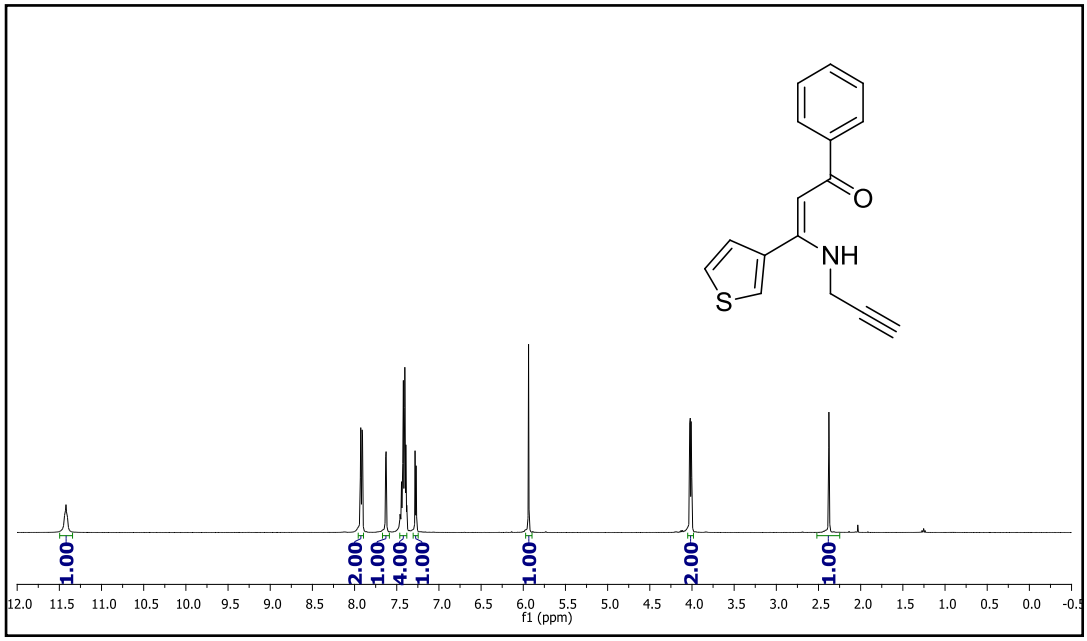

Figure 61. ^{1}H NMR spectrum of compound **25B**.

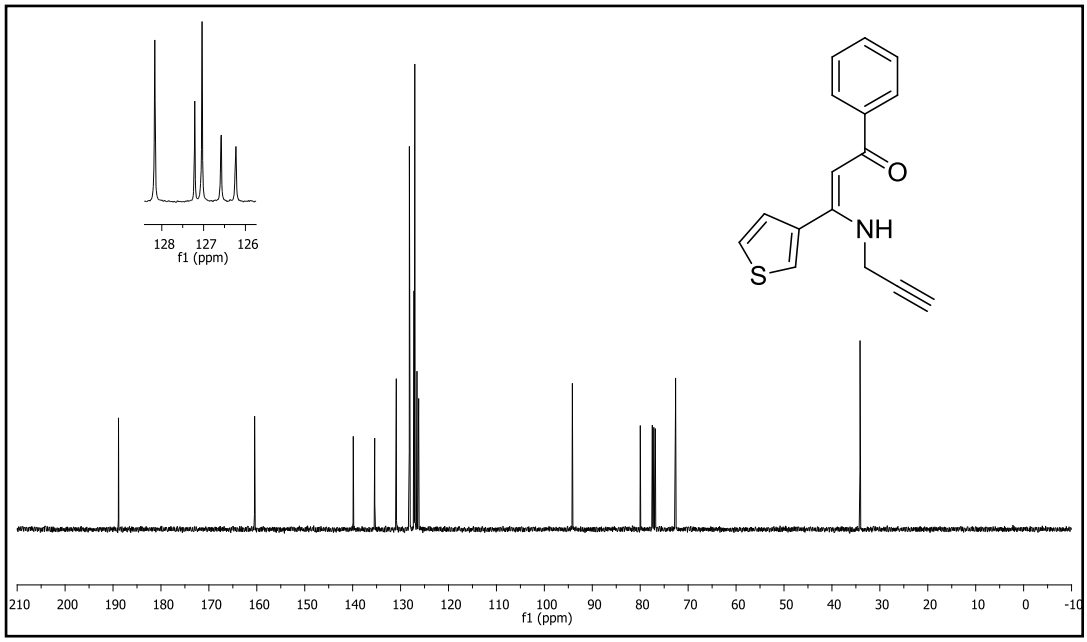

Figure 62. ^{13}C NMR spectrum of compound **25B**.

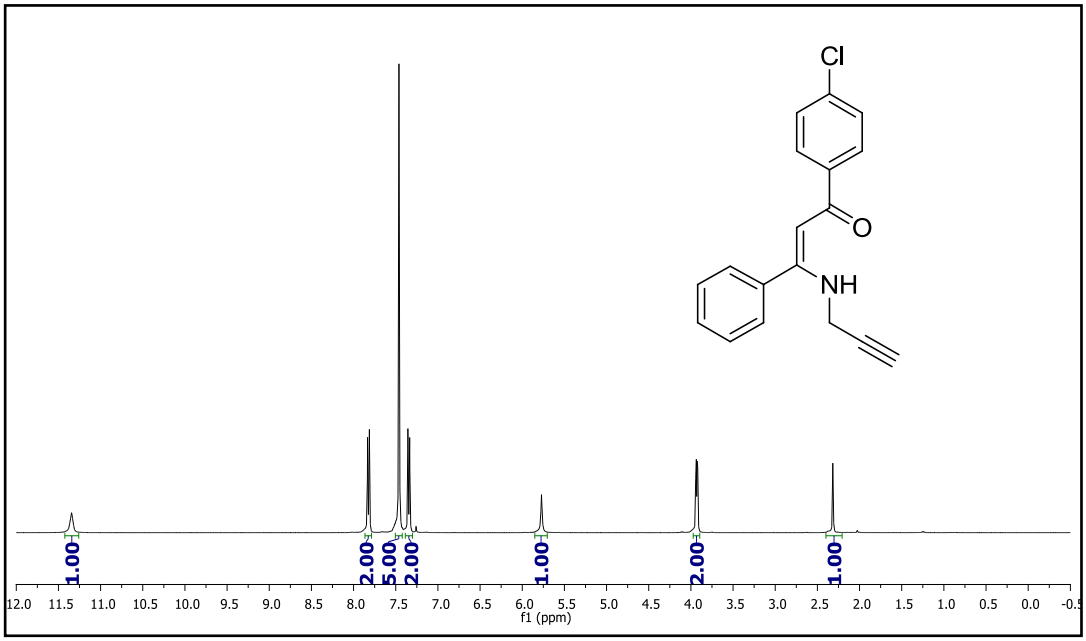

Figure 63. ^{1}H NMR spectrum of compound **25C**.

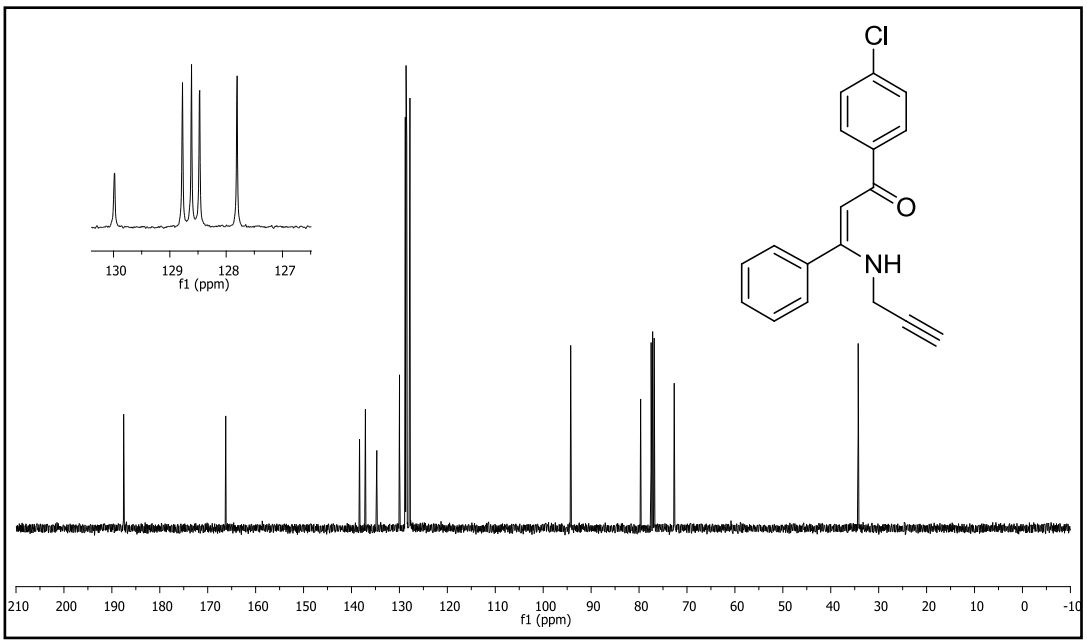

Figure 64. ^{13}C NMR spectrum of compound **25C**.

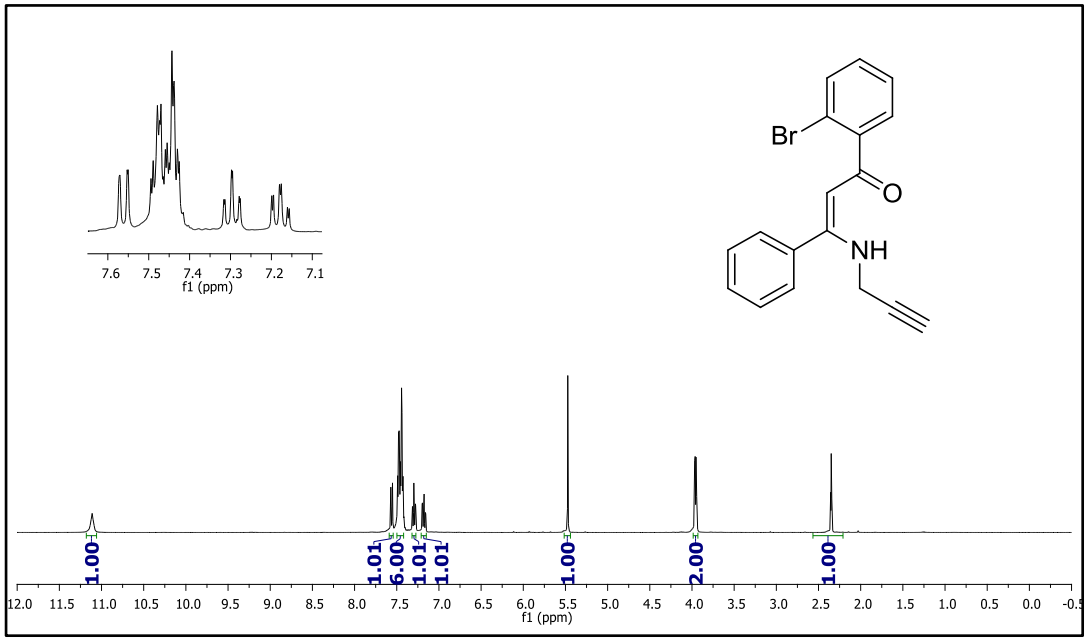

Figure 65. ^{1}H NMR spectrum of compound **25D**.

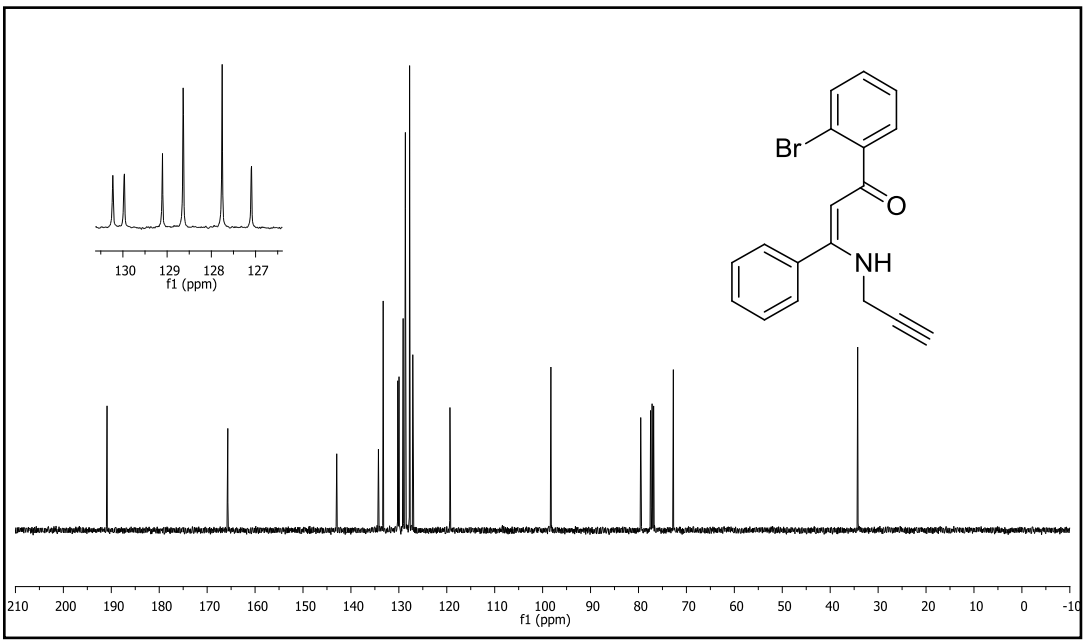

Figure 66. ^{13}C NMR spectrum of compound **25D**.

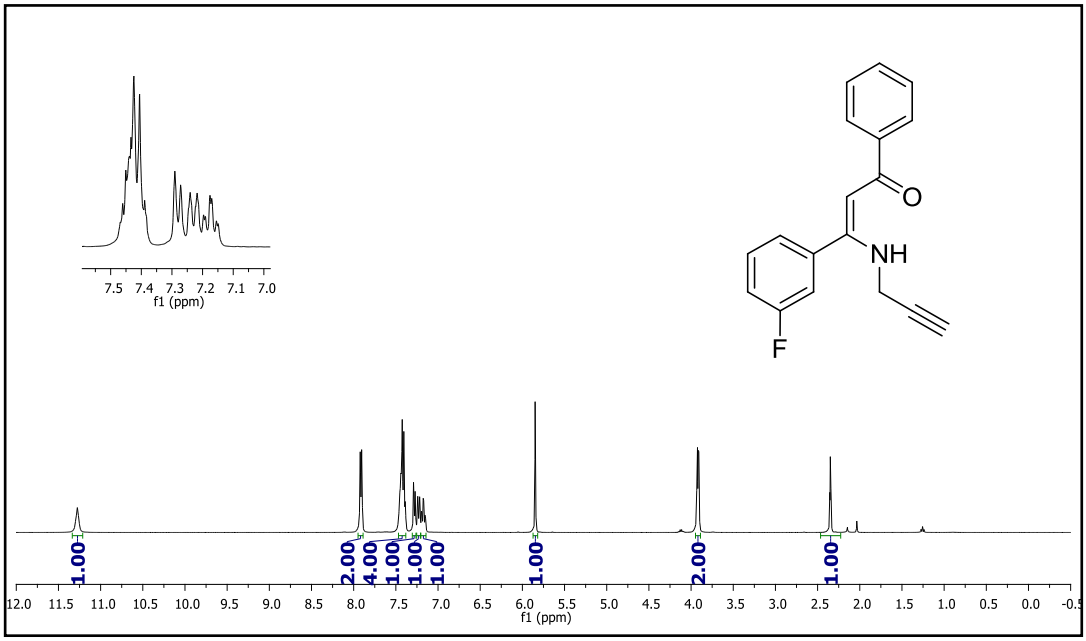

Figure 67. ^{1}H NMR spectrum of compound **25E**.

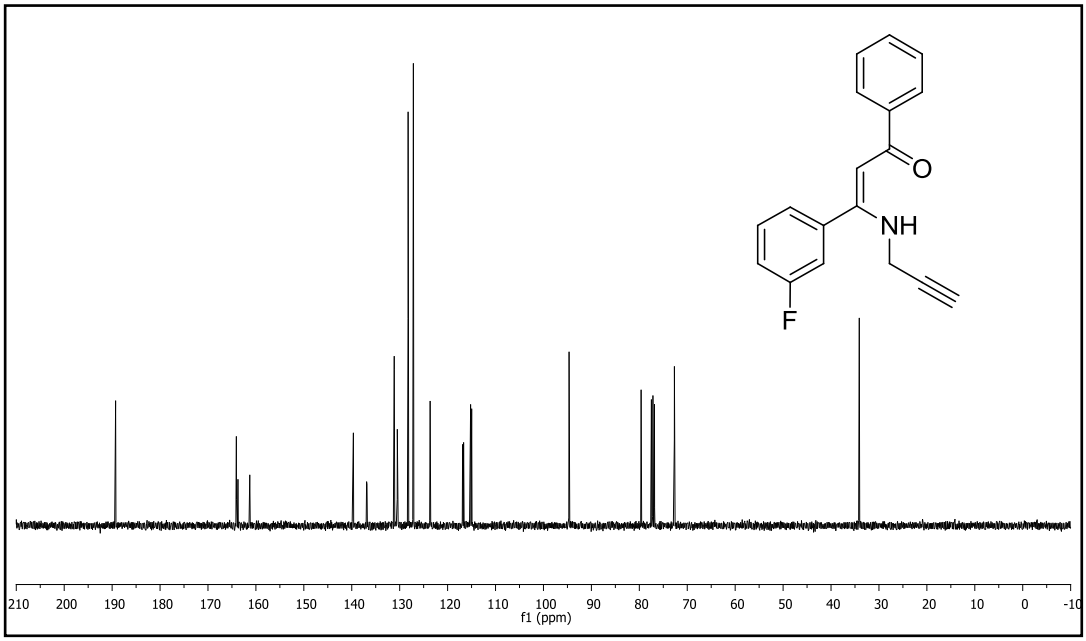

Figure 68. ^{13}C NMR spectrum of compound **25E**.

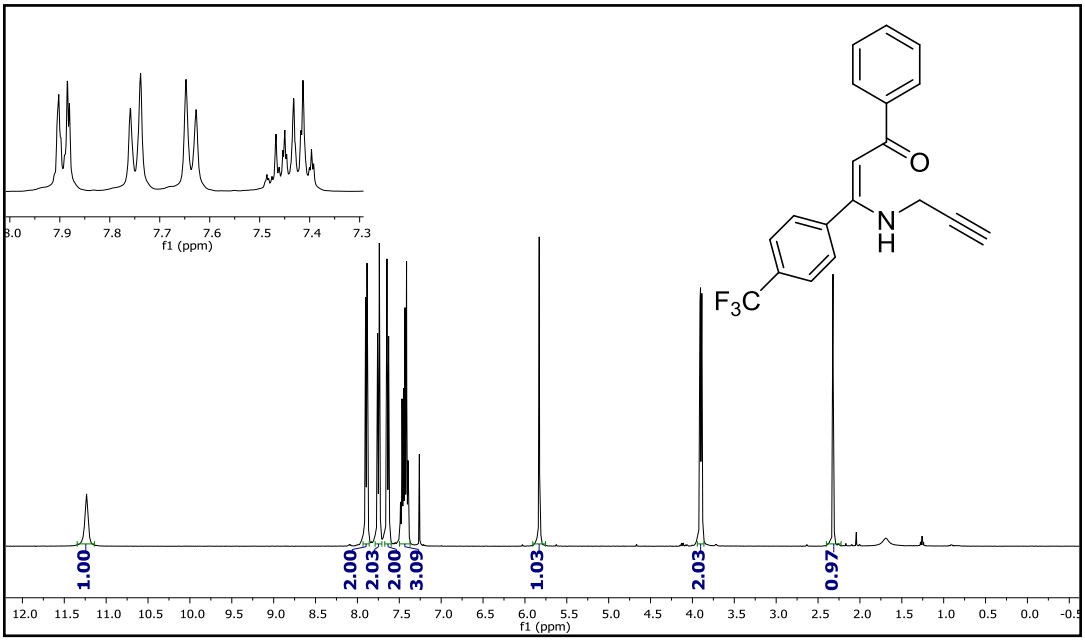

Figure 69. ^{1}H NMR spectrum of compound **25F**.

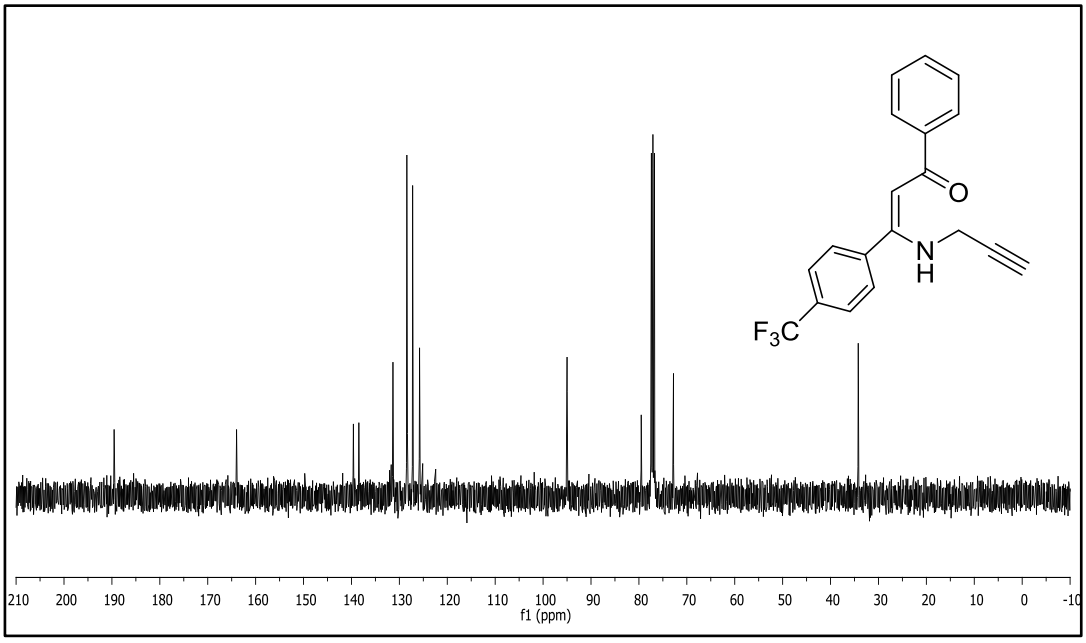

Figure 70. ^{13}C NMR spectrum of compound **25F**.

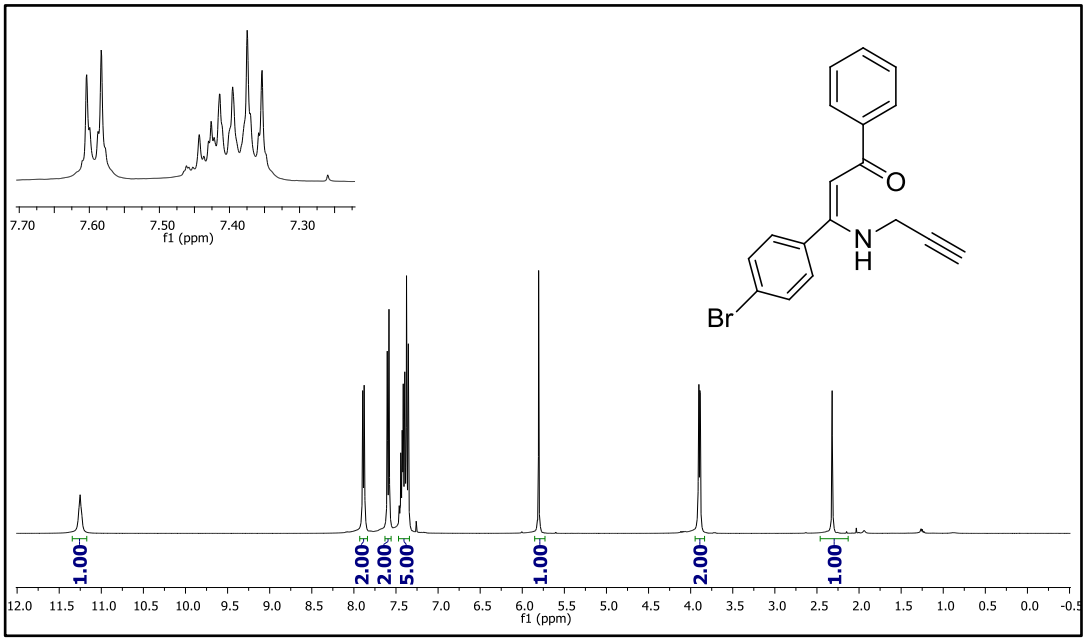

Figure 71. ^{1}H NMR spectrum of compound **25G**.

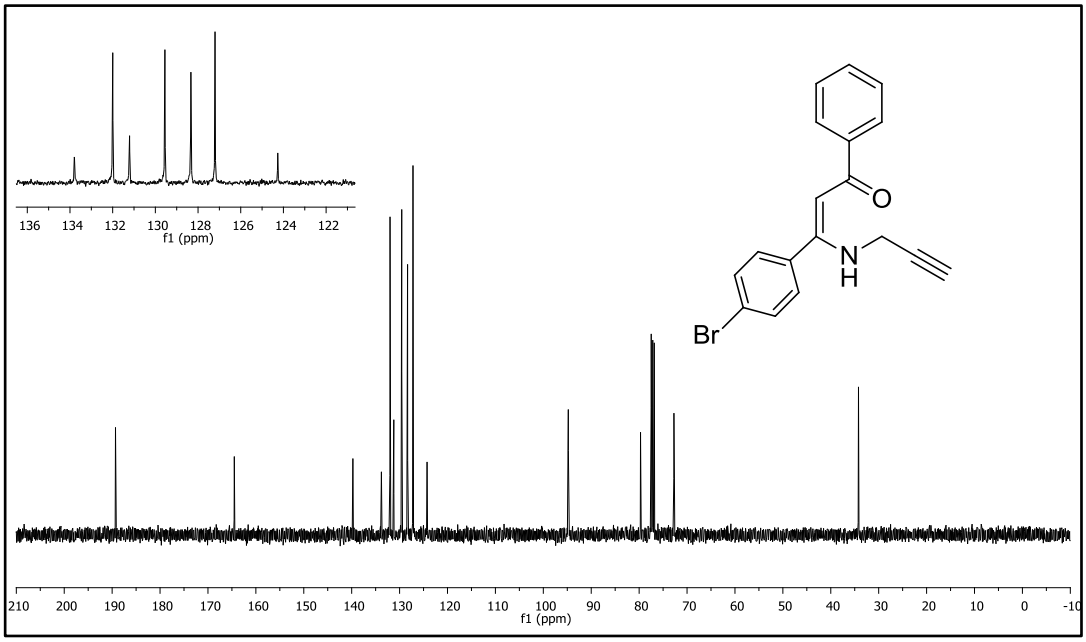

Figure 72. ^{13}C NMR spectrum of compound **25G**.

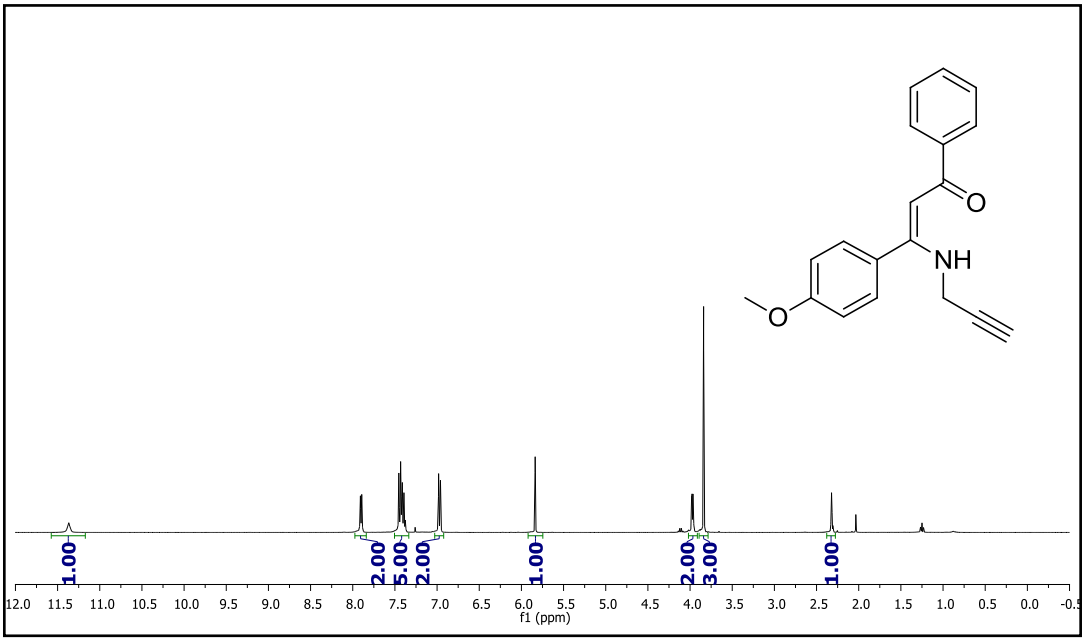

Figure 73. ^{1}H NMR spectrum of compound **25H**.

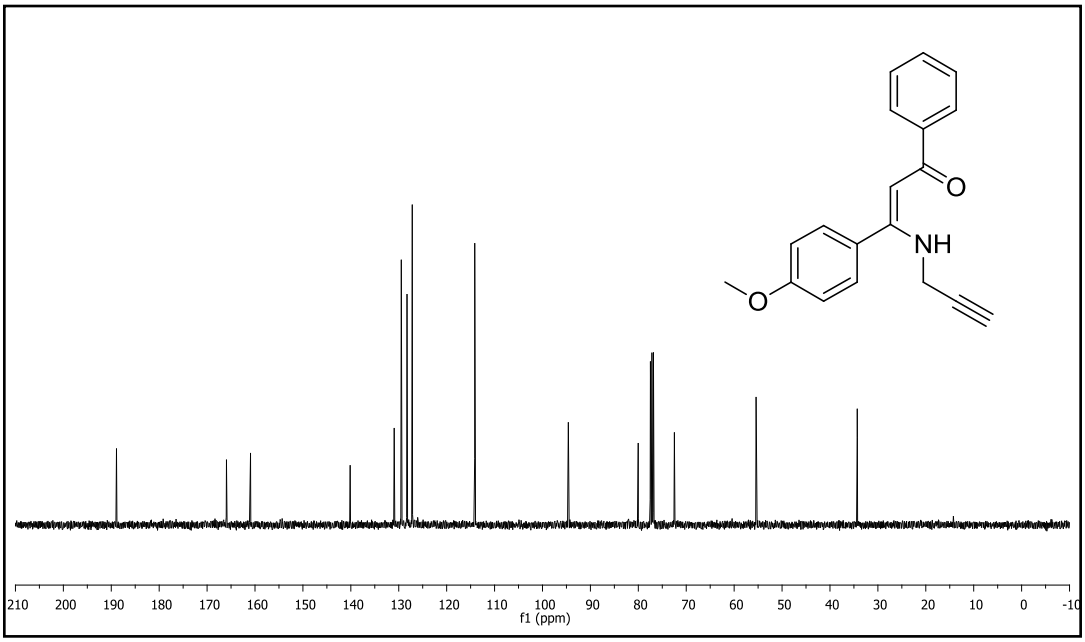

Figure 74. ^{13}C NMR spectrum of compound **25H**.

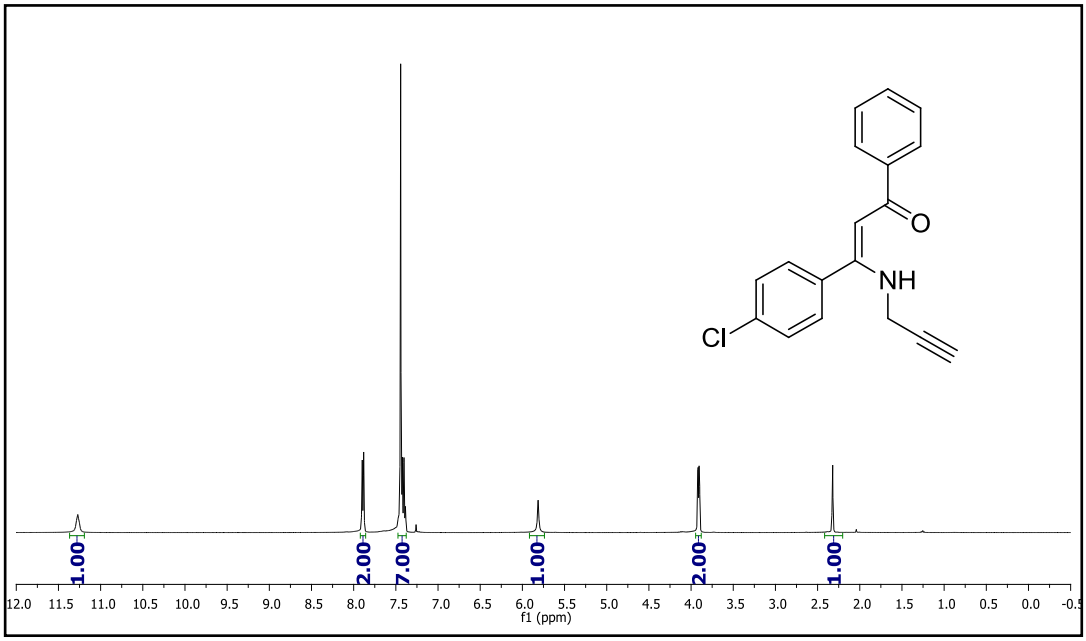

Figure 75. ^{1}H NMR spectrum of compound **25I**.

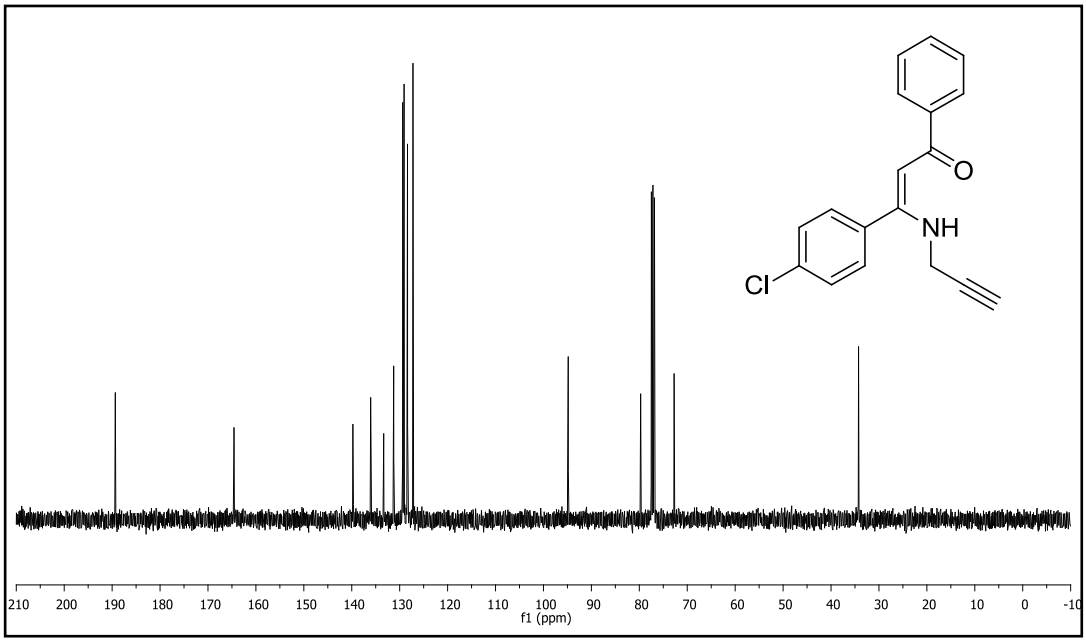

Figure 76. ^{13}C NMR spectrum of compound **25I**.

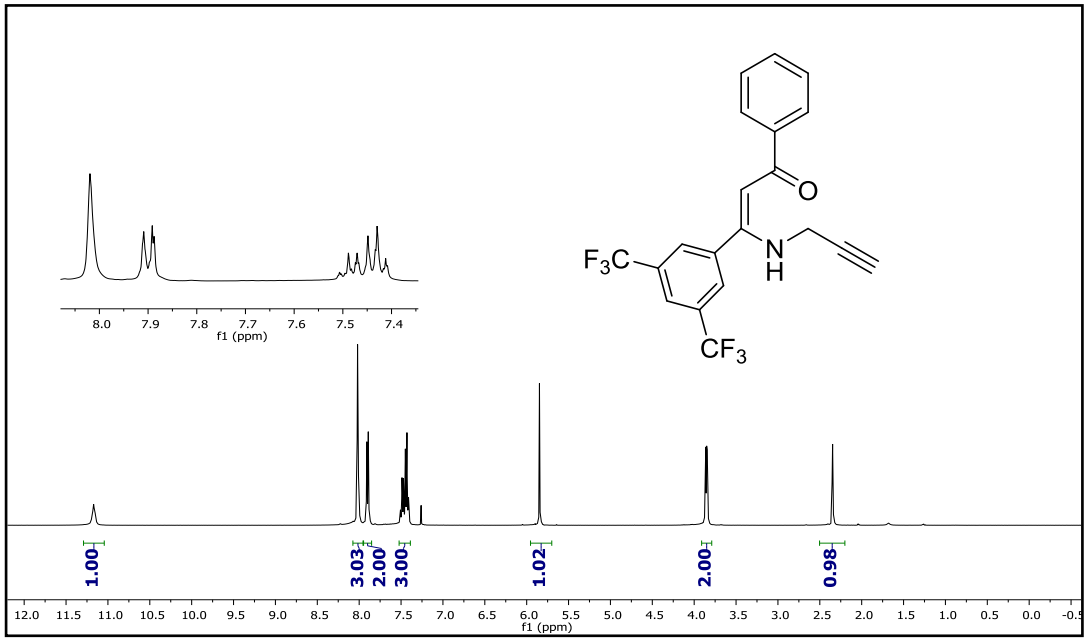

Figure 77. ^{1}H NMR spectrum of compound **25J**.

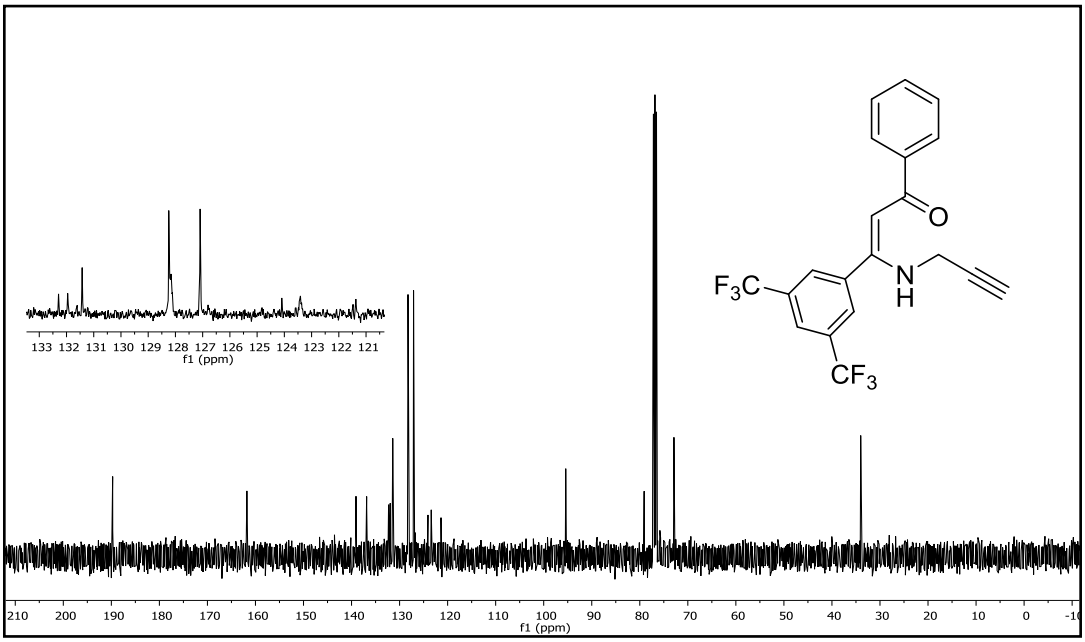

Figure 78. ^{13}C NMR spectrum of compound **25J**.

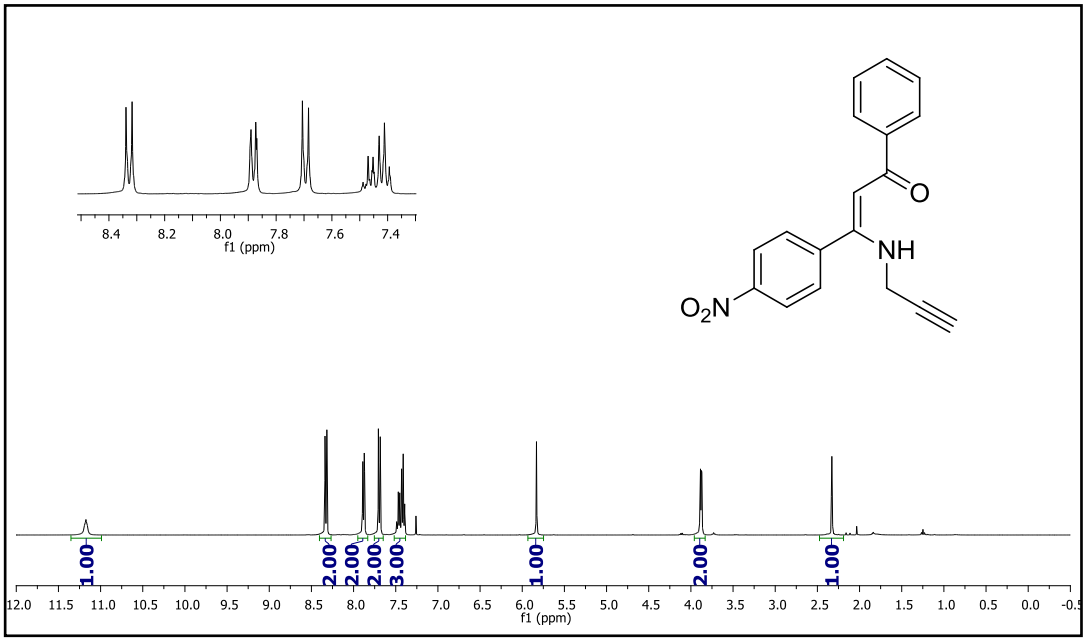

Figure 79. ^{1}H NMR spectrum of compound **25K**.

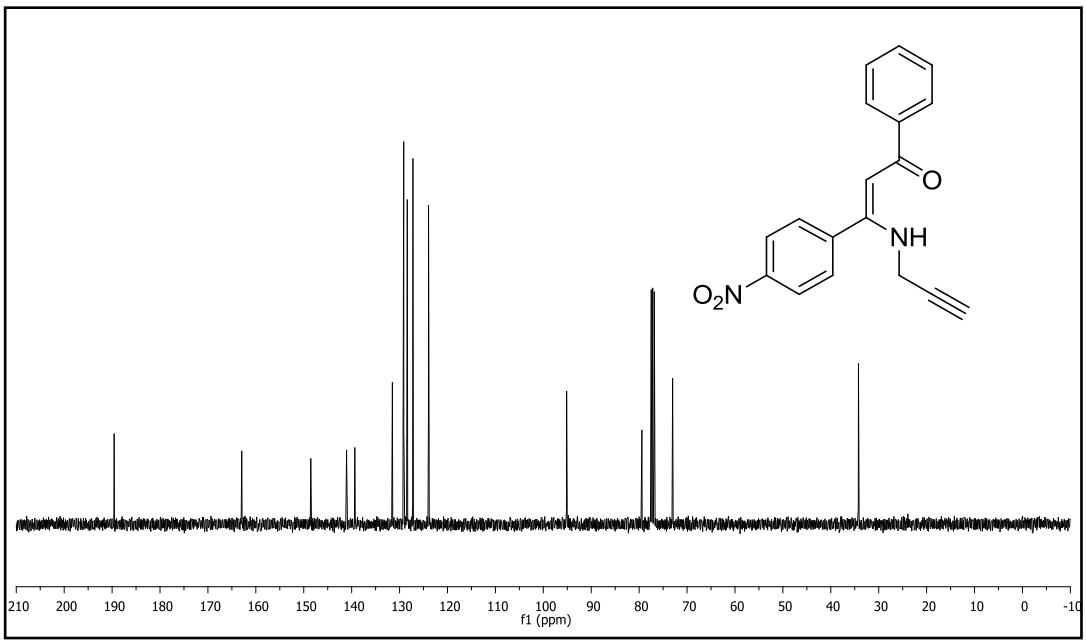

Figure 80. ^{13}C NMR spectrum of compound **25K**.

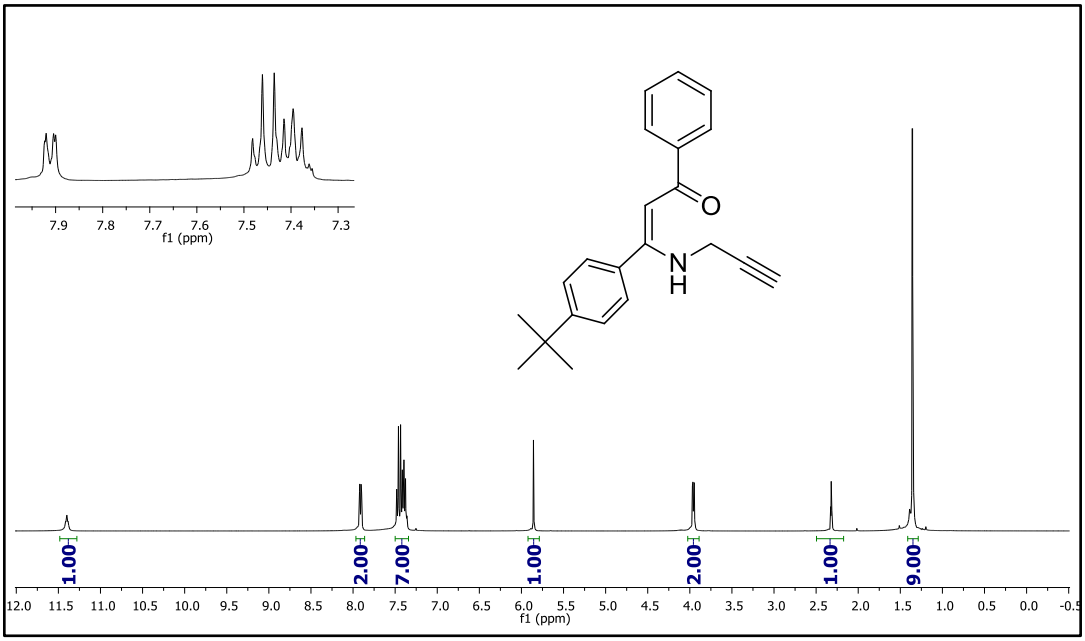

Figure 81. ^{1}H NMR spectrum of compound **25L**.

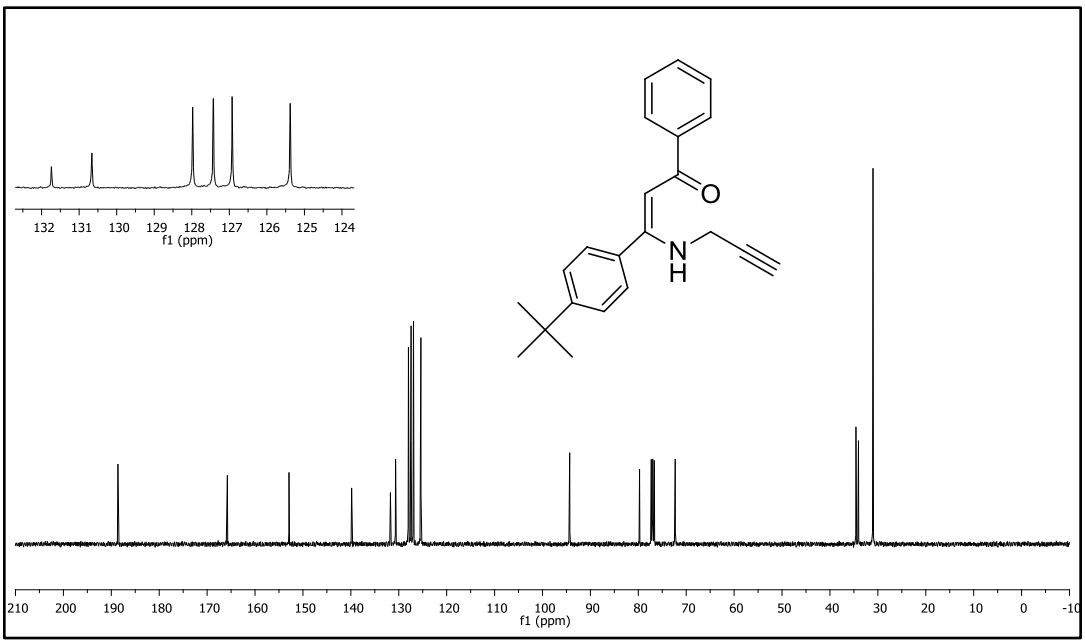

Figure 82. ^{13}C NMR spectrum of compound **25L**.

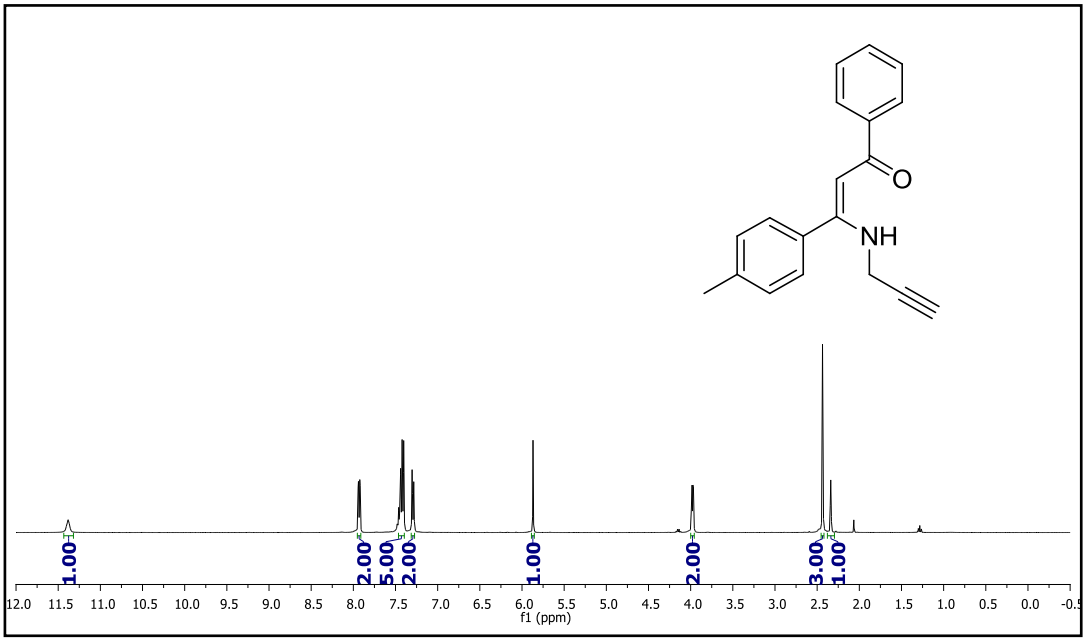

Figure 83. ^{1}H NMR spectrum of compound **25M**.

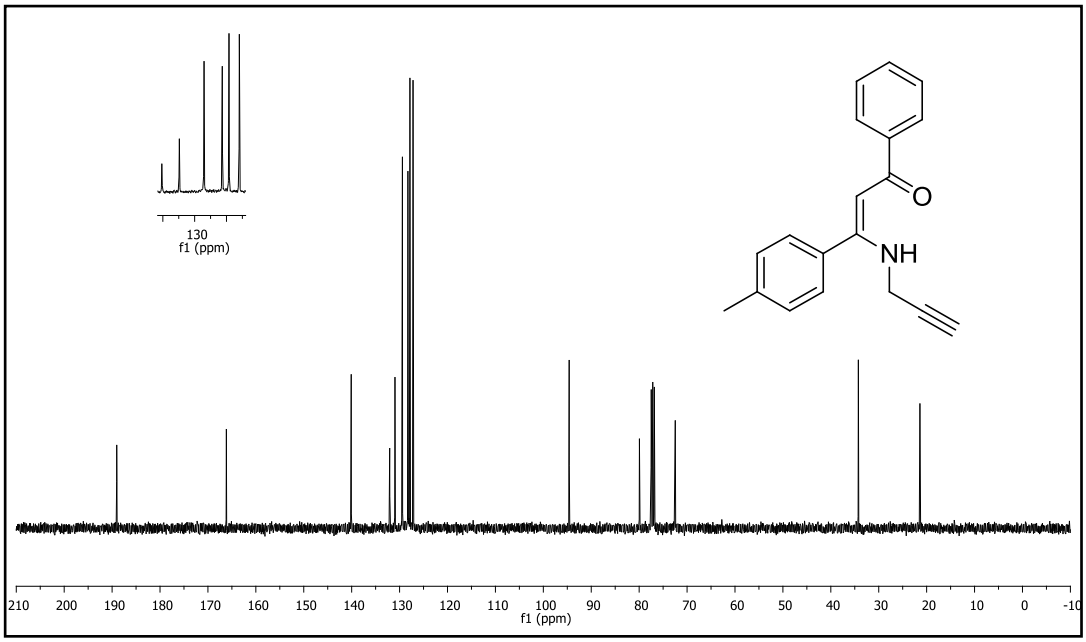

Figure 84. ^{13}C NMR spectrum of compound **25M**.

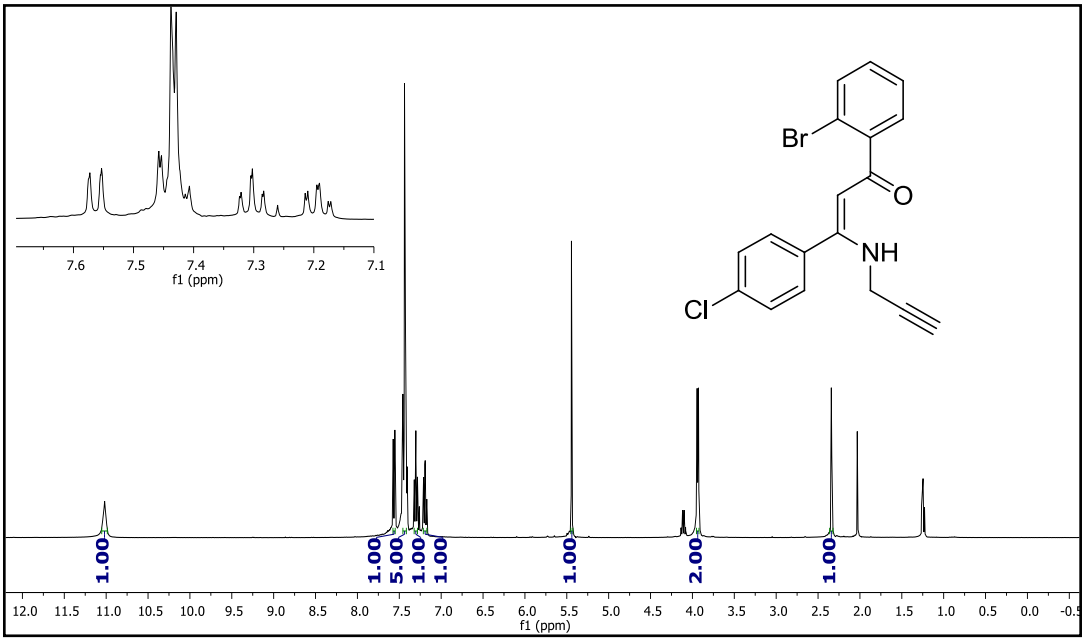

Figure 85. ^{1}H NMR spectrum of compound **25N**.

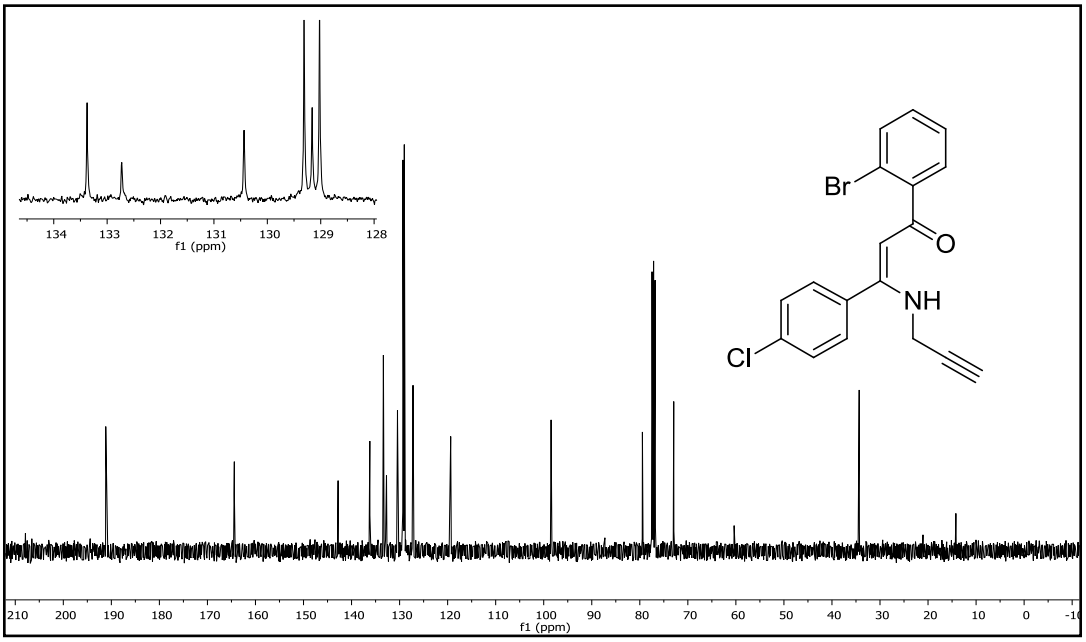

Figure 86. ^{13}C NMR spectrum of compound **25N**.

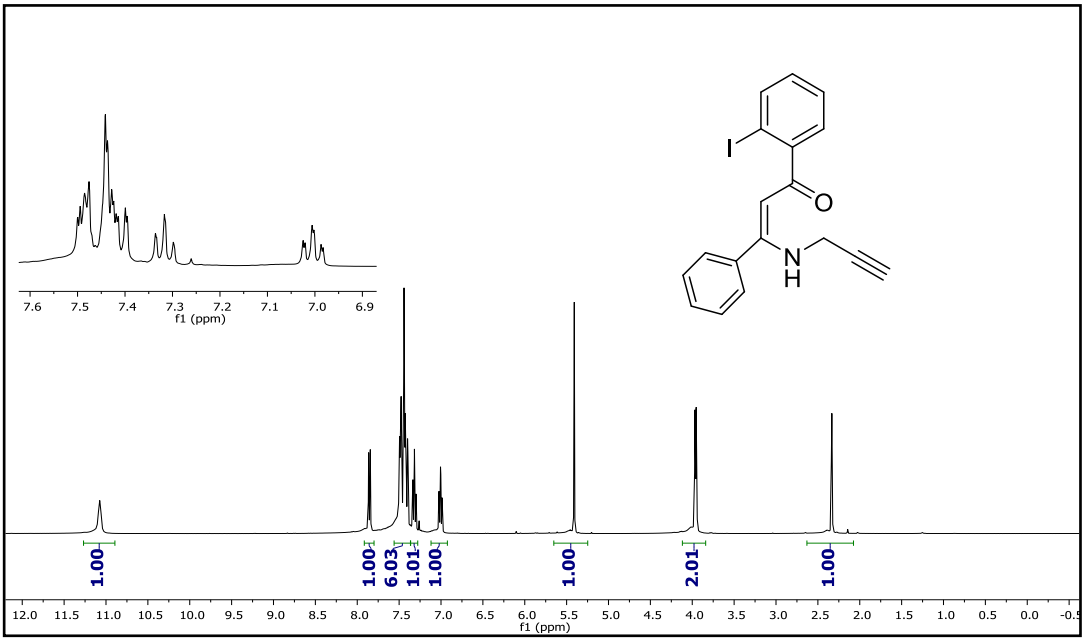

Figure 87. ^{1}H NMR spectrum of compound **25O**.

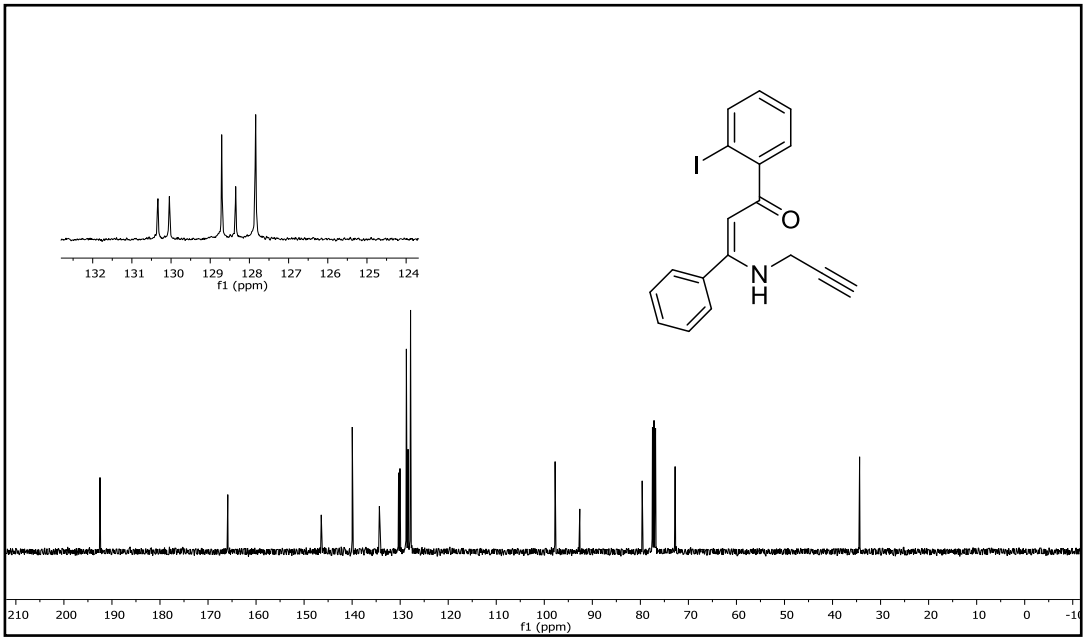

Figure 88. ^{13}C NMR spectrum of compound **25O**.

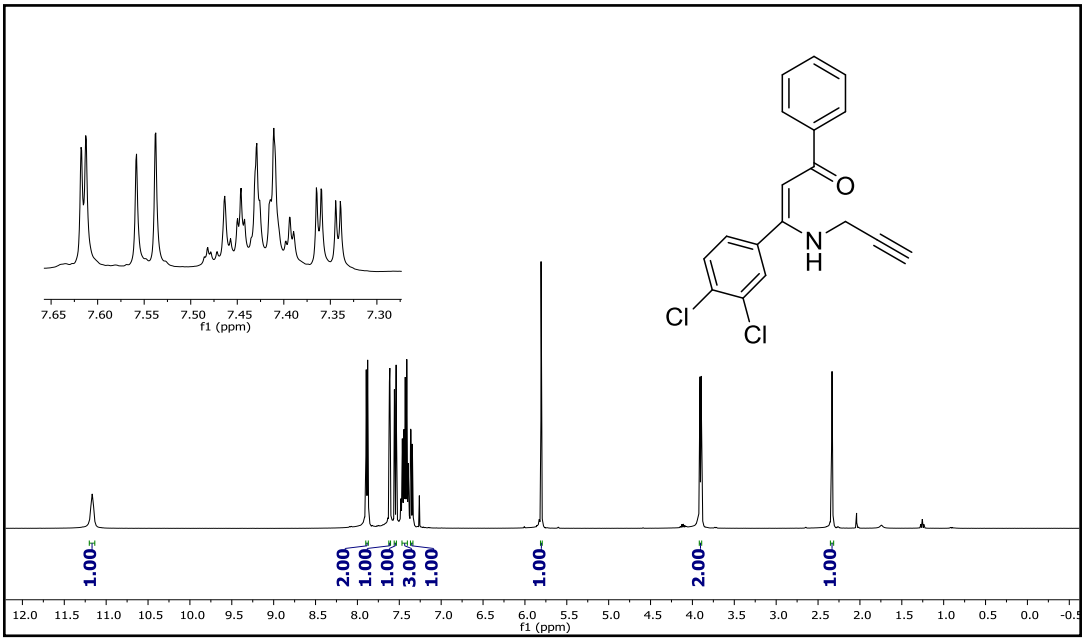

Figure 89. ^{1}H NMR spectrum of compound **25P**.

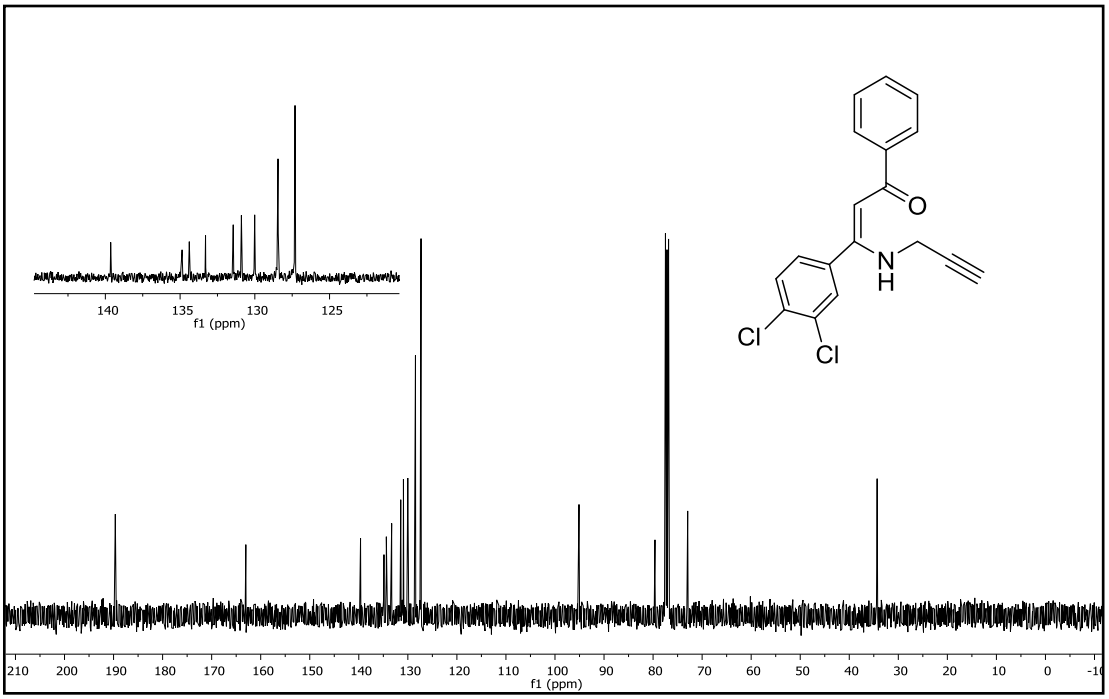

Figure 90. ^{13}C NMR spectrum of compound **25P**.

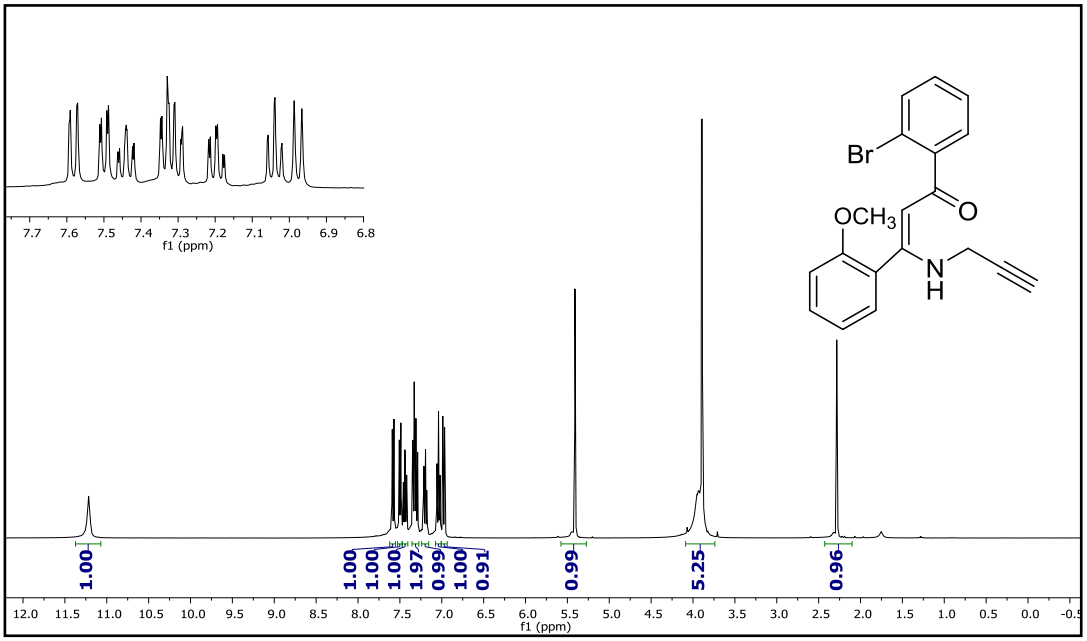

Figure 91. ^{1}H NMR spectrum of compound **25Q**.

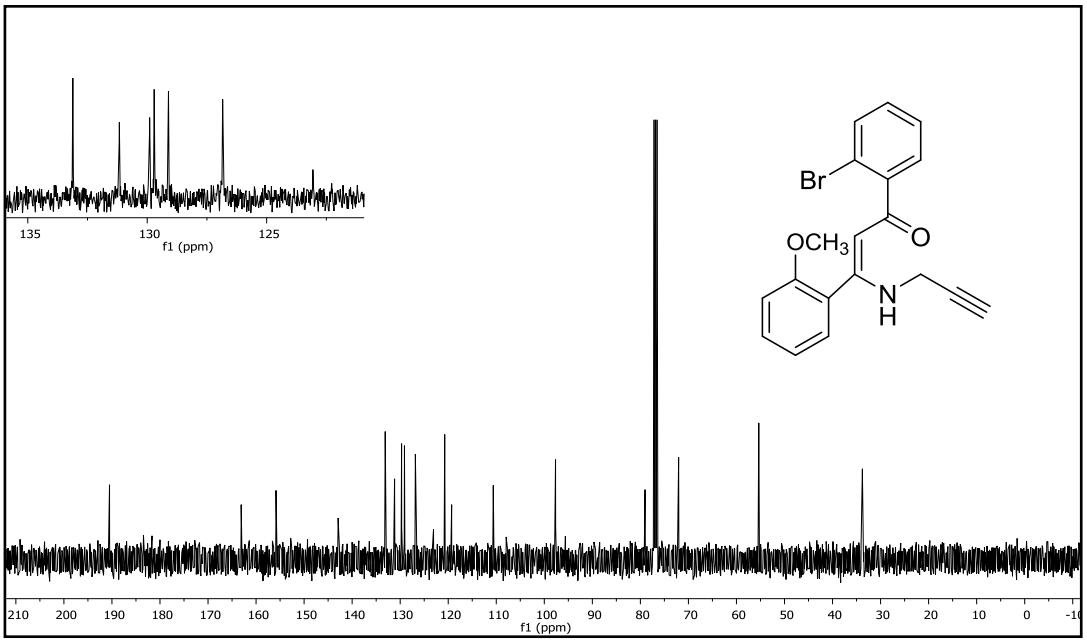

Figure 92. ^{13}C NMR spectrum of compound **25Q**.

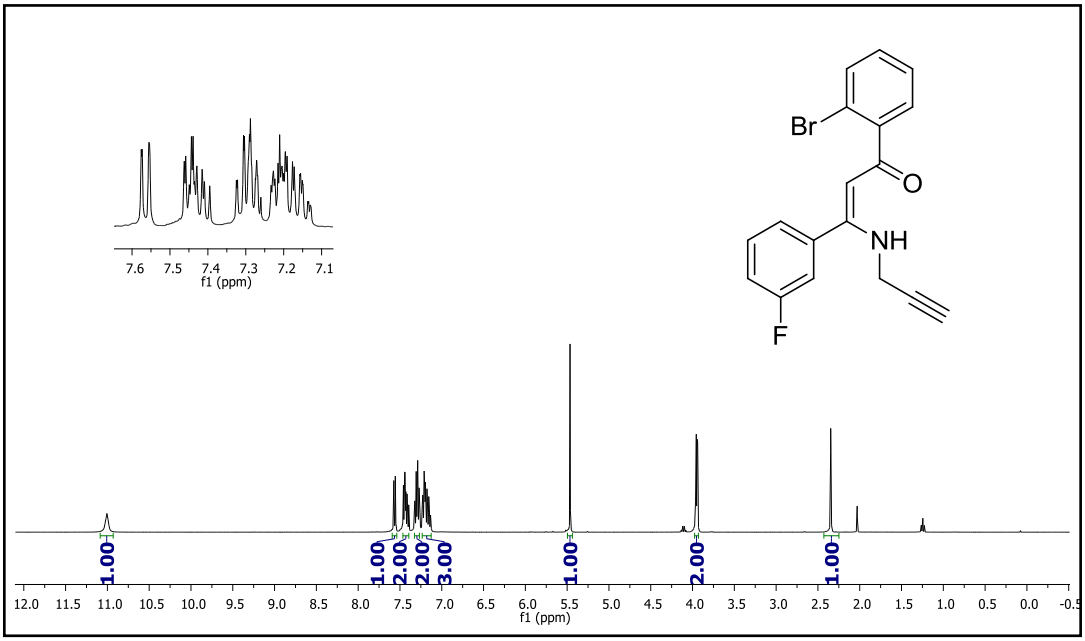

Figure 93. ^{1}H NMR spectrum of compound **25R**.

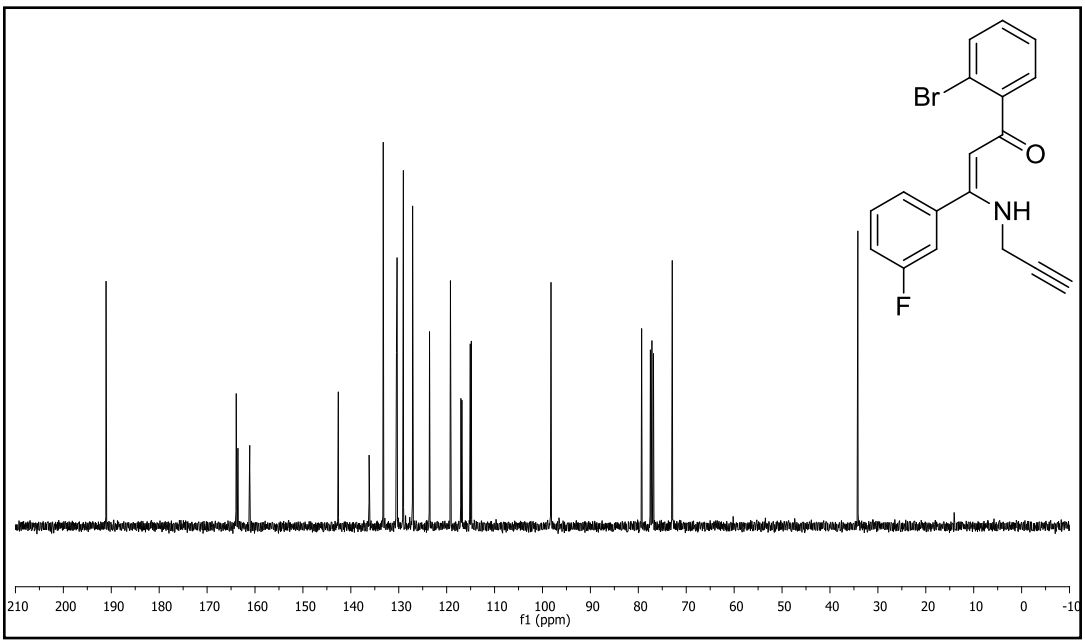

Figure 94. ^{13}C NMR spectrum of compound **25R**.

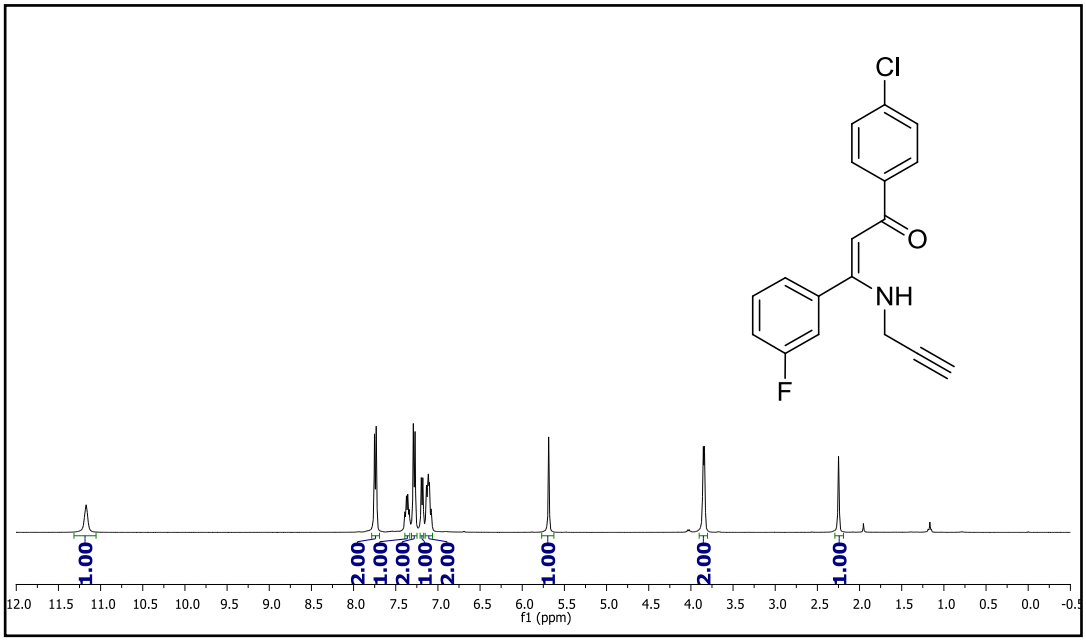

Figure 95. ^{1}H NMR spectrum of compound **25S**.

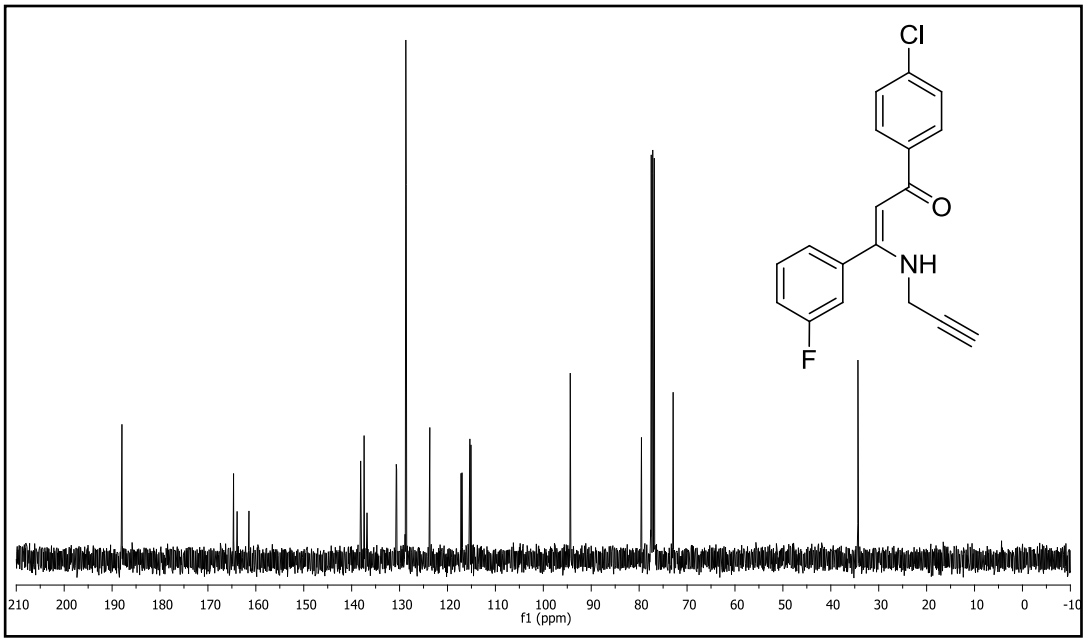

Figure 96. ^{13}C NMR spectrum of compound **25S**.

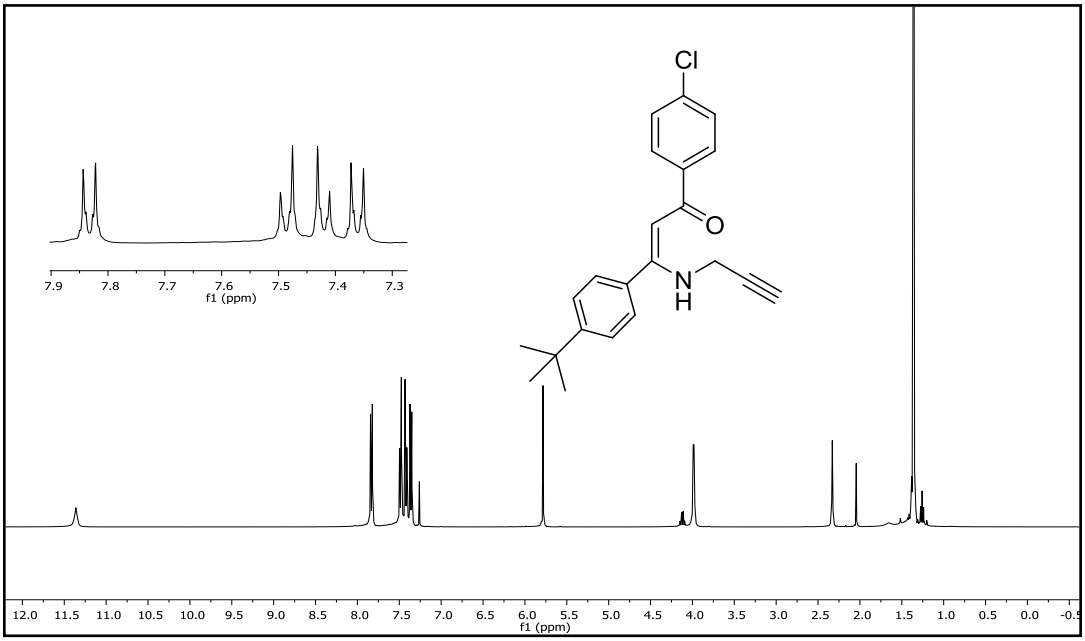

Figure 97. ^{1}H NMR spectrum of compound **25T**.

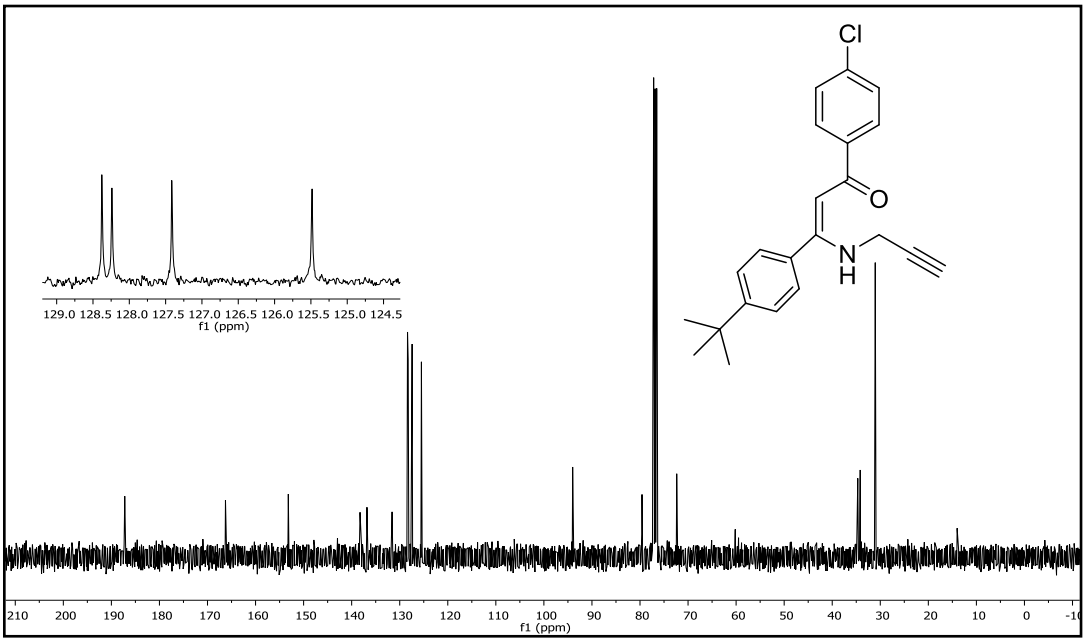

Figure 98. ^{13}C NMR spectrum of compound **25T**.

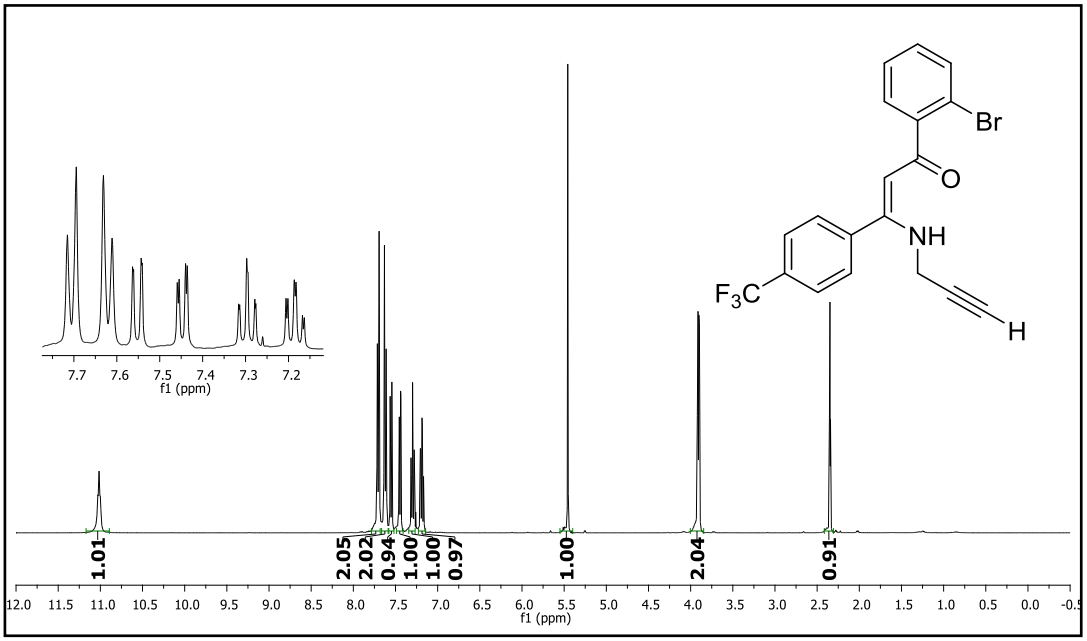

Figure 99. ^{1}H NMR spectrum of compound **25U**.

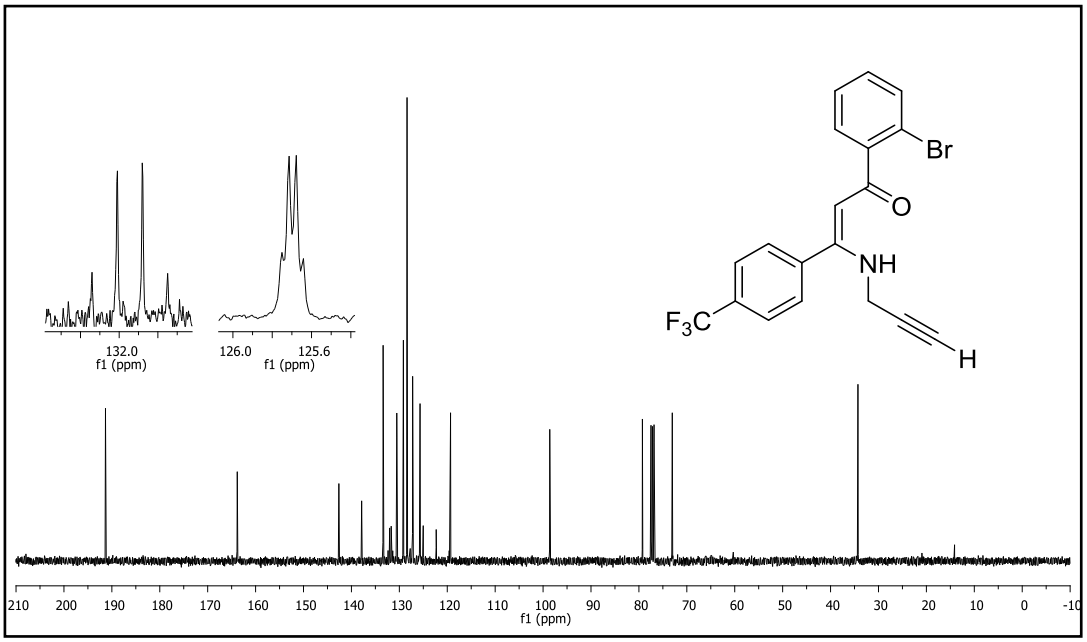

Figure 100. ^{13}C NMR spectrum of compound **25U**.

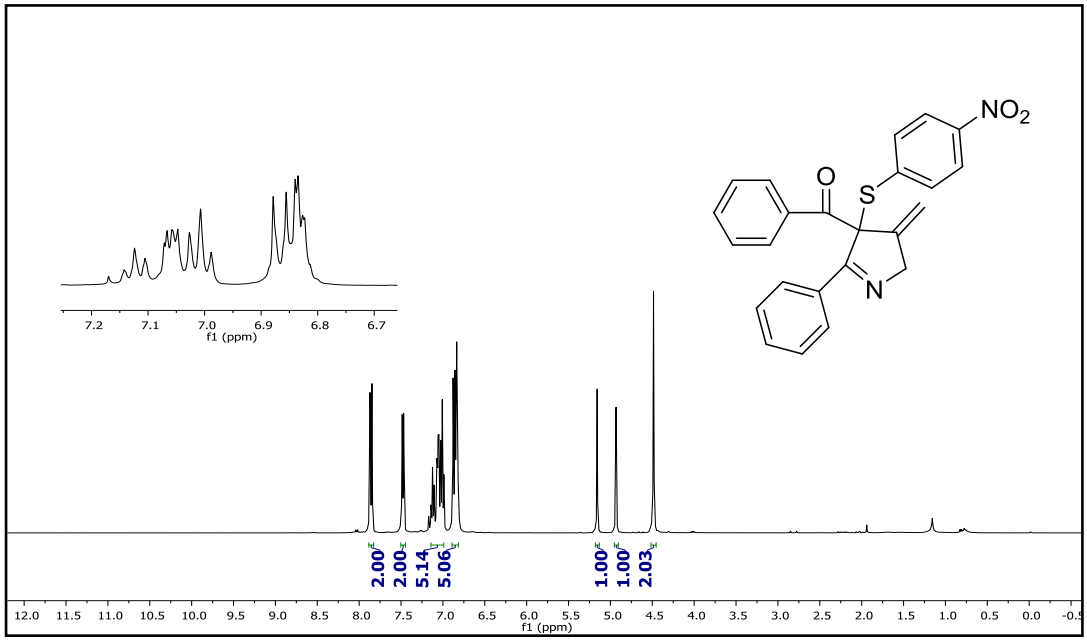

Figure 101. ^{1}H NMR spectrum of compound **32A**.

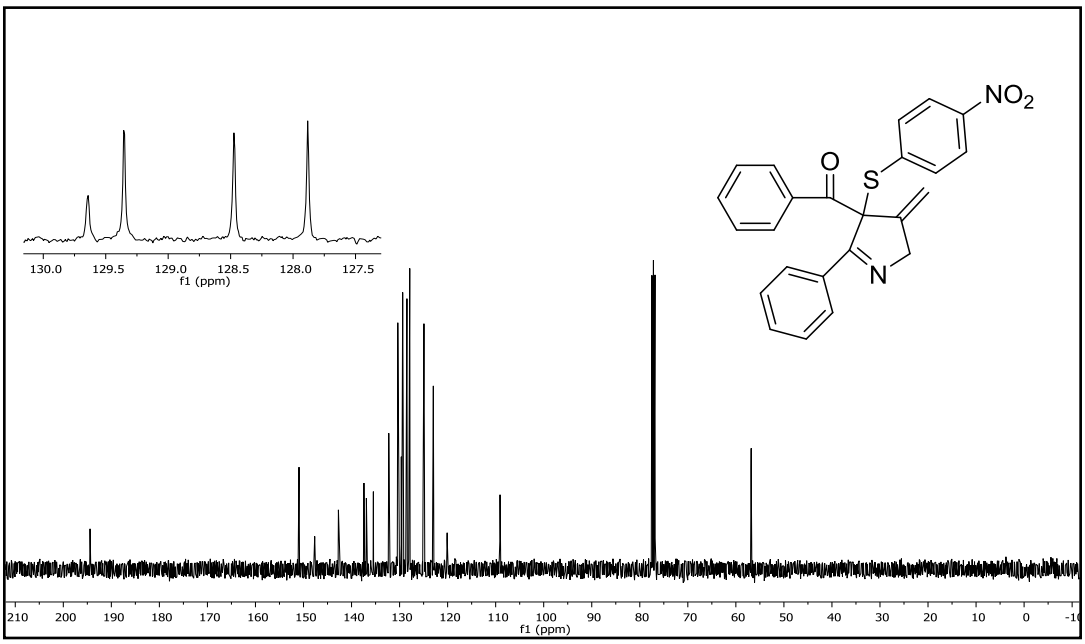

Figure 102. ^{13}C NMR spectrum of compound **32A**.

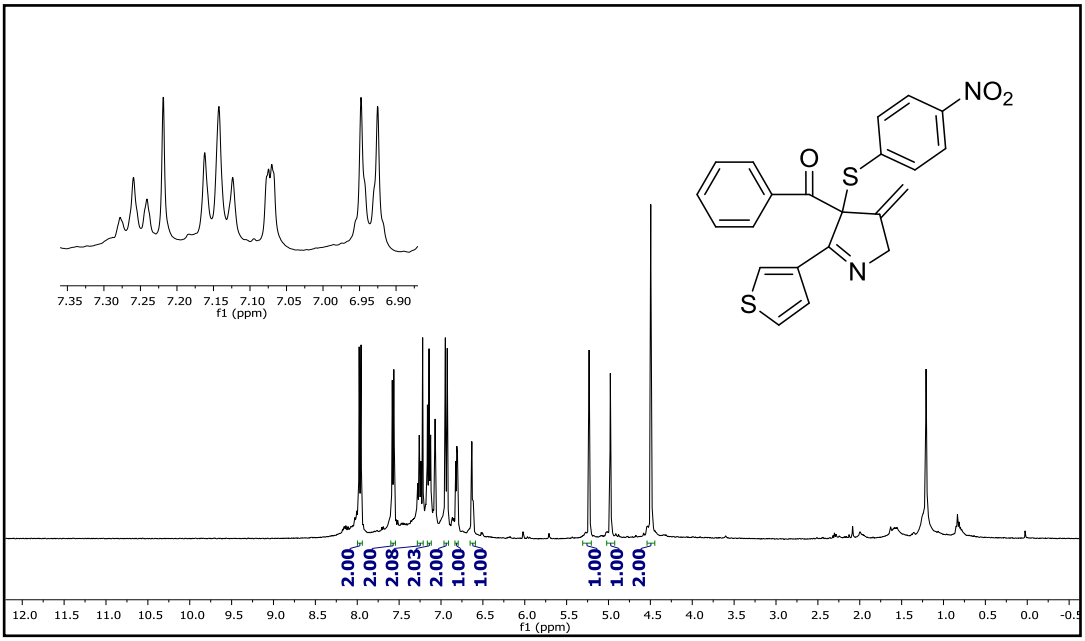

Figure 103. ^{1}H NMR spectrum of compound **32B**.

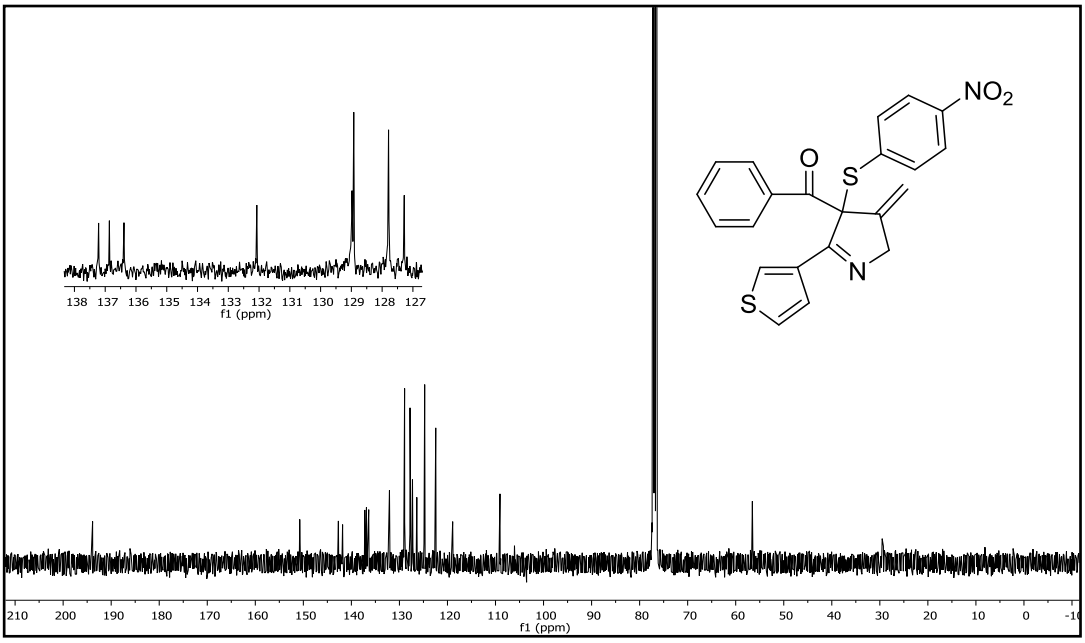

Figure 104. ^{13}C NMR spectrum of compound **32B**.

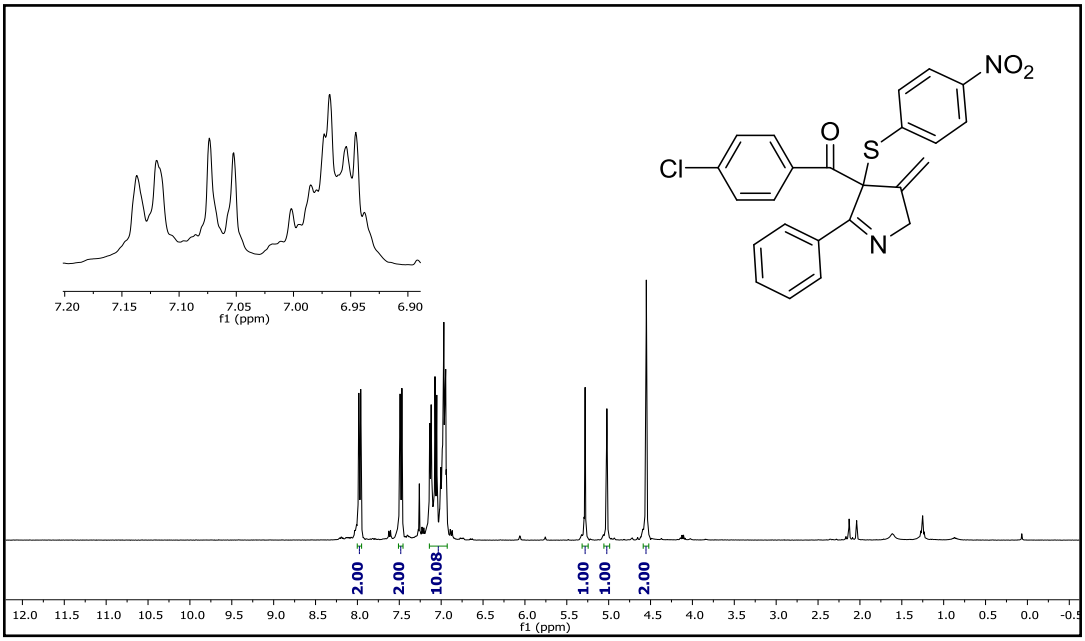

Figure 105. ^{1}H NMR spectrum of compound **32C**.

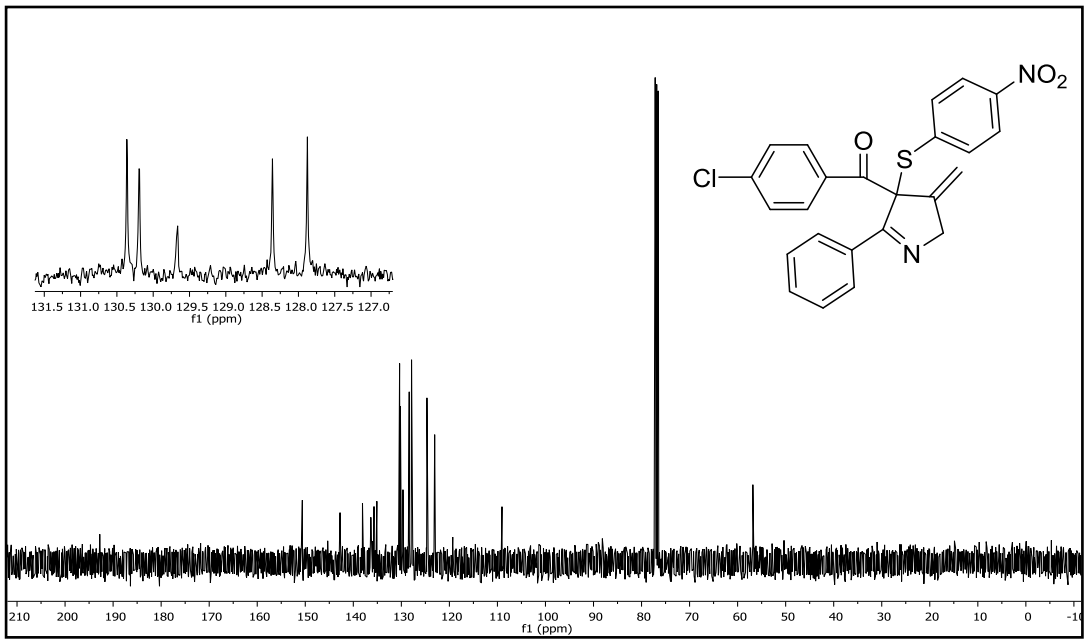

Figure 106. ^{13}C NMR spectrum of compound **32C**.

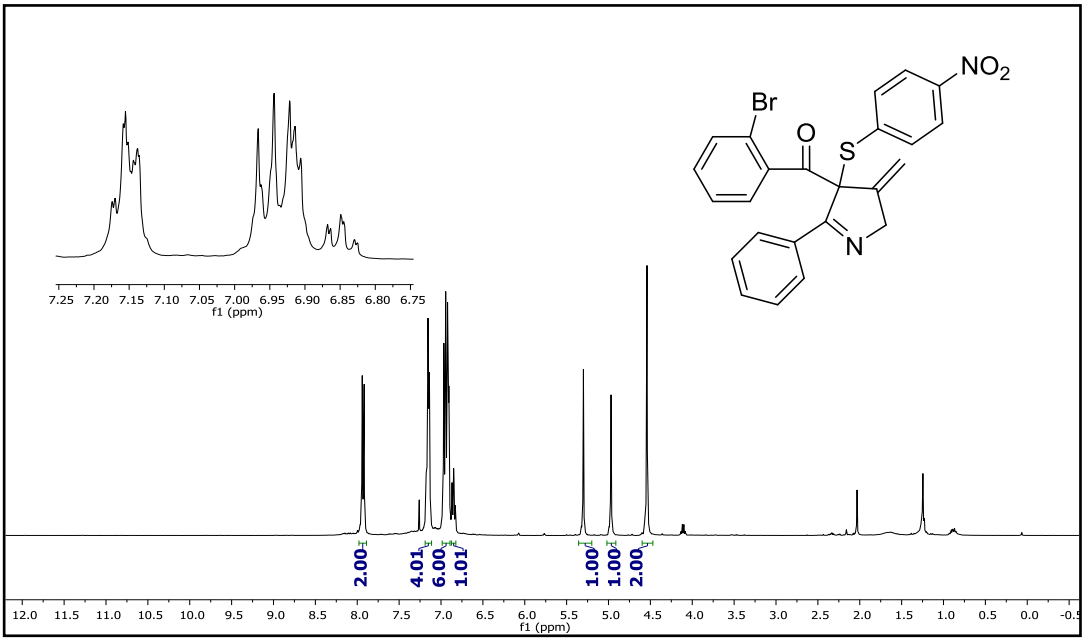

Figure 107. ^{1}H NMR spectrum of compound **32D**.

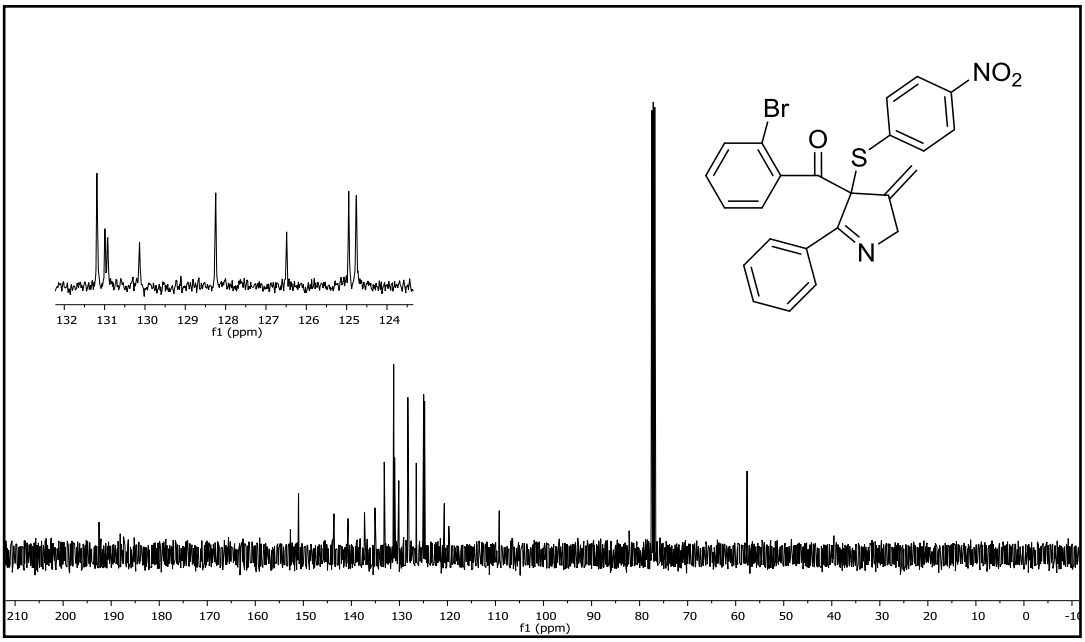

Figure 108. ^{13}C NMR spectrum of compound **32D**.

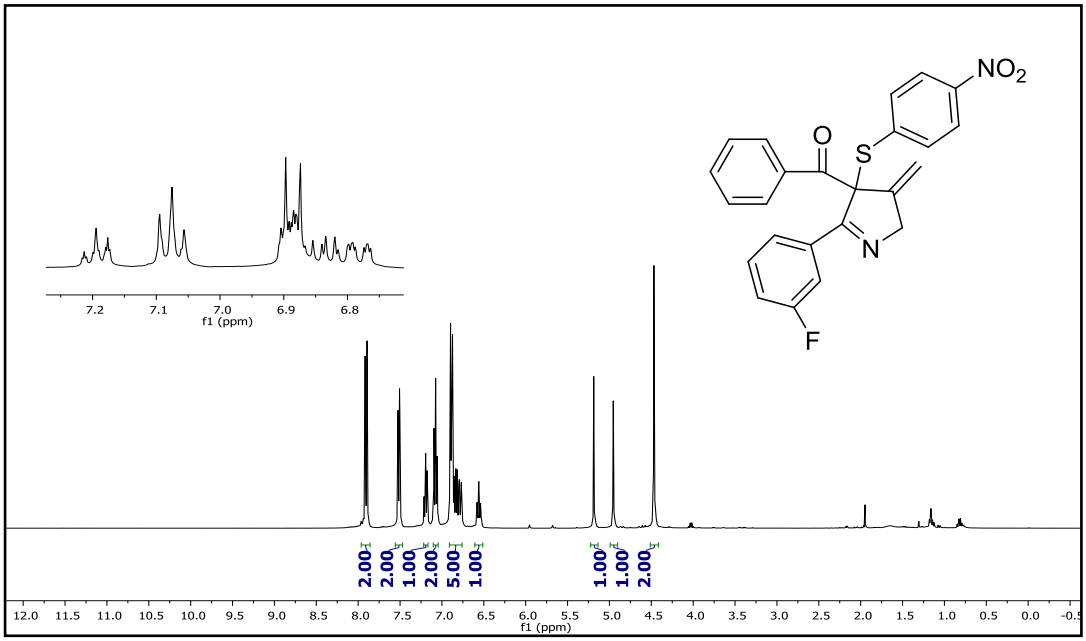

Figure 109. ^{1}H NMR spectrum of compound **32E**.

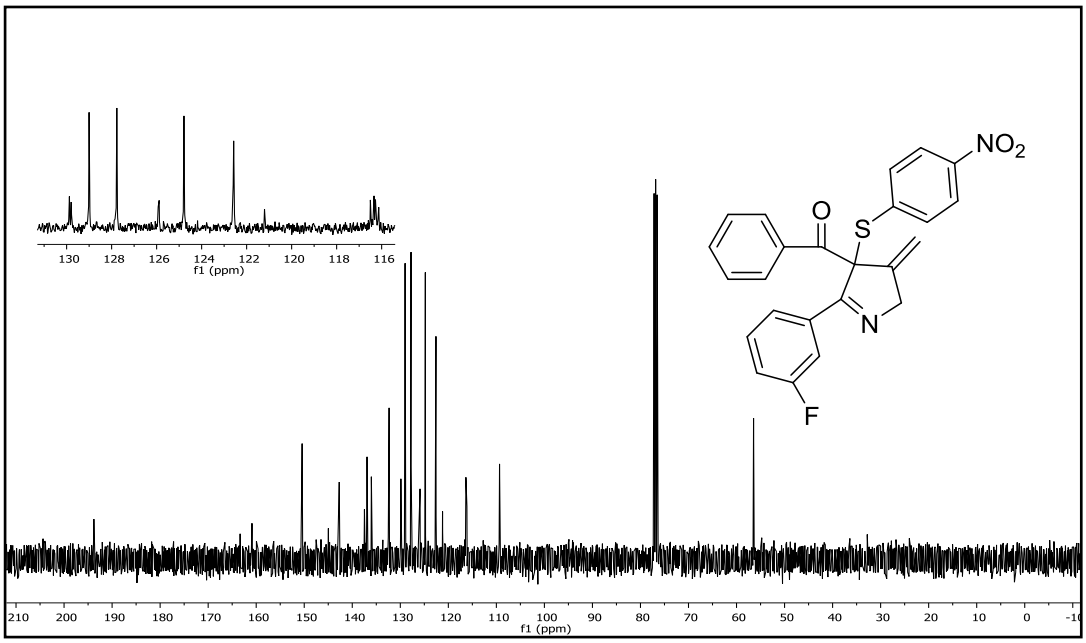

Figure 110. ^{13}C NMR spectrum of compound **32E**.

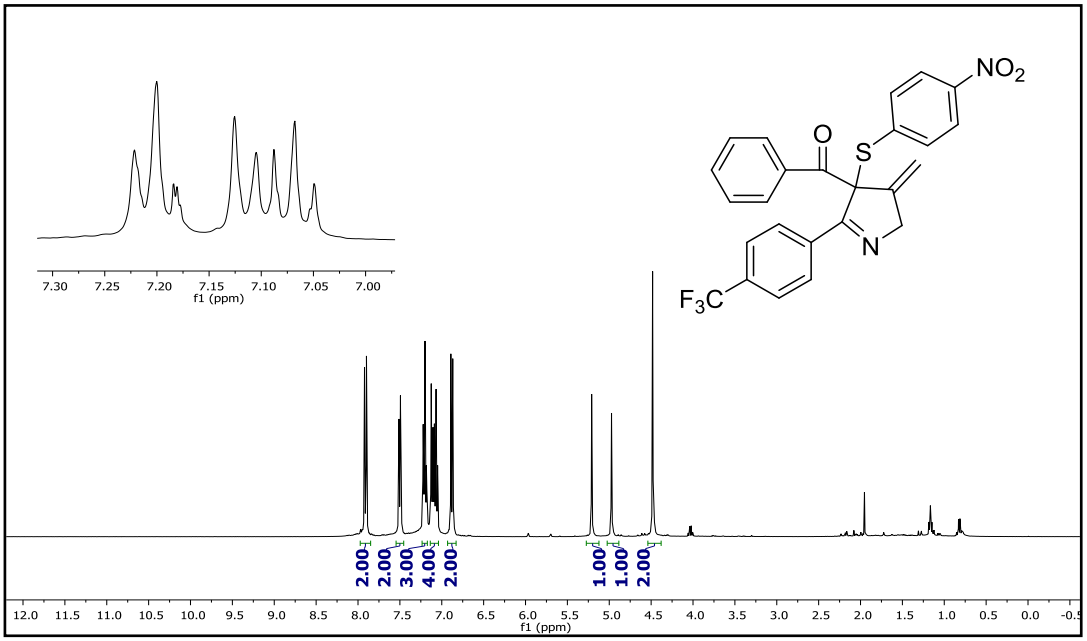

Figure 111. ^{1}H NMR spectrum of compound **32F**.

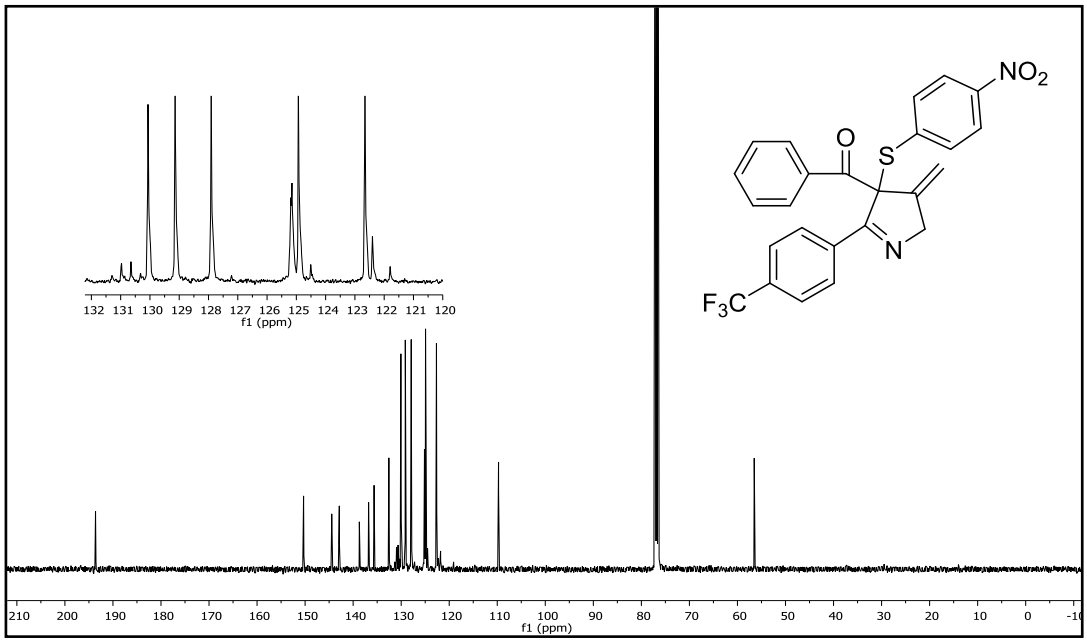

Figure 112. ^{13}C NMR spectrum of compound **32F**.

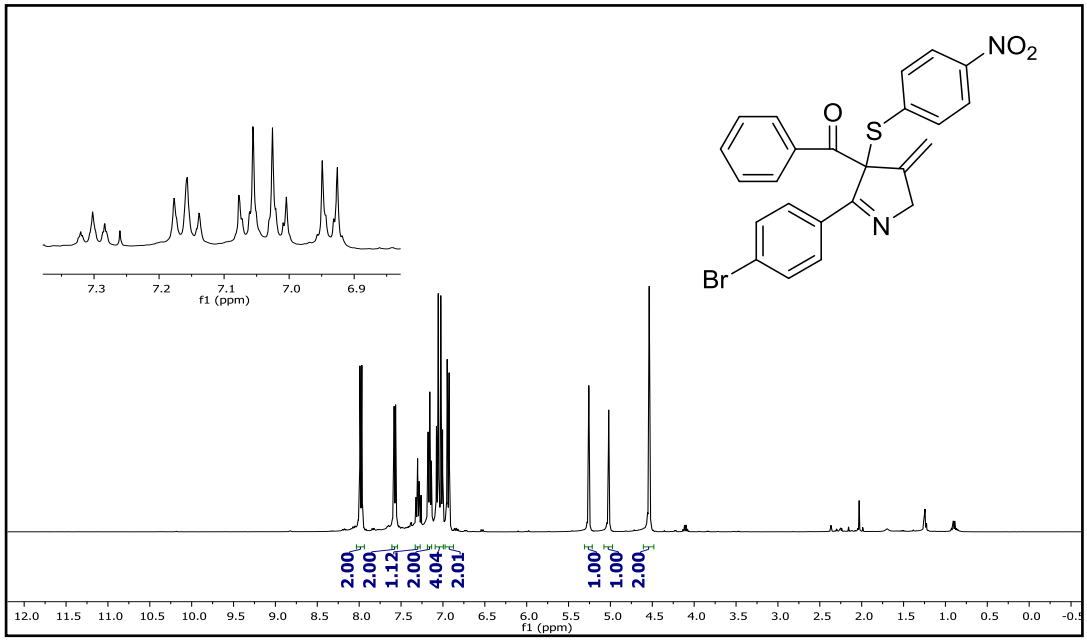

Figure 113. ^{1}H NMR spectrum of compound **32G**.

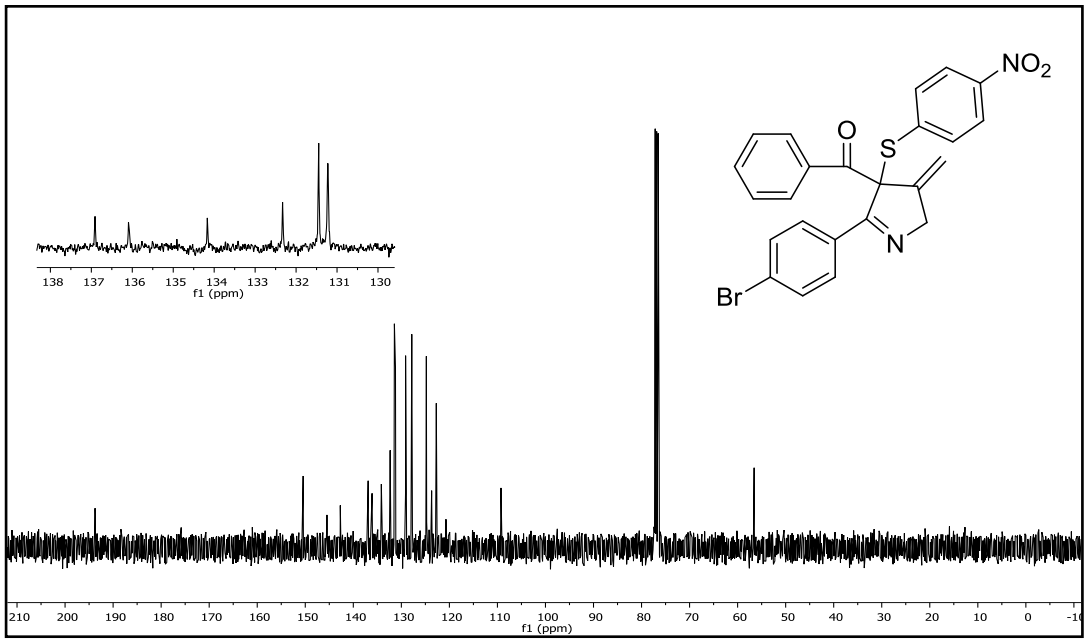

Figure 114. ^{13}C NMR spectrum of compound **32G**.

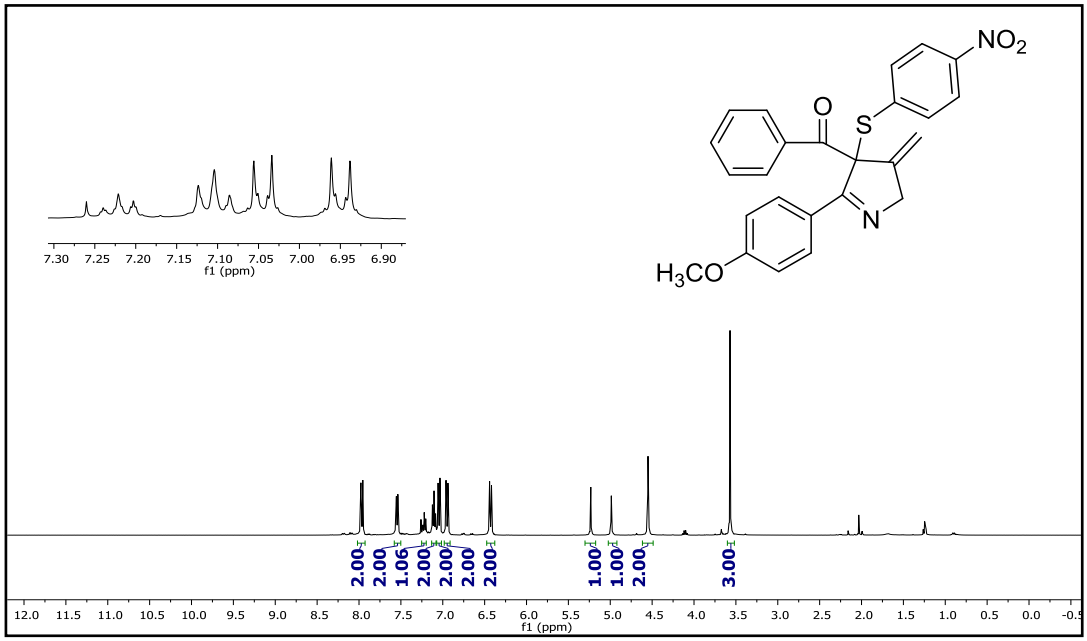

Figure 115. ^{1}H NMR spectrum of compound **32H**.

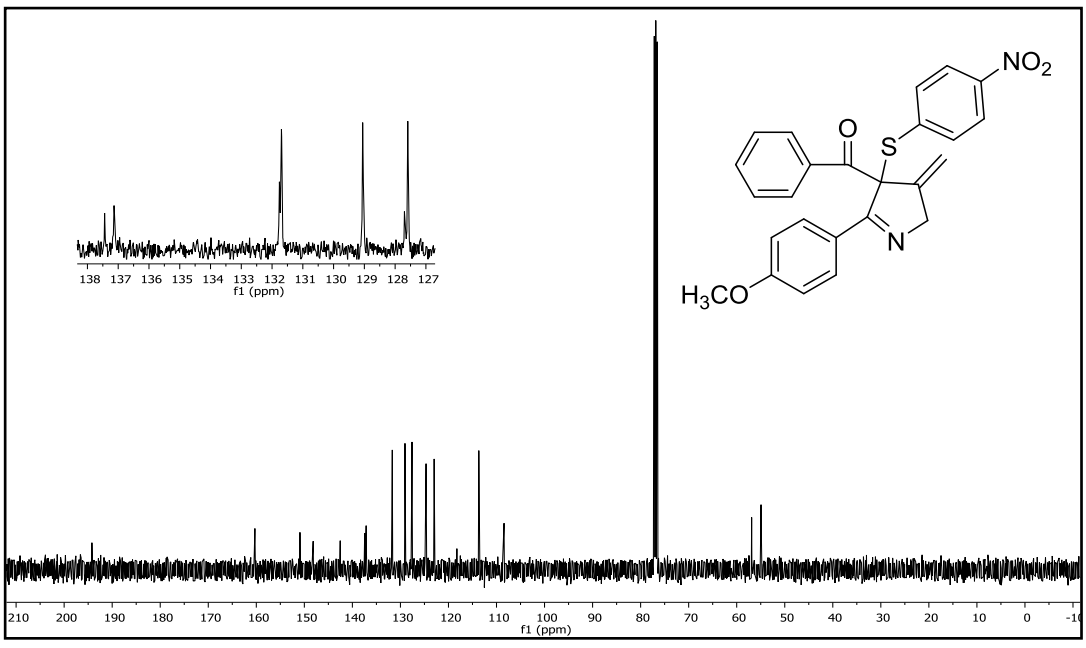

Figure 116. ^{13}C NMR spectrum of compound **32H**.

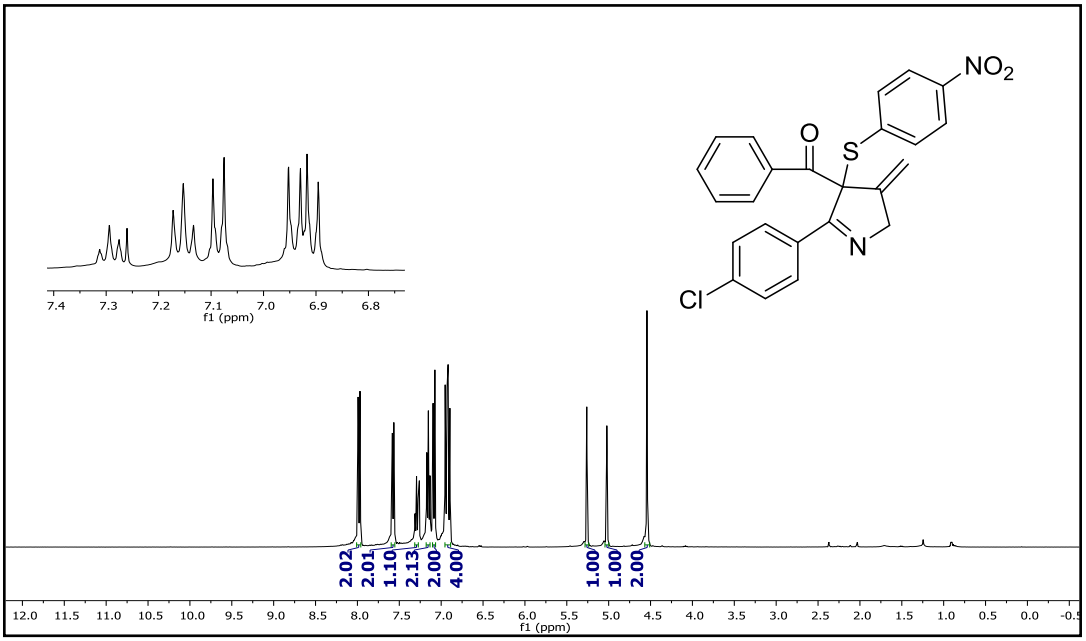

Figure 117. ^{1}H NMR spectrum of compound **32I**.

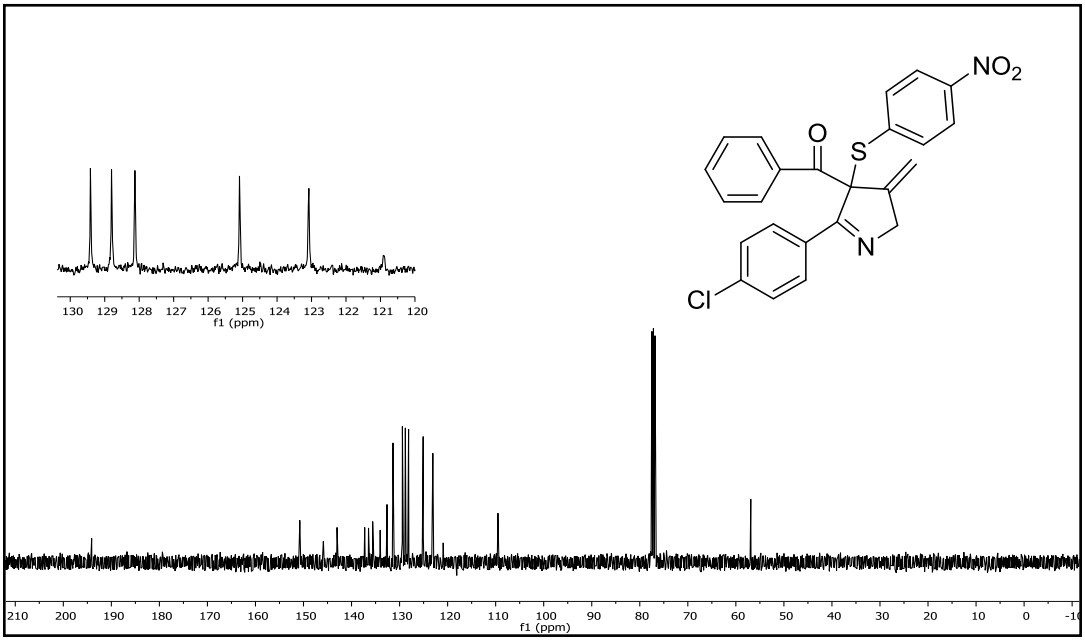

Figure 118. ^{13}C NMR spectrum of compound **32I**.

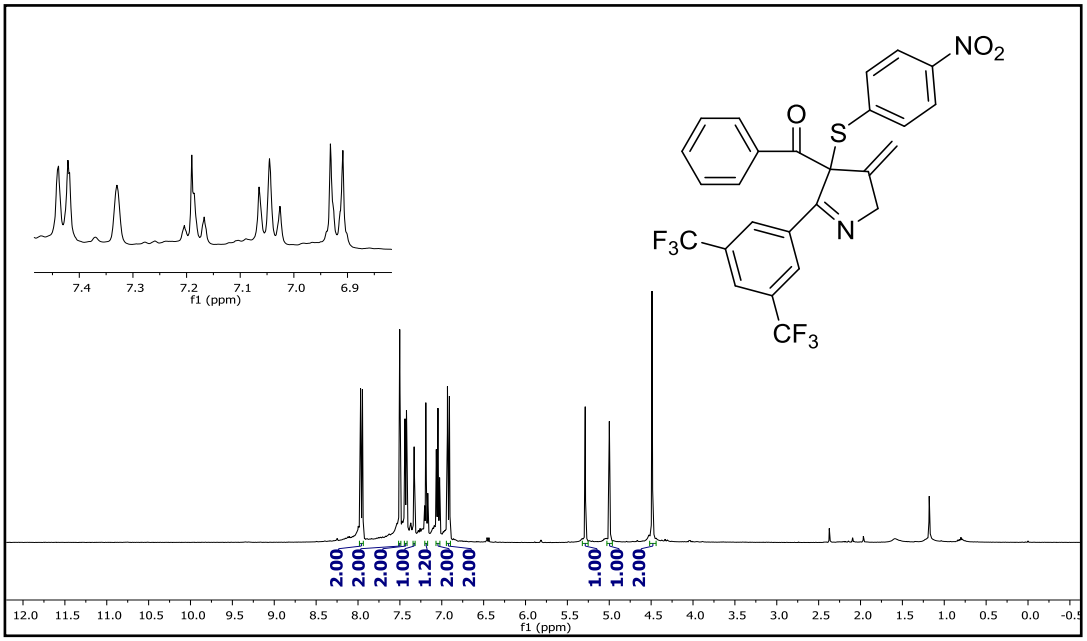

Figure 119. ^{1}H NMR spectrum of compound **32J**.

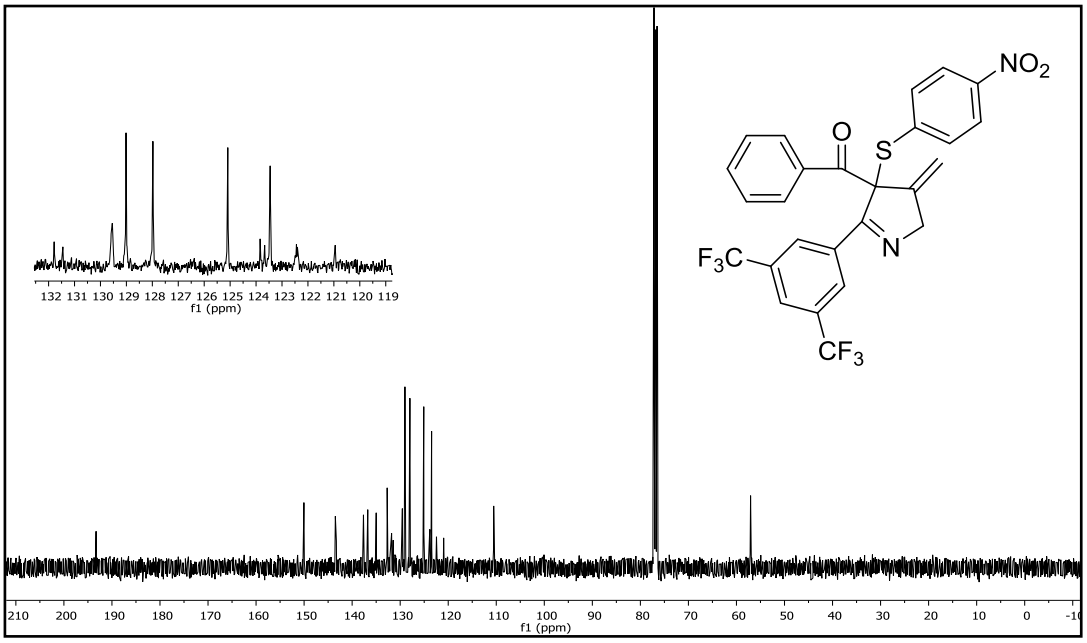

Figure 120. ^{13}C NMR spectrum of compound **32J**.

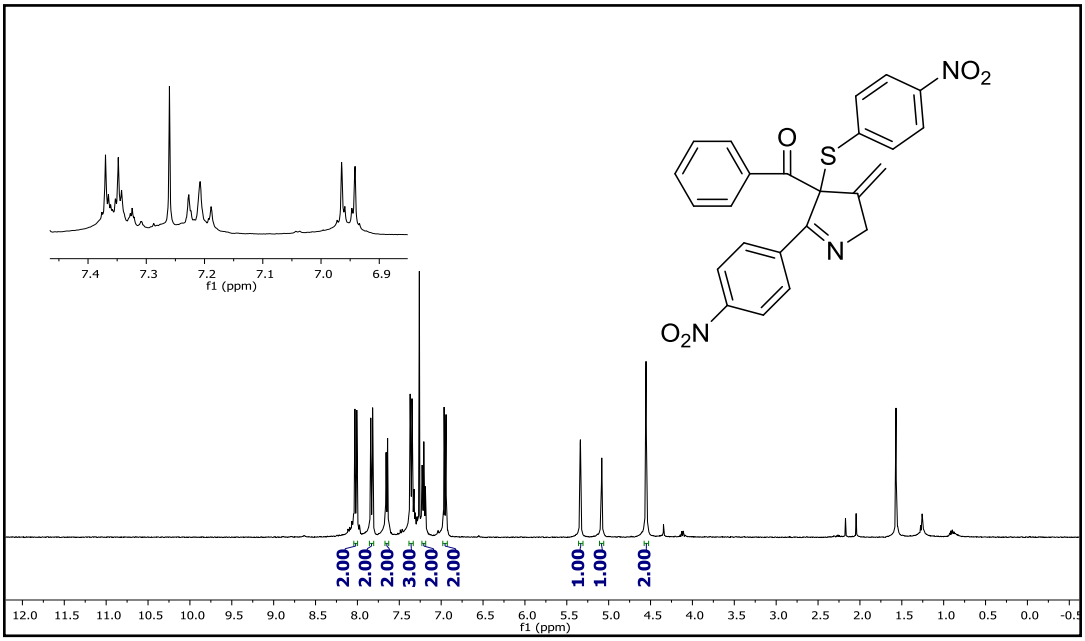

Figure 121. ^{1}H NMR spectrum of compound **32K**.

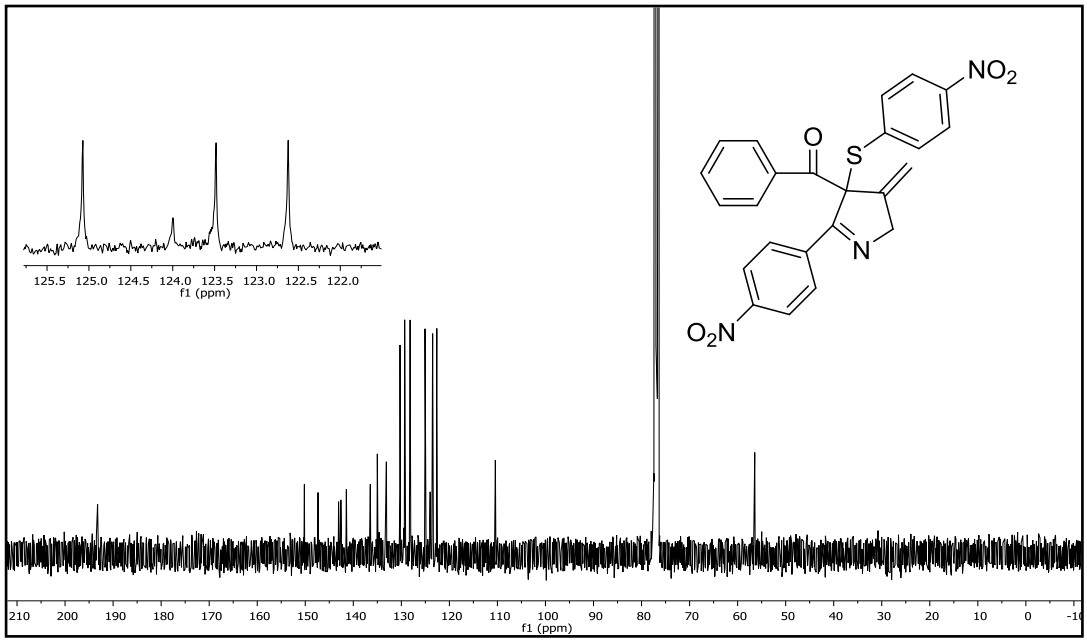

Figure 122. ^{13}C NMR spectrum of compound **32K**.

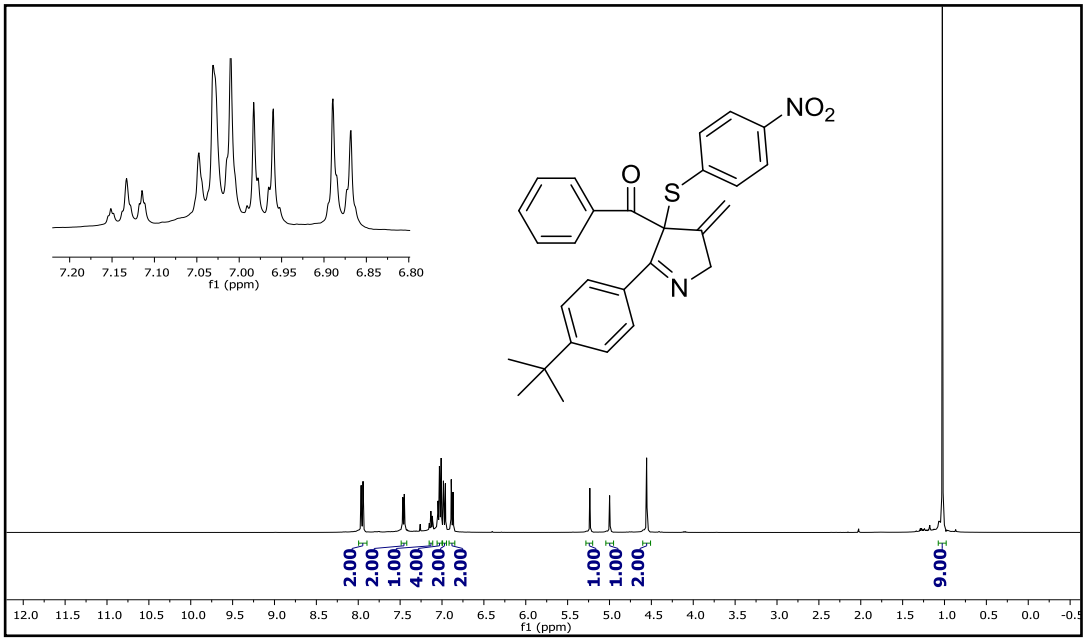

Figure 123. ^{1}H NMR spectrum of compound **32L**.

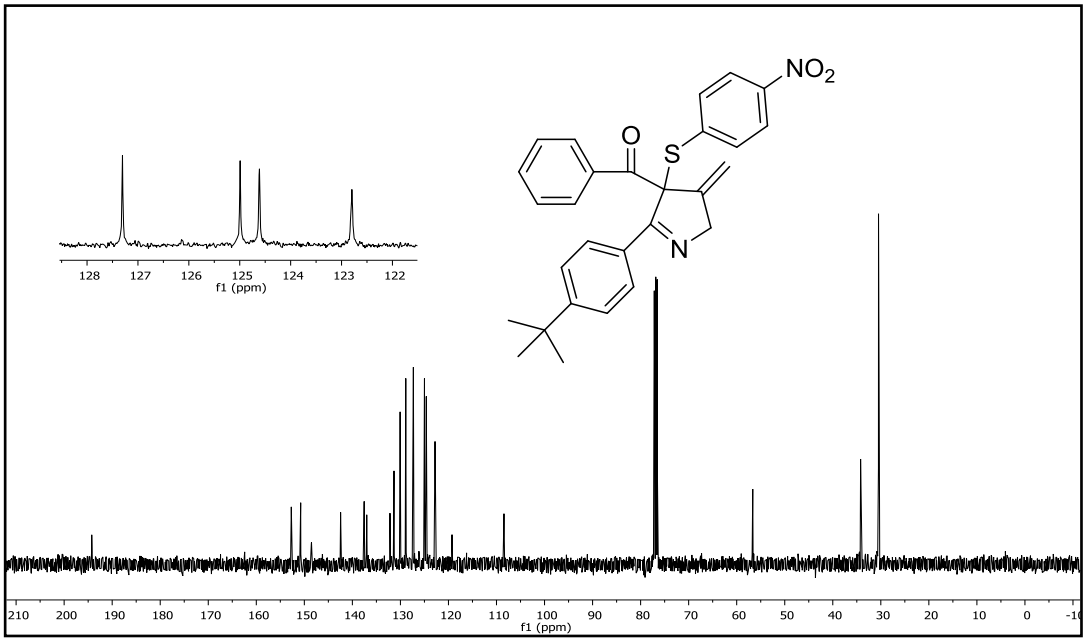

Figure 124. ^{13}C NMR spectrum of compound **32L**.

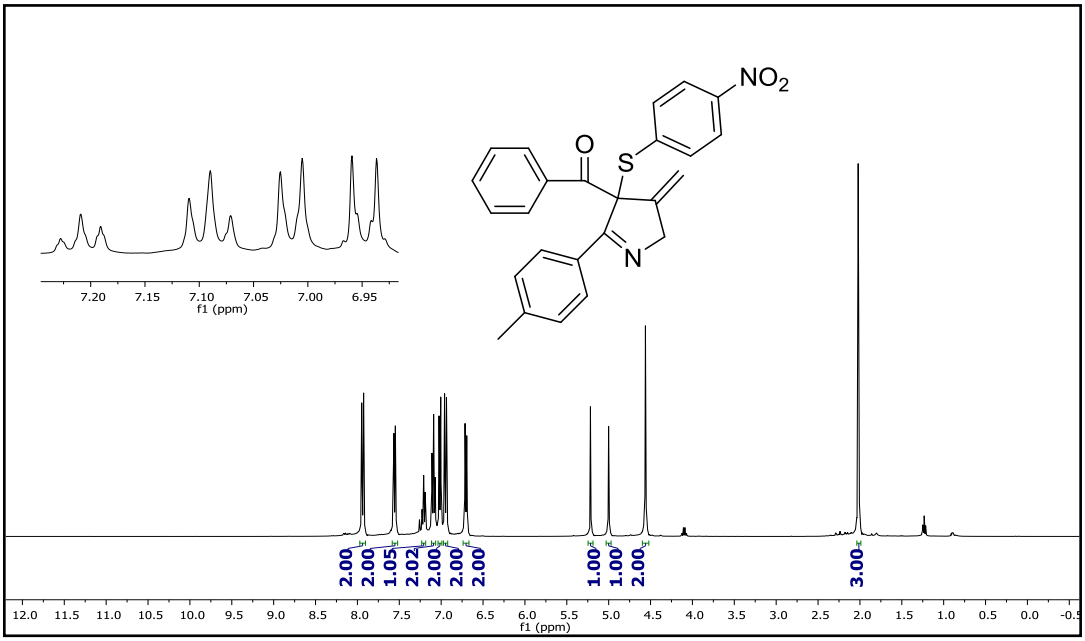

Figure 125. ^{1}H NMR spectrum of compound **32M**.

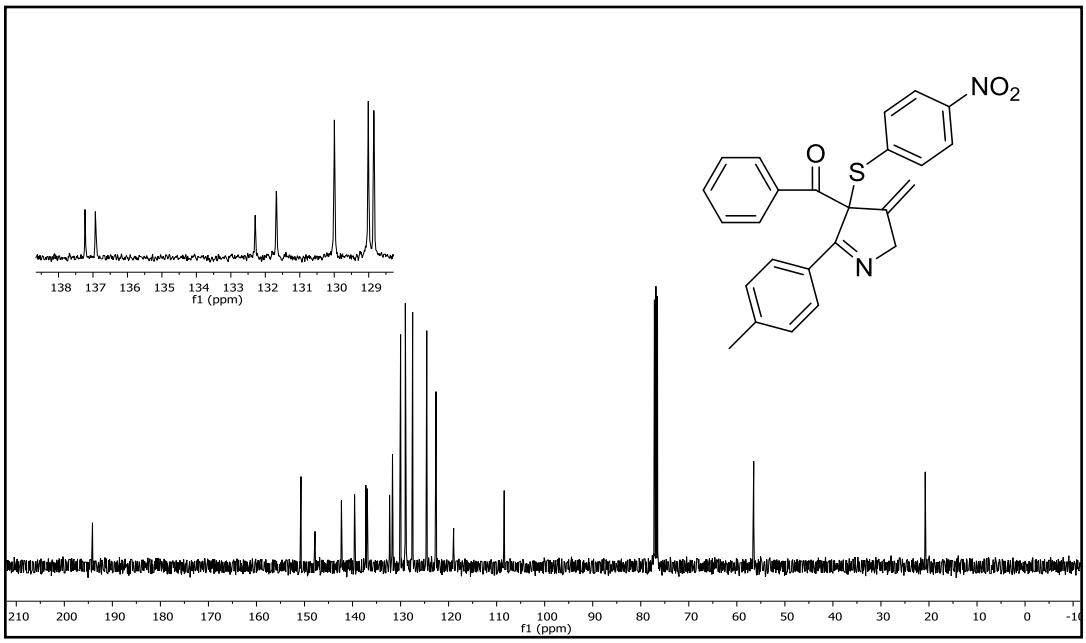

Figure 126. ^{13}C NMR spectrum of compound **32M**.

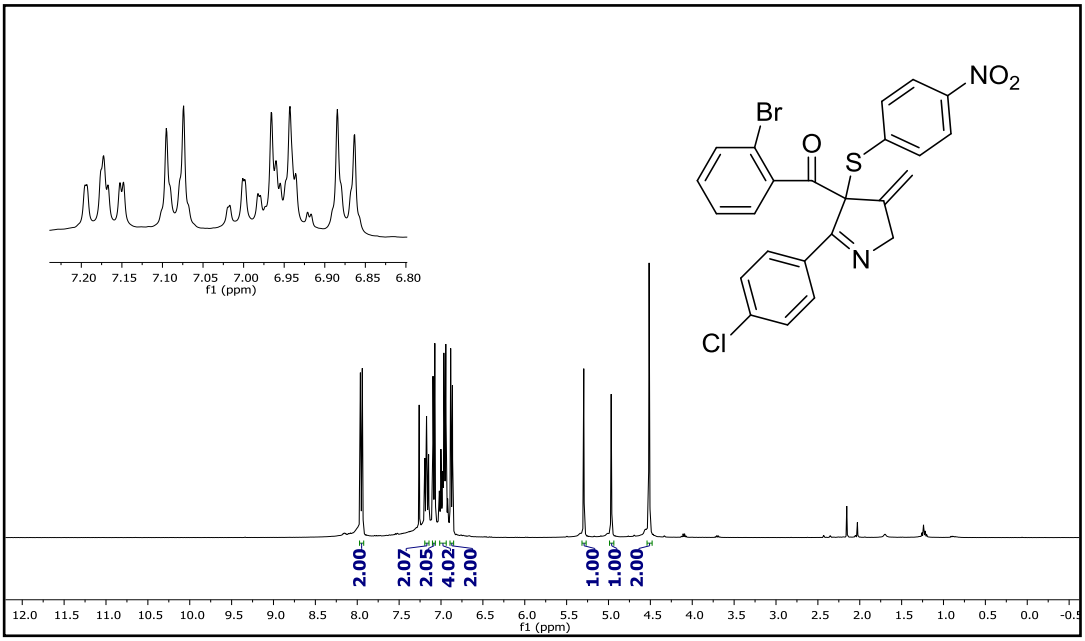

Figure 127. ^{1}H NMR spectrum of compound **32N**.

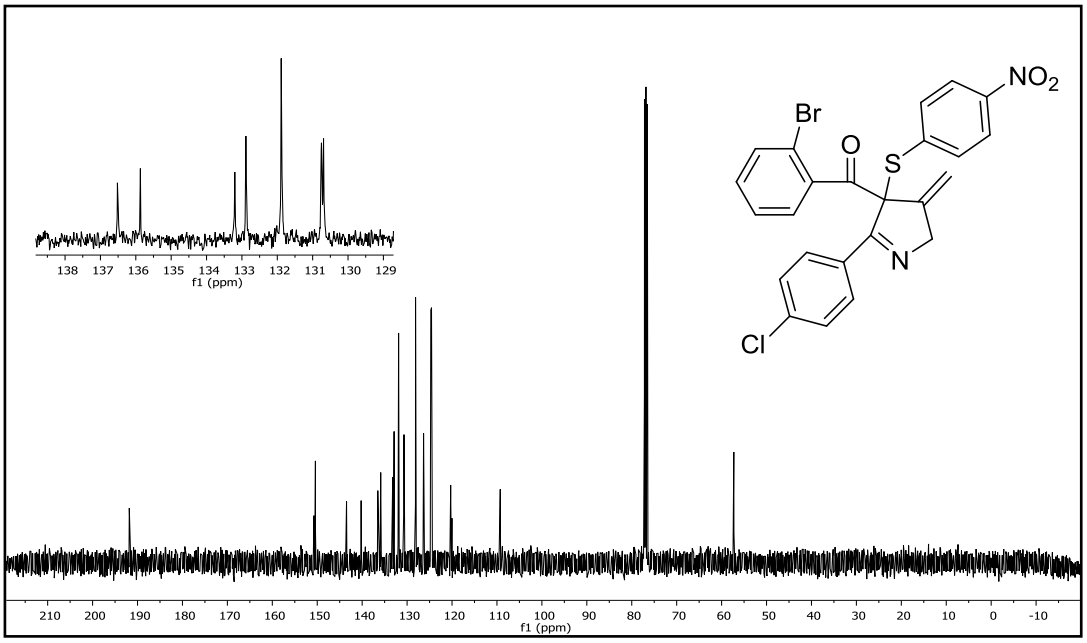

Figure 128. ^{13}C NMR spectrum of compound **32N**.

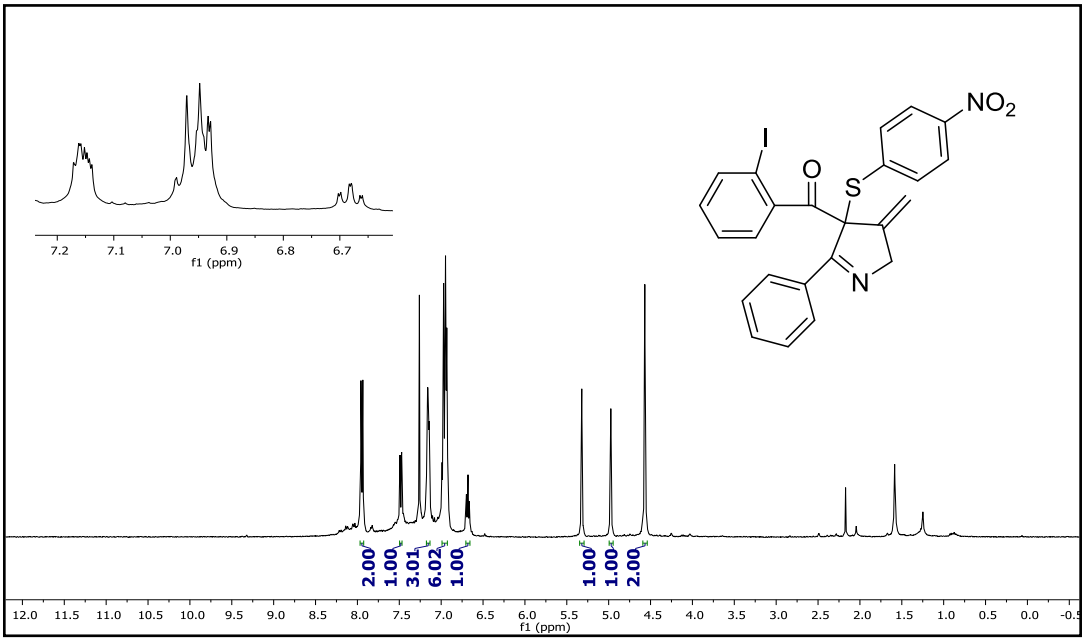

Figure 129. ^{1}H NMR spectrum of compound **32O**.

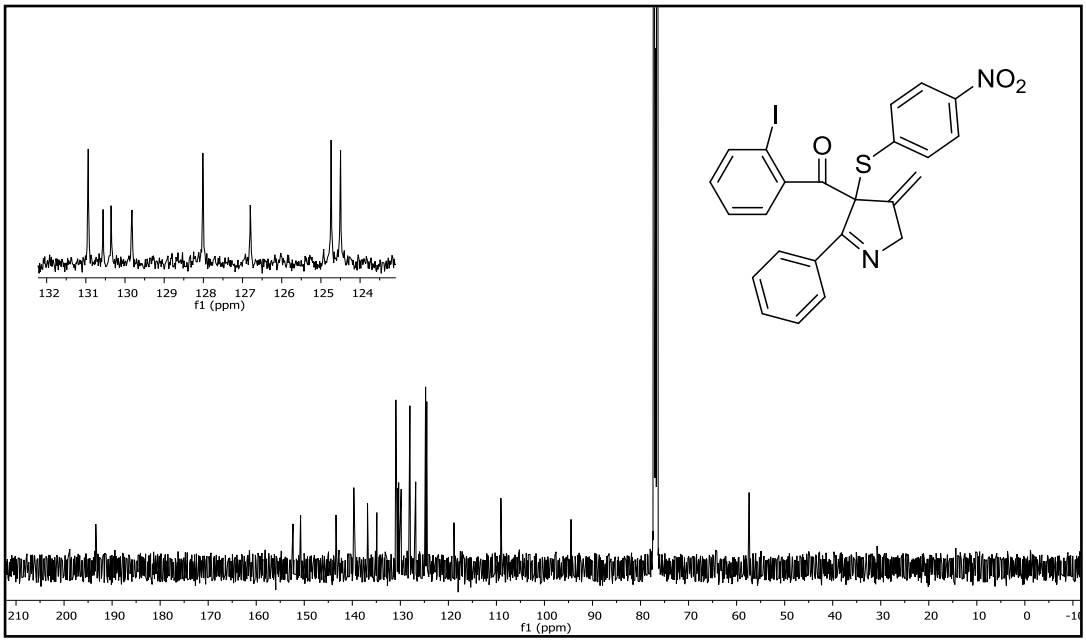

Figure 130. ^{13}C NMR spectrum of compound **32O**.

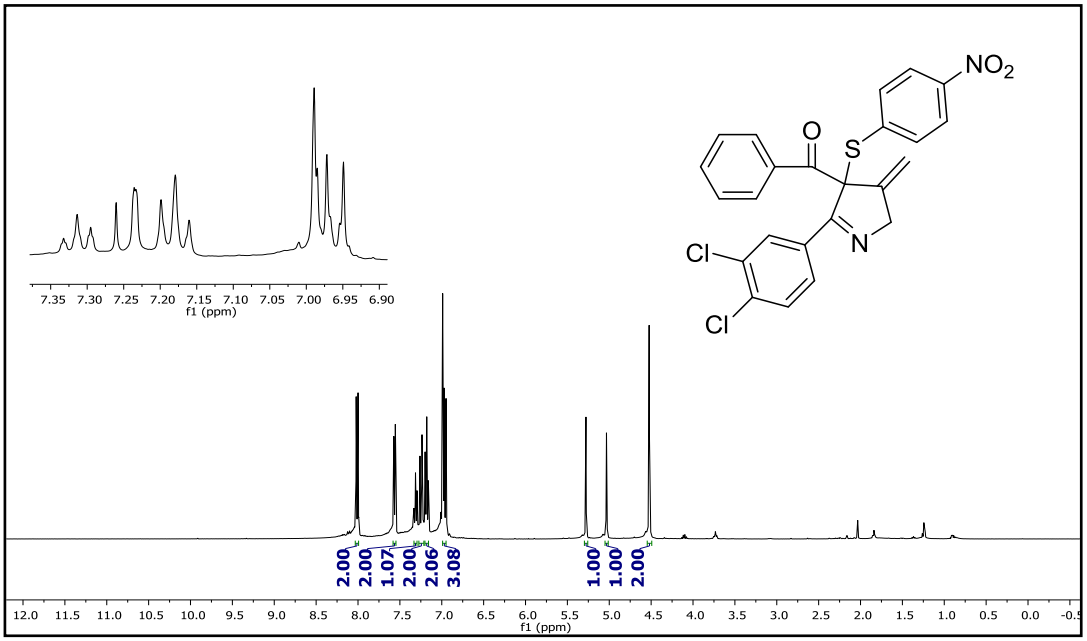

Figure 131. ^{1}H NMR spectrum of compound **32P**.

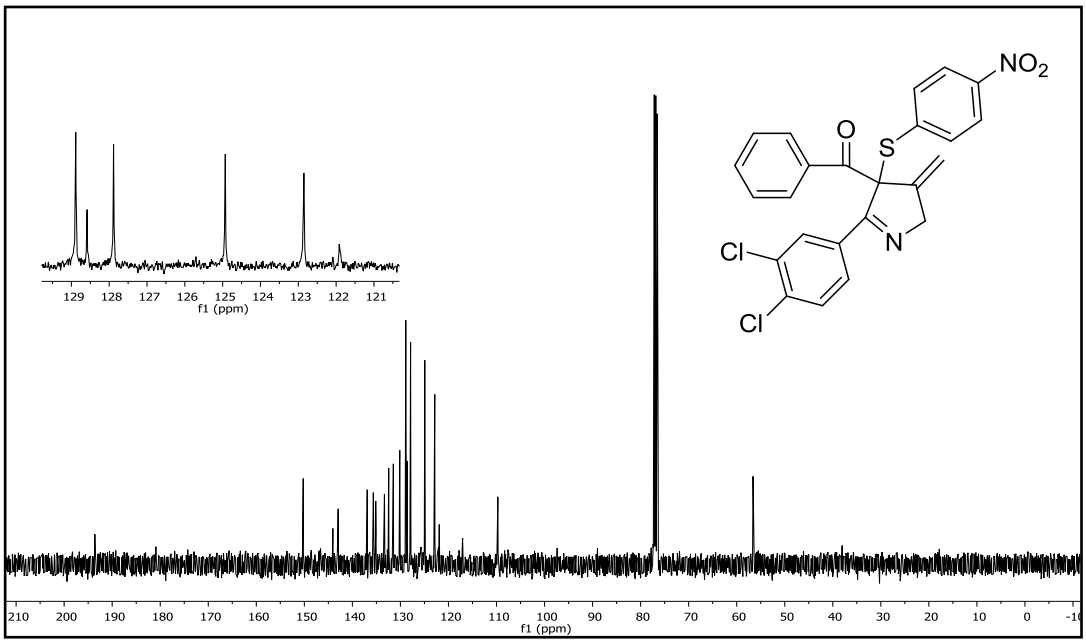

Figure 132. ^{13}C NMR spectrum of compound **32P**.

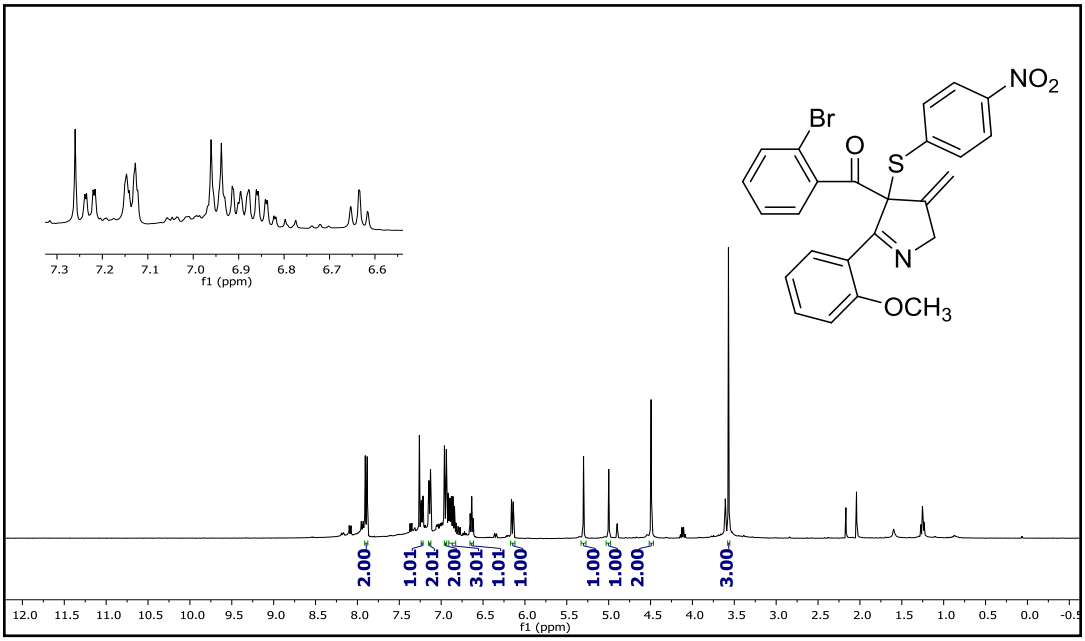

Figure 133. ^{1}H NMR spectrum of compound **32Q**.

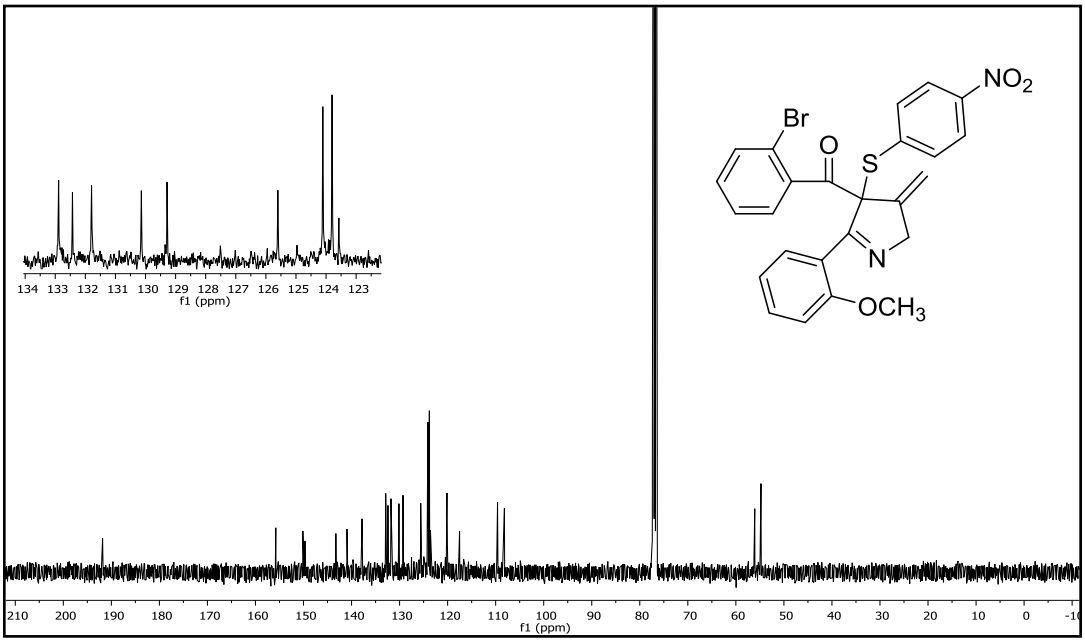

Figure 134. ^{13}C NMR spectrum of compound **32Q**.

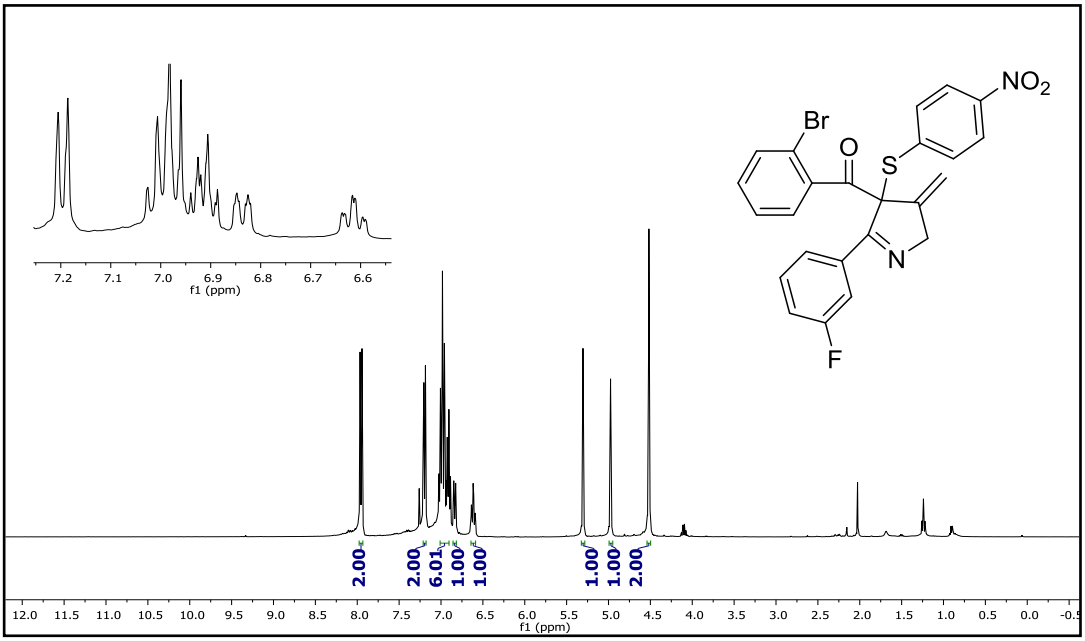

Figure 135. ^{1}H NMR spectrum of compound **32R**.

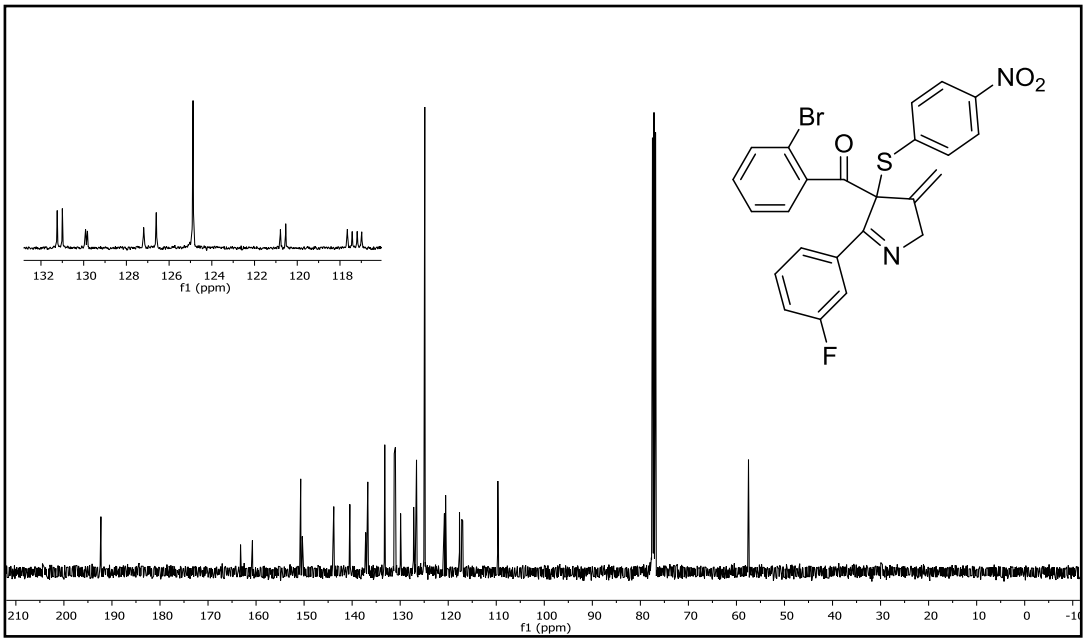

Figure 136. ^{13}C NMR spectrum of compound **32R**.

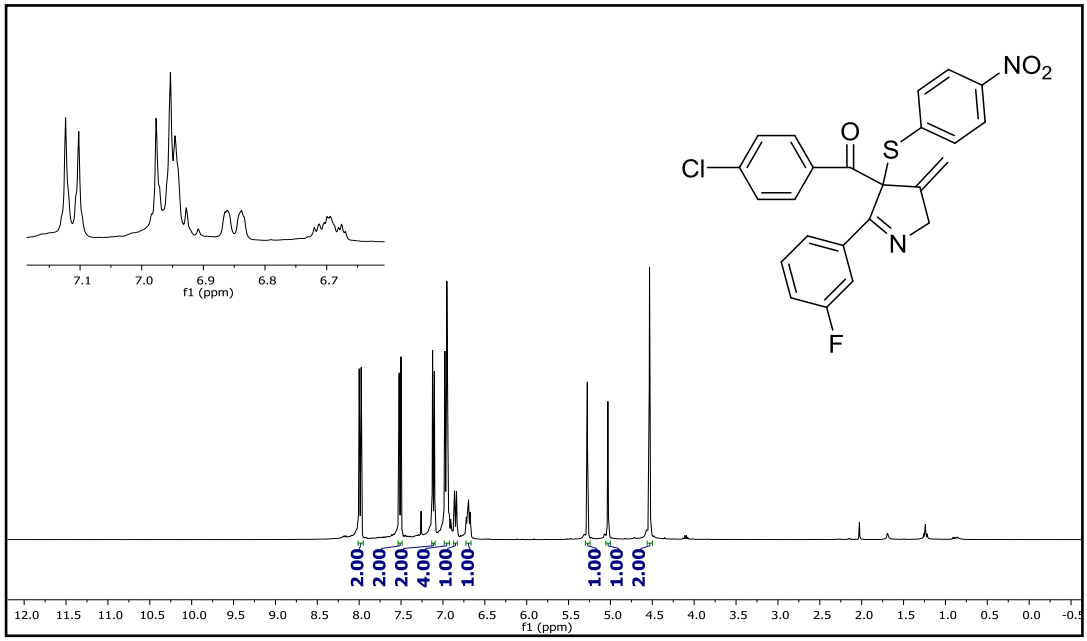

Figure 137. ^{1}H NMR spectrum of compound **32S**.

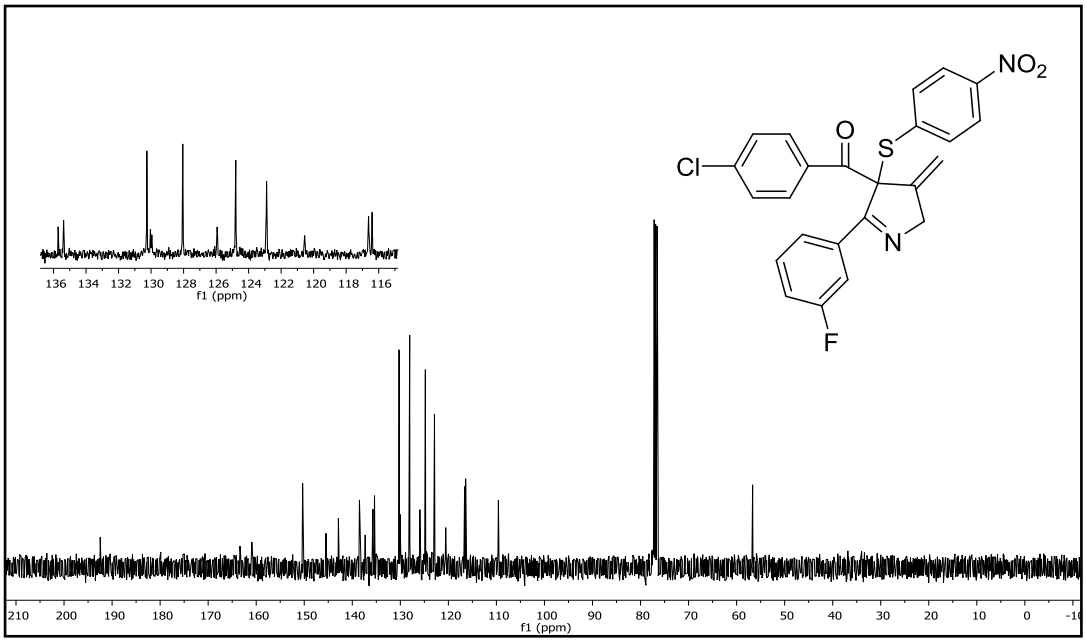

Figure 138. ^{13}C NMR spectrum of compound **32S**.

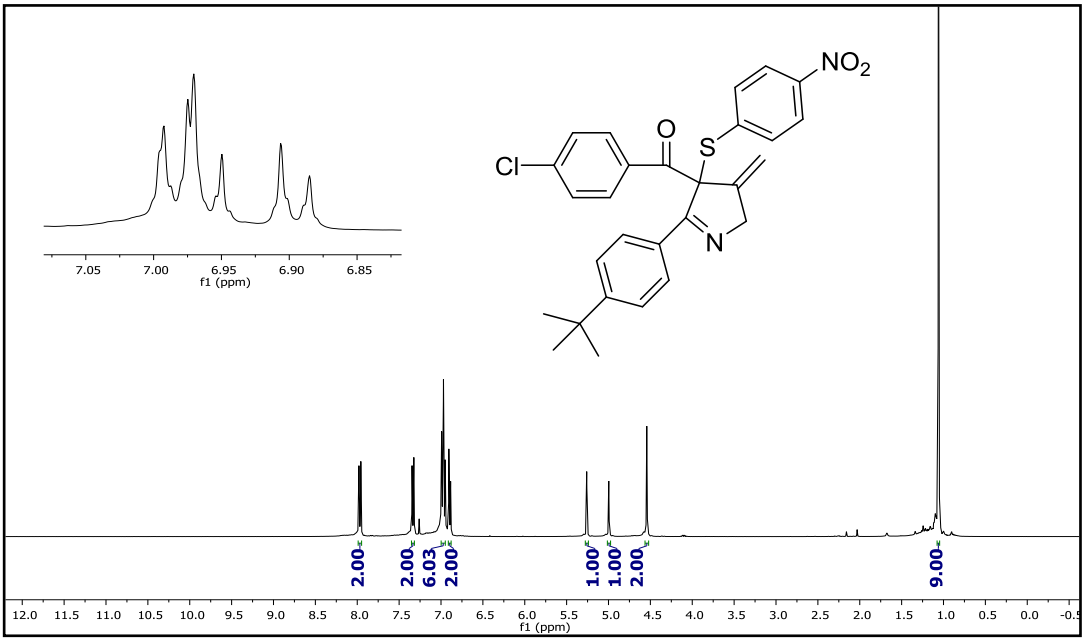

Figure 139. ^{1}H NMR spectrum of compound **32T**.

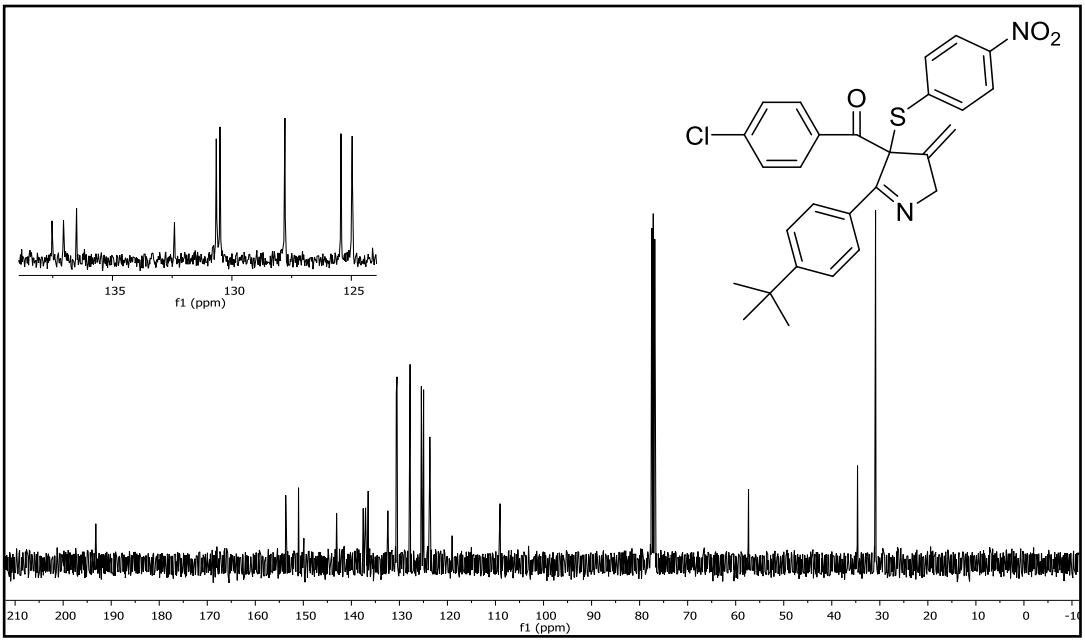

Figure 140. ^{13}C NMR spectrum of compound **32T**.

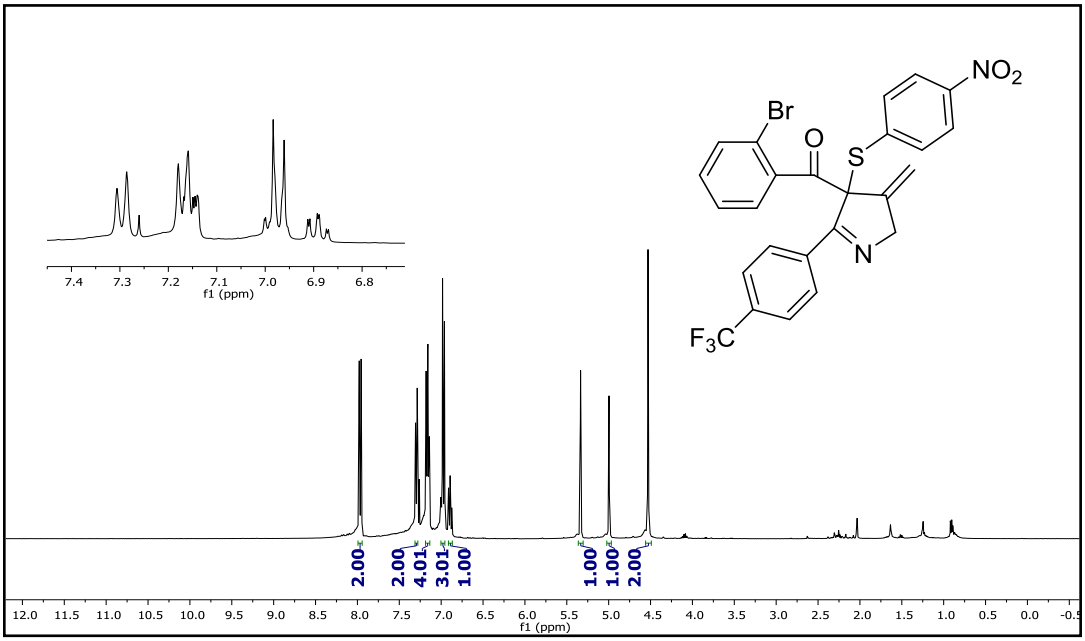

Figure 141. ^{1}H NMR spectrum of compound **32U**.

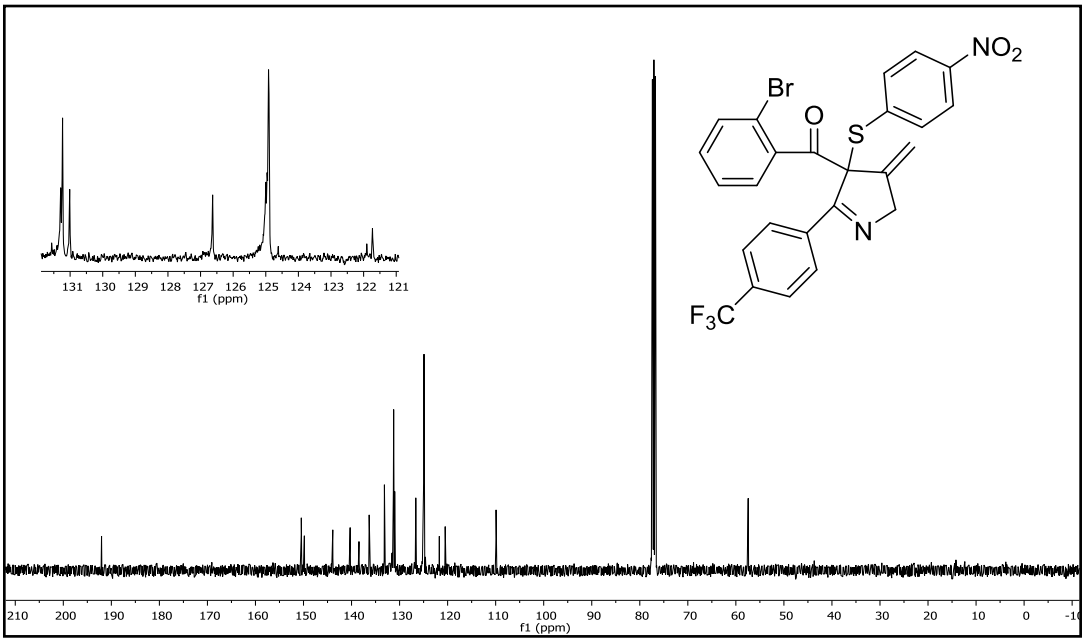

Figure 142. ^{13}C NMR spectrum of compound **32U**.