# Reactivity Control of Alkenes, Alkynes and Alcohols for C–S Bond Formation Reactions


*By*

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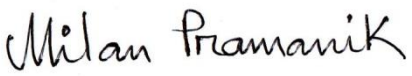

Milan Pramanik

# DECLARATION

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

Milan Pramanik

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12. **Pramanik, M.**; Mal, P., "C-S Bond Formation Reaction by C-H Functionalization" Wiley 2021, *In Press* (Book Chapter)

13. S, Sau[†].; Pramanik, M[†].; Mal, P., "The Reported Hydrofunctionalization Reactions that Proceed in the Absence of Catalyst: The Importance of Control Experiment" .([†]Equally contributed) *The Chemical Record*, **2021,** DOI: org/10.1002/tcr.202100208.

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2. **Poster Presentation:** Frontier in Chemical Science (FICS-2018) at IIT Guwahati on (6-8)$^{th}$ December 2018, Title: 'N-iodosuccinimide as Bifunctional Reagent in (E)-Selective C($_{sp2}$)–H sulfonylation of Styrenes'
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Milan Pramanik

*Dedicated*

*To*

# *My Parents*

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*...Milan Pramanik*

# CONTENTS

# SUMMARY

Chemists have the unremitting curiosity to conceptualize new reactivity paradigms towards shortening and modifying synthetic routes for the construction of molecular architecture *via* applying milder reaction conditions, utilizing new synthons, enhancing atom and step-economic processes, etc. In this context, the central focus of this thesis describes the reactivity of alkenes, alkynes, and alcohols in C–S bond formation reactions. Various sustainable tactics like the use of N-iodosucinimide (NIS) as iodine reagents, utilization of non-covalent interactions as the driving force, and use of visible light photocatalyst were operated to control C–S bond formation reaction. Initially, we started our journey with styrenes as an alkene source for the formation of (*E*)-selective vinyl sulfones. To our delight, the addition of styrene into aryl sulfonyl hydrazine in the presence of NIS (2.5 equiv) and $K_2CO_3$ (1.5 equiv) at 70 $^oC$ temperature under an open atmosphere could provide (*E*)-selective vinyl sulfones. In this particular reaction, NIS has shown here dual role: a) generation of sulfonyl radical; b) for iodination to afford *β*-iodo sulfone as one of the intermediate. At the final step, $K_2CO_3$ was used for the elimination of HI from *β*-iodo sulfone to produce final (*E*)-vinyl sulfones as a product. Overall, a mild and convenient approach was introduced for controlling the reaction of alkenes like styrenes. Again, moving on to the reactivity of alkynes, it has been understood that co-operative non-covalent interaction like H-bonding interaction could help to control the regio- and stereo-selectivity of internal alkynes. Pleasingly, neat mixing of thiophenol to *N*,3-diphenylpropiolamide as internal alkyne could provide (*Z*)-*anti*-Markovnikov vinyl sulfides *via* N-H…S H-bonding. Again, when 2-amino thiophenol was taken, due to N-H…N type H-bonding interaction switching of selectivity from (*Z*)-*anti*-Markovnikov to (*Z*)-Markovnikov vinyl sulfide was observed. In continuation, we also

sought to examine the reactivity of terminal alkynamide via using appropriate non-covalent interaction. In this case, newly identified S…O interaction was responsible for controlling the (*Z*)-selectivity of vinyl sulfides when the reaction of terminal propiolamide and thiols were carried out in the presence of $^{t}$BuOLi in ethanol within 10 min. It was anticipated that S…O interaction was originated from the delocalization of lone pair of carbonyl oxygen to σ-hole of sulfur of C–S. In the final chapter, we have also discussed the use of photocatalysis for the C–S bond formation reaction from benzyl alcohol *via* C-O bond functionalization. To our delight, when benzyl alcohol and thiols were irradiated under 3W blue LEDs and in the presence of 5 mol % 9-mesityl-10-methylacridinium perchlorate organophotocatalyst, dithioacetals or thioethers was observed. Several control experiments also revealed that excited state photocatalyst could take part in the single electron transfer (SET) process with benzyl alcohol and molecular oxygen. Thus, the reactivity of benzyl alcohol was also controlled by using an appropriate photocatalyst.

# LIST OF SCHEMES

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## List of Abbreviations Used

| | |
|---|---|
| Å | Angstrom |
| Ar | Aryl/Aromatic |
| Ac | Acetyl |
| br | Broad |
| BHT | Butylated hydroxy toluene |
| ºC | Degree Celcius |
| Calcd | Calculated |
| cm | Centimeter |
| d | Doublet, Days |
| DBU | 1,8-Diazabicyclo-(5.4.0)-undec-7-ene |
| DCE | 1,2-Dichloroethane |
| DCM | Dichloromethane |
| dd | Doublet of a Doublet |
| Dil | Dilute |
| DMF | *N*,*N*-Dimethyl Formamide |
| DMAc | Dimethyl acetamide |

| | |
|---|---|
| DMPO | 5,5-Dimethyl-1-pyrroline N-oxide |
| DMSO | Dimethyl Sulfoxide |
| DTBP | Di-tert-butyl peroxide |
| DFT | Density Functional Theory |
| Equiv | Equivalent |
| ESI-TOF | Electrospray ionization time-of-flight |
| Et | Ethyl |
| EtOAC | Ethyl Acetate |
| EtOH | Ethyl Alcohol |
| g | Grams |
| h | Hours |
| HFIP | 1,1,1,3,3,3-Hexafluoro-2-propanol |
| HRMS | High-Resolution Mass Spectrometry |
| $H_2O$ | Water |
| Hz | Hertz |
| IR | Infrared |
| $K_2S_2O_8$ | Potasium persulfate |
| NIS | *N*-iodosuccinimide |
| NCS | *N*-chlorosuccinimide |
| MeCN | Acetonitrile |
| mp | Melting point |
| Me | Methyl |
| Min | Minutes |
| mL | Milliliter |
| mmol | Millimole |
| mol | Mole |
| M | Molar |
| m | Multiplet |
| MS | Mass Spectra, Molecular Sieves |
| M/Z | Mass to charge ratio |
| nm | Nanometer |

| | |
|---|---|
| NMR | Nuclear Magnetic Resonance |
| [O] | Oxidation |
| $O_2$ | Oxygen |
| OTf | Trifluromethanesulfonate |
| Py | Pyridine |
| Ph | Phenyl |
| rt | Room Temperature |
| s | Singlet, Seconds |
| *t* | *Tert* |
| TBHP | Tert-Butylhydroperoxide |
| TBAI | Tetrabutylammonium iodide |
| TEMPO | (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl |
| TEC | Thiol-Ene-Click |
| TFE | 2,2,2-Trifluoroethanol |
| THF | Tetrahydrofuran |
| TLC | Thin Layer Chromatography |
| TMS | Trimethylsilyl |
| Ts | *p*-Toluenesulfonyl |
| TFA | Trifluoroacetic acid |
| TYC | Thiol-Yne-Click |
| XRD | X-Ray Diffraction |

# CHAPTER 1

# Importance of Organo-Sulfur Compounds and Their Synthesis

## 1.1 ABSTRACT

This chapter summarizes a concise overview of organo-sulfur compounds and strategies for their synthesis. The chapter is categorized into two main parts: (i) the significance of sulfur in daily life and (ii) brief notes on the organo-sulfur reagents and their uses in C–S bond formation reactions. The second part is also classified into four sub-categories based on the sustainable strategies: (i) iodine reagent mediated metal-free C–S bond formation reaction, (ii) non-covalent interaction controlled C–S bond formation reaction, (iii) visible-light-driven photocatalytic C–S bond formation reaction, and (iv) electrochemical oxidative C–S bond formation reaction. Finally, the chapter is concluded with a brief outline of the research focus of the current thesis.

## 1.2 INTRODUCTION

Sulfur is recognized from ancient times as the 10$^{th}$ most abundant element per weight and the 5$^{th}$ highest element on earth[1]. It is found on earth as a sulfate mineral and also exited in a pure native form. It is relatively rare in the Earth's layer (~ 6%). Generally, elemental sulfur[2] is located on earth, including hydrothermal vents, salt domes, hot springs, volcanic emissions, etc. In olden times, the counties such as India, China, Greece, and Egypt used to exploit sulfur as an ignition source in the spiritual ceremonial due to its abundance in native form. Sulfur is also called

brimstone[3], or burn stone. In 1777, an alchemist Antoine Lavoisier, recognized sulfur which was basically an element, however, not a compound in terms of the principle of combustibility. Later on, French chemists Joseph Gay-Lussac and Louis Thenard envisioned its elemental properties. Indeed, sulfur is an element symbolized as 'S' with atomic number 16. It mainly belongs to p-block, group 16 in the periodic table with electronic configuration $[Ne]3s^2 3p^4$. Therefore the common oxidation state of sulfur varies from -2 to +6. Again, because of its electropositive nature, large size, and amphoteric behavior, sulfur can form a stable compound with all types of elements except noble gas. It can form multivalent compounds with electronegative elements such as oxygen[4], nitrogen[5], pseudo halide[6,] or sulfur[7] too. Sulfur forms octasulfur as allotropes, and it burns in the presence of blue flame to form sulfur dioxide.

## 1.3 SULFUR IN DAILY LIFE

Sulfur is one of the essential elements found in all living bodies. Next to calcium (Ca) and phosphorus (P), it is also the 3rd most abundant mineral in the human body. It is found within the body in the form of organosulfur compounds like proteins[8], amino acids[9], etc. Among 20 amino acids, sulfur-containing amino acids are cysteine and methionine. Among vitamins, biotin and thiamine also contain sulfur. National Academics Food and Nutrition Board have identified that a human body needs 0.2-1.5 g of sulfur per day. Our nature always stands for us with an enriched source of sulfur[10] as a structure of fruits and vegetables (Figure 1.1).

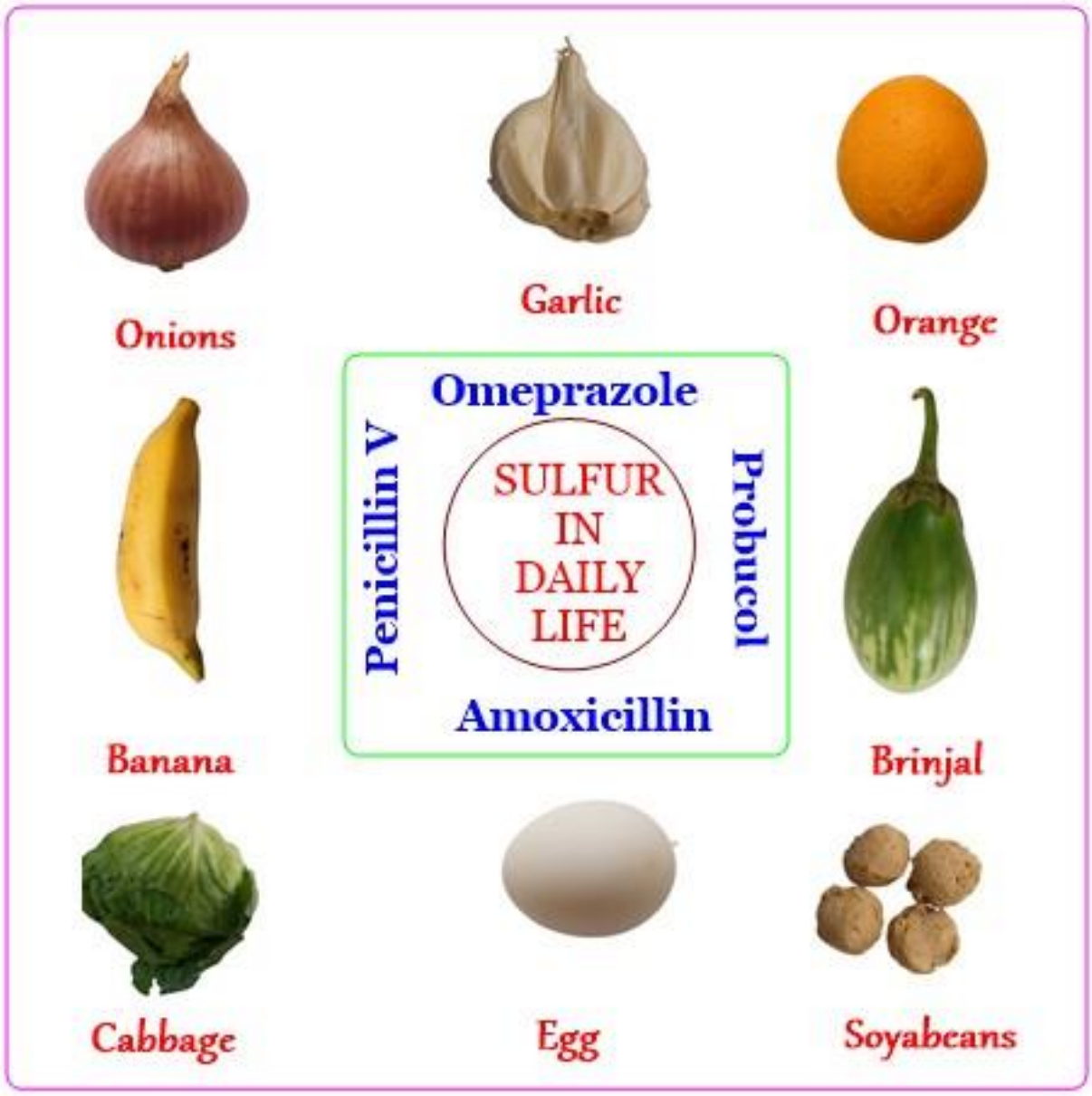



**Figure 1.1.** Few examples of natural organo-sulfur compounds used in daily life.

In addition, organosulfur compounds are omnipresent in varieties of natural products, and they are also widely used in the pharmaceutical industry, agrochemicals, material sciences, and medical sciences[11]. Some of the commercial drug candidates, such as Omeprazole, Penicillin V, Amoxicillin, ATI2 (Ativan), Nelfinavir, etc., are used to treat diseases like gastric disorder, bacterial infection, anxiety, and HIV, respectively (Figure 1.2).

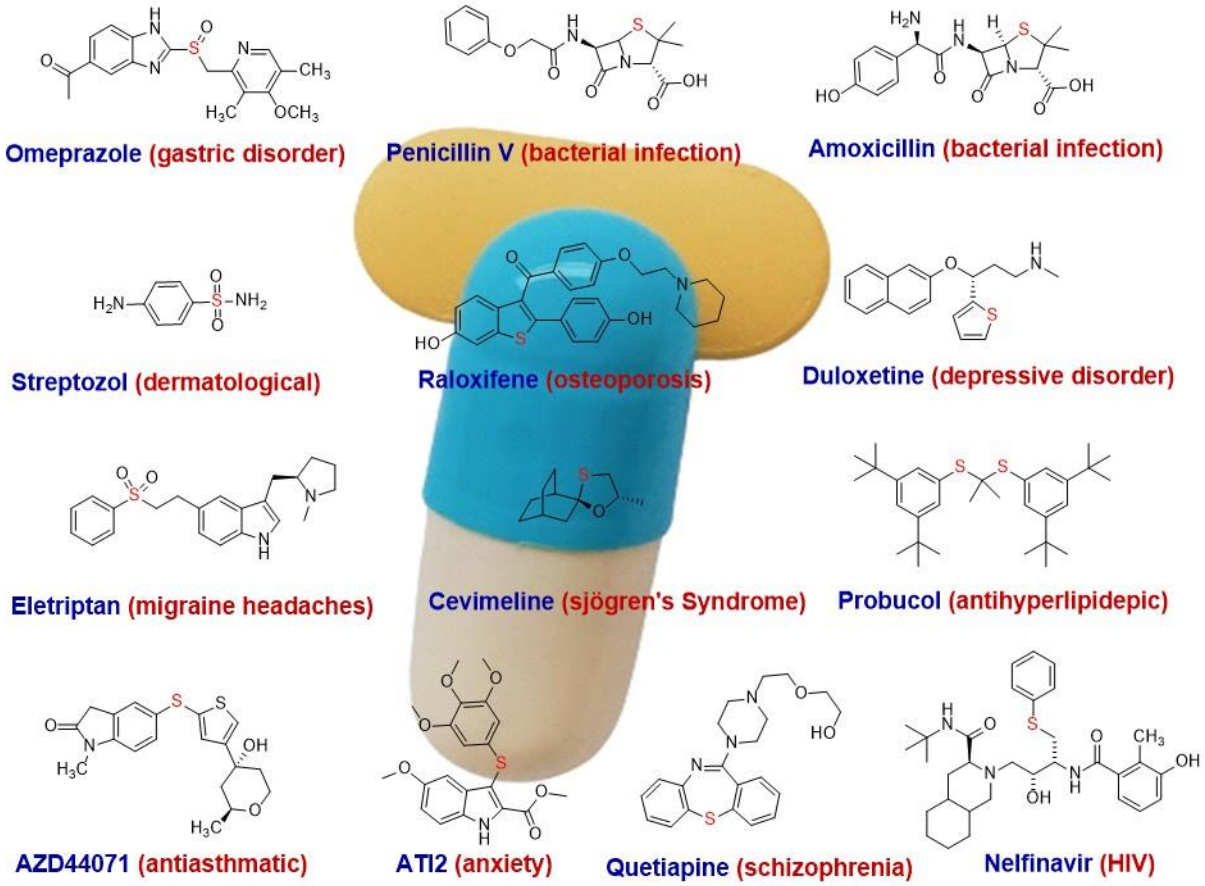



**Figure 1.2.** Few examples of pharmaceutically active sulfur-based drugs.

## 1.4 SULFUR PRECURSORS AND THEIR USE IN C–S BOND FORMATION REACTIONS.

Sulfur precursors are mainly classified into two categories: a) organo-sulfur reagents such as thiophenol, aryl sulfonyl hydrazine, etc. b) salt of sulfur such as $PhSO_2Na$, $Na_2S$, etc. Herein, we have mainly covered organo-sulfur precursors which are used to construct C–S bonds under mild reaction condition[12]. Figure 1.3 displays examples of organo-sulfur reagents (thiophenol, elemental sulfur, thiosuccinimide, thiobenzoic acid, benzene sulfonic acid, sulfonyl chloride, sulfonyl hydrazine, diphenyl disulfide, benzenesulfonothioate, dimethyl sulfoxide, etc.) used in

C–S bond formation reactions. We have subjectively selected some samples of organo-sulfur precursors, which are commercially available or very easy to prepare.

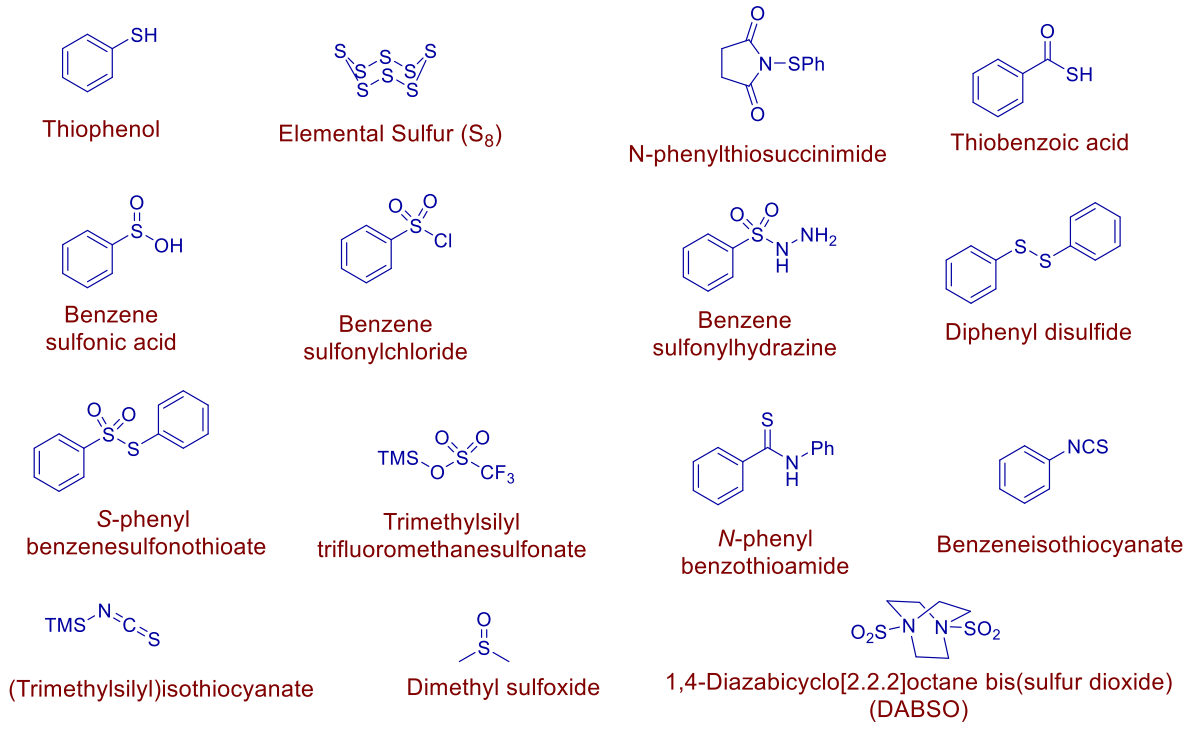



**Figure 1.3.** Commonly used sulfur precursors for C–S bond formation reactions.

Our planet always faces critical challenges due to pollution from different aspects like hazardous chemicals used in the chemical industry. Therefore, it is very urgent to find out more sustainable resources which can minimize global pollution. Transition metal-catalyzed carbon-sulfur (C–S) bond formation reaction has significantly expanded the synthetic toolbox in the organic research field since 1960[11]. It catches immense achievement[13] by obtaining Nobel Prize in 2010. Notwithstanding, there are huge limitations, challenges, and drawbacks observed in metal-catalyzed reactions. First of all, transition metal catalysts and ligands are expensive, tricky to prepare. Second, most of them are toxic. Therefore, the consumption of transition metal does not lead to the sustainability of the reaction condition. Third, the removal of trace amounts of metal

catalysts from the reaction is challenging and tricky as well. As a result, this strategy is not recommended for the pharmaceutical industry. Fourth, most importantly, many transition metals are unstable in air and moisture sensitive, thus, required an inert reaction environment. Fifth, the requirement of co-catalyst and additives make the procedure amateur and sporadic. In this regard, the experimental chemist has an unrelieved effort to visualize a new reactivity archetype to make greener methods in constructing organic molecules. Therefore, we have herein considered methodologies for C–S bond formation reaction in terms of sustainable chemistry. The examples are classified into four categories: i) iodine reagent mediated metal-free C–S bond formation reactions, ii) non-covalent interaction controlled C–S bond formation reactions, iii) visible-light-driven photocatalytic C–S bond formation reactions, and iv) electrochemical oxidative C–S bond formation reactions.

### 1.4.1 Iodine reagent mediated metal-free C–S bond formation reactions.

Because of the persistent pursuit of sustainable and green methods, step chasing new conditions and new reactivity towards efficient and selective transition- metal- free C–S coupling reaction by using iodine reagents would expect to be never ceased. Herein, we have mainly focused on the use of various iodine reagents in the C–S coupling reactions. We have also summarized some of the iodine reagents which are commonly used for oxidative C–S coupling (Figure 1.4).

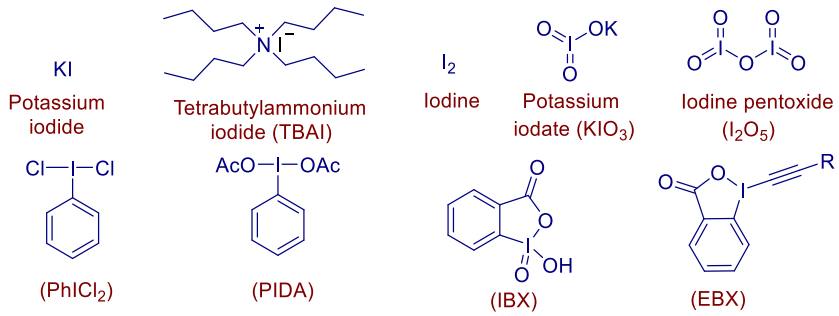
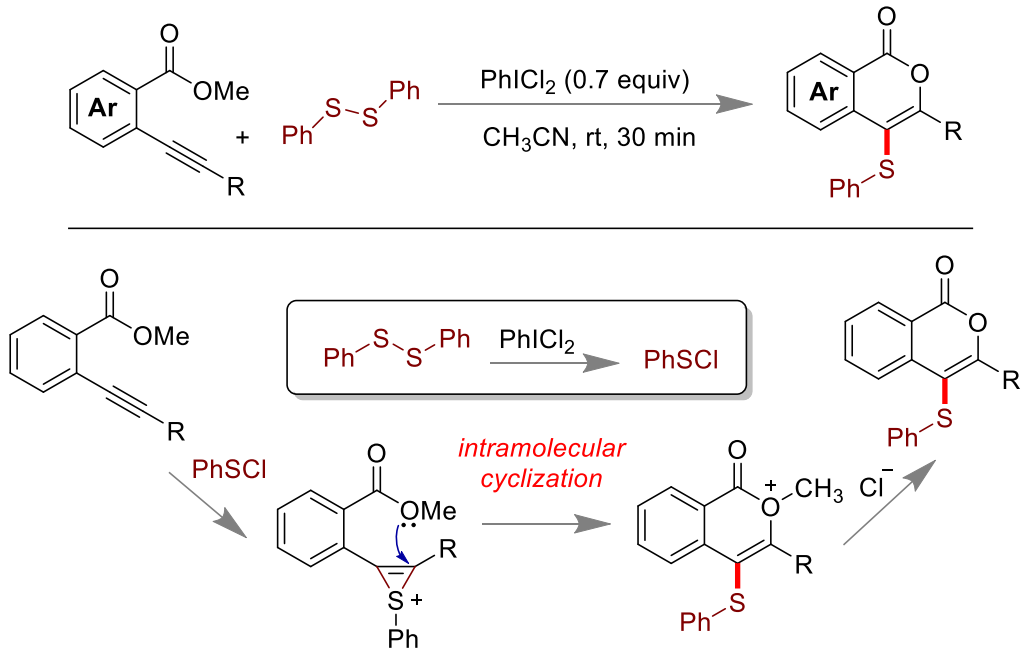



**Figure 1.4.** Iodine reagents used for C–S coupling reactions.

### 1.4.1.1 $PhICl_2$ mediated synthesis of sulfenylated isocoumarins.

Recently, Du's group demonstrated a regioselective synthesis of sulfenylated isocumarins from disulfides as sulfenylating agents and $PhICl_2$ as oxidant (Scheme 1.1)[14]. As described below, aryl sulfenyl chloride formed a cyclic intermediate in the presence of iodine reagent. Following, intramolecular cyclization by neighboring oxygen could lead to the formation of the final product.

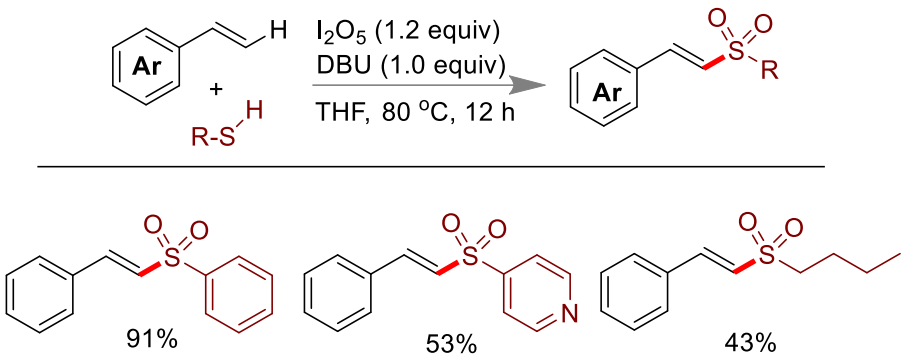



**Scheme 1.1.** Lei's approach for the synthesis of sulfenylated isocoumarin.

### 1.4.1.2 $I_2O_5$ mediated synthesis of (*E*)-vinyl sulfone from styrene and thiol.

Wang's group reported $I_2O_5$ mediated C–S coupling of olefins and thiols *via* oxidative pathway (Scheme 1.2)[15]. Here, $I_2O_5$ could help in the generation of sulfonyl radical as well as the formation of β-iodo sulfone as an intermediate. In this reaction, DBU was used in the final step for the elimination of hydro-iodic acid (HI), which led to the formation of the desired sulfone.

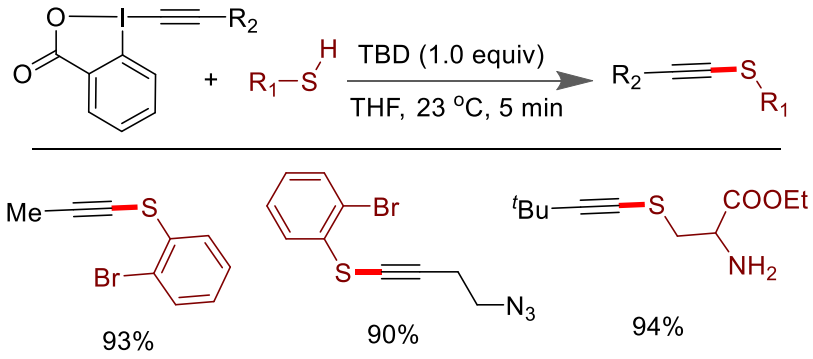
This methodology was well compatible with various thiols like aliphatic, aromatic, and hetero-aromatic thiols.




**Scheme 1.2.** Wang's work is based on the iodine-mediated synthesis of vinyl sulfone.

### 1.4.1.3 EBX mediated alkynylation of thiol.

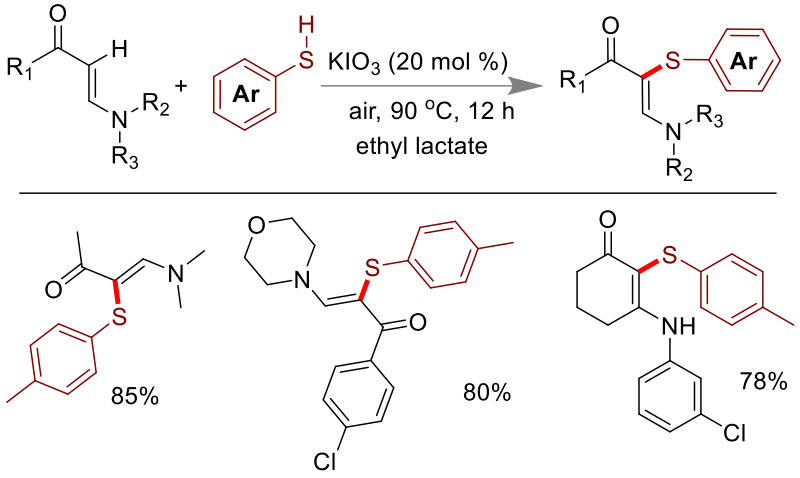
Waser's group has shown a strategy to functionalize thiol derivatives with ethynyl benziodoxolone (EBX) in the presence of 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) as a base (Scheme 1.3)[16]. The reaction was found to be efficient for varieties of alkynes and thiols with good to excellent yields.




**Scheme 1.3.** Waser's approach towards alkynylation of thiols by EBX.

### 1.4.1.4 $KIO_3$ catalyzed sulfenylation of enaminone.

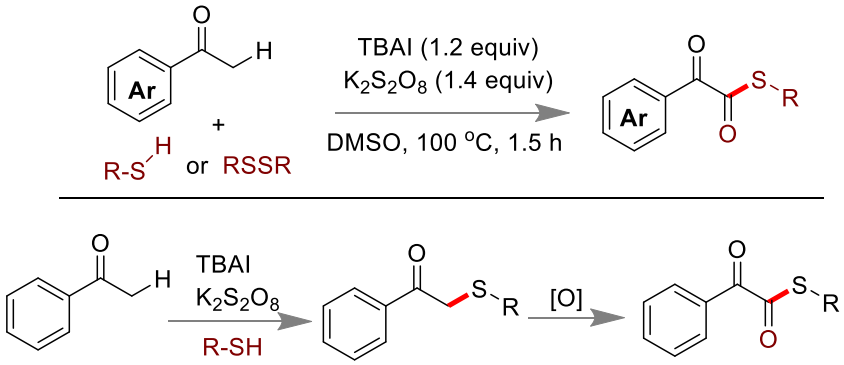
Potassium iodate ($KIO_3$) catalyzed C-H sulfenylation of enaminones was experienced by Wan's group *via* the *anti*-Michael pathway (Scheme 1.4)[17]. Aerial oxygen was used as a co-oxidant for this transformation. Substrate tolerability was found to be excellent.




**Scheme 1.4.** Wan's report for $KIO_3$ catalyzed sulfenylation of enaminones.

### 1.4.1.5 TBAI mediated thioesterification of a methyl ketone.

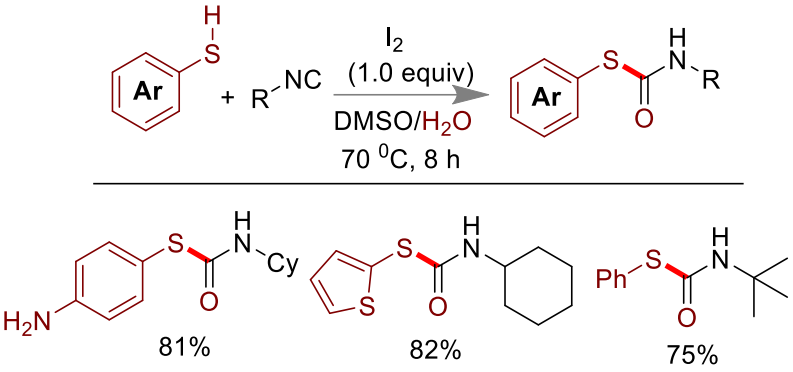
A direct $C_{sp3}$-H thioesterification of methyl ketones was demonstrated by Yan and co-workers using TBAI/ $K_2S_2O_8$ as reaction controller (Scheme 1.5)[18]. They have shown that a combination of TBAI/ $K_2S_2O_8$ could facilitate the SET process, which further resulted in C–S coupled product followed by oxidation to afford α-keto thioesterification as the desired product.




**Scheme 1.5.** Yu's report for oxidative thioesterification of methyl ketones.

### 1.4.1.6 Iodine-mediated synthesis of thiocarbamate.

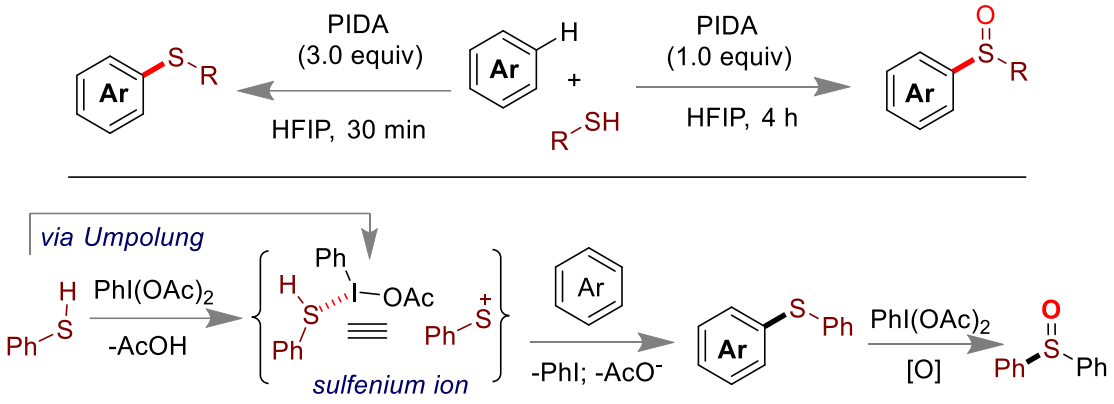
In 2018, He's group reported the iodine-mediated synthesis of thiocarbamates from thiols and isocyanides using water as an oxygen source (Scheme 1.6)[19]. This methodology was treated as excellent access for synthesizing thiocarbamates under metal-free and mild reaction conditions.




**Scheme 1.6.** He's report for the synthesis of thiocarbamates.

### 1.4.1.7 PIDA mediated synthesis of aryl thioether and aryl sulfoxide.

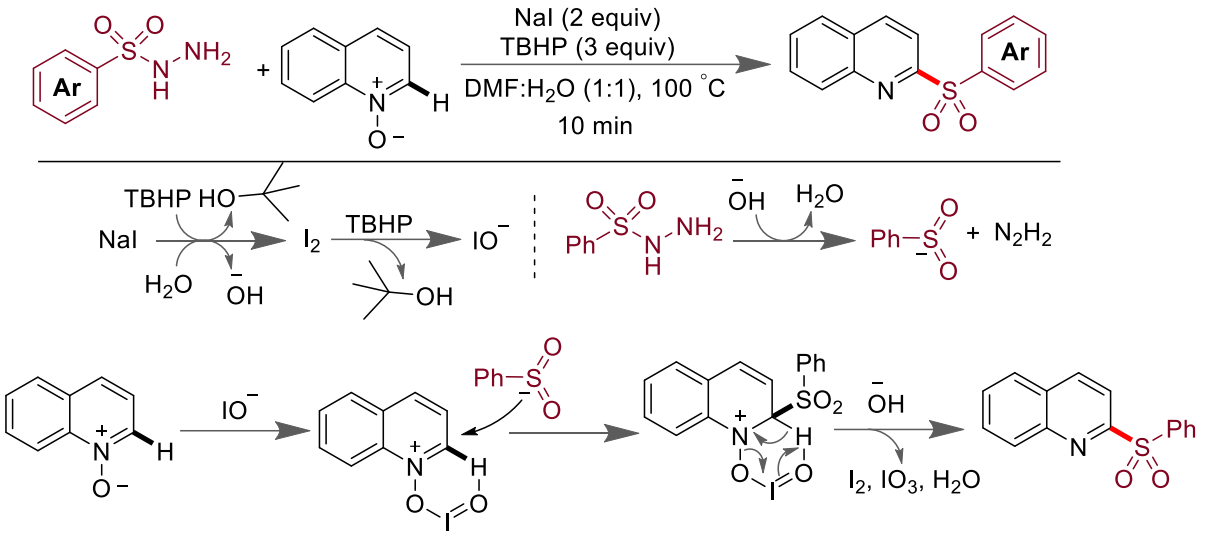
Mal and co-workers have established that synthesis of either thioethers or diaryl sulfoxides could be achieved from electron-rich arenes and thiophenols *via* the formation of sulfenium ion as intermediate (Scheme 1.7).[20] It was anticipated that sulfenium ions were generated from the treatment of thiols and iodine(III) reagent $PhI(OAc)_2$ (PIDA) in HFIP solvent. Subsequently, aromatic electrophilic substitution (EArS) between sulfenium ion and electron-rich arene led to diaryl sulfide as a product. Following, the addition of excess PIDA helped in the oxidation of sulfur center to produce diaryl sulfoxides as a product. They have also assumed that sulfenium ion intermediate was stabilized by HFIP through hydrogen bonding. Along with the remarkable hydrogen bonding capacity, HFIP also could ionize PIDA, which helped to accelerate the EArS reaction with electron-rich arenes.




**Scheme 1.7.** Mal's approach for dehydrogenative C–S coupling of arene and thiol.

### 1.4.1.8 NaI mediated $C_2$-sulfonylation of quinoline *N*-oxide.

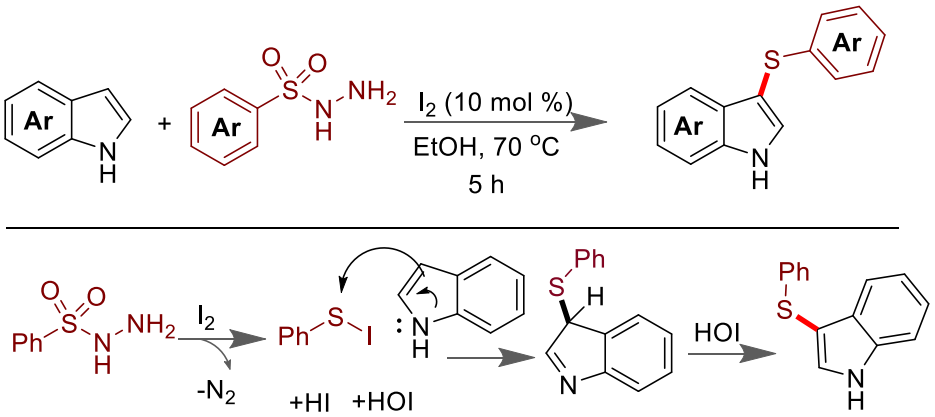
An efficient method for the Synthesis of $C_2$-sulfonylation pyridine *N*-oxide was established by He and co-worker[21]. In this protocol, quinoline *N*-oxide was treated with sulfonyl hydrazine in the presence of sodium iodide and TBHP in DMF: $H_2O$ (1:1) at 100 $^oC$ temperature, which led to the formation of $C_2$-sulfonylated quinoline (Scheme 1.8). Interestingly, NaI and TBHP combination was served as an efficient generator of phenyl sulfenium anion, which further reacted with quinoline *N*-oxide to form a six-membered intermediate followed by nucleophilic attack from sulfenium anion, led to producing $C_2$-sulfonylated quinoline.




**Scheme1.8.** He's approach for $C_2$-sulfonylation of quinoline *N*-oxide.

### 1.4.1.9 Iodine mediated $C_3$-sulfenylation of indole.

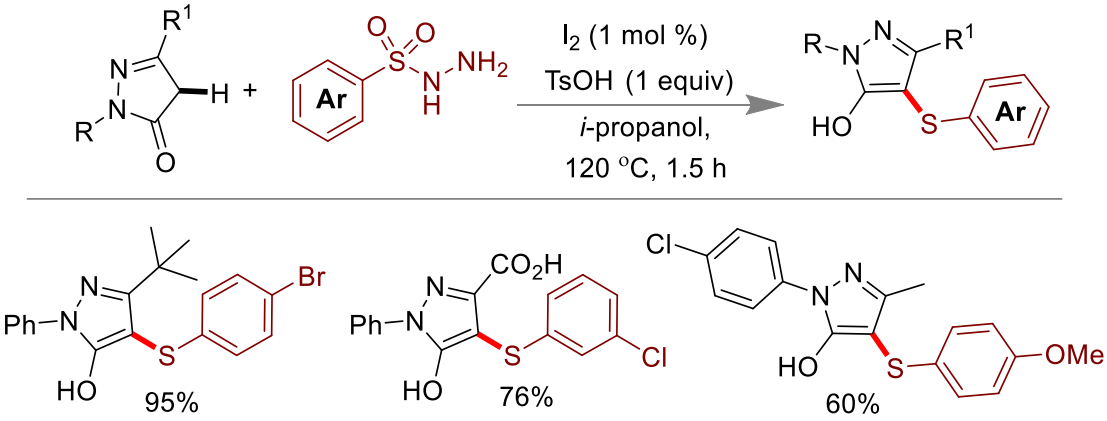
Tian and co-workers have introduced a method for regioselective sulfenylation of indoles using aryl sulfonyl hydrazine as sulfenylating source and 10 mol % molecular iodine as oxidant (Scheme 1.9)[22]. As shown below, PhSI could be generated from the reaction of aryl sulfonyl hydrazine and iodine. Following, nucleophilic attack by indole to PhSI, resulted in sulfenylated indole derivatives.




**Scheme 1.9.** Tian's approach for $C_3$-sulfonylation of indole.

### 1.4.1.10 Iodine mediated synthesis of pyrazolone thioether.

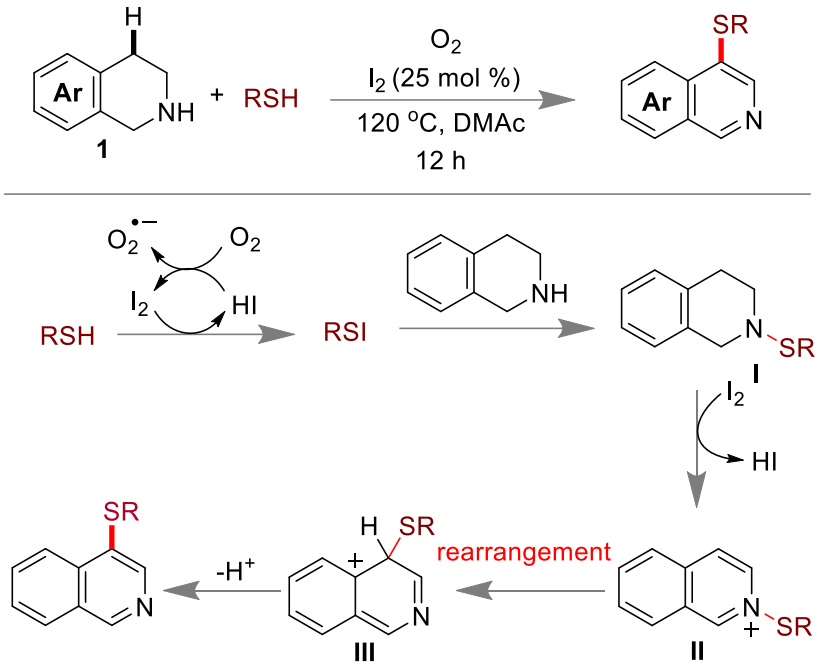
Zhao's group has shown that the C–H functionalization of pyrazolone with aryl sulfonyl hydrazine in 1 mol % iodine and tosyl sulfonic acid (1equiv) led to the formation of pyrazolone thioethers (Scheme 1.10)[23]. The reaction displayed high functional group tolerance by providing pyrazolone thioethers with good to excellent yields.




**Scheme 1.10.** Zhao's approach for pyrazolone thioethers.

### 1.4.1.11 Iodine promoted *β*-Thiolation of piperdine.

Lei and co-workers have described iodine promoted oxidative C($sp^3$)–H thiolation of piperdine (Scheme 1.11)[24]. Authors have proposed that molecular iodine and aerial oxygen helped in oxidative N-S bond formation followed by aromatization and rearrangement with the help of iodine to provide thioled isoquinolines.




**Scheme 1.11.** Lei's approach for C($sp^3$)-H thiolation of piperdine.

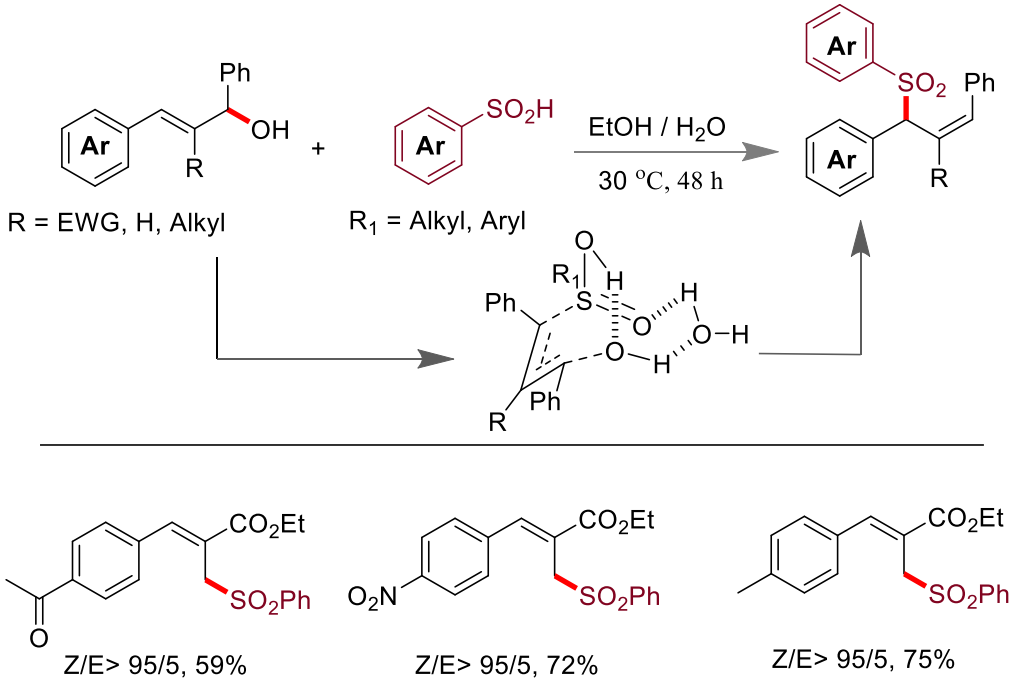
## 1.4.2 Non-covalent interaction controlled C–S bond formation reactions.

To understand the role of non-covalent interaction[25, 26] in a chemical reaction, click chemistry[27], system chemistry[28], and supramolecular approaches have gained enormous attention in the chemical community. Indeed, stabilization of reactive intermediate through the use of non-covalent interactions[29] like halogen bonding[30, 31], anion-π[32], hydrogen bonding[33-35], π- π stacking[36] is significant as well as highly desirable because many complicated reactions could be performed easily. In this regard, our major research focus is to find out how do the multiple non-covalent interactions control a chemical reaction to move it in a forward direction?

### 1.4.2.1 Hydrogen bonding assisted allylic sulfonylation reaction.

Recently Loh's group experienced a water-promoted allylic sulfonylation reaction of sulfinic acid in a highly regioselective manner (Scheme 1.12)[37]. It has been proposed that H-bonding

interactions led to the formation of a six-membered cyclic transition state within the hydroxyl group of allylic alcohol, sulfinic acid, and water. Thus, co-operative non-covalent interaction helped to enhance not only the nucleophilicity of sulfinic acid but also to activate the C-O bond *via* the elimination of the hydroxyl group. This unique methodology served as excellent functional group tolerance for the carbonyl group, electron-donating, electron-withdrawing, hetero-substituted allylic alcohol, and aliphatic sulfinic acid.

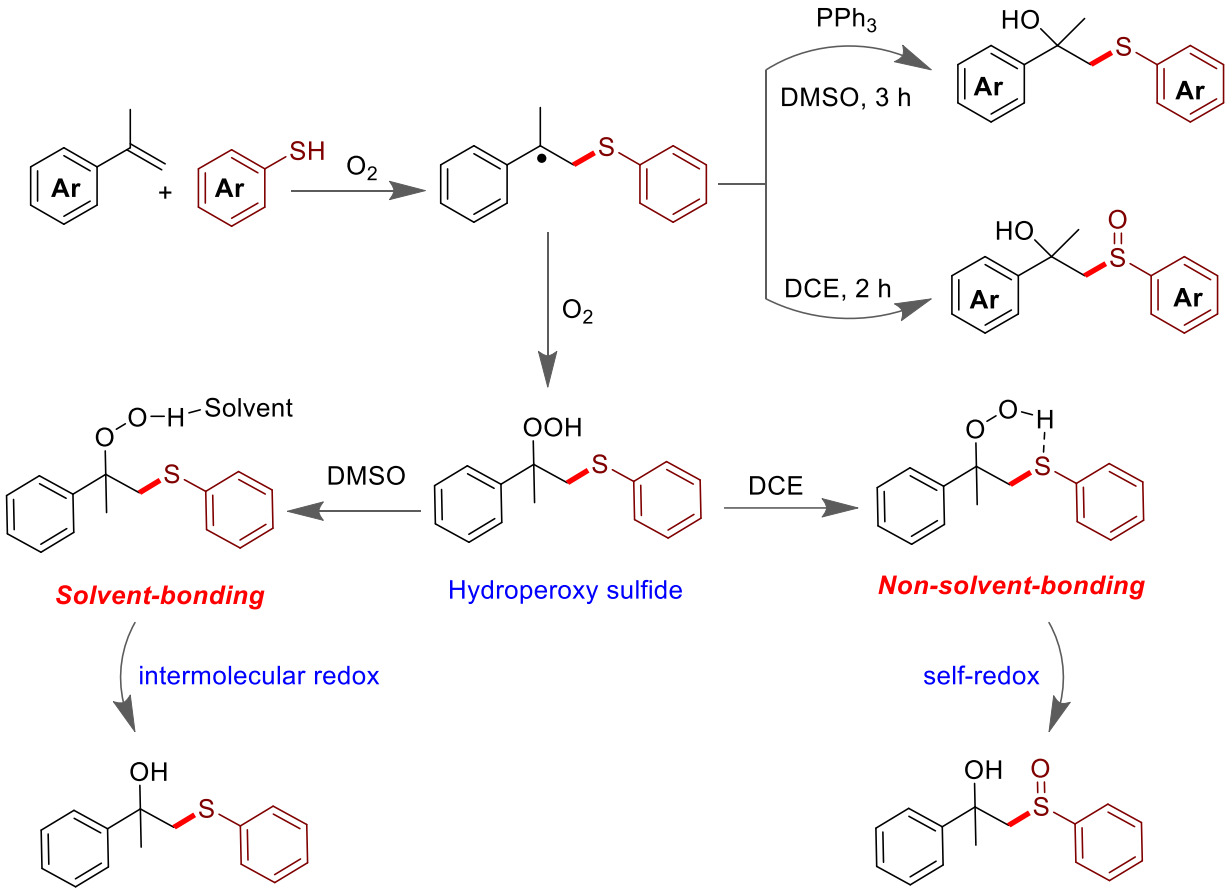



**Scheme 1.12.** Loh's approach for allylic sulfonylation reaction of sulfinic acid.

### 1.4.2.2 Solvent bonding in the synthesis of β-hydroxy sulfides and sulfoxides.

In 2016, Lei described a radical-mediated synthesis of β-hydroxy sulfides and sulfoxide from alkene and thiophenol through solvent bonding (Scheme 1.13)[38]. Interestingly, solvent-solute interaction experienced to have β-hydroxy sulfides product selectively. It has been shown that weakly hydrogen bonding solvents such as $CHCl_3$, DCE preferred to get β-hydroxy sulfoxide

products due to solute-solute interaction rather than solvent-solute interaction. On the other hand, DMSO formed hydrogen bonding strongly with solute, and thus β-hydroxy sulfides could be obtained with the assistant of solvent-solute interaction. From the proposed mechanistic study, it was confirmed that stabilization of benzylic radical was the key and important intermediate.

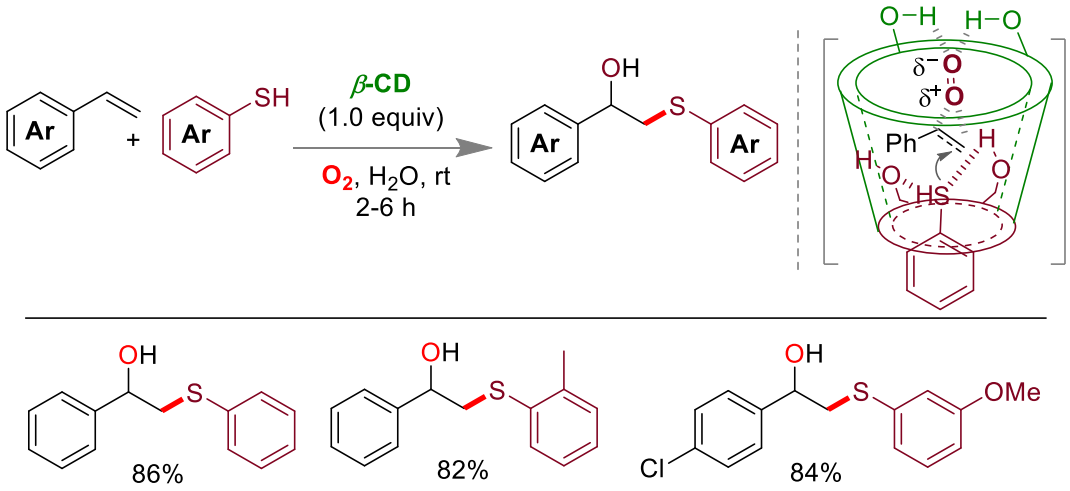



**Scheme 1.13.** Lei's approach for the synthesis of β-hydroxy sulfide or sulfoxide.

### 1.4.2.3 Supramolecular catalysis in synthesis of *β*-hydroxysulfides.

*β*- Hydroxysulfides were also reported by Rao's group using supramolecular catalysis (Scheme 1.14)[39]. They showed that cyclodextrin catalyzed the reaction of styrene and thiophenol under aerobic conditions. Here cyclodextrin, being an excellent host, formed a host-guest complex through its hydrophobic cavities. It stabilized thiophenol and aerobic molecular oxygen through

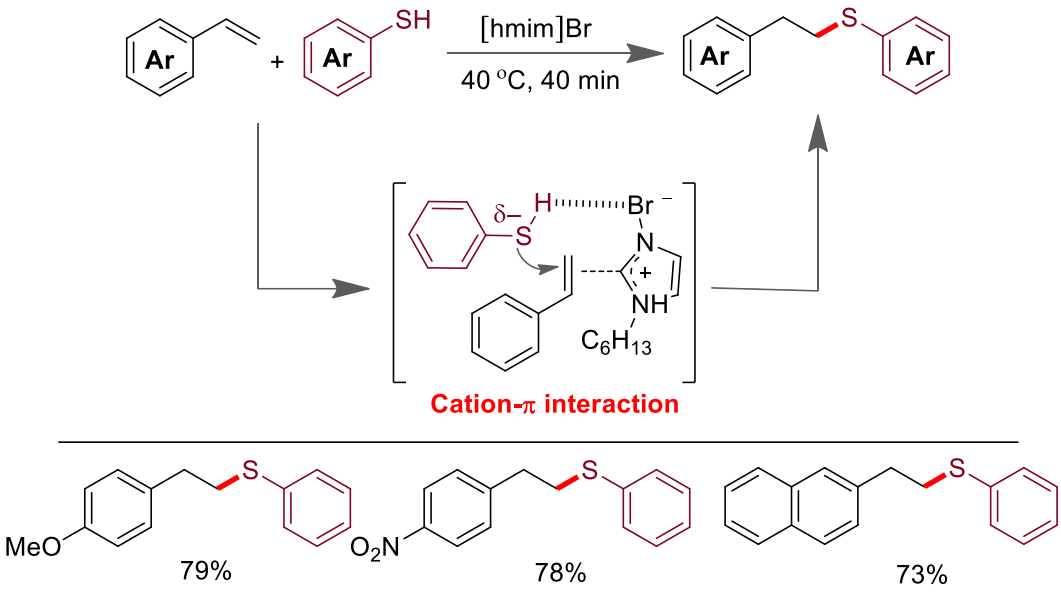
intermolecular hydrogen bonding. Consequently, hydrophobic styrene was stabilized through complexation with the host molecule. Following, a favorable nucleophilic attack was occurred by thiol to maintain proper regioselectivity. Finally, oxygen insertion from the cavity led to the formation of *β*- hydroxy sulfides product.




**Scheme 1.14.** Lei's approach for the synthesis of β-hydroxy sulfide or sulfoxide.

### 1.4.2.4 Cation… π interaction in thiol-ene-click(TEC) reaction.

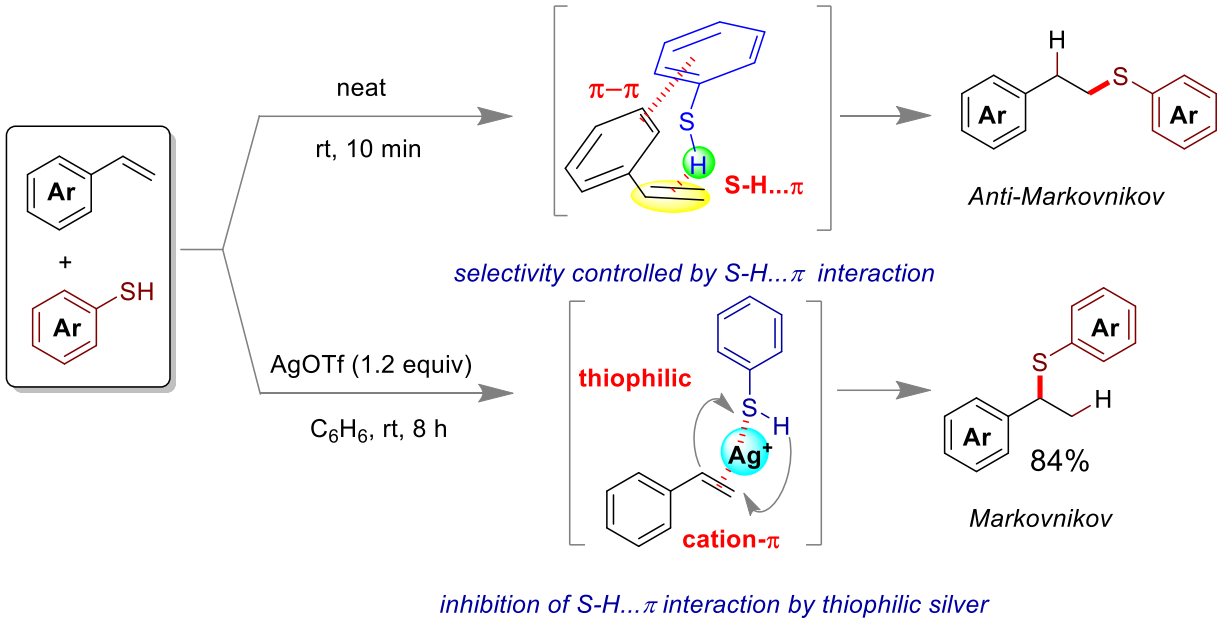
Continuous effort towards the development of non-covalent interaction could include more convenient strategies. In 2015, Sinha and co-workers established ionic liquid mediated anti-Markovnikov selective thiol-ene-click reaction (Scheme 1.15)[40]. The ionic liquid [hmim]Br operated both as the catalyst and as solvent here. The electrophilic, as well as nucleophilic nature of [hmim]Br, promoted to activate both thiophenol and olefin. Here, counter anion ($Br^-$) of ionic liquid formed halogen bonding with the proton of thiophenol and thus improved the nucleophilic character of thiophenol. On the other hand, C-2 hydrogen of $[hmim]^+$ activated olefin through cation…π or C–H…π interaction. As a result, nucleophilic attack of thiophenol to styrene occurred *via* anti-Markovnikov fashion to afford selective linear thioethers with excellent yield.




**Scheme 1.15.** Sinha's approach for the synthesis of linear thioethers.

### 1.4.2.5 S–H… π interaction in thiol-ene-click (TEC) reaction.

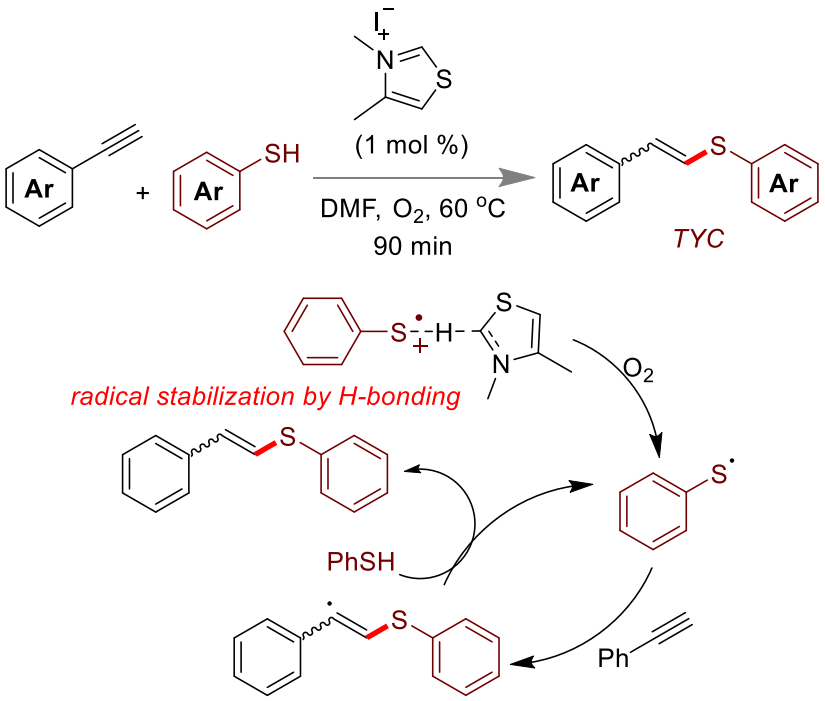
Interestingly, Mal's group envisioned that mixing of styrene and thiophenol under neat conditions could lead to anti-Markovnikov selective thioethers (Scheme 1.16)[41]. After careful investigation on this mechanistic pathway, it was realized that S–H…π interaction between olefin and hydrogen of thiophenol could help to attain the *anti*-Markovnikov selective linear thioethers. Not only S–H…π interaction, π -π stacking interaction between two phenyl groups of styrene and thiophenols was also operated as an additional driving force for this click reaction. Notifying, tunning of selectivity from *anti*-Markovnikov to Markovnikov selective product was also carried out by the addition of thiophilic silver in the same reaction system. It was assumed that Ag(OTf) inhibited S-H…π interaction through coordination of sulfur's lone pair and cation-π interaction with olefin and silver.




**Scheme 1.16.** Mal's approach for the anti-Markovnikov and Markovnikov selective thioethers.

### 1.4.2.6 H-bonding interaction in thiol-yne-click (TYC) reaction.

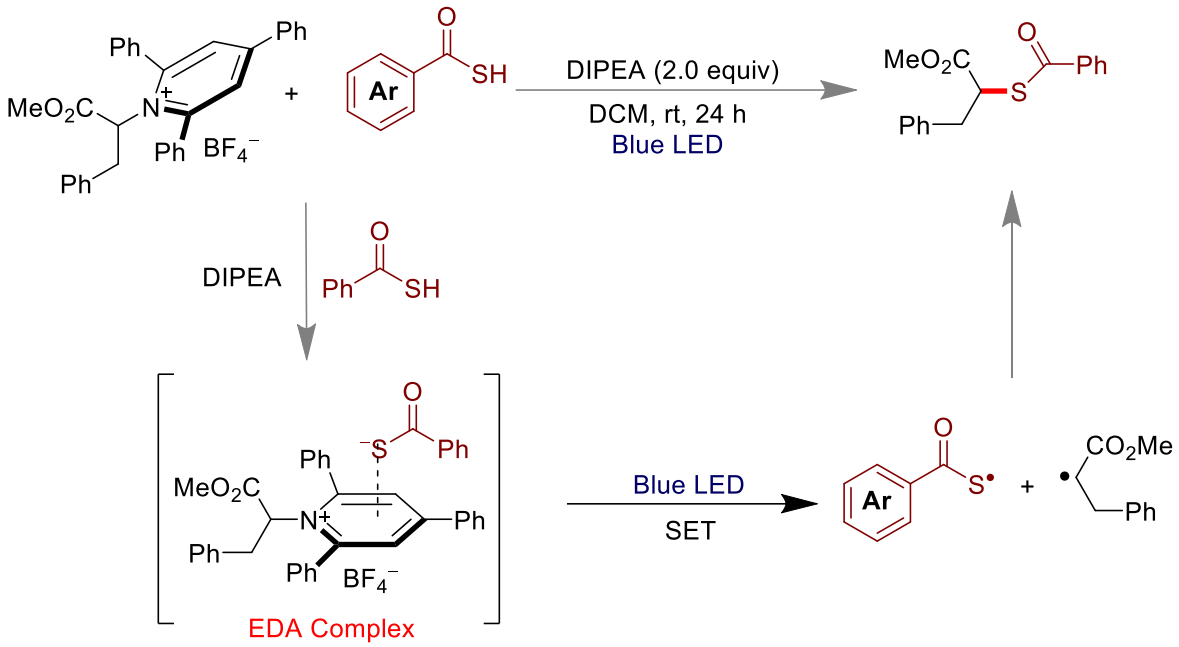
Chung and co-workers also proposed *anti*-Markovnikov addition of thiophenols to phenylacetylene using ionic liquid 3,4-dimethyl-5-vinylthiazolium iodide as a catalyst in DMF solvent and under air (Scheme 1.17).[42] As shown below, a thiyl radical was generated in the presence of air, which was further stabilized by ionic liquid (thiazolium salt) *via* H-bonding. Finally, thiyl radical was added to alkynes to attain *anti*-Markovnikov vinyl sulfide as (*E*)-and -(*Z*) isomeric mixture.




**Scheme 1.17.** Chung's approach for the synthesis of anti-Markovnikov selective vinyl sulfide.

### 1.4.2.7 EDA complexation in thioesterification reaction.

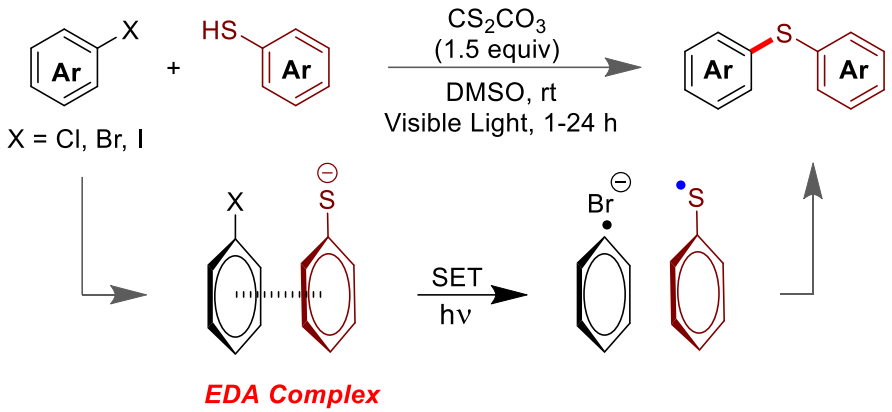
Visible-light-induced and base-mediated thioesterification could be done from amino acid containing Katritzky salt and thiobenzoic acid (Scheme 1.18)[43]. In this reaction, DIPEA, a nitrogenous base as well as an excellent single electron donor species, assisted in forming a thioacetic acid anion at the beginning. Afterward, the thiolate ion was stabilized by the EDA complex with Katritzky salt and thiobenzoic acid. Again DIPEA took part in SET to generate alkyl radical intermediate by fragmenting pyridine as a by-product. Finally, radical-radical cross-coupling yielded thioesterification products.




**Scheme 1.18.** Thioesterification of amino acids using Katritzky salts.

### 1.4.2.8 EDA complexation in the synthesis of thioether.

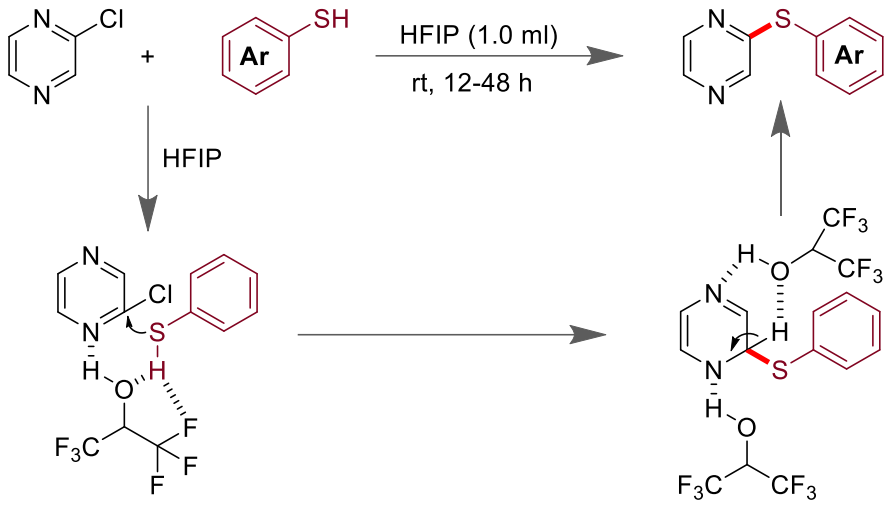
In the past few years, thioether synthesis had continuously been reported under metal-free and visible light conditions. In 2017 Miyake and co-workers developed visible-light-induced C–S coupling of aromatic thiol and aryl halide in the absence of any catalyst (Scheme 1.19)[44]. It was proposed that thiolate anion and aryl halide formed an EDA complex through π-π stacking with the shortest distance. Here EDA complex and π-π stacking interaction were stabilized by DMSO solvent. Afterward, intermolecular charge transfer occurred from thiolate anion to aryl halide, resulting in which thiyl radicals and aryl radicals were generated *via* the SET process. Thereafter, radical-radical cross-coupling yielded desired thioethers.




**Scheme 1.19.** Miyake's approach for the synthesis of thioethers.

### 1.4.2.9 H-bonding interaction in the synthesis of hetero-aromatic thioether.

Recently, Kapdi and co-workers have shown that aromatic nucleophilic substitution of chloro-heteroarene could lead to forming a new C–S bond by breaking the C–Cl bond in the presence of HFIP as solvent (Scheme 1.20)[45]. Indeed, HFIP showed versatility in many chemical transformations because of its strong hydrogen bonding donor capability, acidic nature, and outstanding ability to ionize a substrate. Utilizing the hydrogen bonding interaction, HFIP coordinated with nitrogen center of hetero-chloro arene through N…H hydrogen bonding. As a result, the C–Cl bond strength became weakened. Consequently, it also promoted nucleophilic attack of thiol through halogen bonding within fluorine of HFIP and proton of thiophenol.




**Scheme 1.20.** Kapdi's approach for the synthesis of heteroaromatic thioethers.

## 1.4.3 Visible light-driven photocatalytic C–S bond formation reactions.

Visible light-driven photocatalysis has been considered as one of the dominant tools in organic synthesis because the energy of photons could easily be converted into chemical energy[46, 47]. Not only this but the photocatalyst is also involved in the single electron transfer (SET) process, which served as an attractive alternative strategy in terms of green chemistry. Many of the photocatalysts such as Eosin Y, Rose bengal, Benzophenone, Riboflavin, etc. have been employed for a wide range of elegant C–S bond formation reaction (Figure 1.5). Most of the photocatalyst shown below has strong visible absorption, long excited-state lifetime, and stability under photolytic conditions.

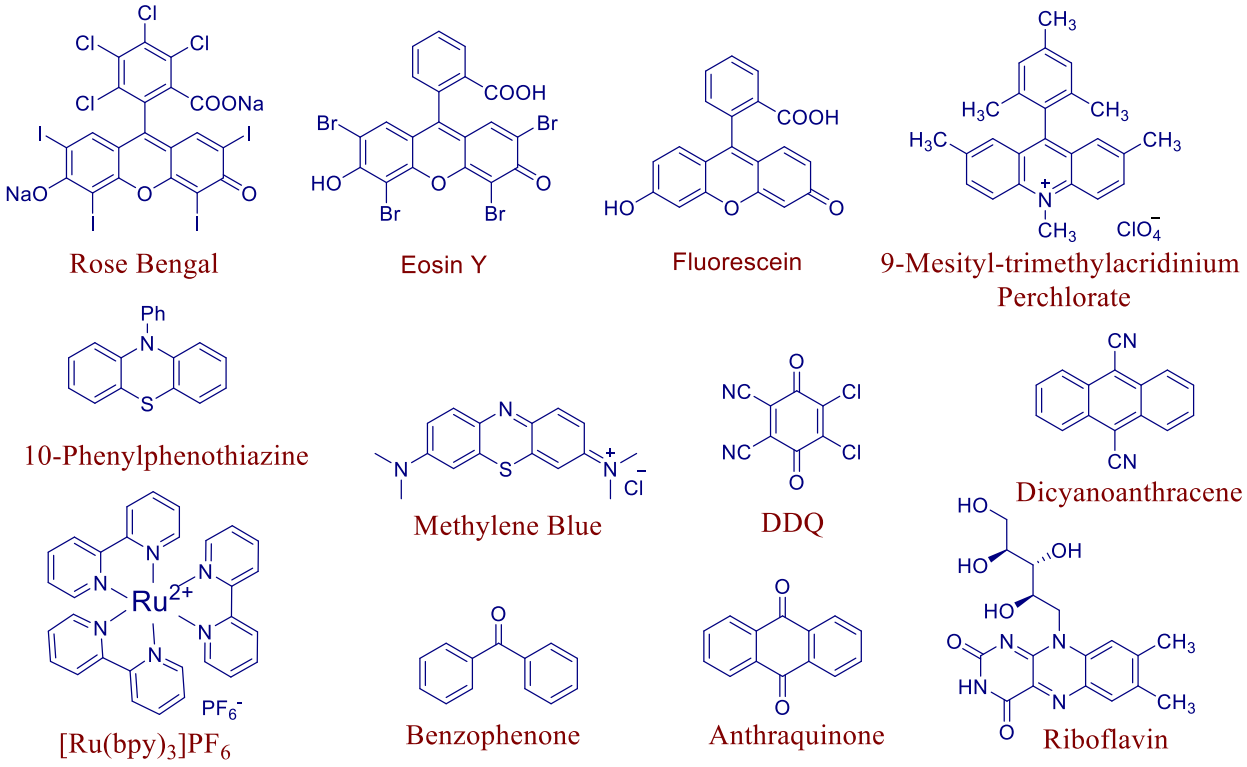



**Figure 1.5.** Common photocatalyst used in C–S bond formation reaction.

The typical nature of a photocatalyst is either to transfer energy to a substrate or to take part in a single electron transfer process (Figure 1.6). However, it needs to be excited initially by irradiation of visible light, which can therefore participate in the oxidative-reductive or energy transfer process. During an oxidative cycle, the excited state photocatalyst (PC*) can be oxidized by an acceptor, which can take one electron from the photocatalyst. Following, oxidized PC can acquire one electron from the substrate and returns to its ground state. Notably, the substrate, which has now be short of one electron, can easily take part in reaction through a single electron transfer process. Similarly, a photocatalyst also involves in a reductive cycle. In this case, the excited photocatalyst (PC*) can take up one electron from a donor and itself reduced. Following, reduced PC can give one electron to the substrate, which can have one extra electron available

for reaction. Simultaneously, the photocatalyst is regenerated. Some of the recent photocatalytic oxidative and reductive C–S bond formation reactions are summarized below.

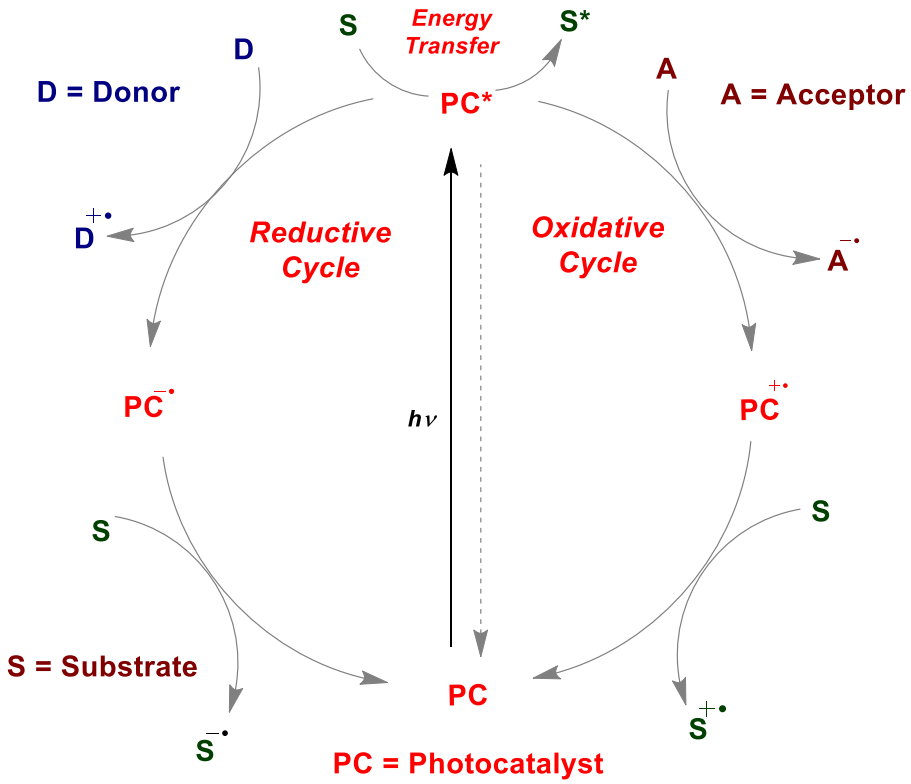
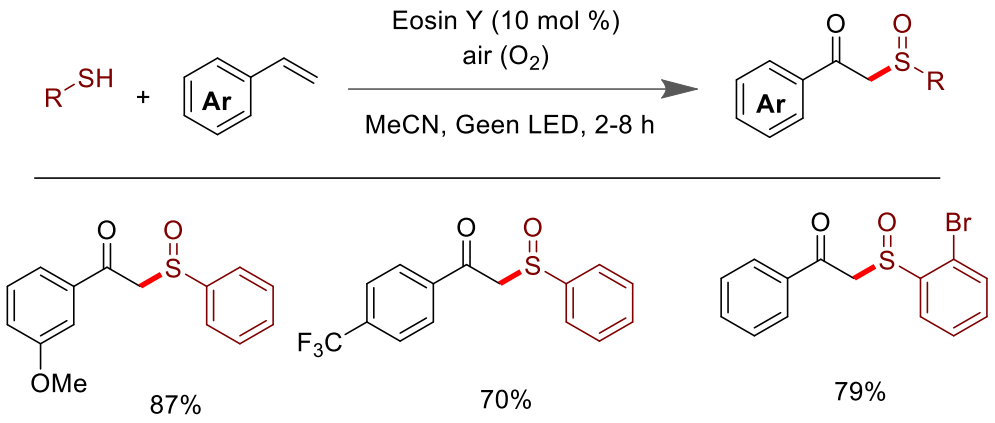



**Figure 1.6.** Function of a photocatalyst in the catalytic cycle.

### 1.4.3.1 Eosin Y as photocatalyst for *β*-ketosulfoxide from styrene and thiol.

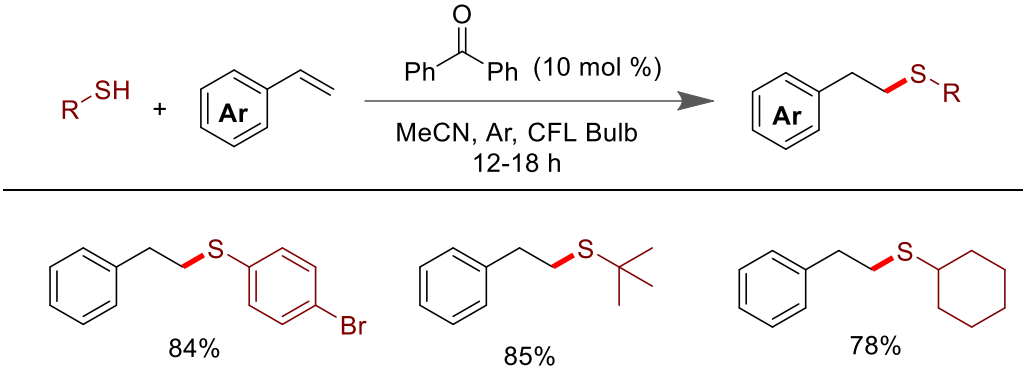
In 2014, Yadav *et. al.* group also introduced Eosin Y as a photocatalyst for the synthesis of *β*-keto-sulfoxide from a radical addition reaction between thiols and styrenes (Scheme 1.21)[48]. In this reaction, molecular oxygen played a dual role: i) incorporation of oxygen at the *β*-position of styrene ii) oxidation of sulfur center.




**Scheme 1.21.** *β*-ketosulfoxide from styrene and thiols.

### 1.4.3.2 Benzophenone as photocatalyst for thiol-ene reaction.

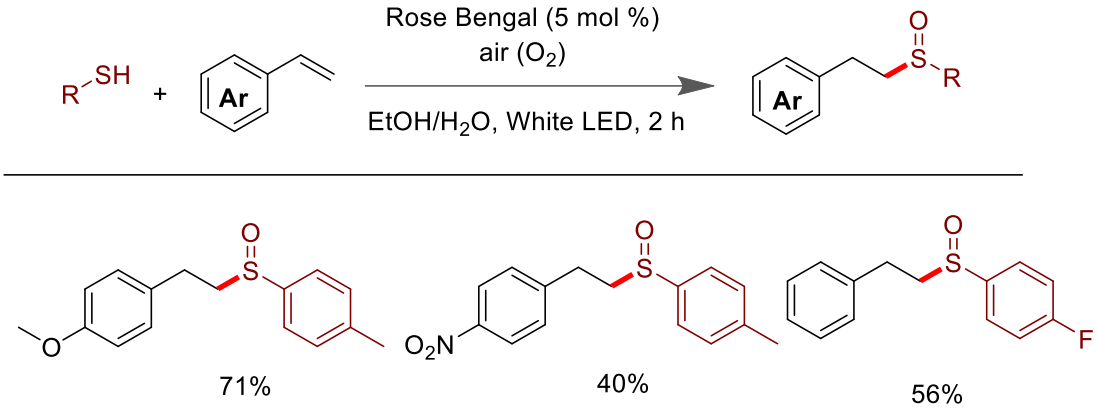
Later on, the same group envisioned that visible light-mediated thiol ene reaction was catalyzed by 10 mol % benzophenone as catalyst without any additional external oxidant (Scheme 1.22)[49]. The reaction proceeded *via* a radical pathway to afford various anti-Markovnikov selective products with good yields.




**Scheme 1.22.** Thiol-ene reaction by benzophenone.

### 1.4.3.3 Rose Bengal as photocatalyst for synthesis of vinyl sulfoxide.

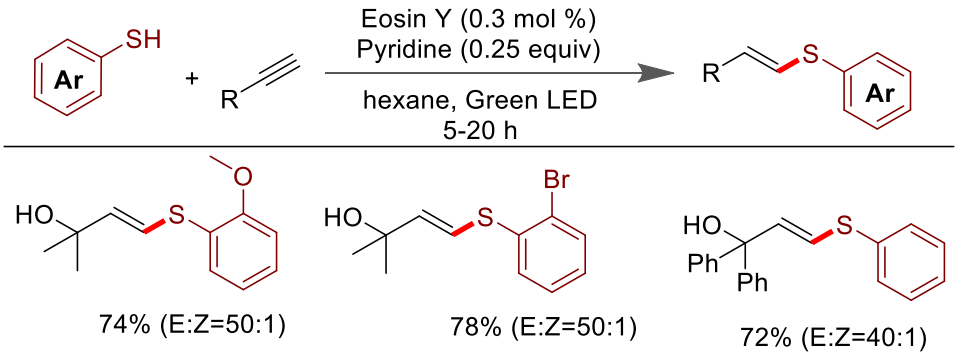
Wei's group has also illustrated that synthesis of vinyl sulfoxide could be achieved from styrene and thiols under irradiation of 5 mol % Rose Bengal by white LED in the air (Scheme 1.23)[50]. The radical-mediated reactions delivered vinyl sulfoxides with reasonable yields.




**Scheme 1.23.** Synthesis of vinyl sulfoxide by Rose Bengal.

### 1.4.3.4 Eosin Y as a photocatalyst for Synthesis of (*E*)-vinyl sulfide.

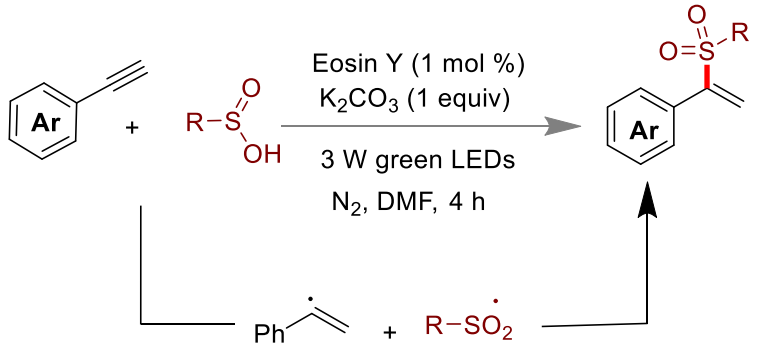
The addition of thiol to alkyne gives anti-Markovnikov vinyl sulfide with E-Z isomeric mixture. In 2016, Ananikov and co-workers developed Eosin Y catalyzed (*E*)-selective vinyl sulfide from the addition of thiol to terminal alkyne (Scheme 1.24)[51]. In this reaction, pyridine was used to deprotonate the acidic proton of thiols.




**Scheme 1.24.** Synthesis of (*E*)-vinyl sulfide by Eosin Y.

### 1.4.3.5 Eosin Y catalyzed Markovnikov vinyl sulfone.

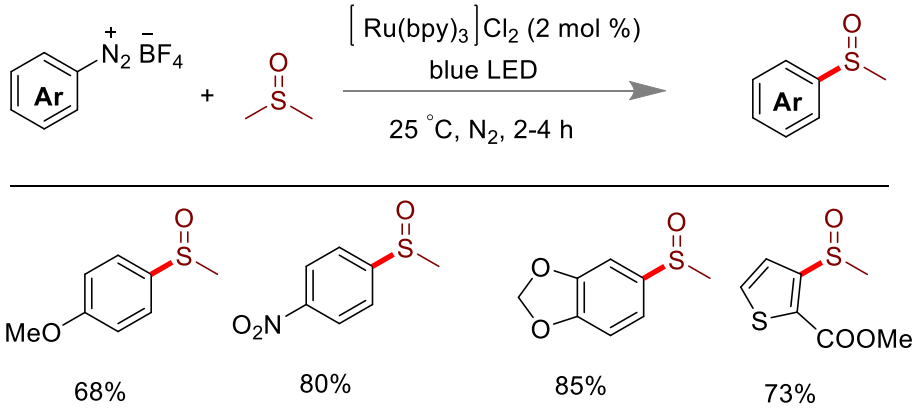
Lei's group reported that Markovnikov selective vinyl sulfones could be obtained from the addition of aryl sulfinic acid to terminal alkyne using green LED as a visible light source and 1 mol % Eosin Y as organo-photocatalyst in the presence of $K_2CO_3$ as a base under an argon atmosphere (Scheme 1.25)[52]. Mechanistically they have proposed that reaction proceeded through vinyl radical and sulfonyl radical intermediate as shown below.




**Scheme 1.25.** Markovnikov selective vinyl sulfone from terminal alkyne.

### 1.4.3.6 Ruthenium catalyzed methylsulfoxidation using diazonium salt.

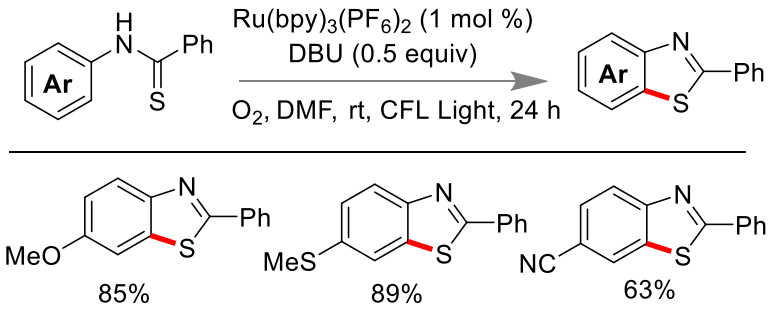
N. Rastogi and co-worker showed that dimethylsulfoxide (DMSO) was used as methyl sulfinyl source for the synthesis of methyl aryl sulfoxide (Scheme 1.26)[53]. In this particular reaction, they have shown that $Ru(bpy)_3Cl_2$ was used for the generation of the aryl radical from aryl diazonium salt *via* single electron transfer (SET) process.




**Scheme 1.26.** Visible light-mediated methyl-sulfoxidation.

### 1.4.3.7 Ruthenium catalyzed synthesis of 2-substituted benzothiazole.

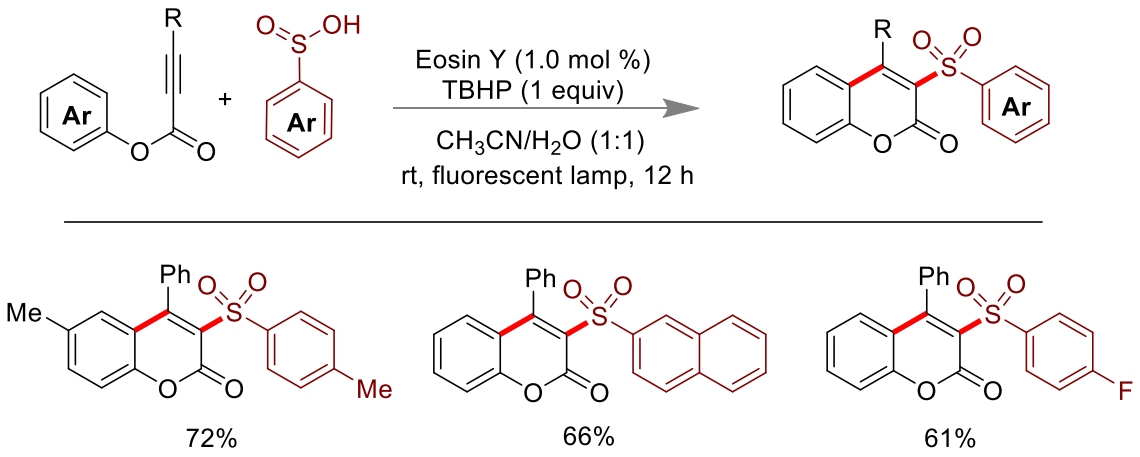
Li's group disclosed a photochemical synthesis of 2-substituted benzothiazoles *via* C–H functionalization reaction using 1 mol % $Ru(bpy)_3Cl_2$ catalyst and DBU as a base under oxygen atmosphere and CFL light (Scheme 1.27)[54]. In this reaction, DBU helped in the deprotonation of thioanilide, and molecular oxygen assisted in oxidizing the photocatalyst, which took part in SET with the deprotonated form of thioanilide to produce 2-substituted benzothiazoles.




**Scheme 1.27.** Visible light-mediated 2-substituted benzothiazoles.

### 1.4.3.8 Eosin Y catalyzed synthesis of 3-sulfonated coumarin.

Wang's group also experienced synthesis of 3-sulfonated coumarin from aryl propiolate and sulfinic acid using Eosin Y as photocatalyst and TBHP as terminal oxidant (Scheme 1.28)[55]. The internal alkyne could be functionalized to afford 3-sulfonated coumarin via cascaded formation of the C–C and C–S bond in a single step.




**Scheme 1.28.** Wang's report for visible light initiated synthesis of coumarin.

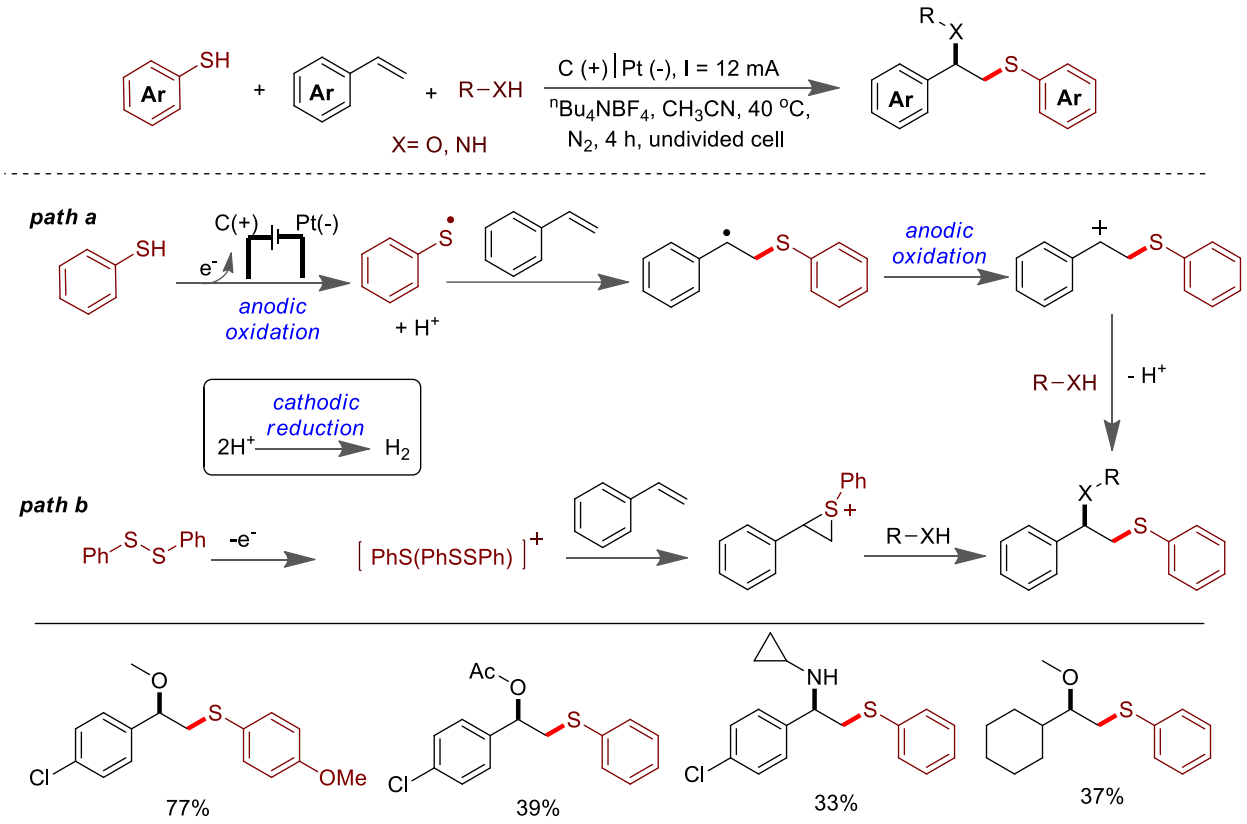
## 1.4.4 Electrochemical oxidative C–S bond formation reactions.

With growing public awareness of the conservation of renewable energy due to global warming, it is essential to reduce the wastage of chemicals in organic synthetic methodology. Indeed, electrochemical synthesis is an alternative way to minimize the use of chemicals, mainly hazardous chemicals. Some of the recent C–S bond formation reaction using electrochemical oxidative process has been discussed below.

### 1.4.4.1 Vicinal di-functionalization of olefin.

In 2018, Lei's group demonstrated an electrochemical oxidative oxy-sulfenylation and amino-sulfenylation of olefins using thiophenol as a C–S coupling partner under 12 mA current in an undivided cell (Scheme 1.29)[56]. This oxidative strategy could be applied for hydroxyl-

sulfenylation and acyloxy-sulfenylation of alkenes, as shown in the scheme. Authors have suggested that oxidation of thiophenol at carbon anode helped to generated thiyl radical. Subsequently, the addition of thiyl radical to olefin produces a radical intermediate, which was oxidized to create a cationic benzyl intermediate. Finally, the nucleophilic attack by a nucleophile on carbocationic intermediate helped to get the desired product. On the other hand, concomitant cathodic reduction at platinum electrodes led to $H_2$ evaluation.

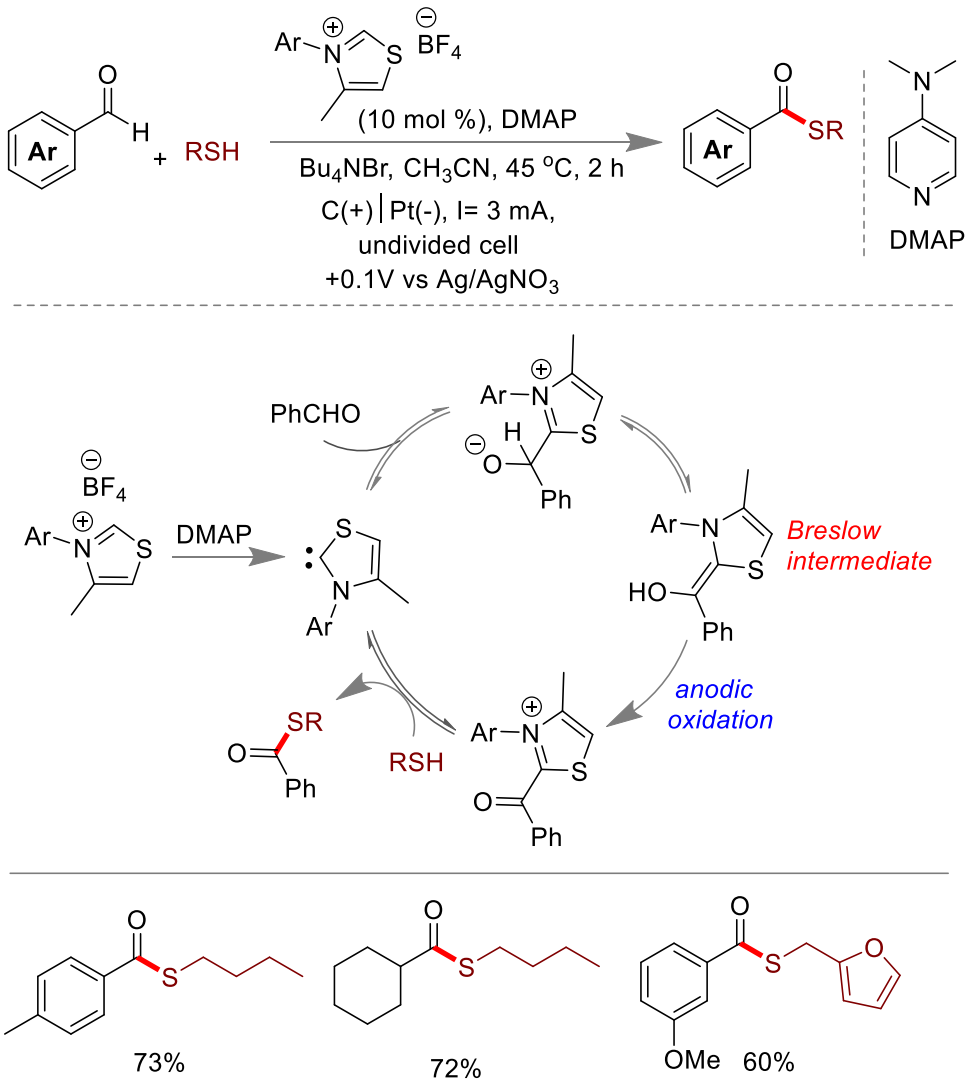



**Scheme 1.29.** Electrochemical difunctionalization of olefins.

## 1.4.4.2 Organocatalyzed thioesterification of aldehyde.

Boydston and co-workers have experienced that thioesterification of aldehydes could be achieved from aldehydes and thiols *via* organocatalytic electrosynthesis[57]. The reactions offered

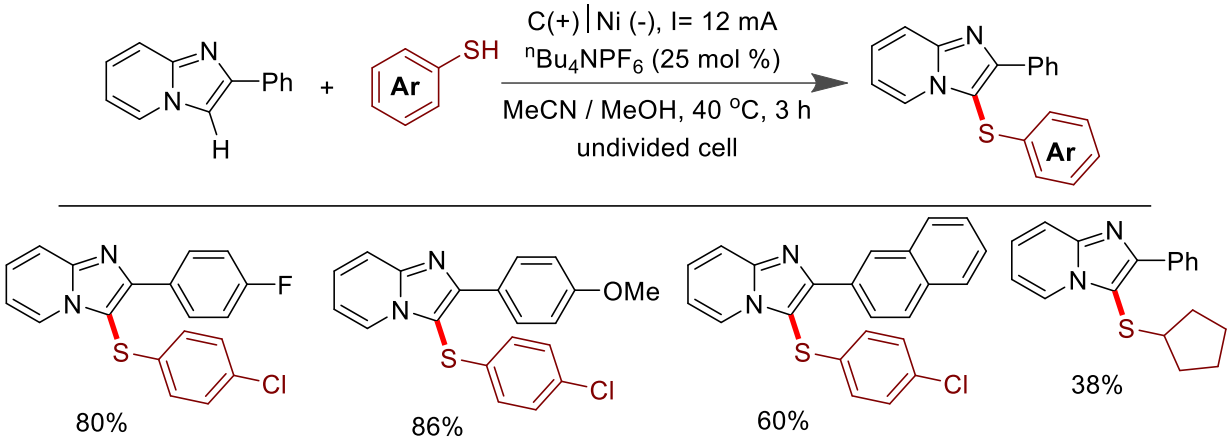
excellent tolerability towards the thioesterification reaction. The organocatalyst thiazolium was utilized here to activate the aldehyde *via* the formation of a well-known Breslow intermediate, as shown in Scheme 1.30. The oxidation of Breslow intermediate at anode center generated acyl thiazolium species which was immediately coupled with thiols to deliver related products.




**Scheme 1.30.** Organocatalyzed oxidative thioesterification of aldehyde.

### 1.4.4.3 C–H sulfenylation of imidazopyridine.

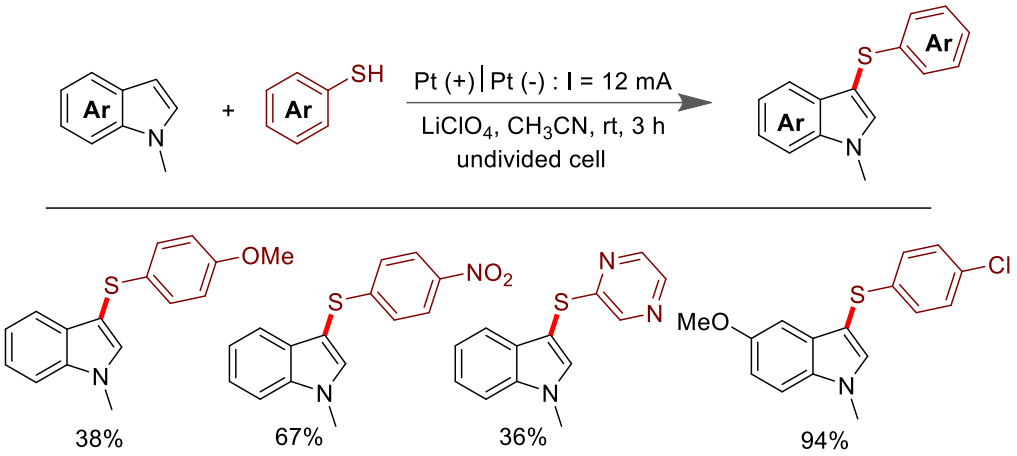
Lei and co-workers introduced a regioselective oxidative C–H sulfenylation of imidazopyridine in an undivided cell without any external oxidant (Scheme 1.31)[58]. The reaction was performed under carbon as an anode, nickel as cathode, and tetrabutylammonium hexafluorophosphate as an electrolyte in the presence of a 12 mA constant current. The electron-donating, electron-withdrawing, and aliphatic substituents were well compatible in the reaction condition to provide sulfenylation product with excellent yield.




**Scheme 1.31.** Electrochemical oxidative cross-coupling of thiophenol and imidazopyridines.

## 1.4.4.4 C-H sulfenylation of indole.

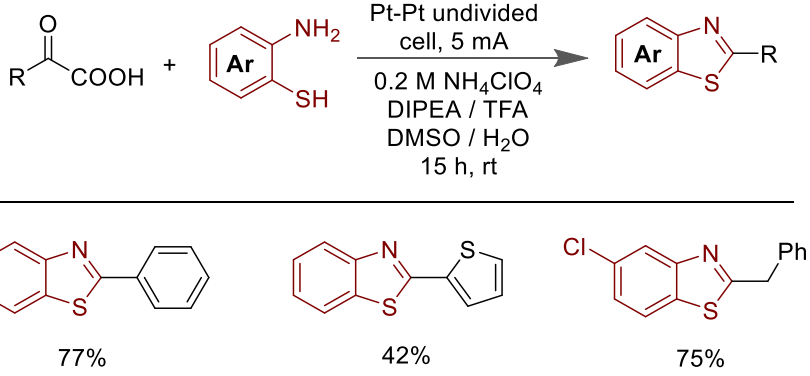
It was also reported that indoles and thiophenols were coupled electrochemically to give 3-sulfenylated indoles (Scheme 1.32)[59]. The reaction was carried out in 12 mA current and lithium perchlorate salt as electrolyte under an undivided cell where platinum plates were used as cathode and anode. The scopes of the substrate were found to be broad, as shown below.




**Scheme 1.32.** Dehydrogenative C–S coupling of indoles and thiols.

### 1.4.4.5 Benzothiazole synthesis from α-keto acid.

Benzothiazoles are recognized as an important category of scaffold which is found in many biologically active molecules. Therefore synthesis of benzothiazole using mild reaction conditions is always desirable. In 2016 Huang's group realized an electrochemical decarboxylative synthesis of substituted benzothiazoles from α-keto acids when 2-amino thiophenol was used as another coupling partner (Scheme 1.33)[60]. In this work, the authors have used Pt-Pt combination as cathode and anode in 0.2 M ammonium perchlorate as an electrolyte in the presence of 5 mA current for this oxidative cyclization reaction.




**Scheme 1.33.** Electrochemical decarboxylative benzothiazole synthesis.

## 1.5 OBJECTIVE

In summary, we have discussed the historical background of the C–S bond formation reaction using various sustainable strategies. Most of the reports include control of the reactivity of sulfur compounds with various types of olefins, alkynes, carbonyls, and heterocyclic cores containing C–S bonds. The objective of the current thesis was to develop sustainable methods like use of iodine reagent, non-covalent interactions, and visible light photocatalysis in C–S bond formation reaction *via* controlling the reactivity of alkenes, alkynes, and alcohols. Below is the pictorial representation of the objective of the present thesis (Figure 1.7).

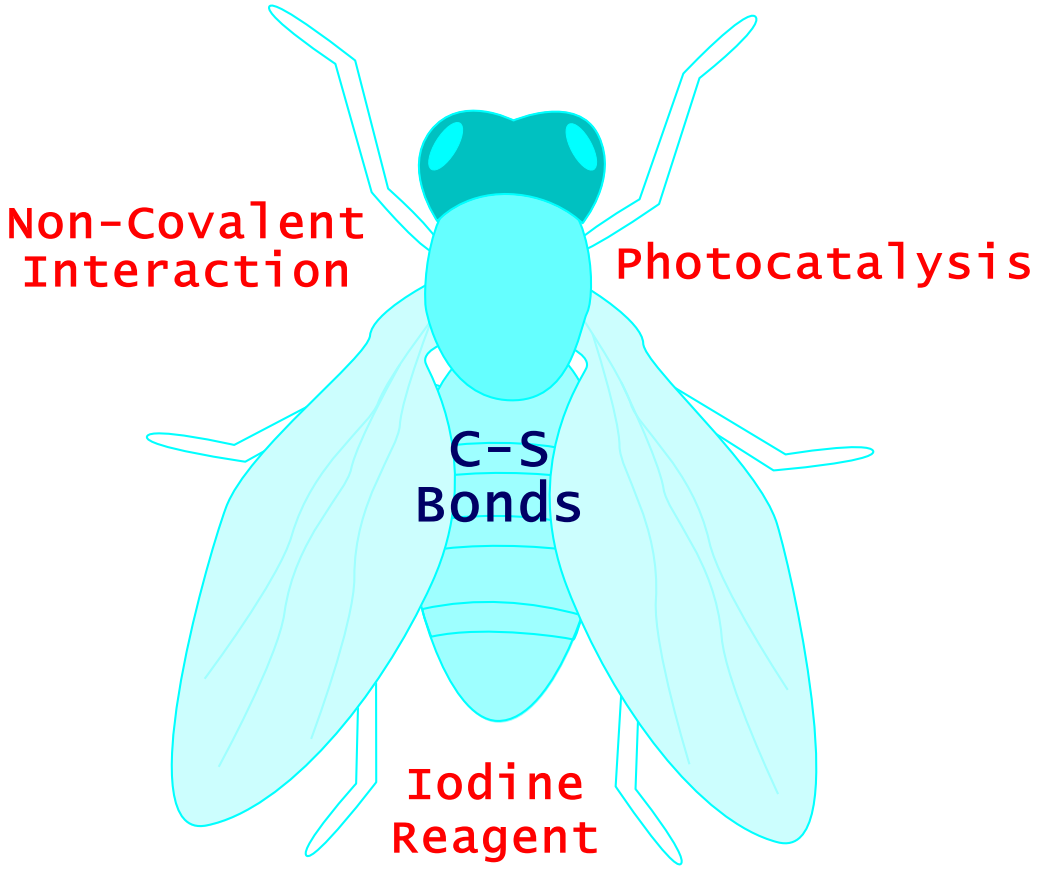



**Figure 1.7.** The objective of the present thesis at a glance.

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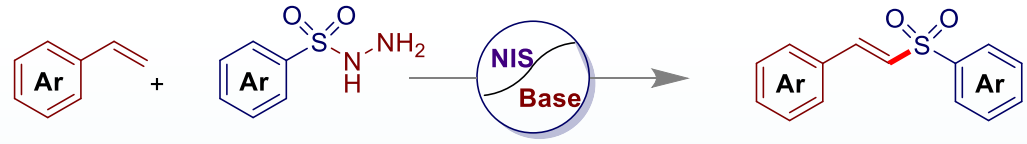
# CHAPTER 2

## *N*-Iodosuccinimide in C($sp^2$)–H Functionalization of Styrene: Synthesis of (*E*)-Vinyl Sulfones

### 2.1 ABSTRACT



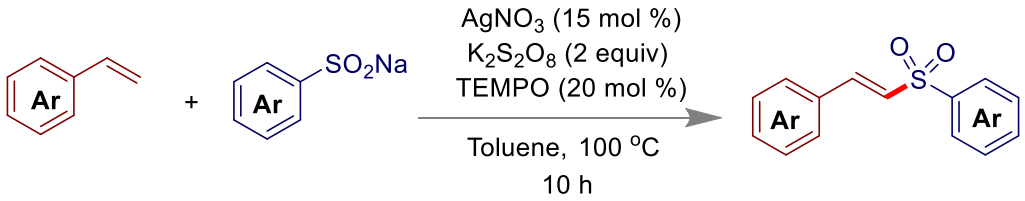

- 26 examples, up to 98 % yield
- E- selectivity
- scalable
- operationally simple
- mild condition
- metal free

A facile regio and stereoselective $C_{sp2}$–H sulfonylation reaction of unactivated olefins with aryl and alkyl sulfonyl hydrazides have been disclosed using *N*-iodosuccinimide (NIS) and $K_2CO_3$ under an open atmosphere within a short reaction time (ca~2 hours). Here, NIS displayed dual function which could play a pivotal role in forming aryl sulfonyl radicals from aryl sulfonyl hydrazides at a primary stage, and it gave *β*-iodosulfone as the second intermediate, which was immediately transformed to (*E*)-vinyl sulfones when $K_2CO_3$ was added. As a whole, a sustainable strategy for the straight synthesis of (*E*)-vinyl sulfones from styrenes is established.

### 2.2 INTRODUCTION

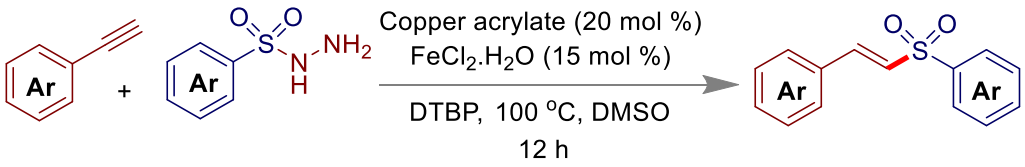
Vinyl sulfone motifs have gained enormous attention in organic research fields because of their wide application in medicine and biologically active compounds.[1-6] Synthetically, vinyl sulfone could be served as efficient dienophiles or Michael acceptors in cycloaddition,[7, 8]epoxidation[9]

and cyclopropanation reaction.[10, 11] Over the past decades, classical methods to synthesize vinyl sulfone implicates Knoevenagel condensation,[12] olefination reactions such Peterson, Wittig, Horner-Wadsworth-Emmons (HWE).[13] Afterward, many methods have been explored using efficient Pd, Cu or Fe catalyzed cross-coupling of vinyl halide,[14] terminal epoxide,[15] vinyl tosylate,[16] *β*-nitrostyrene,[17] vinyl boronic acid,[18] vinyl triflates,[19]propiolic acid,[20, 21,] and various alkenes.[22,23] Very recently, Jiang's group reported silver catalyzed synthesis of vinyl sulfone starting from styrene derivatives and aryl sulfonates at elevated temperatures (Scheme 2.1).[24] This strategy suffered from the use of toxic metals, expensive additives.




**Scheme 2.1.** Jiang's approach for silver catalyzed sulfonylation reaction of styrene.

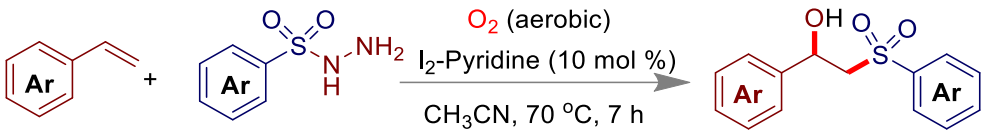
Similarly, Zhang's work also demonstrated the synthesis of vinyl sulfones from aryl sulfonyl hydrazides using Fe/Cu co-catalyst and di-*tert* butyl peroxide at 100 °C (Scheme 2.2).[21] This method also suffered from the use of harmful peroxide reagents and metal co-catalyst.




**Scheme 2.2.** Zhang's approach for iron catalyzed sulfonylation reaction of styrene.

As the development of alternative sustainable methodology, Mal's group also used sulfonyl hydrazides as a sulfone source for the synthesis of β-hydroxy sulfones (Scheme 2.3).[25a] They

have used a combination of iodine-pyridine as reaction promoter and aerial dioxygen as oxygen source at elevated temperature for selective formation of β-hydroxy sulfones.




**Scheme 2.3.** Mal's approach for iodine promoted oxysulfonylation reaction of styrene.

In our work, we developed an unprecedented concept that explained that N-iodosuccinimide (NIS) has dual role to synthesize vinyl sulfone (Figure 2.1)[25b]. Styrenes and sulfonyl hydrazides were allowed to react in ethanol at 70 ºC for 2 h with the help of NIS and potassium carbonate ($K_2CO_3$), which resulted in (*E*)-vinyl sulfones exclusively (Figure 2.1a). NIS could primarily help to produce sulfonyl radicals from sulfonyl hydrazide, as indicated below (Figure 2.1b). Afterward, NIS was again utilized for the formation of *β*-iodo sulfone, which was further transformed to (*E*)-vinyl sulfones by eliminating hydro-iodic acid (HI).

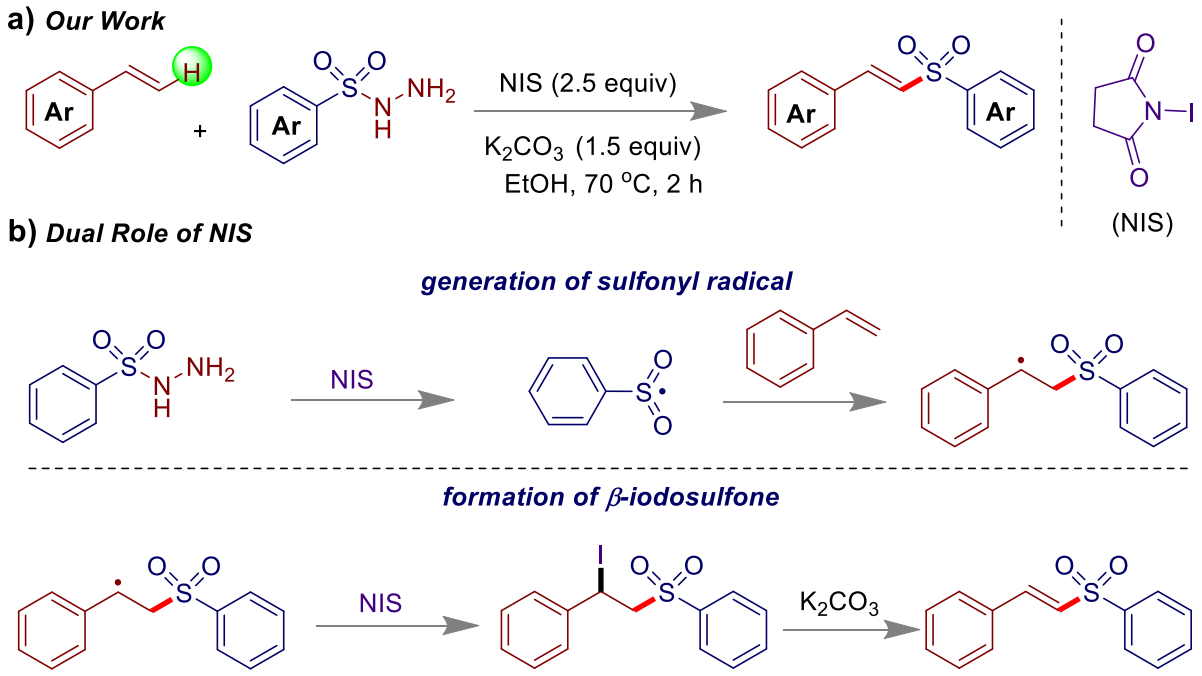
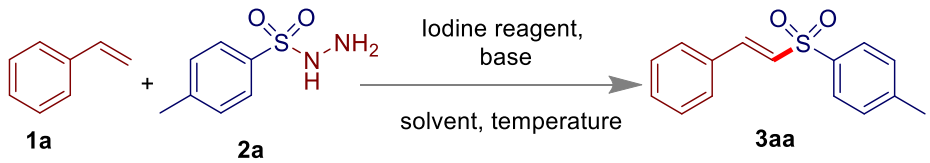


**Figure 2.1.** Our work: a) Synthesis of (*E*)-vinyl sulfone from styrenes and aryl sulfonyl hydrazides using *N*-iodosuccinimide (NIS) b) The multiple role of NIS is shown.

## 2.3 RESULT AND DISCUSSION

To our initial screening of proper reaction conditions, styrene (**1a**) and p-toluenesulfonyl hydrazide (**2a**) were selected as representative substrates for the C–S coupling reaction (Table 2.1). The reaction was performed with NIS (2.5 equiv) and $K_2CO_3$ (1.5 equiv) in acetonitrile solvent at 70 ºC temperature. The desired vinyl sulfone **3aa** was obtained in 84% yield (entry 1). Following, solvent screening was done with DMSO, $H_2O$, DCE, EtOH (entries 2-5). Notable that, EtOH was found to be the best choice in which compound **3aa** was isolated in 98% yield (entry 5). Similarly, other bases like $Cs_2CO_3$, KOH, pyridine, and 1,4-diazabicyclo[2.2.2]octane (DABCO) were not well effective as $K_2CO_3$ to produce desired product (entries 6-9). Variety of iodine reagents such as iodine, potassium iodide (KI), phenyl iodine diacetate (PIDA) were tested where iodine was found to be most efficient (entries 10-12). As expected, the reaction was unproductive in the absence of base (entry 13) and oxidant (entry 14). The nature of the reaction was sluggish at either room temperature (entry 15) or 50 ºC temperature (entry 16). The yield of desired product was remained unchanged during the inert atmosphere reaction indicating that there was no role of molecular oxygen in this transformation (entry 17). Again, the optimization of oxidant (NIS) and base ($K_2CO_3$) equivalents were discussed in Table 2.2.

**Table 2.1**. Effect of reaction parameter




| entry | oxidant | solvent | base | yield[a] |
|---|---|---|---|---|
| 1 | NIS | $CH_3CN$ | $K_2CO_3$ | 84 |
| 2 | NIS | DMSO | $K_2CO_3$ | 54 |
| 3 | NIS | $H_2O$ | $K_2CO_3$ | 57 |
| 4 | NIS | DCE | $K_2CO_3$ | 66 |
| 5 | NIS | EtOH | $K_2CO_3$ | 98 |
| 6 | NIS | EtOH | $Cs_2CO_3$ | 97 |
| 7 | NIS | EtOH | KOH | 68 |
| 8 | NIS | EtOH | pyridine | 45 |
| 9 | NIS | EtOH | DABCO | 51 |
| 10 | $I_2$ | EtOH | $K_2CO_3$ | 69 |
| 11 | KI | EtOH | $K_2CO_3$ | 0 |
| 12 | PIDA | EtOH | $K_2CO_3$ | 0 |
| 13 | NIS | EtOH | - | 0 |
| 14 | - | EtOH | $K_2CO_3$ | 0 |
| 15 | NIS | EtOH | $K_2CO_3$ | 85[b] |
| 16 | NIS | EtOH | $K_2CO_3$ | 89[c] |
| 17 | NIS | EtOH | $K_2CO_3$ | 97[d] |

[a]Isolated yields, **1a** (0.576 mmol), **2a** (0.864 mmol), solvent (2 mL), oxidant (2.5 equiv) and base (1.5 equiv) were used for 2 h at 70 °C. [b]Room temperature, 4 h. [c]50 °C; [d]Inert atmosphere.

With the optimal condition in hand, the scope of styrenes was explored in Figure 2.2. A variety of styrene derivatives having electron-donating groups such as -Me, -$^{i}$Pr, -OMe (**3ba**, **3ca**, **3da**, **3ea,** and **3ha**) were isolated with good to excellent yields (60-91%). On the other hand, biphenyl and naphthalene substituted styrenes also worked well to produce **3fa** and **3ga** with 75% and 68% yield, respectively. Likewise, the electron-withdrawing group -Cl, -$CF_3$, -CN, and -$NO_2$ (**3ia**, **3ja**, **3ka**, **3la**, **3ma**) resulted in desired sulfones in satisfactory yield (70-96%). Pyridine containing olefin (2-vinyl pyridine) was also tolerated to deliver **3na** with a 34% yield. In scale-up synthesis, desired product **3aa** was isolated in 92%.

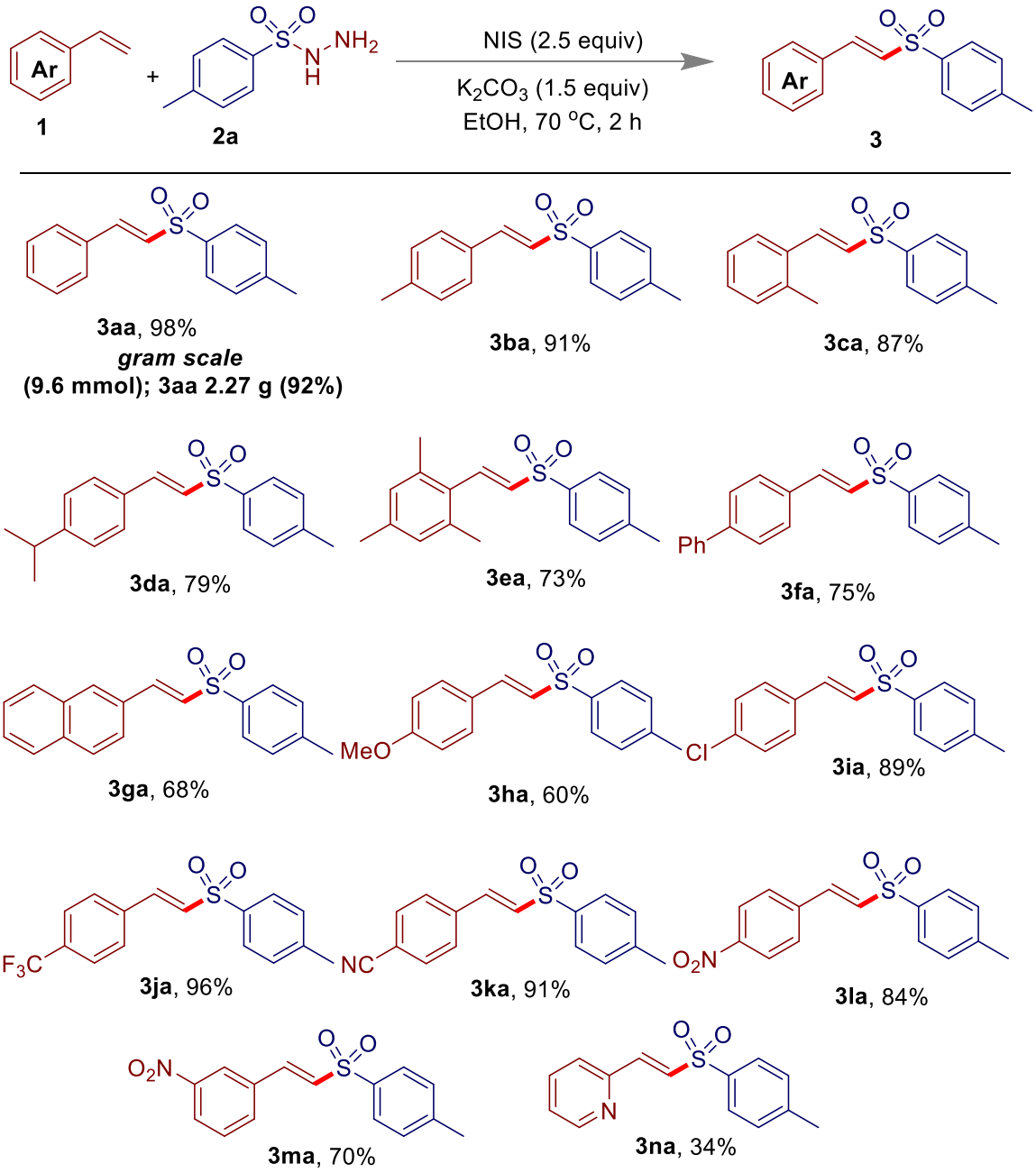



**Figure 2.2.** Scopes of styrenes for the synthesis of vinyl sulfones.

Next, we sought to explore the scopes of several sulfonyl hydrazides (Figure 2.3). Benzenesulfonyl hydrazide offered **3ob** and **3ib** with 93% and 89% yield, respectively. In addition, the electron-donating group containing sulfonyl hydrazides such as -$^{t}$Bu, -OMe, -$^{i}$Pr

(**3ac**, **3oc**, **3pc**, **3ad**, **3od,** and **3ae**) were well productive (yield 72-82%). Similarly, the *p*-nitro-phenylhydrazine delivered the desired product **3af** with only a 57% yield. This is due to the fact that the nucleophilicity of sulfonyl radical was de-minimized by the electron-withdrawing effect of the nitro group. Likewise, the sulfonyl group having naphthalene scaffold yielded **3ga** with 71% yield. On the other hand, the aliphatic sulfonyl hydrazides produced products **3ah** and **3gh** in satisfactory results (58% and 67%, respectively).

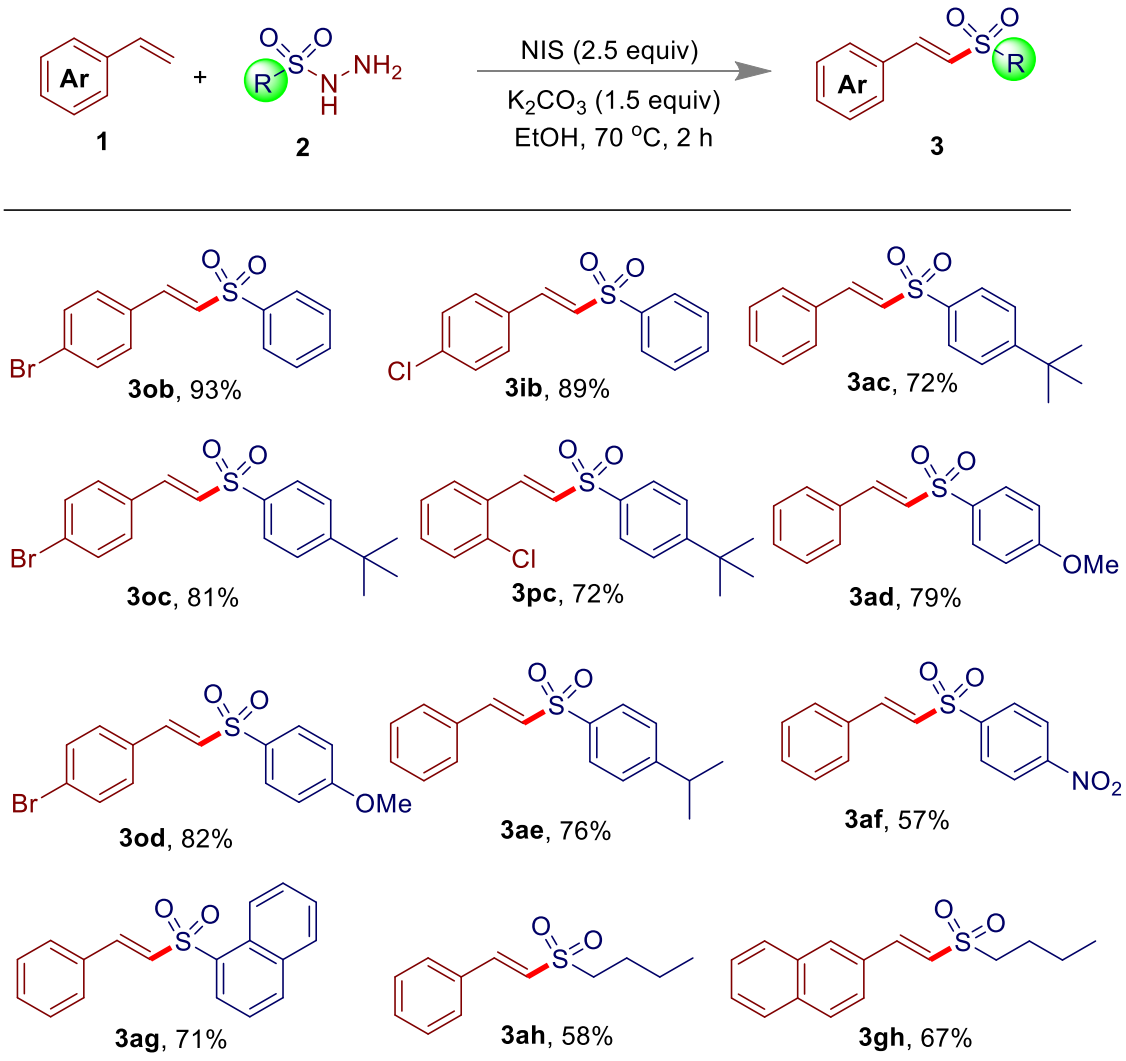



**Figure 2.3.** Scopes of sulfonyl hydrazides for the synthesis of vinyl sulfones.

A couple of control experiments was carried out in order to understand the reaction pathway (Figure 2.4). Compounds **1a** and **2a** were utterly hampered when radical inhibitors like 2,2,6,6-tetramethylpiperidin-1-yl) oxidanyl (TEMPO), and butylated hydroxytoluene (BHT) were added under standard conditions (Figure 2.4a), which confirmed that the radical pathway is involved in the reaction. Additionally, *p*-methyl-benzene-sulfonyl iodide 4a[26] (Figure 2.4b, left) and sulfonothioate derivative **5a**[27] (Figure 2.4b, right) did not lead to desired product. These observations also indicated that there was no such kind of intermediates involved in the reaction medium. When *β*-iodo sulfone **6a** was employed under standard reaction conditions, compound **3aa** was isolated in a 75% yield, indicating that *β*-iodo sulfone could be the reliable intermediate (Figure 2.4c).[28]

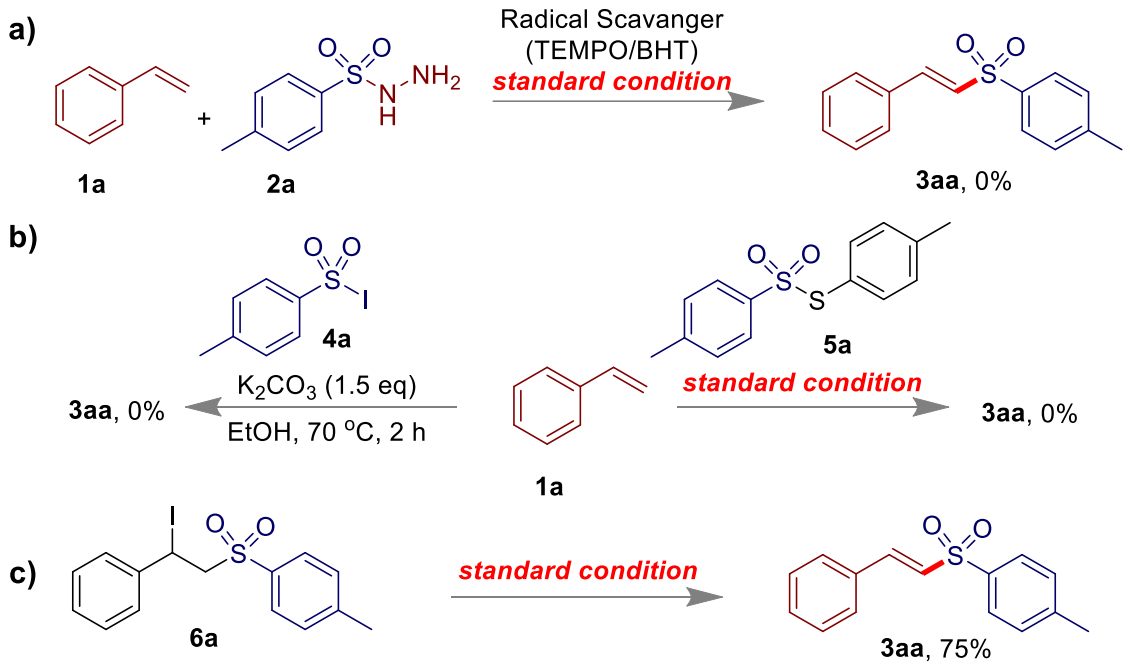



**Figure 2.4.** Several control experiments were performed to understand the reaction mechanism.

Based on the above control experiments and literature reports,[25, 29] a possible mechanism was described in Figure 2.5. Initially, NIS was cleaved homolytically and abstracted hydrogen from N-H consecutively from sulfonyl hydrazide to produce sulfonyl radical **IV** *via* intermediate **I**, **II,** and **III,** followed by nitrogen gas were evolved to give sulfonyl radical intermediate **IV**. Subsequently, generated sulfonyl radical **IV** could further combine with styrenes to form stable benzylic radical **V**. Next, benzylic radical **V** reacted with NIS to furnish *β*-iodo sulfone **7a** as intermediate. At the final stage, $K_2CO_3$ eliminated the hydroiodic acid (HI) to get the desired product **3aa**.

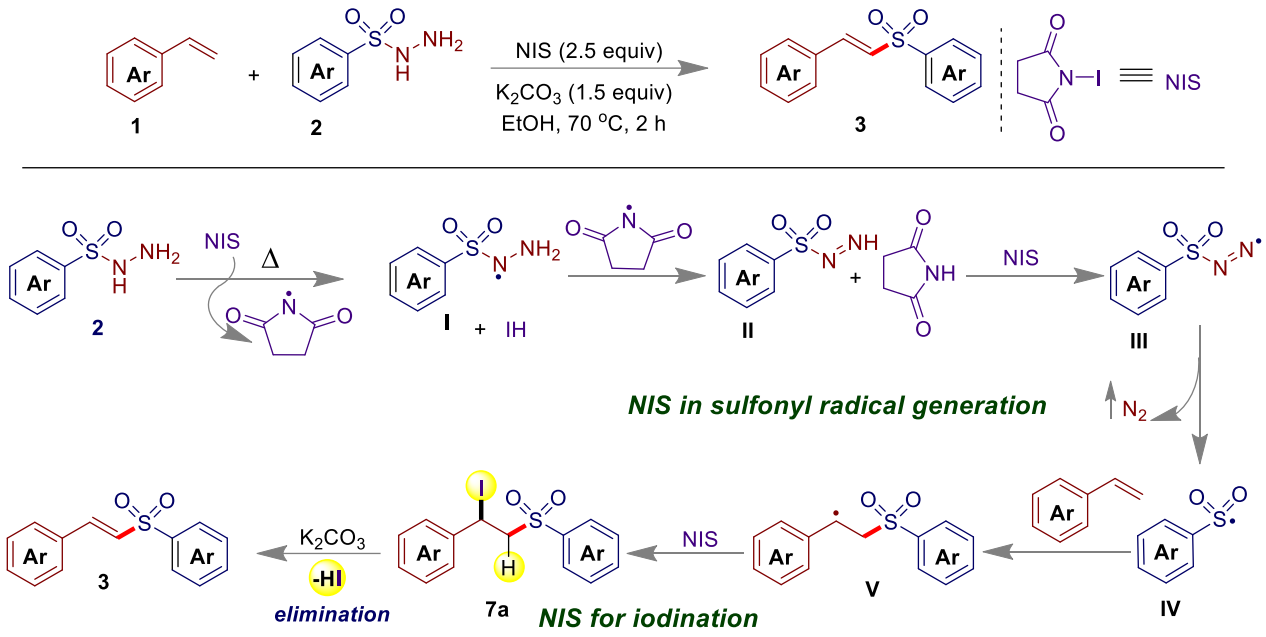



**Figure 2.5.** Plausible mechanism.

Furthermore, unsuccessful substrates were listed in Figure 2.6. Compounds like allylbenzene and hex-1-ene did not result in related products **3qa** and **3ra** because of the instability of radical intermediate. Likewise, compound **3sa** was also not formed because N-iodosuccinimide could

possibly react with a nitrogen atom.[30] Similarly, amino styrenes **1u** was failed to give vinyl sulfone **3ua** because of the strong acid-base reaction between iodine and amine**.** On the other hand, the steric factor was also implemented for $\alpha$-methyl styrenes which failed to provide **3va**.

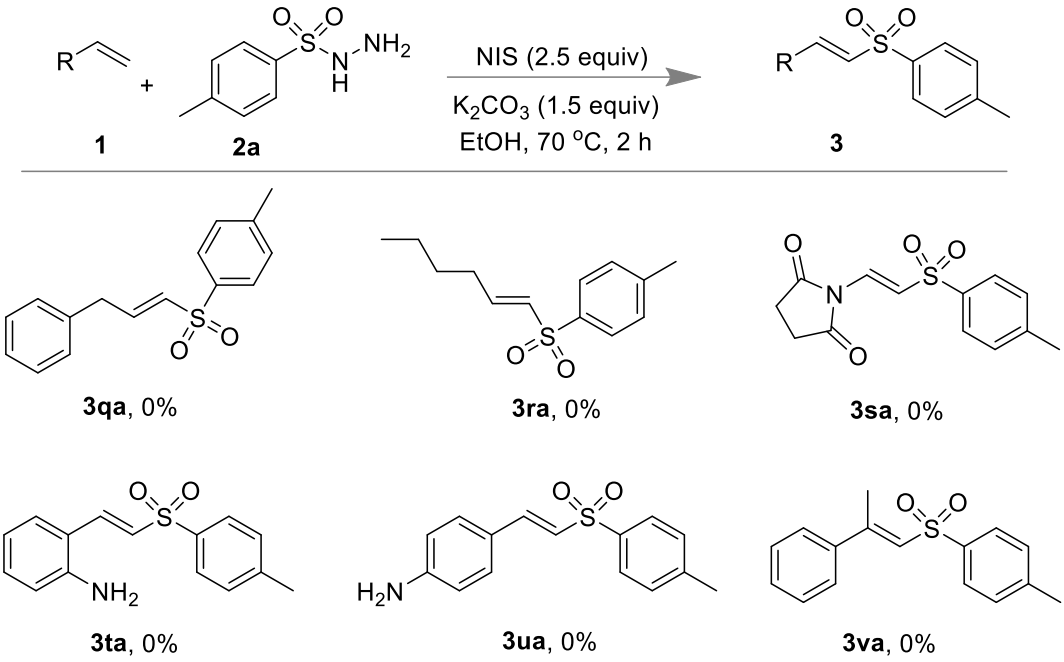



**Figure 2.6.** Unsuccessful substrates.

## 2.4 CONCLUSION

In summary, we have developed a new efficient method for synthesizing vinyl sulfone for the first time by using *N*-iodosuccinimide as an oxidant. Significantly, neither any additive nor any radical initiator like peroxide was needed in this reaction. This protocol shows operationally simple, scalable synthesis, short reaction time, highly regio and stereoselectivity, broad substrate scopes, implying a more convenient approach over the traditional methods.

## 2.5 EXPERIMENTAL SECTION

**General aspects**

All reactions were carried out under an open atmosphere unless otherwise noted .All solvents were generally distilled by following the standard procedures prior to use. All reactions were monitored by TLC on Merck 60 F254 aluminum sheets pre-coated with silica gel .Column chromatography was performed using Chemlabs silica-gel 230-400 mesh. The NMR studies were carried out by Bruker 400 and 700 MHz at room temperature in $CDCl_3$ solutions; $^1H$ chemical shifts are given in $\delta$ (ppm) related to TMS as internal standard, coupling constants *J* values in Hz, and the chemical shift value (δ, ppm) are reported in chloroform-$d_3$ (7.26 for $^1H$ and 77.16 ppm for $^{13}C$. Mass spectroscopy was recorded using an ESI-TOF instrument (Bruker). Infra-red spectroscopic studies were performed and described in wavenumber ($cm^{-1}$). The single-crystal XRD was analyzed in a Rigaku Oxford diffractometer, and the crystal is deposited in the Cambridge Crystallographic Data Centre. Melting point are recorded in $^oC$. The elaborate procedure for the preparation of target molecules and the other intermediates are described below.

**General procedure for preparation of sulfonyl hydrazide (2):**

To an oven-dried round-bottomed flask, *p*-toluenesulfonyl chloride (5 g, 26.2 mmol) in THF (15 mL) was allowed to stir at 0 $^oC$. Following, hydrazine monohydrate (2.7 g, 55 mmol) was injected in a dropwise manner to cold the solution, followed by the whole reaction mixture was allowed for 30 min. Afterward, THF was removed under reduced pressure, and content was extracted with ethyl acetate and water, dried with sodium sulfate. Next, the organic layer was

reduced under vacuum to get crude solid. Finally, recrystallization was done with EtOH to afford the desired hydrazines in 96% yield (4.65 g).

**General procedure for the synthesis of (*E*)-vinyl sulfone (3aa).**

In a oven dried sealed tube, styrene **1a** (60 mg, 0.576 mmol), *p*-toluenesulfonyl hydrazide **2a** (160 mg, 0.864 mmol) were dissolved in 3 mL of EtOH. Following, potassium carbonate ($K_2CO_3$) (0.864 mmol) was added to this. Next, N-iodosuccinimide (324 mg, 1.44 mmol) was slowly added. After that, the whole reaction mixture was kept at 70 ºC for a reaction time like 2 h. After completion of the reaction, the reaction mixture was allowed to cool, and excess ethanol was removed under pressure. Next, the crude mixture was extracted with EtOAc/$H_2O$ and saturated $Na_2S_2O_3$ solution. The organic part was dried over sodium sulfate (anhydrous) and reduced in a vacuum. The crude product was further purified by using chromatography in ethyl acetate and hexane (1:9 v/v) mixture as eluent to get the pure desired product in 98% yield (145 mg).

**Scale-up synthesis for 3aa.**

In a sealed tube, styrene (**1a)** (1.0 g, 9.6 mmol), *p*-toluenesulfonyl hydrazide (**2a)** (3.5 g, 19.2 mmol) were dissolved in 3 mL of EtOH. Following, potassium carbonate ($K_2CO_3$) (2.6 g, 19.2 mmol) was added to this. Next, N-iodosuccinimide (NIS) (5.4 g, 24 mmol) was slowly added. After that, the whole mixture was kept at 70 ºC for a reaction time like 2 h. After completion of the reaction, the reaction mixture was allowed to cool, and excess ethanol was removed under pressure. Next, the crude mixture was extracted with EtOAc/$H_2O$ and saturated $Na_2S_2O_3$ solution. The organic solutions were dried over sodium sulfate (anhydrous) and concentrated in a

vacuum. The crude reaction mixture was further purified by chromatography using ethyl acetate and hexane (1:9 v/v) mixture as eluent to get the pure desired product in 92% yield (2.27 g).

**Radical trapping experiment in the presence of TEMPO/BHT.**

Compound **1a** (0.576 mmol, 66 μL) and **2a** (0.864 mmol) were mixed in an oven-dried sealed tube (50 mL). Following, $K_2CO_3$ (120 mg, 0.864 mmol) and TEMPO (0.864 mmol) were put in the solution, and content was further dissolved in 2 mL of EtOH. Afterward, N-iodosuccinimide (1.44 mmol) was added portion-wise. The container was further permitted to heat at 70 ºC for another 2 h. Progress of the reaction was monitored by using TLC, but no desired product was found. Similarly, the addition of BHT (190 mg, 0.864 mmol) also displayed failure of product formation.

**The reaction of 1a with 4-methylbenzenesulfonyl iodide (4a).**

Styrenes **1a** (66 μL, 0.576 mmol), 4-methylbenzenesulfonyl iodide **4a** (243 mg, 0.864 mmol), potassium carbonate (120 mg, 0.864 mmol), were taken in EtOH (2 mL) in a sealed tube (50 mL). Following, the reaction tube was heated at 70 ºC for 2 h. Progress of the reaction was examined by using TLC, but the desired product was not detected.

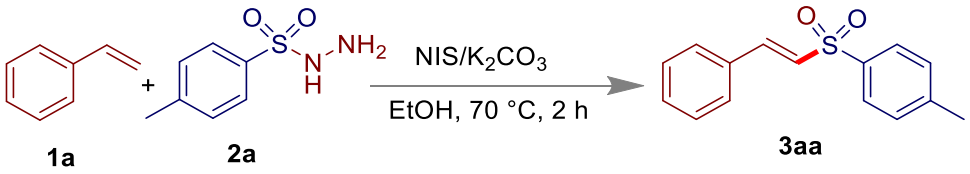
**The reaction of 1a with sulfothionic acid (5a).**

Styrene (**2a)** (66 μL, 0.576 mmol), sulfothionic acid (**5a)** (240 mg, 0.864 mmol) and $K_2CO_3$ (120 mg, 0.864 mmol) were dissolved in 2 mL of EtOH. Following, NIS (324 mg, 1.44 mmol) was added portion-wise. The reaction tube was allowed to stir at 70 ºC for 2 h. Progress of the reaction was scrutinized by using TLC, but the desired product was not found.

**The reaction of *β*-iodosulfone (6a) under standard conditions.**

In a 50 mL sealed tube, *β*-iodosulfone (6**a**) (90 mg, 0.233 mmol); and $K_2CO_3$ (48 mg, 0.349 mmol) were mixed in 2 mL of EtOH. Following, N-iodosuccinimide (131 mg, 0.582 mmol) was added portion-wise. The reaction tube was stirred at 70 ºC for 2 h. After completion of the reaction, the resulting solution was cooled, concentrated under vacuum. The solid residue was purified by column chromatography using ethyl acetate/hexane as an eluent to afford desired product in 75% yield (46 mg).

**Table 2.2.** Optimization of reaction condition[a]




| entry | NIS load (equiv) | $K_2CO_3$ load (equiv) | yield (%) |
|---|---|---|---|
| 1 | 1.0 | 1.0 | 33 |
| 2 | 1.5 | 1.5 | 39 |
| 3 | 2.0 | 1.5 | 86 |
| 4 | 2.5 | 1.5 | 98 |
| 5 | 2.5 | 1.0 | 63 |

Reaction condition[a]: **1a** (0.576 mmol), **2a** (0.864 mmol), solvent (2 mL), isolated yield.

**Crystallographic Investigation**

The compound **3aa** was recrystallized in ethanol and water mixture (ca. 30%). The crystals data were collected with a Bruker SMART D8 goniometer equipped with an APEX CCD detector and

with an INCOATEC micro source (Cu-Kα radiation, λ = 0.71073 Å). SAINT+[31] and SADABS[32] were used to integrate the intensities and to correct the absorption, respectively. The structure was resolved by direct methods and refined on $F^2$ with SHELXL-97.[33]

Compound (**3aa**) (CCDC 1859757)

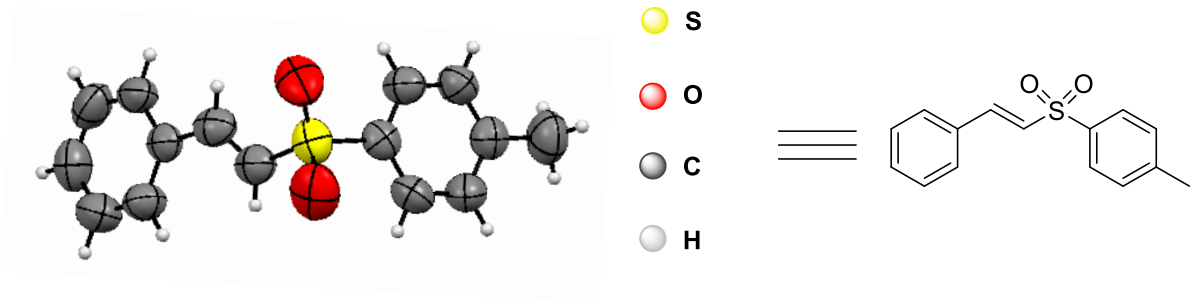



**Figure 2.7**. Crystal structure of (**3aa**) (CCDC 1859757).

Crystallographic Data for **3aa**

| | |
|---|---|
| Empirical formula | $C_{15}H_{14}O_2S$ |
| Formula weight | 258.32 |
| Temperature/K | 293 |
| Crystal system | orthorhombic |
| Space group | $P2_12_12_1$ |
| a/Å | 5.5953(3) |
| b/Å | 8.2183(4) |
| c/Å | 29.7693(18) |
| α/° | 90 |
| β/° | 90 |

| | |
|---|---|
| γ/° | 90 |
| Volume/Å$^3$ | 1368.90(13) |
| Z | 4 |
| $\rho_{calc}$g/cm$^3$ | 1.253 |
| μ/mm$^{-1}$ | 2.027 |
| F(000) | 544.0 |
| Crystal size/mm$^3$ | 0.24 × 0.19 × 0.18 |
| Radiation | CuKα (λ = 1.54184) |
| Reflections collected | 9014 |
| Independent reflections | 2761 [$R_{int}$ = 0.0661, $R_{sigma}$ = 0.0385] |
| Goodness-of-fit on $F^2$ | 1.061 |
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.0664, $wR_2$ = 0.2024 |
| Final R indexes [all data] | $R_1$ = 0.0964, $wR_2$ = 0.2783 |
| Largest diff. peak/hole / e Å$^{-3}$ | 0.34/-0.35 |

## CHARACTERIZATION DATA

**(*E*)-1-Methyl-4-(styrylsulfonyl)benzene (3aa):**[34] $R_f$ = 0.65 (20% ethyl acetate in hexane); white solid; yield 98% (145 mg); mp 120-122 ºC (lit.[34] 124-125 ºC); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.2 Hz, 2H), 7.66 (d, *J* = 15.4 Hz, 1H), 7.49-7.46 (m, 2H), 7.41-7.38 (m, 3H), 7.34 (d, *J* = 8.2 Hz, 2H), 6.85 (d, *J* = 15.4 Hz, 1H), 2.43 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 144.5, 142.1, 137.9, 132.6, 131.2, 130.1, 129.2, 128.7, 127.9, 127.9, 21.8.

**(*E*)-1-Methyl-4-((4-methylstyryl)sulfonyl)benzene (3ba):**[34] $R_f$ = 0.75 (20% ethyl acetate in hexane); white solid; yield 91% (126 mg); mp 144-146 ºC (lit.[34] 145-147 ºC); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.2 Hz, 2H), 7.62 (d, *J* = 15.4 Hz, 1H), 7.37 (d, *J* = 8.2 Hz, 2H), 7.34 (d, *J* = 8.2 Hz, 2H), 7.19 (d, *J* = 8.2 Hz, 2H), 6.79 (d, *J* = 15.4 Hz, 1H), 2.43 (s, 3H), 2.37 (s, 3H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 144.4, 142.2, 141.9, 138.1, 130.1, 129.9, 129.9, 128.7, 127.8, 126.5, 21.8, 21.7.

**(*E*)-1-Methyl-2-(2-tosylvinyl)benzene (3ca):**[35] $R_f$ = 0.7 (20% ethyl acetate in hexane); white solid; yield 87% (120 mg); mp 125-127 ºC (lit.[35] 126-127 ºC); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 15.4 Hz, 1H), 7.83 (d, *J* = 8.2 Hz, 2H), 7.42 (d, *J* = 7.8 Hz, 1H), 7.35 (d, *J* = 8.2 Hz, 2H), 7.32-7.27 (m, 1H), 7.22-7.16 (m, 2H), 6.77 (d, *J* = 15.4 Hz, 1H), 2.45 (s, 3H), 2.44 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 144.5, 139.7, 138.3, 137.8, 131.4, 131.1, 131.0, 130.1, 128.6, 127.8, 126.9, 126.6, 21.8, 19.9.

**(*E*)-1-Isopropyl-4-(2-tosylvinyl)benzene (3da):** $R_f$ = 0.8 (20% ethyl acetate in hexane); brownish white solid; yield 79% (97 mg); mp 110-113 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.2 Hz, 2H), 7.63 (d, *J* = 15.4 Hz, 1H), 7.40 (d, *J* = 8.2 Hz, 2H), 7.33 (d, *J* = 8.2 Hz, 2H), 7.24 (d, *J* = 8.2 Hz, 2H), 6.79 (d, *J* = 15.4 Hz, 1H), 2.91 (sept, *J* = 6.8 Hz, 1H), 2.43 (s, 3H), 1.24 (d, *J* = 6.8 Hz, 6H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 152.7, 144.4, 142.2, 138.1, 130.2, 130.1, 128.8, 127.8, 127.3, 126.6, 34.3, 23.8, 21.7; IR (KBr) ῡ 3049, 2957, 1613, 1458, 1302, 1142, 585, 528; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{21}O_2S$ 301.1257; found 301.1228.

**(*E*)-1,3,5-Trimethyl-2-(2-tosylvinyl)benzene (3ea):**[36] $R_f$ = 0.85 (20% ethyl acetate in hexane); white solid; yield 73% (90 mg); mp 103-106 ºC (lit.[36] 104-106 ºC); $^1$H NMR (700 MHz, $CDCl_3$) δ 7.85-7.81 (m, 3H), 7.34 (d, *J* = 8.0 Hz, 2H), 6.87 (s, 2H), 6.52 (d, *J* = 15.8 Hz, 1H), 2.44 (s, 3H), 2.28 (s, 6H), 2.27 (s, 3H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 144.4, 140.5, 139.5, 138.1, 137.2, 132.1, 130.1, 129.5, 128.7, 127.8, 21.8, 21.2, 21.2.

**(*E*)-4-(2-Tosylvinyl)-1,1'-biphenyl (3fa):** $R_f$ = 0.75 (20% ethyl acetate in hexane); white solid; yield 75% (83 mg); mp 226-228 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.2 Hz, 2H), 7.69 (d, *J* = 15.4 Hz, 1H), 7.62 (d, *J* = 8.2 Hz, 2H), 7.59 (d, *J* = 7.4 Hz, 2H), 7.55 (d, *J* = 8.2 Hz, 2H), 7.45 (t, *J* = 7.4 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.35 (d, *J* = 8.2 Hz, 2H), 6.87 (d, *J* = 15.4 Hz, 1H), 2.44 (s, 3H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 144.5, 144.0, 141.7, 134.1, 137.9, 131.5, 130.1, 129.2, 129.1, 128.2, 127.9, 127.8, 127.5, 127.2, 21.8; IR (KBr) ῡ 2950, 1635, 1408, 1305, 1142, 661, 530; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{19}O_2S$ 335.1100; found 335.1071.

**(*E*)-2-(2-Tosylvinyl)naphthalene (3ga):**[34] $R_f$ = 0.7 (20% ethyl acetate in hexane); white solid; yield 67% (80 mg); mp 157-160 ºC (lit.[34] 159-160 ºC); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.87-7.80 (m, 6H), 7.56-7.50 (m, 3H), 7.35 (d, *J* = 8.2 Hz, 2H), 6.95 (d, *J* = 15.4 Hz, 1H), 2.44 (s, 3H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 144.5, 142.1, 138.0, 134.6, 133.3, 131.0, 130.14, 130.06, 129.1, 128.8, 128.0, 127.9 (×2), 127.8, 127.1, 123.6, 21.8.

**(*E*)-1-Methoxy-4-(2-tosylvinyl)benzene (3ha):**[37] $R_f$ = 0.5 (20% ethyl acetate in hexane);pale yellow solid; yield 60% (77 mg); mp 95-97 ºC (lit.[37] 96-98 ºC); $^1$H NMR (400 MHz, $CDCl_3$) δ

7.81 (d, *J* = 8.2 Hz, 2H), 7.60 (d, *J* = 15.4 Hz, 1H), 7.42 (d, *J* = 8.8 Hz, 2H), 7.33 (d, *J* = 8.2 Hz, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 6.69 (d, *J* = 15.4 Hz, 1H), 3.83 (s, 3H), 2.43 (s, 3H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 162.1, 144.3, 141.9, 138.3, 130.4, 130.0, 127.7, 125.2, 124.9, 114.6, 55.6, 21.7.

**(*E*)-1-Chloro-4-(2-tosylvinyl)benzene (3ia):**[21] $R_f$ = 0.5 (20% ethyl acetate in hexane); white solid; yield 89% (130 mg); mp 152-154 ºC (lit.[21] 149-151 ºC); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.2 Hz, 2H), 7.60 (d, *J* = 15.4 Hz, 1H), 7.40 (d, *J* = 8.6 Hz, 2H), 7.37-7.34 (m, 4H), 6.82 (d, *J* = 15.4 Hz, 1H), 2.44 (s, 3H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 144.7, 140.6, 137.6, 137.3, 131.1, 130.2, 129.8, 129.5, 128.4, 127.9, 21.8.

**(*E*)-1-Methyl-4-((4-(trifluoromethyl)styryl)sulfonyl)benzene (3ja):**[21] $R_f$ = 0.4 (20% ethyl acetate in hexane); white solid; yield 96% (128 mg); mp 120-124 ºC (lit.[21] 120-122 ºC); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.2 Hz, 2H),7.67 (d, *J* = 15.4 Hz, 1H), 7.64 (d, *J* = 8.2 Hz, 2H), 7.58 (d, *J* = 8.2 Hz, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 6.94 (d, *J* = 15.4 Hz, 1H), 2.44 (s, 3H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 145.0, 140.0, 137.3, 136.0, 132.7 (q, $^2J_{C\text{-}F}$ = 32.9 Hz), 130.5, 130.2, 128.8, 128.0, 126.2 (q, $^3J_{C\text{-}F}$ = 3.7 Hz), 123.7 (q, $^1J_{C\text{-}F}$ = 272.4 Hz), 21.8.

**(*E*)-4-(2-Tosylvinyl)benzonitrile (3ka):**[21] $R_f$ = 0.4 (20% ethyl acetate in hexane); white solid; yield 91% (120 mg); mp 125-128 ºC (lit.[21] 125-127 ºC); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.2 Hz, 2H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.64 (d, *J* = 15.4 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.2 Hz, 2H), 6.95 (d, *J* = 15.4 Hz, 1H), 2.45 (s, 3H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 145.2, 139.4, 137.0, 136.9, 132.9, 131.5, 130.3, 129.0, 128.1, 118.2, 114.4, 21.8.

**(*E*)-1-Methyl-4-((4-nitrostyryl)sulfonyl)benzene (3la):**[38] $R_f$ = 0.45 (20% ethyl acetate in hexane); white solid; yield 84% (103 mg); mp 172-174 ºC (lit.[38] 172-175 ºC); $^1$H NMR (700 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.8 Hz, 2H), 7.84 (d, *J* = 8.2 Hz, 2H), 7.69 (d, *J* = 15.4 Hz, 1H), 7.63 (d, *J* = 8.8 Hz, 2H), 7.38 (d, *J* = 8.2 Hz, 2H), 6.99 (d, *J* = 15.4 Hz, 1H), 2.45 (s, 3H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 149.1, 145.2, 138.8, 138.7, 136.9, 132.2, 130.3, 129.3, 128.1, 124.4, 21.9.

**(*E*)-1-Methyl-4-((4-nitrostyryl)sulfonyl)benzene (3la):**[38] $R_f$ = 0.45 (20% ethyl acetate in hexane); white solid; yield 84% (103 mg); mp 172-174 ºC (lit.[38] 172-175 ºC); $^1$H NMR (700 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.8 Hz, 2H), 7.84 (d, *J* = 8.2 Hz, 2H), 7.69 (d, *J* = 15.4 Hz, 1H), 7.63 (d, *J* = 8.8 Hz, 2H), 7.38 (d, *J* = 8.2 Hz, 2H), 6.99 (d, *J* = 15.4 Hz, 1H), 2.45 (s, 3H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 149.1, 145.2, 138.8, 138.7, 136.9, 132.2, 130.3, 129.3, 128.1, 124.4, 21.9.

**(*E*)-1-Nitro-3-(2-tosylvinyl)benzene (3ma):**[37] $R_f$ = 0.45 (20% ethyl acetate in hexane); white solid; yield 70% (85 mg); mp 126-128 ºC (lit.[37] 129-131 ºC); $^1$H NMR (400 MHz, $CDCl_3$) δ 8.32 (brs, 1H), 8.25 (d, *J* = 8.2 Hz, 1H), 7.84 (d, *J* = 8.2 Hz, 2H), 7.78 (d, *J* = 7.8 Hz, 1H), 7.69 (d, *J* = 15.4 Hz, 1H), 7.60 (t, *J* = 8.0, 1H), 7.37 (d, *J* = 8.2 Hz, 2H), 7.01 (d, *J* = 15.4 Hz, 1H), 2.45 (s, 3H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 148.8, 145.1, 138.9, 137.0, 134.4, 134.3, 131.2, 130.4, 130.3, 128.1, 125.4, 122.9, 21.8.

**(*E*)-2-(2-Tosylvinyl)pyridine (3na):**[34] $R_f$ = 0.5 (20% ethyl acetate in hexane); pale yellow solid; yield 34% (51 mg); mp 92-94 ºC (lit.[34] 91-93 ºC); $^1$H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, *J* = 4.6 Hz, 1H), 7.83 (d, *J* = 8.2 Hz, 2H), 7.73 (td, *J* =7.6, 1.6 Hz, 1H), 7.61 (d, *J* = 14.8 Hz, 1H), 7.43 (d, *J* = 14.8 Hz, 1H), 7.40 (d, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 2H), 7.28 (dd, *J* = 7.6, 4.6 Hz,

1H), 2.42 (s, 3H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 151.1, 150.2, 144.8, 139.9, 137.4, 137.3, 132.5, 130.1, 128.1, 125.6, 125.1, 21.7.

**(*E*)-1-Bromo-4-(2-(phenylsulfonyl)vinyl)benzene (3ob):**[39] $R_f$ = 0.5 (20% ethyl acetate in hexane); white solid; yield 93% (98 mg); mp 103-105 ºC (lit.[39] 104-107 ºC); $^1$H NMR (700 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.6 Hz, 2H), 7.67-7.60 (m, 2H), 7.56 (t, *J* = 7.6 Hz, 2H), 7.53 (d, *J* = 8.2 Hz, 2H), 7.35 (d, *J* = 8.2 Hz, 2H), 6.85 (d, *J* = 15.4 Hz, 1H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 141.2, 140.6, 133.7, 132.5, 131.4, 130.1, 129.6, 128.1, 127.9, 125.8.

**(*E*)-1-Chloro-4-(2-(phenylsulfonyl)vinyl)benzene (3ib):**[40] $R_f$ = 0.6 (20% ethyl acetate in hexane); white solid; yield 89% (107 mg); mp 130-132 ºC (lit. 128-130 ºC); $^1$H NMR (700 MHz, $CDCl_3$) δ 7.95 (*J* = 8.4 Hz, 2H), 7.66-7.61 (m, 2H), 7.56 (t, *J* = 7.8 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 15.4 Hz, 1H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 141.1, 140.6, 137.4, 133.7, 131.0, 129.9, 129.6, 129.5, 128.0, 127.9.

**(*E*)-1-(*tert*-Butyl)-4-(styrylsulfonyl)benzene (3ac):**[38] $R_f$ = 0.6 (20% ethyl acetate in hexane); white solid; yield 72% (124 mg); mp 116-118 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.6 Hz, 2H), 7.67 (d, *J* = 15.4 Hz, 1H), 7.55 (d, *J* = 8.6 Hz, 2H), 7.48-7.46 (m, 2H), 7.40-7.35 (m, 3H), 6.86 (d, *J* = 15.4 Hz, 1H), 1.34 (s, 9H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 157.5, 142.1, 137.8, 132.6, 131.2, 129.2, 128.7, 127.8, 127.7, 126.5, 35.4, 31.2.

**(*E*)-1-Bromo-4-(2-((4-(*tert*-butyl)phenyl)sulfonyl)vinyl)benzene (3oc):** $R_f$ = 0.65 (20% ethyl acetate in hexane); white solid; yield 81% (101 mg); mp 172-174 ºC; $^1$H NMR (700 MHz,

$CDCl_3$) δ 7.85 (d, *J* = 8.4 Hz, 2H), 7.60 (d, *J* = 15.4 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.52 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 15.4 Hz, 1H), 1.34 (s, 9H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 157.7, 140.7, 137.5, 132.5, 131.5, 130.0, 128.5, 127.7, 126.6, 125.7, 35.4, 31.2; IR (KBr) ῡ 2964, 1621, 1487, 1306, 1149, 659, 570; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{20}BrO_2S$ 379.0362; found 379.0343.

**(*E*)-1-(2-((4-(*tert*-Butyl)phenyl)sulfonyl)vinyl)-2-chlorobenzene (3pc):** $R_f$ = 0.75 (20% ethyl acetate in hexane); white solid; yield 72% (104 mg); mp 117-119 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 8.07 (d, *J* = 15.4 Hz, 1H), 7.88 (d, *J* = 8.4 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.33 (t, *J* = 7.4 Hz, 1H), 7.26 (t, *J* = 7.4 Hz, 1H), 6.89 (d, *J* = 15.4 Hz, 1H), 1.34 (s, 9H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 157.7, 138.1, 137.3, 135.4, 131.9, 131.0, 130.5, 130.5, 128.4, 127.9, 127.3, 126.6, 35.4, 31.2; IR (KBr) ῡ 2963, 1610, 1471, 1306, 1149, 635, 565; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{20}ClO_2S$ 335.0867; found 335.0851.

**(*E*)-1-Methoxy-4-(styrylsulfonyl)benzene (3ad):**[21] $R_f$ = 0.4 (20% ethyl acetate in hexane); white solid; yield 79% (125 mg); mp 85-87 ºC (lit.[21] 83-85 ºC); $^1$H NMR (700 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.8 Hz, 2H), 7.63 (d, *J* = 15.4 Hz, 1H), 7.47 (d, *J* = 6.8 Hz, 2H), 7.41-7.37 (m, 3H), 7.01 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 15.4 Hz, 1H), 3.87 (s, 3H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 163.7, 141.5, 132.6, 132.3, 131.2, 130.0, 129.2, 128.6, 128.1, 114.7, 55.8.

**(*E*)-1-Bromo-4-(2-((4-methoxyphenyl)sulfonyl)vinyl)benzene (3od):** $R_f$ = 0.45 (20% ethyl acetate in hexane); white solid; yield 82% (94 mg); mp 150-152 ºC; $^1$H NMR (700 MHz, $CDCl_3$)

δ 7.86 (d, *J* = 8.8 Hz, 2H), 7.56 (d, *J* = 15.4 Hz, 1H), 7.52 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.01 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 15.4 Hz, 1H), 3.87 (s, 3H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 163.8, 140.1, 132.5, 132.0, 131.6, 130.1, 130.0, 128.8, 125.6, 114.8, 55.9; IR (KBr) ῡ 1632, 1490, 1318, 1141, 672, 562; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{15}H_{14}BrO_3S$ 352.9842; found 352.9819.

**(*E*)-1-Isopropyl-4-(styrylsulfonyl)benzene (3ae):** $R_f$ = 0.8 (20% ethyl acetate in hexane); white solid; yield 76% (125 mg); mp 96-98 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.4 Hz, 2H), 7.66 (d, *J* = 15.4 Hz, 1H), 7.48 (d, *J* = 6.6 Hz, 2H), 7.41-7.37 (m, 5H), 6.85 (d, *J* = 15.4 Hz, 1H), 3.35-2.63 (sept, *J* = 6.8 Hz, 1H), 1.27 (d, *J* = 6.8 Hz, 6H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 155.2, 142.1, 138.1, 132.6, 131.2, 129.2, 128.7, 128.0, 127.8, 127.6, 34.4, 23.8; IR (KBr) ῡ 2961, 1626, 1455, 1311, 1142, 652, 556; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{19}O_2S$ 287.1100; found 287.1075.

**(*E*)-1-Nitro-4-(styrylsulfonyl)benzene (3af):**[21] $R_f$ = 0.45 (20% ethyl acetate in hexane); brownish white; yield 57% (95 mg); mp 156-158 ºC (lit.[21] 152-154 ºC); $^1$H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, *J* = 8.8 Hz, 2H), 8.15 (d, *J* = 8.8 Hz, 2H), 7.77 (d, *J* = 15.4 Hz, 1H), 7.51 (d, *J* = 6.6 Hz, 2H), 7.48-7.39 (m, 3H), 6.85 (d, *J* = 15.4 Hz, 1H); $^{13}$C NMR (175 MHz, DMSO-$d_6$) δ 150.7, 146.6, 144.6, 132.7, 132.1, 129.7, 129.5, 129.3, 127.2, 125.4.

**(*E*)-1-(Styrylsulfonyl)naphthalene (3ag):**[34] $R_f$ = 0.7 (20% ethyl acetate in hexane); white solid; yield 71% (121 mg); mp 127-130 ºC (lit.[34] 129-131 ºC); $^1$H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, *J* = 8.6 Hz, 1H), 8.42 (d, *J* = 7.4 Hz, 1H), 8.13 (d, *J* = 8.2 Hz, 1H), 7.96 (d, *J* = 8.2 Hz, 1H), 7.82

(d, *J* = 15.4 Hz, 1H), 7.68 (t, *J* = 7.8 Hz, 1H), 7.61 (dd, *J* = 15.8, 7.8 Hz, 2H), 7.48-7.46 (m, 2H), 7.39-7.34 (m, 3H), 7.00 (d, *J* = 15.4 Hz, 1H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 142.8, 135.6, 135.3, 134.4, 132.5, 131.3, 130.0, 129.3, 129.2, 128.8, 128.7, 128.7, 127.6, 127.1, 124.8, 124.4.

**(*E*)-(2-(Butylsulfonyl)vinyl)benzene (3ah):**[34] $R_f$ = 0.75 (20% ethyl acetate in hexane); yellow liquid; yield 58% (75 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 15.4 Hz, 1H), 7.52 (dd, *J* = 7.4, 1.6 Hz, 2H), 7.44-7.40 (m, 3H), 6.82 (d, *J* = 15.4 Hz, 1H), 3.08-3.04 (m, 2H), 1.84-1.77 (m, 2H), 1.51-1.42 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 144.9, 132.4, 131.5, 129.3, 128.7, 124.8, 55.1, 24.7, 21.8, 13.7.

**(*E*)-2-(2-(Butylsulfonyl)vinyl)naphthalene (3gh):** $R_f$ = 0.75 (20% ethyl acetate in hexane); white solid; yield 67% (72 mg); mp 110-112 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.91-7.81 (m, 3H), 7.76 (d, *J* = 15.4 Hz, 1H), 7.62 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.59-7.53 (m, 2H), 6.92 (d, *J* = 15.4 Hz, 1H), 3.13-3.06 (m, 2H), 1.90-1.74 (m, 2H), 1.52-1.45 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 145.0, 134.7, 133.3, 131.2, 129.9, 129.2, 128.9, 128.0, 128.0, 127.2, 124.8, 123.5, 55.2, 24.7, 21.8, 13.7; IR (KBr) ῡ 3054, 2923, 2870, 1614, 1455, 1311, 1122, 595, 558; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{19}O_2S$ 275.1100; found 275.1072.

## 2.6 NOTES AND REFERENCES

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## NMR Spectrum of Selected Compounds

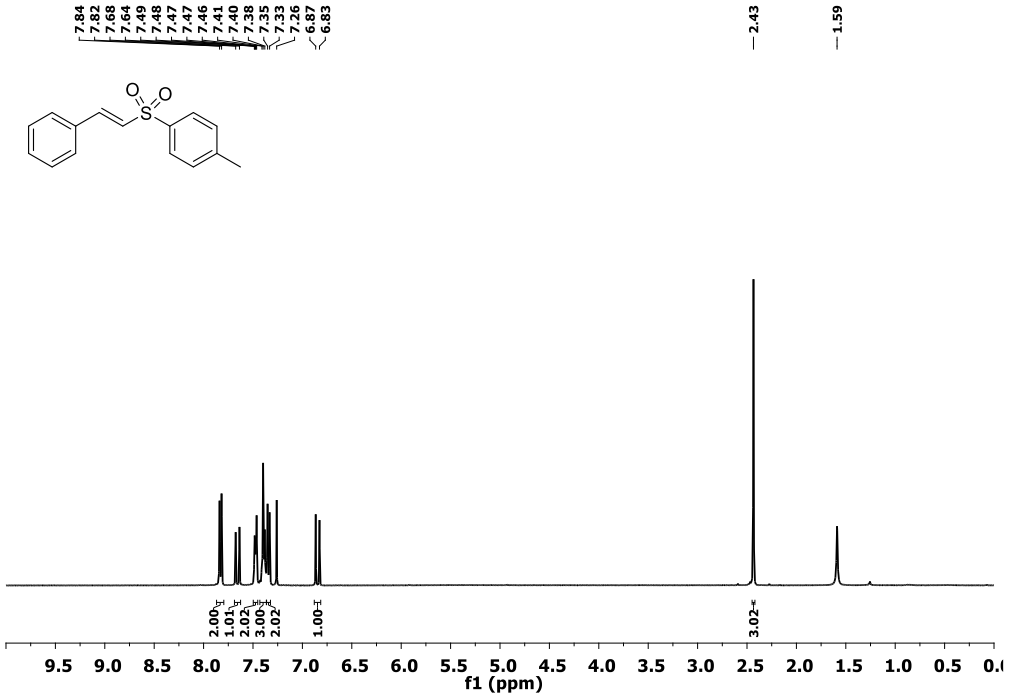



**Figure 2.8.** $^{1}$H NMR spectrum of (*E*)-1-Methyl-4-(styrylsulfonyl)benzene (**3aa**)

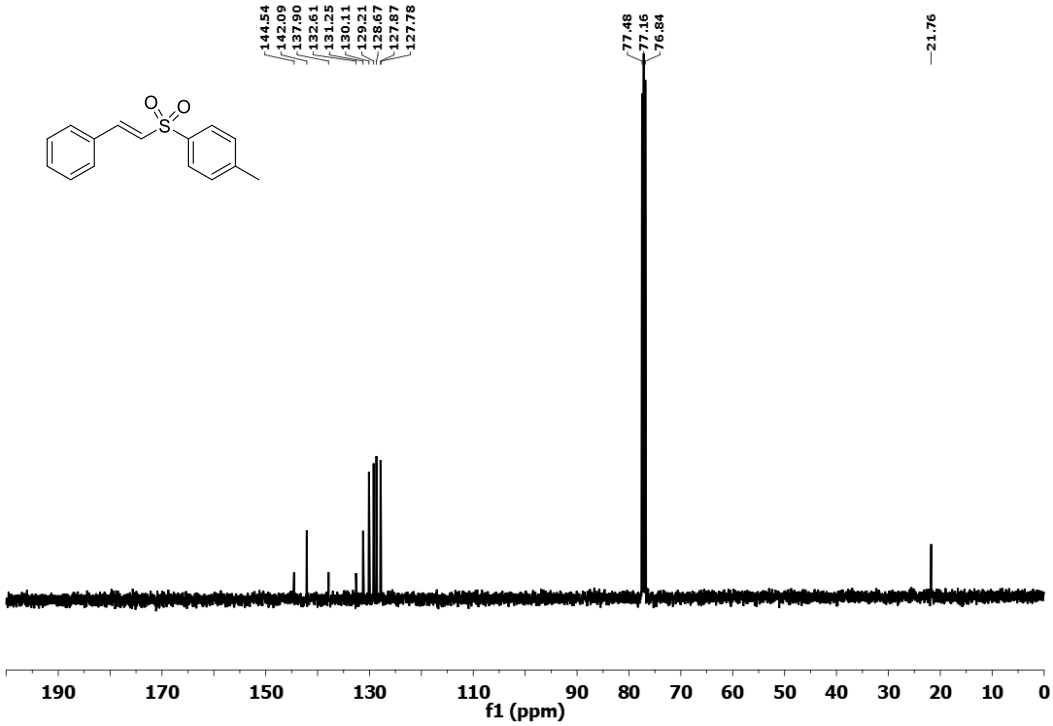



**Figure 2.9.** $^{13}$C NMR spectrum of (*E*)-1-Methyl-4-(styrylsulfonyl)benzene (**3aa**)

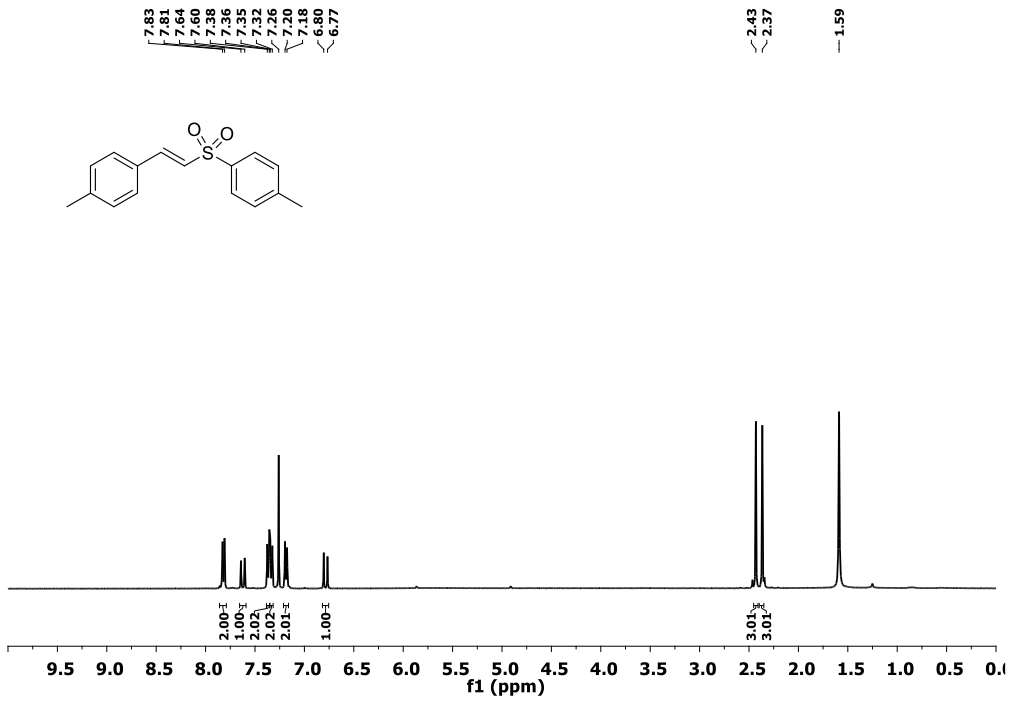



**Figure 2.10.** $^{1}$H NMR spectrum of (*E*)-1-Methyl-4-((4-methylstyryl)sulfonyl)benzene (**3ba**)

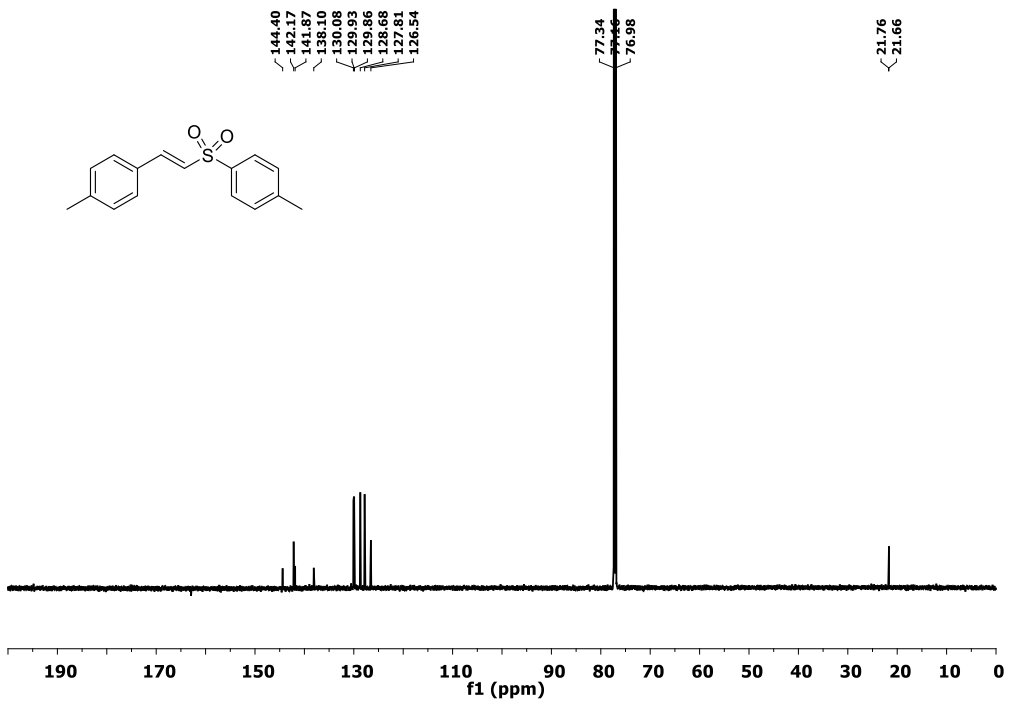



**Figure 2.11.** $^{13}$C NMR spectrum of (*E*)-1-Methyl-4-((4-methylstyryl)sulfonyl)benzene (**3ba**)

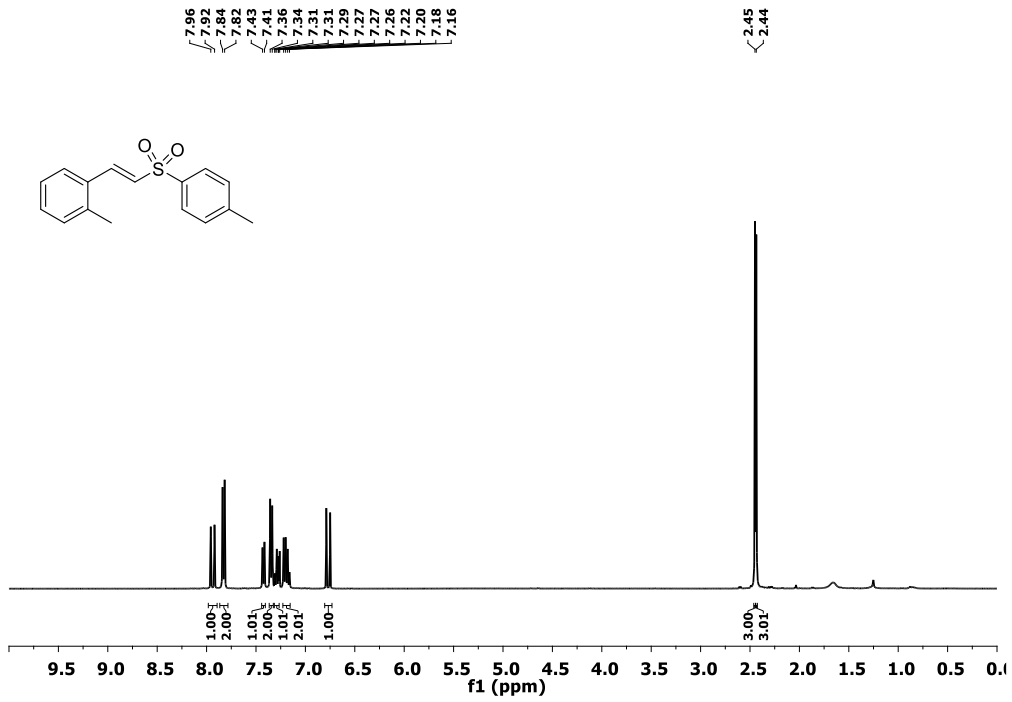



**Figure 2.12.** $^{1}$H NMR spectrum of (*E*)-1-Methyl-2-(2-tosylvinyl)benzene (**3ca**)

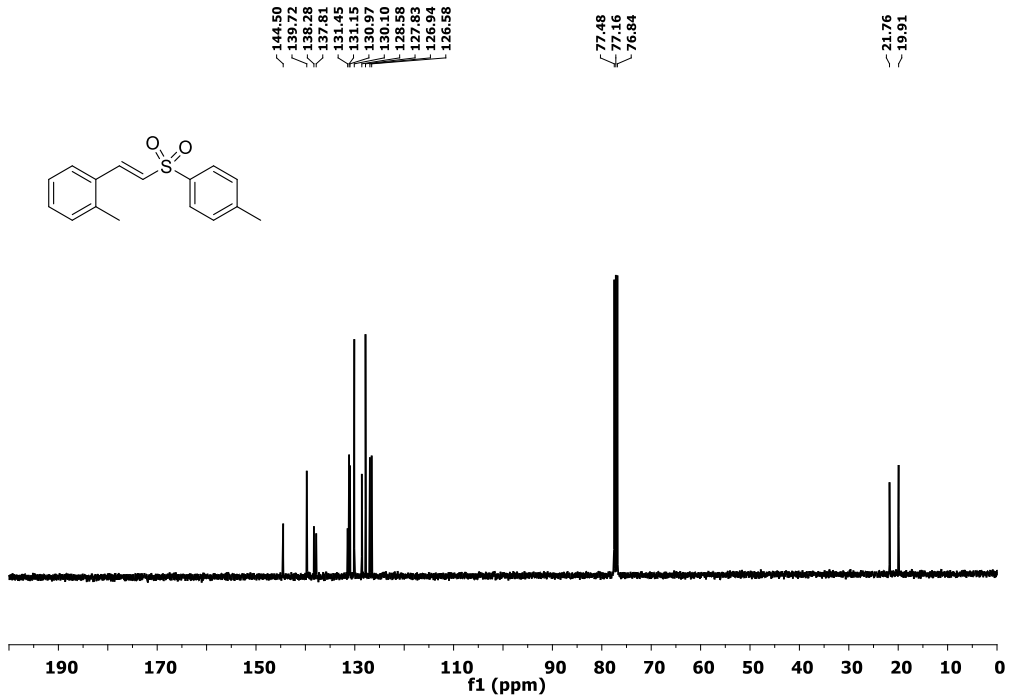



**Figure 2.13.** $^{13}$C NMR spectrum of (*E*)-1-Methyl-2-(2-tosylvinyl)benzene (**3ca**)

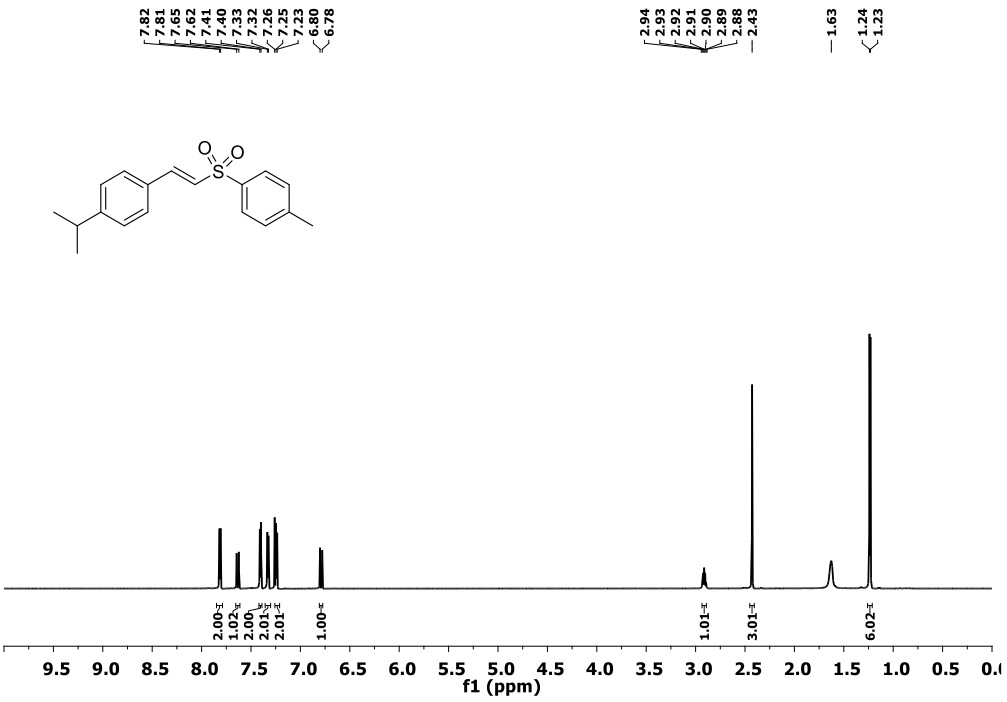



**Figure 2.14.** $^{1}$H NMR spectrum of (*E*)-1-Isopropyl-4-(2-tosylvinyl)benzene (**3da**)

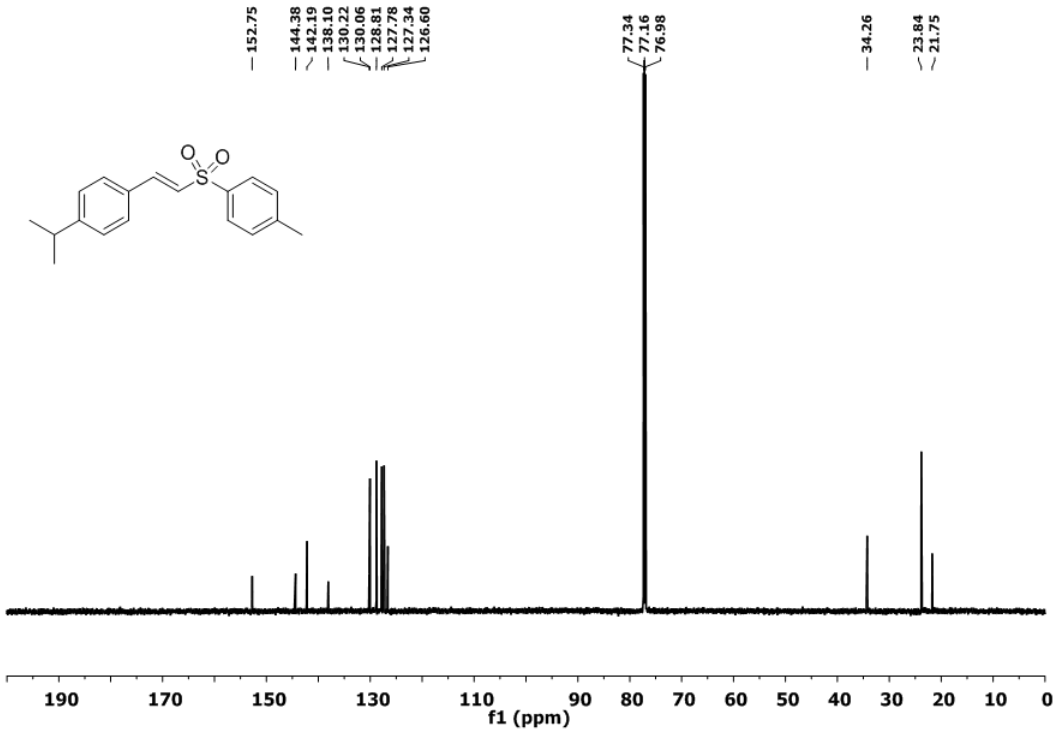



**Figure 2.15.** $^{13}$C NMR spectrum of (*E*)-1-Isopropyl-4-(2-tosylvinyl)benzene (**3da**)

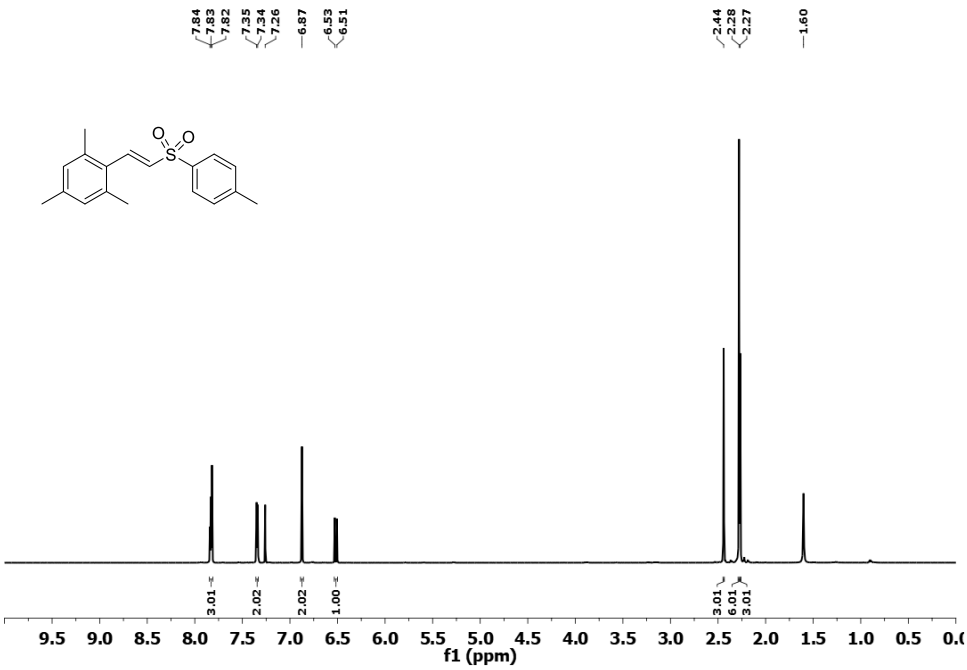



**Figure 2.16.** $^{1}$H NMR spectrum of (*E*)-1,3,5-Trimethyl-2-(2-tosylvinyl)benzene (**3ea**)

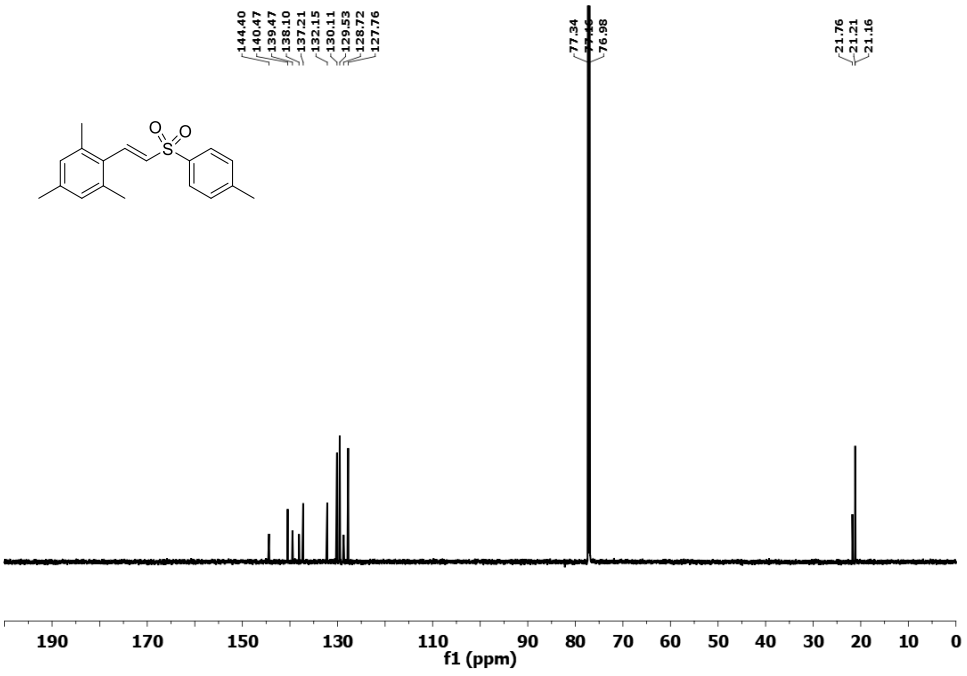



**Figure 2.17.** $^{13}$C NMR spectrum of (*E*)-1,3,5-Trimethyl-2-(2-tosylvinyl)benzene (**3ea**)

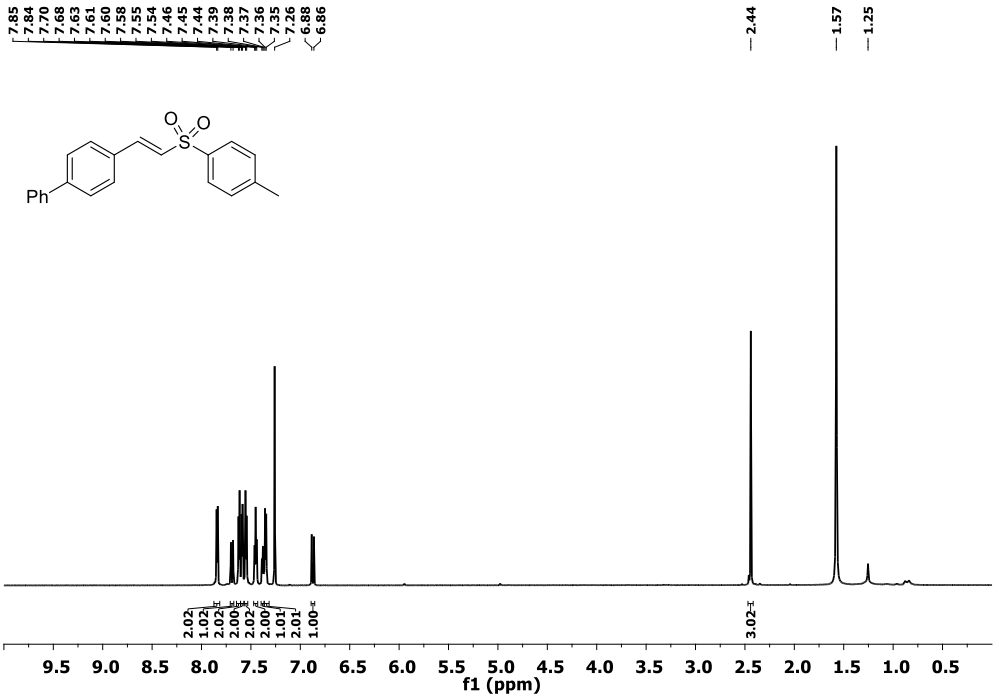



**Figure 2.18.** $^{1}$H NMR spectrum of (*E*)-4-(2-Tosylvinyl)-1,1'-biphenyl (**3fa**)

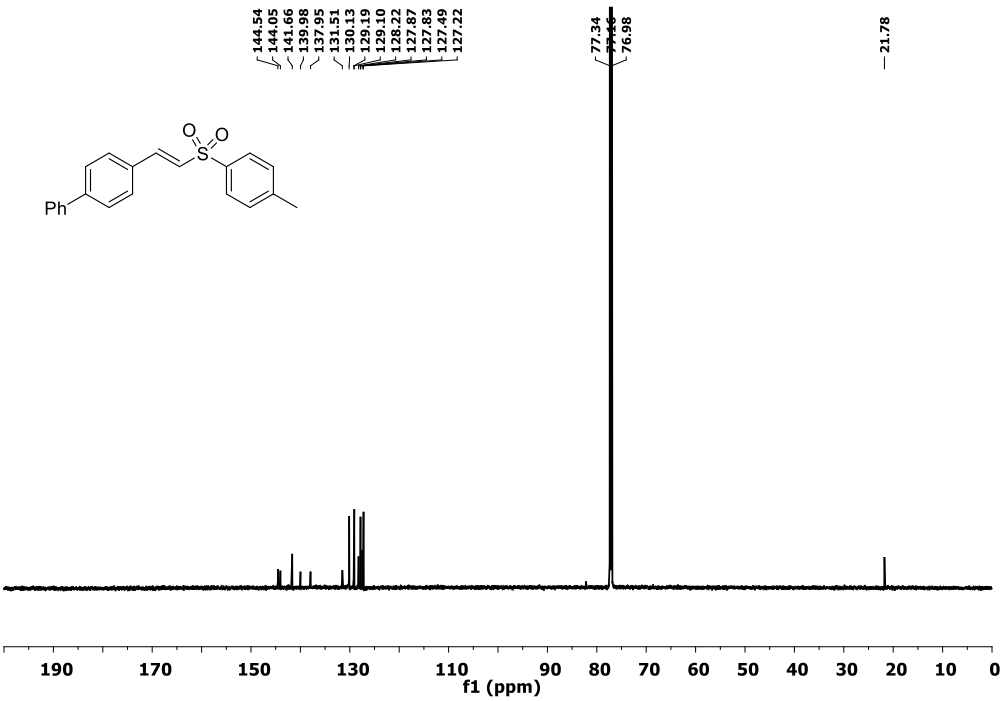



**Figure 2.19.** $^{13}$C NMR spectrum of (*E*)-4-(2-Tosylvinyl)-1,1'-biphenyl (**3fa**)

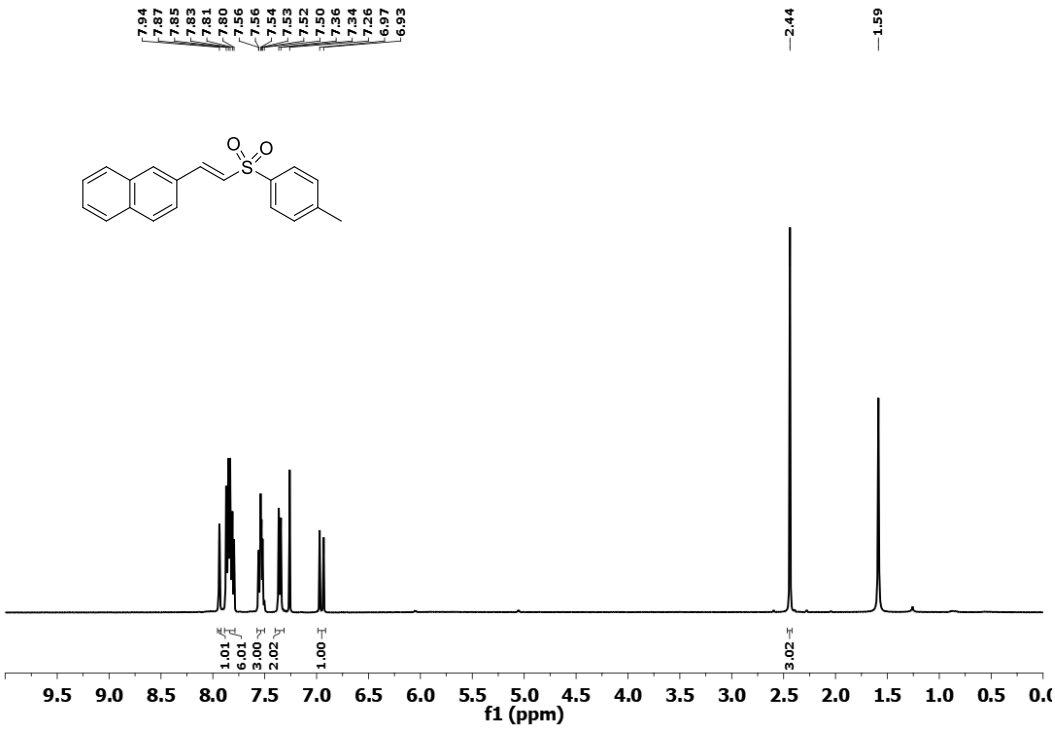



**Figure 2.20.** $^{1}$H NMR spectrum of (*E*)-2-(2-Tosylvinyl)naphthalene (**3ga**)

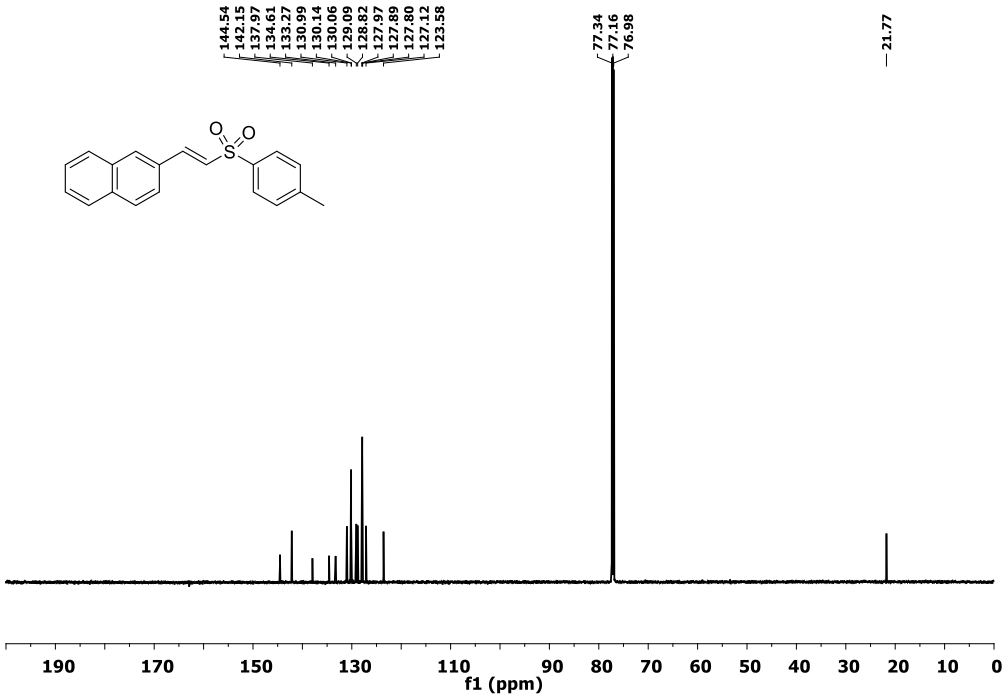



**Figure 2.21.** $^{13}$C NMR spectrum of (*E*)-2-(2-Tosylvinyl)naphthalene (**3ga**)

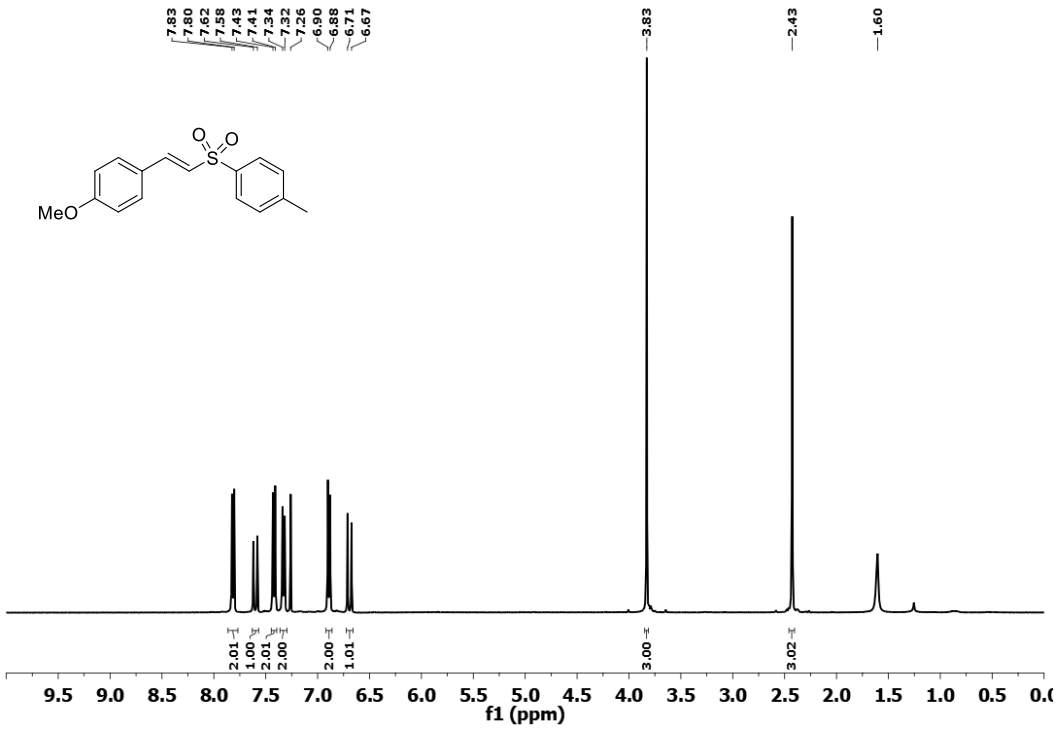



**Figure 2.22.** $^{1}$H NMR spectrum of (*E*)-1-Methoxy-4-(2-tosylvinyl)benzene (**3ha**)

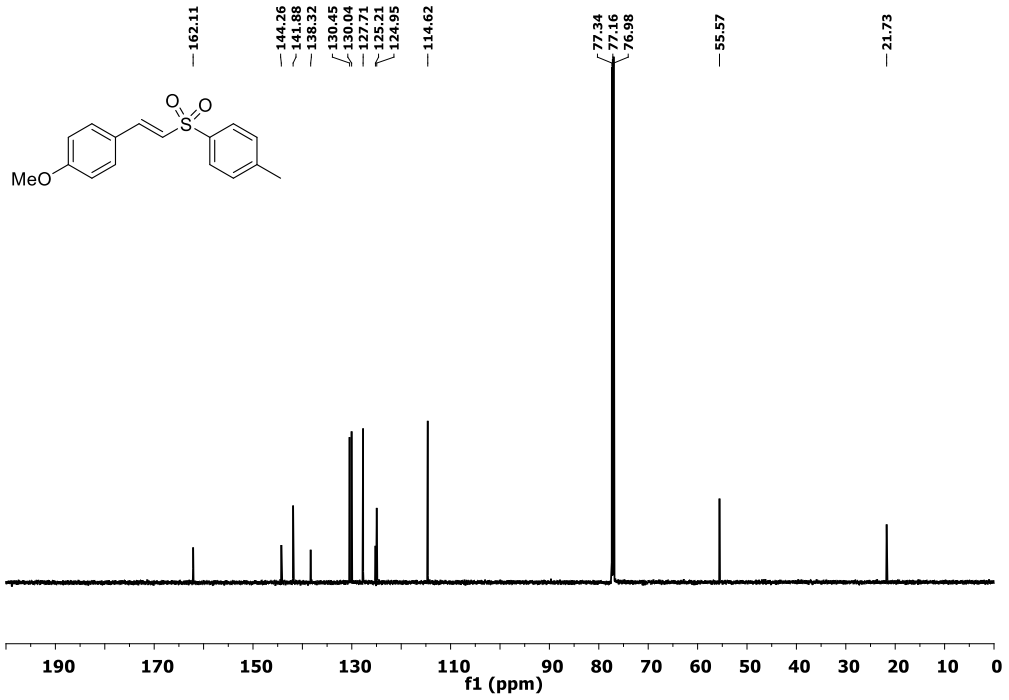



**Figure 2.23.** $^{13}$C NMR spectrum of (*E*)-1-Methoxy-4-(2-tosylvinyl)benzene (**3ha**)

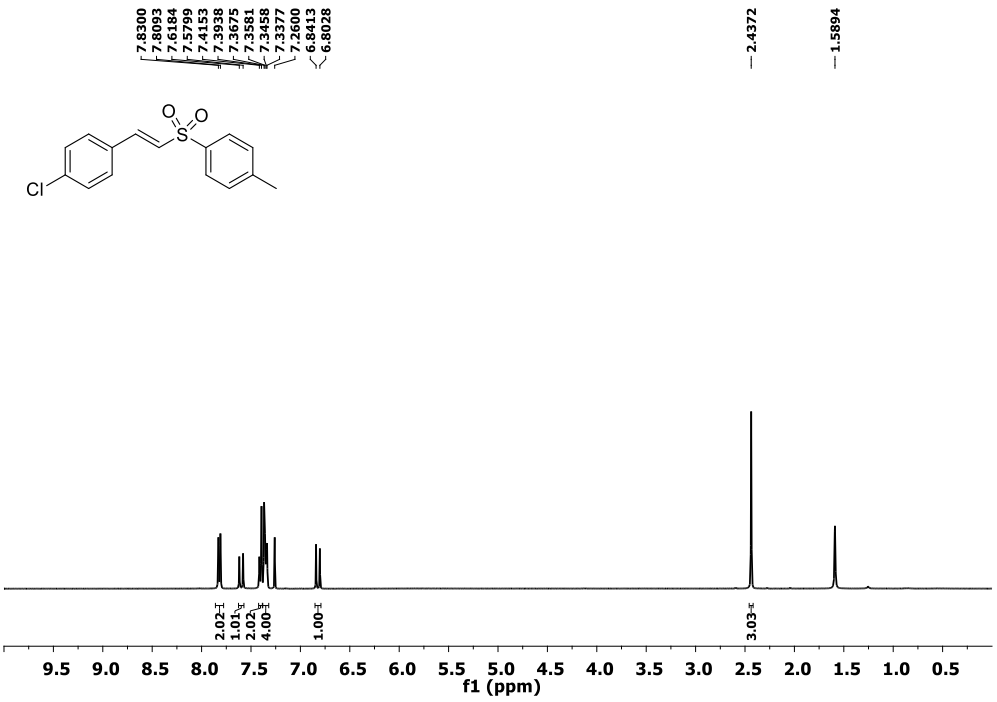



**Figure 2.24.** $^{1}$H NMR spectrum of (*E*)-1-Chloro-4-(2-tosylvinyl)benzene (**3ia**)

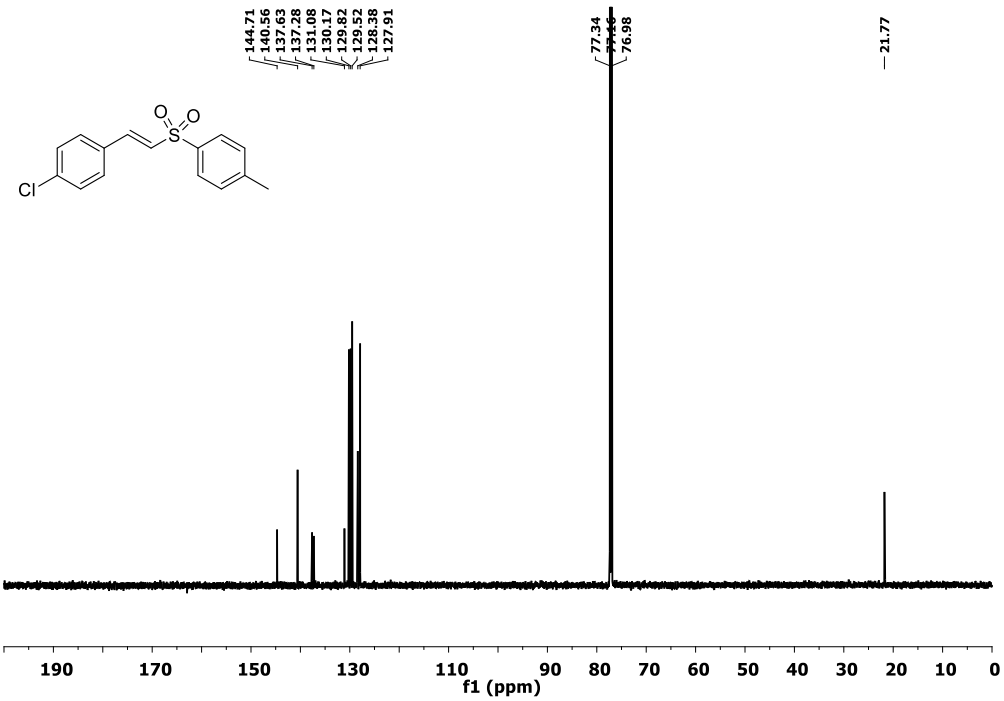



**Figure 2.25.** $^{13}$C NMR spectrum of (*E*)-1-Chloro-4-(2-tosylvinyl)benzene (**3ia**)

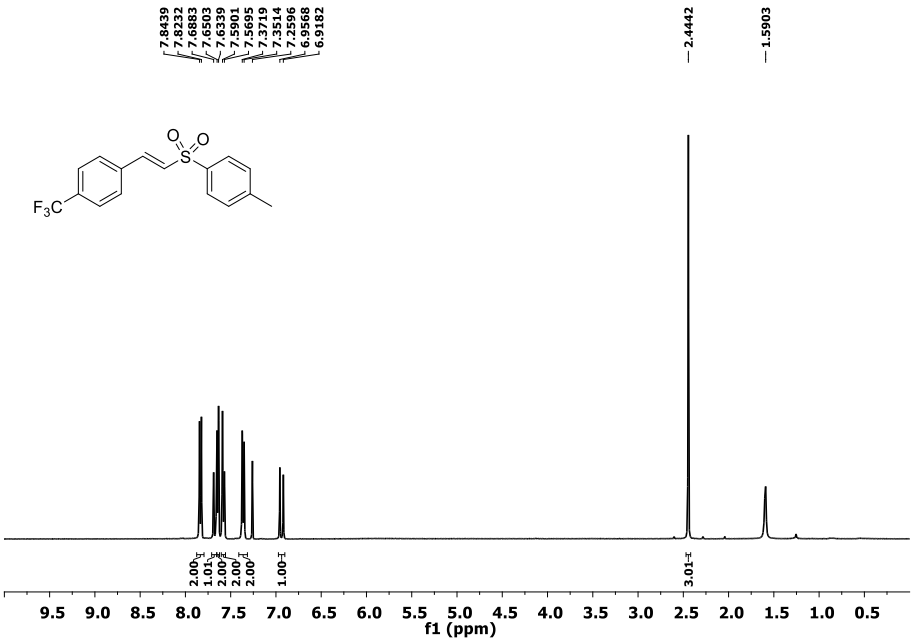



**Figure 2.26.** $^{1}$H NMR spectrum of (*E*)-1-Methyl-4-((4-(trifluoromethyl)styryl)sulfonyl)benzene (**3ja**)

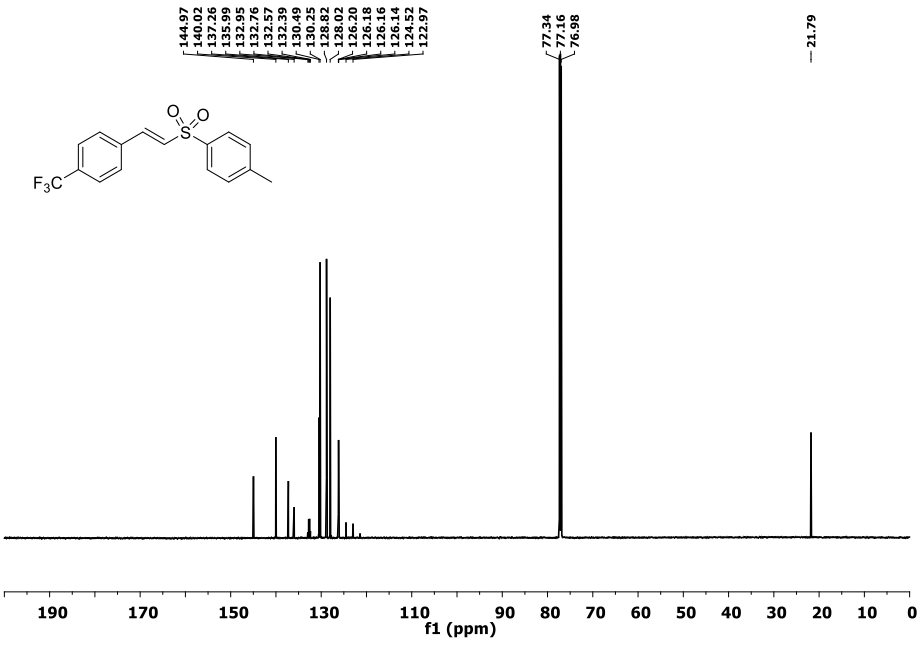



**Figure 2.27.** $^{13}$C NMR spectrum of (*E*)-1-Methyl-4-((4-(trifluoromethyl)styryl)sulfonyl)benzene (**3ja**)

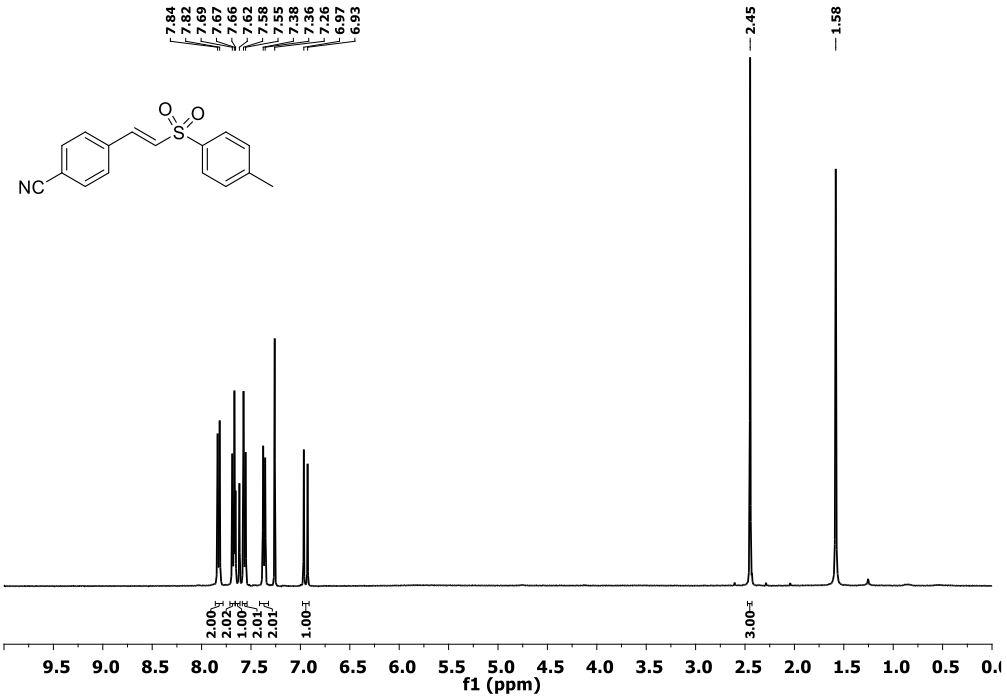



**Figure 2.28.** $^{1}$H NMR spectrum of (*E*)-4-(2-Tosylvinyl)benzonitrile (**3ka**)

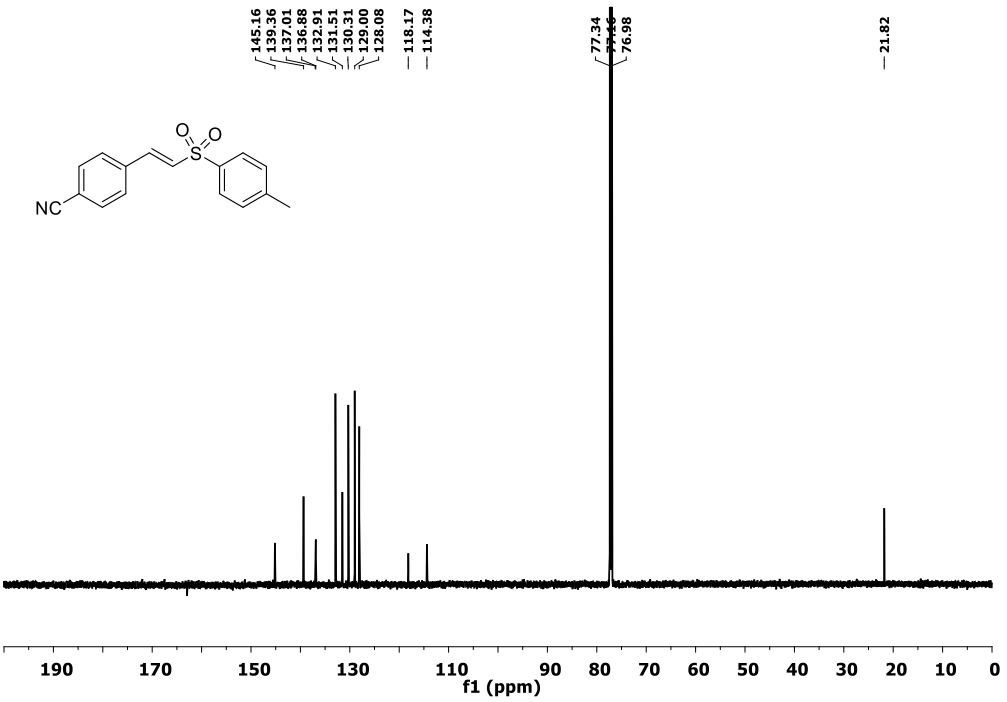



**Figure 2.29.** $^{13}$C NMR spectrum of (*E*)-4-(2-Tosylvinyl)benzonitrile (**3ka**)

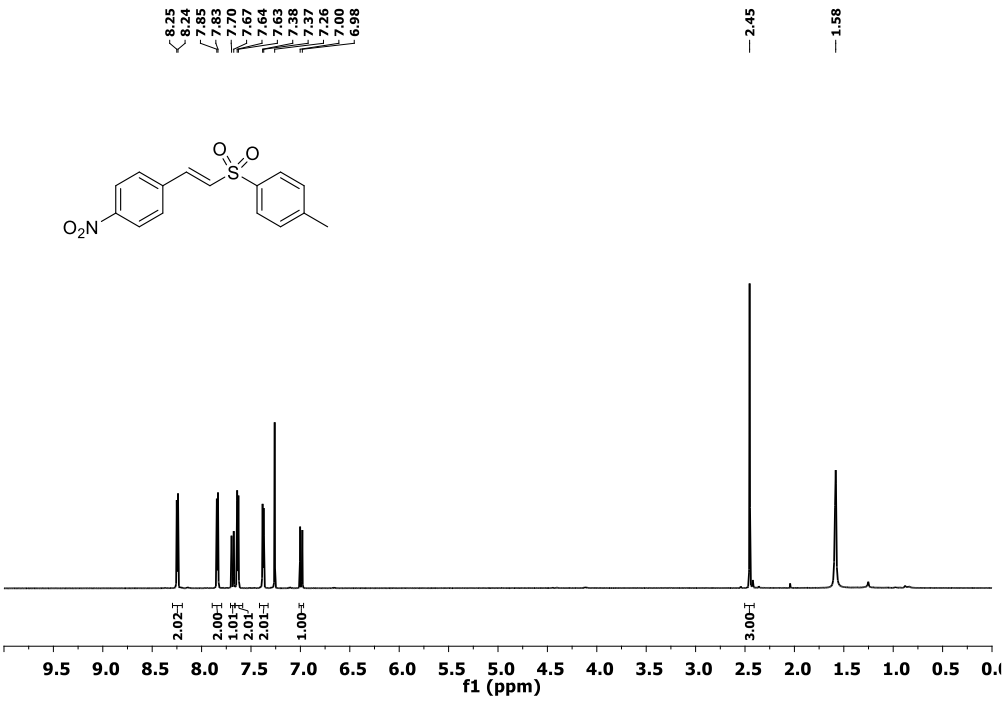



**Figure 2.30.** $^{1}$H NMR spectrum of (*E*)-1-Methyl-4-((4-nitrostyryl)sulfonyl)benzene (**3la**)

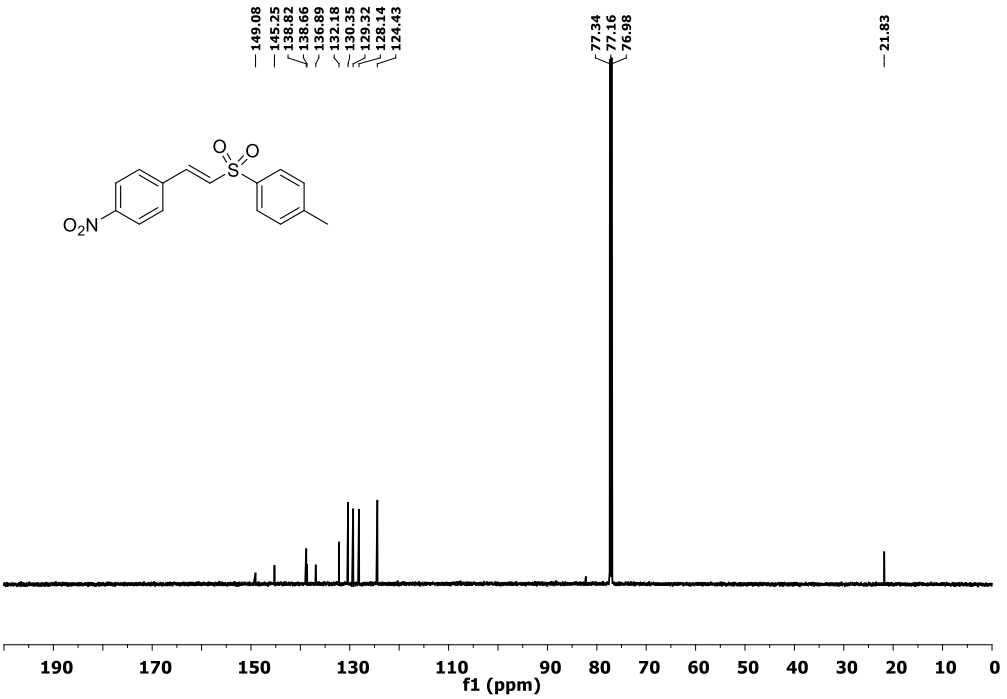



**Figure 2.31.** $^{13}$C NMR spectrum of (*E*)-1-Methyl-4-((4-nitrostyryl)sulfonyl)benzene (**3la**)

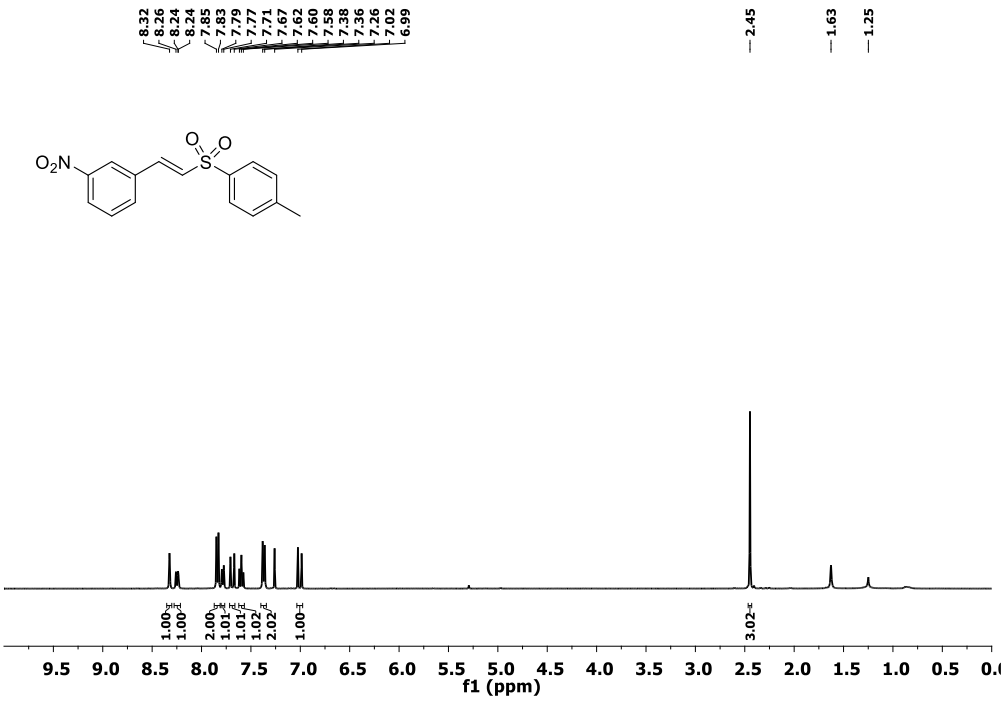



**Figure 2.32.** $^{1}$H NMR spectrum of (*E*)-1-Nitro-3-(2-tosylvinyl)benzene (**3ma**)

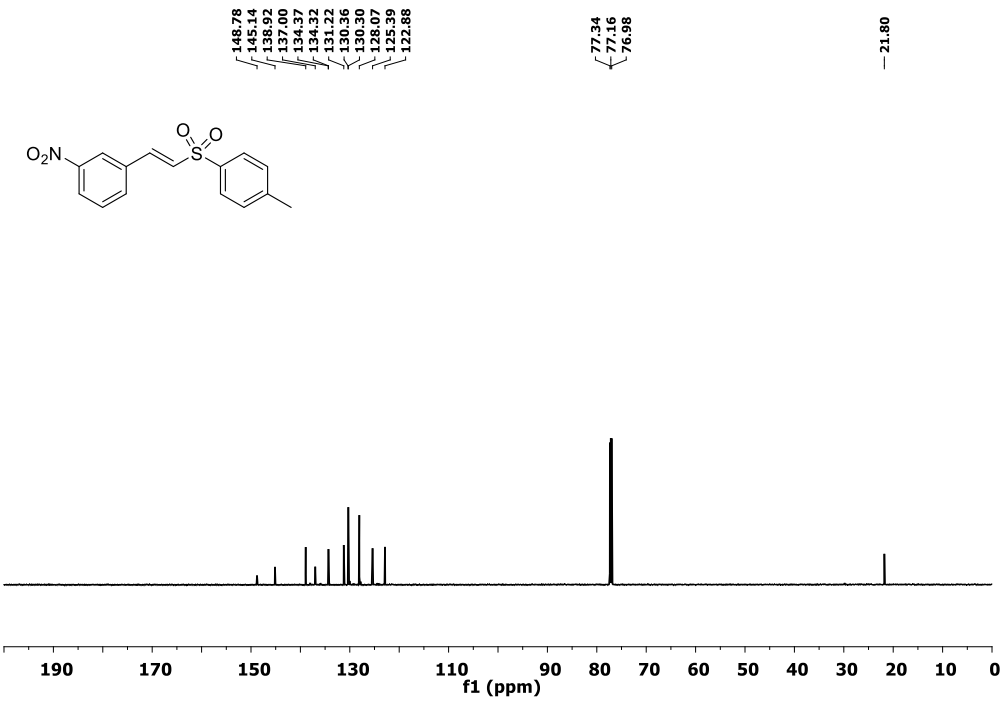



**Figure 2.33.** $^{13}$C NMR spectrum of (*E*)-1-Nitro-3-(2-tosylvinyl)benzene (**3ma**)

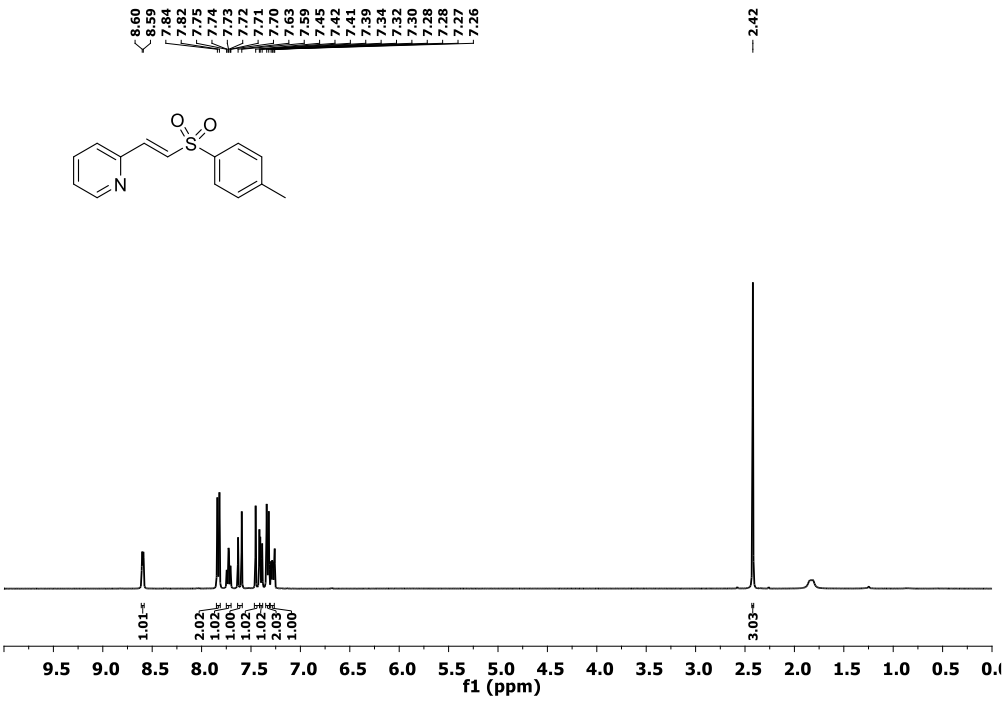



**Figure 2.34.** $^{1}$H NMR spectrum of (*E*)-2-(2-Tosylvinyl)pyridine (**3na**)

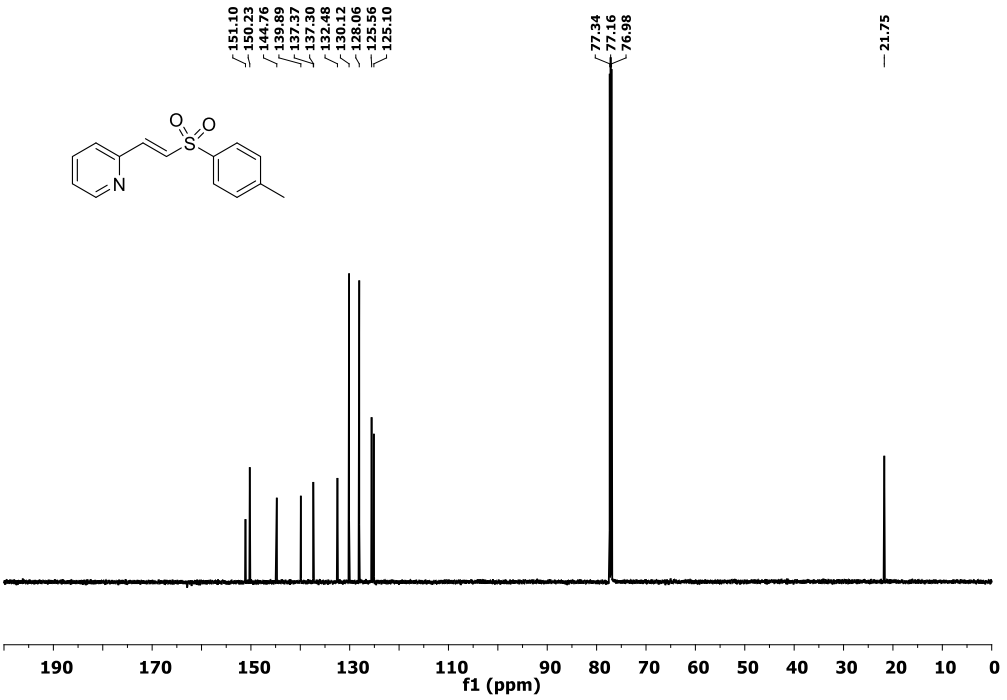



**Figure 2.35.** $^{13}$C NMR spectrum of (*E*)-2-(2-Tosylvinyl)pyridine (**3na**)

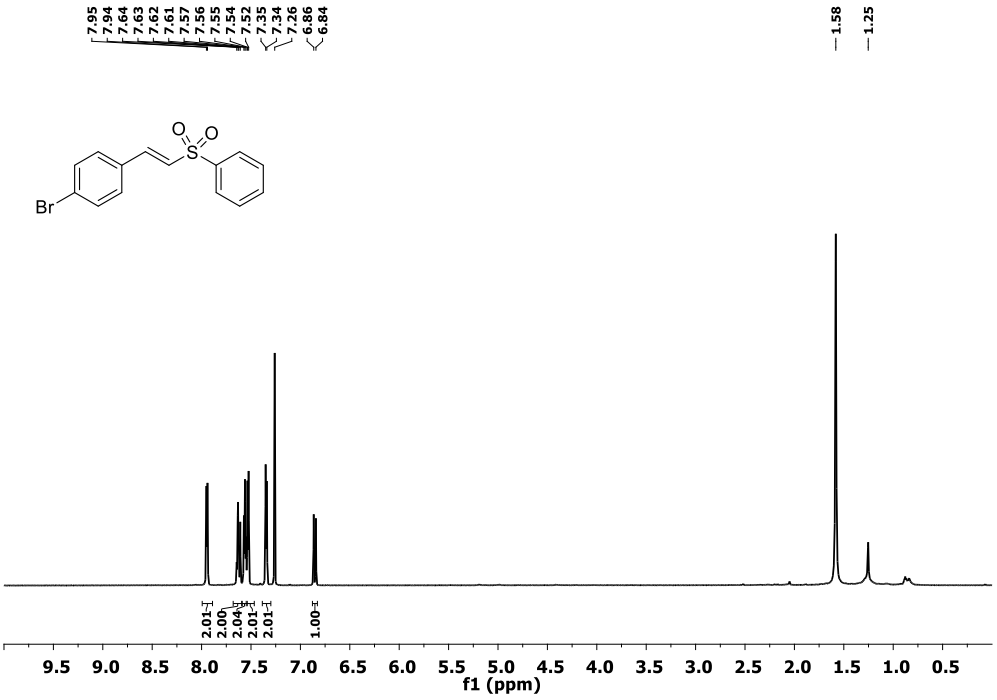



**Figure 2.36.** $^{1}$H NMR spectrum of (*E*)-1-Bromo-4-(2-(phenylsulfonyl)vinyl)benzene (**3ob**)

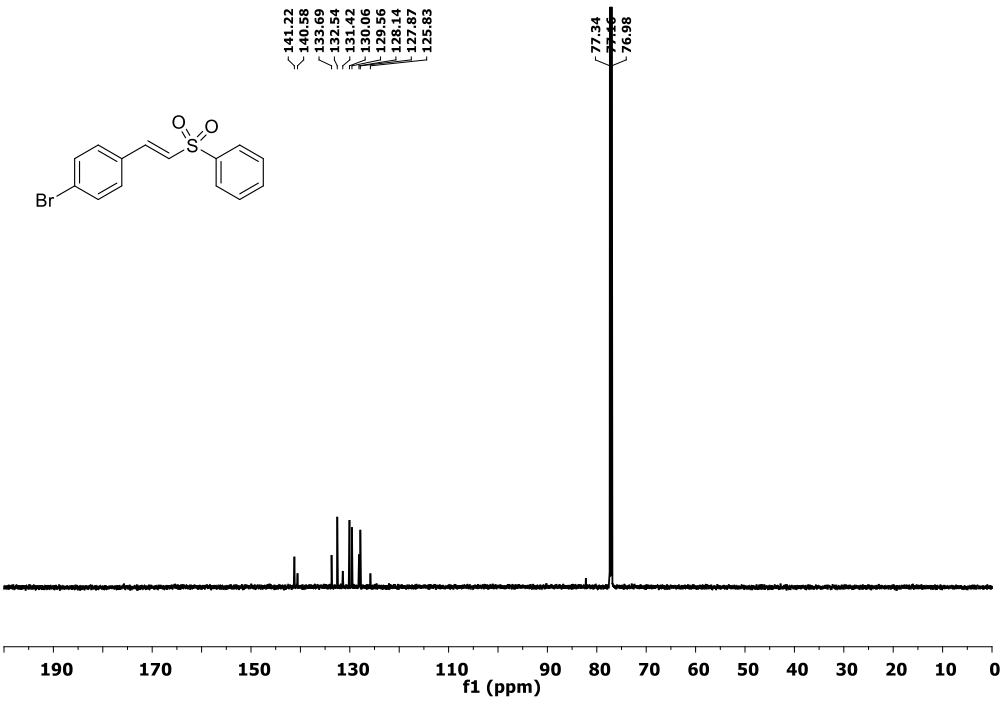



**Figure 2.37.** $^{13}$C NMR spectrum of (*E*)-1-Bromo-4-(2-(phenylsulfonyl)vinyl)benzene (**3ob**)

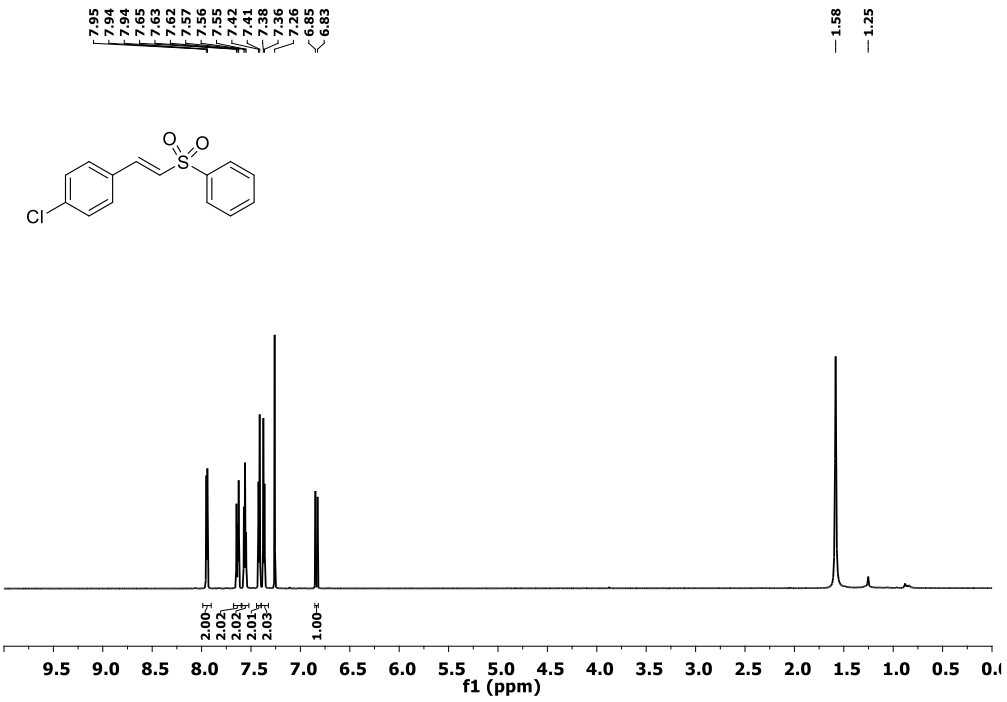



**Figure 2.38.** $^{1}$H NMR spectrum of (*E*)-1-Chloro-4-(2-(phenylsulfonyl)vinyl)benzene (**3ib**)

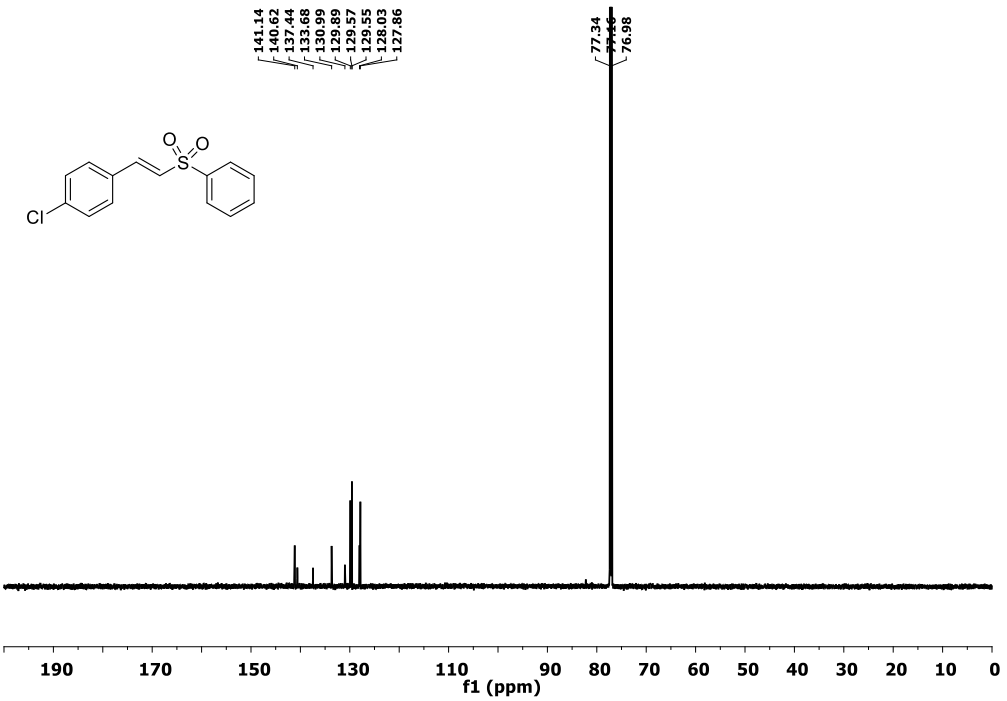



**Figure 2.39.** $^{13}$C NMR spectrum of (*E*)-1-Chloro-4-(2-(phenylsulfonyl)vinyl)benzene (**3ib**)

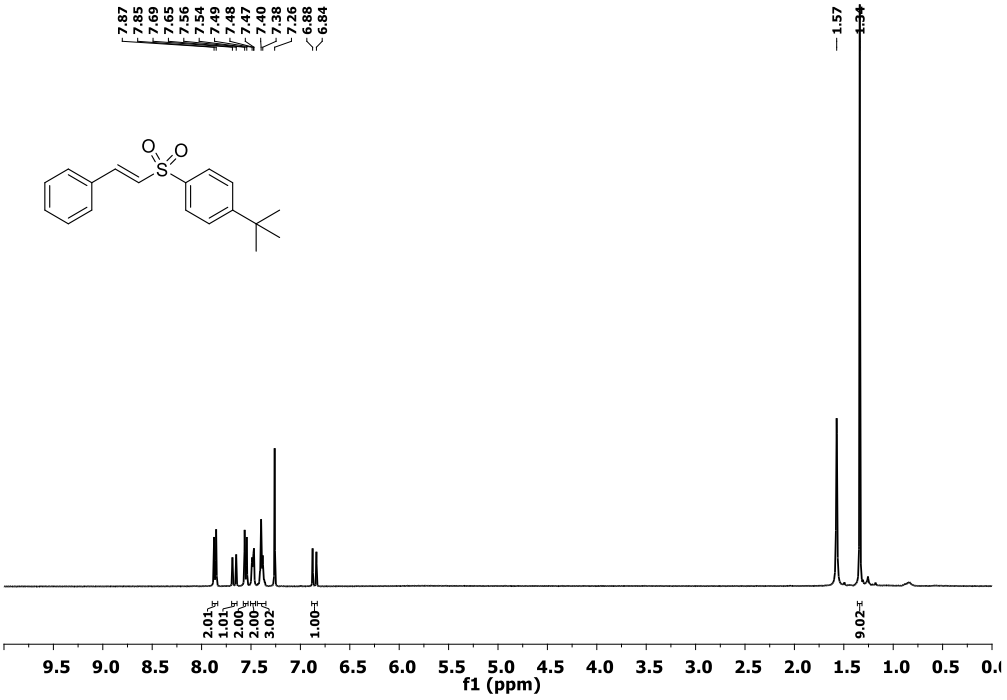



**Figure 2.40.** $^{1}$H NMR spectrum of (*E*)-1-(tert-Butyl)-4-(styrylsulfonyl)benzene (**3ac**)

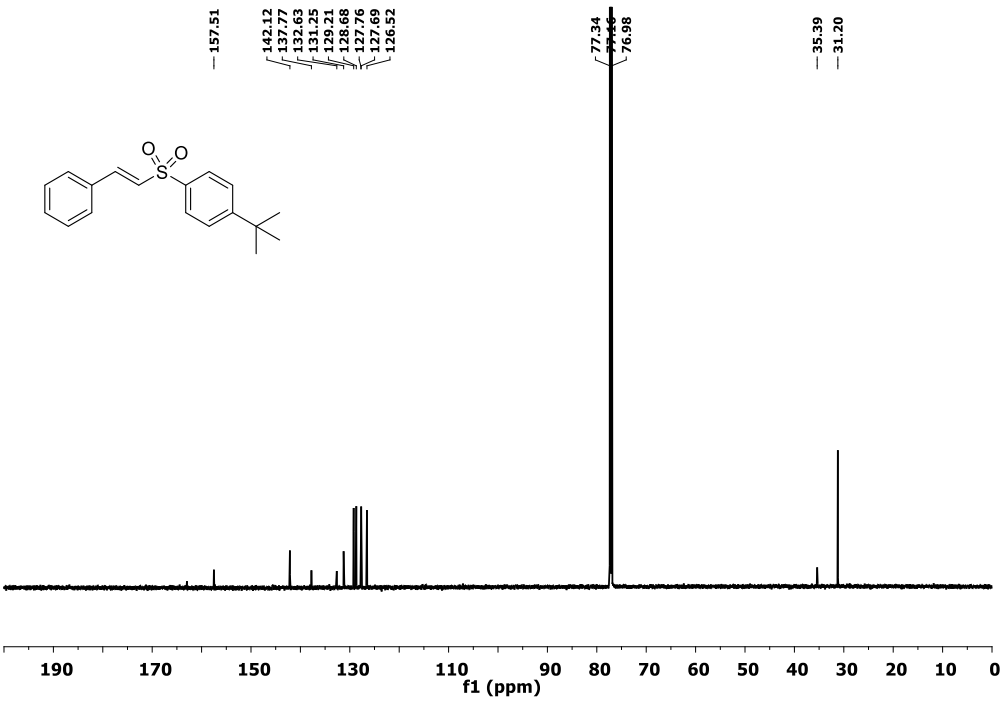



**Figure 2.41.** $^{13}$C NMR spectrum of (*E*)-1-(tert-Butyl)-4-(styrylsulfonyl)benzene (**3ac**)

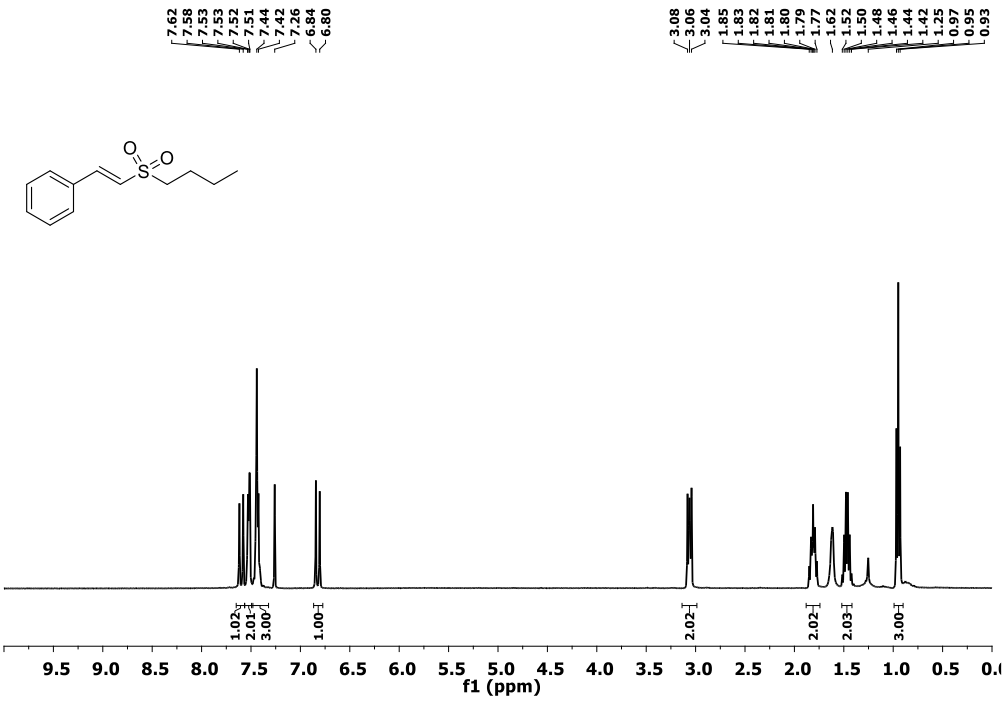



**Figure 2.42.** $^{1}$H NMR spectrum of (*E*)-(2-(Butylsulfonyl)vinyl)benzene (**3ah**)

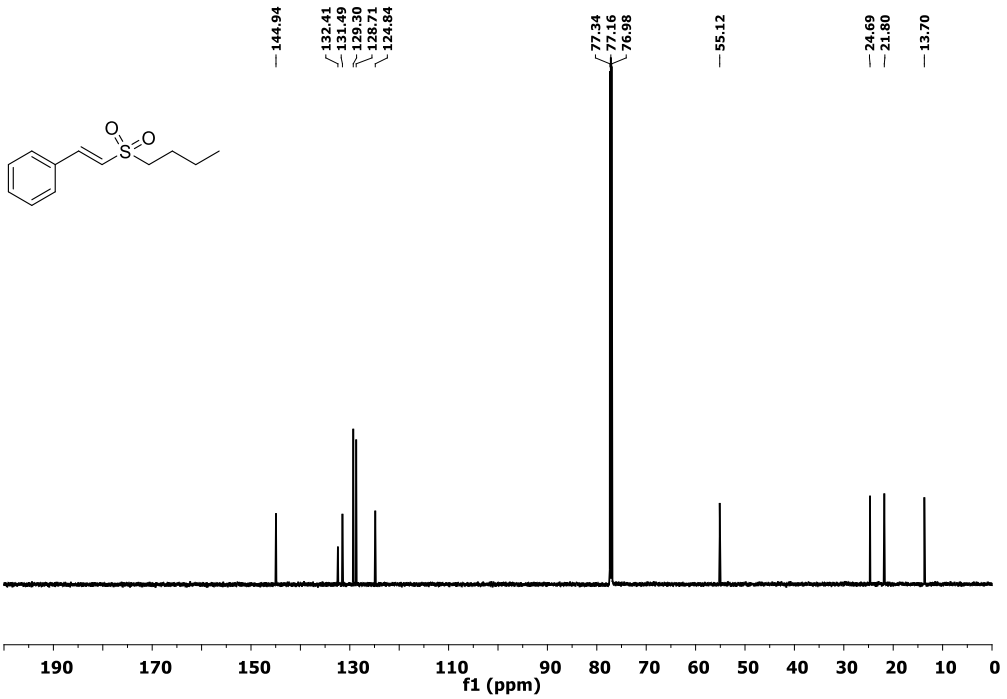



**Figure 2.43.** $^{13}$C NMR spectrum of (*E*)-(2-(Butylsulfonyl)vinyl)benzene (**3ah**)

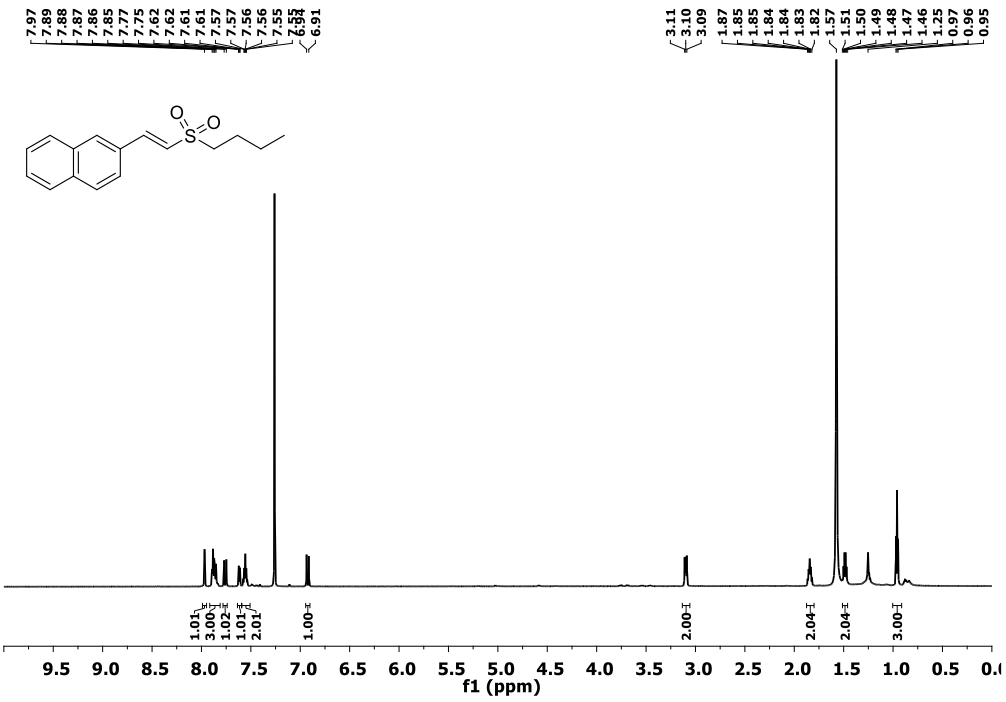



**Figure 2.44.** $^{1}$H NMR spectrum of (*E*)-2-(2-(Butylsulfonyl)vinyl)naphthalene (**3gh**)

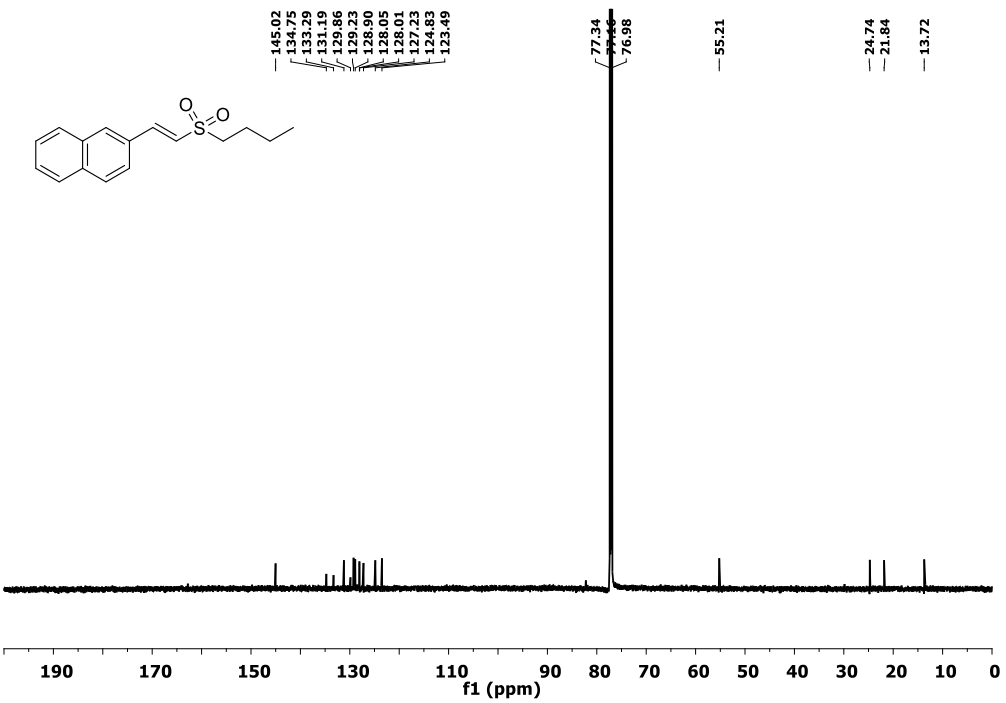
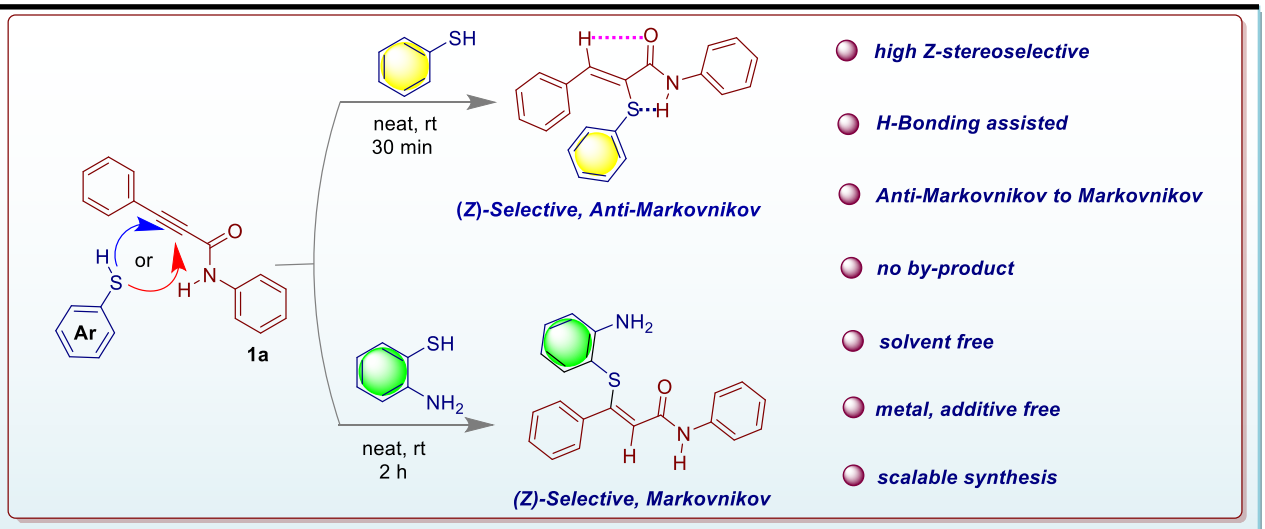



**Figure 2.45.** $^{13}$C NMR spectrum of (*E*)-2-(2-(Butylsulfonyl)vinyl)naphthalene (**3gh**)

# CHAPTER 3

# Amide Hydrogen Bond Controlled (*Z*)-Selective *anti*-Markovnikov or Markovnikov Thiol-Yne-Click Reactions of Internal Alkynes

## 3.1 ABSTRACT

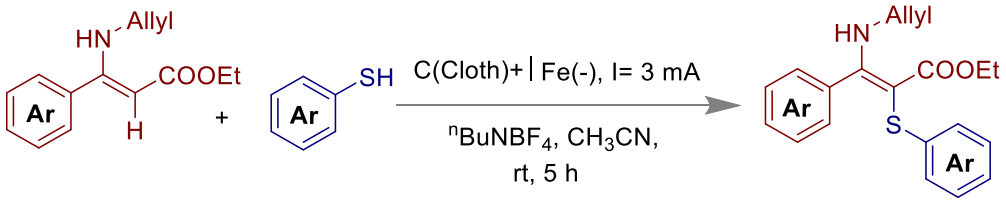



(*E*)-alkenes are thermodynamically more stable and expected to form predominantly in an alkyne addition reaction. So, tuning of stereoselectivity from less energy (*E*)-alkenes to high energy, less stable (*Z*)-alkenes is an unprecedented challenge in organic synthesis. Herein, by applying H-bonding interaction like N–H…S, N–H…N, and C–H…O, we have successfully controlled either (*Z*)-*anti*-Markovnikov or Markovnikov vinyl sulfides from addition reaction of an internal alkyne and thiophenols. Single crystal X-ray diffraction analysis and $^{1}$H NMR study

could help to rationalize the H-bonding interaction, which was a key factor for the origin of regio and stereoselectivity of the desired product.

## 3.2 INTRODUCTION

(*Z*)-alkenes are the reliable core structure of many biologically active compounds and are found in a series of natural products[1-3]. Up to now, many classical methods like Wittig reaction[4], catalytic hydrogenation of alkynes[5-7], alkynes metathesis[8-11], and coupling reactions[12, 13] are the most popular. Apart from these, addition in alkynes *via* radical pathway is a very straight forward[14-16], environment-friendly alternative tool to this family. Although the problem of reactivity is solved, the question of controlling stereoselectivity mainly, (*Z*)-selectivity of alkenes comes into the picture. Hence, nucleophilic addition in alkynes always offers thermodynamic stable (*E*)-alkenes predominantly[17]. Thus it is our outstanding challenge and thus appealing to synthesize high energy, less stable (*Z*)-alkenes. Recently, transition metal-catalyzed the addition of terminal alkynes promised a substantial strategy to ingress (*Z*)-alkenes[18-24]. Thiol-yne-click reaction or, more specifically, hydrothiolation of the alkyne is well established to make many organosulfur compounds[25]. Vinyl sulfide is widely found in bioactive molecules[26-29]. To date, the available methods for synthesizing vinyl sulfides suffer from the multistep synthetic procedure, poor selectivity, unwanted by-product formation, harsh reaction conditions[30-36]. Lei and co-workers reported the electrochemical synthesis of substituted vinyl sulfide from enamines and thiophenols (Scheme 3.1). Although the method was highly sustainable, it required electricity and additional electrolyte[37].



**Scheme 3.1.** Lei's approach for electrochemical oxidative C–H/S–H cross-coupling between enamines and thiophenols.

Very recently, Mal and co-workers reported S–H···π driven thiol-yne-click reaction to access a series of vinyl sulfides[38a]. Although it is the greenest and atom economical approach, it suffers from the lack of stereo-selectivity, and it was applicable only for terminal alkyne like phenylacetylene. Therefore, controlling regio and stereoselectivity to get (*Z*)-specific vinyl sulfide from internal alkyne through a simple strategy is very important and thus a challenging task to an organic chemist.

To understand the role of noncovalent interaction[39, 40] in a chemical reaction, the click chemistry[41], and system chemistry[42] approaches have gained enormous attention in the chemical community. Stabilization of reactive intermediate through the weak interaction[43] like halogen bonding[44, 45], anion-π[46], hydrogen bonding[47-49], π- π stacking[50] is very important as well as highly desirable because many complicated reactions could be performed easily. In this context, the use of hydrogen bonding as a key and fundamental factor to access regio selective high energy *Z*-vinyl sulfides is the unexplored and thus the newest addition to this family[47, 51].

## 3.3 RESULT AND DISCUSSION

Organic solvents have their largest pollution and toxic problem in organic reactions. Therefore, the development of solvent-free reaction conditions is always being demanded and challenged[52]. Although the performance of organic reaction in water as a solvent is a good choice in terms of an environmentally benign but most of the organic compounds are less soluble in water. An ideal

reaction moves in neat conditions, and by the way, it reduces the amount of waste and avoids work-up[38, 53].

To our primary study, internal alkyne such as diphenyl acetylene was unreactive with thiophenol under neat mixing because of uniform electronic distribution over triple bonds. We hypothesize that introduction of an amide scaffold nearby alkyne of diphenyl acetylene would activate the alkyne, and the amide-H will be accessible for H-bonding (Figure 3.1a). Keeping this reliable idea in mind, we attempt to exploit appropriate weak interactions like N–H…S H-bonding, which could help to attain (*Z*)-*anti*-Markovnikov vinyl sulfides **3aa** exclusively when internal alkyne *N*,3-diphenylpropiolamide (**1a**), and thiophenol (**2a**) was mixed at room temperature under solvent-free condition. Mostly, the intramolecular hydrogen bonding interactions like C-H…O and N–H…S could help to achieve (*Z*)-selectivity in the product **3aa** (Figure 3.1b)[38b]. On the other hand, switching of product selectivity from (*Z*)-selective *anti*-Markovnikov vinyl sulfide to (*Z*)-selective Markovnikov vinyl sulfide was accomplished *via* utilizing appropriate N–H…N hydrogen bonding when 2-amino thiophenol (**2k**) was considered as an alternate of thiophenol (**2a**). We could foresee that N–H…S and N–H…N hydrogen-bonding between amide-H and thiophenol's sulfur might help accelerate the reactions towards a forward direction. The amino group at the *ortho*-position of the thiophenol could give Markovnikov product because of strong preference in N–H…N H-bonding shown in Figure 3.1b.

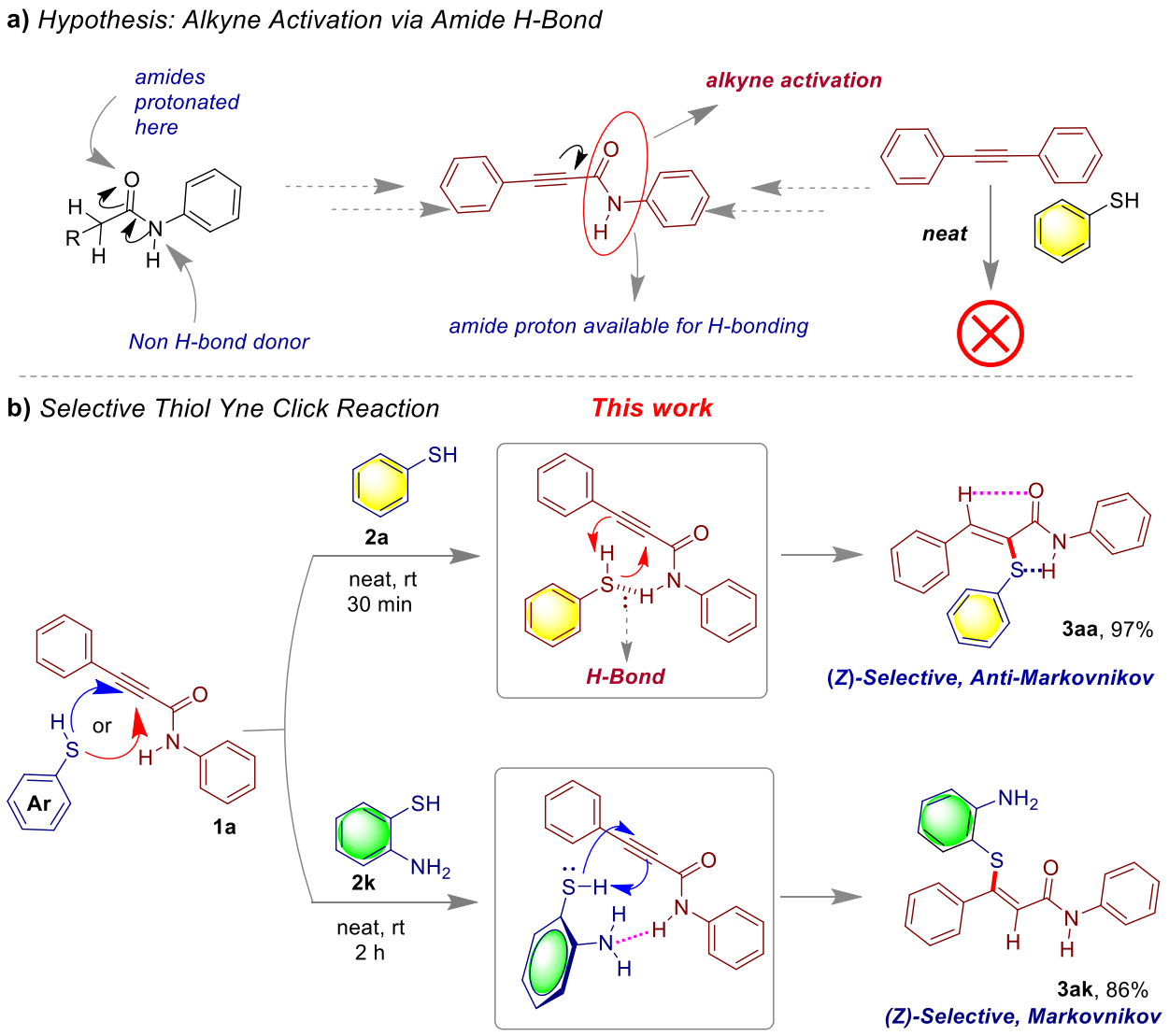
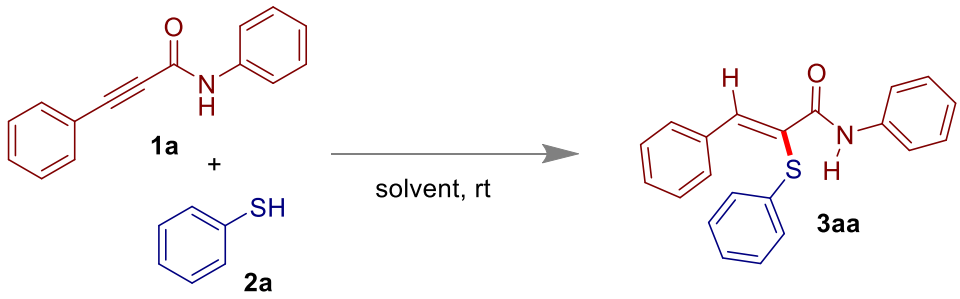



**Figure 3.1.** a) alkyne activation and amide hydrogen bonding. b) Our work for the synthesis of (*Z*)-selective *anti*-Markovnikov or Markovnikov vinyl sulfides.

Initially, diphenylpropiolamide (**1a**) and thiophenol (**2a**) were selected as model substrates with a 1:1 ratio, and the reaction was allowed to stir at room temperature at an open atmosphere under neat conditions. After 30 minutes, desired product **3aa** was isolated in 50% yield (Table 3.1, entry 1). Surprisingly, the yield of the desired product **3aa** was increased with the variation of the thiophenol equivalent (Table 3.1, entry 2-4). To our delight, desired product **3aa** was found in

97% yield in the thiophenol with 3 equivalents. It was noted that 3 equivalent of thiophenol was required, which might be to make the reaction mixture soluble and to assist in intermolecular hydrogen bonding. Notable that, no by-product was observed, and excess thiophenol was recovered after the completion of the reaction. Next, we screened the solvent like ethanol (EtOH), water ($H_2O$), chloroform ($CHCl_3$), dimethyl sulfoxide (DMSO), Toluene (Table 3.1, entry 5-9). It was anticipated that the nature of the reaction was sluggish in toluene because hydrogen bonding interaction is relatively less favored in non-polar solvents like toluene. On the other hand, hydrogen bonding is found to be facile in polar solvents like EtOH, $H_2O$ and thus, it offered relatively good yields (82% and 86%, respectively) (Table 3.1, entries 5 and 6). Chlorinated solvent ($CHCl_3$) gave only 40% yield, and solvent like DMSO yielded 59% yield (Table 3.1, entries 7 and 8). The performance of the reaction was found to be best in neat conditions rather than any solvent.

**Table 3.1.** Effect of reaction parameters[b]




| entry | thiol (equiv) | solvent | yield(%)[a] |
|---|---|---|---|
| 1 | 1 | - | 50 |
| 2 | 1.5 | - | 68 |
| 3 | 2 | - | 81 |

| | | | |
|---|---|---|---|
| 4 | 3 | - | 97 |
| 5 | 3 | EtOH | 82 |
| 6 | 3 | $H_2O$ | 86 |
| 7 | 3 | $CHCl_3$ | 40 |
| 8 | 3 | DMSO | 59 |
| 9 | 3 | Toluene | 27 |
| 10 | 3 | - | 93[c] |

[a]Isolated yields after column chromatograph, [b]Reaction conditions: **1a** (0.271 mmol), **2a** (0.813 mmol), room temperature, 30 minutes. [c]Reaction under $N_2$ atmosphere.

With the optimal condition in hand, we turned our attention to investigate the influence of thiophenol derivatives. Interestingly, thiophenols with the electron-donating groups (-Me, -OMe) yielded the desired products **3ab** and **3ac** in 98% and 66%, respectively, after 1.5 h (Figure 3.2). Again, *p*-methoxy thiophenol produced 82% of **3ac** in the presence of few drops of ethanol. Halo (X = -F, -Cl, -Br) substituted thiols responded smoothly to produce corresponding sulfides (**3ad**, **3ae,** and **3af**) with 81-91% yields. Electron deficient trifluoromethyl group (-$CF_3$) in the *para* position of thiophenol offered **3ag** in 91% yield within 1 h. Likewise, *meta*-substituted thiophenols with -OMe, -Cl reacted nicely to provide corresponding thiolated products with 78% and 90% yields, respectively. Following, *ortho*-fluoro-thiophenol also provided **3aj** in 79% yield within 30 min. Unfortunately, aliphatic thiols (**2l**, **2m**) were unproductive to give corresponding vinyl sulfides because of the less nucleophilicity nature of thiols. We have also scaled up the synthesis, and 87% yield of the **3aa** was isolated from 1 gram of phenylpropiolamide.

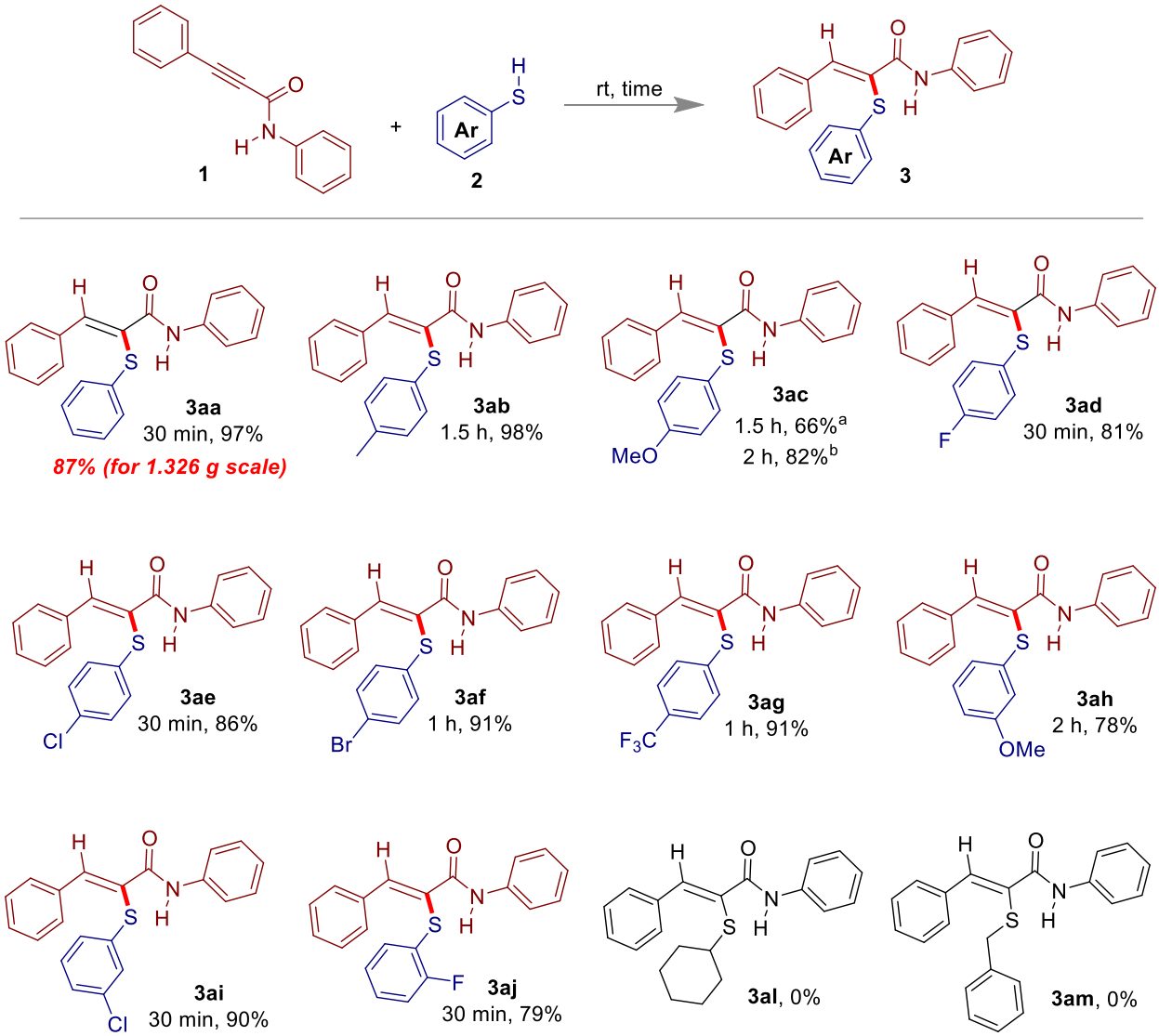



**Figure 3.2.** Scopes of thiophenols for vinyl sulfides. [a]at neat; [b]at few drops EtOH

Furthermore, the scope of internal alkynes was evaluated (Figure 3.3). Gratifyingly, phenylpropanolamine having methyl substituent at *ortho* and *para* position exhibited (*Z*)-selective vinyl sulfides (**3ba**, **3ca**, **3da**) with moderate to excellent yields (88-96%). Likewise, -Et, -$^{i}$Pr, -$^{t}$Bu, -OMe containing phenylpropanolamine also afforded corresponding vinyl sulfides as products (**3ea**, **3fa**, **3ga,** and **3ha**) in a range of 79-97% yield. Similarly, biphenyl-linked

propiolamide resulted in **3ia** only with a 43% yield within 1 h; however, no enhancement in yield was found even after 6 h. Again, phenylpropiolamides having X= -F, -Cl, -Br, and -I, were also well productive to supply corresponding vinyl sulfides (**3ja**, **3ka**, **3la,** and **3ma**) with 76-98% yields, respectively. Notable that compounds **3na** and **3oa** were isolated with 74% and 70% yields. In addition, compounds **3pa** and **3qa** were isolated in good yields within 1.5 hours. Pleasingly, our methodology was also successful for poly-aromatic systems to achieve compounds **3sa**, **3ta,** and **3ua** in 78%, 62%, and 48% yields, respectively. The primary propiolamide was unproductive due to N–H...S type H-bonding within $NH_2$ and thiophenol, which perhaps did not allow the thiol to come up to the close proximity for TYC reaction.

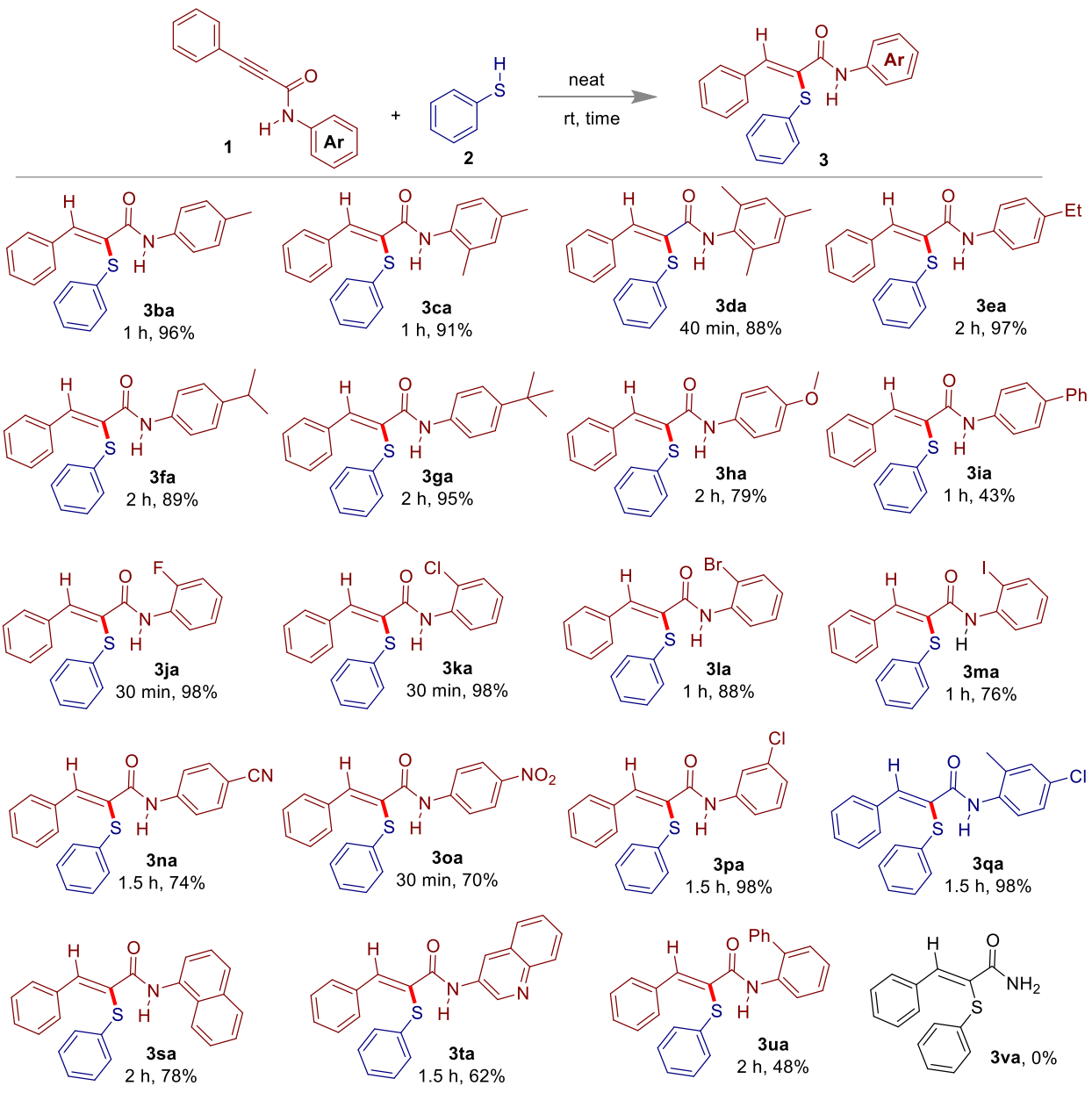



**Figure 3.3.** Scopes of phenylpropiolamide for the synthesis of vinyl sulfides.

In order to understand the mechanistic pathway of the reaction, a couple of control experiments were performed (Figure 3.4). Interestingly, N-methyl-N,3-diphenylpropiolamide **4,** and thiophenol (**2a**) were unproductive under neat conditions (Figure 3.4a), which implied that there was a crucial role of amide proton, which might promote hydrogen bonding with the sulfur atom

of thiophenol and thus helped the reaction to move on forward direction by maintaining proper regio-selectivity. Similarly, when phenylpropiolate **5** was allowed to react with 4-bromo-thiophenol, the mixture of regioisomers **6** and **7** was found (Figure 3.4b). The regio-selectivity was lost; hence amide N–H has a crucial role for N–H…S H-bonding.

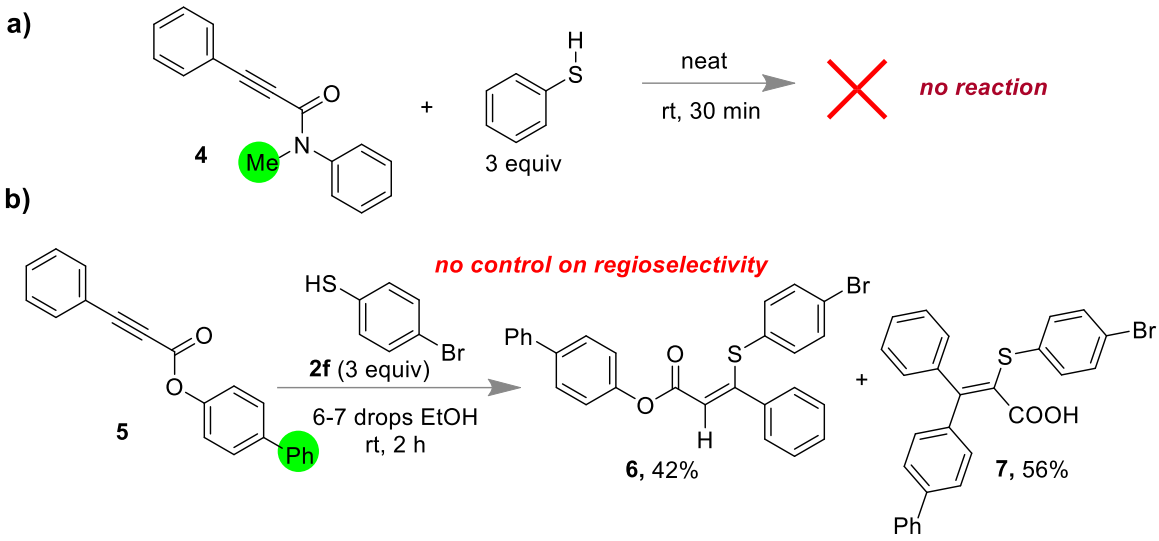



**Figure 3.4.** Control experiments. a) No product when amide-H was absent. b) Selectivity was lost when phenyl 3-phenylpropiolate **5** and thiophenol (**2a**) were reacted.[54]

Furthermore, X-Ray structure analysis of compound **3aa** could help to rationalize the origin of (*Z*)-selectivity (Figure 3.5). It was anticipated that strong intramolecular hydrogen bonding between the carbonyl oxygen and vinylic-H was found to be with a bond distance and angle of $C_7$-$H_7\cdots O_1$ = 2.374 Å and 106.72°, respectively. In addition, sulfur and amide proton showed bond distance and angle of $N_{11}$-$H_{11}\cdots S_{12}$ = 2.469Å and 119.08°, respectively (Figure 3.5). Thus it was concluded that C–H…O and N–H…S interactions during the formation of **3aa** helped to establish (*Z*)-selectivity. On the other hand, the structure elucidation of (*Z*)-selective Markovnikov product (**3ak**) was done by $^1$H-$^1$H ROESY, $^{13}$C-$^1$H HMBC, and $^{13}$C-$^1$H HSQC 2D NMR study, which were discussed later.

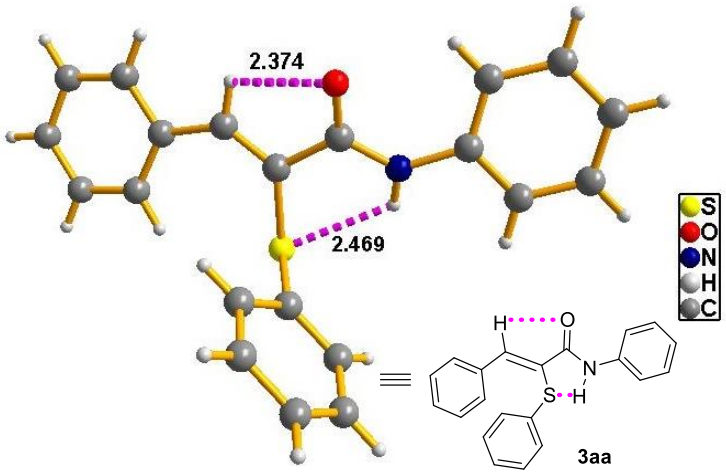



**Figure 3.5.** X-Ray structure of 3aa (CCDC 1910745) showing H-bonding interaction

The low temperature $^{1}$H NMR analysis with the progressive addition of thiophenol (**2a**) in **1a** (1.0 equiv) in $CDCl_3$ also supported the involvement of H-bonding interactions during the course of the reaction (Figure 3.6). When 0.5 equivalent of thiophenol was added at 0 ºC, a considerable shift of N–H signal was noted at 7.93 ppm (Figure 3.6a and 3.6b). This information suggested that the shift of N–H signal was probably due to the existence of N–H…S H-bonding between thiophenol **1a** and phenylpropiolamide **2a**. No shift of S–H indicated the non-existence of S–H...O H-bonding between thiol and carbonyl group. Again, the NH signal of the **3aa** appeared at 9.07 ppm at -45 ºC (Figure 3.6c) in $CD_2Cl_2$; however, it was at 8.96 ppm when the temperature was 25 ºC (Figure 3.6d). This minor change also provided a piece of evidence for the formation of intramolecular H-bonding. Similar observations were also made for the vinylic hydrogen (~8.5 ppm) of **3aa** to participate in C–H…O hydrogen bonding. Cooperatively, N–H…S and C–H…O H-bonding interactions helped to develop the (*Z*)-selective *anti*-Markovnikov product. Thus, from the above control experiment, it was anticipated that the H-bonding interactions like

N–H…S and N–H…N might be the driving force for click reactions and preferable regio-selectivity.

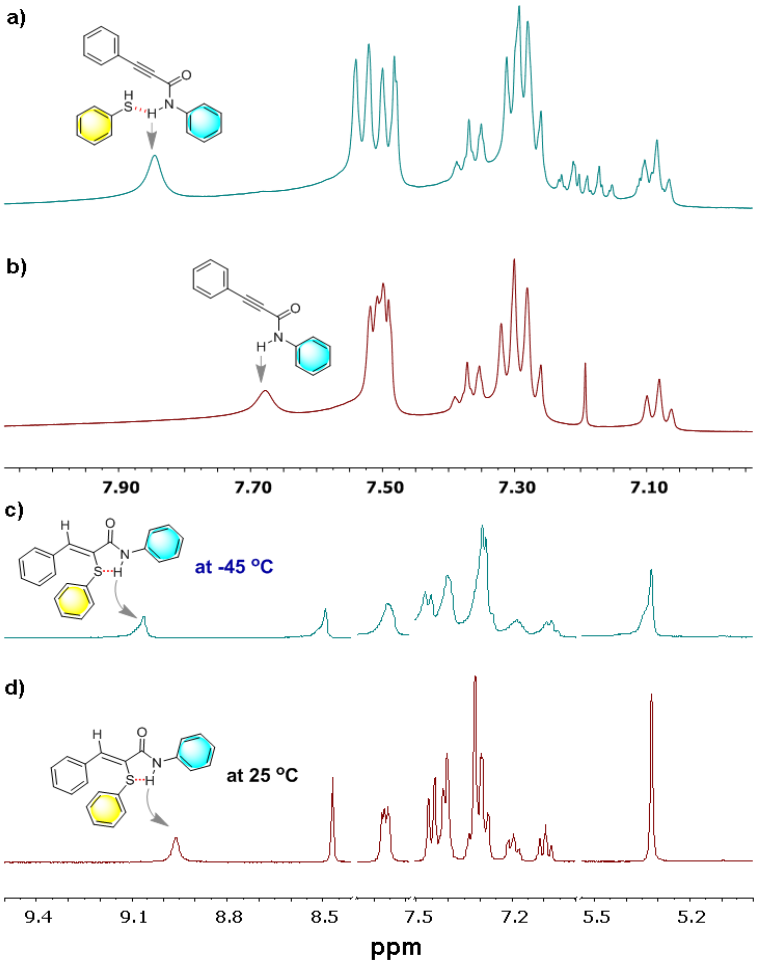



**Figure 3.6.** a) $^{1}$H NMR spectra of the mixture **1a** + 0.5 equiv **2a** at 0 ºC in $CDCl_3$. b) 1a at -5 ºC in $CDCl_3$. c) The product **3aa** at -45 ºC in $CD_2Cl_2$ and d) The compound **3aa** at 25 ºC in $CD_2Cl_2$.

Next, the synthetic utility of the vinyl sulfides was shown in Figure 3.7. Benzamide derivatives were reacted to produce *anti*-Markovnikov product **3ra** in 88% yield (Figure 3.7a). The vinyl sulfide **3aa** was transformed to corresponding vinyl sulfoxide **8** through *m*CPBA oxidation

(Figure 3.7b). Again, suzuki coupling with vinyl sulfide **3la** was carried out to have a 98% yield of **9** from the corresponding bromo derivative (Figure 3.7c).

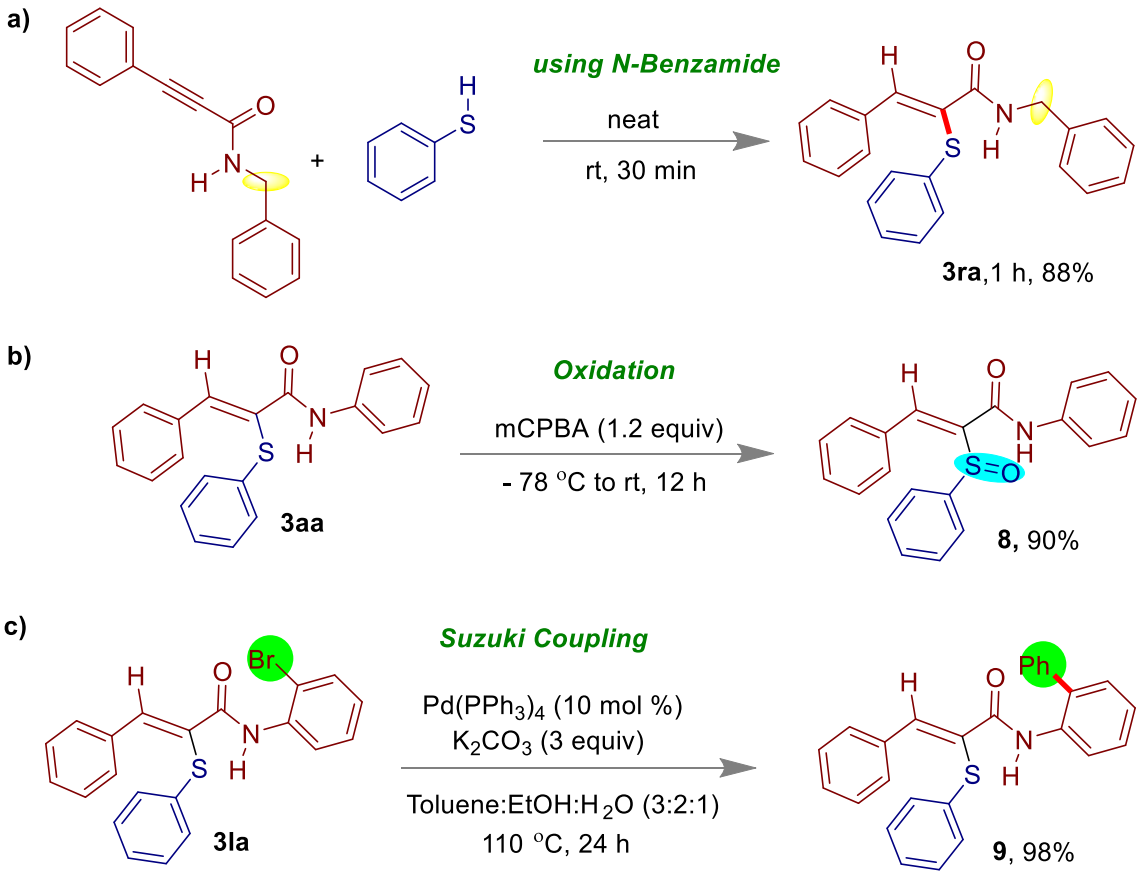



**Figure 3.7.** Synthetic utility. a) synthesis using N-benzamides. b) oxidation. d) suzuki coupling.

## 3.4 CONCLUSION

In summary, we have established that appropriate implementation of amide H-bonding interactions could help to switch the product choice from (*Z*)-selective *anti*-Markovnikov to Markovnikov vinyl sulfides from a reaction of an internal alkyne and thiophenol. A series of

thioacryamides/vinyl sulfides could be achieved in good to excellent yield under mild, solvent-free conditions within a very short reaction time. Hydrogen bonding interaction initiated the reaction and improved the region-selectivity. Also, the origin of stereoselectivity in the desired product has been demonstrated nicely using the hydrogen bonding concept. Therefore, the entire methodology is unique, novel and thus can be treated as more efficient and greenest over other traditional methods for making C–S bonds.

## 3.5 EXPERIMENTAL SECTION

**General aspects**

All reactions were carried out under an open atmosphere chromatography was performed using Chemlabs silica-gel 230-400 mesh.The yields are reported in % (percentage). The NMR studies were carried out by Bruker 400 and 700 MHz at roomunless otherwise noted .All solvents were generally distilled by following the standard procedures prior to use. All reactions were monitored by TLC on Merck 60 F254 aluminum sheets pre-coated with silica gel. Column temperature in $CDCl_3$ solutions; $^1H$ chemical shifts are given in $\delta$ (ppm) related to TMS as internal standard, coupling constants *J* values in Hz, and the chemical shift value (δ, ppm) are reported with respect to the residual chloroform (7.26 for $^1H$ and 77.16 ppm for $^{13}C$. HRMS was recorded using an ESI-TOF instrument. Infra-red spectroscopic studies were performed and described in wavenumber ($cm^{-1}$). The single-crystal XRD was analyzed in a Rigaku Oxford diffractometer, and the crystal is deposited in the Cambridge Crystallographic Data Centre. EPR spectra were obtained in a Bruker EMX (ER 073) instrument. Melting point are recorded in $^oC$. The elaborate procedure for the preparation of target molecules and the other intermediates are described below.

**General procedures for the synthesis of N,3-diphenylpropiolamide derivatives.**

At first, propionic acid (3.54 mmol, 1.1 equiv) was dissolved in 10 mL DCM ($CH_2Cl_2$) and allowed to stir at -20 °C temperature in a round-bottomed flask. Following, 4-dimethylaminopyridine (DMAP) (0.32 mmol, 0.1 equiv), dicyclohexylcarbodiimide (DCC) (3.54 mmol, 1.1 equiv) was dissolved in 5 mL DCM, followed by it was slowly injected to the solution. After that, aniline derivative (3.22 mmol, 1.0 equiv) in DCM (5 mL) was slowly injected to the reaction mixture. Afterward, the whole content was further allowed at room temperature for another 12 h. After completion of the reaction, the whole mixture was washed 3 times with 0.5 Molar aqueous HCl, dried with $Na_2SO_4$, and finally concentrated under vacuum. The crude solid was then purified by column chromatography technique to afford the allied desired N,3-diphenylpropiolamide derivatives as yellow solid.

**Representative synthetic procedure for compound 3aa.**

The N,3-diphenylpropiolamide (**1a**) (60 mg, 0.271 mmol) was kept in a 10 mL round bottom flask. To this thiophenol (**2a**) (89 mg, 0.813 mmol) was injected at open-air, and the content was stirred at room temperature, and the progress of the reaction was monitored by TLC (*for solid mixtures, few drops of EtOH was required to make the mixture soluble*). When the reaction was over, the desired product was isolated through column chromatography eluting in EtOAc/Hexane. In most of the cases, excess thiol around ~1.5 equiv, was recovered.

**Crystallographic Investigation**

The compound (**3aa**) was recrystallized by the slow evaporation of ethanol and water mixture (ca. 50%). The crystals data were collected with Bruker SMART D8 goniometer equipped with

an APEX CCD detector and with an INCOATEC micro source (Cu-Kα radiation, λ = 1.54184 Å). SAINT+ and SADABS were used to integrate the intensities and to correct the absorption, respectively. The structure was resolved by direct methods and refined on $F^2$ with SHELXL-97.[55]

**Compound (3aa) (CCDC 1910745)**

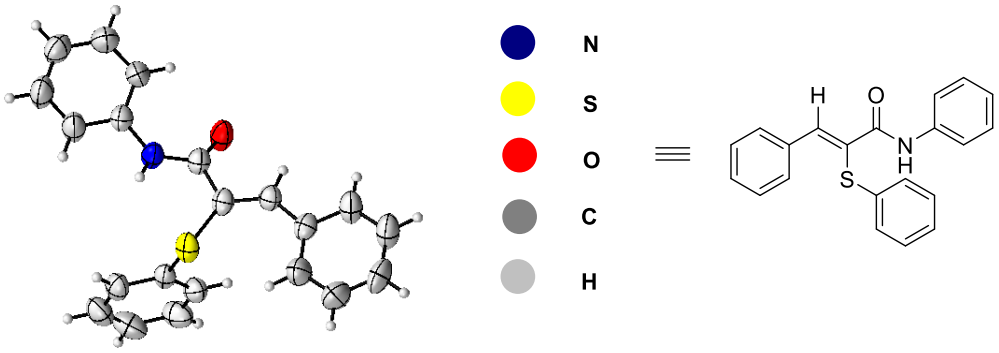



**Figure 3.8**. Crystal structure of (**3aa**) (CCDC 1910745).

**Crystallographic Data for** (**3aa**)

| | |
|---|---|
| Empirical formula | $C_{21}H_{17}NOS$ |
| Formula weight | 331.43 |
| Temperature/K | 299 |
| Crystal system | Orthorhombic |
| Space group | $Pca2_1$ |
| a/Å | 16.2527(7) |
| b/Å | 5.8894(2) |
| c/Å | 18.0008(7) |

| | |
|---|---|
| α/° | 90 |
| β/° | 90 |
| γ/° | 90 |
| Volume/Å | 1723.01(12) |
| Z | 4 |
| $\rho_{calc}$g/cm$^3$ | 1.213 |
| μ/mm$^{-1}$ | 1.703 |
| F(000) | 629.0 |
| Crystal size/mm$^3$ | 0.2×0.2×0.18 |
| Radiation | CuKα (λ = 1.54184) |
| Reflections collected | 13559 |
| Independent reflections | 3374 [$R_{int}$ = 0.1472, $R_{sigma}$ = 0.0660] |
| Goodness-of-fit on $F^2$ | 1.082 |
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.0648, w$R_2$ = 0.1754 |
| Final R indexes [all data] | $R_1$ = 0.0703, w$R_2$ = 0.1855 |
| Largest diff. peak/hole / e Å$^{-3}$ | 0.58/-0.47 |

**Compound 7 (CCDC 1965122)**

The compound **7** was crystallized directly from the reaction mixture of compound **6** and **(2f)** in EtOH. The crystals data were collected with a Bruker SMART D8 goniometer equipped with an APEX CCD detector and with an INCOATEC micro source (Mo-Kα radiation, λ = 0.71073 Å). SAINT+ and SADABS were used to integrate the intensities and to correct the absorption, respectively. The structure was resolved by direct methods and refined on $F^2$ with SHELXL-97.

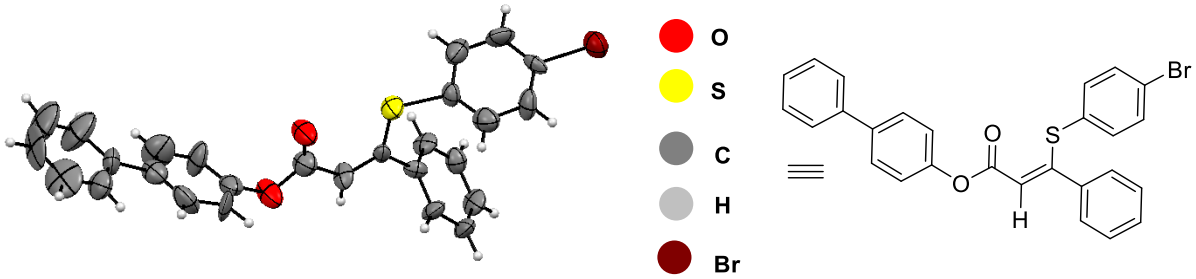



**Figure 3.9**. Crystal structure of compound **6** (CCDC 1965122).

**Crystallographic Data for compound 6**

| | |
|---|---|
| Empirical formula | $C_{27}H_{19}BrO_2S$ |
| Formula weight | 487.41 |
| Temperature/K | 296 |
| Crystal system | Triclinic |
| Space group | P-1 |
| a/Å | 6.5137(5) |
| b/Å | 22.7108(19) |
| c/Å | 32.675(3) |
| α/° | 108.215(5) |
| β/° | 93.851(5) |
| γ/° | 96.920(5) |
| Volume/Å | 4529.7(7) |
| Z | 2 |
| $\rho_{calc}g/cm^3$ | 1.427 |
| $\mu/mm^{-1}$ | 1.928 |
| F(000) | 1982.0 |

| | |
|---|---|
| Crystal size/$mm^3$ | 0.26×0.18×0.12 |
| Radiation | MoKα (λ = 0.71073) |
| Reflections collected | 51290 |
| Independent reflections | 16535 [$R_{int}$ = 0.1142, $R_{sigma}$ = 0.1507] |
| Goodness-of-fit on $F^2$ | 1.047 |
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.1058, $wR_2$ = 0.2309 |
| Final R indexes [all data] | $R_1$ = 0.2549, $wR_2$ = 0.2858 |
| Largest diff. peak/hole / e $Å^{-3}$ | 1.11/-0.71 |

**EPR experiment.**

EPR spectrum was recorded at room temperature (298 K) using the EPR instrument which was derived at 9.4335 GHz. Typical parameters were documented as follows, scan range: 100 G; centre fieldset: 3480.00 G; time constant: 0.16 ms; scan time: 122.88 s; modulation amplitude: 20.0 G; modulation frequency: 100 kHz; receiver gain: $2.00\times10^2$ ; microwave power: $7.14e^{-001}$ mW.

**The reaction of propiolamide 1a with thiophenol 2a in the presence of DMPO under the standard condition.**

A solution of propiolamide **1a** (60 mg, 0.271 mmol)**,** thiophenol (89 mg, 0.813 mmol), and DMPO (20 μL) were allowed to stir for 20 minutes at room temperature. Afterward, 20 μL solutions were quickly transferred into the EPR tube, and 200 μL of toluene was added to the EPR tube. No EPR signal has appeared.

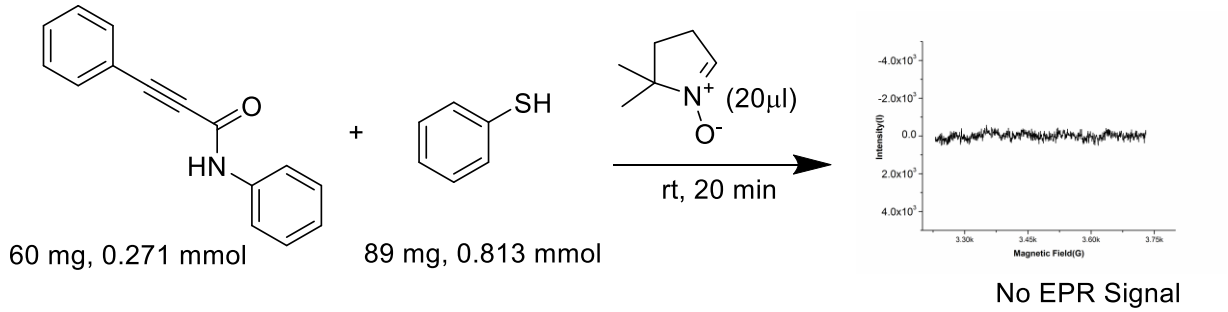
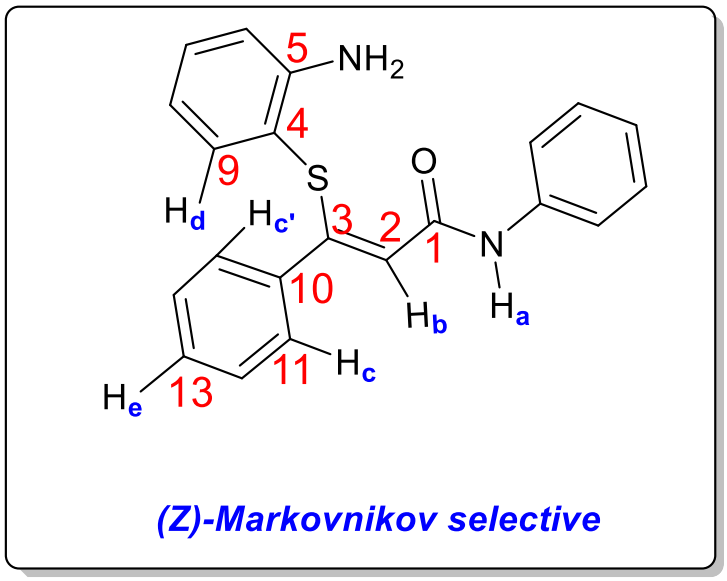



**Figure 3.10**. EPR spectra of reaction mixture **1a** and **2a** in the presence of spin trapping reagent DMPO in toluene solvent.

**Structure elucidation for compound (3ak)**

The proposed structure is given below



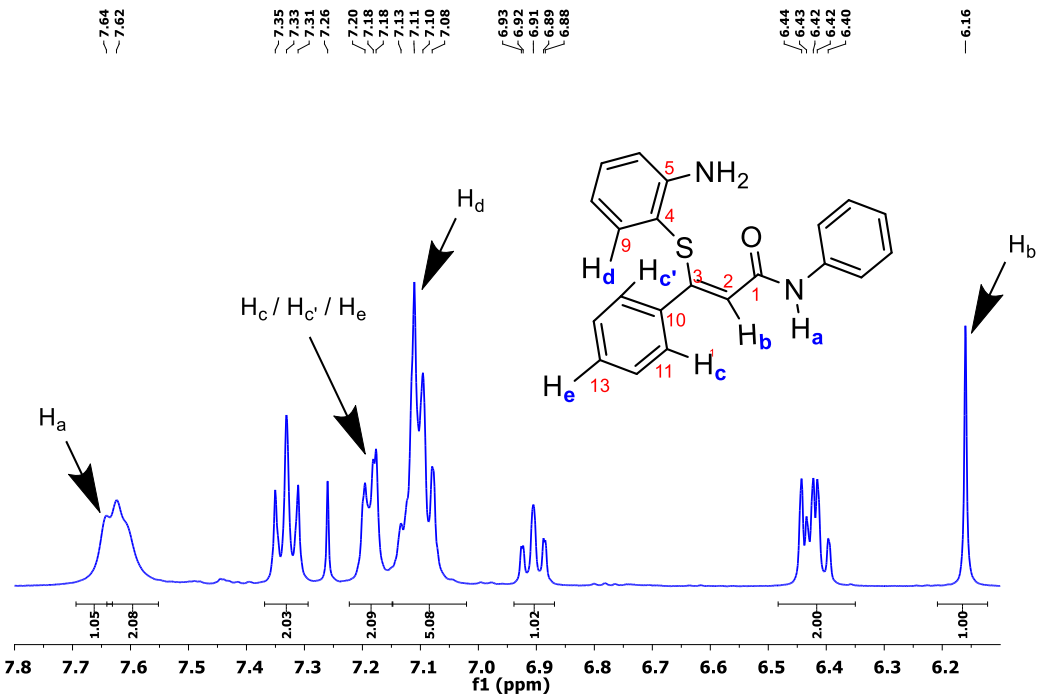



**Figure 3.11.** $^{1}$H NMR spectrum of Compound **(3ak)** with the expanded aromatic region. The signature peaks are assigned through $^{1}$H-$^{13}$C HMBC and HSQC NMR study below.

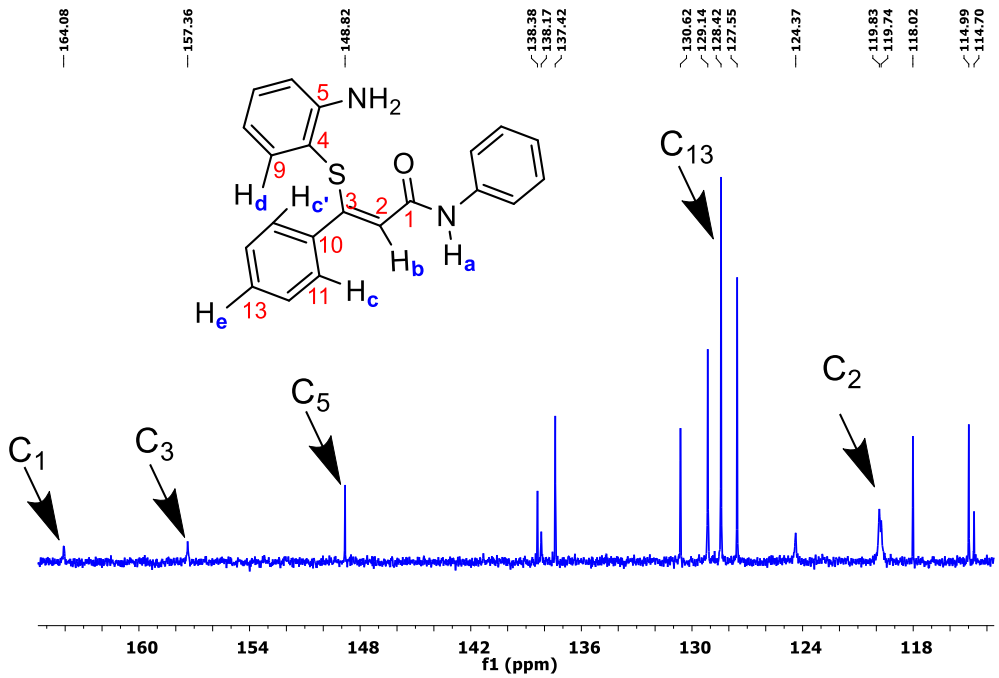



**Figure 3.12.** $^{13}$C NMR spectrum of Compound (3ak) with the expanded aromatic region. The signature peaks are assigned through $^{1}$H-$^{13}$C HMBC and HSQC NMR study below.

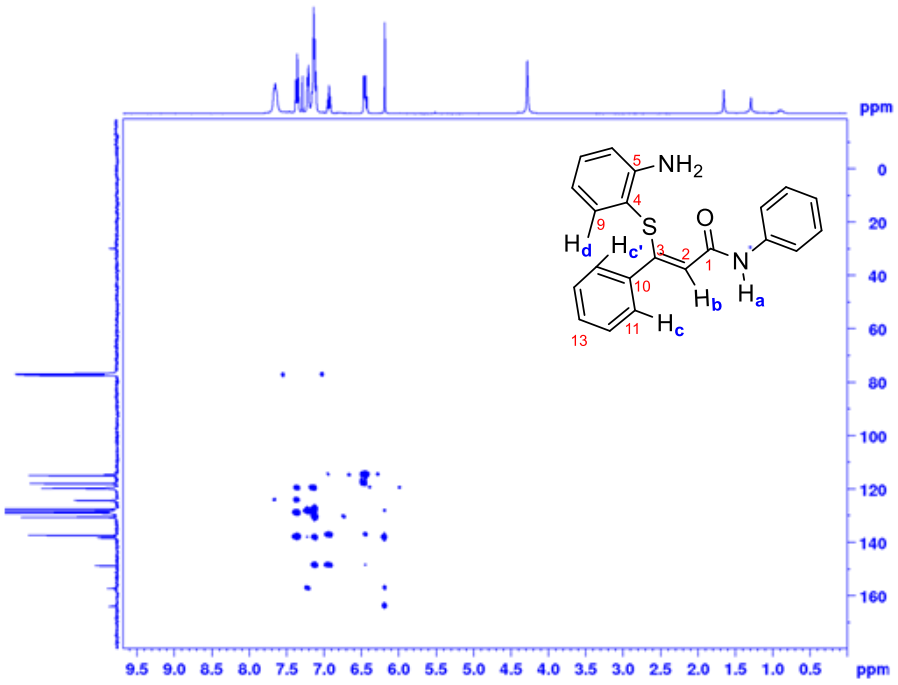



**Figure 3.13.** HMBC spectrum (full). All points used along indirect and direct dimensions were 256 and 2048 with a spectral breadth 23900 Hz and 5200 Hz. 16 transients were performed with a prescan delay of 3s. $CDCl_3$ is not calibrated as 7.284 ppm as a substitute of 7.26 ppm).

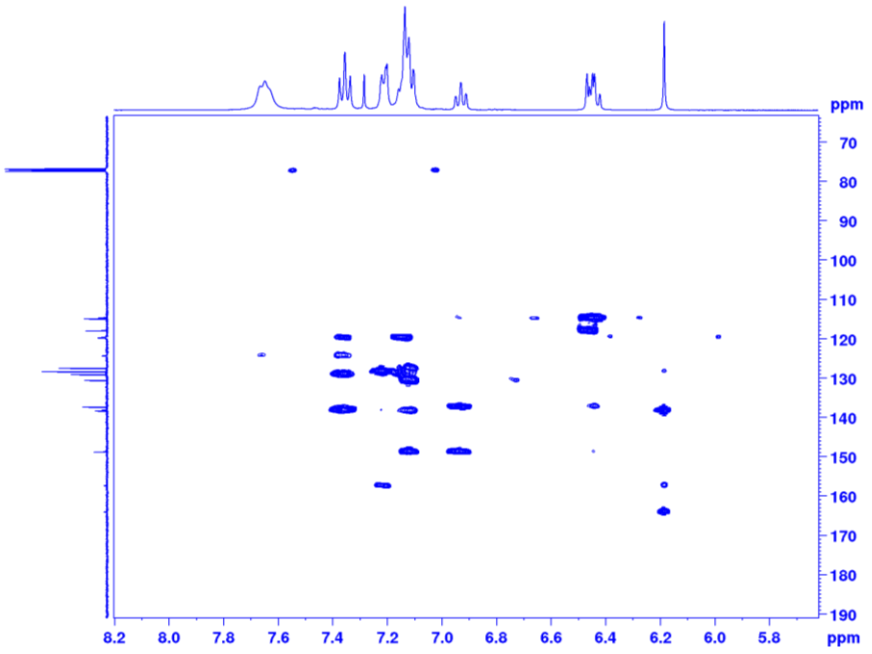



**Figure 3.14.** HMBC spectra are showing strong three bond connectivity and week two bond connectivity.

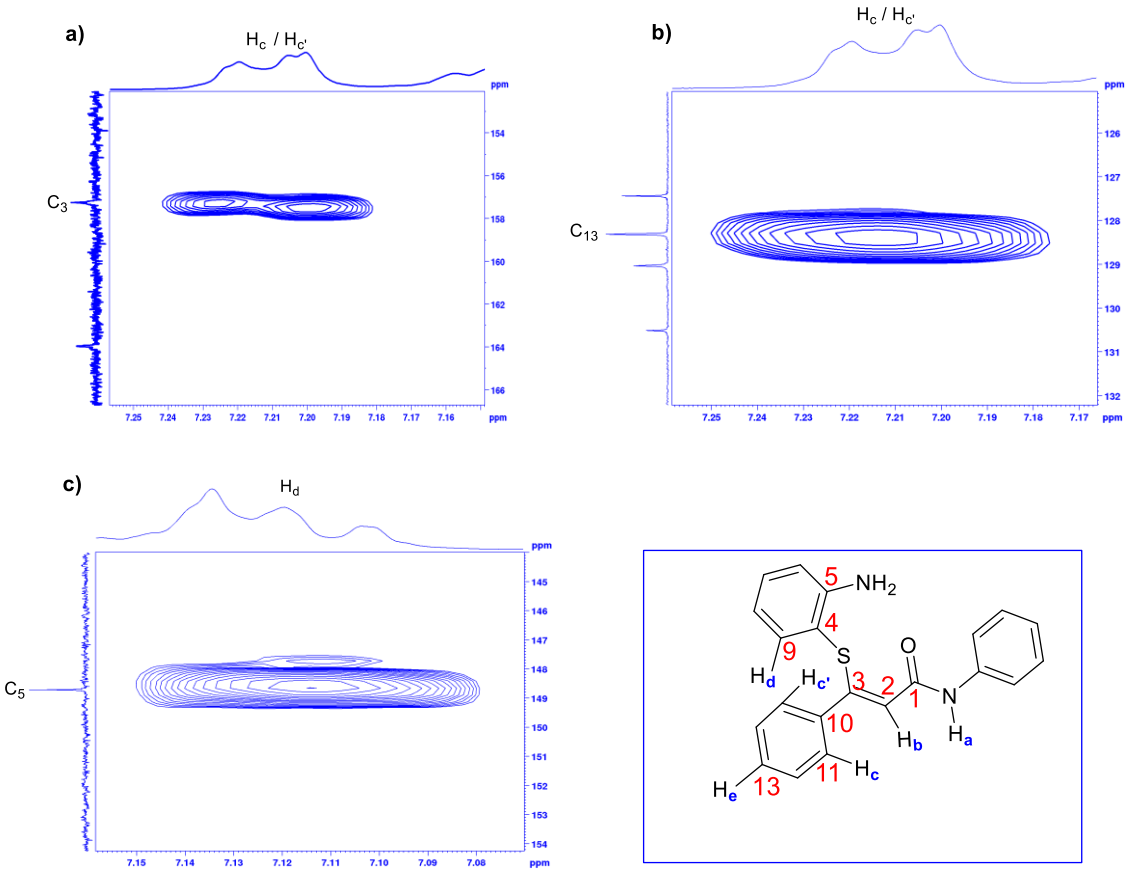



**Figure 3.15.** $^{1}H$-$^{13}C$ HMBC spectrum indicating three bond connectivity: **a)** Three bond connectivity between $H_c/H_{c'}$ and $C_3$. **b)** Three bond connectivity between $H_c/H_{c'}$ and $C_{13}$. **c)** Three bond connectivity between $H_d$ and $C_5$.

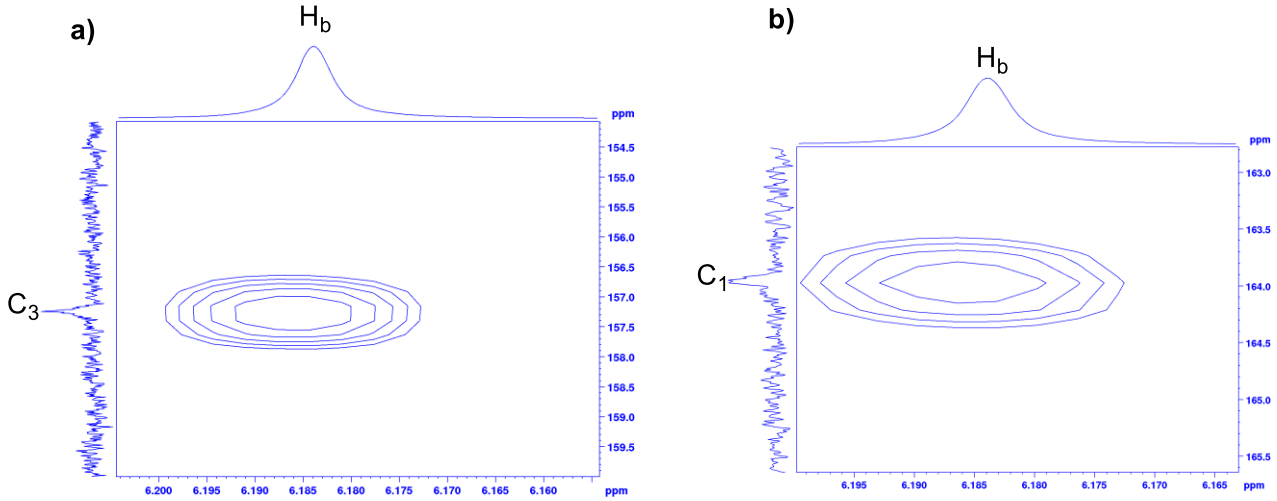



**Figure 3.16.** $^{1}H$-$^{13}C$ HMBC NMR spectra with two bond correlation. **a)** Two bond correlation between $H_b$ and $C_3$. **b)** Two Bond correlation between $H_b$ and $C_1$.

From 2D HMBC analysis, it was concluded that the Hc/Hc' at 7.2 ppm was connected with $C_3$ at 157.2 ppm *via* three bond coupling, and it was also connected with $C_{13}$ at 128.2 ppm via three bond coupling (Figures 3.14-3.16). Therefore it is concluded the resonance at 7.2 ppm must appear from $H_C/_{C'}$. $C_5$(148.7) showed a strong three bond correlation with the proton at 7.1 ppm. Thus it was indicating that this was equivalent to $H_d$.

$H_b$ at 6.18 ppm showed a 2-bond correlation with $C_3$ at 157.2 ppm and $C_1$ at 163.8 ppm. Thus it was confirmed that $C_3$ must equivalent to 157.2.

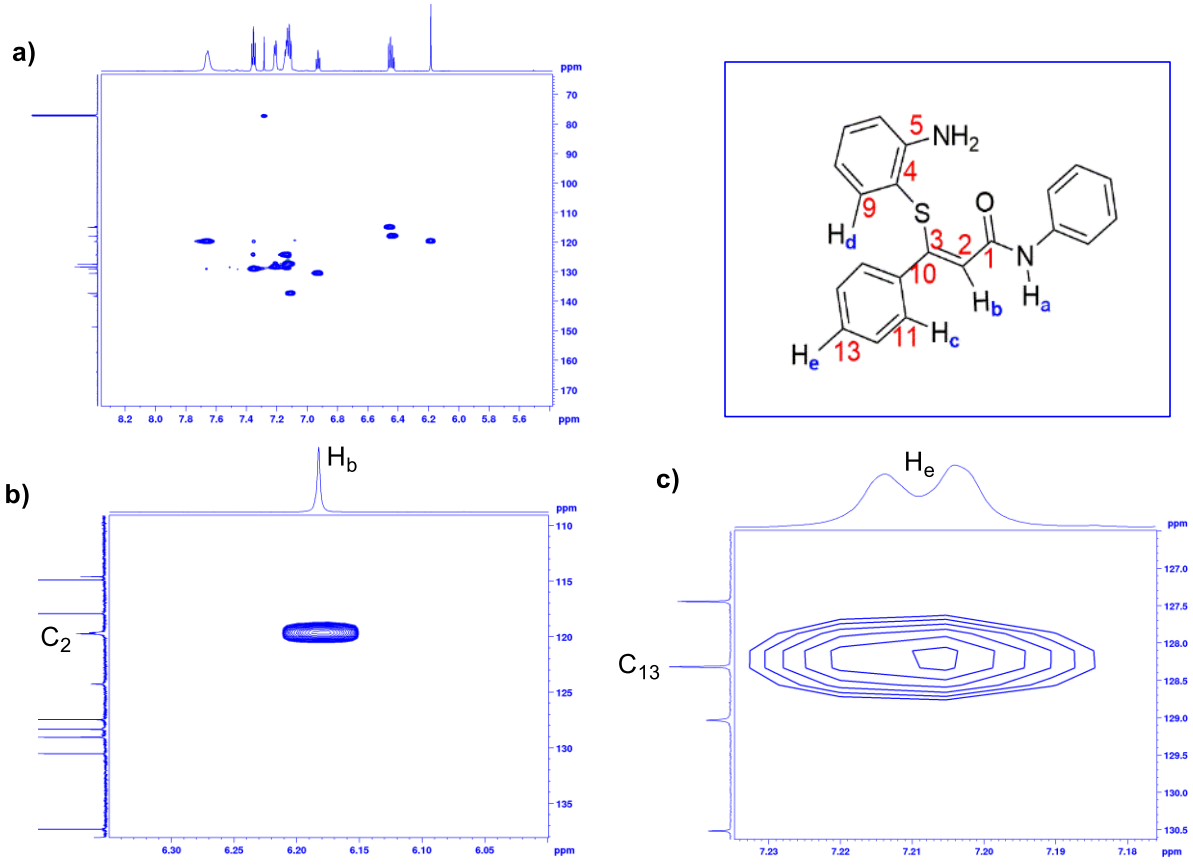



**Figure 3.17.** HSQC Spectra: **a)** Expanded aromatic region. **b)** One bond correlation of $H_b$ with $C_2$. **c)** One bond correlation of $H_e$ with $C_{13}$.

From HSQC analysis, it was seen that single-bond-connectivity of $H_b$ is with $C_2$ at 119.2 ppm (Figure 3.17). $C_{13}$ also showed a one bond correlation with $H_e$, which was resonating 7.2 ppm. Thus, it further concluded that $C_{13}$ resonated at 128.2 ppm.

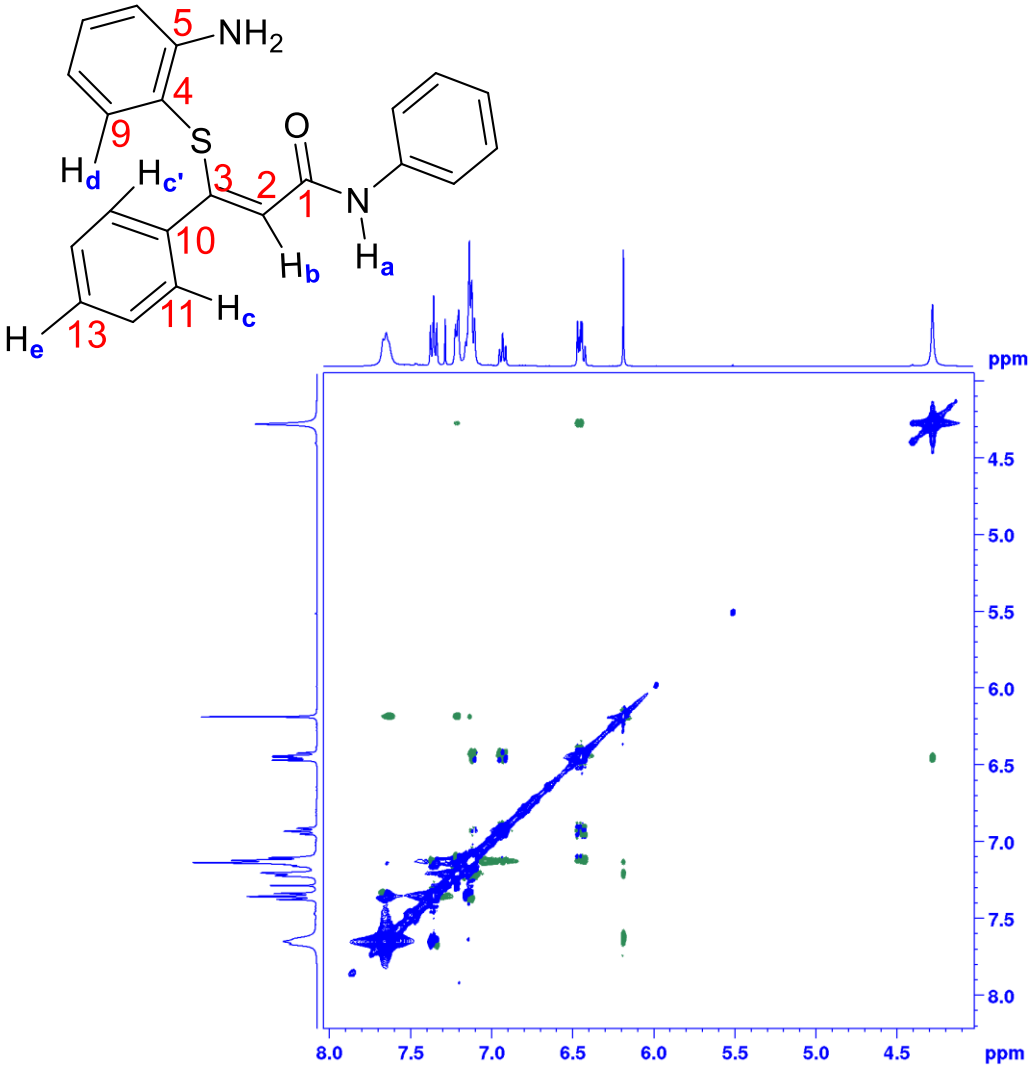



**Figure 3.18.** ROESY spectra of compound **3ak**. The number of points in the acquisition and indirect dimension was 2048 and 256, with a spinlock pulse of a duration of 270ms. 8 transients with a prescan delay of 3 seconds were used to ensure complete relaxation. Spectral with along both indirect and direct dimensions was adjusted to 4125 Hz.

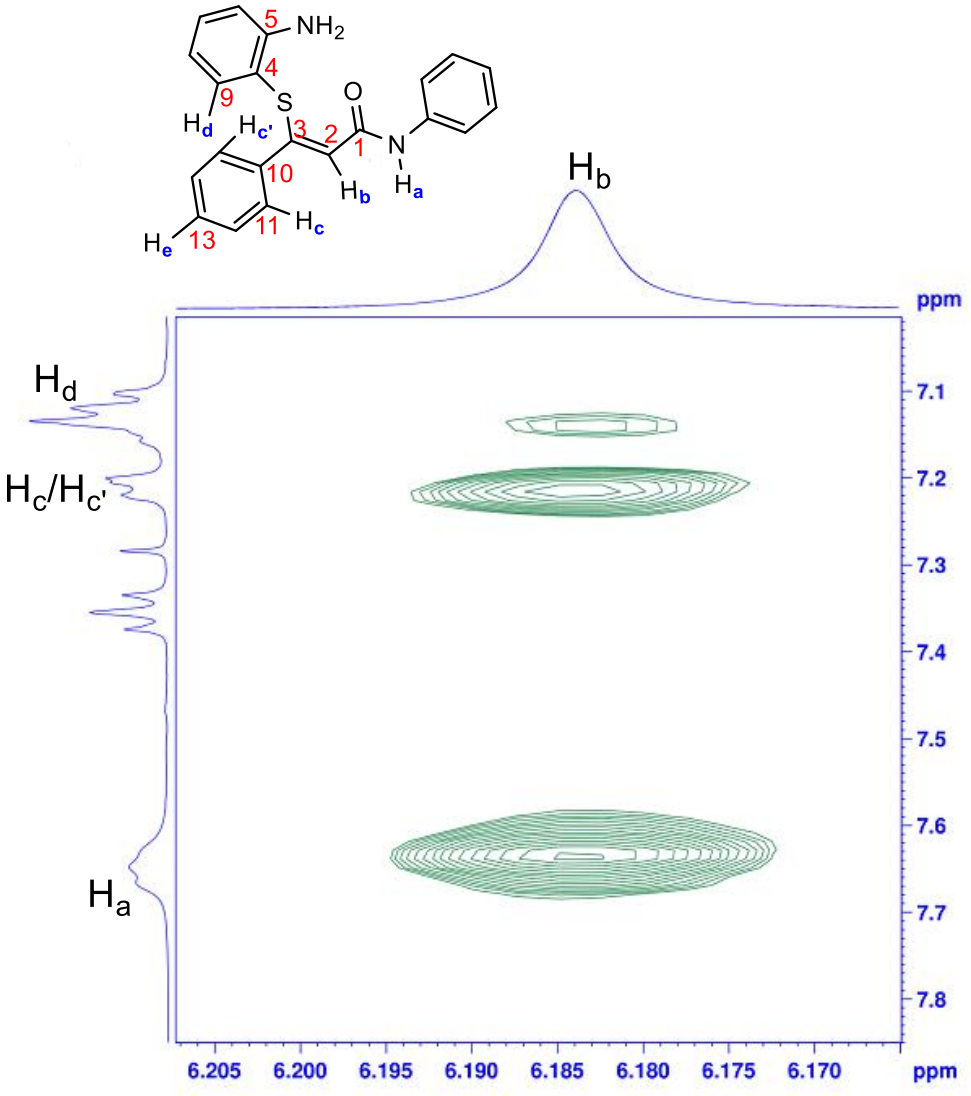



**Figure 3.19.** Expanded region of the ROESY spectra.

$^{1}$H-$^{1}$H ROESY 2D NMR experiment showed a strong correlation between $H_b$(6.18 ppm) and $H_a$ (7.64 ppm) (Figures 3.18 and 3.19). This confirmed the Markovnikov selectivity of the compound (**3ak**). Besides, another strong correlation between $H_b$(6.18 ppm) and Hc/Hc'(7.20 ppm) was also observed. It confirmed the (Z)-selectivity of **3ak**. However, a very weak interaction of $H_b$ with $H_d$ was also observed. Th integrals ratio between two cross-peaks was found to be approximately 1:0.10.

In order to make out the observed interaction, we have carried out optimization of structure through DFT(B3LYP/6311G). The optimized structure was given below.

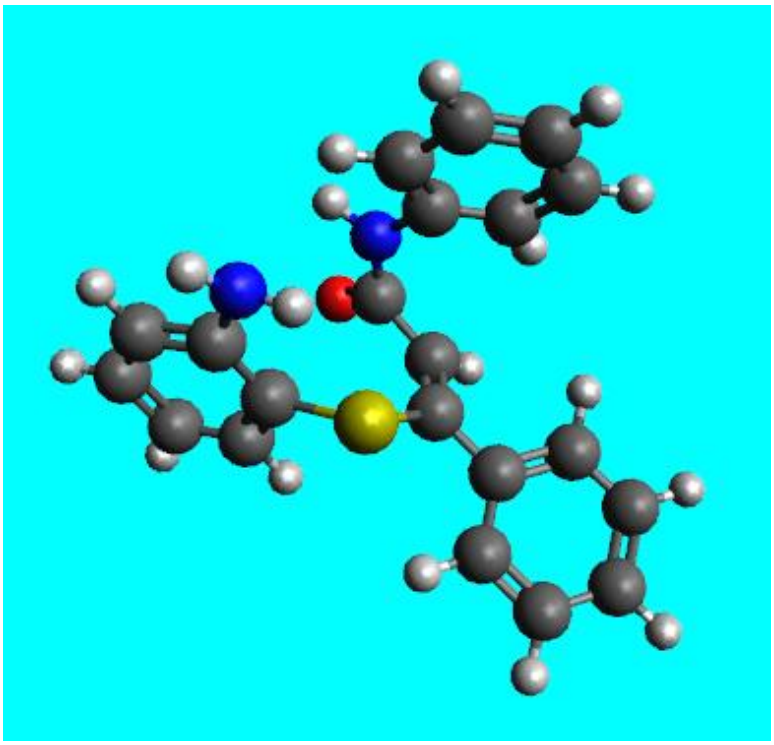


**Figure 3.20.** Optimized geometry via B3LYP DFT method using 6311G basis set with quadratic convergence.

In the optimized figure (Figure 3.20), it was clearly observed that the distance between $H_b$ and $H_d$ was very high (3.90Å) in contrast to $H_b$ and $H_c$ (2.36 Å). As the concentration of ROESY cross-peaks is inversely proportional with the sixth power of distance ($1/r^6$), the intensity ratio in the present case between $H_b$-$H_c$ and $H_b$-$H_d$ was expected to be 1:0.06, which was very close to the experimentally observed ratio of 1:0.10. This confirmed the exclusive configuration of (Z)-selective Markovnikov product**.**

## NMR CHARACTERIZATION DATA

**(Z)-N,3-Diphenyl-2-(phenylthio)acrylamide (3aa):** $R_f$ = 0.6 (20% ethyl acetate in hexane); white solid; yield 97% (87 mg); mp 96-98 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 9.00 (s, 1H), 8.53 (s, 1H), 7.86-7.85 (m, 2H), 7.47 (d, *J* = 7.7 Hz, 2H), 7.40-7.39 (m, 3H), 7.31-7.30 (m, 3H), 7.29-7.27 (m, 3H), 7.18 (t, *J* = 7.2 Hz, 1H), 7.10 (t, *J* = 7.4 Hz, 1H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 163.7, 147.6, 137.8, 134.6, 134.3, 130.9, 130.3, 129.8, 129.1, 128.6, 127.9, 126.9, 124.8, 124.3, 120.2; IR (KBr) ῡ 3347, 3057, 2924, 1674, 691; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{21}H_{17}NOSNa$ 354.0923; found 354.0927.

**(Z)-N,3-Diphenyl-2-(*p*-tolylthio)acrylamide (3ab):** $R_f$ = 0.7 (20% ethyl acetate in hexane); white solid; yield 98% (91 mg); mp 122-124 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 9.01 (s, 1H), 8.48 (s, 1H), 7.89-7.85 (m, 2H), 7.48 (d, *J* = 7.7 Hz, 2H), 7.41-7.37 (m, 3H), 7.30 (t, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 7.7 Hz, 2H), 7.09 (t, *J* = 8.0 Hz, 3H), 2.27 (s, 3H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 163.3, 147.1, 137.9, 137.0, 134.7, 130.9, 130.6, 130.6, 130.2, 129.1, 128.6, 127.4, 124.9, 124.7, 120.2, 21.1; IR (KBr) ῡ 3344, 2923, 1667, 690; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{20}NOS$ 346.1260; found 346.1258.

**(Z)-2-((4-Methoxyphenyl)thio)-N,3-diphenylacrylamide (3ac):** $R_f$ = 0.5 (20% ethyl acetate in hexane); white solid; yield 66% (65 mg); in 1 mL EtOH 82% (80 mg); mp 140-141 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 8.99 (s, 1H), 8.40 (s, 1H), 7.87 (d, *J* = 7.7 Hz, 2H), 7.48 (d, *J* = 7.7 Hz, 2H), 7.42-7.38 (m, 3H), 7.31 (t, *J* = 7.7 Hz, 2H), 7.26-7.24 (m, 2H), 7.10 (t, *J* = 7.4 Hz, 1H), 6.82 (d, *J* = 8.4 Hz, 2H), 3.74 (s, 3H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 163.3, 159.2, 146.1, 137.8, 134.7, 130.9, 130.1, 129.7, 129.1, 128.6, 126.0, 124.7, 124.6, 120.1, 115.5, 55.5; IR (KBr) ῡ

3334, 2924, 2348, 1666, 691; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{22}H_{19}NO_2SNa$ 384.1029; found 384.1041.

**(Z)-2-((4-Fluorophenyl)thio)-N,3-diphenylacrylamide (3ad):** $R_f$ = 0.6 (20% ethyl acetate in hexane); white solid; yield 81% (77 mg); mp 113-114 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 8.94 (s, 1H), 8.47 (s, 1H), 7.85-7.84 (m, 2H), 7.48 (d, *J* = 7.7 Hz, 2H), 7.41-7.40 (m, 3H), 7.31 (t, *J* = 8.0 Hz, 2H), 7.28-7.26 (m, 2H), 7.11 (t, *J* = 7.4 Hz, 1H), 6.99 (t, *J* = 8.6 Hz, 2H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 163.0, 162.0 (d, $^1J_{CF}$ = 247.2 Hz), 147.3, 137.7, 134.4, 130.9, 130.4, 129.3 (d, $^3J_{CF}$ = 8.1 Hz), 129.3 (d, $^4J_{CF}$ = 3.2 Hz), 129.2, 128.6, 124.9(×2), 120.2, 117.0 (d, $^2J_{CF}$ = 22.3 Hz); IR (KBr) ῡ 3353, 2923, 1661, 1314, 690; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{21}H_{16}NFOSNa$ 372.0829; found 372.0846.

**(Z)-2-((4-Chlorophenyl)thio)-N,3-diphenylacrylamide (3ae):** $R_f$ = 0.7 (20% ethyl acetate in hexane); white solid; yield 86% (86 mg); mp 135-138 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 8.94 (s, 1H), 8.53 (s, 1H), 7.83-7.82 (m, 2H), 7.49 (d, *J* = 7.7 Hz, 2H), 7.41-7.40 (m, 3H), 7.32 (t, *J* = 7.7 Hz, 2H), 7.25 (d, *J* = 7.7 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.12 (t, *J* = 7.7 Hz, 1H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 162.9, 148.1, 137.6, 134.3, 132.9, 132.8, 130.9, 130.5, 130.0, 129.2, 128.7, 128.3, 124.9, 123.8, 120.2; IR (KBr) ῡ 3348, 2924, 2853, 1663, 754, 690; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{17}ClNOS$ 366.0714; found 366.0684.

**(Z)-2-((4-Bromophenyl)thio)-N,3-diphenylacrylamide (3af):** $R_f$ = 0.5 (20% ethyl acetate in hexane); white solid; yield 91% (101mg); mp 142-144 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 8.94 (s, 1H), 8.53 (s, 1H), 7.82-7.81 (m, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.41-7.39 (m, 5H), 7.32 (t, *J* = 7.7

Hz, 2H), 7.16 (d, *J* = 8.4 Hz, 2H), 7.12 (t, *J* = 7.4 Hz, 1H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 162.9, 148.3, 137.6, 134.3, 133.6, 132.8, 130.9, 130.5, 129.9, 128.7, 128.5, 124.9, 123.6, 120.7, 120.2; IR (KBr) ῡ 3353, 2924, 2359, 1661, 690, 667; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{17}BrNOS$ 410.0179; found 410.0209.

**(Z)-N,3-Diphenyl-2-((4-(trifluoromethyl)phenyl)thio)acrylamide (3ag):** $R_f$ = 0.6 (20% ethyl acetate in hexane); white solid; yield 91% (99 mg); mp 138-141 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 8.94 (s, 1H), 8.63 (s, 1H), 7.82- 7.80 (m, 2H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 7.7 Hz, 2H), 7.41-7.40 (m, 3H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.32 (t, *J* = 7.7 Hz, 2H), 7.12 (t, *J* = 7.4 Hz, 1H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 162.8, 149.3, 139.5, 137.5, 134.2, 130.9, 130.7, 129.2, 128.8 (q, $^2J_{CF}$ = 32 Hz), 128.7, 126.6 (q, $^4J_{CF}$ = 3.6 Hz), 126.6, 125.0, 124.0 (q, $^1J_{CF}$ = 272 Hz), 122.5, 120.3; IR (KBr) ῡ 3363, 2923, 1659, 1326, 688; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{17}F_3NOS$ 400.0977; found 400.0970.

**(Z)-2-((3-Methoxyphenyl)thio)-N,3-diphenylacrylamide (3ah):** $R_f$ = 0.7 (20% ethyl acetate in hexane); white solid; yield 78% (76 mg); mp 101-103 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 9.00 (s, 1H), 8.53 (s, 1H), 7.86-7.85 (m, 2H), 7.49 (d, *J* = 7.7 Hz, 2H), 7.40-7.39 (m, 3H), 7.31 (t, *J* = 7.7 Hz, 2H), 7.20 (t, *J* = 8.2 Hz, 1H), 7.10 (t, *J* = 7.4 Hz, 1H), 6.90 (dd, *J* = 7.7, 0.7 Hz, 1H), 6.84 (s, 1H), 6.72 (dd, *J* = 8.4, 1.8 Hz, 1H), 3.74 (s, 3H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 163.1, 160.5, 147.8, 137.8, 135.5, 134.5, 130.9, 130.7, 130.3, 129.1, 128.6, 124.7, 124.14, 120.2, 119.3, 112.6, 112.6, 55.4; IR (KBr) ῡ 3345, 2924, 2359, 1668, 689; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{22}H_{19}NO_2SNa$ 384.1029; found 384.1015.

**(Z)-2-((3-Chlorophenyl)thio)-N,3-diphenylacrylamide (3ai):** $R_f$ = 0.6 (20% ethyl acetate in hexane); white solid; yield 90% (89 mg); mp 150-152 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.58 (s, 1H), 7.84-7.81 (m, 2H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.42-7.40 (m, 3H), 7.32 (t, *J* = 8.0 Hz, 2H), 7.30 (s, 1H), 7.23-7.10 (m, 4H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 162.8, 148.7, 137.6, 136.4, 135.6, 134.3, 130.9, 130.8, 130.6, 129.2, 128.7, 127.1, 126.7, 124.9, 124.9, 123.2, 120.3; IR (KBr) ῡ 3348, 2348, 1665, 774, 690; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{17}ClNOS$ 366.0714; found 366.0713.

**(Z)-2-((2-Fluorophenyl)thio)-N,3-diphenylacrylamide (3aj):** $R_f$ = 0.6 (20% ethyl acetate in hexane); white solid; yield 79% (75 mg); mp 105-108 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 9.05 (s, 1H), 8.51 (s, 1H), 7.87-7.86 (m, 2H), 7.53 (d, *J* = 7.7 Hz, 2H), 7.45-7.39 (m, 3H), 7.32 (t, *J* = 7.7 Hz, 2H), 7.21-7.16 (m, 2H), 7.11 (t, *J* = 7.7 Hz, 1H), 7.09 (t, *J* = 8.7 Hz, 1H), 7.03 (t, *J* = 7.7 Hz, 1H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 163.0, 160.2 (d, $^1J_{CF}$ = 245.2 Hz), 147.9, 137.7, 134.4, 130.9, 130.4, 129.9, 129.1, 129.0 (d, $^3J_{CF}$ = 7.6 Hz), 128.6, 125.5 (d, $^4J_{CF}$ = 3.4 Hz), 124.8, 123.7, 121.3 (d, $^2J_{CF}$ = 17.0 Hz), 120.2, 116.1 (d, $^2J_{CF}$ = 21.3 Hz); IR (KBr) ῡ 3355, 3056, 2924, 1652, 1178, 689; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{17}FNOS$ 350.1009; found 350.1003.

**(Z)-3-((2-Aminophenyl)thio)-N,3-diphenylacrylamide (3ak):** $R_f$ = 0.4 (20% ethyl acetate in hexane); brownish white solid; yield 86% (81 mg); mp 175-176 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.64 (s, 1H), 7.63 (d, *J* = 7.4 Hz, 2H), 7.33 (t, *J* = 7.8 Hz, 2H), 7.20-7.18 (m, 2H), 7.13-7.08 (m, 5H), 7.93-6.88 (m, 1H), 6.44-6.40 (m, 2H), 6.16 (s, 1H), 4.25 (s, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.1, 157.4, 148.8, 138.4, 138.2, 137.4, 130.6, 129.1, 128.4, 127.5, 124.4, 119.8,

119.7, 118.0, 115.0, 114.7; IR (KBr) ῡ 3432, 3359, 2923, 2359, 1607, 668; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{21}H_{18}N_2OSNa$ 369.1032 ; found 369.1020.

**(Z)-3-Phenyl-2-(phenylthio)-N-(p-tolyl)acrylamide (3ba):** $R_f$ = 0.4 (20% ethyl acetate in hexane); white solid; yield 96% (85 mg); mp 108-111 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.93 (s, 1H), 8.51 (s, 1H), 7.86-7.84 (m, 2H), 7.42-7.38 (m, 3H), 7.34 (d, *J* = 8.2 Hz, 2H), 7.31-7.26 (m, 4H), 7.19-7.16 (m, 1H), 7.10 (d, *J* = 8.2 Hz, 2H), 2.29 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 163.0, 147.4, 135.2, 134.6, 134.4, 134.4, 130.9, 130.2, 129.8, 129.6, 128.6, 127.2, 126.8, 124.4, 120.3, 21.0; IR (KBr) ῡ 3360, 2921, 2369, 1676, 689; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{20}NOS$ 346.1260; found 346.1277.

**(Z)-N-(2,4-Dimethylphenyl)-3-phenyl-2-(phenylthio)acrylamide (3ca):** $R_f$ = 0.6 (20% ethyl acetate in hexane); white solid; yield 91% (79 mg); mp 143-146 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 8.92 (s, 1H), 8.56 (s, 1H), 7.86-7.85 (m, 2H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.41-7.38 (m, 3H), 7.31-7.27 (m, 4H), 7.18 (t, *J* = 7.0 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 1H), 6.92 (s, 1H), 2.26 (s, 3H), 1.93 (s, 3H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 162.9, 147.9, 134.9, 134.7, 134.6, 133.3, 131.2, 130.8, 130.2, 129.8, 129.1, 128.6, 127.4, 126.9, 126.7, 124.3, 122.4, 21.0, 17.3; IR (KBr) ῡ 3365, 2923,2853, 1673, 690; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{23}H_{21}NOSNa$ 382.1236; found 382.1250.

**(Z)-N-Mesityl-3-phenyl-2-(phenylthio)acrylamide (3da):** $R_f$ = 0.8 (20% ethyl acetate in hexane); white solid; yield 88% (75 mg); mp 158-160 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 8.52 (s, 1H), 8.39 (s, 1H), 7.88-7.87 (m, 2H), 7.42-7.38 (m, 3H), 7.35 (d, *J* = 7.0 Hz, 2H), 7.31 (t, *J* = 7.7

Hz, 2H), 7.21 (t, *J* = 7.4 Hz, 1H), 6.83 (s, 2H), 2.24 (s, 3H), 1.89 (s, 6H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 163.6, 147.4, 137.2, 135.3, 134.8, 134.7, 131.3, 130.8, 130.1, 129.8, 129.0, 128.5, 127.4, 126.8, 124.3, 21.0, 18.1; IR (KBr) ῡ 3259, 2923, 2853, 1646, 689; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{24}H_{24}NOS$ 374.1573; found 374.1576.

**(Z)-N-(4-Ethylphenyl)-3-phenyl-2-(phenylthio)acrylamide (3ea):** $R_f$ = 0.6 (20% ethyl acetate in hexane); white solid; yield 97% (84 mg); mp 115-117 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.52 (s, 1H), 7.86-7.84 (m, 2H), 7.42-7.38 (m, 5H), 7.32-7.26 (m, 4H), 7.19-7.18 (m, 1H), 7.13 (d, *J* = 8.4 Hz, 2H), 2.60 (q, *J* = 7.6 Hz, 2H), 1.20 (t, *J* = 7.6 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 163.0, 147.4, 140.9, 135.4, 134.6, 134.4, 130.9, 130.2, 129.8, 128.6, 128.4, 127.2, 126.8, 124.4, 120.4, 28.5, 15.8; IR (KBr) ῡ 3341, 2959, 1716, 667; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{23}H_{22}NOS$ 360.1417; found 360.1426.

**(Z)-N-(4-Isopropylphenyl)-3-phenyl-2-(phenylthio)acrylamide (3fa):** $R_f$ = 0.7 (20% ethyl acetate in hexane); white solid; yield 89% (76 mg); mp 129-133 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.53 (s, 1H), 7.86-7.85 (m, 2H), 7.41-7.38 (m, 5H), 7.31 (d, *J* = 7.7 Hz, 2H), 7.28 (t, *J* = 7.7 Hz, 2H), 7.18 (d, *J* = 7.7 Hz, 1H), 7.16 (d, *J* = 7.7 Hz, 2H), 2.86 (sept, *J* = 7.0 Hz, 1H), 1.22 (d, *J* = 7.0 Hz, 6H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 163.0, 147.5, 145.5, 135.5, 134.6, 134.4, 130.9, 130.2, 129.8, 128.6, 127.2, 127.0, 126.8, 124.4, 120.4, 33.7, 24.1; IR (KBr) ῡ 3359, 2957, 2868, 2358, 1652, 690; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{24}H_{23}NOSNa$ 396.1393; found 396.1409.

**(Z) N-(4-(*tert*-Butyl)phenyl)-3-phenyl-2-(phenylthio)acrylamide (3ga):** $R_f$ = 0.8 (20% ethyl acetate in hexane); white solid; yield 95% (79 mg); mp 137-139 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.53 (s, 1H), 7.86-7.84 (m, 2H), 7.40-7.38 (m, 5H), 7.33-7.28 (m, 6H), 7.18 (t, *J* = 6.8 Hz, 1H), 1.29 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 163.1, 147.8, 147.5, 135.2, 134.6, 134.4, 130.9, 130.2, 129.8, 128.6, 127.2, 126.8, 125.9, 124.4, 120.0, 34.5, 31.5; IR (KBr) ῡ 3338, 3069, 2962, 1661, 689; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{25}H_{25}NOSNa$ 410.1549; found 410.1562.

**(Z)-N-(4-Methoxyphenyl)-3-phenyl-2-(phenylthio)acrylamide (3ha):** $R_f$ = 0.6 (20% ethyl acetate in hexane); white solid; yield 79% (68 mg); mp 129-131 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.51 (s, 1H), 7.85-7.83 (m, 2H), 7.42-7.39 (m, 3H), 7.35 (d, *J* = 8.8 Hz, 2H), 7.31-7.26 (m, 4H), 7.20-7.17 (m, 1H), 6.83 (d, *J* = 8.8 Hz, 2H), 3.77 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 163.0, 156.8, 147.2, 134.6, 134.5, 130.9, 130.8, 130.2, 129.8, 128.6, 127.2, 126.8, 124.4, 122.0, 114.3, 55.6; IR (KBr) ῡ 3348, 2923, 2359, 1672, 689; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{22}H_{19}NO_2SNa$ 384.1029; found 384.1024.

**(Z)-N-([1,1'-Biphenyl]-4-yl)-3-phenyl-2-(phenylthio)acrylamide (3ia):** $R_f$ = 0.5 (20% ethyl acetate in hexane); brownish white solid; yield 43% (36 mg); mp 163-167 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 9.07 (s, 1H), 8.54 (s, 1H), 7.88-7.86 (m, 2H), 7.56-7.52 (m, 6H), 7.43-7.40 (m, 5H), 7.34-7.28 (m, 5H), 7.19 (t, *J* = 6.8 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 163.2, 147.7, 140.6, 137.7, 137.1, 134.6, 134.3, 130.9, 130.3, 129.9, 128.9, 128.6, 127.7, 127.3, 127.2, 127.0, 126.9, 124.3, 120.5; IR (KBr) ῡ 3316, 2922, 1652, 687; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{27}H_{22}NOS$ 408.1417; found 408.1433.

**(Z)-N-(2-Fluorophenyl)-3-phenyl-2-(phenylthio)acrylamide (3ja):** $R_f$ = 0.7 (20% ethyl acetate in hexane); white solid; yield 98% (86 mg); mp 125-127 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 9.38 (s, 1H), 8.52 (s, 1H), 8.38 (t, *J* = 8.0 Hz, 1H), 7.90-7.89 (m, 2H), 7.43-7.39 (m, 3H), 7.33 (d, *J* = 7.0 Hz, 2H), 7.28 (t, *J* = 8.0 Hz, 2H), 7.18 (t, *J* = 7.0 Hz, 1H), 7.13-7.12 (m, 1H), 7.05-7.01 (m, 2H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 163.2, 152.9 (d, $^1J_{CF}$ = 244.4 Hz), 147.8, 134.4, 134.0, 131.0, 130.4, 129.7, 128.6, 127.6, 127.0, 126.5 (d, $^3J_{CF}$ = 10.0 Hz), 124.6 (d, $^4J_{CF}$ = 1.6 Hz), 124.63, 124.59, 121.5, 114.9 (d, $^2J_{CF}$ = 19.0 Hz); IR (KBr) ῡ 3358, 2924, 1699, 1320, 690; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{21}H_{16}FNOSNa$ 372.0829; found 372.0834.

**(Z)-N-(2-Chlorophenyl)-3-phenyl-2-(phenylthio)acrylamide (3ka):** $R_f$ = 0.75 (20% ethyl acetate in hexane); white solid; yield 98% (84 mg); mp 117-119 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 8.54 (s, 1H), 8.48 (d, *J* = 8.0 Hz, 1H), 7.90-7.89 (m, 2H), 7.41-7.40 (m, 3H), 7.32-7.25 (m, 6H), 7.17 (t, *J* = 7.2 Hz, 1H), 7.01 (t, *J* = 7.6 Hz, 1H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 163.3, 148.3, 134.9, 134.5, 134.1, 131.0, 130.5, 129.7, 129.2, 128.6, 127.8, 127.4, 126.8, 124.8, 124.6, 123.6, 121.3; IR (KBr) ῡ 3330, 3059, 2926, 1699, 738, 689; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{17}ClNOS$ 366.0714; found 366.0718.

**(Z)-N-(2-Bromophenyl)-3-phenyl-2-(phenylthio)acrylamide (3la):** $R_f$ = 0.85 (20% ethyl acetate in hexane); white solid; yield 88% (72 mg); mp 124-126 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 8.55 (s, 1H), 8.47 (d, *J* = 8.4 Hz, 1H), 7.90-7.88 (m, 2H), 7.48 (d, *J* = 8.2 Hz, 1H), 7.41-7.40 (m, 3H), 7.32-7.25 (m, 5H), 7.17 (t, *J* = 7.2 Hz, 1H), 6.95 (t, *J* = 7.6 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 163.4, 148.4, 136.1, 134.5, 134.2, 132.5, 131.0, 130.5, 129.7, 128.6,

128.4, 127.3, 126.8, 125.3, 124.4, 121.6, 114.0; IR (KBr) ῡ 3314, 1672, 737, 688; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{21}H_{16}BrNOSNa$ 432.0028; found 432.0041.

**(Z)-N-(2-Iodophenyl)-3-phenyl-2-(phenylthio)acrylamide (3ma):** $R_f$ = 0.8 (20% ethyl acetate in hexane); white solid; yield 76% (60 mg); mp 128-130 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 9.58 (s, 1H), 8.57 (s, 1H), 8.36 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.89-7.88 (m, 2H), 7.74 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.41-7.4 (m, 3H), 7.35-7.31 (m, 3H), 7.28-7.26 (m, 2H), 7.17 (t, *J* = 7.4 Hz, 1H), 6.82-6.80 (m, 1H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 163.6, 148.6, 139.1, 138.7, 134.5, 134.4, 131.0, 130.5, 129.7, 129.2, 128.6, 127.2, 126.7, 126.1, 124.2, 121.6, 89.8; IR (KBr) ῡ 3293, 3058, 1672, 688, 524; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{21}H_{16}INOSNa$ 479.9889; found 479.9904.

**(Z)-N-(4-Cyanophenyl)-3-phenyl-2-(phenylthio)acrylamide (3na):** $R_f$ = 0.5 (20% ethyl acetate in hexane); brownish white solid; yield 74% (64 mg); mp > 180 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 9.19 (s, 1H), 8.52 (s, 1H), 7.88-7.86 (m, 2H), 7.63-7.57 (m, 4H), 7.42-7.41 (m, 3H), 7.32-7.29 (m, 4H), 7.22-7.20 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 163.6, 148.7(×2), 141.7, 134.2, 133.8, 133.3, 131.0, 130.8, 130.0, 128.7, 127.2, 123.5, 119.9, 118.9, 107.6; IR (KBr) ῡ 3325, 2359, 1661, 687; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{17}N_2OS$ 357.1056; found 357.1067.

**(Z)-N-(4-Nitrophenyl)-3-phenyl-2-(phenylthio)acrylamide (3oa):** $R_f$ = 0.3 (20% ethyl acetate in hexane); brownish white solid; yield 70% (59 mg); mp 156-157 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 9.30 (s, 1H), 8.53 (s, 1H), 8.18 (d, *J* = 8.8 Hz, 2H), 7.88-7.86 (m, 2H), 7.66 (d, *J* = 8.8 Hz, 2H), 7.43-7.41 (m, 3H), 7.31-7.30 (m, 4H), 7.23-7.18 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$)

δ 163.7, 149.0, 143.9, 143.5, 134.1, 133.7, 131.1, 130.8, 130.0, 128.7, 127.23, 127.18, 125.1, 123.5, 119.5; IR (KBr) ῡ 3356, 2924, 2359, 1700, 1558, 689; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{17}N_2O_3S$ 377.0954; found 377.0952.

**(Z)-N-(3-Chlorophenyl)-3-phenyl-2-(phenylthio)acrylamide (3pa):** $R_f$ = 0.8 (20% ethyl acetate in hexane); white solid; yield 98% (84 mg); mp 102-103 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 9.01 (s, 1H), 8.52 (s, 1H), 7.86-7.85 (m, 2H), 7.60 (s, 1H), 7.41-7.40 (m, 3H), 7.31-7.28 (m, 5H), 7.22-7.18 (m, 2H), 7.07 (d, *J* = 7.7 Hz, 1H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 163.3, 148.1, 138.9, 134.8, 134.4, 134.1, 131.0, 130.5, 130.0, 129.9, 128.6, 127.1, 127.0, 124.8, 123.9, 120.2, 118.1; IR (KBr) ῡ 3341, 3059, 1667, 738, 689; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{21}H_{16}ClNOSNa$ 388.0533; found 388.0545.

**(Z)-N-(4-Chloro-2-methylphenyl)-3-phenyl-2-(phenylthio)acrylamide (3qa):** $R_f$ = 0.85 (20% ethyl acetate in hexane); white solid; yield 98% (82 mg); mp 137-139 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 8.97 (s, 1H), 8.57 (s, 1H), 7.92 (d, *J* = 9.1 Hz, 1H), 7.87-7.85 (m, 2H), 7.42-7.40 (m, 3H), 7.30-7.29 (m, 4H), 7.21-7.18 (m, 1H), 7.17 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.09 (s, 1H), 1.94 (s, 3H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 163.0, 148.5, 134.6, 134.5, 134.4, 130.9, 130.6, 130.4, 130.2, 130.0, 129.8, 128.6, 126.84, 126.83, 126.81, 123.8, 123.3, 17.3; IR (KBr) ῡ 3351, 3056, 1670, 765, 690; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{22}H_{18}ClNOSNa$ 402.0690; found 402.0674.

**((Z)-N-Benzyl-3-phenyl-2-(phenylthio)acrylamide (3ra):** $R_f$ = 0.45 (20% ethyl acetate in hexane); white solid; yield 88% (68 mg); mp 102-103 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 8.44 (s,

1H), 7.82 (d, *J* = 6.3 Hz, 2H), 7.39-7.36 (m, 4H), 7.28-7.26 (m, 2H), 7.23-7.21 (m, 3H), 7.20-7.17 (m, 3H), 6.91 (d, *J* = 6.3 Hz, 2H), 4.46 (d, *J* = 6.3 Hz, 2H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 165.1, 146.7, 137.9, 134.8, 134.7, 130.8, 130.0, 129.7, 128.7, 128.5, 127.4, 127.4, 127.3, 126.6, 124.4, 44.4; IR (KBr) ῡ 3314, 2924, 2853, 1651, 690; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{22}H_{19}NOSNa$ 368.1080; found 368.1080.

**(Z)-N-(Naphthalen-1-yl)-3-phenyl-2-(phenylthio)acrylamide (3sa):** $R_f$ = 0.4 (10% ethyl acetate in hexane); white solid; yield 78% (64 mg); mp 160-164 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 9.48 (s, 1H), 8.63 (s, 1H), 7.98 (d, *J* = 7.7 Hz, 1H), 7.91-7.89(m, 2H), 7.82 (d, *J* = 8.2 Hz, 1H), 7.67 (d, *J* = 8.2 Hz, 1H), 7.49-7.45 (m, 2H), 7.45-7.41 (m, 6H), 7.34 (t, *J* = 7.8 Hz, 3H), 7.30-7.20 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 163.6, 148.3, 134.6, 134.57, 134.1, 132.5, 130.9, 130.4, 129.9, 128.8, 128.6, 127.3 127.2, 126.9, 126.4, 126.0, 125.9, 125.9, 124.3, 120.6, 120.5; IR (KBr) ῡ 3366, 3052, 2360, 1671, 689; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{25}H_{19}NOSNa$ 404.1080; found 404.1093.

**(Z)-3-Phenyl-2-(phenylthio)-N-(quinolin-3-yl)acrylamide (3ta):** $R_f$ = 0.4 (30% ethyl acetate in hexane); white solid; yield 62% (52 mg); mp 169-173 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 9.23 (s, 1H), 8.73 (d, *J* = 2.4 Hz, 1H), 8.60 (d, *J* = 2.5 Hz, 1H), 8.56 (s, 1H), 8.02 (d, *J* = 8.4 Hz, 1H), 7.90-7.88 (m, 2H), 7.80 (d, *J* = 8.2 Hz, 1H), 7.64-7.60 (m, 1H), 7.54-7.50 (m, 1H), 7.43-7.41 (m, 3H), 7.36- 7.28 (m, 4H), 7.21-7.17 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 163.9, 148.2, 145.9, 144.3, 134.3, 134.0, 131.3, 131.0, 130.6, 130.0, 129.2, 128.7, 128.6, 128.3, 127.9, 127.4, 127.3, 127.2, 124.2, 123.9; IR (KBr) ῡ 3346, 2954, 2339, 1663, 688; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{24}H_{19}N_2OS$ 383.1213; found 383.1235.

**(Z)-N-([1,1'-Biphenyl]-2-yl)-3-phenyl-2-(phenylthio)acrylamide (3ua):** $R_f$ = 0.75 (10% ethyl acetate in hexane); colorless liquid; yield 48% (39 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 9.45 (s, 1H), 8.66 (d, *J* = 8.2 Hz, 1H), 8.55 (s, 1H), 7.83-7.81 (m, 2H), 7.43-7.40 (m, 4H), 7.37-7.35 (m, 3H), 7.26-7.24 (m, 2H), 7.22-7.10 (m, 5H), 6.92-6.90 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 163.1, 147.8, 138.0, 135.3, 134.5, 134.2, 132.3, 130.8, 130.2, 129.5, 129.4, 129.4, 129.1, 128.5, 128.5, 127.9, 126.7, 126.3, 124.4, 124.1, 120.0; IR (KBr) ῡ 3331, 2359, 1668, 689; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{27}H_{21}NOSNa$ 4430.1236; found 430.1239.

**(*R*,*Z*)-N,3-Diphenyl-2-(phenylsulfinyl)acrylamide 8:** $R_f$ = 0.55 (20% ethyl acetate in hexane); white solid; yield 90% (66 mg); mp 141-142 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 10.33 (s, 1H), 8.40 (s, 1H), 7.68-7.66 (m, 2H), 7.60-7.59 (m, 2H), 7.50-7.44 (m, 8H), 7.29 (t, *J* = 7.7 Hz, 2H), 7.09 (t, *J* = 7.7 Hz, 1H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 161.4, 147.8, 141.4, 137.8, 134.9, 132.5, 131.3, 130.94, 130.90, 129.8, 129.1(×2), 124.7, 124.4, 120.8; IR (KBr) ῡ 3352, 3058, 2348, 1677, 1316, 690; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{21}H_{17}NO_2SNa$ 370.0872; found 370.0862.

**(Z)-N-([1,1'-Biphenyl]-2-yl)-3-phenyl-2-(phenylthio)acrylamide 9:** $R_f$ = 0.85 (20% ethyl acetate in hexane); liquid; yield 98% (58 mg); $^1$H NMR (700 MHz, $CDCl_3$) δ 9.41 (s, 1H), 8.62 (d, *J* = 7.7 Hz, 1H), 8.52 (s, 1H), 7.81-7.80 (m, 2H), 7.43-7.35 (m, 7H), 7.24 (dd, *J* = 7.7, 1.4 Hz, 2H), 7.20-7.20-7.18 (m, 1H), 7.18-7.15 (m, 2H), 7.14 (dd, *J* = 7.7, 0.7 Hz, 1H), 7.11 (t, *J* = 7.4 Hz, 1H), 6.89 (d, *J* = 7.7 Hz, 2H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 163.1, 147.9, 138.0, 135.3, 134.5, 134.2, 132.3, 130.9, 130.2, 129.5, 129.4, 129.2(×2), 128.6, 128.5, 128.0, 126.7, 126.4,

124.4, 124.2, 120.1; IR (KBr) ῡ 3334, 3057, 1642, 1495, 691; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{27}H_{22}NOS$ 408.1417; found 408.1423.

**[1,1'-Biphenyl]-4-yl (Z)-3-((4-bromophenyl)thio)-3-phenylacrylate 6:** $R_f$ = 0.4 (10% ethyl acetate in hexane); white solid; yield 42% (41 mg); mp 108-112 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.56-7.51 (m, 4H), 7.43-7.27 (m, 5H), 7.22-7.12 (m, 6H), 6.98-6.88 (m, 3H), 6.26 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.1, 161.9, 150.3, 140.6, 139.0, 137.9, 137.0, 135.5, 133.4, 131.8, 129.2, 128.9, 128.9, 128.3, 127.4, 127.3, 122.6, 122.1, 115.5; IR (KBr) ῡ 3055, 2923, 2360, 1712, 690.

**(*E*)-3-([1,1'-Biphenyl]-4-yl)-2-((4-bromophenyl)thio)-3-phenylacrylic acid 7[56]:** $R_f$ = 0.5 (40% ethyl acetate in hexane); yellow solid; yield 56% (54 mg); $^1$H NMR (400 MHz, DMSO) δ 12.99 (s, 1H), 7.68-7.65 (m, 4H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.42-7.37 (m, 3H), 7.36-7.33 (m, 3H), 7.31-7.28 (m, 4H); $^{13}$C NMR (100 MHz, DMSO) δ 167.4, 149.6, 140.4, 140.1, 139.8, 139.3, 133.7, 132.0, 131.3, 129.1, 129.0, 128.8, 128.5, 128.3, 127.8, 126.6, 126.5, 125.9, 120.1; IR (KBr) ῡ 3475, 2924, 1680, 698.

**N,3-Diphenylpropiolamide 1a:**[57] $R_f$ = 0.7 (20% ethyl acetate in hexane); brownish white solid; yield 90% (650 mg); mp 126-128 ºC (lit.[57]124-125 ºC); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.59-7.55 (m, 4H), 7.43 (t, *J* = 7.4 Hz, 1H), 7.38-7.32 (m, 4H), 7.14 (t, *J* = 7.4 Hz, 1H).

**3-Phenyl-N-(p-tolyl)propiolamide 1b:**[58] $R_f$ = 0.8 (20% ethyl acetate in hexane); yellow solid; yield 91% (598 mg); mp 144-145 ºC (lit.[58]143-145); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.64 (s, 1H),

7.58-7.56 (m, 2H), 7.46-7.42 (m, 3H), 7.37 (t, *J* = 7.2 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 2.33 (s, 3H).

**N-(2,4-Dimethylphenyl)-3-phenylpropiolamide 1c:**[59] $R_f$ = 0.85 (20% ethyl acetate in hexane); brown solid; yield 74% (450 mg); mp 136-138 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.2 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 2H), 7.46-7.43 (m, 1H), 7.38 (t, *J* = 7.2 Hz, 2H), 7.31-7.26 (m, 1H), 7.09-7.02 (m, 2H), 2.31 (s, 3H), 2.29 (s, 3H).

**N-Mesityl-3-phenylpropiolamide 1d:** $R_f$ = 0.85 (20% ethyl acetate in hexane); yellow solid; yield 63% (355 mg); mp 140-142 ºC; $^1$H NMR (400 MHz, DMSO) δ 10.02 (s, 1H), 7.58 (d, *J* = 7.2 Hz, 2H), 7.48-7.40 (m, 3H), 6.83 (s, 2H), 2.16 (s, 3H), 2.06 (s, 6H); $^{13}$C NMR (100 MHz, DMSO) δ 150.8, 136.2, 134.9, 132.3, 131.2, 130.4, 129.1, 128.4, 119.8, 84.1, 83.7, 20.5, 18.1; IR (KBr) ῡ 3212, 2981, 2920, 2217, 1634; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{18}H_{17}NONa$ 286.1202; found 286.1216.

**N-(4-Ethylphenyl)-3-phenylpropiolamide 1e:** $R_f$ = 0.5 (20% ethyl acetate in hexane); yellow solid; yield 93% (575 mg); mp 126-128 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.64 (s, 1H), 7.57 (d, *J* = 6.8 Hz, 2H), 7.48 (d, *J* = 7.6 Hz, 2H), 7.43 (d, *J* = 7.2 Hz, 1H), 7.39-7.35 (m, 2H), 7.17 (d, *J* = 7.6 Hz, 2H), 2.63 (q, *J* = 7.6 Hz, 2H), 1.22 (t, *J* = 7.6 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 141.1, 135.2, 132.7, 130.3, 128.6, 128.4, 120.35, 120.30, 120.1, 85.7, 83.7, 28.4, 15.7; IR (KBr) ῡ 3262, 2964, 2209, 1636; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{16}NO$ 250.1226; found 250.1235.

**N-(4-Isopropylphenyl)-3-phenylpropiolamide 1f:** $R_f$ = 0.6 (20% ethyl acetate in hexane); brown solid; yield 82% (480 mg); mp 133-136 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.6 Hz, 2H), 7.52 (s, 1H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 7.2 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 2.90 (sept, *J* = 6.8 Hz, 1H), 1.24 (d, *J* = 6.8 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 151.0, 145.9, 135.1, 132.7, 130.4, 128.7, 127.2, 120.25, 120.17, 85.7, 83.6, 33.8, 24.1; IR (KBr) ῡ 3259, 2956, 2209, 1639; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{18}NO$ 264.1383; found 264.1394.

**N-(4-(*tert*-Butyl)phenyl)-3-phenylpropiolamide 1g:** $R_f$ = 0.8 (20% ethyl acetate in hexane); yellow solid; yield 87% (489 mg); mp 148-150 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.0 Hz, 2H), 7.52 (s, 1H); 7.51-7.47 (m, 2H), 7.43 (d, *J* = 7.2 Hz, 1H), 7.40-7.36 (m, 4H), 1.31 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 151.1, 148.1, 134.8, 132.7, 130.4, 128.7, 126.1, 120.2, 119.9, 85.7, 83.7, 34.6, 31.4; IR (KBr) ῡ 3258, 3055, 2962, 2211, 1632; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{19}H_{19}NONa$ 300.1359; found 300.1344.

**N-(4-Methoxyphenyl)-3-phenylpropiolamide 1h:**[60] $R_f$ = 0.4 (20% ethyl acetate in hexane); brownish solid; yield 93% (570 mg); mp 128-130 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.58-7.56 (m, 2H), 7.48 (d, *J* = 8.8 Hz, 2H), 7.43 (d, *J* = 7.2 Hz, 1H), 7.39-7.36 (m, 2H), 7.32-7.30 (m, 1H), 6.88 (d, *J* = 8.8 Hz, 2H), 3.80 (s, 3H).

**N-([1,1'-Biphenyl]-4-yl)-3-phenylpropiolamide 1i:** $R_f$ = 0.7 (20% ethyl acetate in hexane); yellow solid; yield 75% (399 mg); mp 184-186 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.66-7.64 (m, 3H), 7.60-7.57 (m, 6H), 7.47-7.32 (m, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 151.1, 140.5, 138.0,

136.7, 132.8, 130.5, 129.0, 128.8, 127.9, 127.4, 127.0, 120.4, 120.1, 86.0, 83.6; IR (KBr) $\bar{\upsilon}$ 3258, 2923, 2359, 1639; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{16}NO$ 298.1226; found 298.1227.

**N-(2-Fluorophenyl)-3-phenylpropiolamide 1j:** $R_f$ = 0.8 (20% ethyl acetate in hexane); yellow solid; yield 85% (550 mg); mp 110-113 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.35 (t, *J* = 8.0 Hz, 1H), 7.77 (s, 1H), 7.60 (d, *J* = 7.6 Hz, 2H), 7.49-7.44 (m, 1H), 7.40 (t, *J* = 8.0 Hz, 2H), 7.17-7.08 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 153.4, 151.00, 150.9, 132.8, 130.6, 128.7, 125.1 (d, $^3J_{CF}$ = 7.6 Hz), 124.8 (d, $^4J_{CF}$ = 3.5 Hz), 122.1, 119.9, 115.0 (d, $^2J_{CF}$ = 19.1 Hz), 86.3, 83.3; IR (KBr) $\bar{\upsilon}$ 3232, 2212, 1649, 1322; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{10}FNONa$ 262.0639; found 262.0629.

**N-(2-Chlorophenyl)-3-phenylpropiolamide 1k:**[61] $R_f$ = 0.8 (20% ethyl acetate in hexane); off white solid; yield 84% (620 mg); mp 104-105 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 8.4 Hz, 1H), 8.00 (s, 1H), 7.62 (d, *J* = 7.2 Hz, 2H), 7.48-7.45 (m, 1H), 7.42-7.38 (m, 3H), 7.31 (t, *J* = 8.0 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H).

**N-(2-Bromophenyl)-3-phenylpropiolamide 1l:**[61] $R_f$ = 0.6 (20% ethyl acetate in hexane); yellowish white solid; yield 76% (401 mg); mp 101-103 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 8.0 Hz, 1H), 7.99 (s, 1H), 7.63-7.56 (m, 3H), 7.48-7.45 (m, 1H), 7.42-7.38 (m, 2H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.03 (t, *J* = 7.4 Hz, 1H).

**N-(2-Iodophenyl)-3-phenylpropiolamide 1m:**[61] $R_f$ = 0.8 (20% ethyl acetate in hexane); brown solid; yield 66% (315 mg); mp 100-103 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.82 (d, *J* = 7.6 Hz, 2H), 7.62 (d, *J* = 7.2 Hz, 2H), 7.42-7.36 (m, 4H), 6.89 (t, *J* = 7.2 Hz, 1H).

**N-(4-Cyanophenyl)-3-phenylpropiolamide 1n:** $R_f$ = 0.3 (20% ethyl acetate in hexane); brown solid; yield 64% (401 mg); mp 156-158 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.71 (d, *J* = 8.8 Hz, 2H), 7.64 (d, *J* = 8.8 Hz, 2H), 7.59 (d, *J* = 7.6 Hz, 2H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 2H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 151.1, 141.4, 133.5, 132.9, 130.9, 128.9, 119.8, 119.5, 118.7, 108.0, 87.3, 83.0; IR (KBr) ῡ 3288, 2923, 2210, 1650, 1592; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{11}N_2O$ 247.0866; found 247.0859.

**N-(4-Nitrophenyl)-3-phenylpropiolamide 1o:** $R_f$ = 0.45 (20% ethyl acetate in hexane); yellowish white solid; yield 67% (389 mg); mp 166-168 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.8 Hz, 2H), 7.91 (s, 1H), 7.76 (d, *J* = 8.8 Hz, 2H), 7.59 (d, *J* = 7.6 Hz, 2H), 7.50-7.45 (m, 1H), 7.42-7.36 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 151.4, 144.0, 143.2, 133.2, 132.8, 131.0, 128.8, 125.3, 119.5, 87.7, 82.9; IR (KBr) ῡ 3266, 2207, 1642, 1552, 1331; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{15}H_{10}N2O_3$ 267.0764; found 267.0767.

**N-(3-Chlorophenyl)-3-phenylpropiolamide 1p:**[62] $R_f$ = 0.6 (20% ethyl acetate in hexane); brown solid; yield 95% (686 mg); mp 110-112 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.59-7.56 (m, 2H), 7.47-7.36 (m, 4H), 7.29-7.26 (m, 2H), 7.13 (d, *J* = 8.0 Hz, 1H).

**N-(4-Chloro-2-methylphenyl)-3-phenylpropiolamide 1q:** $R_f$ = 0.55 (20% ethyl acetate in hexane); off white solid; yield 86% (585 mg); mp 146-148 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.8 Hz, 1H), 7.60 (d, *J* = 7.2 Hz, 2H), 7.48-7.44 (m, 1H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.30 (s, 1H), 7.21 (s, 2H), 2.32 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 151.3, 133.7, 132.8, 130.95, 130.92, 130.6, 130.5, 128.8, 127.1, 124.5, 119.9, 86.2, 83.3, 17.9; IR (KBr) ῡ 3195, 2359, 1628, 1518, 756; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{13}ClNO$ 270.0680; found 270.0686.

**N-Benzyl-3-phenylpropiolamide 1r:**[63] $R_f$ = 0.6 (20% ethyl acetate in hexane); yellowish white solid; yield 90% (586 mg); mp 116-118 ºC (lit[63].108-110 ºC); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.53-7.51 (m, 2H), 7.43-7.40 (m, 2H), 7.37-7.31 (m, 7H), 4.55 (d, *J* = 6.0 Hz, 2H).

**N-(Naphthalen-1-yl)-3-phenylpropiolamide (1s):**[64] $R_f$ = 0.45 (10% ethyl acetate in hexane); yellow solid; yield 61% (350 mg); mp 177-181 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.2 Hz, 1H), 7.95 (d, *J* = 7.8 Hz, 2H), 7.90 (d, *J* = 7.8 Hz, 1H), 7.75 (d, *J* = 8.2 Hz, 1H), 7.64 (d, *J* = 7.4 Hz, 2H), 7.59-7.51 (m, 3H), 7.50-7.47 (m, 1H), 7.43-7.39 (m, 2H).

**3-Phenyl-N-(quinolin-3-yl)propiolamide (1t):** $R_f$ = 0.35 (30% ethyl acetate in hexane); white solid; yield 35% (200 mg); mp 154-156 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.87 (s, 1H), 8.85 (s, 1H), 8.05 (d, *J* = 8.4 Hz, 1H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 7.4 Hz, 2H), 7.51-7.48 (m, 2H), 7.42-7.39 (m, 1H), 7.33-7.30 (m, 2H); IR (KBr) ῡ 3345, 2929, 2360, 1663; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{13}N_2O$ 273.1022; found 273.1037.

**N-([1,1'-Biphenyl]-2-yl)-3-phenylpropiolamide (1u):**[61] $R_f$ = 0.6 (20% ethyl acetate in hexane); brownish white solid; yield 62% (330 mg); mp 171-174 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.2 Hz, 1H), 7.54-7.46 (m, 5H), 7.44-7.38 (m, 5H), 7.36-7.32 (m, 2H), 7.29 (d, *J* = 7.2 Hz, 1H), 7.24-7.20 (m, 1H).

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## NMR Spectrum of Selected Compounds

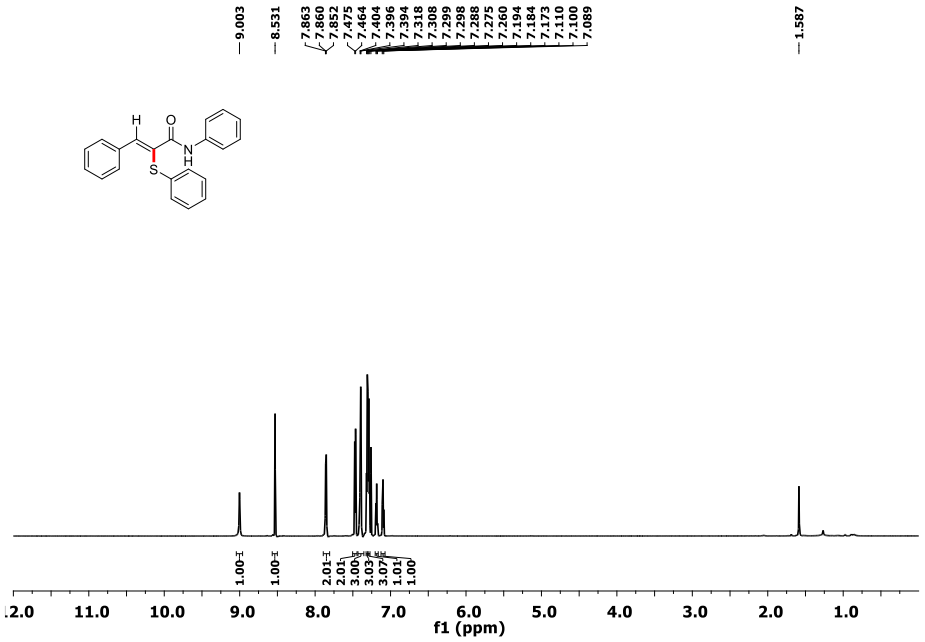



**Figure 3.21.** $^{1}$H NMR spectrum of (Z)-N,3-diphenyl-2-(phenylthio)acrylamide (**3aa**)

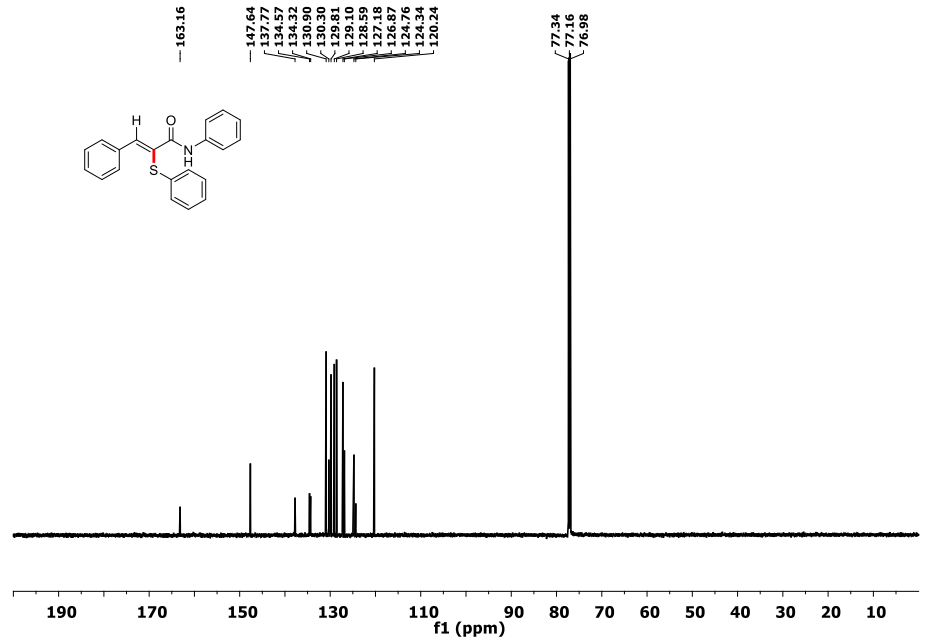



**Figure 3.22.** $^{13}$C NMR spectrum of (Z)-N,3-diphenyl-2-(phenylthio)acrylamide (**3aa**)

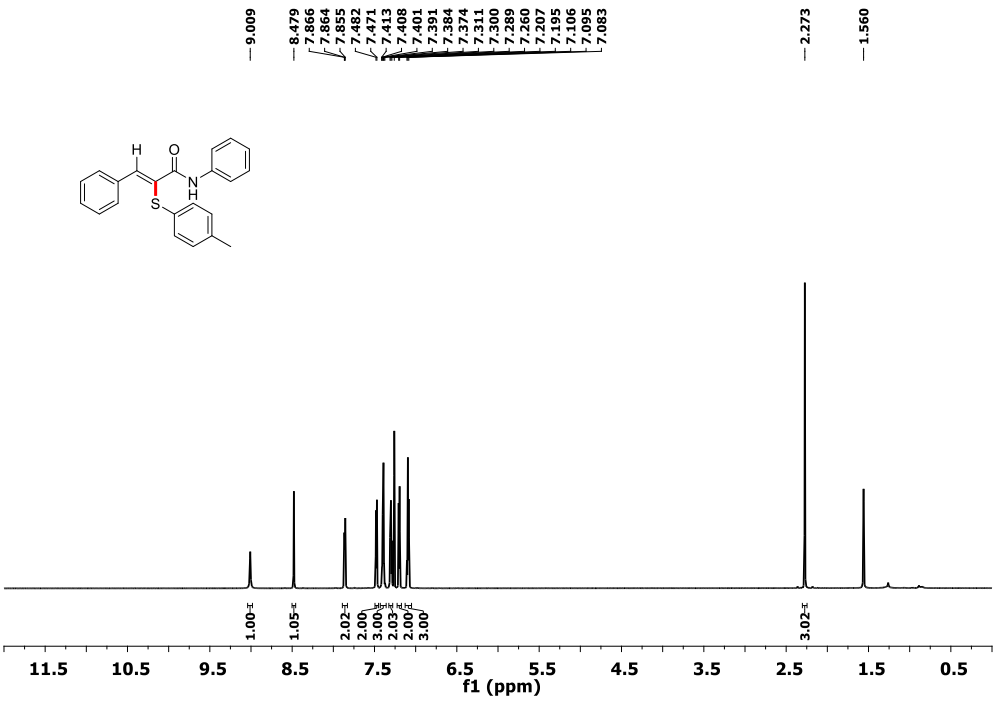



**Figure 3.23.** $^{1}$H NMR spectrum of (Z)-N,3-diphenyl-2-(p-tolylthio)acrylamide (**3ab**)

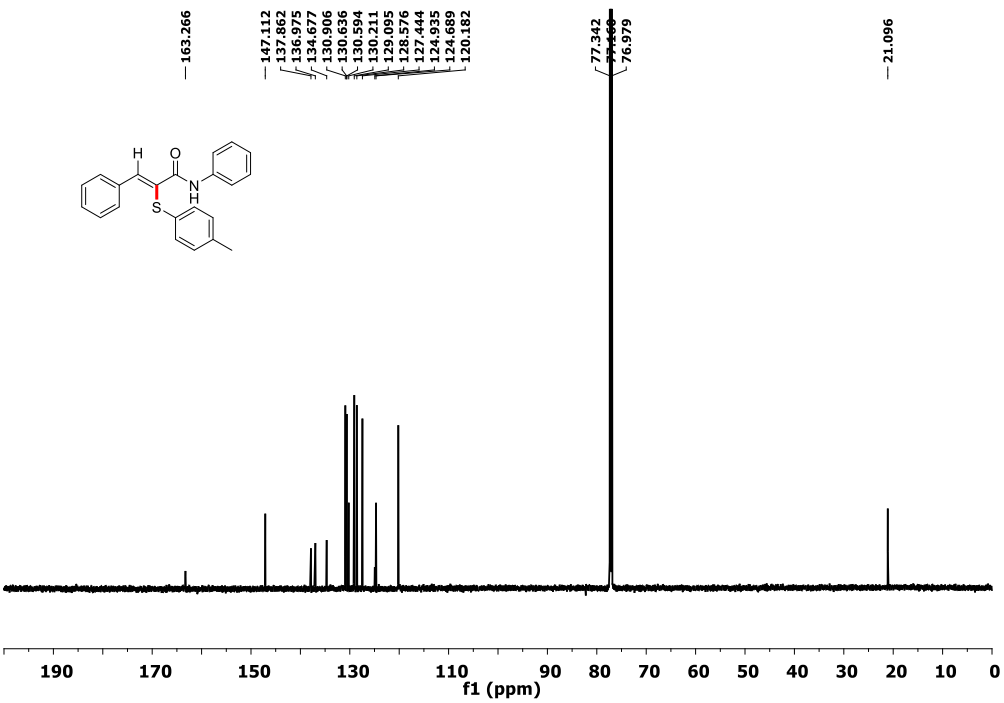



**Figure 3.24.** $^{13}$C NMR spectrum of (Z)-N,3-diphenyl-2-(p-tolylthio)acrylamide (**3ab**)

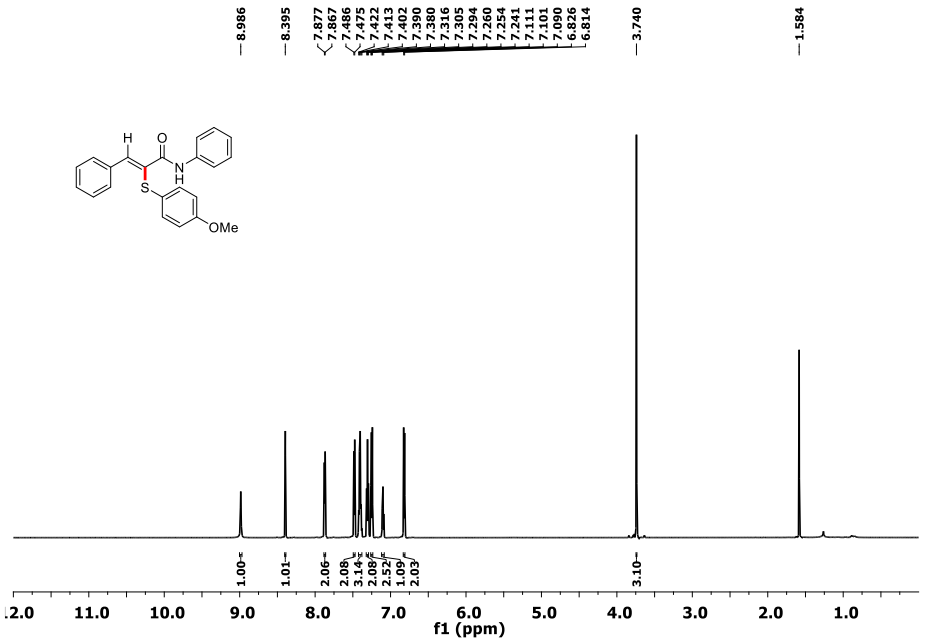



**Figure 3.25.** $^{1}$H NMR spectrum of (Z)-2-((4-methoxyphenyl)thio)-N,3-diphenylacrylamide **(3ac)**

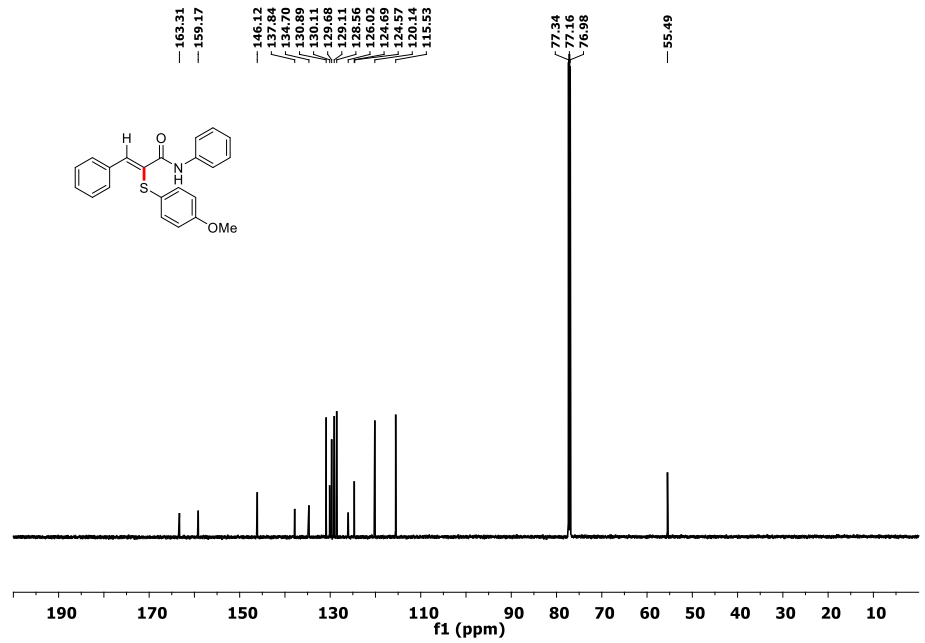



**Figure 3.26.** $^{13}$C NMR spectrum of (Z)-2-((4-methoxyphenyl)thio)-N,3-diphenylacrylamide **(3ac)**

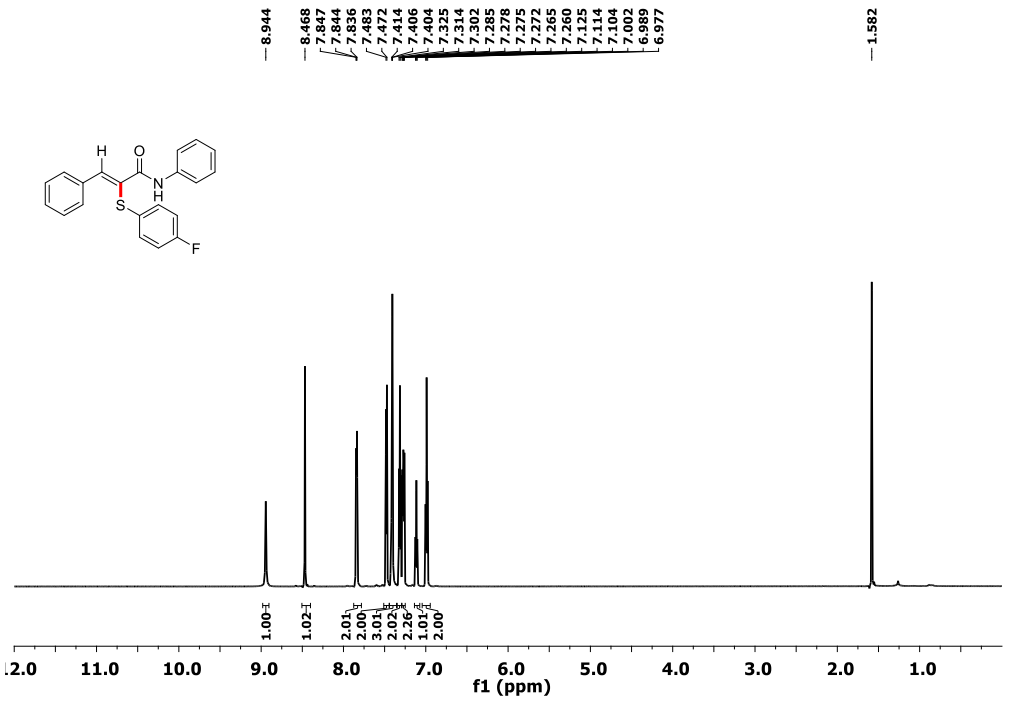



**Figure 3.27.** $^{1}$H NMR spectrum of (Z)-2-((4-fluorophenyl)thio)-N,3-diphenylacrylamide **(3ad)**

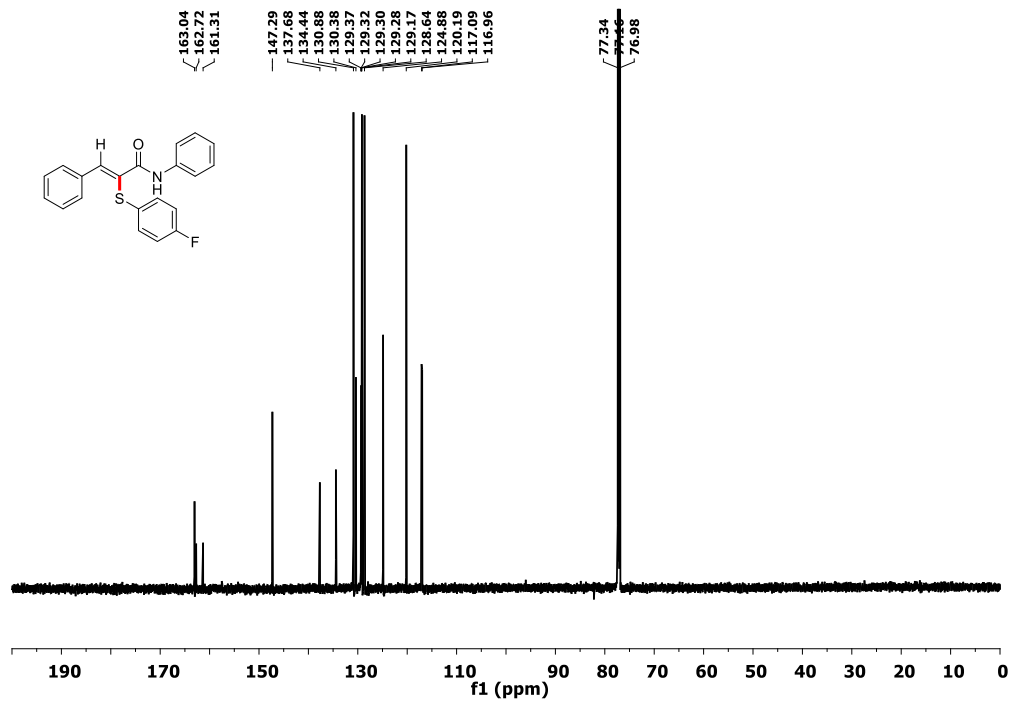



**Figure 3.28.** $^{13}$C NMR spectrum of (Z)-2-((4-fluorophenyl)thio)-N,3-diphenylacrylamide **(3ad)**

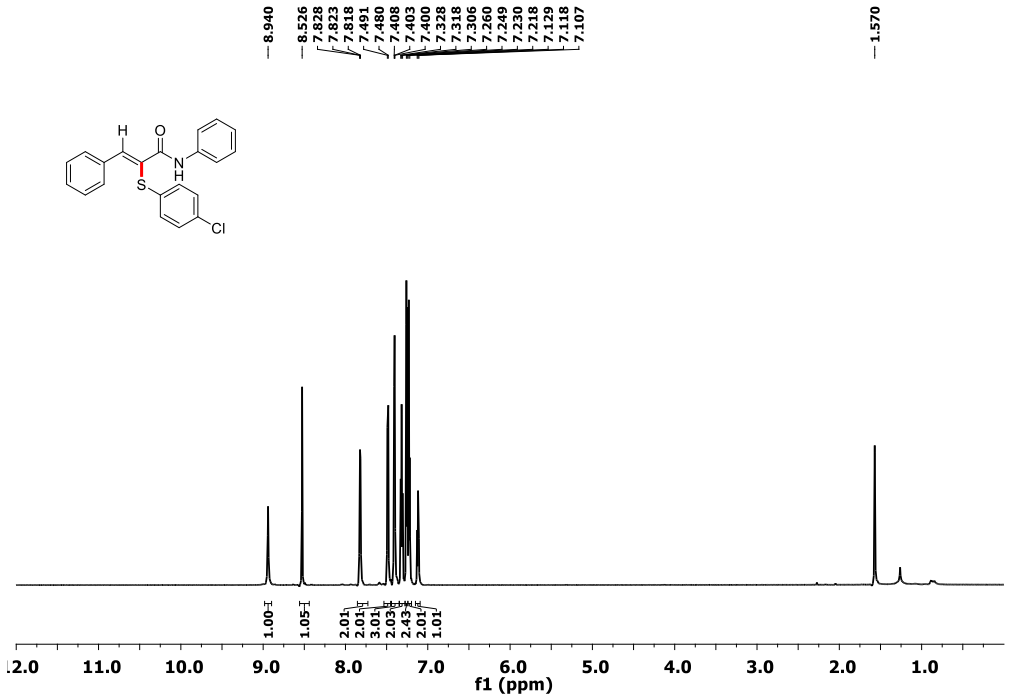



**Figure 3.29.** $^{1}$H NMR spectrum of (Z)-2-((4-chlorophenyl)thio)-N,3-diphenylacrylamide **(3ae)**

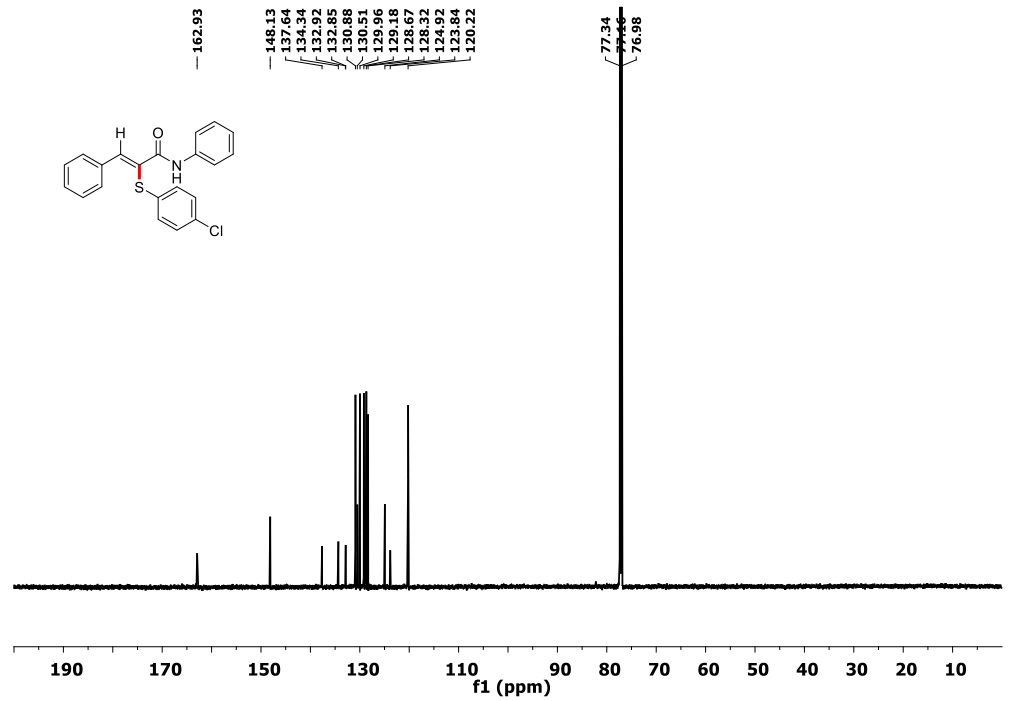



**Figure 3.30.** $^{13}$C NMR spectrum of (Z)-2-((4-chlorophenyl)thio)-N,3-diphenylacrylamide **(3ae)**

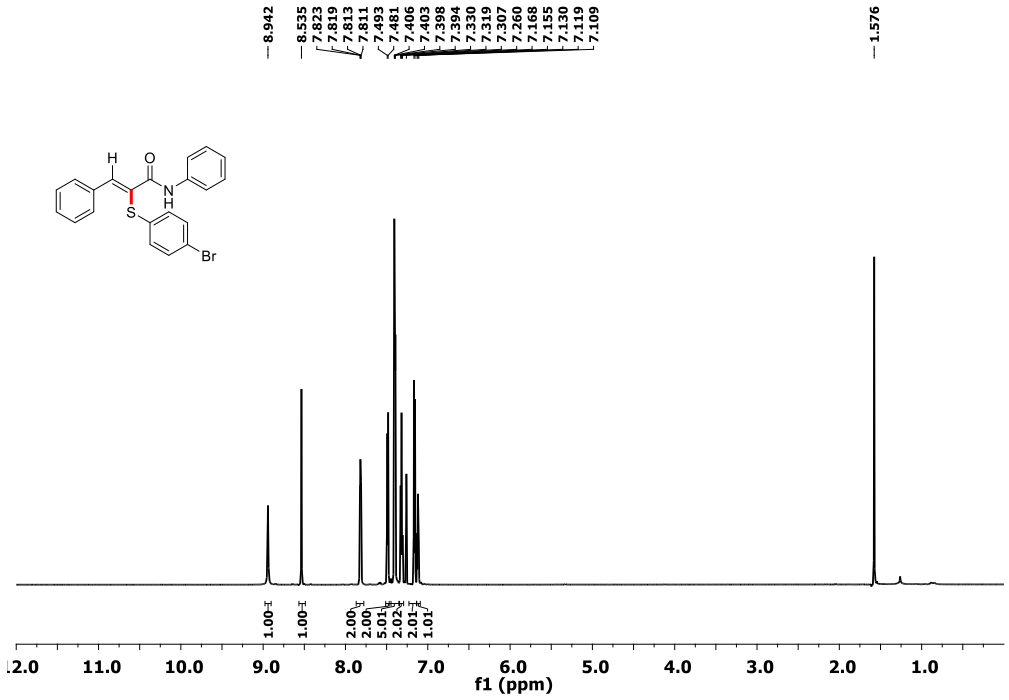



**Figure 3.31.** $^{1}$H NMR spectrum of (Z)-2-((4-bromophenyl)thio)-N,3-diphenylacrylamide **(3af)**

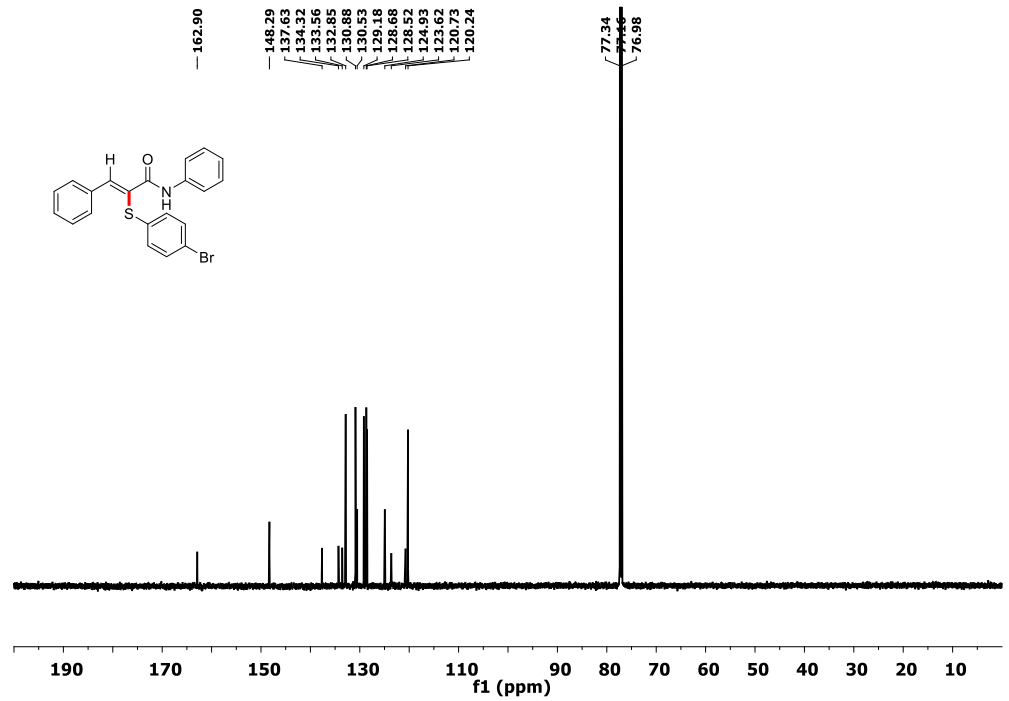



**Figure 3.32.** $^{13}$C NMR spectrum of (Z)-2-((4-bromophenyl)thio)-N,3-diphenylacrylamide **(3af)**

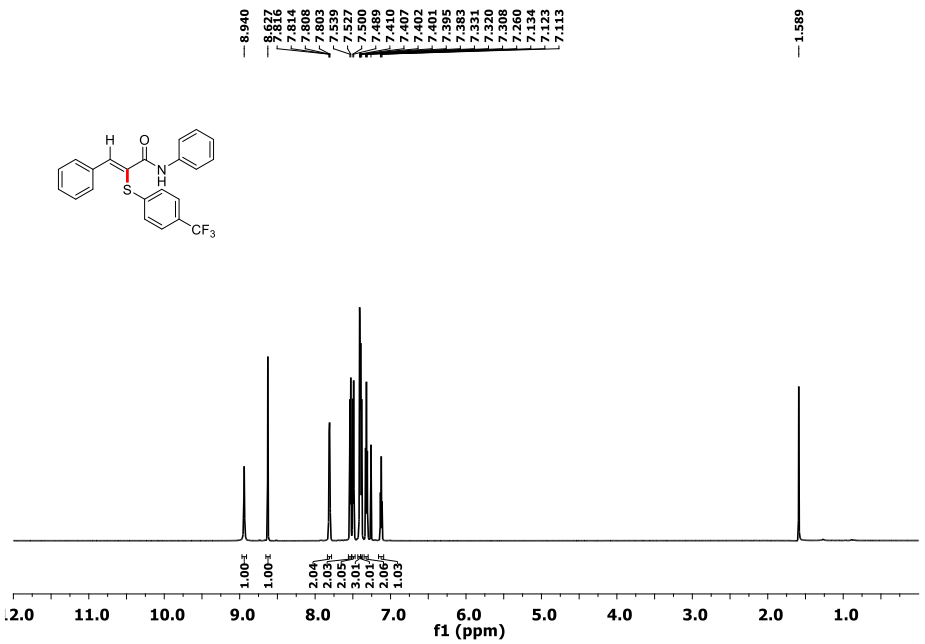



**Figure 3.33.**[1]H NMR spectrum of (Z)-N,3-diphenyl-2((4(trifluoromethyl)phenyl)thio)acrylamide **(3ag)**

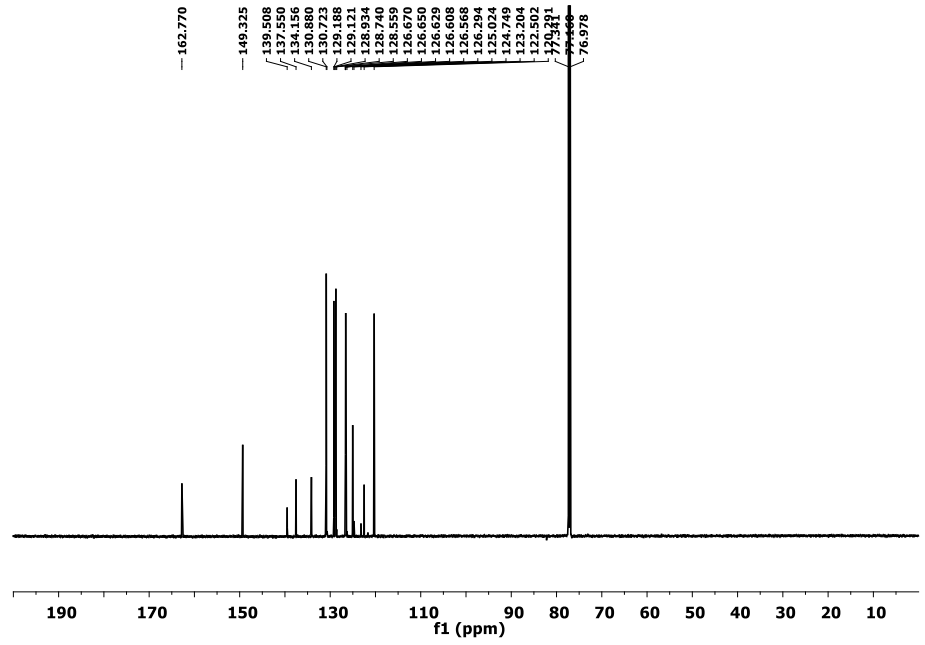



**Figure3.34.** [13]C NMR spectrum of (Z)-N,3-diphenyl-2-((4-(trifluoromethyl)phenyl)thio)acrylamide **(3ag)**

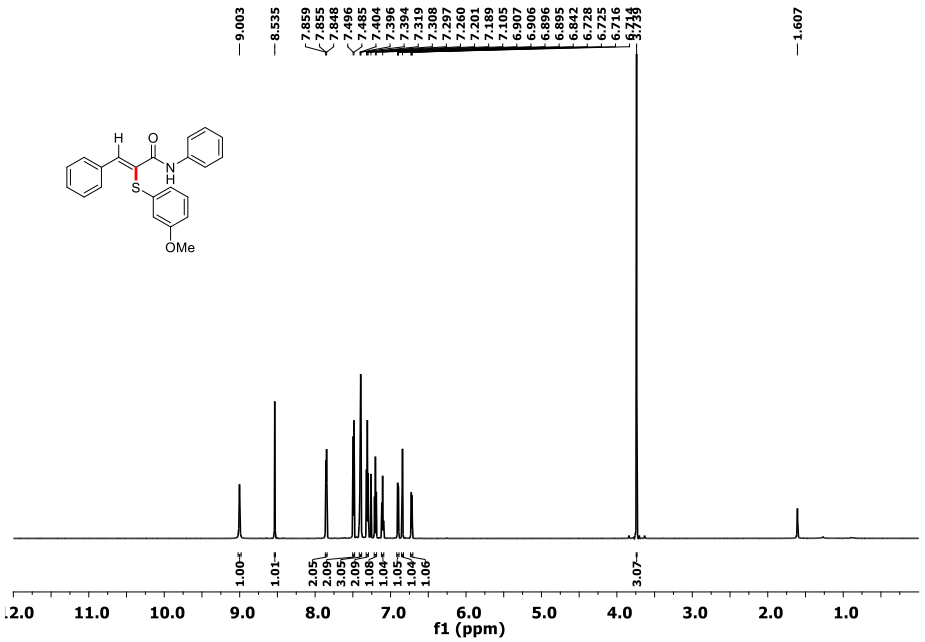



**Figure 3.35.** $^{1}$H NMR spectrum of (Z)-2-((3-methoxyphenyl)thio)-N,3-diphenylacrylamide **(3ah)**

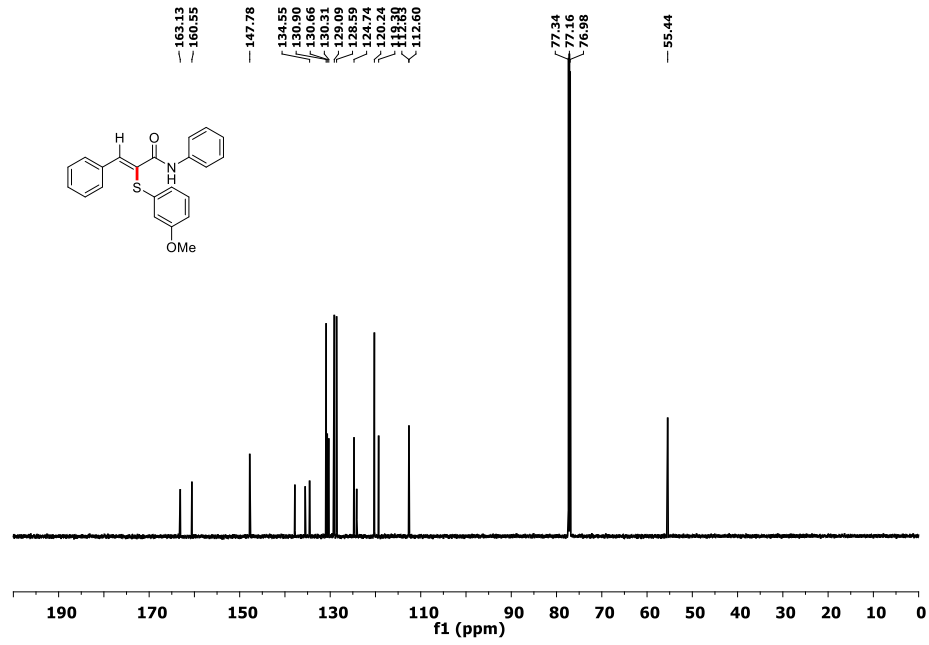



**Figure 3.36.** $^{13}$C NMR spectrum of (Z)-2-((3-methoxyphenyl)thio)-N,3-diphenylacrylamide **(3ah)**

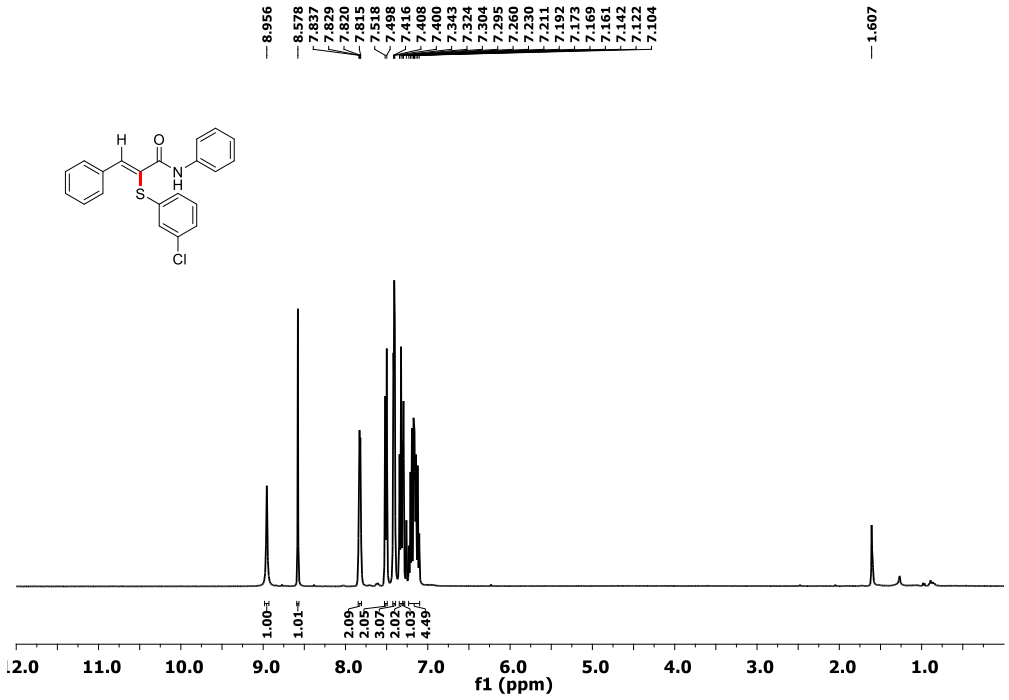



**Figure 3.37.** $^{1}$H NMR spectrum of (Z)-2-((3-chlorophenyl)thio)-N,3-diphenylacrylamide **(3ai)**

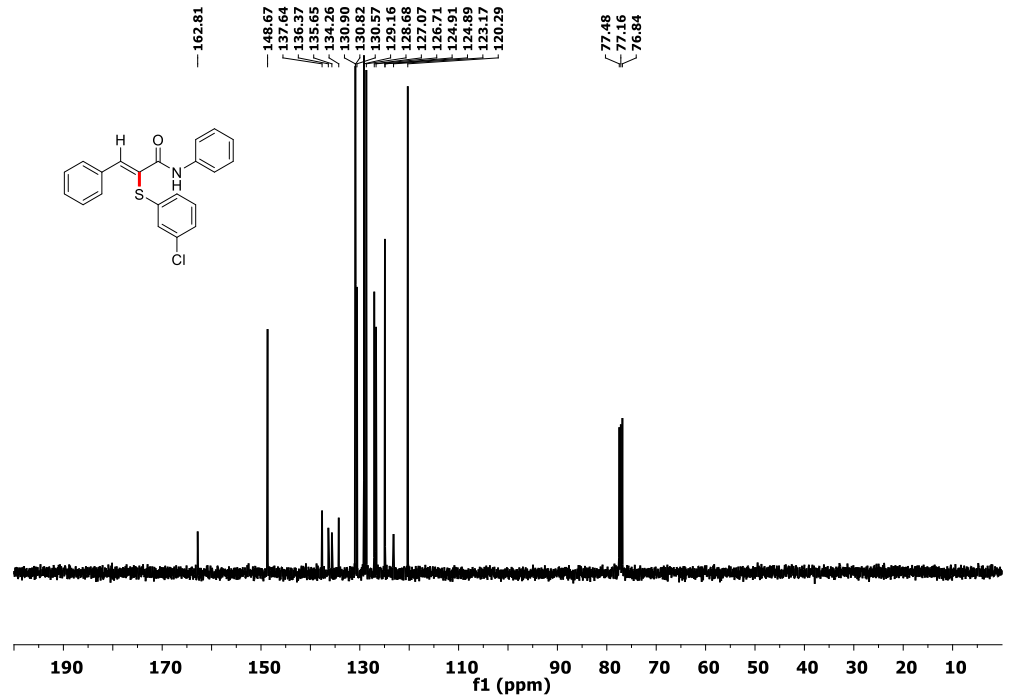



**Figure 3.38.** $^{13}$C NMR spectrum of (Z)-2-((3-chlorophenyl)thio)-N,3-diphenylacrylamide **(3ai)**

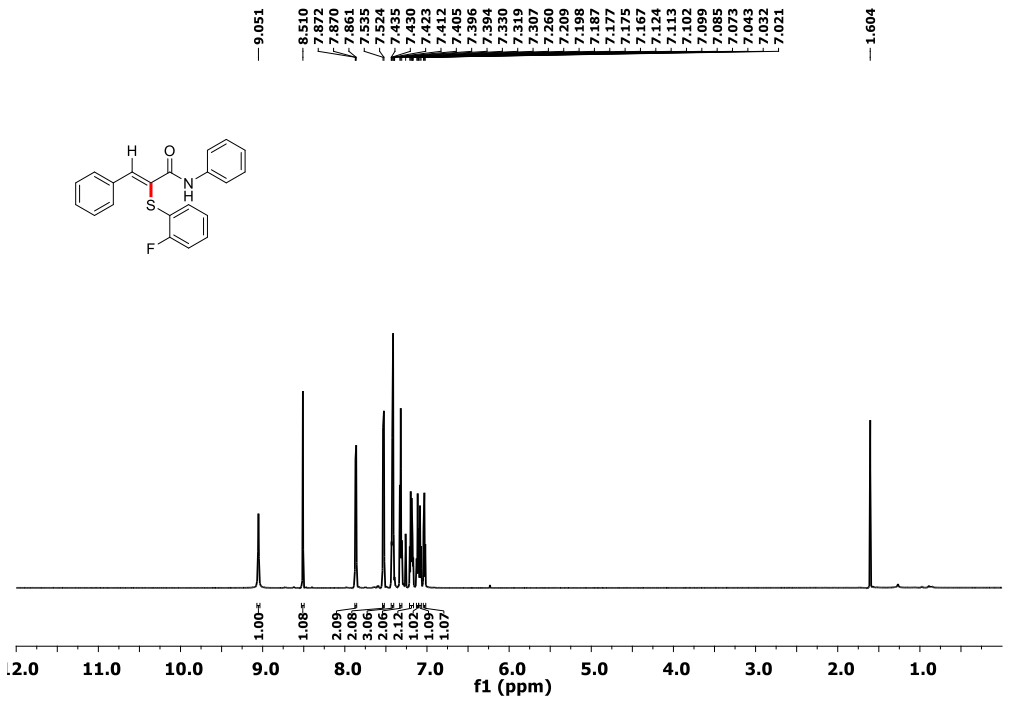



**Figure 3.39.** $^{1}$H NMR spectrum of (Z)-2-((2-fluorophenyl)thio)-N,3-diphenylacrylamide **(3aj)**

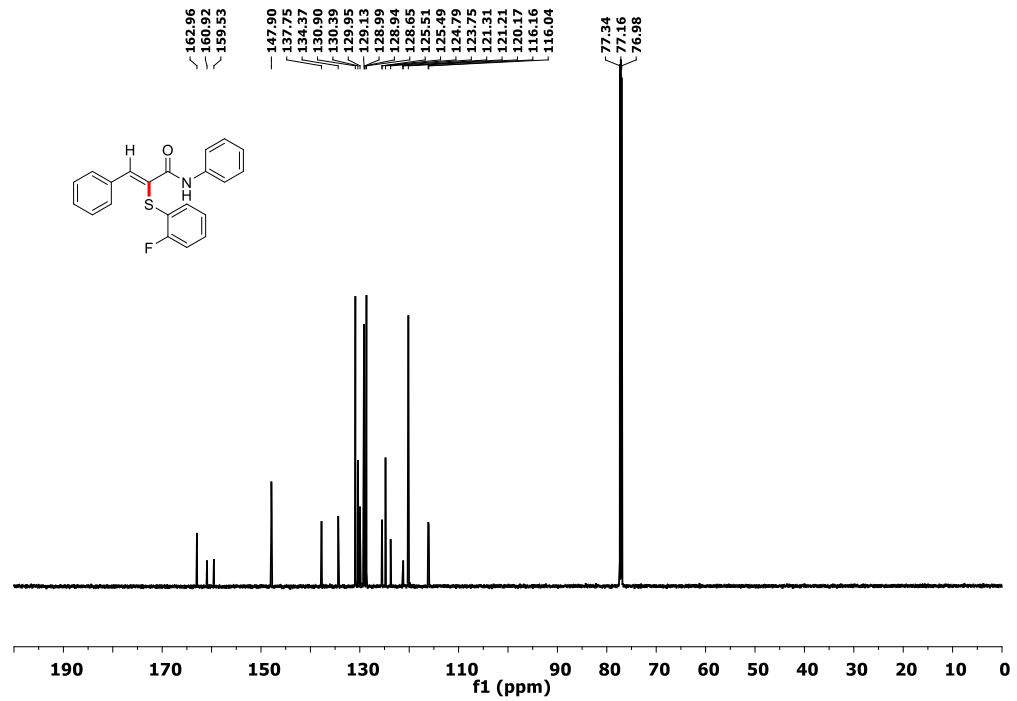



**Figure 3.40.** $^{13}$C NMR spectrum of (Z)-2-((2-fluorophenyl)thio)-N,3-diphenylacrylamide **(3aj)**

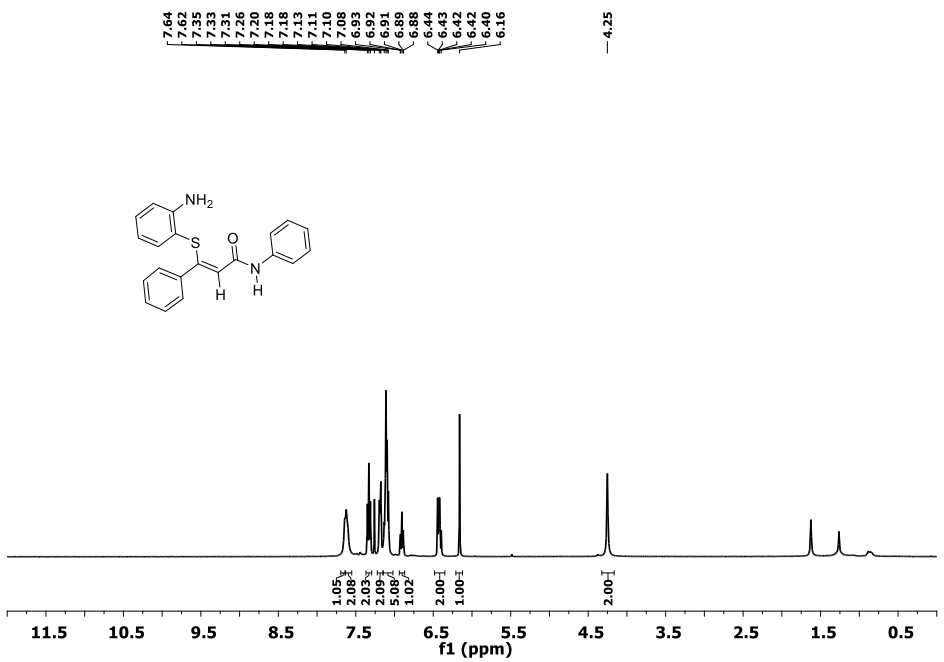



**Figure 3.41.** $^{1}$H NMR spectrum of (Z)-3-((2-aminophenyl)thio)-N,3-diphenylacrylamide **(3ak)**

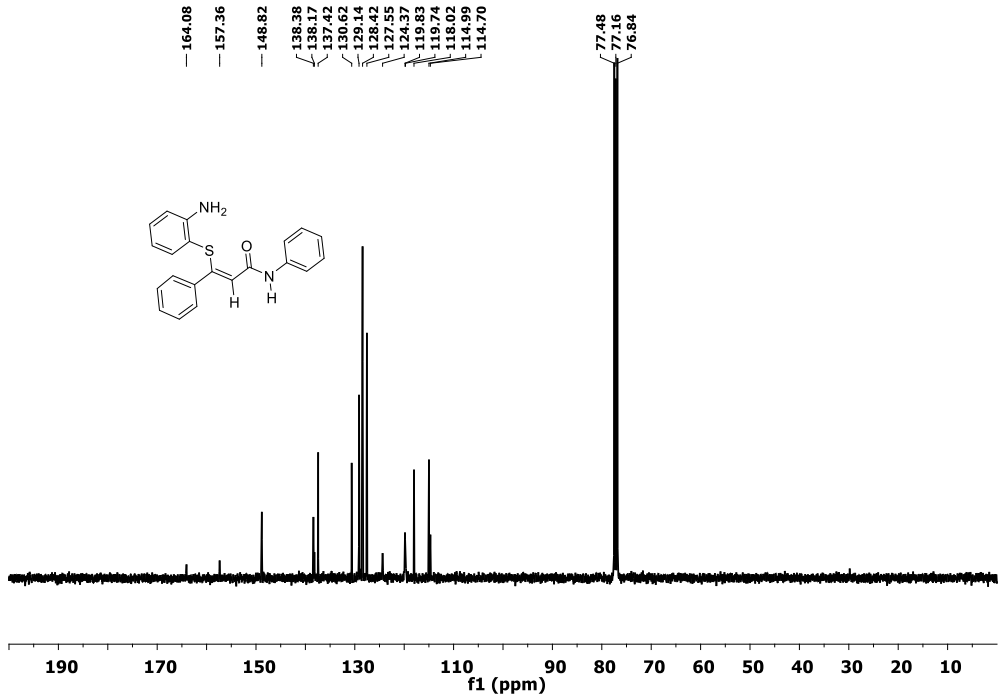



**Figure 3.42.** $^{13}$C NMR spectrum of (Z)-2-((2-aminophenyl)thio)-N,3-diphenylacrylamide **(3ak)**

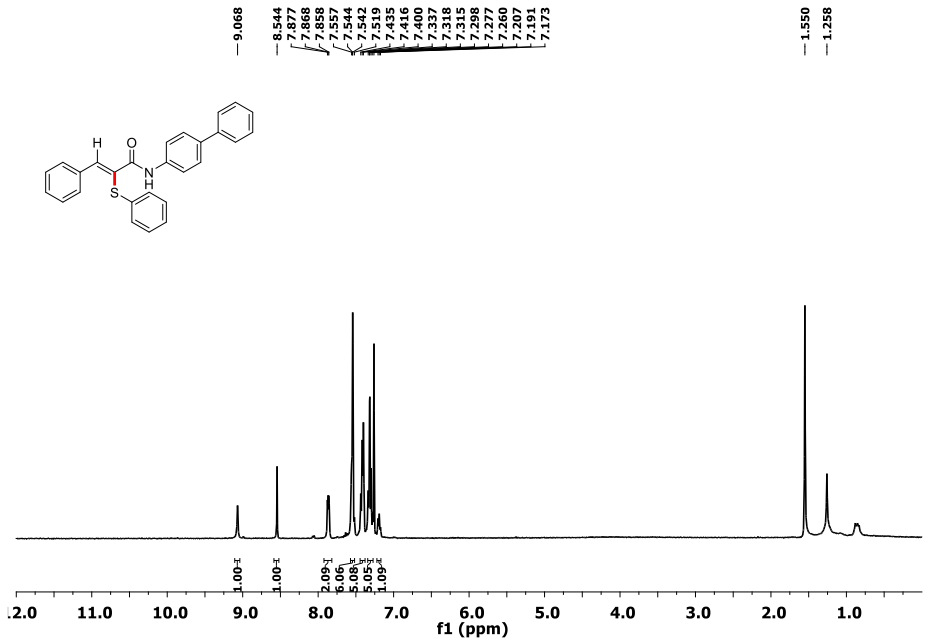



**Figure 3.43.** $^{1}$H NMR spectrum of (Z)-N-([1,1'-biphenyl]-4-yl)-3-phenyl-2-(phenylthio)acrylamide **(3ia)**

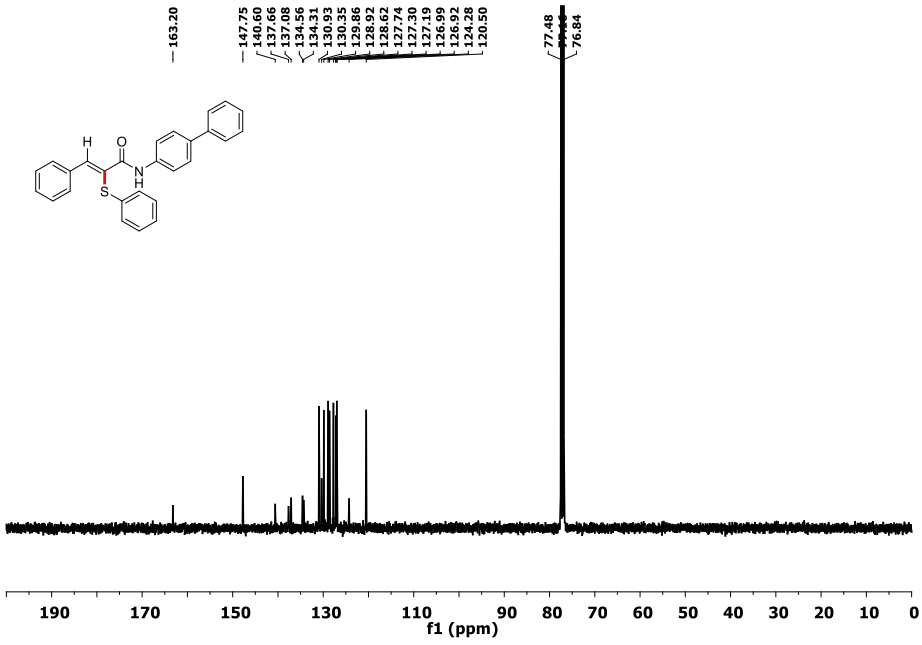



**Figure 3.44.** $^{13}$C NMR spectrum of (Z)-N-([1,1'-biphenyl]-4-yl)-3-phenyl-2-(phenylthio)acrylamide **(3ia)**

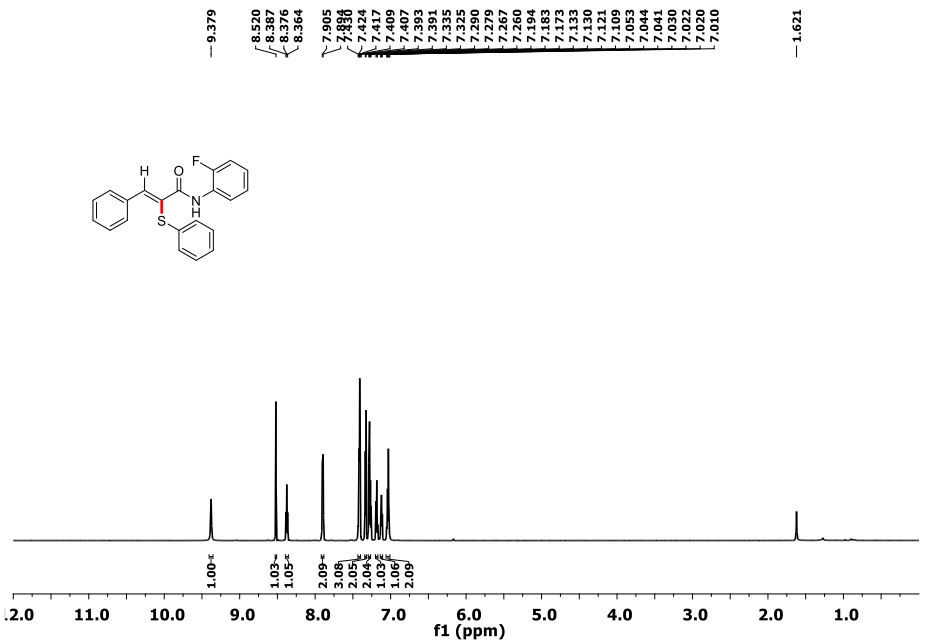



**Figure 3.45.** $^{1}$H NMR spectrum of (Z)-N-(2-fluorophenyl)-3-phenyl-2-(phenylthio)acrylamide **(3ja)**

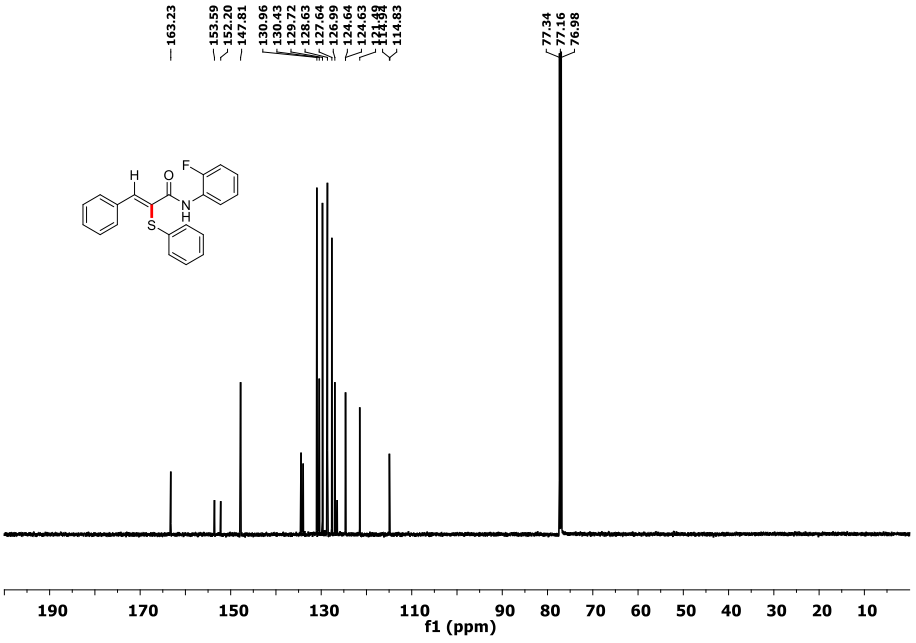



**Figure 3.46.** $^{13}$C NMR spectrum of (Z)-N-(2-fluorophenyl)-3-phenyl-2-(phenylthio)acrylamide **(3ja)**

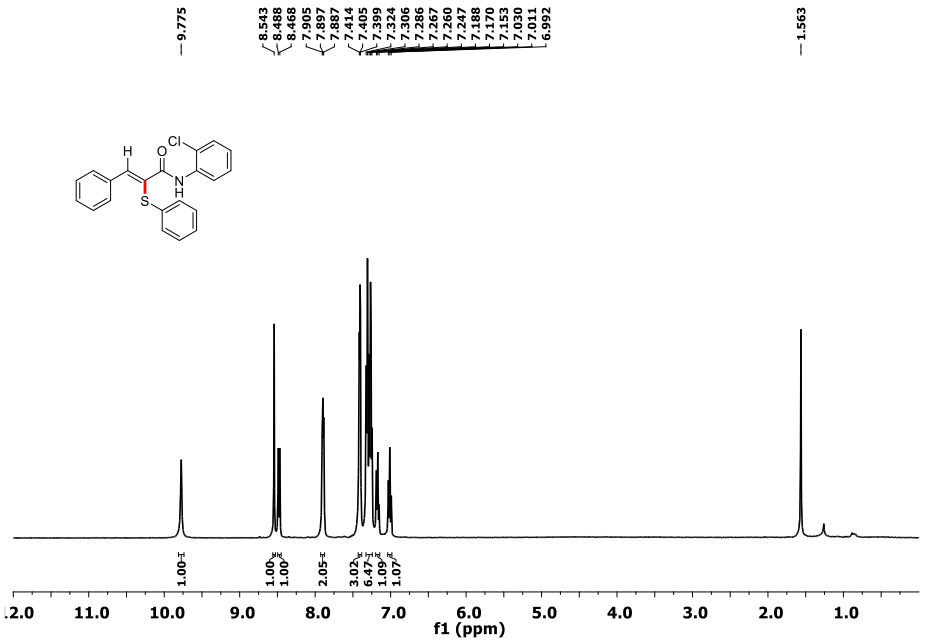



**Figure 3.47.** $^{1}$H NMR spectrum of (Z)-N-(2-chlorophenyl)-3-phenyl-2-(phenylthio)acrylamide **(3ka)**

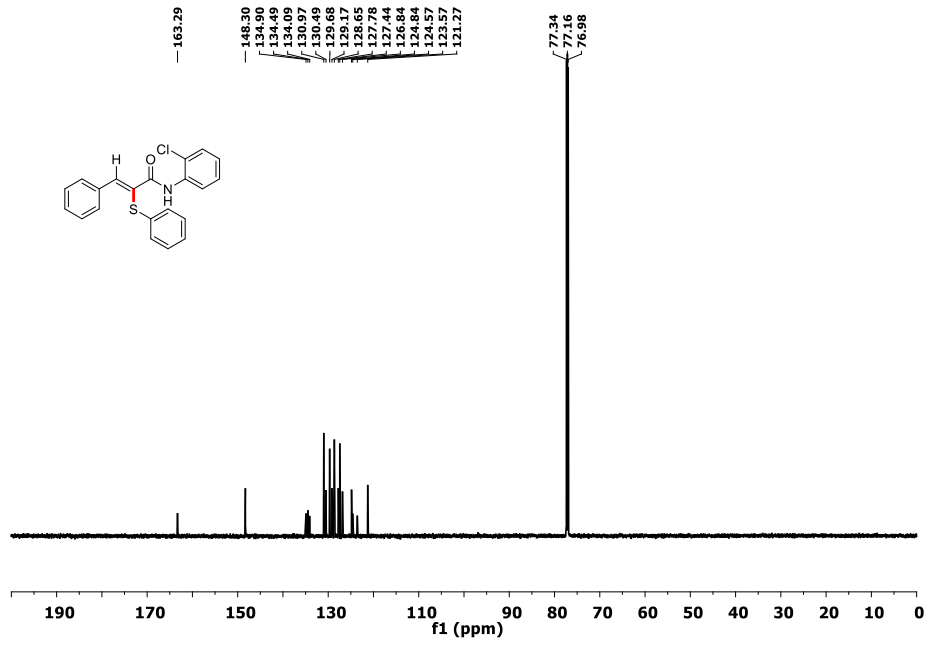



**Figure 3.48.** $^{13}$C NMR spectrum of (Z)-N-(2-chlorophenyl)-3-phenyl-2-(phenylthio)acrylamide **(3ka)**

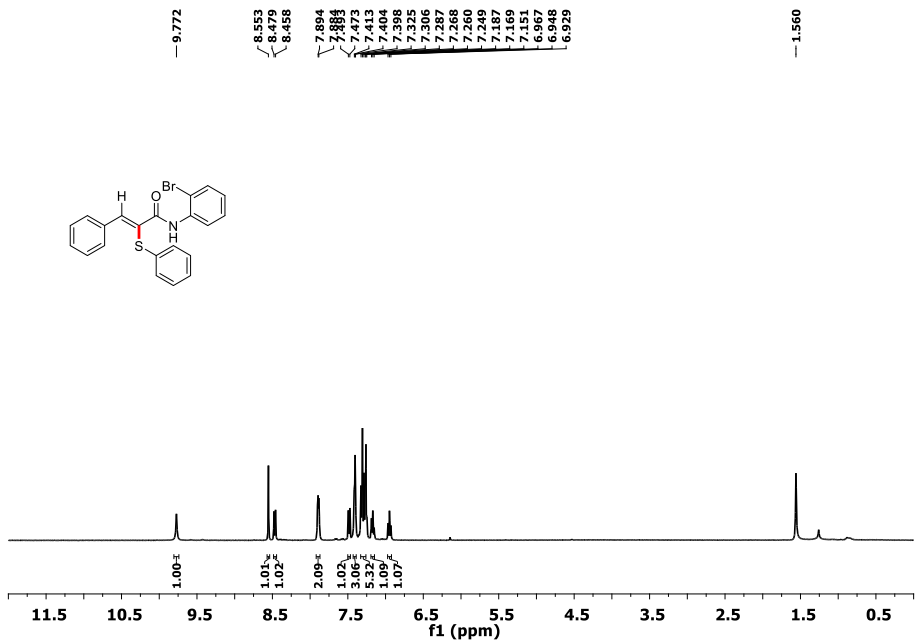



**Figure 3.49.** $^{1}$H NMR spectrum of (Z)-N-(2-bromophenyl)-3-phenyl-2-(phenylthio)acrylamide **(3la)**

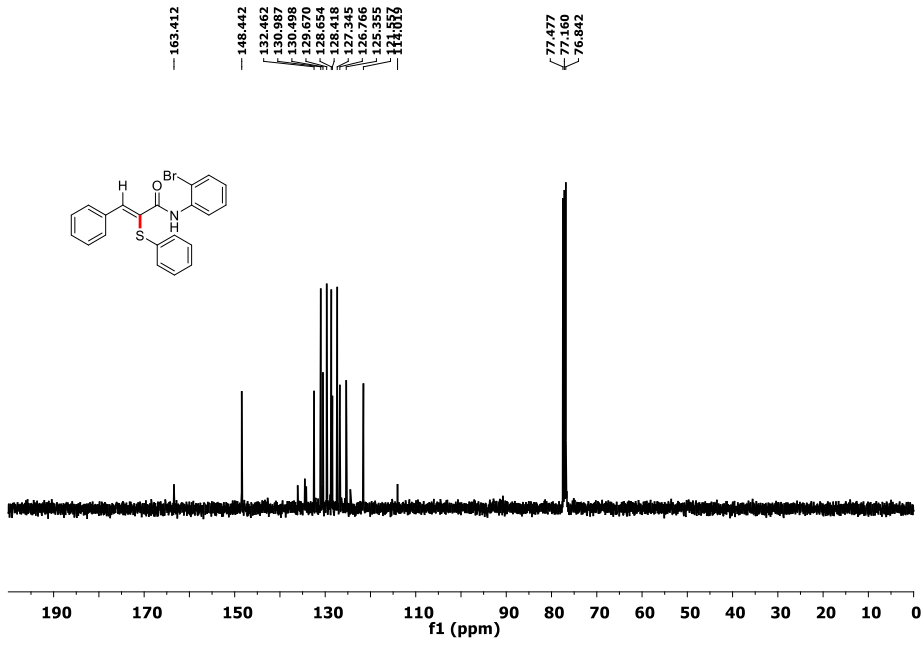
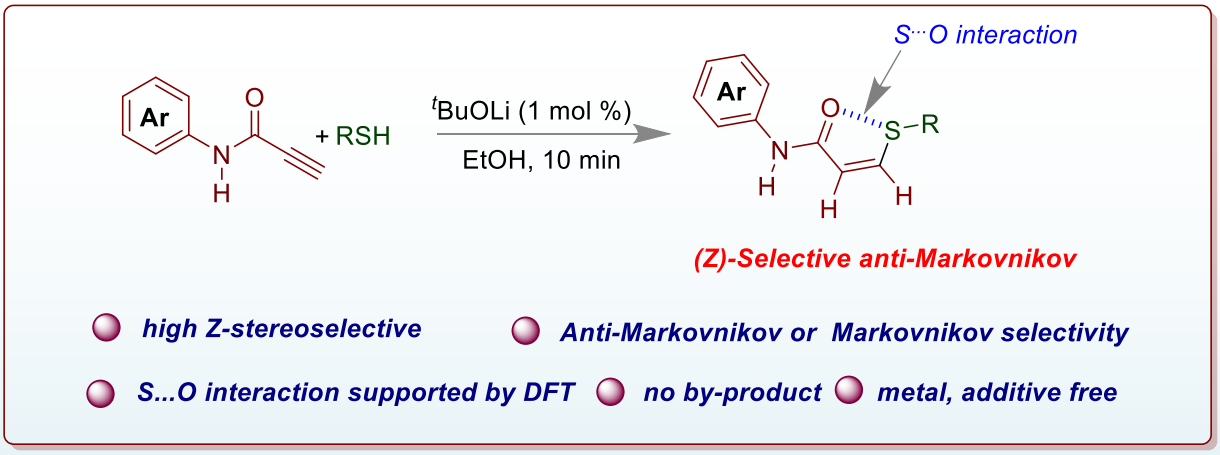



**Figure 3.50.** $^{13}$C NMR spectrum of (Z)-N-(2-bromophenyl)-3-phenyl-2-(phenylthio)acrylamide **(3la)**

# CHAPTER 4

# S...O Interaction Controlled (*Z*)-Selective *anti*-Markovnikov Thiol-Yne-Click Reactions of Terminal Alkynes

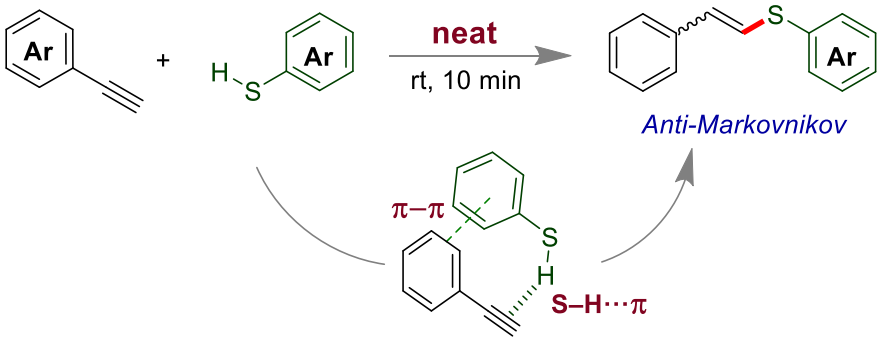
## 4.1 ABSTRACT




(*E*)-vinyl sulfides are primarily formed in an addition reaction of terminal alkyne with thiols because it is thermodynamically stable. Therefore, the synthesis of high-energy Z-vinyl sulfides is highly challenging and also popular in organic synthetic chemistry. Herein, by utilizing novel S…O interaction, we had effectively controlled selectivity of (*Z*)-*anti*-Markovnikov vinyl sulfides when phenylpropiolamide and thiols were added in the presence of 1 mol% $^{t}$BuOLi in EtOH solvent. The single-crystal X-ray diffraction analysis and Density Functional Theory (DFT) confirmed that S…O interaction was initiated from the delocalization of oxygen lone pair to σ* orbital of sulfur of C–S.

## 4.2 INTRODUCTION

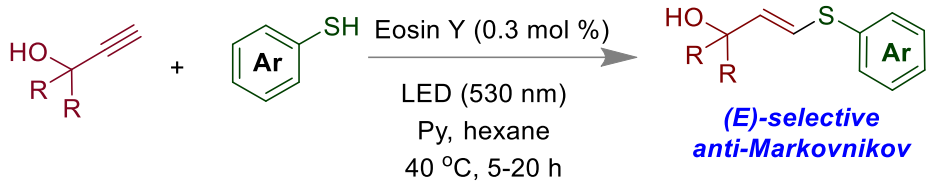
Recently, radical-mediated addition reaction in alkynes becomes a straight, straightforward, and environment-friendly alternative tool in the organic research area[1-3]. In this context, alkyne hydrothiolation reaction is one of the convenient platforms to construct C–S bonds in synthetic methodology[4]. Though the reactivity of alkyne or hydrothiolation reaction is well introduced yet it suffers from poor stereo-selectivity, formation of unwanted by-products, and harsh reaction conditions[5-9]. Mal group has experienced that simple, neat mixing of phenylacetylene and thiophenol could lead to *anti*-Markovnikov vinyl sulfides within 10 min reaction time (Scheme 4.1)[10a]. They envisioned that the intermolecular π-π stacking between two phenyl rings, S–H…π interaction between S–H of thiophenol, and triple bond of phenylacetylene. Although *anti*-Markovnikov selectivity was successfully identified, the issues of *E* or *Z*-selectivity were still unresolved.




**Scheme 4.1.** *anti*-Markovnikov vinyl sulfides by Mal's group.

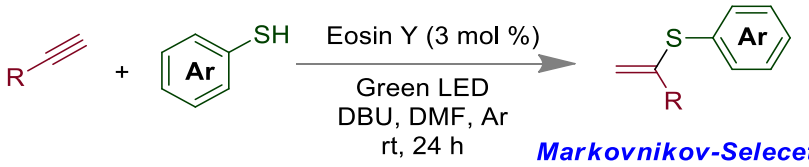
Later on, selectivity issues have been controlled, but in most cases, low-energy (*E*)-vinyl sulfides are predominantly formed because (*E*)-vinyl sulfides are thermodynamically more stable than (*Z*)-vinyl sulfides. Therefore, control of radical addition for achieving selective configuration of (Z)-vinyl sulfides is of high interest and challenge. There are many reports available on selective

formation of either *anti*-Markovnikov or Markovnikov vinyl sulfides. In 2016 Ananikov's group demonstrated the synthesis of (*E*)-*anti*-Markovnikov vinyl sulfides by visible light photo-catalysis (Scheme 4.2)[11].




**Scheme 4.2.** (*E*)-*anti*-Markovnikov vinyl sulfides by Ananikov's group.

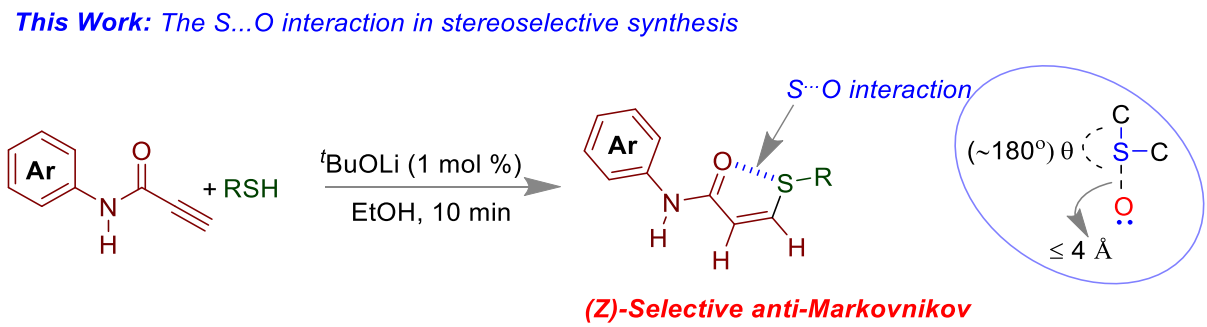
Recently, the same group introduced the switching of selectivity from anti-Markovnikov to Markovnikov selective vinyl sulfides in the presence of DBU as a base under irradiation of visible light (Scheme 4.3)[12].




**Scheme 4.3.** Markovnikov vinyl sulfides from terminal alkynes by Ananikov's group.

Soft forces or weak interactions such as S–H…O, S–H…S, O–H…S, N–H…S, etc., associated with sulfur atoms are still under characterization in both theoretical[13] and experimental[14] point of view. Apart from these well-known non-covalent interactions, the sulfur oxygen (S…O) interaction[15-18] is unexplored. Theoretical chemist has shown that S…O interaction can be used widely for designing drug molecules.[19, 20] Notable that, the S…O interaction is involved with low lying vacant σ* orbital of divalent sulfur center and the lone pairs of X (X = O/N) where the angle of C–S…X is found to be ~180°, and the distance between sulfur and X would be within 4 Å.[15] Herein, we disclosed that the unique S…O interaction was used to obtain (*Z*)-selective *anti*-

Markovnikov vinyl sulfides from the reaction of phenylpropiolamide and thiol in the presence of 1 mol % $^{t}$BuOLi in EtOH solvent (Scheme 4.4)[10b].



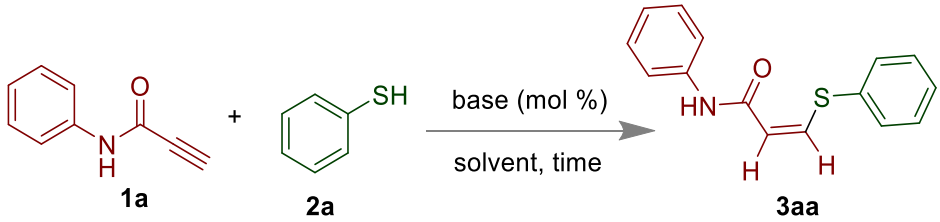

**Scheme 4.4.** Our work based on S…O interaction controlled (*Z*)-*anti*-Markovnikov vinyl sulfide.

## 4.3 RESULT AND DISCUSSION

The development of low-cost and commercially available catalysts or reagents instead of precious metals has recently been a chemical trend in both the research area of academia and industry. In this regard, the exploitation of heterogeneous catalysis, electrocatalysis[21], and organocatalysis in organic synthesis is exceedingly desirable. Keeping this reliable idea in mind, 1 mol % of lithium *tert*-butoxide ($^{t}$BuOLi) was considered for the generation of thiyl radical to conduct the click reaction between N-phenylpropiolamide and thiophenol. Delightfully, *anti*-Markovnikov and *Z*-selective vinyl sulfide was successfully achieved in EtOH medium within 10 min reaction time. The reaction between **1a** and **2a** yielded the desired product **3aa** in 90% yield with high *Z*-selectivity (Z/E=92:8) when 5 mol % of $^{t}$BuOLi was employed in our initial screening in $CH_3CN$ solvent for 30 min (Table 4.1, entry 1). Following, the effect of solvents like $CCl_4$, $H_2O$, $CHCl_3$, MeOH, and EtOH were examined, and EtOH was proved to be the best solvent for this transformation (Table 4.1, entries 2-6). Potassium *tert*-butoxide ($^{t}$BuOK) was taken instead of $^{t}$BuOLi, but no sacrificial change in reactivity was observed (Table 4.1, entry 7).

Afterward, the load of base and reaction time was monitored. It was notified that 1 mol% of $^{t}$BuOLi is sufficient to get 95% of desired (*Z*)-*anti*-Markovnikov selective product within 10 min (Table 4.1, entries 8 and 9). The reaction was very sluggish in the absence of catalyst under open air, producing 76% of desired product **3aa** (*Z*/*E*=82:18) (Table 4.1, entry 10). Also, no product was found in the absence of catalyst under an inert atmosphere (Table 4.1, entry 11). These two observations indicated that aerial oxygen might be helping in the generation of thiyl radical. No appreciable change in yield was observed for reaction in dry EtOH and inert atmosphere (Table 4.1, entry 12).

**Table 4.1.** Effect of reaction parameters[a]




| entry | solvent | initiator (mol %) | time | yield of 3aa (%)[a] | ratio of *Z*/*E*[b] |
|---|---|---|---|---|---|
| 1 | $CH_3CN$ | $^{t}$BuOLi (5.0) | 30 min | 90 | 92:8 |
| 2 | $CCl_4$ | $^{t}$BuOLi (5.0) | 30 min | 78 | 80:20 |
| 3 | $H_2O$ | $^{t}$BuOLi (5.0) | 2 h | 73 | 80:20 |
| 4 | $CHCl_3$ | $^{t}$BuOLi (5.0) | 30 min | 85 | 86:14 |
| 5 | MeOH | $^{t}$BuOLi (5.0) | 30 min | 81 | 90:10 |
| 6 | EtOH | $^{t}$BuOLi (5.0) | 30 min | 95 | 97:3 |
| 7 | EtOH | $^{t}$BuOK (5.0) | 30 min | 94 | 97:3 |

| | | | | | |
|---|---|---|---|---|---|
| 8 | EtOH | $^t$BuOLi (1.0) | 30 min | 95 | 97:3 |
| 9 | EtOH | $^t$BuOLi (1.0) | 10 min | 95 | 97:3 |
| 10 | EtOH | - | 16 h | 76 | 82:18 |
| 11 | EtOH | - | 24 h | 0[c] | - |
| 12 | EtOH | $^t$BuOLi (1.0) | 10 min | 93[d] | 97:3 |

[a]Isolated yields after column chromatography, [b]mixture of *Z/E* isomers determined by crude $^1$H NMR analysis; Reaction conditions: **1a** (60 mg, 0.413 mmol), **2a** (54 mg, 0.0.495 mmol) and $^t$BuOLi (0.33mg, 0.00413 mmol) in 1 mL EtOH under open air at room temperature. [c]Reaction was performed under an inert atmosphere in the absence of $^t$BuOLi. [d]In dry EtOH at argon atmosphere.

Next, we turned our attention to explore the substrate scopes of N-phenylpropiolamide derivatives. As shown in Figure 4.1, the electron-donating groups such as methyl, isopropyl, *tert*-butyl at *ortho* and *para* position of N-phenyl, could produce corresponding *Z*-selective vinyl sulfides (**3aa-3fa**) with high yields (76-95%). Again,-OEt and -$OCF_3$ containing N-phenylpropiolamides showed 90% and 95% of **3ga** and **3ha**, respectively. On the other hand, N-phenylpropiolamides having halo substituents (X= F, Cl, Br, I) were also screened, however; fluoro, chloro substituted propiolamides produced moderate yields (**3ia**,76% and **3la**,78% respectively), and bromo, iodo substituted alkyne partners showed excellent yields (**3ja**, 83% and **3ka**, 89% respectively) with high *Z*-selectivity. Also, dihalo-substituted N-phenylpropiolamides were also well-productive offering (*Z*)-anti-Markovnikov selective vinyl sulfides **3ma** and **3na** with 77% and 68% yields, respectively. Besides, compound **3oa** was produced with 93% yields.

Consequently, N-methylated phenylpropiolamide also took part in addition reaction to deliver (*Z*)-selective **3pa** in 68% yield.

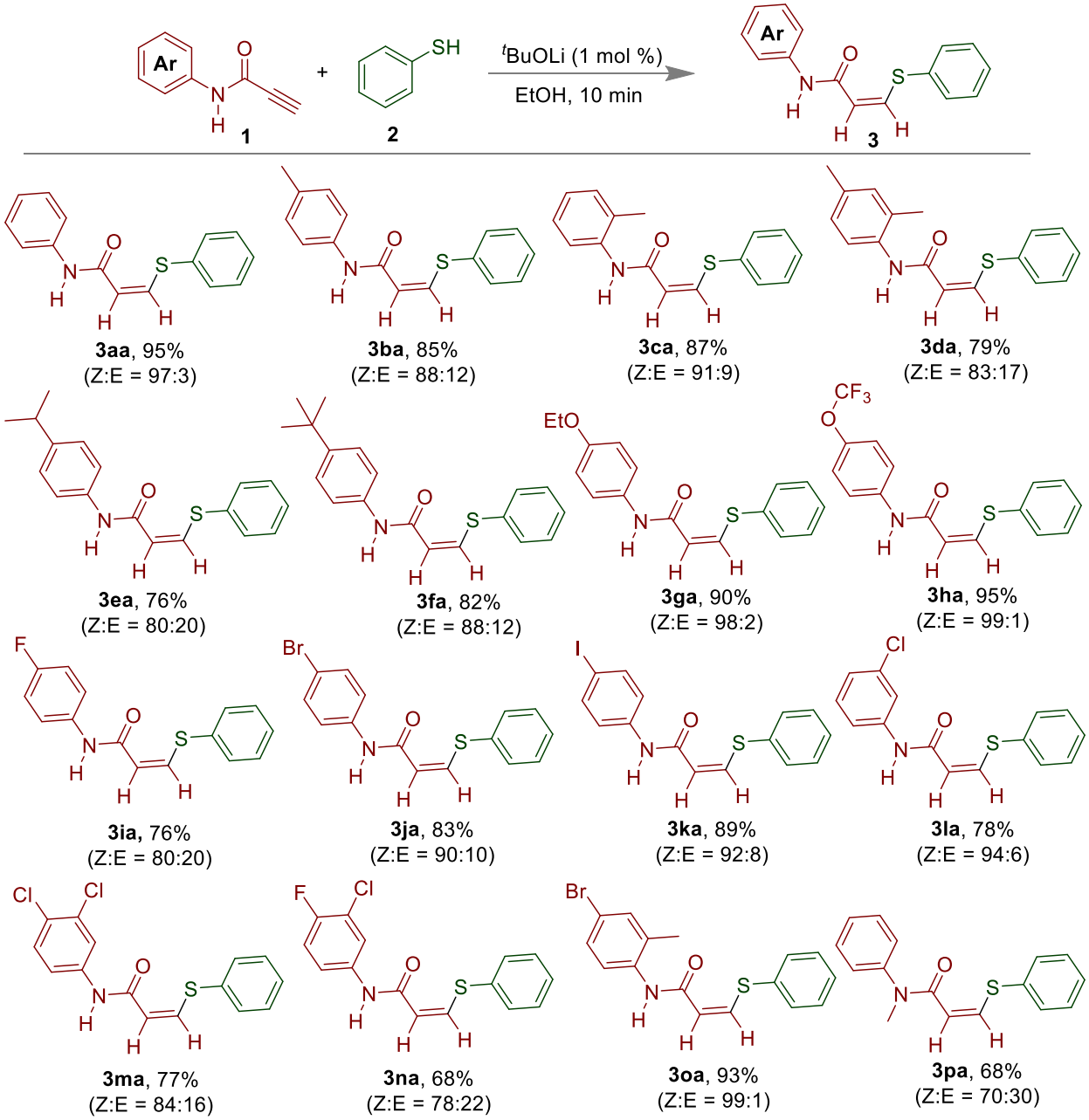



**Figure 4.1.** Scope of N-phenylpropiolamides for the synthesis of (Z)-vinyl sulfides.

Following, scopes of various thiols were examined (Figure 4.2). To our delight, *o*-and *p*-substituted thiophenols with -$CH_3$ and -$OCH_3$ group underwent addition reaction smoothly to

afford compounds **3ab**-**3af** with 69-82% yields (Figure 4.2a). Besides, 2-Amino thiophenol was tolerated with this mild basic medium offering **3gg** in a 73% yield. Again, halo-substituted thiophenols were well productive towards click reaction to generate **3ai**-**3an** with good to excellent results (80-96% yields) (Figure 4.2b). Interestingly, thiophenols containing electron-withdrawing partners such as $-CF_3$, $-NO_2$ also showed unique (Z)-selectivity by delivering compound **3ah** and **3oa** with 87% and 88% yields, respectively. On the other hand, hetero-substituted thiols, which were well compatible with this optimized reaction condition, produced **3ap** and **3aq** with excellent productivity (90% and 93%, respectively). In addition, aromatic dithiols (benzene-1,4-dithiol) displayed (*ZZ*)-and (*ZE*)-isomer of **3ar** with 96% and 1% yields, respectively (Figure 4.2c). Again, aliphatic dithiols (propane-1,3-dithiol) have also shown (*ZZ*)- and (*ZE*)-selectivity of **3as** with 72% and 12% yields; and (*EE*)-isomers of **3as** with 7% yield. Other aliphatic thiols were also screened; however, (*Z*)-selective vinyl sulfides (**3at**-**3aw**) were isolated in 62-92% yields (Figure 4.2d).

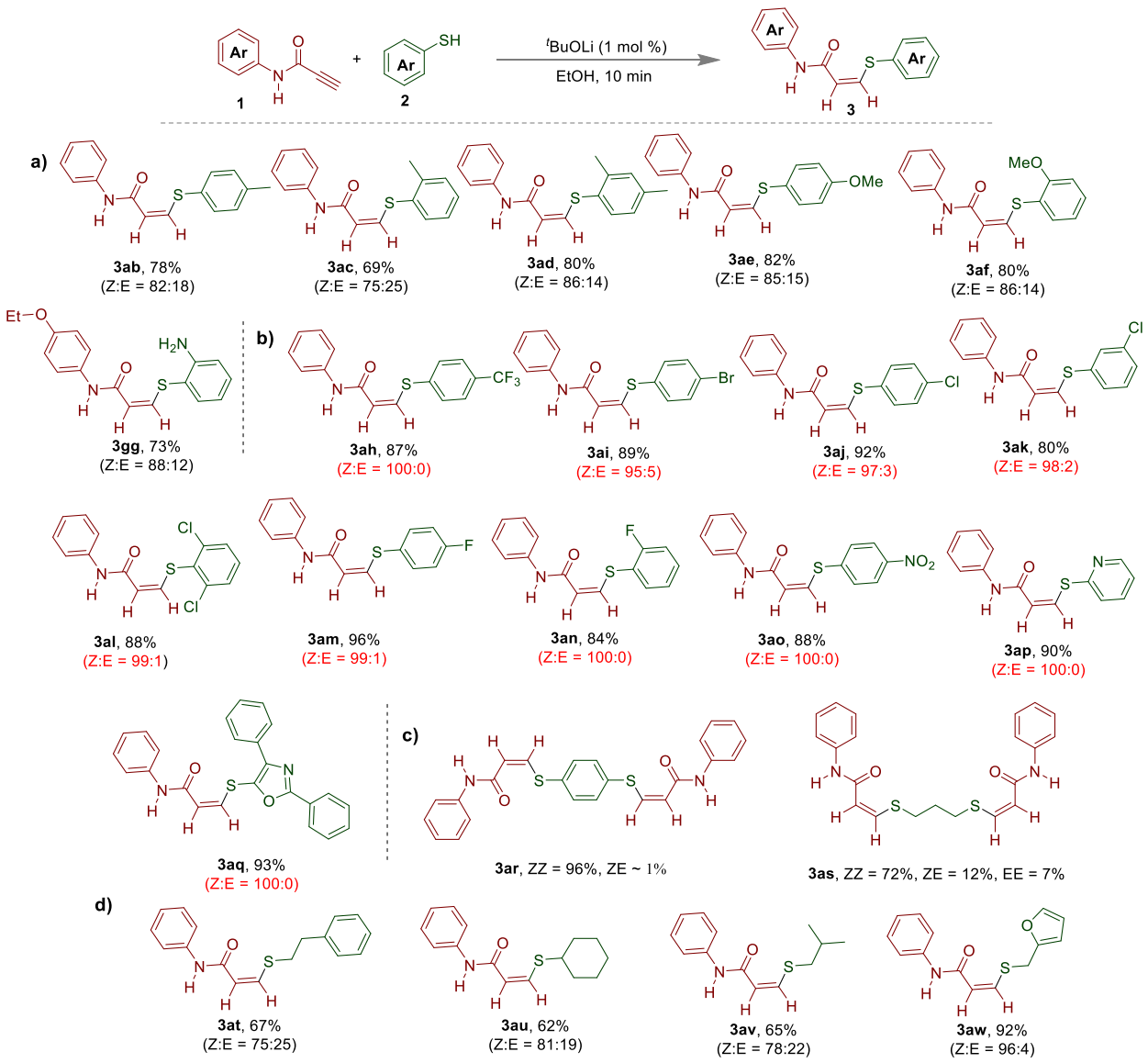



**Figure 4.2.** Scopes of a) electron-donating and b) electron-withdrawing and hetero-aromatic c) dithiols and d) aliphatic thiols.

In addition, several mechanistic studies were performed to elucidate the radical-mediated reaction pathway and identify the origin of (Z)-selectivity (Figure 4.3). The addition of thiophenol in phenylacetylene under standard conditions could show an inseparable mixture of non-selective vinyl sulfides **4** (Figure 4.3a). Again, *N*-(prop-2-yn-1-yl)-aniline

and thiophenol **2a** did not give any product under standard conditions, which indicated that the carbonyl group has a crucial role in the addition reaction. In addition, *p*-tolyl propiolate and thiophenol **2a** also gave inferior results. Surprisingly, 1-phenylprop-2-yn-1-one having carbonyl group was instantly converted into dithioacetal **5**. These phenomena also directed that the amide group acted as reaction controller for the (*Z*)-selective product. The EPR studies helped to rationalize the radical mechanism. On the other hand, a sharp EPR signal was observed when DMPO (5,5-dimethyl-1-pyrroline-*N*-oxide) was added as a free-radical scavenger under standard reaction conditions (Figure 4.3b). Again, the addition of TEMPO also exhibited no product formation, which proved that the reaction possibly goes through the generation of thiyl radical.

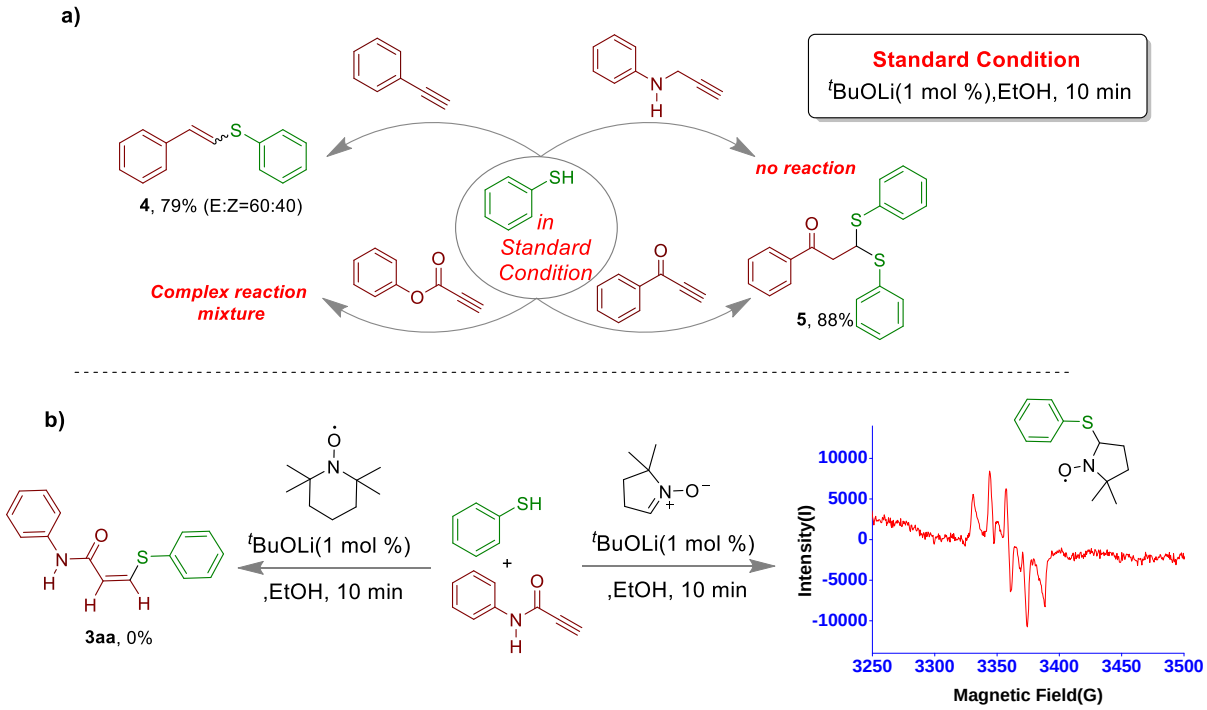



**Figure 4.3.** Control experiments: a) unselective reactions of various terminal alkynes; b) EPR experiment with DMPO; g = 2.00752 (right side) and the radical quenching experiment using TEMPO (left side).

X-ray structure of compound **3ga** also revealed that the bond distance between the carbonyl oxygen and sulfur was found to be C=O···S = 2.85 Å, and the bond angle of $C_1$-S(of PhSH)…O is 169.48$^{o,}$ thus assumed that a weak interaction between sulfur and oxygen (S…O) might help to attain the (*Z*)-selectivity (Figure 4.4a). This S…O interaction was further supported by density functional theory (DFT) (Figure 4.4b). The geometry of Z-vinyl sulfide (**3ga**) was optimized by density functional theory (DFT) at BYLYP/6-31+G (d, p) level. The optimized structure also showed the distance between the carbonyl oxygen and sulfur is 2.809A$^{o,}$ and the angle between the carbonyl oxygen and C–S is 172.24$^{o}$. The natural bond orbital (NBO) analysis on the optimized structure of Z-vinyl sulfide (**3ga**) also displayed second-order perturbation energy $E_{n\text{-}\sigma^*}$ is 2.65 kcal/mol which substantiated gorgeous S···O interaction which is due to the delocalization of lone pair of electrons on the oxygen atom into adjacent C–S σ* orbital. In addition, the geometry of corresponding (*E*)-vinyl sulfide (**3ga**) was also optimized where such type of delocalization of lone pair of electrons is not possible because of the huge distance between the carbonyl oxygen and C–S. In Figure 4.4c, the pictorial form of molecular HOMO and LUMO residing on carbonyl oxygen and C–S are displayed.

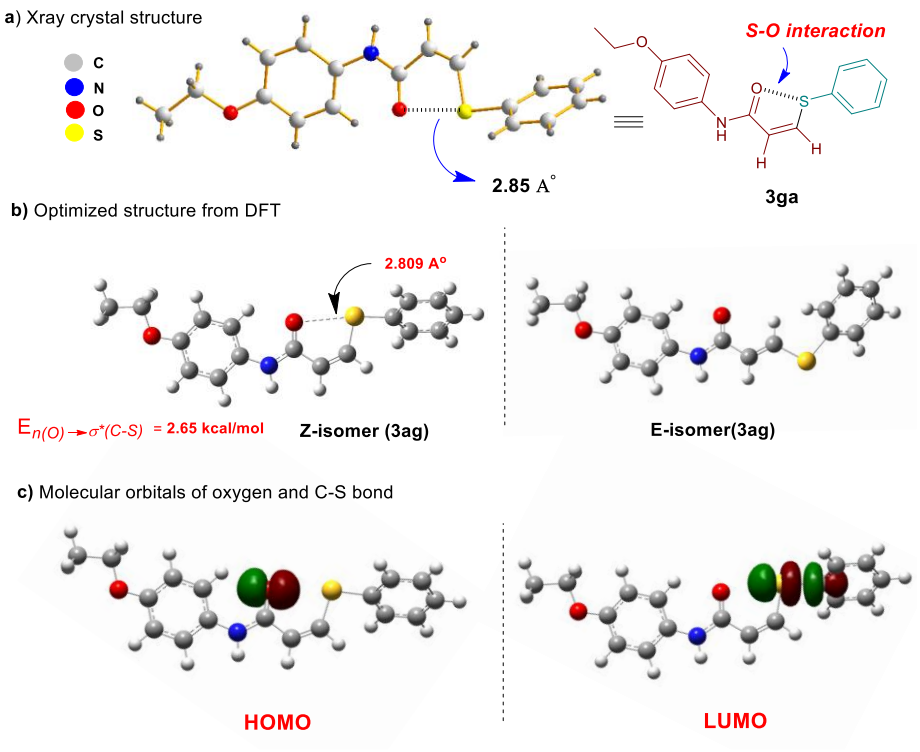



**Figure 4.4.** a) Crystal structure of compound **3ga** and the S…O interaction is indicated; b) The optimized geometry of **3ga** (*Z*) and (E)-isomer obtained from B3LYP/6-31+G(d,p) calculations is shown. c) HOMO and LUMO are located on carbonyl oxygen and C–S.

To our delight, the S…O interaction was also further verified by the nature of the electronic effect on substituent of thiophenols (Figure 4.2b, *vide supra*). The electronegative and hetero-substituent on thiols offered the (*Z*)-selectivity exclusively. This is due to the fact that electron-withdrawing substituent on thiol or hetero-substituent could stabilize the sulfur's lone pair through delocalization of π electron cloud within the aromatic ring. As a result, divalent sulfur with low lying σ* orbital participated in S…O interaction with neighboring oxygen's lone pair. But such stability was hampered when electron-donating substituent on thiophenol was introduced; thus, the expected ratio of (*E*)-selective product gradually increased[15].

Based on the previous literature reports[22] and control experiment, a plausible mechanism was outlined (Figure 4.5a). Initially, $^{t}$BuOLi was involved in the generation of thiyl radical *via* the formation of a complex **I** with thiol. Consequently, thiyl radical **II** was reacted with N-phenylpropiolamide to generate vinylic radical **III**. Now, (*Z*)-selectivity was conserved by S…O interaction. Following, hydrogen atom transfer took place from thiol to radical intermediate **III** to offer (Z)-selective vinyl sulfides with regeneration of thiyl radical. The thiyl radical once again participated in a chain reaction to form the final product. Next, the newly formed (Z)-vinyl sulfides exhibited versatile reactivity towards oxidation and suzuki coupling reaction, as shown in Figure 4.5b. (*Z*)-vinyl sulfide was converted to (*Z*)-vinyl sulfoxide **6** with excellent yield. Also, suzuki coupling reaction between **3ai** and phenylboronic acid offered substituted (*Z*)-vinyl sulfide **7** with 76% yield (Figure 4.5c).

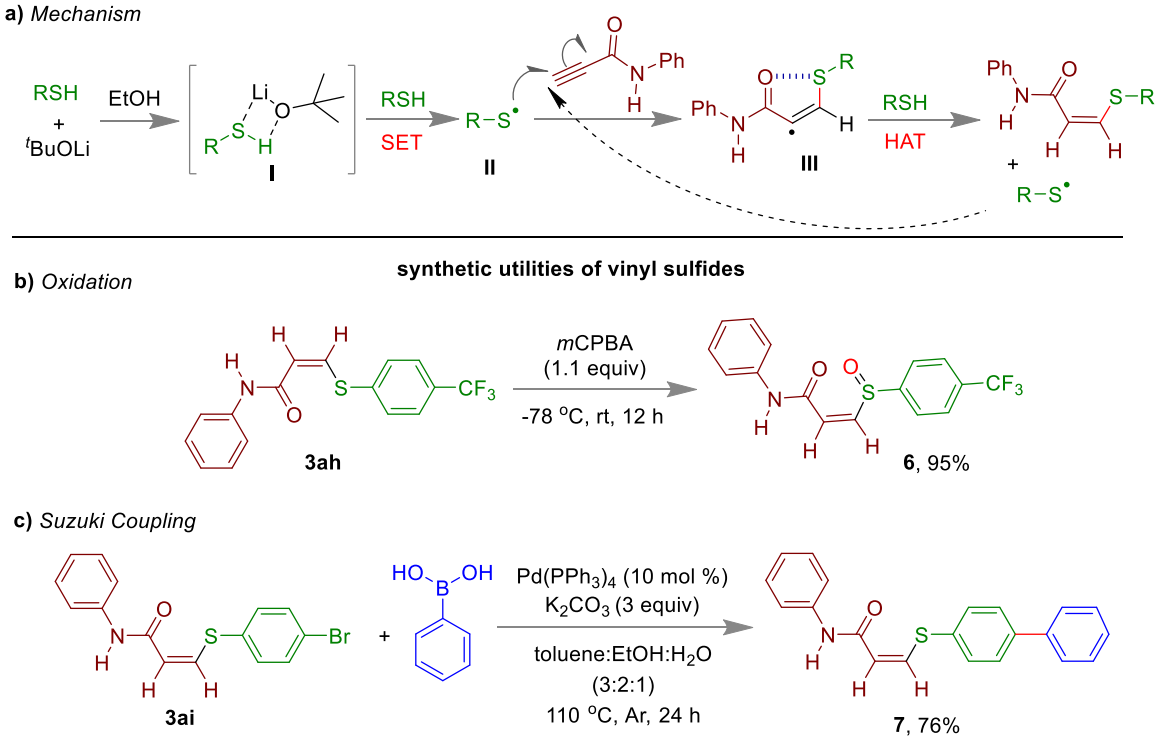



**Figure 4.5.** a) Plausible mechanism of the reaction; b) Oxidation of sulfide to sulfoxide **6** c) Suzuki coupling reaction of (*Z*)-vinyl sulfide to afford **7**.

## 4.4 CONCLUSION

In conclusion, we have demonstrated a simple protocol for the synthesis of stereo and regio-selective vinyl sulfides from the addition reaction of N-phenylpropiolamides and thiols *using* $^{t}$BuOLi as radical initiator. A newly identified S…O interaction is recognized for the first time to demonstrate the origin of the (*Z*)-selectivity of vinyl sulfide. In addition, the thiol-yne-click reaction provided a wide range of substrate scopes and excellent synthetic utilities. Overall, the current work offers special instruction for a stereoselective radical addition to alkynes by using suitable weak interaction.

## 4.5 EXPERIMENTAL SECTION

**General aspects**

All reactions were carried out under an open atmosphere unless otherwise noted .All solvents were generally distilled by following the standard procedures prior to use. All reactions were monitored by TLC on Merck 60 F254 aluminum sheets pre-coated with silica gel .Column chromatography was performed using Chemlabs silica-gel 230-400 mesh. The NMR studies were carried out by Bruker 400 and 700 MHz at room temperature in $CDCl_3$ solutions; $^{1}$H chemical shifts are given in $\delta$ (ppm) related to TMS as internal standard, coupling constants *J* values in Hz, and the chemical shift value (δ, ppm) are reported with respect to the residual chloroform (7.26 for $^{1}$H and 77.16 ppm for $^{13}$C). High resolution mass spectroscopy was recorded using an ESI-TOF instrument. Infra-red spectroscopic studies were performed and described in wavenumber ($cm^{-1}$). Melting reported are in degree centigrade. The single-crystal XRD was analyzed in a Rigaku Oxford diffractometer, and the crystal is deposited in the Cambridge Crystallographic Data Centre. EPR spectra were obtained in a Bruker EMX (ER 073)

instrument. The elaborate procedure for the preparation of target molecules and the other intermediates are described below.

**General procedures for the synthesis of N-phenylpropiolamide derivatives.**

In an oven-dried round-bottomed flask, propiolic acid (3.54 mmol, 1.1 equiv) and 4-dimethylaminopyridine (0.32 mmol, 0.1 equiv) in 10 mL $CH_2Cl_2$ (DCM) were stirred at -20 °C. To this, dicyclohexylcarbodiimide (3.54 mmol, 1.1 equiv) in 5 mL $CH_2Cl_2$ were injected drop-wise. Following, aniline (3.22 mmol, 1.0 equiv) in 5 mL $CH_2Cl_2$ was then added dropwise. Afterward, the reaction mixture was kept at room temperature overnight. After the end of the reaction, the crude reaction mixture was washed, dried over $Na_2SO_4$, and finally concentrated under a rotary evaporator. The crude starting material was purified by column chromatography to get the desired N-phenylpropiolamide derivatives as solid.

**General procedure for the synthesis of 3aa.**

In a 10 mL round bottom flask, the thiophenol (**2a**) (54 mg, 0.0.495 mmol) and Lithium *tert*-butoxide (0.33 mg, 0.00413 mmol) were dissolved in 1 mL EtOH. After that, N-phenylpropiolamide (**1a**) (60 mg, 0.413 mmol) was added to the solution, and the resulting reaction mixture was stirred in an open atmosphere for 10 min. The progress of the reaction was monitored by TLC. After completion of the reaction, excess EtOH was removed column chromatography was done in EtOAc/Hexane to isolate the desired product **3aa**.

**EPR experiment.**

EPR spectra were recorded at 298 K using an EPR spectrometer derived at 9.4335 GHz. Typical spectrometer parameters are shown as follows, scan range: 100 G; center fieldset: 3480.00 G;

time constant: 0.16 ms; scan time: 122.88 s; modulation amplitude: 20.0 G; modulation frequency: 100 kHz; receiver gain: $2.00\times10^{2}$ ; microwave power: $7.14e^{-001}$ mW.

**Spin-trapping experiment in the presence of DMPO.**[3]

A mixture of thiophenol **2a** (0.495 mmol)**,** *N*-phenylpropiolamide **1a** (0.413 mmol), $^{t}$BuOLi (0.00413 mmol, 1 mol %), and DMPO (20 μL) were stirred in 1.0 mL $CH_3CN$ for 2 min. Following, 20 μL solutions were quickly transferred into an EPR tube, and toluene (200 μL) was added to analyze EPR. A similar experiment was performed without thiophenol **2a**. A sharp signal was observed for the first case, but no signal was found when the experiment was carried out in the absence of thiophenol.

**Crystallographic Investigation**

Good quality crystals of compounds **3ga** and **6** were obtained after slow evaporation of ethanol and water mixture (ca. 50%). The crystals data were collected from the same instrument which was mentioned in the above chapter.

**Compound (3ga) (CCDC 2044667)**

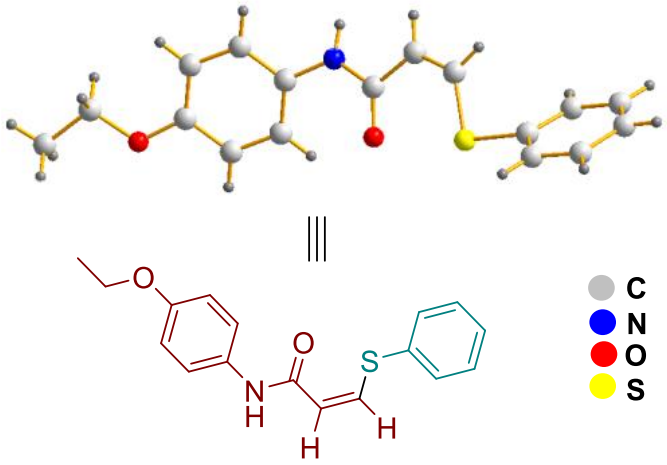



**Figure 4.6.** Crystal structure of (**3ga**) (CCDC 2044667).

**Crystallographic Data for (3ga)**

| | |
|---|---|
| Empirical formula | $C_{17}H_{17}NO_2S$ |
| Formula weight | 299.37 |
| Temperature/K | 100.00(10) |
| Crystal system | Monoclinic |
| Space group | $P2_1/n$ |
| a/Å | 9.77820(12) |
| b/Å | 17.7960(2) |
| c/Å | 18.3352(2) |
| α/° | 90 |
| β/° | 101.9230(12) |
| γ/° | 90 |
| Volume/Å$^3$ | 3121.73(7) |
| Z | 8 |

| | |
|---|---|
| ρcalcg/cm$^3$ | 1.274 |
| μ/mm$^{-1}$ | 1.868 |
| F(000) | 1264.0 |
| Crystal size/mm$^3$ | 0.2 × 0.18 × 0.18 |
| Radiation | CuKα (λ = 1.54184) |
| Reflections collected | 47713 |
| Independent reflections | 6378 [Rint = 0.0731, Rsigma = 0.0307] |
| Goodness-of-fit on F2 | 1.029 |
| Final R indexes [I>=2σ (I)] | R1 = 0.0416, wR2 = 0.1117 |
| Final R indexes [all data] | R1 = 0.0430, wR2 = 0.1128 |
| Largest diff. peak/hole / e Å$^{-3}$ | 0.36/-0.38 |

**Compound 6 (CCDC 2044669)**

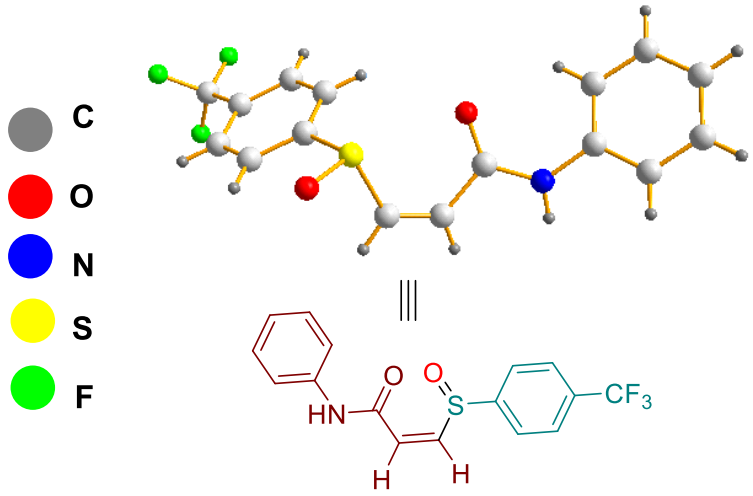



**Figure 4.7.** Crystal structure of **6** (CCDC 2044669).

**Crystallographic Data for 6**

| | |
|---|---|
| Empirical formula | $C_{16}H_{12}F_3NO_2S$ |
| Formula weight | 339.33 |
| Temperature/K | 298.9(2) |
| Crystal system | Monoclinic |
| Space group | $P2_1/c$ |
| a/Å | 14.97283(16) |
| b/Å | 5.15517(5) |
| c/Å | 20.2206(3) |
| α/° | 90 |
| β/° | 90.3507(11) |
| γ/° | 90 |
| Volume/Å$^3$ | 1560.74(3) |
| Z | 4 |
| ρcalcg/cm$^3$ | 1.444 |
| μ/mm$^{-1}$ | 2.227 |
| F(000) | 696.0 |
| Crystal size/mm$^3$ | 0.2 × 0.18 × 0.17 |
| Radiation | CuKα (λ = 1.54184) |
| Reflections collected | 24037 |
| Independent reflections | 3304 [Rint = 0.0375, Rsigma = 0.0194 |
| Goodness-of-fit on F2 | 1.129 |
| Final R indexes [I>=2σ (I)] | R1 = 0.0566, wR2 = 0.1674 |
| Final R indexes [all data] | R1 = 0.0596, wR2 = 0.1708 |

## NMR CHARACTERIZATION DATA

**(Z)-N-Phenyl-3-(phenylthio)acrylamide (3aa):** $R_f$ = 0.45 (20% ethyl acetate in hexane); yellow solid; yield 95% (100 mg); mp 154-156 ºC; $^1$H NMR (400 MHz, DMSO-$d_6$) δ 10.13 (s, 1H), 7. 65 (d, *J* = 8.0 Hz, 2H), 7.53 (d, *J* = 7.4 Hz, 2H), 7.43 (t, *J* = 7.4 Hz, 2H), 7.40-7.35 (m, 2H), 7.32 (t, *J* = 7.8 Hz, 2H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.25 (d, *J* = 9.8 Hz, 1H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 164.0, 144.0, 139.2, 136.9, 129.7, 129.4, 128.8, 127.6, 123.1, 118.8, 117.0; IR (KBr) ῡ 3303, 3054, 2935, 1644, 690; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{13}NOSNa$ 278.0610; found 278.0636.

**(Z)-3-(Phenylthio)-N-(p-tolyl)acrylamide (3ba):** $R_f$ = 0.5 (20% ethyl acetate in hexane); pale yellow solid; yield 85% (86 mg); mp 163-167 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.50-7.48 (m, 4H), 7.41 (s, 1H) , 7.38-7.29 (m, 3H), 7.17 (d, *J* = 9.8 Hz, 1H), 7.10 (d, *J* = 8.0 Hz, 2H), 6.00 (d, *J* = 9.8 Hz, 1H), 2.30 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.3, 147.0, 137.2, 135.5, 133.9, 131.0, 129.6, 129.4, 128.1, 119.8, 115.8, 21.0; IR (KBr) ῡ 3310, 2915, 2339, 1657, 688; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{16}NOS$ 270.0947; found 270.0966.

**(Z)-3-(Phenylthio)-N-(o-tolyl)acrylamide (3ca):** $R_f$ = 0.55 (20% ethyl acetate in hexane); white solid; yield 87% (88 mg); mp 160-164 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.51 (d, *J* = 7.8 Hz, 2H), 7.39-7.31 (m, 3H), 7.23-7.18 (m, 3H), 7.08-7.00 (m, 2H), 6.02 (d, *J* = 9.8 Hz, 1H), 2.29 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.5, 147.5, 137.3, 135.9, 131.1, 130.5, 129.7, 129.4, 128.2, 127.0, 125.0, 122.7, 115.6, 18.0; IR (KBr) ῡ 3206, 3034, 2922, 1634, 689; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{16}H_{15}NOSNa$ 292.0767; found 292.0761.

**(Z)-N-(2,4-Dimethylphenyl)-3-(phenylthio)acrylamide (3da):** $R_f$ = 0.6 (20% ethyl acetate in hexane); white solid; yield 79% (78 mg); mp 182-184 ºC; $^1$H NMR (700 MHz, $CDCl_3$) δ 7.85-7.84 (m, 1H), 7.49 (d, *J* = 7.4 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 1H), 7.19 (d, *J* = 9.0 Hz, 1H), 7.03-6.99 (m, 3H), 6.03 (d, *J* = 9.0 Hz, 1H), 2.29 (s, 3H), 2.24 (s, 3H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 164.4, 147.0, 137.3, 134.7, 133.2, 131.14, 131.08, 129.4, 128.6, 128.1, 127.4, 123.0, 115.7, 21.0, 17.9; IR (KBr) ῡ 3387, 3003, 1733, 1274, 657; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{17}H_{17}NOSNa$ 306.0923; found 306.0925.

**(Z)-N-(4-Isopropylphenyl)-3-(phenylthio)acrylamide (3ea):** $R_f$ = 0.5 (20% ethyl acetate in hexane); white solid; yield 76% (72 mg); mp 173-174 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.50 (d, *J* = 6.8 Hz, 3H), 7.38-7.34 (m, 2H), 7.34-7.30 (m, 2H), 7.20-7.16 (m, 3H), 5.99 (d, *J* = 9.8 Hz, 1H), 2.87 (sept, *J* = 6.8 Hz, 1H), 1.23 (d, *J* = 6.8 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.3, 147.1, 145.0, 137.3, 135.8, 131.1, 129.4, 128.1, 127.0, 119.9, 115.7, 33.7, 24.1; IR (KBr) ῡ 3294, 2955, 1600, 822, 691; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{18}H_{19}NOSNa$ 320.1080; found 320.1065.

**(Z)-N-(4-(tert-Butyl)phenyl)-3-(phenylthio)acrylamide (3fa):** $R_f$ = 0.65 (20% ethyl acetate in hexane); white solid; yield 82% (76 mg); mp 183-185 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.52-7.50 (m, 3H), 7.39-7.30 (m, 6H), 7.20 (d, *J* = 9.8 Hz, 1H), 5.99 (d, *J* = 9.8 Hz, 1H), 1.30 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.4, 147.30, 147.27, 137.3, 135.4, 131.1, 129.4, 128.1, 125.9, 119.5, 115.6, 34.5, 31.5; IR (KBr) ῡ 3299, 2962, 1597, 694; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{19}H_{21}NOSNa$ 334.1236; found 334.1236.

**(Z)-N-(4-Ethoxyphenyl)-3-(phenylthio)acrylamide (3ga):** $R_f$ = 0.55 (30% ethyl acetate in hexane); white solid; yield 90% (85 mg); mp 163-165 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.50-7.48 (m, 4H), 7.40-7.30 (m, 4H), 7. 17 (d, *J* = 9.8 Hz, 1H), 6.84 (d, *J* = 8.8 Hz, 2H), 5.97 (d, *J* = 9.8 Hz, 1H), 4.00 (q, *J* = 6.8 Hz, 2H), 1.39 (t, *J* = 6.8 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.2, 155.8, 146.8, 137.3, 131.11, 131.06, 129.4, 128.1, 121.5, 115.7, 114.9, 63.8, 15.0; IR (KBr) ῡ 3321, 2977, 2339, 1632, 685; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{17}H_{17}NO_2SNa$ 322.0872; found 322.0869.

**(Z)-3-(Phenylthio)-N-(4-(trifluoromethoxy)phenyl)acrylamide (3ha):** $R_f$ = 0.45 (30% ethyl acetate in hexane); white solid; yield 95% (85 mg); mp 170-174 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.6 H z, 2H), 7.51-7.47 (m, 2H), 7.44 (s, 1H), 7.39-7.31 (m, 3H), 7.26-7.24 (m, 1H), 7.16 (d, *J* = 8.6 Hz, 2H), 6.00 (d, *J* = 9.8 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.5, 148.4, 145.4, 136.9, 136.7, 131.1, 129.5, 128.3, 121.8, 120.9, 119.3, 115.1; $^{19}$F NMR (376 MHz, $CDCl_3$) δ -58.11; IR (KBr) ῡ 3330, 3057, 2359, 1636, 668; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{16}H_{12}F_3NO_2SNa$ 362.0433; found 362.0415.

**(Z)-N-(4-Fluorophenyl)-3-(phenylthio)acrylamide (3ia):** $R_f$ = 0.5 (30% ethyl acetate in hexane); white solid; yield 76% (76 mg); mp 153-157 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.56-7.50 (m, 2H), 7.49 (d, *J* = 7.4 Hz, 2H), 7.44-7.38 (m, 1H), 7.37-7.31 (m, 3H), 7.21 (d, *J* = 9.8 Hz, 1H), 7.00 (t, *J* = 8.4 Hz, 2H), 5.99 (dd, *J* = 9.8, 1.2 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.4, 159.5 (d, $^1J_{CF}$ = 243.4 Hz), 147.8, 137.0, 134.1, 131.0, 129.4, 128.2, 121.6 (d, $^3J_{CF}$ = 6.2 Hz), 115.7 (d, $^2J_{CF}$ = 22.4 Hz), 115.4; $^{19}$F NMR (376 MHz, $CDCl_3$) δ -118.12; IR (KBr) ῡ 3305,

2921, 2341, 1634, 688; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{15}H_{13}FNOS$ 274.0696; found 274.0694.

**(Z)-N-(4-Bromophenyl)-3-(phenylthio)acrylamide (3ja):** $R_f$ = 0.55 (30% ethyl acetate in hexane); white solid; yield 83% (74 mg); mp 166-168 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.52 (s, 1H), 7.50-7.48 (m, 3H), 7.42-7.31 (m, 6H), 7.23 (d, *J* = 9.8 Hz, 1H), 5.98 (d, *J* = 9.8 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.4, 148.3, 137.2, 136.9, 132.1, 131.1, 129.5, 128.3, 121.3, 116.9, 115.2; IR (KBr) ῡ 3327, 3052, 2964, 1624, 690, 681; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{15}H_{13}BrNOS$ 333.9896; found 333.9885.

**(Z)-N-(4-Iodophenyl)-3-(phenylthio)acrylamide (3ka):** $R_f$ = 0.6 (30% ethyl acetate in hexane); white solid; yield 89% (75 mg); mp 165-167 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.63-7.60 (m, 2H), 7.51-7.48 (m, 2H), 7.41-7.37 (m, 3H), 7.36-7.32 (m, 2H), 7.25 (d, *J* = 9.8 Hz, 1H), 7.23 (s, 1H), 5.96 (d, *J* = 9.8 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.4, 148.4, 138.0, 137.9, 136.9, 131.1, 129.5, 128.3, 121.6, 115.2, 87.5; IR (KBr) ῡ 3327, 3077, 2324, 1651, 681, 506; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{15}H_{13}INOS$ 381.9757; found 381.9743.

**(Z)-N-(3-Chlorophenyl)-3-(phenylthio)acrylamide (3la):** $R_f$ = 0.65 (30% ethyl acetate in hexane); pale yellow solid; yield 78% (63 mg); mp 156-160 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.52-7.50 (m, 2H), 7.42-7.32 (m, 4H), 7.32-7.26 (m, 2H), 7.23 (t, *J* = 8.0 Hz, 1H), 7.08 (d, *J* = 7.8 Hz, 1H), 5.98 (d, *J* = 9.8 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.4, 148.7, 139.2, 136.9, 134.9, 131.1, 130.1, 129.5, 128.3, 124.4, 119.9, 117.6, 115.0; IR (KBr) ῡ 3302,

2922, 2851, 1674, 745, 691; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{15}H_{13}ClNOS$ 290.0401; found 290.0379.

**(Z)-N-(3,4-Dichlorophenyl)-3-(phenylthio)acrylamide (3ma):** $R_f$ = 0.6 (30% ethyl acetate in hexane); white solid; yield 77% (70 mg); mp 154-156 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.88-7.87 (m, 1H), 7.64 (s, 1H), 7.49-7.46 (m, 2H), 7.40-7.37 (m, 2H), 7.35-7.31 (m, 2H), 7.27-7.24 (m, 2H), 6.01 (d, *J* = 9.8 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.6, 148.9, 137.5, 136.6, 132.9, 131.1, 130.5, 129.5, 128.4, 127.4, 121.5, 119.1, 114.9; IR (KBr) ῡ 3319, 3060, 2916, 1537, 745, 690; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{11}Cl_2NOSNa$ 345.9831; found 345.9836.

**(Z)-N-(3-Chloro-4-fluorophenyl)-3-(phenylthio)acrylamide (3na):** $R_f$ = 0.55 (30% ethyl acetate in hexane); yellow solid; yield 68% (63 mg); mp 162-164 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.84-7.83 (m, 1H), 7.50 (d, *J* = 7.4 Hz, 2H), 7.39-7.32 (m, 5H), 7.27-7.25 (m, 1H), 7.09-7.05 (t, *J* = 8.6 Hz, 1H ), 5.97 (d, *J* = 9.8 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.4, 154.9 (d, $^1J_{CF}$ = 246.2 Hz), 148.7, 136.8, 134.7 (d, $^4J_{CF}$ = 3.2 Hz), 131.1, 129.5, 128.4, 122.0, 121.3 (d, $^2J_{CF}$ = 18.4 Hz), 119.4 (d, $^{4'}J_{CF}$ = 3.4 Hz), 116.7 (d, $^{2'}J_{CF}$ = 22.0 Hz), 114.8; $^{19}$F NMR (376 MHz, $CDCl_3$) δ -120.68; IR (KBr) ῡ 3294, 2957, 2852, 1652, 1241, 745, 692; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{11}ClFNOSNa$ 330.0126; found 330.0120.

**(Z)-N-(4-Bromo-2-methylphenyl)-3-(phenylthio)acrylamide (3oa):** $R_f$ = 0.6 (30% ethyl acetate in hexane); white solid; yield 93% (81 mg); mp 166-170 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.61 (s, 1H), 7.50-7.47 (m, 2H), 7.43 (d, *J* = 8.6 Hz, 1H), 7.39-7.31 (m, 4H), 7.26-7.21 (m,

2H), 5.98 (d, *J* = 9.8 Hz, 1H), 2.35 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.4, 148.1, 138.7, 137.3, 137.0, 132.7, 131.1, 129.5, 128.3, 121.9, 119.5, 118.6, 115.3, 23.1; IR (KBr) ῡ 3327, 3055, 2341, 1634, 680, 555; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{16}H_{14}BrNOSNa$ 369.9872; found 369.9865.

**(Z)-N-methyl-N-phenyl-3-(phenylthio)acrylamide (3pa):** $R_f$ = 0.75 (20% ethyl acetate in hexane); colorless liquid; yield 68% (69 mg); $^1$H NMR (700 MHz, $CDCl_3$) δ 7.48 -7.47 (m, 2H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.34-7.31 (m, 3H), 7.30-7.28 (m, 1H), 7.22 (d, *J* = 7.4 Hz, 2H), 6.99 (d, *J* = 9.8 Hz, 1H), 5.79 (d, *J* = 9.8 Hz, 1H), 3.37 (s, 3H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 166.5, 146.7, 143.9, 137.8, 131.1, 129.8, 129.3, 127.9, 127.6, 127.4, 113.7, 37.1; IR (KBr) ῡ 3052, 2930, 2322, 1680, 680; HRMS (ESI/Q-TOF) m/z: [M + Na]+ calcd for $C_{16}H_{15}NOSNa$ 292.0767; found 292.0778.

**(Z)-N-Phenyl-3-(p-tolylthio)acrylamide (3ab):** $R_f$ = 0.5 (20% ethyl acetate in hexane); yellow solid; yield 78% (86 mg); mp 183-187 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 6.2 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.33-7.29 (m, 3H), 7.19-7.16 (m, 3H), 7.10 (t, *J* = 7.4 Hz, 1H), 5.96 (d, *J* = 9.8 Hz, 1H), 2.36 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.4, 148.5, 138.4, 138.1, 133.7, 131.3, 130.2, 129.1, 124.3, 119.7, 115.2, 21.3; IR (KBr) ῡ 3300, 3033, 2849, 2335, 1633, 692; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{16}H_{15}NOSNa$ 292.0767; found 292.0758.

**(Z)-N-Phenyl-3-(o-tolylthio)acrylamide (3ac):** $R_f$ = 0.55 (20% ethyl acetate in hexane); pale yellow solid; yield 69% (77 mg); mp 155-157 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.4 Hz, 2H), 7.49 (d, *J* = 7.2 Hz, 1H), 7.36 (s, 1H), 7.32 (t, *J* = 7.8 Hz, 2H), 7.27-7.19 (m, 3H), 7.11

(d, *J* = 7.4 Hz, 1H), 7.07 (d, *J* = 9.8 Hz, 1H), 6.00 (d, *J* = 9.8 Hz, 1H), 2.46 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.5, 148.1, 139.9, 138.1, 136.2, 132.6, 130.7, 129.1, 128.7, 127.0, 124.3, 119.7, 115.6, 21.0; IR (KBr) ῡ 3357, 3054, 1596, 691; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{16}NOS$ 270.0947; found 270.0923.

**(Z)-3-((2,4-Dimethylphenyl)thio)-N-phenylacrylamide (3ad):** $R_f$ = 0.7 (20% ethyl acetate in hexane); yellow solid; yield 80% (94 mg); mp 186-188 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 6.6 Hz, 2H), 7.38 (d, *J* = 7.8 Hz, 1H), 7.32 (t, *J* = 7.8 Hz, 2H), 7.26 (s, 1H), 7.12-7.07 (m, 2H), 7.04-7.02 (m, 2H), 5.96 (d, *J* = 9.8 Hz, 1H), 2.43 (s, 3H), 2.33 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.7, 148.9, 139.9, 138.9, 138.2, 133.0, 132.7, 131.6, 129.1, 127.8, 124.3, 119.7, 115.3, 21.2, 21.0; IR (KBr) ῡ 3454, 2919, 2312, 1634, 686; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{17}H_{17}NOSNa$ 306.0923; found 306.0915.

**(Z)-3-((4-Methoxyphenyl)thio)-N-phenylacrylamide (3ae):** $R_f$ = 0.45 (30% ethyl acetate in hexane); white solid; yield 82% (96 mg); mp 171-173 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 6.6 Hz, 2H), 7.43 (d, *J* = 8.8 Hz, 2H), 7.33-7.26 (m, 3H), 7.12-7.07 (m, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 5.93 (d, *J* = 9.8 Hz, 1H), 3.81 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.7, 160.1, 149.5, 138.1, 133.5, 129.1, 127.9, 124.3, 119.7, 115.0, 114.9, 55.5; IR (KBr) ῡ 3266, 3129, 2357, 1618, 1210, 694; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{16}NO_2S$ 286.0896; found 286.0871.

**(Z)-3-((2-Methoxyphenyl)thio)-N-phenylacrylamide (3af):** $R_f$ = 0.4 (30% ethyl acetate in hexane); white solid; yield 80% (94 mg); mp 169-171 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.61 (d,

*J* = 6.6 Hz, 2H), 7.53 (s, 1H), 7.46 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.34-7.30 (m, 1H), 7.28-7.26 (m, 2H), 7.11 (d, *J* = 9.8 Hz, 1H), 7.07 (t, *J* = 7.4 Hz, 1H), 6.96-6.90 (m, 2H), 6.01 (d, *J* = 9.8 Hz, 1H), 3.84 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.6, 158.4, 147.6, 138.2, 133.3, 130.1, 129.0, 124.5, 124.1, 121.2, 119.8, 115.5, 111.5, 56.0; IR (KBr) ῡ 3305, 3052, 2934, 1645, 692; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{16}NO_2S$ 286.0896; found 286.0869.

**(Z)-3-((4-Fluorophenyl)thio)-*N*-phenylacrylamide (3am):** $R_f$ = 0.45 (20% ethyl acetate in hexane); white solid; yield 96% (108 mg); mp 182-184 ºC; $^1$H NMR (400 MHz, DMSO-$d_6$) δ 10.14 (s, 1H), 7.65 (d, *J* = 7.4 Hz, 2H), 7.59-7.56 (m, 2H), 7.33-7.25 (m, 5H), 7.05 (t, *J* = 7.3 Hz, 1H), 6.23 (d, *J* = 9.8 Hz, 1H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 164.0, 161.8 (d, $^1J_{CF}$ = 245.3 Hz), 144.6, 139.2, 132.6 (d, $^4J_{CF}$ = 3.0 Hz), 132.5 (d, $^3J_{CF}$ = 8.4 Hz), 128.8, 123.2, 118.9, 116.8, 116.4 (d, $^2J_{CF}$ = 22.0 Hz); $^{19}$F NMR (377 MHz, DMSO-$d_6$) δ -114.17; IR (KBr) ῡ 3309, 3055, 2337, 1625, 1303, 688; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{15}H_{13}FNOS$ 274.0696; found 274.0696.

**(Z)-3-((2-Fluorophenyl)thio)-N-phenylacrylamide (3an):** $R_f$ = 0.35 (20% ethyl acetate in hexane); pale yellow solid; yield 84% (94 mg); mp 145-148 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 6.8 Hz, 2H), 7.51 (td, *J* = 7.8, 1.6 Hz, 1H), 7.43 (s, 1H), 7.37-7.29 (m, 3H), 7.16-7.06 (m, 4H), 6.04 (d, *J* = 9.8 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.5, 161.6 (d, $^1J_{CF}$ = 247.6 Hz), 146.6, 138.0, 134.1, 130.7 (d, $^3J_{CF}$ = 7.8 Hz), 129.1, 124.9 (d, $^4J_{CF}$ = 3.8 Hz), 124.4, 123.8 (d, $^2J_{CF}$ = 17.8 Hz), 119.9, 116.4 (d, $^2J_{CF}$ = 22.4 Hz), 116.1; $^{19}$F NMR (376 MHz, $CDCl_3$) δ -108.61; IR (KBr) ῡ 3322, 2923, 2851, 1652, 1309, 692; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{12}FNOSNa$ 296.0516; found 296.0513.

**(Z)-3-((4-Chlorophenyl)thio)-N-phenylacrylamide (3aj):** $R_f$ = 0.5 (20% ethyl acetate in hexane); yellow solid; yield 92% (110 mg); mp 205-210 ºC; $^1$H NMR (400 MHz, DMSO-$d_6$) δ 10.16 (s, 1H), 7.65 (d, *J* = 7.8 Hz, 2H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 9.8 Hz, 1H), 7.32 (t, *J* = 7.8 Hz, 2H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.27 (d, *J* = 9.8 Hz, 1H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 164.0, 143.3, 139.1, 135.9, 132.4, 131.4, 129.3, 128.8, 123.2, 118.9, 117.3; IR (KBr) ῡ 3345, 3035, 2923, 2359, 1633, 692; HRMS (ESI/Q-TOF) m/z: [M + Na]$^+$ calcd for $C_{15}H_{12}ClNOSNa$ 312.0220; found 312.0207.

**(Z)-3-((3-Chlorophenyl)thio)-N-phenylacrylamide (3ak):** $R_f$ = 0.65 (30% ethyl acetate in hexane); white solid; yield 80% (95 mg); mp 156-158 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 6.8 Hz, 2H), 7.48-7.47 (m, 1H), 7.38-7.29 (m, 6H), 7.16 (dd, *J* = 9.8, 1.2 Hz, 1H), 7.11 (t, *J* = 7.2 Hz, 1H), 6.04 (d, *J* = 9.8 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.3, 146.1, 139.1, 137.9, 135.1, 130.6, 130.5, 129.2, 129.0, 128.3, 124.5, 119.8, 116.3; IR (KBr) ῡ 3305, 2955, 1733, 779, 694; HRMS (ESI/Q-TOF) m/z: [M + Na]$^+$ calcd for $C_{15}H_{12}ClNOSNa$ 312.0220; found 312.0212.

**(Z)-3-((2,6-Dichlorophenyl)thio)-*N*-phenylacrylamide (3al):** $R_f$ = 0.6 (30% ethyl acetate in hexane); pale yellow solid; yield 88% (118 mg); mp 186-188 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.4 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.34-7.30 (m, 3H), 7.27-7.23 (m, 1H), 7.11 (t, *J* = 7.4 Hz, 1H), 6.82 (d, *J* = 9.8 Hz, 1H), 6.06 (d, *J* = 9.8 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.5, 146.8, 140.1, 137.9, 134.6, 130.7, 129.1, 129.0, 124.4, 119.7, 115.8; IR (KBr) ῡ 3446, 2924, 1700, 778, 690; HRMS (ESI/Q-TOF) m/z: [M + Na]$^+$ calcd for $C_{15}H_{11}Cl_2NOSNa$ 345.9831; found 345.9814.

**(Z)-3-((4-Bromophenyl)thio)-N-phenylacrylamide (3ai):** $R_f$ = 0.55 (20% ethyl acetate in hexane); yellow solid; yield 89% (124 mg); mp 211-215 ºC; $^1$H NMR (400 MHz, DMSO-$d_6$) δ 10.16 (s, 1H), 7.64 (d, *J* = 7.8 Hz, 2H), 7.61 (d, *J* = 7.8 Hz, 2H), 7.49-7.47 (m, 2H), 7.38 (d, *J* = 9.8 Hz, 1H), 7.32 (t, *J* = 7.8 Hz, 2H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.27 (d, *J* = 9.8 Hz, 1H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 164.0, 143.1, 139.1, 136.4, 132.2, 131.6, 128.8, 123.2, 120.8, 118.9, 117.4; IR (KBr) ῡ 3340, 2918, 2359, 1637, 692, 602; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{12}BrNOSNa$ 355.9715; found 355.9721.

**(Z)-3-((2-Aminophenyl)thio)-N-(4-ethoxyphenyl)acrylamide (3gg):** $R_f$ = 0.35 (30% ethyl acetate in hexane); white solid; yield 73% (72 mg); mp 169-173 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 7.4 Hz, 2H), 7.17 (t, *J* = 7.6 Hz, 1H), 6.85-6.82 (m, 3H), 6.75-6.70 (m, 2H), 5.98 (d, *J* = 9.8 Hz, 1H), 4.24 (s, 2H), 3.99 (q, *J* = 6.8 Hz, 2H), 1.39 (t, *J* = 7.0 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.4, 155.9, 148.2, 147.8, 135.4, 131.1, 130.9, 121.6, 119.2, 118.8, 116.5, 115.5, 114.9, 63.8, 15.0; IR (KBr) ῡ 3305, 2978, 1557, 1181, 694; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{17}H_{18}N_2O_2SNa$ 337.0981; found 337.0966.

**(Z)-*N*-Phenyl-3-((4-(trifluoromethyl)phenyl)thio)acrylamide (3ah):** $R_f$ = 0.5 (30% ethyl acetate in hexane); yellow solid; yield 87% (116 mg); mp 202-206 ºC; $^1$H NMR (400 MHz, DMSO-$d_6$) δ 10.21 (s, 1H), 7.78-7.73 (m, 4H), 7.65 (d, *J* = 7.8 Hz, 2H), 7.53 (d, *J* = 9.8 Hz, 1H), 7.32 (t, *J* = 7.8 Hz, 2H), 7.06 (t, *J* = 7.4 Hz, 1H), 6.34 (d, *J* = 9.8 Hz, 1H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 163.9, 142.4, 141.3, 139.1, 129.4, 128.8, 127.6 (q, $^2J_{CF3}$ = 32.0 Hz), 126.1 (q, $^4J_{CF3}$ = 3.4 Hz), 124.10 (q, $^1J_{CF3}$ = 272.0 Hz), 123.3, 118.9, 118.2; $^{19}$F NMR (376 MHz, DMSO-$d_6$) δ -

61.02; IR (KBr) ῡ 3344, 3045, 2922, 1643, 1225, 693; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{16}H_{12}F_3NOSNa$ 346.0484; found 346.0471.

**(Z)-3-((4-Nitrophenyl)thio)-N-phenylacrylamide (3ao):** $R_f$ = 0.4 (30% ethyl acetate in hexane); yellow solid; yield 88% (108 mg); mp 210-215 ºC; $^1$H NMR (400 MHz, DMSO-$d_6$) δ 10.26 (s, 1H), 8.23 (d, *J* = 8.8 Hz, 2H), 7.79 (d, *J* = 8.8 Hz, 2H), 7.66 (s, 1H), 7.66-7.62 (m, 2H) 7.33 (t, *J* = 7.8 Hz, 2H), 7.07 (t, *J* = 7.4 Hz, 1H), 6.40 (d, *J* = 9.8 Hz, 1H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 163.8, 146.1, 145.9, 139.6, 139.0, 130.3, 128.8, 124.2, 123.4, 119.0, 118.9; IR (KBr) ῡ 3208, 2920, 1568, 694; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{15}H_{13}N_2O_3S$ 301.0641; found 301.0641.

**(Z)-*N*-Phenyl-3-(pyridin-2-ylthio)acrylamide (3ap):** $R_f$ = 0.45 (30% ethyl acetate in hexane); yellow solid; yield 90% (95 mg); mp 103-108 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.49-8.48 (m, 1H), 8.46-8.43 (m, 1H), 7.87 (s, 1H), 7.62-7.60 (m, 2H), 7.56-7.52 (m, 1H), 7.29-7.26 (m, 3H), 7.09-7.05 (m, 2H), 6.22 (d, *J* = 9.8 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.8, 156.0, 149.6, 139.2, 138.1, 136.9, 129.0, 124.3, 123.4, 121.3, 119.9, 116.4; IR (KBr) ῡ 3303, 2955, 1645, 1136, 691; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{14}H_{12}N_2OSNa$ 279.0563; found 279.0562.

**(Z)-3-((2,4-Diphenyloxazol-5-yl)thio)-N-phenylacrylamide (3aq):** $R_f$ = 0.5 (20% ethyl acetate in hexane); yellow solid; yield 93% (153 mg); mp 168-173 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 9.8 Hz, 1H), 7.67 (d, *J* = 6.8 Hz, 2H), 7.59 (s, 1H), 7.59-7.57 (m, 3H), 7.41-7.33 (m, 9H), 7.14 (t, *J* = 7.0 Hz, 1H), 6.24 (d, *J* = 9.8 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.1,

158.8, 147.9, 139.0, 137.6, 136.51, 132.1, 129.3, 128.90(×2), 128.86, 128.8, 128.6, 128.1, 126.6, 124.8, 120.0, 117.7; IR (KBr) ῡ 3274, 3045, 2922, 1596, 689; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{24}H_{18}N_2O_2SNa$ 421.0981; found 421.0959.

**(2Z, 2'Z)-3,3'-(1,4-Phenylenebis(sulfanediyl))bis(N-phenylacrylamide) (3ar):** $R_f$ = 0.5 (30% ethyl acetate in hexane); pale yellow solid; yield 96% (175 mg); mp >230 ºC; $^1$H NMR (400 MHz, DMSO-$d_6$) δ 10.16 (s, 2H), 7.65 (d, *J* = 7.4 Hz, 4H), 7.64-7.56 (m, 4H), 7.41 (d, *J* = 9.8 Hz, 2H), 7.32 (t, *J* = 7.8 Hz, 4H), 7.05 (t, *J* = 7.4 Hz, 2H), 6.28 (d, *J* = 9.8 Hz, 2H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 164.0, 143.2, 139.2, 136.3, 130.4, 128.8, 123.2, 118.9, 117.3; IR (KBr) ῡ 3222, 3049, 1637, 1258, 692; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{24}H_{20}N_2O_2S_2Na$ 455.0858; found 455.0848.

**(Z)-3-((4-(((E)-3-Oxo-3-(phenylamino)prop-1-en-1-yl)thio)phenyl)thio)-N-phenylacrylamide (3ar):** $R_f$ = 0.55 (30% ethyl acetate in hexane); solid; yield ~1% (~2 mg); $^1$H NMR (400 MHz, DMSO-$d_6$) δ 10.19 (s, 1H), 9.93 (s, 1H), 7.68-7.64 (m, 5H), 7.61-7.57 (m, 4H), 7.48 (d, *J* = 9.8 Hz, 1H), 7.34-7.31 (m, 2H), 7.30-7.27 (m, 2H), 7.08-7.01 (m, 2H), 6.31 (d, *J* = 9.8 Hz, 1H), 6.06 (d, *J* = 14.8 Hz, 1H); $^{13}$C NMR (175 MHz, DMSO-$d_6$) δ 164.0, 161.9, 142.5, 140.5, 139.2, 139.1(×2), 138.2, 133.2, 130.5, 129.6, 128.8, 128.8, 123.3, 120.0, 119.2(×2), 118.9(×2), 117.7; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{24}H_{20}N_2O_2S_2Na$ 455.0858; found 455.0821.

**(2Z,2'Z)-3,3'-(Propane-1,3-diylbis(sulfanediyl))bis(N-phenylacrylamide) (3as):** $R_f$ = 0.7 (30% ethyl acetate in hexane); quasi-solid; yield 72% (160 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ

7.60 (d, *J* = 6.8 Hz, 4H), 7.33 (t, *J* = 7.8 Hz, 4H), 7.22 (s, 2H), 7.11 (t, *J* = 7.4 Hz, 2H), 7.00 (d, *J* = 9.8 Hz, 2H), 5.96 (d, *J* = 9.8 Hz, 2H), 2.94 (t, *J* = 6.8 Hz, 4H), 2.09 (p, *J* = 6.8 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.9, 146.9, 138.2, 129.0, 124.2, 119.9, 116.3, 34.6, 30.5; IR (KBr) ῡ 3301, 2918, 2849, 1652, 743, 686; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{21}H_{22}N_2O_2S_2Na$ 421.1015; found 421.1015.

**(2E,2'E)-3,3'-(Propane-1,3-diylbis(sulfanediyl))bis(N-phenylacrylamide) (3as):** $R_f$ = 0.75 (30% ethyl acetate in hexane); solid; yield 7% (16 mg); $^1$H NMR (400 MHz, DMSO-$d_6$) δ 9.89 (s, 2H), 7.63 (d, *J* = 7.8 Hz, 4H), 7.59 (d, *J* = 15.0 Hz, 2H), 7.30 (t, *J* = 7.8 Hz, 4H), 7.04 (t, *J* = 7.4 Hz, 2H), 6.16 (d, *J* = 15.0 Hz, 2H), 3.02 (t, *J* = 7.2 Hz, 4H), 2.07-2.01 (m, 2H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 162.1, 141.2, 139.3, 128.7, 123.1, 119.1, 118.2, 30.1, 27.9; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{21}H_{22}N_2O_2S_2Na$ 421.1015; found 421.1018.

**(Z)-3-((3-(((E)-3-Oxo-3-(phenylamino)prop-1-en-1-yl)thio)propyl)thio)-Nphenylacrylamide (3as):** $R_f$ = 0.75 (30% ethyl acetate in hexane); semi-solid; yield 12% (27 mg); $^1$H NMR (700 MHz, $CDCl_3$) δ 8.63 (s, 1H), 8.15 (s, 1H), 7.69 (d, *J* = 7.1 Hz, 2H), 7.62-7.59 (m, 3H), 7.27-7.25 (m, 4H), 7.09-7.06 (m, 2H), 6.89 (d, *J* = 9.9 Hz, 1H), 6.07 (d, *J* = 9.9 Hz, 1H), 6.04 (d, *J* = 14.7 Hz, 1H), 2.81-2.78 (m, 4H), 1.97-1.93 (m, 2H); $^{13}$C NMR (175 MHz, $CDCl_3$) δ 165.0, 163.4, 146.7, 142.2, 138.7, 138.1, 129.1, 129.0, 124.4, 124.1, 120.2, 119.9, 117.4, 116.6, 35.4, 29.5, 28.7; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{21}H_{22}N_2O_2S_2Na$ 399.1195; found 399.1197.

**(Z)-3-(Phenethylthio)-*N*-phenylacrylamide (3at):** $R_f$ = 0.45 (20% ethyl acetate in hexane); white solid; yield 67% (78 mg); mp 160-164 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.0 Hz, 2H), 7.38 (s, 1H), 7.32-7.27 (m, 4H), 7.24-7.21 (m, 3H), 7.08 (t, *J* = 7.4 Hz, 1H), 6.92 (d, *J* = 9.8 Hz, 1H), 5.91 (d, *J* = 9.8 Hz, 1H), 3.03-2.94 (m, 4H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 165.0, 147.4, 139.7, 138.2, 129.0, 128.7, 128.7, 126.7, 124.1, 119.6, 115.7, 37.9, 36.9; IR (KBr) ῡ 3222, 3023, 2944, 1634, 692; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{17}H_{17}NOSNa$ 306.0923; found 306.0922.

**(Z)-3-(cyclohexylthio)-*N*-phenylacrylamide (3au):** $R_f$ = 0.55 (10% ethyl acetate in hexane); white solid; yield 62% (67 mg); mp 137-140 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.2 Hz, 2H), 7.42 (s, 1H), 7.29-7.25 (m, 2H), 7.07-7.04 (m, 2H), 5.92 (d, *J* = 10.1 Hz, 1H), 2.83-2.76 (m, 1H), 2.03-1.99 (m , 2H), 1.82-1.78 (m, 2H), 1.63-1.59 (m, 1H), 1.50-1.40 (m, 2H), 1.38-1.21 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.8, 145.7, 138.3, 129.0, 124.0, 119.7, 115.3, 47.9, 33.6, 25.9, 25.5; IR (KBr) ῡ 3308, 2927, 2851, 1668, 691; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{19}NOSNa$ 284.1080; found 284.1091.

**(Z)-3-(*iso*-Butylthio)-*N*-phenylacrylamide (3av):** $R_f$ = 0.75 (20% ethyl acetate in hexane); white solid; yield 65% (63 mg); mp 120-123 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 6.8 Hz, 2H), 7.29 (t, *J* = 7.8 Hz, 2H), 7.23 (s, 1H), 7.08 (t, *J* = 7.4 Hz, 1H), 6.97 (d, *J* = 10.0 Hz, 1H), 5.89 (d, *J* = 10.0 Hz, 1H), 2.66 (d, *J* = 6.8 Hz, 2H), 1.90 (nonet, *J* = 6.6 Hz, 1H), 1.03 (d, *J* = 6.6 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.7, 148.8, 138.3, 129.1, 124.1, 119.6, 115.2, 46.0, 29.5, 21.8; IR (KBr) ῡ 3341, 3054, 2359, 1627, 750, 689; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{13}H_{17}NOSNa$ 258.0923; found 258.0928.

**(Z)-3-((Furan-2-ylmethyl)thio)-*N*-phenylacrylamide (3aw):** $R_f$ = 0.35 (20% ethyl acetate in hexane); white solid; yield 92% (98 mg); mp 111-115 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 6.6 Hz, 2H), 7.37-7.36 (m, 1H ), 7.29 (t, *J* = 8.0 Hz, 2H), 7.23 (s, 1H), 7.09-7.06 (m, 2H), 6.33-6.31 (m, 1H), 6.25 (d, *J* = 3.2 Hz, 1H), 5.94 (d, *J* = 9.8 Hz, 1H), 3.91 (s, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 164.5, 151.1, 146.1, 142.7, 138.1, 129.0, 124.2, 119.7, 116.0, 110.7, 108.2, 32.1; IR (KBr) ῡ 3312, 2923, 1642, 691; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{14}H_{13}NO_2SNa$ 282.0559; found 282.0562.

**(Z)-*N*-Phenyl-3-((4-(trifluoromethyl)phenyl)sulfinyl)acrylamide 6:** $R_f$ = 0.45 (50% ethyl acetate in hexane); white solid; yield 95% (60 mg); mp >230 ºC; $^1$H NMR (400 MHz, DMSO-$d_6$) δ 10.68 (s, 1H), 8.06 (d, *J* = 8.2 Hz, 2H), 7.95 (d, *J* = 8.0 Hz, 2H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.37 (t, *J* = 7.8 Hz, 2H), 7.13 (t, *J* = 7.4 Hz, 1H), 6.93 (d, *J* = 9.8 Hz, 1H), 6.69 (d, *J* = 9.8 Hz, 1H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 161.7, 152.7, 150.3, 138.2, 130.9 (q, $^2J_{CF3}$ = 32.0 Hz), 129.0, 128.7, 126.3 (q, $^3J_{CF3}$ = 3.4 Hz), 125.8, 124.4, 123.8 (q, $^1J_{CF3}$ = 272.6 Hz), 119.6; $^{19}$F NMR (376 MHz, $CDCl_3$) δ -56.54; IR (KBr) ῡ 3305, 3033, 2974, 1668, 1000, 696; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{13}F_3NO_2S$ 340.0614; found 340.0587.

**(Z)-3-([1,1'-Biphenyl]-4-ylthio)-N-phenylacrylamide 7:** $R_f$ = 0.45 (20% ethyl acetate in hexane); white solid; yield 76% (60 mg); mp 177-180 ºC; $^1$H NMR (400 MHz, DMSO-$d_6$) δ 10.15 (s, 1H), 7.74-7.60 (m, 8H), 7.55-7.44 (m, 3H), 7.39 (t, *J* = 6.8 Hz, 1H), 7.33 (t, *J* = 7.8 Hz, 2H), 7.06 (t, *J* = 7.4 Hz, 1H), 6.28 (d, *J* = 9.8 Hz, 1H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 164.1, 143.7, 139.3, 139.20, 139.18, 136.0, 130.2, 129.0, 128.8, 127.8, 127.6, 126.6, 123.2, 118.9,

117.1; IR (KBr) ῡ 3397, 3040, 2916, 1657, 697; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{21}H_{17}NOSNa$ 354.0923; found 354.0919.

***N*-Phenylpropiolamide 1a:**[23] $R_f$ = 0.75 (20% ethyl acetate in hexane); yellow solid; yield 64% (301 mg); mp 81-84 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.52 (d, *J* = 7.8 Hz, 2H), 7.34 (t, *J* = 7.8 Hz, 2H), 7.15 (t, *J* = 7.4 Hz, 1H), 2.92 (s, 1H).

***N*-(*p*-Tolyl)propiolamide 1b:**[24] $R_f$ = 0.35 (20% ethyl acetate in hexane); yellow solid; yield 61% (270 mg); mp 126-129 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.14 (d, *J* = 8.4 Hz, 2H), 2.90 (s, 1H), 2.32 (s, 3H).

***N*-(*o*-Tolyl)propiolamide 1c:** $R_f$ = 0.35 (20% ethyl acetate in hexane); yellow solid; yield 89% (400 mg); mp 133-135 ºC; $^1$H NMR (400 MHz, DMSO-$d_6$) δ 10.24 (s, 1H), 7.29-7.23 (m, 2H), 7.20-7.13 (m, 2H), 4.34 (s, 1H), 2.19 (s, 3H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 150.2, 134.8, 132.7, 130.4, 126.3, 126.1, 125.8, 78.4, 76.9, 17.8; IR (KBr) ῡ 3256, 3023, 2926, 2359, 2107, 1677; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{10}H_{10}NO$ 160.0757; found 160.0764.

***N*-(2,4-Dimethylphenyl)propiolamide 1d:** $R_f$ = 0.35 (20% ethyl acetate in hexane); yellow solid; yield 70% (300 mg); mp 151-153 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.6 Hz, 1H), 7.24 (s, 1H ), 7.03-7.01 (m, 2H), 2.91 (s, 1H), 2.30 (s, 3H), 2.25 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 150.1, 136.1, 132.0, 131.4, 129.5, 127.6, 123.6, 77.8, 74.0, 21.0, 17.8; IR (KBr) ῡ 3279, 3088, 2969, 2107, 1672, 745; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_{12}NO$ 174.0913; found 174.0937.

***N*-(4-*iso*-Propylphenyl)propiolamide 1e:** $R_f$ = 0.35 (20% ethyl acetate in hexane); semi solid; yield 67% (280 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 2.90 (s, 1H), 2.93-2.83 (m, 1H), 1.23 (d, *J* = 6.8 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 150.3, 145.9, 134.9, 126.9, 120.5, 77.7, 74.4, 33.6, 24.0; IR (KBr) ῡ 3273, 2959, 2108, 1699, 833; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{12}H_{14}NO$ 188.1070; found 188.1088.

***N*-(4-(*tert*-Butyl)phenyl)propiolamide 1f:** $R_f$ = 0.4 (20% ethyl acetate in hexane); semi solid; yield 58% (234 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.45 (d, *J* = 8.6 Hz, 2H), 7.34 (d, *J* = 8.6 Hz, 2H), 2.90 (s, 1H), 1.30 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 150.0, 148.3, 134.5, 126.0, 120.1, 77.8, 74.2, 34.5, 31.4; IR (KBr) ῡ 3299, 2981, 2109, 1599, 741; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_{16}NO$ 202.1226; found 202.1245.

***N*-(4-Ethoxyphenyl)propiolamide 1g:** $R_f$ = 0.30 (20% ethyl acetate in hexane); grey solid; yield 85% (350 mg); mp 95-103 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.42-7.39 (m, 3H), 6.87-6.85 (d, *J* = 9.0 Hz, 2H), 4.01 (q, *J* = 7.0 Hz, 2H), 2.90 (s, 1H), 1.40 (t, *J* = 7.0 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 156.4, 149.9, 130.1, 122.0, 114.9, 77.8, 74.2, 63.9, 14.9; IR (KBr) ῡ 3292, 3064, 2970, 2340, 2109, 1635; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_{12}NO_2$ 190.0863; found 190.0865.

***N*-(4-(Trifluoromethoxy)phenyl)propiolamide 1h:** $R_f$ = 0.4 (30% ethyl acetate in hexane); yellow solid; yield 91% (210 mg); mp 123-127 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.58-7.56 (m, 2H), 7.19 (d, *J* = 8.6 Hz, 2H), 2.95 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 149.9, 146.0, 135.7, 122.0, 121.4, 120.6 (q, *J* = 257.8 Hz), 77.4, 74.8; IR (KBr) ῡ 3303, 3073, 2111,

1670, 1240; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{10}H_7F_3NO_2$ 230.0423; found 230.0437.

***N*-(4-Fluorophenyl)propiolamide 1i:** $R_f$ = 0.35 (20% ethyl acetate in hexane); yellow solid; yield 79% (350 mg); mp 175-177 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.50-7.47 (m, 2H), 7.03 (t, *J* = 8.6 Hz, 2H), 2.93 (s, 1H).

***N*-(4-Bromophenyl)propiolamide 1j**:[24] $R_f$ = 0.35 (20% ethyl acetate in hexane); yellow solid; yield 62% (241 mg); mp 184-188 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.46 (d, *J* = 9.0 Hz, 2H), 7.41 (d, *J* = 9.0 Hz, 2H), 2.95 (s, 1H).

***N*-(4-Iodophenyl)propiolamide 1k:** $R_f$ = 0.25 (20% ethyl acetate in hexane); white solid; yield 64% (237 mg); mp 206-211 ºC; $^1$H NMR (400 MHz, DMSO-$d_6$) δ 10.90 (s, 1H), 7.66 (d, *J* = 8.6 Hz, 2H), 7.43 (d, *J* = 8.6 Hz, 2H), 4.44 (s, 1H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 149.7, 138.0, 137.5, 121.8, 88.1, 78.2, 77.5; IR (KBr) ῡ 3294, 2922, 2108, 1655, 508; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_9H_7INO$ 271.9567; found 271.9558.

***N*-(3-Chlorophenyl)propiolamide 1l:**[24] $R_f$ = 0.6 (20% ethyl acetate in hexane); yellow solid; yield 54% (230 mg); mp 164-166 ºC; $^1$H NMR (400 MHz, DMSO-$d_6$) δ 10.99 (s, 1H), 7.75 (t, *J* = 2.0 Hz, 1H), 7.50-7.48 (m, 1H), 7.36 (t, *J* = 8.0 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 1H), 4.48 (s, 1H).

***N*-(3,4-Dichlorophenyl)propiolamide 1m:** $R_f$ = 0.3 (20% ethyl acetate in hexane); yellow solid; yield 88% (350 mg); mp 179-184 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 2.0 Hz, 1H),

7.55 (s, 1H), 7.40 (d, *J* = 8.6 Hz, 1H), 7.36-7.33 (m, 1H), 2.98 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 149.8, 137.6, 132.1, 130.1, 127.0, 121.5, 119.3, 77.8, 74.3; IR (KBr) ῡ 3284, 3096, 2110, 1643, 675; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_9H_6Cl_2NO$ 213.9821; found 213.9812.

***N*-(3-Chloro-4-fluorophenyl)propiolamide 1n:** $R_f$ = 0.3 (30% ethyl acetate in hexane); yellow solid; yield 68% (280 mg); mp 153-155 ºC; $^1$H NMR (400 MHz, DMSO-$d_6$) δ 11.00 (s, 1H), 7.86 (d, *J* = 5.2 Hz, 1H), 7.52-7.50 (m, 1H), 7.40-7.38 (m, 1H), 4.48 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 154.8 (d, $^1J_{CF}$ = 246.4 Hz), 145.0, 134.6, 122.3, 120.8 (d, $^2J_{CF}$ = 18.4 Hz), 119.9 (d, $^3J_{CF}$ = 6.8 Hz), 116.46 (d, $^2J_{CF}$ = 22.0 Hz), 77.9, 74.2; IR (KBr) ῡ 3268, 2925, 2850, 2108, 1645, 1238, 686; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_9H_6ClFNO$ 198.0116; found 198.0106.

***N*-(4-Bromo-2-methylphenyl)propiolamide 1o:** $R_f$ = 0.36 (20% ethyl acetate in hexane); yellow solid; yield 57% (220 mg); mp 123-126 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.46-7.44 (m, 2H), 7.23 (dd, *J* = 8.6, 2.6 Hz, 1H), 2.93 (s, 1H), 2.36 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 149.8, 139.0, 136.2, 132.9, 122.3, 120.6, 119.1, 77.6, 74.5, 23.2; IR (KBr) ῡ 3280, 2925, 2853, 2109, 1607, 671; HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{10}H_9BrNO$ 237.9862; found 237.9879.

**3-Phenyl-N-(p-tolyl)propiolamide 1r:**[2] $R_f$ = 0.75 (20% ethyl acetate in hexane); yellow solid; yield 76% (499 mg); mp 146-148 ºC (lit.[2]143-145); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.64 (s, 1H),

7.58-7.56 (m, 2H), 7.44 (t, *J* = 7.4 Hz, 3H), 7.37 (t, *J* = 7.4 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 2.33 (s, 3H).

**1-phenyl-3,3-bis(phenylthio)propan-1-one 5:**[25] $R_f$ = 0.45 (5% ethyl acetate in hexane); colorless liquid; yield 88% (142 mg); $^1$H NMR (400 MHz, DMSO-$d_6$) δ 7.92-7.90 (m, 2H), 7.67-7.64 (m, 1H), 7.52 (t, *J* = 7.6 Hz, 2H), 7.46-7.43 (m, 4H), 7.39-7.30 (m, 6H), 5.16 (t, *J* = 6.6 Hz, 1H), 3.59 (d, *J* = 6.6 Hz, 2H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 196.1, 136.1, 133.6, 133.4, 131.9, 129.2, 128.8, 128.1, 127.9, 54.1, 43.9.

**phenyl(styryl)sulfane 4:**[10] $R_f$ = 0.85 (in hexane); colorless liquid; yield 79% (98 mg); 1H NMR (400 MHz, CDCl3) δ 7.58-7.28 (m, 10H), 6.92 (d, J = 15.5 Hz, 1H), 6.76 (d, J = 15.5 Hz, 1H), 6.63 (d, J = 10.8 Hz, 1H), 6.53 (d, J = 10.7 Hz, 1H).

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## NMR Spectrum of Selected Compounds

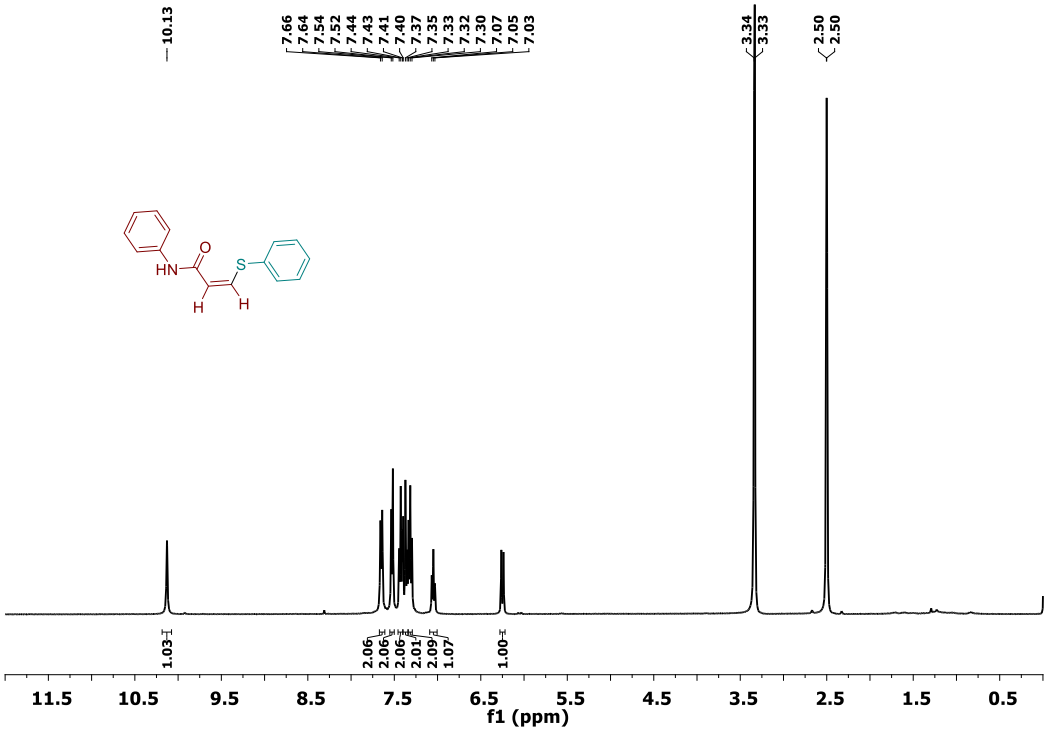



**Figure 4.8.** $^{1}$H NMR spectrum of (Z)-N-phenyl-3-(phenylthio) acrylamide (**3aa**)

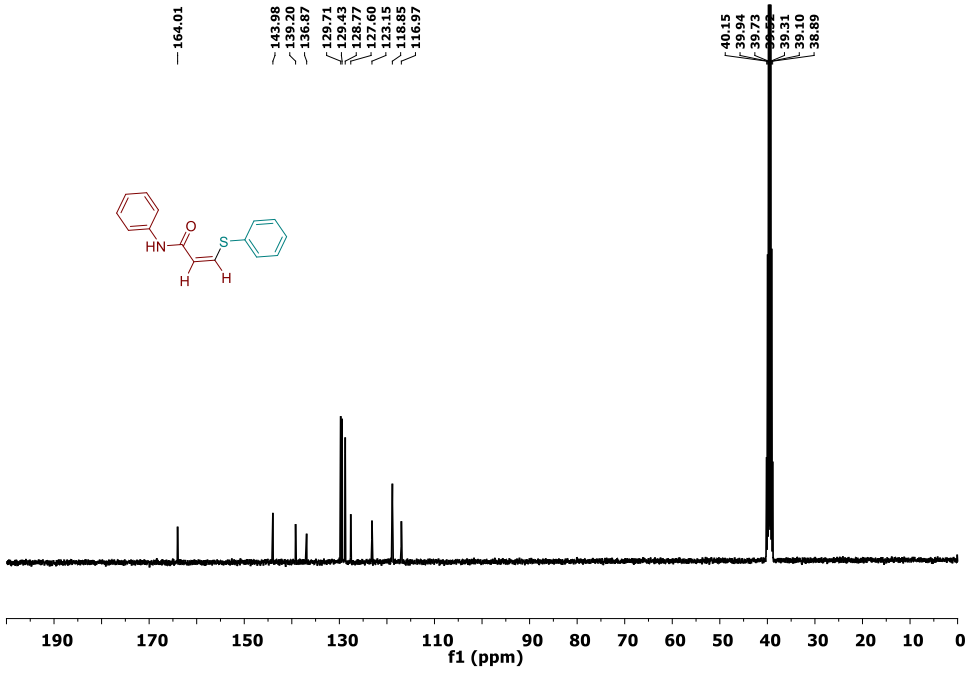



**Figure 4.9.** $^{13}$C NMR spectrum of (Z)-N-phenyl-3-(phenylthio)acrylamide (**3aa**)

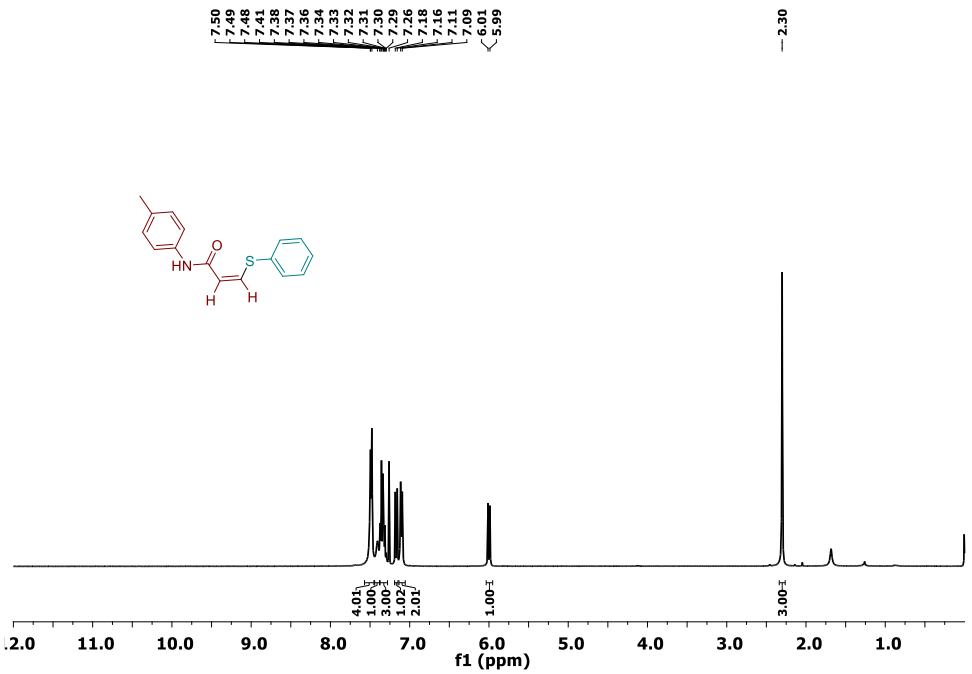



**Figure 4.10.** $^{1}$H NMR spectrum of (Z)-3-(phenylthio)-N-(p-tolyl)acrylamide (**3ba**)

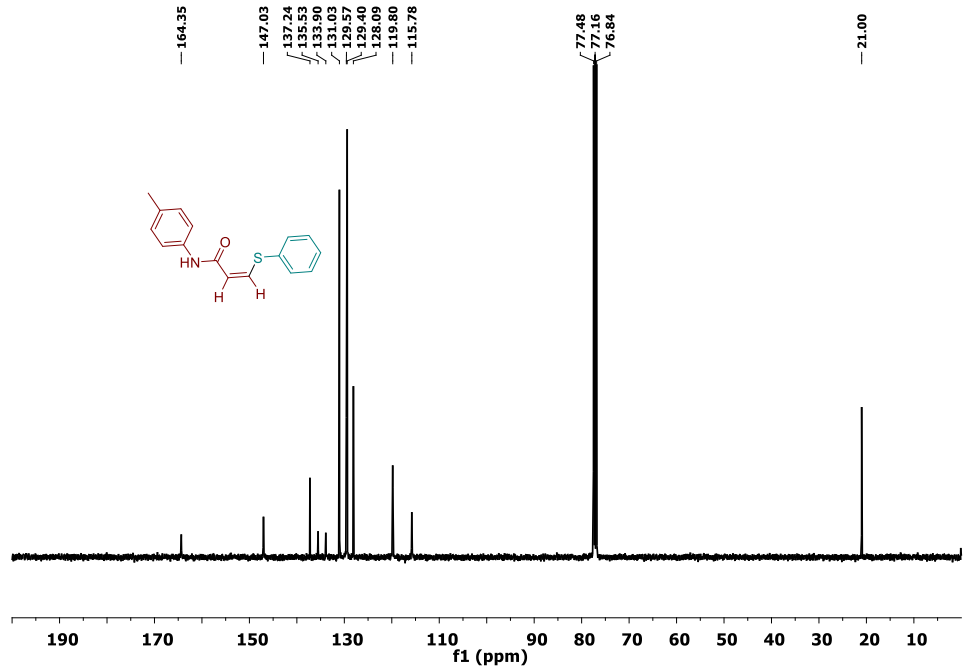



**Figure 4.11.** $^{13}$C NMR spectrum of (Z)-3-(phenylthio)-N-(p-tolyl)acrylamide (**3ba**)

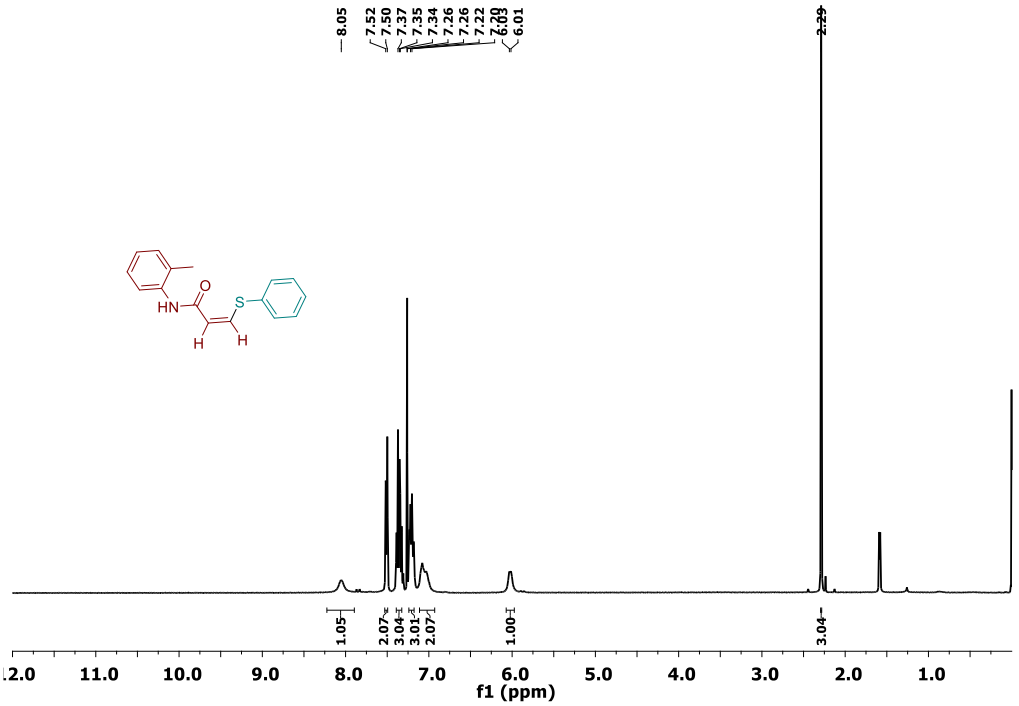



**Figure 4.12.** $^{1}$H NMR spectrum of (Z)-3-(phenylthio)-N-(o-tolyl)acrylamide (**3ca**)

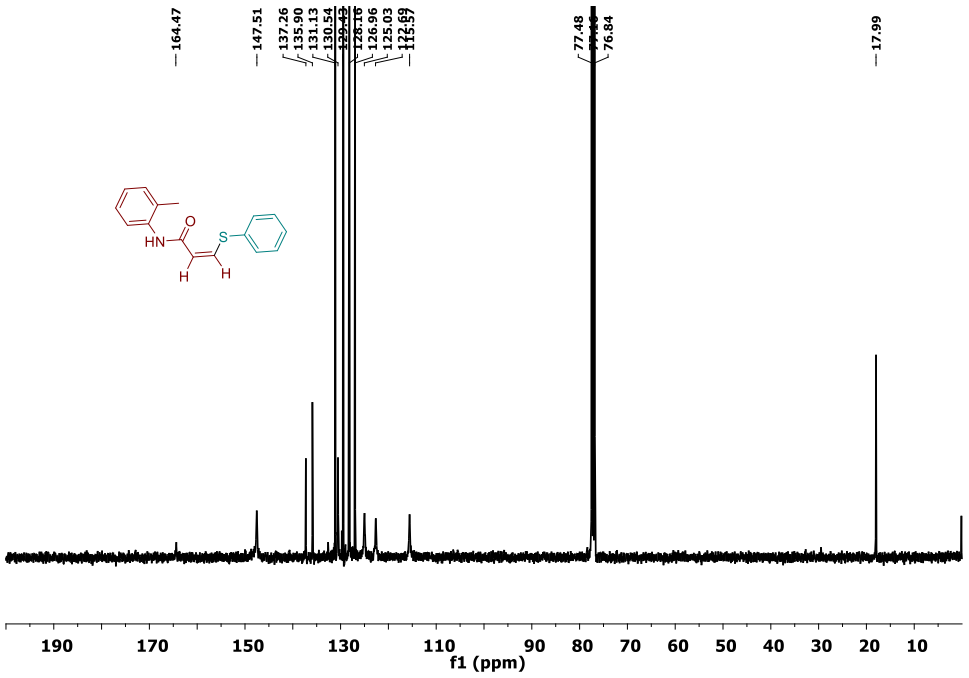



**Figure 4.13.** $^{13}$C NMR spectrum of (Z)-3-(phenylthio)-N-(o-tolyl)acrylamide (**3ca**)

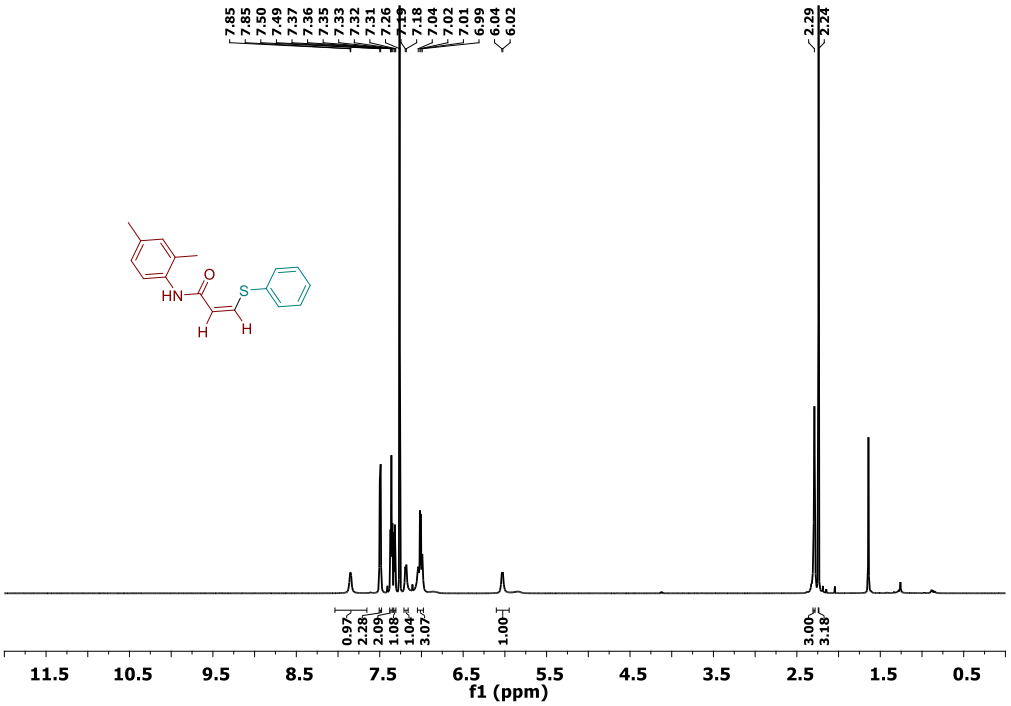



**Figure 4.14.** $^{1}$H NMR spectrum of (Z)-N-(2,4-dimethylphenyl)-3-(phenylthio)acrylamide (**3da**)

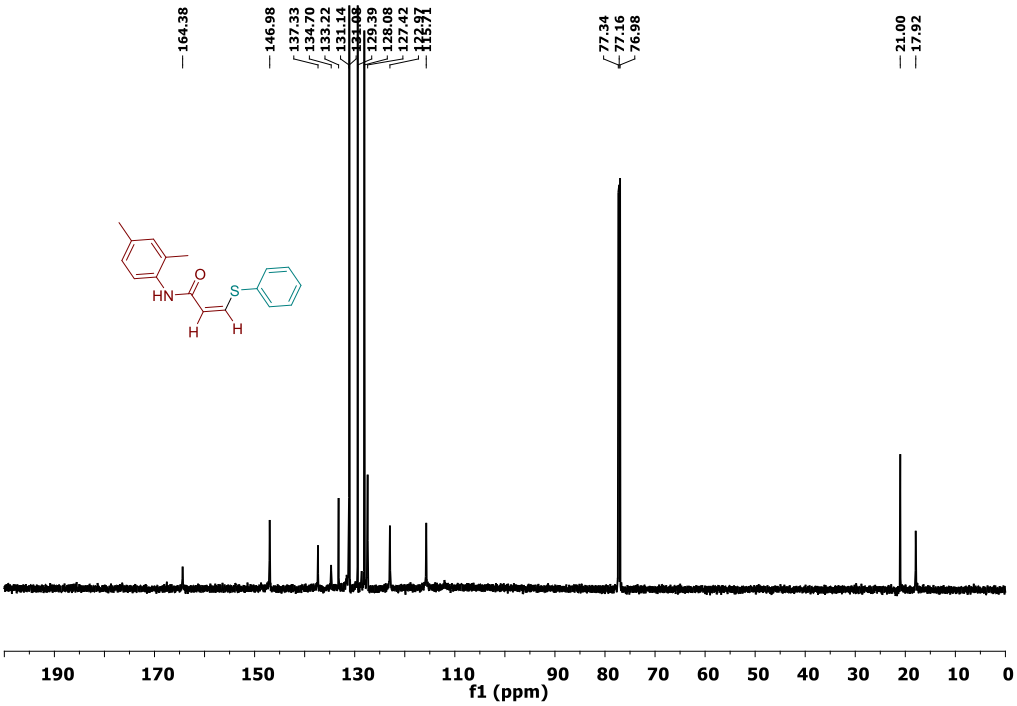



**Figure 4.15.** $^{13}$C NMR spectrum of (Z)-N-(2,4-dimethylphenyl)-3-(phenylthio)acrylamide (**3da**)

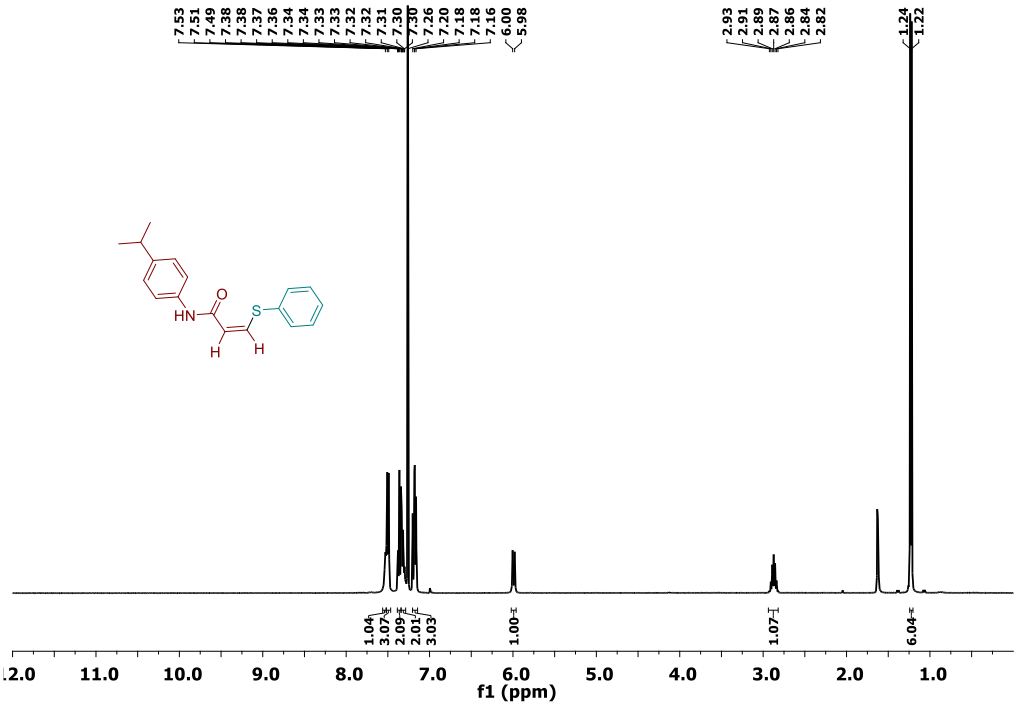



**Figure 4.16.** $^{1}$H NMR spectrum of (Z)-N-(4-isopropylphenyl)-3-(phenylthio)acrylamide (**3ea**)

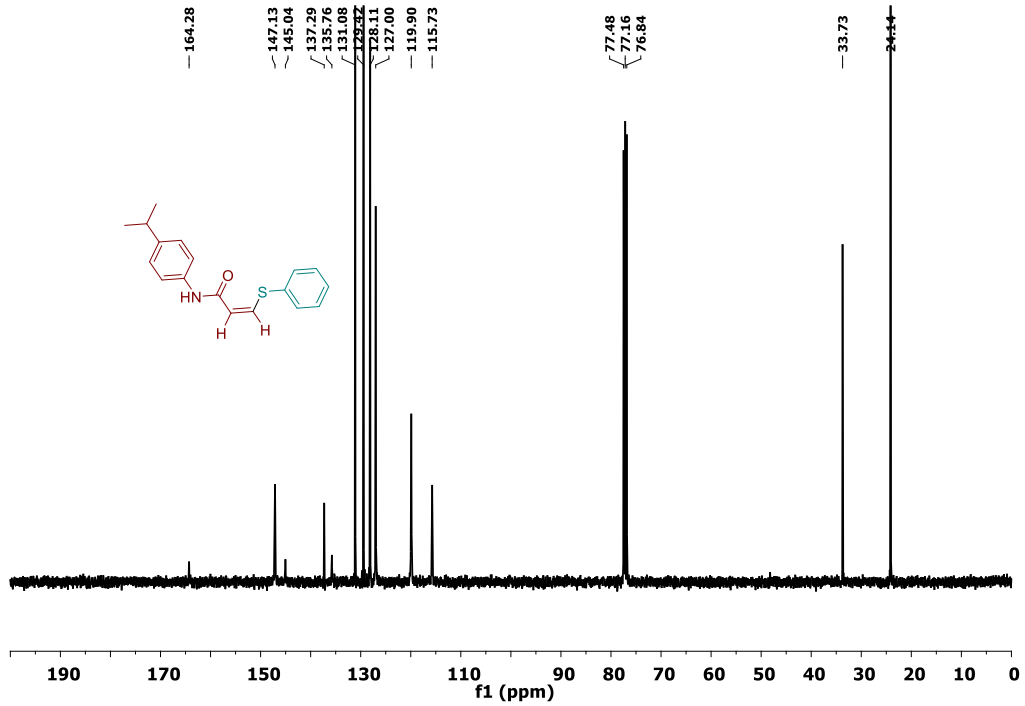



**Figure 4.17.** $^{13}$C NMR spectrum of (Z)-N-(4-isopropylphenyl)-3-(phenylthio)acrylamide (**3ea**)

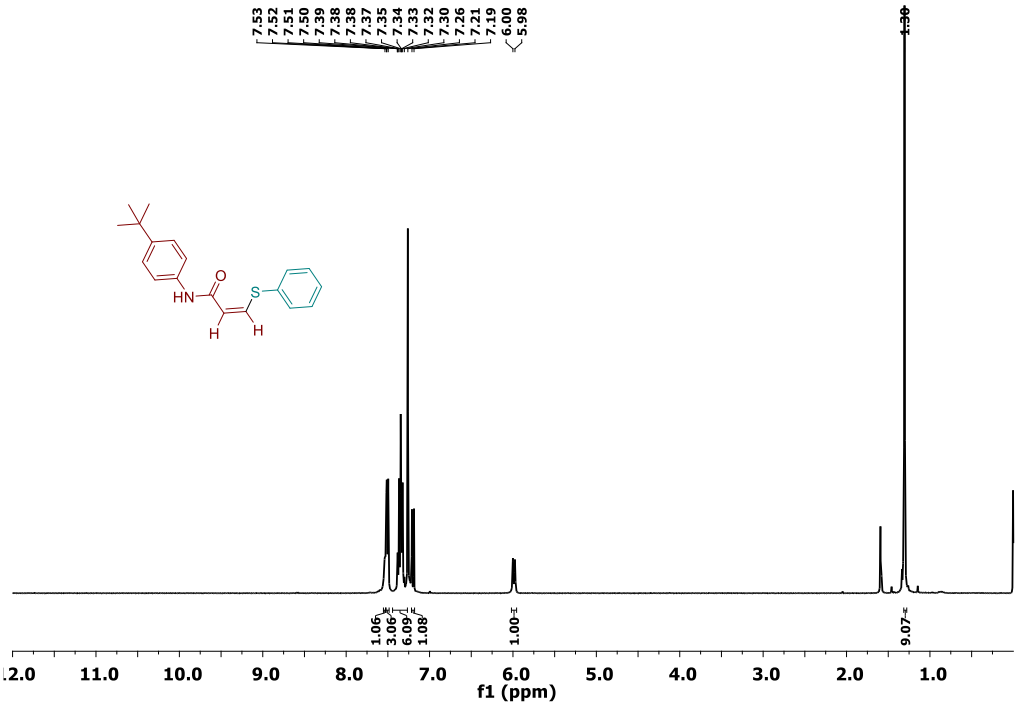



**Figure 4.18.** $^{1}$H NMR spectrum of (Z)-N-(4-(tert-butyl)phenyl)-3-(phenylthio)acrylamide (**3fa**)

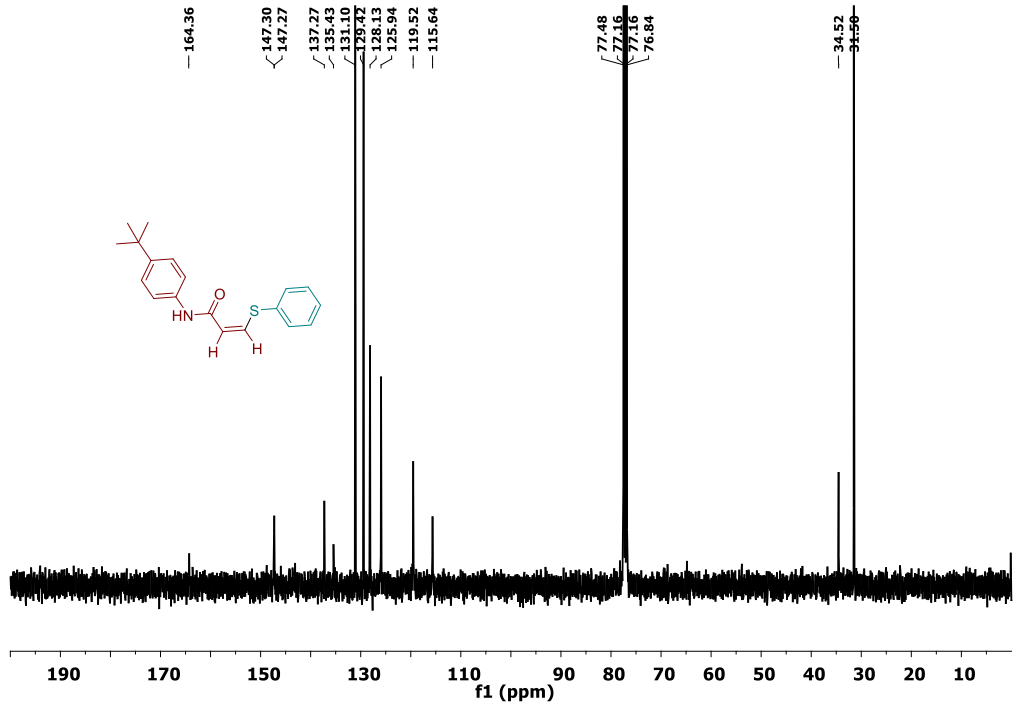



**Figure 4.19.** $^{13}$C NMR spectrum of (Z)-N-(4-(tert-butyl)phenyl)-3-(phenylthio)acrylamide (**3fa**)

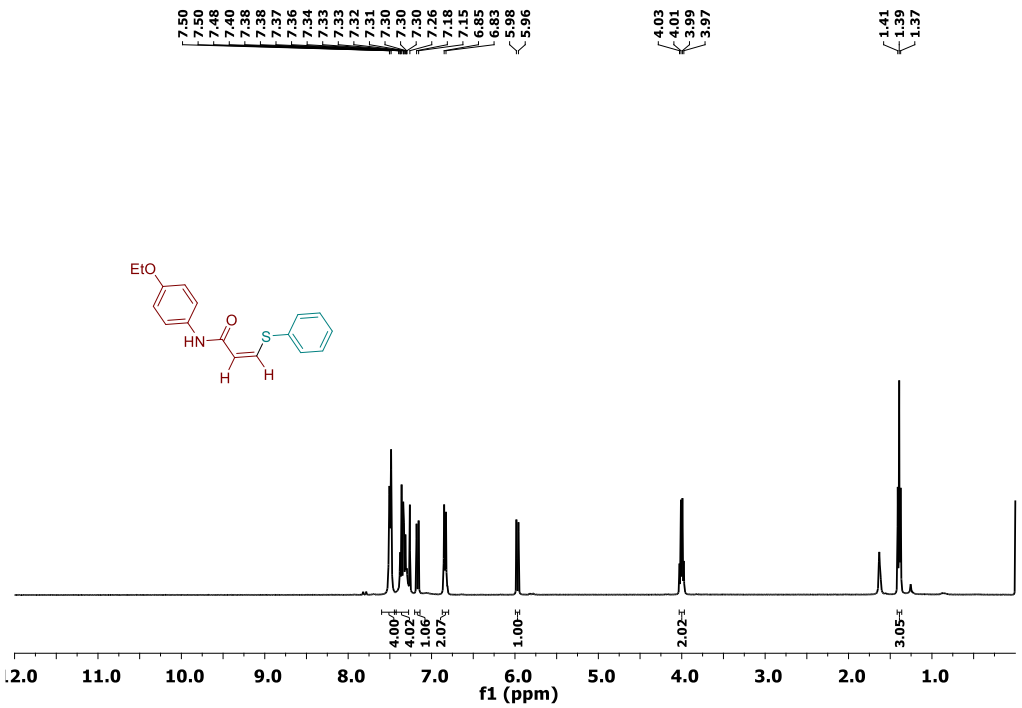



**Figure 4.20.** $^{1}$H NMR spectrum of (Z)-N-(4-ethoxyphenyl)-3-(phenylthio)acrylamide (**3ga**)

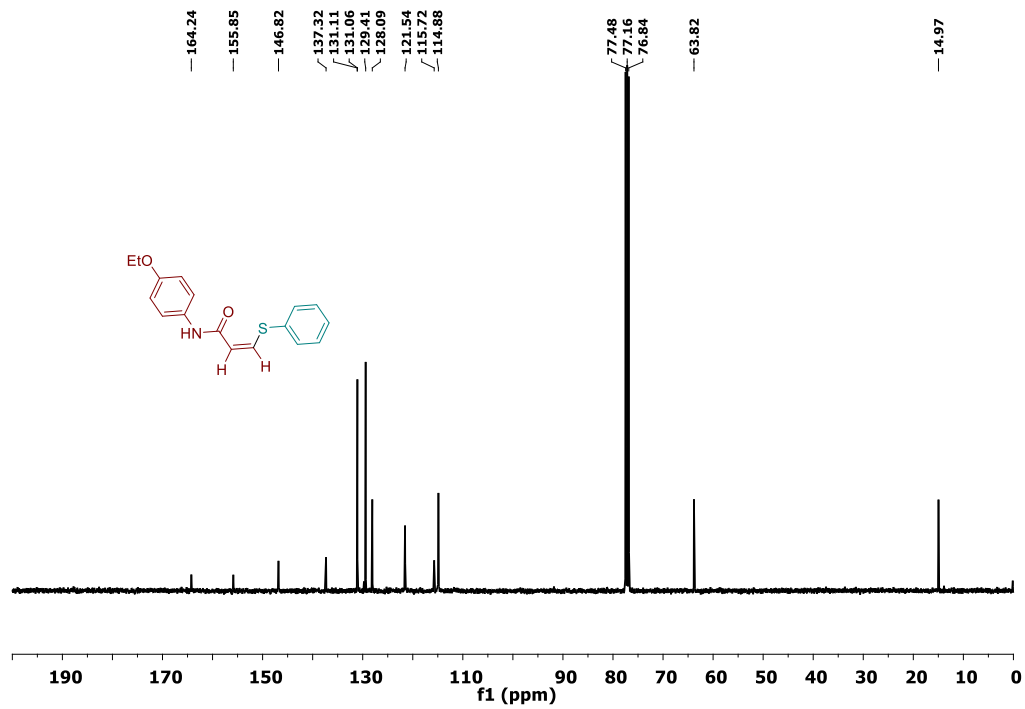



**Figure 4.21.** $^{13}$C NMR spectrum of (Z)-N-(4-ethoxyphenyl)-3-(phenylthio)acrylamide (**3ga**)

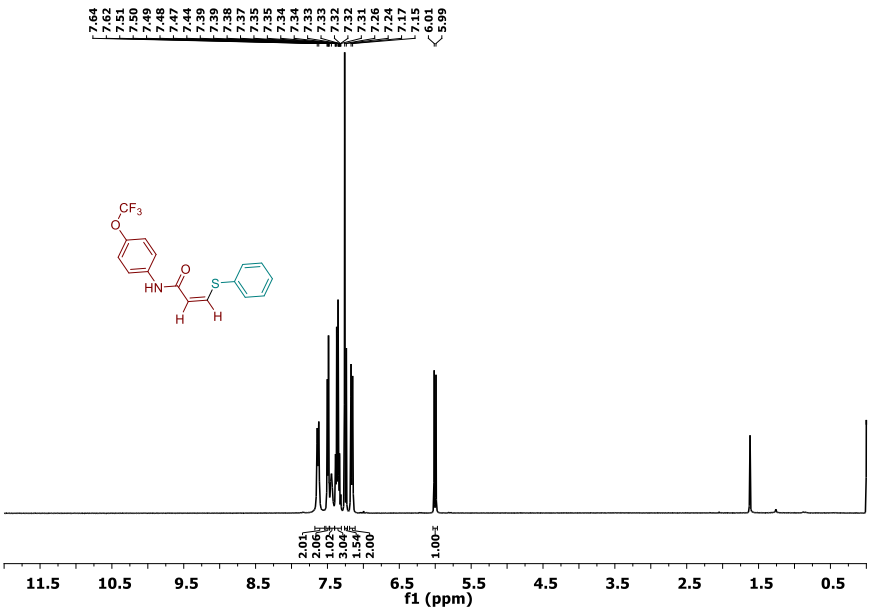



**Figure4.22.** $^{1}$H NMR spectrum of (Z)-3-(phenylthio)-N-(4-(trifluoromethoxy)phenyl)acrylamide (**3ha**)

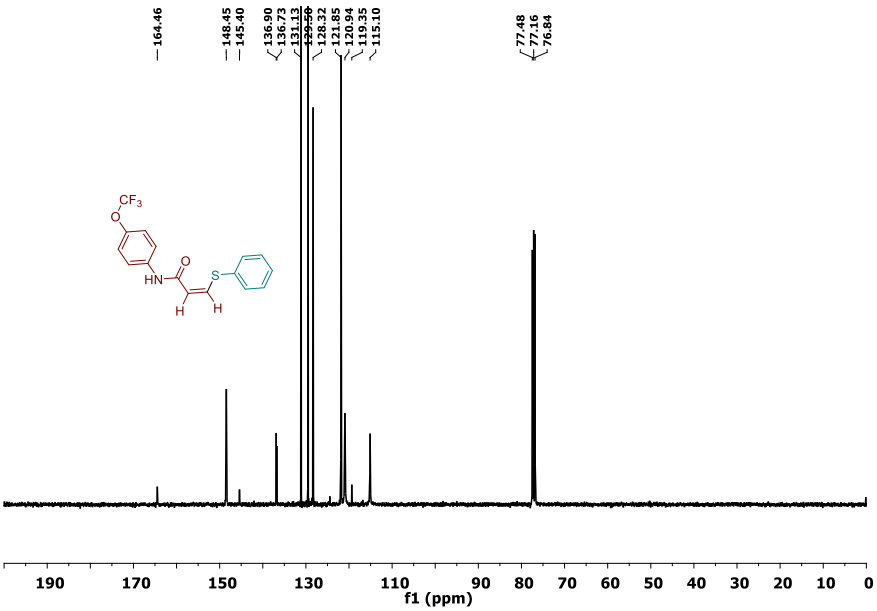



**Figure4.23.** $^{13}$C NMR spectrum of (Z)-3-(phenylthio)-N-(4-(trifluoromethoxy)phenyl)acrylamide (**3ha**)

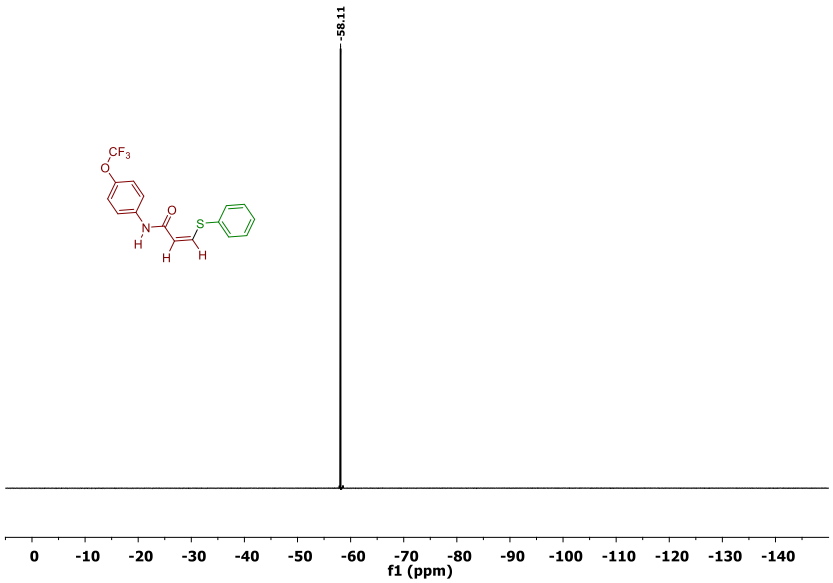



**Figure4.24.** $^{19}F$ NMR spectrum of (Z)-3-(phenylthio)-N-(4-(trifluoromethoxy)phenyl)acrylamide (**3ha**)

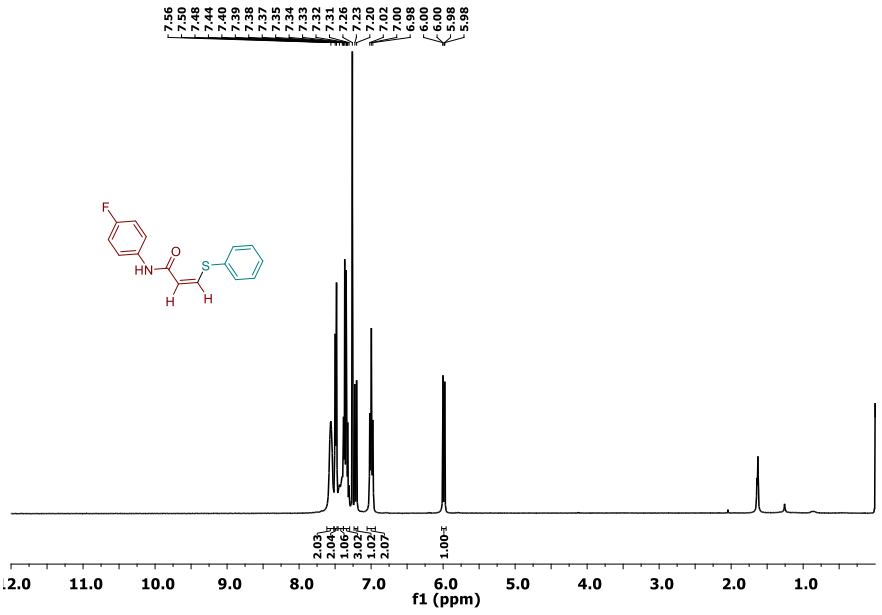



**Figure 4.25.** $^{1}H$ NMR spectrum of (Z)-N-(4-fluorophenyl)-3-(phenylthio)acrylamide (**3ia**)

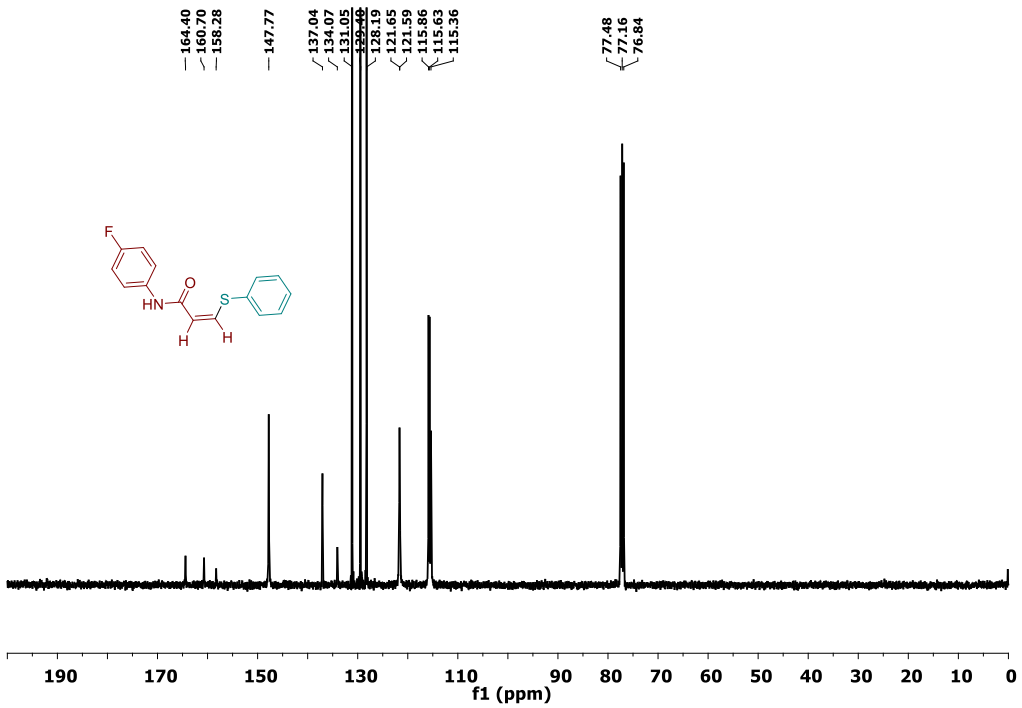



**Figure 4.26.** $^{13}$C NMR spectrum of (Z)-N-(4-fluorophenyl)-3-(phenylthio)acrylamide (**3ia**)

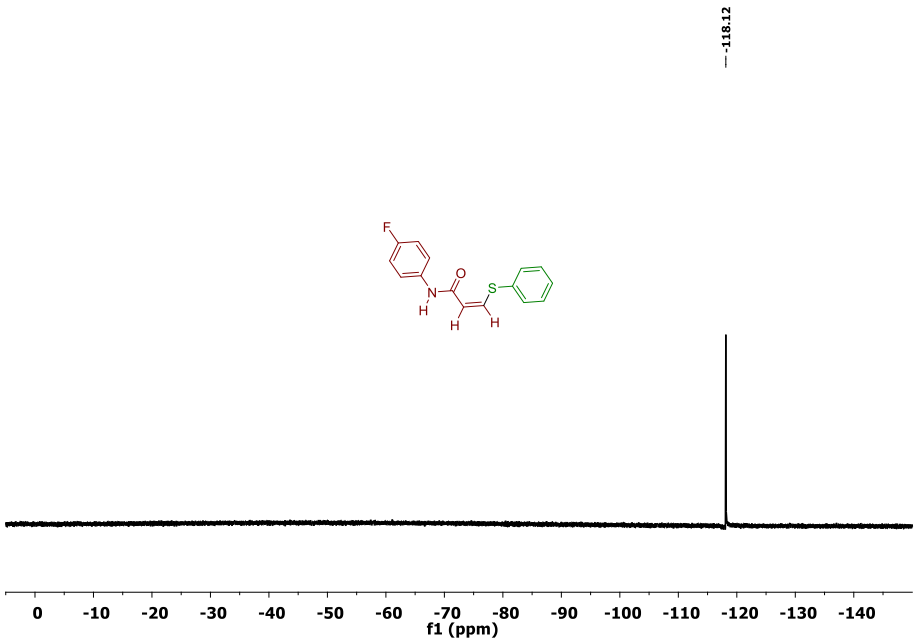



**Figure 4.27.** $^{19}$F NMR spectrum of (Z)-N-(4-fluorophenyl)-3-(phenylthio)acrylamide (**3ia**)

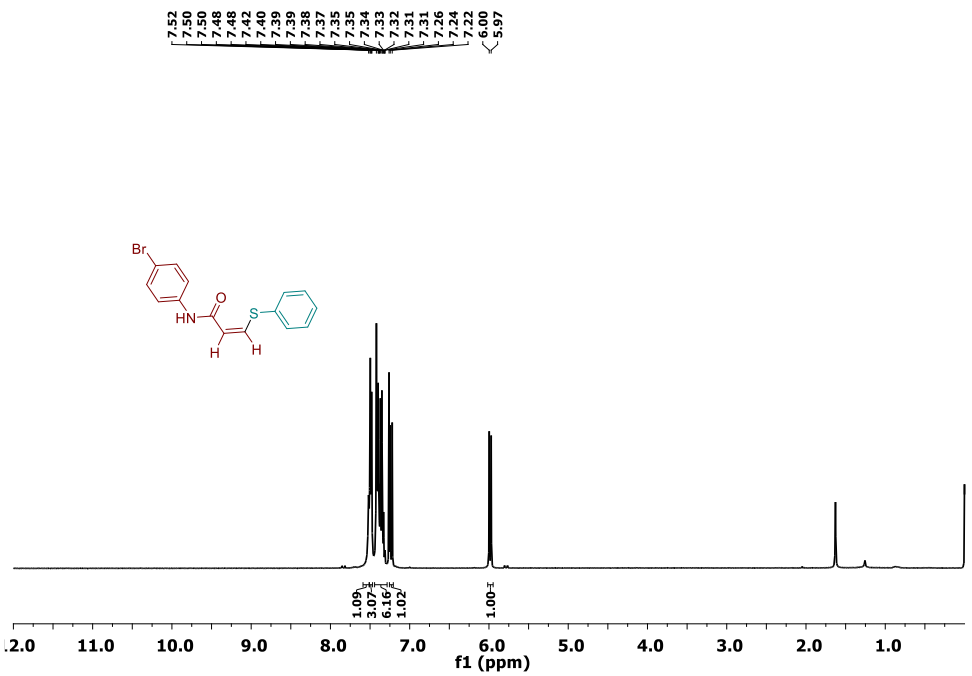



**Figure 4.28.** $^{1}$H NMR spectrum of (Z)-N-(4-bromophenyl)-3-(phenylthio)acrylamide (**3ja**)

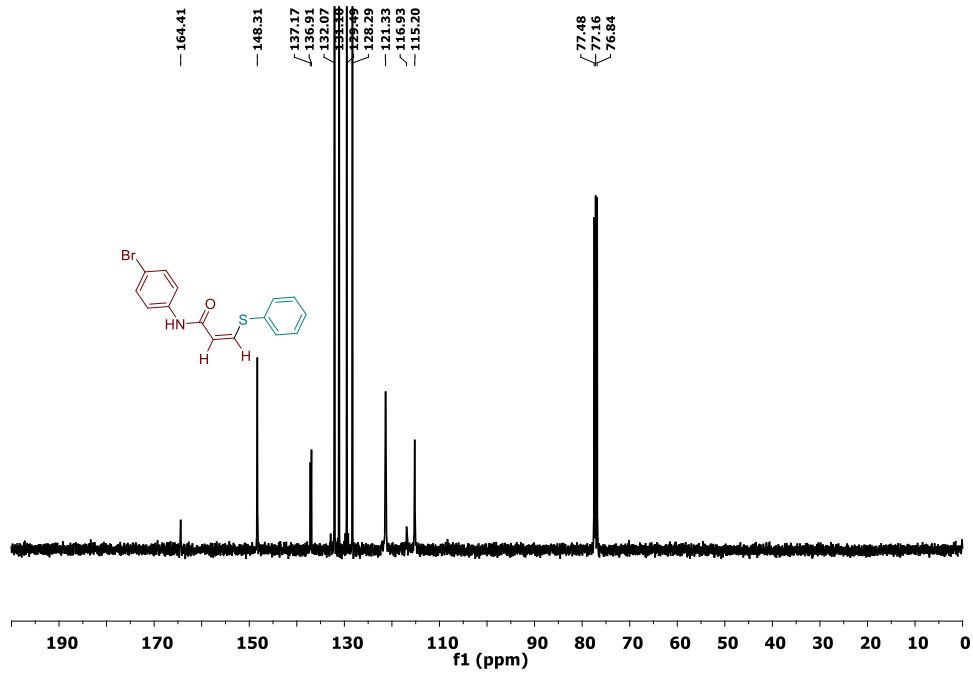



**Figure 4.29.** $^{13}$C NMR spectrum of (Z)-N-(4-bromophenyl)-3-(phenylthio)acrylamide (**3ja**)

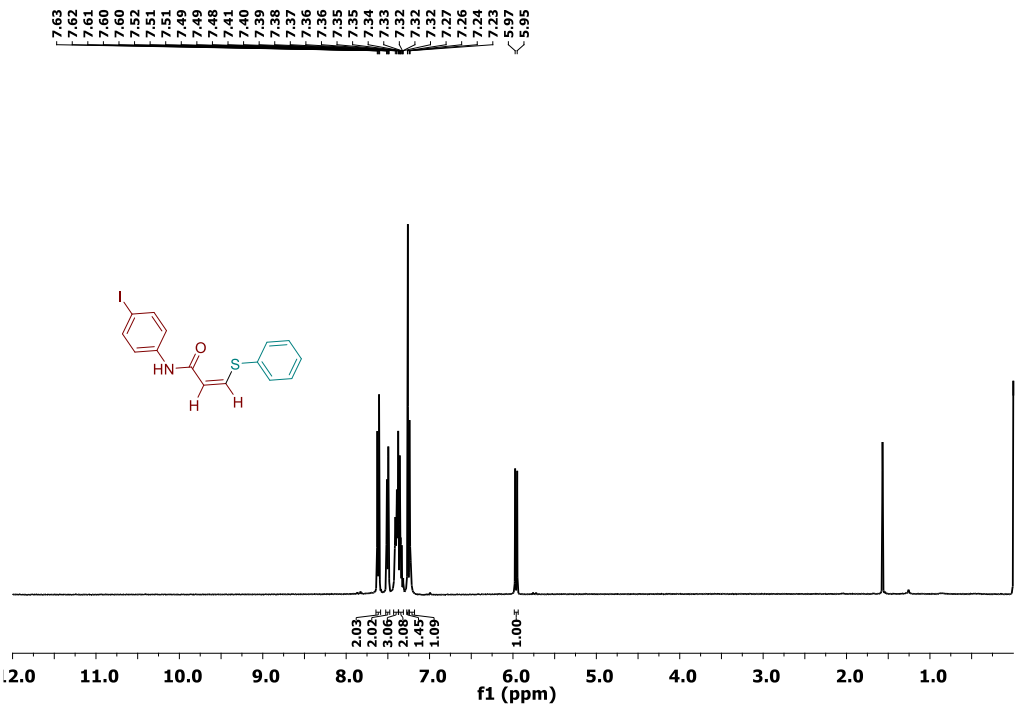



**Figure 4.30.** $^{1}$H NMR spectrum of (Z)-N-(4-iodophenyl)-3-(phenylthio)acrylamide (**3ka**)

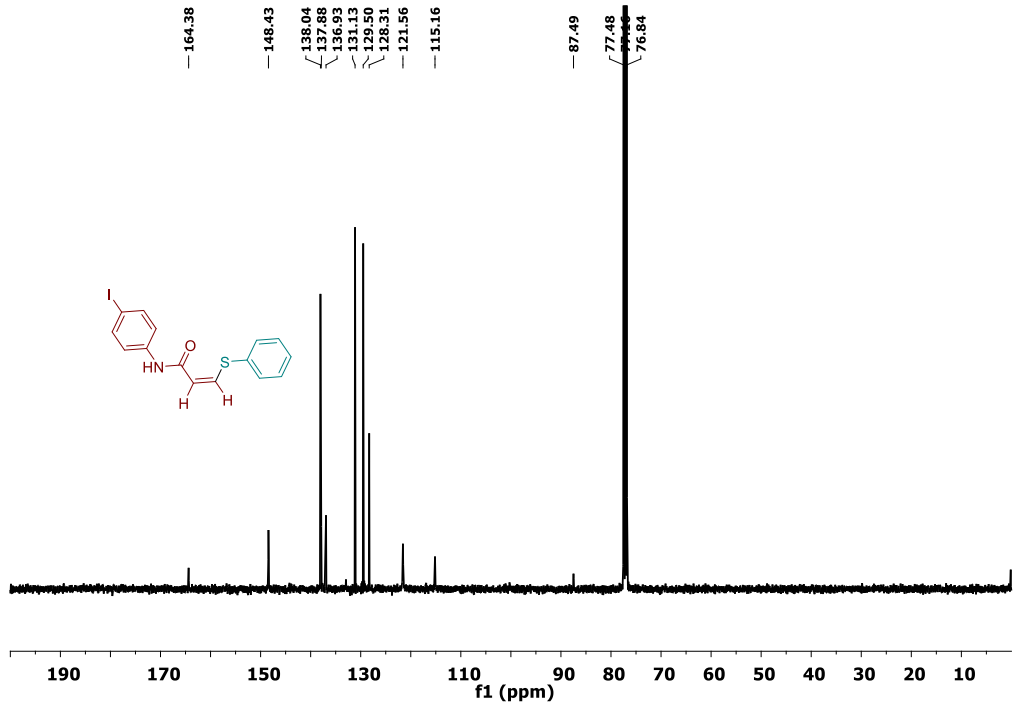



**Figure 4.31.** $^{13}$C NMR spectrum of (Z)-N-(4-iodophenyl)-3-(phenylthio)acrylamide (**3ka**)

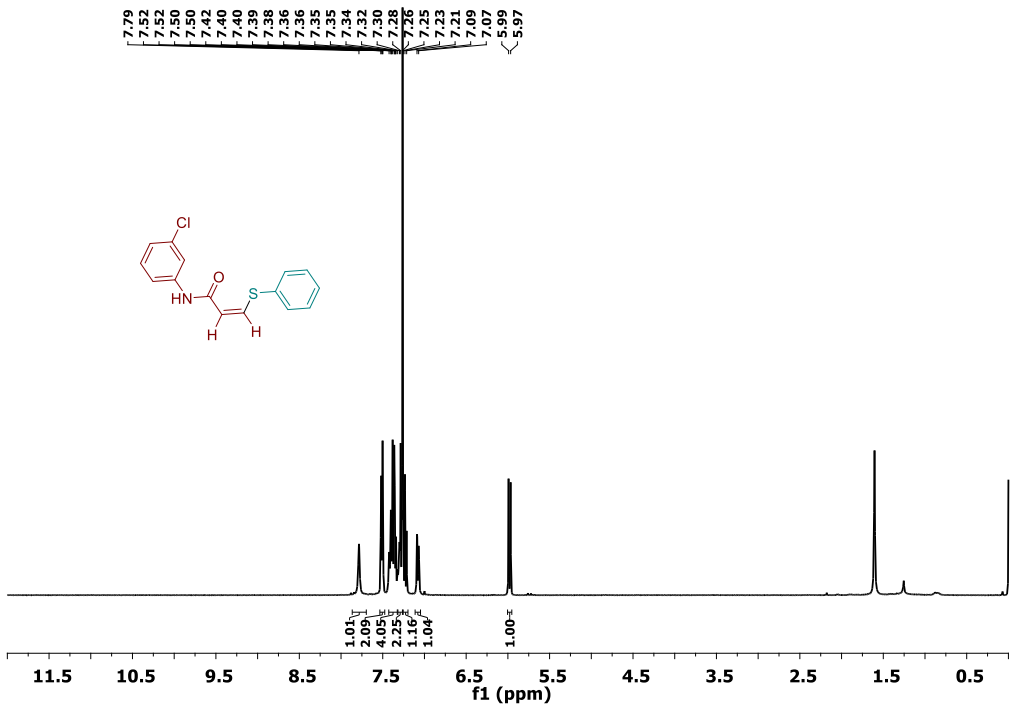



**Figure 4.32.** $^{1}$H NMR spectrum of (Z)-N-(3-chlorophenyl)-3-(phenylthio)acrylamide (**3la**)

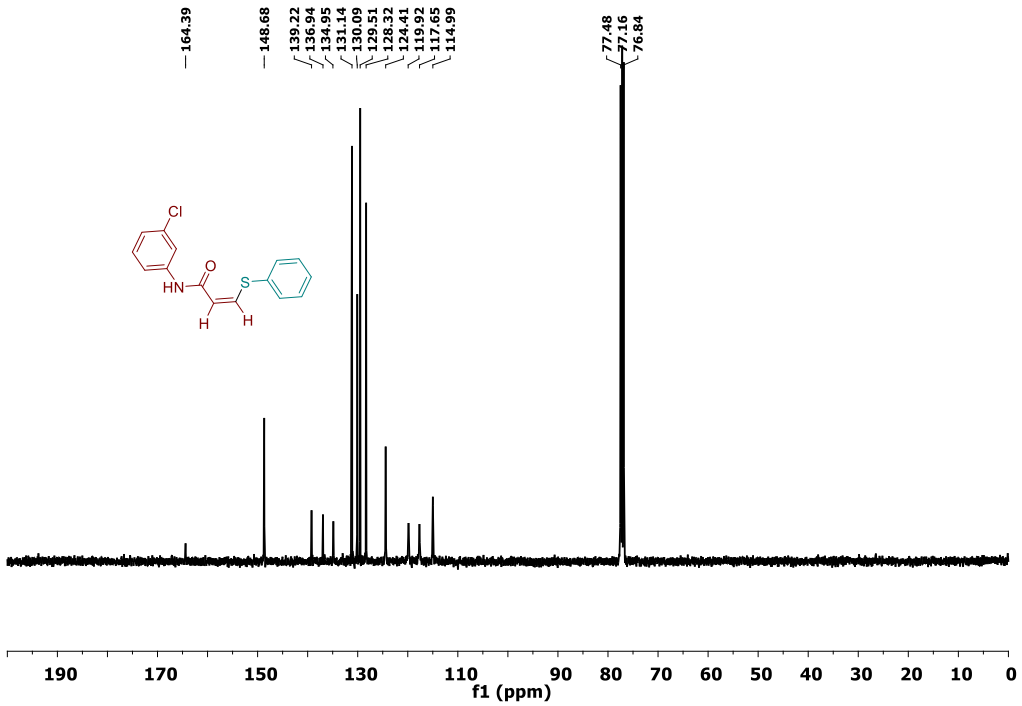



**Figure 4.33.** $^{13}$C NMR spectrum of (Z)-N-(3-chlorophenyl)-3-(phenylthio)acrylamide (**3la**)

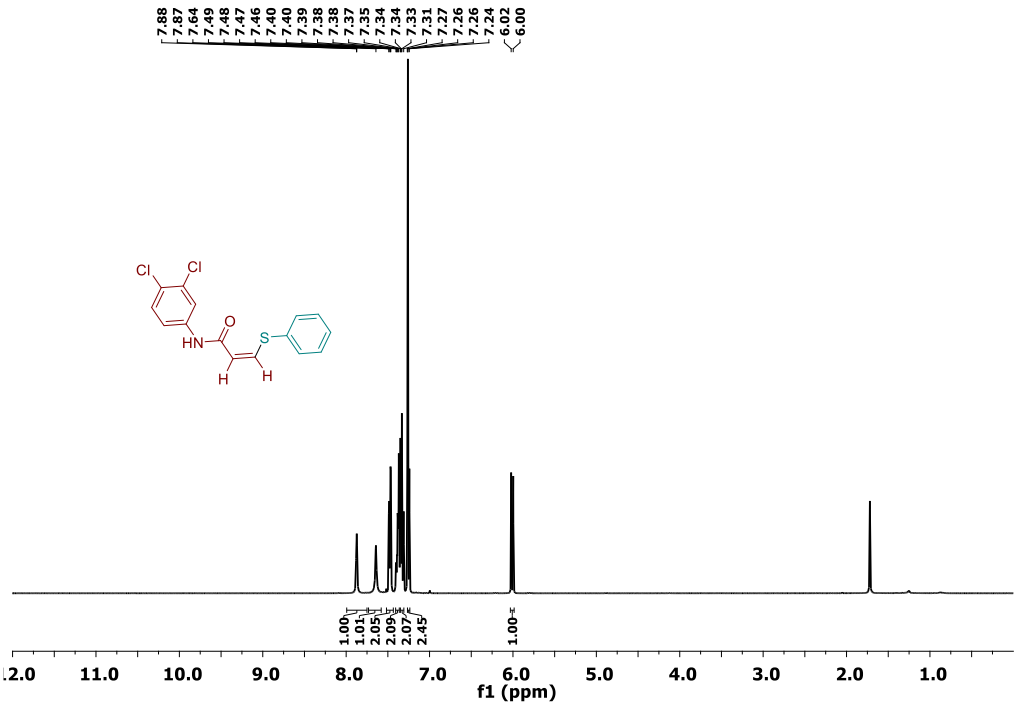



**Figure 4.34.** $^{1}$H NMR spectrum of (Z)-N-(3,4-dichlorophenyl)-3-(phenylthio)acrylamide (**3ma**)

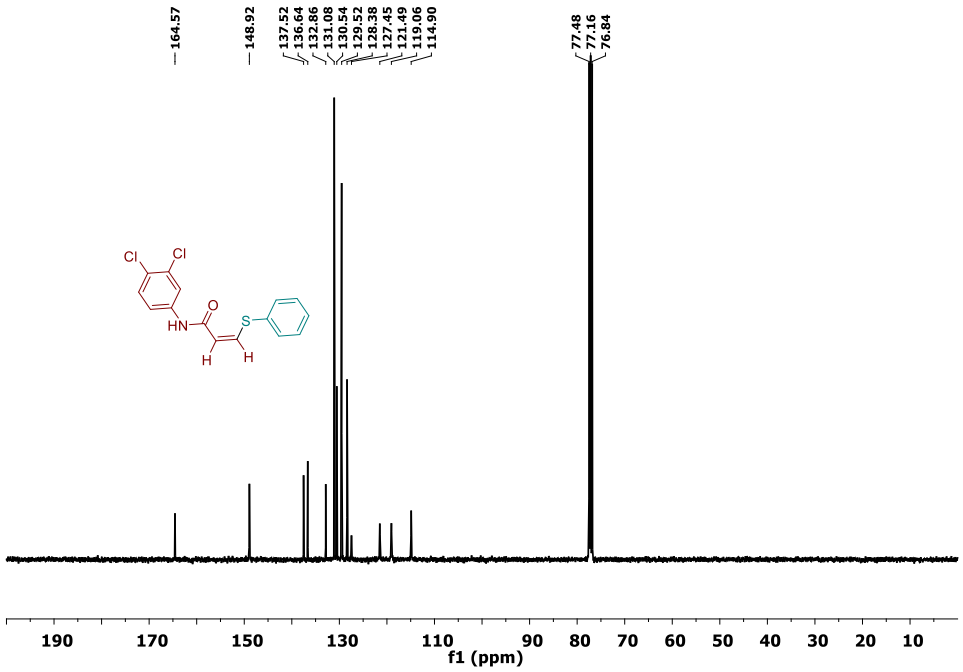



**Figure 4.35.** $^{13}$C NMR spectrum of (Z)-N-(3,4-dichlorophenyl)-3-(phenylthio)acrylamide (**3ma**)

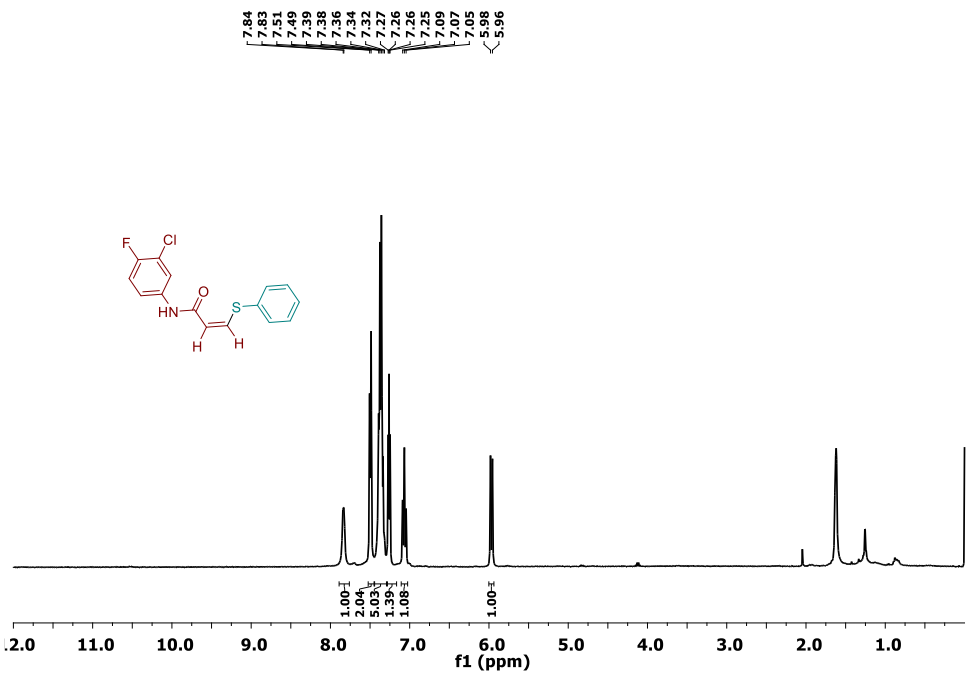



**Figure 4.36.** $^{1}$H NMR spectrum of (Z)-N-(3-chloro-4-fluorophenyl)-3-(phenylthio)acrylamide(**3na**)

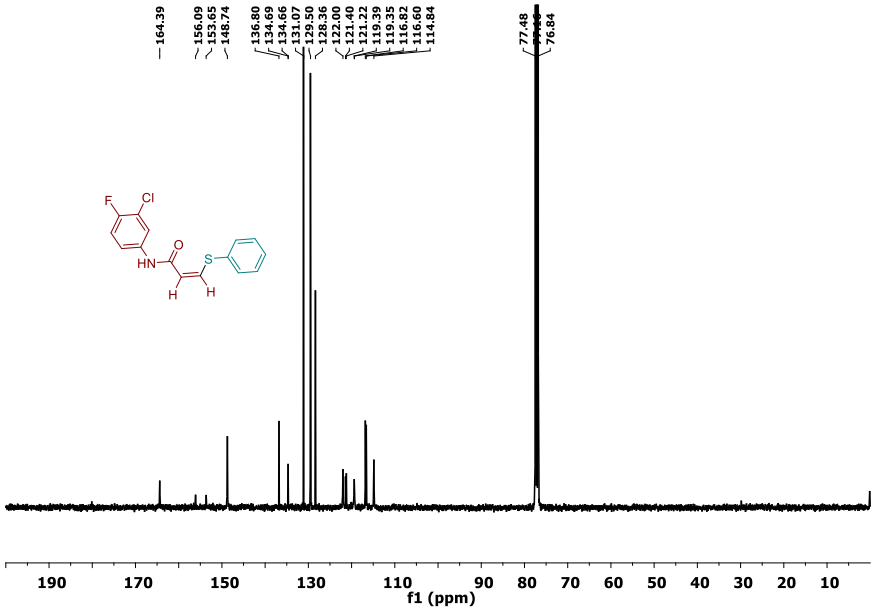



**Figure 4.37.** $^{13}$C NMR spectrum of (Z)-N-(3-chloro-4-fluorophenyl)-3-(phenylthio)acrylamide(**3na**)

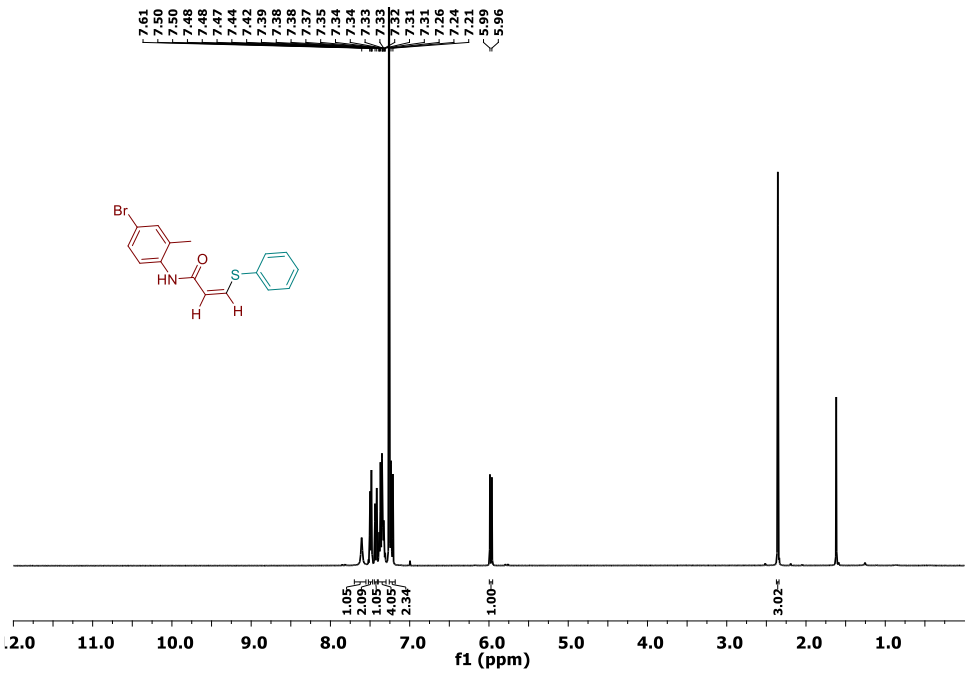



**Figure 4.38.** $^{1}$H NMR spectrum of (Z)-N-(4-bromo-2-methylphenyl)-3-(phenylthio)acrylamide (**3oa**)

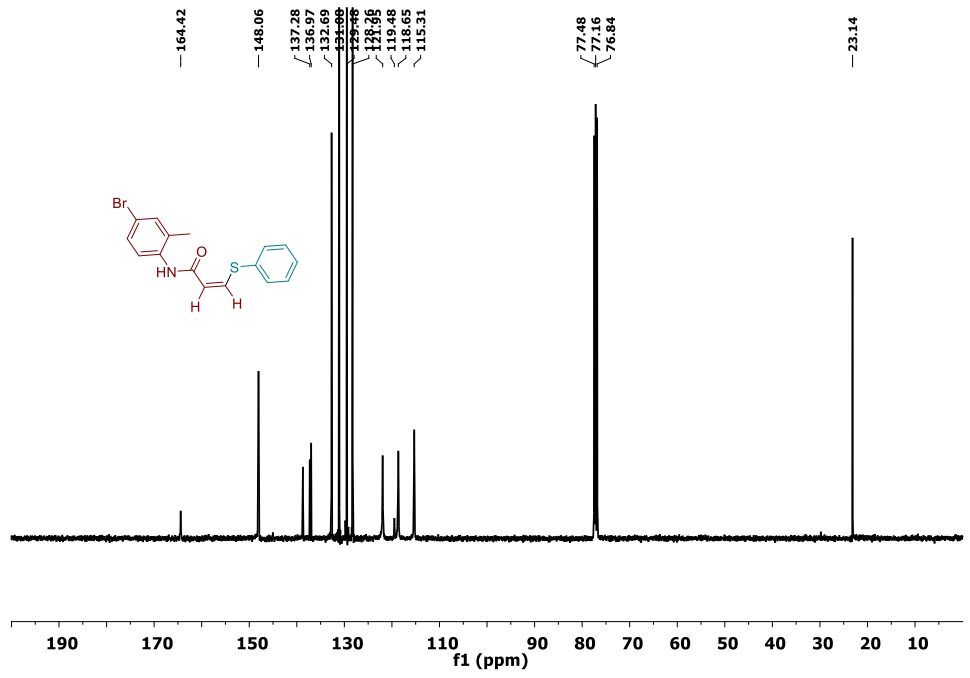



**Figure 4.39.** $^{13}$C NMR spectrum of (Z)-N-(4-bromo-2-methylphenyl)-3-(phenylthio)acrylamide (**3oa**)

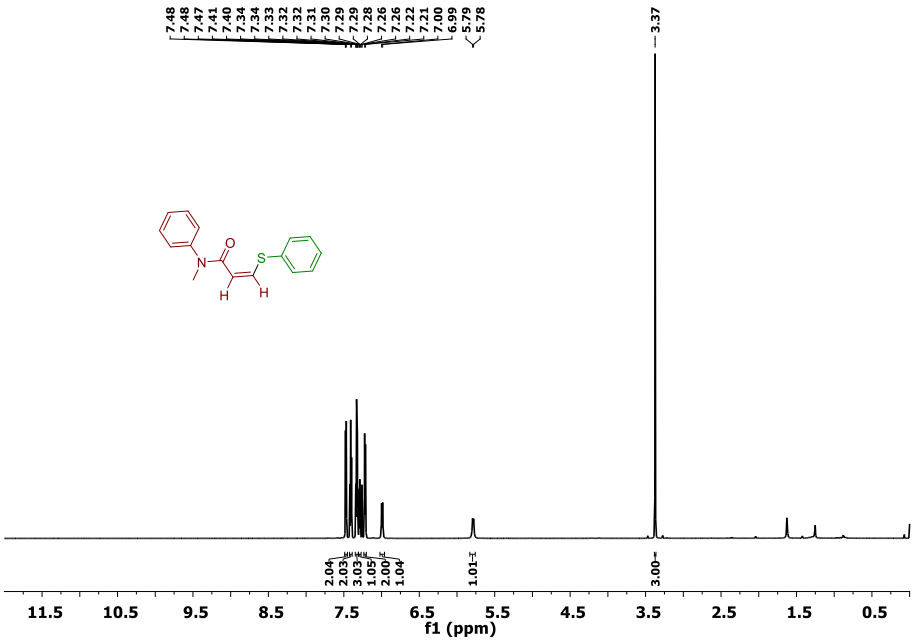



**Figure 4.40.** $^{1}$H NMR spectrum of (Z)-N-methyl-N-phenyl-3-(phenylthio)acrylamide (**3pa**)

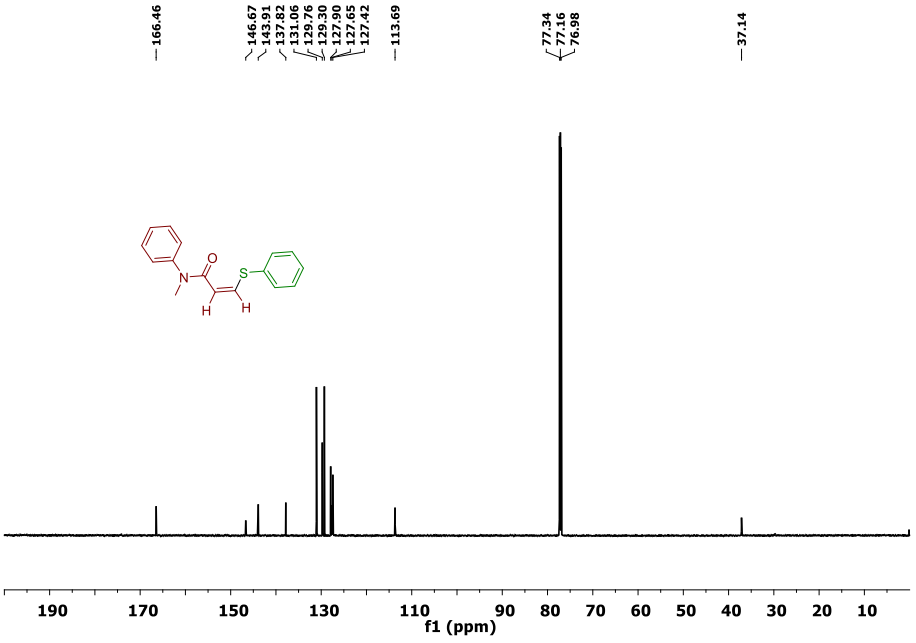



**Figure 4.41.** $^{13}$C NMR spectrum of (Z)-N-methyl-N-phenyl-3-(phenylthio)acrylamide (**3pa**)

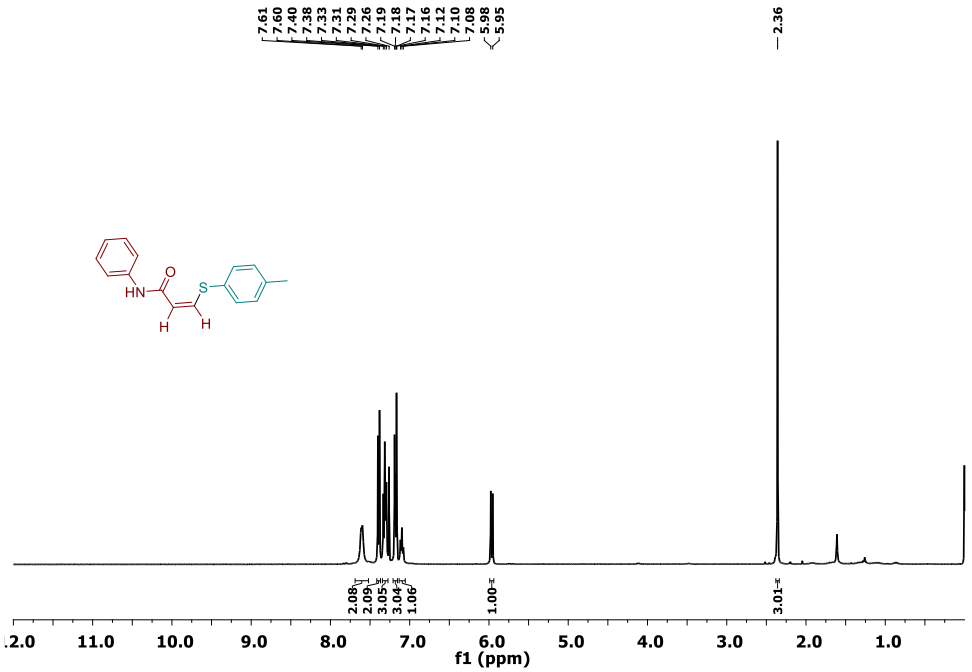



**Figure 4.42.** $^{1}$H NMR spectrum of (Z)-N-phenyl-3-(p-tolylthio)acrylamide (**3ab**)

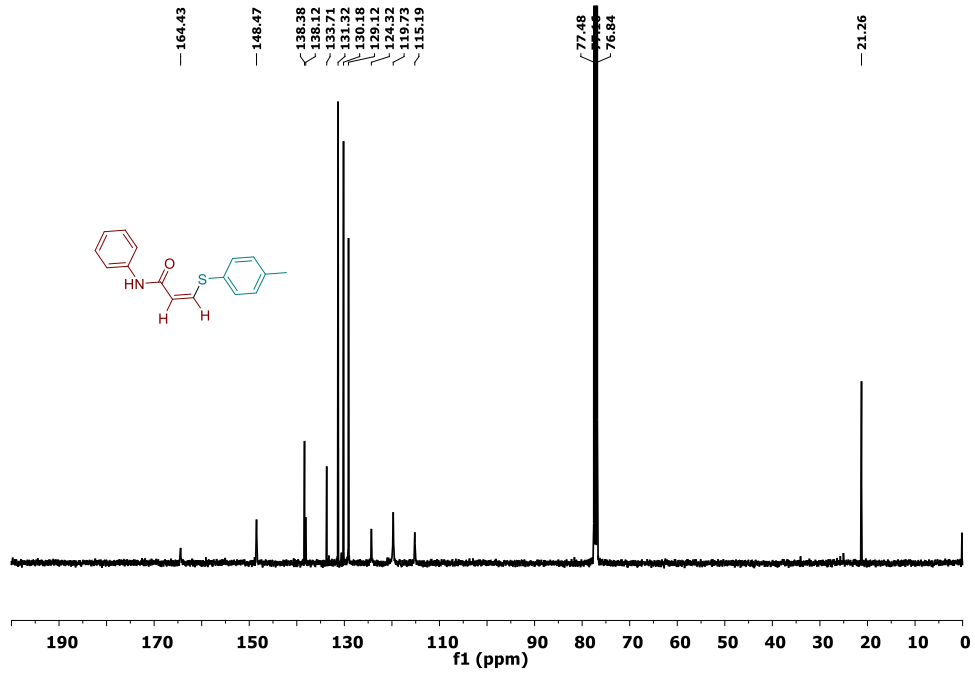



**Figure 4.43.** $^{13}$C NMR spectrum of (Z)-N-phenyl-3-(p-tolylthio)acrylamide (**3ab**)

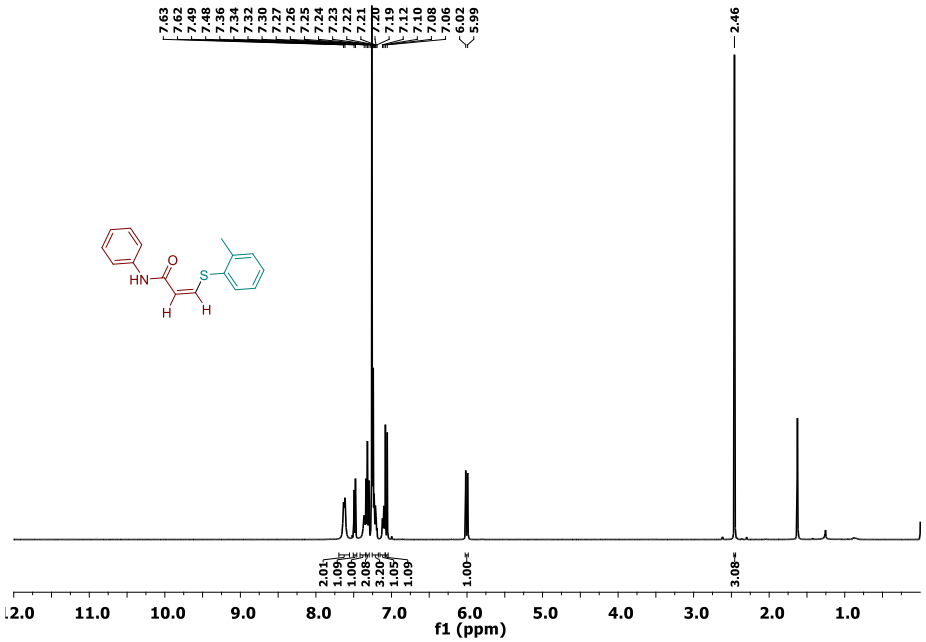



**Figure 4.44.** $^{1}$H NMR spectrum of (Z)-N-phenyl-3-(o-tolylthio)acrylamide (**3ac**)

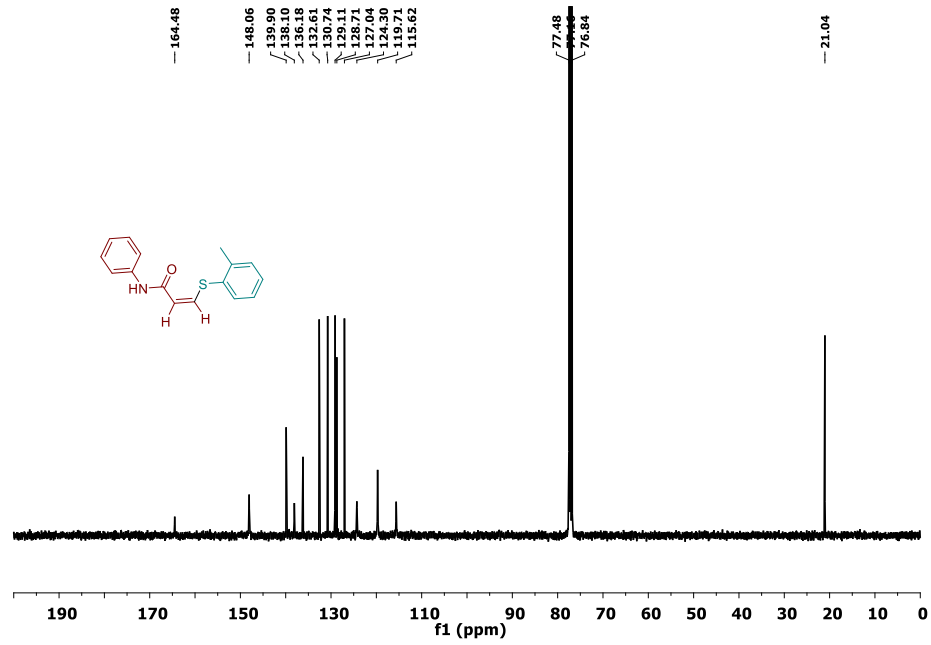



**Figure 4.45.** $^{13}$C NMR spectrum of (Z)-N-phenyl-3-(o-tolylthio)acrylamide (**3ac**)

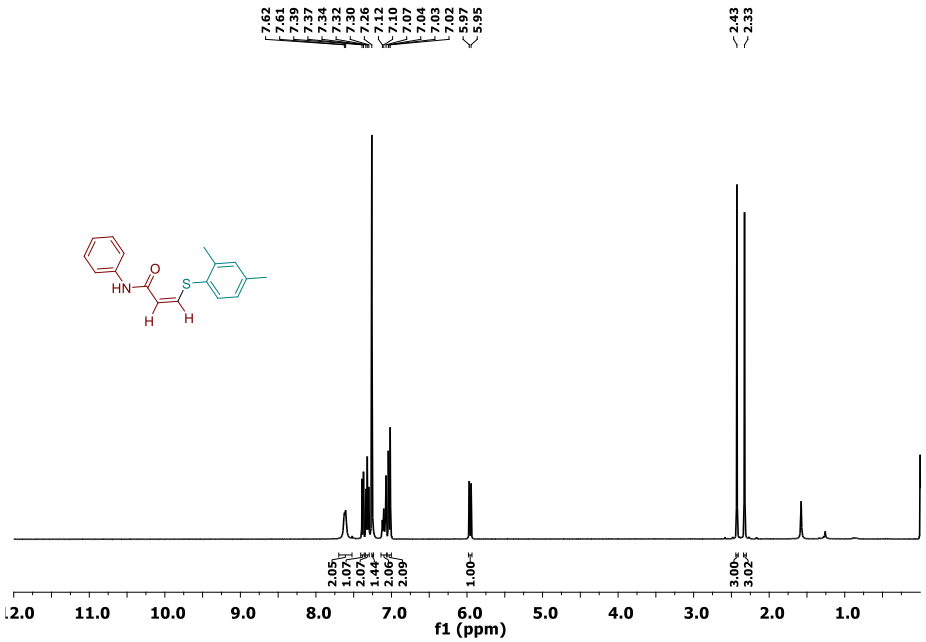



**Figure 4.46.** $^{1}$H NMR spectrum of (Z)-3-((2,4-dimethylphenyl)thio)-N-phenylacrylamide (**3ad**)

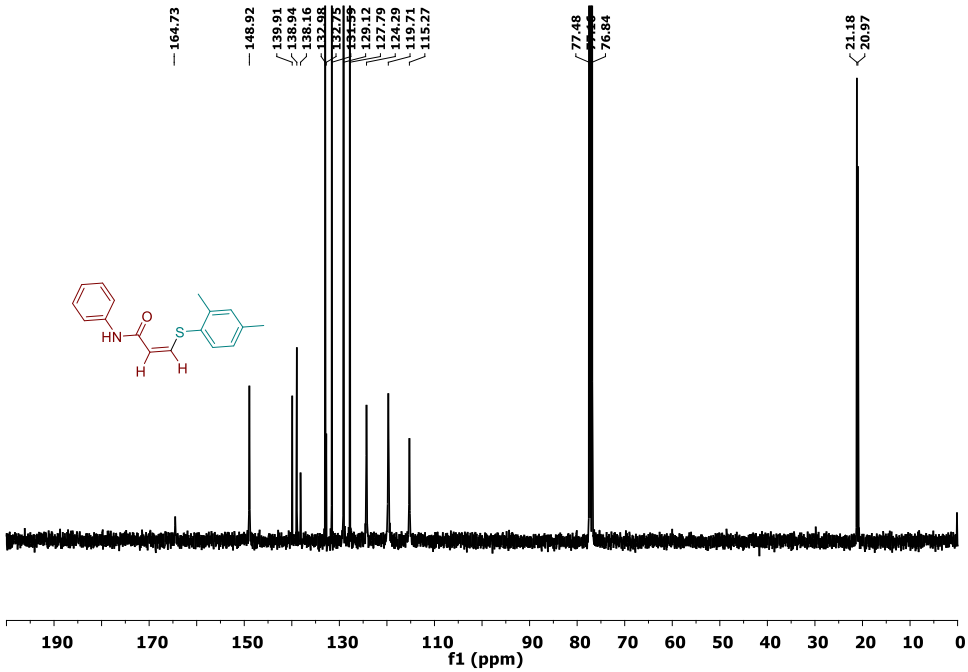



**Figure 4.47.** $^{13}$C NMR spectrum of (Z)-3-((2,4-dimethylphenyl)thio)-N-phenylacrylamide (**3ad**)

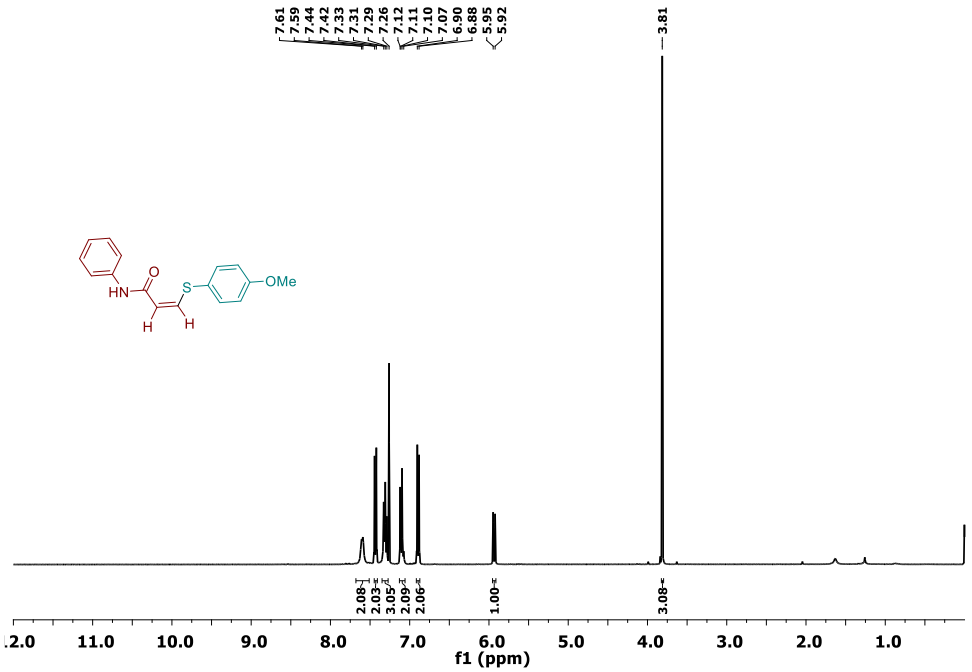



**Figure 4.48.** $^{1}$H NMR spectrum of (Z)-3-((4-methoxyphenyl)thio)-N-phenylacrylamide (**3ae**)

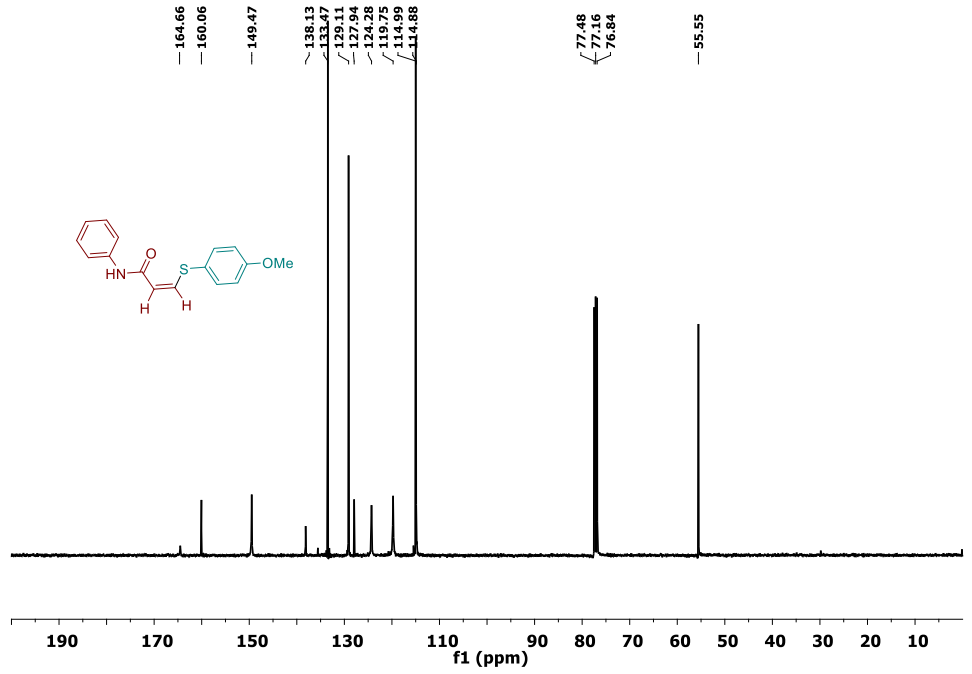



**Figure 4.49.** $^{13}$C NMR spectrum of (Z)-3-((4-methoxyphenyl)thio)-N-phenylacrylamide (**3ae**)

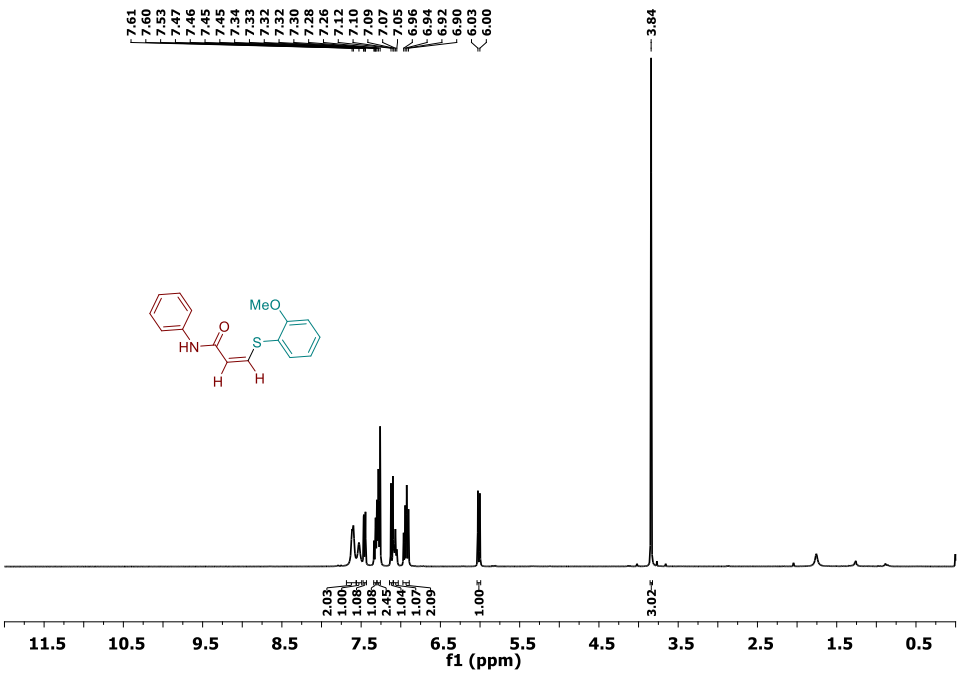



**Figure 4.50.** $^{1}$H NMR spectrum of (Z)-3-((2-methoxyphenyl)thio)-N-phenylacrylamide (**3af**)

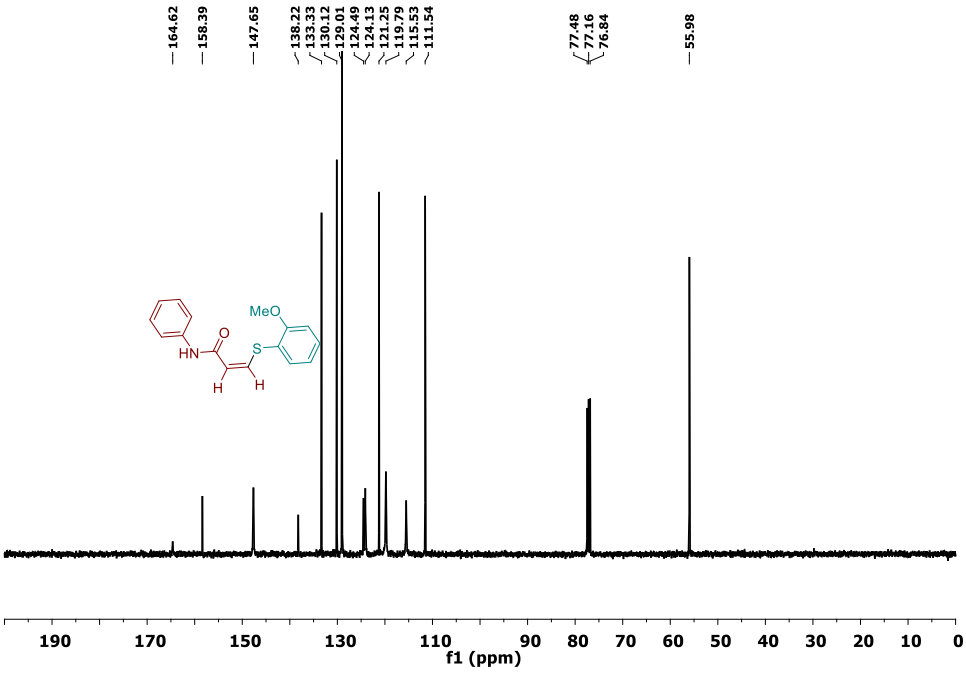



**Figure 4.51.** $^{13}$C NMR spectrum of (Z)-3-((2-methoxyphenyl)thio)-N-phenylacrylamide (**3af**)

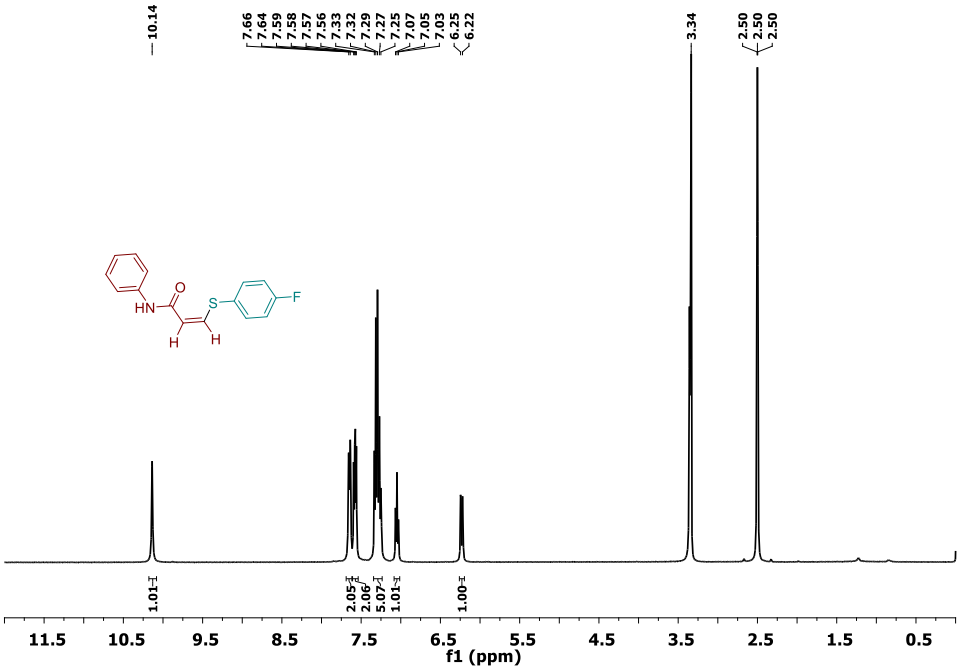



**Figure 4.52.** $^{1}$H NMR spectrum of (Z)-3-((4-fluorophenyl)thio)-N-phenylacrylamide (**3am**)

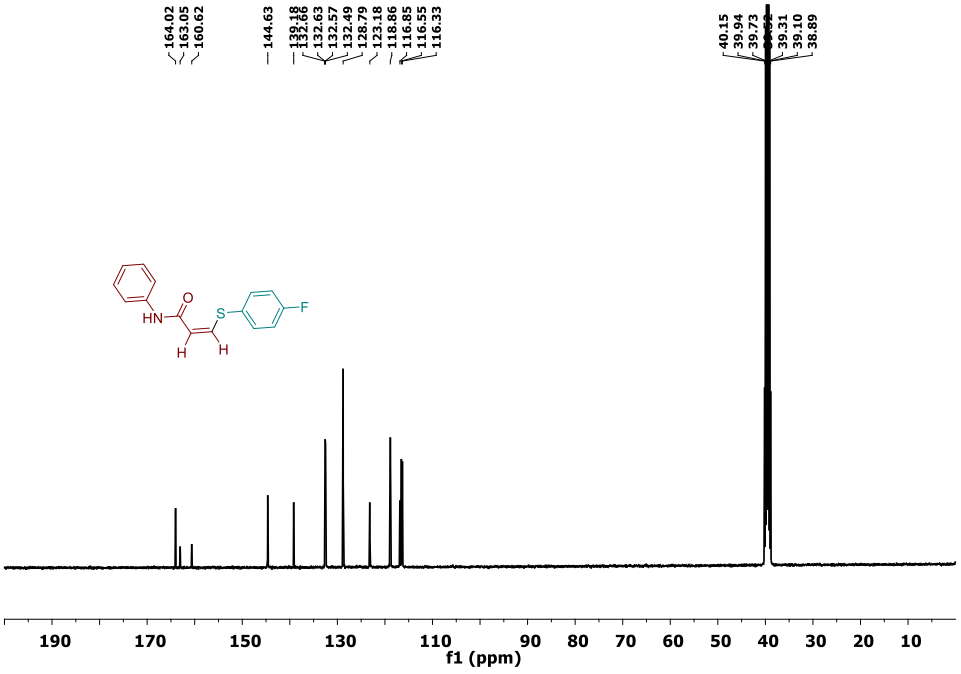
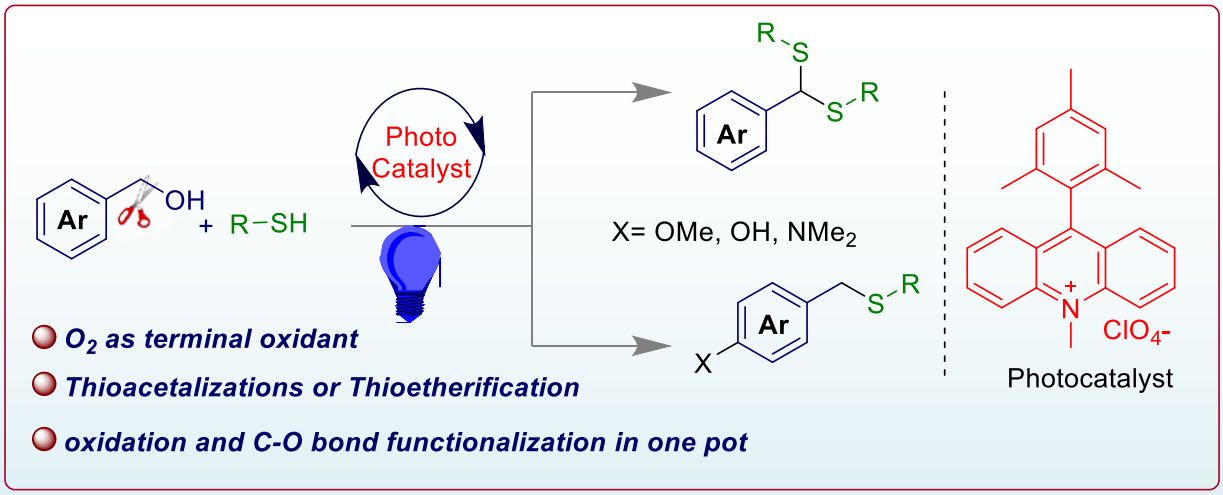



**Figure 4.53.** $^{13}$C NMR spectrum of (Z)-3-((4-fluorophenyl)thio)-N-phenylacrylamide (**3am**)

# CHAPTER 5

# Oxidative C–O Bond Functionalization of Benzyl Alcohol by Visible Light Photocatalyst: Synthesis of Dithioacetals and Thioethers

## 5.1 ABSTRACT




A mild and operationally simple protocol for C–S bond formation reaction is disclosed *via* a two-step oxidative process of benzyl alcohol in one pot by using 9-mesityl-10-methylacridinium perchlorate as photocatalyst and aerial oxygen as the terminal oxidant. Various types of thioacetals and benzyl thioethers could be achieved selectively from visible light irradiation of unactivated benzyl alcohols and thiophenols. Detail mechanistic study helped to establish the role of molecular oxygen and photocatalyst in the single electron transfer (SET) process. EPR experiment confirmed the involvement of the radical pathway.

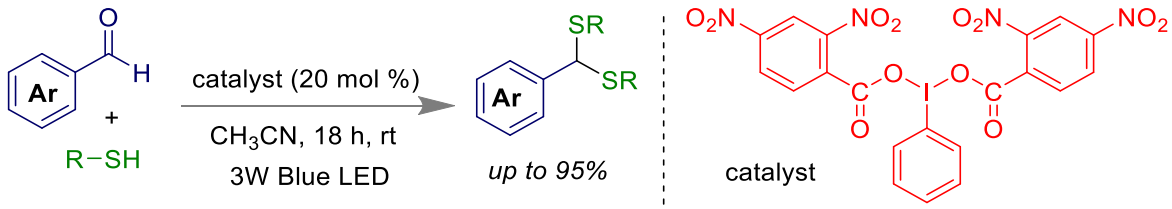
## 5.2 INTRODUCTION

In recent years, the oxidation technique is gaining enormous attention. It has rapidly started to find applications in various synthetic research fields because many domino syntheses could be performed in one pot using *in situ* oxidative strategy[1]. In particular, oxidation of benzyl alcohol is one of the fundamental and desirable topics in organic methodology because of the following reasons. Primarily, benzyl alcohols are very unreactive because the hydroxyl group shows bad leaving ability until unless the exiting C–O bond is activated by Lewis acid or catalysis[2, 3]. Secondly, oxidation of benzyl alcohol leads to either aldehyde or ketone, which is generally a reactive species towards any nucleophile in the same reaction pot[4, 5]. For oxidation of benzyl alcohols, most of the literature demonstrated the use of stoichiometric oxidants[6, 7] like hypervalent iodine, peroxides, and metal salts, etc., which have poor practicability towards the birth and growth of green chemistry. In this regard, aerial oxygen is one of the most ecological and sustainable oxidants, which can act both to be functionalized within a molecule and oxidize a substrate by utilizing superoxide anion radical, singlet oxygen, and hydroxy radical[8].

In the last two decades, visible-light-driven photocatalysis has become a powerful tool in organic synthesis as the energy of a photon can easily be converted to chemical energy[9, 10]. Not only this, it also involves a single electron transfer (SET) process to access a wide range of elegant chemical transformation[11]. In particular, recent photocatalytic studies on benzyl alcohol as benzyl synthon are of course attractive[2].

Sulfur-containing molecules are ubiquitously found in natural products, drugs, and many smart materials[12]. Thus, C–S bond-forming reaction under mild and sustainable conditions is always desirable for synthetic chemist[13]. Thioacetals act as an excellent protecting group for the synthesis of many drugs because of their high tolerance under acidic or basic condition[14]. Apart

from this, thioacetal shows umpolung reactivity with respect to carbonyl compound[15]. Many traditional methods are reported; however, they involve acidic, basic, or metal catalysis, which resulted in toxicity, waste of precious metal, poor functional group tolerance, and lack of chemoselectivity[16-21]. Recently Mal's group has introduced chemo-selective dithioacetalization of aldehydes by iodine (III) reagent as visible-light-induced radical initiator (Scheme 5.1)[22].




**Scheme 5.1**. Mal's work is based on iodine (III) reagent in dithioacetalization reaction.

Recently, Lee[23] and Xie[24] groups established individually thioacetalization reactions, but both the methods are limited to only aliphatic thiols and required inert atmosphere conditions. Again, Sekar and coworkers also reported a carbene mediated thioactalization reaction as an alternative approach from N-tosyl hydrazones and disulfides[25]. Aldehydes used as the precursor of most of the thioacetalization reactions, are generally unstable in the open atmosphere and prone to get oxidized by air. Conversely, photoredox catalyzed oxidation of stable benzyl alcohols to aldehydes by Das's group[26], and Kokotos's group[27] received our attention towards *in situ* oxidation strategy for direct C–S bond formation reaction from benzyl alcohol (Figure 5.1).

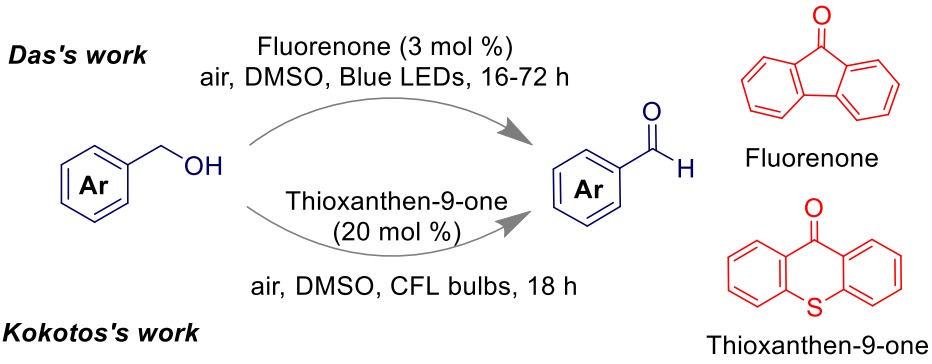
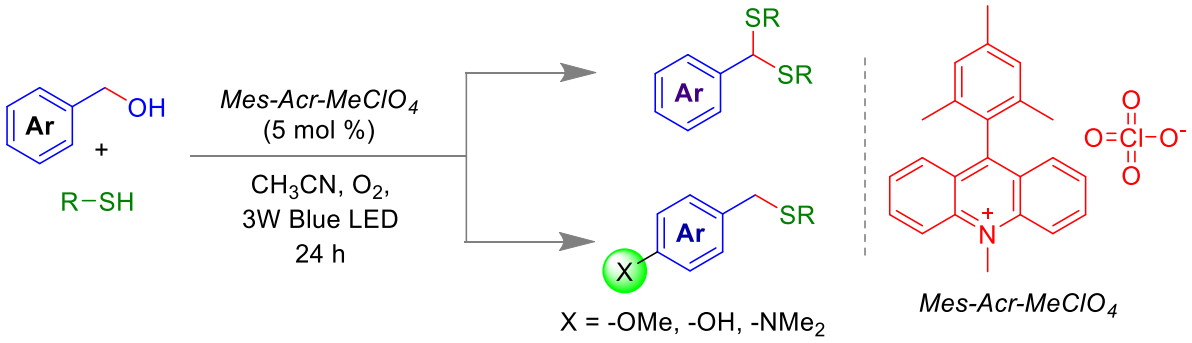



**Figure 5.1**. Das and Kototos's individual strategies for oxidation of benzylic alcohols.

After careful observation of previous reports, we realize that the design of thioacetal from air-stable and commercially available benzyl alcohol can be a good start for thioacetalization reaction *via* oxidative two-step photo-redox process in one pot (Scheme 5.2). Here, the use of 9-mesityl-10-methylacridinium perchlorate (Mes-Acr-MeClO$_4$) as the photocatalyst and aerial oxygen as the terminal oxidant for the reaction of benzyl alcohol and thiols in acetonitrile solvent using 3W blue LED light led to either dithioacetals or thioethers as a product (Scheme 5.2)[28].



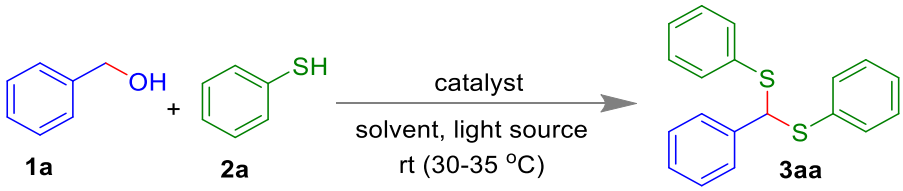

**Scheme 5.2**. Our work is based on *in situ* oxidation of benzyl alcohols followed by thioacetalization or thioetherification reaction *via* photocatalysis.

## 5.3 RESULT AND DISCUSSION

The literature report suggested that ground state reduction potential of 9-mesityl-10-methylacridinium (-0.49 V vs. SCE) is found to be comparable with the reduction potential of molecular oxygen (-0.87 V vs. SCE). Thus, it was anticipated that excited Mes-Acr-$Me^+$ after single electron transfer with benzyl alcohol would again give back the electron to $O_2$ by reducing into its superoxide radical form[9, 26] Keeping this reliable thought in mind, we forced to irradiate benzyl alcohol **1a** and thiophenol **2a** under 3W blue LEDs in $O_2$ atmosphere in $CH_3CN$ as solvent (Table 5.1). Delightfully, no sacrificial by-product other than water was observed, and the excess thiophenol was recovered as such after the reaction. Initially, the desired compound **3aa** was isolated in 32% yield in the presence of 5 mol% 9-mesityl-10-methylacridinium tetrafluoroborate as photocatalyst in 0.5 ml thiophenol and 1.0 mL $CH_3CN$ solvent under 3w blue LEDs irradiation in oxygen atmosphere after 24 h reaction time (entry 1). Other photocatalysts showed inferior results (entries 2-4) for this oxidative transformation. Screening of other solvents ($CHCl_3$, DCE, Toluene, DMSO) did not encourage the yield of the desired product (entries 5-8). Next, the reaction was irradiated in white and green LEDs, but no satisfactory yield was observed (entries 9 and 10). The use of 4 equivalent thiophenols led to a decrease in yield (entry 11). Finally, the best condition was achieved in 9-mesityl-10-methylacridinium perchlorate as photocatalyst under $O_2$ atmosphere in 3W blue LEDs in $CH_3CN$ solvent (entry 12). The yield of the product was moved down when 2 mol % of the photocatalyst was used (entry 13). The optimized reaction time was found to be 24 hours as a 68% yield of the desired product **3aa** was isolated after 12 hours (entry 14). Notably, the reaction was failed in the absence of either photocatalyst or light (entries 15-16), thus indicated that excitation of photocatalyst with visible light is required for this oxidative process to facilitate C–S bond

formation reaction. The reaction was also unsuccessful in the argon atmosphere, indicated that molecular oxygen acted as an oxidant for this oxidative process (entry 17).

**Table 5.1.** Optimization of reaction conditions.[a]




| entry | catalyst (mol %) | solvent | light source | yield (%) |
|---|---|---|---|---|
| 1 | Mes-Acr-$MeBF_4$ (5) | $CH_3CN$ | Blue LED (3W) | 32 |
| 2 | Rose Bengal(5) | $CH_3CN$ | Blue LED (3W) | - |
| 3 | Eosin Y(5) | $CH_3CN$ | Blue LED (3W) | - |
| 4 | $Ru(bipy)_3(PF_6)_2$(5) | $CH_3CN$ | Blue LED (3W) | 26 |
| 5 | Mes-Acr-$MeBF_4$ (5) | $CHCl_3$ | Blue LED (3W) | 21 |
| 6 | Mes-Acr-$MeBF_4$ (5) | DCE | Blue LED (3W) | 29 |
| 7 | Mes-Acr-$MeBF_4$ (5) | Toluene | Blue LED (3W) | - |
| 8 | Mes-Acr-$MeBF_4$ (5) | DMSO | Blue LED (3W) | - |
| 9 | Mes-Acr-$MeBF_4$ (5) | $CH_3CN$ | White LED (14W) | 31 |
| 10 | Mes-Acr-$MeBF_4$ (5) | $CH_3CN$ | Green LED (26W) | - |
| 11 | Mes-Acr-$MeClO_4$ (5) | $CH_3CN$ | Blue LED (3W) | 74[b] |
| 12 | Mes-Acr-$MeClO_4$ (5) | $CH_3CN$ | Blue LED (3W) | 96 |
| 13 | Mes-Acr-$MeClO_4$ (2) | $CH_3CN$ | Blue LED (3W) | 77 |
| 14 | Mes-Acr-$MeClO_4$ (5) | $CH_3CN$ | Blue LED (3W) | 68[c] |
| 15 | ---------- | $CH_3CN$ | Blue LED (3W) | - |

| | | | | |
|---|---|---|---|---|
| 16 | Mes-Acr-$MeClO_4$ (5) | $CH_3CN$ | ---------- | - |
| 17 | Mes-Acr-$MeClO_4$ (5) | $CH_3CN$ | Blue LED (3W) | $0^d$ |

Reaction Condition[a]: **1a** (0.555 mmol, 60 mg), Mes-Acr-$MeClO_4$ (5 mol %, 0.027 mmol, 11 mg) 0.5 mL thiol and 1.0 mL $CH_3CN$ in $O_2$ atmosphere for 24 h at rt in Blue LEDs; [b]4.0 equiv of thiophenol; [c]after 12 h; [d]at argon atmosphere.

With the optimal condition in hand, a variety of benzyl alcohol derivatives were examined for the aerobic oxidative C–S coupling reaction. As illustrated in Figure 5.2a, benzyl alcohol-containing electron pushing groups such as -Me, -$^i$Pr, and -$^t$Bu afforded efficient transformations of **3aa-3ea** in a range of 76%-96% yields. Again, 4-fluoro benzyl alcohol and 4-nitro benzyl alcohol were also compatible in the oxidative process to deliver dithioacetals **3fa** and **3ga** in 65% and 42% yields, respectively. Other functional groups like -OPh and -SMe in benzyl alcohols were also provided **3ha** and **3ia** in 98% and 74% yield, respectively. In addition, benzyl alcohols having ester, keto, and ether linkage could provide thioacetals **3ja**, **3ka,** and **3la** with 72%, 58%, and 80% yields, respectively. Again, 2-thiophenemethanol, heterocyclic alcohol, also responded to give dithioacetal **3ta** with a 68% yield.

Furthermore, scopes of thiols were also examined under standard reaction conditions (Figure 5.2b). The methyl and methoxy substituted thiophenol could deliver compound **3ab** and **3ac** with 84% and 70% yield, respectively. Similarly, *para*-halo substituted (X= -Br, -Cl, -F) thiophenols could be transformed into corresponding thioacetals (**3ad, 3ae,** and **3ag**) in 77%, 94%, and 88% yields, respectively. 3-Chloro, 2-fluoro, and 4-$CF_3$ containing thiophenols also yielded 91%, 79%, and 61% yields of compound **3af**, **3ah,** and **3ai**, respectively. Aliphatic thiols were also suitable to produce compounds **3bj, 3bk,** and **3ul** with 54%, 62%, and 69% yields, respectively.

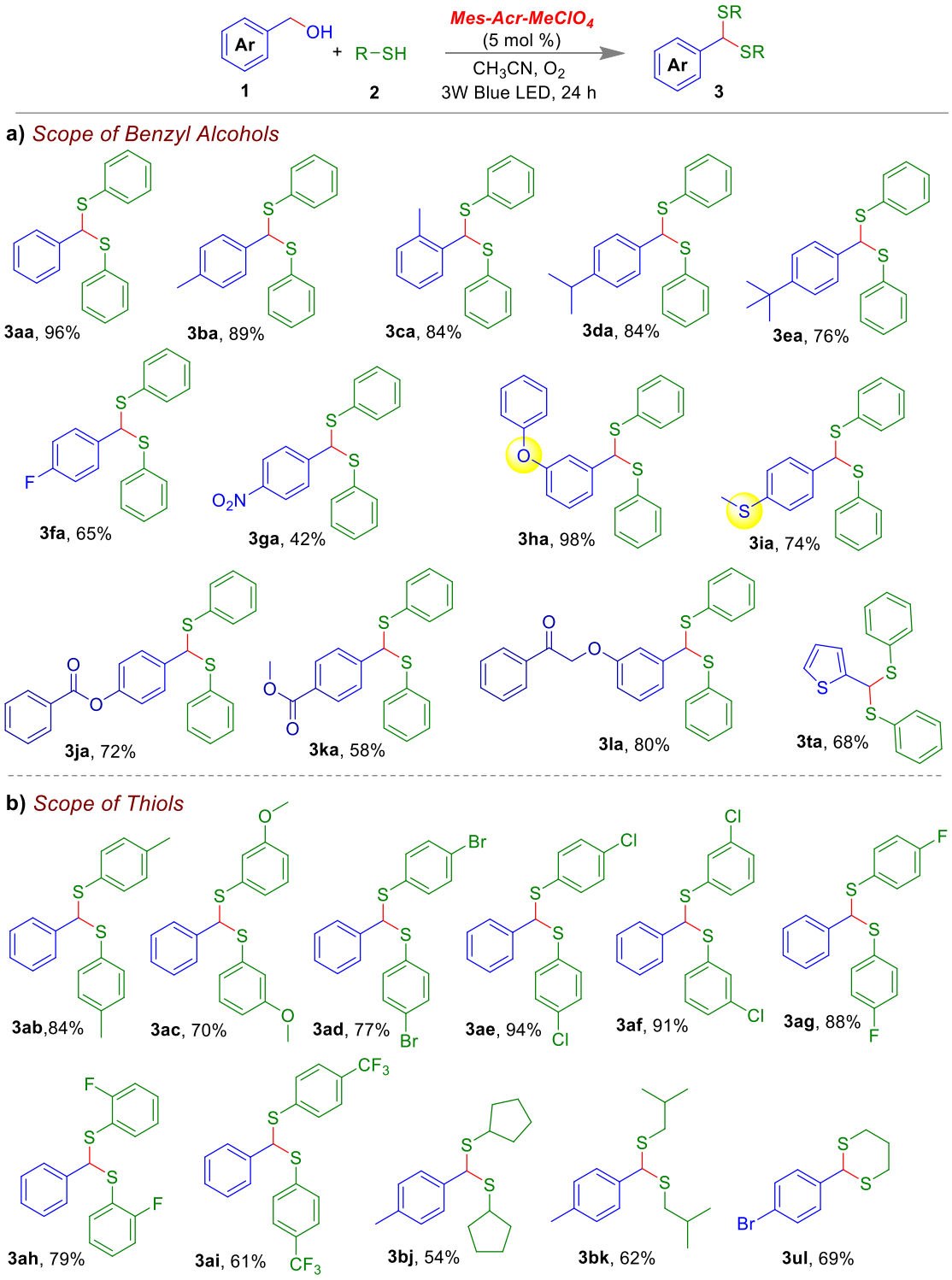



**Figure 5.2**. Scopes of a) benzyl alcohols and b) thiols

Gratifyingly, when *para*-methoxy benzyl alcohol was employed under the same strategy, the reaction was found to be attractive by delivering benzyl sulfane as a product (Figure 5.3). Here, an electronically rich methoxy group with a +R effect took part in the SET process to produce benzyl sulfane over thioacetal as a C–S coupled product. Not only the *para*-methoxy group but the -$NMe_2$ and -OH group also experienced the same examination under the standard reaction condition. Thiophenols with -Me and -OMe group at -*o,* -*p,* and -*m* position resulted in benzyl sulfanes **4ma-4mc** in a range of 63%-93% yields. Again, 2,4-Dimethoxy benzyl alcohol also yielded 81% of benzyl sulfane **4na**. Notable that, incorporation of another methoxy group at the 3-position of *para*-methoxy thiophenol led to the mixture of benzyl sulfane and thioacetal (**4oa**, **3oa**) with 53% and 26% yields, respectively. Again, benzyl alcohol **1p** also reacted similarly to form the mixture of sulfane **4pa** and thioacetal **3pa** with 52% and 45% yields, respectively. Besides, 3,4,5-methoxy benzyl alcohol was treated under this photolytic condition to produce a mixture of **4qa** and **3qa** in 29% and 59% yields. In addition, 4-N,N-dimethylamino benzyl alcohol could able to give the desired product **4ra** exclusively with excellent yield (97%). Notable that vanillyl phenyl sulfide **4sa** could also be derived from vanillyl alcohol with a 79% yield. Furfuryl alcohol could be oxidized under this photolytic condition to afford **4vb** with a 59% yield.

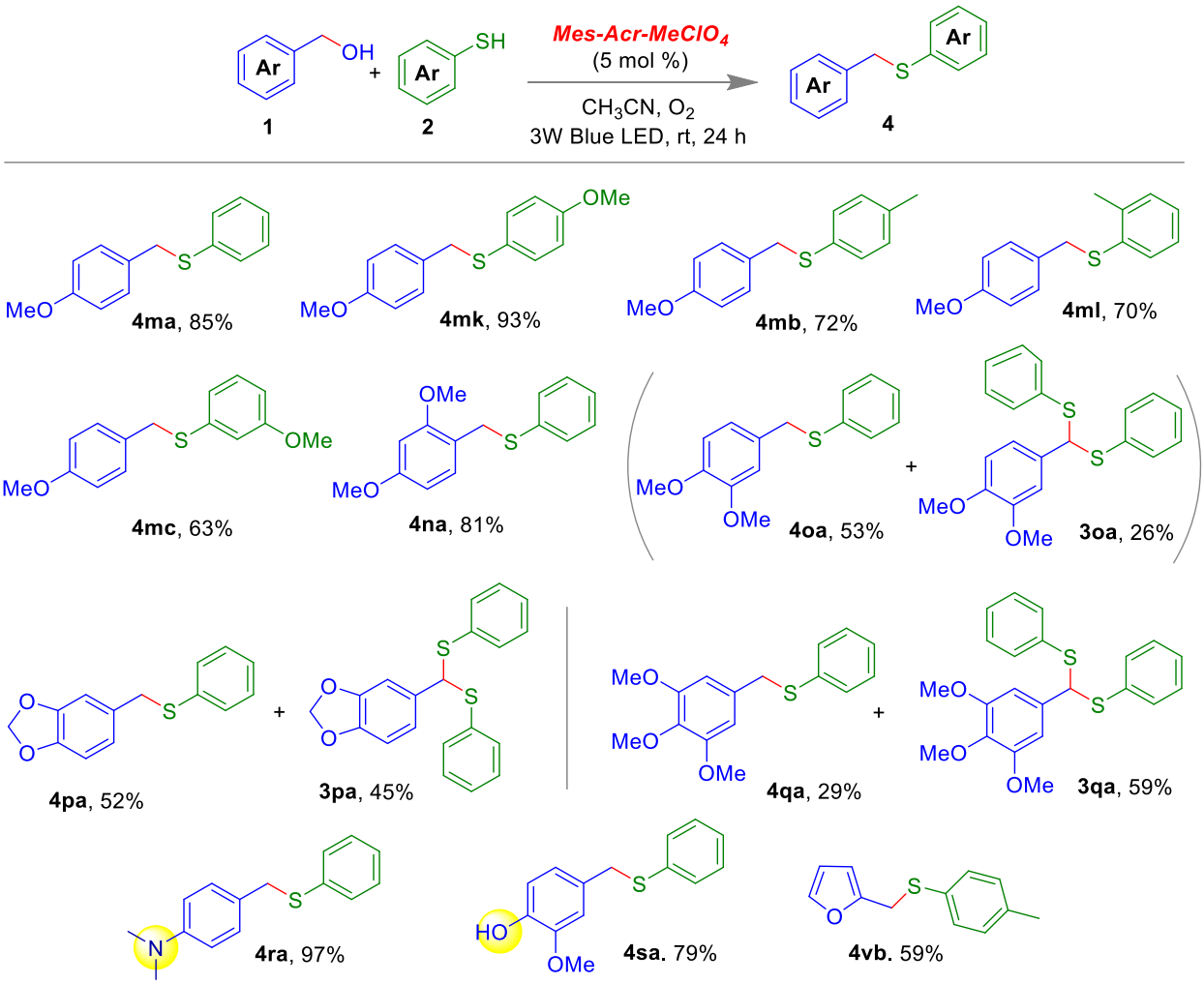



**Figure 5.3**. Scopes of benzyl alcohols and thiophenols for thioetherification reaction.

Chemically we have also shown a series of control experiments in Figure 5.4. In order to check the radical preceded reaction pathway, a reaction was performed with disulfide, but no formation of desired product indicated that there is no possibility of disulfide as intermediate (Figure 5.4a). The performance of reaction under an inert atmosphere led to no product, which indicated molecular oxygen is useful for this oxidative process. The step-wise formation of benzaldehyde and dithioacetals from benzyl alcohol confirmed that aldehyde was the sole intermediate for this C–S coupling reaction (Figure 5.4b). During formation of benzaldehyde, hydrogen peroxide ($H_2O_2$) was produced. The addition of KI and dil $H_2SO_4$ (catalytic) in the reaction medium

showed generation of tri-iodide ($\lambda_{max}$ = 359 nm at UV-Vis spectra), which confirmed formation of $H_2O_2$ in the reaction. Again, treatment of TEMPO as a radical trapping candidate inhibited the formation of product **3aa,** which was evidenced as a radical-mediated mechanism (Figure 5.4c). The methodology was unsuccessful in the absence of Mes-Acr-$ClO_4$ as the catalyst, which implied that the catalyst was essential for the SET process. In addition, benzyl sulfane could be derived from intermediate **6**. To verify this, compound **8** and **2a** were irradiated under standard condition, but desired benzyl sulfane was not detected indicating compound **4ma** could be achieved from hemithioacetal intermediate (Figure 5.4d). Again, 4-methoxy benzyl alcohol did not respond in the absence of catalyst and light, which confirmed that thioether **4ma** could not be the result of $S_N^2$ type reaction between 4-methoxy benzyl alcohol **1m** and thiophenol **2a**. Again, the step-wise formation of 4-methoxy benzaldehyde and corresponding dithioacetals from 4-methoxybenzyl alcohol confirmed that *in-situ* 4-methoxy benzaldehyde was also formed as intermediate here (Figure 5.4e). Unfortunately, aliphatic alcohol, such as amyl alcohol, neither resulted in amyl aldehyde nor dithioacetal product (Figure 5.4f). This is due to the fact that generation of an unstable alkyl radical intermediate as shown in the mechanism.

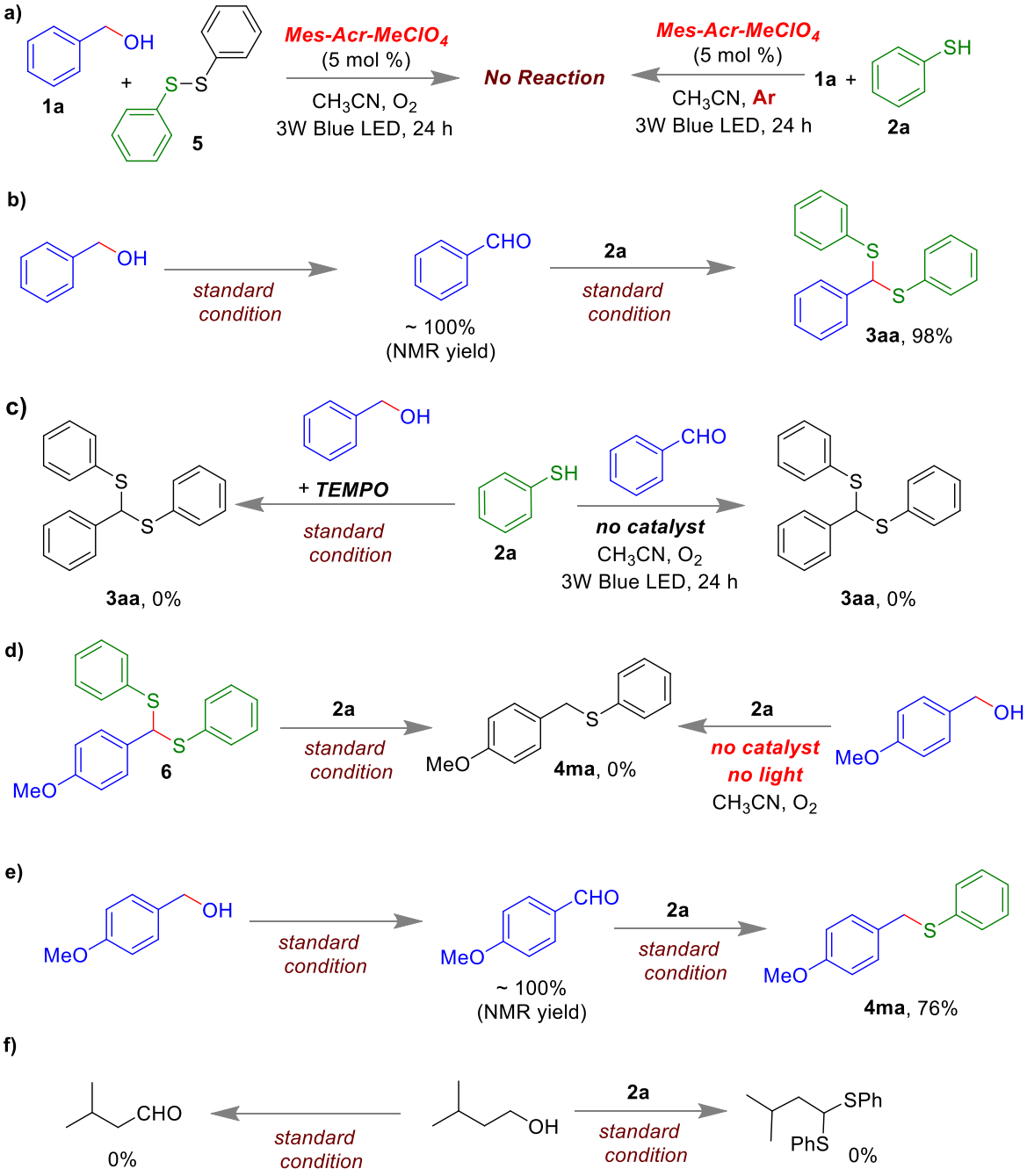



**Figure 5.4**. Control experiments.

A distinct EPR signal was found when DMPO (5,5-Dimethyl-1-pyrroline *N*-oxide) was added under standard reaction conditions (red color line in Figure 5.5a), and the signal had vanished

when the experiment was performed without thiophenol (black color linear line in Figure 5.5a). On the other hand, the light On-Off experiments have suggested that light is required for the excitation of the photocatalyst (Figure 5.5b).

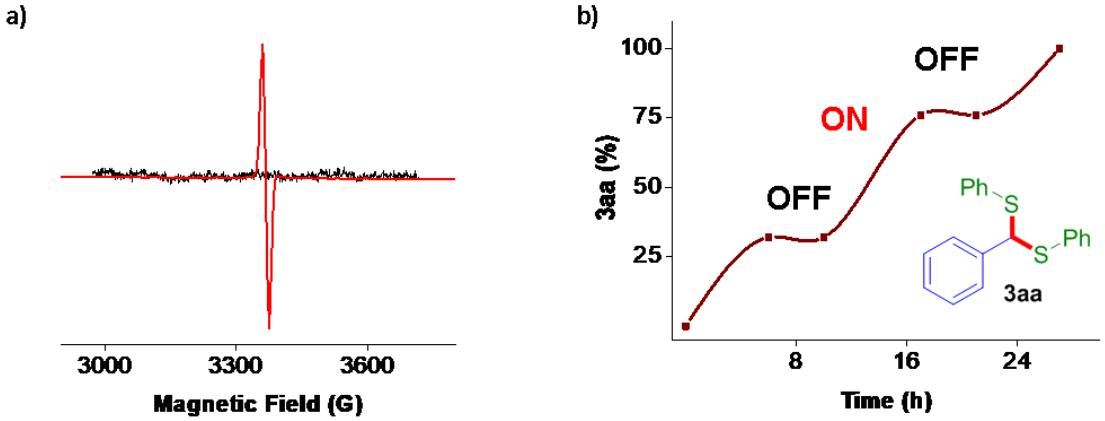



**Figure 5.5**. EPR spectrum using DMPO and Light On-Off experiment under standard condition.

Initially, the radical mechanism was anticipated in the presence of $O_2$ and photocatalyst. In order to confirm that, various types of radical and singlet oxygen quenching experiments were performed shown in Table 5.2. When BHT was employed under the standard as a radical scavenger, but no desired product was isolated, indicating that reaction follows radical pathway. Similarly, $NaN_3$ and DABCO were also used in the reaction mixture as singlet oxygen quenchers. Both of the quenchers partially inhibited the product formation indicating the necessity of singlet oxygen in the reaction pathway. Again, treatment of benzoquinone reduced the yield of the product confirmed the presence of superoxide radical anion in the reaction mechanism.

**Table 5.2.** Quenching experiment[a]

| Entry | Quincher(equiv) | Note | Yield(%)[b] |
|---|---|---|---|

| | | | |
|---|---|---|---|
| 1 | BHT(2) | Radical scavenger | 0 |
| 2 | $NaN_3$(1) | Singlet oxygen scavenger | 0 |
| 3 | DABCO(1) | Singlet oxygen scavenger | 21 |
| 4 | Benzoquinone (1) | Super oxide radical anion scavenger | 19 |

Reaction Condition[a]: **1a** (0.277 mmol, 30 mg), $Acr^+$-$MesClO4^-$ (5 mol %, 0.0135 mmol, 5 mg) 0.2 ml thiol and 0.5 ml $CH_3CN$ in $O_2$ atmosphere for 24 hours in Blue LEDs. Yield[b] [is] determined by $^1H$ NMR where dibromomethane is used as an internal standard.

The Stern-Volmer quenching study using fluorescence measurement of catalyst *vs.* benzyl alcohol or thiophenol rationalized that the excited state of the photocatalyst was quenched by benzyl alcohol and thiophenol as well (Figure 5.6).

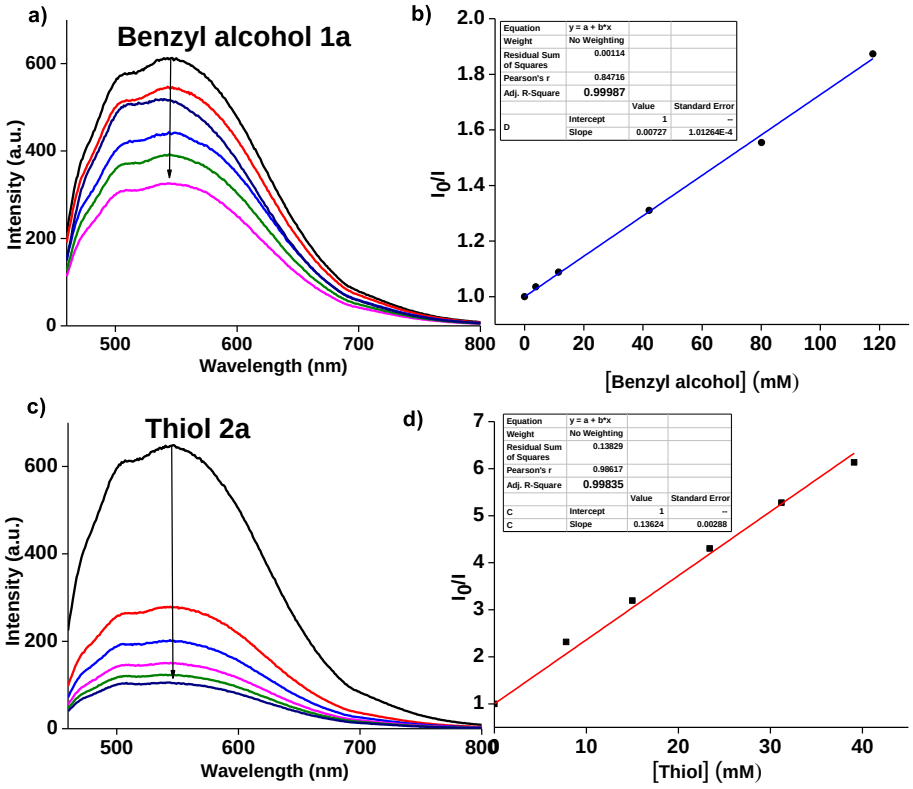


**Figure 5.6**. a) Fluorescence quenching of catalyst by benzyl alcohol **1a**; b) Stern-Volmer plot of **1a**; c) Fluorescence quenching of catalyst by thiophenol; d) Stern-Volmer plot of **2a**.

Based on the above shreds of evidence and literature reports,[26, 29] a reliable mechanism is proposed in Figure 5.7. Initially, Mes-Acr-$MeClO_4$ (PC) got excited to its [Mes-Acr-$MeClO_4$]* upon irradiation of visible light. Following, the excited photocatalyst (PC*) generated intermediate **7** from benzyl alcohol *via* SET process[30], and itself got reduced to $PC^{\cdot-}$. The intermediate **7** was converted to the radical intermediate **8** by losing $H^+$. Afterward, the $PC^{\cdot-}$ helped to generate superoxide radical anion from molecular oxygen. Now, the superoxide radical anion oxidized the intermediate **8** to the corresponding aldehyde followed by photocatalyst was regenerated. Similarly, thiophenol **2a** is also participated in the oxidative cycle to generate thiyl radical **10** (Figure 5.7a). At the pre-final stage (Figure 5.7b), thiyl radicals attacked benzaldehyde to form hemithioacetal as intermediate **11** in the presence of another molecule of thiophenol.[29] Following, hemithioacetal **11** resulted in either intermediates **12** or **13**, based on the substitution at the *para*-substituent of benzyl alcohol (as shown groups like -OMe or $-NMe_2$ favored intermediate **13**). Intermediate **12** was further transformed to **14** with the help of thiyl radical, which afforded the dithioacetal **3aa** *via* reduction of $PC^{\cdot-}$. On the other hand, electronic rich intermediate **13** was converted to cation radical **15** *via* HAT from thiophenol[31], which led to the formation of **4ma** by SET with $PC^{\cdot-}$.

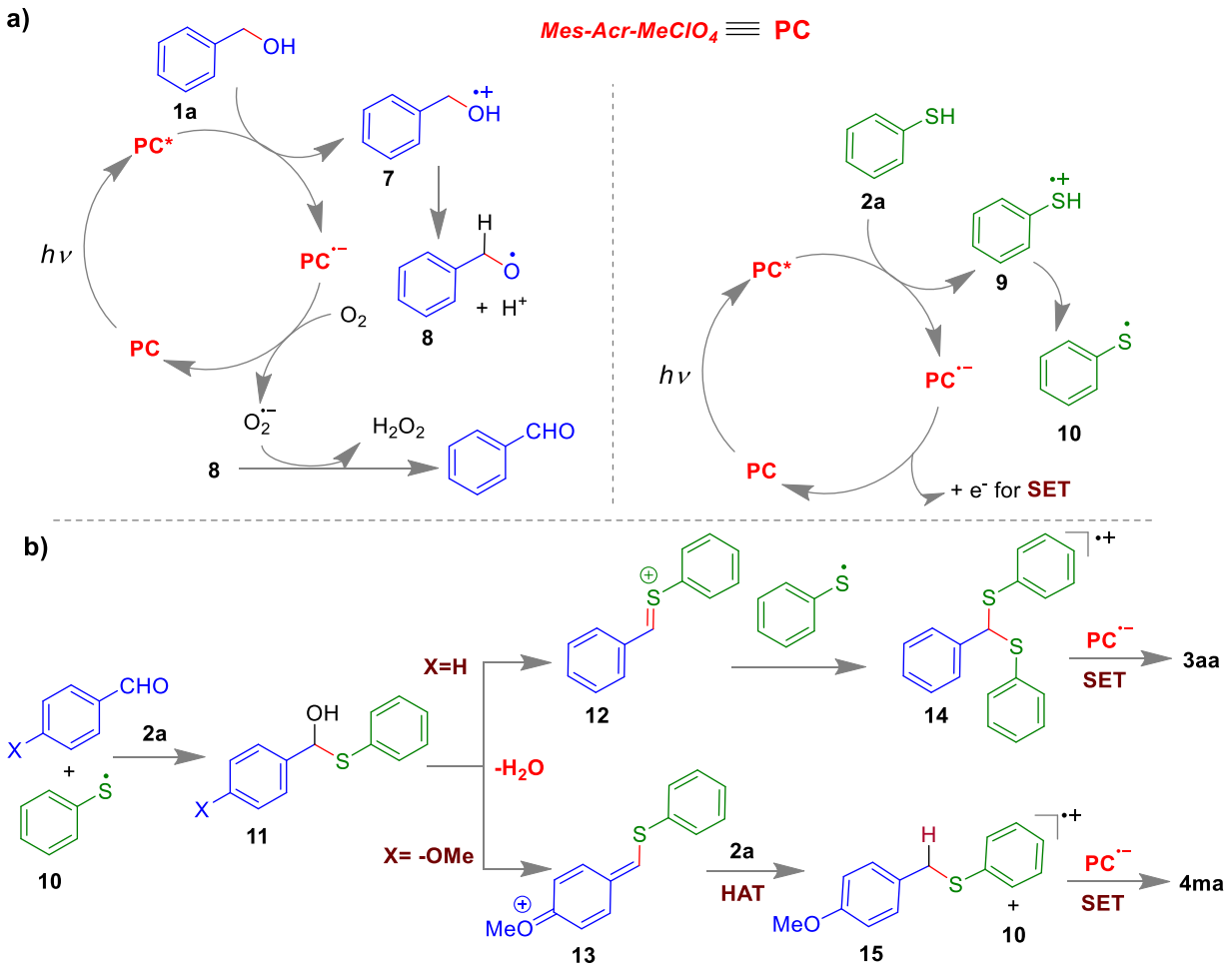



**Figure 5.7**. Plausible mechanism.

## 5.4. CONCLUSION

We have developed a unique and new strategy for C–S bond-forming reaction *via* two steps oxidative process in one pot under irradiation of visible light photocatalyst. A wide range of functional group tolerance thioacetals and thioethers were achieved from unactivated benzyl alcohols. Thus we foresee that this two-step oxidative C–O bond functionalization reaction in a single step would offer a new synthetic route for many cascaded process in organic transformation.

## 5.5. EXPERIMENTAL SECTION

**General Aspects.**

All the chemicals were purchased from commercial sources and used as received. All the reactions were generally carried out under an open atmosphere unless otherwise noted. Chromatographic purifications of the compounds were performed using silica gel (Mess 230-400) and ethyl acetate/hexane as eluent. $^{1}H$ and $^{13}C$ spectra of the compounds were recorded on Bruker 400 and 700 MHz instruments at 25 ºC. The chemical shift value (δ, ppm) were reported with respect to the residual chloroform (7.26 for $^{1}H$ and 77.16 ppm for $^{13}C$). Mass spectra were recorded as ESI-TOF (HRMS). Infrared spectra were recorded on neat solids using KBr pellets and described in wavenumber ($cm^{-1}$). Digital melting point apparatus was used to record the melting point of the compound. Fluorescence spectra were recorded in Perkin Elmer, LS 55 spectrophotometer with an optical cell of 1 cm per length. EPR spectra were obtained in a Bruker EMX (ER 073) instrument.

**Representative procedure for the preparation of sulfanes**.

In an oven-dried schlenk tube benzylic alcohol **1a** (0.555 mmol, 60 mg) and Mes-Acr-$MeClO_4$ (5 mol %, 0.027 mmol, 11 mg) were dissolved in 1.0 mL acetonitrile solvent (*for solid thiophenols 5.0 equiv was used*). Following, Thiophenol **2a** (0.5 mL) was added to the reaction mixture and irradiated by 3W Blue LED light for 24 h at room temperature (30-35 ºC). After completion of the reaction, acetonitrile was removed under reduced pressure. The pure product **3aa** was isolated through column chromatography using ethyl acetate and hexane as eluent. Generally, for 60 mg (0.555 mmol) of **1a**, 0.5 ml of **2a** was used and after reaction, approximately 0.3 mL of **2a** was recovered by column chromatography.

**Light ON-OFF-ON experiment.**

Benzylic alcohol derivatives **1a** (0.555 mmol, 60 mg), and Mes-Acr-$MeClO_4$ (5 mol %, 0.027 mmol, 11 mg) were dissolved in 1.0 mL acetonitrile. Following, Thiophenol **2a** (0.5 mL) was added to the reaction mixture and irradiated by 3W Blue LEDs light for 24 h. Successive progress of the reaction was monitored every 4 h and 6 h in the presence light and absence of light by $^1H$ NMR experiment using dibromomethane as internal standard.

**EPR experiments.**

EPR spectra were recorded at 298 K using an EPR spectrometer derived at 9.4335 GHz. Typical spectrometer parameters are shown as follows, scan range: 100 G; center fieldset: 3480.00 G; time constant: 0.16 ms; scan time: 122.88 s; modulation amplitude: 20.0 G; modulation frequency: 100 kHz; receiver gain: $2.00\times10^2$ ; microwave power: $7.14e^{-001}$ mW.

**Spin-trapping experiment in the presence DMPO.**[32]

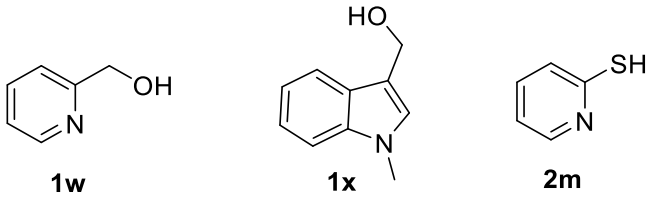
A mixture of benzyl alcohol (0.555 mmol)**,** thiophenol (0.5 mL), Mes-Acr-$MeClO_4$ (5 mol %), and DMPO (20 μL) were stirred in 1.0 mL $CH_3CN$ and irradiated in 3W Blue LEDs for 10 min. Afterward, 20 μL solution was quickly transferred into an EPR tube, and 200 μL toluene was added to analyze EPR. A similar experiment was performed without thiophenol.

**Fluorescence quenching studies.**

The photocatalyst Mes-Acr-$MeClO_4$ was excited at 440 nm. After irradiation of Mes-Acr-$MeClO_4$ ($4\times 10^{-5}$ M in MeCN) at 440 nm under $N_2$ atmosphere, maximum emission was observed at 615 nm. When the amount of benzyl alcohol under saturated air and oxygen was

increased, fluorescence intensity was gradually decreased. After irradiation of Mes-Acr-$MeClO_4$ ($4\times 10^{-5}$ M in MeCN) at 440 nm under $N_2$ atmosphere, maximum emission was observed at 648 nm. Similarly, when the amount of thiophenol was increased, fluorescence intensity was gradually decreased.

**Unsuccessful substrates**




**1w** **1x** **2m**

**Figure 5.8.** The alcohols and thiol were not compatible with the methodology.

**CHARACTERIZATION DATA**

**(Phenylmethylene)bis(phenylsulfane) (3aa).**[25] $R_f$ = 0.4 (hexane); colorless liquid; yield 96% (164 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.36-7.33 (m, 6H), 7.28-7.26 (m, 2H), 7.24-7.22 (m, 7H), 5.42 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 139.8, 134.7, 132.7, 129.0, 128.6, 128.2, 128.0, 127.9, 60.6.

**(*p*-Tolylmethylene)bis(phenylsulfane) (3ba).** $R_f$ = 0.45 (hexane); white solid; yield 89% (140 mg); mp 55-57 ºC (lit.[25] 56-58 ºC); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.36-7.34 (m, 4H), 7.27 (d, *J* = 7.8 Hz, 2H), 7.26-7.23 (m, 6H), 7.08 (d, *J* = 7.8 Hz, 2H), 5.42 (s, 1H), 2.32 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 138.0, 136.8, 134.9, 132.4, 129.3, 128.9, 127.9, 127.8, 60.3, 21.3.

**(*o*-Tolylmethylene)bis(phenylsulfane) (3ca).**[25] $R_f$ = 0.5 (hexane); colorless liquid; yield 84% (133 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.65-7.63 (m, 1H), 7.35-7.33 (m, 4H), 7.26-7.22 (m, 6H), 7.19-7.15 (m, 2H), 7.13-7.09 (m, 1H), 5.66 (s, 1H), 2.31 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 137.5, 135.2, 135.0, 132.4, 130.5, 129.0, 128.4, 128.0, 127.8, 126.6, 57.2, 19.4.

**((4-Isopropylphenyl)methylene)bis(phenylsulfane) (3da).**[25] $R_f$ = 0.45 (hexane); colorless liquid; yield 84% (118 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.36-7.34 (m, 2H), 7.34-7.32 (m, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 7.26-7.22 (m, 6H), 7.13 (d, *J* = 8.2 Hz, 2H), 5.43 (s, 1H), 2.88 (sept, *J* = 7.0 Hz, 1H), 1.23 (d, *J* = 7.0 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 148.9, 137.1, 135.0, 132.5, 128.9, 127.8, 127.8, 126.7, 60.4, 33.9, 24.0.

**((4-(Tert-butyl)phenyl)methylene)bis(phenylsulfane) (3ea).**[25] $R_f$ = 0.3 (hexane); white semi solid; yield 76% (101 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.36-7.35 (m, 2H), 7.34-7.32 (m, 2H), 7.31-7.28 (m, 4H), 7.26-7.24 (m, 3H), 7.24-7.22 (m, 3H), 5.44 (s, 1H), 1.30 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 151.2, 136.7, 135.0, 132.4, 128.9, 127.7, 127.6, 125.6, 60.4, 34.7, 31.4

**((4-Fluorophenyl)methylene)bis(phenylsulfane) (3fa).**[25] $R_f$ = 0.4 (hexane); colorless liquid; yield 65% (101 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.36-7.33 (m, 4H), 7.32-7.29 (m, 2H), 7.27-7.24 (m, 6H), 6.94 (t, *J* = 8.6 Hz, 2H), 5.42 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 162.4 (d, $^1J_{C-F}$ = 247.2 Hz), 135.6 (d, $^4J_{C-F}$ = 3.0 Hz), 134.3, 132.9, 129.7 (d, $^3J_{C-F}$ = 8.3 Hz), 129.0, 128.12, 115.5 (d, $^2J_{C-F}$ = 21.8 Hz), 59.8.

**((4-Nitrophenyl)methylene)bis(phenylsulfane) (3ga).**[25] $R_f$ = 0.45 (5% ethyl acetate in hexane); yellow liquid; yield 42% (58 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.6 Hz, 2H), 7.45 (d, *J* = 8.6 Hz, 2H), 7.35-7.34 (m, 2H), 7.34-7.32 (m, 2H), 7.29-7.25 (m, 6H), 5.44 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 147.2, 133.4, 129.2, 129.2, 128.9, 128.7, 127.7, 123.8, 59.9.

**((3-Phenoxyphenyl)methylene)bis(phenylsulfane) (3ha):** $R_f$ = 0.2 (hexane); colorless liquid; yield 98% (117 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.37-7.35 (m, 4H), 7.33 (d, *J* = 7.6 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 1H), 7.27-7.23 (m, 7H), 7.15 (d, *J* = 7.6 Hz, 1H), 7.10 (t, *J* = 7.4 Hz, 1H), 6.99 (s, 1H), 6.89 (d, *J* = 8.0 Hz, 3H), 5.39 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 157.2, 157.1, 141.7, 134.4, 132.9, 130.0, 129.8, 129.0, 128.0, 123.3, 123.0, 118.8, 118.76, 118.68, 60.2; IR (KBr) ῡ 2923, 1489, 1248, 1024, 689 $cm^{-1}$; HRMS (ESI/Q-TOF) m/z: $[M\text{-}SC_6H_5]^+$ calcd for $C_{19}H_{15}OS$ 291.0838; found 291.0815.

**((4-(Methylthio)phenyl)methylene)bis(phenylsulfane) (3ia).** $R_f$ = 0.4 (2% ethyl acetate in hexane); white solid; yield 74% (102 mg); mp 86-90 ºC (lit.[25] 88-90 ºC); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.36-7.33 (m, 4H), 7.29 (d, *J* = 8.4 Hz, 2H), 7.26-7.23 (m, 6H), 7.14 (d, *J* = 8.4 Hz, 2H), 5.40 (s, 1H), 2.46 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 138.5, 136.5, 134.6, 132.6, 129.0, 128.4, 127.9, 126.4, 60.1, 15.8.

**(Phenylmethylene)bis(p-tolylsulfane) (3ab).** $R_f$ = 0.2 (hexane); white solid; yield 84% (156 mg); mp 66-67 ºC (lit.[25] 64-66 ºC); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 7.4 Hz, 2H), 7.25 (d, *J* = 6.8 Hz, 3H), 7.24 (d, *J* = 7.8 Hz, 4H), 7.05 (d, *J* = 7.8 Hz, 4H), 5.31 (s, 1H), 2.31 (s, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 140.1, 138.1, 133.3, 131.0, 129.7, 128.5, 128.0 (×2), 61.4, 21.3.

**(Phenylmethylene)bis((3-methoxyphenyl)sulfane) (3ac):** $R_f$ = 0.4 (5% ethyl acetate in hexane); colorless liquid; yield 70% (142 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.40-7.37 (m, 2H), 7.30-7.29 (m, 1H), 7.28-7.26 (m, 1H), 7.24-7.23 (m, 1H), 7.15 (t, *J* = 8.0 Hz, 2H), 6.95 (d, *J* = 7.8 Hz, 2H), 6.86-6.84 (m, 2H), 6.77 (d, *J* = 8.2 Hz, 1H), 6.76 (d, *J* = 8.2 Hz, 1H), 5.45 (s, 1H), 3.70 (s, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 159.7, 141.4, 135.9, 129.7, 128.7, 128.2, 128.1, 124.5, 117.3, 114.0, 60.1, 55.4; IR (KBr) ῡ 2833, 2359, 1590, 1283, 685 cm$^{-1}$; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{21}H_{20}O_2S_2Na$ 391.0797; found 391.0770.

**(Phenylmethylene)bis((4-bromophenyl)sulfane) (3ad):** $R_f$ = 0.4 (2% ethyl acetate in hexane); white solid; yield 77% (200 mg); mp 64-66 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.4 Hz, 4H), 7.34-7.31 (m, 2H), 7.30-7.26 (m, 3H), 7.18 (d, *J* = 8.4 Hz, 4H), 5.35 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 139.0, 134.4, 133.3, 132.1, 128.8, 128.5, 128.0, 122.5, 60.6; IR (KBr) ῡ 3059, 1471, 1088, 695, 592 cm$^{-1}$; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$calcd for $C_{19}H_{14}Br_2S_2Na$ 488.8775; found 488.8753.

**(Phenylmethylene)bis((4-chlorophenyl)sulfane) (3ae).**[25] $R_f$ = 0.5 (2% ethyl acetate in hexane); colorless liquid; yield 94% (197 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.34-7.32 (m, 2H), 7.31-7.28 (m, 2H), 7.28-7.26 (m, 5H), 7.23-7.21 (m, 4H), 5.36 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 139.0, 134.4, 134.3, 132.6, 129.1, 128.7, 128.4, 127.9, 60.9.

**(Phenylmethylene)bis((3-chlorophenyl)sulfane) (3af):** $R_f$ = 0.55 (2% ethyl acetate in hexane); colorless liquid; yield 91% (191 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.38-7.36 (m, 2H), 7.33-7.31 (m, 2H), 7.31-7.28 (m, 3H), 7.25-7.15 (m, 6H), 5.45 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ

138.8, 136.3, 134.6, 132.2, 130.5, 130.0, 128.8, 128.6, 128.2, 128.0, 60.3; IR (KBr) ῡ 3069, 1574, 1083, 778, 679 $cm^{-1}$; HRMS (ESI/Q-TOF) m/z: $[M-C_6H_4ClS]^+$ calcd for $C_{13}H_{10}ClS$ 233.0186; found 233.0177.

**(Phenylmethylene)bis((4-fluorophenyl)sulfane) (3ag).**[25] $R_f$ = 0.4 (hexane); colorless liquid; yield 88% (168 mg); $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.34-7.29 (m, 5H), 7.26-7.23 (m, 4H), 6.94 (t, *J* = 8.6 Hz, 4H), 5.23 (s, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 163.0 (d, $^1J_{C-F}$ = 248.9 Hz), 139.4, 136.0 (d, $^3J_{C-F}$ = 8.3 Hz), 129.3 (d, $^4J_{C-F}$ = 3.4 Hz), 128.6, 128.3, 128.0, 116.1 (d, $^2J_{C-F}$ = 21.8 Hz), 62.3.

**(Phenylmethylene)bis((2-fluorophenyl)sulfane) (3ah):** $R_f$ = 0.35 (hexane); colorless liquid; yield 79% (151 mg); $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 7.4 Hz, 2H), 7.37 (d, *J* = 7.4 Hz, 2H), 7.28-7.22 (m, 5H), 7.02 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 8.0 Hz, 2H), 5.71 (s, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 162.5 (d, $^1J_{C-F}$ = 246.8 Hz), 139.0, 135.4, 130.5 (d, $^3J_{C-F}$ = 8.3 Hz), 128.7, 128.5, 128.0, 124.6 (d, $^4J_{C-F}$ = 3.9 Hz), 121.4 (d, $^2J_{C-F}$ = 18.3 Hz), 115.9 (d, $^2J_{C-F}$ = 23.0 Hz), 57.9; IR (KBr) ῡ 3065, 1671, 1471, 1226, 697 $cm^{-1}$; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{19}H_{14}F_2S_2Na$ 367.0397; found 367.0372.

**(Phenylmethylene)bis((4-(trifluoromethyl)phenyl)sulfane) (3ai):** $R_f$ = 0.35 (hexane); colorless liquid; yield 61% (86 mg); $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.2 Hz, 4H), 7.44 (d, *J* = 7.8 Hz, 2H), 7.41 (d, *J* = 8.2 Hz, 4H), 7.36-7.30 (m, 3H), 5.60 (s, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 139.5, 138.2, 131.2, 129.5 (q, $^2J_{C-F}$ = 32.5 Hz), 129.0, 128.9, 128.0, 125.9 (q, $^4J_{C-F}$ =

3.6 Hz), 125.4 (q, $^{1}J_{C\text{-}F}$ = 272.4 Hz), 58.6; IR (KBr) ῡ 2925, 1606, 1166, 1674, 702 $cm^{-1}$; HRMS (ESI/Q-TOF) m/z: $[M\text{-}C_7H_4F_3S]^+$ calcd for $C_{14}H_{10}F_3S$ 267.0450; found 267.0442.

**(*p*-Polylmethylene)bis(cyclopentylsulfane) (3bj):** $R_f$ = 0.6 (hexane); colorless liquid; yield 54% (81 mg); $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 7.8 Hz, 2H), 7.12 (d, *J* = 7.8 Hz, 2H), 4.86 (s, 1H), 3.12-3.07 (m, 2H), 2.33 (s, 3H), 1.98-1.88 (m, 4H), 1.71-1.63 (m, 4H), 1.53-1.48 (m, 8H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 138.3, 137.5, 129.3, 127.7, 52.7, 44.4, 33.7, 25.0, 21.3; IR (KBr) ῡ 2954, 1652, 1509, 459, 667 $cm^{-1}$; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{18}H_{26}S_2Na$ 329.1368; found 329.1377.

**(4-Methoxybenzyl)(phenyl)sulfane (4ma).** $R_f$ = 0.4 (5% ethyl acetate in hexane); white solid; yield 85% (85 mg); mp 83-85 ºC (lit.[33] 85 ºC); $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.33-7.31 (m, 2H), 7.28-7.26 (m, 1H), 7.24-7.23 (m, 2H), 7.21-7.16 (m, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 4.09 (s, 2H), 3.79 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 158.9, 136.7, 130.1, 129.9, 129.5, 128.9, 126.4, 114.0, 55.4, 38.6.

**(4-Methoxybenzyl)(4-methoxyphenyl)sulfane (4mk).** $R_f$ = 0.65 (5% ethyl acetate in hexane); white solid; yield 93% (105 mg); mp 89-90 ºC (lit.[34] 89 ºC); $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.6 Hz, 2H), 7.11 (d, *J* = 8.6 Hz, 2H), 6.79 (d, *J* = 8.6 Hz, 4H), 3.95 (s, 2H), 3.78 (s, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 159.3, 158.8, 134.2, 130.3, 130.1, 126.4, 114.5, 113.9, 55.4, 55.4, 40.8.

**(4-Methoxybenzyl)(p-tolyl)sulfane (4mb).** $R_f$ = 0.65 (5% ethyl acetate in hexane); white solid; yield 72% (76 mg); mp 63-65 ºC (lit.[33] 66 ºC); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 8.6 Hz, 2H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.81 (d, *J* = 8.6 Hz, 2H), 4.03 (s, 2H), 3.79 (s, 3H), 2.31 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 158.9, 136.6, 132.9, 130.8, 130.1, 129.9, 129.7, 114.0, 55.4, 39.3, 21.2.

**(4-Methoxybenzyl)(o-tolyl)sulfane (4ml).**[35] $R_f$ = 0.65 (5% ethyl acetate in hexane); white solid; yield 70% (74 mg); mp 62-64 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 7.4 Hz, 1H), 7.24 (d, *J* = 8.2 Hz, 2H), 7.16 (t, *J* = 6.8 Hz, 2H), 7.13-7.09 (m, 1H), 6.84 (d, *J* = 8.2 Hz, 2H), 4.06 (s, 2H), 3.80 (s, 3H), 2.35 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 158.9, 137.9, 136.1, 130.14, 130.10, 129.3, 128.9, 126.5, 126.1, 114.0, 55.4, 37.8, 20.4.

**(4-Methoxybenzyl)(3-methoxyphenyl)sulfane (4mc):** $R_f$ = 0.3 (5% ethyl acetate in hexane); colorless liquid; yield 63% (70 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.6 Hz, 2H), 7.17 (t, *J* = 8.0 Hz, 1H), 6.90 (d, *J* = 7.8 Hz, 1H), 6.83 (d, *J* = 8.6 Hz, 3H), 6.72 (dd, *J* = 8.2, 2.2 Hz, 1H), 4.09 (s, 2H), 3.79 (s, 3H), 3.76 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 159.8, 158.9, 138.1, 130.1, 129.7, 129.4, 121.8, 114.8, 114.1, 112.2, 55.4, 55.3, 38.3; IR (KBr) ῡ 2924, 1634, 1511, 1034, 686 $cm^{-1}$; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{16}O_2SNa$ 283.0763; found 283.0755.

**(2,4-Dimethoxybenzyl)(phenyl)sulfane (4na):** $R_f$ = 0.4 (5% ethyl acetate in hexane); colorless liquid; yield 81% (75 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.34-7.32 (m, 2H), 7.27-7.25 (m, 1H), 7.24 (d, *J* = 7.8 Hz, 1H), 7.19-7.16 (m, 1H), 7.09 (d, *J* = 8.2 Hz, 1H), 6.45-6.44 (m, 1H), 6.39

(dd, *J* = 8.2, 2.4 Hz, 1H), 4.10 (s, 2H), 3.80 (s, 3H), 3.79 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 160.6, 158.4, 137.3, 130.8, 129.9, 128.8, 126.1, 118.3, 104.2, 98.8, 55.6, 55.5, 33.1; IR (KBr) ῡ 2934, 2358, 1505, 1209, 691 $cm^{-1}$; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{16}O_2SNa$ 283.0763; found 283.0762.

**(3,4-Dimethoxybenzyl)(phenyl)sulfane (4oa).**[36] $R_f$ = 0.35 (5% ethyl acetate in hexane); white solid; yield 53% (49 mg); mp 78-80 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 7.8 Hz, 2H), 7.26 (t, *J* = 7.4 Hz, 2H), 7.19 (t, *J* = 6.8 Hz, 1H), 6.82 (d, *J* = 8.4 Hz, 1H), 6.79-6.76 (m, 2H), 4.08 (s, 2H), 3.86 (s, 3H), 3.82 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 149.0, 148.3, 136.5, 130.2, 130.0, 128.9, 126.5, 121.1, 112.0, 111.1, 56.0, 55.9, 39.2.

**((3,4-Dimethoxyphenyl)methylene)bis(phenylsulfane) (3oa).**[37] $R_f$ = 0.3 (5% ethyl acetate in hexane); colorless liquid; yield 26% (41 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.38-7.36 (m, 4H), 7.28-7.25 (m, 6H), 6.91 (s, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 6.74 (d, *J* = 8.2 Hz, 1H), 5.42 (s, 1H), 3.86 (s, 3H), 3.81 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 148.9, 148.8, 134.6, 132.7, 132.1, 128.9, 127.9, 120.3, 110.9, 110.8, 60.2, 55.9(×2).

**5-((Phenylthio)methyl)benzo[d][1,3]dioxole (4pa).**[38] $R_f$ = 0.55 (2% ethyl acetate in hexane); colorless liquid; yield 52% (50 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.32-7.30 (m, 2H), 7.28-7.24 (m, 2H), 7.21-7.17 (m, 1H), 6.82 (s, 1H), 6.73-6.69 (m, 2H), 5.93 (s, 2H), 4.04 (s, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 147.9, 146.9, 136.4, 131.3, 130.0, 129.0, 126.5, 122.2, 109.3, 108.2, 101.1, 39.2.

**5-(Bis(phenylthio)methyl)benzo[d][1,3]dioxole (3pa).**[37] $R_f$ = 0.5 (2% ethyl acetate in hexane); colorless liquid; yield 45% (62 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.38-7.36 (m, 4H), 7.29-7.26 (m, 6H), 6.99 (d, *J* = 1.7 Hz, 1H), 6.79 (dd, *J* = 8.0, 1.8 Hz, 1H), 6.67 (d, *J* = 8.0 Hz, 1H), 5.97 (s, 2H), 5.37 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 147.9, 147.5, 134.7, 133.7, 132.5, 129.0, 127.9, 121.6, 108.4, 108.0, 101.4, 60.3.

**Phenyl(3,4,5-trimethoxybenzyl)sulfane (4qa).**[39] $R_f$ = 0.25 (5% ethyl acetate in hexane); colorless liquid; yield 29% (25 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.36-7.32 (m, 2H), 7.28 (d, *J* = 7.2 Hz, 1H), 7.26-7.23 (m, 1H), 7.22-7.18 (m, 1H), 6.47 (s, 2H), 4.05 (s, 2H), 3.82 (s, 3H), 3.79 (s, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 153.3, 137.3, 136.3, 133.2, 130.5, 129.0, 126.7, 105.9, 61.0, 56.2, 39.9.

**((3,4,5-Trimethoxyphenyl)methylene)bis(phenylsulfane) (3qa).**[40] $R_f$ = 0.2 (5% ethyl acetate in hexane); colorless liquid; yield 59% (71 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.38-7.36 (m, 4H), 7.27-7.25 (m, 6H), 6.55 (s, 2H), 5.36 (s, 1H), 3.83 (s, 3H), 3.77 (s, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 153.1, 137.7, 135.2, 134.4, 132.9, 129.0, 128.0, 105.0, 61.0, 60.9, 56.2;

**N,N-Dimethyl-4-((phenylthio)methyl)aniline (4ra).**[41] $R_f$ = 0.65 (10% ethyl acetate in hexane); white solid; yield 97% (93 mg); mp 95-97 ºC (lit. 95-105 ºC); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 7.8 Hz, 2H), 7.26 (t, *J* = 7.4 Hz, 2H), 7.17 (t, *J* = 8.2 Hz, 3H), 6.67 (d, *J* = 8.2 Hz, 2H), 4.09 (s, 2H), 2.93 (s, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 150.0, 137.3, 129.8, 129.5, 128.9, 126.1, 124.9, 112.7, 40.8, 38.6.

**2-Methoxy-4-((phenylthio)methyl)phenol (4sa):** $R_f$ = 0.5 (10% ethyl acetate in hexane); white solid; yield 79% (76 mg); mp 94-96 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.33-7.30 (m, 2H), 7.28-7.26 (m, 1H), 7.26-7.24 (m, 1H), 7.21-7.17 (m, 1H), 6.82 (d, *J* = 7.8 Hz, 1H), 6.78-6.75 (m, 2H), 5.54 (s, 1H), 4.06 (s, 2H), 3.83 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 146.6, 144.9, 136.5, 130.2, 129.4, 129.0, 126.5, 121.9, 114.3, 111.4, 56.0, 39.3; IR (KBr) ῡ 2996, 1601, 1279, 1034, 748, 699 $cm^{-1}$; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{14}H_{14}O_2SNa$ 269.0607; found 269.0605.

**4-(Bis(phenylthio)methyl)phenyl benzoate (3ja).**[22] $R_f$ = 0.4 (5% ethyl acetate in hexane); white solid; yield 72% (81 mg); mp 116-118 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 7.8 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.38-7.36 (m, 4H), 7.27-7.26 (m, 6H), 7.14 (d, *J* = 8.4 Hz, 2H), 5.45 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 165.3, 150.7, 137.4, 134.4, 133.8, 132.9, 130.3, 129.6, 129.2, 129.1, 128.7, 128.1, 121.8, 60.1.

**Methyl 4-(bis(phenylthio)methyl)benzoate (3ka).**[25] $R_f$ = 0.45 (5% ethyl acetate in hexane); colorless liquid; yield 58% (76 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.2 Hz, 2H), 7.39 (d, *J* = 8.2 Hz, 2H), 7.35-7.34 (m, 4H), 7.26-7.24 (m, 6H), 5.44 (s, 1H), 3.91 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 166.8, 144.9, 133.9, 133.1, 129.9, 129.8, 129.1, 128.3, 128.1, 60.3, 52.3.

**2-(3-(Bis(phenylthio)methyl)phenoxy)-1-phenylethan-1-one (3la).**[22] $R_f$ = 0.55 (5% ethyl acetate in hexane); white solid; yield 80% (87 mg); mp 89-91 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.8 Hz, 1H), 7.97 (s, 1H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 2H), 7.35-7.32 (m, 4H), 7.24-7.23 (m, 6H), 7.18 (t, *J* = 7.8 Hz, 1H), 6.98 (d, *J* = 7.8 Hz, 1H), 6.97-6.95 (m, 1H),

6.84 (dd, *J* = 8.2, 2.4 Hz, 1H), 5.37 (s, 1H), 5.18 (s, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 194.5, 158.1, 141.5, 134.8, 134.5, 134.0, 132.8, 129.8, 129.0 (×2), 128.3, 128.0, 121.4, 115.0, 114.3, 71.0, 60.4.

**(2-(Bis(phenylthio)methyl)thiophene) (3ta):**[25] $R_f$ = 0.35 (hexane); colorless liquid; yield 68% (112 mg ); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.42-7.39 (m, 4H), 7.29-7.26 (m, 6H), 7.23-7.21 (m, 1H), 6.95-6.94 (m, 1H), 6.86-6.84 (m, 1H), 5.71 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 143.9, 134.3, 132.9, 129.0, 128.2, 126.64, 126.63, 125.9, 55.7.

**(p-Tolylmethylene)bis(isobutylsulfane) (3bk):** $R_f$ = 0.4 (hexane); colorless liquid; yield 62% (86 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.2 Hz, 2H), 7.13 (d, *J* = 8.2 Hz, 2H), 4.80 (s, 1H), 2.49-2.38 (m, 4H), 2.34 (s, 3H), 1.85-1.72 (m, 2H), 0.98-0.94 (m, 12H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 137.8, 137.6, 129.3, 127.7, 54.0, 41.4, 28.5, 22.2, 21.3; IR (KBr) ῡ 2835, 2366, 1587, 1278, 688 $cm^{-1}$; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{16}H_{26}S_2Na$ 305.1368; found 305.1355.

**2-(4-Bromophenyl)-1,3-dithiane (3ul):** $R_f$ = 0.45 (2% ethyl acetate in hexane); white solid; yield 69% (61 mg); mp 88-90 ºC (lit.[24] 93-94 ºC); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.4 Hz, 2H), 5.11 (s, 1H), 3.08-3.00 (m, 2H), 2.93-2.87 (m, 2H), 2.19-2.13 (m, 1H), 1.99-1.86 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 138.3, 132.0, 129.6, 122.4, 50.7, 32.1, 25.1.

**(2-((p-Tolylthio)methyl)furan) (4vb):** $R_f$ = 0.45 (hexane); colorless liquid; yield 59% (74 mg); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.35-7.34 (m, 1H), 7.26 (d, *J* = 7.8 Hz, 2H), 7.09 (d, *J* = 7.8 Hz, 2H), 6.27 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.07 (d, *J* = 3.2 Hz, 1H), 4.05 (s, 2H), 2.32 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 151.4, 142.2, 137.2, 131.8, 131.6, 129.8, 110.5, 107.9, 32.5, 21.2; IR (KBr) ῡ 2923, 2358, 1547, 1298, 699 $cm^{-1}$; HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{12}H_{12}OSNa$ 227.0501; found 227.0497.

## 5.6 NOTES AND REFERENCES

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## NMR Spectrum of Selected Compounds

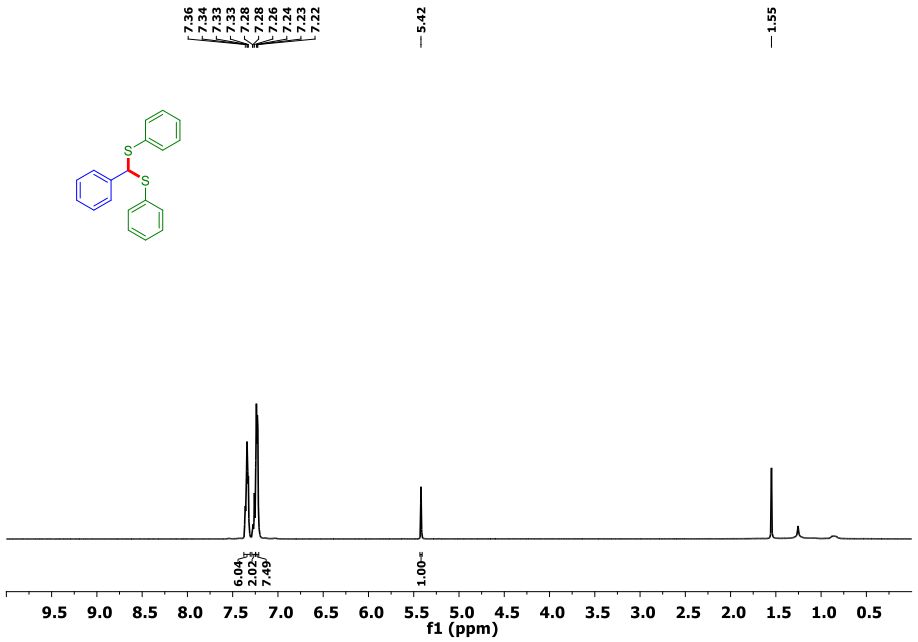



**Figure 5.9.** $^{1}$H NMR spectrum of (phenylmethylene)bis(phenylsulfane) (**3aa**)

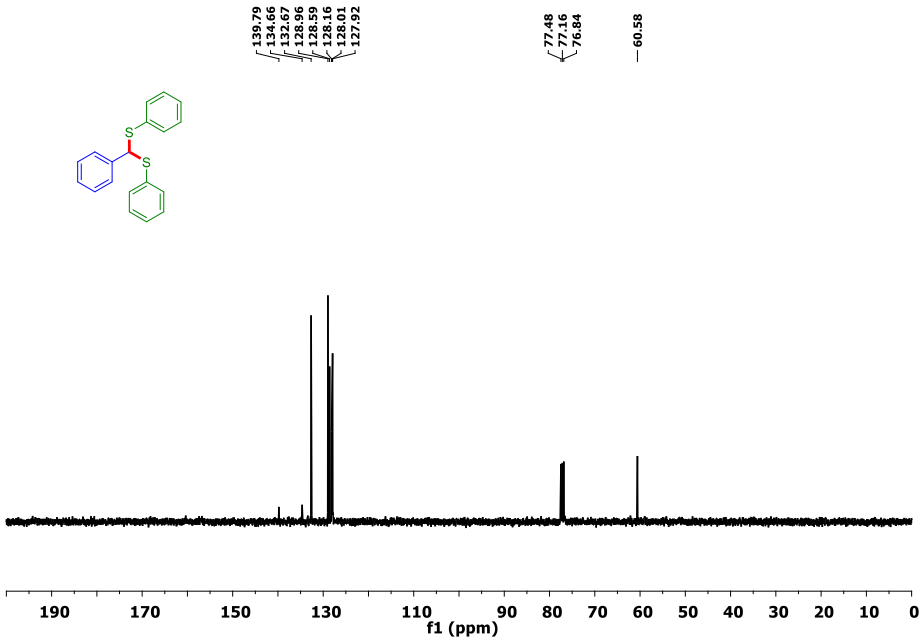



**Figure 5.10.** $^{13}$C NMR spectrum of (phenylmethylene)bis(phenylsulfane) (**3aa**)

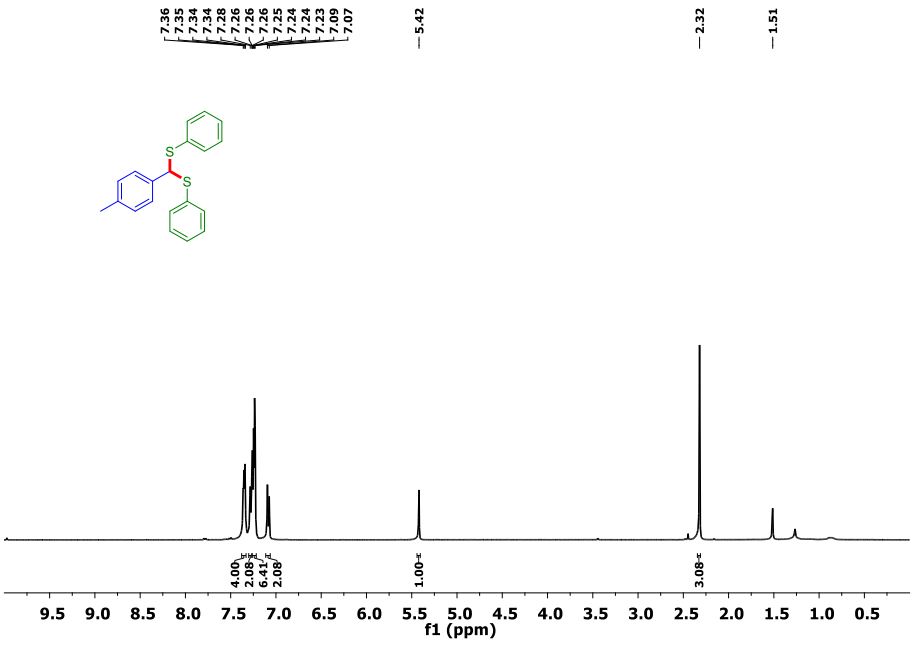



**Figure 5.11.** $^{1}$H NMR spectrum of (p-tolylmethylene)bis(phenylsulfane) (**3ba**)

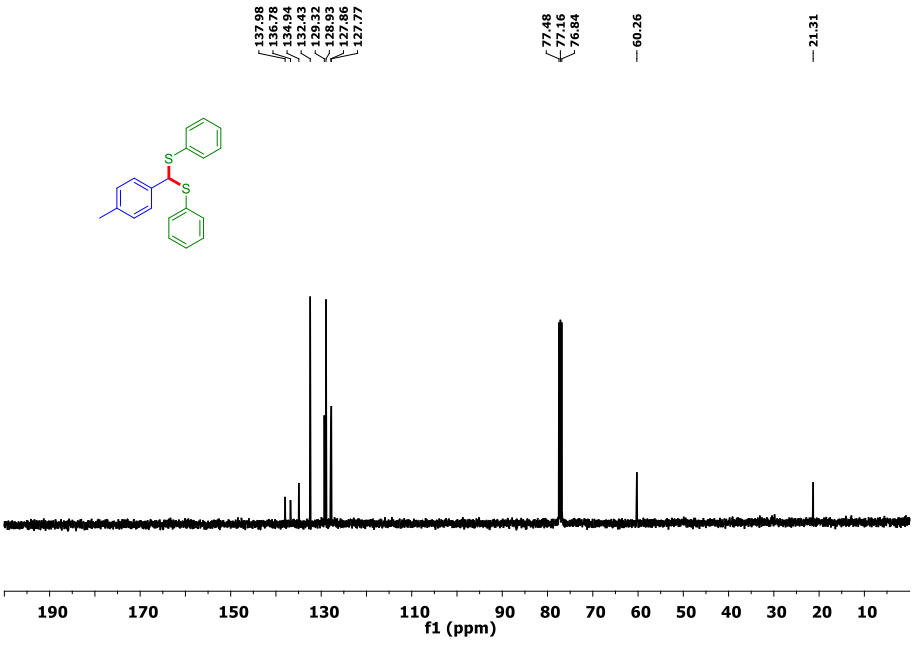



**Figure 5.12.** $^{13}$C NMR spectrum of (phenylmethylene)bis(phenylsulfane) (**3ba**)

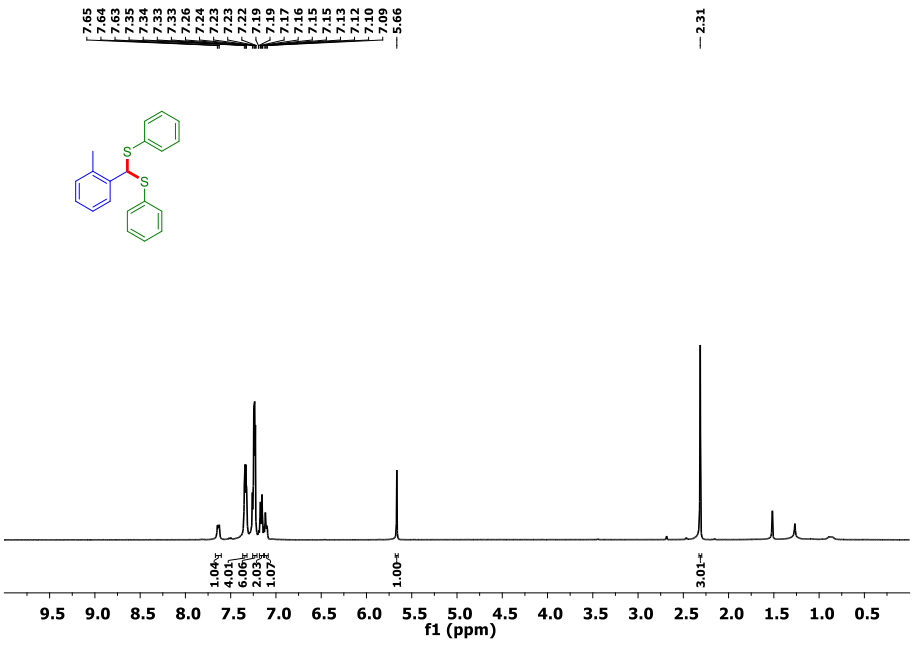



**Figure 5.13.** $^{1}$H NMR spectrum of (o-tolylmethylene)bis(phenylsulfane) (**3ca**)

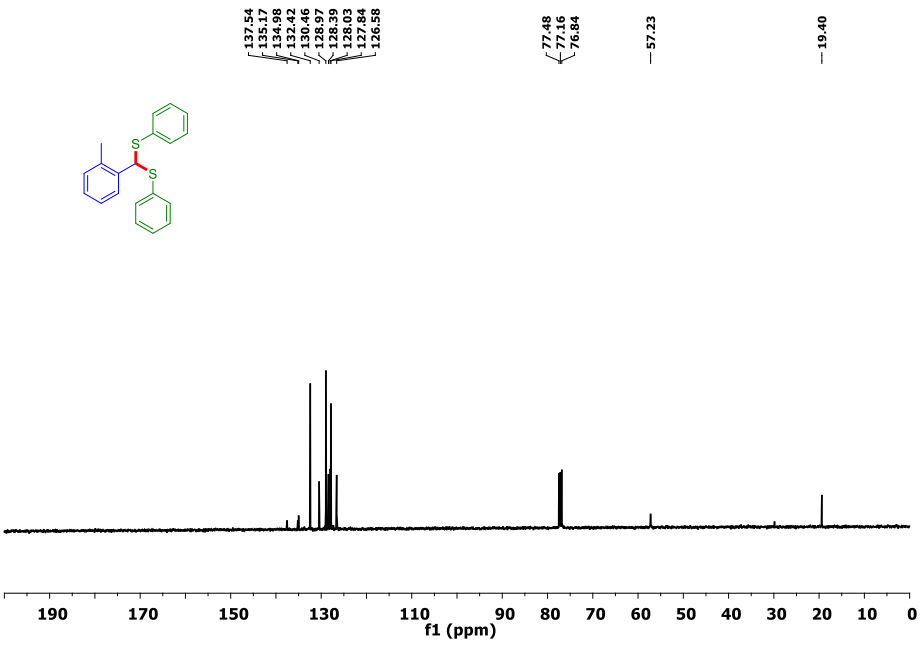



**Figure 5.14.** $^{13}$C NMR spectrum of (*o*-tolylmethylene)bis(phenylsulfane) (**3ca**)

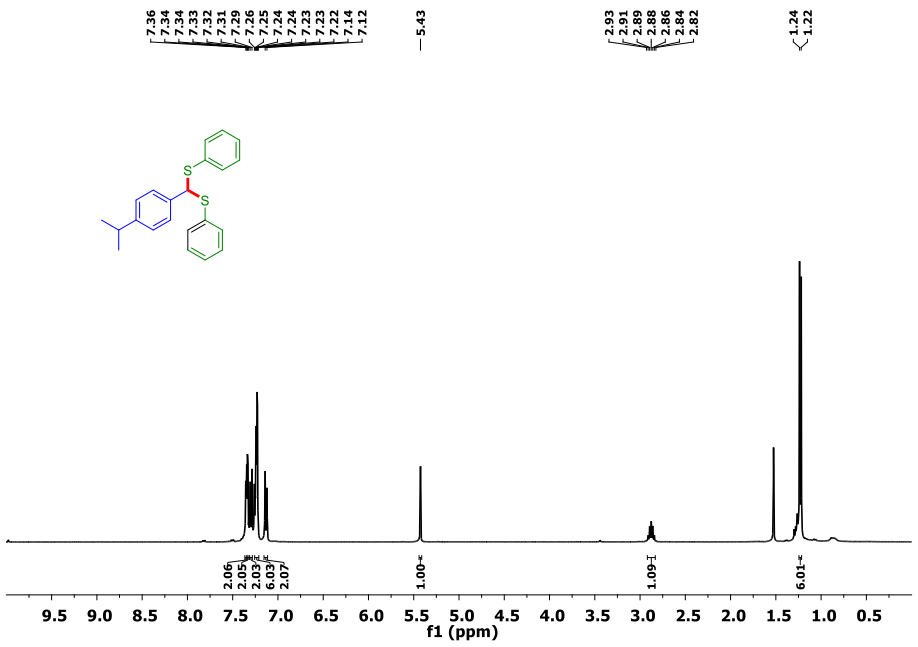



**Figure 5.15.** $^{1}$H NMR spectrum of ((4-isopropylphenyl)methylene)bis(phenylsulfane) (**3da**)

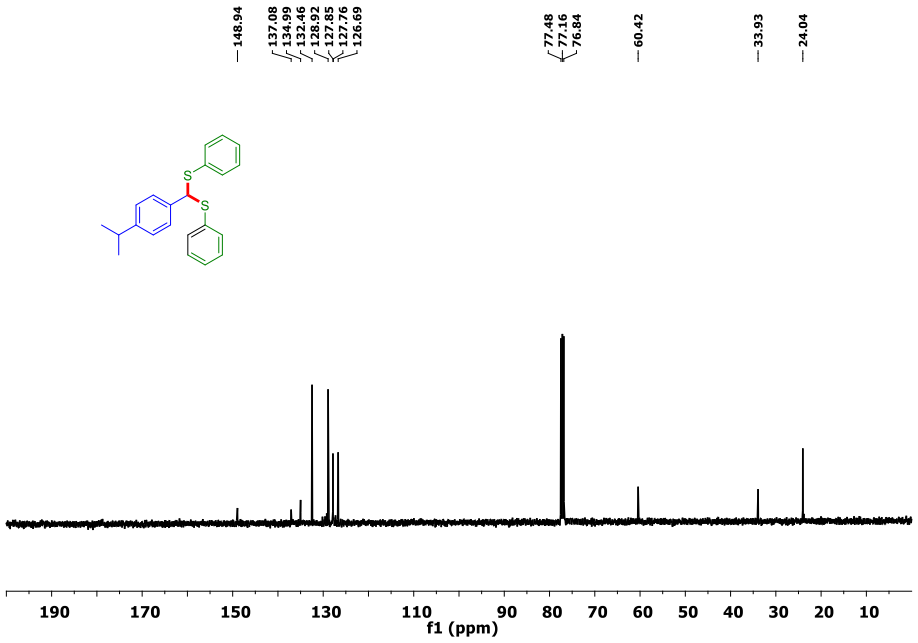



**Figure 5.16.** $^{13}$C NMR spectrum of ((4-isopropylphenyl)methylene)bis(phenylsulfane) (**3da**)

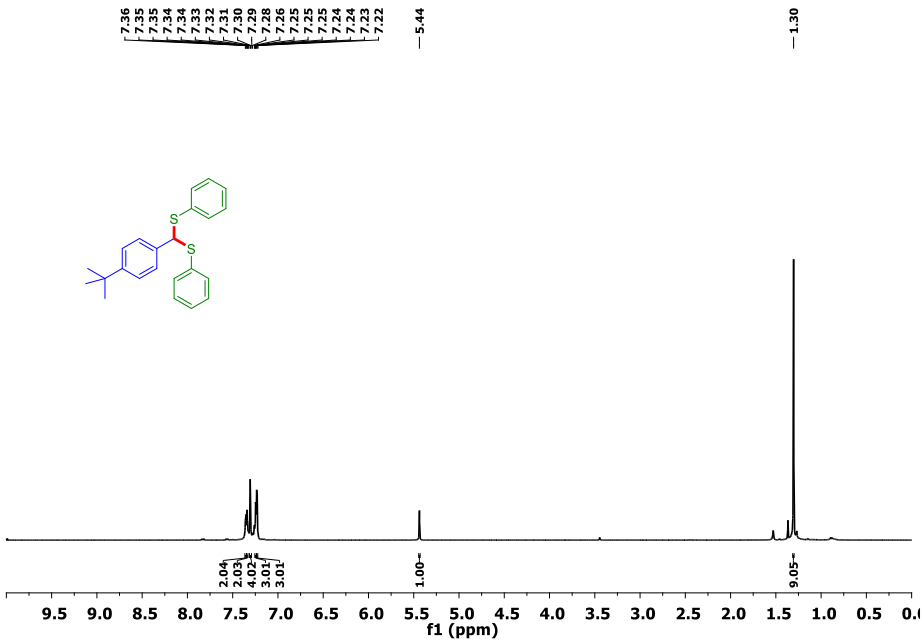



**Figure 5.17.** $^{1}$H NMR spectrum of ((4-(tert-butyl)phenyl)methylene)bis(phenylsulfane) (**3ea**)

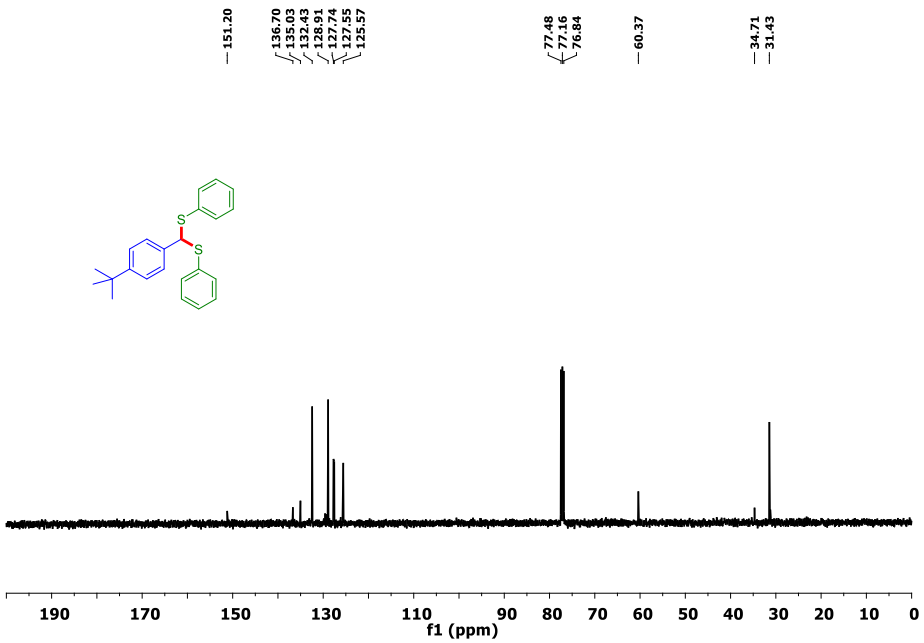



**Figure 5.18.** $^{13}$C NMR spectrum of ((4-(tert-butyl)phenyl)methylene)bis(phenylsulfane) (**3ea**)

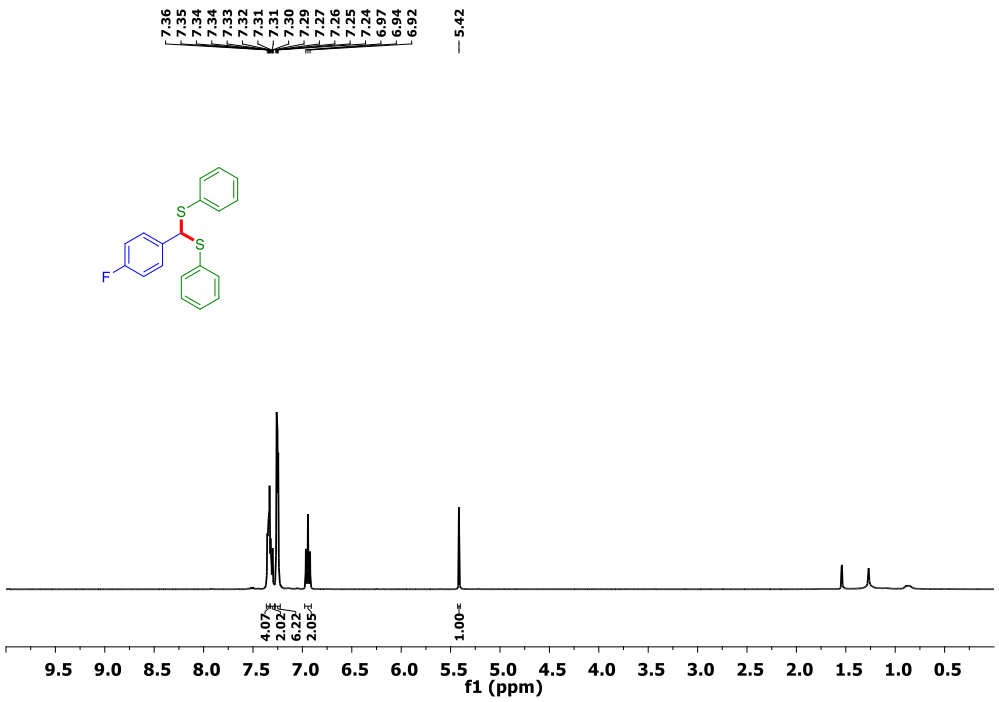



**Figure 5.19.** $^{1}$H NMR spectrum of ((4-fluorophenyl)methylene)bis(phenylsulfane) (**3fa**)

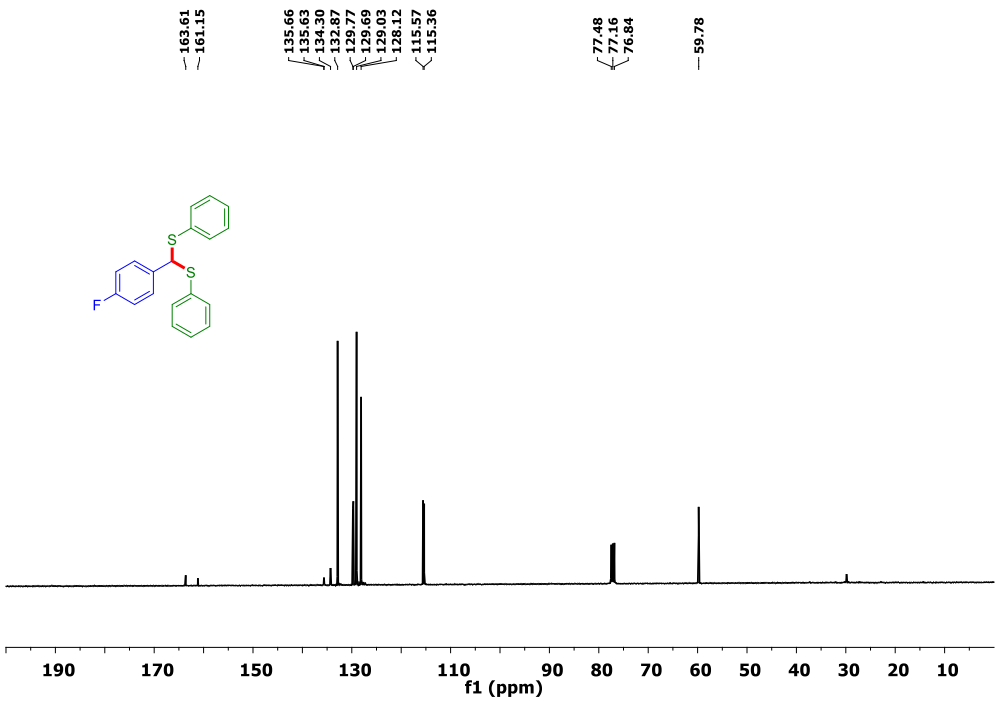



**Figure 5.20.** $^{13}$C NMR spectrum of ((4-fluorophenyl)methylene)bis(phenylsulfane) (**3fa**)

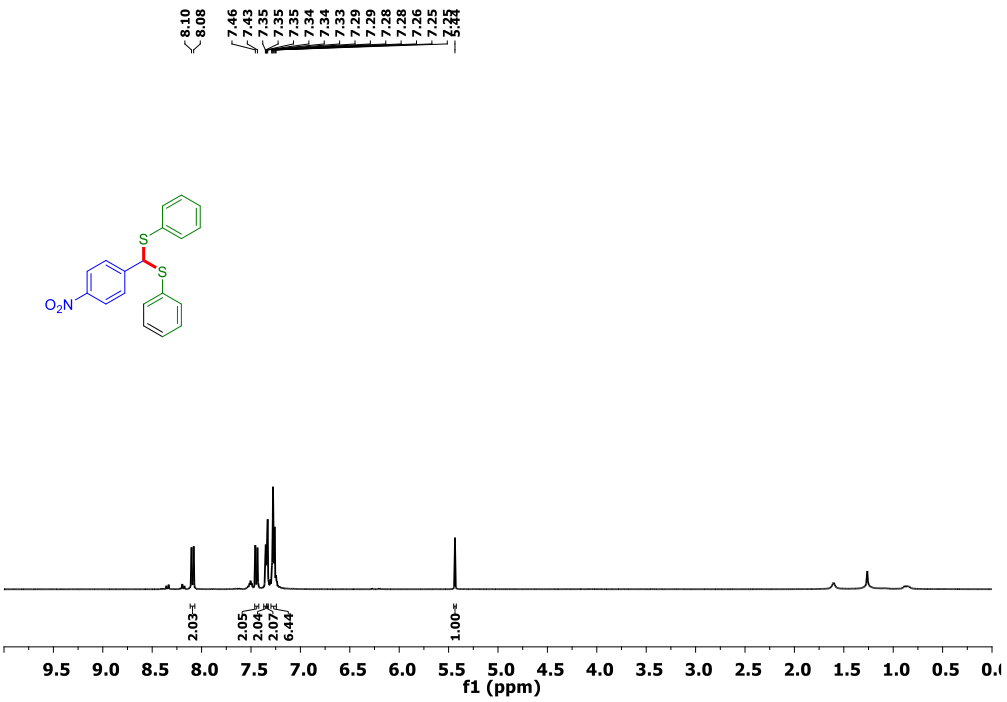



**Figure 5.21.** $^{1}$H NMR spectrum of ((4-nitrophenyl)methylene)bis(phenylsulfane) (**3ga**)

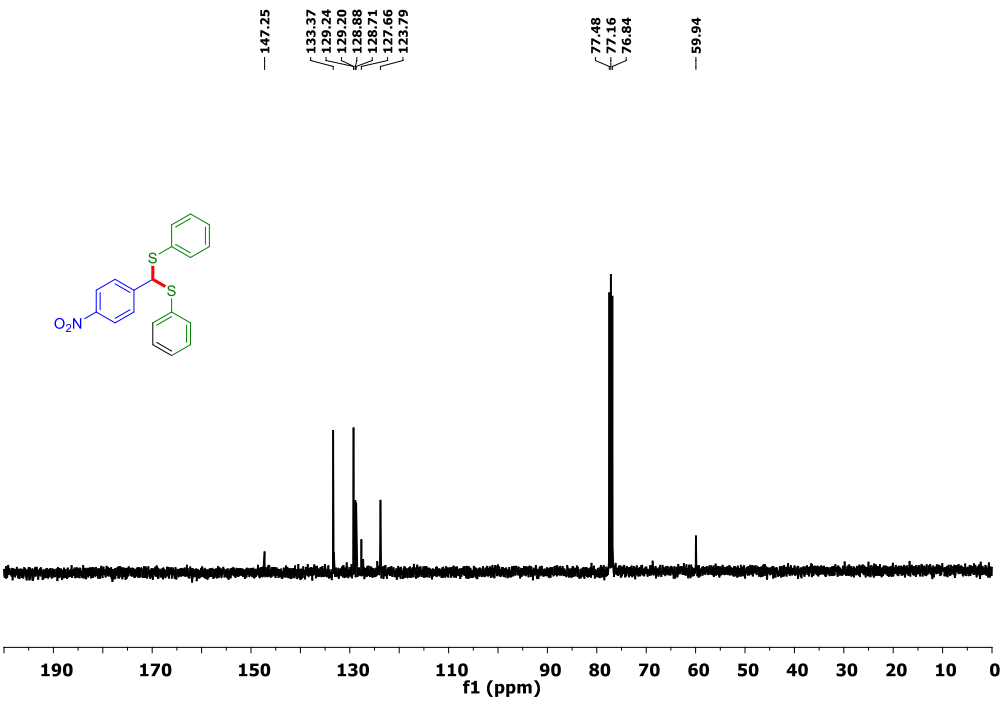



**Figure 5.22.** $^{13}$C NMR spectrum of ((4-nitrophenyl)methylene)bis(phenylsulfane) (**3ga**)

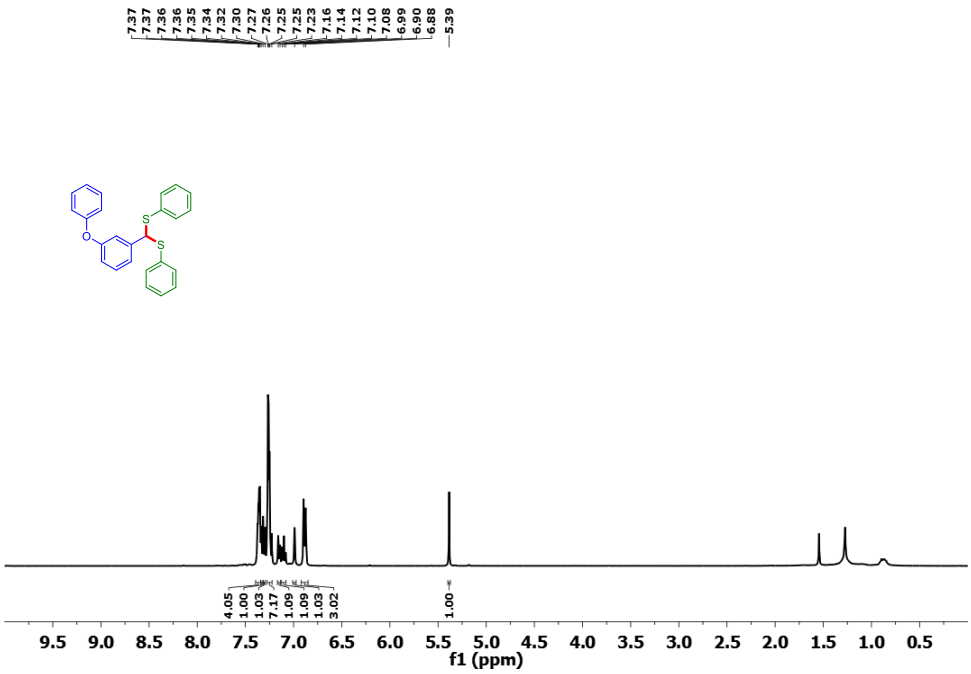



**Figure 5.23.** $^{1}$H NMR spectrum of ((3-phenoxyphenyl)methylene)bis(phenylsulfane) (**3ha**)

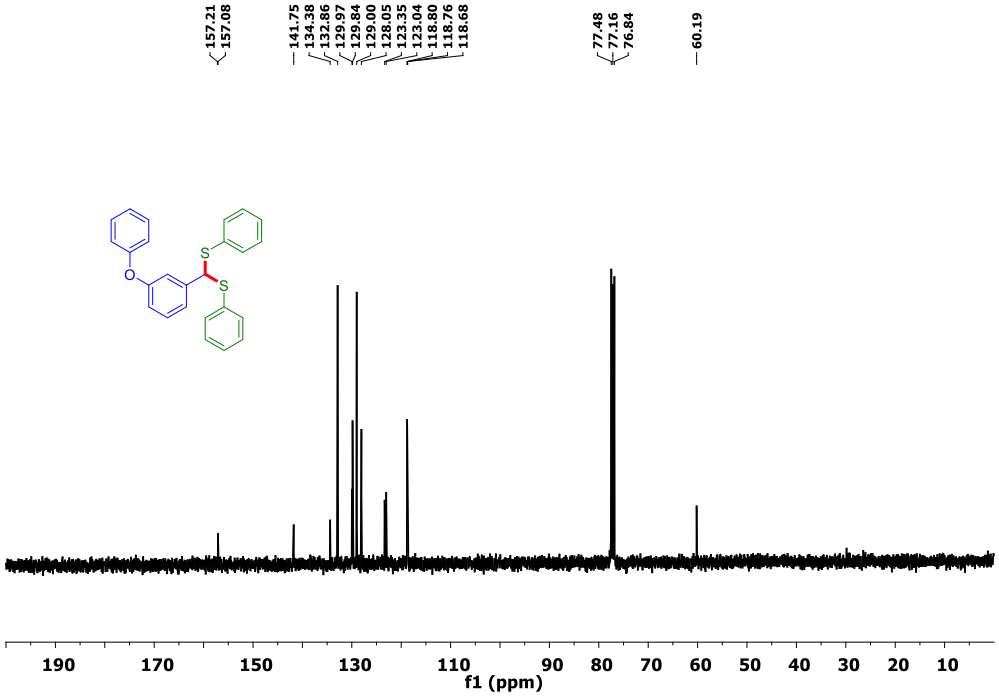



**Figure 5.24.** $^{13}$C NMR spectrum of ((3-phenoxyphenyl)methylene)bis(phenylsulfane) (**3ha**)

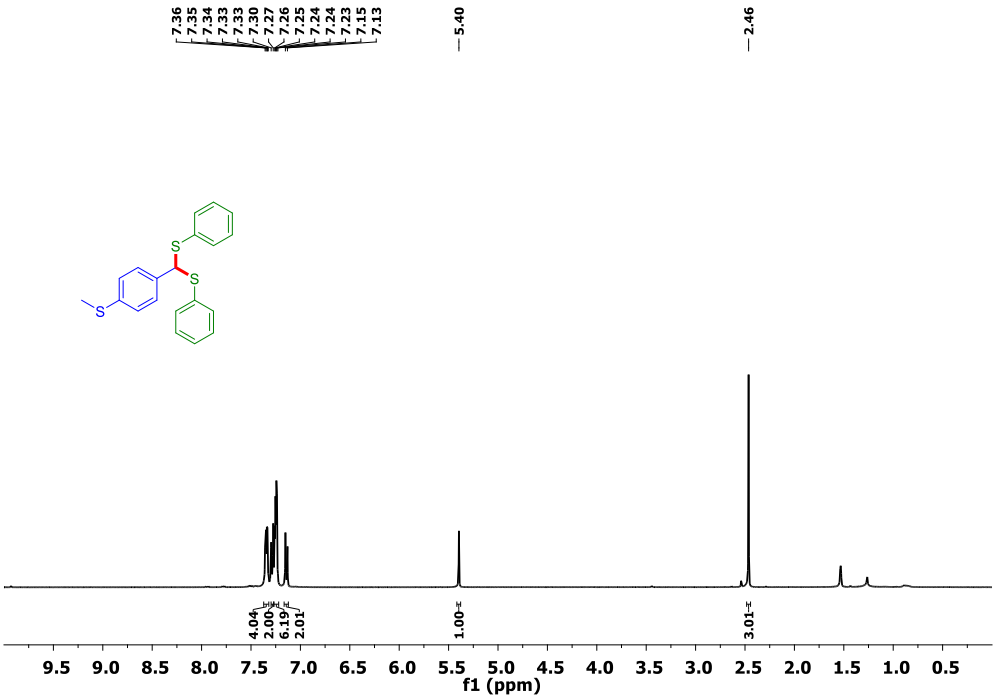



**Figure 5.25.** $^{1}$H NMR spectrum of ((4-(methylthio)phenyl)methylene)bis(phenylsulfane) (**3ia**)

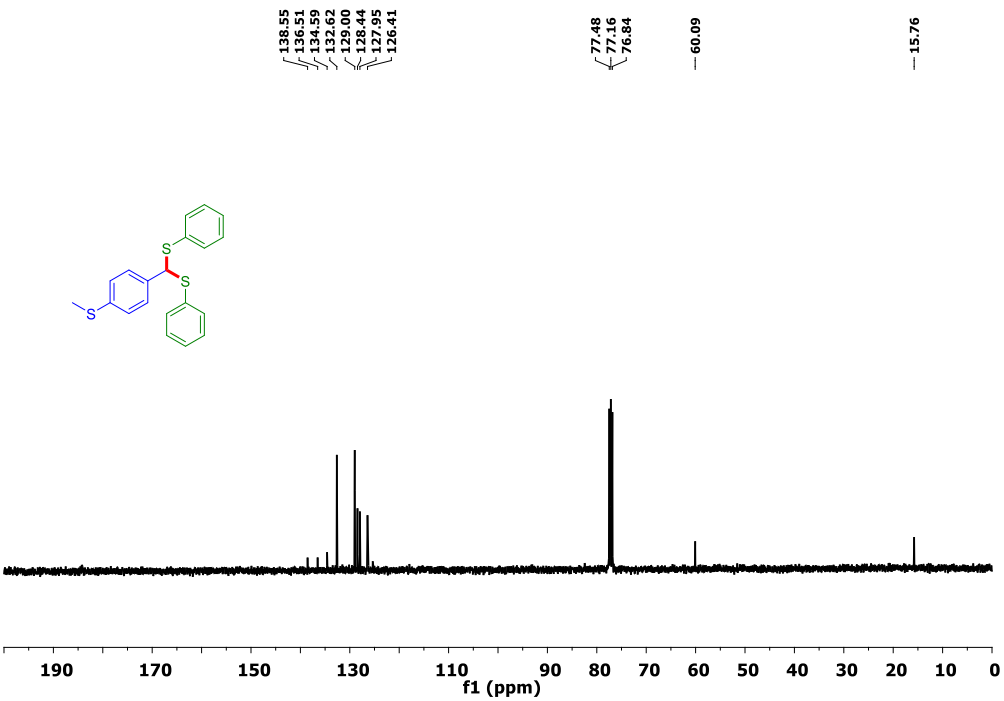



**Figure 5.26.** $^{13}$C NMR spectrum of ((4-(methylthio)phenyl)methylene)bis(phenylsulfane) (**3ia**)

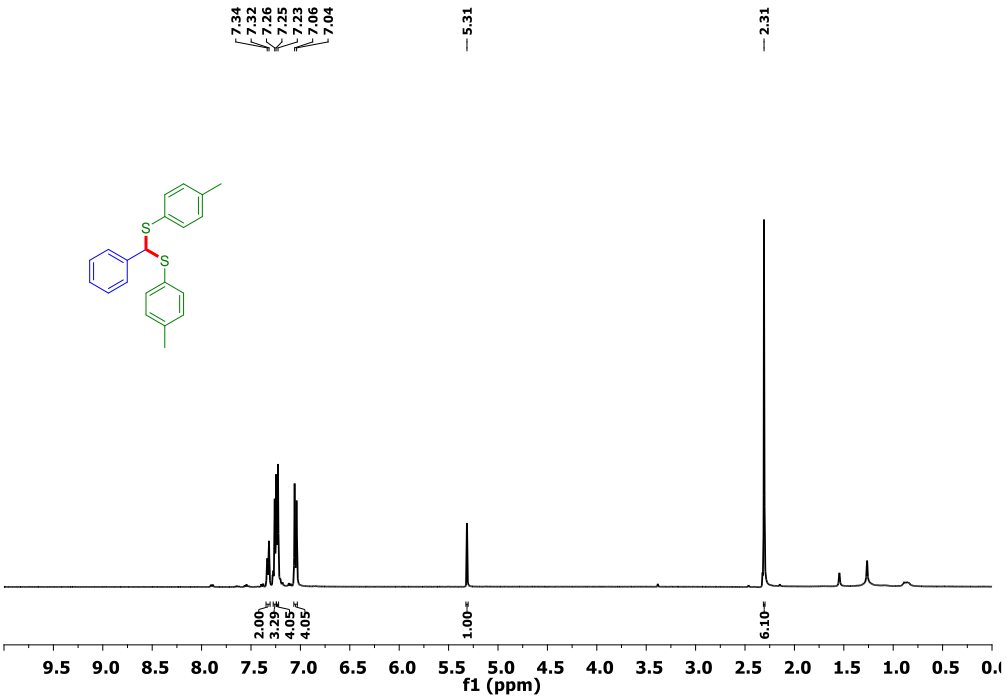



**Figure 5.27.** $^{1}$H NMR spectrum of (phenylmethylene)bis(p-tolylsulfane) (**3ab**)

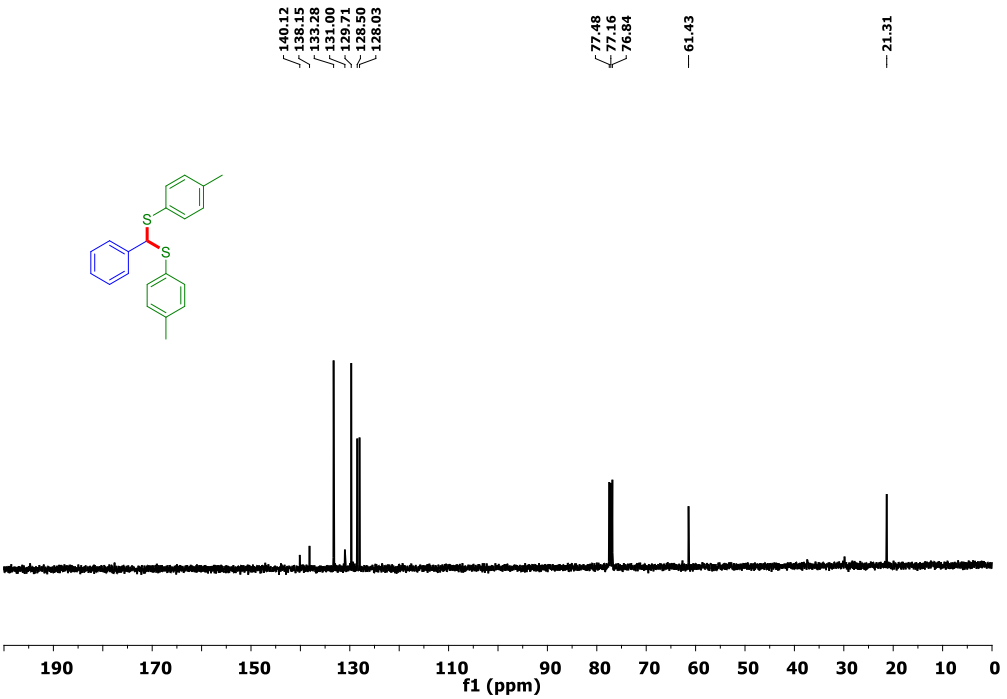



**Figure 5.28.** $^{13}$C NMR spectrum of (phenylmethylene)bis(p-tolylsulfane) (**3ab**)

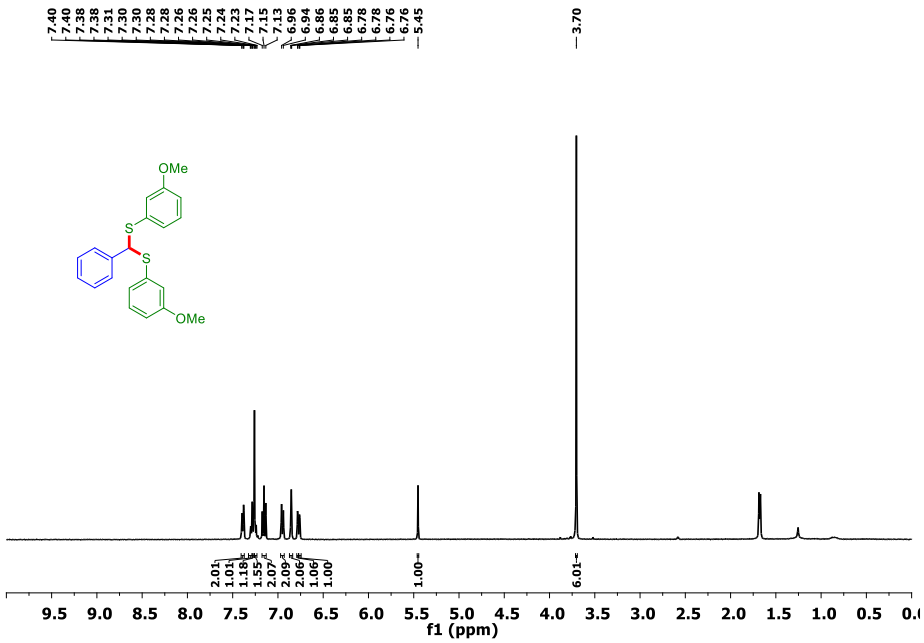



**Figure 5.29.** $^{1}$H NMR spectrum of (phenylmethylene)bis((3-methoxyphenyl)sulfane) (**3ac**)

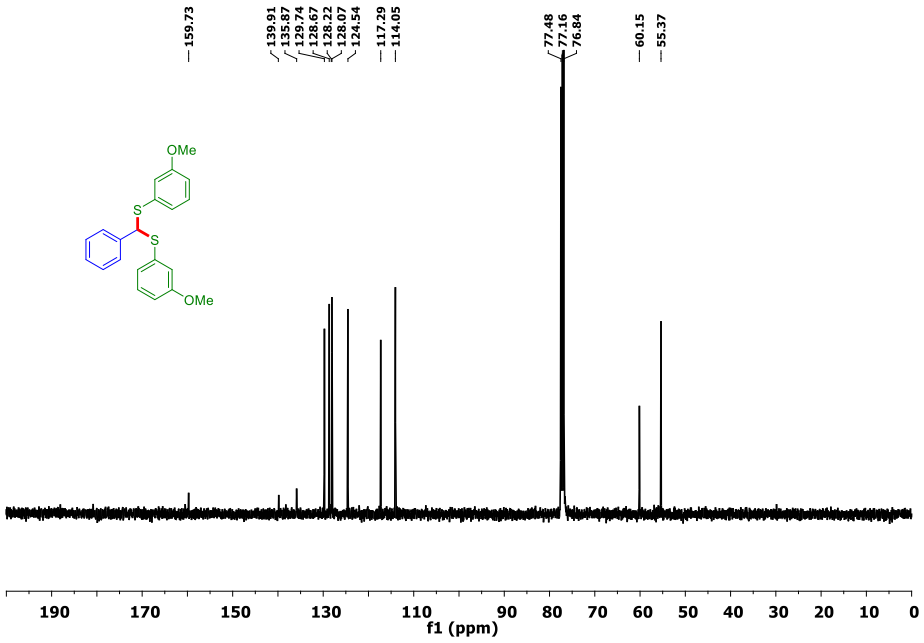



**Figure 5.30.** $^{13}$C NMR spectrum of (phenylmethylene)bis((3-methoxyphenyl)sulfane) (**3ac**)

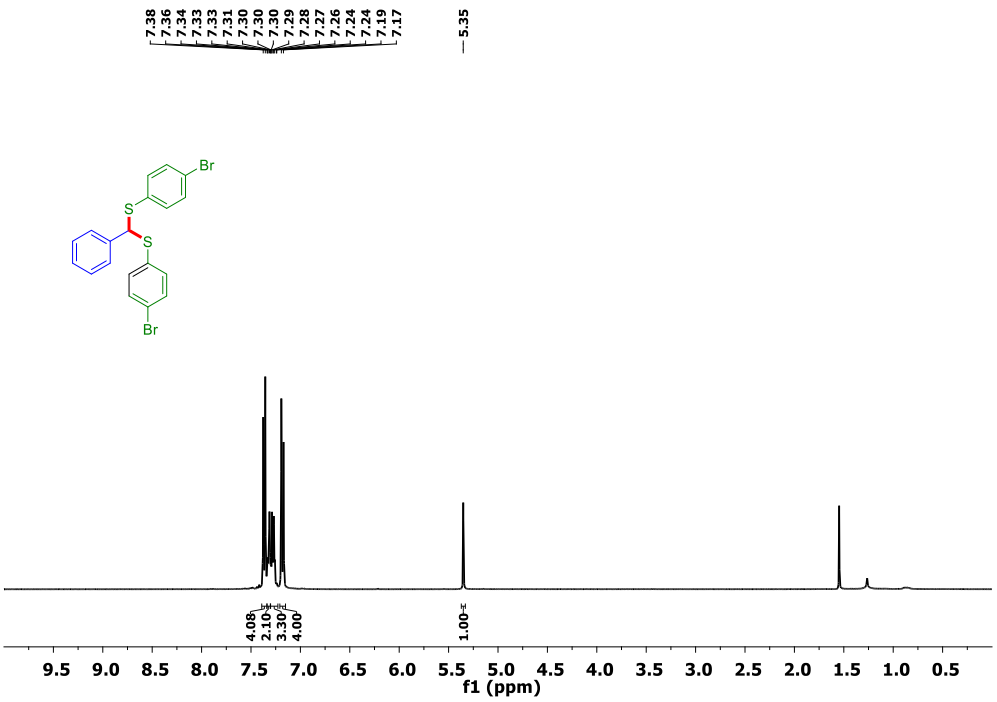



**Figure 5.31.** $^{1}$H NMR spectrum of (phenylmethylene)bis((4-bromophenyl)sulfane) (**3ad**)

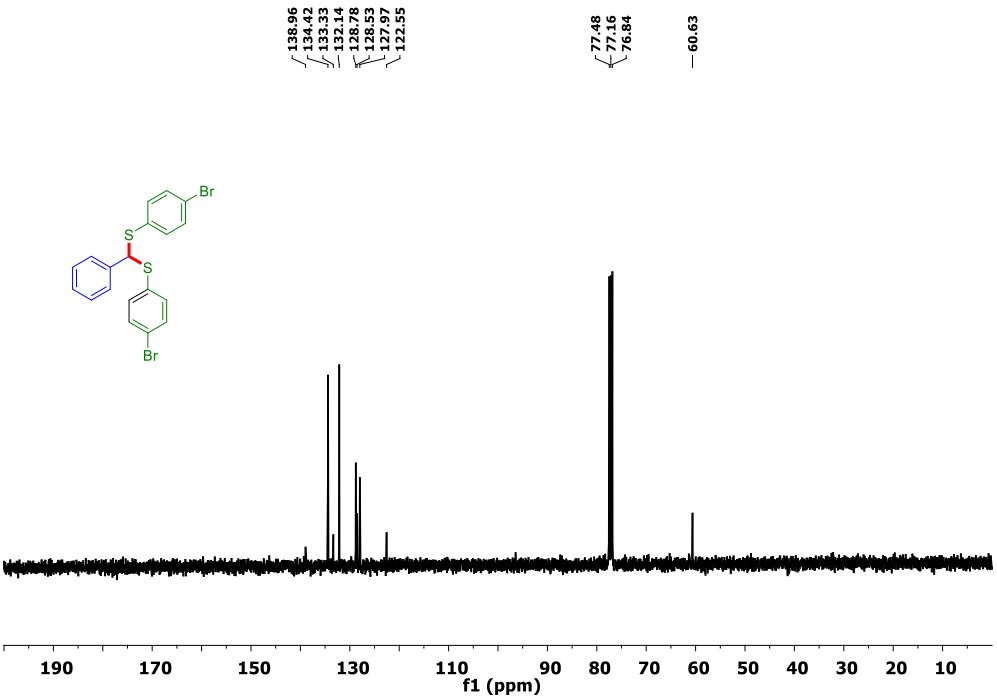



**Figure 5.32.** $^{13}$C NMR spectrum of (phenylmethylene)bis((4-bromophenyl)sulfane) (**3ad**)

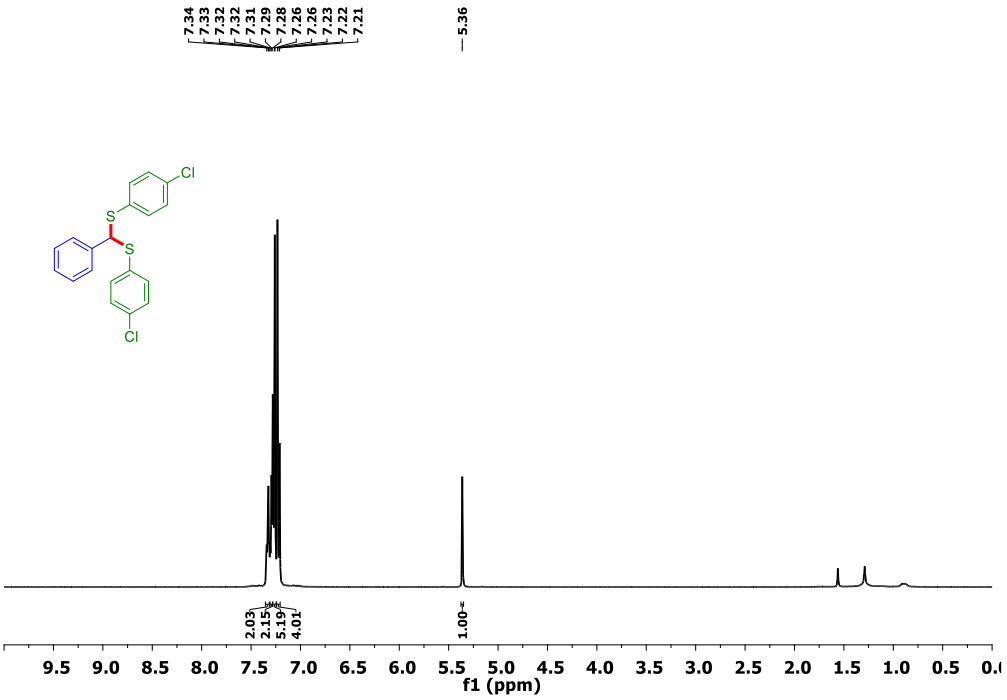



**Figure 5.33.** $^{1}$H NMR spectrum of (phenylmethylene)bis((4-chlorophenyl)sulfane) (**3ae**)

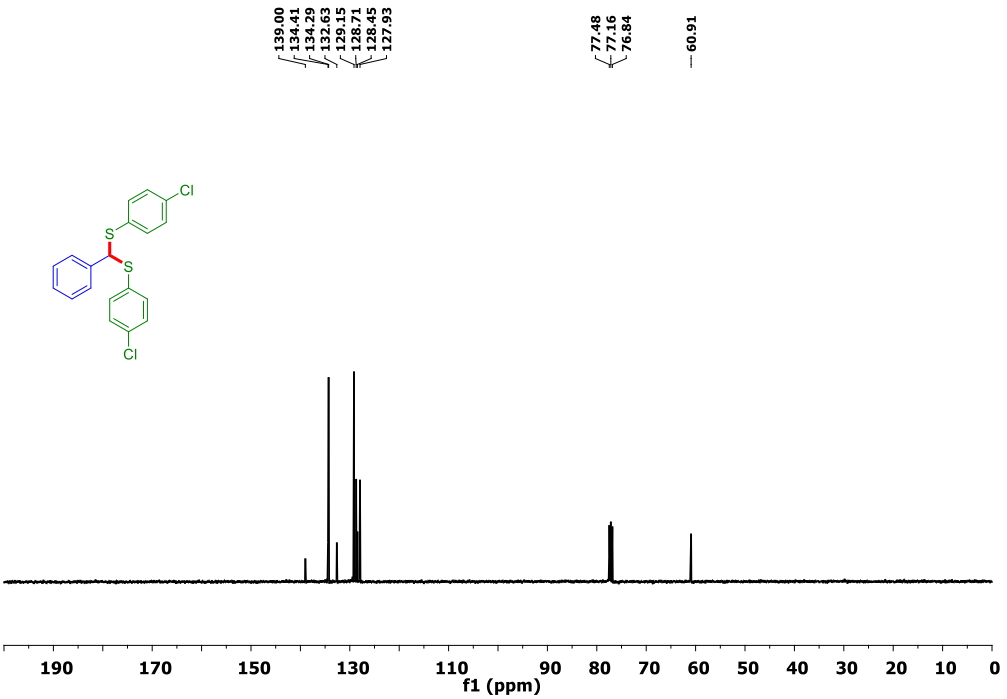



**Figure 5.34.** $^{13}$C NMR spectrum of (phenylmethylene)bis((4-chlorophenyl)sulfane) (**3ae**)

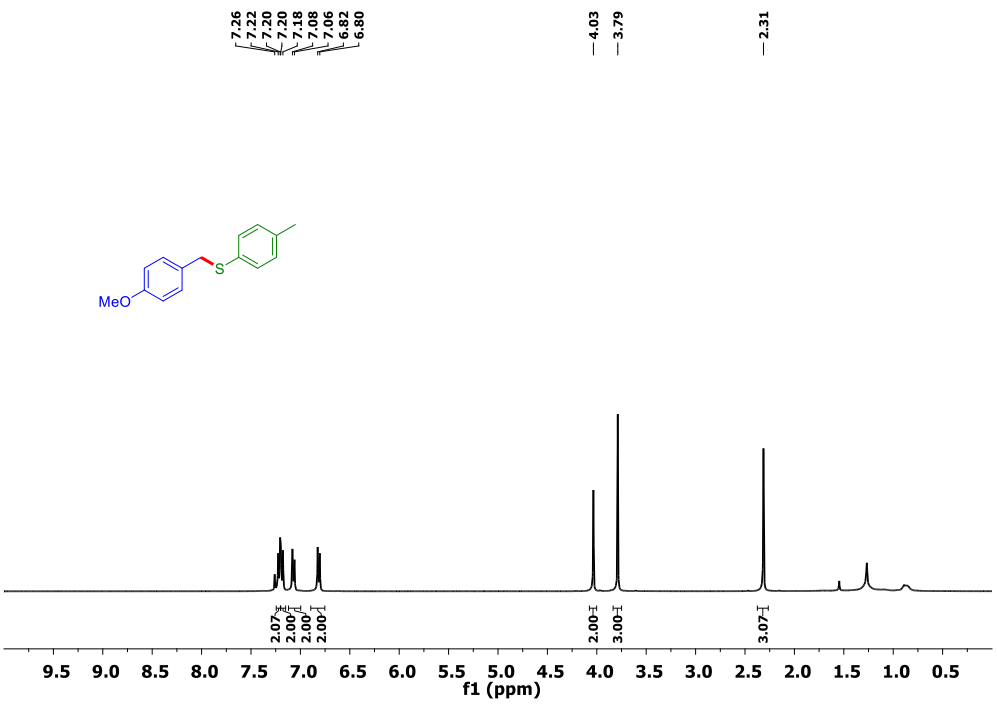



**Figure 5.35.** $^{1}$H NMR spectrum of (4-methoxybenzyl)(p-tolyl)sulfane (**4mb**)

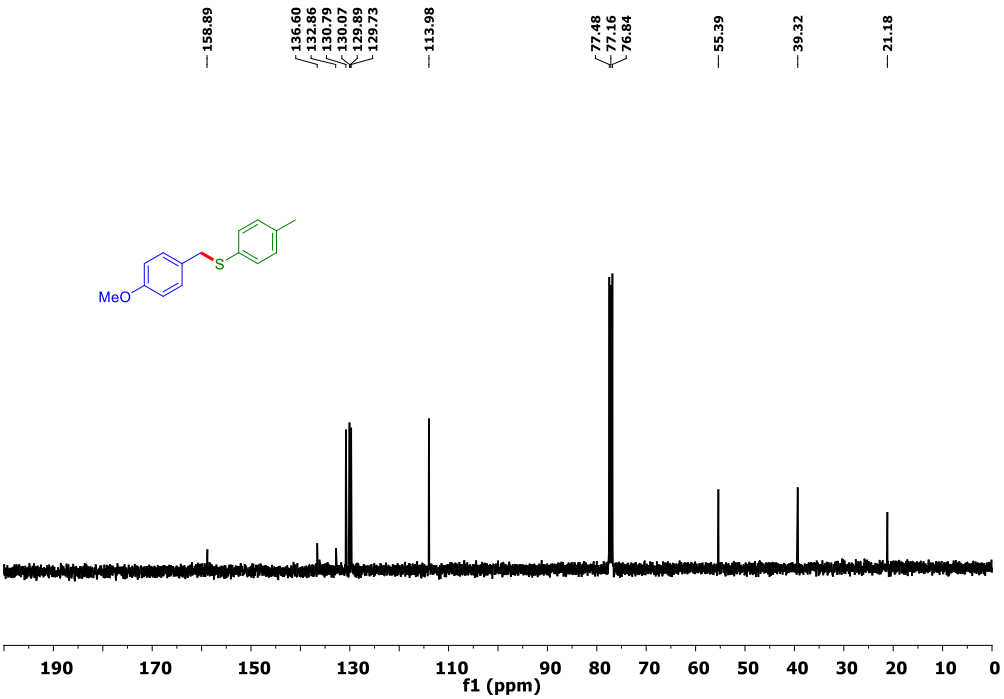



**Figure 5.36.** $^{13}$C NMR spectrum of (4-methoxybenzyl)(p-tolyl)sulfane (**4mb**)

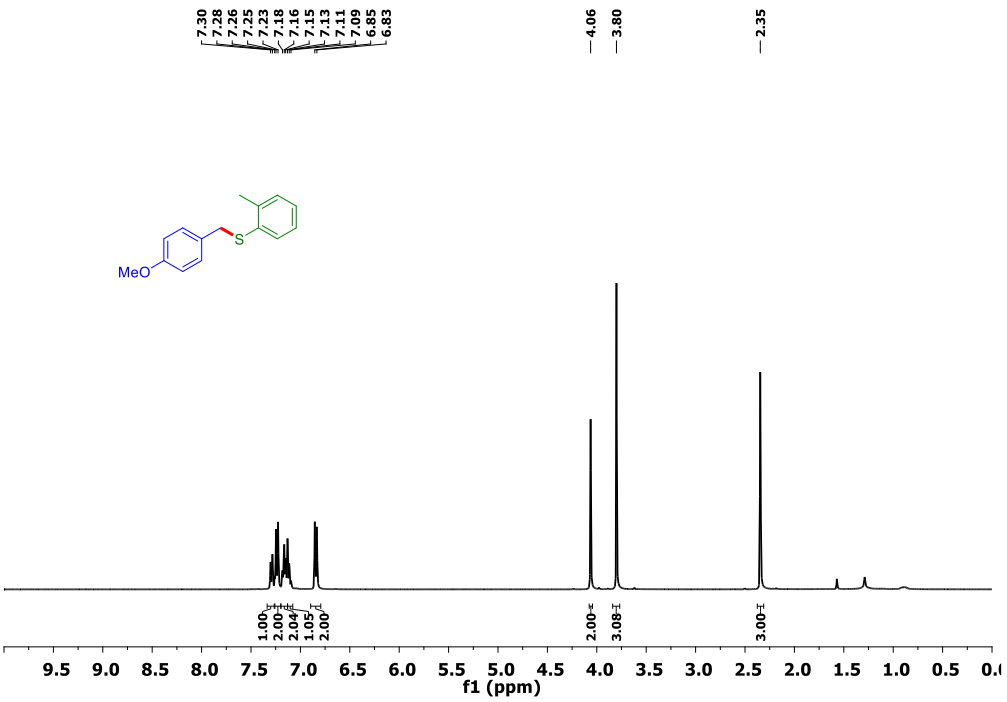



**Figure 5.37.** $^{1}$H NMR spectrum of (4-methoxybenzyl)(o-tolyl)sulfane (**4ml**)

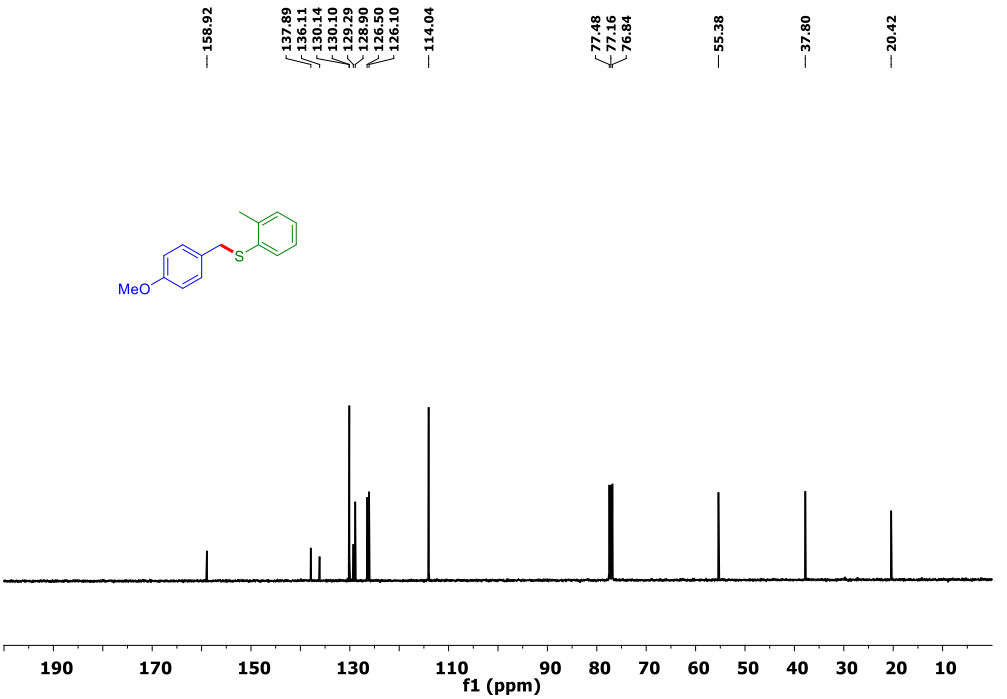



**Figure 5.38.** $^{13}$C NMR spectrum of (4-methoxybenzyl)(o-tolyl)sulfane (**4ml**)

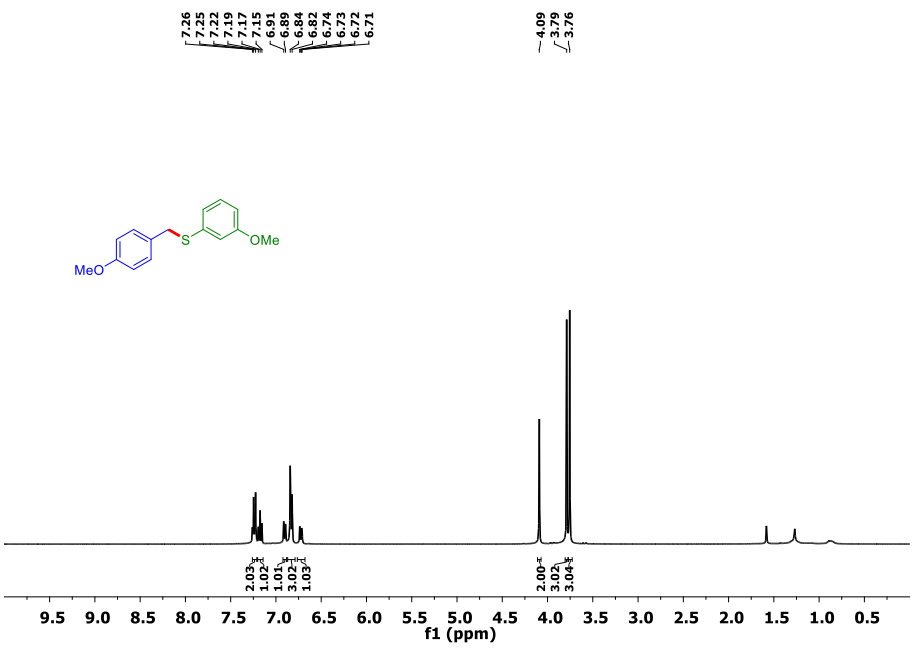



**Figure 5.39.** $^{1}$H NMR spectrum of (4-methoxybenzyl)(3-methoxyphenyl)sulfane (**4mc**)

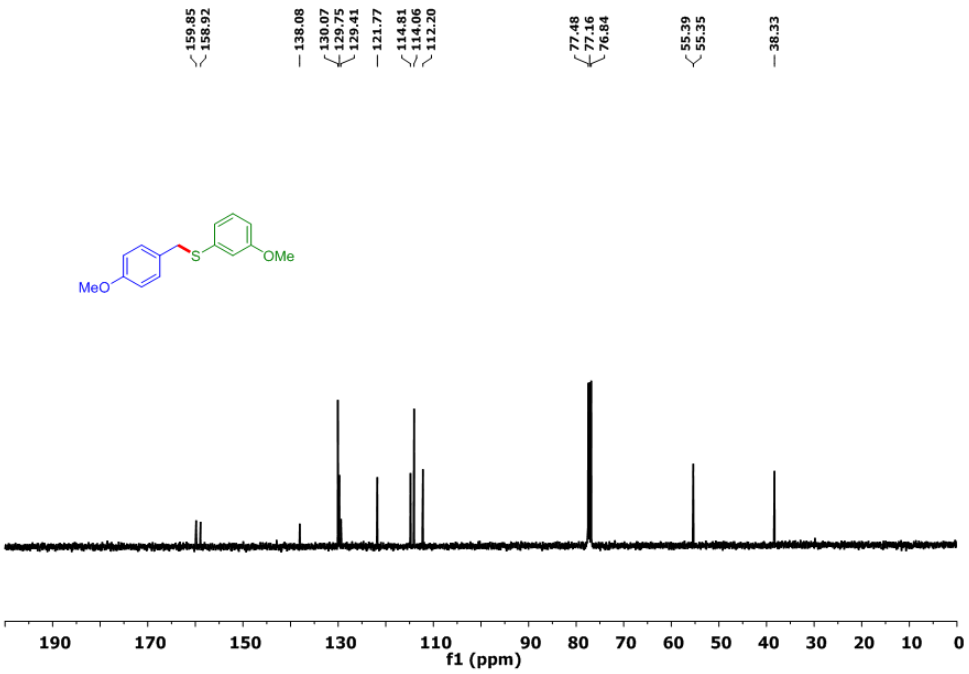



**Figure 5.40.** $^{13}$C NMR spectrum of (4-methoxybenzyl)(3-methoxyphenyl)sulfane (**4mc**)

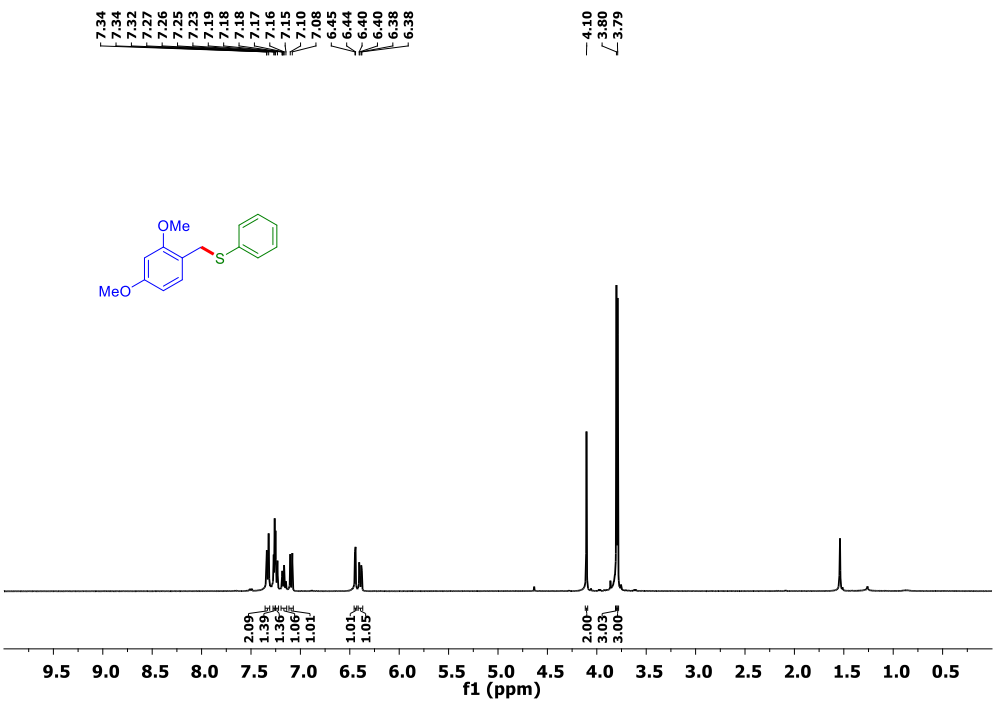



**Figure 5.41.** $^{1}$H NMR spectrum of (2,4-dimethoxybenzyl)(phenyl)sulfane (**4na**)

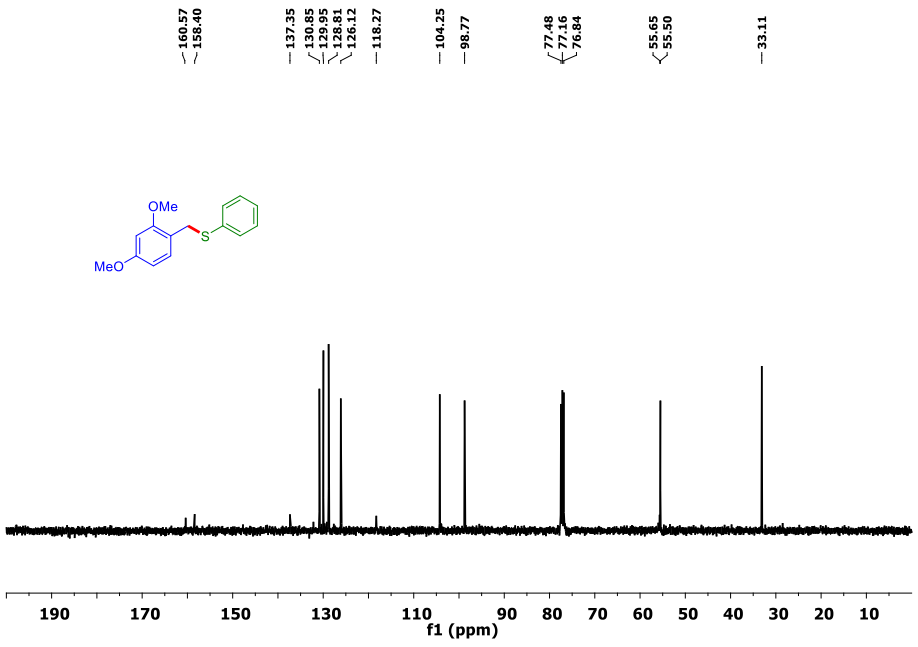



**Figure 5.42.** $^{13}$C NMR spectrum of (2,4-dimethoxybenzyl)(phenyl)sulfane (**4na**)

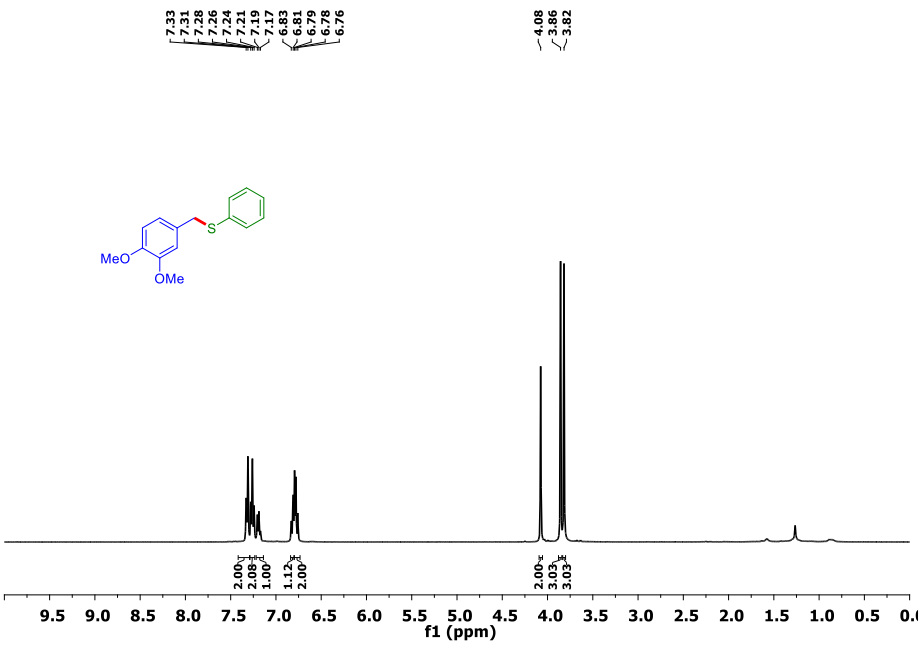



**Figure 5.43.** $^{1}$H NMR spectrum of (3,4-dimethoxybenzyl)(phenyl)sulfane (**4oa**)

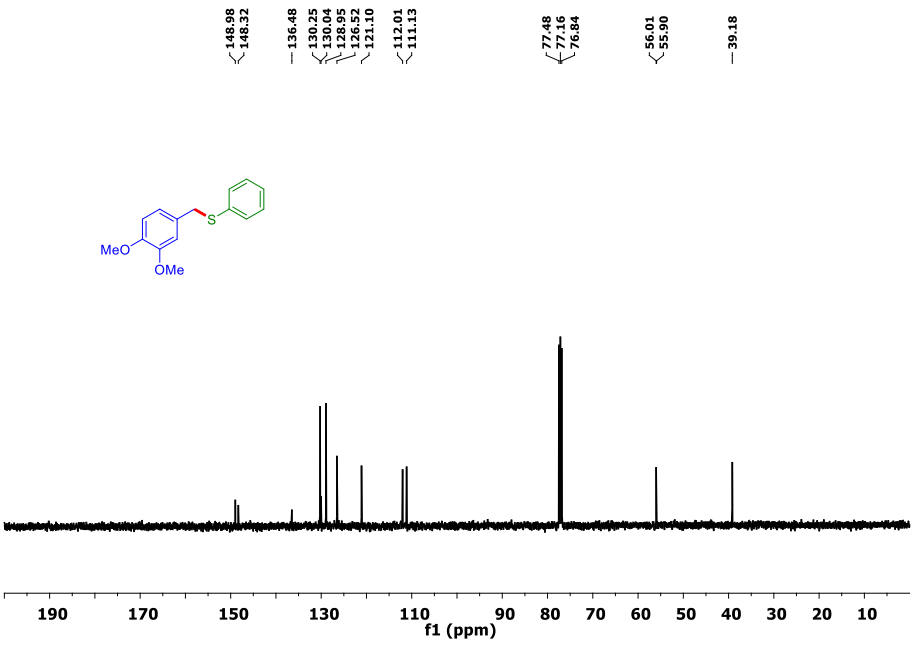



**Figure 5.44.** $^{13}$C NMR spectrum of (3,4-dimethoxybenzyl)(phenyl)sulfane (**4oa**)

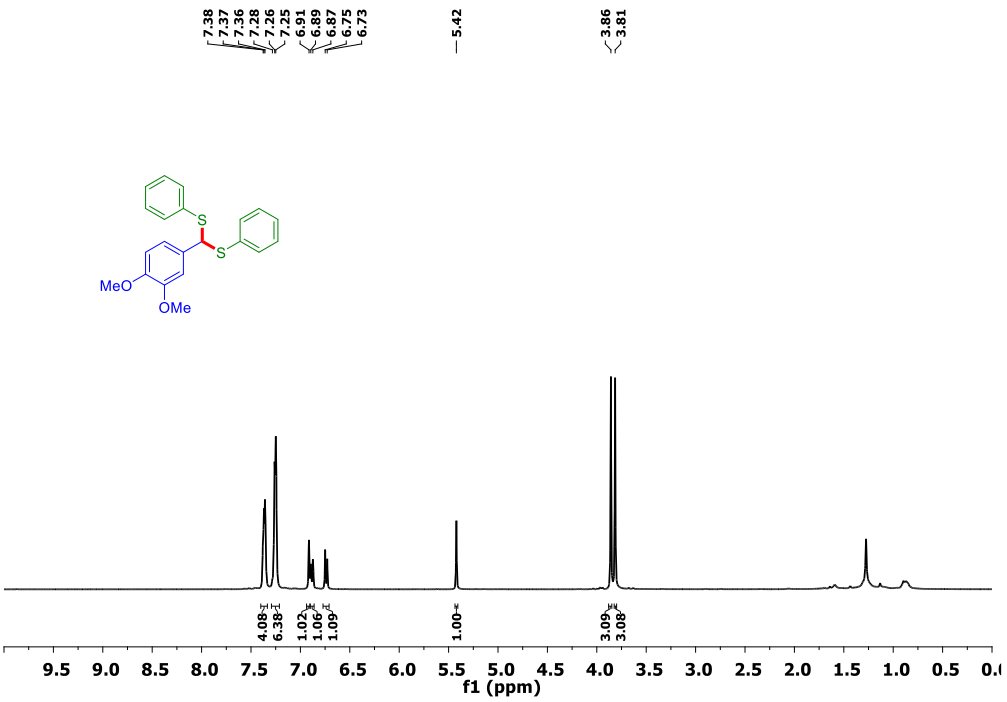



**Figure 5.45.** $^{1}$H NMR spectrum of ((3,4-dimethoxyphenyl)methylene)bis(phenylsulfane) (**3oa**)

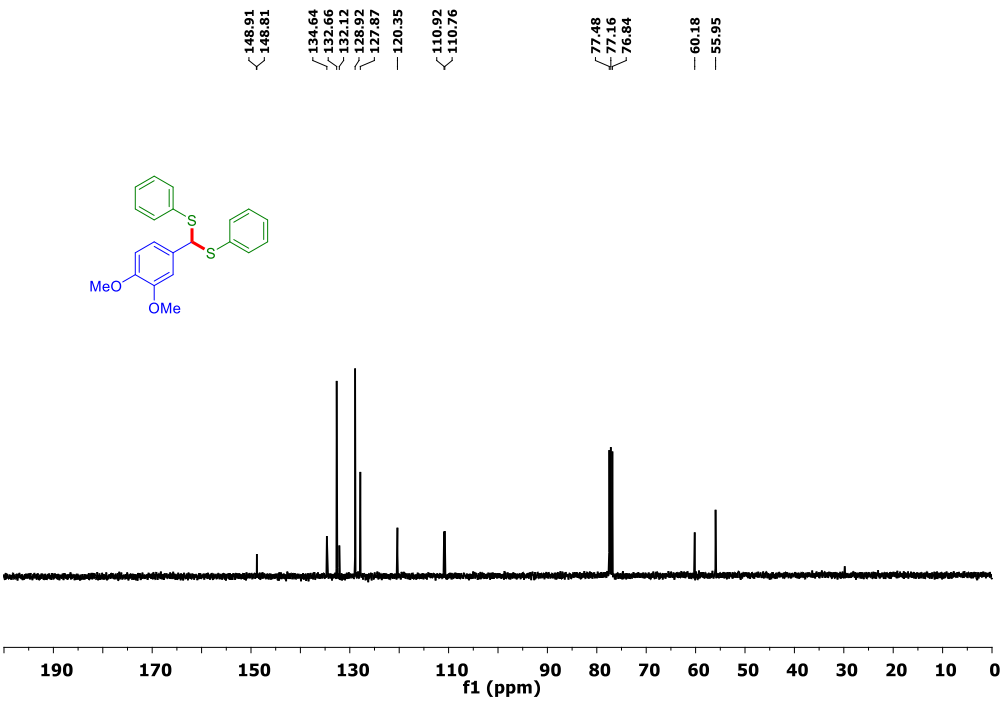



**Figure 5.46.** $^{13}$C NMR spectrum of ((3,4-dimethoxyphenyl)methylene)bis(phenylsulfane) (**3oa**)

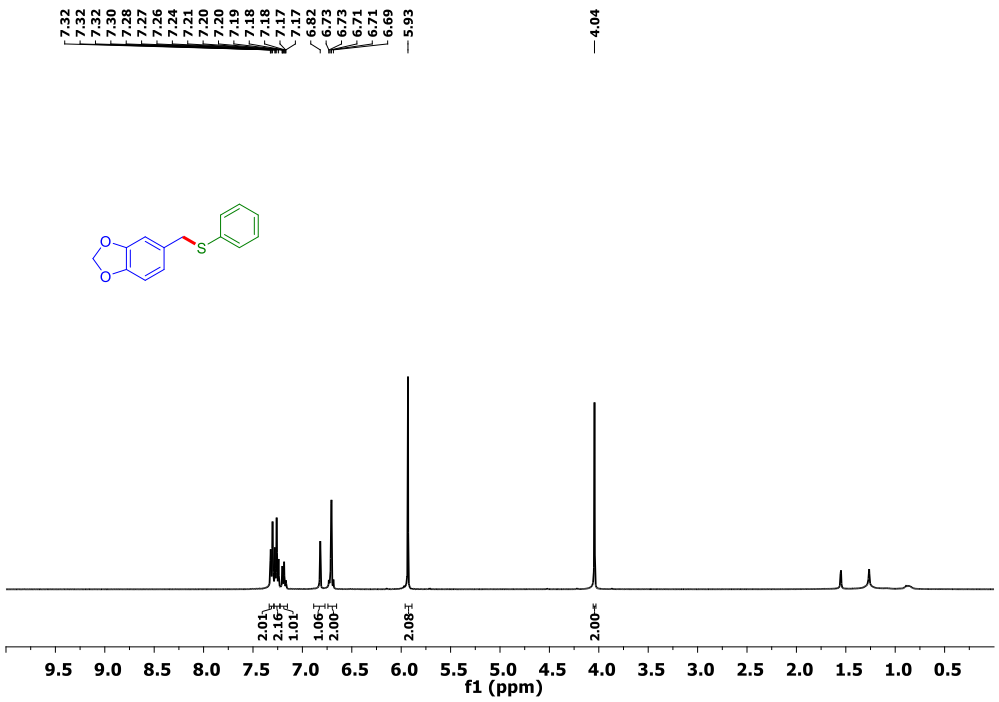



**Figure 5.47.** $^{1}$H NMR spectrum of 5-((phenylthio)methyl)benzo[d][1,3]dioxole (**4pa**)

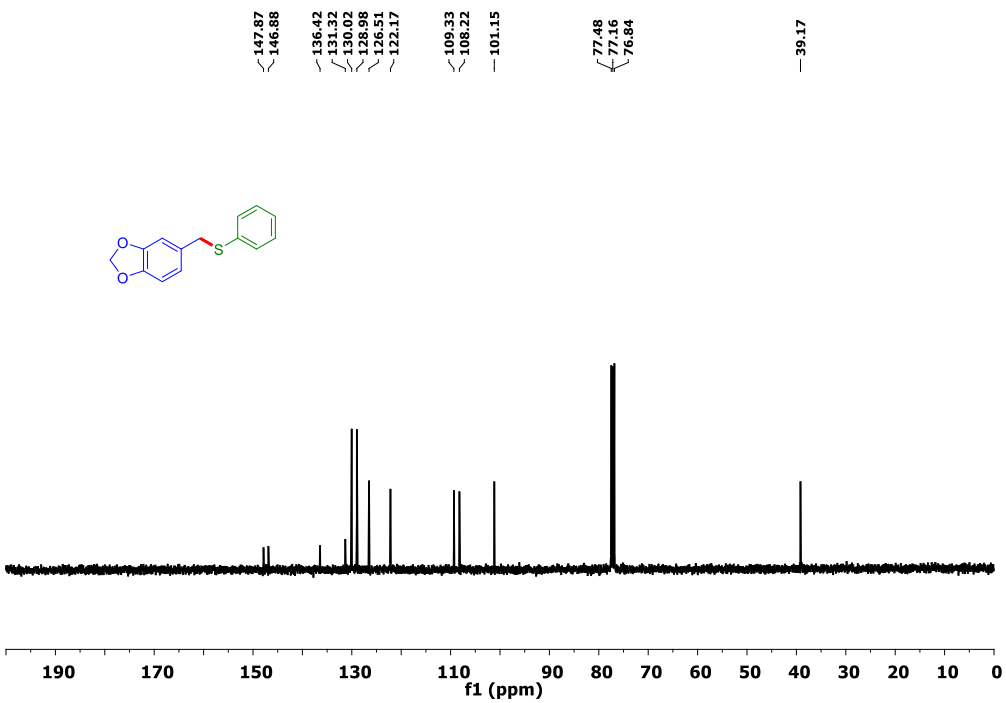



**Figure 5.48.** $^{13}$C NMR spectrum of 5-((phenylthio)methyl)benzo[d][1,3]dioxole (**4pa**)

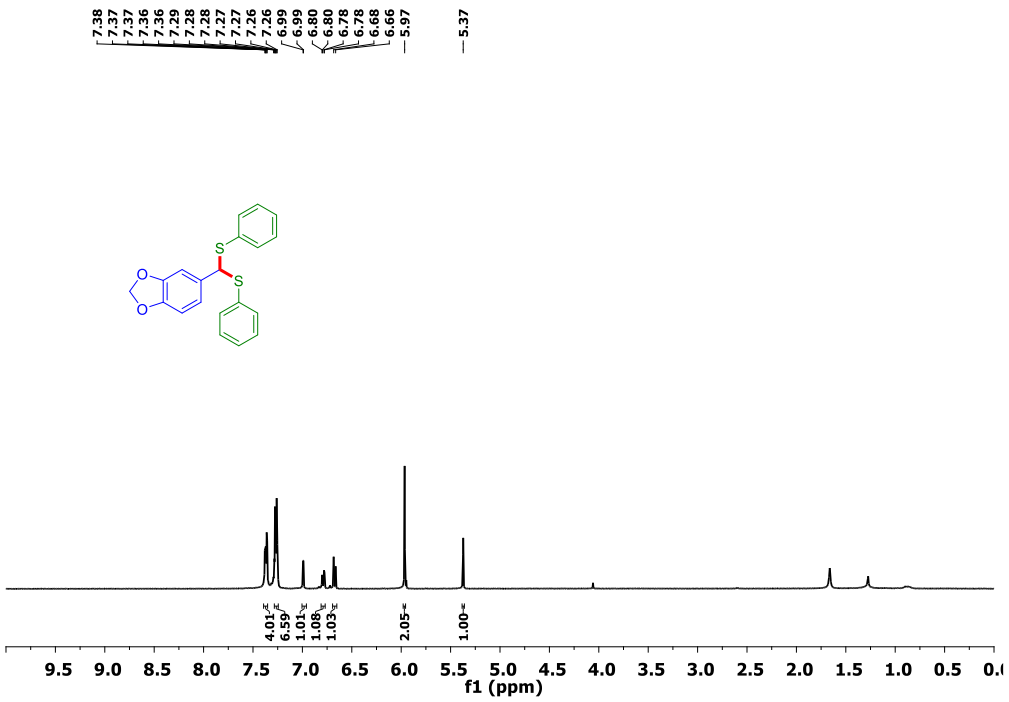



**Figure 5.49.** $^{1}$H NMR spectrum of 5-(bis(phenylthio)methyl)benzo[d][1,3]dioxole (**3pa**)

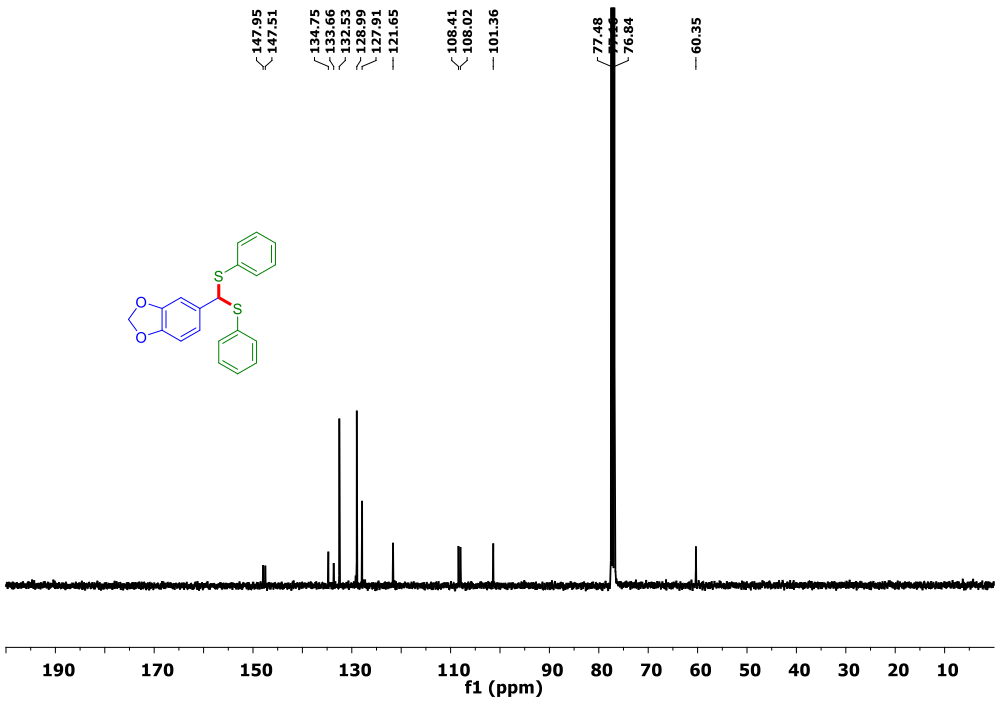



**Figure 5.50.** $^{13}$C NMR spectrum of 5-(bis(phenylthio)methyl)benzo[d][1,3]dioxole (**3pa**)

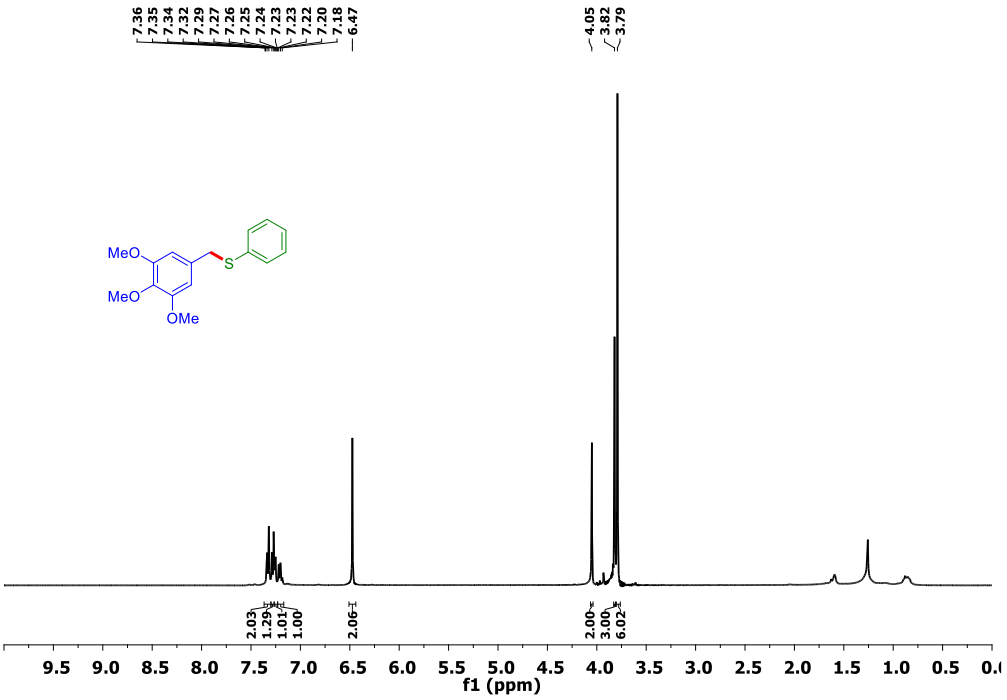



**Figure 5.51.** $^{1}$H NMR spectrum of phenyl(3,4,5-trimethoxybenzyl)sulfane (**4qa**)

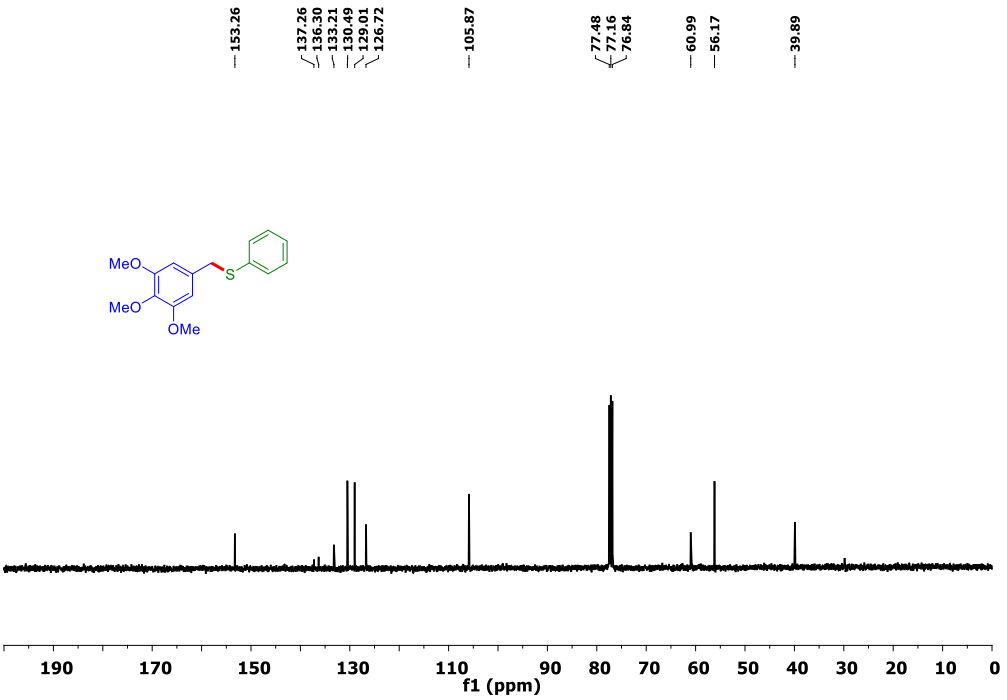



**Figure 5.52.** $^{13}$C NMR spectrum of phenyl(3,4,5-trimethoxybenzyl)sulfane (**4qa**)

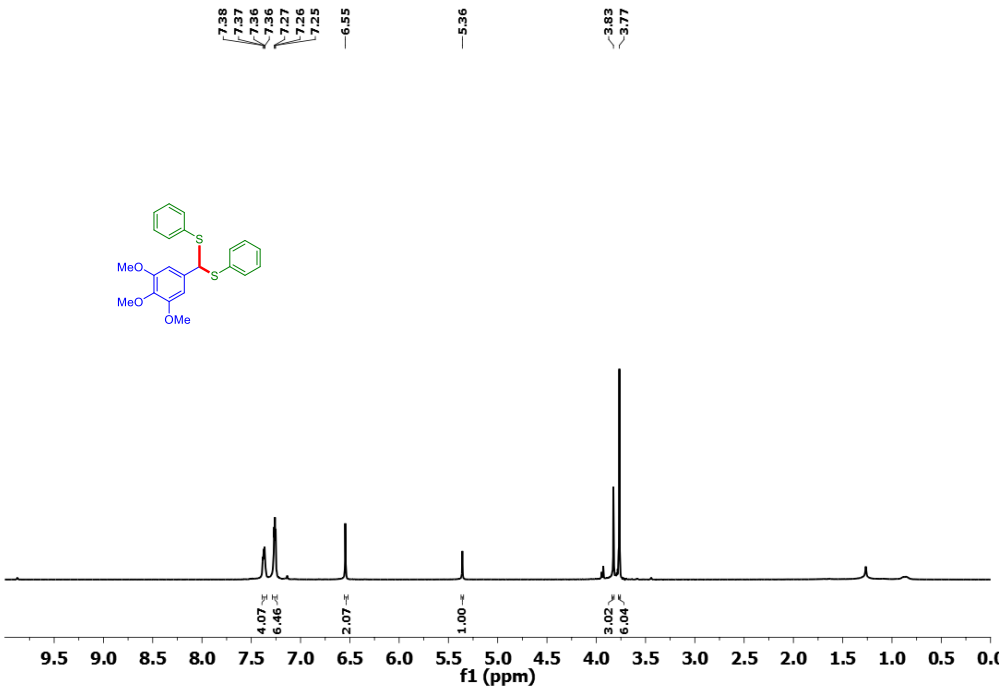



**Figure 5.53.** $^{1}$H NMR spectrum of ((3,4,5-trimethoxyphenyl)methylene)bis(phenylsulfane) (**3qa**)

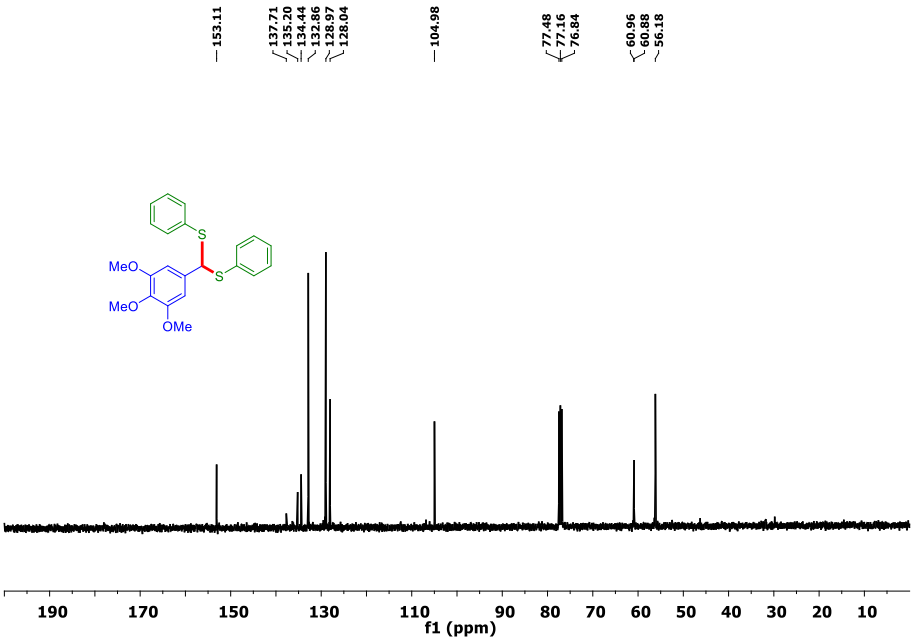



**Figure 5.54.** $^{13}$C NMR spectrum of ((3,4,5-trimethoxyphenyl)methylene)bis(phenylsulfane) (**3qa**)

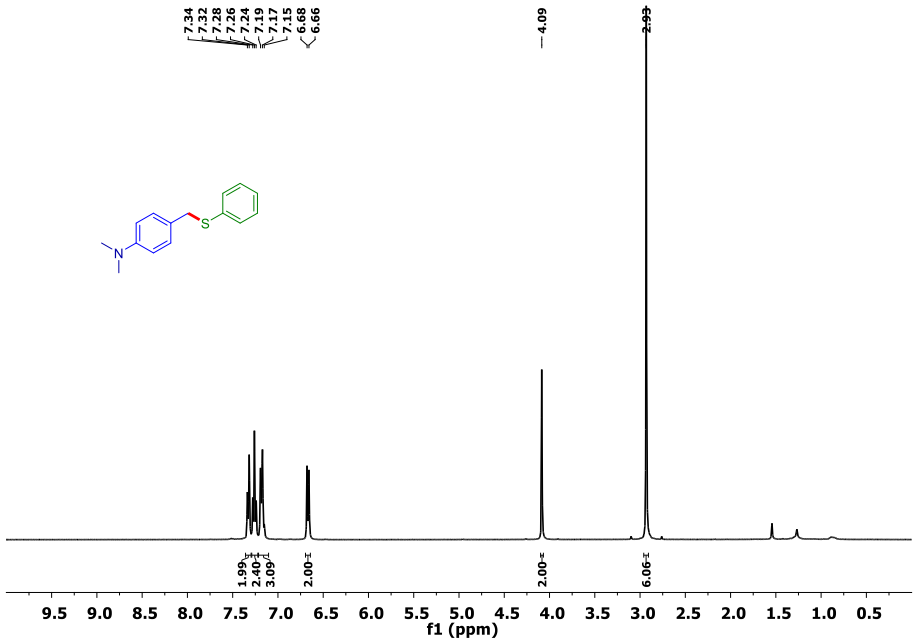



**Figure 5.55.** $^{1}$H NMR spectrum of N,N-dimethyl-4-((phenylthio)methyl)aniline (**4ra**)

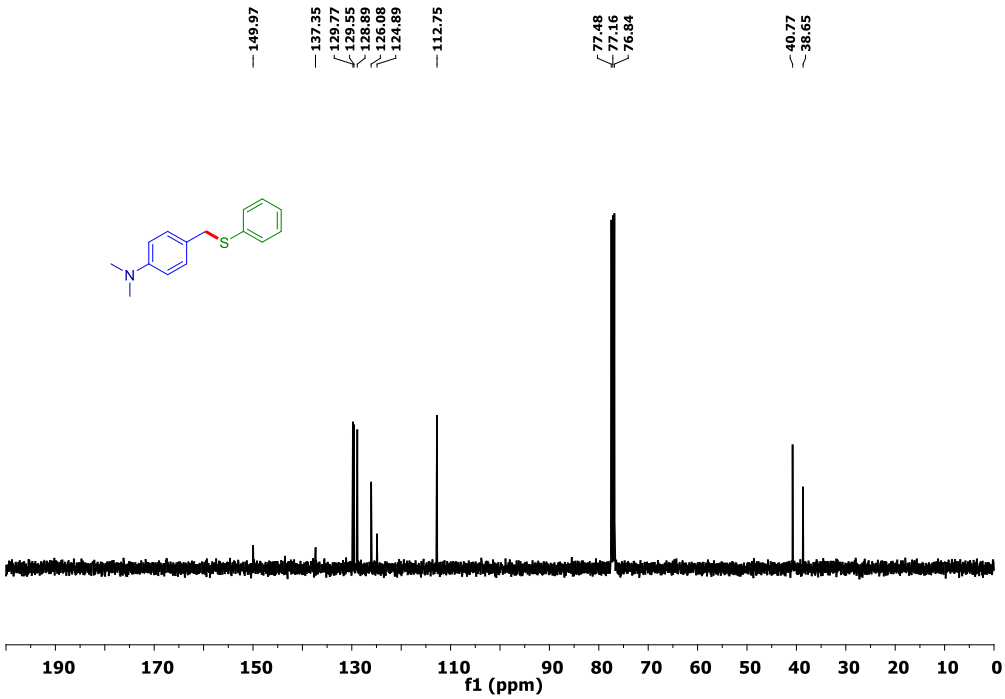



**Figure 5.56.** $^{13}$C NMR spectrum of N,N-dimethyl-4-((phenylthio)methyl)aniline (**4ra**)

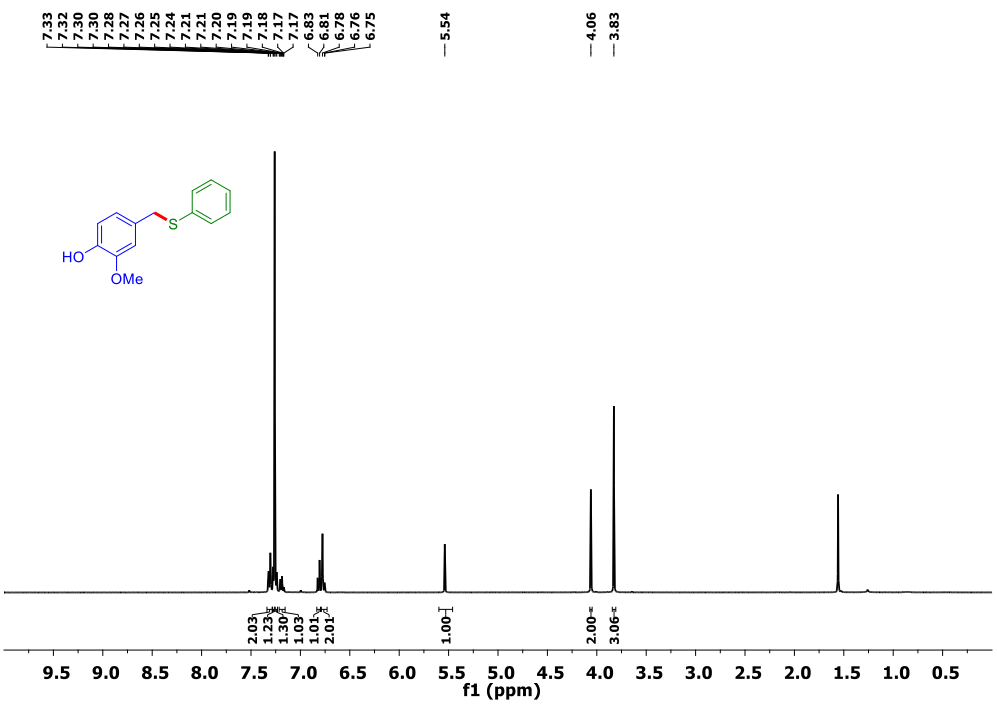



**Figure 5.57.** $^{1}$H NMR spectrum of 2-methoxy-4-((phenylthio)methyl)phenol (**4sa**)

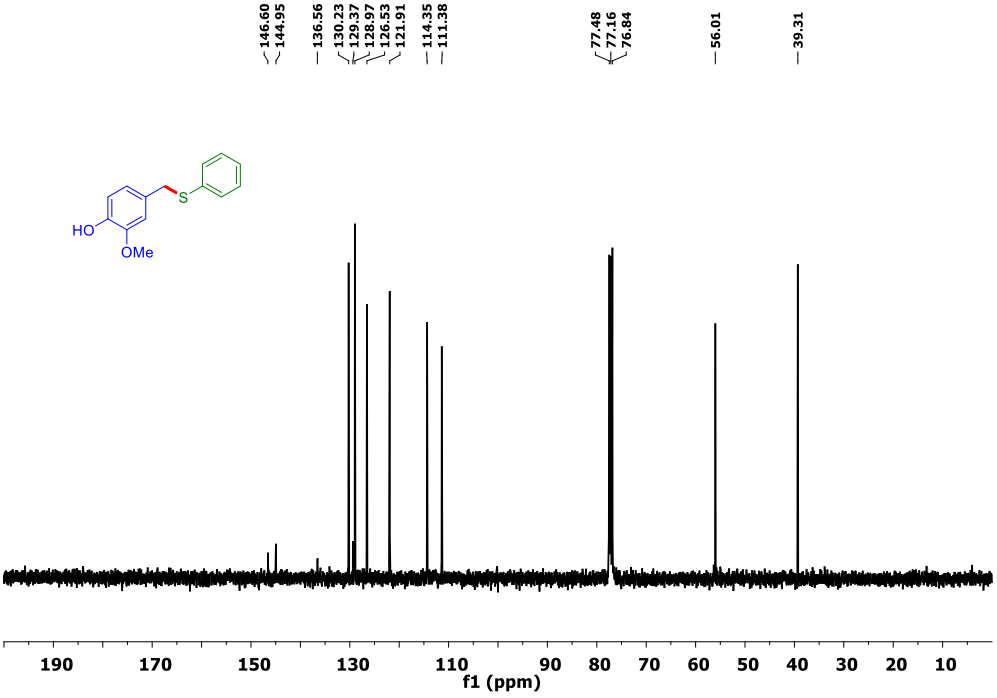
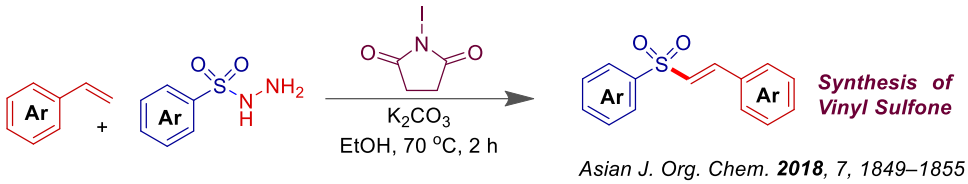



**Figure 5.58.** $^{13}$C NMR spectrum of 2-methoxy-4-((phenylthio)methyl)phenol (**4sa**)

# Thesis at a Glance

## Reactivity of Alkenes

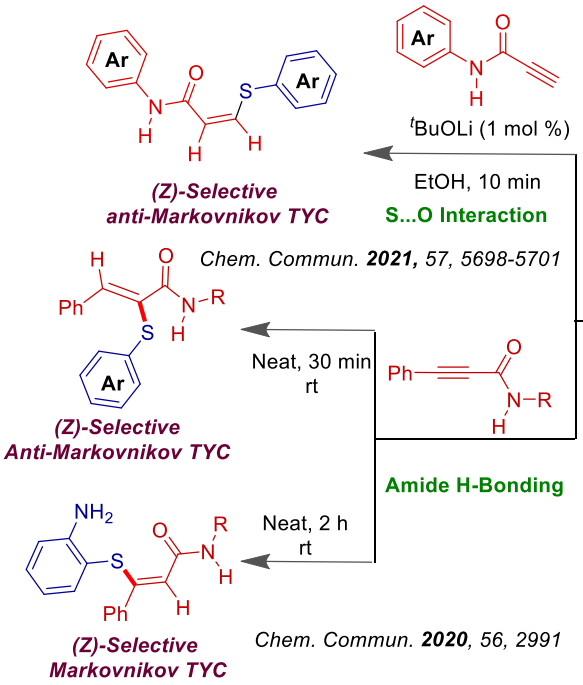
**a)** NIS in Sulfonylation




*Asian J. Org. Chem.* ***2018****, 7, 1849–1855*

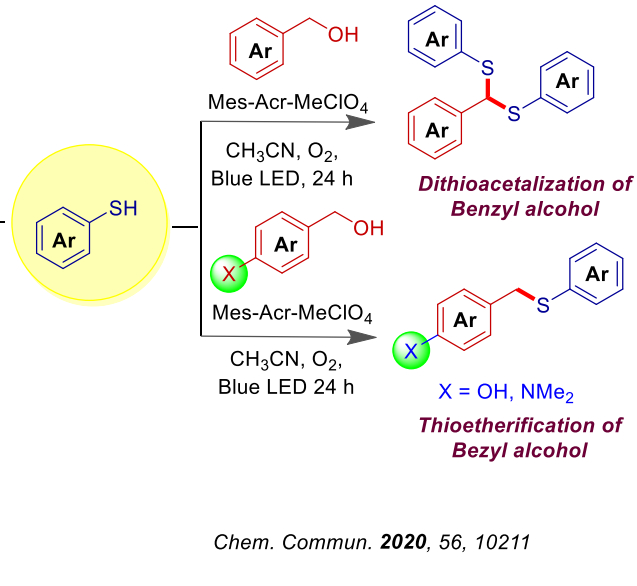
## Reactivity of Alkynes

**b)** Non Covalent Interactions

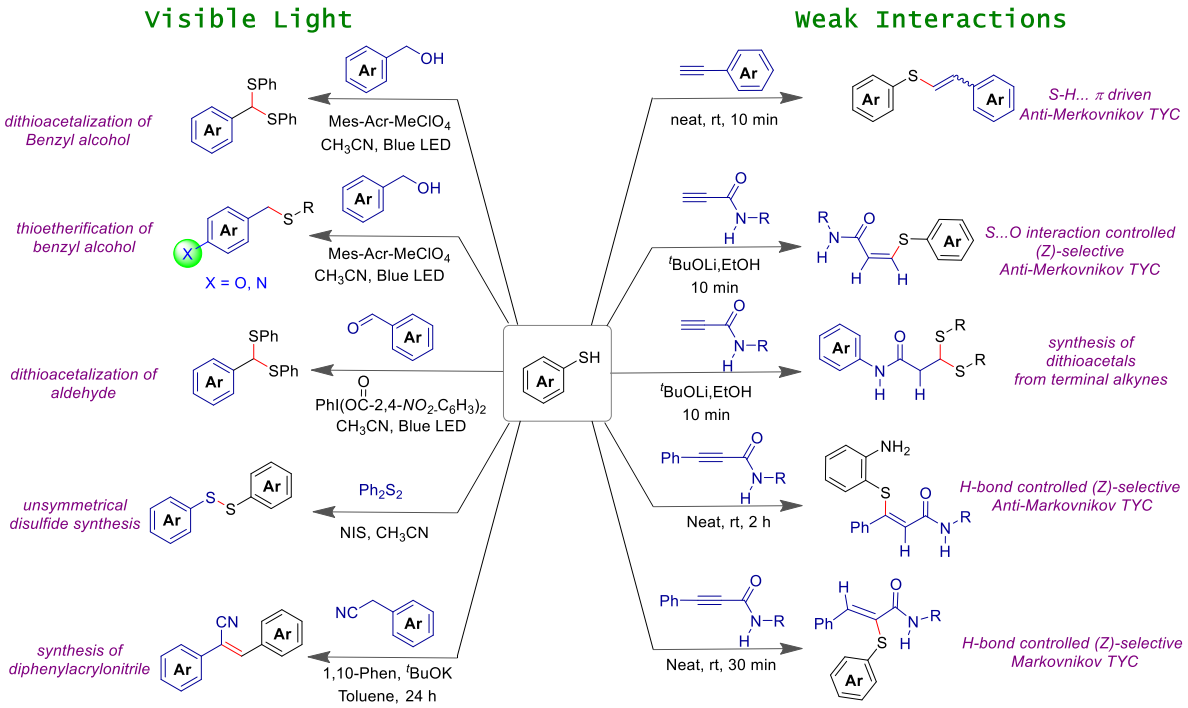



## Reactivity of alcohols

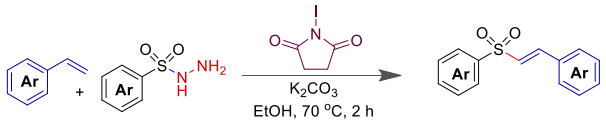
**c)** Visible Light Photocatalyst



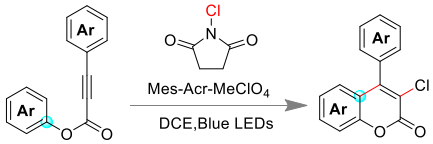
# Overall Work




## NXS and Their Dual Role (X=-Cl,-I)

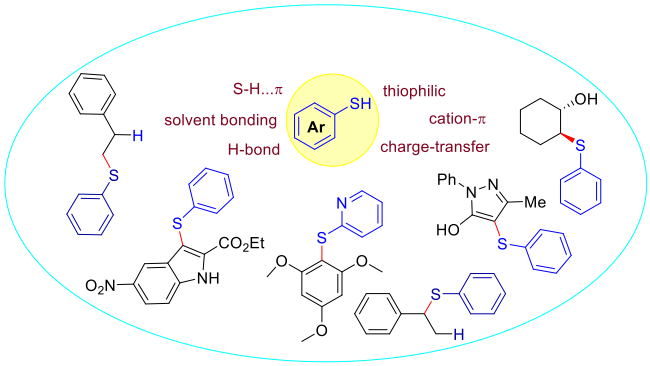



*synthesis of vinyl sulfone*



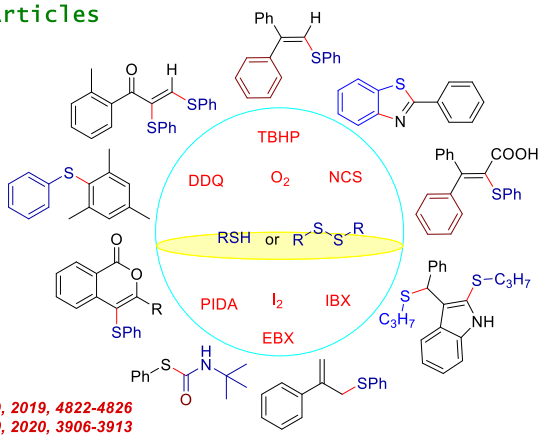

*synthesis of 3-chlorocoumarin*

## weak interactions in C-S coupling




## Review Articles

## metal-free C-S coupling




*Chem. Commun. 2020, 56, 2991-2994*
*Chem. Commun. 2021, 57, 5698-5701*
*Chem. Commun. 2020, 56, 10211-10214*

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*The Chemical Record, 2021, DOI: org/10.1002/tcr.202100208*
*Org. Lett. 2021, 23, 8088-8092*

*J. Org. Chem. 2020, 85, 11997-12011*
*Org. Biomol. Chem. 2020, 18, 8771-8792*
*Org. Biomol. Chem., 2021, 19, 8539-8543*