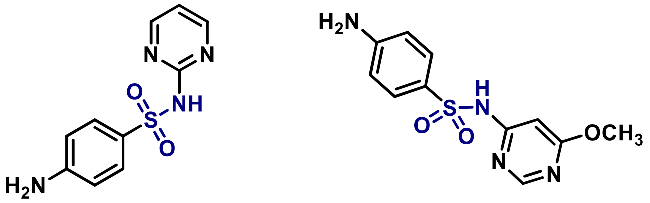
Chapter-4

Visible-Light Induced Arylation via Electron-Donor-Acceptor Complex: a Catalyst-Free Approach for the Synthesis of N-(Hetero)Aryl Sulfonamides

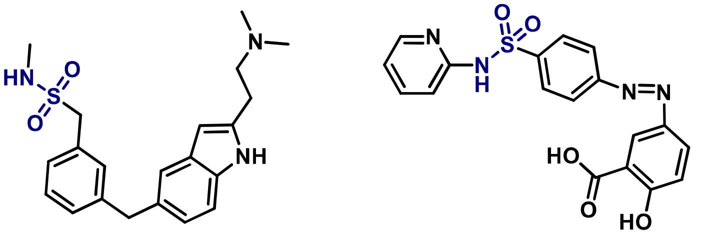
4.1 Introduction

N-Arylsulfonamides [1] are quite common structural motifs as a class of critical building blocks found in many biologically active compounds and pharmaceutical intermediates [2-5], and these structures play significant roles in organic synthesis as well as biological and medicinal research [6-12](Figure 4.1).



sulfadizine
as antibacterial drug

sulfamonomethoxine
as antibiotic

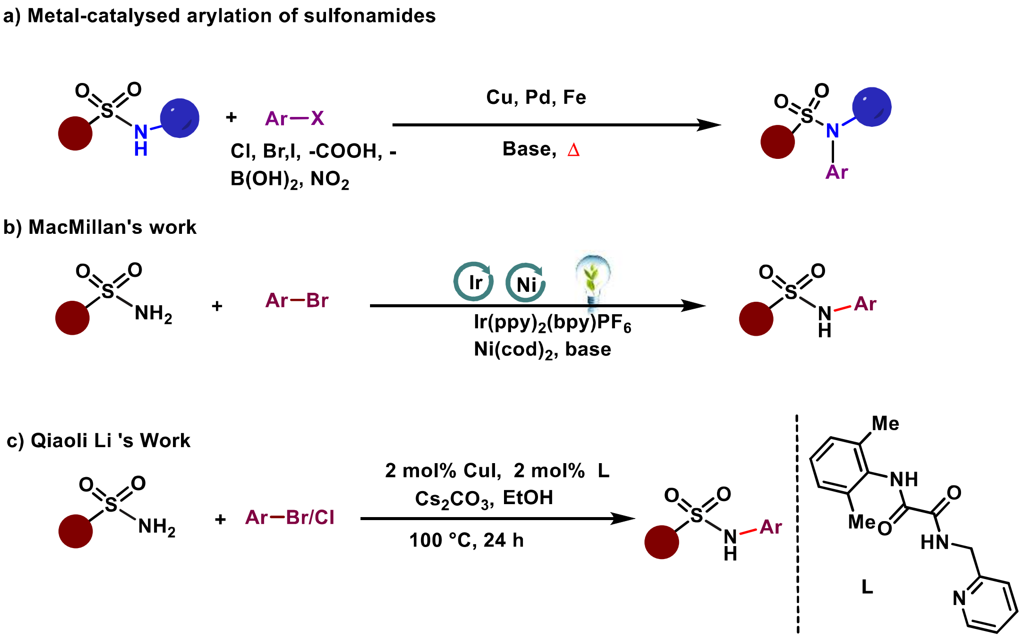


sumatriptan drug
migraine headache

sulfasalazine drug
for rheumatoid arthritis

Figure 4.1 Biologically active N-arylsulfonamides

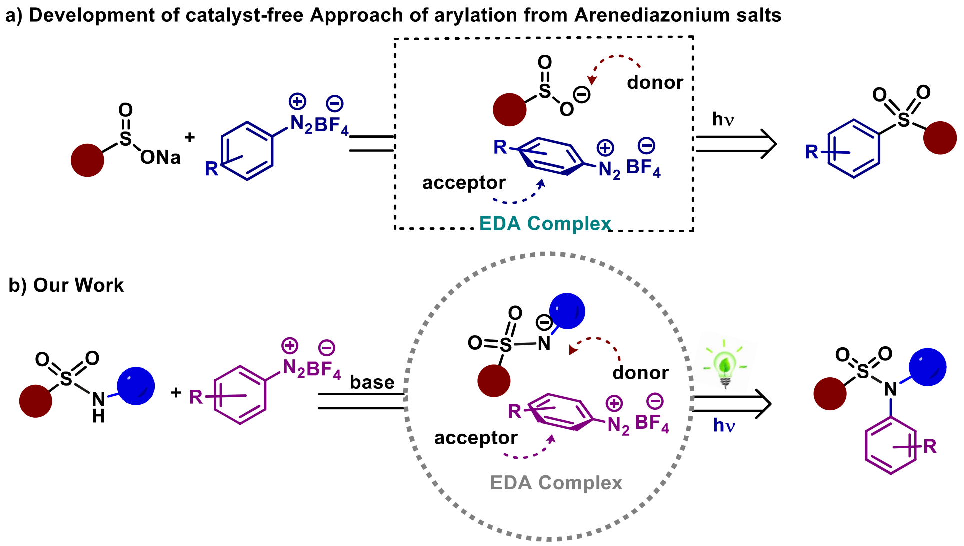
As a result, organic and pharmaceutical chemists are interested in developing efficient and environmentally friendly methods for synthesizing N-arylsulfonamides under mild conditions. Various efforts have been made in recent years to construct sulfonamides [2, 13]. One of the most common routes to synthesize N-arylsulfonamides involves the direct formation of N-S bonds. While this approach is generally effective, it frequently suffers from the use of aromatic amines as nitrogen sources, which are genotoxic and undesirable potential impurities in the synthesis of active pharmaceutical ingredients. The synthesis of N-arylsulfonamides via metal-catalyzed C-N bond formation has been extensively researched in recent years to overcome this limitation. However, their toxicity and environmental pollution issues greatly limit their further application [14-24](Scheme 4.1a**).** Notably, in 2018, the MacMillan group [25] presented the visible-light photoredox Ir/Ni dual catalysis as a potential path for C-N bond formation. These methods require transition metal catalysts and organometallic complexes (Scheme 4.1b**).** In 2022, Qiaoli Li group [26] reported direct N-arylsulfonamide from (hetero)aryl bromides/chlorides in the presence of 2–5 mol% copper salts and oxalamides at 100 °C (Scheme 4.1c).



Scheme 4.1 Previous works

In 2021, Xin Liang et al. [27] reported catalyst-free photochemical sulfonylation of diazonium salt driven by the photochemically activated EDA complexes (Scheme 4.2a).

Inspired by this strategy, we have generated aryl radicals by taking advantage of EDA complex. The anionic nitrogen of the sulfonamide group was engaged in an EDA complex with a diazonium salt. The EDA complex-enabled reaction has emerged as a valuable strategy for functionalized molecule synthesis. Under visible-light [28-31] catalyst-free conditions, the reaction proceeds efficiently due to the formation of an EDA complex between the electron-efficient reagent (acceptor) and the electron-rich reagent (donor) [27, 32-39]. Due to their widespread availability and high reactivity as arylation reagents, organic chemists have used arene diazonium salts [30, 31] more frequently in cross-coupling reactions. The current study aims to assess the readily available phenyl/heterocyclic diazonium salts and sulfonamides as acceptors and donors, respectively, for the construction of N-arylsulfonamides through radical coupling (Scheme 4.2b).



Scheme 4.2 Catalyst-free approach of arylation

In continuouation of our work [40-45] in the field of green synthetic chemistry from an environmental and economic standpoint of view, we would like to report herein a visible-light-driven EDA-complex-induced N-arylation of sulfonamides for the coupling of phenyl/heterocyclic diazonium salts and sulfonamides without the use of transition metals and catalysts. The currently developed protocol has many attractive features, including non-toxic, catalyst-free, lower energy, cost, and waste, which are interesting for developing sustainable processes. Furthermore, this benign protocol could be successfully applied to the late-stage functionalization of a complex molecule relevant to medicine (Scheme 4.3b).

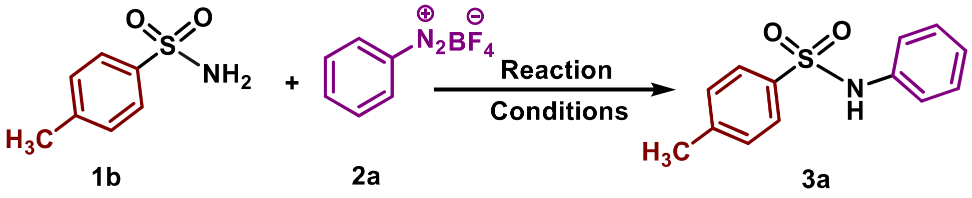
4.2 Results and discussion

First, the reaction's optimization was carried out. Avoiding transition-metal catalysts was the original intention of this research. Based on this idea, we commenced our investigation with benzenediazonium salt **2a**, *p*-toluene sulfonamide **1b**, $NaHCO_3$ as a base in MeCN solvent under blue LED irradiation, gratifyingly desired product N-arylsulfonamide (**3a**) was obtained in 76% isolated yield in 6 hours (Table 4.1, entry 1). Inspired by this result, benzene diazonium salt and *p*-toluene sulfonamide were selected as the model reaction to optimize reaction conditions such as base, solvents, and blue LED light (Tables 4.1 & 4.2). Preliminary studies revealed that the base significantly impacted the photoreaction, and Cs_2CO_3 was the best, giving the N-aryl sulfonamides **3a** with a 90% yield (Table 4.1, entry 4). Other bases, including Na_2CO_3, K_2CO_3, Et_3N, and DBU are less efficient than Cs_2CO_3, giving **3a** in 27−86% yields (Table 4.1, entries 1−6). With Cs_2CO_3 as the base, solvent screening revealed that CH_3CN was the best solvent (Table 4.1, entries 7−14). No reaction occurred without a solvent and base (Table 4.1, entries 15&16).

Moreover, upon extensive reaction optimization (Table 4.2), the best reaction conditions with 90% yield of the desired product **3a** were obtained using CH_3CN (4mL), **2a**, **1b,** and cesium carbonate Cs_2CO_3 as a base under blue light-emitting diodes (LEDs) at room temperature for 6 hr. (Table 4.2, entry 8). A significant drop in yield was observed while switching from blue LED to other light sources like green, purple, white LED, and 20W CFL (Table 4.2, entries 2-5). After that, the reaction without light gave no product, revealing that light is indispensable in this arylation reaction (Table 4.2, entry 6). Finally, if we prolonged the reaction time, 6 h to 8 h, the yield of the target product was still 90%. (Table 4.2 entry 7).

Different derivatives of diazonium salts and sulfonamides were used to examine the generality and substrate range under optimal reaction conditions. Initially, the reaction of the different diazonium salt with primary sulfonamide was studied. As shown in Table 4.3, diazonium salt with electron donating group methyl, methoxy, and hydroxy **(3b-3e)** were successfully tolerated in this transformation (84- 88% yield). Moreover, various electron-deficient groups, including cyano and nitro, as well as halide (Cl, Br, F) substituents **(3f-3m),** produced good to excellent yield of arylation (86- 92% yield). Naphthyl and para-ketone benzene diazonium salt was amenable for the process, providing the corresponding product **(3n&3o)** in 90 and 82% yield, respectively. Importantly, heteroaryl derivatives of diazonium salt (**3p-3u**) worked well and afforded the target product 79-86% yields.

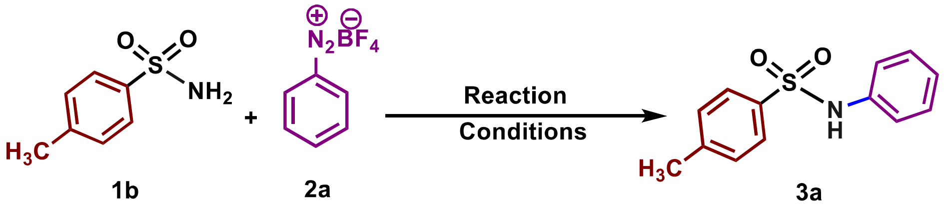
Table 4.1 Optimization of reaction conditions[a]



Entry	base	Solvent	Yield[b]%
1	$NaHCO_3$	CH_3CN	76
2	Na_2CO_3	CH_3CN	74
3	Cs_2CO_3	CH_3CN	90
4	K_2CO_3	CH_3CN	80
5	NEt_3	CH_3CN	38
6	DBU	CH_3CN	27
7	Cs_2CO_3	DCM	40
8	Cs_2CO_3	Ethanol	74
9	Cs_2CO_3	DMC	78
10	Cs_2CO_3	Water	nr
11	Cs_2CO_3	THF	nr
12	Cs_2CO_3	2-MeTHF	nr
13	Cs_2CO_3	DMF	nr
14	Cs_2CO_3	DMSO	nr
15	Cs_2CO_3	-	nr
16	-	CH_3CN	nr
17[c]	Cs_2CO_3	CH_3CN	87

[a] Reaction conditions: **1b** (0.6 mmol), **2** (0.3 mmol), base (0.6 mmol), solvent (4 mL), blue LED, ambient room temperature, and 6 h. [c]1.2 mmol Cs_2CO_3.[b] Isolated yield.

Table 4.2 Reaction conditions[a]



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

Entry	variations in the reaction conditions	Yield (%)[b]
1	Blue LEDs	90
2	green LEDs instead of blue LEDs	28
3	Purple LEDs instead of blue LEDs	46
4	white LEDs instead of blue LEDs	63
5	20W CFL instead of blue LEDs	49
6	no light	nr
7	reaction for 8 hrs	90
8	Standard Conditions	90

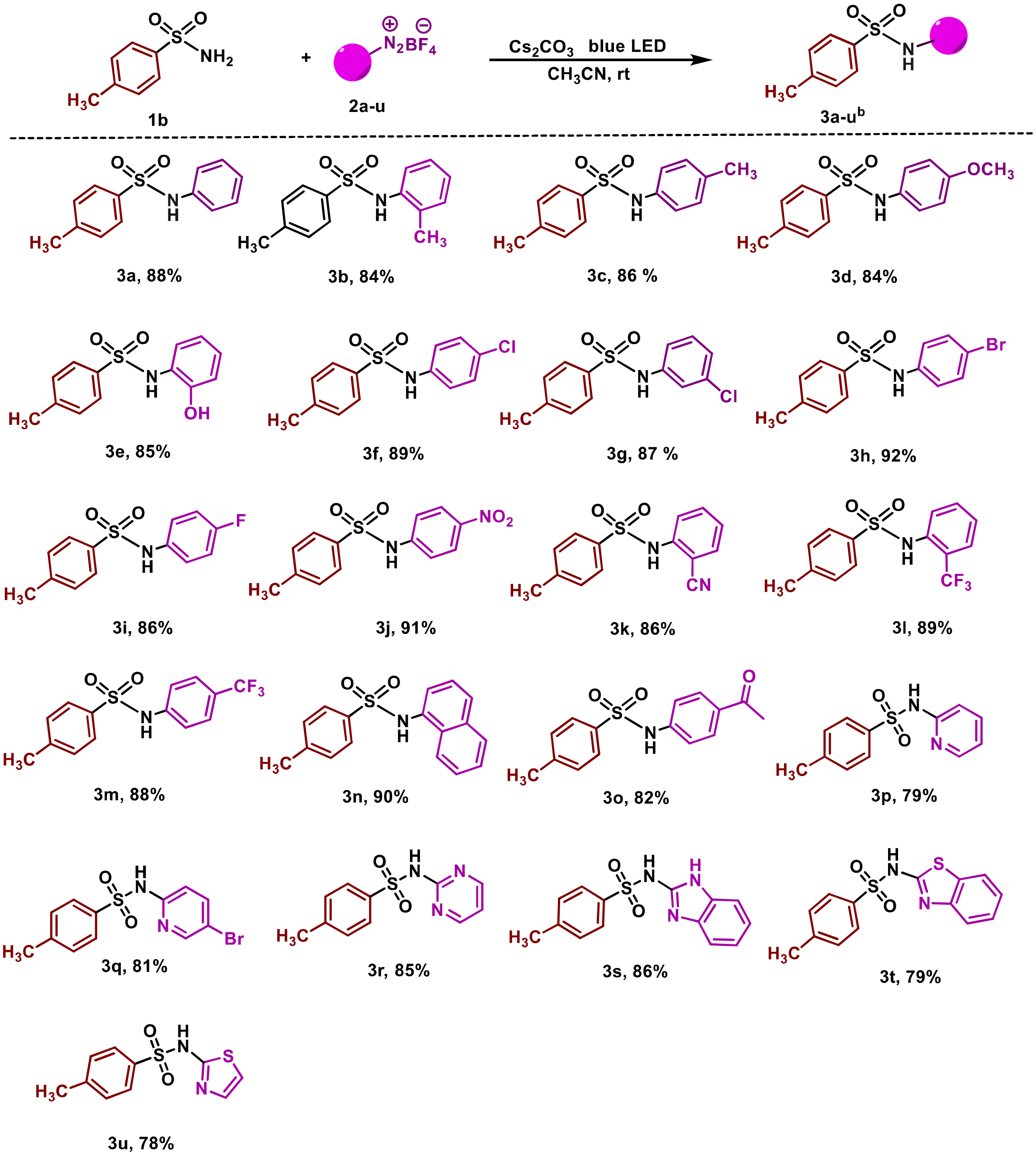
[a] Reaction conditions: **1b** (0.6 mmol), **2a** (0.3 mmol), Cs_2CO_3 (0.6 mmol), CH_3CN as a solvent (4 mL), blue LED, ambient room temperature, and 6 h. [b] Isolated yield.

We next investigated the substrate scope of the different derivatives of primary sulfonamide with respect to a benzene diazonium salt (Table 4.4). It was found that electronically and sterically, different derivatives of primary sulfonamide were successfully engaged in this transformation to deliver the target product in excellent yield with good functional group tolerance. Generally, the functional group such as Cl, Br, OH, Me, and OMe were equally reactive and gave the target products **4a-4i** in 81-93% yields. Also, this approach afforded well with naphthyl, para-ketone, and the nitro group provided the desired product with a good yield. We also examined that methyl sulfonamide and 2,4,6-trimethylbenzenesulfonamide were also suitable, giving rise to the target products **4c** and **4n** in 88% and 48% yields, respectively (Table 4.4).

Next, the reactivity of diazonium salt was also evaluated with a secondary sulfonamide (Table 4.5**).** It was found that likewise, in table 4.3, a variety of diazonium salt derivatives (**2a-2i**) was well tolerated by steric and sensitive functional groups like halides, methyl methoxy, Cl, and Br, hydroxyl, and nitro, providing a plentiful opportunity for further functionalization.

To demonstrate the viability of this approach, a gram-scale synthesis (Scheme 4.3a) was carried out with **1b** (6 mmol), **2a** (3 mmol), and Cs_2CO_3 (6 mmol) the target product **3a** was produced in 63% yield. Furthermore, to demonstrate the synthetic application of the new technique, we first synthesized the antibacterial medicine sulfanilamide (**4o**) with 71% yield by reducing 4-acetamidobenzene-sulfonamide (**1o**) [12]. Recent research has shown that the sulfanilamide moiety integrated with aromatic heterocyclic nitrogen-containing groups could exhibit various pharmacological activities and biological activities [13].

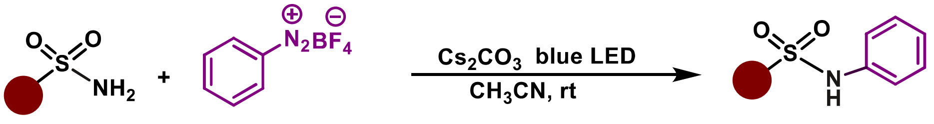
Table 4.3 Scope of the diazonium salt[a]



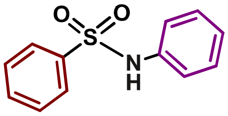
3a, 88%
3b, 84%
3c, 86 %
3d, 84%
3e, 85%
3f, 89%
3g, 87 %
3h, 92%
3i, 86%
3j, 91%
3k, 86%
3l, 89%
3m, 88%
3n, 90%
3o, 82%
3p, 79%
3q, 81%
3r, 85%
3s, 86%
3t, 79%
3u, 78%

[a] Reaction conditions: **1b** (0.6 mmol), **2** (0.3 mmol), Cs_2CO_3 (0.6 mmol), CH_3CN as a solvent (4 mL), blue LED, ambient room temperature, and 6 h. [b] Isolated yield.

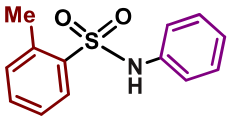
Table 4.4 Scope of the primary sulfonamide[a]



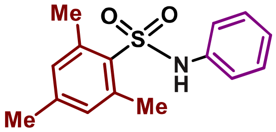
1a-n **2a** **4a-n**



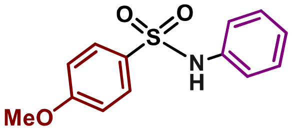
4a, 90%



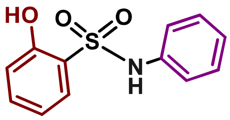
4b, 82%



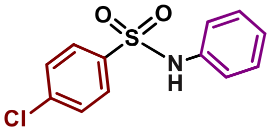
4c, 48%



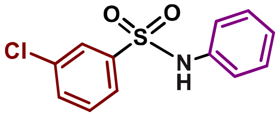
4d, 93%



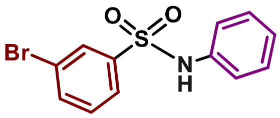
4e, 88%



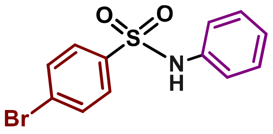
4f, 82%



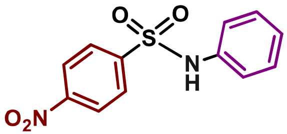
4g, 81%



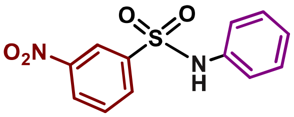
4h, 85%



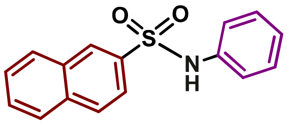
4i, 87%



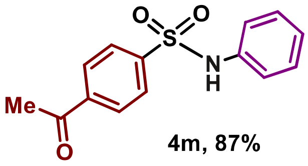
4j, 84%



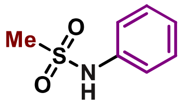
4k, 83%



4l, 87%



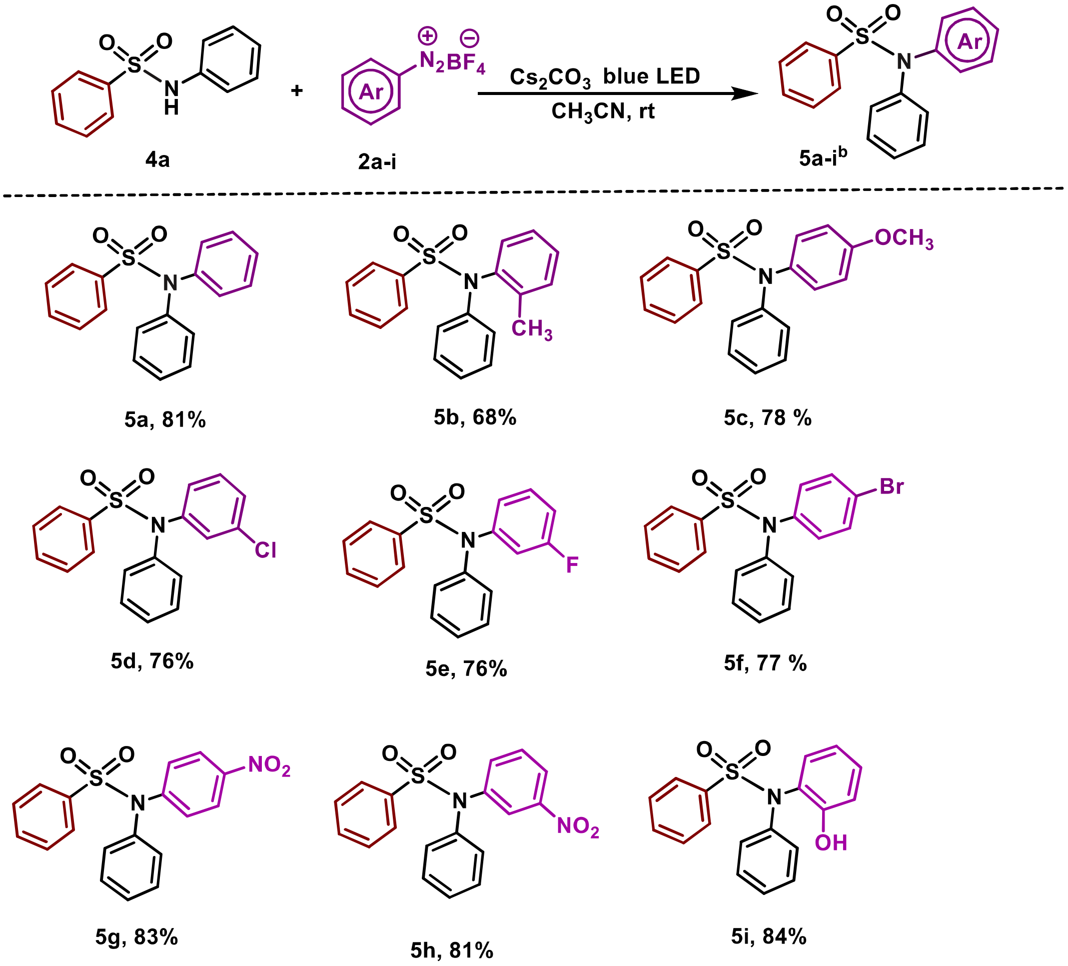
4m, 87%



4n, 88%

[a]Reaction conditions:**1** (0.6 mmol), **2a** (0.3 mmol), Cs$_2$CO$_3$ (0.6 mmol), CH$_3$CN as a solvent (4 mL), blue LED, ambient room temperature, and 6h. [b] Isolated yield.

Table 4.5 Scope of the secondary sulfonamides



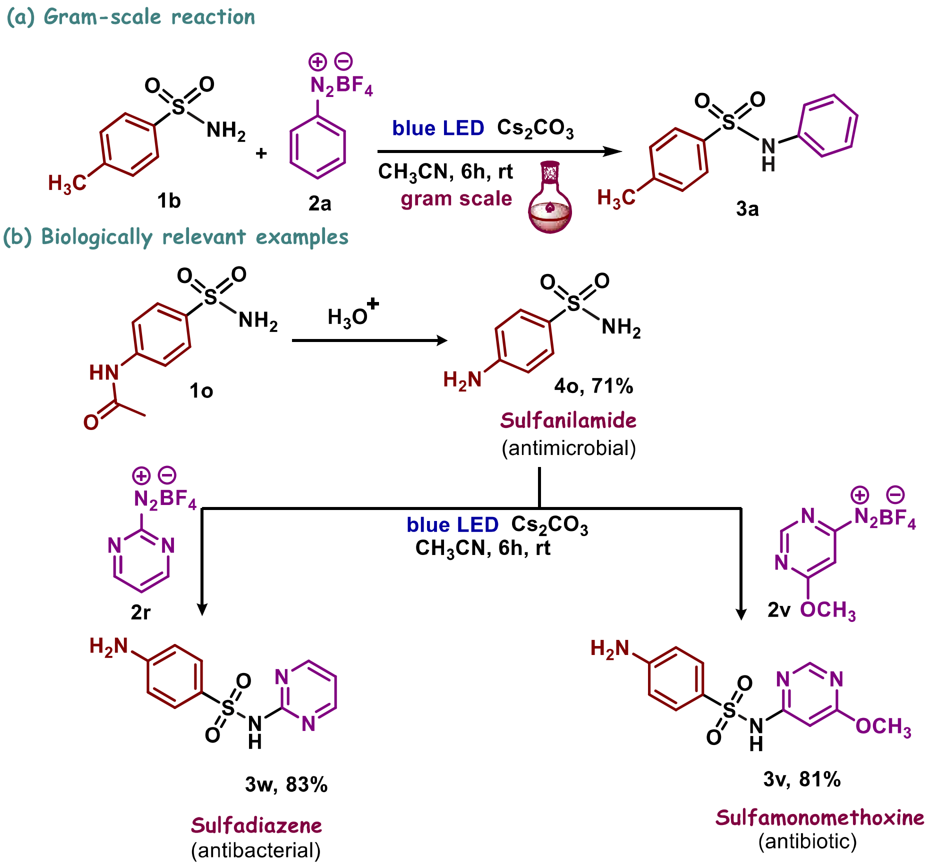
5a, 81% **5b**, 68% **5c**, 78 %

5d, 76% **5e**, 76% **5f**, 77 %

5g, 83% **5h**, 81% **5i**, 84%

[a]Reaction conditions: **4a** (0.6 mmol), **2** (0.3 mmol), Cs_2CO_3 (0.6 mmol), CH_3CN as a solvent (4 mL), blue LED, ambient room temperature, and 6h. [b]Isolated yield.

Direct arylation was achieved with two distinct heteros (aryl) diazonium salts employing sulfanilamide drug **4o** as a coupling partner. We obtained the antibacterial sulfadiazine (**3w**) as a marketable medication in 83% yield by coupling sulfanilamide (**4o**) with pyrimidine-2-diazonium salt (**2r**) under our standard conditions. Following that, we used this approach to produce an satisfactory yield of 81% of Sulfamonomethoxine (**3v**), a long-acting sulfonamide antibiotic medication (Scheme 4.3b).

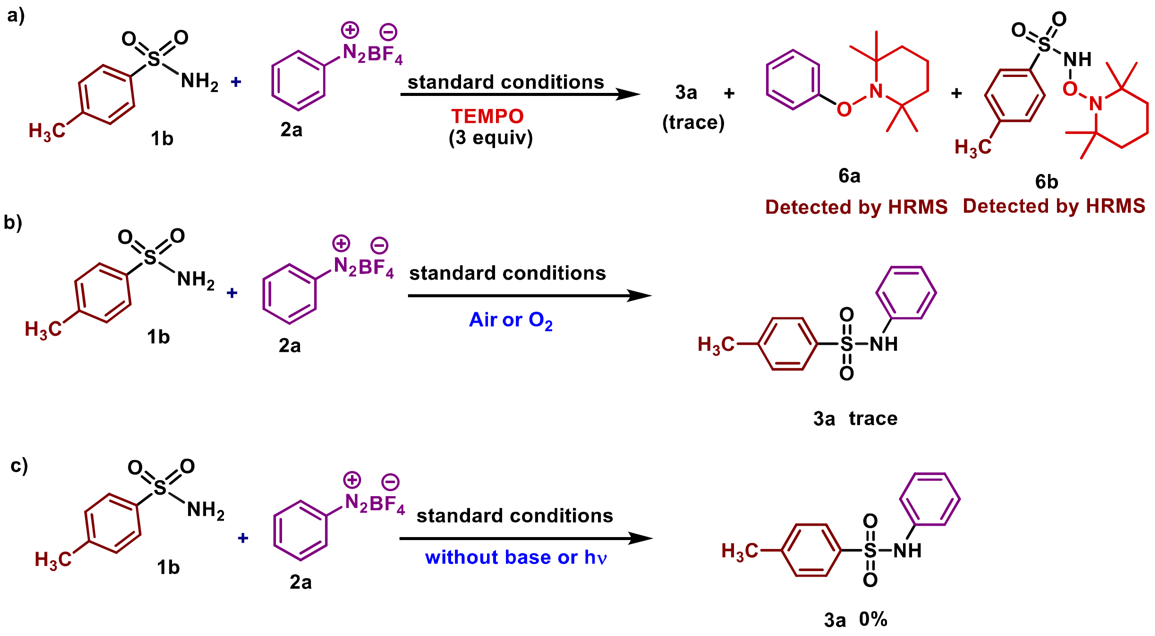


Scheme 4.3 (a) Gram-scale reaction (b) Synthesis of biologically relevant molecules

4.3 Control experiments

A series of control experiments were conducted to gain insight into this transformation, as shown in Scheme 4.4. We first examined the UV-visible absorption spectra of substrates **1b** (colourless) and **2a** (yellow colour for benzene diazonium salt, different derivatives of diazonium salt show different colour), showed that **1b** could absorb light with wavelengths less than 290 nm, while **2a** could absorb light with wavelengths between 340 and 490 nm

(Figure 4.2). Moreover, the mixture of **1b** and **2a** did not affect the waveform or the strength of the spectra. The electron donor-acceptor (EDA) complex generated by the interaction of the sulfonamide anion **[A]** and **2a** is assumed to be responsible for the peak observed when **1b**, **2a**, and Cs_2CO_3 were mixed. This EDA complex is observably dark red and displays visible-light absorption tailing to the 390–515 nm area (Figure 4.2). Further, We studied the nature of this interaction by Jobs plot experiments (Figure 4.3). These experiments revealed a parabolic curve with a maximum absorbance value at 50% mole fraction of **2a**, confirming a 1:1 stoichiometric ratio of the EDA complex between **1a** and **2a**. The light on/off experiments proved the critical role of blue light (Figure 4.6) and excluded the nucleophile reaction pathway. The addition of TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) under standard conditions resulted in the inhibition of the arylation reaction. High-resolution mass spectrometry (HRMS) was used to identify the TEMPO-trapped products **6a** and **6b**, which confirmed the presence of aryl and sulfonamide radicals in this transformation. The control experiment revealed that no target product **4a** was found without base or light irradiation, indicating that the base and light were all indispensable for the reaction; the reaction is sensitive to air or oxygen atmosphere (Scheme 4.4).



Scheme 4.4 Mechanistic studies. (a) Radical-inhibiting and trapping experiments. (b&c) Some control experiments.

4.3.1 UV/Vis absorption spectrometry.

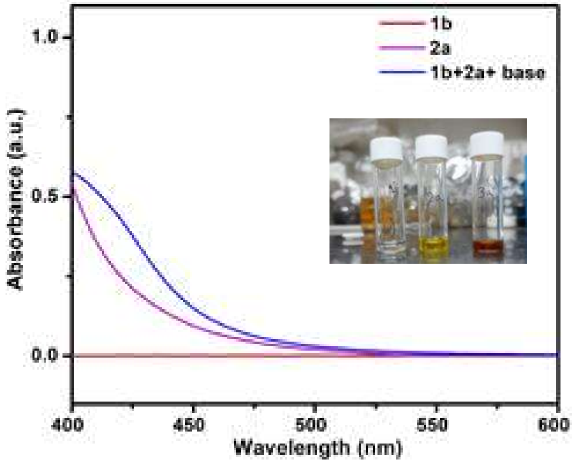


Figure 4.2. Absorption spectra of **1b, 2a**, and mixture of **1b+2a** + base. (Dissolved in MeCN).

4.3.2 Stoichiometry of the EDA complex 1b+2a (Jobs plot)

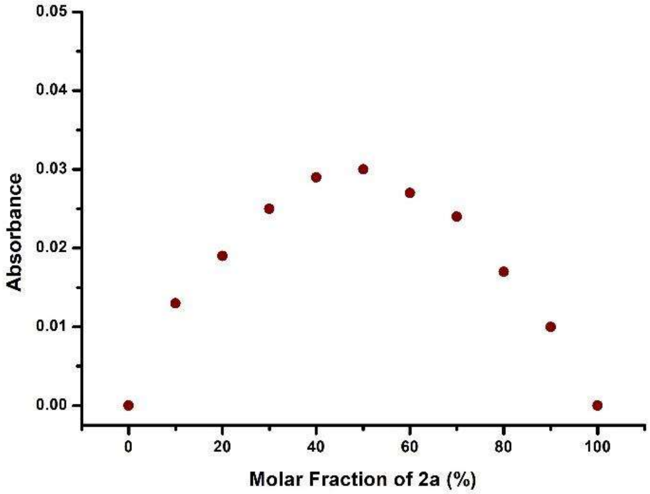
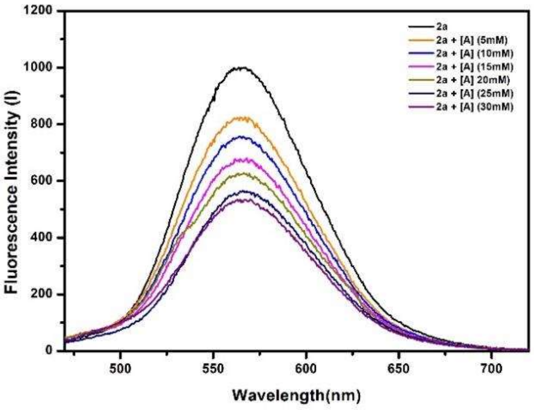


Figure 4.3 Jobs plot

The stoichiometry of the EDA complexes **1b** & **2a** was calculated using the Job's plot method. The Job's plot of the EDA complex between **1b** and **2a** was calculated by measuring the absorption of acetonitrile solutions at 410 nm with different donor/acceptor ratios with constant concentration (0.02 M) of the two components. The absorbance values were plotted against the molar fraction (%) of **2a**. The Job's plot analysis of the EDA complex between **1b** and **2a** showed a maximal absorbance at 50% molar fraction of **2a,** indicating the 1:1 stoichiometry of the EDA complex in solution.

4.3.3 Stern-Volmer fluorescence quenching studies

In a typical experiment, the solution of **2a** in MeCN was added to the appropriate amount of sulfonamide anion **[A]**. The addition of **[A]** was repeated six consecutive times. After each addition, emission spectra were recorded. All the solutions were excited at **410 nm;** the emission was acquired from 0 nm to 700 nm. The result shown in figure 4.4 indicates that **[A]** quenches the excited state of **2a** and its emission.



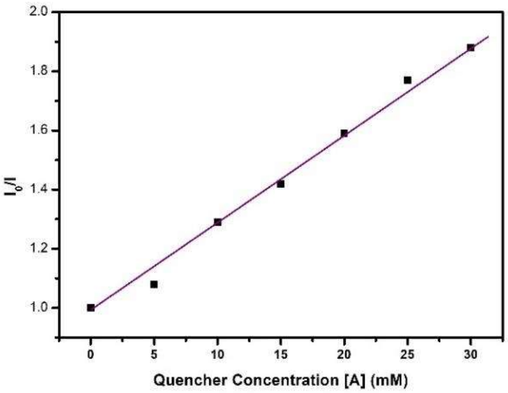


Figure 4.4. The fluorescence emission spectra of **2a** with different concentrations of quencher **[A]. Figure 4.5.** Stern-Volmer fluorescence quenching plot

The Stern-Volmer plot (shown in figure 4.5)indicated a linear relationship between the concentration of [A] and the ratio I_0/I. The Stern-Volmer constant K_{SV} was calculated using **equation 1**.

$$I_0/I = 1 + K_{SV}[Q] \qquad \text{..........}\textbf{Eq. 1}$$

Where, I_0 = the intensity of fluorescence of 2a, without quencher [A]
I = the intensity of fluorescence of 2a, with quencher [A]
[Q] = concentration of the quencher [A]

4.3.4 ON-OFF Experiments

The reaction between **1b** and **2a** was conducted under standard conditions. Sequential intervals of stirring the reaction mixture in the presence of visible light (blue LED) were followed by stirring in the absence of light. One reaction system was suspended at each time point, followed by column chromatography purification to produce the corresponding products **3a.** The weight of the product measured the yield of **3a**.

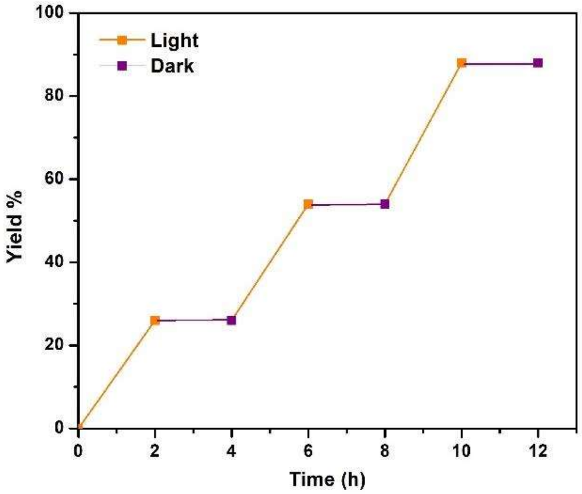
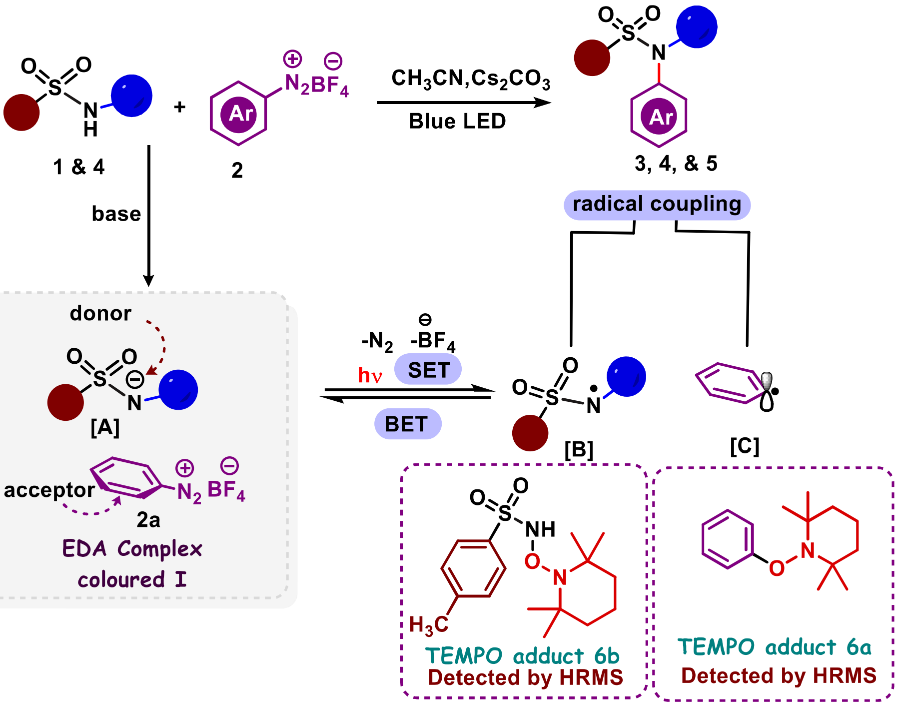


Figure 4.6 ON-OFF Experiments

4.4 Proposed mechanism

Based on the above results and previous literature[27, 34-36, 46], we suggested a plausible mechanism in Scheme 4.5. First, with the assistance of the base, a sulfonamide anion intermediate **[A]** is promptly produced from the sulfonamide **1 & 4**. Subsequently, formed EDA complex between the electron-deficient diazonium salts **2** and electron-rich intermediate anion **[A]** via anion- π interaction. Then under visible-light irradiation, a single electron is transferred from donor to acceptor within the EDA complex. Aryl radical **[C]** is produced by irreversible fragmentation, which disrupts the back electron transport and intermediate sulfonamide radical **[B]**. Finally, sulfonamide radical **[B]** rapidly interacts with aryl radical intermediate **[C]** through radical coupling**,** thus generating the target N-arylated sulfonamide products **3, 4 & 5**.



Scheme 4.5 Plausible mechanism

4.5 Conclusions

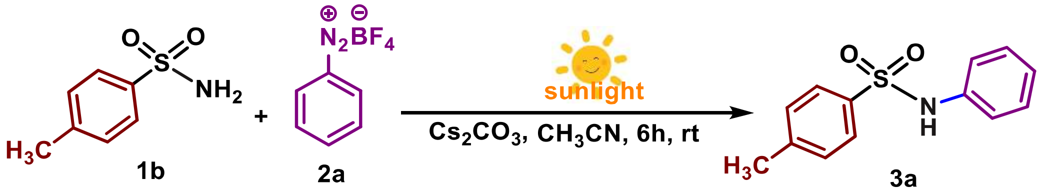
In this study, we have demonstrated the catalyst-free synthesis of N-(Hetero)aryl Sulfonamides from functionalized diazonium salt and complex aryl amines using Cs_2CO_3 and visible light irradiation through the EDA complex. The mechanistic study suggested that the sulfonamide was formed via a radical coupling pathway of the sulfonamide radical and aryl radical intermediate using visible light. The pharmaceutical industry became more interested in structural importance as more sulfur-containing drugs and bioactive chemicals were discovered. In order to build the sulfonamide library for drug discovery and scale-up synthesis in a useful, affordable, and environmentally friendly manner, this methodology demonstrated a high tolerance of various functional groups substituted on sulfonamides and diazonium salts. It is anticipated that our methodologies will find widespread use in academic and professional settings.

4.6 Experimental procedures

4.6.1 General procedure for the preparation of N-Aryl Sulfonamide.

A 10 mL reaction tube equipped with a magnetic stirring bar was charged with sulfonamide derivatives **1** (0.6 mmol), diazonium salt derivatives **2** (0.3 mmol), Cs_2CO_3(0.6 mmol) as a base, and solvent CH_3CN (4 mL). The mixture was then stirred at room temperature and irradiated with a (80 cm) blue LEDs lights strip for 6 h. After completion of the reaction, the reaction mixture was extracted with ethyl acetate (3x50 mL). The combined organic phases were dried over anhydrous Na_2SO_4, and the solvent was removed under a vacuum. The residue was purified by column chromatography on neutral silica gel (ethyl acetate: hexane).

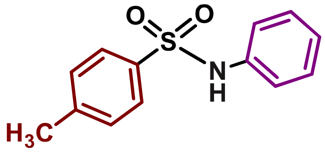
4.6.2 Application under the sunlight



The reaction tube was charged with **1b** (0.6 mmol), **2a** (0.3 mmol), and Cs_2CO_3 (0.6 mmol) in CH_3CN (4 mL) at room temperature, then the reaction system was irradiated under sunlight for 6 h (from 10:00 to 16:00; 14/09/2022. IIT BHU, Varanasi, UP India. Temperature: 25 °C – 35 °C) to provide 61% yield of the desired product **3a.**

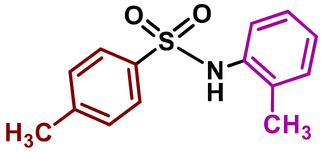
4.7 Characterization of the target products

4-Methyl-N-phenylbenzenesulfonamide (3a)



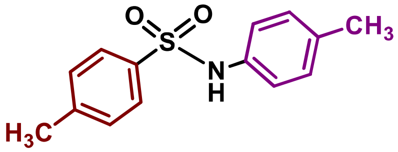
88% yield. Pale green solid. m.p.: 104-105ºC. ^{1}H NMR (500 MHz, DMSO) δ 10.13 (s, 1H), 7.73 (d, J = 9.6 Hz, 2H), 7.59 (t, J = 8.0 Hz, 1H), 7.53 (m, J = 8.6 Hz, 2H), 7.02 (d, J = 8.3 Hz, 2H), 6.97 (d, J = 8.5 Hz, 2H), 2.17 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 139.98, 135.45, 133.88, 133.23, 130.03, 129.64, 127.11, 121.11, 20.75. HRMS (ESI) m/z: [M+H] + calculated for $C_{13}H_{14}NO_2S$ 248.0745; found: 248.0733

4-Methyl-N-(o-tolyl)benzenesulfonamide (3b)



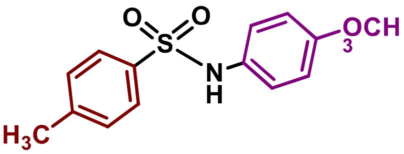
84% yield. Pink solid. m.p.: 106-107 ºC. ^{1}H NMR (500 MHz, DMSO) δ 9.59 (s, 1H), 7.48 (d, J = 8.0 Hz, 2H), 7.36 (m, 2H), 7.29 (m, J = 7.5 Hz, 2H), 7.12 (d, J = 7.8 Hz, 2H), 2.30 (d, J = 6.9 Hz, 6H). ^{13}C NMR (126 MHz, DMSO) δ 146.04, 138.18, 131.80, 131.58, 128.56, 128.15, 127.64, 125.95, 123.18, 21.25, 17.29. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{16}NO_2S$ 262.0901; found: 263.0917

4-Methyl-N-(p-tolyl)benzenesulfonamide (3c)



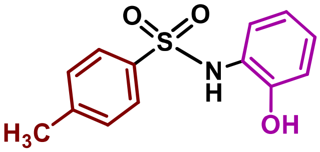
86% yield. White solid. m.p.: 114-116ºC. ^{1}H NMR (500 MHz, DMSO) δ 9.95 (s, 1H), 7.51 (d, J = 7.9 Hz, 2H), 7.31 (d, J = 8.3 Hz, 2H), 7.26 (d, J = 8.2 Hz, 2H), 7.14 (d, J = 7.9 Hz, 2H), 2.32 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 145.53, 138.53, 138.40, 130.68, 129.21, 128.68, 125.95, 123.54, 21.26, 20.99. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{16}NO_2S$ 262.0901; found: 262.0912

N-(4-Methoxyphenyl)-4-methylbenzenesulfonamide (3d)



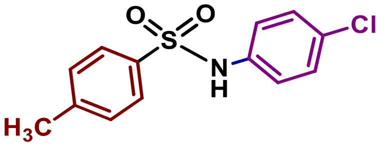
85% yield. Pale pink solid. m.p.: 115-117 °C. ^{1}H NMR (500 MHz, DMSO) δ 7.97 (s, J = 6.3 Hz, 1H), 7.68 (d, J = 8.2 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.7 Hz, 2H), 6.84 (d, J = 8.7 Hz, 2H), 3.87 (d, J = 6.3 Hz, 2H), 3.72 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 151.61, 145.41, 138.60, 134.45, 132.93, 128.69, 125.98, 118.53, 116.71, 115.92, 94.23, 21.26. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{16}NO_3S$ 278.0850; found: 278.0852

N-(2-Hydroxyphenyl)-4-methylbenzenesulfonamide (3e)



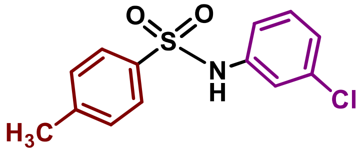
84% yield. Gray solid. m.p.: 137-138°C. ^{1}H NMR (500 MHz, DMSO) δ 10.70 (s, 1H), 9.73 (s, 1H), 7.50 (d, J = 8.1 Hz, 2H), 7.31 (m, 2H), 7.13 (d, J = 7.8 Hz, 2H), 7.02 (d, J = 8.1 Hz, 1H), 6.89 (t, J = 8.3 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 151.17, 145.96, 138.24, 129.90, 128.58, 125.96, 124.52, 119.96, 119.32, 116.62, 21.26. HRMS (ESI) m/z: [M+H] + calculated for $C_{13}H_{14}NO_3S$ 264.0694; found: 264.0698.

N-(4-Chlorophenyl)-4-methylbenzenesulfonamide (3f)



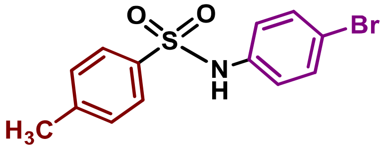
87% yield. White solid. m.p.: 120-122°C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, J = 8.3 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 7.21 (m, 2H), 7.06 (d, J = 8.8 Hz, 2H), 2.40 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.23, 135.61, 135.22, 130.77, 129.82, 129.40, 127.29, 122.79, 21.57. HRMS (ESI) m/z: [M+H] + calculated for $C_{13}H_{13}NO_2SCl$ 282.0355; found: 282.0358

N-(3-Chlorophenyl)-4-methylbenzenesulfonamide (3g)



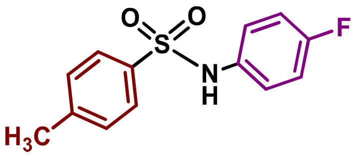
87% yield. White solid. m.p.: 114-115 °C. ^{1}H NMR (500 MHz, DMSO) δ 7.50 (d, J = 8.0 Hz, 2H), 7.36 (d, J = 8.0 Hz, 1H), 7.19 (t, J = 7.7 Hz, 1H), 7.14 (d, J = 7.8 Hz, 2H), 7.08 (d, J = 8.0 Hz, 1H), 6.89 (t, J = 7.6 Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 145.71, 139.43, 138.41, 130.00, 128.63, 128.51, 125.96, 122.22, 121.34, 119.53, 21.26. HRMS(ESI) m/z: [M+H] + calculated for $C_{13}H_{13}NO_2SCl$282.0355; found: 282.0362

N-(4-Bromophenyl)-4-methylbenzenesulfonamide (3h)



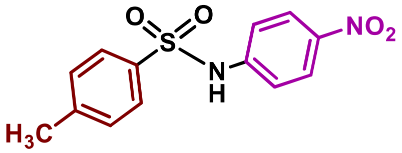
92% yield. White solid. m.p.: 140-145°C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, J = 8.3 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 7.21 (d, J = 8.8 Hz, 2H), 7.05 (d, J = 8.8 Hz, 2H), 2.40 (s, 26H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.23, 135.62, 135.16, 130.84, 129.81, 129.42, 127.28, 122.86, 21.59. HRMS (ESI) m/z: [M+H] + calculated for $C_{13}H_{13}NO_2SBr$ 325.9850; found: 325.9851

N-(4-Fluorophenyl)-4-methylbenzenesulfonamide (3i)



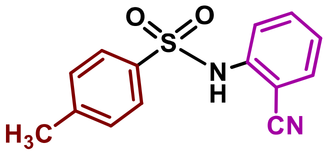
86% yield. White solid. m.p.: 98-99 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, J = 8.1 Hz, 2H), 7.25 (d, J = 8.1 Hz, 2H), 7.07 (m, J = 7.3 Hz, 2H), 6.94 (t, J = 8.6 Hz, 2H), 2.41 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.06, 135.66, 132.32, 129.72, 127.30, 124.60, 21.58 (s). ^{19}F NMR (471 MHz, $CDCl_3$) δ -116.24 – -116.48. HRMS (ESI) m/z: [M+H] + calculated for $C_{13}H_{13}NO_2SF$ 266.0651; found: 266.0654

4-Methyl-N-(4-nitrophenyl)benzenesulfonamide (3j)



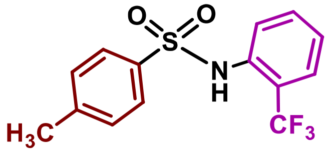
91% yield. Pale gray solid. m.p.: 180-182ºC. ^{1}H NMR (500 MHz, DMSO) δ 7.95 (d, J = 9.2 Hz, 2H), 7.52 (d, J = 8.1 Hz, 2H), 7.16 (m, 2H), 6.63 (d, J = 9.2 Hz, 2H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 155.84, 145.25, 138.71, 136.28, 128.73, 126.83, 125.97, 113.12, 21.25. HRMS(ESI) m/z: [M+H] + calculated for $C_{13}H_{13}N_2O_4S$ 293.0596; found: 293.0599

N-(2-Cyanophenyl)-4-methylbenzenesulfonamide (3k)



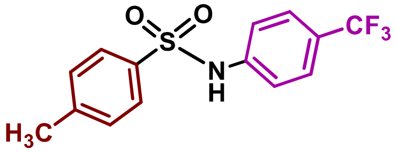
86% yield. White solid. m.p.: 172-173ºC. ^{1}H NMR (500 MHz, DMSO) δ 7.51 (d, J = 8.1 Hz, 2H), 7.38 (m, J = 7.8 Hz, 1H), 7.31 (m, J = 7.2 Hz, 1H), 7.16 (m, 2H), 6.81 (m, J = 8.4 Hz, 1H), 6.61 (m, J = 7.8 Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 151.61, 145.41, 138.60, 134.45, 132.93, 128.69, 125.98, 118.53, 116.71, 115.92, 94.23, 21.26. HRMS(ESI) m/z: [M+H] + calculated for $C_{14}H_{13}N_2O_2S$273.0697; found: 273.0699

4-Methyl-N-(2-(trifluoromethyl)phenyl)benzenesulfonamide (3l)



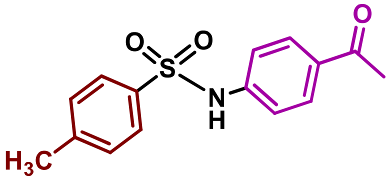
84% yield. White solid. m.p.: 124-125 ºC. ^{1}H NMR (500 MHz, DMSO) δ 10.83 (s, 1H), 7.72 (d, J = 8.3 Hz, 2H), 7.60 (d, J = 8.6 Hz, 2H), 7.37 (d, J = 8.1 Hz, 2H), 7.29 (d, J = 8.5 Hz, 2H), 2.34 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 158.92, 142.96, 138.35, 130.04, 129.97, 129.39, 127.01, 114.09, 55.53, 21.43. ^{19}F NMR (471 MHz, DMSO) δ -61.43. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{13}NO_2SF_3$ 316.0619; found: 316.0619

4-Methyl-N-(4-(trifluoromethyl)phenyl)benzenesulfonamide (3m)



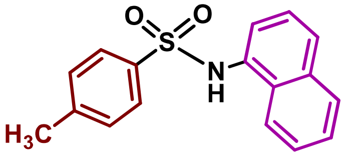
88% yield. Cream solid. m.p.: 144-145ºC. ^{1}H NMR (500 MHz, DMSO) δ 10.82 (s, 1H), 7.72 (d, J = 8.3 Hz, 2H), 7.60 (d, J = 8.6 Hz, 2H), 7.38 (d, J = 8.1 Hz, 2H), 7.29 (d, J = 8.5 Hz, 2H), 2.34 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 144.21, 142.16, 136.80, 130.36, 127.16, 127.01, 126.98, 119.10, 21.42. ^{19}F NMR (471 MHz, CDCl3) δ -62.23 (s). HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{13}NO_2SF_3$ 316.0619; found: 315.0620

N-(4-Acetylphenyl)-4-methylbenzenesulfonamide (3n):



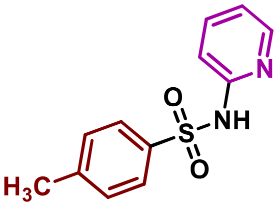
79% yield. Brown solid. m.p.: 198-200. ^{1}H NMR (500 MHz, DMSO) δ 7.84 (d, J = 8.7 Hz, 2H), 7.50 (d, J = 8.1 Hz, 2H), 7.14 (d, J = 7.8 Hz, 2H), 6.96 (d, J = 8.6 Hz, 2H), 2.47 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 196.31, 145.50, 138.54, 130.73, 128.68, 125.96, 117.61, 26.72, 21.26. HRMS(ESI) m/z: [M+H] + calculated for $C_{15}H_{16}NO_3S$ 290.0850; found: 290.0844

4-Methyl-N-(naphthalen-1-yl)benzenesulfonamide (3o)



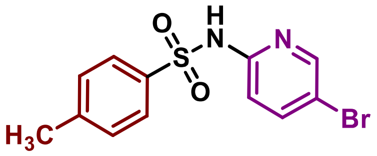
90% yield. brownish gray solid. m.p.: 109-111°C. ^{1}H NMR (500 MHz, DMSO) δ 10.49 (s, 1H), 7.80 (m, 3H), 7.71 (d, J = 8.3 Hz, 2H), 7.58 (s, 1H), 7.46 (m, 1H), 7.38 (t, J = 6.9 Hz, 1H), 7.32 (m, 3H), 2.27 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 143.76, 137.06, 135.98, 133.70, 130.40, 130.15, 129.48, 127.95, 127.62, 127.23, 127.11, 125.44, 120.70, 116.20, 21.37. HRMS(ESI) m/z: [M+H] + calculated for $C_{17}H_{16}NO_2S$ 298.0901; found: 298.0912

4-Methyl-N-(pyridin-2-yl)benzenesulfonamide (3p)



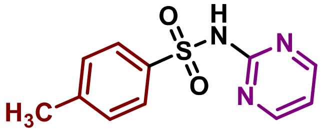
79% yield. light yellow solid m.p.: 213-214°C. ^{1}H NMR (500 MHz, DMSO) δ 11.87 (s, 1H), 8.02 (d, J = 6.1 Hz, 1H), 7.76 (d, J = 8.3 Hz, 2H), 7.70 (t, J = 8.9 Hz, 1H), 7.34 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.6 Hz, 1H), 6.90 (m, 1H), 2.34 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 153.44, 142.94, 140.60, 139.39, 129.85, 127.08, 116.25, 114.01, 21.40. HRMS (ESI) m/z: [M+H] + calculated for $C_{12}H_{13}N_2O_2S$ 249.0697; found: 249.0699

N-(5-Bromopyridin-2-yl)-4-methylbenzenesulfonamide (3q)



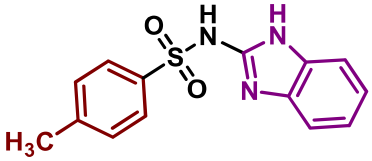
81% yield. Yellow liquid b.p.: 222-224°C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (s, 2H), 7.55 (m, J = 8.8 Hz, 1H), 7.37 (d, J = 8.9 Hz, 1H), 7.27 (d, J = 8.2 Hz, 2H), 6.49 (d, J = 8.8 Hz, 1H), 4.84 (s, 1H), 2.41 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.76, 149.18, 144.39, 141.43, 140.75, 129.91, 127.18, 113.47, 110.57, 21.60. HRMS (ESI) m/z: [M+H] + calculated for $C_{12}H_{12}N_2O_2SBr$ 326.9802; found: 326. 97.98

4-Methyl-N-(pyrimidin-2-yl)benzenesulfonamide (3r)



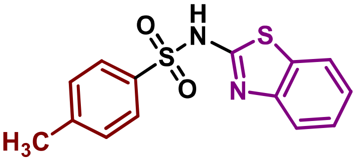
85% yield. White solid. m.p.: 213-214°C. ^{1}H NMR (500 MHz, DMSO) δ 8.65 (d, J = 7.6 Hz, 2H), 7.54 (d, J = 7.8 Hz, 2H), 7.14 (d, J = 7.8 Hz, 2H), 7.02 (m, 2H), 7.00 (d, J = 8.8 Hz, 1H), 2.29 (s, 3H). HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{14}N_3O_2S$ 250.0650; found: 250.0654

N-(1H-Benzo[d]imidazol-2-yl)-4-methylbenzenesulfona mide (3s)



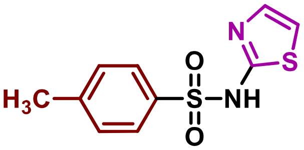
86% yield. White solid. m.p.: 213-214°C. ^{1}H NMR (500 MHz, DMSO) δ 8.44 (s, 2H), 7.52 (d, J = 7.6 Hz, 2H), 7.39 – 7.33 (m, 1H), 7.24 – 7.19 (m, 2H), 7.14 (d, J = 7.8 Hz, 2H), 2.28 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 151.06, 145.30, 138.70, 130.06, 128.73, 125.9, 123.54, 111.81, 21.24. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{14}N_3O_2S$ 288.0806; found: 288.0802

N-(Benzo[d]thiazol-2-yl)-4-methylbenzenesulfonamide (3t)



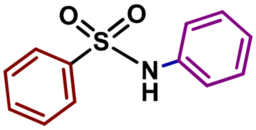
79% yield. Cream white solid. m.p.: 243-245ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 6.3 Hz, 4H), 7.13 (d, J = 4.6 Hz, 2H), 6.52 (d, J = 4.6 Hz, 1H), 5.60 (s, 1H), 2.42 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.79, 143.21, 138.10, 129.46, 126.75, 124.38, 107.84, 29.72, 21.56. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{13}N_2O_2S_2$ 304.0340; found: 304.0339

4-Methyl-N-(thiazol-2-yl)benzenesulfonamide (3u)



78% yield. Yellow solid. m.p.: 137-138ºC. ^{1}H NMR (500 MHz, DMSO) δ 12.69 (s, 1H), 7.69 (d, J = 8.2 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 7.6 Hz, 1H), 6.82 (d, J = 7.6 Hz, 1H), 2.35 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 169.27, 142.62, 140.00, 129.80, 126.29, 124.89, 108.60, 21.40. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{13}N_2O_2S_2$ 254.0184; found: 254.0183

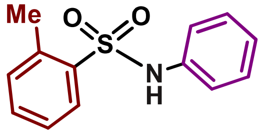
N-Phenylbenzenesulfonamide (4a)



92% yield, White solid. m.p.: 105-106ºC. ^{1}H NMR (500 MHz, DMSO) δ 7.60 (t, J = 7.9 Hz, 1H), 7.50 (d, J = 8.0 Hz, 4H), 7.46 (s, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.14 (d, J = 8.3 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ

145.53, 138.53, 138.40, 130.68, 129.21, 128.68, 125.95, 123.54. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{13}N_2O_2S_2$ 233.0510; found: 233.0509

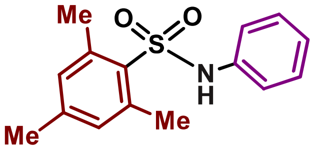
2-Methyl-N-phenylbenzenesulfonamide (4b):



82% yield, White solid. m.p.: 68-70ºC. ^{1}H NMR (500 MHz, DMSO) δ 9.59 (s, 1H), 7.65 (d, J = 7.3 Hz, 3H), 7.55 (t, J = 7.8 Hz, 2H), 7.15 – 7.12 (m, 1H), 7.09 (m, J = 6.7 Hz, 2H), 6.98 – 6.94 (m, 1H), 1.96 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 141.01, 135.21, 134.61, 133.18, 131.19, 129.64, 126.97, 126.95, 126.79, 17.99. HRMS(ESI) m/z: [M+H] + calculated for $C_{14}H_{13}N_2O_2S_2$ 247.0667; found: 247.0668

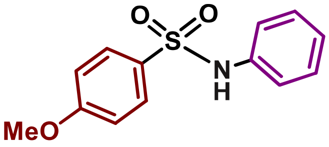
2,4,6-Trimethyl-N-phenylbenzenesulfonamide (4c)

48% yield, White solid. m.p.: 168-169ºC. ^{1}H NMR (500 MHz, DMSO) δ 10.18 (s, 1H),



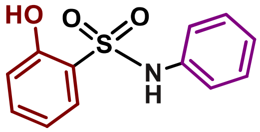
7.21 (t, J = 7.9 Hz, 2H), 7.01 – 6.95 (m, 5H), 2.55 (s, 6H), 2.22 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 142.48, 139.09, 138.11, 134.30, 132.25, 129.60, 123.99, 119.55, 22.91, 20.83. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{13}N_2O_2S_2$ 275.0980; found: 275.0982

4-Methoxy-N-phenylbenzenesulfonamide (4d)



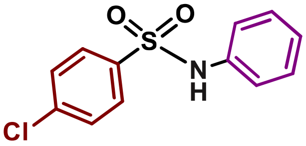
93% yield, White solid. m.p.: 105-106ºC. ^{1}H NMR (500 MHz, DMSO) δ 9.92 (s, 1H), 7.70 (m, 2H), 7.62 (m, 1H), 7.53 (t, J = 7.5 Hz, 2H), 6.97 (d, J = 9.0 Hz, 2H), 6.80 (d, J = 9.0 Hz, 2H), 3.66 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 157.00, 139.91, 133.17, 130.52, 129.59, 127.13, 123.93, 114.74, 55.59. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{13}N_2O_2S_2$ 263.0616; found: 263.0318

2-Hydroxy-N-phenylbenzenesulfonamide (4e)



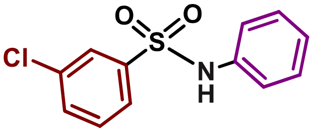
88% yield, brown solid. m.p.: 121-122°C. ^{1}H NMR (500 MHz, DMSO) δ 9.23 (s, 2H), 7.73 (d, J = 7.3 Hz, 2H), 7.53 (t, J = 7.3 Hz, 1H), 7.47 (t, J = 7.4 Hz, 2H), 7.07 (d, J = 7.8 Hz, 1H), 6.80 (t, J = 7.6 Hz, 1H), 6.67 (d, J = 7.7 Hz, 1H), 6.62 (t, J = 7.6 Hz, 1H). ^{13}C NMR (126 MHz, DMSO) δ 150.53, 142.56, 132.23, 129.12, 127.00, 124.60, 123.47, 119.23, 114.89. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{13}N_2O_2S_2$ 249.0460; found: 249.0461

4-Chloro-N-phenylbenzenesulfonamide (4f)



83% yield, White solid. m.p.: 103-105°C. ^{1}H NMR (500 MHz, DMSO) δ 7.74 (m, J = 7.0 Hz, 2H), 7.55 (m, J = 6.7 Hz, 1H), 7.51 (m, J = 8.1 Hz, 2H), 7.23 (m, 2H), 7.05 (m, 2H). ^{13}C NMR (126 MHz, DMSO) δ 141.33, 139.84, 132.71, 129.51, 129.29, 126.99, 126.79, 122.09. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{13}N_2O_2S_2$ 267.0120; found: 267.0117

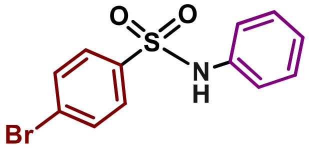
3-Chloro-N-phenylbenzenesulfonamide (4g)



81% yield, White solid. m.p.: 90-92°C. ^{1}H NMR (500 MHz, DMSO) δ 7.74 (d, J = 9.6 Hz, 2H), 7.46 (d, J = 7.3 Hz, 3H), 7.04

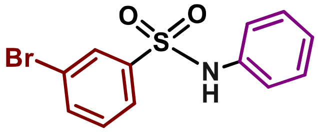
(t, J = 8.1 Hz, 1H), 6.94 (s, 1H), 6.83 (d, J = 8.2 Hz, 1H), 6.71 (d, J = 9.7 Hz, 1H). ^{13}C NMR (126 MHz, DMSO) δ 144.14, 133.31, 131.39, 130.82, 130.39, 129.06, 126.80, 119.63, 119.16, 115.36. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{13}N_2O_2S_2$ 267.0120; found: 267.0115

4-Bromo-N-phenylbenzenesulfonamide (4h)



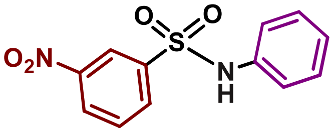
87% yield, Yellowish white solid. m.p.: 120-121°C. ^{1}H NMR (500 MHz, DMSO) δ 7.76 (m, 2H), 7.53 (m, 3H), 7.15 (d, J = 8.9 Hz, 2H), 6.97 (d, J = 8.9 Hz, 2H). ^{13}C NMR (126 MHz, DMSO) δ 142.49, 132.13, 129.31, 129.07, 126.91, 124.53, 122.09. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{13}N_2O_2S_2$ 310.9616; found: 310.9617

3-Bromo-N-phenylbenzenesulfonamide (4i)



87% yield, White solid. m.p.: 105-106°C. ^{1}H NMR (500 MHz, DMSO) δ 7.96 (m, 2H), 7.80 (d, J = 8.2 Hz, 2H), 7.49 (d, J = 7.3 Hz, 2H), 7.01 (d, J = 9.3 Hz, 1H), 6.74 (s, 1H), 6.60 (d, J = 9.2 Hz, 1H). ^{13}C NMR (126 MHz, DMSO) δ 138.83, 136.09, 131.91, 129.28, 126.88, 126.76, 125.68, 119.03, 112.84. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{13}N_2O_2S_2$ 310.9616; found: 310.9614

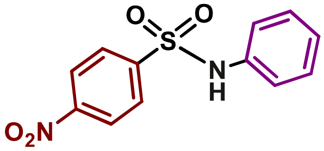
3-Nitro-N-phenylbenzenesulfonamide (4j)



83% yield, Orange solid. m.p.: 110-111°C. ^{1}H NMR (500 MHz, DMSO) δ 7.75 (m, 2H), 7.65 (t, J = 7.2 Hz, 1H), 7.37

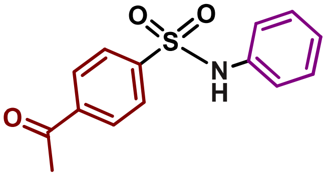
(d, J = 7.7 Hz, 3H), 7.28 (d, J = 6.7 Hz, 1H), 7.15 (t, J = 7.9 Hz, 1H), 7.11 (d, J = 7.4 Hz, 1H). ^{13}C NMR (126 MHz, DMSO) δ 152.01, 148.77, 146.64, 130.14, 129.26, 128.62, 127.57, 126.57, 113.57, 110.92. HRMS(ESI) m/z: [M+H] + calculated for $C_{14}H_{13}N_2O_2S_2$ 278.0361; found: 278.0360

4-Nitro-N-phenylbenzenesulfonamide (4k)



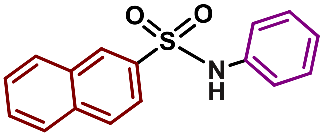
87% yield, Yellow solid. m.p.: 137-138°C. ^{1}H NMR (500 MHz, DMSO) δ 7.72 (m, J = 7.8 Hz, 2H), 7.46 (m, J = 7.2 Hz, 3H), 7.08 (d, J = 8.0 Hz, 2H), 6.95 (m, 2H). ^{13}C NMR (126 MHz, DMSO) δ 150.15, 143.79, 131.65, 129.10, 128.85, 126.84, 122.10, 115.62. HRMS(ESI) m/z: [M+H] + calculated for $C_{14}H_{13}N_2O_2S_2$ 278.0361; found: 278.0363

4-Acetyl-N-phenylbenzenesulfonamide (4l)



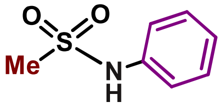
87% yield, Cream white solid. m.p.: 134-135°C. ^{1}H NMR (500 MHz, DMSO) δ 7.76 (d, J = 7.9 Hz, 1H), 7.66 (m, J = 7.9 Hz, 2H), 7.51 (m, 2H), 6.94 (d, J = 8.8 Hz, 1H), 6.56 (d, J = 8.8 Hz, 2H), 6.04 (s, 1H), 2.38 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 195.40, 154.09, 131.04, 130.00, 129.06, 126.77, 125.28, 119.14, 112.91, 26.32. HRMS(ESI) m/z: [M+H] + calculated for $C_{14}H_{13}NO_3S$ 275.0616; found: 275.0615

N-Phenylnaphthalene-2-sulfonamide (4m)



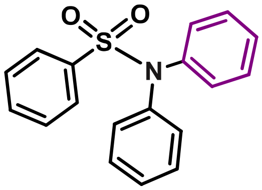
87% yield, White solid. m.p.: 133-134ºC. ^{1}H NMR (500 MHz, DMSO) δ 7.77 (m, 2H), 7.59 (m, 1H), 7.54 (m, 2H), 7.37 (s, 3H), 7.22 (d, J = 8.9 Hz, 2H), 7.04 (d, J = 8.9 Hz, 2H). ^{13}C NMR (126 MHz, DMSO) δ 141.08, 139.45, 132.83, 129.56, 129.34, 128.80, 127.01, 124.73, 123.61, 122.08. HRMS(ESI) m/z: [M+H] + calculated for $C_{14}H_{13}NO_3S$ 283.0667; found: 283.0666

N-Phenylmethanesulfonamide(4n)



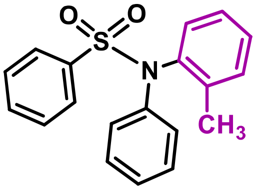
88% yield, White solid. m.p.: 100-10ºC. ^{1}H NMR (500 MHz, DMSO) δ 7.34 (t, J = 7.9 Hz, 2H), 7.22 (m, J = 8.6 Hz, 2H), 7.10 (t, J = 7.4 Hz, 1H), 2.98 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 138.93, 129.76, 124.26, 120.23, 39.64. HRMS(ESI) m/z: [M+H] + calculated for $C_{14}H_{13}NO_3S$ 173.0354; found: 173.0355

N,N-Diphenylbenzenesulfonamide(5a)



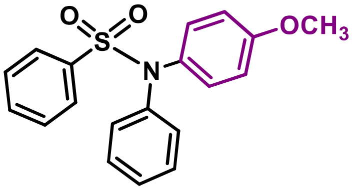
71% yield, White solid. m.p.:135-136ºC. ^{1}H NMR (500 MHz, DMSO) δ 7.73 (d, J = 9.5 Hz, 2H), 7.54 – 7.48 (m, 3H), 7.17 (m, J = 8.1 Hz, 4H), 7.00 (d, J = 8.7 Hz, 2H), 6.76 (d, J = 8.6 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 157.79, 132.37, 129.83, 129.39, 129.16, 126.94, 122.08, 119.25, 115.69. HRMS(ESI) m/z: [M+H] + calculated for $C_{14}H_{13}NO_3S$ 309.0823; found: 309.0821

N-Phenyl-N-(o-tolyl)benzenesulfonamide (5b)



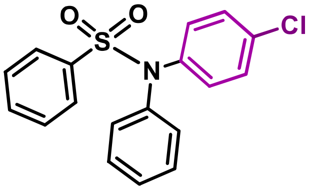
68% yield, White solid. m.p.: 128-129ºC. ^{1}H NMR (500 MHz, DMSO) δ 9.59 (d, J = 8.0 Hz, 1H), 9.41 (m, 1H), 7.65 (m, J = 8.6 Hz, 3H), 7.55 (t, J = 7.6 Hz, 2H), 7.16 (m, J = 7.2 Hz, 2H), 7.10 (m, J = 8.8 Hz, 3H), 6.98 – 6.95 (m, 1H), 6.81 – 6.72 (m, 3H), 1.97 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 157.77, 141.03, 135.22, 134.63, 133.17, 131.19, 129.84, 129.63, 126.98, 126.94, 126.78, 119.28, 115.69, 17.99. HRMS(ESI) m/z: [M+H] + calculated for $C_{14}H_{13}NO_3S$ 323.0980; found: 323.0981

N-(4-Methoxyphenyl)-N-phenylbenzenesulfonamide (5c)



78% yield, White solid. m.p.: 112-113ºC. ^{1}H NMR (500 MHz, DMSO) δ 7.70 (m, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.53 (t, J = 7.5 Hz, 2H), 7.18 – 7.15 (m, 2H), 6.97 (d, J = 7.0 Hz, 2H), 6.80 (d, J = 9.0 Hz, 2H), 6.77 – 6.75 (m, 3H), 3.66 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 157.77, 157.00, 139.88, 133.18, 130.51, 129.84, 129.59, 127.13, 123.93, 119.27, 115.68, 114.73, 55.58. HRMS(ESI) m/z: [M+H] + calculated for $C_{14}H_{13}NO_3S$ 339.0929; found: 339.0931

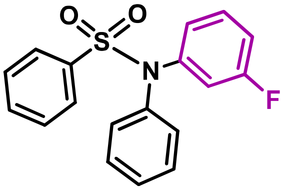
N-(4-Chlorophenyl)-N-phenylbenzenesulfonamide (5d)



76% yield, White solid. m.p.: 138-139 ºC. ^{1}H NMR (500 MHz, DMSO) δ 7.73 (m, J = 7.5 Hz, 2H), 7.47(m, 3H), 7.18 (m, 2H), 7.04 (t, J = 8.1 Hz, 1H), 6.93 (t, J = 7.1 Hz, 1H), 6.83 (d, J =

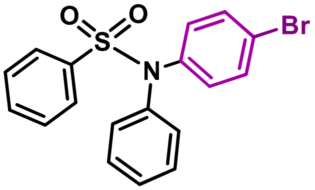
9.0 Hz, 1H), 6.78 (m, 3H), 6.70 (d, J = 9.1 Hz, 1H). ^{13}C NMR (126 MHz, DMSO) δ 157.79, 133.30, 131.36, 130.38, 129.84, 129.05, 126.78, 119.59, 119.25, 119.17, 115.69. HRMS(ESI) m/z: [M+H] + calculated for $C_{14}H_{13}NO_3S$ 343.0434; found: 343.0433

N-(3-Fluorophenyl)-N-phenylbenzenesulfonamide (5e)



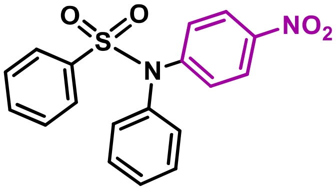
76 % yield, White solid. m.p.: 137-138°C. ^{1}H NMR (500 MHz, DMSO) δ 7.74 (d, J = 8.0 Hz, 1H), 7.56 (m, 2H), 7.19 (m, 5H), 7.00 (d, J = 8.9 Hz, 1H), 6.78 (m, 5H). ^{13}C NMR (126 MHz, DMSO) δ 157.79, 132.31, 129.84, 129.37, 129.14, 126.94, 122.08, 119.25, 115.69. HRMS(ESI) m/z: [M+H] + calculated for $C_{14}H_{13}NO_3S$ 327.0729; found: 327.0731

N-(4-Bromophenyl)-N-phenylbenzenesulfonamide (5f)



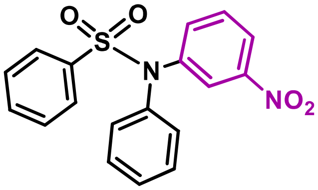
77% yield, White solid. m.p.: 137-138°C. ^{1}H NMR (500 MHz, DMSO) δ 7.75 (d, J = 7.0 Hz, 2H), 7.58 (t, J = 7.9 Hz, 1H), 7.52 (t, J = 7.3 Hz, 2H), 7.24 (d, J = 8.9 Hz, 2H), 7.16 (t, J = 7.2 Hz, 2H), 7.06 (d, J = 8.9 Hz, 2H), 6.77 (t, J = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 157.80, 140.76, 138.95, 132.98, 129.83, 129.61, 129.40, 127.41, 127.04, 122.08, 119.25, 115.69. HRMS(ESI) m/z: [M+H] + calculated for $C_{14}H_{13}NO_3S$ 386.9929; found: 386.9926

N-(4-Nitrophenyl)-N-phenylbenzenesulfonamide (5g)



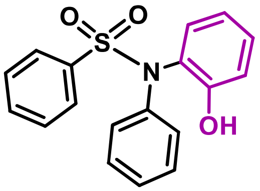
83% yield, Yellow solid. m.p.: 130-131ºC. ^{1}H NMR (500 MHz, DMSO) δ 8.24 (s, 2H), 7.93 (d, J = 8.8 Hz, 2H), 7.21 (m, 2H), 7.01 (t, J = 8.9 Hz, 2H), 6.89 (d, J = 7.3 Hz, 2H), 6.81 (m, 3H), 6.65 (m, J = 7.2 Hz, 1H). ^{13}C NMR (126 MHz, DMSO) δ 157.80, 129.81, 128.89, 128.84, 128.08, 128.05, 124.23, 124.19, 121.29, 119.22, 115.69. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{13}NO_3S$ 354.0674; found: 354.0679

N-(3-Nitrophenyl)-N-phenylbenzenesulfonamide (5h)



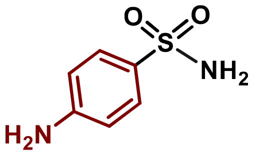
81% yield, Orange solid. m.p.: 136-137ºC. ^{1}H NMR (500 MHz, DMSO) δ 7.72 (s, 1H), 7.50 (m, J =7.8 Hz, 2H), 7.20 (m, 5H), 7.00 (d, J = 8.9 Hz, 1H), 6.76 (s, 5H). ^{13}C NMR (126 MHz, DMSO) δ 157.89, 129.84, 129.49, 129.14, 126.94, 122.17, 119.25, 115.69. HRMS(ESI) m/z: [M+H] + calculated for $C_{14}H_{13}NO_3S$ 354.0674; found: 354.0671

N-(2-Hydroxyphenyl)-N-phenylbenzenesulfonamide (5i)



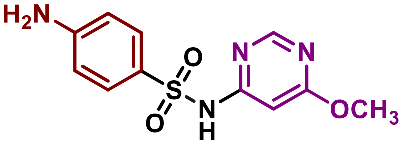
84% yield, White solid. m.p.: 112-113ºC. ^{1}H NMR (500 MHz, DMSO) δ 9.16 (s, 1H), 7.73 (d, *J* = 8.6 Hz, 3H), 7.58 – 7.53 (m, 2H), 7.49 (t, *J* = 7.5 Hz, 3H), 7.20 – 7.13 (m, 1H), 7.10 – 7.07 (m, 1H), 6.84 (d, *J* = 7.8 Hz, 1H), 6.76 (d, *J* = 8.6 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 6.64 (d, *J* = 6.3 Hz, 1H). ^{13}C NMR (126 MHz, DMSO) δ 157.78, 150.62, 142.08, 132.47, 129.83, 129.18, 127.05, 126.44, 125.30, 124.01, 119.28, 119.26, 115.69, 115.29.

4-Aminobenzenesulfonamide (Sulfanilamide) (4o)



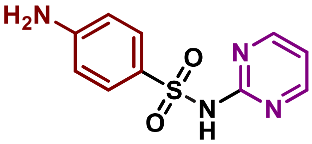
71% yield, White solid. m.p.: 164-166ºC. ^{1}H NMR (500 MHz, DMSO) δ 7.47 – 7.44 (m, 1H), 6.89 (s, 1H), 6.61 – 6.57 (m, 1H), 5.81 (s, 1H). ^{13}C NMR (126 MHz, DMSO) δ 152.38, 130.50, 127.89, 112.89.

4-Amino-N-(6-methoxypyrimidin-4-yl)benzenesulfonamide(Sulfamonomethoxine)(3v)



81% yield, White solid. m.p.: 206-208ºC. ^{1}H NMR (500 MHz, DMSO) δ 11.32 (s, 1H), 8.39 (d, *J* = 0.9 Hz, 1H), 7.57 – 7.53 (m, 2H), 6.61 – 6.56 (m, 2H), 6.31 (d, *J* = 0.9 Hz, 1H), 6.09 (s, 2H), 3.84 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 170.25, 159.26, 153.81, 129.66, 113.00, 91.07, 54.35.

4-Amino-N-(pyrimidin-2-yl)benzenesulfonamide (*Sulfadiazine*) (3w)



83% yield, White solid. m.p.: 252-256ºC. ^{1}H NMR (500 MHz, DMSO) δ 11.25 (s, 1H), 8.48 (d, *J* = 4.8 Hz, 2H), 7.63 – 7.59 (m, 2H), 7.01 (t, *J* = 4.8 Hz, 1H), 6.59 – 6.54 (m, 2H), 6.00 (s, 2H). ^{13}C NMR (126 MHz, DMSO) δ 158.72, 157.72, 153.49, 130.28, 125.37, 119.81, 115.98, 112.59.

4.8 Spectral Data of Products

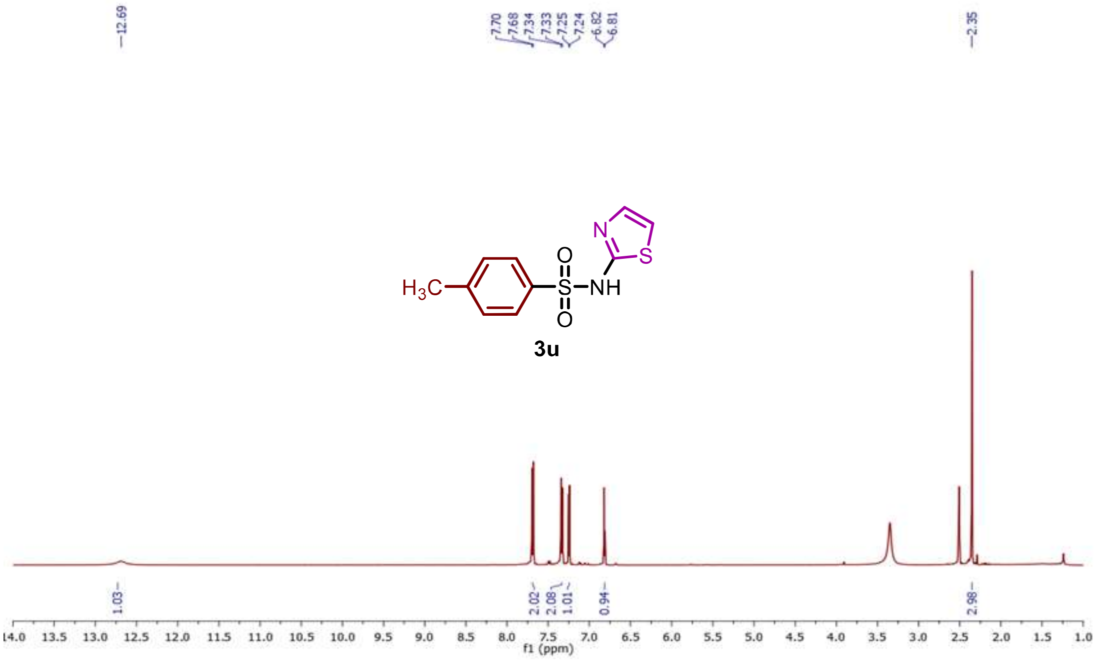


Figure 4.7 ^{1}H NMR spectrum of compound **3u**

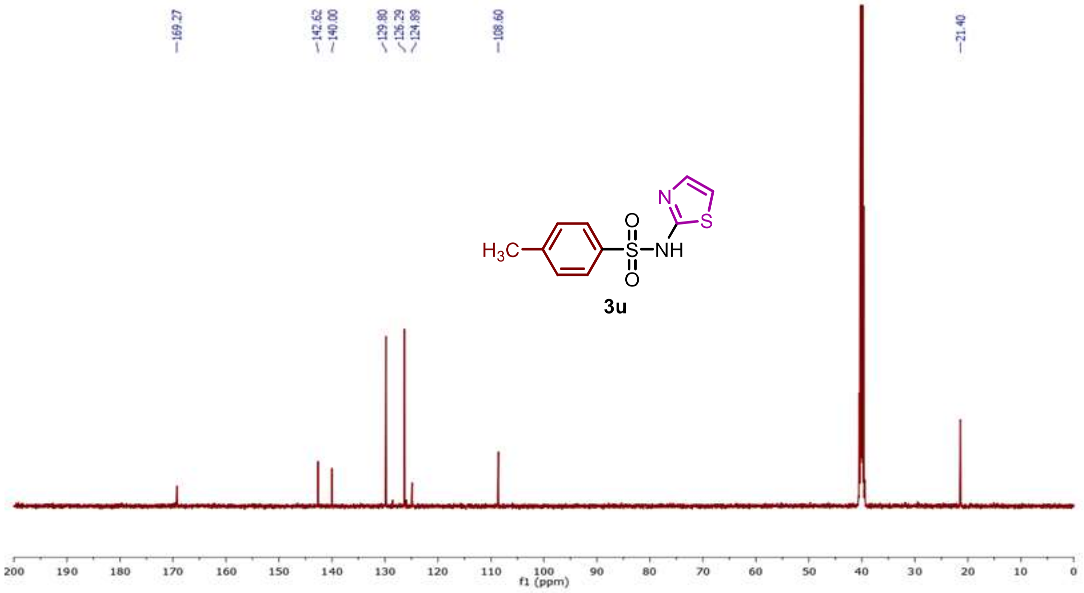


Figure 4.8 ^{13}C NMR spectrum of compound **3u**

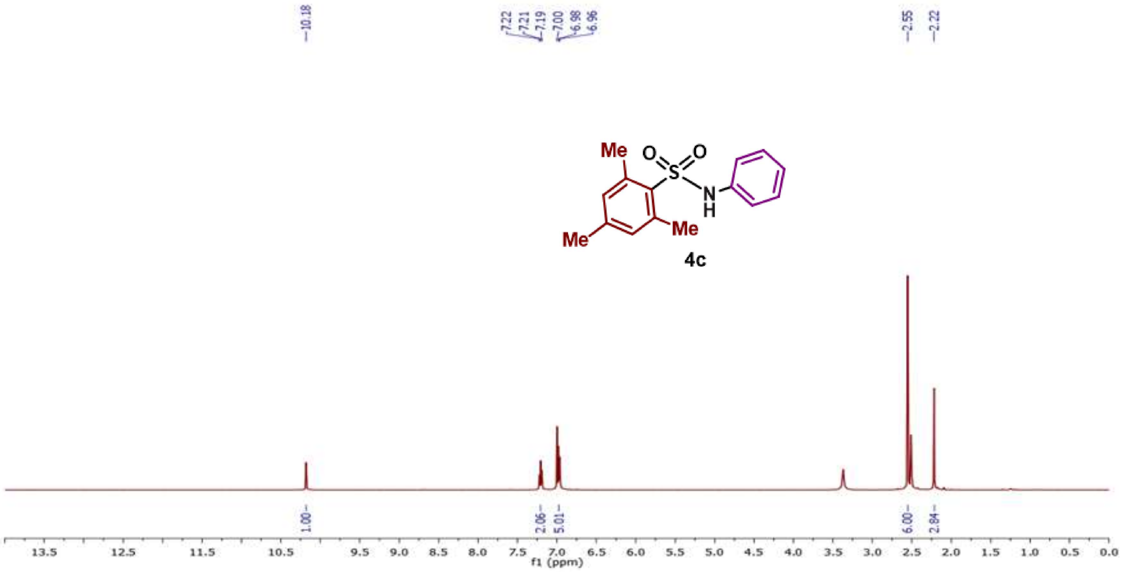


Figure 4.9 ^{1}H NMR spectrum of compound **4c**

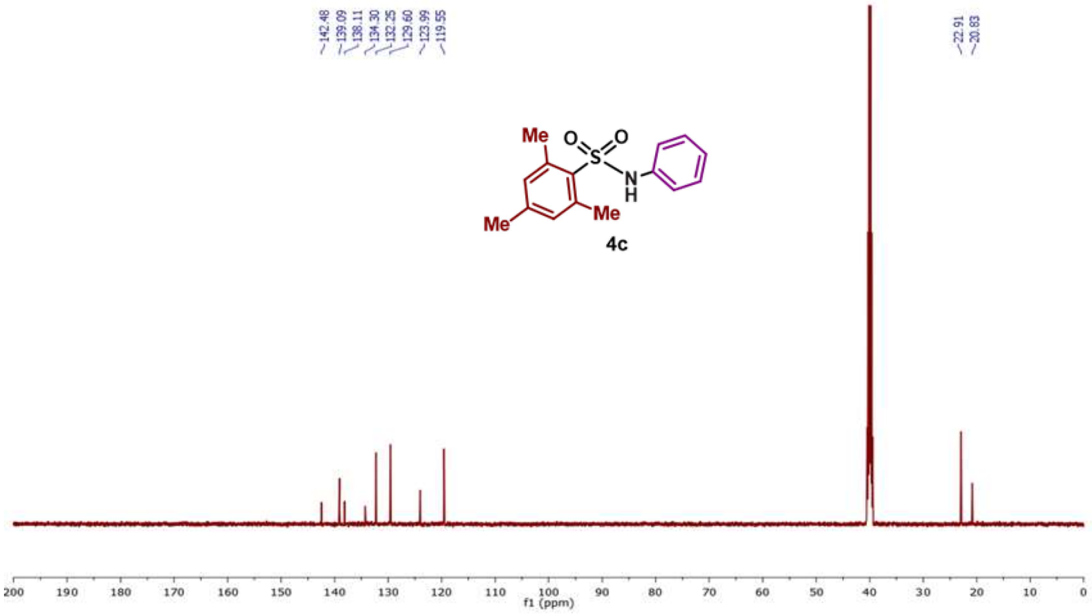


Figure 4.10 ^{13}C NMR spectrum of compound **4c**

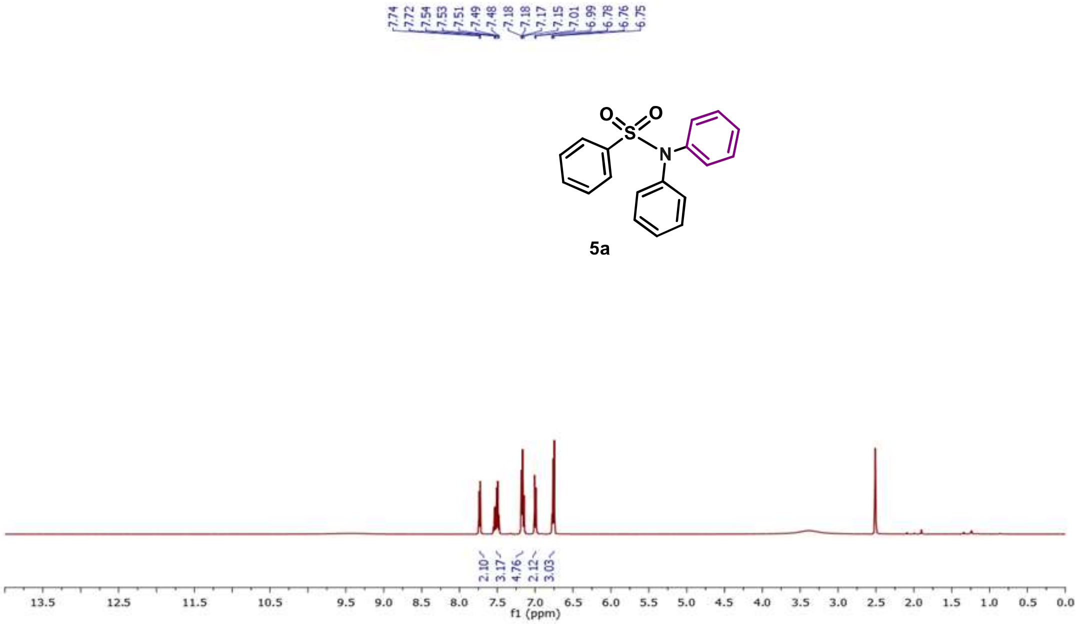


Figure 4.11 ^{1}H NMR spectrum of compound **5a**

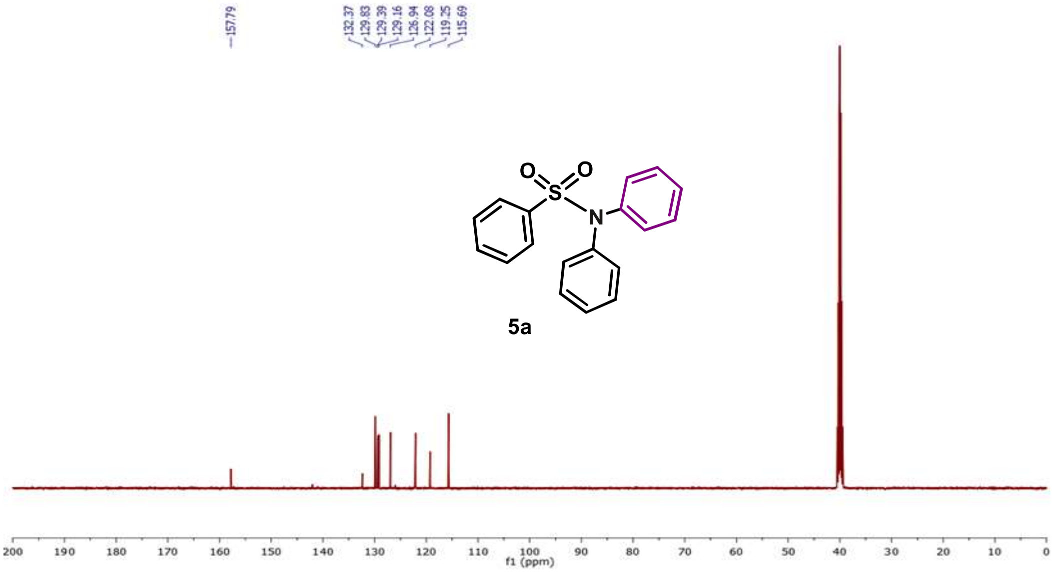


Figure 4.12 ^{13}C NMR spectrum of compound **5a**

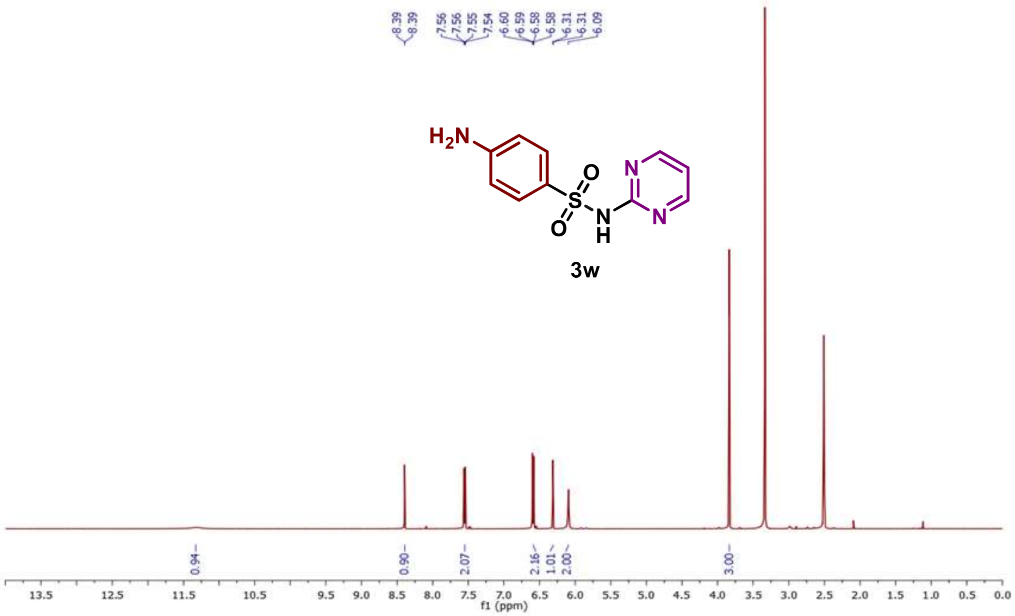


Figure 4.13 ^{1}H NMR spectrum of compound **3w**

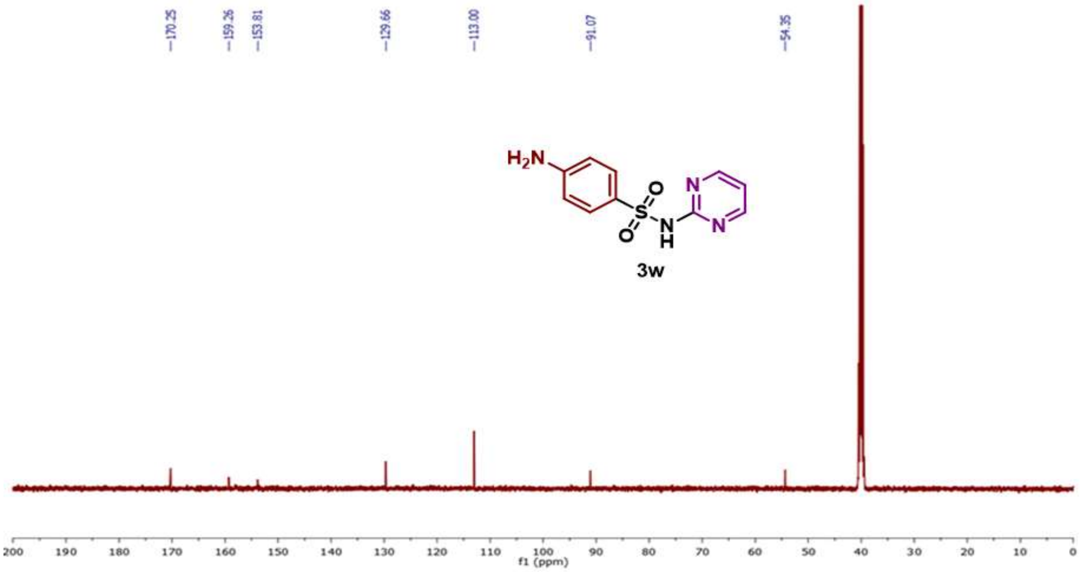
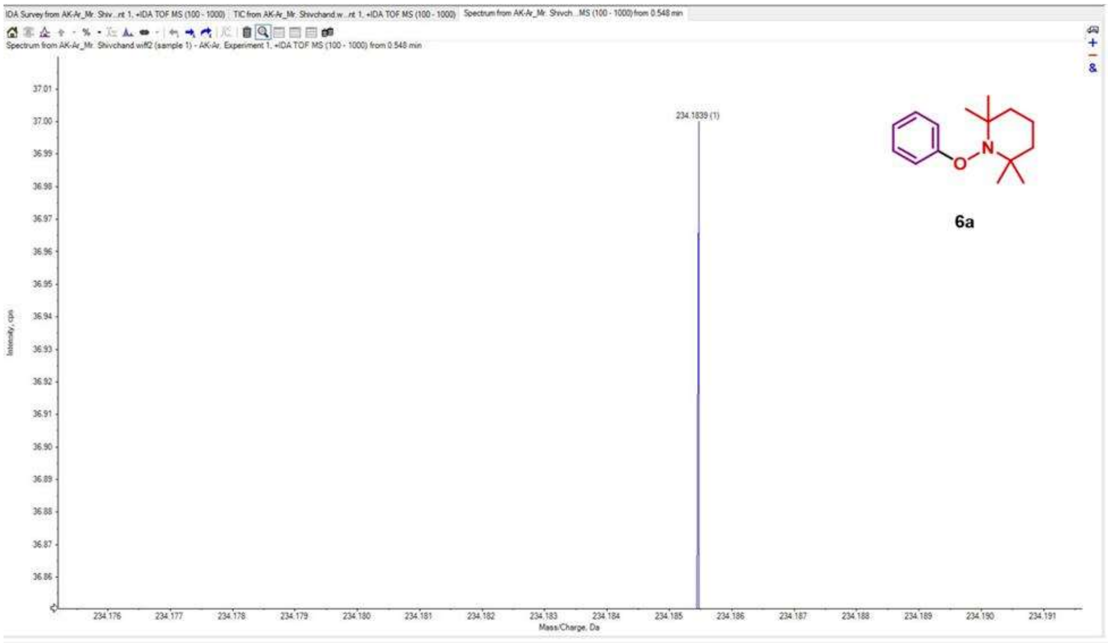


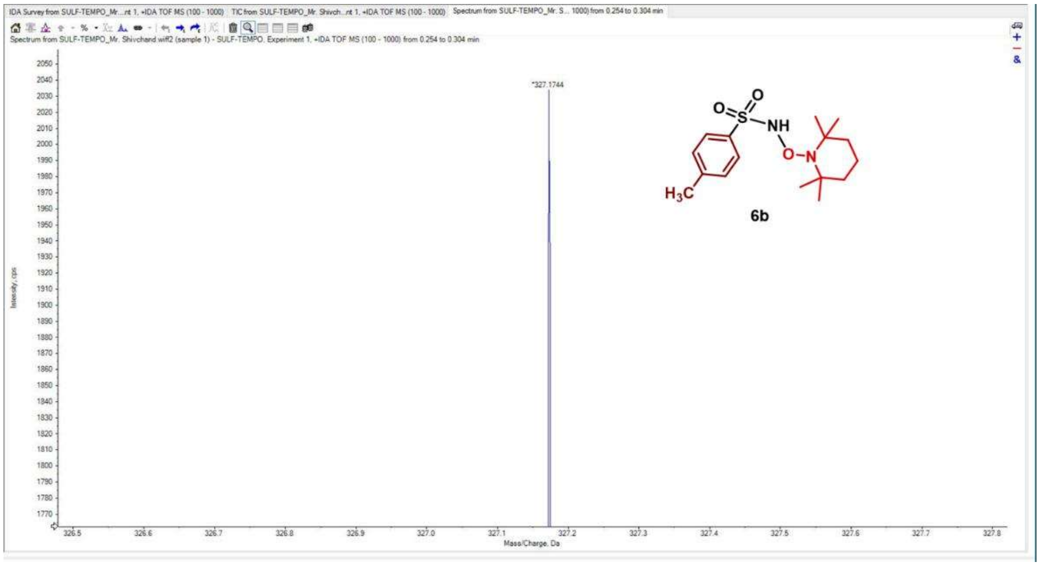
Figure 4.14 ^{13}C NMR spectrum of compound **3w**

4.9 HRMS Spectra



Spectrum from AK-Ar_Mr. Shivchand.wiff2 (sample 1) - AK-Ar, Experiment 1, +IDA TOF MS (100 - 1000) from 0.548 min

Figure 4.15 HRMS spectra of **6a**



Spectrum from SULF-TEMPO_Mr. Shivchand.wiff2 (sample 1) - SULF-TEMPO, Experiment 1, +IDA TOF MS (100 - 1000) from 0.254 to 0.304 min

Figure 4.16 HRMS spectra of **6b**

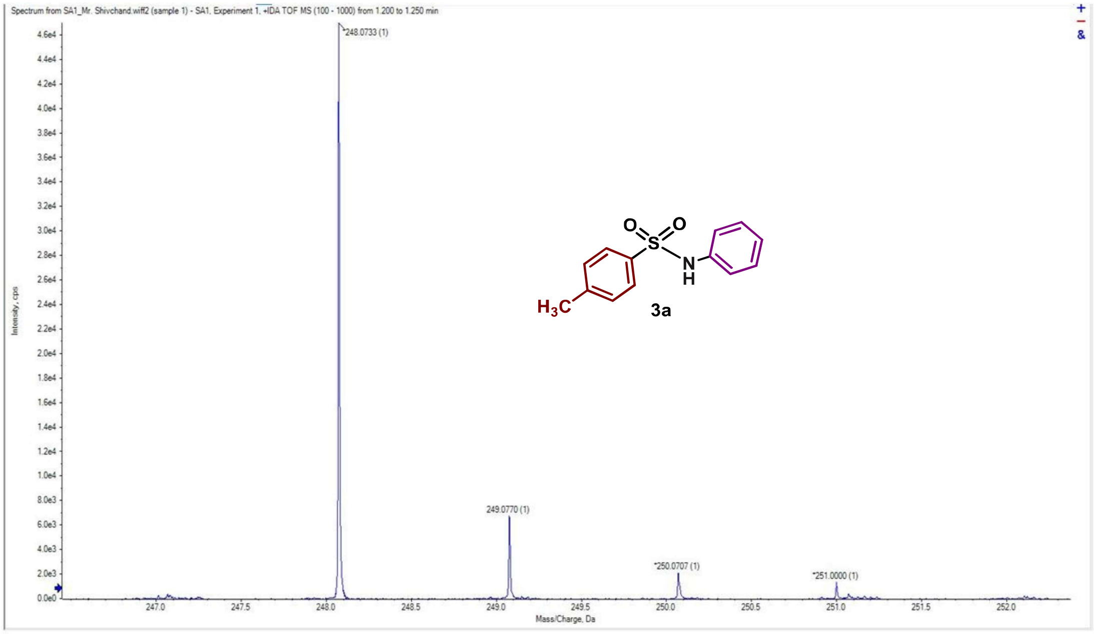


Figure 4.17 HRMS spectra of **3a**

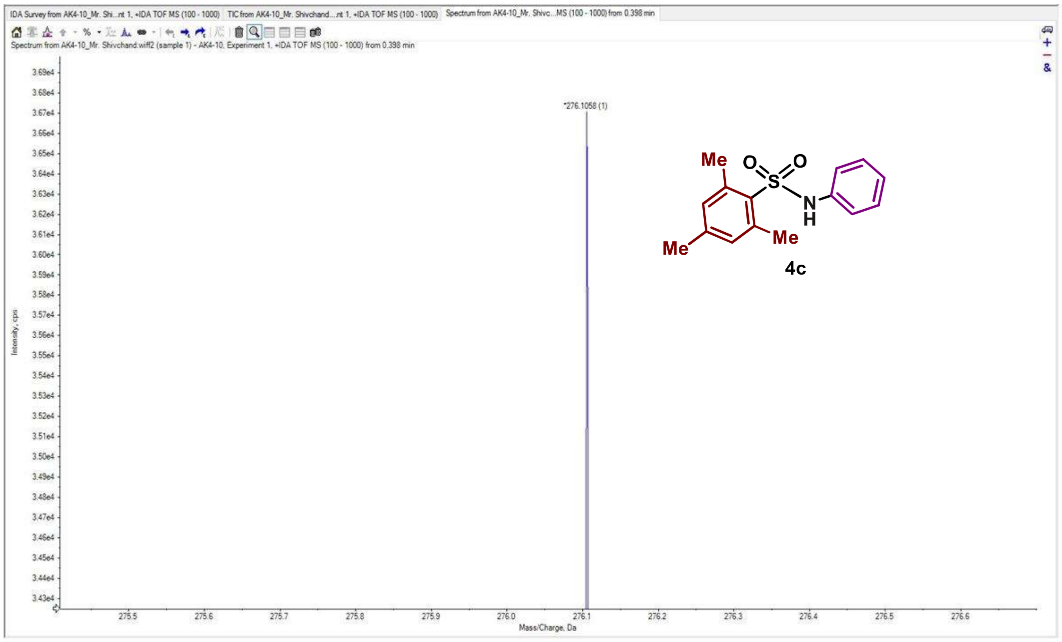


Figure 4.18 HRMS spectra of **4c**

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