Chapter-3

Photo-triggered Synthesis of Sulfonamides in a Sustainable Solvent via Electron Donor-Acceptor Complex

3.1 Introduction

Recently, the development of environmentally friendly and ecological procedures based on the principle of Green Chemistry has been done due to concerns about pollutants and dangerous waste produced in chemical laboratories and industries. Visible-light [1-11] photocatalysis as a renewable, clean, and abundant energy source has attracted substantial consideration from chemists and industrialists since it requires everlasting sunlight or cheap and abundant domestic lamps for irradiation rather than the costly and unsafe thermal activation conventional method. The exploitation of photocatalysts for the visible light-initiated reaction has many advantages even though it suffers from various shortcomings, like the use of expensive and complex metal catalysts and the generation of waste material. Hence there is a demand for developing a catalyst-free approach for visible light-initiated reactions [12-16]. Thus, the visible light-initiated reaction is an unpolluted, cost-effective, and environmentally friendly alternative method for organic synthesis [17-23].

Sulfonamides [24-33] are a significant compound in synthetic and medicinal chemistry with various biological activities [34-36]. They also show various therapeutic and agricultural applications such as antibacterial [37], antiviral [38], antiprotozoal, antifungal, antitumor, anti-inflammatory, anti-HIV agents, herbicides, pesticides, and surfactants [39] (Figure 3.1). Moreover, Sulfa drugs are the oldest prepared antimicrobial agent [40, 41], and even now, they have been broadly used to treat various microbial infections. Medical treatment through

sulfonamides has recuperated sureness with a mixture of trimethoprim and sulfamethoxazole to treat urinary tract bacterial infections.

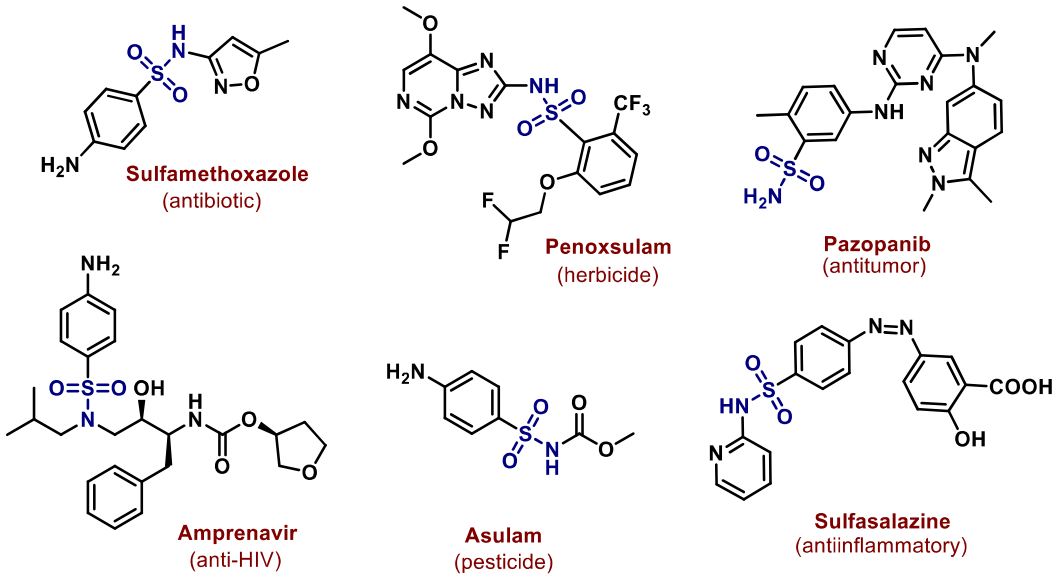
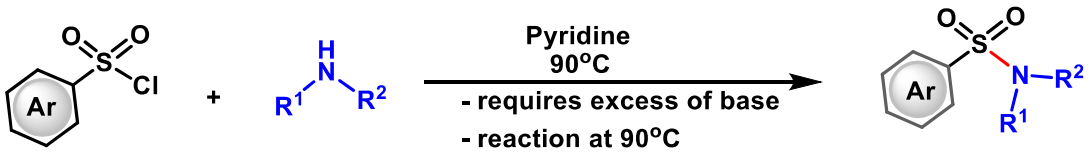
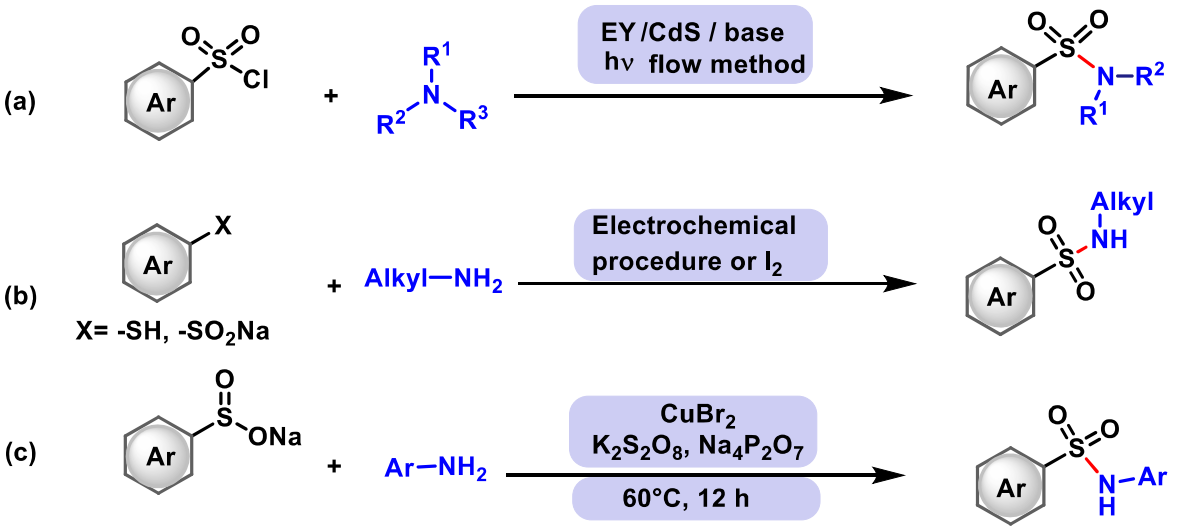


Figure 3.1 Examples of biologically relevant sulfonamides

Nowadays, they are extensively used as antimicrobial agents [42], mainly due to their non-toxic, inexpensive, and excellent activity of bacterial infection. Subsequently, sulfonamides have been widened as antimicrobial agents to anticancer agents [43], antiglaucoma agents, cyclooxygenase-2 and lipoxygenase inhibitors, gamma-secretase, hypoglycemic agents, and anticonvulsant agents [44-46].



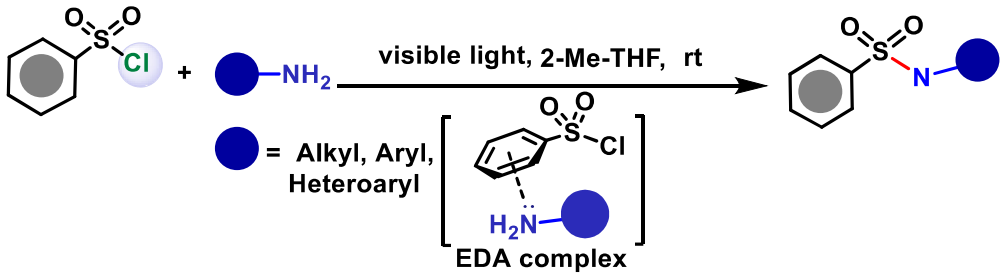
Scheme 3.1 Conventional method



Scheme 3.2 Some recent previous methods for the synthesis of sulfonamide

Attributable to their pronounced significance, many powerful methodologies have been reported to synthesize sulfonamide derivatives [47-54]. However, the main drawbacks of sulfonamide synthesis include the use of organic amine bases, high temperatures, inorganic salts, hazardous/explosive compounds, the creation of toxic by-products, and thermal conditions, which are occasionally unavoidable in reaction conditions. Although some methodologies have been reported to reduce hazards by selecting sustainable conditions [50, 51, 55-58] such as photochemical synthesis and the use of water as a solvent, there are still some limitations, such as the use of photocatalysts, and base as waste generation, long reaction times, and limited functional group compatibilities. Thus, it is crucial to develop a green, efficient, eco-friendly approach for synthesizing sulfonamide via readily available sulfonyl chloride, which is biocompatible, more reactive, relatively cheap, and easy to the experimental procedure. As a continuous work in the field of green synthetic chemistry [59-

64], wherein we would like to report a facile, catalyst-free, and visible light-mediated approach for synthesizing sulfonamides by electron donor-acceptor (EDA) complexes as a catalyst-free strategy [65]. To the best of my knowledge, there have been no reports to date referring to the synthesis of sulfonamide using *p*-toluene sulfonyl chloride and a variety of amines in 2-Me-THF as green sustainable solvents under blue LED at room temperature (Scheme 3.3).



Scheme 3.3 A catalyst-/additive-free photocatalytic method

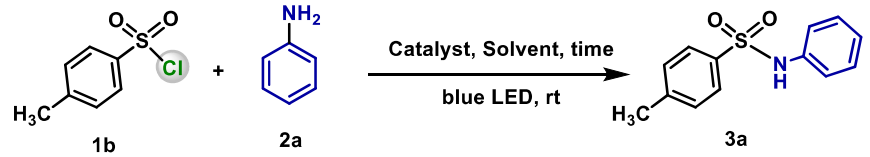
3.2 Results and discussion

Initially, we commenced our strategy by synthesizing 4-methyl-N-phenyl benzene sulfonamide **3a** with aniline **2a**, *p*-toluene sulfonyl chloride **1b**, with eosin Y as photocatalyst in MeCN solvent under blue LED irradiation. To our delight, desired product **3a** was obtained in 75% isolated yield in 6 hours. IR, ^{1}H NMR, and ^{13}C NMR spectra identified the structure of product 3a. Inspired by this result, aniline and *p*-toluene sulfonyl chloride are selected as the model reaction to optimize reaction conditions such as photoredox catalysts, solvents, time, and blue LED light (Table 3.1). The excellent yield of the product with eosin Y encouraged us to optimize various photoredox catalysts such as Rose Bengal and Acridine

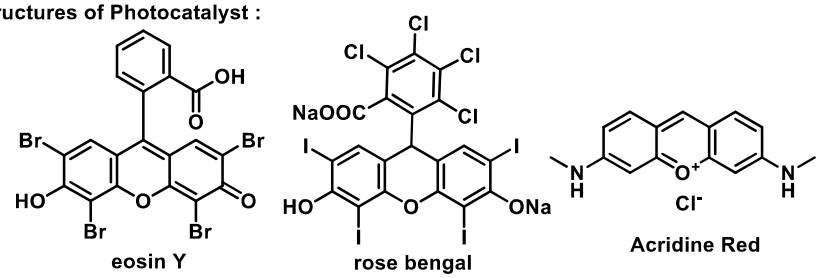
Red. Still, they provide only 41% and 46%, respectively (Table 3.1, entries 2&3). This result revealed that eosin Y is a more efficient photoredox catalyst delivering a 75% yield (Table 3.1, entry 1). Furthermore, we tested various solvents such as DCM, DMF, and DMSO with eosin Y, but they did not provide the target product effectively (Table 3.1, entries 4-6). Then, we tried the reaction in a catalyst-free condition with MeCN solvent and, surprisingly 82% yield of the product was obtained (Table 3.1, Entry 7). Next, some green solvents such as 2-Me-THF, dimethyl carbonate (DMC), water, and ethanol were examined to improve the reaction efficiency. Among them, biomass-derived solvent 2-Me-THF was found to be a solvent of choice, providing the expected product in 86% yield (Table 3.1, entries 8-11). After that, the reaction in the dark gave no product, demonstrating the significance of light irradiation (Table 3.1, entry 12).

Subsequently, various light sources were investigated, and a more satisfactory yield was not obtained (Table 3.1 entries 13 and 14). Further, the reaction was carried out by heating at 60˚C, and the yield of the product was still found to be 78 % (Table 3.1, entry 15). Also, the reaction was tried without solvent, and no product was obtained (Table 3.1 entries 16). Finally, we prolonged the reaction time, and the yield of the target product was still 86% (Table 3.1 entry 17). After rigorous experiments, the optimal condition was established as follows: **1b** (0.5 mmol), **2a** (0.5 mmol), 2-Me-THF (5 ml) at room temperature for 6 h, and irradiated under blue LED.

Table 3.1 Optimization of the Reaction Conditions[a]



Structures of Photocatalyst :



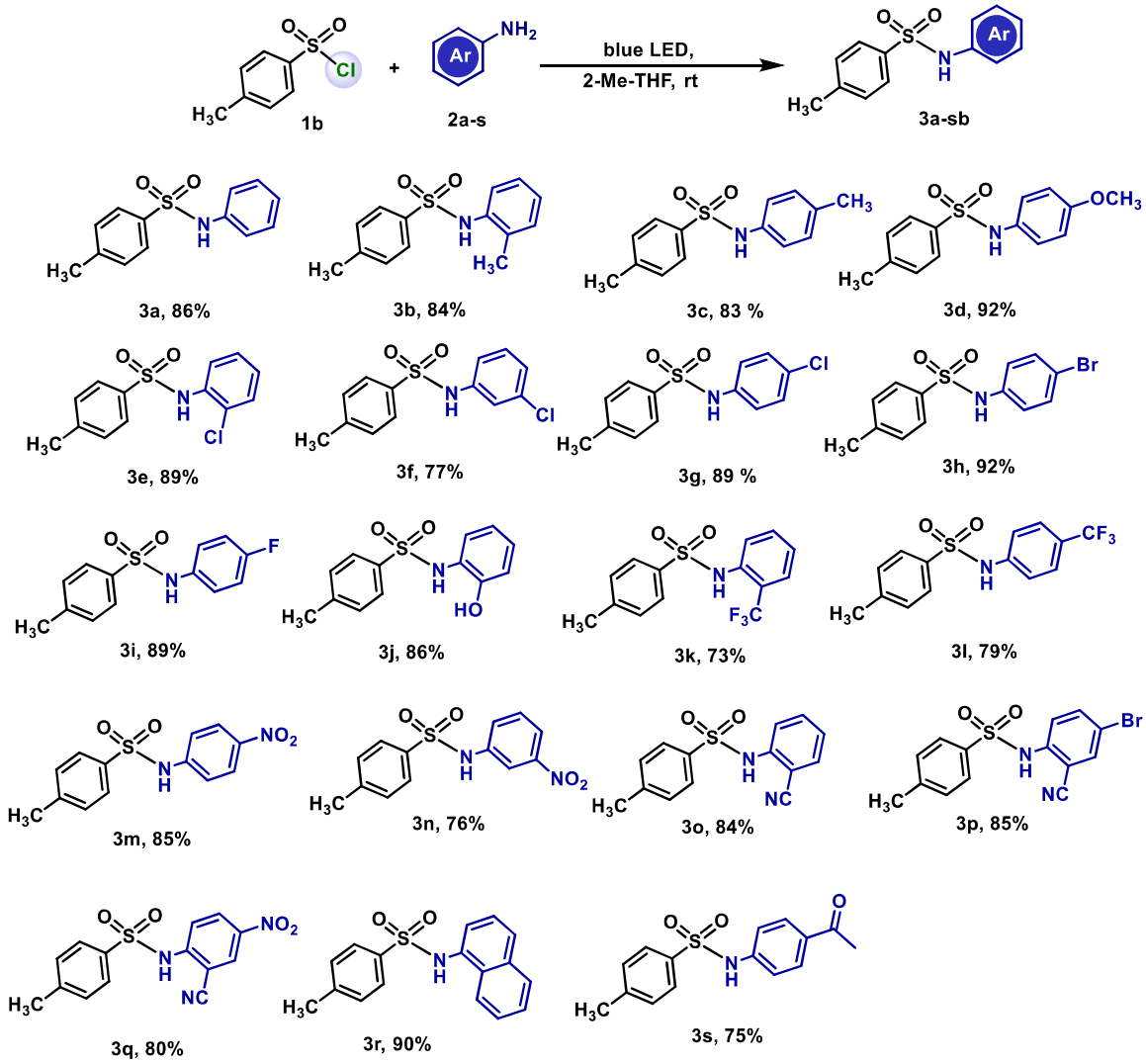
Entry	Catalyst	Solvent	Yield[b] %
1	eosin Y	MeCN	75
2	rose bengal	MeCN	41
3	acridine red	MeCN	46
4	eosin Y	DCM	29
5	eosin Y	DMF	trace
6	eosin Y	DMSO	trace
7	–	MeCN	82
8	–	2-Me-THF	86
9	–	DMC	trace
10	–	H_2O	nd
11	–	Ethanol	nd
12[c]	–	2-Me-THF	nr
13[d]	–	2-Me-THF	25
14[e]	–	2-Me-THF	70
15[f]	–	2-Me-THF	78
16	–	none	nr
17[g]	–	2-Me-THF	86

[a]Reaction condition: **1b** (0.25mmol), **2a** (0.25 mmol) , solvents (8 mL) at room temperature, for 6 h, and irradiate under blue LED. [b] Isolated yield, [c] In the dark, [d] A green LED, [e] 20 W CFL, [f] reaction temperature was found to be 60˚C, [g] reaction for 8 h. (nr = no reaction, nd = not detected)

After optimizing reaction conditions, we focused on studying the reaction's scope and limitations concerning aromatic amines (Table 3.2). Firstly, anilines bearing different substituents were tested. Generally, aniline containing both electron-rich and neutral substituents provided high yields of sulfonamide products (Table 3.2, **3a-d**). At the same time, halo-substituted anilines provided excellent results (Table 3.2, **3e-h**). The halo-substituted group in sulfonamide can provide good reactivity sites for further synthetic transformations. Also, this green approach works well for electron-withdrawing substitutions (Table 3.2 **3i-k**). All secondary aromatic amine and aliphatic amines showed excellent reactivity and gave the target product moderate to good yield (Table 3.3, **3aa-ae**). After that, we looked at the many types of heterocyclic amines (Table 3.3). Some heterocyclic amine derivatives (**2af, 2ag, 2ah, 2ai, and 2aj**) interacted with sulphonyl chloride to produce the corresponding products (**3af, 3ag, 3ah, 3ai, and 3aj**) in good yield (70-77%). Regrettably, some heterocyclic amines **2ak** and **2al** do not provide the product. It's unclear why these substrates are incompatible.

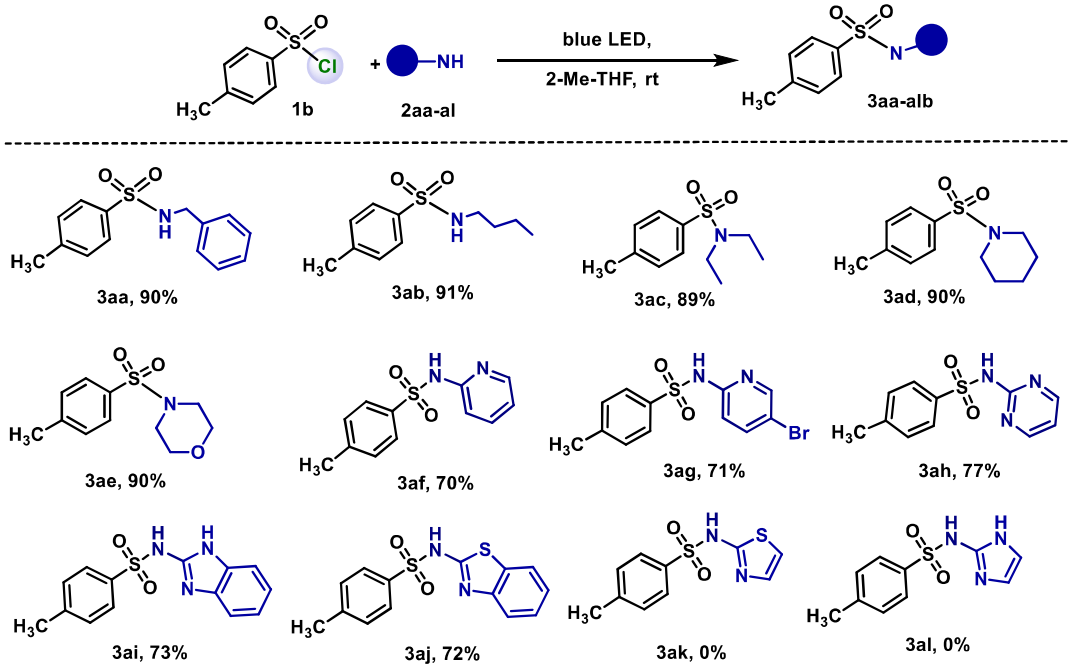
After confirming this methodology's applicability for a broad range of amines, different sulfonyl chloride (**1a–1h**) were assessed. Sulfonyl chloride bearing common functionalities, such as chloride, bromide, nitro, and carbonyl groups, reacted smoothly with aniline **1a** under visible-light irradiation, and sulfonamide **4a–4h** were produced in isolated yields of 84%–92%. (Table 3.4). Due to this wide range of functional group tolerability, this is a universal method for forming sulfonamide in green, catalyst-free, base-free conditions at room temperature.

Table 3.2 Substrate scope of anilines[a]



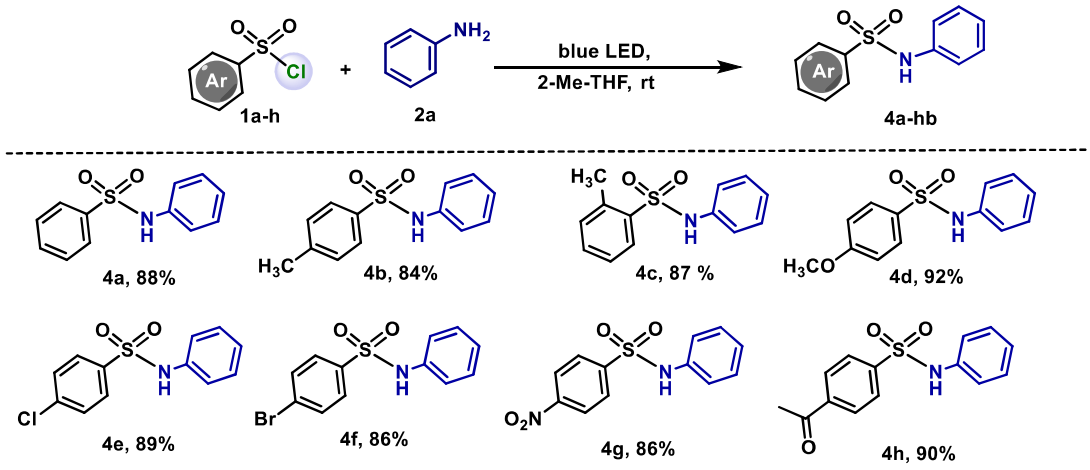
[a]Reaction condition: **1b** (0.25 mmol), **2** (0.25 mmol), solvents (8 mL) at room temperature, for 6 h, and irradiated under blue LED. [b] Isolated yield

Table 3.3 Substrate scope of some primary, secondary and heterocyclic amines[a]



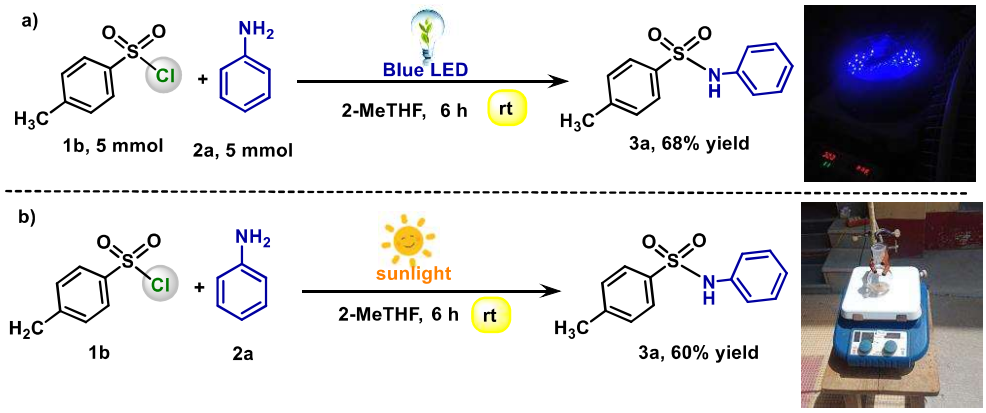
[a]Reaction condition: **1b** (0.25 mmol), **2** (0.25 mmol) , solvents (8 mL) at room temperature, for 6 h, and irradiate under blue LED. [b] Isolated yield.

Table 3.4: Substrate scope of sulfonyl chloride[a]



[a]Reaction condition: **1** (0.25 mmol), **2a** (0.25 mmol) , solvents (8 mL) at room temperature, for 6 h, and irradiate under blue LED. [b] Isolated yield.

To examine the viability of this visible-light-promoted synthesis of sulfonamides, a gram-scale reaction was charged with **1b** (5 mmol) and **2a** (5 mmol), for the synthesis of desired product **3a** under standard conditions (Scheme 3.4a). The reaction proceeds smoothly with a satisfactory yield of 68%. Gratifyingly, the chosen product **3a** was also obtained with a yield of 60% when the reaction was carried out under sunlight irradiation for 6 hours. (Scheme 3.4b). The results showed that sunlight could be used as an efficient and renewable light source in this strategy.

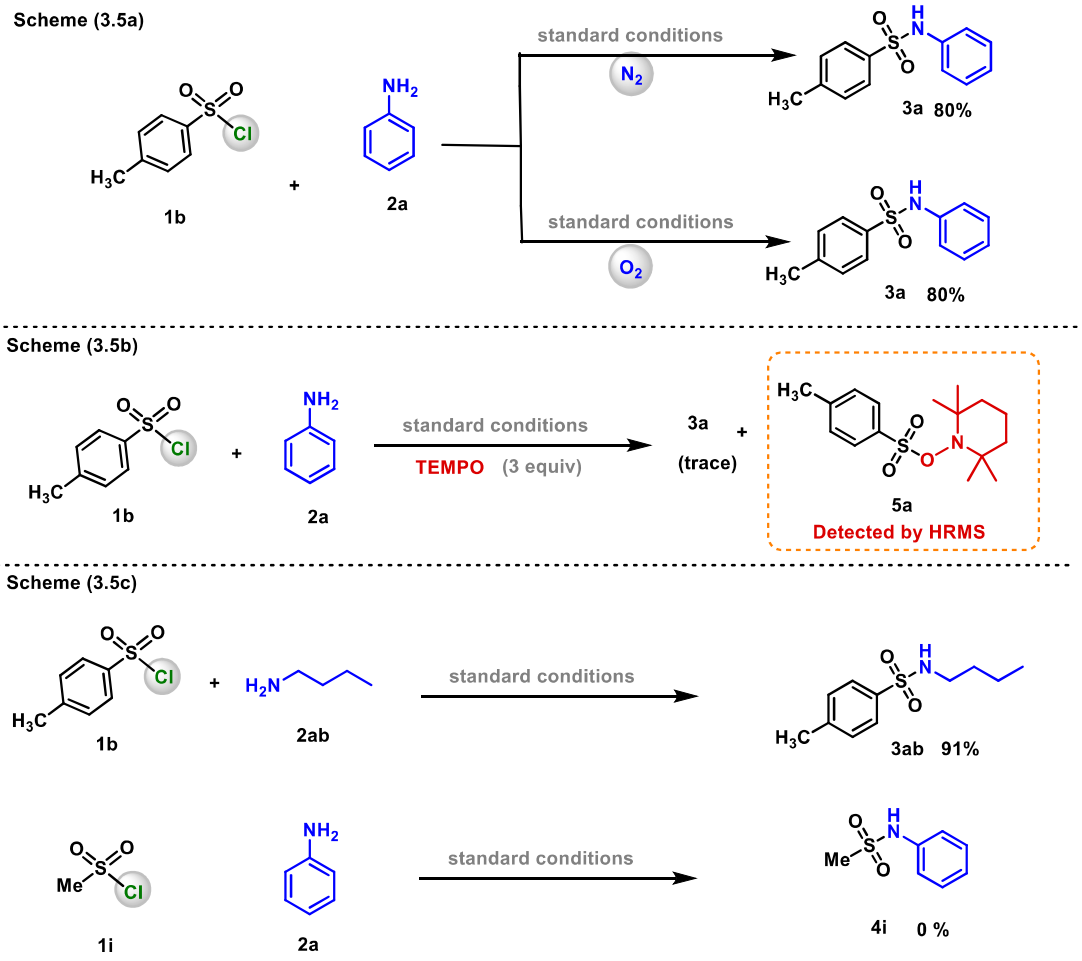


Scheme 3.4 The gram-scale reaction and the reaction under sunlight

3.3 Control experiment

To probe the reaction mechanism, several control experiments were carried out. Firstly, the UV-visible absorption spectra of substrates **1b** and **2a** revealed that **1b** could absorb light with wavelengths less than 280 nm, while **2a** could absorb light with wavelengths between 290 and 345 nm. The combined spectrum of **1b** and **2a** showed that adding **2a** increased the absorbance and that a red shift (bathochromic shift) was seen, suggesting an electron-donor-acceptor (EDA) complex developing between **1b** and **2a** (Figure 3.2) [65].

Following that, several Stern-Volmer experiments were carried out, and the results showed that photo-excited **2a** was effectively quenched by **1b**. The quenching effect becomes more observable as the concentration of **1b** increases, as shown in Figure 3.4. The light on/off experiments proved the critical role of blue light (Figure 3.6) and excluded the nucleophile reaction pathway. When the reaction was carried out under an N_2 atmosphere and an O_2 atmosphere (balloon), 80% of the intended product **3a** was obtained; this reveals that the O_2 atmosphere was not essential for the reaction (Scheme 3.5a). Next, we believe that our procedure follows a radical pathway. As a result, radical scavenging experiments were carried out to support our hypothesis. In the presence of 2, 2, 6, 6-tetramethylpiperidine-1-oxyl (TEMPO), the reaction was suppressed, and no desired product **3a** was formed as expected, implying that the reaction proceeded via a radical mechanism (Scheme 3.5b). High-resolution mass spectroscopy (HRMS) findings confirmed that the trapped adduct **5a** was formed, indicating that the sulfonyl radical was generated as a key intermediate in this reaction. We also tried the reaction with aliphatic amine and aliphatic sulfonyl chloride. We got the product with amine but not with aliphatic sulfonyl chloride because the latter could not produce the EDA complex (Scheme 3.5c).



Scheme 3.5 Control experiments

3.3.1 UV-Vis absorption experiment

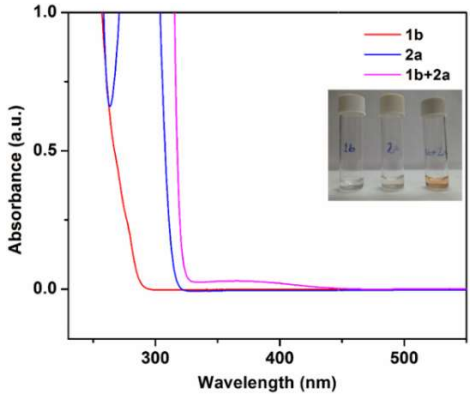


Figure 3.2 Absorption spectra of **1b**, **2a**, and mixture of **1b+2a**. (Dissolved in MeCN)

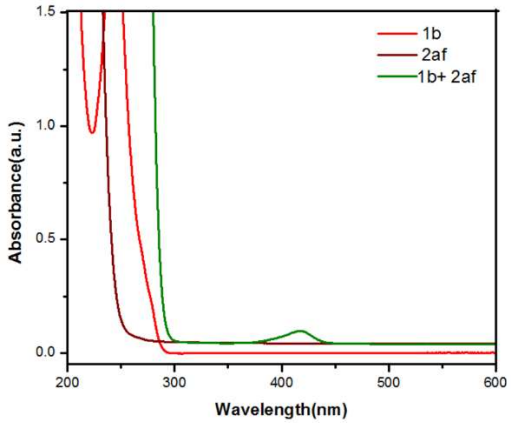


Figure 3.2a Absorption spectra of **1b, 2af**, and the mixture of **1b+2af**. (Dissolved in MeCN).

3.3.2 Stern-Volmer Fluorescence quenching studies

3.3.2.1 Emission spectra

The fluorescence emission intensities were recorded on a PerkinElmer LS 55 Fluorescence spectrometer 1.0 mM stock solution of 1b and 2a was prepared and diluted with MeCN. The solution was placed in a screw-top 1.0 cm quartz cuvette and emission spectra of the sample were collected. The excitation wavelength was fixed at 265 nm and 345 nm respectively.

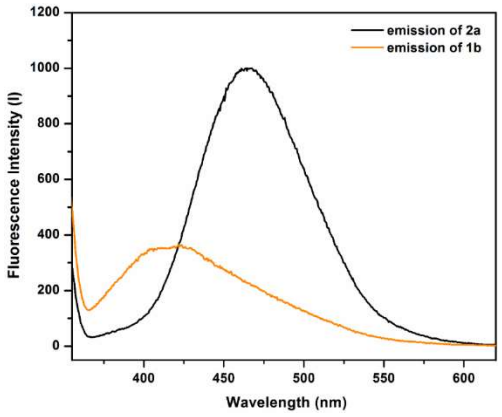


Figure 3.3. Emission spectra of the **2a** and **1b**

3.3.2.2 Stern-Volmer fluorescence quenching experiments

In a typical experiment, the solution of **2a** in MeCN was added to the appropriate amount of TsCl **1b**. The addition of **1b** was repeated six consecutive times. After each addition, emission spectra were recorded. All the solutions were excited at 345 nm; the emission was acquired from 0 nm to 600 nm. The result shown in figure 3.4a indicates that **1b** quenches the excited state of **2a** and its emission.

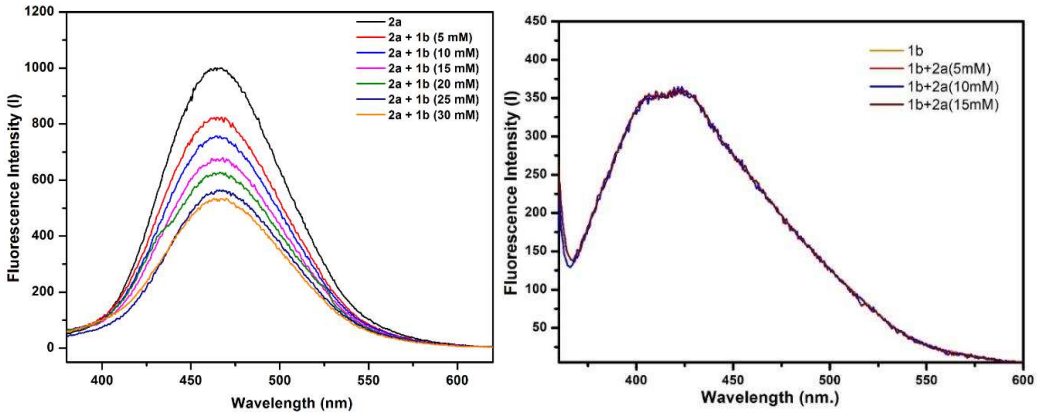


Figure 3.4. (a) The fluorescence emission spectra of **2a** with different concentrations of quencher **1b**. **(b)**The fluorescence emission spectra of **1b** with different concentration of quencher **2a**.

The Stern-Volmer plot (shown in Figure 3.5) indicated a linear relationship between the concentration of 1 and the ratio I_0/I. The Stern-Volmer constant K_{SV} was calculated using **equation 1**.

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

Where, I_0 = the intensity of fluorescence of 2a, without quencher 1b

I = the intensity of fluorescence of 2a, with quencher 1b

[Q] = concentration of the quencher 1b

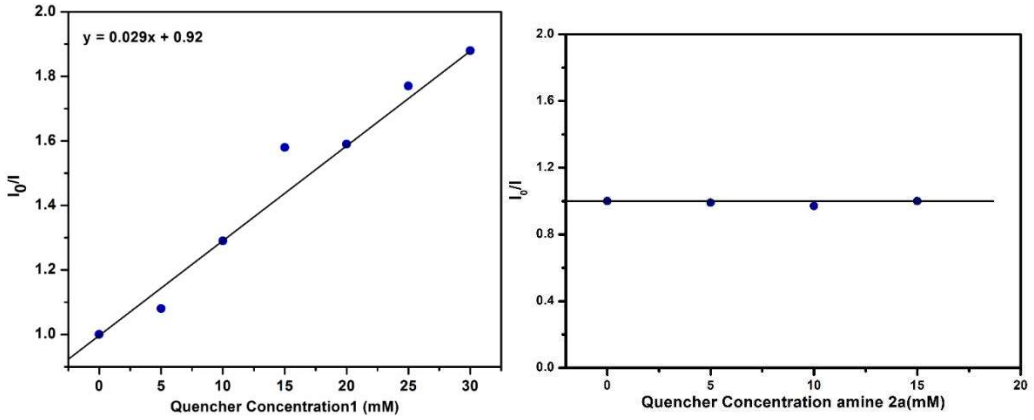


Figure 3.5. Stern-Volmer fluorescence quenching plot

3.3.3 ON/OFF experiments

The reaction between **1b** and **2a** was conducted under the standard conditions on a 0.25 mmol scale. The reaction mixture was subjected to sequential periods of stirring under visible light irradiation (blue LED) followed by stirring in the absence of light. At each time point, one reaction system was suspended, which was then purified with column chromatography on silica gel (Ethyl acetate: hexane) to give the corresponding products **3a**. The yield of **3a** was measured by the weight of the product.

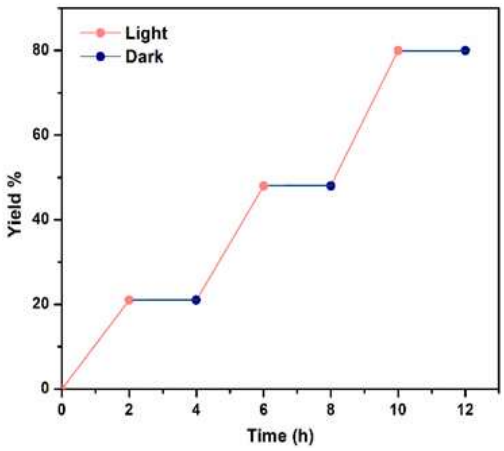
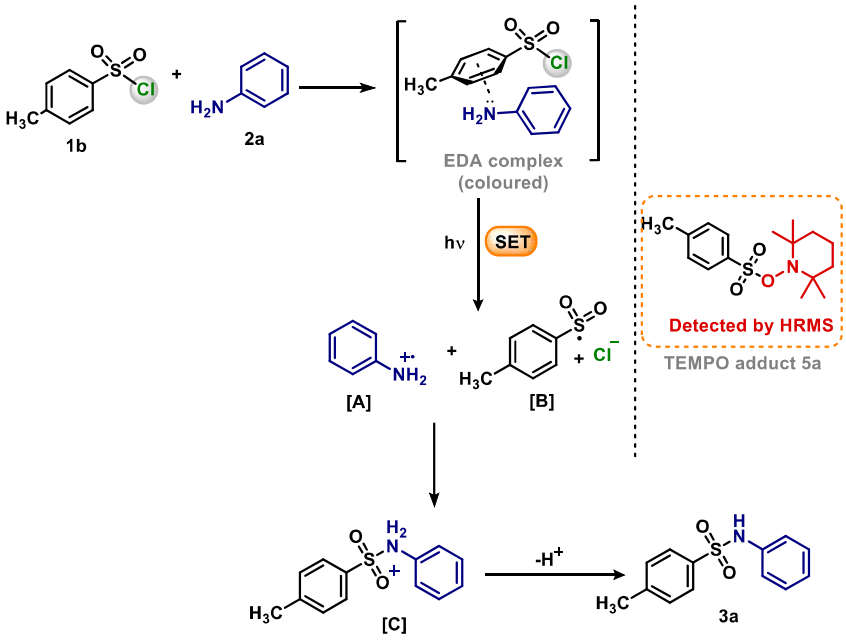


Figure 3.6 ON-OFF experiments

3.4 Proposed mechanism

Based on literature precedents [20, 66-69] and experimental results, we proposed a new plausible mechanism as depicted in scheme 5. Initially, an EDA complex was formed between electron-rich amine **(2a)** and electron-deficient sulfonyl chloride (**1b)** [70-72]. EDA complex undergoes a visible-light-induced single electron transfer (SET) process and generates radical cation **A**, *p*-toluene sulfonyl radical [68] **B**, releasing a chloride ion. The recombination of radical cation **A** and the sulfonyl radical **B** provided a cationic adduct **C**, which led to product **3a** after deprotonation.



Scheme 3.6 Plausible mechanism

3.5 Conclusions

In conclusion, the synthesis of sulfonamide has been developed at room temperature without external photocatalyst, base, and transition metals using green 2-MeTHF as the only solvent.

This new approach is recognized as an environmentally friendly and efficient visible light-triggered and EDA complex-promoted sulfonation of amine. This reaction could accomplish a gram-scale synthesis of sulfonamide using a simple reaction setup and validated for sunlight. Furthermore, the reaction has many advantages, including readily available raw ingredients, straightforward operation, and functional group compatibility.

3.6 Experimental Setup

Reactions were performed using a blue LED strip as the light source. A reaction tube was fixed at 5-6 cm from a commercial 80 cm blue LED strip, while a fan was used to cool down the reactor (the reaction temperature within the reaction vessel was measured to be between 30-35 ºC) shown in Figure 3.7.

3.6.1 The visible light irradiation setup.

Figure 3.7 A reaction setup showing the reaction tube was fixed at 5-6 cm from the blue LED stripped (80 cm). [Personal photo made by one of the authors- Arsala Kamal]

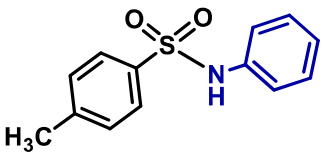
3.7 Experimental procedures

3.7.1 General procedure for the preparation of compound 3a-3s & 3aa-3aj

A 10 mL reaction tube equipped with a magnetic stirring bar was charged with *p*-toluene sulfonyl chlorides **1b** (0.25 mmol), amine derivatives **2** (0.25 mmol), and solvent 2-MeTHF (8 mL). The mixture was then stirred at room temperature and irradiated with a (80 cm) blue LEDs lights strips for 6 h. After completion of the reaction, the reaction mixture was extracted with ethyl acetate (3**x**50 mL). The combined organic phases were dried over anhydrous Na_2SO_4, and then the solvent was removed under a vacuum. The residue was purified by column chromatography on neutral silica gel (ethyl acetate: hexane)

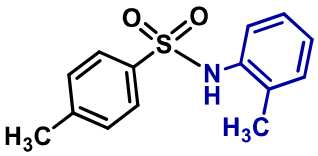
3.8 Characterization data of compounds

4-Methyl-N-phenylbenzenesulfonamide (3a)



86% yield. Pale green solid. m.p.: 104-105 °C. ^{1}H NMR (500 MHz, CDCl3) δ 7.69 (d, J = 8.2 Hz, 2H), 7.30 – 7.21 (m, 3H), 7.17 – 7.05 (m, 4H), 6.97 (s, 1H), 2.40 (s, 3H). ^{13}C NMR (126 MHz, CDCl3) δ 143.91, 136.51, 136.04, 129.67, 129.33, 127.28, 125.34, 121.58, 21.56. HRMS (ESI) m/z: [M+H] + calculated for $C_{13}H_{14}NO_2S$ 248.0745; found: 248.0733

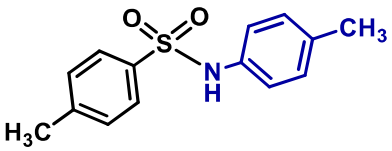
4-Methyl-N-(o-tolyl)benzenesulfonamide (3b)



84% yield. Pink solid. m.p.: 106-107 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 7.8 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.18 – 7.13 (m, 1H), 7.12 – 7.07 (m, 2H), 6.41 (s, 1H), 2.41 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.80, 136.77, 134.51,

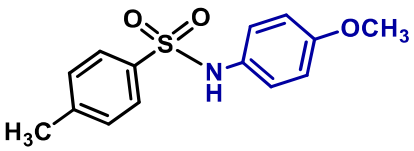
131.26, 130.77, 129.60, 127.18, 126.97, 126.20, 124.30, 21.54, 17.54. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{16}NO_2S$ 262.0901; found: 263.0917

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



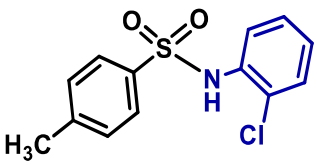
83% yield. White solid. m.p.: 114-116 °C. ^{1}H NMR (500 MHz, DMSO) δ 7.50 (d, *J* = 6.7 Hz, 2H), 7.34 (d, *J* = 6.4 Hz, 2H), 7.33 – 7.28 (m, 2H), 7.13 (d, *J* = 7.8 Hz, 2H), 2.32 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 138.40, 132.03, 131.84, 131.21, 128.61, 127.6, 125.93, 123.47, 21.25, 17.25. 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)



92% yield. Pale pink solid. m.p.: 115-117 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, J = 8.2 Hz, 2H), 7.34 (d, J = 8.1 Hz, 2H), 7.13 (d, J = 8.6 Hz, 2H), 6.82 (d, J = 8.6 Hz, 2H), 4.61 (s, 1H), 3.80 (s, 3H), 2.46 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 159.34, 143.52, 136.87, 129.76, 129.29, 128.24, 127.21, 114.08, 55.31, 21.57. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{16}NO_3S$ 278.0850; found: 278.0852.

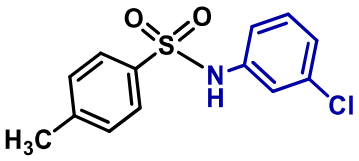
N-(2-Chlorophenyl)-4-methylbenzenesulfonamide (3e)



89% yield. White solid. m.p.: 102-104 °C. ^{1}H NMR (500 MHz, DMSO) δ 7.51 (d, *J* = 7.9 Hz, 2H), 7.38 (d, *J* = 7.8 Hz, 1H), 7.33 – 7.27 (m, 1H), 7.15 (d, *J* = 7.9 Hz, 2H), 6.82 (d, *J* = 8.4 Hz, 1H),

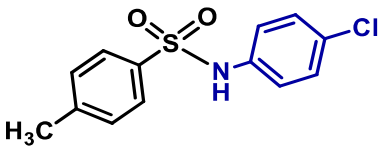
6.61 (dd, J = 10.7, 4.3 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 151.32, 145.08, 138.81, 134.47, 132.95, 128.76, 125.96, 118.51, 116.93, 116.06, 21.25. HRMS (ESI) m/z: [M+H] + calculated for $C_{13}H_{13}NO_2SCl$ 282.0355; found: 282.0358

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



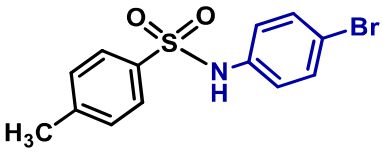
77% yield. White solid. m.p.: 114-115 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, J = 8.3 Hz, 2H), 7.28 (d, J = 8.2 Hz, 2H), 7.18 (d, J = 8.0 Hz, 1H), 7.14 (t, J = 2.0 Hz, 1H), 7.10 – 7.06 (m, 1H), 7.00 (d, J = 8.0 Hz, 1H), 2.41 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 144.32, 137.86, 135.72, 134.92, 130.34, 129.85, 127.27, 125.23, 120.95, 118.94, 21.59. HRMS (ESI) m/z: [M+H] + calculated for $C_{13}H_{13}NO_2SCl$ 282.0355; found: 282.0362

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



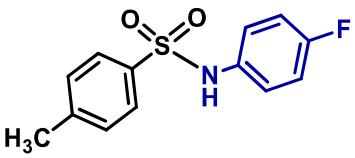
89% yield. White solid. m.p.: 120-122 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, J = 8.3 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 7.21 – 7.18 (m, 2H), 7.06 (d, J = 8.8 Hz, 2H), 2.40 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.23, 135.61, 135.22, 130.77, 129.82, 129.40, 127.29, 122.79, 21.57.HRMS (ESI) m/z: [M+H] + calculated for $C_{13}H_{13}NO_2SCl$ 282.0355; found: 282.0358

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



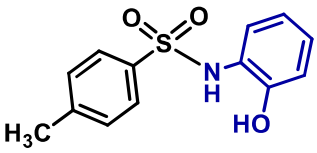
92% yield. White solid. m.p.: 140-145°C. ^{1}H NMR (500 MHz, CDCl3) δ 7.69 (d, J = 8.3 Hz, 18H), 7.28 (s, 3H), 7.26 (d, J = 8.0 Hz, 19H), 7.21 (d, J = 8.8 Hz, 16H), 7.05 (d, J = 8.8 Hz, 18H), 2.40 (s, 26H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.23, 135.62, 135.16, 130.84, 129.81, 129.42, 127.28, 122.86, 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)



89% yield. White solid. m.p.: 98-99 °C. ^{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 (dd, J = 5.3, 3.4 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, CDCl3) δ -116.24 – -116.48. HRMS (ESI) m/z: [M+H] + calculated for $C_{13}H_{13}NO_2SF$ 266.0651; found: 266.0654

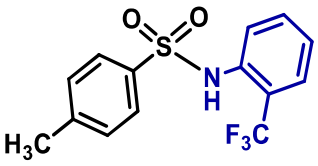
N-(2-Hydroxyphenyl)-4-methylbenzenesulfonamide (3j)



86% yield. Gray solid. m.p.: 137-138 °C. ^{1}H NMR (500 MHz, DMSO) δ 10.69 (s, 1H), 9.72 (s, 1H), 7.50 (d, *J* = 8.1 Hz, 2H), 7.31 – 7.21 (m, 2H), 7.13 (d, *J* = 7.8 Hz, 2H), 7.02 (dd, *J* = 8.1, 1.2 Hz, 1H), 6.89 (td, *J* = 7.7, 1.3 Hz, 1H), 2.30 (s, 2H). ^{13}C NMR (126 MHz, DMSO) δ 151.14 (s), 145.88 (s), 138.27 (s), 129.85 (s), 128.57 (s), 125.95 (s), 124.49 (s), 119.94 (s),

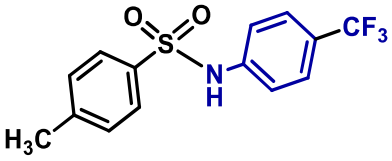
119.34 (s), 116.62 (s), 21.24 (s). HRMS (ESI) m/z: [M+H] + calculated for $C_{13}H_{14}NO_3S$ 264.0694; found: 264.0698

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



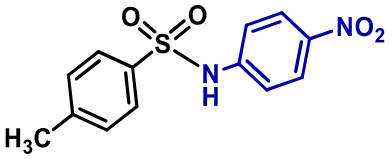
73% yield. White solid. m.p.: 124-125 °C. ^{1}H NMR (500 MHz, DMSO) δ 7.61 (t, J = 7.9 Hz, 1H), 7.51 (dt, J = 14.9, 7.4 Hz, 4H), 7.44 (d, J = 8.0 Hz, 1H), 7.13 (d, J = 7.9 Hz, 2H), 7.01 – 6.87 (m, 1H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, CDCl3) δ 144.3, 137.85, 135.74, 134.92, 130.34, 129.85, 127.27, 125.24, 120.98, 118.97, 21.59. ^{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 (3l)



79% yield. Cream solid. m.p.: 144-145 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (t, J = 8.2 Hz, 2H), 7.51 – 7.46 (m, 2H), 7.30 – 7.26 (m, 2H), 7.23 (d, J = 7.0 Hz, 2H), 2.40 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 144.57, 140.03, 135.69, 129.96, 127.27, 126.61, 125.01, 122.85, 119.60, 21.54. ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.23 (s).HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{13}NO_2SF_3$ 316.0619; found: 315.0620

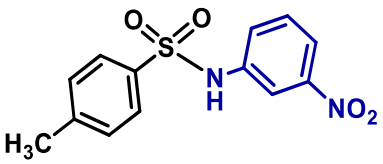
4-Methyl-N-(4-nitrophenyl)benzenesulfonamide (3m)



85% yield. Pale gray solid. m.p.: 180-182 °C. ^{1}H NMR (500 MHz, DMSO) δ 7.53 – 7.47 (m, 4H), 7.43 – 7.38 (m, 1H),

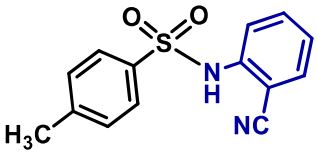
7.36 (dd, J = 5.8, 3.8 Hz, 2H), 7.14 (d, J = 7.8 Hz, 2H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 156.08, 145.72, 138.40, 136.14, 128.63, 126.86, 125.97, 112.93, 21.26. HRMS (ESI) m/z: [M+H] + calculated for $C_{13}H_{13}N_2O_4S$ 293.0596; found: 293.0599

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



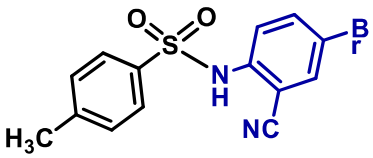
76% yield. Pale yellow solid. m.p.: 177-180 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 2H), 7.17 (s, 1H), 7.13 (d, *J* = 2.0 Hz, 1H), 7.08 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.00 (dd, *J* = 8.1, 1.2 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.31, 137.85, 135.74, 134.92, 130.34, 129.85, 127.27, 125.24, 120.98, 118.97, 21.59. HRMS (ESI) m/z: [M+H] + calculated for $C_{13}H_{13}N_2O_4S$ 293.0596; found: 293.0597.

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



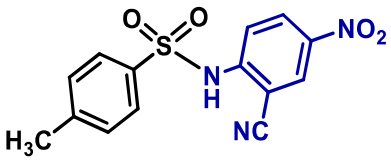
84% yield. White solid. m.p.: 172-173 °C. ^{1}H NMR (500 MHz, DMSO) δ 7.50 (d, *J* = 8.1 Hz, 2H), 7.39 – 7.35 (m, 1H), 7.30 (ddd, *J* = 8.7, 7.2, 1.6 Hz, 1H), 7.14 (d, *J* = 7.8 Hz, 2H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.60 (ddd, *J* = 8.2, 7.3, 1.0 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 151.84, 145.63, 138.45, 134.44, 132.89, 128.63, 125.97, 118.55, 116.56, 115.77, 94.05, 21.24. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{13}N_2O_2S$ 273.0697; found: 273.0699

N-(4-Bromo-2-cyanophenyl)-4-methylbenzenesulfonamide (3p)



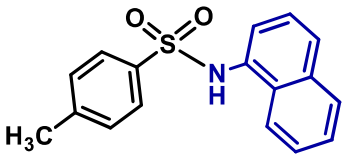
85% yield. White solid. m.p.: 180-182 °C. ^{1}H NMR (500 MHz, DMSO) δ 7.49 (dd, *J* = 7.6, 5.3 Hz, 3H), 7.32 (dd, *J* = 9.0, 2.6 Hz, 1H), 7.14 (d, *J* = 7.8 Hz, 2H), 6.80 (d, *J* = 9.0 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 151.11, 145.59, 138.48, 134.54, 131.56, 128.64, 125.96, 119.04, 117.53, 117.33, 94.85, 21.24. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{12}N_2O_2SBr$ 350.9802; found: 273.072

N-(2-Cyano-4-nitrophenyl)-4-methylbenzenesulfonamide (3q)



80% yield. Yellow solid. m.p.: 170-172 °C. ^{1}H NMR (500 MHz, DMSO) δ 7.50 (d, *J* = 7.9 Hz, 3H), 7.32 (dd, *J* = 9.0, 2.6 Hz, 1H), 7.13 (d, *J* = 7.8 Hz, 2H), 6.80 (d, *J* = 9.0 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 151.13 (s), 145.62 (s), 138.45 (s), 134.55 (s), 131.58 (s), 128.64 (s), 125.97 (s), 118.99 (s), 117.52 (s), 117.35 (s), 94.82 (s), 21.26 (s). HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{12}N_3O_4S$ 318.0548; found: 318.0555

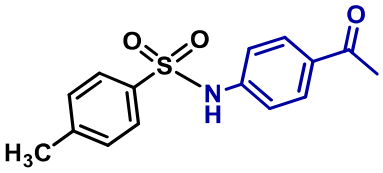
4-Methyl-N-(naphthalen-1-yl)benzenesulfonamide (3r)



90% yield. Pinkish gray solid. m.p.: 109-111 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 17.7, 8.3 Hz, 5H), 7.58 (s, 1H), 7.44 (dd, *J* = 14.3, 7.5 Hz, 2H), 7.29 – 7.26 (m, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 2.35 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.97, 136.04,

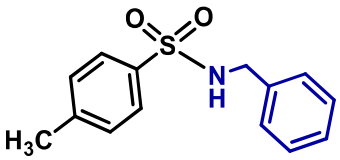
134.23, 133.68, 131.04, 129.73, 129.36, 127.58, 127.33, 126.65, 125.44, 120.95, 118.18, 21.50. HRMS (ESI) m/z: [M+H] + calculated for $C_{17}H_{16}NO_2S$ 298.0901; found: 298.0912

N-(4-Acetylphenyl)-4-methylbenzenesulfonamide (3s)



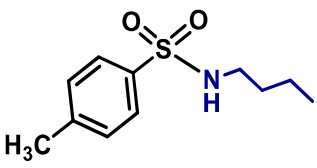
75% yield. Brown solid. m.p.: 198-200 °C. ^{1}H NMR (500 MHz, DMSO) δ 7.86 (d, J = 8.6 Hz, 2H), 7.51 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 7.9 Hz, 2H), 7.03 (d, J = 8.6 Hz, 2H), 2.48 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 196.49, 145.32, 138.66, 130.68, 128.71, 125.96, 118.37, 26.78, 21.26. HRMS (ESI) m/z: [M+H] + calculated for $C_{15}H_{16}NO_3S$ 290.0850; found: 290.0844

N-Benzyl-4-methylbenzenesulfonamide (3aa)



90% yield. Cream white solid. m.p.: 113-114 °C. ^{1}H NMR (500 MHz, CDCl3) δ 7.79 (d, J = 8.2 Hz, 2H), 7.33 (d, J = 8.3 Hz, 2H), 7.29 (dd, J = 8.6, 5.7 Hz, 3H), 7.22 (dd, J = 4.4, 3.6 Hz, 2H), 4.70 (s, 1H), 4.15 (s, 2H), 2.46 (s, 3H). ^{13}C NMR (126 MHz, CDCl3) δ 143.55, 136.90, 136.28, 129.76, 128.72, 127.91, 127.21, 47.30, 21.54. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{16}NO_2S$ 262.0901; found: 262.0902

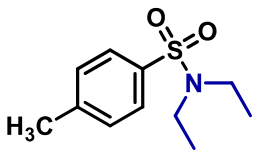
N-Butyl-4-methylbenzenesulfonamide (3ab)



91% yield. Cream solid. m.p.: 77-80 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.2 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 4.12

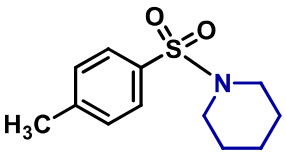
(d, *J* = 20.1 Hz, 1H), 2.94 (t, *J* = 7.1 Hz, 2H), 2.44 (s, 3H), 1.48 – 1.41 (m, 2H), 1.30 (dd, *J* = 15.1, 7.6 Hz, 3H), 0.86 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.30, 137.04, 130.24, 129.67, 127.08, 42.92, 31.57, 21.49, 19.68, 13.51. HRMS (ESI) m/z: [M+H] + calculated for $C_{11}H_{18}NO_2S$ 228.1058; found: 228.1062

N,N-Diethyl-4-methylbenzenesulfonamide (3ac)



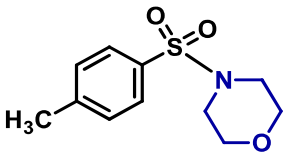
89% yield. Yellow liquid. ^{1}H NMR (500 MHz, DMSO) δ 7.67 (d, *J* = 8.2 Hz, 2H), 7.41 (d, *J* = 8.1 Hz, 2H), 3.13 (q, *J* = 7.1 Hz, 4H), 2.51 – 2.50 (m, 6H), 2.39 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 143.37, 137.34, 130.27, 127.21, 42.24, 21.41, 14.55. HRMS (ESI) m/z: [M+H] + calculated for $C_{11}H_{18}NO_2S$ 228.1058; found: 228.1059

1-Tosylpiperidine (3ad)



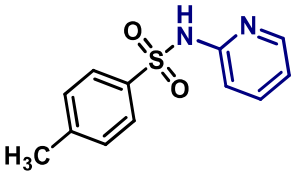
90% yield. White solid. m.p.: 142-143 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.2 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 3.01 – 2.95 (m, 4H), 2.45 (s, 3H), 1.68 – 1.63 (m, 4H), 1.42 (dt, *J* = 11.7, 5.9 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.31, 133.22, 129.55, 127.73, 46.95, 29.71, 25.17, 23.53, 21.54. HRMS (ESI) m/z: [M+H] + calculated for $C_{12}H_{18}NO_2S$ 240.1058; found: 240.1044

4-Tosylmorpholine (3ae)



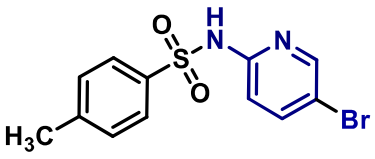
90% yield. Yellow liquid. 1H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, J = 8.2 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 3.78 – 3.73 (m, 4H), 3.02 – 2.97 (m, 4H), 2.46 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.99, 132.00, 129.77, 127.92, 66.11, 46.01, 21.57. HRMS (ESI) m/z: [M+H] + calculated for $C_{11}H_{16}NO_3S$ 242.0850; found: 242.0842

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



70% yield. Light yellow solid m.p.: 213-214 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 8.37 (d, *J* = 5.1 Hz, 3H), 7.82 (d, *J* = 8.3 Hz, 6H), 7.67 (ddd, *J* = 9.0, 7.1, 1.9 Hz, 3H), 7.42 (d, *J* = 8.9 Hz, 3H), 7.27 (d, *J* = 8.0 Hz, 5H), 6.81 (t, *J* = 6.5 Hz, 3H), 2.41 (s, 8H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.15 (s), 142.84 (s), 142.05 (s), 140.82 (s), 138.75 (s), 129.58 (s), 126.84 (s), 115.10 (s), 114.21 (s), 21.51 (s). HRMS (ESI) m/z: [M+H] + calculated for $C_{12}H_{13}N_2O_2S$ 249.0697; found: 249.0699

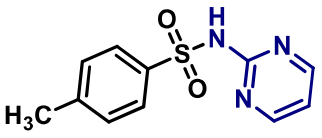
N-(5-Bromopyridin-2-yl)-4-methylbenzenesulfonamide (3ag)



71% yield. Yellow liquid b.p.: 222-224 °C (reptd.). ^1H NMR (500 MHz, $CDCl_3$) δ 7.76 (s, 2H), 7.55 (dd, *J* = 8.8, 2.4 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,

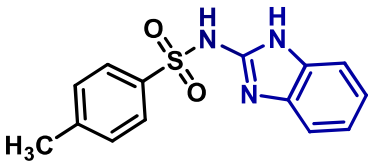
144.39, 141.43, 140.75, 129.91, 127.18, 113.47, 110.57, 21.60. HRMS (ESI) m/z: [M+H] + calculated for $C_{12}H_{12}N_2O_2SBr$ 326.9802; found: 326. 97.98

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



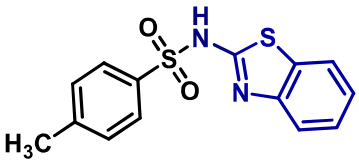
77% yield. White solid. m.p.: 213-214 °C. ^{1}H NMR (500 MHz, DMSO) δ 8.65 (d, *J* = 7.6 Hz, 2H), 7.54 (d, *J* = 7.8 Hz, 2H), 7.14 (d, *J* = 7.8 Hz, 2H), 7.02 – 7.01 (m, 2H), 7.00 (d, *J* = 8.8 Hz, 1H), 2.29 (s, 3H). HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{14}N_3O_2S$ 250.0650; found: 250.0654

N-(1H-Benzo[d]imidazol-2-yl)-4-methylbenzenesulfonamide (3ai)



73% 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

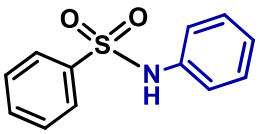
N-(Benzo[d]thiazol-2-yl)-4-methylbenzenesulfonamide (3aj)



72% yield. Cream white solid. m.p.: 243-245 °C. ^{1}H NMR (500 MHz, CDCl3) 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),

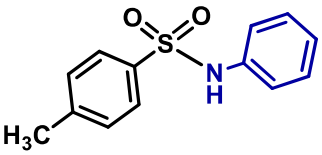
5.60 (s, 1H), 2.42 (s, 3H). ^{13}C NMR (126 MHz, CDCl3) δ 169.79, 143.21, 138.10, 129.46, 126.75, 124.38, 107.84, 29.72, 21.56. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{13}N_2O_2S_2$ 304.0340; found: 304.0339

N-Phenylbenzenesulfonamide (4a)



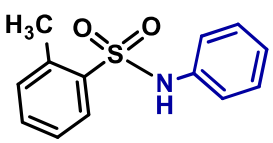
88% yield. White solid. m.p.: 105-106 °C. ^{1}H NMR (500 MHz, DMSO) δ 7.60 (t, *J* = 7.9 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 4H), 7.46 (s, 1H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.14 (d, *J* = 8.3 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 145.53, 138.53, 138.40, 130.68, 129.21, 128.68, 125.95, 123.54. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{13}N_2O_2S_2$ 233.0510; found: 233.0512

4-Methyl-N-phenylbenzenesulfonamide (4b)



84% yield. White solid. m.p.: 106-107 °C. ^{1}H NMR (500 MHz, DMSO) δ 7.95 (d, *J* = 9.2 Hz, 2H), 7.52 (d, *J* = 8.1 Hz, 3H), 7.18 – 7.12 (m, 2H), 6.63 (d, *J* = 9.2 Hz, 2H), 2.29 (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. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{13}N_2O_2S_2$ 247.0667; found: 247.0666

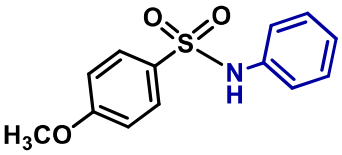
2-Methyl-N-phenylbenzenesulfonamide (4c)



87% yield. White solid. m.p.: 68-70 °C. ^{1}H NMR (500 MHz, DMSO) δ 8.19 (s, 1H), 7.51 (d, *J* = 8.1 Hz, 2H), 7.46 (d, *J* = 7.7 Hz, 2H), 7.44 – 7.37 (m, 3H), 7.14 (d, *J* = 7.8 Hz, 2H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 146.04,

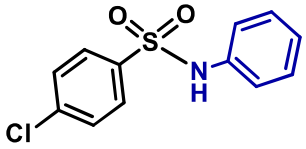
138.18, 131.81, 131.69, 128.56, 128.15, 127.64, 125.95, 123.18, 17.29. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{13}N_2O_2S_2$ 247.0667; found: 247.0668

4-Methoxy-N-phenylbenzenesulfonamide (4d)



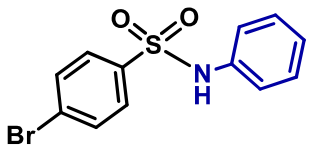
92% yield. White solid. m.p.: 105-106 °C. ^{1}H NMR (500 MHz, DMSO) δ 7.97 (t, *J* = 6.3 Hz, 1H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 3.72 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 158.92, 142.96, 138.35, 130.00, 129.39, 127.01, 114.09, 55.53. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{13}N_2O_2S_2$ 263.0616; found: 263.0318

4-Chloro-N-phenylbenzenesulfonamide (4e)



89% yield. White solid. m.p.: 103-105 °C. ^{1}H NMR (500 MHz, DMSO) δ 10.46 (s, 1H), 7.77 – 7.74 (m, 2H), 7.63 (m, *J* = 8.3, 6.4 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 2H), 7.30 (d, *J* = 8.8 Hz, 2H), 7.10 (d, *J* = 8.9 Hz, 2H). ^{13}C NMR (126 MHz, DMSO) δ 139.61, 137.12, 133.54, 129.81, 129.61, 128.64, 127.09, 122.07. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{13}N_2O_2S_2$ 267.0120; found: 267.0117

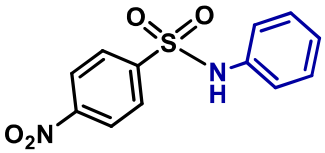
4-Bromo-N-phenylbenzenesulfonamide (4f)



86% yield. White solid. m.p.: 118-119 °C. ^{1}H NMR (500 MHz, DMSO) δ 7.51 (d, *J* = 8.1 Hz, 2H), 7.38 (m, *J* = 7.8, 1.2 Hz, 1H), 7.31 (m, *J* = 8.7, 7.2, 1.6 Hz, 1H), 7.19 – 7.09 (m, 3H), 6.81 (m, *J* = 8.4, 0.4 Hz, 1H), 6.61 (m, *J* = 7.8, 1.0 Hz, 1H). ^{13}C NMR (126 MHz, DMSO) δ 145.72, 138.41, 134.42,

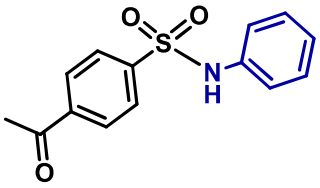
129.34, 129.10, 128.97, 128.64, 125.97. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{13}N_2O_2S_2$ 310.9616; found: 310.9612

4-Nitro-N-phenylbenzenesulfonamide (4g)



86% yield. Yellow solid. m.p.: 137-138 °C. ^{1}H NMR (500 MHz, DMSO) δ 10.73 (s, 1H), 7.96 (d, *J* = 7.6 Hz, 2H), 7.83 (m, *J* = 16.5, 8.7 Hz, 2H), 7.27 (t, *J* = 7.9 Hz, 2H), 7.14 – 7.05 (m, 3H). ^{13}C NMR (126 MHz, DMSO) δ 148.39, 137.06, 135.12, 133.00, 131.79, 130.34, 129.80, 125.16, 120.94. 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 (4h)



90% yield. Cream white solid. m.p.: 134-135 °C. ^{1}H NMR (500 MHz, DMSO) δ 7.84 (d, *J* = 8.7 Hz, 2H), 7.50 (d, *J* = 8.1 Hz, 3H), 7.14 (d, *J* = 7.8 Hz, 3H), 6.95 (s, 1H), 2.47 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 196.31, 146.70, 145.50, 138.54, 130.73, 130.13, 128.68, 125.96, 117.61, 26.72. HRMS (ESI) m/z: [M+H] + calculated for $C_{14}H_{13}NO_3S$ 275.0616; found: 275.061

3.9 Spectral data of few product

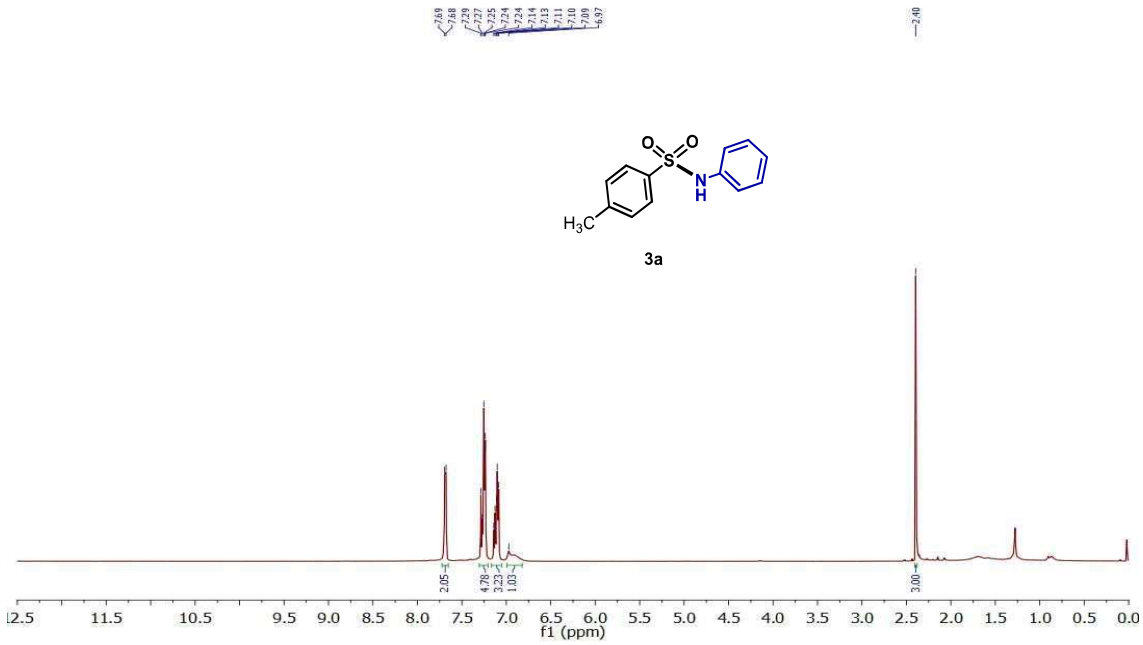


Figure 3.8 ^{1}H NMR of product **3a**

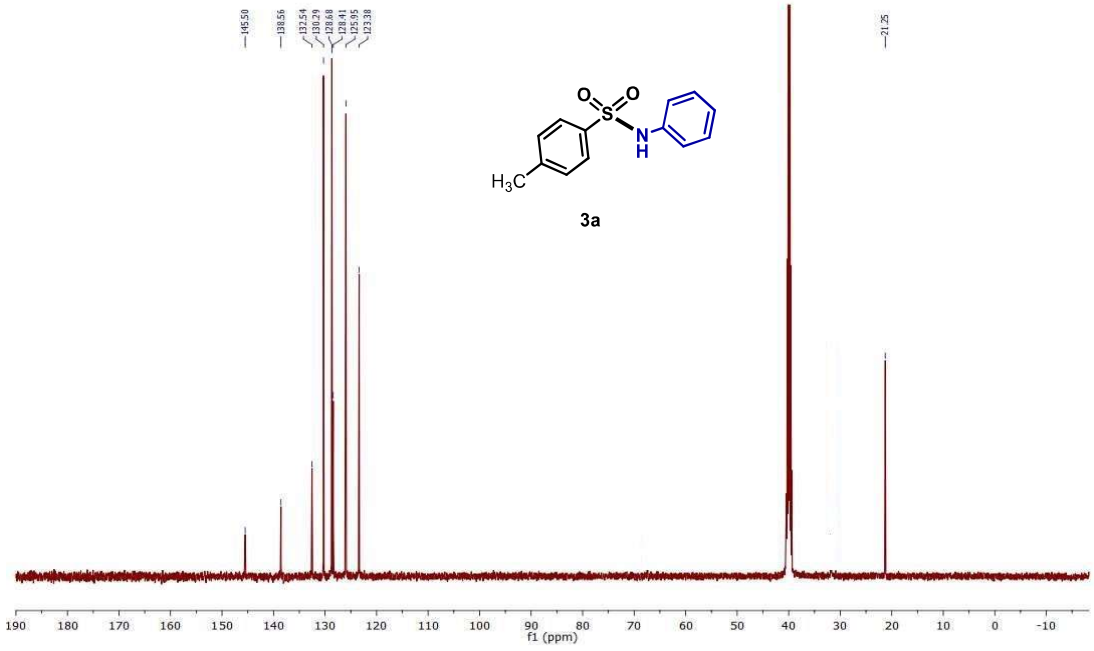


Figure 3.9 ^{13}CNMR of product **3a**

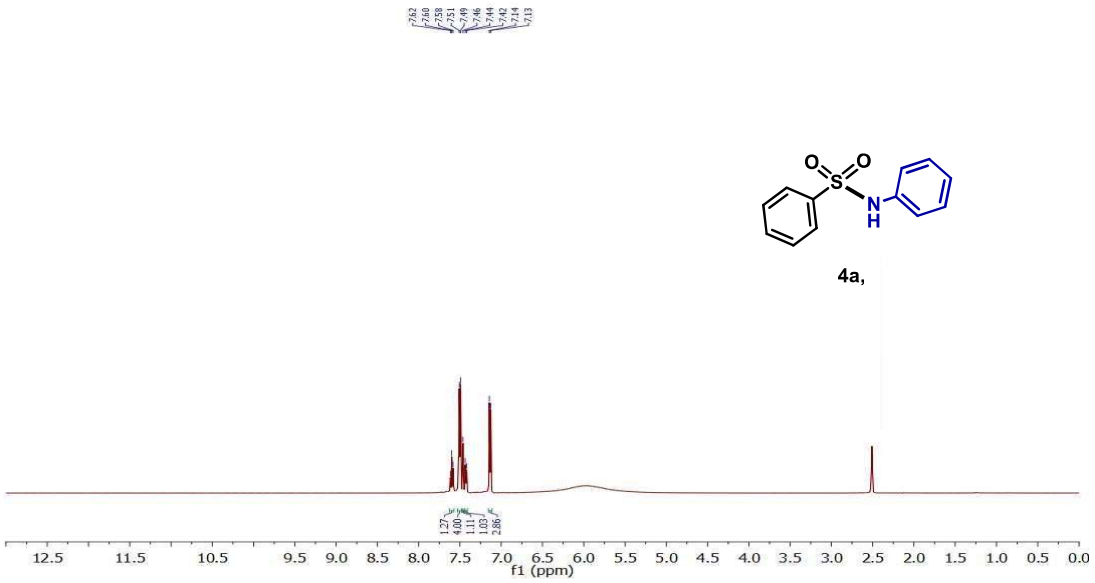


Figure 3.10 ^{1}H NMR of product **4a**

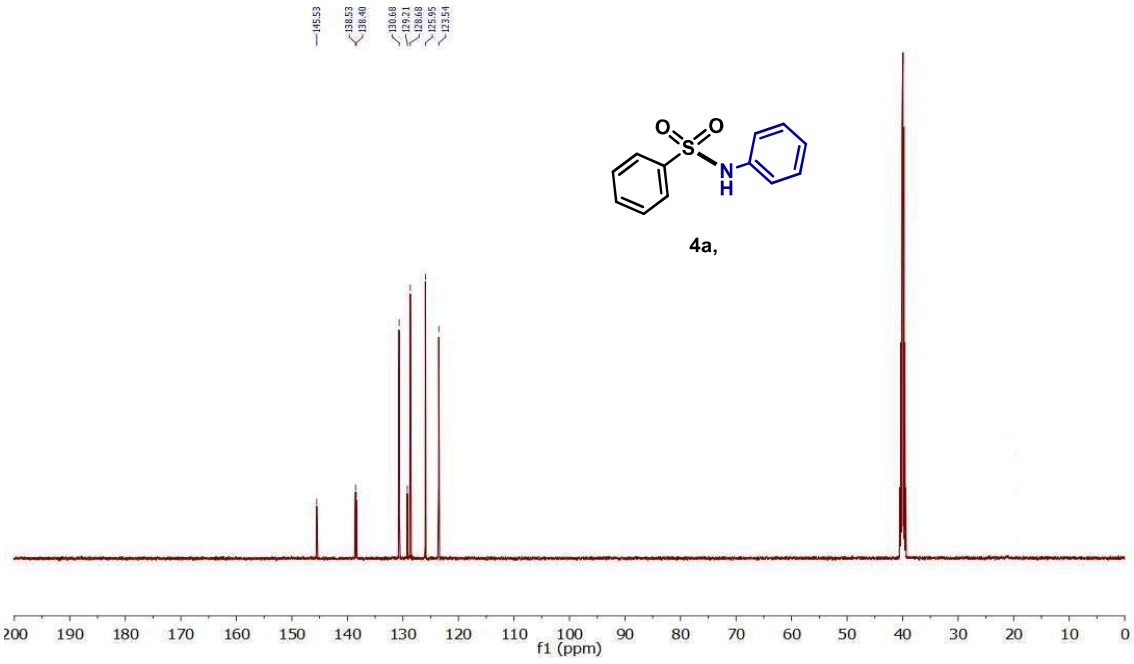


Figure 3.11 ^{13}C NMR of product **4a**

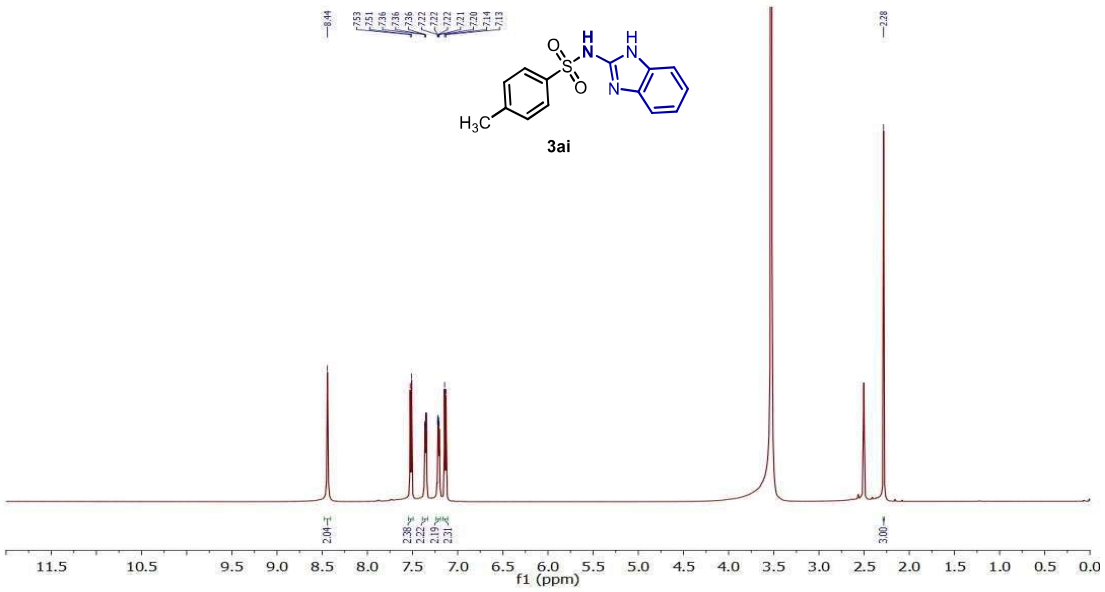


Figure 3.12 ^{1}H NMR of product **3ai**

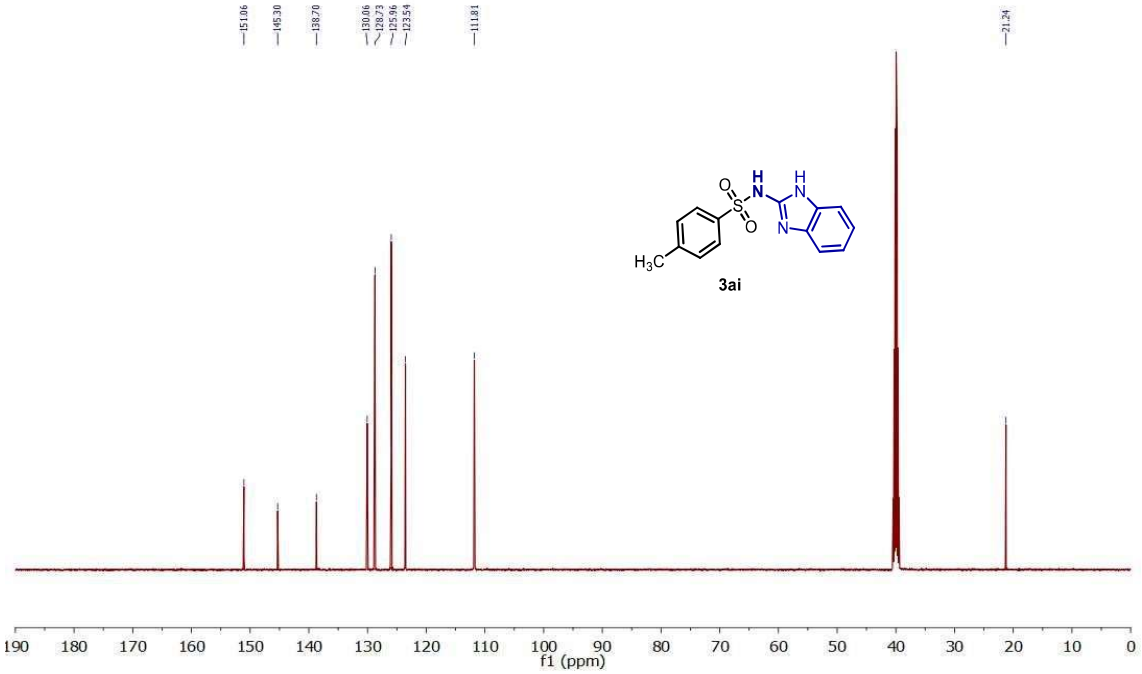


Figure 3.13 ^{13}C NMR of product **3ai**

3.10 HRMS spectra

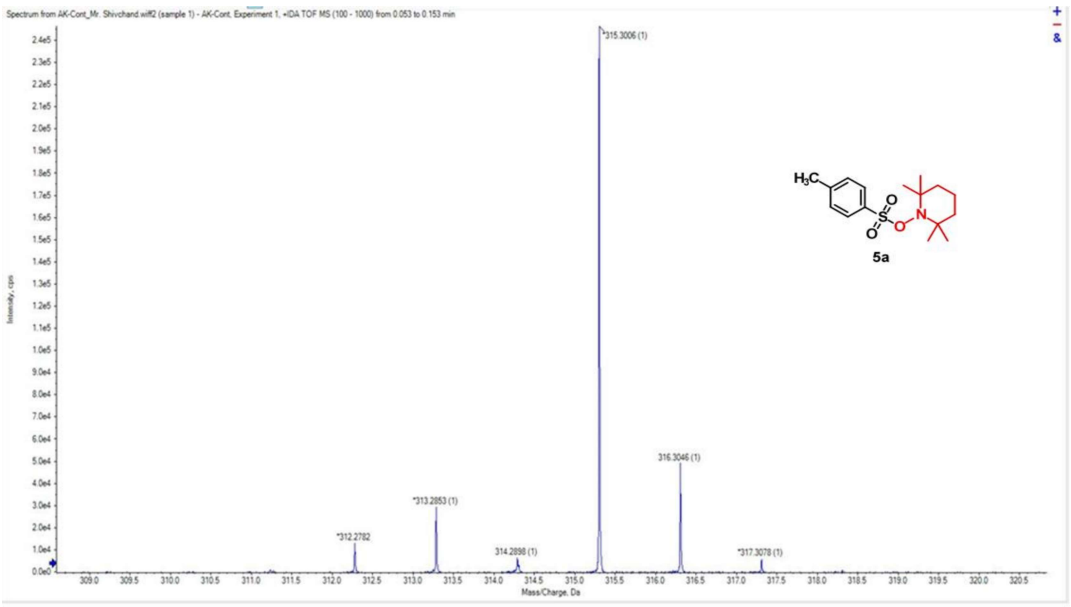


Figure 3.14 HRMS Spectra of **5a**

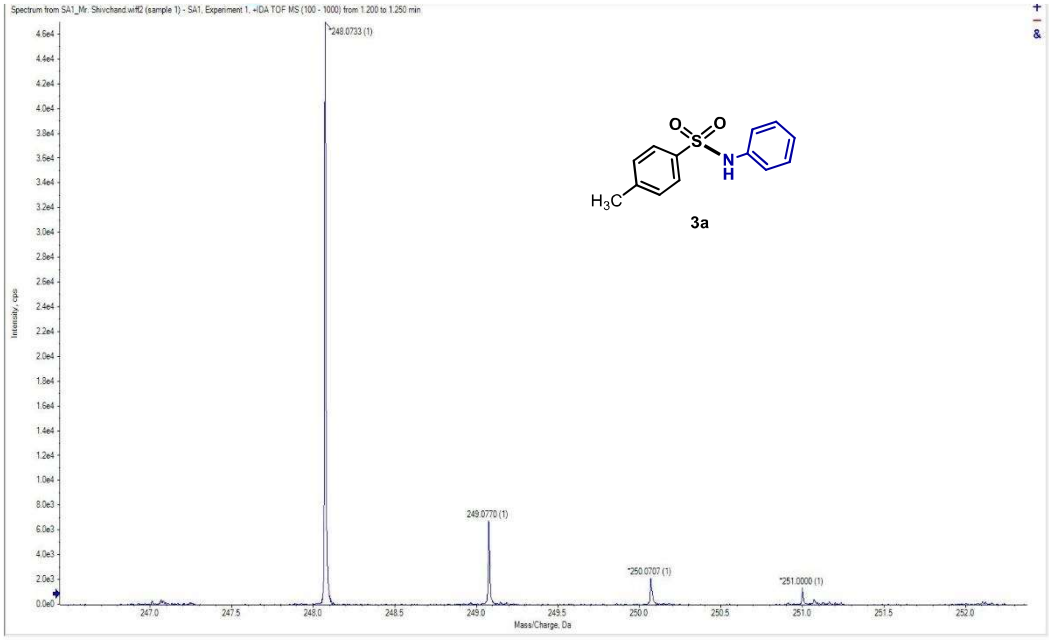


Figure 3.15 HRMS Spectra of **3a**

3.11 References

[1] J. Xuan, X.-K. He, W.-J. Xiao, "Visible light-promoted ring-opening functionalization of three-membered carbo-and heterocycles", *Chemical Society Reviews*, **49** (2020) 2546-2556.
[2] Q.Q. Zhou, Y.Q. Zou, L.Q. Lu, W.J. Xiao, "Visible-light-induced organic photochemical reactions through energy-transfer pathways," *Angewandte Chemie International Edition,* **58** (2019) 1586-1604.
[3] X. Zhang, K. Rakesh, L. Ravindar, H.-L. Qin, "Visible-light initiated aerobic oxidations: a critical review," *Green Chemistry,* **20** (2018) 4790-4833.
[4] Q. Liu, L.-Z. Wu, "Recent advances in visible-light-driven organic reactions," *National Science Review,* **4** (2017) 359-380.
[5] N.F. Nikitas, D.I. Tzaras, I. Triandafillidi, C.G. Kokotos, "Photochemical oxidation of benzylic primary and secondary alcohols utilizing air as the oxidant," *Green Chemistry,* **22** (2020) 471-477.
[6] Q. Guo, Q. Peng, H. Chai, Y. Huo, S. Wang, Z. Xu, "Visible-light promoted regioselective amination and alkylation of remote C (sp3)-H bonds," *Nature communications,* **11** (2020) 1-10.
[7] Q. Xu, X. Zhou, S. Zhang, L. Pan, Q. Liu, Y. Li, "Visible-Light-Induced Sulfur-Alkenylation of Alkenes," Organic Letters, **23** (2021) 4870-4875.
[8] M. Li, T. Liu, J. Li, H. He, H. Dai, J. Xie, "Visible-Light-Mediated Deoxyalkynylation of Activated Tertiary Alcohols," *The Journal of Organic Chemistry,* **86** (2021) 12386-12393.
[9] Q. Yan, W. Cui, X. Song, G. Xu, M. Jiang, K. Sun, J. Lv, D. Yang, "Sulfonylation of Aryl Halides by Visible Light/Copper Catalysis," *Organic Letters,* **23** (2021) 3663-3668.
[10] P. Pan, S. Liu, Y. Lan, H. Zeng, C.-J. Li, "Visible-light-induced cross-coupling of aryl iodides with hydrazones via EDA-complex," *Chemical Science,* (2022).
[11] Y. Wang, Y. Lang, C.-J. Li, H. Zeng, "Visible-light-induced transition metal and photosensitizer free decarbonylative addition of amino-arylaldehydes to ketones," *Chemical Science,* **13** (2022) 698-703.
[12] M. Tavakolian, M. Hosseini-Sarvari, "Catalyst-Free Organic Transformations under Visible-Light," *ACS Sustainable Chemistry & Engineering,* **9** (2021) 4296-4323.
[13] Y. Wei, Q.-Q. Zhou, F. Tan, L.-Q. Lu, W.-J. Xiao, "Visible-light-driven organic photochemical reactions in the absence of external photocatalysts," *Synthesis,* **51** (2019) 3021-3054.
[14] Q. Xiao, Q.-X. Tong, J.-J. Zhong, "Recent Advances in Visible-Light Photoredox Catalysis for the Thiol-Ene/Yne Reactions," *Molecules,* **27** (2022) 619.
[15] G.-Z. Wang, D.-G. Liu, M.-T. Liu, Y. Fu, "Photocatalyst-and additive-free site-specific C (sp 3)–H hydrazination of glycine derivatives and peptides," *Green Chemistry*, **23** (2021) 5082-5087.
[16] M.T. Liu, D.G. Liu, Z.W. Qin, G.Z. Wang, "Visible Light-induced Decarboxylative Alkylations Enabled by Electron Donor-Acceptor Complex," *Asian Journal of Organic Chemistry,* (2022) e202200335.

[17] G. Li, Q. Yan, X. Gong, X. Dou, D. Yang, "Photocatalyst-free regioselective C–H thiocyanation of 4-anilinocoumarins under visible light," *ACS Sustainable Chemistry & Engineering,* **7** (2019) 14009-14015.
[18] F.-L. Zeng, K.-C. Xie, Y.-T. Liu, H. Wang, P.-C. Yin, L.-B. Qu, X. Chen, B. Yu, "Visible-light-promoted catalyst-/additive-free synthesis of aroylated heterocycles in sustainable solvent," *Green Chemistry,* (2022).
[19] Q. Fan, L. Zhu, X. Li, H. Ren, G. Wu, H. Zhu, W. Sun, "Catalyst-free visible light-mediated selective oxidation of sulfides into sulfoxides under clean conditions," *Green Chemistry,* **23** (2021) 7945-7949.
[20] B. Sun, H. Ding, H.X. Tian, P.Y. Huang, C. Jin, C.L. Wu, R.P. Shen, "Photo-Triggered Self-Induced Homolytic Dechlorinative Sulfonylation/Cyclization of Unactivated Alkenes: Synthesis of Quinazolinones Containing a Sulfonyl Group," *Advanced Synthesis & Catalysis,* **364** (2022) 766-772.
[21] S. Engl, O. Reiser, "Catalyst-Free Visible-Light-Mediated Iodoamination of Olefins and Synthetic Applications," *Organic Letters,* **23** (2021) 5581-5586.
[22] Z.-P. Ye, P.-J. Xia, F. Liu, Y.-Z. Hu, D. Song, J.-A. Xiao, P. Huang, H.-Y. Xiang, X.-Q. Chen, H. Yang, Visible-Light-Induced, "Catalyst-Free Radical Cross-Coupling Cyclization of N-Allylbromodifluoroacetamides with Disulfides or Diselenides," *The Journal of Organic Chemistry,* **85** (2020) 5670-5682.
[23] J. Li, J.-X. Wen, X.-C. Lu, G.-Q. Hou, X. Gao, Y. Li, L. Liu, "Catalyst-Free Visible-Light-Promoted Cyclization of Aldehydes: Access to 2, 5-Disubstituted 1, 3, 4-Oxadiazole Derivatives," *ACS omega,* **6** (2021) 26699-26706.
[24] S.-C. He, J. Ponmani, S. Avula, X.-L. Wang, H.-Z. Zhang, C.-H. Zhou, "Recent advance in sulfonamide-based medicinal chemistry," *SCIENTIA SINICA Chimica,* **46** (2016) 823-847.
[25] T.C. Das, S.A. Quadri, M. Farooqui, "Recent advances in synthesis of sulfonamides: A review," *Chemistry & Biology Interface,* **8** (2018).
[26] K.H. Oudah, M.A. Najm, A.B. Roomi, H.A. Al-sa, "The recent progress of sulfonamide in medicinal chemistry," *Systematic Reviews in Pharmacy,* **11** (2020) 1473-1477.
[27] A. Kołaczek, I. Fusiarz, J. Ławecka, D. Branowska, "Biological activity and synthesis of sulfonamide derivatives: a brief review," *Chemik,* **68** (2014) 620-628.
[28] M.A. Pasha, N. Shrivatsa, "N-Sulfonylation of amines, imides, amides and anilides using p-TsCl in presence of atomized sodium in EtOH–THF under sonic condition," *Ultrasonics Sonochemistry,* **26** (2015) 15-21.
[29] R. Hosseinzadeh, M. Tajbakhsh, M. Mohadjerani, M. Alikarami, "Copper-catalysed N-arylation of arylsulfonamides with aryl bromides and aryl iodides using KF/Al2O3," *Journal of chemical sciences,* **122** (2010) 143-148.
[30] D.C. Loukrakpam, P. Phukan, "CuI catalyzed sulfamidation of arylboronic acid using TsNBr2 at room temperature," *Tetrahedron Letters,* **58** (2017) 4855-4858.
[31] K. Zhang, Y. Zhang, Q. Liu, D. He, J. Tian, H. Zhou, "Metal-Free One-Pot Synthesis of Sulfonamides from Nitroarenes and Arylsulfonyl Chlorides in Water," *ChemistrySelect,* **4** (2019) 7413-7415.

[32] S.Y. Chow, M.Y. Stevens, L.R. Odell, "Sulfonyl azides as precursors in ligand-free palladium-catalyzed synthesis of sulfonyl carbamates and sulfonyl ureas and synthesis of sulfonamides," *The Journal of organic chemistry,* **81** (2016) 2681-2691.
[33] J. Baffoe, M.Y. Hoe, B.B. Toure, "Copper-mediated N-heteroarylation of primary sulfonamides: synthesis of mono-N-heteroaryl sulfonamides," *Organic Letters,* **12** (2010) 1532-1535.
[34] İ. Gulçin, P. Taslimi, "Sulfonamide inhibitors: a patent review 2013-present," *Expert opinion on therapeutic patents,* **28** (2018) 541-549.
[35] M. Ashfaq, S.S. Shah, T. Najjam, S. Shaheen, G. Rivera, "Synthetic routes of sulfonamide derivatives: a brief review," *Mini-Reviews in Organic Chemistry,* **10** (2013) 160-170.
[36] M. Siddique, A.B. Saeed, S. Ahmad, N.A. Dogar, "Synthesis and biological evaluation of hydrazide based sulfonamides," *J Sci Innovative Res,* **2** (2013) 627-633.
[37] E.E. Connor, "Sulfonamide antibiotics," *Primary care update for ob/gyns,* **5** (1998) 32-35.
[38] C.T. Supuran, A. Innocenti, A. Mastrolorenzo, A. Scozzafava, "Antiviral sulfonamide derivatives," *Mini reviews in medicinal chemistry,* **4** (2004) 189-200.
[39] C.T. Supuran, A. Casini, A. Scozzafava, "Protease inhibitors of the sulfonamide type: anticancer, antiinflammatory, and antiviral agents," *Medicinal Research Reviews,* **23** (2003) 535-558.
[40] K.O. Mohamed, Y.M. Nissan, A.A. El-Malah, W.A. Ahmed, D.M. Ibrahim, T.M. Sakr, M.A. Motaleb, "Design, synthesis and biological evaluation of some novel sulfonamide derivatives as apoptosis inducers," *European Journal of Medicinal Chemistry,* **135** (2017) 424-433.
[41] J. Chen, S. Xie, "Overview of sulfonamide biodegradation and the relevant pathways and microorganisms," *Science of the Total Environment,* **640** (2018) 1465-1477.
[42] R. Hosseini, R. Ranjbar-Karimi, K. Mohammadiannejad, "Synthesis of N-substituted sulfonamides containing perhalopyridine moiety as bio-active candidates," *Journal of Fluorine Chemistry,* **233** (2020) 109507.
[43] C.T. Supuran, "Indisulam: an anticancer sulfonamide in clinical development," *Expert opinion on investigational drugs,* **12** (2003) 283-287.
[44] S. Bowers, G.D. Probst, A.P. Truong, R.K. Hom, A.W. Konradi, H.L. Sham, A.W. Garofalo, K. Wong, E. Goldbach, K.P. Quinn, "N-Bridged bicyclic sulfonamides as inhibitors of γ-secretase," *Bioorganic & medicinal chemistry letters,* **19** (2009) 6952-6956.
[45] C.T. Supuran, F. Briganti, S. Tilli, W.R. Chegwidden, A. Scozzafava, "Carbonic anhydrase inhibitors: sulfonamides as antitumor agents?," *Bioorganic & medicinal chemistry,* **9** (2001) 703-714.
[46] K. Rakesh, S.-M. Wang, J. Leng, L. Ravindar, A.M. Asiri, H.M. Marwani, H.-L. Qin, "Recent development of sulfonyl or sulfonamide hybrids as potential anticancer agents: a key review," *Anti-Cancer Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Anti-Cancer Agents),* **18** (2018) 488-505.

[47] G. Meshram, V.D. Patil, "A simple and efficient method for sulfonylation of amines, alcohols and phenols with cupric oxide under mild conditions," *Tetrahedron Letters,* **50** (2009) 1117-1121.
[48] M. Harmata, P. Zheng, C. Huang, M.G. Gomes, W. Ying, K.-O. Ranyanil, G. Balan, N.L. Calkins, "Expedient synthesis of sulfinamides from sulfonyl chlorides," *The Journal of organic chemistry,* **72** (2007) 683-685.
[49] R. Sridhar, B. Srinivas, V.P. Kumar, M. Narender, K.R. Rao, "β-Cyclodextrin-catalyzed monosulfonylation of amines and amino acids in water," *Advanced Synthesis & Catalysis,* **349** (2007) 1873-1876.
[50] Y. Cai, R. Zhang, D. Sun, S. Xu, Q. Zhou, "Eosin Y-sensitized photocatalytic reaction of tertiary aliphatic amines with arenesulfonyl chlorides under visible-light irradiation," *Synlett,* **28** (2017) 1630-1635.
[51] S. Firoozi, M. Hosseini-Sarvari, "Nanosized CdS as a reusable photocatalyst: the study of different reaction pathways between tertiary amines and aryl sulfonyl chlorides through visible-light-induced N-dealkylation and C–H activation processes," *The Journal of Organic Chemistry,* **86** (2021) 2117-2134.
[52] K. Yang, M. Ke, Y. Lin, Q. Song, "Sulfonamide formation from sodium sulfinates and amines or ammonia under metal-free conditions at ambient temperature," *Green Chemistry,* **17** (2015) 1395-1399.
[53] Y. He, S.-G. Li, I.I. Mbaezue, A.C. Reddy, Y.S. Tsantrizos, "Copper-boryl mediated transfer hydrogenation of N-sulfonyl imines using methanol as the hydrogen donor," *Tetrahedron,* **85** (2021) 132063.
[54] S. Chung, J. Kim, "Cu-catalyzed aerobic oxidative synthesis of sulfonamides from sulfonyl hydrazides and amines," *Tetrahedron Letters,* **60** (2019) 792-795.
[55] A. Gioiello, E. Rosatelli, M. Teofrasti, P. Filipponi, R. Pellicciari, "Building a sulfonamide library by eco-friendly flow synthesis," *ACS Combinatorial Science,* **15** (2013) 235-239.
[56] M. Jafarpour, A. Rezaeifard, T. Golshani, "A green, catalyst-free method for the synthesis of sulfonamides and sulfonylazides, Phosphorus, Sulfur, and Silicon," **186** (2010) 140-148.
[57] S. Mondal, "Sulfonamide synthesis under green conditions," *Synthetic Communications,* **51** (2021) 1023-1044.
[58] S.K.R. Parumala, R.K. Peddinti, "Metal-free synthesis of sulfonamides via iodine-catalyzed oxidative coupling of sulfonyl hydrazides and amines," *Tetrahedron Letters,* **57** (2016) 1232-1235.
[59] A. Kamal, H.K. Singh, S.K. Maury, S. Kumari, A.K. Kushwaha, V. Srivastava, S. Singh, "Visible Light-Driven Synthesis of Amine–Sulfonate Salt Derivatives: A Step towards Green Approach," *Journal of Molecular Structure,* (2022) 132523.
[60] H.K. Singh, A. Kamal, S. Kumari, D. Kumar, S.K. Maury, V. Srivastava, S. Singh, "Eosin Y-catalyzed synthesis of 3-aminoimidazo [1, 2-a] pyridines via the HAT process under visible light through formation of the C–N bond," *ACS omega,* **5** (2020) 29854-29863.

[61] A. Kamal, H.K. Singh, D. Kumar, S.K. Maury, S. Kumari, V. Srivastava, S. Singh, "Visible Light-Induced Cu-Catalyzed Synthesis of Schiff's Base of 2-Amino Benzonitrile Derivatives and Acetophenones," *ChemistrySelect,* **6** (2021) 52-58.
[62] S. Kumari, S. Kumar Maury, H. Kumar Singh, A. Kamal, D. Kumar, S. Singh, V. Srivastava, "Visible Light Mediated, Photocatalyst-Free Condensation of Barbituric Acid with Carbonyl Compounds," *ChemistrySelect,* **6** (2021) 2980-2987.
[63] S.K. Maury, S. Kumari, A.K. Kushwaha, A. Kamal, H.K. Singh, D. Kumar, S. Singh, "Grinding induced catalyst free, multicomponent synthesis of indoloindole pyrimidine," *Tetrahedron Letters,* **61** (2020) 152383.
[64] D. Kumar, S.K. Maury, S. Kumari, A. Kamal, H.K. Singh, S. Singh, V. Srivastava, "TBAI-catalyzed C–N bond formation through oxidative coupling of benzyl bromides with amines: a new avenue to the synthesis of amides," *Synthetic Communications,* (2022) 1-9.
[65] Y. Sumida, H. Ohmiya, "Direct excitation strategy for radical generation in organic synthesis," *Chemical Society Reviews,* **50** (2021) 6320-6332.
[66] J. Tong, H. Li, Y. Zhu, P. Liu, P. Sun, "Visible-light-induced dehydrogenative sulfonylation of tertiary amines under transition-metal-and photocatalyst-free conditions," *Green Chemistry,* (2022).
[67] L. Lin, Z. Yang, J. Liu, J. Wang, J. Zheng, J.-L. Li, X. Zhang, X.-W. Liu, H. Jiang, J. Li, "Visible-light-induced surfactant-promoted sulfonylation of alkenes and alkynes with sulfonyl chloride by the formation of an EDA-complex with NaI in water at room temperature," *Green Chemistry,* **23** (2021) 5467-5473.
[68] X.-X. Meng, Q.-Q. Kang, J.-Y. Zhang, Q. Li, W.-T. Wei, W.-M. He, "Visible-light-initiated regioselective sulfonylation/cyclization of 1, 6-enynes under photocatalyst-and additive-free conditions," *Green Chemistry,* **22** (2020) 1388-1392.
[69] H. Qiao, S. Sun, F. Yang, Y. Zhu, W. Zhu, Y. Dong, Y. Wu, X. Kong, L. Jiang, Y. Wu, "Copper (I)-catalyzed sulfonylation of 8-aminoquinoline amides with sulfonyl chlorides in air," *Organic letters,* **17** (2015) 6086-6089.
[70] G.E. Crisenza, D. Mazzarella, P. Melchiorre, "Synthetic methods driven by the photoactivity of electron donor–acceptor complexes," *Journal of the American Chemical Society,* **142** (2020) 5461-5476.
[71] P. Wade, H. Morrison, N. Kornblum, "The effect of light on electron-transfer substitution at a saturated carbon atom," *Journal of organic chemistry,* **52** (1987) 3102-3107.
[72] J.D. Anunziata, N.S. Galaverna, J.O. Singh, J.J. Silber, "n-π Electron donor–acceptor complexes. III. Aliphatic amines with dicyanobenzenes. Electric and steric effects of the N-substituents on complex formation," *Canadian journal of chemistry,* **64** (1986) 1491-1495.