Chapter-5

Visible Light-Driven Synthesis of Amine–Sulfonate Salt Derivatives: A Step towards Green Approach

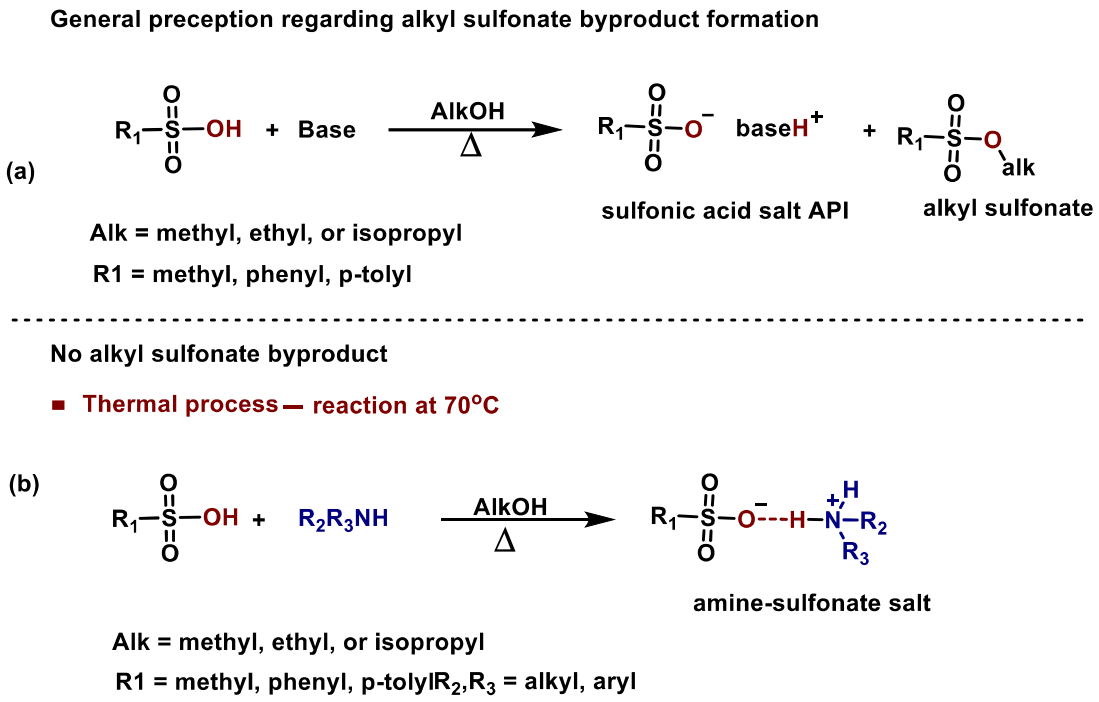
5.1 Introduction

In the modern era, visible light initiated significant chemical reactions are an encouraging and green approach in organic synthesis. The use of visible light is advantageous because it is a clean, cheap, renewable, abundant, and ecologically favorable energy source for carrying out organic reactions[1-4]. Various examples of visible light-initiated organic reactions without external photocatalysts are available in the literature, in contrast to the use of photocatalyzed organic transformations. Therefore, the exploitation of visible light for the energy transfer process for the excitation of organic molecules to accomplish important photochemical reactions would work as a valued aid in sustainable organic synthesis [5-7].

Organic sulphonic acid salt work as an anionic surface-active agent, and hence they are extensively utilized in the detergent industry. Organic sulphonic acid salts containing soaps are better than ordinary soap because they do not form insoluble salts with magnesium & calcium ions and foam in hard water. These salts are used as emulsion breakers and electrolytes in zinc-cerium and lead-acid flow batteries. They are the main intermediate in synthesizing dyes and chemicals for electroplating. Such salts are also used in photo imaging and as an etching agent for semiconductors and ceramic compounds [8, 9].

In addition, sulfonic acid salts are also enormously valuable for drug development. Sulphonate salts do not form hydrates like other strong acid salts and, thus it, become more suitable for secondary processing like wet granulation. In the pharmaceutical industry, more than half of the top drugs are given in the salt form to optimize the pharmaceutical,

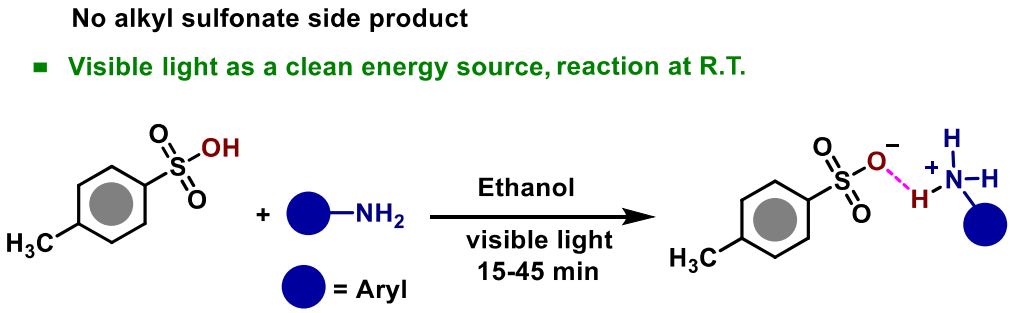
physicochemical, therapeutic, active pharmaceutical ingredients, and processing properties of ionizable drug substances [10]. However, the potential active pharmaceutical ingredients (APIs) properties (i.e. crystallinity, chemical purity, solubility, and stability) are extremely valuable. Sulfonic acid salts have better physical or chemical properties than other salts of the same organic base [10-12].



Scheme 5.1 Previous works

Although not a worldwide remedy to the issue of the formation of salt, they do provide important benefits as substitutes to traditional anions, for instance, acetate or chloride. Due to the recognized potential contamination problem with genotoxic alkyl sulfonate [13-15], there appears to be no such crowded use of sulfonic acid salts. The use of the Viracept (nelfinavir mesylate) drug pulls out from the market because it is contaminated with EMS

(Ethyl methane sulfonate)[13]. Thus, the use of mesylate anion was exempted as such and highlighted the necessity for a strong GMP (Good manufacturing practice) regulator and a systematic understanding of the development of sulfonate ester [14, 15]. Even though the synthesis of ester in the presence of alcohol from a sulfonic acid under strongly acidic conditions is a very slow and thermodynamically unfavorable reaction to yield even a small transformation. The acid salts form immediately by proton transfer when an equimolar amount of sulphonic acid is added to a pharmaceutical base; as a result, the acid is neutralized, and ester is not formed as a side product, albeit an alcoholic solvent is used. If certain direct techniques and precautions are followed, evidence suggests that it is possible to synthesize a sulfonic acid salt of an amine-containing drug substance that is free of alkyl sulfonate contamination using short-chain alcohol as a solvent [16, 17].



Scheme 5.2 Visible light-mediated synthesis of amine-sulfonate salt

As far as we know, the synthesis of amine-sulfonate salt is not yet explored, and it is of great importance in medicinal and synthetic chemistry to explore an efficient approach for the synthesis of amine-sulfonate salt without any side product. In view of the above facts and in order to explore our research towards green technology [18-20]. It is worthwhile to report

the synthesis of sulfonate salt from an efficient method under visible light at room temperature within 15-45 min (Scheme 5.2).

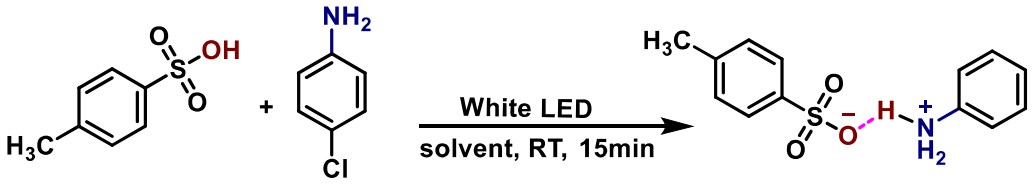
5.2 Results and discussion

In the initial state of the study of optimum reaction condition, *p*-toluenesulfonic acid **1** and *p*-chloroaniline **2b** was taken as model substrate under visible light irradiation. First, various solvents, such as toluene, DCM, DME, CH_3CN, and ethanol were screened, and it was observed that ethanol is the superior solvent compared to others (Table-5.1 entries 1-4, 9, and 10). However, the other solvents like THF, DMF, DMSO, water, and without solvent did not give the desired product (table 5.1 entries 5-8 and 10, respectively).

Afterward the selection of the solvent, we concentrated on studying the effect of various visible light sources (Table 5.2) on the reaction. The experiment was carried out using visible light of different intensities (CFL, blue LED, green LED, and white LED), (Table 5.2, entries 1–6) to get excellent yield. These experiments reveal that the product yield and reaction time was best when a 12 W white LED was used (Table 5.2, entries 1).

Furthermore, the product was formed only in trace amounts in the dark, and 40% of the yield was obtained without white LEDs (Table 5.2, entries 7& 8). The following experiment was carried out in the presence of catalyst eosin Y (0.1 mol%) for 120 min (Table 5.2, entry 9), but the product was not obtained. However, as soon as the same reaction was performed for 120 min in the presence of nitrogen (Table 5.2, entry 11), no product was obtained. Finally, the reaction was also tried in the presence of sunlight instead of white LEDs (Table 5.2, entries 10) on the other hand there was no significant effect on our reaction.

Table 5.1: Optimization of the reaction condition[a]



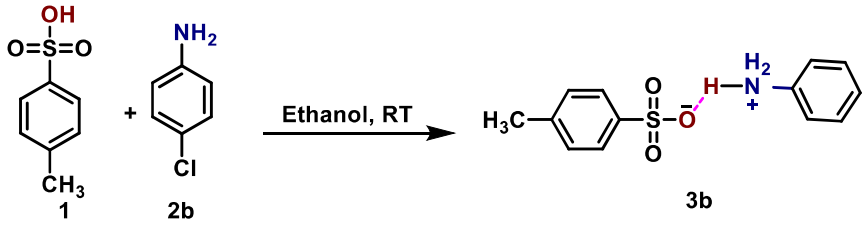
1 2b 3b

Entry	Solvent	Yield[b]%
1	PhMe	88
2	DCM	40
3	Ethanol	96
4	DME	78
5	Water	nr
6	THF	nr
7	DMF	nr
8	DMSO	nr
9	CH_3CN	trace
10	-	nr

[a]Conditions: *p*-Toluenesulfonic acid **1** (1.0 equiv),4-chloroaniline **2b** (1.0 equiv) in solvent , irradiation with 12 W white LEDs at room temperature for 15 minutes, [b]isolated yield.

With the optimized reaction conditions, the substrate scope of the synthesis of sulphonate salt was explored using various amine derivatives. The reaction proceeds smoothly with all amines 2a-o and provided the desired product (3a-3o) shown in Table 5.3 in excellent yield.

Table 5.2 Optimization of the Conditions[a]

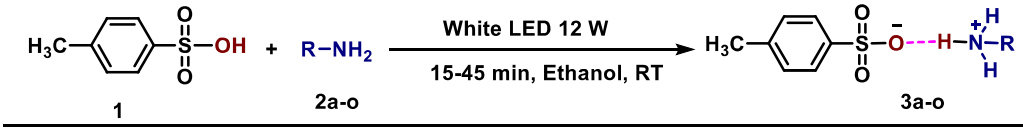


Entry	variations in the reaction conditions	Time (min.)	Yield of 3a (%)[b]
1	12 W white LEDs	15	96
2	15 W white LEDs	30	82
3	20 W white LEDs	60	80
4	15W CFL instead of white LEDs	60	78
5	blue LEDs instead of white LEDs	60	79
6	green LEDs instead of white LEDs	60	63
7	without white LED	60	40
8	Dark	120	27
9	with eosin Y	120	nr
10	sunlight instead of white LEDs	120	63
11	under N2 atmosphere	120	nr

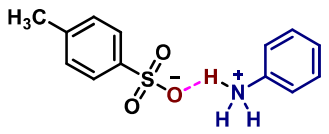
[a]Conditions: p-Toluenesulfonic acid **1** (1.0 equiv),4-chloroaniline **2b** (1.0 equiv) in ethanol at room temprature [b]Isolated yield

Generally, amine with a functional group such as Cl, Br, OMe, and Me provided the product in excellent yield. Remarkably, the most withdrawing group like F, CF_3, and NO_2 (Table 5.3, **3i-3m**) provided low yield as compared to other groups. The molecular structure of all the synthesized compounds was characterized by ^{1}H NMR, ^{13}C NMR, and mass spectrometry. The structure of **3b** was confirmed by single-crystal X-ray crystallographic analysis.

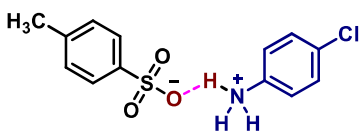
Table 5.3. Scope and versatility of the reaction



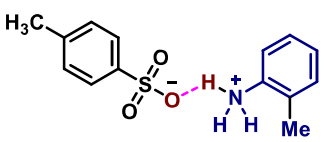
1 2a-o 3a-o



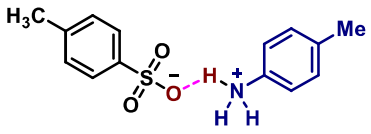
3a, 91%, 15 min



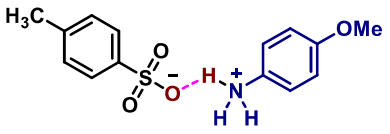
3b, 96%, 15 min



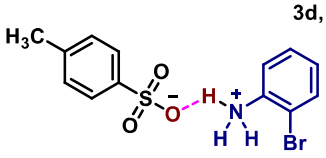
3c, 94%, 20 min



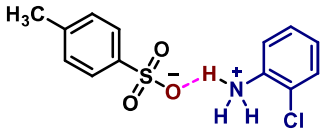
3d, 93%,20 min



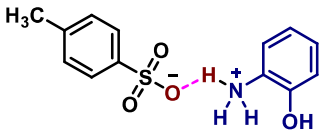
3e, 92%, 25 min



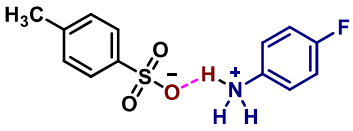
3f, 95%, 20 min



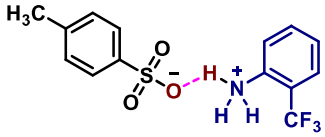
3g, 90%, 25 min



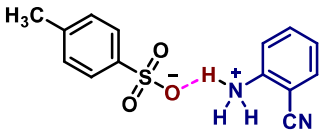
3h, 93%,15 min



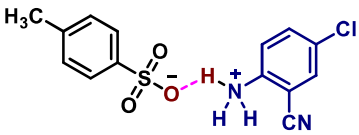
3i, 88%, 20 min



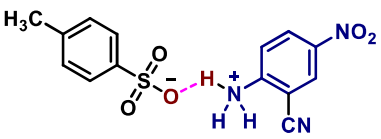
3j, 81%, 45 min



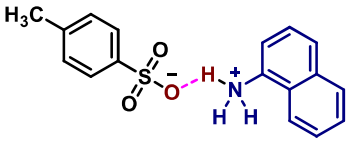
3k, 88%, 30 min



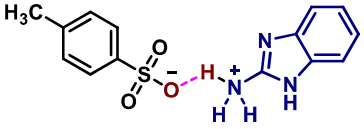
3l, 89%, 25 min



3m, 79%, 45 min



3n, 86%, 35 min



3o, 90%, 30 min

[a]Conditions: p-Toluenesulfonic acid **1** (1.0 equiv),4-chloroaniline **2b** (1.0 equiv) in ethanol , irradiation with 12 W white LEDs at room temperature, [b]Isolated yield.

5.3. X-ray crystallographic study of 3b method for single crystals growth

The single crystal for compound **3b** [Ak_S2A_Lt_Cu] was prepared from a mixture of solvent DCM and ethanol (v/v = 1:1). A pure solid sample (15–20 mg) was dissolved in DCM (4 mL) in a vial at room temperature, and ethanol (3-4 mL) was added into the above solution slowly while keeping the sample completely dissolved. The vial was properly sealed with parafilm and kept at room temperature to allow the slow evaporation of the solvents until a single crystal was obtained. Tables 5.4 and 5.5 (Figure 5.1).

Table 5.4 Crystal data and structure refinement for Ak_S2A_Lt_Cu.

Identification code	Ak_S2A_Lt_Cu
Empirical formula	$C_{13}H_{14}ClNO_3S$
Formula weight	299.76
Temperature/K	150.01(11)
Crystal system	triclinic
Space group	P-1
a/Å	5.7053(13)
b/Å	7.4896(14)
c/Å	15.760(2)
α/°	95.035(14)
β/°	96.062(16)
γ/°	92.300(17)
Volume/Å^3	666.2(2)
Z	2
ρ_{calc}g/cm^3	1.494
μ/mm^{-1}	4.044
F(000)	312.0
Crystal size/mm^3	0.389 × 0.353 × 0.233
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	11.34 to 133.78
Index ranges	$-6 \le h \le 6$, $-6 \le k \le 8$, $-18 \le l \le 18$
Reflections collected	3156
Independent reflections	2114 [R_{int} = 0.1199, R_{sigma} = 0.0723]
Data/restraints/parameters	2114/0/174
Goodness-of-fit on F^2	1.130

Final R indexes [I>=2σ (I)]	R_1 = 0.0886, wR_2 = 0.2426
Final R indexes [all data]	R_1 = 0.0967, wR_2 = 0.2588
Largest diff. peak/hole / e $Å^{-3}$	0.65/-0.73

Table 5.5 Hydrogen Bonds for Ak_S2A_Lt_Cu.

D	H	A	d(D-H)/Å	d(H-A)/Å	d(D-A)/Å	D-H-A/°
N1	H1A	O2	0.89	2.00	2.871(4)	165.7

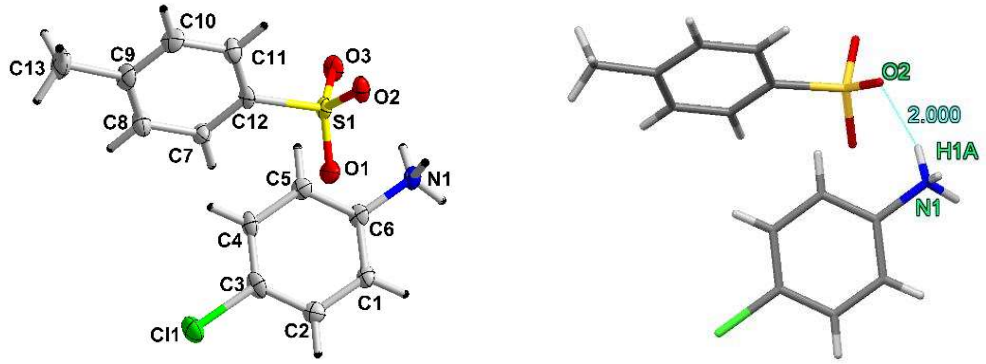
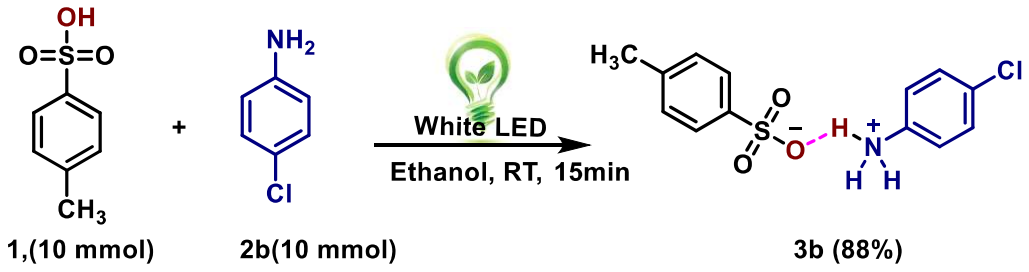


Figure 5.1 Crystal structure of 3b.

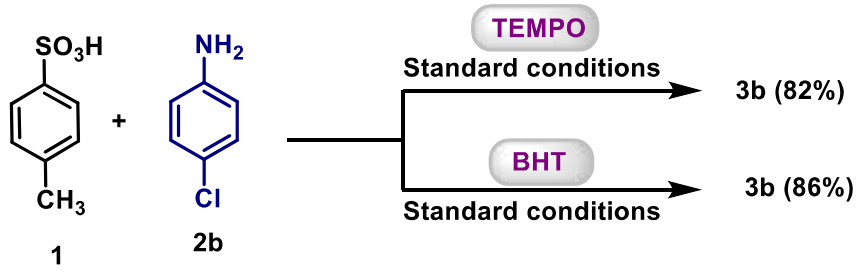
Additionally, we have also investigated the gram-scale applications for this reaction. Surprisingly this reaction is feasible (Scheme 5.3) and provided 88% of **3b**, with no significant loss of efficiency.



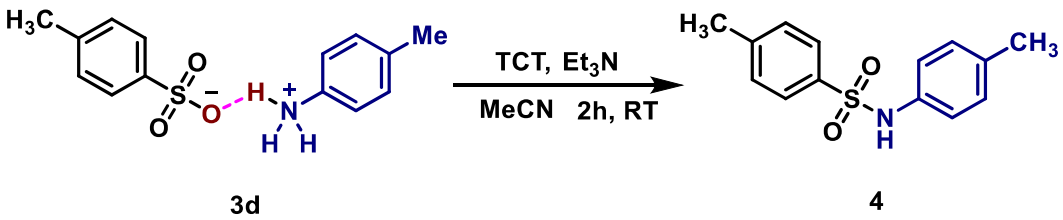
Scheme 5.3 Synthesis of 3b product on gram-scale

In order to propose the mechanism, some control experiments i.e., the model reaction, were performed with TEMPO (2,2,6,6-Tetramethyl-1-piperidinyloxy) and BHT (butylated

hydroxytoluene). However, there was no significant effect on the reaction. These reactions indicate that there is no involvement of the radical pathway. On the other hand, experimental data and UV spectra (UV-visible absorption spectra Figure 5.2) proved that the reaction occurs in the presence of visible light.



Scheme 5.4 Control Experiment



Scheme 5.5 Synthesis of sulfonamide from amine-sulfonate salt

Having generated a library of amine-sulfonate salt, some transformations of synthesized products were investigated. As shown in Scheme 5.5, sulfonamide was synthesized from amine–sulfonate salts using organic base triethylamine and cyanuric chloride as a catalyst in the presence of acetonitrile at room temperature in good to excellent yields [21].

5.4. Conclusions

In conclusion, we have successfully developed a mild, green, catalyst-free, and environment-friendly protocol for visible-light-initiated amine-sulfonate salts at room temperature. The prepared thermally stable and irreversible amine sulfonate salts are extremely useful in the

pharmaceutical industry. Mechanistic investigations reveal that reaction occurs in visible light, and there is no formation of genotoxic sulfonate ester as a side product.

5.5 Experimental procedures

5.5.1 General procedure for the preparation of compound 3a-3o

A mixture of amine derivatives **2** and *p*-toluenesulfonic acid **1** in ethanol solvent was stirred and irradiated by commercially available 12 W white LED for 15-45 min at room temperature. After completion of the reaction, the resulting precipitate of the product was recrystallized from ethanol.

5.5.2 General procedure for the preparation of compound 4

The solution of freshly prepared amine-derived sulfonate salt (0.01 mol) in anhydrous MeCN (40 mL) was added to TCT (0.0033 mol) and the reaction mixture was stirred at r.t. for 30 minutes. Next, Et_3N (0.012 mol) was added, and the solution was stirred for 30–90 min. The reaction mixture was concentrated under a vacuum, and the residue was dissolved in $CHCl_3$ (100 mL). The organic layer was washed with water (2 × 100 mL), dried over anhydrate Na_2SO_4, and evaporated in a vacuum. The residue was purified by short column chromatography on silica gel eluting with a mixture of PE–EtOAc.

5.6 UV-Visible absorption spectra

The sample was prepared by mixing *p*-toluenesulfonic acid and amine derivatives in a methanol solvent [Conc. reaction mixture = 1.25×10-4mol/L] in a light path quartz UV cuvette (Figure 5.2).

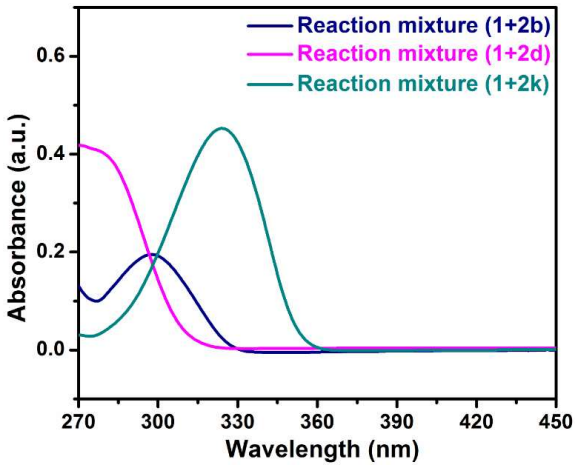


Figure 5.2. UV-vis absorption spectra of reaction mixtures of **(1+2b), (1+2d),** and **(1+2k)** in methanol at concentrations of 1.25×10^{-4}mol/L for each species.

5.7 Time profile of photocatalytic reaction with and without visible Light.

To explore the effect of visible light on the system, we carried out "On/Off" experiment (Figure 5.3). The On/Off experiments revealed that visible light irradiation could significantly promote the reaction (Figure 5.3a). In the dark reaction condition, it was observed that the reaction was stopped, and only a trace amount of product was obtained (Figure 5.3b). When the visible light source LED was turned off, the yields increased slowly with the prolongation of reaction time (Figure 5.3c). These experiments show that visible-light irradiation could significantly speed up the reaction.

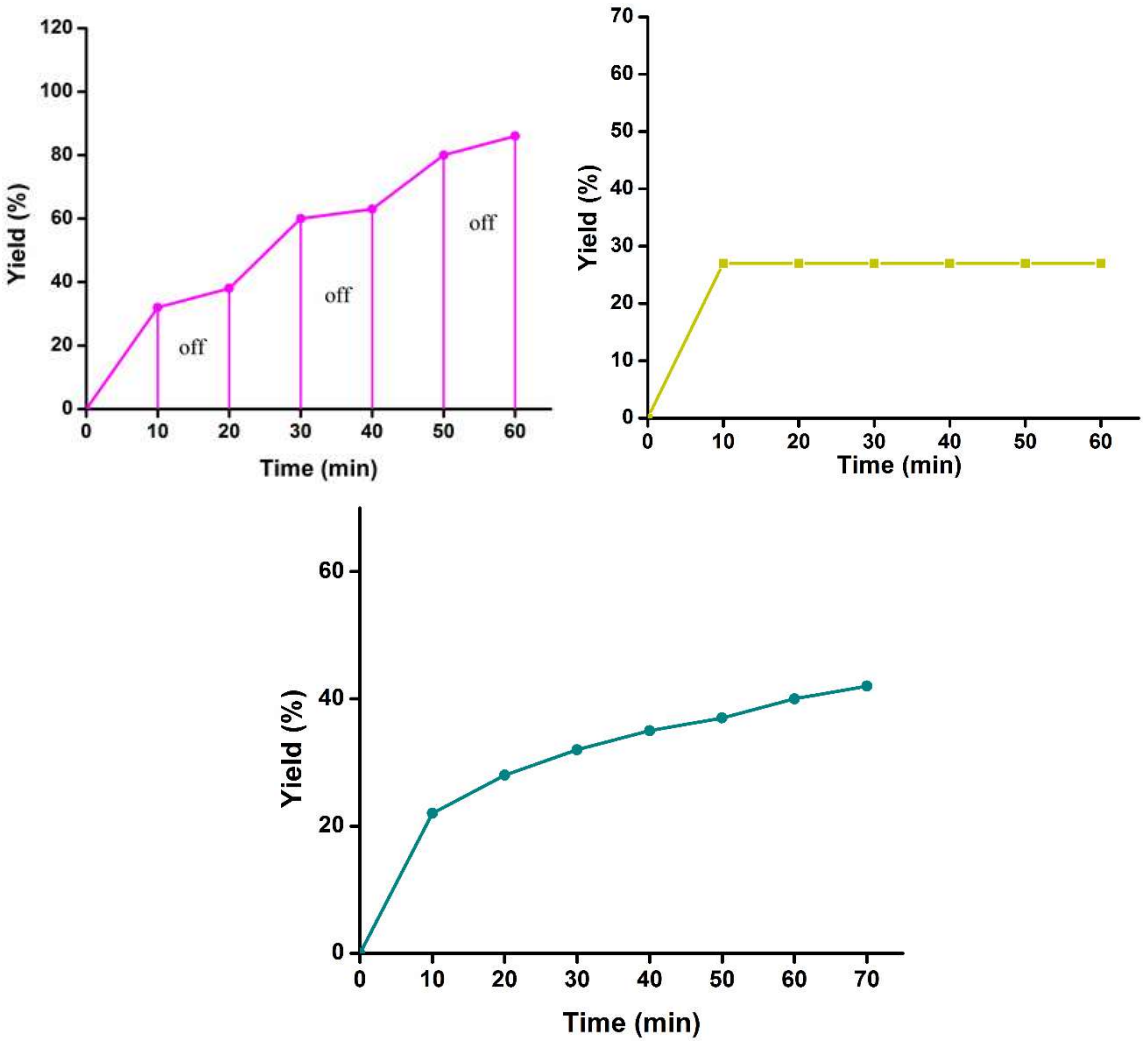
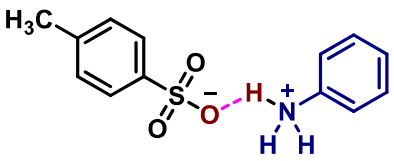


Figure 5.3 a) The "On–off" switching of the light source experiments to explore the effect of visible light; b) Dark experiments effect of reaction time (reaction carried out under dark reaction conditions c) Turn off white LED experiment (reaction without the light source)

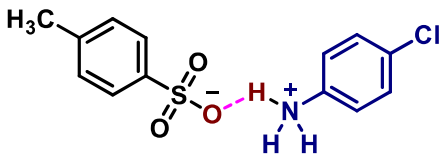
5.8 Characterisation of the products.

Aniline-sulfonate salt (3a)



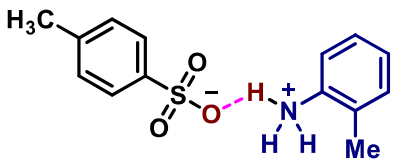
91% yield, Olive green crystal, m.p.: 182-183°C, ^{1}H NMR (500 MHz, DMSO) δ 7.52 – 7.47 (m, 4H), 7.44 – 7.39 (m, 1H), 7.34 (dd, *J* = 5.3, 3.3 Hz, 2H), 7.14 (d, *J* = 7.9 Hz, 2H), 2.28 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 145.56 (s), 138.50 (s), 132.47 (s), 130.31 (s), 128.66 (s), 128.47 (s), 125.94 (s), 123.41 (s), 21.25 (s). HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_{16}NO_3S$, 266.0850; found, 266.0849.

4-Chloroaniline-sulfonate salt (3b)



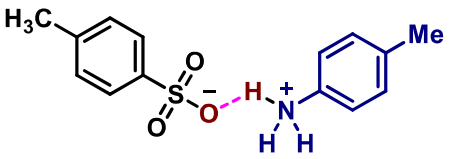
96% yield, White crystal, m.p.: 170-172°C, ^{1}H NMR (500 MHz, DMSO) δ 7.52 – 7.46 (m, 4H), 7.27 (d, *J* = 8.7 Hz, 2H), 7.13 (d, *J* = 7.9 Hz, 2H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 145.38 (s), 138.60 (s), 133.77 (s), 131.06 (s), 130.08 (s), 128.67 (s), 125.93 (s), 124.04 (s), 21.23 (s). HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_{15}ClNO_3S$, 300.0461; found, 300.0461.

2-Methylaniline-sulfonate salt (3c)



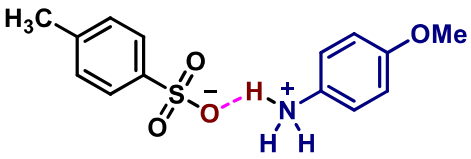
94% yield, White solid, m.p.: 192-193°C, ^{1}H NMR (500 MHz, DMSO) δ 9.72 (s, 3H), 7.49 (d, *J* = 7.9 Hz, 2H), 7.38 – 7.20 (m, 4H), 7.13 (d, *J* = 7.7 Hz, 2H), 2.31 (d, *J* = 11.4 Hz, 6H). ^{13}C NMR (126 MHz, DMSO) δ 145.81, 138.33, 131.91, 131.30, 128.58, 127.65, 125.94, 123.50, 21.26, 17.26. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{14}H_{18}NO_3S$, 280.1007; found, 280.1001.

4-Methylaniline-sulfonate salt (3d)



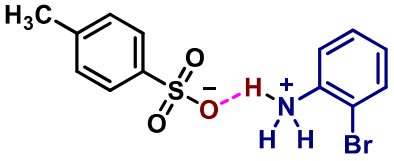
93% yield, White crystal, m.p.: 172-175°C, ^{1}H NMR (500 MHz, DMSO) δ 9.92 (s, 3H), 7.51 – 7.48 (m, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.28 – 7.24 (m, 2H), 7.14 – 7.12 (m, 2H), 2.32 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 145.69, 138.40, 130.68, 129.22, 128.63, 125.95, 123.52, 21.25, 20.99. HRMS (ESI-TOF) m/z: [M + H]+ calcd for $C_{14}H_{18}NO_3S$, 280.1007; found, 280.1001

4-Methoxyaniline-sulfonate salt (3e)



92% yield, White crystal, m.p.: 115-117°C, ^{1}H NMR (500 MHz, DMSO) δ 7.51 – 7.47 (m, 2H), 7.30 (d, *J* = 8.9 Hz, 2H), 7.13 (d, *J* = 7.8 Hz, 2H), 7.06 – 7.03 (m, 2H), 3.76 (d, *J* = 7.9 Hz, 3H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 159.37 (s), 145.80 (s), 138.34 (s), 128.61 (s), 125.95 (s), 124.91 (s), 124.21 (s), 115.40 (s), 55.93 (s), 21.25 (s). HRMS (ESI-TOF) m/z: [M + H]+ calcd for $C_{14}H_{18}NO_4S$, 296.0956; found, 296.0961.

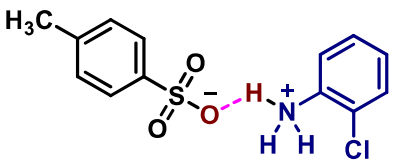
2-Bromoaniline-sulfonate salt (3f)



93% yield, White crystal, m.p.: 183-186°C, ^{1}H NMR (500 MHz, DMSO) δ 7.53 – 7.49 (m, 2H), 7.40 – 7.28 (m, 2H), 7.14 (d, *J* = 7.8 Hz, 2H), 6.83 – 6.79 (dd, *J* = 8.4, 0.5 Hz, 1H), 6.63 – 6.58 (m, 1H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 151.09, 145.38,

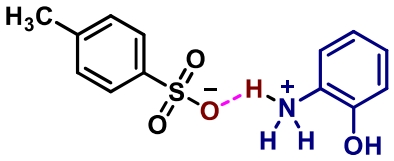
138.61, 134.53, 131.56, 128.69, 125.97, 119.05, 117.55, 117.33, 21.25. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_{15}BrNO_3S$, 343.9956; found, 343.9959

2-Chloroaniline-sulfonate salt (3g)



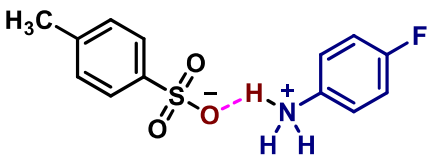
90% yield, White crystal, m.p.: 180-181°C, ^{1}H NMR (500 MHz, DMSO) δ 7.52 – 7.47 (m, 2H), 7.39 – 7.26 (m, 2H), 7.14 (dd, *J* = 8.4, 0.6 Hz, 2H), 6.80 (dd, *J* = 8.4, 0.5 Hz, 1H), 6.63 – 6.57 (m, 1H), 2.29 (s, 3H).^{13}C NMR (126 MHz, DMSO) δ 151.79, 145.57, 138.42, 134.44, 132.91, 128.63, 125.96, 118.56, 116.52, 115.77, 21.25. HRMS (ESI-TOF) m/z: [M + H]+ calcd for $C_{13}H_{15}ClNO_3S$, 300.0461; found, 300.0460

2-Hydroxyaniline-sulfonate salt (3h)



93% yield, Gray crystal, m.p.: 198-200°C, ^{1}H NMR (500 MHz, DMSO) δ 10.75 (s, 1H), 7.51 – 7.48 (m, 2H), 7.28 – 7.22 (m, 2H), 7.14 – 7.11 (m, 2H), 7.01 (dd, *J* = 8.1, 1.2 Hz, 1H), 6.88 (td, *J* = 7.7, 1.3 Hz, 1H), 2.29 (s, 3H).^{13}C NMR (126 MHz, DMSO) δ 154.43, 144.84, 144.60.138.99, 136.27, 128.83, 125.94, 113.95, 112.62, 21.25. HRMS (ESI-TOF) m/z: [M + H]+ calcd for $C_{13}H_{16}NO_4S$, 282.0800; found, 282.0808.

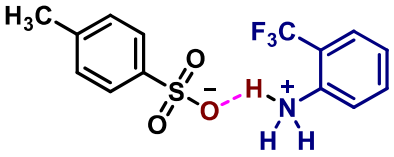
4-Floroaniline-sulfonate salt (3i)



88% yield, White solid, m.p.: 172-173°C, ^{1}H NMR (500 MHz, DMSO) δ 7.63 – 7.45 (m, 4H), 7.40 (d, *J* = 8.7 Hz, 2H), 7.08 (d, *J* = 7.04 Hz, 2H), 2.33 (s, 3H). ^{13}C NMR

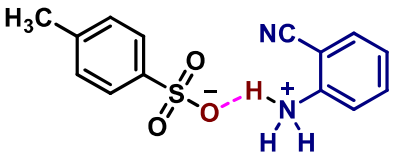
(126 MHz, DMSO) δ 151.79, 145.57, 138.42, 134.44, 132.91, 128.63, 125.96, 118.56, 21.25. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_{15}FNO_3S$, 284.6756; found, 284.6760

2-Trifluoromethylaniline-sulfonate salt (3j)



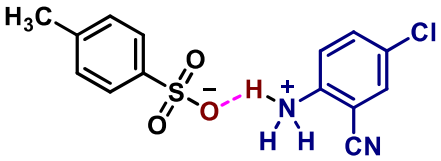
81% yield, white crystal, m.p.: 172-173°C, ^{1}H NMR (500 MHz, DMSO) δ 7.62 (t, *J* = 7.8 Hz, 1H), 7.55 (d, *J* = 6.2 Hz, 1H), 7.50 (d, *J* = 8.1 Hz, 3H), 7.46 (d, *J* = 6.6 Hz, 1H), 7.13 (d, *J* = 7.8 Hz, 2H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 145.37 (s), 138.61 (s), 137.70 (s), 131.35 (s), 130.92 (s), 130.66 (s), 130.41 (s), 128.68 (s), 125.93 (s), 125.30 (s), 123.13 (s), 121.92 (s), 117.76 (s), 21.23 (s). HRMS (ESI-TOF) m/z: [M + H]+ calcd for $C_{14}H_{15}F_3NO_3S$, 334.0724; found, 334.0729.

2-Cyanoaniline-sulfonate salt (3k)



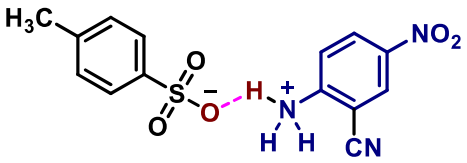
88% yield, White crystal, m.p.: 173°C, ^{1}H NMR (500 MHz, DMSO) δ 7.51 (d, *J* = 7.9 Hz, 2H), 7.32 (ddd, *J* = 20.3, 8.5, 4.6 Hz, 2H), 7.15 (d, *J* = 7.9 Hz, 2H), 6.82 (d, *J* = 8.4 Hz, 1H), 6.66 – 6.56 (m, 1H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 151.32 (s), 145.08 (s), 138.81 (s), 134.47 (s), 132.95 (s), 128.76 (s), 125.96 (s), 118.51 (s), 116.93 (s), 116.06 (s), 94.41 (s), 21.25 (s). HRMS (ESI-TOF) m/z: [M + H]+ calcd for $C_{14}H_{15}N_2O_3S$, 291.0803; found, 291.0800.

2-Chloro,5-cyanoaniline-sulfonate salt (3l)



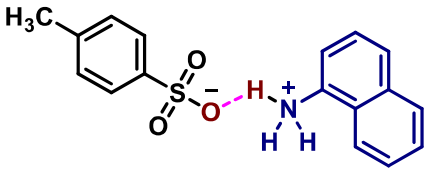
89% yield, White crystal, m.p.: 180°C, ^{1}H NMR (500 MHz, DMSO) δ 7.52 – 7.47 (m, 3H), 7.32 (dd, *J* = 9.0, 2.6 Hz, 1H), 7.13 (d, *J* = 7.8 Hz, 2H), 6.80 (d, *J* = 9.0 Hz, 1H), 5.84 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 151.13 (s), 145.62 (s), 138.45 (s), 134.54 (s), 131.58 (s), 128.64 (s), 125.97 (s), 118.99 (s), 117.52 (s), 117.35 (s), 94.82 (s), 21.26 (s). HRMS (ESI-TOF) m/z: [M + H]+ calcd for $C_{14}H_{14}ClN_2O_3S$, 325.0413; found, 325.0420.

2-Cyano,5-nitroaniline-sulfonate salt (3m)



79% yield, Yellow solid, m.p.: 184-185°C, ^{1}H NMR (500 MHz, DMSO) δ 7.52 – 7.47 (m, 3H), 7.32 (dd, *J* = 9.0, 2.6 Hz, 1H), 7.16 – 7.11 (m, 2H), 6.80 (d, *J* = 9.0 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 151.47 (s), 145.17 (s), 138.73 (s), 134.45 (s), 132.91 (s), 128.72 (s), 125.95 (s), 118.50 (s), 116.81 (s), 115.96 (s), 94.30 (s), 21.25 (s).HRMS (ESI-TOF) m/z: [M + H]+ calcd for $C_{14}H_{14}N_3O_5S$, 336.0654; found, 336.0650.

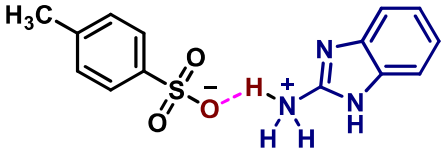
1-Naphthylamine-sulfonate salt (3n)



86% yield, Brown crystal, m.p.: 187°C, ^{1}H NMR (500 MHz, DMSO) δ 8.07 (d, *J* = 8.7 Hz, 1H), 7.99 (t, *J* = 6.8 Hz, 2H), 7.89 (s, 1H), 7.64 – 7.55 (m, 2H), 7.53 – 7.45 (m, 3H), 7.13 (d, *J* = 7.9 Hz, 2H), 2.28 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 145.55 (s), 138.53 (s), 133.15 (s), 132.40 (s), 130.43 (s), 129.90 (s), 128.66 (s), 128.35 (s), 128.17 (s),

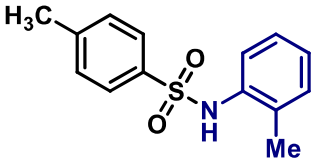
127.86 (s), 127.34 (s), 125.95 (s), 121.75 (s), 121.54 (s), 21.24 (s). HRMS (ESI-TOF) m/z: [M + H]+ calcd for $C_{17}H_{17}NO_3S$, 316.1007; found, 316.1017.

2-Aminobenzimidazole -sulfonate salt (3o)



90% yield, Yellow viscous liquid, ^{1}H NMR (500 MHz, DMSO) δ 12.49 (s, 2H), 8.44 (s, 2H), 7.55 (d, *J* = 8.1 Hz, 2H), 7.39 – 7.34 (m, 2H), 7.24 – 7.19 (m, 2H), 7.15 (d, *J* = 7.9 Hz, 2H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 151.06 (s), 145.30 (s), 138.70 (s), 130.06 (s), 128.73 (s), 125.96 (s), 123.54 (s), 111.81 (s), 21.24 (s).HRMS (ESI-TOF) m/z: [M + H]+ calcd for $C_{15}H_{17}N_2O_3S$, 305.0950; found, 305.0951.

4-Methyl-N-(o-tolyl) benzene sulfonamide (4)



92% yield, White crystal, m.p.: 106-108°C, ^{1}H NMR (500 MHz, DMSO) δ 9.97 (s, 1H), 7.55 – 7.49 (m, 2H), 7.29 (dd, J = 18.2, 8.3 Hz, 4H), 7.14 (d, J = 7.8 Hz, 2H), 2.31 (d, J = 12.4 Hz, 6H). HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{14}H_{16}NO_2S$, 262.0901; found, 262.0949.

5.9 Spectral data of products

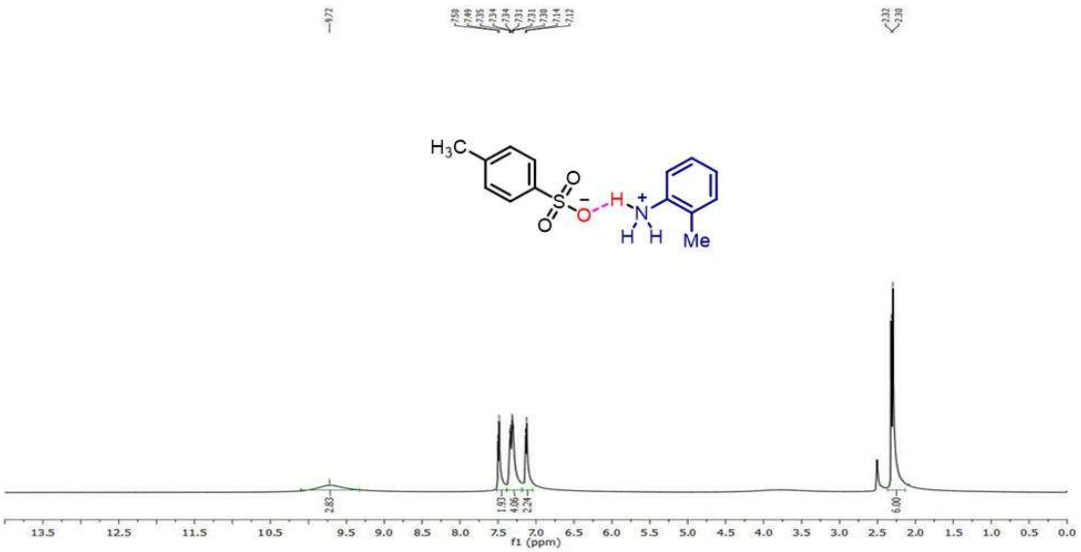


Figure 5.4 ^{1}H NMR spectrum of compound **3c**

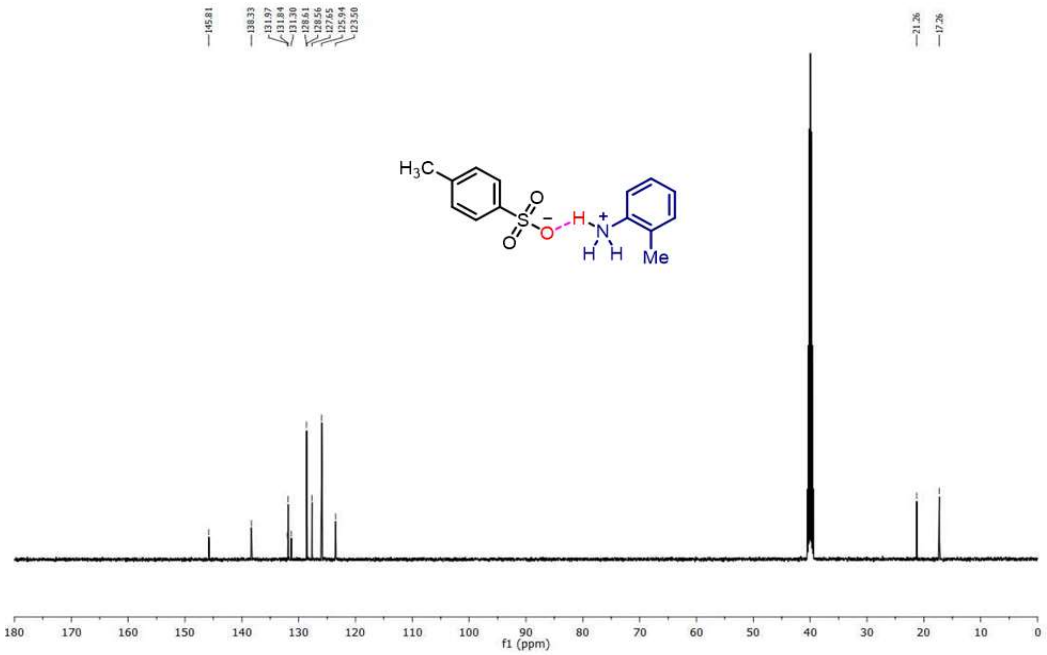


Figure 5.5 ^{13}C NMR spectrum of compound **3c**

5.10 References

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