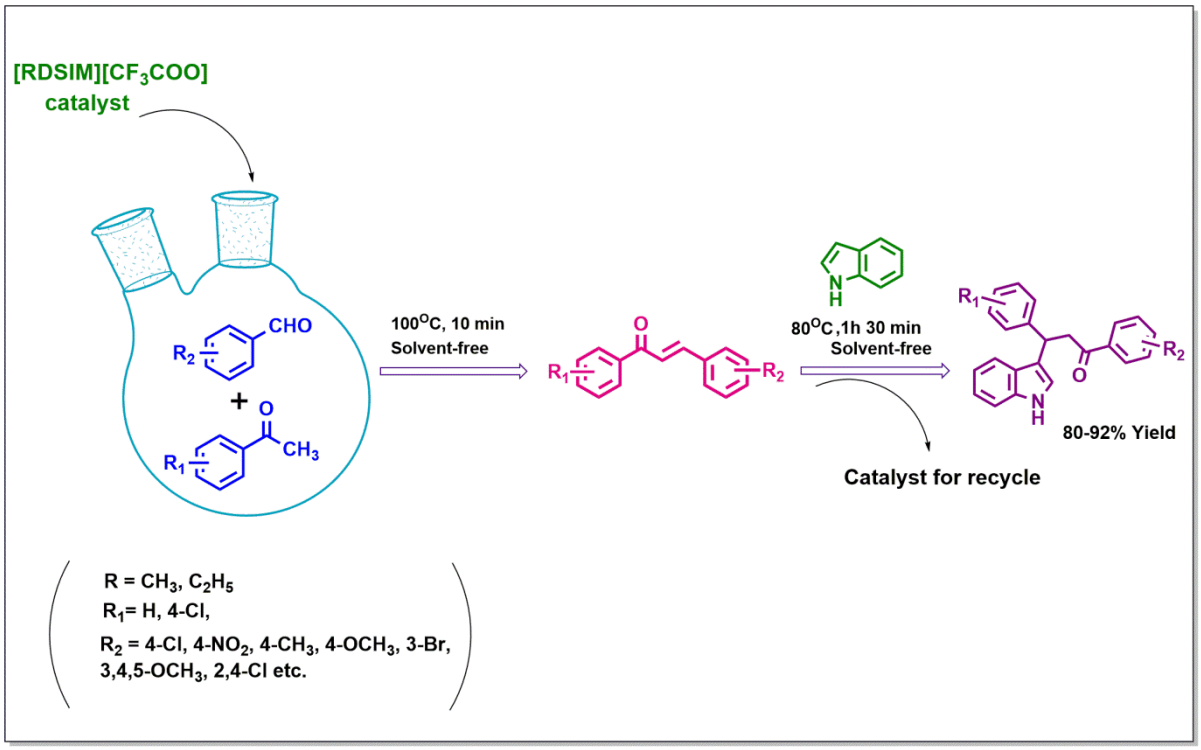
Chapter 5A

N-SO_3H functionalized Imidazolium Ionic Liquids Catalysed Sequential Michael-like Addition of Indole with Chalcones via Claisen-Schmidt Condensation



5A.1 Introduction

Heterocyclic compounds are extensively distributed in the form of various natural products like alkaloids, amino acids, vitamins and plant pigments. Indole derivatives form an important class of heterocycles and possess variety of biological activities like antifungal, antimicrobial, antiviral, anti-inflammatory and analgesic activities [1, 2]. They are abundant in nature as flower scents, perfumes, and coal tar. It has been observed that 3-alkylated indoles are important building blocks for synthesis of various biologically potent compounds. The 3- position of indole moiety is the preferred site for electrophilic substitution and this fact is often utilized for the preparation of 3-alkylated derivatives of indole [3].

The primary preparation route of 3- alkylated indole involves Michael-like addition reaction of indole with α, β-unsaturated ketones using either Brønsted or Lewis acid catalysts. Chalcones represent a class of α, β-unsaturated aromatic ketones that are present as the core unit in variety of biologically active molecules with antibacterial, anti-inflammatory, antiviral, antioxidant, antituberculosis, anticancer and antifungal activities [4-6]. Chalcones are also naturally available precursors of flavonoids and isoflavonoids [7]. Further, they are also employed as reaction precursors to get pyrazoles [8], isoxazoles [9] and thiazoles [10]. The conventional synthetic route for the synthesis of chalcones involves Claisen-Schmidt condensation between acetophenone derivatives and aromatic aldehydes and utilize strong acidic or basic reagents/catalysts like NaOH, $Ba(OH)_2$, KOH, $AlCl_3$ and HCl [11, 12]. This traditional catalysts however come with several drawbacks like difficulty in catalyst recovery, side product formation, less product selectivity, longer reaction time, extreme reaction conditions and complicated isolation of products [11]. A number of Lewis /Brønsted acids, [13,14], solid acids [15,16] and solid bases [17-21] were later introduced for this condensation reaction to overcome the earlier difficulties. However, only to moderate success was obtained with these catalysts. Additionally, environmentally benign strategies were employed for the synthesis of chalcones using ionic liquids [22-26], supercritical fluids [27], glycerine [28], microwave irradiation [29] and ultrasound-assisted conditions [30]. The literature review provided us a few examples involving the use of task-specific acidic ionic liquids in the synthesis of chalcones. Dong et al. utilised N-alkane sulfonic acid functionalized Brønsted acidic ammonium based ionic liquids as dual solvent-catalyst systems for the Claisen-Schmidt condensation between acetophenone derivatives and aromatic

aldehydes at 140 °C for 4 hours under inert atmosphere [25]. Shen et al. employed N-alkylsulfonic functionalized imidazolium ILs for the synthesis of chalcones at 140 °C under solvent-free conditions [22]. Kunde et al. [23], Qian et al. [30], Davoodonia et al. [31] and Sarda et al. [32] also reported the synthesis of chalcones using task-specific ionic liquids (TSILs). These task-specific ionic liquids (ILs) functioned as non-corrosive and recyclable safer alternatives to the conventional non-reusable and corrosive acidic/basic reagents/catalysts [33].

The Michael-like addition of indoles to the chalcones that gives us the biologically important 3-substituted indoles have been conducted using various catalysts such as cerium trichloride, antimony chloride, triflic acid, bismuth nitrate, niobium pentachloride etc. [34-38]. Recent reports on the use of acidic ionic liquids as catalysts/solvents in the synthesis of 3-substituted indoles are also available. Liu and co-workers reported the use of N-alkyl $–SO_3H$ functionalized pyridinium, benzimidazolium and thiazolium based BAILs as catalysts in acetonitrile for the above synthesis of [39-41]. Gu et al. [42], Hagiwara et al. [43] and Yadav et al. [44] have also utilised ILs as dual solvent-catalyst in the Michael-like addition of indoles to chalcones.

Based on the advantages of the task-specific ionic liquids as environmentally safer catalysts/solvents and the success obtained from their use in various organic transformations, we planned the use of N-SO_3H functionalized BAILs in the sequential synthesis of 3-substituted indoles by Michael-like addition of indole with chalcones via Claisen-Schmidt condensation. In this work, we were interested to explore the catalytic activities of two series of direct N-SO_3H functionalized imidazolium ILs i.e. 2-methyl/2-ethyl-1,3-disulfoimidazolium carboxylate ionic liquids [MDSIM][X] and [EDSIM][X], (where, X = CF_3COO^-, CCl_3COO^-, CH_3COO^-) (**Scheme 3.1, Chapter 3**) for one-pot synthesis of 3-substitited indoles after selective formation of the chalcones involving Claisen-Schmidt condensation and consecutive Michael-like addition of indole (**Scheme 5A.1**).

5A.2 Results and Discussion

5A.2.1 Characterization of the N-SO_3H functionalized Brønsted acidic ionic liquids (BAILs)

In the present work, total eight numbers of (**Fig.5A.1**) 2-methyl/2-ethyl-1,3-disulfoimidazolium carboxylate ionic liquids [MDSIM][X] and [EDSIM][X] (where X = Cl-, CF_3COO^-, CCl_3COO^-, CH_3COO^-) were synthesized as per the standard method given in **Chapter 3 (Experimental section 3.4, Scheme 3.1)** [45]**.** The characterization of the four Cl- and CF_3COO^- anion containing ionic liquids is already given in the **Chapter 3**. The structural characterization of the other four BAILs containing CCl_3COO^- and CH_3COO^- anions were done using NMR (^1H & ^{13}C), FT-IR and elemental analysis. Comparative thermogravimetric analysis (TGA) and UV-vis Hammett acidity study of the synthesized ILs were performed to identify the most acidic and thermally stable BAILs for their exploration as efficient reusable acidic catalyst for the two-step one-pot preparation of 3-substituted indole derivatives (**Scheme 5A.1**).

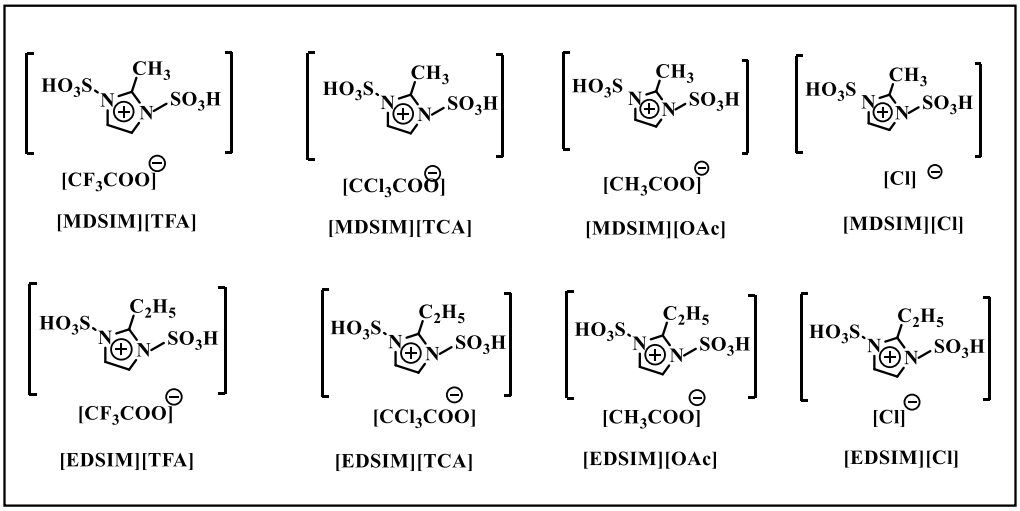
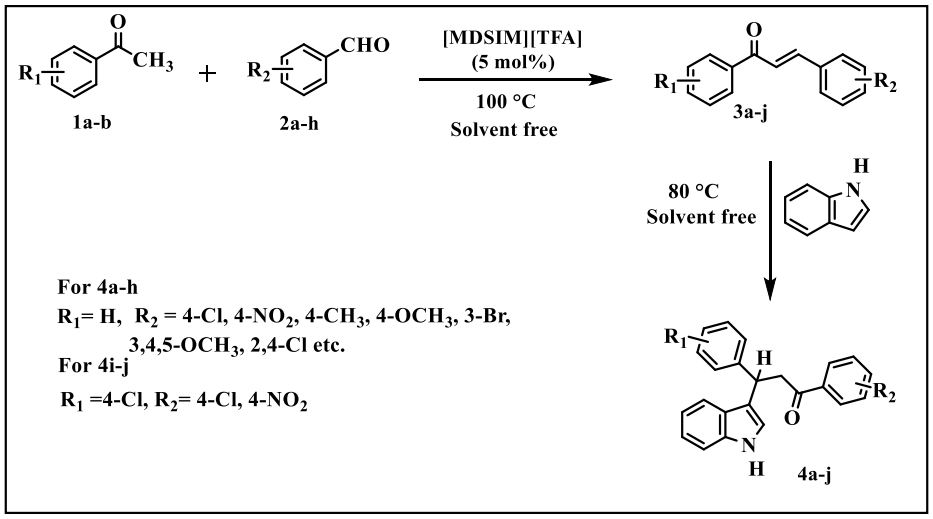


Fig. 5A.1: Structures of the eight ([MDSIM]/[EDSIM]) based ILs.

5A.2.1.1 FT-IR analysis

The pairing of carboxylate anions with the 2-alkyl-1,3-disulfoimidazolium cation can be confirmed from the FT-IR spectra of the six [MDSIM]/[EDSIM] carboxylate ILs in the region of 500-2000 cm^{-1}. **Fig.5A.2 (A & B)** displays the FT-IR spectra of the [MDSIM] and [EDSIM] carboxylate ILs respectively. The FT-IR band assignments of the ILs are listed in **Table 5A.1**.



Scheme 5A.1: One pot two step synthesis of 3-substituted indoles.

Table 5A.1. FT-IR band assignments of the ILs.

Peaks (cm^{-1})	Assignments
572–587	$–SO_3H$ (bending)
750-760	out of plane ring bending of C-H bond
870-885	N–S stretching
1040–1060	S–O symmetric stretching
1165–1195	S–O asymmetric stretching
1441-1468	C-H bending of $-CH_3$ group
1620–1640	-C=C- stretching
1720–1780	C=O stretching

5A.2.1.2 NMR analysis

The ^{1}H NMR spectra of these ILs clearly show two acidic proton signals around 13.9-11.9 ppm for the $-SO_3H$ groups. For the two -CH protons of the imidazolium ring we get peaks at 7.5-7.3 ppm. The proton signals of CH_3/C_2H_5 groups at C-2 position of the imidazolium cation are observed in aliphatic region. The pairing of carboxylate anions with the 2-alkyl-1,3-disulfoimidazolium cations can be confirmed from the presence of ^{13}C NMR peak of C=O group at 155-170 ppm.

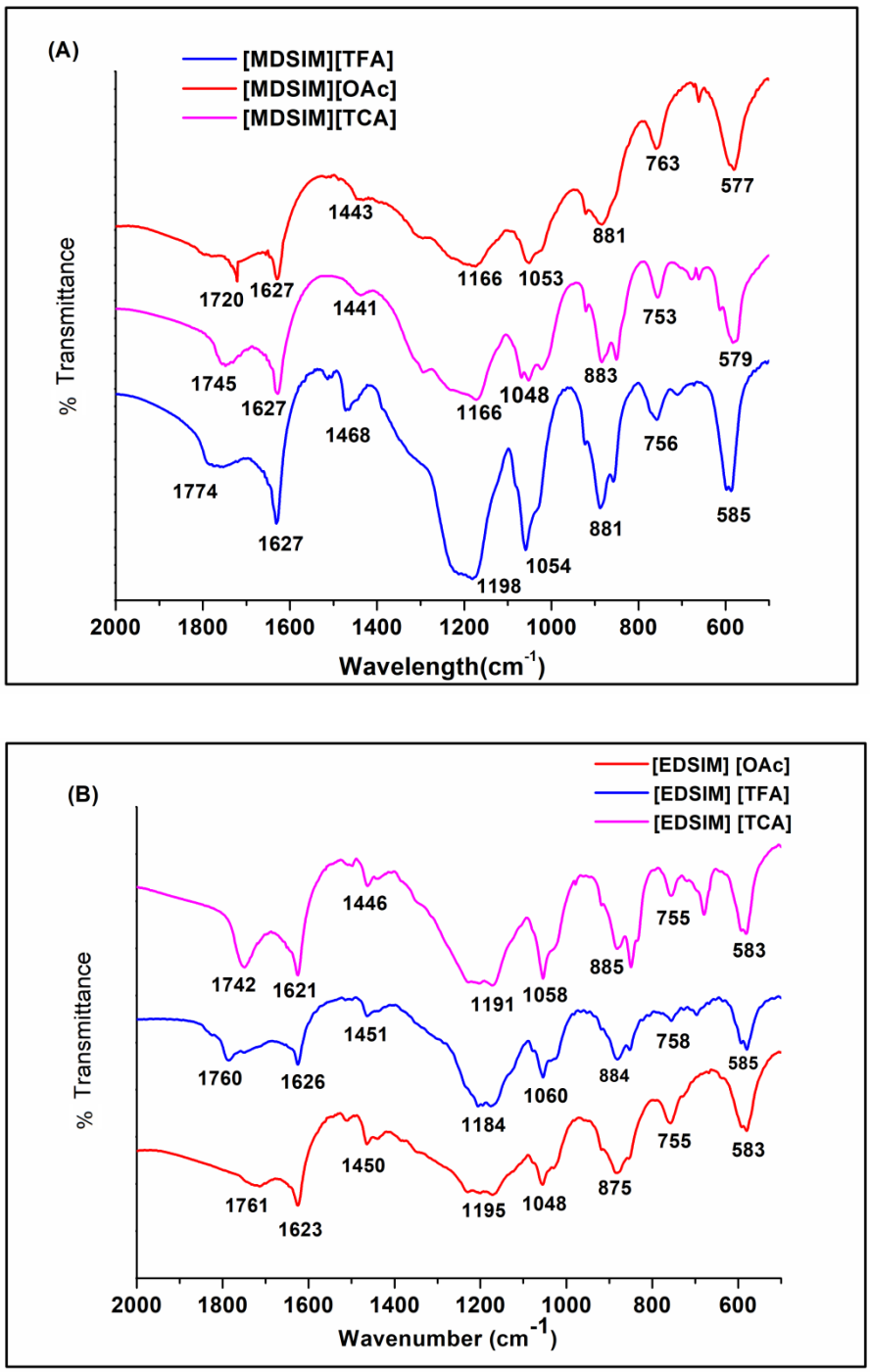


Fig. 5A.2: FT-IR spectra of (A) [MDSIM] series ILs (B) [EDSIM] series ILs in the 500-2000 cm^{-1} region.

5A.2.1.3 Hammett acidity of the BAILs

The Brønsted acidities of the two series of ionic liquids [MDSIM][X] and [EDSIM][X] (where X = Cl^-, CF_3COO^- (TFA), CCl_3COO^- (TCA) & CH_3COO^- (TCA)) were determined from the UV-visible Hammett plots **Fig. 5A.3 (A & B)** by calculating their

Hammett acidity functions H^o using the **Equation 1.4** from **Chapter 1**. The lowering of observed H^o values for any IL expresses more acidic strength among all the ILs. **Table 5A.2** contains the calculated H^o values of all the ILs. The decreasing order of Hammett acidities of the two series of ILs can be written as : [MDSIM] series : [MDSIM][TFA] > [MDSIM][TCA] > [MDSIM][OAc] > [MDSIM][Cl] and [EDSIM] series : [EDSIM][TFA] > [EDSIM][TCA] > [EDSIM][OAc] > [EDSIM][Cl]. This is the exact order of the pKa values of the corresponding carboxylic acids: CF_3COOH (1.2), CCl_3COOH (1.6), CH_3COOH (2.2). Furthermore, from the H^o values, it can be seen that the [MDSIM] series is slightly more acidic compared to the [EDSIM] series. Thus, the acidity of the two series of ILs were both affected by the alkyl chain length of the imidazolium cation and the nature of the anion.

Table 5A.2: Hammett acidity functions H^o of the ionic liquids**.**

Entry	IL	A_{max}	[I]%	[HI]%	H^o
1	4-nitroaniline	0.95	100	-	-
2	[MDSIM][Cl]	0.46	48.42	51.57	0.97
3	[MDSIM][TFA]	0.29	30.42	69.58	0.64
4	[MDSIM][TCA]	0.32	33.68	66.31	0.70
5	[MDSIM][OAc]	0.36	37.89	62.10	0.78
6	[EDSIM][Cl]	0.51	53.15	46.85	1.05
7	[EDSIM][TFA]	0.33	35.08	64.92	0.72
8	[EDSIM][TCA]	0.41	42.75	57.25	0.86
9	[EDSIM][OAc]	0.47	52.31	47.69	1.03

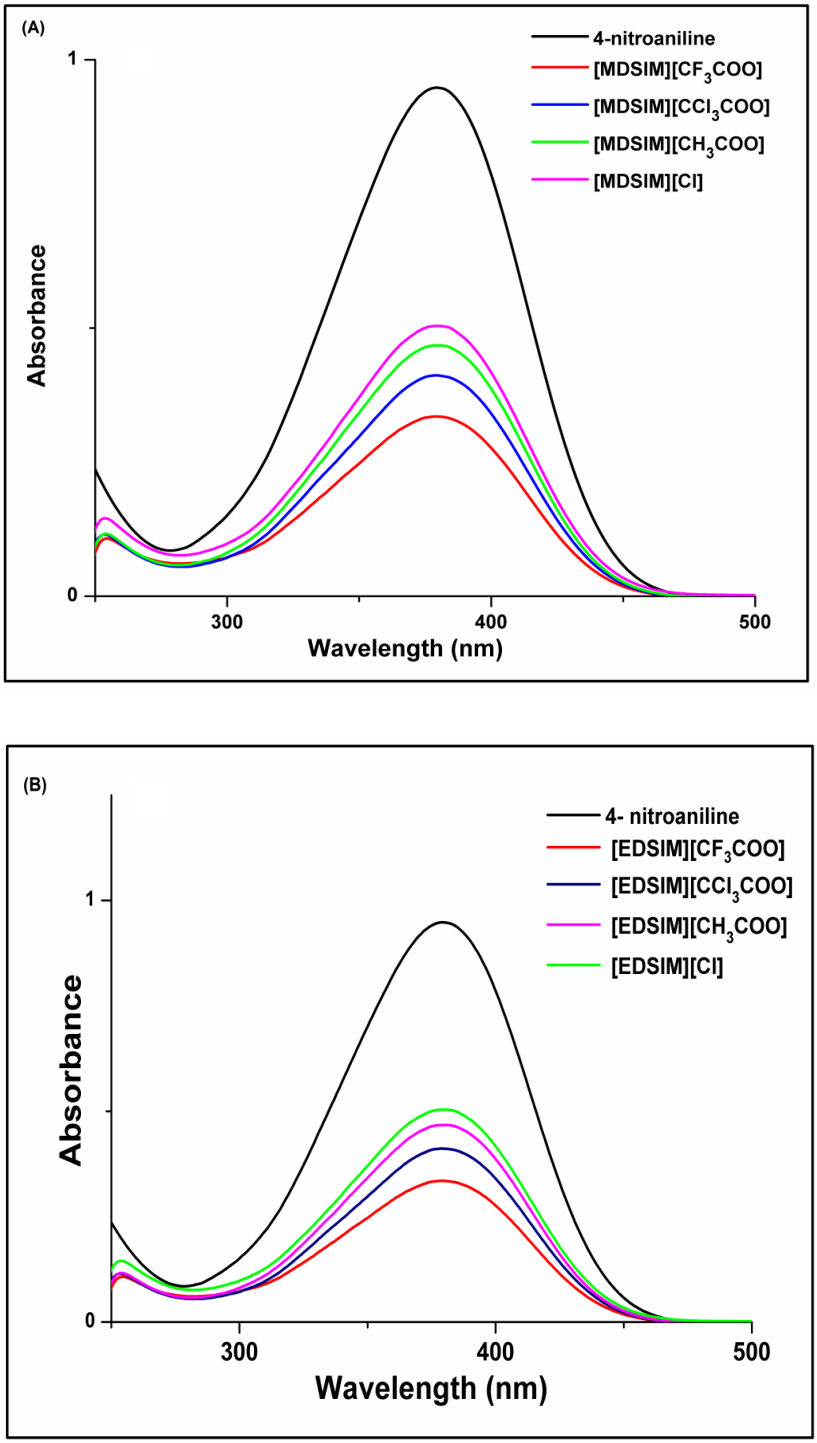


Fig. 5A.3: Hammett plot of BAILs (A) [MDSIM] series ILs and (B) [EDSIM] series ILs.

5A.2.1.4 Thermogravimetric analysis

The two series of ILs displayed a similar three step degradation pattern as seen from their TGA plots in **Fig. 5A.4 (A & B)**. The first degradation was observed around 100 °C, which can be attributed to the release of physisorbed water. For the [MDSIM][X] series, a maximum weight loss of 37% around 100 °C for the physisorbed water was observed

in case of [MDSIM][OAc]. It was followed by [MDSIM][TCA] with 29% weight loss. Among the four ILs, [MDSIM][TFA] and [MDSIM][Cl] were the least hydrophilic ones with only 16% and 17% weight loss around 100 °C. For the [EDSIM][X] series, [EDSIM][Cl] was found to be the least hydrophilic one with only 11% weight loss around 100°C. It was followed by [EDSIM][TFA] and [EDSIM][OAc] with 15% and 20% weight loss around 100°C. However, [EDSIM][TCA] showed a slightly different behaviour than the other ILs. Its TGA profile exhibited a 48% weight loss that started around 100 °C and extended up to 173 °C, making it the least thermally stable of the eight ILs. The other seven ILs displayed thermal stability up to 250-260 °C, with only a slight variation based on the sizes of alkyl groups and anions. A further weight loss was observed in the range of 320-350 °C.

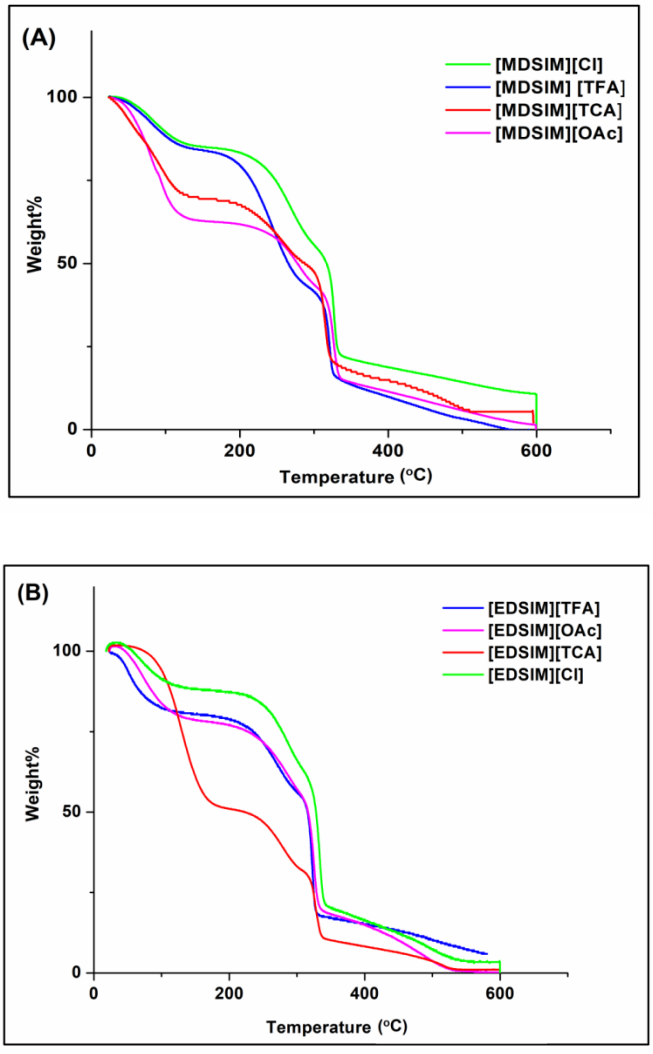


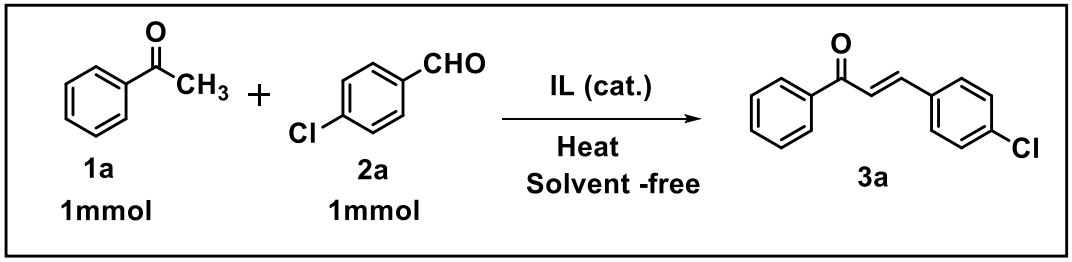
Fig. 5A.4: TGA plots of (A) [MDSIM] series ILs (B) [EDSIM] series ILs.

5A.2.2 Catalytic Study

The catalytic activities of the most acidic and thermally stable ionic liquid from each series, i.e. [MDSIM][TFA] and [EDSIM][TFA], were explored for the synthesis of 3-substituted indoles according to **Scheme 5A.1**. The catalytic activities of these two Ils were compared to that of CF_3COOH for the preparation of chalcones in the first step.

5A.2.2.1 Selective formation of chalcones

Catalyst amount and reaction temperature were optimized by conducting a model reaction (**Scheme 5A.2**) of 4-Cl benzaldehyde (1 mmol) and acetophenone (1 mmol) using 2 and 5 mol% of the [MDSIM][TFA] and [EDSIM][TFA] IL catalysts under solvent-free conditions at different temperatures (100 °C, 80 °C, 60 °C and 25 °C, **Table 5A.3**). It was found that 5 mol% of the [MDSIM][TFA] provided the best yield (98%) for the product **3a** at 100 °C in 10 minutes (**Table 5A.3,** entry 2**)**. The same catalyst however took 20 minutes at 80 °C to give a yield of 90 % (**Table 5A.3,** entry 5**)**. The reaction required more time with 2 mol% of both the IL catalysts at 100 °C (**Table 5A.3,** entries 1, 3). The use of CF_3COOH (2 and 5 mol%) produced a mixture of products with lower yields of **3a** at 40 °C and 60°C (**Table 5A.3, entries** 11, 12, 13). The results implied that CF_3COOH is not a suitable catalyst for the preparation of chalcones as a single product and both the ILs displayed better catalytic activity. Thus, [MDSIM][TFA] was identified as the best catalyst for the preparation of chalcones. On the other hand, no reaction occurred in absence of the [MDSIM][TFA] catalyst under solvent-free treatment at 100 °C for several hours.



Scheme 5A.2: Synthesis of chalcone by Claisen-Schmidt condensation.

Table 5A.3: Optimization of reaction conditions for Claisen-Schmidt condensation.

Entry	Catalyst	IL mol%	Temperature (°C)	Time (min.)	% Yield[a] (3a)
1	[MDSIM][TFA]	2	100	25	95
2	[MDSIM][TFA]	5	100	10	98
3	[EDSIM][TFA]	2	100	30	92
4	[EDSIM][TFA]	5	100	15	94
5	[MDSIM][TFA]	5	80	20	90
6	[EDSIM][TFA]	5	80	35	85
7	[MDSIM][TFA]	5	60	30	84
8	[EDSIM][TFA]	5	60	45	80
9	[MDSIM][TFA]	5	25[b]	4h	66
10	[EDSIM][TFA]	5	25[b]	6h	58
11	CF_3COOH	2	60	5h	45
12	CF_3COOH	5	60	4h	50
13	CF_3COOH	5	40	7h	40

[a] Isolated yields, [b] Room-temperature grinding.

After that the model reaction (**Scheme 5A.2**) was conducted in a variety of solvents, both polar and non-polar (water, ethanol, ethyl acetate, acetonitrile, and dichloromethane) using 5 mol% of the [MDSIM][TFA]. The products were obtained with 50-80 % yields for 2.5-12-hour reactions (**Table 5A.4**).

Table 5A.4: Study of solvent effects on the model compound (**3a**).

Entry	Solvent	Temperature (°C)	Time (h)	% Yield[a] (3a)
1	CH_3CN	82	8	60
2	CH_2Cl_2	25	12	58
3	EtOH	78	6	65
4	EtOAc	77	2.5	80
3	H_2O	100	24	50

[a] Isolated yields

The use of solvents didn't exhibit any beneficial effects on the product yield and in fact increased the reaction time. Hence, we extended our study in solvent-free conditions by varying the substituted aromatic aldehydes and ketones to produce a variety of the chaconnes (**Fig. 5A.5**).

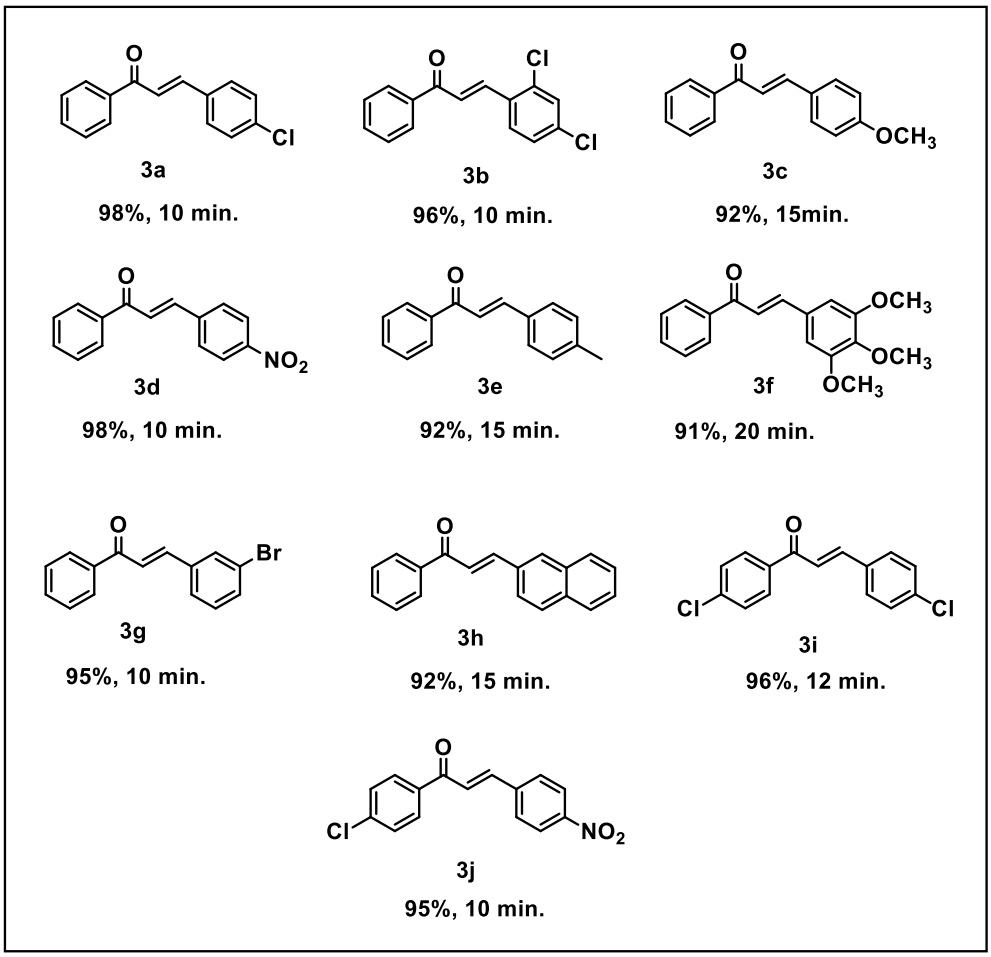


Fig. 5A.5: Structures of the synthesised chalcones.

5A.2.2.2 Sequential synthesis of 3-substituted indoles

The crude mixture of chalcone **3a** obtained in the 1st step, using 5 mol% of [MDSIM][TFA] under solvent-free conditions, was treated with the indole (1 mmol) by varying the reaction temperature (60°C, 80°C and 100 °C) to obtain the optimum reaction temperature (**Scheme 5A.1, Table 5A.5**). The optimum temperature for the conjugate addition of indole with the crude chalcone **3a** to produce the 3-substituted indole **4a** was found to be 80 °C (**Table 5A.5,** entry 2).

Utilising the optimized conditions (**Table 5A.3,** entry 2 **and Table 5A.5,** entry 2), a number of Michael adducts were prepared by varying the aromatic aldehydes and

ketones. The reaction proceeded successfully for all the different combinations of aromatic aldehydes and ketones (**Fig.5A.5**). However, a slightly better yield was observed in case of the chalcnoes prepared from aromatic aldehydes with electron withdrawing groups (**Fig.5A.6, 4a, 4d, 4i & 4j**).

Table 5A.5: Optimisation of the reaction temperature for the 2nd step**.**

Entry	1st step		2nd step		% Yield[a]
	Temperature (°C)	Time (min.)	Temperature (°C)	Time (min.)	
1	100	10	100	1h 20 min.	90
2	100	10	80	1h 30 min.	90
3	100	10	60	2h 15 min.	85

[a] Isolated yields

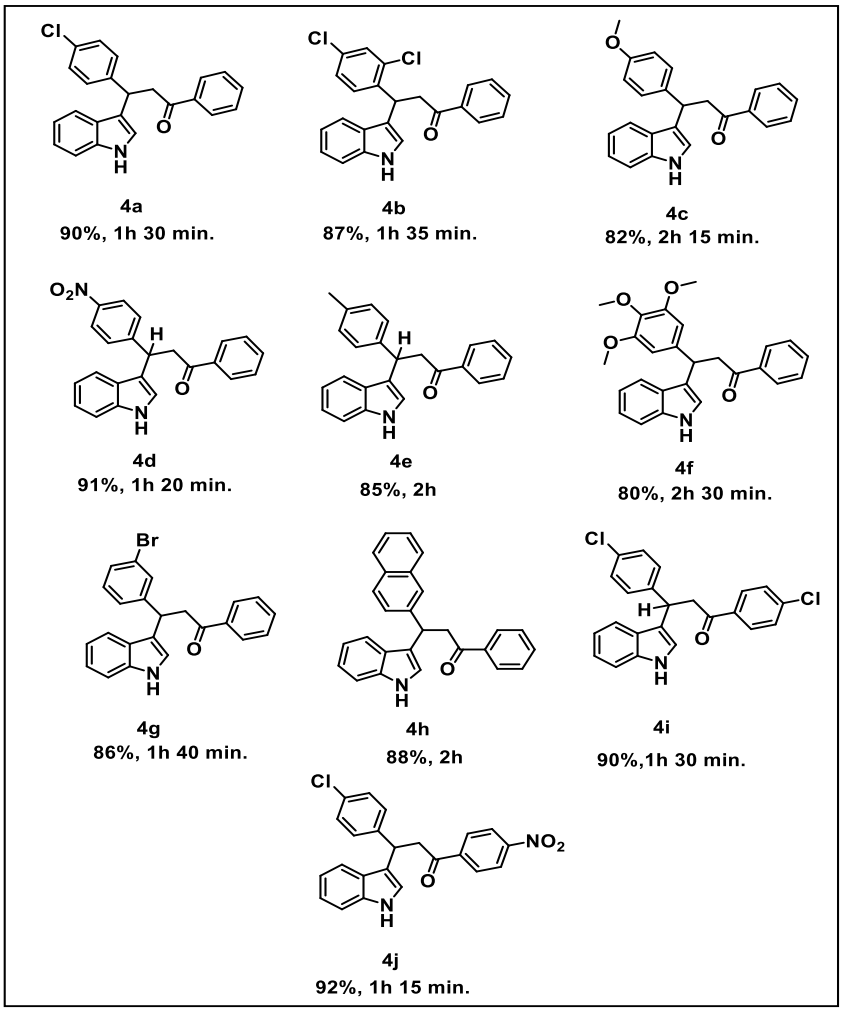
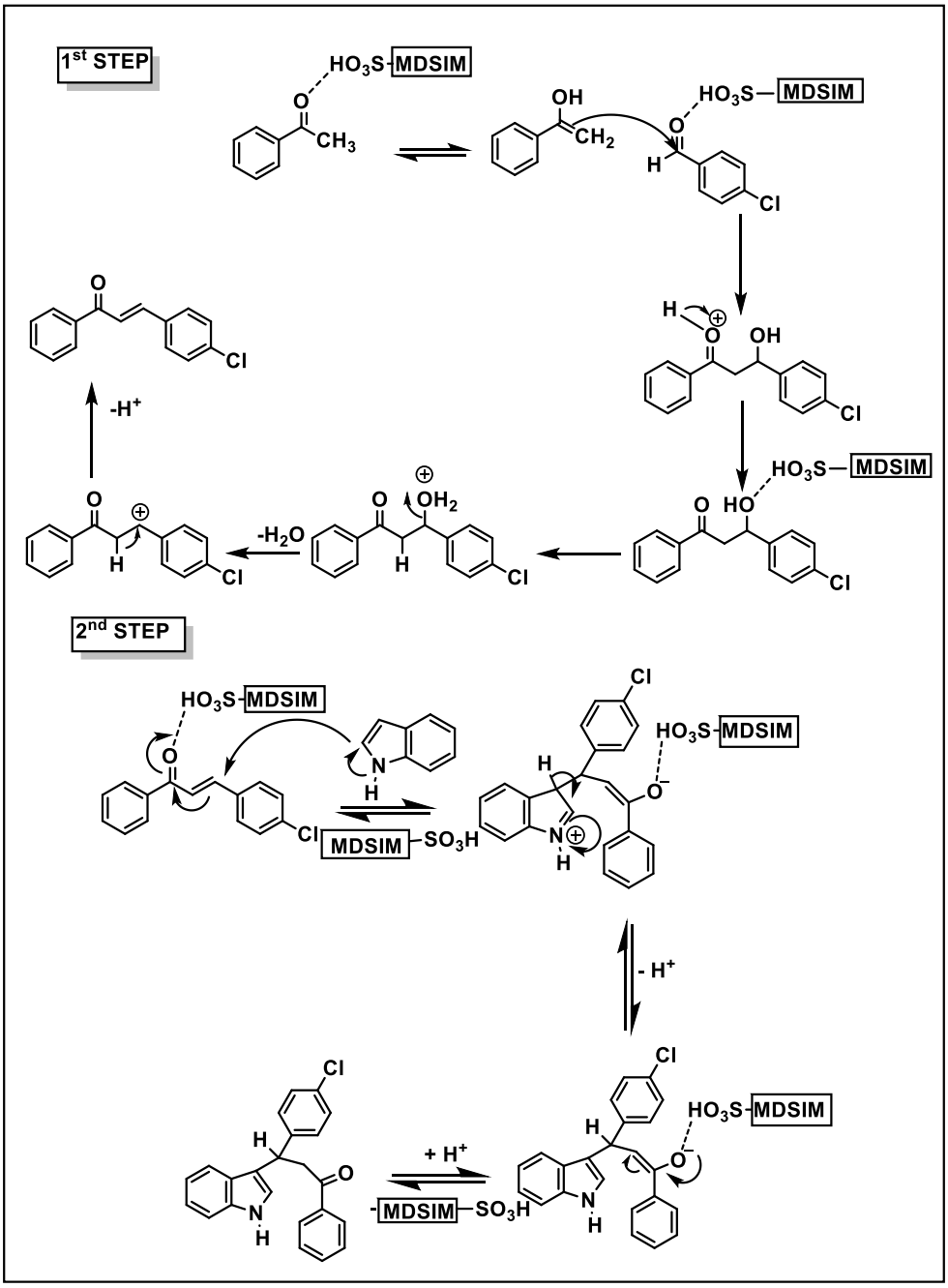


Fig. 5A.6: Structures of the synthesised 3-substituted indoles.

5A.2.2.3 Plausible mechanism

The acid catalysed activation of the carbonyl groups in both the substrate molecules of the Claisen-Schmidt condensation is the key factor for selective formation of the chalcones in the 1st step of reaction. This is followed by activation of the carbonyl group of chalcones by the same IL in the 2nd step, facilitating the Michael like addition of the indole, as shown in **Scheme 5A.3.**



Scheme 5A.3: The plausible mechanism for the formation of Chalcone (**3a**) and 3-substituted indole (**4a**) catalysed by the IL [MDSIM][TFA].

5A.2.2.4 Catalyst recyclability

The catalyst [MDSIM][TFA] was successfully recycled up to four times for the model reaction in 3 mmol scale by dissolving the product **4a** in ethyl acetate (**Scheme 5A.1**). The catalyst is insoluble in ethyl acetate and hence, could be easily separated as a viscous liquid inside the reaction vessel and can be used for the next cycle. The recyclability study revealed that the reaction time increased after each consecutive cycle **(Fig. 5A.7)**, with only a slight decrease in the activity of the BAIL. This decrease can be attributed to the repeated washing of the catalyst with organic solvents during the work-up steps. The FT-IR spectrum of the recycled catalyst after the 4th cycle supported the retention of original peaks of the fresh one **(Fig. 5A.8)**.

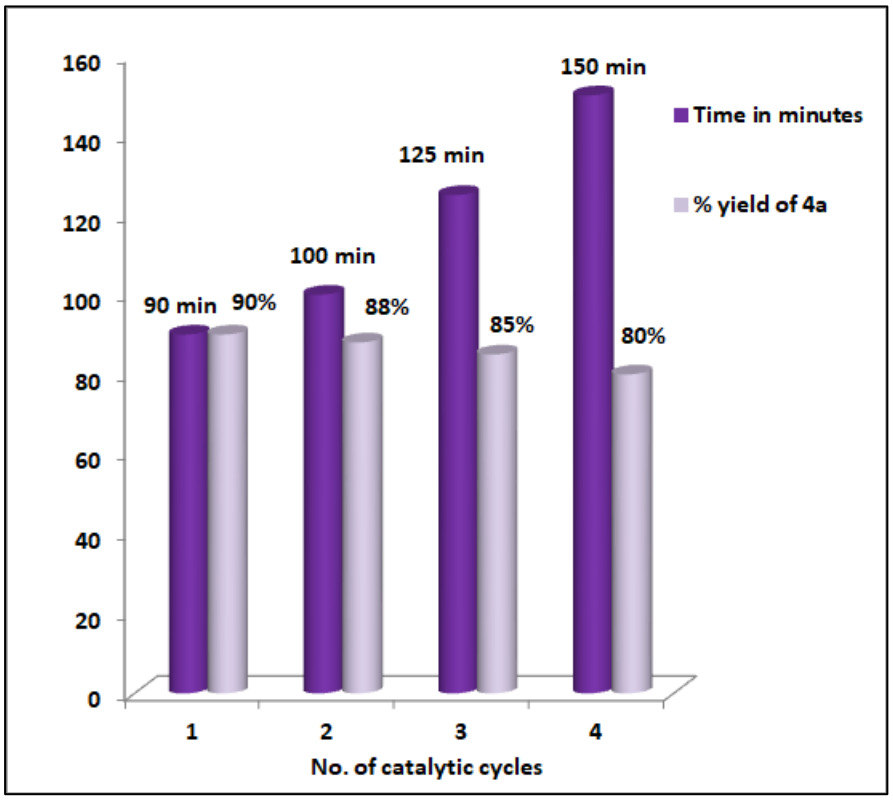


Fig. 5A.7: Recyclability profile of the IL [MDSIM][TFA].

5A.3 Summary

This work was focused on exploring the catalytic activity of -SO_3H functionalized imidazolium ILs in the one-pot sequential synthesis of 3-substitued indoles via selective formation of the chalcones as precursors. The high thermal stability and Brønsted acidity

of the two series of -SO_3H functionalized imidazolium ionic liquids made them suitable candidates for catalyzing the titled reactions. [MDSIM][TFA] was found to be the best catalyst. This is a simple and efficient acidic ionic liquid catalyzed strategy for preparation of the chalcones and also for the 3-substituted indoles under environmentally safe and acceptable conditions, avoiding the complicated separation techniques and toxic/or corrosive catalysts/reagents. Moreover, the easy recycling of catalyst and isolation of products, along with the wide functional group tolerance make this procedure eligible for further catalytic applications.

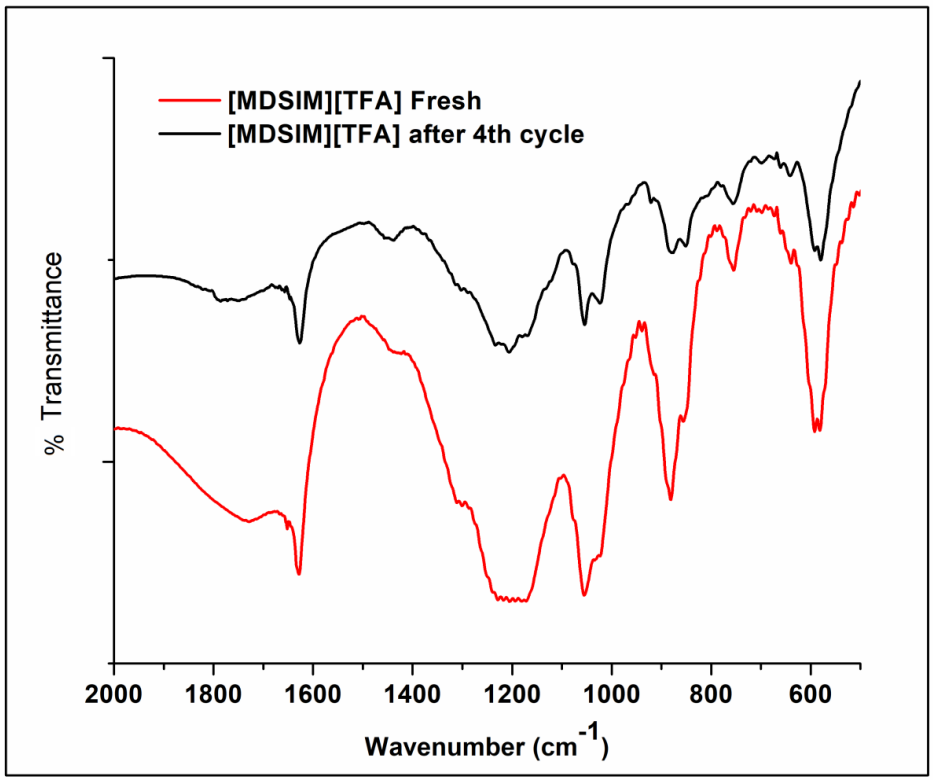


Fig. 5A.8: FT-IR spectra of the used [MDSIM][TFA] (after 4th cycle) along with the fresh one.

5A.4 Experimental section

5A.4.1 Synthesis of the N-SO_3H functionalized Brønsted acidic ionic liquids (BAILs)

The preparations of two known ([MDSIM][TFA] and [EDSIM][TFA]) and four new ionic liquids ([MDSIM][TCA], [EDSIM][TCA], [MDSIM][OAc] and [EDSIM][OAc]) were done as per the two-step standard method [45] described in **Chapter 3, sub-section 3.4.1**. Treatment of [RDSIM][Cl] obtained in the 1st step with 20 mmol of CF_3COOH/CCl_3COOH/CH_3COOH at 80°C for 2 hours to produce the anion exchanged

Brønsted acidic ionic liquids **(**BAILs), [RDSIM][TFA], [RDSIM][TCA] and [RDSIM][OAc] respectively. Further purification was carried out by washing the crude ionic liquids in the immiscible dry DCM solvent (3 × 5 mL) followed by decantation of the solvent, to obtain analytically pure ionic liquids.

5A.4.2 General procedure for preparation of chalcone derivatives

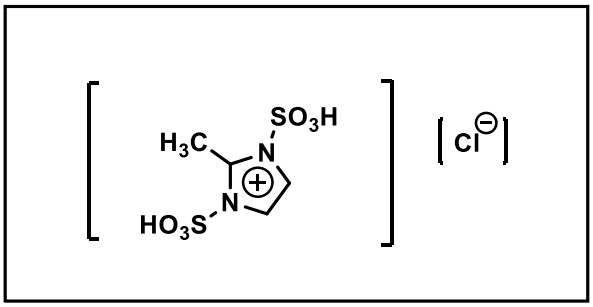
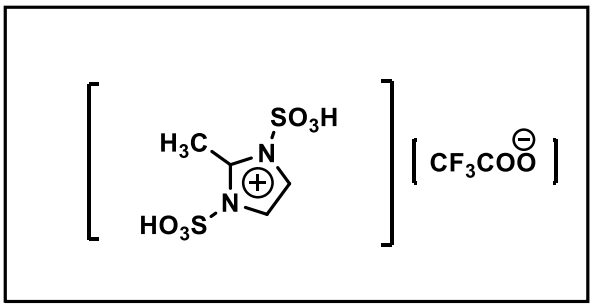
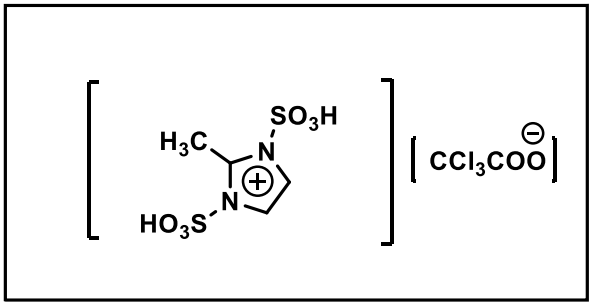
The Claisen-Schmidt condensation of acetophenone/4-Cl-acetophenone and aromatic aldehydes was carried out by mixing equimolar amount (1 mmol) of each substrate in a two neck 100 mL round bottomed flask using 5 mol % of the ([MDSIM][TFA] catalyst, at 100^{o}C (oil bath) for about 10 minutes with continuous stirring. The progress of the reaction was monitored by thin layer chromatography technique. After completion of the reaction, the product was dissolved in 3 mL of dry DCM and decanted from the round bottomed flask, leaving the DCM insoluble viscous IL catalyst behind in the reaction vessel. The ionic liquid catalyst was recycled after washing with more amount of the DCM and then dried in vacuum oven at 40^{o}C. The DCM extract containing the product was washed with aqueous $NaHCO_3$ solution and then dried over anhydrous Na_2SO_4. The crude product was obtained as solid residue after evaporation of the DCM extract under reduced pressure. Further purification was done by recrystallizing the product from aqueous ethanol to obtain analytically pure product.

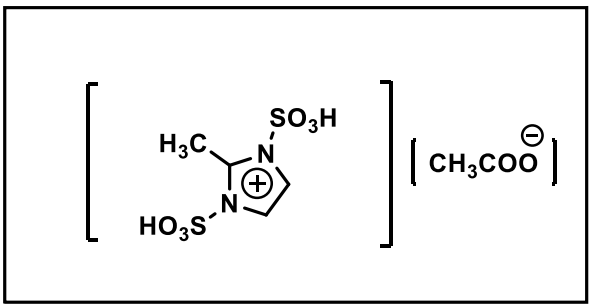
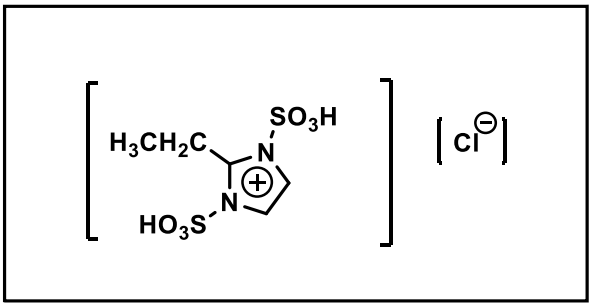
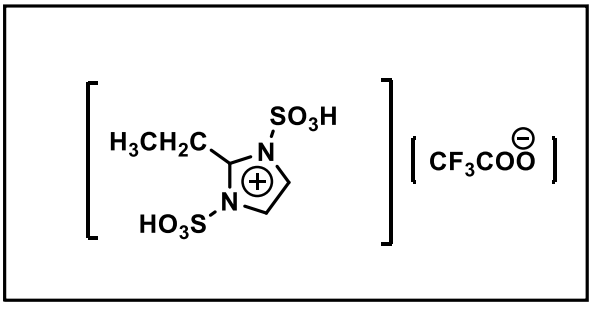
5A.4.3 General procedure for one-pot synthesis of 3-substituted indole derivatives

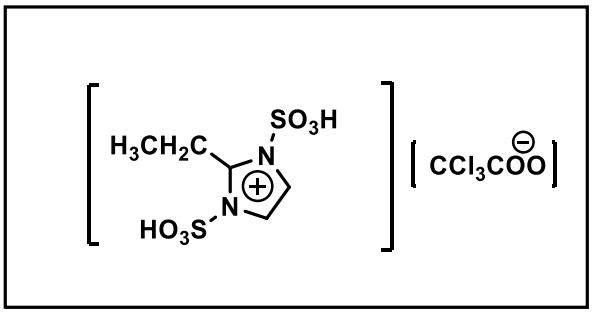
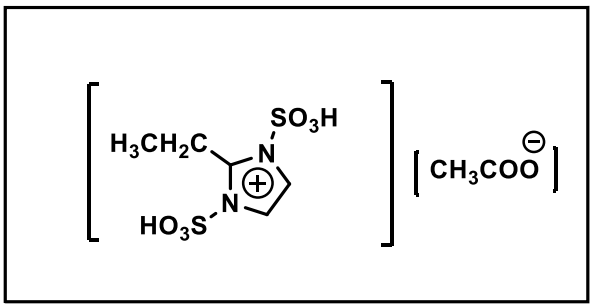
The sequential synthesis of 3-substituted indole derivatives was done from the crude mixture of chalcone with the catalyst [MDSIM][TFA], as obtained in the 1st step of the reaction. To this crude mixture, indole (1 mmol) was added and was stirred at 80°C for about 1.5-2 hours, till the completion of the reaction. The catalyst being insoluble in ethyl acetate was easily separated as a viscous residue inside the flask by dissolving the conjugate addition product in ethyl acetate (3 mL). This solution of ethyl acetate containing the Michael addition product was then decanted from the reaction vessel and washed with aqueous $NaHCO_3$ solution to remove any acidic impurities present. It was followed by the separation of the organic phase from the aqueous. The organic extract was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure to isolate the crude product as solid residue. This product was again recrystallized from aqueous-ethanol solution to get analytically pure product. The ionic liquid catalyst inside the flask

was again recycled after washing with ethyl acetate (2 × 2 mL) for two more times and dried in the vacuum oven at 60 °C.

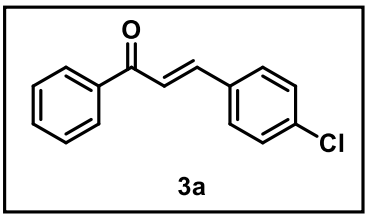
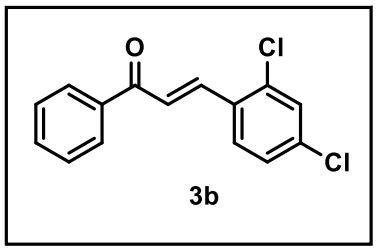
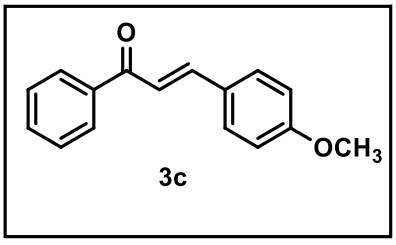
5A.4.4 Spectral data of the ILs

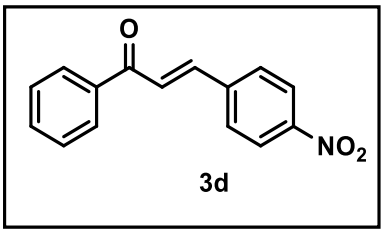
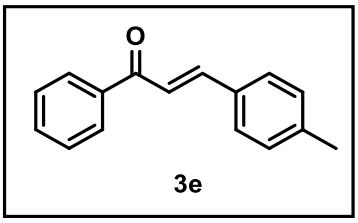
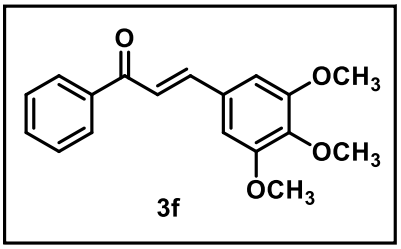
Structure	Spectral data
 2-methyl-1,3-disulfoimidazolium chloride [MDSIM][Cl]	Yellow viscous liquid; FT-IR (KBr) υ cm^{-1} = 3425, 3067, 2917, 1627, 1445, 1314, 1191, 1050, 873, 753 and 580; ^{1}H NMR (DMSO-d_6, 400MHz) : δ 13.91 (s, 1H), 11.90 (s, 1H), 7.46 (s, 2H), 2.51 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz,): δ 144.9, 119.1 and 11.7; CHN analysis(%) : Cal. C 17.05, H 3.58, N 9.94; Found C 17.11, H 3.54, N 9.90.
 2-methyl-1,3-disulfoimidazolium trifluoroacetate [MDSIM][TFA]	Brown viscous liquid; FT-IR (KBr) υ cm^{-1} = 3445, 3016, 2910, 1774, 1627, 1468, 1306, 1198, 1054, 881, 756 and 585; ^{1}H NMR (DMSO-d_6, 400 MHz) :δ 13.93 (s, 1H), 12.95 (s, 1H), 7.47-7.41 (m, 2H), 2.51 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) : δ 160.4, 144.9, 119.1 and 11.3; CHN analysis(%) : Cal. C 20.06, H 2.81, N 7.80; Found C 20.10, H 2.74, N 7.93.
	Brown viscous liquid; FT-IR (KBr) υ cm-1 = 3407, 2990, 2867, 1745, 1627, 1441, 1294, 1166, 1048, 883, 754 and 572; 1H NMR (DMSO-d6, 400 MHz); δ 13.85 (s, 1H), 13.10 (s, 1H). 7.42 (s, 1H), 2.49 (s, 3H); 13C NMR (DMSO-

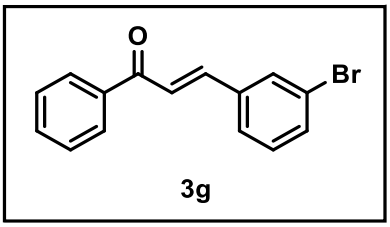
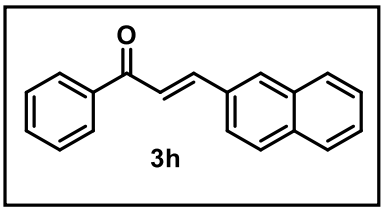
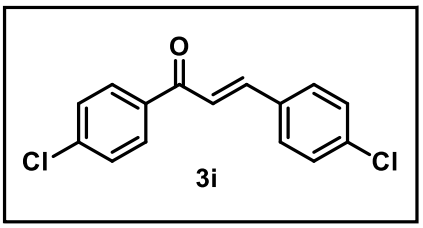
2-methyl-1,3-disulfoimidazolium trichloroacetate [MDSIM][TCA]	d6, 100 MHz): δ 163.3, 144.3, 119.5, and 10.7; CHN analysis(%) : Cal. C 17.64, H 2.47, N 6.86; Found C 17.47, H 2.64, N 6.93.
 2-methyl-1,3-disulfoimidazolium acetate [MDSIM][OAc]	Light brown viscous liquid; FT-IR (KBr) υ cm^{-1} = 3420, 2987, 2858, 1720, 1627, 1443, 1298, 1166, 1053, 881, 763 and 577; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 13.79 (s, 1H), 12.41 (s, 1H), 7.34 (s, 2H), 2.46 (s, 3H), 1.99-1.78 (m, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz,): δ 172.4, 143.9, 119.0, 21.9 and 10.9; CHN analysis(%) : Cal. C 23.64., H 4.29, N 9.18; Found C 23.55, H 4.36, N 9.14.
 2-ethyl-1,3-disulfoimidazolium chloride [EDSIM][Cl]	Yellow viscous liquid; FT-IR (KBr) υ cm^{-1} = 3437, 2929, 2860, 1629, 1453, 1176, 1054, 872, 750, 581; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 13.95 (s, 1H) 12.96 (s, 1H), 7.4-7.42 (m, 2H), 2.88-2.84 (m, 2H), 1.24-1.18 (m, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 149.3, 118.9, 18.8 and 12.4; CHN analysis (%) : Cal. C 20.31, H 4.09, N 9.47; Found C 20.25, H 4.11, N 9.60.
	Brown viscous liquid; FT-IR (KBr) υ cm^{-1} = 3448, 2923, 2853,1760, 1626, 1451, 1184, 1060, 884, 758 and 585; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 13.79 (s, 2H), 7.47 (s, 2H), 2.88 (q, *J* = 8 Hz, 2H), 1.22 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) : δ 159.2, 149.5,

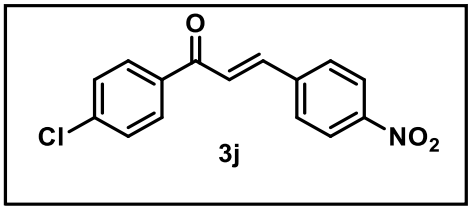
2-ethyl-1,3-disulfoimidazolium trifluoroacetate [EDSIM][TFA]	119.4, 116.4, 19.6 and 10.9; CHN analysis(%) : Cal. C 22.52, H 3.24, N 7.50; Found C 22.47, H 3.36, N 7.62.
 2-ethyl-1,3-disulfoimidazolium trichloroacetate [EDSIM][TCA]	Brown viscous liquid; FT-IR (KBr) υ cm^{-1} = 3450, 2923, 2858, 1742, 1621, 1446, 1191, 1058, 885,755 and 583; ^{1}H NMR: (DMSO-d_6, 400 MHz): δ 13.2 (s, 2H), 7.45 (s, 2H), 2.88 (q, *J* = 8 Hz, 2H), 1.23 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 163.1, 148.8, 119.2, 19.4, and 12.2; CHN analysis(%) : Cal. C 19.89, H 2.86, N 6.63; Found C 19.97, H 2.82, N 6.62.
 2-ethyl-1,3-disulfoimidazolium acetate [EDSIM][OAc]	Yellow viscous liquid; FT-IR (KBr) υ cm^{-1} = 3457, 2934, 2855, 1761, 1623, 1450, 1195, 1048, 875, 755 and 583; ^{1}H NMR: δ (DMSO-d_6, 400 MHz): δ 13.91 (s, 2H), 7.52 (s, 2H), 2.88 (q, *J* = 8.0 Hz, 2H), 1.87 (s, 3H), 1.23 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) : δ 173.1, 149.1, 119.1, 21.9, 18.8, and 11.3; CHN analysis(%) : Cal. C 26.33, H 4.74, N 8.77; Found C 26.85, H 4.62, N 8.57.

5A.4.5 Spectral data of the chalcones

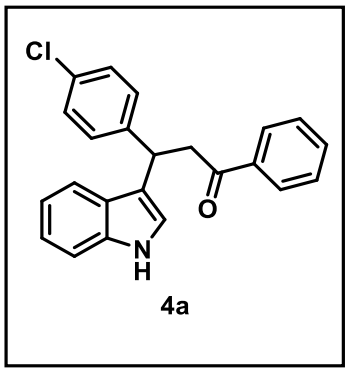
Structure	Spectral analysis
 3a 3-(4-chlorophenyl)-1-phenylprop-2-en-1-one	Yellowish white solid; m.p. 113.4-114.6^{o}C ^{o}C (lit. 112-114^{o}C) [31]; FT-IR (KBr) υ cm^{-1}: 3405,3060, 3030, 2980, 1669, 1610, 1565,1482, 1332, 1204, 1002, 814, 769, 664 and 469; ^{1}H NMR ($CDCl_3$, 400 MHz) : δ 8.01 (d, *J* = 8.0 Hz, 2H), 7.74 (d, *J* = 7.7 Hz, 1H), 7.61-7.56 (m, 3H), 7.52-7.48 (m, 3H), 7.39 (d, *J* = 7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 190.3, 143.1, 138.6, 136.7, 132.9, 132.9, 129.6, 128.4 and 122.1.
 3b 3-(2,4-dichlorophenyl)-1-phenylprop-2-en-1-one	Yellowish white solid; m.p. 71.3-73.5^{o}C (lit.72-74^{o}C)[46]; FT-IR (KBr) υ cm^{-1} : 3406, 3067, 3044, 2924, 1670, 1603, 1565, 1460, 1422, 1385, 1340, 1303, 1250, 1197, 1100, 1010, 972, 867, 824, 800, 790, 732, 687, 649, 544, 439; ^{1}H NMR ($CDCl_3$, 400 MHz) : δ 8.09 (d, *J* = 16 Hz, 1H), 8.01-7.99 (m, 2H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.61-7.57 (m, 1H), 7.52-7.45 (m, 4H) 7.31-7.28 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 189.6, 139.7, 137.5, 135.9, 133.3, 131.5, 130.4, 128.4, 127.3 and 125.4
 3c 3-(4-methoxyphenyl)-1-phenylprop-2-en-1-one	Light yellow solid; m.p. 71.6-73.2^{o}C (lit.74-75^{o}C) [25]; FT-IR (KBr) υ cm^{-1}: 3387, 2956, 2922, 2835, 1665, 1602, 1575, 1490, 1448, 1340, 1310, 1265, 1204, 1171, 1081, 1032, 972, 822, 777, 664 507; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.00 (d, *J* = 6.9 Hz, 2H), 7.79 (d, *J* = 15.6 Hz, 1H),7.61-7.55 (m, 3H), 7.51-7.39 (m, 3H), 6.93 (d, *J* = 8.7 Hz, 2H) 3.85

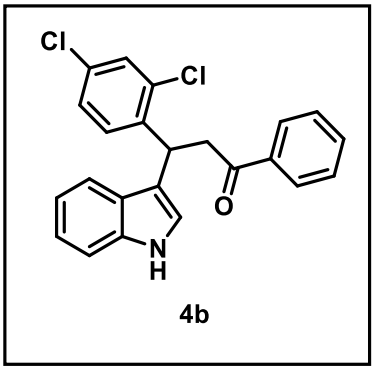
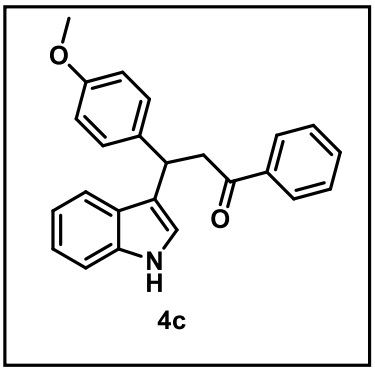
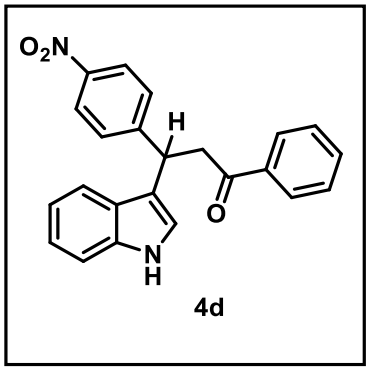
	(s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 190.7, 161.7, 144.6, 138.6, 133.0, 130.4, 127.7, 126.7, 120.1, 113.8, and 55.4.
 3d 3-(4-nitrophenyl)-1-phenylprop-2-en-1-one	Yellowish white solid; m.p. 158.7-160.4^{o}C (lit.158-161^{o}C) [47]; FT-IR (KBr) υ cm^{-1} :3412, 3098, 3074, 2922, 1655, 1609, 1515, 1443, 1409, 1337, 1219, 1104, 1015, 981, 841, 744; ^{1}H NMR ($CDCl_3$, 400 MHz) : δ 7.98-7.96 (m, 4H), 7.67-7.64 (m, 2H), 7.53-7.49 (m, 5H) ; ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 194.5, 135.3, 132.8, 129.8 and 129.0.
 3e 1-phenyl-3-p-tolylprop-2-en-1-one	Yellow solid; m.p. 89.6-90.6^{o}C (lit. 90-92^{o}C) [31]; FT-IR (KBr) υ cm^{-1}: 3402, 3023, 3063, 2916, 2845, 1659, 1595, 1560, 1443, 1347, 1197, 1010, 979, 822, 771, 664, 484; ^{1}H NMR ($CDCl_3$, 400 MHz) : δ 8.01 (d, *J* = 7.3 Hz, 2H), 7.80 (d, *J* = 8 Hz, 1H), 7.59-7.47 (6H, m), 7.25-7.21 (m, 2H), 2.39 (s, 3H); ^{13}C ($CDCl_3$, 100 MHz) : δ 190.9, 145.4, 141.1, 138.0, 132.9, 131.9, 129.4, 128.6, 120.7, and 21.8.
 3f 3-(3,4,5-trimethoxyphenyl)-1-phenylprop-2-en-1-one	Orange solid; m.p. 137.6-139.4 ^{o}C; FT-IR (KBr) υ cm^{-1}: 3397, 3001, 2957, 2935, 2829, 1656, 1595, 1568, 1490, 1408, 1265, 1121, 1020, 979, 829, 774, 694, 589; ^{1}H NMR ($CDCl_3$, 400 MHz) : δ 8.00 (d, *J* = 8 Hz, 2H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.61-7.48 (m, 3H), 7.40 (d, *J* = 7.6 Hz, 1H), 6.85 (s, 2H), 3.91 (s, 6H), 3.89 (s, 3H); ^{13}C ($CDCl_3$, 100 MHz) : δ 190.7, 153.2, 144.9, 140.1, 137.8, 132.9, 130.4, 128.8, 121.3, 105.2, 60.8 and 56.7.

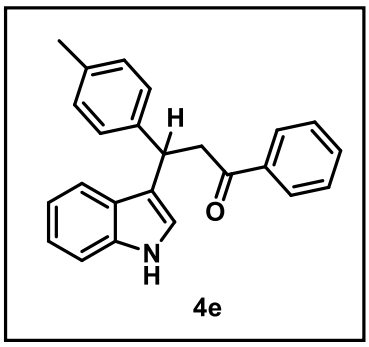
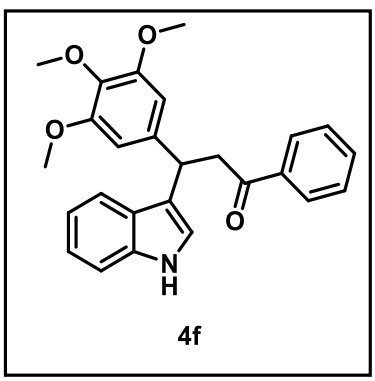
 3-(3-bromophenyl)-1-phenylprop-2-en-1-one	Light yellow amorphous solid; m.p. 82.5-84.3°C (lit. 83-85°C) [31]; FT-IR (KBr) cm^{-1}: 3067, 3030, 2949, 1663, 1610, 1592,1400, 1310, 1219, 1017, 972, 770, 679; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.00 (d, *J* = 8.02 Hz, 2H), 7.79 (m, 1H), 7.72 (d, *J* = 7.72, 1H), 7.62-7.58 (m, 1H), 7.55 - 7.49 (m, 5H), 7.31-7.27 (m, 1H) ; ^{13}C ($CDCl_3$, 100 MHz): δ 190.0, 143.5, 138.3, 136.7, 132.5, 130.4, 128.4, 126.9, and 122.8.
 3-(naphthalen-3-yl)-1-phenylprop-2-en-1-one	Light yellow solid; m.p. 153.3-155.4°C (lit.155-156°C) [48]; FT-IR (KBr) υ cm^{-1}: 3400, 3062, 3030, 2917, 1665, 1605, 1585, 1560, 1453, 1355, 1295, 1204, 1002, 994, 814, 784, 701, 687, 649, 469; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.07-8.02 (m, 3H), 8.00-7.94 (m, 2H), 7.89 -7.79 (4H, m), 7.67-7.58 (m, 2H), 7.54-7.50 (3H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 190.7, 145.1, 138.5, 134.1, 133.7, 132.6, 130.8, 128.5, 128.1, 127.2, 126.5, 123.7 and 121.9.
 1,3-bis(4-chlorophenyl)prop-2-en-1-one	Light yellow solid; m.p. 163.3-165.2°C; FT-IR (KBr) υ cm^{-1}: 3418, 3084, 3033, 1654, 1590, 1558, 1474, 1397, 1333, 1101, 1008, 979, 811, 727, 663, 547, 476; ^{1}H NMR ($CDCl_3$, 400 MHz) : δ 7.94 (d, *J* = 8.0 Hz, 2H), 7.74 (d, *J* = 16.0 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.47-7.37 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 188.5, 143.1, 139.7, 136.6, 136.4, 133.3, 129.6, 129.5, 128.8, 128.5 and 121.3.
	Light orange solid; m.p. 160.1-163.4°C; FT-

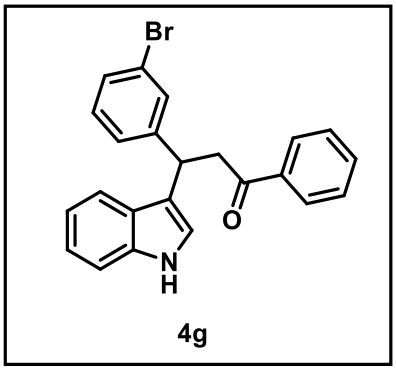
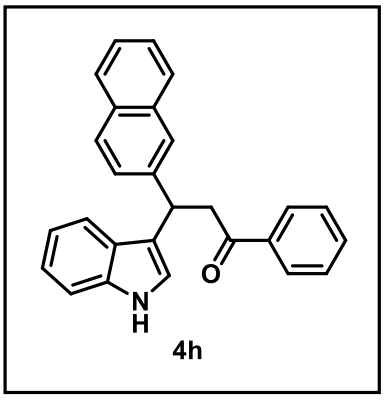
 1-(4-chlorophenyl)-3-(4-nitrophenyl)prop-2-en-1-one	IR (KBr) υ cm^{-1}: 3422, 3122, 1664, 1613, 1553, 1407, 1344, 1213, 1100, 1006, 812, 756, 656, 537; ^{1}H NMR ($CDCl_3$, 400 MHz) : δ 8.27 (d, *J* = 8.0 Hz, 2H), 7.97 (d, *J* = 8.0 Hz, 2H), 7.83-7.76 (m, 3H), 7.58 (d, *J* = 16.0Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 2H) ; ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 188.1, 149.1, 141.9, 140.4, 139.9, 136.0, 130.3, 129.1, 128.6, 125.2 and 124.2.

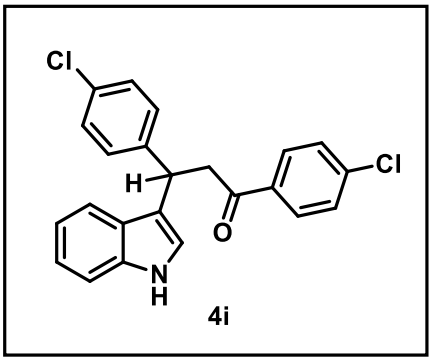
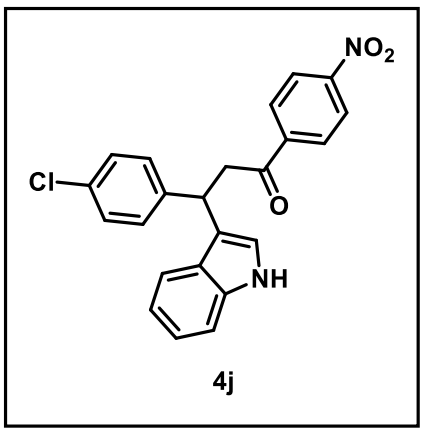
5A.4.6 Spectral data of Michael addition products

Structure	Spectral data
 3-(4-chlorophenyl)-3-(1H-indol-3-yl)-1-phenylpropan-1-one	Light pink solid; m.p. 129.4-131.3°C (reported value:129-132 °C) [39]; FT-IR (KBr) υ cm^{-1}: 3405, 3051, 2923, 2884,2859,1680, 1590, 1493, 1456, 1417, 1262, 1185, 1081, 1011, 966, 785, 734,702, 580, 509 and 425; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.98 (s, 1H), 7.93 (d , *J* = 8.0 Hz, 1H),7.54 (t, *J* = 8.0 Hz, 1H), 7.45-7.38 (m, 2H), 7.34 (d, *J* = 8.0Hz, 1H), 7.28-7.19 (m, 6H), 7.15(t, *J* = 8.0 Hz, 1H), 7.04-6.99 (m, 1H), 5.05-5.02 (m, 1H), 3.81 (dd, *J* = 16Hz, 8Hz, 1H), 3.70 (dd, *J* = 16 Hz, 8Hz, 1H); ^{13}C NMR ($CDCl_3$, 100MHz): δ 198.2, 142.8, 137.0, 133.2, 129.3, 128.2, 126.2, 122.4, 121.4, 119.6, 119.0, 111.2, 45.0 and 37.6.
	Light brown solid; m.p. 131-133.7 °C; FT-IR (KBr) υ cm^{-1}: 3425, 3058, 2923, 2848, 1687, 1590, 1468,1390, 1352, 1320, 1262, 1198, 1094, 1049, 979, 869, 818, 747, 690, 580, 444 and 419; ^{1}H

 **4b** 3-(2,4-dichlorophenyl)-3-(1H-indol-3-yl)-1-phenylpropan-1-one	NMR ($CDCl_3$, 400 MHz): δ 7.97-7.95 (d, *J* = 8.0Hz, 2H), 7.57-7.53 (m, 1H), 7.46-7.37 (m,4H), 7.33-7.31 (d, *J* = 8.0 Hz, 1H), 7.17-7.13 (m, 2H), 7.09-7.00 (m, 3H), 5.48 (t, *J* = 8.0 Hz, 1H), 3.78 (dd, *J* = 16 Hz, 8Hz, 1H), 3.64(dd, *J* = 16Hz, 4Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 179.8, 139.1, 129.6, 128.9, 128.1, 127.2, 121.8, 119.2, 112.5, 46.9, and 34.1.
 **4c** 3-(1H-indol-3-yl)-3-(4-methoxyphenyl)-1-phenylpropan-1-one	Orange solid; m.p. 132.1-134.5°C; FT-IR (KBr) υ cm^{-1}: 3412, 2922, 2851, 1680, 1609, 1506, 1448,1332, 1249, 1178, 1101, 1030, 824, 740, 688, 579, 549 and 425; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.96 (s, 1H), 7.92 (d, *J* = 12 Hz, 2H), 7.55-7.51 (m, 1H), 7.44-7.40 (m, 2H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.26-7.23 (m, 4H), 7.15-7.11 (m, 1H), 7.02-6.98 (m, 2H), 6.78 (d, *J* = 8.0Hz, 1H), 5.00(t, *J* = 8.0Hz, 1H), 3.88-3.65 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 193.4, 151.4, 134.9, 133.1, 128.8, 128.6, 128.1, 122.2, 119.8, 119.5, 113.8, 111.1, 87.2, 55.3, 42.8 and 31.0.
 **4d**	Dirty white solid ; m.p. 166.2-168.5°C; FT-IR (KBr) υ cm^{-1}: 3392, 3128, 3058, 2298, 2851, 1738,1687, 1596, 1506, 1461, 1345, 1223, 1101, 1010, 978, 849, 785, 740, 688, 586, 521 and 425; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.28 (d, *J* = 8.0 Hz, 2H), 8.11(d, *J* = 8.0 Hz, 2H), 8.03-8.02 (m,1H), 7.93-7.91 (m, 1H),

3-(1H-indol-3-yl)-3-(4-nitrophenyl)-1-phenylpropan-1-one	7.84-7.77 (m, 2H), 7.66-7.61 (m,1H), 7.54-7.51 (m, 3H),7.36-7.34 (m, 1H), 7.18-7.15 (m,1H), 5.19-5.14 (m, 1H), 3.85(dd, *J* = 16 Hz, 8 Hz, 1H), 3.78(dd, *J* = 16 Hz, 8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.7, 151.8, 141.7, 136.6, 133.2,129.0, 128.8, 128.6, 128.1, 125.6, 124.2, 123.8, 122.7, 121.4, 119.9, 119.1, 117.9, 111.4,44.6 and 37.8.
 **4e** 3-(1H-indol-3-yl)-1-phenyl-3-p-tolylpropan-1-one	Dark pink solid; m.p. 133.5-135.7°C ; FT-IR (KBr) υ cm^{-1}: 3425, 3058, 3025, 2916, 2877, 1906,1667, 1596, 1506, 1455, 1416, 1332, 1268, 1204, 1101, 1023, 972, 811, 740, 688, 579, 496, 463 and 418; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.03(s, H), 7.96 (d, *J* = 8.0Hz, 2H), 7.58-7.54 (m, 1H), 7.50-7.41 (m, 3H), 7.30-7.27 (m, 3H), 7.18-7.14 (m, 1H), 7.11-7.03 (m, 3H), 6.93-6.92 (m, 1H), 5.07 (t, *J* = 8.0 Hz, 1H), 3.83 (dd, *J* = 16 Hz, 8.0 Hz, 1H), 3.73 (dd, *J* = 16 Hz,8.0Hz, 1H), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.6, 140.8, 137.5, 136.7, 135.6,133.3, 129.2, 128.6, 128.1, 127.8, 126.9, 122.4, 121.2, 119.3, 110.9, 99.9, 45.3, 37.8 and 20.8.
 **4f**	Dark yellow solid; m.p. 135.5-137.3°C; FT-IR (KBr) υ cm^{-1}: 3392, 3058, 2922, 2851, 2247, 1738,1674, 1590, 1506, 1461, 1416, 1332, 1236, 1120, 998, 907, 824, 734, 688, 650 and 415; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.02 (d, *J* = 12.0 Hz, 3H), 7.73-7.69 (m, 1H), 7.60-7.56

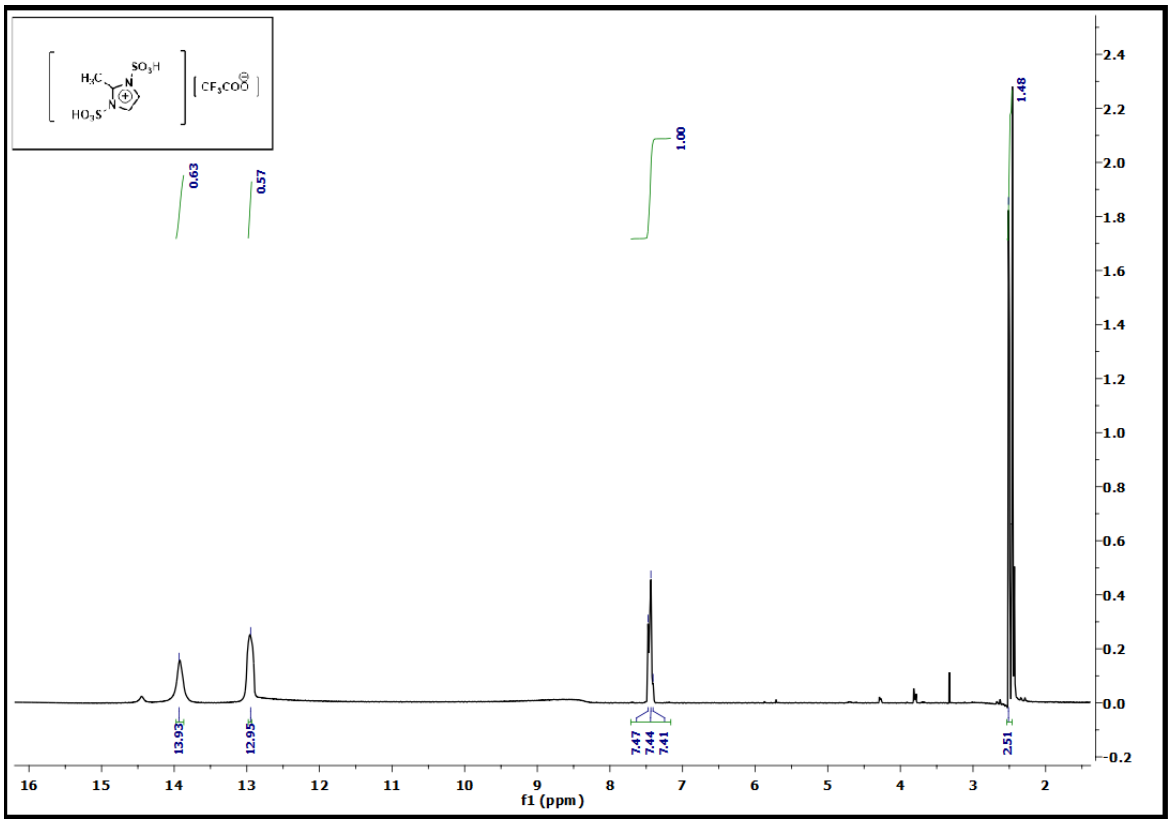
3-(1H-indol-3-yl)-3-(3,4,5-trimethoxyphenyl)-1-phenylpropan-1-one	(m, 1H),7.50-7.48 (m, 3H), 7.41-7.37 (m, 1H), 6.86 (s, 3H), 3.92 (s, 7H), 3.89 (s, 3H), 1.57 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 191.0, 153.5, 145.0, 140.4, 137.8, 132.7, 130.4, 128.6, 121.4,105.6, 60.6 and 56.2.
 **4g** 3-(3-bromophenyl)-3-(1H-indol-3-yl)-1-phenylpropan-1-one	Light yellow solid; m.p 99.3-101.2°C.; FT-IR (KBr) υ cm^{-1}: 3405, 3052, 2922, 1674, 1590, 1564,1442, 1423, 1332, 1204, 1171, 1088, 1074, 978, 920, 889, 740, 688, 599 and 418; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.92 (s, 1H), 7.47-7.41 (m, 5H), 7.33-7.27 (m, 4H), 7.15-7.09 (m, 3H), 6.99 (m, 1H), 5.03 (t, *J* = 8.0 Hz, 1H), 3.79 (dd, *J* = 16.0 Hz, 8.0Hz, 1H), 3.67 (dd, *J* = 16.0Hz, 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 197.9, 146.8, 143.1, 137.0, 136.7, 133.3, 130.9, 129.6, 128.9, 128.1, 126.7, 123.2, 122.6, 111.3, 45.0 and 37.7.
 **4h** 3-(1H-indol-3-yl)-3-(naphthalene-2-yl)-1-phenylpropan-1-one	Light yellow solid; m.p. 156.2-157.8°C; FT-IR (KBr) υ cm^{-1}: 3425, 3399, 3052, 2922, 2844, 1667,1596, 1506, 1455, 1410, 1332, 1262, 1197, 1094, 978, 901, 831, 740, 682, 657, 579, 483 and 425; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.61 (s, 1H), 8.06 (s, 1H), 7.94 (d, *J* = 12.0 Hz, 1H), 7.80 (s, 1H), 7.76-7.72 (m, 2H), 7.54-7.38 (m, 7H), 7.32-7.30 (m, 1H), 7.13 (t, *J* = 8.0 Hz,1H), 7.01-6.96 (m, 2H) 5.24 (t, *J* = 8.0 Hz, 1H), 3.93-3.80 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.3, 141.9, 137.2, 133.3, 133.1,132.5, 128.6,

	128.1, 127.9, 127.6, 126.8, 125.9, 125.4, 122.1, 119.6, 119.5, 119.3, 119.2, 110.9, 44.8 and 38.8.
 4i 1,3-bis(4-chlorophenyl)-3-(1H-indol-3-yl)propan-1-one	Light yellow solid; m.p. 126.2-128.4℃; FT-IR (KBr) υ cm^{-1}: 3397, 3041, 2909, 1676, 1585, 1494, 1394, 1328, 1196, 1088, 1014, 972, 807, 724, 592, 526 and 427; ^{1}H NMR ($CDCl_3$, 400 MHz) : δ 8.02 (s, 1H), 7.96 (d, *J* = 8.0Hz, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.49-7.46 (m, 1H), 7.40-7.37 (m, 3H), 7.34(d, *J* = 8.0 Hz, 1H), 7.26 (m, 1H), 7.21-7.19 (m, 1H), 7.16 (t, *J* = 8.0 Hz, 1H),7.02 (t, *J* = 8.0 Hz, 1H), 6.97 (d, *J* = 4.0 Hz, 1H), 5.02-4.99 (m, 1H), 3.74(dd, *J* = 16Hz, 8Hz,1H), 3.63 (dd, *J* = 16Hz, 8Hz, 1H) ; ^{13}C NMR ($CDCl_3$, 100MHz) : δ 197.1, 143.9, 142.4, 135.1,133.2, 130.0,129.4, 129.2, 128.9, 128.6, 122.4, 121.4, 119.6, 118.4, 111.2, 86.6 and 44.8.
 4j 3-(4-chlorophenyl)-3-(1H-indol-3-yl)-1-(4-nitrophenyl)propan-1-one	Light orange solid; m.p. 167.1-170.2℃; FT-IR (KBr) υ cm^{-1}: 3405, 3066, 2876, 1676, 1585, 1502, 1345, 1254, 1088, 1006, 815, 758, 691 and 518; ^{1}H NMR (DMSO-d6, 400MHz) : δ 10.94 (s, 1H), 8.27-8.13 (m, 2H), 8.09 (d, *J* = 8.0 Hz, 1H),8.04 (d, *J* = 8.0 Hz, 1H),7.69-7.62 (m, 2H), 7.55(d, *J* = 8.0 Hz, 2H),7.43-7.40 (m, 2H), 7.28 (d, *J* = 8.0 Hz, 1H), 6.99 (t, *J* = 8.0 Hz, 1H), 6.87(t, *J* = 8.0 Hz, 1H), 4.97-4.94 (m, 1H), 4.02-3.89(m, 2H) ; ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 196.3, 151.7, 146.4, 139.7, 137.1, 134.4,

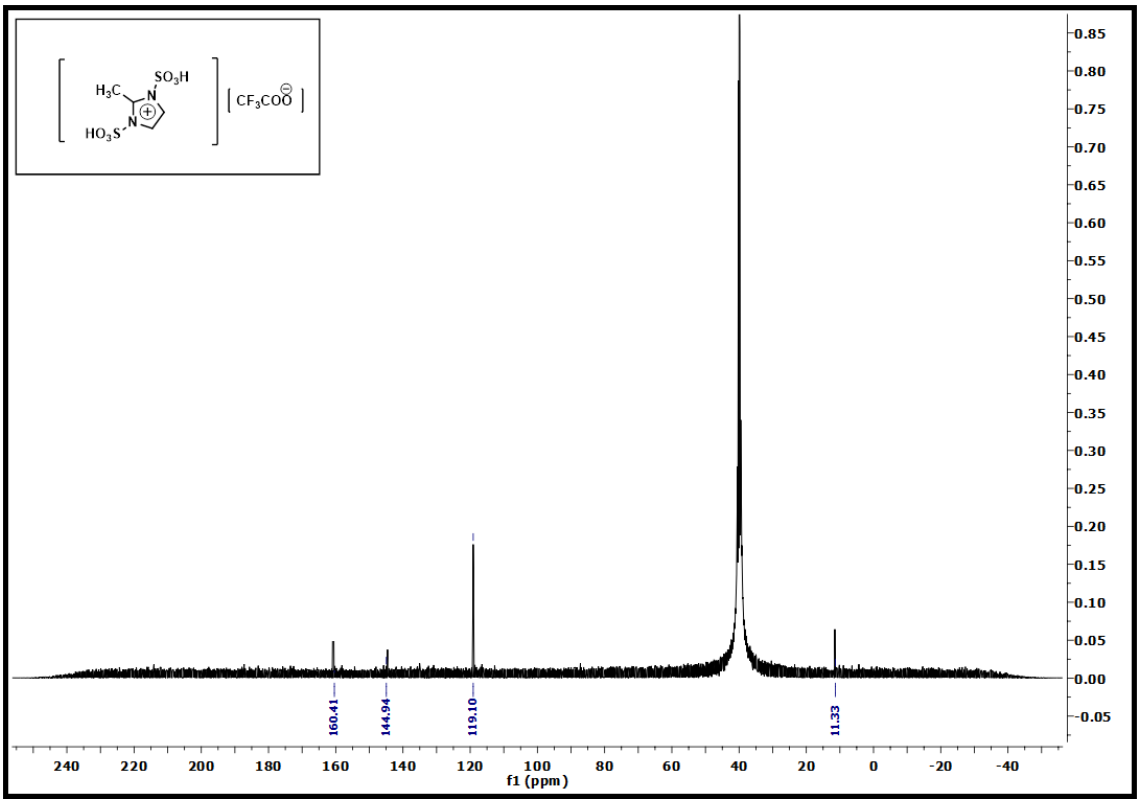
	130.4, 129.6, 128.8, 125.8, 123.9, 121.1, 119.6, 118.9, 117.9 and 44.71.

5A.4.7 NMR spectra of [MDSIM][TFA] ionic liquid

1. ^{1}H NMR spectra of [MDSIM[TFA]

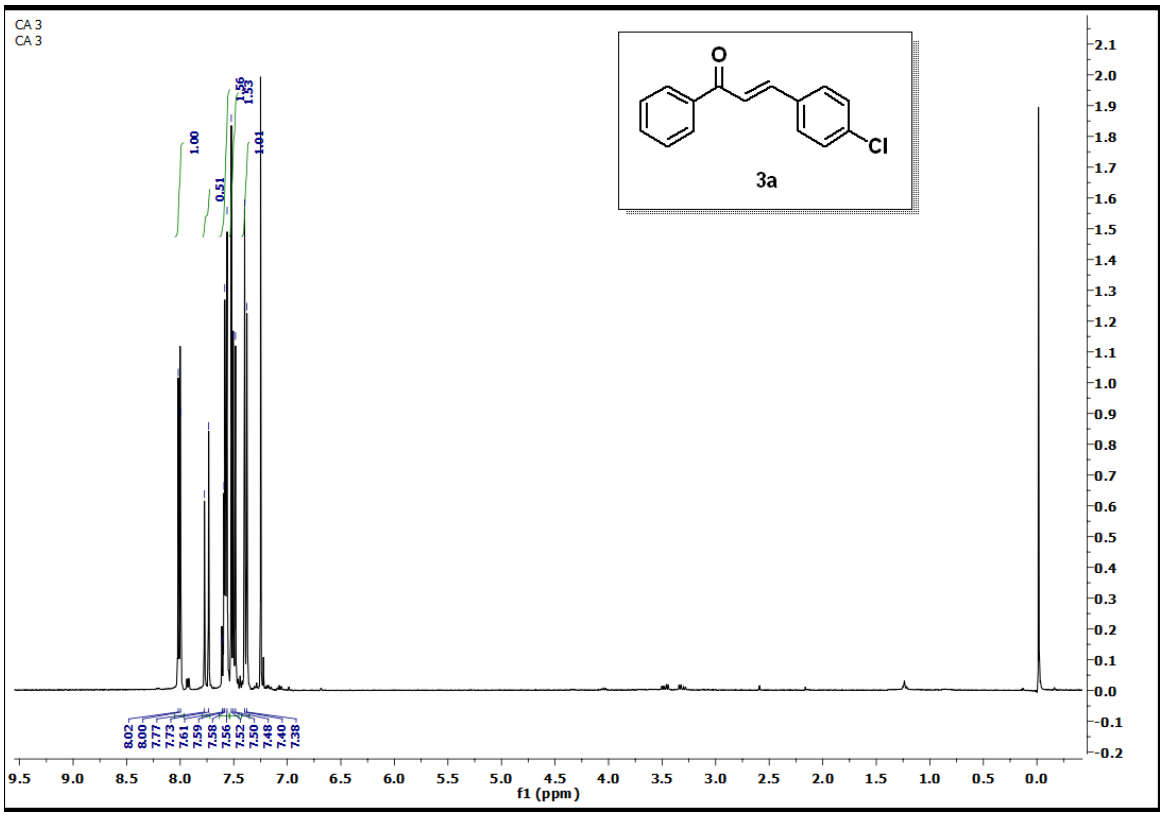


2. ^{13}C NMR spectra of [MDSIM][TFA]

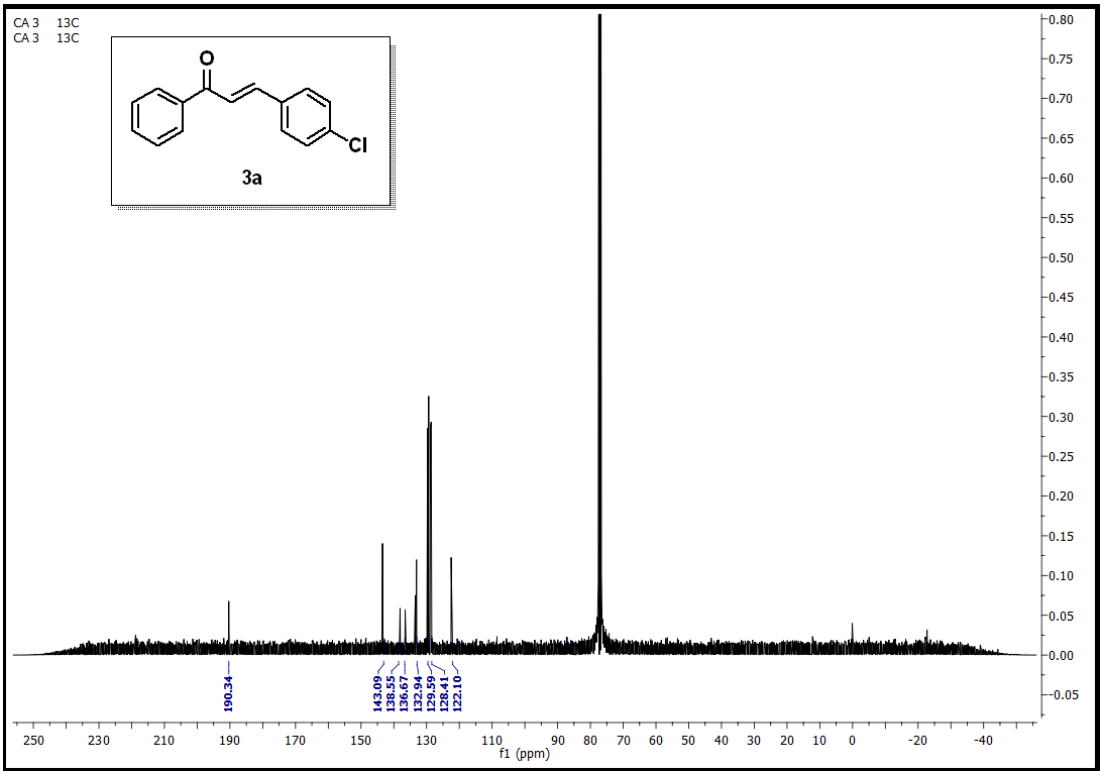


5A.4.8 NMR spectra of 3a

1. ^{1}H NMR spectra of 3a

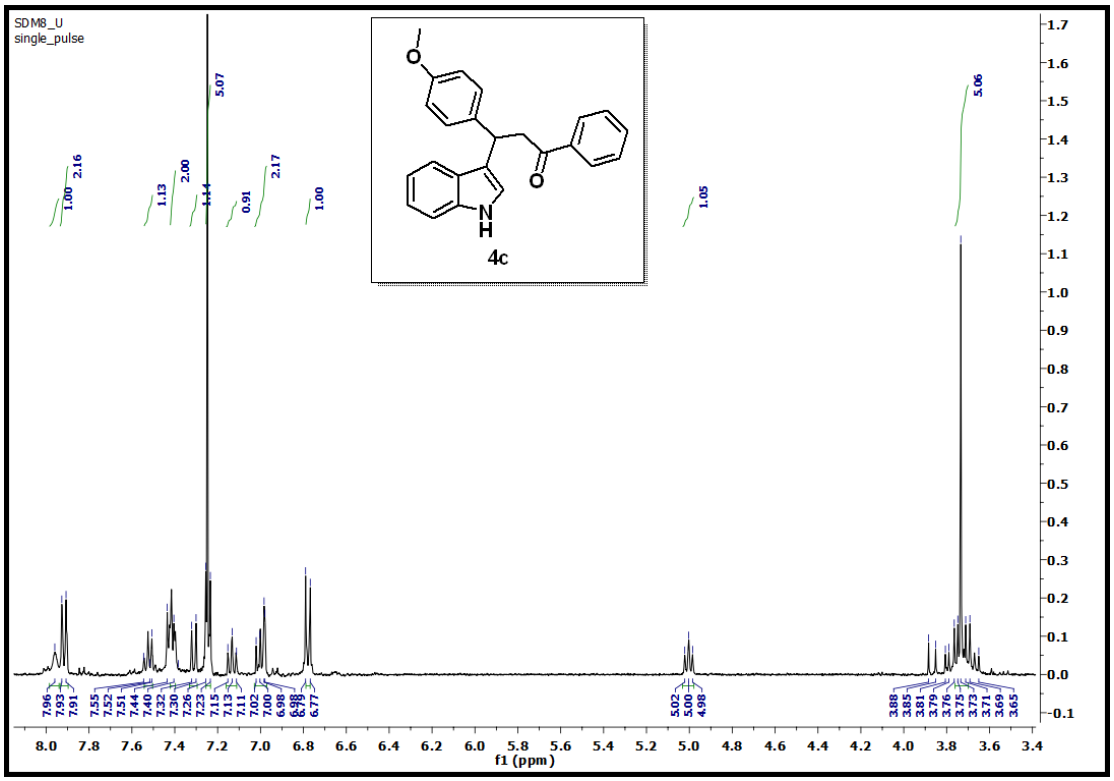


2. ^{13}C NMR spectra of 3a

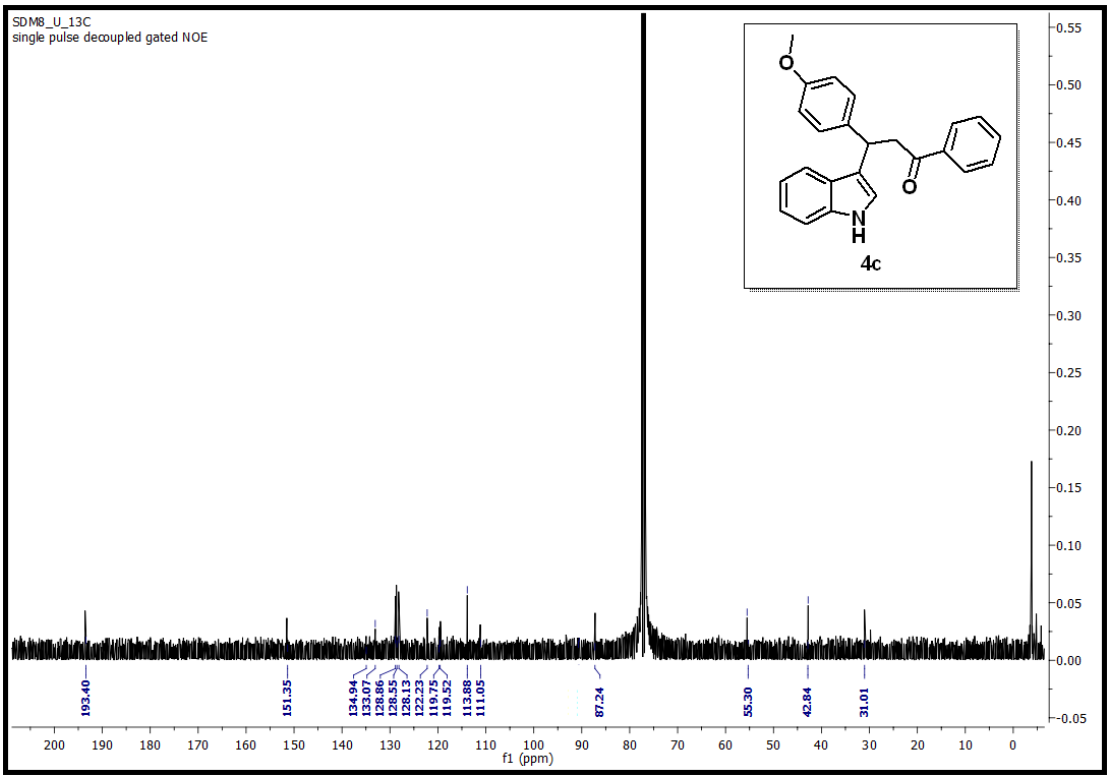


5A.4.9 NMR spectra of 4c

1. ^{1}H NMR spectra of 4c



2. ^{13}C NMR spectra of 4c



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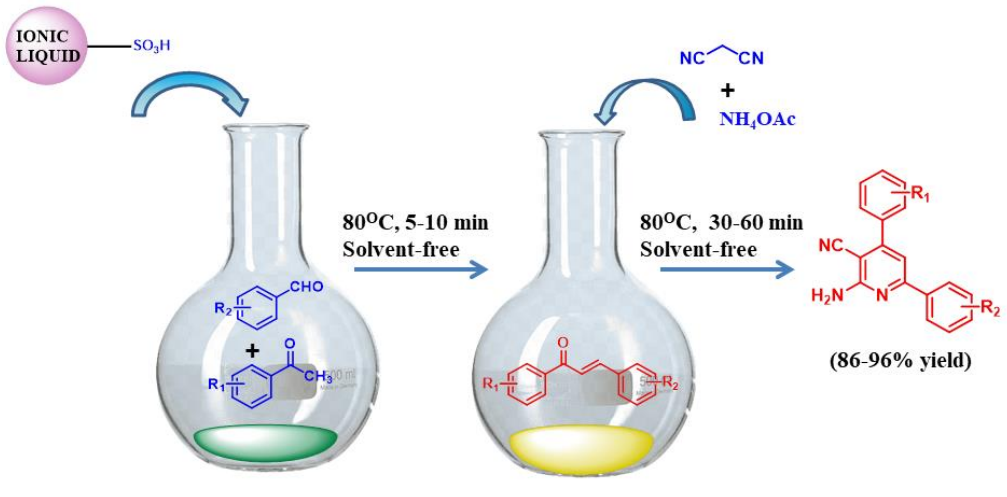
Chapter 5B

N-SO_3H Functionalised Ionic Liquid Catalysed Sequential One-Pot Multicomponent Synthesis of 2-Amino-3-cyanopyridines



Where,
R_1 = H, 4-Cl; R_2 = 4-Cl, 2,4-Cl, 4-OCH_3, 4-NO_2, 4-CH_3 etc.

5B.1 Introduction

Heterocyclic compounds are widely known for their biological activities. Among these heterocycles, pyridine ring is an important scaffold present in many significant biological molecules like Vitamin B6, nicotinic acid, dipicolinic acid etc. Functionalized pyridines have received considerable recognition over the past few decades for their broad range of biological activities [1, 2]. 2-Amino-3-cyanopyridines are one type of pyridine derivatives with broad range of pharmaceutical activities including anti-bacterial activity [3], IKK-β inhibition [4], A2A adenosine receptor antagonistic properties [5], HIV-1 integrase inhibition [6], carbonic anhydrase inhibition [7], antifungal [8], anti-inflammatory [4], anticancer [9], anti-parkinsonism properties [6] and many more. Due to the prominence of biologically active pyridine derivatives, their synthesis occupies a pivotal place in organic chemistry and several methods for their synthesis using a variety of catalysts have been developed. The literature review reveals their different synthetic approaches involving multistep reactions [10, 11] as well as one-pot multicomponent reactions [2, 3] employing variety of catalysts in solvent-free medium or in solution under thermal conditions, microwave irradiation, or ultrasound assisted conditions etc. [4, 5, 12]. Most of these synthetic routes however utilize expensive metal catalysts like Yb(PFO_3), Cu nanoparticles, Fe_3O_4 magnetic nanoparticles etc.[2, 13-16] and toxic solvents like benzene/toluene[17]. Additionally, these synthetic routes also present us with other difficulties like multiple steps, longer reaction time, less product selectivity, expensive catalysts, and lower yields. Thus, the development of efficient, economic, and environmentally benign strategies for the synthesis of 2-amino-3-cyanopyridines is quintessential. Some success in this regard was achieved with ionic liquids [18-23], trifluoroethanol [24], graphene oxide [25], microwave irradiation [3], ultrasound-assisted [12], and urease enzyme [26].

The use of nanoparticle catalyst for the same was also observed. Asadbegi et al. designed poly N,N-dimethylaniline-formaldehyde supported on silica-coated magnetic nanoparticles (PDMAF NPs) as catalyst for the multicomponent synthesis of 2-amino-3-cyanopyridines in ethanol [27]. Further reports on the use of Cu nanoparticles supported on charcoal [15], urea based acidic nanomagnetic catalysts Fe_3O_4@SiO_2@$(CH_2)_3$-urea-benzimidazole sulfonic acid [13] and Fe_3O_4@THAM-SO_3H magnetic nanoparticles [28] are also available.

The literature of multicomponent synthesis of 2-amino-3-cyanopyridines using ionic liquids as solvent/catalyst systems is discussed in **Chapter 1, sub-section 1.3.1.3**. The applications of ionic liquids as solvent/catalyst systems eliminated the various limitations of the earlier reported catalytic systems for the multicomponent synthesis of 2-amino-3-cyanopyridines (**Chapter 1, sub-section 1.3.1.3)**.

The task-specific ionic liquids have emerged to be efficient and recyclable safer alternatives to the conventional non-reusable corrosive acidic/basic reagents/catalysts in various organic transformations [29-35]. The development of task-specific ionic liquids (TSILs) has paved the way for several organic transformations to be carried out successfully with higher yields, lower reaction time and eliminating of tedious purification methods. Thus, in continuation of the previous work on TSILs catalysed organic transformations and utilization of chalcones as reaction precursors for synthesis of heterocycles **(Chapter 5A)**, we designed the present work to explore the catalytic activities of TSILs in the synthesis of 2-amino-3-cyanopyridines using chalcones as precursors. In the current work, four different types of direct N-SO_3H functionalized Brønsted acidic ionic liquids (BAILs) N, N, N', N'- tetrasulfopiperazinium chloride $[TSPi][Cl]_2$, 1,3-disulfoimidazolium trifluoroacetate [DSIM][TFA], 2-ethyl-1,3-disulfoimidazolium trifluoroacetate [EDSIM][TFA], N,N-dibutyl-disulfo-ammonium trifluoroacetate [DBDSA][TFA] were explored as reusable homogeneous catalysts **(Fig. 5B.1 and Scheme 5B.1)** for the one-pot two-step sequential synthesis of 2-amino-3-cyanopyridines in a solvent-free thermal method. Unlike the earlier methods, employing four-component synthesis route of 2-amino-3-cyanopyridines [20] or directly using chalcone as a reactant [19], this method involved *in situ* generation of the chalcones in the first step *via* acidic TSIL-catalysed Claisen-Schmidt condensation between aromatic aldehyde and ketone. It was followed by a multi-component reaction of the *in situ* generated chalcones with malononitrile and ammonium acetate (NH_4OAc) in presence of the same TSIL catalyst, which selectively produced 2-amino-3-cyanopyridines under solvent-free conditions at 80 ℃ **(Scheme 5B.2)**. The multicomponent sequential "one-pot" approach utilized here incorporates various advantages like operational simplicity, minimization of waste generation, shorter reaction times, and energy efficiency.

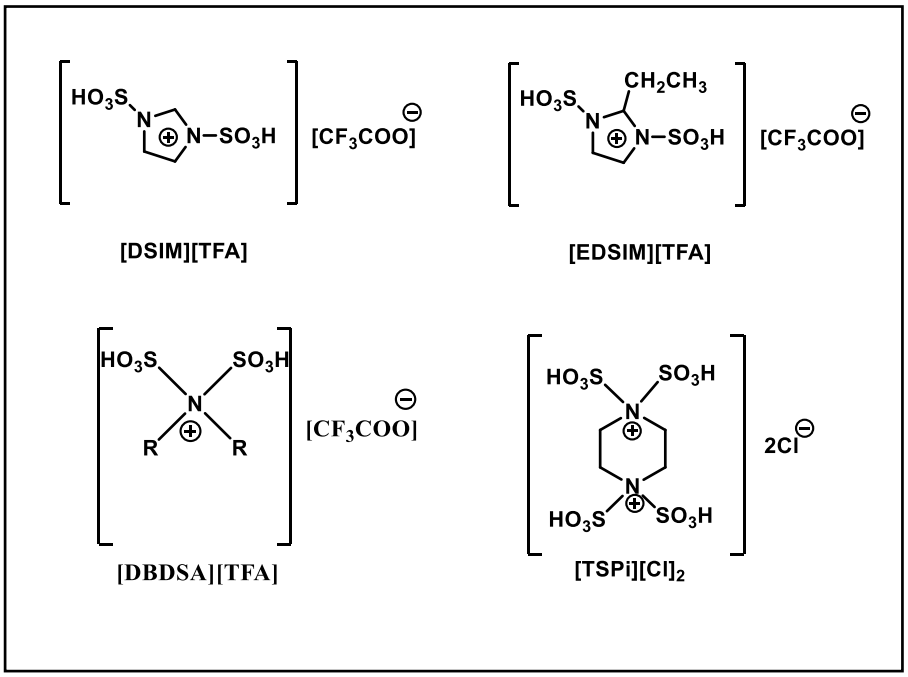
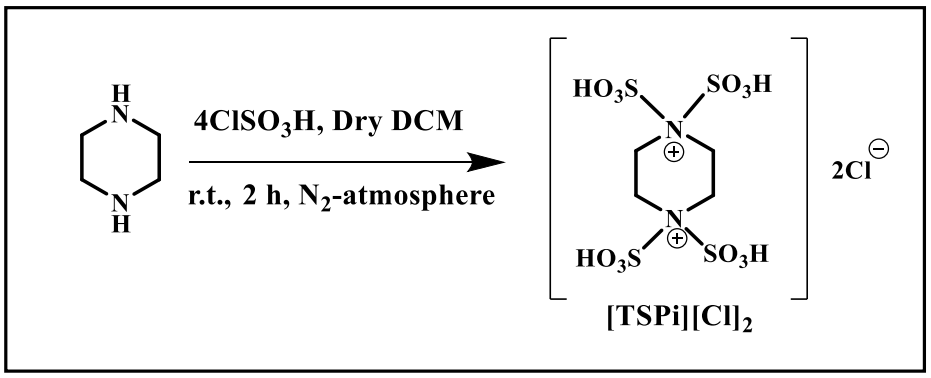


Fig. 5B.1: Structure of the N-SO_3H functionalized Brønsted acidic ionic liquids (BAILs).

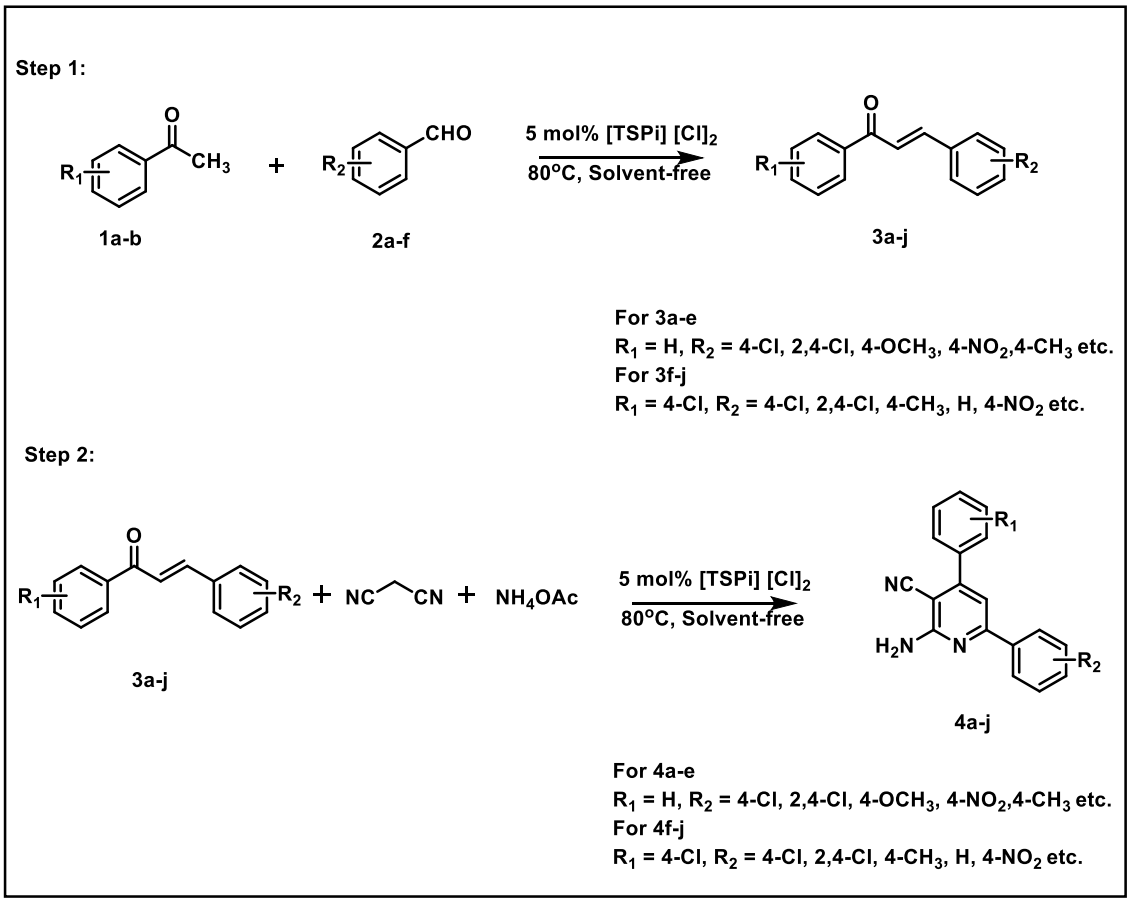
5B.2 Results and Discussion

5B.2.1 Characterization of the N-SO_3H functionalized Brønsted acidic ionic liquids

The three N-SO_3H functionalized BAILs, 1,3-disulfoimidazolium trifluoroacetate [DSIM][TFA], 2-ethyl-1,3-disulfoimidazolium trifluoroacetate [EDSIM][TFA] and N,N-dibutyl-disulfo-ammonium trifluoroacetate [DBDSA][TFA] were synthesized according to the standard procedures mentioned in **Chapter 3** and **4** [30]. N, N, N', N'-tetrasulfopiperazinium chloride $[TSPi][Cl]_2$ BAIL was synthesized according to **Scheme 5B.1** [31]. The detailed synthetic procedure is given in the experimental section **5B.3**. Their structures were confirmed using ^{1}H NMR, ^{13}C NMR and FT-IR analysis. Comparative thermogravimetric analysis and Hammett acidity study of the BAILs were performed to determine their acidity and thermal stability to investigate their catalytic activities in the sequential one pot synthesis of 2-amino-3-cyanopyridines derivatives **(Scheme 5B.2)**.



Scheme 5B.1: Synthesis of the ionic liquid $[TSPi][Cl]_2$.



Scheme 5B.2: One-pot two-step synthesis of 2-amino-3-cyanopyridines.

5B.2.1.1 FT-IR analysis

Fig.5B.2 displays the FT-IR spectra of the four BAILs respectively. The FT-IR band assignments of the BAILs are listed in **Table 5B.1**.

Table 5B.1: FT-IR band assignments of the BAILs.

Peaks (cm^{-1})	Assignments
572–587	$-SO_3H$ (bending)
750–760	Out of plane ring bending of -CH bond
870–885	N-S stretching
1040–1060	S-O symmetric stretching
1165–1195	S-O asymmetric stretching
1200-1340	C- N stretching
1441–1468	C-H bending of $-CH_3$ group
1620–1630	-C=C- stretching
1790-1750	C=O stretching
3000-2840	C-H stretching
3450-3400	-OH stretching due to intermolecular H-bonding among IL molecules

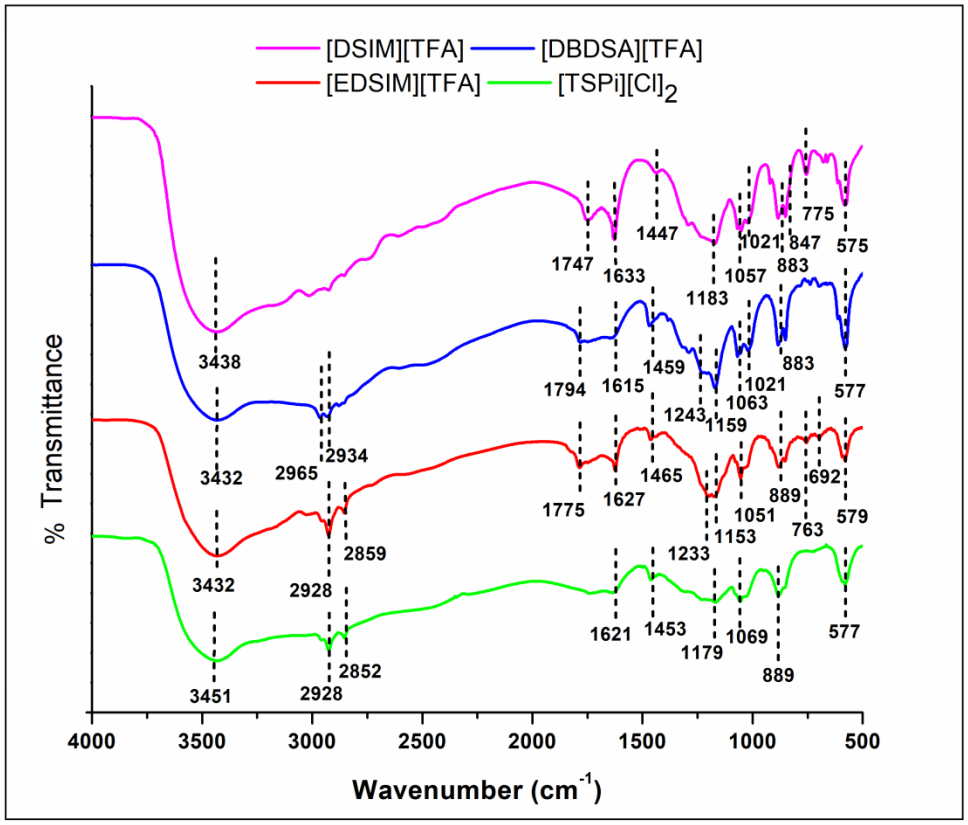


Fig. 5B.2: FT-IR spectra of the BAILs.

5B.2.1.2 NMR analysis

The ^1H NMR spectral data of [DSIM][TFA], [EDSIM][TFA] & $[TSPi][Cl]_2$ clearly show the acidic proton signals around 13.9-11.9 ppm for the $-SO_3H$ groups. In case of [DBDSA][TFA] we observe the $–SO_3H$ protons near 8.3 ppm. For the two -CH protons

of the imidazolium ring we get peaks at 7.5-7.3 ppm. The eight –CH protons of $[TSPi][Cl]_2$ appear as a single peak in the aliphatic region near 3.5 ppm. The proton signals for the $-C_2H_5$ group at C-2 position of the imidazolium cation are observed in the aliphatic region. The pairing of carboxylate anions with the imidazolium cations can be confirmed from the presence of ^{13}C NMR peak of C=O group at 155-170 ppm.

5B.2.1.3 Hammett acidity of the BAILs

The Brønsted acidities of the four $N–SO_3H$ functionalized ionic liquids were determined from the Hammett function (H°) values obtained from their UV-visible Hammett acidity plots **(Fig. 5B.3)**. The Hammett functions H° **(Table 5B.2)** of the BAILs were calculated using **Equation 1.4** from **Chapter 1**. The H° values decreased with the increasing acidity of the BAILs. From the H° values of ILs obtained, the decreasing order of acidity of the BAILs can be written as: $[TSPi][Cl]_2$ > [DSIM][TFA]> [EDSIM][TFA] > [DBDSA][TFA]. The four $–SO_3H$ groups containing $[TSPi][Cl]_2$ was found to be the most acidic, whereas the two bulkier alkyl group and two sulfonic group containing ammonium based ionic liquid [DBDSA][TFA] was found to be the least acidic. The slight differences in the acidities of [EDSIM][TFA] than the [DSIM][TFA] can be attributed to the reduction of electron deficient character of the imidazolium cation with increasing +I inductive effect of the C-2 methyl substituent.

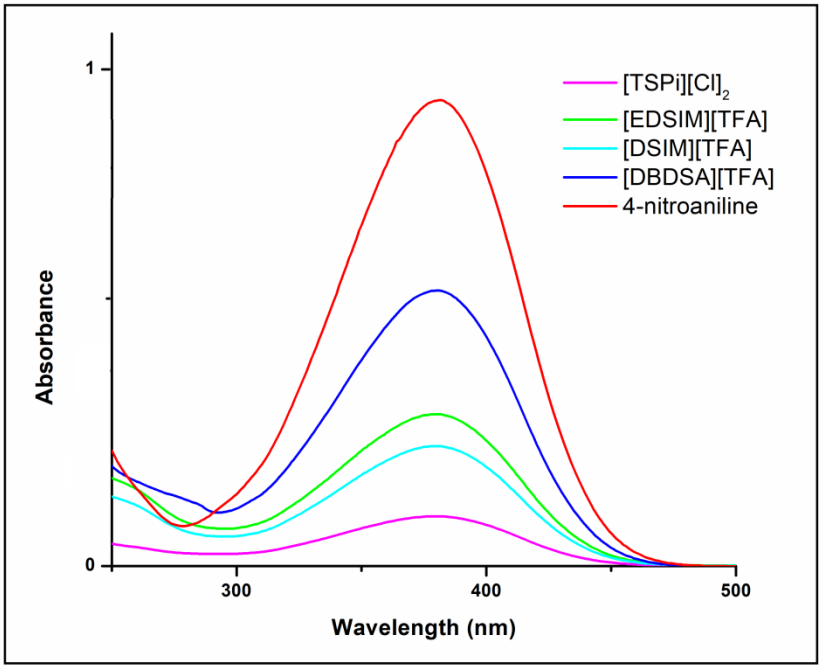


Fig. 5B.3: Hammett plot of the BAILs.

Table 5B.2: Hammett acidity functions of the BAILs.

Entry	IL	A_{max}	[I]%	[HI]%	H^O
1	4-Nitroaniline	0.99	100	-	-
2	[DSIM][TFA]	0.22	22.22	77.78	0.53
3	[EDSIM][TFA]	0.35	35.35	64.65	0.74
4	$[TSPi][Cl]_2$	0.11	11.11	88.89	0.09
5	[DBDSA][TFA]	0.45	46.46	53.54	0.93

5B.2.1.4 Thermogravimetric analysis

Thermogravimetric (TG) plots of the BAILs as shown in **Fig. 5B.4** display their two or three step decomposition patterns. The first degradation step observed in the plots around 100 °C can be accounted for release of physisorbed water. A maximum weight loss of 21% for the physisorbed water was observed in case of [DBDSA][TFA] and was followed by [EDSIM][TFA] with 15% weight loss. Among the four BAILs considered, [DSIM][TFA] is the least hydrophilic one with only 7% weight loss around 100 °C. In case of $[TSPi][Cl]_2$, around 13 % weight loss due to moisture was observed near 100 °C. It was followed by another decomposition around 193 °C. The TGA curves of the other three BAILs showed thermal stability up to 230-250 °C.

5B.2.2 Catalytic Study

Catalytic activities of the four BAILs were compared in the one-pot two-step sequential synthesis of 2-amino-3-cyanopyridines. The catalytic activities of these ILs were compared to that of CF_3COOH for the preparation of chalcones in the first step.

5B.2.2.1 Synthesis of chalcones via Claisen-Schmidt condensation

Initially, the catalytic activity of most acidic IL catalyst $[TSPi][Cl]_2$ was studied by varying its amount i.e., 2 and 5 mol% for optimization of the model Claisen-Schmidt condensation **(Scheme 5B.5)** (**Table 5B.3, Entries 1, 2**) of 4-chloro benzaldehyde (1 mmol) with acetophenone (1 mmol) under solvent-free conditions **(Scheme 5B.3)** at 80

°C to form the chalcone 3a. It was observed that using 5 mol% of the $[TSPi][Cl]_2$ gave higher yield **(98 %, Table 5B.3, Entry 2)** of 3a in 5 minutes.

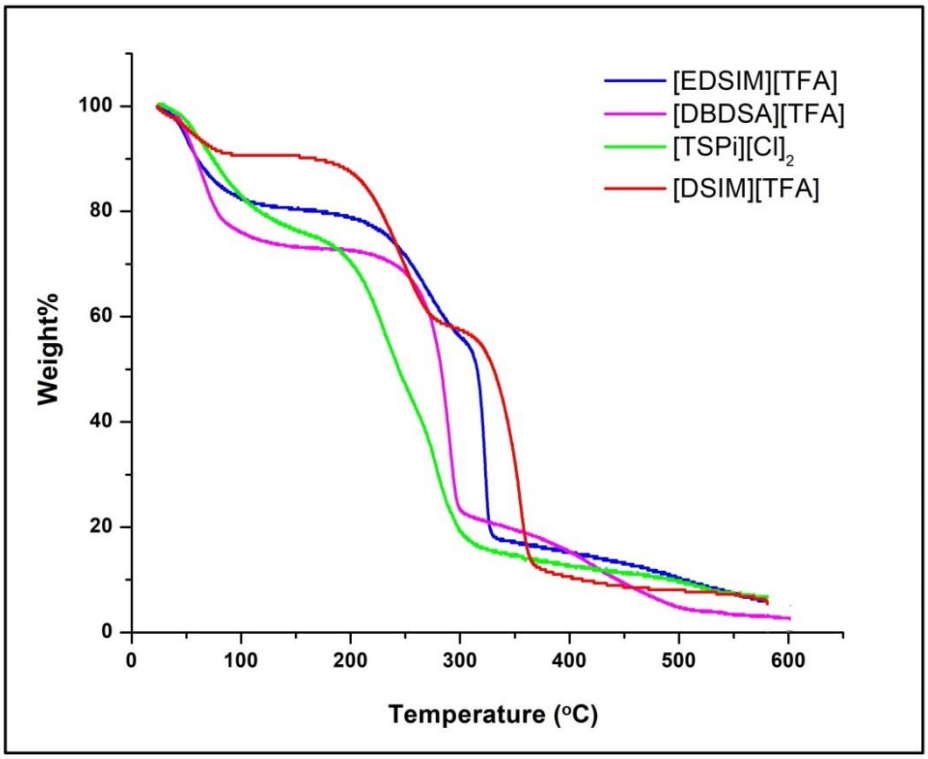
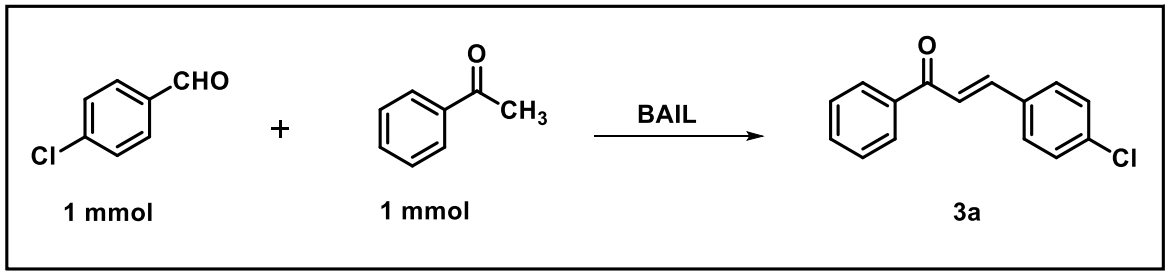


Fig. 5B.4: TGA plots of the BAILs.

Further improvements in product yields were not observed when the reaction was performed at 60 °C and at room temperature using solvent-free grinding method (**Table 5B.3, Entry 3 & 4**). From these observations, it was decided to screen the catalytic activity of [DSIM][TFA] and [DBDSA][TFA] as well at 80 °C for the model product of chalcone (3a). The catalytic activity of [EDSIM][TFA] was reported previously for the Claisen-Schmidt condensation (**Chapter 5A, sub-section 5A.2.2.1, Table 5A.3, Entries 3, 4, 6, 8, 10)** and those results were considered for comparison with the catalytic activities of the other three ILs (**Table 5B.3, Entries 5-10**). The effects of increasing reaction temperature to 100 °C along with variation of the catalyst amount (2 mol% and 5 mol%) were studied for the [DSIM][TFA], [DBDSA][TFA] and the results (**Table 5B.3, Entries 11-16**) were compared with the earlier data of [EDSIM][TFA] from **Chapter 5A.3**.

Further, the catalytic activities of the ILs were compared with CF_3COOH (**Table 5B.3, Entries 17, 18**) for the model product 3a and it was observed that the ILs had better

catalytic activities. These results were also previously reported in **Chapter 5A (Table 5A.3, Entries 11-13)**. Among the four ILs, 5 mol% of the $[TSPi][Cl]_2$ showed the best result for selective formation of the 3a at 80 °C due to its higher acidic strength.



Scheme 5B.3: Synthesis of chalcone by Claisen-Schmidt condensation.

Table 5B.3: Optimization of the reaction conditions for Claisen-Schmidt condensation.

Entry	Catalyst	IL mol%	Temperature (°C)	Time (min.)	% Yield (3a)[a],[b]
1	$[TSPi][Cl]_2$	2	80	10	95
2	$[TSPi][Cl]_2$	5	80	5	98
3	$[TSPi][Cl]_2$	5	60	25	88
4	$[TSPi][Cl]_2$	5	25	120	70[c]
5	[DSIM][TFA]	2	80	30	86
6	[DSIM][TFA]	5	80	20	90
7	[DBDSA][TFA]	2	80	100	80
8	[DBDSA][TFA]	5	80	60	84
9	[EDSIM][TFA]	2	80	50	82
10	[EDSIM][TFA]	5	80	35	85
11	[DSIM][TFA]	2	100	20	96
12	[DSIM][TFA]	5	100	10	98

13	[DBDSA][TFA]	2	100	45	87
14	[DBDSA][TFA]	5	100	30	90
15	[EDSIM][TFA]	2	100	30	92
16	[EDSIM][TFA]	5	100	15	94
17	CF_3COOH	2	60	5h	45
18	CF_3COOH	5	60	4h	50

[a] Isolated yields; [b] reaction conditions:4-Cl benzaldehyde (1 mmol), acetophenone (1 mmol); [c] solvent-free grinding method

Further to investigate the effects of solvent on the product yields, the model reaction (**Scheme 5B.3)** was conducted in both polar (ethanol, ethyl acetate, acetonitrile, tetrahydrofuran, water) and non-polar solvents (dichloromethane, hexane) using 5 mol% of $[TSPi][Cl]_2$. The reactions yielded 50-70% of the product 3a for 1.5–5 h reaction time (**Table 5B.4**). The presence of solvent displayed an increase in the reaction time with a decreasing product yield and didn't exhibit any beneficial outcome. This can be attributed to the self-aggregation tendencies of the IL catalysts in presence of solvents as well as forming H-bonding interactions with the protic solvents which reduces the number of Brønsted acidic catalytic sites. Hence, the solvent free condition at 80 ℃ with 5 mol % of the $[TSPi][Cl]_2$ was considered as the optimum reaction condition and a series of chalcone derivatives were synthesized by varying the substituted aromatic aldehydes and ketones to showcase the broad scope and generality of this method (**Fig. 5B.5**). Thus, the optimised condition was 5 mol% of the $[TSPi][Cl]_2$ at 80 °C under solvent free conditions (**Table 5B.3, Entry 2**), for *in situ* formation of chalcone derivatives. These chalcones were then utilized for the sequential one-pot three component reactions with malononitrile and ammonium acetate to form 2-amino-3-cyanopyridines as the final products.

5B.2.2.2 Synthesis of 2-amino-3-cyanopyridine derivatives

After optimization of the model reaction for **Step 1 (Scheme 5B.3)**, the catalytic activity of $[TSPi][Cl]_2$ was investigated for **Step 2 (Scheme 5B.4)** i.e., synthesis of 2-amino-3-cyanopyridine (4a). The crude chalcone 3a (1 mmol) obtained in the **step 1** using 5 mol% of $[TSPi][Cl]_2$ (**Table 5B.3, Entry 2**), was treated with malononitrile (1 mmol)

and different amounts of ammonium acetate (NH_4OAc) under solvent-free conditions by varying the reaction temperatures (80 °C, 60 °C and room temperature) (**Table 5B.5**). NH_4OAc was used as the source of ammonia.

Table 5B.4: Solvent effects on the model compound (3a) catalysed by $[TSPi][Cl]_2$.

Entry	Solvent	Temperature (°C)	Time (h)	%Yield[a],[b] (3a)
1	CH_2Cl_2	r.t.	3	50
2	Hexane	68	2.5	57
3	CH_3CN	82	2	60
4	EtOH	78	2	65
5	EtOAc	77	1.5	70
6	THF	77	5	44
7	H_2O	100	12	52

[a] Isolated yields, [b] reaction conditions:4-Cl benzaldehyde (1 mmol), acetophenone (1 mmol);

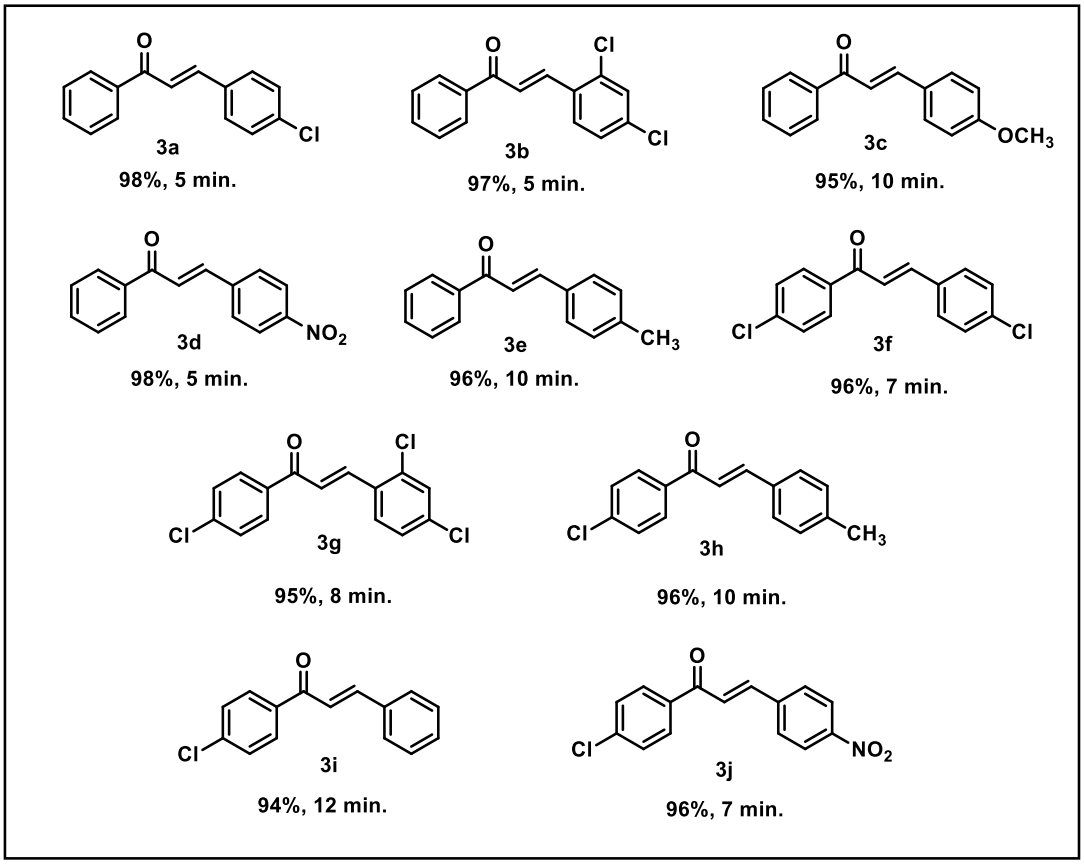
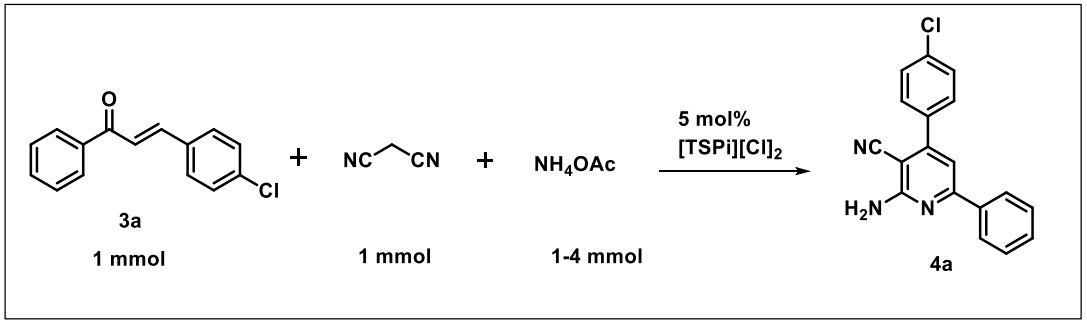


Fig. 5B.5: Substrate-scope study for chalcones using $[TSPi][Cl]_2$ catalyst.

The optimized reaction temperature and amount of NH_4OAc for the multi-component reaction were found to be 80 °C and 1.5 mmol respectively **(Table 5B.5, Entry 2)**.

Further studies were carried out to explore the catalytic activity of $[TSPi][Cl]_2$ in the one-pot, four-component general synthesis of 2-amino-3-cyano-pyridine (4a) (4-Cl-benzaldehyde (1 mmol), acetophenone (1 mmol), malononitrile (1 mmol), and NH_4OAc (1.5 mmol)) at 80℃ under solvent-free conditions. However, this route resulted in a decrease in the yield of 4a (80%) due to the formation of side products. To avoid the parallel reactions involved in the four-component reaction route which lead to the formation of side products, we continued our further studies with the sequential two-step one-pot multicomponent approach for the synthesis of 2-amino-3-cyanopyridines, with selective formation of chalcones in the first step.



Scheme 5B.4: Synthesis of 2-amino-3-cyanopyridine (4a) from crude chalcone (3a).

Table 5B.5. Optimization of the reaction temperature and amount of NH_4OAc for the synthesis of 2-amino-3-cyanopyridine (4a)

Entry	Temp. (℃) (2^{nd} step)	Time (min.) (2^{nd} step)	NH_4OAc (mmol)	% Yield[a],[b] (4a)
1	80	35	1	92
2	80	30	1.5	95
3	80	30	2	95
4	80	30	4	95
5	60	60	1.5	88
6	r.t.	5h	1.5	54[c]

[a] Isolated Yields; [b] reaction conditions: *in situ* generated chalcone 3a (1 mmol), malononitrile (1 mmol);

[c] solvent-free grinding method

5B.2.2.3 Substrate scope study for 2-amino-3-cyanopyridines derivatives

The above optimized conditions **(Table 5B.3, Entry 2 and Table 5B.5, Entry 2)** were utilised to synthesize several 2-amino-3-cyanopyridines.The reactions proceeded successfully for all the different combinations of aromatic aldehydes and ketones used in the synthesis of chalcones. However, a slightly better yield was observed in case of the 2-amino-3-cyanopyridines prepared from the chalcones having electron-withdrawing groups **(Fig.5B.6, 4a, 4b, 4d, 4f & 4j)**.

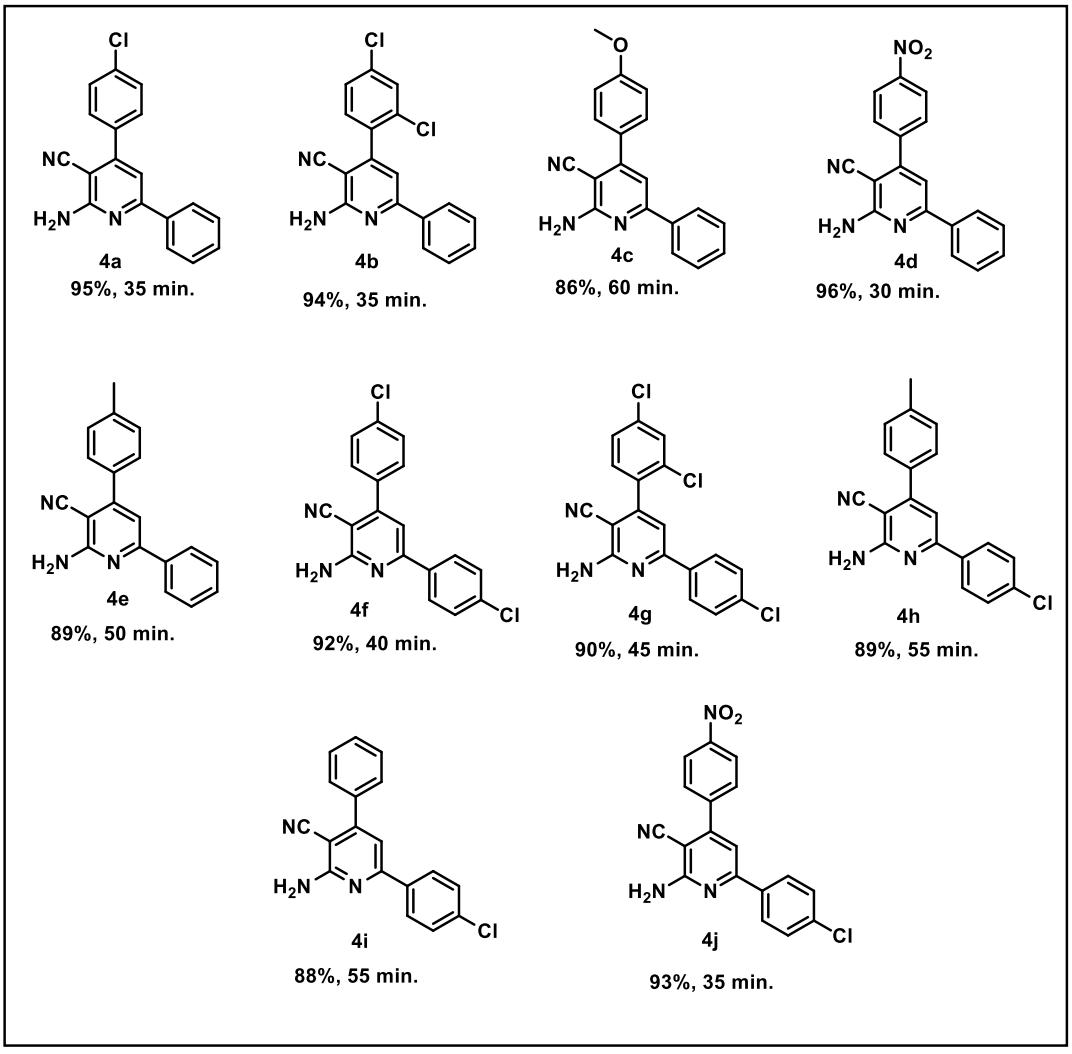


Fig. 5B.6: Substrate scope study for 2-amino-3-cyanopyridines.

5B.2.2.4 Recycling of the catalyst [TSPi][Cl]$_2$

The catalyst [TSPi][Cl]$_2$ was successfully recycled up to three times for the model reaction performed in 3 mmol scale of substrates (**Scheme 5B. 3 & 4**) by dissolving the product in dry dichloromethane. The catalyst being insoluble in dry dichloromethane

(DCM) could be easily recovered as a viscous liquid inside the reaction vessel. The ionic liquid catalyst was washed with more amount of the DCM (2 × 3 mL) and dried for 6-8 hours in the vacuum oven at 70 °C to be used in the next run. Recyclability study indicated the high catalytic activity of $[TSPi][Cl]_2$ even after the fourth run with a slight increase in reaction time. It can be attributed to the repeated washing of the used catalyst with DCM solvent under atmospheric conditions which causes absorption of atmospheric moisture by the IL catalyst *via* H-bonding with the $-SO_3H$ groups. Absorption of moisture makes the Brønsted acidic sites become less reactive and hence decreasing the product yield. The results obtained are summarized in the **Fig. 5B.7** below. FT-IR spectrum of the used catalyst even after the 4th cycle displayed the retention of original peaks present in the fresh one (**Fig. 5B.8**).

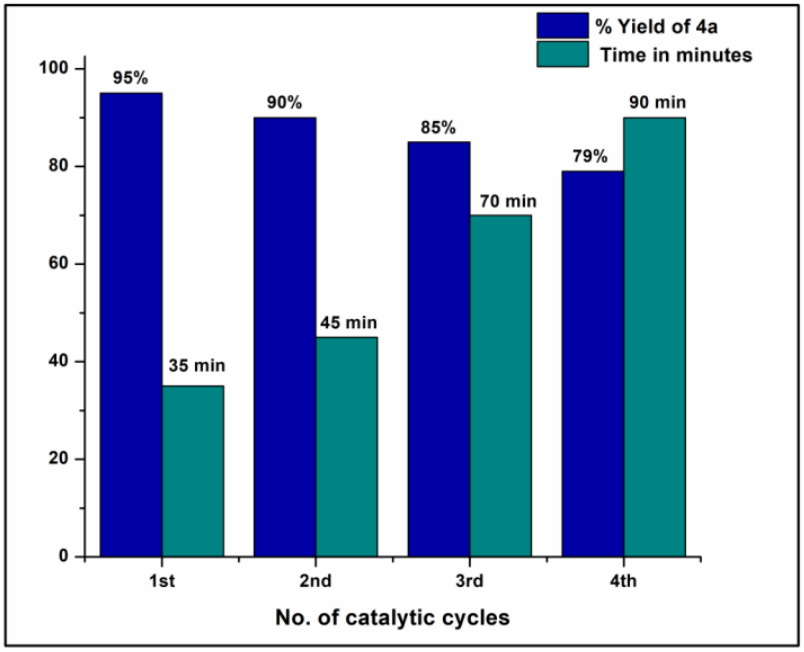


Fig. 5B.7: Recyclability profile of the BAIL $[TSPi][Cl]_2$ for the synthesis 4a.

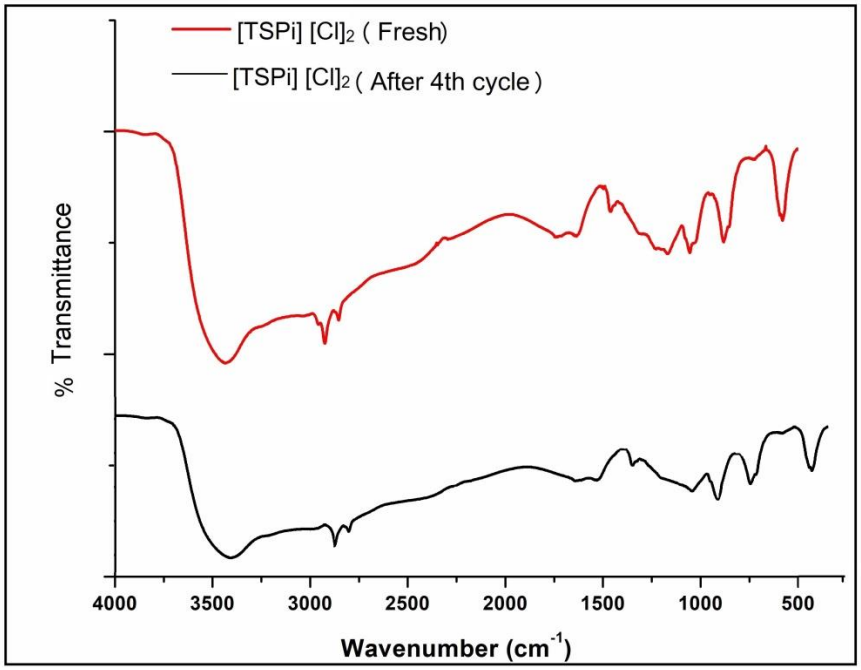
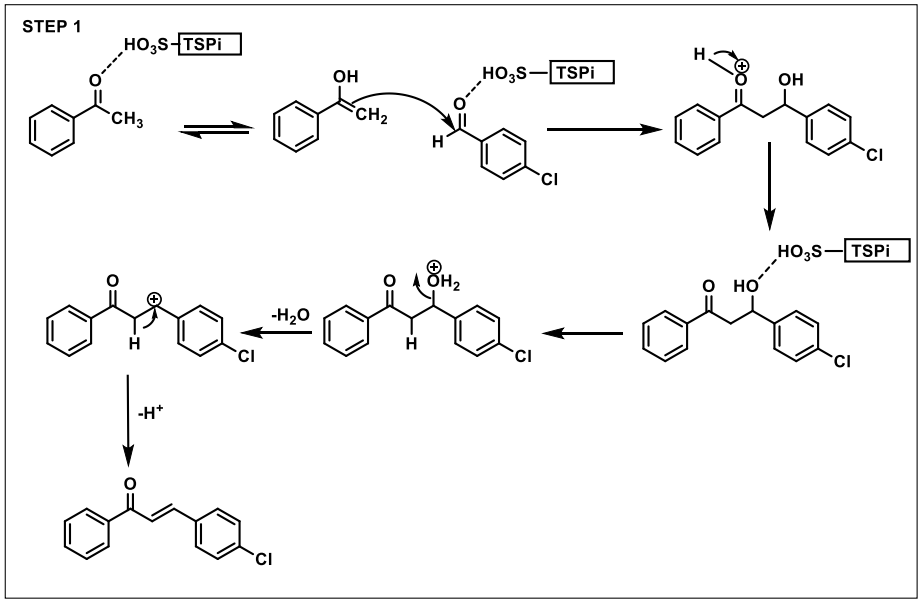


Fig. 5B.8: FT-IR spectra of the fresh $[TSPi][Cl]_2$ along with the used one (after 4th cycle) for synthesis of 4a.

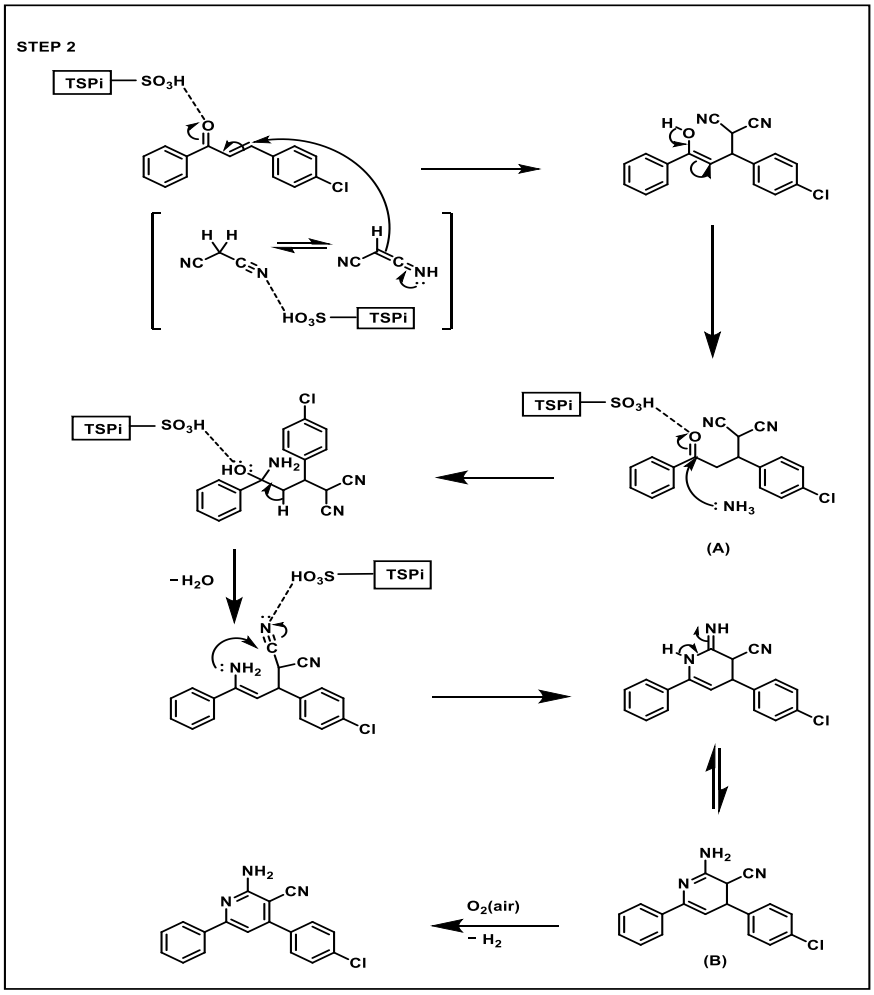
5B.2.2.5 Plausible mechanism

The mechanism of this sequential one-pot two-step reaction follows a different path compared to the general four-component multicomponent reaction of acetophenone, malononitrile, aromatic aldehydes and ammonium acetate. The activation of carbonyl groups of both the substrates by the $–SO_3H$ group of IL catalyst is the key factor for selective formation of the chalcones through Claisen-Schmidt condensation in **step 1 (Scheme 5B.5A)**.

The **step 2** of the reaction may involve IL catalysed activation of malononitrile as well as the carbonyl group of chalcones for a 1,4-addition to get the Michael adduct (A). It is followed by the nucleophilic attack of the ammonia molecule on the carbonyl group of the Michael adduct in presence of the IL catalyst to produce a cyclic intermediate B (**Scheme 5B.5A**). The subsequent aerial oxidation of the intermediate B under the reaction condition produces our desired 2-amino-3-cyanopyridine derivative.



Scheme 5B.5A: Plausible mechanism for the formation of chalcone 3a.



Scheme 5B.5B: Plausible mechanism for the formation of compound 4a.

5B.3 Summary

This work presents an efficient and green method for the synthesis of 2-amino-3-cyanopyridine derivatives via N-SO_3H functionalized ionic liquid catalysed one-pot two-step sequential reaction. The reaction involves the selective formation of chalcones in the first step as precursors for the multi-component reaction with malononitrile and ammonium acetate in the second step to yield 2-amino-3-cyanopyridine derivatives. The Brønsted acidity and high thermal stability of the N-SO_3H functionalized ionic liquids make them excellent candidates for catalysing these reactions. $[TSPi][Cl]_2$ was found to be the best catalyst for this reaction. The dual solvent-catalyst role of the Brønsted acidic ILs in this two-step one-pot route eliminates the use of toxic organic solvents and metals, tedious chromatographic separations of reaction intermediates/products and strong acidic or basic conditions. This method exhibits a broad substrate scope, and the catalyst could be easily recycled and reused for at least three times without a significant loss of activity. At the same time, it provides the benefits of selective formation of chalcones /2-amino-3-cyanopyridines, shorter reaction times, and higher yields of products using a simple isolation process, which are essential components to define it as an environmentally sustainable approach.

5B.4 Experimental section

5B.4.1 Synthesis of the N-SO_3H functionalized Brønsted acidic ionic liquids (BAILs)

The preparation of 1,3-disulfoimidazolium trifluoroacetate [DSIM][TFA] and 2-ethyl-1,3-disulfoimidazolium trifluoroacetate [EDSIM][TFA] ionic liquids were done in two steps [30] according to the standard method described in **Chapter 3, sub-section 3.4.1.** N, N-dibutyl-disulfo-ammonium trifluoroacetate [DBDSA][TFA] was synthesized according to the standard procedure mentioned in **Chapter 4, sub-section 4.4.1**.

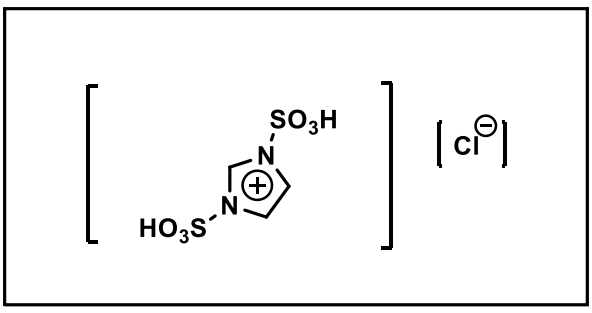
The tetrasulfopiperazinium ionic liquid N, N, N', N'- tetrasulfopiperazinium chloride $[TSPi][Cl]_2$ was prepared in a single step [31]. Piperazine (10 mmol) was mixed with 40 mmol chlorosulfonic acid in a two neck 100 mL round bottom flask at room temperature with continuous stirring for two hours in dry dichloromethane, under nitrogen atmosphere to obtain $[TSPi][Cl]_2$ as a brownish yellow viscous liquid [31]. Solvent dichloromethane was removed under reduced pressure to obtain the IL in pure form.

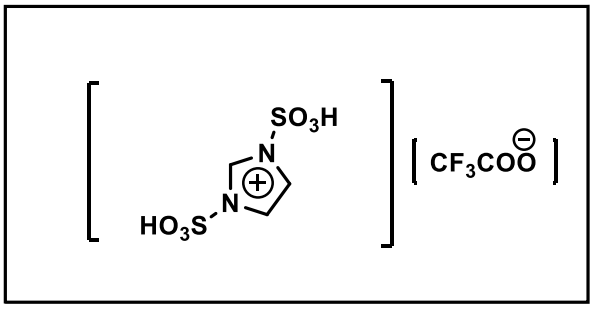
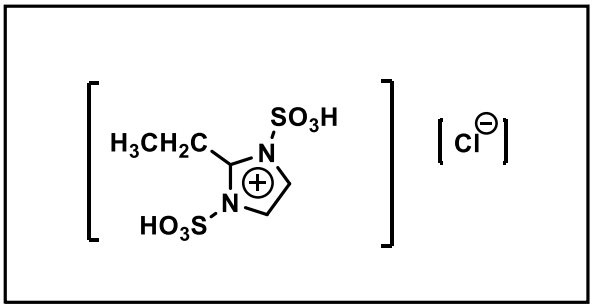
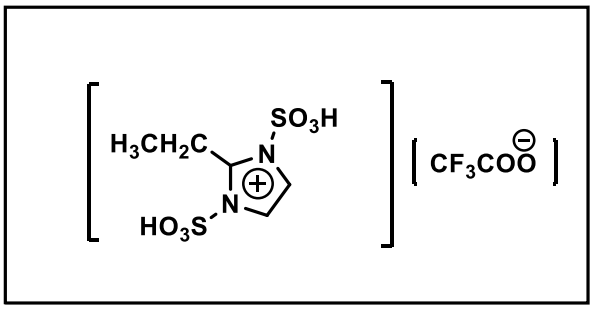
5B.4.2 Synthesis of 2-amino-3-cyanopyridine derivatives through one-pot sequential reaction

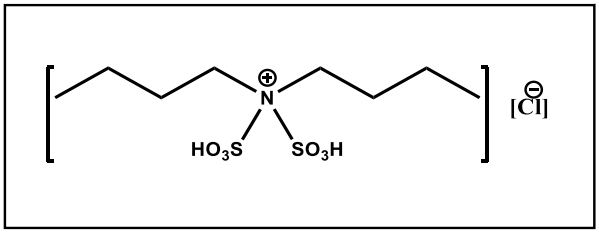
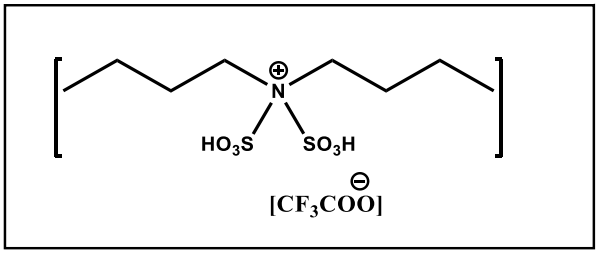
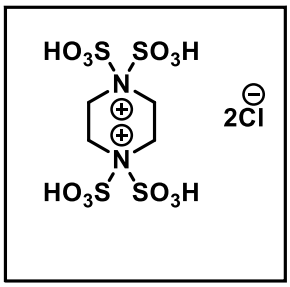
The one pot synthesis of 2-amino-3-cyanopyridine derivatives was conducted in a sequential two-step method. The initial step involves *in situ* formation of chalcone derivatives (1 mmol) via Claisen-Schmidt condensation of acetophenone/4-Cl-acetophenone (1 mmol) and aromatic aldehydes in presence of 5 mol% of $[TSPi][Cl]_2$ catalyst at 80 ^{o}C followed by reaction with malononitrile (1 mmol) and ammonium acetate (1.5 mmol) at the same temperature under solvent-free conditions to get the crude 2-amino-3-cyanopyridines for the specified reaction period. The progress of reaction was monitored by thin layer chromatography for both the steps. On completion of the 2nd step of the reaction, as observed from the TLC analysis, the mixture was diluted with dichloromethane and was decanted to separate the DCM immiscible viscous IL catalyst from the crude product solution. The ionic liquid catalyst was washed with more amount of the DCM (2 × 3 mL) and dried for 6-8 hours in the vacuum oven at 70 °C for use in the next run. The DCM layer was washed with aqueous $NaHCO_3$ solution for removal of any acidic impurities and then it was separated from the aqueous phase. The organic layer containing product was then dried over anhydrous sodium sulphate (Na_2SO_4) and distilled under reduced pressure to get the 2-amino-3-cyanopyridines as crude solid residue. The product was further purified by recrystallization from aqueous ethanol solution.

Additionally, to get analytically pure chalcones, the crude reaction mixture obtained in the 1st step was treated according to the method described in **Chapter 5A, sub-section 5A.4.2.**

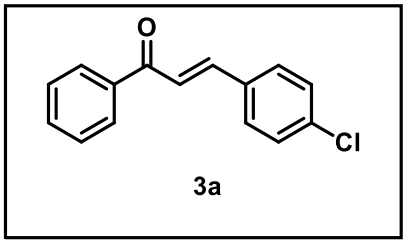
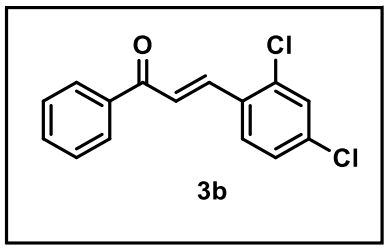
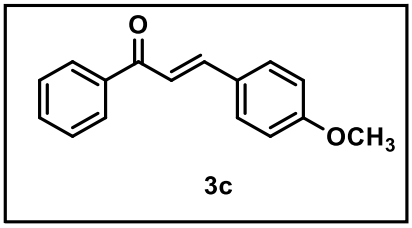
5B.4.3 Spectral data of the ILs

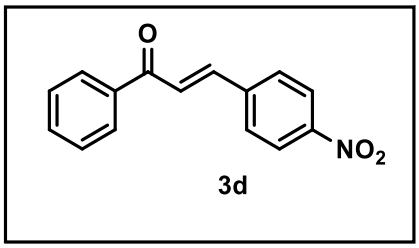
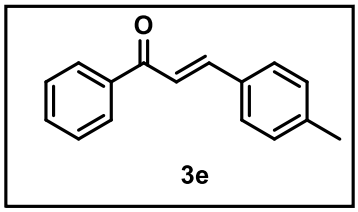
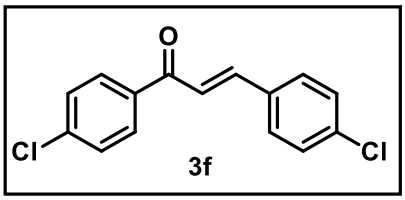
Structure	Spectral data
	Yellow viscous liquid; FT-IR (KBr) cm^{-1} : 3433, 3351,1591, 1523, 1436, 1045, 875.4, 757, 617, 585, 455, 437; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 14.35 (s, 1H), 13.23-13.04 (m, 1H), 9.00 (s, 1H), 7.72-7.57 (m, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz,) δ 135.2,

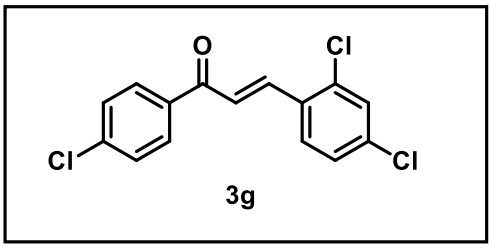
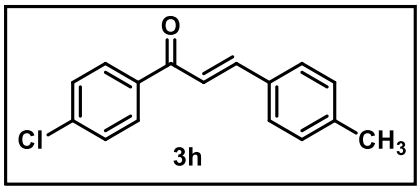
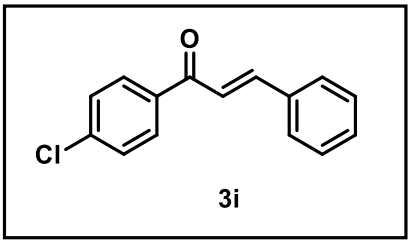
1,3-disulfoimidazolium chloride [DSIM][Cl]	120.5 and 119.9.
 1,3-disulfoimidazolium trifluoroacetate [DSIM][CF_3COO]	Brown viscous liquid; FT-IR (KBr) cm^{-1} : 3438, 1747, 1633, 1447, 1183, 1057, 1021, 883, 847, 775, 575; ^1H NMR (DMSO-d_6, 400 MHz): δ 14.15 (s, 1H), 13.42 (s, 1H), 9.05-8.88 (m, 1H), 7.60-7.48 (m, 2H);^{13}C NMR (DMSO-d_6, 100 MHz,): δ 158.5, 136.7, 134.6, 119.6 and 62.37.
 2-ethyl-1,3-disulfoimidazolium chloride [EDSIM][Cl]	Yellow viscous liquid; FT-IR (KBr) cm^{-1} : 3437, 2929, 2860, 1629, 1453, 1176, 1054, 872, 750 581; ^1H NMR (DMSO-d_6, 400 MHz): δ 13.95 (s, 1H) 12.96 (s, 1H), 7.47-7.42 (m, 2H), 2.88-2.84 (m, 2H), 1.24-1.18 (m, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 149.3, 118.9, 18.8 and 12.4.
 2-ethyl-1,3-disulfoimidazolium trifluoroacetate [EDSIM][TFA]	Brown viscous liquid; FT-IR (KBr) cm^{-1} : 3432, 2928, 2859, 1775, 1627, 1465, 1233, 1153, 1051, 889, 763, 692, 579; ^1H NMR (DMSO-d_6, 400 MHz) : δ 13.79 (s, 2H), 7.47 (s, 2H), 2.88 (q, *J* = 8.0 Hz, 2H), 1.22 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) : δ 159.2, 149.5, 119.4, 116.4, 19.6 and 10.9.
	Brown viscous liquid; FT-IR (KBr) cm^{-1}: 3429, 2959, 2923, 2855,1627, 1467, 1238, 1165, 1047, 1019, 882,

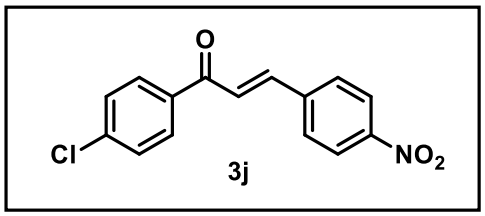
 N,N-Disulfodibutylammonium chloride [DBDSA][Cl]	874, 586; ^{1}H NMR (DMSO-d_6, 400 MHz) : δ 8.52 (s, 2H), 2.73 (s, 4H), 1.49-1.48 (m, 4H), 1.20-1.19 (s, 4H), 0.77 - 0.76 (m, 6H) ; ^{13}C NMR (DMSO-d_6, 100 MHz): δ 47.2, 27.4, 19.9 and 13.2.
 N,N-Disulfodibutylammonium trifluoroacetate [DBDSA][TFA]	Dark brown viscous liquid; FT-IR (KBr) cm^{-1}: 3432, 2965, 2934, 1794, 1615, 1459, 1243, 1159, 1063, 1021, 883, 577; ^{1}H NMR (DMSO-d_6,400 MHz) : δ 8.38 (s, 2H), 2.79 (s, 4H), 1.53-1.48 (m, 4H), 1.28-1.23 (m, 4H), 0.84-0.81 (m, 6H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 159.6, 46.9, 27.9, 19.6, and 12.8
 1,4-tetrasulfopiperazinium chloride $[TSPi][Cl]_2$	Brownish yellow viscous liquid; FT-IR (KBr) cm^{-1}: 3438, 2924, 2842, 1741, 1635, 1455, 1170, 1064, 868, 574; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 13.48 (s, 4H), 3.75 (s, 8H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 52.3.

5B.4.4 Spectral data of Chalcones

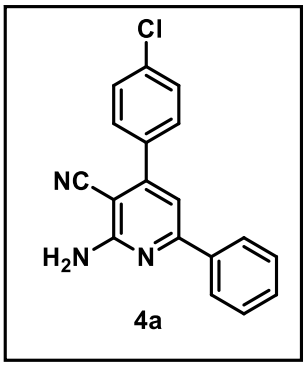
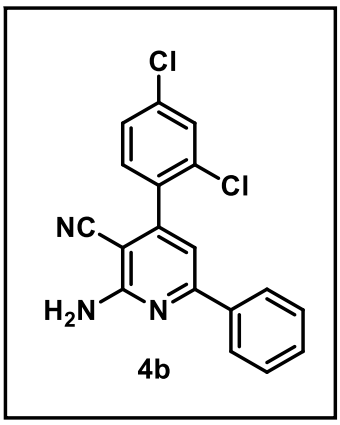
Structure	Spectral data
 3a 3-(4-chlorophenyl)-1-phenylprop-2-en-1-one	Yellowish white solid; m.p. 113.4-114.6^{o}C (lit. 112-114^{o}C) [36]; FT-IR (KBr) cm^{-1}: 3060, 3030, 2980, 1669, 1610, 1565,1482, 1332, 1204, 1002, 814, 769, 664, 469; ^{1}H NMR ($CDCl_3$, 400 MHz) : δ 8.01 (d, *J* = 8.0 Hz, 2H), 7.75 (d, *J* = 7.7 Hz, 1H), 7.61-7.56 (m, 3H), 7.52-7.48 (m, 3H), 7.39 (d, *J* = 7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 190.2, 143.3, 137.9, 133.3, 132.9, 129.6, 129.2, 128.6, 128.5 and 122.4.
 3b 3-(2,4-dichlorophenyl)-1-phenylprop-2-en-1-one	Yellowish white solid; m.p. 71.3-73.5^{o}C (lit.72-74^{o}C)[37]; FT-IR (KBr) υ cm^{-1} : 3406, 3067, 3044, 2924, 1670, 1603, 1565, 1460, 1422, 1385, 1340, 1303, 1250, 1197, 1100, 1010, 972, 867, 824, 800, 790, 732, 687, 649, 544, 439; ^{1}H NMR ($CDCl_3$, 400 MHz) : δ 8.09 (d, *J* = 16 Hz, 1H), 8.01-7.99 (m, 2H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.61-7.57 (m, 1H), 7.52-7.45 (m, 4H) 7.31-7.28 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 189.6, 139.7, 137.5, 135.9, 133.3, 131.5, 130.4, 128.4, 127.3 and 125.4.
 3c 3-(4-methoxyphenyl)-1-phenylprop-2-en-1-one	Light yellow solid; m.p. 71.6-73.2^{o}C (lit.74-76^{o}C) [37]; FT-IR (KBr) υ cm^{-1}: 3387, 2956, 2922, 2835, 1665, 1602, 1575, 1490, 1448, 1340, 1310, 1265, 1204, 1171, 1081, 1032, 972, 822, 777, 664, 507; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.00 (d, *J* = 6.9 Hz, 2H), 7.79 (d, *J* = 15.6 Hz, 1H),7.61-7.55 (m, 3H), 7.51-7.39 (m, 3H), 6.93 (d, *J*

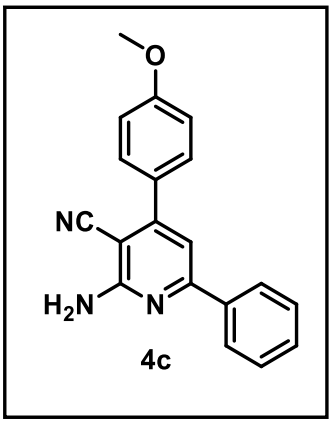
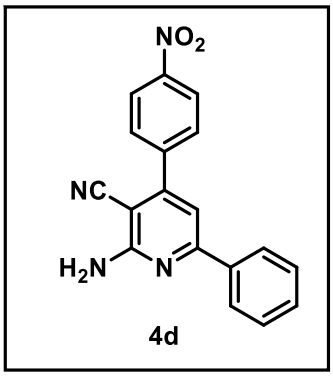
	= 8.7 Hz, 2H) 3.85 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 190.7, 161.7, 144.6, 138.6, 133.0, 130.4, 127.7, 126.7, 120.1, 113.8 and 55.4.
 3-(4-nitrophenyl)-1-phenylprop-2-en-1-one	Yellowish white solid; m.p. 158.7-160.4^{o}C (lit.160-162^{o}C) [37]; FT-IR (KBr) υ cm^{-1} :3412, 3098, 3074, 2922, 1655, 1609, 1515, 1443, 1409, 1337, 1219, 1104, 1015, 981, 841, 744; ^{1}H NMR ($CDCl_3$, 400 MHz) : δ 7.98-7.96 (m, 4H), 7.67-7.64 (m, 2H), 7.53-7.49 (m, 5H) ; ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 194.5, 135.3, 132.8, 129.8 and 129.0.
 1-phenyl-3-p-tolylprop-2-en-1-one	Yellow solid; m.p. 89.6-90.6^{o}C (lit. 90-92^{o}C) [36]; FT-IR (KBr) υ cm^{-1}: 3402, 3023, 3063, 2916, 2845, 1659, 1595, 1560, 1443, 1347, 1197, 1010, 979, 822, 771, 664. 484; ^{1}H NMR ($CDCl_3$, 400 MHz) : δ 8.01 (d, *J* = 7.3 Hz, 2H), 7.80 (d, *J* = 8 Hz, 1H), 7.59-7.47 (6H, m), 7.25-7.21 (m, 2H), 2.39 (s, 3H); ^{13}C ($CDCl_3$, 100 MHz) : δ 190.9, 145.4, 141.1, 138.0, 132.9, 131.9, 129.4, 128.6, 120.7 and 21.8
 1,3-bis(4-chlorophenyl)prop-2-en-1-one	Light yellow solid; m.p. 163.3-165.2°C; FT-IR (KBr) υ cm^{-1}: 3418, 3084, 3033, 1654, 1590, 1558, 1474, 1397, 1333, 1101, 1008, 979, 811, 727, 663, 547, 476; ^{1}H NMR ($CDCl_3$, 400 MHz) : δ 7.94 (d, *J* = 8.0 Hz, 2H), 7.74 (d, *J* = 16.0 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.47-7.37 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 188.5, 143.1, 139.7, 136.6, 136.4, 133.3, 129.6, 129.5, 128.8, 128.5, and 121.3.

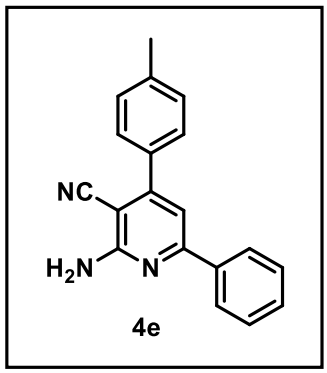
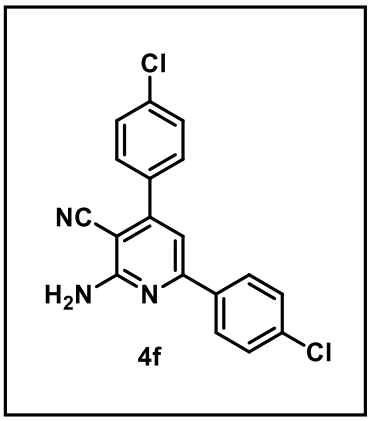
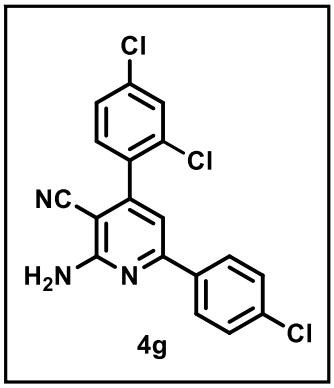
 1-(4-chlorophenyl)-3-(2,4-dichlorophenyl) prop-2-en-1-one	Light yellow solid; m.p. 139.2-141.2°C; FT-IR (KBr) υ cm^{-1} : 3403, 3060, 3044, 2929, 1670, 1612, 1565, 1462, 1427, 1385, 1341, 1303, 1255, 1197, 1100, 1016, 972, 867, 824, 806, 790, 737, 687, 650, 548, 436; ^{1}H NMR ($CDCl_3$, 400 MHz) : δ 8.10 (d, *J* = 8.09 Hz, 1H), 7.95-7.87 (m, 3H), 7.66 (d, *J* = 7.66, 1H), 7.48-7.39 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 189.2, 140.1, 138.9, 136.7, 135.9, 134.8, 131.8, 130.4, 127.3 and 124.4.
 1-(4-chlorophenyl)-3-(p-tolyl)prop-2-en-1-one	Yellow solid; m.p. 143-145.2°C; FT-IR (KBr) υ cm^{-1}: 3400, 3030, 3063, 2918, 2850, 1662, 1595, 1561, 1440, 1347, 1197, 1012, 979, 823, 773, 664, 484; ^{1}H NMR ($CDCl_3$, 400 MHz) : δ 7.97-7.75 (m, 2H), 7.48-7.39 (m, 8H), 2.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 188.5, 139.7, 136.0, 134.4, 129.9, 128.8, 128.1, 123.9 and 19.9.
 1-(4-chlorophenyl)-3-phenylprop-2-en-1-one	Light yellow solid; m.p. 98.5-99.7°C; FT-IR (KBr) cm^{-1}: FT-IR (KBr) cm^{-1}: 3056, 3028, 2980, 1671, 1610, 1565,1485, 1330, 1210, 1007, 814, 769, 665, 467; ^{1}H NMR ($CDCl_3$, 400 MHz) : δ 8.01(d, *J* = 8.01 Hz, 2H), 7.75 (d, *J* = 7.7 Hz, 1H), 7.59-7.56 (m, 3H), 7.52-7.49 (m, 3H), 7.38 (d, *J* = 7.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 190.1, 143.5, 138.3,136.4,133.3, 129.6, 129.2, 128.4 and 122.4.
	Light orange solid; m.p. 160.1-163.4°C; FT-IR (KBr) υ cm^{-1}: 3422, 3122, 1664, 1613, 1553, 1407, 1344, 1213, 1100, 1006, 812, 756, 656, 537; ^{1}H NMR ($CDCl_3$, 400

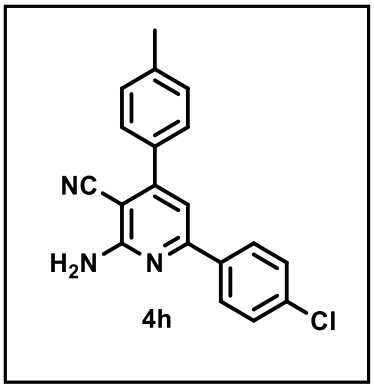
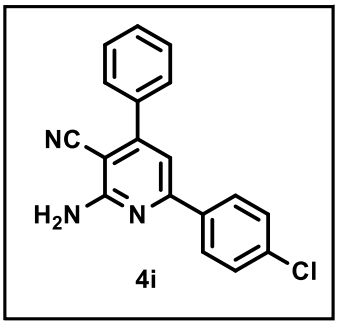
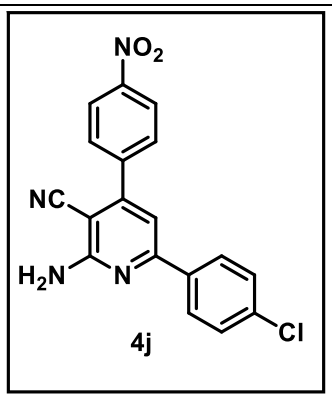
 3j 1-(4-chlorophenyl)-3-(4-nitrophenyl)prop-2-en-1-one	MHz) : δ 8.27 (d, *J* = 8.0 Hz, 2H), 7.97 (d, *J* = 8.0 Hz, 2H), 7.83-7.76 (m, 3H), 7.58 (d, *J* = 16.0Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 2H) ; ^{13}C NMR ($CDCl_3$, 100 MHz) :δ 188.1, 149.1, 141.9, 140.4, 139.9, 136.0, 130.3, 129.1, 128.6, 125.2 and 124.2.

5B.4.5 Spectral data of 2-amino-3-cyanopyridine

Structure	Spectral data
 4a 2-amino-4-(4-chlorophenyl)-6-phenylpyridine-3-carbonitrile	Light yellow solid, m.p. 226.3-227.2 ℃ (lit. 234-236 ^{o}C) [19] ; FT-IR (KBr) cm^{-1}: 3480, 3356, 3215, 2213, 1618, 1543, 1478, 1444, 1370, 1254, 1088, 1006, 815, 758, 683, 625, 551, 418; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99-7.97 (m, 2H), 7.57-7.55 (m, 2H), 7.50-7.46 (m, 5H), 7.15 (s, 1H), 5.39 (s, 2H) ; ^{13}C NMR (100 MHz, $CDCl_3$) : δ 160.3, 153.5, 137.5, 136.4, 135.2, 130.4, 129.9, 129.5, 128.8, 127.2, 117.4, 110.8 and 87.7.
 4b 2-amino-4-(2,4-dichlorophenyl)-6-phenylpyridine-3-carbonitrile	Dark orange solid, m.p. 177-178 ℃; FT-IR (KBr) cm^{-1}: 3504, 3372, 3272, 3190, 3074, 2213, 1610, 1577, 1490, 1353, 1246, 1122, 857,766, 683, 625 , 526; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98-7.96 (m, 2H), 7.56 (m, 1H), 7.47-7.45 (m, 3H), 7.40-7.37 (m, 1H), 7.32-7.30 (m, 1H), 7.11 (s, 1H) 5.39 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 159.8, 151.9, 137.6, 136.2, 134.4, 133.3, 131.2, 130.5,

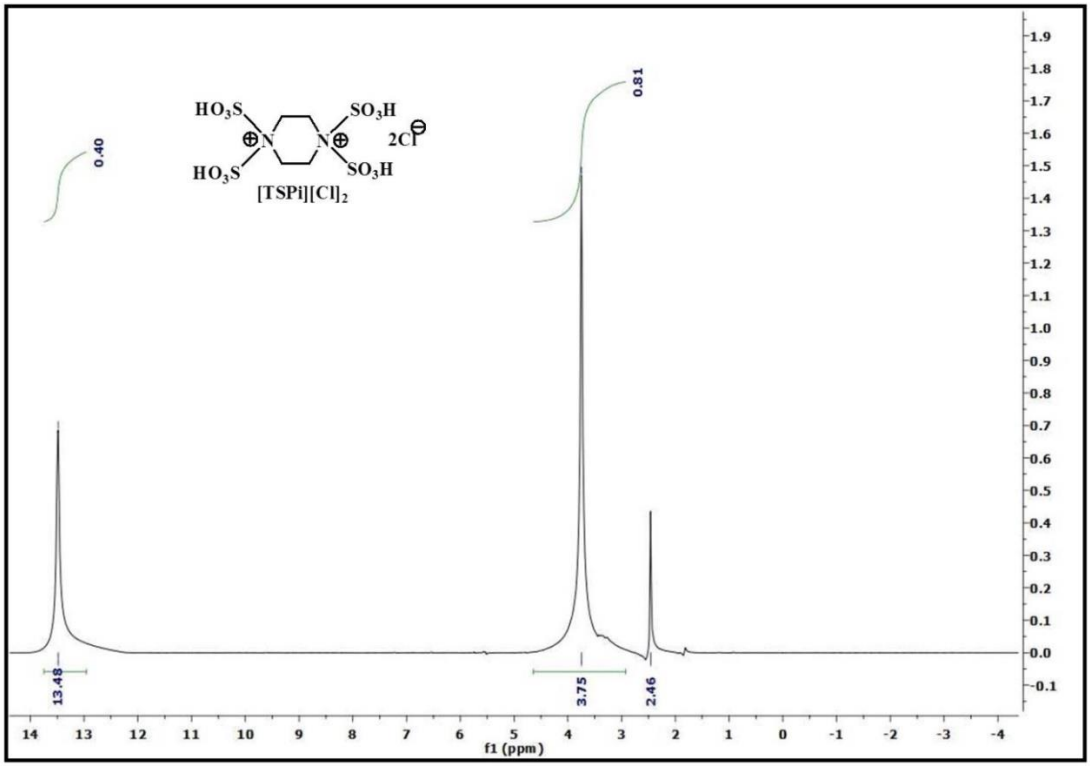
	130.3, 128.9, 127.6, 127.5, 116.2, 112.1 and 89.9.
 2-amino-4-(4-methoxyphenyl)-6-phenylpyridine-3-carbonitrile	Pale yellow solid, m.p.183 − 184 °C (lit. 180 − 182 °C) [2] ; FT- IR(KBr) cm^{-1}: 3472, 3314, 3182, 2933, 2213, 1634, 1510, 1378, 1254, 1179, 1014, 823, 758, 699, 518; ^1H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 12.0 Hz, 2H), 7.47-7.45 (m, 3H), 7.17 (s, 1H), 7.03 (d, *J* = 8.0 Hz, 2H), 5.32 (s, 2H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.1, 160.5, 159.5, 154.8, 138.2, 130.1, 129.3, 128.9, 127.3, 114.5, 111.1, 87.9 and 58.4.
 2-amino-4-(4-nitrophenyl)-6-phenylpyridine-3-carbonitrile	Orange yellow solid, m.p. 212.9-213.9 °C (lit. 210-211 °C) [28]; FT-IR (KBr) cm^{-1}: 3488, 3372, 2917, 2859, 2213,1626, 1560, 1510, 1353, 1254, 1113, 998, 840, 749, 691; ^1H NMR (400 MHz, $CDCl_3$): δ 8.37 (d, *J* = 8.0Hz, 2H), 8.01-7.98 (m, 2H), 7.78 (d, *J* = 8.0 Hz, 2H), 7.49-7.46 (m, 3H), 7.19 (s, 1H), 5.44 (s, 2H) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.5, 152.7, 143.3, 137.5, 130.8, 129.7, 129.0, 128.4, 127.4, 124.0, 114.1, 100.1 and 87.8.
	Dark yellow solid, m.p. 175-177.1 °C (lit. 175-176 °C) [10]; FT-IR (KBr) cm^{-1}: 3472, 3289, 3173, 2909, 2205, 1907, 1626, 1560, 1343, 1444, 1362, 1246, 1171, 1105, 923, 857, 766, 693, 642, 526, 482; ^1H NMR (400MHz, $CDCl_3$): δ 8.00-

 2-amino-4-(p-tolyl)-6-phenylpyridine-3-carbonitrile	7.97 (m, 2H), 7.55-7.47 (m, 5H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.18 (s, 1H), 5.38(s, 2H), 2.43 (s, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.7, 159.2, 155.1, 139.3, 138.3, 133.7, 129.9, 129.5 128.6, 128.2, 127.3, 117.7, 110.7, 100.2, 88.1 and 21.3.
 2-amino-4-(4-chlorophenyl)-6-(4-chlorophenyl) pyridine-3-carbonitrile	Yellow solid, m.p**.** 248.2-249.5 ℃ (lit. 248-250℃) [38]; FT-IR (KBr) cm^{-1}: 3442, 3354, 3226, 2911, 2844, 2214, 1794, 1644, 1550, 1520, 1503, 1463, 1396, 1295, 1242, 1095, 1013, 819, 725, 504; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95-7.93 (m, 2H), 7.57-7.54 (m, 2H), 7.50-7.48 (m, 2H), 7.44-7.42 (m, 2H), 7.12 (s, 1H), 5.35 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 160.2, 148.9, 136.9, 136.2, 135.5, 129.9, 129, 128.2, 115.5, 100.4 and 94.8.
 2-amino-6-(4-chlorophenyl)-4-(2,4-dichlorophenyl)-3-carbonitrile	Yellow solid, m.p**.** 227.6-228.4℃; FT-IR (KBr) cm^{-1}: 3462, 3349, 2951, 2891, 2844, 2221, 1618, 1577, 1543, 1476, 1376, 1255, 1101, 1027, 813, 618, 524, 490; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94-7.91 (m, 2H), 7.56 (s, 1H), 7.44-7.42 (m, 2H), 7.40-7.37 (m, 1H), 7.31-7.29 (m, 1H) 7.07 (s, 1H), 5.35 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 160.1, 138.9, 135.2, 134.4, 131.8, 130.4, 128.1, 123.6, 111.2 and 99.9.

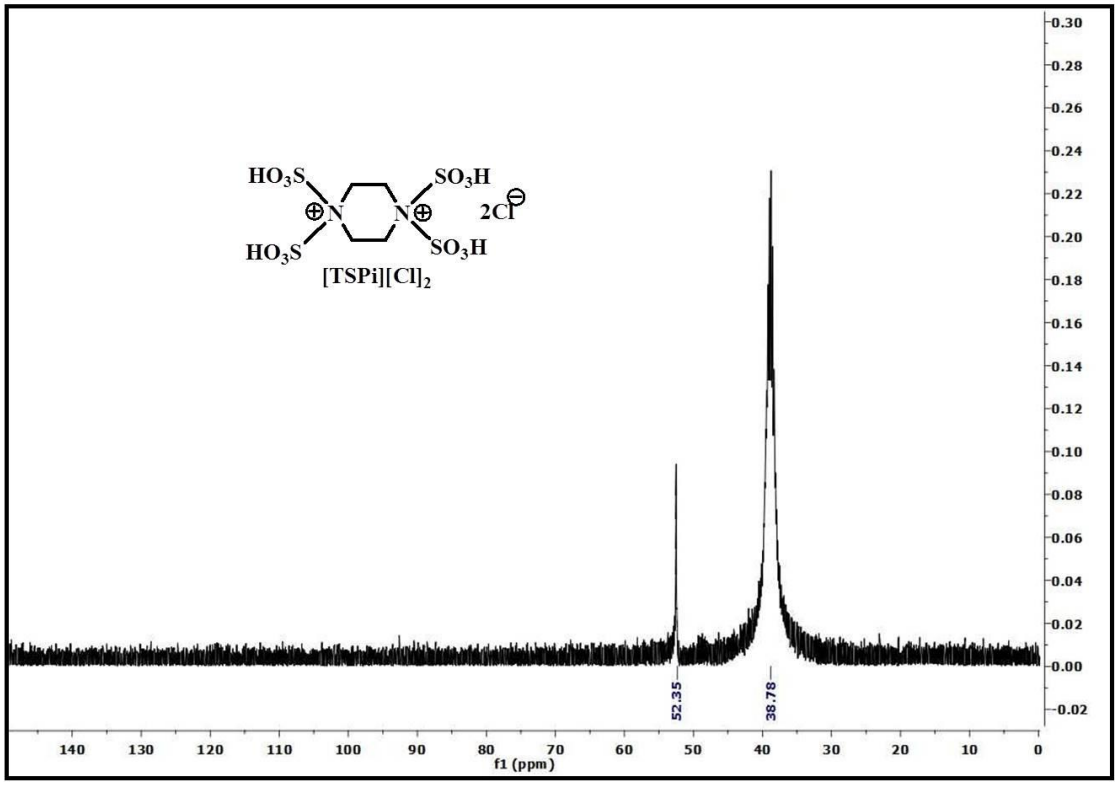
 2-amino-4-(p-tolyl)-6-(4-chlorophenyl)pyridine-3-carbonitrile	Orange yellow solid, m.p. 219-220 ℃; FT-IR (KBr) cm^{-1}: 3495, 3387, 2925, 2865, 2201, 1610, 1590, 1543, 1483, 1449, 1429, 1369, 1235, 1013, 799, 725, 644 , 497;^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95-7.91 (m, 2H), 7.53-7.51 (m, 2H),7.44-7.42 (m, 2H), 7.41-7.31 (m, 2H), 7.15 (s, 1H), 5.35 (s, 2H) 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 160.7, 158.8, 155.8, 140.8, 137.1, 134.1, 129.2, 117.2, 88.6 and 21.9.
 2-amino-4-benzyl-6-(4-chlorophenyl) pyridine-3-carbonitrile	Orange solid, m.p. 239.3-240.1 ℃ (lit. 240-242℃) [19]; FT-IR (KBr) cm^{-1}: 3440, 3352, 3226, 2994, 2844, 2195, 1784, 1629, 1559, 1503, 1495, 1426, 1357, 1260, 1102, 1087, 824, 729, 675; ^{1}H NMR (400 MHz, $CDCl_3$):δ 7.96-7.93 (m, 2H), 7.62-7.60 (m, 2H),7.52-7.50 (m, 2H), 7.45-7.42 (m, 3H), 7.16 (s, 1H), 5.35 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 162.9, 149.4, 146.8, 139.7, 137.1, 135.9, 128.8, 111.2, 111.1 and 99.9.
 2-amino-4-(4-nitrophenyl))-6-(4-chlorophenyl) pyridine-3-carbonitrile	Orange yellow solid, m.p. 257.6-260.1℃; FT-IR (KBr) cm^{-1}: 3476, 3382, 2921, 2859, 2213,1626, 1562, 1511, 1353, 1262, 1123, 988, 840, 747, 690; ^{1}H NMR (400 MHz, $CDCl_3$):δ 8.20 (d, *J* = 8.0Hz, 2H), 7.83-7.80 (m, 2H), 7.74-7.72 (m, 2H), 7.64 (d, *J* = 8.0Hz, 2H), 7.37 (s, 1H), 5.35 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 161.5, 142.7,140.8, 139.3, 136, 130.7, 128.4, 124.4, 124, 100.4 and 87.9.

5B.4.6 NMR spectra of $[TSPi][Cl]_2$ ionic liquid

1. ^{1}H NMR spectra of $[TSPi][Cl]_2$

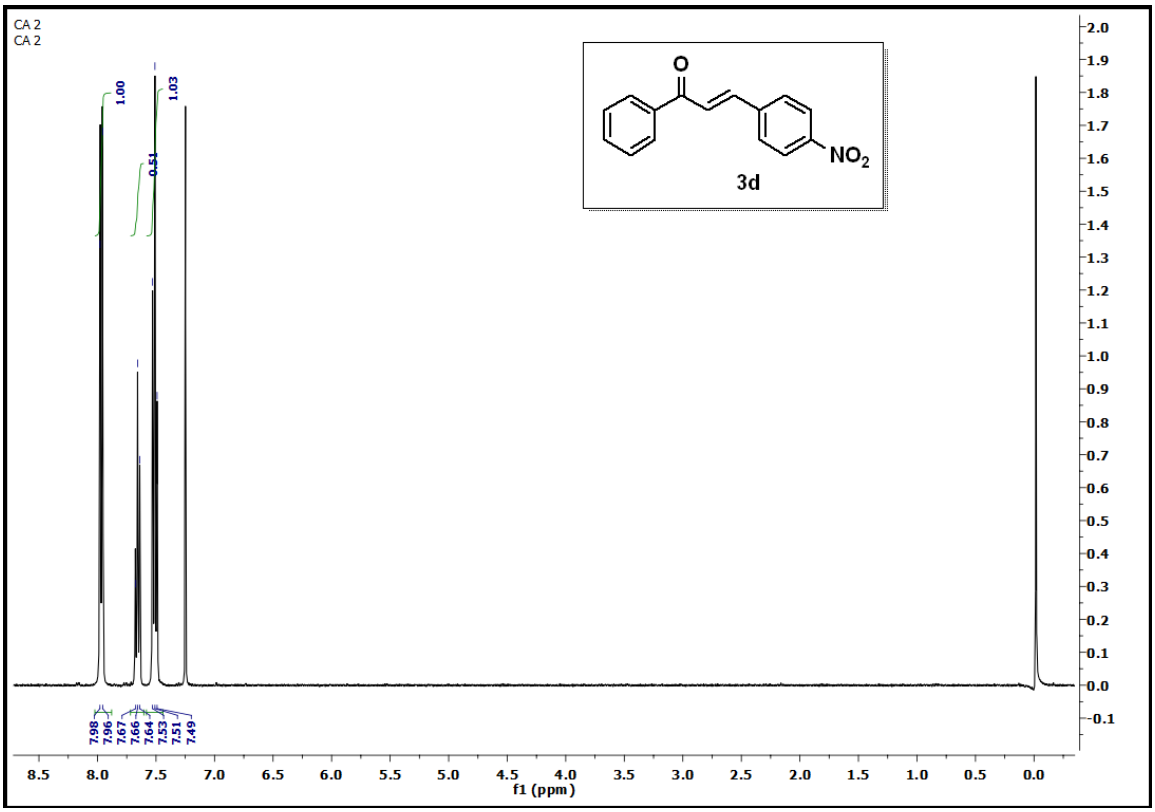


2. ^{13}C NMR spectra of $[TSPi][Cl]_2$

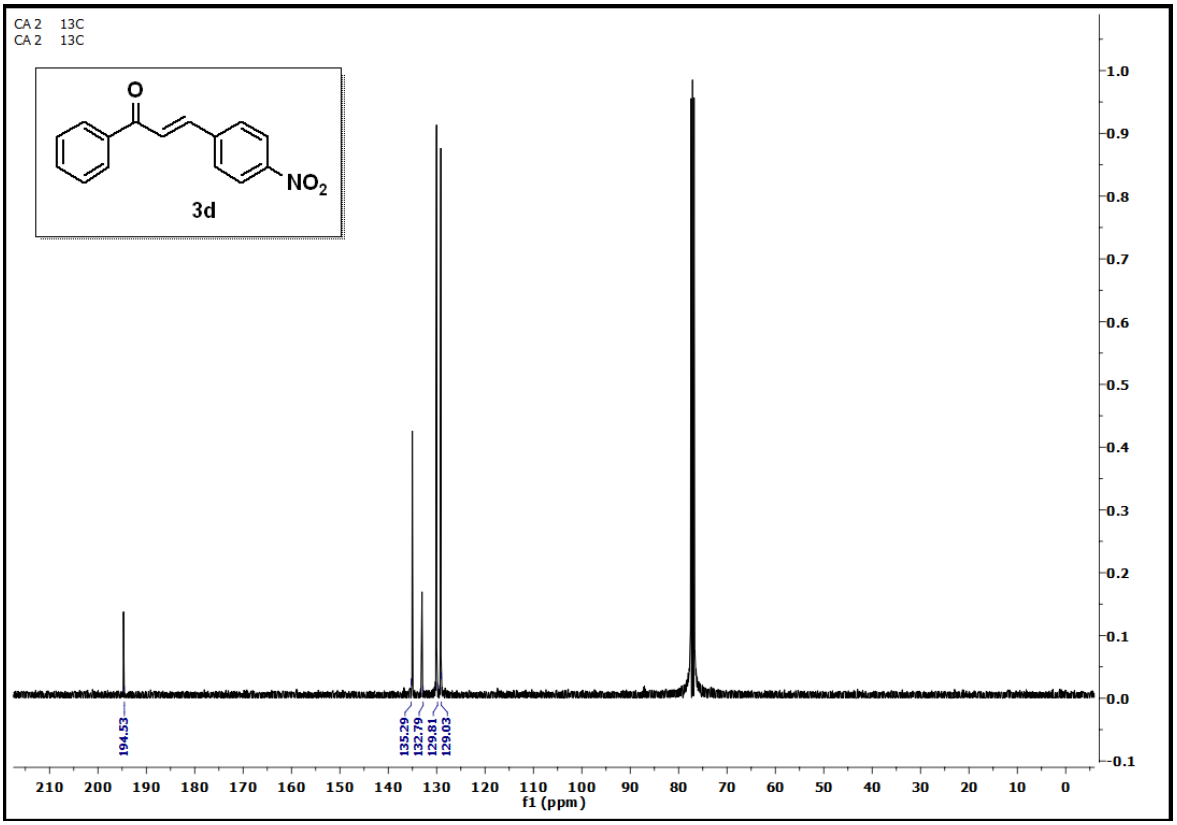


5B.4.7 NMR spectra of 3d

1. ^{1}H NMR spectra of 3d

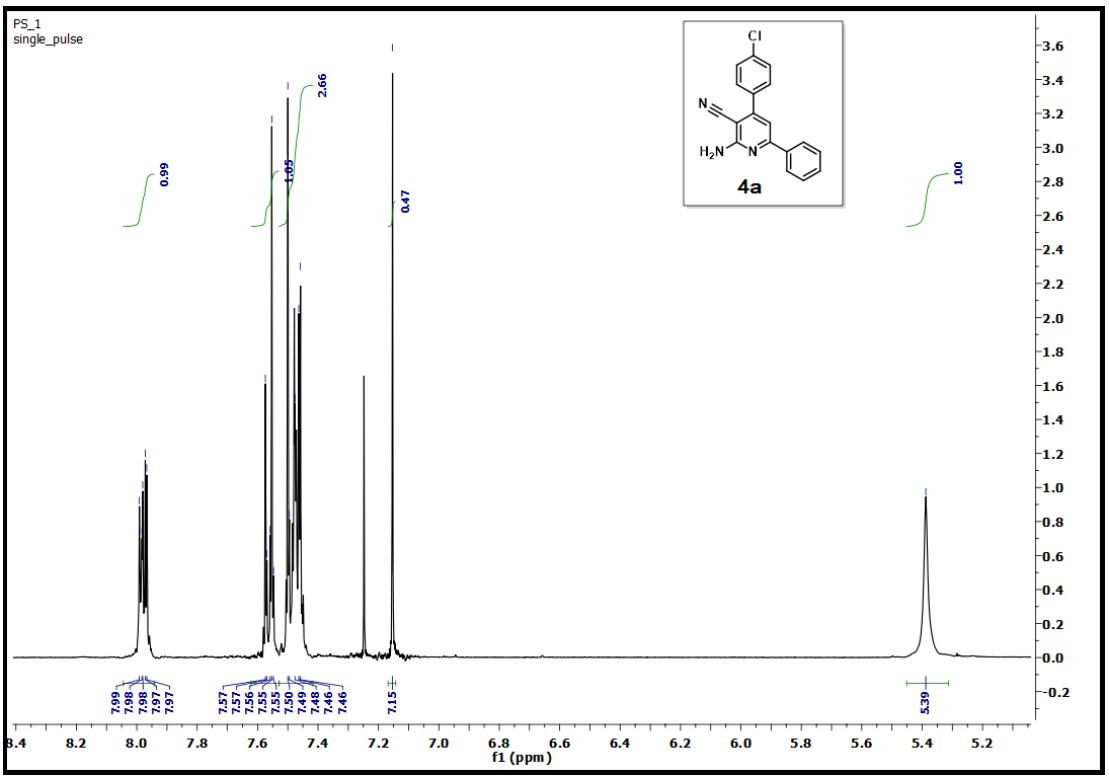


2. ^{13}C NMR spectra of 3d

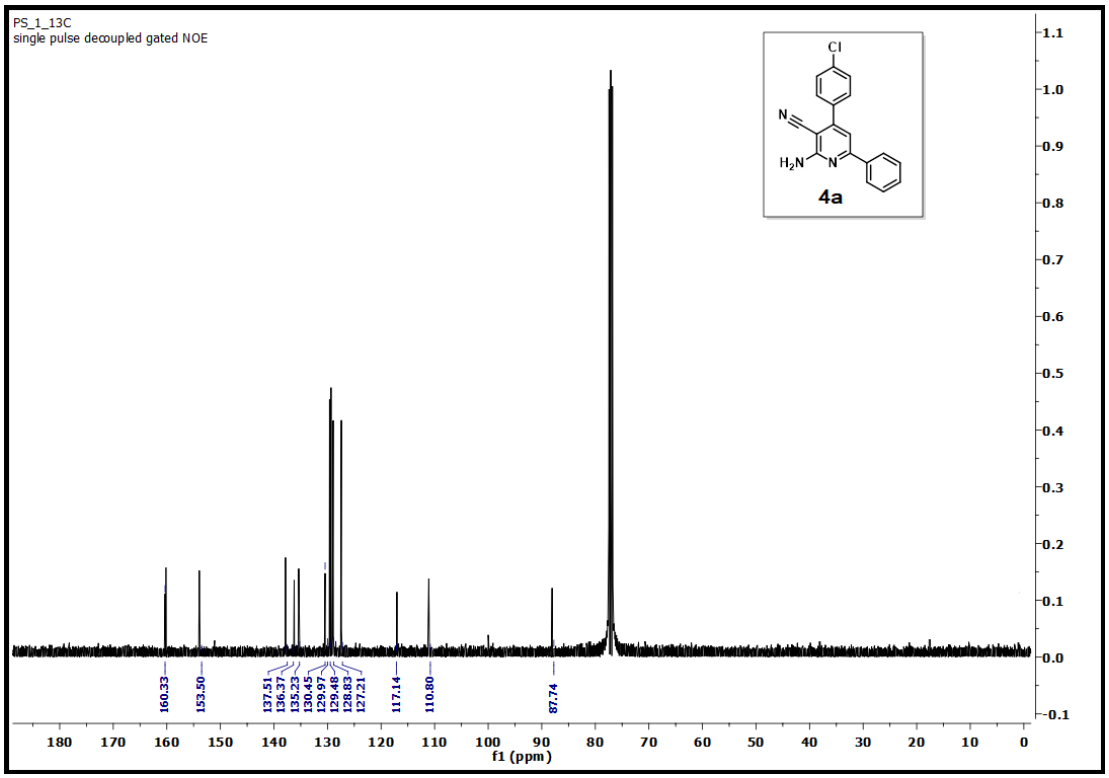


5B.4.8 NMR spectra of 4a

1. ^{1}H NMR spectra of 4a



2. ^{13}C NMR spectra of 4a



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