Chapter 6

N, N, N', N'-tetrasulfopiperazinium dicationic ionic liquids as prominent acidic catalyst for one pot synthesis of 2-amino-4, 6-diaryl pyrimidines

6A.1 An insight into the behavior of monocationic and dicationic ionic liquids

Monocationic ionic liquids (MILs) have been synthesized and studied extensively while the area of dicationic ionic liquids (DILs) is still to be explored more. Transition from monocationic to dicationic analogue involving similar class of compound often results into variations in behavior of the material. **Subunit 1.2.6** (**Chapter 1**) discusses the classification and applications of the DILs which clearly displays the compositional diversity according to their dicationic existence. The DILs facilitate more combinations of cationic components, counter anions and also bridging groups in between the cations which brings many additional advantages to this class of ILs as compared to the MILs [1, 2]. It was mentioned in literature that some physicochemical properties of the DILs are superior to the corresponding MILs such as viscosity, surface tension, wide temperature window to exist in liquid state, thermal stability *etc.* [1]. Most of the developments of DILs have been studied till date centered on imidazolium and ammonium ionic liquids. Considering the limited study on structure property relationship of the DILs, Majhi and his group explained the differences in the behavior of dicationic and monocationic ionic liquids by time resolved-fluorescence, NMR and fluorescence correlation spectroscopy (FCS) [3]. Also, Montalbán *et al.* assessed ecotoxicity of the dicationic versus monocationic ionic liquids and concluded dicationic ILs as more environmentally friendly for industrial applications [4].

6A.2 Piperazine as a unique dicationic core

Large number of symmetric or asymmetric DILs are synthesized from organic cations containing one or two –N atom in each heterocyclic unit which include mainly imidazolium, pyridinium cations (subunit **1.2.6**, **Chapter 1**). Interestingly, in the wide range of N-heterocyclic compounds more specifically where two N atoms are present, only one of the N atoms is capable of acquiring positive charge. Therefore, those cations have to be connected *via* a linker like alkyl chain to another cation to form a dication. But piperazine avoids the complexity of linker and requirement of another cationic part by utilizing both the N-atoms present in the same structure to form dications. Being able to form dications on its own makes the piperazinium ILs somehow different from the other DILs. Surge of literature gives very few reports on piperazinium DILs. In 1987, Creighton and Taylor reported the synthesis of dihalide salts of the 1, 1, 4, 4-tetramethylpiperazinium dication. The reaction of N, N, N', N'-tetramethyl-l, 2-

diaminoethane (tmen) with 1, 2-dihalogenoethanes gave the dicationic salts of piperazine. But this work was about the formation of piperazinium core itself. Piperazine did not involve directly in the synthesis of dicationic salt from the beginning [5]. Also, Harmon and Brooks (1993) synthesized N, N, N', N'-tetramethyl piperazinium (TMP^{2+}) iodide, chloride, fluoride and bromide utilizing N, N'-dimethyl piperazine and methylhalide and studied the thermodynamic behavior of them [6] (**Fig.6A.1**).

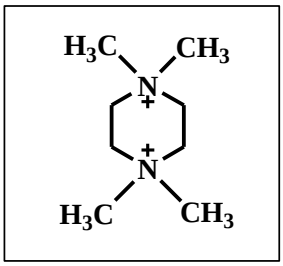
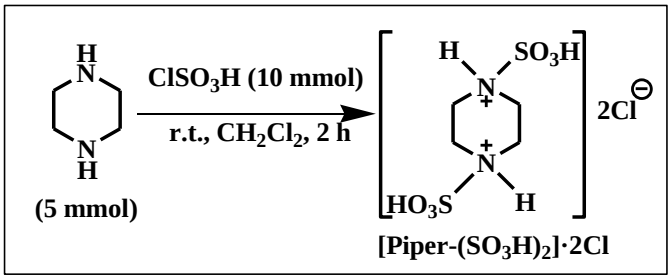


Fig.6A.1: Structure of N, N, N', N'-tetramethylpiperazinium dication

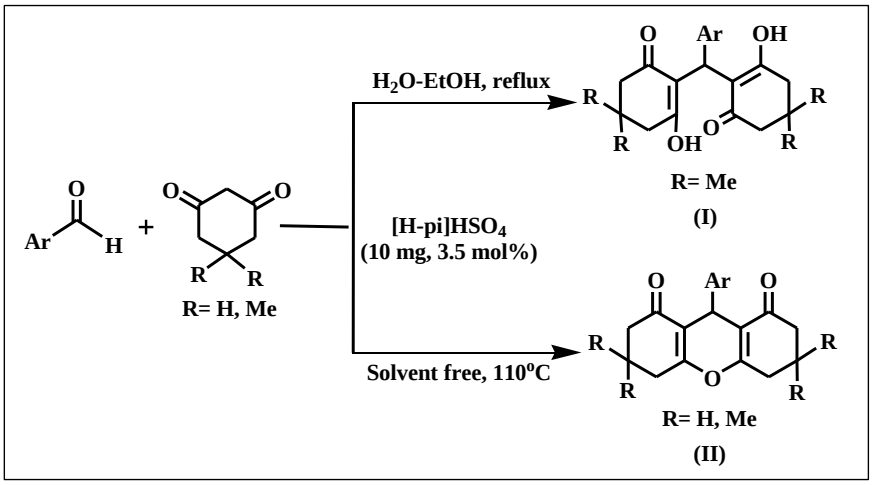
In 2016, Koodehi *et al.* synthesized 1, 4-disulfopiperazine-1, 4-diiumchloride ([Piper-$(SO_3H)_2$]2Cl), as Brönsted acidic ionic solid and used as efficient catalyst for N-Boc protection of amines without solvent interference at room temperature (**Scheme 6A.1**) [7]. Chemoselectivity, short reaction time, excellent yield of the products and reusability of the catalyst were the advantages of this method. Only 5 mol% of the catalyst was used for the N-Boc protection of aniline within 3 min to give excellent yield of the product.



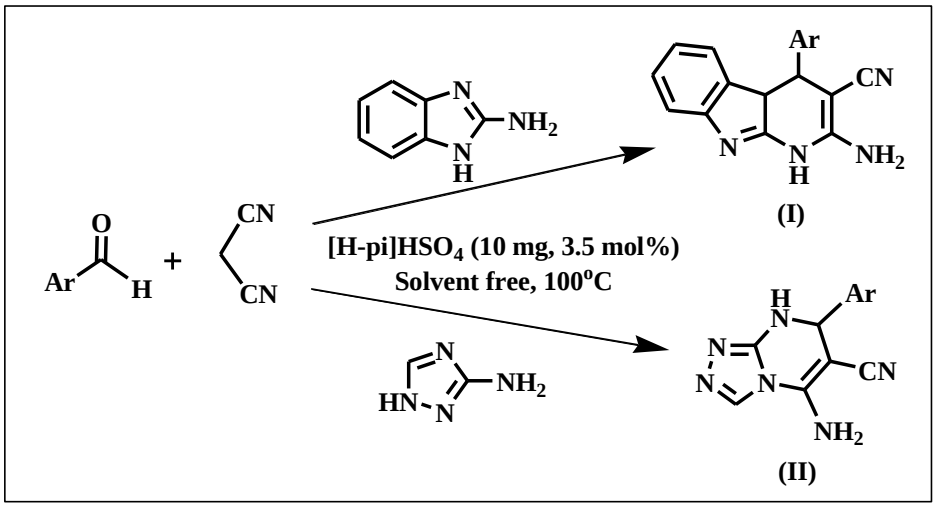
Scheme 6A.1: Synthesis of 1, 4-disulfopiperazine-1, 4-diiumchloride

A DIL 1, 4-piperazinium hydrogen sulfate ([H-pi]HSO_4) was synthesized from the reaction of piperazine with sulfuric acid by Jashnani *et al.* (**Fig.6A.2**) [8] and was analyzed by various analytical techniques. This IL was examined as efficient catalyst for preparation of 2, 2'-arylmethylene-*bis*(3-hydroxy-5, 5-dimethyl-2-cyclohexene-1-one) in aqueous EtOH under reflux condition and 1, 8-dioxooctahydroxanthene derivatives under solvent-free method at 100°C (**Scheme 6A.2**). Also, the same IL was used to catalyze the

three-component reaction of aldehydes, malononitrile and 2-aminobenzimidazole and or 3-amino [1, 2, 4] triazole to produce imidazo [1, 2-a] pyrimidines and triazolo [4, 3-a] pyrimidines (**Scheme 6A.3**) respectively. In all the catalytic reactions, the IL catalyst was recycled successfully up to five cycles.



Scheme 6A.2: Preparation of 2, 2'-arylmethylene-*bis*(3-hydroxy-5, 5-dimethyl-2-cyclohexene-1-one) (**I**) & 1, 8-dioxooctahydroxanthene (**II**) derivatives using [H-pi]HSO_4



Scheme 6A.3: [H-pi]HSO_4 catalyzed synthesis of imidazo [1, 2-a] pyrimidines (**I**) and triazolo [4, 3-a] pyrimidines (**II**)

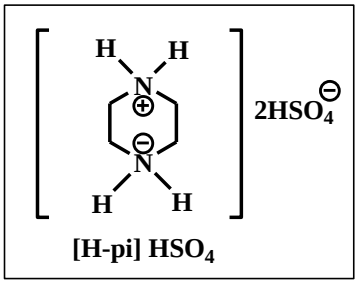
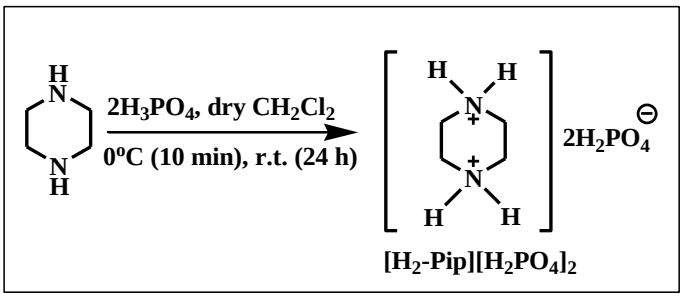
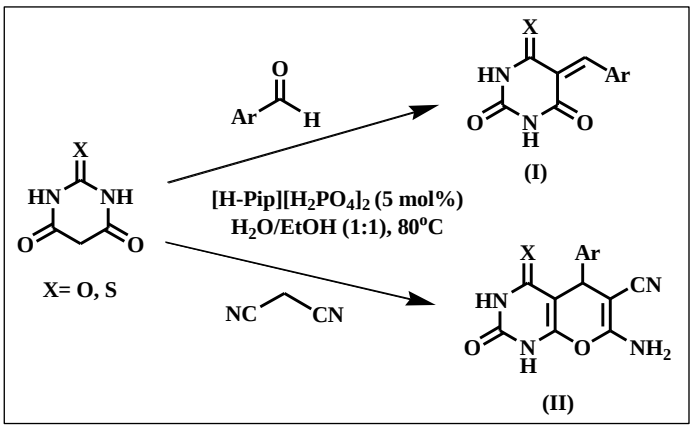


Fig.6A.2: Structure of 1, 4-piperazinium hydrogen sulfate

Recently, Darvishzad *et al.* (2019) developed another new piperazine-based dicationic Brönsted acidic ionic salt named as piperazine-1, 4-diium dihydrogen phosphate [H_2-Pip][H_2PO_4]$_2$ (**Scheme 6A.4**) and it was used as an efficient reusable catalyst for the synthesis of 5-arylidenepyrimidine-2, 4, 6 (1*H*, 3*H*, 5*H*)-trione and pyrano [2, 3-d]pyrimidinone (thione) derivatives [9]. 5 mol% of [H_2-Pip][H_2PO_4]$_2$ at 80^{o}C in H_2O/EtOH (1:1) afforded 74-96% yield of 5-arylidene barbituric acid derivatives and 70-95% yield of pyrano [2, 3, *d*] pyrimidinone(thione) derivatives (**Scheme 6A.5**).

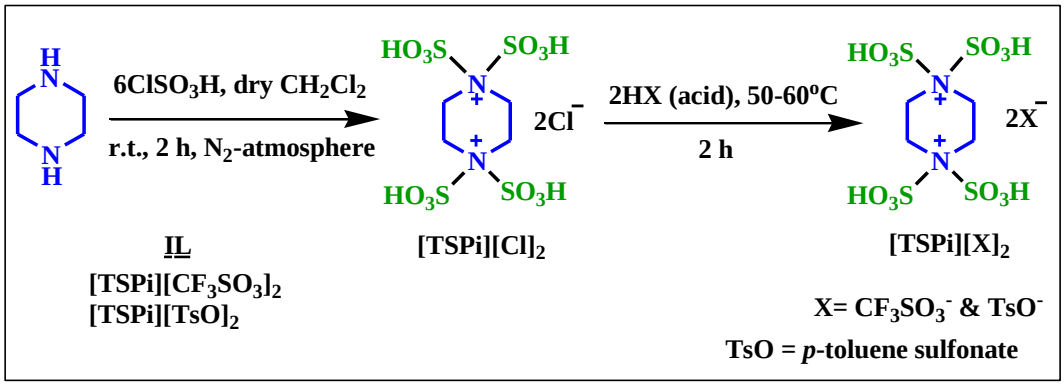


Scheme 6A.4: Synthesis of piperazine-1, 4-diium dihydrogenphosphate



Scheme 6A.5: Synthesis of 5-arylidene barbituric acid derivatives (**I**) & pyrano [2, 3, *d*] pyrimidinone(thione) derivatives (**II**) using [H_2-Pip][H_2PO_4]$_2$

Based on the limited literature on dicationic piperazinium ionic liquids we planned to design a series of -SO_3H functionalized Brönsted acidic piperazinium dicationic ionic liquids $[TSPi][X]_2$ with four sulfonic groups in presence of different counter anions (X) such as chloride (Cl), triflate (-SO_3CF_3) and *p*-toluene sulfonate (TsO) (**Scheme 6A.6**).



Scheme 6A.6: Synthesis of $[TSPi][X]_2$ (X = Cl, CF_3SO_3 & TsO)

6A.3 Pharmacological activities of pyrimidine derivatives

Pyrimidines are aromatic heterocycles containing pyridine like structure with two nitrogen atoms at 1 and 3 positions of the six membered rings. They also represent a broad class of natural and synthesized fused pyrimidine derivatives with variety of biological, clinical and pharmacological activities [10, 11]. Pyrimidine derivatives are integral part of building blocks of nucleic acids DNA and RNA in the form of necleobases thymine, uracil and cytosine [12]. Their pharmacological activities include antibacterial [13], antifungal [14], anti-inflammatory [15], analgesic [16], antiviral [17], antidiabetic [18], anticonvulsant [19], antioxidant [20], anticancer [21], calcium channel blockers activities [22] in addition to potential central nervous system(CNS) depressant properties [23].

Several literature reviews express pyrimidine derivatives as significant biologically active molecules of new era in medicinal chemistry [24-28]. They mentioned the drugs available in market that have pyrimidine nucleus in their structure and used for treatment of several disorders (**Fig.6A.3a-d**). Most of them are mono, di- , tri- and tetra- substituted pyrimidine derivatives. In addition, many pyrimidines and fused pyrimidines are vascular endothelial growth receptors that can be used as cancer therapy agents for various types of cancers as approved by the US Food and Drug Administration [29, 30].

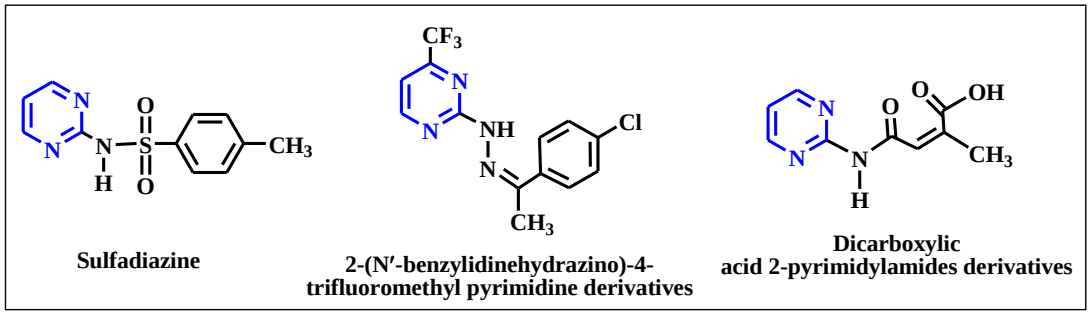


Fig.6A.3a: Some monosubstituted pyrimidine based antibacterial drugs

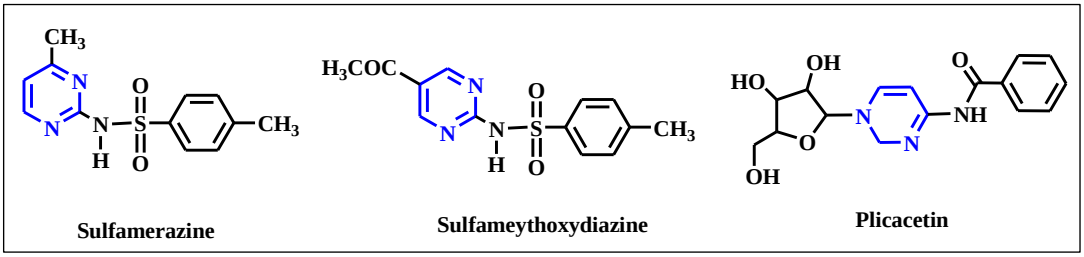


Fig.6A.3b: Some disubstituted pyrimidine based drugs

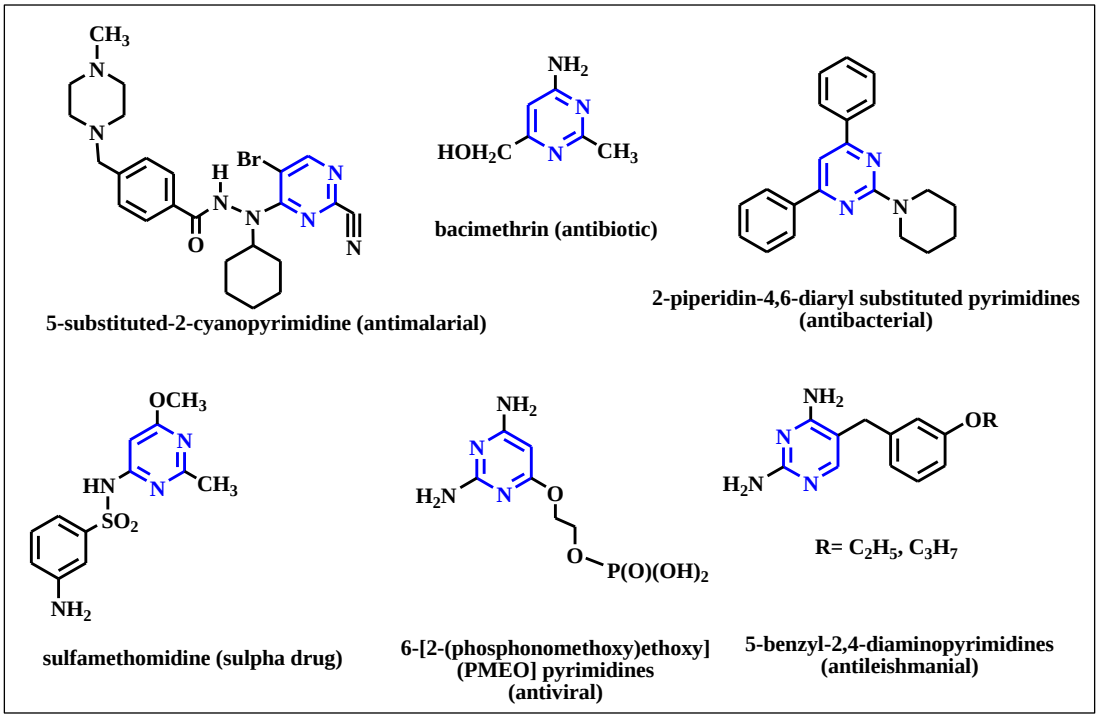


Fig.6A.3c: Some trisubstituted pyrimidine derivatives

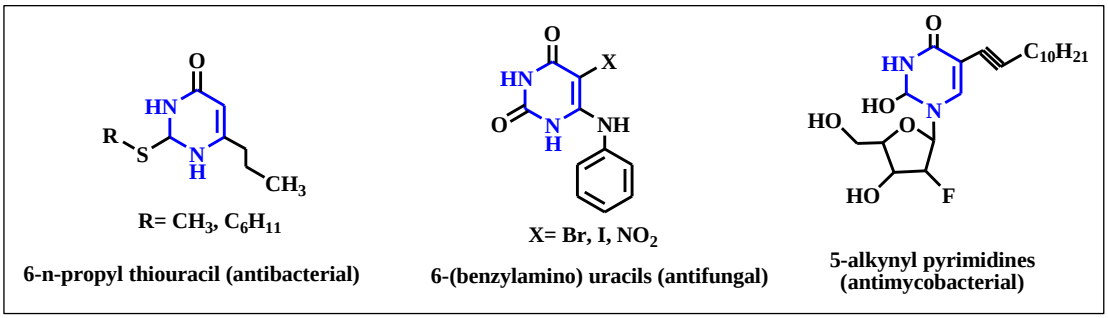


Fig.6A.3d: Some important tetrasubstituted pyrimidine derivatives

Some examples of pyrimidine based anti-cancer drugs are shown in **Fig.6A.4** [27].

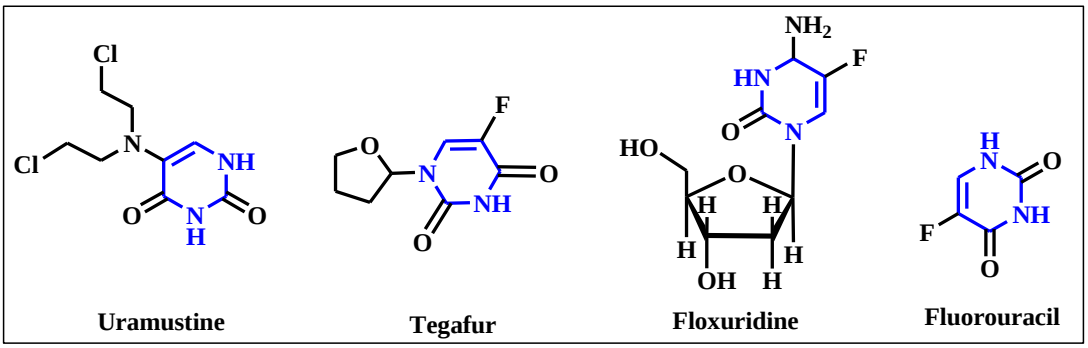
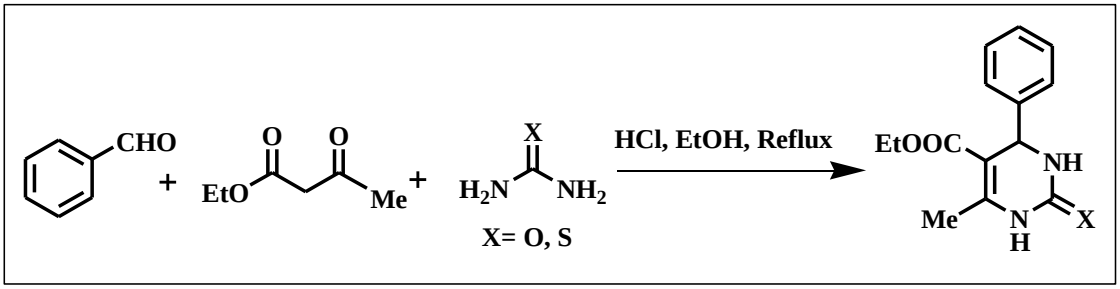


Fig.6A.4: Pyrimidine molecules containing drugs with anti-cancer activities

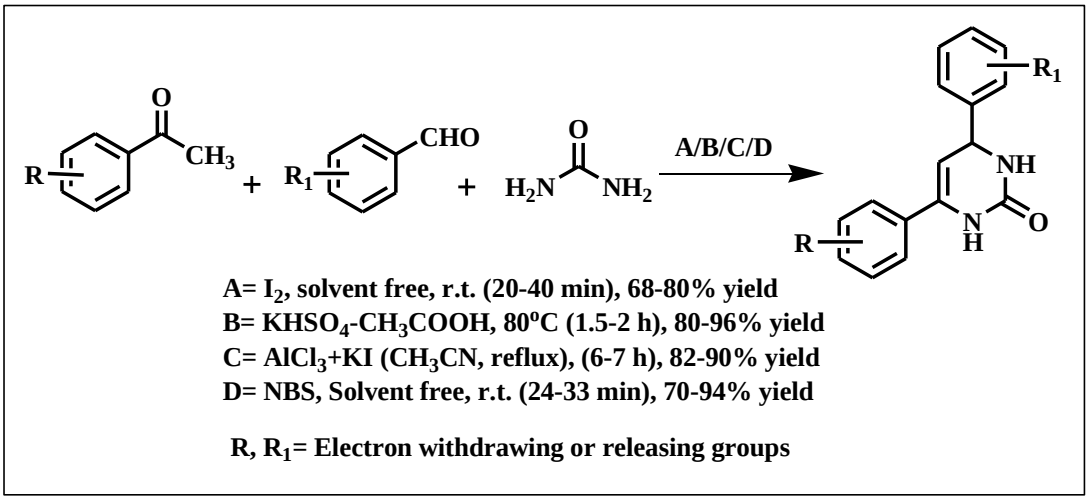
It seems that one can change the pharmacological activities of pyrimidines by incorporation of different substituents as well as fusion of different heterocycles with the pyrimidine nucleus.

6A.4 3, 4-dihydropyrimidin-2(1H)-one (or thione) derivatives via Biginelli-like reaction protocols and involvement of ionic liquids as catalysts/medium

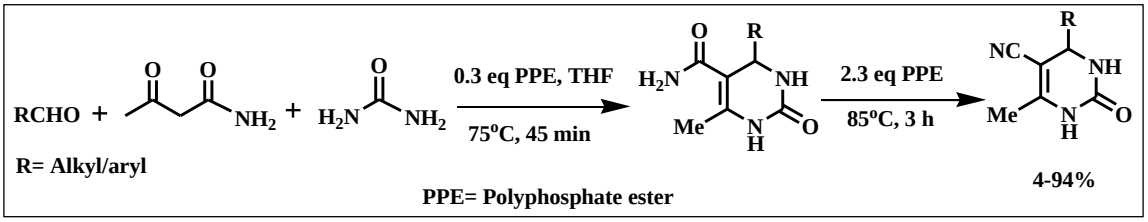
Biginelli-like reaction is an extension of classical acid (or base) catalyzed three-component Biginelli reaction of β-ketoester, aldehydes and urea (or thiourea) (**Scheme 6A.7**) after replacement of the β-ketoester component with other types of carbonyl derivatives including enolizable ketones, cyclic or acyclic β-diketones, β-ketolactones, cyclic β-diesters or β-diamides, α-ketoacids and benzocyclic ketones to produce variety of Biginelli scaffolds i.e. 3, 4-dihydropyrimidin-2(1*H*)-one (DHPM) derivatives (**Scheme 6A.8-6A.15**) [31-41].



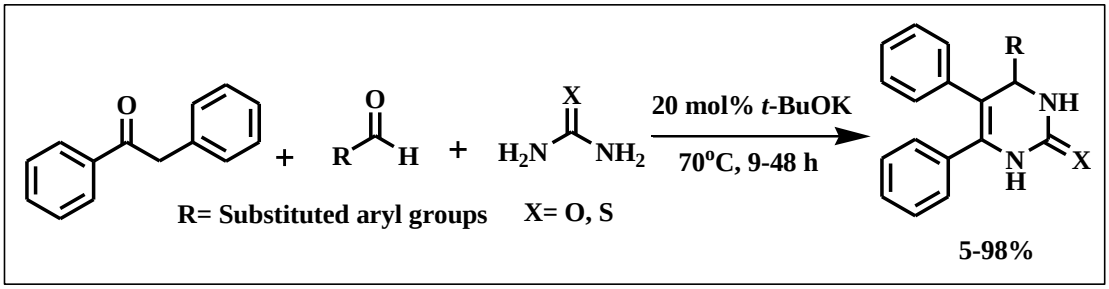
Scheme 6A.7: Classical Biginelli reaction



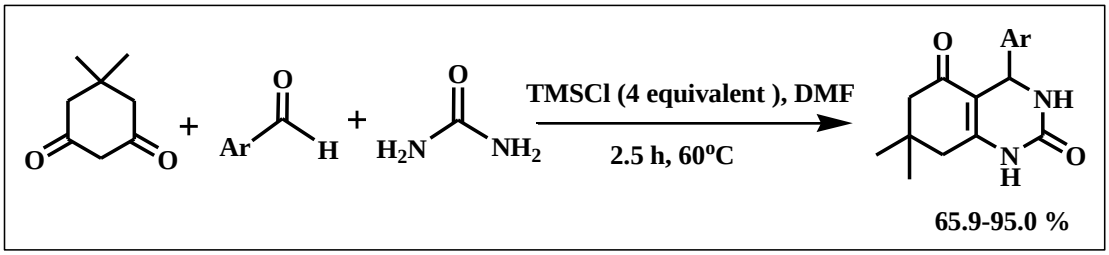
Scheme 6A.8: Synthesis of 5-unsubstituted-3, 4-dihydropyrimidin-2(1H)-ones [31-34]



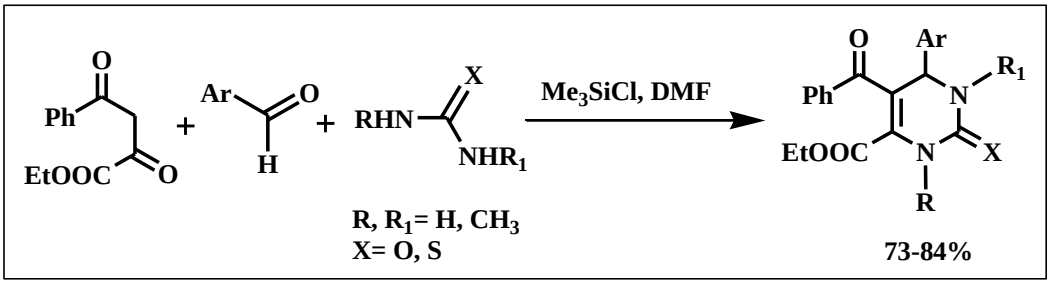
Scheme 6A.9: Synthesis of 5-cyano-dihydropyrimidinones reported by Schmidt *et al.* [35]



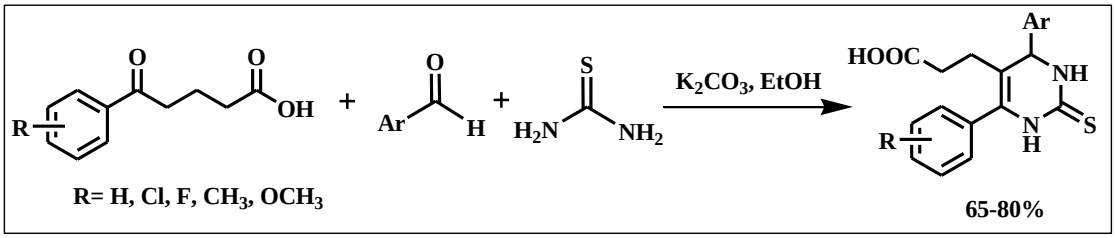
Scheme 6A.10: Biginelli-type reaction mediated by Brönsted base [36]



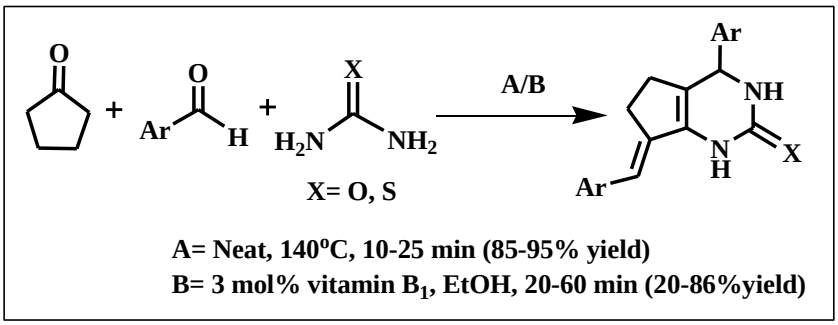
Scheme 6A.11: TMSCl catalyzed synthesis of DHPMs from dimedone [37]



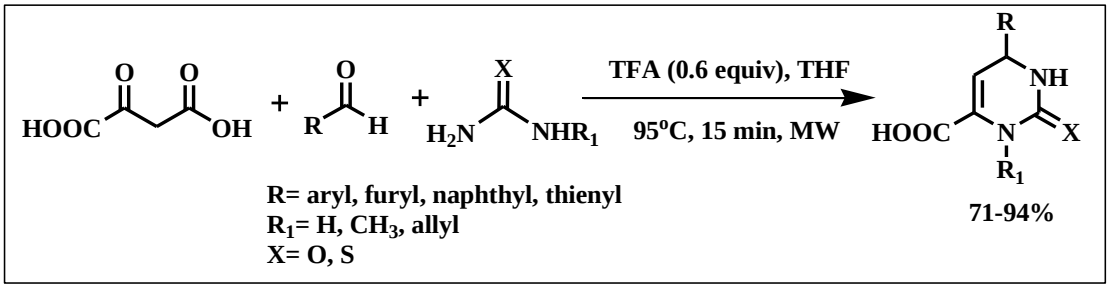
Scheme 6A.12: One-pot synthesis of dihydropyrimidines [38]



Scheme 6A.13: Synthesis of 4, 6-(4-substituted aryl)-2-thioxo-1,2,3,4-tetrahydro-pyrimidin-5-yl-propanoic acid [39]

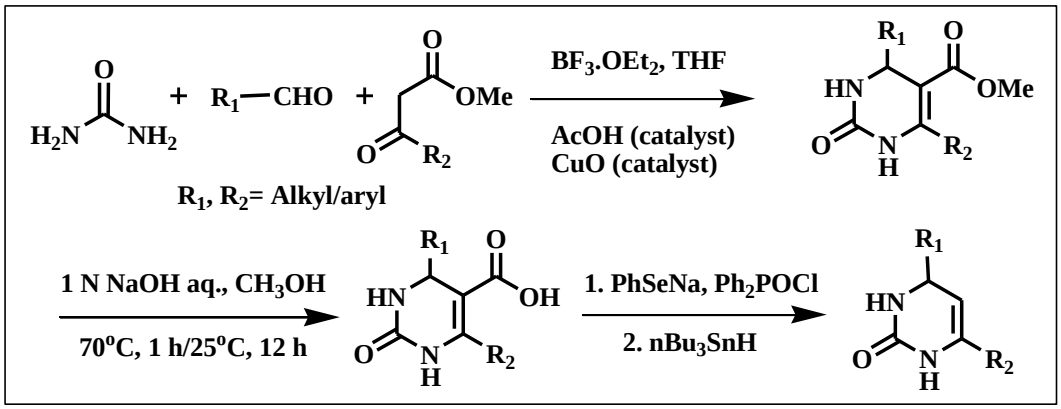


Scheme 6A.14: Biginelli reaction involving cyclopentanone [40]



Scheme 6A.15: Microwave assisted synthesis of DHPMs [41]

For development of effective drug molecules *via* the Biginelli DHPMs, it requires scope for variation of substituent at every position of the pyrimidine nucleus. The structures of classical Biginelli DHPMs are very rigid in presence of C-6 methyl and C-5 substituents. They are not readily functionalized or transformed to other functional groups. In absence of them, C_5-C_6 bond displays typical enamine character and on this basis, several manipulation of the Biginelli DHPM nucleus has been done to explore wide range of pharmacological properties [42-45] by employing various cyclic and acyclic CH-acid components instead of the β-ketoester. It was also observed in literature that one method reported by Steele *et al.* [46] for preparation of 5-unsubstituted 3,4-dihydropyrimidin-2(1*H*)-ones used multistep strategies involving sequential saponification of C-5 ester on precursor pyrimidine followed by thermal decarboxylation along with formation of multiple side-products (**Scheme 6A.16**). As compared to this method, the Biginelli-like condensation of acetopheneone, urea and aromatic aldehydes represents a simple alternative for the multistep synthesis of 5-unsubstituted Biginelli DHPMs.



Scheme 6A.16: Multistep route for 5-unsubstituted 3, 4-dihydropyrimidin-2(1*H*)-ones

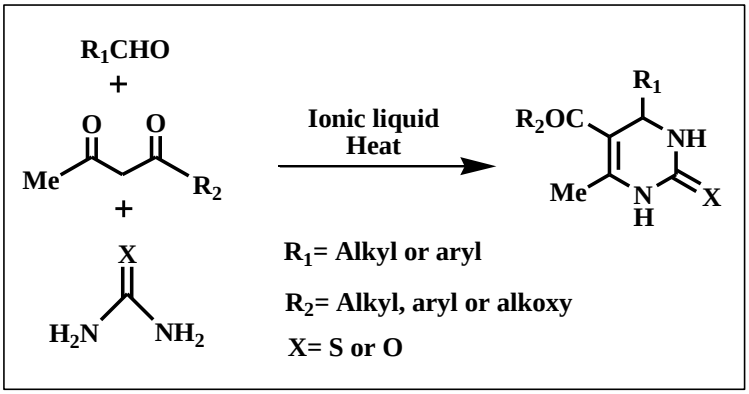
A large number of the Biginelli-like reactions employed strong Brönsted or Lewis acid catalysts at high temperature for longer time to get good yields of the products. For example, Bussolari and his coworkers (2000) tested concentrated H_2SO_4 in ethanol and CF_3COOH (TFA) in dichloroethane as non-reusable catalysts for the Biginelli-like reaction of β-Keto carboxylic acid under reflux for 12 h (similar to **Scheme 6A.15**) [47]. The catalytic activity of TFA was better than sulfuric acid.

The use of conc. HCl acid was described by Yarim *et al.* (2003) for the reaction of N-methyl urea with 5, 5-dimethyl-1, 3-cyclohexanedione and aromatic aldehydes under reflux condition in ethanol (reaction scheme is similar to **Scheme 6A.11**) [48].

Similarly, Wang *et al.* [49] described the Biginelli-like condensation of acetophenone, urea and aromatic aldehydes in acetonitrile under reflux for 12 h using catalytic amount of $FeCl_3.6H_2O$ and stoichiometric amount of TMSCl to afford 75-88% yield of the product (reaction scheme is similar to **Scheme 6A.8**).

Later on, other Lewis acids catalysts such as $AlCl_3$ under reflux condition [50], $Fe(NO_3)_3.9H_2O$ using solvent-free grinding [51], ZnI_2 under MW irradiation [52], iodotrimethylsilane in CH_3CN at room temperature [53] *etc.* were introduced for the Biginelli–like reaction of acetopheneone to produce the corresponding 5-unsubstituted-3,4- dihydropyrimidinones with variety of substituted aromatic aldehydes.

As a part of designing of sustainable development approach, the uses of ionic liquids have been also observed in the Biginelli (or like) reactions (**Scheme 6A.17**) of β-dicarbonyl compounds with aldehydes and urea (or thiourea) as recyclable medium or dual specific solvent-catalyst systems with selective formation of required product at normal or moderate temperature within short period as compared to the conventional acid catalyzed reactions. Example of some of these IL solvent/catalytic systems are [hmim][HSO_4]-$NaNO_3$ [54], [C_4mim][HSO_4] [55], [bmim][Sac] [56], [bmim][$FeCl_4$] [57], 3-carboxymethyl-1-methylimidazolium bisulfate (CMImHSO_4) [58], -SO_3H functionalized ammonium based ILs [59], glycine nitrate [Gly][NO_3] [60], 1-butyl-1,3-thiazolidine-2-thione *p*-toluenesulfate [Btto][*p*-TSA] [61], 2-pyrrolidonium hydrogen sulfate [Hnhp][HSO_4], N-methyl-2-pyrrolidonium hydrogen sulfate [nmp][HSO_4], and N-methyl-2-pyrrolidonium dihydrogen phosphate [nmp][H_2PO_4] [62], 3-(2-carboxybenzoyl-1-methyl-1*H*-imidazolium chloride [Cbmim][Cl] [63] *etc.*



Scheme 6A.17: General scheme for Biginelli reaction

Above all, a few supported or immobilized IL catalysts were known to catalyze Biginelli synthesis of 3, 4-dihydropyrimidin-2(1H)-ones. Silica-supported sulfonic acid–functionalized ionic liquid (Si-[sbSipim][PF_6]) [64], 1-methyl-3-(3-trimethoxysilylpropyl) imidazolium hydrogen sulfate ionic liquid grafted on Fe_3O_4 magnetic nanoparticles (MNPs-IL-HSO_4) [65] and $CuCl_2$–supported imidazolium-based ionic liquid [bmim][PF_6]-$CuCl_2$ [66] (**Fig.6A.5**). Also, Brönsted-Lewis acidic ionic liquid [msi]$_3$[PW] was tested as efficient catalyst for the synthesis of DHPMs (**Fig.6A.6**) [67].

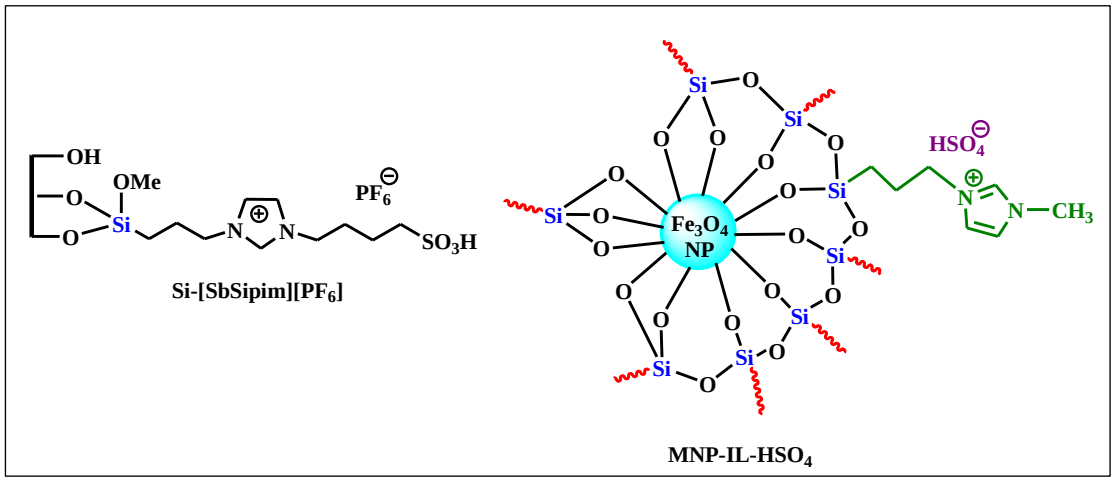


Fig.6A.5: Structures of Si-[sbSipim][PF_6] and MNPs-IL-HSO_4

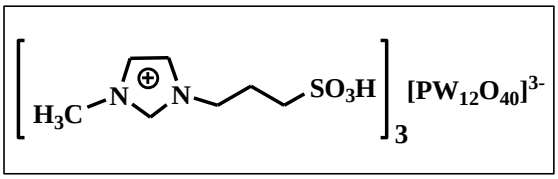


Fig.6A.6: Structure of [msi]$_3$[PW]

For the Biginelli-like reactions, only few studies have been done involving ionic liquids as catalyst as compared to the Biginelli reaction of β-dicarbonyl compounds.

Hajipour and his group (2011) applied N-(4-sulfonic acid) butyl triethyl ammonium hydrogen sulfate ([TEBSA][HSO_4]) as reusable Brönsted acidic IL catalyst for the preparation of Biginelli-like DHPMs (similar to **Scheme 6A.14**) at 100°C under solvent-free condition within 5-25 min reaction time (75-91% yield) [68].

Wang *et al.* in 2012 [69] introduced $[MeC(OH)_2]^+ClO_4^-$ as super acidic ionic liquid catalyst for the Biginelli-type reactions of various aliphatic or aromatic aldehydes, 1,3-dicarbonyl compound and urea at 90°C under solvent-free condition for 15–60 min reaction time. This method was also very effective for the inactive aliphatic aldehydes.

In 2016, Zhou *et al.* [70] screened the catalytic efficiencies of a series of functionalized Brönsted acidic ILs (**Fig.6A.7**) for the same reaction of aromatic aldehydes, urea or thiourea and cyclopentanone in solvent-free medium at 80°C (**Scheme 6A.14**). Among all the –SO_3H functionalized ILs, [C_3SO_3HDoim][HSO_4] ionic liquid worked as the best catalyst and could be reused for at least 7 times with the similar catalytic activity.

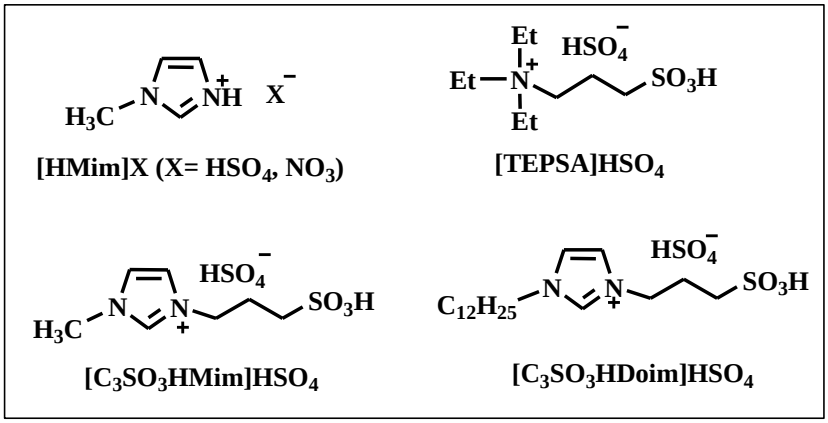


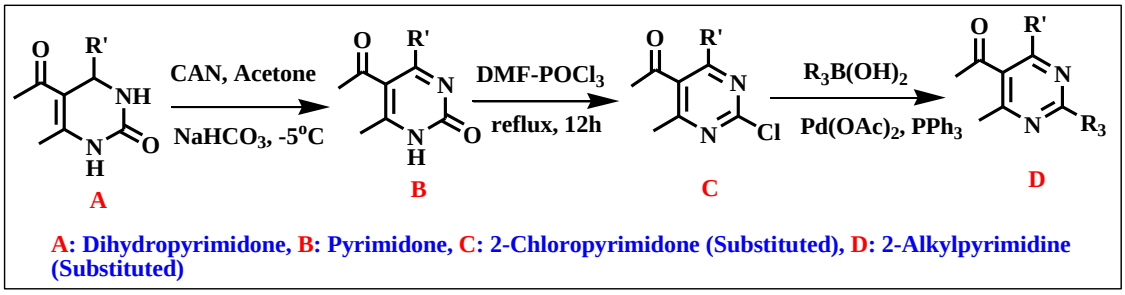
Fig.6A.7: Structures of BAIL catalysts used for Biginelli-type reaction

The above review of literature reflects the lack of efficient Brönsted acidic IL catalysts for preparation of Biginelli-like DHPM scaffolds starting from three-component mixture of aceotophenone, aromatic aldehydes and urea and also then subsequent conversion into substituted pyrimidines without isolation of the DHPMs intermediate in one pot reaction.

6A.5 Strategies for conversion of Biginelli DHPMs to pyrimidines

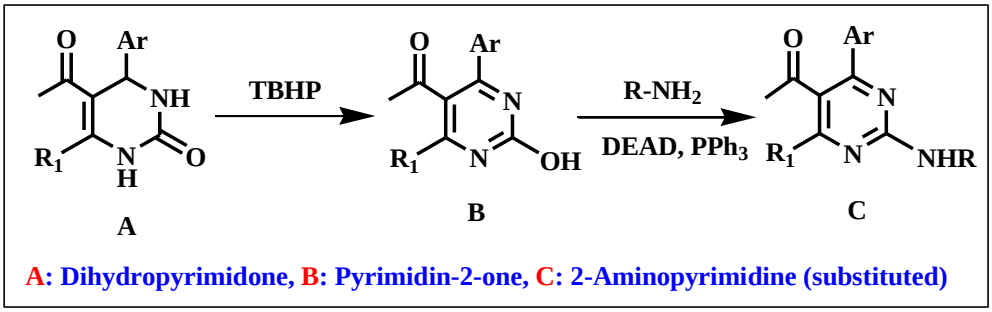
Although the number of catalytic reports published on the Biginelli (or like) DHPMs scaffolds are increasing tremendously, still there has been deficiency of efficient methodologies to convert the DHPMs to pyrimidine nucleus. One route utilizes dehydrogenation of the DHPMs followed by nucleophilic substitution at 2-position of pyrimidine ring [71-73]. A number of oxidants such as concentrated HNO_3, ceric ammonium nitrate, (diacetoxyiodo) benzene, $Mn(OAc)_3$ and MnO_2, tert-butyl hydroperoxide were used for oxidative aromatization of 1,4-dihydropyrimidine [74-78]. Functionalization of the C-2 position of pyrimidines was achieved *via* Kappe dehydrogenation of the DHPMs and PyBroP-mediated coupling with nucleophiles for 24 hour reaction at room temperature [79]. Most of these dehydrogenation methods require longer reaction time (36–67 h) and higher temperature in addition to lower yields and inefficiency of the oxidizing agents [71-73]. A modified sequential five steps microwave assisted conversion of DHPMs to 2-amino-4- aryl pyrimidine derivatives was performed at high temperature in sealed vessel by Matoobi *et al.* They identified isolation of each intermediate involved in S-alkylation, oxidation and nucleophilic substitution steps [80].

One of the important methods for the conversion of Biginelli dihydropyrimidones (**Scheme 6A.18**) to pyrimidines involves conversion to pyrimidone followed by halogenation and Suzuki Coupling [81].



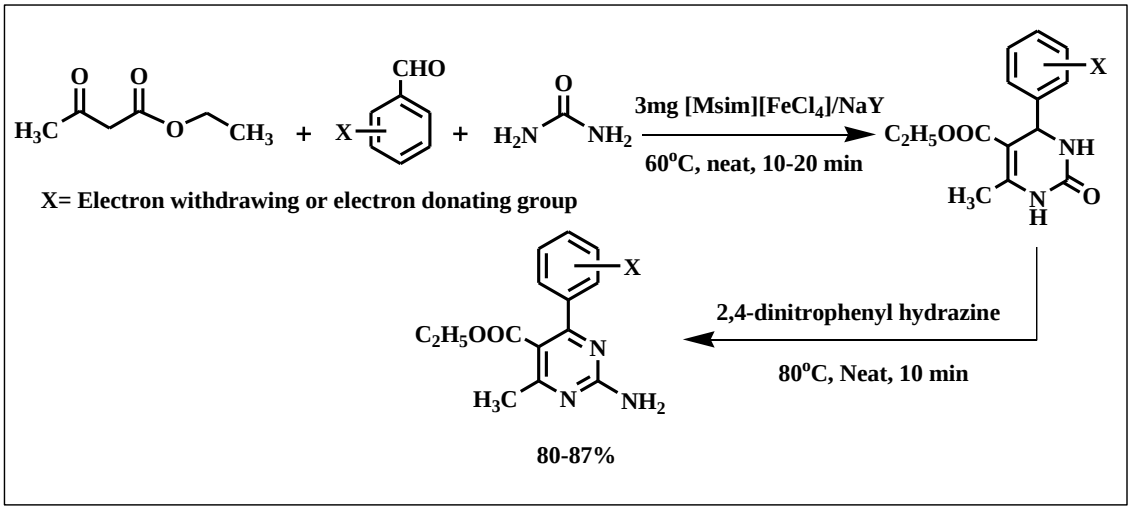
Scheme 6A.18: Conversion of dihydropyrimidones to 2-alkyl pyrimidines *via* Suzuki coupling

Another procedure involves the conversion of dihydropyrimidone to pyrimidin-2-ol followed by conversion to pyrimidin-2-amine through Mitsunobu reaction (**Scheme 6A.19**) [82].



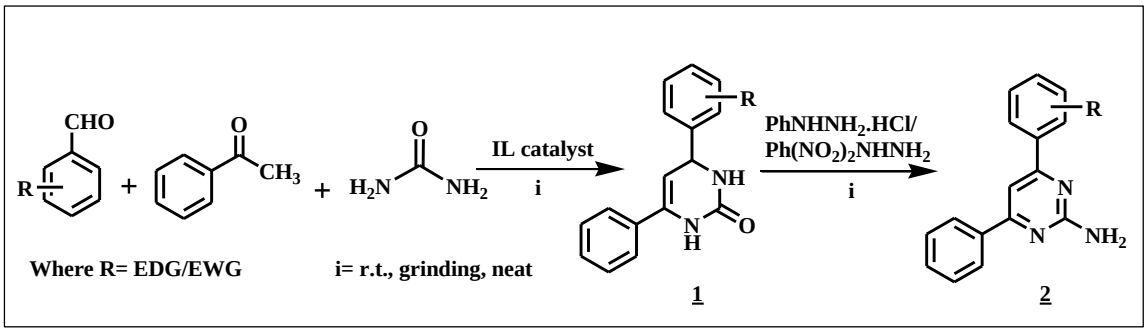
Scheme 6A.19: Transformation of dihydropyrimidones to pyrimidin-2-amines *via* Mitsunobu reaction

The only method involving heterogenized Brönsted-Lewis acidic IL supported on zeolite was reported by Gogoi *et al.* which introduced 1-sulfonic-3-methylimidazolium ferric chloride [Msim][$FeCl_4$] supported on NaY zeolite as catalyst for one-pot consecutive formation of the Biginelli-DHPMs to 2-amino-4-arylpyrimidines (**Scheme 6A.20**) [83].



Scheme 6A.20: Synthesis of 2-amino-4-arylpyrimidines

After observing the above findings of catalytic uses of ionic liquids in Biginelli-like reactions, it was planned to utilize four –SO_3H group bearing dicationic piperazinium ILs catalysts for one-pot two step synthesis of substituted pyrimidines from *in-situ* generated Biginelli-like DHPMs scaffold (**Scheme 6A.21**) under solvent-free grinding method at room temperature.



Scheme 6A.21: One pot two step synthesis of 2-amino pyrimidine derivatives

6B.1 Synthesis and characterization of N, N, N', N'-tetrasulfopiperazinium dicationic ionic liquids [TSPi][X]$_2$ with X = Cl, CF_3SO_3, TsO

This section describes preparation of three new members of $–SO_3H$ functionalized dicationic ionic liquids of N, N, N', N'-tetrasulfopiperazinium cation [TSPi] in pair with three anions [X] (X = Cl, CF_3SO_3, TsO) (**Scheme 6A.6**, **Section 6A**). The structures of these ILs were determined through ^{1}H NMR, ^{13}C NMR and FT-IR spectroscopic techniques and also CHN elemental analysis. Their Brönsted acidities were compared by UV-Vis absorbance spectra *via* Hammett plot. Their catalytic uses as acidic ILs were studied for one-pot two step synthesis of 2-amino-4, 6-diaryl pyrimidines through Biginelli-like reaction of acetophenone, aromatic aldehyde and urea to form DHPMs scaffold followed by subsequent condensation-aromatization reaction of phenylhydrazones of DHPMs (**Scheme 6A.21**, **Section 6A**).

FT-IR analysis

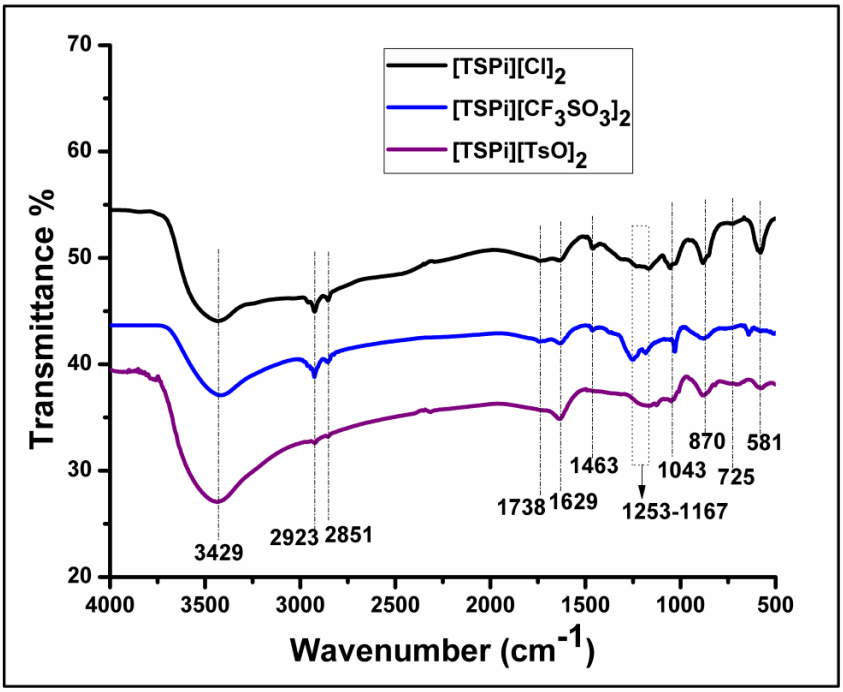


Fig.6B.1: FT-IR spectra of [TSPi][X]$_2$ (X = Cl, CF_3SO_3, TsO)

Table 6B.1 summarizes assignment of all IR peaks of the three ILs in **Fig.6B.1**. Typical vibrations of $–SO_3H$ groups were observed in finger-print region of the IR spectra. The IR spectra clearly displayed broad band for O-H stretch of $–SO_3H$ groups in 3400-3500 cm^{-1} region. Apart from this, the increase in intensity of this broad band in case of

$[TSPi][TsO]_2$ may be reasoned for presence of strong intermolecular H-bonded water molecules with *p*-toluene sulfonate anion in association with $–SO_3H$ groups of piperazinium cation. It was reported that in solid *p*-toluenesulfonic acid monohydrate, this anion exists as stable complex $(H_3O)^+\cdots(C_6H_4(CH_3)SO_3)^-$ with one water molecule and each of the H_3O^+ cation is surrounded by three other *p*-toluene sulfonate anions *via* H-bonding interactions to generate stable crystalline structure [84].

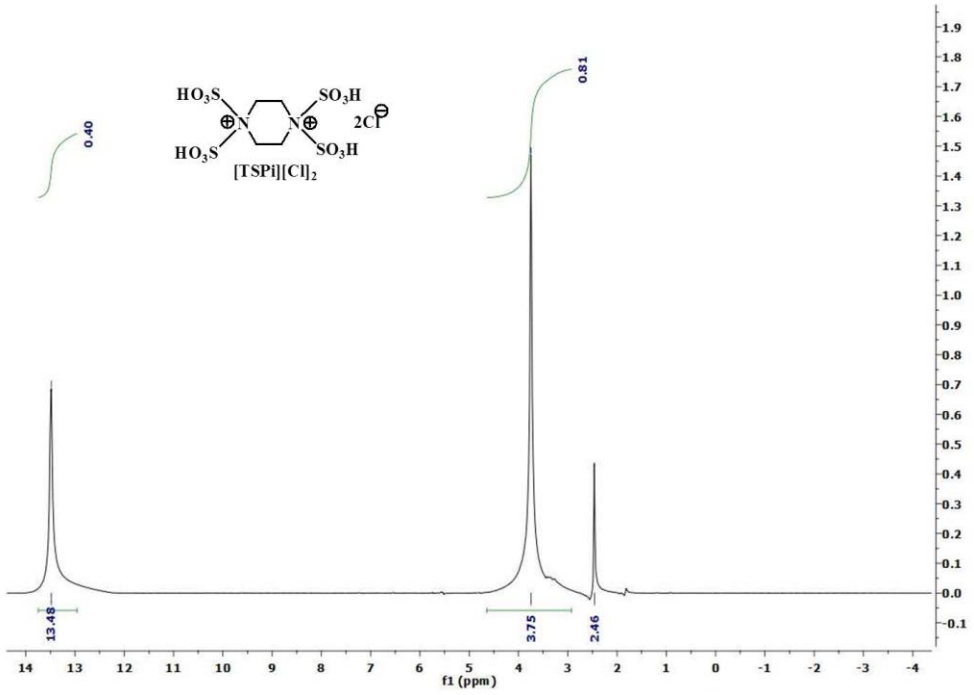
Table 6B.1: FT-IR band assignments of piperazinium ionic liquids

Bands (cm^{-1})	Assignment
581	S-O bending
725	Out-of-plane ring C-H bending
870	N-S stretch
1043	S-O antisymmetric stretch
1167-1253	S-O symmetric stretch
1463	Out of phase C-H bending of methyl group
1629	Aromatic C=C stretch
2851 & 2923	C-H stretch (CH_2)
3429	O-H stretch of $-SO_3H$ group

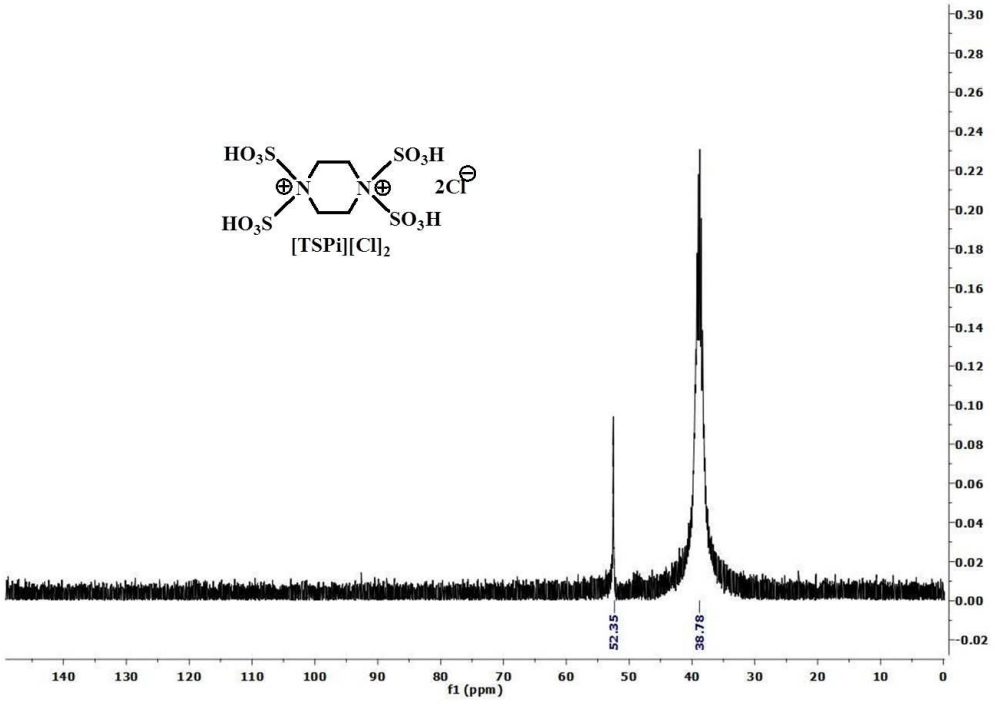
NMR analysis

^1H NMR spectra of the three ILs indicated attachment of four $–SO_3H$ groups with the piperazinium cation by four protons singlet at 12.82-13.50 ppm in addition to another eight protons singlet of ring carbons in the range of 3.26-3.79 ppm. Two *p*-toluene sulfonate anions showed two methyl singlets at 2.17 ppm and 2.14 ppm along with two four protons multiplets in aromatic region for the two phenyl protons at 7.05 ppm and 7.45 ppm. The representative NMR (proton and ^{13}C NMR) spectra of $[TSPi][Cl]_2$ and $[TSPi][TsO]_2$ ILs are expressed in (**Fig.6B.2**) and (**Fig.6B.3**) respectively. The ^{13}C peak corresponding to eight carbons of piperazinium cation is slightly shifted to down field from its initial value of the parent IL at 52.4 ppm to 87.3 ppm for the *p*-toluene sulfonate based IL in **Fig.6B.3**. Other characteristic peaks of phenyl carbon atoms are also observed at 143.9, 139.4, 129.1 and 126.0 ppm. The methyl carbon of *p*-toluene sulfonate anion is

found at 21.2 ppm. Thus, the NMR analysis distinctly evidenced the formation of these ILs.

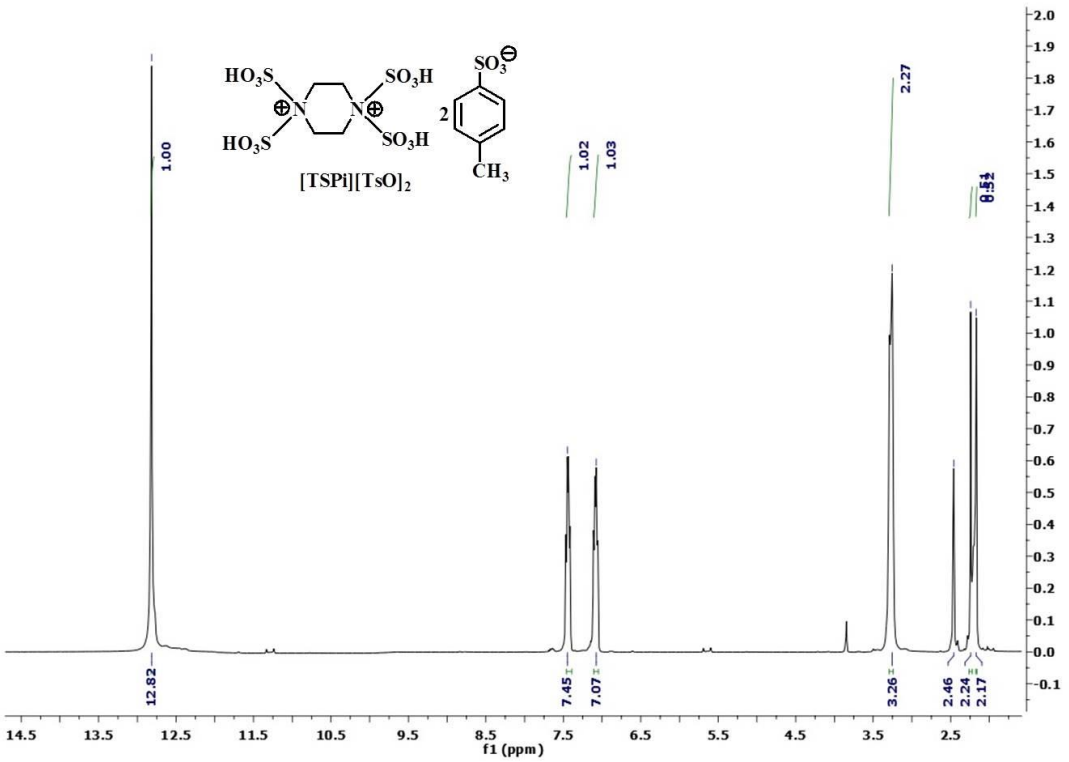


(a)

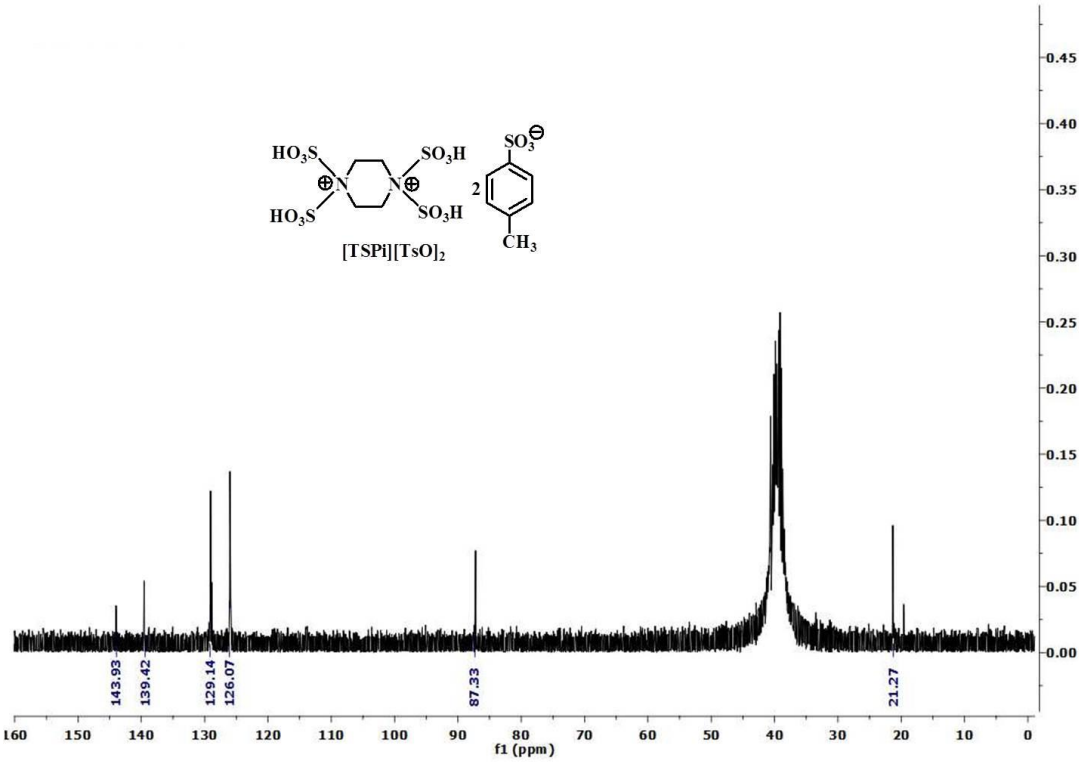


(b)

Fig.6B.2: (a) ^{1}H NMR and (b) ^{13}C NMR of $[TSPi][Cl]_2$



(a)



(b)

Fig.6B.3: (a) ^{1}H NMR and (b) ^{13}C NMR of $[TSPi][TsO]_2$

TGA analysis

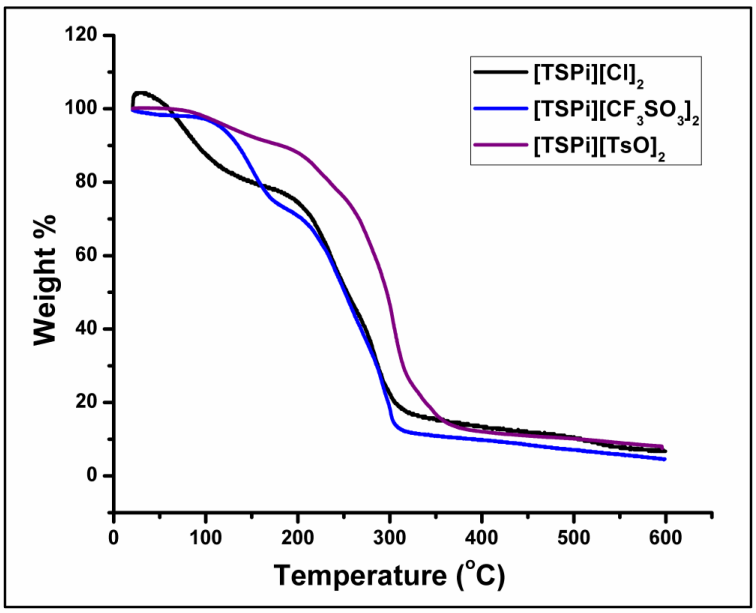


Fig.6B.4: TGA graph of $[TSPi][X]_2$ (X = Cl, CF_3SO_3, TsO)

TGA patterns of the three ILs were represented in **Fig.6B.4** and expressed absence of physisorbed water in $[TSPi][CF_3SO_3]_2$ and $[TSPi][TsO]_2$ in contrast to approximate 13% loss of moisture for initial ionic liquid $[TSPi][Cl]_2$ below 100°C. These patterns reflect low moisture sensitivity of both the triflate and *p*-toluene sulfonate based ILs. The rapid decomposition of chloride based IL was observed at 200°C to 300°C. Around 30% weight loss was found in temperature range of 140°C to 160°C for the $[TSPi][CF_3SO_3]_2$ whereas only 3-4% decrease of weight was seen for the $[TSPi][TsO]_2$ in between 140°C to 200°C. This small amount of weight loss for the $[TSPi][TsO]_2$ can be expected for release of strongly H-bonded water molecules as discussed in FT-IR spectrum at temperature above 100°C. This thermal studies displayed greater stability of the $[TSPi][TsO]_2$ up to 200°C due to presence of more number of resonating structures of *p*-toluene sulfonate anion. The lower stability of triflate based IL indicates weak ionic interaction between the ion-pair for minimum number of delocalized structures of triflate anion.

Hammett acidity determination

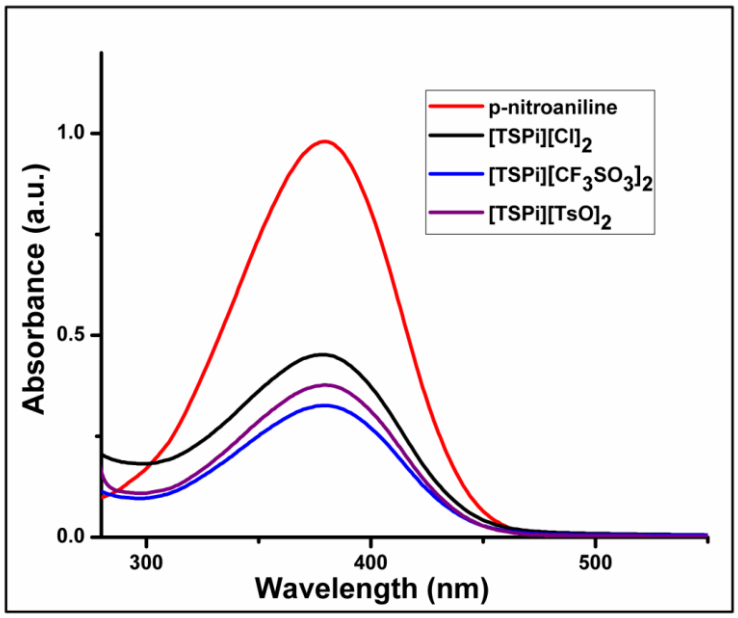


Fig.6B.5: Hammett plot of dicationic ionic liquids in ethanol

The Brönsted acidities of three dicationic ILs were determined from Hammett acidity function using UV-Visible Hammett plots (**Fig.6B.5**) (referred to **Section 2B**, **Chapter 2**). The trend in acidity with respect to the initial chloride IL was obtained as: $[TSPi][CF_3SO_3]_2$>$[TSPi][TsO]_2$>$[TSPi][Cl]_2$ in accordance with the Hammett acidity function (**Table 6B.2**).

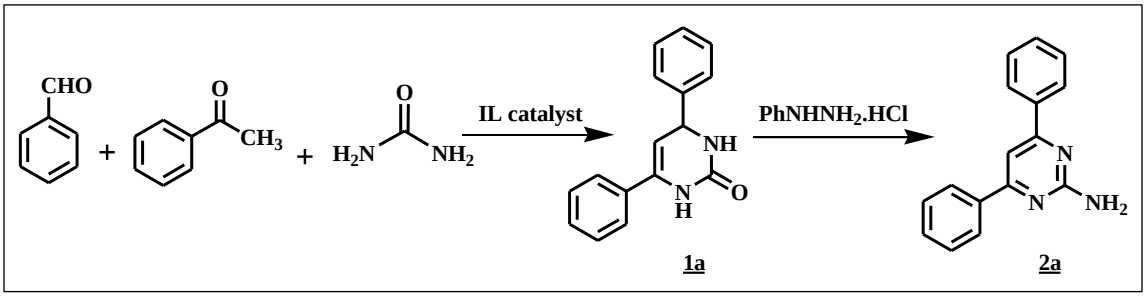
Table 6B.2: Hammett acidity calculation (A_{max}= 379 nm)

Entry	A_{max}	[I]%	$[IH^+]$%	H^o
p-Nitroaniline	0.98	100	0	-
$[TSPi][Cl]_2$	0.45	45.9	54.1	0.919
$[TSPi][TsO]_2$	0.37	37.7	62.3	0.772
$[TSPi][CF_3SO_3]_2$	0.32	32.6	67.4	0.674

6B.2 Catalytic study

The catalytic activities of three acidic ILs were investigated for one pot two-step synthesis of 4 ,6-diphenylpyrimidin-2-amine (**2a**) under solvent-free grinding and also in solution involving *in situ* formation of Biginelli-like dihydropyrimidinone (DHPM) from

the reaction of acetophenone, benzaldehyde and urea followed by treatment with phenyl hydrazine (**Scheme 6B.1)**. Optimization studies were conducted to determine the best reaction condition for the model reaction in terms of catalyst amount, reaction temperature and also solvents. Three catalyst amounts such as 2, 2.5 and 5 mol% were employed for each of the three ILs under solvent-free grinding condition at normal temperature using mortar and pestle as shown in **Table 6B.3** (entries 1-3). Only 2.5 mol% of the $[TSPi][CF_3SO_3]_2$ ionic liquid was able to give 89% yield of the product within 16 minute reaction for the two step reactions (**Table 6B.3**, entry 2). The other two ILs also showed good activities with the same amount of catalyst (entries 1 & 3). The trend of catalytic activity of the three ILs was identical with the Hammett acidity order which clearly supported the maximum catalytic activity of the $[TSPi][CF_3SO_3]_2$ ionic liquid. Using 2.5 mol% of the $[TSPi][CF_3SO_3]_2$ catalyst, solvent study was done only for ethanol and dichloromethane under reflux which showed better yield of the product in ethanol whereas the result was not good for non-polar solvent CH_2Cl_2 (**Table 6B.3**, entry 5). The reaction wasn't occurred in the 1st step in absence of catalyst in solvent-free grinding condition (**Table 6B.3**, entry 4). Finally, it was decided to utilize only 2.5 mol% as the most suitable amount of this catalyst for preparation of DHPMs using different substituted aromatic aldehydes and then subsequent aromatization of phenyl hydrazones of DHPMs to corresponding 4, 6-diaryl pyrimidin-2-amines under solvent-free mechanochemical process (**Table 6B.4**).



Scheme 6B.1: Synthesis of 2-amino-4, 6-phenyl pyrimidine

Table 6B.3: Optimization of the reaction condition for the synthesis of **2a**

Entry	Catalyst	Time (min)[a]			Yields [a, c] **2a** (%)		
		2 mol% [b]	2.5 mol%	5 mol%			
1	$[TSPi][Cl]_2$	15/20	15/25	10/25	75	78	78
2	**$[TSPi][CF_3SO_3]_2$**	7/10	**6/10**	6/12	87	**89**	86
3	$[TSPi][TsO]_2$	10/10	8/10	8/12	82	85	80
4	No catalyst	-	-	-	-	-	-
5	$[TSPi][CF_3SO_3]_2$[d]	30/25[d]			55/80[d]		

[a] The two step reactions from entry 1-4 were conducted by room temperature grinding method; [b] Reaction time was recorded separately for both steps using TLC technique; [c] Isolated yields; [d] Reaction was performed in CH_2Cl_2 and EtOH under reflux using 2.5 mol% of $[TSPi][CF_3SO_3]_2$.

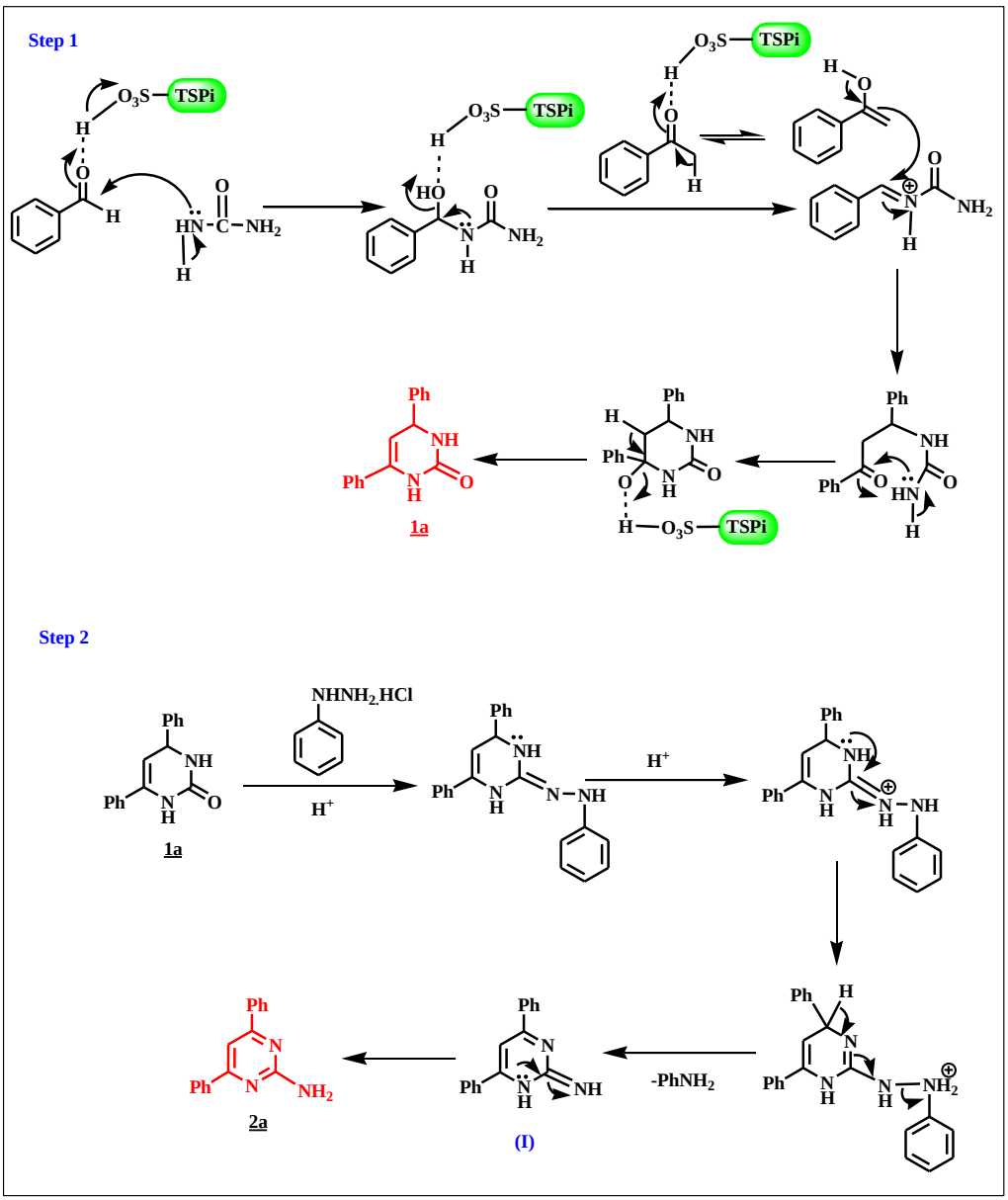
Table 6B.4: Substrate scope study for the synthesis of **2a** using 2.5 mol% of $[TSPi][CF_3SO_3]_2$ under solvent-free grinding condition

Entry	R	Product	Time (min)[c]	Yield (%)[d]
1	H[a]	**2a**	16	89
2	4-OCH_3[b]	**2b**	25	82
3	2-OH[a]	**2c**	18	82
4	2, 4-dichloro[a]	**2d**	15	88
5	4-OH[b]	**2e**	20	85
6	4-CH_3[a]	**2f**	16	88
7	4-NO_2[a]	**2g**	15	85
8	3, 4, 5-trimethoxy[a]	**2h**	20	84
9	4-Cl[a]	**2i**	15	90
10	Naphthaldehyde[b]	**2j**	20	80

[a] Reaction was carried out using phenylhydrazine hydrochloride; [b] Reaction was carried out using 2, 4-dinitrophenyl hydrazine; [c] Reaction time was given as total reaction time including both steps; [d] Isolated yield.

Plausible mechanism

Mechanism for first step of this reaction is proposed (**Scheme 6B.2**) to proceed with formation of iminium intermediate after nucleophilic addition of urea to activated aldehyde in presence of the acid catalyst. Enolised form of acetophenone attacks the iminium ion and produces 1-(3-oxo-1, 3-diphenylpropyl) urea which undergoes cyclocondensation to give the required Biginelli-like DHPM (**1a**). Second step involves acid catalyzed rearrangement of initially formed phenylhydrazone derivative to produce 4, 6-diphenylpyrimidin-2(1H)-imine (**I**), with expulsion of aniline molecule for subsequent aromatization to give 4, 6-diphenylpyrimidin-2-amine (**2a**).



Scheme 6B.2: Mechanism for two step synthesis of 2-amino pyrimidine derivative

Recyclability study

The model reaction performed for recyclability test of the $[TSPi][CF_3SO_3]_2$ catalyst (**Scheme 6B.1**) involved 5 mmol of each substrate and solvent-free grinding method under optimized condition. The IL catalyst was easily separated as viscous liquid inside the mortar by dissolving only product mixture in dry CH_2Cl_2 after completion of the reaction. The organic extract of dichloromethane was decanted and the IL catalyst was washed two times more with the dichloromethane solvent. Then it was dried at 40°C for one hour in vacuum oven and reused for the next cycle. This study expressed gradual loss of catalytic activity of the spent catalyst with increasing reaction time up to 4th cycle (**Fig.6B.6**). The FT-IR spectrum of recycled catalyst after the 3rd cycle expressed similar IR vibrations like the fresh catalyst (**Fig.6B**.7).

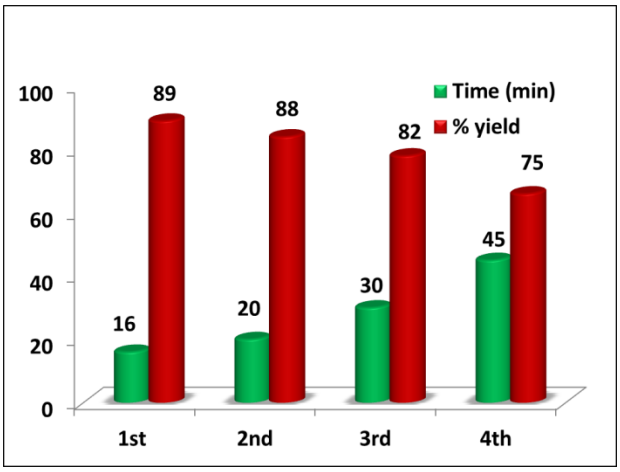


Fig.6B.6: Recyclability profile of $[TSPi][CF_3SO_3]_2$

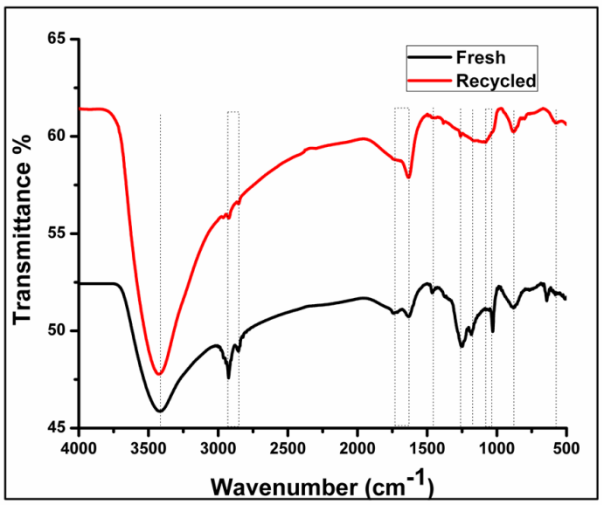


Fig.6B.7: FTIR spectra of used catalyst (after 3rd cycle) with parent IL

6B.3 Conclusion

In summary, three members of –N-SO_3H functionalized piperazinium based Brönsted acidic ILs were synthesized successfully using three anions including Cl^-, $CF_3SO_3^-$ and TsO^-. Thermal analysis demonstrated hydrophilic properties of the parent chloride IL which was found opposite for the other two liquids with increasing ionic strength of constituent ion-pairs. TGA analysis also expressed the release of 3-4% of strong H-bonded water molecule involving –SO_3H groups of piperazinium cation and tosylate anion of $[TSPi][TsO]_2$ above 100^oC. The Hammett acidity values of the three ILs identified $[TSPi][CF_3SO_3]_2$ as the most acidic IL catalyst for the preparation of 2-amino-4, 6-diaryl- pyrimidines involving *in situ* formation of Biginelli-like DHPMs as reaction intermediate under solvent-free grinding without isolation of the DHPMs for the 2nd step of reaction. This method offers a simple and efficient route for selective synthesis of variety of substituted 2-amino-pyrimidine derivatives under mild condition.

6B.4 Experimental section

General techniques

The necessary chemicals were purchased from Sigma Aldrich and TCI Chemicals. The structures of ionic liquids and pyrimidine derivatives were identified using similar instruments such as NMR, IR, TGA, UV-Vis and elemental analysis already mentioned in "**General Information**" of **Chapter 2**, **Section 2B** under experimental section.

Typical procedure for synthesis of $[TSPi][X]_2$ where X= Cl, CF_3SO_3 & TsO

The parent ionic liquid $[TSPi][Cl]_2$ was initially formed after dropwise addition of chlorosulfonic acid (30 mmol) to the CH_2Cl_2 (DCM) solution of piperazine (5 mmol) at 0°C for 2-3 min in a two necked 100 mL round bottom flask under nitrogen atmosphere. The process was continued for two hour with continuous stirring to complete the formation of $[TSPi][Cl]_2$. The ionic liquid was isolated in pure form after washing 3-4 times with dry DCM (15 mL) followed by evaporation of the DCM in rotary evaporator. In next step of reaction, the N, N, N', N'-tetrasulfopiperazinium chloride $[TSPi][Cl]_2$ was treated with 10 mmol of triflic acid (CF_3SO_3H) and *p*-toluene sulfonic acid monohydrate (TsOH) separately at 50-60^oC to obtain the respective two dicationic ionic liquids $[TSPi][X]_2$ as brown viscous liquids, where X = CF_3SO_3, TsO (**Scheme 6A.6**, **Section**

6A). Then, the crude liquids were washed with immiscible DCM solvent for three times to dissolve unreacted organic acids from the viscous liquid through decantation process. Finally, they were dried in vacuum oven at 40^{o}C to get almost pure products for spectral analysis.

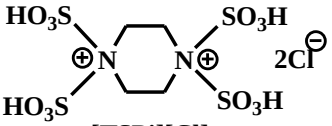
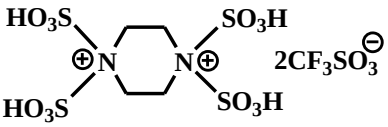
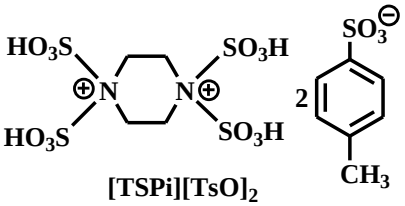
Method for preparation of 4, 6-disubstituted-pyrimidin-2-amine derivatives

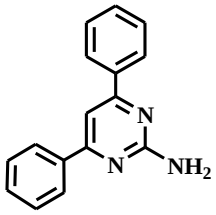
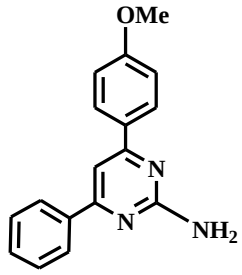
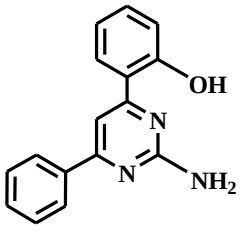
A mixture of acetophenone (1 mmol), aromatic aldehyde (1 mmol) and urea (1 mmol) was grinded homogeneously in presence of 2.5 mol% of [TSPi][CF_3SO_3]$_2$ catalyst under solvent-free condition using mortar and pestle at ambient temperature for a definite period as monitored by TLC to give Biginelli-like DHPM as single product (**Table 6B.3**). To the crude product of DHPM derivative, phenyl hydrazine hydrochloride (1 mmol) was added with continuous grinding with the same amount of IL catalyst to get desired pyrimidines within the specific reaction time (**Table 6B.3**). After completion of the reaction as observed from TLC, addition of dichloromethane was done to dissolve the reaction mixture leaving the IL catalyst as insoluble viscous liquid in the mortar. The solvent was then decanted and evaporated to get the solid product mixture. The solid mixture was first treated with ethanol to dissolve unreacted reaction intermediate at normal temperature and then filtered to get the crude solid product. The product was further recrystallized from absolute ethanol to get analytically pure product. The viscous IL catalyst was again washed with dichloromethane and then dried in vacuum oven for reuse.

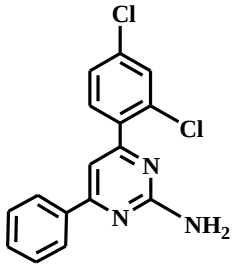
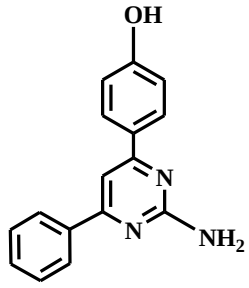
Isolation procedure for Biginelli 3, 4-dihydropyrimidin-2(1H)-ones (DHPMs)

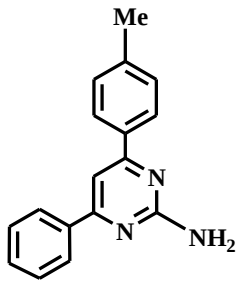
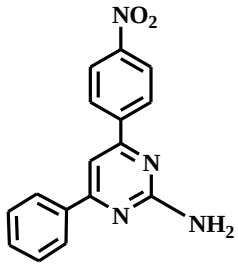
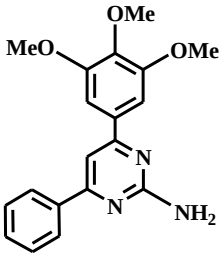
The isolation of only two Biginelli-like DHPMs was done for confirmation of the formation of DHPM intermediates in the first step of reaction during the preparation of 2-aminopyrimidine derivatives. At first the reaction mixture was diluted with ethanol to dissolve the IL catalyst and also the unreacted acetophenone if present from the solid mixture at room temperature. Then it was filtered and the residue was further washed with a saturated solution of sodium bicarbonate to remove any acidic component. The crude product was isolated after decantation of the aqueous bicarbonate solution and air dried for few hours. For analytical purpose, it was again recrystallized from saturated solution of absolute ethanol.

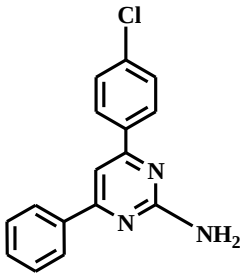
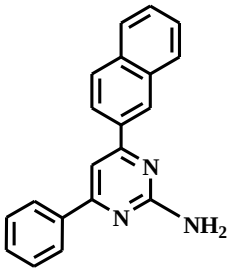
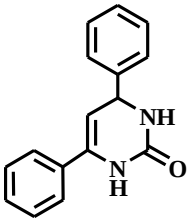
6B.5 Spectral data of [TSPi][X]$_2$, 2-amino pyrimidine derivatives (2a-2j) and two Biginelli dihydropyrimidone derivatives (1a & 1i)

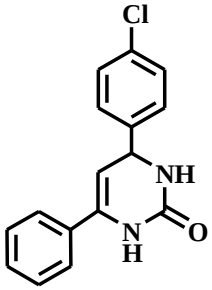
Entry	Spectral data
 **[TSPi][Cl]$_2$**	Brown viscous liquid, FTIR (KBr) cm^{-1}: 3429, 2923, 2851, 1629, 1463, 1167, 1043, 870, 725, 581; ^{1}H NMR (DMSO-d$_6$, 400 MHz): δ 13.48 (s, 4H), 3.75 (s, 8H); ^{13}C NMR (DMSO-d$_6$, 100 MHz): δ 52.4; CHN analysis $C_4H_{12}Cl_2N_2O_{12}S_4$: Calcd. C, 10.02; H, 2.52; N, 5.84; Found: C, 9.92; H, 2.77; N, 5.86.
 **[TSPi][CF$_3$SO$_3$]$_2$**	Brown viscous liquid, FTIR (KBr) cm^{-1}: 3429, 2923, 2851, 1629, 1463, 1167, 1043, 870, 725, 639, 581; ^{1}H NMR (DMSO-d$_6$, 400 MHz): δ 13.50 (s, 4H), 3.79 (s, 8H); ^{13}C NMR (DMSO-d$_6$, 100 MHz): δ 87.4, 100.1; CHN analysis $C_6H_{12}F_6N_2O_{18}S_6$: Calcd. C, 10.20; H, 1.71; N, 3.96; Found: C, 10.32; H, 1.77; N, 3.86.
 **[TSPi][TsO]$_2$**	Brown viscous liquid, FTIR (KBr) cm^{-1}: 3429, 2923, 2851, 1629, 1463, 1167, 1043, 870, 725, 581; ^{1}H NMR (DMSO-d$_6$, 400 MHz): δ 2.17 (s, 3H), 2.24 (s, 3H), 3.26 (s, 8H), 7.07(s, 4H), 7.45 (s, 4H), 12.82 (s, 4H); ^{13}C NMR (DMSO-d$_6$, 100 MHz): δ 143.9, 139.4, 129.1, 126.0, 87.3, 21.2; CHN analysis $C_{18}H_{26}N_2O_{18}S_6$: Calcd. C, 28.80; H, 3.49; N, 3.73; Found: C, 28.92; H, 3.57; N, 3.76.

 **4,6-diphenylpyrimidin-2-amine** **2a**	Orange solid, Mp.: 148°C; FTIR (KBr) cm^{-1}: 3444, 3284, 2916, 1622, 1578, 1506, 1413, 1325, 1253, 1131, 747, 689, 596; ^1H NMR (DMSO-d_6, 400 MHz): δ 11.62 (s, 1H), 8.84 (s, 1H), 8.66 (s, 1H), 8.35-8.32 (m, 1H), 8.05-8.02 (m, 1H), 7.76 (s, 2H), 7.44 (m, 5H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 149.9, 144.9, 137.4, 134.0, 131.0, 130.2, 129.6, 127.8, 123.4, 117.3, 87.2; CHN analysis $C_{17}H_{14}N_2$: Calcd. C, 82.90; H, 5.73; N, 11.37; Found: C, 82.92; H, 5.77; N, 11.36.
 **4-(4-methoxyphenyl)-6-phenylpyrimidin-2-amine** **2b**	Orange solid, Mp.: 277°C; FTIR (KBr) cm^{-1}: 3458, 3270, 2916, 1622, 1578, 1506, 1413, 1332, 1246, 1138, 827, 740, 624, 581; ^1H NMR (DMSO-d_6, 400 MHz): δ 11.57 (s, 1H), 8.83 (s, 1H), 8.61 (s, 1H), 8.34-8.31 (m, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 3H), 7.03 (d, *J* = 8.0 Hz, 3H), 3.79 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 161.8, 150.0, 145.0, 137.2, 130.2, 129.6, 126.8, 123.6, 117.2, 115.0, 55.9; CHN analysis $C_{17}H_{15}N_3O$: Calcd.; C, 73.63; H, 5.45; N, 15.15; Found: C, 73.92; H, 5.60; N, 15.26.
 **2-(2-amino-6-phenylpyrimidin-4-yl)phenol** **2c**	Yellow solid, Mp.: 144°C; FTIR (KBr) cm^{-1}: 3444, 3313, 2923, 1607, 1535, 1492, 1355, 1275, 1159, 1065, 870, 740, 689; ^1H NMR (DMSO-d_6, 400 MHz): δ 10.4 (s, 1H), 10.3 (s, 1H), 8.10 (s, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.20 (t, *J* = 8.0 Hz, 2H), 7.13 (t, *J* = 8.0 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 2H), 6.81-6.85 (m, 2H), 6.73 (t, *J* = 8.0 Hz,

	1H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 156.0, 145.4, 137.8, 129.6, 127.7, 120.9, 119.8, 119.4, 116.4, 112.1; CHN analysis $C_{16}H_{13}N_3O$; Calcd.; C, 72.99; H, 4.98; N, 15.96; Found: C, 72.92; H, 5.00; N, 15.99.
 **4-(2,4-dichlorophenyl)-6-phenylpyrimidin-2-amine** **2d**	Orange solid, Mp.: 282°C; FTIR (KBr) cm^{-1}: 3408, 3306, 2916, 1666, 1593, 1513, 1456, 1377, 1253, 1152, 1095, 870, 754, 689, 560; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 10.7 (s, 1H), 8.10 (s, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.57 (s, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.18-7.22 (m, 2H), 7.05-7.07 (m, 2H), 6.76 (t, *J* = 8.0 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 145.2, 132.9, 132.6, 132.1, 131.3, 129.7, 129.6, 128.2, 127.4, 120.0, 112.7; CHN analysis $C_{16}H_{11}Cl_2N_3$; Calcd.; C, 60.78; H, 3.51; N, 13.29; Found: C, 61.02; H, 3.60; N, 13.35.
 **4-(2-amino-6-phenylpyrimidin-4-yl)phenol** **2e**	Orange solid, Mp.: 278°C; IR (KBr) cm^{-1}: 3427, 3271, 2915, 1624, 1587, 1513, 1506, 1417, 1335, 1268, 1128, 1076, 831, 742; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 11.5 (d, *J* = 12.0 Hz, 1H), 10.0 (s, 1H), 8.79-8.81 (m, 1H), 8.55 (d, *J* = 8.0 Hz, 1H), 8.32-8.27 (m, 1H), 7.99 (t, *J* = 8.0 Hz, 1H), 7.61-7.57 (m, 2H), 7.81-7.86 (m, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 160.5, 150.2, 144.9, 137.2, 129.7, 125.1, 124.9, 116.4, 86.8; CHN analysis $C_{16}H_{13}N_3O$; Calcd.; C, 72.99; H, 4.98; N, 15.96; Found: C, 72.92; H, 5.00; N, 15.85.

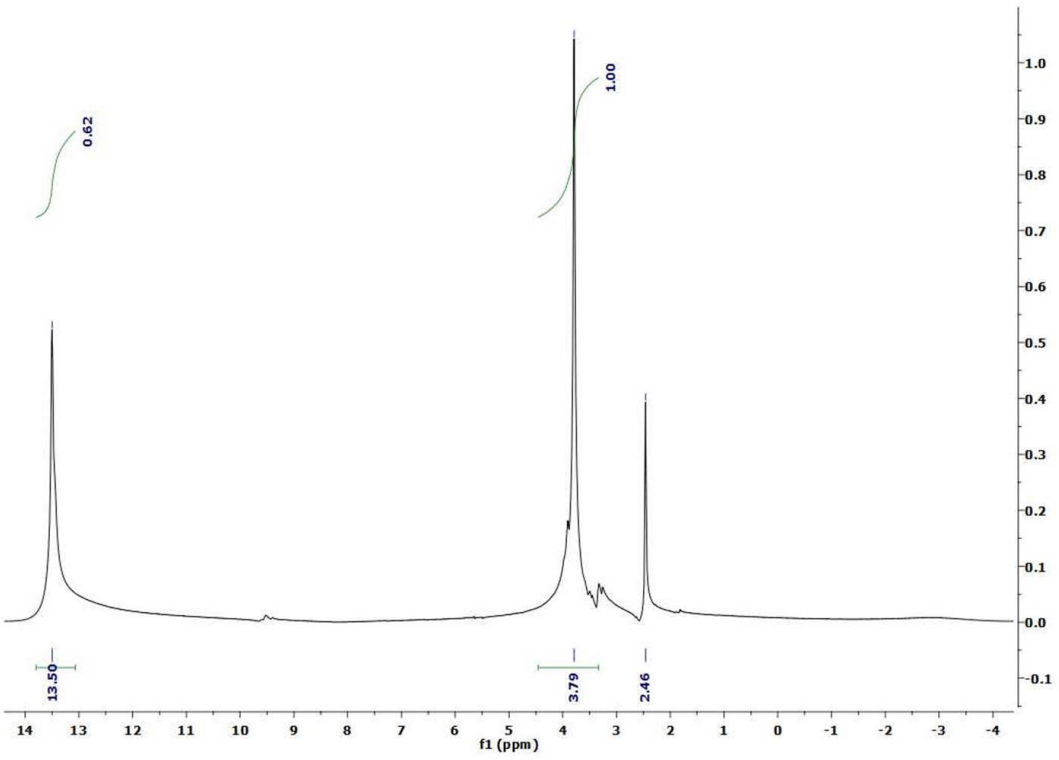
 **4-phenyl-6-p-tolylpyrimidin-2-amine** **2f**	Brick red solid, Mp.: 94°C; FTIR (KBr) cm^{-1}: 3444, 3299, 2916, 1658, 1593, 1492, 1253, 1123, 1065, 820, 740, 689; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 10.2 (s, 1H), 7.79 (s, 1H), 7.51 (d, *J* = 12.0 Hz, 2H), 7.19-7.15 (m, 4H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.71 (t, *J* = 8.0 Hz, 1H), 2.25 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 145.8, 137.8, 136.8, 133.6, 129.8, 125.9, 118.8, 112.3, 21.1; CHN analysis $C_{17}H_{15}N_3$; Calcd.; C, 78.13; H, 5.79; N, 16.08; Found: C, 78.22; H, 5.80; N, 16.85.
 **4-(4-nitrophenyl)-6-phenylpyrimidin-2-amine** **2g**	Orange solid, Mp.: 158.3°C; FTIR (KBr) cm^{-1}: 3444, 3299, 2923, 1600, 1571, 1513, 1340, 1260, 1145, 1109, 834, 754, 689, 596; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 10.85 (s, 1H), 8.19 (d, *J* = 8.0 Hz, 2H), 8.0 (s, 1H), 7.85 (d, *J* = 8.0 Hz, 2H), 7.23-7.22 (m, 2H), 7.12-7.10 (m, 2H), 6.91-6.77 (m, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 146.6, 144.9, 143.2, 134.1, 129.8, 126.6, 124.6, 120.4, 113.1; CHN analysis $C_{16}H_{12}N_4O_2$; Calcd.; C, 65.75; H, 4.14; N, 19.17; Found: C, 65.80; H, 4.24; N, 19.25.
 **4-(3,4,5-trimethoxyphenyl)-6-phenylpyrimidin-2-amine** **2h**	Brick red solid, Mp.: 80°C; FTIR (KBr) cm^{-1}: 3444, 3291, 2945, 1694, 1593, 1499, 1449, 1405, 1332, 1260, 1217, 1123, 993, 820, 740, 675; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 10.24 (s, 1H), 7.75 (s, 1H), 7.22-7.16 (m, 2H), 7.04 (d, *J* = 8.0 Hz, 2H), 6.91 (s, 2H), 6.70 (t, *J* = 8.0 Hz, 1H), 3.78 (s, 6H), 3.64 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 153.7, 145.7, 138.0, 136.8,

	131.8, 129.6, 118.9, 112.3, 103.2, 60.6, 56.1; CHN analysis $C_{19}H_{19}N_3O_3$; Calcd.; C, 67.64; H, 5.68; N, 12.46; Found: C, 68.10; H, 5.74; N, 12.25.
 **4-(4-chlorophenyl)-6-phenylpyrimidin-2-amine** **2i**	Light pink solid, Mp.: 119.7°C; FTIR (KBr) cm^{-1}: 3451, 3313, 3053, 2923, 2844, 1600, 1521, 1485, 1441, 1355, 1260, 1138, 1080, 827, 747, 689; ^1H NMR (DMSO-d_6, 400 MHz): δ 7.63 (s, 1H), 7.59 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.29-7.25 (m, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 6.86-6.89 (m, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 144.4, 135.8, 133.9, 129.4, 128.8, 127.2, 120.3, 112.8; CHN analysis $C_{16}H_{12}ClN_3$; Calcd.; C, 68.21; H, 4.29; N, 14.91; Found: C, 68.30; H, 4.34; N, 14.85.
 **4-(naphthalen-2-yl)-6-phenylpyrimidin-2-amine** **2j**	Orange solid, Mp.: 265°C; FTIR (KBr) cm^{-1}: 3444, 3291, 3090, 2916, 1622, 1578, 1506, 1420, 1340, 1260, 1145, 827, 740, 581; ^1H NMR (DMSO-d_6, 400 MHz): δ 11.70 (s, 1H), 8.82 (s, 2H), 8.34-8.37 (m, 1H) 8.13-8.15 (m, 2H), 7.91-8.05 (m, 5H), 7.54-7.56 (m, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz: δ 165.1, 162.7, 133.7, 133.3, 132.1, 130.7, 129.5, 128.8, 126.6, 126.2, 125.2, 124.3, 98.2; CHN analysis $C_{20}H_{15}N_3$; Calcd.;C, 80.78; H, 5.08; N, 14.13; Found: C, 80.82; H, 5.24; N, 14.85.
 **3,4-dihydro-4,6-diphenylpyrimidin-2(1*H*)-one**	White solid, Mp.: 247°C; FTIR (KBr) cm^{-1}: 3237, 3093, 3058, 1674, 1350, 755; ^1H NMR (DMSO-d_6, 400 MHz): δ 7.91 (s, 1H), 7.29-7.23 (m, 5H), 7.10-7.06 (m, 5H), 6.15 (brs, 1H), 5.60 (brs, 1H), 4.23 (s, 1H);

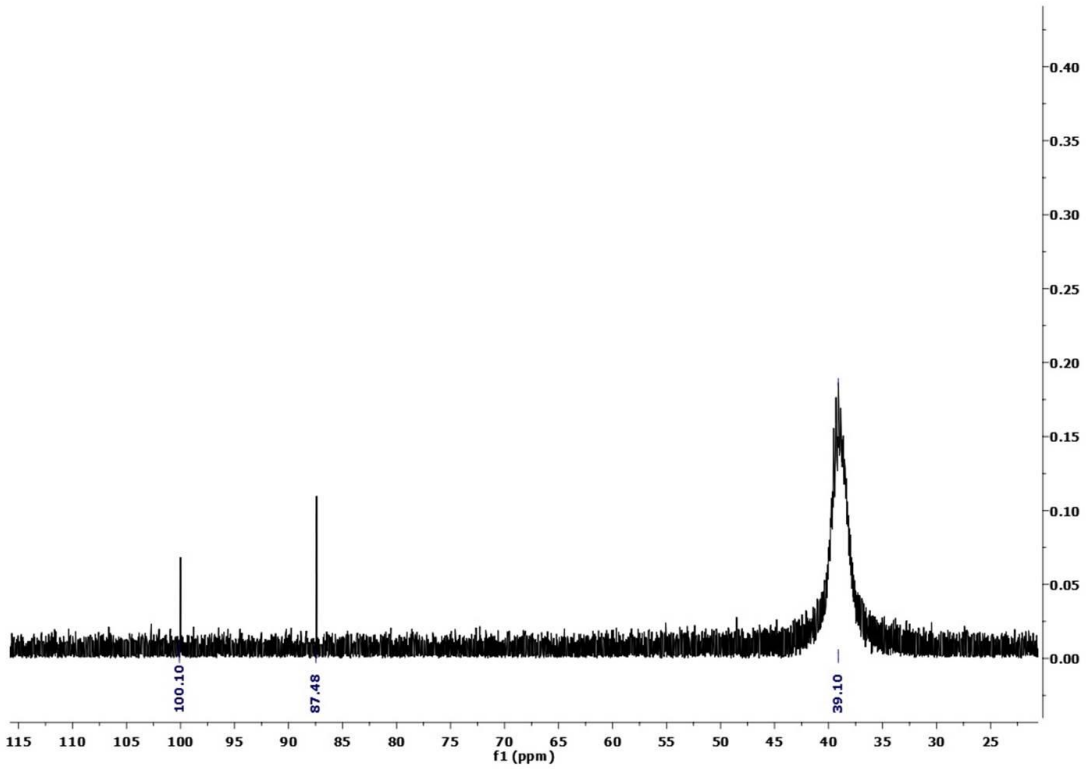
1a	^{13}C NMR (DMSO-d_6, 100 MHz): δ 157.8, 154.8, 141.8, 133.7, 129.2, 128.6, 128.4, 127.8, 127.4, 127.1, 54.5; CHN analysis $C_{16}H_{14}N_2O$; Calcd.;C, 76.78; H, 5.64; N, 11.19; Found: C, 77.01; H, 5.74; N, 11.85.
 **4-(4-chlorophenyl)-3,4-dihydro-6-phenylpyrimidin-2(1*H*)-one** **1i**	White solid, Mp.: 292^{o}C; FTIR (KBr) cm^{-1}: 3237, 3073, 1666, 1343, 820, 763; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 7.36-7.30 (m, 2H), 7.13 (s, 3H), 6.96 (s, 4H), 6.73 (brs, 1H), 5.65 (brs, 1H), 4.19 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 154.6, 142.4, 140.7, 131.9, 129.0, 128.4, 127.9, 127.2, 53.9; CHN analysis; $C_{16}H_{13}ClN_2O$; Calcd.; C, 67.49; H, 4.60; N, 9.84; Found: C, 67.55; H, 4.74; N, 9.88.

6B.6 NMR spectra of some selected compounds

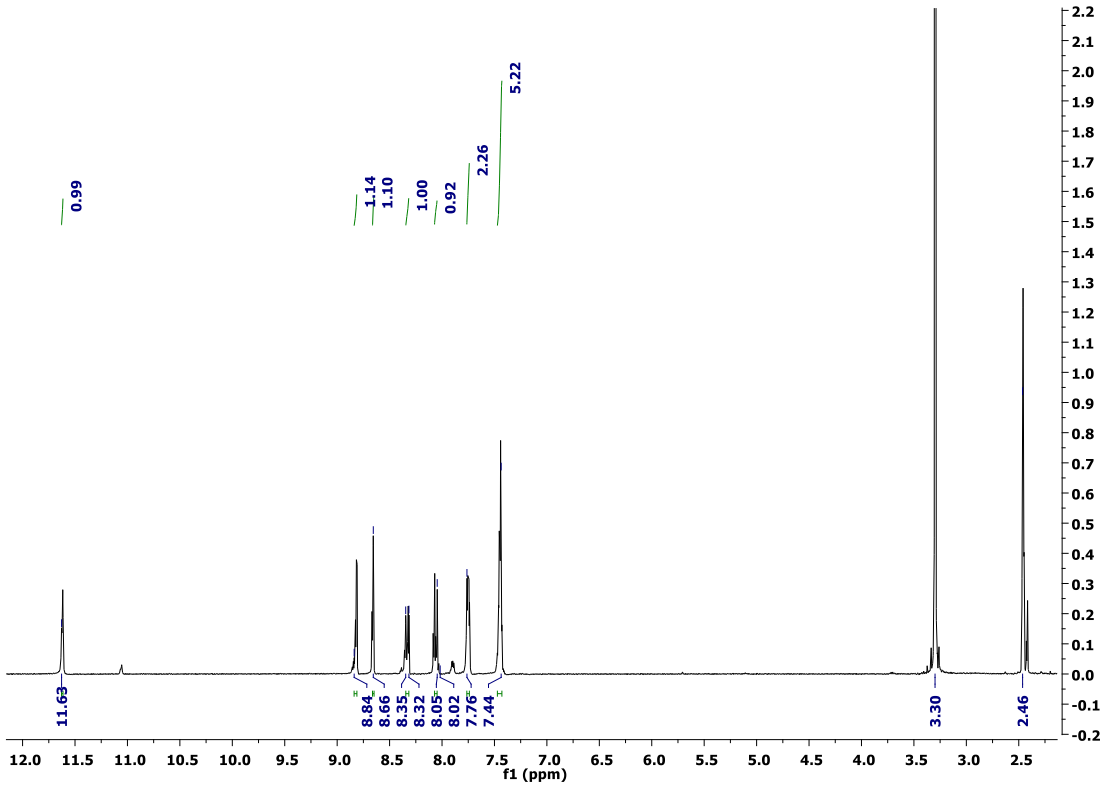
1. ^{1}H NMR of $[TSPi][CF_3SO_3]_2$



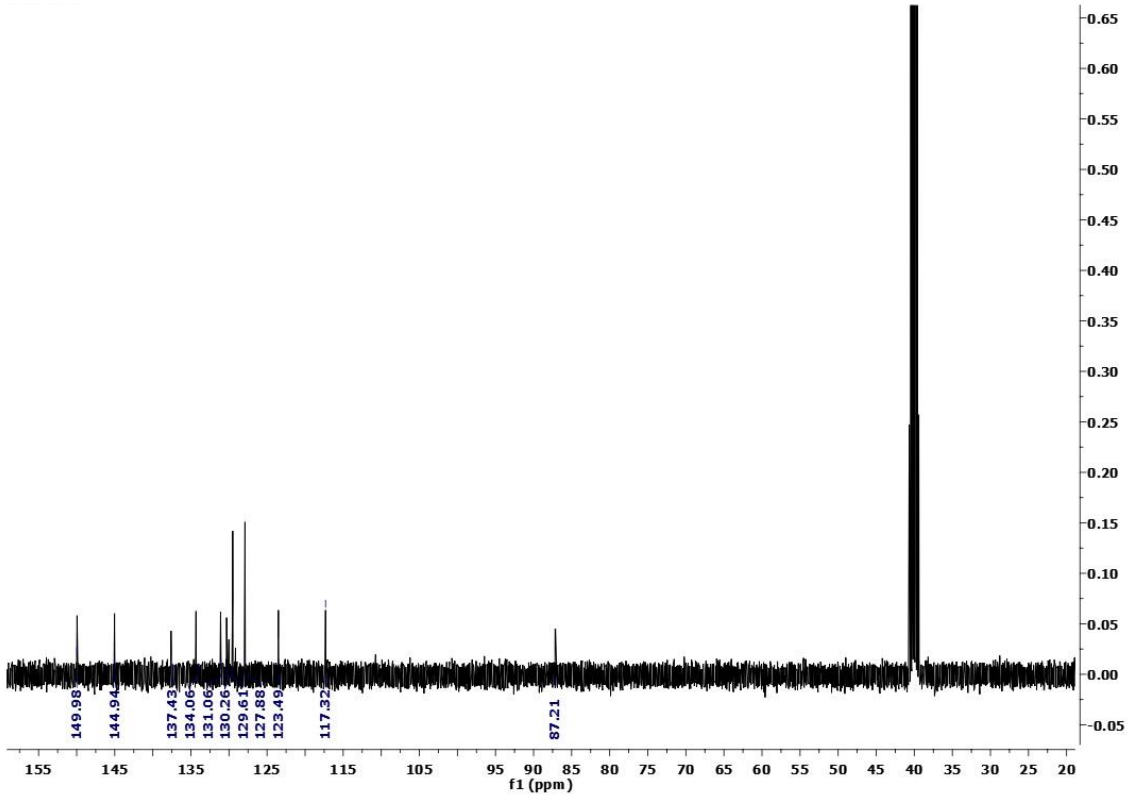
^{13}C NMR of $[TSPi][CF_3SO_3]_2$



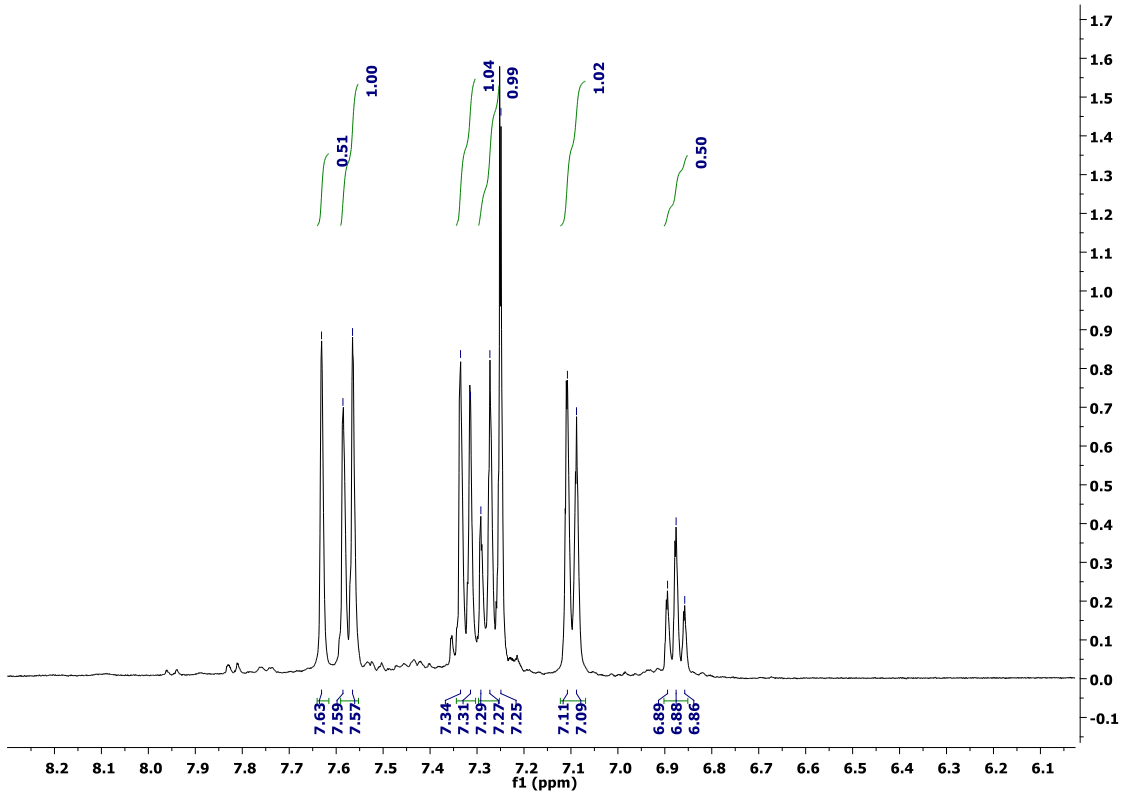
2. ^{1}H NMR of **2a**



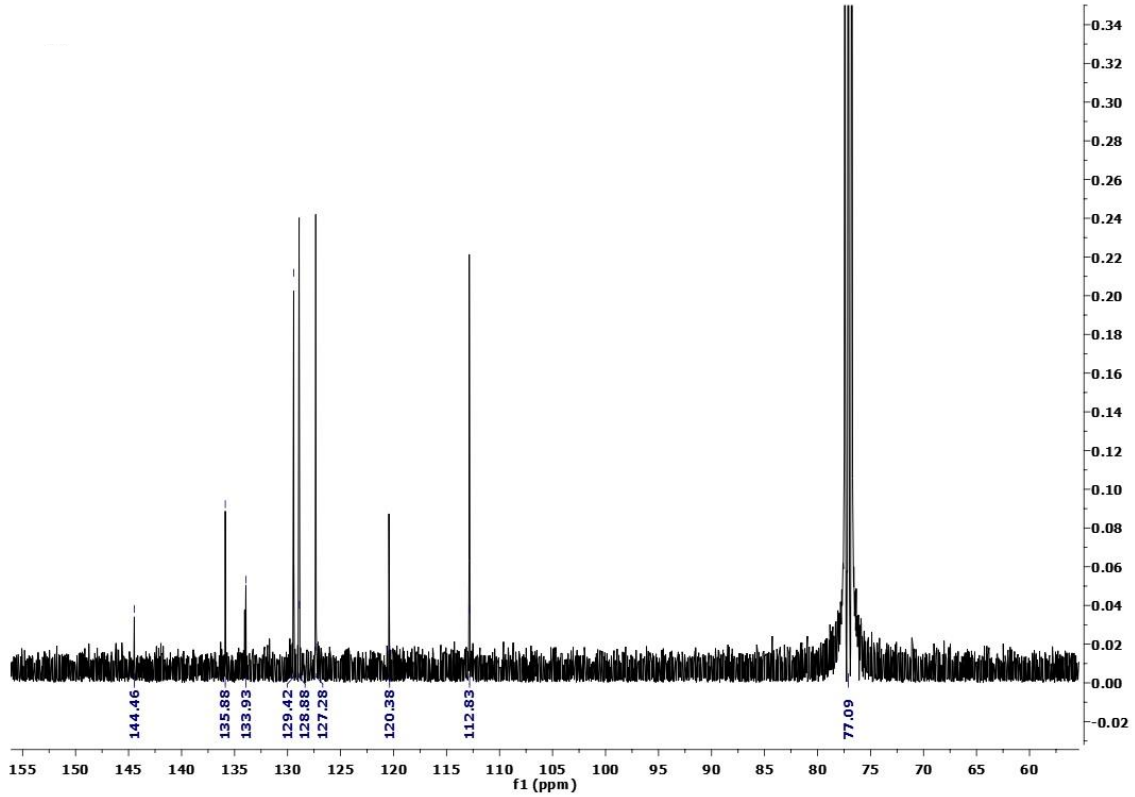
^{13}C NMR of **2a**



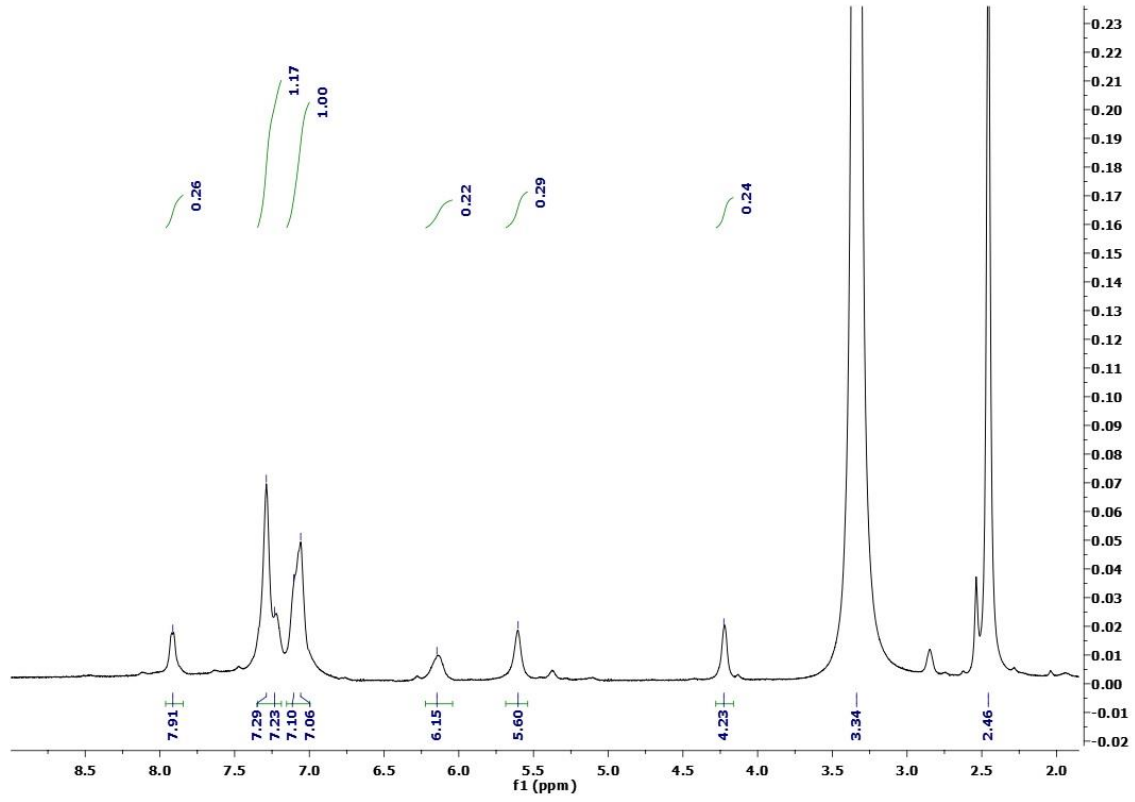
3. ^{1}H NMR of **2i**



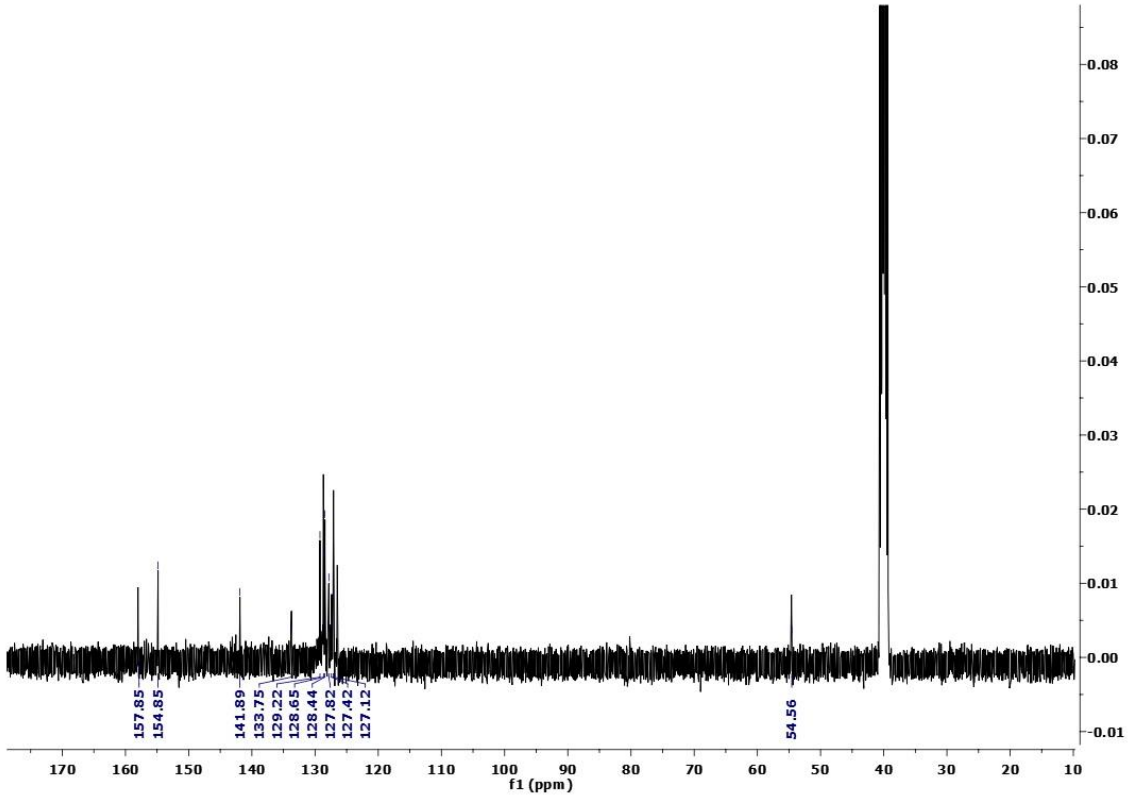
^{13}C NMR of **2i**



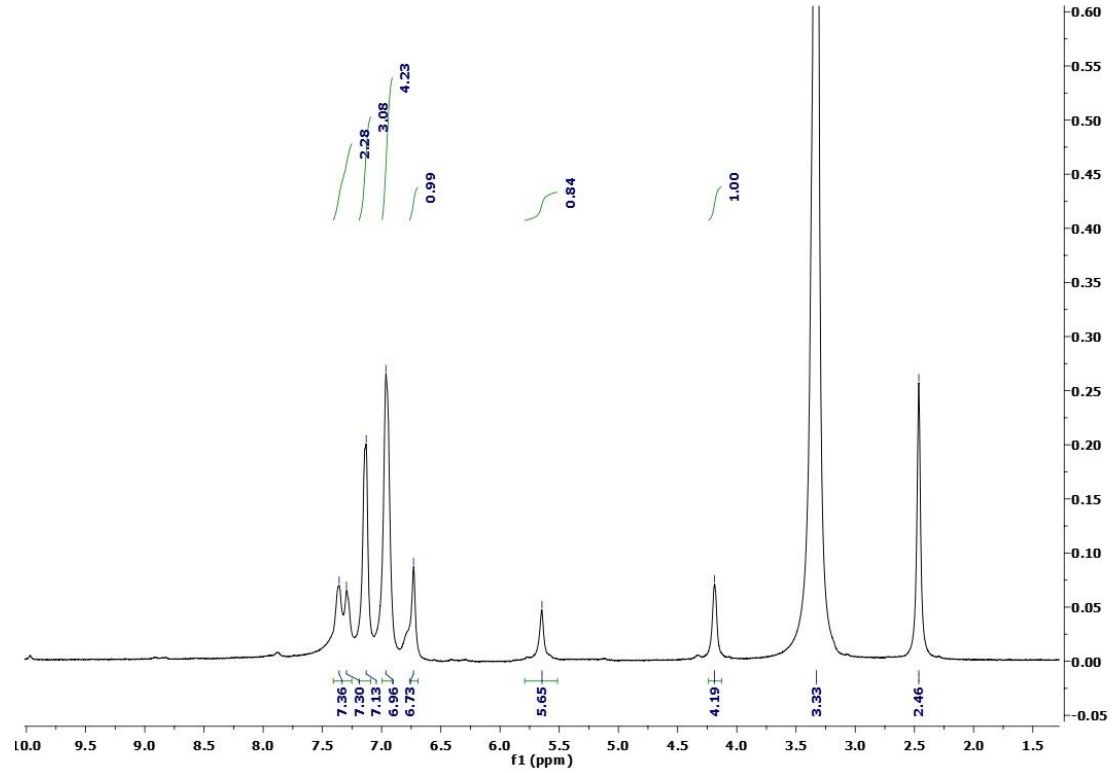
4. ^{1}H NMR of **1a**



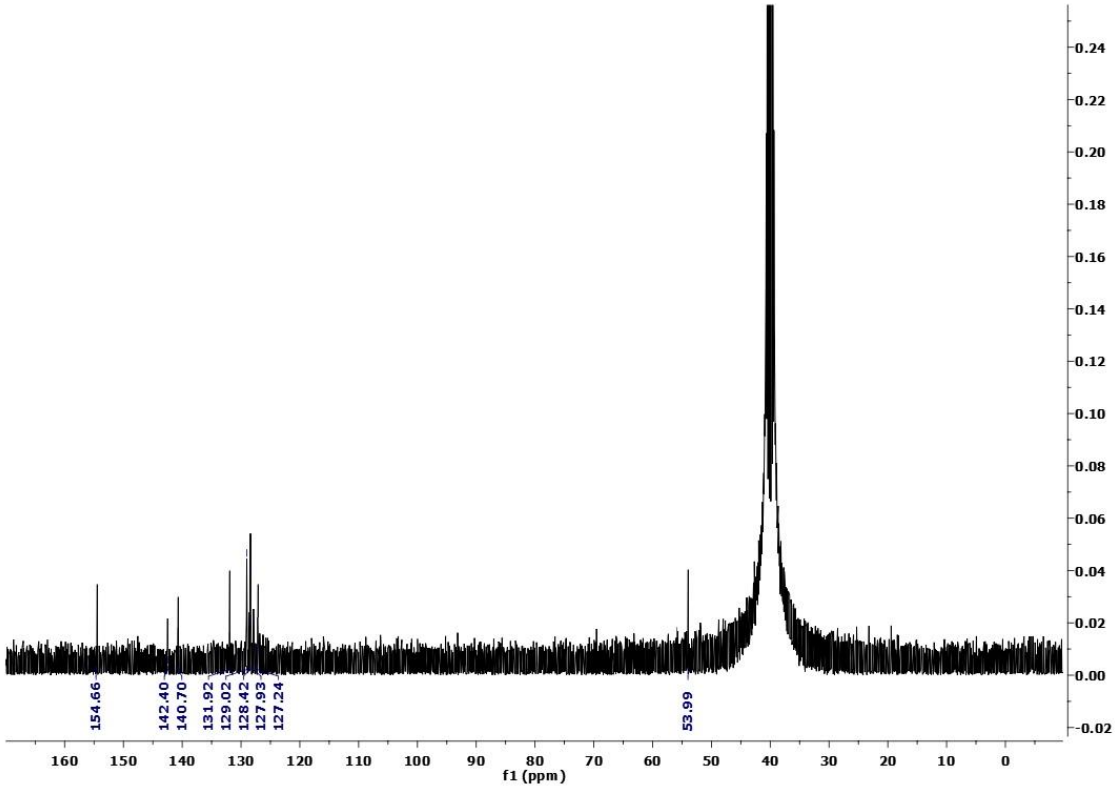
^{13}C NMR of **1a**



5. ^{1}H NMR of **1i**



^{13}C NMR of **1i**



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