RSC Advances

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View Article Online
DOI: 10.1039/C6RA21865B

Synthesis of Dual Functional Pyrimidinium Ionic Liquids (PyrILs) as Reaction Media and Antimicrobial Agents

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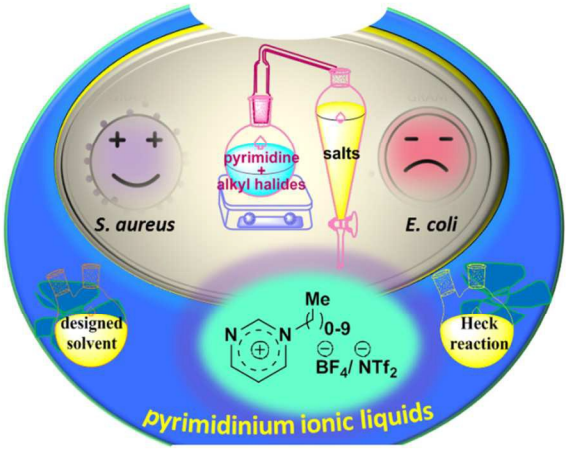

ABSTRACT: The development of materials with intrinsic synergistic properties has attracted great interest in the fields of chemistry and materials science. This article described the design and a concise two-step synthetic route of twenty antibacterial *N*-alkyl pyrimidinium ionic liquids with ability to be used as reaction media. These synergistic materials have been synthesized by the *N*-alkylation of pyrimidine, precursor of nucleobases, with varied *n*-alkyl (C_1-C_{10}) halides followed by anion metathesis of the resulting pyrimidinium halides using the salt of the counter anions, tetrafluoroborate (BF_4^-) and bis(trifluoromethanesulfonyl)amide (NTf_2^-) in good to excellent yields. With these newly synthesized quaternized pyrimidinium ionic liquids (PyrILs), the studies of solubility/miscibility in common solvents, solute-solvent interactions using UV-visible spectroscopy, compatibility as designed solvent for chemical reaction and evaluation of antimicrobial properties were conducted. The assessment of biological properties of all the PyrILs with (BF_4^-) counteranion against several microorganisms revealed that the $[C_9Pyr]BF_4$ and $[C_{10}Pyr]BF_4$ containing longer alkyl chain are the potential antibacterial agents showing excellent bioactivity against both Gram-positive *S. aureus* (MIC = 8 and 4 μg/mL, respectively), as well as Gram-negative *E. coli* bacteria (MIC = 8 and 4 μg/mL, respectively).

Keywords: Ionic liquids, pyrimidine, Heck reaction, anion metathesis, *N*-alkylation, UV-visible, antibacterial activity

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INTRODUCTION

Currently, ionic liquids (ILs) are in the frontline of academic and industrial centric research and discussion, particularly, in green chemical synthesis of the potential materials due to their unusual reactivity in synthetic and photophysical applications, unexpected compatibility, excellent solubility and miscibility in wide range of organic solvents, as well as aqueous medium. They are molten salts that are liquid around ambient condition and consisting of bulky organic cation and either an organic or inorganic anion,[1] endured by weak columbic force of attraction. The unique-array of physicochemical properties, including low vapor pressure, wide liquid window, reduced flammability, high polarity, excellent stability (*e.g*. thermal, physical, chemical, redox, radiochemical) and so forth are evident parameters for making these organic salts as more greener solvents, and suitable for numerous applications over the hazardous and toxic traditional volatile organic compounds (VOCs).[2,3] Thus, due to these appealing properties, ILs promise extensive application in various fields, such as organic synthesis, catalysis, bio-catalysis, polymerization, absorption of toxic gases, liquid-liquid extraction *etc*.[4,5] In particular, these are used as a less toxic reaction medium in hydrogenation, transition metal catalyzed reactions, cycloaddition, intramolecular aldolization, C-C coupling reactions and so on.[6,7]

It is obvious that nitrogen-containing heterocycles, which are immensely distributed in nature and present in DNA, RNA, hormones, proteins, including biologically and physiologically urged molecules, are playing a vital role in metabolism of all living cells. These are also important starting materials in the synthesis of ionic liquids *via* quaternisation of nitrogen atom. Presently, the majority of research on ILs is dominated mostly by the common cationic moieties, such as imidazolium, pyrazolium, triazolium, thiazolium, pyridinium, pyrylium, pyrrolidinium, ammonium and phosphonium, including the anions, $BF_4^-, PF_6^-, CF_3CO_2^-, CF_3SO_3^-, AlCl_4^-, OH^-, NO_3^-, SCN^-, Br^-, Cl^-$, $(SO_2CF_3)_2N^-$ and I^- (Figure 1).[8-12] However, to the best of our knowledge, to date, very little efforts have been devoted towards the development of neucleobase precursor, pyrimidine-based ionic liquids as of the recent publications.[13]

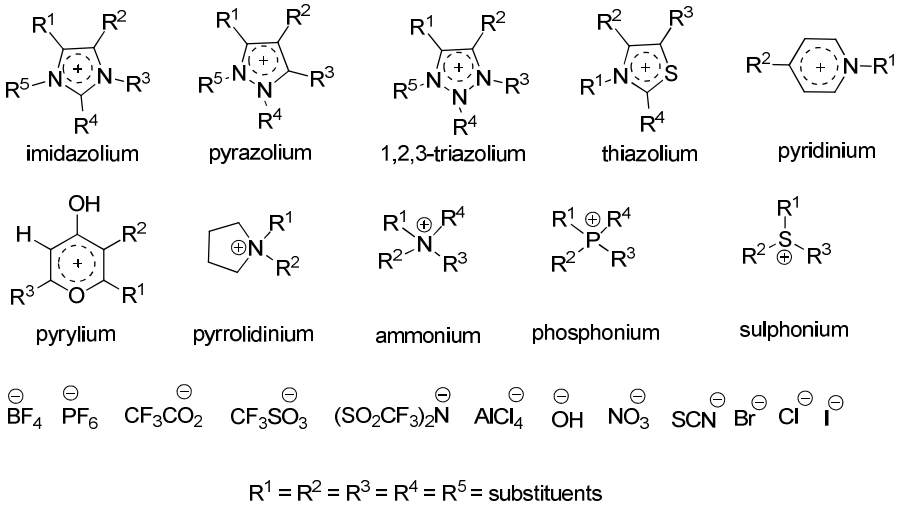

Figure 1. Common cationic and anionic units of ionic liquids

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Moreover, the ionic liquids, which could act as pharmaceutical agents, such as antibacterial, antiseptic and antifungal *etc*., are not well documented in literature.[14] However, our studies have revealed the inner potential of the newly synthesized pyrimidinium ionic liquids to exhibit excellent antimicrobial activity, inspiring the exciting possibility to be used as biocidal agents in the control of contamination and infection by the potential microorganisms. Pyrimidine is ubiquitous in many important biologically active molecules, such as nucleobases, nucleosides, nucleotides, synthetic drugs and drug candidates with a wide range of pharmacological activities depending on the functionalization of the pyrimidine moiety. Compounds containing densely functionalized pyrimidine moiety exhibit a wide spectrum of biological activities,[15,16] such as antifungal, anticancer, antimalarial, antibacterial, anti-HIV, anti-hypertensive *etc.* (Figure 2).[17] Due to emerging challenges faced by the bacterial resistance and multidrug resistant bacteria (MDR) against several clinical and life-saving drugs, including the allied toxicity problems, it is a pressing need for the development of new antibiotics with a unique mode of action. It is noteworthy to mention that the cationic lipids,[18,19] which contain a hydrophilic polar head and hydrophobic lipid part, have been developed to facilitate the permeation after disruptions of the bacterial envelope induced by removal (substitution) of positively charged divalent counterions by ammonium ions.[20] Additionally, the alkyl chain plays important role in membrane permeability for showing better antimicrobial activity. Cationic lipids including dodine,[21] benzalkonium chlorides,[22] sphingosine[23] and fatty amines,[20] chlorohexidine,[24] cationic polymers[25] and other cationic amphiphiles[26,27] are known to exhibit broad spectrum antibacterial activities (Figure 2). Spurred by the presence of pyrimidine moiety in the potential drugs, and also the lack of literatures of unexplored work on pyrimidine-based ionic liquid, we have described herein, a concise synthetic strategy for the generation of twenty pyrimidinium ionic liquids, which might shed some light on the development of therapeutic agents in new and future drug development for disinfectants and antimicrobials, as well as the useful greener solvents for chemical synthesis.

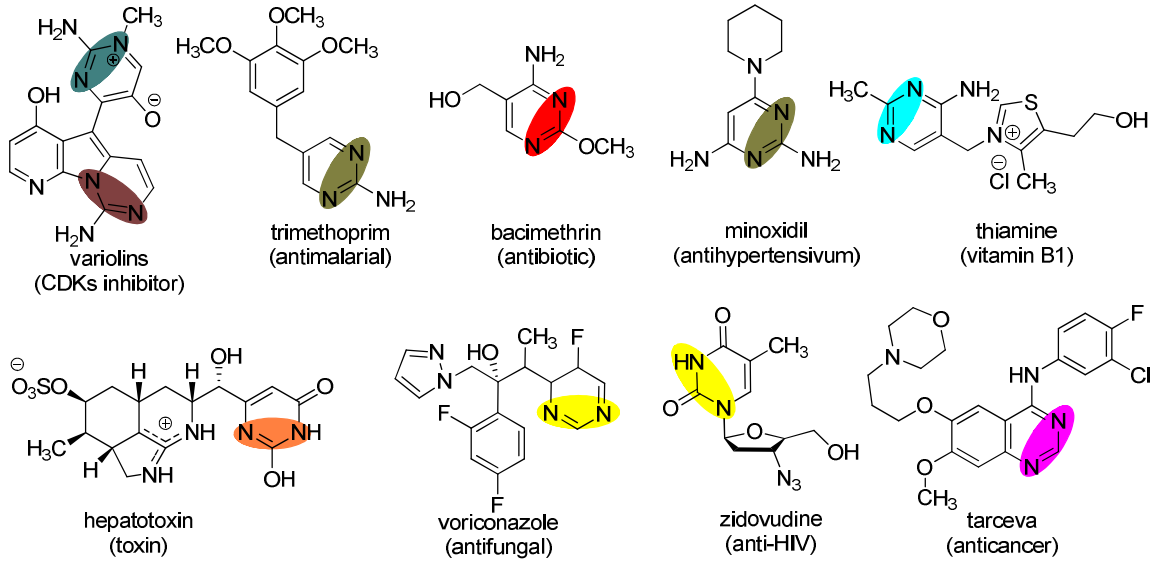

Figure 2. Pharmacological profile of pyrimidine core

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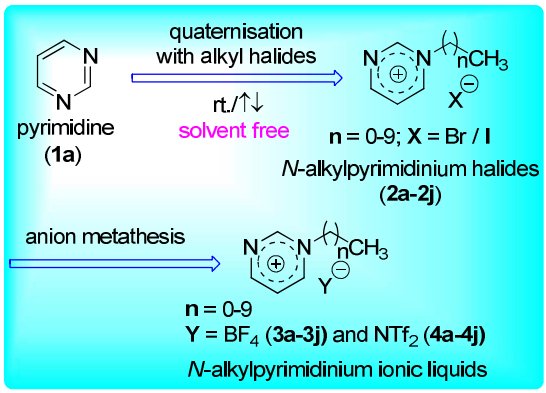
As a designer solvent, ionic liquids acquire tunable physicochemical properties, such as viscosity, hydrophobicity, boiling point, melting point and solubility by changing the anion and functionality attached with cation. Henceforth, to prepare a designer solvent for synthetic and biological application as antiseptics and disinfectants alleviating the antibacterial resistance, twenty pyrimidinium ionic liquids consisting a pyrimidine core tethered with *n*-alkyl chain of different lengths (C_1-C_{10}) as cation coupled with tetrafluoroborate (BF_4^-) and bis(trifluoromethanesulfonyl)amide (NTf_2^-) as non-coordinating counter anions have been designed and synthesized. The structural characterization of the newly synthesized compounds were carried out with NMR, mass, FTIR spectroscopy and elemental analysis. Herein, a simple and effective technique was used for the synthesis, isolation and most challenging purification of ionic liquids. Additionally, to find the synthetic applications of pyrimidinium ionic liquids as reaction medium, the $[C_6Pyr]BF_4$ (**3f**) ionic liquid as a representative of all the newly developed PyrILs was successfully employed as a compatible solvent in Heck coupling reaction for the formation of new carbon-carbon bond[28] and the medicinal applications of these PyrILs were further assessed exhibiting their antibacterial properties against several Gram-positive and Gram-negative bacteria.

RESULTS AND DISCUSSION

Synthetic strategy for N-alkylpyrimidinium halides and ionic liquids

As a part of our continuous interest in developing new ionic liquids as designer solvent, alternative to traditional volatile organic solvents (VOS), we have recently succeeded in developing indazolium ionic liquids and applied it to aldol condensation reaction.[8] Encouraged by these successful efforts for developing the indazolium ionic liquids as efficient reaction medium from the biologically active indazole, we have focused our recent attention on the synthesis of pyrimidinium ionic liquids derived from pyrimidine (**1a**) as constituent of natural bioactive compounds. As a target to synthesize *N*-alkylpyrimidinium ionic liquids (**3a-3j/4a-4j)**, a concise and practical two-step protocol involving quaternisation of a nitrogen atom using alkyl halides to produce *N*-alkylpyrimidinium salts (**2a-2j**) followed by anion metathesis to replace halide with the desired anion has been deliberated (Scheme 1).



Scheme 1. Synthetic strategy for *N*-alkylpyrimidinium halides and ionic liquids

Synthesis of *N*-alkylpyrimidinium halides

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Accordingly, the initial study was the quaternisation of nitrogen atom present in the pyrimidine ring with different alkyl halides varying the chain length from C_1 to C_{10}; compared to pyridine, *N*-alkylation of pyrimidine ring was challenging due to less availability of electron lone pair on *N*-atom compared to pyridine and more susceptible to photolytical and thermal decomposition of the pyrimidine ring into uracil and nucleophilic aromatic substitution.[29] After exhaustive hit and trial attempt for *N*-alkylation on pyrimidine ring with least amount of decomposition and formation of substituted pyrimidine, a solvent free method was developed as a safest and suitable method in which the pyrimidine was treated with neat methyl iodide in excess amount at room temperature under an inert atmosphere and light protected environment, affording *N*-methylpyrimidinium iodide salt **2a** as a yellow solid in 93% yield (Scheme 2, Table 1: Entry 1). The reaction was monitored by TLC and the nonpolar impurities in crude salt were removed by washing with diethyl ether (2-3 times) and its structure was confirmed by spectroscopic methods. In the ^{1}H NMR spectrum, the shifting of signals of pyrimidinium salts **(2a)** towards lower field at around δ 8.14-9.57 ppm from δ 7.38-8.90 ppm compared to that of parent pyrimidine **(1a)** corroborated the quaternisation of *N*-atom present in pyrimidine *via N*-alkylation followed by the positive charge distribution into the pyrimidine ring. Similarly, in the ^{13}C NMR spectrum of **2a,** the peaks appeared at 123.9-164.4 ppm is slightly more deshielded than that of the characteristic peak at 122.3-157.1 ppm for pyrimidine. In addition to this, further noticeable feature is the observation of peak at δ 4.33 ppm due to appearance of proton signals of alkyl chain connected with *N*-atom (-NCH_3), which is on close agreement with the reported one.[13] The low-resolution ESI$^+$-QTOF mass of **2a** produced at *m/z* = 95.0631 for $[C_5H_7N_2]^+$ (calcd mass = 95.0604 for $[C_5H_7N_2]^+$) confirmed the formation of salt $[C_5H_7N_2]^+I^-$ **(2a)**. Having synthesized the quaternised methyl pyrimidinium iodide salt (**2a**) through quaternisation of the *N*-atom of the pyrimidine ring using methyl iodide followed by unambiguous thorough characterization of the same, we have investigated the alkylation of pyrimidine ring with higher alkyl halides ranging from C_2 to C_{10} under refluxing condition at 65-80 °C for 5 h to 2 days. It is necessary to mention that quaternisation of pyrimidine with methyl, ethyl, and *n*-propyl groups afforded **2a**, **2b,** and **2c** in almost quantitative yield, whereas *n*-butyl to *n*-decyl halides produced the salts **2d-2j** in moderate to high yields (Scheme 2, Table 1: Entries 1 to 10). The comparatively lower yield of the salts **2d-2j** are believed to be responsible for the higher bulkiness allied with greater flexibility of the comparatively longer alkyl side chain, which reduces the rate of quaternisation of *N*-atom of the pyrimidine **(1a)** with corresponding alkyl halides. The reaction was monitored carefully with a precise temperature control, as prolonged heating at higher temperature leads to darken brown oil and enhancement of unidentified and intricate impurities, which were much difficult to remove from the resulting products. Hence, the reactions were performed at constant temperature with continuous monitoring by TLC for the fixed time period rather than the use of longer reaction time. The residual unreacted starting material and unidentified complex mixture was removed from the reaction mixture by repeated washing with diethyl ether and the purified products were confirmed by spectroscopic analysis. Purity of the ionic liquids has been confirmed by NMR and elemental analysis and found to be reasonable.

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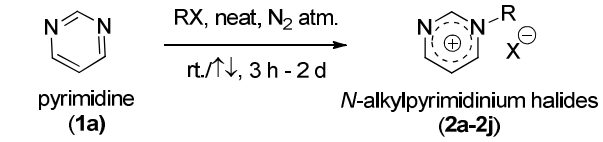

R = Me, Et; X = I
R = *n*-Pr, *n*-Bu, *n*-Pent, *n*-Hex, *n*-Hept, *n*-Oct, *n*-Non, *n*-Dec; X = Br

Scheme 2. Synthesis of *N*-alkylpyrimidinium salts

Table 1. Reaction parameters, yields and state of *N*-alkylpyrimidinium salts

Entry	RX	time (h)	product	isolated yield (%)	state/MP
1.	1-iodomethane	3	2a	93	solid/142 °C
2.	1-iodoethane	5	2b	92	solid/114 °C
3.	1-bromopropane	24	2c	92	viscous liquid
4.	1-bromobutane	24	2d	89	semi solid
5.	1-bromopentane	32	2e	90	semi solid
6.	1-bromohexane	32	2f	87	semi solid
7.	1-bromoheptane	36	2g	87	semi solid
8.	1-bromooctane	42	2h	84	semi solid
9.	1-bromononane	48	2i	79	semi solid
10.	1-bromodecane	48	2j	72	semi solid

To surmount the difficulties that are encountered during temperature control and also due to longer reaction period, the microwave-assisted and sonochemical methods were also attempted for the quaternisation of pyrimidine ring using bromoalkanes in neat condition at different time and temperatures, but the reaction proved unsuccessful.

Synthesis of *N*-alkylpyrimidinium ionic liquids

However, the synthesized quaternised salts of pyrimidine (**2a-2j**) were subjected to convert into the corresponding ionic liquids by anion metathesis. These halide-free salts could be useful as dual functional agents, such as green solvents for organic synthesis as well as antibacterial agents for the control of contamination and infection by the potential pathogens. A library of *N*-alkylpyrimidinium ionic liquids (**3a-3j** and **4a-3j)** comprising of weakly coordinating tetrafluoroborate (BF_4^-) and bis(trifluoromethanesulfonyl)amide (NTf_2^-) anions were synthesized (Scheme 3). The hydrophobic NTf_2^- anion was preferred one for the formation of new ionic liquids because it is hydrolytically stable and having strong delocalization of the electron cloud towards the fluoroalkyl group, which weakens its interaction with the cation leading to lower melting and boiling points of the NTf_2^- counteranion-based ionic liquids in comparison to the BF_4^- counteranion-based ILs. The most challenging part in this metathesis step was the purification of the crude ionic liquids from the unreacted starting materials as well as other impurities generated during the course of the reaction and thus, an efficient and practical method for purification was developed sans column chromatography, the most commonly used technique for purification in organic synthesis. To overcome the problem, numerable combinations of pentane and ether in different ratio were used for washing purposes depending on the alkyl chain length and anion, which is discussed in the text.

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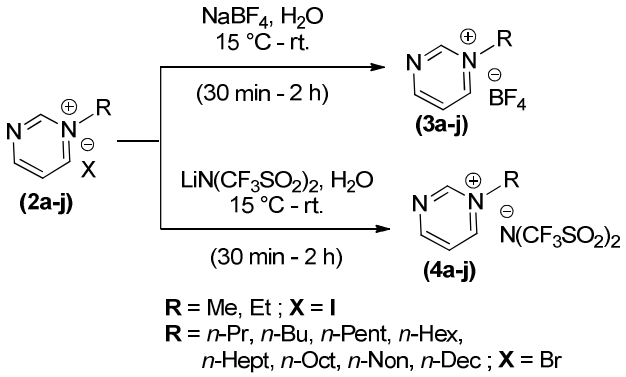
Initially, the studies of metathesis step were performed with the ionic liquids synthesized using the shortest alkyl halide, *N*-methylpyrimidinium iodide (**2a**) and the longest alkyl halide, *N*-decylpyrimidinium (**2j**) bromide in most benign solvent, *i.e.*, aqueous solution by portion wise addition of sodium tetrafluoroborate at 15 °C for 10-15 min and then allowed to room temperature for 30 min to 2 h to afford the desired *N*-methylpyrimidinium (**3a**) and *N*-decylpyrimidinium (**3j**) tetrafluoroborate ionic liquids in 71% and 94% yield (Scheme 3, Table 2: Entries 1 and 10), respectively. Whereas the same reaction of other *N*-alkylpyrimidinium halides (alkyl = Ethyl to *n*-Nonyl) with sodium tetrafluoroborate afforded almost quantitative yield of the products. Ionic liquids (**3e-3g**) were liquid at room temperature and hence termed as room temperature ionic liquids (RTLIs), whereas the ionic liquids **3a-3d** and **3h-3j** are found as sticky substances, which melts below 100 °C. With this optimized conditions, the anion metathesis reaction was then examined with lithium bis(trifluoromethylsulfonyl)amide for the formation of *N*-alkylpyrimidinium bis(trifluoromethylsulfonyl)amide ionic liquids. In this case, the resulted room temperature ionic liquids **4a-4j** are obtained in higher yields except *N*-propylpyrimidinium bis(trifluoromethylsulfonyl)amide ionic liquid affording 70% yield (Scheme 3, Table 2: Entries 1 to 10).



Scheme 3. Synthesis of *N*-alkylpyrimidinium ionic liquids

Table 2. *N*-alkylpyrimidinium ionic liquids

Entry	Ionic liquids (**3a-3g**)	Isolated yield (%) (**3a-3g**)	Solvent for purification (**3a-3g**)	Ionic liquids (**4a-4g**)	Solvent/s for purification (**4a-4g**)	Ratio (v/v)	Isolated yield (%) (**4a-4g**)
1.	$[C_1Pyr]BF_4$ **3a**	71	Et_2O	$[C_1Pyr]NTf_2$ **4a**	pentane:Et_2O	0:1	84
2.	$[C_2Pyr]BF_4$ **3b**	74	Et_2O	$[C_2Pyr]NTf_2$ **4b**	pentane:Et_2O	0:1	86
3.	$[C_3Pyr]BF_4$ **3c**	76	Et_2O	$[C_3Pyr]NTf_2$ **4c**	pentane:Et_2O	0:1	70

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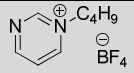
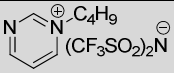
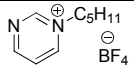
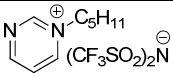
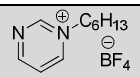
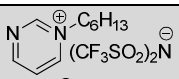
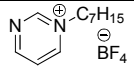
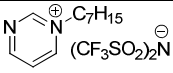
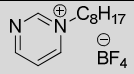
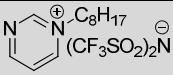
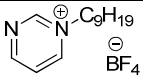
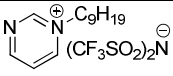
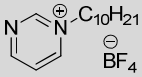
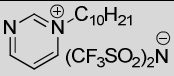
4.	 [C_4Pyr]BF_4 **3d**	79	Et_2O	 [C_4Pyr]NTf_2 **4d**	pentane:Et_2O	0:1	87
5.	 [C_5Pyr]BF_4 **3e**	81	Et_2O	 [C_5Pyr]NTf_2 **4e**	pentane:Et_2O	0:1	90
6.	 [C_6Pyr]BF_4 **3f**	87	Et_2O	 [C_6Pyr]NTf_2 **4f**	pentane:Et_2O	0:1	91
7.	 [C_7Pyr]BF_4 **3g**	89	Et_2O	 [C_7Pyr]NTf_2 **4g**	pentane:Et_2O	2:8	91
8.	 [C_8Pyr]BF_4 **3h**	90	Et_2O	 [C_8Pyr]NTf_2 **4h**	pentane:Et_2O	2.5:7.5	93
9.	 [C_9Pyr]BF_4 **3i**	92	Et_2O	 [C_9Pyr]NTf_2 **4i**	pentane:Et_2O	3:7	94
10.	 [$C_{10}Pyr$]BF_4 **3j**	94	Et_2O	 [$C_{10}Pyr$]NTf_2 **4j**	pentane:Et_2O	3:7	95

Solubility studies of various ionic liquids

Since, room-temperature ionic liquids (ILs) have potential for different applications, including catalysis and synthesis, thus, after successful synthesis of pyrimidinium salts, ionic liquids *via* metathesis and purification by washing out the impurities, reagents and unreacted materials with a minimum amount of cold solvent mixture in a fixed ratio, the synthetic application of the synthesized ionic liquids to form C-C bond was explored. To figure out the appropriate solvent mixture for purification of the synthesized PyrILs, the solubility/miscibility of the ionic liquid with different solvents was investigated; the observations of this study could have greater potential as crucial parameters for conducting chemical reaction in these newly synthesized PyrILs in combination with aqueous and/or non-aqueous solvents, photophysical study in binary solvent mixture, investigation of its catalytic activity for chemical reactions and their recycling purposes. Therefore, the solubility of *N*-alkylpyrimidinium tetrafluoroborate (**3a-3j**) ionic liquids in several common organic solvents was extensively studied (Table 3). It is found that the ionic liquids do not dissolve in hexane or Et_2O, but are comfortably soluble in MeOH and CH_3CN and the solubility increases with the increase of dielectric constant of the organic solvents. However, the length of alkyl chains (C_1-C_{10}) of the cation have greater influences in determining the solubility of these PyrILs in different solvents ($CHCl_3$,

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EtOAc, CH_2Cl_2 and H_2O); with increase of chain length of the attached alkyl groups with cationic part of these PyrILs increases in $CHCl_3$, EtOAc, and CH_2Cl_2 while it decreases in H_2O. Thus, the PyrILs (**3a-3f**) formed with the moderate alkyl chain length are completely miscible in H_2O, however, **3g-3h** derived with long alkyl groups is partially miscible and **3i-3j** synthesized with longer alkyl chains are immiscible; the variation of solubility properties of all these PyrILs is the function of hydrophobicity of the newly synthesized the ionic liquids.[9b,e] Since the $(NTf_2)^-$ is more hydrophobic than BF_4^-, so it is believed that the solubility of the ionic liquids with $(NTf_2)^-$ counterions will be less in aqueous solution rather than in organic solvents. Further, the feasibility of the Heck-coupling reaction in the RTILs of PYrILs was explored.

Table 3. Miscibility/solubility of various ionic liquids (**3a-3j**) in organic and aqueous solvents

Ionic liquids	**Pentane**	**Hexane**	**Et_2O**	**$CHCl_3$**	**EtOAc**	**CH_2Cl_2**	**MeOH**	**CH_3CN**	**H_2O**
$[C_1Pyr]BF_4$ (**3a**)	nm	nm	nm	nm	nm	pm	m	m	m
$[C_2Pyr]BF_4$ (**3b**)	nm	nm	nm	nm	nm	pm	m	m	m
$[C_3Pyr]BF_4$ (**3c**)	nm	nm	nm	nm	nm	pm	m	m	m
$[C_4Pyr]BF_4$ (**3d**)	nm	nm	nm	nm	pm	pm	m	m	m
$[C_5Pyr]BF_4$ (**3e**)	nm	nm	nm	m	m	m	m	m	m
$[C_6Pyr]BF_4$ (**3f**)	nm	nm	nm	m	m	m	m	m	m
$[C_7Pyr]BF_4$ (**3g**)	nm	nm	nm	m	m	m	m	m	pm
$[C_8Pyr]BF_4$ (**3h**)	nm	nm	nm	m	m	m	m	m	pm
$[C_9Pyr]BF_4$ (**3i**)	nm	nm	nm	m	m	m	m	m	nm
$[C_{10}Pyr]BF_4$ (**3j**)	nm	nm	nm	m	m	m	m	m	nm

m = miscible, nm = non-miscible, pm = partially miscible. Dielectric constant (ε) at 20 °C: Pentane = 1.84, Hexane = 1.89, Et_2O = 4.33, $CHCl_3$ = 4.81, EtOAc = 6.02 (25 °C), CH_2Cl_2 = 8.93 (25 °C), MeOH = 32.70, CH_3CN = 37.50, and H_2O = 80.10

Pd-catalyzed Heck-coupling reaction

In a preliminary study, the palladium acetate, $Pd(OAc)_2$ catalyzed Heck-coupling reaction on styrene derivative as a simple model substrate with bromo benzene for C-C bond formation was accomplished using one of the RTILs, 1-hexylpyrimidinium tetrafluoroborate, $[C_6Pyr]BF_4$ **(3f)** affording **7** in 85% yield**;** in this context, it could be mentioned that the same method could find an wider application as a potential greener synthetic method of an important cancer-preventive drug, resveratrol (Scheme 4). In brief, the reaction was monitored by TLC and the product was extracted with diethyl ether (3 × 3 mL). The combined organic layers were concentrated by rotary evaporator. The residue was purified by flash column chromatography on silica gel (ethyl acetate:hexane, 5:95) furnishing the desired product **7,** whose spectroscopic data are fully corroborated with the literature precedent.[30] It was interesting to mention that the recyclability of the ILs was also explored by the same experimental IL, which was recovered from the Heck-coupling reaction, and reused for the second time and found that the yield of the reaction was reasonable (≥ 77%).

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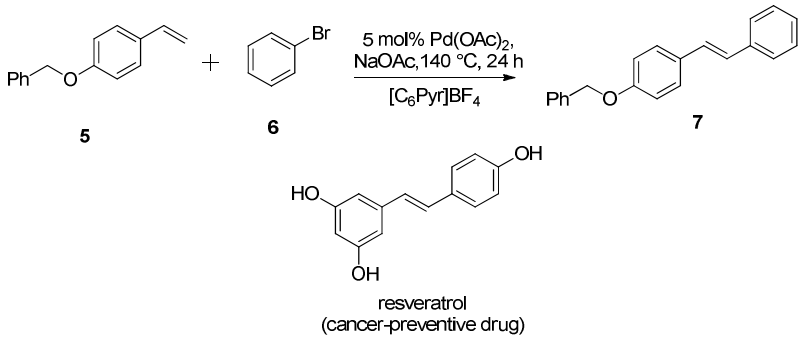
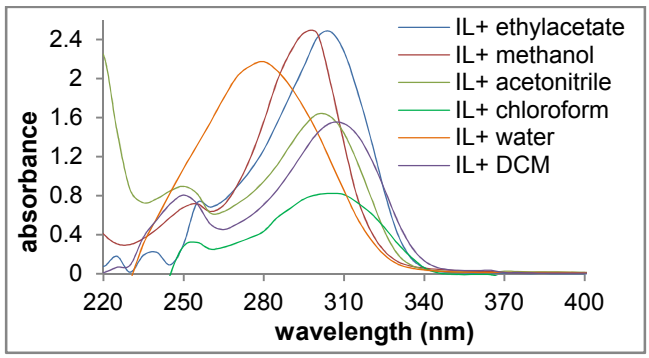


Scheme 4. Pd-catalyzed Heck-coupling reaction in ionic liquid $[C_6Pyr][BF_4]$

Photophysical study

For unwrapping the photophysical properties of the series of PyrILs, the interaction of 1-hexylpyrimidinium tetrafluoroborate, $[C_6Pyr][BF_4]$ as an representative of all the synthesized PyrILs with different solvents (H_2O, EtOAc, CH_3OH, CH_3CN, $CHCl_3$ and CH_2Cl_2) was studied by UV–visible spectroscopy. It is worthy to mention that the UV-visible study revealed the blue shift of hexylpyrimidinium tetrafluoroborate, $[C_6Pyr]BF_4$ in different solvents (H_2O, EtOAc, CH_3OH, CH_3CN, $CHCl_3$ and CH_2Cl_2) at 2.5×10^{-4} M concentration with increase of solvent polarity as UV absorption is the function of concentration of dissolved solute, *i.e.*, ionic liquid. As per the UV-visible spectroscopic study, it is clearly observed that the λ_{max} value of 2.5×10^{-4} M ionic liquid, $[C_6Pyr]BF_4$ (**3f**) in different organic solvents (295-305 nm) is red shifted with respect to that of in water (280 nm) (Figure 3). It is also evident that the λ_{max} shifts to lower wavelengths [$\lambda_{max}CH_2Cl_2$ (310 nm)< $\lambda_{max}CHCl_3$ (306 nm)< λ_{max}EtOAc (305 nm) < $\lambda_{max}CH_3OH$ (300 nm) < $\lambda_{max}CH_3CN$ (295 nm) < $\lambda_{max}H_2O$ (280 nm)] with the increase of solvent polarity [CH_2Cl_2 (3.1)< $CHCl_3$ (4.1)< EtOAc (4.4)< CH_3OH (5.1)< CH_3CN (5.8)< H_2O (10.8)]. The intensity of the UV absorbance data of **3f** at 2.5×10^{-4} M concentration varies in different solvent [EtOAc (2.5) ≈ CH_3OH (2.5) > H_2O (2.2) > CH_3CN (1.6) > CH_2Cl_2 (1.5) > $CHCl_3$ (0.8)] indicating that the solubility of the IL (**3f**) may not depend upon the solvent polarity only but also upon other factors, such as intermolecular forces. Generally, this unique behavior could be understood by the difference of solubility of the ionic liquid in different solvents. Thus, the variations in the position, intensity, and shape of the absorption spectra can be direct measures of the specific interactions between the solute and solvent molecules.[31] Thereby the UV spectroscopic study could provide useful information about the solubility limit of ionic liquids in different solvent (Figure 3).



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DCM = dichloromethane

Figure 3. Photophysical study of 2.5×10^{-4} M ionic liquid, $[C_6Pyr]BF_4$ (**3f**) by UV-Visible spectroscopy

Water content, Melting Temperature, and Glass Transition Temperature

To determine the operational range of ILs, the melting point, glass transition temperature, and water content were measured. The melting point or glass transition temperature determines the lowest temperature at which the IL can be used as a liquid. The ILs are tabulated in Table 1S to facilitate easy comparison of the parameters of their thermal analysis. The melting point (T_m) and the glass transition temperature (T_g) was determined considering the onset temperature of an endothermic peak upon heating, and the temperature at the midpoint of a small heat capacity change, respectively. Accordingly, the DSC curve of $[C_9Pyr]BF_4$, $[C_9Pyr]NTf_2$ and $[C_2Pyr]NTf_2$ shown in the Figure S1 and S2 produced a sharp phase transition assigning as their melting point (T_m) at 47.66, -52.40 and 46.90 ºC, respectively. Figure S1 shows that the $[C_9Pyr]NTf_2$ have the heat absorption peak at -52.40 º, which is lower temperature than that of the $[C_9Pyr]BF_4$ (47.66 ºC); it is probably due to the weak coulombic interaction of pyrimidinium cation with NTf_2^- anion. While in Figure S2, the $[C_1Pyr]NTf_2$ and $[C_8Pyr]NTf_2$ shows heat capacity (ΔC_p) of 0.267 $J.g^{-1}.°C$ and 0.059 $J.g^{-1}.°C$, assigning as glass transition temperature (T_g) thus no melting points were observed in the temperature range scanned for these ILs. In addition, the water content was less than 0.016% in all of the ILs with counter anion BF_4^- and less than 0.012% in all the ILs with counter anion NTf_2^- which was analyzed by Karl Fischer titration (Metrohm coulometer) as the ILs with counter anion BF_4^- are relatively hydrophilic in comparison to the series of ILs with counter anion NTf_2^-.

Antibacterial assay

Considering their potential versatility as active constituent in biologically active natural products and drug molecules allied with the unexplored results of the pyrimidine moiety as a part of cationic lipid in pharmacological activities, the *in vitro* antibacterial activities of the synthesized ionic liquids against Gram-positive *Staphylococcus aureus* (NCIM 2079), *Bacillus subtilis* (NCIM 2250) and *Bacillus pumilis* (NCIM 2327) and Gram-negative *Escherichia coli* (NCIM 2109), *Pseudomonas aerugenosa* (NCIM 2036) and *Klebsiella pneumoniae* (NCIM 2719) bacterial strains with that of chloramphenicol (CP) as positive control are investigated. During the assessment of their medicinal properties, the antibacterial activities of the ten pyrimidinium ionic liquids containing various hydrophobic alkyl chain lengths with BF_4^- as counteranion at different concentration (μg/mL) using double dilution method have been explored. It is interesting to report that, the antibacterial activities of the ILs (**3h-3j**) with alkyl chain length (C_8-C_{10}) exhibited good to moderate growth inhibition activity (MIC = 4-32 μg/mL) against Gram-positive bacteria. In particular, the ILs $[C_9Pyr]BF_4$ **3i**, and $[C_{10}Pyr]BF_4$ **3j,** which are relatively hydrophobic, revealed excellent bioactivity against Gram-positive *S. aureus* with MIC = 8 μg/mL and 4 μg/mL, respectively. The antibacterial profile of the $[C_1Pyr]BF_4$ **3a** to $[C_{10}Pyr]BF_4$ **3j** suggests that higher alkyl chain length induces optimal antibacterial activity. Surprisingly, it is found that the ionic liquid, $[C_{10}Pyr]BF_4$ **3j** shows the similar antibacterial activity of the clinically used ciprofloxacin (MIC = 4 μg/mL) against Gram negative *E. coli,* which is very interesting and could lead as one of the promising antibacterial and disinfectant drug candidates. On the other hand, a moderate antibacterial activity was also observed for the ILs (**3h-3j**) (C_8-C_{10}) against *B. subtilis* and *B. pumilis* as shown in Table 4.

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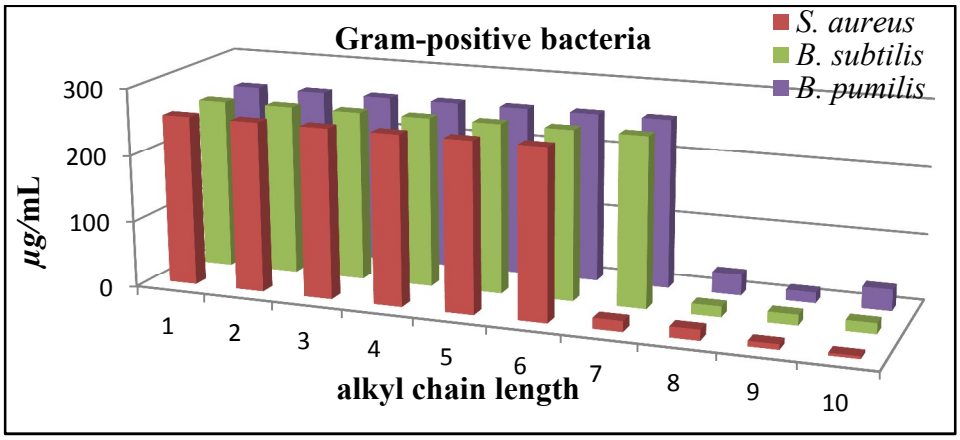
Table 4. In vitro antibacterial assay of $[C_1Pyr]BF_4$ to $[C_{10}Pyr]BF_4$ (**3a-3j**) against various bacterial strains (MIC in µg/mL); chloramphenicol (CP)

Organism	C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}	CP
S. aureus	256	256	256	256	256	256	16	16	8	4	0.1
B. subtilis	256	256	256	256	256	256	256	16	16	16	0.2
B. Pumilis	256	256	256	256	256	256	256	32	16	32	0.2
E. coli	256	256	16	256	256	256	256	32	8	4	4.0
P. aruginosa	>256	>256	>256	>256	>256	>256	64	32	64	64	8.0
K. pneumoniae	>256	>256	16	>256	>256	>256	>256	32	32	32	4.0

Although the assessment of medicinal properties suggested that the antibacterial activities of the tested ILs is modulated by alkyl chain length, however any obvious trends are not documented rather different level of antibacterial activity are shown depending on the microorganisms tested. The expression of the antibacterial properties of these ionic liquids is due to the presence of the cationic charge, which disrupts the bacterial membrane leading to cell death. The high activity of C_9- or C_{10}-lipid chain containing ionic liquids against Gram-positive as well as Gram-negative bacteria could open a new window for the development of potential antiseptics and antimicrobial disinfectants or drug entity in curing the topical infections. Moreover, cationic surface-active detergents, such as benzalkonium chloride are clinically used as strong disinfectants being effective on both Gram-positive and Gram-negative organisms; the MIC of optimized benzalkonium chlorides is 6.25 µg/mL on MRSA[24]. A bar diagram for the antibacterial activity of the *N*-alkylpyrimidinium tetrafluoroborate (**3a-3j**) ionic liquids are shown in Figure 4.



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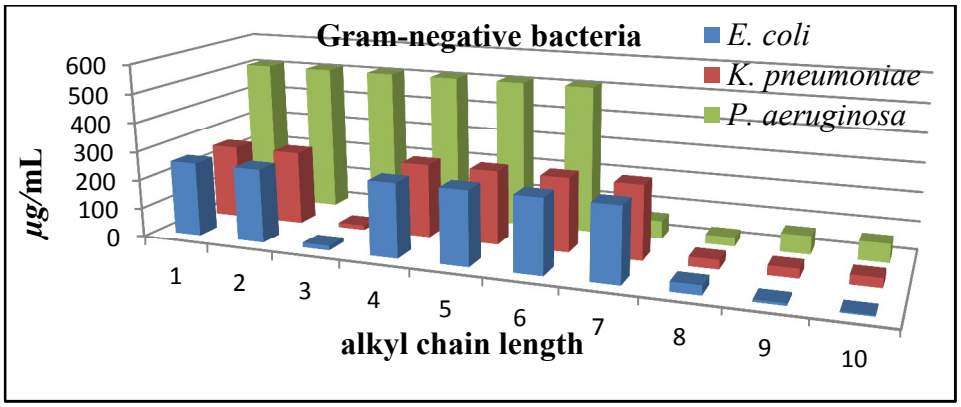

Figure 4. Bar diagram for the antibacterial activity of ionic liquids **3a-3j**

Microbial Study

The *in vitro* antibacterial activities were carried out at Department of Microbiology, R. C. Patel Arts Commerce and Science College Shirpur, Dhule (Maharashtra). The antibacterial activities were assessed against Gram-positive (*Staphylococcus aureus* NCIM 2079, *Bacillus subtilis*, NCIM 2250 and *Bacillus pumilis* NCIM 2327) and Gram-negative (*Escherichia coli* NCIM 2109, *Pseudomonas aerugenosa* NCIM 2036 and *Klebsiella pneumoniae* NCIM 2719) bacterial strains. Cultures used in the experiment were obtained from National Collection of Industrial Microorganisms (NCIM), National Chemical Laboratory (NCL), Pune (India). Nutrient agar microbiological media used for Gram-positive and Gram-negative strains was obtained from Hi-media (India) and the ingredients (g/L) of the composition is sodium chloride, 5.0; beef extract 10.0 and peptone 10.0 at pH 7.2.The chloramphenicol was used as standard drug for Gram-positive and Gram-negative bacterial strains. The MIC values of ILs (**3a-j**) were evaluated by double dilution method.[32] Stock solution of 1024 μg/mL of each IL was prepared in DMSO and further serial dilution were prepared to final concentration of 512, 256, 128, 64, 32, 16, 8, 4, 2, 1, 0.5, 0.25, 0.125 μg/mL in water. The MIC which inhibits the visible growth after 24 h, was determined visually after incubation for 24 h, at 37 °C and pH 7.2. The lowest concentration which showed no visible growth was taken as end point for MIC values.

Evaluation of cell cytotoxicity

Cell Culture

Human colorectal cells Caco-2 were maintained in Eagle's Minimum Essential Medium in 20% fetal bovine serum and 100 units/ml penicillin-streptomycin solution. Cells were grown at 37 ^{0}C in humidified 5% CO_2 incubator (Thermo Fisher Scientific) as adherent monolayers and fresh media was added after every 24 h and passaged when cells reached near 80% confluency.[33] These cells developed morphological characteristics of normal enetrocuytes when grown on plastic plates.[34]

MTT assay

The MTT assay is a well-established assay to study the viability of cells *in vitro*. NAD(P)H-dependent cellular oxidoreductase enzymes present in mitochondria can convert MTT dye to insoluble formazan crystals, producing purple colour. The intensity of the colour is directly proportional to the number of viable cells. In our experiment,

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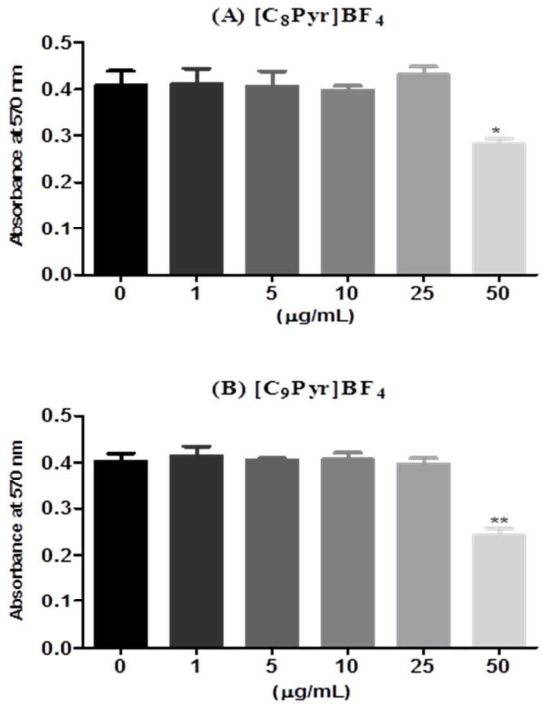
10,000 cells were counted through a haemocytometer and seeded to a 96 well plate. After 24 h of incubation, spent media was aspirated and fresh media with different concentration (1, 5, 10, 25 and 50 µg/mL) of three potential ILs $[C_8Pyr]BF_4$, $[C_9Pyr]BF_4$, and $[C_{10}Pyr]BF_4$ were added to wells. After 24 h, media containing compounds were removed and 5 mg/mL MTT dye (100µL/well) in phosphate buffer saline (PBS, pH 7.4) was added to each well and incubation was done in a humidified incubator at 37 ^{0}C for 4 h. After incubation, dye was aspirated out and 100 µL/well DMSO was added to solubilize the formazan crystals. Finally, absorbance was taken at 570 nm by microplate reader (Synergy H1 Hybrid Reader, Biotek, Winooski, VT).[34,35]

Statistical Analysis

Statistical significance of differences between control and treated samples were calculated using Student's t-test (Graphpad Prism version 5). P-value of less than 0.05 were considered to be significant.

Result

To investigate the effect of three potential ILs $[C_8Pyr]BF_4$, $[C_9Pyr]BF_4$ and $[C_{10}Pyr]BF_4$ on growth and viability of Caco-2 cells MTT assay was performed. Studied ILs did not show significant decrease in the viability of cells on initial four concentrations *i.e.* 1, 5, 10, 25 µg/mL. However, on highest concentration (50 µg/mL) ILs showed decrease in cell viability with increase in chain length from C_8-C_{10} after 24 h of incubation (Figure 5). ILs $[C_8Pyr]BF_4$, $[C_9Pyr]BF_4$ and $[C_{10}Pyr]BF_4$ shows 68.86, 60.90 and 37.55% cell viability and cell cytotoxicity 31.13, 39.90 and 63.45% respectively at 50 µg/mL.



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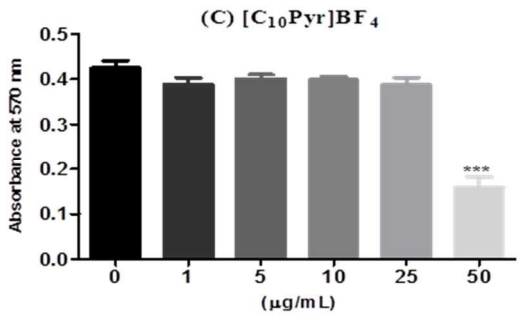

Figure 5. Effect of ILs ILs (A) $[C_8Pyr]BF_4$, (B) $[C_9Pyr]BF_4$ and (C) $[C_{10}Pyr]BF_4$ (1-50 µg/mL) on cytotoxicity of Caco-2 cells

CONCLUSION

In conclusion, a two-step and concise protocol for the synthesis of pyrimidine-based ionic liquids tethered with alkyl substituent of varying chain length (as cation) and tetrafluoroborate and bis(trifluoromethylsulfonyl)amide as the counter anion in moderate to good yields have been developed. Their photophysical and chemical reactivity are demonstrated in view of the solubility in aqueous and non-aqueous solvents, solute-solvent interaction by UV-visible spectroscopy and the synthetic utility as reaction media. In order to evaluate their potentiality in different field, one of the room-temperature pyrimidinium ionic liquids, $[C_6Pyr]BF_4$ **(3f)** was used in palladium catalyzed Heck-coupling reaction to study the ability as reaction medium. In the preparation of ionic liquids, the purification method of anion metathesis, which is one of the challenging steps, was established by using different combination of solvent mixture for rinsing the crude products to get the pure PyrILs. It is pertinent to mention that in due course, the other ionic liquids are also being studied for their application as catalysts in different chemical reactions and as well as alternatives to conventional organic solvents in organic synthesis. As these ionic liquid contain a polar quaternary nitrogen atom and hydrophobic lipid part, their structures resemble with the cationic lipid, like benzoalkonium chloride, a disinfectant and hence some of the ionic liquids were tested against Gram-positive and Gram-negative microorganisms and $[C_9Pyr]BF_4$ and $[C_{10}Pyr]BF_4$ are found to exhibit promising results against Gram-positive *S. aurues* (MIC = 8 and 4 mg/mL, respectively) as well as Gram-negative *E. coli* (MIC = 8, 4 mg/mL, respectively). With the alkyl chain C_9 and C_{10}, $[C_9Pyr]BF_4$ and $[C_{10}Pyr]BF_4$ are assumed to easily permeate the cell membrane in addition to electrostatic interaction. In the meantime, the biological activities of other ionic liquids with bis(trifluoromethylsulfonyl)amide as the counter anion are currently undergoing *in vitro* testing for antimicrobial and anticancer activities. These data will be published in due course.

EXPERIMENTAL SECTION

General information and methods

The required reagents and solvents were purchased from commercial suppliers (Sigma Aldrich, Merck and Rankem) and were used as received without further purification. Progress of the reaction was monitored by thin layer chromatography (TLC) on pre-coated silica gel 60-F254 alumina plates (Merck) and visualization was accomplished

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using UV light. All the quaternised salts and ionic liquids were purified either using diethyl ether or the mixture of diethyl ether and pentane and yield refers to those obtained after purification unless otherwise stated. ^{1}H and ^{13}C NMR spectra were recorded with a 500 MHz Bruker Avance spectrometer in D_2O and acetone-d_6 with tetramethylsilane (TMS) as internal standard. The chemical shifts are noted in part per million (ppm) and the coupling constants are given in Hertz. Low-resolution mass spectra were recorded with a Q-TOF, Agilent Technologies G6520B mass spectrometer with the electrospray ionization (ESI^+) technique. Perkin-Elmer spectrum 65 FTIR spectrophotometer was used for recording IR spectra and the values are expressed as % transmittance. Elemental analyses were performed by Euro Vector elemental analyzer. The absorption transition (λ_{max}) was recorded using Analytical UV spectro 2060 plus within the range of 200-600 nm at room temperature. Experiments were performed in 1 cm path length quartz cuvette. Melting points were determined in open capillaries and are uncorrected. Differential scanning calorimetery curve were performed with Perkin Elmer DSC 6000 and Scanning sequence involves freezing of an ILs sample to -70 ºC, maintaining this temperature for 10 min, and then heating the sample to 150 ºC at 10 ºC/min under nitrogen atmosphere. MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) and molecular biology grade DMSO were purchased from Sigma Aldrich (St. Louis, MO). 100 mm and 96 well tissue culture treated plates were procured from Corning. Fetal bovine serum, Trypsin-EDTA and penicillin-streptomycin solution were purchased from (Gibco Life Technologies, Grand Island, NY, Invitrogen). Human colorectal cells Caco-2 were purchased from NCCS Pune, India.

General procedure of quaternisation for *N*-alkyl pyrimidinium halides (2a-2j). To a vessel containing pyrimidine (**1**) (650 mg, 8.12 mmol), alkyl halides (1.39 g, 8.93 mmol) was added and stirred at 65-80 °C for 5 to 48 h under neat condition to afford corresponding alkyl substituted pyrimidinium salts except the reaction with methyl iodide at room temperature for 3 h. Primarily the completion of reaction was marked by the separation of oil from the initially taken clear and homogenous mixture of pyrimidine and alkyl halide. After complete consumption of starting materials monitored by TLC, the residue was treated with diethyl ether to remove the unreacted starting materials. Additionally, these synthesised pyrimidinium salts were purified with diethyl ether to remove unidentified complex impurities and dried in *vacuum* to remove the residual solvent. The reaction was carried out at dark environment to avoid the light exposure under nitrogen atmosphere.

General procedure for the synthesis of *N*-alkyl pyrimidinium tetrafluoroborate (3a-3j).

To a solution of pyrimidinium salts (340 mg, 1.18 mmol) in water (2 mL), sodium tetrafluoroborate ($NaBF_4$) salt (142.44 mg, 1.30 mmol) was added in portion with vigorous stirring over 10-15 min at 15 °C and then stirring was continued at room temperature for another 2h. The water was removed under reduced pressure at 80 °C until we reached at constant weight. To the remaining residue, CH_2Cl_2 (10×10 mL) was added followed by filtration of the salts (metal halides). The ionic liquids with alkyl chain (C_5-C_{10}) tethered with pyrimidinium cation immediately formed a colloidal solution and extracted with CH_2Cl_2 (5×5 mL). The organic layer was separated and the combined CH_2Cl_2 layers were dried over Na_2SO_4, concentrated in rotary evaporator to afford the desired ILs. The crude

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products were further purified with diethyl ether *via* decantation method and dried in *vaccum* as metathesis product **(3a-3j)**.

General procedure for the synthesis of N-alkyl pyrimidinium bis(trifluoromethanesulphonyl)amide (4a-4j).
To a solution of pyrimidinium salts (552 mg, 1.92 mmol) in water (4 mL), bis(trifluoromethane sulphonamide)lithium ($LiN(SO_2CF_3)_2$) salt (606.88 mg, 2.11 mmol) was added in portion wise with continuous stirring over 10-15 min at 15 °C and then stirring was continued at room temperature for 2 h. Then, the mixture was transferred to a separating funnel and extracted with CH_2Cl_2 (5×5 mL). The organic layer was separated and the combined CH_2Cl_2 layers were dried over Na_2SO_4 and concentrated in rotary evaporator. The crude products were further purified with diethyl ether or diethyl ether/pentane depending on alkyl chain as discussed in Table 2 and dried in *vaccum* to get ionic liquid (**4a-4j).**

Procedure for Heck coupling for the synthesis of 1-(benzyloxy)-4-styrylbenzene (7).
In a preliminary study, the Heck-coupling reaction of bromobenzene (0.05 mmol, 16 mg) **(5)** and 1-(benzyloxy)-4-vinylbenzene (0.076 mmol, 30 mg) **(6)** was accomplished (as a model reaction) by employing palladium (II) acetate (5 mol%) and sodium acetate (0.075 mmol, 12.30 mg) in 1-hexylpyrimidin-1-ium tetrafluoroborate ($[C_6Pyr]BF_4$) **(3f)** (1mL) as the reaction medium affording the *(cis)*-1-(benzyloxy)-4-styrylbenzene **(7)** in 85% yield (Scheme 4). The reaction was carried out under nitrogen atmosphere, and before heating, the reaction mixture was deareated by nitrogen flow for 5 min. The reaction was accomplished by heating at 140 °C after 24 h, monitored by TLC. The cooled reaction mixture was extracted with diethyl ether (4×5 mL) and the combined extracts were concentrated on a rotary evaporator followed by purification of the crude mixture with flash silica gel chromatography (ethyl acetate: hexane, 5:95) to afford the desired coupled product. The product was dried in *vacuum* at 50 °C to remove the residual solvent. The product formation was confirmed by ^{1}H NMR, which is in close agreement with the reported literature.

*Pyrimidine (**1a**).* Colorless liquid; ^{1}H NMR (500 MHz, D_2O): δ 8.98 (s, 1 H, -NCHN-), 8.67 (m, 2 H, -N-CH-) ,7.47 (m, 1 H, -CH-) ppm; ^{13}C NMR (500 MHz, D_2O): δ 157.1, 157.0, 122.3 (pyrimidine ring) ppm; FTIR (KBr pellet): 3042 (aromatic -CH str.), 1615 (-C=N str.), 1577, 1566, 1467 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI^+) *m/z* Calcd for $[C_4H_5N_2]^+$: 81.0453 $(M+H)^+$, Found: 81.0485; Elemental analysis Calcd for $C_4H_4N_2$: C 59.99, H 5.03, N 34.98, Found. C 60.22, H 5.21, N 35.01%.

1-*Methylpyrimidin-1-ium iodide (**2a**).* Yellow solid; yield 90%; mp 142 °C; ^{1}H NMR (500 MHz, D_2O): δ 9.65 (s, 1 H, -NCHN^+-), 9.43(m, 1 H, -$^+$N-CH-), 9.25 (d, *J* = 5.1Hz, 1 H, -N-CH-), 8.22 (m, 1 H, -CH-), 4.42 (s, 3H, -$^+$N-CH_3) ppm; ^{13}C NMR (500 MHz, D_2O): δ 164.4, 154.1, 153.0, 123.9 (pyrimidine ring), 45.6 (-$^+$N-CH_3) ppm; FTIR (KBr pellet): 3068, 3027 (aromatic -CH str.), 2992, 2971 (aliphatic -CH str.), 1620 (-C=N str.), 1566, 1493, 1444 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI^+) *m/z* Calcd for $[C_5H_7N_2]^+$:

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95.0604 $(M\text{-}I)^+$, Found: 95.0631; Elemental analysis Calcd for $C_5H_7IN_2$: C 27.05, H 3.18, N 12.62, Found: C 27.24, H 3.08, N 12.79%.

All spectroscopic data were in close agreement with the reported ones.[13]

*1-Ethylpyrimidin-1-ium iodide (**2b**).* Yellow solid; Yield: 92%; mp 119 °C; ^{1}H NMR (500 MHz, D_2O): δ 9.73 (s, 1 H, -NCHN$^+$-), 9.43 (m, 1 H, -$^+$N-CH-), 9.34 (m,1 H, -N-CH-), 8.25 (m, 1 H, -CH-), 4.72 (br q, J = 7.2 Hz, 2 H, -$^+$N-CH_2-), 1.69 (br t, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, D_2O): δ 164.5, 153.4, 151.8, 124.2 (pyrimidine ring), 55.0 (-$^+$N-CH_2-), 15.1 (-CH_3) ppm; FTIR (KBr pellet): 3051 (aromatic -CH str.), 2979 (aliphatic -CH str.), 1627 (-C=N str.), 1569, 1498, 1452 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI$^+$) *m/z* Calcd for $[C_6H_9N_2]^+$: 109.0760 $(M\text{-}I)^+$, Found: 109.0751; Elemental analysis Calcd for $C_6H_9IN_2$: C 30.53, H 3.84, N 11.87, Found: C 30.71, H 3.98, N 11.71%.

*1-Propylpyrimidin-1-ium bromide (**2c**)*. Brownish viscous liquid; yield 89%; ^{1}H NMR (500 MHz, D_2O): δ 9.76 (s, 1 H, -NCHN$^+$-) , 9.49 (m, 1 H, -$^+$N-CH-), 9.36 (br d, J = 5.1 Hz, 1 H, -N-CH-), 8.30 (m, 1 H, -CH-), 4.68 (t, J = 7.3 Hz, 2 H, -$^+$N-CH_2-), 2.10-2.15 (m, 2 H, -CH_2-), 1.05 (t, J = 6.9 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, D_2O): δ 164.6, 153.5, 152.1, 124.3 (pyrimidine ring), 60.9 (-$^+$N-CH_2-), 23.9 (-CH_2-), 9.8 (-CH_3) ppm; FTIR (KBr pellet): 3037 (aromatic -CH str.), 2971, 2936, 2875 (aliphatic -CH str.), 1625 (-C=N str.), 1569, 1498, 1465 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI$^+$) *m/z* Calcd for $[C_7H_{11}N_2]^+$: 123.0917 $(M\text{-}Br)^+$, Found: 123.0904; Elemental analysis Calcd for $C_7H_{11}BrN_2$: C 41.40, H 5.46, N 13.79, Found: C 41.62, H 5.37, N 13.61%.

*1-Butylpyrimidin-1-ium bromide (**2d**)*. Brownish semi solid; yield 70%; ^{1}H NMR (500 MHz, D_2O): δ 9.73 (s, 1 H, -NCHN$^+$-), 9.46 (m, 1H, -$^+$N-CH-), 9.34 (br d, J = 5.1 Hz, 1 H, -N-CH-), 8.26 (m, 1 H, -CH-), 4.69 (t, J = 7.3 Hz, 2 H, -$^+$N-CH2-), 2.04-2.07 (m, 2 H, -CH_2-), 1.42- 1.47 (m, 2 H, -CH_2-), 0.98 (t, J =7.1 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, D_2O): δ 164.5, 153.5, 152.0, 124.2 (pyrimidine ring), 59.3 (-$^+$N-CH_2-), 32.2, 18.8 (-CH_2-), 12.7 (-CH_3) ppm; FTIR (KBr pellet): 3042 (aromatic -CH str.), 2966, 2931, 2875 (aliphatic -CH str.), 1622 (-C=N str.), 1566, 1498, 1467, 1437 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI$^+$) *m/z* Calcd for $[C_8H_{13}N_2]^+$: 137.1073 $(M\text{-}Br)^+$, Found: 137.1060; Elemental analysis Calcd for $C_8H_{13}BrN_2$: C 44.26, H 6.04, N 12.90, Found: C 44.46, H, 6.21, N 13.11%.

*1-Pentylpyrimidin-1-ium bromide (**2e**)*. Brownish semi solid; yield: 83%; ^{1}H NMR (500 MHz, D_2O): δ 9.72 (s, 1 H, -NCHN$^+$-), 9.45 (m, 1 H, -$^+$N-CH-), 9.33 (br d, J = 5.0 Hz, 1 H, -N-CH-), 8.26 (m, 1 H, -CH-), 4.68 (t, J = 7.5 Hz, 2 H, -$^+$N-CH_2-), 2.05-2.10 (m, 2 H, -CH_2-), 1.37-1.41 (m, 4 H, -CH_2-), 0.90 (br t, J = 7.3 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, D_2O): δ 164.5, 153.5, 152.0, 124.2 (pyrimidine ring), 59.5

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(-$^{+}$N-CH_2-), 29.9, 27.4, 21.4 (-CH_2-), 13.0 (-CH_3) ppm; FTIR (KBr pellet): 3027 (aromatic -CH str.), 2961, 2926, 2865 (aliphatic -CH str.), 1622 (-C=N str.), 1569, 1495, 1467, 1437 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI^+) *m/z* Calcd for $[C_9H_{15}N_2]^+$: 151.1230 $(M\text{-}Br)^+$, Found: 151.1217; Elemental analysis Calcd for $C_9H_{15}BrN_2$: C 46.77, H 6.54, N 12.12, Found: C 46.43, H 6.85, N 11.97%.

*1-Hexylpyrimidin-1-ium bromide (**2f**)*. Brownish semi solid; yield 89%; ^{1}H NMR (500 MHz, D_2O + CD_3OD; 4:1): δ 9.68 (s, 1 H, -NCHN^{+}-), 9.41 (m, 1 H, -$^{+}$N-CH-), 9.28 (br d, *J* = 5.0 Hz, 1 H, -N-CH-), 8.21 (m, 1 H, -CH-), 4.63 (t, *J* = 7.1 Hz, 2 H, -$^{+}$N-CH_2-), 2.00-2.05 (m, 2 H, -CH_2-), 1.29-1.37 (m, 6 H, -CH_2-), 0.84 (br t, *J* = 7.0 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, D_2O + CD_3OD; 4:1): δ 165.5, 154.4, 152.9, 125.1 (pyrimidine ring), 60.4 (-$^{+}$N-CH2-), 31.3, 31.1, 25.9, 22.7 (-CH_2-), 14.1 (-CH_3) ppm; FTIR (KBr pellet): 3027 (aromatic -CH str.), 2961, 2926, 2865 (aliphatic -CH str.), 1622 (-C=N str.), 1566, 1495, 1467, 1437 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI^+) *m/z* Calcd for $[C_{10}H_{17}N_2]^+$: 165.1386 $(M\text{-}Br)^+$, Found: 165.1358; Elemental analysis Calcd for $C_{10}H_{17}BrN_2$: C 48.99, H 7.09, N 11.43, Found: C 49.19, H, 7.14, N 11.62%.

*1-Heptylpyrimidin-1-ium bromide (**2g**)*. Brownish semi solid; yield 55%; ^{1}H NMR (500 MHz, acetone-d_6): δ 10.35 (s, 1 H, -NCHN^{+}), 10.18 (m, 1 H, -$^{+}$N-CH-), 9.61 (m, 1 H, -N-CH-), 8.51 (m, 1 H, -CH-), 5.08 (t, *J* = 7.2 Hz, 2 H, -$^{+}$N-CH_2-), 2.18-2.20 (m, 2 H,-CH_2-), 1.30-1.51 (m, 8 H,-CH_2-), 0.88 (br t, *J* = 7.1 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, acetone-d_6): δ 165.4, 154.9, 153.6, 125.0 (pyrimidine ring), 59.5 (-$^{+}$N-CH2-), 32.3, 31.8, 29.4, 26.7, 23.2 (-CH_2-), 14.3 (-CH_3) ppm; FTIR (KBr pellet): 3022 (aromatic -CH str.), 2961, 2931, 2860 (aliphatic -CH str.), 1622 (-C=N str.), 1566, 1495, 1467, 1439 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI^+) *m/z* Calcd for $[C_{11}H_{19}N_2]^+$:179.1543 $(M\text{-}Br)^+$, Found: 179.1517; Elemental analysis Calcd for $C_{11}H_{19}BrN_2$: C 50.97, H 7.39, N 10.81, Found: C 51.12, H 7.49, N 11.04%.

*1-Octylpyrimidin-1-ium bromide (**2h**)*. Brownish semi solid; yield 58%; ^{1}H NMR (500 MHz, acetone-d_6): δ 10.40 (s, 1 H, -NCHN^{+}-), 10.19 (m, 1 H, -$^{+}$N-CH-), 9.64 (m, 1 H, -N-CH-), 8.54 (m, 1 H, -CH-), 5.09 (t, *J* = 7.5 Hz, 2 H, -$^{+}$N-CH_2-), 2.18- 2.21 (m, 2 H, -CH_2-), 1.29-1.50 (m, 10 H,-CH_2-), 0.87 (br t, *J* = 7.3 Hz, 3 H,-CH_3) ppm; ^{13}C NMR (500 MHz, acetone-d_6): δ 165.5, 154.9, 153.6, 125.1 (pyrimidine ring), 59.5 (-$^{+}$N-CH_2-), 32.4, 31.8, 29.8, 29.7, 26.7, 23.2 (-CH_2-), 14.3 (-CH_3) ppm; FTIR (KBr pellet): 3017 (aromatic -CH str.), 2961, 2926, 2860 (aliphatic -CH str.), 1625 (-C=N str.), 1569, 1498, 1467, 1434 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI^+) *m/z* Calcd for $[C_{12}H_{21}N_2]^+$: 193.1699 $(M\text{-}Br)^+$, Found: 193.1751; Elemental analysis Calcd for $C_{12}H_{21}BrN_2$: C 52.75, H 7.75, N 10.25, Found: C 52.91, H 7.85, N 10.47%.

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1-Nonylpyrimidin-1-ium bromide ***(2i)***. *Golden-b*rown semi solid; yield 62%; ^{1}H NMR (500 MHz, acetone-d_6 + CD_3OD; 4:1): δ 10.15 (s, 1 H, -NCHN^{+}-), 9.89 (m, 1 H, -$^{+}$N-CH=), 9.59 (m, 1 H, -N-CH=), 8.45 (m, 1 H, -CH-), 4.97 (br t, *J* = 7.5 Hz, 2 H, -$^{+}$N-CH_2-), 2.17-2.21 (m, 2 H, -CH_2-), 1.29-1.50 (m, 12 H, -CH_2-), 0.87 (br t, *J* = 7.5 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, acetone-d_6 + CD_3OD; 4:1): δ 165.6, 154.8, 153.4, 125.1 (pyrimidine ring), 59.9 (-$^{+}$N-CH_2-), 32.5, 31.8, 30.1, 29.9, 29.8, 26.8, 23.3 (-CH_2-), 14.3 (-CH_3) ppm; FTIR (KBr pellet): 3053, 3012 (aromatic -CH str.), 2961, 2926, 2855 (aliphatic -CH str.), 1622 (-C=N str.), 1571, 1495, 1462, 1434 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI^{+}) *m/z* Calcd for $[C_{13}H_{23}N_2]^{+}$: 207.1856 (M-Br)$^{+}$, Found: 207.1895; Elemental analysis Calcd for $C_{13}H_{23}BrN_2$: C 54.36, H 8.07, N 9.75, Found: C 54.49, H 8.27, N 9.91%.

1-Decylpyrimidin-1-ium bromide ***(2j)***. *Golden-b*rown semi solid; yield 63%; ^{1}H NMR (500 MHz, acetone-d_6 + CD_3OD; 4:1): δ 10.21 (s, 1 H, -NCHN^{+}-), 9.95 (m, 1 H, -$^{+}$N-CH-), 9.61 (m, 1 H, -N-CH-), 8.47 (m, 1 H, -CH-), 5.00 (t, *J* = 7.0 Hz, 2 H, -$^{+}$N-CH_2-), 2.18-2.20 (m, 2 H, -CH_2-), 1.29-1.50 (m, 14 H, -CH_2-), 0.88 (br t, *J* = 6.9 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, acetone-d_6 + CD_3OD; 4:1): δ 165.1, 154.4, 153.0, 124.6 (pyrimidine ring), 59.3 (-$^{+}$N-CH_2-), 32.1, 31.4, 29.8, 29.7, 29.6, 29.3, 26.3, 22.8 (-CH_2-), 13.9 (-CH_3) ppm; FTIR (KBr pellet): 3012 (aromatic -CH str.), 2956, 2921, 2855 (aliphatic -CH str.), 1622 (-C=N str.),1569, 1498, 1467, 1434 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI^{+}) m/z Calcd for $[C_{14}H_{25}N_2]^{+}$: 221.2012 (M-Br)$^{+}$, Found: 221.2065; Elemental analysis Calcd for $C_{14}H_{25}BrN_2$: C 55.81, H 8.36, N 9.30, Found: C 55.93, H 8.44, N 9.47%.

1-Methylpyrimidin-1-ium tetrafluoroborate ***(3a)***. Yellow solid; yield 71%; mp 110 °C; ^{1}H NMR (500 MHz, D_2O): δ 9.66 (s, 1 H, -NCHN^{+}-), 9.44 (m, 1 H, -$^{+}$N-CH-), 9.26 (m, 1 H, -N-CH-), 8.25 (m, 1 H, -CH-), 4.44 (s, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, D_2O): δ 164.3, 154.1, 152.9, 123.8 (pyrimidine ring), 45.4 (-$^{+}$NCH_3) ppm; FTIR (KBr pellet): 3068, 3027 (aromatic -CH str.), 2992, 2971 (aliphatic -CH str.), 1620 (-C=N str.), 1566, 1493, 1448 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI^{+}) *m/z* Calcd for $[C_5H_7N_2]^{+}$: 95.0604 (M-BF_4)$^{+}$, Found: 95.0631; Elemental analysis Calcd for C_5H_7 BF_4N_2: C 33.01, H 3.88, N 15.40, Found: C 33.19, H 4.02, N 15.62%.

1-Ethylpyrimidin-1-ium tetrafluoroborate ***(3b)***. Yellow viscous liquid; yield 74%; ^{1}H NMR (500 MHz, D_2O): δ 9.72 (s, 1 H, -NCHN^{+}-), 9.43 (m, 1 H, -$^{+}$N-CH-), 9.33 (br d, *J* = 5.0 Hz, 1 H, -N-CH-), 8.24 (m, 1 H, -CH-), 4.72 (br q, *J* = 7.1 Hz, 2 H, -$^{+}$N-CH_2-), 1.68 (br t, *J* = 7.2 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, D_2O): δ 164.5, 153.4, 151.8, 124.1 (pyrimidine ring), 55.0 (-$^{+}$N-CH_2-), 15.0 (-CH_3) ppm; FTIR (KBr pellet): 3051 (aromatic -CH str.), 2979 (aliphatic -CH str.), 1627 (-C=C str.), 1569, 1498, 1452, 1437 (-C=N str.) cm^{-1}; (Q-TOF) LC-MS (ESI^{+}) *m/z* Calcd for $[C_6H_9N_2]^{+}$: 109.0760 (M-BF_4)$^{+}$, Found:

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DOI: 10.1039/C6RA21865B

109.0751; Elemental analysis Calcd for $C_6H_9BF_4N_2$: C 36.78, H 4.63, N 14.30, Found: C 36.88, H 4.91, N 14.41%.

1-Propylpyrimidin-1-ium tetrafluoroborate ***(3c)***. Brownish viscous liquid; yield 76%; ^{1}H NMR (500 MHz, D_2O): δ 9.69 (s, 1 H, -NCHN$^+$-), 9.42 (m, 1 H, -$^+$N-CH-), 9.29 (br d, J = 5.1Hz, 1 H, -N-CH-), 8.22 (m, 1 H, -CH-), 4.61 (br t, J = 7.3 Hz, 2 H, -$^+$N-CH_2-), 2.04-2.08 (m, 2 H,-CH_2-), 0.99 (br t, J = 7.2 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, D_2O): δ 164.5, 153.5, 152.0, 124.1 (pyrimidine ring), 60.7 (-$^+$N-CH_2-), 23.8 (-CH_2-), 9.6 (-CH_3) ppm; FTIR (KBr pellet): 3084 (aromatic -CH str.), 2977, 2939, 2883 (aliphatic -CH str.), 1627 (-C=N str.),1571, 1498, 1464, 1440 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI$^+$) *m/z* Calcd for $[C_7H_{11}N_2]^+$: 123.0917 $(M\text{-}BF_4)^+$, Found: 123.0904; Elemental analysis Calcd for $C_7H_{11}BF_4N_2$: C 40.04, H 5.28, N 13.34, Found: C 40.24, H 5.41, N 13.51%.

1-Butylpyrimidin-1-ium tetrafluoroborate ***(3d)***. Brownish viscous liquid; yield 79%; ^{1}H NMR (500 MHz, D_2O): δ 9.71 (s, 1 H, -NCHN$^+$-), 9.44 (m, 1 H, -$^+$N-CH-) , 9.31 (br d, J = 5.0 Hz, 1 H, -N-CH-), 8.25 (m, 1 H, -CH-), 4.67 (br t, J = 7.2 Hz, 2 H,- $^+$N-CH_2-), 2.03-2.06 (m, 2 H, -CH_2-), 1.41-1.44 (m, 2 H, -CH_2-), 0.98 (t, J = 7.3 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, D_2O): δ 164.5, 153.5, 152.0, 124.2 (pyrimidine ring), 59.3 (-$^+$N-CH_2-), 32.2, 18.8 (-CH_2-), 12.6 (-CH_3) ppm; FTIR (KBr pellet): 3088 (aromatic -CH str.), 2971, 2936, 2880 (aliphatic -CH str.), 1622 (-C=N str.), 1566, 1500, 1470, 1439 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI$^+$) *m/z* Calcd for $[C_8H_{13}N_2]^+$: 137.1073 $(M\text{-}BF_4)^+$, Found: 137.1060; Elemental analysis Calcd for $C_8H_{13}BF_4N_2$: C 42.89, H 5.85, N 12.51, Found: C 43.08, H 6.05, N 12.67%.

1-Pentylpyrimidin-1-ium tetrafluoroborate ***(3e)***. Brownish semi-solid; yield 81%; ^{1}H NMR (500 MHz, acetone-d_6): δ 9.94 (s, 1 H, -NCHN$^+$-), 9.57 (m, 1 H, -$^+$N-CH-), 9.53 (m, 1H, -N-CH-), 8.39 (m, 1H, -CH-), 4.85 (br t, J = 7.2 Hz, 2 H, -$^+$N-CH_2-), 2.16-2.19 (m, 2H, -CH_2-), 1.40-1.47 (m, 4 H, -CH_2-), 0.91 (br t, J = 7.0 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, acetone-d_6): δ 165.7, 154.7, 153.1, 125.2 (pyrimidine ring), 60.1 (-$^+$N-CH_2-), 31.3, 28.8, 22.7 (-CH_2-), 14.1 (-CH_3) ppm; FTIR (KBr pellet): 3083 (aromatic -CH str.), 2961, 2936, 2875 (aliphatic -CH str.), 1625 (-C=N str.),1617, 1569, 1500, 1465, 1439 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI$^+$) *m/z* Calcd for $[C_9H_{15}N_2]^+$: 151.1230 $(M\text{-}BF_4)^+$, Found: 151.1217; Elemental analysis Calcd for $C_9H_{15}BF_4N_2$: C 45.41, H 6.35, N 11.77, Found: C 45.52, H 6.48, N 11.54%.

1-Hexylpyrimidin-1-ium tetrafluoroborate ***(3f)***. Brownish viscous liquid; yield 87 %; ^{1}H NMR (500 MHz, acetone-d_6): δ 9.91 (s, 1 H, -NCHN$^+$-), 9.55 (m, 1 H, -$^+$N-CH-), 9.50 (br d, J = 5.0 Hz, 1 H, -N-CH-), 8.37 (m, 1 H, -CH-), 4.83 (t, J = 6.9 Hz, 2 H, -$^+$N-CH_2-), 2.14-2.17 (m, 2 H, -CH_2-), 1.32-1.51 (m, 6 H, -CH_2-), 0.88 (br t, J = 7.0 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, acetone-d_6): δ 165.6, 154.6, 153.0,

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125.1(pyrimidine ring), 60.0 (-$^{+}$N-CH_2-), 31.7, 31.4, 26.3, 22.9 (-CH_2-), 14.1 (-CH_3) ppm; FTIR (KBr pellet): 3088 (aromatic -CH str.), 2961, 2931, 2860 (aliphatic -CH str.), 1627 (-C=N str.),1569, 1500, 1470, 1457, 1439(-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI^+) *m/z* Calcd for $[C_{10}H_{17}N_2]^+$: 165.1386 (M-BF_4)$^+$, Found: 165.1358; Elemental analysis Calcd for $C_{10}H_{17}BF_4N_2$: C 47.65, H 6.80, N 11.11, Found: C 47.76, H 7.04, N 11.21%.

1-Heptylpyrimidin-1-ium tetrafluoroborate ***(3g).*** Brownish viscous liquid; yield 89%; ^{1}H NMR (500 MHz, acetone-d_6): δ 9.97 (s, 1 H, -NCHN$^+$-), 9.56 (m, 2 H, -$^+$N-CH- and -N-CH-), 8.41 (m, 1 H, -CH-), 4.87 (t, *J* = 6.9 Hz, 2 H, -$^+$N-CH_2-), 2.17-2.20 (m, 2 H, -CH_2-), 1.30-1.51 (m, 8 H, -CH_2-), 0.87 (br t, *J* = 7.0 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, acetone-d_6): δ 165.7, 154.7, 153.1, 125.2 (pyrimidine ring), 60.1 (-$^+$N-CH_2-), 32.2, 31.6, 29.4, 26.7, 23.1 (-CH_2-), 14.3 (-CH_3) ppm; FTIR (KBr pellet): 3088 (aromatic -CH str.), 2961, 2926, 2865 (aliphatic -CH str.), 1625 (-C=N str.), 1571, 1498, 1470, 1455, 1442 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI^+) *m/z* Calcd for $[C_{11}H_{19}N_2]^+$: 179.1543 (M-BF_4)$^+$, Found: 179.1517; Elemental analysis Calcd for $C_{11}H_{19}BF_4N_2$: C 49.65, H 7.20, N 10.53, Found: C 49.79, H 7.37, N 10.69%.

1-Octylpyrimidin-1-ium tetrafluoroborate ***(3h).*** Brownish viscous liquid; yield 90%; ^{1}H NMR (500 MHz, acetone-d_6): δ 9.90 (s, 1 H, -NCHN$^+$-), 9.54 (m, 1 H, -$^+$N-CH-), 9.49 (m, 1 H, -N-CH-), 8.36 (m, 1 H, -CH-), 4.82 (br t, *J* = 7.1 Hz, 2 H, -$^+$N-CH_2-), 2.15-2.17 (m, 2 H, -CH-), 1.28-1.49 (m, 10 H, -CH_2-), 0.87 (br t, *J* = 7.0 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, acetone-d_6): δ 165.5, 154.5, 152.9, 125.0 (pyrimidine ring), 60.0 (-$^+$N-CH_2-), 32.3, 31.5, 29.6, 29.5, 26.6, 23.1 (-CH_2-), 14.2 (-CH_3) ppm; FTIR (KBr pellet): 3088 (aromatic -CH str.), 2961, 2931, 2860 (aliphatic -CH str.), 1625 (-C=N str.), 1569, 1500, 1467, 1442 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI^+) *m/z* Calcd for $[C_{12}H_{21}N_2]^+$: 193.1699 (M-BF_4)$^+$, Found: 193.1751; Elemental analysis Calcd for $C_{12}H_{21}BF_4N_2$: C 51.45, H 7.56, N 10.00, Found: C 51.61, H 7.74, N 10.12%.

1-Nonylpyrimidin-1-ium tetrafluoroborate ***(3i)***. Brownish semi-solid; yield 92%; ^{1}H NMR (500 MHz, acetone-d_6): δ 9.96 (s, 1 H, -NCHN$^+$-), 9.55-9.57 (m, 2 H, -$^+$N-CH- and -N-CH-), 8.40 (m, 1 H, -CH-), 4.86 (t, *J* = 7.5 Hz, 2 H, -$^+$N-CH_2-) , 2.17-2.19 (m, 2 H, -CH_2-), 1.27-1.51 (m, 12 H, -CH_2-), 0.87 (br t, *J* = 7.3 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, acetone-d_6): δ 165.7, 154.7, 153.1, 125.2 (pyrimidine ring), 60.1 (-$^+$N-CH_2-), 32.5, 31.6, 30.0, 29.8, 29.7, 26.7, 23.3 (-CH_2-), 14.3 (-CH_3) ppm; FTIR (KBr pellet): 3098 (aromatic -CH str.), 2961, 2931, 2860 (aliphatic -CH str.), 1630 (-C=N str.), 1566, 1516, 1500, 1472, 1457, 1442 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI^+) *m/z* Calcd for $[C_{13}H_{23}N_2]^+$:207.1856 (M-

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DOI: 10.1039/C6RA21865B

$BF_4)^+$, Found: 207.1895; Elemental analysis Calcd for $C_{13}H_{23}BF_4N_2$: C 53.08, H 7.88, N 9.52, Found: C 53.23, H 8.03, N 9.71%.

1-Decylpyrimidin-1-ium tetrafluoroborate ***(3j).*** Brownish semi-solid; yield 94%; ^{1}H NMR (500 MHz, acetone-d_6): δ 9.96 (s, 1 H, -NCHN$^+$-), 9.57 (m, 1 H, -$^+$N-CH-), 9.55 (m, 1 H, -N-CH-), 8.40 (m, 1 H, -CH-), 4.86 (t, J = 7.5 Hz, 2 H, -$^+$N-CH_2-), 2.16-2.20 (m, 2 H, -CH_2-), 1.28-1.50 (m, 14 H, -CH_2-), 0.88 (br t, J = 7.3 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, acetone-d_6): δ 165.7, 154.7, 153.1, 125.2 (pyrimidine ring), 60.1 (-$^+$N-CH_2-), 32.6, 31.6, 30.1, 30.0, 29.7, 29.5, 26.7, 23.3 (-CH_2-), 14.3 (-CH_3) ppm; FTIR (KBr pellet): 3093 (aromatic -CH str.), 2961, 2931, 2860 (aliphatic -CH str.), 1620 (-C=N str.), 1566, 1500, 1470, 1457, 1439 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI$^+$) *m/z* Calcd for $[C_{14}H_{25}N_2]^+$: 221.2012 (M-$BF_4)^+$, Found: 221.2065; Elemental analysis Calcd for $C_{14}H_{25}BF_4N_2$: C 54.56, H 8.18, N 9.09, Found: C 54.77, H 8.28, N 9.31%.

1-Methylpyrimidin-1-ium bis(trifluoromethanesulfonyl)amide ***(4a).*** Yellow solid; yield 84%; mp 89 °C; ^{1}H NMR (500 MHz, acetone-d_6): δ 9.90 (s, 1 H, -NCHN$^+$-), 9.57 (m, 1 H, -$^+$N-CH-), 9.50 (br d, J = 5.0 Hz, 1 H, -N-CH-), 8.40 (m, 1 H, -CH-), 4.62 (s, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, acetone-d_6): δ 165.4, 155.3, 154.0, 124.6 (pyrimidine ring), 120.9 (q, J_{CF} = 321.1 Hz, $N(SO_2CF_3)_2$), 46.3 (-$^+$N-CH_3) ppm; FTIR (KBr pellet): 3087 (aromatic -CH str.), 2987 (aliphatic -CH str.),1633 (-C=N str.), 1573,1497, 1457, 1418 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI$^+$) *m/z* Calcd for $[C_5H_7N_2]^+$: 95.0604 $(M\text{-}NTf_2)^+$, Found: 95.0631; Elemental analysis Calcd for $C_7H_7F_6N_3O_4S_2$: C 22.40, H 1.88, N 11.20, Found: C 22.50, H 1.92, N 11.33%.

1-Ethylpyrimidin-1-ium bis(trifluoromethanesulfonyl) amide ***(4b)****.* Yellow solid; yield 86%; mp 81 °C; ^{1}H NMR (500 MHz, acetone-d_6): δ 10.01 (s, 1 H, -NCHN$^+$-), 9.61 (m, 2 H, -$^+$N-CH- and -N-CH-), 8.45 (m, 1 H, -CH-), 4.97 (br q, J = 6.8 Hz, 2 H, -$^+$N-CH_2-), 1.81 (br t, J = 7.0 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, acetone-d_6): δ 165.8, 154.8, 152.8, 125.1 (pyrimidine ring), 121.0 (q, J_{CF} = 321.2 Hz, $N(SO_2CF_3)_2$), 55.8 (-$^+$N-CH_2-), 16.1 (-CH_3) ppm; FTIR (KBr pellet): 3087 (aromatic -CH str.), 2996 (aliphatic -CH str.), 1627 (-C=N str.), 1570, 1497, 1454, 1439 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI$^+$) *m/z* Calcd for $[C_6H_9N_2]^+$: 109.0760 $(M\text{-}NTf_2)^+$, Found: 109.0751; Elemental analysis Calcd for $C_8H_9F_6N_3O_4S_2$: C 24.68, H 2.33, N 10.79, Found: C 24.71, H 2.46, N 10.81%.

1-Propylpyrimidin-1-ium bis(trifluoromethanesulfonyl) amide ***(4c).*** Brownish thick viscous liquid: yield 70%; ^{1}H NMR (500 MHz, acetone-d_6): δ 9.93 (s, 1 H, -NCHN$^+$-), 9.58 (m, 1 H, -$^+$N-CH-), 9.53 (m, 1 H, -N-CH-), 8.39 (m, 1 H, -CH-), 4.82 (br t, J = 7.2 Hz, 2 H, -$^+$N-CH_2-), 2.20-2.23 (m, 2 H, -CH_2-), 1.07 (br t,

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J = 7.2 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, acetone-d_6): δ 165.7, 154.5, 152.8, 125.0 (pyrimidine ring), 120.8 (q, J_{CF} = 321.0 Hz, $N(SO_2CF_3)_2$), 61.4 (-$^+$N-CH_2-), 24.9 (-CH_2-), 10.5 (-CH_3) ppm; FTIR (KBr pellet) :3078 (aromatic -CH str.), 2980, 2945, 2889 (aliphatic -CH str.), 1619 (-C=N str.), 1459 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI$^+$) *m/z* Calcd for $[C_7H_{11}N_2]^+$: 123.0917 $(M\text{-}NTf_2)^+$, Found: 123.0904; Elemental analysis Calcd for $C_9H_{11}F_6N_3O_4S_2$: C 26.80, H 2.75, N 10.42, Found: C 26.99, H 2.91, N 10.39%.

All spectroscopic data were in close agreement with the reported ones.[13]

1-Butylpyrimidin-1-ium bis(trifluoromethanesulfonyl) amide ***(4d).*** yellowish viscous liquid; yield 87%; ^{1}H NMR (500 MHz, acetone-d_6): δ 9.99 (s, 1 H, -NCHN$^+$-), 9.58-9.61 (m, 2 H, -$^+$N-CH- and -N-CH-), 8.44 (m, 1 H, -CH-), 4.89 (t, J = 7.5 Hz, 2 H, -$^+$N-CH_2-), 2.16-2.20 (m, 2 H, -CH_2-), 1.50-1.54 (m, 2 H, -CH_2-), 0.99 (t, J = 7.0 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, acetone-d_6): δ 165.8, 154.7, 153.0, 125.2 (pyrimidine ring), 120.9 (q, J_{CF} = 321.2 Hz, $N(SO_2CF_3)_2$), 60.0 (-$^+$N-CH_2-), 33.5, 20.0 (-CH_2-), 13.6 (-CH_3) ppm; FTIR (KBr pellet): 3081 (aromatic -CH str.), 2969, 2945, 2882 (aliphatic -CH str.), 1626 (-C=N str.),1570, 1496, 1468, 1440 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI$^+$) *m/z* Calcd for $[C_8H_{13}N_2]^+$: 137.1073 $(M\text{-}NTf_2)^+$, Found: 137.1060; Elemental analysis Calcd for $C_{10}H_{13}F_6N_3O_4S_2$: C 28.78, H 3.14, N 10.07, Found: C 28.69, H 3.04, N 10.27%.

1-Pentylpyrimidin-1-ium bis(trifluoromethanesulfonyl) amide ***(4e).*** Brownish viscous liquid; yield 90%; ^{1}H NMR (500 MHz, acetone-d_6): δ 9.97 (s, 1 H, -NCHN$^+$-), 9.58-9.59 (m, 2 H, -$^+$N-CH- and -N-CH-), 8.41 (m, 1 H, -CH-), 4.87 (br t, J = 7.5 Hz, 2 H, -$^+$N-CH_2-), 2.18-2.21 (m, 2 H, -CH_2-), 1.41-1.48 (m, 4 H, -CH_2-), 0.91 (br t, J = 7.2 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, acetone-d_6): δ 165.8, 154.7, 152.9, 125.1 (pyrimidine ring), 120.9 (q, J = 321.1Hz, $N(SO_2CF_3)_2$), 60.2 (-$^+$N-CH_2-), 31.3, 28.8, 22.7 (-CH_2-), 13.9 (-CH_3) ppm; FTIR (KBr pellet): 3081 (aromatic -CH str.), 2966, 2939, 2878 (aliphatic -CH str.), 1624 (-C=N str.), 1570, 1497, 1473, 1442 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI$^+$) *m/z* Calcd for $[C_9H_{15}N_2]^+$: 151.1230 $(M\text{-}NTf_2)^+$, Found: 151.1217; Elemental analysis Calcd for $C_{11}H_{15}F_6N_3O_4S_2$: C 30.63, H 3.50, N 9.74, Found: C 30.77, H 3.71, N 9.81%.

Hexylpyrimidin-1-ium bis(trifluoromethanesulfonyl)amide ***(4f)***. Brownish viscous liquid; yield 91%; ^{1}H NMR (500 MHz, acetone-d_6): δ 9.98 (s, 1 H, -NCHN$^+$-), 9.57-9.60 (m, 2 H, -$^+$N-CH- and -N-CH-), 8.43 (m, 1 H, -CH-), 4.88 (br t, J = 7.4 Hz, 2 H, -$^+$N-CH_2-), 2.18-2.21 (m, 2 H, -CH_2-), 1.49-1.51 (m, 2 H, -CH_2-), 1.34-1.37 (m, 4 H, -CH_2-), 0.88 (br t, J = 7.3, 3H, -CH_3) ppm; ^{13}C NMR (500 MHz, acetone-d_6): δ 165.8, 154.7, 153.0, 125.1(pyrimidine ring), 120.9 (q, J_{CF} = 321.3 Hz, $N(SO_2CF_3)_2$), 60.2 (-$^+$N-CH_2-), 31.8, 31.5, 26.4, 22.9 (-CH_2-), 14.1 (-CH_3) ppm; FTIR (KBr pellet): 3080 (aromatic -CH str.), 2964, 2937,

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2865 (aliphatic -CH str.), 1626 (-C=N str.), 1566, 1495, 1471, 1439 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI^+) *m/z* Calcd for $[C_{10}H_{17}N_2]^+$: 165.1386 $(M\text{-}NTf_2)^+$, Found: 165.1358 ; Elemental analysis Calcd $C_{12}H_{17}F_6N_3O_4S_2$: C 32.36, H 3.85, N 9.43, Found: C 32.22, H 3.77, N 9.49%.

1-Heptylpyrimidin-1-ium bis(trifluoromethanesulfonyl) amide ***(4g).*** Brownish viscous liquid; yield 91%; ^1H NMR (500 MHz, acetone-d_6): δ 10.01 (s, 1 H, -NCHN$^+$-), 9.61 (m, 2 H, -$^+$N-CH- and -N-CH-), 8.46 (m, 1 H, -CH-), 4.91 (br t, *J* = 7.1 Hz, 2 H, -$^+$N-CH_2-), 2.19-2.22 (m, 2 H, -CH_2-), 1.29-1.50 (m, 8 H, -CH_2-), 0.87 (br t, *J* = 7.0 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, acetone-d_6): δ 165.8, 154.8, 153.0, 125.2 (pyrimidine ring), 121.0 (q, J_{CF} = 321.3 Hz, $N(SO_2CF_3)_2$), 60.2 (-$^+$N-CH_2-), 32.2, 31.6, 26.7, 23.1, 18.8 (-CH_2-), 14.2 (-CH_3) ppm; FTIR (KBr pellet): 3077 (aromatic -CH str.), 2961, 2934, 2863 (aliphatic -CH str.), 1623 (-C=N str.), 1566, 1498, 1471, 1439 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI^+) *m/z* Calcd for $[C_{11}H_{19}N_2]^+$: 179.1543 $(M\text{-}NTf_2)^+$, Found: 179.1517; Elemental analysis Calcd for $C_{13}H_{19}F_6N_3O_4S_2$: C 33.99, H 4.17, N 9.15, Found: C 34.19, H 4.34, N 8.95%.

1-Octylpyrimidin-1-ium bis(trifluoromethanesulfonyl) amide ***(4h)***. Brownish viscous liquid; yield 93%; ^1H NMR (500 MHz, acetone-d_6): δ 9.99 (s, 1 H, -NCHN$^+$-), 9.59-9.61 (m, 2 H, -$^+$N-CH- and -N-CH-), 8.44 (m, 1 H, -CH-), 4.89 (br t, *J* = 7.1 Hz, 2H, -$^+$N-CH_2-), 2.18-2.22 (m, 2 H, -CH_2-), 1.28-1.50 (m, 10 H, -CH_2-), 0.86 (br t, *J* = 7.1 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, acetone-d_6): δ 165.8, 154.7, 153.0, 125.1 (pyrimidine ring), 120.9 (q, J_{CF} = 321.2 Hz, $N(SO_2CF_3)_2$), 60.2 (-$^+$N-CH_2-), 32.3, 31.6, 29.7, 29.6, 26.7, 23.2 (-CH_2-), 14.3 (-CH_3) ppm; FTIR (KBr pellet): 3080 (aromatic -CH str.), 2931, 2863 (aliphatic -CH str.), 1623(-C=N str.), 1569, 1495, 1468 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI^+) *m/z* Calcd for $[C_{12}H_{21}N_2]^+$: 193.1699 $(M\text{-}NTf_2)^+$, Found: 193.1751; Elemental analysis Calcd for $C_{14}H_{21}F_6N_3O_4S_2$: C 35.52, H 4.47, N 8.88, Found: C 35.69, H 4.59, N 8.66%.

1-Nonylpyrimidin-1-ium bis(trifluoromethanesulfonyl) amide ***(4i).*** Brownish viscous liquid; yield 94%; ^1H NMR (500 MHz, acetone-d_6): δ 10.02 (s, 1 H, -NCHN$^+$-), 9.62 (m, 2 H, -$^+$N-CH- and -N-CH-), 8.47 (m, 1H, -CH-), 4.91 (br t, *J* = 7.1 Hz, 2 H, -$^+$N-CH_2-), 2.20-2.23 (m, 2 H, -CH_2), 1.29-1.50 (m, 12 H, -CH_2-), 0.87 (br t, *J* = 7.1 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, acetone-d_6): δ 165.8, 154.8, 153.0, 125.2 (pyrimidine ring), 121.0 (q, J_{CF} = 321.3 Hz, $N(SO_2CF_3)_2$), 60.2 (-$^+$N-CH_2-), 32.5, 31.7, 30.1, 30.0, 29.7, 26.8, 23.3 (-CH_2-), 14.3 (-CH_3) ppm; FTIR (KBr pellet): 3080 (aromatic -CH str.), 2931, 2860 (aliphatic -CH str.), 1623 (-C=N str.), 1566, 1495, 1468, 1442 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI^+) *m/z* Calcd for $[C_{13}H_{23}N_2]^+$: 207.1856 $(M\text{-}NTf_2)^+$, Found: 207.1895; Elemental analysis Calcd for $C_{15}H_{23}F_6N_3O_4S_2$: C 36.96, H 4.76, N 8.62, Found: C 36.81, H 4.59, N 8.69%.

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1-Decylpyrimidin-1-ium bis(trifluoromethanesulfonyl) amide ***(4j).*** Brownish viscous liquid; yield 95%; ^{1}H NMR (500 MHz, acetone-d_6): 10.01 (s, 1 H, -NCHN$^+$-), 9.60-9.62 (m, 2 H, -$^+$N-CH- and -N-CH-), 8.45 (m, 1 H, -CH-), 4.90 (br t, J = 7.2 Hz, 2 H, -$^+$N-CH_2-), 2.19-2.22 (m, 2 H, -CH_2-), 1.22-1.50 (m, 14H, -CH_2-), 0.87 (br t, J = 7.1 Hz, 3 H, -CH_3) ppm; ^{13}C NMR (500 MHz, acetone-d_6): δ 165.8, 154.8, 153.0, 125.2 (pyrimidine ring), 121.0 (q, J_{CF} = 321.3 Hz, $N(SO_2CF_3)_2$), 60.2 (-$^+$N-CH_2-), 32.5, 31.6, 30.0, 29.9, 29.5, 26.7, 23.3 (-CH_2-), 14.3 (-CH_3) ppm; FTIR (KBr pellet): 3080 (aromatic -CH str.), 2931, 2860 (aliphatic -CH str.), 1626 (-C=N str.),1566, 1498, 1468, 1439 (-C=C str.) cm^{-1}; (Q-TOF) LC-MS (ESI$^+$) *m/z* Calcd for $[C_{14}H_{25}N_2]^+$: 221.2012 $(M\text{-}NTf_2)^+$, Found: 221.2065; Elemental analysis Calcd for $C_{16}H_{25}F_6N_3O_4S_2$: C 38.32, H 5.02, N 8.38, Found: C 38.12, H 4.98, N 8.51%.

1-(Benzyloxy)-4-vinylbenzene ***(5)****. White solid;* ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30-7.48 (m, 7 H, Ar ring), 6.94 (d, J = 7.7 Hz, 2 H, Ar ring), 6.66 (dd, J = 17.3, 11.0 Hz, 1 H, -CH=CH_2), 5.61 (d, J = 17.5 Hz, 1 H, -CH_2=CH-), 5.13 (d, J = 10.8 Hz, 1 H, -CH_2=CH-), 5.07 (s, 2 H, -O-CH_2-Ar ring) ppm.

1-(Benzyloxy)-4-styrylbenzene ***(7).*** *White solid;* ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38-7.47 (m, 12 H, Ar ring), 6.95-6.97 (m, 2 H, Ar ring), 6.75 (d, J = 7.4 Hz, 1 H, -CH=CH-), 5.09 (d, J = 7.5 Hz, 1H, -CH=CH-), 5.01 (s, 2 H, -O-CH_2-Ar) ppm.

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra of all the synthesized ionic liquid are available free of charge via the Internet at http://rsc.org

ACKNOWLEDGEMENTS

KG is grateful for the financial support from University Grant Commission and thankful to Central University of Gujarat, Gandhinagar-382030 for instrumentation and infrastructural facilities. The authors are also very much thankful to Mr. Akash Sabarwal, School of Life Sciences, CUG for his kind support to assess the cytotoxicity of the synthesized ionic liquids.

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