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Basic Task-specific Ionic Liquid as Catalyst and Reaction Medium: A Green Protocol for the Synthesis of 4-Oxo-6-aryl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile Derivatives

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A novel basic ionic liquid, based on imidazolium cation, is designed, synthesized and successfully used as a catalyst for the one-pot synthesis of 4-oxo-6-aryl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile derivatives. The remarkable features of this new catalyst are its ethyleneoxy bridge which participates in dissolving organic compound in the ionic liquid and its strong base counterion. The application of this ionic liquid is studied in a new one-pot method for the synthesis of heterocyclic compounds under solvent-free conditions. A simple and convenient procedure, high conversion, reusability of catalyst, easy purification and shorter reaction time are the advantageous features of this method.

Keywords: Ionic liquid, Imidazolium cation, Pyrimidine, Reusable catalyst, Ethyleneoxy bridge

INTRODUCTION

Ionic liquids have attracted extensive research interest in the area of green chemistry [1-3]. Their use as solvents for organic synthesis has been widely explored [4]. Recently, basic ionic liquids (BILs) were reported to be used as green catalysts and are being of interest in numerous synthetic studies due to the combination of the advantages of inorganic bases, stability in water and air, easy separation, and reusability [5]. Bronsted basic ionic liquids often involve organic salts with OH^- anion. Most research on Bronsted basic ionic liquids is related to OH (1-butyl-3-methylimidazolium hydroxide) that has been used as a strong base in the condensation reaction [6-9] and synthesis of organic compounds [10-13]. These strong BILs exhibit great potential for the replacement of conventional basic catalysts because they are flexible, nonvolatile, noncorrosive, and immiscible with many organic solvents [14,15]. In order to increase the basic strength, ionic liquid containing two OH groups has also been reported [16]. In recent year, dicationic ILs would be interesting research targets due to their high thermal stability, broad liquid range, and biological activities such as antiviral, antifungal and anticancer activities. In particular, imidazolium based dicationic ILs showing high thermal stability were used as effective reaction media for high temperature organic reactions [17-20]. In continuation of our previous works about novel ionic liquids, as catalyst and solvent [21,22], we became interested in the synthesis of a novel basic dicationic ionic liquid and application of this novel catalyst as a new and efficient method for the synthesis of 4-oxo-6-aryl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile derivatives in the presence of catalytic amount of this novel basic ionic liquid under solvent-free conditions. Also, many pyrimidine-5-carbonitrile derivatives proved to exhibit potent anticancer [23,24] as well as antimicrobial [25,26] and antiplasmodial activities [27]. Several methods have been reported for the synthesis of 4-oxo-6-aryl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile derivatives in the presence of a catalyst such as K_2CO_3 [28,29], KOH [30],

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and pipyridine [31] in ethanol. In designing this novel ionic liquid, we used 1,2-bis(2-chloroethoxy)ethane as a linker between imidazolium rings that participates in dissolving organic compound in ionic liquid. We believe that this novel basic ionic liquid can be applied as a catalyst in many different organic transformations.

EXPERIMENTAL

Materials and Instrumentation

All reagents were purchased from Merck Company and used without further purification. The melting points of products were determined with an electro thermal type 9100 melting point apparatus. The FT-IR spectra were recorded on an Avatar 370 FT-IR Therma Nicolet spectrometer. The mass spectra were recorded on a 5973 Network Mass Selective Detector. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-400 Avance spectrometers at 400 MHz, using DMSO-d_6 or $CDCl_3$ as the deuterated solvents. Chemical shifts are reported in ppm downfield from TMS as internal standard; coupling constants *J* are given in Hertz.

Synthesis of 1,2-bis(2-(1*H*-imidazol-1-yl)ethoxy) ethane (1). A mixture of imidazole (32 mmol, 2.176 g) and potassium hydroxide (32 mmol, 1.792 g) in DMSO (25 ml) was stirred at 70 °C for one hour. Then, 1,2-bis(2-chloroethoxy)ethane (16 mmol, 2.48 ml) was added to the reaction mixture and stirred for 24 h. The resulting mixture was poured into 100 ml of water and extracted with methylene chloride (5 × 20 ml). The combined organic layer was washed with water (3 × 20 ml), dried with anhydrous Na_2SO_4, and concentrated to give 1,2-bis(2-(1H-imidazol-1-yl)ethoxy)ethane (1) as a pale yellow viscous oil, 3.10 g, 77% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.45 (s, 4H), 3.59 (t, 4H, *J* = 4.8 Hz), 4.01 (t, 4H, *J* = 4.8 Hz), 6.90 (t, 2H, *J* = 1.2 Hz), 6.94 (t, 2H, *J* = 1.2 Hz), 7.45 (s, 2H). ^{13}C NMR ($CDCl_3$, 400 MHz) δ: 46.9, 70.3, 70.4, 119.4, 128.9, 137.5. IR (KBr, cm^{-1}): 1642, 1525, 1425. m/z, calcd. for $C_{12}H_{18}N_4O_2[M]^+$: 250.30, found: 250.0.

Synthesis of 1,1'- ((ethane-1,2-diylbis(oxy) bis (ethane-2,1-diyl))bis (3-propyl-1*H*-imidazol-3-ium) bromide (2). A 25 ml round-bottomed flask was charged with 1,2-bis(2-(1*H*-imidazol-1-yl)ethoxy)ethane (1) (12.4 mmol, 3.1 g) and 1-bromopropane (24.8 mmol, 3.05 g) without any solvent was stirred at 70 °C for 24 h. After this time, the reaction mixture was cooled to room temperature, the residue was washed with dry CH_2Cl_2 (3 × 20 ml) and dried under vacuum to give 1,1'-((ethane-1,2-diylbis(oxy)) bis(ethane-2,1-diyl))bis(3-propyl-1H-imidazol-3-ium) bromide (2) as a viscous yellowish oil, 2.37 g, 96.3%.yield. ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 0.809 (t, 6H, *J* = 7.2 Hz), 1.74-1.89 (m, 4H), 3.52 (s, 4H), 3.76 (t, 4H, *J* = 4.8 Hz), 4.207 (t, 4H, *J* = 6.8 Hz), 4.38 (t, 4H, *J* = 4.8 Hz), 7.84 (d, 2H, *J* = 1.2 Hz), 7.90 (s, 2H), 9.39 (s, 2H). ^{13}C NMR (DMSO-d_6, 400 MHz) δ: 10.8, 23.4, 49.2, 50.6, 68.5, 69.8, 122.7, 123.2, 136.7. IR (KBr, cm^{-1}): 3137, 3075, 2965, 2876, 1630, 1563, 1456, 1167, 1113, 768, 643. m/z, calcd. for $C_{18}H_{32}Br_2N_4O_2$ $[M]^+$: 496.2, found: 495.8.

Synthesis of 1,1'-((ethane-1,2-diylbis(oxy))bis(ethane-2,1-diyl))bis(3-propyl-1*H*-imidazol-3-ium) hydroxide (3). A mixture of 1,1'-((ethane-1,2-diylbis(oxy))bis(ethane-2,1-diyl))bis(3-propyl-1H-imidazol-3-ium) bromide (2) (10 mmol, 5.0 g) and potassium hydroxide (20 mmol, 1.12 g) in DMSO (5 ml) was stirred at room temperature for 24 h. Then, the reaction mixture was filtered and the residue was washed with dry ethylacetate (3 × 20 ml) and dried under vacuum to give 1,1'-((ethane-1,2-diylbis(oxy))bis(ethane-2,1-diyl))bis(3-propyl-1*H*-imidazol-3-ium) hydroxide (3) as a viscous yellowish oil. ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 0.80 (t, 6H, *J* = 7.0 Hz), 1.70-1.88 (m, 4H), 3.50 (s, 4H), 3.74 (t, 4H, *J* = 4.6 Hz), 4.20 (t, 4H, *J* = 6.8 Hz), 4.40 (t, 4H, *J* = 4.6 Hz), 7.82 (d, 2H, *J* = 1.2 Hz), 7.92 (s, 2H), 9.45 (s, 2H). ^{13}C NMR (DMSO-d_6, 400 MHz) δ: 10.7, 24.4, 48.1, 52.2, 68.0, 69.5, 121.8, 122.9, 136.3, IR (KBr, cm^{-1}): 3502, 3427, 2965, 2915, 2875, 1662, 1568, 1436, 1405, 1115, 1023, 953, 705.

General Procedure for Preparation of 4-Oxo-6-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile Derivatives

A mixture of ethylcyano acetate (2 mmol), thiourea (2 mmol), an appropriate amount of aldehyde (2 mmol) and ionic liquid (1 mmol) was stirred at 100 °C for 4-10 h. The progress of the reaction was monitored by TLC. When the reaction was completed, the mixture was cooled to room temperature, and water (30 ml) was added to the mixture. The resulting solid product was filtered and washed with water. The crude product was purified by recrystallization

from ethyl acetate and n-hexane or ethanol.

Selected Spectroscopic Data

4-Oxo-6-phenyl-2-thioxo-1,2,3,4-tetrahydro-pyrimidine-5-carbonitrile (4a). m.p.: 259 °C. ^{1}H-NMR (DMSO-d6, 400 MHz) δ: 7.20-7.35 (m, 5H, Ar-H), 13.05 (b, 2H, NH, SH). ^{13}C NMR (DMSO-d6, 100 MHz) δ: 92.5, 114.2, 127.1, 129.2, 130.5, 137.1, 159.2, 160.4, 174.2. .IR (KBr, cm^{-1}): 3166, 3080, 2929, 2239, 1699, 1576, 1224, 1147, 757.

4-Oxo-2-thioxo-6-(*p*-tolyl)-1,2,3,4-tetrahydro-pyrimidine-5-carbonitrile (4b). m.p.: 248 °C. ^{1}H NMR (DMSO-d6, 400 MHz) δ: 2.34 (s, 3H, CH3), 7.40-7.54 (m, 4H, Ar-H), 13.10 (b, 2H, NH, SH). ^{13}C NMR (DMSO-d6, 100 MHz) δ: 21.9, 90.5, 115.2, 127.8, 129.4, 129.9, 138.0, 159.5, 161.2, 176.1. .IR (KBr, cm^{-1}): 3129, 3056, 2946, 2872, 2229, 1679, 1555, 1457, 1222, 1148, 821. m/z, calcd. for $C_{12}H_9N_3OS$ [M]$^+$: 243.05, found: 243.0.

4-Oxo-2-thioxo-6-(*m*-tolyl)-1,2,3,4-tetrahydro-pyrimidine-5-carbonitrile (4c). m.p.: 249 °C, ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.38 (s, 3H, CH3), 7.45-7.50 (m, 4H, Ar-H), 13.14 (b, 2H, NH, SH). ^{13}C NMR (DMSO-d6, 100 MHz) δ: 21.3, 90.9, 115.2, 126.3, 128.8, 129.5, 129.7, 133.2, 138.3, 159.0, 161.4, 176.7. IR (KBr, cm^{-1}): 3176, 3092, 2921, 2230, 1678, 1547, 1442, 1224, 1205, 1133, 704. m/z, calcd. for $C_{12}H_9N_3OS$ [M]$^+$: 243.05, found: 243.0.

6-(4-Isopropylphenyl)-4-oxo-2-thioxo-1,2,3,4-tetra-hydropyrimidine-5-carbonitrile (4d). m.p.: 279 °C, ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.20 (d, 6H, J= 6.5, CH_3), 2.80-2.90 (m, 2H, CH), 7.20-7.24 (m, 2H, Ar-H), 7.30-7.34 (m, 2H, Ar-H), 13.11 (bs, 2H, OH, SH). ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 23.1, 33.8, 91.0, 111.6, 114.8, 115.7, 132.5, 150.8, 157.5, 159.1, 175.8 IR (KBr, cm^{-1}): 3129, 2959, 2864, 2230, 1679, 1569, 1459, 1222, 1147, 836. m/z, calcd. for $C_{14}H_{13}N_3OS$ [M]$^+$: 271.08, found: 271.0.

6-(3-Methoxyphenyl)-4-oxo-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile (4e). m.p.: 239 °C, ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.83 (s, 3H, CH_3), 7.18-7.21 (m, 1H, Ar-H), 7.23-7.25 (m, 2H, Ar-H), 7.48 (t, 1H, *J* = 8, Ar-H), 13.16 (bs, 2H, OH, SH). ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 55.9, 91.1, 114.4, 115.1, 118.4, 121.3, 130.2, 130.9, 158.9, 159.2, 161.1, 176.6. IR (KBr, cm^{-1}): 3558, 3382, 3158, 2933, 2230, 1698, 1538, 1445, 1221, 1139, 775. m/z, calcd. for C12H9N3O2S [M]$^+$: 259.04, found: 259.0.

6-(4-(Dimethylamino)phenyl)-4-oxo-2-thioxo-1,2,3,4-tetrahydropyrimidine-carbonitrile (4f). m.p.: 285 °C. ^{1}H NMR (CD_3COCD_3, 400 MHz) δ: 3.02 (s, 6H, CH_3), 6.80 (d, 2H, *J* = 9.0, Ar-H), 7.65 (d, 2H, *J* = 9.0, Ar-H), 11.50 (s, 1H, NH), 11.80 (s, 1H, NH). ^{13}C NMR (CD_3COCD_3, 100 MHz) δ: 41.2, 89.0, 110.6, 112.8, 115.4, 132.5, 150.2, 159.5, 160.6, 174.9. IR (KBr, cm^{-1}): 2926, 2214, 1663, 1566, 1523, 1386, 1292, 1190, 1171, 814.

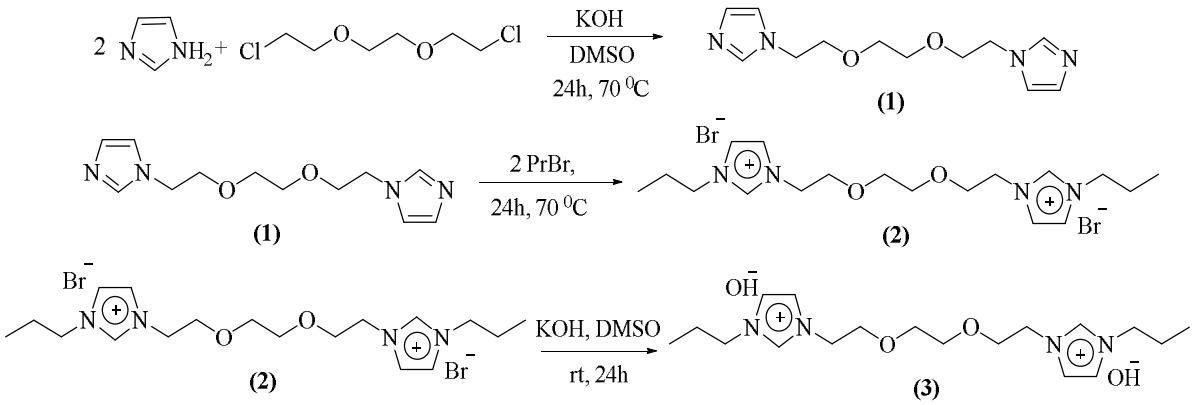
6-(4-(Diethylamino)phenyl)-4-oxo-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile (4g). m.p.: 255 °C. ^{1}H NMR (CD_3COCD_3, 400 MHz) δ: 1.23 (t, 6H, *J* = 7.2, CH_3), 3.55 (q, 4H, *J* = 7.2, CH_2), 6.87 (d, 2H, *J* = 9.2, Ar-H), 7.74 (d, 2H, *J* = 9.2, Ar-H), 11.43 (s, 1H, NH), 11.64 (s, 1H, NH). ^{13}C NMR (CD_3COCD_3, 100 MHz) δ: 11.8, 44.2, 87.0, 110.6, 113.8, 115.0, 130.5, 151.2, 158.5, 159.6, 176.2. IR (KBr, cm^{-1}): 3223, 2970, 2929, 2208, 1658, 1517, 1450, 1331, 1225, 1133, 784. m/z, calcd. for $C_{15}H_{16}N_4OS$ [M]$^+$: 300.10, found: 300.0. Anal. calcd for $C_{15}H_{16}N_4OS$: C, 59.98, H, 5.37, N, 18.65, found: C, 57.92, H, 5.16, N, 18.28.

6-(Furan-2-yl)-4-oxo-2-thioxo-1,2,3,4-tetrahydro-pyrimidine-5-carbonitrile (4h). m.p. > 300 °C. ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 6.89 (d, d, 1H, J_1 = 2.0 Hz, J_2 = 1.6 Hz, Ar-H), 7.88 (d, 1H, *J* = 3.6 Hz, Ar-H), 8.21 (d, 1H, *J* = 1.2 Hz, Ar-H), 12.72 (b, 1H, NH), 13.06 (s, 1H, SH). ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 85.7, 114.1, 115.0, 120.2, 142.3, 147.2, 149.3, 159.1, 176.5. IR (KBr, cm^{-1}): 3158, 3120, 2233, 1668, 1548, 1224, 1179, 1038, 768. m/z, calcd. for $C_9H_5N_3O_2S$ [M]$^+$: 219.01, found: 219.0.

RESULTS AND DISCUSSION

Preparation and Characterization of Ionic Liquid

We designed and synthesized a novel ionic liquid, based on imidazolium cation, with a triethylenoxy spacer. 1,2-Bis(2-(1H-imidazol-1-yl)ethoxy)ethane (1) has been synthesized according to our previously published method [22]. Treatment of compound (1) with propyl bromide led to the formation of 1,1'-((ethane-1,2-diylbis(oxy))bis(ethane-2,1-diyl))bis(3-propyl-1H-imidazol-3-ium) bromide (2) in 96% yield as viscous oil. This compound (2) is then converted into the novel basic ionic liquid (3) by the reaction with potassium hydroxide in the presence of dimethyl sulfoxide at room temperature in 85% yield as



Scheme 1. Synthesis of dicationic basic ionic liquid

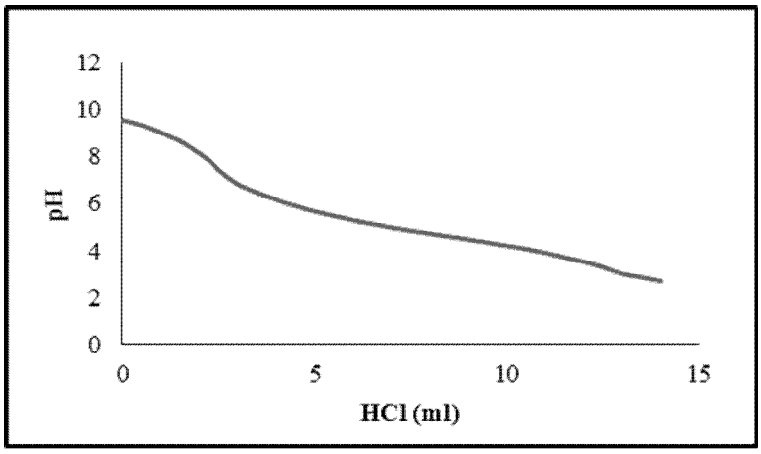


Fig. 1. pH meter titration curve of the novel dicationic BIL.

viscous oil. In designing this novel ionic liquids, propyl group that is covalently bonded to the imidazolium rings helps to increase hydrophobicity of ionic liquid. Also, short oligo (ethylene glycol) chain that is used as a linker between two imidazolium ring increases the flexibility and hydrophobicity of the ionic liquid. In addition this synthesized dicationic basic ionic liquid is hydrophilic in nature. Oligo chain spacer is responsible for hydrophilicity.

Actually the oxygen atoms in ethyleneoxy bridges act as hydrogen bond acceptor and also help to form strong hydrogen bond with organic compounds and polar solvent [32,33].

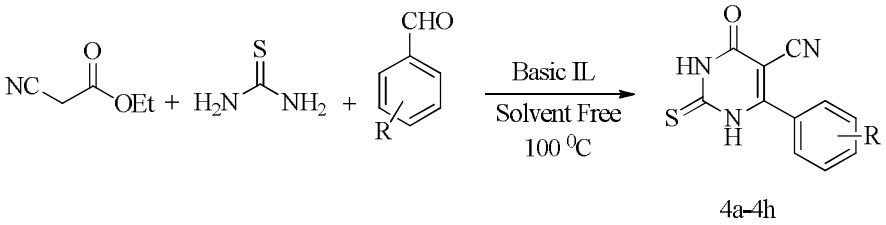
Additionally, in the synthesis of this novel basic ionic liquid, we used hydroxy groups to produce basic ionic liquid as catalyst and solvent for basic condition reaction. This part of ionic liquid can increase hydrophilicity of the BIL. These features lead to dissolve polar organic compounds and enhance the significant catalytic activity of this novel dicationic basic ionic liquid in organic transformations.

pK_b Measurement of Basic Ionic Liquid

The pK_b value for the mentioned basic ionic liquid was determined using 0.1 M solution of ionic liquid and was titrated with 0.1 M of HCl. The pH of the solution was measured using a calibrated glass electrode pH meter at 25 °C. As shown in Fig. 1, the pK_b value of basic ionic liquid is 8.78. This novel basic ionic liquid can be used as catalyst in

Table 1. Solubility Property of the Synthesized Dicationic Basic Ionic Liquid

Solvents	H_2O	CH_3OH	EtOAc	$(Et)_2O$	$CHCl_3$	DMSO	DMF	C_6H_{12}	Toluene
M	M	M				M	M		
cible									
Immiscible			IM	IM	IM			IM	IM



4a-4h

Scheme 2. Synthesis of 4-oxo-6-aryl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile derivatives

many different organic transformations.

Solubility of Basic Ionic Liquid

Solubility of the synthesized dicationic RTIL was determined in several selected solvents at ambient temperature and all results are summarized in Table 1. In general, all dicationic ionic liquids showed good solubility in polar solvents while insoluble in ethyl acetate, diethyl ether, cyclohexane, and toluene. This synthesized dicationic basic ionic liquid is hydrophilic in nature and this property, due to the presence of ethyleneoxy bridges and formation of hydrogen bonding, has a good solubility in polar solvents such as dimethylsulfoxide (DMSO) and *N,N*-dimethyl-formamide (DMF). Also, due to the presence of hydroxide ions in the two active sites of the synthesized basic catalyst, hydrophilic property and excellent solubility in protic solvents such as water, ethanol and methanol are increased.

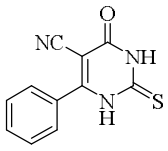
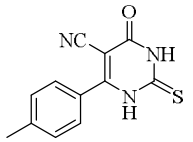
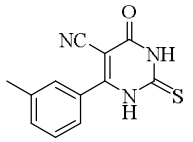
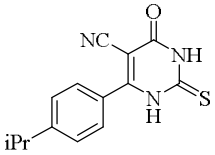
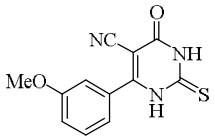
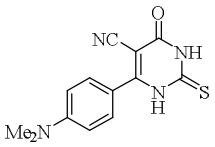
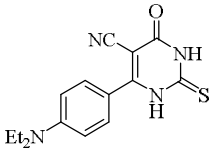
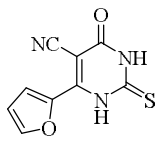
The application of this novel basic ionic liquid is studied in a new one-pot method for the synthesis of 4-oxo-6-Aryl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile derivatives from ethyl cyanoacetate, thiourea and various aromatic aldehydes, in the presence of catalytic amount of this novel ionic liquid under solvent-free conditions (Scheme 2). The corresponding desired products were isolated in excellent yields and the results are summarized in Table 2.

In order to investigate the effect of temperature on the reaction, the concentration of ionic liquid was kept constant at 0.5 mmol and a mixture of substrates was treated with ionic liquid. The reaction was monitored by TLC at different temperatures ranging from 50 to 120 °C. (Table 3). Our results indicate that after stirring the reaction mixture at 50 °C for 24 h, the yield of the corresponding product was low (Table 3, entry 1). Subsequently, the mixture was heated in an oil bath. Increasing the reaction temperature from 100 to 120 °C gave better results in terms of yield and reaction time. Further increase in temperature did not show any significant improvement in the yield and the reaction time. Therefore, 100 °C was selected as the reaction temperature for all further reactions (Table 3, entry 2-4).

Molecular Geometry of Basic Ionic Liquid

The optimized geometry of synthesized dicationic basic ionic liquid is shown in Fig. 2, and the minimum-energy geometries of the novel ionic liquid were computed by performing *ab initio* geometry optimizations at the RHF/6-31G level of theory. All calculations were carried out using Gaussian 09 [34]. The optimized molecular structure of the novel ionic liquid is demonstrated in Figs. 2 and 3. The results are shown in Table 4. This optimized structure

Table 2. Results of the Synthesis of 4-Oxo-6-aryl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile Derivatives Using Novel Basic Ionic Liquid (3)

Entry	Aldehydes	Product	Time (h)	Isolated yield (%)	M.p. (°C)	Repoted/Ref.
4a	C_6H_5CHO		4	72	257	261-263/[36]
4b	4-Me C_6H_4CHO		7	63	241	245-246/[36]
4c	3-Me C_6H_4CHO		6	71	249	-
4d	4-iPr C_6H_4CHO		9	53	279	-
4e	3-MeO C_6H_4CHO		6	65	238	-
4f	4-Me_2N C_6H_4CHO		5	82	283	287-288/[37]
4g	4-Et_2N C_6H_4CHO		5	78	255	-
4h	C_4H_3OCHO		4	65	>300	>300/[38]

[a]All compounds were characterized on the basis of ^{1}H NMR and IR spectral data, which were consistent with those reported in the literature.

Table 3. Temperature Optimization for the Synthesis of 4-Oxo-6-aryl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile Derivatives

Entry	ILOH (mmol)	Temperature (°C)	Time (h)	Isolated yield (%)
1	0.5	50	24	30
2	0.5	80	10	88
3	0.5	100	4	72
4	0.5	120	4	74

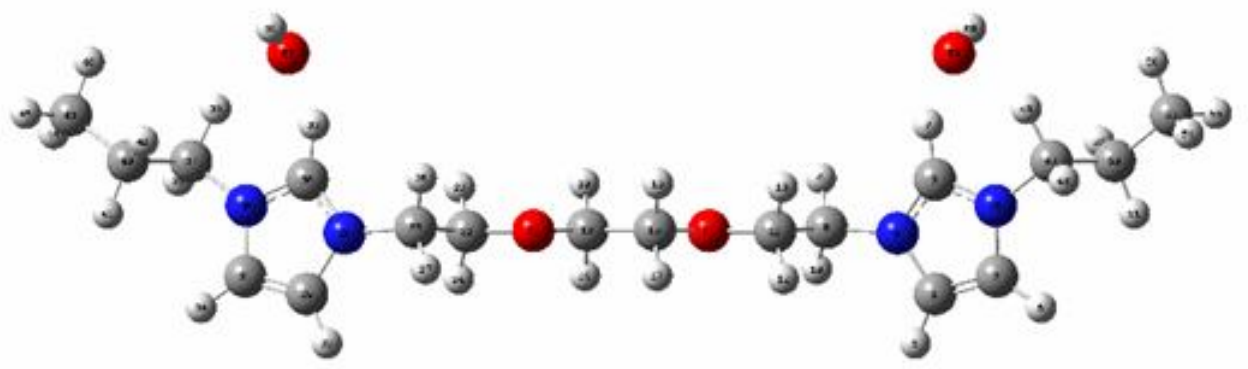


Fig. 2. Optimized molecular structure of basic ionic liquid (3) using RHF/6-31G..

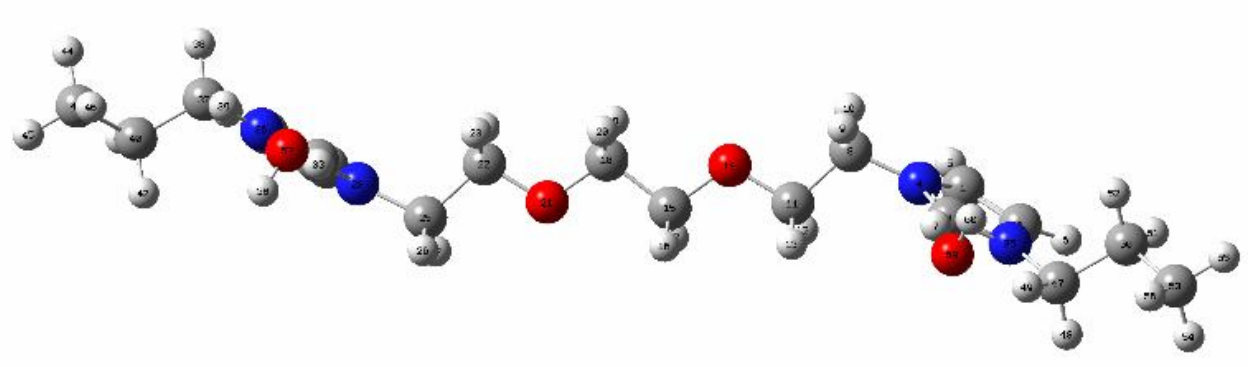
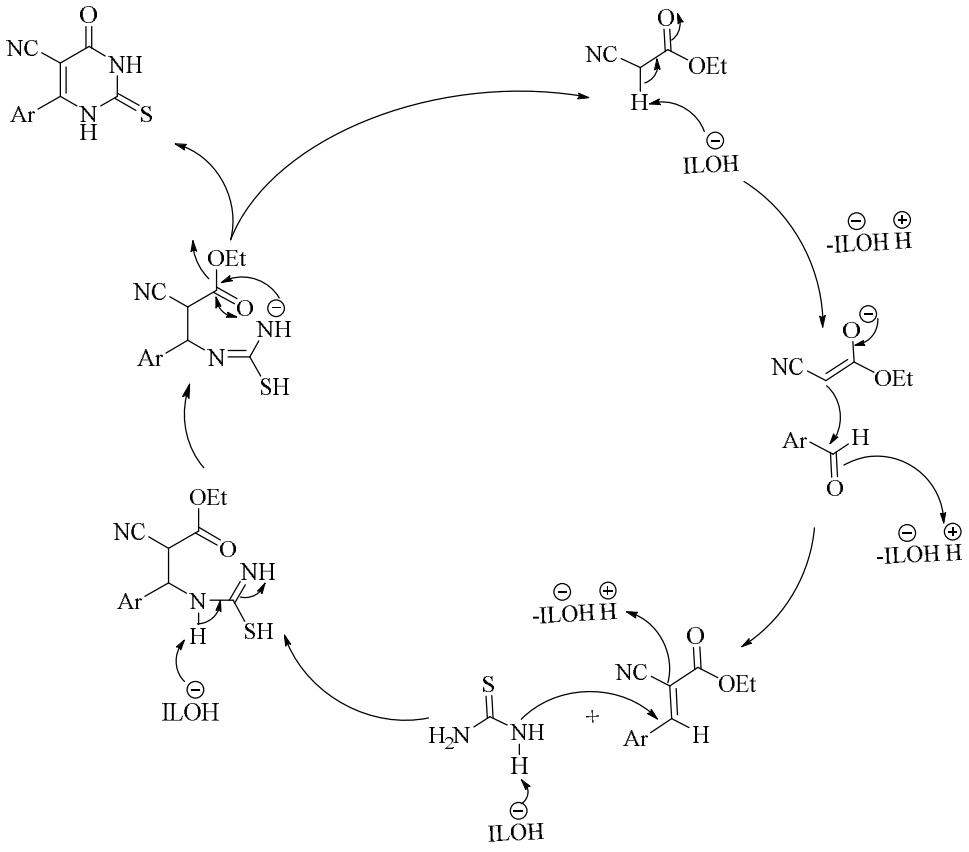


Fig. 3. Top view and anti-direction of the optimized molecular structure of basic ionic liquid (3) using RHF/6-31G..

reveals that the most stable form of the novel ionic liquid is anti-direction of hydroxy ions in addition to the anti-direction of two imidazolium rings toward each other (Fig. 3). The distances of hydroxy ion from hydrogen and nitrogen of imidazolium rings, for two active sites, are (H_{49}-O_{59} = 1.85720 Å), (H_{39}-O_{57} = 1.85716 Å), (N_{35}-O_{59} = 3.05277 Å) and (N_{36}-O_{57} = 3.05269 Å) showing the symmetrical structure of this novel ionic liquid. The distance of hydroxy ion from the imidazolium ring hydrogen ($(N)_2C$-H) was confirmed that hydrogen bond is

Table 4. The Geometry Parameters of the Ionic Liquid Calculated at RHF/6-31G Level of Theory

Parameter		
Bond distance (Å)		
(N)2C-H	C3-H7 = 1.06986	C30-H33 = 1.06986
(N)2C-H---OH	H7-O59 = 1.50846	H33-O57 = 1.50848
H---OH	H49-O59 = 1.85720	H39-O57 = 1.85716
N---OH	N35-O59 = 3.05277	N36-O57 = 3.05269
(N)2C-H---OH (angle)	C3-H7-O59 = 151.17198	C30-H33-O57 = 151.16766
E (a.u.)	-1226.14298446	
Dipole Moment (D)	14.5010	



Scheme 3. The suggested mechanism for the formation of 4-oxo-6-aryl-2-thioxo-1,2,3,4-tetrahydro-pyrimidine-5-carbonitrile derivatives

Table 5. The Comparison of some other Methods with Basic Ionic Liquid Catalyst for the Synthesis of 4-Oxo-6-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile Derivatives

Entry	Catalyst	Solvent	Temperature (ºC)	Time (h)	Isolated yield (%)	Ref.
1	K_2CO_3	Ethanol	reflux	19	45	[36]
2	Piperidine	Ethanol	reflux	12	67	[31]
3	K_2CO_3	Ethanol	MW	0.1	83	[28]
4	Piperidine	Methanol	MW	0.06	55	[39]
5	Sodium ethoxide	Ethanol	rt	48	51	[40]
6	Basic-IL	-	100	4	72	[a]

[a]This work.

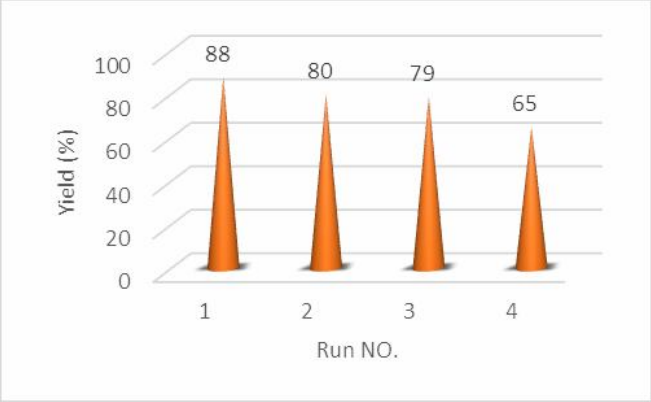


Fig. 4. Reusability of the BIL in the synthesis of 4-oxo-6-phenyl-2-thioxo-1,2,3,4-tetrahydro-pyrimidine-5-carbonitrile derivatives.

present between cationic and anionic moiety in the synthesized ionic liquid.

In a possible mechanism, the reaction initially proceeds by Knoevenagel condensation, as the basic ionic liquid, which promotes the reaction by abstracting a proton from the active methylene of ethyl cyanoacetate. As a result, an alkene intermediate (A) may be formed with the aldehyde. This compound (A) reacts with thiourea *via* Michael addition to give the 4-oxo-6-aryl-2-thioxo-1,2,3,4-tetra-hydropyrimidine-5-carbonitrile derivatives (Scheme 3) [35].

In order to illustrate the catalyst activity of the novel basic ionic liquid in comparison with other reported results, we compared the results and reaction conditions of this work with some other methods reported in the literature used in the synthesis of 4-oxo-6-Aryl-2-thioxo-1,2,3,4 tetrahydropyrimidine-5-carbonitrile derivatives (Table 5). As shown in Table 5, this novel basic ionic liquid is an effective, green and eco-friendly catalyst with high catalytic

activity and short reaction time for the synthesis of 4-oxo-6-aryl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile derivatives.

Recycling of Basic Ionic Liquid

The recycling performance of basic ionic liquid was investigated in the reaction of ethyl cyanoacetate, thiourea and benzaldehyde. The catalyst was recovered by washing the aqueous layer thoroughly with ethyl acetate and evaporation of the water at 50-60 °C in a vacuum oven and gave 88% yields and reused for the same experiment for four times (Fig. 4).

CONCLUSIONS

In conclusion, we have designed and synthesized a novel basic ionic liquid, based on imidazolium cation, and have successfully used it as a catalyst for the one-pot synthesis of 4-oxo-6-aryl-2-thioxo-1,2,3,4-tetrahydro-pyrimidine-5-carbonitrile derivatives. The remarkable feature of this new catalyst is its ethyleneoxy bridge which participates in dissolving organic compounds. The application of this basic ionic liquid is studied in a new one-pot method for the synthesis of tetrahydropyrimidine derivatives under solvent-free conditions. The advantages offered by this protocol include reusability of the catalyst, high conversion, short reaction time, and simple experimental procedure.

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