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Short Communication

1-Methylimidazolium hydrogen sulfate/chlorotrimethylsilane: An effective catalytic system for the synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones and hydroquinazoline-2,5-diones

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ABSTRACT

Brønsted acidic ionic liquid, 1-methylimidazolium hydrogen sulfate, in the presence of catalytic amount of chlorotrimethylsilane has been used as an efficient and reusable catalyst for the one-pot synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones and hydroquinazoline-2,5-diones under thermal and solvent-free conditions. High yields of the products were obtained in a few minutes by using this new catalysis system.

1. Introduction

Biginelli reaction is ranked as one of the most powerful routs for the synthesis of complex heterocyclic scaffolds for therapeutic and pharmacological properties [1–3]. Classical Biginelli reaction involves one-pot condensation of an aldehyde, a β-ketoester, and urea under strongly acidic conditions [4].

In recent decades, the scope of the original Biginelli reaction was extended by variation of the 1,3-dicarbonyl compound building blocks. Many groups have elegantly demonstrated the synthetic versatility of numerous 1,3-dicarbonyl compounds, including β-ketoester and cyclic β-diketones [5–34]. However, in spite of their potential utility, all of the reported synthetic methods suffer from limitations such as the use of expensive reagents, strong acidic conditions, low yields and long reaction times. Also, the requirement for the use of stoichiometric amount of catalyst and un-recoverability of strong acids or solvents as well as harsh reaction conditions are of the other limitations of these reports. Therefore, to avoid these limitations, introducing milder and more efficient methods are needed.

Due to environmental concerns, the use of benign solvents as alternatives to volatile organic solvents is of much interest to organic chemists. The use of ionic liquids as reaction media and catalyst can offer a solution to solvent emission and catalyst recycle problems [35,36]. Ionic liquids posses the advantages like negligible vapor pressure, reasonable thermal stability and recyclability. They dissolve many organic and inorganic substrates and are tunable to specific chemical tasks [37]. Recently, ionic liquids have been successfully employed as solvents with catalytic activity for a variety of reactions [38].

In this study, in continuation of our effort to develop applicability of Biginelli reaction [39,40], an efficient, facile and solvent-free procedure was introduced for the synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones (Table 1) and hydroquinazoline-2,5-diones/thiones (Table 2). For this purpose, the reaction of aromatic aldehydes, cyclic or acyclic ketones and urea/thiourea using Brønsted acidic ionic liquid (1-methylimidazolium hydrogen sulfate, [Hmim]HSO_4), in the presence of catalytic amount of chlorotrimethylsilane (TMSCl) (Schemes 1, 2) as an effective catalytic system was investigated for the first time. The procedure presented here not only gives the desired products in good yields, but also avoids the problems associated with conventional solvents such as cost, handling, safety and pollution, and moreover the reaction times are reduced to a few minutes.

2. Experimental

All reagents were purchased from Merck and Fluka and used without further purification. Melting points were obtained in open capillary tubes and were measured on an Electro-thermal IA 9100 apparatus. IR spectra were recorded on KBr pellets on a Shimadzu FT-IR 8600 spectrophotometer. ^{1}H and ^{13}C NMR spectra were determined on a Bruker 500 DRX Avance instrument at 500 and 125 MHz.

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Table 1
Synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones and comparison of efficiency 1-methylimidazolium hydrogen sulfate/chlorotrimethylsilane catalytic system with other catalysts and methods[a].

Products	R^1	R^2	R^3	X	Found			Reported			
					m.p. (°C)	Time (min)	Yield (%)	m.p. (°C)	Time (min)	Yield (%)	Ref.
4a	3-NO_2	Ph	Ph	O	221–223	40	96(95,92,90)[b]	222–224	7	96	[39][c]
4b	4-NO_2	Ph	Ph	O	256–258	25	96	–	–	–	–
4c	3-OMe	Ph	Ph	O	191–193	35	87	191–193	7	91	[39][c]
4d	3-Br	Ph	Ph	O	201–203	50	88	–	–	–	–
4e	4-Me	Ph	Ph	O	236–238	60	80	–	–	–	–
4f	H	Ph	Ph	S	260–261	45	94	259–261	5	97	[39][c]
4g	3-Cl	Ph	Ph	S	263–264	50	92	263–265	5	95	[39][c]
4h	4-Cl	Ph	Ph	S	284–286	35	89	–	–	–	–
4k	4-NO_2	Ph	Ph	S	276–277	35	96	–	–	–	–
4l	2,4-diCl	Me	COOEt	O	253–255	25	91	–	–	–	–
4m	H	Me	COOEt	O	204-205	30	92	206–208	240	97	[27]
4n	3-NO_2	Me	COOEt	O	230–232	20	96	230–232	240	94	[27]
4o	3-OMe	Me	COOEt	O	210–211	25	91	206–208	240	94	[27]
4p	2-OMe	Me	COOEt	O	260–261	35	86	–	–	–	–
4q	H	Me	COOEt	S	205–206	30	90	207–208	240	92	[27]
4r	2-OMe	Me	COOEt	S	193–195	25	92	–	–	–	–
4s	3-NO_2	Me	COOEt	S	205–207	25	94	206–207	240	92	[27]

[a] Reaction condition: aromatic aldehyde (1 mmol), ketone or β-ketoester (1 mmol), urea (2 mmol) or thiourea (2 mmol), [Hmim]HSO_4 (0.5 mmol), TMSCl (0.5 mmol) in an oil bath at 80 °C.
[b] The yields of reaction with recycled ionic liquid after three successive runs.
[c] Reaction carried out under microwave irradiation.

2.1. Preparations of 1-methylimidazolium hydrogen sulfate, [Hmim]HSO_4, as Brønsted acidic ionic liquid

The ionic liquid of [Hmim]HSO_4 was prepared by reported procedure [41]. 1-Methylimidazole (1.59 mL, 20 mmol) and acetonitrile (5 mL) were charged into a 25 mL round-bottom flask. Then, the mixture was stirred at 0 °C for 1 min. Stoichiometric amount of concentrated sulfuric acid (97%, 1.03 g/mL) was added dropwise and the mixture stirred for 1 h at 0 °C and then stirred for 2 h at room temperature. The [Hmim]HSO_4 was washed repeatedly with diethyl ether (2.5 mL) to remove non-ionic residues and then it was dried in a vacuum evaporator.

2.2. General procedure for preparation of 4a-s and 7a-p

A mixture of aldehyde (1 mmol), cyclic or acyclic ketone (1 mmol), urea or thiourea (2 mmol), [Hmim]HSO_4 (0.5 mmol) and TMSCl (0.5 mmol) was heated at 80 °C for the appropriate time according to Tables 1, 2. After completion of reaction, as indicated by TLC, the reaction mixture was allowed to cool to room temperature. Then, 5 mL distilled water was added into the beaker and stirred. The obtained precipitate was filtered off. The crude product was recrystallized from ethanol and dried to afford powder compounds of 4a-s, 7a-p.

The filtrate was concentrated under reduced pressure and washed with diethyl ether. Then, it was dried in a vacuum evaporator to recover the ionic liquid for subsequent use.

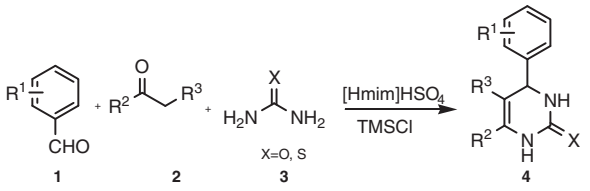
3,4-Dihydro-4-(*4-NO_2*-phenyl)-5,6-diphenylpyrimidine-2(1*H*)-one (4b). White powder; mp: 256–258 °C; IR (KBr) ν_{max}: 3232, 3097, 2928, 1702, 1651, 1530 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ_H: 5.35 (d, J = 4.2 Hz, 1H), 6.80–7.26 (m, 10H), 7.61 (d, J = 8.6 Hz, 2H), 8.25 (d, J = 8.6 Hz, 2H), 8.58 (s, 1H, NH), 9.46 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6) δ_c: 58.1, 110.2, 124.9, 127.3, 128.7, 128.8, 129.2, 129.4, 129.9, 130.5, 134.3, 134.7, 137.4, 147.9, 150.2, 153.4.

3,4-Dihydro-4-(*3-Br*-phenyl)-5,6-diphenylpyrimidine-2(1*H*)-one (4d). White powder; mp: 201–203 °C; IR (KBr) ν_{max}: 3220, 3091, 2918, 1689, 1595, 1471 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ_H:

Table 2
Synthesis of hydroquinazoline-2,5-diones/thiones and comparison of efficiency 1-methylimidazolium hydrogen sulfate/chlorotrimethylsilane catalytic system with other catalysts.

Products	R^1	R^2	R^3	X	Found			Reported			
					Time (min)	Yield (%)	m.p.(°C)	Time (h)[a]	Yield (%)[b]	m.p.(°C)	Ref.
7a	3-NO_2	H	H	O	15	94	308–310	–	–	–	–
7b	2- NO_2	H	H	O	15	85	271–273	–	–	–	–
7c	2-Cl	H	H	O	15	84	299–301	–	–	–	–
7d	3,5-Cl	H	H	O	15	82	324–326	–	–	–	–
7e	4-Br	H	H	S	15	78	306–308	–	–	–	–
7f	H	H	H	O	15	86	307–308	10, 6.5	70, 94	308–309	[23,34]
7g	2-Br	H	H	O	15	88	289–290	10	66	291–292	[23]
7h	3-Br	H	H	O	15	95	302–303	10	68	304–305	[23]
7i	4-NO_2	H	H	O	15	82	299–300	10, 6.5	67, 81	302–303	[23,34]
7j	4-Cl	H	H	O	15	93	285–287	10, 6	76, 88	287–288	[23,34]
7k	4-OMe	H	H	O	15	68	277–278	10	74	279–280	[23]
7l	4-Cl	CH_3	CH_3	O	10	91	296–297	2, 10	94, 72	296–297	[33,23]
7m	2-Cl	CH_3	CH_3	O	10	87	276–288	0.42	75	277–279	[24]
7n	H	CH_3	CH_3	O	10	89	286–288	1.5, 2.5, 0.33	95, 92, 73	287–290	[33,34,24]
7o	4-Cl	CH_3	CH_3	S	10	86	271–274	0.5	52	271–274	[24]
7p	3-NO_2	CH_3	CH_3	S	10	82	251–253	0.58	46	250–252	[24]

[a] Numbers of this column refer to reported time (h) in literatures that are shown in the reference column, respectively.
[b] Numbers of this column refer to reported yield in literatures that are shown in the reference column, respectively.



Scheme 1. Synthesis of 3,4-dihydropyrimidin-2(1H)-ones/thiones.

5.19 (d, $J=2.7$ Hz, 1H), 6.78–7.24 (m, 10H), 7.30 (s, 1H), 7.31–7.38 (m, 3H), 7.53 (s, 1H, NH), 8.66 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6) δ_c: 58.7, 108.9, 125.5, 125.9, 126.8, 127.4, 127.8, 127.9, 128.1, 129.2, 129.3, 130.5, 133.0, 134.7, 153.0, 137.6, 146.2, 152.8.

3,4-Dihydro-4-(*4-Me*-phenyl)-5,6-diphenylpyrimidine-2(1*H*)-one (4e). White powder; mp: 236–238 °C; IR (KBr) ν_{max}: 3209, 3018, 2943, 1649, 1569, 1479 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 2.28 (s, 3H), 5.07 (d, $J=2.8$ Hz, 1H), 6.79 (m, 2H), 7.00–7.28 (m, 12H), 8.87 (s, 1H, NH), 9.28 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6) δ_c: 20.6, 58.6, 111.2, 126.3, 127.0, 127.8, 128.0, 129.2, 128.4, 129.2, 133.3, 133.8, 137.1, 137.3, 139.5, 153.0.

3,4-Dihydro-4-(*4-Cl*-phenyl)-5,6-diphenylpyrimidine-2(1*H*)-thione (4h). White powder; mp: 284–286 °C; IR (KBr) ν_{max}: 3211, 3060, 2906, 1658, 1596, 1490 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 5.20 (d, $J=3.4$ Hz, 1H), 6.79–7.24 (m, 10H), 7.37 (d, $J=8.38$ Hz, 2H), 7.42 (d, $J=8.38$ Hz, 2H), 8.72 (s, 1H, NH), 9.35 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6) δ_c: 59.5, 110.0, 126.8, 126.8, 128.7, 128.9, 129.0, 129.5, 129.8, 130.2, 132.8, 135.7, 135.8, 138.7, 143.7, 172.5.

3,4-Dihydro-4-(*4-NO_2*-phenyl)-5,6-diphenylpyrimidine-2(1*H*)-thione (4k). White powder; mp: 276–277 °C; IR (KBr) ν_{max}: 3228, 3089, 2926, 1685, 1649, 1531 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 5.36 (d, $J=3.4$ Hz, 1H), 6.81–7.05 (m, 10H), 7.60 (d, $J=8.6$ Hz, 2H), 8.25 (d, $J=8.6$ Hz, 2H), 9.46 (s, 1H, NH), 10.12 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6) δ_c: 59.1, 111.3, 124.9, 127.4, 128.8, 128.9, 129.4, 129.5, 129.9, 130.6, 134.4, 134.8, 137.6, 147.9, 150.3, 174.8.

3,4-Dihydro-5-etoxycarbonyl-4-(2,4-dichlorophenyl)-6-methylpyrimidine-2(1*H*)-one (4l). White powder; mp: 253–255 °C; IR (KBr) ν_{max}: 3244, 3216, 2977, 1724, 1702, 1647, 1463 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 1.00 (t, 3H), 2.28 (s, 3H), 3.89 (q, 2H), 5.59 (d, $J=1.5$ Hz, 1H), 7.30–7.55 (m, 3H), 7.73 (s, 1H, NH), 9.30 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6) δ_c: 14.7, 18.5, 52.0, 60.0, 98.3, 128.8, 129.5, 130.1, 133.4, 133.5, 141.8, 150.4, 152.0, 165.7, 187.0.

3,4-Dihydro-5-etoxycarbonyl-4-(*2-OMe*-phenyl)-6-methylpyrimidine-2(1*H*)-thione (4r). White powder; mp: 193–195 °C; IR (KBr) ν_{max}: 3176, 3132, 2985, 1703, 1645, 1583, 1479 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 1.00 (t, 3H), 2.28 (s, 3H), 3.78 (s, 3H), 3.90 (m, 2H), 5.50 (d, $J=3.2$ Hz, 1H), 6.87–7.27 (m, 4H), 9.21 (s, 1H, NH), 10.20 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6) δ_c: 14.8, 17.8, 50.3, 56.3, 60.2, 100.2, 112.1, 121.0, 128.6, 129.9, 131.4, 145.9, 157.5, 166.0, 175.0.

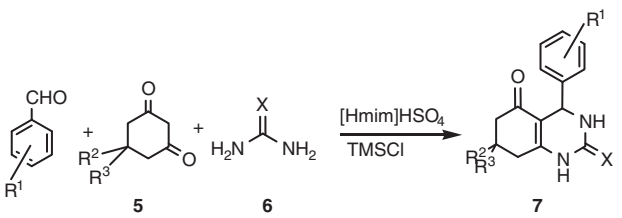
4-(*3-NO_2*-phenyl)-3,4,7,8-tetrahydro-1*H*,6*H*-quinazolin-2,5-dione (7a). Yellow powder; mp: 308–310 °C; IR (KBr) ν_{max}: 3338, 3209, 3091, 2952, 1706, 1622, 1527, 1446 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 1.82 (m, 1H), 1.92 (m, 1H), 2.23 (m, 1H), 2.25 (m, 1H), 2.43 (m, 1H), 2.52 (m, 1H), 5.33 (s, 1H), 7.62 (t, 1H), 7.70 (d, $J=7.7$ Hz, 1H), 7.9 (s, 1H, NH), 8.08 (s, 1H), 8.10 (d, $J=6.8$ Hz, 1H), 9.6 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6) δ_c: 21.5, 26.7, 37.0, 52.3, 108.3, 121.8, 123.1, 130.9, 133.8, 147.5, 148.6, 152.3, 156.0, 194.2.

4-(*2-NO_2*-Phenyl)-3,4,7,8-tetrahydro-1*H*,6*H*-quinazolin-2,5-dione (7b). Yellow powder; mp: 271–273 °C; IR (KBr) ν_{max}: 3429, 3211, 3120, 2966, 1699, 1645, 1604, 1519 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 1.82 (m, 1H), 1.90 (m, 1H), 2.08 (m, 1H), 2.16 (m, 1H), 2.46 (m, 1H), 2.49 (m, 1H), 5.85 (s, 1H), 7.47 (t, 1H), 7.49 (d, $J=7.7$ Hz, 1H), 7.68 (t, 1H), 7.74 (s, 1H, NH), 7.84 (d, $J=8.0$ Hz, 1H), 9.60 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6) δ_c: 21.5, 26.6, 36.8, 48.8, 108.2, 124.7, 129.3, 130.1, 134.6, 139.5, 148.6, 151.7, 155.8, 193.9.

4-(*2-Cl*-Phenyl)-3,4,7,8-tetrahydro-1*H*,6*H*-quinazolin-2,5-dione (7c). Yellow powder; mp: 299–301 °C; IR (KBr) ν_{max}: 3382, 3222, 3120, 2958, 1701, 1645, 1604, 1494 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 1.88 (m, 1H), 1.92 (m, 1H), 2.14 (m, 1H), 2.21 (m, 1H), 3.32 (m, 1H), 3.43 (m, 1H), 5.56 (s, 1H), 7.22 (m, 1H), 7.24 (m, 1H), 7.26 (m, 1H), 7.38 (d, $J=7.43$ Hz, 1H), 7.62 (s, 1H, NH), 9.50 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6) δ_c: 21.7, 26.8, 37.1, 51.1, 107.7, 128.3, 129.8, 130.0, 130.3, 132.8, 141.8, 151.8, 156.0, 193.8.

4-(3,5-Dichlorophenyl)-3,4,7,8-tetrahydro-1*H*,6*H*-quinazolin-2,5-dione (7d). Yellow powder; mp: 324–326 °C; IR (KBr) ν_{max}: 3228, 3116, 2956, 1701, 1614, 1581, 1465 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 1.81 (m, 1H), 1.90 (m, 1H), 2.22 (m, 2H), 2.45 (t, 1H), 2.49 (t, 1H), 5.20 (s, 1H), 7.21 (s, 1H), 7.22 (s, 1H), 7.46 (t, 1H), 7.82 (s, 1H, NH), 9.60 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6) δ_c: 21.5, 26.7, 37.0, 52.1, 107.9, 125.9, 127.7, 134.8, 149.4, 152.2, 156.2, 194.2.

4-(*4-Br*-Phenyl)-3,4,7,8-tetrahydro-1*H*,6*H*-2-thioxoquinazolin-5-one (7e). Yellow powder; mp: 306–307 °C; IR (KBr) ν_{max}: 3242, 3184, 2991, 1623, 1566, 1460 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ_H: 1.80 (m, 1H), 1.91 (m, 1H), 2.22 (m, 1H), 2.27 (m, 1H), 2.48 (m, 1H), 2.51 (m, 1H), 5.17 (s, 1H), 7.15 (d, $J=8.55$ Hz, 2H), 7.51 (d, $J=8.55$ Hz, 2H), 9.60 (s, 1H, NH), 10.6 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6) δ_c: 21.3, 26.1, 37.1, 52.3, 109.5, 121.5, 129.5, 132.2, 143.4, 151.7, 175.3, 194.8.



Scheme 2. Synthesis of hydroquinazoline-2,5-diones/thiones.

3. Results and discussion

Recently, chlorotrimethylsilane has been used as a mild and efficient promoter for various organic reactions [28–32]. It has been reported as a useful and inexpensive Lewis acid catalyst for the synthesis of octahydroquinazolinones. In 2006, reaction of dimedone, aromatic aldehydes and urea in the presence of TMSCl was carried out by Kantevari, in the MeCN/DMF at 80 °C. There are disadvantages for this report due to long reaction time (1.5–3 h), use of stoichiometric amount of TMSCl and unrecoverable solvent [33]. In 2010, the synthesis of octahydroquinazolinones using cyclohexadione instead of dimedone in the presence of TMSCl in [Bmim]BF_4 was reported by refluxing for 6.5–8 h [34], yet the reaction time was very high.

In our previous work [39], the condensation reaction of aromatic aldehyde, deoxybenzoin, and urea in the presence of TMSCl/$Co(OAc)_2\cdot 4H_2O$ under microwave irradiation was studied. Herein, to introduce a milder method, our initial attempts were directed toward the synthesis of 3,4-dihydro-4-aryl-5,6-diphenylpyrimidin-2(1*H*)-ones. In order to find the optimum conditions, for the formation of 4a, reaction of 3-nitrobenzaldehyde (1 mmol) 1a, deoxybenzoin (1 mmol) 2a, and urea (2 mmol) 3 was performed in the presence of various ionic liquids such as [Hmim]HSO_4, 1-buthyl-3-methyimidazolium bromide ([Bmim]Br), 1-methyl-2-pyrolidonium hydrogen sulfate ([NMP]HSO_4). We found that, all of the above ionic liquids could promote the reaction, but the yields were not so high (Table 3, entries 1–3).

However, satisfactory results were obtained when the reactions were carried out in the presence of TMSCl. The amount of ionic liquid and TMSCl was examined, and the results are summarized in Table 3. It could be seen that 0.5 mmol [Hmim]HSO_4 and 0.5 mmol TMSCl gave the best yield (96%) at 80 °C (entry 4, Table 3).

Table 3
Effects of the type and amount of ionic liquid and TMSCl on the formation of 4a.

Entry	Ionic liquid (mmol)	TMSCl (mmol)	t (min)	Yield (%)
1	[Hmim]HSO_4(0.5)	–	40	72
2	[Bmim]Br(0.5)	–	60	60
3	[NMP]HSO_4(0.5)	–	90	22
4	[Hmim]HSO_4(0.5)	0.5	40	96
5	[Bmim]Br(0.5)	0.5	40	82
6	[NMP]HSO_4(0.5)	0.5	90	35
7	[Hmim]HSO_4 (0.5)	0.25	45	81
8	[Hmim]HSO_4 (0.5)	0.75	50	84
9	[Hmim]HSO_4 (0.5)	1	60	78
10	[Hmim]HSO_4 (0.25)	0.5	60	75
11	[Hmim]HSO_4 (0.75)	0.5	40	85
12	[Hmim]HSO_4 (1)	0.5	60	77

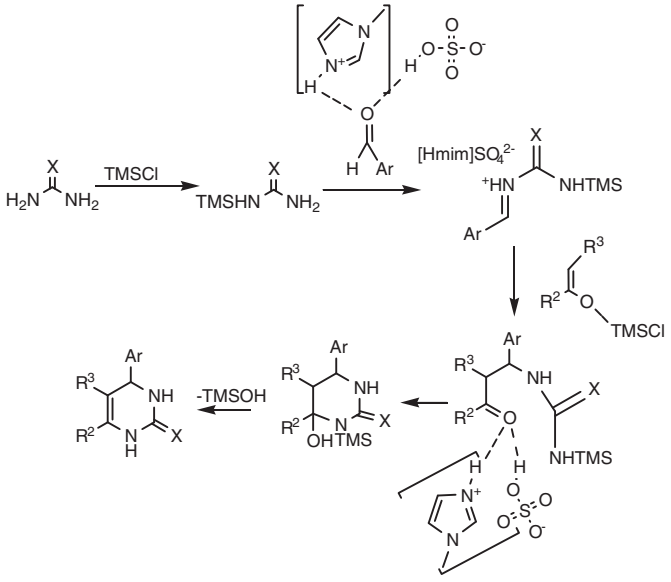
Reaction condition: 3-Nitrobenzaldehyde (1 mmol), deoxybenzoin (1 mmol), urea (2 mmol), 80 °C.

In order to examine the substrate scope of Biginelli reaction, the reaction of various aromatic aldehydes and urea (or thiourea) with deoxybenzoin (or ethyl acetoacetate) under the optimized reaction conditions was examined (Scheme 1). The results are shown in Table 1. According to the table, we could see that all the reactions afforded the corresponding DHPMs 4a-s in good to high yields.

Prompted by this success and in order to explore the generality of the method, we extended the reaction of various aldehydes and urea (or thiourea) with cyclic diketones such as dimedone and cyclohexanedione under similar conditions and as the results hydroquinazoline-2,5-diones/thiones 7a-p were obtained as products (Table 2, Scheme 2).

A brief comparison of the present method with those previously reported in literature in terms of reaction times and yields reveals the merit of this method for the synthesis of the desired products. As shown in Tables 1 and 2, reaction times were considerably decreased and yield of reaction increased. Thus, the [Hmim]HSO_4 and TMSCl act as a suitable catalytic medium with respect to reaction times and yields of the products.

According to the mechanism suggested by Kappe [42], a proposed reaction mechanism for the Biginelli condensation via an acylimine intermediate, is presented in Scheme 3. The intermediate acylimine is formed by the reaction of the aldehyde and urea (or thiourea) and subsequent addition of ketone enolate to the acylimine, followed by cyclization and dehydration, affords the corresponding products.



Scheme 3. Plausible mechanism for the formation of 3,4-dihydropyrimidin-2(1H)-ones/thiones.

Brønsted acidic ionic liquid ([Hmim]HSO_4) can activate the carbonyl groups of aldehyde via hydrogen bonding between the carbonyl group and the cationic (N^+–H) or anionic component (HSO_4^-) of ionic liquid to decrease the energy of transition state. The TMSCl effects may be explained in terms of hard–soft reagent, which activates the carbonyl group of deoxybenzoin and considerably accelerates the reaction.

After reaction, the ionic liquid is easily separated from the reaction medium by washing with distilled water (IL is soluble in water). The washed ionic liquid is distilled under vacuum to recover solvent for reuse in subsequent reactions. After three successive runs, recycled ionic liquid showed no loss of efficiency with regard to reaction time and yield (Table 1).

4. Conclusion

The ionic liquid, [Hmim]HSO_4, in the presence of TMSCl can efficiently catalyze the condensation of an aromatic aldehyde, cyclic or acyclic ketones or β-ketoester and urea (or thiourea) that affords the corresponding 3,4-dihydropyrimidin-2(1*H*)-ones/thiones and hydroquinazoline-2,5-diones/thiones. A simple procedure for product isolation, lack of problems connected with conventional solvent use, descend reaction time with improved yield and use of catalytic amount of TMSCl as compared to other reported methods are advantages of the proposed procedure.

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