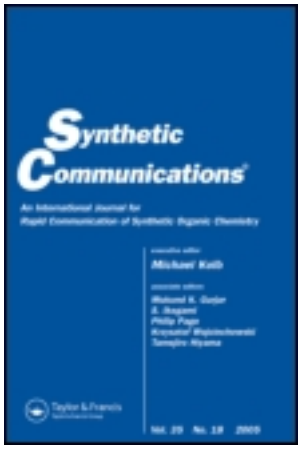


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Pyridinium-Based Brønsted Acidic Ionic Liquid as a Highly Efficient Catalyst for One-Pot Synthesis of Dihydropyrimidinones

Abdol R. Hajipour [a] [b] & Mohadeseh Seddighi [b]

[a] Department of Pharmacology, University of Wisconsin, Medical School, Madison, Wisconsin, USA

[b] Department of Chemistry, Isfahan University of Technology, Isfahan, Iran

Accepted author version posted online: 06 Jul 2011.Version of record first published: 14 Sep 2011.

To cite this article: Abdol R. Hajipour & Mohadeseh Seddighi (2012): Pyridinium-Based Brønsted Acidic Ionic Liquid as a Highly Efficient Catalyst for One-Pot Synthesis of Dihydropyrimidinones, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 42:2, 227-235

To link to this article: http://dx.doi.org/10.1080/00397911.2010.523488

Synthetic Communications®, 42: 227–235, 2012

ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397911.2010.523488

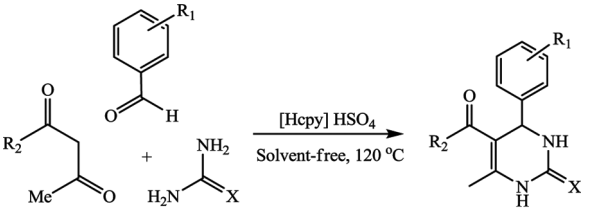
PYRIDINIUM-BASED BRØNSTED ACIDIC IONIC LIQUID AS A HIGHLY EFFICIENT CATALYST FOR ONE-POT SYNTHESIS OF DIHYDROPYRIMIDINONES

Abdol R. Hajipour[1,2] and Mohadeseh Seddighi[2]

[1]*Department of Pharmacology, University of Wisconsin, Medical School, Madison, Wisconsin, USA*

[2]*Department of Chemistry, Isfahan University of Technology, Isfahan, Iran*

GRAPHICAL ABSTRACT



R_2 = OEt or Me X = O or S

Abstract *In this work, the synthesis and characterization of 3-carboxypyridinium hydrogensulfate ([Hcpy]HSO_4) as a new Brønsted acidic ionic liquid are reported. This reusable, inexpensive, and green catalyst was employed for one-pot condensation of 1,3-dicarbonyl compounds, aromatic aldehydes and urea or thiourea for the synthesis of the corresponding 3,4-Dihydropyrimidin-2(1*H*)-ones. The reactions were carried out under solvent-free and green conditions. The procedure gave the products in excellent yields within very short reaction times.*

Keywords Biginelli reaction; Brønsted acidic ionic liquid; 3-carboxypyridinium hydrogensulfate; dihydropyrimidinone; one-pot; solvent-free

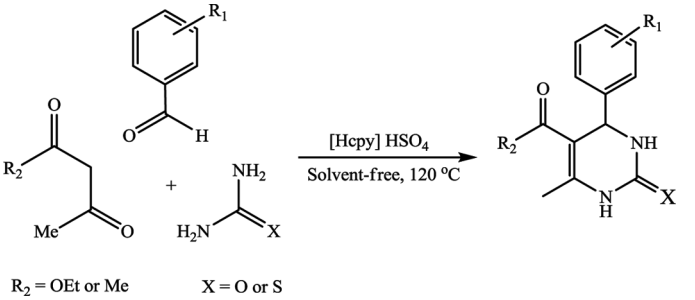
INTRODUCTION

3,4-Dihydropyrimidin-2(1*H*)-ones an most important class of multicomponent reaction products because they have a wide range of biological and pharmacological properties such as antiviral, antibacterial, anticancer, antitumor, and anti-inflammatory activities.[1] Also, these heterocyclic compounds have been employed as calcium channel blocker[2] and selective α_{1A} receptor antagonists.[3]

One of the most important methods for the synthesis of these compounds is the one-pot condensation of aldehydes with ß-ketoester and urea under acidic

Received February 1, 2010.

Address correspondence to Abdol R. Hajipour, Department of Chemistry, Isfahan University of Technology, Isfahan, Iran. E-mail: arhajipour@wisc.edu; haji@cc.iut.ac.in



Scheme 1.

conditions, which was reported for the first time by Biginelli.[4] Many Brønsted and Lewis acid catalysts such as LiBr,[5] $Cu(OTf)_2$,[6] [bmim][$FeCl_4$],[7] 1,1,3,3-tetramethylguanidinium trifluoroacetate (TMGT),[8] $SnCl_2 \cdot 2H_2O$–LiCl,[9] Al_2O_3-SO_3H,[10] $CuCl_2 \cdot 2H_2O$,[11] $InBr_3$,[12] MoO_3/Al_2O_3,[13] Pyrazolidine dihydrochloride,[14] aluminosilicate (AlKIT-5),[15] acidic ionic liquids,[16] ruthenium(III) chloride,[17] and yttria-zirconia-based Lewis acid have been used.[18] However, these methods suffer from disadvantages such as long reaction times, preparation of the starting materials, poor yields, excess reagents or catalysts, organic solvents, and harsh reaction conditions.

Recently, ionic liquids have been used as solvent or catalyst in organic synthesis because of their remarkable properties such as nonflammability; negligible vapor pressure; high thermal, chemical, and electrochemical stability; easy recyclability; and high solvating ability. Brønsted acidic ionic liquids as catalyst or in the dual rule of catalyst and solvent have improved many reactions such as synthesis of benzoxanthenes,[19] oxidation of benzylic alcohol,[20] chemoselective synthesis of 1,1-diacetates,[21] deprotection of S,S-acetals,[22] Fischer indol synthesis,[23] chemoselective thioacetalization of aldehydes,[24] N-Boc protection of amines,[25] azidation of alcohols,[26] and synthesis of 1-amidoalkyl 2-naphthols.[27]

In continuation of our effort to develop efficient methods in organic synthesis, herein we report the synthesis of 3-carboxypyridinium hydrogensulfate [Hcpy] HSO_4, a novel, inexpensive, green, and efficient Brønsted acidic ionic liquid and its application as an efficient catalyst for the one-pot condensation of aromatic aldehydes with ß-ketoester or 1,3-diketone and urea for the synthesis of 3,4-dihydropyrimidin-2-(1H)-ones under solvent-free conditions (Scheme 1).

RESULTS AND DISCUSSION

The studies of Brønsted-acidic ionic liquid showed that the acidity of the ionic liqiuds were dependent on their counteranion and showed that the acidic ionic liquids with $[HSO_4]^-$ as anion are more acidic than other anions such as HPO_4^-, NO_3^-, $CF_3SO_3^-$, *p*TSA^- and PF_6^-.[28] Therefore, we used HSO_4 as anion for our Brønsted-acidic ionic liquid, and two techniques were employed to measure the acidity of this ionic liquid.

In the first method, the pK_a values of 3-carboxypyridinium hydrogensulfate ([Hcpy]HSO_4) was determined using 0.1 mol L^{-1} solution of ionic liquid and was

titrated with 0.05 mol L^{-1} of NaOH. The pH of the solution was measured using a calibrated glass electrode pH meter at 25 °C. As shown in Figure 1 the first change happened at 40 ml of consumed NaOH and the second at 60 ml. It seems that the first change belonged to the two hydrogens with the same pK_a. The pK_a value of carboxyl group of nicotinic acid is 4.9. When ionic liquid is prepared from this compound, the nitrogen is protonated and a delocalized positive charge is created. This suggests that the inductive effect of the positive charge of the imidazolium group affects the acidity of carboxyl-substituted group and the inductive effect drops dramatically when the chain length is increased.[26] Similarly, the positive charge of pyridinium ring can increase the acidity of the carboxyl group. Therefore, it is reasonable to have two hydrogens with the same pK_a belonging to the carboxyl group and HSO_4^-. The third pK_a of this compound was 4.76, which belonged to the NH group.

The Hammett acidity function (H_0) also was studied for this acidic catalyst by the ultraviolet–visible (UV-vis) technique. The Hammett function is defined as

$$H_0 = \mathrm{pK(I)_{aq}} + \log([\mathrm{I}]_s/[\mathrm{IH}^+]_s)$$

where the $pK\ (I)_{aq}$ is the pK_a value of the aqueous solution of the indicator and $[IH^+]_s$ and $[I]_s$ are the molar concentrations of protonated and unprotonated forms of the indicator in the solution, respectively. The 2-nitroaniline ($pK_a = -0.2$) in water was used as an indicator in our procedure. As shown in Figure 2, the maximum absorbance of the unprotonated 2-nitroaniline was observed at 412 nm, and the H_0 of the acidic ionic liquid was 0.8 for 20 mmol/L of catalyst.

To assess the potential of this catalyst for the Biginelli reaction, initially we used the reaction between 3-nitrobenzaldehyde (1 mmol), urea (1.5 mmol), ethylacetoacetate, and ionic liquid as a model and optimized the amounts of ionic liquid, ethylacetoacetate, and solvent and the temperature. The best result was obtained using 7 mol% of ionic liquid and 1 mmol ethylacetoacetate at 120 °C under solvent-free

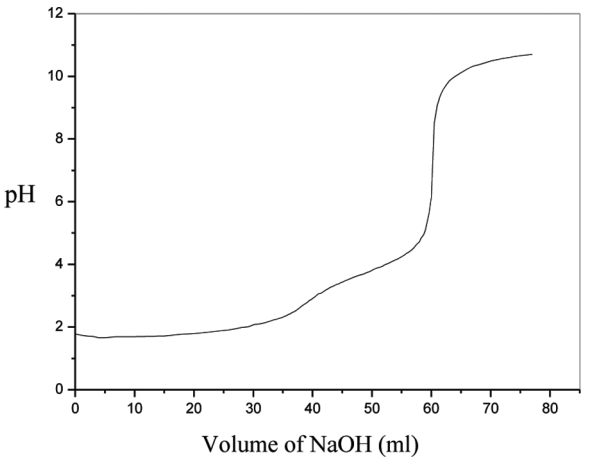


Figure 1. pH meter titration curve of 3-carboxypyridinium hydrogen sulfate [Hcpy]HSO_4.

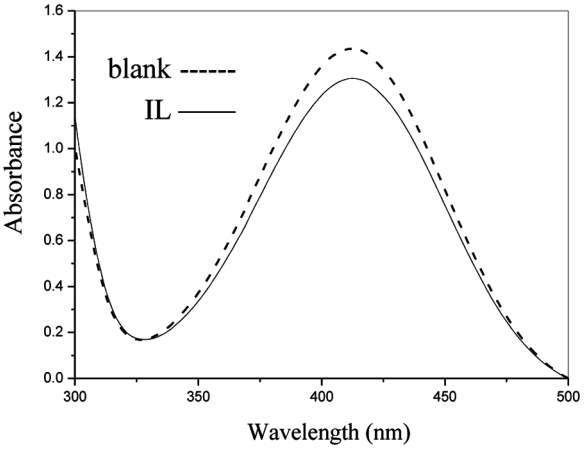


Figure 2. UV-vis absorbances of 2-nitroaniline in the presence of catalyst.

conditions (Table 1). Reaction in different solvents was not suitable for these reactions, and solvent-free conditions gave the best results, as demonstrated in Table 1, entries 1–3. These optimized conditions were applied for various aromatic aldehydes with electron-donating or electron-withdrawing substituent in the *ortho*, *meta*, and *para* positions of the benzene ring to afford the desired 3,4-dihydropyrimidin-2(1*H*)-ones (Table 2). Also, acetylacetone was employed in this procedure, and the corresponding dihydropyrimidones were obtained in good yields within short reaction times. Furthermore, we employed the thiourea to produce the corresponding 3,4-dihydropyrimidin-2-(1H)-thiones in good yields (Table 2, entries 18 and 19).

The aromatic aldehydes with electron-donating as well as electron-withdrawing groups gave the desired products in excellent yields within very short times. Also, the steric effects did not show any significant effect on the yields and reaction times. For example, *ortho*-substituted aromatic aldehydes such as 2-bromobenzaldehyde

Table 1. Optimization of reaction conditions catalysed by Brønsted-acidic ionic liquid[a]

Entry	Ethylacetoacetate (mmol)	IL as catalyst (mol%)	Reaction conditions	Time (min)	Yield (%)[b]
1	1	5	Reflux in ethanol	60	25
2	1	5	Reflux in ethyl acetate	60	10
3	1	5	Reflux in water	60	–
4	1	5	Neat/100 °C	12	61
5	1	5	Neat/120 °C	5	76
6	1.2	5	Neat/120 °C	5	75
7	1.5	5	Neat/120 °C	5	75
8	1	0	Neat/120 °C	120	–
9	1	3	Neat/120 °C	8	60
10	1	7	Neat/120 °C	4	94
11	1	10	Neat/120 °C	4	94

[a]3-Nitrobenzaldehyde (1 mmol), urea (1.5 mmol), ethylacetoacetate, and IL as catalyst.
[b]Isolated yields after purification.

Table 2. Synthesis of 3,4-dihydropyrimidinones under solvent-free conditions catalyzed by [Hcpy]HSO_4 ionic liquid

Entry	R_1	R_2	X	Time (min)	Yield (%)[a]	Melting point (°C)	
						Found	Reported
1	4-NO_2	OEt	O	3	93	206–207	205–207[29]
2	4-Cl	OEt	O	5	84	209–210	209–211[33]
3	4-Br	OEt	O	5	85	218–220	197–198[8]
4	4-CH_3	OEt	O	5	86	211–212	213–216[31]
5	3-NO_2	OEt	O	4	94	226–227	226–228[32]
6	3-OCH_3	OEt	O	5	88	207–208	205–207[33]
7	2-Cl	OEt	O	6	89	213–214	215–218[29]
8	2-Br	OEt	O	8	83	205–207	206–208[32]
9	H	OEt	O	5	91	199–200	200–202[29]
10	2,6-di Cl	OEt	O	4	74	234–235	234–236[9]
11	4-NO_2	CH_3	O	7	85	229–230	230[32]
12	4-Cl	CH_3	O	6	64	216–218	217–218[11]
13	3-OCH_3	CH_3	O	4	76	230–231	—
14	3-NO_2	CH_3	O	4	92	264–266	274–276[11]
15	2-Cl	CH_3	O	5	85	228–230	—
16	2-Br	CH_3	O	5	79	206–208	—
17	H	CH_3	O	4	84	236–237	233–236[32]
18	3-NO_2	OEt	S	10	74	207–208	206–207[29]
19	H	OEt	S	11	68	206–207	205–206[29]

[a]Isolated yields after purification.

Table 3. Comparison result of [Hcpy]HSO_4 with results obtained by other groups for synthesis of 5-ethoxycarbonyl-6-methyl-4-(3-nitrophenyl)-3,4-dihydropyrimidin-2-(1H)-one (Table 2, entry 5)

Entry	Catalyst (mol%)	Reaction conditions	Time	Yield (%)	Ref.
1	LiBr (10)	Reflux in acetonitril	5 h	93	[5]
2	$Cu(OTf)_2$ (1)	Acetonitril/50 °C	6 h	80	[6]
3	[bmim][$FeCl_4$] (10)	Neat/90 °C	3 h	68	[7]
4	TMGT (40)	Neat/100 °C	20 min	93	[8]
5	Al_2O_3-SO_3H (0.23 g)	Reflux in ethanol	6 h	94	[10]
6	$InBr_3$ (10)	Reflux in ethanol	7 h	86	[12]
7	MoO_3/Al_2O_3 (5)	Neat/80 °C	1.5 h	94	[13]
8	[Hcpy] HSO_4 (7)	Neat/120 °C	3 min	94	—

(Table 2, Entry 8) gave 83% yields in comparison to 85% yields of *para*-substituted para with less steric hindrance (Table 2, entry 3)

To evaluate the efficiency of [Hcpy]HSO_4, we compared our results with the reported procedure. As demonstrated in Table 3, our catalyst is superior to reported methods because it uses less catalyst, has very short reaction times, gives good yields, involves green reaction conditions, and has straightforward isolation of the product.

CONCLUSION

In the present study, one-pot condensation of 1,3-dicarbonyl compounds, aromatic aldehydes, and urea or thiourea was employed for the synthesis of the

corresponding 3,4-dihydropyrimidin-2-(1*H*)-ones in the presence of 3-carboxypyridinium hydrogensulfate Brønsted acidic ionic liquid as an inexpensive, efficient, and green catalyst. High catalytic efficiency, very short reaction times, excellent yields, environmentally benign method, easy preparation of catalyst, and straightforward isolation of products are advantages of this method over reported methods.

EXPERIMENTAL

The products are known and were characterized by comparing their infrared (IR), ^{1}H NMR and ^{13}C NMR spectra, and melting points with those reported in the literature. All yields refer to the isolated products after purification. Melting points were measured on an Electrothermal apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded by a 500-MHz instrument in 500 and 125 MHz respectivly in $CDCl_3$ or dimethylsulfoxide (DMSO-d_6) using tetramethylsilane (TMS) as an internal standard. FT-IR spectra were recorded on a Jasco 680-plus spectrophotometer, using the KBr disk technique. UV spectra were recorded on a Jasco V-570 UV-vis/NIR spectrophotometer.

Synthesis of Brønsted Acidic Ionic Liquid (3-Carboxypyridinium Hydrogensulfate [Hcpy] HSO_4)

In a round-bottomed flask, 0.53 ml sulfuric acid (98%, d = 1.84) was added dropwise to a mixture of nicotinic acid (1.23 g, 10 mmol) in 10 ml of dichloromethane on an ice bath. The reaction mixture was stirred at room temperature for 30 min, and then the solvent was evaporated under reduced pressure to obtain 3-carboxypyridinium hydrogensulfate [Hcpy]HSO_4 in quantitative yield. FT-IR (KBr, cm^{-1}): 2465–3270, 1733, 1603, 1531, 1465, 1397, 1271, 1033, 735, 665. ^{1}H NMR (300 MHz, D_2O): $\delta = 7.89$ (m, 1H, CH), 8.68 (m, 1H, CH), 8.72 (m, 1H, CH), 8.99 (m, 1H, CH) ppm. ^{13}C NMR (75 MHz, D_2O): $\delta = 127.67$, 130.41, 127.24, 144.35, 147.17, 164.59 ppm.

General Procedure for the Synthesis of 3,4-Dihydropyrimidin-2-(1*H*)-ones

A mixture of aldehyde (1 mmol), urea or thiourea (1.5 mmol), ethylacetoacetate or acetylacetone (1 mmol), and ionic liquid (7 mol%) in a round-bottomed flask was stirred at 120 °C for the appropriate time (Table 2). After completion of the reaction as mentioned by thin-layer chromatography (TLC), the solidified reaction mixture was cooled to room temperature and 5 ml cool water were added. The mixture was stirred for 5 min, and the product was filtered off. The products were purified by recrystallization from aqueous ethanol.

Selected Data

4-(2-Bromophenyl)-5-ethoxycarbonyl-6-methyl-3,4-dihydropyrimidin-2-(1H)-one (Table 2, Entry 8). FT-IR (KBr, cm^{-1}): 3347, 3227, 1695, 1638, 1567, 1450, 1371.^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.01$ (3H, t, $J = 7.1$ Hz), 2.39 (3H, s),

3.95 (2H, q, $J = 7$ Hz), 5.78 (1H, d, $J = 2.6$ Hz), 5.86 (1H, s, NH), 7.08 (1H, m), 7.21 (2H, m), 7.5 (1H, d, $J = 8.3$), 8.69 (1H, s, NH).

5-Acetyl-4-(3-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2-(1H)-one (Table 2, Entry 13). FT-IR (KBr, cm^{-1}): 3340, 3273, 3051, 1714, 1678, 1599, 1487, 1453, 1330. ^{1}H NMR (500 MHz, $CDCl_3$/DMSO-d_6): $\delta = 2.09$ (3H, s), 2.34 (3H, s), 2.76 (3H, s), 5.36 (1H, s), 5.97 (1H, s, NH), 6.78 (1H, d, $J = 7.4$ Hz), 6.83 (1H, s), 6.87 (1H, d, $J = 7.6$ Hz), 7.23 (1H, m), 7.86 (1H, s, NH).

5-Acetyl-6-methyl-4-(3-nitrophenyl)-3,4-dihydropyrimidin-2-(1H)-one (Table 2, Entry 14). FT-IR (KBr, cm^{-1}): 3348, 3272, 3061, 1681, 1600, 1530, 1436. ^{1}H NMR (500 MHz, 500 MHz, $CDCl_3$/DMSO-d_6): $\delta = 2.12$ (3H, s), 2.29 (3H,s), 5.43 (1H, d, $J = 3.4$ Hz), 6.93 (1H, s, NH), 7.38 (1H, t, $J = 7.9$ Hz), 7.58 (1H, d, $J = 7.7$ Hz), 7.99 (1H, d, $J = 7.8$ Hz), 8.14 (1H, s), 8.65 (1H, s, NH).

5-Acetyl-4-(2-chlorophenyl)-6-methyl-3,4-dihydropyrimidin-2-(1H)-one (Table 2, Entry 15). FT-IR (KBr, cm^{-1}): 3341, 3292, 1704, 1622, 1551, 1461, 1333.^{1}H NMR (500 MHz, $CDCl_3$/DMSO-d_6): $\delta = 1.97$ (3H, s), 2.52 (3H, s), 5.77 (1H,s), 5.81 (1H, s, NH), 7.18 (3H, m), 7.33 (1H, m), 8.38 (1H, s, NH).

ACKNOWLEDGMENTS

We gratefully acknowledge the funding support received for this project from the Isfahan University of Technology (IUT), Iran (A. R. H.). Further financial support from the Center of Sensor and Green Chemistry Research (IUT) is gratefully acknowledged.

REFERENCES

1. (a) Russowsky, D.; Canto, R. F.; Sanches, S. A.; D'Oca, M. J.; Fátima, A. D.; Pilli, R. A.; Kohn, L. K.; Antônio, M. A.; Carvalho, J. A. Synthesis and differential antiproliferative activity of Biginelli compounds against cancer cell lines: Monastrol, oxo-monastrol and oxygenated analogues. *Bioorg. Chem.* **2006**, *34*, 173–182; (b) Kappe, C. O. Biologically active dihydropyrimidones of the Biginelli-type—A literature survey. *Eur. J. Med. Chem.* **2000**, *35*, 1043–1052.
2. (a) Atwal, K. S.; Swanson, B. N.; Unger, S. E.; Floyd, D. M.; Moreland, S.; Hedberg, A.; O'Reilly, B. C. Dihydropyrimidine calcium channel blockers: 3-Carbamoyl-4-aryl-1,2,3,4-tetrahydro-6-methyl-5 pyrimidinecarboxaycliidc esters as orally effective antihypertensive agents. *J. Med. Chem.* **1991**, *34*, 806–811; (b) Rovnyak, G. C.; Atwal, K. S.; Hedberg, A.; Kimball, S. D.; Moreland, S.; Gougoutas, J. Z.; O'Reilly, B. C.; Schwartz, J.; Malley, M. F. Dihydropyrimidine calcium channel blockers, 4: Basic 3-substituted-4-aryl-1,4-dihydropyrimidine-5-carboxyaliccid esters: Potent antihypertensive agents. *J. Med. Chem.* **1992**, *35*, 3254–3263; (c) Rovnyak, G. C.; Kimball, S. D.; Beyer, B.; Cucinotta, G.; DiMarco, J. D.; Gougoutas, J.; Hedberg, A.; Malley, M.; McCarthy, J. P.; Zhang, R.; Morelande, S. Calcium entry blockers and activators: Conformational and structural determinations of dihydropyrimidine calcium channel modulators. *J. Med. Chem.* **1996**, *38*, 119–129.
3. (a) Nagarathnam, D.; Miao, S. W.; Lagu, B.; Chiu, G.; Fang, J.; Dhar, T. G. M.; Zhang, J.; Tyagarajan, S.; Marzabadi, M. R.; Zhang, F.; Wong, W. C.; Sun, W.; Tian, D.; Wetzel, J. M.; Forray, C.; Chang, R. S. L.; Broten, T. P.; Ransom, R. W.; Schorn, T. W.; Chen, T. B.; O'Malley, S.; Kling, P.; Schneck, K.; Bendesky, R.; Harrell, C. M.; Vyas, K. P.;

Gluchowski, C. Design and synthesis of novel α_{1A} adrenoceptor-selective antagonists, 1: Structure–activity relationship in dihydropyrimidinones. *J. Med. Chem.* **1999**, *42*, 4764–4777; (b) Barrow, J. C.; Nantermet, P. G.; Selnick, H. G.; Glass, K. L.; Rittle, K. E.; Gilbert, K. F.; Steele, T. G.; Homnick, C. F.; Freidinger, R. M.; Ransom, R. W.; Kling, P.; Reiss, D.; Broten, T. P.; Schorn, T. W.; Chang, R. S. L.; O'Malley, S. S.; Olah, T. V.; Ellis, J. D.; Barrish, A.; Kassahun, K.; Leppert, P.; Nagarathnam, D.; Forray, C. In vitro and in vivo evaluation of dihydropyrimidinone C-5 amides as potent and aelective α_{1A} receptor antagonists for the treatment of benign prostatic hyperplasia. *J. Med. Chem.* **2000**, *43*, 2703–2718.

4. Biginelli, P. Aldureides of ethylic acetoacetate and ethylic oxalacetate. *Gazz. Chim. Ital.* **1893**, *23*, 360.
5. Maiti, G.; Kundu, P.; Guin, C. One-pot synthesis of dihydropyrimidinones catalysed by lithium bromide: An improved procedure for the Biginelli reaction. *Tetrahedron Lett.* **2003**, *44*, 2757–2758.
6. Paraskar, A. S.; Dewkar, G. K.; Sudalai, A. $Cu(OTf)_2$: A reusable catalyst for high-yield synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones. *Tetrahedron Lett.* **2003**, *44*, 3305–3308.
7. Chen, X.; Peng, Y. Chloroferrate(III) ionic liquid: Efficient and recyclable catalyst for solvent-free synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones. *Catal. Lett.* **2008**, *122*, 310–313.
8. Shaabani, A.; Rahmati, A. Ionic liquid–promoted efficient synthesis of 3,4-dihydropyrimidin-2-(1H)-ones. *Catal. Lett.* **2005**, *100*, 177–179.
9. Shailaja, M.; Rao, B. V.; Parvathi, N. Simple protocol for the synthesis of 3,4-dihydropyrimidin-2(1H)-ones using $SnCl_2 \cdot 2H_2O$-LiCl as an inexpensive catalyst system. *Synth. Commun.* **2004**, *34*, 1559–1564.
10. (a) Salehi, P.; Dabiri, M.; Zolfigol, M. A.; Bodaghi Fard, M. A. Silica sulfuric acid: An efficient and reusable catalyst for the one-pot synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones. *Tetrahedron Lett.* **2004**, *44*, 2889–2891; (b) Shaterian, H. R.; Hosseinian, A.; Ghashang, M. An efficient synthesis of multisubstituted 3,4-Dihydropyrimidin-2(1H)-ones/thiones under solvent-free microwave irradiation using alumina sulfuric acid. *Phosphorus, Sulfur Silicon Relat. Elem.* **2009**, *184*, 197–205.
11. Xu, F.; Wang, J.; Tian, Y. New procedure for one-pot synthesis of 3,4-dihydropyrimidin-2(1H)-ones by Biginelli reaction. *Synth. Commun.* **2008**, *38*, 1229–1310.
12. Fu, N.; Yuan, Y.; Cao, Z.; Wang, S.; Wang, J.; Peppe, C. Indium (III) bromide–catalyzed preparation of dihydropyrimidinones: Improved protocol conditions for the Biginelli reaction. *Tetrahedron* **2002**, *58*, 4801–4807.
13. Jain, S. L.; Prasad, V. V. D. N.; Sain, B. Alumina-supported MoO_3: An efficient and reusable heterogeneous catalyst for synthesis of 3,4-dihydropyridine-2(1H)-ones under solvent-free conditions. *Catal. Commun.* **2008**, *9*, 499–503.
14. Suzuki, I.; Iwata, Y.; Takeda, K. Biginelli reactions catalyzed by hydrazine-type organocatalyst. *Tetrahedron Lett.* **2008**, *49*, 3238–3241.
15. Shobha, D.; Chari, M. A.; Mano, A.; Selvan, S. T.; Mukkanti, K.; Vinu, A. Synthesis of 3,4-dihydropyrimidin-2-ones (DHPMs) using mesoporous aluminosilicate (AlKIT-5) catalyst with cage-type pore structure. *Tetrahedron* **2009**, *65*, 10608–10611.
16. Gui, J. Z.; Liu, D.; Wang, C.; Lu, F.; Lian, J. Z.; Jiang, H.; Sun, Z. L. One-pot synthesis of 3,4-dihydropyrimidin-2(1H)-ones catalyzed by acidic ionic liquids under solvent-free conditions. *Synth. Commun.* **2009**, *39*, 3436–3443.
17. De, S. K.; Gibbs, R. A. Ruthenium(III) chloride–catalyzed one-pot synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones under solvent-free conditions. *Synthesis* **2005**, 1748–1750.
18. Ramalingam, S.; Kumar, P. Yttria-zirconia-based Lewis acid catalysis of the biginelli reaction: An efficient one-pot Synthesis of 3,4-dihydropyrimidin-2-(1H)-ones. *Synth. Commun.* **2009**, *39*, 1299–1309.

19. Gong, K.; Fang, D.; Wang, H.; Zhou, X.; Liu. The one-pot synthesis of 14-alkyl- or aryl-14H-dibenzo[a,j]xanthenes catalyzed by task-specific ionic liquid. *Dyes Pigments* **2009**, *80*, 30–33.
20. Hajipour, A. R.; Rafiee, F.; Ruoho, A. E. Facile and selective oxidation of benzylic alcohols to their corresponding carbonyl compounds with sodium nitrate in the presence of brønsted acidic ionic liquids. *Synlett* **2007**, 1118–1120.
21. Hajipour, A. R.; Khazdooz, L.; Ruoho, A. E. Brønsted acidic ionic liquid as an efficient catalyst for chemoselective synthesis of 1,1-diacetates under solvent-free conditions. *Catal. Commun.* **2008**, *9*, 89–96.
22. Hajipour, A. R.; Khazdooz, L.; Ruoho, A. E. Brönsted acidic ionic liquid/NH_4NO_3 as a new reagent for the deprotection of S,S-acetals under solvent-free conditions. *J. Sulfur Chem.* **2009**, *30*, 46–52.
23. Xu, D.; Yang, W.; Luo, S.; Wang, B.; Wu, J.; Xu, Z. Fischer indole synthesis in Brønsted acidic ionic liquids: A green, mild, and regiospecific reaction system. *Eur. J. Org. Chem.* **2007**, 1007–1012.
24. Hajipour, A. R.; Azizi, G.; Ruoho, A. E. An efficient method for chemoselective thioacetalization of aldehydes in the presence of a catalytic amount of acidic ionic liquid under solvent-free conditions. *Synlett* **2009**, 1974–1978.
25. Sunitha, S.; Kanjilal, S.; Reddy, P. S.; Prasad, R. B. N. An efficient and chemoselective Brønsted acidic ionic–liquid-catalyzed N-Boc protection of amines. *Tetrahedron Lett.* **2008**, *49*, 2527–2532.
26. Hajipour, A. R.; Rajaei, A.; Ruoho, A. E. A mild and efficient method for preparation of azides from alcohols using acidic ionic liquid [H-NMP]HSO_4. *Tetrahedron Lett.* **2009**, *50*, 708–711.
27. Hajipour, A. R.; Ghayeb, Y.; Sheikhan, N.; Ruoho, A. E. Brønsted acidic ionic liquid as an efficient and reusable catalyst for one-pot synthesis of 1-amidoalkyl 2-naphthols under solvent-free conditions. *Tetrahedron Lett.* **2009**, *50*, 5649–5651.
28. (a) Xing, H.; Wang, T.; Zhou, Z.; Dai, Y. The sulfonic acid–functionalized ionic liquids with pyridinium cations: Acidities and their acidity–catalytic activity relationships. *J. Mol. Catal. A: Chem.* **2007**, *264*, 53–59; (b) Gu, Y.; Zhang, J.; Duan, Z.; Deng, Y. Pechmann reaction in non-chloroaluminate acidic ionic liquids under solvent-free conditions. *Adv. Synth. Catal.* **2005**, *347*, 512–516; (c) Li, X.; Eli, W.; Li, G. Solvent-free synthesis of benzoic esters and benzyl esters in novel Brønsted acidic ionic liquids under microwave irradiation. *Catal. Commun.* **2008**, *9*, 2264–2268; (d) Xu, D.; Yang, W.; Luo, S.; Wang, B.; Wu, J.; Xu, Z. Fischer indole synthesis in Brønsted acidic ionic liquids: A green, mild, and regiospecific reaction system. *Eur. J. Org. Chem.* **2007**, *1007*, 1012; (e) Weng, J.; Wang, C.; Li, H.; Wang, Y. Novel quaternary ammonium ionic liquids and their use as dual solvent-catalysts in the hydrolytic reaction. *Green Chem.* **2006**, *8*, 96–99.
29. Fei, Z.; Zhao, D.; Geldbach, T. J.; Scopelliti, R.; Dyson, P. J. Brønsted acidic ionic liquids and their zwitterions: Synthesis, characterization, and pK_a determination. *Chem. Eur. J.* **2004**, *10*, 4886–4893.
30. Kumar, A.; Maurya, R. A. Synthesis of 3,4-dihydropyrimidin-2(1H)-ones using Ziegler–Natta catalyst system under solvent-free conditions. *J. Mol. Catal. A: Chem.* **2007**, *272*, 53–56.
31. Yu, Y.; Liu, D.; Liu, C.; Luo, G. One-pot synthesis of 3,4-dihydropyrimidin-2(1H)-ones using chloroacetic acid as catalyst. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 3508–3510.
32. Ma, Y.; Qian, C.; Wang, L.; Yang, M. Lanthanide triflate–catalyzed Biginelli reaction: One-pot synthesis of dihydropyrimidinones under solvent-free conditions. *J. Org. Chem.* **2000**, *65*, 3864–3868.
33. Shaabani, A.; Bazgir, A.; Teimouri, F. Ammonium chloride–catalyzed one-pot synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones under solvent-free conditions. *Tetrahedron Lett.* **2003**, *44*, 857–859.