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Journal of Molecular Catalysis A: Chemical 258 (2006) 133–138
JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL
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One-pot synthesis of Biginelli and Hantzsch products catalyzed by non-toxic ionic liquid (BMImSac) and structural determination of two products

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Received 12 March 2006; received in revised form 15 May 2006; accepted 15 May 2006
Available online 23 June 2006

Abstract

In this paper, both 1,4-dihydropyridinones (Hantzsch products) and 3,4-dihydropyrimidinones (Biginelli products) are synthesized in one-pot of aldehydes, β-dicarbonyl compounds and urea, catalyzing by non-toxic room temperature ionic liquid 1-*n*-butyl-3-methylimidazolium saccharinate (BMImSac). The ionic liquid (BMImSac) is environmentally benign associated with ionic liquid with F^-. In order to improve the yield and selectivity, the effects of the mole proportion of reactants and solvents are investigated. Interestingly, by increasing the amount of ethyl acetoacetate or utilizing water as solvent, an unexpected by-product, Hantzsch product which is distinct from Biginelli product, is generated. All Biginelli and Hantzsch products are simultaneously purified and characterized by IR, ^{1}H NMR and ^{13}C NMR, of which one Biginelli product (**4h**) and one Hantzsch product (**5b**) are structurally determinated by X-ray single crystal diffraction. The crystal data for **4h**: triclinic system, *P*-1 space group, $a = 7.515(3)$ Å, $b = 9.011(4)$ Å, $c = 11.218(5)$ Å, $\alpha = 106.288(6)^\circ$, $\beta = 104.644(6)^\circ$, $\gamma = 100.234(6)^\circ$, $Z = 2$, $V = 679.7(5)$ Å^3, $D_c = 1.36$ g/cm^3, $R_1 = 0.0603$. The crystal data for **5b**: monoclinic system, *P*2(1)/*c* space group, $a = 9.765(3)$ Å, $b = 7.391(2)$ Å, $c = 24.795(7)$ Å, $\beta = 93.669(5)^\circ$, $Z = 4$, $V = 1785.7(9)$ Å^3, $D_c = 1.292$ g/cm^3, $R_1 = 0.0440$.

Keywords: Ionic liquid; Biginelli reaction; Hantzsch product; Dihydropyrimidinones; One-pot synthesis

1. Introduction

Considerable attentions are paid on the usage of room temperature ionic liquids (RTILs) in procedure of organic reactions, due to their lack of vapor pressure, environmentally benign, high catalysis and ease of reuse [1]. In the past decade, a variety of classic reactions have been successfully investigated by utilizing RTILs as catalyst, such as Friedel–Crafts reaction, Heck reaction, Suzuki reaction, Diels–Alder reaction, Wittig reaction, Mannich reaction, oxidation and Beckmann rearrangement reaction [2]. Since the Biginelli products, dihydropyrimidinone, can act as calcium channel blocker, antihypertensive agents and α-1a-antagonist [3], the Biginelli reaction [4], a one-pot but low yield (20–50%) condensation of β-dicarbonyl compounds with aldehydes and urea or thiourea in the presence of catalytic amount of acid, has increasingly attracted intense interest. In general, Lewis acids including $BF_3{\cdot}OEt_2$ [5], $CdCl_2$ [6], $NiCl_2{\cdot}6H_2O$ or $FeCl_3{\cdot}6H_2O$ [7], $In(OTf)_3$ [8], $InBr_3$ [9], $ZnCl_2$ [10], $RuCl_3$ [11], $ZrCl_4$ [12], $CeCl_3{\cdot}7H_2O$ [13], $Mn(OAc)_3{\cdot}2H_2O$ [14], $Yb(OTf)_3$ [15], $La(OTf)_3$ [16], $Sc(OTf)_3$ [17] and other catalysts such as 12-tungstophosphoric acid [18], natural HEU type zeolite [19], silicagel supported sodium hydrogensulfate [20], *N*-bromosuccinimide [21] and iodine [22] can also catalyze the reaction. In addition, new methods, including microwave irradiation [23] and synthesis of solid phase [24], are also employed. Peng and Deng [25] have been reported by using $BMImBF_4$ and $BMImPF_6$ to catalyze the Biginelli reaction at high yield and high selectivity. However, Swatlowski et al. [26] recently refer to what ILs with fluorous anions can do harm to the environment.

In this paper, we attempt to use ILs without fluorous anions—1-*n*-butyl-3-methylimidazolium saccharinate (BMImSac) to catalyze the Biginelli reaction. By modifying the mole proportion of reactants, besides the Biginelli products another type of products are obtained. Through spectrum and X-ray single crystal diffraction analysis, they are demonstrated as Hantzsch products. Stadler and Kappe [27] have reported this phenomenon under the microwave irradiation, where only one

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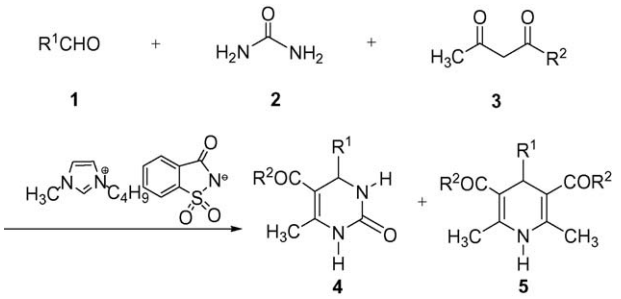
doi:10.1016/j.molcata.2006.05.028



Scheme 1.

dihydropyridine was obtained as a by-product. Through changing the substitutes on the aldehyde, we discuss the phenomenon that both Biginelli and Hantzsch products are obtained in detail (Scheme 1). In the meantime, one Biginelli product (**4h**) and one Hantzsch product (**5b**) are structurally determinated by X-ray single crystal diffraction.

2. Experimental

2.1. General

Melting point was determined with RY-1 apparatus in open glass capillaries and was uncorrected. IR spectra were recorded on a Nicolet 510P FT-IR spectrometer using KBr pellets or film. NMR spectra were recorded on a JEOL JMR-ECP 600M in DMSO-d_6 with TMS as an internal standard. Elemental analyses were performed on Elemento EL-III. The crystals data were collected on BRUKER SMART 1000 CCD diffractometer using Mo Kα radiation (λ = 0.71073 Å) at room temperature.

2.2. Preparation of the RTILs—1-n-butyl-3-methylimidazolium saccharinate (BMImSac)

The sodium saccharinate (27.0 g, 0.112 mol) was added into a solution of 1-*n*-butyl-3-methylimidazolium bromide (BMImBr) (24.6 g, 0.112 mol) in 100 mL acetone at room temperature. After stirring for 30 h, the reaction mixture was filtered through a plug of celite (l = 2 cm). The volatiles were removed under reduced pressure overnight. Viscous oil was yielded with 31.0 g (86%). IR (film) υ: 766, 951, 1148, 1166, 1260, 1332, 1458, 1580, 1633, 2873, 2961, 3097, 3147 cm^{-1}; ^{1}H NMR (DMSO-d_6, 600 MHz) δ: 0.89 (t, 3H, J = 7.6 Hz), 1.25 (m, 2H), 1.76 (m, 2H), 3.88 (s, 1H), 4.19 (t, 2H, J = 7.0 Hz), 7.59–7.61 (m, 4H), 7.75 (s, 1H), 7.82 (s, 1H), 9.24 (s, 1H). ^{13}C NMR (DMSO-d_6, 600 MHz) δ: 13.23, 18.73, 31.33, 35.73, 48.44, 119.09, 122.23, 122.45, 123.55, 128.25, 130.99, 131.56, 134.78, 136.50, 167.88.

2.3. General experimental procedure

The typical synthesis was to mix aldehydes (20 mmol), β-dicarbonyl compounds (30 mmol), urea (30 mmol) and BMImSac (0.1 mmol) in a 100 mL flask, and heat at 100 °C for 2–4 h (monitored by TLC). After the solid product was filtered, washed with water and dried, the primary product was obtained. The pure products **4** and **5** were isolated via flash column chromatography (petroleum ether/ethyl acetate, 3:1).

2.3.1. 5-Ethoxycarbonyl-4-phenyl-6-methyl-3,4-dihydropyrimidin-2(1H)-one (*4a*)

IR (KBr) υ: 1094, 1225, 1648, 1702, 1725, 3119, 3247 cm^{-1}. ^{1}H NMR (DMSO-d_6, 600 MHz) δ: 1.09 (t, J = 7.0 Hz, 3H), 2.25 (s, 3H), 3.98 (q, J = 7.0 Hz, 2H), 5.14 (d, J = 3.3 Hz, 1H), 7.23–7.34 (m, 5H, ArH), 7.75 (s, 1H, NH), 9.21 (s, 1H, NH). ^{13}C NMR (DMSO-d_6, 600 MHz) δ: 14.17, 17.78, 53.95, 59.19, 99.23, 126.25, 127.27, 128.40, 144.87, 148.38, 152.13, 165.33. Anal. Calcd. for $C_{14}H_{16}N_2O_3$ (%): C, 64.60; H, 6.20; N, 10.76. Found: C, 64.42; H, 6.16; N, 10.73.

2.3.2. 4-Phenyl-2,6-dimethyl-1,4-dihydro-3,5-pyridinedicarboxylate (*5a*)

IR (KBr) υ: 1093, 1213, 1489, 1652, 1688, 3342 cm^{-1}. ^{1}H NMR (DMSO-d_6, 600 MHz) δ: 1.12 (t, J = 7.0 Hz, 6H), 2.26 (s, 6H), 3.98 (m, 4H), 4.86 (s, 1H), 7.09–7.21 (m, 5H, ArH), 8.81 (s, 1H, NH). ^{13}C NMR (DMSO-d_6, 600 MHz) δ: 14.15, 18.21, 38.83, 58.96, 101.81, 125.85, 127.33, 127.82, 145.33, 148.15, 166.92. Anal. Calcd. for $C_{19}H_{23}NO_4$ (%): C, 69.28; H, 7.04; N, 4.25. Found: C, 69.03; H, 7.00; N, 4.23.

2.3.3. 5-Ethoxycarbonyl-4-(4-fluorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one (*4b*)

IR (KBr) υ: 1092, 1223, 1649, 1702, 1726, 3122, 3245 cm^{-1}. ^{1}H NMR (DMSO-d_6, 600 MHz) δ: 1.10 (t, J = 7.0 Hz, 3H), 2.28 (s, 3H), 3.99 (q, J = 7.0 Hz, 2H), 5.16 (d, J = 3.7 Hz, 1H), 7.18–7.27 (m, 4H, ArH), 7.82 (s, 1H, NH), 9.36 (s, 1H, NH). ^{13}C NMR (DMSO-d_6, 600 MHz) δ: 14.05, 17.25, 53.62, 59.34, 100.28, 115.44, 115.95, 128.43, 128.48, 139.75, 145.22, 152.87, 160.72 and 162.33 (split), 165.13. Anal. Calcd. for $C_{14}H_{15}FN_2O_3$ (%): C, 60.43; H, 5.43; N, 10.07. Found: C, 60.23; H, 5.41; N, 10.04.

2.3.4. 4-(4-Fluorophenyl)-2,6-dimethyl-1,4-dihydro-3,5-pyridinedicarboxylate (*5b*)

IR (KBr) υ: 1091, 1211, 1490, 1653, 1688, 3343 cm^{-1}. ^{1}H NMR (DMSO-d_6, 600 MHz) δ: 1.10 (t, J = 7.0 Hz, 6H), 2.25 (s, 6H), 4.00 (m, 4H), 4.89 (s, 1H), 7.15–7.28 (m, 4H, ArH), 8.83 (s, 1H, NH). ^{13}C NMR (DMSO-d_6, 600 MHz) δ: 14.11, 18.07, 38.90, 58.93, 101.58, 125.85, 127.14, 127.57, 145.38, 158.69, 166.16. Anal. Calcd. for $C_{19}H_{22}FNO_4$ (%): C, 65.69; H, 6.38; N, 4.03. Found: C, 65.48; H, 6.35; N, 4.02.

2.3.5. 5-Acetyl-4-phenyl-6-methyl-3,4-dihydropyrimidin-2(1H)-one (*4l*)

IR (KBr) υ: 1237, 1602, 1678, 1702, 3145, 3262 cm^{-1}. ^{1}H NMR (DMSO-d_6, 600 MHz) δ: 2.10 (s, 3H), 2.29 (s, 3H), 5.25 (d, J = 3.7 Hz, 1H), 7.23–7.34 (m, 5H, ArH), 7.84 (s, 1H, NH), 9.20 (s, 1H, NH). ^{13}C NMR (DMSO-d_6, 600 MHz) δ: 18.93, 30.34, 53.79, 109.57, 126.43, 127.35, 128.52, 144.24, 148.15, 152.13, 194.25. Anal. Calcd. for $C_{13}H_{14}N_2O_2$ (%): C, 67.81; H, 6.13; N, 12.17. Found: C, 67.58; H, 6.09; N, 12.13.

Table 1
Reaction of benzaldehyde, ethyl acetoacetate and urea under different conditions

Entry	The proportion[a]	IL (mmol)	Solvent	Time (h)	Final product(s)	Yield (%)[b]
1	1:1:1.5	0	None	6	None	0
2	1:1:1.5	0.1	None	2	**4**	90
3	1:1:1.5	0.2	None	2	**4**	87
4	1:1:1.5	0.1	THF	6	None	0
5	1:1:1.5	0.1	CH_2Cl_2	6	None	0
6	1:1:1.5	0.1	Ethanol	6	**4**	81
7	1:1:1.5	0.1	Water	6	**4** + **5**	28 + 13
8	1:1:1.5	0.1	Ethanol/water[c]	6	**4** + **5**	35 + 18
9	1:1.5:1.5	0.1	Ethanol/water	6	**4** + **5**	36 + 25
10	1:1.5:1.5	0.1	None	2	**4** + **5**	60 + 24
11	1:2:1.5	0.1	None	2	**4** + **5**	30 + 19

[a] The proportion of benzaldehyde, ethyl acetoacetate and urea.
[b] Isolated yield, based on benzaldehyde.
[c] The proportion of ethanol/water is 1:1.

2.3.6. 4-Phenyl-2,6-dimethyl-3,5-diacetyl-1, 4-dihydropyridine (**5l**)

IR (KBr) υ: 1380, 1462, 1638, 1675, 3328 cm^{-1}. ^1H NMR (DMSO-d_6, 600 MHz) δ: 2.19 (s, 6H), 2.27 (s, 6H), 5.03 (s, 1H), 7.09–7.22 (m, 5H, ArH), 8.91 (s, 1H, NH). ^{13}C NMR (DMSO-d_6, 600 MHz) δ: 19.08, 30.18, 38.68, 112.56, 126.00, 127.10, 128.20, 144.44, 147.13, 196.38. Anal. Calcd. for $C_{17}H_{19}NO_2$ (%): C, 75.81; H, 7.11; N, 5.20. Found: C, 75.62; H, 7.08; N, 5.18.

2.4. Structural determination of Biginelli product (**4h**) and Hantzsch product (**5b**)

The X-ray single crystal diffraction measurement was performed on the BRUKER SMART 1000 CCD diffracometer equipped with the graphite monochromatized Mo Kα radiation ($\lambda = 0.71073$ Å) at $T = 293$ K. The structures of both compounds were solved by the direct-method routine of SHELXS-97 and refined by full-matrix least-squares method on F^2 by using SHELXL-97.

A single crystal of 0.24 mm × 0.12 mm × 0.08 mm of **4h** was selected. A total of 3705 reflections, of which 2368 were unique [R(int) = 0.0157], were collected in the region $2.00^\circ < \theta < 25.03^\circ$. All non-hydrogen atoms were refined anisotropically. $R_1 = 0.0603$ for 2368 reflections with $F_o > 2\sigma(F_o)$ and $R_1 = 0.0922$ for all 3705 reflections, $wR_2(F^2) = 0.1801$, GOF = 1.081. The largest difference map peak and hole were 0.865 and $-0.306\ e\ Å^{-3}$, respectively.

A single crystal of 0.24 mm × 0.20 mm × 0.14 mm of **5b** was selected. A total of 10,063 reflections, of which 3674 were unique [R(int) = 0.035], were collected in the region $1.65^\circ < \theta < 26.46^\circ$. All non-hydrogen atoms were refined anisotropically. $R_1 = 0.044$ for 3674 reflections with $F_o > 2\sigma(F_o)$ and $R_1 = 0.0822$ for all 10,063 reflections, $wR_2(F^2) = 0.1096$, GOF = 1.007. The largest difference map peak and hole were 0.226 and $-0.177\ e\ Å^{-3}$, respectively.

CCDC 274115 for **4h** and CCDC 253641 for **5b** contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge

Table 2
Synthesis of Biginelli and Hantzsch products by the condensation of aldehydes, β-dicarbonyl compounds and urea under solventless catalyzed by IL[a]

	R^1	R^2	Time (h)	Yield (%)[b]	MP (°C)	
				4 + **5**	**4**	**5**
a	C_6H_5	OEt	2	60 + 24	204–205 [5]	157–159 [31]
b	4-(F)-C_6H_4	OEt	2	64 + 26	184–186 [5]	150–152 [33]
c	4-(Cl)-C_6H_4	OEt	3	52 + 30	208–211 [5]	147–148 [31]
d	4-(OCH_3)-C_6H_4	OEt	2.5	55 + 28	206–208 [5]	161–163 [31]
e	4-(NO_2)-C_6H_4	OEt	3	67 + 21	209–212 [5]	129–131 [31]
f	4-(NMe_2)-C_6H_4	OEt	4	46 + 18	230–232 [12]	203–205 [32]
g	4-(OH)-C_6H_4	OEt	2	58 + 26	201–202 [12]	229–232 [34]
h	2-(F)-C_6H_4	OEt	2	62 + 22	233–235 [29]	205–207 [34]
I	2-(Cl)-C_6H_4	OEt	2.5	65 + 20	226–228 [9]	125–126 [34]
j	2-(OCH_3)-C_6H_4	OEt	3	54 + 23	262–265 [30]	140–142 [34]
k	2-Furyl	OEt	2.5	69 + 22	206–208 [12]	163–164 [31]
l	C_6H_5	CH_3	2	72 + 15	211–213 [5]	183–184 [34]

[a] Products MPs and their IR and ^1H NMR were compared with those reported in the literature.
[b] Isolated yield, based on aldehydes.

Table 3
Data collection parameters and crystal data for the compounds **4h** and **5b**

	Compound	
	4h	**5b**
Empirical formula	$C_{14}H_{15}FN_2O_3$	$C_{19}H_{22}FNO_4$
Formula weight	278.28	347.38
Crystal system	Triclinic	Monoclinic
Space group	*P*-1	*P*2(1)/*c*
a (Å)	7.515(3)	9.765(3)
b (Å)	9.011(4)	7.391(2)
c (Å)	11.218(5)	24.795(7)
α (°)	106.288(6)	90
β (°)	104.644(6)	93.669(5)
γ (°)	100.234(6)	90
Volume (Å^3)	679.7(5)	1785.7(9)
Z	2	4
Density calcd. (g/cm^3)	1.360	1.292
Absorption coefficient (mm^{-1})	0.105	0.097
F(0 0 0)	292	736
Crystal size (mm)	0.24 × 0.12 × 0.08	0.24 × 0.20 × 0.14
Temperature (K)	293(2)	293(2)
θ ranges (°)	2.00–25.03	1.65–26.46
Index range	$-8 \le h \le 8$, $-10 \le k \le 8$, $-13 \le l \le 13$	$-8 \le h \le 12$, $-9 \le k \le 9$, $-25 \le l \le 30$
Collected reflections	3705	10063
Independent reflections	2368	3674
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/restrains/parameters	2368/1/183	3674/1/233
Final *R* indices [$I > 2\sigma(I)$]	$R_1 = 0.0603$, $wR_2 = 0.1801$	$R_1 = 0.0440$, $wR_2 = 0.1096$
R indices (all data)	$R_1 = 0.0922$, $wR_2 = 0.2020$	$R_1 = 0.0822$, $wR_2 = 0.1305$
Goodness-of-fit on F^2	1.081	1.007
Largest difference peak/hole (*e* Å^{-3})	0.865 and −0.306	0.226 and −0.177

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3. Results and discussion

3.1. Experimentation

A summary of the optimized experiments with benzaldehyde, ethyl acetoacetate and urea is listed in Table 1. The results show that the reactants hardly react when no IL is added (entry 1), and the yield of Biginelli product is up to 90% with modifying the amount of RTILs (0.1 mmol) (entries 2 and 3) [28]. Entries 4–8 indicate the effects of different solvents. In THF (entry 4) or dichloromethane (entry 5), the reactants do not react, probably owing to the lower boiling point of both solvents. However, in ethanol (entry 6), Biginelli product is obtained in moderate yield, when the water as solvent is added into the reaction system. An unknown compound is generated (entry 7). The unknown compound increases with the ethanol added and the amount of ethyl acetoacetate increasing. Moreover, the unknown compound is

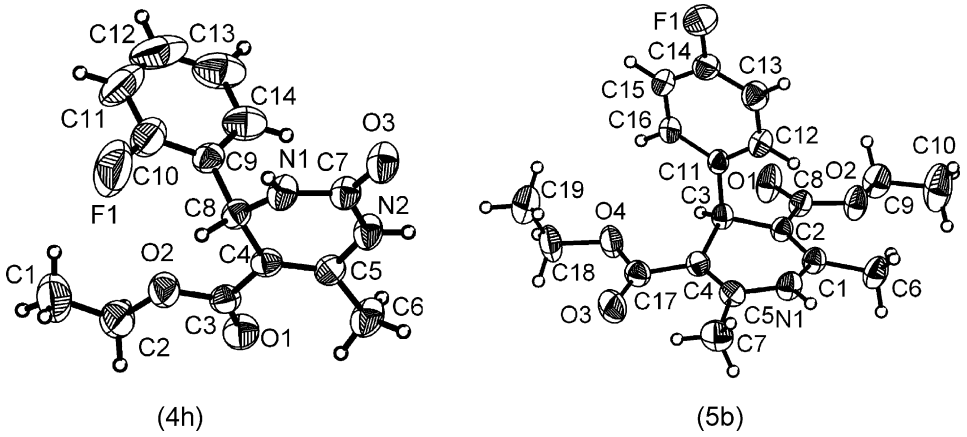

Fig. 1. ORTEP plot of the asymmetric unit of 5-ethoxycarbonyl-4-(2-fluorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one (**4h**) and 4-(4-fluorophenyl)-2,6-dimethyl-1,4-dihydro-3,5-pyridine dicarboxylate (**5b**) (the thermal ellipsoids represent 50% possibility).

also genarated by adding the amount of ethyl acetoacetate without any solvent (entries 10 and 11). The unknown compound is isolated by column chromatography. At last, the purified unknown compound is obtained as the crystal. The structure of unknown compound is determinated by X-ray single crystal diffraction. The result indicates that the unknown compound is Hantzsch product.

In order to exhibit the effects of Hantzsch reaction, different reactants are employed under the condition (entry 10, Table 1). The results (Table 2) show that the generality of the present protocol is effective for both ethyl acetoacetate and acetyl acetone (**a** and **l**) of 10 different aldehydes. For aromatic aldehydes carrying either electron-donating (**d** and **g**) or electron-withdrawing (**c** and **e**) substituents, two products are obtained in high yield. By replacing urea with thiourea to reaction system under the proportion of 1:1.5:1.5 (benzaldehyde:ethyl acetoacetate:thiourea), the unexpected phenomenon is not found, and Biginelli product is obtained in 74% yield.

*3.2. Structural description of 5-ethoxycarbonyl-4-(2-fluorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one (**4h**) and 4-(4-fluorophenyl)-2,6-dimethyl-1,4-dihydro-3,5-pyridinedicarboxylate (**5b**)*

A summary of experiment data and refinement parameters of 4h and 5b is given in Table 3; the molecular structure of 4h and 5b is shown in Fig. 1; the configuration of 4h and 5b is shown in Fig. 2. In the structure of **4h**, the bond lengths and angels are in agreement with literature values [35]. The pyrimidine moiety is non-planar, which forms a twist-boat configuration, as indicated by the largest displacement at atom N1 from the least-squares plane −0.129(2) Å and by the C(7)–N(1)–C(8)–C(4) torsion angle 25.2(3)°. The benzene ring is planar, and the largest displacement observed being −0.006(2) and 0.006(2) Å for atoms C(9) and C(10), respectively. The dihedral angel between the pyrimidine moiety and the benzene ring is 88.90(3)°, close to the value of 91.57° found in 4-(2-chlorophenyl)-6-methyl-5-ethoxycarbonyl-3,4-dihydropyrimidin-2(1H)-one [36]. The ester group of **4h** is antiperiplanar to the double bond of pyrimidine with an O(2)–C(2)–C(4)–C(8) torsion angle of −10.0(3)°.

In the structure of **5b**, the DHP ring is non-planar, which forms a shallow boat configuration with the displacement of N(1) and C(3) −0.154(2) and −0.212(2) Å, respectively. The atoms N(1) and C(3) are defining the stern and bow positions, above the four-atom plan through C(1), C(2), C(4) and C(5). Bond lengths and angles within the 1,4-dihydropyridine ring, as well as for the 2-, 3-, 5- and 6-substituents, are unexceptional [37,38]. The DHP ring is found to have an extremely puckered boat conformation with a torsion angle magnitude sum of 115.2°, similar to the dimethyl 2,6-dimethyl-4-[*trans*-(2-nitrophenyl)ethylene]-1,4-dihydropyridine-3,5-dicarboxylate (sum of 118°) [39]. The extreme puckering of the DHP ring would be increase the receptor binding and activity of the calcium channel drugs. The benzene ring is planar, the largest displacement observed being 0.007(2) for atom C(11), and the dihedral angel between the DHP ring and the benzene ring is 87.24(9)°, close to the early reported 88.3(3)° [40]. The two ester groups are twisted in different directions. One is synperiplanar to the ring double bonds with a C(3)–C(2)–C(8)–O(1) torsion angle of −15.2(3)°; the other is antiperiplanar to the ring double bonds with a C(3)–C(4)–C(17)–O(3) torsion angle of −172.90(19)°, slightly oriented out of the DHP plane.

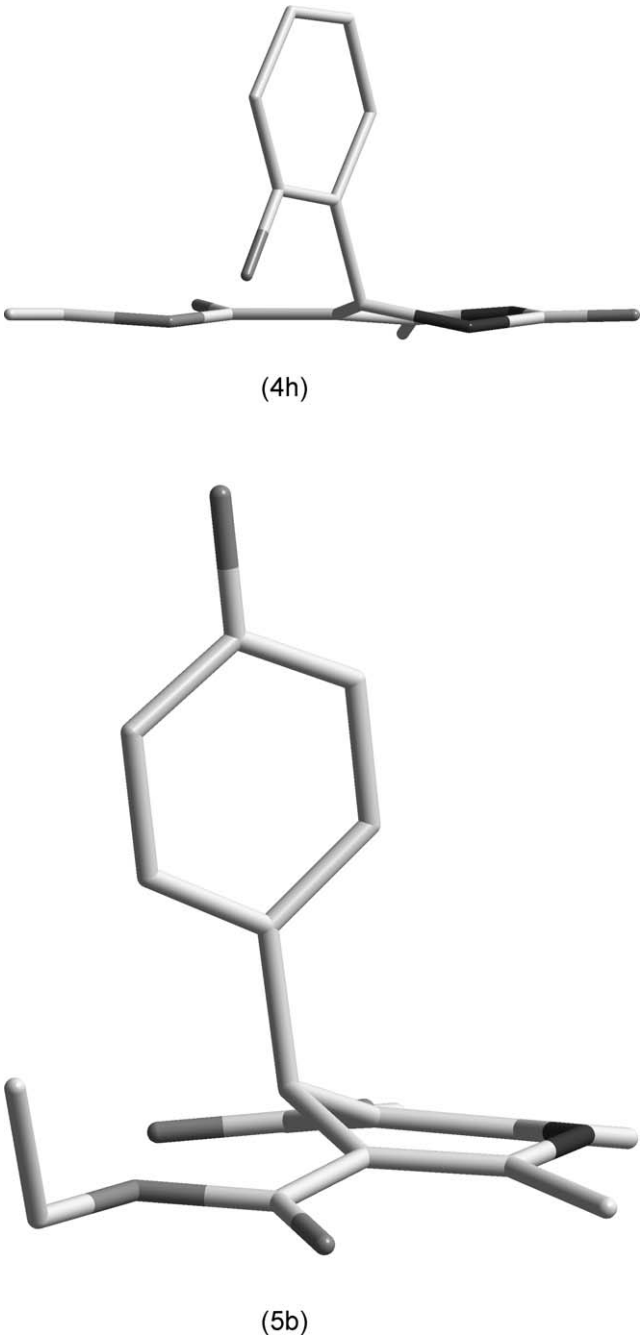

Fig. 2. Twist-boat configuration of the pyrimidine ring in **4h**; shallow boat configuration of the pyridine ring in **5b**. The nitrogen atom is represented in dark grey, carbon atom in light grey and oxygen and fluorine atoms in medium grey.

4. Conclusion

In conclusion, we use the ionic liquid 1-*n*-butyl-3-methylimidazolium saccharinate to catalyze the Biginelli reaction, from

which both the Biginelli and Hantzsch products were obtained. In order to improve the selectivity and yield, the effects of solvents and mole proportion of reactants are investigated. Mild reaction conditions, non-toxic catalyst and environmental benign are the advantages of this new procedure.

Acknowledgements

The authors are very grateful to the National Science Foundation of China (No. 20572057) and the Natural Science Foundation of Shandong Province (No. Y2003B01) for financial supports.

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