Month 2014

Novel SO_3H-Functionalized Ionic Liquids – Catalyzed Facile and Efficient Synthesis of Polyhydroquinoline Derivatives via Hantzsch Condensation under Ultrasound Irradiation

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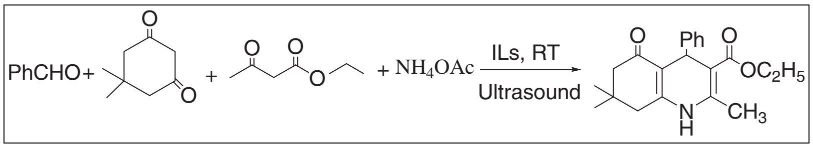
Received March 23, 2012
DOI 10.1002/jhet.2070



A facile and efficient synthesis of polyhydroquinolines has been developed via four-component condensation reactions of aldehydes, dimedone, ethyl acetoacetate, and ammonium acetate in the presence of Novel SO_3H-functionalized ionic liquid catalysts through Hantzsch reaction under ultrasound irradiation without solvent. Simple work-up procedure, environmentally friendly, inexpensive, and non-toxic catalyst, shorter reaction times along with excellent product yields are the significant features of this practical method.

J. Heterocyclic Chem., **00,** 00 (2014).

INTRODUCTION

Compounds containing the 4-substituted 1,4-dihydropyridine (DHP) nucleus comprise a large family of medicinally important compounds. They can cure the disordered heart ratio as a chain-cutting agent of factor IV channel, possess the calcium channel agonist–antagonist modulation activities [1–3], and also behave as neuroprotectants, cerebral antiischaemic agents, and chemosensitizers [4,5]. A recent computational analysis of the comprehensive medicinal chemistry database found the DHP framework to be among the most prolific chemotypes found. Thus, the synthesis of 4-substituted 1,4-dihydro-pyridines (1,4-DHPs) is of continuing interest. Recently, several methods have been reported comprising the use of conditions such as conventional heating [6], solar thermal energy [7], ionic liquid [8], TMSCl-NaI [9], metal triflates [10], grinding [11], Hy-Zeolite [12], montmorillonite K-10 [13], cerium(IV) ammonium nitrate [14], iron(III) trifluoroacetate [15], $HClO_4$-SiO_2 [16], heteropoly acid [17], molecular iodine [18], *p*-TSA [19], L-proline and derivatives [20], nickel [21], polymers [22], Baker's yeast [23], Glycine [24], L-proline [25], guanidine hydrochloride [26], ZnO-nanoparticle [27]. Most of these processes, however, suffer from one or other drawbacks such as longer reaction time, lower product yield, harsh conditions, high costs, difficult to reuse, usually required in large amounts, and use of hazardous catalysts. As a result, an eco-safe and efficient alternative method for the preparation of polyhydroquinoline is highly desirable.

Ultrasonic chemistry has received an increasing attention in recent years [28]. A large number of organic reactions can be carried out in higher yields, shorter reaction time and milder conditions under ultrasound irradiation than that of conventional methods. In our previous work, the novel SO_3H-functionalized ILs that have two alkyl sulfonic acid groups in imidazolium cations were designed and applied for xanthenedione derivatives synthesis in water under ultrasound irradiation (Fig. 1) [29]. However, there is no report on the use of SO_3H-functionalized ionic liquids (ILs) as a catalyst in the Hantzsch condensation, we wish to demonstrate the catalytic activity of these ILs in the synthesis of polyhydroquinolines under ultrasound irradiation without solvent.

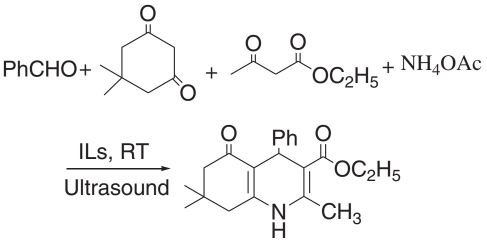
RESULTS AND DISCUSSION

We report herein a benign, rapid, and efficient four-component, one-pot synthesis of polyhydroquinolines in excellent yields by using aromatic aldehydes, dimedone, ethyl acetoacetate, and ammonium acetate in the presence of catalytic amount of ILs (1 mol %) under ultrasound irradiation without solvent. Initially, the model reaction was carried out under ultrasound irradiation (Scheme 1). The results of ILs catalyzed condensation reactions are shown in Table 1. First, 97.0% yields obtained when the reaction was catalyzed by 1.0 % fresh ILs (Table 1, entry 1). Because the products are insoluble in water, the reaction mixture was washed with cold water to remove the ILs after the reaction completed, the remaining ILs could be reused for the subsequent catalytic cycle of the reaction directly after removal of water under vacuum, without an obvious decrease in the reaction performance after 10 recycles in terms of the rate and the yield. We also carried out the model reaction without any catalyst, but the product was isolated in poor yield after 40 min (entry 11).

As ILs have a similar structure and property with *P*-TSA [19], its mechanism as a catalyst for the Hantzsch reaction under solvent-free conditions is proposed (Scheme 2). It

Figure 1. Novel Brønsted acidic ionic liquids (ILs) bearing two alkyl sulfonic acid groups.

Scheme 1



might catalyze the Knoevenagel-type coupling of aldehydes with active methylene compounds and then the Michael-type addition of intermediates through either path A or path B to give the 1,4-DHPs.

Encouraged by the previous results, we have treated a variety of substituted aldehydes, dimedone, ethyl acetoacetate, and ammonium acetate in the presence of ILs catalyst to form the corresponding polyhydroquinolines. Excellent yields of polyhydroquinolines were obtained by carrying out the reaction under ultrasound irradiation at room temperature for 0. 5–3 min (Table 2). This method has the ability to tolerate a variety of functional groups such as hydroxyl, methoxy, methyl, nitro, and halides under the reaction conditions. Both the electron-rich and electron-deficient aldehydes as well as heterocyclic aldehydes (entries 16, 17) worked well, leading to high yields of product. However, aliphatic aldehydes afforded relevant lower yields (entry 21). (Scheme 3)

CONCLUSIONS

In conclusion, we have demonstrated that the four-component ultrasound-asisted Hantzsch reaction can effectively be performed with the promotion of novel SO_3H-functionalized ionic liquids, which provide a simple and efficient method for the synthesis of polyhydroquinoline derivatives. The present method has many obvious advantages compared with those reported in the previous literatures, including the avoidance of discharging harmful organic solvents, the high yields, the short reaction times, the generality, and the simplicity of the methodology and recycling of the catalyst.

EXPERIMENTAL

General melting points were determined on a Kofler hot-stage apparatus and were uncorrected. IR spectra were recorded on a NicoletFT/IR-5700 spectrophotometer.^{1}H-NMR spectra were recorded on a BRUKER AVANCE DPX spectrometer at 200 MHz. NMR spectra were obtained on solutions in $CDCl_3$ by using TMS as an internal standard. Ultrasound reaction was conducted by using XO-SM100 ultrasound synthesis system (NAN JING SINO INSTRUMENTS MANUFACTURE Co., LTD) (Sinopharm Chemical Reagent Co., Ltd, ShangHai, China). TLC was carried out on GF254 silica gel plates. Commercially available chemicals were used without further purification.

General experimental procedure. A mixture of aldehyde (10 mmol), dimedone (10 mmol), ethyl acetoacetate (10 mmol), ammonium acetate (11 mmol), and ILs (0.1 mmol) was irradiated at 35 kHz for 0.5–3 mins, after the reaction was complete, the reaction mixture was cooled to room temperature, poured into crushed ice, and stirred for several minutes. The resulting solid was filtered under suction and recrystallized from hot ethanol to afford the pure products. Finally, the remaining $[(HSO_3\text{-p})_2im][CF_3SO_3]$ was reused after removal of water under vacuum. The spectral and analytical data for the compounds are presented in the later text (**5a–5u**).

5a IR (KBr): 3287, 3077, 2964, 1696, 1610 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$): $\delta = 0.92$ (s, 3H), 1.07 (s, 3H), 1.18 (t, $J = 7.3$ Hz, 3H), 2.13–2.25 (m, 4H), 2.38 (s, 3H), 4.05 (q, $J = 7.33$ Hz, 2H), 5.02 (s, 1H), 5.8 (s, 1H, NH), 6.85–6.89 (m, 2H), 7.23–7.27 (m, 2H); ^{13}C-NMR (62.5 MHz, $CDCl_3$): $\delta = 195.70$, 167.47, 148.72, 147.05, 143.67, 127.96, 127.83, 125.98, 111.92, 105.93, 59.78, 50.72, 40.85, 36.55, 32.64, 29.41, 27.08, 19.24, 14.17.

5b IR (KBr): 3275, 3080, 2960, 1700, 1650 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$): 0.95 (s, 3H), 1.07 (s, 3H), 1.21 (t, $J = 6.4$ Hz, 3H), 2.17–2.25 (m, 4H), 2.23 (s, 3H), 2.35 (s, 3H), 4.04 (q, $J = 7.0$ Hz, 2H), 5.00 (s, 1H), 6.09(s, 1H), 7.01 (d, $J = 7.6$ Hz, 2H), 7.18 (d, $J = 8.0$ Hz, 2H); ^{13}C-NMR (62.5 MHz, $CDCl_3$): $\delta = 195.68$, 167.39, 148.74, 146.95, 143.71, 127.97, 127.83, 126.07, 112.01, 105.98, 59.83, 50.77, 40.92, 36.59, 32.73, 29.45, 27.06, 19.81, 19.23, 14.16.

Table 1

Recycling of the catalyst in the condensation reaction.

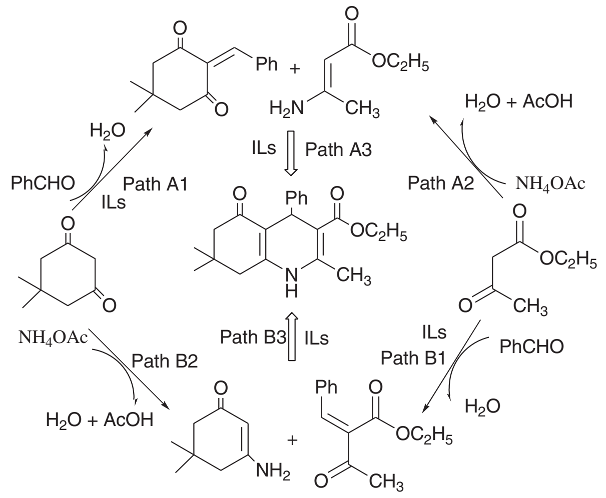
Entry	1	1[a]	2[a]	3[a]	4[a]	5[a]	6[a]	7[a]	8[a]	9[a]	10[a]	11[b]
Time (min)	5	5	5	5	5	5	5	5	5	5	5	40
Yield (%)[c]	97	97	96	95	96	95	95	95	95	94	94	85

[a] Reaction conditions: benzaldehyde (10 mmol), dimedone(10 mmol), ethyl acetoacetate (10 mmol), ammonium acetate (11 mmol), and ILs (0.1 mmol); ultrasound irradiation for 5 min, $[(HSO_3\text{-p})_2im][CF_3SO_3]$ was reused.

[b] The reaction was carried out without any catalyst for 40 min.

[c] Isolated yield.

Scheme 2



5c IR (KBr): 3276, 2957, 1705, 1647, 1605, 1497, 1382, 1217, 1030, 767 cm^{-1}; ^{1}H-NMR (200 MHz, CDCl$_3$): 0.94 (s, 3H), 1.06 (s, 3H), 1.21 (t, J = 7.0 Hz, 3H), 2.17-2.27 (m, 4H), 2.23 (s, 3H), 2.36 (s, 3H), 3.73 (s, 3H), 4.06 (q, J = 7.0 Hz, 2H), 5.99 (s, 1H), 6.19(s, 1H), 6.73 (d, J = 6.6 Hz, 2H), 7.21 (d, J = 8.6 Hz, 2H); ^{13}C-NMR (62.5 MHz, CDCl$_3$): δ = 195.65, 167.51, 157.72, 148.18, 143.21, 139.60, 128.91, 113.20, 112.21, 106.24, 59.75, 55.08, 50.73, 40.95, 35.67, 32.64, 29.41, 27.13, 19.31, 14.21.

5d ^{1} IR (KBr): 3274, 3206, 3085, 2938, 1705, 1606 cm^{-1}; ^{1}H-NMR (200 MHz, CDCl$_3$) : 0.92 (s, 3H), 1.07 (s, 3H), 1.19 (t, J = 7.2 Hz, 3H), 2.09–2.29 (m, 4H), 2.37 (s, 3H), 4.05 (q, J = 7.2 Hz, 2H), 5.02(s, 1H), 6.10 (s, 1H), 7.14–7.27 (m, 4H); ^{13}C-NMR (62.5 MHz, CDCl$_3$): δ = 195.64, 167.31, 149.20, 144.53, 133.55, 129.11, 128.08, 126.23, 111.14, 105.12, 59.79, 50.67, 40.64, 36.58, 32.59, 29.34, 27.01, 19.06, 14.13.

5e IR (KBr): 3291, 2961, 1695, 1610, 1490, 1380, 1221, 1025, 764 cm^{-1}; ^{1}H-NMR (200 MHz, CDCl$_3$): 0.93 (s, 3H), 1.07 (s, 3H), 1.19 (t, J = 7.0 Hz, 3H), 2.15–2.30 (m, 4H), 2.37 (s, 3H), 4.05 (q, J = 7.0 Hz, 2H), 5.03 (s, 1H), 6.14 (s, 1H), 6.83–6.92 (m, 2H), 7.23–7.29 (m, 2H); ^{13}C-NMR (62.5 MHz, CDCl$_3$): δ = 195.65, 167.55, 153.72, 149.27, 144.60, 138.63, 129.51, 112.17, 106.25, 59.84, 50.78, 40.97, 36.12, 32.71, 29.42, 27.15, 19.31, 14.22.

5f IR (KBr): 3391, 2956, 1702, 1645, 1590, 1480, 1385, 1220, 782 cm^{-1}; ^{1}H-NMR (200 MHz, CDCl$_3$): 0.85 (s, 3H), 1.00 (s, 3H), 1.13 (t, J = 7.0 Hz, 3H), 1.97–2.48 (m, 4H), 2.50 (s, 3H), 3.97 (q, J = 6.8 Hz, 2H), 4.73(s, 1H), 6.54 (d, J = 8.6 Hz, 2H), 6.92 (d, J = 8.4 Hz, 2H), 8.98 (s, 1H), 9.05 (s, 1H); ^{13}C-NMR (62.5 MHz, CDCl$_3$): δ = 195.69, 167.47, 148.70, 147.02, 143.57, 127.86, 127.82, 125.96, 111.90, 105.91, 59.76, 50.71, 40.83, 36.52, 32.61, 29.40, 27.05, 19.22, 14.16.

5g IR (KBr): 3283, 3078, 2930, 2885, 2841, 1688, 1650, 1610, 1574, 1558, 1487, 1443 cm^{-1}; ^{1}H-NMR (200 MHz, CDCl$_3$): 0.91 (s, 3H), 1.04 (s, 3H), 1.17 (t, J = 7.0 Hz, 3H), 2.11–2.28 (m, 4H), 2.26 (s, 3H), 3.78 (s, 3H), 3.99 (q, J = 1.2 Hz, 2H), 5.23(s, 1H), 5.98 (s, 1H), 6.75–6.83 (m, 2H), 6.91–7.21 (m, 1H), 7.25–7.29 (m, 1H); ^{13}C-NMR (62.5 MHz, CDCl$_3$): δ = 195.67, 167.51, 157.72, 148.18, 143.21, 139.60, 128.91, 126.81, 114.31, 113.20, 112.21, 106.24, 59.75, 55.08, 50.73, 40.95, 35.67, 32.64, 29.41, 27.13, 19.31, 14.21.

5h IR (KBr): 3296, 3093, 2969, 2940, 1699, 1612, 1525 cm^{-1}; ^{1}H-NMR (200 MHz, CDCl$_3$): 0.88 (s, 3H), 1.05 (s, 3H), 1.09 (t, J = 7.0 Hz, 3H), 2.12–2.28 (m, 4H), 2.35 (s, 3H), 4.02 (q,

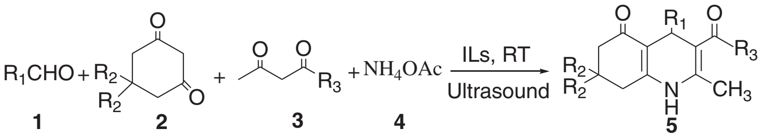
Table 2

Synthesis of polyhydroquinolines catalyzed by ionic liquids (ILs) under ultrasound irradiation.[a]

Product	R$_1$	R$_2$	R$_3$	Products	Time (min)	Yield [b] (%)	mp (°C) Obs	mp (°C) Lit
1	C$_6$H$_5$	CH$_3$	OEt	**5a**	1	97	202–203	203–205[24]
2	4-CH$_3$C$_6$H$_4$	CH$_3$	OEt	**5b**	1	95	258–260	259–260[24]
3	4-CH$_3$OC$_6$H$_4$	CH$_3$	OEt	**5c**	1	93	255–257	256–257[24]
4	4-ClC$_6$H$_4$	CH$_3$	OEt	**5d**	1	94	245–248	246–248[24]
5	4-FC$_6$H$_4$	CH$_3$	OEt	**5e**	1	92	184–187	184–185[24]
6	4-HOC$_6$H$_4$	CH$_3$	OEt	**5f**	1.5	94	230–234	232–234[19]
7	2-CH$_3$OC$_6$H$_4$	CH$_3$	OEt	**5g**	1	93	250–253	251–254[19]
8	2-NO$_2$C$_6$H$_4$	CH$_3$	OEt	**5h**	3	91	201–203	203–206[19]
9	2-HOC$_6$H$_4$	CH$_3$	OEt	**5i**	2	93	208–211	207–210[19]
10	2-ClC$_6$H$_4$	CH$_3$	OEt	**5j**	3	92	205–207	206–208[19]
11	3-CH$_3$OC$_6$H$_4$	CH$_3$	OEt	**5k**	0.5	98	201–203	202–204[15]
12	3-ClC$_6$H$_4$	CH$_3$	OEt	**5l**	1	98	192–194	192–193[19]
13	3-BrC$_6$H$_4$	CH$_3$	OEt	**5m**	0.5	98	234–235	235–237[19]
14	2-Cl-5-NO$_2$C$_6$H$_3$	CH$_3$	OEt	**5n**	1	90	234–236	234–235[19]
15	2-Naphthal	CH$_3$	OEt	**5o**	1	91	197–199	198–200[15]
16	2-Furyl	CH$_3$	OEt	**5p**	1	98	245–247	247–248[19]
17	2-Thioanyl	CH$_3$	OEt	**5q**	0.5	97	240–243	241–242[19]
18	C$_6$H$_5$	H	OEt	**5r**	1	91	240–242	240–241[15]
19	C$_6$H$_5$	CH$_3$	OMe	**5s**	0.5	96	263–274	—
20	C$_6$H$_5$	CH$_3$	Me	**5t**	1	93	199–201	—
21	(CH$_3$)$_2$CH	CH$_3$	OEt	**5u**	3	88	157–158	—

[a] Reaction conditions: aldehyde **1** (10 mmol), dimedone **2** (10 mmol), **3** (10 mmol), ammonium acetate **4** (11 mmol), and ILs (0.1 mmol).
[b] Isolated yield.

Scheme 3



J = 7.0 Hz, 2H), 5.87 (s, 1H), 6.23 (s, 1H), 7.22–7.27(m, 1H), 7.44–7.49 (m, 2H), 7.71–7.75 (m, 1H); ^{13}C-NMR (62.5 MHz, CDCl$_3$): δ = 195.79, 167.51, 141.02, 132.33, 131.12, 128.74, 127.15, 125.96, 114.25, 109.24, 101.34, 55.13, 52.94, 50.52, 48.91, 46.85, 42.47, 32.37, 31.26, 29.16, 26.55.

5i IR (KBr): 3284, 3080, 2936, 2880, 1730, 1652, 1575, 1558, 1515, 1457 cm^{-1}; ^{1}H-NMR (200 MHz, CDCl$_3$): 0.88 (s,3H), 1.01 (s, 3H), 1.23 (t, J = 7.4 Hz, 3H), 1.89 (s, 3H), 2.15 (s, 4H), 4.10 (m, 2H), 4.67 (d, J = 2.8 Hz, 1H), 5.30 (s, 1H), 6.76-6.85 (m, 2H), 6.76–6.85 (m, 2H), 7.00–7.05 (m, 1H),7.33–7.37 (m, 1H); ^{13}C-NMR (62.5 MHz, CDCl$_3$): δ = 195.69, 167.47, 148.70, 147.02, 143.57, 127.86, 127.82, 125.96, 121.30, 114.12, 111.90, 105.91, 59.76, 50.71, 40.83, 36.52, 32.61, 29.40, 27.05, 19.22, 14.16.

5j IR (KBr): 3292, 3072, 2956, 2930, 1698, 1637, 1607, 1423, 1379, 1279, 1072 cm^{-1}; ^{1}H-NMR (200 MHz, CDCl$_3$): 0.94 (s,3H), 1.06 (s, 3H), 1.27 (t, J = 7.4 Hz, 3H), 2.14–2.22 (m, 4H), 2.26 (s, 3H), 4.04 (q, J = 2.2 Hz, 2H), 5.38 (s, 1H), 6.37 (s, 1H), 7.02–7.13 (m, 2H), 7.21–7.27 (m, 1H), 7.37–7.42 (m, 1H); ^{13}C-NMR (62.5 MHz, CDCl$_3$): δ = 195.41, 167.23, 149.38, 142.42, 133.67, 132.78, 132.04, 129.13, 126.86, 111.13, 104.59, 60.11, 50.58, 41.07, 32.73, 29.12, 27.37, 19.11, 14.17.

5k IR (KBr): 3283, 3078, 2930, 2885, 2841, 1688, 1650, 1610, 1574, 1558, 1487 cm^{-1}; ^{1}H-NMR (200 MHz, CDCl$_3$): 0.95 (s,3H), 1.07 (s, 3H), 1.21 (t, J = 7.0 Hz, 3H), 2.15–2.29 (m, 4H), 2.36 (s, 3H), 3.75 (s, 3H), 4.08 (q, J = 7.0 Hz, 2H), 5.04 (s, 1H), 6.00 (s, 1H), 6.62–6.68 (m, 1H), 6.86–6.92 (m, 2H), 7.08–7.15 (m, 1H); ^{13}C-NMR (62.5 MHz, CDCl$_3$): δ = 195.66, 167.50, 157.71, 148.17, 143.20, 139.61, 128.90, 126.80, 114.30, 113.19, 112.21, 106.23, 59.74, 55.07, 50.72, 40.95, 35.66, 32.63, 29.41, 27.12, 19.30, 14.21.

5l IR (KBr): 3274, 3202, 3074, 2934, 1704, 1605 cm^{-1}; ^{1}H-NMR (200 MHz, CDCl$_3$) : 0.95 (s, 3H), 1.07 (s, 3H), 1.21 (t, J = 7.2 Hz, 3H), 2.18–2.29 (m, 4H), 2.36 (s, 3H), 4.02–4.13 (m, 2H), 5.03(s, 1H), 6.42 (s, 1H), 7.08–7.17 (m, 2H), 7.21–7.27 (m, 2H); ^{13}C-NMR (62.5 MHz, CDCl$_3$): δ = 195.40, 167.22, 149.37, 142.41, 133.66, 132.76, 132.02, 129.12, 126.85, 111.12, 104.58, 60.11, 50.58, 41.06, 32.72, 29.12, 27.36, 19.11, 14.15.

5m IR (KBr): 3275, 3204, 3074, 2957, 1703, 1605 cm^{-1}; ^{1}H-NMR (200 MHz, CDCl$_3$) : 0.96 (s, 3H), 1.08 (s, 3H), 1.21 (t, J = 7.4 Hz, 3H), 2.19–2.29 (m, 4H), 2.37 (s, 3H), 4.06 (q, J = 5.8 Hz, 2H), 5.02 (s, 1H), 7.00–7.10(m, 1H), 7.21–7.27 (m, 2H), 7.39–7.40 (m, 2H); ^{13}C-NMR (62.5 MHz, CDCl$_3$): δ = 196.40, 168.25, 149.37, 144.42, 133.64, 132.73, 132.02, 129.10, 126.84, 111.13, 104.55, 60.12, 50.59, 41.08, 32.74, 29.15, 27.40, 19.13, 14.17.

5n IR (KBr): 3294, 3093, 2969, 2940, 1699, 1612, 1525, 1379, 1279, 1072 cm^{-1}; ^{1}H-NMR (200 MHz, CDCl$_3$) : 0.96 (s, 3H), 1.08 (s, 3H), 1.21 (t, J = 7.4 Hz, 3H), 2.19−2.29 (m, 4H), 2.37 (s, 3H), 4.06 (q, J = 5.8 Hz, 2H), 5.02 (s, 1H), 7.38–7.40 (m, 1H), 7.88–7.90 (m, 1H), 8.02–8.12 (m, 1H); ^{13}C-NMR (62.5 MHz, CDCl$_3$): δ = 196.41, 168.28, 150.12, 145.42, 134.61, 133.70, 133.02, 129.20, 127.34, 112.13, 105.55, 60.22, 50.64, 41.38, 32.75, 29.16, 27.41, 19.15, 14.19.

5o IR (KBr): 3199, 3058, 2958, 2922, 1676, 1635, 1602, 1448 cm^{-1}; ^{1}H-NMR (200 MHz, CDCl$_3$): 0.89 (s,3H), 1.04 (s, 3H), 1.19 (t, J = 7.0 Hz, 3H), 2.14–2.26 (m, 4H), 2.42 (s, 3H), 4.04 (q, J = 7.0 Hz, 2H), 5.23 (s, 1H), 6.16 (s, 1H), 7.35–7.53 (m, 3H), 7.67–7.76 (m, 4H); ^{13}C-NMR (62.5 MHz, CDCl$_3$): δ = 195.71, 167.46, 148.71, 147.05, 143.67, 127.96, 127.83, 127.58, 126.31, 126.01, 125.98, 125.52, 111.92, 105.93, 59.78, 50.72, 40.85, 36.55, 32.64, 29.41, 27.08, 19.24, 14.17.

5p IR (KBr): 3288, 3078, 2969, 1687, 1602, 1493, 1034, 941, 877, 826 cm^{-1}; ^{1}H-NMR (200 MHz, CDCl$_3$): 1.03 (3H, s), 1.12 (3H, s), 1.26 (3H, t, J = 6.9 Hz), 2.21–2.27 (3H, m), 2.35–2.38 (4H, m), 4.10–4.18 (2H, m), 5.25 (1H, s), 5.80 (1H, s), 6.02 (1H, s), 6.20 (1H, s), 7.17 (1H, s); ^{13}C-NMR (62.5 MHz, CDCl$_3$): δ = 195.57, 167.34, 157.94, 150.61, 144.26, 140.85, 111.13, 105.03, 103.07, 59.83, 50.63, 36.88, 32.48, 29.71, 27.03, 19.08, 14.17.

5q IR (KBr): 3218, 3079, 2963, 2934, 1695, 1652, 1611, 1457, 1447, 1383, 1398, 1282 cm^{-1}; ^{1}H-NMR (200 MHz, CDCl$_3$): 0.93 (s, 3H), 1.02 (s, 3H), 1.18 (t, J = 7.0 Hz, 3H), 2.08–2.51 (m, 4H), 2.33 (s, 3H), 4.05 (q, J = 7.2 Hz, 2H), 5.16(s, 1H), 6.64–6.66 (m, 1H), 6.79–6.83 (m, 1H),7.15–7.18 (s, 1H), 9.25 (s, 1H); ^{13}C-NMR (62.5 MHz, CDCl$_3$): δ = 195.56, 167.33, 157.92, 150.61, 144.23, 140.85, 115.15, 108.03, 103.06, 59.83, 50.65, 36.85, 32.47, 29.71, 27.03, 19.08, 14.17.

5r IR (KBr): 3283, 3077, 2962, 2879, 1690, 1645, 1607 cm^{-1}; ^{1}H-NMR (200 MHz, CDCl$_3$): 1.18 (t, J = 7.4 Hz, 3H), 1.62 (s, 2H), 1.94–1.99 (m, 2H), 2.29–2.44 (m, 7H), 4.04 (q, J = 7.0 Hz, 2H), 5.08 (s, 1H), 5.98 (s, 1H), 7.09–7.32 (m, 5H); ^{13}C-NMR (62.5 MHz, CDCl$_3$): δ = 195.69, 167.47, 148.71, 147.04, 143.65, 127.95, 127.82, 125.96, 111.91, 105.93, 59.77, 40.85, 36.54, 32.65, 29.41, 19.24, 14.17.

5s IR (KBr): 3277, 3078, 2937, 2873, 1683, 1648, 1606 cm^{-1}; ^{1}H-NMR (200 MHz, CDCl$_3$): 0.93 (s, 3H), 1.07 (s, 3H), 2.16–2.29 (m, 4H), 2.38 (s, 3H),3.60 (s, 3H), 5.07 (s, 1H), 6.05 (s, 1H), 7.09–7.32 (m, 5H); ^{13}C-NMR (62.5 MHz, CDCl$_3$): δ = 195.70, 167.47, 148.72, 147.05, 143.67, 127.96, 127.83, 125.98, 111.92, 105.93, 59.78, 50.72, 40.85, 36.55, 32.64, 29.41, 27.08, 19.24, 14.17. *Anal*. Calcd. for $C_{20}H_{23}NO_3$: C, 73.82; H, 7.12; N, 4.31. Found: C, 73.73; H, 4.38; N, 4.29.

5t IR (KBr): 3271, 3072, 2961, 2871, 1647, 1595,1506 cm^{-1}; ^{1}H-NMR (200 MHz, CDCl$_3$): 1.10 (s, 6H), 1.24 (s, 3H), 2.37 (s, 3H), 2.35–2.43 (m, 4H), 5.54(s, 1H), 7.07–7.12 (m, 2H), 7.07–7.12 (m, 2H), 11.87 (s, 1H); ^{13}C-NMR (62.5 MHz, CDCl$_3$): δ = 195.70, 167.47, 148.72, 147.05, 143.67, 127.96, 127.83, 125.98, 111.92, 105.93, 50.72, 40.85, 36.55, 32.64, 29.41, 27.08, 22.21, 19.24. *Anal*. Calcd. for $C_{20}H_{23}NO_2$: C, 77.64; H, 7.49; N, 4.53. Found: C, 77.70; H, 4.50; N, 4.51.

5u IR (KBr): 3271, 3072, 2964, 2870, 1717, 1652, 1583, 1418, 1363, 1339 cm^{-1}; ^{1}H-NMR (200 MHz, CDCl$_3$, δppm): 0.84(d, J = 6.4 Hz, 6H), 1.07(s, 6H), 1.18 (t, J = 7.0 Hz, 3H), 2.29 (s, 3H), 2.25–2.31 (m, 4H), 2.43–2.51 (m, 1H), 2.87–3.01(s, 1H), 4.06 (q, J = 5.8 Hz, 2H), 12.45 (s, 1H); ^{13}C-NMR (62.5 MHz, CDCl$_3$): δ = 195.70, 167.47, 148.72, 147.05, 111.92, 105.93, 59.78, 50.72, 36.55, 32.64, 30.18, 29.41, 27.08, 21.21, 19.23, 14.15. *Anal*. Calcd. for $C_{18}H_{27}NO_3$: C, 70.79; H, 8.91; N, 4.59. Found: C, 70.80; H, 8.93; N, 4.58.

Acknowledgment. We are pleased to acknowledge the financial support from Tai zhou University.

REFERENCES AND NOTES

[1] Kawase, M.; Shah, A.; Gaveriya, A.; Motohashi, N.; Sakagami, H.; Varga, A.; Molnar, J. Bioorg Med Chem 2002, 10, 1051.

[2] Shan, R.; Velazquez, C.; Knaus, E. E. J Med Chem 2004, 47, 254.

[3] Sawada, Y.; Kayakiri, H.; Abe, Y.; Mizutani, T.; Inamura, N.; Asano, M.; Hatori, C.; Aramori, I.; Oku, T.; Tanaka, H. J Med Chem 2004, 47, 2853.

[4] Klusa, V. Drugs Future 1995, 20, 135.

[5] Boer, R.; Gekeler, V. Drugs Future 1995, 20, 499.

[6] (a) Sufirez, M.; Ochoa, E.; Verdecia, Y.; Verdecia, B.; Moran, L.; Martin, N.; Quinteiro, M.; Seoane, C.; Soto, J. L.; Novoa, H.; Blaton, N.; Peters, O. M. Tetrahedron 1999, 55, 875; (b) Suresh, D.; Kumar, J.; Sandhu, S. Synth Commun 2009, 39, 1957.

[7] Mekheimer, R. A.; Hameed, A. A.; Sadek, K. U. Green Chem 2008, 10, 592.

[8] [a] Ji, S. J.; Jiang, Z. Q.; Lu, J.; Loa, T. P. Synlett 2004, 5, 831; [b] Zhang, X. Y.; Li, Y. Z.; Fan, X. S.; Qu, G. R.; Hu, X. Y.; Wang, J.; J. Chin Chem Lett 2006, 17, 150.

[9] Sabitha, G.; Reddy, G. S. K.; Reddy, C. S.; Yadav, J. S. Tetrahedron Lett 2003, 44, 4129.

[10] (a) Wang, L. M.; Sheng, J.; Zhang, L.; Han, J. W.; Fan, Z. Y.; Tian, H.; Qian, C. T. Tetrahedron 2005, 61, 1539; (b) Donelson, J. L.; Gibbs, A.; De, S. K. J Mol Catal A: Chem 2006, 256, 309.

[11] Kumar, S.; Sharma, P.; Kapoor, K. K.; Hundal, M. S. Tetrahedron 2008, 64, 536.

[12] Das, B.; Ravikanth, B.; Ramu, R.; Rao, V. B. Chem Pharm Bull 2006, 54, 1044.

[13] Song, G.; Wang, B.; Wu, X.; Kang, Y.; Yang, L. Synth Commun 2005, 35, 2875.

[14] Reddy, C. S.; Raghu, M. Chin Chem Lett 2008, 19, 775.

[15] Adibi, H. ; Samimi, H. A.; Beygzadeh, M. Catal Commun 2007, 8, 2119.

[16] Maheswara, M.; Siddaiah, V.; Damu, G. L. V.; Rao, C. V. Arkivoc 2006, 2, 201.

[17] (a) Heravi, M. M.; Bakhtiri, K.; Javadi, N. M.; Bamoharram, F. F.; Saeedi, M.; Oskooi, H. A. J Mol Catal A: Chem 2007, 264, 50; (b) Nagarapu, L.; Apuri, S.; Gaddam, S.; Bantu, R.; Mahankhali, V. C.; Kantevari, S. Lett Org Chem 2008, 5, 60.

[18] Ko, S.; Sastry, M. N. V.; Lin, C.; Yao, C. F. Tetrahedron Lett 2005, 46, 5771.

[19] Cherkupally, S. R.; Mekalan, R. Chem Pharm Bull 2008, 56, 1002.

[20] (a) Evans, C. G.; Gestwicki, J. E. Org Lett 2009, 11, 2957; (b) Kumar, A.; Maurya, R. A. Tetrahedron 2007, 63, 1946.

[21] Sapkal, S. B.; Shelke, K. F.; Shingate, B. B.; Shingare, M. Tetrahedron Lett 2009, 50, 1754.

[22] (a) Breitenbucher, J. G.; Figliozzi, G. Tetrahedron Lett 2000, 41, 4311; (b) Dondoni, A.; Massi, A.; Minghini, E.; Bertolasi, V. Tetrahedron 2004, 60, 2311.

[23] Kumar, A.; Maurya, R. A. Tetrahedron Lett 2007, 48, 3887.

[24] Singh, S. K.; Singh, K. N. J.Heterocyclic Chem. 2010, 47, 194.

[25] Guo, S. R.; Yuan, Y. Q. Chin J Chem 2010, 28, 811.

[26] Baghbanian, S. M.; Khaksar, S.; Vahdat, S. M.; Farhang, M.; Tajbakhsh, M. Chin Chem Lett 2010, 21, 563.

[27] Kassaee, M. Z.; Masrouri, H.; Movahedi, F. Monatsh Chem 2010, 141, 317.

[28] Mason, T. J.; Peters, D. Practical Sonochemistry, Seconded; Ellis Horwood: London, 2002.

[29] Li, B. L.; Liang, H. D.; Zhong, A. G.; Xu, D. Q. Adv Mater Res 2012, 391, 1354.