

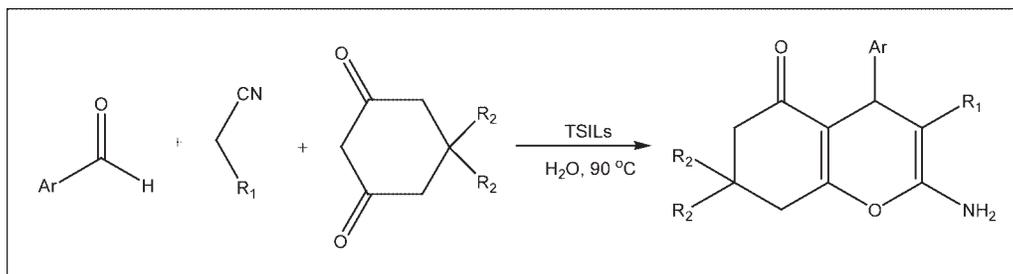
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Some halogen-free acyclic task-specific ionic liquids (TSILs) were synthesized as novel and recyclable catalysts for the synthesis of 5-oxo-5,6,7,8-tetrahydro-4*H*-benzo[*b*]pyrans by one-pot three-component condensation of aromatic aldehyde, malononitrile (or ethyl cyanoacetate), and dimedone (or 1,3-cyclohexanedione) in water. The condensation accomplished successfully with good yields ranged from 86 to 94%. After the reaction, the products could simply be separated from the catalyst/water, and the catalyst could be reused at least 10 times without noticeably decreasing the catalytic activity.

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INTRODUCTION

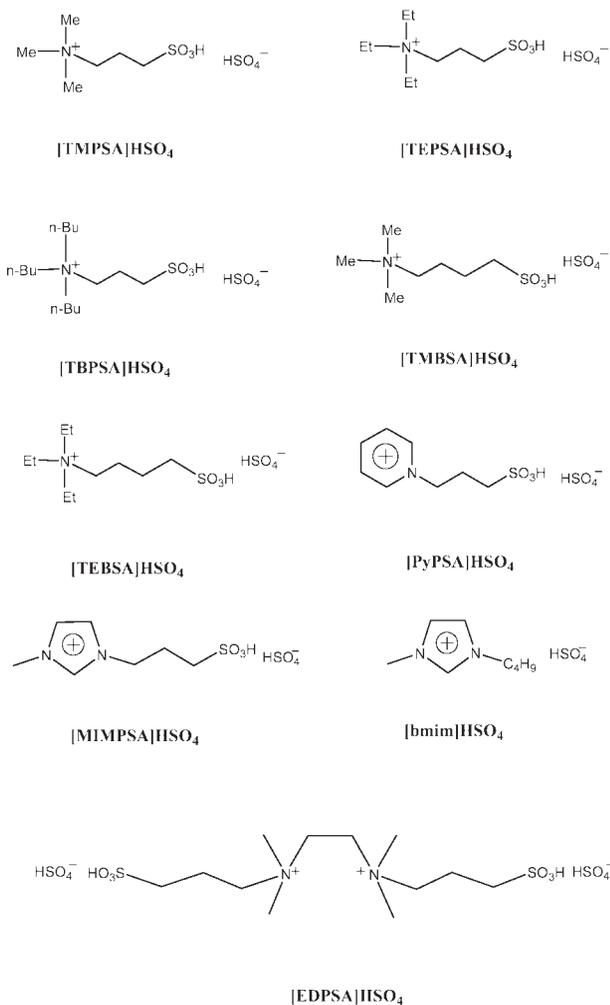
4*H*-Benzopyrans have attracted considerable attention because of their useful biological and pharmacological properties [1]. The synthesis of 5-oxo-5,6,7,8-tetrahydro-4*H*-benzo[*b*]pyrans usually involves a condensation of appropriate active methylene carbonyl compounds, aromatic aldehydes, and malononitrile (or cyanoacetates) catalyzed mainly by organic and mineral acids in organic solvents, which often suffer from the drawbacks of low yield, high reaction temperature, toxicity and difficulty in product separation. Recently, many synthetic methods for preparing these compounds have been reported by the condensation of aromatic aldehydes and active methylene carbonyl compounds in the presence of phase transfer catalyst [2], rare earth perfluorooctanoates [3], KF-Alumina [4], sodium selenate [5], and proline [6] as catalysts, as well as with the assistance of microwave [7] or ultrasound irradiation [8]. However, the search for the new readily available and green catalysts is still being actively pursued these years.

Ionic liquids have attracted wide interest as environmental benign catalysts or excellent alternatives to organic solvents these years because of their favorable properties such as negligible volatility, high thermal sta-

bility [9]. Brønsted acidic or basic task-specific ionic liquids (TSILs) are designed to replace traditional acids or bases in organic synthetic procedure. In view of both the advantages and disadvantages of homogeneous and heterogeneous catalytic reactions, the use of TSILs as reaction medium/catalytic system may offer a convenient solution to both the solvent emission and catalytic recycling problem. Some researchers have already used ionic liquids as solvents/catalysts in condensation reactions [10–12]. Recently, Luo and coworkers [13] reported a new temperature-dependent biphasic system comprising PEG-1000-based acidic ionic liquid/toluene, and it is used in preparation of benzopyrans. Chen *et al.* [14] used *N,N*-dimethylamino-functionalized basic ionic liquid to catalyze one-pot multicomponent reaction for the synthesis of benzopyrans. In fact, the use of Brønsted-acidic or basic TSILs as catalysts is an area of ongoing activity; however, the development and exploration of TSILs are currently in the preliminary stage. On the other hand, reactions in aqueous media may offer many advantages such as simple operation and high efficiency in many organic reactions. Thus, it is necessary to carry out this condensation using TSILs as catalysts in aqueous media.

In our previous work, some novel and cheap SO₃H-functional halogen-free acidic ionic liquids that bear an

Scheme 1



alkane sulfonic acid group in an acyclic trialkylammonium cation have been synthesized to catalyze some organic reactions [15]. In continuation of our work in studying acid-catalyzed reactions in ionic liquids, we report here the synthesis of 5-oxo-5,6,7,8-tetrahydro-4*H*-benzo[b]pyrans by condensation of aromatic aldehyde, malononitrile (or ethyl cyanoacetate), and dimedone (or 1,3-cyclohexanedione) in water catalyzed by acidic ionic liquids.

RESULTS AND DISCUSSION

The preparation of SO₃H-functionalized halogen-free acidic ionic liquids (Scheme 1) was made up of two-step atom economic reaction. The chemical yields for both the zwitterions formation and acidification steps were essentially quantitative since neither reaction produced byproducts. The preparation of [bmim]HSO₄ was accomplished by anion metathesis with NaHSO₄ in good yield of 96%.

The fresh new TSILs with HSO₄⁻ anion are somewhat viscous colorless or pale brown liquids at room tempera-

ture. All produced TSILs are entirely miscible with water and soluble or partly soluble in organic solvents.

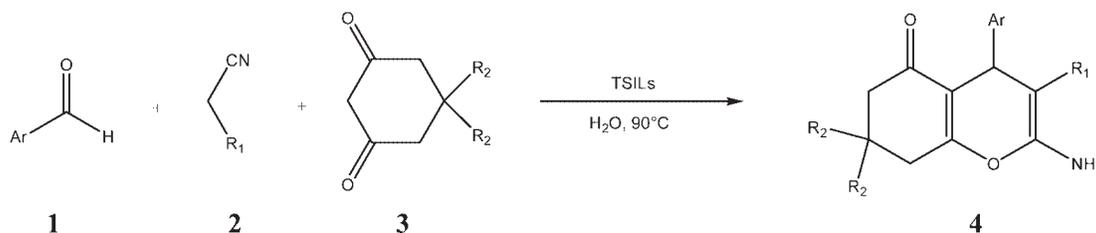
To optimize the reaction conditions (Scheme 2), for the beginning of this study, benzaldehyde, malononitrile, and dimedone were used as the model reactants at 90°C in TSILs/water for a length of time to compare the catalytic performance of the TSILs in aqueous medium. As shown in Table 1, no desirable product could be detected when a mixture of model reactants was heated at 90°C for 8 h in the absence of ionic liquid (Table 1, entry 1), which indicated that the catalysts should be absolutely necessary for this condensation. All the nine TSILs proved to be very active, leading to 82–90% yield of 5-oxo-5,6,7,8-tetrahydro-4*H*-benzo[b]pyrans in the presence of 10% TSILs (entries 5, 10–17). In addition, ionic liquids containing the longer length of alkyl chain are relatively efficient; however, the better immiscibility of the resulted product with the shorter length of alkyl chain ionic liquids should facilitate the separation in work-up procedure. Hence, [TEBSA]HSO₄ should be the best catalyst for this condensation among these ionic liquids and the optimized reaction conditions went to entry 5 in Table 1.

Condensation reaction in [TEBSA]HSO₄/H₂O gave a yield of 89%, which was nearly the same as that in organic solvents. The chemical industry is under considerable pressure to replace many of the volatile organic compounds (VOCs) that are currently used as solvents in organic synthesis. As a clean and cheap solvent, it is of great importance to carry out this reaction in water for the environmental and economic reasons.

While optimizing the reaction condition, the recycling performance of [TEBSA]HSO₄ was investigated using the above-mentioned model reaction. After the separation of the products **4**, the catalyst-containing filtrate was reused in the next run without further purification. The data listed in Table 2 showed that the [TEBSA]HSO₄ could be reused at least 10 times without obviously decreasing of the catalytic activity. Compared with the traditional solvents and catalysts, the easy and efficient recycling performance is also an attractive property of the ionic liquids for the environmental protection and economic reasons.

Then, the condensation reaction of various aromatic aldehyde, malononitrile (or ethyl cyanoacetate), and dimedone (or 1,3-cyclohexanedione) in the presence of [TEBSA]·HSO₄ as an environmentally benign ionic liquid was explored under the optimized reaction conditions described earlier, and the results are presented in Table 3. It can easily be seen that in all cases the reactions gave the products in good yields ranged from 86 to 94%. Aromatic aldehydes carrying either electron-donation or electron-withdrawing substituents afforded good yields of 5-oxo-5,6,7,8-tetrahydro-4*H*-benzo[b]pyrans in high purity. However, the product obtained is

Scheme 2



racemic, which indicated that the reaction was accomplished with no regioselectivity in this procedure.

In conclusion, some acyclic TSILs such as [TEBSA]·H₂SO₄, [TBPSA]·H₂SO₄, [EDPSA]·H₂SO₄, and so on were synthesized in an atom-economic procedure. These ionic liquids were found to be efficient catalysts for the synthesis of 5-oxo-5,6,7,8-tetrahydro-4*H*-benzo[*b*]pyrans in aqueous media, offering the practical convenience in the product separation from the ionic liquid/water system. The merit of this methodology is that it is simple, mild, and efficient, and the raw materials are cheaper than TSILs with imidazole or triphenylphosphine as the cation. Therefore, we believe that the work reported here would have potential application in green chemistry.

EXPERIMENTAL

Melting points were determined on X-6 microscope melting apparatus. The IR spectra were run on a Nicolette spectrometer and expressed in cm⁻¹ (KBr). ¹H NMR spectra were recorded on Bruker DRX300 (300 MHz) and ¹³C NMR spectra on

Bruker DRX300 (75.5 MHz) spectrometer. Elemental analyses were recorded on Perkin-Elmer C spectrometer. Mass spectra were obtained with automated FININIGAN Trace Ultra-Trace DSQ GC/MS spectrometer. All chemicals (AR grade) were commercially available and used without further purification.

Synthesis of halogen-free SO₃H-functional acidic ionic liquids (TSILs). All acyclic SO₃H-functionalized halogen-free acidic ionic liquids, such as [TEBSA]H₂SO₄, [TBPSA]H₂SO₄, were synthesized according to our previous methods [15d], and the pyridine, imidazole-based acidic ionic liquids for comparison were synthesized according to reported methods [15c]. Their structures were analyzed by ¹H NMR, ¹³C NMR, and MS spectral data. The selected spectral data for acidic halogen-free TSILs.

N,N,N-Triethyl-*N*-butanesulfonic acid ammonium hydrogen sulfate ([TEBSA]H₂SO₄). ¹H NMR (300 MHz, D₂O): δ 3.15 (q, *J* = 7.2 Hz, 6H, N-CH₂-CH₃), 3.07 (t, *J* = 8.4 Hz, 2H, N-CH₂-C-C-SO₃), 2.82 (t, *J* = 7.2 Hz, 2H, N-C-C-CH₂-SO₃), 1.63–1.70 (m, 4H, N-C-C₂H₄-C-SO₃), 1.09–1.13 (m, 9H, N-CH₂-CH₃). ¹³C NMR (75.5 MHz, D₂O): δ 56.21, 52.85, 50.32, 21.50, 20.20, 6.90. MS (*m/z*): 335.35 (M⁺), 208.36 (100).

N,N,N-Tributyl-*N*-propanesulfonic acid ammonium hydrogen sulfate ([TBPSA]H₂SO₄). ¹H NMR (500 MHz, D₂O): δ 3.28 (t, 2H, *J* = 4.0 Hz, N-CH₂-C-C-SO₃), 3.13 (t, 6H, *J*

Table 1

Synthesis of 5-oxo-5,6,7,8-tetrahydro-4*H*-benzo[*b*]pyrans catalyzed by acidic ionic liquids.^a

Entry	Catalyst	TSILs (mol%) ^b	<i>T</i> (°C)	Time (h)	Yields (%) ^c
1	–	–	100	8.0	–
2	[TEBSA]·H ₂ SO ₄	4	90	6.0	87
3	[TEBSA]·H ₂ SO ₄	6	90	4.5	89
4	[TEBSA]·H ₂ SO ₄	8	90	1.5	89
5	[TEBSA]·H ₂ SO ₄	10	90	1.0	89
6	[TEBSA]·H ₂ SO ₄	12	90	1.0	90
7	[TEBSA]·H ₂ SO ₄	15	90	1.0	91
8	[TEBSA]·H ₂ SO ₄	10	70	3.5	86
9	[TEBSA]·H ₂ SO ₄	10	80	2.0	90
10	[TMBSA]·H ₂ SO ₄	10	90	1.0	84
11	[TMPSA]·H ₂ SO ₄	10	90	1.0	82
12	[TEPSA]·H ₂ SO ₄	10	90	1.0	84
13	[TBPSA]·H ₂ SO ₄	10	90	1.0	90
14	[PyPSA]·H ₂ SO ₄	10	90	1.0	83
15	[MIMPSA]·H ₂ SO ₄	10	90	1.0	85
16	[bmim]·H ₂ SO ₄	10	90	1.5	82
17	[EDPSA]·H ₂ SO ₄	10	90	1.0	86

^a Acidic ionic liquids are 5 mmol benzaldehyde, 5 mmol malononitrile, 5 mmol dione, and water is used as a solvent.

^b Molar ration of TSILs to benzaldehyde.

^c Isolated yields.

Table 2
Reusing of the ionic liquid [TEBSA]·HSO₄^a

Entry	Run	Isolated yield (%)
1	Fresh	89
2	1	90
3	2	90
4	3	88
5	4	89
6	5	90
7	6	89
8	7	88
9	8	88
10	9	86
11	10	87

^a Acidic ionic liquids are 5 mmol benzaldehyde, 5 mmol malononitrile, 5 mmol dimedone, 0.5 mmol catalyst, 90°C, 1.0 h.

= 8.5 Hz, N—CH₂—C—C—CH₃), 2.85 (t, 2H, *J* = 7.0 Hz, N—C—C—CH₂—SO₃), 2.00–2.06 (m, 2H, N—C—CH₂—C—SO₃), 1.53–1.59 (m, 6H, N—C—CH₂—C—CH₃), 1.22–1.30 (m, 6H, N—C—C—CH₂—CH₃), 0.84 (t, 9H, *J* = 7.5 Hz, N—C—C—C—CH₃). ¹³C NMR (75.5 MHz, D₂O): δ 58.49, 50.66, 48.42, 23.93, 20.36, 19.16, 14.46. MS (*m/z*): 405.29 (M⁺), 406.28, 404.28 (100).

***N*-Propanesulfonic acid pyridinium hydrogen sulfate ([PyPSA]HSO₄).** ¹H NMR (300 MHz, D₂O): δ 8.62 (d, *J* = 6.0 Hz, 2H, H-2, H-6), 8.30 (t, *J* = 7.8 Hz, 1H, H-4), 7.84 (t, *J* = 6.9 Hz, 2H, H-3, H-5), 4.51 (t, *J* = 7.5 Hz, 2H, N—CH₂—C—C—SO₃), 2.73 (t, *J* = 7.2 Hz, 2H, N—C—C—C—CH₂—SO₃), 2.18–2.23 (m, 2H, N—C—CH₂—C—SO₃). ¹³C NMR (75.5 MHz, D₂O): δ 146.35, 144.70, 128.82, 60.28, 47.48, 26.47.

***1*-Methyl-3-propanesulfonic acid imidazolium hydrogen sulfate ([MIMPSA]HSO₄).** ¹H NMR (300 MHz, D₂O): δ 8.47 (s, 1H, CH), 7.24 (d, *J* = 1.5 Hz, 1H, CH), 7.17 (d, *J* = 1.5 Hz, 1H, CH), 4.08 (t, *J* = 6.9 Hz, 2H, N—CH₂—C—C—SO₃), 3.62 (s, 3H, N—CH₃), 2.64 (t, 2H, *J* = 7.5 Hz, 2H, N—C—C—CH₂—SO₃), 2.01–2.06 (m, 2H, N—C—CH₂—C—SO₃). ¹³C NMR (75.5 MHz, D₂O): δ 136.53, 124.32, 122.57, 48.13, 47.66, 36.46, 25.48. MS (*m/z*): 302.0 (M⁺), 300.93 (100).

***1*-Butyl-3-methylimidazolium hydrogen sulfate ([bmim]HSO₄).** ¹H NMR (300 MHz, D₂O): δ 8.62 (s, 1H, H-2), 7.33v7.38 (m, 2H, H-4, H-5), 4.09 (t, 2H, *J* = 7.1 Hz), 3.79 (s, 3H), 1.68–1.78 (m, 2H), 1.16–1.24 (m, 2H), 0.79 (t, 3H, *J* = 7.4 Hz). ¹³C NMR (75.5 MHz, D₂O): δ 136.35, 124.07, 122.80, 49.85, 36.33, 31.80, 19.31, 13.25. *m/z*: 236 (M⁺), 139 (100, M⁺-HSO₄).

***N,N,N',N'*-Tetramethyl-*N,N'*-dipropanesulfonic acid ethylenediammonium hydrogen sulfate ([EDPSA]·HSO₄).** ¹H NMR (300 MHz, D₂O): δ 3.60 (s, 4H, —CH₂—), 3.24 (t, 4H, *J* = 8.4 Hz, —CH₂—), 2.89 (s, 12H, CH₃), 2.64 (t, 4H, *J* = 6.9 Hz, —CH₂—), 1.85–1.95 (q, 4H, *J* = 7.65 Hz, —CH₂—). Anal. Calcd. For C₁₂H₃₂N₂O₁₄S₄: C, 25.89; H, 5.79; N, 5.03; Found: C, 25.65; H, 5.80; N, 4.81. *m/z*: 556.88 (M⁺), 361.07 (M⁺-2H₂SO₄, 100).

General procedure for the synthesis of 5-oxo-5,6,7,8-tetrahydro-4H-benzo[b]pyrans. To a round-bottomed flask charged with aromatic aldehyde (5 mmol) **1**, malononitrile or ethyl cyanoacetate (5 mmol) **2**, 5,5-dimethyl-1,3-cyclohexanedione (dimedone) or 1,3-cyclohexanedione (5 mmol) **3** in 5 mL of water was added acidic ionic liquid (0.5 mmol) under stirring. The mixture was then stirred for a certain time at 90°C. On completion (monitored by TLC), the precipitated crude product was collected by filtration and recrystallized from ethanol (95%) to afford pure 5-oxo-5,6,7,8-tetrahydro-4H-benzo[b]pyrans **4**. The filtrated containing ionic liquid

Table 3
Synthesis of 5-oxo-5,6,7,8-tetrahydro-4H-benzo[b]pyrans catalyzed by [TEBSA]·HSO₄^a

Entry	Ar	R ₁	R ₂	Time (h)	Mp (°C) [Lit.]	Yields (%) ^b
1	C ₆ H ₅	CN	CH ₃	1.0	226–228 [13]	89
2	<i>p</i> -CH ₃ OC ₆ H ₄	CN	CH ₃	1.0	197–199 [13]	93
3	<i>o</i> -CH ₃ C ₆ H ₄	CN	CH ₃	1.0	212–214 [13]	86
4	<i>m</i> -HOC ₆ H ₄	CN	CH ₃	1.0	230–232 [13]	92
5	<i>p</i> -FC ₆ H ₄	CN	CH ₃	1.5	191–193 [2b]	87
6	<i>o</i> -ClC ₆ H ₄	CN	CH ₃	1.0	214–215 [13]	91
7	<i>m</i> -ClC ₆ H ₄	CN	CH ₃	1.0	230–232 [13]	91
8	<i>p</i> -ClC ₆ H ₄	CN	CH ₃	1.0	209–211 [13]	91
9	<i>p</i> -BrC ₆ H ₄	CN	CH ₃	1.0	205–207 [13]	94
10	<i>m</i> -NO ₂ C ₆ H ₄	CN	CH ₃	1.0	208–210 [13]	92
11	<i>p</i> -NO ₂ C ₆ H ₄	CN	CH ₃	1.0	179–180 [13]	93
12	2,4-Cl ₂ C ₆ H ₃	CN	CH ₃	1.0	189–191 [13]	87
13	<i>p</i> -CH ₃ OC ₆ H ₄	CN	H	1.0	190–192 [2b]	92
14	<i>o</i> -ClC ₆ H ₄	CN	H	1.0	210–212 [2b]	86
15	<i>p</i> -ClC ₆ H ₄	CN	H	1.0	225–227 [6b]	93
16	<i>m</i> -NO ₂ C ₆ H ₄	CN	H	1.0	198–200 [2b]	92
17	2,4-Cl ₂ C ₆ H ₃	CN	H	1.5	220–222 [2b]	87
18	<i>p</i> -ClC ₆ H ₄	CO ₂ Et	CH ₃	1.5	155–157 [13]	88
19	<i>m</i> -NO ₂ C ₆ H ₄	CO ₂ Et	CH ₃	1.5	185–187 [13]	89

^a Acidic ionic liquids are 5 mmol benzaldehyde, 5 mmol malononitrile (or ethyl cyanoacetate), 5 mmol dimedone (or 1,3-cyclohexanedione), 0.5 mmol catalyst, 90°C.

^b Isolated yields.

could be reused directly in the next run without further purification. The products were identified by IR, ¹H NMR, and physical data (Mp) with those reported in the literatures.

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