Chinese Science Bulletin

Synthesis of a novel multi-SO_3H functionalized strong Brønsted acidic ionic liquid and its catalytic activities for acetalization

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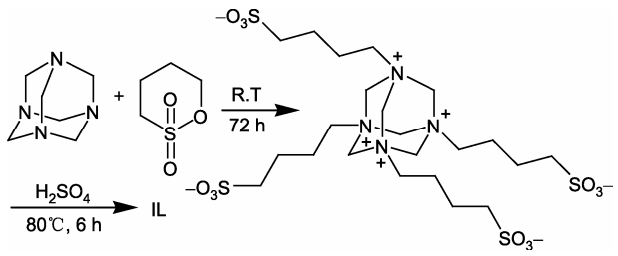
The novel multi-SO_3H functionalized strong Brønsted acidic ionic liquid has been prepared and its catalytic activities were investigated through the acetalization. The results showed that the novel catalyst was very efficient for the reaction with the average yield over 90% under solvent-free condition at room temperature. Operational simplicity, without need of any solvent, a small amount of usage, low cost of the catalyst used, high yields, applicability to large-scale reactions and reusability are the key features of this methodology. The novel catalyst also has great potential for the green process.

acetals, ionic liquids, catalysis, green chemistry, protecting groups

Currently, ionic liquids are receiving widespread attention as mediums for a variety of reactions[1–4] for their properties such as very low or practically no vapor pressure, remarkable solubility behavior and possibility to vary structure to manipulate the parameters like density, solubility, etc.[5–7] Recently, the alkane sulfonic acid group functionalized ionic liquids (FIL) were reported offering a new possibility for developing environmentally friendly acidic catalysts due to the combination of the advantages of liquid acids and solid acids, e.g. uniform acid sites, stability in water and air, easy separation and reusability[8]. Since 2002, Cole et al.[9] first published an article about sulfonic FIL with strong Brønsted acidity, and the research and application of various $–SO_3H$ functionalized strong Brønsted acidic ionic liquids have received more and more attention for their potential in replacement of conventional homogenous/heterogeneous acidic catalysts because they are fluxible, nonvolatile, non-corrosive and immiscible in many organic solvents and could be used as dual solvent and catalysts[10–15]. To the best of our knowledge, most ionic liquids were functionalized with just one sulfonic group, which results in the low acidity as the acid catalysts. Hence,we present a novel strong Brønsted acidic ionic liquid with four $–SO_3H$ groups. The catalyst was synthesized through the addition of hexamethylenetetramine and 1,4-butane sulfonate (Scheme 1). The catalytic activities of the novel ionic liquid have been observed through the acetaliztion. The results showed that the catalyst was very efficient for the reactions with the yield over 95% under solvent-free condition at room temperature. The additional advantage of extremely high density of



Scheme 1 The synthetic route of the novel catalyst.

Received February 11, 2009; accepted May 20, 2009
doi: 10.1007/s11434-009-0437-3
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Supported by the National Key Project of Scientific and Technical Supporting Programs of Ministry of Science and Technology of China (Grant No. 2006BAE03B06), Shanghai Leading Academic Discipline Project (Grant No. B409) and Shanghai International Cooperation of Science and Technology Project (Grant No. 06SR07101).

Citation: Zhang J, Bao S H, Yang J G. Synthesis of a novel multi-SO_3H functionalized strong Brønsted acidic ionic liquid and its catalytic activities for acetalization. Chinese Sci Bull, 2009, 54: 3958−3964, doi: 10.1007/s11434-009-0437-3

acidity made the catalyst hold greater potential for the acid-catalyzed reactions than the other acid catalysts.

1 Experimental

All organic reagents were commercial products being of the highest purity (>98%) and used for the reaction without further purification. Cyclohexanone, Hexamethylenetetramine, 1,4-butane sulfonate, 3-pentanone, butanone, propionaldehyde, mercaptoethanol, *n*-butyraldehyde, iso-butyraldehyde, diphenyl ketone, and benzaldehyde were purchased from Shanghai Chemicals Co. *n*-valeraldehyde was obtained from Fluck.

1.1 Synthesis of the catalyst

(i) Preparation of zwitterions. Hexamethylenetetramine and quadruplemolar 1,4-butane sulfonate were mixed without other solvent and stirred magnetically for 72 h at 25℃. Then, a white solid zwitterion was formed and washed repeatedly with ether. After being dried in vacuum (110℃, 0.01 Torr), the white solid zwitterion was obtained in good yield (>90%) and sufficient purity as assessed by a Varian DRX-400 NMR spectroscopy. Spectroscopic data for zwitterions: ^{1}H NMR (400 MHz, D_2O, TMS): δ 1.423 (m, 2H), 1.584 (m, 2H), 2.593 (t, J = 7.6Hz, 2H), 3.964 (t, J = 7.6Hz, 2H), 8.463 (s, 3H). ^{13}C NMR (100 MHz, D_2O, TMS): δ 21.180, 21.879, 50.368, 52.193, 79.999.

(ii) Preparation of $-SO_3H$ functionalized ionic liquids. A stoichiometric amount of sulfuric acid was added to the above obtained zwitterion and the mixture was stirred for 6 h at 80℃ to form the ionic liquid. The ionic liquid phase was then washed repeatedly with toluene and ether to remove non-ionic residues, and dried in vacuum (110℃, 0.01 Torr). The product was formed quantitatively and in high purity assessed by mass balance and ^{1}H NMR spectroscopies. ^{1}H NMR (400 MHz, D_2O, TMS): δ 1.323 (m, 2H), 1.483 (m, 2H), 2.503 (t, J = 7.6Hz, 2H), 3.874 (t, J = 7.6Hz, 2H), 8.263 (s, 3H).

1.2 The acetalization of carbonyl compounds

The following is a typical procedure: Into a mixture of carbonyl compound (30 mmol) and diol (30 mmol) is added the catalyst (68 mg (0.01 mmol)) at room temperature and left for stirring at the same temperature. After completion of the reaction as indicated by TLC, the reaction mixture was extracted with ethyl acetate: ethyl ether = 1∶1, and the extract was washed with brine, dried (Na_2SO_4), evaporated and purified by column chromatography over silica gel (25% ethyl acetate in petroleum ether) to obtain the pure product. All the known compounds were fully detected by GC-MS (Agilent 6890N GC/5973N MS, DM-5MS) and the usual spectral methods (NMR and IR).

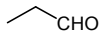
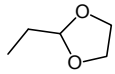
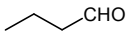
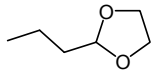
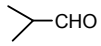
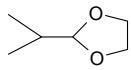
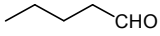
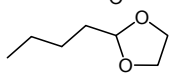
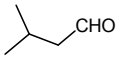
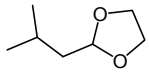
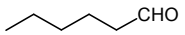
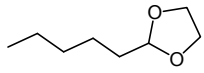
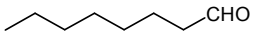
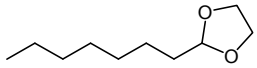
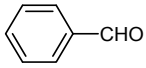
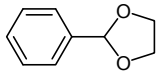
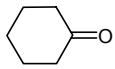
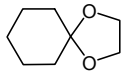
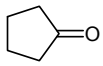
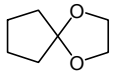
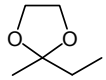
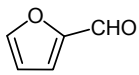
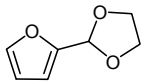
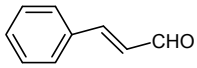
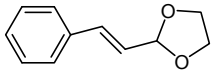
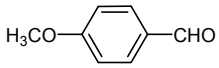
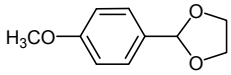
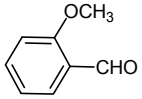
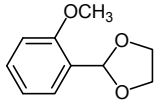
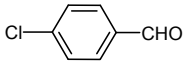
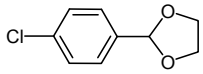
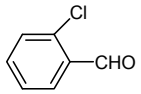
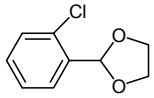
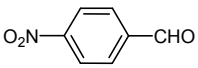
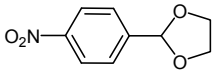
2 Results and discussion

2.1 The acetalization of carbonyl compounds

Various carbonyl compounds have been used as substrates to react with glycol over the novel catalyst (Table 1). The results in Table 1 clearly demonstrate that the novel catalyst is efficient, with almost quantitative conversion and exclusive selectivity for most reactions between carbonyl compounds and glycol. Aliphatic aldehydes transformed to the corresponding acetals smoothly under the reaction conditions (entries 1－7). Aromatic aldehydes, such as *p*-chlorobenzaldehyde, *p*-methoxybenzaldehyde, and *p*-nitrobenzaldehye, could also be acetalized to afford the corresponding 1,3-dioxolanes with 95%, 94% and 95% yields respectively (entries 14－18). Cinnamaldehyde was converted to the corresponding products in high yield (91.3%) without any damage of the double bond (entry 13). The ketalization reactions were also examined over the system. The linear chain ketones butanone can also be converted to the corresponding ketals in moderate yields (entry 11). Cyclohexanone and cyclopentanone also worked well, but the reactivity of cyclopentanone seemed to be slightly lower than that of cyclohexanone (entries 9 and 10). The reactions were also very efficient for the heterocyclic compounds. 2-Furaldehyde was successfully acetalized, and the conversion of the aromatic aldehyde was 92% (entry 12), further expanding the generality of this catalytic system to heterocyclic aromatic aldehydes. In our system, many acid-labile substrates, such as 4-methoxybenzaldehyde, and cinnamaldehyde, all worked well (entries 13－15). These results indicate the usefulness of the novel ionic liquid as catalyst for the reactions.

O/S-acetals are very important in different aspects. They can be used as either acyl anion equivalents for C－C bond formation[16−18] or carbonyl protecting group[19]. Moreover, their considerable stability in acidic conditions rather than O/O-acetals and their easy removal in comparison with S－S acetals make them good protecting tools in organic synthesis[20]. So the reactions of carbonyl compounds with mercaptoethanol are also

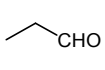
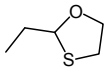
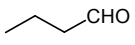
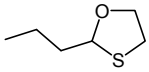
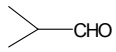
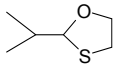
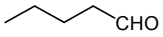
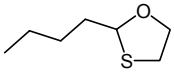
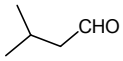
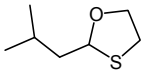
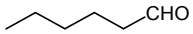
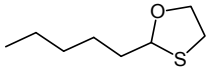
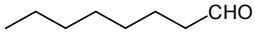
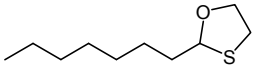
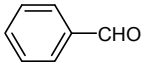
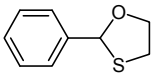
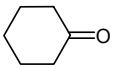
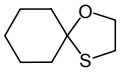
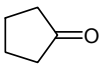
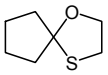
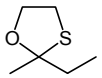
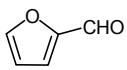
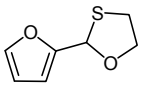
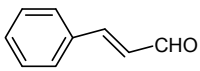
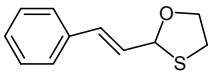
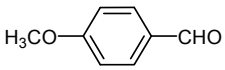
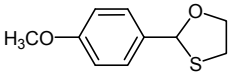
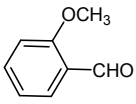
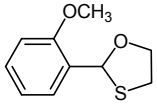
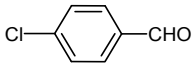
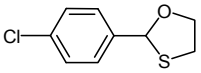
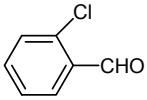
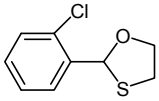
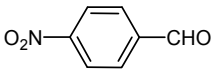
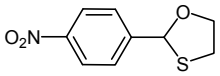
Table 1 The reactions between carbonyl compounds and glycol

Entry	Substrate	Product	Reaction time (h)	Yield (%)[a, b]
1			1.5	99.5
2			4.0	95.3
3			3.5	96.3
4			5.0	94.5
5			6.0	94.2
6			7.0	93.5
7			12	90.5
8			3.0	96.5
9			4.0	93.2
10			7.0	91.8
11			14	79.8
12			12	92.4
13			8.0	91.3
14			8.0	94.6
15			9.0	91.5
16			5.0	95.2
17			7.0	93.4
18			3.0	96.4

a) All reactions were triggered at room temperature (25℃). Conditions: carbonyl compounds: 20 mmol; glycol: 24 mmol; catalyst: 68 mg (0.01mmol); b) Isolated yield.

commonly used in our catalytic system (Table 2). As summarized in Table 2, the novel ionic liquid is also very efficient for the acetalization of a wide variety of carbonyl compounds and mercaptoethanol. Using a small amount of the catalyst under mild and simple reaction conditions (at room temperature in air), aromatic aldehydes, a conjugated aldehyde, aliphatic aldehydes, and cyclic ketones all underwent smooth transformation to the corresponding acetals in good yields. An acid-sensitive 2-furancarboxaldehyde was converted to the corresponding dimethylacetal with 92.4% yield (entry 12). The double bond in cinnamaldehyde did not under-

Table 2 Preparation of various oxathioacetals from the corresponding carbonyl compounds

Entry	Substrate	Product	Reaction time (min)	Yield (%)a, b)
1			1.0	98.9
2			2.0	97.3
3			3.0	95.3
4			4.0	95.5
5			5.0	95.2
6			7.0	94.5
7			12	93.5
8			3.0	97.5
9			4.0	94.2
10			5.0	92.8
11			14	87.8
12			8.0	92.4
13			7.0	92.3
14			6.0	95.3
15			8.0	94.5
16			3.0	96.1
17			5.0	93.7
18			3.0	97.3

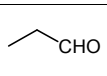
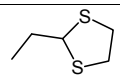
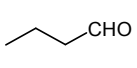
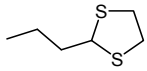
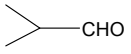
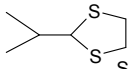
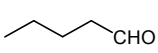
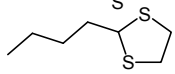
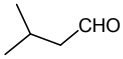
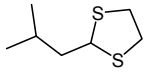
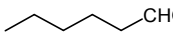
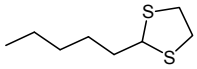
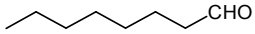
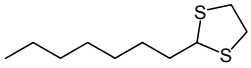
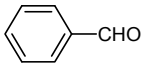
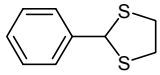
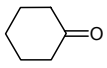
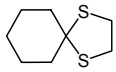
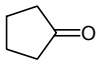
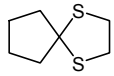
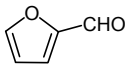
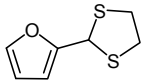
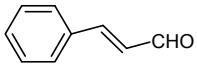
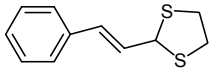
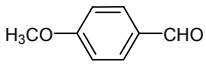
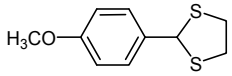
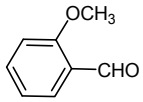
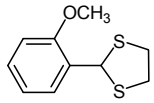
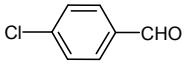
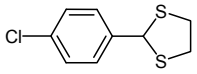
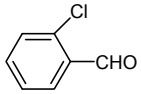
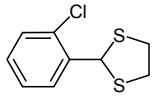
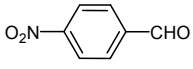
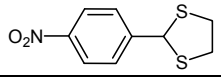
a) All reactions were triggered at room temperature (25℃). Conditions: carbonyl compounds: 20 mmol; glycol: 24 mmol; catalyst: 68 mg (0.01mmol); b) Isolated yield.

go isomerization during acetal formation (entry 13). These results indicate that the reaction conditions are mild and not sufficiently acidic to cause side-reactions.

S/S-acetals derived from aldehydes are good precursors for the formation of C—C bond under basic conditions[21]. Their synthesis was also very important in organic syntheses. Many of the reagents and catalysts used in the preparation of O/S-acetals and O/O-acetals from carbonyl compounds did not work successfully in the preparation of S/S-acetals[22–24]. So the preparation of S/S acetals was discussed (Table 3). A wide variety of carbonyl compounds was successfully transformed to

the corresponding S/S-acetals using the novel catalyst under solvent-free condition. It can be seen from Table 3 that catalyst was very efficient for the reactions with the average yield above 90%. Also it can be deduced that the reactivity of glycol, mercaptoethanol and dithioethylene was different and the reactivity became higher with –SH increasing. Benzaldehyde or aromatic aldehydes containing electron withdrawing substituent attached to the aromatic ring react very fast to furnish acetals due to the better electrophilicity at the carbonyl center compared to the aromatic aldehydes with electron donating substituent present in the aromatic nucleus,

Table 3 The synthesis of various dithiolanes from carbonyl compounds and 1,2-ethanedithiol

Entry	Substrate	Product	Reaction time (min)	Yield (%)a, b)
1			1.0	99.3
2			2.0	98.3
3			2.5	95.6
4			3.0	96.5
5			4.5	96.2
6			6.5	95.5
7			10	93.5
8			2.5	98.1
9			3.5	94.6
10			4.5	93.8
11			12	88.4
12			8.0	93.4
13			6.0	93.3
14			5.0	95.8
15			7.5	94.9
16			3.0	98.8
17			4.5	96.7
18			2.5	98.1

a) All reactions were triggered at room temperature (25℃). Conditions: carbonyl compounds: 20 mmol; glycol: 24 mmol; catalyst: 68 mg (0.01mmol); b) Isolated yield.

which may reduce the electophilicity at the carbonyl center by virtue of the conjugation (entries 14—18). In addition, the formation of acetals from aliphatic aldehydes also differs for the steric hindrance (entries 1—7).

2.2 The comparative study on the catalytic activities of the different catalysts

A comparative study on the catalytic activities of the novel catalyst with the reported catalyst was carried out using benzaldehyde and glycol as a model substrates (Table 4). From this study, it can be concluded that the novel catalyst has much higher activity than others, furthermore it has the advantage of reusability. It is clearly shown that the novel catalyst should be considered as one of the best choices for economic convenient, and user-friendly catalyst and scaling up.

Table 4 The comparison of different catalysts

Entry	Catalyst	Catalyst amount (mg)	Reaction time (h)	Yield (%)
1	Novel catalyst	68	3	96.5
2	$[Et_3NH][HSO_4]$	240	12	90.5
3	[Bmim] $[HSO_4]$	145	14	91.3
4	[Spmim]$[HSO_4]$	232	10	89.6
5	[Sbpr]$[HSO_4]$	128	13	92.8

2.3 The reuse of the catalyst

One property of the novel catalyst is the reusability. After reactions, the reaction mixture was extracted with ethyl acetate: ethyl ether = 1∶1 and the lower phase, and the ionic liquid could be reused without any disposal. The recovered activities were investigated through the reaction of benzaldehyde and glycol carefully (Figure 1). The yields and the sample composition remained unchanged even after the catalyst had been recycled for five times.

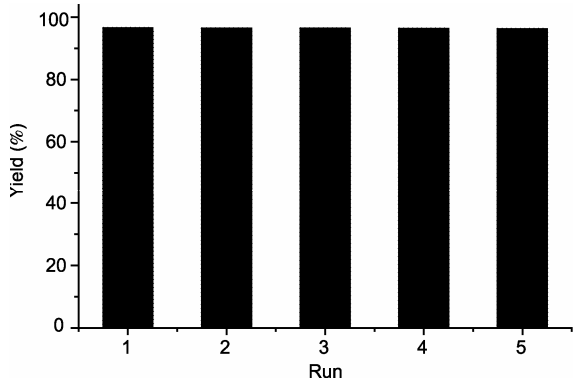


Figure 1 The reuse of the catalyst.

2.4 The probable mechanism

The probable mechanism is illustrated in Figure 2. Here, the acidity of the catalyst showed great importance for the reactions. The novel ionic liquid owned much higher acidity, which resulted in the high activities.

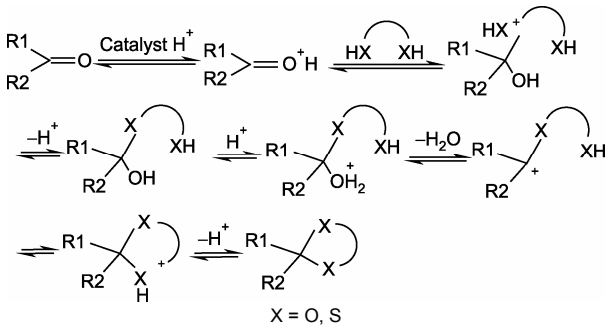


Figure 2 The probable mechanism.

3 Conclusions

A novel ionic liquid with high acidity has been found to be highly efficient for different acetals formation from aliphatic and aromatic aldehydes. Operational simplicity, with no need of any solvent, a small amount of usage, low cost of the catalyst used, high yields, and applicability to large-scale reactions are the key features of this methodology. The novel catalyst also owned great potential for the green process.

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