

## Application of Functional Ionic Liquids Possessing Two Adjacent Acid Sites for Acetalization of Aldehydes

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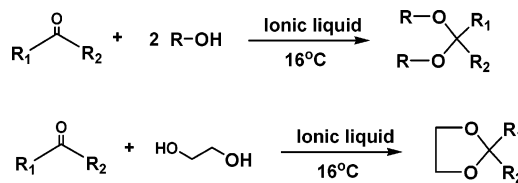
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**Abstract:** Several acid functional ionic liquids, in which cations possess two adjacent acid sites, were synthesized and used for the acetalization of aldehydes with good catalytic performance under mild reaction conditions.

The acetalization reaction is a process that is widely used in organic synthesis to protect the carbonyl group of aldehydes and ketones.<sup>1</sup> Afterward, acetals became important reactants for synthesis of enantiomerically pure compounds which were widely used as steroids, pharmaceuticals, and fragrances.<sup>2</sup> Previously, the catalysts used in the acetalization reactions were generally proton acids, Lewis acids, and a number of transitional metal complexes including Rh, Pd, and Pt.<sup>3</sup> Although good results were obtained, the separation of the products from the catalyst system after the reaction was still difficult to overcome and the noble metal catalysts used were quite expensive and usually unstable.<sup>4</sup> Therefore, to design and synthesize a catalytic system that may be stable, easily separable, and reusable has long been pursued. Furthermore, the basic requirements for achieving high catalytic activity, as it was reported in previous literature, were the presence of sufficient acidity and the existence of two adjacent acid sites to have the reactants



**FIGURE 1.** Acetalization reactions with acid functional ionic liquid as catalyst.

in a mutually cis position,<sup>4</sup> and all these studies offered us the possibility of designing suitable catalysts for this reaction.

On the other hand, because of the great potential of room temperature ionic liquids as environmentally benign media for catalytic processes,<sup>5</sup> much attention has currently been focused on the organic reactions catalyzed with or in ionic liquids, and many organic reactions, especially in the reactions promoted with acid–base catalysts, were performed in ionic liquids with high performances.<sup>6</sup> At the same time, the acidic ionic liquid used in previous literature was usually based on  $\text{AlCl}_3$ , which was not stable, and the reusability was also difficult.<sup>7</sup> Recently, the syntheses of “task-specific” ionic liquids with special functions according to the requirement of a specific reaction have become an attractive field.<sup>8</sup> Herein, according to the requirement of the catalysts for the acetalization reactions as mentioned above, a series of acid functional ionic liquids with two adjacent acid sites, i.e., the acid group introduced and the  $\text{N}^+$  in the imidazolium, were synthesized and used for the acetalization reactions with good results (Figure 1).

Our new approach reported here involves the use of room temperature ionic liquids based on  $-\text{CO}_2\text{H}$ ,  $-\text{SO}_3\text{H}$ , and  $-\text{SO}_3\text{H}$ , Figure 2. All chemical reagents were purified by distillation before use. The ionic liquids  $[\text{AcMim}]\text{Cl}$ ,  $[\text{AcBim}]\text{Cl}$ ,  $[\text{AcOim}]\text{Cl}$ ,  $[(\text{CH}_2)_4\text{SO}_3\text{HMim}]\text{CF}_3\text{SO}_3$ ,  $[(\text{CH}_2)_4\text{SO}_3\text{HMim}]\text{TSO}$ , and  $\text{Mim}(\text{CH}_2)_4\text{SO}_3$  were synthesized according to the procedures reported in previous literature.<sup>8b,e,f</sup>

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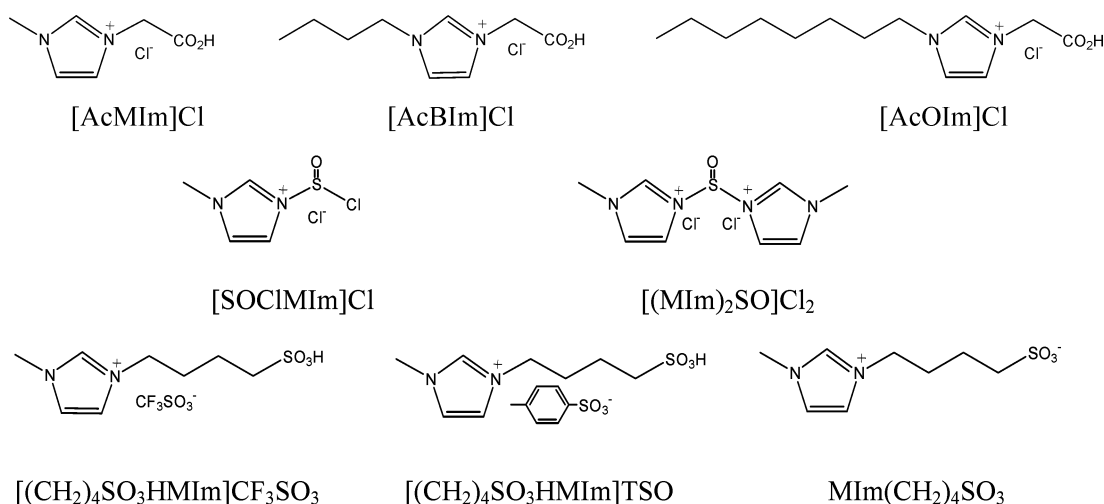
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**FIGURE 2.** Functional ionic liquids synthesized and used in acetalization reactions.

Ionic liquid [SOCIMIm]Cl was synthesized as follows: A mixture containing 60 mL of acetonitrile and 36.3 mL (0.5 mol) of thionyl chloride was charged into a 250-mL three-necked flask equipped with a condenser tube. Then, under rigorous stirring, 39.8 mL (0.5 mol) of methyl imidazole was dropped into the mixture after ca. 30 min. After further reaction at room temperature for 12 h, the acetonitrile was separated with distillation and the desired ionic liquid [SOCIMIm]Cl was obtained. Ionic liquid [(MIm)<sub>2</sub>SO]Cl<sub>2</sub> was synthesized as follows: A mixture containing 60 mL of acetonitrile and 79.6 mL (1 mol) of methyl imidazole was charged into a 250-mL three-necked flask equipped with a condenser tube. Then, under rigorous stirring, 36.3 mL (0.5 mol) of thionyl chloride was dropped into the mixture after ca. 30 min. After further reaction at room temperature for 12 h, the acetonitrile was separated by distillation and the desired ionic liquid [(MIm)<sub>2</sub>SO]Cl<sub>2</sub> was obtained. The ionic liquids were further purified through drying in a vacuum (ca. 5 mmHg) at 150 °C to remove the residual acetonitrile, methyl imidazole, and thionyl chloride.

For each acetalization reaction, aldehydes (2 mL), alcohols (5 mL), and 1 g of catalysts (about 2–3 mmol) were charged into a 25-mL round-bottomed flask equipped with a magnetic stirrer. All reactions were performed at 16–40 °C for 2–23 h. After reaction, a liquid mixture with two phases was obtained in most cases, into which an additional amount of ethanol (3–5 mL) was added to allow the two-phase liquid mixture to become a single phase for analysis. Qualitative analyses were conducted with a GC-MS with a 30 m × 0.25 mm × 0.33 μm capillary column with a chemstation containing a NIST Mass Spectral Database. Quantitative analyses were conducted with a GC equipped with a FID detector, 30 m × 0.25 mm × 0.33 μm capillary column. Conversion and selectivity were calculated according to the chromatograph peak areas given by the chemstation. The isolated yields were obtained by using a separating funnel and by removal of the aldehyde and alcohol by evaporation. The ionic liquid was reused for the next time after it was dried in a vacuum (ca. 5 mmHg) at 120 °C for 1 h.

Butyl aldehyde and isoamyl alcohol were first selected to test the catalytic activity of the ionic liquid catalysts.































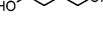


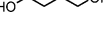


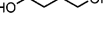






**TABLE 1.** Results of Acetalization of Butyl Aldehyde over Different Functional Ionic Liquids<sup>a</sup>

| entry           | ionic liquids   | conversion (%) | selectivity (%)        |
|-----------------|---|----------------|------------------------|
| 1               | [AcMIm]Cl   | 7.7            | 66.4                   |
| 2               | [AcBIm]Cl   | 90.1           | 97.8 (84) <sup>b</sup> |
| 3               | [AcOIm]Cl   | 74.8           | 72.9                   |
| 4               | ClCH <sub>2</sub> CO <sub>2</sub> H   | 40.3           | 87.0                   |
| 5               | [SOCIMIm]Cl   | 94.0           | 98.9 (88)              |
| 6               | [(MIm) <sub>2</sub> SO]Cl <sub>2</sub>  | 81.8           | 95.8 (77)              |
| 7               | SOCl <sub>2</sub>   | 60.9           | 66.9                   |
| 8               | [(CH <sub>2</sub> ) <sub>4</sub> SO <sub>3</sub> HMIm]CF <sub>3</sub> SO <sub>3</sub> | 86.6           | 75                     |
| 9               | [(CH <sub>2</sub> ) <sub>4</sub> SO <sub>3</sub> HMIm]TSO                             | 96.9           | 85.5                   |
| 10              | MIm(CH <sub>2</sub> ) <sub>4</sub> SO <sub>3</sub>                                    | 0.4            | 49.8                   |
| 11 <sup>c</sup> | [SOCIMIm]Cl   | 92.9           | 98.9 (83)              |

<sup>a</sup> *t* = 2 h, *T* = 16 °C. <sup>b</sup> Data in parentheses are isolated yields. <sup>c</sup> The ionic liquid was reused a third time.

All results of the acetalization of butyl aldehyde with isoamyl alcohol over different ionic liquids are listed in Table 1. First, the –CH<sub>2</sub>CO<sub>2</sub>H group was introduced into the imidazolium cation. It can be seen that the best result was obtained over [AcBIm]Cl but poor results were observed when using ClCH<sub>2</sub>CO<sub>2</sub>H as catalyst or the butyl in [AcBIm]Cl was substituted by methyl or octyl (entries 1–4). These results showed that the synergism between the N<sup>+</sup> in the imidazolium and the –CO<sub>2</sub>H was the key factor for high catalytic activity and its effect was to promote the conversion of *mono*-acetalization product into *di*-acetalization product because no *mono*-acetalization product was detected. The resulting byproducts given by the GC-MS also indicated that the dominating side reactions occurring in this process were the polymerization and oxidation of butyl aldehyde and they could be effectively inhibited when using this functional ionic liquid as a catalyst. Excellent results were observed when another acid functional ionic liquid, [SOCIMIm]Cl, was employed in this reaction with 94.0% conversion and 98.9% selectivity (entry 5). The conversion decreased remarkably (81.8%) if [(MIm)<sub>2</sub>SO]Cl<sub>2</sub> was used as the catalyst, which may be attributed to the steric hindrance of this ionic liquid, entry 6. At the same time, only 60.9% conversion and 66.9% selectivity were obtained when with use of only SOCl<sub>2</sub> as catalyst, which further indicated that the cooperation between the acid group –SOCl

TABLE 2. Results of Acetalizations of Ethanediol and Butanediol with Aldehydes (Ketones)<sup>a</sup>

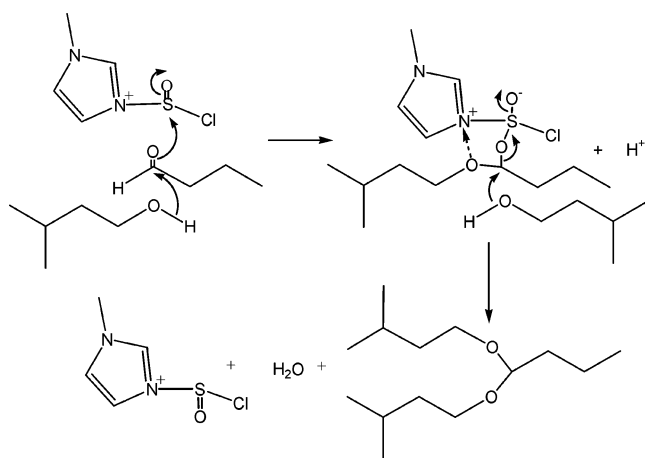
| Entry | alcohols  | ketones/aldehydes   | products  | t (h) <sup>b</sup> | con % <sup>c</sup> |
|-------|---|---|---|--------------------|--------------------|
| 1     |    |    |    | 3                  | 44.5               |
| 2     |    |    |    | 4                  | 97.8               |
| 3     |    |    |    | 4                  | 26                 |
| 4     |    |    |    | 15                 | 70                 |
| 5     |    |    |    | 20                 | 80                 |
| 6     |    |    |    | 4                  | 97                 |
| 7     |    |    |    | 4                  | 99                 |
| 8     |    |    |    | 23                 | 54.2               |
| 9     |    |    |    | 3                  | 37                 |
| 10    |    |    |    | 10                 | 5                  |
| 11    |    |    |    | 10                 | 30                 |
| 12    |  |   |   | 5                  | 72.3               |
| 13    |  |  |  | 15                 | 85.4               |
| 14    | MeOH  |  |  | 17                 | 10.3               |
| 15    | MeOH  |  |  | 7                  | 20                 |

<sup>a</sup> The reaction temperatures were 16 and 40 °C when ethanediol and butanediol were used as reactants, respectively, because the butanediol was solid at room temperature. <sup>b</sup> The given time was an equilibrium point in the reaction. <sup>c</sup> The corresponding selectivities were all ca. 100%.

and the N<sup>+</sup> in the imidazolium cation was indispensable. The -SO<sub>3</sub>H group, which was usually used as an acid catalyst, was also introduced into the imidazolium cation and very interesting results were obtained (entries 8–10), i.e., no acetalization reaction occurred if MIm(CH<sub>2</sub>)<sub>4</sub>SO<sub>3</sub> was used as the catalyst but the catalytic activity could be greatly enhanced when the -(CH<sub>2</sub>)<sub>4</sub>SO<sub>3</sub> group was protonated while the selectivity decreased greatly. All these results suggested that the acid site was indispensable; however, polymerization and oxidation of aldehyde occurred remarkably if such an acid site was too stronger. When the conversions and selectivities were high enough, isolated yields were given by simple decantation and it can be seen that the isolated yields were about 80–90%. As one of the most effective functional ionic liquids, [SOCIMIm]Cl was selected to investigate the possibility of reusability (entry 11). As was shown, no obvious change was observed on the catalytic activity and 83% of isolated yields was maintained when [SOCIMIm]Cl was reused a third time, which showed that the func-

tional ionic liquid was stable enough and the presence of water, which was formed during the reaction, has less impact on the catalytic activity of ionic liquid [SO-CIMIm]Cl.

Then, the reactions of ethanediol and butanediol with different kinds of aldehydes (ketones) were further employed to investigate the universality of these catalysts, and ionic liquid [SOCIMIm]Cl was selected as a typical catalyst because it possessed the highest catalytic activity and was first synthesized in this work (Table 2). Good results were also obtained when using ethanediol and aldehydes (ketones) such as cyclohexanone, benzaldehyde, propionaldehyde, and butyraldehyde as reactants with respectively 97.8%, 80%, 99%, and 97% conversions and approximately 100% selectivities. The corresponding isolated yields were not conducted because the reaction system containing ethanediol was very viscous and the separation could not be performed easily in such a small reaction scale. No good results were obtained with this catalyst system when other aldehydes were used to react



**FIGURE 3.** A possible mechanism of the acetalization reaction over functional ionic liquid.

with ethanediol. Their conversions were ca. 30–70% although high selectivities were maintained. The results were not as good as that with ethanediol as reactant when butanediol, methanol, and ethanol were used in the acetalization reaction. The highest conversion was 85.4%

when butanediol and chloroacetaldehyde were employed as reactants. It is worth noting that the conversion did not increase further even for longer reaction time, which indicated that the aldehyde acetals further reacted with the water formed during the reaction and there was an equilibrium point in acetalization reactions in such a reaction system if the water was not removed.

As to the mechanism of this reaction, the synergistic combination of the acid group and the  $N^+$  in the imidazolium should be the key factor and this process is graphically shown in Figure 3.

In conclusion, a series of functional ionic liquids with two adjacent acid sites were used as catalysts for acetalization reactions and good results were obtained, and it also was determined that they can be easily reused without deactivation occurring in some cases. The results also showed that the synergism between the two acid sites in the functional ionic liquids should be the key factor for the high catalytic activity.

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