Novel Hydrophobic Brønsted Acidic Ionic-liquids as Efficient and Reusable Catalysts for Organic Reactions in Water

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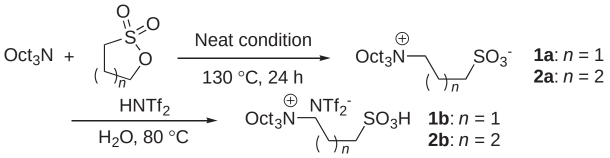
Novel hydrophobic Brønsted acidic ionic liquids (HBAIL) were prepared and utilized as acid catalysts in organic reactions in water. HBAILs were demonstrated, for the first time, to be effective catalysts for Prins cyclization of styrene derivatives in water with a formaldehyde water solution. Many styrene derivatives could be successfully converted to the corresponding 1,3-dioxanes. Other dehydration reactions also proceeded well using HBAILs in water. After reactions, HBAILs could be easily recovered and reused without significant loss of activity.

Organic reactions in water without the use of any harmful organic solvents are of great current interest, because water is an easily available, economical, safe, and environmentally benign solvent.[1] Although various catalysts have been developed to realize organic transformations in water, it is still difficult to achieve recovery and reuse of the catalysts in many cases. Brønsted acid catalysts are widely utilized in organic synthesis, however, traditional Brønsted acid catalysts are hydrophilic and generally less active for organic reactions in water because of the fact that most substrates are not soluble in water. Recently, we have addressed this issue by constructing hydrophobic reaction environments in water utilizing surfactant-type Brønsted acid[2] or styrene-based hydrophobic polymer-supported sulfonic acid catalysts.[3] In these cases, however, substrate scope is rather limited for hydrophobic substrates, and the efficiency of reuse of catalysts are not yet satisfactory.

Ionic liquids constitute a class of solvent entirely composed of ions. Their use as an environmentally friendly alternative for conventional solvents has received much attention recently.[4] Our specific interest in ionic liquids centers on their designability, which allows easy manipulate of their structure and their properties. As a typical example of functionalized ionic liquids, non-chloroaluminate acidic ionic liquids have exhibited great potential in replacement of conventional homogeneous and heterogeneous acidic catalysts, because they are air- and moisture-stable, less volatile and non-corrosive.[5] However, non-chloroaluminate acidic ionic liquids developed to date are all hydrophilic despite the fact that hydrophobic non-functionalized ionic liquids have been widely used in some processes. In the course of our investigations to develop efficient catalysts in water, we reasoned that hydrophobic Brønsted acidic ionic liquids might act as hydrophobic acid catalysts in water. Herein, we describe a novel hydrophobic Brønsted acidic ionic liquid catalyst (HBAIL), which works very efficiently in several acid-catalyzed organic reactions in water. In contract to our previous systems, HBAIL can work well for reactions with hydrophilic substrates in water.



Scheme 1. Preparation of HBAILs.

The structures and the synthetic procedures of two HBAILs are shown in Scheme 1. First, 1,3-propanesultone and 1,4-butanesultone were allowed to react with trioctylamine to prepare sulfobetaines **1a** and **2a**. The sulfobetaines obtained were then treated with trifluoromethanesulfonimide in water to afford hydrophobic products **1b** and **2b**. The compounds **1a**, **2a**, **1b**, and **2b** were well characterized by IR, ^{1}H and ^{13}C NMR and HRMS (see Supporting Information).[10] Compounds **1b** ($H_0 = 1.23$, 1 mmol/L in dichloromethane) and **2b** ($H_0 = 1.27$, 1 mmol/L in dichloromethane) are highly viscous liquid at room temperature, and are stable to air and moisture. Solubility investigation revealed that they are not soluble in water and hexane, but dissolve in ethyl acetate. It should be noted that increases the length of the alkyl group on the nitrogen atom from eight to twelve carbon atoms suppressed the second step reaction, treatment of sulfobetaine with trifluoromethanesulfonimide in water.

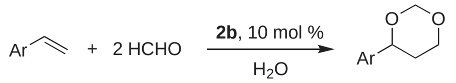
With the hydrophobic Brønsted acidic ionic liquids in hand, some acid-catalyzed reactions were investigated in water. First, we examined the activities of HBAILs in the Prins cyclization reaction, which is an important carbon–carbon bond-forming reaction and widely used in organic synthesis.[6,7] Although there have been many reports on the use of Lewis and Brønsted acids as catalysts for this reaction, most of them include the use of paraformaldehyde as a formaldehyde source, which is slowly soluble in water. To dissolve paraformaldehyde, organic solvents were consequently used in the reaction.[8] From economical and environmental points of view, an aqueous formaldehyde solution should be a better substrate. However, only a few mineral acids can work in water, and yields obtained are still far from satisfactory (<60%).[9] Thus, we decided to use an aqueous formaldehyde solution to investigate the Prins cyclization of styrene using HBAIL. Traditional mineral and organic aromatic sulfonic acids were also examined to compare their efficiency of these catalysts. A typical reaction of styrene with formaldehyde at 75 °C using traditional acids such as H_2SO_4, H_3PO_4, HCl, and TsOH showed low yields (<30%) even after 24 h (Table 1). To our great delight, the reaction took place smoothly in the presence of 10 mol % of **1b** and **2b** to afford 4-phenyl-1,3-dioxane in 92 and 95% yields after 12 h. The reaction also proceeded well using DBSA (dodecylbenzenesulfonic acid) in water. An advantage of HBAIL is the ease with which it can be recovered and reused. With HBAIL **2b**, the ionic liquid catalyst could be easily recovered by removal of water after extraction of the product with hexane. The recovered **2b** showed an unchanged

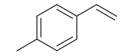
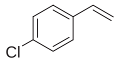
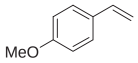
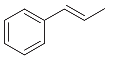
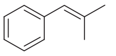
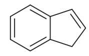
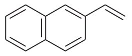
Table 1. Screening of catalyst for Prins cyclization of styrene in water

Entry	Catalyst	Time/h	Yield/%
1	H_2SO_4	24	23
2	H_3PO_4	24	trace
3	HCl	24	11
4	TsOH	24	trace
5	**1b**	12	92
6	**2b**	12	95
7	DBSA	12	82
8[a)]	**2b**	12	95

[a]The catalyst was reused in the second run.[10]

Table 2. Substrate scope for Prins cyclization



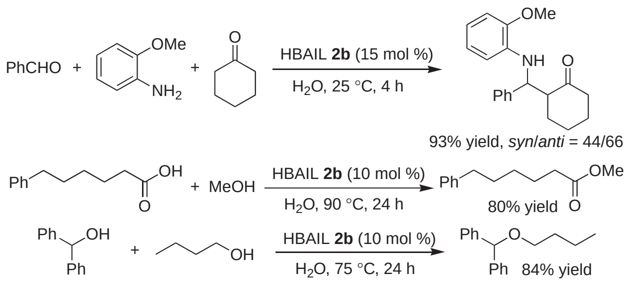
Entry	Styrene	Temp./°C	Time/h	Yield/%
1		75	12	93
2		75	12	81
3		60	12	94
4		75	20	74
5		90	24	54
6		60	24	77
7		60	24	70

activity in the Prins cyclization of styrene with an aqueous formaldehyde solution. DBSA is soluble in hexane, and it would be leached into organic phase during the extraction.

Many styrene derivatives can be used in this Prins cyclization, and good to excellent yields were obtained as shown in Table 2. For highly active substrates, such as 4-methoxystyrene and indene, lower temperature was better for the formation of the desired Prins cyclization products, as high temperatures caused polymerization of the olefins. When the β-position of styrene was substituted by one or two methyl groups, the yield of the reaction decreases presumably due to steric hindrance.

We then tested some dehydrative reactions with HBAIL in water. As shown in Scheme 2, the direct three-component Mannich reaction of benzaldehyde, *o*-anisidine, and cyclohexanone proceeded smoothly in water in the presence of a catalytic amount of HBAIL **2b**. 6-Phenylhexaoic acid was esterified by methanol in water in 80% yield using HBAIL **2b**. Etherification reaction between benzhydrol and *n*-butanol also proceeded well with HBAIL **2b** in water. These results demonstrate that HBAIL can be widely used as a Brønsted acid catalyst in many acid-catalyzed reactions in water.

In summary, novel hydrophobic Brønsted acidic ionic liquids (HBAIL) have been developed and utilized as acid catalysts in organic reactions in water. Furthermore, HBAILs were demonstrated for the first time to be effective catalysts for Prins cyclization of styrene derivatives in water using an aqueous formaldehyde solution. Many styrene derivatives can be successfully converted to the corresponding 1,3-dioxanes in water. Some other dehydrative reactions in water also proceeded well using HBAIL systems. In addition, HBAIL could be easily recovered after reactions and reused in the next run without loss of activity.



Scheme 2. Dehydrative reactions over HBAIL system in water.

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