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Hydrophobic, low-loading and alkylated polystyrene-supported sulfonic acid for several organic reactions in water: remarkable effects of both the polymer structures and loading levels of sulfonic acids†

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A hydrophobic, low-loading and alkylated polystyrene-supported sulfonic acid (LL–ALPS–SO_3H) has been developed for several organic reactions such as the hydrolysis of thioesters, the deprotection of acetals and an acetonide, and the hydration of an epoxide and an alkyne in pure water on the basis of remarkable effects of both the polymer structures and loading levels of the sulfonic acid catalysts.

Organic reactions using solid-supported catalysts are of great significant interest due to their practical advantages such as the simplification of the work-up procedures and the reuse of the catalysts,[1] although solid-supported catalysts sometimes display inferior activities to those of the corresponding homogeneous versions. On the other hand, organic reactions in water have received much attention in modern synthetic organic chemistry, because water is easily available, economical, and harmless to the environment compared with organic solvents.[2] Therefore, organic reactions using solid-supported catalysts in water would be an ideal methodology, provided that the catalysts show high catalytic activity in water.[3,4] Traditional approaches to this goal have been the use of amphiphilic polymer-supported catalysts, which swell adequately in water.[3] Contrary to these, we report here that a water-unswellable hydrophobic polymer-supported sulfonic acid, a low-loading and alkylated polystyrene-supported sulfonic acid (LL–ALPS–SO_3H), is an ideal catalyst for several organic reactions such as the hydrolysis of thioesters, the deprotection of acetals and an acetonide, and the hydration of an epoxide and an alkyne in pure water.

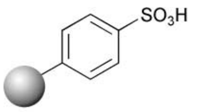
Quite recently, we have found a hydrophobic polystyrene-supported sulfonic acid (PS–SO_3H **1**, loading of –SO_3H group: 0.46 mmol g^{-1}), which works efficiently for the hydrolysis of thioesters in pure water.[5] Based on this preliminary finding, we carried out a detailed study on the effect of the loading levels (sulfonic acid content in the polymer) using polystyrene-supported sulfonic acid (PS–SO_3H **1**).[6,7] Hydrolysis of dodecyl thiolaurate was selected as a model reaction to estimate the effect, because a large activation barrier exists between the material and the product.[8] As shown in Table 1, it was found that the lower the loading, the higher the yields (entries 1–4). The reaction hardly proceeded even using 50 mol% of the catalyst in the case of a high-loading (entry 1).[9] These results indicate that the hydrophobicity, which depends on the loading, is very important for the activity of the catalyst in water. However, when the lowest loading catalyst (0.12 mmol g^{-1}) investigated was used (entry 5), the yield was decreased. It can be presumed that if the loading is lower, the amount of polymer is larger, and as a result, the substrate must be diluted in the polymer. This dilution may lead to the slow reaction rate. In fact, when the amount of the catalyst was decreased to 5 mol% (entries 4 and 5), the lowest loading polymer gave a better yield, probably because the dilution was not a severe problem in the presence of the smaller amount of the polymer.

Table 1 Effects of the loading and the catalyst structure

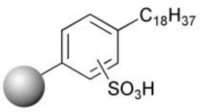
$$C_{11}H_{23}COSC_{12}H_{25} \xrightarrow[H_2O,\ \text{reflux, 24 h}]{\text{10 mol\% Catalyst}} C_{11}H_{23}CO_2H + C_{12}H_{25}SH$$

Entry	Catalyst	Loading (mmol g^{-1})	Yield (%)[a]
1	**1**	1.55	0(5)[b]
2	**1**	0.76	10
3	**1**	0.46	69
4	**1**	0.21	82(25)[c]
5	**1**	0.12	71(36)[c]
6	**2**	0.41	96(46)[c]
7	**3**	0.36	82
8	**4**	0.57	27
9	**5**	0.19	0
10	**6**[d]	0.11	13
11	**2**	1.40	63
12	**2**	1.01	83
13	**2**	0.85	84
14	**2**	0.17	92(55)[c]

[a] Yield of the carboxylic acid. [b] 50 mol% of the catalyst was used. [c] 5 mol% of the catalysts were used. [d] Macroporous PS–SO_3H.



(**1**)



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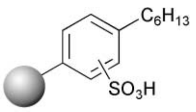

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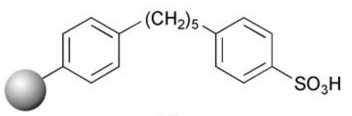

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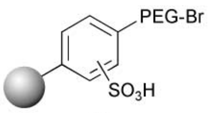

(**5**)

Next, we turned our attention to the polymer structure. Several types of polymer catalysts were synthesized to investigate the effect of the structure.[10] Interestingly, the yield was increased dramatically using a C18-alkylated polystyrene-supported sulfonic acid (**2**, 0.41 mmol g^{-1}) (entry 6).[11] This result suggested that the long alkyl chain increased the hydrophobic nature and, as a result, the affinity for the substrate. When C6-alkylated polystyrene-supported sulfonic acid **3** (0.36 mmol g^{-1}) was used as a catalyst (entry 7), the yield was decreased in comparison with that using **2**, although **3** was more effective than PS–SO_3H **1**. On the other hand, **4**, which

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† Electronic supplementary information (ESI) available: Experimental details. See http://www.rsc.org/suppdata/ob/b3/b305622h/

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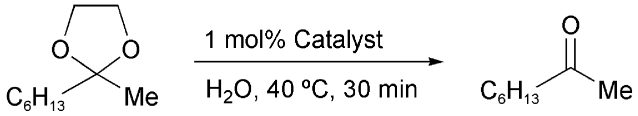
Table 2 Hydrolysis of dodecyl thioacetate in water

$$C_{12}H_{25}SAc \xrightarrow[H_2O,\ \text{reflux},\ 24\ \text{h}]{1\ \text{mol\%}\ \text{Catalyst}} C_{12}H_{25}SH$$

Entry	Catalyst	Loading (mmol g^{-1})	Yield (%)
1	**1**	0.46	44
2	**2**	0.41	82
3	**2**	0.17	94(96)[a]

[a] 2nd use.

Table 3 Deprotection of the ketal derived from 2-octanone



Entry	Catalyst	Loading (mmol g^{-1})	Yield (%)
1[a]	**1**	4.41	3
2	**1**	1.55	17
3	**1**	0.12	78
4	**2**	1.40	80
5	**2**	0.17	96
6	**5**	0.19	6
7	**6**	0.11	24

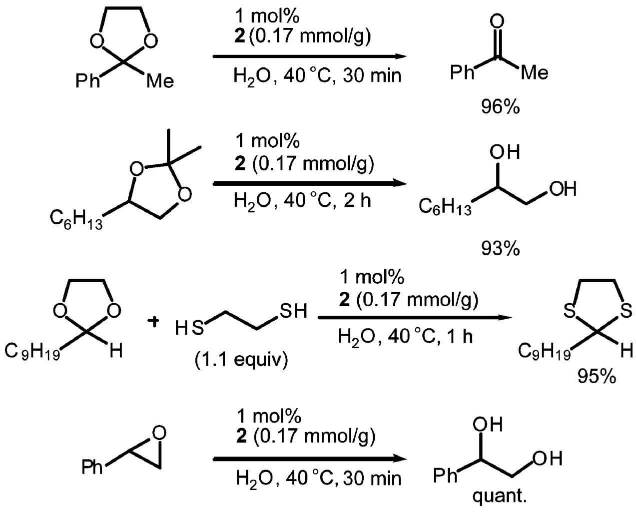
[a] Commercially available DOWEX 50W-X2 was used as a catalyst.

has a spacer, was not so effective for the hydrolysis (entry 8). It is noteworthy that the amphiphilic polymer-supported catalyst **5**, which was prepared by sulfonation of a commercially available TentaGel resin (entry 9), did not catalyze the reaction at all. Activity of macroporous PS–SO_3H **6**, prepared from a commercially available ArgoPore resin, was also low for this reaction even if the catalyst was prepared at a low-loading level (entry 10). Based on these results, we conclude that *the hydrophobic nature of the long alkyl chain is a significant key for the catalyst to exhibit high activity in water*.

We further investigated the effect of the loading of **2**, which was an effective catalyst according to the study of the structural effects (entries 6, 11–14). It is interesting to note that, although the reaction proceeded in good yield even using high loading catalysts, **2** showed the same tendency as PS–SO_3H **1**; the lower the loading, the higher the catalytic activity. These studies on both the effects of the loading levels and the structures revealed that a low-loading and alkylated polystylene-supported sulfonic acid (LL–ALPS–SO_3H) such as **2** (0.17 mmol g^{-1}) is one of the best catalysts for the hydrolysis in pure water as shown in entry 14.

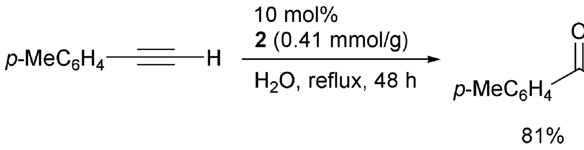
We carried out the hydrolysis of another thioester using LL–ALPS–SO_3H to demonstrate the effectiveness of the catalyst (Table 2). This also showed remarkable effects of the structures and loading levels. To be precise, **2** (0.17 mmol g^{-1}) was the most effective for the hydrolysis of this thioester, and it should be noted that only 1 mol% of the catalyst is enough to complete the reaction (entry 3). In addition, the catalyst was easily recovered after the reactions by simple filtration and washing with water and ether, and could be reused for the next reaction without any loss of the catalytic activity.

LL–ALPS–SO_3H **2** was effective for other organic reactions in water. In the case of the deprotection of the ketal derived from 2-octanone, **2** (0.17 mmol g^{-1}) also showed excellent catalytic activity compared with various types of catalysts in water (Table 3). It is noteworthy that the catalytic activity was much higher than that of commercially available DOWEX 50W-X2 (4.41 mmol g^{-1}). Moreover, it was revealed that LL–ALPS–SO_3H was effective for several other reactions such as deprotection of an aromatic ketal and an acetonide, transthioacetalization of an acetal, and hydration of an epoxide (Scheme 1). It should be noted again that only 1 mol% of the catalyst is sufficient to complete all reactions shown in Table 3 and Scheme 1. Interestingly, the analytically pure product was obtained quantitatively after the reaction mixture was filtered, washed with water, and concentrated in the case of the hydration of the epoxide. This procedure will be extended to a flow system without the use of any organic solvent.



Scheme 1 LL–ALPS–SO_3H-catalyzed organic reactions in water.

Finally, it was found that LL–ALPS–SO_3H can also be used for the hydration of an alkyne as shown in [eqn. (1)]. To the best


(1)

of our knowledge, this is the first example of the hydration of an alkyne using a catalytic amount of a Brϕnsted acid without a metal salt in pure water.[12]

In conclusion, we have investigated loading levels and structures of hydrophobic polymer-supported sulfonic acids, and found LL–ALPS–SO_3H to be one of the best catalysts for several acid-catalyzed organic reactions in pure water. Hydrophobicity of the catalyst was suggested to be a key for efficient catalysis. This concept will be applicable to various types of catalysts for organic reactions in water.

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