Dehydrative Esterification of Carboxylic Acids with Alcohols Catalyzed by Polymer-Supported Sulfonic Acids in Water

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Abstract: Dehydrative esterification of carboxylic acids with alcohols in water was efficiently catalyzed by hydrophobic polystyrene-supported sulfonic acids as recoverable and reusable catalysts. In these reactions, esters were obtained in high yields without using any dehydrating agents or apparatus. The sulfonic acid contents of the catalysts and the presence of long alkyl chains on the benzene rings of polystyrene significantly affected the catalytic activity.

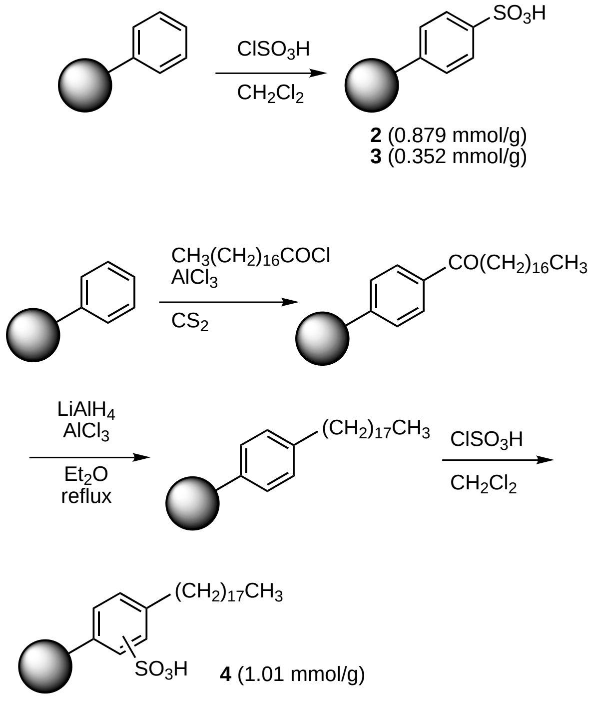
Keywords: aqueous reactions; Brønsted acids; dehydration; esterification; polymer catalysts

Organic reactions in water have been a subject of much recent research.[1] Although various efficient synthetic reactions in aqueous media have been developed so far, there are still some problems to be solved. One of the most serious problems is that large amounts of water as a solvent have detrimental effects on reactions in which water molecules must be removed during the reaction. An example is acid-catalyzed direct esterification of carboxylic acids with alcohols. Usually in this dehydration reaction, water molecules have to be removed (azeotropically or using a dehydrating agent) to shift the equilibrium to the ester formation.[2] On the other hand, we have recently developed surfactant-type Brønsted acid-catalyzed dehydration reactions such as esterification,[3] etherification, thioetherification, and dithioacetalization[4] in water. In these reactions, a surfactant-type Brønsted acid, *p*-dodecylbenzenesulfonic acid (DBSA),[5] and hydrophobic substrates assemble together through hydrophobic interaction to form emulsion droplets whose interior is hydrophobic enough to remove water molecules from the droplets. In addition, DBSA is concentrated onto the surface of the droplets at which the reaction takes place, thus enhancing the rate to reach equilibrium.

Although DBSA catalyzes the dehydration reaction to afford the corresponding products in high yields, it was still difficult to achieve recovery and reuse of the catalyst. Therefore, we aimed to develop a catalyst that can be recovered and reused, and envisioned use of polymer-supported catalysts for this purpose.[6,7] Although polymer-supported sulfonic acids have been used for Brønsted acid-catalyzed reactions including ester hydrolysis in water,[8] there is no example of their use for esterification in the medium. Herein we report that the dehydrative esterification in water was effectively catalyzed by hydrophobic polystyrene-supported sulfonic acids as recoverable and reusable catalysts.

In our search for effective polymer catalysts for dehydration reactions in water, the esterification of lauric acid with 3-phenyl-1-propanol was chosen as a model, which was catalyzed by DBSA to give the corresponding ester in 60% yield after 24 h (Table 1, entry 1).[3] First, a commercially available DOWEX® 50W-X2 (H form, **1**)[9] was tested as a representative polystyrene-supported sulfonic acid. Unexpectedly, it turned out to be totally ineffective even when used in large excess (entries 2 and 3). This resin swells significantly in water due to its high sulfonic acid content.[9] On the other hand, it has been reported that, in hydrolysis of esters, hydrophobic polystyrene-supported sulfonic acids are more active compared with less hydrophobic ones.[8c, d] Therefore, we expected that more hydrophobic resins would be more effective also in the present dehydration reaction.

Thus, we prepared polystyrene-supported sulfonic acids **2** and **3** whose sulfonic acid contents (0.879 and 0.352 mmol/g, respectively) were less than that of **1** (Scheme 1). As shown in Table 1 (entries 4 and 5), **2** and **3** did indeed catalyze the esterification, and the more hydrophobic **3** was found to be superior to **2.** We also prepared another polymer-supported sulfonic acid **4** (1.01 mmol/g) having a long alkyl group (Scheme 1). With this hydrophobic catalyst **4**, the esterification also proceeded smoothly (Table 1, entry 6). Most polymer catalysts reported for aqueous reactions significantly swell or dissolve in water.[7] On the other hand, both **3** and **4** scarcely swelled in water but worked as efficient catalysts. This result indicates that *the highly hydrophobic nature of polymer-supported catalysts plays a very important role for activity in the dehydration reaction in water*.[10]



Scheme 1.

The equilibrium position between the ester and the starting materials restricts the maximum yield of the ester. From the result of the longer reaction time (120 h, Table 1, entry 5), the position was found to be almost identical with that of the DBSA-catalyzed reaction (entry 1).

As expected, the catalysts were recoverable and reusable. For example, resin **3** was easily recovered by filtration after the esterification was completed, and the catalyst was repeatedly reused at least 4 times without loss of the catalytic activity (Scheme 2).

These polymer-supported catalysts were applied to other substrates as shown in Table 2. For some substrates having simple aliphatic chains, the reactions with catalyst **3** proceeded slowly (entries 2 and 4). However, **4** catalyzed the reactions more rapidly (entries 3 and 5). It should be noted that the presence of long alkyl chains on the benzene rings in **4** alters the catalytic activity for these substrates.

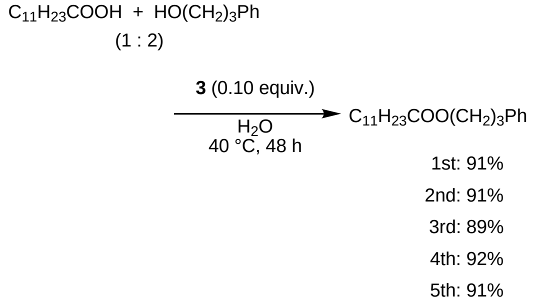
In conclusion, dehydrative esterification of carboxylic acids with alcohols in water was successfully carried out in the presence of hydrophobic polymer-supported sulfonic acids as recoverable and reusable catalysts. The hydrophobic nature and alkyl chains of the catalysts were found to play important roles in the present system. This work will not only lead to a practical synthetic method but also expand the versatility of catalytic organic reactions in water.

Table 1. Effect of catalysts on dehydrative esterification in water.

$$\underset{(1:1)}{C_{11}H_{23}COOH + HO(CH_2)_3Ph} \xrightarrow[\substack{H_2O \\ 40\ °C,\ 24\ h}]{\text{catalyst}} C_{11}H_{23}COO(CH_2)_3Ph$$

Entry	Catalyst (equiv.)	Yield (%)[a]
1	DBSA (0.10)	60 (83, 85[b])[c]
2	**1** (0.10)	0
3	**1** (6.45)	2
4	**2** (0.10)	41
5	**3** (0.10)	74 (81, 84[b])[c]
6	**4** (0.10)	72

[a] Isolated yield.
[b] NMR yield.
[c] For 120 h.



Scheme 2.

Table 2. Dehydrative esterification of other substrates in water.

$$\underset{(1:2)}{RCO_2H + HOR'} \xrightarrow[\substack{H_2O \\ 40\ °C,\ 48\ h}]{\text{catalyst (0.10 equiv)}} RCO_2R'$$

Entry	R	R'	Catalyst	Yield [%][a]
1	$Ph(CH_2)_4$-	-$(CH_2)_{11}CH_3$	**3**	92
2	$CH_3(CH_2)_{10}$-	-$(CH_2)_{11}CH_3$	**3**	71
3	$CH_3(CH_2)_{10}$-	-$(CH_2)_{11}CH_3$	**4**	96
4	$CH_3(CH_2)_7CH=CH(CH_2)_7$-	-$(CH_2)_{11}CH_3$	**3**	45
5	$CH_3(CH_2)_7CH=CH(CH_2)_7$-	-$(CH_2)_{11}CH_3$	**4**	94
6	$Ph(CH_2)_4$-	-$(CH_2)_{12}Br$	**3**	93

[a] Isolated yield.

Experimental Section

Preparation of Polymer-Supported Catalyst 3

To a suspension of polystyrene (3.03 g, 1% DVB cross-linked, 200–400 mesh) in dichloromethane (60 mL) was slowly added chlorosulfonic acid (0.10 mL) at 0 °C, and the whole was stirred for 6 h. Acetic acid (30 mL) was added and, after 1 h, the resin was collected on a glass filter, rinsed with water (50 mL × 3), water/THF (1/1, 50 mL × 3), and dichloromethane (50 mL × 3), and dried under vacuum to give resin **3.** From the result of elemental analysis (found: S 1.13%), the sulfonic acid content was estimated as 0.352 mmol/g. Resin **2** was similarly prepared by increasing the amount of chlorosulfonic acid used.

Preparation of Polymer-Supported Catalyst 4

To a mixture of $AlCl_3$ (4.43 g) in carbon disulfide (50 mL) were added polystyrene (2.31 g, 1% DVB cross-linked, 200–400 mesh) and stearoyl chloride (10.1 g) successively at room temperature. After stirring for 32 h, 1 N aqueous HCl (150 mL) was added. After stirring for 12 h, the carbon disulfide was evaporated, and 1 N aqueous HCl (100 mL) was added. The resin was collected on a glass filter, rinsed with water (300 mL), water/THF (1/1, 300 mL), THF (300 mL), and dichloromethane (300 mL), and dried under vacuum at 60 °C. According to the result of elemental analysis, the acylation proceeded quantitatively. Anal. calcd: C 84.26, H 11.42; found: C 84.13, H 11.42; IR (KBr): $\nu = 1686\ \mathrm{cm^{-1}}$.

The resin was reduced in the following step. $AlCl_3$ (3.91 g) was added to a mixture of $LiAlH_4$ (1.13 g) in ether (60 mL) in several portions at 0 °C. After warming to room temperature, the resin (5.00 g) was added in several portions, and the whole was heated under reflux for 24 h. After cooling to 0 °C, 1 N aqueous HCl (180 mL) was added. The mixture was stirred for 13 h, evaporated to remove the ether, and filtered. The resultant resin was rinsed with 1 N aqueous HCl (100 mL), water (200 mL), water/THF (1/1, 200 mL), THF (200 mL), dichloromethane/methanol (5/2, 70 mL), and dichloromethane (150 mL) and dried under vacuum at 60 °C. According to the result of elemental analysis, the reduction proceeded quantitatively. Anal. calcd: C 87.56, H 12.44; found: C 87.30, H 12.44. IR and swollen resin-magic angle spinning ^{13}C NMR[11] ($CDCl_3$) also confirmed disappearance of the carbonyl group.

The resin was then sulfonated as follows. To a suspension of the resin (724 mg) in dichloromethane (4.0 mL) was added chlorosulfonic acid (0.080 mL) at 0 °C, and the whole was stirred for 12 h. Acetic acid (2 mL) was added, and, after stirring at room temperature for 30 min, water (1 mL) was added. After further stirring for 30 min, the resultant resin was collected on a glass filter, rinsed with water/THF (1/1, 100 mL), THF (50 mL), and dichloromethane (50 mL), and dried under vacuum at 60 °C. From the result of elemental analysis (found: S 3.23%), the sulfonic acid content was estimated as 1.01 mmol/g.

General Procedure for Esterification in Water

A mixture of a carboxylic acid (0.25 mmol), an alcohol (0.25–0.50 mmol), and a polymer-supported catalyst (0.1 equiv. to the carboxylic acid) in water (1.5 mL) was stirred at 40 °C for 24–48 h. Water (5 mL) and ether (for Table 2, entries 1 and 6) or toluene (for entries 2–5) (2 mL) were added, and the polymer was filtered and rinsed with ether. The organic layer was washed with saturated $NaHCO_3$ solution, dried over Na_2SO_4, and concentrated. The product was purified by chromatography on silica gel.

Acknowledgements

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