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Direct Dehydrative Esterification of Alcohols and Carboxylic Acids with a Macroporous Polymeric Acid Catalyst

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ABSTRACT

A macroporous polymeric acid catalyst was prepared for the direct esterification of carboxylic acids and alcohols that proceeded at 50–80 °C without removal of water to give the corresponding esters with high yield. Flow esterification for the synthesis of biodiesel fuel was also achieved by using a column-packed macroporous acid catalyst under mild conditions without removal of water.

Direct dehydrative esterification of alcohols and carboxylic acids is one of the most fundamental yet challenging transformations in organic syntheses,[1] where the use of a small amount of catalysts under neat conditions is among the most ideal methods.[2] This reaction is an equilibrium dehydration process in which a stoichiometric amount of water forms as a coproduct. Therefore, in most cases, large amounts of excess alcohols or carboxylic acids under the azeotropic reflux conditions or with dehydrating agents are required in order to promote the equilibrium reaction and obtain a quantitative yield of the ester.[2−4]

Nature provides us with directions for developing catalysts for in-water dehydrative reactions against equilibrium: nucleic acids and proteins are synthesized via in-water dehydrative reactions mediated by proteins via

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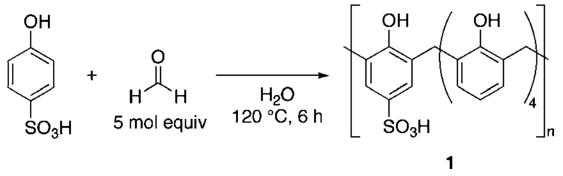
phase separation under nonequilibrium conditions.[5] This phenomena prompted us to develop enzyme-inspired polymeric acid catalysts that realize phase-separated nonequilibrium reaction conditions. We designed a fairly hydrophilic meso/macroporous acid catalyst for this purpose. Fairly hydrophilic meso/macropores in the catalyst should readily capture a fairly hydrophilic substrates and reactants, alcohols and carboxylic acids, to convert to the corresponding more hydrophobic esters that could be kicked out from the hydrophilic nano/macropores not to be captured and mediated by the catalyst. This is our working hypothesis of in-water dehydrative reaction with phase separation under nonequilibrium conditions to afford the desired esters in high yield. Here, we report the development of a macroporous phenolsulfonic acid–formaldehyde resin catalyst as a novel heterogeneous polymeric acid catalyst. By using the catalyst, the direct dehydrative esterification proceeded smoothly in the presence of less than 1 mol % of the macroporous acid catalyst without removal of water to afford the corresponding esters with high yield. Moreover, biodiesel fuel was produced under the flow reaction conditions by using a column-packed macroporous acid catalyst.

Phenolsulfonic acid–formaldehyde resins have been used as cation exchangers or electron-conductive compositions.[6] However, to the best of our knowledge, there are no reports on their catalytic use as heterogeneous catalysts. The phenolsulfonic acid–formaldehyde resin **1** was prepared by the condensative polymerization of *p*-phenolsulfonic acid and formaldehyde (5 mol equiv) in H_2O at 120 °C for 6 h (Scheme 1), after which the reaction mixture was gradually cooled to 25 °C over 12 h to give a pale brownish gel. After being dried under reduced pressure, the gel became a reddish brown, hardly soluble solid. Elemental analysis and the IR spectrum (773 and 708 cm^{-1}) (Figure S1, Supporting Information) of **1** showed 80% degradation of the sulfonic acid group via thermal decomposition.

Scheme 1. Preparation of *p*-Phenolsulfonic Acid–Formaldehyde Resins



When the high-resolution SEM of **1** was observed, we were surprised to find that it was an aggregated macroporous material with a pore size of 1–5 μm wide (Figure 1a,b). Energy-dispersive X-ray spectroscopy analysis on the SEM (EDX/SEM) of **1** showed sulfur atoms uniformly dispersed on the polymeric matrix (Figure 1c,d). The surface area of **1** was 11.5 m^2/g from Kr absorption–BET analysis.

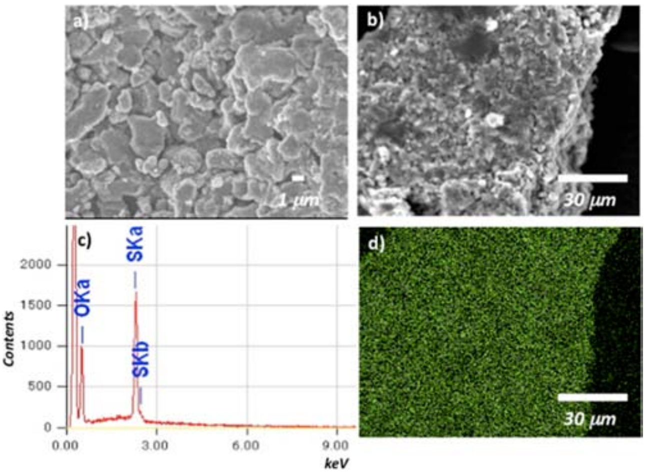


Figure 1. (a, b) SEM images (bar scale: (a) 1 μm, (b) 30 μm), (c) EDX/SEM image of **1**, and (d) EDX/SEM mapping of sulfur atom in **1**.

With a phenolsulfonic acid–formaldehyde resin **1** in hand, we investigated the catalytic activity in the direct esterification of **2a** and acetic acid with a variety of homogeneous and heterogeneous acid catalysts at 50 °C for 12 h without removal of water (Figure 2). When the esterification of benzyl alcohol (**2a**) and acetic acid (1.2 mol equiv) was performed with **1** (0.7 mol % SO_3H) at 50 °C for 12 h, we were pleased to find that the reaction with less than 1 mol % catalyst proceeded smoothly to give benzyl acetate (**3a**) with 96% conversion. While a homogeneous counterpart *p*-phenolsulfonic acid and a common homogeneous catalyst *p*-TsOH led to the formation of **3a** with 72% and 77% within 6 h, a prolonged reaction time did not afford the generation of **3a** owing to the equilibrium (12 h; 79% and 82% conversion, respectively). The catalytic activity of common heterogeneous acid catalysts zeolite (MS3A),[7] Amberlyst,[8] and DOWEX[9] was lower than that of **1** (12 h, 7%, 31%, and 51% conversion, respectively) under similar conditions.

Using the best heterogeneous catalyst **1**, direct esterification of various alcohols and acetic acid (1.2 mol equiv) was performed with **1** (0.7 mol %) at 50 °C for 12 h under similar conditions (Table 1). The esterification of benzyl alcohol (**2a**), 2-phenylethanol (**2b**), and 3-phenyl-1-propanol (**2c**) with acetic acid proceeded smoothly to afford the corresponding acetates (**3a**–**c**) with 93–94% yield (entries 1–3).

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(8) CAS: 125004-35-5, Amberlyst 16 (Fluka) was used.

(9) CAS: 69011-20-7, DOWEX 50WX2-200 (Wako) was used.

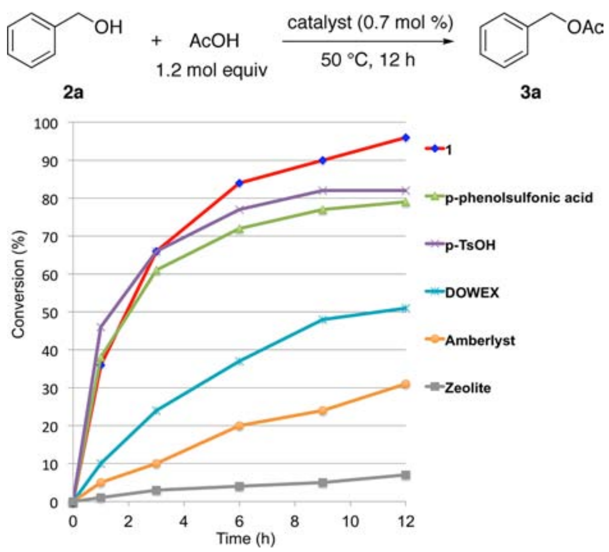
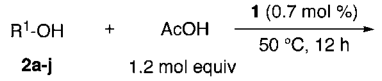


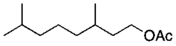
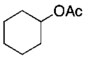
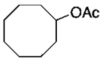
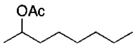
Figure 2. Catalytic activity (time course) of **1** and commercially available homogeneous and heterogeneous acid catalysts (0.7 mol % of SO_3H) for direct esterification.

Aliphatic alcohols 1-octanol (**2d**), 1-decanol (**2e**), and 1-dodecanol (**2f**) were also transformed into the corresponding acetates (**3d**−**f**) with 92−93% yield (entries 4−6). The direct esterification of 3,7-dimethyl-1-octanol (**2g**) and acetic acid gave 3,7-dimethyloctyl acetate (**3g**) in 93% yield. The direct esterification of alicyclic and aliphatic secondary alcohols, cyclohexanol (**2h**), cyclooctanol (**2i**), and 2-octanol (**2j**) led to the formation of the corresponding acetates (**3h**−**j**) with 91−94% yield under similar conditions.

Furthermore, direct esterification of various carboxylic acids and methanol (5 mol equiv) was performed with **1**

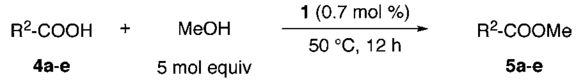
Table 1. Direst Esterification of Various Alcohols and Acetic Acid Catalyzed by **1**[a]



entry	product	3	yield[b]
1	$PhCH_2OAc$	**3a**	94
2	$Ph(CH_2)_2OAc$	**3b**	93
3	$Ph(CH_2)_3OAc$	**3c**	93
4	$CH_3(CH_2)_7OAc$	**3d**	92
5	$CH_3(CH_2)_9OAc$	**3e**	92
6	$CH_3(CH_2)_{11}OAc$	**3f**	93
7	 OAc	**3g**	93
8[c]	 OAc	**3h**	94
9[c]	 OAc	**3i**	91
10[c]	 OAc	**3j**	94

[a] Conditions: **2a** (1.0 mmol), AcOH (1.2 mmol), **1** (0.7 mol %), 50 °C, 12 h. [b] Isolated yield. [c] 80 °C.

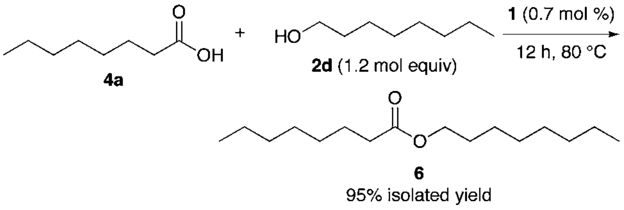
Table 2. Direst Esterification of Various Carboxylic Acids and Methanol Catalyzed by **1**[a]



entry	product	5	yield[b] (%)
1	$CH_3(CH_2)_6CO_2Me$	**5a**	94
2	$CH_3(CH_2)_8CO_2Me$	**5b**	95
3	$CH_3(CH_2)_{10}CO_2Me$	**5c**	93
4	$CH_3(CH_2)_{14}CO_2Me$	**5d**	95
5[c]	$CH_3(CH_2)_{16}CO_2Me$	**5e**	95

[a] Conditions: **4a** (1.0 mmol), MeOH (5.0 mmol), **1** (0.7 mol %), 50 °C, 12 h. [b] Isolated yield. [c] 60 °C.

Scheme 2. Direct Esterification of Octanoic Acid (**4a**) and 1-Octanol (**2d**) Catalyzed by **1**



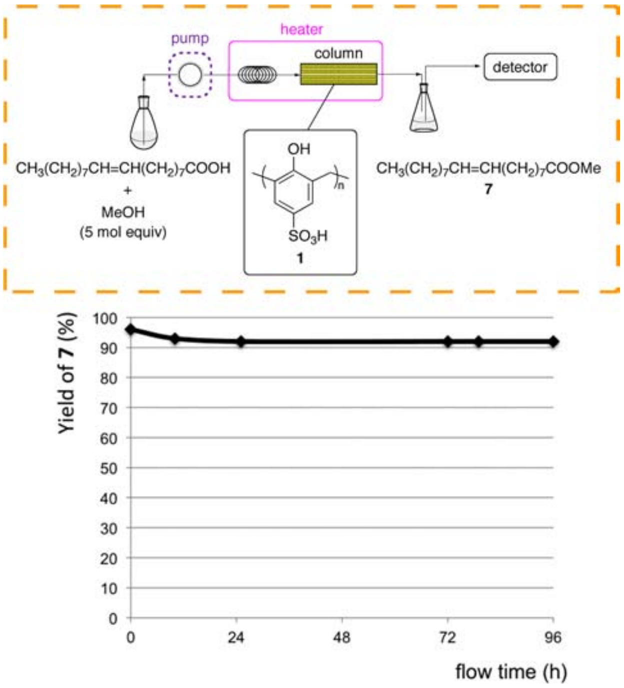


Figure 3. Image of continuous flow esterification for the synthesis of biodiesel fuel **7** by use of column-packed **1** and graphic chart of continuous flow time (*X*-axis) and yield of **7** (*Y*-axis).

(0.7 mol %) at 50 °C for 12 h without removal of water (Table 2). Thus, the direct esterification of octanoic acid (**4a**) and decanoic acid (**4b**) proceeded to afford the corresponding methyl esters (**5a**,**b**) with 94–95% yield. Lauric acid (**4c**) and palmitic acid (**4d**) were also converted to give the corresponding methyl esters **5c**,**d** with 93–95% yield. The direct esterification of stearic acid (**4e**) was performed at 60 °C (**4e** was hardly soluble at 50 °C) under similar conditions to give stearic acid methyl ester (**5e**) with 95% yield. Moreover, direct esterification of an aliphatic acid, octanoic acid, and an aliphatic alcohol, 1-octanol (1.2 mol equiv), also proceeded at 80 °C under similar conditions to give **6** with 95% yield (Scheme 2).

To apply the catalyst **1** for the synthesis of functional materials, the flow continuous esterification of oleic acid and methanol was investigated to provide biodiesel fuel (Figure 3).[10] Into the acid catalyst **1** (900 mg) packed column was injected a neat mixture of oleic acid and methanol (5 mol equiv) continuously by a pump injector at a flow rate of 0.6 mL/h at 80 °C. The esterification proceeded within a residence time of 18 min to give the desired biodiesel fuel **7** with 92–96% yield. The flow system provided **7** with 92–96% yield for 4 days without loss of its catalytic activity.

In conclusion, a porous *p*-phenolsulfonic acid–formaldehyde resin **1** with 0.7 mol % efficiently catalyzed the direct esterification of alcohols and carboxylic acids at 50–80 °C for 12 h without removal of water to give the corresponding esters with 92–96% yield. Moreover, the flow reactor with a **1**-packed column continuously provided biodiesel fuel with high yield.

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Supporting Information Available. Experimental section, NMR data and spectra of the products, and Kr-adsorption isotherm for **1**. This material is available free of charge via the Internet at http://pubs.acs.org.

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The authors declare no competing financial interest.