**Hydrophobic Polymer-Supported Catalyst for Organic Reactions in Water:
Acid-Catalyzed Hydrolysis of Thioesters and Transprotection of Thiols**

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Supporting Information

Experimental Section

General

NMR spectra were recorded on a JEOL JNM-LA300 or JNM-LA400 spectrometer. Tetramethylsilane ($\delta = 0$) was used as an internal standard for ^1H NMR and CDCl_3 ($\delta = 77.0$) for ^{13}C NMR. High-performance liquid chromatography was carried out using following apparatuses; SHIMADZU LC-10AT (liquid chromatography), SHIMADZU SPD-10A (UV detector), and SHIMADZU CR8A Chromatopac. Column chromatography was conducted on Silica gel 60 (Merck) and preparative thin-layer chromatography (TLC) was carried out using Wakogel B-5F. All compounds were confirmed by comparison with commercially available compounds or published data.

Preparation of polymer-supported sulfonic acid (PS-SO₃H).

To a suspension of polystyrene (10.06 g, 1% DVB cross-linked, 200–400 mesh) in dichloromethane (150 mL) was slowly added a solution of chlorosulfonic acid (0.37 mL) in dichloromethane (20 mL) at 0 °C, and the whole was shaken for 6 h. THF/water (5/1,

60 mL) was added, and after shaken at rt for 1 h and left overnight, the resin was collected on a glass filter, rinsed with water, water/THF, THF, and dichloromethane, and dried in vacuo to give the polymer-supported sulfonic acid (PS-SO₃H). From a result of elemental analysis (found: S, 1.48%), the sulfonic acid content was estimated as 0.462 mmol/g.

PS-SO₃H-catalyzed hydrolysis of dodecyl thiolaurate in water (Table 2, entry 1). A mixture of dodecyl thiolaurate (96.3 mg, 0.25 mmol) and the polymer-supported catalyst (PS-SO₃H, 54.5 mg, 0.025 mmol) in degassed water (1.5 mL) was stirred for 72 h under reflux conditions. The polymer was filtered and washed with water and dichloromethane after cooled to rt. The organic layer was dried over Na₂SO₄, and evaporated. The mixture was purified by flash column chromatography (10 g SiO₂) to give dodecanethiol (48.2 mg, 95%) containing the disulfide (2%) from hexane eluate and lauric acid (47.8 mg, 95%) from AcOEt eluate. Dodecanethiol: ¹H NMR (CDCl₃) δ 0.88 (3H, t, *J* = 6.7 Hz), 1.26–1.40 (19H, m), 1.61 (2H, q, *J* = 7.4 Hz), 2.52 (2H, q, *J* = 7.3 Hz); ¹³C NMR (CDCl₃) δ 14.13, 22.71, 24.68, 28.41, 29.11, 29.37, 29.55, 29.62, 29.65, 29.67, 31.94, 34.08. Lauric acid: ¹H NMR (CDCl₃) δ 0.88 (3H, t, *J* = 6.7 Hz), 1.23–1.40 (16H, m), 1.58–1.66 (2H, m), 2.35 (2H, t, *J* = 7.5 Hz); ¹³C NMR (CDCl₃) δ 14.13, 22.72, 24.72, 29.10, 29.28, 29.37, 29.47, 29.63, 31.95, 34.12, 180.15.

PS-SO₃H-catalyzed hydrolysis of ethyl thiolaurate in water (Table 2, entry 2). A mixture of ethyl thiolaurate (61.3 mg, 0.25 mmol) and the polymer-supported catalyst (PS-SO₃H, 54.4 mg, 0.025 mmol) in degassed water (1.5 mL) was stirred for 36 h under reflux conditions. The polymer was filtered and washed with water and dichloromethane after cooled to rt. The organic layer was dried over Na₂SO₄, and evaporated. The mixture was purified by flash column chromatography (5 g SiO₂) to give lauric acid (46.5 mg, 93%)

from AcOEt eluate. ^1H and ^{13}C NMR spectra were identical with those shown in the experimental procedure for Table 2, entry 1.

PS-SO₃H-catalyzed hydrolysis of *tert*-butyl thiolaurate in water (Table 2, entry 3). A mixture of *tert*-butyl thiolaurate (68.2 mg, 0.25 mmol) and the polymer-supported catalyst (PS-SO₃H, 54.5 mg, 0.025 mmol) in degassed water (1.5 mL) was stirred for 168 h under reflux conditions. The polymer was filtered and washed with water and dichloromethane after cooled to rt. The organic layer was dried over Na₂SO₄, and evaporated. The mixture was purified by flash column chromatography (2 g SiO₂) to give lauric acid (50.1 mg, quant.) from AcOEt eluate. ^1H and ^{13}C NMR spectra were identical with those shown in the experimental procedure for Table 2, entry 1.

PS-SO₃H-catalyzed hydrolysis of phenyl thiolaurate in water (Table 2, entry 4). A mixture of phenyl thiolaurate (73.1 mg, 0.25 mmol) and the polymer-supported catalyst (PS-SO₃H, 54.6 mg, 0.025 mmol) in degassed water (1.5 mL) was stirred for 24 h under reflux conditions. The polymer was filtered and washed with water and dichloromethane after cooled to rt. The organic layer was dried over Na₂SO₄, and evaporated. The mixture was purified by preparative TLC on silica gel to give lauric acid (48.9 mg, 98%). ^1H and ^{13}C NMR spectra were identical with those shown in the experimental procedure for Table 2, entry 1.

PS-SO₃H-catalyzed hydrolysis of ethyl 3-phenylthiopropionate in water (Table 2, entry 5). A mixture of ethyl 3-phenylthiopropionate (48.6 mg, 0.25 mmol) and the polymer-supported catalyst (PS-SO₃H, 54.1 mg, 0.025 mmol) in degassed water (1.5 mL) was stirred for 24 h under reflux conditions. The polymer was filtered and washed with

water and dichloromethane after cooled to rt. The organic layer was dried over Na₂SO₄, and evaporated. The mixture was purified by preparative TLC on silica gel to give hydrocinnamic acid (31.8 mg, 85%). ¹H NMR (CDCl₃) δ 2.66–2.71 (2H, m), 2.89–2.99 (2H, m), 7.17–7.32 (5H, m); ¹³C NMR (CDCl₃) δ 30.56, 35.61, 126.38, 128.32, 128.56, 140.13, 179.25.

PS-SO₃H-catalyzed hydrolysis of ethyl thiocinnamate in water (Table 2, entry 6). A mixture of ethyl thiocinnamate (48.2 mg, 0.25 mmol) and the polymer-supported catalyst (PS-SO₃H, 54.3 mg, 0.025 mmol) in degassed water (1.5 mL) was stirred for 168 h under reflux conditions. The polymer was filtered and washed with water and dichloromethane after cooled to rt. The organic layer was dried over Na₂SO₄, and evaporated. The mixture was purified by preparative TLC on silica gel to give cinnamic acid (33.3 mg, 90%). ¹H NMR (CDCl₃) δ 6.46 (1H, dd, *J* = 16.0, 0.6 Hz), 7.39–7.42 (3H, m), 7.53–7.58 (2H, m), 7.80 (2H, d, *J* = 16.0 Hz).

PS-SO₃H-catalyzed hydrolysis of dodecyl thioacetate in water (Table 2, entry 7). A mixture of dodecyl thioacetate (62.0 mg, 0.25 mmol) and the polymer-supported catalyst (PS-SO₃H, 54.3 mg, 0.025 mmol) in degassed water (1.5 mL) was stirred for 24 h under reflux conditions. The reaction mixture was quenched with saturated aq. NaHCO₃ after cooled to rt. The polymer was filtered and washed with water and ethyl acetate. The organic layer was dried over Na₂SO₄, and evaporated. Dodecanethiol (51.4 mg, quant.) was obtained as essentially pure form. ¹H and ¹³C NMR spectra were identical with those shown in the experimental procedure for Table 2, entry 1.

Reaction using 2 mol% PS-SO₃H (Table 2, entry 7). A mixture of dodecyl thioacetate (61.3 mg, 0.25 mmol) and the polymer-supported catalyst (PS-SO₃H, 10.8 mg, 0.005 mmol) in degassed water (1.5 mL) was stirred for 48 h under reflux conditions. The polymer was filtered and washed with water and dichloromethane after cooled to rt. The organic layer was dried over Na₂SO₄, and evaporated. Dodecanethiol (51.1 mg, quant.) was obtained as essentially pure form. ¹H and ¹³C NMR spectra were identical with those shown in the experimental procedure for Table 2, entry 1.

PS-SO₃H-catalyzed hydrolysis of benzyl thioacetate in water (Table 2, entry 8). A mixture of benzyl thioacetate (42.2 mg, 0.25 mmol) and the polymer-supported catalyst (PS-SO₃H, 54.5 mg, 0.025 mmol) in degassed water (1.5 mL) was stirred for 24 h under reflux conditions. The reaction mixture was quenched with saturated aq. NaHCO₃ after cooled to rt. The polymer was filtered and washed with water and ethyl acetate. The organic layer was dried over Na₂SO₄, and evaporated. Benzyl mercaptan (24.8 mg, 80%) was obtained as essentially pure form. ¹H NMR (CDCl₃) δ 1.76 (1H, t, *J* = 7.5 Hz), 3.74 (2H, d, *J* = 7.7 Hz), 7.20–7.33 (5H, m). The yield was 80% because of the volatility of the product.

PS-SO₃H-catalyzed hydrolysis of 3-phenylpropyl thioacetate in water (Table 2, entry 9). A mixture of 3-phenylpropyl thioacetate (48.3 mg, 0.25 mmol) and the polymer-supported catalyst (PS-SO₃H, 54.2 mg, 0.025 mmol) in degassed water (1.5 mL) was stirred for 24 h under reflux conditions. The polymer was filtered and washed with water and dichloromethane after cooled to rt. The organic layer was dried over Na₂SO₄, and evaporated. 3-Phenylpropane-1-thiol (40.0 mg, quant.) was obtained as essentially pure form. ¹H NMR (CDCl₃) δ 1.35(1H, t, *J* = 7.8 Hz), 1.93 (2H, q, *J* = 7.3 Hz), 2.53 (2H, q, *J*

= 7.3 Hz), 2.72 (2H, t, J = 7.5 Hz), 7.16–7.31 (5H, m); ^{13}C NMR (CDCl_3) δ 23.98, 34.35, 35.47, 125.96, 128.40, 128.46, 141.26.

PS-SO₃H-catalyzed hydrolysis of dodecyl thiobenzoate in water (Table 2, entry 10).

A mixture of dodecyl thiobenzoate (76.6 mg, 0.25 mmol) and the polymer-supported catalyst (PS-SO₃H, 108.2 mg, 0.050 mmol) in degassed water (1.5 mL) was stirred for 168 h under reflux conditions. The polymer was filtered and washed with water and dichloromethane after cooled to rt. The organic layer was dried over Na₂SO₄, and evaporated. The mixture was purified by flash column chromatography (5 g SiO₂) to give dodecanethiol (45.3 mg, 89%) containing the disulfide (5%) from hexane eluate. ^1H and ^{13}C NMR spectra were identical with those shown in the experimental procedure for Table 2, entry 1.

PS-SO₃H-catalyzed hydrolysis of the dithioester in water (Table 2, entry 11). A mixture of the dithioester (63.8 mg, 0.25 mmol) and the polymer-supported catalyst (PS-SO₃H, 54.1 mg, 0.025 mmol) in degassed water (1.5 mL) was stirred for 24 h under reflux conditions. The polymer was filtered and washed with water and dichloromethane after cooled to rt. The organic layer was dried over Na₂SO₄, and evaporated. 1,2-Benzenedimethanethiol¹ (42.1 mg, 99%) was obtained as essentially pure form. ^1H NMR (CDCl_3) δ 1.85 (2H, t, J = 7.2 Hz), 3.85 (4H, d, J = 7.2 Hz), 7.17–7.29 (4H, m); ^{13}C NMR (CDCl_3) δ 26.06, 127.90, 129.72, 138.68.

Recycle experiment of PS-SO₃H (Eq. 1). A mixture of dodecyl thioacetate (245.2 mg, 1.0 mmol) and the polymer-supported catalyst (PS-SO₃H, 216.7 mg, 0.10 mmol) in degassed water (6 mL) was stirred for 24 h under reflux conditions. The polymer was

filtered through a glass filter after the reaction mixture was cooled to rt, and the polymer was washed with water and ether. The organic layer was dried over Na₂SO₄, and evaporated. Dodecanethiol (204 mg, quant.) was obtained as essentially pure form. ¹H and ¹³C NMR spectra were identical with those shown in the experimental procedure for Table 2, entry 1. The recovered PS-SO₃H was reused several times without loss of activity after dried under vacuum.

PS-SO₃H-catalyzed hydrolysis of ethyl (*R*)-(-)-2-phenyl-thiopropionate in water (Eq. 2). A mixture of ethyl (*R*)-(-)-2-phenyl-thiopropionate (48.5 mg, 0.25 mmol) and the polymer-supported catalyst (PS-SO₃H, 54.5 mg, 0.025 mmol) in degassed water (1.5 mL) was stirred for 72 h under reflux conditions. The polymer was filtered and washed with water and dichloromethane after cooled to rt. The organic layer was dried over Na₂SO₄, and evaporated. The mixture was purified by preparative TLC on silica gel to give (*R*)-(-)-2-phenylpropionic acid (27.8 mg, 74%). ¹H NMR (CDCl₃) δ 1.51(3H, d, *J* = 7.1 Hz), 3.73 (1H, q, *J* = 7.1 Hz), 7.23–7.36 (5H, m); ¹³C NMR (CDCl₃) δ 18.10, 45.35, 127.40, 127.60, 128.69, 139.76, 180.69. The enantiomeric excess of the product was determined by HPLC analysis (93% ee. Daicel Chiralcel OD, hexane/*i*-PrOH/HCO₂H = 98/2/1).

PS-SO₃H-catalyzed transprotection of dodecanethiol in water (Table 3, entry 1). A mixture of dodecyl thioacetate (122.8 mg, 0.50 mmol), triphenylmethanol (130.6 mg, 0.50 mmol), and the polymer-supported catalyst (PS-SO₃H, 108.5 mg, 0.050 mmol) in degassed water (3.0 mL) was stirred for 48 h under reflux conditions. The reaction mixture was quenched with saturated aq. NaHCO₃ and brine after cooled to rt. The polymer was filtered and washed with water and ethyl acetate. The organic layer was dried over Na₂SO₄, and evaporated. The mixture was purified by preparative TLC on silica gel to

give dodecyl triphenylmethyl sulfide² (202.8 mg, 91%). ¹H NMR (CDCl₃) δ 0.87 (3H, t, J = 6.7 Hz), 1.22–1.41 (20H, m), 2.13 (2H, t, J = 7.3 Hz), 7.15–7.29 (9H, m), 7.39–7.43 (6H, m).

PS-SO₃H-catalyzed transprotection of dodecanethiol in water (Table 3, entry 2). A mixture of dodecyl thioacetate (61.3 mg, 0.25 mmol), benzhydrol (92.2 mg, 0.50 mmol), and the polymer-supported catalyst (PS-SO₃H, 54.4 mg, 0.025 mmol) in degassed water (1.5 mL) was stirred for 48 h under reflux conditions. The reaction mixture was quenched with saturated aq. NaHCO₃ and brine after cooled to rt. The polymer was filtered and washed with water and ethyl acetate. The organic layer was dried over Na₂SO₄, and evaporated. The mixture was purified by preparative TLC on silica gel to give benzhydryl dodecyl sulfide³ (82.8 mg, 90%). ¹H NMR (CDCl₃) δ 0.88 (3H, t, J = 6.6 Hz), 1.23–1.35 (18H, m), 1.49–1.61 (2H, m), 2.37 (2H, t, J = 7.3 Hz), 5.14 (1H, s), 7.19–7.33 (6H, m), 7.41–7.44 (4H, m).

PS-SO₃H-catalyzed transprotection of dodecanethiol in water (Table 3, entry 3). A mixture of dodecyl thioacetate (61.7 mg, 0.25 mmol), 4-methoxybenzyl alcohol (70.6 mg, 0.51 mmol), and the polymer-supported catalyst (PS-SO₃H, 54.3 mg, 0.025 mmol) in degassed water (1.5 mL) was stirred for 48 h under reflux conditions. The reaction mixture was quenched with saturated aq. NaHCO₃ and brine after cooled to rt. The polymer was filtered and washed with water and ethyl acetate. The organic layer was dried over Na₂SO₄, and evaporated. The mixture was purified by preparative TLC on silica gel to give dodecyl 4-methoxybenzyl sulfide³ (56.9 mg, 71%). ¹H NMR (CDCl₃) δ 0.88 (3H, t, 6.8 Hz), 1.24 (18H, s), 1.51–1.58 (2H, m), 2.39 (2H, t, J = 7.4 Hz), 3.66 (2H, s), 3.82 (3H, s), 6.84 (2H, d, J = 8.5 Hz), 7.22 (2H, d, J = 8.5 Hz).

PS-SO₃H-catalyzed transprotection of benzyl mercaptan in water (Table 3, entry 4).

A mixture of benzyl thioacetate (42.1 mg, 0.25 mmol), triphenylmethanol (65.4 mg, 0.25 mmol) and the polymer-supported catalyst (PS-SO₃H, 54.0 mg, 0.025 mmol) in degassed water (1.5 mL) was stirred for 24 h under reflux conditions. The reaction mixture was quenched with saturated aq. NaHCO₃ and brine after cooled to rt. The polymer was filtered and washed with water and ethyl acetate. The organic layer was dried over Na₂SO₄, and evaporated. The mixture was purified by preparative TLC on silica gel to give benzyl triphenylmethyl sulfide³ (80.4 mg, 88%). ¹H NMR (CDCl₃) δ 3.30 (2H, s), 7.11-7.31 (14H, m), 7.45-7.49 (6H, m).

PS-SO₃H-catalyzed dithioacetalization of benzaldehyde using dithioester in water

(Eq. 3). A mixture of benzaldehyde (26.7 mg, 0.25 mmol), the dithioester (53.0 mg, 0.276 mmol) and the polymer-supported catalyst (PS-SO₃H, 54.2 mg, 0.025 mmol) in degassed water (1.5 mL) was stirred for 24 h under reflux conditions. The polymer was filtered and washed with water and dichloromethane after cooled to rt. The organic layer was dried over Na₂SO₄, and evaporated. The mixture was purified by preparative TLC on silica gel to give 2-phenyl-1,3-dithiane⁴ (48.0 mg, 98%). ¹H NMR (CDCl₃) δ 1.88–1.98 (1H, m), 2.14–2.18 (1H, m), 2.87–2.93 (2H, m), 3.02–3.09 (2H, m), 5.17 (1H, s), 7.27–7.35 (3H, m), 7.47 (2H, d, *J* = 7.3 Hz); ¹³C NMR (CDCl₃) δ 25.11, 32.09, 51.48, 127.75, 128.43, 128.72, 139.11.

References

(1) Patney, H. K. *Synth. Commun.* **1993**, 23, 1829.

- (2) Tam-Chang, S.-W.; Mason, J. C. *Tetrahedron* **1999**, *55*, 13333.
- (3) Manabe, K.; Iimura, S.; Sun, X.-M.; Kobayashi, S. *J. Am. Chem. Soc.* **2002**, *124*, 11971.
- (4) Ku, B.; Oh, D. Y. *Synth. Commun.* **1989**, *19*, 433.