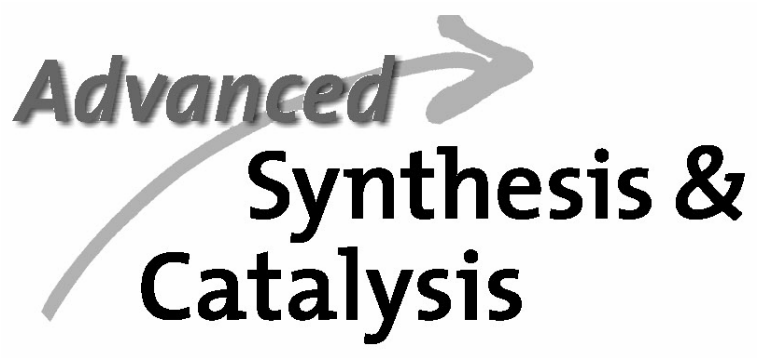

Supporting Information

Supporting Information

Remarkable Activation of a Lipase by the (*R*)-Pyrrolidine-substituted Imidazolium Alkyl PEG Sulfate

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General Procedures

Reagents and solvents were purchased from common commercial sources and were used as received or purified by distillation over appropriate drying agents. Reactions requiring anhydrous conditions were carried out under argon with dry, freshly distilled solvents and magnetic stirring. Reactions except the preparation of the ionic liquids were monitored by thin layer chromatography using silica gel plate and GC. Thin layer chromatography was performed with the indicated solvents and Wako gel B-5F. ^{1}H-NMR spectra and ^{13}C-NMR spectra were recorded on a JEOL JNM MH-500 or JNM MH-400MHz spectrometer. Chemical shifts are expressed in ppm downfield from tetramethylsilane (TMS) in $CDCl_3$ as an internal reference. IR spectra were obtained on SHIMADZU FT-IR 8000 spectrometers. Optical rotation was measured with a JASCO DIP-370 digital polarimeter. The rate was determined by gas chromatography analysis (Quadrex bonded fused silica methyl silicone, ϕ 0.25 mm × 25 m, N_2) .The optical purity was determined by HPLC analysis using Daicel OD, OD-H, OB, AD, or OJ-H and capillary gas chromatography (Chiraldex G-TA, ϕ 0.25 mm × 20 m, 100 ºC, He). MALDI-TOF-MS spectra were obtained on a BRUKER AutoFLEX-T2.

Preparation of amino acid-coated lipase PS

Glycine free PS was prepared by Celite free lipase PS, which was provided by Amano Enzyme, Ltd. and included 20 wt% of glycine as a stabilizer, following the procedure illustrated in Scheme 1: Typically, celite free PS (10 mg) was dissolved in 0.50 ml of deionized water at 4°C in a centrifugal filter device equipped with ultracel YM-10 (Microcon, Millipore) and centrifuged at 13,000 rpm at 4°C for 10 min., repeating the same process several times until (after ca. 10 times) no more glycine was detected from the filtrate. Since the glycine free lipase protein is unstable, it was immediately used for amino acid coated lipase PS. The resulting glycine free protein was dissolved in cold deionized water, dried by lyophilization to give GF-PS powder and stored under argon in a refrigerator. Amino acid coated lipase was prepared by mixing with the corresponding amino acid (100 mol eq. vs. lipase protein) with glycine free lipase PS protein and dried by lyophilization. The amino acid sequence of lipase PS is known, so the exact molecular weight can be given as 32 K dalton. With this data, we evaluated lipase-catalyzed reactions using the same amount of amino acid coated lipase PS as of enzyme protein. For

example, since 8.0 mg of GF-PS (10 mg of the starting celite-free PS) corresponded to 2.5 X 10^{-4} mmol of lipase PS protein (32 K dalton), the amount of enzyme protein involved in each amino acid coated enzyme was estimated as follows: L-Phe-PS: 66 wt%, L-Pro-PS: 73 wt%, Gly-PS: 81wt%, IL1-PS: 19wt%, L-Phe-IL1-PS: 18 wt%, L=Pro-IL1-PS: 18wt%. (Figure S-1)

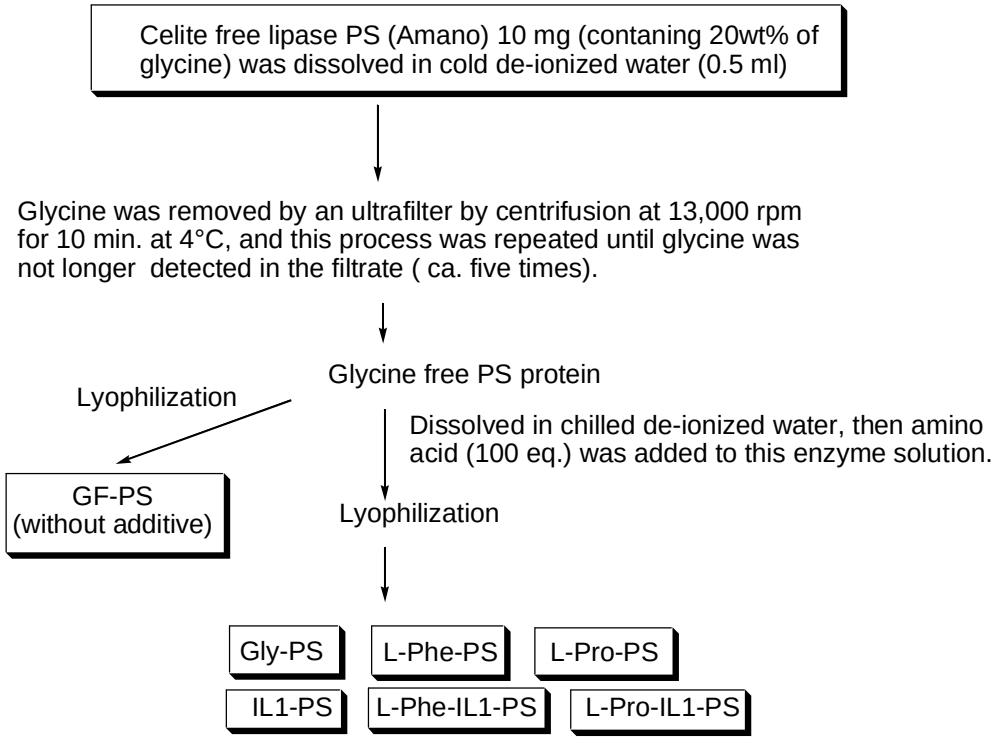
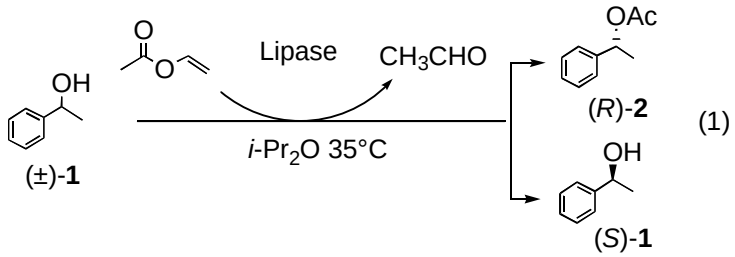


Figure S-1. Prpperation of amino acid-coated lipase PS

Lipase-catalyzed transesterification using amino acid-coated lipase PS.



(1)

To a solution of (±)-**1** (50 mg, 0.41 mmol) and vinyl acetate (55 mg, 0.64 mmol) in i-Pr_2O (2.0 mL) was added GF-PS (5.0 mg) and the mixture was stirred at 35 ºC. The reaction course was monitored by capillary GC-analysis and silica gel TLC. (*R*)-**2** and (*S*)-**1** were obtained by preparative silica gel thin layer chromatography (TLC). The enantioselectivity was determined by HPLC analysis on a chiral column (Chiralcel OB, hexane: 2-propanol = 9 : 1). When the reaction was carried out using amino acid coated enzyme, we used 7.5 mg of L-Phe-PS, 6.8 mg of L-Pro-PS, 6.1 mg of Gly-PS, 26.3 mg of IL1-PS, and 27.8 mg of L-Phe-IL1-PS or L-pro-IL1-PS per 50 mg of (±)-**1**. The results are summarized in Table 1.

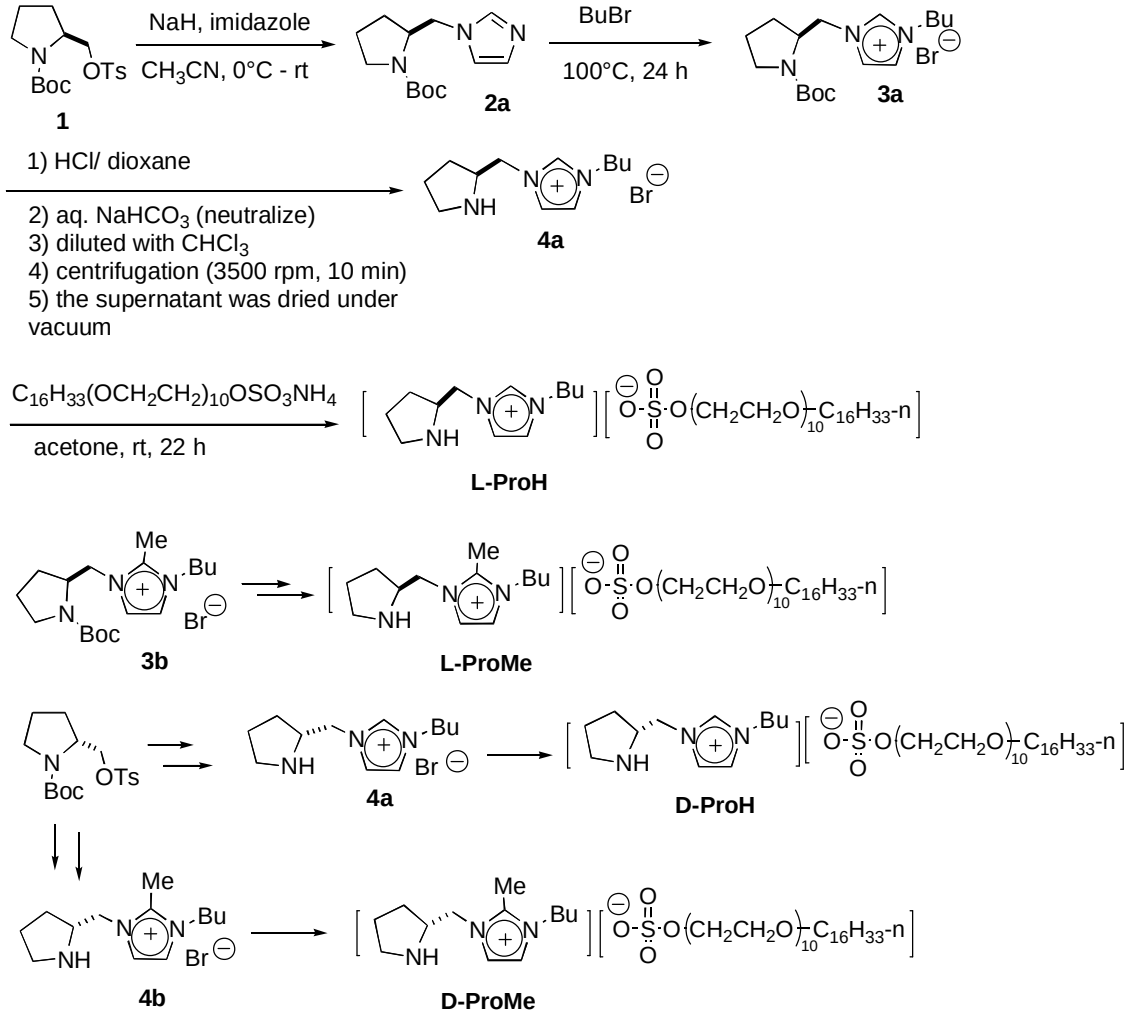
(*R*)-**2**: Rf 0.55 (hexane/ethyl acetate = 4/1); ^{1}H NMR (500 MHz, ppm, $CDCl_3$, *J*= Hz) 1.47 (3H, d, *J*= 6.9 Hz), 2.00 (3H, s), 5.81 (1H, q, *J*= 6.9 Hz), 7.19-7.29 (5H, m); ^{13}C NMR (125 MHz, ppm, $CDCl_3$) d 21.25, 22.12, 72.22, 126.00, 127.77, 128.40, 141.59, 170.21; IR (neat, cm^{-1}) 2980, 1730, 1495, 1370, 1240, 1030, 940, 760.
(*S*)-**1**: Rf 0.25 (hexane/ethyl acetate = 4:1); ^{1}H NMR (500 MHz, ppm, $CDCl_3$, *J*= Hz) d 1.43 (3H, d, *J*= 6.4 Hz), 1.75 (1H, s, OH), 4.83 (1H, q, *J*= 6.4 Hz), 7.28-7.30 (5H, m); ^{13}C NMR (125 MHz, ppm, $CDCl_3$) d 25.01, 70.13, 125.30, 127.26, 128.33, 145.76; IR (neat, cm^{-1}) 3330, 3030, 2970, 2890, 1490, 1450, 1010, 900.

Table 1. Transesterification of 1-phenylethanol (**1**) by glycine free lipase PS or amino acid coated lipase PS

Entry	Lipase	Time (h)	Yield of (*R*)-**2** (ee_P, %)[a]	Yield of (*S*)-**1** (ee_S, %)[a]	%conv.[b]	Relative Rate (%conv/h)	E[b]
1	GF-PS	48	5 (>99)	44 (33)	25	0.52	>200
2	Gly-PS	26	9 (87)	72 (15)	15	0.58	17
3	L-Phe-PS	48	10 (>99)	53 (23)	19	0.40	>200
4	L-Pro-PS	60	14 (97)	58 (23)	19	0.32	91
5	IL1-PS	20	22 (>99)	35 (64)	39	2.0	>200
6	L-Phe-IL1-PS	21	25 (>99)	38 (63)	39	1.9	>200
7	L-Pro-IL1-PS	4	22 (>99)	35 (62)	38	9.5	>200

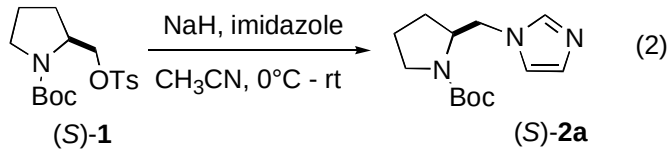
[a]Determined by HPLC, Chiralcel OD-H, *i*-PrOH: hexane = 9:1. [b]Calculated by ee_P and ee_S. E= $\ln[(1-c)(1+ee_P)]/\ln[(1-c)(1-ee_P)]$, here c means conv. which was calculated by the following formula: c = $ee_P/(ee_P+ee_S)$.[13]

Synthesis of (*R*)- or (*S*)-Pyrrolidine–substituted imidazolium salts



Scheme S-1

Preparation of (*S*)-2a[14]

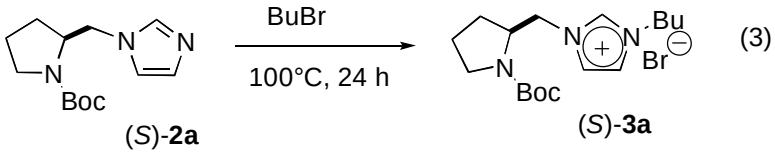


(2)

To a suspension of sodium hydrate (1.72 g, 60% in mineral oil) in dry acetonitrile (60 ml) was added an acetonitrile (10 mL) solution of imidazole (2.42 g, 35.4 mmol) drop-wise at 0°C, following by stirring for 20 min at the same temperature. To this mixture was added an acetonitrile (6 ml) solution of tosylate (*S*)-**1** (8.4 g, 23.6 mmol) and the mixture was stirred under reflux conditions for 1.5 h. After being cooled to rt, the mixture was evaporated to dryness, then diluted with water (75 ml) and extracted with $CHCl_3$ (3 times) and ether (2 times). The organic layers were dried (Na_2SO_4) and

evaporated and subjected to silica gel flash column chromatography (hexane-ethyl acetate= 1:1, ethyl acetate/ methanol= 10:1 then 5:1) to give (*S*)-**2a**[14] (4.6 g, 18.4 mmol) in 78% yield.
$[\alpha]^{26}_{D}$ -66.2 (c1.0, $CHCl_3$); ^{1}H NMR (400 MHz, ppm, $CDCl_3$, *J*= Hz) d 1.29-1.39 (1H, m), 1.50 (9H, s), 1.60-1.75 (2H, m), 1.89-2.00 (1H, m), 3.12-3.42 (2H, m), 3.95-4.10 (2H, m), 4.22-4.28 (1H, m), 6.89 (1H, s), 7.05(1H, s), 7.42 (1H, s); ^{13}CNMR (125 MHz, ppm, $CDCl_3$) d 22.7, 27.9, 28.5, 46.4, 49.1, 56.9, 79.5, 119.3, 128.8, 137.0, 154.1; IR (neat, cm^{-1}) 2978, 1686, 1400, 1169, 754.

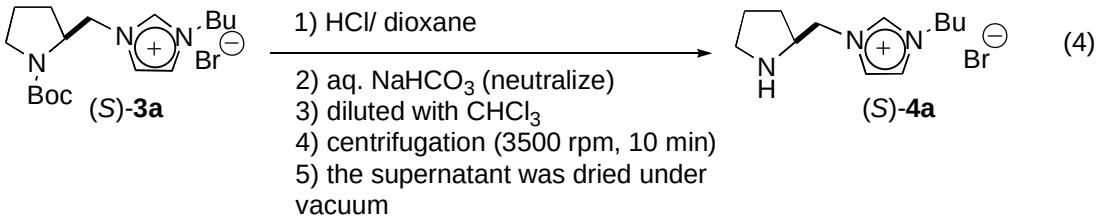
Preparation of (*S*)-3a[14]



(3)

A mixture of (*S*)-**2a**[14] (4.06 g, 16.1 mmol) and 1-bromobutane (3.11 g, 22.7 mmol) was stirred at 100 °C for 24 h under argon. After being cooled to rt, the mixture was diluted with cold water and washed with ether (5 ml x 5 times) and a mixed solvent (hexane/ ethyl acetate= 2:1, 3 times). The resulting aqueous solution was dried by lyophilization to give (*S*)-**3a** [14] (6.08 g, 15.7 mmol) in 97 % yield.
$[\alpha]^{26}_{D}$ -18.2 (c1.0, $CHCl_3$) ; ^{1}H NMR (500 MHz, ppm, $CDCl_3$, *J*= Hz) d 0.98 (3H, t, J= 7.4 Hz), 1.42 (9H, s), 1.40-1.45 (2H, m), 1.82-2.11 (4H, m), 3.22-3.49 (2H, m), 4.12-4.20 (1H, m), 4.25-4.41 (2H, m), 4.48-4.66 (2H, m), 7.29(1H, s), 7.38(1H, s), 10.5 (1H, s); ^{13}CNMR (125 MHz, ppm, $CDCl_3$) d 12.9, 18.8, 23.1, 27.8, 31.4, 46.5, 49.0, 49.1, 51.3, 56.4, 79.5, 121.6, 122.4, 136.4, 154.5; IR (neat, cm^{-1}) 3077, 2964, 1676, 1560, 1452, 1167, 1107, 756.

Preparation of (*S*)-4a[14]

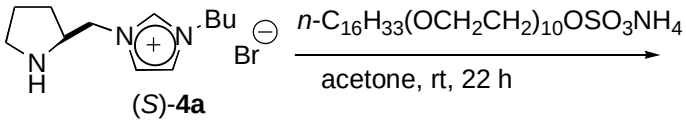


(4)

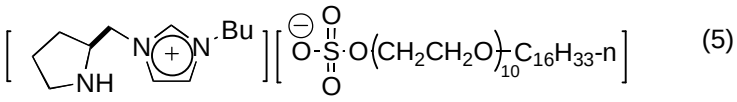
(*S*)-**3a**[14] was dissolved in a mixture of conc. HCl aqueous solution (60 ml) and dioxane (40 ml) at 0°C and evaporated to dryness. The resulting solid was next neutralized by saturated $NaHCO_3$ aqueous solution. The resulting mixture was evaporated to dryness, then diluted with $CHCl_3$ to form NaCl as precipitate which was removed by filtration through a glass sintered filter with a Celite pad; then the filtrate was centrifuged at 3500 rpm for 10 min. The supernatant was evaporated to dryness to give (*S*)-**4a**[14] (5.3 g, 15.6 mmol) in quantitative yield.
$[\alpha]^{28}_{D}$ +21.6 (c1.0, $CHCl_3$) ; ^{1}H NMR (500 MHz, ppm, $CDCl_3$, *J*= Hz) d 0.98 (3H, t, J= 7.4 Hz), 1.36-1.47 (3H, m), 1.67-1.78 (2H, m), 1.88-1.94 (3H, m), 2.08-2.09 (1H, m), 2.86-2.91 (1H, m), 2.95-3.00 (1H, m), 3.69-3.74 (1H, m), 4.14 (1H, dd, J= 13.3 Hz, 8.7 Hz), 4.33 (2H, t, J= 7.8 Hz), 4.44 (1H, dd, J= 13.5 Hz, 3.7 Hz), 7.22 (1H, s), 7.53 (1H, s),

10.48 (1H, s); ^{13}CNMR (125 MHz, ppm, $CDCl_3$) d 13.4, 19.4, 25.9, 29.2, 32.0, 46.6, 49.8, 54.4, 57.4, 120.9, 123.1, 137.3; IR (neat, cm^{-1}) 3414, 2957, 2876, 1560, 1165, 752.

Preparation of L-ProH



(*S*)-**4a**

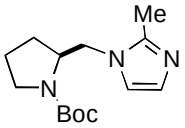


(5)

L-ProH

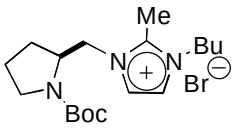
A mixture of (*S*)-**4a**[14] (520 mg, 1.7 mmol) and ammonium cetyl-PEG10 sulfate (1.34 g, 1.7 mmol) [2] in dry acetone (2.0 ml) was stirred at rt for 22 h to form white precipitate (NH4Br). The precipitate was removed by filtration through a glass sintered filter with celite pad. To the filtrate was added activate charcoal and stirred for 1 h at rt, then put through an Al_2O_3 (neutral type I, activated) short column. The resulting filtrate was evaporated and dried under vacuum at 0.1 Torr for 24 h to give **L-ProH** (903 mg, 0.93 mmol) in 55 % as a yellow solid.

L-ProH: $[\alpha]^{27}_D$ +0.2 (c1.13, $CHCl_3$); mp 28-29°C; ^{1}H NMR (500 MHz, ppm, $CDCl_3$, *J*= Hz) d 0.88 (6H t, *J*= 7.4), 1.25 (30H, brs), 1.37-1.44 (2H, m), 1.57 (4H, quin. J= 6.8 Hz), 1.86-1.92 (2H, m), 2.44 (1H, brs), 3.44 (2H, t, J= 6.8 Hz), 3.57-3.61 (4H, m), 3.63 (36H, brs), 3.72 (1H, brs), 4.19 (1H, t, J= 5.1 Hz), 4.23 (1H, t, J= 4.6 Hz), 4.32 (2H, t, J= 7.3 Hz), 7.26 (1H, s), 7.29 (1H, s), 10.02 (1H, s); ^{13}CNMR (125 MHz, ppm, $CDCl_3$) d 13.3, 14.0, 19.3, 22.5, 25.9, 29.2, 29.3, 29.5, 29.6, 31.8, 32.0, 49.7, 64.5, 69.9, 70.1, 70.4, 71.4, 72.5; IR (neat, cm^{-1}) 3449, 2851, 2343, 1736, 1638, 1468, 1346, 1279, 1244, 1119, 949, 845; HRMS (MALDI-TOF MS, matrix: DHB) Calcd for $C_{12}H_{22}N_3$ for the imidazolium cation: 208.1816; found 208.1818.



(*S*)-**2b**

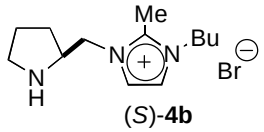
(*S*)-**2b**[14]: $[\alpha]^{21}_D$ -31.0 (c1.0, $CHCl_3$); bp 397 °C; ^{1}H NMR (500 MHz, ppm, $CDCl_3$, *J*= Hz) d 1.26-1.38 (1H, m), 1.49 (9H, s), 1.68-1.70 (2H, m), 1.84-1.91 (1H, m), 2.41 (3H, s), 3.24-3.44 (2H, m), 3.98-4.14 (3H, m), 6.78 (1H, d, J= 9.2 Hz), 6.91(1H, s); ^{13}CNMR (125 MHz, ppm, $CDCl_3$) d 13.1, 23.3, 27.9, 28.4, 46.8, 48.3, 57.2, 80.1, 119.8, 127.4, 145.0, 154.6; IR (neat, cm^{-1}) 2978, 1690, 1400, 1171, 731.



(*S*)-**3b**

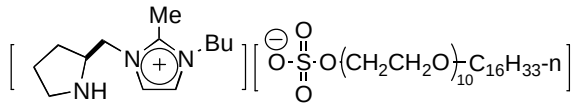
(*S*)-**3b**[14]: $[\alpha]^{20}_D$ +21.9 (c1.1, $CHCl_3$); bp 120-124 °C; ^{1}H NMR (500 MHz, ppm, $CDCl_3$,

J= Hz) d 0.97 (3H, t, J= 7.3 Hz), 1.35 (9H, s), 1.39-1.47 (2H, m), 1.80 (2H, quin, J= 7.3 Hz), 1.92-2.07(3H, m), 2.24 (1H, brs), 2.84 (3H, s), 3.29-3.49 (2H, m), 4.16-4.32 (3H, m), 4.44-4.58 (2H, m), 7.29(1H, s), 7.41 (1H, s), 7.92(1H, s); ^{13}CNMR (125 MHz, ppm, $CDCl_3$) d 10.6, 13.4, 19.5, 23.6, 28.2, 28.3, 31.7, 46.9, 48.5, 51.7, 55.8, 79.7, 120.4, 123.3, 143.9, 155.1; IR (neat, cm^{-1}) 3071, 2964, 2880, 1685, 1452, 1173, 1107, 758.



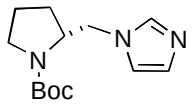
(*S*)-**4b**

(*S*)-**4b**[14]: $[\alpha]^{28}_D$ +21.6 (c1.1, $CHCl_3$) ; ^{1}H NMR (500 MHz, ppm, $CDCl_3$, *J*= Hz) d 0.97 (3H, t, J= 7.4 Hz), 1.41 (2H, sex, J= 7.4 Hz), 1.46-1.52 (1H, m), 1.67-1.74 (1H, m), 1.76-1.86 (3H, m), 1.99-2.06 (1H, m), 2.54 (1H, brs), 2.83 (3H, s), 2.83-2.99 (2H, m), 3.62-3.70 (1H, m), 4.05 (1H, dd, J= 13.8 Hz, 9.2 Hz), 4.23 (2H, t, J= 7.3 Hz), 4.35 (1H, dd, J= 14.0 Hz, 3.2 Hz), 7.52 (1H, s), 7.78 (1H, s); ^{13}CNMR (125 MHz, ppm, $CDCl_3$) d 11.2, 13.4, 19.5, 25.7, 29.2, 31.6, 46.4, 48.5, 53.6, 57.7, 120.8, 122.4, 143.6; IR (neat, cm^{-1}) 3414, 3271, 3063, 2957, 2873, 1583, 1529, 1248, 1117, 752.



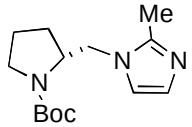
L-ProMe

L-ProMe: $[\alpha]^{27}_D$ -0.6 (c1.03, $CHCl_3$); mp 30-33°C; ^{1}H NMR (500 MHz, ppm, $CDCl_3$, *J*= Hz) d 0.67 (6H t, *J*= 6.9), 1.05 (30H, brs), 1.34-139 (6H, m), 1.94-1.98 (2H, m), 2.42 (3H, s), 3.07 (1H, brs), 3.24 (2H, t, J= 6.9 Hz), 3.36-3.40 (4H, m), 3.44 (36H, brs), 3.49-3.51 (1H, m), 3.57-3.59 (1H, m), 3.89 (1H, t, J= 3.2 Hz), 3.98-4.01 (2H,m), 4.09-4.10 (1H, m), 7.27 (1H, d, J= 2.3 Hz), 7.33 (1H, d, J= 2.2 Hz); ^{13}CNMR (125 MHz, ppm, $CDCl_3$) d 13.6, 22.2, 24.5, 25.4, 25.6, 28.8, 28.9, 29.0, 29.1, 29.2, 32.2, 31.4, 32.3, 53.6, 61.0, 62.0, 68.9, 69.6, 69.8, 70.1, 70.9, 71.5, 72.1; IR (neat, cm^{-1}) 3449, 2916, 2851, 1468, 1113, 949, 845; HRMS (MALDI-TOF MS, matrix: DHB) Calcd for $C_{13}H_{24}N_3$ for the imidazolium cation: 222.1972; found 222.2017.



(*R*)-**2a**

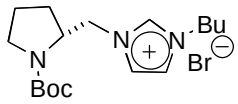
(*R*)-**2a** [14]: $[\alpha]^{24}_D$ +65.6 (c1.0, $CHCl_3$); mp 101-104°C; ^{1}H NMR (400 MHz, ppm, $CDCl_3$, *J*= Hz) d 1.29-1.39 (1H, m), 1.50 (9H, s), 1.68 (2H, brs), 1.91-2.00 (1H, m), 3.07-3.45 (2H, m), 3.94-4.15 (2H, m), 4.27 (1H, dd, J= 13.7 Hz, 5.5 Hz), 6.90 (1H, s), 7.04 (1H, s), 7.42 (1H, s); ^{13}CNMR (125 MHz, ppm, $CDCl_3$) d 23.1, 28.2, 28.9, 46.8, 49.5, 57.3, 79.9, 119.6, 129.3, 137.4, 154.5; IR (neat, cm^{-1}) 3099, 2971, 2874, 1680, 1406, 1163, 773.



(*R*)-**2b**

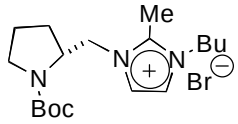
(*R*)-**2b** [14]: $[\alpha]^{24}_D$ +28.0 (c0.97, $CHCl_3$); bp 397 °C/ 760 Torr (Kugelrohr); ^{1}H NMR (500

MHz, ppm, $CDCl_3$, *J*= Hz) d1.49 (9H, s), 1.60-1.96 (4H, m), 2.41 (3H, s), 3.25-3.45 (2H, m), 3.96-4.10 (3H, m), 6.79 (1H, d, J= 8.7 Hz), 6.90(1H, s); ^{13}CNMR (125 MHz, ppm, $CDCl_3$) d 12.9, 23.1, 27.7, 28.2, 46.6, 48.1, 57.0, 79.9, 119.6, 127.1, 144.7, 154.4; IR (neat, cm^{-1}) 2977, 2884, 1686, 1400, 1169, 733.



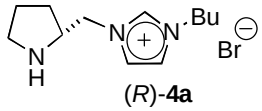
(*R*)-**3a**

(*R*)-**3a**[14]: $[\alpha]^{23}_D$ +31.6 (c1.1, $CHCl_3$); ^{1}H NMR (500 MHz, ppm, $CDCl_3$, *J*= Hz) d 0.97 (3H, t, J= 7.4 Hz), 1.42 (9H, s), 1.87-2.04 (6H, m), 3.39 (2H, brs), 4.21 (1H, brs), 4.36 (2H, brs), 4.46-4.70 (2H, m), 7.29 (1H, s), 7.38 (1H, s), 10.5 (1H, s); ^{13}CNMR (125 MHz, ppm, $CDCl_3$) d 14.0, 18.9, 23.2, 27.9, 31.7, 46.6, 49.2, 49.4, 51.3, 56.6, 79.6, 121.7, 122.4, 136.6, 154.6; IR (neat, cm^{-1}) 3069, 2967, 1686, 1560, 1458, 1391, 1169, 755.



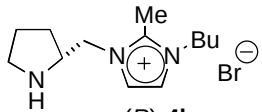
(*R*)-**3b**

(*R*)-**3b**[14]: $[\alpha]^{24}_D$ -21.9 (c1.06, $CHCl_3$); bp 120-124 °C; ^{1}H NMR (500 MHz, ppm, $CDCl_3$, *J*= Hz) d 0.97 (3H, t, J= 7.3 Hz), 1.34 (9H, s), 1.38-1.46 (2H, m), 1.80 (2H, quin, J= 7.3 Hz), 1.89-1.95(2H, m), 1.96-2.03 (1H, m), 2.20-2.29 (1H, m), 2.82 (3H, s), 3.28-3.35 (1H, m), 3.46-3.49 (1H, m), 4.02-4.16 (3H, m), 4.46-4.54 (2H, m), 7.22 (1H, s), 7.85 (1H, s); ^{13}CNMR (125 MHz, ppm, $CDCl_3$) d 10.2, 13.0, 19.0, 23.2, 27.4, 27.8, 31.3, 46.4, 48.1, 51.2, 55.4, 79.3, 120.2, 122.7, 143.5, 154.7; IR (neat, cm^{-1}) 3079, 2967, 2934, 2876, 1685, 1389, 1170, 1107, 758.



(*R*)-**4a**

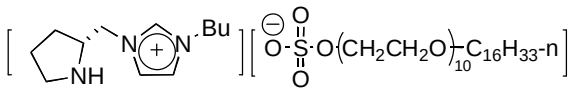
(*R*)-**4a**[14]: $[\alpha]^{24}_D$ -21.9 (c1.06, $CHCl_3$); ^{1}H NMR (500 MHz, ppm, $CDCl_3$, *J*= Hz) d 0.97 (3H, t, J= 7.3 Hz), 1.39-1.40 (2H, m), 1.47-1.54 (1H, m), 1.71-1.84 (2H, m), 1.91 (2H, quin, J= 7.8 Hz, 7.3 Hz), 2.07-2.13 (1H, m), 2.94-3.05 (3H, m), 3.76-3.82 (1H, m), 4.29 (1H, m), 4.14 (3H, t, J= 7.3 Hz), 4.48-4.51 (1H, m), 7.19 (1H, s), 7.56 (1H, s), 10.44 (1H, s); ^{13}CNMR (125 MHz, ppm, $CDCl_3$) d 13.1, 19.1, 25.4, 28.7, 31.7, 46.1, 49.4, 53.5, 57.3, 121.0, 123.0, 136.5; IR (neat, cm^{-1}) 3423, 2960, 2874, 1560, 1165, 754.



(*R*)-**4b**

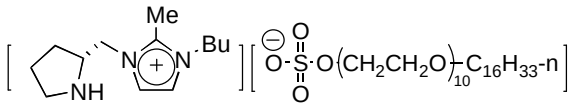
(*R*)-**4b**[14]: $[\alpha]^{24}_D$ -25.4 (c2.64, $CHCl_3$): ^{1}H NMR (500 MHz, ppm, $CDCl_3$, *J*= Hz) d 0.98 (3H, t, J= 7.3 Hz), 1.41 (2H, sex, J= 7.3 Hz), 1.52-1.60 (1H, m), 1.72-1.91 (4H, m), 2.07-2.13 (1H, m), 2.84 (3H, s), 2.92-3.01 (2H, m), 3.38 (1H, brs), 3.68-3.74 (1H,m), 4.19-4.23 (3H, m), 4.44 (1H, dd, J= 14.2 Hz, 3.7 Hz), 7.48 (1H, d, J= 1.8 Hz), 7.85 (1H, d, J= 1.8 Hz); ^{13}CNMR (125 MHz, ppm, $CDCl_3$) d 11.2, 13.4, 19.5, 25.4, 29.0, 31.5, 46.1, 48.6, 52.9, 57.9, 120.9, 122.4, 143.8; IR (neat, cm^{-1}) 3414, 3067, 2960, 2874, 1530, 1115,

756.



R-ProH

D-ProH: $[\alpha]^{23}_{D}$ +0.6 (c0.98, $CHCl_3$); mp 27-28°C; ^{1}H NMR (500 MHz, ppm, $CDCl_3$, *J*= Hz) d 0.88 (6H t, *J*= 7.3), 1.25 (32H, brs), 1.57 (4H, quin. J= 6.8 Hz), 1.80-1.91 (2H, m), 2.72 (1H, brs), 3.44 (2H, t, J= 6.9 Hz), 3.57-3.62 (4H, m), 3.63 (36H, brs), 3.72 (1H, d, J= 8.9 Hz), 4.18-4.23 (2H, m), 4.32 (2H, t, J= 5.5 Hz), 7.54 (1H, dd, J= 5.7 Hz, 3.2 Hz), 7.71 (1H, dd, J= 5.9 Hz, 3.2 Hz), 10.24 (1H, s); ^{13}CNMR (125 MHz, ppm, $CDCl_3$) d 14.1, 22.7, 25.8, 26.1, 29.4, 29.5, 29.6, 29.4, 29.7, 31.9, 32.8, 61.7, 61.8, 70.4, 70.3, 70.6, 71.5, 72.6; IR (neat, cm^{-1}) 3434, 2917, 2851, 1468, 1113, 947, 845; HRMS (MALDI-TOF MS, matrix: DHB) Calcd for $C_{12}H_{22}N_3$ for the imidazolium cation: 208.1816; found 208.1957.



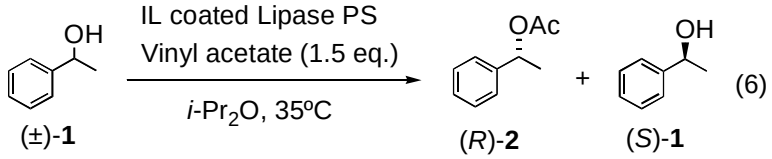
R-ProMe

D-ProMe: $[\alpha]^{27}_{D}$ +1.2 (c1.01, $CHCl_3$); mp 27-28°C; ^{1}H NMR (500 MHz, ppm, $CDCl_3$, *J*= Hz) d 0.88 (6H t, *J*= 6.9), 1.26 (30H, brs), 1.57 (6H, m), 2.27-2.35 (2H, m), 2.62 (3H, s), 2.92 (1H, brs), 3.45 (2H, t, J= 6.9 Hz), 3.57-3.62 (4H, m), 3.66 (36H, brs), 3.72 (1H, brs), 3.78-3.82 (1H, m), 4.15-4.17 (1H, m), 4.22 (2H, t, J= 4.6 Hz), 4.33 (1H, t, J= 4.6 Hz), 7.54 (1H, dd, J= 5.5 Hz, 2.3 Hz), 7.71 (1H, dd, J= 5.8 Hz, 2.2 Hz); ^{13}CNMR (125 MHz, ppm, $CDCl_3$) d 14.0, 22.6, 26.0, 29.3, 29.4, 29.5, 29.5, 29.6, 31.8, 39.8, 61.6, 61.7, 69.9, 70.0, 70.2, 70.5, 71.5, 72.5; IR (neat, cm^{-1}) 3435, 2917, 2851, 1468, 1350, 1109; HRMS (MALDI-TOF MS, matrix: DHB) Calcd for $C_{13}H_{24}N_3$ for the imidazolium cation: 222.1972; found 222.2111.

Preparation of (D)-ProMe-supported lipase PS (D-ProMe-PS) by lyophilization

Lipase PS (Amano) (1.0 g, since this contained 20 wt % of glycine and 1.0 wt % of lipase protein, therefore amount of lipase protein was estimated as $3.1x10^{-4}$ mmol) was dissolved in 8.0 ml of 0.1 M potassium phosphate buffer (pH 7.2) and the mixture was centrifuged at 3,500 rpm for 5 min (3 times). 2.0 ml of 0.1 M potassium phosphate buffer (pH7.2) of **D-ProMe** (30 mg; ca. 3.1×10^{-2} mmol because the estimated molecular weight of the salt was 984.37.) was mixed with the resulting supernatant and dried by lyophilization to give D-ProMe-PS (219 mg) as a hygroscopic white powder. The estimated lipase protein of this enzyme powder was therefore estimated as 4.2 wt%.
L-ProH-PS, **L-ProMe-PS**, and **D-ProH-PS** were prepared by the same procedure.

D-ProMe-PS-catalyzed acylation of (±)-1-phenylethanol (1) in *i*-Pr_2O



(±)-**1** (*R*)-**2** (*S*)-**1**

To a solution of (±)-**1a** (50 mg, 0.41 mmol) and vinyl acetate (53 mg, 0.62 mmol) in *i*-Pr_2O (2.0 mL) was added **D-ProMe-PS** (5.9 mg, corresponding to 0.25 mg of enzyme)

and the mixture was stirred at 35ºC. The reaction course was monitored by capillary GC-analysis and silica gel TLC. The reaction mixture was filtrated through a sintered glass filter with a Celite pad to remove the lipase, and the filtrate was concentrated under vacuum. Preprative silica gel TLC afforded (*R*)-**2** (25.0 mg, 0.15 mmol) in 37% yiled and (*S*)-**1** (19.5 mg, 0.16 mmol) in 39% yield. The enantioselectivity was determined by HPLC analysis using a chiral column (Chiralcel OB, hexane: 2-propanol = 9: 1). (*R*)-**2**: $[\alpha]^{25}_{D}$ +102 (c1.0), $CHCl_3$), >99% ee; (*S*)-**1**: $[\alpha]^{25}_{D}$ -54.0 (c1.0, $CHCl_3$), 97% ee. The results are summarized in Table 2.

Table 2. Second generation IL type activator coated PS-catalyzed transesterification of 1-phenylethanol (**1**)

Entry	Lipase[c]	Acyl donor	Time (h)	Yield of (*R*)-**2** (ee_P, %)[d]	Yield of (*S*)-**1** (ee_S, %)[d]	Rate [e]	conv. [f]	E[f]
1	PS	VA[a]	28	21 (83)	61 (38)	65	0.31	16
2	IL1-PS	VA[a]	2	39 (>99)	48 (88)	200	0.47	>200
3	L-ProH	VA[a]	1	44 (96)	53 (81)	1300	0.46	123
4	L-ProMe	VA[a]	1	37 (98)	42 (91)	1450	0.48	>200
5	D-ProH	VA[a]	0.5	35 (>99)	35 (96)	3400[g]	0.49	>200
6	D-ProMe	VA[a]	0.5	37 (>99)	39 (97)	3800[g]	0.49	>200
7	PS	TFEA[b]	24	17 (>99)	59 (27)	90	0.21	>200
8	D-ProMe	TFEA[b]	2	39 (>99)	43 (87)	2800	0.47	>200

[a] Vinyl acetate (1.5 eq vs (±)-**1**) was used as acyl donor. [b] 2,2,2-trifluoroethyl acetate (1.5 eq.) was used as acyl donor. [c] These enzymes involve 20 wt% of glycine as stabilizing agent. [d] Deternined by HPLC, Chiralcel OD-H, *i*-PrOH: hexane = 9:1. [e] mM, h^{-1}, mg $(enzyme)^{-1}$. The reaction rate of the lipase-catalyzed reaction was determined by capillary GC-analysis: the reaction mixture was sampled at appropriate reaction interval and determined % conversion by GC analysis comparing to the internal reference compound based on the results until 60 min reaction, respectively. [f] Calculated by ee_P and ee_S. $E= \ln[(1-c)(1+ee_P)]/\ln[(1-c)(1-ee_P)]$, here c means conv. which was calculated by the following formula: $c = ee_P/(ee_P+ee_S)$. See ref. [13]. [g] Since the lipase proceeded very rapidly, the initial reaction rate was determined based on the graph of reaction course during 30 min reaction.

Recyclable use of D-ProMe-PS in an ionic liquid solvent system

To a mixture of 1-phenylethanol (±)-**1** (50 mg, 0.41 mmol) and vinyl acetate (52 mg, 0.60 mmol) in $[P_{444ME}]NTf_2$[19] (1.0 mL) was added **D-ProMe-PS** (6.0 mg, corresponding to 0.25 mg of enzyme) and the mixture was stirred at 35 ºC for 35 min. The reaction course was monitored by capillary GC-analysis and silica gel TLC. To the reaction mixture was added 1.5 mL of a mixed solvent of hexane and diethyl ether (3:1) to form biphasic layers and product acetate (*R*)-**2** and alcohol (*S*)-**3** were isolated from the ether layer. It was essential to repeat the extraction with the mixed solvent from the reaction mixture 10 times. The combined extracts were evaporated and preparative silica gel TLC gave (*R*)-**2** (99.1% ee) in 46% and alcohol (*S*)-**3** (91% ee) in 44% yield. Since the lipase was remained in the ionic liquid layer, it was possible to use the lipase repeatedly (Figure S-2); the ionic layer was placed under reduced pressure (2 torr) at rt for 15 min. to remove the ether and to the resulting ionic layer was added (±)-**1** (50 mg, 0.41 mmol) and vinyl acetate (53 mg, 0.62 mmol) and the mixture was stirred at 35°C.

$[P_{444ME}]NTf_2$ will be soon commercially avairable from Tokyo Chemical Industry Co.,

LTD. TEL: +81-3-5640-8857, FAX: +81-3-5640-8868.

The 1st run (35 min.):
(*R*)-**2**: 46% yield, 99.1% ee; $[a]^{25}_{D}$ +101 (c 1.0, $CHCl_3$)
(*S*)-**1**: 44% yield, 91% ee; $[a]^{27}_{D}$ -49.1 (c 1.0, $CHCl_3$)

The 5th run (30 min.):
(*R*)-**2**: 46% yield, 99.5% ee; $[a]^{27}_{D}$ +105 (c 1.0, $CHCl_3$)
(*S*)-**1**: 53% yield, 88% ee; $[a]^{27}_{D}$ -55.4 (c 1.0, $CHCl_3$)

The 10th run (55 min.):
(*R*)-**2**: 37% yield, 99.0% ee; $[a]^{26}_{D}$ +108 (c 1.0, $CHCl_3$)
(*S*)-**1**: 42% yield, 91.5% ee; $[a]^{25}_{D}$ -51.7 (c 1.0, $CHCl_3$)

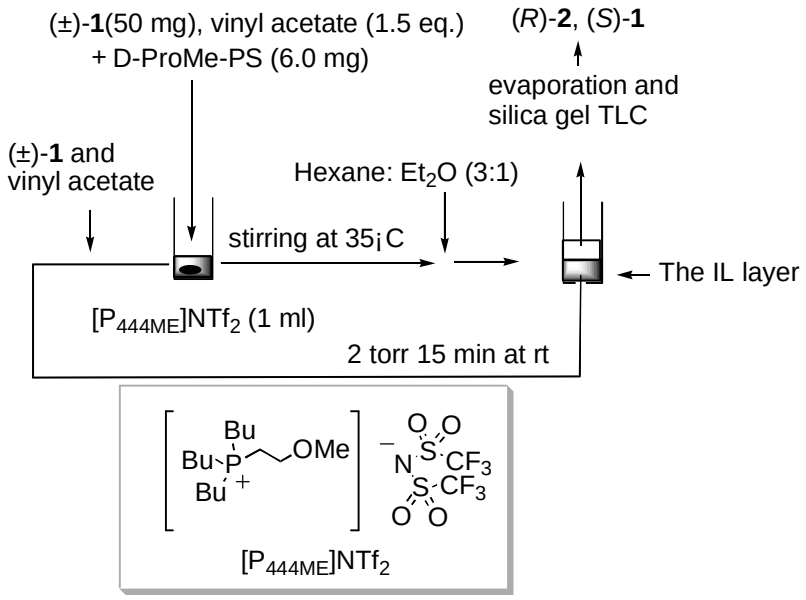
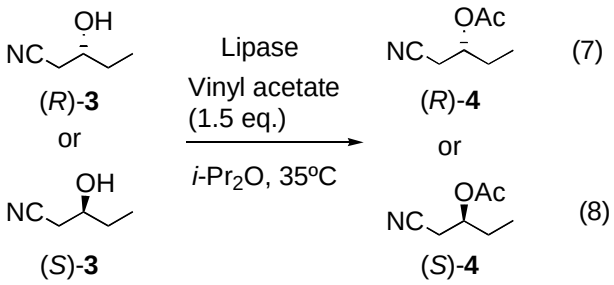


Figure S-2. Recyclable use of D-ProMe-PS in an ionic liquid solvent system

Kinetics experiments for lipase-catalyzed acetylation of 3-hydroxypentanenitrile (3)[8b]

The reaction rate of the lipase-catalyzed reaction was determined by capillary GC-analysis as follows: the reaction mixture was sampled at appropriate reaction intervals and % conversion determined by GC analysis, respectively. The reaction rate of lipase PS-catalyzed reaction was determined based on these results up to 60 min reaction. In contrast, since D-ProMe-PS-catalyzed reaction proceeded very rapidly, the initial reaction rate was determined based on the graph of the reaction course as illustrated. For details of the kinetic experiments, see reference 8. The results are summarized in Table 3.



(7)

(8)

Table 3. Results of kinetic experiments of IL-coated PS-catalyzed transesterification of 3-hydroxypentanenitrile(3)

Entry	Substrate	Enzyme	V_{max}[a]	K_m (M)	K_{cat} (min^{-1})	K_{cat}/K_m
1	(*R*)-**3**	PS	$7.2x10^{-2}$	0.23	0.29	1.3
2	(*R*)-**3**	IL1-PS	$4.4x10^{-1}$	0.30	1.8	6.0
3	(*R*)-**3**	L-ProMe-PS	$9.1x10^{-1}$	0.69	3.6	5.3
4	(*R*)-**3**	D-ProMe-PS	1.2	0.51	5.0	9.7
5	(*S*)-**3**	PS	$5.8x10^{-3}$	0.19	0.023	0.12
6	(*S*)-**3**	IL1-PS	$8.7x10^{-2}$	0.24	0.35	1.4
7	(*S*)-**3**	L-ProMe-PS	$1.1x10^{-1}$	0.31	0.44	1.4
8	(*S*)-**3**	D-ProMe-PS	$1.2x10^{-1}$	0.15	0.49	3.3

[a] M, min^{-1}, mg $(enzyme)^{-1}$.

Here we report only typical results of IL1-PS, D-ProMe-PS and L-ProMe-PS-catalyzed reactions.

Lipase PS

(*R*)-**3**: V_{max} = 0.072 (M min^{-1} mg^{-1}), K_m = 0.23 (M), K_{cat} = 0.29(min^{-1}), K_{cat}/K_m = 1.3 ($M^{-1}min^{-1}$)

[S] (M)	V(M min^{-1}, mg^{-1})	1/[S] (M^{-1})	1/V(M^{-1} min, mg)
0.40	0.046	2.5	22
0.20	0.034	5.0	30
0.133	0.027	7.5	38
0.10	0.024	10	42
0.080	0.018	12.5	57
0.067	0.017	15	59

(S)-**3**: V_{max} = 0.0058 (M min^{-1} mg^{-1}), K_m = 0.19 (M), K_{cat} = 0.023 (min^{-1}), K_{cat}/K_m = 0.12 ($M^{-1}min^{-1}$)

[S] (M)	V(M min^{-1}, mg^{-1})	1/[S] (M^{-1})	1/V(M^{-1} min, mg)
0.4	0.0037	2.5	272
0.2	0.0034	5.0	291
0.133	0.0023	7.5	441
0.1	0.0020	10	490

IL1-PS

(R)-**3:** V_{max} = 0.44 (M min^{-1} mg^{-1}), K_m = 0.30 (M), K_{cat} = 1.8 (min^{-1}), K_{cat}/K_m = 6.0 ($M^{-1}min^{-1}$)

[S] (M)	V(M min^{-1}, mg^{-1})	1/[S] (M^{-1})	1/V(M^{-1} min, mg)
0.20	0.17	5.0	5.9
0.133	0.14	7.5	7.3
0.10	0.12	10	8.3
0.080	0.092	12.5	11
0.067	0.080	15	12

(S)-**3:** V_{max} = 0.087 (M min^{-1} mg^{-1}), K_m = 0.24 (M), K_{cat} = 0.35 (min^{-1}), K_{cat}/K_m = 1.4 ($M^{-1}min^{-1}$)

[S] (M)	V(M min^{-1}, mg^{-1})	1/[S] (M^{-1})	1/V(M^{-1} min, mg)
0.4	0.058	2.5	17
0.2	0.037	5.0	27
0.133	0.030	7.5	33
0.1	0.025	10	40
0.08	0.023	12.5	43
0.067	0.018	15	55

L-ProMe-PS

(R)-**3:** V_{max} = 0.91 (M min^{-1} mg^{-1}), K_m = 0.69 (M), K_{cat} = 3.6 (min^{-1}), K_{cat}/K_m = 5.3 ($M^{-1}min^{-1}$)

[S] (M)	V(M min^{-1}, mg^{-1})	1/[S] (M^{-1})	1/V(M^{-1} min, mg)
0.20	0.19	5.0	5.4
0.133	0.16	7.5	6.4
0.10	0.12	10	8.4
0.080	0.097	12.5	10
0.067	0.078	15	13

(S)-**3:** V_{max} = 0.11 (M min^{-1} mg^{-1}), K_m = 0.31 (M), K_{cat} = 0.44 (min^{-1}), K_{cat}/K_m = 1.4 ($M^{-1}min^{-1}$)

[S] (M)	V(M min^{-1}, mg^{-1})	1/[S] (M^{-1})	1/V(M^{-1} min, mg)
0.4	0.066	2.5	15
0.2	0.041	5.0	25
0.133	0.032	7.5	31
0.1	0.026	10	38
0.08	0.063	12.5	44

D-ProMe-PS

(*R*)-**3:** V_{max} = 1.2 (M min^{-1} mg^{-1}), K_m = 0.51 (M), K_{cat} = 5.0 (min^{-1}), K_{cat}/K_m = 9.7($M^{-1}min^{-1}$)

[S] (M)	V(M min^{-1}, mg^{-1})	1/[S] (M^{-1})	1/V(M^{-1} min, mg)
0.40	0.69	2.5	1.45
0.20	0.29	5.0	3.44
0.133	0.27	7.5	3.66
0.10	0.20	10	5.10
0.080	0.17	12.5	5.99
0.067	0.15	15	6.80

(S)-**3:** V_{max} = 0.12 (M min^{-1} mg^{-1}), K_m = 0.15 (M), K_{cat} = 0.49 (min^{-1}), K_{cat}/K_m = 3.3 ($M^{-1}min^{-1}$)

[S] (M)	V(M min^{-1}, mg^{-1})	1/[S] (M^{-1})	1/V(M^{-1} min, mg)
0.4	0.11	2.5	9.3
0.2	0.070	5.0	14.3
0.133	0.052	7.5	19.3
0.1	0.045	10	22.0
0.08	0.063	12.5	15.9
0.067	0.041	15	24.3