Supporting Information for
Rational Design of an L-Histidine-derived Minimal Artificial Acylase for the Kinetic Resolution of Racemic Alcohols

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General Methods. Infrared (IR) spectra were recorded on a JASCO FT/IR 460 plus spectrometer. ^{1}H NMR spectra were measured on a Varian Gemini-2000 spectrometer (300 MHz) at ambient temperature. Data were recorded as follows: chemical shift in ppm from internal tetramethylsilane on the δ scale, multiplicity (s = singlet; d = doublet; t = triplet; m = multiplet), coupling constant (Hz), integration, and assignment. ^{13}C NMR spectra were measured on Varian Gemini-2000 (75 MHz) spectrometer. Chemical shifts were recorded in ppm from the solvent resonance employed as the internal standard (deuterochloroform at 77.00 ppm). High-performance liquid chromatography (HPLC) analysis was conducted using Shimadzu LC-10 AD coupled diode array-detector SPD-MA-10A-VP and chiral column of Daicel CHIRALCEL OD-H (4.6 mm × 25 cm), AD-H (4.6 mm × 25 cm), or Daicel CHIRALPAK AS-H (4.6 mm × 25 cm). Optical rotations were measured on a RUDOLPH AUTOPOL IV digital polarimeter. GC analysis was performed with Shimadzu 17A instruments using TCI CHIRALDEX γ-TA (0.25 mmI.D. x 20 m x 0.125 μm). Melting points were determined using a Yanaco MP-J3. All experiments were carried out under an atmosphere of dry nitrogen. For thin-layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 GF_{254} 0.25 mm or silica gel NH_2 F_{254S} 0.25 mm) were used. The products were purified by column chromatography on silica gel (E. Merck Art. 9385 or Fuji Silysia Chemical Ltd. Cromatorex® NH-DM1020). Microanalyses were performed at the Graduate School of Agriculture, Nagoya University. High resolution mass spectral analysis (HRMS) was performed at Chemical Instrument Center, Nagoya University. In experiments that required dry solvent, ether, *N*,*N*-dimethylformamide (DMF) and tetrahydorofuran (THF) were purchased from Aldrich or Wako as the "anhydrous" and stored over 4A molecular sieves. Benzene, hexane, toluene, and dichloromethane were freshly distilled from calcium hydride. Other simple chemicals were analytical-grade and obtained commercially.

General Procedure for the Preparation of *N*(π)-Methyl-*N*(α)-(arenesulfonyl)-L-hisitidinol

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(1, X=OH). To a solution of *N*(π)-methyl-L-hisitidinol (**3**)[1] (621 mg, 4.0 mmol) in pyridine (20 mL) was added the corresponding arenesulfonyl chloride (5.5 mmol) at 0 °C. After the mixture was stirred for 5 h at room temperature, the solvent was removed under reduced pressure. The crude product was dissolved in EtOAc, and washed with water and brine. The organic layer was dried over Na_2SO_4, filtrated, and concentrated under reduced pressure. The reside was purified by flah column chromatography on Cromatorex® NH-DM1020 (eluent: EtOAc) to give *N*(π)-methyl-*N*(α)-(arenesulfonyl)-L-hisitidinol (**1**, X=OH) in good yield.

***N*(π)-Methyl-*N*(α)-(benzenesulfonyl)-L-hisitidinol (1, Ar=C_6H_5, X=OH):** TLC (silica gel NH_2 F_{254S}, EtOAc:MeOH=11:1) R_f=0.25; Purification by column chromatography on Cromatorex® NH-DM1020 (EtOAc:MeOH=10:1); $[\alpha]_D^{20}$ = 6.0 (*c* = 1.06, $CHCl_3$); IR (KBr) 3600–3250, 2924, 1636, 1510, 1447, 1324, 1158, 1093, 690, 592 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.75 (dd, *J* = 6.0, 15.3 Hz, 1H), 2.88 (dd, *J* = 7.5, 15.3 Hz, 1H), 3.32–3.38 (m, 1H), 3.39 (s, 3H), 3.49 (d, *J* = 4.2 Hz, 2H), 4.48–4.95 (br, 1H), 6.61 (s, 1H), 7.26 (s, 1H), 7.42 (t, *J* = 7.4 Hz, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.77 (d, *J* = 7.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.9, 31.4, 54.3, 62.3, 126.7 (2C), 127.4, 127.9, 129.0 (2C), 132.4, 137.8, 140.5. Anal. Calcd for $C_{13}H_{17}N_3O_3S$: C, 52.86; H, 5.80. Found: C, 52.81; H, 5.82.

***N*(π)-Methyl-*N*(α)-(4-trifluoromethylbenzenesulfonyl)-L-hisitidinol (1, Ar=4-$CF_3C_6H_2$, X=OH):** ^1H NMR ($CDCl_3$, 300 MHz) δ 2.84 (dd, *J* = 6.0, 15.3 Hz, 1H), 2.92 (dd, *J* = 7.1, 15.5 Hz, 1H), 3.41 (m, 1H), 3.49 (s, 3H), 3.54 (d, *J* = 4.2 Hz, 2H), 6.02 (br, 1H), 6.60 (s, 1H), 7.28 (s, 1H), 7.67 (d, *J* = 8.1 Hz, 2H), 7.93 (d, *J* = 8.4 Hz, 2H). Anal. Calcd for $C_{14}H_{16}F_3N_3O_3S$: C, 46.28; H, 4.44. Found:. C, 46.33; H, 4.41.

***N*(π)-Methyl-*N*(α)-(2,4,6-triisopropylbenzenesulfonyl)-L-hisitidinol (1, Ar=2,4,6-*i*-$Pr_3C_6H_2$, X=OH):** white solid (838 mg, 2.0 mmol, 50% yield); $[\alpha]_D^{20}$ = 20.4 (*c* = 1.0 in $CHCl_3$); IR (KBr) 3486, 3114, 3053, 2958, 2928, 2869, 1601, 1461, 1316, 1294, 1146, 1113, 1059, 1041, 664, 561 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.248 (d, *J* = 6.9 Hz, 12H), 1.255 (d, *J* = 6.9 Hz, 6H), 2.75–3.02 (m, 3H), 3.42–3.52 (m, 3H), 3.53 (s, 3H), 4.13 (septet, *J* = 6.9 Hz, 2H), 5.72 (d, *J* = 6.6 Hz, 1H), 6.58 (s, 1H), 7.16 (s, 2H), 7.27 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.6, 24.9, 25.0, 26.2, 29.8, 31.5, 34.1, 53.7, 61.4, 123.8, 127.5, 128.1, 133.3, 137.7, 150.1, 152.8; MS (FAB+) $[M+H]^+$ *m/z* 422. Anal. Calcd for $C_{22}H_{35}N_3O_3S$: C, 62.67; H, 8.37; N. Found: C, 62.61; H, 8.39.

Procedure for the Preparation of *N*(π)-Methyl-*N*(α)-benzoyl-L-hisitidinol (5, Ar=Ph, X=OH). To a solution of **3** (621 mg, 4 mmol) in pyridine (20 mL) was added benzoyl chloride (0.638 mL, 5.5 mmol) at 0 °C. After the mixture was stirred for 5 h at room temperature, the solvent was removed under reduced pressure. The crude product was dissolved in EtOAc, and washed with water and brine. The organic phase was dried over Na_2SO_4, filtrated, and

concentrated under reduced pressure. The reside was purified by flash column chromatography on NH silica gel (eluent: EtOAc) to give **5** in good yield. TLC (silica gel NH_2 F_{254S}, EtOAc–MeOH=10:1) R_f=0.21; $[\alpha]_D^{20}$ = –28.2 (*c* = 1.0 in $CHCl_3$); IR (neat) 3500–3300 (br), 2923, 2852, 1638, 1542 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.99 (s, 1H), 3.01 (d, *J* = 3.0 Hz, 1H), 3.72 (s, 3H), 3.77 (d, *J* = 1.5 Hz, 1H), 3.78 (d, *J* = 1.2 Hz, 1H), 4.23 (m, 1H), 6.77 (d, *J* = 7.8 Hz, 1H), 6.83 (s, 1H), 7.43 (m, 3H), 7.52 (m, 1H), 7.74 (m, 1H); ^{13}C NMR ($CDCl_3$) 25.0, 31.6, 50.8, 61.5, 126.9, 127.5, 128.5 (2C), 128.7, 131.6, 134.1, 137.8, 167.7. Anal. Calcd for $C_{14}H_{17}N_3O_2$: C, 64.85; H, 6.61. Found: C, 64.90; H, 6.59.

General Procedure for the Preparation of (*S*)-1-*tert*-Butyldiphenylsilyloxy-3-(3'-methyl-3'*H*-imidazol-4'-yl)-2-(arenesulfonylamino)propane (1, X=*t*-BuPh$_2$Si): To a solution of *N*(π)-methyl-*N*(α)-(arenesulfonyl)-L-hisitidinol (**1**, X=OH) (0.95 mmol) in DMF (5 mL) was added *tert*-butylchlorodiphenylsilane (304 μL, 1.17 mmol) and imidazole (163 mg, 2.4 mmol) at 0 °C. After the mixture was stirred for 6 h at room temperature, the solvent was removed under reduced pressure to give the crude product. The residue was purified by flash column chromatography on NH silica gel (eluent: hexane–EtOAc=1:1) to give **1** (X=*t*-BuPh$_2$Si).

(*S*)-1-*tert*-Butyldiphenylsilyloxy-3-(3'-methyl-3'*H*-imidazol-4'-yl)-2-(benzenesulfonylamino)propane (1a): TLC (silica gel NH_2 F_{254S}, hexane:EtOAc=1:2) R_f=0.15; Purification by column chromatography on Cromatorex® NH-DM1020 (hexane:EtOAc=1:2~1:4); $[\alpha]^{20}_D$=2.34 (*c*=0.51, $CHCl_3$); IR (KBr) 3069, 2930, 2857, 1509, 1428, 1324, 1158, 1113, 1070, 823, 706, 588 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.04 (s, 9H), 2.84 (dd, *J*=5.4, 15.0 Hz, 1H), 2.96 (dd, *J*=7.8, 15.0 Hz, 1H), 3.28–3.37 (m, 1H), 3.41 (s, 3H), 3.44 (dd, *J*=4.8, 10.5 Hz, 1H), 3.59 (dd, *J*=3.9, 10.5 Hz, 1H), 5.42 (br, 1H), 6.54 (s, 1H), 7.25 (s, 1H), 7.34–7.58 (m, 13H), 7.66 (d, *J*=8.1 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) 19.2, 26.4, 26.9 (3C), 31.3, 53.8, 63.7, 126.7 (2C), 127.0, 127.9 (4C), 128.0, 129.0 (2C), 130.0 (2C), 132.5 (2C), 135.4 (4C), 138.0 (2C), 140.1. Anal. Calcd for $C_{29}H_{35}N_3O_3SSi$: C, 65.26; H, 6.61. Found: C, 65.18; H, 6.66.

(*S*)-(+)-1-*tert*-Butyldiphenylsilyloxy-3-(3'-methyl-3'*H*-imidazol-4'-yl)-2-(4''-trifluoromethylbenzenesulfonylamino)propane (1b): TLC (silica gel NH_2 F_{254S}, hexane:EtOAc=1:2) R_f=0.26; Purification by column chromatography on silica gel Cromatorex® NH-DM1020 (hexane:EtOAc=1:2~1:4) and recrystallization ($CHCl_3$–hexane); $[\alpha]^{20}_D$ = 1.72 (*c* 0.93, $CHCl_3$); ^1H NMR (300 Hz, $CDCl_3$) δ 1.02 (s, 9H), 2.88 (dd, *J* = 6.0, 15.3 Hz, 1H), 2.98 (dd, *J* = 6.6, 15.3 Hz, 1H), 3.32–3.42 (m, 1H), 3.44 (s, 3H), 3.47 (dd, *J* = 6.0, 10.3 Hz, 1H), 3.57 (dd, *J* = 4.2, 10.3 Hz, 1H), 5.55 (br, 1H), 6.57 (s, 1H), 7.21 (s, 1H), 7.33–7.39 (m, 4H), 7.41–7.48 (m, 2H), 7.50–7.56 (m, 4H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.73 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.2, 26.2, 26.8 (3C), 31.3, 54.1, 63.9, 123.1 (q, *J* = 273 Hz), 126.1 (q, J=3.7 Hz, 2C), 126.9, 127.1 (2C), 127.9 (4C), 128.1, 130.1 (2C), 132.46, 132.53, 133.9 (q, *J* = 33.0 Hz), 135.4 (4C), 134.0,

144.1. Anal. Calcd for $C_{30}H_{34}F_3N_3O_3SSi$: C, 59.88; H, 5.69. Found: C, 59.83; H, 5.73.

(*S*)-1-*tert*-Butyldiphenylsilyloxy-3-(3'-methyl-3'*H*-imidazol-4'-yl)-2-(2'',4'',6''-triisopropylbenzenesulfonylamino)propane (1d): white solid (615 mg, 0.93 mmol, 98% yield): $[\alpha]_D^{20}$ = 4.8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.05 (s, 9H), 1.20 (d, *J* = 6.9 Hz, 6H), 1.23 (d, *J* = 6.9 Hz, 6H), 1.25 (d, *J* = 6.9 Hz, 6H), 2.80–3.02 (m, 3H), 3.43 (s, 3H), 3.61 (brs 3H), 4.10 (septet, *J* = 6.9 Hz, 2H), 4.95–5.15 (br, 1H), 6.48 (s, 1H), 7.08 (s, 2H), 7.26–7.44 (m, 8H), 7.52–7.68 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.3, 23.6, 24.9, 26.2, 27.0, 29.8, 31.3, 34.2, 53.3, 63.6, 123.8, 127.3, 127.9, 128.0, 130.0, 130.1, 132.5, 132.6, 133.4, 135.47, 135.50, 138.0, 150.1, 152.9; IR (KBr) 4325, 3072, 3053, 2959, 2928, 2859, 2739, 1601, 1511, 1463, 1427, 1322, 1152, 1113, 1072, 741, 703, 661, 560 506 cm^{-1}; MS (FAB+) $[M+H]^+$ *m/z* 660. Anal. Calcd for $C_{38}H_{53}N_3O_3SSi$: C, 69.15; H, 8.09. Found: C, 69.19; H, 8.03.

General Procedure for the Preparation of (*S*)-3-(3'-Methyl-3'*H*-imidazol-4'-yl)-2-(arenesulfonylamino)propyl Isobutyrate (1, X=OCO*i*-Pr). To a solution of *N*(π)-methyl-*N*(α)-(arenesulfonyl)-L-hisitidinol (**1**, X=OH) (1 mmol) in $CHCl_3$ (10 mL) was added isobutyryl chloride (105 μL, 1 mmol) and Et_3N (101 μL, 1 mmol) at 0 °C. After the mixture was stirred for 6 h at room temperature, the solvent was removed under reduced pressure. The reside was purified by flah column chromatography on NH silica gel (eluents: EtOAc–MeOH) to give **1** (X=OCO*i*-Pr).

(*S*)-3-(3'-Methyl-3'*H*-imidazol-4'-yl)-2-(2'',4'',6''-triisopropylbenzenesulfonylamino)propyl Isobutyrate (1c): white solid (143 mg, 0.29 mmol, 29% yield); TLC (silica gel NH_2 F_{254S}, hexane:EtOAc=1:2) R_f=0.22; $[\alpha]_D^{20}$ = 15.2 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (s, 1H), 7.15 (s, 1H), 6.70 (d, *J* = 8.1 Hz, 1H), 6.45 (s, 1H), 4.17 (m, 2H), 4.05 (dd, *J* = 4.7, 11.3 Hz, 1H), 3.95 (dd, *J* = 6.5, 11.3 Hz, 1H), 5.79 (m, 1H), 3.65 (s, 3H), 3.01 (dd, *J* = 8.0, 15.5 Hz, 1H), 2.90 (m, 2H), 2.15 (m, 1H), 1.24 (m, 18H), 1.04 (d, *J* = 7.2 Hz, 3H), 0.99 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.76, 18.83, 23.6, 24.8, 25.0, 27.2, 29.7, 31.7, 33.5, 34.1, 51.5, 64.2, 123.8, 126.6, 128.0, 134.0, 137.9, 149.8, 152.6, 176.7; IR (KBr) 3436, 2961, 2929, 2871, 1735, 1601, 1466, 1321, 1194, 1151, 1113, 663, 570 cm^{-1}; MS (FAB+) $[M+H]^+$ *m/z* 492. Anal. Calcd for $C_{26}H_{41}N_3O_4S$: C, 63.51; H, 8.40. Found: 63.55; H, 8.34.

(*S*)-2-[*N*-Isobutyryl(2',4',6'-triisopropylbenzenesulfonyl)amino]-3-(3"-methyl-3"*H*-imidazol-4"-yl)propyl Isobutyrate (4): white solid (185 mg, 0.33 mmol, 33% yield); TLC (silica gel NH_2 F_{254S}, hexane:EtOAc=1:2) R_f=0.37; $[\alpha]_D^{20}$ = –3.9 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (s 1H), 7.23 (s, 2H), 6.59 (s, 1H), 4.32 (m, 3H), 3.95 (m 2H), 3.48 (s, 3H), 3.44 (m, 2H), 2.92 (m, 1H), 2.71 (dd, *J* = 3.6, 15.6 Hz, 1H), 2.38 (m, 1H), 1.26 (m, 18H), 1.12 (d, *J* = 6.6 Hz, 3H), 1.06 (d, *J* = 1.5 Hz, 3H), 1.04 (dd, *J* = 1.5, 6.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.6, 18.8, 19.1, 19.6, 23.5, 24.6, 24.7, 25.9, 29.4, 31.2, 33.7, 34.2, 35.7, 57.7, 64.1, 124.4, 127.7, 128.1,

131.6, 137.9, 151.1, 154.9, 176.3, 179.3; IR (KBr) 3439, 2964, 2934, 2873, 1742, 1689, 1601, 1466, 1386, 1367, 1336, 1204, 1145 952, 664, 588, 564 cm^{-1}; MS (FAB+) $[M+H]^+$ *m/z* 562. Anal. Calcd for $C_{30}H_{47}N_3O_5S$: C, 64.14; H, 8.43. Found; C, 64.23; H, 8.51.

(*S*)-(+)-1-*tert*-Butyldiphenylsilyloxy-3-(3'-methyl-3'*H*-imidazol-4'-yl)-2-benzoylaminopropane (5): TLC (silica gel NH_2 F_{254S}, hexane:EtOAc=1:2) R_f=0.17; Purification by column chromatography on silica gel Cromatorex® NH-DM1020 (hexane:EtOAc=1:2~1:4); $[\alpha]^{20}_D$ = 15.5 (*c* 0.62, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.13 (s, 9H), 2.93 (dd, *J* = 5.0, 15.0 Hz, 1H), 3.05 (dd, *J* = 9.0, 15.0 Hz, 1H), 3.70 (s, 3H), 3.77 (dd, *J* = 3.6, 10.4 Hz, 1H), 3.86 (dd, *J* = 2.7, 10.4 Hz, 1H), 4.20 (m, 1H), 6.64 (br, 1H), 6.66 (s, 1H), 7.42 (m, 10 H), 7.64 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.3, 25.5, 26.9 (3C), 31.4, 50.0, 63.2, 126.7 (2C), 127.87, 127.94 (4C), 128.1, 128.6 (2C), 130.0, 130.1, 131.6, 132.6, 132.9, 134.1, 135.46 (2C), 135.53 (2C), 138.1, 166.9. Anal. Calcd for $C_{30}H_{35}N_3O_2Si$: C, 72.40; H, 7.09. Found: C, 72.48; H, 7.06.

General Procedure for the Preparation of 1-(*N*-Pyrrolidine-1'-carbonyloxy)-2-alcohols (6c, 8, 10, 12, 14) Derived from *meso*-1,2-Diols: The treatment of *meso*-1,2-diols (20 mmol) with bis(trichloromethyl)carbonate (triphosgene) (20 mmol) in dichloromethane (100 mL) in the presence of pyridine (10 mL) at room temperature were converted to the corresponding cyclic carbonates in quantitative yield.[2] Subsequent aminolysis of cyclic carbonates (20 mmol) with pyrrolidine (10 mL) in THF (40 mL) under reflux conditions afforded 1-(*N*-pyrrolidine-1'-carbonyloxy)-2-alcohols **(6c, 8, 10, 12, 14)** in quantitative yield.

General Procedure for the Kinetic Resolution of Racemic Alcohols with Isobutyric Anhydride Induced by Nucleophilic Catalysts. To a solution of racemic alcohol (0.25 mmol) and catalyst (0.0125 mmol) in toluene (2.5 mL) was added *i*-Pr_2NEt (21.8 μL, 0.125 mmol) and isobutyric anhydride (20.7 μL, 0.125 mL). After being stirred for 3 h at room temperature or 0 °C (for each reaction temperature, see Tables 2–4), the reaction mixture was treated with 0.1 M HCl aqueous solution and extracted with EtOAc. The organic layer was washed with saturated aqueous $NaHCO_3$, dried over $NaSO_4$, and concentrated under reduced pressure. Ee values of the recovered alcohol and the acylated product were determined by HPLC analysis of crude products. The conversion (*c*) was estimated by the following equation, *c* (%) = [ee (recovered alcohol)]/[ee (recovered alcohol) + ee (acylated product)].[3] The *S* (k_{fast}/k_{slow}) value was estimated by the following equation, $S = \ln[(1-c)(1-ee_{alcohol})]/\ln[(1-c)(1+ee_{alcohol})]$.[3]

***cis*-1-[*p*-(Dimethylamino)benzoyloxy]-2-cyclohexanol (6a):[4]** TLC (hexane–EtOAc=2:1) R_f=0.11; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34–1.52 (m, 2H), 1.60–1.78 (m, 4H), 1.84 (q, *J* = 8.6 Hz, 1H), 1.99 (q, *J* = 9.8 Hz, 1H), 2.17 (d, *J* = 4.2 Hz, 1H), 3.05 (s, 6H), 3.91–3.98 (m, 1H), 5.15–5.19 (m, 1H), 6.52 (d, *J* = 9.1 Hz, 2H), 7.93 (d, *J* = 9.1 Hz, 2H); HPLC (Daicel Chiralpak OD-H,

hexane:2-propanol = 20:1, flow rate 1.0 mL/min) t_R= 26.9 ((1*R*,2*S*), minor) and 55.5 ((1*S*, 2*R*), major) min.

***cis*-1-[*p*-(Dimethylamino)benzoyloxy]-2-cyclohexyl Isobutyrate (7a):**[4] TLC (hexane–EtOAc=2:1) R_f=0.60; $[\alpha]^{20}_D$ = –48.0 (*c* 1.0, $CHCl_3$) for **7a** of 84% ee; HPLC (Daicel Chiralcel OD-H, hexane:2-propanol = 20:1, flow rate 1.0 mL/min) t_R= 9.4 ((1*R*,2*S*), minor) and 12.1 ((1*S*,2*R*), major) min; IR (film) 3019, 2943, 1725, 1697, 1608, 1526, 1368, 1281, 1216, 1184, 1109, 760, 668 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.15 (q, *J*=3.6 Hz, 6H), 1.42–15.6 (m, 2H), 1.63–1.81 (m, 4H), 1.87–2.02 (m, 2H), 2.54 (septet, *J*=6.9 Hz, 1H), 3.04 (s, 6H), 5.07–5.13 (m, 1H), 5.19–5.26 (m, 1H), 6.64 (d, *J*=6.9 Hz, 2H), 7.90 (d, *J*=8.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.9, 19.0, 27.79 (2C), 27.83, 27.9, 34.2, 40.0 (2C), 70.7, 71.0, 110.6 (2C), 117.2, 131.2 (2C), 153.2, 160.0, 176.3.

***cis*-1-Dimethylcarbamoyloxy-2-cyclohexanol (6b):** TLC (hexane–EtOAc = 2:1) R_f = 0.11; GC (CHIRALDEX γ-TA (20 m), inj. temp. 140 °C, col. temp. 110 °C, N_2 (80 Pa)) t_R = 29.4 ((1*S*,2*R*)-**6b**, minor), 31.6 ((1*R*,2*S*)-**6b**, major) min; ^1H NMR (300 MHz, $CDCl_3$) δ 1.25–1.50 (m, 2H), 1.50–1.64 (m, 2H), 1.64–1.80 (m, 3H), 1.80–1.90 (m, 1H), 2.66 (s, 1H), 2.94 (s, 3H), 2.95 (s, 3H), 3.83 (br, 1H), 4.89–4.95 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.4, 22.0, 28.1, 29.9, 35.9, 36.4, 70.2, 74.6, 156.8. Anal. Calcd for $C_9H_{17}NO_3$: C, 57.73; H, 9.15. Found: C, 57.78; H, 9.22.

***cis*-1-Dimethylcarbamoyloxy-2-cyclohexyl Isobutyrate (7b):** HPLC (Daicel Chiralpack AD-H, hexane:2-propanol = 40:1, flow rate 0.25 mL/min) t_R = 57.8 ((1*S*,2*R*)-**7b**, major), 61.0 ((1*R*,2*S*)-**7b**, minor) min. Anal. Calcd for $C_{13}H_{23}NO_4$: C, 60.68; H, 9.01. Found: C, 60.59; H, 9.14.

***cis*-*N*-(2-Hydroxycyclohexanoxycarbonyl)pyrrolidine (6c):** TLC (hexane–EtOAc = 2:1) R_f=0.17; $[\alpha]^{20}_D$ = –2.7 (*c* 1.0, $CHCl_3$) for 97% ee; HPLC (Daicel Chiralpack AS-H, hexane:2-propanol = 20:1, flow rate = 1.0 mL/min) t_R = 24.7 ((1*S*,2*R*)-**6c** , minor), 30.1 ((1*R*,2*S*)-**6c** , major) min; IR (film) 3500–3350 (br), 2938, 2871, 1680, 1429, 1360, 1181, 1129, 1109, 984, 768 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.24–2.15 (m, 12H), 2.78 (s, 1H), 3.40 (t, *J*=6.6 Hz, 4H), 3.83 (br, 1H), 4.92 (dt, *J*=2.4, 6.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.3, 22.0, 24.9, 25.6, 28.2, 29.8, 45.8, 46.1, 70.1, 74.1, 155.1. Anal. Calcd for $C_{11}H_{19}NO_3$: C, 61.95; H, 8.98. Found: C, 61.91; H, 9.01.

***cis*-*N*-(2-Isobutyryloxycyclohexanoxycarbonyl)pyrrolidine (7c):** TLC (hexane–EtOAc = 2:1) R_f = 0.27; $[\alpha]^{20}_D$ = –19.5 (*c* 1.0, $CHCl_3$) for 72% ee; HPLC (Daicel Chiralpack AS-H, hexane:2-propanol = 20:1, flow rate = 0.5 mL/min) t_R = 13.5 ((1*R*,2*S*)-**7c**, minor), 14.5 ((1*S*,2*R*)-**7c**, major) min; IR ($CHCl_3$) 2876, 2943, 2875, 1728, 1694, 1425, 1372, 1196, 1128, 1105, 756 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.16 (d, *J*=3.3 Hz, 3H), 1.19 (d, *J*=3.3 Hz, 3H), 1.36–1.52 (m, 2H), 1.52–1.75 (m, 4H), 1.75–1.94 (m, 6H), 2.56 (septet, *J*=6.9 Hz, 1H), 3.31 (t, *J*=6.3 Hz, 2H), 3.38 (t, *J*=6.0 Hz, 2H), 4.86–4.93 (m, 1H), 5.04 –5.10 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.9, 19.0, 21.2, 22.2, 24.9, 25.6, 27.8, 28.1, 34.2, 45.6, 46.0, 70.8, 71.7, 154.3, 176.1. Anal. Calcd for $C_{15}H_{25}NO_4$: C,

63.58; H, 8.89. Found: C, 63.46; H, 8.97.

***cis*-1-(*N*-Pyrrolidine-1'-carbonyloxy)-2-cyclopentanol (8):**[4] TLC (hexane–EtOAc = 2:1) R_f = 0.09; $[\alpha]^{20}_D$ = –7.9 (*c* 1.0, $CHCl_3$) for 90% ee; HPLC (Daicel Chiralpak AD-H, hexane:2-propanol = 20:1, flow rate 1.0 mL/min, t_R= 16.8 (major) and 24.8 (minor) min; IR (KBr) 3450–3350, 2980, 2951, 2874, 1661, 1443, 1360, 1173, 1115, 1037, 860, 769, 606, 504 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.49–1.61 (m, 1H), 1.61–1.77 (m, 1H), 1.77–2.02 (m, 8H), 2.54 (d, *J* =3.3 Hz, 1H), 3.34–3.43 (m, 4H), 4.13–4.21 (m, 1H), 4.93 (dt, *J* = 4.7, 6.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.4, 24.9, 25.7, 28.5, 30.5, 45.8, 46.2, 73.7, 77.4, 155.1.

***cis*-1-(*N*-Pyrrolidine-1'-carbonyloxy)-2-cyclopentyl Isobutyrate:**[4] TLC (hexane–EtOAc = 2:1) R_f = 0.28; $[\alpha]^{20}_D$ = –32.4 (*c* 1.0, $CHCl_3$) for 94% ee; HPLC (Daicel Chiralpak AS-H, hexane:2-propanol = 20:1, flow rate 1.0 mL/min, t_R= 8.6 (major) and 10.2 (minor) min; IR (KBr) 2973, 2876, 1736, 1708, 1419, 1345, 1198, 1155, 1128, 1109, 767 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.15 (d, *J* = 1.8 Hz, 3H), 1.17 (d, *J* = 1.8 Hz, 3H), 1.56–1.72 (m, 1H), 1.72–1.80 (m, 1H), 1.80–1.92 (m, 6H), 1.92–2.06 (m, 2H), 2.53 (septet, *J* = 6.9 Hz, 1H), 3.31 (t, *J* = 6.3 Hz, 2H), 3.37 (t, *J* = 6.3 Hz, 2H), 5.08 (dt, *J* = 4.2, 6.0 Hz, 1H), 5.15 (dt, *J* = 4.2, 5.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.8, 18.9, 19.2, 24.9, 25.7, 28.3, 28.4, 34.1, 45.7, 46.1, 74.3, 74.8, 154.4, 176.2.

***cis*-1-(*N*-Pyrrolidine-1'-carbonyloxy)-2-cycloheptanol (9):**[4] TLC (hexane–EtOAc = 2:1), R_f = 0.09; $[\alpha]^{20}_D$ = –8.8 (*c* 1.0, $CHCl_3$) for 93% ee; HPLC (two linear Daicel Chiralcel OD-H columns, hexane:2-propanol = 20:1, flow rate 1.0 mL/min) t_R= 37.0 (major) and 39.6 (minor) min; IR (film) 3500–3400 (br), 2933, 2871, 1678, 1429, 1180, 1129, 1106, 769 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.40–1.62 (m, 4H), 1.62–1.84 (m, 6H), 1.84–2.00 (m, 4H), 3.09 (s, 1H), 3.40 (t, *J* = 6.6 Hz, 4H), 3.88–3.96 (m, 1H), 4.97 (dt, *J* = 2.4, 7.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) 22.5, 22.8, 24.9, 25.7, 26.9, 28.9, 31.4, 73.5, 78.5, 155.4.

***cis*-1-(*N*-Pyrrolidine-1'-carbonyloxy)-2-cycloheptyl Isobutyrate:**[4] TLC (hexane–EtOAc = 2:1), R_f = 0.36; $[\alpha]^{20}_D$ = –17.9 (*c* 1.0, $CHCl_3$) for 92% ee; HPLC (two linear Daicel Chiralcel OD-H columns, hexane:2-propanol = 20:1, flow rate 1.0 mL/min) t_R= 15.4 (minor) and 16.3 (major) min; IR (film) 2936, 2872, 1733, 1703, 1419, 1195, 1157, 1100, 768 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.17 (d, *J* = 7.0 Hz, 3H), 1.18 (d, *J* = 7.0 Hz, 3H), 1.47–1.81 (m, 8H), 1.81–2.01 (m, 6H), 2.58 (septet, *J* = 7.0 Hz, 1H), 3.26–3.43 (m, 4H), 4.94–5.01 (m, 1H), 5.10–5.16 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) 18.9, 19.0, 22.5, 22.7, 24.9, 25.7, 26.6, 28.8, 29.1, 34.2, 45.6, 46.0, 74.5, 75.2, 154.4, 176.2.

(2*RS*,3*SR*)-2-(*N*-Pyrrolidine-1'-carbonyloxy)-3-butanol (10):[5] TLC (hexane–EtOAc=2:1) R_f = 0.10; $[\alpha]^{20}_D$ = –2.3 (*c* 1.0, $CHCl_3$) for 82% ee; HPLC (Daicel Chiralpak AD-H, hexane:2-propanol = 20:1, flow rate 1.0 mL/min, t_R= 15.9 (major) and 20.8 (minor) min; IR (film) 3500–3350 (br), 2977, 2877, 1679, 1426, 1130, 1106, 769 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.16 (d, *J* = 6.3 Hz, 3H), 1.22 (d, *J* = 6.6 Hz, 3H), 1.82–1.95 (m, 4H), 2.81 (s, 1H), 3.33–3.43 (m, 4H), 3.83–3.93

(m, 1H), 4.84 (dq, *J* = 2.7, 12.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.3, 17.2, 24.9, 25.6, 45.8, 46.2, 70.0, 75.1, 155.2.

(2*RS*,3*SR*)-2-(*N*-Pyrrolidine-1'-carbonyloxy)-3-butyl Isobutyrate:[5] TLC (hexane–EtOAc = 2:1) R_f = 0.33; $[\alpha]^{20}_D$ = –25.2 (*c* 1.0, $CHCl_3$) for 93% ee; HPLC (Daicel Chiralpak AD-H, hexane:2-propanol = 20:1, flow rate 1.0 mL/min, t_R= 7.1 (major) and 8.4 (minor) min; IR (film) 2978, 2877, 1734, 1705, 1416, 1196, 1160, 1103, 768 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.16 (d, *J* = 7.2 Hz, 3H), 1.17 (d, *J* = 6.8 Hz, 3H), 1.21 (d, *J* = 6.3 Hz, 3H), 1.24 (d, *J* = 6.8 Hz, 3H), 1.82–1.92 (m, 4H), 2.54 (septet, *J* = 7.0 Hz, 1H), 3.30 (t, *J* = 6.3 Hz, 2H), 3.38 (t, *J* = 6.3 Hz, 2H), 4.88 (dq, *J* = 4.1, 6.5 Hz, 1H), 3.38 (t, *J* = 6.3 Hz, 2H), 4.88 (dq, *J* = 4.1, 6.5 Hz, 1H), 5.03 (dq, *J* = 4.1, 65. Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.3, 15.5, 18.8, 19.0, 24.9, 25.6, 34.1, 45.6, 46.0, 71.3, 72.0, 154.3, 176.3.

***N*-(3-Hydroxy-3-phenylpropionyl)pyrrolidine (11):** TLC (hexane–EtOAc = 2:1) R_f = 0.22; $[\alpha]_D^{20}$ = –51.5 (*c* = 1.0 in $CHCl_3$) for 64% ee; HPLC (Daicel Chiralpak AD-H, hexane:2-propanol = 20:1, flow rate 1.0 mL/min) t_R= 30.2 (minor) and 32.1 (major) min; IR (KBr) 3300–3200 (OH), 1609 (C=O), 1474, 1065, 707 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.80–2.00 (m, 4H), 2.58 (dd, *J* = 8.7, 16.2 Hz, 1H), 2.65 (dd, *J* = 3.6, 16.2 Hz, 1H), 3.31 (t, *J* = 6.6 Hz, 2H), 3.48 (t, *J* = 6.3 Hz, 2H), 4.97 (d, *J* = 3.0 Hz, 1H), 5.16 (dt, *J* = 3.3, 8.7 Hz, 1H), 7.24–7.45 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.3, 25.8, 43.0, 45.5, 46.5, 70.3, 125.6 (2C), 127.4, 128.4 (2C), 143.1, 170.7. Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81. Found: C, 71.19; H, 7.99.

***N*-(3-Isobutyryloxy-3-phenylpropionyl)pyrrolidine:** TLC (hexane–EtOAc = 1:2) R_f = 0.35; $[\alpha]_D^{20}$ = 29.5 (*c* = 1.0 in $CHCl_3$); HPLC (Daicel Chiralpak AD-H, hexane:2-propanol = 20:1, flow rate 1.0 mL/min) t_R= 36.5 (major) and 45.0 (minor) min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.15 (t, *J* = 7.1 Hz, 6 H), 1.76–1.95 (m, 4H), 2.56 (septet, *J* = 7.1 Hz, 1 H), 2.65 (dd, *J* = 5.4, 15.0 Hz, 1H), 2.94 (dd, *J* = 8.3, 15.0 Hz, 1H), 3.22–3.31 (m, 1H), 3.40–3.51 (m, 3H), 6.21 (dd, *J* = 5.4, 8.3 Hz, 1H), 7.24–7.41 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.8 (2C), 24.3 , 26.0, 33.9, 42.0, 45.6, 46.7, 72.6, 126.2 (2C), 127.9, 128.5 (2C), 140.5, 167.6, 175.6. Anal. Calcd for $C_{17}H_{23}NO_3$: C, 70.56; H, 8.01. Found: C, 70.67; H, 7.93.

(2*SR*,3*RS*)-*N*-(3-Hydroxy-2-methyl-3-phenylpropionyl)pyrrolidine (12): TLC (hexane–EtOAc = 1:2) R_f = 0.35; $[\alpha]_D^{20}$ = –80.1 (*c* = 1.0 in $CHCl_3$) for 80% ee; HPLC (Daicel Chiralpak AD-H, hexane:2-propanol = 20:1, flow rate 1.0 mL/min) t_R= 26.6 (major) and 28.4 (minor) min; IR (KBr) 3400–3300 (OH), 2976, 2872, 1613, 1469, 1447, 1047, 756, 702 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (d, *J* = 7.2 Hz, 3H), 1.65–1.87 (m, 4H), 2.86 (dq, *J* = 7.2, 2.1 Hz, 1H), 2.96–3.05 (m, 1H), 3.23–3.32 (m, 1H), 3.34–3.41 (m, 2H), 4.64 (d, *J* = 7.2 Hz, 1H), 4.77 (dd, *J* = 5.1, 6.9 Hz, 1H), 7.21–7.37 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.3, 24.1, 25.8, 44.8, 45.4, 46.5, 76.6, 125.9 (2C), 127.4, 128.2 (2C), 143.3, 174.1. Anal. Calcd for $C_{14}H_{19}NO_2$: C, 72.07; H, 8.21. Found: C, 72.21; H, 8.13.

***N*-(3-Isobutyryloxy-2-methyl-3-phenylpropionyl)pyrrolidine:** TLC (hexane–EtOAc=1:1) R_f = 0.19; $[\alpha]_D^{20}$ = 55.8 (*c* = 1.0 in $CHCl_3$) for 82% ee; HPLC (Daicel Chiralpak AD-H, hexane:2-propanol = 20:1, flow rate 1.0 mL/min) t_R= 27.4 (minor) and 49.7 (major) min; IR (KBr) 2973, 2875, 1731, 1628, 1459, 1438, 1200, 1162, 703 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.91 (d, *J* = 7.2 Hz, 3H), 1.07 (d, *J* = 7.2 Hz, 3H), 1.09 (d, *J* = 7.2 Hz, 3H), 1.82–1.94 (m, 2H), 1.94–2.05 (m, 2H), 2.45 (septet, *J* = 6.9 Hz, 1H), 3.60 (dq, *J* = 3.9, 6.9 Hz, 1H), 3.45–3.56 (m, 3H), 3.68–3.78 (m, 1H), 5.77 (d, *J* =10.2 Hz, 1H), 7.26–7.39 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 18.5, 18.8, 24.4, 26.1, 33.9, 43.6, 45.8, 46.7, 78.4, 127.3 (2C), 128.1, 128.4 (2C), 138.9, 172.1, 174.9. Anal. Calcd for $C_{18}H_{25}NO_3$: C, 71.26; H, 8.31. Found: C, 71.18; H, 8.43.

***cis*-*N*-(2'-Hydroxyindan-1'-yl)pyrrolidine-1-carboxamide (13):[6]** TLC (EtOAc) R_f = 0.40; $[\alpha]^{20}_D$ = –36.6 (*c* 1.0, $CHCl_3$) for 67% ee; HPLC (Daicel Chiralpack AD-H, hexane:2-propanol = 9:1, flow rate = 1.0 mL/min) t_R = 11.9 (major), 15.0 (minor) min; IR (KBr) 3405, 3205, 1618, 1523, 1474, 1404, 1180, 1060, 744 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.90–1.97 (m, 4H), 1.93 (s, 1H), 2.96 (dd, *J* = 3.6, 16.5 Hz, 1H), 3.17 (dd, *J* = 5.6, 16.5 Hz, 1H), 3.34–3.44 (m, 4H), 4.61–4.68 (m, 1H), 4.71 (d, *J* = 7.5 Hz, 1H), 5.29 (dd, *J* = 5.3, 7.4 Hz, 1H), 7.19–7.36 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.5 (2C), 39.1, 45.7 (2C), 58.8, 73.9, 124.7, 125.3, 127.1, 128.3, 140.4, 141.3, 157.2.

***cis*-*N*-(2'-Isobutyryloxyindan-1'-yl)pyrrolidine-1-carboxamide:[6]** TLC (hexane–EtOAc = 1:2) R_f = 0.34; $[\alpha]^{20}_D$ = 63.2 (*c* 1.0, $CHCl_3$) for 84% ee; HPLC (Daicel Chiralpack AD-H, hexane:2-propanol = 9:1, flow rate = 1.0 mL/min) t_R = 16.7 (major), 24.6 (minor) min; IR (KBr) 3550–3300 (br), 1729, 1642, 1622, 1524, 1403, 1189, 1151, 1037 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.03 (d, *J* = 6.0 Hz, 3H), 1.05 (d, *J* = 6.0 Hz, 3H), 1.82–1.90 (m, 4H), 2.40 (septet, *J* = 7.0 Hz, 1H), 2.89 (d, *J* = 17.4 Hz, 1H), 3.16 (dd, *J* = 5.1, 17.4 Hz, 1H), 3.23–3.38 (m, 4H), 4.62 (d, *J* = 9.3 Hz, 1H), 5.48 (dt, *J* = 0.9, 5.6 Hz, 1H), 5.58 (dd, *J* = 5.6, 9.2 Hz, 1H), 7.13–7.21 (m, 3H), 7.25–7.30 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.7, 19.1, 23.5 (2C), 34.0, 37.7, 45.6 (2C), 56.7, 76.0, 123.9, 124.9, 127.1, 127.9, 139.4, 141.9, 156.2, 176.2.

(2*SR*,3*SR*)-2-(*N*-Pyrrolidine-1'-carboxamino)-3-hydroxybutyric Acid Methyl Ester (14): TLC (hexane–EtOAc = 1:5) R_f = 0.17; $[\alpha]^{20}_D$ = –32.0 (*c* 1.0, $CHCl_3$) for 51% ee; HPLC (Daicel Chiralpack AS-H, hexane:2-propanol = 5:1, flow rate = 0.5 mL/min) t_R = 23.5 (major), 27.7 (minor) min; IR (KBr) 3400–3300 (br), 2987, 2956, 2879, 1751, 1616, 1526, 1433, 1191, 1163 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.11 (d, *J* = 6.3 Hz, 3H), 1.91–1.96 (m, 4H), 3.36–3.42 (m, 4H), 3.79 (s, 3H), 4.17–4.27 (m, 1H), 4.40 (d, *J* = 5.4 Hz, 1H), 4.68 (dd, *J* = 3.3, 6.0 Hz, 1H), 5.25 (d, *J* = 5.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.0, 25.5 (2C), 45.7 (2C), 52.6, 59.1, 69.1, 157.0, 171.6. Anal. Calcd for $C_{10}H_{18}N_2O_4$: C, 52.16; H, 7.88. Found: C, 52.11; H, 7.90.

(2*SR*,3*SR*)-2-(*N*-Pyrrolidine-1-carboxamino)-3-isobutyryloxybutyric Acid Methyl Ester: TLC (hexane–EtOAc = 1:2) R_f=0.34; $[\alpha]^{20}_D$ = 1.1 (*c* 1.0, $CHCl_3$) for 80% ee; HPLC (Daicel

Chiralpack AS-H, hexane:2-propanol = 5:1, flow rate = 0.5 mL/min) t_R = 12.6 (major), 15.6 (minor) min; IR (KBr) 3354, 3290, 2979, 2944, 2875, 1739, 1639, 1535, 1416, 1197, 1161 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.14 (d, *J* = 4.8 Hz, 3H), 1.32 (d, *J* = 4.8 Hz, 3H), 1.36 (d, *J* = 6.6 Hz, 3H), 1.89–1.94 (m, 4H), 2.53 (septet, *J* = 7.0 Hz, 1H), 3.33–3.39 (m, 4H), 3.77 (s, 3H), 4.69 (dd, *J*=3.6 , 8.1 Hz, 1H), 5.13 (dq, *J* =3.3, 12.9 Hz, 1H), 5.21 (d, *J* = 8.1 Hz, 1H), 4.69 (dd, *J* = 3.6, 8.1 Hz, 1H), 5.13 (dq, *J* = 3.3, 12.9 Hz, 1H), 5.21 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.2, 18.7, 18.9, 25.5 (2C), 34.0, 45.5 (2C), 52.3, 57.3, 71.4, 155.7, 171.0, 176.9. Anal. Calcd for $C_{14}H_{24}N_2O_5$: C, 55.98; H, 8.05. Found: C, 55.91; H, 8.08.

3-Methyl-2-(*N*-pyrrolidine-1-carboxamino)-1-butanol (15): TLC (EtOAc) R_f = 0.14; $[\alpha]^{20}_D$ = –37.2 (*c* 1.0, $CHCl_3$) for 88% ee; HPLC (Daicel Chiralpack AS-H, hexane:2-propanol = 5:1, flow rate = 0.5 mL/min) t_R = 11.1 (major), 14.5 (minor) min; IR (KBr) 3364, 3292, 2969, 2869, 1608, 1525, 1408, 1335, 1086 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.95 (d, *J* = 5.1 Hz, 3H), 0.97 (d, *J* = 5.1 Hz, 3H), 1.84–1.99 (m. 5H), 3.31–3.39 (m, 4H), 3.55–3.68 (m, 2H), 3.68–3.78 (m, 1H), 3.98 (t, *J* = 4.8 Hz, 1H), 4.39 (d, *J* = 6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.8, 19.6, 25.5 (2C), 29.4, 45.6 (2C), 58.2, 65.4, 157.9. Anal. Calcd for $C_{10}H_{20}N_2O_2$: C, 59.97; H, 10.07. Found: C, 59.89; H, 10.12.

Isobutyryloxy-3-methyl-2-(*N*-pyrrolidine-1-carboxamino)butane: TLC (hexane–EtOAc = 1:5) R_f = 0.33; $[\alpha]^{20}_D$ = 30.6 (*c* 1.0, $CHCl_3$) for 86% ee; HPLC (Daicel Chiralpack AS-H, hexane:2-propanol = 5:1, flow rate = 0.5 mL/min) t_R = 9.0 (minor), 13.0 (major) min; IR (KBr) 3313, 2969, 2872, 1731, 1625, 1533, 1469, 1405, 1195, 1161, 1081 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.96 (d, *J* = 6.6 Hz, 6H), 1.14 (d, *J* = 2.1 Hz, 3H), 1.17 (d, *J* = 2.1 Hz, 3H), 1.84 (septet, *J* = 6.7 Hz, 1H), 1.87–1.94 (m, 4H), 2.56 (septet, *J* = 7.0 Hz, 1H), 3.32 (t, *J* = 6.6 Hz, 4H), 3.90–4.06 (m, 2H), 4.23–4.35 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.6, 18.9, 19.2, 25.5 (2C), 29.9, 34.0, 45.4 (2C), 54.3, 64.7, 156.4, 177.5. Anal. Cald for $C_{14}H_{26}N_2O_3$: C, 62.19; H, 9.69. Found: C, 62.22; H, 9.75.

Procedure for the Preparation of Polystyrene-bound Catalyst 2. (4-Methoxyphenyl)diisopropylsilylpropyl polystyrene (**16**, 1.40 mmol of Si per gram, 50–100 mesh; The polymer matrix is copolystyrene–1% divinylbenzene.)[7,8] that had been dried under vacuum for 12 h was weighed (212 mg, 0.297 mmol) into a flask and swollen in CH_2Cl_2 (2.1 mL, 10 mL of solvent per gram of resin) under N_2 atomosphere for 30 min. The solvent was then drained under positive N_2 pressure, and a 4% trifluoromethanesulfonic acid/CH_2Cl_2 solution (6 equiv of TfOH relative to Si) was added by syringe. The resin turned bright red/orange upon acid treatment and was then gently agitated for 30 min while still under N_2 atmosphere. Once activation was completed, two CH_2Cl_2 washed removed excess acid. Treatment of silyl triflate functionalized resin with 2,6-lutidine (280 μL, 2.40 mmol, 8 equiv relative to Si) for 15 min followed by addition

of an azeotropically dried solution of **1** (Ar=2,4,6-*i*-$Pr_3C_6H_2$, X=OH; 253 mg, 0.600 mmol) in CH_2Cl_2 (1.2 mL) resulted in a colorless resin. The beads are then gently agitated for an additional 10 h under N_2 atmosphere. The beads were drained, exposed to atmosphere, and subjected to the following wash protocol: CH_2Cl_2 (2 × 3 mL × 45 min), THF (2 × 3 mL × 30 min), THF/*i*-Pr_2EtN (3:1, 2 × 3 mL × 30 min), THF/IPA (3:1, 2 × 3 mL × 30 min), THF/H_2O (3:1, 2 × 3 mL × 30 min), and THF/IPA (3:1, 2 × 3 mL × 30 min), DMF (2 x 3 mL x 30 min), THF (2 × 3 mL × 30 min). The resin was air-dried for 3 h and then placed under high vacuum for 24 h to remove trace solvent and H_2O to give **2**. The mass of **2** was 278 mg (0.229 mmol, 0.824 mmol of imidazole moiety per gram), indicating an apparent loading efficiency of 77% based on weight gain.

Procedure for the Kinetic Resolution of (±)-6c Induced by Reusable Catalyst 2. To a suspension of (±)-**6c** (53.3 mg, 0.25 mmol) and **2** (15.2 mg, 0.0125 mmol, 0.824 mmol/g) in CCl_4 (2.5 mL) was added *i*-Pr_2NEt (21.8 μL, 0.125 mmol) and isobutyric anhydride (20.7 μL, 0.125 mmol). After being shaken at 0 °C for 7 h, **2** was recovered by filtration and washing with toluene (3 mL × 2). Thus, **2** was reused more than 6 times without any loss of activity and selectivity. The combined filtrate was concentrated under reduced pressure, and the residue was analyzed without purification. The ee values for the recovered alcohol **6c** and the acylated product **7c** were determined by HPLC analysis: (1*S*,2*R*)-**6c** (major enantiomer), 82–85 % ee and (1*R*,2*S*)-**7c** (major enantiomer), 87–90% ee. The conversion from **6c** to **7c** was determined to be 48–49% by the following equation; conversion (%) = [ee (recovered alcohol)]/[ee (recovered alcohol) + ee (acylated product)].[3]

Computational Methods

Theoretical calculations were performed using the Gaussian 98 program.[10] Gradient-corrected density functional theory (DFT) with Becke's three-parameter exchange with the Lee, Yang and Parr correlation functional (B3LYP),[10] were carried out using the 6-311++G(d,p) basis set. After satisfactory optimization, the vibrational spectrum of each species was calculated.

The Conformers of 3-Acetyl-1,5-dimethylimidazolium Cation

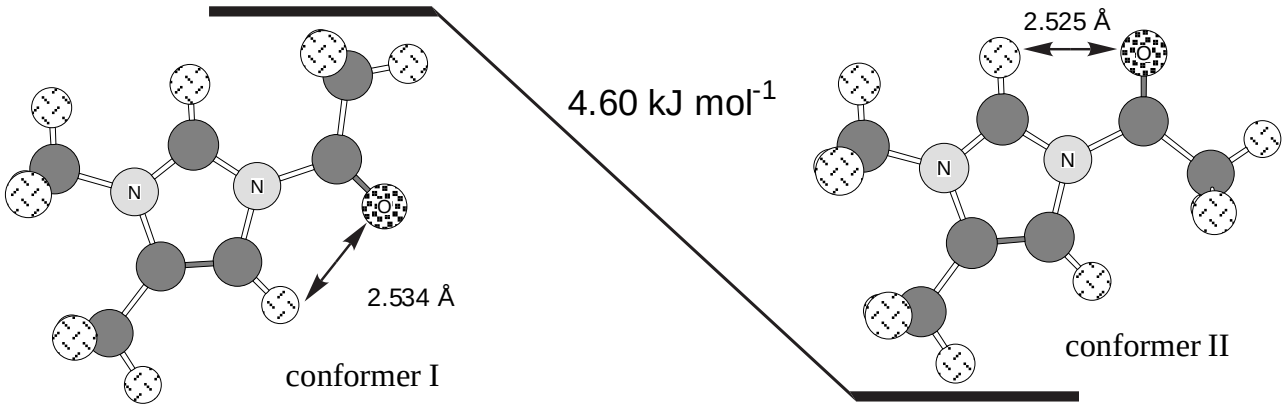

Chart 1.

As shown above, the energy differences between two optimized conformers of 3-acetyl-1,5-dimethylimidazolium cation were calculated at the B3LYP/6-311++G(d,p) level. The calculations show that the attractive interaction between an acyl oxygen and an imidazoyl proton in conformer II is stronger than that in conformer I.

Full Molecules

DMAP

B3LYP/6-311++G(d,p)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	0.179133	-0.000011	-0.049187
2	7	0	1.554736	-0.000004	-0.108986
3	6	0	-0.571897	1.195864	-0.019946
4	6	0	2.284689	1.249997	0.041342
5	6	0	2.284728	-1.249983	0.041337
6	6	0	-0.571913	-1.195880	-0.019942
7	6	0	-1.958056	1.131369	0.012683
8	6	0	-1.958071	-1.131367	0.012684
9	7	0	-2.671936	0.000006	0.027327
10	1	0	-0.093789	2.165334	-0.021143
11	1	0	3.347677	1.059383	-0.099546
12	1	0	2.143995	1.703243	1.032449
13	1	0	1.976366	1.977225	-0.714769

14	1	0	3.347712	-1.059329	-0.099526
15	1	0	1.976451	-1.977211	-0.714792
16	1	0	2.144031	-1.703249	1.032434
17	1	0	-0.093820	-2.165356	-0.021131
18	1	0	-2.529941	2.055731	0.031901
19	1	0	-2.529968	-2.055721	0.031910

E(B3LYP)= -382.3601616

Dipole moment (Debye): X= 4.8342 Y= 0.0000 Z= 0.1015

Tot= 4.8352

1,5-Me_2-IMD

B3LYP/6-311++G(d,p)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	1.236072	0.896166	0.000037
2	7	0	-0.116205	0.676185	-0.000289
3	7	0	1.920180	-0.222594	-0.000543
4	6	0	-0.297102	-0.698820	0.000058
5	6	0	-1.155773	1.690398	0.000189
6	6	0	0.974292	-1.221118	0.000205
7	6	0	-1.639907	-1.348816	0.000207
8	1	0	1.649941	1.894066	-0.000125
9	1	0	-1.787836	1.604638	-0.887232
10	1	0	-0.686145	2.673846	-0.002958
11	1	0	-1.783715	1.608246	0.890907
12	1	0	1.254033	-2.263958	0.000319
13	1	0	-1.518142	-2.432937	0.000462
14	1	0	-2.230733	-1.082735	0.883833
15	1	0	-2.230716	-1.083162	-0.883563

E(B3LYP)= -304.9316185

Dipole moment (Debye): X= -4.1501 Y= 1.6432 Z= 0.0012

Tot= 4.4635

1-Me-IMD

B3LYP/6-311++G(d,p)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-0.198976	-1.085408	0.000186
2	7	0	0.609891	0.016246	-0.000009
3	7	0	-1.473865	-0.767781	-0.000197
4	6	0	-0.227521	1.113342	-0.000179
5	6	0	2.063356	0.031762	0.000013
6	6	0	-1.502442	0.606560	0.000182
7	1	0	0.203649	-2.087586	0.000246
8	1	0	0.153600	2.121246	-0.000330
9	1	0	2.445375	0.536900	-0.889970
10	1	0	2.426754	-0.995600	-0.000053
11	1	0	2.445347	0.536780	0.890077
12	1	0	-2.433408	1.151474	0.000264

E(B3LYP)= -265.6019855

Dipole moment (Debye): X= 4.0735 Y= 1.2684 Z= 0.0004

Tot= 4.2664

1,4-Me_2-IMD

B3LYP/6-311++G(d,p)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-0.608683	1.188791	-0.000077
2	7	0	-1.087221	-0.088539	-0.000152
3	7	0	0.704603	1.228655	0.000085

4	6	0	0.021316	-0.915229	-0.000034
5	6	0	-2.479709	-0.501383	-0.000300
6	6	0	1.117975	-0.086793	0.000148
7	6	0	2.566798	-0.453471	0.000348
8	1	0	-1.268080	2.044569	-0.000152
9	1	0	-0.070891	-1.989239	-0.000067
10	1	0	-2.709471	-1.092418	-0.890158
11	1	0	-3.111359	0.386925	-0.000479
12	1	0	-2.709723	-1.092243	0.889610
13	1	0	3.071624	-0.046156	-0.880308
14	1	0	2.698653	-1.537648	0.000404
15	1	0	3.071396	-0.046090	0.881105

E(B3LYP)= -304.9328651

Dipole moment (Debye): X= -4.1501 Y= 1.6432 Z= 0.0012

Tot= 4.4635

1,2-Me_2-IMD

B3LYP/6-311++G(d,p)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-0.256975	-0.688276	-0.003807
2	7	0	-0.135804	0.679893	-0.022385
3	7	0	0.925605	-1.271328	0.010330
4	6	0	1.218440	0.961976	-0.008571
5	6	0	-1.213901	1.654620	0.015091
6	6	0	1.849112	-0.252483	0.008020
7	6	0	-1.569775	-1.398654	-0.003175
8	1	0	1.588050	1.974218	-0.018017
9	1	0	-0.832899	2.621586	-0.312600
10	1	0	-1.621013	1.761471	1.024936
11	1	0	-2.018130	1.355938	-0.659047
12	1	0	2.909563	-0.451293	0.013538

13	1	0	-2.178337	-1.140578	0.870053
14	1	0	-1.376595	-2.470271	0.018012
15	1	0	-2.160642	-1.174123	-0.897846

E(B3LYP)= -304.9334031

Dipole moment (Debye): X= -2.5782 Y= 3.2048 Z= -0.0103

Tot= 4.1132

3-acetyl-1,5-dimethylimidazolium cation (conformer I; Chart 1.)

B3LYP/6-311++G(d,p)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-0.027811	1.040098	-0.000323
2	7	0	-1.313389	0.696498	-0.000047
3	7	0	0.714366	-0.080551	-0.000024
4	6	0	-1.417998	-0.701657	-0.000034
5	6	0	-2.443153	1.636793	0.000146
6	6	0	2.192882	-0.212847	0.000065
7	6	0	-0.141662	-1.173824	-0.000038
8	8	0	2.628832	-1.319177	0.000286
9	6	0	2.961631	1.072438	-0.000024
10	6	0	-2.721368	-1.420507	-0.000048
11	1	0	0.346306	2.049679	-0.000483
12	1	0	-3.049548	1.478666	-0.891241
13	1	0	-2.056754	2.653933	-0.000824
14	1	0	-3.048347	1.479878	0.892571
15	1	0	0.245338	-2.178366	0.000014
16	1	0	4.022393	0.830931	0.000040
17	1	0	2.730918	1.667133	0.888370
18	1	0	2.730983	1.666981	-0.888536
19	1	0	-2.544491	-2.495614	0.000752
20	1	0	-3.315064	-1.176591	0.885183
21	1	0	-3.314350	-1.177803	-0.886099

E(B3LYP)= -458.0035914

3-acetyl-1,5-dimethylimidazolium cation (conformer II; Chart 1.)

B3LYP/6-311++G(d,p)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	0.108588	-1.082678	-0.000215
2	7	0	1.362366	-0.643507	-0.000056
3	7	0	-0.717857	-0.023848	-0.000022
4	6	0	1.363460	0.758480	0.000010
5	6	0	2.558362	-1.498730	-0.000034
6	6	0	-2.193442	-0.188283	0.000024
7	6	0	0.054500	1.133488	0.000113
8	8	0	-2.609820	-1.303980	-0.000011
9	6	0	-2.977536	1.084007	0.000155
10	6	0	2.610723	1.571109	-0.000015
11	1	0	-0.217087	-2.110084	-0.000356
12	1	0	3.151005	-1.297187	-0.891905
13	1	0	2.244840	-2.540483	-0.000620
14	1	0	3.150440	-1.298007	0.892401
15	1	0	-0.378510	2.118098	0.000259
16	1	0	-4.035748	0.832081	-0.000355
17	1	0	-2.746991	1.682295	-0.885914
18	1	0	-2.747719	1.681506	0.886961
19	1	0	2.358974	2.631245	0.000685
20	1	0	3.220276	1.369248	0.884959
21	1	0	3.219578	1.370255	-0.885707

E(B3LYP)= -458.0053486

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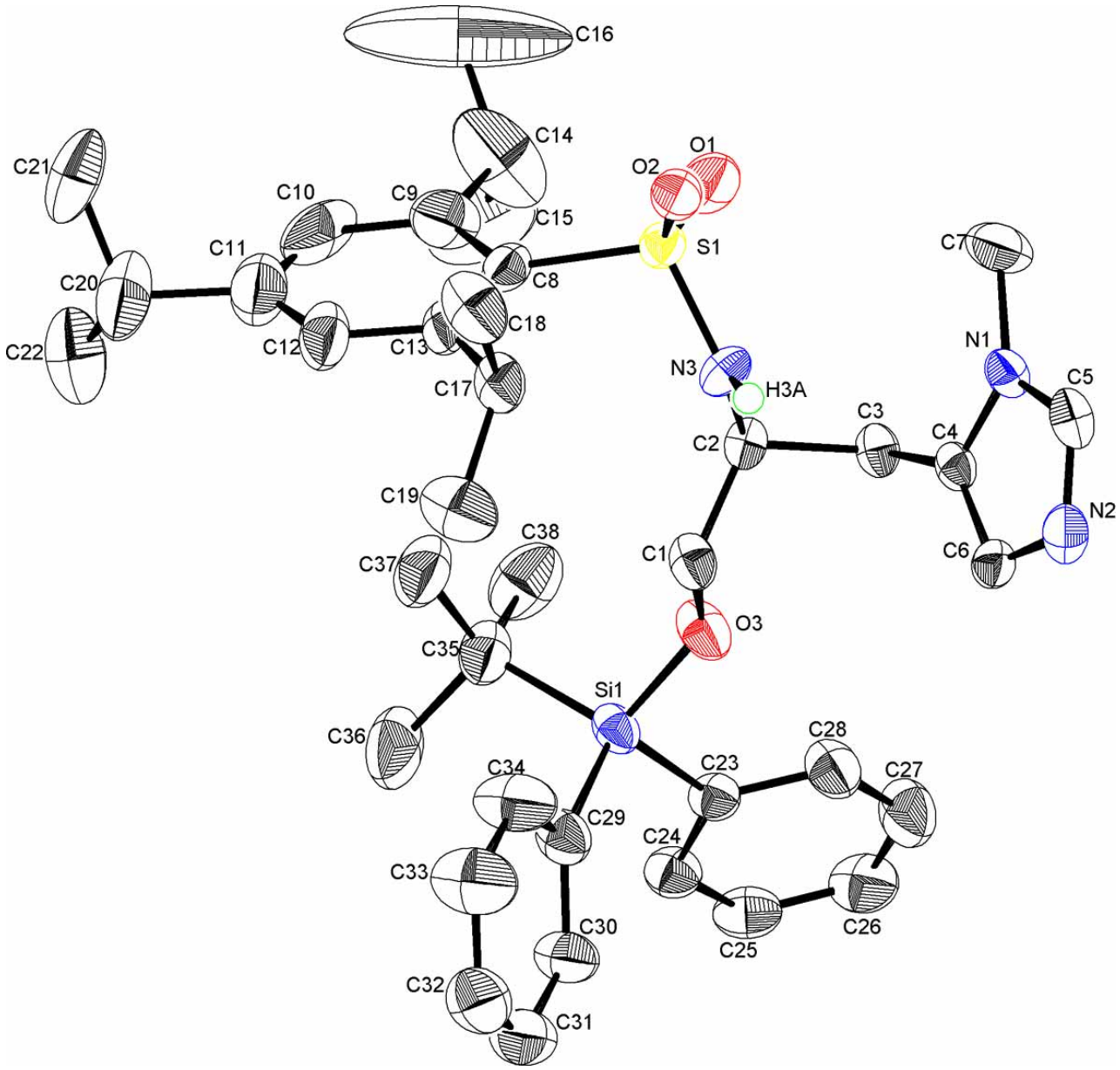

Figure. ORTEP Plot of **1d**. Drawn with 50% probability, and hydrogen atoms except for the SO_2NH moiety are omitted for clarity.