KINETIC RESOLUTION OF ALCOHOLS USING A 1,2-DIHYDROIMIDAZO[1,2-A]QUINOLINE ENANTIOSELECTIVE ACYLATION CATALYST

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SUPPORTING INFORMATION: Experimental procedures (9 pages), ¹H NMR and ¹³C NMR spectra (32 pages).

EXPERIMENTAL PART.

General. All reagents were obtained commercially and used as received unless otherwise specified. First-generation catalyst CF₃-PIP was prepared as previously described.¹ Preparations of catalyst precursors requiring elevated pressures were carried out in thick-wall pressure tubes with Teflon screwcaps available from Chemglass. (±)-1-Phenylethanol (**12**), (±)-1-phenyl-1-propanol (**13**), (±)-2,2-dimethyl-1-phenyl-1-propanol (**15**) and (±)- α -methyl-2-naphthalenemethanol (**16**) are available from Aldrich. (±)-E-4-Phenyl-but-3-en-2-ol (**6**), (±)-E-2-methyl-5-phenyl-pent-4-en-3-ol (**7**), (±)-E-3-methyl-4-phenyl-but-3-en-2-ol (**8**), (±)-E-2,4-dimethyl-5-phenyl-pent-4-en-3-ol (**9**) were prepared by addition of methyl- or isopropyl-Grignard reagents to the corresponding commercially available aldehydes. (±)-2-Methyl-1-phenyl-1-propanol (**14**), (±)- α -methyl-1-naphthalenemethanol (**17**) and 1-(1-cyclohexenyl)-ethanol⁹ (**18**) were prepared by borohydride reduction of the corresponding commercially available ketones. (±)-E-4-(o-Methoxyphenyl)-but-3-en-2-ol (**10**)^{10a} was prepared by borohydride reduction of the corresponding ketone obtained by aldol condensation of o-anisaldehyde with acetone.^{10b} (±)-1-(Chrom-3-en-3-yl)-ethanol (**11**)^{11a} was prepared by borohydride reduction of the corresponding ketone obtained from salicylaldehyde and methyl vinyl ketone.^{11b} Chloroform (OmniSolv® grade, stabilized with nonpolar hydrocarbons) was obtained from EM Science. Solvents used for chromatography were ACS or HPLC grade, as appropriate. Reactions were monitored by thin layer chromatography (TLC) using EM Science 60F silica gel plates. Flash column chromatography was performed over ICN Ecochrom silica gel (32-63 μ m). Deuterated chloroform was obtained from Aldrich. ¹H NMR and ¹³C NMR spectra were recorded on a Unity 300 MHz Varian spectrometer. The chemical shifts are reported as δ values (ppm) relative to TMS using residual CHCl₃ peak (7.26 ppm) as the reference. High-Resolution mass spectral analyses were performed at Washington University MS Center on a Kratos MS-50TA spectrometer using electron impact method (EI). Melting points were measured on a Mel-Temp II capillary melting point apparatus. Infrared spectra were recorded on a Perkin-Elmer Spectrum Bx FTIR spectrophotometer using potassium bromide plates. Optical rotations were measured at room temperature and 589 nm wavelength using a Perkin-Elmer 241 polarimeter. HPLC analyses were performed on a Shimadzu LC system using isopropanol-hexanes mobile phase at a flow rate of 1 mL/min and UV detection at 254 nm as previously described.¹ The absolute chirality of the unreacted alcohols obtained by kinetic resolution was either assigned by comparison of the sign of optical rotation with literature data or determined by Mosher ester analysis.

CATALYST PREPARATION.

(R)-N-(6-chloroquinolinyl-2)-2-Hydroxy-1-phenylethylamine (**5**)

A 15-mL pressure tube charged with 2,6-dichloroquinoline **3** (1.352 g, 6.83 mmol), (R)-phenylglycinol **4** (0.964 g, 7.03 mmol), N, N-diisopropylethylamine (0.991 g, 7.67 mmol) and a stir bar was flushed with nitrogen several times, stoppered and immersed into an oil bath kept at 130 ± 5 °C for 2.5 days. The tube was allowed to cool to room temperature and the content was diluted with CH₂Cl₂, which led to precipitation of a white solid. The mixture was washed with saturated aqueous NH₄Cl to remove N, N-diisopropylethylamine and then with saturated aqueous NaHCO₃. The solution was dried over Na₂SO₄ and evaporated to afford 1.770 g of the crystalline product (87%), which was sufficiently pure for the next step. If necessary, the product can be chromatographed (6% isopropanol, 0.8% triethylamine in hexanes).

¹H NMR (300 MHz, CDCl₃) δ 7.73 (d; J = 9 Hz; 1H), 7.62 (d; J = 8.7 Hz; 1H), 7.62 (d; J = 8.7 Hz; 1H), 7.55 (d; J = 2.2 Hz; 1H), 7.48 (dd; J₁ = 9 Hz, J₂ = 2.2 Hz; 1H), 7.28~7.45 (m; 5H), 6.67 (d; J = 9 Hz; 1H), 5.85 (s; 1H), 5.16 (dt; J₁ = 7.4 Hz, J₂ = 3.6 Hz; 1H), 4.05 (dd; J₁ = 11.3 Hz, J₂ = 7.4 Hz; 1H), 3.00 (dd; J₁ = 11.3 Hz, J₂ = 3.6 Hz; 1H); **¹³C NMR** (75 MHz, CDCl₃) δ 156.7, 144.8, 140.0, 137.0, 130.5, 129.0, 128.05, 127.98, 126.88, 126.81, 126.2, 123.9, 113.0, 68.3, 59.8; **IR** (film, cm⁻¹) 3316 (br) 1618.7, 1498.6, 1398.4; **MS**: HR-EI calculated for C₁₇H₁₅ClN₂O (M⁺) m/z: 298.0873, found: 298.0904; **mp** 172-174 °C; **[α]_D** = -154° (c = 0.26, MeOH).

(R)-7-Chloro-2-phenyl-2, 3-dihydroimidazo[1,2-a]quinoline (Cl-PIQ, **2**)

A solution of **5** (0.365 g, 1.22 mmol) in 6.4 mL of CHCl₃ was treated with SOCl₂ (0.23 mL, 3.15 mmol), and heated to reflux at 60~65 °C. After 1.5 hours, the reaction mixture was allowed to cool somewhat, treated with a few drops of MeOH, and then heated again for 10 minutes and allowed to cool to room temperature. The mixture was treated with saturated aqueous NaHCO₃ until the aqueous phase reached pH 8, then with 1M NaOH to pH 14, and extracted with CH₂Cl₂. The organic extract was dried over Na₂SO₄, concentrated, and chromatographed (10%→15% isopropanol, 2% triethylamine in hexanes) to afford 0.311 g of yellow oil (91%), which crystallized on standing.

¹H NMR (300 MHz, CDCl₃) δ 7.20-7.40 (m; 8H), 6.76 (d; J = 9.3 Hz; 1H), 6.65 (d; J = 8.8 Hz; 1H), 5.40 (dd; J₁ = 11.4 Hz, J₂ = 8.4 Hz; 1H), 4.40 (dd; J₁ = 11.4 Hz, J₂ = 10.3 Hz; 1H), 3.88 (dd; J₁ = 10.3 Hz, J₂ = 8.4 Hz; 1H); **¹³C NMR** (75 MHz, CDCl₃) δ 156.2, 143.9, 137.5, 135.8, 130.2, 128.7, 127.5, 127.4, 126.6, 125.4, 122.2, 118.4, 112.7, 67.7, 54.1; **IR** (film, cm⁻¹) 1640.3, 1568.9,

1433.9; **MS**: HR-EI calculated for $C_{17}H_{13}ClN_2$ (M^+) m/z : 280.0767, found: 280.0770; **mp** 134-136 °C (from Et₂O-hexanes); $[\alpha]_D^{25} = +746^\circ$ ($c = 0.27$, MeOH).

Note: The catalyst recrystallized from Et₂O-hexanes did not show a significant improvement of selectivity compared with the catalyst that was obtained after chromatography (using **17** as the test substrate). The data reported were obtained with the unrecrystallized catalyst.

KINETIC RESOLUTION EXPERIMENTS.

Substrates 6-17.

Kinetic resolution experiments with substrates **6-17** were carried out according to the previously published procedure,¹ except that for the most acid-sensitive substrates **10** and **11** the treatment with dilute HCl during the workup was omitted and the crude mixtures were directly applied to silica gel and chromatographed.

Substrate 18.

- 1) The substrate (63 mg, 0.50 mmol), 0.050 mmol of the catalyst and 0.50 mL of 0.75 M solution of *i*-Pr₂NEt in CDCl₃ were placed in a one-dram vial. The vial was cooled in an ice bath for 15 minutes before propionic anhydride precooled to 0 °C (48 μ L, 0.375 mmol) was added. The vial was left in the ice bath. The progress of acylation was checked periodically by withdrawing a small aliquot of the reaction mixture, diluting it with CDCl₃ and analyzing by ¹H NMR. After reaching conversion over 40% by NMR, the reaction mixture was quenched by adding 0.5 mL of methanol and left at 0 °C for 0.5 h and at room temperature for 1 h. The mixture was diluted with CH₂Cl₂, washed with saturated NH₄Cl, brine, saturated NaHCO₃ and brine again and dried over Na₂SO₄, and rotary evaporated. The propionate ester and the unreacted alcohol were separated by column chromatography (5 $\rightarrow$ 15% Et₂O in hexanes). The ester was hydrolyzed with 2 M aqueous MeOH for 2 h. The resulting alcohol was isolated by standard aqueous workup and purified by chromatography (short column, 15% Et₂O in hexanes).
- 2) The unreacted alcohol and the alcohol obtained by hydrolysis of the propionate ester were benzoylated to permit their separation on a chiral HPLC column. Each sample of the alcohol

was dissolved in 0.5 mL of CH_2Cl_2 and treated with 55 μL of NEt_3 , 2-3 mg of DMAP and 35 μL of benzoyl chloride at room temperature overnight. The reaction mixture was quenched by adding 15 μL of ethylenediamine, diluted with CH_2Cl_2 , and washed with 1 M HCl and then saturated NaHCO_3 . The organic phase was dried over Na_2SO_4 and rotary evaporated. The semisolid residue was taken up in the eluent and chromatographed (4% Et_2O in hexanes). The resulting benzoate **20** was analyzed by HPLC using CHIRALPAK AD analytical column (4.6x250 mm, Chiral Technologies, Inc.) and 0.5% isopropanol in hexane as the mobile phase.

Spectral data for previously uncharacterized substrates and esters.

Propionate of 6: ^1H NMR (300 MHz, CDCl_3) δ 7.40-7.24 (m; 5H), 6.61 (d; J = 15.9 Hz; 1H), 6.20 (dd; J_1 = 15.9 Hz, J_2 = 6.6 Hz; 1H), 5.55 (quintet; J = 6.6 Hz; 1H), 2.36 (qd; J_1 = 7.4 Hz, J_2 = 0.8 Hz; 2H), 1.42 (d; J = 6.6 Hz; 3H), 1.16 (t; J = 7.4 Hz; 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 173.7, 136.3, 131.4, 128.9, 128.5, 127.8, 126.5, 70.7, 27.9, 20.3, 9.1; **MS:** HR-EI calculated for $\text{C}_{13}\text{H}_{16}\text{O}_2$ (M^+) m/z : 204.1150, measured m/z : 204.1150; **IR** (KBr, cm^{-1}) 1734.0, 1187.3.

Propionate of 7: ^1H NMR (300 MHz, CDCl_3) δ 7.40-7.23 (m; 5H), 6.59 (d; J = 15.9 Hz; 1H), 6.12 (dd; J_1 = 15.9 Hz, J_2 = 6.9 Hz; 1H), 5.22 (t; J = 6.9 Hz; 1H), 2.37 (apparent qd; J_1 = 7.6 Hz, J_2 = 1.0 Hz; 2H), 1.96 (octet; J = 6.9 Hz; 1H), 1.16 (t; J = 7.6 Hz; 3H), 0.96 (d; J = 6.9 Hz; 3H), 0.95 (d; J = 6.9 Hz; 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 173.8, 136.5, 133.2, 128.5, 127.8, 126.5, 126.3, 79.1, 32.4, 27.9, 18.2, 9.2; **MS:** HR-EI calculated for $\text{C}_{15}\text{H}_{20}\text{O}_2$ (M^+) m/z : 232.1463, measured m/z : 232.1457; **IR** (KBr) 2964.8, 1732.5, 1185.7 cm^{-1} .

Propionate of 8: ^1H NMR (300 MHz, CDCl_3) δ 7.36-7.19 (m; 5H), 6.52 (s; 1H), 5.43 (q; J = 6.7 Hz; 1H), 2.36 (q; J = 7.7 Hz; 2H), 1.88 (s; 3H), 1.41 (d; J = 6.7 Hz; 3H), 1.16 (t; J = 7.7 Hz; 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 173.6, 137.4, 137.2, 129.0, 128.0, 126.5, 126.2, 75.1, 27.9, 19.3, 13.8, 9.14; **MS:** HR-EI calculated for $\text{C}_{14}\text{H}_{18}\text{O}_2$ (M^+) m/z : 218.1307, measured m/z : 218.1312; **IR** (KBr) 2981.6, 1736.7, 1186.9.

Propionate of 9: ^1H NMR (300 MHz, CDCl_3) δ 7.35-7.21 (m; 5H), 6.49 (s; 1H), 4.99 (d; J = 8.2 Hz; 1H), 2.37 (q; J = 7.5 Hz; 2H), 2.03 (doublet of septets; J_1 = 8.2 Hz; J_2 = 6.7 Hz; 1H), 1.84 (s; 3H), 1.17 (t; J = 7.5 Hz; 3H), 0.96 (d; J = 6.7 Hz; 3H), 0.91 (d; J = 6.7 Hz; 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 173.7, 137.3, 135.4, 129.0, 128.5, 128.0, 126.5, 84.3, 30.2, 27.9, 19.1, 18.5, 13.8, 9.2; **MS:** HR-EI calculated for $\text{C}_{16}\text{H}_{22}\text{O}_2$ (M^+) m/z : 246.1620, measured m/z : 246.1620; **IR** (KBr) 2964.3, 1737.7, 1184.0 cm^{-1} .

Alcohol 10: ^1H NMR (300 MHz, CDCl_3) δ 7.44 (dd; J_1 = 7.7 Hz, J_2 = 1.6 Hz; 1H), 7.23 (td; J_1 = 7.4 Hz, J_2 = 1.6 Hz; 1H), 6.95-6.85 (m; 3H), 6.27 (dd; J_1 = 15.9 Hz, J_2 = 6.3 Hz; 1H), 4.50 (q; J = 6.3 Hz; 1H), 3.85 (s; 3H), 1.66 (s, br; 1H), 1.37 (d; J = 6.3 Hz; 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 156.7, 134.2, 128.7, 126.8, 125.6, 124.3, 120.6, 110.8, 69.4, 55.4, 23.3; **MS:** HR-EI calculated for $\text{C}_{11}\text{H}_{14}\text{O}_2$ (M^+) m/z : 178.0994, measured m/z : 178.994; **IR** (KBr, cm^{-1}) 3356.2 (br), 1489.1, 1243.4.

Propionate of 10: ^1H NMR (300 MHz, CDCl_3) δ 7.43 (d; J = 7.7 Hz; 1H), 7.23 (t; J = 7.1 Hz; 1H), 6.96-6.85 (m; 3H), 6.22 (dd; J_1 = 16.2 Hz, J_2 = 6.7 Hz; 1H), 5.55 (quintet; J = 6.7 Hz; 1H),

3.84 (s; 3H), 2.34 (q; J = 7.4 Hz; 2H), 1.41 (d; J = 6.7 Hz; 3H), 1.15 (t; J = 7.4 Hz; 3H); ¹³C NMR (75 MHz, CDCl₃) □ 173.7, 156.8, 129.4, 128.9, 126.9, 126.2, 125.3, 120.5, 110.8, 71.3, 55.4, 27.9, 20.4, 9.1; MS: HR-EI calculated for C₁₄H₁₈O₃ (M⁺) m/z: 234.1256, measured m/z: 234.1248; IR (KBr) 2979.6, 1731.9 cm⁻¹.

Alcohol 11: ¹H NMR (300 MHz, CDCl₃) □ 7.11 (td; J₁ = 7.4 Hz, J₂ = 1.4 Hz; 1H), 7.00 (dd; J₁ = 7.4 Hz, J₂ = 1.4 Hz; 1H), 6.87 (td; J₁ = 7.4 Hz, J₂ = 1.4 Hz; 1H), 6.80 (d; J = 7.4 Hz; 1H), 6.38 (s; 1H), 4.81 (s; 2H), 4.42 (q; J = 6.2 Hz; 1H), 1.61 (s; 1H), 1.39 (d; J = 6.2 Hz; 3H); ¹³C NMR (75 MHz, CDCl₃) □ 153.5, 137.4, 129.0, 126.7, 122.4, 121.5, 118.4, 115.5, 68.6, 65.4, 21.3; MS: HR-EI calculated for C₁₁H₁₂O₂ (M⁺) m/z: 176.0837, measured m/z: 176.0832; IR (KBr, cm⁻¹) 3368.8 (br), 1487.2.

Propionate of 11: ¹H NMR (300 MHz, CD₃COCD₃) □ 7.14-7.06 (m; 2H), 6.87 (t; J = 7.4 Hz; 1H), 6.75 (d; J = 8.0 Hz; 1H), 6.49 (s; 1H), 5.44 (q; J = 6.4 Hz; 1H), 4.80 (d; J = 14.4 Hz; 1H), 4.72 (d; J = 14.4 Hz; 1H), 2.36 (q; J = 7.3 Hz; 2H); 1.40 (d; J = 6.4 Hz; 3H), 1.09 (t; J = 7.3 Hz; 3H); ¹³C NMR (75 MHz, CD₃COCD₃) □ 173.7, 154.5, 135.0, 130.0, 127.9, 123.3, 122.3, 120.7, 116.2, 70.7, 66.0, 28.1, 18.8, 9.5; MS: HR-EI calculated for C₁₄H₁₆O₃ (M⁺) m/z: 232.1099, measured m/z: 232.1097; IR (KBr) 2980.2, 1735.0, 1185.6 cm⁻¹.

Propionates of 12 and 13: previously reported¹²

Propionate of 14: ¹H NMR (300 MHz, CDCl₃) □ 7.36-7.24 (m; 5H), 5.50 (d; J = 6.9 Hz; 1H), 2.43-2.30 (m; 2H), 2.11 (octet; J = 6.9 Hz; 1H), 1.15 (t; J = 7.6 Hz; 3H), 0.98 (d; J = 6.9 Hz; 3H), 0.82 (d; J = 6.9 Hz; 3H); ¹³C NMR (75 MHz, CDCl₃) □ 173.6, 139.9, 128.1, 127.6, 126.9, 80.6, 33.5, 27.8, 18.7, 18.4, 9.1; MS: HR-EI calculated for C₁₃H₁₈O₂ (M⁺) m/z: 206.1307, measured m/z: 206.1298; IR (KBr) 2964.4, 1738.5, 1186.3 cm⁻¹.

Propionate of 15: ¹H NMR (300 MHz, CDCl₃) □ 7.3-7.2 (m; 5H), 5.49 (s; 1H), 2.37 (apparent qd; J₁ = 7.5 Hz, J₂ = 3.0 Hz; 2H), 1.14 (t; J = 7.5 Hz; 3H), 0.92 (s; 9H); ¹³C NMR (75 MHz, CDCl₃) □ 173.4, 138.6, 127.7, 127.5, 127.4, 82.5, 35.0, 27.9, 26.0, 9.2; MS: HR-EI calculated for C₁₄H₂₀O₂ (M⁺) m/z: 220.1463, measured m/z: 220.1455; IR (KBr) 2972.0, 1738.6, 1176.3 cm⁻¹.

Propionate of 16: ¹H NMR (300 MHz, CDCl₃) □ 7.87-7.83 (m; 4H), 7.54-7.51 (m; 3H), 6.10 (q; J = 6.6 Hz; 1H), 2.41 (apparent qd; J₁ = 7.7 Hz, J₂ = 1.9 Hz; 2H), 1.65 (d; J = 6.6 Hz; 3H), 1.18 (t; J = 7.7 Hz; 3H); ¹³C NMR (75 MHz, CDCl₃) □ 173.7, 139.1, 133.1, 132.9, 128.3, 128.0, 127.6, 126.1, 124.9, 124.0, 72.1, 27.8, 22.2, 9.1; MS: HR-EI calculated for C₁₅H₁₆O₂ (M⁺) m/z: 228.1150, measured m/z: 228.1154; IR (KBr) 2980.2, 1732.0, 1188.6 cm⁻¹.

Propionate of 17: ¹H NMR (300 MHz, CDCl₃) □ 8.12 (d; J = 8.0 Hz; 1H), 7.88-7.80 (m; 2H), 7.63-7.46 (m; 4H), 6.69 (q; J = 6.6 Hz; 1H), 2.42 (apparent qd; J₁ = 7.7 Hz, J₂ = 2.2 Hz; 2H), 1.72 (d; J = 6.6 Hz; 3H), 1.18 (t; J = 7.7 Hz; 3H); ¹³C NMR (75 MHz, CDCl₃) □ 173.7, 137.6, 133.8, 130.2, 128.9, 128.3, 126.2, 125.6, 125.3, 123.2, 123.1, 69.2, 27.9, 21.7, 9.1; MS: HR-EI calculated for C₁₅H₁₆O₂ (M⁺) m/z: 228.1150, measured m/z: 228.1160; IR (KBr) 2980.9, 1735.5, 1186.1 cm⁻¹.

Propionate of 18: $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 5.68 (apparent doublet; $J = 0.8$ Hz; 1H), 5.23 (q; $J = 6.4$ Hz; 1H), 2.30 (q; $J = 7.4$ Hz; 2H), 2.0-1.95 (m; 4H), 1.6-1.5 (m; 4H), 1.27 (d; $J = 6.4$ Hz; 3H), 1.12 (t; $J = 7.4$ Hz; 3H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 173.8, 137.2, 123.4, 73.8, 27.9, 24.8, 24.1, 22.4, 22.3, 18.8, 9.1; **MS:** HR-EI calculated for $\text{C}_{11}\text{H}_{18}\text{O}_2$ (M^+) m/z : 182.1307, measured m/z : 182.1306; **IR** (KBr, cm^{-1}) 2932.0, 1735.7, 1192.4.

Benzoate of 18: $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 8.05 (d; $J = 7.4$ Hz; 2H), 7.55 (t; $J = 7.4$ Hz; 1H), 7.43 (t; $J = 7.4$ Hz; 2H), 5.79 (apparent doublet; $J = 0.8$ Hz; 1H), 5.50 (q; $J = 6.4$ Hz; 1H), 2.1-2.0 (m; 4H), 1.75-1.55 (m; 4H), 1.43 (d; $J = 6.4$ Hz; 3H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 165.8, 137.1, 132.7, 130.9, 129.5, 128.2, 123.7, 74.8, 24.8, 24.1, 22.5, 22.3, 19.0; **MS:** HR-EI calculated for $\text{C}_{15}\text{H}_{18}\text{O}_2$ (M^+) m/z : 230.1307, measured m/z : 230.1314; **IR** (KBr, cm^{-1}) 2929.0, 1716.8, 1271.8.

HPLC separation and properties of alcohol substrates.

Substrate	HPLC conditions ^a	Retention time (min) ^a		Unreacted alcohol ^d	
		(R)-ent	(S)-ent	Sign of rotation	Ref.
3% IPA/hexane	21.2	35.3	(-)	13
5% IPA/hexane	14.5	23.1	(+)	14
5% IPA/hexane	12.9	14.6	(+)	15
1% IPA/hexane	32.5	37.3	(+)	16
18% IPA/hexane	11.1	19.7	(-)	17
0.5% IPA/hexane ^b	13.9 ^b	19.8 ^b	(-)	17
2% IPA/hexane	20.7	26.2	(-)	18
2.5% IPA/hexane	23.4	26.0	(-)	18
1% IPA/hexane	41.7	34.6	(-)	18

2% IPA/hexane	21.1	13.7	(-)	19
10% IPA/hexane	21.1	13.1	(-)	18
100% hexane ^b	27.2 ^b	32.5 ^b	(-)	18
0.5% IPA/hexane	7.3 ^c	9.1 ^c	(-)	20

^a) Unless specified otherwise, HPLC separation of enantiomers was achieved using free alcohols on CHIRALCEL OD-H analytical column (4.6x250 mm, Chiral Technologies, Inc.) with isopropanol/hexane eluent of the concentration indicated;

^b) HPLC separation of enantiomers was achieved using the propionate esters of the alcohols on CHIRALPAK AD analytical column (4.6x250 mm, Chiral Technologies, Inc.)

^c) HPLC separation of enantiomers was achieved using the benzoate ester of the alcohol on CHIRALPAK AD analytical column (4.6x250 mm, Chiral Technologies, Inc.)

^d) Absolute configuration was confirmed to be S in all cases

Kinetic resolution data

Entry	Substrate	Catalyst	t(h)	#	ee _E %	ee _A %	C _{HPLC} %	s	C _{AVG} %	s _{AVG}
1		CF ₃ PIP	8	1	79.1	11.8	13.0	9.6	14	11
				2	82.2	13.6	14.2	11.7		
2		Cl-PIQ	8	1	86.3	66.1	43.4	26.9	44	27
				2	85.7	68.7	44.5	26.7		
3		CF ₃ PIP	8	1	86.9	39.2	31.1	21.0	30	21
				2	86.9	36.4	29.5	20.4		
4		Cl-PIQ	8	1	75.9	90.5	54.4	22.3	53	24
				2	81.3	84.8	51.1	25.9		
5		CF ₃ PIP	8	1	75.2	12.4	14.1	8.0	14	9
				2	80.9	13.4	14.2	10.8		
6		Cl-PIQ	8	1	82.1	53.5	39.4	17.3	38	17
				2	82.0	45.7	35.8	15.8		
7		CF ₃ PIP	8	1	84.1	8.7	9.4	12.6	9	13
				2	84.0	8.4	9.1	12.5		
8		Cl-PIQ	8	1	86.6	42.3	32.8	21.1	32	22
				2	88.2	39.7	31.0	23.6		
9		CF ₃ PIP	8	1	61.6	23.9	27.9	5.3	27	6
				2	71.6	24.2	25.3	7.6		
10		Cl-PIQ	8	1	75.7	96.3	56.0	28.1	56	31
				2	77.8	97.2	55.6	33.3		

11		CF ₃ PIP	8	1	81.9	83.0	50.3	25.9	50	26
12		Cl-PIQ	4	2	82.1	82.4	50.1	25.8		
13		CF ₃ PIP ^a	8	1	80.6	99.7	55.3	58.2	55	57
14		Cl-PIQ	8	2	80.7	99.6	55.3	56.0		
15		CF ₃ PIP ^a	8	1	89.3	42.7	32.3	26.8	32	26
16		Cl-PIQ	8	2	89.2	40.3	31.1	26.0		
17		CF ₃ PIP ^a	8	1	78.3	96.5	55.2	32.6	55	33
18		Cl-PIQ	8	2	78.6	96.2	55.1	32.5		
19		CF ₃ PIP ^a	8	1	90.4	60.8	40.2	36.8	39	36
20		Cl-PIQ	8	2	90.6	57.2	38.7	36.0		
21		CF ₃ PIP	8	1	83.5	95.3	53.3	41.5	53	41
22		Cl-PIQ	8	2	84.1	94.3	52.9	41.3		
23		CF ₃ PIP	8	1	91.5	69.9	43.3	47.4	43	50
24		Cl-PIQ	8	2	92.6	67.8	42.3	52.9		
25		CF ₃ PIP ^a	8	1	89.4	91.1	50.5	57.0	50	59
26		Cl-PIQ	8	2	90.2	90.7	50.1	61.2		
27		CF ₃ PIP ^a	52	1	93.5	88.2	48.6	87.1	48	85
28		Cl-PIQ	8	2	93.8	83.6	47.1	82.5		
29		CF ₃ PIP ^a	8	1	96.7	69.7	41.9	124	42	117
30		Cl-PIQ	8	2	96.1	72.5	43.0	110		
31		CF ₃ PIP	8	1	87.0	86.8	49.9	40.5	50	42
32		Cl-PIQ	2	2	87.2	88.7	50.4	43.1		
33		CF ₃ PIP ^a	8	1	91.0	94.4	50.9	76.1	51	74
34		Cl-PIQ	8	2	90.2	94.9	51.3	71.6		
35		CF ₃ PIP ^a	8	1	90.1	89.1	49.7	57.8	51	56
36		Cl-PIQ	8	2	87.8	94.0	51.7	54.4		
37		CF ₃ PIP ^b	32	1	80.0	99.7	55.5	55.9	56	55
38		Cl-PIQ ^b	11	2	79.8	99.7	55.6	55.0		
39		CF ₃ PIP ^b	32	1	74.5	50.6	40.5	11.2	40	11
40		Cl-PIQ ^b	11	2	73.7	47.8	39.3	10.5		
41		CF ₃ PIP ^b	32	1	78.2	69.6	47.1	16.9	47	17
42		Cl-PIQ ^b	11	2	78.3	71.1	47.6	17.4		

^a) Data from previously published work.¹

^b) 10 mol% of the catalyst was used

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