The ‘reverse-tethered’ ruthenium (II) catalyst for asymmetric transfer hydrogenation: further applications.

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Synthesis of 4-benzoylpiperidine-1-carboxylic acid tert-butyl ester

To a stirred solution of 4-benzoylpiperidine hydrochloride (0.500 g, 2.22 mmol) in 5:2 water:THF (5.2 cm³) was added Boc₂O (0.532 g, 2.44 mmol) followed by sodium carbonate (0.470 g, 4.43 mmol). The reaction mixture was stirred at 80 °C for 1 hour, cooled, diluted with EtOAc (10 cm³) washed with water (10 cm³) and the aqueous layer extracted with EtOAc (10 cm³). The combined extracts were dried (MgSO₄) and concentrated under vacuum to give the product (0.572 g, 89%) as a white solid; ν_max/cm⁻¹ (solid) 1675 (C=O), 770 and 704 (Ph); δ_H (400 MHz; CDCl₃; Me₄Si) 1.47 (9 H, s, C(CH₃)₃), 1.64-1.76 (2 H, m), 1.81-1.88 (2 H, m), 2.85-2.95 (2 H, m), 3.36-3.45 (1 H, m, CH), 4.10-4.22 (2 H, m), 7.48 (2 H, dd (app. t), J 7.3 and 7.3), 7.57 (1 H, m), 7.94 (2 H, d, J 7.3); δ_C (100.6 MHz; CDCl₃; Me₄Si) 28.4 (t), 28.5 (3 x q), 43.5 (overlapping d and t), 79.6 (s), 128.3 (2 x d), 128.8 (2 x d), 133.1 (d), 135.9 (s), 154.7 (s), 202.1 (s); Found (LSIMS) 290.1771 [MH]+, C₁₇H₂₄NO₃ requires 290.1756 (5.0 ppm error); m/z (EI) 290 (MH⁺, 25%), 188 (M-H⁺, 10), 234 (100), 216 (60), 188 (35).

Synthesis of 4-methoxymethylenetetrahydropyran

To a suspension of methoxymethyltriphenylphosphonium chloride (24.82 g, 72.41 mmol) in THF (250 cm³) at 0 °C was added dropwise a solution of 2.5 M n-BuLi (24.0 cm³, 59.93 mmol) in hexane. The reaction mixture was warmed to room temperature, stirred for 1 hour, re-cooled to 0 °C and a solution of tetrahydro-4H-pyran-4-one (5.00 g, 49.94 mmol) in THF (10 cm³) added dropwise. After 20 minutes the reaction mixture was concentrated under vacuum, triturated with ether (4 x 100 cm³), concentrated under vacuum, and the residue was purified by flash column chromatography (2%
EtOAc/Hexane to 10% EtOAc/Hexane) to give the product (2.98 g, 47%) as a colourless mobile oil; $\delta_H$ (300 MHz; CDCl$_3$; Me$_4$Si) 1.65-1.69 (2 H, m), 1.89-1.93 (2 H, m), 3.16 (3 H), 3.22-3.26 (4 H, m), 5.45 (1 H, s); $\delta_C$ (100.6 MHz; CDCl$_3$; Me$_4$Si) 28.3 (t), 39.7 (d), 66.9 (t), 180.0 (s).

Synthesis of tetrahydropyran-4-carboxylic acid

To a stirred solution of 4-methoxymethylenetetrahydropyran (2.90 g, 22.6 mmol) in acetone (45 cm$^3$) was added a solution of 1.2 M HCl (aq.) (1.3 cm$^3$, 1.56 mmol). The reaction mixture was stirred for 3 hours, diluted with further acetone (85 cm$^3$) and Jones reagent (prepared from CrO$_3$ (2.26 g), water (9.6 cm$^3$) and conc. H$_2$SO$_4$ (2.0 cm$^3$)) added dropwise over 1 hour. The resulting green solid was removed and the reaction mixture concentrated under vacuum. The residue was purified by flash column chromatography (10% EtOAc/Hexane to 80% EtOAc/Hexane) to give the product (0.930 g, 32%) as a white solid; $\delta_H$ (400 MHz; CDCl$_3$; Me$_4$Si) 1.75-1.91 (4 H, m), 2.58 (1 H, m, CH), 3.47 (2 H, td, $J$ 11.6 and 2.8), 4.00 (2 H, dt, $J$ 11.6 and 3.8), 11.10 (1 H, s); $\delta_C$ (100.6 MHz; CDCl$_3$; Me$_4$Si) 28.3 (2 x t), 39.7 (d), 66.9 (2 x t), 180.0 (s).

Synthesis of phenyl-(tetrahydropyran-4-yl)-methanone

A stirred solution of tetrahydropyran-4-carboxylic acid (0.758 g, 5.83 mmol) in thionyl chloride (1 cm$^3$) was heated at reflux for 45 minutes, cooled to room temperature, concentrated under vacuum and added dropwise to a suspension of anhydrous aluminium chloride (1.437 g, 10.78 mmol) in benzene (6 cm$^3$). The reaction mixture was stirred at 75 °C for 1 hour, cooled to room temperature, poured onto ice/water (50 cm$^3$) and extracted with chloroform (2 x 50 cm$^3$). The combined extracts were washed with brine (20 cm$^3$), dried (MgSO$_4$) and concentrated under vacuum to give the product (0.890 g, 80%) as a white solid; $\nu_{\text{max}}$ cm$^{-1}$ (solid) 1675 (C=O), 773 and 696 (Ph); $\delta_H$ (400 MHz; CDCl$_3$;
Me₄Si) 1.67-1.85 (4 H, m), 3.38-3.51 (3 H, m), 3.94-3.97 (2 H, m), 7.36-7.41 (2 H, m, m-ArH), 7.48 (1 H, m), 7.84-7.87 (2 H, m); δC (100.6 MHz; CDCl₃; Me₄Si) 29.1 (2 x t), 42.6 (d), 67.3 (2 x t), 128.3 (2 x d), 128.8 (2 x d), 133.1 (d), 135.8 (s), 201.8 (s). Found (LSIMS) 190.0997 [M]+, C₁₂H₁₄O₂ requires 190.0994 (1.6 ppm error); m/z (EI) 290 (MH+, 25%), 188 (M-H+, 10), 234 (100), 216 (60), 188 (35).

Synthesis of 1-(2-bromoethyl)-4-fluorobenzene ³

To a stirred solution of 2-4-fluorophenylethanol (10.00 g, 71.35 mmol) in dichloromethane (120 cm³) at 0 °C was added tetrabromomethane (29.60 g, 89.18 mmol) and then triphenyl phosphine (28.10 g, 107.02 mmol) portionwise over 10 minutes. The reaction mixture was stirred for 1 hour, concentrated under vacuum and diethyl ether added. The resultant solids were removed by filtration and the filtrate concentrated under vacuum. The residue was purified by flash column chromatography (ether) to give the product (14.26 g, 98%) as a pale yellow oil; δH (400 MHz; CDCl₃; Me₄Si) 3.13 (2 H, t, J 7.5), 3.54 (2 H, t, J 7.5), 7.00 (2 H, dd, J 8.8 and 8.5), 7.17 (2 H, dd, J 8.8 and 5.5); δC (100.6 MHz; CDCl₃; Me₄Si) 33.0 (t), 38.5 (t), 115.5 (dd, Jc-F 21.2), 130.2 (dd, Jc-F 7.9), 134.6 (d, Jc-F 3.2), 161.9 (d, Jc-F 245.1).

Synthesis of 1-[2-(fluorophenyl)-ethyl]-piperidine-4-carboxylic acid ethyl ester ²⁵

To a stirred solution of ethyl isonicotinate (3.00 g, 19.1 mmol) in DMF (40 cm³) was added 1-(2-bromoethyl)-4-fluorobenzene (4.27 g, 21.0 mmol) followed by potassium carbonate (7.91 g, 57.3 mmol). The reaction mixture was stirred at 90 °C overnight, cooled to room temperature, filtered and washed with ether (200 cm³). The organics were washed with water (100 cm³), dried (MgSO₄) and concentrated under vacuum. The residue was purified by flash column chromatography (10% EtOAc/Hexane to 40%
EtOAc/Hexane) to give 25 (3.63 g, 68%) as a pale yellow oil; δH (400 MHz; CDCl3; Me4Si) 1.25 (3 H, t, J 7.3), 1.72-1.83 (2 H, m), 1.88-1.95 (2 H, m), 2.04-2.11 (2 H, m), 2.29 (1 H, m), 2.52-2.56 (2 H, m), 2.74-2.79 (2 H, m), 2.91-2.96 (2 H, m), 4.13 (2 H, q, J 7.3), 6.96 (2 H, dd, J 8.8 and 8.5), 7.15 (2 H, dd, J 8.5 and 5.3); δC (100.6 MHz; CDCl3; Me4Si) 14.2 (q), 28.3 (2 x t), 32.9 (t), 41.1 (d), 53.0 (2 x t), 60.3 (t), 60.8 (t), 115.1 (dd, J_{C-F} 21.0), 130.1 (dd, J_{C-F} 7.7), 136.0 (d, J_{C-F} 3.0), 161.4 (d, J_{C-F} 243.7), 175.1 (s).

Synthesis of {1-[2-(4-fluorophenyl)-ethyl]-piperidin-4-yl}-phenylmethanone 23

To a stirred solution of 25 (1.00 g, 3.58 mmol) in THF (20 cm³) was added N,O-dimethylhydroxylamine hydrochloride (0.523 g, 5.36 mmol) followed by a solution of 1 M ethyl magnesium bromide (10.8 cm³, 10.8 mmol) in THF at -15 °C. The reaction mixture was warmed to 0 °C over 1.5 hours and treated dropwise with a solution of 1.9 M PhLi (3.96 cm³, 7.52 mmol) in di-t-butyl ether. The resulting mixture was stirred at room temperature for 3 hours, quenched with sat. NH₄Cl (aq.) (20 cm³), separated and extracted with ether (50 cm³). The combined extracts were dried (MgSO₄), concentrated under vacuum and the residue was purified by flash column chromatography (ether) to give 23 (0.882 g, 79%) as a pale yellow solid; ν_{max}/cm⁻¹ (solid) 1668 (C=O), 822 (p-disubstituted benzene), 770 and 695 (Ph); δH (300 MHz; CDCl3; Me4Si) 1.82-1.94 (4 H, m), 2.12-2.22 (2 H, m), 2.56-2.61 (2 H, m), 2.77-2.82 (2 H, m), 3.02-3.09 (2 H, m, ring CH₂), 3.27 (1 H, m), 6.96 (2 H, dd, J 8.7 and 8.5), 7.16 (2 H, dd, J 8.5 and 5.3), 7.42-7.59 (3 H, m), 7.94 (2 H, d, J 7.2); δC (100.6 MHz; CDCl3; Me4Si) 28.8 (2 x t), 32.9 (t), 43.7 (d), 53.3 (2 x t), 60.8 (t), 115.1 (dd, J_{C-F} 21.1), 128.3 (2 x d), 128.7 (2 x d), 130.1 (dd, J_{C-F} 7.7), 133.0 (d), 136.1 (2 x overlapping s), 161.4 (d, J_{C-F} 243.5), 202.6 (s). Found (EI) 312.1764 [MH]⁺, C₂₀H₂₃NOF requires 312.1764 (0.1 ppm error); m/z (EI) 312 (MH⁺, 30%), 202 (100), 104 (20).
Synthesis of (2,3-dimethoxyphenyl)-{1-[2-(4-fluorophenyl)-ethyl]-piperidin-4-yl}methanone 24

To a stirred solution of veratrole (1.039 g, 7.52 mmol) in THF (14 cm³) at 0 °C was added dropwise a solution of 2.5 M n-BuLi (3.33 cm³, 8.33 mmol) in hexane. The reaction mixture was warmed to room temperature and added to a separate reaction flask containing a solution of 25 (1.00 g, 3.58 mmol) in THF (20 cm³) which had been treated with N,O-dimethylhydroxylamine hydrochloride (0.523 g, 5.36 mmol) and a solution of 1 M ethyl magnesium bromide (10.8 cm³, 10.8 mmol) in THF at -15 °C and warmed to 0 °C over 1.5 hours. The resulting mixture was stirred at room temperature for 3 hours, quenched with sat. NH₄Cl (aq.) (20 cm³), separated and extracted with ether (50 cm³). The combined extracts were dried (MgSO₄), concentrated under vacuum and the residue was purified by flash column chromatography (ether) to give 24 (0.820 g, 62%) as a pale yellow oil; δ_H (400 MHz; CDCl₃; Me₄Si) 1.69-1.80 (2 H, m), 1.85-1.94 (2 H, m), 2.08-2.14 (2 H, m), 2.53-2.57 (2 H, m), 2.74-2.79 (2 H, m), 2.95-3.00 (2 H, m), 3.08 (1 H, m), 3.86 (3 H, s), 3.89 (3 H, s), 6.92-7.16 (7 H, m); δ_C (100.6 MHz; CDCl₃; Me₄Si) 28.1 (2 x t), 32.9 (t), 48.1 (d), 53.3 (2 x t), 55.9 (q), 60.7 (t), 61.8 (q), 114.8 (d), 115.1 (dd, J_C-F 21.1), 120.3 (d), 124.3 (d), 130.0 (dd, J_C-F 7.8), 134.4 (s), 136.1 (d, J_C-F 3.1), 146.9 (s), 152.7 (s), 161.4 (d, J_C-F 243.7), 206.5 (s).

Synthesis of 2-imidazol-1-yl-1-phenylethanone 26

To a stirred solution of imidazole (4.310 g, 63.32 mmol) in dichloromethane (50 cm³) was added 2-bromoacetophenone (6.000 g, 30.15 mmol) portionwise over 10 minutes. The reaction mixture was stirred for 3 hours during which time a precipitate formed. Water (50 cm³) was added and the mixture filtered, separated, washed with sat. NaCl solution (50 cm³), concentrated under vacuum, dissolved in EtOAc (75 cm³), filtered and
then concentrated under vacuum to give 26 (2.152 g, 38%) as a pale yellow solid; \( \nu_{\text{max}}/\text{cm}^{-1} \) (solid) 1693 (C=O), 745 and 691 (Ph); \( \delta_H \) (400 MHz; CDCl\(_3\); Me\(_4\)Si) 5.41 (2 H, s), 6.94 (1 H, m), 7.12 (1 H, m), 7.50-7.56 (3 H, m), 7.65 (1 H, m), 7.96 (2 H, d, J 7.5); \( \delta_C \) (100.6 MHz; CDCl\(_3\); Me\(_4\)Si) 52.5 (t), 120.4 (d), 128.0 (2 x d), 129.1 (2 x d), 129.4 (d), 134.2 (s), 134.4 (d), 138.2 (d), 191.8 (s); Found (EI) 186.0793 [M]+, C\(_{11}\)H\(_{10}\)N\(_2\)O requires 186.0793 (0.3 ppm error); m/z (EI) 186 (M+, 20%), 105 (100), 77 (40).

**Synthesis of 1-(2,4-dichlorophenyl)-2-imidazol-1-ylethanone 27**

To a stirred solution of imidazole (6.390 g, 93.96 mmol) in dichloromethane (27 cm\(^3\)) was added a solution of 2, 2’, 4’-trichloroacetophenone (10.000 g, 44.74 mmol) in dichloromethane (13 cm\(^3\)) over 20 minutes. The reaction mixture was stirred at 40 °C for 2 hours, cooled and stirred at room temperature overnight. Water (150 cm\(^3\)) and further dichloromethane (100 cm\(^3\)) was added, separated, washed successively with water (50 cm\(^3\)) and sat. NaCl solution (50 cm\(^3\)), dried (MgSO\(_4\)) and concentrated under vacuum. The residue was recrystallised twice from methanol to give 27 (3.16 g, 28%) as a white solid; \( \nu_{\text{max}}/\text{cm}^{-1} \) (solid) 1698 (C=O), 806 (2 adjacent ArH); \( \delta_H \) (400 MHz; CDCl\(_3\); Me\(_4\)Si) 5.33 (2 H, s), 6.94 (1 H, m), 7.11 (1 H, m), 7.37 (1 H, dd, J 8.3 and 2.0), 7.51 (2 H, overlapping d and s, J 2.0) 7.56 (1 H, d, J 8.3); \( \delta_C \) (100.6 MHz; CDCl\(_3\); Me\(_4\)Si) 55.5 (t), 120.0 (d), 128.0 (d), 129.8 (d), 130.8 (d), 131.1 (d), 132.5 (s), 134.1 (s), 138.0 (d), 139.2 (s), 193.7 (s); Found (EI) 254.0011 [M]+, C\(_{11}\)H\(_8\)N\(_2\)OCl\(_2\) requires 254.0014 (1.0 ppm error); m/z (EI) 254 (M+, 10%), 219 (10), 175 (70), 173 (100), 145 (20).

**Ketone reduction in FA/TEA, representative procedure:** A solution of ruthenium dimer 9 (9.8 mg, 0.0075 mmol) in formic acid : triethylamine 5 : 2 azeotrope (1.5 mL) was stirred in a flame dried Schlenk tube at 28°C for 30 minutes. The temperature was then adjusted to that indicated in the text. Substrate (3.00 mmol) was added and the reaction mixture was stirred at the same temperature for the time indicated. The reaction
mixture was filtered (silica), washed (50% EtOAc/hexane) and concentrated under vacuum to give the reduction product. The residue was purified by flash chromatography where necessary.

**Reduction of acetylenic ketone in iPrOH:** A mixture of monomer 8 (6.2 mg, 0.010 mmol), was dissolved in iPrOH (19.5 mL) at rt. Potassium hydroxide (2.0 mg in 0.5 mL iPrOH, 0.050 mmol) was added and the mixture was stirred at 28°C for 30 min. A solution of acetylenic ketone (precursor to 22, 0.29mL, 2.0 mmol) in iPrOH (1 mL) was then added. The reaction was stirred for 18h at 28°C. The reaction mixture was filtered (silica), washed (50% EtOAc/hexane) and concentrated under vacuum to give the reduction product. The residue was purified by flash chromatography where necessary.

**Note:** The optical rotations match the e.e.s in the compound listings below, however the quoted value may not match that in the tables in each case. This is because the ketones were reduced in multiple experiments, and optical rotations were only obtained once for each reduction (i.e. to link chiral GC or HPLC retention times to configuration). The Tables will quote the e.e. as determined for that particular run under the conditions listed in each case, as determined by chiral GC or HPLC.

**1-Phenylethanol:** Enantiomeric excess and conversion by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, T = 115 °C, P = 7 psi, ketone 13.2 min., R isomer 19.3 min., S isomer 20.3 min.); [α]_D^22 +49.0 (c 1.0 in CHCl_3) 98% ee (R) (lit.⁶ [α]_D^23 +48.6 (c 1.0 in CH₂Cl₂) 96% ee (R)); δ_H(300 MHz; CDCl₃; Me₄Si) 1.47 (3 H, d, J 6.4), 2.04 (1 H, br s), 4.86 (1 H, q, J 6.4), 7.33-7.35 (5 H, m); δ_C(75.5 MHz; CDCl₃; Me₄Si) 145.6 (s). Data in agreement with commercially available sample.

**1-Cyclohexylethanol:** **Method A:** Enantiomeric excess by HPLC of 2-naptholate ester derivative (Chiralcel OD-H, 4% iso-propanol/hexane (0.7 mL min⁻¹), R isomer 8.3 min., S isomer 9.6 min.), conversion by ^1^H-NMR; **Method B:** Enantiomeric excess and conversion by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, T = 100 °C, P = 7
psi, ketone 17.6 min., \( R \) isomer 26.3 min., \( S \) isomer 26.9 min.; \([\alpha]_D^{18}\) -1.61 (c 1.80 in CHCl₃) 19% ee (\( R \)) (lit.\(^7\) \([\alpha]_D +3.51\) (c 3.1 in CHCl₃) 95% ee (\( S \)); \( \delta_H(400 \text{ MHz; CDCl}_3; \text{Me}_4\text{Si}) 0.92-1.32\) (6 H, m), 1.15 (3 H, d, \( J 6.3 \)),1.46 (1 H, br s), 1.63-1.88 (5 H, m), 3.54 (1 H, dt, \( J 6.3 \) and 6.3); \( \delta_C(100.6 \text{ MHz; CDCl}_3; \text{Me}_4\text{Si}) 20.4\) (q), 26.2 (2 x overlapping t), 26.5 (t), 28.4 (t), 28.7 (t), 45.1 (d), 72.2 (d). Data in agreement with commercially available sample.

**3,3-Dimethylbutan-2-ol:** Enantiomeric excess and conversion by GC analysis (Chrompac cyclodextrin-\( \beta \)-236M-19 50m, \( T = 80 \text{ °C, P = 7 psi, ketone 5.5 min., R isomer 8.7 min., S isomer 8.9 min;}\); \([\alpha]_D^{23}\) +2.0 (c 0.9 in CCl₄) 63% ee (\( S \)) (lit.\(^8\) \([\alpha]_D^{29} -43.0\) (c 1.5 in CCl₄) 99% ee (\( R \)); \( \delta_H(400 \text{ MHz; CDCl}_3; \text{Me}_4\text{Si}) 0.89\) (9 H, s), 1.12 (3 H, d, \( J 6.5 \)), 1.58-1.82 (1 H, br s), 3.44-3.52 (1 H, m); \( \delta_C(100.6 \text{ MHz; CDCl}_3; \text{Me}_4\text{Si}) 17.8\) (q), 25.4 (3 x q), 34.9 (s), 75.6 (d). Data in agreement with commercially available sample.

**1-Adamantanylethanol:** Enantiomeric excess by GC analysis (Chiracel \( \beta \)-DEX-120 25m, \( T = 115 \text{ °C, P = 48 psi, R isomer 57.1 min., S isomer 58.4 min;}\), conversion by \(^1\text{H-}\)NMR; \([\alpha]_D^{18}\) +0.4 (c 1.5 in CHCl₃) 12% ee (\( R \)) (lit.\(^9\) \([\alpha]_D^{25} -1.6\) (c 2.2 in CHCl₃) 99.8% ee (\( S \)); \( \delta_H(400 \text{ MHz; CDCl}_3; \text{Me}_4\text{Si}) 1.10\) (3 H, d, \( J 6.5 \)), 1.32 (1 H, br s), 1.45-1.75 (12 H, m), 1.96-2.02 (3 H, m), 3.28 (1 H, q, \( J 6.5 \)); \( \delta_C(100.6 \text{ MHz; CDCl}_3; \text{Me}_4\text{Si}) 16.5\) (q), 28.4 (3 x d), 36.6 (s), 37.3 (3 x t), 37.7 (3 x t), 75.8 (d). Data in agreement with commercially available sample.

**1-Cyclohexylpropan-1-ol:** Enantiomeric excess and conversion by GC analysis (Chrompac cyclodextrin-\( \beta \)-236M-19 50m, \( T = 100 \text{ °C, P = 15 psi, ketone 19.9 min., S isomer 31.5 min., R isomer 32.1 min;}\); \([\alpha]_D^{23}\) -1.92 (c 0.65 in CHCl₃) 28% ee (\( S \)) (lit.\(^10\) \([\alpha]_D^{25} -3.9\) (c 3.05 in CHCl₃) 99% ee (\( S \)); \( \delta_H(400 \text{ MHz; CDCl}_3; \text{Me}_4\text{Si}) 0.95\) (3 H, t, \( J 7.4 \)), 0.99-1.82 (14 H, m), 3.25-3.30 (1 H, m); \( \delta_C(100.6 \text{ MHz; CDCl}_3; \text{Me}_4\text{Si}) 10.2\) (q), 26.2 (t), 26.4 (t), 26.6 (t), 26.8 (t), 27.7 (t), 29.3 (t), 77.6 (d).
Octan-2-ol: Enantiomeric excess and conversion by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, T = 70 °C, P = 10 psi, ketone 29.3 min., R isomer 54.1 min., S isomer 55.1 min.); [α]D^23 +3.31 (c 0.65 in CHCl₃) 24% ee (S) (lit.11 [α]D^25 +9.0 (c 1.23 in CHCl₃) 99% ee (S)); δH(400 MHz; CDCl₃; Me₄Si) 0.89 (3 H, t, J 6.8), 1.18 (3 H, d, J 6.3), 1.27-1.47 (10 H, m), 1.57 (1 H, br s), 3.78 (1 H, m, CHOH); δC(100.6 MHz; CDCl₃; Me₄Si) 14.1 (q), 22.6 (t), 23.4 (q), 25.7 (t), 29.3 (t), 31.8 (t), 39.4 (t), 68.1 (d).

Cyclohexylphenylmethanol: Enantiomeric excess and conversion by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, T = 160 °C, P = 10 psi, ketone 26.0 min., S isomer 35.3 min., R isomer 35.8 min.); mp 62 °C, [α]D^22 +30.3 (c 0.4 in ether) 85% ee (R) (lit.12 [α]D^25 -36.0 (c 2.25 in ether) 80% ee (S)); δH(400 MHz; CDCl₃; Me₄Si) 0.90-1.99 (12 H, m), 4.35 (1 H, d, J 7.0), 7.19-7.35 (5 H, m); δC(100.6 MHz; CDCl₃; Me₄Si) 26.0 (t), 26.1 (t), 26.4 (t), 28.9 (t), 29.3 (t), 45.0 (d), 79.4 (d), 126.7 (d), 127.4 (d), 128.2 (d), 143.7 (s).

1-Phenylpropan-1-ol: Enantiomeric excess and conversion by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, T = 115 °C, P = 15 psi, ketone 13.6 min., R isomer 20.8 min., S isomer 21.9 min.); [α]D^20 +47.0 (c 1.4 in CHCl₃) 95% ee (R) (lit.11 [α]D^25 -47.2 (c 0.65 in CHCl₃) 99% ee (S)); δH(400 MHz; CDCl₃; Me₄Si) 0.90 (3 H, t, J 7.5), 1.75 (2 H, dq, J 7.5 and 6.5), 1.98 (1 H, br s), 4.57 (1 H, t, J 6.5), 7.24-7.36 (5 H, m); δC(100.6 MHz; CDCl₃; Me₄Si) 10.2 (q), 31.9 (t), 76.0 (d), 126.0 (2 x d), 127.5 (d), 128.4 (2 x d), 144.6 (s).

2-Methyl-1-phenylpropan-1-ol: Enantiomeric excess and conversion by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, T = 120 °C, P = 15 psi, ketone 12.5 min., R isomer 22.4 min., S isomer 22.9 min.); [α]D^20 +39.3 (c 1.25 in ether) 86% ee (R) (lit.11 [α]D^25 -49.1 (c 0.85 in ether) 99% ee (S)); δH(400 MHz; CDCl₃; Me₄Si) 0.99 (3 H, d, J 6.8), 0.99 (3 H, d, J 6.8), 1.91 (1 H, d, J 2.4), 1.95 (1 H, dq, J 7.0, 6.8 and 6.8), 4.34 (1 H, dd, J 7.0 and 2.4), 7.23-7.36 (5 H, m); δC(100.6 MHz; CDCl₃; Me₄Si) 19.0 (2 x q), 35.3 (d), 80.0 (d), 126.6 (2 x d), 127.4 (d), 128.2 (2 x d), 143.7 (s).
**2,2-Dimethyl-1-phenylpropan-1-ol:** Enantiomeric excess and conversion by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, T = 125 °C, P = 15 psi, ketone 12.0 min., S isomer 24.2 min., R isomer 24.8 min.); $[\alpha]_D^{20} +27.0$ (c 1.15 in ether) 78% ee (R) (lit. $[\alpha]_D^{25} +31.0$ (c 4.4 in ether) 87% ee (R)); $\delta_H$(400 MHz; CDCl$_3$; Me$_4$Si) 0.92 (9 H, s), 1.88 (1 H, d, J 2.8), 4.38 (1 H, d, J 2.8), 7.24-7.32 (5 H, m); $\delta_C$(100.6 MHz; CDCl$_3$; Me$_4$Si) 26.0 (3 x q), 35.6 (s), 82.4 (d), 127.3 (d), 127.6 (overlapping d and 2 x d), 142.2 (s).

**Cyclopropylphenylmethanol:** Enantiomeric excess and conversion by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, T = 125 °C, P = 15 psi, ketone 19.8 min., R isomer 30.0 min., S isomer 30.9 min.); $[\alpha]_D^{20} +23.0$ (c 1.25 in CHCl$_3$) 78% ee (S) (lit. $[\alpha]_D^{27} -28.3$ (c 1.0 in CHCl$_3$) 96% ee (R)); $\delta_H$(400 MHz; CDCl$_3$; Me$_4$Si) 0.31-0.64 (4 H, m), 1.18 (1 H, m), 2.31 (1 H, br s), 3.97 (1 H, d, J 8.3), 7.22-7.41 (5 H, m); $\delta_C$(100.6 MHz; CDCl$_3$; Me$_4$Si) 2.8 (t), 3.6 (t), 21.0 (d), 78.5 (d), 126.1 (2 x d), 127.5 (d), 128.4 (2 x d), 143.9 (s).

**Cyclobutylphenylmethanol:** Enantiomeric excess and conversion by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, T = 130 °C, P = 15 psi, ketone 26.2 min., R isomer 38.3 min., S isomer 38.9 min.); $[\alpha]_D^{24} -35.0$ (c 0.8 in CHCl$_3$) 87% ee (S) (lit. $[\alpha]_D^{27} -29.7$ (c 0.05 in CHCl$_3$) 82% ee (S)); $\delta_H$(400 MHz; CDCl$_3$; Me$_4$Si) 1.76-2.12 (7 H, m), 2.63 (1 H, d, quintet, J 8.0 and 7.5), 4.57 (1 H, d, J 8.0), 7.24-7.33 (5 H, m); $\delta_C$(100.6 MHz; CDCl$_3$; Me$_4$Si) 17.8 (t), 24.4 (t), 24.9 (t), 42.5 (d), 78.4 (d), 126.2 (2 x d), 127.5 (d), 128.3 (2 x d), 143.2 (s).

**Cyclopentylphenylmethanol:** $[\alpha]_D^{20} -40.0$ (c 0.8 in CHCl$_3$) 78% ee (S) (lit. $[\alpha]_D$ (+) sign of rotation consistent with R isomer; $\delta_H$(400 MHz; CDCl$_3$; Me$_4$Si) 1.14 (1 H, m), 1.35 (1 H, m), 1.43-1.70 (5 H, m), 1.87 (1 H, m), 2.09 (1 H, br s), 2.19 (1 H, d, quintet, J 8.3 and 8.3), 4.36 (1 H, d, J 8.3), 7.22-7.32 (5 H, m); $\delta_C$(100.6 MHz; CDCl$_3$; Me$_4$Si) 25.4
1-(2-Methoxyphenyl)-ethanol 10: Enantiomeric excess and conversion by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, T = 140 °C, P = 15 psi, ketone 12.9 min., S isomer 14.9 min., R isomer 15.4 min.); \([\alpha]_D^{22}\) -37.2 (c 0.85 in toluene) 70% ee (S) (lit.\(^9\) \([\alpha]_D^{25}\) -57.5 (c 0.45 in toluene) 95% ee (S)); \(\delta_H(400 \text{ MHz}; \text{CDCl}_3; \text{Me}_4\text{Si})\) 1.42 (3 H, d, \(J\) 6.5), 2.63 (1 H, d, \(J\) 5.3), 3.77 (3 H, s), 5.01 (1 H, dt, \(J\) 6.5 and 5.3), 6.79 (1 H, d, \(J\) 8.3), 6.88 (1 H, dd, \(J\) 7.5 and 7.5), 7.16 (1 H, ddd, \(J\) 8.3, 7.5 and 1.5), 7.26 (1 H, dd, \(J\) 7.5 and 1.5); \(\delta_C(100.6 \text{ MHz}; \text{CDCl}_3; \text{Me}_4\text{Si})\) 22.9 (q), 55.3 (q), 66.5 (d), 110.5 (d), 120.8 (d), 126.1 (d), 128.3 (d), 133.5 (s), 156.6 (s).

1-(3-Methoxyphenyl)-ethanol 11: Enantiomeric excess and conversion by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, T = 140 °C, P = 15 psi, ketone 13.0 min., R isomer 18.1 min., S isomer 18.6 min.); \([\alpha]_D^{22}\) -30.9 (c 0.85 in MeOH) 94% ee (S) (lit.\(^11\) \([\alpha]_D^{25}\) -34.9 (c 0.85 in MeOH) >99% ee (S)); \(\delta_H(400 \text{ MHz}; \text{CDCl}_3; \text{Me}_4\text{Si})\) 1.45 (3 H, d, \(J\) 6.5), 2.34 (1 H, br s), 3.77 (3 H, s), 4.81(1 H, q, \(J\) 6.5), 6.79 (1 H, ddd, \(J\) 8.3, 2.5 and 0.8), 6.90-6.92 (2 H, m), 7.23 (1 H, dd, \(J\) 8.3 and 8.3); \(\delta_C(100.6 \text{ MHz}; \text{CDCl}_3; \text{Me}_4\text{Si})\) 25.2 (q), 55.2 (q), 70.3 (d), 110.9 (d), 112.9 (d), 117.7 (d), 129.5 (d), 147.7 (s), 159.8 (s).

1-(4-Methoxyphenyl)-ethanol 12: Enantiomeric excess and conversion by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, T = 130 °C, P = 15 psi, ketone 25.9 min., R isomer 27.0 min., S isomer 27.5 min.); \([\alpha]_D^{22}\) -36.4 (c 1.5 in EtOH) 94% ee (S) (lit.\(^9\) \([\alpha]_D^{25}\) -26.9 (c 0.2 in EtOH) 88% ee (S)); \(\delta_H(300 \text{ MHz}; \text{CDCl}_3; \text{Me}_4\text{Si})\) 1.46 (3 H, d, \(J\) 6.4), 2.39 (1 H, br s), 3.79 (3 H, s), 4.83 (1 H, q, \(J\) 6.4), 6.87 (2 H, d, \(J\) 8.7), 7.28 (2 H, d, \(J\) 8.7); \(\delta_C(75.5 \text{ MHz}; \text{CDCl}_3; \text{Me}_4\text{Si})\) 24.8 (q), 55.0 (q), 69.8 (d), 113.6 (2 x d), 126.5 (2 x d), 137.8 (s), 158.7 (s).

(Tetrahydro-2H-pyran-4-yl)(phenyl)methanol 13: \(^2\) Enantiomeric excess by HPLC analysis (Chialcel OD-H, 10% iso-propanol/hexane (0.8 mL min\(^{-1}\)), ketone 6.1 min., S isomer 7.4 min., R isomer 8.8 min.), conversion by \(^1\)H-NMR; \([\alpha]_D^{26}\) -37.1 (c 1.85 in
tert-Butyl-4-(hydroxy(phenyl)methyl)piperidine-1-carboxylate 14: Enantiomeric excess by HPLC analysis (Chiralcel OD-H, 10% iso-propanol/hexane (0.8 mL min⁻¹), S isomer 6.7 min., R isomer 8.2 min.), conversion by ¹H-NMR; [α]D²⁴ -3.1 (c 2.3 in CHCl₃) 93% ee (S); νmax/cm⁻¹ (thin film) 3419 (OH), 1666 (C=O), 760 and 701 (Ph); δH(400 MHz; CDCl₃; Me₄Si) 1.08-1.31 (3 H, m), 1.44 (9 H, s), 1.74 (1 H, m), 1.85 (1 H, br s), 1.97 (1 H, m), 2.52-2.71 (2 H, m), 3.97-4.22 (2 H, m), 4.38 (1 H, d, J 7.5), 7.28-7.38 (5 H, m); δC(100.6 MHz; CDCl₃; Me₄Si) 28.4 (2 x t), 31.6 (t), 42.6 (d), 53.3 (t), 53.4 (t), 60.0 (t), 78.0 (d), 115.3 (dd, J C-F 21.2), 126.6 (2 x d), 127.7 (d), 128.4 (2 x d), 130.1 (dd, J C-F 8.0), 134.7 (s), 143.1 (s), 161.5 (d, J C-F 244.3). Found (CI) 312.1764 [M-H]⁺, C₂₀H₂₃NOF requires 312.1764 (0.2 ppm error); m/z (CI) 314 (MH⁺, 100%), 204 (90).

{1-[2-(4-Fluorophenyl)-ethyl]-piperidin-4-yl}-phenylmethanol 15: Enantiomeric excess by ¹H-NMR of carbinyl proton¹⁶ of MTPA ester derivative (R alcohol derivative δH 4.07, S alcohol derivative δH 4.14), conversion by ¹H-NMR; [α]D²⁵ -16.0 (c 0.05 in MeOH) 91% ee (S); νmax/cm⁻¹ (solid) 3161 (OH), 764 and 700 (Ph); δH(400 MHz; CDCl₃; Me₄Si) 1.28-1.68 (4 H, m), 2.05-2.21 (3 H, m), 2.63-2.67 (2 H, m), 2.84-2.88 (2 H, m), 3.06 (1 H, m), 3.20 (1 H, m), 4.37 (1 H, d, J 6.8), 6.95 (2 H, dd, J 8.8 and 8.5), 7.12 (2 H, dd, J 8.5 and 5.3), 7.24-7.34 (5 H, m); δC(100.6 MHz; CDCl₃; Me₄Si) 27.5 (2 x t), 31.6 (t), 42.6 (d), 53.3 (t), 53.4 (t), 60.0 (t), 78.0 (d), 115.3 (dd, J C-F 21.2), 126.6 (2 x d), 127.7 (d), 128.4 (2 x d), 130.1 (dd, J C-F 8.0), 134.7 (s), 143.3 (s), 161.5 (d, J C-F 244.3). Found (Cl) 312.1764 [M-H]⁺, C₂₀H₂₃NOF requires 312.1764 (0.2 ppm error); m/z (Cl) 314 (MH⁺, 100%), 204 (90).

(2,3-Dimethoxyphenyl)-{1-[2-(4-fluorophenyl)-ethyl]-piperidin-4-yl}-methanol 16: Enantiomeric excess by HPLC analysis (Chiralcel OD-H, 10% iso-propanol/hexane (0.8
mL min⁻¹), ketone 10.6 min., \( R \) isomer 11.2 min., \( S \) isomer 12.6 min.), conversion by \(^1\)HNMR; \([\alpha]_D^{25}\) -11.5 (c 0.2 in MeOH) 65% ee (\( S \)) (lit. \(^4\) \([\alpha]_D^{22}\) +21.6 (c 2.15 in MeOH) 98% ee (\( R \)); \( \delta_H \) (400 MHz; CDCl₃; Me₄Si) 1.25-1.54 (3 H, m), 1.67 (1 H, m), 1.86-2.10 (3 H, m), 2.50-2.54 (2 H, m), 2.74-2.78 (2 H, m), 2.85-2.96 (2 H, m), 3.08 (1 H), 3.86 (6 H, m), 4.64 (1 H, d, \( J \) 8.0), 6.83-7.14 (7 H, m); \( \delta_C \) (100.6 MHz; CDCl₃; Me₄Si) 28.7 (2 x t), 32.8 (t), 42.8 (d), 53.7 (2 x t), 55.7 (q), 60.8 (t), 60.9 (q), 74.4 (d), 111.4 (d), 115.1 (dd, \( J_C-F \) 21.1), 119.7 (d), 124.0 (d), 130.0 (dd, \( J_C-F \) 7.7), 136.1 (dd, \( J_C-F \) 3.1), 136.4 (s), 146.5 (s), 152.5 (s), 161.4 (dd, \( J_C-F \) 243.5).

**1-(Pyridin-4-yl)ethanol 17**: Enantiomeric excess and conversion by GC analysis (Chrompac cyclodextrin-\( \beta \)-236M-19 50m, \( T \) = 130 °C, \( P \) = 10 psi, ketone 7.9 min., \( R \) isomer 11.4 min., \( S \) isomer 11.6 min.); \([\alpha]_D^{25}\) -48.1 (c 0.45 in EtOH) 83% ee (\( S \)) (lit. \(^17\) \([\alpha]_D^{26}\) -58.3 (c 0.5 in EtOH) 100% ee (\( S \)); \( \delta_H \) (400 MHz; CDCl₃; Me₄Si) 1.48 (3 H, d, \( J \) 6.5), 4.47 (1 H, br s), 4.88 (1 H, q, \( J \) 6.5), 7.29 (1 H, d, \( J \) 5.8), 8.52 (1 H, d, \( J \) 5.8); \( \delta_C \) (100.6 MHz; CDCl₃; Me₄Si) 25.1 (q), 68.4 (d), 120.6 (2 x d), 149.3 (2 x d), 155.8 (s).

**1-(Pyridin-3-yl)ethanol 18**: Enantiomeric excess and conversion by GC analysis (Chrompac cyclodextrin-\( \beta \)-236M-19 50m, \( T \) = 130 °C, \( P \) = 10 psi, ketone 8.2 min., \( R \) isomer 11.8 min., \( S \) isomer 12.1 min.); \([\alpha]_D^{25}\) -42.9 (c 0.15 in EtOH) 72% ee (\( S \)) (lit. \(^17\) \([\alpha]_D^{24}\) -56.3 (c 1.0 in EtOH) 100% ee (\( S \)); \( \delta_H \) (400 MHz; CDCl₃; Me₄Si) 1.47 (3 H, d, \( J \) 6.5), 4.68 (1 H, br s), 4.88 (1 H, q, \( J \) 6.5), 7.23 (1 H, dd, \( J \) 7.8 and 4.8), 7.73 (1 H, ddd, \( J \) 7.8, 2.0 and 1.8), 8.32 (1 H, dd, \( J \) 4.8 and 1.8), 8.42 (1 H, d, \( J \) 2.0); \( \delta_C \) (100.6 MHz; CDCl₃; Me₄Si) 25.1 (q), 67.3 (d), 123.6 (d), 133.7 (d), 142.0 (s), 146.9 (d), 147.8 (d).

**1-(Pyridin-2-yl)ethanol 19**: Enantiomeric excess and conversion by GC analysis (Chrompac cyclodextrin-\( \beta \)-236M-19 50m, \( T \) = 100 °C, \( P \) = 15 psi, ketone 11.8 min., \( R \) isomer 22.5 min., \( S \) isomer 23.0 min.); \([\alpha]_D^{24}\) -54.2 (c 0.65 in CHCl₃) 94% ee (\( S \)) (lit. \(^17\) \([\alpha]_D^{25}\) -58.3 (c 0.5 in EtOH) 96% ee (\( S \)); \( \delta_H \) (400 MHz; CDCl₃; Me₄Si) 1.51 (3 H, d, \( J \) 6.5), 4.38 (1 H, br s), 4.90 (1 H, q, \( J \) 6.5), 7.19 (1 H, dd, \( J \) 7.3 and 4.9), 7.30 (1 H, d, \( J \)
8.0), 7.68 (1 H, ddd, J 8.0, 7.3 and 1.8), 8.52 (1 H, d, J 4.9); δ_C(100.6 MHz; CDCl₃; Me₄Si) 24.2 (q), 68.9 (d), 119.8 (d), 122.2 (d), 136.8 (d), 148.1 (d), 163.2 (s).

1-(Furan-2-yl)ethanol 20: Enantiomeric excess and conversion by GC analysis (Chrompack cyclodextrin-β-236M-19 50m, T = 100 °C, P = 10 psi, ketone 9.5 min., R isomer 11.9 min., S isomer 12.2 min.); [α]_D²⁵ -19.7 (c 0.8 in CHCl₃) 98% ee (S) (lit.¹⁷ [α]_D²⁴ -20.1 (c 1.0 in CHCl₃) 99% ee (S)); δ_H(400 MHz; CDCl₃; Me₄Si) 1.53 (3 H, d, J 6.5), 2.79 (1 H, br s), 4.87 (1 H, q, J 6.5), 6.22 (1 H, d, J 3.3), 6.32 (1 H, dd, J 3.3 and 1.8), 7.36 (1 H, dd, J 1.8 and 0.8); δ_C(75.5 MHz; CDCl₃; Me₄Si) 21.0 (q), 63.3 (d), 104.9 (d), 109.9 (d), 141.7 (d), 157.3 (s).

1-(Thiophen-2-yl)ethanol 21: Enantiomeric excess and conversion by GC analysis (Chrompack cyclodextrin-β-236M-19 50m, T = 125 °C, P = 10 psi, ketone 12.2 min., R isomer 14.6 min., S isomer 14.9 min.); [α]_D²⁴ -26.2 (c 1.65 in CHCl₃) 97% ee (S) (lit.¹⁷ [α]_D²⁴ -26.0 (c 1.0 in CHCl₃) 99% ee (S)); δ_H(400 MHz; CDCl₃; Me₄Si) 1.59 (3 H, d, J 6.5), 2.19 (1 H, br s), 5.11 (1 H, q, J 6.5), 6.94-6.97 (2 H, m), 7.22 (1 H, dd, J 4.8 and 1.8); δ_C(100.6 MHz; CDCl₃; Me₄Si) 25.3 (q), 66.3 (d), 123.2 (d), 124.4 (d), 126.7 (d), 149.9 (s).

4-Phenylbut-3-yn-2-ol 22: Enantiomeric excess by HPLC analysis (Chialcel OD-H, 10% iso-propanol/hexane (0.5 mL min⁻¹), ketone 9.0 min., R isomer 11.1 min., S isomer 28.7 min.), conversion by ¹H-NMR; [α]_D²⁴ -30.8 (c 0.4 in CHCl₃) 89% ee (S) (lit.¹⁸ [α]_D²³ -35.0 (c 1.0 in CHCl₃) 97% ee (S)); δ_H(400 MHz; CDCl₃; Me₄Si) 1.55 (3 H, d, J 6.5), 2.07 (1 H, br s), 4.76 (1 H, q, J 6.5), 7.27-7.30 (3 H, m), 7.38-7.41 (2 H, m); δ_C(100.6 MHz; CDCl₃; Me₄Si) 24.4 (q), 58.9 (d), 84.0 (s), 91.0 (s), 122.6 (s), 128.3 (2 x d), 128.4 (d), 131.7 (2 x d).

(1H-Imidazol-1-yl)(phenyl)methanol 28: Enantiomeric excess by HPLC analysis (Chialcel OD-H, 20% iso-propanol/hexane (0.8 mL min⁻¹), S isomer 19.1 min., R isomer 21.7 min.), conversion by ¹H-NMR; [α]_D²⁴ -42.8 (c 0.4 in EtOH) 99% ee (R) (lit.⁵ [α]_D²⁵
\[+46.1 \text{ (c 0.98 in EtOH) 97\% ee (S)}; \delta_H(400 MHz; DMSO-d_6) 4.07 \text{ (1 H, dd, } J 13.8 \text{ and 7.8)}, 4.17 \text{ (1 H, dd, } J 13.8 \text{ and 4.0)}, 4.85 \text{ (1 H, dd, } J 7.8 \text{ and 4.0)}, 6.86 \text{ (1 H, m), 7.14 \text{ (1 H, m), 7.25-7.40 (5 H, m, Ph), 7.53 \text{ (1 H, d, } J 2.0)}; \delta_C(100.6 MHz; DMSO-d_6) 53.6 \text{ (t), 72.0 (d), 120.1 (d), 126.0 (2 x d), 127.3 (d), 127.5 (d), 128.1 (2 x d), 137.7 (d), 142.5 (s).}

\text{(2,4-Dichlorophenyl)(1H-imidazol-1-yl)methanol 29}: \text{ Enantiomeric excess by HPLC analysis (Chialcel AD, 10\% iso-propanol/hexane (0.8 mL min}^{-1}), S isomer 9.4 \text{ min.}, R isomer 14.2 \text{ min.}, \text{ conversion by } ^1H-NMR; [\alpha]_D^{25} -28.1 \text{ (c 0.55 in MeOH) 71\% ee (R) (lit.}^5 [\alpha]_D^{25} +83.8 \text{ (c 1.0 in MeOH) 91\% ee (S)}; \delta_H(400 MHz; DMSO-d_6) 4.08 \text{ (1 H, dd, } J 14.2 \text{ and 7.0), 4.20 \text{ (1 H, dd, } J 14.2 \text{ and 3.3), 5.11 \text{ (1 H, dd, } J 7.0 \text{ and 3.3), 6.86 \text{ (1 H, m), 7.07 \text{ (1 H, m), 7.40-7.52 (3 H, m), 7.58 \text{ (1 H, d, } J 2.0)); }\delta_C(100.6 MHz; DMSO-d_6) 51.6 \text{ (t), 68.6 (d), 120.1 (d), 127.4 (d), 127.7 (d), 128.4 (d), 129.4 (d), 131.8 (s), 132.7 (s), 137.7 (d), 138.6 (s).}

\text{2-Chloro-1-phenyl ethanol 31 and 2-phenoxy-1-phenylethanol 33}: \text{ These compounds have recently been analysed in very recent work in this group, and the results in this work were obtained by comparison of chiral GC and HPLC to the prior work.}^19 \text{ The best optimized result for 31 (Table 3, entry 6, 97\% e.e.) relates to the use of EtOAC co-solvent at a ratio of 1.4 mL EtOAc per 1 mL FA/TEA(5:2). Reduction without the addition of EtOAc gave a product of 95\% e.e. after a reaction time of 1 hr 30 min (full conversion).}

\text{Kinetic studies using NMR}: \text{ A solution of dimer 9 (7mg, 0.0053 mmol, 0.25mol\% relative to ketone) was dissolved in FA/TEA (5:2, 1 mL) and d6 benzene (0.05 mL) was added. The NMR signal was locked to the d6-benzene and, 30 minutes after making up the solution, acetophenone (0.23 mL, 0.25mg, 2.13 mmol) was added. Upon addition of ketone, time was set to zero. NMR spectra were obtained at fixed intervals following the addition of ketone.}

\text{Procedure for repeated-charging experiment}: \text{ A solution of dimer 9 (10.4mg, 0.0079 mmol) in FA/TEA (5:2, 1.5 mL) and acetophenone (0.35 mL, 0.38 mg, 3.16 mmol) was}
stirred for a fixed time (ca 2-3 h) at 40°C after which a sample was taken and analysed by chiral GC. A further portion of acetophenone (0.35 mL, 0.38 mg, 3.16 mmol) was added to the reaction along with 0.11 mL formic acid. The analysis/addition process was repeated at the intervals indicated in Figure 3.
1H NMR of compound 35:
1H NMR of compound 36:
13C NMR of compound 36:
1H NMR of compound 37:
13C NMR of compound 37.

*** Current Data Parameters ***
NAME : dec07-1
EXPNO : 30
PROCNO : 1

*** Acquisition Parameters ***
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DATE_A : Dec 07 2004
LOCNUC : 2H
NS : 512
NUC1 : 13C
NUC2 : 1H
O1 : 10.05870 Hz
PROBHD : 5 mm Dual 13C/1H TS240A
RG : 49.96,000000
SFO1 : 100.5976527 MHz
SFO2 : 400.916589 MHz
SW : 249.7655 ppm
SW_p : 15125.628 Hz
TD : 65336

*** Processing Parameters ***
AUNMP : proc_Jdk
GB : 0.0600000
LB : 2.60 Hz
WDB : EM
1H NMR of compound 39:
13C NMR of compound 39:
1H NMR of compound 34:
13C NMR of compound 34:
1H NMR of compound 40:
13C NMR of compound 40:
1H NMR of compound 41:
NMR of compound 41:

*** Current Data Parameters ***
NAME : mnr01-l
EXPNO : 20
PROCNO : 1

*** Acquisition Parameters ***
B1 : 199.3876240 MHz
DATE : 04/32.29
DATE_d : Mar 04 2005
DS : 4
LOCNLC : 2H
NS : 512
NUC1 : 1H
NUC2 : 1H
O1 : 100.3370 Hz
PULPROG : pendant
DNP : 1
RG : 4000.0000000
SW : 249.7635 ppm
TD : 65536

*** Processing Parameters ***
GB : 0.0000000
LB : 2.00 Hz
SI : 65536
TDoff : 65536
WOW : 128
References


