Supplementary Information

Ammonium-directed dihydroxylation: metal-free synthesis of the diastereoisomers of 3-amino-cyclohexane-1,2-diol

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Experimental

General Experimental

Reactions involving moisture-sensitive reagents were carried out under a nitrogen or argon atmosphere using standard vacuum line techniques and glassware that was flame dried and cooled under nitrogen before use. Solvents were dried according to the procedure outlined by Grubbs and co-workers.[1] Water was purified by an Elix® UV-10 system. All other solvents were used as supplied (analytical or HPLC grade) without prior purification. Organic layers were dried over $MgSO_4$. Thin layer chromatography was performed on aluminium plates coated with 60 F_{254} silica. Plates were visualised using UV light (254 nm), iodine, 1% aq $KMnO_4$, or 10% ethanolic phosphomolybdic acid. Flash column chromatography was performed either on Kieselgel 60 silica on a glass column, or on a Biotage SP4 automated flash column chromatography platform.

Melting points were recorded on a Gallenkamp Hot Stage apparatus and are uncorrected. IR spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer as either a thin film on NaCl plates (film) or a KBr disc (KBr), as stated. Selected characteristic peaks are reported in cm^{-1}. NMR spectra were recorded on Bruker Avance spectrometers in the deuterated solvent stated. The field was locked by external referencing to the relevant deuteron resonance. Low-resolution mass spectra were recorded on either a VG MassLab 20-250 or a Micromass Platform 1 spectrometer. Accurate mass measurements were run on either a Bruker MicroTOF internally calibrated with polyalanine, or a Micromass GCT instrument fitted with a Scientific Glass Instruments BPX5 column (15 m × 0.25 mm) using amyl acetate as a lock mass.

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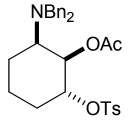
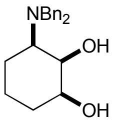
[1] A. B. Pangborn, M. A. Giardello, R. H. Grubbs, R. K. Rosen, F. J. Timmers, *Organometallics*, **1996**, *15*, 1518.

(1*RS*,2*RS*,3*RS*)-1-*p*-Toluenesulphonyloxy-2-acetoxy-3-*N*,*N*-dibenzylaminocyclohexane 10



Ac_2O (0.26 mL, 2.74 mmol) and DMAP (50 mg) were added sequentially to a stirred solution of **3** (851 mg, 1.83 mmol, >98% de) in DCM/pyridine (1:1, 40 mL). The resultant solution was stirred at rt for 24 h before being cooled to 0 °C. H_2O (50 mL) was added, the organic layer was separated and the aqueous layer was extracted with DCM (2 × 50 mL). The combined organic extracts were washed sequentially with 10% aq. $CuSO_4$ (2 × 100 mL), 0.1 M aq. $NaHCO_3$ (2 × 100 mL) and brine (100 mL), dried, and concentrated *in vacuo* to give **10** as a colourless oil (928 mg, quant, >98% de); ν_{max} (film) 2944 (C–H), 1746 (C=O); δ_H (400 MHz, $CDCl_3$) 1.47-1.88 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 1.99 (3H, s, CO*Me*), 2.48 (3H, s, ArCH_3), 2.94-3.04 (1H, m, C(3)*H*), 3.64 (4H, AB system, N(CH_2Ph)$_2$), 4.60-4.65 (1H, br m, C(1)*H*), 5.05-5.09 (1H, br m, C(2)*H*), 7.13-7.51 (12H, m, *Ar*, *Ph*), 7.64 (2H, d, *J* 7.6, *Ar*); δ_C (400 MHz, $CDCl_3$) 19.5, 21.2, 21.8, 22.8, 26.2 (*C*(4), *C*(5), *C*(6), CO*Me*, Ar*C*H_3), 53.6 (*C*(3)), 55.0 (N(*C*H_2Ph)$_2$), 71.1 (*C*(2)), 78.1 (*C*(1)), 126.8, 127.8, 128.2, 128.4, 129.8, 133.7, 140.2, 144.7 (*Ar*, *Ph*), 169.7 (C=O); *m/z* (ESI^+) 508 ($[M+H]^+$, 100%), 396 (50%); HRMS (ESI^+) $C_{29}H_{34}NO_5S^+$ ($[M+H]^+$) requires 508.2152; found 508.2153.

(1*RS*,2*SR*,3*SR*)-3-*N*,*N*-dibenzylaminocyclohexane-1,2-diol 11

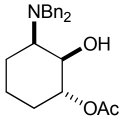


Method A: $CaCO_3$ (1.88 g, 18.8 mmol) was added to a stirred solution of **10** (9.93 g, 18.8 mmol, 90% de) in EtOH/H_2O (6:1, 236 mL) and the resultant suspension was heated at reflux for 48 h. The reaction mixture was concentrated *in vacuo*. H_2O (200 mL) was added to the residue and the mixture was extracted with DCM (3 × 200 mL). The combined organic extracts were dried and concentrated *in vacuo*. The residue was dissolved in MeOH (50 mL) and K_2CO_3 (200 mg) was added. The resulting suspension was stirred at rt for 16 h then concentrated *in vacuo*. H_2O (100 mL) was added and the mixture was extracted with DCM (3 × 100 mL). The combined organic extracts were washed sequentially with H_2O (2 × 250 mL) and brine (250 mL), dried, and concentrated *in vacuo*. Purification *via* flash column chromatography (gradient elution, 5%→100% EtOAc in 40-60 °C petrol) gave **14** as a pale yellow solid (215 mg, 4%, >98% de); mp 103-104 °C; ν_{max} (KBr) 3449 (O–H), 2936 (C–H); δ_H (400 MHz, $CDCl_3$) 1.22-1.47 (2H, m, C(4)H_A, C(6)H_A), 1.57-1.81 (2H, m, C(5)H_2), 1.88-2.09 (2H, m, C(4)H_B, C(6)H_B), 2.41 (2H, br s, 2 × O*H*), 2.91-3.05 (1H, m, C(3)*H*), 3.44 (2H, d, *J* 13.4, N(C$H_A$$H_B$Ph)$_2$), 3.52 (1H, dd, *J* 10.1, 3.0, C(2)*H*), 3.88 (2H, d, *J* 13.4, N(C$H_A$$H_B$Ph)$_2$), 4.14 (1H, q, *J* 3.0, C(1)*H*), 7.24-7.49 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.5 (*C*(5)), 22.1

(*C*(4)), 29.6 (*C*(6)), 53.1, 53.6 (N(CH$_2$Ph)$_2$), 57.4 (*C*(3)), 68.3 (*C*(1)), 71.0 (*C*(2)), 128.2 (*p-Ph*), 128.5, 128.9 (*o-*, *m-Ph*), 139.3 (*i-Ph*); *m*/*z* (ESI$^+$) 312 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{20}H_{26}NO_2^+$ ([M+H]$^+$) requires 312.1958; found 312.1950. Further elution gave **11** as a pale yellow solid (3.48 g, 60%, >98% de); mp 62-63 °C; ν_{max} (KBr) 3416 (O–H), 2936 (C–H); δ_H (400 MHz, CDCl$_3$) 1.07-1.22 (1H, m, C(5)*H*$_A$), 1.52-1.82 (5H, m, C(4)*H*$_2$, C(5)*H*$_B$, C(6)*H*$_2$), 2.55-2.64 (1H, m, C(3)*H*), 2.80 (2H, br s, 2 × O*H*), 3.42 (1H, ddd, *J* 11.4, 5.0, 2.7, C(1)*H*), 3.81 (2H, d, *J* 16.0, N(C*H*$_A$H$_B$Ph)$_2$), 3.93 (2H, d, *J* 16.0, N(CH$_A$*H*$_B$Ph)$_2$), 4.25-4.29 (1H, m, C(2)*H*), 7.22-7.41 (10H, m, *Ph*); δ_C (100 MHz, CDCl$_3$) 22.0, 22.1 (*C*(4), *C*(5)), 28.4 (*C*(6)), 55.1 (N(*C*H$_2$Ph)$_2$), 60.6 (*C*(3)), 71.5, 71.8 (*C*(1), *C*(2)), 126.8 (*p-Ph*), 128.3, 128.4 (*o,m-Ph*), 140.6 (*i-Ph*); *m*/*z* (ESI$^+$) 312 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{20}H_{26}NO_2^+$ ([M+H]$^+$) requires 312.1958; found 312.1956. Further elution gave **5** as a viscous, pale yellow oil (760 mg, 13%, >98% de).

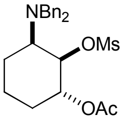
Method B: KOAc (216 mg, 2.21 mmol) was added to a stirred solution of **10** (747 mg, 1.47 mmol, >98% de) in EtOH/H$_2$O (6:1, 40 mL) and the resultant suspension was heated at reflux for 48 h. The reaction mixture was then concentrated *in vacuo*. H$_2$O (100 mL) was added to the residue and the mixture was extracted with DCM (3 × 100 mL). The combined organic extracts were dried and concentrated *in vacuo*. The residue was dissolved in MeOH (10 mL) and K$_2$CO$_3$ (100 mg) was added. The resulting suspension was stirred at rt for 16 h then concentrated *in vacuo*. H$_2$O (50 mL) was added and the mixture was extracted with DCM (3 × 50 mL). The combined organic extracts were washed sequentially with H$_2$O (2 × 100 mL) and brine (100 mL), dried, and concentrated *in vacuo*. Purification *via* flash column chromatography (gradient elution, 5%→100% EtOAc in 40-60 °C petrol) gave **4** as a colourless oil (16 mg, 4%, >98% de). Further elution gave **11** as a pale yellow solid (337 mg, 74%, >98% de). Further elution gave **5** as a viscous, pale yellow oil (31 mg, 7%, >98% de).

(1*RS*,2*RS*,3*RS*)-1-Acetoxy-2-hydroxy-3-*N*,*N*-dibenzylaminocyclohexane 15



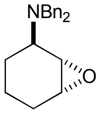
A stirred solution of **4** (5.79 g, 19.8 mmol) in AcOH (15 mL) was heated at 50 ºC for 24 h before being allowed to cool to rt. 0.1 M aq. NaHCO$_3$ (100 mL) was added and the mixture was extracted with DCM (3 × 100 mL). The combined organic extracts were washed with 0.1 M aq. NaHCO$_3$ (5 × 100 mL), dried and concentrated *in vacuo* to give **15** as a yellow solid (6.98 g, quant, >98% de); mp 57-58 °C; ν_{max} (KBr) 3456 (O–H), 2937 (C–H), 1717 (C=O); δ_H (400 MHz, CDCl$_3$) 1.42-1.86 (6H, m, C(4)*H*$_2$, C(5)*H*$_2$, C(6)*H*$_2$), 1.92 (3H, s, CO*Me*), 2.67 (1H, br s, O*H*), 2.88-2.94 (1H, m, C(3)*H*), 3.75 (2H, d, *J* 12.0, N(C*H*$_A$H$_B$Ph)$_2$), 3.84 (2H, d, *J* 12.0, N(CH$_A$*H*$_B$Ph)$_2$), 4.06 (1H, app t, *J* 3.2, C(2)*H*), 4.98-5.02 (1H, m, C(1)*H*), 7.19-7.44 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 20.2, 23.0, 24.6 (*C*(4), *C*(5), *C*(6)), 21.1 (CO*Me*), 54.8 (N(*C*H_2Ph)$_2$), 57.5 (*C*(3)), 68.0 (*C*(2)), 72.5 (*C*(1)), 126.9 (*p-Ph*) 128.3, 128.6 (*o*-, *m-Ph*), 140.1 (*i-Ph*), 170.1 (*C*OMe); *m*/*z* (ESI$^+$) 354 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{22}H_{28}NO_3^+$ ([M+H]$^+$) requires 354.2064; found 354.2059.

(1*RS*,2*RS*,3*RS*)-1-Acetoxy-2-methanesulphonyloxy-3-*N*,*N*-dibenzylaminocyclohexane 16



Et_3N (96 µL, 0.69 mmol), DMAP (5 mg) and MsCl (27 µL, 0.34 mmol) were added sequentially to a stirred solution of **15** (81 mg, 0.23 mmol) DCM (2 mL) at −10 °C. The reaction mixture was stirred at −10 °C for 48 h, after which time H_2O (1 mL) was added and the solution was allowed to warm to rt. The mixture was extracted with DCM (3 × 10 mL). The combined organic extracts were washed sequentially with 10% aq. $CuSO_4$ (3 × 30 mL), H_2O (3 × 30 mL) and 0.1 M aq. $NaHCO_3$ (3 × 30 mL), dried, and concentrated *in vacuo* to give **16** as a colourless oil (99 mg, quant, >98% de); ν_{max} (film) 3028, 2940 (C–H), 1740 (C=O); δ_H (400 MHz, $CDCl_3$); 1.44-1.95 (9H, m, C(4)*H*$_2$, C(5)*H*$_2$, C(6)*H*$_2$, CO*Me*), 2.98-3.04 (1H, m, C(3)*H*), 3.07 (3H, s, S*Me*), 3.73 (2H, d, *J* 14.2, N(C*H*$_A$H$_B$Ph)$_2$), 2.85-3.92 (2H, m, N(CH$_A$*H*$_B$Ph)$_2$), 4.94-4.99 (1H, br m, C(2)*H*), 5.06-5.12 (1H, br m, C(1)*H*), 7.14-7.49 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$); 20.2, 22.3, 24.5 (*C*(4), *C*(5), *C*(6)), 20.7 (CO*Me*), 38.9 (S*Me*), 53.8 (*C*(3)), 54.7 (N(*C*H_2Ph)$_2$), 70.1 (*C*(1)), 78.7 (*C*(2)), 126.9 (*p-Ph*), 128.2, 128.4 (*o*-, *m-Ph*), 140.1 (*i-Ph*), 169.5 (*C*OMe); *m*/*z* (ESI$^+$) 432 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{23}H_{30}NO_5S^+$ ([M+H]$^+$) requires 432.1839; found 432.1839.

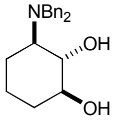
(1*RS*,2*SR*,3*RS*)-1,2-Epoxy-3-*N*,*N*-dibenzylamino-cyclohexane 17



K_2CO_3 (100 mg) was added to a stirred solution of **16** (126 mg, 0.29 mmol) in MeOH (5 mL). The resultant suspension was stirred for 16 h at rt before being concentrated *in vacuo*. H_2O (10 mL) was added and the mixture was extracted with DCM (3 × 10 mL). The combined organic extracts were washed sequentially with H_2O (2 × 10 mL) and brine (10 mL), dried, and concentrated *in vacuo*. Purification *via* flash column chromatography (gradient elution, 0%→100%, EtOAc in 40-60 °C petrol) gave **17** as a white solid (39 mg, 46%, >98% de); mp 48-49 °C; ν_{max} (film) 3061, 2937 (C–H); δ_H (400 MHz, $CDCl_3$) 1.16-1.36 (2H, m, C(4)*H*$_A$, C(5)*H*$_A$), 1.39-1.53 (1H, m, C(5)*H*$_B$), 1.57-1.73 (1H, m, C(6)*H*$_A$), 1.73-1.86 (1H, m, C(4)*H*$_B$), 2.05-2.14 (1H, m, C(6)*H*$_B$), 2.99-3.07 (1H, m, C(3)*H*), 3.21-3.25 (1H, m, C(1)*H*), 3.25-3.30 (1H, m, C(2)*H*), 3.75 (4H, AB system, N(C*H*$_2$Ph)$_2$), 7.23-7.49 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 16.1 (*C*(5)), 22.2 (*C*(4)), 25.2

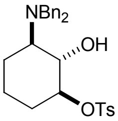
(*C*(6)), 53.1 (*C*(3)), 53.5 (*C*(1)), 54.8 (N(*C*H_2Ph)$_2$), 55.6 (*C*(2)), 127.0 (*p-Ph*), 128.3, 128.4, (*o*-, *m*,-*Ph*), 139.9 (*i-Ph*); *m*/*z* (ESI$^+$) 294 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{20}H_{24}NO^+$ ([M+H]$^+$) requires 294.1852; found 294.1849.

(1*RS*,2*RS*,3*SR*)-3-*N*,*N*-dibenzylaminocyclohexane-1,2-diol 18



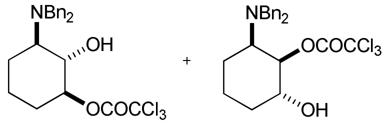
Concentrated H_2SO_4 (0.24 mL) in H_2O (1.4 mL) was added to a stirred solution of **17** (266 mg, 0.91 mmol) in 1,4-dioxane (1 mL) and the resultant mixture was stirred at rt for 16 h before being concentrated *in vacuo*. 0.1 M aq. NaHCO3 was added and the mixture was extracted with Et2O (4 × 10 mL). The combined organic extracts were washed with 0.1 M aq. NaHCO3 (3 × 40 mL), dried and concentrated *in vacuo*. Purification *via* flash column chromatography (gradient elution, 0%→100% EtOAc in 40-60 °C petrol) gave **18** as a pale yellow solid (124 mg, 44%, >98% de); mp 72-73 °C; ν_{max} (KBr) 3417 (O–H), 3061, 3027, 2938 (C–H); δ_H (400 MHz, $CDCl_3$) 1.11-2.00 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 2.37-2.48 (1H, m, C(3)*H*), 3.02 (1H, br s, O*H*), 3.31-3.48 (3H, m, C(2)*H*, N(C$H_A$$H_B$Ph)$_2$), 3.69-3.98 (4H, br m, C(1)*H*, N(CH$_A$$H_B$Ph)$_2$, O*H*), 7.23-7.41 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 21.6, 21.7, 31.5 (*C*(4), *C*(5), *C*(6)), 53.7 (N(*C*H_2Ph)$_2$), 55.0 (*C*(1)), 61.2 (*C*(3)), 74.7 (*C*(2)), 127.3 (*p-Ph*), 128.4, 128.6 (*o*, *m-Ph*), 139.2 (*i-Ph*); *m*/*z* (ESI$^+$) 312 ([M+H]$^+$, 100%); HRMS $C_{20}H_{26}NO_2^+$ ([M+H]$^+$) requires 312.1958; found 312.1962.

(1*RS*,2*RS*,3*SR*)-1-*p*-Toluenesulphonyloxy-2-hydroxy-3-*N*,*N*-dibenzylaminocyclohexane 19



TsOH (800 mg, 4.21 mmol) was added to a stirred solution of **17** (273 mg, 0.93 mmol) in DCM (10 mL) and the reaction mixture was then stirred at rt for 16 h. 0.1 M aq. $NaHCO_3$ (10 mL) was added, the organic layer was separated and the aqueous layer was extracted with DCM (3 × 10 mL). The combined organic extracts were washed with 0.1 M aq. $NaHCO_3$ (5 × 40 mL), dried and concentrated *in vacuo* to give **19** as a white solid (472 mg, quant, >98% de); mp 95-97 °C; ν_{max} (KBr) 3442 (O–H), 2950 (C–H); δ_H (400 MHz, $CDCl_3$) 1.08-1.37 (2H, m, C(4)H_A, C(5)H_A), 1.41-1.54 (1H, app qd *J* 12.0, 4.0 C(6)H_A), 1.75-1.86 (1H, m, C(5)H_B), 1.87-1.96 (1H, m, C(4)H_B), 2.02-2.16 (1H, m, C(6)H_B), 2.38-2.47 (4H, m, C(3)*H*, Ar*Me*), 3.36 (2H, d, *J* 13.3, N(CH_AH$_B$Ph)$_2$), 3.58 (2H, app t, *J* 9.6, C(2)*H*, O*H*), 3.83 (2H, d, *J* 13.3, N(CH$_A$$H_B$Ph)$_2$), 4.34 (1H, ddd, *J* 11.6, 8.5, 4.8, C(1)*H*), 7.21-7.34 (12H, m, *Ar*, *Ph*), 7.82 (2H, d, *J* 8.0, *Ar*); δ_C (100 MHz, $CDCl_3$) 21.4, 21.6, 31.0 (*C*(4), *C*(5), *C*(6), Ar*Me*), 53.6 (N(*C*H_2Ph)$_2$), 61.8 (*C*(3)), 71.3 (*C*(2)), 84.9 (*C*(1)), 127.4, 127.8, 128.5, 128.9, 129.5, 138.7 (*Ar*, *Ph*); *m*/*z* (ESI$^+$) 466 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{27}H_{32}NO_4S^+$ ([M+H]$^+$) requires 466.2047; found 466.2045.

(1*RS*,2*RS*,3*SR*)-1-Trichloroacetoxy-2-hydroxy-3-*N*,*N*-dibenzylaminocyclohexane 20



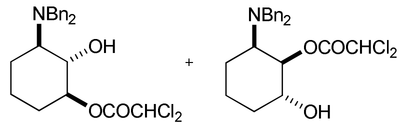
20 **21**

20:**21**, 80:20

Cl_3CCO_2H (59 mg, 0.358 mmol) was added to a stirred solution of **17** (70 mg, 0.24 mmol) in DCM (2 mL) and the reaction mixture was stirred at rt for 16 h. 0.1 M aq. $NaHCO_3$ (10 mL) was added, the organic layer was separated and the aqueous layer was extracted with DCM (3 × 10 mL). The combined organic extracts were washed with 0.1 M aq. $NaHCO_3$ (5 × 40 mL), dried and concentrated *in vacuo* to give an 80:20 mixture of **20**:**21** as a yellow oil (83 mg, 77%); ν_{max} (film) 3419 (O–H), 2940 (C–H), 1762 (C=O); *m*/*z* (ESI$^+$) 456 ([M+H]$^+$, 100%), 313 (79%); HRMS (ESI$^+$) $C_{22}H_{25}{}^{35}Cl_3NO_3^+$ ([M+H]$^+$) requires 456.0895; found 456.0895. Data for **20**: δ_H (400 MHz, $CDCl_3$) 1.21-1.54 (2H, m, C(4)H_A, C(6)H_A), 1.79-1.98 (2H, m, C(5)H_2), 1.98-2.06 (1H, m, C(4)H_B), 2.06-2.15 (1H, m, C(6)H_B), 2.48-2.59 (1H, m, C(3)*H*), 3.33-3.50 (2H, m, N(CH_AH$_B$Ph)$_2$), 3.76 (1H, app t, *J* 9.6, C(2)*H*), 3.89-3.97 (2H, m, N(CH$_A$$H_B$Ph)$_2$), 4.69 (1H, ddd, *J* 11.4, 9.1, 5.1, C(1)*H*), 7.21-7.39 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 21.3, 21.3 (*C*(4), *C*(5)), 28.7 (*C*(6)), 53.5 (N(*C*H$_2$Ph)$_A$), 55.3 (N(*C*H$_2$Ph)$_B$), 61.6 (*C*(3)), 71.0 (*C*(2)), 82.1 (*C*(1)), 90.0 (*C*Cl$_3$), 127.6 (*p-Ph*), 128.7, 129.0 (*o-*, *m-Ph*), 138.3 (*i-Ph*), 161.4 (*C*OCCl$_3$).

K_2CO_3 (100 mg) was added to a stirred solution of an 80:20 mixture of **20**:**21** (83 mg, 0.18 mmol) in MeOH (10 mL) and the resultant suspension was stirred at rt for 16 h before being concentrated *in vacuo*. H_2O (10 mL) was added and the mixture was extracted with DCM (4 × 10 mL). The combined organic extracts were washed with brine (40 mL), dried and concentrated *in vacuo* to give an 80:20 mixture of **18**:**5** as a colourless oil (57 mg, quant).

(1*RS*,2*RS*,3*SR*)-1-Dichloroacetoxy-2-hydroxy-3-*N*,*N*-dibenzylaminocyclohexane 22



22 **23**

22:**23**, 75:25

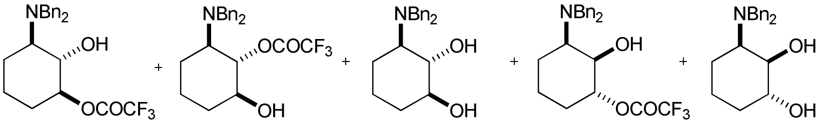
Cl_2CHCO_2H (0.07 mL, 0.86 mmol) was added to a stirred solution of **17** (50 mg, 0.17 mmol) in DCM (2 mL) and the reaction mixture was stirred at rt for 16 h. 0.1 M aq. $NaHCO_3$ (10 mL) was added, the organic layer was separated and the aqueous layer was extracted with DCM (3 × 10 mL). The combined organic extracts were washed with 0.1 M aq. $NaHCO_3$ (5 × 40 mL), dried and concentrated *in vacuo* to give a 75:25 mixture of **22**:**23** (50 mg, 70%).

Data for **22**: δ_H (400 MHz, $CDCl_3$) 1.12-2.17 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 2.52-2.66 (1H, m, C(3)*H*), 3.43-3.57 (2H, d, *J* 13.3, N(C$H_A$$H_B$Ph)$_2$), 3.69-3.80 (1H, m, C(2)*H*), 3.95-4.05 (2H, d, *J* 13.3, N(C$H_A$$H_B$Ph)$_2$), 4.60-4.75 (1H, m, C(1)*H*), 5.98 (1H, s, C*H*Cl_2), 7.22-7.57 (10H, m, *Ph*).

Data for **23**: δ_H (400 MHz, $CDCl_3$) [selected peaks] 4.33-4.42 (1H, m, C(1)*H*) 5.46 -5.51 (1H, m, C(2)*H*), 5.95 (1H, s, C*H*Cl_2).

K_2CO_3 (100 mg) was added to a stirred solution of a 75:25 mixture of **22**:**23** (50 mg, 0.12 mmol) in MeOH (10 mL) and the resultant suspension was stirred at rt for 16 h before being concentrated *in vacuo*. H_2O (10 mL) was added and the mixture was extracted with DCM (4 × 10 mL). The combined organic extracts were washed with brine (40 mL), dried and concentrated *in vacuo* to give a 75:25 mixture of **18**:**5** as a colourless oil (37 mg, quant).

(1*RS*,2*RS*,3*SR*)-1-Trifluoroacetoxy-2-hydroxy-3-*N*,*N*-dibenzylaminocyclohexane 24



24 **25** **18** **26** **5**

24:**25**:**18**:**26**:**5**, 22:4:55:17:2

F_3CCO_2H (39 μL, 0.53 mmol) was added to a stirred solution of **17** (31 mg, 0.106 mmol, >98% de) in DCM (2 mL) and the reaction mixture was stirred at rt for 16 h. 0.1 M aq. $NaHCO_3$ (10 mL) was then added, the organic layer was separated and the aqueous layer was extracted with DCM (3 × 10 mL). The combined organic extracts were washed with 0.1 M aq. $NaHCO_3$ (5 × 40 mL), dried and concentrated *in vacuo* to give a 22:4:55:17:2 mixture of **24**:**25**:**18**:**26**:**5** (57 mg).

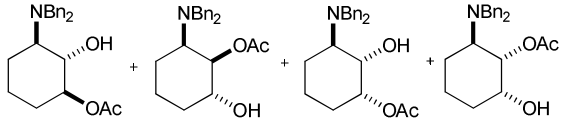
Data for **24**: δ_H (400 MHz, $CDCl_3$) [selected peaks] 3.63-3.77 (1H, m, C(2)*H*), 4.75 (1H, ddd, *J* 12.0, 8.0, 4.0, C(1)*H*).

Data for **25**: δ_H (400 MHz, $CDCl_3$) [selected peaks] 2.73-2.83 (1H, m, C(3)*H*), 5.07-5.14 (1H, m, C(2)*H*).

Data for **26**: δ_H (400 MHz, $CDCl_3$) [selected peaks] 4.00-4.10 (1H, m, C(2)*H*) 5.20-5.26 (1H, m, C(1)*H*).

K_2CO_3 (60 mg) was added to a stirred solution of a 22:4:55:17:2 mixture of **24**:**25**:**18**:**26**:**5** (57 mg) in MeOH (5 mL) and the resultant suspension was stirred at rt for 16 h before being concentrated *in vacuo*. H_2O (5 mL) was added and the mixture was extracted with DCM (4 × 5 mL). The combined organic extracts were washed with brine (40 mL), dried and concentrated *in vacuo* to give an 81:19 mixture of **18**:**5** as a colourless oil (20 mg).

(1*RS*,2*RS*,3*SR*)-1-Acetoxy-2-hydroxy-3-*N*,*N*-dibenzylaminocyclohexane 28



28 **29** **30** **31**

28:**29**:**30**:**31**, 44:36:11:9

A stirred solution **17** (50 g, 0.171 mmol, >98% de) in AcOH (1 mL) was heated at 50 ºC for 24 h before being allowed to cool to rt. 0.1 M aq. $NaHCO_3$ (10 mL) was then added and the aqueous layer was extracted with DCM (3 × 10 mL). The combined organic extracts were then washed with 0.1 M aq. $NaHCO_3$ (5 × 10 mL), dried and concentrated *in vacuo* to give a 44:36:11:9 mixture of **28**:**29**:**30**:**31** (53 mg) as a colourless oil.

Data for **28**: δ_H (400 MHz, $CDCl_3$) [selected peaks] 2.43-2.52 (1H, m, C(2)*H*, 4.49-4.60 (1H, m, C(1)*H*).

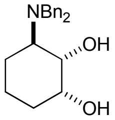
Data for **29**: δ_H (400 MHz, $CDCl_3$) [selected peaks] 3.09-3.16 (1H, m, C(1)*H*), 5.17-5.22 (1H, m, C(2)*H*).

Data for **30**: δ_H (400 MHz, $CDCl_3$) [selected peaks] 5.05-5.10 (1H, m, C(1)*H*).

Data for **31**: δ_H (400 MHz, $CDCl_3$) [selected peaks] 5.34-5.39 (1H, m, C(2)*H*).

K_2CO_3 (100 mg) was added to a stirred solution of a 44:36:11:9 mixture of **28**:**29**:**30**:**31** (53 mg) in MeOH (10 mL) and the resultant suspension was stirred at rt for 16 h before being concentrated *in vacuo*. H_2O (10 mL) was added and the mixture was extracted with DCM (4 × 10 mL). The combined organic extracts were washed with brine (40 mL), dried and concentrated *in vacuo* to give a 44:36:20 mixture of **18**:**5**:**14** as a colourless oil (23 mg).

(1*RS*,2*SR*,3*RS*)-3-*N*,*N*-dibenzylaminocyclohexane-1,2-diol 14



KOAc (23 mg, 0.24 mmol) was added to a stirred solution of **16** (99 mg, 0.23 mmol) in EtOH/H_2O (6:1, 5 mL) and the resultant suspension was heated at reflux for 48 h. The reaction mixture was allowed to cool to rt and concentrated *in vacuo*. H_2O (10 mL) was added and the mixture was extracted with DCM (3 × 10 mL). The combined organic extracts were dried and concentrated *in vacuo*. The residue was dissolved in MeOH (10 mL) and K_2CO_3 (100 mg) were added. The resultant suspension was stirred for 16 h before being concentrated *in vacuo*. H_2O (10 mL) was added and the mixture was extracted with DCM (3 × 10 mL). The combined organic extracts were washed sequentially with H_2O (2 × 30 mL) and brine (30 mL), dried, and concentrated *in vacuo* to give **14** as a pale yellow solid (31 mg, 43%, >98% de).

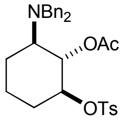
X-ray Crystal Structure Determination for 14

Data were collected using an Enraf-Nonius κ-CCD diffractometer with graphite monochromated Mo-$K\alpha$ radiation using standard procedures at 150 K. The structure was solved by direct methods (SIR92), all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[2]

X-ray crystal structure data for **14** [$C_{20}H_{25}NO_2$]: M = 311.42, monoclinic, space group $P\ 1\ 2_1/a\ 1$, a = 10.83920(10) Å, b = 28.0222(3) Å, c = 12.21180(10) Å, β = 110.5571(5)°, V = 3473.00(6) Å^3, Z = 8, μ = 0.76 mm^{-1}, colourless plate, crystal dimensions = 0.1 × 0.3 × 0.4 mm^3. A total of 7908 unique reflections were measured for $5 < \theta < 27$ and 4662 reflections were used in the refinement. The final parameters were $wR_2 = 0.042$ and $R_1 = 0.040$ [$I > 3.0\sigma(I)$].

Crystallographic data (excluding structure factors) has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 681276. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

(1*RS*,2*RS*,3*SR*)-1-*p*-Toluenesulphonyloxy-2-acetoxy-3-*N*,*N*-dibenzylaminocyclohexane 34



Ac_2O (0.13 mL, 1.4 mmol) and DMAP (50 mg) were added sequentially to a stirred solution of **19** (472 mg, 0.93 mmol) in DCM/pyridine (1:1, 20 mL). The resultant solution was stirred at rt for 24 h before being cooled to 0 °C. H_2O (20 mL) was added, the organic layer was separated and the aqueous layer was extracted with DCM (2 × 20 mL). The combined organic extracts were washed sequentially with 10% aq. $CuSO_4$ (2 × 50 mL), 0.1 M aq. $NaHCO_3$ (2 × 50 mL) and brine (50 mL), dried, and concentrated *in vacuo* to give **34** as a white solid (373 mg, 72%, >98% de); mp 105-106 °C; ν_{max} (KBr) 2942, 2867 (C–H), 1741 (C=O); δ_H (400 MHz, $CDCl_3$) 1.06-1.20 (1H, m, C(5)H_A), 1.29-1.43 (1H, m, C(4)H_A), 1.43-1.56 (1H, m, C(6)H_A), 1.73-1.82 (1H, m, C(5)H_B), 1.94-2.02 (4H, m, C(4)H_B, CO*Me*), 2.03-2.12 (1H, m, C(6)H_B), 2.44 (3H, s, Ar*Me*), 2.67 (1H, app td *J* 12.0, 4.0, C(3)*H*), 3.43 (2H, d, *J* 13.5, N(C$H_A$$H_B$Ph)$_2$), 3.78 (2H, d, *J* 13.5, N(C$H_A$$H_B$Ph)$_2$), 4.45 (1H, ddd, *J* 12.0, 8.0, 4.0, C(1)*H*), 5.18 (1H, app t, *J* 9.9 C(2)*H*), 7.17-7.35 (12H, m, *Ph*, *Ar*), 7.74 (2H, d, *J* 8.1, *Ar*); δ_C (400 MHz, $CDCl_3$) 20.9, 23.7, 31.5 (*C*(4), *C*(5), *C*(6)), 21.1, 21.6 (CO*Me*, Ar*Me*), 53.6 (N(*C*H_2Ph)$_2$), 59.5 (*C*(3)), 72.4 (*C*(2)), 82.4 (*C*(1)), 126.9, 127.5, 128.2, 128.7, 129.7, 139.6 (*Ar*,

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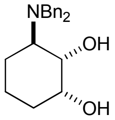
[2] P. W. Betteridge, J. R. Carruthers, R. I. Cooper, C. K. Prout and D. J. Watkin, CRYSTALS, 2001, Issue 11, Chemical Crystallography Laboratory, University of Oxford, UK.

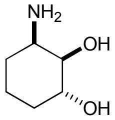
Ph), 170.2 (*C*OMe); *m*/*z* (ESI$^+$) 508 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{29}H_{34}NO_5S^+$ ([M+H]$^+$) requires 508.2152; found 508.2152.

(1*RS*,2*SR*,3*RS*)-3-*N*,*N*-dibenzylaminocyclohexane-1,2-diol 14 from 34



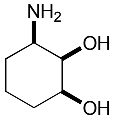
KOAc (73 mg, 0.74 mmol) was added to a stirred solution of **34** (373 mg, 0.74 mmol) in EtOH/H_2O (6:1, 20 mL) and the resultant suspension was heated at reflux for 72 h. The reaction mixture was allowed to cool to rt and concentrated *in vacuo*. H_2O (20 mL) was added and mixture was extracted with DCM (3 × 20 mL). The combined organic extracts were dried and concentrated *in vacuo*. The residue was dissolved in MeOH (10 mL) and K_2CO_3 (100 mg) were added. The resultant suspension was stirred for 16 h at rt before being concentrated *in vacuo*. H_2O (20 mL) was added and mixture was extracted with DCM (3 × 20 mL). The combined organic extracts were washed sequentially with H_2O (2 × 50 mL) and brine (50 mL), dried, and concentrated *in vacuo* to give **14** as a white solid (130 mg, 57%, >98% de).

(1*RS*,2*RS*,3*RS*)-3-Aminocyclohexane-1,2-diol 6



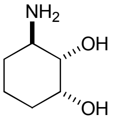
Pd(OH)$_2$/C (78 mg) was added to a vigorously stirred solution of **5** (157 mg, 0.50 mmol) in degassed MeOH (2 mL) and the resultant suspension was stirred at rt under H_2 (1 atm) for 24 h. The suspension was then filtered through a pad of Celite (eluent MeOH) and the filtrate was concentrated *in vacuo* to give **6** as a pale yellow solid (53 mg, 80%, >98% de); mp 115-116 °C; ν_{max} (KBr) 3355 (O–H), 2936, 2867 (C–H); δ_H (400 MHz, *d*$_4$-MeOH) 1.34-1.46 (1H, m, C(6)*H*$_A$), 1.47-1.66 (4H, m, C(4)*H*$_2$, C(5)*H*$_2$), 1.74-1.87 (1H, m, C(6)*H*$_B$), 3.02-3.12 (1H, m, C(3)*H*), 3.52 (1H, dd, *J* 5.3, 3.3, C(2)*H*), 3.74-3.82 (1H, m, C(1)*H*); δ_C (100 MHz, *d*$_4$-MeOH) 18.6, 29.2 (*C*(4), *C*(5)), 47.4 (*C*(6)), 49.9 (*C*(3)), 70.0 (*C*(1)), 74.2 (*C*(2)); *m/z* (ESI$^+$) 132 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_6H_{14}NO_2^+$ ([M+H]$^+$) requires 132.1019; found 132.1022.

(1*RS*,2*SR*,3*SR*)-3-Aminocyclohexane-1,2-diol 7



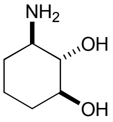
Pd(OH)$_2$/C (121 mg) was added to a vigorously stirred solution of **11** (243 mg, 0.78 mmol) in degassed MeOH (2 mL) and the resultant suspension was stirred at rt under H_2 (1 atm) for 24 h. The suspension was then filtered through a pad of Celite (eluent MeOH) and the filtrate was concentrated *in vacuo* to give **7** as a colourless oil (103 mg, quant, >98% de); ν_{max} (film) 3385 (O–H), 2941, 2867 (C–H); δ_H (400 MHz, d_4-MeOH) 1.11-1.76 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 2.59-2.74 (1H, m, C(3)*H*), 3.46-3.59 (1H, m, C(1)*H*), 3.75-3.81 (1H, m, C(2)*H*); δ_C (100 MHz, d_4-MeOH) 21.0, 27.6, 28.2 (*C*(4), *C*(5), *C*(6)), 52.2 (*C*(3)), 71.8 (*C*(1)), 73.2 (*C*(2)); *m/z* (ESI$^+$) 132 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_6H_{14}NO_2^+$ ([M+H]$^+$) requires 132.1019; found 132.1020.

(1*RS*,2*SR*,3*RS*)-3-Aminocyclohexane-1,2-diol 8



Pd(OH)$_2$/C (25 mg) was added to a vigorously stirred solution of **14** (54 mg, 0.17 mmol) in degassed MeOH (2 mL) and the resultant suspension was stirred at rt under H_2 (1 atm) for 24 h. The suspension was then filtered through a pad of Celite (eluent MeOH) and the filtrate was concentrated *in vacuo* to give **8** as a white solid (14 mg, 64%, >98%); mp 134-135 °C; ν_{max} (KBr) 3384 (O–H), 2940, 2871 (C–H); δ_H (400 MHz, d_4-MeOH) 1.14-1.27 (1H, m, C(4)H_A), 1.44-1.57 (2H, m, C(5)H_A, C(6)H_A), 1.63-1.78 (1H, m, C(5)H_B), 1.79-1.97 (2H, m, C(4)H_B, C(6)H_B), 2.92-3.03 (1H, m, C(3)*H*), 3.21 (1H, dd, *J* 9.6, 3.1, C(2)*H*), 4.00 (1H, app q, *J* 3.0, C(1)*H*); δ_C (100 MHz, d_4-MeOH) 18.7 (*C*(5)) 31.4 (*C*(6)), 32.2 (*C*(4)), 50.4 (*C*(3)), 67.0 (*C*(1)), 77.3 (*C*(2)); *m/z* (ESI$^+$) 132 ([M+H]$^+$, 55%); HRMS (ESI$^+$) $C_6H_{14}NO_2^+$ ([M+H]$^+$) requires 132.1019; found 132.1022.

(1*RS*,2*RS*,3*SR*)-3-Aminocyclohexane-1,2-diol 9



Pd(OH)$_2$/C (55 mg) was added to a vigorously stirred solution of **18** (110 mg, 0.35 mmol) in degassed MeOH (2 mL) and the resultant suspension was stirred at rt under H_2 (1 atm) for 24 h. The suspension was then filtered through a pad of Celite (eluent MeOH) and the filtrate was concentrated *in vacuo* to give **9** as a white solid (47 mg, quant, >98% de); mp 45-46 °C; ν_{max} (KBr) 3356 (O–H), 2934, 2868 (C–H); δ_H (400 MHz, d_4-MeOH) 1.25-1.46 (3H, m, C(4)H_A, C(5)H_A, C(6)H_A), 1.71-1.81 (1H, m, C(5)H_B), 1.88-2.02 (2H, m, C(4)H_B, C(6)H_B), 2.75 (1H, app td, *J* 10.3, 3.7, C(3)*H*), 3.12 (1H, app t, *J* 9,2, C(2)*H*), 3.30-3.43 (1H, m, C(1)*H*); δ_C (100 MHz, d_4-MeOH) 21.3 (*C*(5)), 30.5, 32.9 (*C*(4), *C*(6)), 54.6 (*C*(3)), 73.6 (*C*(1)), 78.6 (*C*(2)); *m/z* (ESI$^+$) 132 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_6H_{14}NO_2^+$ ([M+H]$^+$) requires 132.1019; found 132.1022.