Supplementary Information

Ammonium-directed dihydroxylation of 3-aminocyclohex-1-enes: development of a metal-free dihydroxylation protocol

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Experimental

General Experimental

Water was purified by an Elix® UV-10 system. *m*CPBA was supplied as a 70-77% slurry in water (Aldrich) and titrated according to the procedure of Swern[1] immediately before use. 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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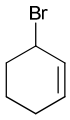
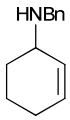
[1] D. Swern, *Org. React.*, **1953**, VII, 392.

(*RS*)-3-Bromocyclohex-1-ene 7



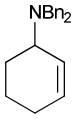
AIBN (cat.) and NBS (160 g, 0.90 mol) were added sequentially to a stirred solution of cyclohexene (91.2 mL, 0.90 mol) in CCl_4 (1 L). The resulting suspension was heated at reflux (80 °C) for 1.5 h then cooled to 0 °C and filtered. The filtrate was concentrated *in vacuo* to give **7** as a brown oil (145 g, quant) which was used immediately without further purification; δ_H (400 MHz, $CDCl_3$) 1.68-1.75 (1H, m), 1.91-2.25 (5H, m), 4.85-4.90 (1H, m, C(3)*H*), 5.80-5.85 (1H, m, C(2)*H*), 5.87-5.93 (1H, m, C(1)*H*).

(*RS*)-3-*N*-Benzylaminocyclohex-1-ene 8



Benzylamine (241 g, 2.25 mmol) and K_2CO_3 (149 g, 1.08 mmol) were added sequentially to a stirred solution of **7** (145 g, 0.90 mmol) in THF (50 mL) at 0 °C. The resulting mixture was stirred for 3 days at 50 °C after which time the mixture was allowed to cool to rt and Et_2O (500 mL) was added. The mixture was washed with H_2O (3 × 1 L) and the organic layer was dried and concentrated *in vacuo*. Purification by flash column chromatography (eluent 30-40 °C petrol) gave **8** as a colourless oil (80.1 g, 48%); δ_H (400 MHz, $CDCl_3$) 1.35-1.61 (2H, m), 1.71-1.81 (1H, m), 1.85-2.06 (3H, m), 3.21-3.29 (1H, m, C(3)*H*), 3.79-3.89 (2H, m, NCH_2Ph), 5.61-5.82 (2H, m, C(1)*H*, C(2)*H*), 7.21-7.49 (5H, m, *Ph*).

(*RS*)-3-*N*,*N*-Dibenzylaminocyclohex-1-ene 9



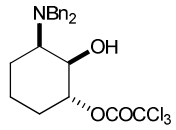
Method A: Dibenzylamine (29.8 mL, 0.16 mmol) and K_2CO_3 (10.3 g, 0.07 mmol) were added sequentially to a stirred solution of **7** (7.14 mL, 0.06 mmol) in THF (50 mL) at 0 °C. The resulting mixture was stirred for 3 days at 50 °C after which time the mixture was allowed to cool to rt and Et_2O (500 mL) was added. The mixture washed with H_2O (3 × 1 L) and the organic layer was dried and concentrated *in vacuo*. Purification by flash column chromatography (euent 30-40 °C petrol) gave **9** as a colourless oil (7.0 g, 41%); δ_H (400 MHz, $CDCl_3$) 1.78-1.99 (2H, m, C(5)H_2), 2.19-2.49 (4H, m, C(4)H_2, C(6)H_2), 3.41 (2H, d, *J* 13.9, N(C$H_A$$H_B$Ph)$_2$), (2H, d, *J* 13.9, N(C$H_A$$H_B$Ph)$_2$), 3.98-4.13 (1H, m, C(3)*H*), 5.65-5.85 (2H, m, C(1)*H*, C(2)*H*), 7.11-7.49 (10H, m, *Ph*).

Method B: Benzyl bromide (50.9 mL, 428 mmol), Hünig's base (82 mL, 471 mmol) and DMAP (cat.) were added sequentially to a stirred solution of **8** (86.1 g, 428 mmol) in DCM (500 mL). The resulting mixture was stirred for 24 h at rt after which time sat. aq. $NaHCO_3$ (500 mL) was added and the mixture was extracted with DCM (3 × 500 mL). The combined organic extracts were washed sequentially with 10% aq. $CuSO_4$ (3 × 500 mL), H_2O (3 × 500 mL) and 3 M aq. HCl (3 × 500 mL). 2 M aq. NaOH was added to the aqueous layer until pH >9 was achieved, and the mixture was then extracted with DCM (3 × 500 mL). The combined organic layers were dried and concentrated *in vacuo* to give **9** as colourless oil (83 g, 70%).

General procedure for ammonium directed dihydroxylation

The requisite acid was added to a stirred solution of the requisite allylic amine in DCM, and the resultant solution was stirred at rt for 5 min. Freshly titrated *m*CPBA was then added and the solution was stirred at rt for 21 h. The mixture was then diluted with DCM and washed with sat. aq. Na_2SO_3 until starch-iodide paper indicated that no *m*CPBA was present. The organic layer was washed four times with 0.1 M aq. $NaHCO_3$, dried and concentrated *in vacuo*.

(1*RS*,2*RS*,3*RS*)-1-Trichloroacetyl-2-hydroxy-3-*N*,*N*-dibenzylaminocyclohexane 11



Following the *general procedure*, Cl_3CCO_2H (294 mg, 1.81 mmol), **9** (100 mg, 0.36 mmol) in DCM (1 mL), and *m*CPBA (81%, 122 mg, 0.58 mmol) gave **11** as colourless oil (165 mg, quant, 90% de); ν_{max} (film) 3424 (O–H), 2941 (C–H), 1762 (C=O); δ_H (400 MHz, $CDCl_3$) 1.50-1.97 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 2.91 (1H, br s, O*H*), 2.99-3.08 (1H, m, C(3)*H*), 3.74 (1H, d, *J* 14.4, N(C$H_A$$H_B$Ph)$_2$), 3.94 (1H, d, *J* 14.4, N(CH$_A$$H_B$Ph)$_2$), 4.14-4.19 (1H, m, C(2)*H*), 5.14-5.20 (1H, m, C(1)*H*), 7.22-7.38 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.8, 22.6, 24.2 (*C*(4), *C*(5), *C*(6)), 54.9 (N(*C*H$_2$Ph)$_2$), 57.5 (*C*(3)), 67.8 (*C*(2)), 77.9 (*C*(1)), 89.9 (*C*Cl$_3$), 127.0 (*p-Ph*), 128.5, 128.6 (*o-*, *m-Ph*), 139.8 (*i-Ph*), 161.0 (*C*=O); *m/z* (ESI$^+$) 456 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{22}H_{25}{}^{35}Cl_3NO_3{}^+$ ([M+H]$^+$) requires 456.0895; found 456.0891.

Rate studies of the ammonium directed dihydroxylation reaction

A solution of **9** (15 mg, 0.054 mmol) in $CDCl_3$ (0.15 mL) was prepared in a 3 mm NMR tube. Cl_3CCO_2H (44 mg, 0.27 mmol) was added and the tube was shaken for 5 min. *m*CPBA (87% by wt, 17 mg, 0.087 mmol) was then added, and the progress of the reaction was monitored by ^{1}H NMR spectroscopic analysis.

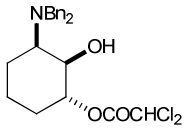
X-ray crystal structure determination for 12

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 **12** [$C_{17.5}H_{18}Cl_{6.67}N_{0.67}O_{4.67}$]: M = 548.69, monoclinic, space group *C 1 2/c 1*, a = 24.5125(2) Å, b = 9.82110(10) Å, c = 30.9595(4) Å, β = 106.7096(5)º, V = 7138.47(13) Å^3, Z = 12, μ = 0.823 mm^{-1}, colourless plate, crystal dimensions = 0.2 × 0.2 × 0.3 mm^3. A total of 7984 unique reflections were measured for $5 < \theta < 27$ and 5826 reflections were used in the refinement. The final parameters were wR_2 = 0.095 and R_1 = 0.092 [$I>3\sigma(I)$].

Crystallographic data (excluding structure factors) has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 679350. 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].

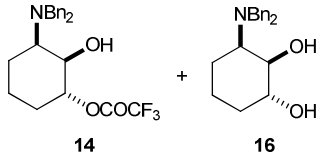
(1*RS*,2*RS*,3*RS*)-1-Dichloroacetoxy-2-hydroxy-3-*N*,*N*-dibenzylaminocyclohexane 13



Following the *general procedure*, Cl_2CHCO_2H (0.15 mL, 1.81 mmol), **9** (100 mg, 0.36 mmol) in DCM (1 mL), and *m*CPBA (81%, 122 mg, 0.58 mmol) gave **13** as a colourless oil (152 mg, quant, 87% de); ν_{max} (film) 3383 (O–H), 3075, 3062, 3027, 2940, 2869, 2864 (C–H), 1758 (C=O); δ_H (400 MHz, $CDCl_3$) 1.40-2.40 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 2.95-3.04 (1H, m, C(3)*H*), 3.75 (2H, d, *J* 14.3, N(CH_AH$_B$Ph)$_2$), 3.90 (2H, d, *J* 14.3, N(CH$_A$$H_B$Ph)$_2$), 4.11 (1H, app t, *J* 3.2, C(2)*H*), 5.14 (1H, app t, *J* 3.2 C(1)*H*), 5.80 (1H, s, C*H*Cl$_2$), 7.22-7.52 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.9, 22.8, 24.3 (*C*(4), *C*(5), *C*(6)), 54.9 (N(CH_2Ph)$_2$), 57.6 (*C*(3)), 64.4 (*C*HCl$_2$), 67.7 (*C*(2)), 76.1 (*C*(1)), 127.0 (*p-Ph*), 128.4, 128.6 (*o*-, *m-Ph*), 139.9 (*i-Ph*), 163.5 (*C*=O); *m/z* (ESI$^+$) 422 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{22}H_{26}{}^{35}Cl_2NO_3^+$ ([M+H]$^+$) requires 422.1284; found 422.1284.

[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.

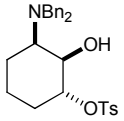
(1*RS*,2*RS*,3*RS*)-1-Trifluoroacetoxy-2-hydroxy-3-*N*,*N*-dibenzylaminocyclohexane 14



14 16

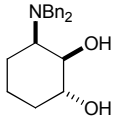
Following the *general procedure*, F_3CCO_2H (0.13 mL, 1.81 mmol), **9** (100 mg, 0.36 mmol) in DCM (1 mL), and *m*CPBA (81%, 122 mg, 0.58 mmol) gave a 53:47 mixture of **14** (90% de) and **16** (90% de) respectively (148 mg).

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



Following the *general procedure*, TsOH (206 mg, 1.08 mmol), **9** (100 mg, 0.36 mmol) in DCM (1 mL), and *m*CPBA (87%, 117 mg, 0.58 mmol) gave **15** as a green oil (167 mg, quant, 90% de); ν_{max} (film) 3050 (O–H), 2946 (C–H); δ_H (400 MHz, $CDCl_3$) 1.43-1.85 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 2.44 (3H, s, ArCH_3), 2.92-3.13 (2H, br m, C(3)*H*, O*H*), 3.77 (4H, AB system, N(CH_2Ph)$_2$), 4.03-4.09 (1H, m, C(2)*H*), 4.75-4.79 (1H, m, C(1)*H*), 7.23-7.37 (12H, m, *Ar*, *Ph*), 7.75-7.81 (2H, d, *J* 7.8, *Ar*); δ_C (100 MHz, $CDCl_3$) 19.2 (*C*H_2), 21.7 (Ar*C*H_3) 23.4, 25.1 (*C*H_2), 54.6 (N(*C*H_2Ph)$_2$), 58.4 (*C*(3)), 67.4 (*C*(2)), 80.1 (*C*(1)), 127.0, 127.8, 128.5, 128.6, 129.9, 133.9, 139.8, 144.8 (*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*RS*)-3-*N*,*N*-Dibenzylaminocyclohexane-1,2-diol 16

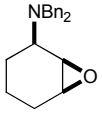


K_2CO_3 (500 mg) was added to a stirred solution of **11** (164 mg, 0.36 mmol) in MeOH (5 mL), and the resultant suspension was stirred at rt for 16 h then concentrated *in vacuo*. H_2O (10 mL) was added and the mixture was extracted with DCM (4 × 10 mL). The combined organic extracts were then washed with brine (50 mL), dried and concentrated *in vacuo*. Purification *via* flash column chromatography (gradient elution, eluent 0%→100% EtOAc in 40-60 °C petrol) gave **16** as a viscous, pale yellow oil (112 mg, quant, 90% de); ν_{max} (film) 3407 (O–H), 3027, 2937 (C–H); δ_H (400 MHz, $CDCl_3$) 1.43-1.89 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 2.14 (1H, br s, O*H*), 3.10-3.20 (1H, m, C(3)*H*), 3.69-3.78 (2H, d, *J* 14.4, N(CH_APh)$_2$), 3.81-3.91 (3H, m, C(2)*H*, N(CH_BPh)$_2$), 3.99-4.06 (1H, m, C(1)*H*), 7.22-7.38 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.9, 23.8, 28.1 (*C*(4), *C*(5), *C*(6)), 55.0 (N(*C*H_2Ph)$_2$), 58.3 (*C*(3)), 70.5 (*C*(1)), 71.1 (*C*(2)), 127.0 (*p*-*Ph*), 128.5,

128.7 (*o*-, *m*-*Ph*), 139.8 (*i*-*Ph*); *m*/*z* (ESI^+) 312 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{20}H_{26}NO_2^+$ ($[M+H]^+$) requires 312.1958; found 312.1952.

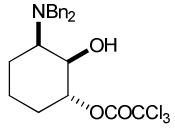
"One-pot" dihydroxylation protocol: Cl_3CCO_2H (29.5 g, 0.18 mol) was added to a stirred solution of **9** (10 g, 36 mmol) in DCM (100 mL) and the resultant solution was stirred at rt for 5 min. Freshly titrated *m*CPBA (87%, 11.5 g, 58 mmol) was then added and the solution was stirred at rt for 21 h. Sat. aq. Na_2SO_3 was then added until starch-iodide paper indicated that no *m*CPBA was present. MeOH (500 mL) and K_2CO_3 (10 g) were then added and the resultant suspension was stirred at rt for 16 h before being concentrated *in vacuo*. H_2O (500 mL) was then added and the mixture was extracted with DCM (4 × 500 mL). The combined organic extracts were washed with brine (1 L), dried and concentrated *in vacuo* to give **16** as a viscous, pale yellow oil (11.4 g, quant, 90% de).

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



DBU (7.94 mL, 52.8 mmol) was added to a stirred solution of **15** (22.3 g, 49 mmol, 90% de) in DCM (100 mL) at rt and the reaction mixture was stirred for 24 h. 10% aq. $CuSO_4$ (500 mL) was added and the mixture was extracted with DCM (3 × 500 mL). The combined organic extracts were washed with H_2O (3 × 500 mL), dried and concentrated *in vacuo*. Purification *via* flash column chromatography (gradient elution, eluent 0%→100% Et_2O in 40-60 °C petrol) gave **17** as a colourless oil (13.6 g, 95%, >98% de); ν_{max} (film) 3061, 2938 (C–H); δ_H (400 MHz, $CDCl_3$) 1.11-1.39 (1H, m, C(5)H_A), 1.55-1.96 (5H, m, C(4)H_2, C(5)H_B, C(6)H_2), 3.00-3.10 (1H, m, C(3)*H*), 3.11-3.17 (1H, m, C(1)*H*), 3.37 (1H, app d, *J* 4.0, C(2)*H*), 3.75 (2H, d, *J* 14.1, N(C$H_A$$H_B$Ph)$_2$), 3.96 (2H, d, *J* 14.1, N(C$H_A$$H_B$Ph)$_2$), 7.24-7.53 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.3, 21.6, 23.1 (*C*(4), *C*(5), *C*(6)), 51.7 (*C*(1)), 54.7 (N(*C*H_2Ph)$_2$), 55.0 (*C*(2)), 55.7 (*C*(3)), 126.7 (*p*-*Ph*), 128.2, 128.6 (*o*-, *m*-*Ph*), 140.7 (*i*-*Ph*); *m*/*z* (ESI^+) 294 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{20}H_{24}NO^+$ ($[M+H]^+$) requires 294.1852; found 294.1853.

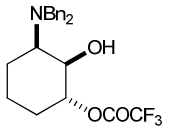
(1*RS*,2*RS*,3*RS*)-1-Trichloroacetyl-2-hydroxy-3-*N*,*N*-dibenzylaminocyclohexane 11 from ring-opening of epoxide 17



Cl_3CCO_2H (171 mg, 1.05 mmol) was added to a stirred solution of **17** (61 mg, 0.21 mmol) in DCM (2 mL) and the reaction mixture was stirred at rt for 16 h. 0.1 M aq. $NaHCO_3$ (5 mL) was then added and the

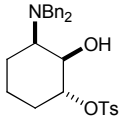
aqueous layer was extracted with DCM (3 × 5 mL). The combined organic extracts were washed with 0.1 M aq. $NaHCO_3$ (5 × 10 mL), dried and concentrated *in vacuo* to give **11** as a colourless oil (96 mg, quant, >98% de).

(1*RS*,2*RS*,3*RS*)-1-Trifluoroacetyl-2-hydroxy-3-*N*,*N*-dibenzylaminocyclohexane 14 from ring-opening of epoxide 17



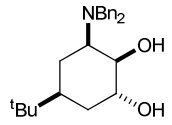
F_3CCO_2H (57 μL, 1.05 mmol) was added to a stirred solution of **17** (45 mg, 0.15 mmol) in DCM (1 mL) and the reaction mixture was stirred at rt for 16 h. 0.1 M aq. $NaHCO_3$ (5 mL) was then added and the aqueous layer was extracted with DCM (3 × 5 mL). The combined organic extracts were washed with 0.1 M aq. $NaHCO_3$ (5 × 10 mL), dried and concentrated *in vacuo* to give **14** as a white solid (63 mg, quant, >98% de); mp 89-90 °C; ν_{max} (KBr) 3405 (O–H), 3086, 3063, 3028, 2943, 2871, 2804 (C–H), 1781 (C=O); δ_H (400 MHz, $CDCl_3$) 1.42-1.97 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 2.92-3.09 (2H, m, C(3)*H*, O*H*), 3.74 (2H, d, *J* 16.0, N(C$H_A$$H_B$Ph)$_2$), 3.88 (2H, d, *J* 16.0, N(C$H_A$$H_B$Ph)$_2$), 4.00-4.10 (1H, m, C(2)*H*), 5.20-5.26 (1H, m, C(1)*H*), 7.21-7.39 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.7, 23.0, 24.3 (*C*(4), *C*(5), *C*(6)), 54.8 (N(*C*H_2Ph)$_2$), 57.8 (*C*(3)), 67.2 (*C*(2)), 77.0 (*C*(1)), 114.5 (q, J_{CF} 286, *C*F_3), 127.1 (*p-Ph*), 128.5, 128.6 (*o*-, *m-Ph*), 139.6 (*i-Ph*), 156.5 (q, J_{CF} 43, *C*=O); *m*/*z* (ESI$^+$) 408 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{22}H_{25}F_3NO_3^+$ ([M+H]$^+$) requires 408.1781; found 408.1772.

(1*RS*,2*RS*,3*RS*)-1-*p*-Toluenesulphonyloxy-2-hydroxy-3-*N*,*N*-dibenzylaminocyclohexane 15 from ring-opening of epoxide 17



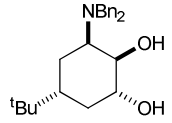
TsOH (324 mg, 1.71 mmol) was added to a stirred solution of **17** (100 mg, 0.34 mmol) in DCM (2 mL) and the reaction mixture was stirred at rt for 16 h. 0.1 M aq. $NaHCO_3$ (5 mL) was then added and the aqueous layer was extracted with DCM (3 × 5 mL). The combined organic extracts were washed with 0.1 M aq. $NaHCO_3$ (5 × 10 mL), dried and concentrated *in vacuo* to give **15** as a colourless oil (119 mg, 86%, >98% de).

(1*RS*,2*RS*,3*RS*,5*SR*)-3-*N*,*N*-Dibenzylamino-5-*tert*-butyl-cyclohexane-1,2-diol 23



Cl_3CCO_2H (44 mg, 0.27 mmol) was added to a solution of *syn*-**21** (13 mg, 0.039 mmol) in $CDCl_3$ (0.15 mL) in a 3mm NMR tube. After 5 min, *m*CPBA (87% by wt, 17 mg, 0.086 mmol) was added and the progress of the reaction monitored by ^{1}H NMR spectroscopy. After completion the reaction mixture was transferred to a round bottom flask and sat. aq. Na_2SO_3 was added until starch-iodide paper indicated that no *m*CPBA remained. MeOH (1 mL) and K_2CO_3 (50 mg) were added and the suspension stirred for 24 h before being concentrated *in vacuo*. H_2O (2 mL) was added and the mixture was extracted with DCM (4 × 2 mL). The combined organic extracts were washed with brine (10 mL), dried, and concentrated *in vacuo* to give **23** as a colourless oil (14 mg, quant, >95% de); ν_{max} (film) 3376 (O–H), 3085, 3063, 3028, 2950, 2689 (C–H); δ_H (400 MHz, $CDCl_3$) 0.81 (9H, s, C*Me*$_3$), 1.06-1.17 (1H, app q, *J* 12.1, C(4)*H*$_{ax}$), 1.40 (1H, br tt, *J* 12.3, 2.8, C(5)*H*), 1.50 (1H, td, *J* 13.0, 2.8, C(6)*H*$_{ax}$), 1.59-1.66 (1H, m, C(6)*H*$_{eq}$), 1.72-1.80 (1H, m, C(4)*H*$_{eq}$), 3.06 (1H, br dt, *J* 12.1, 3.0, C(3)*H*), 3.77 (2H, d, *J* 16.0, N(C*H*$_A$H$_B$Ph)$_2$), 3.87 (2H, d, *J* 16.0 N(CH$_A$*H*$_B$Ph)$_2$), 4.01 (1H, app br t, *J* 2.5, C(2)*H*), 4.15 (1H, app q, *J* 3.0, C(1)*H*), 7.19-7.40 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 25.7 (*C*(4)), 27.4 (C*Me*$_3$), 28.4 (*C*(6)), 32.2 (*C*Me$_3$), 40.2 (*C*(5)), 54.9 (N(*C*H$_2$Ph)$_2$), 59.9 (*C*(3)), 69.3 (*C*(2)), 70.2 (*C*(1)), 126.9 (*p-Ph*), 128.4, 128.5 (*o-*, *m-Ph*), 139.2 (*i-Ph*); *m*/*z* (ESI$^+$) 368 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{24}H_{34}NO_2^+$ ([M+H]$^+$) requires 368.2584; found 368.2584.

(1*RS*,2*RS*,3*RS*,5*RS*)-3-*N*,*N*-Dibenzylamino-5-*tert*-butyl-cyclohexane-1,2-diol 25

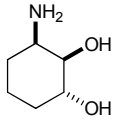


Cl_3CCO_2H (44 mg, 0.27 mmol) was added to a solution of *anti*-**22** (18 mg, 0.054 mmol) in $CDCl_3$ (0.15 mL) in a 3mm NMR tube. After 5 min, *m*CPBA (87% by wt, 17 mg, 0.086 mmol) was added and the progress of the reaction monitored by ^{1}H NMR spectroscopy. After completion the reaction mixture was transferred to a round bottom flask and sat. aq. Na_2SO_3 was added until starch-iodide paper indicated that no *m*CPBA remained. MeOH (1 mL) and K_2CO_3 (50 mg) were added and the suspension stirred for 24 h before being concentrated *in vacuo*. H_2O (2 mL) was added and the mixture was extracted with DCM (4 × 2 mL). The combined organic extracts were washed with brine (10 mL), dried, and concentrated *in vacuo* to give a 22:78 mixture of **24**:**25** as a colourless oil (20 mg); ν_{max} (film) 3354 (O–H), 3068, 3032, 2956, 2871 (C–H); *m*/*z* (ESI$^+$) 368 ([M+H]$^+$, **25**, 100%), 350 ([M+H]$^+$, **24**, 74%); HRMS (ESI$^+$) $C_{24}H_{34}NO_2^+$ ([M+H]$^+$, **25**) requires 368.2584; found 368.2582.

Data for **24**: δ_H (400 MHz, $CDCl_3$) [selected peaks] 0.84 (9H, s, CMe_3), 3.67 (2H, d, *J* 12.0, N(CH_AH$_B$Ph)$_2$), 3.97 (2H, d, *J* 12.0, N(CH$_A$$H_B$Ph)$_2$).

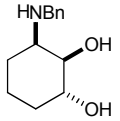
Data for **25**: δ_H (400 MHz, $CDCl_3$) 0.93 (9H, s, CMe_3), 1.03 (1H, app q, *J* 12.5, C(6)H_{ax}), 1.17-1.37 (1H, m, C(4)H_{ax}), 1.57 (1H, br tt, *J* 12.9, 3.4, C(5)*H*), 2.05 (1H, br ddd, *J* 12.4, 6.8, 3.0, C(6)H_{eq}), 2.15-2.23 (1H, m, C(4)H_{eq}), 3.21 (1H, dd, *J* 9.6, 7.3, C(2)*H*), 3.33 (1H, app t, *J* 6.6, C(3)*H*), 3.43 (2H, d, *J* 13.1, N(CH_AH$_B$Ph)$_2$), 3.85 (1H, ddd, *J* 11.4, 9.6, 4.3, C(1)*H*), 3.95 (2H, d, *J* 13.1, N(CH$_A$$H_B$Ph)$_2$), 7.20-7.45 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 23.5 (*C*(4)), 27.3 (CMe_3), 32.3 (*C*(6)), 32.8 (*C*Me$_3$), 43.0 (*C*(5)), 56.1 (*C*(3)), 56.4 (N(*C*H$_2$Ph)$_2$), 73.4 (*C*(1)), 75.0 (*C*(2)), 127.5 (*p-Ph*), 128.6, 129.0 (*o-*, *m-Ph*), 138.8 (*i-Ph*).

(1*RS*,2*RS*,3*RS*)-3-Aminocyclohexane-1,2-diol 35



$Pd(OH)_2$/C (50 mg) was added to a vigorously stirred suspension of **16** (100 mg, 0.32 mmol) in degassed MeOH (1 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 **35** as a pale yellow solid (33 mg, 78%, 90% 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), *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.

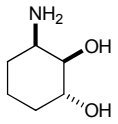
(1*RS*,2*RS*,3*RS*)-3-*N*-Benzylaminocyclohexane-1,2-diol 36



Cl_3CCO_2H (4.37 g, 2.67 mmol) was added to a stirred solution of **8** (1.01 g, 5.39 mmol) in DCM (14.8 mL) and the resultant solution was stirred at rt for 5 min. Freshly titrated *m*CPBA (87%, 1.71 g, 8.62 mmol) was then added and the solution was stirred at rt for 21 h. Sat. aq. Na_2SO_3 was then added until starch-iodide paper indicated that no *m*CPBA remained. MeOH (50 mL) and K_2CO_3 (5 g) were then added and the resultant suspension was stirred at rt for 16 h before being concentrated *in vacuo*. H_2O (50 mL) was then added and the mixture was extracted with DCM (4 × 100 mL). The combined organic extracts were washed with brine (100 mL), dried and concentrated *in vacuo*. Purification *via* flash column chromatography on neutral alumina (gradient elution, 0%→100% MeOH in DCM) gave **36** as white solid (1.11 g, 94%, 90%

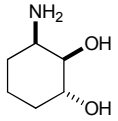
de); mp 150-151 °C; ν_{max} (film) 3500 (O–H), 3045, 2945, 3867 (C–H); δ_H (400 MHz, d_4-MeOH) 1.45-1.90 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 3.25-3.39 (1H, m, C(3)*H*), 3.83-4.04 (2H, m, C(1)*H*, C(2)*H*), 4.05-4.15 (2H, m, NCH_2Ph), 7.31-7.42 (3H, m, *Ph*), 7.44-7.51 (2H, m, *Ph*); δ_C (100 MHz, d_4-MeOH) 18.3, 24.3, 27.6 (*C*(4), *C*(5), *C*(6)), 49.3 (N*C*H_2Ph), 56.1 (*C*(3)), 68.8 (*C*(2)), 69.8 (*C*(1)), 128.9 (*p-Ph*), 129.1, 129.8 (*o*-, *m*-*Ph*), 133.9 (*i-Ph*); *m/z* (ESI$^+$) 222 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{13}H_{20}NO_2^+$ ([M+H]$^+$) requires 222.1489; found 222.1490.

(1*RS*,2*RS*,3*RS*)-3-Aminocyclohexane-1,2-diol 35 from 36



$Pd(OH)_2$/C (131 mg) was added to a vigorously stirred suspension of **36** (262 mg, 1.19 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 **35** as a pale yellow solid (130 mg, 84%, 90% de).

(1*RS*,2*RS*,3*RS*)-3-Aminocyclohexane-1,2-diol 35 from 37



Cl_3CCO_2H (2.07 g, 12.7 mmol) was added to a stirred solution of **37** (500 mg, 2.54 mmol) in DCM (7 mL mL) and the resultant mixture was stirred at rt for 7 days. Concentration *in vacuo* of an aliquot gave **38** as a mixture with Cl_3CCO_2H; δ_H (400 MHz, $CDCl_3$) 1.62-2.18 (6H, m, C(4)H_2, C(5)H_2, C(6)H_2), 3.98-4.11 (1H, br m, C(3)*H*), 5.69-5.76 (1H, m, C(2)*H*), 6.09-6.17 (1H, m, C(1)*H*), 7.04-7.33 (3H, br s, NH_3); δ_H (100 MHz, $CDCl_3$) 18.7, 24.3, 27.1 (*C*(4), *C*(5), *C*(6)), 48.4 (*C*(3)), 121.8 (*C*(2)), 136.0 (*C*(1)); HRMS (ESI$^+$) $C_6H_{12}N^+$ ([M+H]$^+$) requires 98.0964; found 98.0964.

*m*CPBA (87%, 806 mg, 4.06 mmol) was added to the reaction mixture and the resultant solution was stirred for 21 h at rt after which time sat. aq. Na_2SO_3 was added until starch-iodide paper indicated that no *m*CPBA remained. MeOH (1 mL) and K_2CO_3 (25 mg) were then added and the resultant suspension was stirred for 24 h at rt. The suspension was concentrated *in vacuo* and the residue filtered through basic alumina (eluent MeOH). The MeOH filtrate was concentrated *in vacuo* and 3 M aq. NaOH (5 drops) was added to the residue. DCM (2 mL) was added to the residue and then decanted to remove *m*CBA residues. This process was repeated five times. The residue was then dried *in vacuo* to give **35** as a pale yellow solid (114 mg, 34%, 90% de).