Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Rapid synthesis and zebrafish evaluation of a phenanthridine-based small molecule library

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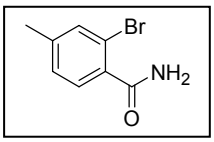
Supporting Information

Contents

General procedure A - Synthesis of aryl amide analogues

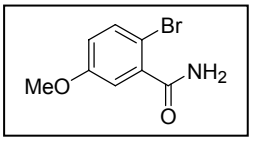
A mixture of the appropriate benzoic acid (approx. 1.00 g) and thionyl chloride (15 mL) was refluxed at 60°C for 3 h. The thionyl chloride was removed under reduced pressure and the residue was dissolved in NH_4OH (15 mL, conc.) and stirred for 16 h at r.t. The reaction mixture was filtered and the precipitate dried on the high vacuum line for several hours to afford the desired amide.

2-Bromo-4-methylbenzamide 11b[1]



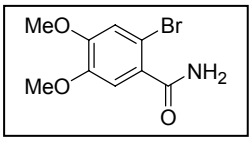
General procedure **A** was followed using 2-bromo-4-methyl benzoic acid (800 mg, 3.70 mmol) and thionyl chloride (12 mL) to afford amide **11b** as a colourless solid (750 mg, 95%). $\mathbf{R_f}$ [CH_2Cl_2:MeOH, 95:5] = 0.45; **MP** 171°C (H_2O), lit 175°C[1]; $\boldsymbol{\upsilon_{max}}$ ($CHCl_3$)/cm^{-1} 3419 (NH), 1636 (C=O); ^{1}**H NMR** δ (250 MHz, CD_3OD) 7.46 (1H, s, Ar*H*), 7.33 (1H, d, *J* 8.0, Ar*H*), 7.19 (1H, dd, *J* 7.5, 0.8, Ar*H*), 2.33 (3H, s, CH_3); ^{13}**C NMR** δ (62.9 MHz, CD_3OD) 173.4 (C), 143.1 (C), 136.6 (C), 134.7 (CH), 129.7 (CH), 129.2 (CH), 120.0 (C), 20.9 (CH_3); ***m/z*** (FAB, 3-NOBA) 216 ([^{81Br}M+H]$^+$, 75%), 214 ([^{79Br}M+H]$^+$, 77), 199 (10), 197 (10), 154 (100), 136 (100), 121 (27); **HRMS** (EI) Found: [^{81Br}M]$^+$, 214.9760. $C_8H_8ON^{81}Br$ requires 214.9763. Found: [^{79Br}M]$^+$, 212.9779. $C_8H_8ON^{79}Br$ requires 212.9784.

2-Bromo-5-methoxybenzamide 11d[2]



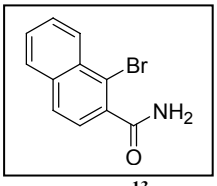
General procedure **A** was followed using 2-bromo-5-methoxy benzoic acid (1.00 g, 4.53 mmol) and thionyl chloride (15 mL) to afford amide **11d** as a colourless solid (650 mg, 65%). $\mathbf{R_f}$ [CH_2Cl_2:MeOH, 95:5] = 0.45; **MP** 154°C, lit 157°C[2]; $\boldsymbol{\upsilon_{max}}$ ($CHCl_3$)/cm^{-1} 3415 (NH), 1635 (C=O); ^{1}**H NMR** δ (250 MHz, CD_3OD) 7.53 (1H, d, *J* 8.8, Ar*H*), 7.04 (1H, d, *J* 3.3, Ar*H*), 6.95 (1H, dd, *J* 8.8, 3.3, Ar*H*), 3.84 (3H, s, CH_3); ^{13}**C NMR** δ (62.9 MHz, CD_3OD) 160.1 (C), 150.8 (C), 134.7 (CH), 128.8 (C), 117.7 (CH), 115.0 (CH), 109.8 (C), 55.8 (CH_3); ***m/z*** (FAB, 3-NOBA) 232 ([^{81Br}M+H]$^+$, 65%), 230 ([^{79Br}M+H]$^+$, 67), 154 (100), 136 (100), 121 (26), 109 (42); **HRMS** (EI) Found: [^{81Br}M]$^+$, 230.9715. $C_8H_8O_2N^{81}Br$ requires 230.9713. Found: [^{79Br}M]$^+$, 228.9733. $C_8H_8O_2N^{79}Br$ requires 228.9733.

2-Bromo-4,5-methoxybenzamide 11e[3]



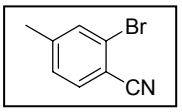
General procedure **A** was followed using 2-bromo-4,5-methoxy benzoic acid (2.00 g, 7.66 mmol) and thionyl chloride (30 mL) to afford amide **11e** as a colourless solid (1.45 g, 73%). $\mathbf{R_f}$ [CH_2Cl_2:MeOH, 95:5] = 0.49; **MP** 178°C, lit 178°C[3]; $\boldsymbol{\upsilon_{max}}$ ($CHCl_3$)/cm^{-1} 3442 (NH), 1676 (C=O); **^{1}H NMR** δ (250 MHz, $(CD_3)_2SO$) 7.73 (1H, br s, N*H*), 7.48 (1H, br s, N*H*), 7.14 (1H, s, Ar*H*), 7.02 (1H, s, Ar*H*), 3.80 (3H, s, CH_3), 3.78 (3H, s, CH_3); **^{13}C NMR** δ (62.9 MHz, $(CD_3)_2SO$) 167.9 (C), 149.1 (C), 147.0 (C), 129.9 (C), 115.1 (CH), 111.4 (CH), 108.6 (C), 55.3 (CH_3), 55.1 (CH_3); ***m/z*** (FAB, 3-NOBA) 262 ([^{81Br}M+H]$^+$, 100%), 260 ([^{79Br}M+H]$^+$, 83), 245 (100), 243 (71), 204 (23), 202 (34), 200 (24), 181 (37), 180 (26), 167 (27), 166 (30); **HRMS** (EI) Found: [^{81Br}M]$^+$, 260.9825. $C_9H_{10}O_3N^{79}Br$ requires 260.9818. Found: [^{79Br}M]$^+$, 258.9838. $C_9H_{10}O_3N^{79}Br$ requires 258.9839.

1-Bromo-naphthalene-2-carboxamide 11f[4]



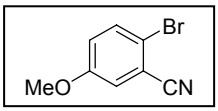
General procedure **A** was followed using 1-bromo-2-naphthoic acid (1.00 g, 3.98 mmol) and thionyl chloride (15 mL) to afford amide **11f** as a colourless solid (995 mg, 99%). $\mathbf{R_f}$ [CH_2Cl_2:MeOH, 95:5] = 0.67; **MP** 202°C (H_2O); $\boldsymbol{\upsilon_{max}}$ ($CHCl_3$)/cm^{-1} 3440 (NH), 1678 (C=O); **^{1}H NMR** δ (250 MHz, $(CD_3)_2SO$) 8.20 (1H, d, *J* 7.5, Ar*H*), 8.17 (1H, br s, N*H*), 8.14 (2H, br s, 2×Ar*H*), 7.88 (1H, br s, N*H*), 7.84 (1H, td, *J* 6.8, 1.5, Ar*H*), 7.79 (1H, td, *J* 6.8, 1.5, Ar*H*), 7.62 (1H, d, *J* 6.8, Ar*H*); **^{13}C NMR** δ (62.9 MHz, $(CD_3)_2SO$) 169.4 (C), 137.7 (C), 133.4 (C), 130.8 (C), 128.1 (2×CH), 127.7 (CH), 127.0 (CH), 126.4 (CH), 124.6 (CH), 117.8 (C); ***m/z*** (FAB, 3-NOBA) 252 ([^{81Br}M+H]$^+$, 76%), 250 ([^{79Br}M+H]$^+$, 90), 235 (12), 233 (13), 154 (100), 149 (26), 138 (41), 136 (97), 107 (46); **HRMS** (EI +ve) Found: [^{81Br}M]$^+$, 250.9765. $C_{11}H_8{}^{81}BrNO$ requires 250.9763. Found: [^{79Br}M]$^+$, 248.9782. $C_{11}H_8{}^{79}BrNO$ requires 248.9784. ^{1}H and ^{13}C NMR data in good agreement with the literature.[4]

2-Bromo-4-methyl benzonitrile 12b[5]



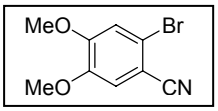
A mixture of amide **11b** (750 mg, 3.50 mmol) and thionyl chloride (5 mL) was refluxed at 60°C for 3 h. The reaction was concentrated under reduced pressure to afford nitrile **12b** as a colourless solid (500 mg, 73%). $\mathbf{R_f}$ [hexane:EtOAc, 3:1] = 0.75; **MP** 55°C, lit 56°C[5]; $\boldsymbol{\upsilon_{max}}$ ($CHCl_3$)/cm^{-1} 2230 (CN); **^{1}H NMR** δ (250 MHz, CD_3OD) 7.38-7.37 (2H, m, 2×Ar*H*), 7.34 (1H, dq, *J* 8.0, 1.5, Ar*H*), 2.43 (3H, s, CH_3); **^{13}C NMR** δ (62.9 MHz, CD_3OD) 146.8 (C), 134.6 (CH), 134.2 (CH), 129.3 (CH), 124.9 (C), 117.5 (C), 112.9 (C), 20.8 (CH_3); ***m/z*** (FAB, 3-NOBA) 198 ([^{81Br}M+H]$^+$, 47%), 196 ([^{79Br}M+H]$^+$, 48), 167 (13), 165 (12), 154 (100); **HRMS** (ES, 3-NOBA) Found: [^{81Br}M]$^+$, 196.9656. $C_8H_6{}^{81}BrN$ requires 196.9658. Found: [^{79Br}M]$^+$, 194.9678. $C_8H_6{}^{79}BrN$ requires 194.9678.

2-Bromo-5-methoxybenzonitrile 12d[6]



A mixture of amide **11d** (630 mg, 2.74 mmol) and thionyl chloride (3 mL) was refluxed at 60°C for 3 h. The reaction was concentrated under reduced pressure to afford nitrile **12d** as a colourless solid (510 mg, 88%). $\mathbf{R_f}$ [hexane:EtOAc, 3:1] = 0.74; **MP** 95°C, lit 98.5-99.5°C[6]; $\boldsymbol{\upsilon_{max}}$ ($CHCl_3$)/cm^{-1} 2229 (CN); **^{1}H NMR** δ (250 MHz, CD_3OD) 7.67 (1H, d, *J* 9.0, Ar*H*), 7.38 (1H, d, *J* 3.1, Ar*H*), 7.18 (1H, dd, *J* 9.0, 3.1, Ar*H*), 3.89 (3H, s, CH_3); **^{13}C NMR** δ (62.9 MHz, CD_3OD) 161.3 (C), 134.9 (CH), 121.9 (CH), 120.0 (CH), 117.6 (C), 116.7 (C), 115.7 (C), 56.2 (CH_3); ***m/z*** (FAB, 3-NOBA) 214 ([^{81Br}M+H]$^+$, 8%), 212 ([^{79Br}M+H]$^+$, 8), 167 (20), 165 (26), 154 (100); **HRMS** (EI) Found: [^{81Br}M]$^+$, 212.9604. $C_8H_6{}^{81}BrNO$ requires 212.9607. Found: [^{79Br}M]$^+$, 210.9622. $C_8H_6{}^{79}BrNO$ requires 210.9627.

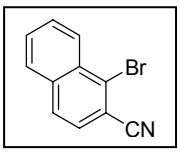
2-Bromo-4,5-methoxybenzonitrile 12e[7]



A mixture of amide **11e** (1.25 g, 4.81 mmol) and thionyl chloride (30 mL) was refluxed at 60°C for 3 h. The reaction was concentrated under reduced pressure to afford nitrile **12e** as a colourless solid (1.15 g, 99%). $\mathbf{R_f}$ [hexane:EtOAc, 3:1] = 0.5; **MP** 113°C (EtOH), lit 117°C[7]; $\boldsymbol{\upsilon_{max}}$ ($CHCl_3$)/cm^{-1} 2229 (CN); **^{1}H NMR** δ

(250 MHz, $(CD_3)_2SO$) 7.49 (1H, s, Ar*H*), 7.39 (1H, s, Ar*H*), 3.87 (3H, s, CH_3), 3.81 (3H, s, CH_3); **^{13}C NMR** δ (90.6 MHz, $(CD_3)_2SO$) 153.4 (C), 148.5 (C), 117.9 (C), 116.9 (C), 116.2 (CH), 115.9 (CH), 105.4 (C), 56.8 (CH_3), 56.3 (CH_3); ***m/z*** (FAB, 3-NOBA) 244 ([^{81Br}M+H]$^+$, 27%), 242 ([^{79Br}M+H]$^+$, 42), 167 (16), 154 (98), 152 (17), 150 (15), 149 (49), 137 (82), 136 (74); **HRMS** (EI) Found: [^{81Br}M]$^+$, 242.9708. $C_9H_8{}^{81}BrNO_2$ requires 242.9713. Found: [^{79Br}M]$^+$, 240.9726. $C_9H_8{}^{79}BrNO_2$ requires 240.9733.

1-Bromo-2-naphthalene-2-carbonitrile 12f[8]

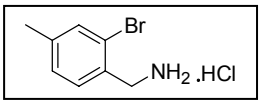


A mixture of amide **11f** (950 mg, 3.80 mmol) and thionyl chloride (6 mL) was refluxed at 60°C for 3 h. The reaction was concentrated under reduced pressure to afford nitrile **12f** as a colourless solid (839 mg, 95%). **R_f** [hexane:EtOAc, 3:1] = 0.83; **MP** 91°C (EtOH), lit 93°C[8]; **υ_{max}** ($CHCl_3$)/cm^{-1} 2226 (CN), 1580 (C=C), 1560 (C=C); **^{1}H NMR** δ (250 MHz, CD_3OD) 8.33-8.29 (1H, m, Ar*H*), 8.04-7.98 (2H, m, 2×Ar*H*), 7.80-7.72 (2H, m, 2×Ar*H*), 7.66 (1H, d, *J* 8.5, Ar*H*); **^{13}C NMR** δ (62.9 MHz, CD_3OD) 136.3 (C), 132.1 (C), 130.2 (CH), 129.6 (CH), 129.5 (CH), 129.2 (CH), 128.3 (CH), 128.2 (C), 127.9 (CH), 118.2 (C), 113.9 (C); ***m/z*** (FAB, 3-NOBA) 234 ([^{81Br}M+H]$^+$, 27%), 232 ([^{79Br}M+H]$^+$, 27), 154 (99), 138 (48), 136 (100); **HRMS** (EI +ve) Found: [^{81Br}M]$^+$, 232.9656. $C_{11}H_6N{}^{81}Br$ requires 232.9658. Found: [^{79Br}M]$^+$, 230.9680. $C_{11}H_6N{}^{79}Br$ requires 230.9678.

General procedure B - Reduction of aryl nitrile analogues

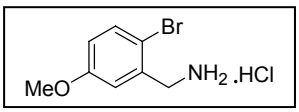
To a suspension of $LiAlH_4$ (2 eq) in Et_2O (10 mL) was added $AlCl_3$ (2 eq) and the reaction stirred for 10 mins at r.t. The mixture was cooled to 0°C and the appropriate nitrile (1 eq) was added portionwise. The reaction was stirred at r.t for 30 mins then heated at 40°C for 18 h. The reaction was quenched by the addition of $Na_2SO_4.5H_2O$ portionwise, then it was filtered and the filtrate stirred vigorously with potassium sodium tartrate (100 mL, sat. aq.) for 1 h. The Et_2O layer was separated and the aqueous phase extracted with Et_2O (3 × 60 mL). The combined organic phases were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was taken up in CH_2Cl_2 (1 mL), and HCl in Et_2O (20.0 mL, 1 M in Et_2O) added. The precipitate was removed by filtration and dried to afford the desired amine hydrochloride.

2-Bromo-4-methylbenzylamine hydrochloride 9b



General procedure **B** was followed using $LiAlH_4$ (186 mg, 4.90 mmol), Et_2O (5 mL), $AlCl_3$ (654 mg, 4.90 mmol) and nitrile **12b** (480 mg, 2.45 mmol), to afford amine hydrochloride **9b** as a colourless solid (465 mg, 80%). **MP** 249°C (Et_2O); **^{1}H NMR** δ (250 MHz, CD_3OD) 7.53 (1H, s, Ar*H*), 7.43 (1H, d, *J* 8.0, Ar*H*), 7.27 (1H, d, *J* 8.0, Ar*H*), 4.23 (2H, s, CH_2), 2.35 (3H, s, CH_3); **^{13}C NMR** δ (62.9 MHz, CD_3OD) 142.8 (C), 134.4 (CH), 131.5 (CH), 130.5 (C), 129.9 (CH), 124.7 (C), 43.6 (CH_2), 20.5 (CH_3); ***m/z*** (FAB, 3-NOBA) 202 ([^{81Br}M+H]$^+$, 91%), 200 ([^{79Br}M+H]+, 93), 185 (95), 183 (95),154 (51); **HRMS** (EI) Found: [^{81Br}M]$^+$, 200.9969. $C_8H_{10}{}^{81}BrN$ requires 200.9971. Found: [^{79Br}M]$^+$, 198.9985 $C_8H_{10}{}^{79}BrN$ requires 198.9991. **Free Amine: R_f** [CH_2Cl_2:MeOH, 95:5] = 0.46; **υ_{max}** ($CHCl_3$)/cm^{-1} 3371 (NH), 3304 (NH), 2922, 1605, 1488; **^{1}H NMR** δ (250 MHz, $CDCl_3$) 7.33 (1H, s, Ar*H*), 7.19 (1H, d, *J* 7.7, Ar*H*), 7.05 (1H, d, *J* 7.7, Ar*H*), 3.81 (2H, s, CH_2), 2.27 (3H, s, CH_3); **^{13}C NMR** δ (62.9 MHz, $CDCl_3$) 138.4 (C), 137.6 (C), 132.4 (CH), 128.0 (CH), 127.6 (CH), 122.4 (C), 45.8 (CH_3), 19.8 (CH_2).

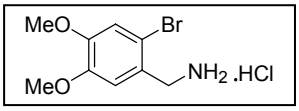
2-Bromo-5-methoxybenzylamine hydrochloride 9d



General procedure **B** was followed using $LiAlH_4$ (36.0 mg, 0.94 mmol), Et_2O (1.00 mL), $AlCl_3$ (432 mg, 0.94 mmol) and nitrile **163c** (100 mg, 0.47 mmol), to afford amine hydrochloride **9d** as a colourless solid (301 mg, 74%). **MP** 201°C; **^{1}H NMR** δ (250 MHz, CD_3OD) 7.62 (1H, d, *J* 8.9, Ar*H*), 7.19 (1H, d, *J* 3.0, Ar*H*), 6.99 (1H, dd, *J* 8.9, 3.0, Ar*H*), 4.27 (2H, s, CH_2), 3.87 (3H, s, CH_3); **^{13}C NMR** δ (62.9 MHz, CD_3OD) 160.6 (C), 146.3 (C), 134.7 (CH), 117.2 (CH), 117.1 (CH), 114.5 (C), 55.7 (CH_3), 43.7 (CH_2); ***m/z*** (FAB, 3-NOBA) 218 ([^{81Br}M+H]$^+$, 51%), 216 ([^{79Br}M+H]$^+$, 62),

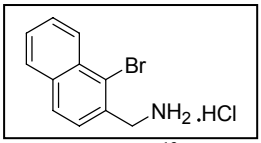
201 (39), 199 (40), 154 (100), 149 (43), 137 (59); **HRMS** (EI) Found: $[^{81Br}M]^+$, 216.9915. $C_8H_{10}ON^{81}Br$ requires 216.9920. Found: $[^{79Br}M]^+$, 214.9935. $C_8H_{10}ON^{79}Br$ requires 214.9940. **Free Amine: R_f** [CH_2Cl_2:MeOH, 95:5] = 0.36; **υ_{max}** ($CHCl_3$)/cm^{-1} 3370 (NH), 1593, 1573, 1470, 1242; **^{1}H NMR** δ (250 MHz, $CDCl_3$) 7.40 (1H, d, *J* 8.7, Ar*H*), 6.93 (1H, d, *J* 3.0, Ar*H*), 6.66 (1H, dd, *J* 8.7, 3.0, Ar*H*), 3.84 (2H, s, CH_2), 3.78 (3H, s, CH_3); **^{13}C NMR** δ (62.9 MHz, $CDCl_3$) 158.8 (C), 142.7 (C), 132.9 (CH), 114.3 (CH), 113.4 (CH), 113.2 (C), 55.0 (CH_3), 46.6 (CH_2).

2-Bromo-4,5-methoxybenzylamine hydrochloride 9e[9]



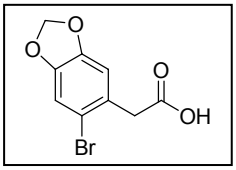
General procedure **B** was followed using $LiAlH_4$ (345 mg, 4.50 mmol), Et_2O (20 mL), $AlCl_3$ (1.21 g, 9.00 mmol) and nitrile **12e** (1.10 g, 4.50 mmol), to afford amine hydrochloride **9e** as a colourless solid (829 mg, 65%). **MP** 194°C; **^{1}H NMR** δ (250 MHz, CD_3OD) 7.25 (1H, s, Ar*H*), 7.21 (1H, s, Ar*H*), 4.25 (2H, s, CH_2), 3.90 (3H, s, CH_3), 3.88 (3H, s, CH_3); **^{13}C NMR** δ (62.9 MHz, CD_3OD) 151.8 (C), 150.2 (C), 125.2 (C), 116.8 (CH), 115.4 (C), 114.9 (CH), 56.5 (2×CH_3), 43.7 (CH_2); ***m/z*** (FAB, 3-NOBA) 248 ($[^{81Br}M+H]^+$, 11%), 246 ($[^{79Br}M+H]^+$, 20), 231 (37), 229 (37), 154 (82), 149 (64), 136 (100); **HRMS** (EI) Found: $[^{81Br}M]^+$, 247.0016. $C_9H_{12}O_2N^{81}Br$ requires 247.0026. Found: $[^{79Br}M]^+$, 245.0034. $C_9H_{12}O_2N^{79}Br$ requires 245.0046. **Free Amine: R_f** [CH_2Cl_2:MeOH, 95: 5] = 0.54; **υ_{max}** ($CHCl_3$)/cm^{-1} 3368 (NH), 2935, 2841, 1602, 1505; **^{1}H NMR** δ (250 MHz, $CDCl_3$) 7.20 (1H, s, Ar*H*), 7.11 (1H, s, Ar*H*), 4.08 (3H, s, CH_3), 4.05 (3H, s, CH_3), 4.03 (2H, s, CH_2), 1.75 (2H, br s, NH_2); **^{13}C NMR** δ (62.9 MHz, $CDCl_3$) 148.2 (C), 148.0 (C), 133.9 (C), 115.3 (CH), 112.8 (C), 111.7 (CH), 55.8 (CH_3), 55.7 (CH_3), 46.2 (CH_2). ^{1}H and ^{13}C NMR data in good agreement with the literature.[9]

(1-Bromo-2-naphthalen-2-yl) methyl amine hydrochloride 9f



General procedure **B** was followed using $LiAlH_4$ (261 mg, 6.89 mmol), Et_2O (10 mL), $AlCl_3$ (920 mg, 6.89 mmol) and nitrile **12f** (800 mg, 3.45 mmol), to afford amine hydrochloride **9f** as a colourless solid (504 mg, 55%). **MP** 270°C (Et_2O); **^{1}H NMR** δ (250 MHz, CD_3OD) 8.37 (1H, d, *J* 9.3, Ar*H*), 8.01 (1H, t, *J* 8.5, Ar*H*), 7.98 (1H, d, *J* 9.5, Ar*H*), 7.75-7.63 (3H, m, 3xAr*H*), 4.54 (2H, s, CH_2); **^{13}C NMR** δ (62.9 MHz, CD_3OD) 136.5 (C), 133.9 (C), 132.3 (C), 130.4 (CH), 130.0 (CH), 129.9 (CH), 129.3 (CH), 128.8 (CH), 128.4 (CH), 126.4 (C) 45.7 (CH_2); ***m/z*** (FAB, 3-NOBA) 238 ($[^{81Br}M+H]^+$, 77%), 236 ($[^{79Br}M+H]^+$, 43), 221 (97), 219 (97)167 (37), 165 (28), 154 (100); **HRMS** (EI +ve) Found: $[^{81Br}M]^+$, 236.9974. $C_{11}H_{10}N^{81}Br$ requires 236.9971. Found: $[^{79Br}M]^+$, 235.0001. $C_{11}H_{10}N^{79}Br$ requires 234.9991. **Free Amine: R_f** [CH_2Cl_2:MeOH, 95:5] = 0.94; **υ_{max}** ($CHCl_3$)/cm^{-1} 3364 (NH), 1596 (NH_2); **^{1}H NMR** δ (250 MHz, $CDCl_3$) 8.15 (1H, d, *J* 8.5, Ar*H*), 7.62 (2H, t, *J* 7.5, 2×Ar*H*), 7.42-7.29 (3H, m, 3xAr*H*), 3.96 (2H, s, CH_2); **^{13}C NMR** δ (62.9 MHz, $CDCl_3$) 140.0 (C), 133.5 (C), 132.2 (C), 127.9 (CH), 127.8 (CH), 127.2 (CH), 126.9 (CH), 126.4 (CH), 126.0 (CH), 122.9 (C), 47.7 (CH_2).

(6-Bromo-benzo[1,3]dioxol-5-yl)-acetic acid 14[10]

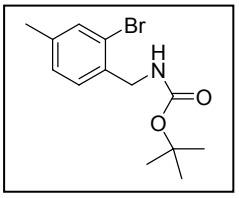


To a solution of 1,3-benzodioxole-5-acetic acid **13**[ref] (700 mg, 3.89 mmol) and NaOH (1.0 mL, 5 M aq.) in H_2O (7 mL) was added DBDMH (600 mg, 2.10 mmol) and the reaction stirred at r.t. under an air atmosphere for 48 h. The reaction was diluted with H_2O (50 mL), acidified to pH 1 with HCl (6 M, aq.) and extracted into Et_2O (3 × 30 mL). The organics were dried ($MgSO_4$) and concentrated under reduced pressure to afford acid **14** as a colourless crystalline powder (909 mg, 91% yield). **R_f** [CH_2Cl_2:MeOH, 95:5] = 0.23; **MP** 191°C (EtOH), lit. 190°C[10]; **υ_{max}** (Nujol)/cm^{-1} 1699 (C=O); **^{1}H NMR** δ (250 MHz, DMSO) 7.21 (1H, s, Ar*H*), 7.02 (1H, s, Ar*H*), 6.07 (2H, s, OCH_2O), 3.63 (2H, s, ArCH_2); **^{13}C NMR** δ (62.9 MHz, DMSO), 171.4 (C), 147.0 (C), 146.8 (C), 127.9 (C), 114.7 (C), 111.9 (CH), 111.4 (CH), 101.7 (CH_2), 40.6 (CH_2); ***m/z*** (EI) 260 ($[^{81Br}M]^+$, 49%), 258 ($[^{81Br}M]^+$, 48), 215 (97), 213 (100), 179 (92), 135 (38), 113 (27); **HRMS** (EI) Found: $[^{79Br}M]^+$, 257.9521. $C_9H_7O_4{}^{79}Br$ requires 257.9522.

General procedure C - Boc protection of aryl analogues

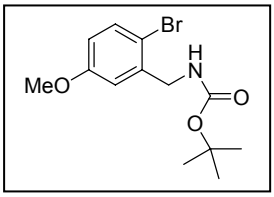
To a suspension of the appropriate amine hydrochloride (1 eq) in CH_2Cl_2 (10 mL) was added Et_3N (1.5 eq) and the reaction stirred for 10 mins. The reaction was cooled to 0°C, Boc_2O (1.1 eq) added and the reaction allowed to warm to r.t. and stirred for 4 h. The reaction was diluted with CH_2Cl_2 (15 mL) and washed with NaCl (3 × 15 mL, sat. aq.). The organics were combined, dried ($MgSO_4$), concentrated under reduced pressure and purified by flash chromatography to afford the desired carbamate.

2-Bromo-4-methylbenzyl-*tert*-butylcarboxamide 16b



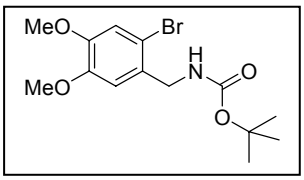
General procedure **C** was followed using amine hydrochloride **9b** (170 mg, 0.72 mmol), CH_2Cl_2 (10 mL), Et_3N (222 µl, 1.58 mmol) and Boc_2O (173 mg, 0.79 mmol). Flash chromatography (hexane:EtOAc, 10:1) afforded carbamate **16b** as a colourless oil (217 mg, 100%). $\mathbf{R_f}$ [3: 1 hexane: EtOAc] = 0.78; $\mathbf{\upsilon_{max}}$ ($CHCl_3$)/cm^{-1} 3346 (NH), 1700 (C=O); **^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 7.36 (1H, s, Ar*H*), 7.25 (1H, d, *J* 7.8, Ar*H*), 7.07 (1H, dd, *J* 7.8, 0.9, Ar*H*), 4.98 (1H, br s, C*H*N), 4.34 (2H, d, *J* 6.2, CH_2Ar), 2.30 (3H, s, CH_3), 1.43 (9H, s, 3×CH_3); **^{13}C NMR** δ (90.6 MHz, 323 K, $CDCl_3$) 155.6 (C), 138.9 (C), 135.0 (C), 133.0 (CH), 129.4 (CH), 128.2 (CH), 123.2 (C), 79.3 (C), 44.6 (CH_2), 28.3 (3×CH_3), 20.4 (CH_3); ***m/z*** (EI) 302 ([^{81Br}M+H]$^+$, 2%), 300 ([^{79Br}M+H]$^+$, 2), 244 (7), 242 (7); **HRMS** (EI) Found: [^{79Br}M]$^+$, 299.0516. $C_{13}H_{18}{}^{79}BrNO_2$ requires 299.0515.

2-Bromo-5-methoxybenzyl-*tert*butylcarboxamide 16d



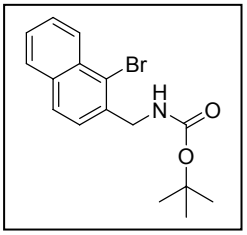
General procedure **C** was followed using amine hydrochloride **9d** (218 mg, 0.86 mmol), CH_2Cl_2 (10 mL), Et_3N (182 µl, 1.30 mmol) and Boc_2O (207 mg, 0.95 mmol). Flash chromatography (hexane:EtOAc, 10:1) afforded carbamate **16d** as a colourless oil (230 mg, 85%). $\mathbf{R_f}$ [hexane:EtOAc, 3:1] = 0.77; $\mathbf{\upsilon_{max}}$ ($CHCl_3$)/cm^{-1} 3350 (NH), 1698 (C=O); **^{1}H NMR** δ (360 MHz, $CDCl_3$) 7.40 (1H, d, *J* 8.7, Ar*H*), 6.93 (1H, d, *J* 3.1, Ar*H*), 6.68 (1H, dd, *J* 8.7, 3.1, Ar*H*), 5.00 (1H, br s, N*H*), 4.33 (2H, d, *J* 6.3, CH_2Ar), 3.77 (3H, s, CH_3),1.46 (9H, s, 3×CH_3); **^{13}C NMR** δ (90.6 MHz, $CDCl_3$) 159.2 (C), 155.6 (C), 139.0 (C), 133.1 (CH), 115.2 (CH), 114.6 (CH), 113.6 (C), 79.5 (C), 55.4 (CH_3), 45.0 (CH_2), 28.3 (3×CH_3); ***m/z*** (EI) 317 ([^{81Br}M]$^+$, 1%), 315 ([^{79Br}M]$^+$, 1), 261 (3), 259 (3), 201 (9), 199 (10), 180 (100); **HRMS** (EI) Found: [^{79Br}M]$^+$, 315.0461. $C_{13}H_{18}{}^{79}BrNO_3$ requires 315.0465.

(2-Bromo-4,5-dimethoxy-benzyl)-carbamic acid *tert*-butyl ester 16e



General procedure **C** was followed using amine hydrochloride **9e** (200 mg, 0.710 mmol), CH_2Cl_2 (10 mL), Et_3N (219 µl, 1.56 mmol) and Boc_2O (155 mg, 0.710 mmol). Flash chromatography (hexane:EtOAc, 10:1) afforded carbamate **16e** as a colourless oil (267 mg, 100%). $\mathbf{R_f}$ [hexane:EtOAc, 3:1] = 0.63; $\mathbf{\upsilon_{max}}$ ($CHCl_3$)/cm^{-1} 3377 (NH), 1701 (C=O); **^{1}H NMR** δ (360 MHz, $CDCl_3$) 6.93 (1H, s, Ar*H*), 6.85 (1H, s, Ar*H*), 5.07 (1H, br s, C*H*N), 4.24 (2H, d, *J* 6.0, CH_2Ar), 3.79 (6H, s, 2×CH_3), 1.39 (9H, s, 3×CH_3); **^{13}C NMR** δ (90.6 MHz, $CDCl_3$) 155.7 (C), 149.1 (C), 148.7 (C), 130.4 (CH), 115.9 (CH), 113.4 (C), 113.2 (C), 79.5 (C), 56.2 (CH_3), 56.1 (CH_3), 44.7 (CH_2), 28.3 (3×CH_3); ***m/z*** (EI) 347 ([^{81Br}M]$^+$, 4%), 345 ([^{79Br}M]$^+$, 4), 290 (27), 288 (27), 242 (13), 210 (100); **HRMS** (EI) Found: [^{79Br}M]$^+$, 345.0570. $C_{14}H_{20}{}^{79}BrNO_4$ requires 345.0570.

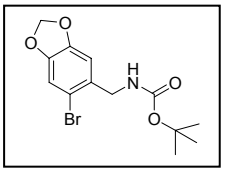
(1-Bromo-naphthalen-2-ylmethyl) carbamic acid *tert*-butyl ester 16f



General procedure **C** was followed using amine hydrochloride 9f (200 mg, 0.73 mmol), CH_2Cl_2 (10 mL), Et_3N (155 µl, 1.10 mmol) and Boc_2O (176 mg, 0.81 mmol). Flash chromatography (hexane:EtOAc, 10:1) afforded carbamate 16f as a colourless solid (222 mg, 90%). $\mathbf{R_f}$ [hexane:EtOAc, 3:1] = 0.64; **MP** 96°C; $\mathbf{\upsilon_{max}}$ ($CHCl_3$)/cm^{-1} 3346 (NH), 1699 (C=O); **^{1}H NMR** δ (250 MHz, $CDCl_3$) 8.21 (1H, d, *J* 8.5, Ar*H*), 7.72 (1H, d, *J* 7.3, Ar*H*), 7.69 (1H, d, *J* 8.3,

Ar*H*), 7.53-7.39 (3H, m, 3xAr*H*), 5.09 (1H, br s, N*H*), 4.54 (2H, d, *J* 6.3, CH_2), 1.37 (9H, s, 3×CH_3); **^{13}C NMR** δ (62.9 MHz, $CDCl_3$) 155.7 (C), 136.0 (C), 133.7 (C), 132.2 (C), 128.0 (CH), 127.8 (CH), 127.4 (CH), 127.0 (CH), 126.8 (CH), 126.3 (CH), 123.4 (C), 79.6 (C), 45.7 (CH_2), 28.3 (3×CH_3); ***m/z*** (EI) 337 ([^{81Br}M+H]$^+$, 1%), 335 ([^{79Br}M+H]$^+$,1), 200 (100); **HRMS** (EI) Found: [^{79Br}M]$^+$, 335.0506. $C_{16}H_{18}{}^{79}BrNO_2$ requires 335.0515.

6-Bromo-benzo[1,3]dioxol-5-ylmethyl)-carbamic acid *tert*-butyl ester 16g

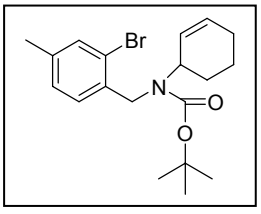


To a suspension of acid **14** (1.72 g, 6.64 mmol) and Et_3N (1.31 mL, 9.40 mmol) in CH_2Cl_2 (50 mL) at 0°C was added diphenylphosphoryl azide (2.00 mL, 9.30 mmol) and the reaction stirred at 0°C for 30 mins. The reaction was warmed to r.t. and stirred for 30 mins before being filtered through a silica gel plug. The crude organics were concentrated under reduced pressure and refluxed in toluene (50 mL) at 80°C for 1 h to ensure complete conversion to isocyanate **15**. The reaction was concentrated under reduced pressure and then refluxed at 80°C in ^{t}BuOH (50 mL) for 19 h. The reaction was concentrated under reduced pressure and purified by flash chromatography (hexane:EtOAc, 100:2–100:8) to afford carbamate **16g** as a colourless oil (1.09 g, 50%). $\mathbf{R_f}$ [hexane:EtOAc, 10:1] = 0.21; $\boldsymbol{\upsilon_{max}}$ ($CHCl_3$)/cm^{-1} 3346 (NH), 1694 (C=O); **^{1}H NMR** δ (250 MHz, $CDCl_3$) 6.99 (1H, s, Ar*H*), 6.95 (1H, s, Ar*H*), 5.97 (2H, s, OCH_2O), 4.99 (1H, br s, N*H*), 4.28 (2H, d, *J* 6.2, CH_2Ar), 1.46 (9H, s, 3×CH_3); **^{13}C NMR** δ (90.6 MHz, $CDCl_3$), 155.6 (C), 147.4 (C), 147.3 (C), 131.1 (C), 113.6 (C), 112.5 (CH), 109.5 (CH), 101.6 (CH_2), 79.4 (C), 44.5 (CH_2), 28.2 (3×CH_3); ***m/z*** (EI) 331 ([^{81Br}M]$^+$, 1%), 329 ([^{79Br}M]$^+$, 1), 274 (1), 272 (1), 194 (7), 49 (100). **HRMS** (EI) Found: [^{79Br}M]$^+$, 329.0258. $C_{13}H_{16}O_4N^{79}Br$ requires 329.0257.

General procedure D – Preparation of cyclisation precursors 5b-g

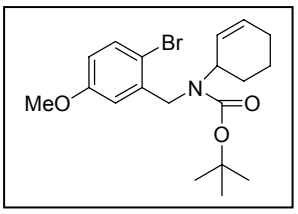
To a solution of Boc carbamate 5 (87 mg, 0.23 mmol) in DMF (1.5 mL) at 0°C was added NaH (2 eq, 60% dispersion in mineral oil) and the reaction warmed to r.t. for 40 mins. The reaction was then cooled to 0°C and 3-bromocyclohexene (2 eq) was added dropwise. The reaction allowed to warm to r.t. and stirred for 16 h. Et_2O (10 mL) was added and the organics washed with NaCl (3 × 15 mL, sat. aq.). The organics were dried ($MgSO_4$), concentrated under reduced pressure and purified by flash chromatography to afford the desired cyclohexenyl amine.

2-Bromo-4-methylbenzyl cyclohex-2-enyl-carbamic acid *tert*-butyl ester 5b



General procedure **D** was followed using Boc carbamate **16b** (198 mg, 0.659 mmol), DMF (5 mL), NaH (53 mg, 60% dispersion in mineral oil, 1.32 mmol) and 3-bromocyclohexene (153 µl, 1.32 mmol). Flash chromatography (hexane-hexane:EtOAc, 100:1) afforded cyclohexenyl amine **5b** as a colourless oil (175 mg, 70%). $\mathbf{R_f}$ [hexane:EtOAc, 3:1] = 0.76; $\boldsymbol{\upsilon_{max}}$ ($CHCl_3$)/cm^{-1} 1640 (C=O); **^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 7.33 (1H, s, Ar*H*), 7.14 (1H, d, *J* 7.9, Ar*H*), 7.07 (1H, d, *J* 7.9, Ar*H*), 5.82-5.80 (1H, m, C*H*=CH), 5.47 (1H, d, *J* 10.2, CH=C*H*), 4.84 (1H, br s, C*H*N), 4.39-4.34 (2H, m, CH_2Ar), 2.30 (3H, s, CH_3), 2.04-1.84 (3H, m, CH_2+CH_AH$_B$), 1.80-1.68 (1H, m, CH$_A$$H_B$), 1.65-1.25 (11H, m, C$H_2$+3×C$H_3$); **^{13}C NMR** δ (90.6 MHz, 323 K, $CDCl_3$) 155.7 (C), 137.6 (C), 135.9 (C), 132.6 (CH), 131.1 (CH), 128.2 (CH), 127.8 (CH), 127.3 (CH), 121.8 (C), 79.5 (C), 53.0 (CH), 47.3 (CH_2), 28.2 (3×CH_3), 28.1 (CH_2), 24.4 (CH_2), 21.3 (CH_2), 20.3 (CH_3); ***m/z*** (FAB, 3-NOBA) 382 ([^{81Br}M+H]$^+$, 12%), 380 ([^{79Br}M+H]$^+$, 15), 326 (100), 324 (100), 185 (96), 183 (97); **HRMS** (EI) Found: [^{79Br}M]$^+$, 379.1142. $C_{19}H_{26}{}^{79}BrNO_2$ requires 379.1141.

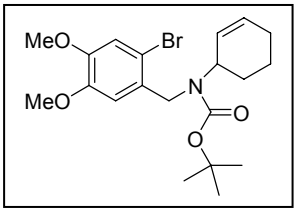
(2-Bromo-5-methoxybenzyl)-(cyclohex-2-enyl)-carbamic acid *tert*-butyl ester 5d



General procedure **D** was followed using Boc carbamate **16d** (222 mg, 0.703 mmol), DMF (5 mL), NaH (56 mg, 60% dispersion in mineral oil, 1.41 mmol) and 3-bromocyclohexene (163 µl, 1.41 mmol). Flash chromatography (hexane:EtOAc, 100:1) afforded cyclohexenyl amine **5d** as a colourless oil (201 mg, 72%). $\mathbf{R_f}$ [hexane:EtOAc, 3:1] = 0.74; $\boldsymbol{\upsilon_{max}}$ ($CHCl_3$)/cm^{-1} 1694 (C=O); **^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 7.45

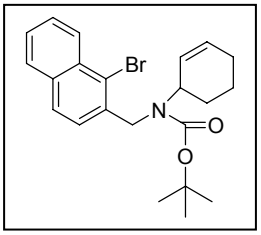
(1H, d, *J* 8.8, Ar*H*), 6.85 (1H, d, *J* 3.1, Ar*H*), 6.66 (1H, dd, *J* 8.8, 3.1, Ar*H*), 5.89-5.80 (1H, m, C*H*=CH), 5.49 (1H, d, *J* 10.1, CH=C*H*), 4.88 (1H, br s, C*H*N), 4.37 (1H, d, *J* 17.4, CH_XH_YAr), 4.30 (1H, d, *J* 17.4, CH_XH_YAr), 3.77 (3H, s, OCH_3), 2.08-1.87 (3H, m, CH_2+CH_AH_B), 1.80-1.71 (1H, m, CH_AH_B), 1.70-1.29 (11H, m, CH_2+3×CH_3); **^{13}C NMR** δ (90.6 MHz, 323 K, $CDCl_3$) 159.1 (C), 155.7 (C), 132.8 (CH), 131.4 (C), 128.2 (2×CH), 113.8 (CH), 113.4 (CH), 112.5 (C), 79.8 (C), 55.3 (CH_3), 53.4 (CH), 47.7 (CH_2), 28.3 (CH_2), 28.2 (3×CH_3), 24.5 (CH_2), 21.3 (CH_2); ***m/z*** (EI) 398 ($[^{81Br}M+H]^+$, 7%), 396 ($[^{79Br}M+H]^+$, 9), 342 (100), 340 (100), 260 (100), 201 (41), 199 (42); **HRMS** (EI) Found: $[^{79Br}M]^+$, 395.1090. $C_{19}H_{26}{}^{79}BrNO_3$ requires 395.1090.

2-Bromo-4,5-dimethoxybenzyl-(cyclohex-2-enyl)-carbamic acid *tert*-butyl ester 5e



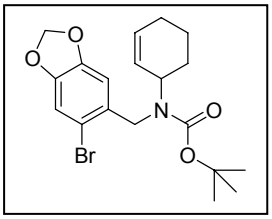
General procedure **D** was followed using Boc carbamate 16e (87 mg, 0.23 mmol), DMF (1.5 mL), NaH (18 mg, 60% dispersion in mineral oil, 0.46 mmol) and 3-bromocyclohexene (53 µl, 0.46 mmol). Flash chromatography (hexane:EtOAc:Et_3N, 100:5:0.5) afforded cyclohexenyl amine 5e as a colourless oil (81 mg, 84%). **R_f** [hexane:EtOAc, 3:1] = 0.49; **υ_{max}** ($CHCl_3$)/cm^{-1} 1640 (C=O); **^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 6.97 (1H, s, Ar*H*), 6.82 (1H, s, Ar*H*), 5.85-5.77 (1H, m, C*H*=CH), 5.44 (1H, d, *J* 10.0, CH=C*H*), 4.80 (1H, br s, C*H*N), 4.35 (1H, d, *J* 16.5, CH_XH_YAr), 4.26 (1H, d, *J* 16.5, CH_XH_YAr), 3.83 (3H, s, CH_3), 3.81 (3H, s, CH_3), 2.05-1.92 (2H, m, CH_2), 1.91-1.80 (1H, m, CH_AH_B), 1.74-1.65 (1H, m, CH_AH_B), 1.65-1.30 (11H, m, CH_2+3×CH_3); **^{13}C NMR** δ (90.6 MHz, 323 K, $CDCl_3$) 155.7 (C), 148.6 (C), 148.3 (C), 131.3 (C), 131.1 (CH), 128.2 (CH), 115.6 (CH), 111.8 (C), 111.2 (CH), 79.6 (C), 56.1 (CH_3), 55.9 (CH_3), 53.1 (CH), 47.1 (CH_2), 28.2 (3×CH_3), 28.1 (CH_2), 24.4 (CH_2), 21.3 (CH_2); ***m/z*** (FAB, 3-NOBA) 428 ($[^{81Br}M+H]^+$, 6%), 426 ($[^{79Br}M+H]^+$, 9), 372 (34), 370 (40), 346 (16), 326 (10), 290 (100), 231 (100), 229 (100); **HRMS** (EI) Found: $[^{79Br}M]^+$, 426.1268. $C_{20}H_{29}{}^{79}BrNO_4$ requires 426.1275.

1-Bromo-naphthalen-2-ylmethyl-(cyclohex-2-enyl)-carbamic acid *tert*-butyl ester 5f



General procedure **D** was followed using Boc carbamate **16f** (165 mg, 0.49 mmol), DMF (5 mL), NaH (40 mg, 60% dispersion in mineral oil, 0.982 mmol) and 3-bromocyclohexene (114 µl, 0.98 mmol). Flash chromatography (hexane:EtOAc, 100:1) afforded cyclohexenyl amine **5f** as a colourless oil (175 mg, 86%). **R_f** [hexane:EtOAc, 3:1] = 0.80; **υ_{max}** ($CHCl_3$)/cm^{-1} 1652 (C=O); **^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 8.33 (1H, d, *J* 8.7, Ar*H*), 7.82 (1H, d, *J* 7.4, Ar*H*), 7.80 (1H, d, *J* 8.4, Ar*H*), 7.58 (1H, t, *J* 6.9, Ar*H*), 7.48 (1H, ddd, *J* 8.3, 7.2, 1.1, Ar*H*), 7.43 (1H, d, *J* 8.6, Ar*H*), 5.83 (1H, br s, C*H*=CH), 5.52 (1H, d, *J* 10.0, CH=C*H*), 4.95 (1H, br s, C*H*N), 4.66 (2H, br s, CH_2Ar), 2.10-1.88 (3H, m, CH_2+CH_AH_B), 1.80-1.71 (1H, m, CH_AH_B), 1.70-1.30 (11H, m, CH_2+3×CH_3);**^{13}C NMR** δ (90.6 MHz, 323 K, $CDCl_3$) 155.9 (C), 137.3 (C), 133.6 (C), 132.2 (C), 131.3 (CH), 128.2 (CH), 127.9 (CH), 127.2 (2×CH), 126.7 (CH), 125.9 (CH), 125.0 (CH), 121.5 (C), 79.8 (C) 53.0 (CH), 48.6 (CH_2), 28.2 (3×CH_3), 28.1 (CH_2), 24.5 (CH_2), 21.3 (CH_2); ***m/z*** (FAB, 3-NOBA) 418 ($[^{81Br}M+H]^+$, 2%), 416 ($[^{79Br}M+H]^+$, 3), 362 (80), 360 (85), 221 (100), 219 (100), 200 (33), 141 (41), 139 (36); **HRMS** (EI) Found: $[^{79Br}M]^+$, 415.1140. $C_{22}H_{26}N{}^{79}BrNO_2$ requires 415.1141.

(4-Bromo-benzo[1,3]dioxol-5-ylmethyl)-(cyclohex-2-enyl)-carbamic acid *tert*-butyl ester 16g



General procedure **D** was followed using Boc carbamate **5g** (140 mg, 0.42 mmol), DMF (4 mL), NaH (34 mg, 60% dispersion in mineral oil, 0.84 mmol) and 3-bromocyclohexene (100 µl, 0.84 mmol). Flash chromatography (hexane:EtOAc, 100:1–100:3) afforded cyclohexene **16g** as a colourless oil (130 mg, 75%). **R_f** [hexane:EtOAc, 3:1] = 0.69; **υ_{max}** ($CHCl_3$)/cm^{-1} 1693 (C=O); **^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 6.95 (1H, s, Ar*H*), 6.78 (1H, s, Ar*H*), 5.93 (2H, s, OCH_2O), 5.83-5.81 (1H, m, C*H*=CH), 5.45 (1H, br d, *J* 10.2, CH=C*H*), 4.76 (1H, br s, C*H*N), 4.34-4.15 (2H, m, CH_2Ar), 2.01-1.97 (2H, m, CH_2), 1.90-1.88 (1H, m, CH_AH_B), 1.75-1.73 (1H, m, CH_AH_B), 1.63-1.59 (2H, m, CH_2), 1.44-1.41 (9H, s, 3×CH_3); **^{13}C NMR** δ (90.6 MHz, 323 K, $CDCl_3$), 155.7 (C), 147.4 (C), 146.8 (C), 132.6 (C), 131.0 (CH), 128.2 (CH), 112.3 (CH), 112.0 (C), 107.7 (CH), 101.4 (CH_2),

79.8 (C), 53.2 (CH), 47.5 (CH_2), 28.3 ($3\times CH_3$), 28.0 (CH_2), 24.5 (CH_2), 21.3 (CH_2); ***m/z*** (EI) 411 ($[^{81Br}M]^+$, 1%), 409 ($[^{79Br}M]^+$, 1), 274 (92), 215 (65), 213 (69), 194 (100); **HRMS** (EI) Found: $[^{79Br}M]^+$, 409.0889. $C_{19}H_{24}O_4N^{79}Br$ requires 409.0883.

General Procedures for Heck cyclisations[11]

General procedure E

Neutral protocol (140°C): To a degassed solution of the aryl halide (1 eq) in DMF was added the Herrmann-Beller palladacycle (5 mol%) and $MeNCy_2$ (4 eq), and the reaction was heated at 140°C. At the conclusion of the reaction (as judged by TLC), the mixture was allowed to cool and then diluted with Et_2O (20 mL) and washed with NaCl (3 × 20 mL, sat. aq.). The organics were combined, dried ($MgSO_4$) and concentrated under reduced pressure to afford the crude product, which was purified by column chromatography to give the stated mixture of double bond isomers.

General procedure F

Neutral protocol (Low temperature): To a degassed solution of the aryl halide (1 eq) and $MeNCy_2$ (4 eq) in MeCN was added $Pd_2(dba)_3$ (5 mol%) and $^tBu_3PHBF_4$ (10 mol%), and the reaction mixture stirred at r.t. or 50°C for the indicated time. At the conclusion of the reaction (as judged by TLC), the mixture was allowed to cool and then diluted with Et_2O (20 mL) and washed with NaCl (3 × 20 mL, sat. aq.). The organics were combined, dried ($MgSO_4$) and concentrated under reduced pressure to afford the crude product, which was purified by column chromatography to give the stated mixture of double bond isomers.

Application of Heck cyclisation protocols

Parent phenanthridine 6-8a[11,12]

Methyl phenanthridine 6-8b

General procedure **E** was followed using cyclohexene **5b** (110 mg, 0.289 mmol), Herrmann-Beller palladacycle (14 mg, 14.5 µmol) and $MeNCy_2$ (245 µl, 1.16 mmol). After 12 h at 140°C, flash chromatography (hexane:EtOAc, 100:1-100:2) afforded the phenanthridine as a colourless solid (65 mg, 76%). ^{1}H NMR of this oil showed it to be 26: 57: 11 mixture of double bond isomers (**6b**:**7b**:**8b**).

Methoxy phenanthridine 6-8d

General procedure **E** was followed using cyclohexene **5d** (110 mg, 0.278 mmol), Herrmann-Beller palladacycle (13 mg, 14.0 µmol) and $MeNCy_2$ (236 µl, 1.11 mmol). After 6 h at 140°C, flash chromatography (hexane:EtOAc, 100:1) afforded the phenanthridine as a colourless oil (64 mg, 73%). ^{1}H NMR of this oil showed it to be a 36: 44: 20 mixture of double bond isomers (**6d**:**7d**:**8d**).

Dimethoxy phenanthridine 6-8e

General procedure **E** was followed using cyclohexene **5e** (50 mg, 0.12 mmol), Herrmann-Beller palladacycle (6 mg, 5.9 µmol) and $MeNCy_2$ (100 µl, 0.47 mmol). After 12 h at 140°C, flash chromatography (hexane:EtOAc, 100:5–100:15) afforded the phenanthridine as a colourless oil (30 mg, 75%). ^{1}H NMR of this oil showed it to be a 41: 32: 27 mixture of double bond isomers (**6e**:**7e**:**8e**).

Naphthyl phenanthridine 6-8f

General procedure **E** was followed using cyclohexene **5f** (110 mg, 0.26 mmol), Herrmann-Beller palladacycle (13 mg, 13 µmol) and $MeNCy_2$ (224 µl, 1.06 mmol). After 5 h at 140°C, flash chromatography (hexane:EtOAc, 100:2–100:3) afforded the phenanthridine as a colourless oil (65 mg, 74%). ^{1}H NMR of this oil showed it to be a 44: 42: 16 mixture of double bond isomers (**6f**:**7f**:**8f**).

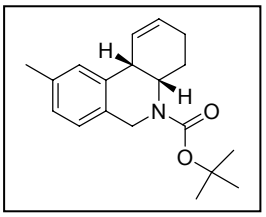
Piperonyl phenanthridine 6-8g

General procedure **E** was followed using cyclohexene **5g** (24 mg, 59 μmol), Herrmann-Beller palladacycle (3 mg, 3.0 μmol), $MeNCy_2$ (52 μl, 0.24 mmol) and DMF (2 mL). After 24 h at 140°C, flash chromatography (hexane:EtOAc, 20:1) afforded the phenanthridine as a colourless oil (12 mg, 59%). ^{1}H NMR of this oil showed it to be a 41:26:33 mixture of double bond isomers (**6g**:**7g**:**8g**). Additionally, 32% of the dehalogenated product was recovered.

General procedure **F** was followed using cyclohexene **5g** (85 mg, 0.21 mmol), $Pd_2(dba)_3$ (9.6 mg, 11 μmol), $P(^tBu)_3HBF_4$ (6.1 mg, 21 μmol) and $MeNCy_2$ (176 μl, 0.83 mmol). After 18 h at r.t., flash chromatography (hexane:EtOAc, 100:4) afforded the phenanthridine as a colourless oil (55 mg, 80%). ^{1}H NMR of this oil showed it to be a 18:46:36 mixture of double bond isomers (**6g**:**7g**:**8g**). Additionally, 11% of the dehalogenated product.

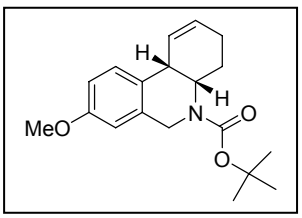
General procedure **F** was followed using cyclohexene **5g** (844 mg, 2.06 mmol), $Pd_2(dba)_3$ (94 mg, 0.10 mmol), $P(^tBu)_3HBF_4$ (56 mg, 0.21 mmol) and $MeNCy_2$ (1.75 mL, 8.24 mmol). After 18 h at 50°C, flash chromatography (hexane:EtOAc, 100:4) afforded the phenanthridine as a colourless oil (676 mg, 99%). ^{1}H NMR of this oil showed it to be a 37:39:24 mixture of double bond isomers (**6g**:**7g**:**8g**).

(4a*SR*,10b*SR*)-9-Methyl-4,4a,6,10b-tetrahydro-3*H*-phenanthridine-5-carboxylic acid *tert*-butyl ester 6b ($\Delta^{1,2}$ isomer)



R_f [hexane:EtOAc, 10:1] = 0.46; **MP** 105°C; **υ_{max}** ($CHCl_3$)/cm^{-1} 1692 (C=O); **^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 7.11 (1H, d, Ar*H*), 7.00 (2H, m, 2×Ar*H*), 6.18-6.12 (1H, m, CHC*H*=CH), 5.88-5.83 (1H, m, CH=C*H*CH_2), 4.68 (1H, d, *J* 16.3, C$H_X$$H_Y$Ar), 4.41 (1H, br s, NC*H*CH), 4.35 (1H, d, *J* 16.3, $CH_X$$H_Y$Ar), 3.54 (1H, br s, NCHC*H*), 2.34 (3H, s, CH_3), 2.29-2.16 (1H, m, C$H_A$$H_B$), 2.15-2.05 (1H, m, $CH_A$$H_B$), 1.74-1.69 (1H, m, C$H_C$$H_D$), 1.61-1.50 (10H, m, 3×CH_3+$CH_C$$H_D$); **^{13}C NMR** δ (90.0 MHz, 323 K, $CDCl_3$) 155.0 (C), 137.6 (C), 136.3 (C), 128.2 (CH), 128.1 (CH), 127.4 (CH), 126.6 (CH), 125.9 (CH), 123.8 (C), 79.6 (CH), 50.5 (CH), 43.3 (CH_2), 37.2 (CH), 28.5 (CH_2), 28.5 (3×CH_3), 25.3 (CH_2), 21.1 (CH_3); ***m/z*** (EI) 299 ([M]$^+$, 1%), 242 (100), 198 (15), 189 (26), 144 (11); **HRMS** (EI) Found: [M]$^+$ 299.1880. $C_{19}H_{25}NO_2$ requires 299.1880. **Diagnostic ^{1}H NMR data for 7b ($\Delta^{2,3}$ isomer) ^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 7.04 (3H, m, 3xAr*H*), 5.70-5.66 (1H, m, C*H*=CH), 5.45-5.40 (1H, m, CH=C*H*), 4.55 (1H, d, *J* 16.2, C$H_X$$H_Y$), 4.48 (1H, d, *J* 16.2, $CH_X$$H_Y$), 4.43 (1H, br s, NC*H*), 3.18 (1H, br s, NCHC*H*), 2.86 (1H, dd, *J* 18.1, 4.9, C$H_A$$H_B$), 2.63-2.56 (1H, m, $CH_A$$H_B$), 2.35 (3H, s, C$H_3$), 2.24-2.19 (1H, m, C$H_C$$H_D$), 1.57-1.48 (10H, m, $CH_C$$H_D$+3×C$H_3$). **Diagnostic ^{1}H NMR data for 8b ($\Delta^{3,4}$ isomer) ^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$); 5.70-5.68 (1H, m, C*H*=CH), 5.53 (1H, dd, *J* 8.5, CH=C*H*), 5.06 (1H, br s, NC*H*), 4.82 (1H, d, *J* 16.7, C$H_X$$H_Y$), 4.21 (1H, d, *J* 16.7, $CH_X$$H_Y$), 3.26 (1H, br s, NCHC*H*), 2.10-1.95 (1H, m, C$H_A$$H_B$), 1.89-1.79 (1H, m, $CH_A$$H_B$).

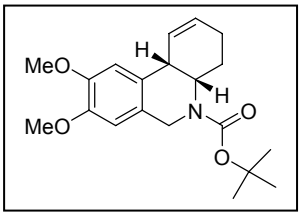
(4a*SR*,10b*SR*)-8-Methoxy-4,4a,6,10b-tetrahydro-3*H*-phenanthridine-5-carboxylic acid *tert*-butyl ester 6d ($\Delta^{1,2}$ isomer)



R_f [hexane:EtOAc, 3:1] = 0.71; **υ_{max}** ($CHCl_3$)/cm^{-1} 1691 (C=O); **^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 7.19 (1H, d, *J* 8.5, Ar*H*), 6.79 (1H, dd, *J* 8.5, 2.7, Ar*H*), 6.66 (1H, d, *J* 2.7, Ar*H*), 6.14-6.09 (1H, m, CHC*H*=CH), 5.84-5.80 (1H, m, CH=C*H*CH_2), 4.69 (1H, d, *J* 16.6, C$H_X$$H_Y$Ar), 4.34 (1H, br s, NC*H*CH), 4.30 (1H, d, *J* 16.6, $CH_X$$H_Y$Ar), 3.79 (3H, s, C$H_3$), 3.51 (1H, br s, NCHC*H*), 2.27-2.16 (1H, m, C$H_A$$H_B$), 2.12-2.04 (1H, m, $CH_A$$H_B$), 1.74-1.65 (1H, m, C$H_C$$H_D$), 1.58-1.47 (10H, m, $CH_C$$H_D$+3×C$H_3$); **^{13}C NMR** δ (90.0 MHz, 323 K, $CDCl_3$) 157.9 (C), 154.9 (C), 130.0 (C), 128.5 (CH), 128.0 (CH), 127.6 (CH), 125.4 (CH), 113.0 (CH), 111.1 (CH), 79.6 (C), 55.2 (CH_3), 50.5 (CH), 43.7 (CH_2), 36.6 (CH), 28.6 (3×CH_3), 26.5 (CH_2), 25.3 (CH_2); ***m/z*** (EI) 315 ([M]$^+$, 2%), 259 (77), 242 (100), 205 (47); **HRMS** (EI) Found: [M]$^+$ 315.1831. $C_{29}H_{25}NO_3$ requires 315.1829. **Diagnostic ^{1}H NMR data for 7d ($\Delta^{2,3}$ isomer) ^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 7.14 (1H, d, *J* 8.6, Ar*H*), 6.73 (1H, d, *J* 2.3, Ar*H*), 5.70-5.62 (1H, m, C*H*=CH), 5.44-5.40 (1H, m, CH=C*H*), 4.52 (2H, s, CH_2Ar), 3.15 (1H, br s, NCHC*H*), 2.81 (1H, dd, *J* 22.9, 4.7, C$H_A$$H_B$), 2.62-2.54 (1H, m, $CH_A$$H_B$). **Diagnostic ^{1}H NMR data for 8d ($\Delta^{3,4}$**

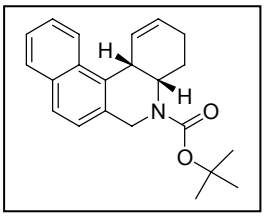
isomer) ^{1}**H NMR** δ (360 MHz, 323 K, $CDCl_3$) 7.26 (1H, d, *J* 8.6, Ar*H*), 6.60 (1H, s, Ar*H*), 5.51 (1H, d, *J* 10.2, C*H*=CH), 5.05 (1H, br s, NC*H*), 4.83 (1H, d, *J* 17.1, CH_XH_Y), 4.22 (1H, d, *J* 17.1, CH_XH_Y), 3.24 (1H, br s, NCHC*H*).

(4a*SR*,10b*SR*)-8,9-Dimethoxy-4,4a,6,10b-tetrahydro-3*H*-phenanthridine-5-carboxylic acid *tert*-butyl ester 6e ($\Delta^{1,2}$ isomer)



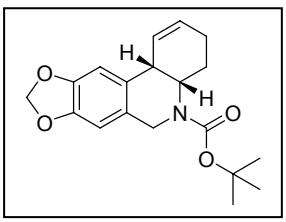
R$_f$ [hexane:EtOAc, 3:1] = 0.44; **MP** 124°C; **υ$_{max}$** ($CHCl_3$)/cm^{-1} 1692 (C=O); ^{1}**H NMR** δ (360 MHz, 323 K, $CDCl_3$) 6.77 (1H, s, Ar*H*), 6.60 (1H, s, Ar*H*), 6.12-6.07 (1H, m, CHC*H*=CH), 5.84-5.81 (1H, m, CH=C*H*CH$_2$), 4.62 (1H, d, *J* 16.3, CH_XH_YAr), 4.37 (1H, br s, NC*H*CH), 4.27 (1H, d, *J* 16.3, CH_XH_YAr), 3.85 (3H, s, CH_3), 3.83 (3H, s, CH_3), 3.47 (1H, br s, NCHC*H*), 2.25-2.20 (1H, m, CH_AH_B), 2.11-2.03 (1H, m, CH_AH_B), 1.69-1.65 (1H, m, CH_CH_D), 1.57 (1H, td, *J* 16.8, 5.8, CH_CH_D), 1.50-1.48 (9H, m, 3×CH_3); ^{13}**C NMR** δ (90.0 MHz, 323 K, $CDCl_3$) 155.0 (C), 148.2 (C), 147.6 (C), 129.8 (C), 128.3 (CH), 127.2 (CH), 124.4 (C), 111.2 (CH), 109.5 (CH), 79.7 (C), 56.0 (2×CH_3), 50.2 (CH), 43.0 (CH_2), 36.6 (CH), 28.4 (3×CH_3), 25.3 (CH_2), 23.9 (CH_2); ***m/z*** (FAB, 3-NOBA) 346 ([M+H]$^+$, 26%), 289 (100), 244 (82), 216 (36), 190 (52), ; **HRMS** (FAB, 3-NOBA) Found: [M+H]$^+$ 346.2017. $C_{20}H_{28}NO_4$ requires 346.2013. **Diagnostic ^{1}H NMR data for 7e ($\Delta^{2,3}$ isomer) ^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 6.75 (1H, s, Ar*H*), 6.66 (1H, s, Ar*H*), 5.67-5.63 (1H, m, C*H*=CH), 5.44-5.40 (1H, m, CH=C*H*), 4.46 (2H, s, CH_2Ar), 3.13 (1H, br s, NCHC*H*), 2.77-2.73 (1H, m, CH_AH_B), 2.61-2.56 (1H, m, CH_AH_B). **Diagnostic ^{1}H NMR data for 8e ($\Delta^{3,4}$ isomer) ^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$); 6.82 (1H, s, Ar*H*), 6.53 (1H, s, Ar*H*), 5.72-5.66 (1H, m, C*H*=CH), 5.48 (1H, dd, *J* 10.1, CH=C*H*), 5.03 (1H, br s, NC*H*), 4.75 (1H, d, *J* 16.5, CH_XH_Y), 4.13 (1H, d, *J* 16.5, CH_XH_Y), 3.21 (1H, br s, NCHC*H*).

(4a*SR*,12c*SR*)-4,4a,6,12c-Tetrahydro-3*H*-benzo[*k*]phenanthridine-5-carboxylic acid *tert*-butyl ester 6f ($\Delta^{1,2}$ isomer)



R$_f$ [hexane:EtOAc, 3:1] = 0.80; **υ$_{max}$** ($CHCl_3$)/cm^{-1} 1688 (C=O); ^{1}**H NMR** δ (360 MHz, 323 K, $CDCl_3$) 8.08 (1H, d, *J* 8.4, Ar*H*), 7.87 (1H, dd, *J* 8.1, 0.7, Ar*H*), 7.71 (1H, d, *J* 8.3, Ar*H*), 7.55 (1H, ddd, *J* 8.3, 6.8, 1.4, Ar*H*), 7.48 (1H, ddd, *J* 8.1, 6.8, 1.3, Ar*H*), 7.29 (1H, d, *J* 8.3, Ar*H*), 5.97-5.92 (1H, m, C*H*=CH), 5.43 (1H, ddd, *J* 9.9, 1.6, 0.8, CH=C*H*), 5.11 (1H, d, *J* 15.1, CH_XH_YAr), 4.62-4.59 (1H, m, C*H*CH=CH), 4.29-4.26 (1H, m, NC*H*), 4.23 (1H, d, *J* 15.1, CH_XH_YAr), 2.56-2.21 (1H, m, CH_CH_D), 2.37-2.25 (1H, m, CH_AH_B), 2.17-2.07 (1H, m, CH_AH_B), 1.91-1.84 (1H, dddd, *J* 13.6, 11.3, 5.2, 2.5, CH_CH_D), 1.49 (9H, m, 3×CH_3); ^{13}**C NMR** δ (90.6 MHz, 323 K, $CDCl_3$) 155.2 (C), 133.7 (C), 133.4 (C), 130.6 (2×C), 129.2 (CH), 129.0 (CH), 126.8 (CH), 126.6 (CH), 126.2 (CH), 125.1 (CH), 124.7 (CH), 122.4 (CH), 79.6 (C) 49.8 (CH), 45.2 (CH_2), 35.2 (CH), 28.5 (3×CH_3), 26.9 (CH_2), 20.6 (CH_2); ***m/z*** (EI) 335 ([M]$^+$, 4%), 307 (30), 242 (35), 136 (100); **HRMS** (EI) Found: [M]$^+$,335.1880. $C_{22}H_{25}NNO_2$ requires 335.1880. **Diagnostic data for 7f ($\Delta^{2,3}$ isomer) ^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 4.98 (1H, d, *J* 16.1, CH_XH_YAr), 4.56 (1H, d, *J* 16.1, CH_XH_YAr), 4.11 (1H, td, *J* 5.7, 2.6, C*H*CH$_2$), 3.95-3.88 (1H, m, NC*H*CH$_2$), 2.97-2.92 (1H, m, CH_AH_B). **Diagnostic data for 8f ($\Delta^{3,4}$ isomer) ^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 4.96 (1H, d, *J* 16.0, CH_XH_YAr), 4.81-4.76 (1H, m, C*H*CH=CH), 4.35 (1H, d, *J* 16.0, CH_XH_YAr), 4.03-3.97 (1H, m, NC*H*CH$_2$).

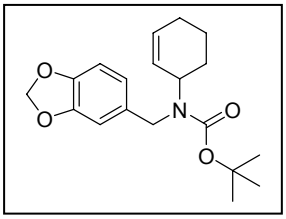
(4a*SR*,11b*SR*)-4,4a,6,11b-Tetrahydro-3*H*-[1,3]dioxolo[4,5-*j*]phenanthridine-5-carboxylic acid *tert*-butyl ester 6g ($\Delta^{1,2}$ isomer)



R$_f$ [hexane:EtOAc, 3:1] = 0.65; **υ$_{max}$** ($CHCl_3$)/cm^{-1} 1692 (C=O); ^{1}**H NMR** δ (360 MHz, 323 K, $CDCl_3$) 6.77 (1H, s, Ar*H*), 6.59 (1H, s, Ar*H*), 6.08-6.03 (1H, m, C*H*=CH), 5.92 (2H, s, OCH_2O), 5.86-5.83 (1H, m, CH=C*H*), 4.58 (1H, d, *J* 16.2, CH_XH_YAr), 4.36 (1H, br s, C*H*CH=CH), 4.29 (1H, d, *J* 16.2, CH_XH_YAr), 3.46 (1H, m, NC*H*), 2.26-2.19 (1H, m, CH_AH_B), 2.16-2.12 (1H, m, CH_AH_B), 2.72-1.68 (1H, m, CH_CH_D), 1.60-1.55 (1H, m, CH_CH_D), 1.51 (1H, s, 3×CH_3); ^{13}**C NMR** δ (90.6 MHz, 323 K, $CDCl_3$) 154.9 (C), 146.7 (C), 145.8 (C), 131.0 (C), 128.5 (CH), 127.2 (CH), 125.7

(C), 107.7 (CH), 106.2 (CH), 100.7 (CH_2), 79.6 (C), 50.4 (CH), 43.6 (CH_2), 37.1 (CH), 28.5 (3×CH_3), 25.3 (CH_2), 24.1 (CH_2); ***m/z*** (EI) 329 ([M]$^+$, 1%), 272 (100); **HRMS** (EI) Found: [M]$^+$, 329.1621. $C_{19}H_{23}O_4N$ requires 329.1622. **Diagnostic ^{1}H NMR data for 7g ($\Delta^{2,3}$ isomer) ^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 6.74 (1H, s, Ar*H*), 6.65 (1H, s, Ar*H*), 5.92 (2H, s, OCH_2O), 5.69-5.65 (1H, m, C*H*=CH), 5.47-5.42 (1H, m, CH=C*H*), 4.41 (2H, s, CH_2Ar), 3.10 (1H, br s, NCHC*H*), 2.72 (1H, dd, *J* 18.3, 4.9, CH_AH$_B$), 2.63-2.56 (1H, m, CH$_A$$H_B$), 2.25-2.20 (1H, m, C$H_CH_D$), 1.63-1.55 (1H, m, CH$_C$$H_D$), 1.52 (9H, s, 3×C$H_3$). **Diagnostic ^{1}H NMR data for 8g ($\Delta^{3,4}$ isomer) ^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 6.82 (1H, s, Ar*H*), 6.52 (1H, s, Ar*H*), 5.90 (2H, s, OCH_2O), 5.73-5.70 (1H, m, C*H*=CH), 5.52-5.48 (1H, m, CH=C*H*), 5.02 (1H, m, NC*H*), 4.74 (1H, d, *J* 16.5, ArCH_XH$_Y$), 4.13 (1H, d, *J* 16.5, ArCH$_X$$H_Y$), 3.20 (1H, m, NCHC*H*).

(Benzo[1,3]dioxol-5-ylmethyl)-(cyclohex-2-enyl)-carbamic acid *tert*-butyl ester (By-product from cyclisation of 5g)

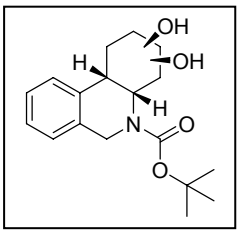


R$_f$ [hexane:EtOAc, 3:1] = 0.69; **υ_{max}** ($CHCl_3$)/cm^{-1} 1686 (C=O); **^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 6.77 (1H, br s, Ar*H*), 6.73 (1H, d, *J* 8.0, Ar*H*), 6.69 (1H, br d, *J* 8.6, Ar*H*), 5.93 (2H, s, OCH_2O), 5.82-5.80 (1H, m, C*H*=CH), 5.49 (1H, d, *J* 10.2, CH=C*H*), 4.71 (1H, br s, C*H*N), 4.34 (1H, d, *J* 16.0, CH_XH$_Y$Ar), 4.20 (1H, d, *J* 16.0, CH$_X$$H_Y$Ar), 1.99-1.97 (2H, m, C$H_2$), 1.90-1.82 (1H, m, C$H_AH_B$), 1.79-1.71 (1H, m, CH$_A$$H_B$), 1.66-1.43 (11H, m, C$H_2$+3×C$H_3$); **^{13}C NMR** δ (90.6 MHz, 323 K, $CDCl_3$), 155.9 (C), 147.6 (C), 146.1 (C), 134.6 (C), 130.5 (CH), 129.0 (CH), 119.8 (CH), 107.8 (CH), 107.5 (CH), 100.7 (CH_2), 79.6 (C), 53.3 (CH), 47.3 (CH_2), 28.4 (3×CH_3), 28.1 (CH_2), 24.6 (CH_2), 21.5 (CH_2); ***m/z*** (EI) 331 ([M]$^+$, 13%), 275 (38), 194 (100), 150 (14), 140 (14), 136 (28), 135 (46); **HRMS** (EI) Found: [M]$^+$, 331.1775. $C_{19}H_{25}O_4N$ requires 331.1778.

General procedure G - Dihydroxylation

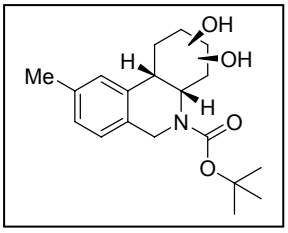
To a solution of the appropriate phenanthridines (1 eq) in THF and H_2O at r.t was added OsO_4 (0.07 eq, 2.5% $^w/_w$ in ^{t}BuOH) and NMO (3 eq) and the reaction was stirred for 16 h. The reaction mixture was poured onto Na_2SO_3 (30 mL, sat. aq.) and extracted with EtOAc (3 × 30 mL). The combined organics were dried ($MgSO_4$), concentrated under reduced pressure and purified to afford the appropriate mixture of diols. Purification by flash chromatography afforded either a mixture of the isolated isomers/diol mixture, or purely the diol mixture. In cases where the isolated isomers were not obtained, further purification by HPLC afforded the corresponding isolated diols.

Dihydroxy-2,3,4,4a,6,10b-hexahydro-1*H*-phenanthridine-5-carboxylic acid *tert*-butyl ester 17-19a



General procedure **G** was followed using phenanthridines **6-8a**[ref] (200 mg, 0.70 mmol), THF (3.92 mL), H_2O (785 µl), OsO_4 (613 µl, 2.5% $^w/_w$ in ^{t}BuOH, 49.1 µmol) and NMO (329 mg, 2.81 mmol). Flash chromatography (CH_2Cl_2-CH_2Cl_2:MeOH, 100:3) afforded mixture of diols **17-19a** as a colourless oil (156 mg, 70%). HPLC (EtOAc:hexane, 3:1) of this mixture afforded $\Delta^{1,2}$ diol **17a** (29 mg, 13%), $\Delta^{2,3}$ diol **18a** (25 mg, 11%), $\Delta^{3,4}$ diol **19a** (26 mg, 12%), and mixed diol fractions (44 mg, 20%), giving an overall yield (124 mg, 56%), all colourless oils.

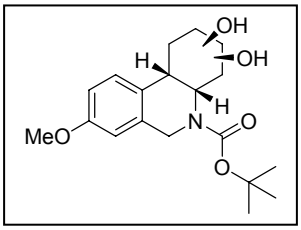
Dihydroxy-9-methyl-2,3,4,4a,6,10b-hexahydro-1*H*-phenanthridine-5-carboxylic acid *tert*-butyl ester 17-19b



General procedure **G** was followed using phenanthridines **6-8b** (84 mg, 0.282 mmol), THF (165 µl), H_2O (820 µl), OsO_4 (247 µl, 2.5% $^w/_w$ in ^{t}BuOH, 19.7 µmol) and NMO (132 mg, 0.846 mmol). Flash chromatography (CH_2Cl_2-CH_2Cl_2:MeOH, 100:2) afforded mixture of diols **17-19b** (73 mg, 78%). Further isolation of the individual diol products **17-19b** was not found to be possible by HPLC so these compounds were

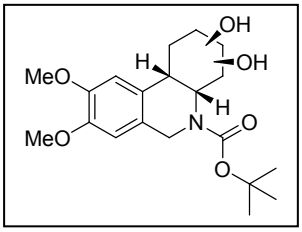
taken on as a mixture. $\mathbf{R_f}$ [CH_2Cl_2:MeOH, 9:1] = 0.57; υ_{max} ($CHCl_3$)/cm^{-1} 3421 (OH), 1664 (C=O); ***m/z*** (EI) 319 ($[M]^+$, 2%), 262 ($[M\text{-}^t Bu]^+$, 100), 218 ($[M\text{-Boc}]^+$, 22), 184 (75).

Dihydroxy-8-methoxy-2,3,4,4a,6,10b-hexahydro-1*H*-phenanthridine-5-carboxylic acid *tert*-butyl ester 17-19d



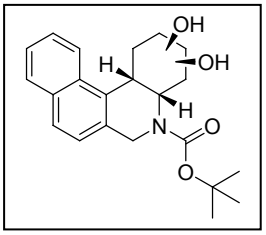
General procedure **G** was followed using phenanthridines **6-8d** (152 mg, 0.482 mmol), THF (2.70 mL), H_2O (541 µl), OsO_4 (423 µl, 2.5% $^w/_w$ in ^{t}BuOH, 33.8 µmol) and NMO (226 mg, 1.93 mmol). Flash chromatography (CH_2Cl_2:MeOH, 100:1-10:1) afforded mixture of diols **17-19d** (159 mg, 95%). HPLC (EtOAc:hexane, 4:1) of this mixture afforded $\Delta^{1,2}$ diol **17d** (21 mg, 13%), $\Delta^{2,3}$ diol **18d** (20 mg, 12%), $\Delta^{3,4}$ diol **19d** (32 mg, 19%), and mixed diol fractions (32 mg, 19%), giving a total yield (105 mg, 63%), all colourless oils.

Dihydroxy-8,9-dimethoxy-2,3,4,4a,6,10b-hexahydro-1*H*-phenanthridine-5-carboxylic acid *tert*-butyl ester 17-19e



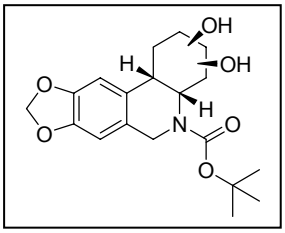
General procedure **G** was followed using phenanthridines **6-8e** (30 mg, 87 µmol), THF (488 µl), H_2O (98 µl), OsO_4 (76 µl, 2.5% $^w/_w$ in ^{t}BuOH, 6.1 µmol) and NMO (31 mg, 0.26 mmol). Flash chromatography (CH_2Cl_2:MeOH, 100:5) afforded mixture of diols **17-19e** (23 mg, 70%). HPLC (EtOAc:hexane, 84:16) afforded $\Delta^{1,2}$ diol **17e** (2 mg, 6%), diol mixture **17e** and **18e** (6.2 mg, 19%) and $\Delta^{3,4}$ diol **19e** (10 mg, 30%), giving an overall yield (18.2 mg, 55%), all colourless oils.

Dihydroxy-2,3,4,4a,6,12c-hexahydro-1*H*-benzo[*k*]phenanthridine-5-carboxylic acid *tert*-butyl ester 17-19f



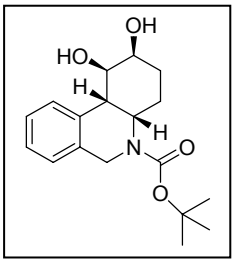
General procedure **G** was followed using phenanthridines **6-8f** (130 mg, 0.39 mmol), THF (2.17 mL), H_2O (434 µl), OsO_4 (338 µl, 2.5% $^w/_w$ in ^{t}BuOH, 27.1 µmol) and NMO (136 mg, 1.16 mmol). Flash chromatography (CH_2Cl_2:MeOH, 100:0.5) afforded $\Delta^{1,2}$ diol **17f** (20 mg, 14%), $\Delta^{2,3}$ diol **18f** (40 mg, 28%), $\Delta^{3,4}$ diol **19f** (23 mg, 16%), and mixed diol (42 mg, 29%) giving a total yield (125 mg, 87%).

Dihydroxy-2,3,4,4a,6,11b-hexahydro-1*H*-[1,3]dioxolo[4,5-*j*]phenanthridine-5-carboxylic acid *tert*-butyl ester 17-19g



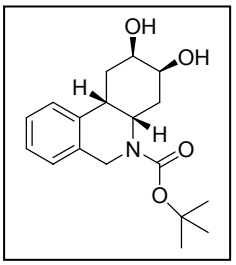
General procedure **G** was followed using phenanthridines **6-8g** (125 mg, 0.38 mmol), THF (2.66 mL), H_2O (531 µl), OsO_4 (332 µl, 2.5% $^w/_w$ in ^{t}BuOH, 26.6 µmol) and NMO (133 mg, 1.14 mmol). Flash chromatography (CH_2Cl_2:MeOH, 98:2) afforded $\Delta^{1,2}$ diol **17g** (13 mg, 9%), $\Delta^{2,3}$ diol **18g** (31 mg, 23%), $\Delta^{3,4}$ diol **19g** (25 mg, 18%), $\Delta^{2,3}$ endo *syn* diol minor diastereomer (3 mg, 2%) and mixed diol (48 mg, 35%) giving a total yield (120 mg, 87%).

(1*RS*,2*SR*,4a*SR*,10b*SR*)-1,2-Dihydroxy-2,3,4,4a,6,10b-hexahydro-1*H*-phenanthridine-5-carboxylic acid *tert*-butyl ester 17a ($\Delta^{1,2}$ isomer)



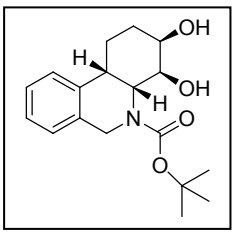
R$_f$ [CH_2Cl_2:MeOH, 9:1] = 0.57; **R$_t$** (EtOAc:hexane, 3:1, flow rate: 8 mL min^{-1}) = 23 min; **υ_{max}** ($CHCl_3$)/cm^{-1} 3421 (OH), 1664 (C=O); **^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 7.36-7.34 (1H, m, Ar*H*), 7.24-7.18 (2H, m, 2×Ar*H*), 7.14-7.12 (1H, m, Ar*H*), 4.74-4.66 (3H, m, C*H*OH+C*H*NBoc+CH_XH$_Y$Ar), 4.35 (1H, d, *J* 17.1, CH$_X$$H_Y$Ar), 3.95 (1H, br s, O*H*), 3.71 (1H, ddd, *J* 11.4, 4.7, 2.8, C*H*OH), 3.40 (1H, br s, C*H*Ar), 1.95-1.85 (1H, m, CH_AH$_B$), 1.70-1.60 (2H, m, CH$_A$$H_B$+C$H_CH_D$), 1.51 (9H, s, 3×C$H_3$), 1.40-1.33 (1H, m, CH$_C$$H_D$); **^{13}C NMR** δ (90.6 MHz, 323 K, $CDCl_3$) 154.9 (C), 133.4 (C), 133.1 (C), 126.9 (CH), 126.6 (C), 126.3 (CH), 125.4 (CH), 79.9 (C), 71.1 (CH), 67.4 (CH), 47.1 (CH), 43.6 (CH_2), 42.8 (CH), 28.4 (3×CH_3), 27.4 (CH_2), 24.2 (CH_2); ***m/z*** (EI) 319 ([M]$^+$, 2%), 262 ([M-^{t}Bu]$^+$, 100), 218 ([M-Boc]$^+$, 22), 184 (75). This compound was also fully characterised by COSY, HSQC and NOESY 2D NMR studies.

(2*RS*,3*SR*,4a*SR*,10b*SR*)-2,3-Dihydroxy-2,3,4,4a,6,10b-hexahydro-1*H*-phenanthridine-5-carboxylic acid *tert*-butyl ester 18a ($\Delta^{2,3}$ isomer)



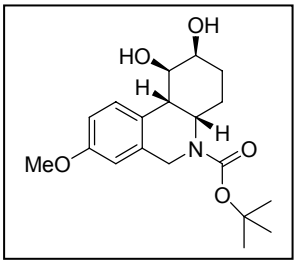
R$_f$ [CH_2Cl_2:MeOH, 9:1] = 0.52; **R$_t$** (EtOAc:hexane, 3:1, flow rate: 8 mL min^{-1}) = 28 min; **υ_{max}** ($CHCl_3$)/cm^{-1} 3414 (OH), 1671 (C=O); **^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 7.47 (1H, d, *J* 7.6, Ar*H*), 7.27-7.20 (2H, m, 2×Ar*H*), 7.12 (1H, d, *J* 6.8, Ar*H*), 4.78-4.72 (1H, m, C*H*NBoc), 4.71 (1H, d, *J* 17.3, CH_XH$_Y$Ar), 4.36 (1H, d, *J* 17.3, CH$_X$$H_Y$*Ar*), 3.92 (1H, m, C*H*OH), 3.64 (1H, dt, *J* 12.0, 3.9, C*H*OH), 3.26 (1H, br s, C*H*Ar), 2.49 (1H, dt, *J* 13.6, 3.1, CH_AH$_B$), 2.25 (1H, ddd, *J* 13.6, 12.0, 4.8, CH$_A$$H_B$), 1.94-1.87 (1H, m, C$H_CH_D$), 1.54-1.45 (10H, m, CH$_C$$H_D$+3×C$H_3$); **^{13}C NMR** δ (90.6 MHz, 323 K, $CDCl_3$) 154.8 (C), 134.5 (C), 133.2 (C), 126.9 (CH), 126.4 (CH), 126.2 (CH), 125.6 (CH), 80.0 (C), 69.4 (CH), 66.7 (CH), 46.3 (CH), 43.6 (CH_2), 36.3 (CH), 31.5 (CH_2), 29.3 (CH_2), 28.4 (3×CH_3); ***m/z*** (EI) 319 ([M]$^+$, 1%), 263 ([M-^{t}Bu]$^+$, 27), 262 (80), 218 ([M-Boc]$^+$, 25), 200 (27), 174 (36), 146 (25), 144 (48); **HRMS** (EI) Found: [M]$^+$, 319.1780. $C_{18}H_{25}O_4N$ requires 319.1778.

(3*RS*,4*SR*,4a*RS*,10b*SR*)-3,4-Dihydroxy-2,3,4,4a,6,10b-hexahydro-1*H*-phenanthridine-5-carboxylic acid *tert*-butyl ester 19a ($\Delta^{3,4}$ isomer)



R$_f$ [CH_2Cl_2:MeOH, 9:1] = 0.58; **R$_t$** (EtOAc:hexane, 3:1, flow rate: 8 mL min^{-1}) = 21 min; **υ_{max}** ($CHCl_3$)/cm^{-1} 3394 (OH), 1668 (C=O); **^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 7.33 (1H, d, *J* 7.5, Ar*H*), 7.27-7.19 (2H, m, 2×Ar*H*), 7.14 (1H, d, *J* 7.1, Ar*H*), 4.80-4.66 (2H, m, C*H*NBoc+CH_XH$_Y$Ar), 4.44 (1H, d, *J* 17.0, CH$_X$$H_Y$Ar), 3.94 (1H, dd, *J* 5.9, 2.9, C*H*OH), 3.31-3.29 (2H, m, C*H*Ar+C*H*OH), 2.29-2.24 (2H, m, CH_2), 1.85-1.80 (1H, m, CH_AH$_B$), 1.58-1.52 (10H, m, CH$_A$$H_B$+3×C$H_3$); **^{13}C NMR** δ (90.6 MHz, 323 K, $CDCl_3$) 156.7 (C), 134.6 (C), 133.3 (C), 126.9 (CH), 126.5 (CH), 126.2 (CH), 125.3 (CH), 80.8 (C), 69.6 (2×CH), 53.1 (CH), 43.9 (CH_2), 36.9 (CH), 28.4 (3×CH_3), 25.4 (CH_2), 20.0 (CH_2); ***m/z*** (EI) 319 ([M]$^+$, 1%), 263 ([M-^{t}Bu], 3), 233 (7), 218 ([M-Boc]$^+$, 6). This compound was also fully characterised by COSY, HSQC and NOESY 2D NMR studies.

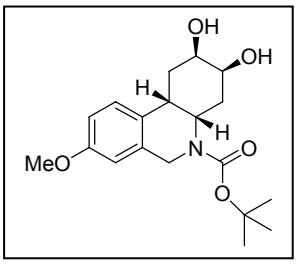
(1*RS*,2*SR*,4a*SR*,10b*SR*)-1,2-Dihydroxy-8-methoxy-2,3,4,4a,6,10b-hexahydro-1*H*-phenanthridine-5-carboxylic acid *tert*-butyl ester 17d ($\Delta^{1,2}$ isomer)



R$_f$ [CH_2Cl_2:MeOH, 9:1] = 0.49; **R$_t$** (EtOAc:hexane, 4:1, flow rate: 10 mL min^{-1}) = 21 min; **υ_{max}** ($CHCl_3$)/cm^{-1} 3423 (OH), 1687 (C=O); **^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 7.24 (1H, d, *J* 8.6, Ar*H*), 6.79 (1H, dd, *J* 8.6, 2.7, Ar*H*), 6.68 (1H, d, *J* 2.7, Ar*H*), 4.72-4.63 (3H, m, 2×C*H*+CH_XH$_Y$Ar), 4.30 (1H, d, *J* 17.1, CH$_X$$H_Y$Ar), 3.80 (3H, s, CH_3), 3.75-3.69 (1H, m, C*H*), 3.35 (1H, br s, C*H*), 2.60 (1H, br s, O*H*), 1.93-1.87 (1H, m, CH_AH$_B$), 1.69-1.64 (1H, m, CH$_A$$H_B$), 1.57-1.41 (11H, m, C$H_2$+3×C$H_3$); **^{13}C NMR** δ (62.9 MHz, $CDCl_3$) 157.9 (C), 154.8 (C), 134.6 (C), 126.5

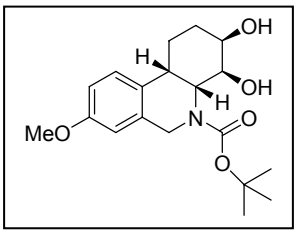
(CH), 124.8 (C), 112.9 (CH), 111.5 (CH), 79.9 (C), 71.1 (CH), 67.3 (CH), 55.2 (CH_3), 46.8 (CH), 43.5 (CH_2), 42.0 (CH), 28.4 ($3\times CH_3$), 27.3 (CH_2), 23.9 (CH_2); ***m/z*** (EI) 349 ($[M]^+$, 4%), 292 ($[M\text{-}^t Bu]^+$, 27), 248 ($[M\text{-Boc}]^+$, 21), 174 (22).

(2*RS*,3*SR*,4a*SR*,10b*SR*)-2,3-Dihydroxy-8-methoxy-2,3,4,4a,6,10b-hexahydro-1*H*-phenanthridine-5-carboxylic acid *tert*-butyl ester 18d ($\Delta^{2,3}$ isomer)



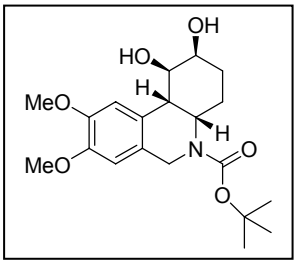
R_f [CH_2Cl_2:MeOH, 9:1] = 0.49; **R_t** (EtOAc:hexane, 4:1, flow rate: 10 mL min^{-1}) = 24 min; **υ_{max}** ($CHCl_3$)/cm^{-1} 3392 (OH), 1672 (C=O); **^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 7.37 (1H, d, *J* 8.5, Ar*H*), 6.82 (1H, dd, *J* 8.5, 2.7, Ar*H*), 6.67 (1H, d, *J* 2.6, Ar*H*), 4.76-4.67 (2H, m, C*H*+C$H_X$$H_Y$Ar), 4.31 (1H, d, *J* 17.4, CH_XH_YAr), 3.92 (1H, d, *J* 3.1, C*H*), 3.81 (3H, s, CH_3), 3.66-3.61 (1H, m, C*H*), 3.21 (1H, m, C*H*), 2.45-2.42 (1H, m, C$H_A$$H_B$), 2.26-2.17 (1H, m, CH_AH_B), 1.91-1.86 (1H, m, C$H_C$$H_D$), 1.60-1.48 (10H, m, CH_CH_D+3×CH_3); **^{13}C NMR** δ (90.6 MHz, 323 K, $CDCl_3$) 158.2 (C), 154.7 (C), 134.5 (C), 126.8 (CH), 126.5 (C), 113.0 (CH), 111.5 (CH), 79.9 (C), 69.6 (CH), 66.7 (CH), 55.2 (CH_3), 46.5 (CH), 43.7 (CH_2), 35.7 (CH), 31.3 (CH_2), 29.5 (CH_2), 28.5 ($3\times CH_3$); ***m/z*** (EI) 349 ($[M]^+$, 5%), 292 ($[M\text{-}^t Bu]^+$, 38), 248 ($[M\text{-Boc}]^+$, 37), 204 (35), 174 (40), 160 (33).

(3*RS*,4*SR*,4a*RS*,10b*SR*)-3,4-Dihydroxy-8-methoxy-2,3,4,4a,6,10b-hexahydro-1*H*-phenanthridine-5-carboxylic acid *tert*-butyl ester 19d ($\Delta^{3,4}$ isomer)



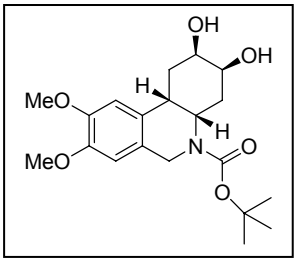
R_f [CH_2Cl_2:MeOH, 9:1] = 0.49; **R_t** (EtOAc:hexane, 4:1, flow rate: 10 mL min^{-1}) = 17 min; **υ_{max}** ($CHCl_3$)/cm^{-1} 3392 (OH), 1668 (C=O); **^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 7.23 (1H, d, *J* 8.6, Ar*H*), 6.82 (1H, dd, *J* 8.6, 2.7, Ar*H*), 6.69 (1H, d, *J* 2.7, Ar*H*), 4.80-4.62 (2H, m, C*H*+C$H_X$$H_Y$Ar), 4.41 (1H, d, *J* 16.7, CH_XH_YAr), 3.94 (1H, d, *J* 2.8, C*H*), 3.81 (3H, s, CH_3), 3.34-3.31 (1H, m, C*H*), 3.24-3.22 (1H, m, C*H*), 2.23-2.21 (1H, m, C$H_A$$H_B$), 1.85-1.80 (1H, m, CH_AH_B), 1.57-1.52 (10H, s, C$H_C$$H_D$+3×C$H_3$), 1.43-1.39 (1H, m, CH_CH_D); **^{13}C NMR** δ (90.6 MHz, 323 K, $CDCl_3$) 158.2 (2×C), 134.5 (C), 126.4 (CH), 123.4 (CH), 113.0 (CH), 111.6 (CH), 80.8 (C), 69.6 (2×CH), 55.3 (CH_3), 53.3 (CH), 46.8 (CH_2), 36.2 (CH), 28.4 ($3\times CH_3$), 25.3 (CH_2), 20.1 (CH_2); ***m/z*** (EI) 349 ($[M]^+$, 21%), 292 ($[M\text{-}^t Bu)]^+$, 100), 257 (56), 248 ($[M\text{-Boc}]^+$, 33), 230 (61), 204 (55).

(1*RS*,2*SR*,4a*SR*,10b*SR*)-1,2-Dihydroxy-8,9-dimethoxy-2,3,4,4a,6,10b-hexahydro-1*H*-phenanthridine-5-carboxylic acid *tert*-butyl ester 17e ($\Delta^{1,2}$ isomer)



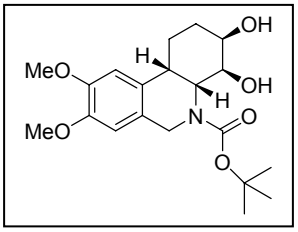
R_f [CH_2Cl_2:MeOH, 9:1] = 0.48; **R_t** (EtOAc:hexane, 84:16, flow rate: 10 mL min^{-1}) = 38 min; **υ_{max}** ($CHCl_3$)/cm^{-1}3423 (OH), 1670 (C=O), 1520, 1406; **^{1}H NMR** δ (360 MHz, $CDCl_3$) 6.83 (1H, s, Ar*H*), 6.61 (1H, s, Ar*H*), 4.70-4.64 (3H, m, 2×C*H*+C$H_X$$H_Y$Ar), 4.24 (1H, d, *J* 16.8, CH_XH_YAr), 3.87 (6H, s, 2×CH_3), 3.70-3.67 (1H, m, C*H*), 3.34 (1H, br s, C*H*), 1.93-1.89 (1H, m, C$H_A$$H_B$), 1.67-1.61 (2H, m, CH_AH_B+C$H_C$$H_D$), 1.53-1.45 (10H, m, CH_CH_D+3×CH_3); **^{13}C NMR** δ (90.6 MHz, $CDCl_3$) 154.8 (C), 147.9 (C), 147.6 (C), 125.3 (C), 124.5 (C), 109.3 (CH), 108.6 (CH), 80.0 (C), 71.3 (CH), 67.5 (CH), 56.1 (CH_3), 55.8 (CH_3), 46.7 (CH), 42.9 (CH_2), 42.2 (CH), 28.4 ($3\times CH_3$), 27.2 (CH_2), 23.8 (CH_2); ***m/z*** (EI) 379 ($[M]^+$, 2%), 322 ($[M\text{-}^t Bu]^+$, 100), 278 ($[M\text{-Boc}]^+$, 6).

(2*RS*,3*SR*,4a*SR*,10b*SR*)-2,3-Dihydroxy-8,9-dimethoxy-2,3,4,4a,6,10b-hexahydro-1*H*-phenanthridine-5-carboxylic acid *tert*-butyl ester 18e ($\Delta^{2,3}$ isomer)



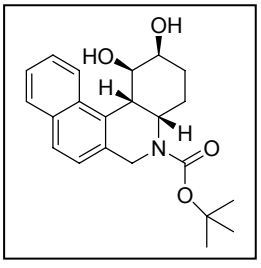
NMR Data for $\Delta^{2,3}$ isomer **18e** was deduced from ^{1}H and ^{13}C NMR of **17e** and **18e** mixture. $\mathbf{R_f}$ [9: 1 CH_2Cl_2:MeOH] = 0.48; $\mathbf{R_t}$ (EtOAc:hexane, 84:16, flow rate: 10 mL min^{-1}) = 38 min; $\boldsymbol{\upsilon_{max}}$ ($CHCl_3$)/cm^{-1} 3425 (OH), 1664 (C=O); **^{1}H NMR** δ (360 MHz, $CDCl_3$) 6.94 (1H, s, Ar*H*), 6.60 (1H, s, Ar*H*), 4.75-4.63 (2H, m, C*H*+CH_XH$_Y$Ar), 4.25 (1H, d, *J* 16.8, CH$_X$$H_Y$Ar), 3.94 (1H, br s, C*H*), 3.89 (3H, s, CH_3), 3.87 (3H, s, CH_3), 3.63-3.60 (1H, m, C*H*), 3.20 (1H, br s, C*H*), 2.43-2.40 (1H, m, CH_AH$_B$), 2.28-2.19 (1H, m, CH$_A$$H_B$), 1.89-1.85 (1H, m, C$H_CH_D$), 1.66-1.61 (1H, m, CH$_C$$H_D$), 1.50 (9H, m, 3×C$H_3$); **^{13}C NMR** δ (90.6 MHz, $CDCl_3$) 154.7 (C), 148.1 (C), 147.6 (C), 128.5 (C), 126.1 (C), 109.2 (CH), 108.6 (CH), 79.9 (C), 69.3 (CH), 66.8 (CH), 56.1 (CH_3), 55.8 (CH_3), 45.8 (CH), 42.9 (CH_2), 35.7 (CH), 31.1 (CH_2), 29.6 (CH_2), 28.4 (3×CH_3); ***m/z*** (EI) 379 ([M]$^+$, 2%), 322 ([M-^{t}Bu]$^+$, 100), 278 ([M-Boc]$^+$, 38), 190 (10).

(3*RS*,4*SR*,4a*RS*,10b*SR*)-3,4-Dihydroxy-8,9-dimethoxy-2,3,4,4a,6,10b-hexahydro-1*H*-phenanthridine-5-carboxylic acid *tert*-butyl ester 19e ($\Delta^{3,4}$ isomer)



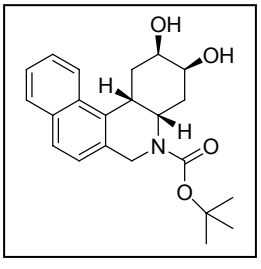
$\mathbf{R_f}$ [9: 1 CH_2Cl_2:MeOH] = 0.51; $\mathbf{R_t}$ (EtOAc:hexane, 84:16, flow rate: 10 mL min^{-1}) = 23 min; $\boldsymbol{\upsilon_{max}}$ ($CHCl_3$)/cm^{-1} 3404 (OH), 1668 (C=O); **^{1}H NMR** δ (250 MHz, $CDCl_3$) 6.80 (1H, s, Ar*H*), 6.63 (1H, s, Ar*H*), 4.66-4.60 (2H, m, C*H*+CH_XH$_Y$Ar), 4.37 (1H, d, *J* 16.8, CH$_X$$H_Y$Ar), 3.96 (1H, br s, C*H*), 3.88 (3H, s, OCH_3), 3.87 (3H, s, OCH_3), 3.35-3.31 (1H, m, C*H*), 3.22 (1H, br s, C*H*), 2.26-2.13 (2H, m, CH_2), 1.86-1.78 (1H, m, CH_AH$_B$), 1.53-1.42 (10H, m, CH$_A$$H_B$+3×C$H_3$); **^{13}C NMR** δ (62.9 MHz, $CDCl_3$) 157.7 (C), 148.0 (C), 147.6 (C), 127.6 (C), 125.2 (C), 109.4 (CH), 108.5 (CH), 80.8 (C), 71.2 (CH), 69.4 (CH), 56.0 (CH_3), 55.9 (CH_3), 52.7 (CH), 43.9 (CH_2), 36.3 (CH), 28.4 (3×CH_3), 25.4 (CH_2), 20.2 (CH_2); ***m/z*** (EI) 379 ([M]$^+$, 1%), 278 ([M-Boc]$^+$, 10), 199 (46), 84 (100).

(1*RS*,2*SR*,4a*SR*,12c*SR*)-1,2-Dihydroxy-2,3,4,4a,6,12c-hexahydro-1*H*-benzo[*k*]phenanthridine-5-carboxylic acid *tert*-butyl ester 17f ($\Delta^{1,2}$ isomer)



$\mathbf{R_f}$ [CH_2Cl_2:MeOH, 9:1] = 0.65; $\boldsymbol{\upsilon_{max}}$ ($CHCl_3$)/cm^{-1} 3418 (OH), 1668 (C=O); **^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 8.08 (1H, d, *J* 8.5, Ar*H*), 7.85 (1H, d, *J* 7.9, Ar*H*), 7.70 (1H, d, *J* 8.3, Ar*H*), 7.54 (1H, t, *J* 7.9, Ar*H*), 7.47 (1H, t, *J* 7.9, Ar*H*), 7.26 (1H, d, *J* 8.2, Ar*H*), 5.11 (1H, d, *J* 15.9, CH_XH$_Y$Ar), 4.41 (1H, m, C*H*), 4.30 (1H, d, *J* 15.9, CH$_X$$H_Y$Ar), 4.17-4.28 (2H, m, 2×C*H*), 3.98-3.95 (1H, m, C*H*), 2.79 (1H, br s, O*H*), 2.27 (1H, br s, O*H*), 2.01-1.93 (2H, m, CH_2), 1.75-1.69 (2H, m, CH_2), 1.49 (9H, m, 3×CH_3); **^{13}C NMR** δ (90.6 MHz, 323 K, $CDCl_3$) 156.0 (C), 134.8 (C), 133.3 (C), 132.6 (C), 130.6 (C), 128.8 (CH), 126.6 (CH), 126.2 (CH), 125.4 (CH), 124.6 (CH), 122.6 (CH), 80.6 (C), 71.2 (CH), 68.9 (CH), 56.7 (CH), 45.3 (CH_2), 30.9 (CH), 28.4 (3×CH_3), 26.6 (CH_2), 26.5 (CH_2); ***m/z*** (EI) 369 ([M]$^+$, 4%), 313 (15), 312 ([M-^{t}Bu], 13), 268 ([M-Boc]$^+$, 71), 223 (31), 180 (36), 141 (21), 84 (100).

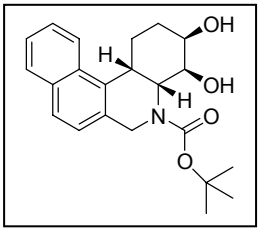
(2*RS*,3*SR*,4a*SR*,12c*SR*)-2,3-Dihydroxy-2,3,4,4a,6,12c-hexahydro-1*H*-benzo[*k*]phenanthridine-5-carboxylic acid *tert*-butyl ester 18f ($\Delta^{2,3}$ isomer)



$\mathbf{R_f}$ [CH_2Cl_2:MeOH, 9:1] = 0.52; $\boldsymbol{\upsilon_{max}}$ ($CHCl_3$)/cm^{-1} 3418 (OH), 1685 (C=O); **^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 8.11 (1H, d, *J* 8.5, Ar*H*), 7.85 (1H, d, *J* 8.1, Ar*H*), 7.71 (1H, d, *J* 8.3, Ar*H*), 7.55 (1H, t, *J* 8.4, Ar*H*), 7.48 (1H, t, *J* 6.8, Ar*H*), 7.27 (1H, d, *J* 8.3, Ar*H*), 5.10 (1H, d, *J* 16.1, CH_XH$_Y$Ar), 4.37 (1H, d, *J* 16.1, CH$_X$$H_Y$Ar), 4.17-4.02 (4H, m, 4xC*H*), 2.71-2.66 (1H, m, CH_AH$_B$), 2.44 (1H, br s, O*H*), 2.15-2.10 (2H, m, CH_2), 1.86-1.78 (1H, m, CH$_A$$H_B$), 1.60 (1H, br s, O*H*), 1.52 (9H, m, 3×CH_3); **^{13}C NMR** δ (90.6 MHz, 323 K, $CDCl_3$) 155.9 (C), 135.0 (C), 133.1 (C), 131.9 (C), 130.3 (C), 128.7

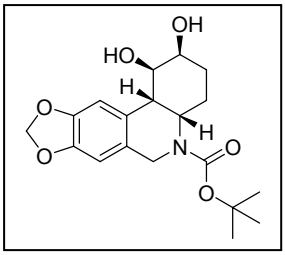
(CH), 126.7 (CH), 126.4 (CH), 125.4 (CH), 124.7 (CH), 122.4 (CH), 80.2 (C), 68.5 (CH), 67.9 (CH), 52.3 (CH), 46.6 (CH_2), 33.5 (CH_2), 31.9 (CH_2), 29.9 (CH), 28.5 (3×CH_3); ***m/z*** (EI) 369 ($[M]^+$, 4%), 312 ($[M\text{-}^tBu]^+$, 100), 268 ($[M\text{-Boc}]^+$, 25), 250 (15), 180 (27).

(3*RS*,4*SR*,4a*SR*,12c*SR*)-3,4-Dihydroxy-2,3,4,4a,6,12c-hexahydro-1*H*-benzo[*k*]phenanthridine-5-carboxylic acid *tert*-butyl ester 19f ($\Delta^{3,4}$ isomer)



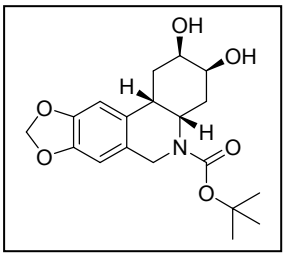
R_f [CH_2Cl_2:MeOH, 9:1] = 0.66; **υ_{max}** ($CHCl_3$)/cm^{-1} 3409 (OH), 1662 (C=O); **^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 8.20 (1H, d, *J* 8.5, Ar*H*), 7.85 (1H, d, *J* 8.1, Ar*H*), 7.76 (1H, d, *J* 8.3, Ar*H*), 7.55 (1H, t, *J* 8.4, Ar*H*), 7.48 (1H, t, *J* 8.1, Ar*H*), 7.33 (1H, d, *J* 8.3, Ar*H*), 5.23 (1H, d, *J* 16.0, CH_XH$_Y$Ar), 4.37 (1H, d, *J* 16.0, CH$_X$$H_Y$Ar), 4.18-4.09 (2H, m, 2×C*H*), 4.01-4.00 (1H, m, C*H*), 3.90-3.86 (1H, m, C*H*), 2.52 (1H, br s, O*H*), 2.44-2.35 (1H, m, CH_AH$_B$), 2.16-2.04 (1H, m, CH$_A$$H_B$), 1.99-1.93 (1H, m, C$H_CH_D$), 1.83-1.79 (1H, m, CH$_C$$H_D$), 1.55 (1H, br s, O*H*), 1.48 (9H, m, 3×CH_3); **^{13}C NMR** δ (90.6 MHz, 323 K, $CDCl_3$) 155.9 (C), 133.3 (2×C), 133.1 (C), 132.0 (C), 128.6 (CH), 127.2 (CH), 126.4 (CH), 125.5 (CH), 125.2 (CH), 123.3 (CH), 80.1 (C), 72.3 (CH), 68.1 (CH), 52.8 (CH), 47.2 (CH_2), 37.8 (CH), 28.4 (3×CH_3), 25.6 (CH_2), 22.8 (CH_2); ***m/z*** (EI) 369 ($[M]^+$, 5%), 313 (26), 312 ($[M\text{-}^tBu]^+$, 100), 268 ($[M\text{-Boc}]^+$, 12), 223 (27), 180 (29).

(1R,2S,4a*SR*,11b*SR*)-1,2-Dihydroxy-2,3,4,4a,6,11b-hexahydro-1*H*-[1,3]dioxolo[4,5-*j*]phenanthridine-5-carboxylic acid *tert*-butyl ester 17g ($\Delta^{1,2}$ isomer)



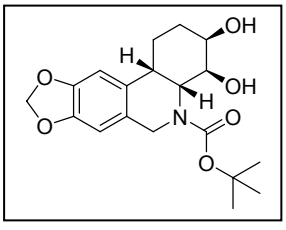
R_f [CH_2Cl_2:MeOH, 9:1] = 0.52; **υ_{max}** ($CHCl_3$)/cm^{-1} 3392 (OH), 1685 (C=O); **^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 6.83 (1H, s, Ar*H*), 6.61 (1H, s, Ar*H*), 5.94-5.93 (2H, m, OCH_2O), 4.66-4.59 (3H, m, 2×C*H*OH+CH_XH$_Y$Ar), 4.24 (1H, d, *J* 16.8, CH$_X$$H_Y$Ar), 3.75-3.71 (1H, m, C*H*), 3.30 (1H, br s, C*H*), 2.41 (1H, br s, O*H*), 2.10-1.83 (3H, m, O*H*+CH_2), 1.70-1.61 (2H, m, CH_2), 1.52 (9H, s, 3×CH_3); **^{13}C NMR** δ (90.6 MHz, 323 K, $CDCl_3$) 154.8 (C), 147.0 (C), 146.2 (C), 126.8 (C), 126.1 (C), 106.7 (CH), 105.7 (CH), 100.9 (CH_2), 79.9 (C), 71.4 (CH), 67.4 (CH), 47.2 (CH), 43.6 (CH_2), 42.8 (CH), 28.9 (3×CH_3), 27.3 (CH_2), 24.0 (CH_2); ***m/z*** (EI) 363 ($[M]^+$, 6%), 306 (53), 252 (22), 224 (30).

(2R,3S,4a*SR*,11b*SR*)-2,3-Dihydroxy-2,3,4,4a,6,11b-hexahydro-1*H*-[1,3]dioxolo[4,5-*j*]phenanthridine-5-carboxylic acid *tert*-butyl ester 18g ($\Delta^{2,3}$ isomer)



R_f [CH_2Cl_2:MeOH, 9:1] = 0.59; **υ_{max}** ($CHCl_3$)/cm^{-1} 3391 (OH), 1684 (C=O); **^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 6.94 (1H, s, Ar*H*), 6.58 (1H, s, Ar*H*), 5.93-5.91 (2H, m, OCH_2O), 4.72-4.65 (1H, m, C*H*), 4.59 (1H, d, *J* 16.9, CH$_X$$H_Y$Ar), 4.23 (1H, d, *J* 16.9, CH$_X$$H_Y$Ar), 3.93 (1H, d, *J* 2.7, C*H*), 3.65-3.61 (1H, m, C*H*), 3.16 (1H, br s, C*H*), 2.51 (1H, br s, O*H*), 2.35-2.30 (1H, m, CH_AH$_B$), 2.26-2.19 (1H, m, CH$_A$$H_B$), 1.90-1.86 (1H, m, C$H_CH_D$), 1.56-1.50 (10H, m, CH$_C$$H_D$+3×C$H_3$); **^{13}C NMR** δ (90.6 MHz, 323 K, $CDCl_3$) 154.7 (C), 147.0 (C), 146.2 (C), 127.7 (C), 126.3 (C), 106.4 (CH), 105.8 (CH), 100.8 (CH_2), 80.0 (C), 69.4 (CH), 66.7 (CH), 46.3 (CH), 43.6 (CH_2), 36.2 (CH), 31.3 (CH_2), 29.7 (CH_2), 28.4 (3×CH_3); ***m/z*** (EI) 363 ($[M]^+$, 1%), 306 (12), 262 (100), 218 (12), 174 (23).

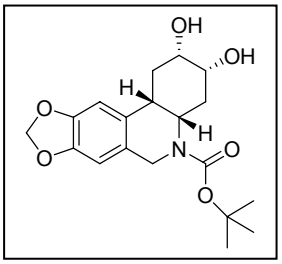
(3R,4S,4a*SR*,11b*SR*)-3,4-Dihydroxy-2,3,4,4a,6,11b-hexahydro-1*H*-[1,3]dioxolo[4,5-*j*]phenanthridine-5-carboxylic acid *tert*-butyl ester 19g ($\Delta^{3,4}$ isomer)



R_f [CH_2Cl_2:MeOH, 9:1] = 0.62; **υ_{max}** ($CHCl_3$)/cm^{-1} 3391 (OH), 1684 (C=O); **^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 6.80 (1H, s, Ar*H*), 6.60 (1H, s, Ar*H*), 5.93-5.91 (2H, m, OCH_2O), 4.67-4.55 (2H, m, C*H*+CH_XH$_Y$Ar), 4.32 (1H, d, *J* 16.1, CH$_X$$H_Y$Ar), 3.95 (1H, d, *J* 2.5, C*H*), 3.34 (1H, br d, *J* 9.6, C*H*), 3.17 (1H, br s, C*H*), 2.61 (1H, br s, O*H*), 2.30-2.20 (1H, m, CH_AH$_B$), 2.13-2.05 (1H, m, CH$_A$$H_B$), 1.83-1.78 (1H, m, C$H_CH_D$), 1.60-

1.45 (11H, m, O*H*+$CH_C H_D$+3×CH_3); **^{13}C NMR** δ (90.6 MHz, 323 K, $CDCl_3$) 157.2 (C), 150.0 (C), 146.1 (C), 128.0 (C), 126.4 (C), 106.6 (CH), 105.6 (CH), 100.9 (CH_2), 80.8 (C), 69.6 (2×CH), 53.0 (CH), 44.2 (CH_2), 36.7 (CH), 28.4 (3×CH_3), 25.4 (CH_2), 20.5 (CH_2); ***m/z*** (EI) 363 ([M]$^+$, 2%), 308 (22), 262 (100), 244 (7), 218 (12).

(2*S*,3*R*,4a*SR*,11b*SR*)-2,3-Dihydroxy-2,3,4,4a,6,11b-hexahydro-1*H*-[1,3]dioxolo[4,5-*j*]phenanthridine-5-carboxylic acid *tert*-butyl ester (Δ^{2,3} isomer, minor diastereomer, endo *syn* diol)

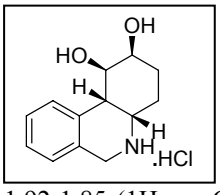


R_f [CH_2Cl_2:MeOH, 95:5] = 0.37; **υ_{max}** ($CHCl_3$)/cm^{-1} 3421 (OH), 1684 (C=O); **^{1}H NMR** δ (360 MHz, 323 K, $CDCl_3$) 6.99 (1H, s, Ar*H*), 6.57 (1H, s, Ar*H*), 5.93 (2H, s, OCH_2O), 4.71 (1H, d, *J* 16.9, $CH_X H_Y Ar$), 4.38-4.32 (1H, m, C*H*), 4.27 (1H, d, *J* 16.9, $CH_X H_Y$Ar), 3.96 (1H, br s, C*H*), 3.71 (1H, br s, C*H*), 3.07 (1H, br s, C*H*), 2.76 (1H, dt, *J* 15.5, 3.3, $CH_A H_B$), 2.02-2.00 (1H, m, $CH_A H_B$), 1.80-1.72 (2H, m, CH_2), 1.51 (9H, s, 3×CH_3); **^{13}C NMR** δ (90.6 MHz, 323 K, $CDCl_3$) 154.5 (C), 146.7 (C), 146.3 (C), 128.5 (C), 125.7 (C), 106.9 (CH), 106.3 (CH), 100.9 (CH_2), 80.1 (C), 70.5 (CH), 69.0 (CH), 49.7 (CH), 43.2 (CH_2), 33.7 (CH), 30.8 (CH_2), 29.4 (CH_2), 28.4 (3×CH_3); ***m/z*** (EI) 364 ([M+H]$^+$, 5%), 363 ([M]$^+$, 2), 306 (16), 262 (100), 218 (16).

General procedure H – Hydrochloride salt formation

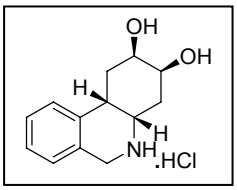
To a solution of the appropriate diol(s) **17-19** in CH_2Cl_2 (2 mL) was added TFA (5 mL) and the reaction was stirred at r.t. for 2 h. The reaction was diluted with H_2O (15 mL), adjusted to pH 8-9 by the addition of NaOH pellets, and then extracted with CH_2Cl_2 (3 × 15 mL). The combined organics were dried ($MgSO_4$) and concentrated under reduced pressure. The resultant oil was taken up in CH_2Cl_2 (1 mL), cooled to 0°C and HCl (excess, 1 M in Et_2O) added. The resultant solid was washed with Et_2O and dried under vacuum to afford the desired amine hydrochloride(s) **20-22**.

(1*RS*,2*SR*,4a*SR*,10b*SR*)-1,2,3,4,4a,5,6,10b-Octahydro-phenanthridine-1,2-diol 20a (Δ^{1,2} isomer)



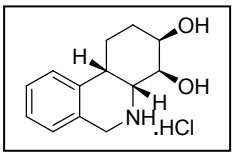
General procedure **H** was followed using diol **17a** (29 mg, 91 μmol), CH_2Cl_2 (2 mL) and TFA (3 mL), then CH_2Cl_2 (1 mL) and HCl (1 mL, 1 M in Et_2O) to afford amine hydrochloride **20a** as a colourless oil (20 mg, 86%). **^{1}H NMR** δ (360 MHz, D_2O) 7.25-7.22 (1H, m, Ar*H*), 7.17-7.13 (2H, m, 2×Ar*H*), 7.06-7.04 (1H, m, Ar*H*), 4.28 (1H, *J* 16.2, $CH_X H_Y$Ar), 4.21 (1H, d, *J* 16.2, $CH_X H_Y$Ar), 3.90 (1H, br d, *J* 7.5, C*H*), 3.75-3.70 (2H, m, 2×C*H*), 3.17 (1H, dd, *J* 7.8, 4.4, C*H*), 1.92-1.85 (1H, m, $CH_A H_B$), 1.76-1.70 (1H, m, $CH_A H_B$), 1.63-1.56 (2H, m, CH_2); **^{13}C NMR** δ (62.9 MHz, D_2O) 131.9 (C), 129.3 (CH), 128.0 (CH), 127.8 (CH), 127.2 (C), 126.9 (C), 70.5 (CH), 67.7 (CH), 51.6 (CH), 43.0 (CH_2), 38.9 (CH), 25.1 (CH_2), 21.4 (CH_2); ***m/z*** (ESI+) 220 ([M+H]$^+$, 77%), 219 (29); **HRMS** (ESI+) Found [M+H]$^+$, 220.1331. $C_{13}H_{18}O_2N$ requires 220.1332.

(2*RS*,3*SR*,4a*SR*,10b*SR*)-1,2,3,4,4a,5,6,10b-Octahydro-phenanthridine-2,3-diol hydrochloride 21a (Δ^{2,3} isomer)



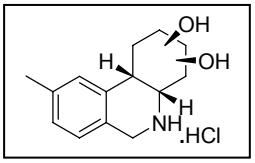
General procedure **H** was followed using diol **18a** (25 mg, 78 μmol), CH_2Cl_2 (2 mL) and TFA (3 mL), then CH_2Cl_2 (1 mL) and HCl (1 mL, 1 M in Et_2O) to afford amine hydrochloride **21a** as a colourless oil (12 mg, 60%). **^{1}H NMR** δ (360 MHz, D_2O) 7.18-7.17 (2H, m, 2×Ar*H*), 7.15-7.10 (1H, m, Ar*H*), 7.02 (1H, d, *J* 7.4, Ar*H*), 4.25-4.17 (2H, m, CH_2Ar), 3.78-3.70 (3H, m, 3×C*H*), 3.24-3.18 (1H, dt, *J* 10.5, 4.6, C*H*Ar), 2.06-1.97 (2H, m, CH_2), 1.85-1.75 (2H, m, CH_2); **^{13}C NMR** δ (150.8 MHz, D_2O) 131.1 (CH), 130.8 (C), 130.0 (CH), 129.4 (C), 129.4 (CH), 129.3 (CH), 70.1 (CH), 68.8 (CH), 54.7 (CH), 46.9 (CH_2), 36.1 (CH_2), 33.7 (CH), 31.6 (CH_2); ***m/z*** (ESI+) 220 ([M+H]$^+$, 100%), 219 (91), 211 (62), 179 (65); **HRMS** (ESI+) Found [M+H]$^+$, 220.1331. $C_{13}H_{18}O_2N$ requires 220.1332.

(3*RS*,4*SR*,4a*RS*,10b*SR*)-1,2,3,4,4a,5,6,10b-Octahydro-phenanthridine-3,4-diol hydrochloride 22a ($\Delta^{3,4}$ isomer)



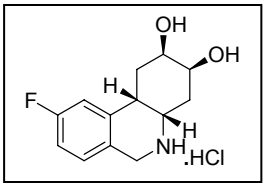
General procedure **H** was followed using diol **19a** (26 mg, 82 μmol), CH_2Cl_2 (2 mL) and TFA (3 mL), then CH_2Cl_2 (1 mL) and HCl (1 mL, 1 M in Et_2O) to afford amine hydrochloride **22a** as a colourless oil (11 mg, 53%). **^{1}H NMR** δ (360 MHz, D_2O) 7.29 (1H, d, *J* 6.9, Ar*H*), 7.20 (1H, t, *J* 7.1, Ar*H*), 7.13 (1H, t, *J* 7.6, Ar*H*), 7.05 (1H, d, *J* 7.5, Ar*H*), 4.24 (1H, d, *J* 16.3, CH_XH$_Y$Ar), 4.18 (1H, d, *J* 16.3, CH$_X$$H_Y$Ar), 3.79-3.73 (2H, m, 2×C*H*), 3.56 (1H, br d, *J* 9.1, C*H*), 3.33-3.29 (1H, m, C*H*), 2.08-1.97 (1H, m, CH_AH$_B$), 1.94-1.85 (1H, m, CH$_A$$H_B$), 1.59-1.53 (1H, m, C$H_CH_D$), 1.34-1.26 (1H, m, CH$_C$$H_D$); **^{13}C NMR** δ (62.9 MHz, D_2O) 133.3 (C), 128.7 (CH), 128.1 (C), 127.4 (CH), 127.0 (CH), 126.8 (CH), 69.0 (CH), 66.7 (CH), 54.5 (CH), 41.3 (CH_2), 33.6 (CH), 25.9 (CH_2), 21.5 (CH_2); ***m/z*** (ESI+) 220 ([M+H]$^+$, 100%), 218 (21); **HRMS** (ESI+) Found [M+H]$^+$, 220.1331. $C_{13}H_{18}O_2N$ requires 220.1332.

9-Methyl-1,2,3,4,4a,5,6,10b-octahydro-phenanthridine-diol hydrochloride 20-22b



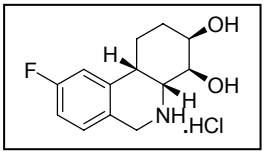
General procedure **H** was followed using diol mixture **17-19b** (16 mg, 48 μmol), CH_2Cl_2 (2 mL) and TFA (5 mL), then CH_2Cl_2 (1 mL) and HCl (2 mL, 1 M in Et_2O) to afford a amine hydrochlorides **20-22b** as a yellow oil (9 mg, 69%). ***m/z*** (ESI+) 234 ([M+H]$^+$, 100%), 232 (44); **HRMS** (ESI+) Found [M+H]$^+$, 234.1489. $C_{14}H_{20}O_2N$ requires 234.1489.

(2*RS*,3*SR*,4a*SR*,10b*SR*) 9-Fluoro-1,2,3,4,4a,5,6,10b-octahydro-phenanthridine-2,3-diol 21c ($\Delta^{2,3}$ isomer)



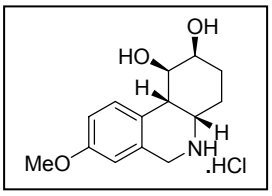
General procedure **H** was followed using diol **18c** (10 mg, 30 μmol), CH_2Cl_2 (2 mL), and TFA (5 mL), then CH_2Cl_2 (1 mL) and HCl (2 mL, 1 M in Et_2O) to afford amine hydrochloride **21c** as a colourless oil (7 mg, 86%). **^{1}H NMR** δ (360 MHz, D_2O) 7.09-7.05 (1H, m, Ar*H*), 6.98 (1H, dd, *J* 10.0, 2.1, Ar*H*), 6.91 (1H, td, *J* 8.7, 2.6, ArH), 4.23 (1H, s, CH_2Ar), 3.81 (1H, dd, *J* 9.8, 4.7, C*H*), 3.77-3.75 (2H, m, 2×C*H*), 3.27-3.23 (1H, m, C*H*), 2.10-2.00 (2H, m, CH_AH$_B$+CH_CH$_D$), 1.87-1.80 (2H, m, CH$_A$$H_B$+CH$_C$$H_D$); **^{13}C NMR** δ (90.6 MHz, D_2O) 162.7 (d, *J* 244.5, C), 137.2 (d, *J* 7.6, C), 129.0 (d, *J* 8.5, CH), 122.8 (C), 115.0 (d, *J* 22.4, CH), 114.8 (d, *J* 22.9, CH), 67.6 (CH), 66.5 (CH), 51.7 (CH), 43.9 (CH_2), 33.2 (CH_2), 31.6 (CH), 29.0 (CH_2); ***m/z*** (ESI+) 238 ([M+H]$^+$, 100%), 211 (12), 179 (12); **HRMS** (ESI+) Found [M+H]$^+$, 238.1234. $C_{13}H_{17}O_2NF$ requires 238.1238.

(3*RS*,4*SR*,4a*RS*,10b*SR*)-9-Fluoro-1,2,3,4,4a,5,6,10b-octahydro-phenanthridine-3,4-diol 22c ($\Delta^{3,4}$ isomer)



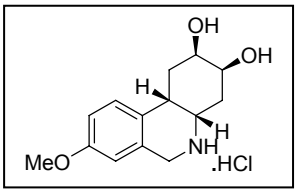
General procedure **H** was followed using diol **19c** (15 mg, 46 μmol), CH_2Cl_2 (2 mL), and TFA (5 mL), then CH_2Cl_2 (1 mL) and HCl (2 mL, 1 M in Et_2O) to afford amine hydrochloride **22c** as a yellow oil (9 mg, 74%). **^{1}H NMR** δ (360 MHz, D_2O) 7.11-7.05 (2H, m, 2×Ar*H*), 6.91 (1H, td, *J* 8.6, 2.7, Ar*H*), 4.23 (1H, d, *J* 16.3, CH_XH$_Y$Ar), 4.17 (1H, d, *J* 16.3, CH$_X$$H_Y$Ar), 3.84-3.82 (1H, m, C*H*), 3.77 (1H, dd, *J* 9.5, 5.3, C*H*), 3.59-3.57 (1H, m, C*H*), 3.32-3.30 (1H, m, C*H*), 2.02-1.92 (2H, m, CH_2), 1.64-1.57 (1H, m, CH_AH$_B$), 1.39-1.31 (1H, m, CH$_A$$H_B$); **^{13}C NMR** δ (90.6 MHz, D_2O) 163.1 (d, *J* 245.1, C), 136.3 (C), 129.8 (d, *J* 8.7, CH), 124.6 (C), 115.1 (d, *J* 22.2, CH), 113.9 (d, *J* 23.3, CH), 69.5 (CH), 67.2 (CH), 54.6 (CH), 49.5 (CH_2), 34.3 (CH), 26.3 (CH_2), 21.9 (CH_2); ***m/z*** (ESI+) 238 ([M+H]$^+$, 100%), 225 (18), 211 (26), 210 (10), 197 (13), 179 (26); **HRMS** (ESI+) Found [M+H]$^+$, 238.1233. $C_{13}H_{17}O_2NF$ requires 238.1238.

(1*RS*,2*SR*,4a*SR*,10b*SR*)-8-Methoxy-1,2,3,4,4a,5,6,10b-octahydro-phenanthridine-1,2-diol 20d ($\Delta^{1,2}$ isomer)



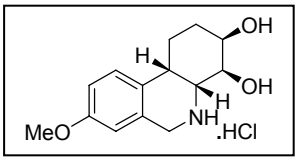
General procedure **H** was followed using diol **17d** (21 mg, 60 μmol), CH_2Cl_2 (2 mL), and TFA (5 mL), then CH_2Cl_2 (1 mL) and HCl (2 mL, 1 M in Et_2O) to afford amine hydrochloride **20d** as a colourless oil (14 mg, 82%). **^{1}H NMR** δ (800 MHz, D_2O) 7.17 (1H, d, *J* 8.8, Ar*H*), 6.76 (1H, d, *J* 8.8, 2.4, Ar*H*), 6.64 (1H, d, *J* 1.6, Ar*H*), 4.23 (1H, d, *J* 16.6, CH_XH$_Y$Ar), 4.18 (1H, d, *J* 16.6, CH$_X$$H_Y$Ar), 3.85 (1H, br s, C*H*), 3.72-3.66 (2H, m, 2×C*H*), 3.61 (3H, s, CH_3), 3.12 (1H, m, C*H*), 1.92-1.89 (1H, m, CH_AH$_B$), 1.73-1.70 (1H, m, CH_CH$_D$), 1.63-1.52 (2H, m, CH$_A$$H_B$+ CH$_C$$H_D$); **^{13}C NMR** δ (200.0 MHz, D_2O) 158.6 (C), 131.1 (CH), 129.0 (C), 124.9 (C), 114.7 (CH), 111.9 (CH), 71.1 (CH), 68.1 (CH), 56.0 (CH_3), 52.2 (CH), 43.4 (CH_2), 38.7 (CH), 25.5 (CH_2), 21.8 (CH_2); ***m/z*** (ESI+) 250 ([M+H]$^+$, 100%), 248 (86), 246 (13); **HRMS** (ESI+) Found [M+H]$^+$, 250.1435. $C_{14}H_{20}O_3N$ requires 250.1438.

(2*RS*,3*SR*,4a*SR*,10b*SR*)-8-Methoxy-1,2,3,4,4a,5,6,10b-octahydro-phenanthridine-2,3-diol 21d ($\Delta^{2,3}$ isomer)



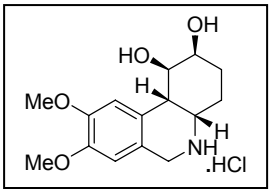
General procedure **H** was followed using diol **18d** (20 mg, 57 μmol), CH_2Cl_2 (2 mL), and TFA (5 mL), then CH_2Cl_2 (1 mL) and HCl (2 mL, 1 M in Et_2O) to afford amine hydrochloride **21d** as a yellow oil (15 mg, 92%). **^{1}H NMR** δ (360 MHz, D_2O) 7.12 (1H, d, *J* 8.6, Ar*H*), 6.79 (1H, dd, *J* 8.6, 2.2, Ar*H*), 6.62 (1H, br s, Ar*H*), 4.23-4.14 (2H, m, CH_2Ar), 3.75-3.64 (3H, m, 3×C*H*), 3.60 (3H, s, OCH_3), 3.18-3.13 (1H, m, C*H*), 2.06-1.94 (2H, m, CH_2), 1.85-1.72 (2H, m, CH_2); **^{13}C NMR** δ (90.6 MHz, D_2O) 158.1 (C), 129.8 (CH), 128.3 (C), 127.3 (C), 115.2 (CH), 111.5 (CH), 67.6 (CH), 66.4 (CH), 55.7 (CH_3), 52.3 (CH), 44.2 (CH_2), 33.6 (CH_2), 30.5 (CH), 29.0 (CH_2); ***m/z*** (ESI+) 250 ([M+H]$^+$, 100%), 249 (28), 248 (89); **HRMS** (ESI+) Found [M+H]$^+$, 250.1438. $C_{14}H_{20}O_3N$ requires 250.1438.

(3*RS*,4*SR*,4a*RS*,10b*SR*)-8-Methoxy-1,2,3,4,4a,5,6,10b-octahydro-phenanthridine-3,4-diol 22d ($\Delta^{3,4}$ isomer)



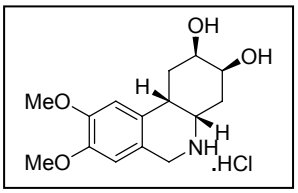
General procedure **H** was followed using diol **19d** (2.1 mg, 6 μmol), CH_2Cl_2 (2 mL), and TFA (5 mL), then CH_2Cl_2 (1 mL) and HCl (2 mL, 1 M in Et_2O) to afford amine hydrochloride **22d** as a colourless oil (1.4 mg, 84%). **^{1}H NMR** δ (800 MHz, D_2O) 7.22 (1H, d, *J* 8.0, Ar*H*), 6.82 (1H, dd, *J* 8.8, 3.2, Ar*H*), 6.67 (1H, d, *J* 2.4, Ar*H*), 4.20 (1H, d, *J* 16.8, CH_XH$_Y$Ar), 4.15 (1H, d, *J* 16.8, CH$_X$$H_Y$Ar), 3.80 (1H, br s, C*H*), 3.71-3.69 (1H, m, C*H*), 3.64 (3H, s, CH_3), 3.60-3.59 (1H, m, C*H*), 3.23 (1H, br s, C*H*), 1.90-1.86 (2H, m, CH_2), 1.59-1.56 (1H, m, CH_AH$_B$), 1.35-1.31 (1H, m, CH$_A$$H_B$); **^{13}C NMR** δ (90.6 MHz, D_2O) 158.0 (C), 130.9 (CH), 130.0 (C), 128.6 (C), 114.9 (CH), 111.8 (CH), 70.1 (CH), 69.1 (CH), 55.8 (CH_3), 54.7 (CH), 41.6 (CH_2), 33.2 (CH), 26.9 (CH_2), 26.0 (CH_2); ***m/z*** (ESI+) 250 ([M+H]$^+$, 100%), 248 (73), 239 (17), 233 (10), 211 (17), 209 (25), 197 (27), 185 (26); **HRMS** (ESI+) Found [M+H]$^+$, 250.1436. $C_{14}H_{20}O_3N$ requires 250.1438.

(1*RS*,2*SR*,4a*SR*,10b*SR*)-8,9-Dimethoxy-1,2,3,4,4a,5,6,10b-octahydro-phenanthridine-1,2-diol hydrochloride 20e ($\Delta^{1,2}$ isomer)



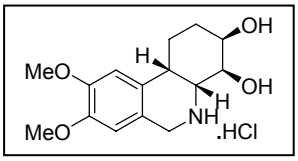
General procedure **H** was followed using diol **17e** (10 mg, 26 μmol), CH_2Cl_2 (2 mL), and TFA (5 mL), then CH_2Cl_2 (1 mL) and HCl (2 mL, 1 M in Et_2O) to afford amine hydrochloride **20e** as a yellow oil (9 mg, 88%). **^{1}H NMR** δ (250 MHz, D_2O) 6.82 (1H, s, Ar*H*), 6.68 (1H, s, Ar*H*), 4.18 (2H, br s, CH_2Ar), 3.83-3.80 (1H, m, C*H*), 3.75-3.68 (2H, m, 2×C*H*), 3.66 (3H, s, CH_3), 3.64 (3H, s, CH_3), 3.09 (1H, dd, *J* 8.8, 4.4, C*H*), 2.04-1.87 (1H, m, CH_AH$_B$), 1.79-1.52 (3H, m, CH_2+CH$_A$$H_B$); **^{13}C NMR** δ (62.9 MHz, D_2O) 148.1 (C), 147.8 (C), 125.2 (C), 120.0 (C), 112.8 (CH), 109.9 (CH), 71.1 (CH), 68.1 (CH), 56.2 (2×CH_3), 52.2 (CH), 43.2 (CH_2), 38.5 (CH), 25.3 (CH_2), 21.6 (CH_2); ***m/z*** (ESI+) 280 ([M+H]$^+$, 61%), 279 ([M]$^+$, 100); **HRMS** (ESI+) Found [M+H]$^+$, 280.1542. $C_{15}H_{22}O_4N$ requires 280.1543.

(2*RS*,3*SR*,4a*SR*,10b*SR*)-8,9-Dimethoxy-1,2,3,4,4a,5,6,10b-octahydro-phenanthridine-2,3-diol hydrochloride 21e ($\Delta^{2,3}$ isomer)



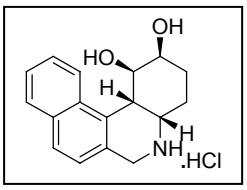
General procedure **H** was followed using diol mixture **17e** and **18e** (6.2 mg, 16 μmol), CH_2Cl_2 (2 mL), and TFA (5 mL), then CH_2Cl_2 (1 mL) and HCl (2 mL, 1 M in Et_2O) to afford amine hydrochlorides **20e** and **21e** as a yellow oil (3 mg, 60%). Data for $\Delta^{2,3}$ isomer **22e** was deduced from ^{1}H, ^{13}C and HSQC NMR data for the mixture of **20e** and **21e**. **^{1}H NMR** δ (500 MHz, D_2O) 6.76 (1H, s, Ar*H*), 6.66 (1H, s, Ar*H*), 4.18-4.15 (2H, m, CH_2Ar), 3.75-3.71 (3H, m, 3×C*H*), 3.67 (3H, s, CH_3), 3.64 (3H, s, CH_3), 3.18-3.15 (1H, m, C*H*), 2.07-2.02 (2H, m, CH_AH$_{B+}$CH_CH$_D$), 1.92-1.88 (1H, m, CH$_A$$H_B$), 1.83-1.78 (1H, m, CH$_C$$H_D$); **^{13}C NMR** δ (125.8 MHz, D_2O) 147.9 (C), 147.6 (C), 125.2 (C), 119.8 (C), 112.7 (CH), 111.1 (CH), 70.9 (CH), 67.5 (CH), 55.9 (2×CH$_3$), 53.3 (CH), 43.9 (CH$_2$), 33.6 (CH), 30.7 (CH$_2$), 28.9 (CH$_2$); ***m/z*** (ESI+) 559 ([2M+H]$^+$, 5%), 280 ([M+H]$^+$, 100), 262 (6); **HRMS** (ESI+) Found [M+H]$^+$, 280.1542. $C_{15}H_{22}O_4N$ requires 280.1543.

(3*RS*,4*SR*,4a*RS*,10b*SR*)-8,9-Dimethoxy-1,2,3,4,4a,5,6,10b-octahydro-phenanthridine-3,4-diol hydrochloride 22e ($\Delta^{3,4}$ isomer)



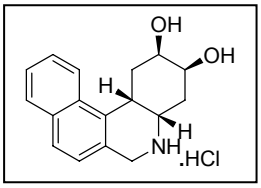
General procedure **H** was followed using diol **19e** (10 mg, 26 μmol), CH_2Cl_2 (2 mL), and TFA (5 mL), then CH_2Cl_2 (1 mL) and HCl (2 mL, 1 M in Et_2O) to afford amine hydrochloride **22e** as a yellow oil (5 mg, 60%). **^{1}H NMR** δ (360 MHz, D_2O) 6.82 (1H, s, Ar*H*), 6.67 (1H, s, Ar*H*), 4.16 (1H, d, *J* 16.1, CH_XH$_Y$Ar), 4.09 (1H, d, *J* 16.1, CH$_X$$H_Y$Ar), 3.78 (1H, br s, C*H*), 3.72-3.65 (1H, m, C*H*), 3.65 (3H, s, CH_3), 3.63-3.60 (1H, m, C*H*), 3.62 (3H, s, CH_3), 3.23 (1H, br s, C*H*), 2.00-1.89 (2H, m, CH_2), 1.64-1.53 (1H, m, CH_AH$_B$), 1.38-1.29 (1H, m, CH$_A$$H_B$); **^{13}C NMR** δ (90.6MHz, D_2O) 148.6 (C), 147.6 (C), 126.3 (C), 120.7 (C), 110.0 (2×CH), 71.7 (CH), 69.1 (CH), 56.1 (2×CH$_3$), 54.6 (CH), 41.0 (CH$_2$), 33.4 (CH), 26.0 (CH$_2$), 21.6 (CH$_2$); ***m/z*** (ESI+) 280 ([M+H]$^+$, 100%); **HRMS** (ESI+) Found [M+H]$^+$, 280.1546. $C_{15}H_{22}O_4N$ requires 280.1543.

(1*RS*,2*SR*,4a*SR*,12c*SR*)-1,2,3,4,4a,5,6,12c-Octahydro-benzo[*k*]phenanthridine-1,2-diol hydrochloride 20f ($\Delta^{1,2}$ isomer)



General procedure **H** was followed using diol **17f** (20 mg, 54 μmol), CH_2Cl_2 (2 mL), and TFA (5 mL), then CH_2Cl_2 (1 mL) and HCl (2 mL, 1 M in Et_2O) to afford amine hydrochloride **20f** as a colourless oil (11 mg, 67%). **^{1}H NMR** δ (500 MHz, D_2O) 8.09 (1H, d, *J* 8.5, Ar*H*), 7.77 (1H, d, *J* 6.5, Ar*H*), 7.76 (1H, d, *J* 9.0, Ar*H*), 7.48-7.41 (2H, m, 2×Ar*H*), 7.19 (1H, d, *J* 8.5, Ar*H*), 4.52 (1H, d, *J* 16.5, CH_XH$_Y$Ar), 4.44 (1H, d, *J* 16.5, CH_XH$_Y$Ar), 4.05-4.03 (2H, m, 2×C*H*), 3.68-3.65 (2H, m, 2×C*H*), 2.22-2.16 (1H, m, CH_AH$_B$), 1.92-1.89 (1H, m, CH$_A$$H_B$), 1.81-1.79 (2H, m, C$H_2$); **^{13}C NMR** δ (125.9 MHz, D_2O) 135.0 (C), 134.7 (C), 132.6 (C), 130.8 (CH), 130.7 (CH), 128.7 (2×CH), 127.7 (C), 127.3 (CH), 126.5 (CH), 74.7 (CH), 71.3 (CH), 56.0 (CH), 46.9 (CH$_2$), 35.7 (CH), 27.8 (CH$_2$), 24.2 (CH$_2$); ***m/z*** (ESI+) 270 ([M+H]$^+$, 38%), 239 (36), 191 (44), 168 (100); **HRMS** (ESI+) Found [M+H]$^+$, 270.1488. $C_{17}H_{20}O_4N$ requires 270.1489.

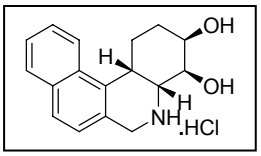
(2*RS*,3*SR*,4a*SR*,12c*SR*)-1,2,3,4,4a,5,6,12c-Octahydro-benzo[*k*]phenanthridine-2,3-diol hydrochloride 21f ($\Delta^{2,3}$ isomer)



General procedure **H** was followed using diol **18f** (40 mg, 66 μmol), CH_2Cl_2 (2 mL), and TFA (5 mL), then CH_2Cl_2 (1 mL) and HCl (2 mL, 1 M in Et_2O) to afford amine hydrochloride **21f** as a colourless oil (20 mg, 61%). **^{1}H NMR** δ (360 MHz, D_2O) 7.85 (1H, d, *J* 8.4, Ar*H*), 7.78 (1H, d, *J* 8.2, Ar*H*), 7.68 (1H, d, *J* 8.6, Ar*H*), 7.51 (1H, t, *J* 7.0, Ar*H*), 7.43 (1H, t, *J* 7.0, Ar*H*), 7.09 (1H, d, *J* 8.6, Ar*H*), 4.37 (2H, s, CH_2Ar), 3.95 (1H, br s, C*H*), 3.81-3.76 (2H, m, 2×C*H*), 3.67 (1H, br s, C*H*), 2.33-2.17 (2H, m, CH_2), 2.04-1.97 (1H, m, CH_AH$_B$), 1.67-1.52 (1H, m, CH$_A$$H_B$); **^{13}C NMR** δ (62.9 MHz, D_2O) 133.9 (C), 131.8 (C), 130.9 (C), 130.0 (CH), 129.1 (CH), 128.4 (CH), 127.6 (CH), 125.1 (CH), 125.0 (C), 123.7 (CH), 69.1 (CH), 66.5

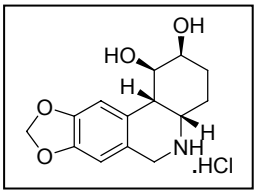
(CH), 54.5 (CH), 46.5 (CH_2), 34.3 (CH), 30.5 (CH_2), 28.1 (CH_2); ***m/z*** (ESI+) 270 ($[M+H]^+$, 100%), 232 (15), 217 (16), 203 (16); **HRMS** (ESI+) Found $[M+H]^+$, 270.1481. $C_{17}H_{20}O_2N$ requires 270.1489.

(3*RS*,4*SR*,4a*RS*,12c*SR*)-1,2,3,4,4a,5,6,12c-Octahydro-benzo[*k*]phenanthridine-3,4-diol hydrochloride 22f ($\Delta^{3,4}$ isomer)



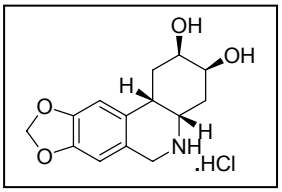
General procedure **H** was followed using diol **19f** (23 mg, 63 μmol), CH_2Cl_2 (2 mL), and TFA (5 mL), then CH_2Cl_2 (1 mL) and HCl (2 mL, 1 M in Et_2O) to afford amine hydrochloride **22f** as a colourless oil (13 mg, 69%). **^{1}H NMR** δ (360 MHz, D_2O) 8.05 (1H, d, *J* 7.5, Ar*H*), 7.77-7.73 (2H, m, 2×Ar*H*), 7.46-7.41 (2H, m, 2×Ar*H*), 7.16 (1H, d, *J* 8.5, Ar*H*), 4.52 (1H, d, *J* 16.5, CH_XH$_Y$Ar), 4.39 (1H, d, *J* 16.5, CH_XH$_Y$Ar), 4.04-3.95 (2H, s, 2×C*H*), 3.64 (1H, d, *J* 11.4, C*H*), 3.54 (1H, br s, CH), 2.22-2.13 (1H, m, CH_AH$_B$), 1.93-1.89 (1H, m, CH$_A$$H_B$), 1.81-1.77 (2H, m, C$H_2$); **^{13}C NMR** δ (62.9 MHz, D_2O) 133.5 (C), 133.2 (C), 130.9 (C), 129.3 (CH), 129.2 (CH), 127.3 (2×CH), 125.9 (CH), 125.7 (C), 125.0 (CH), 73.1 (CH), 69.6 (CH), 54.5 (CH), 45.2 (CH_2), 34.0 (CH), 26.2 (CH_2), 22.6 (CH_2); ***m/z*** (ESI+) 270 ($[M+H]^+$, 71%), 217 (21), 172 (27); **HRMS** (ESI+) Found $[M+H]^+$, 270.1481. $C_{17}H_{20}O_2N$ requires 270.1489.

(1*RS*,2*SR*,4a*SR*,11b*SR*)-1,2,3,4,4a,5,6,11b-Octahydro-[1,3]dioxolo[4,5-*j*]phenanthridine-1,2-diol hydrochloride 20g ($\Delta^{1,2}$ isomer)



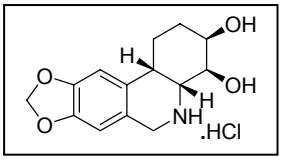
General procedure **H** was followed using diol **17g** (18 mg, 50 μmol), CH_2Cl_2 (2 mL) and TFA (3 mL), then CH_2Cl_2 (1 mL) and HCl (2 mL, 1 M in Et_2O) to afford amine hydrochloride **20g** as a yellow solid (9 mg, 61%). **^{1}H NMR** δ (360 MHz, D_2O) 6.76 (1H, s, Ar*H*), 6.57 (1H, s, Ar*H*), 5.80 (2H, s, OCH_2O), 4.21-4.12 (2H, m, CH_2Ar), 3.95-3.85 (1H, m, C*H*), 3.83-3.75 (2H, m, 2×C*H*), 3.11-3.05 (1H, m, C*H*), 2.04-1.59 (6H, m, 2×CH_2+2xO*H*); **^{13}C NMR** δ (90.6 MHz, D_2O) 147.9 (C), 147.8 (C), 126.6 (C), 121.3 (C), 110.1 (CH), 107.3 (CH), 102.5 (CH_2), 71.7 (CH), 68.6 (CH), 52.6 (CH), 44.0 (CH_2), 39.6 (CH), 26.0 (CH_2), 22.2 (CH_2); ***m/z*** (ESI+) 264 ($[M+H]^+$, 4%), 150 (21), 149 (21); **HRMS** (ESI+) Found $[M+H]^+$, 264.1237. $C_{14}H_{18}O_4N$ requires 264.1230.

(2*RS*,3*SR*,4a*SR*,11b*SR*)-1,2,3,4,4a,5,6,11b-Octahydro-[1,3]dioxolo[4,5-*j*]phenanthridine-2,3-diol hydrochloride 21g ($\Delta^{2,3}$ isomer)



General procedure **H** was followed using diol **18g** (10 mg, 28 μmol), CH_2Cl_2 (2 mL) and TFA (3 mL), then CH_2Cl_2 (1 mL) and HCl (2 mL, 1 M in Et_2O) to afford amine hydrochloride **21g** as a yellow solid (7 mg, 81%). **^{1}H NMR** δ (360 MHz, D_2O) 6.69 (1H, s, Ar*H*), 6.54 (1H, s, Ar*H*), 5.80-5.79 (2H, m, OCH_2O), 4.17-4.09 (2H, m, CH_2Ar), 3.79-3.72 (3H, m, 3×C*H*), 3.14-3.11 (1H, m, C*H*), 2.09-1.98 (2H, m, CH_2), 1.88-1.72 (2H, m, CH_2); **^{13}C NMR** δ (90.6 MHz, D_2O) 148.4 (C), 147.6 (C), 129.2 (C), 120.7 (C), 108.8 (CH), 107.3 (CH), 102.5 (CH_2), 68.3 (CH), 67.1 (CH), 52.9 (CH), 45.1 (CH_2), 34.4 (CH_2), 31.9 (CH), 29.8 (CH_2); ***m/z*** (ESI+) 264 ($[M+H]^+$, 100%), 262 (46); **HRMS** (ESI+) Found $[M+H]^+$, 264.1232. $C_{14}H_{18}O_4N$ requires 264.1230.

(3*RS*,4*SR*,4a*RS*,11b*SR*)-1,2,3,4,4a,5,6,11b-Octahydro-[1,3]dioxolo[4,5-*j*]phenanthridine-3,4-diol hydrochloride 22g ($\Delta^{3,4}$ isomer)



General procedure **H** was followed using diol **19g** (5 mg, 14 μmol), CH_2Cl_2 (2 mL) and TFA (3 mL), then CH_2Cl_2 (1 mL) and HCl (2 mL, 1 M in Et_2O) to afford amine hydrochloride **22g** as a colourless oil (3 mg, 73%). **^{1}H NMR** δ (360 MHz, D_2O) 6.81 (1H, s, Ar*H*), 6.58 (1H, s, Ar*H*), 5.80-5.77 (2H, m, OCH_2O), 4.16 (1H, d, *J* 16.1, CH_XH$_Y$Ar), 4.09 (1H, d, *J* 16.1, CH$_X$$H_Y$Ar), 3.82-3.80 (1H, br s, C*H*), 3.72 (1H, dd, *J* 9.4, 4.5, C*H*), 3.62-3.59 (1H, m, C*H*), 3.22-3.21 (1H, m, C*H*), 1.93-1.85 (1H, m, CH_AH$_B$), 1.63-1.56 (1H, m, CH$_A$$H_B$), 1.39-1.30 (2H, m, C$H_2$); **^{13}C NMR** δ (90.6 MHz, D_2O) 149.8 (C), 148.4 (C), 129.1 (C), 123.2 (C), 108.6 (2×CH), 103.5 (CH_2), 70.9 (CH), 68.6 (CH), 56.3 (CH), 42.8 (CH_2), 35.5 (CH), 27.7 (2×CH_2);

m/z (ESI+) 264 ($[M+H]^+$, 24%), 225 (29), 211 (29), 179 (61); **HRMS** (ESI+) Found $[M+H]^+$, 264.1234. $C_{14}H_{18}O_4N$ requires 264.1230.

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