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

Lauren R. Donaldson, Stephen Wallace, David Haigh, E. Elizabeth Patton, and Alison N. Hulme*

Supporting Information

Contents

S1-S6 Synthesis of N-Boc protected substituted benzyamine building blocks
S6-S8 Synthesis of Heck cyclisation precursors
S8-S11 Heck cyclisation reactions
S11-S17 Dihydroxylation of alkenes
S17-S22 Boc-deprotection to give individual library members
S22 References

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 NH₄OH (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

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%). Rₗ [CH₂Cl₂:MeOH, 95:5] = 0.45; MP 171°C (H₂O), lit 175°C; v max (CHCl₃)/cm⁻¹ 3419 (NH), 1636 (C=O); ¹H NMR δ (250 MHz, CD₃OD) 7.46 (1H, s, ArH), 7.33 (1H, d, J 8.0, ArH), 7.19 (1H, d, J 7.5, 0.8, ArH), 2.33 (3H, s, CH₃); ¹³C NMR δ (62.9 MHz, CD₃OD) 173.4 (C), 143.1 (C), 136.6 (C), 134.7 (CH), 129.7 (CH), 129.2 (CH), 120.0 (C), 20.9 (CH₃); m/z (FAB, 3-NOBA) 216 ([⁸¹BrM-H]+, 75%), 214 ([⁷⁹BrM-H]+, 77), 199 (10), 197 (10), 154 (100), 136 (100), 121 (27); HRMS (EI) Found: [⁸¹BrM]+, 214.9760. C₈H₈ON₈¹Br requires 214.9763. Found: [⁷⁹BrM]+, 212.9779. C₈H₈ON₇⁹Br requires 212.9784.

2-Bromo-5-methoxybenzamide 11d

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%). Rₗ [CH₂Cl₂:MeOH, 95:5] = 0.45; MP 154°C, lit 157°C; v max (CHCl₃)/cm⁻¹ 3415 (NH), 1635 (C=O); ¹H NMR δ (250 MHz, CD₃OD) 7.53 (1H, d, J 8.8, ArH), 7.04 (1H, d, J 3.3, ArH), 6.95 (1H, d, J 8.8, 3.3, ArH), 3.84 (3H, s, CH₃); ¹³C NMR δ (62.9 MHz, CD₃OD) 173.4 (C), 150.8 (C), 134.7 (CH), 128.8 (C), 117.7 (CH), 115.0 (CH), 109.8 (C), 55.8 (CH₃); m/z (FAB, 3-NOBA) 232 ([⁸¹BrM-H]+, 65%), 230 ([⁷⁹BrM-H]+, 67), 154 (100), 136 (100), 121 (26), 109 (42); HRMS (EI) Found: [⁸¹BrM]+, 230.9715. C₈H₈O₂N₈¹Br requires 230.9713. Found: [⁷⁹BrM]+, 228.9733. C₈H₈O₂N₇⁹Br requires 228.9733.
2-Bromo-4,5-methoxybenzamide 11e

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%). Rf [CH2Cl2:MeOH, 95:5] = 0.49; MP 178°C, lit 178°C; \( \nu_{\text{max}} (\text{CHCl3/cm}) \approx 3442 (\text{NH}), 1676 (\text{C=O}); ^1H \text{NMR } \delta (250 \text{MHz, (CD3)2SO}) 7.73 (1H, br s, NH), 7.48 (1H, br s, NH), 7.14 (1H, s, ArH), 7.02 (1H, s, ArH), 3.80 (3H, s, CH3H), 3.78 (3H, s, CH3); ^13C \text{NMR } \delta (62.9 \text{MHz, (CD3)2SO}) 167.9 (C), 149.1 (C), 147.0 (C), 129.9 (C), 115.1 (CH), 111.4 (CH), 108.6 (C), 55.3 (CH3), 55.1 (CH3); m/z (FAB, 3-NOBA) 262 ([\text{[81BrM]+H}]+, 100%), 250 ([\text{[79BrM]+H}]+, 83), 245 (100), 243 (71), 204 (23), 202 (34), 200 (24), 181 (37), 180 (26), 167 (27), 166 (30); HRMS (EI) Found: [\text{[81BrM]}]+, 260.9835. C9H10O3N79Br requires 260.9835.

1-Bromo-naphthalene-2-carboxamide 11f

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%). Rf [CH2Cl2:MeOH, 95:5] = 0.67; MP 202°C (H2O); \( \nu_{\text{max}} (\text{CHCl3/cm}) \approx 3440 (\text{NH}), 1678 (\text{C=O}); ^1H \text{NMR } \delta (250 \text{MHz, (CD3)2SO}) 8.20 (1H, d, J 7.5, ArH), 8.17 (1H, br s, NH), 8.14 (2H, br s, 2xArH), 7.88 (1H, br s, NH), 7.84 (1H, td, J 6.8, 1.5, ArH), 7.79 (1H, td, J 6.8, 1.5, ArH), 7.62 (1H, d, J 6.8, ArH); ^13C \text{NMR } \delta (62.9 \text{MHz, (CD3)2SO}) 169.4 (C), 137.7 (C), 133.4 (C), 130.8 (C), 128.1 (2xCH), 127.7 (CH), 127.0 (CH), 126.4 (CH), 124.6 (CH), 117.8 (C); m/z (FAB, 3-NOBA) 252 ([\text{[81BrM]+H}]+, 76%), 250 ([\text{[79BrM]+H}]+, 90), 235 (12), 233 (13), 154 (100), 149 (26), 138 (41), 136 (97), 107 (46); HRMS (EI +ve) Found: [\text{[81BrM]}]+, 250.9765. C13H8BrNO requires 250.9763. Found: [\text{[79BrM]}], 248.9782. C11H8.84BrNO requires 248.9784. H and \(^13\)C NMR data in good agreement with the literature.4

2-Bromo-4-methyl benzonitrile 12b

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%). Rf [hexane:EtOAc, 3:1] = 0.75; MP 55°C, lit 56°C; \( \nu_{\text{max}} (\text{CHCl3/cm}) \approx 2230 (\text{CN}); ^1H \text{NMR } \delta (250 \text{MHz, (CD3)2OD}) 7.38-7.37 (2H, m, 2xArH), 7.34 (1H, d, J 8.0, 1.5, ArH), 2.43 (3H, s, CH3); ^13C \text{NMR } \delta (62.9 \text{MHz, (CD3)2OD}) 146.8 (C), 134.6 (CH), 134.2 (CH), 129.3 (CH), 124.9 (C), 117.5 (C), 112.9 (C), 20.8 (CH3); m/z (FAB, 3-NOBA) 198 ([\text{[81BrM]+H}]+, 47%), 196 ([\text{[79BrM]+H}]+, 48), 167 (13), 165 (12), 154 (100); HRMS (ES, 3-NOBA) Found: [\text{[81BrM]}]+, 196.9656. C7H6.81BrNO requires 196.9658. Found: [\text{[79BrM]}], 194.9678. C6H6.81BrNO requires 194.9678.

2-Bromo-5-methoxybenzonitrile 12d

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%). Rf [hexane:EtOAc, 3:1] = 0.74; MP 95°C, lit 98.5-99.5°C; \( \nu_{\text{max}} (\text{CHCl3/cm}) \approx 2229 (\text{CN}); ^1H \text{NMR } \delta (250 \text{MHz, (CD3)2OD}) 7.67 (1H, d, J 9.0, ArH), 7.38 (1H, d, J 3.1, ArH), 7.18 (1H, dd, J 9.0, 3.1, ArH), 3.89 (3H, s, CH3); ^13C \text{NMR } \delta (62.9 \text{MHz, (CD3)2OD}) 161.3 (C), 134.9 (CH), 121.9 (CH), 120.0 (CH), 117.6 (C), 115.7 (C), 56.2 (CH3); m/z (FAB, 3-NOBA) 214 ([\text{[81BrM]+H}]+, 8%), 212 ([\text{[79BrM]+H}]+, 8), 167 (20), 165 (26), 154 (100); HRMS (EI) Found: [\text{[81BrM]}]+, 212.9604. C7H6.81BrNO requires 212.9607. Found: [\text{[79BrM]}], 210.9622. C6H6.81BrNO requires 210.9627.

2-Bromo-4,5-methoxybenzonitrile 12c

A mixture of amide 11c (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 12c as a colourless solid (1.15 g, 99%). Rf [hexane:EtOAc, 3:1] = 0.5; MP 113°C (EtOH), lit 117°C; \( \nu_{\text{max}} (\text{CHCl3/cm}) \approx 2229 (\text{CN}); ^1H \text{NMR } \delta
(250 MHz, (CD$_3$)$_2$SO) 7.49 (1H, s, ArH), 7.39 (1H, s, ArH), 3.87 (3H, s, CH$_3$), 3.81 (3H, s, CH$_3$); $^{13}$C NMR δ (90.6 MHz, (CD$_3$)$_2$SO) 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 ([$^{81}$BrM+H$^+$], 27%), 242 ([$^{79}$BrM+H$^+$], 42), 167 (16), 154 (98), 152 (17), 150 (15), 149 (49), 137 (82), 136 (74); HRMS (EI) Found: [$^{81}$BrM$^+$], 242.9708. C$_5$H$_8$BrNO$_2$ requires 240.9733.

1-Bromo-2-naphthalene-2-carbonitrile 12f

To a suspension of LiAlH$_4$ (2 eq) in Et$_2$O (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$_2$SO$_4$·5H$_2$O portionwise, then it was filtered and the filtrate stirred vigorously with potassium sodium tartrate (100 mL, sat. aq.) for 1 h. The Et$_2$O layer was separated and the aqueous phase extracted with Et$_2$O (3× 60 mL). The combined organic phases were washed (MgSO$_4$, 5H$_2$O) then it was filtered and the filtrate stirred vigorously with potassium sodium tartrate (100 mL, sat. aq.) for 1 h. The Et$_2$O layer was separated and the aqueous phase extracted with Et$_2$O (3× 60 mL). The combined organic phases were dried (MgSO$_4$) and 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; $\nu_{max}$ (CHCl$_3$)/cm$^{-1}$ 2226 (CN), 1580 (C=C), 1560 (C=N); $^1$H NMR δ (250 MHz, CD$_3$OD) 7.83-7.29 (1H, m, ArH), 8.04-7.98 (2H, m, 2×ArH), 7.80-7.72 (2H, m, 2×ArH), 7.66 (1H, d, J 8.5, ArH); $^{13}$C NMR δ (62.9 MHz, CD$_2$OD) 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 ([$^{81}$BrM+H$^+$], 27%), 232 ([$^{79}$BrM+H$^+$], 27%), 230 ([$^{79}$BrM$^+$], 27%); HRMS (EI) +ve Found: [$^{81}$BrM$^+$], 229.9656. C$_{11}$H$_6$N$_7$Br requires 229.9678.

General procedure B - Reduction of aryl nitrile analogues

To a suspension of LiAlH$_4$ (2 eq) in Et$_2$O (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$_2$SO$_4$, CH$_2$Cl$_2$ (100 mL, sat. aq.) for 1 h. The Et$_2$O layer was separated and the aqueous phase extracted with Et$_2$O (3× 60 mL). The combined organic phases were washed (MgSO$_4$, 5H$_2$O) then it was filtered 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$_2$O (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$_2$O); $^1$H NMR δ (250 MHz, CD$_2$OD) 7.53 (1H, s, ArH), 6.99 (1H, d, J 8.9, ArH), 7.27 (1H, d, J 8.0, ArH), 7.21 (1H, d, J 8.0, ArH), 4.23 (2H, s, CH$_2$), 2.35 (3H, s, CH$_3$); $^{13}$C NMR δ (62.9 MHz, CD$_2$OD) 142.8 (C), 134.4 (CH), 131.5 (CH), 130.5 (C), 129.9 (CH), 124.7 (C), 43.6 (CH$_3$), 20.5 (CH$_3$); m/z (FAB, 3-NOBA) 202 ([$^{81}$BrM+H$^+$], 91%), 200 ([$^{79}$BrM+H$^+$]+, 93), 185 (95), 183 (95), 154 (51); HRMS (EI) Found: [$^{81}$BrM$^+$], 200.9969. C$_7$H$_{10}$BrN requires 198.9991. Free Amine: $R_f$ [CH$_2$Cl$_2$:MeOH, 95:5] = 0.46; $\nu_{max}$ (CHCl$_3$)/cm$^{-1}$ 3371 (NH), 3304 (NH), 2922, 1605, 1488; $^1$H NMR δ (250 MHz, CDCl$_3$) 7.33 (1H, s, ArH), 7.19 (1H, d, J 7.7, ArH), 7.05 (1H, d, J 7.7, ArH), 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$_3$).

2-Bromo-5-methoxybenzylamine hydrochloride 9d

General procedure B was followed using LiAlH$_4$ (36.0 mg, 0.94 mmol), Et$_2$O (1.00 mL), AlCl$_3$ (432 mg, 4.94 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$_2$OD) 7.62 (1H, d, J 8.9, ArH), 7.19 (1H, d, J 3.0, ArH), 6.99 (1H, dd, J 8.9, 3.0, ArH), 4.27 (2H, s, CH$_2$), 3.87 (3H, s, CH$_3$); $^{13}$C NMR δ (62.9 MHz, CD$_2$OD) 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 ([$^{81}$BrM+H$^+$], 51%), 216 ([$^{79}$BrM+H$^+$], 62), 154 ([$^{79}$BrM], 75%).
238 ([81BrM]+, 77%), 236 ([79BrM]+, 43), 221 (97), 219 (97) 167 (37), 165 (28), 154 (100); [79BrM]+, 257.9521. C9H7O4 (C), 127.9 (C), 114.7 (C), 111.9 (CH), 111.4 (CH), 101.7 (CH2), 40.6 (CH2); 49%), 258 ([81BrM]+, 48), 215 (97), 213 (100), 179 (92), 135 (38), 113 (27); [79BrM]+, 257.9521. C9H7O4 167Br requires 257.9522.

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

General procedure B was followed using LiAlH4 (261 mg, 6.89 mmol), Et2O (10 mL), AlCl3 (920 mg, 6.89 mmol) and nitrile 12e (800 mg, 3.45 mmol), to afford amine hydrochloride 9f as a colourless solid (504 mg, 55%). MP 194°C; 1H NMR δ (250 MHz, CD2OD) 7.25 (1H, s, ArH), 7.21 (1H, s, ArH), 4.25 (2H, s, CH2), 3.90 (3H, s, CH3), 3.88 (3H, s, CH3). 13C NMR δ (62.9 MHz, CD2OD) 151.8 (C), 150.2 (C), 125.2 (C), 116.8 (CH), 115.4 (C), 114.9 (CH), 56.5 (2×CH3), 43.7 (CH2). m/z (FAB, 3-NOBA) 248 ([81BrM]+, 11%), 246 ([79BrM]+, 20), 231 (37), 229 (37), 154 (82), 149 (64), 136 (100); HRMS (EI) Found: [81BrM]+, 248.0016. C9H12O2N81Br requires 247.0026. Found: [79BrM]+, 246.9994. C9H12O2N79Br requires 246.9992.

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

General procedure B was followed using LiAlH4 (261 mg, 6.89 mmol), Et2O (30 mL). The organics were dried (MgSO4) and concentrated under reduced pressure to afford amine hydrochloride 9e as a colourless solid (829 mg, 77%). MP 193°C; 1H NMR δ (250 MHz, CD2OD) 7.20 (1H, s, ArH), 7.11 (1H, s, ArH), 7.02 (1H, d, J 8.5, ArH), 6.07 (1H, s, ArH), 6.66 (1H, dd, J 7.5, 3×ArH), 3.96 (2H, s, CH2); 13C NMR δ (62.9 MHz, CD2OD) 148.2 (C), 148.0 (C), 130.4 (CH), 115.3 (C), 112.8 (C), 111.7 (CH), 55.7 (CH3), 46.2 (CH2). 1H and 13C NMR data in good agreement with the literature.

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

General procedure B was followed using LiAlH4 (261 mg, 6.89 mmol), Et2O (10 mL), AlCl3 (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 (Et2O); 1H NMR δ (250 MHz, CD2OD) 8.37 (1H, d, J 8.5, ArH), 7.98 (1H, d, J 9.5, ArH), 7.75-7.63 (3H, m), 3xArH), 4.54 (2H, s, CH2); 13C NMR δ (62.9 MHz, CD2OD) 136.5 (C), 133.9 (C), 132.3 (C), 130.4 (CH), 130.0 (CH), 129.9 (CH), 129.3 (CH), 128.3 (CH), 128.4 (CH), 126.4 (45.7 (CH2); m/z (FAB, 3-NOBA) 238 ([81BrM]+, 77%), 236 ([81BrM]+, 43), 221 (97), 219 (97)167 (37), 165 (28), 154 (100); HRMS (EI +ve) Found: [81BrM]+, 236.9974. C11H10N81Br requires 236.9971. Found: [79BrM]+, 235.0001. C11H10N79Br requires 234.9991. Free Amine: Rf [CH2Cl2:MeOH, 95:5] = 0.54; vmax (CHCl3/cm-1) 3364 (NH), 1596 (NH2); 1H NMR δ (250 MHz, CDCl3) 8.15 (1H, d, J 8.5, ArH), 7.20 (1H, t, J 6.0, ArH), 7.11 (1H, m, 3xArH), 4.08 (3H, s, CH3), 4.03 (2H, s, CH2), 1.75 (2H, br s, NAr); 13C NMR δ (62.9 MHz, CDCl3) 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 (CH2).

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

To a solution of 1,3-benzodioxole-5-acetic acid 13ref (700 mg, 3.89 mmol) and NaOH (1.0 mL, 5 M aq) in H2O (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 H2O (50 mL), acidified to pH 1 with HCl (6 M, aq.) and extracted into Et2O (3 × 30 mL). The organics were dried (MgSO4) and concentrated under reduced pressure to afford acid 14 as a colourless crystalline powder (909 mg, 91% yield). Rf [CH2Cl2:MeOH, 95:5] = 0.23; MP 191°C (EtOH), lit. 190°C19; vmax (Nujol)/cm-1 1699 (C=O); 1H NMR δ (250 MHz, DMSO) 7.21 (1H, s, ArH), 7.02 (1H, s, ArH), 6.07 (2H, s, OCH2O), 3.63 (2H, s, ArCH2); 13C 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 (CH2), 40.6 (CH2); m/z (EI) 260 ([81BrM]+, 49%), 258 ([81BrM]+, 48), 215 (97), 213 (100), 179 (92), 135 (38), 113 (27); HRMS (EI) Found: [81BrM]+, 257.9521. C9H8O316Br requires 257.9522.
General procedure C - Boc protection of aryl analogues

To a suspension of the appropriate amine hydrochloride (1 eq) in CH₂Cl₂ (10 mL) was added Et₃N (1.5 eq) and the reaction stirred for 10 mins. The reaction was cooled to 0°C, Boc₂O (1 eq) added and the reaction allowed to warm to r.t. and stirred for 4 h. The reaction was diluted with CH₂Cl₂ (15 mL) and washed with NaCl (3 × 15 mL, sat. aq.). The organics were combined, dried (MgSO₄), concentrated under reduced pressure and purified by flash chromatography to afford the desired carbamate.

2-Bromo-4-methylbenzyl-carbamic acid 16b

General procedure C was followed using amine hydrochloride 9b (170 mg, 0.72 mmol), CH₂Cl₂ (10 mL), Et₃N (222 µl, 1.58 mmol) and Boc₂O (173 mg, 0.79 mmol). Flash chromatography (hexane:EtOAc, 10:1) afforded carbamate 16b as a colourless oil (217 mg, 100%). Rᶠ [3: 1 hex:EtOAc] = 0.78; νmax (CHCl₃)/cm⁻¹ 3346 (NH), 1700 (C=O); ¹H NMR δ (360 MHz, CDCl₃) 7.36 (1H, s, ArH), 7.25 (1H, d, J 7.8, ArH), 7.07 (1H, d, J 7.8, 0.9, ArH), 4.98 (1H, br s, CH(N)), 4.34 (2H, d, J 6.2, CH₂Ar), 2.30 (3H, s, CH₃), 1.43 (9H, s, 3×CH₃); ¹³C NMR δ (90.6 MHz, CDCl₃) 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 (CH₂), 28.3 (3×CH₃), 20.4 (CH₃); m/z (EI) 302 ([⁸¹BrM⁺H]+, 2%), 300 ([⁷⁹BrM⁺H]+, 2), 244 (7), 242 (7); HRMS (EI) Found: [⁷⁹BrM⁺], 299.0515. C₁₃H₁₈⁷⁹BrNO requires 299.0515.

2-Bromo-5-methoxybenzyl-carbamic acid 16c

General procedure C was followed using amine hydrochloride 9d (218 mg, 0.86 mmol), CH₂Cl₂ (10 mL), Et₃N (155 µl, 1.10 mmol) and Boc₂O (176 mg, 0.85 mmol). Flash chromatography (hexane:EtOAc, 10:1) afforded carbamate 16c as a colourless oil (230 mg, 85%). Rᶠ [hex:EtOAc, 3:1] = 0.77; νmax (CHCl₃)/cm⁻¹ 3350 (NH), 1698 (C=O); ¹H NMR δ (360 MHz, CDCl₃) 7.40 (1H, d, J 8.7, ArH), 6.93 (1H, d, J 3.1, ArH), 6.68 (1H, dd, J 8.7, 3.1, ArH), 5.00 (1H, br s, NHz), 4.33 (2H, d, J 6.3, CH₂Ar), 3.77 (3H, s, CH₃), 2.30 (3H, s, C₆H₅); ¹³C NMR δ (90.6 MHz, CDCl₃) 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 (CH₃), 45.0 (CH₂), 28.3 (3×CH₃); m/z (EI) 317 ([⁸¹BrM⁺], 1%), 315 ([⁷⁹BrM⁺], 1), 261 (3), 259 (3), 201 (9), 199 (10), 180 (100); HRMS (EI) Found: [⁷⁹BrM⁺], 315.0461. C₁₃H₁₈⁷⁹BrNO₃ requires 315.0465.

2-Bromo-4,5-dimethoxy-benzyl-carbamic acid tert-butyl ester 16d

General procedure C was followed using amine hydrochloride 9e (200 mg, 0.710 mmol), CH₂Cl₂ (10 mL), Et₃N (219 µl, 1.56 mmol) and Boc₂O (207 mg, 0.95 mmol). Flash chromatography (hexane:EtOAc, 10:1) afforded carbamate 16d as a colourless oil (267 mg, 100%). Rᶠ [hex:EtOAc, 3:1] = 0.63; νmax (CHCl₃)/cm⁻¹ 3377 (NH), 1701 (C=O); ¹H NMR δ (360 MHz, CDCl₃) 6.93 (1H, s, ArH), 6.85 (1H, s, ArH), 5.07 (1H, br s, CH(N)), 4.24 (2H, d, J 6.0, CH₂Ar), 3.79 (6H, s, 2×CH₃), 1.39 (9H, s, 3×CH₃); ¹³C NMR δ (90.6 MHz, CDCl₃) 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 (CH₃), 56.1 (CH₂), 44.7 (CH₃), 28.3 (3×CH₃); m/z (EI) 347 ([⁸¹BrM⁺], 4%), 345 ([⁷⁹BrM⁺], 4), 290 (27), 288 (27), 242 (13), 210 (100); HRMS (EI) Found: [⁷⁹BrM⁺], 345.0570. C₁₄H₂₉⁷⁹BrNO₄ 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), CH₂Cl₂ (10 mL), Et₃N (155 µl, 1.10 mmol) and Boc₂O (176 mg, 0.81 mmol). Flash chromatography (hexane:EtOAc, 10:1) afforded carbamate 16f as a colourless solid (222 mg, 90%). Rᶠ [hex:EtOAc, 3:1] = 0.64; MP 96°C; νmax (CHCl₃)/cm⁻¹ 3346 (NH), 1699 (C=O); ¹H NMR δ (250 MHz, CDCl₃) 8.21 (1H, d, J 8.5, ArH), 7.72 (1H, d, J 7.3, ArH), 7.69 (1H, d, J 8.3,
ArH), 7.53-7.39 (3H, m, 3×ArH), 5.09 (1H, br s, NH2), 4.54 (2H, d, J 6.3, CH3), 1.37 (9H, s, 3×CH3). 13C NMR δ (62.9 MHz, CDCl3) 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 (CH2), 28.3 (3×CH3); m/z (EI) 337 ([81BrM+H]+, 1%), 329 ([79BrM+H]+, 1), 274 (1), 272 (1), 194 (7), 49 (100). HRMS (EI) Found: [79BrM]+, 335.0506. C16H18BrNO2 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 Et3N (1.31 mL, 9.40 mmol) in CH2Cl2 (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 refuxed in toluene (50 mL) at 80°C for 1 h to ensure complete conversion to isocyanate 15. The reaction was then concentrated under reduced pressure and again refuxed at 80°C in 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 cyclohexenyl amine 16g as a colourless oil (1.09 g, 50%). Rf [hexane:EtOAc, 10:1] = 0.21; vmax (CHCl3)/cm⁻¹ 1694 (C=O); 1H NMR δ (360 MHz, 323 K, CDCl3) 7.45 (1H, d, J 7.9, ArH), 7.07 (1H, d, J 7.9, ArH), 5.82-5.80 (1H, m, CH=CH), 5.47 (1H, d, J 10.2, CH=CH), 4.84 (1H, br s, CHN), 4.39-3.4 (2H, m, CH2Ar), 2.30 (3H, s, CH3), 2.04-1.84 (3H, m, CH2+CH3CH2), 1.80-1.68 (1H, m, CH2CH2), 1.65-1.25 (11H, m, CH2+3×CH3); 13C NMR δ (90.6 MHz, CDCl3) 155.6 (C), 155.3 (C), 135.9 (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 (CH2), 28.2 (3×CH3), 28.1 (CH3), 21.3 (CH2), 20.3 (CH3); m/z (FAB, 3-NOBA) 382 ([10BrM+H]+, 12%), 380 ([9BrM+H]+, 15), 326 (100), 324 (100), 185 (96), 183 (97); HRMS (EI) Found: [10BrM]+, 379.1142. C10H16O3Br requires 379.1141.

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, 1.32 mmol) and the reaction stirred at 0°C for 30 mins. The reaction was then cooled to 0°C and 3-bromocyclohexene (2 eq) was added dropwise. The reaction was allowed to warm to r.t. and stirred for 16 h. Et2O (10 mL) was added and the organics washed with NaCl (3×15 mL, sat. aq.). The organics were dried (MgSO4), 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%). Rf [hexane:EtOAc, 10:1] = 0.81; vmax (CHCl3)/cm⁻¹ 1640 (C=O); 1H NMR δ (90.6 MHz, CDCl3) 7.33 (1H, s, ArH), 7.14 (1H, d, J 7.9, ArH), 7.07 (1H, d, J 7.9, ArH), 5.82-5.80 (1H, m, CH=CH), 5.47 (1H, d, J 10.2, CH=CH), 4.84 (1H, br s, CHN), 4.39-3.4 (2H, m, CH2Ar), 2.30 (3H, s, CH3), 2.04-1.84 (3H, m, CH2+CH3CH2), 1.80-1.68 (1H, m, CH2CH2), 1.65-1.25 (11H, m, CH2+3×CH3); 13C NMR δ (90.6 MHz, CDCl3) 155.7 (C), 137.6 (C), 135.9 (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 (CH2), 28.2 (3×CH3), 28.1 (CH3), 21.3 (CH2), 20.3 (CH3); m/z (FAB, 3-NOBA) 382 ([10BrM+H]+, 12%), 380 ([9BrM+H]+, 15), 326 (100), 324 (100), 185 (96), 183 (97); HRMS (EI) Found: [10BrM]+, 379.1142. C10H16O3Br 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%). Rf [hexane:EtOAc, 3:1] = 0.74; vmax (CHCl3)/cm⁻¹ 1694 (C=O); 1H NMR δ (360 MHz, 323 K, CDCl3) 7.45
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:Et3N, 100:5:0.5) afforded cyclohexenyl amine 5e as a colourless oil (81 mg, 84%). Rf [hexane:EtOAc, 3:1] = 0.49; $\nu_{\text{max}}$ (CHCl3)/cm$^{-1}$ 1640 (C=O); ¹H NMR δ (360 MHz, 323 K, CDCl3) 6.97 (1H, s, ArH), 6.82 (1H, s, ArH), 5.85-5.77 (1H, m, CH=CH), 5.44 (1H, d, J = 10.0, CH=CH), 4.80 (1H, br s, CHN), 4.35 (1H, d, J = 16.5, CHH$_2$Ar), 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$_2$H$_2$Ar), 1.74-1.65 (1H, m, CH$_2$H$_2$Ar), 1.65-1.30 (1H, m, CH$_2$=CHCH$_2$); ¹³C NMR δ (90.6 MHz, 323 K, CDCl3) 155.7 (C), 147.4 (C), 132.8 (C), 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 (C), 47.7 (CH$_2$), 28.3 (2×CH$_2$), 24.5 (CH$_2$), 21.3 (CH$_3$); m/z (EI) 398 ([$^{79}$BrM$^{+}$H]$^+$, 7%), 396 ([$^{79}$BrM$^{+}$H]$^+$, 9), 342 (100), 340 (100), 260 (100), 201 (41), 199 (42); HRMS (EI) Found: [M$^{+}$]$^+$, 395.1090. C$_{19}$H$_{26}^{79}$BrNO$_2$ requires 395.1090.

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 mg, 0.98 mmol). Flash chromatography (hexane:EtOAc, 100:1) afforded cyclohexenyl amine 5f as a colourless oil (175 mg, 86%). Rf [hexane:EtOAc, 3:1] = 0.80; $\nu_{\text{max}}$ (CHCl3)/cm$^{-1}$ 1652 (C=O); ¹H NMR δ (360 MHz, 323 K, CDCl3) 8.33 (1H, d, J = 8.7, ArH), 7.82 (1H, d, J = 7.4, ArH), 7.80 (1H, d, J = 8.4, ArH), 7.58 (1H, t, J = 6.9, ArH), 7.48 (1H, d, J = 8.3, ArH, 7.32, 7.1, 1.2, ArH), 7.43 (1H, d, J = 8.6, ArH), 5.83 (1H, br s, CH=CH), 5.52 (1H, d, J = 10.0, CH=CH), 4.95 (1H, br s, CHN), 4.66 (2H, br s, CH$_2$Ar), 2.10-1.88 (3H, m, CH$_3$CH$_2$H$_2$Ar), 1.80-1.71 (1H, m, CH$_2$H$_2$Ar), 1.70-1.30 (1H, m, CH$_2$=CHCH$_2$); ¹³C NMR δ (90.6 MHz, 323 K, CDCl3) 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$_2$), 24.5 (CH$_2$), 21.3 (CH$_3$); m/z (FAB, 3-NOBA) 428 ([$^{79}$BrM$^{+}$H]$^+$, 6%), 426 ([$^{79}$BrM$^{+}$H]$^+$, 9), 372 (34), 370 (40), 346 (16), 326 (10), 290 (100), 231 (100), 229 (100); HRMS (EI) Found: [M$^{+}$]$^+$, 426.1268. C$_{23}$H$_{29}^{79}$BrNO$_2$ requires 426.1275.

(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%). Rf [hexane:EtOAc, 3:1] = 0.69; $\nu_{\text{max}}$ (CHCl3)/cm$^{-1}$ 1693 (C=O); ¹H NMR δ (360 MHz, 323 K, CDCl3) 6.95 (1H, s, ArH), 6.78 (1H, s, ArH), 5.93 (2H, s, OCH$_2$O), 5.83-5.81 (1H, m, CH=CH), 5.45 (1H, br d, J = 10.2, CH=CH), 4.76 (1H, br s, CHN), 4.34-4.15 (2H, m, CH$_2$Ar), 2.01-1.97 (2H, m, CH$_3$), 1.90-1.88 (1H, m, CH$_2$H$_2$Ar), 1.75-1.73 (1H, m, CH$_2$H$_2$Ar), 1.63-1.59 (2H, m, CH$_2$), 1.44-1.41 (9H, s, 3×CH$_3$); ¹³C NMR δ (90.6 MHz, 323 K, CDCl3) 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$_2$), 90.6 (C).
General Procedures for Heck cyclisations\textsuperscript{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 MeNC\textsubscript{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\textsubscript{2}O (20 mL) and washed with NaCl (3 \times 20 mL, sat. aq.). The organics were combined, dried (MgSO\textsubscript{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 MeNC\textsubscript{2} (4 eq) in MeCN was added Pd\textsubscript{2}(dba)\textsubscript{3} (5 mol\%) and tBu\textsubscript{3}PHBF\textsubscript{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\textsubscript{2}O (20 mL) and washed with NaCl (3 \times 20 mL, sat. aq.). The organics were combined, dried (MgSO\textsubscript{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\textsuperscript{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 \mu mol) and MeNC\textsubscript{2} (245 \mu l, 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\%). \textsuperscript{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 \mu mol) and MeNC\textsubscript{2} (236 \mu l, 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\%). \textsuperscript{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 \mu mol) and MeNC\textsubscript{2} (100 \mu l, 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\%). \textsuperscript{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 \mu mol) and MeNC\textsubscript{2} (224 \mu l, 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\%). \textsuperscript{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, 0.59 μmol), Herrmann-Beller palladacycle (3 mg, 3.0 μmol), MeNC2 (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%). ¹H 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), Pd₂{(dbp)₃} (9.6 mg, 0.11 μmol), P(Bu)₂HBF₄ (6.1 mg, 21 μmol) and MeNC2 (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%). ¹H 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), Pd₂{(dbp)₃} (94 mg, 0.10 mmol), P(Bu)₂HBF₄ (56 mg, 0.21 mmol) and MeNC2 (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%). ¹H NMR of this oil showed it to be a 37:39:24 mixture of double bond isomers (6g:7g:8g).

(4aSR,10bSR)-9-Methyl-4,4a,6,10b-tetrahydro-3H-phenanthridine-5-carboxylic acid tert-butyl ester 6b (Δ³⁻² isomer)

Rₜ [hexane:EtOAc, 10:1] = 0.46; MP 105°C; v_max (CHCl₃) cm⁻¹ 1692 (C=O); ¹H NMR δ (360 MHz, 323 K, CDCl₃) 7.11 (1H, d, ArH), 7.00 (2H, m, 2×ArH), 6.18-6.12 (1H, m, CHCH=CH), 5.88-5.83 (1H, m, CH=CHCH₂), 4.68 (1H, d, J 16.3, CH₂H₂Ar), 4.41 (1H, br s, NCHCH), 4.35 (1H, d, J 16.3, CH₂H₂Ar), 3.54 (1H, br s, NCHCH), 2.34 (3H, s, CH₃), 2.29-2.16 (1H, m, CH₂H₂), 2.15-2.05 (1H, m, CH₃H₂), 1.74-1.69 (1H, m, CH₃H₂), 1.61-1.50 (10H, m, 3×CH₂+CH₃H₂); ¹³C NMR δ (90.0 MHz, 323 K, CDCl₃) 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 (CH₂), 37.2 (CH), 28.5 (CH₂), 28.5 (3×CH₂), 25.3 (CH₂), 21.1 (CH₃); m/z (EI) [M⁺]¹, 3% 442 (100), 198 (15), 189 (26), 144 (11); HRMS (EI) Found: [M⁺] ²99.1880. C₁₉H₂₅NO₂ requires 299.1880.

Diagnostic ¹H NMR data for 7b (Δ³⁻² isomer) ¹H NMR δ (360 MHz, 323 K, CDCl₃) 7.04 (3H, m, 3×ArH), 5.70-5.66 (1H, m, CH=CH), 5.45-5.40 (1H, m, CH=CH), 4.55 (1H, d, J 16.2, CH₂H₂), 4.48 (1H, d, J 16.2, CH₂H₂), 4.43 (1H, br s, NCHCH), 3.18 (1H, br s, NCHCH), 2.86 (1H, dd, J 18.1, 4.9, CH₂H₂), 2.63-2.56 (1H, m, CH₃H₂), 2.35 (3H, s, CH₃), 2.24-2.19 (1H, m, CH₃H₂), 1.57-1.48 (10H, m, CH₃H₂+3×CH₃). Diagnostic ¹H NMR data for 8b (Δ³⁻⁴ isomer) ¹H NMR δ (360 MHz, 323 K, CDCl₃) 7.50-5.68 (1H, m, CH=CH), 5.53 (1H, dd, J 8.5, CH=CH), 5.06 (1H, br s, NCHCH), 4.82 (1H, d, J 16.7, CH₂H₂), 4.21 (1H, d, J 16.7, CH₂H₂), 3.26 (1H, br s, NCHCH), 2.10-1.95 (1H, m, CH₂H₂), 1.89-1.79 (1H, m, CH₂H₂).

(4aSR,10bSR)-8-Methoxy-4,4a,6,10b-tetrahydro-3H-phenanthridine-5-carboxylic acid tert-butyl ester 6d (Δ³⁻²⁻² isomer)

Rₜ [hexane:EtOAc, 3:1] = 0.71; v_max (CHCl₃) cm⁻¹ 1691 (C=O); ¹H NMR δ (360 MHz, 323 K, CDCl₃) 7.19 (1H, d, J 8.5, ArH), 6.79 (1H, dd, J 8.5, 2.7, ArH), 6.66 (1H, d, J 2.7, ArH), 6.14-6.09 (1H, m, CH=CHCH₂), 5.84-5.80 (1H, m, CH=CHCH₂), 4.69 (1H, d, J 16.6, CH₂H₂Ar), 4.34 (1H, br s, NCHCH), 4.30 (1H, d, J 16.6, CH₂H₂Ar), 3.79 (3H, s, CH₃), 3.51 (1H, br s, NCHCH), 2.27-2.16 (1H, m, CH₂H₂), 2.12-2.04 (1H, m, CH₂H₂), 1.74-1.65 (1H, m, CH₂H₂), 1.58-1.47 (10H, m, CH₂H₂+3×CH₃); ¹³C NMR δ (90.0 MHz, 323 K, CDCl₃) 157.9 (C), 154.9 (C), 150.0 (C), 128.5 (CH), 128.0 (CH), 127.6 (CH), 125.4 (CH), 113.0 (CH), 111.1 (CH), 79.6 (C), 55.2 (CH₃), 50.5 (CH), 43.7 (CH₂), 36.6 (CH), 28.6 (3×CH₂), 26.5 (CH₂), 25.3 (CH₃); m/z (EI) [M⁺]¹, 2% 315.1831. C₁₉H₂₅NO₂ requires 315.1829. Diagnostic ¹H NMR data for 7d (Δ³⁻²⁻² isomer) ¹H NMR δ (360 MHz, 323 K, CDCl₃) 7.14 (1H, d, J 8.6, ArH), 6.73 (1H, d, J 7.2, ArH), 5.70-5.62 (1H, m, CH=CH), 5.44-5.40 (1H, m, CH=CH), 4.52 (3H, s, CH₂Ar), 3.15 (1H, br s, NCHCH), 2.81 (1H, dd, J 22.9, 4.7, CH₂H₂), 2.62-2.54 (1H, m, CH₂H₂). Diagnostic ¹H NMR data for 8d (Δ³⁻⁴⁻²⁻² isomer)
(4aSR,10bSR)-8,9-Dimethoxy-4,4a,6,10b-tetrahydro-3H-phenanthridine-5-carboxylic acid tert-butyl ester 6e (Δ12 isomer)

\[ \text{R}_t \{\text{hexane:EtOAc, 3:1}\} = 0.44; \text{ MP} 124^\circ \text{C}; \nu_{\text{max}} (\text{CHCl}_3)/\text{cm}^{-1} 1692 (\text{C}=\text{O}); ^1\text{H NMR} \delta (360 \text{ MHz, 323 K, CDCl}_3) 7.67 (1\text{H}, d, J 8.6, \text{ArH}), 6.60 (1\text{H}, s, \text{ArH}), 5.51 (1\text{H}, d, J 10.2, \text{CH}=\text{CH}), 5.05 (1\text{H}, br s, NCH), 4.83 (1\text{H}, d, J 17.1, \text{CH}_3\text{H}_3\text{H}), 4.22 (1\text{H}, d, J 17.1, \text{CH}_3\text{H}_3\text{H}), 3.24 (1\text{H}, br s, NCHCH).\]

(4aSR,12cSR)-4,4a,6,12c-Tetrahydro-3H-benzol[4,5]phenanthridine-5-carboxylic acid tert-butyl ester 6f (Δ12 isomer)

\[ \text{R}_t \{\text{hexane:EtOAc, 3:1}\} = 0.80; \nu_{\text{max}} (\text{CHCl}_3)/\text{cm}^{-1} 1688 (\text{C}=\text{O}); ^1\text{H NMR} \delta (360 \text{ MHz, 323 K, CDCl}_3) 8.08 (1\text{H}, d, J 8.4, \text{ArH}), 7.87 (1\text{H}, dd, J 8.1, 0.7, \text{ArH}), 7.71 (1\text{H}, d, J 8.3, \text{ArH}), 7.55 (1\text{H}, ddd, J 8.3, 6.8, 1.4, \text{ArH}), 7.48 (1\text{H}, ddd, J 8.1, 6.8, 1.3, \text{ArH}), 7.29 (1\text{H}, d, J 8.3, \text{ArH}), 5.97-5.92 (1\text{H}, m, \text{CH} = \text{CH}), 5.43 (1\text{H}, ddd, J 9.9, 1.6, 0.8, \text{CH} = \text{CH}), 5.11 (1\text{H}, d, J 15.1, \text{CH}_3\text{H}_3\text{H}), 4.62-4.59 (1\text{H}, m, \text{CH(CH)=CH}), 4.29-4.26 (1\text{H}, m, \text{NCH}), 4.23 (1\text{H}, d, J 15.1, \text{CH}_3\text{H}_3\text{H}), 2.56-2.21 (1\text{H}, m, \text{CH}_3\text{H}_3\text{H}), 2.37-2.25 (1\text{H}, m, \text{CH}_3\text{H}_3\text{H}), 2.17-2.07 (1\text{H}, m, \text{CH}_3\text{H}_3\text{H}), 1.97-1.84 (1\text{H}, ddd, J 13.6, 11.3, 3.2, 2.5, 2.5, \text{CH}_3\text{H}_3\text{H}), 1.49 (9\text{H}, m, 3\times \text{CH}_3); ^13\text{C NMR} \delta (90.6 \text{ MHz, 323 K, CDCl}_3) 155.2 (\text{C}), 133.7 (\text{C}), 133.4 (\text{C}), 130.6 (2\times \text{C}), 129.2 (\text{CH}), 129.0 (\text{CH}), 126.8 (\text{CH}), 126.6 (\text{CH}), 126.2 (\text{CH}), 125.1 (\text{CH}), 124.7 (\text{CH}), 122.4 (\text{CH}), 79.6 (\text{C}), 49.8 (\text{CH}), 45.2 (\text{CH}), 35.2 (\text{CH}), 28.5 (3\times \text{CH}_3), 26.9 (\text{CH}_3), 20.6 (\text{CH}_2); \nu_{\text{max}} (\text{FAB, 3-NBA}) 346 ([M]+, 26%), 289 (100), 244 (82), 216 (36), 190 (52); \nu_{\text{HRMS}} (\text{FAB, 3-NBA}) \text{ Found: [M]+} 346.17, 343.16. \nu_{\text{HRMS}} \text{ for 7f (Δ13 isomer) } ^1\text{H NMR} \delta (360 \text{ MHz, 323 K, CDCl}_3) 8.03 (1\text{H}, d, J 8.4, \text{ArH}), 6.66 (1\text{H}, s, \text{ArH}), 5.67-5.63 (1\text{H}, m, \text{CH} = \text{CH}), 5.44-5.40 (1\text{H}, m, \text{CH} = \text{CH}), 4.46 (2\text{H}, m, \text{CH}_3\text{H}_3\text{H}), 3.13 (1\text{H}, br s, \text{NCHCH}), 2.77-2.73 (1\text{H}, m, \text{CH}_3\text{H}_3\text{H}), 2.61-2.56 (1\text{H}, m, \text{CH}_3\text{H}_3\text{H}); \nu_{\text{HRMS}} \text{ for 8e (Δ14 isomer) } ^1\text{H NMR} \delta (360 \text{ MHz, 323 K, CDCl}_3) 6.82 (1\text{H}, s, \text{ArH}), 6.53 (1\text{H}, s, \text{ArH}), 5.72-5.66 (1\text{H}, m, \text{CH} = \text{CH}), 5.48 (1\text{H}, dd, J 10.1, \text{CH} = \text{CH}), 5.03 (1\text{H}, br s, \text{NCH}), 4.75 (1\text{H}, d, J 16.5, \text{CH}_3\text{H}_3\text{H}), 4.13 (1\text{H}, d, J 16.5, \text{CH}_3\text{H}_3\text{H}), 3.21 (1\text{H}, br s, \text{NCHCH}).\]

(4aSR,11bSR)-4,4a,6,11b-Tetrahydro-3H-[1,3]dioxolo[4,5-j]phenanthridine-5-carboxylic acid tert-butyl ester 6g (Δ12 isomer)

\[ \text{R}_t \{\text{hexane:EtOAc, 3:1}\} = 0.65; \nu_{\text{max}} (\text{CHCl}_3)/\text{cm}^{-1} 1692 (\text{C}=\text{O}); ^1\text{H NMR} \delta (360 \text{ MHz, 323 K, CDCl}_3) 6.77 (1\text{H}, s, \text{ArH}), 6.59 (1\text{H}, s, \text{ArH}), 6.08-6.03 (1\text{H}, m, \text{CH} = \text{CH}), 5.92 (2\text{H}, s, \text{OCH}_2\text{O}), 5.86-5.83 (1\text{H}, m, \text{CH} = \text{CH}), 4.58 (1\text{H}, d, J 16.2, \text{CH}_3\text{H}_3\text{H}), 4.36 (1\text{H}, br s, \text{CHCHCH}), 4.29 (1\text{H}, d, J 16.2, \text{CH}_3\text{H}_3\text{H}), 3.46 (1\text{H}, m, \text{NCH}), 2.62-2.19 (1\text{H}, m, \text{CH}_3\text{H}_3\text{H}), 2.16-2.12 (1\text{H}, m, \text{CH}_3\text{H}_3\text{H}), 2.72-1.68 (1\text{H}, m, \text{CH}_3\text{H}_3\text{H}), 1.60-1.55 (1\text{H}, m, \text{CH}_3\text{H}_3\text{H}), 1.51 (1\text{H}, s, 3\times \text{CH}_3); ^13\text{C NMR} \delta (90.6 \text{ MHz, 323 K, CDCl}_3) 154.9 (\text{C}), 146.7 (\text{C}), 145.8 (\text{C}), 131.0 (\text{C}), 128.5 (\text{CH}), 127.2 (\text{CH}), 125.7
(C), 107.7 (CH), 106.2 (CH), 100.7 (CH2), 79.6 (C), 43.6 (CH2), 37.1 (CH), 28.5 (3×CH3), 25.3 (CH2), 24.1 (CH); m/z (EI) 329 ([M]+, 1%), 272, (100); HRMS (EI) Found: [M]+, 329.1621. C19H25O4N requires 329.1622.

Diagnostic 1H NMR data for 7g (A2 3 isomer) 1H NMR δ (360 MHz, 323 K, CDCl3) 6.74 (1H, s, ArH), 6.82 (1H, s, ArH), 5.92 (2H, s, OCH2O), 5.69-5.65 (1H, m, CH=C), 5.47-5.42 (1H, m, CH=CH), 4.41 (2H, s, CH2Ar), 3.10 (1H, br s, NCH), 2.72 (1H, dd, J 18.3, 4.9, CH2), 2.63-2.56 (1H, m, CH2), 2.25-2.20 (1H, m, CH2), 1.63-1.55 (1H, m, CH2), 1.52 (9H, s, 3×CH3). Diagnostic 1H NMR data for 8g (A3 4 isomer) 1H NMR δ (360 MHz, 323 K, CDCl3) 6.52 (1H, s, ArH), 5.90 (2H, s, OCH2O), 5.73-5.70 (1H, m, CH=CH), 5.52-5.48 (1H, m, CH=CH), 5.02 (1H, m, NCH), 4.74 (1H, d, J 16.5, ArCH2), 4.13 (1H, d, J 16.5, ArCH2), 3.20 (1H, s, ArH), 2.72-2.56 (1H, m, CHA).Diagnostic 1H NMR data for 6g (360 MHz, 323 K, CDCl3) 6.77 (1H, br s, ArH), 5.93 (2H, s, OCH2O), 5.82-5.80 (1H, m, CH=C), 5.49 (1H, d, J 10.2, CH=CH), 4.71 (1H, br s, CH2N), 4.34 (1H, d, J 16.0, CH2), 4.20 (1H, d, J 16.0, CH2), 1.99-1.97 (2H, m, CH2), 1.90-1.82 (1H, m, CH2), 1.79-1.71 (1H, m, CH2), 1.66-1.43 (11H, m, CH3×3×CH3); 13C NMR δ (90.6 MHz, 323 K, CDCl3) 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 (CH2), 79.6 (C), 53.3 (CH), 47.3 (CH2), 28.4 (3×CH3), 28.1 (CH2), 24.6 (CH2), 21.5 (CH2); m/z (EI) 331 ([M]+, 13%), 275 (38), 194 (100), 150 (14), 140 (14), 136 (28), 135 (46); HRMS (EI) Found: [M]+, 331.1775. C19H25O4N requires 331.1778.

**General procedure G - Dihydroxylation**

To a solution of the appropriate phenanthridines (1 eq) in THF and H2O at rt was added OsO4 (0.07 eq, 2.5% w/w in BuOH) and NMO (3 eq) and the reaction was stirred for 16 h. The reaction mixture was poured onto Na2SO4 (30 mL, sat. aq.) and extracted with EtOAc (3×30 mL). The combined organics were dried (MgSO4), concentrated under reduced pressure and purified to afford the appropriate diol 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-1H-phenanthridine-5-carboxylic acid tert-butyl ester 17-19a**

General procedure G was followed using phenanthridines 6-8a (200 mg, 0.70 mmol), THF (3.92 mL), H2O (785 µl), OsO4 (613 µl, 2.5% w/w in BuOH, 49.1 µmol) and NMO (329 mg, 2.81 mmol). Flash chromatography (CH2Cl2-CH2Cl2: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 Δ1 2 diol 17a (29 mg, 13%), Δ2 3 diol 18a (25 mg, 11%), Δ3 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-1H-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), H2O (820 µl), OsO4 (247 µl, 2.5% w/w in BuOH, 19.7 µmol) and NMO (132 mg, 0.846 mmol). Flash chromatography (CH2Cl2-CH2Cl2: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. \( R_f \) [CH\(_2\)Cl\(_2\):MeOH, 9:1] = 0.57; \( \nu_{\text{max}} \) (CHCl\(_3\))/cm\(^{-1}\) 3421 (OH), 1664 (C=O); \( m/z \) (EI) 319 ([M]+, 2%), 262 ([M-'Bu]+, 100), 218 ([M-Boc]+, 22), 184 (75).

Dihydroxy-8-methoxy-2,3,4a,6,10b-hexahydro-1\( \text{H} \)-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\(_2\)O (541 \( \mu \)l), OsO\(_4\) (423 \( \mu \)l, 2.5% w/w in 'BuOH, 33.8 \( \mu \)mol) and NMO (226 mg, 1.93 mmol). Flash chromatography (CH\(_2\)Cl\(_2\):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\( \text{H} \)-phenanthridine-5-carboxylic acid tert-butyl ester 17-19e

General procedure G was followed using phenanthridines 6-8e (30 mg, 87 \( \mu \)mol), THF (488 \( \mu \)l), H\(_2\)O (98 \( \mu \)l), OsO\(_4\) (76 \( \mu \)l, 2.5% w/w in 'BuOH, 6.1 \( \mu \)mol) and NMO (31 mg, 0.26 mmol). Flash chromatography (CH\(_2\)Cl\(_2\):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\( \text{H} \)-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\(_2\)O (434 \( \mu \)l), OsO\(_4\) (338 \( \mu \)l, 2.5% w/w in 'BuOH, 27.1 \( \mu \)mol) and NMO (136 mg, 1.16 mmol). Flash chromatography (CH\(_2\)Cl\(_2\):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\( \text{H} \)-[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\(_2\)O (531 \( \mu \)l), OsO\(_4\) (332 \( \mu \)l, 2.5% w/w in 'BuOH, 26.6 \( \mu \)mol) and NMO (133 mg, 1.14 mmol). Flash chromatography (CH\(_2\)Cl\(_2\):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%), \( \Delta^{3,6} \) endo syn diol minor diastereomer (3 mg, 2%) and mixed diol (48 mg, 35%) giving a total yield (120 mg, 87%).
(1S,2S,4aSR,10bSR)-1,2-Dihydroxy-2,3,4,4a,6,10b-hexahydro-1H-phenanthridine-5-carboxylic acid tert-buty1 ester 17a (Δ1,2 isomer)

Rf [CH2Cl2:MeOH, 9:1] = 0.57; Rf (EtOAc:hexane, 3:1, flow rate: 8 mL min⁻¹) = 28 min; v_{max} (CHCl₃) cm⁻¹ = 3414 (OH), 1671 (C=O); ¹H NMR δ (360 MHz, 323 K, CDCl₃) 7.47 (1H, d, J = 7.6, ArH), 7.27-7.20 (2H, m, 2×ArH), 7.12 (1H, d, J = 6.8, ArH), 4.78-4.72 (1H, m, CHNBoc), 4.71 (1H, d, J = 17.3, CH₂H₂Ar), 4.36 (1H, d, J = 17.3, CH₂Ar), 3.92 (1H, m, CHOH), 3.64 (1H, dt, J = 12.0, 3.9, CHOH), 3.26 (1H, br s, CHTAr), 2.49 (1H, dt, J = 13.6, 3.1, CH₂HTAr), 2.25 (1H, ddd, J = 13.6, 12.0, 4.8, CH₂HTB), 1.94-1.87 (1H, m, CH₂HTB+3×CH₂); ¹³C NMR δ (90.6 MHz, 323 K, CDCl₃) 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 (CH₂), 28.4 (3×CH₂), 27.4 (CH₂), 24.2 (CH₂); m/z (EI) 319 ([M]+, 2%), 262 ([M⁺-Bu]+), 100, 218 ([M⁺-Boc]+), 22, 184 (75). This compound was also fully characterised by COSY, HSQC and NOESY 2D NMR studies.

(2RS,3SR,4aSR,10bSR)-2,3-Dihydroxy-2,3,4,4a,6,10b-hexahydro-1H-phenanthridine-5-carboxylic acid tert-buty1 ester 18a (Δ3 isomer)

Rf [CH2Cl2:MeOH, 9:1] = 0.52; Rf (EtOAc:hexane, 3:1, flow rate: 8 mL min⁻¹) = 28 min; v_{max} (CHCl₃) cm⁻¹ = 3414 (OH), 1671 (C=O); ¹H NMR δ (360 MHz, 323 K, CDCl₃) 7.47 (1H, d, J = 7.6, ArH), 7.27-7.20 (2H, m, 2×ArH), 7.12 (1H, d, J = 6.8, ArH), 4.78-4.72 (1H, m, CHNBoc), 4.71 (1H, d, J = 17.3, CH₂H₂Ar), 4.36 (1H, d, J = 17.3, CH₂Ar), 3.92 (1H, m, CHOH), 3.64 (1H, dt, J = 12.0, 3.9, CHOH), 3.26 (1H, br s, CHTAr), 2.49 (1H, dt, J = 13.6, 3.1, CH₂HTAr), 2.25 (1H, ddd, J = 13.6, 12.0, 4.8, CH₂HTB), 1.94-1.87 (1H, m, CH₂HTB+3×CH₂); ¹³C NMR δ (90.6 MHz, 323 K, CDCl₃) 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 (CH₂), 28.4 (3×CH₂), 27.4 (CH₂), 24.2 (CH₂); m/z (EI) 319 ([M]+, 1%), 263 ([M⁺-Bu]+), 27, 262 (80), 218 ([M⁺-Boc]+), 25, 200 (27), 174 (36), 146 (25), 144 (48); HRMS (EI) Found: [M]+, 319.1780. C₁₈H₂₅O₄N requires 319.1778.

(3RS,4SR,4aRS,10bSR)-3,4-Dihydroxy-2,3,4,4a,6,10b-hexahydro-1H-phenanthridine-5-carboxylic acid tert-buty1 ester 19a (Δ3,4 isomer)

Rf [CH2Cl2:MeOH, 9:1] = 0.58; Rf (EtOAc:hexane, 3:1, flow rate: 8 mL min⁻¹) = 21 min; v_{max} (CHCl₃) cm⁻¹ = 3394 (OH), 1668 (C=O); ¹H NMR δ (360 MHz, 323 K, CDCl₃) 7.33 (1H, d, J = 7.5, ArH), 7.27-7.19 (2H, m, 2×ArH), 7.14 (1H, d, J = 7.1, ArH), 4.80-4.66 (2H, m, CHNBoc+CH₂H₂Ar), 4.44 (1H, d, J = 17.0, CH₂H₂Ar), 3.94 (1H, dd, J = 5.9, 2.9, CHOH), 3.31-3.29 (2H, m, CHAr+CHOH), 2.29-2.24 (2H, m, CH₂), 1.85-1.80 (1H, m, CH₂HTB), 1.58-1.52 (10H, m, CH₂HTB+3×CH₂); ¹³C NMR δ (90.6 MHz, 323 K, CDCl₃) 156.7 (C), 134.6 (C), 133.3 (C), 126.9 (CH), 126.5 (CH), 125.6 (CH), 80.8 (C), 69.6 (2×CH), 53.1 (CH), 43.9 (CH₂), 36.9 (CH), 28.4 (3×CH₂), 25.4 (CH₂), 20.0 (CH₂); m/z (EI) 319 ([M]+, 1%), 263 ([M⁺-Bu]+), 27, 233 (7), 218 ([M⁺-Boc]+), 25. This compound was also fully characterised by COSY, HSQC and NOESY 2D NMR studies.

(1RS,2SR,4aSR,10bSR)-1,2-Dihydroxy-8-methoxy-2,3,4,4a,6,10b-hexahydro-1H-phenanthridine-5-carboxylic acid tert-buty1 ester 17d (Δ1,2 isomer)

Rf [CH2Cl2:MeOH, 9:1] = 0.49; Rf (EtOAc:hexane, 4:1, flow rate: 10 mL min⁻¹) = 21 min; v_{max} (CHCl₃) cm⁻¹ = 3423 (OH), 1687 (C=O); ¹H NMR δ (360 MHz, 323 K, CDCl₃) 7.24 (1H, d, J = 8.6, ArH), 6.78 (1H, dd, J = 8.6, 2.7, ArH), 6.68 (1H, d, J = 2.7, ArH), 4.72-4.63 (3H, m, 2×CH=CH₂H₂Ar), 4.30 (1H, d, J = 17.1, CH₂H₂Ar), 3.80 (3H, s, CH₃), 3.75-3.69 (1H, m, CH₂), 3.35 (1H, br s, CH), 2.60 (1H, br s, CH₂), 1.93-1.87 (1H, m, CH₂HTB), 1.69-1.64 (1H, m, CH₂HTB), 1.57-1.41 (11H, m, CH₂=3×CH₂); ¹³C NMR δ (62.9 MHz, CDCl₃) 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 (CH3), 46.8 (CH), 43.5 (CH2), 42.0 (CH), 28.4 (3×CH3), 27.3 (CH2), 23.9 (CH3); m/z (EI) 349 ([M]+, 4%), 292 ([M-Boc]+), 27, 248 ([M-Boc]+), 21, 174 (22).

(2RS,3SR,4aSR,10bSR)-2,3-Dihydroxy-8-methoxy-2,3,4,4a,6,10b-hexahydro-1H-phenanthridine-5-carboxylic acid tert-butyl ester 18d (Δ13 isomer)

Rf [CH2Cl2:MeOH, 9:1] = 0.49; Rf (EtOAc:hexane, 4:1, flow rate: 10 mL min-1) = 24 min; vmax (CHCl3)/cm-1 3392 (OH), 1672 (C=O); 1H NMR δ (360 MHz, CDCl3) 7.37 (1H, d, J 8.5, ArH), 6.82 (1H, dd, J 8.5, 2.7, ArH), 6.67 (1H, d, J 2.6, ArH), 4.76-4.67 (2H, m, CH=CH2H3Ar), 4.31 (1H, d, J 17.4, CH2H3Ar), 3.92 (1H, d, J 3.1, CH), 3.81 (3H, s, CH3), 3.66-3.61 (1H, m, CH), 3.21 (1H, m, CH2), 2.45-2.42 (1H, m, CH3H6), 2.26-2.17 (1H, m, CH3H6), 1.91-1.86 (1H, m, CH3H6), 1.60-1.48 (10H, m, CH3H6+3×CH3); 13C NMR δ (90.6 MHz, 323 K, CDCl3) 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 (CH3), 46.5 (CH), 43.7 (CH2), 35.7 (CH), 31.3 (CH2), 29.5 (CH2), 28.5 (3×CH3); m/z (EI) 349 ([M]+, 5%), 292 ([M-Boc]+), 38, 248 ([M-Boc]+), 37, 204 (35), 174 (40), 160 (33).

(3RS,4SR,4aRS,10bSR)-3,4-Dihydroxy-8-methoxy-2,3,4,4a,6,10b-hexahydro-1H-phenanthridine-5-carboxylic acid tert-butyl ester 19d (Δ14 isomer)

Rf [CH2Cl2:MeOH, 9:1] = 0.49; Rf (EtOAc:hexane, 4:1, flow rate: 10 mL min-1) = 17 min; vmax (CHCl3)/cm-1 3392 (OH), 1668 (C=O); 1H NMR δ (360 MHz, CDCl3) 7.23 (1H, d, J 8.6, ArH), 6.82 (1H, dd, J 8.6, 2.7, ArH), 6.69 (1H, d, J 2.7, ArH), 4.80-4.62 (2H, m, CH=CH2H3Ar), 4.41 (1H, d, J 16.7, CH2H3Ar), 3.94 (1H, d, J 2.8, CH), 3.81 (3H, s, CH3), 3.34-3.31 (1H, m, CH), 3.24-3.22 (1H, m, CH), 2.23-2.21 (1H, m, CH3H6), 1.85-1.80 (1H, m, CH3H6), 1.57-1.52 (10H, s, CH3H6+3×CH3), 1.43-1.39 (1H, m, CH3H6); 13C NMR δ (90.6 MHz, 323 K, CDCl3) 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 (CH3), 53.3 (CH), 46.8 (CH2), 36.2 (CH), 28.4 (3×CH3), 25.3 (CH2), 20.1 (CH2); m/z (EI) 349 ([M]+, 21%), 292 ([M-Boc]+), 100, 257 (56), 248 ([M-Boc]+), 33, 230 (61), 204 (55).

(1RS,2SR,4aSR,10bSR)-1,2-Dihydroxy-8,9-dimethoxy-2,3,4,4a,6,10b-hexahydro-1H-phenanthridine-5-carboxylic acid tert-butyl ester 17e (Δ12 isomer)

Rf [CH2Cl2:MeOH, 9:1] = 0.48; Rf (EtOAc:hexane, 84:16, flow rate: 10 mL min-1) = 38 min; vmax (CHCl3)/cm-1 3423 (OH), 1670 (C=O), 1520, 1406; 1H NMR δ (360 MHz, CDCl3) 6.83 (1H, s, ArH), 6.61 (1H, s, ArH), 4.70-4.64 (3H, m, 2×CH=CH2H3Ar), 4.24 (1H, d, J 16.8, CH2H3Ar), 3.87 (6H, s, 2×CH3), 3.70-3.67 (1H, m, CH), 3.34 (1H, br s, CH), 1.93-1.89 (1H, m, CH3H6), 1.67-1.61 (2H, m, CH3H6+CH2H3), 1.53-1.45 (10H, m, CH3H6+3×CH3); 13C NMR δ (90.6 MHz, CDCl3) 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 (CH3), 55.8 (CH3), 46.7 (CH), 42.9 (CH2), 42.2 (CH), 28.4 (3×CH3), 27.2 (CH2), 23.8 (CH2); m/z (EI) 379 ([M]+, 2%), 322 ([M-Boc]+), 100), 278 ([M-Boc]+), 6).
NMR Data for Δ2,3 isomer 18e was deduced from 1H and 13C NMR of 17e and 18e mixture. Rf [9: 1 CH2Cl2:MeOH] = 0.48; Rf (EtOAc:hexane, 84:16, flow rate: 10 ml min⁻¹) = 38 min; νmax (CHCl3)/cm⁻¹ 3425 (OH), 1664 (C=O); 1H NMR δ (360 MHz, CDCl3) 6.94 (1H, s, ArH), 6.60 (1H, s, ArH), 4.75-6.63 (2H, m, CH=CH₂ArH₃), 4.25 (1H, d, J 16.8, CH₃H₂Ar), 3.94 (1H, br s, CH₃), 3.89 (3H, s, CH₃), 3.87 (3H, s, CH₃), 3.63-3.60 (1H, m, CH₃), 3.20 (1H, br s, CH₃), 2.43-2.40 (1H, m, CH₃CH₂), 2.28-2.19 (1H, m, CH₃CH₂), 1.89-1.85 (1H, m, CH₃CH₂), 1.66-1.61 (1H, m, CH₃CH₂), 1.50 (9H, m, 3×CH₃); 13C NMR δ (90.6 MHz, CDCl₃) 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 (CH₃), 55.8 (CH₃), 45.0 (CH), 42.9 (CH₃), 35.7 (CH), 31.1 (CH₃), 29.6 (CH₂), 28.4 (3×CH₃); m/z (EI) 379 ([M]+, 2%), 322 ([M-Bu]+, 100), 278 ([M-Boc]+, 38), 190 (10).

Rf [9: 1 CH2Cl2:MeOH] = 0.51; Rf (EtOAc:hexane, 84:16, flow rate: 10 ml min⁻¹) = 23 min; νmax (CHCl₃)/cm⁻¹ 3404 (OH), 1668 (C=O); 1H NMR δ (250 MHz, CDCl₃) 6.80 (1H, s, ArH), 6.63 (1H, s, ArH), 4.66-4.60 (2H, m, CH=CH₂ArH₃), 4.37 (1H, d, J 16.8, CH₃H₂Ar), 3.96 (1H, br s, CH₃), 3.88 (3H, s, OCH₃), 3.87 (3H, s, OCH₃), 3.35-3.31 (1H, m, CH₃), 3.22 (1H, br s, CH₃), 2.26-2.13 (1H, m, CH₂), 1.86-1.78 (1H, m, CH₃CH₂), 1.53-1.42 (10H, m, CH₃H₃+3×CH₃); 13C NMR δ (62.9 MHz, CDCl₃) 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 (C), 56.0 (CH), 55.9 (CH₃), 52.7 (CH), 43.9 (CH₂), 36.3 (CH), 28.4 (3×CH₃), 25.4 (CH₂), 20.2 (CH₂); m/z (EI) 379 ([M]+, 1%), 278 ([M-Boc]+, 10), 199 (46), 84 (100).

Rf [CH2Cl2:MeOH; 9:1] = 0.65; νmax (CHCl₃)/cm⁻¹ 3418 (OH), 1668 (C=O); 1H NMR δ (360 MHz, 323 K, CDCl₃) 8.08 (1H, d, J 8.5, ArH), 7.85 (1H, d, J 7.9, ArH), 7.70 (1H, d, J 8.3, ArH), 7.54 (1H, t, J 7.9, ArH), 7.47 (1H, t, J 7.9, ArH), 7.26 (1H, d, J 8.2, ArH), 5.11 (1H, d, J 15.9, CH₂H₂Ar), 4.41 (1H, m, CH₂), 4.30 (1H, d, J 15.9, CH₂H₂Ar), 4.17-4.28 (2H, m, 2×CH₂), 3.98-3.95 (1H, m, CH), 2.79 (1H, br s, CH₂), 2.27 (1H, br s, CH₂), 2.01-1.93 (2H, m, CH₂), 1.75-1.69 (2H, m, CH₂), 1.49 (9H, m, 3×CH₃); 13C NMR δ (90.6 MHz, 323 K, CDCl₃) 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 (CH₂), 30.9 (CH), 28.4 (3×CH₃), 26.6 (CH₂), 26.5 (CH₂); m/z (EI) 369 ([M]+, 4%), 313 (15), 312 ([M-Bu]+, 13), 268 ([M-Boc]+, 71), 223 (31), 180 (36), 141 (21), 84 (100).

Rf [CH2Cl2:MeOH; 9:1] = 0.52; νmax (CHCl₃)/cm⁻¹ 3418 (OH), 1685 (C=O); 1H NMR δ (360 MHz, 323 K, CDCl₃) 8.11 (1H, d, J 8.5, ArH), 7.85 (1H, d, J 8.1, ArH), 7.71 (1H, d, J 8.3, ArH), 7.55 (1H, t, J 8.4, ArH), 7.48 (1H, t, J 6.8, ArH), 7.27 (1H, d, J 8.3, ArH), 5.10 (1H, d, J 16.1, CH₂H₂Ar), 4.37 (1H, d, J 16.1, CH₂H₂Ar), 4.17-4.02 (2H, m, 2×CH₂), 3.98-3.95 (1H, m, CH), 2.79 (1H, br s, CH₂), 2.27 (1H, br s, CH₂), 2.01-1.93 (2H, m, CH₂), 1.75-1.69 (2H, m, CH₂), 1.49 (9H, m, 3×CH₃); 13C NMR δ (90.6 MHz, 323 K, CDCl₃) 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 (CH2), 33.5 (CH2), 31.9 (CH2), 29.9 (CH), 28.5 (3×CH3); m/z (EI) 369 ([M]+, 4%), 312 ([M–Bu]+, 100), 268 ([M–Boc]+, 25), 250 (15), 180 (27).

(3R,4S,4aSR,12cSR)-3,4-Dihydroxy-2,3,4,4a,6,12c-hexahydro-1H-benzo[k]phenanthridine-5-carboxylic acid tert-butyl ester 19f (Δ1,2 isomer)

(1R,2S,4aSR,11bSR)-1,2-Dihydroxy-2,3,4,4a,6,11b-hexahydro-1H-[1,3]dioxolo[4,5-j]phenanthridine-5-carboxylic acid tert-butyl ester 17g (Δ1,2 isomer)

(2R,3S,4aSR,11bSR)-2,3-Dihydroxy-2,3,4,4a,6,11b-hexahydro-1H-[1,3]dioxolo[4,5-j]phenanthridine-5-carboxylic acid tert-butyl ester 18g (Δ2,3 isomer)

(3R,4S,4aSR,11bSR)-3,4-Dihydroxy-2,3,4,4a,6,11b-hexahydro-1H-[1,3]dioxolo[4,5-j]phenanthridine-5-carboxylic acid tert-butyl ester 19g (Δ3,4 isomer)
1.45 (1H, m, OH), CH,H,3×CH3), 13C NMR δ (90.6 MHz, 323 K, CDCl3) 157.2 (C), 150.0 (C), 146.1 (C), 128.0 (C), 126.4 (C), 106.6 (CH), 105.6 (CH), 100.9 (CH3), 80.8 (C), 69.6 (2CH), 53.0 (CH), 44.2 (CH2), 36.7 (CH), 28.4 (3CH3), 25.4 (CH2), 20.5 (CH3); m/z (EI) 363 ([M]+, 2%), 308 (22), 262 (100), 244 (7), 218 (12).

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

\[
\text{Rf} \ [\text{CH}_2\text{Cl}_2:\text{MeOH}, 95:5] = 0.37; \text{v}_{\text{max}} \text{(CHCl}_3)/\text{cm}^{-1} 3421 \text{ (OH), 1684 (C=O)}. \]

\[
\text{1}^\text{H NMR} \delta \ (360 \text{ MHz, D}_2\text{O}) 7.25-7.22 (1H, m, Ar\ H), 7.18-7.17 (2H, m, 2\ CH), 7.15-7.10 (1H, m, Ar\ H), 6.90 \text{ (CH)}; 5.93 (2H, s, OC\ H), 4.71 (1H, d, J 16.9, CH3H\ Ar), 3.71 (1H, br s, CH), 2.76 (1H, dt, J 15.5, 3.3, CH3H\ Ar), 2.02-2.00 (1H, m, CH2\ H), 1.51 (9H, s, 3\ CH3); 13C NMR δ (90.6 MHz, 323 K, CDCl3) 154.5 (C), 146.7 (C), 146.3 (C), 128.5 (C), 125.7 (C), 106.9 (CH), 106.3 (CH), 100.9 (CH3), 80.1 (C), 70.5 (CH), 69.0 (CH), 49.7 (CH), 43.2 (CH2), 33.7 (CH), 30.8 (CH2), 29.4 (CH2), 28.4 (3CH3); 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 CH2Cl2 (2 mL) was added TFA (5 mL) and the reaction was stirred at r.t. for 2 h. The reaction was diluted with H2O (15 mL), adjusted to pH 8-9 by the addition of NaOH pellets, and then extracted with CH2Cl2 (3 mL), cooled to 0°C and HCl (excess, 1 M in Et2O) added. The resultant solid was washed with Et2O and dried under vacuum to afford the desired amine hydrochloride(s) 20-22.

\[(1\text{RS,2SR,4aSR,10bSR})-1,2,3,4,4a,5,6,10b-\text{Octahydro-phenanthridine-1,2-diol 20a (\(\Delta^{1,2}\) isomer)}\]

General procedure H was followed using diol 17a (29 mg, 91 µmol), CH2Cl2 (2 mL) and TFA (3 mL), then CH2Cl2 (1 mL) and HCl (1 mL, 1 M in EtO) to afford amine hydrochloride 20a as a colourless oil (20 mg, 86%). \[\text{1}^\text{H NMR} \delta \ (360 \text{ MHz, D}_2\text{O}) 7.25-7.22 (1H, m, Ar\ H), 7.17-7.13 (2H, m, 2\timesAr\ H), 7.06-7.04 (1H, m, Ar\ H), 4.28 (1H, J 16.2, CH3H\Ar), 4.21 (1H, d, J 16.2, CH3H\Ar), 3.90 (1H, br d, J 7.5, CH), 3.75-3.70 (2H, m, 2\timesCH2), 3.17 (1H, dd, J 7.8, 4.4, CH), 1.92-1.85 (1H, m, CH3H\Ar), 1.76-1.70 (1H, m, CH3H\Ar), 1.63-1.56 (2H, m, CH2); 13C NMR δ (62.9 MHz, D2O) 131.9 (C), 129.3 (C), 128.0 (CH), 127.8 (CH), 127.2 (C), 126.9 (C), 70.5 (CH), 67.7 (CH), 51.6 (CH), 43.0 (CH2), 38.9 (CH), 25.1 (CH2), 21.4 (CH3); m/z (ESI+) 220 ([M+H]+, 77%), 219 (29); HRMS (ESI+) Found [M+H]+, 220.1331. C13H18O2N requires 220.1332.

\[(2\text{RS,3SR,4aSR,10bSR})-1,2,3,4,4a,5,6,10b-\text{Octahydro-phenanthridine-2,3-diol hydrochloride 21a (\(\Delta^{2,3}\) isomer)}\]

General procedure H was followed using diol 18a (25 mg, 78 µmol), CH2Cl2 (2 mL) and TFA (3 mL), then CH2Cl2 (1 mL) and HCl (1 mL, 1 M in EtO) to afford amine hydrochloride 21a as a colourless oil (12 mg, 60%). \[\text{1}^\text{H NMR} \delta \ (360 \text{ MHz, D}_2\text{O}) 7.18-7.17 (2H, m, 2\timesAr\ H), 7.15-7.10 (1H, m, Ar\ H), 7.02 (1H, d, J 7.4, Ar\ H), 4.25-4.17 (2H, m, CH2\Ar), 3.78-3.70 (3H, m, 3\timesCH), 3.24-3.18 (1H, dt, J 10.5, 4.6, CH\ Ar), 2.06-1.97 (2H, m, CH2), 1.85-1.75 (2H, m, CH2); 13C NMR δ (150.8 MHz, D2O) 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 (CH3), 36.1 (CH2), 33.7 (CH), 31.6 (CH2); m/z (ESI+) 220 ([M+H]+, 100%), 219 (91), 211 (62), 179 (65); HRMS (ESI+) Found [M+H]+, 220.1331. C13H18O2N requires 220.1332.
**Supplementary Material (ESI) for Organic & Biomolecular Chemistry**

**Supplementary Material (ESI)** for Organic & Biomolecular Chemistry

This journal is (c) The Royal Society of Chemistry 2010

---

(3RS,4RS,4aRS,10bSR)-1,2,3,4,4a,5,6,10b-Octahydro-phenanthridine-3,4-diol hydrochloride 22a (A\(^{34}\) isomer)

General procedure H was followed using diol 19a (26 mg, 82 µmol), CH₂Cl₂ (2 mL) and TFA (3 mL), then CH₂Cl₂ (1 mL) and HCl (1 mL, 1 M in Et₂O) to afford amine hydrochloride 22a as a colourless oil (11 mg, 53%). \(^1\)H NMR δ (360 MHz, D₂O) 7.29 (1H, d, J 6.9, ArH), 7.20 (1H, t, J 7.1, ArH), 7.13 (1H, t, J 7.6, ArH), 7.05 (1H, d, J 7.5, ArH), 4.24 (1H, d, J 16.3, CH₂H₂Ar), 4.18 (1H, d, J 16.3, CH₂H₂Ar), 3.79-3.73 (2H, m, 2×CH₂), 3.56 (1H, br d, J 9.1, CH), 3.33-3.29 (1H, m, CH), 2.08-1.97 (1H, m, CH₂), 1.94-1.85 (1H, m, CH₂H₂), 1.59-1.53 (1H, m, CH₂H₂), 1.34-1.26 (1H, m, CH₂H₂); \(^13\)C NMR δ (77.0 MHz, D₂O) 162.7 (d, J 22.4, CH), 127.4 (CH), 127.0 (CH), 126.8 (CH), 69.0 (CH), 54.5 (CH), 41.3 (CH₂), 33.6 (CH), 25.9 (CH₂); m/z (ESI+ (M+H)) 238 ([M+H]+, 100%), 211 (26), 179 (26); HRMS (ESI+) Found [M+H]+, 238 (100%).

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

General procedure H was followed using diol mixture 17-19b (16 mg, 48 µmol), CH₂Cl₂ (2 mL) and TFA (5 mL), then CH₂Cl₂ (1 mL) and HCl (2 mL, 1 M in Et₂O) to afford amine hydrochlorides 20-22b as a yellow oil (9 mg, 69%). m/z (ESI+ (M+H)) 234 ([M+H]+, 100%), 232 (44); HRMS (ESI+) Found [M+H]+, 234.1489. C₁₃H₁₇O₂N₂ requires 234.1489.

(2RS,3SR,4aSR,10bSR) 9-Fluoro-1,2,3,4,4a,5,6,10b-Octahydro-phenanthridine-2,3-diol 21c (A\(^{2,3}\) isomer)

General procedure H was followed using diol 18c (10 mg, 30 µmol), CH₂Cl₂ (2 mL), and TFA (5 mL), then CH₂Cl₂ (1 mL) and HCl (2 mL, 1 M in Et₂O) to afford amine hydrochloride 21c as a colourless oil (7 mg, 86%). \(^1\)H NMR δ (360 MHz, D₂O) 7.09-7.05 (1H, m, ArH), 6.98 (1H, d, J 10.0, 2.1, ArH), 6.91 (1H, td, J 8.7, 2.6, ArH), 4.23 (1H, s, CH₂Ar), 3.81 (1H, dd, J 9.8, 4.7, CH₂), 3.77-3.75 (2H, m, 2×CH₂), 3.27-3.23 (1H, m, CH), 2.10-2.00 (2H, m, CH₂H₂+CH₂H₂); \(^13\)C NMR δ (90.6 MHz, D₂O) 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 (CH₂), 33.2 (CH₂), 31.6 (CH), 29.0 (CH₂); m/z (ESI+ (M+H)) 238 ([M+H]+, 100%), 211 (12), 179 (12); HRMS (ESI+) Found [M+H]+, 238.1234. C₁₃H₁₇FNO₂ requires 238.1238.

(3RS,4SR,4aRS,10bSR)-9-Fluoro-1,2,3,4,4a,5,6,10b-Octahydro-phenanthridine-3,4-diol 22c (A\(^{34}\) isomer)

General procedure H was followed using diol 19c (15 mg, 46 µmol), CH₂Cl₂ (2 mL), and TFA (5 mL), then CH₂Cl₂ (1 mL) and HCl (2 mL, 1 M in Et₂O) to afford amine hydrochloride 22c as a yellow oil (9 mg, 74%). \(^1\)H NMR δ (360 MHz, D₂O) 7.11-7.05 (2H, m, 2×ArH), 6.91 (1H, td, J 8.6, 2.7, ArH), 4.23 (1H, d, J 16.3, CH₂H₂Ar), 4.17 (1H, d, J 16.3, CH₂H₂Ar), 3.84-3.82 (1H, m, CH), 3.77 (1H, dd, J 9.5, 5.3, CH₂), 3.59-3.57 (1H, m, CH₂), 3.32-3.30 (1H, m, CH₂), 2.02-1.92 (2H, m, CH₂), 1.64-1.57 (1H, m, CH₂H₂), 1.39-1.31 (1H, m, CH₂H₂); \(^13\)C NMR δ (90.6 MHz, D₂O) 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 (CH₂), 49.5 (CH₂), 34.3 (CH), 26.3 (CH₂), 21.9 (CH₂); m/z (ESI+ (M+H)) 238 ([M+H]+, 100%), 225 (18), 211 (26), 210 (10), 197 (13), 179 (26); HRMS (ESI+) Found [M+H]+, 238.1233. C₁₃H₁₁FNO₂ requires 238.1238.

---

- S18 -
(1RS,2SR,4aSR,10bSR)-8-Methoxy-1,2,3,4,4a,5,6,10b-octahydro-phenanthridine-1,2-diol 20d (Δ^{1,2} isomer)

General procedure H was followed using diol 17d (21 mg, 60 µmol), CH₂Cl₂ (2 mL), and TFA (5 mL), then CH₂Cl₂ (1 mL) and HCl (2 mL, 1 M in Et₂O) to afford amine hydrochloride 20d as a colourless oil (14 mg, 82%). ¹H NMR δ (800 MHz, D₂O) 7.17 (1H, d, J 8.8, ArH), 6.76 (1H, d, J 8.8, 2.4, ArH), 6.64 (1H, d, J 1.6, ArH), 4.23 (1H, d, J 16.6, CH₂H₁Ar), 4.18 (1H, d, J 16.6, CH₂H₁Ar), 3.85 (1H, br s, CH₃), 3.72-3.66 (2H, m, 2×CH₂), 3.61 (3H, s, CH₃), 3.12 (1H, m, CH₃), 1.92-1.89 (1H, m, CH₂H₃α), 1.73-1.70 (1H, m, CH₂H₃β), 1.63-1.52 (2H, m, CH₃H₄+ CH₃H₅); ¹³C NMR δ (200.0 MHz, D₂O) 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 (CH₂), 52.2 (CH), 43.4 (CH₃), 38.7 (CH), 25.5 (CH₂), 21.8 (CH₃); m/z (ESI+) 250 ([M+H]+, 100%), 248 (86), 246 (13); HRMS (ESI+) Found [M+H]+, 250.1435. C₁₄H₂₃O₃N requires 250.1438.

(2RS,3SR,4aSR,10bSR)-8-Methoxy-1,2,3,4,4a,5,6,10b-octahydro-phenanthridine-2,3-diol 21d (Δ^{2,3} isomer)

General procedure H was followed using diol 18d (20 mg, 57 µmol), CH₂Cl₂ (2 mL), and TFA (5 mL), then CH₂Cl₂ (1 mL) and HCl (2 mL, 1 M in Et₂O) to afford amine hydrochloride 21d as a yellow oil (15 mg, 92%). ¹H NMR δ (360 MHz, D₂O) 7.12 (1H, d, J 8.6, ArH), 6.79 (1H, dd, J 8.6, 2.2, ArH), 6.62 (1H, br s, ArH), 4.23-4.14 (2H, m, CH₂H₂Ar), 3.75-3.64 (3H, m, 3×CH₃), 3.60 (3H, s, OCH₃), 3.18-3.13 (1H, m, CH), 2.06-1.94 (2H, m, CH₂), 1.85-1.72 (2H, m, CH₃). ¹³C NMR δ (90.6 MHz, D₂O) 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 (CH₂), 52.3 (CH), 44.2 (CH₂), 33.6 (CH₂), 30.5 (CH₂), 29.0 (CH₂); m/z (ESI+) 250 ([M+H]+, 100%), 249 (28), 248 (89); HRMS (ESI+) Found [M+H]+, 250.1438. C₁₄H₂₃O₃N requires 250.1438.

(3RS,4SR,4aRS,10bSR)-8-Methoxy-1,2,3,4,4a,5,6,10b-octahydro-phenanthridine-3,4-diol 22d (Δ^{3,4} isomer)

General procedure H was followed using diol 19d (2.1 mg, 6 µmol), CH₂Cl₂ (2 mL), and TFA (5 mL), then CH₂Cl₂ (1 mL) and HCl (2 mL, 1 M in Et₂O) to afford amine hydrochloride 22d as a colourless oil (1.4 mg, 84%). ¹H NMR δ (800 MHz, D₂O) 7.22 (1H, d, J 8.0, ArH), 6.82 (1H, dd, J 8.8, 3.2, ArH), 6.67 (1H, d, J 2.4, ArH), 4.20 (1H, d, J 16.8, CH₂H₃Ar), 4.15 (1H, d, J 16.8, CH₂H₃Ar), 3.80 (1H, br s, CH₃), 3.71-3.69 (1H, m, CH), 3.64 (3H, s, CH₃), 3.60-3.59 (1H, m, CH₃), 3.23 (1H, br s, CH₃), 1.90-1.86 (2H, m, CH₂), 1.59-1.56 (1H, m, CH₃H₄), 1.35-1.31 (1H, m, CH₃H₅); ¹³C NMR δ (90.6 MHz, D₂O) 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 (CH₃), 54.7 (CH), 41.6 (CH₂), 33.2 (CH), 26.9 (CH₂), 26.0 (CH₃); 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. C₁₄H₂₃O₃N requires 250.1438.

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

General procedure H was followed using diol 17e (10 mg, 26 µmol), CH₂Cl₂ (2 mL), and TFA (5 mL), then CH₂Cl₂ (1 mL) and HCl (2 mL, 1 M in Et₂O) to afford amine hydrochloride 20e as a yellow oil (9 mg, 88%). ¹H NMR δ (250 MHz, D₂O) 6.82 (1H, s, ArH), 6.68 (1H, s, ArH), 4.18 (2H, br s, CH₂H₂Ar), 3.83-3.80 (1H, m, CH₃), 3.75-3.68 (2H, m, 2×CH₃), 3.66 (3H, s, CH₃H₃), 3.64 (3H, s, CH₃), 3.09 (1H, dd, J 8.8, 4.4, CH₂), 2.04-1.87 (1H, m, CH₃H₅Ar), 1.79-1.52 (3H, m, CH₃+CH₃H₅Ar); ¹³C NMR δ (62.9 MHz, D₂O) 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×CH₃), 52.2 (CH), 43.2 (CH₂), 38.5 (CH), 25.3 (CH₃), 21.6 (CH₂); m/z (ESI+) 280 ([M+H]+, 61%), 279 ([M]+, 100); HRMS (ESI+) Found [M+H]+, 280.1542. C₁₃H₂₁O₄N requires 280.1543.

- S19 -
(2RS,3SR,4aSR,10bSR)-8,9-Dimethoxy-1,2,3,4,4a,5,6,10b-octahydro-phenanthridine-2,3-diol hydrochloride 21e (Δ²⁻³ isomer)

General procedure H was followed using diol mixture 17e and 18e (6.2 mg, 16 µmol), CH₂Cl₂ (2 mL), and TFA (5 mL), then CH₂Cl₂ (1 mL) and HCl (2 mL, 1 M in Et₂O) to afford amine hydrochlorides 20e and 21e as a yellow oil (3 mg, 60%). Data for Δ²⁻³ isomer 22e was deduced from ¹H, ¹³C and HSQC NMR data for the mixture of 20e and 21e. ¹H NMR δ (300 MHz, D₂O) 6.76 (1H, s, ArtH), 6.66 (1H, s, ArtH), 4.18-4.15 (2H, m, CH₂Ar), 3.75-3.71 (3H, m, 3×CH), 3.67 (3H, s, CH₃), 3.64 (3H, s, CH₃), 3.18-3.15 (1H, m, CH₃), 2.07-2.02 (2H, m, CH₂H₁₁CH₂H₁₁), 1.92-1.88 (1H, m, CH₂H₁₁), 1.83-1.78 (1H, m, CH₂H₁₂); ¹³C NMR δ (125.8 MHz, D₂O) 147.9 (C), 147.6 (C), 125.2 (C), 119.8 (C), 112.7 (CH), 111.1 (CH), 70.9 (CH), 59.2 (2×CH₂), 53.3 (CH), 43.9 (CH₂), 33.6 (CH₂), 30.7 (CH₂), 28.9 (CH₂); m/z (ESI⁺) 559 ([2M+H]⁺, 5%), 280 ([M+H]⁺, 100); HRMS (ESI⁺) Found [M+H]⁺, 280.1542. C₁₅H₂₂O₄N requires 280.1543.

(3RS,4aSR,10bSR)-8,9-Dimethoxy-1,2,3,4,4a,5,6,10b-octahydro-phenanthridine-3,4-diol hydrochloride 22e (Δ³⁻⁴ isomer)

General procedure H was followed using diol 19e (10 mg, 26 µmol), CH₂Cl₂ (2 mL), and TFA (5 mL), then CH₂Cl₂ (1 mL) and HCl (2 mL, 1 M in Et₂O) to afford amine hydrochloride 22e as a yellow oil (5 mg, 60%). ¹H NMR δ (360 MHz, D₂O) 6.82 (1H, s, ArtH), 6.67 (1H, s, ArtH), 4.16 (1H, d, J 16.1, CH₂H₁₁Ar), 4.09 (1H, d, J 16.1, CH₂H₁₁Ar), 3.78 (1H, br s, CH₃), 3.72-3.65 (1H, m, CH₃), 3.65 (3H, s, CH₃), 3.63-3.60 (1H, m, CH₃), 3.62 (3H, s, CH₃), 3.23 (1H, br s, CH₃), 2.00-1.89 (2H, m, CH₂), 1.64-1.53 (1H, m, CH₂H₁₁), 1.38-1.29 (1H, m, CH₂H₁₁), ¹³C NMR δ (90.6MHz, D₂O) 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×CH₂), 54.6 (CH), 41.0 (CH₃), 33.4 (CH), 26.0 (CH₂), 21.6 (CH₂); m/z (ESI⁺) 280 ([M+H]⁺, 100%); HRMS (ESI⁺) Found [M+H]⁺, 280.1546. C₁₇H₂₀O₄N requires 280.1543.

(1RS,2SR,4aSR,12cSR)-1,2,3,4,4a,5,6,12c-Octahydro- benzo[k]phenanthridine-1,2-diol hydrochloride 20f (Δ²⁻⁴ isomer)

General procedure H was followed using diol 17f (20 mg, 54 µmol), CH₂Cl₂ (2 mL), and TFA (5 mL), then CH₂Cl₂ (1 mL) and HCl (2 mL, 1 M in Et₂O) to afford amine hydrochloride 20f as a colourless oil (11 mg, 67%). ¹H NMR δ (500 MHz, D₂O) 7.48-7.41 (2H, m, 2×Ar), 7.22-7.16 (1H, t, J 7.7, Ar), 7.19 (1H, d, J 8.5, ArH), 7.16 (1H, m, CH₂H₁₁), 7.05 (1H, m, CH₂H₁₂), 6.97-6.74 (5H, m, 5×CH₂), 6.73 (1H, s, CH₃), 6.63 (1H, s, CH₃), 3.68-3.65 (2H, m, 2×CH₂), 4.05-4.03 (2H, m, 2×CH₂), 3.62 (3H, s, CH₃), 1.89-1.79 (1H, m, CH₂H₁₂), 1.61-1.51 (1H, m, CH₂H₁₁); ¹³C NMR δ (125.9 MHz, D₂O) 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 (CH₃), 35.7 (CH), 27.8 (CH₃), 24.2 (CH₂); m/z (ESI⁺) 280 ([M+H]⁺, 38%), 239 (36), 191 (44), 168 (100); HRMS (ESI⁺) Found [M+H]⁺, 270.1488. C₁₃H₁₈O₂N requires 270.1489.
(NH), 54.5 (CH), 46.5 (CH2), 34.3 (CH), 30.5 (CH2), 28.1 (CH3); m/z (ESI+) 270 ([M+H]+, 100%), 232 (15), 217 (16), 203 (16); HRMS (ESI+) Found [M+H]+, 270.1481. C17H20O2N requires 270.1489.

(3RS,4SR,4aRS,12cSR)-1,2,3,4,4a,5,6,12c-Octahydro-benzo[k]phenanthridine-3,4-diol hydrochloride 22f (Δ23-isomer)

General procedure H was followed using diol 19f (23 mg, 63 µmol), CH2Cl2 (2 mL), and TFA (5 mL), then CH2Cl2 (1 mL) and HCl (2 mL, 1 M in EtO) to afford amine hydrochloride 22f as a colourless oil (13 mg, 69%). 1H NMR δ (360 MHz, D2O) 8.05 (1H, d, J 7.5, ArH), 7.77-7.73 (2H, m, 2×ArH), 7.46-7.41 (2H, m, 2×ArH), 7.16 (1H, d, J 8.5, ArH), 4.52 (1H, d, J 16.5, CH2Ar), 4.39 (1H, d, J 16.5, CH2Ar), 4.04-3.95 (2H, s, 2×CHH), 3.64 (1H, d, J 11.4, CH), 3.54 (1H, br s, CH), 2.22-2.13 (1H, m, CHA), 1.93-1.89 (1H, m, CHA), 1.81-1.77 (2H, m, CH2); 13C NMR δ (62.9 MHz, D2O) 133.5 (C), 133.2 (C), 130.9 (C), 129.3 (CH), 129.2 (CH), 127.3 (2×CH), 125.9 (C), 125.7 (C), 125.0 (CH), 73.1 (CH), 69.6 (CH), 54.5 (CH), 45.2 (CH2), 34.0 (CH), 26.2 (CH2), 22.6 (CH2); m/z (ESI+) 270 ([M+H]+, 71%), 217 (21), 172 (27); HRMS (ESI+) Found [M+H]+, 270.1481. C17H20O2N requires 270.1489.

(1RS,2SR,4aSR,11bSR)-1,2,3,4,4a,5,6,11b-Octahydro-[1,3]dioxolo[4,5-j]phenanthridine-1,2-diol hydrochloride 20g (Δ3-isomer)

General procedure H was followed using diol 17g (18 mg, 50 µmol), CH2Cl2 (2 mL) and TFA (3 mL), then CH2Cl2 (1 mL) and HCl (2 mL, 1 M in EtO) to afford amine hydrochloride 20g as a yellow solid (9 mg, 61%). 1H NMR δ (360 MHz, D2O) 6.76 (1H, s, ArH), 6.57 (1H, s, ArH), 5.80 (2H, s, OCH3O), 4.21-4.12 (2H, m, CH2Ar), 3.95-3.85 (1H, m, CH), 3.83-3.75 (2H, m, 2×CH), 3.11-3.05 (1H, m, CH), 2.04-1.59 (6H, m, 2×CH2+2×OH); 13C NMR δ (90.6 MHz, D2O) 147.9 (C), 147.8 (C), 126.6 (C), 121.3 (C), 110.1 (CH), 107.3 (CH), 102.5 (CH2), 71.7 (CH), 68.6 (CH), 52.6 (CH2), 44.0 (CH2), 39.6 (CH), 26.0 (CH2), 22.2 (CH2); m/z (ESI+) 264 ([M+H]+, 4%), 150 (21), 149 (21); HRMS (ESI+) Found [M+H]+, 264.1237. C14H16O3N requires 264.1230.

(2RS,3SR,4aSR,11bSR)-1,2,3,4,4a,5,6,11b-Octahydro-[1,3]dioxolo[4,5-j]phenanthridine-2,3-diol hydrochloride 21g (Δ23-isomer)

General procedure H was followed using diol 18g (10 mg, 28 µmol), CH2Cl2 (2 mL) and TFA (3 mL), then CH2Cl2 (1 mL) and HCl (2 mL, 1 M in EtO) to afford amine hydrochloride 21g as a yellow solid (7 mg, 81%). 1H NMR δ (360 MHz, D2O) 6.69 (1H, s, ArH), 6.54 (1H, s, ArH), 5.80-5.79 (2H, m, OCH3O), 4.17-4.09 (2H, m, CH2Ar), 3.79-3.72 (3H, m, 3×CHH), 3.14-3.11 (1H, m, CH), 2.09-1.98 (2H, m, CH2), 1.88-1.72 (2H, m, CH2); 13C NMR δ (90.6 MHz, D2O) 148.4 (C), 147.6 (C), 129.2 (C), 120.7 (C), 108.8 (CH), 107.3 (CH), 102.5 (CH2), 68.3 (CH), 67.1 (CH), 52.9 (CH), 45.1 (CH2), 34.4 (CH2), 31.9 (CH), 29.8 (CH2); m/z (ESI+) 264 ([M+H]+, 100%), 262 (46); HRMS (ESI+) Found [M+H]+, 264.1232. C14H16O3N requires 264.1230.

(3RS,4SR,4aSR,11bSR)-1,2,3,4,4a,5,6,11b-Octahydro-[1,3]dioxolo[4,5-j]phenanthridine-3,4-diol hydrochloride 22g (Δ3-isomer)

General procedure H was followed using diol 19g (5 mg, 14 µmol), CH2Cl2 (2 mL) and TFA (3 mL), then CH2Cl2 (1 mL) and HCl (2 mL, 1 M in EtO) to afford amine hydrochloride 22g as a colourless oil (3 mg, 73%). 1H NMR δ (360 MHz, D2O) 6.81 (1H, s, ArH), 6.58 (1H, s, ArH), 5.80-5.77 (2H, m, OCH3O), 4.16 (1H, d, J 16.1, CH3HAr), 4.09 (1H, d, J 16.1, CH3HAr), 3.82-3.80 (1H, br s, CHH), 3.72 (1H, dd, J 9.4, 4.5, CH2), 3.62-3.59 (1H, m, CH), 3.22-3.21 (1H, m, CH), 1.93-1.85 (1H, m, CH2H3Ar), 1.63-1.56 (1H, m, CH2H3Ar), 1.39-1.30 (2H, m, CH2); 13C NMR δ (90.6 MHz, D2O) 149.8 (C), 148.4 (C), 129.1 (C), 123.2 (C), 108.6 (2×CH), 103.5 (CH2), 70.9 (CH), 68.6 (CH), 56.3 (CH), 42.8 (CH2), 35.5 (CH), 27.2 (2×CH2);
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_{4}N requires 264.1230.

**References**