Supporting Information

An efficient one-pot decarboxylative aromatization of tetrahydro-β-carbolines by using *N*-chlorosuccinimide: Total synthesis of norharmane, harmane and eudistomins

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Experimental Section

General information

Unless otherwise stated, all the starting materials and other reagents of the best grade were commercially available and were used without further purification. TLC was performed on 0.25 mm silica gel 60-F254 plates. Spots were visualized by UV light. All the melting points were taken by Electrothermal apparatus and the values are uncorrected. ¹H and ¹³C NMR spectra were recorded on 300 MHz, 400 MHz and 500 MHz NMR instruments using tetramethylsilane as the internal standard. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane. Spin multiplicities are described as s (singlet), bs (broad singlet), d (doublet), dd (double doublet), t (triplet), q (quartet), or m (multiplet). Coupling constants are reported in hertz (Hz). HRMS analyses were acquired on single quadruple and carried out using the ESI techniques at 70 eV. Wherever required column chromatography was performed using silica gel of 60–120 mm with hexane, ethyl acetate and methanol as eluents.

Pictet-Spengler reaction and decarboxylative aromatization of L-tryptophan.



Scheme S1: Synthesis of β -carboline (2a-t) unsing NCS.

General Procedure

To a stirred solution of L-tryptophan (1, 1 mmol) in acetic acid was added aldehyde (1.1 mmol), stirred at 80 °C for 1 h and the acetic acid was removed under reduced pressure and dried well. This residue was taken in DMF, added TEA (3 mmol) and solution of NCS (2.1 mmol) in DMF. Then the reaction mixture was stirred for 30 min at room temperature. After completion of the reaction (monitored by TLC), the reaction mixture was quenched with water, extracted with ethyl acetate and washed with saturated Na₂CO₃ solution. The combined organic layers were washed with water, brine solution, dried over sodium sulfate, filtered and concentrated under reduced pressure. The residue obtained was purified by column chromatography by using ethyl acetate and hexane to afford the desired β -carbolines (**2a-t**).

9H-Pyrido[3,4-b]indole (norharmane, 2a).¹



Yellow solid: 80% yield; mp:195–198 °C (ref. 1: (195–197 °C); ¹H NMR (300 MHz, CDCl₃) δ: 9.16 (bs, 1H), 8.94 (s, 1H),
8.47 (d, J = 4.9 Hz, 1H), 8.14 (d, J = 7.9 Hz, 1H), 7.98 (d, J = 4.9 Hz, 1H), 7.58–7.51 (m, 2H), 7.30 (t, J = 7.7 Hz, 1H); ¹³C NMR (125 MHz, DMSO–d₆) δ; 140.4, 137.9, 135.8, 133.9, 128.0, 127.3, 121.6, 120.5, 119.1, 114.5, 111.8; MS (ESI): *m/z*

169 $[M + H]^+$; HRMS (ESI): calcd for C₁₁H₉N₂ m/z 169.0760 $[M + H]^+$; found: 169.0757.

1-Methyl-9*H*-pyrido[3,4-*b*]indole (harmane, 2b).²



Off white solid: 82% yield; mp: 230–233 °C (ref. 2: 235–236 °C); ¹H NMR (300 MHz, CDCl₃ + DMSO– d_6) δ : 10.77 (bs, 1H), 8.30 (d, J = 4.7 Hz, 1H), 8.10 (d, J = 7.5 Hz, 1H), 7.81 (d, J = 4.7 Hz, 1H), 7.63–7.48 (m, 2H), 7.23 (t, J = 6.9 Hz, 1H), 2.86 (s, 3H); ¹³C NMR (75 MHz, CDCl₃ + DMSO– d_6) δ : 141.6, 140.2, 136.8, 134.3, 127.3, 126.9, 121.0, 120.7, 118.8, 112.1,

111.5, 20.0; MS (ESI): *m/z* 183 [M + H]⁺; HRMS (ESI): calcd for C₁₂H₁₁N₂ *m/z* 183.0916 [M + H]⁺; found: 183.0916.

1-Propyl-9*H*-pyrido[3,4-*b*]indole (2c).³

Brown colour solid: 78% yield; mp: 170–175 °C (ref. 3: 218–220 °C); ¹H NMR (300 MHz, DMSO– d_6) δ: 11.05 (bs, 1H), 8.30 (d, J = 5.3 Hz, 1H), 8.09 (d, J = 7.7 Hz, 1H), 7.80 (d, J = 5.3 Hz, 1H), 7.58 (d, J = 8.1 Hz, 1H), 7.50 (t, J = 7.5 Hz, 1H), 7.22 (t, J = 7.5 Hz, 1H), 3.14 (t, J = 7.5 Hz, 2H), 1.92 (q, J = 7.5, 15.1 Hz, 2H), 1.05 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, DMSO– d_6) δ: 145.6, 140.2, 137.3, 134.0, 127.6, 126.9, 121.5, 120.9, 119.0, 112.4, 111.7, 35.3, 21.3, 13.8; MS (ESI): m/z 211 [M + H]⁺; HRMS (ESI): calcd for C₁₄H₁₅N₂ m/z 211.1229 [M + H]⁺; found: 211.1216.

1-(4-Methoxybenzyl)-9*H*-pyrido[3,4-*b*]indole (2d)



Yellow solid: 90% yield; mp: 142–144 °C; ¹H NMR (300 MHz, DMSO– d_6) δ : 11.67 (s, 1H), 8.26 (d, J = 5.3 Hz, 1H), 8.21 (d, J = 7.7 Hz, 1H), 7.96 (d, J = 5.1 Hz, 1H), 7.62 (d, J = 8.1 Hz, 1H), 7.54 (t, J = 7.2 Hz, 1H), 7.31 (d, J = 8.7 Hz, 2H), 7.23 (t, J = 7.7 Hz, 1H), 6.82 (d, J = 8.5 Hz, 2H), 4.38 (s, 2H), 3.67 (s, 3H); ¹³C NMR (100 MHz, DMSO– d_6) δ : 157.5, 144.7, 140.3, 137.6, 133.8, 131.1, 129.6, 127.9, 127.6, 121.6, 120.9, 119.2, 113.6, 112.8, 111.8, 54.8, 38.4; MS (ESI): m/z 289 [M + H]⁺; HRMS (ESI): calcd for C₁₉H₁₇ON₂ m/z 289.1335 [M + H]⁺; found: 289.1328.

1-Phenyl-9*H*-pyrido[3,4-*b*]indole (2e).²



Yellow solid: 85% yield; mp: 241–244 °C (ref. 2: 241–242 °C); ¹H NMR (300 MHz, DMSO– d_6) δ : 11.52 (bs, 1H), 8.47 (d, J = 5.2 Hz, 1H), 8.26 (d, J = 7.7 Hz, 1H), 8.13 (d, J = 5.3 Hz, 1H), 8.03 (d, J = 7.0 Hz, 2H), 7.67–7.49 (m, 5H), 7.26 (t, J = 7.5 Hz, 1H); ¹³C NMR (75 MHz, DMSO– d_6) δ : 142.1, 141.0, 138.3, 138.3, 132.9, 129.0, 128.6, 128.4, 128.3, 128.0, 121.5, 120.7, 119.4, 113.8, 112.3; MS (ESI): m/z 245 [M + H]⁺; HRMS (ESI): calcd for C₁₉H₁₅O₂N₂ m/z 245.1073 [M + H]⁺; found:

245.1074.

1-(*p*-Tolyl)-9*H*-pyrido[3,4-*b*]indole (2f).⁴



White solid: 88% yield; mp: 192–195 °C (ref. 4: 190.3–191.6 °C); ¹H NMR (300 MHz, CDCl₃ + DMSO– d_6) δ: 11.23 (bs, 1H), 8.38 (d, J = 5.1 Hz, 1H), 8.11 (d, J = 7.9 Hz, 2H), 7.89 (t, J = 5.4 Hz, 3H), 7.59 (d, J = 8.2 Hz, 1H), 7.45 (t, J = 7.3 Hz, 1H), 7.34 (d, J = 7.9 Hz, 2H), 7.19 (t, J = 7.3 Hz, 1H), 2.41 (s, 3H); ¹³C NMR (75 MHz, CDCl₃ + DMSO– d_6) δ: 142.2, 140.8, 137.8, 137.5, 135.4, 132.8, 128.8, 127.9, 127.5, 120.8, 120.6, 118.9, 112.9, 112.0, 20.6; MS (ESI): m/z 259 [M + H]⁺; HRMS (ESI): calcd for C₁₈H₁₅N₂ m/z 259.1229 [M + H]⁺; found: 259.1219.

1-(2-Methoxyphenyl)-9*H*-pyrido[3,4-*b*]indole (2g).⁵



White solid: 93% yield; mp: 157–160 °C (ref. 5: 172–174 °C); ¹H NMR (500 MHz, CDCl₃) δ : 8.58 (bs, 1H), 8.55 (d, J = 5.2 Hz, 1H), 8.17 (d, J = 7.9 Hz, 1H), 7.93–7.90 (m, 3H), 7.55 (t, J = 7.1 Hz, 1H), 7.51 (t, J = 8.1 Hz, 1H), 7.32 (t, J = 7.6 Hz, 1H), 7.11 (d, J = 8.6 Hz, 2H), 3.90 (s, 3H); ¹³C NMR (75 MHz, CDCl₃ + DMSO– d_6) δ : 158.7, 141.5, 140.2, 137.2, 132.2, 130.1, 128.7, 128.2, 126.8, 120.1, 118.3, 113.0, 111.9, 111.3, 54.2; MS (ESI): m/z 275 [M + H]⁺; HRMS (ESI):

calcd for $C_{18}H_{15}ON_2 m/z 275.1178 [M + H]^+$; found: 275.1166.

1-(3,4,5-Trimethoxyphenyl)-9*H*-pyrido[3,4-*b*]indole (2h).⁶



White solid: 92% yield; mp: 169–172 °C (ref. 6: 167–169 °C); ¹H NMR (500 MHz, CDCl₃) δ : 8.77 (bs, 1H), 8.55 (d, J = 5.1 Hz, 1H), 8.16 (d, J = 7.9 Hz, 1H), 7.94 (d, J = 5.1 Hz, 1H), 7.60–7.52 (m, 2H), 7.33 (t, J = 7.5 Hz, 1H), 7.13 (s, 1H), 3.92 (s, 9H); ¹³C NMR (CDCl₃, 75 MHz) δ : 153.5, 143.0, 140.5, 139.0, 138.2, 134.0, 133.4, 129.8, 128.4, 121.8, 121.7, 120.1, 113.7, 111.6, 105.2, 60.8, 56.1; MS (ESI): m/z 335 [M + H]⁺; HRMS (ESI): calcd for C₁₉H₁₅O₂N₂ m/z 335.1390 [M + H]⁺; found: 335.1391.

White solid: 83% yield; mp: 262–264 °C (ref. 7: 260–262 °C); ¹H NMR (300 MHz, CDCl₃ + DMSO– d_6) δ: 11.17 (s, 0.8H), 8.98 (s, 0.8H), 8.35 (d, J = 5.1 Hz, 1H), 8.07 (d, J = 7.9 Hz, 2H), 7.87–7.83 (m, 1H), 7.58 (d, J = 8.1 Hz, 1H), 7.51 (d, J = 1.7 Hz, 0.8H), 7.46–7.40 (m, 2H), 7.17 (d, J = 7.7 Hz, 1H), 6.98 (d, J = 8.1 Hz, 1H), 3.92 (s, 2.5H), peaks at 11.29, 9.22, 7.54 and 3.96 are due to 20% minor rotamers; ¹³C NMR (75 MHz, CDCl₃ + DMSO– d_6) δ: 147.4, 146.9, 142.5, 140.8, 137.6, 132.6, 129.5, 128.6, 127.4, 120.9, 120.7, 118.9, 115.2, 112.5, 112.1, 111.8, 55.2; MS (ESI): m/z 291 [M + H]⁺; HRMS (ESI): calcd for C₁₈H₁₅O₂N₂ m/z 291.1128 [M + H]⁺; found: 291.1115.

3-(9*H*-Pyrido[3,4-*b*]indol-1-yl)phenol (2j).⁵



Cream colour solid: 78% yield; mp: 213–216 °C (ref. 5: 215–216 °C); ¹H NMR (300 MHz, CDCl₃ + DMSO–*d*₆) δ: 10.79 (s, 1H), 9.14 (bs, 1H), 8.38 (d, *J* = 5.1 Hz, 1H), 7.85 (d, *J* = 7.7 Hz, 1H), 7.54 (d, *J* = 5.1 Hz, 1H), 7.61 (d, *J* = 3.0 Hz, 1H), 7.47–7.37 (m, 3H), 7.30 (t, *J* = 7.7 Hz, 1H), 7.17 (t, *J* = 7.4 Hz, 1H), 6.87 (d, *J* = 7.2 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃ + DMSO–*d*₆) δ: 156.9, 142.1, 140.4, 139.0, 137.4, 132.6, 128.9, 128.6, 127.1, 120.4, 120.4, 118.6, 115.0, 114.8,

112.6, 111.5; MS (ESI): m/z 261 [M + H]⁺; HRMS (ESI): calcd for C₁₇H₁₃ON₂ m/z 261.1022 [M + H]⁺; found: 261.1019.

1-(4-Chlorophenyl)-9*H*-pyrido[3,4-*b*]indole (2k).



Light yellow solid: 80% yield; mp: 200–265 °C; ¹H NMR (300 MHz, CDCl₃ + DMSO– d_6) δ : 11.42 (s, 1H), 8.39 (d, J = 5.3 Hz, 1H), 8.13 (d, J = 7.7 Hz, 1H), 8.00 (s, 1H), 7.99 (d, J = 8.3 Hz, 2H), 7.61 (d, J = 8.3 Hz, 1H), 7.55 (d, J = 8.5 Hz, 2H), 7.48 (t, J = 7.2 Hz, 1H), 7.21 (t, J = 7.7 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃ + DMSO–d6) δ : 141.1, 140.7, 137.8, 136.7, 133.4, 132.9, 129.8, 129.4, 128.4, 127.9, 121.1, 120.6, 119.3, 113.7, 112.1; MS (ESI): m/z 279 [M + H]⁺; HRMS (ESI): calcd for C₁₇H₁₂ClN₂ m/z 279.0689 [M + H]⁺; found: 279.0942.

1-(4-Fluorophenyl)-9*H*-pyrido[3,4-*b*]indole (2l).⁴



White solid: 83% yield; mp: 206–209 °C (ref. 4: 203–205 °C); ¹H NMR (300 MHz, CDCl₃ + DMSO– d_6) δ: 11.03 (bs, 1H), 8.39 (d, J = 5.3 Hz, 1H), 8.06 (d, J = 7.7 Hz, 1H), 7.98 (q, J = 5.5, 8.5 Hz, 2H), 7.87 (d, J = 5.1 Hz, 1H), 7.56 (d, J = 8.1 Hz, 1H), 7.45 (t, J = 7.5 Hz, 1H), 7.25–7.14 (m, 3H); ¹³C NMR (75 MHz, CDCl₃ + DMSO– d_6) δ: 163.7 and 160.4 (d, J = 247.5 Hz), 141.1, 140.8, 137.8, 134.4, 132.8, 129.9 (d, J = 7.7 Hz), 1289.1, 127.5, 120.7, 120.6, 119.0, 115.0 (d, J = 20.9 Hz), 113.6, 111.8; MS (ESI): m/z 263 [M + H]⁺; HRMS (ESI): calcd for C₁₇H₁₂N₂F m/z 263.0979 [M + H]⁺; found: 263.0979.

4-(9*H*-Pyrido[3,4-*b*]indol-1-yl)benzonitrile (2m).⁵



White solid: 81% yield; mp: 230–233 °C (ref. 5: 230–232 °C); ¹H NMR (300 MHz, CDCl₃ + DMSO– d_6) δ: 11.03 (bs, 1H), 8.45 (d, J = 5.3 Hz, 1H), 8.15 (d, J = 8.1 Hz, 2H), 8.07 (d, J = 7.7 Hz, 1H), 7.93 (d, J = 5.3 Hz, 1H), 7.80 (d, J = 8.1 Hz, 2H), 7.55 (d, J = 7.9 Hz, 1H), 7.47 (t, J = 5.5 Hz, 1H), 7.20 (t, J = 7.7 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃ + DMSO– d_6) δ: 142.6, 140.9, 139.6, 138.2, 133.2, 131.8, 129.8, 128.7, 127.9, 120.9, 120.6, 119.4, 118.3, 114.1, 111.8, 110.9; MS (ESI): m/z 270 [M + H]⁺; HRMS (ESI): calcd for C₁₈H₁₂N₃ m/z 270.1025 [M + H]⁺; found: 270.1026.

1-(4-Nitrophenyl)-9*H*-pyrido[3,4-*b*]indole (2n).⁵



Yellow solid: 79% yield; mp: 243–246 °C (ref. 5: 244–246 °C); ¹H NMR (300 MHz, CDCl₃ + DMSO– d_6) δ: 10.82 (bs, 1H), 8.31 (d, J = 5.3 Hz, 1H), 8.17 (d, J = 8.9 Hz, 2H), 8.06 (d, J = 8.9 Hz, 2H), 7.92 (d, J = 7.9 Hz, 1H), 7.79 (d, J = 5.1 Hz, 1H), 7.40 (d, J = 8.1 Hz, 1H), 7.32 (t, J = 7.7 Hz, 1H), 7.06 (t, J = 7.0 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃ + DMSO– d_6) δ: 146.8, 144.5, 141.0, 139.2, 138.2, 133.3, 129.9, 129.0, 128.0, 123.2, 120.9, 120.5, 119.4, 114.4, 111.9; MS (ESI): m/z 290 [M + H]⁺; HRMS (ESI): calcd for C₁₇H₁₂O₂N₃ m/z 290.0924 [M + H]⁺; found: 290.0927.



White solid: 91% yield; mp: 169–173 °C (Ref. 2: 171–172 °C); ¹H NMR (300 MHz, CDCl₃ + DMSO– d_6) δ: 11.06 (bs, 1H), 8.35 (d, J = 5.1 Hz, 1H), 8.06 (d, J = 7.9 Hz, 1H), 7.84 (d, J = 5.1 Hz, 1H), 7.57 (d, J = 8.1 Hz, 1H), 7.52–7.40 (m, 3H), 7.17 (t, J = 7.2 Hz, 1H), 6.95 (d, J = 7.9 Hz, 1H), 6.02 (s, 2H); ¹³C NMR (75 MHz, CDCl₃ + DMSO– d_6) δ: 146.6, 146.5, 140.9, 140.0, 136.9, 131.8, 131.4, 128.1, 126.7, 121.1, 119.9, 119.8, 118.2, 112.0, 111.1, 107.6, 107.1, 99.9; MS (ESI): m/z 289 [M + H]⁺; HRMS (ESI): calcd for C₁₈H₁₃O₂N₂ m/z 289.0971 [M + H]⁺; found: 289.0973.

1-(Naphthalen-1-yl)-9*H*-pyrido[3,4-*b*]indole (2p).⁵



Off white solid: 94% yield; mp: 177–180 °C (ref. 5: 178–180 °C); ¹H NMR (300 MHz, CDCl₃ + DMSO– d_6) δ : 10.80 (bs, 1H), 8.46 (d, J = 5.3 Hz, 1H), 8.12 (d, J = 7.9 Hz, 1H), 8.00 (d, J = 5.5 Hz, 1H), 7.95 (d, J = 5.5 Hz, 1H), 7.84–7.79 (m,

1H), 7.72–7.67 (m, 2H), 7.62 (d, J = 7.5 Hz, 1H), 7.47 (t, J = 7.7 Hz, 1H), 7.45–7.40 (m, 2H), 7.34 (t, J = 8.1 Hz, 1H), 7.21–7.15 (m, 1H); ¹³C NMR (75 MHz, CDCl₃ + DMSO-*d*₆) δ: 141.3, 139.7, 136.4, 134.3, 133.4, 132.3, 130.0, 127.4, 127.2, 126.7, 126.6, 126.0, 124.8, 124.5, 124.3, 124.0, 119.9, 119.5, 117.9, 112.3, 110.8; MS (ESI): m/z 295 [M + H]⁺; HRMS (ESI): calcd for C₂₁H₁₄N₂ m/z 295.1229 [M+H]⁺; found: 295.1232.

1-(Phenanthren-9-yl)-9*H*-pyrido[3,4-*b*]indole (2q).



Off white solid: 95% yield; mp: 230–235 °C; ¹H NMR (300 MHz, CDCl₃ + DMSO– d_6) δ : 11.51 (bs, 1H), 8.88 (t, J = 8.6 Hz, 2H), 8.52 (d, J = 5.3 Hz, 1H), 8.22 (d, J = 7.9 Hz, 1H), 7.95 (d, J = 5.5 Hz, 1H), 8.13 (d, J = 5.3 Hz, 1H), 8.04 (s, 1H), 8.03 (d, J = 5.5 Hz, 1H), 7.78–7.64 (m, 4H), 7.53–7.42 (m, 3H), 7.26–7.19 (m, 1H); ¹³C NMR (125 MHz, CDCl₃+ DMSO- d_6) δ : 142.4, 140.9, 137.6, 137.5, 134.8, 133.8, 130.9, 130.3, 130.0, 128.9, 128.7, 128.2, 127.9, 127.2, 126.8, 126.6, 126.6, 126.3, 122.8, 122.4, 121.3, 120.7, 119.2, 113.8, 112.0; MS (ESI): m/z 345 [M + H]+; HRMS (ESI): calcd

for $C_{25}H_{17}N_2 m/z$ 345.1386 [M + H]⁺; found: 345.1369.

1-(Pyridin-3-yl)-9*H*-pyrido[3,4-*b*]indole (2r).⁵

White solid: 91% yield; mp: 203–208 °C (ref. 5: 205–208 °C); ¹H NMR (300 MHz, CDCl₃ + DMSO– d_6) δ : 11.08 (bs, 1H), 9.32 (s, 1H), 8.69 (dd, J = 1.1, 4.5 Hz, 1H), 8.55 (d, J = 5.2 Hz, 1H), 8.38 (d, J = 7.9 Hz, 1H), 8.16 (d, J = 7.9 Hz, 1H), 7.99 $(d, J = 5.1 \text{ Hz}, 1\text{H}), 7.63 (d, J = 8.1 \text{ Hz}, 1\text{H}), 7.57-7.49 (m, 2\text{H}), 7.28 (t, J = 7.1 \text{ Hz}, 1\text{H}); {}^{13}\text{C} \text{ NMR} (75 \text{ MHz}, \text{DMSO}-d_6) \delta:$ 149.3, 148.9, 141.1, 139.3, 138.5, 135.8, 134.0, 133.2, 129.3, 128.3, 123.8, 121.6, 120.6, 119.5, 114.4, 112.3; MS (ESI): *m/z* 246 $[M + H]^+$; HRMS (ESI): calcd for C₁₆H₁₂N₃ m/z 246.1025 $[M + H]^+$; found: 246.1012.

1-(4-Fluoro-3-methoxyphenyl)-9H-pyrido[3,4-b]indole (2s).



Creamish solid: 88% yield; mp: 130–135 °C; ¹H NMR (300 MHz, CDCl₃ + DMSO– d_6) δ : 11.45 (bs, 1H), 8.41 (d, J = 5.1Hz, 1H), 8.17 (d, J = 6.7 Hz, 1H), 8.01 (d, J = 5.1 Hz, 1H), 7.71 (dd, J = 1.7, 8.5 Hz, 1H), 7.62 (d, J = 8.3 Hz, 1H), 7.59–7.53 (m, 1H), 7.50 (t, J = 7.9 Hz, 1H), 7.33 (dd, J = 8.3, 11.1 Hz, 1H), 7.22 (t, J = 7.2 Hz, 1H), 3.98 (s, 3H); ¹³C NMR (125 MHz, $CDCl_3 + DMSO - d_6) \delta$: 152.7 and 150.7 (d, J = 247.0 Hz), 147.1 (d, J = 10.9 Hz), 141.2, 141.0, 137.7 (d, J = 17.2 Hz), 134.8 (d, J = 2.7 Hz), 132.8, 129.1, 127.9, 127.8, 121.1, 120.6, 119.2, 115.6 (dd, J = 3.6, 17.2 Hz), 113.6,

113.5, 112.2, 55.7; MS (ESI): m/z 293 [M + H]⁺; HRMS (ESI): calcd for C₁₈H₁₄ON₂F m/z 293.1084 [M + H]⁺; found: 293.1066.

1-(4-(trifluoromethyl)phenyl)-9H-pyrido[3,4-b]indole (2t).

Light yellow solid: 85% yield; mp: 150–153 °C; ¹H NMR (400 MHz, DMSO– d_6) δ : 8.51 (d, J = 5.1 Hz, 1H), 8.30 (d, J = 7.9 Hz, 1H), 8.25 (d, J = 8.1 Hz, 2H), 8.20 (d, J = 5.2 Hz, 1H), 7.97 (d, J = 8.2 Hz, 2H), 7.65 (d, J = 1H), 7.58 (t, J = 5.8 Hz, 2H), 7.65 (d, J = 1H), 7.58 (t, J = 5.8 Hz, 2H), 7.65 (d, J = 1H), 7.58 (t, J = 5.8 Hz, 2H), 7.65 (d, J = 1H), 7.58 (t, J = 5.8 Hz, 2H), 7.65 (d, J = 1H), 7.58 (t, J = 5.8 Hz, 2H), 7.65 (d, J = 1H), 7.58 (t, J = 5.8 Hz, 2H), 7.65 (d, J = 1H), 7.58 (t, J = 5.8 Hz, 2H), 7.65 (t, J = 1H), 7.29 (t, J = 6.7 Hz, 1H); ¹³C NMR (125 MHz, DMSO- d_6) δ : 142.2, 141.1, 140.3, 138.4, 133.1, 129.5, 129.1, 128.7, 128.4, 128.3, 125.4, 121.6, 120.6, 119.6, 114.6, 112.3; MS (ESI): *m/z* 313 [M + H]⁺. CF_3

Synthesis of Eudistomin I (6)

1-(Pyrrolidin-2-yl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole-3-carboxylic acid dihydrochloride (5)



A stirred solution of L-tryptophan (1.0 g, 4.90 mmol) and N-boc-L-prolinal (0.975 g, 4.90 mmol) in glacial acetic acid was heated at 80 °C for 2 h. After cooling to rt, the acetic acid was removed, the residue was taken in 1,4-dioxane (10 mL) and was added 2N HCl in 1,4-dioxane (5 ml) at 0 °C. The resulting reaction mixture was stirred at room temperature for 4 h. After total consumption of the starting material (monitored by TLC), the reaction mixture was concentrated under reduced pressure and dried well. The crude product was triturated in acetone, the resulted solid filtered and dried to afford the dihydrochloride salt 5 as white solid (1.57 g, 90% yield). mp: 238–240 °C; ¹H NMR (300 MHz, DMSO– d_6) δ :

11.61 (s, 0.2H), 11.47 (s, 0.8H), 10.36 (bs, 0.3H), 9.98 (bs, 0.8H), 9.61 (bs, 1H), 7.53 (d, J = 7.9 Hz, 1H), 7.39 (d, J = 8.1 Hz, 1H), 7.16 (t, J = 1.00 Hz, 1H), 7.10 (t, J = 1.00 7.3 Hz, 1H), 7.04 (t, J = 7.1 Hz, 1H), 5.44–5.24 (m, 1H), 4.74–4.63 (m, 1H), 4.61–4.51 (m, 1H), 4.30–4.15 (m, 1H), 3.46–3.27 (m, 3H),

3.04–2.92 (m, 1H), 2.22–1.76 (m, 4H); ¹³C NMR (75 MHz, DMSO–*d*₆) δ: 169.9, 136.5, 125.2, 125.1, 122.5, 119.2, 118.3, 111.6, 106.4, 59.2, 51.5, 51.2, 44.5, 27.5, 22.7, 22.1; MS (ESI): *m/z* 286 [M + H]⁺; HRMS (ESI): calcd for C₁₆H₂₀O₂N₃ *m/z* 286.1550 [M + H]⁺; found: 286.1545.

1-(3,4-Dihydro-2*H*-pyrrol-5-yl)-9*H*-pyrido[3,4-*b*]indole (or) eudistomin I (6).⁸



To a stirred solution of dihydrochloride salt **5** (500 mg, 1.39 mmol) in DMF (4 mL) was added TEA (0.97 mL, 6.98 mmol), cooled to 0 °C and added a solution of NCS (0.575 mg, 4.32 mmol) in DMF (5 mL) and the reaction mixture was allowed to stir at room temperature 30 min. After the completion of starting material (monitored by TLC) reaction mixture was diluted with water and extracted with ethyl acetate (2x50 mL), washed with water (50 mL), brine (50 mL), dried over sodium sulfate

and concentrated under reduced pressure. The crude product was purified by column chromatography using 20% ethyl acetate in `n-hexane to afford the eudistomin I (**6**, 288 mg, 70% yield) as a light yellow solid, mp: 151–154 °C (ref. 8: 153–155 °C); ¹H NMR (500 MHz, CDCl₃) δ : 10.85 (s, 1H), 8.50 (d, *J* = 5.0 Hz, 1H), 8.15 (d, *J* = 7.9 Hz, 1H), 8.00 (d, *J* = 5.1 Hz, 1H), 7.61–7.53 (m, 2H), 7.32–7.28 (m, 1H), 4.30–4.26 (m, 2H), 3.37–3.31 (m, 2H), 2.14–2.05 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) δ : 176.8, 140.8, 138.2, 135.8, 135.4, 129.5, 128.5, 121.8, 121.2, 120.1, 116.1, 111.9, 62.2, 34.9, 21.9; MS (ESI): *m/z* 236 [M + H]⁺. HRMS (ESI): calcd for C₁₅H₁₄N₃ *m/z* 236.1182 [M + H]⁺; found: 236.1185.

6-Bromo-9*H*-pyrido[3,4-*b*]indole (or) Eudistomin N (7)⁸



To a mixture of 0.1 N H_2SO_4 (1.5 mL) and 37% formaldehyde (0.8 mL) was added L-tryptophane (0.5 g, 2.4 mmol) with stirring. After being stirred for 4 h at room temperature, the resulted white solid was collected by filtration and dried well. The solid material was taken in DMF (7 mL), added TEA (0.61 mL, 7.34 mmol), cooled to 0 °C and added solution of

NCS (0.69 g, 5.14 mmol) in DMF. The reaction mixture was stirred for 30 min at room temperature, diluted with water (50 mL), extracted with ethylacetate (2x50 mL) and washed with water (50 mL). The combined extracts were dried over sodium sulfate, filtered, concentrated *in vacuo* and the crude product was purified by silica gel column chromatography using ethyl acetate:n-hexane (1:1) to afford norharmane (**2a**, 0.33 g, 80% yield). To the stirred solution of **2a** in acetic acid (10 mL) was added NBS (0.38 g, 2.16 mmol) and stirred for 5 h at room temperature. The solvent most removed *in vacuo* and neutralized with saturated Na₂HCO₃ solution and extracted with ethylacetate (2x30 mL) and washed with water (30 mL). The combined extracts were dried over sodium sulfate, filtered, concentrated *in vacuo* and the crude product was purified by silica gel column chromatography using ethyl acetate:n-hexane (1:1) to afford eudistomin N (7, 0.43 g, 89% yield) as creamish solid. Mp: 265–270 °C (ref. 8: 265–268 °C); ¹H NMR (300 MHz, CDCl₃ + DMSO–*d*₆) δ : 11.09 (bs, 1H), 8.84 (s, 1H), 8.31 (d, *J* = 5.3 Hz, 1H), 8.16 (S, 1H), 7.83 (d, *J* = 5.1 Hz, 1H), 7.51 (dd, *J* = 1.7, 8.6 Hz, 1H), 7.38 (d, *J* = 8.7 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃ + DMSO–*d*₆) δ : 139.1, 137.6, 136.0, 133.7, 130.2, 126.8, 123.6, 122.2, 114.0, 113.1, 111.3; MS (ESI): *m/z* 247 [M]⁺ and 249 [M + 2H]⁺; HRMS (ESI): calcd for C₁₁H₈N₂Br *m/z* 246.9865 [M + H]⁺; found: 246.9855.

Synthesis of eudistomin T (9)

tert-Butyl 2-phenyl-1-(9H-pyrido[3,4-b]indol-1-yl)ethylcarbamate (8)⁹



A stirred solution of L-tryptophan (1.0 g, 4.90 mmol) and *N*-boc-L-alaninal (1.22 g, 4.90 mmol) in glacial acetic acid was heated at 80 °C for 2 h. After cooling to rt, the acetic acid was removed, the residue was taken DMF (7 mL), added TEA (2.0 mL, 14.70 mmol), cooled to 0 °C and added solution of NCS (1.37 g, 10.29 mmol) in DMF. The reaction mixture was stirred for 30 min at room temperature, diluted with water (70 mL), extracted with ethyl acetate (2x70 mL) and washed with water (100 mL). The combined extracts were dried over sodium sulfate, filtered, concentrated *in vacuo* and the crude

product was purified by silica gel column chromatography using ethyl acetate:n-hexane (1:1) to afford compound **8** (1.51 g, 80% yield) as white solid. Mp: 236–240 °C (ref. 9: 230–232 °C); ¹H NMR (400 MHz, DMSO– d_6) δ : 8.29 (d, J = 5.1 Hz, 1H), 8.21 (d, J = 7.8 Hz, 1H), 8.01 (d, J = 5.1 Hz, 1H), 7.62 (d, J = 8.1 Hz, 1H), 7.55 (t, J = 7.4 Hz, 1H), 7.32–7.1 (m, 7H), 5.50 (q, J = 6.9, 13.8 Hz, 0.8H), 3.21–3.09 (m, 2H), 1.28 (s, 8H), peaks at 5.32 and 0.99 are due to the 20% minor rotamer; ¹³C NMR (100 MHz, DMSO– d_6) δ : 155.1, 145.1, 140.3, 138.1, 137.1, 137.0, 132.6, 129.3, 127.9, 127.8, 127.7, 125.9, 121.6, 121.5, 120.7, 119.2, 113.5, 111.8, 77.8, 53.1, 28.0; MS (ESI): m/z 388 [M + H]⁺; HRMS (ESI): calcd for C₂₄H₂₆O₂N₃ m/z 388.2019 [M + H]⁺; found: 388.2020.

2-Phenyl-1-(9*H*-pyrido[3,4-*b*]indol-1-yl)ethanone (or) Eudistomin T (9)⁹



To a stirred solution of boc product **8** (0.3 g, 1.04 mmol) in 1,4-dioxane (20 mL) was added 2 N HCl in 1,4-dioxane solution (1 mL) at 0°C and stirred for 3 h. After consumption of the starting material (monitored by TLC), the solvent removed *in vacuo* and dried. The crude product was dissolved in methanol (10 mL) and added sodium carbonate (4 g), followed by aq. NaOCl (1 mL, 5.9 % w/w) over a period of 15 mins. After being stirred for 1 h at room temperature, reaction mixture was diluted with 1 N HCl solution (30 mL), extracted with DCM (2x30 mL), washed with saturated

sodium bicarbonate solution (30 mL) and water (50 mL). The combined organic phases were dried over sodium sulfate, filtered and evaporated *in vacuo*. The crude product was purified by column chromatography using ethyl acetate and n-hexane (3:7) to afford eudistomin T (**9**) as yellow solid (0.19 g, 88% yield). Mp: 163–165°C (ref. 9: 155–157 °C); ¹H NMR (400 MHz, CDCl₃) δ : 10.26 (bs, 1H), 8.59 (d, *J* = 4.9 Hz, 1H), 8.15 (d, *J* = 5.5 Hz, 1H), 8.14 (d, *J* = 8.9 Hz, 1H), 7.61–7.56 (m, 1H), 7.51 (d, *J* = 8.2 Hz, 1H), 7.43–7.40 (m, 2H), 7.37–7.30 (m, 3H), 7.29–7.24 (m, 1H), 4.74 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ : 202.3, 141.0, 138.2, 135.9, 135.3, 134.9, 131.6, 130.0, 129.2, 128.4, 126.7, 121.8, 120.7, 120.5, 119.2, 111.9, 43.9; MS (ESI): *m/z* 287 [M + H]⁺; HRMS (ESI): calcd for C₁₉H₁₅ON₂*m/z* 287.1178 [M + H]⁺; found: 287.1175.

Synthesis of 1-(1*H*-indol-3-yl)-9*H*-pyrido[3,4-*b*]indole (or) Eudistomin U (10)¹⁰



A stirred solution of L-tryptophan (0.50 g, 2.45 mmol) and indole-3-carbaldehyde (0.35 g, 2.45 mmol) in glacial acetic acid (5 mL) was heated at 80 °C for 2 h. After cooling to rt, the solvent most was removed *in vacuo*, the residue was taken DMF (5 mL), added TEA (1.02 mL, 7.35 mmol), cooled to 0 °C and added solution of NCS (0.69 g, 5.14 mmol) in DMF (5 mL). The reaction mixture was stirred for 30 min at room temperature, diluted with water (30 mL), extracted with ethyl

acetate (2x50 mL) and washed with water (30 mL). The combined extracts were dried over sodium sulfate, filtered, evaporated *in vacuo* and the crude product was purified by silica gel column chromatography using ethyl acetate/methanol (9:1) to afford eudistomin U (**10**, 0.59 g, 85% yield) as light yellow solid. Mp: 230–235 °C (ref. 10: 235–236 °C); ¹H NMR (500 MHz, DMSO– d_6) δ : 11.72 (s, 1H), 11.31 (s, 1H), 8.55 (d, J = 7.9 Hz, 1H), 8.4 (d, J = 5.1 Hz, 1H), 8.30 (d, J = 2.7 Hz, 1H), 8.23 (d, J = 7.9 Hz, 1H), 7.95 (d, J = 5.1 Hz, 1H), 7.69 (d, J = 8.1 Hz, 1H), 7.56–7.50 (m, 2H), 7.25 (t, J = 7.3 Hz, 1H), 7.21 (t, J = 7.0 Hz, 1H), 7.14 (t, J = 7.9 Hz, 1H); ¹³C NMR (100 MHz, DMSO– d_6) δ : 140.6, 140.3, 137.8, 136.4, 131.9, 128.0, 127.6, 126.1, 125.9, 122.2, 121.9, 121.3, 121.1, 119.7, 119.3, 113.1, 112.3, 111.5, 111.4; MS (ESI): m/z 284 [M + H]⁺; HRMS (ESI): calcd for C₁₉H₁₄N₃ m/z 284.1182 [M + H]⁺; found: 284.1185.

Pictet-Spengler reaction and aromatization of tetrahydro-β-carboline esters.



Scheme S2: Synthesis of methyl-β-carbolinecarboxylates (4a-h)

General Procedure

To a stirred solution of L-tryptophan methyl ester hydrochloride (**3**, 1 mmol) in ethanol was added aldehyde (1 mmol), stirred at 80 °C for 4 h and the ethanol was evaporated *in vacuo* and dried well. This residue was directly taken in DMF, added TEA (2.5 mmol) and NCS (2.1 mmol) in DMF. Then the reaction mixture was stirred for 30 min at room temperature and after completion of the reaction (monitored by TLC), added ice cold water, the resulted solid was filtered, washed with water and dried well. The solid product was then triturated in 20-50% ethyl acetate and hexane solvent system, filtered and dried to afford the pure desired β -carboline esters (**4a-h**).

Methyl 1-phenethyl-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4a).

Brown solid: 81% yield; mp: 165–170 °C; ¹H NMR (300 MHz, CDCl₃) δ : 8.77 (s, 1H), 8.30 (bs, 1H), 8.13 (d, *J* = 7.9 Hz, 1H), 7.52 (t, *J* = 8.2 Hz, 1H), 7.37 (d, *J* = 8.2 Hz, 1H), 7.30 (t, *J* = 7.1 Hz, 1H), 7.21–7.15 (m, 3H), 7.12 (d, *J* = 7.9 Hz, 2H), 4.05 (s, 3H), 3.47 (t, *J* = 7.3 Hz, 2H), 3.18 (t, *J* = 7.7 Hz, 2H); ¹³C NMR (100 MHz, DMSO–*d*₆) δ : 166.1, 144.8, 141.5, 140.6, 135.9, 135.6, 128.4, 128.3, 128.1, 127.1, 125.8, 121.9, 121.2, 120.6, 116.0, 112.2, 51.8, 35.1, 33.5; MS (ESI): *m/z* 331 [M + H]⁺; HRMS (ESI): calcd for C₂₁H₁₉O₂N₂*m/z* 331.1441 [M + H]⁺; found: 331.1428.

Methyl 1-(3,4,5-trimethoxyphenyl)-9H-pyrido[3,4-b]indole-3-carboxylate (4b).¹¹



Off white solid: 94% yield; mp: 226–229 °C (ref. 11: 229–230 °C); ¹H NMR (300 MHz, CDCl₃ + DMSO– d_6) δ : 8.79 (s, 1H), 8.22 (d, J = 7.9 Hz, 1H), 7.64 (d, J = 8.3 Hz, 1H), 7.51 (t, J = 7.2 Hz, 1H), 7.26 (t, J = 7.2 Hz, 1H), 7.17 (s, 2H), 3.93 (s, 3H), 3.92 (s, 6H), 3.79 (s, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ : 165.8, 152.7, 142.2, 141.2, 137.8, 136.2, 134.5, 132.9, 128.7, 128.0, 121.1, 120.9, 119.9, 116.1, 112.4, 105.5, 59.9, 55.5, 51.6; MS (ESI): m/z 393 [M + H]⁺; HRMS (ESI): calcd for C₂₂H₂₁O₅N₂ m/z 393.1445 [M + H]⁺; found: 393.1432.

Methyl 1-(naphthalen-1-yl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4c).



White solid: 95% yield; mp: 294–297 °C; ¹H NMR (300 MHz, DMSO–d₆) δ : 11.61 (s, 1H), 9.05 (s, 1H), 8.48 (d, J = 7.7 Hz, 1H), 8.16 (dd, J = 2.5, 6.8 Hz, 1H), 8.11 (d, J = 8.1 Hz, 1H), 7.78–7.73 (m, 2H), 7.62–7.53 (m, 4H), 7.44 (t, J = 6.9 Hz, 1H), 7.33 (t, J = 7.7 Hz, 1H), 3.90 (s, 3H): ¹³C NMR (125 MHz, DMSO–d₆) δ : 166.0, 142.4, 141.2, 136.3, 136.2, 134.6, 133.4, 131.1, 128.9, 128.6, 128.4, 128.2, 127.5, 126.5, 126.1, 125.5, 125.2, 122.1, 121.1, 120.2, 116.9, 112.5, 51.9; MS (ESI): m/z 353 [M + H]⁺; HRMS (ESI): calcd for C₂₃H₁₇O₂N₂ m/z 353.1284 [M + H]+; found:

353.1288.

Methyl 1-(4-chlorophenyl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4d).¹²



Yellow solid: 92% yield; mp: 268–272 °C (ref. 12: 270 °C); ¹H NMR (300 MHz, CDCl₃ + DMSO– d_6) δ (ppm): 8.81 (s, 1H), 8.23 (d, J = 7.7 Hz, 1H), 8.01 (d, J = 8.3 Hz, 1H), 7.64 (d, J = 8.3 Hz, 1H), 7.59–7.51 (m, 3H), 7.27 (t, J = 7.2 Hz, 1H), 6.92 (d, J = 7.4 Hz, 1H), 3.93 (s, 3H); ¹³C NMR (100 MHz, DMSO– d_6) δ (ppm); 165.8, 141.4, 140.6, 136.5, 136.2, 134.4, 133.6, 130.3, 129.3, 128.7, 125.4, 121.9, 120.9, 120.4, 116.8, 112.6, 51.9; MS (ESI): m/z 337 [M + H]⁺; HRMS (ESI): calcd for C₁₉H₁₄O₂N₂Cl m/z 337.0738 [M + H]⁺; found: 337.0729.

Methyl 1-(phenanthren-9-yl)-9H-pyrido[3,4-b]indole-3-carboxylate (4e).9



White solid: 96% yield; mp: 290–295 °C; ¹H NMR (300 MHz, DMSO– d_6 + CDCl₃) & 11.56 (s, 1H), 8.98 (s, 1H), 8.89 (t, J = 8.7 Hz, 2H), 8.34 (d, J = 7.9 Hz, 1H), 8.03 (d, J = 6.6 Hz, 2H), 7.80–7.60 (m, 4H), 7.52–7.45 (m, 3H), 7.29 (t, J = 7.9 Hz, 1H), 3.92 (s, 3H): ¹³C NMR (125 MHz, DMSO– d_6 + CDCl₃) & 165.9, 142.3, 141.2, 136.4, 136.2, 133.2, 130.8, 130.2, 130.1, 130.0, 128.9, 128.4, 128.3, 127.2, 126.8, 126.7, 126.6, 126.1, 122.8, 122.5, 121.5, 121.0, 120.0, 116.8, 112.3, 51.8; MS (ESI): m/z 403 [M + H]⁺; HRMS (ESI): calcd for C₂₇H₁₉O₂N₂ m/z 403.1441 [M + H]+; found: 403.1427.

Methyl 1-(4-fluoro-3-methoxyphenyl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4f).



Off white solid: 94% yield; mp: 215–220 °C; ¹H NMR (300 MHz, DMSO– d_6) δ : 8.94 (s, 1H), 8.44 (d, J = 7.9 Hz, 1H), 7.73–7.66 (m, 2H), 7.61 (t, J = 7.2 Hz, 1H), 7.55–7.43 (m, 2H), 7.34 (t, J = 7.4 Hz, 1H), 3.99 (s, 3H), 3.93 (s, 3H); ¹³C NMR (725 MHz, DMSO– d_6) δ : 165.8, 152.8 and 150.9 (d, J = 246.1 Hz), 147.1 (d, J = 10.9 Hz), 141.3 (d, J = 3.6 Hz), 136.4, 134.5, 134.2 (d, J = 3.6 Hz), 129.0, 128.6, 121.9, 121.1 (d, J = 7.2 Hz), 121.0, 120.3, 116.7, 116.1, 116.0, 114.0 (1.8 Hz), 112.6, 55.9, 51.9; MS (ESI): m/z 351 [M + H]⁺; HRMS (ESI): calcd for C₂₀H₁₆O₃N₂ F m/z 351.1139 [M + H]⁺; found: 351.1128.

Methyl 1-(4-(trifluoromethyl)phenyl)-9H-pyrido[3,4-b]indole-3-carboxylate (4g).⁵

White solid: 91% yield; mp: 303–306°C (ref. 5: 306–310 °C); ¹H NMR (300 MHz, DMSO– d_6) δ : 8.80 (s, 1H), 8.13 (t, J = 7.4 Hz, 3H), 7.75 (d, J = 8.3 Hz, 2H), 7.60 (d, J = 8.1 Hz, 1H), 7.50 (t, J = 7.7 Hz, 1H), 7.26 (t, J = 7.5 Hz, 1H), 3.95 (s, 3H); ¹³C NMR (75 MHz, DMSO– d_6) δ : 165.6, 141.4, 141.2, 140.2, 136.6, 134.6, 129.4, , 129.3, 129.2, 129.2, 128.5, 125.3 (q, J = 3.8, 7.7 Hz), 121.7, 120.9, 120.3, 116.9, 112.5, 51.8; MS (ESI): m/z 371 [M + H]⁺; HRMS (ESI): calcd for C₂₀H₁₄O₂N₂F₃ m/z 371.1001 [M + H]⁺; found: 371.0993.

Methyl 1-(1-((*tert*-butoxycarbonyl)amino)-2-phenylethyl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4h)



White solid: 88% yield; mp: 147–150 °C; ¹H NMR (400 MHz, DMSO– d_6) δ: 12.01 (bs, 1H), 8.85 (s, 1H), 8.38 (d, J = 7.8 Hz, 1H), 7.69 (d, J = 8.2 Hz, 1H), 7.62 (t, J = 7.2 Hz, 1H), 7.37–7.26 (m, 4H), 7.22 (t, J = 7.2 Hz, 2H), 7.14 (d, J = 7.2 Hz, 1H), 5.52 (q, J = 7.2, 14.7 Hz, 1H), 3.94 (s, 3H), 3.22 (d, J = 7.1 Hz, 2H), 1.30 and 0.96 (s, 8H and s, 1H); ¹³C NMR (100 MHz, DMSO– d_6) δ: 165.8, 155.1, 145.2, 140.7, 137.9, 135.7, 134.5, 129.4, 128.5, 127.9, 127.7, 126.0, 121.9, 120.9, 120.2, 116.7, 112.2, 78.0, 53.6, 51.9, 40.0, 28.0; MS (ESI): m/z 446 [M + H]⁺; HRMS (ESI): calcd for $C_{26}H_{28}O_4N_3$ m/z 446.2074 [M + H]⁺; found: 446.2063.

1-(4-Methoxyphenyl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (14).¹³



Creamish solid: 85% yield; mp: 185–188 °C (ref. 13: 196–197 °C); ¹H NMR (300 MHz, DMSO–*d*₆) δ: 7.78 (d, *J* = 7.6 Hz, 1H), 7.46–7.39 (m, 1H), 7.34–7.28 (m, 2H), 6.76 (d, *J* = 8.8 Hz, 2H), 6.29 (d, *J* = 8.8 Hz, 2H), 4.67–4.55 (m, 1H), 4.51–4.39 (m, 1H), 3.52 (s, 3H), 2.94 (m, 1H), 2.31–2.21 (m, 1H); ¹³C NMR (75 MHz, DMSO–*d*₆) δ: 174.1, 167.5, 160.1, 153.5, 143.8, 128.6, 128.5, 127.7, 125.3, 122.6, 121.9, 113.1, 72.5, 59.8, 54.6, 36.9; MS (ESI): *m/z* 277 [M + H]⁺.

1-(4-Nitrophenyl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (15)¹⁴



Yellow solid: 82% yield; mp: 218–220 °C (ref. 14: 220–222 °C); ¹H NMR (300 MHz, DMSO– d_6 + CDCl₃) δ : 11.04 (s, 1H), 8.30 (d, J = 8.7 Hz, 2H), 7.99 (d, J = 8.7 Hz, 2H), 7.55 (d, J = 7.9 Hz, 1H), 7.38 (d, J = 8.1 Hz, 1H), 7.17 (t, J = 7.5 Hz, 1H), 7.04 (t, J = 7.5 Hz, 1H), 3.96 (t, J = 7.9 Hz, 2H), 2.89 (t, J = 8.3 Hz, 2H); ¹³C NMR (75 MHz, DMSO– d_6 + CDCl₃) δ : 155.8, 146.4, 141.6, 135.5, 127.6, 125.3, 123.0, 122.3, 121.6, 118.0, 117.8, 115.3, 110.9, 47.1, 17.3; MS (ESI): m/z 292 [M + H]⁺.

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9*H*-Pyrido[3,4-*b*]indole (norharmane, 2a) ¹H NMR (300 MHz, CDCl₃)



¹³C NMR (125 MHz, DMSO-*d*₆)









1-Methyl-9*H*-pyrido[3,4-*b*]indole (harmane, 2b)





¹³C NMR (75 MHz, $CDCl_3 + DMSO-d_6$)





Harmane (2b)

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150	140	130	120	110	100	90	80	70	<mark>60</mark>	5 0	40	30	20	10	0

1-Propyl-9*H*-pyrido[3,4-*b*]indole (2c)

¹H NMR (300 MHz, DMSO-*d*₆)



¹³C NMR (100 MHz, DMSO-*d*₆)





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150	140	130	120	110	100	90	80	70	60	50	40	30	20	10	0

1-(4-Methoxybenzyl)-9*H*-pyrido[3,4-*b*]indole (2d)

¹H NMR (300 MHz, DMSO– d_6)



¹³C NMR (100 MHz, DMSO-*d*₆)





1-Phenyl-9*H*-pyrido[3,4-*b*]indole (2e)

¹H NMR (300 MHz, DMSO-*d*₆)



¹³C NMR (75 MHz, DMSO-*d*₆)







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150	140	120	120	110	100		••••				40	20	20	10	•••••
150	140	130	120	110	100	90	80	70	00	50	40	30	20	10	0

1-(*p*-Tolyl)-9*H*-pyrido[3,4-*b*]indole (2f)

¹H NMR (300 MHz, $CDCl_3 + DMSO-d_6$)



¹³C NMR (75 MHz, CDCl₃ + DMSO-*d*₆)



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140	130	120	110	100	90	80	70	60	50	40	30	20	10	0

1-(2-Methoxyphenyl)-9*H*-pyrido[3,4-*b*]indole (2g)

¹H NMR (500 MHz, CDCl₃)



¹³C NMR (75 MHz, CDCl₃ + DMSO-*d*₆)



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160	150	140	130	120	110	100	90	80	70	60	50	40	30	20	10	0

1-(3,4,5-Trimethoxyphenyl)-9*H*-pyrido[3,4-*b*]indole (2h)

¹H NMR (500 MHz, CDCl₃)



¹³C NMR (CDCl₃, 75 MHz)



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160	150	140	130	120	110	100	<mark>90</mark>	80	70	60	50	40	<u>30</u>	20	10	••••• <u>0</u>

2-Methoxy-4-(9*H*-pyrido[3,4-*b*]indol-1-yl)phenol (2i) ¹H NMR (300 MHz, CDCl₃ + DMSO-*d*₆)



¹³C NMR (75 MHz, CDCl₃ + DMSO $-d_6$)



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150	140	130	120	110	100	90	80	70	60	50	40	30	20	10	•••••

3-(9H-Pyrido[3,4-b]indol-1-yl)phenol (2j)

NMR (300 MHz, CDCl₃+DMSO-d₆)



¹³C NMR (75 MHz, CDCl₃ + DMSO-d6)





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160	150	140	130	120	110	100	90	<mark>80</mark>	70	60	50	40	30	<mark>2</mark> 0	10	••••••••••••••••••••••••••••••••••••••

1-(4-Chlorophenyl)-9*H*-pyrido[3,4-*b*]indole (2k) ¹H NMR (300 MHz, CDCl₃ + DMSO-*d*₆)



¹³C NMR (125 MHz, CDCl₃ + DMSO-*d6*)





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S20

1-(4-Fluorophenyl)-9*H*-pyrido[3,4-*b*]indole (2l) ¹H NMR (300 MHz, CDCl₃ + DMSO–*d*₆)



¹³C NMR (75 MHz, CDCl₃ + DMSO $-d_6$)





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170	160	150	140	130	120	110	100	<mark>90</mark>	<mark>80</mark>	7 0	<mark>60</mark>	<mark>50</mark>	40	30	20	10	0

4-(9*H*-Pyrido[3,4-*b*]indol-1-yl)benzonitrile (2m)

¹H NMR (300 MHz, $CDCl_3 + DMSO-d_6$)



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C NMR (75 MHz, $CDCl_3 + DMSO-d_6$)





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							****				*****		*****		
150	140	130	120	110	100	90	80	70	60	50	40	30	20	10	0

1-(4-Nitrophenyl)-9*H*-pyrido[3,4-*b*]indole (2n)

¹H NMR (300 MHz, $CDCl_3 + DMSO-d_6$)



¹³C NMR (75 MHz, $CDCl_3 + DMSO-d_6$)



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150 140	130	120	110	100	90	80	70	60	50	40	30	20	10	••••• <u>0</u>

1-(Benzo[*d*][1,3]dioxol-5-yl)-9*H*-pyrido[3,4-*b*]indole (20) ¹H NMR (300 MHz, CDCl₃ + DMSO-*d*₆)



¹³C NMR (75 MHz, CDCl₃ + DMSO-d₆)







S24

1-(Naphthalen-1-yl)-9*H*-pyrido[3,4-*b*]indole (2p)

¹H NMR (300 MHz, $CDCl_3 + DMSO-d_6$)



¹³C NMR (75 MHz, CDCl₃+DMSO- d_6)







S25

1-(Phenanthren-9-yl)-9*H*-pyrido[3,4-*b*]indole (2q)

¹H NMR (300 MHz, $CDCl_3 + DMSO-d_6$)



¹³C NMR (125 MHz, CDCl₃ + DMSO $-d_6$)







S26

1-(Pyridin-3-yl)-9*H*-pyrido[3,4-*b*]indole (2r)





¹³C NMR (75 MHz, DMSO-*d*₆)







1-(4-Fluoro-3-methoxyphenyl)-9*H*-pyrido[3,4-*b*]indole (2s) ¹H NMR (300 MHz, CDCl₃ + DMSO-*d*₆)



¹³C NMR (125 MHz, CDCl₃ + DMSO-*d*₆)







55.704

1-(4-(trifluoromethyl)phenyl)-9H-pyrido[3,4-b]indole (2t)

¹H NMR (400 MHz, DMSO-*d*₆)



¹³C NMR (125 MHz, DMSO-*d*₆)







1-(Pyrrolidin-2-yl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole-3-carboxylic acid dihydrochloride (5) ¹H NMR (300 MHz, DMSO-*d*₆)



¹³C NMR (75 MHz, DMSO-*d*₆)



2HCI

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5

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170	160	150	140	130	120	110	100	00	80	70	60	50	10	30	20	10	•••••

1-(3,4-Dihydro-2*H*-pyrrol-5-yl)-9*H*-pyrido[3,4-*b*]indole (or) eudistomin I (6) ¹H NMR (500 MHz, CDCl₃)



³C NMR (125 MHz, CDCl₃)



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180	170	160	150	140	130	120	11(100	90	80	70	60	50	40	30	20	10	0

6-Bromo-9*H*-pyrido[3,4-*b*]indole (or) Eudistomin N (7) ¹H NMR (300 MHz, CDCl₃ + DMSO-*d*₆)



¹³C NMR (125 MHz, CDCl₃ + DMSO-*d*₆)





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140	130	120	110	100	90	80	70	60	50	40	30	20	10	••••

tert-Butyl 2-phenyl-1-(9*H*-pyrido[3,4-*b*]indol-1-yl)ethylcarbamate (8)

¹H NMR (400 MHz, DMSO-*d*₆)



¹³C NMR (100 MHz, DMSO-*d*₆)



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160	150	140	130	120	110	100	90	80	7 0	60	50	40	30	20	10	0

2-Phenyl-1-(9*H*-pyrido[3,4-*b*]indol-1-yl)ethanone (or) Eudistomin T (9) ¹H NMR (400 MHz, CDCl₃)



¹³C NMR (100 MHz, CDCl₃)



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200	175	150	125	100	75	50	25	0

Synthesis of 1-(1*H*-indol-3-yl)-9*H*-pyrido[3,4-*b*]indole (or) Eudistomin U (10) ¹H NMR (500 MHz, DMSO-*d*₆)



¹³C NMR (100 MHz, DMSO-*d*₆)





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140	130	120	110	100	<mark>90</mark>	80	70	60	50	40	30	20	10	0

Methyl 1-phenethyl-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4a)

¹H NMR (300 MHz, CDCl₃)



¹³C NMR (100 MHz, DMSO-*d*₆)



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170	160	150	140	130	120	110	100	<mark>90</mark>	80	7 0	60	<mark>50</mark>	40	30	20	10	0

Methyl 1-(3,4,5-trimethoxyphenyl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4b)

¹H NMR (300 MHz, $CDCl_3 + DMSO-d_6$)



¹³C NMR (CDCl₃, 75 MHz)



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170 160	150	140	130	120	110	100	90	80	70	60	50	4 0	30	20	10	0

Methyl 1-(naphthalen-1-yl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4c) ¹H NMR (300 MHz, DMSO-d₆)



¹³C NMR (125 MHz, DMSO-*d*₆)



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170	160	150	140	130	120	110	100	90	80	70	60	50	40	30	20	10	0

Methyl 1-(4-chlorophenyl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4d)

¹H NMR (300 MHz, $CDCl_3 + DMSO-d_6$)



¹³C NMR (100 MHz, DMSO-*d*₆)



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170	160	150	140	130	120	110	100	90	80	70	60	<mark>5</mark> 0	<mark>40</mark>	30	20	10	••••••••••••••••••••••••••••••••••••••

Methyl 1-(phenanthren-9-yl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4e) ¹H NMR (300 MHz, DMSO-*d*₆ + CDCl₃)



¹³C NMR (125 MHz, DMSO $-d_6$ + CDCl₃)



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170	160	150	140	130	120	110	100	90	80	70	60	50	40	30	20	10	0

Methyl 1-(4-fluoro-3-methoxyphenyl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4f) ¹H NMR (300 MHz, DMSO-*d*₆)



¹³C NMR (725 MHz, DMSO–*d*₆)



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170	160	150	140	130	120	110	100	90	80	70	60	50	40	30	20	10	••••••••••••••••••••••••••••••••••••••

Methyl 1-(4-(trifluoromethyl)phenyl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4g)

¹H NMR (300 MHz, DMSO-*d*₆)



¹³C NMR (75 MHz, DMSO-*d*₆)



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170	160	150	140	130	120	110	100	<u>90</u>	80	70	60	50	40	30	20	10	0

Methyl 1-(1-((*tert*-butoxycarbonyl)amino)-2-phenylethyl)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate (4h) ¹H NMR (400 MHz, DMSO-*d*₆)



¹³C NMR (100 MHz, DMSO-*d*₆)



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															l		
170	160	150	140	130	120	110	100	90	80	70	60	50	40	30	20	10	0

1-(4-Methoxyphenyl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (15)

¹H NMR (300 MHz, DMSO– d_6)



¹³C NMR (75 MHz, DMSO-*d*₆)



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175		1	150)			1	125	I	,	2	51	100)	13	I		75	1	I.			50	1			2	25	5					0	

1-(4-Nitrophenyl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (16) ¹H NMR (300 MHz, DMSO-*d*₆ + CDCl₃)



¹³C NMR (75 MHz, DMSO– d_6 + CDCl₃)





S45