Electronic Supplementary Material (ESI) for MedChemComm.

Electronic Supplementary Information

Integrating Multicomponent Flow Synthesis and Computational Approaches for the Generation of a Tetrahydroquinoline Compound Based Library

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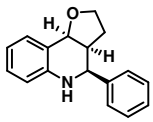
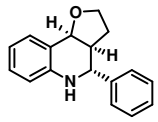
Spectral data of TC-THQ derivatives

(±)-*cis* 4-phenyl-2,3,3a,4,5,9b-hexahydro-furo[3,2-c]quinoline (4a)[1]



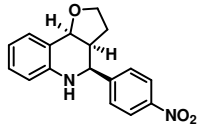
Isolated yield: 65% (164 mg, 0.6526 mmol). White solid (m.p. 93-95 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.51-1.55 (m, 1H), 2.19-2.24 (m, 1H), 2.78-2.81 (m, 1H), 3.69-3.75 (m, 1H), 3.81-3.86 (m, 1H), 4.71 (d, *J*= 2.89 Hz, 1H), 5.29 (d, *J*= 7.96 Hz, 1H), 6.61 (d, *J*= 8.01 Hz, 1H), 6.83 (t, *J*= 8.01 Hz, 1H), 7.09 (t, *J*= 8.01 Hz, 1H), 7.32-7.48 (m, 6H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 24.6, 45.7, 57.5, 66.8, 75.9, 114.9, 119.2, 122.7, 126.5, 127.6, 128.3, 128.6, 130.1, 142.1, 144.9. GC-MS: m/z = 251.

(±)-*trans* 4-phenyl-2,3,3a,4,5,9b-hexahydro-furo[3,2-c]quinoline (4b)[1]



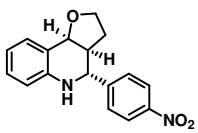
Isolated yield: 13% (33 mg, 0.1313 mmol). Viscous oil. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.71-1.74 (m, 1H), 2.00-2.04 (m, 1H), 2.47-2.49 (m, 1H), 3.79-3.88 (m, 2H), 4.01-4.08 (m, 1H), 4.61 (d, *J*= 5.03 Hz, 1H), 6.63 (d, *J*= 8.09 Hz, 1H), 6.82 (t, *J*= 7.42 Hz, 1H), 7.13 (t, *J*= 7.76 Hz, 1H), 7.36-7.47 (m, 6 H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 28.8, 43.3, 57.7, 65.2, 76.2, 114.7, 118.4, 120.0, 126.5, 128.1, 128.3, 128.9, 131.2, 141.6, 145.4. GC-MS: m/z = 251.

(±)-*cis* 4-(4-nitrophenyl)-2,3,3a,4,5,9b-hexahydro-furo[3,2-c]quinoline (12a)[2,3]



Isolated yield: 84% (250 mg, 0.8428 mmol). Yellow solid (m.p. 159-161 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.44-1.56 (m, 1H), 2.04-2.12 (m, 1H), 2.68-2.76 (m, 1H), 2.82-3.24 (m, 2H), 4.84 (d, *J*= 3.20 Hz, 1H), 5.36 (d, *J*= 7.60 Hz, 1H), 6.62 (d, *J*= 9.06 Hz, 1H), 6.88 (t, *J*= 7.62 Hz, 1H), 7.18 (t, *J*= 7.86 Hz, 1H), 7.47 (d, *J*= 7.62 Hz, 1H), 7.64 (d, *J*= 8.44 Hz, 2H), 8.27 (d, *J*= 8.44 Hz, 2H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 24.7, 44.8, 56.5, 66.8, 74.9, 113.9, 118.8, 125.7, 126.5, 127.0, 128.2, 128.8, 129.1, 140.6, 149.8. GC-MS: m/z = 297.

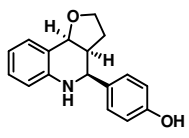
(±)-*trans* 4-(4-nitrophenyl)-2,3,3a,4,5,9b-hexahydro-furo[3,2-c]quinoline (12b)[2,3]



Isolated yield: 5% (15 mg, 0.0506 mmol). Yellow solid (m.p. 154-157 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.64-1.72 (m, 1H), 2.08-2.22 (m, 1H), 2.82-2.91 (m, 1H), 3.78-3.90 (m, 2H), 4.12 (m, 1H), 4.72 (d, *J*= 5.60 Hz, 1H), 6.64 (d, *J*= 8.12 Hz, 1H), 6.89 (t, *J*= 7.66 Hz, 1H), 7.21 (t, *J*= 7.82 Hz, 1H), 7.42 (d, *J*= 7.58 Hz, 1H), 7.72 (d, *J*= 8.37 Hz, 2H), 8.29 (d,

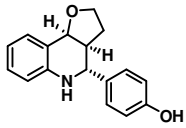
J= 8.36 Hz, 2H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 25.1, 47.2, 54.6, 58.4, 68.8, 114.6, 119.9, 122.4, 124.8, 125.4, 127.4, 129.2, 131.1, 143.8, 147.4. GC-MS: m/z = 297.

(±)-*cis* 4-(4-hydroxyphenyl)-2,3,3a,4,5,9b-hexahydro-furo[3,2-c]quinoline (13a)[4]



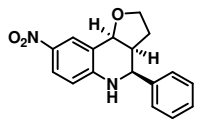
Isolated yield: 40% (108 mg, 0.4040 mmol). Whitish solid (m.p. 156-157 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.52-1.58 (m, 1H), 2.23-2.29 (m, 1H), 2.76-2.81 (m, 1H), 3.65 (brs, 1H), 3.74-3.90 (m, 2H), 4.62 (d, *J*= 2.68 Hz, 1H), 5.28 (d, *J*= 8.0 Hz, 1H), 5.72 (brs, 1H), 6.53 (d, *J*= 14.56 Hz, 1H), 6.67 (dd, J_1= 2.76 Hz, J_2= 8.54 Hz, 1H), 6.94 (d, *J*= 2.76 Hz, 1H), 7.30-7.33 (m, 1H), 7.39 (t, *J*= 7.15 Hz, 2H), 7.40-7.47 (m, 2H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 24.6, 45.7, 57.5, 66.8, 75.9, 114.1, 114.8, 121.6, 126.5, 127.6, 128.3, 128.6, 130.1, 143.2, 154.1. GC-MS: m/z = 268.

(±)-*trans* 4-(4-hydroxyphenyl)-2,3,3a,4,5,9b-hexahydro-furo[3,2-c]quinoline (13b)[4]



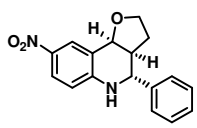
Isolated yield: 18% (48 mg, 0.1796 mmol). Pale yellow solid (m.p. 147-149 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.51-1.56 (m, 1H), 2.08-2.21 (m, 1H), 2.66-2.78 (m, 1H), 3.68-3.85 (m, 3H), 4.63 (d, *J*= 4.96 Hz, 1H), 5.73 (brs, 1H), 6.56 (d, *J*= 8.56 Hz, 1H), 6.72 (dd, J_1= 2.78 Hz, J_2= 8.76 Hz, 1H), 6.92 (d, *J*= 2.76 Hz, 1H), 7.29-7.32 (m, 1H), 7.38 (t, *J*= 7.15 Hz, 2H), 7.42-7.48 (m, 2H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 28.7, 43.2, 57.6, 66.0, 76.1, 114.5, 118.2, 122.5, 127.5, 128.2, 128.7, 129.1, 131.1, 142.1, 152.3. GC-MS: m/z = 268.

(±)-*cis* 8-nitro-4-phenyl-2,3,3a,4,5,9b-hexahydro-furo[3,2-c]quinoline (14a)[3]



Isolated yield: 66% (196 mg, 0.6614 mmol). Yellow solid (m.p. 169-170 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.42-1.54 (m, 1H), 2.19-2.24 (m, 1H), 3.64-3.78 (m, 3H), 3.81 (brs, 1H), 4.70 (d, *J*= 2.98 Hz, 1H), 5.32 (d, *J*= 7.98 Hz, 1H), 6.63 (d, *J*= 8.87 Hz, 1H), 7.24-7.42 (m, 5H), 7.87 (dd, J_1= 8.87 Hz, J_2= 2.49 Hz, 1H), 8.16 (s, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 22.8, 49.4, 54.1, 58.4, 69.2, 114.9, 115.8, 121.6, 122.4, 123.8, 125.3, 127.2, 130.1, 144.6, 146.8. GC-MS: m/z = 297.

(±)-*trans* 8-nitro-4-phenyl-2,3,3a,4,5,9b-hexahydro-furo[3,2-c]quinoline (14b)[3]

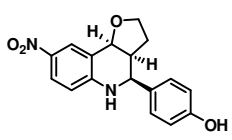


Isolated yield: 13% (38 mg, 0.1282 mmol). Yellow solid (m.p. 163-166 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.56-1.64 (m, 1H), 1.88-1.92 (m, 1H), 2.38-2.46 (m, 1H), 3.78-3.82 (m, 2H), 3.98-4.04 (m, 1H), 4.56 (d, *J*= 4.92 Hz, 1H), 6.64 (d, *J*= 8.85 Hz, 1H),

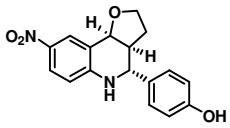
7.24-7.42 (m, 5H), 7.86 (dd, J_1= 8.85 Hz, J_2= 2.51 Hz, 1H), 8.15 (s, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 22.8, 49.4, 54.1, 58.4, 69.2, 114.9, 115.8, 121.6, 122.4, 123.8, 125.3, 127.2, 130.1, 144.6, 146.8. GC-MS: m/z = 297.

8-nitro-4-(4-hydroxyphenyl)-2,3,3a,4,5,9b-hexahydro-furo[3,2-c]quinoline (15)

Isolated yield: 82% (255 mg, 0.8164 mmol) as mixture *cis/trans* 78:22.

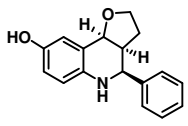


(±)-*cis* **15a** (partial characterization from the inseparable diasteromeric mixture). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.61-1.64 (m, 1H), 2.07-2.12 (m, 1H), 2.81-2.84 (m, 1H), 3.80-3.86 (m, 1H), 3.93-3.96 (m, 1H), 4.90 (d, *J*= 3.05 Hz, 1H), 5.28 (d, *J*= 7.42 Hz, 1H), 6.60 (d, *J*= 8.91 Hz, 2H), 6.92-6.96 (m, 1H), 7.02 (d, *J*= 2.50 Hz, 2H), 8.00 (d, *J*= 8.91 Hz, 1H), 8.13 (s, 1H).



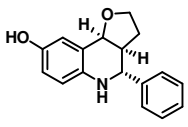
(±)-*trans* **15b** (partial characterization from the inseparable diasteromeric mixture). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.78-1.82 (m, 1H), 2.07-2.12 (m, 1H), 2.43-2.48 (m, 1H), 3.80-3.86 (m, 2H), 4.08-4.10 (m, 1H), 4.62 (d, *J*= 4.58 Hz, 1H), 6.62 (d, *J*= 8.85 Hz, 2H), 6.92-6.96 (m, 1H), 7.04 (d, *J*= 2.36 Hz, 2H), 7.98 (d, *J*= 8.54 Hz, 1H), 8.12 (s, 1H).

(±)-*cis* 8-hydroxy-4-phenyl-2,3,3a,4,5,9b-hexahydro-furo[3,2-c]quinoline (16a)



Isolated yield: 39% (104 mg, 0.3890 mmol). White solid (m.p. 183-186 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.50-1.58 (m, 1H), 2.20-2.31 (m, 1H), 2.79 (dq, J_1= 2.87, J_2= 8.12, 1H), 3.64 (brs, 1H), 3.76 (q, *J*= 8.54, 1H), 3.87 (dt, J_1= 3.30, J_2= 8.39, 1H), 4.62 (d, *J*= 2.68 Hz, 1H), 5.28 (d, *J*= 8.00 Hz, 1H), 5.72 (brs, 1H), 6.53-6.55 (m, 1H), 6.67 (dd, J_1= 2.76, J_2= 8.54, 1H), 6.94 (d, *J*= 2.76 Hz, 1H), 7.30-7.33 (m, 1H), 7.39 (t, *J*= 7.15 Hz, 2H), 7.46-7.48 (m, 2H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 24.4, 45.7, 57.9, 67.0, 76.3, 116.0, 116.3, 117.4, 123.2, 126.5, 127.6, 128.6, 138.8, 142.2, 149.1. GC-MS: m/z = 268.

(±)-*trans* 8-hydroxy-4-phenyl-2,3,3a,4,5,9b-hexahydro-furo[3,2-c]quinoline (16b)

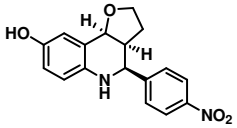


Isolated yield: 25% (68 mg, 0.2544 mmol). Pale yellow solid (m.p. 179-181 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.62-1.68 (m, 1H), 1.96-2.04 (m, 1H), 2.42-2.48 (m, 1H), 3.64 (brs, 1H), 3.78-3.86 (m, 2H), 4.10-4.16 (m, 1H), 4.60 (d, *J*= 5.02 Hz, 1H), 6.56-6.58 (m, 1H), 6.68 (dd, J_1= 2.72, J_2= 8.22, 1H), 6.97 (d, *J*= 2.72 Hz, 1H), 7.28-7.32 (m, 1H), 7.40 (t, *J*=

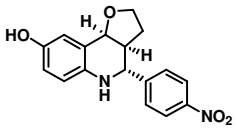
7.2 Hz, 2H), 7.45-7.47 (m, 2H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 28.6, 43.4, 58.1, 65.4, 76.6, 114.8, 115.8, 116.0, 121.4, 126.5, 127.6, 128.8, 139.9, 141.6, 149.8. GC-MS: m/z = 268.

4-(4-nitrophenyl)-8-hydroxy-4-phenyl-2,3,3a,4,5,9b-hexahydro-furo[3,2-c]quinoline (17)

Isolated yield: 66% (206 mg, 0.6595 mmol) as mixture *cis/trans* 75:25.

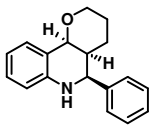


(±)-*cis* **17a** (partial characterization from the inseparable diasteromeric mixture). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.55-1.59 (m, 1H), 2.02-2.09 (m, 1H), 2.79-2.81 (m, 1H), 3.77-3.85 (m, 1H), 3.90-3.93 (m, 1H), 4.88 (d, *J*= 2.83 Hz, 1H), 5.26 (d, *J*= 7.41 Hz, 1H), 6.56-6.60 (m, 1H), 6.64 (s, 1H), 6.72-6.76 (m, 1H), 7.36-7.43 (m, 2H), 8.31-8.34 (m, 2H).



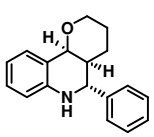
(±)-*trans* **17b** (partial characterization from the inseparable diasteromeric mixture). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.72-1.78 (m, 1H), 2.02-2.09 (m, 1H), 2.42-2.46 (m, 1H), 3.77-3.85 (m, 2H), 4.06-4.08 (m, 1H), 4.89 (d, *J*= 4.72 Hz, 1H), 6.56-6.60 (m, 1H), 6.64 (s, 1H), 6.72-6.76 (m, 1H), 7.36-7.43 (m, 4H), 8.31-8.34 (m, 2H).

(±)-*cis* 5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (18a)[1]



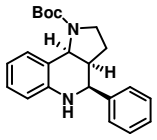
Isolated yield: 10% (27 mg, 0.1017 mmol). White solid (m.p. 128-129 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.46-1.51 (m, 1H), 1.53-1.58 (m, 3H), 2.16-2.18 (m, 1H), 3.44 (dt, J_1= 11.40 Hz, J_2= 2.40 Hz, 1H), 3.59 (dd, J_1= 11.40, J_2= 2.40 Hz, 1H), 4.70 (d, *J*= 2.40 Hz, 1H), 5.34 (d, *J*= 5.60 Hz, 1H), 6.63 (d, *J*= 8.01 Hz, 1H), 6.82 (t, *J*= 7.81 Hz, 1H), 7.11 (t, *J*= 8.01 Hz, 1H), 7.26-7.45 (m, 6H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 18.0, 25.3, 38.8, 59.3, 60.6, 72.7, 114.1, 118.4, 120.2, 126.8, 127.5, 127.6, 128.1, 128.4, 141.1, 145.2. GC-MS: m/z = 265.

(±)-*trans* 5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (18b)[1]



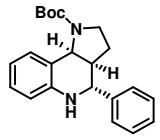
Isolated yield: 64% (170 mg, 0.6407 mmol). Pale yellow viscous oil. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.28-1.37 (m, 2H), 1.51-1.52 (m, 1H), 1.58-1.67 (m, 1H), 1.78-1.85 (m, 1H), 2.08-2.13 (m, 1H), 3.74 (dt, J_1= 11.40 Hz, J_2= 2.50 Hz, 1H), 4.10-4.14 (m, 1H), 4.41 (d, *J*= 2.60 Hz, 1H), 4.74 (d, *J*= 10.80 Hz, 1H), 6.54 (d, *J*= 8.08 Hz, 1H), 6.73 (t, *J*= 7.60 Hz, 1H), 7.10 (t, *J*= 8.08 Hz, 1H), 7.25 (d, *J*= 7.61 Hz, 1H), 7.34-7.45 (m, 5H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 23.3, 24.2, 38.8, 54.8, 68.6, 74.5, 114.1, 118.4, 120.2, 127.8, 127.9, 128.6, 129.3, 130.9, 142.3, 144.6. GC-MS: m/z = 265.

(±)-*cis* 4-phenyl-2,3,3a,4,5,9b-hexahydro-pyrrolo[3,2-c]quinoline-1-carboxylic acid *tert*-butyl ester (19a)[5]



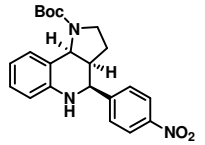
Isolated yield: 41% (144 mg, 0.4109 mmol). White solid (m.p. 122-126 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.48-1.51 (m, 10H), 2.04-2.24 (m, 1H), 2.55-2.56 (m, 1H), 3.28-3.34 (m, 1H), 3.90-3.94 (m, 1H), 4.73-4.75 (m, 1H), 5.36 (dd, J_1= 42.85 Hz, J_2= 7.19 Hz, 1H), 6.58 (d, J= 7.95 Hz, 1H), 6.78 (t, J= 7.42 Hz, 1H), 7.05-7.07 (m, 1H), 7.31-7.47 (m, 5H), 7.55-7.72 (m, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 28.5, 28.7, 44.3, 45.2, 53.4, 56.7, 79.8, 114.6, 119.0, 121.9, 123.0, 126.5, 127.8, 128.6, 130.6, 141.9, 143.6, 145.8. GC-MS: m/z = 351.

(±)-*trans* 4-phenyl-2,3,3a,4,5,9b-hexahydro-pyrrolo[3,2-c]quinoline-1-carboxylic acid *tert*-butyl ester (19b)[5]



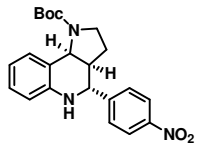
Isolated yield: 25% (86 mg, 0.2454 mmol). Pale yellow viscous oil. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.52 (s, 9H), 2.07-2.12 (m, 2H), 2.60-2.62 (m, 1H), 3.37-3.40 (m, 1H), 3.48-3.53 (m, 1H), 4.28 (brs, 1H), 4.37 (d, J= 2.83 Hz, 1H), 4.84 (brs, 1H), 6.58 (d, J= 7.96 Hz, 1H), 6.72 (t, J= 7.42 Hz, 1H), 7.10 (t, J= 7.71 Hz, 1H), 7.18 (dt, J_1= 7.71, J_2= 1.86 Hz, 1H), 7.26-7.29 (m, 4H), 7.52 (brs, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 28.3, 28.6, 44.8, 52.5, 53.4, 56.1, 79.5, 115.1, 117.8, 118.5, 125.9, 127.2, 128.1, 128.7, 129.3, 142.6, 145.1, 146.4. GC-MS: m/z = 351.

(±)-*cis* 4-(4-nitrophenyl)-2,3,3a,4,5,9b-hexahydro-pyrrolo[3,2-c]quinoline-1-carboxylic acid *tert*-butyl ester (20a)[6]



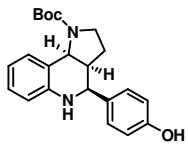
Isolated yield: 58% (228 mg, 0.5766 mmol). Yellow solid (m.p. 153-155 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.46-1.48 (m, 10H), 2.02-2.16 (m, 1H), 2.52-2.58 (m, 1H), 3.26-3.32 (m, 1H), 3.92-3.94 (m, 1H), 4.74-4.76 (m, 1H), 5.34 (dd, J_1= 40.68 Hz, J_2= 7.08 Hz, 1H), 6.60 (d, J= 8.85 Hz, 1H), 6.84 (t, J= 7.52 Hz, 1H), 7.18 (t, J= 7.86 Hz, 1H), 7.48 (d, J= 7.48 Hz, 1H), 7.62 (d, J= 8.36 Hz, 2H), 8.28 (d, J= 8.36 Hz, 2H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 28.4, 28.6, 44.2, 46.4, 53.2, 56.8, 79.6, 114.2, 119.2, 125.4, 126.6, 127.2, 128.3, 128.8, 129.2, 141.0, 145.4, 149.8.

(±)-*trans* 4-(4-nitrophenyl)-2,3,3a,4,5,9b-hexahydro-pyrrolo[3,2-c]quinoline-1-carboxylic acid *tert*-butyl ester (20b)[6]



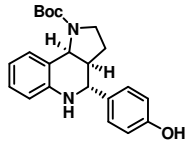
Isolated yield: 16% (62 mg, 0.1568 mmol). Yellow solid (m.p. 150-151 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz): 1.56 (s, 9H), 2.06-2.12 (m, 2H), 2.60-2.62 (m, 1H), 3.36-3.38 (m, 1H), 3.48-3.52 (m, 1H), 4.32 (brs, 1H), 4.48 (d, *J*= 2.96 Hz, 1H), 4.88 (brs, 1H), 6.60 (d, *J*= 8.84 Hz, 1H), 6.85 (t, *J*= 7.50 Hz, 1H), 7.18 (t, *J*= 7.87 Hz, 1H), 7.48 (d, *J*= 7.48 Hz, 1H), 7.61 (d, *J*= 8.33 Hz, 2H), 8.27 (d, *J*= 8.32 Hz, 2H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 28.2, 28.8, 44.8, 52.6, 54.2, 56.4, 79.6, 114.9, 118.4, 125.2, 126.5, 127.4, 128.2, 128.9, 129.3, 141.1, 144.9, 149.6.

(±)-*cis* 4-(4-hydroxyphenyl)-2,3,3a,4,5,9b-hexahydro-pyrrolo[3,2-c]quinoline-1-carboxylic acid *tert*-butyl ester (21a)



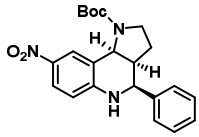
Isolated yield: 24% (87 mg, 0.2374 mmol). White solid (m.p. 201-202 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.50-1.59 (m, 9H), 1.84 (brs, 1H), 2.12-2.18 (m, 1H), 2.55 (brs, 1H), 3.25-3.38 (m, 2H), 3.94 (brs, 1H), 4.73 (d, *J*= 10.83 Hz, 1H), 5.36 (dd, J_1= 41.24 Hz, J_2= 7.08 Hz, 1H), 6.57 (d, *J*= 6.87 Hz, 1H), 6.77 (t, *J*= 7.27 Hz, 1H), 7.05-7.08 (m, 1H), 7.31-7.50 (m, 4H), 7.63 (dd, J_1= 62.37 Hz, J_2= 7.54 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 28.4, 28.7, 44.3, 45.2, 56.2, 56.6, 79.3, 114.7, 119.0, 123.0, 126.6, 127.8, 128.6, 130.6, 141.9, 143.7, 155.1, 156.2. GC-MS: m/z = 367.

(±)-*trans* 4-(4-hydroxyphenyl)-2,3,3a,4,5,9b-hexahydro-pyrrolo[3,2-c]quinoline-1-carboxylic acid *tert*-butyl ester (21b)



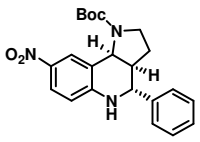
Isolated yield: 22% (80 mg, 0.2183 mmol). Whitish solid (m.p. 193-196 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.48-1.53 (m, 9H), 2.06-2.11 (m, 2H), 2.59-2.61 (m, 1H), 3.33-3.38 (m, 1H), 3.50 (brs, 1H), 4.28 (brs, 1H), 4.37 (s, 1H), 4.84 (brs, 1H), 6.57 (d, *J*= 7.96 Hz, 1H), 6.73 (t, *J*= 7.42 Hz, 1H), 7.08 (t, *J*= 7.52 Hz, 1H), 7.26-7.27 (m, 4 H), 7.50 (brs, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 26.2, 28.6, 42.8, 46.2, 54.0, 58.2, 79.5, 114.0, 118.1, 121.4, 126.6, 127.2, 128.8, 130.1, 141.2, 142.9, 154.9, 156.3. GC-MS: m/z = 367.

(±)-*cis* 8-nitro-4-phenyl-2,3,3a,4,5,9b-hexahydro-pyrrolo[3,2-c]quinoline-1-carboxylic acid *tert*-butyl ester (22a)



Isolated yield: 53% (210 mg, 0.5310 mmol). Yellow solid (m.p. 207-209 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.48-1.52 (m, 9H), 2.04-2.24 (m, 2H), 2.54-2.58 (m, 1H), 3.28-3.36 (m, 1H), 3.92-3.96 (m, 1H), 4.74-4.78 (m, 1H), 5.42 (dd, J_1= 36.52 Hz, J_2= 6.88 Hz, 1H), 6.54 (d, *J*= 8.78 Hz, 1H), 7.22-7.36 (m, 5H), 7.92 (d, *J*= 8.78 Hz, 1H), 8.12 (s, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 25.6, 28.4, 44.9, 49.4, 59.9, 64.6, 79.6, 114.9, 121.6, 122.4, 125.3, 126.2, 128.2, 128.6, 136.0, 140.6, 150.2, 157.8. GC-MS: m/z = 396.

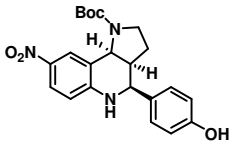
(±)-*trans* 8-nitro-4-phenyl-2,3,3a,4,5,9b-hexahydro-pyrrolo[3,2-c]quinoline-1-carboxylic acid *tert*-butyl ester (22b)



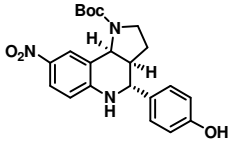
Isolated yield: 15% (60 mg, 0.1517 mmol). Yellow solid (m.p. 199-201 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.54 (s, 9H), 2.08-2.12 (m, 2H), 2.58-2.62 (m, 1H), 3.38-3.42 (m, 1H), 3.48-3.52 (m, 1H), 4.32 (brs, 1H), 4.38 (d, *J*= 2.88 Hz, 1H), 4.92 (brs, 1H), 6.56 (d, *J*= 8.81 Hz, 1H), 7.24-7.35 (m, 5H), 7.94 (d, *J*= 8.82 Hz, 1H), 8.14 (s, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 28.4, 28.6, 44.2, 48.4, 56.2, 62.1, 79.6, 114.3, 122.2, 123.3, 124.9, 126.5, 128.7 (2x), 135.8, 142.2, 149.1, 157.6. GC-MS: m/z = 396.

8-nitro-4-(4-hydroxyphenyl)-2,3,3a,4,5,9b-hexahydro-pyrrolo[3,2-c]quinoline-1-carboxylic acid *tert*-butyl ester (23)

Isolated yield: 52% (215 mg, 0.5225 mmol) as mixture *cis/trans* 63:37.

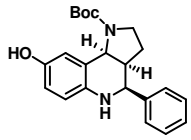


(±)-*cis* **23a** (partial characterization from the inseparable diasteromeric mixture). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.46-1.48 (m, 9H), 1.98-2.04 (m, 2H), 2.62-2.66 (m, 1H), 3.18-3.24 (m, 1H), 3.78-3.84 (m, 1H), 4.70-4.72 (m, 1H), 5.24-5.46 (m, 1H), 6.61 (d, *J*= 8.86 Hz, 2H), 6.94-7.00 (m, 1H), 7.06 (d, *J*= 2.67 Hz, 2H), 7.96 (d, *J*= 8.86 Hz, 1H), 8.11 (s, 1H).



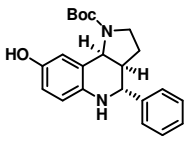
(±)-*trans* **23b** (partial characterization from the inseparable diasteromeric mixture). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.52 (s, 9H), 2.12-2.16 (m, 2H), 2.48-2.52 (m, 1H), 3.32-3.36 (m, 1H), 3.50-3.56 (m, 1H), 4.44 (brs, 1H), 4.56 (m, 1H), 4.87 (brs, 1H), 6.64 (d, *J*= 8.85 Hz, 2H), 6.94-7.00 (m, 1H), 7.04 (d, *J*= 2.35 Hz, 2H), 7.96 (d, *J*= 8.86 Hz, 1H), 8.09 (s, 1H).

(±)-*cis* 8-hydroxy-4-phenyl-2,3,3a,4,5,9b-hexahydro-pyrrolo[3,2-c]quinoline-1-carboxylic acid *tert*-butyl ester (24a)



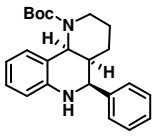
Isolated yield: 27% (100 mg, 0.2729 mmol). White solid (m.p. 192-196 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.50-1.53 (m, 9H), 2.04-2.10 (m, 2H), 2.55-2.58 (m, 1H), 3.34-3.45 (m, 1H), 3.89-3.90 (m, 1H), 4.72-4.74 (m, 1H), 5.34 (dd, J_1= 49.85 Hz, J_2= 9.57 Hz, 1H), 6.58 (d, J= 8.01 Hz, 1H), 6.78 (t, J= 7.06 Hz, 1H), 6.97-7.27 (m, 1H), 7.34-7.46 (m, 5H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 24.5, 28.6, 45.2, 51.1, 57.4, 66.9, 76.6, 115.6, 116.0, 117.5, 123.0, 126.4, 127.7, 128.8, 138.7, 142.4, 148.6, 152.1. GC-MS: m/z = 367.

(±)-*trans* 8-hydroxy-4-phenyl-2,3,3a,4,5,9b-hexahydro-pyrrolo[3,2-c]quinoline-1-carboxylic acid *tert*-butyl ester (24b)



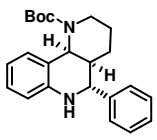
Isolated yield: 22% (80 mg, 0.2183 mmol). White solid (m.p. 188-192 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.50 (m, 9H), 2.06 (m, 2H), 2.61 (m, 1H), 3.35-3.36 (m, 1H), 3.51 (brs, 1H), 4.28 (s, 1H), 4.83 (brs, 1H), 6.49 (d, J= 8.32 Hz, 1H), 6.65 (d, J= 8.32 Hz, 1H), 7.10 (brs, 1H), 7.27-7.39 (m, 5H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 28.6, 29.7, 45.1, 53.2, 56.7, 57.3, 79.8, 114.8, 115.9, 116.1, 122.9, 126.0, 127.2, 128.7, 138.2, 145.0, 148.2, 154.2. GC-MS: m/z = 367.

(±)-*cis* *tert*-butyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-benzo[h][1,6]naphthyridine-1(2*H*)-carboxylate (26a)[5]



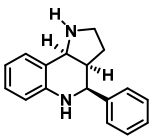
Isolated yield: 15% (55 mg, 0.1508 mmol). White solid (m.p. 140-142 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.51-1.60 (m, 12H), 1.98-2.12 (m, 2H), 2.52-2.72 (ddt, J_1= 38.97 Hz, J_2= 12.40 Hz, J_3= 2.21 Hz, 1H), 3.89-4.14 (m, 1H), 4.85 (s, 1H), 5.81 (dd, J_1= 68.23 Hz, J_2= 5.23 Hz, 1 H), 6.65 (t, J= 7.00 Hz, 1H), 6.79 (dt, J_1= 7.62 Hz, J_2= 1.88 Hz, 1H), 7.00 (d, J= 7.62 Hz, 1H), 7.12 (q, J= 8.07 Hz, 1H), 7.32-7.50 (m, 5H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 25.0, 28.4, 33.8, 40.9, 52.5, 53.8, 59.6, 79.7, 114.4, 118.3, 118.9, 126.8, 127.0, 127.4, 127.7, 128.3, 141.3, 145.0, 155.8. GC-MS: m/z = 365.

(±)-*trans* *tert*-butyl-5-phenyl 3,4,4a,5,6,10b-hexahydro-benzo[h][1,6]naphthyridine-1(2*H*)-carboxylate (26b)[5]



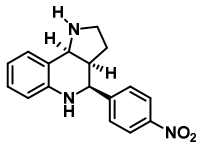
Isolated yield: 47% (170 mg, 0.4664 mmol). White solid (m.p. 137-140 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.29-1.65 (m, 12H), 1.83-1.85 (m, 2H), 2.07-2.10 (m, 1H), 2.69-2.74 (m, 1H), 4.04 (brs, 1H), 4.36 (s, 1H), 4.46 (brs, 1H), 6.67 (d, *J*= 7.89 Hz, 1H), 6.75 (t, *J*= 7.44 Hz, 1H), 6.97 (brs, 1H), 7.15 (t, *J*= 7.44 Hz, 1H), 7.28-7.34 (m, 5H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 25.4, 28.4, 33.8, 40.8, 48.3, 60.3, 65.7, 79.3, 112.9, 117.0, 125.4, 126.8, 126.9, 127.8 (2x), 128.4, 143.5, 145.1, 155.6. GC-MS: m/z = 365.

(±)-*cis* 4-phenyl-2,3,3a,4,5,9b-hexahydro-1H-pyrrolo[3,2-c]quinoline (27a)



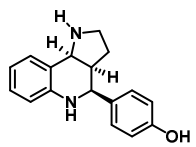
Isolated yield: 84% (42 mg, 0.1678 mmol). White solid (m.p. 190°C dec). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.64-1.68 (m, 1H), 2.31 (q, *J*= 12.25 Hz, 1H), 3.03 (q, *J*= 7.71 Hz 1H), 3.19 (brs, 1H), 3.30 (brs, 1H), 3.90 (brs, 2H), 4.64 (d, *J*= 2.27 Hz, 1H), 5.51 (d, *J*= 5.78 Hz, 1H), 6.67 (d, *J*= 8.07 Hz, 1H), 6.83 (t, *J*= 7.45 Hz, 1H), 7.16 (t, *J*= 7.67 Hz, 1H), 7.32-7.44 (m, 6H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 22.7, 43.8, 44.7, 56.6, 58.0, 115.5, 116.0, 120.0, 126.3, 128.2, 128.9, 129.5, 130.0, 140.2, 145.9. GC-MS: m/z = 251.

(±)-*cis* 4-(4-nitrophenyl)-2,3,3a,4,5,9b-hexahydro-1H-pyrrolo[3,2-c]quinoline (28a)



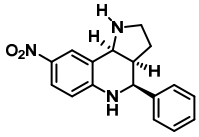
Isolated yield: 85% (50 mg, 0.1693 mmol). Yellow solid (m.p. >200 °C dec). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.92-1.98 (m, 1H), 2.22-2.28 (m, 1H), 3.26-3.32 (m, 4H), 3.92 (d, *J*= 3.72 Hz, 1H), 4.43 (d, *J*= 2.96 Hz, 1H), 5.64 (d, *J*= 6.02 Hz, 1H), 6.72 (d, *J*= 8.78 Hz, 1H), 6.89 (t, *J*= 7.66 Hz, 1H), 7.04 (t, *J*= 7.72 Hz, 1H), 7.48 (d, *J*= 7.58 Hz, 1H), 7.59 (d, *J*= 8.19 Hz, 2H), 8.24 (d, *J*= 8.18 Hz, 2H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 28.6, 44.4, 49.2, 56.8, 59.2, 114.1, 117.2, 122.1, 128.2, 128.6, 131.8, 133.6, 138.8, 140.4, 142.8.

(±)-*cis* 4-(4-hydroxyphenyl)-2,3,3a,4,5,9b-hexahydro-1H-pyrrolo[3,2-c]quinoline (29a)



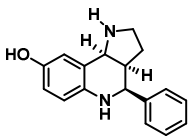
Isolated yield: 88% (47 mg, 0.1765 mmol). White solid (m.p. 194-196 °C). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.57-1.61 (m, 1H), 2.25-2.30 (m, 1H), 2.84-2.87 (m, 1H), 3.74-3.81 (m, 1H), 3.86-3.91 (m, 1H), 4.76 (d, *J*= 2.98 Hz, 1H), 5.34 (d, *J*= 5.95 Hz, 1H), 6.65 (d, *J*= 0.80 Hz, 1H), 6.84-6.87 (m, 1H), 7.12-7.16 (m, 1H), 7.31-7.46 (m, 4H), 7.53-7.54 (m, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 25.4, 42.6, 48.8, 54.5, 58.8, 114.2, 116.8, 120.0, 122.2, 128.8, 129.2, 130.6, 132.4, 142.6, 158.2.

(±)-*cis* 8-nitro-4-phenyl-2,3,3a,4,5,9b-hexahydro-1H-pyrrolo[3,2-c]quinoline (30a)



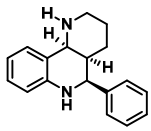
Isolated yield: 81% (48 mg, 0.1625 mmol). Yellow solid (m.p. > 200 °C dec). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.46-1.54 (m, 1H), 2.18-2.22 (m, 1H), 3.56-3.82 (m, 3H), 3.81 (brs, 1H), 3.92 (brs, 1H), 4.74 (d, *J*= 2.88 Hz, 1H), 5.34 (d, *J*= 6.34 Hz, 1H), 6.62 (d, *J*= 8.77 Hz, 1H), 7.21-7.36 (m, 5H), 7.85 (dd, J_1= 8.77 Hz, J_2= 2.47 Hz, 1H), 8.18 (s, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 26.8, 42.8, 49.1, 56.2, 58.8, 112.6, 116.2, 123.4, 124.2, 126.9, 128.2, 128.8, 136.4, 144.6, 146.8.

(±)-*cis* 8-hydroxy-4-phenyl-2,3,3a,4,5,9b-hexahydro-1H-pyrrolo[3,2-c]quinoline (31a)



Isolated yield: 94% (50 mg, 0.1877 mmol). Pale yellow solid (m.p. 193-196 °C). ^{1}H-NMR (CD_3OD, 400 MHz): δ 1.65-1.69 (m, 1H), 1.97-2.02 (m, 1H), 2.53-2.57 (m, 1H), 3.06 (q, *J*= 9.94 Hz, 1H), 3.21-3.25 (m, 1H), 4.52 (s, 1H), 5.18 (d, *J*= 5.56 Hz, 1H), 6.56 (s, 2H), 6.84 (s, 1H), 7.32-7.41 (m, 3H), 7.47-7.49 (m, 2H). ^{13}C-NMR (CD_3OD, 100.6 MHz): δ 27.6, 41.7, 42.9, 58.0, 58.7, 115.7, 116.5, 116.6, 119.2, 127.8, 128.1, 128.3, 139.3, 141.6, 149.4.

(±)-*cis* 5-phenyl-1,2,3,4,4a,5,6,10b-octahydrobenzo[h][1,6]naphthyridine (32a)



Isolated yield: 92% (49 mg, 0.1853 mmol). White solid (m.p. >200 °C dec). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 1.68-1.72 (m, 2H), 1.99-2.14 (m, 2H), 2.54-2.76 (m, 2H), 3.32 (brs, 1H), 3.76 (brs, 1H), 3.88-4.11 (m, 1H), 4.78 (brs, 1H), 5.62 (d, *J*= 5.54 Hz, 1 H), 6.64 (t, *J*= 7.12 Hz, 1H), 6.76 (m, 1H), 6.96 (d, *J*= 7.64 Hz, 1H), 7.07 (d, *J*= 8.12 Hz, 1H), 7.34-7.46 (m, 5H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ 24.6, 28.8, 36.9, 40.4, 52.6, 58.8, 114.2, 117.8, 122.1, 126.8, 127.2, 127.6, 127.7, 131.6, 141.1, 144.4. GC-MS: m/z = 264.

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