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SUPPLEMENTARY MATERIAL TO

Synthetic route towards 1,2,3,4-tetrahydroquinoxaline/ /piperidine combined tricyclic ring system

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SPECTROSCOPIC DATA AND YIELDS OF SYNTHESIZED COMPOUNDS **3**–**12**

*Methyl 1-benzyl-4-((2-bromophenyl)amino)-1,2,5,6-tetrahydropyridine-3-carboxylate [**3a**]*

Yield: 5.60 g (70 %); off-white solid; mp: 87-88°C; R_f=0.37. (SiO_2; petroleum ether/EtOAc, 9:1). IR (ATR): 3239, 3027, 2947, 2807, 2763, 1664, 1615, 1490, 1440, 1367, 1250, 1117, 1059, 738 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ = 10.53 (s, 1H), 7.58 (dd, J = 7.9, 1.5 Hz, 1H), 7.39 – 7.29 (m, 4H), 7.29 – 7.24 (m, 1H), 7.25 – 7.20 (m, 1H), 7.20 – 7.14 (m, 1H), 6.98 (td, J = 7.6, 7.5, 1.7 Hz, 1H), 3.72 (s, 3H), 3.64 (s, 2H), 3.35 (br. s, 2H), 2.50 (t, J = 5.7, 5.7 Hz, 2H), 2.39 (t, J = 5.6, 5.6 Hz, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 169.3, 153.7, 138.2, 138.0, 133.1, 129.0, 128.3, 127.6, 127.1, 126.6, 125.9, 120.1, 93.2, 62.4, 51.9, 50.8, 48.5, 28.5 ppm.

*Methyl 1-benzyl-4-((2-iodophenyl)amino)-1,2,5,6-tetrahydropyridine-3-carboxylate [**3b**]*

Yield: 6.70 g (75 %); off-white solid; mp: 106-108°C; R_f=0.37. (SiO_2; petroleum ether/EtOAc, 9:1). IR (ATR): 3130, 3027, 2950, 2791, 2742, 1652, 1606, 1494. 1446, 1364, 1243, 1149, 1060, 776 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ = 10.34 (s, 1H), 7.83 (dd, J = 7.9, 1.5 Hz, 1H), 7.37 – 7.28 (m, 4H), 7.28 – 7.21 (m, 2H), 7.18 – 7.11 (m, 1H), 6.85 (td, J = 7.6, 7.6, 1.6 Hz, 1H), 3.71 (s, 3H), 3.62 (s, 2H), 3.33 (br. s, 2H), 2.48 (t, J = 5.7, 5.7 Hz, 2H), 2.27 (t, J = 5.6, 5.6 Hz, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 169.3, 153.9, 141.2, 139.3, 138.2, 129.0, 128.6, 128.3, 127.1, 126.9, 126.9, 98.0, 92.9, 62.4, 51.8, 50.8, 48.5, 28.4 ppm.

*Methyl (±)-cis-1-benzyl-4-((2-bromophenyl)amino)piperidine-3-carboxylate [(±) cis-**4a**]*

Obtained from **2a**. Yield: 2.31 g (61 %); colorless viscous oil; R_f=0.39. (SiO_2; petroleum ether/EtOAc, 9:1). IR (ATR): 3392, 3027, 2949, 2804, 1730,

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1594, 1510, 1435, 1321, 1215, 1020, 741 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ = 7.47 – 7.41 (m, 1H), 7.38 – 7.29 (m, 4H), 7.32 – 7.25 (m, 1H), 7.21 – 7.12 (m, 1H), 6.71 – 6.65 (m, 1H), 6.61 – 6.53 (m, 1H), 5.24 (s, 1H), 3.87 – 3.74 (m, 1H), 3.67 (s, 3H, partially overlapped), 3.64 (d, *J* = 13.4 Hz, 1H, partially overlapped), 3.50 (d, *J* = 13.3 Hz, 1H), 3.02 (br. s, 1H, partially overlapped), 2.96 (br. s, 1H, partially overlapped), 2.78 – 2.63 (m, 1H), 2.60 – 2.46 (m, 1H), 2.46 – 2.35 (m, 1H), 2.14 – 2.03 (m, 1H), 1.93 – 1.83 (m, 1H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 172.7, 143.8, 138.2, 132.7, 128.8, 128.3, 128.1, 127.0, 117.8, 111.8, 110.6, 62.6, 53.1, 51.5, 49.9, 44.5, 28.7 ppm.

*Methyl (±)-trans-1-benzyl-4-((2-bromophenyl)amino)piperidine-3-carboxylate [(±) trans-**4a**]*

Obtained from **2a**. Yield: 1.36 g (36 %); colorless viscous oil; R_f=0.53. (SiO_2; petroleum ether/EtOAc, 9:1). IR (ATR): 3398, 3027, 2924, 2807, 1735, 1596, 1511, 1437, 1320, 1197, 1020, 743 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ = 7.41 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.37 – 7.32 (m, 4H), 7.33 – 7.26 (m, 1H), 7.20 – 7.11 (m, 1H), 6.75 – 6.69 (m, 1H), 6.60 – 6.53 (m, 1H), 4.31 (d, *J* = 8.9 Hz, 1H), 3.74 – 3.68 (m, 1H), 3.61 (s, 2H, partially overlapped), 3.59 (s, 3H, partially overlapped), 3.01 (d, *J* = 10.2 Hz, 1H), 2.90 (d, *J* = 11.4 Hz, 1H), 2.80 – 2.71 (m, 1H), 2.47 (t, *J* = 10.8, 10.8 Hz, 1H), 2.30 (t, *J* = 11.3, 11.3 Hz, 1H), 2.22 – 2.13 (m, 1H), 1.60 (d, *J* = 11.8 Hz, 1H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 173.1, 143.6, 137.1, 132.5, 129.1, 128.4, 128.3, 127.3, 118.1, 112.3, 110.3, 62.4, 54.0, 52.3, 51.8, 51.6, 48.3, 31.3 ppm.

*Methyl (±)-cis-1-benzyl-4-((2-iodophenyl)amino)piperidine-3-carboxylate [(±) cis-**4b**]*

Obtained from **3b**. Yield: 2.41 g (57 %); colorless viscous oil; R_f=0.39. (SiO_2; petroleum ether/EtOAc, 9:1). IR (ATR): 3381, 3026, 2804, 1733, 1588, 1508, 1454, 1319, 1215, 1005, 742, 700 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ = 7.64 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.32 – 7.25 (m, 4H), 7.26 – 7.21 (m, 1H), 7.18 – 7.12 (m, 1H), 6.59 – 6.54 (m, 1H), 6.40 (td, *J* = 7.6, 7.5, 1.5 Hz, 1H), 5.01 (s, 1H), 3.87 – 3.73 (m, 1H), 3.64 (s, 3H), 3.61 (d, *J* = 3.9 Hz, 1H), 3.58 (d, *J* = 4.7 Hz, 1H), 2.97 (br. s, 1H, partially overlapped), 2.95 – 2.87 (m, 1H, partially overlapped), 2.71 – 2.60 (m, 1H), 2.59 – 2.47 (m, 1H), 2.44 – 2.32 (m, 1H), 2.09 – 1.98 (m, 1H), 1.87 – 1.78 (m, 1H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 172.7, 146.1, 139.3, 138.2, 129.2, 128.8, 128.1, 127.1, 118.7, 111.2, 86.4, 62.7, 53.0, 51.6, 50.4, 44.6, 28.7 ppm.

*Methyl (±)-trans-1-benzyl-4-((2-iodophenyl)amino)piperidine-3-carboxylate [(±) trans-**4b**]*

Obtained from **3b**. Yield: 1.52 g (36 %); colorless oil; R_f=0.53. (SiO_2; petroleum ether/EtOAc, 9:1). IR (ATR): 3385, 2950, 2807, 1735, 1589, 1510, 1454, 1318, 1197, 1005, 743, 700 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ = 7.66 – 7.58 (m, 1H), 7.37 – 7.27 (m, 4H), 7.30 – 7.21 (m, 1H), 7.21 – 7.12 (m, 1H), 6.68 – 6.61 (m, 1H), 6.46 – 6.37 (m, 1H), 4.14 (d, *J* = 8.7 Hz, 1H), 3.75 – 3.66 (m, 1H), 3.59 (s, 3H), 3.55 (d, *J* = 5.4 Hz, 2H), 2.94 (d, *J* = 6.4 Hz, 1H), 2.89 – 2.79

(m, 1H), 2.70 (td, *J* = 9.5, 9.5, 3.6 Hz, 1H), 2.43 (t, *J* = 10.6, 10.6 Hz, 1H), 2.27 (d, *J* = 11.1 Hz, 1H), 2.19 – 2.12 (m, 1H), 1.60 – 1.49 (m, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 173.3, 146.0, 139.1, 138.0, 129.4, 128.9, 128.2, 127.1, 119.0, 111.7, 86.3, 62.5, 54.0, 52.7, 51.8, 48.4, 31.4 ppm.

*(±)-cis-1-benzyl-4-((2-bromophenyl)amino)piperidine-3-carboxamide [(±) cis-**5a**]*

Obtained from *cis*/*trans*-**4a** mixture. Yield: 0.45 g (27 %); off-white solid; mp: 185-187°C; R_f=0.45. (SiO_2; CH_2Cl_2/MeOH, 95:5). IR (ATR): 3377, 3331, 3186, 2954, 2820, 1664, 1597, 1507, 1427, 1316, 745 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.50 (s, 1H), 7.40 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.39 – 7.27 (m, 3H), 7.25 (dd, *J* = 6.4, 2.0 Hz, 2H), 7.16 – 7.07 (m, 1H), 6.57 – 6.46 (m, 2H), 6.09 (s, 1H), 5.61 (d, *J* = 7.0 Hz, 1H), 3.59 (d, *J* = 12.7 Hz, 1H), 3.56 – 3.48 (m, 1H, partially overlapped), 3.47 (d, *J* = 12.8 Hz, 1H, partially overlapped), 3.17 (d, *J* = 12.1 Hz, 1H), 3.01 (d, *J* = 8.6 Hz, 1H), 2.79 – 2.72 (m, 1H), 2.30 (dd, *J* = 12.2, 2.9 Hz, 1H), 2.21 (td, *J* = 12.0, 11.9, 2.8 Hz, 1H), 2.09 (d, *J* = 10.5 Hz, 1H), 1.66 (qd, *J* = 12.3, 12.3, 12.3, 4.0 Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 175.0, 143.7, 136.9, 132.8, 129.1, 128.6, 128.1, 127.7, 117.2, 110.7, 109.9, 62.8, 54.1, 52.3, 51.3, 44.6, 28.0 ppm.

*(±)-trans-1-benzyl-4-((2-bromophenyl)amino)piperidine-3-carboxamide [(±) trans-**5a**]*

Obtained from *cis*/*trans*-**4a** mixture. Yield: 0.84 g (49 %); off-white solid; mp: 124-126°C; R_f=0.40. (SiO_2; CH_2Cl_2/MeOH, 95:5). IR (ATR): 3327, 3175, 2954, 2811, 1667, 1593, 1516, 1410, 1326, 736 cm^{-1}. ^{1}H NMR (400 MHz, DMSO) δ = 7.39 (s, 1H), 7.38 – 7.31 (m, 1H), 7.35 – 7.20 (m, 5H), 7.15 – 7.06 (m, 1H), 6.85 (s, 1H), 6.79 – 6.72 (m, 1H), 6.52 – 6.43 (m, 1H), 4.46 (d, *J* = 8.5 Hz, 1H), 3.52 – 3.43 (m, 3H, overlapped CH-H with $PhCH_2$-H), 2.83 (d, *J* = 10.0 Hz, 1H), 2.76 (d, *J* = 12.3 Hz, 1H), 2.58 (td, *J* = 10.6, 10.6, 3.8 Hz, 1H), 2.14 (t, *J* = 11.1, 11.1 Hz, 1H, partially overlapped), 2.11 – 2.03 (m, 1H, partially overlapped), 1.96 (d, *J* = 12.9 Hz, 1H), 1.30 (qd, *J* = 12.2, 12.2, 12.2, 3.9 Hz, 1H) ppm. ^{13}C NMR (101 MHz, DMSO) δ = 174.3, 144.4, 138.7, 132.8, 129.4, 129.1, 128.7, 127.5, 117.8, 112.7, 109.2, 62.2, 55.8, 52.4, 52.2, 49.0, 31.5 ppm.

*(±)-cis-1-benzyl-4-((2-iodophenyl)amino)piperidine-3-carboxamide [(±) cis-**5b**]*

Obtained from *cis*/*trans*-**4b** mixture. Yield: 0.58 g (30 %); off-white solid; mp: 197-199°C; R_f=0.45. (SiO_2; CH_2Cl_2/MeOH, 95:5). IR (ATR): 3410, 3334, 3273, 2951, 2804, 1637, 1582, 1510, 1313, 746, 649 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.48 (s, 1H), 7.68 – 7.60 (m, 1H), 7.38 – 7.21 (m, 5H), 7.19 – 7.09 (m, 1H), 6.49 – 6.42 (m, 1H), 6.42 – 6.33 (m, 1H), 5.85 (s, 1H), 5.44 (d, *J* = 7.0 Hz, 1H), 3.59 (d, *J* = 12.7 Hz, 1H), 3.57 – 3.48 (m, 1H, partially overlapped), 3.47 (d, *J* = 12.8 Hz, 1H, partially overlapped), 3.17 (d, *J* = 12.2 Hz, 1H), 3.00 (d, *J* = 11.5 Hz, 1H), 2.80 – 2.73 (m, 1H), 2.30 (dd, *J* = 12.2, 2.9 Hz, 1H), 2.20 (td, *J* = 11.9, 11.9, 2.8 Hz, 1H), 2.09 (dd, *J* = 13.7, 3.4 Hz, 1H), 1.65 (qd, *J* = 12.2, 12.2, 12.1, 4.0 Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 174.8, 146.1,

139.6, 137.0, 129.2, 129.0, 128.6, 127.7, 118.1, 110.1, 85.3, 62.9, 54.2, 52.3, 51.9, 44.6, 28.0 ppm.

*(±)-trans-1-benzyl-4-((2-iodophenyl)amino)piperidine-3-carboxamide [(±) trans-**5b**]*

Obtained from *cis*/*trans*-**4b** mixture. Yield: 1.05 g (55 %); off-white solid; mp:118-120°C; R_f=0.40. (SiO_2; CH_2Cl_2/MeOH, 95:5). IR (ATR): 3383, 3324, 3206, 2943, 2801, 1682, 1671, 1589, 1508, 1452, 1321, 735, 702 cm^{-1}. ^1H NMR (400 MHz, DMSO) δ = 7.56 (dd, J = 7.8, 1.5 Hz, 1H), 7.43 (s, 1H), 7.33 – 7.18 (m, 5H), 7.16 – 7.07 (m, 1H), 6.86 (s, 1H), 6.69 – 6.62 (m, 1H), 6.38 – 6.29 (m, 1H), 4.15 (d, J = 8.3 Hz, 1H), 3.53 – 3.42 (m, 3H, overlapped CH_2-H with $PhCH_2$-H), 2.82 (d, J = 9.3 Hz, 1H), 2.74 (d, J = 11.7 Hz, 1H), 2.55 (td, J = 10.4, 10.4, 3.7 Hz, 1H), 2.14 (t, J = 11.2, 11.2 Hz, 1H, partially overlapped), 2.13 – 2.01 (m, 1H, partially overlapped), 2.03 – 1.92 (m, 1H), 1.33 – 1.22 (m, 1H) ppm. ^{13}C NMR (101 MHz, DMSO) δ = 174.1, 146.7, 139.3, 138.7, 129.8, 129.3, 128.7, 127.4, 118.8, 112.0, 86.0, 62.2, 55.7, 52.7, 52.1, 49.2, 31.5 ppm.

*(±)-cis-1-benzyl-4-(N-(2-bromophenyl)propionamido)piperidine-3-carboxamide [(±) cis-**9a**]*

Obtained from *cis*-**5a.** Yield: 0.38 g (78 %); off-white solid; mp: 189-191°C; R_f=0.54. (SiO_2; CH_2Cl_2/MeOH, 95:5). IR (ATR): 3378, 3176, 2939, 2761, 1681, 1646, 1472, 1384, 1267, 729, 699 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ = 8.65 (s, 1H), 7.60 – 7.53 (m, 1H), 7.55 – 7.48 (m, 1H), 7.34 – 7.12 (m, 7H), 5.65 (s, 1H), 4.50 (dt, J = 13.3, 4.9, 4.9 Hz, 1H), 3.58 – 3.53 (m, 1H), 3.43 (q, J = 12.8, 12.8, 12.8 Hz, 2H), 3.07 (d, J = 12.2 Hz, 1H), 2.86 (d, J = 9.6 Hz, 1H), 2.37 (dd, J = 12.3, 3.1 Hz, 1H), 2.09 (td, J = 11.8, 11.8, 2.9 Hz, 1H), 1.93 – 1.77 (m, J = 7.7, 7.7, 7.1, 7.1, 7.1, 7.1, 7.1 Hz, 2H), 1.47 – 1.37 (m, 1H), 1.30 (qd, J = 12.9, 12.9, 12.8, 4.2 Hz, 1H), 1.02 (t, J = 7.4, 7.4 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 175.4, 174.1, 139.2, 137.0, 133.1, 132.9, 129.7, 129.0, 128.6, 128.5, 127.5, 126.7, 62.6, 55.4, 54.1, 52.4, 42.9, 28.6, 25.4, 9.1 ppm.

*(±)-trans-1-benzyl-4-(N-(2-bromophenyl)propionamido)piperidine-3-carboxamide [(±) trans-**9a**]*

Due to impurities that could not be successfully separated by recrystallization or chromatography, the structure of compound *trans*-**9a** was determined by comparing the spectroscopic data of crude product with those for *cis*-**9a**, *cis*-**9b** and *trans*-**9b**, and by performing the Hofmann rearrangement that yielded corresponding carbamate trans-10a. For this reasons the spectroscopic data of *trans*-**9a** are omitted from supplemental material, while approximate yield was determined by TLC.

*(±)-cis-1-benzyl-4-(N-(2-iodophenyl)propionamido)piperidine-3-carboxamide [(±) cis-**9b**]*

Obtained from *cis*-**5b**. Yield: 0.51 g (94 %); off-white solid; mp: 173-175°C; R_f=0.54. (SiO_2; CH_2Cl_2/MeOH, 95:5). IR (ATR): 3379, 3059, 2934, 2817, 1661, 1638, 1465, 1379, 1283, 745, 676 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ = 8.61 (s, 1H), 7.79 (dd, J = 7.9, 1.4 Hz, 1H), 7.49 (dd, J = 7.9, 1.6 Hz, 1H), 7.30 (td, J = 7.6, 7.6, 1.5 Hz, 1H), 7.29 – 7.16 (m, 3H), 7.17 – 7.10 (m, 2H), 6.98 (td, J = 7.6,

7.6, 1.6 Hz, 1H), 5.73 (s, 1H), 4.44 (dt, *J* = 13.3, 4.8, 4.8 Hz, 1H), 3.63 – 3.55 (m, 1H), 3.43 (q, 2H), 3.06 (d, *J* = 12.3 Hz, 1H), 2.88 – 2.80 (m, 1H), 2.35 (dd, *J* = 12.3, 3.2 Hz, 1H), 2.07 (td, *J* = 11.9, 11.8, 2.9 Hz, 1H), 1.92 – 1.73 (m, 2H), 1.42 – 1.35 (m, 1H), 1.26 (qd, *J* = 12.9, 12.9, 12.9, 4.2 Hz, 1H), 1.02 (t, *J* = 7.4, 7.4 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 175.4, 173.8, 142.7, 139.1, 137.0, 132.4, 129.6, 129.4, 129.0, 128.4, 127.5, 104.9, 62.6, 55.3, 54.1, 52.4, 42.5, 29.1, 25.9, 9.1 ppm.

*(±)-trans-1-benzyl-4-(N-(2-iodophenyl)propionamido)piperidine-3-carboxamide [(±) trans-**9b**]*

Obtained from *trans*-**5b**. Yield: 0.48 g (89 %); off-white solid; mp: 205-208°C; R_f=0.32. (SiO_2; CH_2Cl_2/MeOH, 95:5). IR (ATR): 3385, 3183, 3064, 2939, 2811, 1651, 1465, 1368, 1259, 733, 697 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.93 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.47 – 7.40 (m, 1H), 7.41 – 7.33 (m, 1H), 7.28 – 7.18 (m, 3H), 7.22 – 7.13 (m, 3H), 7.09 – 7.01 (m, 1H), 6.78 (s, 1H), 5.67 (s, 1H), 5.10 (td, *J* = 11.9, 11.9, 4.1 Hz, 1H), 3.48 – 3.37 (m, 2H), 3.23 – 3.14 (m, 1H), 2.67 (td, *J* = 11.5, 11.4, 3.7 Hz, 1H), 2.31 – 2.24 (m, 1H), 2.16 (t, *J* = 11.1, 11.1 Hz, 1H), 2.12 – 2.00 (m, 2H), 1.87 – 1.74 (m, 1H), 1.27 – 1.12 (m, 1H), 0.98 (t, *J* = 7.4, 7.4 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 175.3, 174.7, 140.7, 140.5, 137.4, 131.2, 130.0, 129.9, 129.0, 128.2, 127.1, 103.6, 62.4, 57.1, 53.9, 52.5, 50.6, 29.0, 28.3, 9.6 ppm.

*Methyl (±)-trans-[1-benzyl-4-((2-bromophenyl)amino)piperidin-3-yl]carbamate [(±) trans-**6a**]*

Obtained from *trans*-**5a.** Yield: 0.28 g (66 %); pale-yellow viscous oil; R_f=0.86. (SiO_2; petroleum ether/EtOAc, 6:4). IR (ATR): 3388, 2947, 2809, 1718, 1595, 1506, 1457, 1322, 1239, 1066, 739 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.48 – 7.43 (m, 1H), 7.34 (ddd, *J* = 25.4, 13.1, 7.1 Hz, 5H), 7.26 (t, *J* = 7.8, 7.8 Hz, 1H), 7.04 (s, 1H), 6.61 (t, *J* = 7.4, 7.4 Hz, 1H), 5.40 (br. s, 1H), 4.58 (d, *J* = 7.1 Hz, 1H), 3.93 – 3.86 (m, 1H), 3.74 (s, 3H), 3.62 – 3.51 (m, 3H, overlapped CH_2-H with $PhCH_2$-H), 2.88 – 2.71 (m, 1H), 2.69 – 2.55 (m, 1H), 2.53 – 2.41 (m, 2H), 2.33 – 2.18 (m, 1H), 1.72 – 1.62 (m, 1H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 156.6, 143.5, 137.9, 132.4, 128.9, 128.3, 127.3, 117.8, 111.9, 109.8, 62.7, 54.3, 52.1, 49.4, 27.9 ppm.

*Methyl (±)-trans-[1-benzyl-4-(N-(2-bromophenyl)propionamido)piperidin-3-yl]carbamate [(±) trans-**10a**]*

Obtained from *trans*-**9a.** Yield: 0.26 g (55 %); off-white solid; mp 129-134°C; R_f=0.58. (SiO_2; petroleum ether/EtOAc, 6:4). IR (ATR): 3367, 2937, 2871, 1719, 1657, 1513, 1455, 1377, 1253, 1035, 743, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.64 (d, *J* = 8.1 Hz, 1H), 7.45 – 7.39 (m, 2H), 7.28 – 7.16 (m, 6H), 5.44 (d, *J* = 8.9 Hz, 1H), 4.68 (td, *J* = 12.0, 11.7, 4.0 Hz, 1H), 3.89 – 3.76 (m, 1H), 3.63 (s, 3H), 3.52 (d, *J* = 13.3 Hz, 1H), 3.37 (d, *J* = 13.0 Hz, 1H), 3.16 (d, *J* = 10.8 Hz, 1H), 2.72 (d, *J* = 11.1 Hz, 1H), 2.11 – 1.98 (m, 2H, partially overlapped), 1.94 (t, *J* = 10.6, 10.6 Hz, 3H, partially overlapped), 1.89 – 1.80 (m,

1H, partially overlapped), 0.99 (t, *J* = 7.4, 7.4 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 176.1, 157.0, 138.0, 137.6, 133.7, 131.5, 129.9, 129.3, 128.9, 128.1, 127.1, 125.9, 62.2, 58.8, 55.9, 52.8, 52.0, 51.7, 28.2, 27.0, 9.6 ppm.

*Methyl (±)-cis-[1-benzyl-4-(N-(2-iodophenyl)propionamido)piperidin-3-yl]carbamate [(±) cis-**10b**]*

Obtained from *cis*-**9b.** Yield: 0.39 g (73 %); yellow amorphous solid; R_f=0.60. (SiO_2; petroleum ether/EtOAc, 6:4). IR (ATR): 3422, 3027, 2938, 1729, 1667, 1501, 1465, 1375, 1259, 1088, 734, 701 cm^{-1}. ^{1}H NMR (400 MHz, DMSO) δ = 7.92 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.49 (td, *J* = 7.6, 7.6, 1.5 Hz, 1H), 7.38 – 7.31 (m, 2H), 7.27 (t, *J* = 7.4, 7.4 Hz, 2H), 7.25 – 7.16 (m, 3H), 7.14 (td, *J* = 7.7, 7.6, 1.5 Hz, 1H), 6.84 (d, *J* = 10.0 Hz, 1H), 4.54 (d, *J* = 9.9 Hz, 1H), 4.11 (d, *J* = 13.1 Hz, 1H), 3.61 (s, 3H), 3.48 – 3.35 (m, 2H), 2.69 (d, *J* = 11.3 Hz, 2H, overlapped CH_2-H with CH_2-H), 2.24 (d, *J* = 11.5 Hz, 1H), 1.94 (t, *J* = 11.5, 11.5 Hz, 1H), 1.73 – 1.58 (m, 2H), 1.33 – 1.24 (m, 1H), 1.12 – 0.99 (m, 0H), 0.88 (t, *J* = 7.4, 7.4 Hz, 3H) ppm. ^{13}C NMR (101 MHz, DMSO) δ = 172.3, 156.7, 142.6, 139.1, 138.3, 131.4, 129.9, 129.4, 128.5, 128.0, 126.8, 105.4, 61.3, 56.7, 55.7, 52.1, 51.5, 46.7, 28.5, 24.5, 9.2 ppm.

*Methyl (±)-trans-[1-benzyl-4-(N-(2-iodophenyl)propionamido)piperidin-3-yl]carbamate [(±) trans-**10b**]*

Obtained from *trans*-**9b.** Yield: 0.32 g (60 %); yellow amorphous solid; R_f=0.58. (SiO_2; petroleum ether/EtOAc, 6:4). IR (ATR): 3310, 3054, 2937, 1722, 1650, 1543, 1495, 1464, 1391, 1274, 1046, 742, 698 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.93 – 7.86 (m, 1H), 7.50 – 7.38 (m, 2H), 7.27 – 7.20 (m, 2H), 7.22 – 7.15 (m, 3H), 7.10 – 7.01 (m, 1H), 5.47 (d, *J* = 8.9 Hz, 1H), 4.67 (td, *J* = 11.9, 11.8, 4.0 Hz, 1H), 3.85 (qd, *J* = 10.5, 10.5, 10.5, 4.2 Hz, 1H), 3.62 (s, 3H), 3.52 (d, *J* = 13.1 Hz, 1H), 3.38 (d, *J* = 13.1 Hz, 1H), 3.19 – 3.10 (m, 1H), 2.72 (d, *J* = 8.5 Hz, 1H), 2.11 – 2.03 (m, 1H, partially overlapped), 2.03 – 1.99 (m, 2H, partially overlapped), 1.99 – 1.92 (m, 2H, partially overlapped), 1.90 – 1.78 (m, 1H), 0.99 (t, *J* = 7.5, 7.5 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 176.2, 157.0, 141.4, 140.2, 137.4, 130.7, 130.2, 129.9, 129.0, 128.2, 127.1, 103.8, 62.1, 58.7, 55.9, 53.0, 52.0, 51.7, 28.9, 27.4, 9.7 ppm.

*(±)-trans-1-benzyl-N^4-(2-bromophenyl)piperidine-3,4-diamine [(±) trans-**7a**]*

Obtained from trans-**6a**. Yield: 0.074 g (93 %); dark-brown viscous oil; R_f=0.25. (SiO_2; CH_2Cl_2/MeOH, 95:5). IR (ATR): 3357, 3027, 2924, 2805, 1595, 1508, 1458, 1320, 1124, 1016, 743 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.41 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.36 – 7.28 (m, 4H), 7.30 – 7.23 (m, 1H), 7.18 – 7.11 (m, 1H), 6.77 – 6.71 (m, 1H), 6.55 (td, *J* = 7.7, 7.6, 1.5 Hz, 1H), 4.20 (d, *J* = 8.9 Hz, 1H), 3.54 (q, *J* = 13.1, 13.1, 13.1 Hz, 2H), 3.14 – 3.05 (m, 1H), 2.98 (d, *J* = 11.5 Hz, 1H), 2.90 (td, *J* = 8.9, 8.9, 4.0 Hz, 1H), 2.85 – 2.79 (m, 1H), 2.21 – 2.13 (m, 1H), 2.13 – 2.04 (m, 1H), 2.00 (t, *J* = 10.1, 10.1 Hz, 1H), 1.74 (br. s, 2H),

1.56 – 1.44 (m, 1H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 144.6, 138.1, 132.6, 129.0, 128.4, 128.2, 127.1, 118.0, 112.2, 110.5, 62.7, 60.0, 57.8, 53.3, 52.2, 30.8 ppm.

*(±)-trans-N-(3-amino-1-benzylpiperidin-4-yl)-N-(2-bromophenyl)propionamide [(±) trans-**11a**]*

Obtained from *trans*-**10a.** Yield: 0.089 g (97 %); pale-yellow viscous oil; R_f=0.2. (SiO_2; CH_2Cl_2/MeOH, 95:5). IR (ATR): 2934, 2807, 1655, 1581, 1471, 1374, 1259, 1028, 734, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.69 – 7.61 (m, 2H), 7.45 – 7.36 (m, 1H), 7.30 – 7.18 (m, 6H), 4.80 – 4.69 (m, 1H), 3.68 (br. s, 2H), 3.57 – 3.48 (m, 2H), 3.16 (d, *J* = 10.9 Hz, 1H), 3.08 (td, *J* = 10.4, 10.4, 4.2 Hz, 1H), 2.84 – 2.76 (m, 1H), 2.25 – 2.11 (m, 2H), 2.09 – 1.96 (m, 3H), 1.21 – 1.11 (m, 1H), 1.04 (t, *J* = 7.3, 7.3 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 176.0, 137.7, 136.7, 133.8, 132.2, 130.0, 129.3, 129.1, 128.3, 127.4, 125.9, 62.1, 60.1, 57.9, 52.0, 51.7, 28.5, 27.1, 9.5 ppm.

*(±)-cis-N-(3-amino-1-benzylpiperidin-4-yl)-N-(2-iodophenyl)propionamide [(±) cis-**11b**]*

Obtained from *cis*-**10b**. Yield: 0.09 g (97 %); pale-yellow viscous oil; R_f=0.2. (SiO_2; CH_2Cl_2/MeOH, 95:5). IR (ATR): 3375, 3059, 3027, 2931, 2808, 1659, 1577, 1466, 1377, 1274, 733, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.88 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.82 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.38 (td, *J* = 7.7, 7.6, 1.4 Hz, 1H), 7.30 – 7.21 (m, 4H), 7.22 – 7.17 (m, 1H), 7.06 – 6.98 (m, 1H), 4.10 (dt, *J* = 13.3, 3.9, 3.9 Hz, 1H), 3.91 (s, 1H), 3.52 – 3.33 (m, 4H, overlapped $PhCH_2$-H with NH_2-H), 2.86 (dt, *J* = 11.7, 2.9, 2.9 Hz, 1H), 2.79 – 2.71 (m, 1H), 2.35 (dd, *J* = 11.8, 1.9 Hz, 1H), 2.03 – 1.95 (m, 1H), 1.87 (q, *J* = 7.4, 7.4, 7.4 Hz, 2H), 1.50 – 1.36 (m, 1H), 1.31 – 1.22 (m, 1H), 1.00 (t, *J* = 7.4, 7.4 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 174.5, 143.9, 139.3, 138.0, 132.4, 129.6, 129.2, 128.9, 128.2, 127.1, 104.1, 62.3, 59.3, 58.8, 52.6, 47.4, 29.4, 24.5, 9.2 ppm.

*(±)-trans-N-(3-amino-1-benzylpiperidin-4-yl)-N-(2-iodophenyl)propionamide [(±) trans-**11b**]*

Obtained from *trans*-**10b.** Yield: 0.10 g (98 %); pale-yellow viscous oil; R_f=0.2. (SiO_2; CH_2Cl_2/MeOH, 95:5). IR (ATR): 3366, 3059, 3027, 2935, 2805, 1658, 1577, 1467, 1376, 1260, 749, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.95 – 7.88 (m, 1H), 7.59 – 7.52 (m, 1H), 7.45 – 7.37 (m, 1H), 7.29 – 7.15 (m, 5H), 7.09 – 7.00 (m, 1H), 4.75 – 4.64 (m, 1H), 3.46 (s, 2H), 3.03 (d, *J* = 12.4 Hz, 1H), 2.87 (td, *J* = 10.4, 10.4, 4.3 Hz, 1H), 2.79 (d, *J* = 11.8 Hz, 1H), 2.61 (br. s, 2H), 2.18 – 2.10 (m, 1H, partially overlapped), 2.10 – 1.98 (m, 3H, partially overlapped), 1.99 – 1.86 (m, 1H, partially overlapped), 1.17 – 1.08 (m, 1H, partially overlapped), 1.05 (t, *J* = 7.5, 7.5 Hz, 3H, partially overlapped) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 175.5, 141.4, 140.3, 137.5, 131.3, 129.8, 129.7, 129.1, 128.2, 127.2, 104.0, 77.3, 77.0, 76.7, 62.4, 61.5, 58.6, 52.5, 52.0, 29.0, 27.8, 9.6 ppm.

*(±)-trans-2-benzyl-1,2,3,4,4a,5,10,10a-octahydropyrido[3,4-b]quinoxaline [(±) trans-**8**]*

Obtained from *trans*-**7a.** Yield: 0.014 g (29 %); dark-brown viscous oil; R_f=0.47. (SiO_2; CH_2Cl_2/MeOH, 95:5) IR (ATR): 3353, 2926, 2853, 2806, 1599, 1505, 1462, 1368, 1303, 742 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ = 7.39 – 7.33 (m, 4H), 7.33 – 7.26 (m, 1H), 6.64 – 6.58 (m, 2H), 6.56 – 6.52 (m, 1H), 6.52 – 6.48 (m, 1H), 3.69 (d, *J* = 13.0 Hz, 1H), 3.58 (d, *J* = 13.1 Hz, 1H, partially overlapped), 3.51 (br. s, 2H, partially overlapped), 3.23 – 3.15 (m, 1H), 3.05 – 2.96 (m, 2H, partially overlapped), 2.99 – 2.92 (m, 1H, partially overlapped), 2.25 (td, *J* = 12.1, 12.0, 2.7 Hz, 1H), 1.93 (t, *J* = 10.5, 10.5 Hz, 1H, partially overlapped), 1.91 – 1.83 (m, 1H, partially overlapped), 1.69 (td, *J* = 12.1, 11.9, 4.0 Hz, 1H) ppm.^{13}C NMR (126 MHz, $CDCl_3$) δ = 137.6, 133.8, 133.6, 129.2, 128.3, 127.3, 119.1, 119.1, 115.0, 114.9, 62.5, 56.7, 54.1, 53.0, 52.0, 30.5 ppm. HRMS (HESI-OT): *m/z* $[M + H]^+$ calcd for $C_{18}H_{21}N_3$: 280.18082; found: 280.18112.

*(±)-cis-1-(2-benzyl-2,3,4,4a,10,10a-hexahydropyrido[3,4-b]quinoxalin-5(1H)-yl)propan-1-one [(±) cis-**12**]*

Obtained from *cis*-**11b.** Yield: 0.032 g (58 %); pale-yellow viscous oil; R_f=0.5. (SiO_2; CH_2Cl_2/MeOH, 95:5). IR (ATR): 3357, 2934, 2808, 1649, 1502, 1379, 1318, 745 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ = 7.37 – 7.14 (m, 6H), 7.04 – 6.93 (m, 1H), 6.76 – 6.61 (m, 2H), 4.85 (s, 1H), 3.85 (s, 1H), 3.55 (d, *J* = 13.2 Hz, 1H), 3.45 (d, *J* = 13.2 Hz, 1H, partially overlapped), 3.38 (s, 1H, partially overlapped), 2.88 (d, *J* = 12.5 Hz, 1H, partially overlapped), 2.85 – 2.77 (m, 1H, partially overlapped), 2.70 – 2.56 (m, 1H, partially overlapped), 2.58 – 2.44 (m, 1H, partially overlapped), 2.35 (dd, *J* = 12.5, 2.2 Hz, 1H), 2.14 (td, *J* = 11.6, 11.5, 3.6 Hz, 1H), 1.51 – 1.35 (m, 2H), 1.13 (t, *J* = 7.4, 7.4 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 173.3, 138.0, 134.7, 128.9, 128.4, 127.3, 126.0, 125.3, 121.8, 116.7, 115.2, 62.3, 56.5, 52.2, 50.3, 44.5, 27.9, 24.7, 10.1 ppm. HRMS (HESI-OT): *m/z* $[M + H]^+$ calcd for $C_{21}H_{25}N_3O$: 336.20704; found: 336.20618.

*(±)-trans-1-(2-benzyl-2,3,4,4a,10,10a-hexahydropyrido[3,4-b]quinoxalin-5(1H)-yl)propan-1--one [(±) trans-**12**]*

Obtained from *trans*-**11b.** Yield: 0.026 g (47 %); pale-yellow viscous oil; R_f=0.5. (SiO_2; CH_2Cl_2/MeOH, 95:5). IR (ATR): 3310, 2928, 2803, 1654, 1501, 1368, 1281, 746 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ = 7.32 – 7.26 (m, 4H), 7.27 – 7.20 (m, 1H), 7.10 – 7.03 (m, 1H), 7.00 – 6.91 (m, 1H), 6.79 – 6.71 (m, 1H), 6.66 – 6.59 (m, 1H), 3.70 – 3.58 (m, 2H, overlapped $PhCH_2$-H with CH-H), 3.45 (d, *J* = 13.1 Hz, 2H, overlapped $PhCH_2$-H with NH-H), 3.07 (td, *J* = 10.4, 10.4, 3.6 Hz, 1H), 3.04 – 2.92 (m, 2H), 2.61 – 2.50 (m, 1H), 2.53 – 2.40 (m, 1H), 2.41 – 2.30 (m, 1H), 2.26 (td, *J* = 11.9, 11.7, 2.7 Hz, 1H), 2.09 (t, *J* = 10.1, 10.1 Hz, 1H), 1.94 (qd, *J* = 12.1, 12.1, 12.1, 3.9 Hz, 1H), 1.04 (t, *J* = 7.3, 7.3 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = 175.4, 142.7, 138.3, 129.0, 128.9, 128.3,

127.1, 125.4, 125.3, 118.8, 115.6, 65.5, 62.2, 58.6, 57.5, 53.0, 30.1, 28.8, 9.7 ppm. HRMS (HESI-OT): *m/z* $[M + H]^+$ calcd for $C_{21}H_{25}N_3O$: 336.20704; found: 336.20703.

SPECTRA OF THE FINAL COMPOUNDS

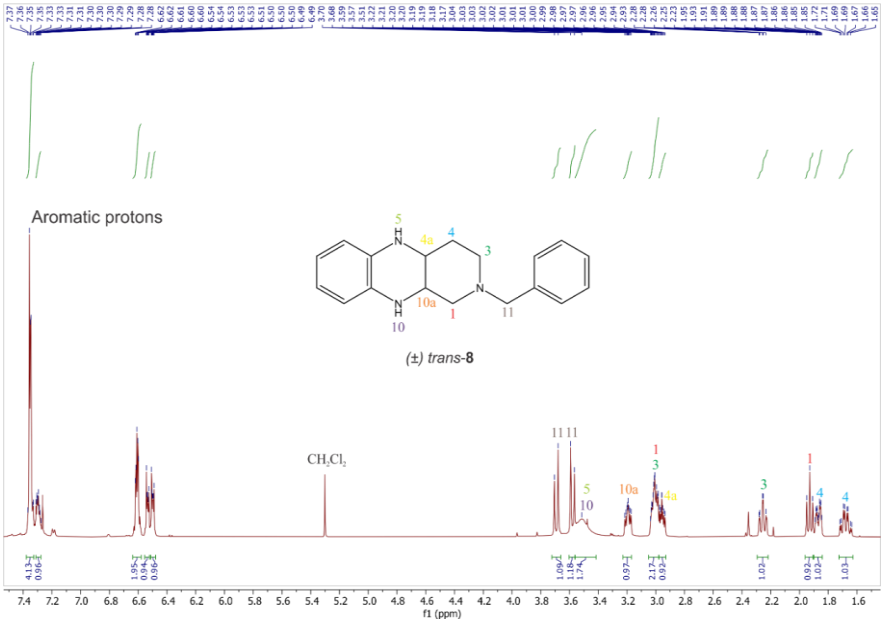

Figure S-1. ^{1}H NMR of (±)-*trans*-2-benzyl-1,2,3,4,4a,5,10,10a-octahydro-pyrido[3,4-b]quinoxaline [(±) *trans*-**8**].

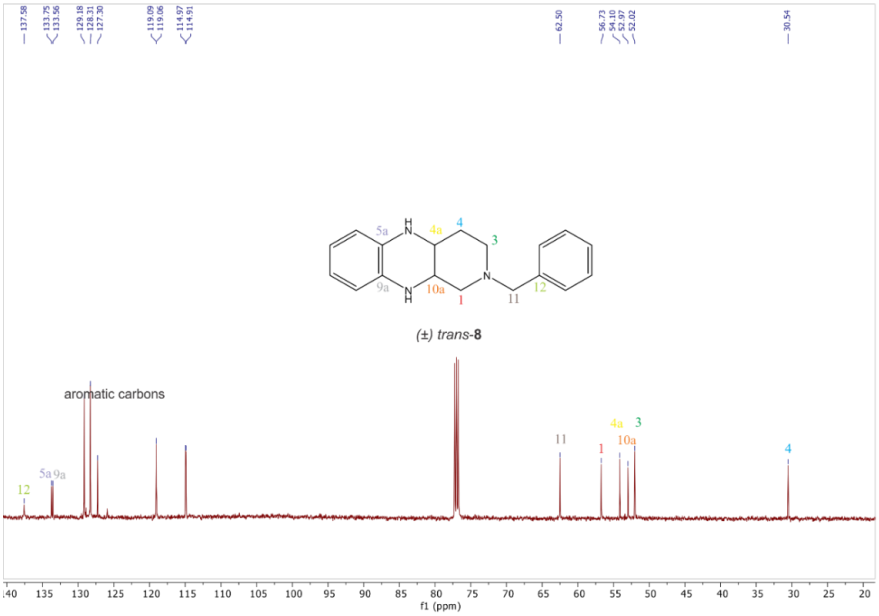

Figure S-2. ^{13}C NMR of (±)-*trans*-2-benzyl-1,2,3,4,4a,5,10,10a-octahydro-pyrido[3,4-b]quinoxaline [(±) *trans*-**8**].

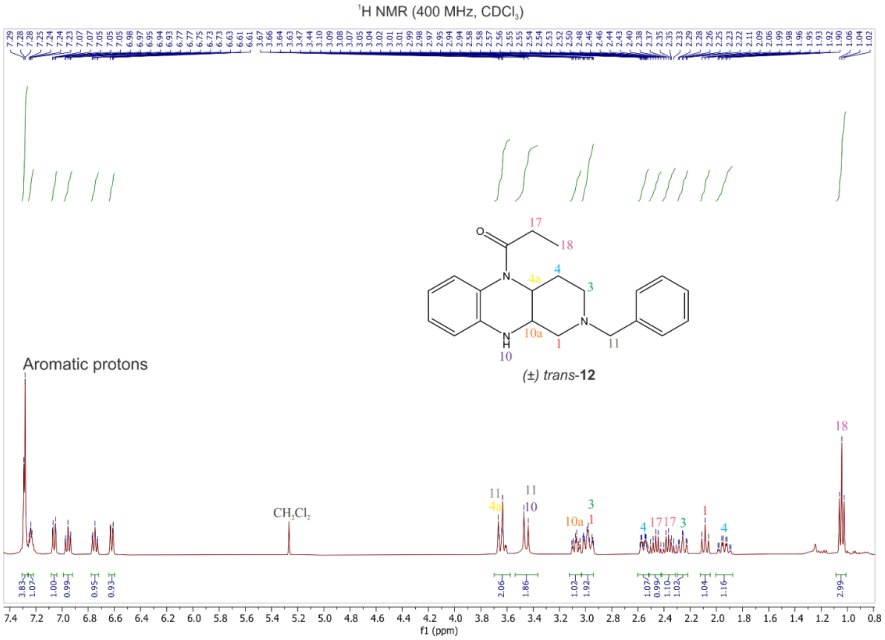

Figure S-3. ^{1}H NMR of (±)-*trans*-1-(2-benzyl-2,3,4,4a,10,10a-hexahydro-pyrido[3,4-b]quinoxalin-5(1H)-yl)propan-1-one [(±) *trans*-**12**]

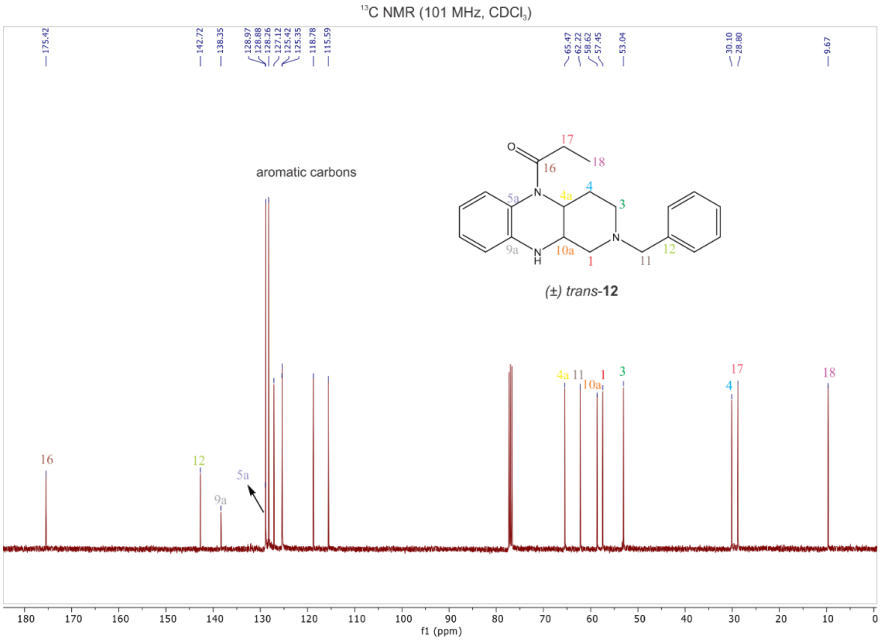

Figure S-4. ^{13}C NMR of (±)-*trans*-1-(2-benzyl-2,3,4,4a,10,10a-hexahydro-pyrido[3,4-b]quinoxalin-5(1H)-yl)propan-1-one [(±) *trans*-**12**]

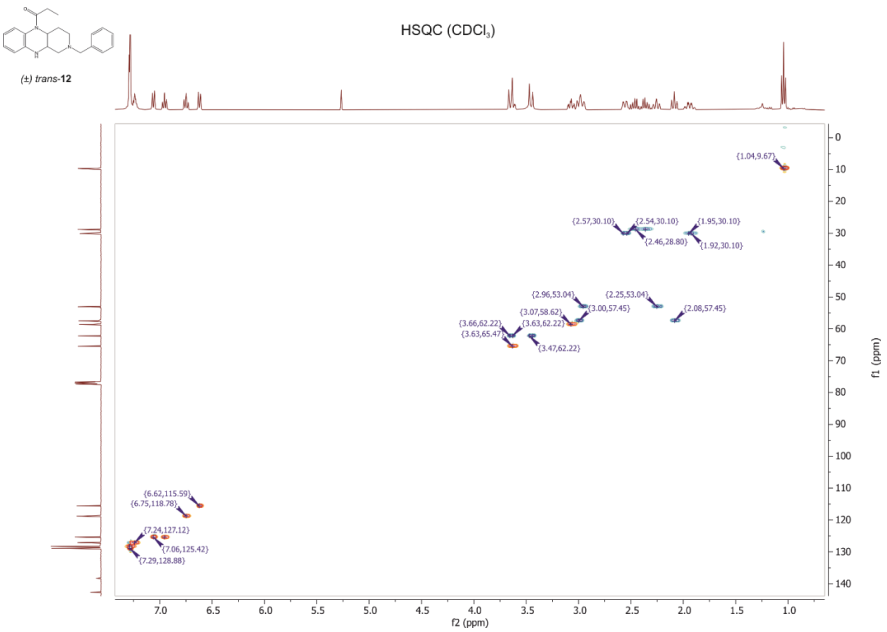

Figure S-5. HSQC of (±)-*trans*-1-(2-benzyl-2,3,4,4a,10,10a-hexahydro-pyrido[3,4-b]quinoxalin-5(1H)-yl)propan-1-one [(±) *trans*-**12**]

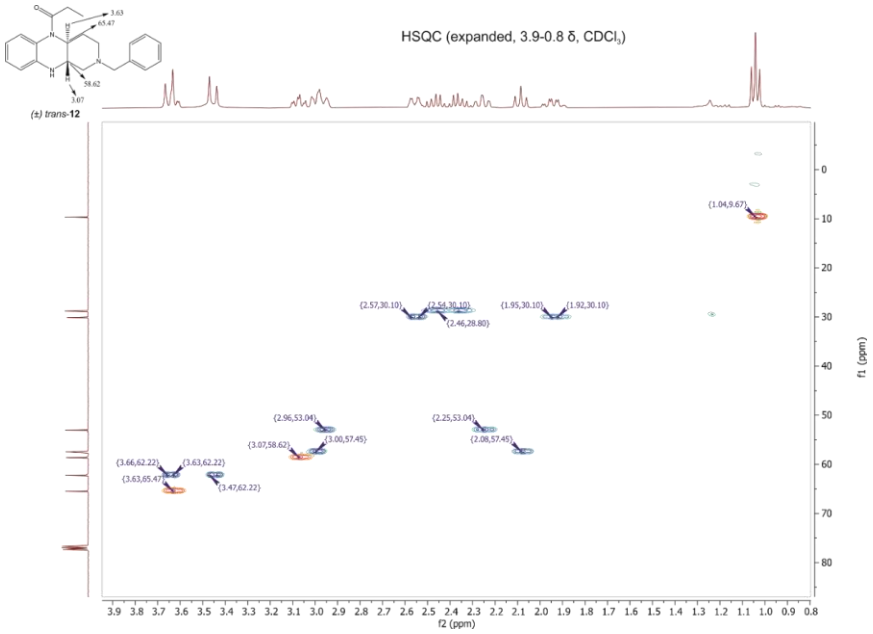

Figure S-6. Expanded HSQC of (±)-*trans*-1-(2-benzyl-2,3,4,4a,10,10a-hexahydro-pyrido[3,4-b]quinoxalin-5(1H)-yl)propan-1-one [(±) *trans*-**12**]

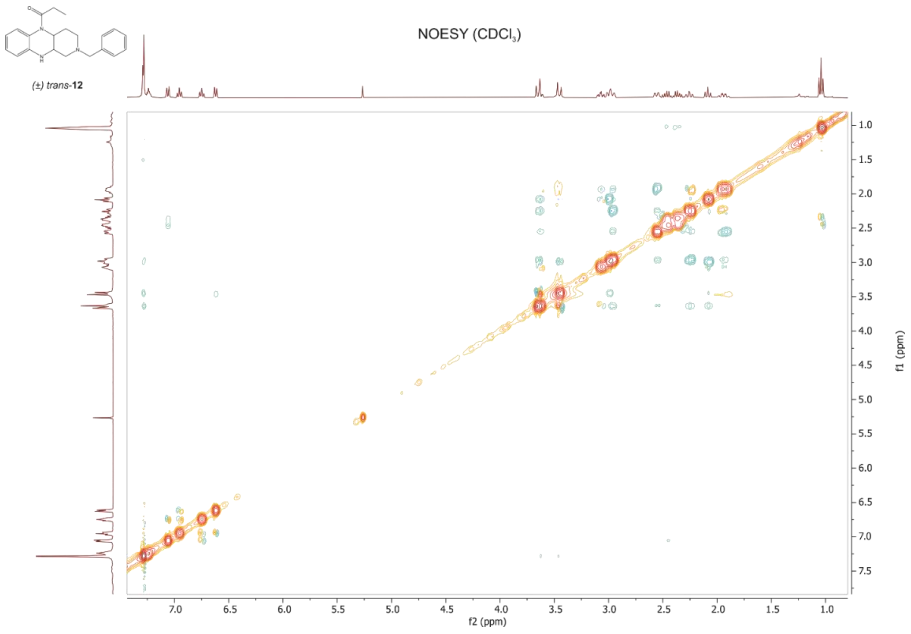

Figure S-7. NOESY of (±)-*trans*-1-(2-benzyl-2,3,4,4a,10,10a-hexahydro-pyrido[3,4-b]quinoxalin-5(1H)-yl)propan-1-one [(±) *trans*-**12**]

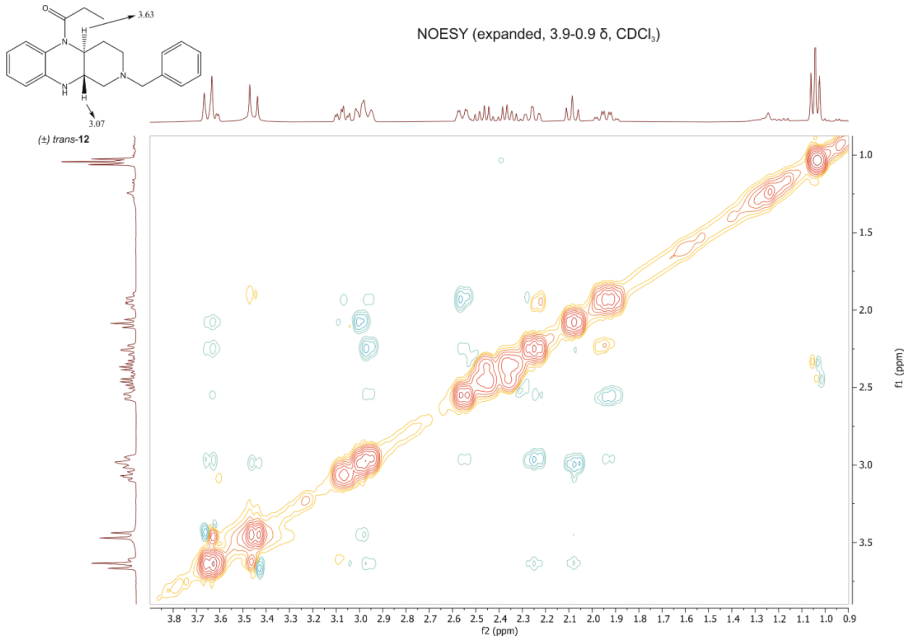

Figure S-8. Expanded NOESY of (±)-*trans*-1-(2-benzyl-2,3,4,4a,10,10a-hexahydro-pyrido[3,4-b]quinoxalin-5(1H)-yl)propan-1-one [(±) *trans*-12]

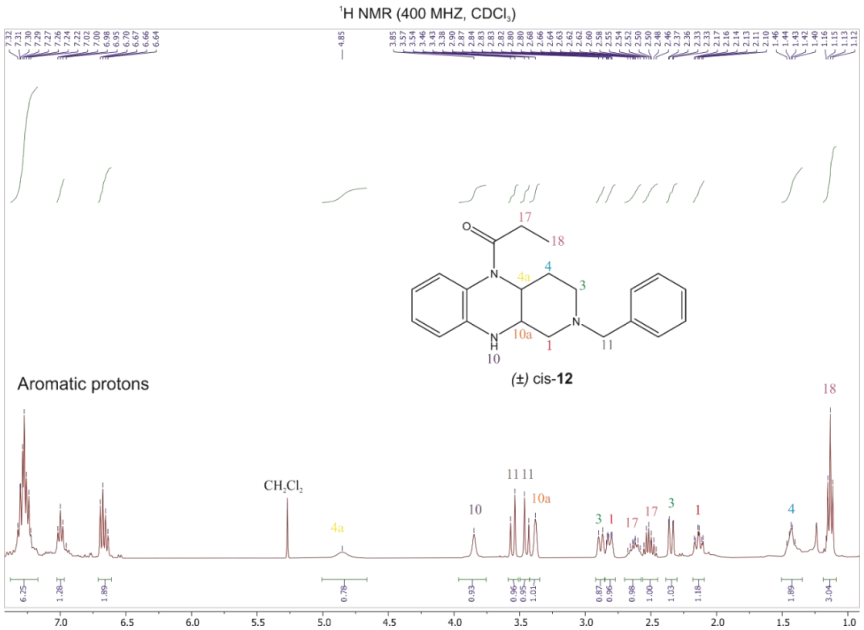

Figure S-9. ^{1}H NMR of (±)-*cis*-1-(2-benzyl-2,3,4,4a,10,10a-hexahydro-pyrido[3,4-b]quinoxalin-5(1H)-yl)propan-1-one [(±) *cis*-**12**]

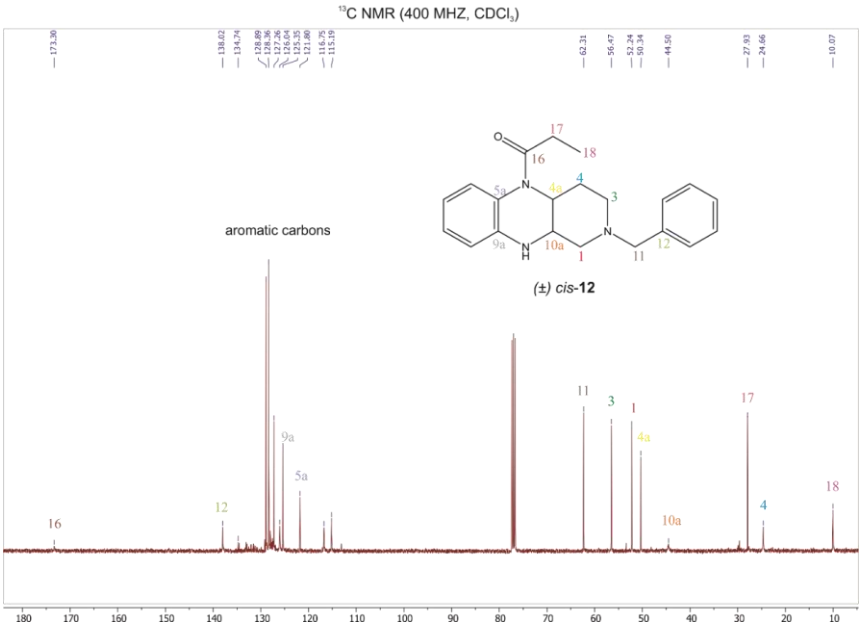

Figure S-10. ^{13}C NMR of (±)-*cis*-1-(2-benzyl-2,3,4,4a,10,10a-hexahydro-pyrido[3,4-b]quinoxalin-5(1H)-yl)propan-1-one [(±) *cis*-**12**]

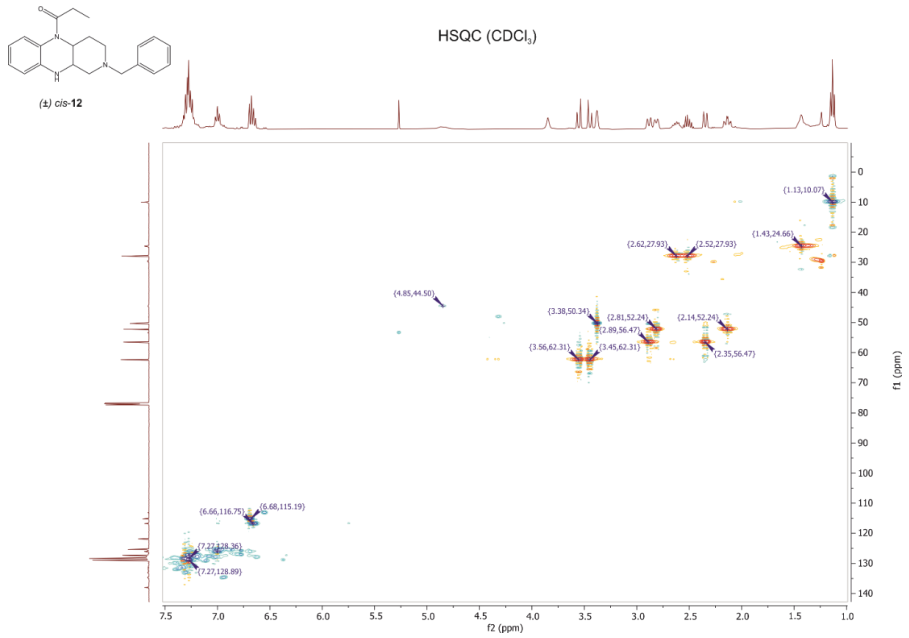

Figure S-11. HSQC of (±)-*cis*-1-(2-benzyl-2,3,4,4a,10,10a-hexahydro-pyrido[3,4-b]quinoxalin-5(1H)-yl)propan-1-one [(±) *cis*-**12**]

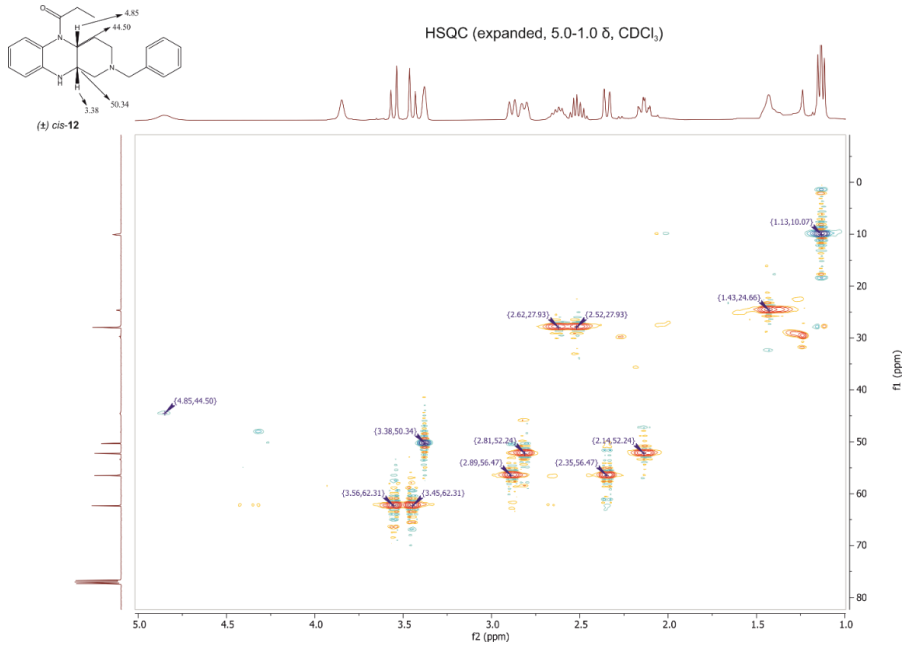

Figure S-12. Esxpanded HSQC of of (±)-*cis*-1-(2-benzyl-2,3,4,4a,10,10a-hexahydro-pyrido[3,4-b]quinoxalin-5(1H)-yl)propan-1-one [(±) *cis*-12]

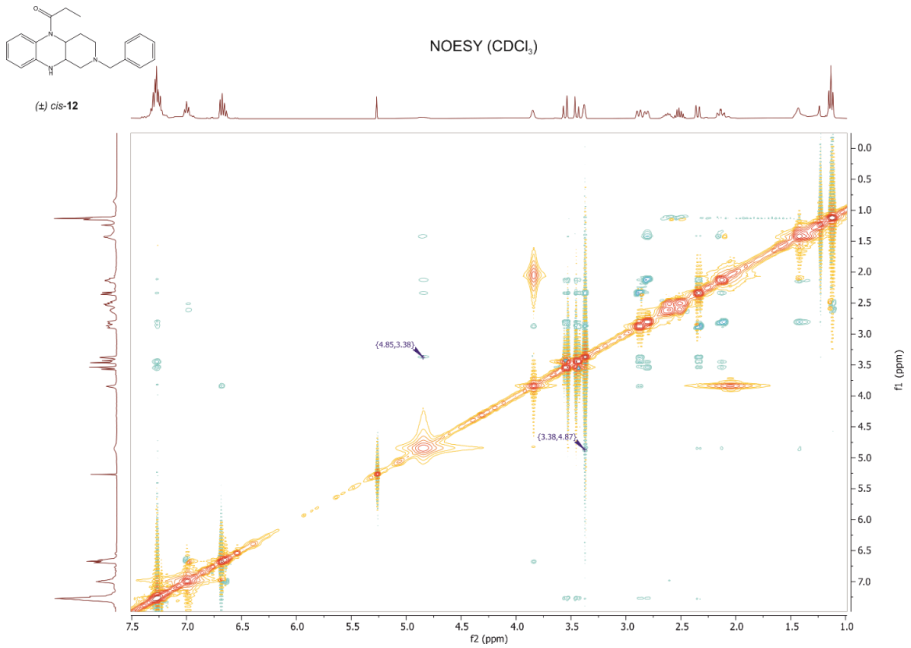

Figure S-13. NOESY of (±)-*cis*-1-(2-benzyl-2,3,4,4a,10,10a-hexahydro-pyrido[3,4-b]quinoxalin-5(1H)-yl)propan-1-one [(±) *cis*-12]

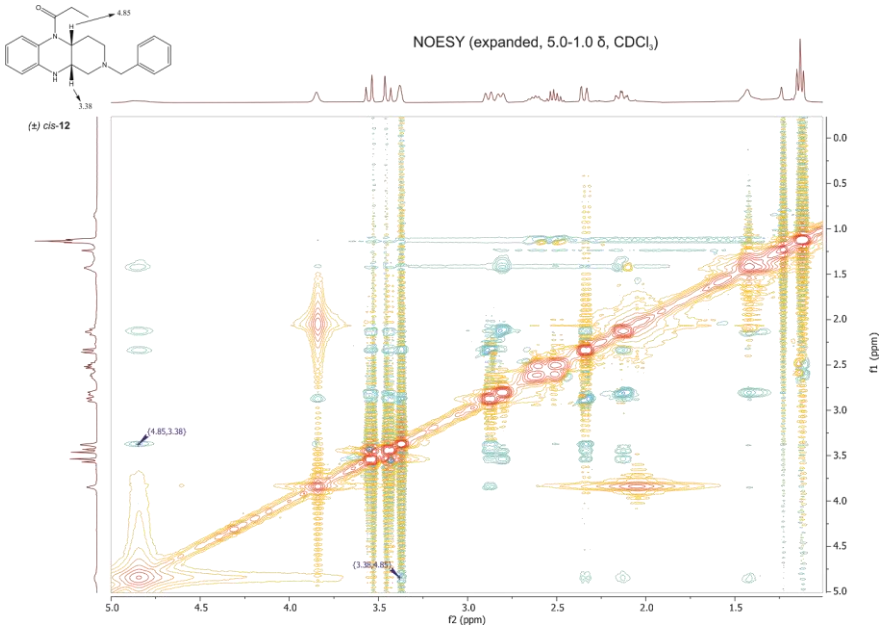

Figure S-14. Expanded NOESY of (±)-*cis*-1-(2-benzyl-2,3,4,4a,10,10a-hexahydro-pyrido[3,4-b]quinoxalin-5(1H)-yl)propan-1-one [(±) *cis*-12].