Supplementary Material For:

Enantiopure Tetrahydro-ß-carbolines via Pictet-Spengler Reactions with *N*-Sulfinyl Tryptamines

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General Information. Nuclear Magnetic Resonance spectra were recorded on a Bruker ARX 400 (400 MHz) spectrometer. Chemical shifts are reported as parts per million (δ) relative to TMS. Coupling constants (*J* values) are reported in hertz (Hz) and spin multiplicities are indicated by the following symbols: s (singlet), bs (broad singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Infrared spectra were recorded on a Bruker IFS 28 FT spectrophotometer. Band positions are reported in reciprocal centimeters (cm^{-1}). Mass spectra were obtained on a JEOL JMS-SX/SX tandem mass spectrometer using Electron Ionisation (EI). Melting points were meassured on a Leitz melting point microscope and are used uncorrected. Flash column chromatography was performed using silica gel (Fluka, 230-400 mesh). Tetrahydrofuran was distilled from sodium/benzophenone ketyl. Chloroform and methylene chloride were distilled from phosphorous pentoxide before use. Acetaldehyde, propionaldehyde and butyraldehyde were distilled prior to use. All other reagents that were commercially obtained were used without further purification.

Preparation of sulfinamines

General procedure To a vigorous stirred mixture of saturated K_2CO_3 (25 mL), methylene chloride (35 mL) and tryptamine (3.2 g, 20 mmol) at 5 ^{0}C was added dropwise a solution of the sulfinyl chloride (22 mmol) in dichloromethane (50 mL). After stirring for 2 hours at ambient temperature the product partially precipitated as a white crystalline material which was obtained by filtration and washed thoroughly with water (30 mL), acetone (30 mL) and ethyl acetate (three times 30 mL). The layers of the filtrate were separated and after drying (Na2SO4), removal of the solvents *in vacuo* and recrystallization the rest of the product was obtained. Yields: **3a**, 75%; **3b**, 70%; **3c**, 65%.

***N*-*p*-Tolylsulfinyl tryptamine 3a** (75%) m.p. 109 °C; ^{1}H-NMR ($CDCl_3$) δ 8.07 (s, 1H), 7.55 (d, *J* = 4 Hz, 2H), 7.50 (d, *J* = 4 Hz, 1H), 7.36 (d, *J* = 4 Hz, 1H), 7.27 (d, *J* = 4 Hz, 2H), 7.20 (t, *J* = 1 Hz, 1H), 7.08 (t, *J* = 1 Hz, 1H), 7.04 (d, *J* = 1 Hz, 1H), 4.15 (t, *J* = 4 Hz, 1H), 3.42 ((m, 1H), 3.16 (m, 1H), 2.98 (t, *J* = 7 Hz, 2H), 2.40 (s, 3H); IR ($CHCl_3$): 3479, 1059; HRMS (EI): Calcd. for $C_{17}H_{18}N_2SO$ 298.1136, Found: 298.1143.

***N*-2-Ethoxynaphtylsulfinyl tryptamine 3b** (70%) m.p. 93-95 °C; ^{1}H-NMR ($CDCl_3$) δ 8.67 (d, *J* = 4 Hz, 1H), 8.10 (bs, 1H), 7.87 (d, *J* = 5 Hz, 1H), 7.78 (d, *J* = 4 Hz, 1H), 7.56-7.49 (m, 2H), 7.39 (t, *J* = 3 Hz, 1H), 7.36 (d, *J* = 4 Hz, 1H), 7.23-7.15 (m, 2H), 7.21-7.03 (m, 2H), 5.78 (bs, 1H), 4.23-4.04 (m, 2H), 3.74-3.65 (m, 1H), 3.65-3.54 (m, 1H), 3.19-3.03 (m, 2H), 1.22 (t, *J* = 6 Hz, 3H); IR ($CHCl_3$): 3479, 1057; HRMS (EI): Calcd. for $C_{22}H_{23}N_2SO$ 363.1562, Found: 363.1568.

***N*-tert-Butylsulfinyl tryptamine 3c** (65%) m.p. 114-117 °C; ^{1}H-NMR ($CDCl_3$) δ 8.33 (s, 1H), 7.62 (d, *J* = 4 Hz, 1H), 7.38 (d, *J* = 4 Hz, 1H), 7.20 (t, *J* = 3 Hz, 1H), 7.12 (t, *J* = 3 Hz, 1H), 7.07 (d, *J* = 1 Hz, 1H), 3.58-3.48 (m, 1H), 3.46-3.28 (m, 2H), 3.15-2.98 (m, 2H), 1.18 (s, 9H); IR ($CHCl_3$): 3479, 1051; HRMS (EI): Calcd. for $C_{14}H_{20}N_2SO$ 264.1292, Found: 264.1288.

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Synthesis of *(R)*-*N*-*p*-Tolylsulfinyl tryptamine *(R)*-3a To a solution of tryptamine (20 mmol, 3.2 g) in THF (200 mL) at -78 ^{0}C was added a solution of n-butyllithium (25.6 mL, 41 mmol 1,6 mL^{-1}) in hexanes. The reaction mixture was allowed to warm to ambient temperature and chlorotrimethylsilane (21 mmol, 2.66 mL) was added. After stirring for 30 min n-butyllithium (21 mmol, 13.1 mL) in hexanes was added and the reaction mixture was stirred for an additional 45 min. The reaction mixture was added to a solution of *(1S,2R,5S)-(S)*-menthyl-*p*-toluenesulfinate (10 mmol) in THF. The reaction was quenched after 1 hour by the addition of an aqueous solution of Na_2HPO_4 (200 mL, 0.1 M). The organic layer was separated and the water layer was extracted with three 100 mL portions of ethyl acetate. The combined organic layers were dried (Na_2SO_4) and the solvents removed *in vacuo*. Flash chromatography (ethyl acetate/light petroleum 1:1) and recrystallisation (ethyl acetate) yielded *(R)*-**3a** in 73% (m.p. 109 ^{0}C, $[\alpha]_D$ = 102^0). Following the same procedure starting from *(1S,2R,5S)-(R)*-menthyl-*p*-toluenesulfinate *(S)*-**3a** was obtained in 68 % (m.p. 109 ^{0}C, $[\alpha]_D$ = -108^0).

Pictet-Spengler reactions of *(R)*-*N*-*p*-Tolylsulfinyl tryptamine *(R)*-3a

General procedure A solution of *(R)*-**3a** (60 mg, 0.2 mmol) and the aldehyde (1.0 mmol) in a mixture of methylene chloride/chloroform (2 mL, 1:1) was cooled to -78 ^{0}C. The indicated quantity of 10-camphorsulfonic acid was added and the reaction mixture was stirred at -78 ^{0}C for the indicated time. The reaction was quenched with triethylamine (0.7 mL, 5 mmol) and the solvents were removed *in vacuo*. Flash chromatography (ethyl acetate/light petroleum 1:1) yielded the mixture products from which the major diastereomer was obtained by crystallization (diethyl ether).

***(+)*-4** (57 %) $[\alpha]_D$ = 212^0; m.p. 205-207 ^{0}C; ^{1}H-NMR ($CDCl_3$) δ 7.82 (bs, 1H), 7.60 (d, *J* = 4 Hz, 2H), 7.44 (d, *J* = 4 Hz, 1H), 7.32-7.28 (m, 3H), 7.15 (t, *J* = 3 Hz, 1H), 7.08 (t, *J* = 3 Hz, 1H), 4.78 (q, *J* = 3 Hz, 1H), 3.52-3.39 (m, 2H), 2.94-2.86 (m, 1H), 2.68 (d, *J* = 7 Hz, 1H), 2.43 (s, 3H), 1.69 (d, *J* = 3 Hz, 3H); IR ($CHCl_3$): 3470, 1466, 1060; HRMS (EI): Calcd. for $C_{19}H_{20}N_2SO$ 324.1292, Found: 324.1297.

***(+)*-5** (61 %) $[\alpha]_D$ = 196^0; m.p. 229-233 ^{0}C; ^{1}H-NMR ($CDCl_3$) δ 7.77 (bs, 1H), 7.61 (d, *J* = 4 Hz, 2H), 7.42 (d, *J* = 4 Hz, 1H), 7.33-7.27 (m, 3H), 7.13 (t, *J* = 3 Hz, 1H), 7.08 (t, *J* = 3 Hz, 1H), 4.71 (t, *J* = 3 Hz, 1H), 3.51-3.45 (m, 1H), 3.29-3.22 (m, 1H), 3.00-2.94 (m, 1H), 2.67-2.62 (m, 1H), 2.42 (s, 3H), 2.17-2.14 (m, 1H), 2.11-1.91 (m, 1H), 1.09 (t, *J* = 5 Hz, 3H); IR ($CHCl_3$): 3470, 1466, 1060; HRMS (EI): Calcd. for $C_{20}H_{22}N_2SO$ 338.1448, Found: 338.1454.

***(+)*-6** (58 %) $[\alpha]_D$ = 190^0; m.p. 204-206 ^{0}C; ^{1}H-NMR ($CDCl_3$) δ 7.80 (s, 1H), 7.60 (d, *J* = 4 Hz, 2H), 7.41 (d, *J* = 4 Hz, 1H), 7.33-7.28 (m, 3H), 7.14 (t, *J* = 4 Hz, 1H), 7.09 (t, *J* = 4 Hz, 1H), 4.77 (t, *J* = 3 Hz, 1H), 3.52-3.46 (m, 1H), 3.29-3.21 (m, 1H), 3.03-2.96 (m, 1H), 2.63 (d, *J* = 7 Hz, 1H), 2.43 (s, 3H), 2.05-1.87 (m, 2H), 1.63-1.52 (m, 2H), 1.00 (t, *J* = 3 Hz, 3H); IR ($CHCl_3$): 3470, 1466, 1060; HRMS (EI): Calcd. for $C_{21}H_{24}N_2SO$ 352.1604, Found: 352.1602.

***(+)*-7** (60 %) $[\alpha]_D$ = 167^0; m.p. 208-211 ^{0}C; ^{1}H-NMR ($CDCl_3$) δ 7.88 (bs, 1H), 7.61 (d, *J* = 4 Hz, 2H), 7.42 (d, *J* = 4 Hz, 1H), 7.33-7.28 (m, 3H), 7.13 (t, *J* = 4 Hz, 1H), 7.07 (t, *J* = 4 Hz, 1H), 4.76 (t, *J* = 3 Hz, 1H), 3.50-3.45 (m, 1H), 3.28-3.21 (m, 1H), 3.02-2.95 (m, 1H), 2.63 (d, *J* = 7 Hz, 1H), 2.42 (s, 3H), 2.06-2.02 (m, 1H), 2.00-1.86 (m, 1H), 1.58-1.34 (m, 4H), 0.94 (t, *J* = 7 Hz, 3H); IR ($CHCl_3$): 3471, 1468, 1060; HRMS (EI): Calcd. for $C_{22}H_{26}N_2SO$ 366.1760, Found: 366.1764.

***(+)*-8** (57 %) $[\alpha]_D$ = 158^0; m.p. 179-182 ^{0}C; ^{1}H-NMR ($CDCl_3$) δ 7.87 (bs, 1H), 7.61 (d, *J* = 4 Hz, 2H), 7.42 (D, *J* = 4 Hz, 1H), 7.33-7.27 (m, 3H), 7.12 (t, *J* = 3 Hz, 1H), 7.05 (t, *J* = 3 Hz, 1H), 4.75 (t, *J* = 3 Hz, 1H), 3.51-3.45 (m, 1H), 3.28-3.20 (m, 1H), 3.02-2,95 (m, 1H), 2.63 (d, *J* = 7 Hz, 1H), 2.43 ((s, 3H), 2.05-1.87 (m, 2H), 1.57-1.49 (m, 2H), 1.40-1.34 (m, 4H), 0.90 (t, *J* = 4 Hz, 3H); IR ($CHCl_3$): 3470, 1468, 1059; HRMS (EI): Calcd. for $C_{23}H_{28}N_2SO$ 380.1916, Found: 380.1913.

***(+)*-9** (59 %) $[\alpha]_D = 190^0$; m.p. 190-193 ^{0}C; ^{1}H-NMR ($CDCl_3$) δ 7.80 (bs, 1H), 7.66 (d, *J* = 4 Hz, 2H), 7.44 (d, *J* = 4 Hz, 1H), 7.40-7.31 (m, 3H), 7.15 (t, *J* =3 Hz, 1H), 7.05 (t, *J* = 3 Hz, 1H), 4.63 (bs, 1H), 3.40-3.31 (m, 1H), 3.24-3.01 (m, 3H), 2.40 (s, 1H), 1.98-1.94 (m, 1H), 1.65-1.47 (m, 2H), 1.06 (d, *J* = 4 Hz, 3H), 1.97 (d, *J* = 4 Hz, 3H); IR ($CHCl_3$): 3467, 1466, 1061; HRMS (EI): Calcd. for $C_{22}H_{26}N_2SO$ 366.1760, Found: 366.1754.

***(+)*-10** (63 %) $[\alpha]_D = 215^0$; m.p. 222-224 ^{0}C; ^{1}H-NMR ($CDCl_3$) δ 7.76 (bs, 1H), 7.65 (d, *J* = 4 Hz, 2H), 7.45 (d, *J* = 4 Hz, 1H), 7.35-7.28 (m, 3H), 7.17 (t, *J* = 3 Hz, 1H), 7.08 (t, *J* = 3 Hz, 1H), 4.59 (d, *J* = 4 Hz, 1H), 3.61-3.54 (m, 1H), 3.26-3.16 (m, 1H), 3.08-2.98 (m, 1H), 2.65 (d, *J* = 7 Hz, 1H), 2.42 (s, 3H), 2.31-2.21 (m, 1H), 1.20 (d, *J* = 5 Hz, 3H), 1.10 (d, *J* = 5 Hz, 3H); IR ($CHCl_3$): 3471, 1465, 1058; HRMS (EI): Calcd. for $C_{21}H_{24}N_2SO$ 352.1604, Found: 352.1609.

***(+)*-11** (57 %) $[\alpha]_D = 196^0$; m.p. 240-241 ^{0}C; ^{1}H-NMR ($CDCl_3$) δ 7.75 (bs, 1H), 7.62 (d, *J* = 4 Hz, 2H), 7.44 (d, *J* = 4 Hz, 1H), 7.35-7.27 (m, 3H), 7.18 (t, *J* = 3 Hz, 1H), 7.08 (t, *J* = 3 Hz, 1H), 4.55 (d, *J* = 4 Hz, 1H), 3.63-3.52 (m, 1H), 3.26-3.16 (m, 1H), 3.09-2.98 (m, 1H), 2.65 (d, *J* = 7 Hz, 1H), 2.42 (s, 3H), 1.96-1.78 (m, 4H), 1.77-1.68 (m, 1H), 1.43-1.14 (m, 6H); IR ($CHCl_3$): 3468, 1466, 1060; HRMS (EI): Calcd. for $C_{24}H_{28}N_2SO$ 392.1916, Found: 392.1917.

Removal of *p*-tolylsulfinyl chiral auxiliary

General procedure To a solution of the Pictet-Spengler product (0.1 mmol) in ethanol (3 mL) at 0 ^{0}C was added concentrated hydrochloric acid (200 µL). The reaction mixture was stirred for 5 min and made alkaline with saturated K_2CO_3 (3 mL). After addition of ethyl acetate (5 mL) and stirring for an additional 15 min the organic layer was removed. The aqueous layer was extracted with two 5 mL portions of ethyl acetate. The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated*in vacuo*. Flash chromatography (ethyl acetate/ethanol/NH_4OH(aq) 85:10:5) yielded the corresponding tetrahydro-ß-carboline as a syrup.

***(-)*-18** (89 %) $[\alpha]_D = -44.0^0$; ^{1}H-NMR ($CDCl_3$) δ 8.05 (bs, 1H), 7.50 (d, *J* = 4 Hz, 1H), 7.30 (d, *J* = 4 Hz, 1H), 7.18-7.09 (m, 2H), 4.17 (q, *J* = 3 Hz, 1H), 3.41-3.35 (m, 1H), 3.10-3.03 (m, 1H), 2.83-2.70 (m, 2H), 1.45 (d, *J* = 4 Hz, 3H); IR ($CHCl_3$): 3473, 1467; HRMS (EI): Calcd. for $C_{12}H_{14}N_2$ 186.1154, Found: 186.1157.

***(-)*-19** (93 %) $[\alpha]_D = -62.6^0$; ^{1}H-NMR ($CDCl_3$) δ 7.72 (bs, 1H), 7.48 (d, *J* = 4 Hz, 1H), 7.31 (d, *J* = 4 Hz, 1H), 7.18-7.05 (m, 2H), 4.06-3.99 (m, 1H), 3.42-3.31 (m, 1H), 3.09-2.99 (m, 1H), 2.81-2.68 (m, 2H), 2.00-1.89 (m, 1H), 1.78-1.67 (m, 1H), 1.08 (t, *J* = 5 Hz, 3H); IR ($CHCl_3$): 3473, 1469; HRMS (EI): Calcd. for $C_{13}H_{16}N_2$ 200.1310, Found: 200.1303.

***(-)*-20** (91 %) $[\alpha]_D = -30.0^0$; ^{1}H-NMR ($CDCl_3$) δ 7.80 (bs, 1H), 7.48 (d, *J* = 4 Hz, 1H), 7.30 (d, *J* = 4 Hz, 1H), 7.16-7.07 (m, 2H), 4.09-4.06 (m, 1H), 3.39-3.33 (m, 1H), 3.06-2.99 (m, 1H), 2.80-2.70 (m, 2H), 1.89-1.80 (m ,1H), 1.72-1.45 (m, 3H), 1.00 (t, *J* = 7 Hz, 3H); IR ($CHCl_3$): 3471, 1466; HRMS (EI): Calcd. for $C_{14}H_{18}N_2$ 214.1466, Found: 214.1458.

***(-)*-21** (93 %) $[\alpha]_D = -65.8^0$; ^{1}H-NMR ($CDCl_3$) δ 7.79 (bs, 1H), 7.48 (d, *J* = 4 Hz, 1H), 7.31 (d, *J* = 4 Hz, 1H), 7.18-7.06 (m, 2H), 4.11-4.03 (m, 1H), 3.41-3.34 (m, 1H), 3.08-2.98 (m, 1H), 2.80-2.70 (m, 2H), 1.96-1.84 (m, 2H), 1.75-1.63 (m, 1H), 1.58-1.36 (m, 3H), 0.94 (t, *J* = 5 Hz, 3H); IR ($CHCl_3$): 3473, 1466; HRMS (EI): Calcd. for $C_{15}H_{20}N_2$ 228.1622, Found: 228.1614.

***(-)*-22** (82 %) $[\alpha]_D$ = -40.0 ^{0}; ^{1}H-NMR ($CDCl_3$) δ 7.79 (bs, 1H), 7.48 (d, *J* = 4 Hz, 1H), 7.32 (d, *J* = 4 Hz, 1H), 7.17-7.06 (m, 2H), 4.13-4.06 (m, 1H), 3.42-3.33 (m, 1H), 3.10-2.99 (m, 1H), 2.83-2.69 (m, 2H), 1.95-1.82 (m, 1H), 1.78-1.65 (m, 1H), 1.62-1.42 (m, 2H), 1.42-1.38 (, 4H), 0.91 (t, *J* = 5 Hz, 3H); IR ($CHCl_3$): 3473, 1465; HRMS (EI): Calcd. for $C_{16}H_{22}N_2$ 242.1778, Found: 242.1770.

***(-)*-23** (90 %) $[\alpha]_D$ = -47.1 ^{0}; ^{1}H-NMR ($CDCl_3$) δ 7.76 (bs, 1H), 7.48 (d, *J* = 4 Hz, 1H), 7.80 (d, *J* = 4 Hz, 1H), 7.18-7.07 (m, 2H), 4.18-4.09 (m, 1H), 3.40-3.31 (m, 1H), 3.09-3.00 (m, 1H), 2.81-2.69 (m, 2H), 2.05-1.94 (m, 1H), 1.68-1.59 (m, 2H), 1.04 (d, *J* = 3 Hz, 3H) , 0.98 (d, *J* =3 Hz, 3H); IR ($CHCl_3$): 3471, 1466; HRMS (EI): Calcd. for $C_{15}H_{20}N_2$ 228.1622 , Found: 228.1620.

***(-)*-24** (93 %) $[\alpha]_D$ = -58.3 ^{0}; ^{1}H-NMR ($CDCl_3$) δ 7.76 (bs, 1H),), 7.48 (d, *J* = 4 Hz, 1H), 7.30 (d, *J* = 4 Hz, 1H), 7.19-7.07 (m, 2H), 4.07 (bs, 1H), 3.36-3.29 (m, 1H), 3.15-3.07 (m, 1H), 2.78-2.96 (m, 2H), 1.81-1.87 (m, 1H), 1.04 (t, *J* = 4 Hz, 3H), 0.95 (t, *J* = 4 Hz, 3H); IR ($CHCl_3$): 3473, 1467; HRMS (EI): Calcd. for $C_{14}H_{18}N_2$ 214.1466, Found: 214.1470.

***(-)*-25** (86 %) $[\alpha]_D$ = -68.5 ^{0}; ^{1}H-NMR ($CDCl_3$) δ 7.78 (bs, 1H), 7.47 (d, *J* = 4 Hz, 1H), 7.31 (d, *J* = 4 Hz, 1H), 7.18-7.07 (m, 2H), 4.00 (bs, 1H), 3.42-3.34 (m, 1H), 3.05-2.95 (m, 1H), 2.79-2.68 (m, 2H), 1.88-1.67 (m, 4H), 1.59-1.11 (m, 7H); IR ($CHCl_3$): 3473, 1464; HRMS (EI): Calcd. for $C_{17}H_{22}N_2$ 254.1778, Found: 254.1769.