Supporting Information

for

Enantioselective Synthesis of the Pyrroloquinoline Core of the Martinellines

Authors:

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General: Proton and carbon magnetic resonance spectra were recorded in $CDCl_3$ at 300 and 75.5 MHz, respectively, and are reported in ppm on the δ scale. Infrared spectra, mass spectra, combustion analysis, and optical rotation were determined by Structure and Analytical Chemistry, Pharmacia & Upjohn. Anhydrous THF was distilled prior to use from sodium metal/benzophenone ketyl. Dry benzene, DMF and acetonitrile were purchased from Aldrich in Sure-Seal® bottles. For the high pressure carbon monoxide reactions, a stainless steel 100 mL high-pressure mini reactor or "bomb" (Parr Instrument Company, Series 4560) equipped with a thermocouple, gas inlet, gas outlet, pressure gauge (to 2000 psi), and mechanical stirrer was used. Unless otherwise noted, all non-aqueous reactions were carried out under a nitrogen atmosphere using oven-dried glassware.

(4b*S*,7*R*,10a*R*)-7-Phenyl-6,7,10,10a,11,12-hexahydro-9H-benzo[g][1,3]oxazolo[2,3-i]indol-9-one (8)

2-(1-Oxo-1,2,3,4-tetrahydro-2-naphthalenyl)acetic acid (**7b**)[4] (1.04 g, 5.09 mmol) and (*R*)-(-)-2-phenylglycinol (0.771 g, 5.18 mmol) were dissolved in toluene (40 mL). The solution was refluxed with azeotropic removal of water until HPLC analysis showed complete consumption of **7b**. The toluene was removed *in vacuo* and the resulting crude product was purified by silica gel column chromatography (1:2 ethyl acetate - *n*-heptane, the sample was loaded as a solution in chloroform) to give **8** (1.18 g, 3.86 mmol, 76% yield) as a extremely viscous orange oil. IR (liq.) 1718, 1450, 1329, 1290, 1268, 1245, 1195, 1046, 1033, 1025, 902, 768, 750, 715, 698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.45 - 7.32 (m, 5 H), 7.19 (d, *J* = 4 Hz, 2 H), 6.94 (dt, *J* = 4, 8 Hz, 1 H), 6.88 (d, *J* = 8 Hz, 1 H), 5.32 (t, *J* = 8 Hz, 1 H), 4.68 (dd, *J* = 8, 9 Hz, 1 H), 4.18 (dd, *J* = 8, 9 Hz, 1 H), 3.06 - 2.97 (m, 2 H), 2.84 - 2.72 (m, 3 H), 2.59 (dd, *J* = 12, 16 Hz, 1 H), 2.39 - 2.32 (m, 1 H), 1.51 - 1.43 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 179.0, 140.1, 138.6, 134.5, 128.7, 128.4, 127.7, 127.4, 126.8, 126.3, 125.9, 100.5, 71.1, 58.7, 44.0, 41.0, 28.2, 28.0; MS (FAB) *m/z* 306 (MH^+), 460, 459, 307, 306, 304, 187, 186, 133, 91, 87; HRMS (FAB) calcd for $C_{20}H_{19}NO_2 + H_1$ 306.1494, found 306.1496. $[\alpha]_D^{25}$ -191 (*c* 0.46, chloroform).

(2*R*)-2-[(3a*R*,9b*S*)-2,3,3a,4,5,9b-hexahydro-1H-benzo[g]indol-1-yl]-2-phenyl-1-ethanol (9b)

Compound **8** (106 mg, 0.346 mmol) was dissolved in anhydrous THF (6 mL) and the resulting solution was cooled to –78 °C. Diisobutylaluminum hydride (1.73 mL, 1.73 mmol, 1.0 M in toluene) was added and the solution was slowly warmed to room temperature overnight. The reaction was quenched by slow addition of methanol (1 mL), followed by CH_2Cl_2 (15 mL) and sodium potassium tartrate (5 mL, saturated aqueous). The resulting mixture was stirred vigorously for 0.5 h. The CH_2Cl_2 layer was separated and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The product was purified by silica gel column chromatography (1:2 ethyl acetate - *n*-heptane, the sample was loaded as a solution in chloroform) to give **9b** (72.8 mg, 0.248 mmol, 72% yield) as a light orange oil. IR (liq.) 3026, 2932, 2863, 2841, 1491, 1453, 1131, 1111, 1075, 1055, 1035, 1028, 751, 704, 626 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.47 - 7.21 (m, 9 H), 3.99 (dd, *J* = 4, 11 Hz, 1 H), 3.87 (t, *J* = 10 Hz, 1 H), 3.70 (d, *J* = 9 Hz, 1 H), 3.43 (dd, *J* = 5, 10 Hz, 1 H), 3.03 (bt, *J* = 8 Hz, 1 H), 2.89 (t, *J* = 12 Hz, 1 H), 2.55 (dt, *J* = 4, 15 Hz, 1 H), 2.45 (t, *J* = 8 Hz, 1 H), 2.28 - 2.19 (m, 1 H), 2.06 - 1.97 (m, 1 H), 1.74 - 1.65 (m, 2 H), 1.55 (ddt, *J* = 4, 7, 13 Hz,1 H); ^{13}C NMR ($CDCl_3$) δ 141.5, 136.5, 135.0, 130.5, 129.6, 128.5, 128.2, 127.8, 127.4, 127.3, 125.6, 61.2, 60.9, 44.6, 34.8, 30.8, 29.5, 26.4; MS (FAB) *m/z* 294 (MH^+), 295, 294, 293, 292, 263, 262, 172, 157, 129, 91; HRMS (FAB) calcd for $C_{20}H_{23}NO + H_1$ 294.1858, found 294.1851. $[\alpha]_D^{25}$ -190 (*c* 1.00, chloroform).

(3a*R*,9b*S*)-1-[(1*R*)-2-Hydroxy-1-phenylethyl]-1,3,3a,4,5,9b-hexahydro-2H-benzo[g]indol-2-one (9a)

Compound **8** (589 mg, 1.93 mmol) was dissolved in CH_2Cl_2 (8.5 mL) and the resulting solution was cooled to –78 °C. Triethylsilane (0.678 mL, 4.24 mmol) was added and the solution was stirred for 15

min prior to slow addition of titanium tetrachloride (4.24 mL, 4.24 mmol, 1.0 M in CH_2Cl_2). The reaction was stirred for 2 h more before warming to room temperature. After stirring for 45 min at room temperature the reaction was poured into saturated aqueous NH_4Cl. The CH_2Cl_2 layer was separated and the aqueous layer was extracted twice more with CH_2Cl_2. The CH_2Cl_2 layers were combined, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The product was purified by silica gel column chromatography (2:1 ethyl acetate – *n*-heptane, the sample was loaded as a solution in chloroform) to give **9a** (0.545 g, 1.77 mmol, 92% yield) as a colorless oil. IR (liq.) 3353, 2937, 1666, 1494, 1454, 1436, 1420, 1351, 1273, 1259, 1069, 749, 700, 680, 632 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.43 - 7.38 (m, 2 H), 7.34 (d, *J* = 7 Hz, 1 H), 7.29 (dd, *J* = 1, 7 Hz, 1 H), 7.23 - 7.17 (m, 4 H), 6.91 (d, *J* = 7 Hz, 1 H), 4.58 (d, *J* = 7 Hz, 1 H), 4.33 (bs, 1 H), 4.07 - 4.00 (m, 2 H), 3.87 - 3.79 (m, 1 H), 3.01 (dd, *J* = 9, 18 Hz, 1 H), 2.88 - 2.74 (m, 2 H), 2.68 (dt, *J* = 6, 10 Hz, 1 H), 2.44 (dd, *J* = 2, 17 Hz, 1 H), 1.88 - 1.70 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 176.9, 140.5, 137.1, 131.7, 130.6, 128.8, 128.7, 128.6, 127.6, 127.4, 125.8, 64.6, 61.9, 61.5, 39.6, 30.6, 29.3, 27.0; MS (FAB) *m/z* 308 (MH^+), 462, 461, 384, 309, 308, 306, 188, 143, 129, 91; HRMS (FAB) calcd for $C_{20}H_{21}NO_2$ $+H_1$ 308.1650, found 308.1651. $[\alpha]_D^{25}$ +132 (*c* 1.00, chloroform).

(3a*R*,9b*S*)-1,3,3a,4,5,9b-Hexahydro-2H-benzo[g]indol-2-one (11a)

Compound **9a** (3.41 g, 11.1 mmol) was dissolved in DMSO (80 mL), lithium hydroxide monohydrate was added and the solution was heated to 140 °C. The progress of the reaction was followed by HPLC and after complete consumption of the starting material the DMSO was removed *in vacuo*. To the resulting brown oil was added a mixture of water and ethyl acetate. The ethyl acetate layer was separated and the aqueous layer was extracted three times with ethyl acetate. The ethyl acetate layers were combined, dried over $MgSO_4$, and concentrated *in vacuo*. The isolated impure orange oil (3.69 g, **10**) was dissolved in THF (80 mL). To the THF solution was added a 1 N aqueous solution of HCl (20 mL). The reaction solution was heated to reflux for 8 h after which it was cooled and poured into water. The aqueous layer was extracted three times with ethyl acetate. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification of the product was accomplished by silica gel chromatography (9:1 ethyl acetate – *n*-heptane, the sample was loaded as a solution in chloroform) to give **11a** (1.57 g, 8.39 mmol, 76% yield) as a white solid. mp 194.0 – 194.6 °C. IR (drift) 3198, 2924, 2856, 1710, 1328, 1296, 1275, 1260, 792, 761, 752, 745, 716, 672, 632 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.24 - 7.18 (m, 3 H), 7.16 - 7.12 (m, 1 H), 6.88 (bs, 1 H), 4.77 (d, *J* = 6.5 Hz, 1 H), 2.84 - 2.65 (m, 4 H), 2.23 - 2.14 (m, 1 H), 1.86 (dq, *J* = 5, 13 Hz, 1 H), 1.75 - 1.63 (m, 1 H);^{13}C NMR (75 MHz, $CDCl_3$) δ 177.2, 137.2, 134.2, 129.0, 128.9, 127.6, 126.7, 54.7, 37.6, 33.9, 27.6, 26.1; MS (EI) *m/z* 187 (M^+), 186, 159, 143, 130, 128, 115, 91, 89, 64, 59; HRMS (FAB) calcd for $C_{12}H_{13}NO$ $+H_1$ 188.1075, found 188.1070. Anal. Calcd for $C_{12}H_{13}NO$: C, 76.98; H, 7.00; N, 7.48. Found: C, 76.92; H, 7.08; N, 7.42. $[\alpha]_D^{25}$ +70 (*c* 0.99, chloroform).

Some physical characteristics for the enantiomer of **11a** were reported in a paper by Koot *et al.*[8] The authors reported a melting point for the enantiomer of **11a** of 196.5 – 197.5 °C, which is consistent with the value we obtained (194.0 – 194.6 °C). However, for the enantiomer of **11a** they also report an optical rotation of $[\alpha]_D^{20}$ -23 (*c* 0.84, chloroform). We repeatedly observed a value of $[\alpha]_D^{25}$ +70 (*c* 0.99, chloroform) for **11a**.

(3a*R*,9b*S*)-2,3,3a,4,5,9b-Hexahydro-1H-benzo[g]indole (11b)

Compound **11a** (135 mg, 0.719 mmol) was dissolved in THF (7 mL) and the resulting solution was cooled to 0 °C. A solution of lithium aluminum hydride (3.60 mL, 3.60 mmol, 1.0 M in THF) was added slowly. **Caution: vigorous bubbling.** After cessation of the bubbling the ice bath was removed and the reaction was stirred at room temperature overnight. The reaction was quenched by slow addition of 1 ml of a 1 N aqueous NaOH solution. The suspension was stirred vigorously for 0.5 h, filtered through a pad of Celite®, and washed with ethyl acetate. The filtrate was concentrated *in vacuo*

producing crude product. Purification was accomplished by silica gel column chromatography (9:1 CH_2Cl_2 – MeOH with 0.5% NH_4OH, the sample was loaded as a solution in chloroform) resulting in the isolation of **11b** (106 mg, 0.611 mmol, 85% yield) as a low melting white solid. mp 35.6 - 38.2 °C. IR (liq.) 3287, 3061, 3045, 3019, 2927, 2867, 2839, 1489, 1453, 1434, 1410, 1395, 1364, 1341, 770, 744 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.44 - 7.42 (m, 1 H), 7.21 - 7.09 (m, 3 H), 4.02 (d, *J* = 6.8 Hz, 1 H), 3.10 (ddd, *J* = 5, 8, 11 Hz, 1 H), 2.90 (ddd, *J* = 7, 9, 11 Hz, 1 H), 2.79 - 2.61 (m, 3 H), 2.40 - 2.29 (m, 1 H), 2.21 - 2.09 (m, 1 H), 1.77 (dq, *J* = 5, 13 Hz, 1 H), 1.64 - 1.53 (m, 1 H), 1.50 - 1.37 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 137.5, 136.6, 129.8, 128.3, 126.6, 126.0, 59.6, 45.5, 37.4, 33.0, 29.0, 26.4; MS (EI) *m/z* 173 (M^+), 173, 171, 144, 130, 128, 116, 115, 102, 63, 51; HRMS (FAB) calcd for $C_{12}H_{15}N + H_1$ 174.1283, found 174.1288. $[\alpha]_D^{25}$ +34 (*c* 1.14, chloroform).

Benzyl 3-(2-methoxy-2-oxoethyl)-4-oxo-3,4-dihydro-1(2H)-quinolinecarboxylate (13a)

Compound **12** (356 mg, 0.905 mmol), benzene (10 mL), acetonitrile (10 mL), triethylamine (0.252 mL, 1.81 mmol), methanol (0.733 mL, 0.87 M), and $Pd(PPh_3)_2Cl_2$ (30.8 mg, 0.0439 mmol) were placed in a 100 mL bomb. The apparatus was assembled, stirring was commenced, and the bomb was purged thoroughly with CO before charging to 1600 psi. **Caution: carbon monoxide is highly toxic**. The bomb was warmed to 65 °C using a Parr Temperature Controller (Model 4841) and Bomb Support and Stirrer Drive System. As the reaction temperature increased small quantities of gas were released to maintain the desired pressure (1600 psi). After the reaction had been maintained at the desired pressure and temperature for 18 h it was cooled, depressurized and poured into water. The resulting mixture was extracted three times with ethyl acetate. The ethyl acetate layers were combined, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was purified by silica gel column chromatography (1:5 ethyl acetate - *n*-heptane, the sample was loaded as a solution in chloroform) producing **13a** (192 mg, 0.543 mmol, 60% yield) as a light orange viscous oil which solidified upon standing. mp 70.6 - 74.6 °C. IR (mull) 1737, 1709, 1690, 1483, 1403, 1324, 1299, 1277, 1230, 1200, 1169, 1157, 1057, 769, 743 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.01 (dd, *J* = 2, 8 Hz, 1 H), 7.86 (d, *J* = 8 Hz, 1 H), 7.52 (dt, *J* = 2, 7 Hz, 1 H), 7.44 - 7.34 (m, 5 H), 7.19 (dt, *J* = 1, 8 Hz, 1 H), 5.33 (d, *J* = 12 Hz, 1 H), 5.27 (d, *J* = 12 Hz, 1 H), 4.64 (dd, *J* = 5, 13 Hz, 1 H), 3.79 (dd, *J* = 12, 13 Hz, 1 H), 3.69 (s, 3 H), 3.27 - 3.17 (m, 1 H), 2.88 (dd, *J* = 5, 17 Hz, 1 H), 2.57 (dd, *J* = 8, 17 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 194.3, 171.6, 153.5, 143.3, 135.5, 134.1, 128.5, 128.3, 128.0, 127.5, 124.2, 124.1, 123.1, 68.1, 51.8, 48.3, 44.0, 31.7; MS (EI) *m/z* 353 (M^+), 147, 146, 92, 91, 78, 77, 65, 64, 59, 51; HRMS (FAB) calcd for $C_{20}H_{19}NO_5 + Na_1$ 376.1161, found 376.1177. Anal. Calcd for $C_{20}H_{19}NO_5$: C, 67.98; H, 5.42; N, 3.96. Found: C, 67.76; H, 5.53; N, 3.98.

Compound **13a** could be produced on a larger scale under more concentrated conditions with a slight reduction in yield. This reaction was performed in a 200 mL Parr bomb at 60 °C under 1600 psi CO pressure with the following quantities: **12**, 8.37 g (21.3 mmol); benzene, 65 mL; acetonitrile, 65 mL; triethylamine 4.45 mL (31.9 mmol); methanol, 5.2 mL; and $Pd(PPh_3)_2Cl_2$, 370 mg (0.527 mmol). Silica gel column chromatography produced 3.90 g of pure compound **13a** (11.0 mmol, 52% yield).

2-{1-[(Benzyloxy)carbonyl]-4-oxo-1,2,3,4-tetrahydro-3-quinolinyl}acetic acid (13b)

Compound **13a** (860 mg, 2.43 mmol) was dissolved in dioxane (30 mL), water (10 mL) was added and the solution was cooled to 0 °C. An aqueous solution of LiOH (9.73 mL, 9.73 mmol, 1.0 M) was added and the reaction mixture was stirred for 1.5 h. The reaction was quenched by the addition of an aqueous saturated citric acid solution until the pH ≤ 3. The resulting solution was extracted three times with chloroform. The chloroform layers were combined, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was purified by silica gel column chromatography (1:1 ethyl acetate - *n*-heptane with 1% acetic acid, the sample was loaded as a solution in chloroform) resulting in the isolation of **13b** (782 mg, 2.31 mmol, 95% yield) as a light yellow solid. mp 142.2 - 143.0 °C (dec.). IR (drift) 1706, 1688, 1484, 1459, 1453, 1403, 1362, 1323, 1313, 1304, 1287, 1233, 1201, 767, 734 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.01 (dd, *J* = 2, 8 Hz, 1 H), 7.86 (d, *J* = 8 Hz, 1 H), 7.53 (dt, *J* = 2, 7 Hz, 1

H), 7.43 - 7.32 (m, 5 H), 7.20 (t, *J* = 8 Hz, 1 H), 5.34 (d, *J* = 12 Hz, 1 H), 5.27 (d, *J* = 12 Hz, 1 H), 4.69 (dd, *J* = 5, 13 Hz, 1 H), 3.78 (t, *J* = 12 Hz, 1 H), 3.27 - 3.17 (m, 1 H), 2.95 (dd, *J* = 5, 17 Hz, 1 H), 2.61 (dd, *J* = 8, 17 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 194.4, 177.0, 153.6, 143.5, 135.5, 134.4, 128.6, 128.4, 128.1, 127.7, 124.4, 124.1, 123.3, 68.4, 48.4, 43.9, 31.8; MS (EI) *m/z* 339 (M^+), 236, 158, 146, 130, 91, 77, 65, 64, 63, 51; HRMS (FAB) calcd for $C_{19}H_{17}NO_5$ +H_1 340.1185, found 340.1189. Anal. Calcd for $C_{19}H_{17}NO_5$: C, 67.25; H, 5.05; N, 4.13. Found: C, 66.89; H, 5.15; N, 4.10.

Benzyl (2a*S*,8b*S*,11*R*)-1-oxo-11-phenyl-1,2,2a,3,10,11-hexahydro-4H-[1,3]oxazolo[3',2':1,2]pyrrolo [3,2-c]quinoline-4-carboxylate (14)

Compound **13b** (779 mg, 2.29 mmol) and (*R*)-(-)-2-phenylglycinol (430 mg, 2.52 mmol) were dissolved in toluene (50 mL). The solution was refluxed with azeotropic removal of water until **13b** was consumed (~21 h). The toluene was then removed *in vacuo*. Purification of the crude product was accomplished by radial column chromatography (4 mm plate, 1:1 ethyl acetate - *n*-heptane, the sample was loaded as a solution in chloroform) resulting in the isolation of **14** (772 mg, 1.75 mmol, 77% yield) as a viscous light yellow oil which solidified upon standing. mp 72.4 - 78.8 °C. IR (drift) 1710, 1490, 1453, 1402, 1361, 1327, 1289, 1265, 1214, 1144, 1046, 761, 732, 716, 698 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.56 (bd, *J* = 7 Hz, 1 H), 7.41 - 7.29 (m, 8 H), 7..21 - 7.18 (m, 3 H), 6.81 - 6.74 (m, 2 H), 5.44 (t, *J* = 6 Hz, 1 H), 5.29 (s, 2 H), 4.60 (t, *J* = 8 Hz, 1 H), 4.46 (dd, *J* = 5, 9 Hz, 1 H), 4.03 (dd, *J* = 5, 14 Hz, 1 H), 3.80 (dd, *J* = 6, 14 Hz, 1 H), 3.25 - 3.15 (m, 1 H), 2.74 (d, *J* = 10 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 178.4, 154.1, 138.9, 138.4, 135.9, 129.6, 128.8, 128.5, 128.4, 128.2, 128.0, 127.7, 127.4, 126.0, 124.4, 124.0, 98.6, 71.9, 67.9, 58.9, 46.9, 45.7, 36.7; MS (FAB) *m/z* 441 (MH^+), 442, 441, 440, 371, 321, 129, 92, 91, 57, 43; HRMS (FAB) calcd for $C_{27}H_{24}N_2O_4$ +H_1 441.1814, found 441.1805. $[\alpha]_D^{25}$ -114 (*c* 0.91, chloroform).

Benzyl (3a*S*,9b*S*)-1-[(1*R*)-2-hydroxy-1-phenylethyl]-2-oxo-1,2,3,3a,4,9b-hexahydro-5H-pyrrolo[3,2-c]quinoline-5-carboxylate (15b) and (3a*S*,9b*S*)-1-[(1*R*)-2-hydroxy-1-phenylethyl]-1,3,3a,4,5,9b-hexahydro-2H-pyrrolo[3,2-c]quinolin-2-one (15a)

Compound **14** (772 mg, 1.75 mmol) was dissolved in CH_2Cl_2 (8 mL) and cooled to –78 °C. Triethylsilane (1.68 mL, 10.5 mmol) was added and the reaction was stirrred for 15 min. before slow addition of a solution of $TiCl_4$ (10.5 mL, 10.5 mmol, 1.0 M in CH_2Cl_2). The reaction was slowly warmed to room temperature over 2 h. More CH_2Cl_2 (10 mL) was added to wash down the solid on the sides of the reaction flask and the reaction was stirred for an additional hour at room temperature. The reaction was quenched by the slow addition of saturated aqueous $NaHCO_3$ followed by water. The organic phase was separated and the aqueous layer was extracted with ethyl acetate three times. The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude material was triturated with $CHCl_3$ and the material that dissolved was subjected to radial column chromatography (4 mm plate, 9:1 ethyl acetate – *n*-heptane, the sample was loaded as a solution in chloroform). Both **15b** (R_f = 0.29) and **15a** (R_f = 0.14) were isolated off the column. Compound **15a** isolated off the column was recombined with the triturated solid.

15b: (169 mg, 0.382 mmol, 22% yield) was obtained as a light orange oil. IR (liq.) 1703, 1667, 1494, 1454, 1438, 1405, 1363, 1350, 1307, 1281, 1257, 1216, 1186, 756, 699 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.60 (d, *J* = 8 Hz, 1 H), 7.43 - 7.31 (m, 9 H), 7.21 (d, *J* = 9 Hz, 1 H), 7.20 (d, *J* = 7 Hz, 1 H), 7.15 (dd, *J* = 1, 7 Hz, 1 H), 7.01 (dd, *J* = 1, 8 Hz, 1 H), 5.30 (d, *J* = 12 Hz, 1 H), 5.22 (d, *J* = 12 Hz, 1 H), 4.67 (dd, *J* = 5, 9 Hz, 1 H), 4.55 (d, *J* = 8 Hz, 1 H), 4.23 (d, *J* = 13 Hz, 1 H), 4.40 - 3.92 (m, 2 H), 3.81 - 3.78 (m, 1 H), 3.27 (dd, *J* = 5, 13 Hz, 1 H), 3.04 (bs, 1 H), 2.99 – 2.90 (m, 1 H), 2.67 (dd, *J* = 3, 17 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 175.6, 154.4, 141.0, 136.8, 135.9, 130.4, 129.3, 128.9, 128.6, 128.3, 128.1, 127.9, 127.5, 127.4, 125.2, 124.8, 68.0, 64.2, 62.4, 59.8, 49.4, 36.9, 34.3; MS (EI) *m/z* 442 (M^+), 277, 130, 106, 105, 104, 103, 91, 77, 65, 51; HRMS (FAB) calcd for $C_{27}H_{26}N_2O_4$ +H_1 443.1971, found 443.1961. $[\alpha]_D^{25}$ +79 (*c* 0.66, chloroform).

15a: (338 mg, 1.09 mmol, 63% yield) was obtained as a white solid. mp 215.0 - 216.2 °C. IR (drift) 3409, 3339, 1678, 1611, 1524, 1498, 1413, 1349, 1308, 1288, 1037, 756, 750, 713, 703 cm^{-1}; ^1H NMR (DMSO-d_6) δ 7.38 - 7.25 (m, 5 H), 7.02 (t, *J* = 7 Hz, 1 H), 6.69 (d, *J* = 7 Hz, 1 H), 6.59 (d, *J* = 8 Hz, 1 H), 6.47 (t, *J* = 7 Hz, 1 H), 6.13 (s, 1 H), 4.86 (t, *J* = 6 Hz, 1 H), 4.45 (d, *J* = 5 Hz, 1 H), 4.32 (t, *J* = 6 Hz, 1 H), 4.08 - 4.00 (m, 1 H), 3.94 - 3.87 (m, 1 H), 3.14 - 3.08 (m, 1 H), 2.92 (t, *J* = 11 Hz, 1 H), 2.73 (dd, *J* = 7, 16 Hz, 1 H), 2.44 - 2.40 (m, 1 H), 2.03 (d, *J* = 16 Hz, 1 H); ^{13}C NMR (DMSO-d_6) δ 174.7, 146.6, 139.2, 132.2, 129.1, 128.4, 127.6, 127.0, 115.0, 114.7, 114.5, 62.9, 59.4, 57.5, 41.2, 36.0, 30.2; MS (EI) *m/z* 308 (M^+), 277, 144, 130, 116, 115, 106, 103, 91, 78, 77; HRMS (FAB) calcd for $C_{19}H_{20}N_2O_2 + H_1$ 309.1603, found 309.1596. Anal. Calcd for $C_{19}H_{20}N_2O_2$: C, 74.00; H, 6.54; N, 9.08. Found: C, 73.60; H, 6.58; N, 8.92. $[\alpha]_D^{21}$ +79 (c 0.79, DMSO).

(3a*S*,9b*S*)-1,3,3a,4,5,9b-Hexahydro-2H-pyrrolo[3,2-c]quinolin-2-one (16)

Compound **16** can be formed in two steps from either **15a** or **15b**.

A: Compound **15b** (134 mg, 0.302 mmol) was dissolved in DMSO (3 mL), $LiOH \cdot H_2O$ (63.3 mg, 1.51 mmol) was added and the solution was heated to 140 °C for 15 h. The DMSO was remove *in vacuo*, and the residue was dissolved in a mixture of water and ethyl acetate. The ethyl acetate was separated and the aqueous layer was extracted three times with ethyl acetate. The ethyl acetate layers were combined, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The product was purified by radial column chromatography (1 mm plate, 9:1 ethyl acetate - *n*-heptane, the sample was loaded as a solution in chloroform) which gave the elimination product (3a*S*,9b*S*)-1-(1-phenylvinyl)-1,3,3a,4,5,9b-hexahydro-2H-pyrrolo[3,2-c]quinolin-2-one (72.5 mg, 0.250 mmol, 83% yield).

B: Compound **15a** (338 mg, 1.09 mmol) was dissolved in DMSO (13 mL), $LiOH \cdot H_2O$ (183 mg, 4.36 mmol) was added and the solution was heated to 140 °C for 18 h. The DMSO was removed *in vacuo*, and the residue was dissolved in a mixture of water and ethyl acetate. The ethyl acetate was separated and the aqueous layer was diluted with brine and extracted three times with ethyl acetate. The ethyl acetate layers were combined, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The product was purified by radial column chromatography (4 mm plate, 9:1 ethyl acetate - *n*-heptane, the sample was loaded as a solution in chloroform) which gave (3a*S*,9b*S*)-1-(1-phenylvinyl)-1,3,3a,4,5,9b-hexahydro-2H-pyrrolo[3,2-c]quinolin-2-one (266 mg, 0.914 mmol, 84% yield).

Compound (3a*S*,9b*S*)-1-(1-phenylvinyl)-1,3,3a,4,5,9b-hexahydro-2H-pyrrolo[3,2-c]quinolin-2-one was produced as a light orange viscous oil. IR (liq.) 1691, 1628, 1611, 1499, 1494, 1445, 1391, 1340, 1298, 1266, 1219, 777, 753, 726, 696 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.39 - 7.30 (m, 5 H), 7.03 (dt, *J* = 1, 8 Hz, 1 H), 2.82 (d, *J* = 8 Hz, 1 H), 6.58 (d, *J* = 8 Hz, 1 H), 6.57 (dt, *J* = 1, 8 Hz, 1 H), 5.72 (s, 1 H), 5.13 (s, 1 H), 4.87 (d, *J* = 7 Hz, 1 H), 3.91 (bs, 1 H), 3.27 (dd, *J* = 4, 12 Hz, 1 H), 3.17 (dd, *J* = 6, 12 Hz, 1 H), 2.98 - 2.88 (m, 1 H), 2.84 - 2.67 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 174.1, 145.3, 141.4, 135.9, 131.2, 128.7, 128.6, 128.5, 126.1, 118.8, 117.6, 115.4, 115.1, 57.3, 43.1, 34.7, 32.1; MS (EI) *m/z* 290 (M^+), 290, 143, 131, 115, 103, 91, 89, 77, 65, 51; HRMS (FAB) calcd for $C_{19}H_{18}N_2O + H_1$ 291.1497, found 291.1494. $[\alpha]_D^{25}$ +42 (*c* 0.57, chloroform).

To (3a*S*,9b*S*)-1-(1-phenylvinyl)-1,3,3a,4,5,9b-hexahydro-2H-pyrrolo[3,2-c]quinolin-2-one (1.50 g, 5.18 mmol) was added THF (43 mL) followed by 1 N HCl (8.8 mL). The reaction was refluxed for 9 h, cooled to room temperature and quenched by slow addition of saturated $NaHCO_3$ until the bubbling stopped. The solution was extracted with ethyl acetate three times. The ethyl acetate layers were combined, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was triturated with warm acetone and the dissolved material was subjected to radial column chromatography (4 mm plate, eluting sequentially with *n*-heptane, 1:1 ethyl acetate – *n*-heptane, 9:1 ethyl acetate – *n*-heptane, and finally ethyl acetate with 1% methanol, the sample was loaded as a solution in acetone and the plate was dried prior to running the column). The compound off the column was recombined with the triturated solid which yielded **16** (778 mg, 4.13 mmol, 80% yield) as a white solid. mp 198.8 - 199.6 °C. IR (drift) 3336, 1684, 1644, 1610, 1501, 1371, 1335, 1302, 1276, 758, 747, 704, 671, 667, 633 cm^{-1}; ^1H NMR (CD_3OD) δ 7.12 (d, *J* = 8 Hz, 1 H), 7.01 (dt, *J* = 1, 7 Hz, 1 H), 6.66 (dt, *J* = 1, 7 Hz, 1

H), 6.63 (d, *J* = 8 Hz, 1 H), 4.72 (d, *J* = 6.8 Hz, 1 H), 3.16 (dd, *J* = 4, 11 Hz, 1 H), 2.92 (dd, *J* = 8, 11 Hz, 1 H), 2.83 - 2.75 (m, 1 H), 2.59 (dd, *J* = 8, 17 Hz, 1 H), 2.21 (dd, *J* = 4, 17 Hz, 1 H); ^{13}C NMR (CD_3OD) δ 177.8, 145.4, 129.3, 127.4, 119.9, 117.1, 114.5, 52.5, 41.9, 33.7, 33.3; MS (EI) *m/z* 188 (M^+), 189, 188, 145, 144, 131, 130, 78, 77, 52, 51; HRMS (FAB) calcd for $C_{11}H_{12}N_2O$ $+H_1$ 189.1028, found 189.1036. $[\alpha]_D^{25}$ -71 (*c* 0.94, DMSO).

(3a*S*,9b*S*)-2,3,3a,4,5,9b-Hexahydro-1H-pyrrolo[3,2-c]quinoline (3)

To **16** (258 mg, 1.37 mmol) was added anhydrous THF (9 mL). To this suspension was added slowly a lithium aluminum hydride solution (6.86 mL, 6.86 mmol, 1.0 M solution in THF). **Caution: hydrogen evolved.** The solution was then refluxed for 8 h. After cooling to room temperature, very slowly 1.30 mL of a 1 N NaOH solution was added to the reaction. **Caution: hydrogen evolved.** After the bubbling ceased ethyl acetate was added and the solution was stirred vigorously for 0.5 h. The suspension was filtered through Celite® and washed with ethyl acetate. The filtrate was concentrated *in vacuo* which produced **3** (220 mg, 1.26 mmol, 92% yield) as a pure light yellow powder (mp 127.6 – 129.1 °C). An analytically pure sample could be obtained by crystallization from ethyl acetate (very light yellow colored needles). mp 132.2 – 132.8 °C. IR (drift) 3280, 2953, 2946, 2863, 1610, 1510, 1499, 1368, 1335, 1309, 1272, 1068, 843, 745, 729 cm^{-1}; ^{1}H NMR (CD_3OD) δ 7.23 (d, *J* = 7 Hz, 1 H), 6.99 (dt, *J* = 1, 7 Hz, 1 H), 6.65 (t, *J* = 6 Hz, 1 H), 6.63 (d, *J* = 8 Hz, 1 H), 3.81 (d, *J* = 6.3 Hz, 1 H), 3.08 - 2.99 (m, 2 H), 2.86 - 2.77 (m, 1 H), 2.71 (t, *J* = 11 Hz, 1 H), 2.35 - 2.28 (m, 1 H), 2.22 - 2.08 (m, 1 H), 1.64 - 1.53 (m, 1 H); ^{13}C NMR (CD_3OD) δ 145.4, 130.0, 127.1, 121.0, 116.8, 114.4, 57.0, 43.0, 42.3, 35.6, 28.9; MS (EI) *m/z* 174 (M^+), 174, 156, 144, 131, 129, 118, 102, 86, 52, 51; HRMS (FAB) calcd for $C_{11}H_{14}N_2$ $+H_1$ 175.1235, found 175.1233. Anal. Calcd for $C_{11}H_{14}N_2$: C, 75.82; H, 8.10; N, 16.08. Found: C, 75.60; H, 8.04; N, 15.94. $[\alpha]_D^{25}$ -89 (*c* 0.66, methanol).