Supporting Information

An Efficient Synthesis of Optically Active Physostigmine from Tryptophan *via* Alkylative Cyclization

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Preparation of 3a-methylthio-1-methoxycarbonyl-8-methyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*] indole (7, Table 1, run 3): To a solution of **6** (115 mg, 0.5 mmol) and Bu_4NI (369 mg, 1.0 mmol) in CH_2Cl_2 (5 mL), was added chloromethy methyl sulfide (0.24 mL, 3 mmol). The mixture was stirring for 70 h at room temperature. The reaction mixture was treated with cold brine (4 mL) and exracted with CH_2Cl_2 (3 mL). Combined organic layers were washed with brine (4 mL) and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography on silica gel (AcOEt/ *n*-hexane 1/ 5 to1/ 2) and afforded **7** (86.4 mg, 59 %) as a colorless oil.

7: IR (neat) cm^{-1} 2952, 1699, 1606, 1446 1385, 1198, 1113, 1001, 885, 744; ^{1}H-NMR (400 MHz, DMSO-d_6, 149.5 °C) δ 2.02 (3H, s, SMe), 2.05 (1H, ddd, *J*=12.4, 6.6, 2.6 Hz, 3-H), 2.17 (1H, ddd, *J*=12.4, 10.0, 8.0 Hz, 3-H), 2.90 (1H, d, *J*=13.1 Hz, SCH_2), 2.92 (3H, s, NMe), 2.95 (1H, ddd, *J*=10.8, 10.0, 6.6 Hz, 2-H), 2.97 (1H, d, *J*=13.1 Hz, SCH_2), 3.69 (3H, s, OMe), 3.77 (1H, ddd, *J*=10.7, 8.0, 2.7 Hz, 2-H), 5.33 (1H, s, 8a-H), 6.40 (1H, d, *J*=8.0 Hz, Ar-H), 6.62 (1H, td, *J*=7.4, 0.9 Hz, Ar-H), 7.06 (1H, td, *J*=7.5, 1.2 Hz, Ar-H), 7.12 (1H, dd, *J*=7.4, 1.0 Hz, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6, 149.5 °C) δ 15.74, 31.94, 35.81, 38.87, 44.67, 51.08, 56.40, 85.40, 105.24, 116.49, 121.89, 127.69, 131.07, 150.22. 154.30; MS (FAB),, m/z 292 (M^+, 100); HRMS (FAB),, m/z calcd for $C_{15}H_{22}N_2O_4S$ 292.1245, found. 292.1260.

Typical procedure for alkylative cyclization using Corey-Kim reagent: synthesis of 3a-methylthiomethly-1-methoxycarbonyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (10, Scheme 2).

To a solution of *N*-chloro succinimide (133 mg, 1.0 mmol) in CH_2Cl_2, was added dimethyl sulfide (75 mg, 1.2 mmol) at -78 °C and the mixture was stirred for 1 h. To this reaction mixture, was added a solution of **9** (109 mg, 0.5 mmol) in CH_2Cl_2 and diisipropylethylamine (155 mg, 1.2 mmol) and the whole was stirred for 2 h at -78 °C. The mixture was treated with cooled brine and extracted with CH_2Cl_2. Combined organic layers were washed, and dried over $MgSO_4$. After evaporation of the solvent, a residue was purified by column chromatography on silica gel (AcOEt/ *n*-hexane 1/ 5 to1/ 2) and afforded **10** (139 mg, 92 %) and **11** (12 mg, 7 %) .

10: white powder (Et_2O); mp. 86.5-87.5 °C; IR (KBr) cm^{-1} 3363, 2954, 1695, 1608, 1454, 1385, 1327, 1201, 1120, 1043, 973, 887, 750, 665; ^{1}H-NMR (400 MHz, DMSO-d_6, 130 °C) δ 2.07 (3H, s, SCH_3), 2.13 (1H, ddd, *J*=12.5, 6.6 , 2.2 Hz, 3-H),

2.23 (1H, ddd, *J*=12.5 , 10.3, 8.1 Hz, 3-H), 2.88 (2H, s, SCH_2), 2.96 (1H, ddd, *J*=10.5, 10.2, 6.6 Hz, 2-H), 3.62 (1H, ddd, *J*=10.5, 8.0, 2.4 Hz, 2-H), 3.66 (3H, s, OMe), 5.27 (1H, s, 8a-H), 5.96 (1H, s, NH), 6.56 (1H, d, *J*=7.8 Hz, Ar-H), 6.63 (1H, t, *J*=7.4 Hz, Ar-H), 6.99 (1H, t, *J*=7.5 Hz, Ar-H), 7.10 (1H, d, *J*=7.6 Hz, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6, 130 °C) δ 16.09, 34.54, 41.84, 44.56, 51.10, 57.24, 79.02, 108.04, 117.01, 122.40, 127.53, 130.55, 149.09, 153.75; LRMS (EI) m/z 278 (M^+, 100); HRMS (FAB), calcd for $C_{14}H_{18}N_2O_2S$ 278.1089, found 278.1090; Anal. calcd for $C_{14}H_{18}N_2O_2S$: C, 60.40; H, 6.52; N, 10.06. Found: C, 60.26; H, 6.51; N, 9.97.

3a,8-Bis(methylthiomethly)-1-methoxycarbonyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (11): IR (neat) cm^{-1} 2916, 1700, 1604, 1490, 1448, 1388, 1206, 10339, 980, 885, 745; ^{1}H-NMR (400 MHz, DMSO-d_6, 149.6 °C) δ 1.97-2.26 (8H, m, 2 x SCH_3 and 3-H), 2.93-3.01 (3H, m, 2-H and SCH_2), 3.69 (3H, s, OCH_3), 3.74-3.79 (1H, m, 2-H), 4.64 (1H, d. *J*=13.7 Hz, NCH_2S), 4.76 (1H, d, *J*=13.7, NCH_2S), 5.65 (1H, s, 8-H), 6.65 (1H, d, *J*=7.6 Hz, Ar-H), 6.70 (1H, t, *J*=7.4 Hz, Ar-H), 7.09 (1H, t, *J*=7.4 Hz, Ar-H), 7.16 (1H, d, *J*=7.5 Hz, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6, 149.6 °C, two sets of signals due to carbamate group were observed.) δ (13.29, 13.65), (15.87, 15.94), (34.51, 35.76), 42.09, (44.30, 44.56), (50.51, 50.82), (51.06, 51.33), 56.52, 82.79, (106.66, 106.94), (116.95, 117.62), (122.19, 122.31), (127.54, 127.62), 131.64, (146.67, 147.69), 154.15; LRMS (EI) m/z: 338 (M^+, 10), 291 (100); HRMS (FAB), calcd for $C_{16}H_{22}N_2O_2S_2$ 338.1123, found 338.1119.

5-Methoxy-3a-methylthiomethly-1-methoxycarbonyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (13): IR (neat) cm^{-1} 3367, 2952, 2831, 1695, 1599, 1454, 1385, 1282, 1198, 1043, 872, 771; ^{1}H-NMR (400 MHz, DMSO-d_6, 149.5 °C) δ 2.06 (3H, s, SMe), 2.16 (1H, ddd, *J*=12.7, 6.8, 2.3 Hz, 3-H), 2.22 (1H, ddd, *J*=12.7, 10.1, 8.1 Hz, 3-H), 2.90 (2H, s, SCH_2), 2.98 (1H, ddd, *J*=10.2, 6.9, 6.3 Hz, 2-H), 3.57-3.62 (1H, m, 2-H), 3.66 (3H, s, OMe), 3.69 (3H, s, OMe), 5.26 (1H, s, 8a-H), 6.50 (1H, d, *J*=8.5 Hz, Ar-H), 6.63, (1H, dd, *J*=8.5, 2.4 Hz, Ar-H), 6.83 (1H, d, *J*=2.5 Hz, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6, 149.7 °C) δ 16.78, 24.67, 35.05, 40.90, 45.23, 51.70, 56.14, 72.80, 80.50, 109.37, 110.55, 110.62, 114.37, 153.23, 162.23; LRMS (EI) m/z 308 (M^+, 100); HRMS (FAB), calcd for $C_{15}H_{20}N_2O_3S$ 308.1195, found 308.1198.

3a-Methylthiomethyl-1-methoxycarbonyl-8-methyl-1,2,3,3a,8,8a-

hexahydropyrrolo[2,3-*b*]indole (14): IR (neat) cm^{-1} 2953, 1713, 1608, 1494, 1446, 1386, 1234, 1201, 1107, 745; ^{1}H-NMR (400 MHz, DMSO-d_6, 150 °C) δ 1.38 (3H, CMe), 1.95 (1H, ddd, *J*=12.5, 8.8, 7.8 Hz, 3-H), 2.04 (1H, ddd, *J*=12.5, 6.6, 3.9 Hz, 3-H), 2.90 (3H, s, N-Me), 3.00 (1H, ddd, *J*=10.7, 8.8, 6.7 Hz, 2-H), 3.68 (3H, s, OMe), 3.73 (1H, ddd, *J*=10.6, 7.8, 3.9 Hz, 2-H), 5.09 (1H, s, 8a-H), 6.39 (1H, d, *J*=7.8 Hz, Ar-H), 6.63 (1H, t, *J*=7.3 Hz, Ar-H), 7.02-7.06 (2H, m, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6, 150 °C) δ 23.80, 32.01, 37.80, 42.05, 45.02, 51.05, 88.22, 105.19, 116.55, 120.88, 121.89, 127.15, 127.69, 133.66, 149.49; LRMS (FAB), m/z 246 (M^+, 100); HRMS (FAB), calcd for $C_{14}H_{18}O_2N_2$ 246.1368, found 246.1367.

(-)-14 from 30: $[\alpha]_D^{27}$ -319 (*c* 1.05, $CHCl_3$)

(+)-14 from 25: $[\alpha]_D^{27}$ 322 (*c* 0.93, $CHCl_3$)

HPLC; Chiralpak AD, eluent: *n*-hexane/ 2-PrOH 95/ 5, flow rate:1.0 mL/ min,
retention time: 6.56 min for (-)-**14**, 8.27 min for (+)-**14**.

5-Methoxy-3a-methylhiomethyl-1-methoxycarbonyl-8-methyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (15): IR (neat) cm^{-1}: 2954, 2885, 2829, 1700, 1597, 1498, 1446, 1385, 1281, 1198, 1092, 1032, 995, 856, 800, 769, 723, 692; ^{1}H-NMR (400 MHz, $CHCl_3$, 55 °C) δ 1.40 (3H, brs, C_{3a}-Me), 1.86-2.11 (2H, m, 3-H), 2.90 (3H, brs, N_8-Me), 3.13-3.20 (1H, m, 2-H), 3.73 (7H, m, 2 x OMe, 2-H), 5.10 (1H, brs, 8a-H), 6.30 (1H, d, *J*=8.0 Hz, Ar-H), 6.64 (1H, d, *J*=2.4 Hz, Ar-H), 6.66 (1H, dd, *J*=8.0, 2.4 Hz, Ar-H); ^{13}C-NMR (100 MHz, $CHCl_3$, two sets of signals due to carbamate group were observed.) δ (24.01, 24.33), (33.61, 34.30), (38.22, 38.71), (46.14, 46.38), 51.64, (52.34, 52.82), 55.92, (89.14, 89.91), (106.70, 106.84), 109.65, 112.31, (135.58, 135.69), (144.59, 144.75), 152.86, (155.52, 156.41); LRMS (FAB), m/z 276 (M^+, 100); HRMS (FAB), calcd for $C_{15}H_{20}O_3N_2$ 276.1474, found, 276.1488.

3a-Methylthiomethyl-1,8-bis(methoxycarbonyl)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (16): IR (neat) cm^{-1} 2952, 1712, 1600, 1483, 1446, 1392, 1321, 1267, 1196, 1051, 976, 756; 1H-NMR (400 MHz, $CDCl_3$, 55 °C) δ 2.00 (3H, SCH_3), 2.25 (2H, m, 3-H), 3.86 (2H, s, CH_2S), 2.93 (1H, td, *J*=11.1, 6.1 Hz, 2-H), 3.72 (3H, s, OCH_3), 3.83 (1H, m, 2-H), 3.86 (3H, s, OCH_3), 6.15 (1H, s, 8a-H), 7.03 (1H, m, Ar-H), 7.20-7.28 (2H, m, Ar-H), 7.72 (1H, d, *J*=8.1 Hz, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$, 55 °C) δ 17.50, 35.41, 42.67, 45.81, 52.38, 52.61, 57.49, 80.21, 116.38, 122.92, 122.52, 128.86, 133.57, 142.38, 153.86, 154.90;

LRMS (EI) m/z: 337 (M^++H, 85), 336 (M^+, 70), 289 (100); HRMS (FAB), calcd for $C_{16}H_{21}N_2O_4S_2$ (M^++H) 337.1222, found 337.1213.

(-)-(2*S*, 3a*R*, 8a*S*)-3a-Methylthiomethyl-1,2-bis(methoxycarbonyl)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (20): $[\alpha]_D^{24}$ -451.1 (*c* 1.35, $CHCl_3$); IR (neat) cm^{-1} 3386, 3000, 2952, 2917, 1749, 1701, 1608, 1450, 1381, 1317, 1271, 1201, 1047, 968, 889, 779, 748; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.05 (4/9H, s, SCH_3), 2.07 (5/9H, s, SCH_3), 2.35-3.43 (1H, m, 3-H), 2.62 (4/9H, dd, *J*=12.7, 7.4 Hz, 3-H), 2.68 (5/9H, dd, *J*=13.0, 7.8 Hz, 3-H), 2.83 (10/9H, s, SCH_2), 2.87 (8/9H, s, SCH_2), 3.63 (5/3H, s, OCH_3) , 3.74 (5/3H, s, OCH_3) , 3.76 (4/3H, s, OCH_3), 3.79 (4/3H, s, OCH_3), 4.08-4.16 (1H, m, 2-H), 4.94 (5/9H, brs, NH), 5.13 (4/9H, brs, NH), 5.42 (1H, s, 8a-H), 6.61-7.20 (4H, m, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6, 150 °C, two sets of signals due to carbamate group were observed.) δ (ppm) : (16.14, 16.22), 38.10, 41.41, (50.59, 50.66), 51.49, 56.43, (58.40, 58.65), 80.01, 108.07, 116.66, (122.57, 122.68), 127.75, 129.74, 149.35, 153.74, 170.33; LRMS (FAB), m/z 336 (M^+, 100); HRMS (FAB), calcd for $C_{16}H_{20}N_2O_4S$ (M^+) 336.1144, found 336.1119.

(-)-(2*S*, 3a*S*, 8a*R*)-3a-Methylthiomethyl-1,2-bis(methoxycarbonyl)- 1, 2, 3, 3a, 8, 8a-hexahydropyrrolo[2,3-*b*]indole (21): white powder (AcOEt-*n*-Hex), mp. 151-152 °C; $[\alpha]_D^{24}$ -248.1 (*c* 1.028, $CHCl_3$); IR (KBr) cm^{-1} 3371, 2952, 2925, 1759, 1709, 1603, 1466, 1448, 1365, 1317, 1292, 1220, 1124, 1043, 853, 885, 773, 7476, 680, 601, 557, 459, 409; ^{1}H-NMR (400 MHz, DMSO-d_6, 149.5 °C) δ 2.05 (3H, s, SCH_3), 2.47 (1H, m, 3-H), 2.65 (1H, dd, *J*=12.9, 9.0 Hz, 3-H), 2.84 (1H, d, *J*=13.5 Hz, SCH_2), 2.89 (1H, d, *J*=13.4 Hz, SCH_2), 3.20 (3H, s, CO_2Me), 3.68 (3H, s, NCO_2Me), 4.52 (1H, dd, *J*=9.1, 2.1 Hz, 2-H), 5.32 (1H, s, 8a-H), 5.86 (1H, brs, NH), 6.55-6.59 (2H, m, Ar-H), 6.97 (1H, td, *J*=7.6, 1.2 Hz, Ar-H), 7.06 (1H, d, *J*=7.3 Hz, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6, 150 °C) δ 16.04, 38.11. 41.50, 51.43, 51.32, 56.41, 58.50, 80.04, 108.02, 116.35, 122.50, 122.50, 127.63, 129.77, 149.18, 153.68, 170.18; LRMS (FAB), m/z: 336 (M^+, 100); HRMS (FAB), Calcd for $C_{16}H_{20}N_2O_4S$ 336.1144, found. 336.1119; Anal. calcd for $C_{16}H_{20}N_2O_4S$ C, 57.12; H, 5.99; N, 8.33, found: C, 57.00; H, 5.94; N, 8.19.

(-)-(2*S*, 3a*R*, 8a*S*)-5-Methoxy-3a-methylthiomethyl-1,2-bis(methoxycarbonyl)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (22): $[\alpha]_D^{24}$ -363.3 (*c* 0.98, $CHCl_3$); IR (neat) cm^{-1} 3381, 2952, 2832, 1747, 1713, 1599,

1494, 1454, 1379, 1203, 1042, 966, 812, 779, 661; ^{1}H-NMR (400 MHz, DMSO-d_6, 149.5 °C) δ 1.97 (3H, s, SCH_3), 2.26 (1H, dd, *J*=13.0, 7.6 Hz, 3-H), 2.50 (1H, dd, *J*=12.9, 7.8 Hz, 3-H), 2.77 (1H, d, *J*=13.3 Hz, SCH_2), 2.83 (1H, d, *J*=13.2 Hz, SCH_2), 3.61 (3H, s, OCH_3), 3.62 (6H, s, 2 x OCH_3), 3.98 (1H, t, *J*=7.8 Hz, 2-H), 5.31 (1H, s, 8a-H), 6.46 (1H, d, *J*=8.3 Hz, Ar-H), 6.57 (1H, dd, *J*=8.4, 2.5 Hz, Ar-H), 6.78 (1H, d, *J*=2.4 Hz, Ar-H);
^{13}C-NMR (100 MHz, DMSO-d_6, 150 °C) δ 15.99, 38.59, 40.96, 50.95, 51.28, 55.45, 56.68, 58.36, 80.85, 109.05, 109.78, 113.96, 132.01, 142.17, 152.64, 153.76, 171.37; LRMS (FAB), m/z 366 (M^+, 80); HRMS (FAB), calcd for ($C_{17}H_{22}N_2O_5S$) 366.1249, found 366.1245.

(+)-(2*S*, 3a*S*, 8a*R*)-5-Methoxy-3a-methylthiomethyl-1,2-bis(methoxycarbonyl)- 1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (23): $[\alpha]_D^{27}$ 145.6 (*c* 0.91, $CHCl_3$); IR (neat) cm^{-1} 3368, 2951, 2833, 1751, 1701, 1491, 1457, 1377, 1206, 1121, 1040, 963, 875, 809, 771, 665; ^{1}H-NMR (400 MHz, DMSO-d_6, 149.5 °C) δ 1.97 (3H, s, SCH_3), 2.37-2.40 (1H, m, 3-H), 2.54 (1H, dd, *J*=13.1, 9.0 Hz, 3-H), 2.75 (1H, d, *J*=13.2 Hz, SCH_2), 2.79 (1H, d, *J*=13.4 Hz, SCH_2), 3.14 (3H, s, CO_2Me), 3.58 (3H, s, OCH_3), 3.57 (3H, s, OCH_3), 4.42 (1H, dd, *J*=9.1, 2.1 Hz, 2-H), 5.21 (1H, s, 8a-H), 6.39 (1H, d, *J*=8.5 Hz, Ar-H), 6.51 (1H, dd, *J*=8.4, 2.5 Hz, Ar-H), 6.65 (1H, d, *J*=2.5 Hz, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6, 150 °C, two sets of signals due to carbamate group were observed.) δ 15.98, 28.74, 37.87, 41.24, 50.46, 55.52, 56.75, (58.35, 58. 58), (80.71, 80.79), 108.62, 109.98, 114.10, 131.08, 143.30, 152.27, 153.68, 170.15; LRMS (EI) m/z 366 (M^+, 30), 305 (100); HRMS (FAB), m/z calcd for $C_{17}H_{22}N_2O_5S$ 366.1249, found.366.1241.

(-)-(2*S*, 3a*S*, 8a*S*)-1,2-Bis(methoxycarbonyl)-3a,8-dimethyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (24): $[\alpha]_D^{23.5}$ -184.5 (*c* 0.55, $CHCl_3$); IR (neat) cm^{-1} 2954, 1734, 1701, 1608, 1491, 1446, 1375, 1233, 1200, 1105, 877, 742, 661; ^{1}H-NMR (400 MHz, DMSO-d_6, 149.5 °C) δ 1.39 (3H, s, C_{3a}-CH_3), 2.11 (1H, dd, *J*=13.1, 4.6 Hz, 3-H), 2.40 (1H, dd, *J*=13.1, 9.1 Hz, 3-H), 2.96 (3H, s, N-Me), 3.66 (3H, s, OMe), 3.70 (3H, s, OMe), 4.21 (1H, dd, J=9.0, 4.6 Hz, 2-H), 5.17 (1H, s, 8a-H), 6.45 (1H, d, *J*=7.8 Hz, Ar-H), 6.66 (1H, t, *J*=7.5 Hz, Ar-H), 7.03-7.06 (2H, m, Ar-H); ^{13}C-NMR (100 MHz, $CHCl_3$, two sets of signals due to carbamate group were observed.) δ (23.54, 23.67), (34.68, 35.47), (42.17, 43.14), 50.58, 51.96, (52.29, 52.63), (59.92, 60.10), (90.81, 91.86), (107.24, 107.34), (118.07, 118.22), 121.44, 128.49, (134.41, 134.71), (149.58, 149.78), (155.03, 155.36), (173.27,

172.74); LRMS (EI) m/z 304 (M^+, 50) , 277 (100); HRMS (FAB), m/z calcd for $C_{16}H_{20}N_2O_4$ 304.1423, found. 304.1423.

(+)-(2*S*, 3a*R*, 8a*R*)-1,2-Bis(methoxycarbonyl)-3a,8-dimethyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (25): $[\alpha]_D^{27}$ 149.7 (*c* 1.07, $CHCl_3$); IR (neat) cm^{-1} 2954, 1751, 1716, 1608, 1491, 1448, 1373, 1300, 1203, 1120, 985, 744; ^{1}H-NMR (400 MHz, DMSO-d_6, 149.5 °C) δ 1.37 (3H, s, C_{3a}-Me), 2.30 (1H, d, *J*=4.9 Hz, 3-H), 2.33 (1H, d, *J*=7.8 Hz, 3-H), 2.92 (3H, s, N-Me), 3.29 (3H, s, CO_2Me), 3.69 (3H, s, NCO_2Me), 4.61 (1H, dd, *J*=7.6, 5.0 Hz, 2-H), 5.19 (1H, s, 8a-H), 6.35 (1H, d, *J*=6.8 Hz, Ar-H), 6.57 (1H, t, *J*=7.3 Hz, Ar-H), 6.96-7.03 (2H, m, Ar-H); ^{13}C-NMR (100 MHz, $CHCl_3$, two sets of signals due to carbamate group were observed.) δ (ppm) : 24.08, (31.70, 32.08), (41.87, 42.61), (51.23, 52.02), (52.37, 52.81), (59.99, 60.32), (88.55, 88.95), 105.94, (117.21, 117.44), (122.07, 122.18), 128.67, 132.78, (150.09, 150.34), (155.62, 155.93), (155.62, 155.93), (171.66, 171.83); LRMS (EI) m/z: 304 (M^+, 50), 144 (100); HRMS (FAB), m/z calcd for $C_{16}H_{20}N_2O_4$ 304.1423, found. 304.1404.

(-)-(2*S*, 3a*S*, 8a*S*)-5-Methoxy-1,2-bis(methoxycarbonyl)-3a,8-dimethyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (26): $[\alpha]_D^{27}$ -143.3 (*c* 0.94, $CHCl_3$); IR (neat) cm^{-1} 2952, 1753, 1716, 1497, 1449, 1370, 1201, 1160, 1091, 1026, 1008, 980, 872, 796, 769; ^{1}H-NMR (400 MHz, DMSO-d_6, 149.5 °C) δ 1.39 (3H, s, SCH_3), 2.09 (1H, dd, *J*=13.2, 4.6 Hz, 3-H), 2.40 (1H, dd, *J*=13.2, 9.2 Hz, 3-H), 2.91 (3H, s, N-CH_3), 3.65 (3H, s, OCH_3), 3.69 (3H, s, OCH_3), 3.70 (3H, s, OCH_3), 4.22 (1H, dd, *J*=9.3, 4.6 Hz, 2-H), 5.10 (1H, s, 8a-H), 6.38 (1H, d, *J*=8.5 Hz, Ar-H), 6.68 (1H, d, *J*=8.3 Hz, Ar-H), 6.70 (1H, s , Ar-H).; ^{13}C-NMR (100 MHz, DMSO-d_6, 150 °C) δ 23.29, 35.17, 41.64, 50.42, 50.93, 51.22, 55.39, 59.11, 91.22, 107.14, 108.73, 113.06, 135.42, 143.39, 152.65, 154.37, 171.56; LRMS (EI) m/z 334 (M^+, 40) 149 (100); HRMS (FAB), m/z calcd for $C_{17}H_{22}N_2O_5$ (M^+) 334.1529, found 334.1505.

(+)-(2*S*, 3a*R*, 8a*R*)-5-Methoxy-1,2-bis(methoxycarbonyl)-3a,8-dimethyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (27): $[\alpha]_D^{27}$ 146.0 (*c* 0.69, $CHCl_3$); IR (neat) cm^{-1}: 2953, 1756, 1706, 1498, 1447, 1385, 1281, 1222, 1200, 1114, 1030, 867, 799, 772, 667; ^{1}H-NMR (400 MHz, $CDCl_3$, 55 °C) δ 1.39 (3H, s, SCH_3), 2.25 (1H, dd, *J*=12.7, 8.8 Hz, 3-H), 2.46 (1H, dd, *J*=12.7, 3.9 Hz, 3-H), 2.94 (3H, brs, N-CH_3), 3.37 (3H, s, OCH_3), 3.71 (6H, brs, 2 x OCH_3), 4.62 (1H, brs, 2-H), 5.24 (1H, brs, 8a-H), 6.27 (1H, d, *J*=8.3 Hz, Ar-H), 6.61 (1H, d, *J*=2.4 Hz, Ar-H),

6.65 (1H, dd, *J*=8.3, 2.5 Hz, Ar-H). ^{13}C-NMR (100 MHz, $CDCl_3$, two sets of signals due to carbamate group were observed.) δ 23.11, (32.65, 32.98), (41.66, 42.43), (51.26, 52.01), (52.37, 52.76), 56.11, (59.55, 59.93), (59.97, 60.32), (89.55, 89.93), 106.54, 109.83, 113.10, 136.21, (144.51, 144.80), (152.59, 152.71), (155.66, 155.96), (171.60, 171.77); LRMS (EI) m/z 344 (M^+, 50), 149 (100); HRMS (FAB), calcd for $C_{17}H_{22}N_2O_5$ 334.1529, found, 334.1510.

(-)-(2*S*, 3a*S*, 8a*R*)-5-Methoxy-2-hydroxymethyl-1,3a,8-trimethyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (28): $[\alpha]_D^{27}$ -117 (*c* 0.5, $CHCl_3$) [lit. $[\alpha]_D^{31}$ -118 (*c* 0.99, $CHCl_3$)][3c]; IR (neat) cm^{-1} 3421, 2925, 1506, 1458, 1276, 1218, 1108, 1028; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.45 (3H, s, C_{3a}-Me), 1.95 (1H, dd, *J*=12.2, 6.6 Hz, 3-H), 2.03 (1H, dd, *J*=10.3, 2.2 Hz, 3-H), 2.44 (3H, s, N-Me), 2.71-2.76 (1H, m, 2-H), 2.90 (3H, s, N-Me), 3.45 (1H, dd, *J*=11.5, 1.4 Hz, CH2O), 3.71 (1H, dd, *J*=11.4, 3.4 Hz, CH_2O), 3.75 (3H, s, O-Me), 4.34 (1H, s, 8a-H), 6.39 (1H, d, *J*=8.3 Hz, Ar-H), 6.64 (1H, d, *J*=2.6 Hz, A-H), 6.66 (1H, dd, *J*=8.3, 2.7 Hz, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) : 27.55, 33.63, 39.60, 43.33, 49.86, 55.93, 59.44, 62.55, 99.21, 108.12, 109.53, 112.36, 138.34, 146.86, 153.29; LRMS (EI) m/z 262 (M^+, 60), 174 (100); HRMS (FAB), calcd for $C_{15}H_{22}N_2O_2$ 262.1681, found 262.1675.

(=)-(2*S*, 3a*R*, 8a*S*)-5-Methoxy-2-hydroxymethyl-1,3a,8-trimethyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (29): $[\alpha]_D^{27}$ 37.2 (*c* 0.5, $CHCl_3$) [lit. $[\alpha]_D^{30.5}$ 36.3 (*c* 1.01, $CHCl_3$)][3c]; IR (neat) cm^{-1} 3386, 2952, 2863, 1494, 1458, 1279, 1223, 1122, 1030; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.37 (3H, s, C_{3a}-Me), 1.95 (1H, dd, *J*=12.7, 6.8 Hz, 3-H), 2.10 (1H, dd, *J*=12.7, 9.3 Hz, 3-H), 2.63 (3H, s, N-Me), 2.84 (3H, s, N-Me), 3.08 (1H, dddd, *J*=9.3, 6.8, 3.6, 2.4 Hz, 2-H), 3.34 (1H, dd, *J*=10.9, 2.4 Hz, CH_2O), 3.62 (1H, dd, *J*=10.9, 3.6 Hz, CH_2O), 3.73 (3H, s, OMe), 3.94 (1H, s, 8a-H), 6.33 (1H, d, *J*=8.0 Hz, Ar-H), 6.63 (1H, d, *J*=2.5 Hz, Ar-H), 6.65 (1H, dd, *J*=8.2, 2.6 Hz, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 25.32, 34.99, 40.59, 40.92, 50.80, 56.00, 60.83, 66.80, 102.38, 107.60, 109.68, 112.11, 137.96, 144.03, 152.99; 262 (M^+, 60), 174 (100); HRMS (FAB), calcd for $C_{15}H_{22}N_2O_2$ 262.1681, found 262.1673.

(-)-(2*S*, 3a*S*, 8a*S*)-1-Methoxycarbonyl-3a,8-dimethyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole-2-carboxylic acid (30): $[\alpha]_D^{24}$ -17.9 (*c* 1.1, $CHCl_3$); IR (neat) cm^{-1}: 3448, 3147, 2959, 1737, 1672, 1609, 1491, 1455, 1385, 1302,

1211, 991, 794, 745; ^{1}H-NMR (400 MHz, DMSO-d_6, 149.5 °C) δ 1.41 (3H, s, C_{3a}-Me), 2.14 (1H, dd, *J*=13.1, 3.6 Hz, 3-H), 2.33 (1H, dd, *J*=12.9, 9.4 Hz, 3-H), 2.95 (3H, s, N-Me), 3.64 (3H, s, OMe), 4.14 (1H, dd, *J*=9.5, 3.6 Hz, 2-H), 5.16 (1H, s, 8a-H), 6.44 (1H, d, *J*=8.0 Hz, Ar-H), 6.65 (1H, d, *J*=7.3 Hz, Ar-H), 7.01-7.07 (2H, m, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$ two sets of signals due to carbamate group were observed.) δ (23.56, 23.64), (34.91, 35.56), (42.04, 43.04), (50.68, 52.06), (52.70, 52.80), (60.04, 60.46), (91.05, 91.92), (107.47, 107.51), (118.24, 118.43), 128.54, (134.33, 134.64), (149.46, 149.65), (155.64, 156.08), (177.07, 178.07); LRMS (FAB), 290 (M^+, 100); HRMS (FAB), calcd for $C_{15}H_{18}N_2O_4$ 290.1267, found 290.1170.

Desoxyeseroline (3): IR (neat) cm^{-1} 2957, 2864, 2790, 1605, 1492, 1451, 1346, 1299, 1255, 1191, 1124, 1034, 957, 897, 737; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.43 (3H, s, C-Me), 1.94-1.97 (2 H, m, 3-H), 2.55 (3H, N_1-Me), 2.60-2.74 (2H, m, 2-H), 2.95 (3H, s, N_8-Me), 4.10 (1H, s, 8a-H), 6.40 (1H, d, *J*=7.8 Hz, Ar-H), 6.66 (1H, t, *J*=7.4 Hz, Ar-H), 6.98 (1H, d, *J*=7.8 Hz, Ar-H), 7.07 (1H, t, *J*=7.6 Hz, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$) 27.32, 36.46, 38.45, 40.81, 52.57, 53.18, 97.47, 106.49, 117.43, 122.14, 127.61, 136.63, 151.90; LRMS (EI) m/z 202 (M^+, 20), 158 (100); HRMS (FAB), calcd for $C_{13}H_{18}N_2$ 202.1470, found 202.1465.
(-)-3 from (-)-14: $[\alpha]_D^{25}$ -74 (*c* 0.5, $CHCl_3$)
(+)-3 from (+)-14: $[\alpha]_D^{25}$ +73 (*c* 0.46, $CHCl_3$)

Esermethole (2): IR (neat) cm^{-1} 2955, 2863, 1595, 1495, 1423, 1346, 1280, 1220, 1121, 1066, 1032, 958, 866, 798, 707; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.43 (3H, s, C-Me), 1.97 (2H, m, 3-H), 2.53 (3H, s, N_1-Me), 2.64 (1H, m, 2-H), 2.72 (1H, m, 2-H), 2.89 (3H, s, N_8-Me), 3.75 (3H, s, OMe), 4.05 (1H, s, 8a-H), 6.36 (1H, d, *J*=8.1 Hz, Ar-H), 6.63 (1H, s, Ar-H), 6.65 (1H, d, *J*=8.3 Hz, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 27.38, 37.90, 38.14, 40.78, 52.69, 53.01, 55.96, 98.32, 107.39, 109.75, 112.12, 138.22, 146.53, 152.90; LRMS (FAB), m/z 232 (M^+, 100); HRMS (FAB), calcd for $C_{14}H_{20}ON_2$ 232.1576, found 232.1577.