Enantioselective Organocatalytic Indole Alkylations. Design of a New and Highly Effective Chiral Amine for Iminium Catalysis.

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Supporting Information

General Information. Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego.[1] Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator. Methylene chloride was distilled from calcium hydride prior to use. Chromatographic purification of products was accomplished using forced-flow chromatography on ICN 60 32-64 mesh silica gel 63 according to the method of Still.[2] Thin-layer chromatography (TLC) was performed on EM Reagents 0.25 mm silica gel 60-F plates. Visualization of the developed chromatogram was performed by fluorescence quenching or anisaldehyde stain.

^{1}H and ^{13}C NMR spectra were recorded on Varian Mercury 300 (300 MHz and 75 MHz respectively) as noted, and are internally referenced to residual protio solvent signals. Data for ^{1}H are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, coupling constant (Hz) and assignment. Data for ^{13}C NMR are reported in terms of chemical shift. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in terms of frequency of absorption (cm^{-1}). Mass spectra were obtained from the UC Irvine Mass Spectral facility. High performance liquid chromatography (HPLC) was performed on Hewlett-Packard 1100 Series chromatographs using

[1]Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals;* 3rd ed., Pregamon Press, Oxford, 1988.
[2]Still, W. C.; Kahn, M.; Mitra, A. J. *J. Org. Chem.* **1978,** *43*, 2923.

Chiralcel AD column (1.6 x 25 cm) and AD guard (1.6 x 5 cm), Chiralcel OD–H (1.6 x 25 cm) and OD guard (1.6 x 5 cm), or Chiralcel AS (1.6 x 25 cm) and AS guard (1.6 x 5 cm) as noted.

General Procedure: An amber 2-dram vial equipped with a magnetic stir bar and containing (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one was charged with CH_2Cl_2, isopropanol, and the appropriate acid, then placed in a bath of a desired temperature. The solution was stirred for 5 min before addition of the α,β-unsaturated aldehyde. After stirring for an additional 10 minutes the indole substrate was added in one portion. The resulting suspension was stirred at constant temperature until complete consumption of the indole as determined by TLC. The reaction mixture was then passed cold through a silica gel plug with Et_2O and then concentrated. The resulting residue was purified by silica gel chromatography (solvents noted) to afford the title compounds. The enantioselectivity was determined by subjecting approximately 10 mg of the title compound to an excess of $NaBH_4$ and 1 mL of ethanol. After 15 min, the solution was treated with saturated aqueous $NaHCO_3$, and the mixture was extracted with CH_2Cl_2. The organic layer was separated, filtered through a silica gel plug and subjected to chiral HPLC analysis (conditions noted).

(*R*)-3-(1-Methyl-1*H*-indol-3-yl)-butanal (Table 1, entry 6). Prepared according to the general procedure from crotonaldehyde (125 μL, 1.50 mmol), 1-methyl-1*H*-indole (64 μL, 0.50 mmol), TFA (7.7 μL, 0.10 mmol) and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one (24.6 mg, 0.100 mmol) in CH_2Cl_2 (0.85 mL) and isopropanol (0.15 mL) at –83 °C for 19 h to provide, after silica gel chromatography (benzene), the title compound as a colorless oil (83 mg, 82% yield, 92% ee). IR (film) 3054, 2960, 2824, 2722, 1720, 1616, 1550, 1474, 1374, 1329, 1241, 740 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.75 (dd, *J* = 2.1, 2.1 Hz, 1H, CHO), 7.63 (d, *J* = 7.8 Hz, 1H, ArH), 7.32-7.21 (m, 2H, ArH), 7.12 (ddd, *J* = 1.5, 7.4, 8.1 Hz, 1H, ArH), 6.84 (s, 1H, NCH), 3.75 (s, 3H, NCH_3), 3.68 (dt, *J* = 6.9, 13.8 Hz, 1H, ArCH), 2.88 (ddd, *J* = 2.7, 6.9, 16.2 Hz, 1H, C**H**$_2$CO); 2.71 (ddd, *J* = 2.7, 6.9, 16.2 Hz, 1H, C**H**$_2$CO); 1.44 (d, *J* = 7.2 Hz, 3H,

CHC**H**$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.8, 137.2, 126.6, 125.2, 121.8, 119.1, 118.9, 118.8, 109.5, 51.2, 32.8, 26.0, 21.9; HRMS (CI) exact mass calcd for ($C_{13}H_{15}NO$) requires *m/z* 201.1154, found *m/z* 201.1152. $[\alpha]_D = -4.2$ (c = 1.0, $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiracel AD and AD guard column (2:98 ethanol/hexanes, 1 mL/min); *S* isomer t_r = 25.2 min and *R* isomer t_r = 27.8 min.

(*R*)-3-(1-Methyl-1*H*-indol-3-yl)-hexanal (Table 2, entry 2). Prepared according to the general procedure from 2-hexenal (174 μL, 1.50 mmol), 1-methyl-1*H*-indole (64μL, 0.50 mmol), TFA (7.7 μL, 0.10 mmol) and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one (24.6 mg, 0.100 mmol) in CH_2Cl_2 (0.85 mL) and isopropanol (0.15 mL) at −60 °C for 6 h to provide, after silica gel chromatography (5:95 EtOAc/hexanes), the title compound as a colorless oil (92 mg, 80% yield, 93% ee). IR (film) 2959, 2923, 2870, 1720, 1483, 1470, 1425, 1376, 1327, 1244, 1159, 1132, 1016, 734 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.71 (dd, *J* = 2.1, 2.1 Hz, 1H, CHO), 7.67 (d, *J* = 8.4 Hz, 1H, ArH), 7.35-7.24 (m, 2H, ArH), 7.12 (ddd, *J* = 1.5, 7.2, 8.1 Hz, 1H, ArH), 6.87 (s, 1H, NCH), 3.76 (s, 3H, NCH_3), 3.55 (m, 1H, ArCH), 2.83 (m, 2H, C**H**$_2$CO), 1.79 (m, 2H, CHC**H**$_2$CH$_2$), 1.34 (dt, *J* = 7.2, 22.8 Hz, 2H, CHC**H**$_2$CH$_3$), 0.92 (dd, *J* = 7.2, 7.2 Hz, 3H, CH$_2$C**H**$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.0, 137.2, 127.0, 126.0, 121.6, 119.2, 118.7, 117.0, 109.4, 49.7, 38.5, 32.8, 31.4, 20.8, 14.2; HRMS (CI) exact mass calcd for ($C_{15}H_{19}NO$) requires *m/z* 229.1467, found *m/z* 229.1464. $[\alpha]_D = -1.7$ (c = 1.0, $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiracel AS and AS guard column (2:98 ethanol/hexanes, 1 mL/min); *S* isomer t_r = 16.1 min and *R* isomer t_r = 18.1 min.

(*S*)-4-Methyl-3-(1-methyl-1*H*-indol-3-yl)-pentanal (Table 2, entry 3). Prepared according to the general procedure from 4-methyl-2-pentenal (175 μL, 1.50 mmol), 1-methyl-

1*H*-indole (64μL, 0.50 mmol), TFA (7.7 μL, 0.10 mmol) and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one (24.6 mg, 0.100 mmol) in CH_2Cl_2 (0.90 mL) and isopropanol (0.10 mL) at −50 °C for 32 h to provide, after silica gel chromatography (10:90 EtOAc/hexanes), the title compound as a colorless oil (85 mg, 74% yield, 93% ee). IR (film) 3052, 2958, 2870, 2834, 2716, 1723, 1609, 1546, 1482, 1469, 1423, 1373, 1328, 1246, 1160, 1138, 1015, 743 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.61 (dd, *J* = 2.4, 2.4 Hz, 1H, CHO), 7.63 (dt, *J* = 0.9, 8.1 Hz, 1H, ArH), 7.33-7.22 (m, 2H, ArH), 7.13 (ddd, *J* = 1.5, 6.9, 8.1 Hz, 1H, ArH), 6.82 (s, 1H, NCH), 3.75 (s, 3H, NCH_3), 3.40 (dt, *J* = 6.6, 7.8 Hz, 1H, ArCH), 2.81 (d, *J* = 2.4 Hz, 1H, C**H**$_2$CO); 2.79 (d, *J* = 2.4 Hz, 1H, C**H**$_2$CO); 2.10 (ddd, *J* = 6.6, 13.2, 19.8 Hz, 1H, C**H**$(CH_3)_2$, 0.96 (d, *J* = 2.1, 3H, CH(C**H**$_3)_2$, 0.94 (d, *J* = 2.1 Hz, 3H, CH(C**H**$_3)_2$; ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.4, 137.0, 127.6, 126.7, 121.6, 119.4, 118.8, 115.6, 109.3, 46.1, 38.0, 32.9, 32.9, 20.6, 20.4; HRMS (CI) exact mass calcd for ($C_{15}H_{19}NO$) requires *m/z* 229.1467, found *m/z* 229.1465. $[\alpha]_D$ = + 15.8 (c = 1.0, $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiracel AS and AS guard column (4% ethanol / hexanes, 1 mL/min); *R* isomer t_r = 13.4 min and *S* isomer t_r = 16.7 min.

(*S*)-3-(1-Methyl-1*H*-indol-3-yl)-3-phenyl-propanal (Table 2, entry 5). Prepared according to the general procedure from cinnamaldehyde (190 μL, 1.50 mmol), 1-methyl-1*H*-indole (64μL, 0.50 mmol), TFA (7.7 μL, 0.10 mmol) and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one (24.6 mg, 0.100 mmol) in CH_2Cl_2 (0.85 mL) and isopropanol (0.15 mL) at −55 °C for 45 h to provide, after silica gel chromatography (10:90 EtOAc/hexanes), the title compound as a colorless oil (110 mg, 84% yield, 90% ee). IR (film) 3051, 3026, 2945, 2888, 2822, 2733, 1722, 1616, 1604, 1547, 1474, 1429, 1376, 1331, 1245, 1225, 1156, 1131, 1013, 765, 740, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.76 (dd, *J* = 2.4, 2.4 Hz, 1H, CHO), 7.43 (dt, *J* = 0.9, 8.1 Hz, 1H, ArH), 7.36-7.28 (m, 7H, ArH), 7.04 (ddd, *J* = 1.2, 6.9, 8.1 Hz, 1H, ArH), 6.88 (s, 1H, NCH), 4.88 (t, *J* = 7.5 Hz, 1H, ArCH), 3.76 (s, 3H, NCH_3), 3.22 (ddd, *J* = 2.7, 8.4,

16.5 Hz, 1H, C**H**$_2$CO); 3.10 (ddd, *J* = 2.7, 8.4, 16.5 Hz, 1H, C**H**$_2$CO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.8, 143.5, 137.3, 128.6, 127.6, 126.8, 126.6, 126.4, 121.9, 119.4, 119.0, 116.6, 109.3, 50.0, 37.4, 32.9; HRMS (CI) exact mass calcd for ($C_{15}H_{17}NO$) requires *m/z* 263.1310, found *m/z* 263.1306. $[\alpha]_D$ = + 30.9 (c = 1.0, $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiracel AD and AD guard column (3:97 ethanol/hexanes, 1 mL/min); *S* isomer t_r = 48.5 min and *R* isomer t_r = 38.9 min.

(*R*)-4-Benzyloxy-3-(1-methyl-1*H*-indol-3-yl)-butanal (Table 2, entry 4). Prepared according to the general procedure from 4-benzyloxy-but-2-enal (286 mg, 1.50 mmol), 1-methyl-1*H*-indole (64μL, 0.50 mmol), TFA (7.7 μL, 0.10 mmol) and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one (24.6 mg, 0.100 mmol) in CH_2Cl_2 (0.85 mL) and isopropanol (0.15 mL) at −83 °C for 18.5 h to provide, after silica gel chromatography (50:50 Et_2O/hexanes), the title compound as a colorless oil (134 mg, 84% yield, 96% ee). IR (film) 3056, 2957, 2894, 2830, 2722, 1717, 1618, 1600, 1582, 1550, 1478, 1451, 1370, 1331, 1309, 1272, 1223, 1173, 1110, 1070, 1024, 772, 740, 714 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.77 (dd, *J* = 2.1, 2.1 Hz, 1H, CHO), 8.04 (d, *J* = 7.2 Hz, 2H, ArH), 7.75 (d, *J* = 8.1 Hz, 1H, ArH), 7.61-724 (m, 5H, ArH), 7.17 (ddd, *J* = 1.5, 6.6, 8.1 Hz, 1H, ArH), 6.96 (s, 1H, NCH), 4.73 (dd, *J* = 5.1, 11.1 Hz, 1H, C**H**$_2$O), 4.42 (dd, *J* = 8.7, 11.1 Hz, 1H, C**H**$_2$O), 4.12 (m, 1H, ArCH), 3.76 (s, 3H, NCH_3), 3.06 (ddd, *J* = 2.1, 6.3, 16.8 Hz, 1H, C**H**$_2$CO); 2.96 (ddd, *J* = 2.7, 8.4, 16.8 Hz, 1H, C**H**$_2$CO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.5, 166.4, 137.1, 133.1, 129.9, 129.6, 128.5, 126.8, 126.4, 122.1, 119.3, 119.0, 112.9, 109.6, 68.1, 46.5, 33.0, 31.2; HRMS (CI) exact mass calcd for ($C_{20}H_{19}NO$) requires *m/z* 321.1365, found *m/z* 321.1354. $[\alpha]_D$ = – 2.0 (c = 1.0, $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiracel AS and AS guard column (4:96 ethanol/hexanes, 1 mL/min); *S* isomer t_r = 42.9 min and *R* isomer t_r = 53.2 min.

(*R*)-2-(1-Methyl-1*H*-indol-3-yl)-4-oxo butyric acid methyl ester (Table 2, entry 6). Prepared according to the general procedure from methyl 4-oxo-butenoate (171 mg, 1.50 mmol), 1-methyl-1*H*-indole (64μL, 0.50 mmol), TFA (7.7 μL, 0.10 mmol) and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one (24.6 mg, 0.100 mmol) in CH_2Cl_2 (0.90 mL) and isopropanol (0.10 mL) at −85 °C for 21 h to provide, after silica gel chromatography (5:47:47 acetone/CH_2Cl_2/hexanes), the title compound as a colorless oil (109 mg, 89% yield, 91% ee). IR (film) 2937, 2833, 2729, 1732, 1623, 1545, 1477, 1436, 1379, 1332, 1228, 1171, 1042, 1016, 980, 773, 742 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.81 (s, 1H, CHO), 7.67 (d, *J* = 8.4 Hz, 1H, ArH), 7.33-7.23 (m, 2H, ArH), 7.15 (ddd, *J* = 1.2, 7.6, 7.8 Hz, 1H, ArH), 6.98 (s, 1H, NCH), 4.44 (dd, *J* = 5.4, 9.3 Hz, 1H, ArH), 3.76 (s, 3H, NCH_3), 3.69 (s, 3H, OCH_3), 3.47 (dd, *J* = 9.3, 18.6 Hz, 1H, C**H**$_2$CO); 2.94 (dd, *J* = 5.1, 18.3 Hz, 1H, C**H**$_2$CO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.1, 173.8, 137.0, 126.9, 126.5, 122.1, 119.5, 119.1, 110.8, 109.6, 52.5, 46.8, 36.5, 33.0; HRMS (CI) exact mass calcd for ($C_{14}H_{15}NO_3$) requires *m/z* 245.1048, found *m/z* 153.1151. $[\alpha]_D$ = – 123.6 (c = 1.0, $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiracel AS and AS guard column (3:97 isopropanol / hexanes, 1 mL/min); *S* isomer t_r = 71.7 min and *R* isomer t_r = 76.3 min.

(*R*)-3-(1*H*-Indol-3-yl)-butanal (Table 3, entry 2). Prepared according to general procedure from crotonaldehyde (100 μL, 1.25 mmol), indole (146 mg, 1.25 mmol), 2,4-dinitrobenzoic acid (53 mg, 0.25 mmol) and (2*S*, 5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one (62 mg, 0.25 mmol) in CH_2Cl_2 (2.25 mL) and isopropanol (0.25 mL) at –60 °C for 19 h at which time an additional 30 μL (0.36 mmol) of crotonaldehyde was added. The reaction was allowed to continue stirring for an additional 3 h to provide, after silica gel chromatography (20:80 EtOAc/hexanes), the title compound as a colorless oil (168 mg, 72%

yield, 91% ee). IR (film) 3408, 2962, 2875, 2833, 2729, 1716, 1617, 1451, 1420, 1337, 1223, 1099, 1010, 772, 741 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.77 (dd, *J* = 2.1, 2.1 Hz, 1H, CHO), 8.15 (s, 1H, NH), 7.68 (dt, *J* = 0.6, 7.8 Hz, 1H, ArH), 7.35 (dt, J = 1.5, 7.8 Hz, 1H, ArH), 7.27-7.15 (m, 2H, ArH), 6.94 (d, *J* = 2.4 Hz, 1H, NCH), 3.68 (dt, *J* = 7.2, 21 Hz, 1H, ArCH), 2.91 (ddd, *J* = 2.4, 6.9, 16.2 Hz, 1H, C**H**$_2$CO); 2.73 (ddd, *J* = 2.1, 7.2, 16.2 Hz, 1H, C**H**$_2$CO); 1.47 (d, *J* = 6.9 Hz, 3H, CHC**H**$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.0, 136.5, 126.1, 122.1, 120.7, 120.1, 119.3, 118.9, 111.4, 50.9, 26.0, 21.6; HRMS (CI) exact mass calcd for ($C_{12}H_{13}NO$) requires *m/z* 187.0997, found *m/z* 153.0993. $[\alpha]_D$ = – 2.2 (c = 1.0, $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiracel OD–H and OD guard column (10:90 ethanol/hexanes, 1 mL/min); *S* isomer t_r = 20.2 min and *R* isomer t_r = 17.6 min.

(*R*)-3-(1-Allyl-1*H*-indol-3-yl)-butanal (Table 3, entry 3). Prepared according to general procedure from crotonaldehyde (125 μL, 1.50 mmol), 1-allyl-1*H*-indole (78.5 mg, 0.500 mmol), TFA (7.7 μL, 0.10 mmol) and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one (24.6 mg, 0.100 mmol) in CH_2Cl_2 (0.90 mL) and isopropanol (0.10 mL) at –72 °C for 21 h to provide, after silica gel chromatography (7:93 EtOAc/hexanes), the title compound as a colorless oil (80 mg, 70% yield, 92% ee). IR (film) 3041, 2966, 2919, 2822, 2834, 2712, 1722, 1469, 1375, 1328, 1309, 1262, 192, 1018, 995, 929, 736 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.76 (dd, *J* = 2.1, 2.1 Hz, 1H, CHO), 7.64 (dt, *J* = 0.9, 7.8 Hz, 1H, ArH), 7.33-7.20 (m, 2H, ArH), 7.13 (ddd, *J* = 0.9, 6.9, 7.8 Hz, 1H, ArH), 6.89 (s, 1H, NCH), 5.98 (ddd, *J* = 5.4, 9.9, 22.5 Hz, 1H, CH_2C**H**CH_2), 5.20 (dd, *J* = 1.5, 10.2 Hz, 1H, CH_2CHC**H**$_2$), 5.10 (dt, *J* = 1.5, 17.1 Hz, 1H CH_2CHC**H**$_2$), 4.68 (d, *J* = 5.4 Hz, 2H NCH_2), 3.69 (dt, *J* = 6.9, 21.3 Hz, 1H, ArCH), 2.88 (ddd, *J* = 2.4, 6.6, 16.2 Hz, 1H, C**H**$_2$CO); 2.71 (ddd, *J* = 2.1, 7.2, 16.2 Hz, 1H, C**H**$_2$CO); 1.44 (d, *J* = 6.9 Hz, 3H, CHC**H**$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.8, 136.7, 133.5, 126.8, 124.1, 121.8, 119.3, 119.2, 119.0, 117.4, 109.8, 51.1, 48.9, 26.1, 21.8; HRMS (CI) exact mass calcd for ($C_{15}H_{17}NO$)

requires *m/z* 227.1310, found *m/z* 227.1309. $[\alpha]_D = -4.4$ (c = 1.0, $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiracel AD and AD guard column (2:98 ethanol/hexanes, 1 mL/min); *S* isomer t_r = 38.7 min and *R* isomer t_r = 42.2 min.

(*R*)-3-(1-Benzyl-1*H*-indol-3-yl)-butanal (Table 3, entry 4). Prepared according to the general procedure from crotonaldehyde (125 μL, 1.50 mmol), 1-benzyl-1*H*-indole (104 mg, 0.500 mmol), 2,4-dinitrobenzoic acid (21.2 mg, 0.100 mmol) and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one (24.6 mg, 0.100 mmol) in CH_2Cl_2 (0.90 mL) and isopropanol (0.10 mL) at −60 °C for 41 h, at which time an additional 125 μL (1.50 mmol) of crotonaldehyde was added. The reaction was continued for an additional 70 h, at which time an additional 42 μL (0.50 mmol) of crotonaldehyde was added. The reaction was continued at this temperature for an additional 5 h, at which time the temperature was raised to −40 °C for 2 h, then −10 °C for an additional 2 h to provide, after silica gel chromatography (15:85 EtOAc/hexanes), the title compound as a colorless oil (110 mg, 80% yield, 89% ee). IR (film) 3062, 3030, 2965, 2925, 2877, 2820, 2724, 1722, 1613, 1589, 1549, 1496, 1480, 1468, 1452, 1392, 1372, 1356, 1331, 1303, 1251, 1203, 1174, 1017 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.76 (dd, *J* = 2.4, 2.4 Hz, 1H, CHO), 7.66 (dt, *J* = 0.6, 7.5 Hz, 1H, ArH), 7.33-7.08 (m, 8H, ArH), 6.92 (s, 1H, NCH), 5.28 (s, 2H, NCH_2), 3.70 (dt, *J* = 6.9, 21 Hz, 1H, ArCH), 2.89 (ddd, *J* = 2.4, 6.6, 16.5 Hz, 1H, C**H**$_2$CO); 2.72 (ddd, *J* = 1.8, 7.8, 15.9 Hz, 1H, C**H**$_2$CO); 1.44 (d, *J* = 6.9 Hz, 3H, CHC**H**$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.7, 137.5, 131.9, 128.8, 127.6, 126.9, 126.8, 124.6, 122.0, 119.6, 119.3, 119.2, 110.0, 51.2, 50.1, 26.1, 21.0; HRMS (CI) exact mass calcd for ($C_{19}H_{19}NO$) requires *m/z* 277.1467, found *m/z* 277.1464. $[\alpha]_D = +3.5$ (c = 1.0, $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiracel AD and AD guard column (2:98 isopropanol / hexanes, 1 mL/min); *S* isomer t_r = 26.5 min and *R* isomer t_r = 29.5 min.

(*R*)-4-Benzyloxy-3-(4-methoxy-1-methyl-1*H*-indol-3-yl)-butanal (Table 3, entry 6). Prepared according to the general procedure from 4-benzyloxy-but-2-enal (285 mg, 1.50 mmol), 4-methoxy-1-methyl-1*H*-indole (80.5 mg, 0.500 mmol), TFA (7.7 μL, 0.10 mmol) and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one (24.6 mg, 0.100 mmol) in CH_2Cl_2 (0.90 mL) and isopropanol (0.10 mL) at −87 °C for 19.5 h to provide, after silica gel chromatography (20:80 EtOAc/hexanes), the title compound as a colorless oil (158 mg, 90% yield, 94% ee). IR (film) 3081, 2961, 2850, 2730, 1719, 1608, 1582, 1548, 1501, 1466, 1454, 1424, 1381, 1334, 1321, 1274, 1261, 1180, 1116, 1073, 1026, 782, 714 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.78 (dd, *J* = 2.4, 2.4 Hz, 1H, CHO), 8.03-8.01 (m, 2H, ArH), 7.59-7.53 (m, 1H, ArH), 7.47-7.41 (m, 2H, ArH), 7.16 (t, *J* = 8.4 Hz, 1H, ArH), 6.92 (dd, *J* = 0.6, 8.4 Hz, 1H, ArH), 6.83 (s, 1H, NCH), 6.52 (d, *J* = 7.5 Hz, 1H, ArH), 4.71 (dd, *J* = 5.1, 10.5 Hz, 1H, C**H**$_2$O), 4.50 (dd, *J* = 8.4, 10.5 Hz, 1H, C**H**$_2$O), 4.35 (m, 1H, ArCH), 3.94 (s, 1H, OCH_3), 3.71 (s, 3H, NCH_3), 2.98 (d, *J* = 2.4 Hz, 1H, C**H**$_2$CO); 2.96 (d, *J* = 2.7 Hz, 1H, C**H**$_2$CO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.5, 166.3, 154.2, 133.0, 130.3, 129.6, 128.6, 128.4, 125.4, 122.9, 116.8, 113.6, 102.8, 99.4, 68.8, 55.3, 47.3, 33.2, 32.2; HRMS (CI) exact mass calcd for ($C_{21}H_{21}NO_4$) requires *m/z* 351.1471, found *m/z* 351.1466. $[\alpha]_D$ = −13.9 (c = 1.0, $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiracel AD and AD guard column (4:96 ethanol/hexanes, 1 mL/min); *S* isomer t_r = 58.7 min and *R* isomer t_r = 47.5 min.

(*R*)-4-Benzyoxy-3-(4-methyl-1*H*-indol-3-yl)-butanal (Table 3, entry 5). Prepared according to the general procedure from benzoic acid 4-benzyloxy-but-enal (143 mg, 0.750 mmol), 4-methyl-1*H*-indole (80.5 mg, 0.500 mmol), 2,4-dinitrobenzoic acid (21.2 mg, 0.100 mmol) and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one (24.6 mg, 0.100 mmol) in CH_2Cl_2 (0.90 mL) and isopropanol (0.10 mL) at −60 °C for 2.5 h to provide, after silica gel

chromatography (15:85 EtOAc/hexanes), the title compound as a colorless oil (150 mg, 94% yield, 94% ee) after silica gel chromatography in 15% EtOAc / hexanes. IR (film) 3406, 2947, 2923, 2843, 2738, 1717, 1620, 1604, 1584, 1451, 1411, 1383, 1344, 1315, 1271, 1178, 1114, 1066, 1226, 969 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.82 (dd, *J* = 2.1, 2.1 Hz, 1H, CHO), 8.14 (s, 1H, NH), 8.02 (dt, *J* = 1.5, 7.2 Hz, 2H, ArH), 7.58 (tt, *J* = 1.5, 6.6 Hz, 1H, ArH), 7.45 (tt, *J* = 1.2, 6.9 Hz, 2H, ArH), 7.24-7.08 (m, 3H, ArH, NCH), 6.91 (dt, *J* = 0.9, 7.2 Hz, 1H, ArH), 4.74 (dd, *J* = 4.2, 10.5 Hz, 1H, C**H**$_2$O), 4.52-4.43 (m, 1H, ArCH), 4.32 (dd, *J* = 8.4, 10.8 Hz, 1H, C**H**$_2$O), 3.05 (ddd, *J* = 2.1, 6.9, 16.8 Hz, 1H, C**H**$_2$CO); 2.95 (ddd, *J* = 2.1, 7.8, 16.8 Hz, 1H, C**H**$_2$CO), 2.82 (s, 3H, $ArCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.3, 166.3, 136.5, 133.2, 130.5, 130.0, 129.7, 128.5, 125.1, 122.6, 122.1, 121.7, 115.8, 109.4, 68.9, 47.8, 31.7, 21.0; HRMS (CI) exact mass calcd for ($C_{20}H_{19}NO_3$) requires *m/z* 321.1365, found *m/z* 321.1353. $[\alpha]_D$ = –26.6 (c = 1.0, $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiracel AD and AD guard column (10:90 ethanol/hexanes, 1 mL/min); *S* isomer t_r = 47.8 min and *R* isomer t_r = 42.4 min.

(*R*)-4-Benzyloxy-3-(6-chloro-1*H*-indol-3-yl)-butanal (Table 3, entry 7). Prepared according to the general procedure from 4-benzyloxy-but-2-enal (143 mg, 0.750 mmol), 6-chloro-1*H*-indole (75.8, 0.500 mmol), 2,4-dinitrobenzoic acid (21.2 mg, 0.100 mmol) and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one (24.6 mg, 0.100 mmol) in CH_2Cl_2 (0.90 mL) and isopropanol (0.10 mL) at -60 °C for 12.75 h to provide, after silica gel chromatography (CH_2Cl_2), the title compound as a colorless oil (124 mg, 73% yield, 97% ee) after silica gel chromatography in CH_2Cl_2. IR (film) 3383, 2953, 2930, 2834, 2734, 1718, 1623, 1603, 1548, 1453, 1403, 1378, 1273, 1184, 1104, 1069, 1019, 909, 804, 774, 714 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.77 (dd, *J* = 1.8, 1.8 Hz, 1H, CHO), 8.15 (s, 1H, NH), 8.02-7.99 (m, 2H, ArH), 7.65 (dd, *J* = 0.6, 8.7 Hz, 1H, ArH), 7.58 (tt, *J* = 1.5, 6.6 Hz, 1H, ArH), 7.48-7.42 (m, 2H, ArH), 7.37 (d, *J* = 1.8 Hz, 1H NCH), 7.12 (dt, *J* = 2.1, 8.7 Hz, 2H, ArH), 4.70 (dd, *J* = 5.1, 10.8

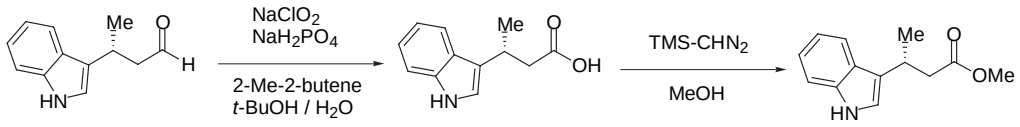
Hz, 1H, C**H**$_2$O), 4.42 (dd, J = 8.4, 11.1 Hz, 1H, C**H**$_2$O), 4.08 (m, 1H, ArCH), 3.06 (ddd, *J* = 1.8, 6.3, 16.8 Hz, 1H, C**H**$_2$CO); 2.95 (ddd, *J* = 2.1, 7.8, 16.5 Hz, 1H, C**H**$_2$CO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.9, 166.5, 136.7, 135.4, 133.2, 129.9, 129.6, 128.5. 125.1, 122.3, 120.7, 119.8, 115.0, 111.4, 67.8, 46.5, 31.0; HRMS (CI) exact mass calcd for ($C_{19}H_{16}ClNO_3$) requires *m/z* 341.0819, found *m/z* 341.0814. $[\alpha]_D = -3.3$ (c = 1.0, $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiracel AD and AD guard column (10:90 ethanol/hexanes, 1 mL/min); *S* isomer t_r = 38.8 min and *R* isomer t_r = 43.3 min.

(*R*)-3-[1-(4-Bromo-benzyl)-5-methoxy-2-methyl-1*H*-indol-3-yl]-butanal (eq 3). To 1-(4-bromo-benzyl)-5-methoxy-2-methyl-1*H*-indole (110 mg, 0.333 mmol) in a 2-dram amber vial was added CH_2Cl_2 (0.60 mL), isopropanol (0.066 mL), dichloroacetic acid (5.5 μL, 0.066 mmol) and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one (16.4 mg, 0.066 mmol). This solution was stirred for 10 min at room temperature, then placed in a −70 °C bath for an additional 10 min. At this time, crotonaldehyde (82 μL, 1.0 mmol) was added and the reaction was stirred at −70 °C for 9 h. The reaction mixture was then transferred cold through a silica plug into a flask and concentrated to provide, after silica gel chromatography (20:80 EtOAc/hexanes), the title compound as a colorless oil (111 mg, 84% yield, 87% ee). IR (film) 2930, 2823, 2730, 1722, 1618, 1581, 1530, 1483, 1452, 1405, 1229, 1156, 1073, 1037, 1011, 902, 798, 476 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.69 (dd, *J* = 1.8, 1.8 Hz, 1H, CHO), 7.38 (dt, *J* = 2.4, 9.0 Hz, 2H, ArH), 7.12 (d, *J* = 2.1 Hz, 1H, ArH), 7.05 (d, *J* = 9.0, 1H, ArH), 6.79-6.75 (m, 3H, ArH), 5.19 (s, 2H NCH_2), 3.88 (s, 3H, OCH_3), 3.66 (dt, *J* = 7.2, 22.2 Hz, 1H ArCH), 3.02 (ddd, *J* = 1.8, 8.1, 16.5 Hz, 1H, C**H**$_2$CO); 2.85 (ddd, *J* = 2.1, 6.6, 16.5 Hz, 1H, C**H**$_2$CO); 2.30 (s, 3H, $ArCH_3$) 1.48 (d, *J* = 7.2 Hz, 3H, CHC**H**$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.5, 153.6, 137.0, 132.7, 132.0, 131.9, 127.6, 126.6, 121.1, 114.5, 110.0, 109.8, 102.3, 56.2, 50.6, 46.2, 26.4, 21.4, 10.9; HRMS (CI) exact mass calcd for ($C_{21}H_{22}BrNO_2$) requires *m/z* 399.0834,

found *m/z* 399.0833. $[\alpha]_D = -20.8$ (c = 1.0, $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiracel OD–H and OD guard column (4:96 ethanol/hexanes, 1 mL/min); *S* isomer t_r = 45.1 min and *R* isomer t_r = 35.9 min.

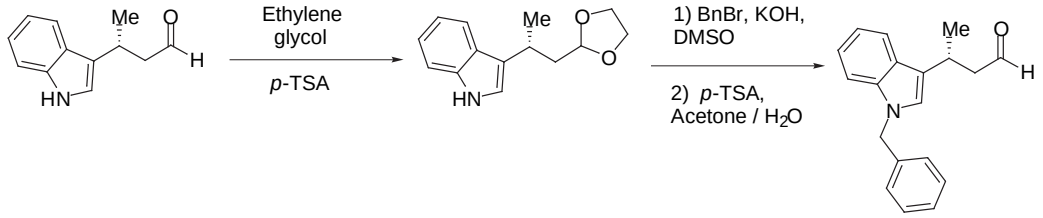
(*R*)-3-[1-(4-Bromo-benzyl)-5-methoxy-2-methyl-1*H*-indol-3-yl]-butyric acid (eq 3). A solution of (*R*)-3-[1-(4-Bromo-benzyl)-5-methoxy-2-methyl-1*H*-indol-3-yl]-butanal (110 mg, 0.250 mmol) and silver nitrate (59.7mg, 0.275mmol) in 1.3ml absolute ethanol was treated with a solution of 5N NaOH in ethanol (1:5, 0.9ml, 0.75 mmol NaOH). After 45 min this was treated with 10ml water, acidified to pH 3 and extracted with $CHCl_3$ (5x20ml) rinsing each extract with brine. The combined organics were dried over Na_2SO_4 and concentated *in vacuo* to provide, after silica gel chromatography the title compound as a pale yellow solid (101 mg, 97% yield). IR (film) 3425, 2961, 2934, 2833, 1706, 1483, 1451, 1405, 1228, 1156, 1010, 796, 755 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36 (d, *J* = 9.0 Hz, 2H, ArH), 7.11 (d, *J* = 2.4 Hz, 1H, ArH), 7.04 (d, *J* = 8.7, 1H, ArH), 6.77-6.73 (m, 3H, ArH), 5.18 (s, 2H NCH_2), 3.86 (s, 3H, OCH_3), 3.56 (dt, *J* = 7.2, 21.9 Hz, 1H ArCH), 2.86 (d, *J* = 3.6 Hz, 1H, C**H**$_2$CO); 2.83 (d, *J* = 3.3 Hz, 1H, C**H**$_2$CO); 2.27 (s, 3H, $ArCH_3$) 1.49 (d, *J* = 7.2 Hz, 3H, CHC**H**$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.0, 153.7, 137.3, 133.8, 133.0, 132.0, 127.7, 126.7, 121.2, 118.8, 114.6, 110.1, 109.9, 102.4, 56.3, 46.3, 41.5, 28.6, 21.1, 10.9; HRMS (CI) exact mass calcd for ($C_{21}H_{23}BrNO_3$) (M+1) requires *m/z* 416.0861, found *m/z* 416.0867. $[\alpha]_D = -30.9$ (c = 1.0, $CHCl_3$).

Determination of absolute stereochemistry

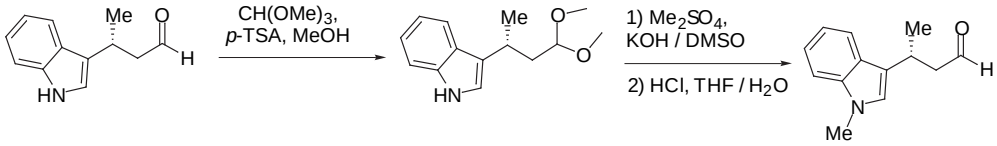


Determination of the absolute stereochemistry of (*R*)-3-(1*H*-indol-3-yl)-butanal by correlation to (*S*)-3-(1*H*-indol-3-yl)-butyric acid methyl ester.[3] 3-(1*H*-Indol-3-yl)-butanal (130 mg, 0.690 mmol) was dissolved in *tert*-butyl alcohol (27 mL) and 2-methyl-2-butene (4.7 mL) and subsequently was stirred for 10 min. To this solution was added an aqueous solution (4.7 mL) of $NaClO_2$ (75 mg, 0.83 mmol) and NaH_2PO_4 (115 mg, 0.830 mmol) in one portion. The reaction mixture was stirred at room temperature for 12 h. The organics were removed by concentrating *in vacuo*. The residue was diluted with 10 mL of H_2O, and adjusted to a neutral pH with 1M HCl. Extraction with EtOAc (3x10 mL), drying over Na_2SO_4, and concentration *in vacuo* provided 3-(1*H*-indol-3-yl)-butanoic acid. TMS-diazomethane was added dropwise to a solution of the crude 3-(1*H*-indol-3-yl)-butanoic acid in methanol (7 mL) until a yellow color persisted. The residual TMS-diazomethane was quenched by the dropwise addition of acetic acid until the yellow color disappeared. The reaction was then treated with an excess of saturated aqueous sodium bicarbonate, extracted with Et_2O (3 x 20ml), dried over Na_2SO_4 and purified by silica gel chromatography (20:80 EtOAc/hexanes to provide (*R*)-3-(1*H*-indol-3-yl)-butyric acid methyl ester. $[\alpha]_D = -7.6$ (c = 1.0, benzene); reported rotation for (*S*)-3-(1*H*-indol-3-yl)-butyric acid methyl ester $[\alpha]_D = +10.9$ (c = 2.12, benzene).

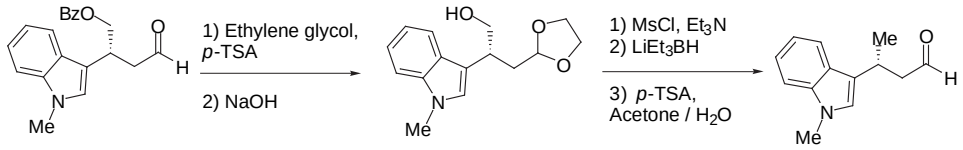
[3] Takeda, T.; Mukaiyama, T. *Chem. Lett*. **1980**, 163



Determination of the absolute stereochemistry of (*R*)-3-(1-Benzyl-1*H*-indol-3-yl)-butanal by correlation to (*R*)-3-(1*H*-indol-3-yl)-butanal. (*R*)-3-(1*H*-Indol-3-yl)-butanal (89.5 mg, 0.479 mmol) was treated with ethylene glycol (130 μL, 2.4 mmol) and a catalytic amount of *p*-TSA in CH_2Cl_2 (2 mL). The reaction was stirred at room temperature for 12 h, at which time the organics were removed *in vacuo*. The solution was diluted with H_2O (10 mL) and extracted with Et_2O (3x20 mL). The collected organics where washed with brine, dried over Na_2SO_4 and concentrated *in vacuo* to provide (*R*)-3-(2-[1,3]dioxolan-2-yl-1-methyl-ethyl)-1*H*-indole (15.7 mg, 0.0680 mmol) after silica gel chromatography (20:80 EtOAc/hexanes). This residual material was then exposed to 1 mL of DMSO, finely crushed KOH (15.3 mg, 0.272 mmol), and benzyl bromide (12 μL, 0.13 mmol) at 0°C, then the solution was allowed to warm to room temperature and stirred for 12 h. The reaction was then treated with water (10ml), and extracted with Et_2O (2x20ml). The aqueous layer was acidifid to pH 4, extracted with Et_2O 3x20ml), dried over Na_2SO_4 and concentrated *in vacuo* to provide 14.7 mg of (*R*)-1-benzyl-3-(2-[1,3]dioxolan-2-yl-1-methyl)-1*H*-indole after preparative TLC (20:80 EtOAc/hexanes). The benzylated product was then refluxed with a catalytic amount of *p*-TSA in H_2O (1 mL) / acetone (2 mL) overnight. The reaction mixture was diluted with H_2O (5 mL), and extracted with Et_2O (3x10 mL). The collected organics were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo* to provide (*R*)-3-(1-benzyl-1*H*-indol-3-yl)-butanal (5.5 mg, 0.020 mmol) after preparative TLC. $[\alpha]_D$ = + 3.8 (c = 1.0, $CHCl_3$); reported rotation for (*R*)-3-(1-benzyl-1*H*-indol-3-yl)-butanal $[\alpha]_D$ = + 3.5 (c = 1.0, $CHCl_3$).



Determination of the absolute stereochemistry of (*R*)-3-(1-methyl-1*H*-indol-3-yl)-butanal by correlation to (*R*)-3-(1*H*-indol-3-yl)-butanal. (*R*)-3-(1*H*-Indol-3-yl)-butanal (236 mg, 1.26 mmol) was dissolved in methanol (15 mL) and treated with trimethyl orthoformate (275 μl, 2.50 mmol) and a catalytic amount of *p*-TSA. The reaction was stirred at room temperature for 3 hours, at which time H_2O (10 mL) was added and the reaction was extracted with ether (3x20 mL). The collected organics were rinsed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to provide 3-(3,3-dimethoxy-1-methyl-propyl)-1*H*-indole (228 mg, 1.17 mmol). 3-(3,3-dimethoxy-1-methyl-propyl)-1*H*-indole (39.9 mg, 0.171 mmol) was dissolved in a KOH (38.4 mg, 0.684 mmol) / DMSO (2 mL) solution and allowed to stir at 0°C for 10 min, at which time dimethyl sulfate (32.5 μl, 0.340 mmol) was added and the reaction was allowed to warm to room temperature. The reaction was left to stir at room temperature until it appeared done by TLC. The reaction was quenched with H_2O (1 mL) and brought to a neutral pH with dropwise addition of 1M HCl. The solution was extracted with Et_2O (3x5 mL), and the collected organics were rinsed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to provide 3-(3,3-dimethoxy-1-methyl-propyl)-1-methyl-indole. This crude residual material was dissolved in THF (5 mL) and 1M HCl (1 mL) to give (*R*)-3-(1-methyl-1*H*-indol-3-yl)-butanal (1.9 mg, 0.0094 mmol) after preparative TLC (25:75 EtOAc/hexanes). . $[\alpha]_D = -4.1$ (c = 1.0, $CHCl_3$); reported rotation for (*R*)-3-(1-methyl-1*H*-indol-3-yl)-butanal $[\alpha]_D = -4.2$ (c = 1.0, $CHCl_3$).



Determination of the absolute stereochemistry (*R*)-4-benzyloxy-3-(1-methyl-1*H*-indol-3-yl)-butanal by correlation to (*R*)-3-(1*H*-indol-3-yl)-butanal. (*R*)-Benzoic acid 2-(1-methyl-1*H*-indol-3-yl)-4-oxo-butyt ester (1.65g, 5.10 mmol) was dissolved in CH_2Cl_2 (50 mL). This solution was treated with *p*-TSA (20 mg) and ethylene glycol (1.4 mL, 26 mmol). The reaction was stirred at room temperature overnight, at which time the organics were removed *in vacuo*. The solution was diluted with H_2O (10 mL) and extracted with Et_2O (3x20 mL). The collected organics were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo* to provide (*R*)-benzoic acid 3-[1,3]dioxolan-2-yl-2-(1-methyl-1*H*-indol-3-yl)-propyl ester. The unpurified product was dissolved in MeOH/THF (18 mL / 18 mL) and allowed to stir at room temperature for 10 min. To this was added a 4% NaOH / MeOH (18 mL) solution. The reaction was allowed to stir at room temperature for 1 h. The solution was diluted with H_2O (10 mL) and extracted with Et_2O (3x20 mL). The collected organics were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo* to provide (*R*)-3-[1,3]dioxolan-2-yl-2-(1-methyl-1*H*-indol-3-yl)-propan-1-ol (600 mg, 2.30 mmol) after silica gel chromatography (50:50 Et_2O/hexanes). 50% Et_2O / hexanes). (*R*)-3-[1,3]Dioxolan-2-yl-2-(1-methyl-1*H*-indol-3-yl)-propan-1-ol (69.5 mg, 0.267 mmol) was dissolved in CH_2Cl_2 (8 mL) and Et_3N (56 µl, 0.40 mmol). The reaction was cooled to 0 °C and treated with methanesulfonyl chloride (31 µl, 0.40 mmol). The reaction stirred for 1.5 h at this temperature then was allowed to warm to room temperature and stirred for an additional 10 min. The solution was diluted with H_2O (5 mL) and extracted with Et_2O (3x10 mL). The collected organics were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo* to provide (*R*)-methanesulfonic acid 3-[1,3]dioxolan-2-yl-2-(1-methyl-1*H*-indol-3-yl)-propyl ester. Deoxygenation was performed following the method of Holder and Matturro.[4] The

[4] Holder, R.W.; Matturro, M.G. *J. Org. Chem.* **1977**, *42*, 2166.

unpurified material was dissolved in THF (2.7 mL) and the system was purged with an inert nitrogen atmosphere. Lithium triethylborohydride (560 µl, 1M solution in THF) was added in one portion and the reaction was allowed to reflux for 1 h under an nitrogen. The system was allowed to come to room temperature and was then cooled to 0 °C via an ice bath. Excess hydride was quenched by the dropwise addition of H_2O. Organoboranes were oxidized by adding 190 µl of a 3N NaOH solution followed by slow dropwise addition of 115 µl of 50% H_2O_2. The ice bath was removed and the reaction mixture was allowed to reflux for an additional hour. After cooling to room temperature, the mixture was diluted with 2.7 mL H_2O and extracted with pentane. The collected pentane layers were washed with H_2O, dried with $MgSO_4$, and concentrated *in vacuo* to provide (*R*)-3-(2-[1,3]dioxolan-2-yl-1-methyl-ethyl)-1-methyl-1*H*-indole. The unpurified material was dissolved in 8 ml acetone and 2 ml H_2O , treated with PPTS and warmed to reflux for 24 h. The reaction was diluted with H_2O (5 mL) and extracted with Et_2O (3x10 mL). The collected organics were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo* to provide (*R*)-3-(1-methyl-1*H*-indol-3-yl)-butanal after preparative TLC (benzene). $[\alpha]_D = -4.6$ (c = 1.0, $CHCl_3$); reported rotation for (*R*)-3-(1-methyl-1*H*-indol-3-yl)-butanal $[\alpha]_D = -4.2$ (c = 1.0, $CHCl_3$).