Angew. Chem. **1999**.

Supporting Information for:

Facile, Novel Methodology for the Synthesis of Pyrrolidine-spiro-oxindoles: Metal-Catalyzed Ring Expansion Reactions of Cyclopropanes by Aldimines

Phil B. Alper, Christiane Meyers, Dionicio R. Siegel, and Erick M. Carreira*

General Methods. All reagents were obtained from commercial sources and used as received unless specified. All non-aqueous reactions were performed using oven-dried glassware under an atmosphere of argon. Air and moisture sensitive liquids and solutions were transferred *via* syringe or stainless steel cannula. Organic solutions were concentrated by rotary evaporation below 40 C using a membrane pump. Dimethylformamide was purchased anhydrous over molecular sieves and used as received. *M*-Xylene was distilled from sodium prior to use. Tetrahydrofuran was distilled from sodium benzophenone ketyl prior to use. Chromatography was performed over Fluka silica gel 60 according to the method of Still[1]. Thin layer chromatography was performed over 0.25 mm silica gel 60F plates (230-400 mesh). Visualization of the developed TLC plates was performed using either UV light or ceric ammonium molybdate (CAM) stain.

NMR spectra were recorded on a Gemini 200 or 300 or a Bruker DRX-500 or DRX-400 instrument and are referenced internally to a residual protio solvent signal. 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 constants. Data for ^{13}C are reported in terms of

chemical shift. IR spectra were recorded on a Perkin-Elmer Spectrum RX-I FT-IR brand instrument using either material pressed into a KBr pellet or a chloroform solution in a NaCl cell. Melting points were recorded on a Büchi 510 instrument and are uncorrected. HPLC analysis was performed on a Hitachi 7000 series instrument using a Säulentechnik 4 mm ID column packed with 5 µm spherisorb SW silica gel.

1-benzyl-spiro-3-cyclopropyl-indole-2-one (1)

A solution of 1-benzyl-indoline-2-one[2] (4.62 g, 20.1 mmol) in DMF (20 mL) was treated with dibromoethane (4.28 g, 22.8 mmol) and cooled in an ice/water bath. Then, NaH (1.49 g, 62.1 mmol) was added in portions. After ~2/3 of the NaH had been added, the cold bath was removed. After stirring at room temperature for 1 h, the reaction was quenched by addition of MeOH (5 mL). The reaction was then diluted with EtOAc (150 mL) and washed with water 4 times (50 mL each) and once with brine (30 mL). The organic solutions were dried over Na_2SO_4, the solvent was removed and the residue was purified on ~150 g of silica gel using 400 mL each of 15 % and 20 % of EtOAc in hexane. The resulting yellow material was crystallized by dissolving it in a minimum amount of toluene and layering cyclohexane on top of this solution. The title material was obtained as colorless crystals in two crops. 3.76 g, 73 % yield; mp 103 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.33-7.26 (m, 5H), 7.15 (dt, 1H, J = 7.5 Hz, 1.3 Hz), 6.99 (dt, 1H, J = 7.5 Hz, 0.9 Hz), 6.86-6.84 (m, 1H), 6.80 (d, 1H, J = 7.8 Hz), 5.00 (s, 2H), 1.81 (dd, 2H, J = 7.8 Hz, 4.1 Hz), 1.56 (dd, 2H, J = 7.8 Hz, 4.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 177.5, 136.5, 131.1, 129.0, 127.8, 127.6, 126.9, 122.3, 118.6, 11.2, 109.2, 44.2, 27.1, 19.5;

IR (KBr) ν 1703, 1616, 1496, 1490, 1466, 1384, 1367, 1339, 1181, 1008, 948, 754, 738, 700, 457; MS (DEI) Calc. for $C_{17}H_{15}NO$: 249.1, Found: 249.1; Anal. Calc. for $C_{17}H_{15}NO$: C 81.90, H 6.06, N 5.62, Found: C 81.92, H 6.22, N 5.73.

Bicyclic oxindole (entry 1)

A sealable tube was charged with 1-benzyl-spiro-3-cyclopropyl-indole-2-one (0.200 g, 0.802 mmol), tetrahydropyridine trimer **(8)**[3] (86.7 mg, 0.348 mmol) and anhydrous MgI_2 (11 mg, 0.040 mmol). The tube was then evacuated and back filled with argon. THF (1 mL) was added and the tube was sealed. The reaction was then dipped into a preheated 125 C oil bath. After 19 h, the reaction was cooled to room temperature and water and EtOAc (2 mL each) were added along with a few crystals of $Na_2S_2O_4$ (to quench the I_2 formed in the reaction). The reaction was diluted with EtOAc, extracted with brine and the organics were dried over Na_2SO_4. After removal of solvent, the reaction was purified by column chromatography using a gradient of 15 to 35 % EtOAc in hexane to obtain the less polar (*R**,*S**)-diastereomer (156 mg) as an oil which solidified upon prolonged exposure to high vacuum. The minor (*R**,*R**)-diastereomer was eluted with a gradient of 2 to 6 % MeOH in CH_2Cl_2 (26 mg) as an oil. Total: 182 mg, 68 % in a diastereomeric ratio of 86:14.

(*R**,*S**)-diastereomer: mp 89-90 C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.43-7.41 (m, 1H), 7.35-7.21 (m, 5H), 7.13 (ddd, 1H, J = 7.8 Hz, 7.8 Hz, 1.3 Hz), 7.02 (ddd, 1H, J = 7.8 Hz, 7.8 Hz, 1.3 Hz), 6.71-6.67 (m, 1H), 5.05 (d, 1H, J = 15.6 Hz), 4.79 (d, 1H, J = 15.6 Hz), 3.31 (ddd, 1H, J = 8.7 Hz, 8.7 Hz, 2.2 Hz), 3.25-3.16 (m, 1H), 2.60-2.35 (m, 3H), 2.15-1.97 (m, 2H), 1.68-1.56 (m, 1H),

1.54-1.37 (m, 1H), 1.30-1.08 (m, 2H), 0.98-0.82 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 179.8, 142.2, 136.1, 133.6, 128.7, 127.5, 127.3, 127.1, 124.9, 122.3, 108.6, 72.1, 56.6, 54.2, 53.6, 43.8, 34.9, 26.4, 25.1, 23.7; IR (KBr) ν 2936, 2793, 1714, 1611, 1487, 1465, 1383, 1363, 1170, 751, 696; MS (DEI) Calc. for $C_{22}H_{24}N_2O$: 332.2, Found: 332.1; Anal. Calc. for $C_{22}H_{24}N_2O$: C 79.48, H 7.28, N 8.43, Found C 79.41, H 7.39, N 8.32.

(*R**,*R**)-diastereomer: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.34-7.20 (m, 6H), 7.12 (ddd, 1H, J = 7.8 Hz, 7.8 Hz, 1.1 Hz), 7.02 (ddd, 1H, J = 7.5 Hz, 7.5 Hz, 0.9 Hz), 6.66-6.62 (m, 1H), 5.16 (d, 1H, J = 15.9 Hz), 4.65 (d, 1H, J = 15.9 Hz), 3.46-3.35 (m, 1H), 3.33- 3.25 (m, 1H), 2.55-2.39 (m, 2H), 2.21 (dd, 1H, J = 11.1 Hz, 2.7 Hz), 2.07-1.88 (m, 3H), 1.80-1.40 (m, 4H), 1.31-1.22 (m, 1H), 1.17-1.00 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 179.0, 142.9, 136.2, 133.5, 128.6, 127.6, 127.4, 127.3, 122.8, 122.4, 108.6, 75.3, 55.8, 55.3, 53.7, 43.8, 34.7, 25.6, 24.7, 24.1; IR (KBr) ν 2935, 2855, 2779, 1714, 1611, 1487, 1466, 1351, 1168, 752, 697; HRMS (FAB) Calc. for $C_{22}H_{24}N_2O$: 332.1889, Found: 332.1898.

2’-(phenyl)-1’-(butyl)-1-benzyl-spiro-(indole-3,3’-pyrrolidine)-2-one (entry 5)

The following procedure is typical for the synthesis of 1’-(alkyl)-1-benzyl-spiro-(indole-3,3’-pyrrolidine)-2-ones:

A sealable tube was charged with 1-benzyl-spiro-3-cyclopropyl-indole-2-one (0.100 g, 0.401 mmol) and anhydrous MgI_2 (11 mg, 0.040 mmol). The tube was then evacuated and back filled with argon. THF (1 mL) was added followed by freshly distilled N-butyl benzyl imine[4] (84 mg, 0.52 mmol). The tube was then sealed and dipped into an oil bath preheated to 80 C. After 2 h, the reaction was cooled to room temperature and water and EtOAc (2 mL each) were added along with a few crystals of $Na_2S_2O_4$ (to quench

the I_2 formed in the reaction). The reactionmixture was diluted with EtOAc, washed with brine and the organic solution was dried over Na_2SO_4. After removal of the solvent, the crude product was purified by column chromatography using a gradient of 0 to 20 % EtOAc in hexane to obtain the (*R**,*S**)-diastereomer (129 mg) first as an off-white solid followed by the (*R**,*R**)-diastereomer (30.8 mg) also as an off-white solid. Total: 129 mg, 97 % yield in a diastereomeric ratio of 81:19.

(*R**,*S**)-diastereomer: mp 108-111 C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.56-7.48 (m, 1H), 7.23-6.87 (m, 12H), 6.39-6.30 (m, 1H), 5.07 (d, 1H, J = 15.9 Hz), 4.55 (d, 1H, J = 15.9 Hz), 4.06 (s, 1H), 3.66 (ddd, 1H, J = 4.7 Hz, 8.7 Hz, 13.4 Hz), 2.81-2.58 (m, 3H), 2.20-2.04 (m, 2H), 1.71-1.26 (m, 4H), 0.93 (dd, 3H, J = 7.2 Hz, 7.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 178.5, 141.8, 136.9, 135.5, 132.4, 128.5, 128.2, 127.4, 127.3, 127.2, 126.8, 125.6, 121.9, 108.4, 77.4, 59.4, 53.5, 51.6, 43.6, 34.2, 30.9, 20.5, 14.2; IR (KBr) ν 1703, 1612, 1487, 1467, 1368, 1171, 909, 651; MS (DEI) Calc. for $C_{28}H_{30}N_2O$: 410.2, Found: 410.2; Anal. Calc. for $C_{28}H_{30}N_2O$: C 81.91, H 7.32, N 6.82, Found: C 81.84, H 7.43, N 6.85.

(*R**,*R**)-diastereomer: mp 112-115 C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.45 (m, 1H), 7.29-7.04 (m, 10H), 6.46-6.35 (m, 3H), 4.99 (d, 1H, J = 15.9), 4.12 (d, 1H, J = 15.9), 3.83-3.69 (m, 1H), 3.74 (s, 1H), 2.70-2.54 (m, 3H), 2.28-2.14 (m, 1H), 2.01 (ddd, 1H, J = 11.9 Hz, 8.6 Hz, 4.2 Hz), 1.74-1.20 (m, 4H), 0.90 (dd, 3H, J = 7.2 Hz, 7.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 178.2, 142.9, 136.9, 135.6, 133.1, 128.4, 128.3, 128.0, 127.9, 127.6, 126.9, 126.6, 122.8, 122.3, 108.7, 81.0, 58.8, 54.1, 53.3, 43.5, 34.8, 30.6, 20.6, 14.1; IR (KBr) ν 1712, 1612, 1489, 1467, 1454, 1362, 1308, 1176, 972; MS (DEI) Calc. for $C_{28}H_{30}N_2O$: 410.2, Found: 410.2; Anal. Calc. for $C_{28}H_{30}N_2O$: C 81.91, H 7.32, N 6.82, Found: C 82.13, H 7.56, N 6.78.

2′-(ethyl)-1′-(allyl)-1-benzyl-spiro-(indole-3,3′-pyrrolidine)-2-one (entry 2)

1-Benzyl-spiro-3-cyclopropyl-indole-2-one (0.200 g, 0.802 mmol), MgI_2 (111 mg, 401 mmol) and freshly distilled N-allyl-propyl imine[5] (312 mg, 3.21 mmol) were allowed to react in 1 mL of THF. The reaction was worked up after 21 h of heating and yielded 50 % of the desired material in a diastereomeric ratio of 91:9 after chromatography.

(*R**,*S**)-diastereomer: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.44 (dd, 1H, J = 0.8 Hz, 7.4 Hz), 7.34-7.20 (m, 5H), 7.16 (ddd, 1H, J = 7.7 Hz, 7.7 Hz, 1.3 Hz), 7.02 (ddd, 1H, J = 7.6 Hz, 7.6 Hz, 1.0 Hz), 6.75 (d, 1H, J = 7.5 Hz), 6.04-5.94 (m, 1H), 5.31-5.25 (m, 1H), 5.18-5.13 (m, 1H), 4.90 (s, 2H), 3.57 (dddd, 1H, J = 13.7 Hz, 4.9 Hz, 1.7 Hz, 1.7 Hz), 3.32 (ddd, 1H, J = 9.2 Hz, 8.2 Hz, 4.0 Hz), 2.92 (dd, 1H, J = 13.7Hz, 7.6 Hz), 2.87 (dd, 1H, J = 9.9 Hz, 3.9 Hz), 2.65 (ddd, 1H, J = 9.2 Hz, 9.2 Hz, 7.8 Hz), 2.34 (ddd, 1H, J = 12.8 Hz, 9.0 Hz, 4.0 Hz), 1.94 (ddd, 1H, J = 12.6 Hz, 7.9 Hz, 7.9 Hz), 1.62-1.51 (m, 1H), 1.17-1.05 (M, 1H), 0.39 (dd, 3H, J = 7.5 Hz, 7.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 180.2, 142.3, 136.0, 132.7, 128.7, 128.5, 127.6, 127.4, 127.3, 127.1, 125.2, 122.3, 116.7, 108.7, 72.8, 56.5, 52.4, 44.0, 36.6, 22.7, 16.2, 10.3, 10.2; IR ($CHCl_3$) ν 4213, 3018, 2974, 2400, 1700, 1612, 1486, 1467, 1363, 1349, 1216, 1047, 1029, 928, 751 (vb), 668; MS (DEI) Calc. for $C_{23}H_{26}N_2O$: 346.2, Found: 346.2; Anal. Calc. for $C_{23}H_{26}N_2O$: C 79.73, H 7.56, N 8.09, Found: C 79.83, H 7.75, N 7.86.

(*R**,*R**)-diastereomer: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.35-7.27 (m, 5H), 7.23 (dd, 1H, J = 7.6 Hz, 1.0 Hz), 7.13 (ddd, 1H, J = 7.7 Hz, 7.7 Hz, 1.3 Hz), 7.01 (ddd, 1H, J = 7.6 Hz, 7.6 Hz, 1.0 Hz), 6.71 (d, 1H, J = 7.4 Hz), 6.10-6.00 (m, 1H), 5.28-5.23 (m, 1H), 5.18-5.13 (m, 1H), 4.99 (d, 1H, J = 15.5 Hz), 4.84 (d, 1H, J = 15.5), 3.62-

3.56 (m, 1H), 3.41 (ddd, 1H, J = 9.8 Hz, 7.5 Hz, 2.5 Hz), 2.97 (dd, 1H, 13.5 Hz, 7.7 Hz), 2.75 (dd, 1H, J = 8.8 Hz, 4.5 Hz), 2.66 (ddd, 1H, 9.8 Hz, 9.8 Hz, 7.2 Hz), 2.42 (ddd, 1H, J = 12.6 Hz, 9.9 Hz, 7.5 Hz), 1.95 (ddd, 1H, J = 9.8 Hz, 7.2 Hz, 2.6 Hz), 1.77-1.61 (m, 3H), 0.46 (dd, 3H, J = 7.5 Hz, 7.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 178.9, 142.1, 136.2, 135.7, 135.6, 128.7, 127.6, 127.5, 122.7, 122.5, 117.2, 108.7, 75.8, 56.7, 56.4, 53.3, 43.9, 37.2, 22.3, 11.1; IR ($CHCl_3$) ν 4213, 3688, 3619, 3018, 2397, 1700, 1521, 1419, 1220, 1046, 929, 737 (vb), 669, 627; MS (DEI) Calc. for $C_{23}H_{26}N_2O$: 346.2, Found: 346.2; Anal. Calc. for $C_{23}H_{26}N_2O$: C 79.73, H 7.56, N 8.09, Found: C 79.89, H 7.74, N 8.12.

2’-(isopropyl)-1’-(allyl)-1-benzyl-spiro-(indole-3,3’-pyrrolidine)-2-one (entry 3)

1-Benzyl-spiro-3-cyclopropyl-indole-2-one (0.200 g, 0.802 mmol), MgI_2 (111 mg, 401 mmol) and freshly distilled N-allyl-isobutyl imine[5] (357 mg, 3.21 mmol) were reacted in 1 mL of THF. The reaction was worked up after 20 h of heating. The two diastereomers could be separated but equilibrated within hours. NMR spectra were obtained separately for the diastereomers, but the other data is reported for the mixture. The total yield was 83 % of the desired material in an equilibrated diastereomeric ratio of 80 to 20.

^{1}H NMR ($CDCl_3$, 300 MHz) ((*R**,*S**)-diastereomer) δ 7.44 (dd, 1H, J = 7.5 Hz, 0.9 Hz), 7.34-7.21 (m, 5H), 7.17 (ddd, 1H, J = 7.8 Hz, 1.2 Hz, 1.2 Hz), 6.99 (ddd, 1H, J = 7.5 Hz, 0.9 Hz, 0.9 Hz), 6.77 (d, 1H, J = 7.5 Hz), 6.09-5.94 (m, 1H), 5.33-5.24 (m, 1H), 5.19-5.13 (m, 1H), 4.92 (s, 2H), 3.53-3.44 (m, 1H), 3.41 (ddd, 1H, J = 10.9 Hz, 8.7 Hz, 6.5 Hz), 3.19-3.10 (m, 1H), 3.01 (d, 1H, J= 8.1 Hz), 2.85 (ddd, 1H, J = 10.9Hz, 8.7 Hz, 4.0 Hz), 2.40 (dt, J(t) =

8.6 Hz, J = 12.1 Hz), 1.84-1.65 (m, 2H), 0.86 (d, 3H, J = 6.9 Hz), 0.38 (d, 3H, J= 6.9 Hz); ((*R**,*R**)-diastereomer) δ 7.36-7.21 (m, 5H), 7.22 (dd, 1H, J = 7.5 Hz, 0.9 Hz), 7.14 (ddd, 1H, J = 7.8 Hz, 1.2 Hz, 1.2 Hz), 7.02 (ddd, 1H, J = 7.5 Hz, 0.9 Hz, 0.9 Hz), 6.65-6.62 (m, 1H), 6.09-5.93 (m, 1H), 5.33-5.24 (m, 1H), 5.19-5.12 (m, 1H), 4.91 (s, 2H), 3.56 (ddd, 1H, J = 11.2 Hz, 6.2 Hz, 6.2 Hz), 3.54-3.44 (m, 1H), 3.32-3.23 (m, 1H), 2.90 (d, 1H, J = 9.0 Hz), 2.92-2.82 (m, 1H), 2.34 (ddd, 1H, J = 12.8 Hz, 6.9 Hz, 6.9 Hz), 2.24-2.10 (m, 1H), 2.08-1.98 (m, 1H), 0.97 (d, 3H, J = 6.5 Hz), 0.44 (d, 3H, J = 6.8); ^{13}C NMR ($CDCl_3$, 75 MHz) ((*R**,*S**)-diastereomer) δ 136.5, 136.0, 128.7, 127.6, 127.5, 125.4, 122.3, 122.0, 116.5, 108.9, 76.8, 59.3, 57.8, 52.1, 44.0, 39.2, 38.1, 30.4, 20.5, 19.1 ((*R**,*R**)-diastereomer) δ 179.0, 141.9, 136.7, 136.1, 135.5, 128.7, 127.6, 127.4, 122.6, 122.3, 116.8, 110.0, 108.8, 80.5, 57.7, 57.5, 52.2, 43.9, 39.2, 29.5, 21.2, 20.2; IR ($CHCl_3$) (mixture) ν 4213, 3683, 3618, 3019, 2975, 2400, 1704, 1611, 1521, 1487, 1467, 1420, 1363, 1215, 1046, 1029, 929, 776 (vb), 671; MS (DEI) (mixture) Calc. for $C_{24}H_{28}N_2O$: 360.2, Found: 360.1; Anal. Calc. (mixture) for $C_{24}H_{28}N_2O$: C 79.96, H 7.83, N 7.77, Found: C 79.82, H 8.01, N 7.61.

2’-(phenyl)-1’-(allyl)-1-benzyl-spiro-(indole-3,3’-pyrrolidine)-2-one (entry 5)

Total yield: 156 mg, 99 % in a diastereomeric ratio of 79:21. (*R**,*S**)-diastereomer: mp 87-91 C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.56-7.48 (m, 1H), 7.23-7.15 (m, 3H), 7.12-6.88 (m, 10H), 6.40-6.32 (m, 1H), 6.05-5.90 (m, 1H), 5.31-5.21 (m, 1H), 5.18-5.11 (m, 1H), 5.06 (d, 1H, J = 15.9 Hz), 4.56 (d, 1H, J = 15.9), 4.13 (3, 1H), 3.62 (ddd, 1H, J = 14.0 Hz, 9.0 Hz, 5.0 Hz), 3.46-3.36 (m, 1H), 2.86-2.72 (m, 2H), 2.62 (ddd, 1H, J = 12.6 Hz, 10.5 Hz, 5.0 Hz),

2.12 (ddd, 1H, J = 13.0 Hz, 9.0 Hz, 6.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 178.5, 141.8, 136.5, 135.8, 135.5, 132.3, 132.3, 128.5, 128.2, 127.6, 127.4, 127.3, 127.2, 126.9, 125.6, 122.0, 116.4, 108.4, 76.7, 59.2, 56.3, 51.7, 43.6, 34.3, 29.7; IR (KBr) ν 1705, 1612, 1496, 1487, 1467, 1453, 1358, 1262, 1212, 1173, 1153, 1103, 1073, 1027, 988, 935, 798, 758, 746, 735, 721, 696; MS (DEI) Calc. for $C_{27}H_{26}N_2O$: 394.2, Found: 394.2; Anal. Calc. for $C_{27}H_{26}N_2O$; C 82.20, H 6.64, N 7.10, Found: C 82.28, H 6.87, N 7.01.

(*R**,*R**)-diastereomer: mp 121-125 C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.46-7.36 (m, 1H), 7.32-7.03 (m, 10H), 6.46-6.36 (m, 3H), 6.10-5.95 (m, 1H), 5.26-5.16 (m, 1H), 5.07-4.97 (m, 1H), 5.01 (d, 1H, J = 15.9 Hz), 4.12 (d, 1H, J = 15.9), 3.81 (s, 1H), 3.75-3.65 (m, 1H), 3.47-3.37 (m, 1H), 2.74-2.54 (m, 3H), 2.25-2.16 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 142.9, 136.3, 135.5, 135.3, 128.4, 128.2, 128.1, 127.9, 127.8, 126.9, 126.6, 122.8, 122.4, 117.0, 108.7, 79.8, 58.7, 56.5, 53.1, 43.5, 34.7; IR (KBr) 2788, 1723, 1611, 1489, 1464, 1452, 1430, 1383, 1360, 1337, 1172, 912, 747, 725, 698; HRMS (FAB) Calc. for $C_{27}H_{26}N_2O$: 394.2045, Found: 394.2048.

N-(alkyl- or aryl-)arylsulfonamides were prepared according to the procedure of Albrecht *et. al.*[6] from the appropriate dialkyl acetals. Data for previously unknown compounds are reported below:

***N*-(2-bromo-benzylidene)-*p*-toluenesulfonamide**

Reaction temperature: 138 °C, recrystallization: toluene, yield: 75 %, white solid.

mp 104-106 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.46 (s, 1H), 8.20-8.15 (m, 1H), 7.95-7.91 (m, 2H), 7.71-7.67 (m, 1H), 7.50-7.37 (m, 4H), 2.47 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.1, 144.8, 135.6, 134.5, 133.7, 131.1, 130.5, 129.8, 128.8, 127.9, 21.6; IR (KBr) ν 1597, 1582, 1557, 1430, 1320, 1290, 1273, 1215, 1157, 1086, 1048, 1075, 861, 807, 787, 760, 705, 689, 657, 614, 546, 498; MS (DEI) Calc. for $C_{14}H_{12}BrNO_2S$: 338.2, Found: 339.0; Anal. Calc. for $C_{14}H_{12}BrNO_2S$: C 68.20, H 5.72, N 4.68, Found: C 68.14, H 5.88, N 4.72.

***N*-(2-methyl-3-phenylallylidene)-*p*-toluenesulfonamide**

Reaction temperature: 140-200 °C, recrystallization: toluene, yield: 57 %, orange solid.

mp 104-106 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.72 (d, 1H,J = 0.5 Hz), 7.89-7.86 (m, 2H), 7.51-7.36 (m, 7H), 2.44 (s, 3H), 2.17 (d, 3H, J = 1.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.6, 151.3, 144.3, 135.6, 135.1, 134.9, 130.3, 129.9, 129.7, 128.7, 128.0, 21.6, 12.8; IR (KBr) ν 1615, 1595, 1557, 1439, 1409, 1323, 1315, 1305, 1281, 1209, 1154, 1087, 1021, 841, 813, 801, 793, 750, 701, 696, 680, 656, 589, 556, 532, 515, 513; MS (DEI) Calc. for $C_{17}H_{17}NO_2S$: 299.1, Found: 298.0; Anal. Calc. for $C_{17}H_{17}NO_2S$: C 68.20, H 5.72, N 4.68, Found: C 68.14, H 5.88, N 4.72.

_N_-(4-trifluoromethyl-benzylidene)-_p_-toluenesulfonamide

reaction temperature: 160 °C, recrystallization: toluene, yield: 74 %, colorless solid.

mp 152-153 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.08 (s, 1H), 8.05 (d, 2H, J = 8.0 Hz), 7.90 (ddd, 2H, J = 8.3 Hz, 8.3 Hz, 2.0 Hz), 7.75 (d, 2H, J = 8.3 Hz), 7.36 (ddd, 2H, J = 8.0 Hz, 8.0 Hz, 2.0 Hz), 2.45 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.4, 145.1, 136.0, 133.6, 135.6, 135.4, 134.5, 131.4, 130.0, 128.3, 21.7; IR (KBr) ν 1616, 1590, 1576, 1413, 1327, 1309, 1291, 1172, 1160, 1130, 1103, 1089, 1063, 1013, 873, 841, 789, 677, 644, 561, 551, 501; MS (DEI) Calc. for $C_{15}H_{12}F_3NO_2S$: 327.1, Found: 326.9; Anal. Calc. for $C_{15}H_{12}F_3NO_2S$: C 55.04, H 3.70, N 4.28, Found: C 55.09, H 3.93, N 4.33.

N-((tri-_iso_propylsilyl)-acetylenilidene)-_p_-toluenesulfonimide

Reaction temperature: 175 C, Kugel-Rohr distillation (160 C at 0.04 Torr), yield: 57 %, colorless oil which solidifies upon standing.

mp 39-44 C; ^{1}H NMR ($CDCl_3$, 300 MHz, minor isomer*) δ 8.26 (s, 1H), 8.25 (s*), 7.87-7.81 (m, 2H), 7.39-7.33 (m, 2H), 2.45 (s, 3H), 1.18-1.02 (m, 21H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 154.6, 145.4, 133.9, 130.0, 128.6, 113.8, 100.7, 21.6, 18.3, 10.8; IR (KBr) ν 2943, 2890, 2866, 2179, 1668, 1595, 1572, 1462, 1329, 1306, 1295, 1189, 1160, 1080, 1019, 997, 882, 818, 706, 685, 629, 552; MS (DEI) Calc. for $C_{19}H_{21}NO_2SSi$: 363.1, Found: 363.2; Anal. Calc. for $C_{19}H_{21}NO_2SSi$: C 62.76, H 8.04, N 3.85, Found: C 62.75, H 7.88, N 3.83.

2’-(phenyl)-1’-(toluene-4-sulfonyl)-1-benzyl-spiro-(indole-3,3’-pyrrolidine)-2-one (entry 6)

The following procedure is typical for the synthesis of 1’-(toluene-4-sulfonyl)-1-benzyl-spiro-(indole-3,3’-pyrrolidine)-2-ones

A solution of 1-benzyl-spiro-3-cyclopropyl-indole-2-one (0.100 g, 0.401 mmol), MgI_2 (11 mg, 0.040 mmol) and *N*-(benzylidine)-*p*-toluenesulfonimide (135 mg, 0.521 mmol) in 1 THF (1 mL) was heated to 60 °C for 8h. The reaction mixture was allowed to cool to room temperature before being quenched with 1 mL of water, a few crystals of $Na_2S_2O_4$ (to quench the I_2 formed in the reaction) and diluted with 1 mL of EtOAc. The phases were separated, the aqueous layer extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with water and brine (20 mL each), dried over Na_2SO_4. After removal of solvent, the crude product was purified by column chromatography using a gradient of 15 to 30 % EtOAc in hexane. The concentrated chromatographed product was dissolved in CH_2Cl_2 (10 mL), washed with 1M NaOH and water (10 mL each) to remove toluene-4-sulfonamide and afford 198 mg (97 %) of the product (both diastereomers) as a colorless solid.

HPLC retention time: (*R**,*S**)-diastereomer (major): 13.8 min, (*R**,*R**)-diastereomer (minor): 15.2 min (80:20 hexanes/EtOAc), diastereomeric ratio: 91:9; mp 160-167 C; ^{1}H NMR ($CDCl_3$, 500 MHz, minor isomer*) δ 7.78-7.72 (m, 2H), 7.38-7.33 (m, 2H), 7.27-7.20 (m, 3H), 7.15-6.96 (m, 8H), 6.88-6.80 (m, 2H), 6.49 (d, 1H, J = 7.8 Hz), 6.45 (d*, J = 7.7 Hz), 5.05 (s*), 4.94 (d, 1H, J = 15.7 Hz), 4.93 (d*, J = 15.7 Hz), 4.88 (s, 1H), 4.59 (d, 1H, J =

15.7 Hz), 4.43 (ddd*, J = 11.3 Hz, 11.3 Hz, 5.7 Hz), 4.20-4.03 (m, 2H), 3.97 (ddd, 1H, J = 10.8 Hz, 8.6 Hz, 4.8 Hz), 2.47 (s*), 2.46 (s, 3H), 2.20-2.03 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 176.5, 176.0*, 143.9, 143.8*, 142.8*, 142.0, 137.0, 136.5*, 135.3, 135.2*, 135.0*, 133.4, 129.7, 128.9*, 128.8*, 128.7, 128.6, 128.4, 128.3, 128.2, 127.9*, 127.8, 127.6, 127.5, 127.2*, 127.0, 126.7*, 125.3, 122.8*, 122.2, 109.2*, 108.9, 71.7*, 70.5, 60.4*, 59.8*, 59.1, 49.0*, 48.3, 43.7, 43.4*, 35.8*, 34.2, 21.6, 21.0*, 14.2*; IR (KBr) ν 3029, 2922, 2359, 2340, 1709, 1611, 1488, 1467, 1454, 1350, 1164, 1093, 1029, 971, 815, 776, 754, 727, 699, 660, 588, 575, 550; MS (DEI) Calc. for $C_{19}H_{21}NO_2SSi$: 508.2, Found: 508.1; Anal. Calc. for $C_{31}H_{28}N_2O_3S$: C 73.20, H 5.55, N 5.51, Found: C 73.05, H 5.75, N 5.46.

2’-(2-methyl-phenyl)-1’-(toluene-4-sulfonyl)-1-benzyl-spiro-(indole-3,3’-pyrrolidine)-2-one (entry 7)

HPLC retention time: (*R**,*S**)-diastereomer (major): 15.5 min, (*R**,*R**)-diastereomer (minor): 12.8 min (80:20 hexanes/EtOAc), diastereomeric ratio: 98:2; mp 204-205 °C; ^{1}H NMR (C_6D_6, 500 MHz) δ 7.98-7.96 (m, 2H), 7.69 (dd, 1H, J = 7.8 Hz, 0.9 Hz), 7.16-6.94 (m, 9H), 6.73 (d, 1H, J = 7.5 Hz), 6.67 (ddd, 1H, J = 1.2 Hz, 7.7 Hz, 7.7 Hz), 6.37 (ddd, 1H, J = 7.6 Hz, 7.6 Hz, 1.0 Hz), 6.23 (d, 1H, J = 7.5 Hz), 5.80-5.78 (m, 1H), 5.44 (s, 1H), 4.58 (d, 1H, J = 15.5 Hz), 4.23 (d, 1H, J = 15.5 Hz) , 4.11 (ddd, 1H, J = 10.3 Hz, 9.0 Hz, 6.7 Hz), 3.85 (ddd, 1H, J = 9.0 Hz, 6.0 Hz, 2.2 Hz), 1.99 (ddd, 1H, J = 13.0 Hz, 10.3 Hz, 8.0 Hz), 1.94 (s, 3H), 1.66 (ddd, 1H, J = 13.0 Hz, 6.7 Hz, 2.2 Hz), 1.53 (s, 3H); ^{13}C NMR (C_6D_6, 125 MHz, one apparent isomer) δ 178.1, 143.0, 138.7, 136.5, 136.2, 135.8, 130.2, 129.5, 129.5, 128.9, 128.7, 128.4, 128.1, 127.9, 127.6, 127.5, 127.5, 126.1, 125.4, 121.9, 108.3, 65.1, 57.1, 47.3, 43.2, 34.4, 21.3, 18.8; IR (KBr) ν 1706 (vs), 1608,

1487, 1465, 1341, 1305, 1164, 1094, 1031, 774, 751, 671, 658, 588, 552; MS (DEI) Calc. for $C_{32}H_{30}N_2O_3S$: 522.2, Found: 522.3; Anal. Calc. for $C_{32}H_{30}N_2O_3S$: C 73.54, H 5.79, N 5.36, Found: C 73.64, H 5.93, N 5.44.

2'-(4-methyl-phenyl)-1'-(toluene-4-sulfonyl)-1-benzyl-spiro-(indole-3,3'-pyrrolidine)-2-one (entry 8)

HPLC retention time: (*R**,*S**)-diastereomer (major): 15.0 min, (*R**,*R**) diastereomer (minor): 13.8 min (80:20 hexanes/EtOAc), diastereomeric ratio: 64:36; mp 178 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, minor diastereomer*) δ 7.74-7.71 (m, 2H), 7.76-7.73 (m, 2H*), 7.36-6.61 (m, 2H, 2H*), 7.25-6.84 (m, 11H, 12H*), 6.50 (d, 1H, J = 7.3 Hz), 6.44 (d, 1H*, J = 7.4 Hz), 6.48-6.46 (m, 1H), 5.00 (s, 1H*), 4.99 (d, 1H, J = 15.7 Hz), 4.97 (d, 1H, J = 15.8 Hz), 4.78 (s, 1H), 4.55 (d, 1H, J = 15.8 Hz), 4.42 (ddd, 1H*, J = 11.4 Hz, 11.4 Hz, 5.7 Hz), 4.16 (d, 1H*, J = 15.7 Hz), 4.15-4.04 (m, 1H, 1H*), 3.93 (ddd, 1H, J = 10.8 Hz, 8.8 Hz, 4.6 Hz), 2.48 (s, 3H*), 2.46 (s, 3H), 2.31 (s, 3H*), 2.24 (s, 3H), 2.19-2.11 (m, 1H, 1H*), 2.08-2.02 (m, 1H), 1.96 (ddd, 1H*, J = 12.6 Hz, 11.4 Hz, 8.22 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz, minor diastereomer*) δ 176.4, 176.1*, 143.9, 143.7*, 142.8*, 142.0, 137.4, 137.3*, 135.3, 135.1*, 135.0*, 133.6, 129.7, 128.9*, 128.7, 128.6, 128.5*, 128.4, 128.4, 128.3, 128.2, 127.8, 127.5, 127.5, 127.2*, 126.9, 126.9, 126.7, 125.4, 122.8*, 122.3, 122.2*, 109.3*, 109.0, 71.6*, 70.5, 59.7*, 59.1, 49.0*, 48.3, 43.6, 43.4*, 35.7*, 34.0, 21.6, 21.6*, 21.3*, 21.2; IR (KBr) ν 1711, 1612, 1597, 1489, 1467, 1459, 1380, 1351, 1164, 1092, 1029, 1019, 816, 751, 733, 709, 698, 660, 591, 584, 572, 550, 542; MS (DEI) Calc. for $C_{32}H_{30}N_2O_3S$: 522.2, Found: 522.0; Anal. Calc. for $C_{32}H_{30}N_2O_3S$: C 73.54, H 5.79, N 5.36, Found: C 73.43, H 5.95, N 5.48.

2′-(2-bromo-phenyl)-1′-(toluene-4-sulfonyl)-1-benzyl-spiro-(indole-3,3′-pyrrolidine)-2-one (entry 9)

HPLC retention time: (*R**,*S**)-diastereomer (major): 19.7 min, (*R**,*R**)-diastereomer (minor): 16.1 min (80:20 hexanes/EtOAc), diastereomeric ratio: 98:2; mp 204-205 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.84-7.81 (m, 3H), 7.43-7.19 (m, 9H), 7.12-7.07 (m, 1H), 7.03 (ddd, 1H, J = 7.7 Hz, 7.7 Hz, 1.1 Hz), 6.62-6.60 (m, 1H), 6.54 (ddd, 1H, J = 7.7 Hz, 7.7 Hz, 1.1 Hz), 5.74 (ddd, 1H, J = 7.7 Hz, 7.7 Hz, 1.1 Hz), 5.27 (s, 1H), 4.91 (d, 1H, J = 15.4 Hz), 4.54 (d, 1H, J = 15.4 Hz), 4.04-4.01 (m, 1H), 3.94 (ddd, 1H, J = 11.4 Hz, 8.9 Hz, 6.2 Hz), 2.47 (s, 3H), 2.38 (ddd, 1H, J = 13.1 Hz, 11.35 Hz, 7.9 Hz), 2.09 (ddd, 1H, J = 13.1 Hz, 6.2 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 178.0, 143.7, 143.2, 139.0, 135.8, 133.4, 132.2, 129.5, 129.2, 128.6, 128.4, 128.4, 127.8, 127.7, 127.2, 126.8, 124.4, 124.3, 121.8, 108.5, 66.8, 56.7, 47.2, 43.5, 34.4, 29.7, 21.7; IR (KBr) ν 1710, 1612, 1489, 1465, 1372, 1354, 1341, 1159, 1091, 1013, 814, 776, 751, 741, 700, 652, 587, 547; MS (DEI) Calc. for $C_{31}H_{27}BrN_2O_3S$: 588.1, Found: 588.0; Anal. Calc. for $C_{31}H_{27}BrN_2O_3S$: C 63.37, H 4.63, N 4.77, Found: C 63.23, H 4.88, N 4.84.

2′-(4-bromo-phenyl)-1′-(toluene-4-sulfonyl)-1-benzyl-spiro-(indole-3,3′-pyrrolidine)-2-one (entry 10)

HPLC retention time: (*R**,*S**)-diastereomer (major): 19.7 min, (*R**,*R**)-diastereomer (minor): 16.8 min (80:20 hexanes/EtOAc), diastereomeric ratio: 82:12; mp 153-154 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, minor diastereomer*) δ 7.75-7.69 (m, 2H, 2H*), 7.38-7.35 (m, 2H, 2H*), 7.27-6.89 (m, 12H, 12H*), 6.53-6.48 (m, 1H, 1H*), 5.02 (s, 1H*), 4.96 (d, 1H*, J = 15.9 Hz), 4.96 (d, 1H, J = 15.7 Hz),

4.75 (s, 1H), 4.57 (d, 1H, J = 15.7 Hz), 4.42 (ddd, 1H*, J = 11.5 Hz, 11.5 Hz, 5.6 Hz), 4.15 (d, 1H*, J = 15.9 Hz), 4.15-4.04 (m, 1H, 1H*), 3.93 (ddd, 1H, J = 11.0 Hz, 9.0 Hz, 3.9 Hz), 2.49 (s, 3H*), 2.47 (s, 3H), 2.20-2.12 (m, 1H, 1H*), 2.04-1.99 (m, 1H, 1H*); ^{13}C NMR ($CDCl_3$, 125 MHz, minor diastereomer*) δ 178.8*, 175.9, 144.2, 144.1*, 142.8*, 142.9, 135.7*, 135.6, 135.1, 134.9*, 134.8*, 132.8, 131.1, 130.7, 129.8, 129.2, 129.1*, 128.8*, 128.7, 128.2, 127.8*, 127.7, 127.5*, 126.9, 126.7, 125.2, 123.0*, 122.5, 122.2*, 121.9*, 121.8, 109.4*, 109.2, 71.0*, 70.2, 59.7*, 59.2, 49.0*, 48.5, 43.7, 43.5*, 35.8*, 34.0, 21.7; IR (KBr) ν 1710, 1612, 1488, 1466, 1385, 1368, 1351, 1338, 1176, 1160, 1097, 1033, 1010, 808, 753, 740, 706, 657, 589, 548; MS (DEI) Calc. for $C_{31}H_{27}BrN_2O_3S$: 588.1, Found: 588.0; Anal. Calc. for $C_{31}H_{27}BrN_2O_3S$: C 63.37, H 4.63, N 4.77, Found: C 63.42, H 4.83, N 4.66.

2’-(4-trifluoromethyl-phenyl)-1’-(toluene-4-sulfonyl)-1-benzyl-spiro-(indole-3,3’-pyrrolidine)-2-one (entry 11)

HPLC retention time: (*R**,*S**)-diastereomer (major): 27.6 min, (*R**,*R**)-diastereomer (minor): 21.1 min (80:20 hexanes/EtOAc), diastereomeric ratio: 84:16; mp 197 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, minor diastereomer*) δ 7.74-7.71 (m, 2H, 2H*), 7.39-6.95 (m, 13H, 13H*), 6.88 (ddd, 1H, J = 7.6 Hz, 7.6, 1.0 Hz), 6.54-6.50 (m, 2H*), 6.53 (d, 1H, J = 12.9 Hz), 5.09 (s, 1H*), 4.95 (d, 1H, J = 15.6 Hz), 4.93 (d, 1H*, J = 15.8 Hz), 4.90 (s, 1H), 4.59 (d, 1H, J = 15.6 Hz), 4.43 (ddd, 1H*, J = 11.5 Hz, 11.5 Hz, 5.7 Hz), 4.18 (d, 1H*, J = 15.8 Hz), 4.15-4.06 (m, 1H, 1H*), 3.97 (ddd, 1H, J = 11.0 Hz, 8.9 Hz, 3.9 Hz), 2.47 (s, 3H), 2.47 (s, 3H*), 2.22-2.13 (m, 1H, 1H*), 2.06-2.00 (m, 1H, 1H*); ^{13}C NMR ($CDCl_3$, 125 MHz, minor diastereomer*) δ 175.9, 175.7*, 144.3, 144.2*, 141.9, 142.7*, 140.9, 135.1, 134.8*, 132.8, 130.0*, 129.9, 129.8,

129.6*, 129.2*, 128.8, 128.7, 128.6*, 128.2, 127.9, 127.8, 127.6*, 127.5*, 127.0, 126.6, 125.3*, 125.1, 124.8*, 124.5, 124.5, 124.5*, 122.5, 122.3*, 109.5*, 109.2, 70.9*, 70.2, 59.7*, 59.3, 49.0*, 48.6, 43.8, 43.5*, 36.1*, 34.3, 21.6, 21.6*; IR (KBr) ν 1711, 1615, 1488, 1466, 1375, 1370, 1353, 1340, 1328, 1160, 1112, 1068, 1029, 1016, 836, 810, 751, 744, 700, 657, 589, 548; MS (DEI) Calc. for $C_{32}H_{27}F_3N_2O_3S$: 576.2, Found: 576.0; Anal. Calc. for $C_{32}H_{27}F_3N_2O_3S$: C 66.65, H 4.72, N 4.86, Found: C 66.47, H 4.81, N 4.66.

2′-(4-methoxy-phenyl)-1′-(toluene-4-sulfonyl)-1-benzyl-spiro-(indole-3,3′-pyrrolidine)-2-one (entry 12)

HPLC retention time: (*R**,*S**)-diastereomer (major): 20.5 min, (*R**,*R**)-diastereomer (minor): 17.8 min (80:20 hexanes/EtOAc), diastereomeric ratio: 67:33; mp 153-155 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, minor diastereomer*) δ 7.75-7.72 (m, 2H*), 7.72-7.69 (m, 2H), 7.36-7.34 (m, 2H, 2H*), 7.22-6.87 (m, 11H, 11H*), 6.66-6.64 (m, 1H*), 6.62-6.60 (m, 1H), 6.45 (d, 1H, J = 8.5 Hz), 6.48 (d, 1H*, J = 7.1 Hz), 5.00 (d, 1H*, J = 16.4 Hz), 4.97 (d, 1H, J = 15.8 Hz), 4.98 (s, 1H*), 4.73 (s, 1H), 4.53 (d, 1H, J = 15.8 Hz), 4.44 (ddd, 1H*, J = 11.4 Hz, 11.4 Hz, 5.7 Hz), 4.16 (d, 1H*, J = 16.4 Hz), 4.12-4.04 (m, 1H, 1H*), 3.92 (ddd, 1H, J = 10.7 Hz, 9.0 Hz, 4.5 Hz), 3.75 (s, 3H*), 3.72 (s, 3H), 2.48 (s, 3H*), 2.46 (s, 3H), 2.21-2.13 (m, 1H, 1H*), 2.09-2.02 (m, 1H), 2.01-1.93 (m, 1H*); ^{13}C NMR ($CDCl_3$, 125 MHz, minor diastereomer*) δ 176.3, 176.2*, 159.3*, 159.2, 143.9, 143.7*, 142.8*, 142.0, 135.2, 135.2*, 135.0*, 133.2, 129.7, 129.7*, 128.9, 128.9*, 128.7, 128.6*, 128.5, 128.5*, 128.5*, 128.4, 128.2, 128.2*, 127.8, 127.8*, 127.5, 127.3*, 126.9, 126.7*, 125.3, 122.8*, 122.3, 122.3*, 113.3*, 113.0, 109.2*, 109.0, 71.4*, 70.3, 59.8*, 59.2, 55.1, 55.0*, 49.0*, 48.0, 43.6, 43.3*, 35.5*, 33.7, 21.6, 21.6*;

IR (KBr) ν 1708, 1514, 1493, 1360, 1350, 1249, 1176, 1160, 1092, 1023, 824, 757, 699, 668, 659, 575, 543; MS (DEI) Calc. for $C_{32}H_{30}N_2O_4S$: 539.2, Found: 538.1; Anal. Calc. for $C_{32}H_{30}N_2O_4S$: C 71.35, H 5.61, N 5.20, Found: C 71.24, H 5.74, N 5.18.

2′-(α-furyl)-1′-(toluene-4-sulfonyl)-1-benzyl-spiro-(indole-3,3′-pyrrolidine)-2-one (entry 13)

HPLC retention time: (*R**,*S**)-diastereomer (major): 15.2 min, (*R**,*R**)-diastereomer (minor): 12.8 min (80:20 hexanes/EtOAc), diastereomeric ratio: 89:11; mp 161-162 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.75-7.72 (m, 2H), 7.33-7.07 (m, 9H), 6.84 (ddd, 1H, J = 7.6 Hz, 7.6 Hz, 1.0 Hz), 6.70-6.68 (m, 1H), 6.61 (d, 1H, J = 7.5 Hz), 6.21-6.19 (m, 1H), 6.16-6.15 (m, 1H), 4.98 (s, 1H), 4.94 (d, 1H, J = 15.7 Hz), 4.69 (d, 1H, J = 15.7 Hz), 3.95-3.92 (m, 2H), 2.44 (s, 3H), 2.35-2.28 (m, 1H) 2.18-2.11 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz, one apparent isomer) δ 176.6, 151.2, 143.6, 142.3, 141.8, 135.5, 134.3, 129.6, 128.8, 128.6, 127.9, 127.6, 127.1, 124.4, 122.5, 110.4, 109.2, 108.9, 63.2, 57.5, 47.3, 43.6, 34.5, 21.6; IR (KBr) ν 1706, 1614, 1600, 1489, 1466, 1459, 1450, 1369, 1353, 1340, 1311, 1221, 1176, 1161, 1098, 1081, 1037, 1009, 831, 815, 756, 744, 699, 661, 601, 588, 547, 532, 473; MS (DEI) Calc. for $C_{29}H_{26}N_2O_4S$: 498.2, Found: 498.1; Anal. Calc. for $C_{29}H_{26}N_2O_4S$: C 69.86, H 5.26, N 5.62, Found: C 69.88, H 5.37, N 5.68.

2′-(4-methyl-phenyl)-1′-(napthalene-4-sulfonyl)-1-benzyl-spiro-(indole-3,3′-pyrrolidine)-2-one

HPLC retention time: (*R**,*S**)-diastereomer (major): 25.4 min, (*R**,*R**)-diastereomer (minor): 23.9 min (85:15 hexanes/EtOAc), diastereomeric ratio: 89:11; mp 181°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ

8.33 (d, 2H, J = 1.5 Hz), 8.16 (d, 2H, J = 8.7 Hz), 7.95-7.93 (m, 2H), 7.85 (dd, 1H, J = 8.4 Hz, 1.9 Hz), 7.69-7.58 (m, 2H), 7.22-6.82 (m, 12H), 6.47 (d, 1H, J = 7.5 Hz), 4.95 (d, 1H, J = 16.4 Hz), 4.90 (s, 1H), 4.52 (d, 1H, J = 16.4 Hz), 4.14-4.05 (m, 2H), 2.22 (s, 3H), 2.21-2.08 (m, 2H);); ^{13}C NMR ($CDCl_3$, 125 MHz, major isomer reported) δ 176.4, 142.1, 137.5, 136.8, 135.3, 135.1, 133.7, 133.5, 129.6, 129.3, 129.2, 128.8, 128.6, 128.4, 128.0, 127.7, 127.5, 127.4, 126.9, 125.4, 123.4, 122.2, 109.0, 70.5, 59.0, 48.2, 43.6, 33.9, 21.2; IR (KBr) ν 1711, 1612, 1488, 1469, 1455, 1348, 1241, 1164, 1132, 1075, 1020, 969, 864, 817, 794, 750, 698, 657, 618, 580, 568, 547, 477; MS (DEI) Calc. for $C_{35}H_{30}N_2O_3S$: 558.2, Found: 558.2; Anal. Calc. for $C_{35}H_{30}N_2O_3S$: C 75.24, H 5.41, N 5.01, Found: C 74.99, H 5.58, N 5.02.

2’-cinnamoyl-1’-(toluene-4-sulfonyl)-1-benzyl-spiro-(indole-3,3’-pyrrolidine)-2-one (entry 14)

HPLC retention time: (*R**,*S**)-diastereomer (major): 17.6 min, (*R**,*R**) diastereomer (minor): 15.1 min (80:20 hexanes/EtOAc), diastereomeric ratio: 74:16; mp 182 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, minor diastereomer*) δ 7.77-7.74 (m, 2H), 7.75-7.72 (m, 2H*), 7.60-7.58 (m, 1H), 7.36-7.33 (m, 2H), 7.26-6.94 (m, 10H, 13H*), 6.86-6.82 (m, 2H*), 6.82-6.78 (m, 2H), 6.56-6.53 (m, 1H*), 6.55 (dd, 1H, J = 7.7 Hz, 1.0 Hz), 6.41 (d, 1H, J = 16.0 Hz), 6.17 (d, 1H*, J = 16.0 Hz), 6.03 (dd, 1H*, J = 16.0, 8.7 Hz), 5.82 (dd, 1H, J = 16.0 Hz, 8.9 Hz), 5.16 (d, 1H, J = 16.0 Hz), 5.12 (d, 1H*, J = 17.0 Hz), 4.54 (d, 1H*, J = 8.7 Hz), 4.47 (d, 1H*, J = 17.0 Hz), 4.41 (d, 1H, J = 16.0 Hz), 4.17 (ddd, 1H*, J = 16.7 Hz, 9.9 Hz, 6.5 Hz), 4.09-3.99 (m, 1H, 1H*), 4.03 (dd, 1H, J = 8.9 Hz, 0.7 Hz), 3.67 (ddd, 1H, J = 13.8 Hz, 10.5 Hz, 3.3 Hz), 2.46 (s, 3H), 2.39 (s, 3H*), 2.35-2.29 (m, 1H, 1H*), 2.18 (ddd, 1H*, J = 12.8 Hz, 9.9 Hz, 8.3 Hz), 2.02 (ddd, 1H, J = 11.3 Hz, 8.0 Hz,

3.3 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz, minor diastereomer*) δ 176.3*, 175.5, 144.1, 143.4*, 142.6*, 141.9, 136.0, 135.9*, 135.1*, 134.7, 133.0, 133.3*, 132.6, 129.8, 129.6, 129.5*, 129.4*,128.8*, 128.7, 128.6, 128.6*, 128.5, 128.4*, 128.1, 127.9, 127.9*, 127.7*, 127.4*, 127.3, 126.9, 126.8*, 126.8*, 126.5, 125.4, 125.1*, 124.5, 123.1, 123.0*, 109.6, 109.3*, 72.5*, 69.9, 58.8, 58.6*, 48.0, 43.9, 43.5*, 35.2*, 33.0, 21.6, 21.5*; IR (KBr) ν 1709, 1613, 1494, 1481, 1467, 1452, 1375, 1352, 1362, 1341, 1327, 1173, 1163, 1153, 1106, 1098, 1085, 979, 971, 749, 738, 697, 664, 610, 584, 547; MS (DEI) Calc. for $C_{33}H_{30}N_2O_3S$: 534.2, Found: 534.1; Anal. Calc. for $C_{33}H_{30}N_2O_3S$: C 74.13, H 5.66, N 5.24, Found: C 74.09, H 5.83, N 5.17.

2’-(1-methylcinnamoyl)-1’-(toluene-4-sulfonyl)-1-benzyl-spiro-(indole-3,3’-pyrrolidine)-2-one (entry 15)

HPLC retention time: (*R**,*S**)-diastereomer (major): 15.3 min, (*R**,*R**)-diastereomer (minor): 11.6 min (80:20 hexanes/EtOAc), diastereomeric ratio: 52:48; mp 143 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, minor diastereomer*) δ 7.86 (d, 2H, J = 8.2 Hz), 7.83-7.80 (m, 2H*), 7.41-6.93 (m, 14H, 15H*), 6.79 (d, 1H, J = 7.5 Hz), 6.71 (d, 1H*, J = 7.7 Hz), 6.67 (d, 1H, J = 7.7 Hz), 5.06 (d, 1H, J = 15.6 Hz), 5.03 (d, 1H*, J = 15.2 Hz), 4.62 (d, 1H*, J = 15.2 Hz), 4.52 (d, 1H, J = 15.6 Hz), 4.50 (s, 1H), 4.46 (s, 1H), 4.19-4.11 (m, 1H), 4.01-3.87 (m, 1H, 2H*), 2.47 (s, 3H), 2.45 (s, 3H*), 2.41-2.35 (m, 1H), 2.10-1.81 (m, 1H, 2H*), 1.78 (s, 3H), 1.44 (s, 3H*);); ^{13}C NMR ($CDCl_3$, 125 MHz, minor diastereomer*) δ 176.9*, 175.6, 144.0*, 143.7, 142.3*, 142.2, 137.1, 137.1*, 135.5*, 135.4, 135.0, 135.0*, 129.8, 129.7*, 129.4, 129.2 , 128.8, 128.7, 128.6*, 128.2, 128.2*, 128.0, 127.9*, 127.8, 127.8*, 127.7, 127.6*, 127.5, 127.3*, 127.1, 127.0*, 126.5*, 126.4, 125.4, 125.3*, 123.4*, 122.9, 122.4, 122.3*, 109.3, 109.0*, 77.2, 75.0*,

63.9*, 58.5, 48.7*, 48.6, 44.0, 43.8*, 35.5*, 35.4, 21.7, 21.6*, 16.6*, 15.8; IR (KBr) ν 1711, 1611, 1597, 1489, 1466, 1455, 1349, 1164, 1093, 1029, 1015, 750, 731, 698, 667.9, 667.5, 588, 581, 550; MS (DEI) Calc. for $C_{34}H_{32}N_2O_3S$: 548.2, Found: 548.1; Anal. Calc. for $C_{34}H_{32}N_2O_3S$: C 74.43, H 5.88, N 5.11, Found: C 74.43, H 6.04, N 4.99.

2’-(tri-*iso*propylsilyl)-acetylenyl)-1’-(toluene-4-sulfonyl)-1-benzyl-spiro-(indole-3,3’-pyrrolidine)-2-one (entry 16)

HPLC retention time: (*R**,*S**)-diastereomer (major): 7.8 min, (*R**,*R**)-diastereomer (minor): 15.6 min (85:15 hexanes/EtOAc), diastereomeric ratio: 98:2; mp 133-137 C; ^{1}H NMR ($CDCl_3$, 300 MHz, minor isomer*) δ 7.90-7.84 (m, 2H), 7.49-7.44 (m, 1H), 7.39-7.21 (m, 7H), 7.17 (ddd, 1H, J = 1.2 Hz, 7.8 Hz, 7.8 Hz), 7.03 (ddd, 1H, J = 0.9 Hz, 7.5 Hz, 7.5 Hz), 6.72 (d, 1H, J = 7.5 Hz), 4.93 (d, 1H, J = 15.6 Hz), 4.78 (d, 1H, J = 15.9 Hz), 4.50 (s*), 4.49 (s, 1H), 3.90-3.70 (m, 2H), 2.46 (s, 3H), 2.20 (ddd, 1H, J = 9.0 Hz, 9.0 Hz, 12.5 Hz), 2.02 (ddd, 1H, J = 4.0 Hz, 7.2 Hz, 12.6 Hz) 0.90-0.80 (m, 21H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 175.7, 144.0, 142.3, 135.6, 134.1, 129.9, 128.9, 128.7, 128.0, 127.8, 127.3, 125.0, 123.1, 109.2, 100.6, 89.5, 58.3, 57.8, 47.6, 44.0, 34.3, 21.5, 18.2, 10.8; IR (KBr) ν 2947.1, 2863.5, 2360.2, 2343.0, 1717.0, 1611.9, 1487.5, 1466.7, 1366.8, 1352.2, 1167.1, 1092.9, 816.0, 747.7, 698.1, 681.3, 661.7, 573.3, 548.3; MS calc’d for $C_{36}H_{44}N_2O_3SSi$: 612.1, Found: 612.3; Anal. Calc. for $C_{36}H_{44}N_2O_3SSi$: C 70.55, H 7.24, N 4.57, Found: C 70.53, H 7.35, N 4.76.

2-phenyl-1-phenylsulfonyl-pyrrolidine-3-(*N,N*-diphenyl)-amide (13)

To MgI_2 (88 mg,0.32 mmol) and *N,N*-diphenyl-cyclopropanecarboxamide (101 mg, 0.410 mmol) 1 mL of a degassed solution of *N,N*-dimethylacetamide (59 μL, 0.64 mmol) in *m*-xylene (2 mL) was added. The reaction mixture was heated to 145 °C for 48h, then allowed to cool to room temperature before being quenched with 1 mL of water, a few crystals of $Na_2S_2O_3$ (to quench the I_2 formed in the reaction) and diluted with 1 mL of EtOAc. The phases were separated and the aqueous layer extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine and water (20 mL each), dried over $NaSO_4$, filtered, concentrated, and purified by chromatography (SiO_2, 75:25 hexanes/EtOAc) to afford the two diastereomers. The concentrated chromatographed products were each dissolved in CH_2Cl_2 (10 mL), washed with 1M NaOH and water (10 mL each) to remove benzene-sulfonamide and afford the pyrrolidine, one as a colorless oil and the other as a colorless solid. diastereomer 1: 51 mg (33 %), diastereomer 2: 33 mg (21 %).

Diastereomer 1: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.83-7.79 (m, 2H), 7.61-7.48 (m, 4H), 7.32-7.16 (m, 12H), 7.08-6.98 (m, 1H), 6.72-6.62 (m, 1H), 4.92 (d, 1H, J = 8.1 Hz), 3.78 (ddd, 1H, J = 11.0 Hz, 6.2 Hz, 5.0 Hz), 4.43 (ddd, 1H, J = 11.0 Hz, 11.0 Hz, 8.1 Hz), 3.07 (q, 1H, J = 8.1 Hz), 1.90-1.82 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.4, 141.3, 137.7, 133.0, 129.3, 128.8, 127.9, 126.7, 111.2, 68.4, 53.3, 49.8, 29.3; IR (KBr) ν 1738, 1669, 1594, 1490, 1447, 1377, 1347, 1263, 1163, 1098, 761, 722, 692, 599; MS (FAB) Calc. for $C_{29}H_{26}N_2O_3S + H^+$: 483.1743, Found: 483.1746.

Diastereomer 2: mp: 189 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.53-7.45 (m, 4H), 7.37-7.06 (m, 14H), 6.57-6.53 (m, 2H), 4.67 (d, 1H, J = 8.3 Hz), 3.86-3.77 (m, 1H), 3.56-3.33 (m, 2H), 2.70 (ddd, 1H, J = 13.3, 9.5, 8.3 Hz), 2.06-1.96 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ

169.6, 143.0, 139.0, 132.2, 130.0, 128.8, 128.8, 128.6, 128.2, 128.2, 127.1, 126.1, 110.5, 64.4, 47.8, 47.7, 27.4; IR (KBr) ν 1674, 1493, 1444, 1347, 1308, 1177, 1163, 1099, 1075, 1052, 1018, 757, 717, 710, 697, 689, 668, 602, 572; MS (FAB) Calc. for $C_{29}H_{26}N_2O_3S + H^+$: 483.1743, Found: 483.1737.

References and Notes

[1] W. C. Still, M. Kahn, A.Mitra, *J. Org. Chem.* **1978**, *43*, 2923.

[2] C. Crestini, R. Saladino *Syn. Comm.* **1994**, *24 (20)*, 2835.

[3] G. P. Claxton, L. Allen, J. M. Grisar *Org. Synth., Coll. Vol. VI* **1988**, 968.

[4] Prepared by refluxing an equimolar amount of the aldehyde and amine in benzene with removal of water followed by removal of solvent and distillation.

[5] R. Tiollias *Bull. Soc. Chim. Fr.* **1947**, 708.

[6] R. Albrecht, G. Kresze, B. Mlakar *Chem. Ber.* **1964**, *24*, 483.