Supporting Information

A Highly Efficient Method for the Construction of Cyclopropane-Containing Dihydroindole Derivatives from Indolemethylenecyclopropanes with DIAD and DEAD

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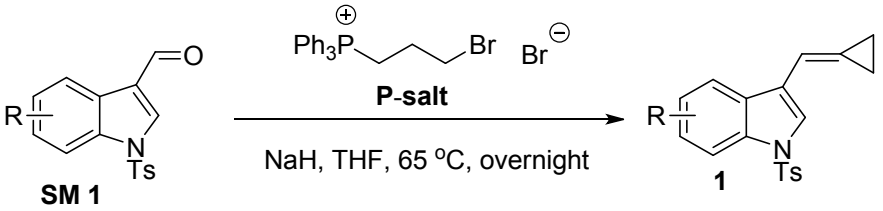
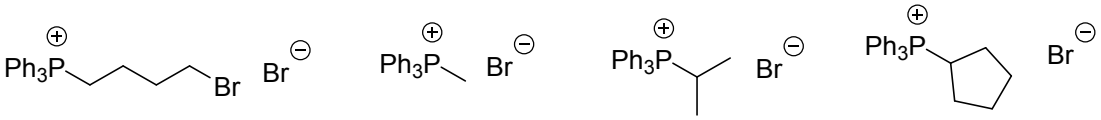
General Remarks

^{1}H NMR spectra were recorded on a Varian Mercury-300 and 400 spectrometer for solution in $CDCl_3$ with tetramethylsilane (TMS) as an internal standard; coupling constants *J* are given in Hz. ^{13}C NMR spectra were recorded on a Varian Mercury-300 and 400 spectrophotometers (75 or 100 MHz) with complete proton decoupling spectrophotometers ($CDCl_3$: 77.0 ppm). Mass and HRMS spectra were recorded by EI method. Organic solvents used were dried by standard methods when necessary. Infrared spectra were recorded on a Perkin-Elmer PE-983 spectrometer with absorption in cm^{-1}. Melting points were determined on a digital melting point apparatus and temperatures were uncorrected. Commercially obtained reagents were used without further purification. All these reactions were monitored by TLC with silica gel coated plates or ^{19}F NMR. Flash column chromatography was carried out using silica gel at increased pressure. All the MCPs involved are known compounds prepared according to a general procedure in literature.[1]

General Procedure for the Preparation of 1



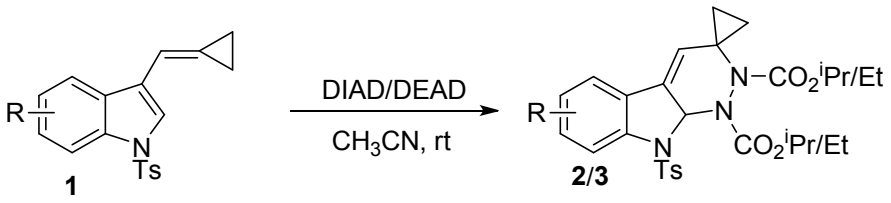
Another procedure for the preparation of **1**: **P-salt** ((3-bromopropyl)triphenylphosphonium bromide) (2.78 g, 6 mmol) and NaH (480 mg, 12 mmol) were placed in a 100 mL flask equipped with a reflux condenser. The reaction set was evacuated and backfilled with Ar for three times. Then 30 mL THF was injected and the reaction mixture was stirred and refluxed at about 65-70 °C overnight. Afterwards compound **SM 1** (10 mmol) dissolved in THF (5 mL) was injected slowly into the reaction system and it continued to reflux for another 6 h. When it completed, the mixture was cooled to room temperature and the reaction was quenched with H_2O. The mixture was filtered through a celite. The filtrate was concentrated on a rotary evaporator and the residue was purified by a silica gel chromatography (PE:EA = 4:1) to afford the corresponding product **1** in moderate yields.



For the synthesis of substrate **1m**, the procedure is the same as that mentioned above and the only difference is that the **P-salt** should be replaced with **p-salt-m**.

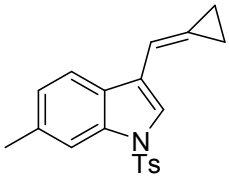
The procedure for the synthesis of **1n - 1p** is different: The corresponding salt (**P-salt-n**/**o**/**p**) (6.0 mmol) was placed in a 50 mL flask and 20 mL THF was added. Then ^{t}BuLi (2.5 M, 2.4 mL) was injected at -78 °C and the mixture was stirred for 2 h. Afterwards the $PhSO_2$-protected indole-3-adehyde (5.0 mmol) dissolved in 10 mL THF was injected and the mixture was allowed to warm up to room temperature. The resulting mixture was continuously stirred for about 5 h and then water was added to quench the reaction. The mixture was filtered under reduced pressure and the filtrate was concentrated on a rotary evaporator. The residue was purified by ae silica gel chromatography (PE:EA = 10:1) to afford the products **1n-1p** in excellent yields.

General Procedure for the reaction of 1 with DIAD/DEAD



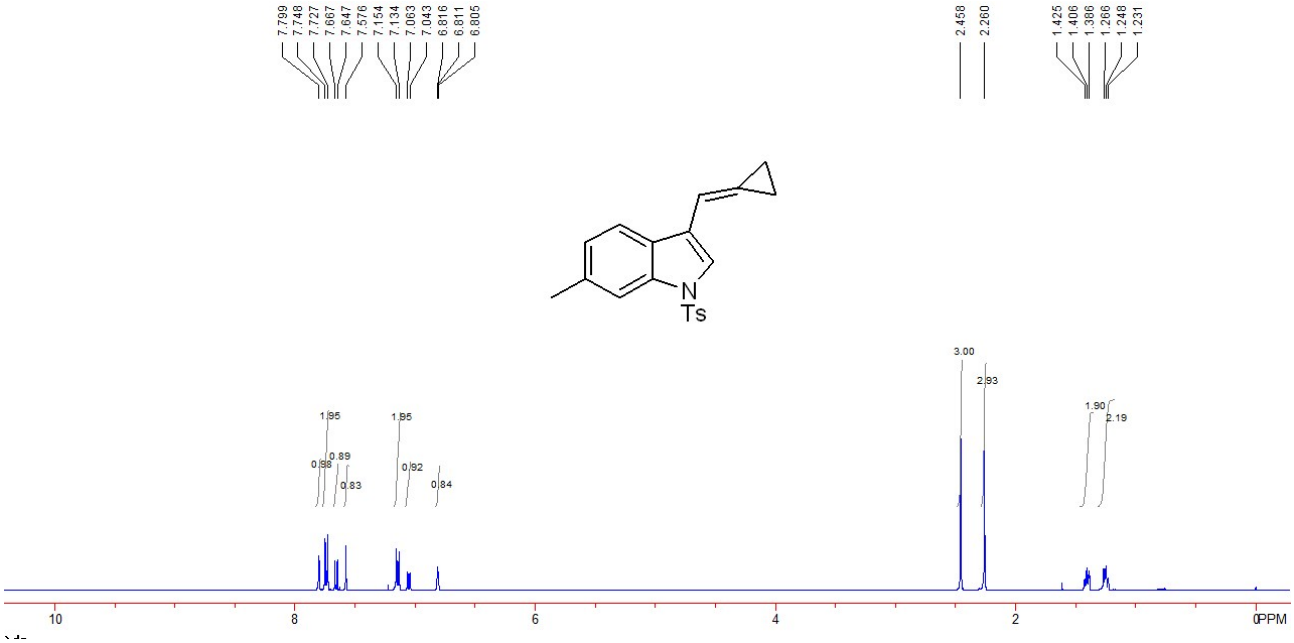
Compound **1** (0.2 mmol) and DIAD (0.4 mL (1.0 M), 0. 4 mmol)/DEAD (0.066 mL, 0.4 mmol) were placed in a 50 mL flask and 3 mL CH_3CN was added. The mixture was stirred at room temperature for about 8 h (If the transformation could not be completed within this period, the reaction mixture could also be heated to 60 ^oC). When the reaction finished, the solution was concentrated on a rotary evaporator and the residue was purified by a silica gel flash chromatography (PE: EA=4:1) to give pure product **2**/**3**.

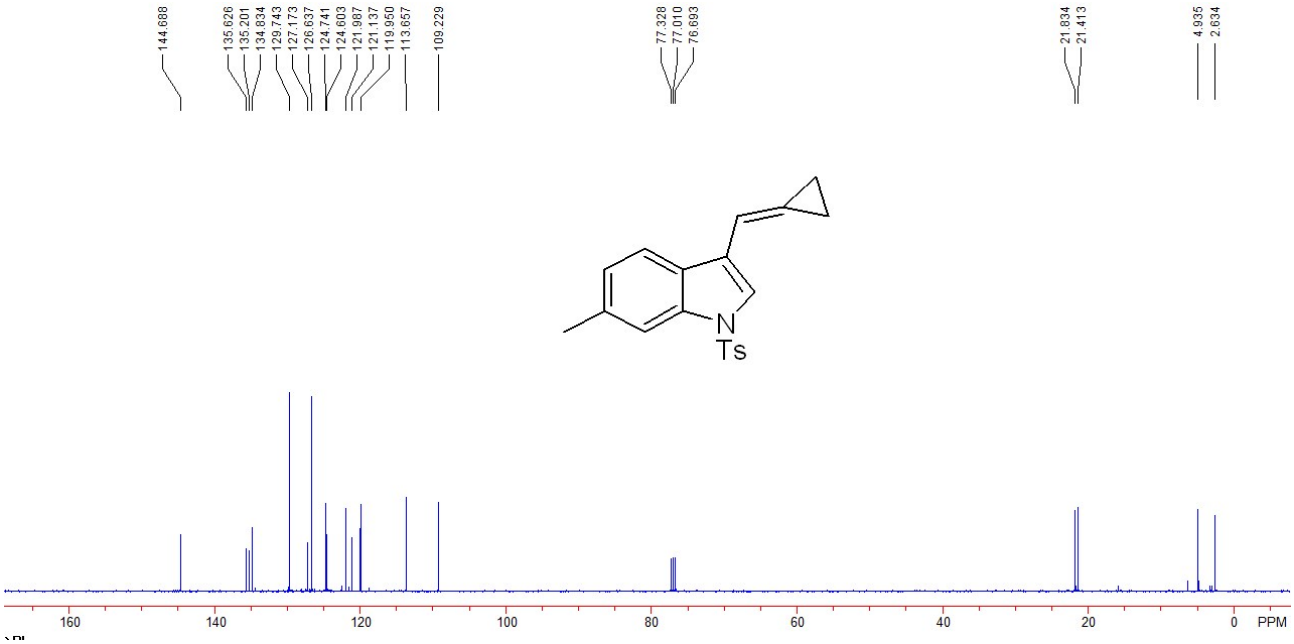
Spectroscopic Data of Compounds 1, 2 and 3.

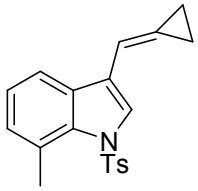


3-(cyclopropylidenemethyl)-6-methyl-1-tosyl-1H-indole (1b).

A white solid, 134.8 mg, 20% yield. M.p.: 156-158 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.25 (t, *J* = 7.6 Hz, 2H, CH_2), 1.40 (t, *J* = 7.6 Hz, 2H, CH_2), 2.26 (s, 3H, CH_3), 2.46 (s, 3H, CH_3), 6.81 (t, *J* =2.0 Hz, 1H, ArH), 7.05 (d, *J* = 8.0 Hz, 1H, ArH), 7.14 (d, *J* = 8.0 Hz, 1H, ArH), 7.58 (s, 1H, ArH), 7.66 (d, *J* = 8.0 Hz, 1H, ArH), 7.74 (d, *J* = 8.4 Hz, 2H, ArH), 7.80 (s, 1H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 2.6, 4.9, 21.4, 21.8, 109.2, 113.6, 120.0, 121.1, 122.0, 124.6, 124.7, 126.6, 127.2, 129.7, 134.8, 135.2, 135.6, 144.7. IR (CH_2Cl_2) ν 2956, 2922, 2848, 1736, 1597, 1370, 1170, 1122, 1093, 803, 703, 671 cm^{-1}. HRMS (DART) calcd. for $C_{20}H_{20}NO_2S$ ($+H^+$): 338.1209, Found: 338.1207.

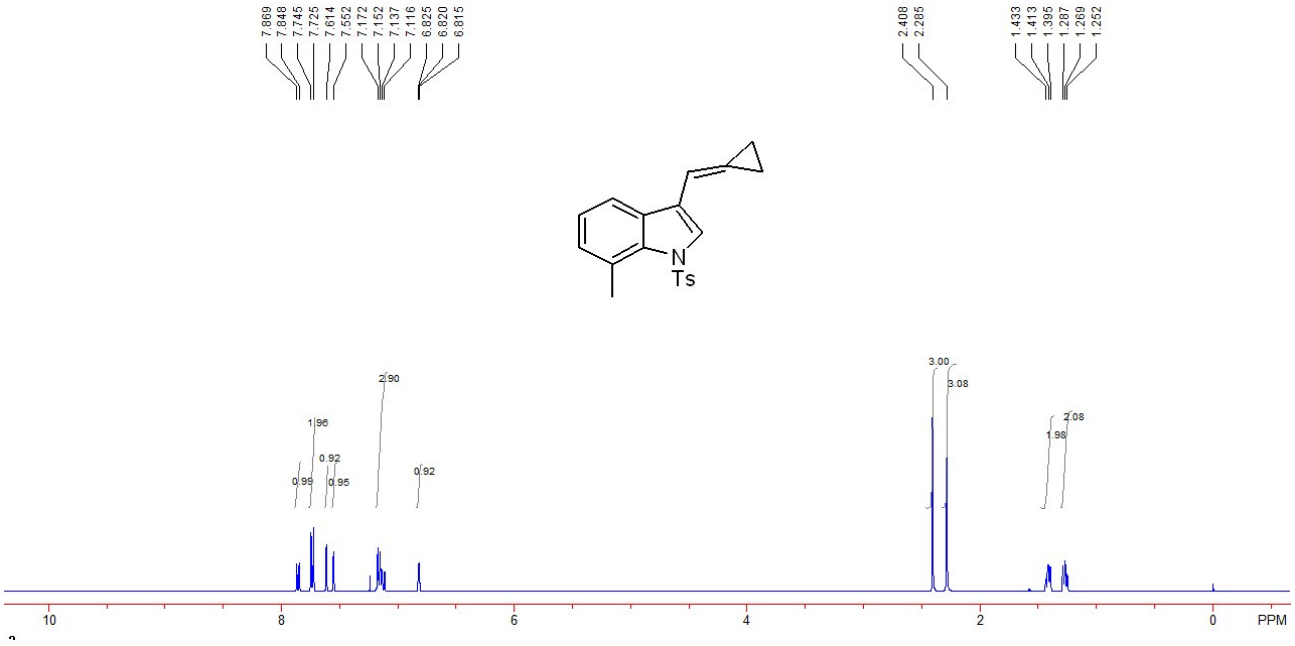


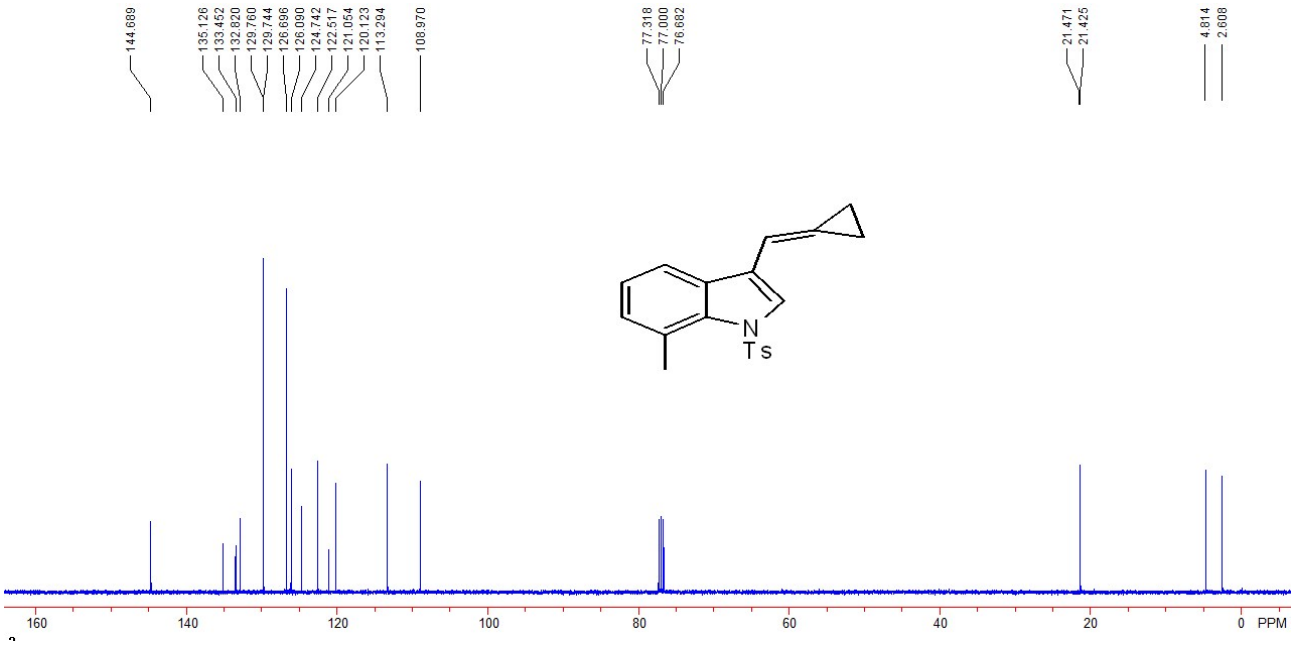


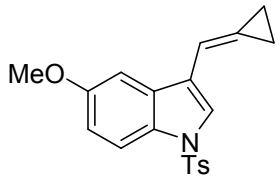


3-(cyclopropylidenemethyl)-7-methyl-1-tosyl-1H-indole (1c).

A white solid, 121.3 mg, 18% yield. M.p.: 149-151 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.27 (t, J = 7.2 Hz, 2H, CH_2), 1.41 (t, J = 7.2 Hz, 2H, CH_2), 2.28 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 6.82 (t, J =2.0 Hz, 1H, ArH), 7.12-7.17 (m, 3H, ArH), 7.55 (s, 1H, ArH), 7.61 (s, 1H, ArH), 7.74 (d, J = 8.0 Hz, 2H, ArH), 7.86 (d, J = 8.4 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 2.6, 4.8, 21.4, 21.5, 109.0, 113.3, 120.1, 121.0, 122.5, 124.7, 126.1, 126.7, 129.7, 129.8, 132.8, 133.4, 135.1, 144.7. IR (CH_2Cl_2) ν 2958, 2919, 2848, 1736, 1597, 1367, 1171, 1123, 1089, 809, 671 cm^{-1}. HRMS (DART) calcd. for $C_{20}H_{20}NO_2S$ (+H^+): 338.1209, Found: 338.1211.



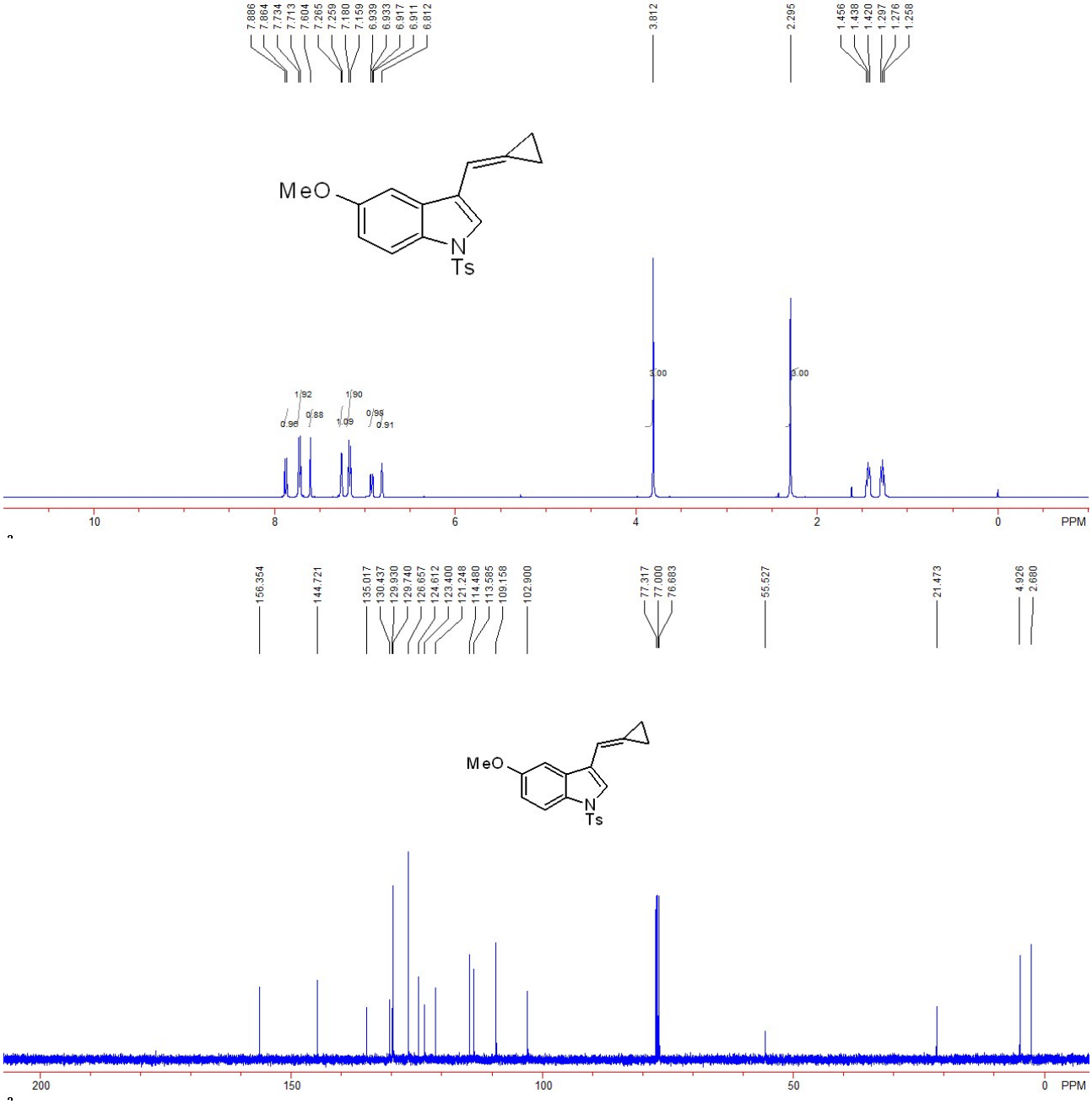


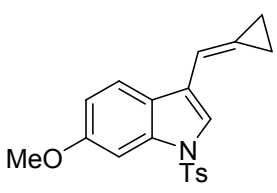


3-(cyclopropylidenemethyl)-5-methoxy-1-tosyl-1H-indole (1d).

A white solid, 70.6 mg, 20% yield. M.p.: 152-154 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.28 (t, J = 7.2 Hz, 2H, CH_2), 1.44 (t, J = 7.2 Hz, 2H, CH_2), 2.30 (s, 3H, CH_3), 3.81 (s, 3H, CH_3), 6.81 (s, 1H, ArH), 6.92 (dd, J = 2.4 Hz, 8.8 Hz, 1H, ArH), 7.17 (d, J =8.4 Hz, 2H, ArH), 7.26 (d, J = 2.4 Hz, 1H, ArH), 7.60 (s, 1H, ArH), 7.72 (d, J = 8.4 Hz, 1H, ArH), 7.88 (d, J = 8.8 Hz, 1H, ArH). ^{13}C

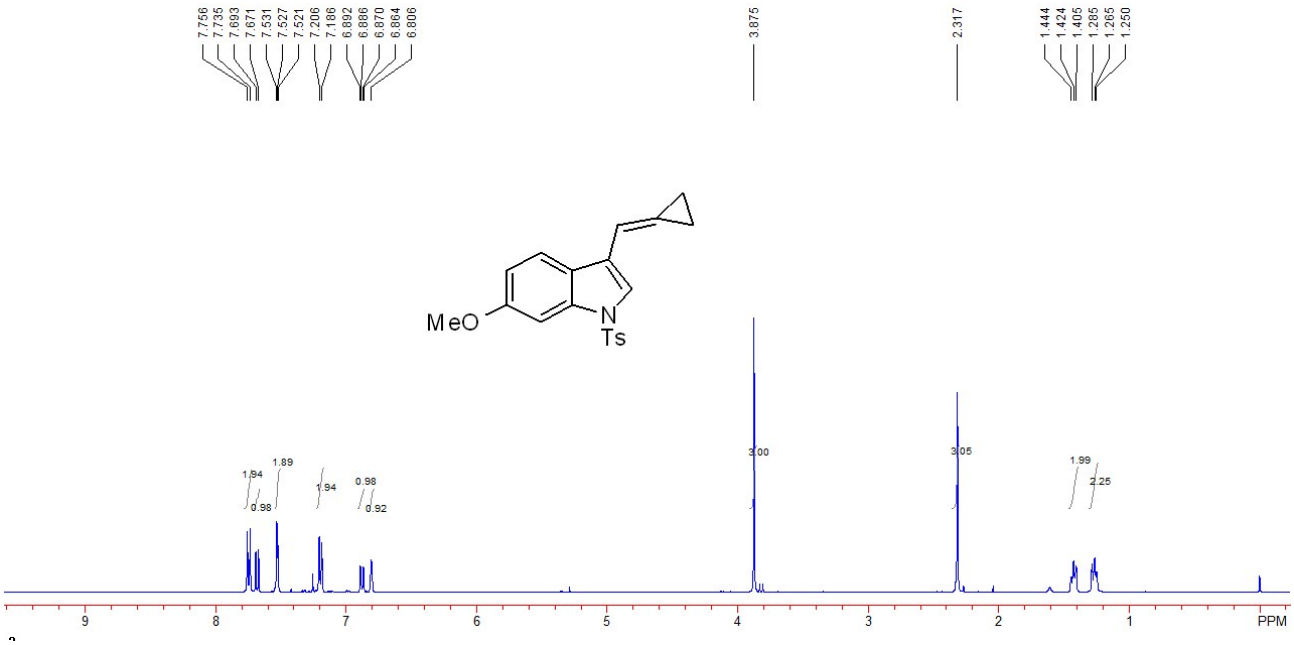
NMR ($CDCl_3$, TMS, 100 MHz) δ 2.7, 4.9, 21.5, 55.5, 102.9, 109.2, 113.6, 114.5, 121.2, 123.4, 124.6, 126.6, 129.7, 130.0, 130.4, 135.0, 144.7, 158.4. IR (CH_2Cl_2) ν 2956, 2919, 2843, 1592, 1364, 1171, 1118, 1026, 809, 780, 676 cm^{-1}. HRMS (DART) calcd. for $C_{20}H_{20}NO_3S$ ($+H^+$): 354.1158, Found: 354.116.

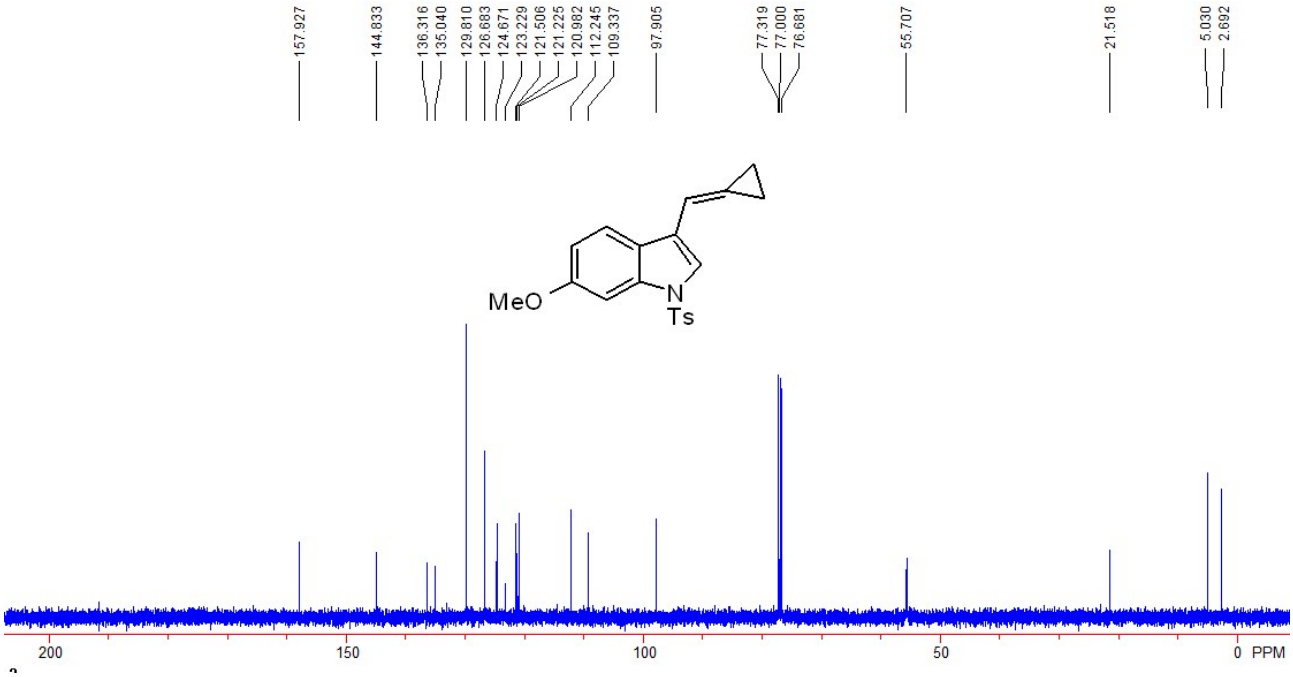


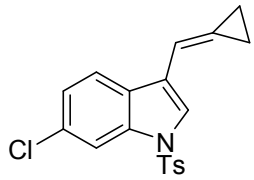


3-(cyclopropylidenemethyl)-6-methoxy-1-tosyl-1H-indole (1e).

A white solid, 148.3 mg, 21% yield. M.p.: 134-136 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.26 (t, *J* = 8.0 Hz, 2H, CH_2), 1.42 (t, *J* =8.0 Hz, 2H, CH_2), 2.32 (s, 3H, CH_3), 3.88 (s, 3H, CH_3), 6.81 (s, 1H, ArH), 6.88 (dd, *J* = 2.4 Hz, 8.8 Hz, 1H, ArH), 7.20 (d, *J* =8.0 Hz, 2H, ArH), 7.52-7.53 (m, 2H, ArH), 7.68 (d, *J* = 8.8 Hz, 1H, ArH), 7.74 (d, *J* = 8.4 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 2.7, 5.0, 21.5, 55.7, 97.9, 109.3, 112.2, 121.0, 121.2, 121.5, 123.2, 124.7, 126.7, 129.8, 135.0, 136.3, 144.8, 157.9. IR (CH_2Cl_2) ν 2964, 2924, 1718, 1610, 1485, 1367, 1288, 1172, 1113, 1029, 812, 671 cm^{-1}. HRMS (DART) calcd. for $C_{20}H_{20}NO_3S$ (+H$^+$): 354.1158, Found: 354.1159.

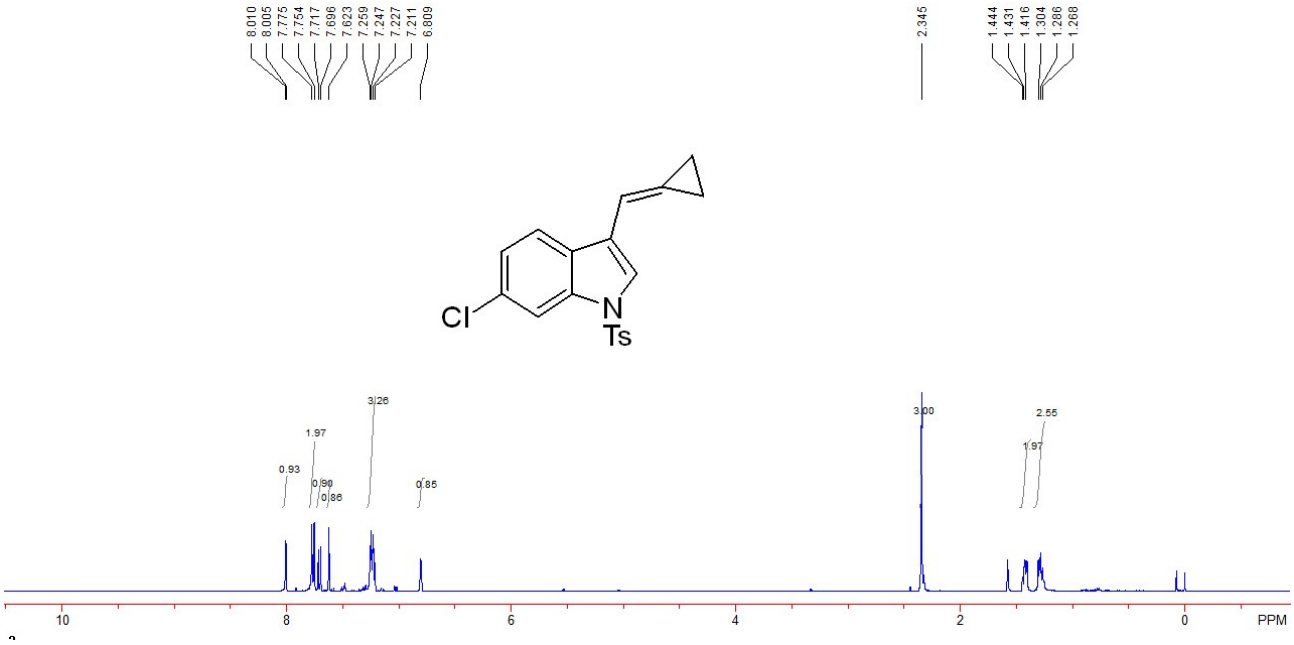


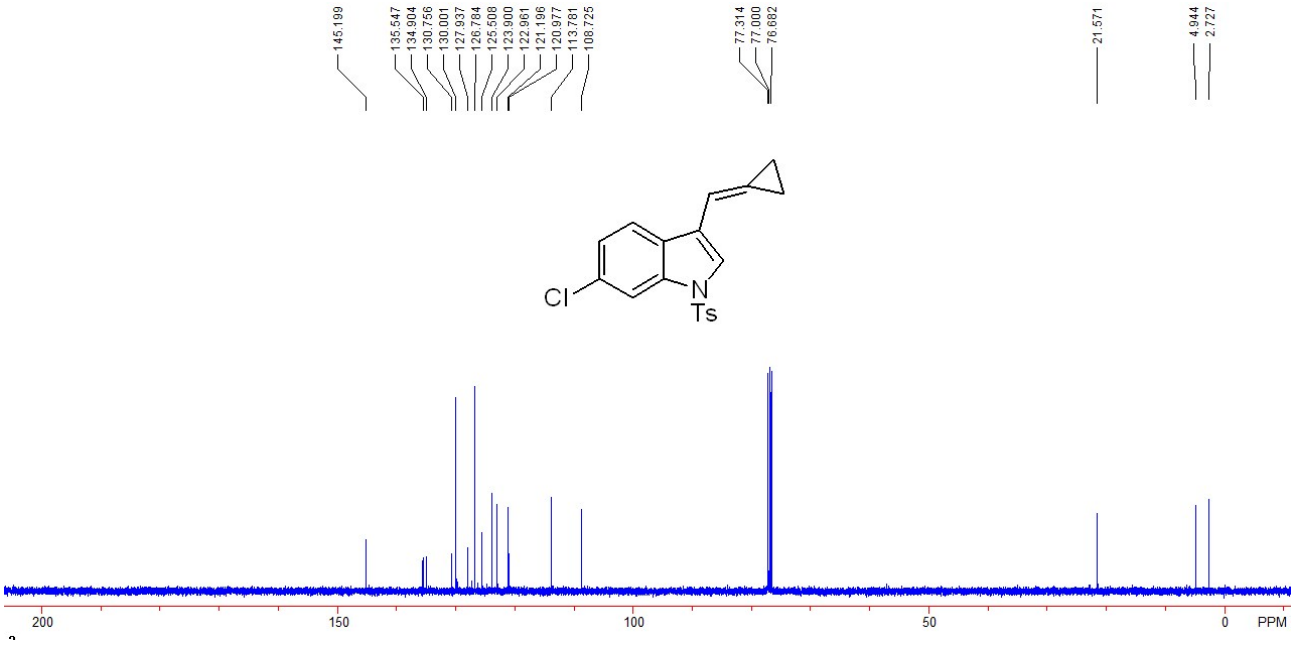


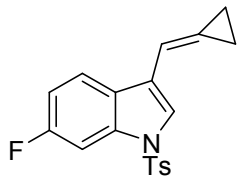


6-chloro-3-(cyclopropylidenemethyl)-1-tosyl-1H-indole (1f).

A white solid, 53.7 mg, 15% yield. M.p.: 189-191 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.29 (t, J = 7.2 Hz, 2H, CH_2), 1.43 (t, J = 7.2 Hz, 2H, CH_2), 2.34 (s, 3H, CH_3), 6.81 (s, 1H, ArH), 7.21-7.26 (m, 3H, ArH), 7.62 (s, 1H, ArH), 7.71 (d, J = 8.4 Hz, 1H, ArH), 7.76 (d, J = 8.4 Hz, 2H, ArH), 8.00 (d, J = 2.0 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 2.7, 4.9, 21.6, 108.7, 113.8, 121.0, 121.2, 123.0, 123.9, 125.5, 126.8, 127.9, 130.0, 130.8, 134.9, 135.5, 145.2. IR (CH_2Cl_2) ν 2958, 2922, 2854, 1380, 1173, 1134, 1087, 809, 667 cm^{-1}. HRMS (DART) calcd. for $C_{19}H_{17}NO_2SCl$ (+H^{+}): 358.0663, Found: 358.0664.

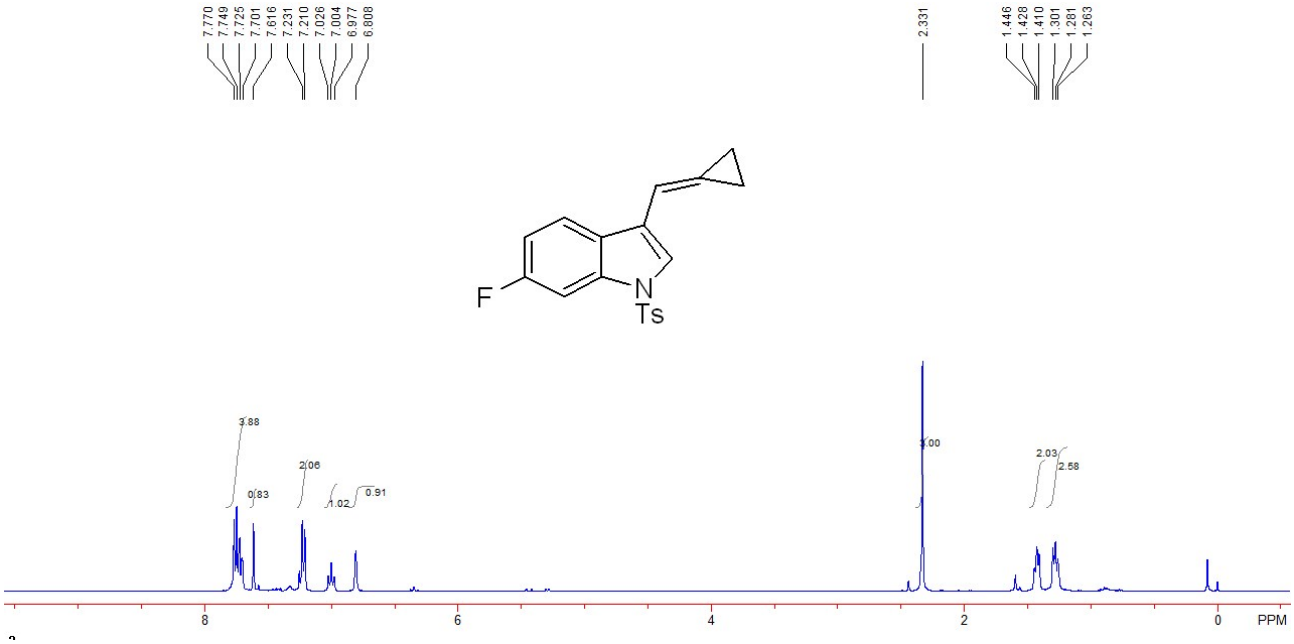






3-(cyclopropylidenemethyl)-6-fluoro-1-tosyl-1H-indole (1g).

A white solid, 78.4 mg, 23% yield. M.p.: 165-167 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.28 (t, J = 7.2 Hz, 2H, CH_2), 1.43 (t, J = 7.2 Hz, 2H, CH_2), 2.33 (s, 3H, CH_3), 6.81 (s, 1H, ArH), 7.00 (t, J = 8.8 Hz, 1H, ArH), 7.22 (d, J = 8.4 Hz, 2H, ArH), 7.62 (s, 1H, ArH), 7.70-7.77 (m, 4H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 2.7, 5.0, 21.5, 101.0 (d, J = 27.8 Hz), 108.9, 111.6 (d, J = 23.8 Hz), 121.0 (d, J = 1.2 Hz), 121.2 (d, J = 9.6 Hz), 122.7, 125.3, 125.7 (d, J = 1.6 Hz), 126.8, 130.0, 134.8, 135.3 (d, J = 12.5 Hz), 145.1, 160.9 (d, J = 240.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -116.30. IR (CH_2Cl_2) ν 2958, 2924, 2859, 1600, 1492, 1373, 1175, 1093, 857, 724, 671, 663 cm^{-1}. HRMS (DART) calcd. for $C_{19}H_{17}NO_2SF$ (+H^+): 342.0959, Found: 342.0958.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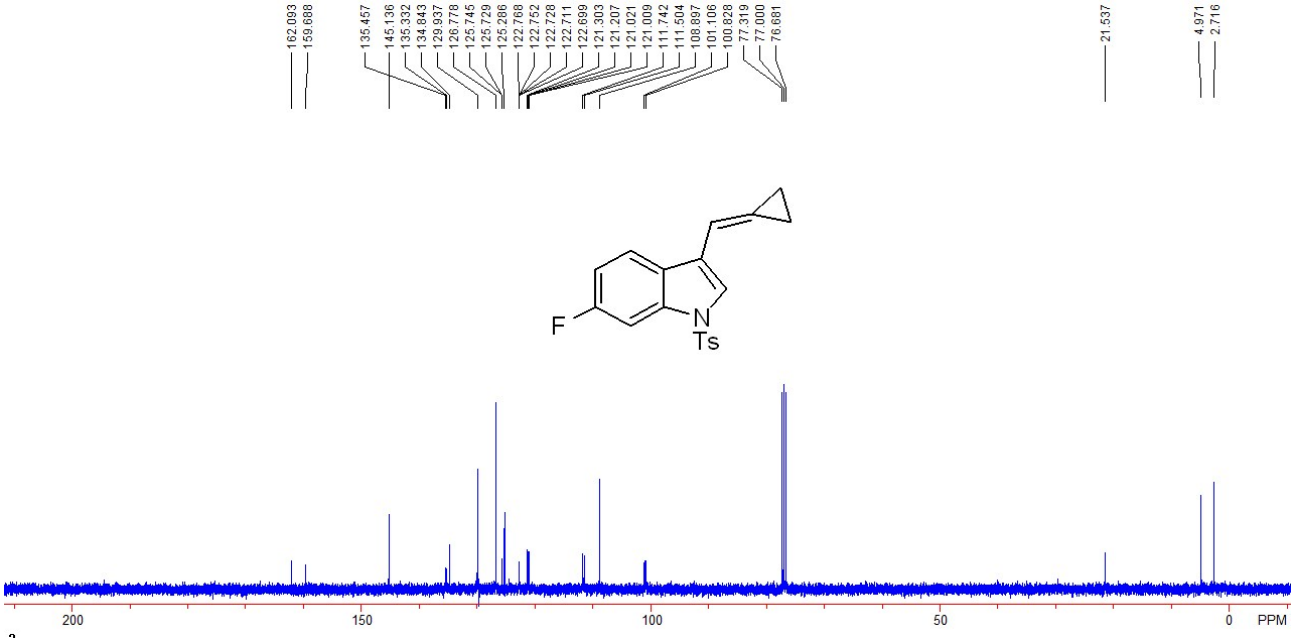
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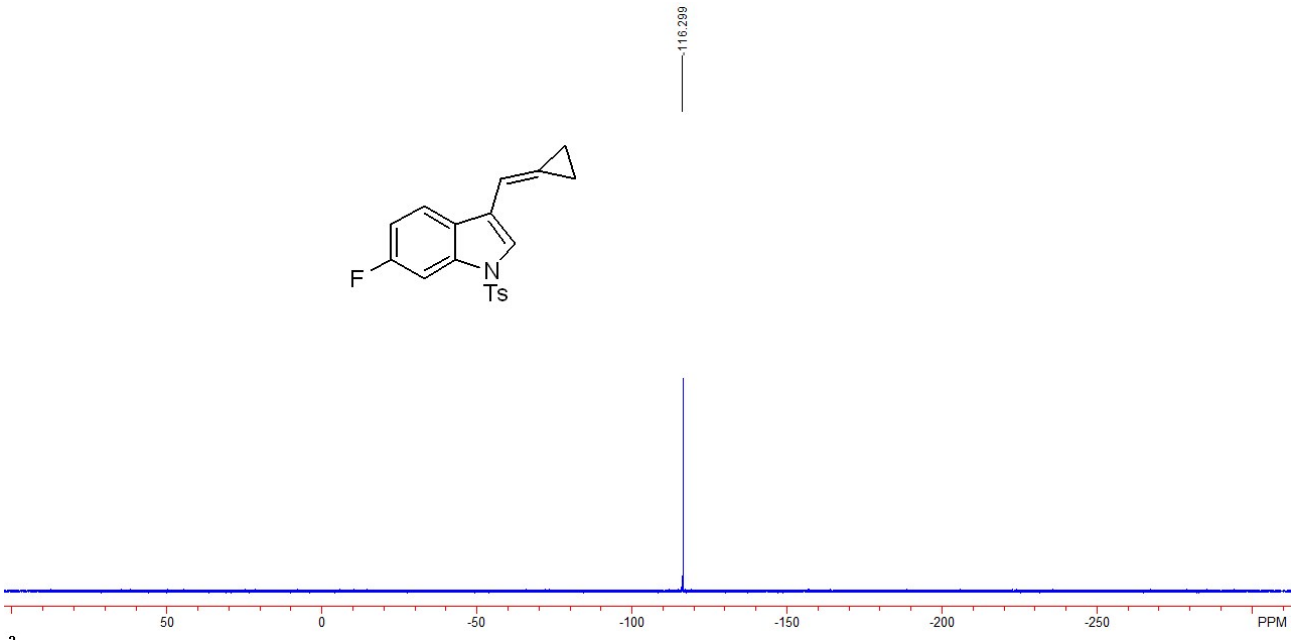
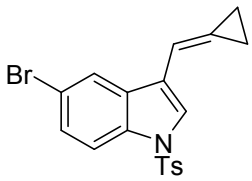
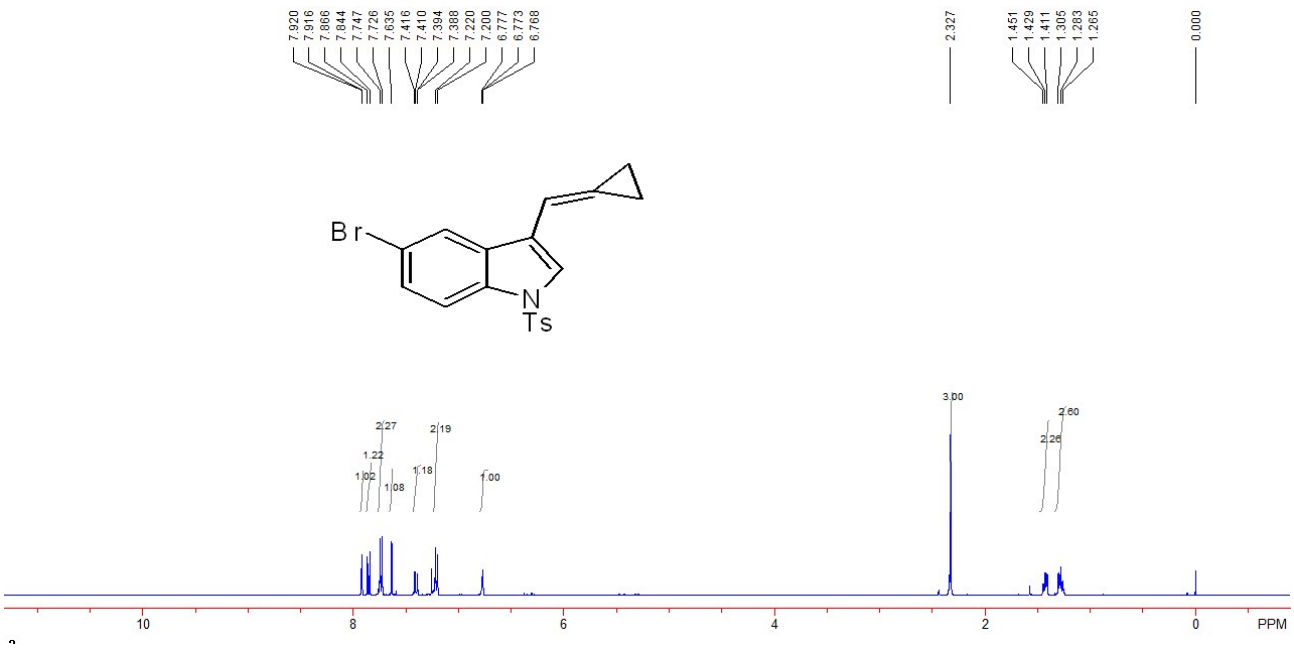
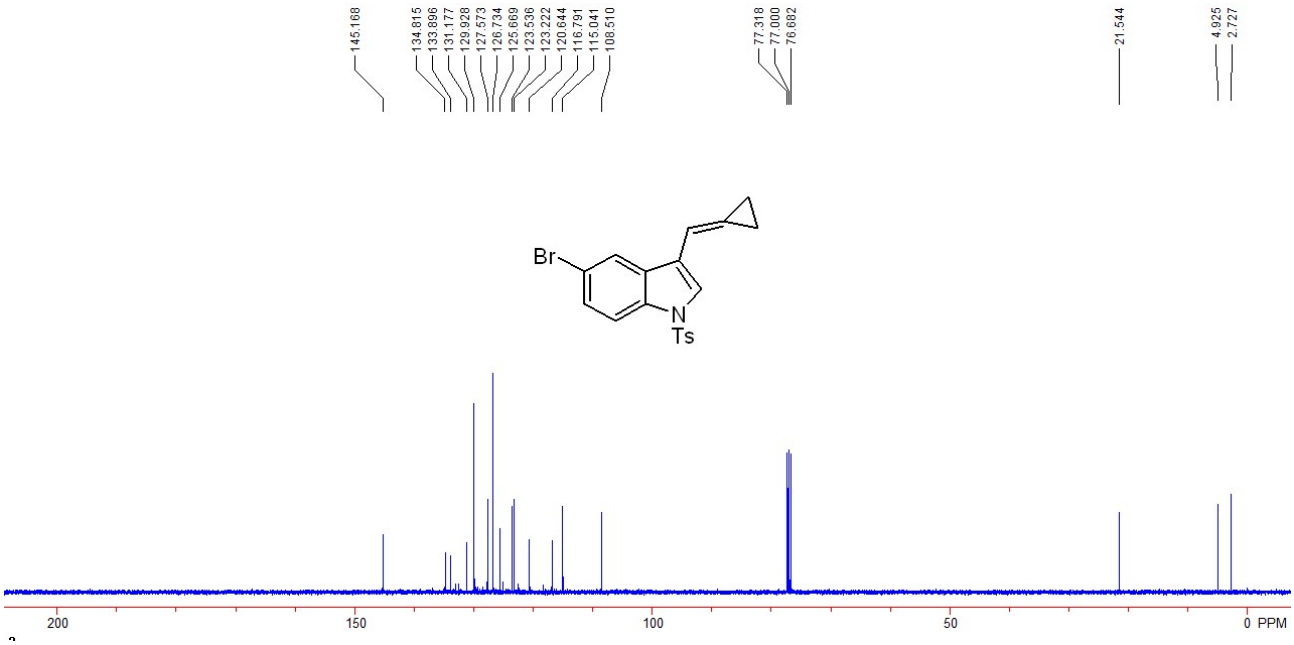


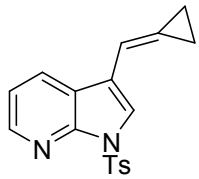


5-bromo-3-(cyclopropylidenemethyl)-1-tosyl-1H-indole (1h).

A white solid, 1.09 g, 26% yield. M.p.: 159-161 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.28 (t, *J* = 8.0 Hz, 2H, CH_2), 1.43 (t, *J* = 8.0 Hz, 2H, CH_2), 2.33 (s, 3H, CH_3), 6.77 (t, *J* = 2.0 Hz, 1H, ArH), 7.21 (d, *J* =8.0 Hz, 2H, ArH), 7.40 (dd, *J* = 2.4 Hz, 8.8 Hz, 1H, ArH), 7.64 (s, 1H, ArH), 7.74 (d, *J* = 8.4 Hz, 2H, ArH), 7.86 (d, *J* = 8.8 Hz, 1H, ArH), 7.92 (d, *J* = 1.6 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 2.7, 4.9, 21.5, 108.5, 115.0, 116.8, 120.6, 123.2, 123.5, 125.6, 126.7, 127.6, 129.9, 131.2, 133.9, 134.8, 145.2. IR (CH_2Cl_2) ν 2956, 2919, 2851, 1597, 1435, 1373, 1174, 1091, 815, 666 cm^{-1}. HRMS (DART) calcd. for $C_{19}H_{17}NO_2SBr$ (+H^+): 402.0158, Found: 402.0158.



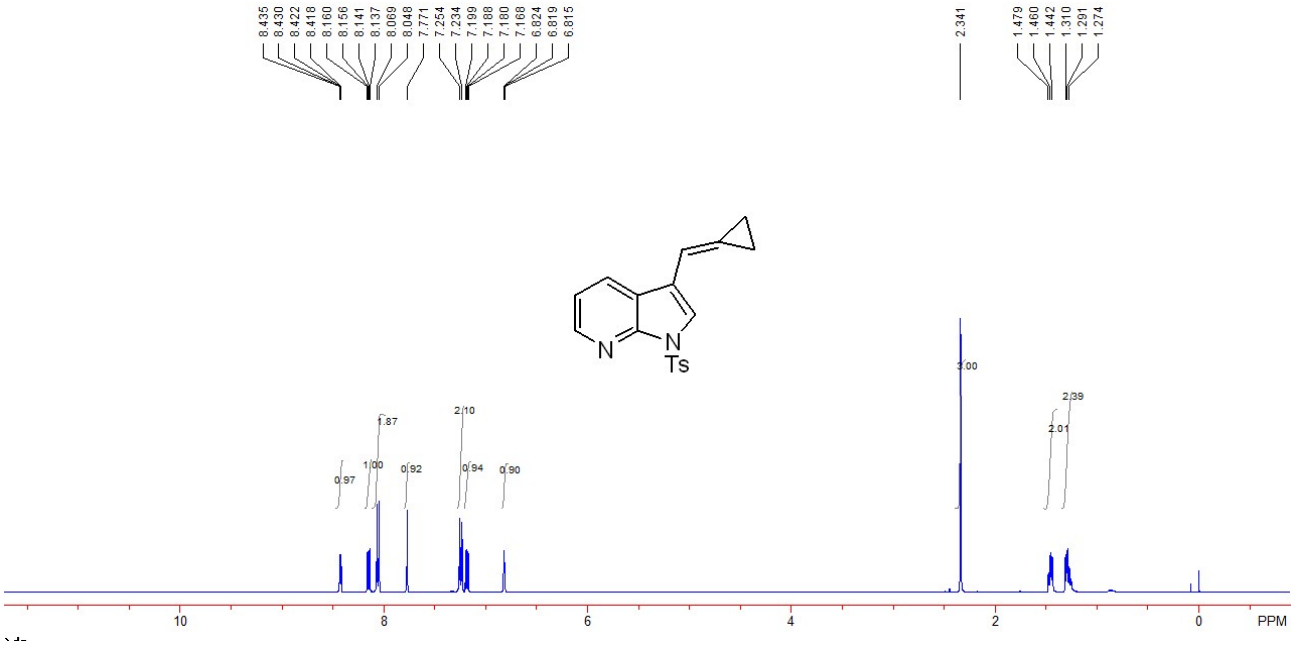


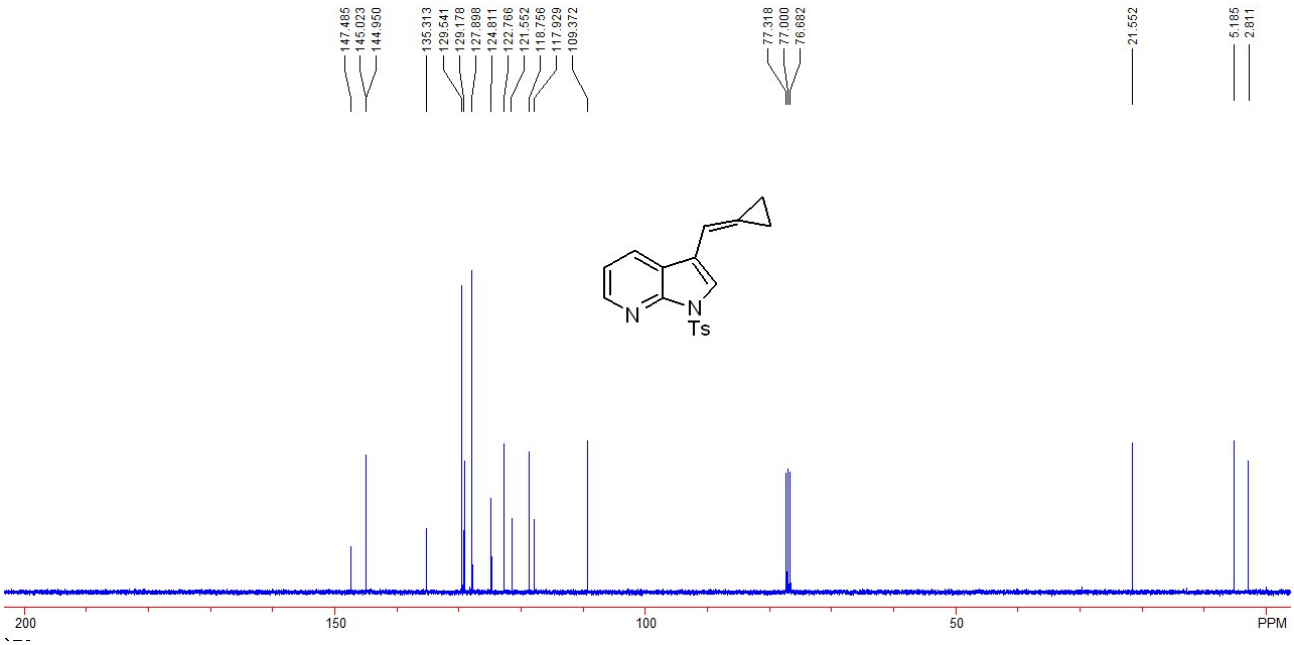


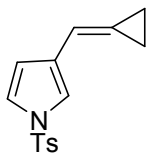
3-(cyclopropylidenemethyl)-1-tosyl-1H-pyrrolo[2,3-b]pyridine (1i).

A white solid, 259.2 mg, 40% yield. M.p.: 184-186 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.29 (t, J = 7.2 Hz, 2H, CH_2), 1.46 (t, J = 7.2 Hz, 2H, CH_2), 2.34 (s, 3H, CH_3), 6.82 (t, J = 2.0 Hz, 1H, ArH), 7.17-7.20 (m, 1H, ArH), 7.24 (d, J = 8.0 Hz, 2H, ArH), 7.77 (s, 1H, ArH), 8.06 (d, J = 8.4 Hz, 2H, ArH), 8.15 (dd, J = 1.6 Hz, 7.6 Hz, 1H, ArH), 8.43 (dd, J = 1.6 Hz, 5.2 Hz, 1H, ArH). ^{13}C NMR

($CDCl_3$, TMS, 100 MHz) δ 2.8, 5.2, 21.6, 109.4, 117.9, 118.8, 121.6, 122.8, 124.8, 127.9, 129.2, 129.5, 135.3, 144.9, 145.0, 147.5. IR (CH_2Cl_2) ν 2956, 2927, 2848, 1597, 1397, 1375, 1191, 1177, 1159, 1091, 666 cm^{-1}. HRMS (DART) calcd. for $C_{18}H_{17}N_2O_2S$ ($+H^+$): 325.1005, Found:325.1005.



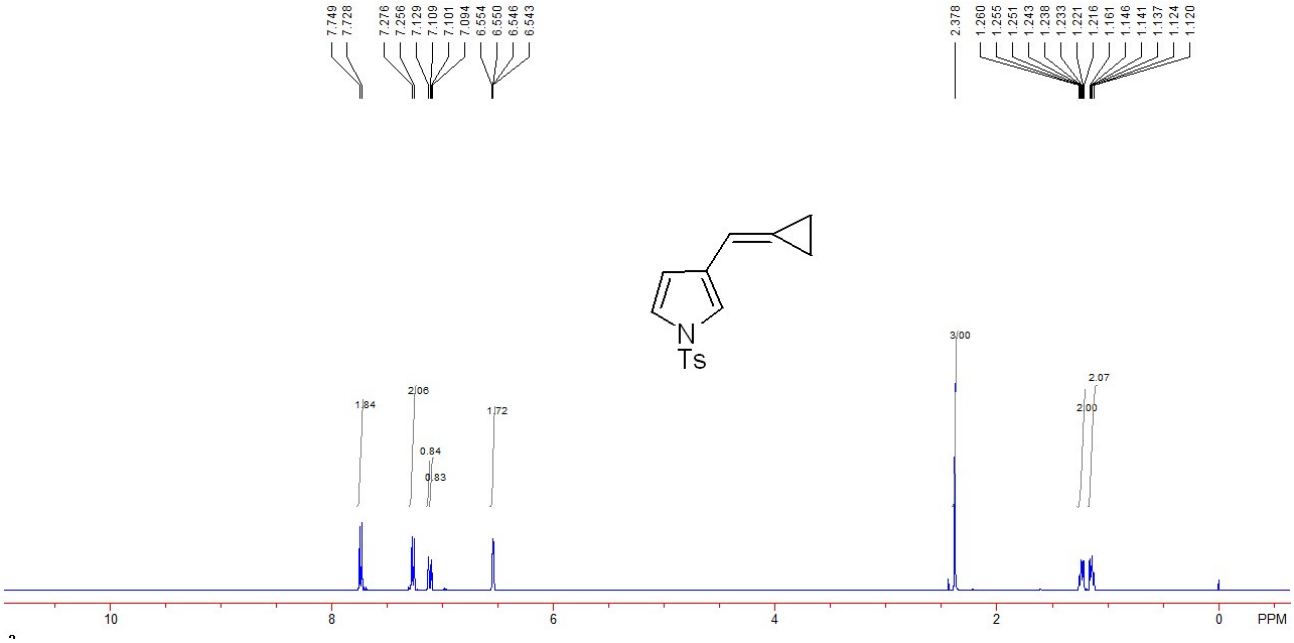


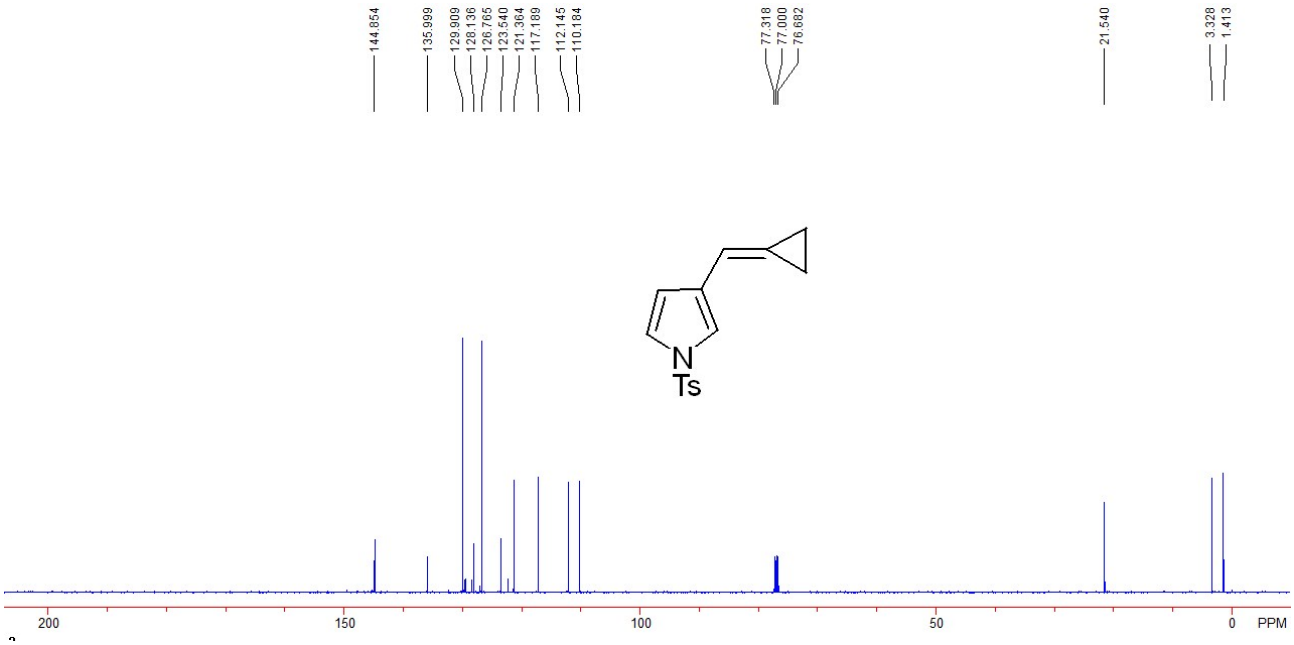


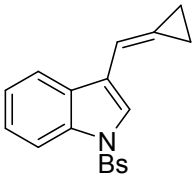
3-(cyclopropylidenemethyl)-1-tosyl-1H-pyrrole (1j).

A white solid, 136.5 mg, 25% yield. M.p.: 119-121 °C. ^1H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.12-

1.16 (m, 2H, CH_2), 1.22-1.26 (m, 2H, CH_2), 2.38 (s, 3H, CH_3), 6.54-6.55 (m, 2H, ArH), 7.10 (t, *J* =2.8 Hz, 1H, ArH), 7.13(s, 1H, ArH), 7.27 (d, *J* = 8.0 Hz, 1H, ArH), 7.74 (d, *J* = 8.4 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 1.4, 3.3, 21.5, 110.2, 112.1, 117.2, 121.4, 123.5, 126.8, 128.1, 129.0, 136.0, 144.8. IR (CH_2Cl_2) ν 3131, 2977, 2930, 1733, 1367, 1172, 1100, 1061, 812, 673 cm^{-1}. HRMS (DART) calcd. for $C_{15}H_{16}NO_2S$ ($+H^+$): 274.0896, Found: 274.0897.

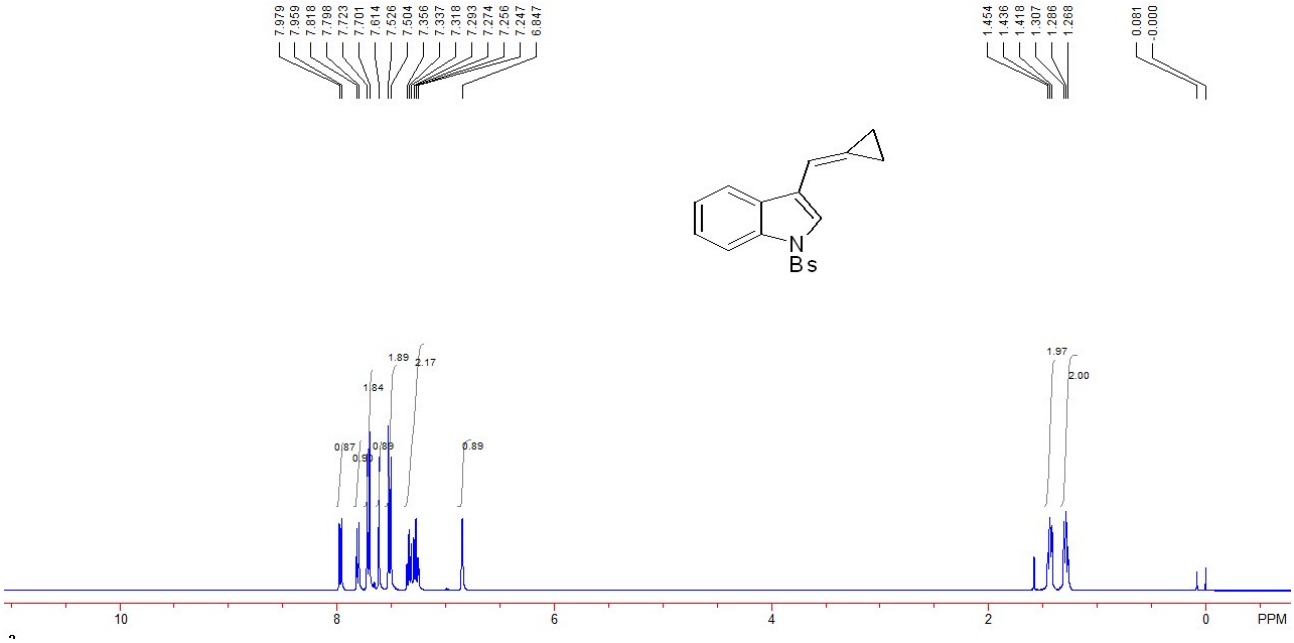


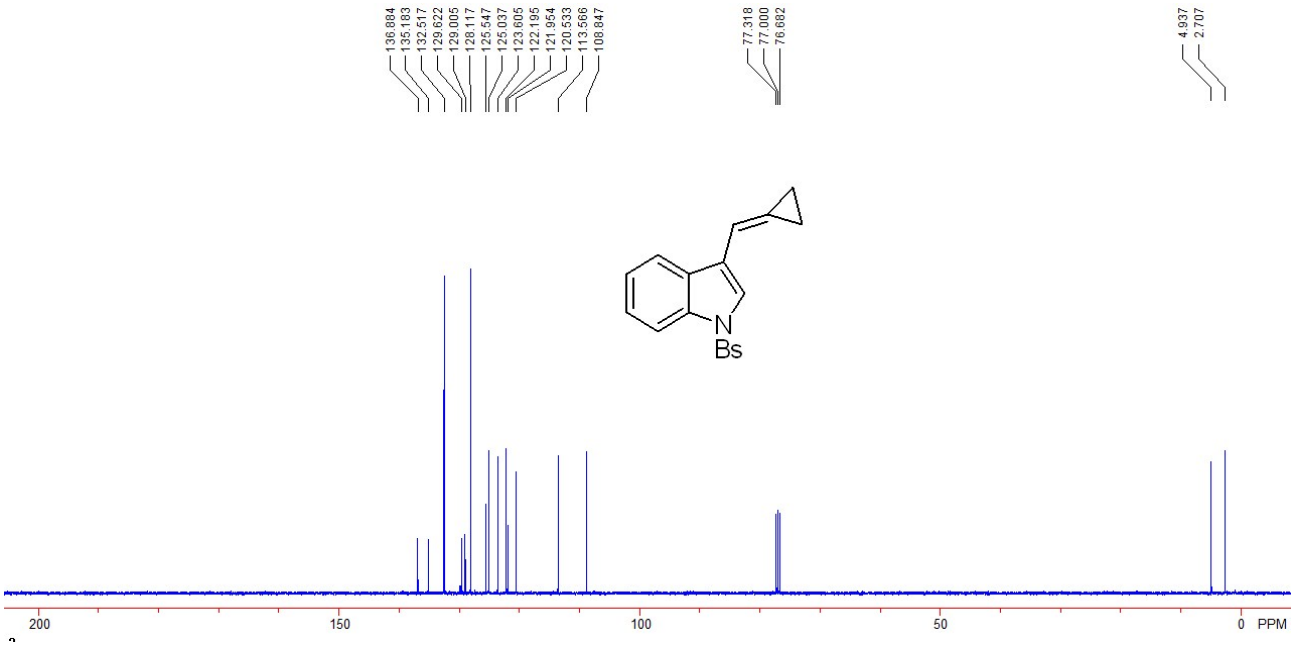


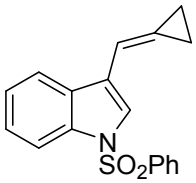


(Z)-4-(2-bromophenyl)-3-chlorobut-3-en-1-ol (1k).

A white solid, 232.8 mg, 30% yield. M.p.: 124-126 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.29 (t, *J* = 7.2 Hz, 2H, CH_2), 1.44 (t, *J* = 7.2 Hz, 2H, CH_2), 6.85 (s, 1H, ArH), 7.25-7.36 (m, 2H, ArH), 7.52 (d, *J* = 8.8 Hz, 2H, ArH), 7.61 (s, 1H, ArH), 7.71 (d, *J* = 8.8 Hz, 2H, ArH), 7.81 (d, *J* = 8.0 Hz, 1H, ArH), 7.97 (d, *J* = 8.0 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 2.7, 4.9, 108.8, 113.6, 120.5, 122.0, 122.2, 123.6, 125.0, 125.5, 128.1, 129.0, 129.6, 132.5, 135.2, 136.9. IR (CH_2Cl_2) ν 3089, 2982, 2916, 1575, 1490, 1376, 1198, 1176, 1146, 1091, 1069, 1011, 861, 782, 751 cm^{-1}. HRMS (DART) calcd. for $C_{18}H_{15}NO_2SBr$ ($+H^+$): 388.0001, Found: 388.0002.

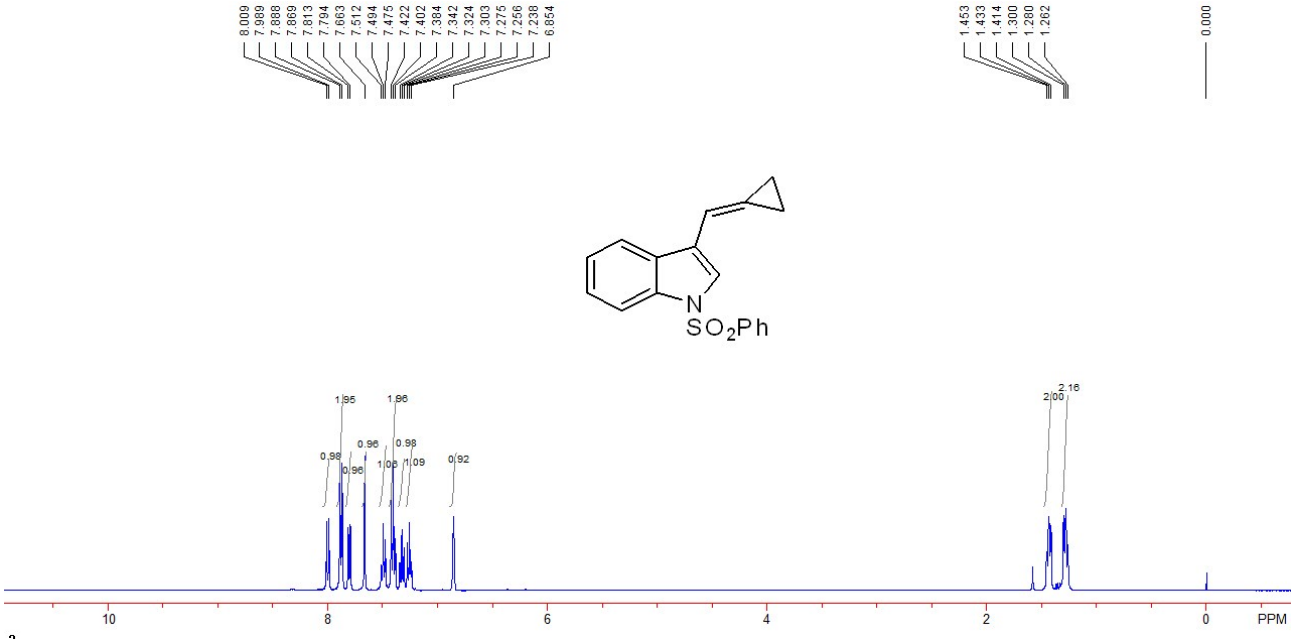


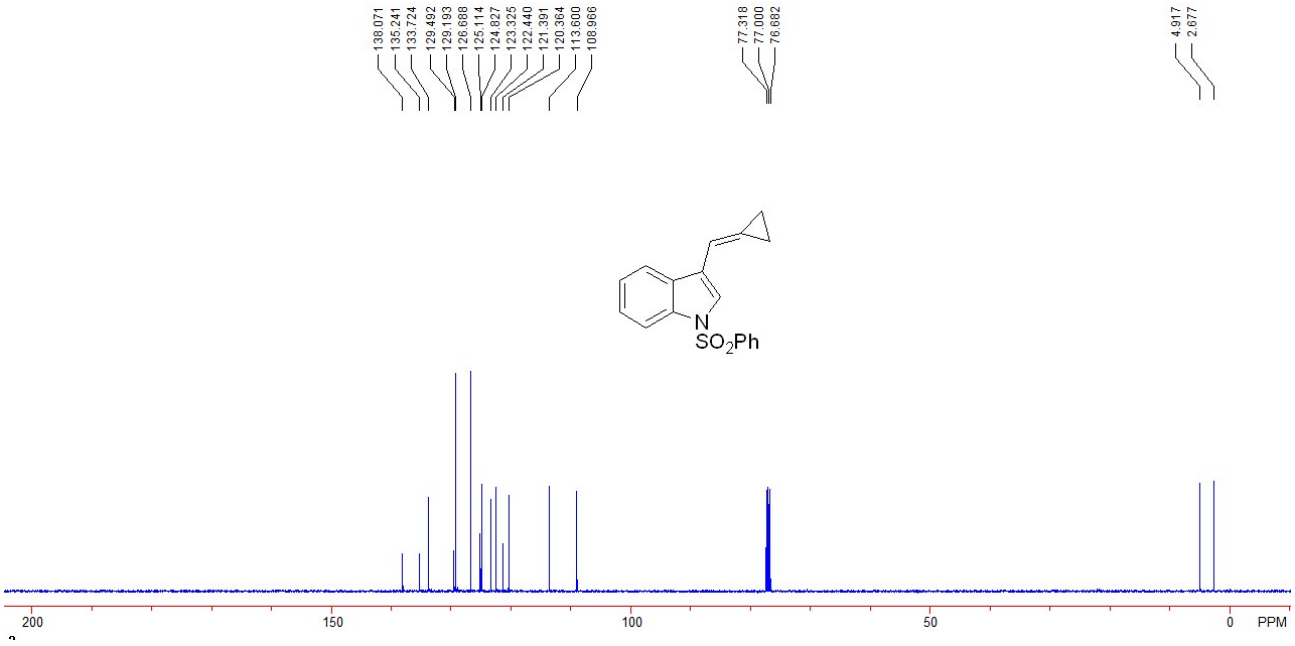


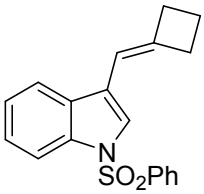


1-((4-bromophenyl)sulfonyl)-3-(cyclopropylidenemethyl)-1H-indole (1l).

A white solid, 148.3 mg, 24% yield. M.p.: 154-156 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.28 (t, *J* = 8.0 Hz, 2H, CH_2), 1.43 (t, *J* = 8.0 Hz, 2H, CH_2), 6.85 (s, 1H, ArH), 7.26 (t, *J* = 7.2 Hz, 1H, ArH), 7.32 (t, *J* = 8.0 Hz, 1H, ArH), 7.40 (t, *J* = 7.6 Hz, 2H, ArH), 7.49 (t, *J* = 7.2 Hz, 1H, ArH), 7.66 (s, 1H, ArH), 7.80 (d, *J* = 7.6 Hz, 1H, ArH), 7.88 (d, *J* = 7.6 Hz, 2H, ArH), 8.00 (d, *J* = 8.0 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 2.7, 4.9, 109.0, 113.6, 120.4, 121.4, 122.4, 123.3, 124.8, 125.1, 126.7, 129.2, 129.5, 133.7, 135.2, 138.1. IR (CH_2Cl_2) ν 2922, 1715, 1451, 1358, 1257, 1173, 1111, 1098, 1085, 1032, 808, 762, 752, 723, 683 cm^{-1}. HRMS (DART) calcd. for $C_{18}H_{16}NO_2S$ (+H^+): 310.0896, Found: 310.0898.

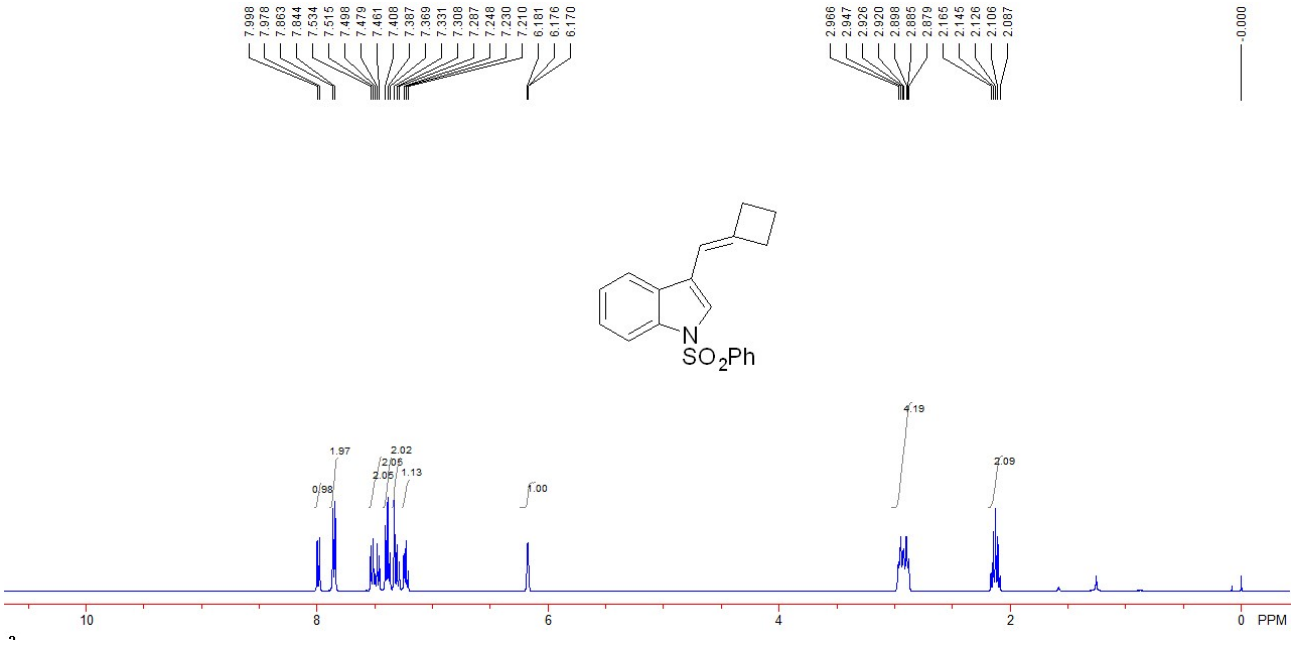


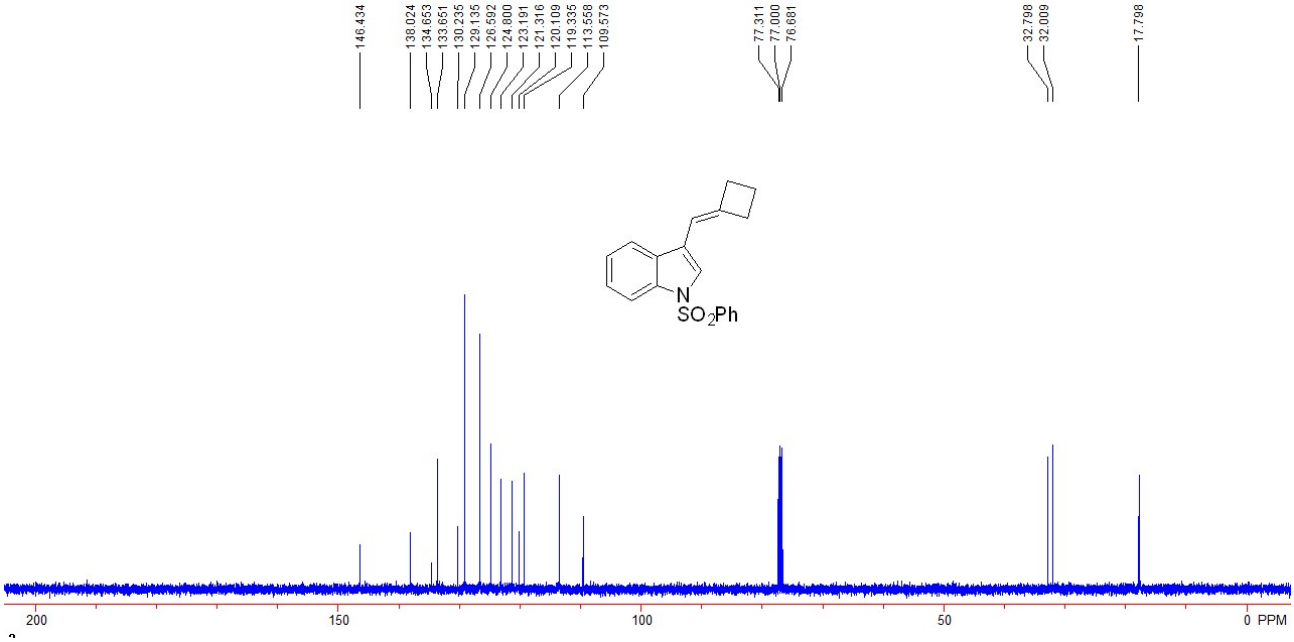


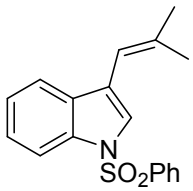


3-(cyclobutylidenemethyl)-1-(phenylsulfonyl)-1H-indole (1m).

A white solid, 245.5 mg, 38% yield. M.p.: 174-176 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.09-2.16 (m, 2H, ArH), 2.88-2.97 (m, 4H, ArH), 6.18 (t, J = 2.4 Hz, 1H, ArH), 7.21-7.25 (m, 1H, ArH), 7.29-7.33 (m, 2H, ArH), 7.39 (t, J = 8.0 Hz, 2H, ArH), 7.46-7.53 (m, 2H, ArH), 7.85 (d, J = 7.6 Hz, 2H, ArH), 7.99 (d, J = 8.0 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 17.8, 32.0, 32.8, 109.6, 113.6, 119.3, 120.1, 121.3, 123.2, 124.8, 126.6, 129.1, 130.2, 133.6, 134.6, 138.0, 146.4. IR (CH_2Cl_2) ν 2922, 2854, 1447, 1359, 1179, 1167, 1134, 1122, 1088, 749, 721, 682 cm^{-1}. MS (%) m/e 323 (30.55), 182 (M^+, 100.00), 181 (22.89), 180 (25.45), 167 (41.05), 154 (41.40), 127 (37.95), 77 (36.05). HRMS (EI) calcd. for $C_{19}H_{17}NO_2S$: 323.0980, Found: 323.0973.



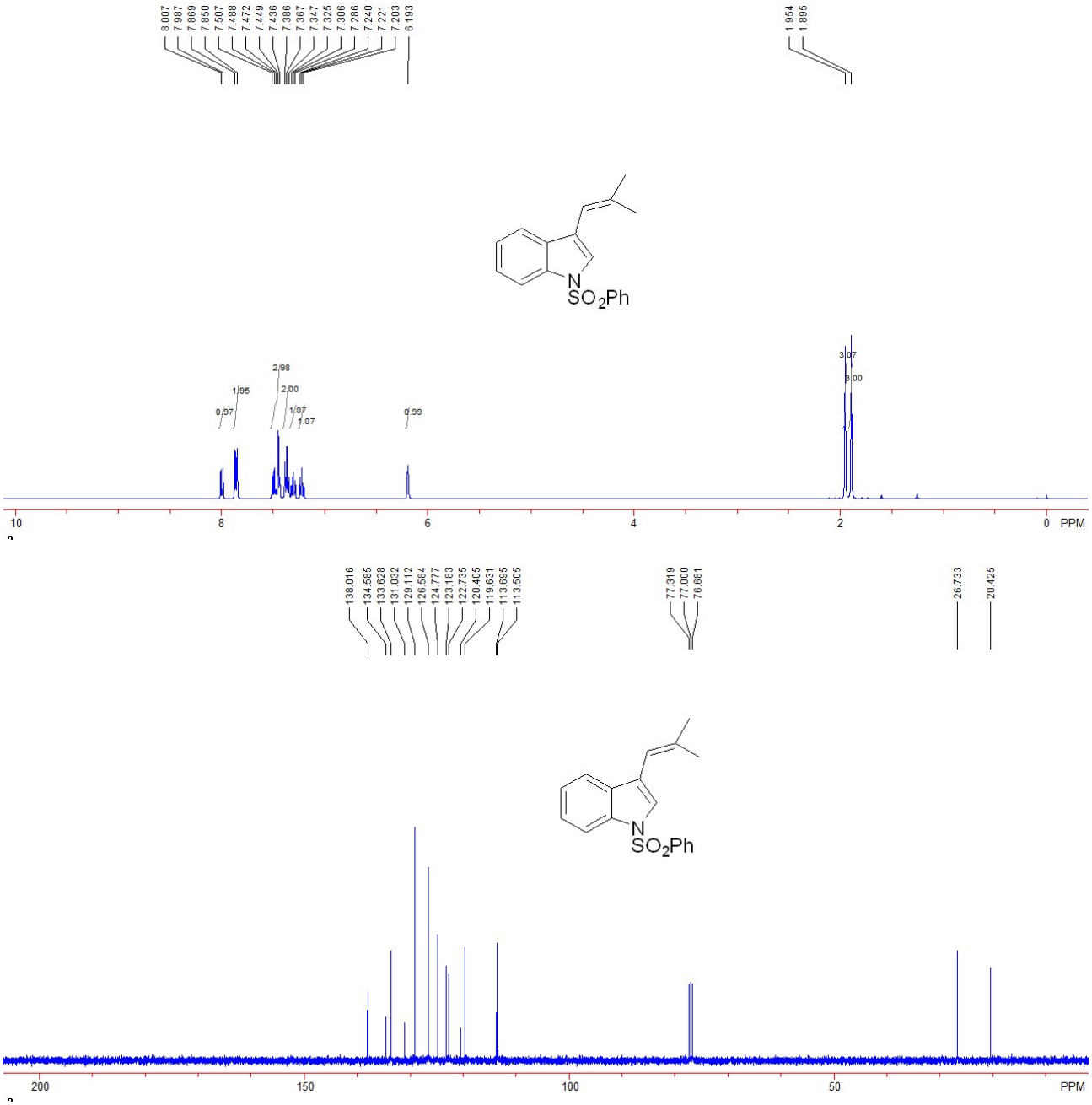


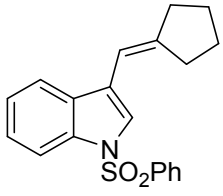


3-(2-methylprop-1-en-1-yl)-1-(phenylsulfonyl)-1H-indole (1o).

A white solid, 547.4 mg, 88% yield. M.p.: 123-125 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.90 (s, 3H, CH_3), 1.95 (s, 3H, CH_3), 6.19 (s, 1H, ArH), 7.22 (t, J = 7.2 Hz, 1H, ArH), 7.31 (t, J = 7.6 Hz, 1H, ArH), 7.37 (t, J = 7.6 Hz, 1H, ArH), 7.44-7.51 (m, 3H, ArH), 7.86 (d, J = 7.6 Hz, 2H, ArH), 8.00 (d, J = 7.6 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 20.4, 26.7, 113.5, 113.7, 119.6,

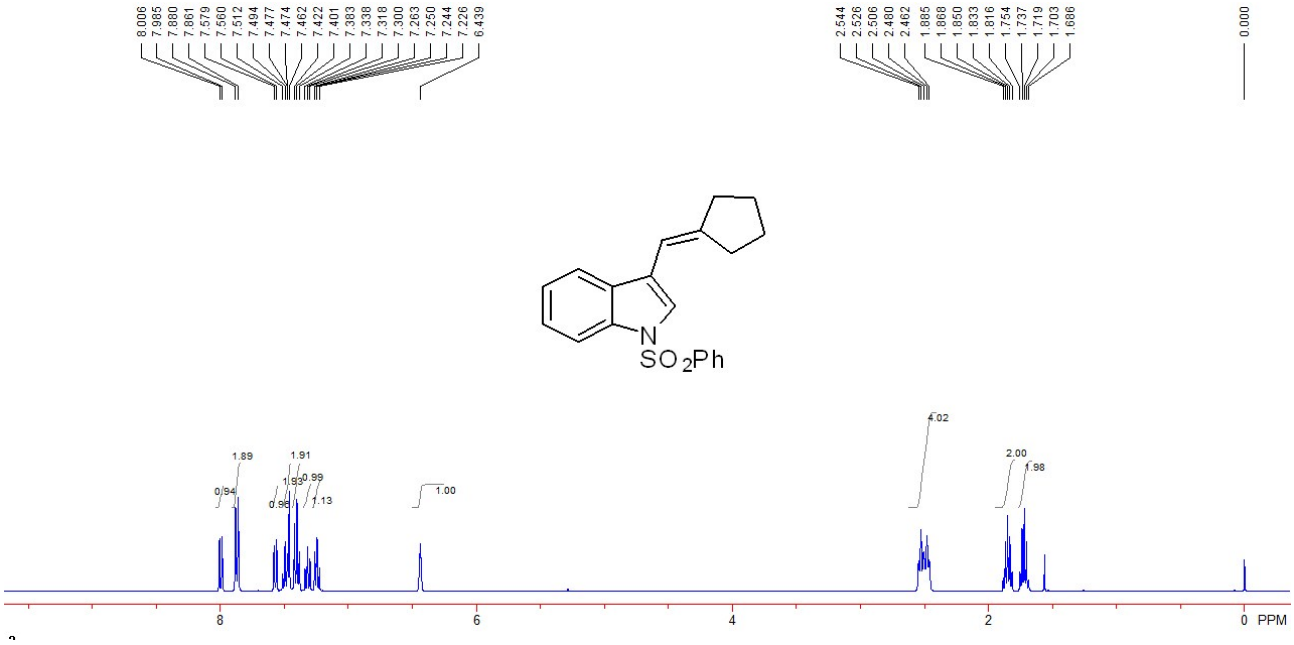
120.4, 122.7, 123.2, 124.8, 126.6, 129.1, 131.0, 133.6, 134.6, 138.0. IR (CH_2Cl_2) ν 3065, 2972, 1447, 1363, 1180, 1173, 1134, 761, 741, 724 cm^{-1}. MS (%) m/e 311 (38.92), 171 (14.49), 170 (M^+, 100.00), 168 (11.58), 155 (14.15), 154 (23.20), 128 (16.57), 77 (26.67). HRMS (EI) calcd. for $C_{18}H_{17}O_2NS$: 311.0980, Found: 311.0977.

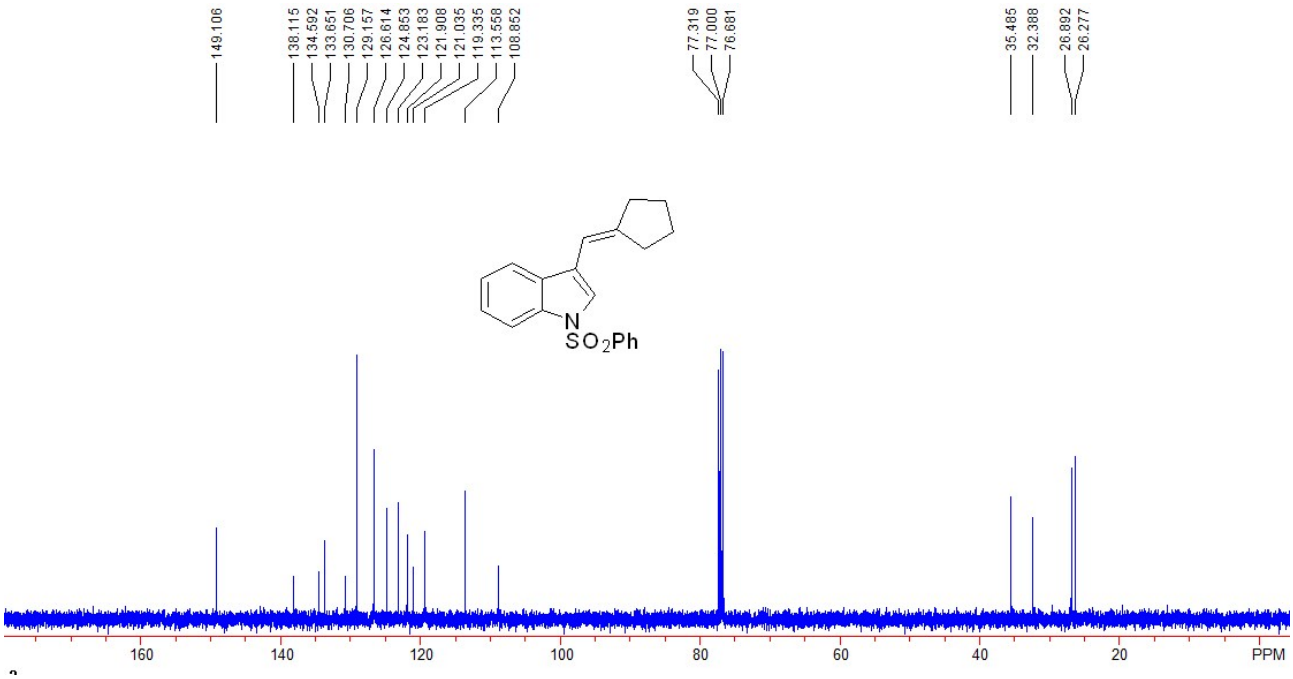


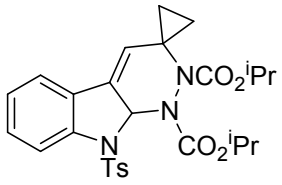


3-(cyclopentylidenemethyl)-1-(phenylsulfonyl)-1H-indole (1p).

A white solid, 532.5 mg, 79% yield. M.p.: 153-155 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.69-1.75 (m, 2H, CH_2), 1.82-1.88 (m, 2H, CH_2), 2.46-2.54 (m, 4H, CH_2), 6.44 (s, 1H, ArH), 7.24 (t, *J* = 7.2 Hz, 1H, ArH), 7.32 (t, *J* = 7.2 Hz, 1H, ArH), 7.40 (t, *J* = 8.0 Hz, 2H, ArH), 7.46-7.51 (m, 2H, ArH), 7.57 (d, *J* = 7.6 Hz, 1H, ArH), 7.87 (d, *J* = 7.6 Hz, 2H, ArH), 8.00 (d, *J* = 8.4 Hz, 1H, ArH),. ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 26.3, 26.9, 32.4, 35.5, 108.8, 113.6, 119.3, 121.0, 121.9, 123.2, 124.8, 126.6, 129.2, 130.7, 133.6, 134.6, 138.1, 149.1. IR (CH_2Cl_2) ν 2958, 2919, 2869, 1447, 1369, 1175, 1130, 1094, 1021, 975, 743, 723, 686 cm^{-1}. MS (%) m/e 337 (42.24), 197 (16.01), 196 (M^+, 100.00), 194 (13.07), 168 (19.05), 167 (22.72), 142 (14.69), 77 (22.87)。 HRMS (EI) calcd. for $C_{20}H_{19}O_2NS$: 337.1137, Found: 337.1140.

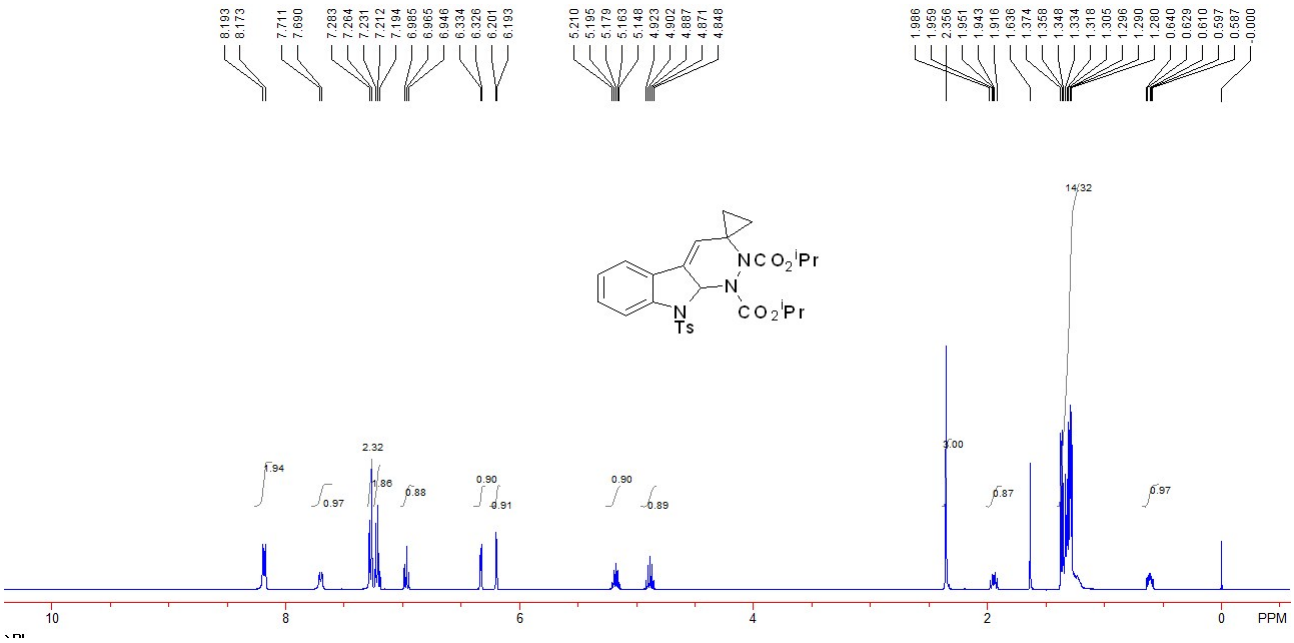


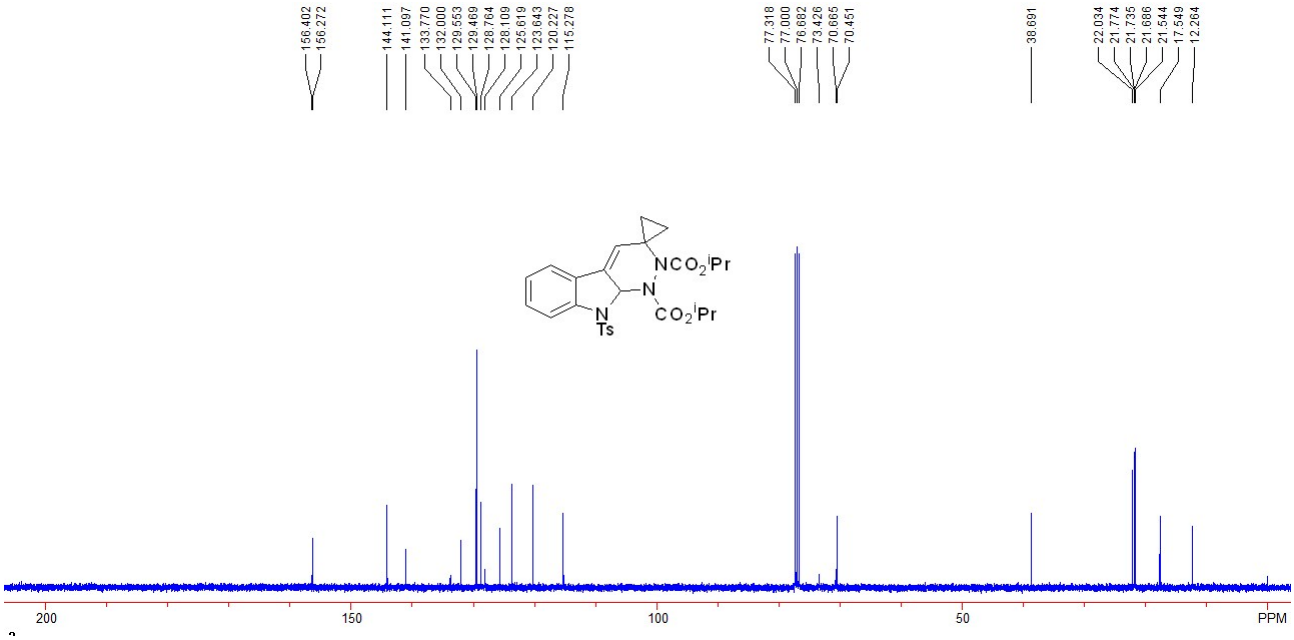


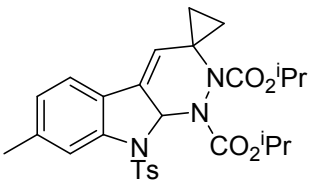


Diisopropyl 9'-tosyl-9',9a'-dihydrospiro[cyclopropane-1,3'-pyridazino[3,4-b]indole]-1',2'-dicarboxylate (2a).

A white solid, 97.8 mg, 86% yield. M.p.: 189-191 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.59-0.64 (m, 1H, CH_2), 1.28-1.37 (m, 14H), 1.92-1.99 (m, 1H, CH_2), 2.35 (s, 3H, CH_3), 4.85-4.92 (m, 1H, CH), 5.15-5.21 (m, 1H, CH), 6.19 (d, *J* = 3.2 Hz, 1H, CH), 6.33 (d, *J* = 3.2 Hz, 1H, CH), 6.96 (t, *J* = 7.6 Hz, 1H, ArH), 7.21 (t, *J* = 7.2 Hz, 2H, ArH), 7.27 (d, *J* = 7.6 Hz, 2H, ArH), 7.70 (d, *J* = 8.4 Hz, 1H, ArH), 8.18 (d, *J* = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.3, 17.5, 21.5, 21.6, 21.7, 21.8, 22.0, 38.7, 70.4, 70.7, 73.4, 115.3, 120.2, 123.6, 125.6, 128.1, 128.8, 129.5, 129.6, 132.0, 133.8, 141.1, 144.1, 156.3, 156.4. IR (CH_2Cl_2) ν 2977, 2924, 1717, 1370, 1313, 1173, 1110, 804, 660 cm^{-1}. HRMS (DART) calcd. for $C_{27}H_{32}O_6N_3S$ (+H^+): 526.2006, Found: 526.2011.



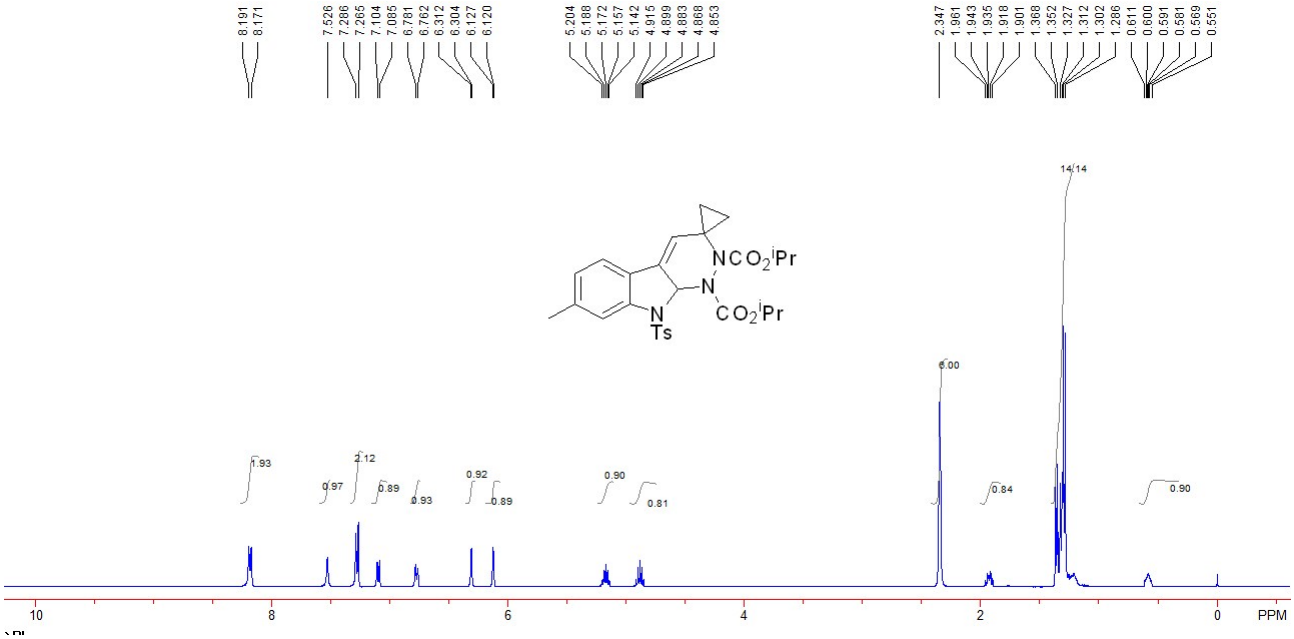


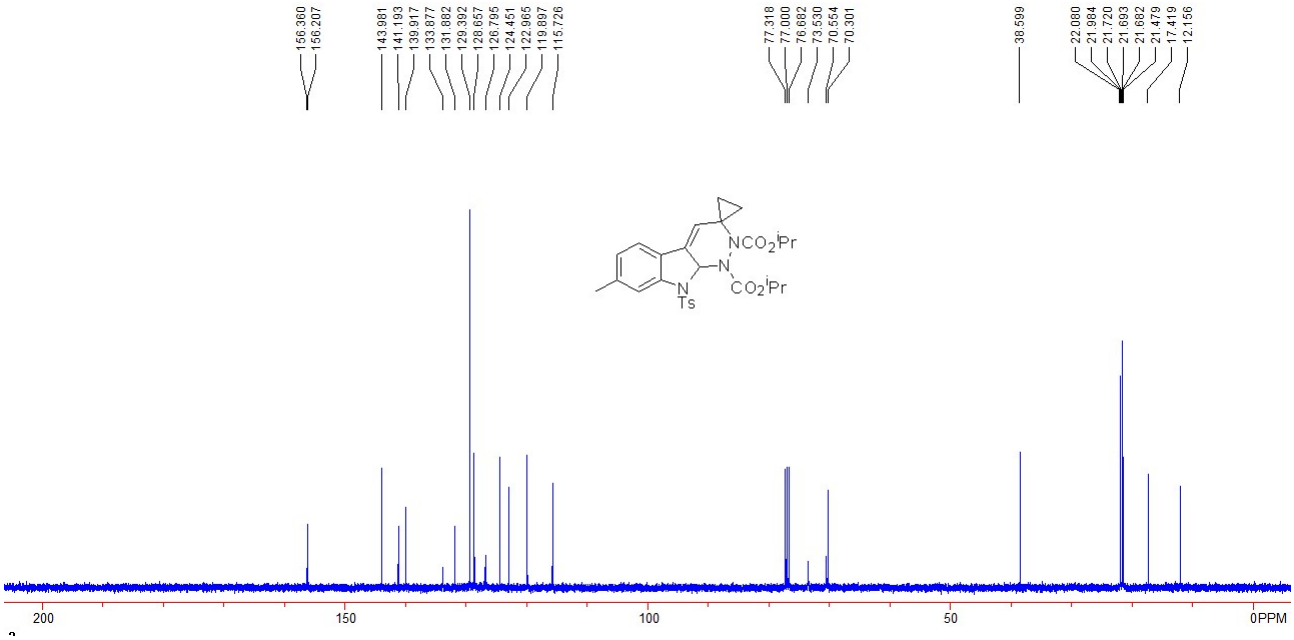


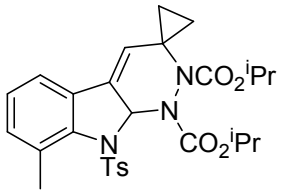
Diisopropyl 7'-methyl-9'-tosyl-9',9a'-dihydrospiro[cyclopropane-1,3'-pyridazino[3,4-b]indole]-1',2'-dicarboxylate (2b).

A white solid, 91.8 mg, 85% yield. M.p.: 211-213 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.55-0.61 (m, 1H, CH_2), 1.29-1.37 (m, 14H), 1.90-1.96 (m, 1H, CH_2), 2.35 (s, 6H, CH_3), 4.85-4.92 (m, 1H, CH), 5.14-5.20 (m, 1H, CH), 6.12 (d, J = 2.8 Hz, 1H, CH), 6.32 (d, J = 3.2 Hz, 1H, CH), 6.77

(d, J = 7.6 Hz, 1H, ArH), 7.09 (d, J = 7.62 Hz, 1H, ArH), 7.27 (d, J = 8.4 Hz, 2H, ArH), 7.53 (s, 1H, ArH), 8.18 (d, J = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.2, 17.4, 21.5, 21.68, 21.69, 21.7, 22.0, 22.1, 38.6, 70.3, 70.6, 73.5, 115.7, 119.9, 123.0, 124.4, 126.8, 128.6, 129.4, 131.9, 133.9, 140.0, 141.2, 144.0, 156.2, 156.4. IR (CH_2Cl_2) ν 2922, 2859, 1717, 1371, 1313, 1175, 1110, 812, 662 cm^{-1}. HRMS (DART) calcd. for $C_{28}H_{34}N_3O_6S$ ($+H^+$): 540.2163, Found: 540.2160.

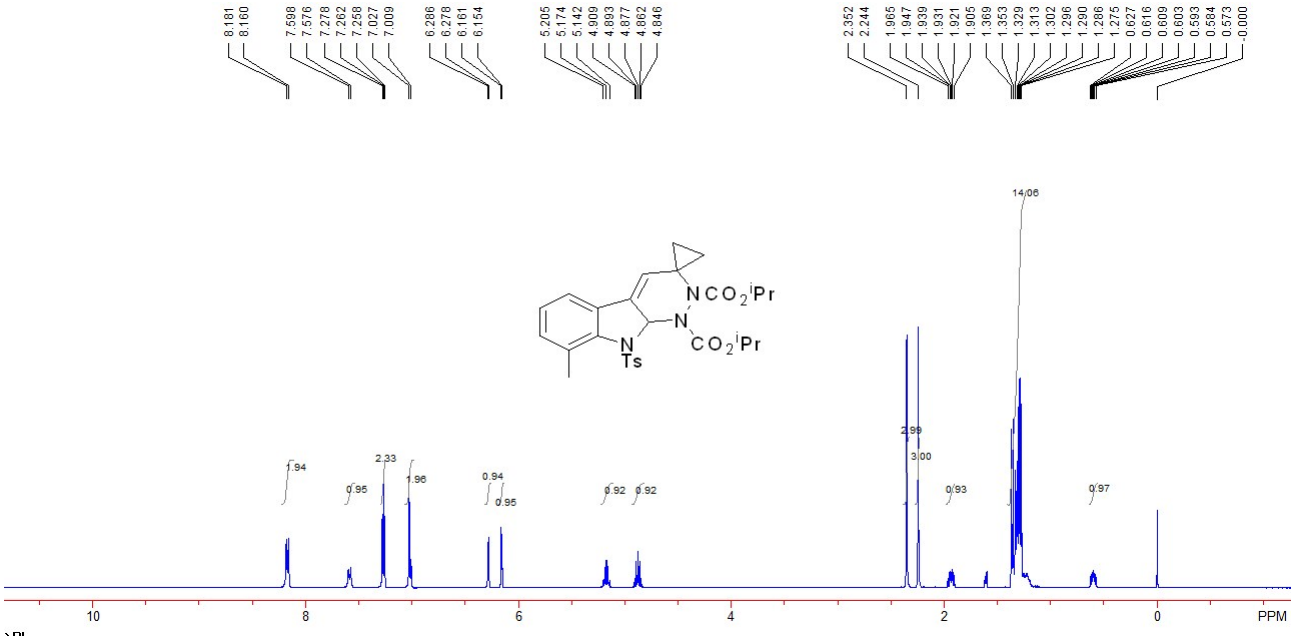


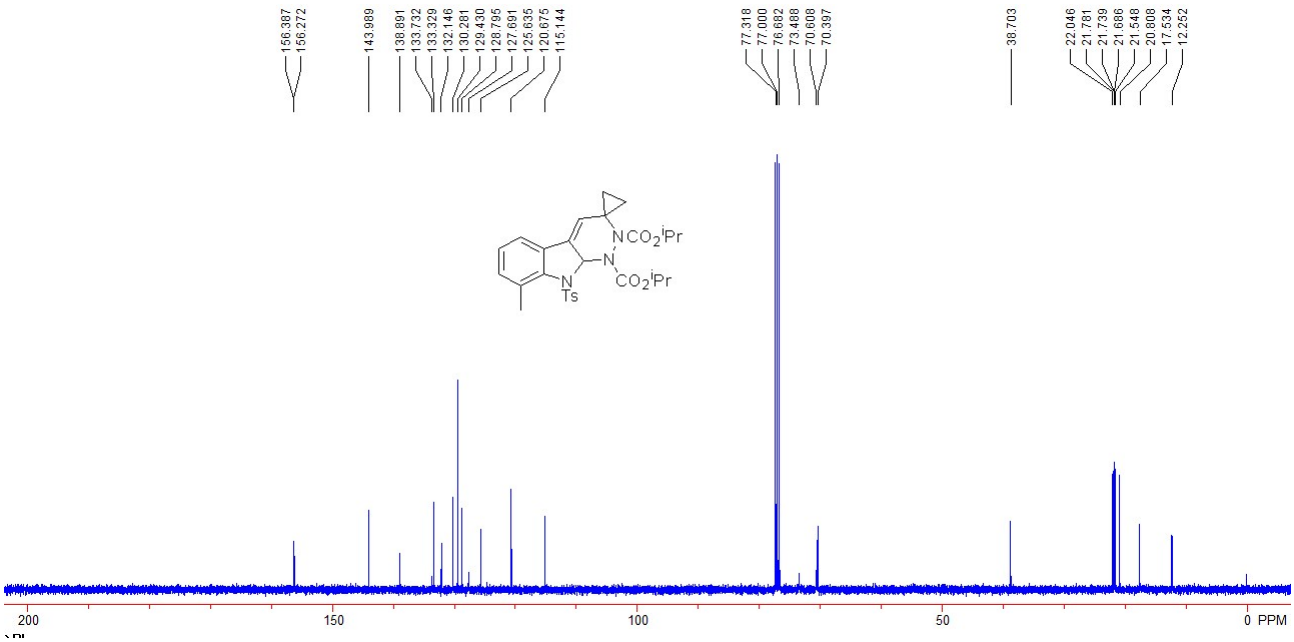


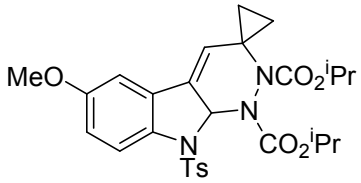


Diisopropyl 8'-methyl-9'-tosyl-9',9a'-dihydrospiro[cyclopropane-1,3'-pyridazino[3,4-b]indole]-1',2'-dicarboxylate (2c).

A white solid, 94.0 mg, 87% yield. M.p.: 219-221 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.57-0.63 (m, 1H, CH_2), 1.28-1.37 (m, 14H), 1.902-1.969 (m, 1H, CH_2), 2.24 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 4.83-4.92 (m, 1H, CH), 5.14-5.21 (m, 1H, CH), 6.16 (d, *J* = 2.8 Hz, 1H, CH), 6.28 (d, *J* = 3.2 Hz, 1H, CH), 7.02 (d, *J* = 7.2 Hz, 2H, ArH), 7.27 (d, *J* = 8.0 Hz, 2H, ArH), 7.59 (d, *J* = 8.8 Hz, 1H, ArH), 8.17 (d, *J* = 8.4 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.2, 17.5, 20.8, 21.5, 21.6, 21.7, 21.8, 22.0, 38.7, 70.4, 70.6, 73.5, 115.1, 120.7, 125.6, 128.8, 129.5, 129.6, 130.3, 132.1, 133.3, 133.7, 138.9, 144.0, 156.3, 156.4. IR (CH_2Cl_2) ν 2922, 2848, 1717, 1369, 1311, 1172, 1110, 1096, 961, 815, 662 cm^{-1}. HRMS (DART) calcd. for $C_{28}H_{34}N_3O_6S$ (+H$^+$): 540.2163, Found: 540.2164.

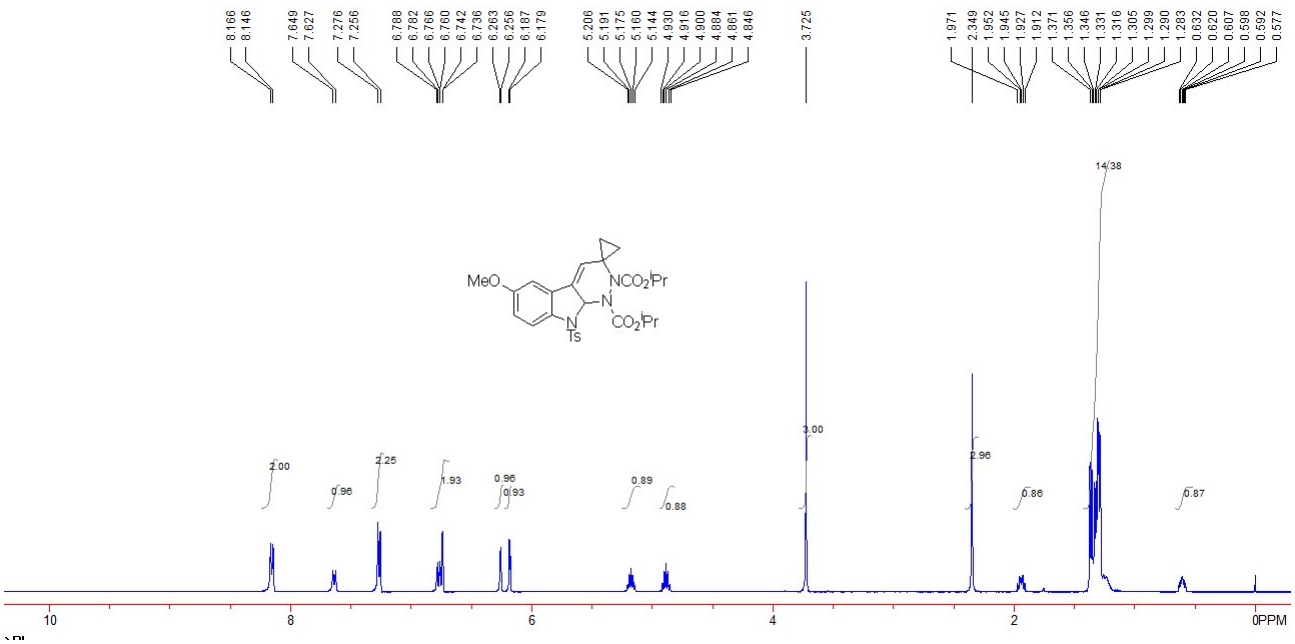


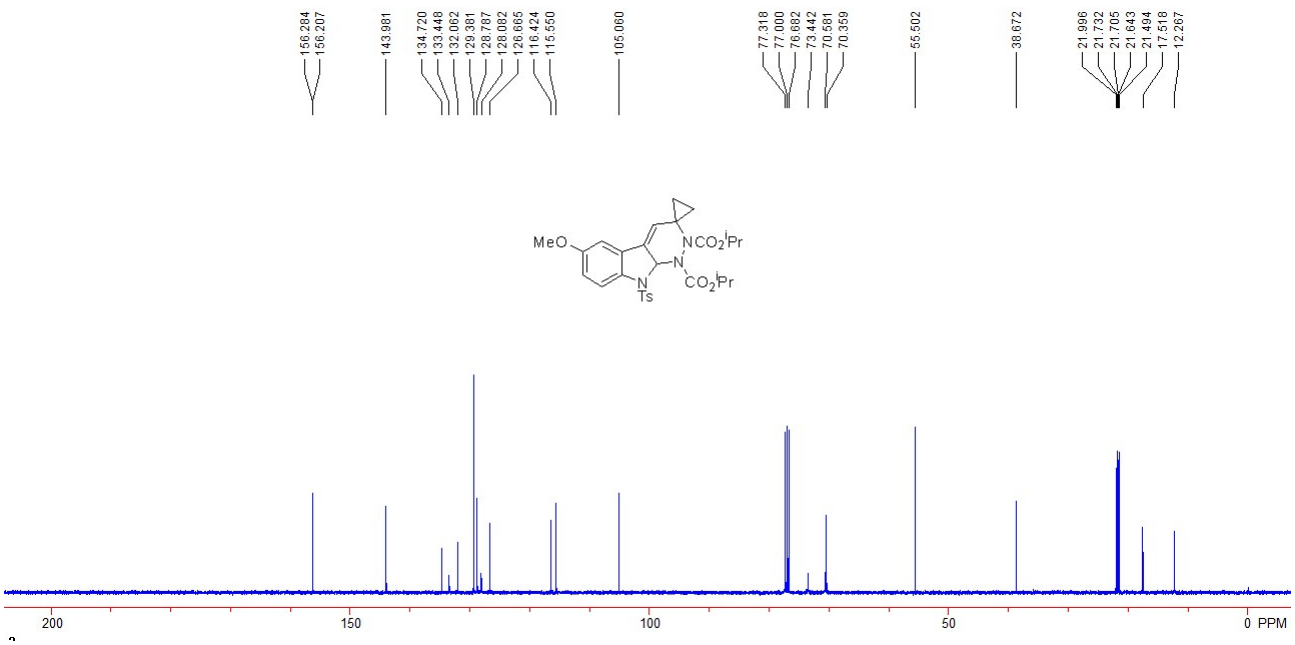


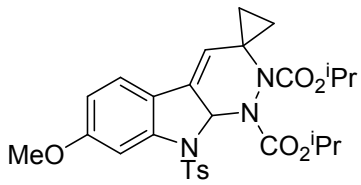


Diisopropyl 6'-methoxy-9'-tosyl-9',9a'-dihydrospiro[cyclopropane-1,3'-pyridazino[3,4-b]indole]-1',2'-dicarboxylate (2d).

A white solid, 73.4 mg, 66% yield. M.p.: 226-228 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.58-0.63 (m, 1H, CH_2), 1.28-1.37 (m, 14H), 1.91-1.97 (m, 1H, CH_2), 2.35 (s, 3H, CH_3), 3.72 (s, 3H, CH_3), 4.85-4.93 (m, 1H, CH), 5.14-5.21 (m, 1H, CH), 6.18 (d, J = 3.2 Hz, 1H, CH), 6.26 (d, J = 2.8 Hz, 1H, CH), 6.74-6.79 (m, 2H, ArH), 7.27 (d, J = 8.0 Hz, 2H, ArH), 7.64 (d, J = 8.8 Hz, 1H, ArH), 8.16 (d, J = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.3, 17.5, 21.5, 21.6, 21.70, 21.73, 22.0, 38.7, 55.5, 70.4, 70.6, 73.4, 105.1, 115.6, 116.4, 126.7, 128.1, 128.8, 129.4, 132.1, 133.4, 134.7, 144.0, 156.2, 156.3. IR (CH_2Cl_2) ν 2961, 2924, 1715, 1363, 1311, 1260, 1170, 1097, 1027, 802, 699, 661 cm^{-1}. HRMS (DART) calcd. for $C_{28}H_{34}N_3O_7S$ (+H$^+$): 556.2112, Found: 556.2111.



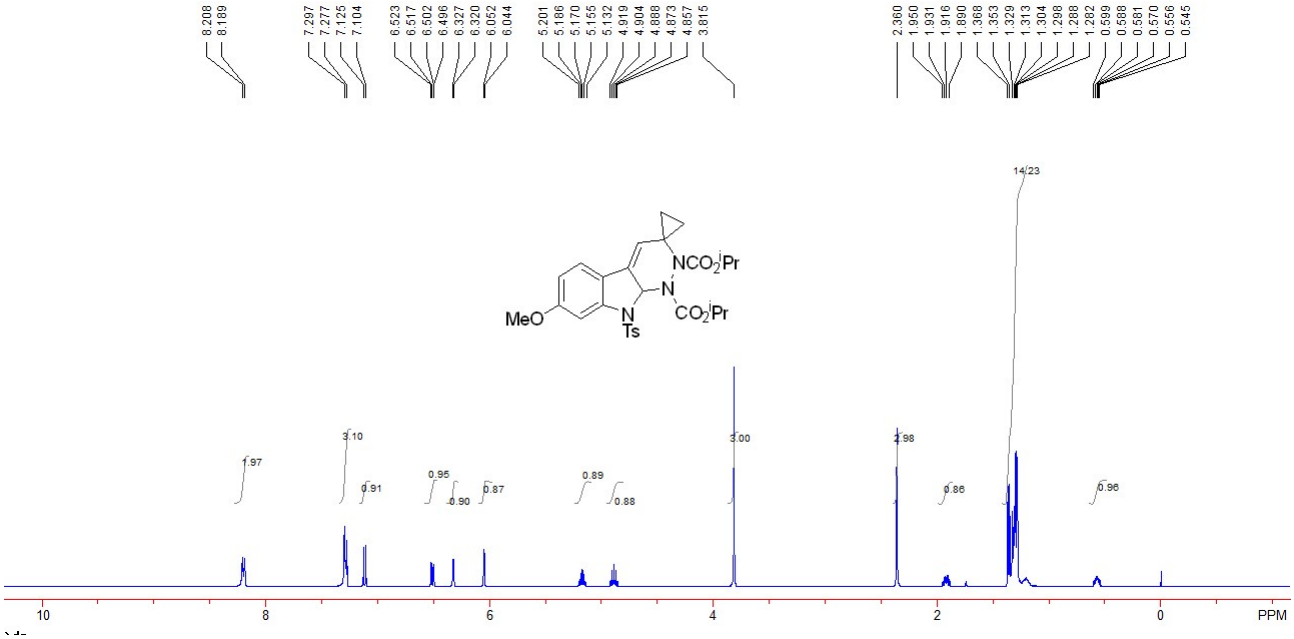


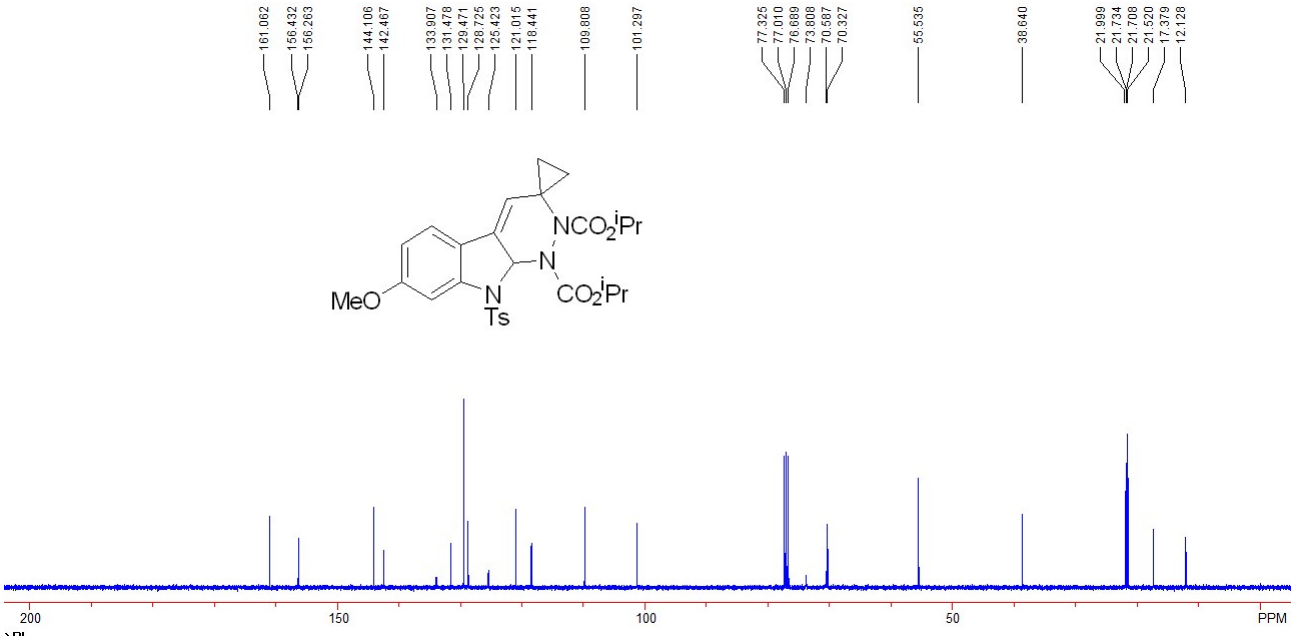


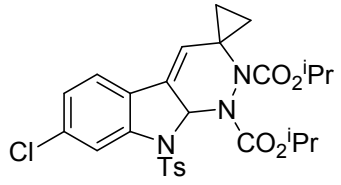
Diisopropyl 7'-methoxy-9'-tosyl-9',9a'-dihydrospiro[cyclopropane-1,3'-pyridazino[3,4-b]indole]-1',2'-dicarboxylate (2e).

A white solid, 61.2 mg, 55% yield. M.p.: 226-228 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.54-0.60 (m, 1H, CH_2), 1.28-1.37 (m, 14H), 1.90-1.95 (m, 1H, CH_2), 2.36 (s, 3H, CH_3), 3.82 (s, 3H, CH_3), 4.86-4.92 (m, 1H, CH), 5.13-5.20 (m, 1H, CH), 6.05 (d, J = 3.2 Hz, 1H, CH), 6.32 (d, J = 2.8

Hz, 1H, CH), 6.51 (dd, J = 2.4 Hz, 8.8 Hz, 1H, ArH), 7.11 (d, J = 8.4 Hz, 1H, ArH), 7.29 (d, J = 8.0 Hz, 3H, ArH), 8.20 (d, J = 7.6 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.1, 17.4, 21.5, 21.71, 21.73, 22.0, 38.6, 55.5, 70.3, 70.6, 73.8, 101.3, 109.8, 118.4, 121.0, 125.4, 128.7, 129.5, 131.5, 133.9, 142.5, 1441, 156.3, 156.4, 161.1. IR (CH_2Cl_2) ν 2958, 1717, 1372, 1261, 1092, 1023, 801, 668 cm^{-1}. HRMS (DART) calcd. for $C_{28}H_{34}N_3O_7S$ ($+H^+$): 556.2112, Found: 556.2112.

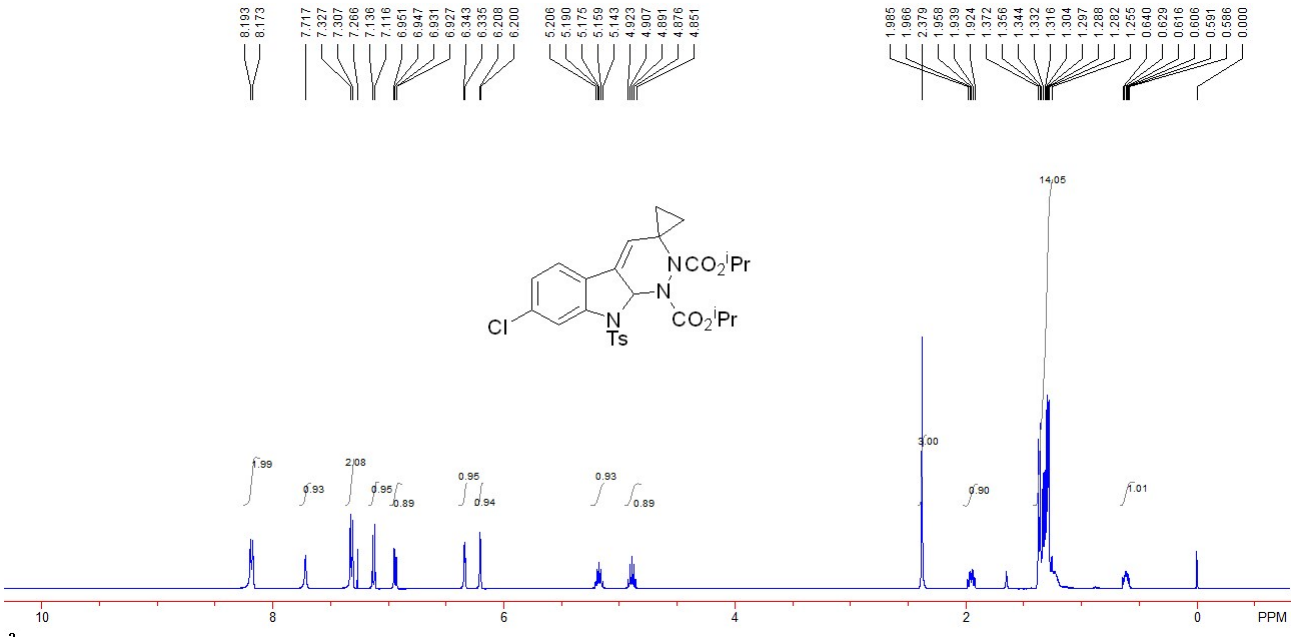


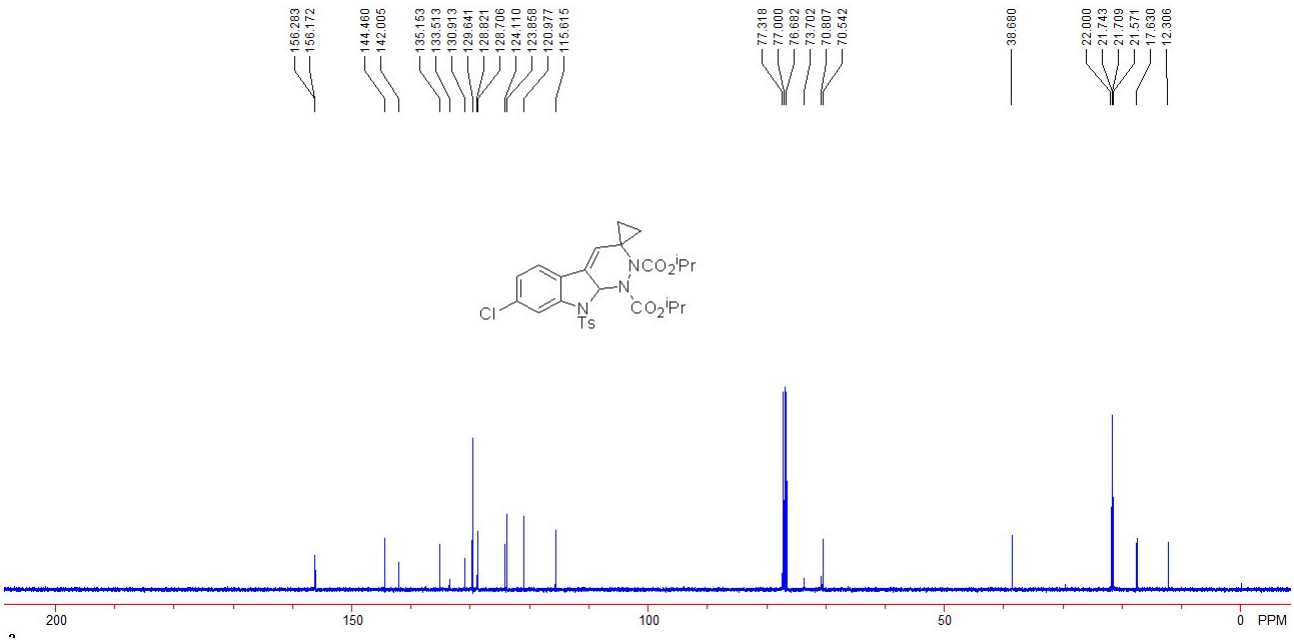


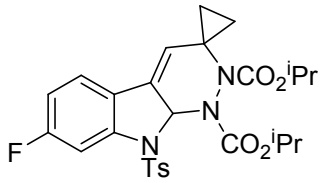


diisopropyl 7'-chloro-9'-tosyl-9',9a'-dihydrospiro[cyclopropane-1,3'-pyridazino[3,4-b]indole]-1',2'-dicarboxylate (2f).

A white solid, 67.2 mg, 60% yield. M.p.: 229-231 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.59-0.64 (m, 1H, CH_2), 1.26-1.37 (m, 14H), 1.92-1.99 (m, 1H, CH_2), 2.38 (s, 3H, CH_3), 4.85-4.92 (m, 1H, CH), 5.14-5.21 (m, 1H, CH), 6.20 (d, *J* = 3.2 Hz, 1H, CH), 6.34 (d, *J* = 3.2 Hz, 1H, CH), 6.94 (dd, *J* = 1.6 Hz, 8.0 Hz, 1H, ArH), 7.13 (d, *J* = 8.0 Hz, 1H, ArH), 7.32 (d, *J* = 8.0 Hz, 2H, ArH), 7.72 (s, 1H, ArH), 8.18 (d, *J* = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.3, 17.6, 21.6, 21.71, 21.74, 22.0, 38.7, 70.5, 70.8, 73.7, 115.6, 121.0, 123.8, 124.1, 128.7, 128.8, 129.6, 130.9, 133.5, 135.2, 142.0, 144.5, 156.2, 156.3. IR (CH_2Cl_2) ν 2984, 2919, 2854, 1717, 1374, 1313, 1174, 1110, 959, 815, 655 cm^{-1}. HRMS (DART) calcd. for $C_{27}H_{31}N_3O_6SCl$ (+H^+): 560.1617, Found: 560.1616.

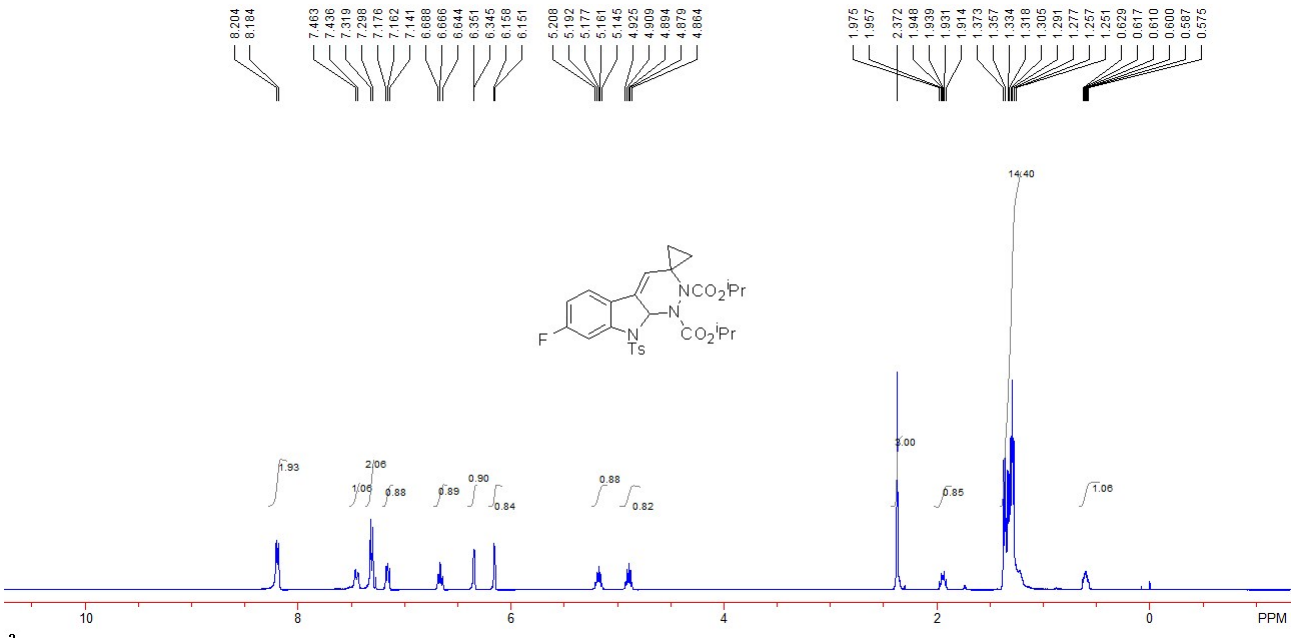






diisopropyl 7'-fluoro-9'-tosyl-9',9a'-dihydrospiro[cyclopropane-1,3'-pyridazino[3,4-b]indole]-1',2'-dicarboxylate (2g).

A white solid, 76.2 mg, 70% yield. M.p.: 223-225 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.58-0.63 (m, 1H, CH_2), 1.25-1.37 (m, 14H), 1.91-1.98 (m, 1H, CH_2), 2.37 (s, 3H, CH_3), 4.86-4.92 (m, 1H, CH), 5.14-5.21 (m, 1H, CH), 6.15 (d, *J* = 2.8 Hz, 1H, CH), 6.35 (d, *J* = 2.42 Hz, 1H, CH), 6.67 (t, *J* = 8.8 Hz, 1H, ArH), 7.14-7.18 (m,1H, ArH), 7.31 (d, *J* = 8.4 Hz, 2H, ArH), 7.45 (d, *J* = 10.8 Hz, 1H, ArH), 8.19 (d, *J* = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.2, 17.5, 21.5, 21.65, 21.67, 21.72, 22.0, 38.6, 70.4, 70.7, 73.8, 103.5 (d, *J* = 28.8 Hz), 110.6 (d, *J* = 23.4 Hz), 121.2 (d, *J* = 10.0 Hz), 121.6 (d, *J* = 2.7 Hz), 127.8, 128.7, 129.6, 130.9 (d, *J* = 1.1 Hz), 133.6, 142.4 (d, *J* = 11.9 Hz), 144.4, 156.2, 156.3, 163.5 (d, *J* = 245.1 Hz). ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -108.73. IR (CH_2Cl_2) ν 2961, 2924, 1716, 1374, 1311, 1261, 1093, 1023, 987, 802, 662 cm^{-1}. HRMS (DART) calcd. for $C_{27}H_{31}N_3O_6SF$ (+H^+): 544.1912, Found: 544.1912.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7.298
7.176
7.162
7.141
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6.345
6.158
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1.914
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1.357
1.334
1.318
1.305
1.291
1.277
1.257
1.251
0.629
0.617
0.610
0.600
0.587
0.575
NCO2iPr
N
CO2iPr
F
N
Ts
14.40
9.00
1.93
2.06
1.06
0.88
0.89
0.90
0.84
0.88
0.82
0.85
1.06
10
8
6
4
2
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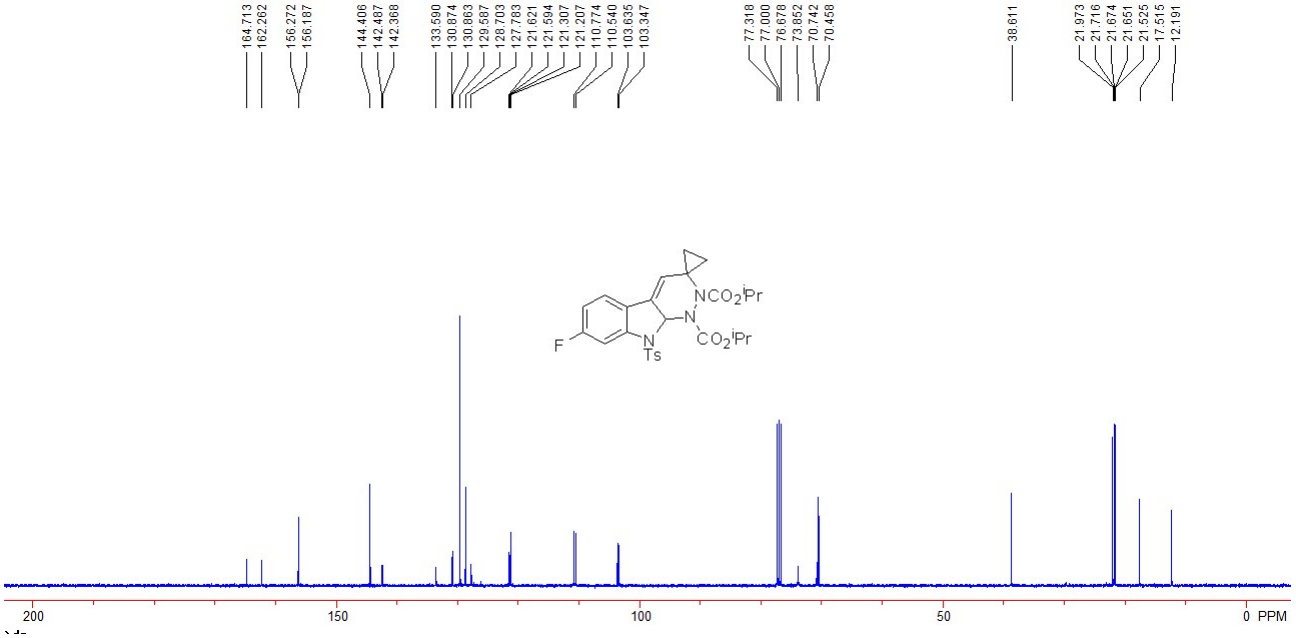
PPM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70.458
38.611
21.973
21.716
21.674
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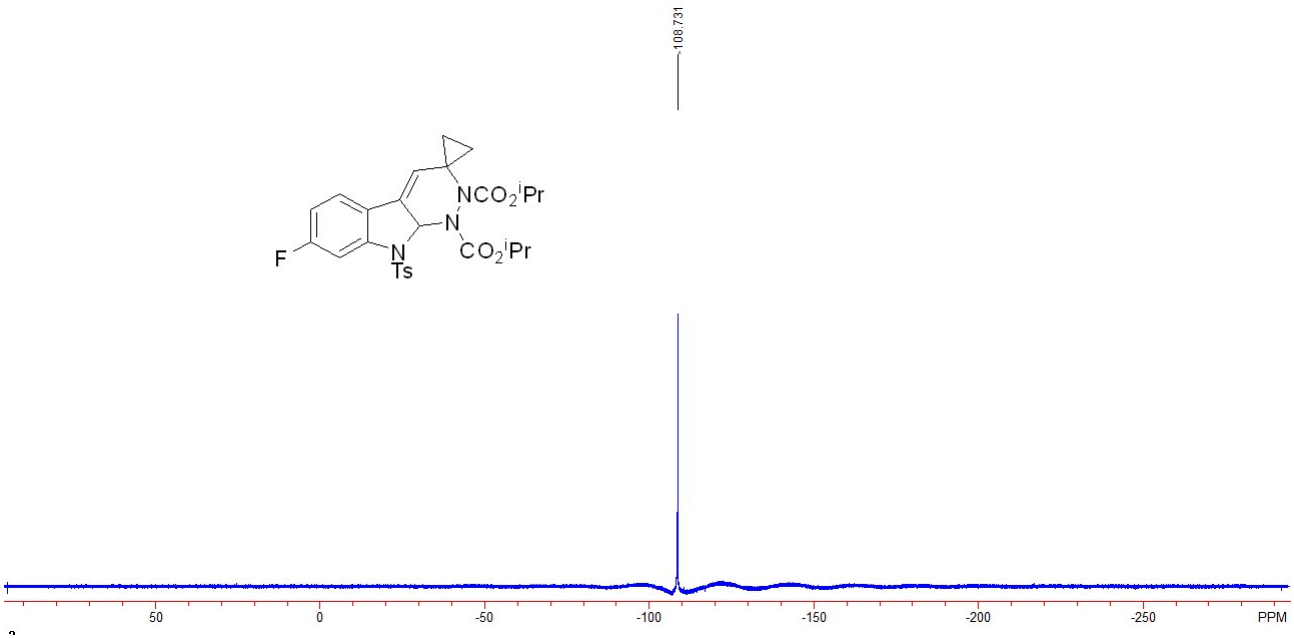
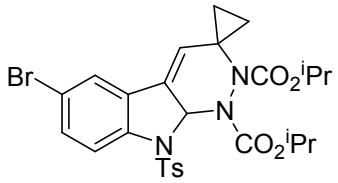
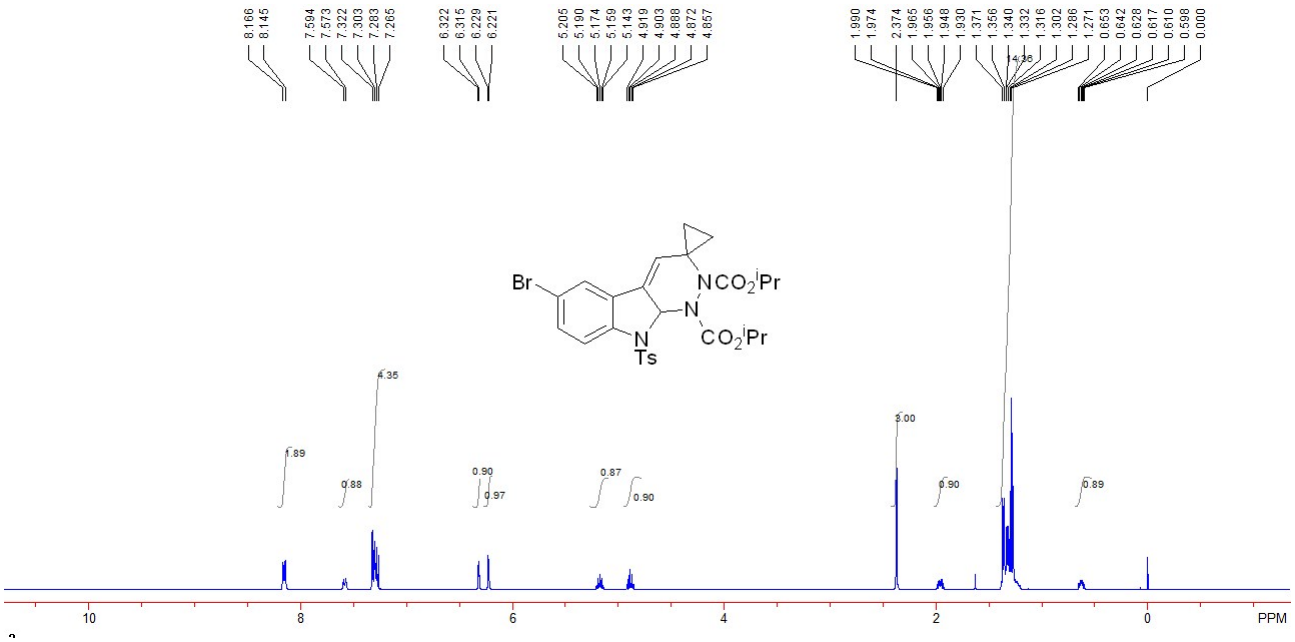
F
N
Ts
200
150
100
50
0 PPM

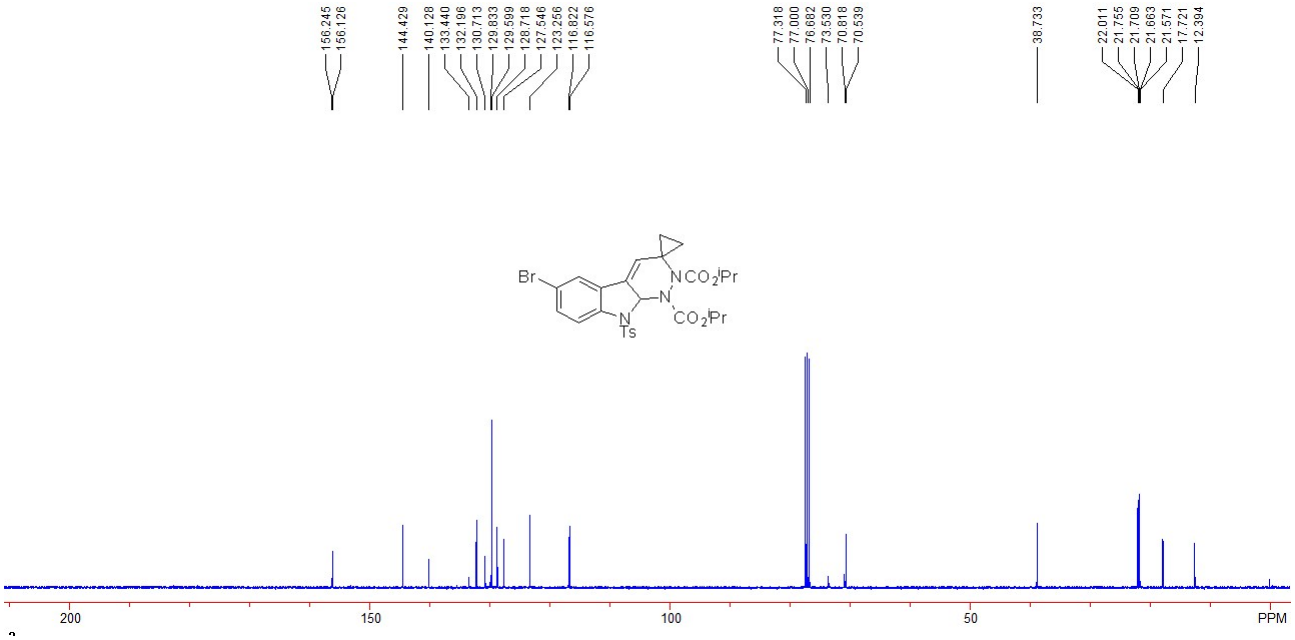


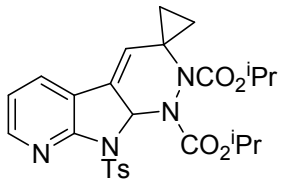


diisopropyl 6'-bromo-9'-tosyl-9',9a'-dihydrospiro[cyclopropane-1,3'-pyridazino[3,4-b]indole]-1',2'-dicarboxylate (2h).

A white solid, 76.1 mg, 63% yield. M.p.: 229-231 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.60-0.65 (m, 1H, CH_2), 1.27-1.37 (m, 14H), 1.93-1.99 (m, 1H, CH_2), 2.37 (s, 3H, CH_3), 4.86-4.92 (m, 1H, CH), 5.14-5.20 (m, 1H, CH), 6.22 (d, J = 3.2 Hz, 1H, CH), 6.32 (d, J = 2.8 Hz, 1H, CH), 7.26-7.32 (m, 4H, ArH), 7.58 (d, J = 8.4 Hz, 1H, ArH), 8.15 (d, J = 8.4 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.4, 17.7, 21.57, 21.66, 21.71, 21.8, 22.0, 38.7, 70.5, 70.8, 73.5, 116.6, 116.8, 123.2, 127.5, 128.7, 129.6, 129.8, 130.7, 132.2, 133.4, 140.1, 144.4, 156.1, 156.2. δ -38.93. IR (CH_2Cl_2) ν 2984, 2916, 1716, 1456, 1372, 1316, 1174, 1105, 812, 661 cm^{-1}. HRMS (DART) calcd. for $C_{27}H_{31}N_3O_6SBr$ ($+H^+$): 604.1111, Found: 604.1109.



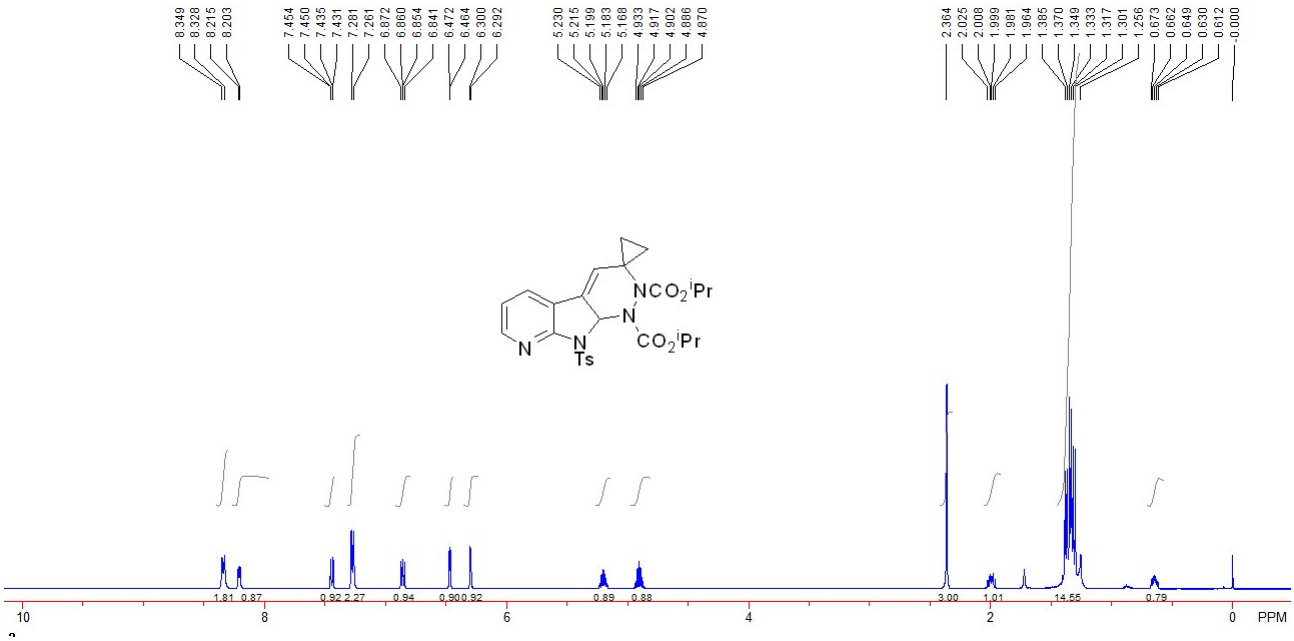


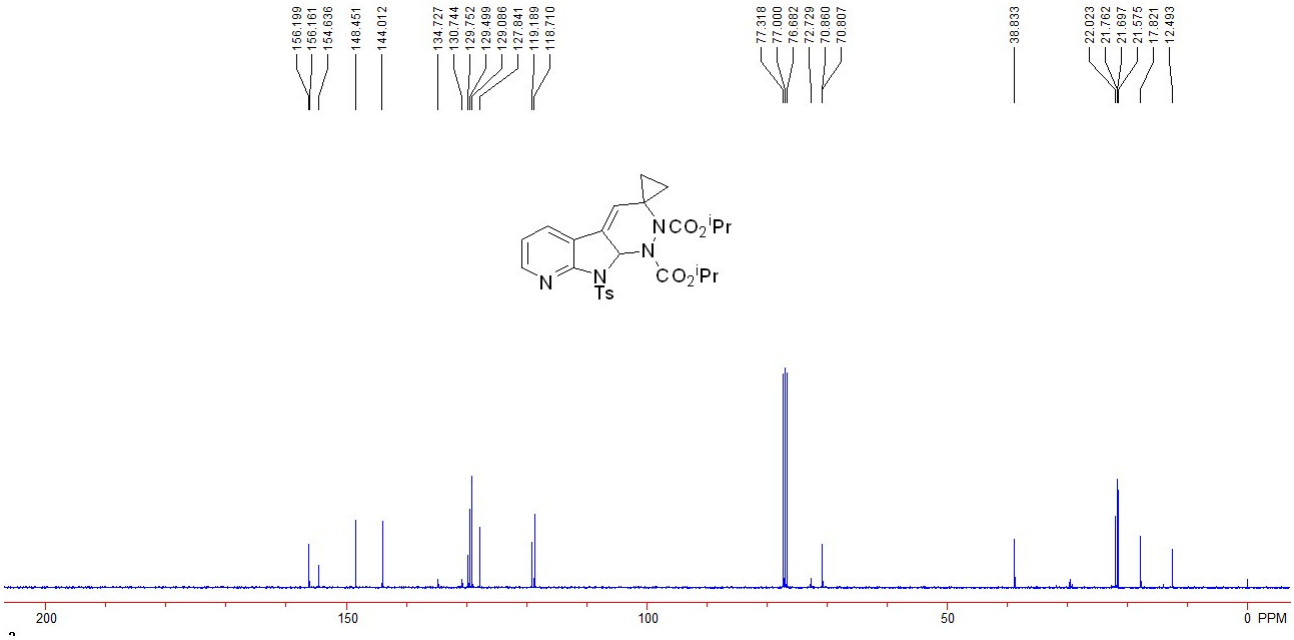


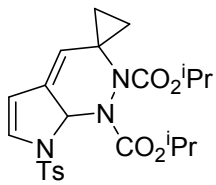
diisopropyl 9'-tosyl-9',9a'-dihydrospiro[cyclopropane-1,3'-pyrido[3',2':4,5]pyrrolo[2,3-c]pyridazine]-1',2'-dicarboxylate (2i).

A white solid, 42.1 mg, 40% yield. M.p.: 214-216 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.61-0.67 (m, 1H, CH_2), 1.26-1.38 (m, 14H), 1.96-2.02 (m, 1H, CH_2), 2.36 (s, 3H, CH_3), 4.87-4.93 (m, 1H, CH), 5.17-5.23 (m, 1H, CH), 6.29 (d, *J* = 3.2 Hz, 1H, CH), 6.47 (d, *J* = 3.2 Hz, 1H, CH), 6.84-

6.87 (m, 1H, ArH), 7.27 (d, J = 8.0 Hz, 2H, ArH), 7.44 (dd, J = 1.6 Hz, 7.6 Hz, 1H, ArH), 8.21 (d, J = 4.8 Hz, 1H, ArH), 8.34 (d, J = 8.4 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.5, 17.8, 21.6, 21.7, 21.8, 22.0, 38.8, 70.8, 70.9, 72.7, 118.7, 119.2, 127.8, 129.1, 129.5, 129.8, 130.7, 134.7, 144.0, 148.4, 154.6, 156.16, 156.20. IR (CH_2Cl_2) ν 2979, 2930, 1716, 1373, 1312, 1176, 1108, 954, 812, 666 cm^{-1}. HRMS (DART) calcd. for $C_{26}H_{31}N_4O_6S$ ($+H^+$): 527.1959, Found: 527.1959.

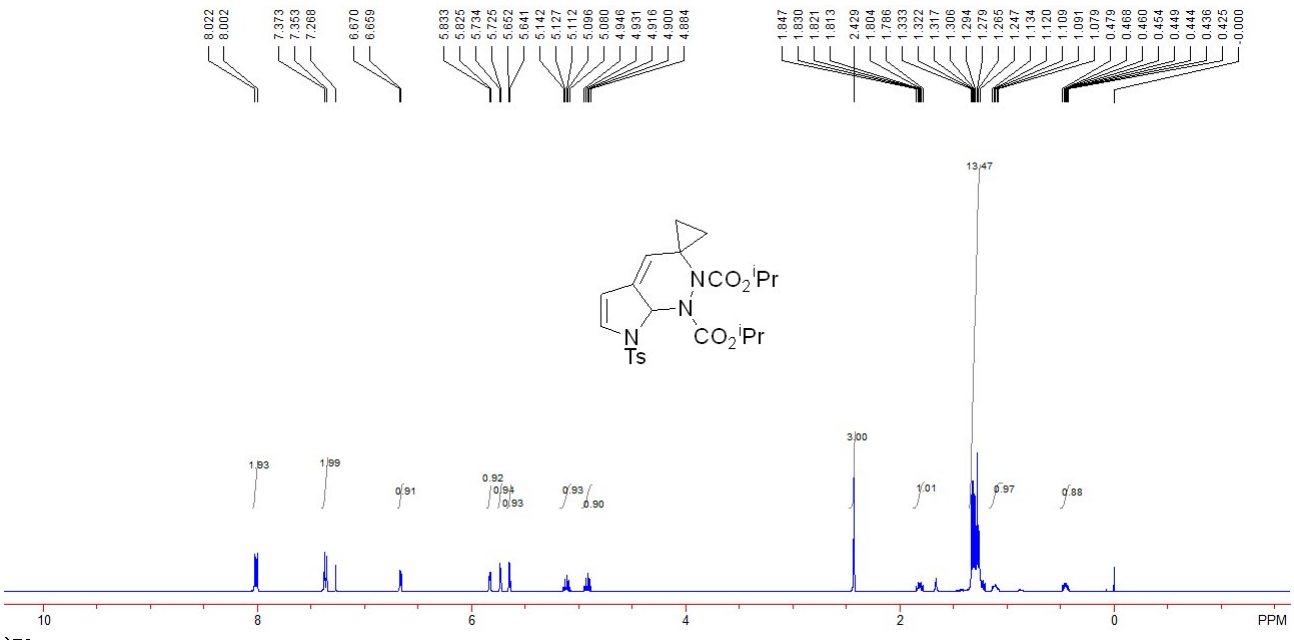


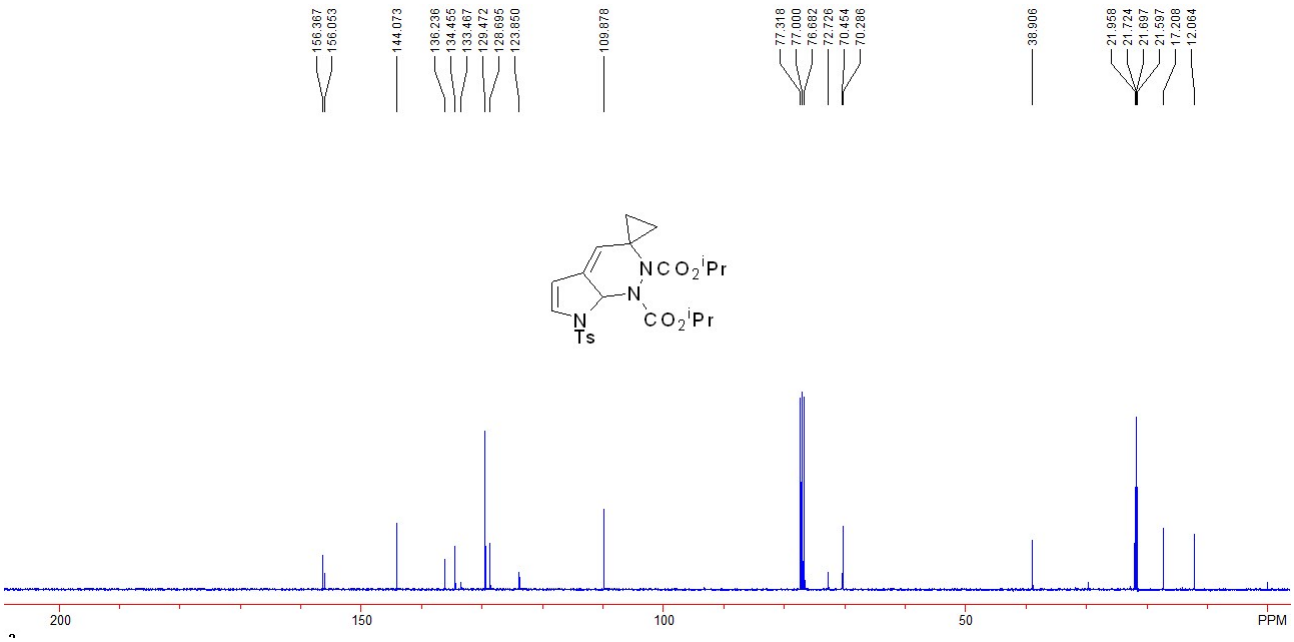


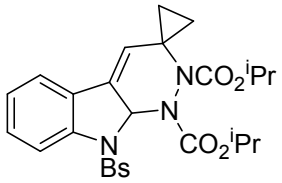


diisopropyl 7'-tosyl-7',7a'-dihydrospiro[cyclopropane-1,3'-pyrrolo[2,3-c]pyridazine]-1',2'-dicarboxylate (2j).

A white solid, 57.1 mg, 60% yield. M.p.: 161-163 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.42-0.48 (m, 1H, CH_2), 1.08-1.13 (m, 1H, CH_2), 1.25-1.33 (m, 13H), 1.79-1.85 (m, 1H, CH_2), 2.43 (s, 3H, CH_3), 4.88-4.95 (m, 1H, CH), 5.08-5.14 (m, 1H, CH), 5.64 (d, *J* = 4.4 Hz, 1H), 5.73 (d, *J* = 3.6 Hz, 1H), 5.83 (d, *J* = 3.2 Hz, 1H), 6.66 (d, *J* = 4.4 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 1H, ArH), 8.01 (d, *J* = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.1, 17.2, 21.6, 21.70, 21.72, 22.0, 38.9, 70.3, 70.4, 72.7, 109.9, 123.8, 128.7, 129.5, 133.5, 134.4, 136.2, 144.1, 156.0, 156.4. IR (CH_2Cl_2) ν 2982, 2922, 1716, 1368, 1313, 1169, 1108, 1096, 964, 741, 664 cm^{-1}. HRMS (DART) calcd. for $C_{23}H_{30}N_3O_6S$ (+H$^+$): 476.1850, Found: 476.1851.

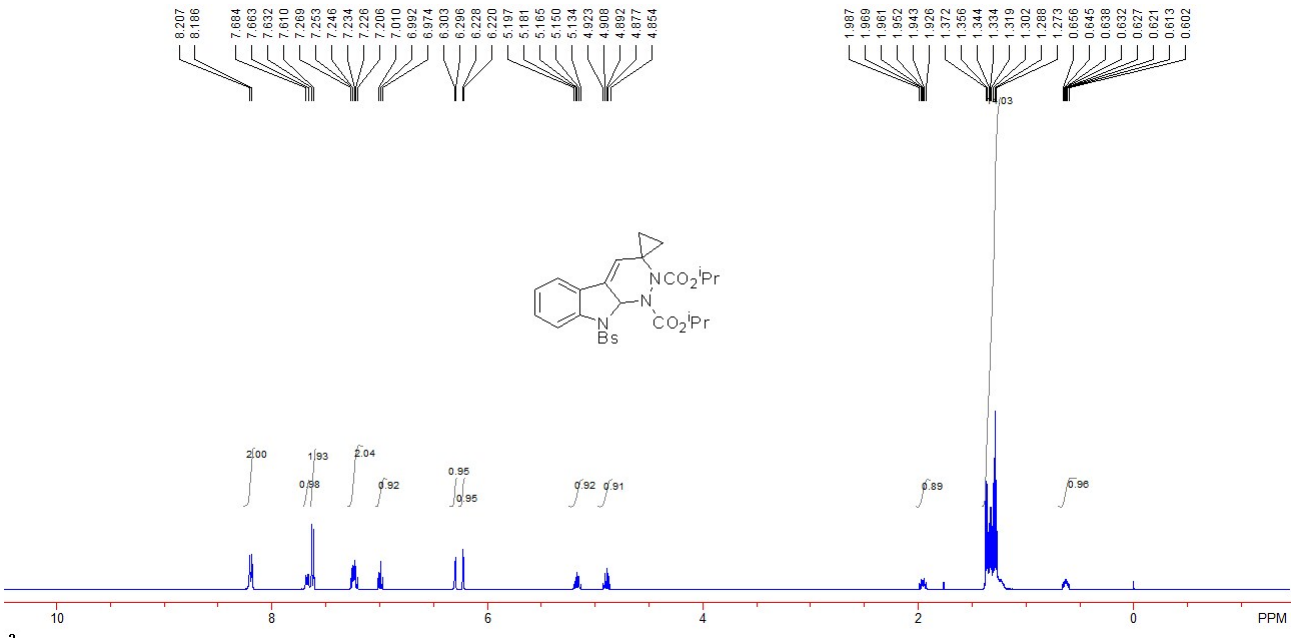


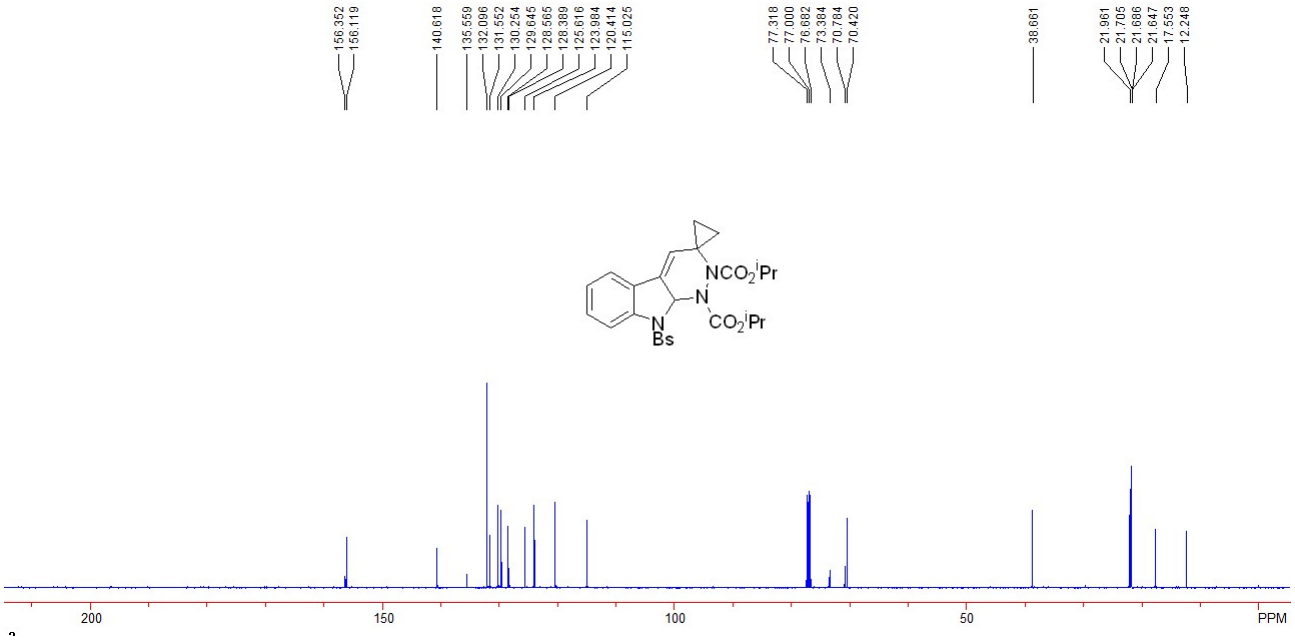


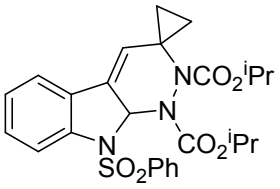


diisopropyl 9'-((4-bromophenyl)sulfonyl)-9',9a'-dihydrospiro[cyclopropane-1,3'-pyridazino[3,4-b]indole]-1',2'-dicarboxylate (2k).

A white solid, 102.7 mg, 87% yield. M.p.: 181-183 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.60-0.66 (m, 1H, CH_2), 1.27-1.37 (m, 14H), 1.93-1.99 (m, 1H, CH_2), 4.85-4.92 (m, 1H, CH), 5.13-5.201 (m, 1H, CH), 6.22 (d, *J* = 3.2 Hz, 1H, CH), 6.30 (d, *J* = 2.8 Hz, 1H, CH), 6.99 (t, *J* = 7.2 Hz, 1H, ArH), 7.21-7.27 (m, 2H, ArH), 7.62 (d, *J* = 8.8 Hz, 2H, ArH), 7.67 (d, *J* = 8.4 Hz, 1H, ArH), 8.20 (d, *J* = 8.4 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.2, 17.6, 21.65, 21.69, 21.7, 22.0, 38.7, 70.4, 70.8, 73.4, 115.0, 120.4, 124.0, 125.6, 128.4, 128.6, 129.6, 130.2, 131.6, 132.1, 135.6, 140.6, 156.1, 156.4. IR (CH_2Cl_2) ν 2919, 2848, 1716, 1453, 1372, 1313, 1275, 1175, 1110, 943, 740 cm^{-1}. HRMS (DART) calcd. for $C_{26}H_{29}N_3O_6SBr$ ($+H^+$): 590.0955, Found: 590.0955.



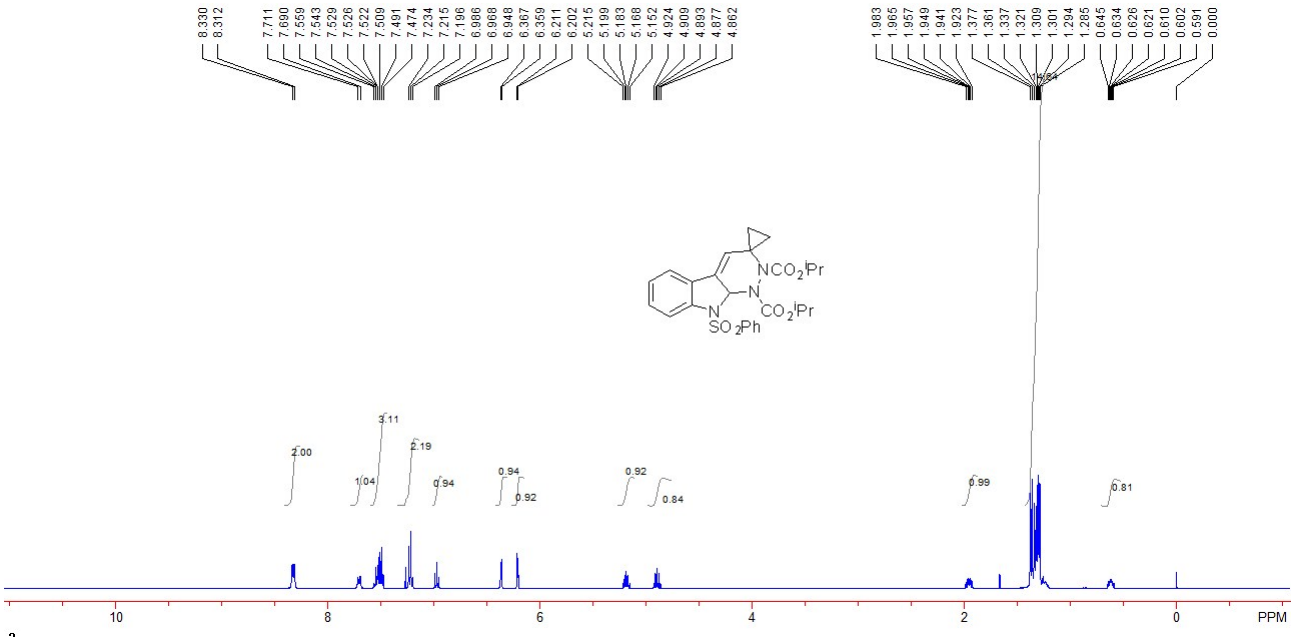


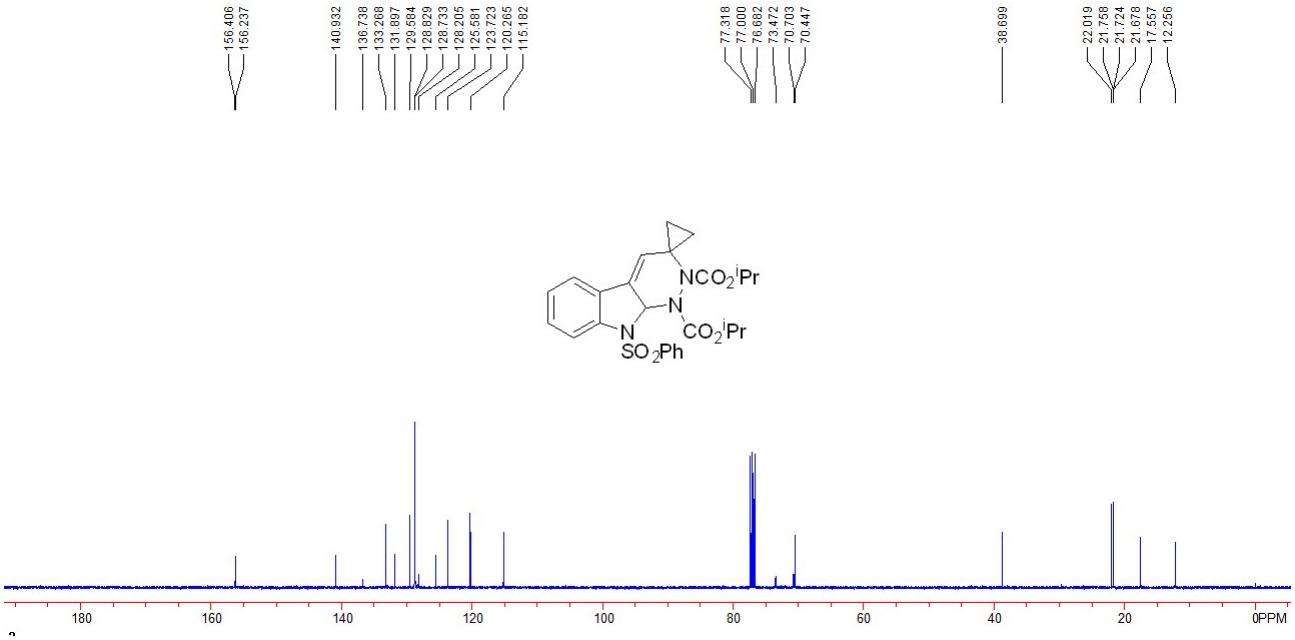


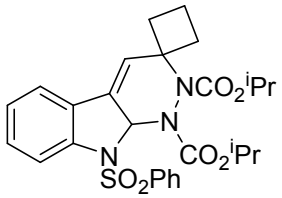
diisopropyl 9'-(phenylsulfonyl)-9',9a'-dihydrospiro[cyclopropane-1,3'-pyridazino[3,4-b]indole]-1',2'-dicarboxylate (2l).

A white solid, 71.7 mg, 70% yield. M.p.: 179-181 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.59-0.64 (m, 1H, CH_2), 1.28-1.38 (m, 14H), 1.92-1.98 (m, 1H, CH_2), 4.86-4.92 (m, 1H, CH), 5.15-5.22

(m, 1H, CH), 6.21 (d, J = 3.6 Hz, 1H), 6.36 (d, J = 3.2 Hz, 1H), 6.97 (t, J = 7.6 Hz, 1H, ArH), 7.22 (t, J = 7.6 Hz, 2H, ArH), 7.47-7.56 (m, 3H, ArH), 7.70 (d, J = 8.4 Hz, 1H, ArH), 8.18 (d, J = 7.2 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.2, 17.6, 21.67, 21.72, 21.76, 22.0, 38.7, 70.4, 70.7, 73.5, 115.2, 120.3, 123.7, 125.6, 128.2, 128.7, 128.8, 129.6, 131.9, 133.3, 136.7, 140.9, 156.2, 156.4. IR (CH_2Cl_2) ν 2977, 2922, 2851, 1716, 1453, 1370, 1313, 1275, 1177, 1110, 950, 754 cm^{-1}. HRMS (DART) calcd. for $C_{26}H_{30}N_3O_6S$ (+H$^+$): 512.1850, Found: 512.1849.

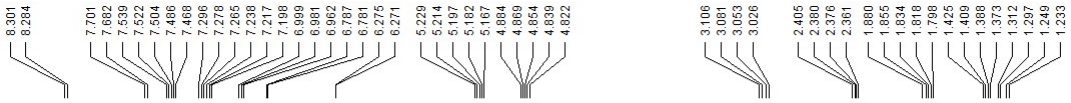


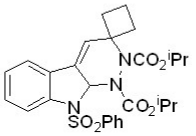


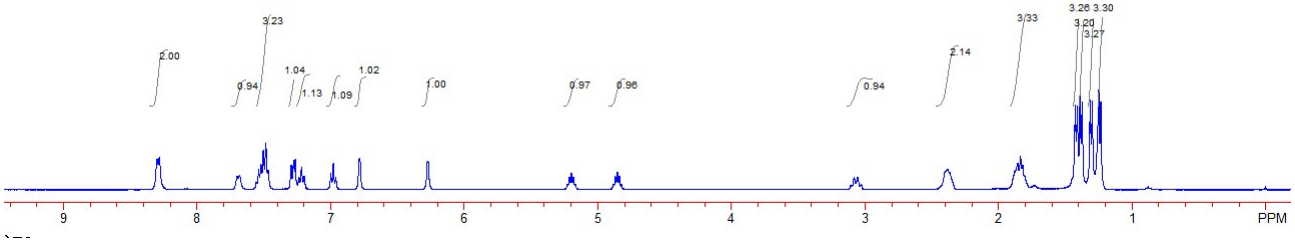


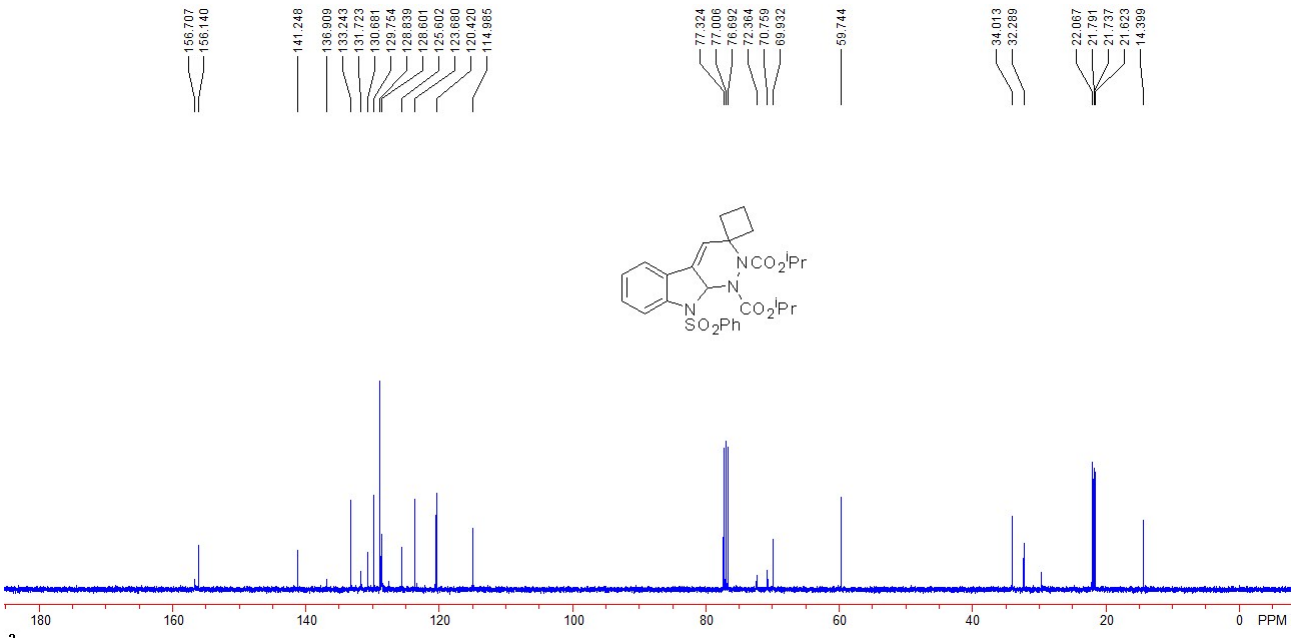
diisopropyl 9'-(phenylsulfonyl)-9',9a'-dihydrospiro[cyclobutane-1,3'-pyridazino[3,4-b]indole]-1',2'-dicarboxylate (2m).

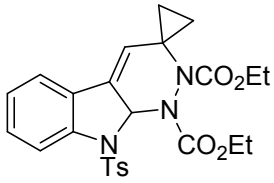
A white solid, 57.7 mg, 55% yield. M.p.: 173-175 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.24 (d, *J* = 6.4 Hz, 3H, CH_3), 1.30 (d, *J* = 6.0 Hz, 3H, CH_3), 1.38 (d, *J* = 6.0 Hz, 3H, CH_3), 1.42 (d, *J* = 6.4 Hz, 3H, CH_3), 1.80-1.88 (m, 3H, CH_2), 2.36-2.40 (m, 2H, CH_2), 3.03-3.11 (m, 1H, CH_2), 4.82-4.88 (m, 1H, CH), 5.17-5.23 (m, 1H, CH), 6.27 (d, *J* = 1.6 Hz, 1H, CH), 6.78 (d, *J* = 2.4 Hz, 1H, CH), 6.98 (t, *J* = 7.2 Hz, 1H, ArH), 7.22 (t, *J* = 8.0 Hz, 1H, ArH), 7.29 (d, *J* = 7.2 Hz, 1H, ArH), 7.47-7.54 (m, 3H, ArH), 7.69 (d, *J* = 7.6 Hz, 1H, ArH), 8.29 (d, *J* = 6.8 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 14.4, 21.6, 21.7, 21.8, 22.1, 32.3, 34.0, 59.7, 69.9, 70.7, 72.4, 115.0, 120.4, 123.7, 125.6, 128.6, 128.8, 129.8, 130.7, 131.7, 133.2, 136.9, 141.2, 156.1, 156.7. IR (CH_2Cl_2) ν 2977, 1715, 1456, 1370, 1314, 1288, 1176, 1109, 980, 754 cm^{-1}. HRMS (DART) calcd. for $C_{27}H_{32}N_3O_6S$ (+H$^+$): 526.2006, Found: 526.2005.





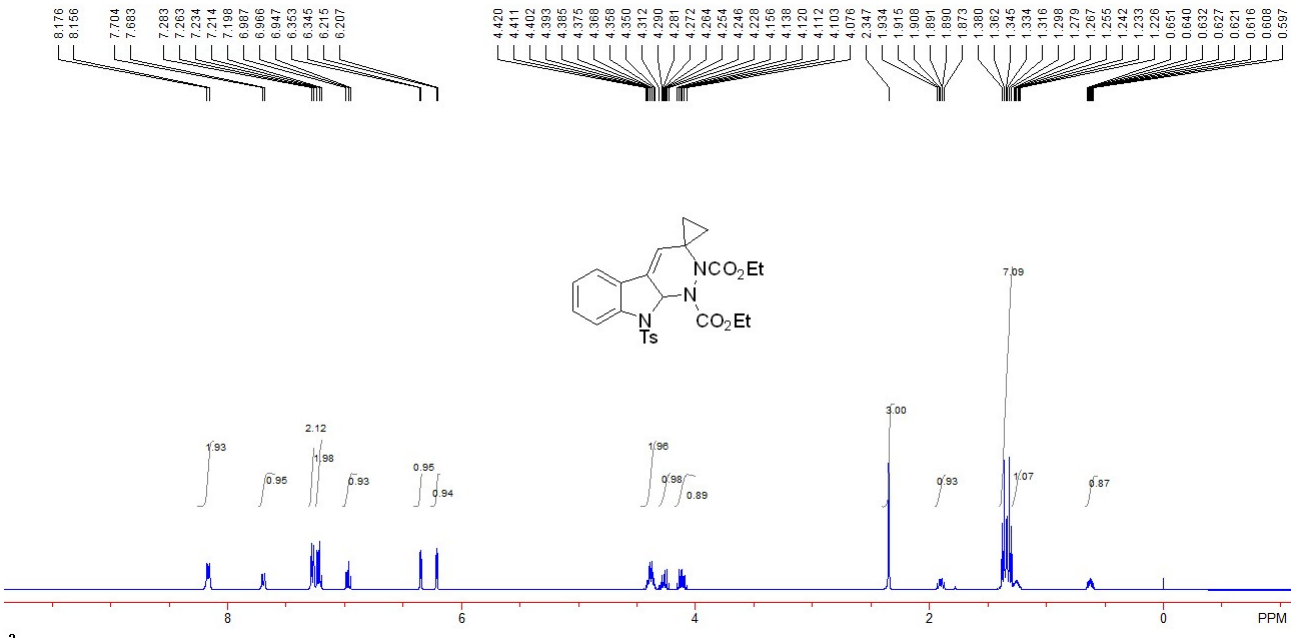


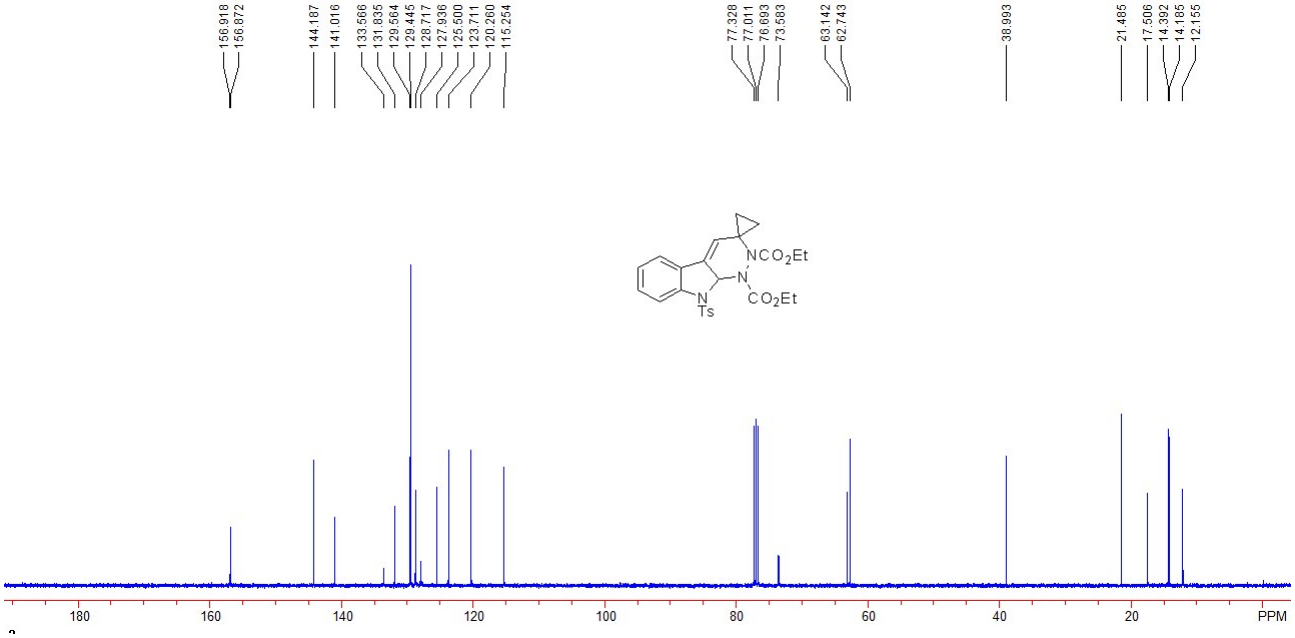


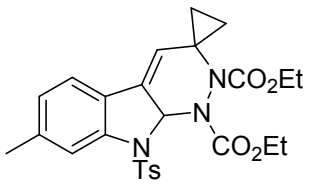


diethyl 9'-tosyl-9',9a'-dihydrospiro[cyclopropane-1,3'-pyridazino[3,4-b]indole]-1',2'-dicarboxylate (3a).

A white solid, 66.6 mg, 67% yield. M.p.: 220-222 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.60-0.65 (m, 1H, CH_2), 1.22-1.28 (m, 1H), 1.30-1.38 (m, 7H), 1.87-1.93 (m, 1H, CH_2), 2.35 (s, 3H, CH_3), 4.08-4.16 (m, 1H), 4.23-4.31 (m, 1H), 4.37-4.39 (m, 2H), 6.21 (d, *J* = 3.2 Hz, 1H, CH), 6.35 (d, *J* = 3.2 Hz, 1H, CH), 6.97 (t, *J* = 8.0 Hz, 1H, ArH), 7.22 (d, *J* = 8.0 Hz, 2H, ArH), 7.27 (d, *J* = 8.0 Hz, 2H, ArH), 7.69 (d, *J* = 8.4 Hz, 1H, ArH), 8.17 (d, *J* = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.2, 14.2, 14.4, 17.5, 21.5, 39.0, 62.7, 63.1, 73.6, 115.2, 120.3, 123.7, 125.5, 127.9, 128.7, 129.4, 129.6, 131.8, 133.6, 141.0, 144.2, 156.87, 156.92. IR (CH_2Cl_2) ν 2956, 2924, 2846, 1718, 1458, 1367, 1324, 1272, 1168, 1089, 945, 754, 662 cm^{-1}. HRMS (DART) calcd. for $C_{25}H_{28}N_3O_6S$ ($+H^+$): 498.1693, Found: 498.1691.



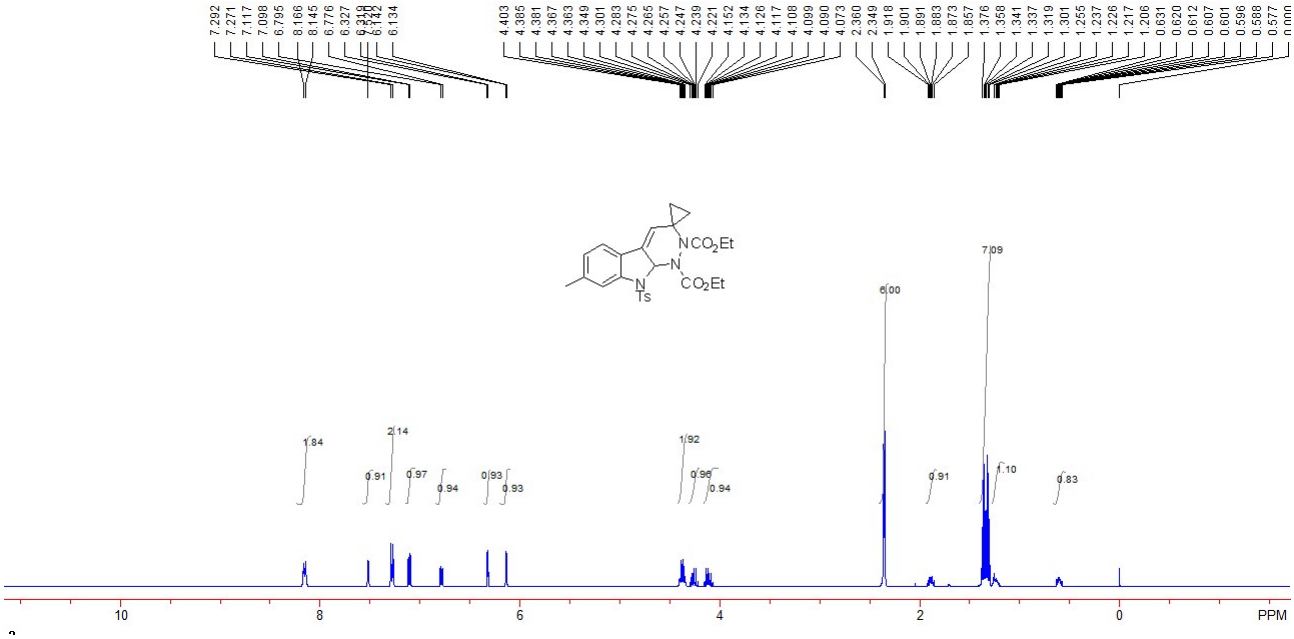


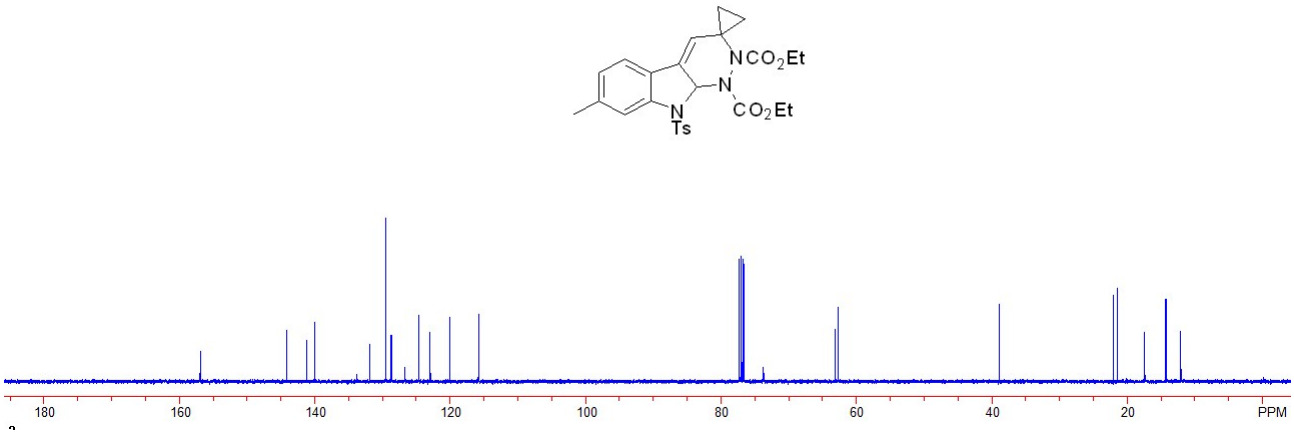


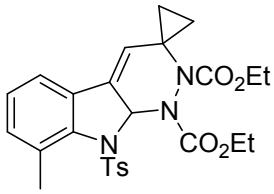
diethyl 7'-methyl-9'-tosyl-9',9a'-dihydrospiro[cyclopropane-1,3'-pyridazino[3,4-b]indole]-1',2'-dicarboxylate (3b).

A white solid, 67.4 mg, 66% yield. M.p.: 229-231 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.58-0.63 (m, 1H, CH_2), 1.21-1.26 (m, 1H, CH_2), 1.30-1.38 (m, 7H), 1.86-1.92 (m, 1H, CH_2), 2.35 (s, 3H, CH_3), 2.36 (s, 3H, CH_3), 4.07-4.15 (m, 1H), 4.22-4.30 (m, 1H), 4.35-4.40 (m, 2H), 6.14 (d, J = 3.2

Hz, 1H, CH), 6.32 (d, *J* = 3.2 Hz, 1H, CH), 6.79 (d, *J* = 7.6 Hz, 1H, ArH), 7.11 (d, *J* = 7.6 Hz, 1H, ArH), 7.28 (d, *J* = 8.4 Hz, 2H, ArH), 7.52 (s, 1H, ArH), 8.16 (d, *J* = 8.4 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.1, 14.2, 14.4, 17.5, 21.5, 22.1, 39.0, 62.7, 63.1, 73.8, 115.8, 120.0, 122.9, 124.6, 126.7, 128.7, 129.4, 131.8, 133.8, 140.0, 141.2, 144.1, 156.9, 157.0. IR (CH_2Cl_2) ν 2927, 1715, 1359, 1315, 1275, 1165, 1091, 872, 809, 731 cm^{-1}. HRMS (DART) calcd. for $C_{26}H_{30}O_6N_3S$: 512.1850, Found: 512.1843.

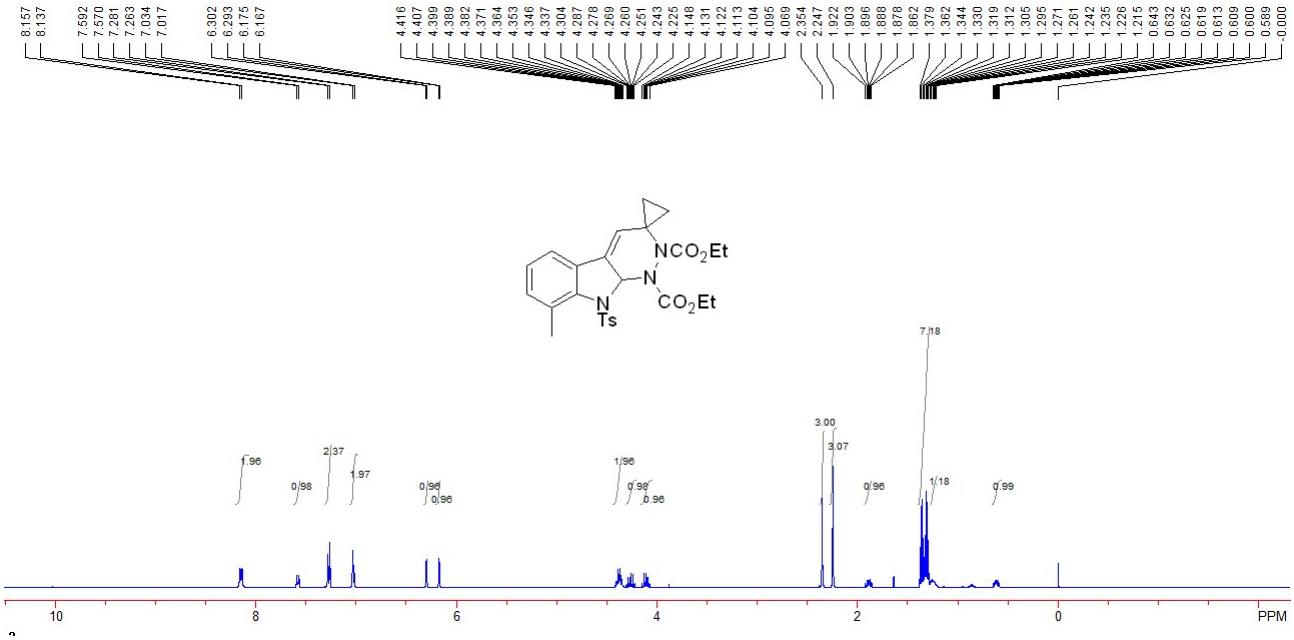


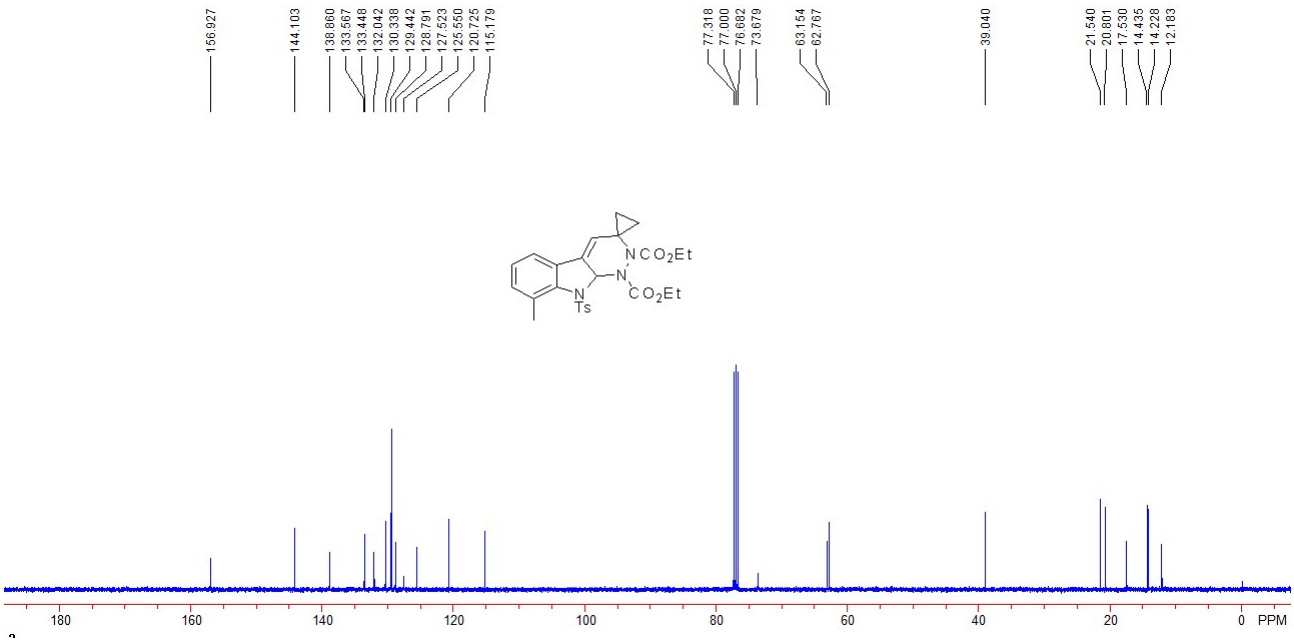


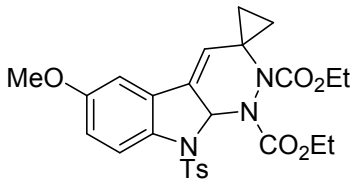


diethyl 8'-methyl-9'-tosyl-9',9a'-dihydrospiro[cyclopropane-1,3'-pyridazino[3,4-b]indole]-1',2'-dicarboxylate (3c).

A white solid, 69.5 mg, 68% yield. M.p.: 239-241 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.59-0.62 (m, 1H, CH_2), 1.22-1.27 (m, 1H, CH_2), 1.30-1.38 (m, 7H), 1.86-1.92 (m, 1H, CH_2), 2.25 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 4.07-4.15 (m, 1H), 4.22-4.30 (m, 1H), 4.35-4.42 (m, 2H), 6.17 (d, *J* = 3.2 Hz, 1H, CH), 6.30 (d, *J* = 3.6 Hz, 1H, CH), 7.02 (d, *J* = 6.8 Hz, 2H, ArH), 7.27 (d, *J* = 7.2 Hz, 2H, ArH), 7.58 (d, *J* = 8.8 Hz, 1H, ArH), 8.15 (d, *J* = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.2, 14.2, 14.4, 17.5, 20.8, 21.5, 39.0, 62.8, 63.2, 73.7, 115.2, 120.7, 125.6, 127.5, 128.8, 129.4, 130.3, 132.0, 133.4, 133.6, 138.9, 144.1, 156.9. IR (CH_2Cl_2) ν 2958, 2922, 2851, 1717, 1469, 1375, 1325, 1272, 1170, 1089, 812, 663 cm^{-1}. HRMS (DART) calcd. for $C_{26}H_{30}O_6N_3S$: 512.1850, Found: 512.1848.

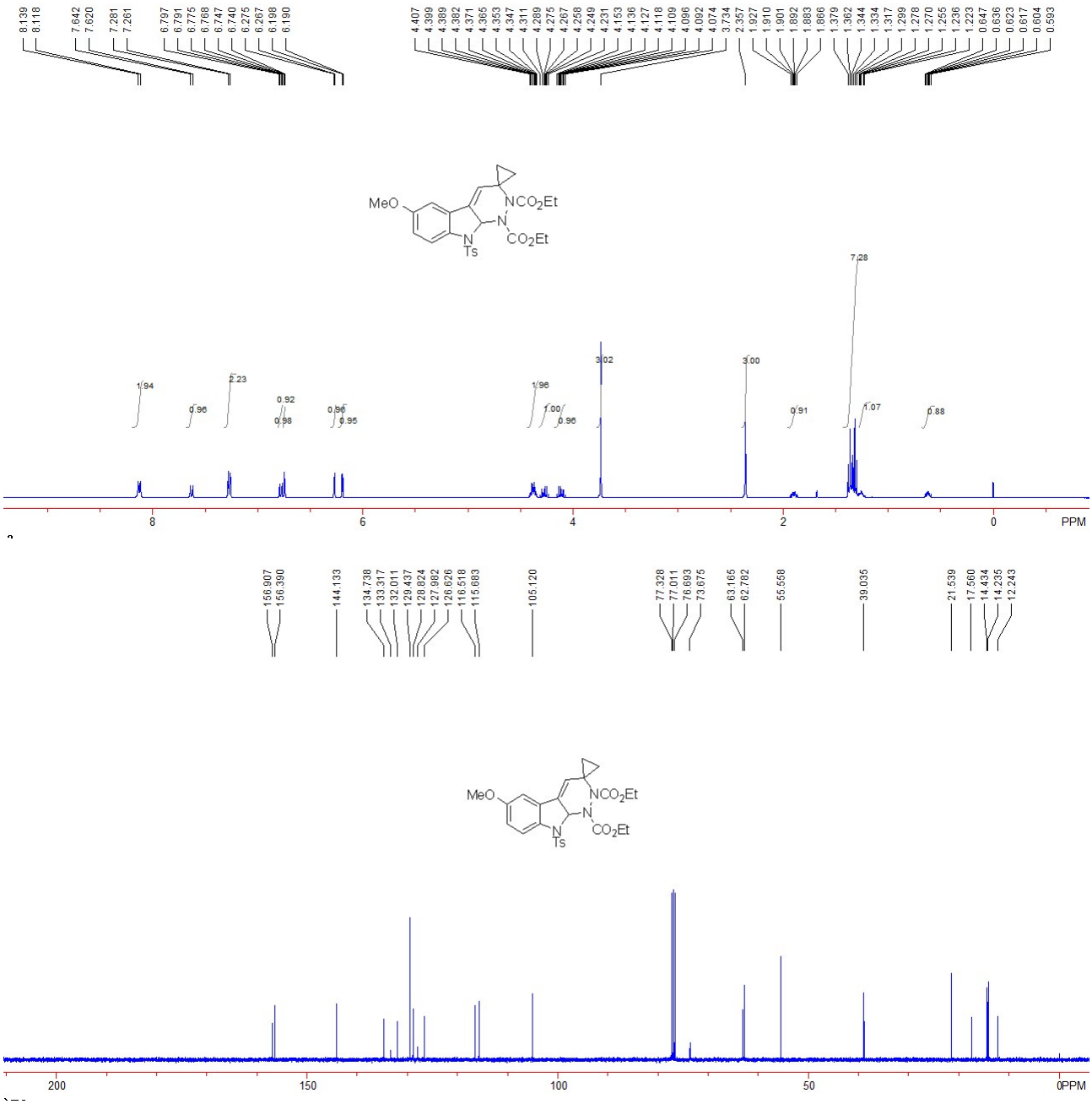


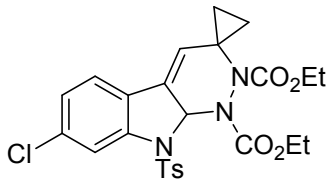




diethyl 6'-methoxy-9'-tosyl-9',9a'-dihydrospiro[cyclopropane-1,3'-pyridazino[3,4-b]indole]-1',2'-dicarboxylate (3d).

A white solid, 84.5 mg, 80% yield. M.p.: 224-226 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.60-0.65 (m, 1H, CH_2), 1.22-1.28 (m, 1H, CH_2), 1.30-1.38 (m, 7H), 1.87-1.93 (m, 1H, CH_2), 2.36 (s, 3H, CH_3), 3.73 (s, 3H, CH_3), 4.07-4.15 (m, 1H), 4.23-4.31 (m, 1H), 4.35-4.41 (m, 2H), 6.19 (d, *J* = 3.2 Hz, 1H, CH), 6.27 (d, *J* = 3.2 Hz, 1H, CH), 6.74 (d, *J* = 2.8 Hz, 1H, ArH), 6.78 (dd, *J* = 2.4 Hz, 8.8 Hz, 1H, ArH), 7.27 (d, *J* = 8.0 Hz, 2H, ArH), 7.63 (d, *J* = 8.8 Hz, 1H, ArH), 8.13 (d, *J* = 8.4 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.2, 14.2, 14.4, 17.6, 21.5, 39.0, 55.6, 62.8, 63.2, 73.7, 105.1, 115.7, 116.5, 126.6, 128.0, 128.8, 129.4, 132.0, 133.3, 134.7, 144.1, 156.4, 156.9. IR (CH_2Cl_2) ν 2950, 2922, 2851, 1715, 1466, 1317, 1170, 662 cm^{-1}. HRMS (DART) calcd. for $C_{26}H_{30}O_7N_3S$: 528.1799, Found: 528.1797.

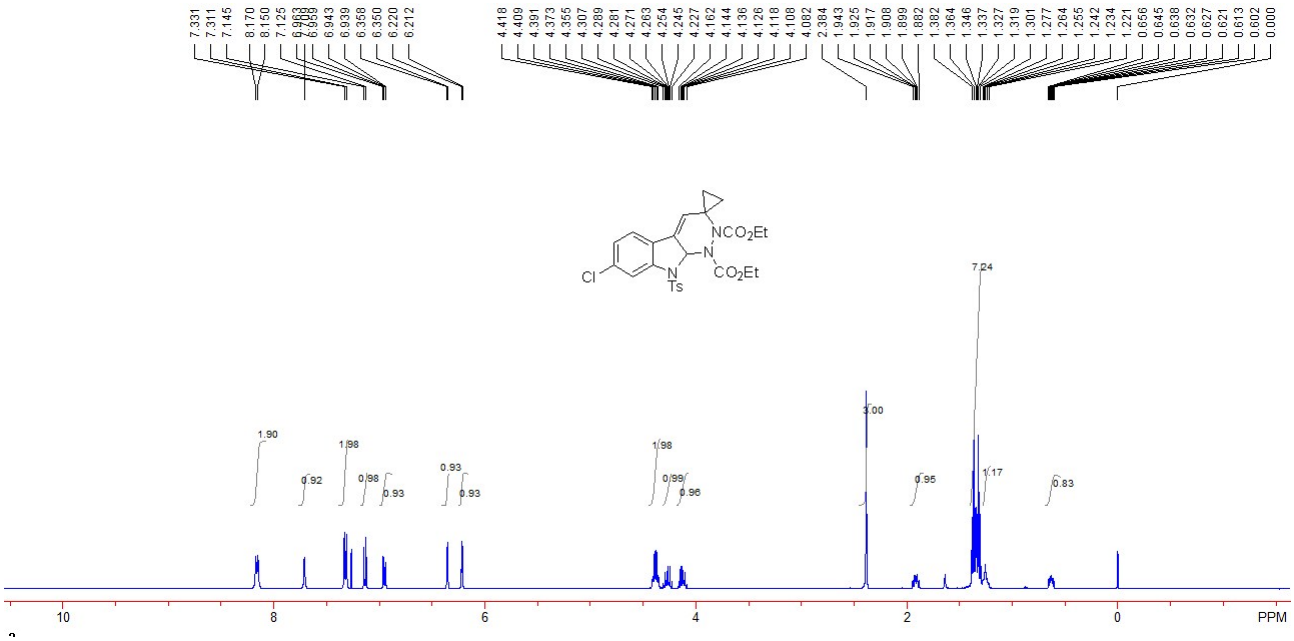


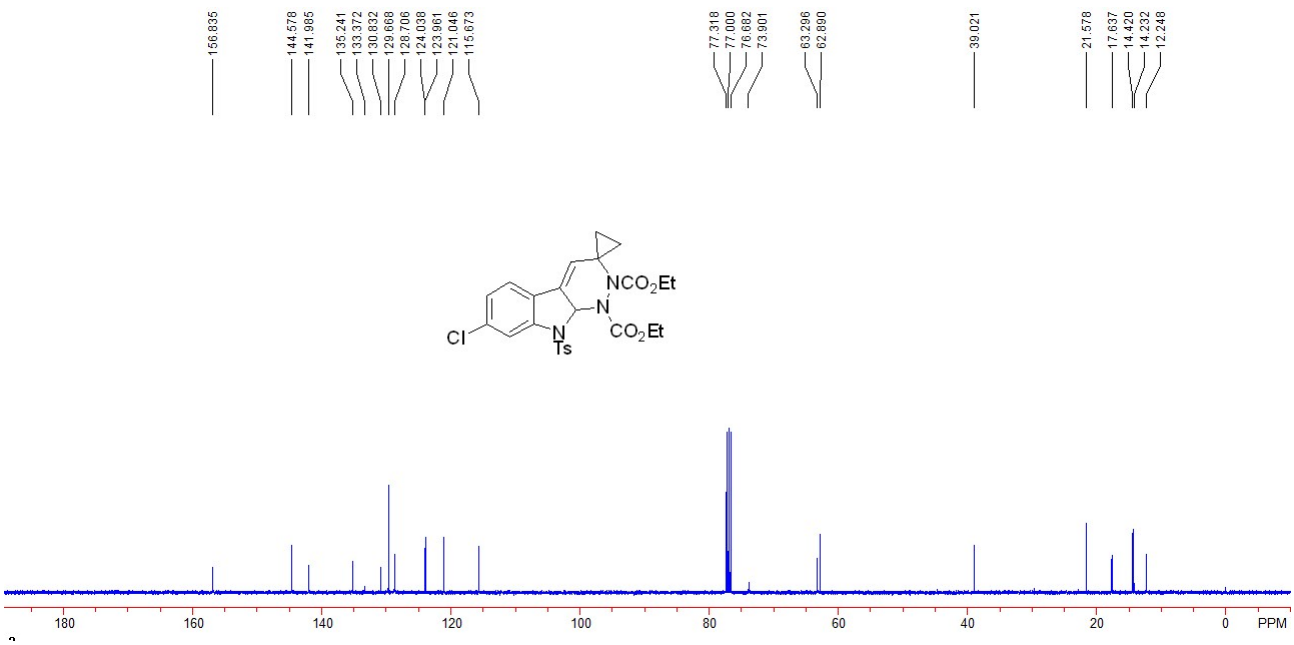


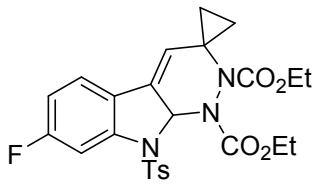
diethyl 7'-chloro-9'-tosyl-9',9a'-dihydrospiro[cyclopropane-1,3'-pyridazino[3,4-b]indole]-1',2'-dicarboxylate (3f).

A white solid, 55.3 mg, 52% yield. M.p.: 226-228 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.60-0.66 (m, 1H, CH_2), 1.22-1.28 (m, 1H, CH_2), 1.30-1.38 (m, 7H), 1.88-1.94 (m, 1H, CH_2), 2.38 (s, 3H, CH_3), 4.087-4.16 (m, 1H, CH_2), 4.23-4.31 (m, 1H, CH_2), 4.36-4.42 (m, 2H, CH_2), 6.22 (d, J = 3.2

Hz, 1H, ArH), 6.35 (d, *J* = 3.2 Hz, 1H, ArH), 6.95 (dd, *J* = 1.6 Hz, 8.0 Hz, 1H, ArH), 7.14 (d, *J* = 8.0 Hz, 1H, ArH), 7.32 (d, *J* = 8.0 Hz, 1H, ArH), 7.71 (s, 1H, ArH), 8.16 (d, *J* = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.2, 14.2, 14.4, 17.6, 21.6, 39.0, 62.9, 63.3, 73.9, 115.7, 121.0, 123.9, 124.0, 128.7, 129.7, 130.8, 133.4, 135.2, 142.0, 144.6, 156.8. IR (CH_2Cl_2) ν 3071, 2961, 2922, 1723, 1372, 1315. 1260, 1090, 1021, 799, 697 cm^{-1}. HRMS (DART) calcd. for $C_{25}H_{27}O_6N_3SCl$: 532.1304, Found: 532.1301.

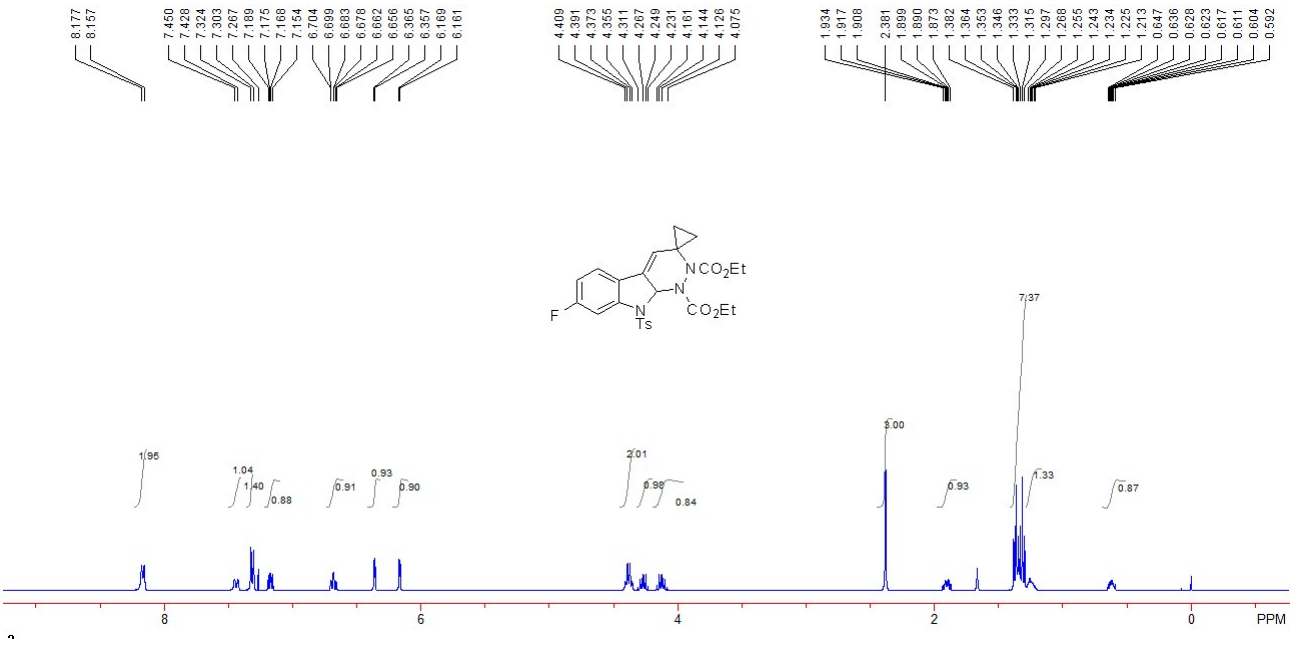


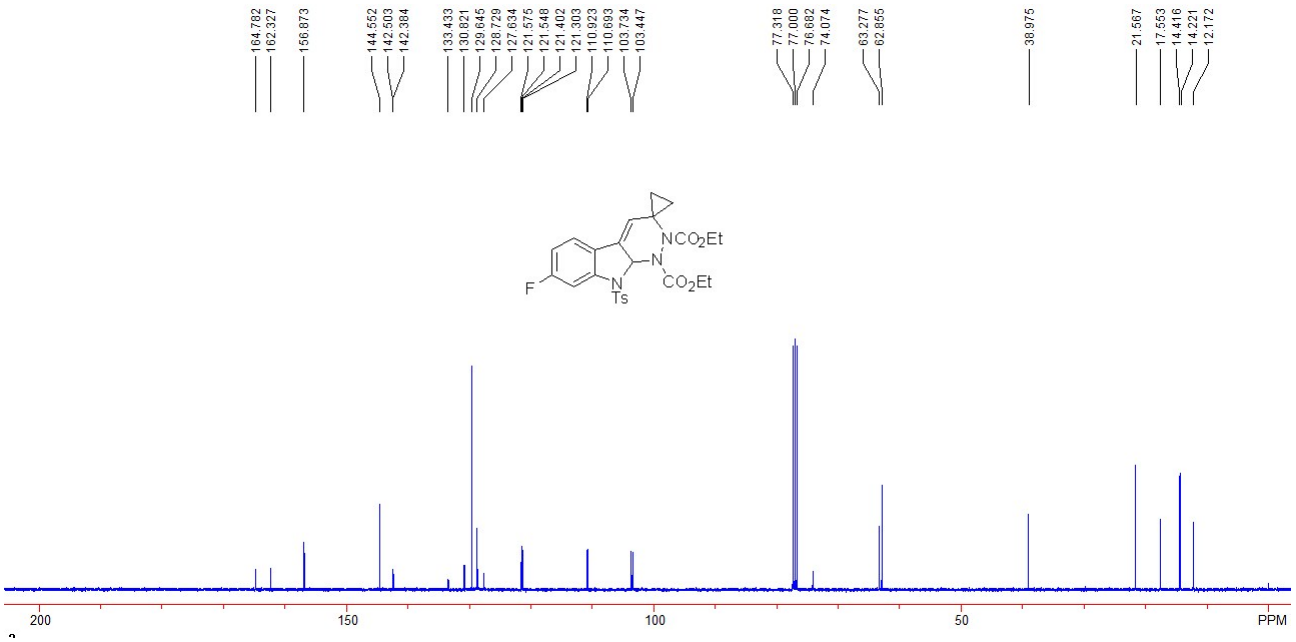


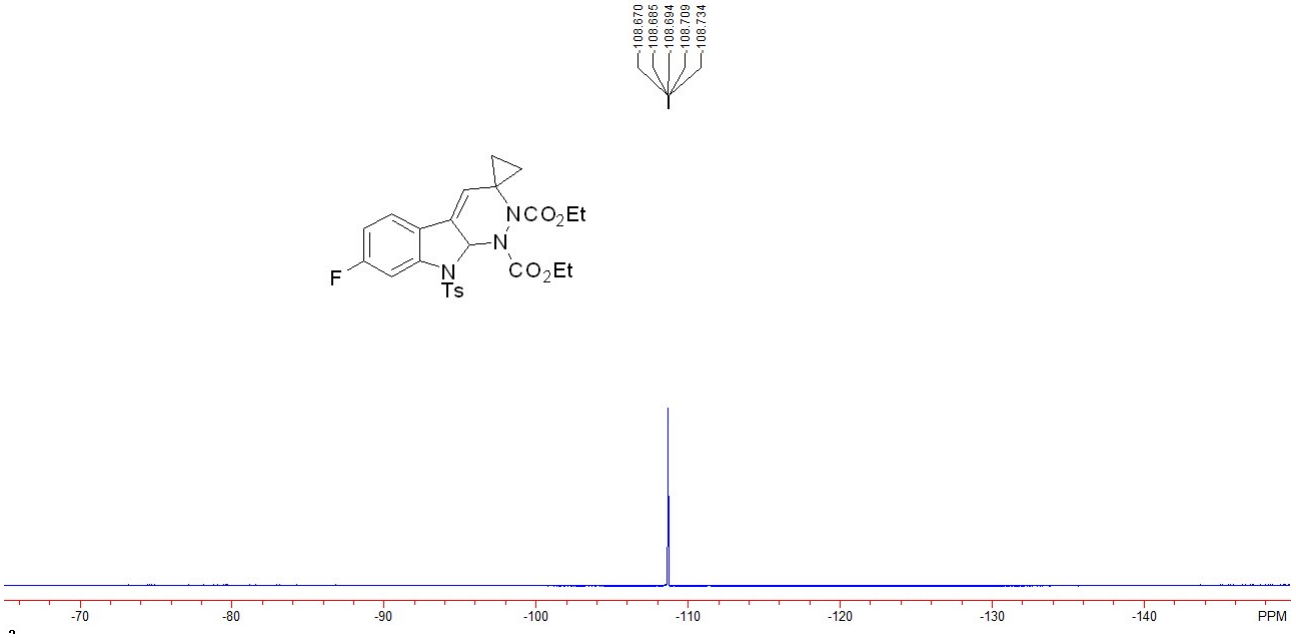


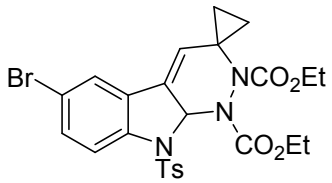
diethyl 7'-fluoro-9'-tosyl-9',9a'-dihydrospiro[cyclopropane-1,3'-pyridazino[3,4-b]indole]-1',2'-dicarboxylate (3g).

A white solid, 54.7 mg, 53 % yield. M.p.: 214-216 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.60-0.65 (m, 1H, CH_2), 1.21-1.27 (m, 1H, CH_2), 1.30-1.38 (m, 7H), 1.87-1.93 (m, 1H, CH_2), 2.38 (s, 3H, CH_3), 4.08-4.16 (m, 1H, CH_2), 4.23-4.31 (m, 1H, CH_2), 4.36-4.41 (m, 2H, CH_2), 6.16 (d, *J* = 3.2 Hz, 1H, CH), 6.36 (d, *J* = 3.2 Hz, 1H, CH), 6.68 (dt, *J* = 2.0 Hz, 8.4 Hz, 1H, ArH), 7.15-7.19 (m, 1H, ArH), 7.31 (d, *J* = 8.4 Hz, 1H, ArH), 7.44 (d, *J* = 8.8 Hz, 1H, ArH), 8.17 (d, *J* = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.2, 14.2, 14.4, 17.6, 21.6, 39.0, 62.8, 63.3, 74.1, 103.6 (d, *J* = 28.7 Hz), 110.8 (d, *J* = 23.0 Hz), 121.4 (d, *J* = 9.9 Hz), 121.6 (d, *J* = 2.7 Hz), 127.6, 128.7, 129.6, 130.8, 133.4, 142.4 (d, *J* = 11.9 Hz), 144.6, 156.9, 163.6 (d, *J* = 245.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -108.69. IR (CH_2Cl_2) ν 2979, 2930, 1722, 1590, 1374, 1320, 1267, 1170, 1093, 980, 815, 662 cm^{-1}. HRMS (DART) calcd. for $C_{25}H_{27}O_6N_3SF$: 516.1599, Found: 516.1598.





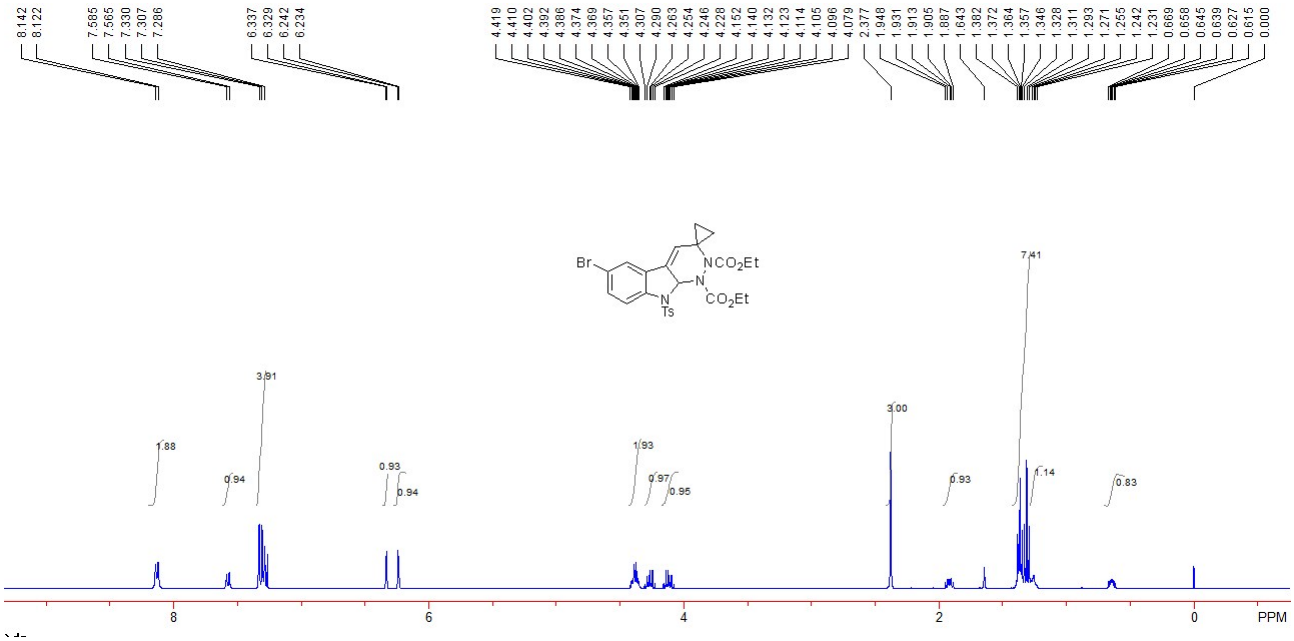


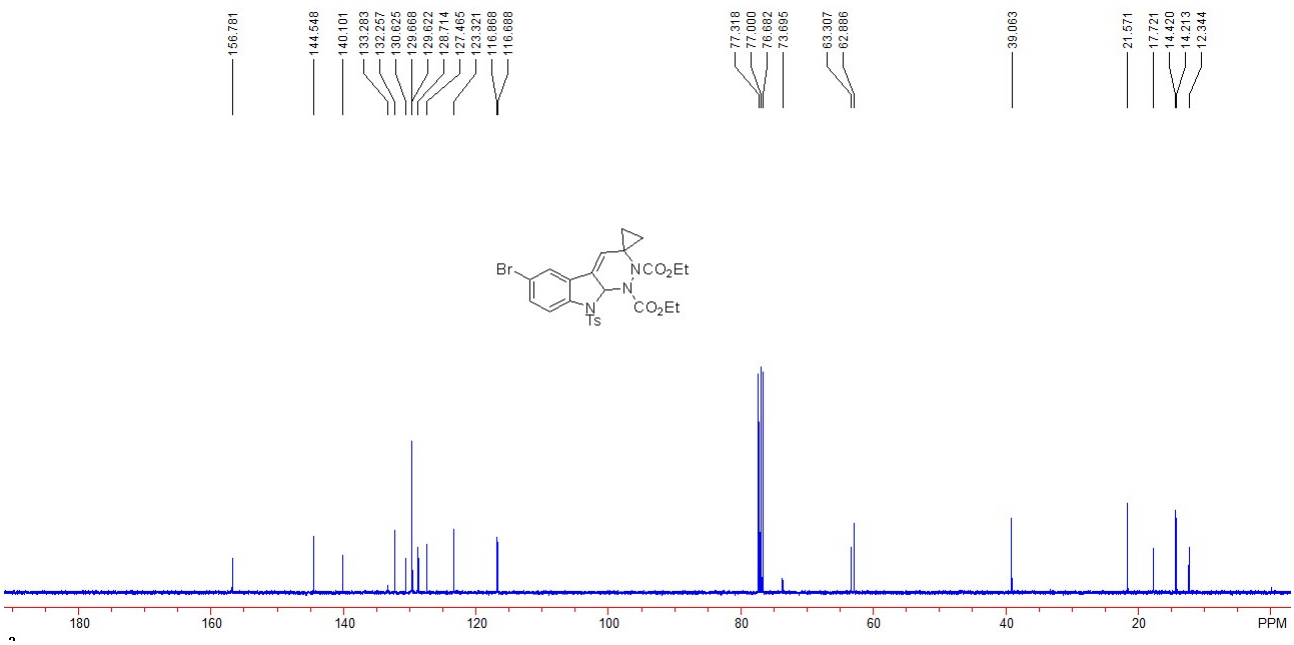


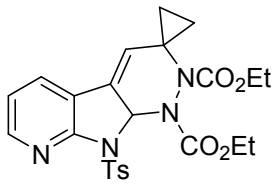
diethyl 6'-bromo-9'-tosyl-9',9a'-dihydrospiro[cyclopropane-1,3'-pyridazino[3,4-b]indole]-1',2'-dicarboxylate (3h).

A white solid, 62.2 mg, 54% yield. M.p.: 219-221 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ0.62-0.67 (m, 1H, CH_2), 1.23-1.27 (m, 1H, CH_2), 1.29-1.38 (m, 7H), 1.89-1.95 (m, 1H, CH_2), 2.38 (s, 3H, CH_3), 4.08-4.15 (m, 1H, CH_2), 4.23-4.31 (m, 1H, CH_2), 4.35-4.42 (m, 2H, CH_2), 6.24 (d, J = 3.2 Hz,

1H, CH), 6.33 (d, J = 3.2 Hz, 1H, CH), 7.29-7.33 (m, 4H, ArH), 7.58 (d, J = 8.0 Hz, 1H, ArH), 8.13 (d, J = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.3, 14.2, 14.4, 17.7, 21.6, 39.1, 62.9, 63.3, 73.7, 116.7, 116.9, 123.3, 127.5, 128.7, 129.6, 129.7, 130.6, 132.2, 133.3, 140.1, 144.5, 156.8. IR (CH_2Cl_2) ν 2958, 1723, 1261, 1090, 1022, 801, 694 cm^{-1}. HRMS (DART) calcd. for $C_{25}H_{27}O_6N_3SBr$: 576.0798, Found: 576.0799.

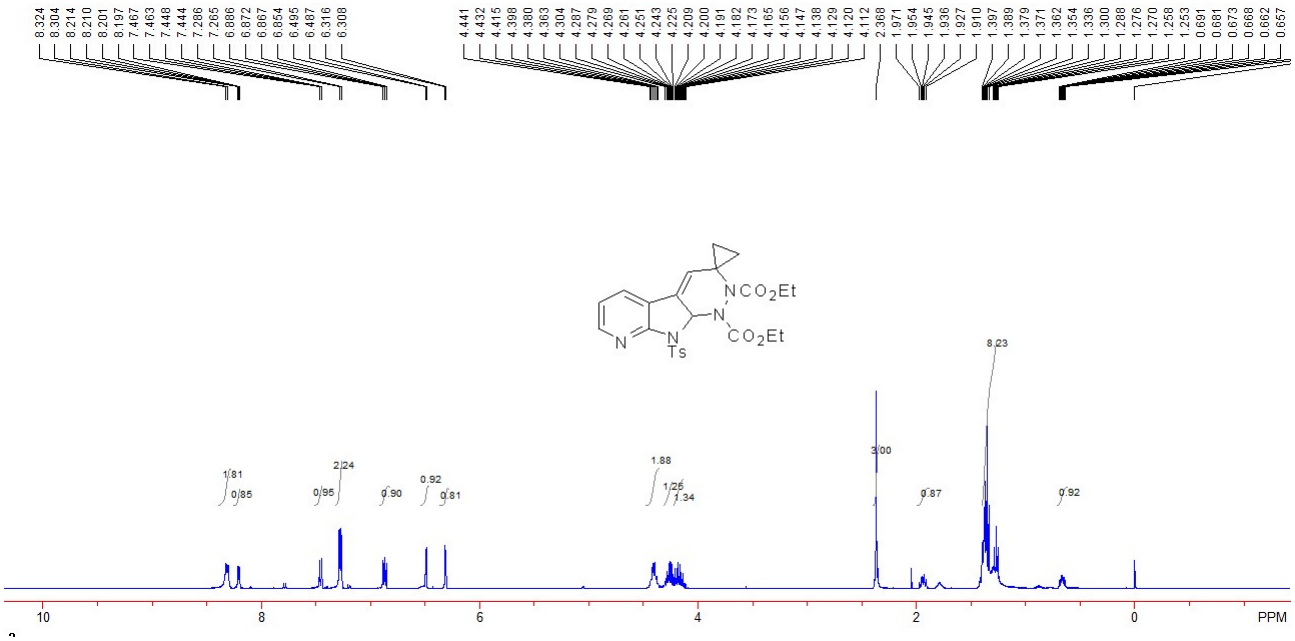


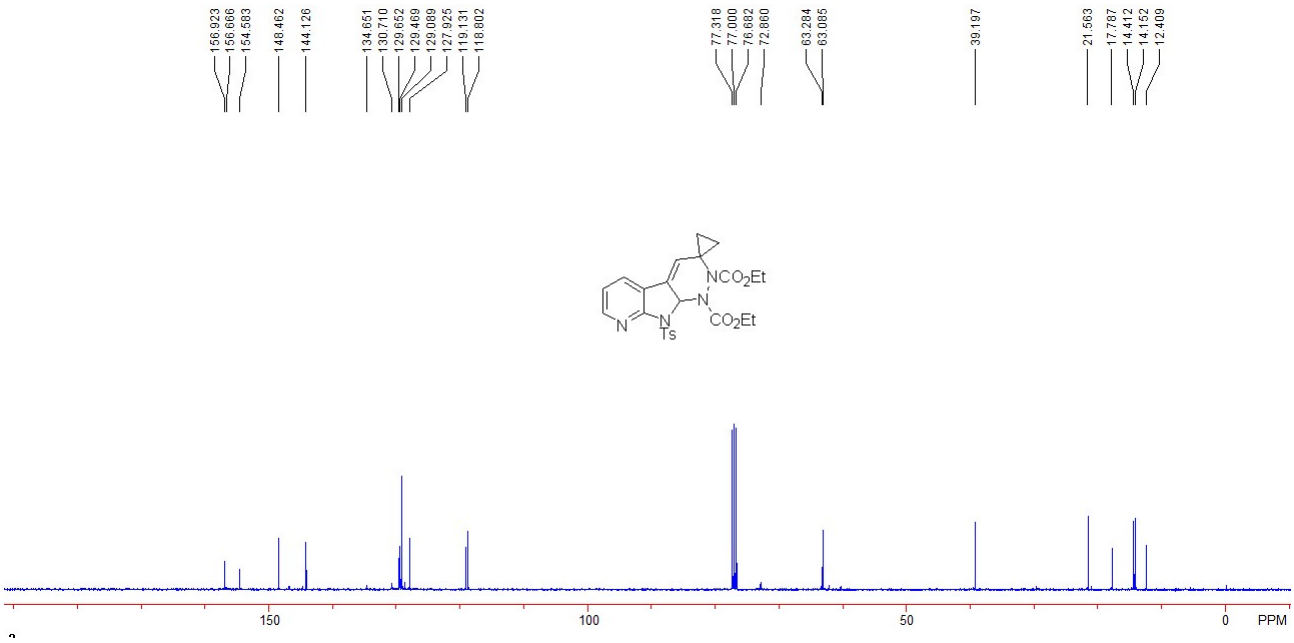


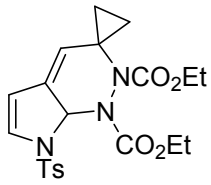


diethyl 9'-tosyl-9',9a'-dihydrospiro[cyclopropane-1,3'-pyrido[3',2':4,5]pyrrolo[2,3-c]pyridazine]-1',2'-dicarboxylate (3i).

A white solid, 49.8 mg, 50% yield. M.p.: 199-201 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.64-0.69 (m, 1H, CH_2), 1.25-1.40 (m, 8H), 1.91-1.97 (m, 1H, CH_2), 2.37 (s, 3H, CH_3), 4.11-4.211 (m, 1H, CH_2), 4.22-4.30 (m, 1H, CH_2), 4.36-4.44 (m, 2H, CH_2), 6.31 (d, *J* = 3.2 Hz, 1H, CH), 6.49 (d, *J* = 3.2 Hz, 1H, CH), 6.85-6.89 (m,1H, ArH), 7.28 (d, *J* = 8.4 Hz, 2H, ArH), 7.6 (dd, *J* = 1.6 Hz, 7.6 Hz, 1H, ArH), 8.21 (dd, *J* = 1.6 Hz, 5.2 Hz, 1H, ArH), 8.31 (d, *J* = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.4, 14.2, 14.4, 17.8, 21.6, 39.2, 63.1, 63.3, 72.9, 118.8, 119.1, 127.9, 129.1, 129.5, 129.6, 130.7, 134.6, 144.1, 148.5, 154.6, 156.7, 156.9. IR (CH_2Cl_2) ν 2924, 1743, 1660, 1409, 1367, 1277, 1259, 1173, 1090, 1035, 665 cm^{-1}. HRMS (DART) calcd. for $C_{24}H_{27}O_6N_4S$: 499.1646, Found: 499.1643.

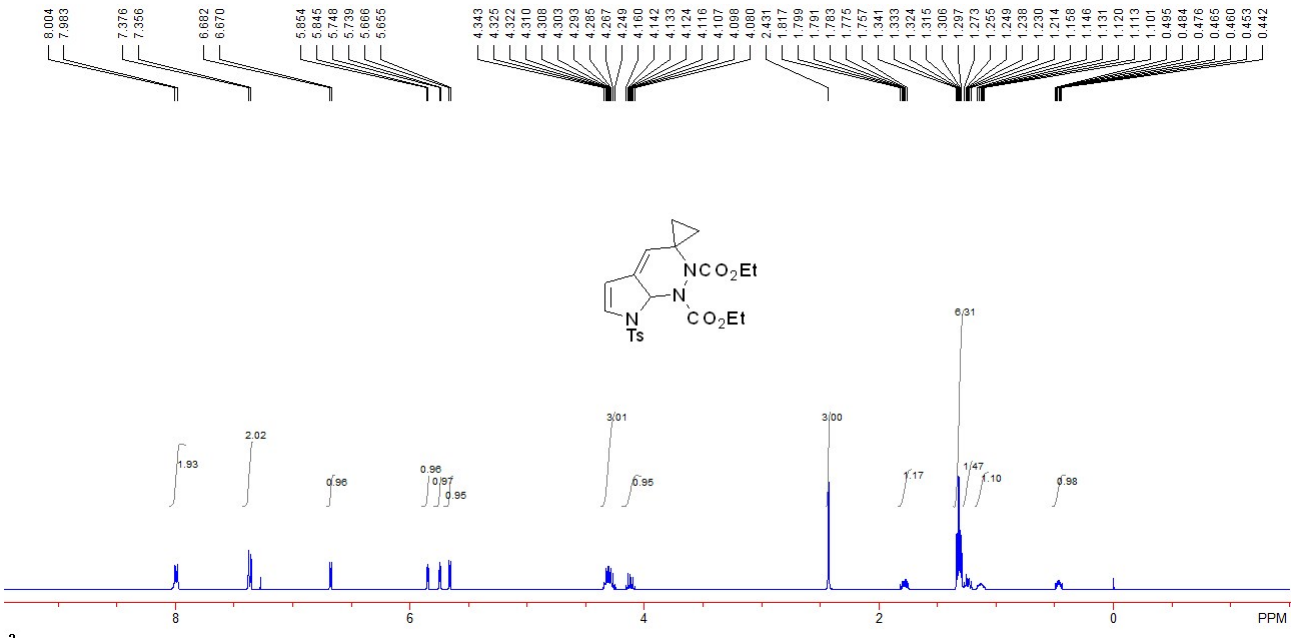


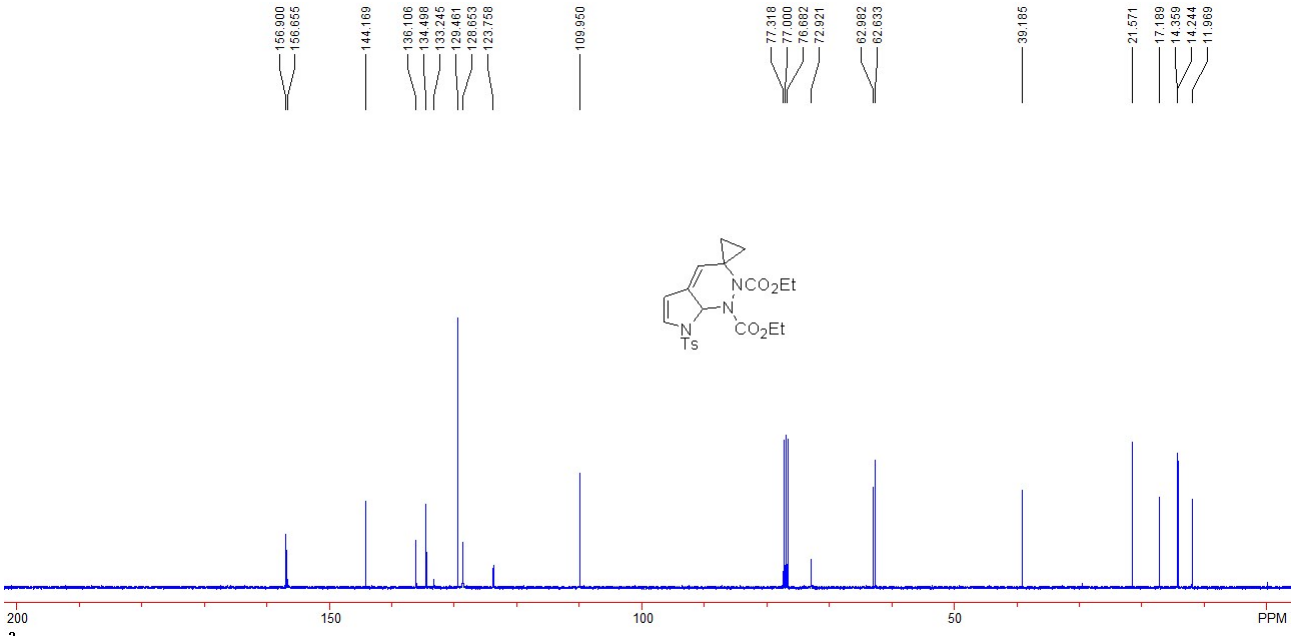


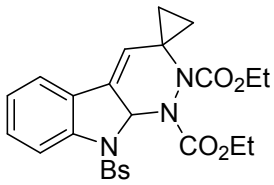


diethyl 7'-tosyl-7',7a'-dihydrospiro[cyclopropane-1,3'-pyrrolo[2,3-c]pyridazine]-1',2'-dicarboxylate (3j).

A white solid, 62.6 mg, 70% yield. M.p.: 173-175 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.44-0.50 (m, 1H, CH_2), 1.10-1.16 (m, 1H, CH_2), 121-1.27 (m, 1H, CH_2), 1.30-1.34 (m, 6H, CH_3), 1.76-1.82 (m, 1H, CH_2), 2.43 (s, 3H, CH_3), 4.08-4.16 (m, 1H), 4.25-4.34 (m, 3H, CH_2), 5.66 (d, J = 4.4 Hz, 1H, ArH), 5.74 (d, J = 3.6 Hz, 1H, ArH), 5.85 (d, J = 3.6 Hz, 1H, ArH), 6.68 (d, J = 4.8 Hz, 1H, ArH), 7.37 (d, J = 8.0 Hz, 2H, ArH), 8.00 (d, J = 8.4 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.0, 14.2, 14.4, 17.2, 21.6, 39.2, 62.6, 63.0, 72.9, 110.0, 123.8, 128.6, 129.5, 133.2, 134.5, 136.1, 144.2, 156.6, 156.9. IR (CH_2Cl_2) ν 2982, 2924, 1716, 1373, 1322, 1166, 1093, 1035, 666 cm^{-1}. HRMS (DART) calcd. for $C_{21}H_{26}O_6N_3S$: 448.1537, Found:448.1536.



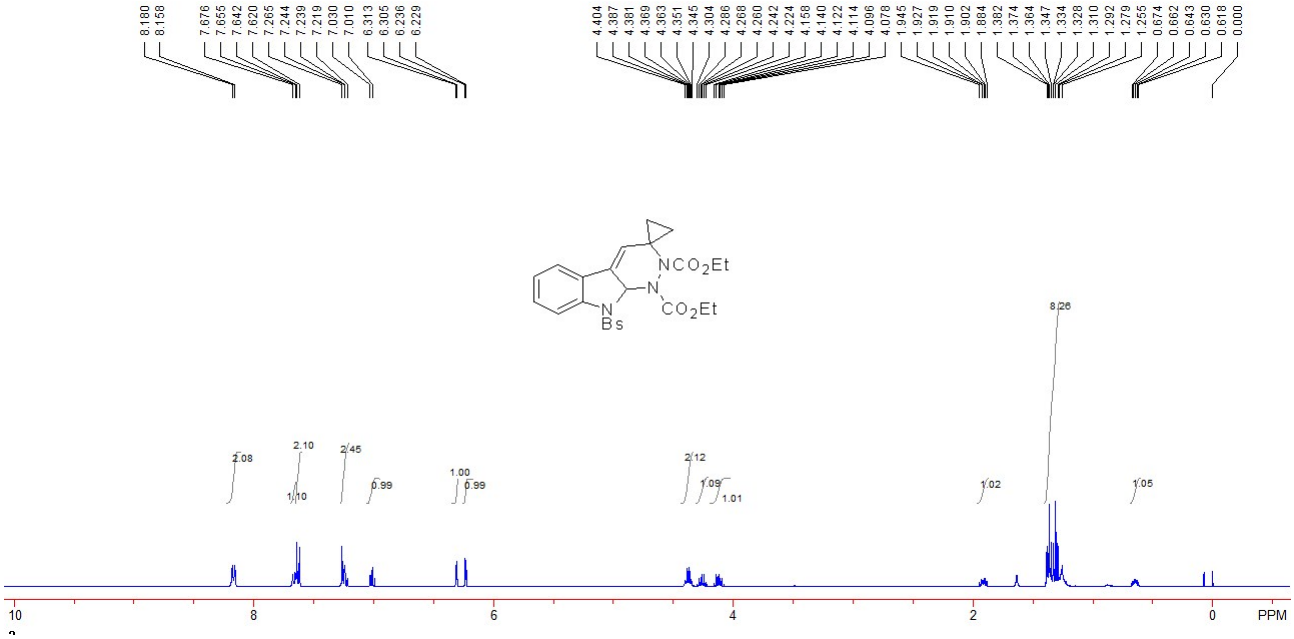


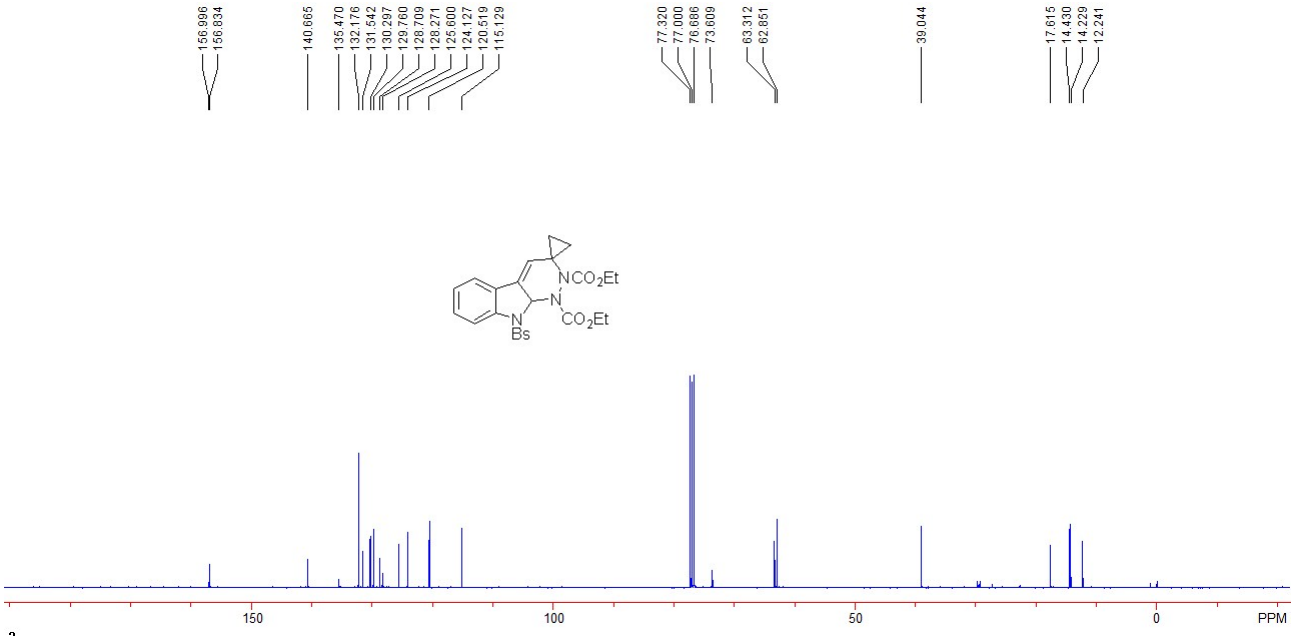


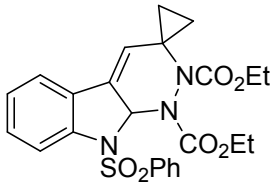
diethyl 9'-((4-bromophenyl)sulfonyl)-9',9a'-dihydrospiro[cyclopropane-1,3'-pyridazino[3,4-b]indole]-1',2'-dicarboxylate (3k).

A white solid, 68.6 mg, 61% yield. M.p.: 213-215 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.62-0.67 (m, 1H, CH_2), 1.26-1.38 (m, 8H,), 1.88-1.94 (m, 1H, CH_2), 4.08-4.16 (m, 1H, CH_2), 4.22-4.30 (m, 1H, CH_2), 4.34-4.40 (m, 2H, CH_2), 6.23 (d, J = 2.8 Hz, 1H, CH), 6.31 (d, J = 3.2 Hz, 1H, CH),

7.01 (t, *J* = 8.0 Hz, 1H, ArH), 7.22-7.26 (m, 2H, ArH), 7.63 (d, *J* = 8.8 Hz, 2H, ArH), 7.67 (d, J = 8.4 Hz, 1H, ArH), 8.17 (d, *J* = 8.8 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.2, 14.2, 14.4, 17.6, 39.0, 62.8, 63.3, 73.6, 115.1, 120.5, 124.1, 125.6, 128.3, 128.7, 129.8, 130.3, 131.5, 132.2, 135.5, 140.7, 156.8, 157.0. IR (CH_2Cl_2) ν 2958, 1717, 1370, 1321, 1175, 1113, 1097, 1070, 1012, 793, 739, 697 cm^{-1}. HRMS (DART) calcd. for $C_{24}H_{25}O_6N_3SBr$: 562.0642, Found: 562.0634.

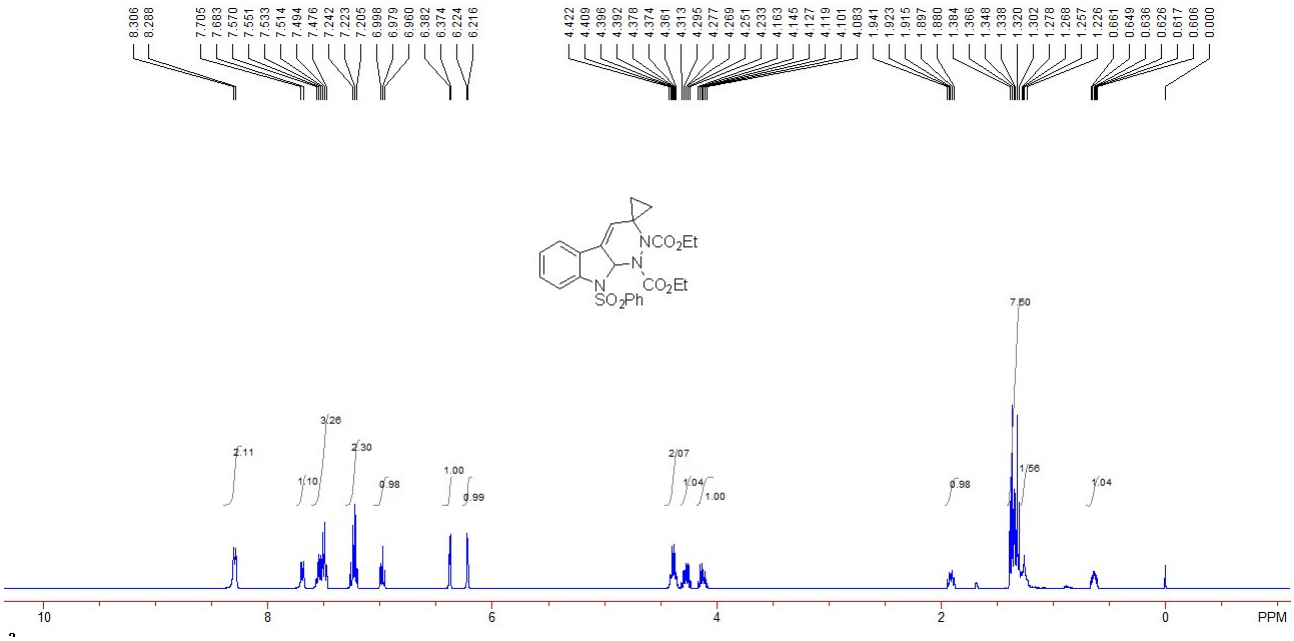


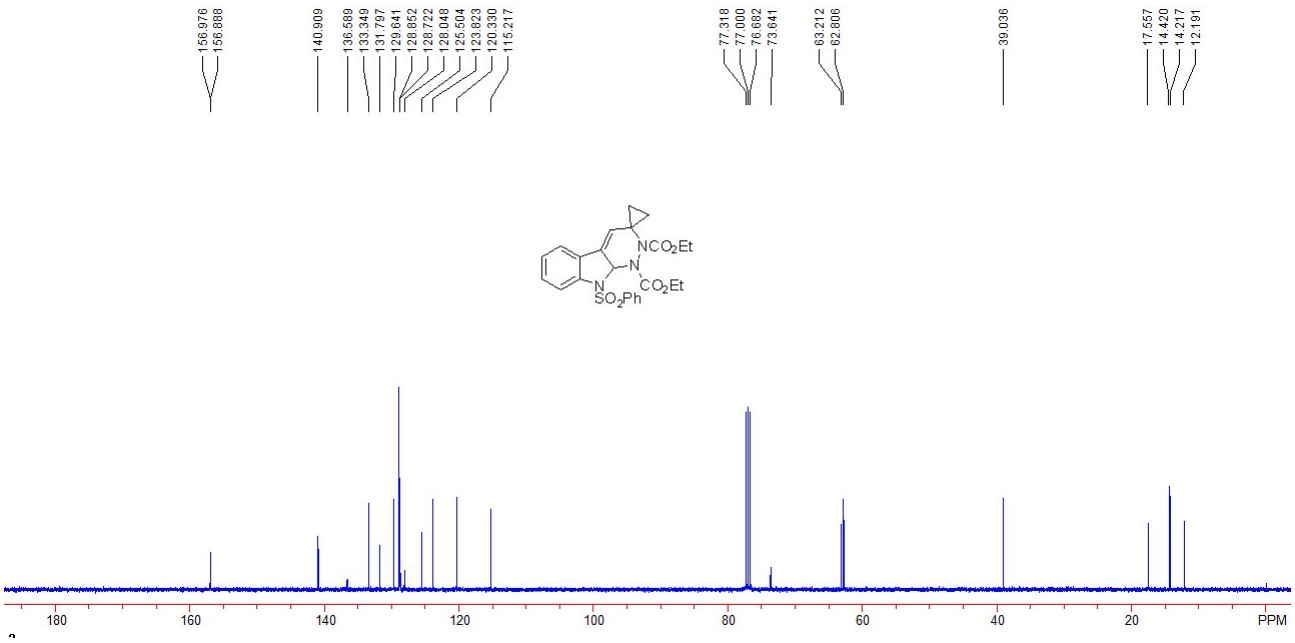


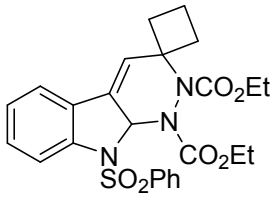


diethyl 9'-(phenylsulfonyl)-9',9a'-dihydrospiro[cyclopropane-1,3'-pyridazino[3,4-b]indole]-1',2'-dicarboxylate (3l).

A white solid, 58.0 mg, 60% yield. M.p.: 203-205 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.61-0.66 (m, 1H, CH_2), 1.23-1.28 (m, 1H, CH_2), 1.30-1.38 (m, 7H), 1.89-1.94 (m, 1H, CH_2), 4.08-4.16 (m, 1H, CH_2), 4.23-4.31 (m, 1H, CH_2), 4.36-4.42 (m, 2H, CH_2), 6.22 (d, *J* = 3.2 Hz, 1H, CH), 6.38 (d, *J* = 3.2 Hz, 1H, CH), 6.98 (t, *J* = 7.6 Hz, 1H, ArH), 7.22 (t, *J* = 7.6 Hz, 2H, ArH), 7.48-7.57 (m, 3H, ArH), 7.69 (d, *J* = 8.8 Hz, 1H, ArH), 8.29 (d, *J* = 7.2 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.2, 14.2, 14.4, 17.6, 39.0, 62.8, 63.2, 73.6, 115.2, 120.3, 123.8, 125.5, 128.0, 128.7, 128.8, 129.6, 131.8, 133.3, 136.6, 140.9, 156.9, 157.0. IR (CH_2Cl_2) ν 2964, 1721, 1372, 1321, 1261, 1176, 1090, 1048, 1023, 799 cm^{-1}. HRMS (DART) calcd. for $C_{24}H_{26}O_6N_3S$: 484.1537, Found: 484.1536.

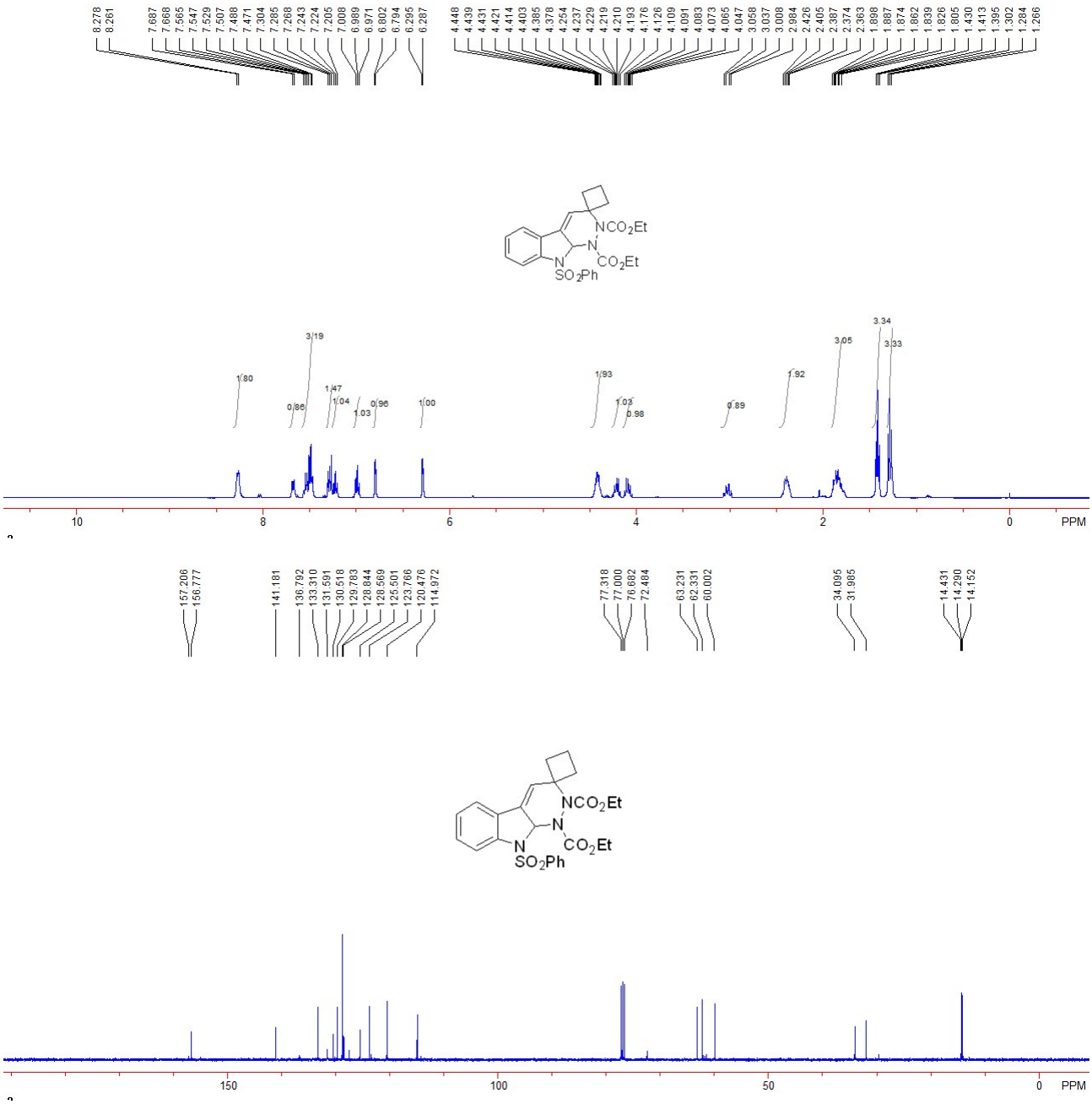


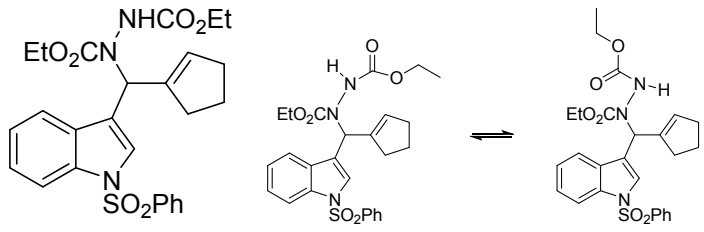




diethyl 9'-(phenylsulfonyl)-9',9a'-dihydrospiro[cyclobutane-1,3'-pyridazino[3,4-b]indole]-1',2'-dicarboxylate (3m).

A white solid, 50.8 mg, 51% yield. M.p.: 179-181 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.28 (t, *J* = 7.2 Hz, 3H, CH_3), 1.41 (t, *J* = 7.2 Hz, 3H, CH_3), 1.80- 1.90 (m, 3H, CH_2), 2.36-2.43 (m, 2H, CH_2), 2.98-3.06 (m, 1H, CH_2), 4.05-4.13 (m, 1H, CH_2), 4.18-4.25 (m, 1H, CH_2), 4.38-4.45 (m, 2H, CH_2), 6.29 (d, *J* = 3.2 Hz, 1H, CH), 6.80 (d, *J* = 3.2 Hz, 1H, CH), 6.99 (t, *J* = 7.6 Hz, 1H, ArH), 7.22 (t, *J* = 7.6 Hz, 1H, ArH), 7.28 (t, *J* = 7.6 Hz, 1H, ArH), 7.47-7.56 (m, 3H, ArH), 7.68 (d, *J* = 7.6 Hz, 1H, ArH), 8.27 (d, *J* = 6.8 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 14.2, 14.3, 14.4, 32.0, 34.1, 60.0, 62.3, 63.2, 72.5, 115.0, 120.5, 123.8, 125.5, 128.6, 128.8, 129.8, 130.5, 131.6, 133.3, 136.8, 141.2, 156.8, 157.2. IR (CH_2Cl_2) ν 2982, 1717, 1464, 1371, 1322, 1286, 1176, 1100, 982, 760, 694 cm^{-1}. HRMS (DART) calcd. for $C_{25}H_{28}O_6N_3S$: 498.1693, Found: 498.1694.

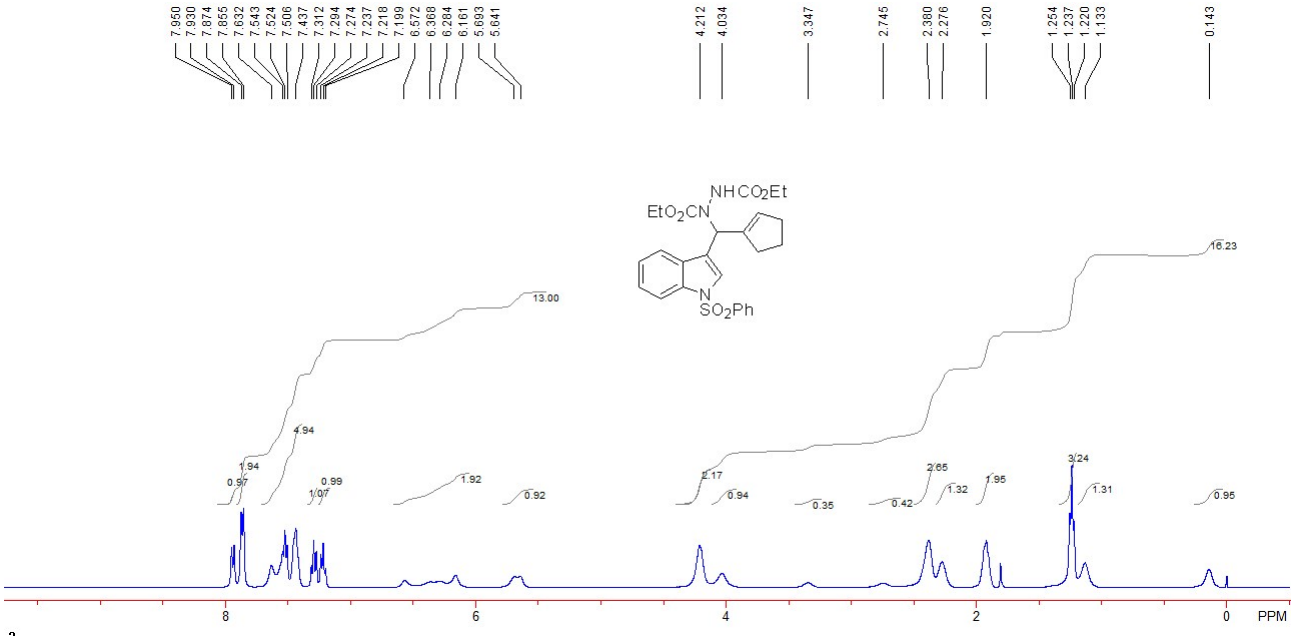


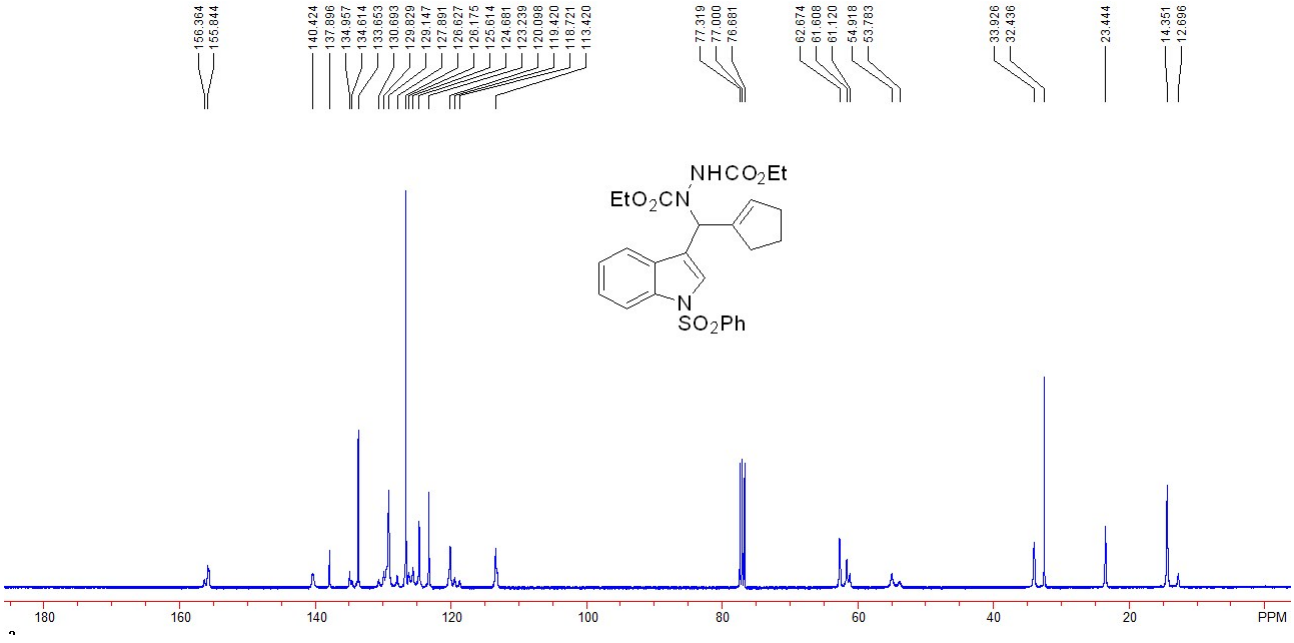


diethyl 1-(cyclopent-1-en-1-yl(1-(phenylsulfonyl)indolin-3-yl)methyl)hydrazine-1,2-dicarboxylate (3p).

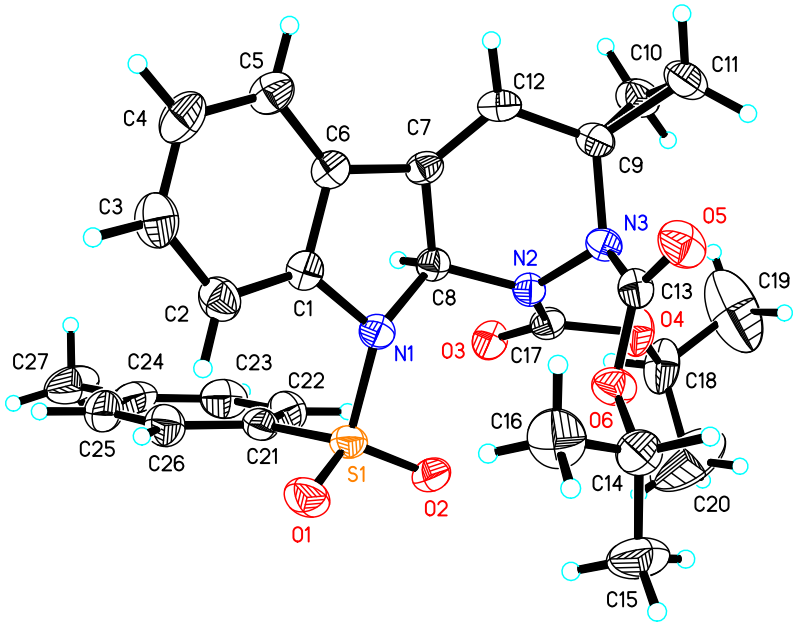
A white solid, 71.8 mg, 70% yield. M.p.: 163-165 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.14 (s, 0.95H, CH_2), 1.13 (s, 1.31H), 1.24 (t, J = 6.8 Hz, 3.24H, CH_3), 1.92 (s, 1.95H), 2.78 (s, 1.32H),

2.38 (s, 2.65H), 2.74 (s, 0.42H), 3.35 (s, 0.35H), 4.03 (s, 0.94H), 4.21 (s, 2.17H), 5.64-5.70 (br, 0.92H), 6.16-6.57 (br, 1.92H), 7.22 (t, J = 7.6 Hz, 0.99H, ArH), 7.29 (t, J = 7.6 Hz, 1.07H, ArH), 7.44-7.63 (m, 4.94H), 7.86 (d, J = 7.6 Hz, 1.91H, ArH), 7.94 (d, J = 8.0 Hz, 0.97H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.7, 14.4, 23.4, 32.4, 33.9, 53.8, 54.9, 61.1, 61.6, 62.7, 113.4, 118.7, 119.4, 120.1, 123.2, 124.7, 125.6, 126.2, 126.6, 127.9, 129.1, 129.8, 130.7, 133.6, 134.6, 145.1, 137.9, 140.4, 155.8, 156.4. IR (CH_2Cl_2) ν 3283, 2977, 2848, 1704, 1447, 1376, 1292, 1176, 1128, 1113, 1095, 754, 726, 686 cm^{-1}. MS (%) m/e 338 (10.96), 337 (32.34), 336 (M^+, 100.00), 195 (21.20), 194 (56.97), 168 (6.46), 167 (23.76), 77 (14.11). HRMS (EI) calcd. for $C_{26}H_{29}N_3O_6S$: 511.1777, Found: 511.1778.



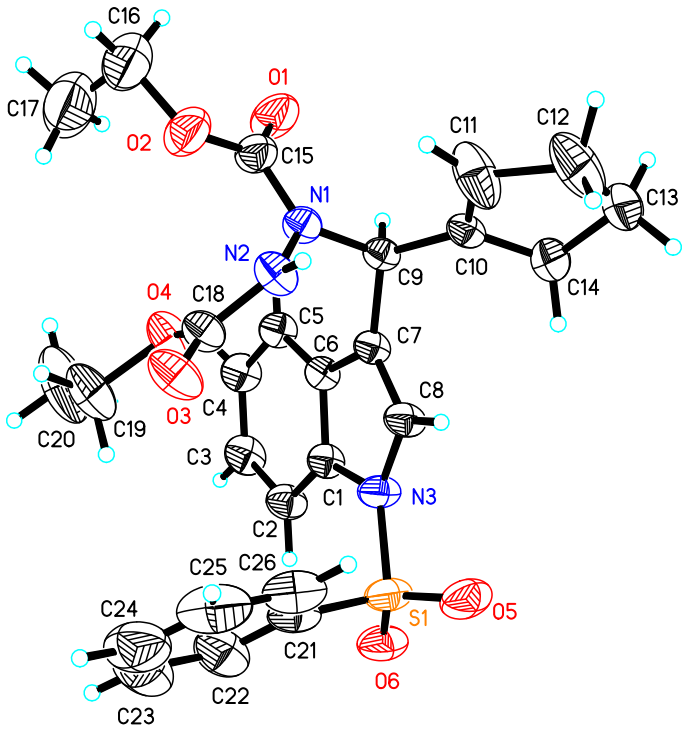


The Crystal Data of 2a



The crystal data of **2a** have been deposited in CCDC with number 1428617. Empirical Formula: $C_{27}H_{31}N_3O_6S$; Formula Weight: 525.61; Crystal Color, Habit: colorless, Crystal Dimensions: 0.210 x 0.180 x 0.140 mm^3; Crystal System: Monoclinic; Lattice Parameters: a = 12.7729(17)Å, b = 16.694(2)Å, c = 14.8793(19)Å, $\alpha = 90^o$, $\beta = 104.131(3)^o$, $\gamma = 90^o$, V = 3076.7(7)$Å^3$; Space group: P 21/n; Z = 4; D_{calc}= 1.135 g/cm^3; F_{000} = 1112; Final R indices [I>2sigma(I)] R1 = 0.0506, wR2 = 0.1322.

The Crystal Data of 3p



The crystal data of **3p** have been deposited in CCDC with number 1855996. Empirical formula: $C_{26}H_{29}N_3O_6S$, Formula weight: 511.58, Crystal system: Monoclinic, Space group: P 21/n, Unit cell dimensions: a = 10.0889(2) Å, α = 90°; b = 23.6964(6) Å, β = 91.1750(10)°; c = 11.1762(3) Å, γ = 90°. Volume: 2671.34(11) $Å^3$, Z = 4, Density (calculated): 1.272 Mg/m^3, F(000) = 1080, Crystal size: 0.200 x 0.170 x 0.130 mm^3, Final R indices [I>2sigma(I)]: R1 = 0.0588, wR2 = 0.1505.

Calculation Details

The geometries of compounds have been optimized at B3LYP/6-31G(d) level; The subsequent frequency calculations on the stationary points were carried out at the same level of theory to ascertain the nature of the stationary points as minima on the respective potential energy surfaces. The conformational space of flexible systems has first been searched manually. Thermochemical corrections to 298.15 K have been calculated for all minima from unscaled vibrational frequencies obtained at this same level. The thermochemical corrections have been combined with single-point energies calculated at the CPCM/B3LYP/6-311+G(d,p)//B3LYP/6-31G(d) level to yield free energy G_{298} at 298.15 K. All quantum mechanical calculations have been performed with Gaussian 09.

Table S1. The total energies, enthalpies and free energies of all species in gas phase shown in Figure 3.

	E_{tot}	H_{298}	G_{298}
A	-1982.543966	-1982.019235	-1982.134585
TS1	-1982.516342	-1981.992784	-1982.100428
B	-1982.549777	-1982.023973	-1982.125538
TS2	-1982.542886	-1982.017938	-1982.120307
C	-1982.597698	-1982.069241	-1982.171619

Table S2. The total energies, enthalpies and free energies of all species in CH_3CN shown in Figure 3, $\varepsilon = 35.688$

	E_{tot}	H_{298}	G_{298}
A	-1983.020067	-1982.495336	-1982.610686
TS1	-1982.992499	-1982.468942	-1982.576586
B	-1983.022131	-1982.496327	-1982.597892
TS2	-1983.020004	-1982.495056	-1982.597425
C	-1983.067711	-1982.539254	-1982.641632

Archive Entries

A

1\1\GINC-A761\SP\RB3LYP\6-311+G(d,p)\C25H27N3O6S1\SIOC001\16-Jun-2019\
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TS1

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B

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TS2

1\1\GINC-A716\SP\RB3LYP\6-311+G(d,p)\C25H27N3O6S1\SIOC001\13-Jun-2019\0\\#p b3lyp/6-311+(d,p) geom=check scrf=(iefpcm,cpcm,solvent=Acetonitrile)\\Title Card Required\\0,1\C,0,-2.6568637338,2.4026953294,-0.3019178444\C,0,-1.5637517757,1.6213607808,0.0645348494\C,0,-0.6923733407,1.9789594684,1.1137811943\C,0,-0.9303595694,3.1568831586,1.8265764042\C,0,-2.0355680008,3.9367715919,1.4892891897\C,0,-2.8850232915,3.5640972205,0.4374962511\H,0,-3.2865603023,2.135924801,-1.1416246428\H,0,-0.262380078,3.4648651471,2.6260515391\H,0,-2.2328390231,4.8529676384,2.0383651382\H,0,-3.7297744363,4.1965531889,0.1803064737\C,0,0.3606549505,0.9646342534,1.1819638875\C,0,0.0803197774,0.0325518556,0.1538232496\N,0,-1.0736481339,0.4089667041,-0.4895537438\S,0,-1.9305100032,-0.6484865785,-1.5712057391\O,0,-2.5726347615,0.2189430619,-2.5523109672\O,0,-0.9600642467,-1.6759370216,-1.9259423767\C,0,-3.18968665,-1.3761803804,-0.5319584296\C,0,-2.8575690151,-2.4706378694,0.2717821137\C,0,-4.486094709,-0.8597805761,-0.5504137293\C,0,-3.8405268249,-3.0373515922,1.076976081\H,0,-1.8542632195,-2.8826582803,0.2479793201\C,0,-5.4557568354,-1.4443250417,0.2619106989\H,0,-4.7338129951,-0.0330301594,-1.2063390096\C,0,-5.150064347,-2.5318332577,1.0913797851\H,0,-3.5903171926,-3.8932280306,1.6985139137\H,0,-6.4691924148,-1.0519820264,0.2450245921\C,0,-6.1991630283,-3.1379056164,1.9913884999\H,0,-6.0473088542,-4.2150293335,2.115120462\H,0,-6.1625248906,-2.6867891345,2.9917797166\H,0,-7.2074605139,-2.9773085329,1.5973547428\C,0,1.5093045414,0.9897043656,1.9568590628\H,0,1.5865333783,1.7280451995,2.7477671819\C,0,2.5662222428,-0.0175502164,1.9106479934\C,0,3.6381556535,0.0638814486,2.9764853304\H,0,4.6038317213,-0.338525492,2.6925973484\C,0,2.5375894327,-0.9289928684,3.1698771042\H,0,1.7487357975,-0.7166712519,3.8855369341\H,0,2.7693264658,-1.9733193242,3.0149759161\H,0,3.6690135944,0.9687917949,3.57811363\N,0,2.8820841413,-0.5118936599,0.5629527101\N,0,2.4747001365,0.1504528599,-0.5929600791\H,0,0.5067347369,-0.9324234846,-0.0499696966\C,0,2.5973664361,1.4875007497,-0.5025818601\C,0,3.4908256709,-1.7467256527,0.3789954383\O,0,3.9519309095,-2.4263355638,1.2879914072\O,0,2.9414103634,2.1504404237,0.4992805192\O,0,3.5513695715,-2.0987632225,-0.9150992106\O,0,2.1914604753,2.0872505164,-1.6560721727\C,0,4.227591536,-3.3459519683,-1.1787395875\H,0,5.248125094,-3.2896209343,-0.7858768735\

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C

1\1\GINC-A744\SP\RB3LYP\6-311+G(d,p)\C25H27N3O6S1\SIOC001\13-Jun-2019\0\\#p b3lyp/6-311+(d,p) geom=check scrf=(iefpcm,cpcm,solvent=Acetonitrile)\\Title Card Required\\0,1\C,0,2.81773653,-10.1392051998,0.3039470269\C,0,3.2316963137,-8.8135163619,0.4167892261\C,0,4.3610072035,-8.4648213044,1.1870834968\C,0,5.1024755011,-9.456625468,1.8287819524\C,0,4.7158975351,-10.7912587636,1.693461592\C,0,3.5831543068,-11.121144144,0.9432301676\H,0,1.9237786002,-10.3969791589,-0.2494039936\H,0,5.9742982161,-9.190510853,2.4204795518\H,0,5.2909293687,-11.5733045144,2.1806479892\H,0,3.2786078055,-12.1606858095,0.8583449547\C,0,4.4555299505,-7.0110468121,1.2159515432\C,0,3.4642787453,-6.4806190842,0.186585807\N,0,2.6166217525,-7.640294082,-0.1183834772\S,0,1.7828706836,-7.636980968,-1.6136479425\O,0,0.8777259845,-8.7858398194,-1.5738483666\O,0,1.3008436939,-6.2698392661,-1.7837823924\C,0,3.0252287906,-7.9372398569,-2.8717372849\C,0,3.6809202247,-6.8470868131,-3.4517439386\C,0,3.344121174,-9.2463208649,-3.2419535517\C,0,4.670554608,-7.0799313559,-4.4045717477\H,0,3.4039090326,-5.8370959747,-3.1685064227\C,0,4.3351774634,-9.4568561685,-4.1974671118\H,0,2.8130394873,-10.0811676945,-2.7995636544\C,0,5.0130475612,-8.3827714809,-4.7926155458\H,0,5.1816780175,-6.2346952051,-4.8586972035\H,0,4.5841146501,-10.4739635998,-4.4898843962\C,0,6.0630191286,-8.6235341457,-5.8505285671\H,0,5.6083282948,-8.6785049079,-6.8484949454\H,0,6.8017182467,-7.8160015611,-5.8729355396\H,0,6.592469583,-9.5669623078,-5.6823131256\C,0,5.0557499761,-6.1608678558,2.0633389359\H,0,5.6875933152,-6.5233297727,2.8709260541\C,0,4.7446768439,-4.7080664453,2.055514266\C,0,4.4766292982,-4.064970185,3.4253770625\H,0,3.655607333,-3.3563514559,3.4438099053\C,0,5.7107579634,-3.7095270882,2.657038245\H,0,6.6643339892,-4.1164212703,2.9845468967\H,0,5.7708430626,-2.7405439031,2.1804741934\H,0,4.557236307,-4.7022705628,4.3016746069\N,0,3.8688848493,-4.3350404829,0.9535769513\N,0,2.8440515979,-5.2476767317,0.7078965359\H,0,3.98092323,-6.1588867426,-0.7280270771\C,0,1.6577794633,-5.0392452213,1.4064585155\C,0,4.1302269307,-3.3536133985,0.0057018763\O,0,5.054143572,-2.5633565523,0.057534233\O,0,1.398977

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4813,-6.7432829\PG=C01 [X(C25H27N3O6S1)]\\@

References

1. Z.-Z. Zhu, K. Chen, L.-Z. Yu, X.-Y. Tang, M. Shi. *Org. Lett.* **2015**, *17*, 5994