Supporting Information

for

Stereoselective Synthesis of 3-Spiropiperidino Indolenines via S_N2-Type Ring Opening of Activated Aziridines with 1*H*-Indoles/Pd-Catalyzed Spirocyclization with Propargyl Carbonates

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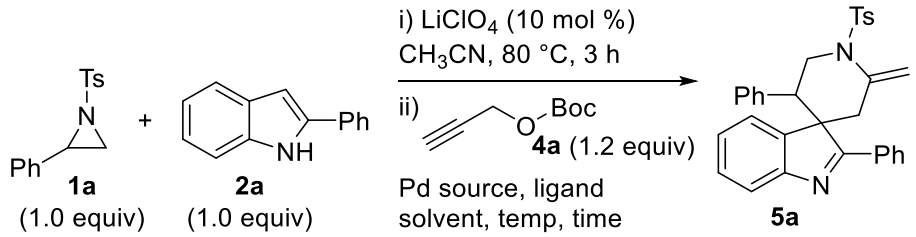
1. Optimization Studies

The reaction conditions were optimized to obtain **5a** in an improved yield (Table S1). No reaction ensued either when the catalyst was altered to bis(dibenzylideneacetone) palladium(0) (entry 2) or the solvent to acetonitrile (entry 3). Marginal increases in yields were observed when the reactions were performed in the presence of 10 mol % $Pd(PPh_3)_4$ and 20 mol % (±)-BINAP in DMF (55%, entry 4) and in toluene (62%, entry 5) at elevated temperatures. Notable increase in yield was observed when DMSO was used and **5a** formed in 84% yield at 120 °C in 5 min (entry 6). Next, several commercially available phosphine ligands were screened. While the usage of Xantphos provided **5a** in slightly decreased yield (73%, entry 7), the best result was obtained with relatively inexpensive 1,1'-bis(diphenylphosphino)ferrocene (dppf) ligand and **5a** was obtained in 86% yield (entry 8). Increase in the catalyst and ligand loading (20 and 40 mol %, respectively) was found to be inconsequential in boosting the efficiency of the transformation (entry 9). When the catalyst loading was reduced to 5 mol % along with 10 mol % dppf, the transformation furnished **5a** in 67% yield (entry 10). Attempts to further increasing the yield of the transformation either with PPh_3 and or with expensive palladium(II) acetate resulted in the formation of **5a** in reduced yield (entry 12) or no yield at all (entry 13), respectively.

Table S1. Optimization studies for the one-pot synthesis of 3-spiropiperidino indolenine **5a**[a]



entry	Pd source	ligand	solvent	T (°C)	time	yield (%)
1	$Pd(PPh_3)_4$	(±)-BINAP	1,2-DCE	85	9 h	51
2	$Pd(dba)_2$	(±)-BINAP	1,2-DCE	85	9 h	NR
3	$Pd(PPh_3)_4$	(±)-BINAP	CH_3CN	85	9 h	NR
4	$Pd(PPh_3)_4$	(±)-BINAP	DMF	120	5 h	55
5	$Pd(PPh_3)_4$	(±)-BINAP	toluene	110	6 h	62
6	$Pd(PPh_3)_4$	(±)-BINAP	DMSO	120	5 min	84
7	$Pd(PPh_3)_4$	Xantphos	DMSO	120	5 min	73
8	**$Pd(PPh_3)_4$**	**dppf**	**DMSO**	**120**	**5 min**	**86**
9[b]	$Pd(PPh_3)_4$	dppf	DMSO	120	5 min	86
10[c]	$Pd(PPh_3)_4$	dppf	DMSO	120	15 min	67
11	$Pd(PPh_3)_4$	Xphos	DMSO	120	5 min	82
12	$Pd(PPh_3)_4$	PPh_3	DMSO	120	2 h	45
13	$Pd(OAc)_2$	PPh_3	DMSO	120	6 h	NR

[a]Unless noted otherwise, all the reactions were carried out in the presence of 10 mol % metal source and 20 mol % ligand. [b]The reaction was carried out with 20 mol % $Pd(PPh_3)_4$ and 40 mol % dppf. [c]The reaction was carried out with 5 mol % $Pd(PPh_3)_4$ and 10 mol % dppf. NR denotes no reaction.

2. Diagnostic NOE Observations

The relative stereochemistry of the two phenyl groups at the 3′ and 5′-positions of **5q** was determined by nuclear overhauser effect (NOE) experiments. When proton H_b was irradiated, peak enhancement for the protons H_a and H_c was observed along with the enhancement of the *ortho* protons H_e of the phenyl group at 5′-position of the piperidine ring. On the other hand, when H_a was irradiated, significant enhancement of H_b and the *ortho* protons H_f of the phenyl group at 3′-position of the piperidine ring was observed. Noteworthily, in this case, no enhancement was observed for the proton H_d. All of these diagnostic NOE observations evidently suggest that the relative stereochemistry at the 3′ and 5′-positions of the 3-spiropiperidine indolenine is *trans*. The spatial interactions of the protons are shown in Figure S1.

Figure S1. Diagnostic NOE Observations for 3-Spiropiperidino Indolenine **5q**

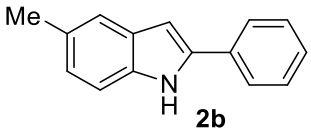
3. Experimental Section

General Procedures. The analytical thin layer chromatography (TLC) was carried out for monitoring the progress of the reactions using silica gel 60 F_{254} precoated plates. Visualizations of the spots were accomplished with a UV lamp or I_2 stain. Silica gel 230–400 mesh size was used for flash column chromatographic purification using a combination of ethyl acetate and petroleum ether as the eluent. Unless otherwise mentioned, all of the reactions were carried out in oven-dried glassware under an atmosphere of nitrogen or argon using anhydrous solvents.

Where appropriate, the solvents and all of the reagents were purified prior to use following the guidelines of Armarego and Chai.[1] The monosubstituted *N*-tosylaziridines (**1a-g**)[2] and *N*-arylsulfonylaziridines (**1h**–**i**)[3] were prepared by following the earlier reports. The propargyl carbonates (**4a**–**c**) were also prepared by following an earlier report.[4] All of the commercial reagents were used as received without further purification unless otherwise mentioned. Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded at 400 MHz and 500 MHz. The chemical shifts were recorded in parts per million (ppm, δ) using tetramethylsilane (δ 0.00) as the internal standard. Splitting patterns of the ^{1}H NMR are mentioned as singlet (s), doublet (d), doublet of doublet (dd), triplet (t), multiplet (m) etc. Proton-decoupled carbon nuclear magnetic resonance (^{13}C{^{1}H} NMR) spectra were recorded at 100 MHz and 125 MHz. HRMS were obtained using (ESI) mass spectrometer (TOF). KBr pellets were used for IR spectra of solid compounds. The melting point measurements were made using a hot stage apparatus and are reported as uncorrected. The enantiomeric excess (ee) was determined by chiral HPLC with a Chiralcel OD-H (detection at 254 nm) using hexane and isopropanol as the mobile phase and an UV/VIS detector. Optical rotations were measured using a 6.0 mL cell with a 1.0 dm path length and are reported as $[\alpha]^{25}_{D}$ (*c* in g per 100 mL solvent) at 25 °C.

4. Spectral Data

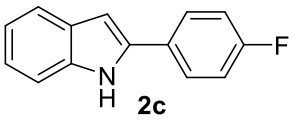
5-Methyl-2-phenyl-1*H*-indole (2b). Acetophenone (0.48 mL, 4.166 mmol, 1.0 equiv) and 4-methylphenylhydrazine hydrochloride (991.0 mg, 6.250 mmol, 1.5 equiv) were mixed with polyphosphoric acid (7.8 g), and the mixture was heated with stirring. The temperature of the reaction mixture was kept at 100–110 °C for 4 h. It was poured into ice water (25 mL) and extracted with EtOAc (8 × 20 mL). The combined extracts were dried over anhydrous Na_2SO_4. The dried extracts were concentrated, and the crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 5% ethyl acetate in petroleum ether as eluent to afford the pure product **2b** (672.8 mg,



2b

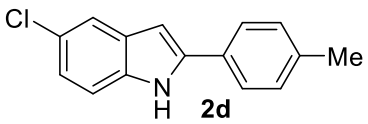
3.250 mmol) as a white solid in 78% yield. mp 190−192 °C; R_f 0.34 (ethyl acetate/petroleum ether, 1:9); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3430, 2928, 1704, 1584, 1492, 1448, 1403, 1348, 1315, 1299, 1243, 1204, 1027, 1007, 879, 789, 758, 740, 686, 589, 505; ^{1}H NMR (500 MHz, $CDCl_3$/DMSO, 10:1) δ 8.39 (s, 1H), 7.66–7.65 (m, 2H), 7.44–7.41 (m, 3H), 7.32–7.25 (m, 2H), 7.02 (d, J = 8.0 Hz, 1H), 6.75–6.72 (m, 1H), 2.46 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$/DMSO, 10:1) δ 137.9, 135.2, 132.6, 129.4, 129.0, 128.7, 127.3, 125.0, 123.6, 120.0, 110.6, 99.2, 21.3; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{14}N$ 208.1126; Found 208.1122.

2-(4-Fluorophenyl)-1*H*-indole (2c). 4-Fluorocetophenone (0.43 mL, 3.619 mmol, 1.0 equiv) and phenylhydrazine (0.53 mL, 5.429 mmol, 1.5 equiv) were mixed with polyphosphoric acid (7.8 g), and the mixture was heated with stirring. The temperature of the reaction mixture was kept at 100–110 °C for 4 h. It was poured into ice water (25 mL) and extracted with EtOAc (8 × 20 mL). The combined extracts were dried over anhydrous Na_2SO_4. The dried extracts were concentrated and the crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 5% ethyl acetate in petroleum ether as eluent to afford the pure product **2c** (581.0 mg, 2.750 mmol) as a white solid in 76% yield. mp 160−162 °C; R_f 0.34 (ethyl acetate/petroleum ether, 1:9); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3415, 1499, 1454, 1427, 1346, 1236, 1100, 836, 794, 752, 522, 509; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.63–7.59 (m, 3H), 7.39–7.38 (m, 1H), 7.22–7.19 (m, 1H), 7.15–7.12 (m, 3H), 6.75 (d, J = 1.3 Hz, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 162.4 (d, $^1J_{C–F}$ = 245.9 Hz), 137.0, 136.8, 129.2, 128.77, 128.75, 126.9, 126.8, 122.4, 120.6, 120.3, 116.1, 115.9, 110.8, 99.9; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{11}FN$ 212.0876; Found 212.0872.

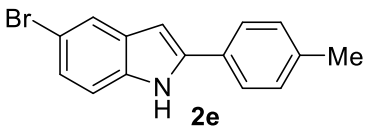


2c

5-Chloro-2-(*p*-tolyl)-1*H*-indole (2d). 4-Methylacetophenone (0.5 mL, 3.726 mmol, 1.0 equiv) and 4-chlorophenylhydrazine hydrochloride (1.0 g, 5.589 mmol, 1.5 equiv) were mixed with polyphosphoric acid (7.8 g), and the mixture was heated with stirring. The temperature of the reaction mixture was kept at 100–110 °C for 4 h. It was poured into ice water (25 mL) and extracted with EtOAc (8 × 20 mL). The combined extracts were dried over anhydrous Na_2SO_4. The dried extracts were concentrated, and the crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 5% ethyl acetate in petroleum ether as eluent to afford the pure product **2d** (675.5 mg, 2.790 mmol) as a white solid in 75% yield. mp 210−212 °C; R_f 0.31 (ethyl acetate/petroleum ether, 1:9); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3443, 1446, 1422, 1283, 1123, 1062, 921, 873, 821, 799, 781, 738, 692, 587, 508; ^1H NMR (500 MHz, $CDCl_3$/DMSO, 6:1) δ 10.13 (s, 1H), 7.54 (d, J = 8.0 Hz, 2H), 7.42 (s, 1H), 7.23 (d, J = 8.6 Hz, 1H), 7.14 (d, J = 8.0 Hz, 2H), 2.29 (s, 3H), 6.98–6.96 (m, 1H), 6.58 (s, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$/DMSO, 6:1) δ139.5, 137.4, 135.2, 130.0, 129.3, 129.2, 125.1, 124.8, 121.4, 119.1, 111.9, 97.8, 20.9; HRMS (ESI-TOF) *m/z*: $[M-H]^-$ Calcd for $C_{15}H_{11}ClN$ 240.0580; Found 240.0584.

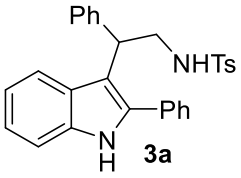


5-Bromo-2-(*p*-tolyl)-1*H*-indole (2e). 4-Methylacetophenone (0.5 mL, 3.726 mmol, 1.0 equiv) and 4-bromophenylhydrazine hydrochloride (1.249 g, 5.589 mmol, 1.5 equiv) were mixed with polyphosphoric acid (7.8 g), and the mixture was heated with stirring. The temperature of the reaction mixture was kept at 110–120 °C for 4 h. It was poured into ice water (25 mL) and extracted with EtOAc (8 × 20 mL). The combined extracts were dried over anhydrous Na_2SO_4. The dried extracts were concentrated, and the crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 5% ethyl acetate in petroleum ether as eluent to afford the pure product **2e** (767.8 mg, 2.680 mmol) as a white solid in 72% yield. mp 216−218 °C; R_f 0.31 (ethyl acetate/petroleum ether, 1:9); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3441, 2257, 1650, 1497, 1443, 1420, 1310,



1225, 1048, 1025, 998, 910, 822, 797, 778, 736, 661, 581, 509; ^{1}H NMR (500 MHz, $CDCl_3$/DMSO, 2:1) δ 10.94 (s, 1H), 7.58–7.55 (m, 3H), 7.22–7.06 (m, 4H), 6.57 (s, 1H), 2.29 (s, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$/DMSO, 2:1) δ 138.9, 136.6, 135.0, 130.0, 128.6, 128.5, 124.5, 123.1, 121.3, 112.0, 111.5, 96.7, 20.3; HRMS (ESI-TOF) *m/z*: $[M-H]^-$ Calcd for $C_{15}H_{11}BrN$ 284.0075; Found 284.0074.

4-Methyl-*N*-(2-phenyl-2-(2-phenyl-1*H*-indol-3-yl)ethyl)benzenesulfonamide (3a). The

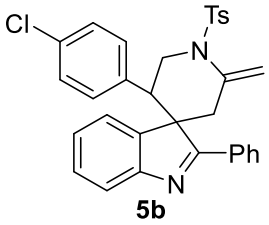


3a

mixture of aziridine **1a** (50.0 mg, 0.182 mmol, 1.0 equiv), **2a** (35.3 mg, 0.182 mmol, 1.0 equiv) and anhydrous $LiClO_4$ (1.9 mg, 0.018 mmol, 0.1 equiv) in CH_3CN (0.2 mL) were taken under argon atmosphere in a double necked round bottom flask. The reaction mixture was stirred at 80 °C for 3 h. After completion of the reaction, the reaction mixture was quenched with water, extracted with ethyl acetate (3 × 15.0 mL) and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 20% ethyl acetate in petroleum ether to afford the pure product **3a** (78.5 mg, 0.168 mmol) as white solid in 92% yield. mp 130−132 °C; R_f 0.18 (ethyl acetate/petroleum ether, 2:8); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3360, 3058, 2924, 1599, 1492, 1450, 1401, 1324, 1265, 1159, 1184, 1119, 1092, 1029, 1017, 975, 835, 813, 743, 700, 664, 578, 551, 528; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.46–7.36 (m, 8H), 7.25–7.17 (m, 7H), 7.11 (d, *J* = 8.3 Hz, 2H), 6.96–6.92 (m, 1H), 4.46 (dd, *J* = 6.0, 10.9 Hz, 1H), 4.23–4.21 (m, 1H), 3.78–3.72 (m, 1H), 3.67–3.62 (m, 1H), 2.38 (s, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 143.1, 141.5, 137.7, 136.1, 136.0, 132.0, 129.5, 128.8, 128.63 (2C), 128.60, 128.3, 127.6, 126.9, 126.6, 122.4, 120.2, 120.0, 111.4, 109.3, 46.6, 42.1, 21.5; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{29}H_{27}N_2O_2S$ 467.1793; Found 467.1797.

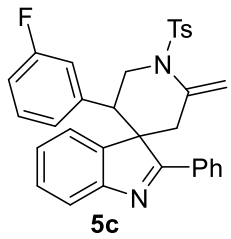
(*S*)-2′-Methylene-2,5′-diphenyl-1′-tosylspiro[indole-3,4′-piperidine] ((*S*)-5a). The mixture of (*R*)-**1a** (50.0 mg, 0.182 mmol, 1.0 equiv), **2a** (35.3 mg, 0.182 mmol, 1.0 equiv) and anhydrous $LiClO_4$ (1.9 mg, 0.018 mmol, 0.1 equiv) in CH_3CN (0.2 mL) was taken in a dried double necked round bottom flask under argon atmosphere and was stirred at 80 °C for 3 h. After the complete consumption of aziridine, $Pd(PPh_3)_4$ (21.0 mg, 0.018 mmol, 0.1 equiv), DPPF (20.2 mg, 0.036 mmol, 0.2 equiv) and propargylic carbonate (**4a**, 34.2 mg, 0.219 mmol, 1.2 equiv) in 3.0 mL of dry DMSO were added. The reaction mixture was then immediately heated at 120 °C and the reaction completed within 5 min as indicated by TLC. The reaction mixture was filtered through a small plug of silica gel followed by concentration under reduced pressure. The crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 15% ethyl acetate in petroleum ether as eluent to afford (*S*)-**5a** (79.3 mg, 0.157 mmol) as a white solid in 86% yield. mp 154−156 °C; $[\alpha]^{25}_D$ −32.4 (*c* 0.166 in CH_2Cl_2) for a 99% ee sample. Optical purity was determined by chiral HPLC analysis (Chiralcel OD-H column), hexane−2-propanol, 95:5; flow rate = 1.0 mL/min; t_R 1: 16.17 min (minor), t_R 2: 18.91 min (major): R_f 0.28 (ethyl acetate/petroleum ether, 2:8); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3060, 2923, 2851, 1647, 1596, 1522, 1493, 1453, 1441, 1398, 1352, 1266, 1238, 1183, 1164, 1110, 1093, 1025, 1015, 946, 894, 879, 816, 765, 736, 694, 672, 643, 625, 582, 541, 522; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.1 Hz, 2H), 7.71 (d, *J* = 7.4 Hz, 1H), 7.66–7.65 (m, 2H), 7.48–7.24 (m, 8H), 6.97 (t, *J* = 7.4 Hz, 1H), 6.81 (t, *J* = 7.7 Hz, 2H), 6.15 (d, *J* = 7.4 Hz, 2H), 5.53 (d, *J* = 1.3 Hz, 1H), 5.05 (d, *J* = 1.7 Hz, 1H), 4.37 (dd, *J* = 4.5, 14.4 Hz, 1H), 4.07–4.02 (m, 1H), 3.58 (dd, *J* = 4.5, 12.5 Hz, 1H), 3.19–3.17 (m, 1H), 2.57 (s, 3H), 2.09 (d, *J* = 13.6 Hz, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 178.3, 154.3, 143.7, 140.2, 137.9, 137.6, 135.5, 133.3, 130.4, 130.0, 128.7, 128.4, 128.1, 127.69, 127.61, 127.37, 127.31, 125.1, 124.6, 121.4, 115.3, 61.2, 47.9, 45.7, 37.9, 21.8; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{32}H_{29}N_2O_2S$ 505.1950; Found 505.1941.

5′-(4-Chlorophenyl)-2′-methylene-2-phenyl-1′-tosylspiro[indole-3,4′-piperidine] (5b). The mixture of **1b** (50.0 mg, 0.162 mmol, 1.0 equiv), **2a** (31.4 mg, 0.162 mmol, 1.0 equiv) and anhydrous $LiClO_4$ (1.7 mg, 0.016 mmol, 0.1 equiv) in CH_3CN (0.2 mL) was taken in a dried double necked round bottom flask under argon atmosphere and was stirred at 80 °C for 3 h. After the complete consumption of aziridine, $Pd(PPh_3)_4$ (18.7 mg, 0.016 mmol, 0.1 equiv), DPPF (17.9 mg, 0.032 mmol, 0.2 equiv) and propargylic carbonate (**4a**, 30.4 mg, 0.194 mmol, 1.2 equiv) in 3.0 mL of dry DMSO were added. The reaction mixture was then immediately heated at 120 °C and the reaction completed within 15 min as indicated by TLC. The reaction mixture was filtered through a small plug of silica gel followed by concentration under reduced pressure. The crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 15% ethyl acetate in petroleum ether as eluent to afford **5b** (73.5 mg, 0.136 mmol) as a white solid in 84% yield. mp 140−142 °C; R_f 0.33 (ethyl acetate/petroleum ether, 2:8); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3059, 2923, 1735, 1647, 1595, 1521, 1493, 1465, 1441, 1411, 1353, 1325, 1266, 1183, 1165, 1112, 1092, 1013, 933, 947, 895, 879, 857, 827, 777, 759, 736, 707, 692, 677, 641, 617, 608, 582, 554, 541, 518; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, J = 8.2 Hz, 2H), 7.70–7.69 (m, 3H), 7.50–7.36 (m, 7H), 7.27–7.23 (m, 1H), 6.78 (d, J = 8.4 Hz, 2H), 6.07 (d, J = 8.3 Hz, 2H), 5.50 (d, J = 1.6 Hz, 1H), 5.05 (d, J = 1.8 Hz, 1H), 4.33 (dd, J = 4.6, 14.1 Hz, 1H), 3.99 (dd, J = 12.9, 14.7 Hz, 1H), 3.59 (dd, J = 4.3, 12.3 Hz, 1H), 3.21 (dt, J = 1.8, 13.7 Hz, 1H), 2.56 (s, 3H), 2.11 (d, J = 13.8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 178.1, 154.4, 144.0, 140.0, 137.9, 137.6, 134.1, 133.5, 133.2, 130.7, 130.2, 129.0, 128.7, 128.6, 128.2, 128.0, 127.5, 125.3, 124.6, 121.7, 115.6, 61.2, 47.7, 45.2, 37.9, 21.9; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{32}H_{28}ClN_2O_2S$ 539.1560; Found 539.1566.



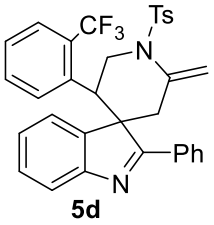
5b

5′-(3-Fluorophenyl)-2′-methylene-2-phenyl-1′-tosylspiro[indole-3,4′-piperidine] (5c). The mixture of **1c** (50.0 mg, 0.171 mmol, 1.0 equiv), **2a** (33.1 mg, 0.171 mmol, 1.0 equiv) and anhydrous $LiClO_4$ (1.8 mg, 0.017 mmol, 0.1 equiv) in CH_3CN (0.2 mL) was taken in a dried double necked round bottom flask under argon atmosphere and was stirred at 80 °C for 3 h. After the complete consumption of aziridine, $Pd(PPh_3)_4$ (19.7 mg, 0.017 mmol, 0.1 equiv), DPPF (21.3 mg, 0.034 mmol, 0.2 equiv) and propargylic carbonate (**4a**, 32.1 mg, 0.205 mmol, 1.2 equiv) in 3.0 mL of dry DMSO were added. The reaction mixture was then immediately heated at 120 °C and the reaction completed within 5 min as indicated by TLC. The reaction mixture was filtered through a small plug of silica gel followed by concentration under reduced pressure. The crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 15% ethyl acetate in petroleum ether as eluent to afford **5c** (78.9 mg, 0.150 mmol) as a white solid in 88% yield. mp 172−174 °C; R_f 0.29 (ethyl acetate/petroleum ether, 2:8); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3062, 2924, 1649, 1614, 1588, 1522, 1491, 1447, 1351, 1325, 1265, 1239, 1184, 1165, 1111, 1090, 1024, 964, 868, 816, 786, 773, 756, 736, 691, 676, 644, 579, 545, 521; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, J = 8.3 Hz, 2H), 7.70–7.66 (m, 3H), 7.51–7.34 (m, 7H), 7.28–7.24 (m, 1H), 6.81–6.69 (m, 1H), 6.68–6.65 (m, 1H), 5.97 (d, J = 7.8 Hz, 1H), 5.82–5.79 (m, 1H), 5.52 (d, J = 1.5 Hz, 1H), 5.06 (d, J = 1.8 Hz, 1H), 4.36 (dd, J = 4.4, 14.3 Hz, 1H), 3.99 (dd, J = 12.6, 14.2 Hz, 1H), 3.58 (dd, J = 4.6, 12.6 Hz, 1H), 3.20–3.18 (m, 1H), 2.57 (s, 3H), 2.10 (d, J = 13.9 Hz, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 178.1, 161.8 (d, $^1J_{C–F}$ = 244.4 Hz), 154.3, 143.9, 139.9, 138.1, 138.0, 137.9, 137.5, 133.2, 130.6, 130.1, 129.19, 129.12, 128.9, 128.5, 128.1, 127.4, 125.3, 124.5, 123.2, 121.6, 115.4, 114.6, 114.4, 114.3, 114.1, 61.1, 47.7, 45.5, 37.9, 21.7; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{32}H_{28}FN_2O_2S$ 523.1856; Found 523.1858.



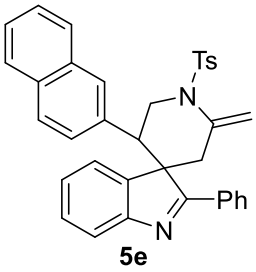
5c

2′-Methylene-2-phenyl-1′-tosyl-5′-(2-(trifluoromethyl)phenyl)spiro[indole-3,4′-piperidine] (5d). The mixture of **1d** (50.0 mg, 0.146 mmol, 1.0 equiv), **2a** (28.3 mg, 0.146 mmol, 1.0 equiv) and anhydrous $LiClO_4$ (1.5 mg, 0.014 mmol, 0.1 equiv) in CH_3CN (0.2 mL) was taken in a dried double necked round bottom flask under argon atmosphere and was stirred at 80 °C for 3 h. After the complete consumption of aziridine, $Pd(PPh_3)_4$ (16.8 mg, 0.014 mmol, 0.1 equiv), DPPF (16.1 mg, 0.029 mmol, 0.2 equiv) and propargylic carbonate (**4a**, 27.4 mg, 0.175 mmol, 1.2 equiv) in 3.0 mL of dry DMSO were added. The reaction mixture was then immediately heated at 120 °C and the reaction completed within 10 min as indicated by TLC. The reaction mixture was filtered through a small plug of silica gel followed by concentration under reduced pressure. The crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 15% ethyl acetate in petroleum ether as eluent to afford **5d** (54.5 mg, 0.095 mmol) as a white solid in 65% yield. mp 180−182 °C; R_f 0.28 (ethyl acetate/petroleum ether, 2:8); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3059, 2921, 1647, 1520, 1492, 1455, 1349, 1308, 1163, 1111, 1092, 1038, 944, 890, 816, 762, 670, 642, 626, 581, 550; ^1H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, J = 8.3 Hz, 2H), 7.74 (d, J = 7.5 Hz, 1H), 7.67 (d, J = 7.6 Hz, 1H), 7.53–7.50 (m, 1H), 7.44–7.31 (m, 5H), 7.25–7.20 (m, 4H), 7.14 (t, J = 7.7 Hz, 1H), 6.91 (t, J = 7.4 Hz, 1H), 6.06 (d, J = 8.1 Hz, 1H), 5.69 (d, J = 1.3 Hz, 1H), 4.95 (d, J = 1.8 Hz, 1H), 4.56 (dd, J = 4.4, 14.3 Hz, 1H), 3.90 (dd, J = 4.3, 12.2 Hz, 1H), 3.74 (dd, J = 12.3, 14.0 Hz, 1H), 3.04–3.02 (m, 1H), 2.56 (s, 3H), 1.97 (d, J = 13.3 Hz, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 179.7, 154.4, 143.7, 140.5, 137.3, 137.1, 135.3, 133.5, 131.5, 130.4, 129.7, 129.0, 128.2, 128.1, 128.0, 127.68, 127.61, 126.7, 126.48, 126.43, 126.3, 125.62 (q, $^1J_{C–F}$ = 274.7 Hz), 125.61, 125.1, 122.0, 114.2, 60.9, 48.9, 42.2, 39.6, 21.6; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{33}H_{28}F_3N_2O_2S$ 573.1824; Found 573.1828.



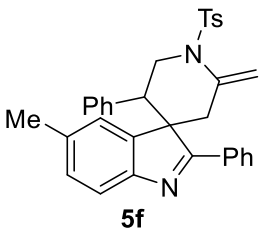
5d

2′-Methylene-5′-(naphthalen-2-yl)-2-phenyl-1′-tosylspiro[indole-3,4′-piperidine] (5e). The mixture of **1e** (50.0 mg, 0.154 mmol, 1.0 equiv), **2a** (29.8 mg, 0.154 mmol, 1.0 equiv) and anhydrous $LiClO_4$ (1.9 mg, 0.015 mmol, 0.1 equiv) in CH_3CN (0.2 mL) was taken in a dried double necked round bottom flask under argon atmosphere and was stirred at 80 °C for 8 h. After the complete consumption of aziridine, $Pd(PPh_3)_4$ (17.8 mg, 0.015 mmol, 0.1 equiv), DPPF (17.1 mg, 0.030 mmol, 0.2 equiv) and propargylic carbonate (**4a**, 28.9 mg, 0.185 mmol, 1.2 equiv) in 3.0 mL of dry DMSO were added. The reaction mixture was then immediately heated at 120 °C and the reaction completed within 15 min as indicated by TLC. The reaction mixture was filtered through a small plug of silica gel followed by concentration under reduced pressure. The crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 15% ethyl acetate in petroleum ether as eluent to afford **5e** (60.0 mg, 0.107 mmol) as a white solid in 70% yield. mp 122−124 °C; R_f 0.27 (ethyl acetate/petroleum ether, 2:8); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3056, 2921, 2850, 1736, 1647, 1597, 1522, 1491, 1458, 1440, 1352, 1265, 1164, 1110, 1091, 1024, 945, 886, 857, 816, 772, 748, 710, 681, 671, 658, 640, 609, 547, 519, 477; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, J = 8.1 Hz, 2H), 7.79 (d, J = 7.4 Hz, 1H), 7.65–7.63 (m, 2H), 7.57 (d, J = 7.9 Hz, 1H), 7.51–7.23 (m, 12H), 6.52 (s, 1H), 6.30–6.28 (m, 1H), 5.55 (d, J = 1.7 Hz, 1H), 5.08 (d, J = 1.8 Hz, 1H), 4.42 (dd, J = 4.6, 14.2 Hz, 1H), 4.14 (dd, J = 12.6, 14.2 Hz, 1H), 3.73 (dd, J = 4.6, 12.6 Hz, 1H), 3.27–3.24 (m, 1H), 2.58 (s, 3H), 2.16 (d, J = 13.7 Hz, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 178.4, 154.4, 143.8, 140.2, 137.9, 137.7, 133.5, 133.0, 132.59, 132.57, 130.5, 130.0, 128.8, 128.4, 128.2 (2C), 127.6, 127.4, 127.27, 127.21, 126.6, 125.7, 125.3, 125.1, 124.7, 121.6, 115.2, 61.4, 48.0, 45.9, 38.0, 21.8; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{36}H_{31}N_2O_2S$ 555.2106; Found 555.2109.



5e

(*S*)-5-Methyl-2′-methylene-2,5′-diphenyl-1′-tosylspiro[indole-3,4′-piperidine] ((*S*)-5f).

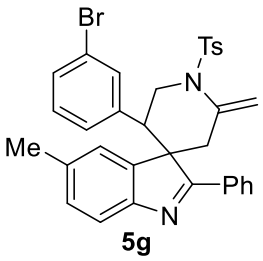


5f

The mixture of (*R*)-**1a** (50.0 mg, 0.182 mmol, 1.0 equiv), **2b** (37.9 mg, 0.182 mmol, 1.0 equiv) and anhydrous $LiClO_4$ (1.9 mg, 0.018 mmol, 0.1 equiv) in CH_3CN (0.2 mL) was taken in a dried double necked round bottom flask under argon atmosphere and was stirred at 80 °C for 6 h. After the complete consumption of aziridine, $Pd(PPh_3)_4$ (21.0 mg, 0.018 mmol, 0.1 equiv), DPPF (20.2 mg, 0.036 mmol, 0.2 equiv) and propargylic carbonate (**4a**, 34.2 mg, 0.219 mmol, 1.2 equiv) in 3.0 mL of dry DMSO were added. The reaction mixture was then immediately heated at 120 °C and the reaction completed within 15 min as indicated by TLC. The reaction mixture was filtered through a small plug of silica gel followed by concentration under reduced pressure. The crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 15% ethyl acetate in petroleum ether as eluent to afford (*S*)**-5f** (75.9 mg, 0.145 mmol) as a white solid in 80% yield. mp 200−202 °C; $[\alpha]^{25}_D$ −76.3 (*c* 0.183 in CH_2Cl_2) for a 98% ee sample. Optical purity was determined by chiral HPLC analysis (Chiralcel OD-H column), hexane−2-propanol, 95:5; flow rate = 1.0 mL/min; t_R 1: 13.15 min (minor), t_R 2: 15.50 min (major): R_f 0.33 (ethyl acetate/petroleum ether, 2:8); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3059, 3029, 2922, 1894, 1736, 1647, 1596, 1522, 1493, 1467, 1453, 1442, 1399, 1352, 1333, 1268, 1237, 1183, 1165, 1114, 1090, 1025, 1015, 946, 937, 865, 819, 762, 720, 696, 677, 667, 587, 570, 551, 542; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.2 Hz, 2H), 7.62–7.60 (m, 2H), 7.50 (s, 1H), 7.46–7.43 (m, 3H), 7.36–7.31 (m, 3H), 7.19 (d, *J* = 7.7 Hz, 1H), 6.97 (t, *J* = 7.3 Hz, 1H), 6.82 (t, *J* = 7.6 Hz, 2H), 6.15 (d, *J* = 7.4 Hz, 2H), 5.57 (d, *J* = 1.3 Hz, 1H), 5.06 (d, *J* = 1.6 Hz, 1H), 4.35 (dd, *J* = 4.5, 14.4 Hz, 1H), 4.08–4.02 (m, 1H), 3.53 (dd, *J* = 4.4, 12.6 Hz, 1H), 3.15–3.12 (m, 1H), 2.57 (s, 3H), 2.46 (s, 3H), 2.08 (d, *J* = 13.8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 177.5, 152.3, 143.8, 140.5, 138.0, 137.7, 135.8, 135.1, 133.6, 130.3, 130.1, 129.4, 128.4, 128.1,

127.8, 127.6, 127.5, 127.4, 125.4, 121.1, 115.3, 61.1, 48.0, 45.8, 38.1, 21.97, 21.91; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{33}H_{31}N_2O_2S$ 519.2106; Found 519.2102.

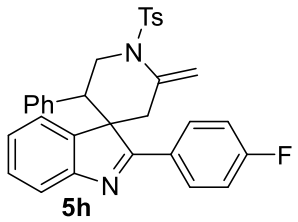
5′-(3-Bromophenyl)-5-methyl-2′-methylene-2-phenyl-1′-tosylspiro[indole-3,4′-piperidine] (5g). The mixture of **1f** (50.0 mg, 0.141 mmol, 1.0 equiv), **2b** (29.4 mg, 0.141 mmol, 1.0 equiv) and anhydrous $LiClO_4$ (1.5 mg, 0.014 mmol, 0.1 equiv) in CH_3CN (0.2 mL) was taken in a dried double necked round bottom flask under argon atmosphere and was stirred at 80 °C for 3.5 h. After the complete consumption of aziridine, $Pd(PPh_3)_4$ (16.2 mg, 0.014 mmol, 0.1 equiv), DPPF (15.6 mg, 0.028 mmol, 0.2 equiv) and propargylic carbonate (**4a**, 26.5 mg, 0.170 mmol, 1.2 equiv) in 3.0 mL of dry DMSO were added. The reaction mixture was then immediately heated at 120 °C and the reaction completed within 15 min as indicated by TLC. The reaction mixture was filtered through a small plug of silica gel followed by concentration under reduced pressure. The crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 15% ethyl acetate in petroleum ether as eluent to afford **5g** (66.9 mg, 0.111 mmol) as a white solid in 79% yield. mp 208−210 °C; R_f 0.31 (ethyl acetate/petroleum ether, 2:8); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3060, 2923, 2853, 1740, 1651, 1592, 1565, 1521, 1459, 1440, 1352, 1322, 1278, 1163, 1092, 996, 941, 891, 876, 819, 785, 767, 745, 678, 643, 627, 592, 561, 525; ^1H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, J = 8.2 Hz, 2H), 7.60 (d, J = 7.4 Hz, 2H), 7.48–7.44 (m, 4H), 7.39–7.34 (m, 3H), 7.21 (d, J = 7.9 Hz, 1H), 7.11–7.10 (m, 1H), 6.69 (t, J = 7.9 Hz, 1H), 6.21–6.20 (m, 1H), 6.08 (d, J = 7.8 Hz, 1H), 5.55 (d, J = 1.3 Hz, 1H), 5.07 (d, J = 1.8 Hz, 1H), 4.32 (dd, J = 4.5, 14.4 Hz, 1H), 4.01–3.96 (m, 1H), 3.46 (dd, J = 4.4, 12.6 Hz, 1H), 3.18–3.15 (m, 1H), 2.56 (s, 3H), 2.46 (s, 3H), 2.12 (d, J = 13.7 Hz, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 177.1, 152.2, 143.9, 139.9, 137.8, 137.7, 137.4, 135.2, 133.3, 130.7, 130.6, 130.4, 130.1, 129.6, 129.1, 128.4, 128.0, 127.4, 125.8, 125.2, 121.5,



5g

121.2, 115.5, 60.8, 47.5, 45.4, 37.7, 21.85, 21.80; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{33}H_{30}BrN_2O_2S$ 597.1211; Found 597.1219.

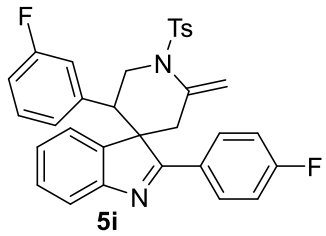
(*S*)-2-(4-Fluorophenyl)-2′-methylene-5′-phenyl-1′-tosylspiro[indole-3,4′-piperidine] ((*S*)-5h). The mixture of (*R*)-**1a** (50.0 mg, 0.182 mmol, 1.0 equiv), **2c** (38.6 mg, 0.182 mmol, 1.0 equiv) and anhydrous $LiClO_4$ (1.9 mg, 0.018 mmol, 0.1 equiv) in CH_3CN (0.2 mL) was taken in a dried double necked round bottom flask under argon atmosphere and was stirred at 80 °C for 3 h. After the complete consumption of aziridine, $Pd(PPh_3)_4$ (21.0 mg, 0.018 mmol, 0.1 equiv), DPPF (20.2 mg, 0.036 mmol, 0.2 equiv) and propargylic carbonate (**4a**, 34.2 mg, 0.219 mmol, 1.2 equiv) in 3.0 mL of dry DMSO were added. The reaction mixture was then immediately heated at 120 °C and the reaction completed within 10 min as indicated by TLC. The reaction mixture was filtered through a small plug of silica gel followed by concentration under reduced pressure. The crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 15% ethyl acetate in petroleum ether as eluent to afford (*S*)-**5h** (82.1 mg, 0.157 mmol) as a white solid in 86% yield. mp 252−254 °C; $[\alpha]^{25}_D$ −52.9 (*c* 0.170 in CH_2Cl_2) for a 98% ee sample. Optical purity was determined by chiral HPLC analysis (Chiralcel OD-H column), hexane−2-propanol, 98:2; flow rate = 1.0 mL/min; t_R 1: 30.71 min (minor), t_R 2: 43.20 min (major): R_f 0.36 (ethyl acetate/petroleum ether, 2:8); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3061, 2923, 1649, 1598, 1505, 1453, 1406, 1353, 1302, 1267, 1234, 1165, 1095, 1027, 946, 894, 841, 817, 767, 736, 700, 675, 629, 582, 567, 541, 521; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.3 Hz, 2H), 7.71–7.67 (m, 3H), 7.47–7.44 (m, 3H), 7.40–7.37 (m, 1H), 7.27–7.24 (m, 1H), 7.05–7.01 (m, 2H), 6.99–6.96 (m, 1H), 6.82 (t, *J* = 7.8 Hz, 2H), 6.13 (d, *J* = 7.4 Hz, 2H), 5.51 (d, *J* = 1.6 Hz, 1H), 5.06 (d, *J* = 1.8 Hz, 1H), 4.36 (dd, *J* = 4.4, 14.4 Hz, 1H), 4.03 (dd, *J* = 12.7, 14.3 Hz, 1H), 3.53 (dd, *J* = 4.4, 12.6 Hz, 1H), 3.15–3.13 (m, 1H), 2.57 (s, 3H), 2.10 (d, *J* = 13.7 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 177.3, 164.0 (d,



5h

$^{1}J_{C–F}$ = 253.8 Hz), 154.3, 143.9, 140.2, 138.1, 137.6, 135.5, 130.5, 130.4, 130.1, 129.7, 128.9, 127.85, 127.80, 127.5, 127.3, 125.3, 124.7, 121.5, 115.7, 115.6, 115.5, 61.3, 48.0, 45.9, 38.0, 21.8; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{32}H_{28}FN_2O_2S$ 523.1856; Found 523.1859.

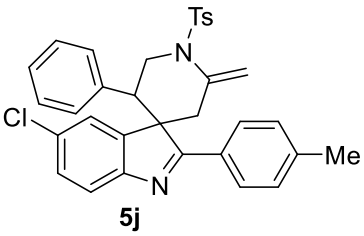
5′-(3-Fluorophenyl)-2-(4-fluorophenyl)-2′-methylene-1′-tosylspiro[indole-3,4′-piperidine] (5i). The mixture of **1c** (50.0 mg, 0.171 mmol, 1.0 equiv), **2c** (36.2 mg, 0.171 mmol, 1.0 equiv) and anhydrous $LiClO_4$ (1.8 mg, 0.017 mmol, 0.1 equiv) in CH_3CN (0.2 mL) was taken in a dried double necked round bottom flask under argon atmosphere and was stirred at 80 °C for 3 h. After the complete consumption of aziridine, $Pd(PPh_3)_4$ (19.7 mg, 0.017 mmol, 0.1 equiv), DPPF (21.3 mg, 0.034 mmol, 0.2 equiv) and propargylic carbonate (**4a**, 32.1 mg, 0.205 mmol, 1.2 equiv) in 3.0 mL of dry DMSO were added. The reaction mixture was then immediately heated at 120 °C and the reaction completed within 5 min as indicated by TLC. The reaction mixture was filtered through a small plug of silica gel followed by concentration under reduced pressure. The crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 15% ethyl acetate in petroleum ether as eluent to afford **5i** (81.6 mg, 0.151 mmol) as a white solid in 88% yield. mp 194−196 °C; R_f 0.28 (ethyl acetate/petroleum ether, 2:8); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3066, 2924, 1649, 1613, 1596, 1522, 1505, 1492, 1449, 1406, 1352, 1325, 1303, 1266, 1236, 1184, 1165, 1110, 1099, 1027, 922, 887, 869, 842, 787. 773, 736, 705, 675, 632, 604, 548, 537, 522, 464; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.3 Hz, 2H), 7.72–7.68 (m, 3H), 7.49–7.39 (m, 4H), 7.28–7.25 (m, 1H), 7.06–7.02 (m, 2H), 6.82–6.78 (m, 1H), 6.70–6.66 (m, 1H), 5.97 (d, *J* = 7.9 Hz, 1H), 5.82–5.79 (m, 1H), 5.50 (d, *J* = 1.6 Hz, 1H), 5.06 (d, *J* = 1.8 Hz, 1H), 4.36 (dd, *J* = 4.4, 14.3 Hz, 1H), 3.98 (dd, *J* = 12.6, 14.1 Hz, 1H), 3.56 (dd, *J* = 4.6, 12.5 Hz, 1H), 3.17–3.14 (m, 1H), 2.57 (s, 3H), 2.11 (d, *J* = 13.7 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 176.9, 164.0 (d, $^{1}J_{C–F}$ = 251.2 Hz), 161.8 (d, $^{1}J_{C–F}$ = 244.4 Hz), 154.2, 143.9, 139.8, 137.99, 137.93, 137.4, 130.38,



5i

130.31, 130.1, 129.52, 129.50, 129.3, 129.2, 129.1, 129.0, 127.4, 127.3, 125.3, 124.5, 123.2, 121.6, 115.78, 115.71, 115.6, 114.7, 114.5, 114.2, 114.1, 61.0, 47.7, 45.6, 37.9, 21.7; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{32}H_{27}F_2N_2O_2S$ 541.1761; Found 541.1763.

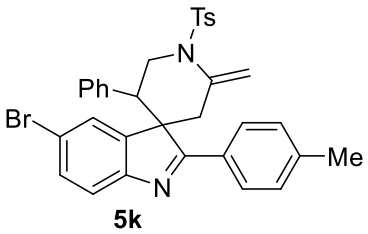
(*S*)-5-Chloro-2′-methylene-5′-phenyl-2-(*p*-tolyl)-1′-tosylspiro[indole-3,4′-piperidine] ((*S*)-5j). The mixture of (*R*)-**1a** (50.0 mg, 0.182 mmol, 1.0 equiv), **2d** (44.2 mg, 0.182 mmol, 1.0 equiv) and anhydrous $LiClO_4$ (1.9 mg, 0.018 mmol, 0.1 equiv) in CH_3CN (0.1 mL) and 1,2-DCE (0.2 mL) was taken in a dried double necked round bottom flask under argon atmosphere and was stirred at 80 °C for 4 h. After the complete consumption of aziridine, $Pd(PPh_3)_4$ (21.0 mg, 0.018 mmol, 0.1 equiv), DPPF (20.2 mg, 0.036 mmol, 0.2 equiv) and propargylic carbonate (**4a**, 34.2 mg, 0.219 mmol, 1.2 equiv) in 3.0 mL of dry DMSO were added. The reaction mixture was then immediately heated at 120 °C and the reaction completed within 10 min as indicated by TLC. The reaction mixture was filtered through a small plug of silica gel followed by concentration under reduced pressure. The crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 15% ethyl acetate in petroleum ether as eluent to afford (*S*)-**5j** (86.0 mg, 0.155 mmol) as a white solid in 85% yield. mp 154−156 °C; $[\alpha]^{25}_D$ −75.0 (*c* 0.080 in CH_2Cl_2) for a 95% ee sample. Optical purity was determined by chiral HPLC analysis (Chiralcel OD-H column), hexane−2-propanol, 95:5; flow rate = 1.0 mL/min; t_R 1: 13.19 min (minor), t_R 2: 14.80 min (major): R_f 0.31 (ethyl acetate/petroleum ether, 2:8); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3060, 3030, 2922, 2853, 1646, 1597, 1576, 1509, 1494, 1450, 1415, 1353, 1330, 1254, 1184, 1165, 1113, 1090, 1028, 945, 887, 818, 770, 711, 699, 677, 633, 592, 549, 541, 522; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.2 Hz, 2H), 7.65–7.63 (m, 3H), 7.46 (d, *J* = 8.1 Hz, 2H), 7.35–7.31 (m, 2H), 7.17 (d, *J* = 7.5 Hz, 2H), 6.98 (t, *J* = 7.6 Hz, 1H), 6.84 (t, *J* = 7.6 Hz, 2H), 6.21 (d, *J* = 7.4 Hz, 2H), 5.53 (d, *J* = 1.4 Hz, 1H), 5.09 (d, *J* = 1.5 Hz, 1H), 4.37 (dd, *J* = 4.6, 14.3 Hz, 1H), 3.99 (dd, *J* = 12.7,



5j

14.2 Hz, 1H), 3.67 (dd, *J* = 4.4, 12.6 Hz, 1H), 3.23–3.20 (m, 1H), 2.57 (s, 3H), 2.43 (s, 3H), 2.09 (d, *J* = 13.9 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 178.7, 153.1, 143.8, 142.1, 141.2, 137.8, 137.5, 135.3, 130.5, 130.2, 130.1, 129.3, 128.8, 128.2, 127.79, 127.72, 127.4, 127.3, 124.6, 121.9, 115.5, 61.6, 47.7, 45.8, 38.0, 21.7, 21.5; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{33}H_{30}ClN_2O_2S$ 553.1717; Found 553.1713.

5-Bromo-2′-methylene-5′-phenyl-2-(*p*-tolyl)-1′-tosylspiro[indole-3,4′-piperidine] (5k). The mixture of **1a** (50.0 mg, 0.182 mmol, 1.0 equiv), **2e** (52.3 mg, 0.182 mmol, 1.0 equiv) and anhydrous $LiClO_4$ (1.9 mg, 0.018 mmol, 0.1 equiv) in CH_3CN (0.1 mL) and 1,2-DCE (0.2 mL) was taken in a dried double necked round bottom flask under argon atmosphere and was stirred at 80 °C for 7 h. After the complete consumption of aziridine, $Pd(PPh_3)_4$ (21.0 mg, 0.018 mmol, 0.1 equiv), DPPF (20.2 mg, 0.036 mmol, 0.2 equiv) and propargylic carbonate (**4a**, 34.2 mg, 0.219 mmol, 1.2 equiv) in 3.0 mL of dry DMSO were added. The reaction mixture was then immediately heated at 120 °C and the reaction completed within 10 min as indicated by TLC. The reaction mixture was filtered through a small plug of silica gel followed by concentration under reduced pressure. The crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 15% ethyl acetate in petroleum ether as eluent to afford **5k** (92.9 mg, 0.155 mmol) as a white solid in 85% yield.

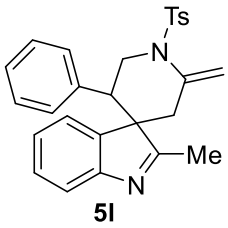


5k

mp 210−212 °C; R_f 0.34 (ethyl acetate/petroleum ether, 2:8); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3060, 2922, 2852, 1646, 1508, 1449, 1353, 1329, 1255, 1184, 1164, 1090, 1014, 945, 883, 818, 769, 733, 709, 633, 590, 539; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.5 Hz, 2H), 7.79–7.78 (m, 1H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.49–7.45 (m, 3H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 2H), 6.98 (t, *J* = 7.4 Hz, 1H), 6.84 (t, *J* = 7.4 Hz, 2H), 6.20 (d, *J* = 7.4 Hz, 2H), 5.53 (d, *J* = 1.1 Hz, 1H), 5.09 (d, *J* = 2.2 Hz, 1H), 4.37 (dd, *J* = 4.6, 14.3 Hz, 1H), 3.98 (dd, *J* = 12.6, 13.8 Hz, 1H), 3.66 (dd, *J* = 4.6, 12.6 Hz, 1H), 3.22–3.20 (m, 1H), 2.57 (s, 3H), 2.43 (s, 3H), 2.09 (d, *J* = 14.3

Hz, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 178.6, 153.4, 143.8, 142.5, 141.3, 137.8, 137.4, 135.2, 131.7, 130.1, 129.3, 128.9, 128.2, 127.79, 127.73, 127.4 (2C), 127.3, 122.4, 118.4, 115.6, 61.6, 47.7, 45.8, 37.9, 21.7, 21.5; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{33}H_{30}BrN_2O_2S$ 597.1211; Found 597.1215.

(*S*)-2-Methyl-2′-methylene-5′-phenyl-1′-tosylspiro[indole-3,4′-piperidine] ((*S*)-5l). The

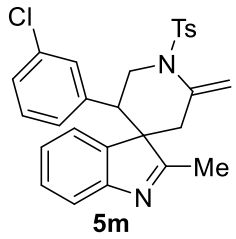


5l

mixture of (*R*)-**1a** (50.0 mg, 0.182 mmol, 1.0 equiv), **2f** (23.9 mg, 0.182 mmol, 1.0 equiv) and anhydrous $LiClO_4$ (1.9 mg, 0.018 mmol, 0.1 equiv) in CH_3CN (0.2 mL) was taken in a dried double necked round bottom flask under argon atmosphere and was stirred at 80 °C for 2.5 h. After the complete consumption of aziridine, $Pd(PPh_3)_4$ (21.0 mg, 0.018 mmol, 0.1 equiv), DPPF (20.2 mg, 0.036 mmol, 0.2 equiv) and propargylic carbonate (**4a**, 34.2 mg, 0.219 mmol, 1.2 equiv) in 3.0 mL of dry DMSO were added. The reaction mixture was then immediately heated at 120 °C and the reaction completed within 5 min as indicated by TLC. The reaction mixture was filtered through a small plug of silica gel followed by concentration under reduced pressure. The crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 20% ethyl acetate in petroleum ether as eluent to afford (*S*)-**5l** (65.4 mg, 0.147 mmol) as a white solid in 81% yield. mp 174−176 °C; $[\alpha]^{25}_D$ −120.0 (*c* 0.125 in CH_2Cl_2) for a 99% ee sample. Optical purity was determined by chiral HPLC analysis (Chiralcel OD-H column), hexane−2-propanol, 95:5; flow rate = 1.0 mL/min; t_R 1: 23.49 min (minor), t_R 2: 36.97 min (major): R_f 0.32 (ethyl acetate/petroleum ether, 4:6); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3060, 3030, 2948, 1735, 1649, 1590, 1578, 1494, 1452, 1429, 1399, 1379, 1351, 1323, 1305, 1290, 1280, 1250, 1206, 1164, 1118, 1107, 1092, 1032, 1019, 943, 908, 891, 862, 817, 800, 767, 736, 702, 671, 636, 587, 570, 547, 526, 484; ^1H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.1 Hz, 2H), 7.60 (d, *J* = 7.4 Hz, 1H), 7.42 (d, *J* = 8.3 Hz, 2H), 7.34–7.32 (m, 2H), 7.21–7.18 (m, 1H), 7.06–7.03 (m, 1H), 6.94 (t, *J* = 7.6 Hz, 2H), 6.41 (d, *J* = 7.6 Hz, 2H), 5.40 (d, *J* = 1.4 Hz, 1H), 4.95 (d, *J*

= 1.7 Hz, 1H), 4.32 (dd, *J* = 4.4, 14.1 Hz, 1H), 3.88–3.83 (m, 1H), 3.12 (dd, *J* = 4.3, 12.4 Hz, 1H), 2.58–2.55 (m, 1H), 2.50 (s, 3H), 2.04 (s, 3H), 1.81 (d, *J* = 13.2 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 182.5, 154.9, 144.1, 138.9, 137.89, 137.86, 135.9, 130.0, 128.6, 128.2, 127.9, 127.5, 127.2, 124.7, 124.4, 120.6, 114.2, 60.8, 48.3, 45.7, 37.9, 21.7, 15.9; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{27}N_2O_2S$ 443.1793; Found 443.1790.

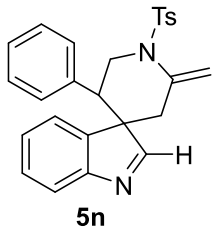
5′-(3-Chlorophenyl)-2-methyl-2′-methylene-1′-tosylspiro[indole-3,4′-piperidine] (5m). The mixture of **1g** (50.0 mg, 0.162 mmol, 1.0 equiv), **2f** (21.3 mg, 0.162 mmol, 1.0 equiv) and anhydrous $LiClO_4$ (1.7 mg, 0.016 mmol, 0.1 equiv) in CH_3CN (0.2 mL) was taken in a dried double necked round bottom flask under argon atmosphere and was stirred at 80 °C for 3 h. After the complete consumption of aziridine, $Pd(PPh_3)_4$ (18.7 mg, 0.016 mmol, 0.1 equiv), DPPF (17.9 mg, 0.032 mmol, 0.2 equiv) and propargylic carbonate (**4a**, 30.4 mg, 0.194 mmol, 1.2 equiv) in 3.0 mL of dry DMSO were added. The reaction mixture was then immediately heated at 120 °C and the reaction completed within 5 min as indicated by TLC. The reaction mixture was filtered through a small plug of silica gel followed by concentration under reduced pressure. The crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 20% ethyl acetate in petroleum ether as eluent to afford **5m** (59.6 mg, 0.125 mmol) as a white solid in 77% yield. mp 178−180 °C; R_f 0.38 (ethyl acetate/petroleum ether, 4:6); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3062, 2921, 1648, 1594, 1577, 1493, 1478, 1452, 1431, 1351, 1324, 1279, 1249, 1205, 1164, 1118, 1107, 1091, 944, 887, 816, 789, 779, 765, 735, 667, 627, 606, 589, 572, 543, 524; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.2 Hz, 2H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.41 (d, *J* = 8.2 Hz, 2H), 7.37–7.35 (m, 2H), 7.22–7.18 (m, 1H), 7.03–7.01 (m, 1H), 6.86 (t, *J* = 8.2 Hz, 1H), 6.38–6.36 (m, 1H), 6.29–6.27 (m, 1H), 5.38 (d, *J* = 1.4 Hz, 1H), 4.96 (d, *J* = 1.8 Hz, 1H), 4.29 (dd, *J* = 4.5, 14.2 Hz, 1H), 3.83–3.77 (m, 1H), 3.10 (dd, *J* = 4.1, 12.4 Hz, 1H), 2.58–2.54 (m, 1H), 2.50 (s, 3H), 2.04 (s, 3H), 1.83 (d, *J* = 13.3 Hz, 1H); $^{13}C\{^{1}H\}$



5m

NMR (100 MHz, $CDCl_3$) δ 182.1, 154.9, 144.2, 138.5, 137.9, 137.72, 137.70, 133.9, 130.0, 129.4, 128.9, 128.1, 127.5 (2C), 125.3, 124.9, 124.3, 120.7, 114.4, 60.6, 48.0, 45.5, 37.7, 21.7, 15.9; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{26}ClN_2O_2S$ 477.1404; Found 477.1405.

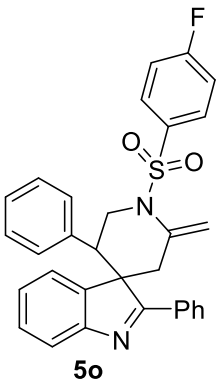
2′-Methylene-5′-phenyl-1′-tosylspiro[indole-3,4′-piperidine] (5n). The mixture of **1a** (50.0 mg, 0.182 mmol, 1.0 equiv), **2g** (21.3 mg, 0.182 mmol, 1.0 equiv) and anhydrous $LiClO_4$ (1.9 mg, 0.018 mmol, 0.1 equiv) in CH_3CN (0.2 mL) was taken in a dried double necked round bottom flask under argon atmosphere and was stirred at 80 °C for 2.5 h. After the complete consumption of aziridine, $Pd(PPh_3)_4$ (21.0 mg, 0.018 mmol, 0.1 equiv), DPPF (20.2 mg, 0.036 mmol, 0.2 equiv) and propargylic carbonate (**4a**, 34.2 mg, 0.219 mmol, 1.2 equiv) in 3.0 mL of dry DMSO were added. The reaction mixture was then immediately heated at 120 °C and the reaction completed within 5 min as indicated by TLC. The reaction mixture was filtered through a small plug of silica gel followed by concentration under reduced pressure. The crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 15% ethyl acetate in petroleum ether as eluent to afford **5n** (47.0 mg, 0.109 mmol) as a white solid in 60% yield.



5n

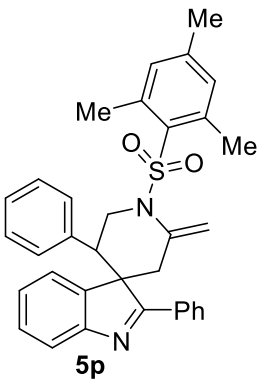
mp 160−162 °C; R_f 0.28 (ethyl acetate/petroleum ether, 2:8); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3030, 2923, 2853, 1738, 1650, 1597, 1552, 1494, 1455, 1377, 1346, 1263, 1184, 1162, 1089, 1031, 948, 909, 770, 738, 700, 641, 605, 583, 548, 524; ^1H NMR (500 MHz, $CDCl_3$) δ 8.45 (s, 1H), 7.84 (d, *J* = 8.3 Hz, 2H), 7.40 (d, *J* = 7.9 Hz, 2H), 7.36–7.34 (m, 1H), 7.19–7.17 (m, 2H), 7.11–7.10 (m, 1H), 7.02–6.97 (m, 3H), 6.76–6.74 (m, 2H), 5.27 (d, *J* = 1.1 Hz, 1H), 4.97 (d, *J* = 1.6 Hz, 1H), 4.46 (dd, *J* = 4.4, 13.7 Hz, 1H), 3.85–3.80 (m, 1H), 3.33 (dd, *J* = 4.4, 12.4 Hz, 1H), 2.61–2.58 (m, 1H), 2.50 (s, 3H), 2.02 (d, *J* = 13.9 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.3, 154.5, 144.1, 140.3, 140.1, 137.5, 136.0, 130.0, 128.4, 128.0, 127.6, 127.5, 126.4, 121.42, 121.40, 111.7, 61.7, 50.0, 47.5, 38.8, 21.7; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{26}H_{25}N_2O_2S$ 429.1637; Found 429.1631.

1′-((4-Fluorophenyl)sulfonyl)-2′-methylene-2,5′-diphenylspiro[indole-3,4′piperidine] (5o). The mixture of **1h** (50.0 mg, 0.180 mmol, 1.0 equiv), **2a** (34.8 mg, 0.180 mmol, 1.0 equiv) and anhydrous $LiClO_4$ (1.9 mg, 0.018 mmol, 0.1 equiv) in CH_3CN (0.2 mL) was taken in a dried double necked round bottom flask under argon atmosphere and was stirred at 80 °C for 4 h. After the complete consumption of aziridine, $Pd(PPh_3)_4$ (20.7 mg, 0.018 mmol, 0.1 equiv), DPPF (19.9 mg, 0.036 mmol, 0.2 equiv) and propargylic carbonate (**4a**, 33.7 mg, 0.216 mmol, 1.2 equiv) in 3.0 mL of dry DMSO were added. The reaction mixture was then immediately heated at 120 °C and the reaction completed within 5 min as indicated by TLC. The reaction mixture was filtered through a small plug of silica gel followed by concentration under reduced pressure. The crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 15% ethyl acetate in petroleum ether as eluent to afford **5o** (70.6 mg, 0.138 mmol) as a white solid in 77% yield. mp 152−154 °C; R_f 0.32 (ethyl acetate/petroleum ether, 2:8); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3062, 2926, 1734, 1648, 1590, 1522, 1493, 1466, 1453, 1441, 1404, 1357, 1266, 1236, 1169, 1155, 1110, 1095, 1025, 946, 894, 879, 841, 777, 765, 736, 694, 678, 625, 582, 540, 499; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05–8.01 (m, 2H), 7.71 (d, J = 7.5 Hz, 1H), 7.64–7.62 (m, 2H), 7.50–7.47 (m, 2H), 7.41–7.32 (m, 5H), 7.28–7.26 (m, 1H), 6.98 (t, J = 7.4 Hz, 1H), 6.82 (t, J = 7.8 Hz, 2H), 6.16 (d, J = 7.1 Hz, 2H), 5.53 (d, J = 1.8 Hz, 1H), 5.08 (d, J = 1.9 Hz, 1H), 4.37 (dd, J = 4.4, 14.5 Hz, 1H), 4.06 (dd, J = 12.7, 14.5 Hz, 1H), 3.56 (dd, J = 4.6, 12.7 Hz, 1H), 3.18–3.15 (m, 1H), 2.10 (d, J = 13.8 Hz, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 178.2, 165.3 (d, $^1J_{C–F}$ = 254.2 Hz), 154.3, 140.0, 137.5, 137.1, 137.0, 135.3, 133.3, 130.6, 130.0, 129.9, 128.8, 128.5, 128.0, 127.75, 127.72, 127.2, 125.1, 124.5, 121.5, 116.8, 116.6, 115.8, 61.2, 48.0, 45.6, 37.8; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{31}H_{26}FN_2O_2S$ 509.1699; Found 509.1691.



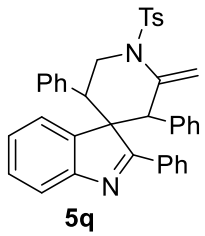
5o

1′-(Mesitylsulfonyl)-2′-methylene-2,5′-diphenylspiro[indole-3,4′-piperidine] (5p). The



mixture of **1i** (50.0 mg, 0.165 mmol, 1.0 equiv), **2a** (32.0 mg, 0.165 mmol, 1.0 equiv) and anhydrous $LiClO_4$ (1.7 mg, 0.016 mmol, 0.1 equiv) in CH_3CN (0.2 mL) was taken in a dried double necked round bottom flask under argon atmosphere and was stirred at 80 °C for 2 h. After the complete consumption of aziridine, $Pd(PPh_3)_4$ (19.0 mg, 0.016 mmol, 0.1 equiv), DPPF (18.3 mg, 0.033 mmol, 0.2 equiv) and propargylic carbonate (**4a**, 31.0 mg, 0.198 mmol, 1.2 equiv) in 3.0 mL of dry DMSO were added. The reaction mixture was then immediately heated at 120 °C and the reaction completed within 5 min as indicated by TLC. The reaction mixture was filtered through a small plug of silica gel followed by concentration under reduced pressure. The crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 15% ethyl acetate in petroleum ether as eluent to afford **5p** (69.8 mg, 0.130 mmol) as a white solid in 79% yield. mp 78−80 °C; R_f 0.38 (ethyl acetate/petroleum ether, 2:8); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3060, 3030, 2927, 2854, 1736, 1651, 1603, 1565, 1522, 1493, 1466, 1454, 1441, 1378, 1320, 1266, 1186, 1152, 1106, 1056, 1032, 934, 909, 875, 802, 778, 766, 757, 737, 721, 692, 682, 660, 596, 584, 542, 491; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19–8.17 (m, 2H), 7.77 (d, J = 7.5 Hz, 1H), 7.53–7.48 (m, 4H), 7.39–7.36 (m, 1H), 7.26–7.23 (m, 1H), 7.00–6.94 (m, 3H), 6.81 (t, J = 7.7 Hz, 2H), 6.27 (d, J = 7.3 Hz, 2H), 4.92 (d, J = 1.8 Hz, 1H), 4.78 (d, J = 1.7 Hz, 1H), 4.42 (dd, J = 4.2, 13.8 Hz, 1H), 4.11 (dd, J = 4.1, 12.6 Hz, 1H), 4.01–3.96 (m, 1H), 3.85–3.82 (m, 1H), 2.69 (s, 6H), 2.34 (s, 3H), 2.20 (d, J = 13.6 Hz, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 178.5, 154.4, 142.7, 140.9, 140.1, 139.6, 135.8, 133.4, 133.3, 131.9, 130.6, 128.7, 128.6, 128.4, 127.6, 127.5, 127.4, 124.9, 124.4, 121.4, 114.8, 61.7, 47.0, 46.4, 38.3, 22.9, 21.0; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{34}H_{33}N_2O_2S$ 533.2263; Found 533.2261.

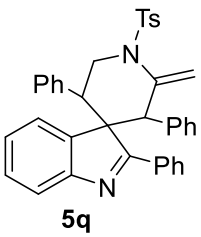
2′-Methylene-2,3′,5′-triphenyl-1′-tosylspiro[indole-3,4′-piperidine] (5q). The mixture of



5q

1a (50.0 mg, 0.182 mmol, 1.0 equiv), **2a** (35.3 mg, 0.182 mmol, 1.0 equiv) and anhydrous $LiClO_4$ (1.9 mg, 0.018 mmol, 0.1 equiv) in CH_3CN (0.2 mL) was taken in a dried double necked round bottom flask under argon atmosphere and was stirred at 80 °C for 3 h. After the complete consumption of aziridine, $Pd(PPh_3)_4$ (21.0 mg, 0.018 mmol, 0.1 equiv), DPPF (20.2 mg, 0.036 mmol, 0.2 equiv) and *tert*-butyl (3-phenylprop-2-yn-1-yl) carbonate (**4b**, 50.9 mg, 0.219 mmol, 1.2 equiv) in 3.0 mL of dry DMSO were added. The reaction mixture was then immediately heated at 120 °C and the reaction completed within 15 min as indicated by TLC. The reaction mixture was filtered through a small plug of silica gel followed by concentration under reduced pressure. The crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 15% ethyl acetate in petroleum ether as eluent to afford **5q** (59.4 mg, 0.102 mmol) as a white solid in 56% yield. mp 148−150 °C; R_f 0.29 (ethyl acetate/petroleum ether, 2:8); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3060, 3028, 2924, 1734, 1640, 1597, 1523, 1493, 1453, 1441, 1353, 1265, 1183, 1165, 1112, 1093, 1018, 957, 904, 887, 841, 766, 733, 698, 660, 621, 601, 586, 575, 552, 539, 517; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01–7.99 (m, 1H), 7.96 (d, J = 8.1 Hz, 2H), 7.56–7.50 (m, 4H), 7.47–7.41 (m, 2H), 7.38–7.35 (m, 2H), 7.28–7.25 (m, 2H), 6.97–6.93 (m, 2H), 6.79 (t, J = 7.8 Hz, 4H), 6.18–6.13 (m, 4H), 5.74 (d, J = 1.7 Hz, 1H), 4.81 (d, J = 1.8 Hz, 1H), 4.55 (dd, J = 4.7, 14.9 Hz, 1H), 4.32 (dd, J = 12.7, 14.9 Hz, 1H), 4.16 (s, 1H), 3.83 (dd, J = 4.5, 12.7 Hz, 1H), 2.65 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 177.5, 155.7, 143.8, 141.3, 138.3, 138.2, 135.3, 135.0, 133.9, 130.3, 130.1, 129.1, 128.18, 128.10, 127.9 (2C), 127.66 (2C), 127.61 (2C), 127.3, 125.6, 125.0, 121.7, 118.0, 66.4, 52.8, 47.7, 47.6, 21.8; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{38}H_{33}N_2O_2S$ 581.2263; Found 581.2261.

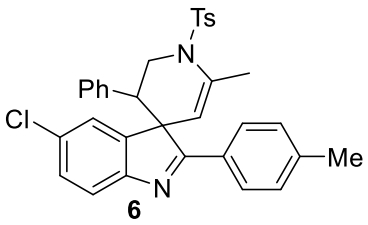
2′-Methylene-2,3′,5′-triphenyl-1′-tosylspiro[indole-3,4′-piperidine] (5q). The mixture of



5q

1a (50.0 mg, 0.182 mmol, 1.0 equiv), **2a** (35.3 mg, 0.182 mmol, 1.0 equiv) and anhydrous $LiClO_4$ (1.9 mg, 0.018 mmol, 0.1 equiv) in CH_3CN (0.2 mL) was taken in a dried double necked round bottom flask under argon atmosphere and was stirred at 80 °C for 3 h. After the complete consumption of aziridine, $Pd(PPh_3)_4$ (21.0 mg, 0.018 mmol, 0.1 equiv), DPPF (20.2 mg, 0.036 mmol, 0.2 equiv) and *tert*-butyl (1-phenylprop-2-yn-1-yl) carbonate (**4c**, 50.9 mg, 0.219 mmol, 1.2 equiv) in 3.0 mL of dry DMSO were added. The reaction mixture was then immediately heated at 120 °C and the reaction completed within 5 min as indicated by TLC. The reaction mixture was filtered through a small plug of silica gel followed by concentration under reduced pressure. The crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 15% ethyl acetate in petroleum ether as eluent to afford **5q** (67.9 mg, 0.117 mmol) as a white solid in 64% yield. All the analytical data matched those reported above.

5-Chloro-6′-methyl-3′-phenyl-2-(*p*-tolyl)-1′-tosyl-2′,3′-dihydro-1′*H*-spiro[indole-3,4′-pyridine] (6). The mixture of **5j** (20.0 mg, 0.036 mmol, 1.0 equiv), anhydrous $ZnBr_2$ (16.2 mg,

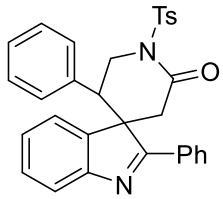


6

0.072 mmol, 2.0 equiv) in benzene (0.7 mL) was taken under argon atmosphere in a dried double necked round bottom flask. The reaction mixture was stirred at 80 °C for 1 h and the progress of reaction was monitored by TLC. After the completion of reaction, the reaction mixture was cooled to room temperature and quenched with water. The aqueous layer was extracted with ethyl acetate (3 × 10.0 mL). Combined extracts were washed with brine and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 10% ethyl acetate in petroleum ether to afford **6** (16.4 mg, 0.029 mmol) as a white solid in 82% yield. mp 238−240 °C; R_f 0.37 (ethyl acetate/petroleum

ether, 2:8); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3031, 2923, 2853, 1736, 1640, 1597, 1580, 1525, 1507, 1496, 1450, 1415, 1357, 1249, 1223, 1183, 1169, 1089, 1063, 1015, 984, 899, 873, 825, 769, 725, 700, 685, 661, 635, 576, 559, 543, 506; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86–7.80 (m, 4H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.25–7.15 (m, 5H), 6.98 (t, *J* = 7.3 Hz, 1H), 6.88 (t, *J* = 7.6 Hz, 2H), 6.24 (d, *J* = 7.3 Hz, 2H), 4.84 (s, 1H), 4.53 (dd, *J* = 3.2, 13.8 Hz, 1H), 4.11–4.06 (m, 1H), 3.42 (dd, *J* = 3.0, 12.5 Hz, 1H), 2.48 (s, 3H), 2.44 (s, 3H), 2.35 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 179.5, 153.2, 144.1, 142.8, 141.4, 137.6, 136.2, 135.3, 130.8, 130.2, 130.1, 129.5, 128.7, 128.0, 127.5, 127.4, 127.3, 127.0, 124.3, 121.3, 110.3, 63.0, 47.9, 44.5, 22.9, 21.64, 21.63; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{33}H_{30}ClN_2O_2S$ 553.1717; Found 553.1712.

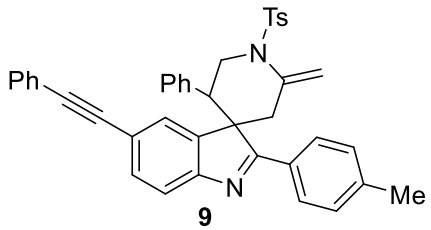
2,5′-Diphenyl-1′-tosylspiro[indole-3,4′-piperidin]-2′-one (7). The mixture of **5a** (30.0 mg, 0.059 mmol, 1.0 equiv), $RuCl_3$ (0.6 mg, 0.002 mmol, 0.05 equiv), $NaIO_4$ (76.2 mg, 0.356 mmol, 6.0 equiv) and $CH_3CN/CCl_4/H_2O$ (0.4 mL, 2:1:1) was taken in a sealed tube. The reaction mixture was stirred at rt for 40 mins and the progress of reaction was monitored by TLC. After the completion of reaction, the reaction mixture was diluted with ethyl acetate (10 mL), quenched with aqueous sodium thiosulfate and filtered through the plug of celite. The filtrate was washed with water and brine, dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 20% ethyl acetate in petroleum ether to afford **7** (19.5 mg, 0.038 mmol) as a white solid in 65% yield. mp 174−176 °C; R_f 0.23 (ethyl acetate/petroleum ether, 2:8); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3061, 2923, 2852, 1693, 1595, 1524, 1493, 1467, 1453, 1359, 1306, 1238, 1186, 1170, 1133, 1113, 1087, 1028, 871, 849, 814, 766, 734, 696, 665, 597, 567, 547, 504; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.2 Hz, 2H), 7.83–7.81 (m, 2H), 7.55–7.39 (m, 7H), 7.17–7.13 (m, 1H), 7.07–7.02 (m, 2H), 6.89 (t, *J* = 7.8 Hz, 2H), 6.28 (d, *J* = 7.3 Hz, 2H), 4.44 (dd, *J* = 5.5, 12.8 Hz, 1H), 4.26–4.19 (m, 1H), 4.00 (dd, *J* = 5.5, 12.3 Hz, 1H), 3.64–3.59 (m, 1H), 2.54–2.50 (m,



7

4H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 177.2, 167.4, 154.4, 145.5, 139.7, 135.3, 134.5, 133.0, 130.9, 129.5, 129.3, 129.2, 128.7, 128.3, 128.1, 128.0, 127.2, 126.2, 122.5, 121.9, 59.8, 49.4, 46.1, 41.2, 21.7; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{31}H_{27}N_2O_3S$ 507.1742; Found 507.1741.

2′-Methylene-5′-phenyl-5-(phenylethynyl)-2-(*p*-tolyl)-1′-tosylspiro[indole-3,4′-piperidine] (9). The mixture of **5k** (30.0 mg, 0.050 mmol, 1.0 equiv), $Pd(PPh_3)_2Cl_2$ (1.7 mg, 0.002 mmol, 0.05 equiv), CuI (0.9 mg, 0.005, 0.1 equiv), phenylacetylene (**8**, 10.2 mg, 0.100 mmol, 2.0 equiv) and Et_3N (0.5 mL) in DMF (0.5 mL) solvent was taken in a sealed tube under argon atmosphere. The reaction mixture was stirred at 90 °C for 5 h and the progress of reaction was monitored by TLC. After the completion of reaction, the reaction mixture was cooled to rt, diluted with ethyl acetate (10 mL) and filtered through the plug of celite. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography on silica gel (230–400 mesh) using 15% ethyl acetate in petroleum ether to afford **9** (21.9 mg, 0.035 mmol) as a white solid in 71% yield. mp 142−144 °C; R_f 0.30 (ethyl acetate/petroleum ether, 2:8); IR $\tilde{\nu}_{max}$ (KBr, cm^{-1}) 3060, 3030, 2922, 2852, 1736, 1647, 1596, 1508, 1492, 1462, 1405, 1353, 1331, 1268, 1238, 1184, 1165, 1091, 1027, 1014, 938, 886, 866, 834, 817, 757, 736, 710, 699, 678, 637, 612, 597, 584, 556, 517; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.4 Hz, 2H), 7.85 (s, 1H), 7.65–7.54 (m, 5H), 7.46 (d, *J* = 7.8 Hz, 2H), 7.40–7.34 (m, 4H), 7.16 (d, *J* = 7.9 Hz, 2H), 6.98 (t, *J* = 7.5 Hz, 1H), 6.83 (t, *J* = 7.6 Hz, 2H), 6.22 (d, *J* = 7.1 Hz, 2H), 5.57 (d, *J* = 1.5 Hz, 1H), 5.12 (d, *J* = 1.7 Hz, 1H), 4.39 (dd, *J* = 4.4, 14.5 Hz, 1H), 4.09 (dd, J = 12.6, 14.1 Hz, 1H), 3.66 (dd, *J* = 4.5, 12.6 Hz, 1H), 3.22–3.19 (m, 1H), 2.56 (s, 3H), 2.44 (s, 3H), 2.11 (d, *J* = 13.9 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 179.2, 154.4, 143.7, 141.2, 140.6, 137.9, 137.4, 135.4, 132.6, 131.6, 130.2, 130.1, 129.3, 128.4, 128.3, 128.2, 127.7, 127.6, 127.45, 127.41,



9

127.3, 123.1, 121.1, 119.6, 115.8, 89.9, 89.8, 61.3, 47.7, 45.8, 38.0, 21.7, 21.5; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{41}H_{35}N_2O_2S$ 619.2419; Found 619.2413.

5. X-ray crystallographic studies:

The crystals used in the analyses were glued to a glass fiber and mounted on CCD diffractometer. The instrument was equipped with CCD area detector and data were collected using graphite-monochromated Mo Kα radiation (λ = 0.71073) at low temperature (100K). Cell constants were obtained from the least-squares refinement of three-dimensional centroids through the use of CCD recording of narrow ω rotation frames, completing almost all-reciprocal space in the stated θ range. All data were collected with SMART 5.628 and were integrated with the SAINT[5] program. An empirical absorption correction was applied to collect reflections with SADABS[6] using XPREP.[7] The structure was solved using SIR-97[8] and refined using SHELXL-97.[9] The space group of the compounds was determined based on the lack of systematic absence and intensity statistics. Full-matrix least squares / difference Fourier cycles were performed which located the remaining non-hydrogen atoms. All non-hydrogen atoms were refined with anisotropic displacement parameters. The hydrogen atoms of the hydroxyl groups were located by differential Fourier map, all other hydrogen atoms are fixed by using geometrical constrains using idealized geometries. All the hydrogen atoms have been defined isotropically.

6. X-ray crystallographic structure of 5f.

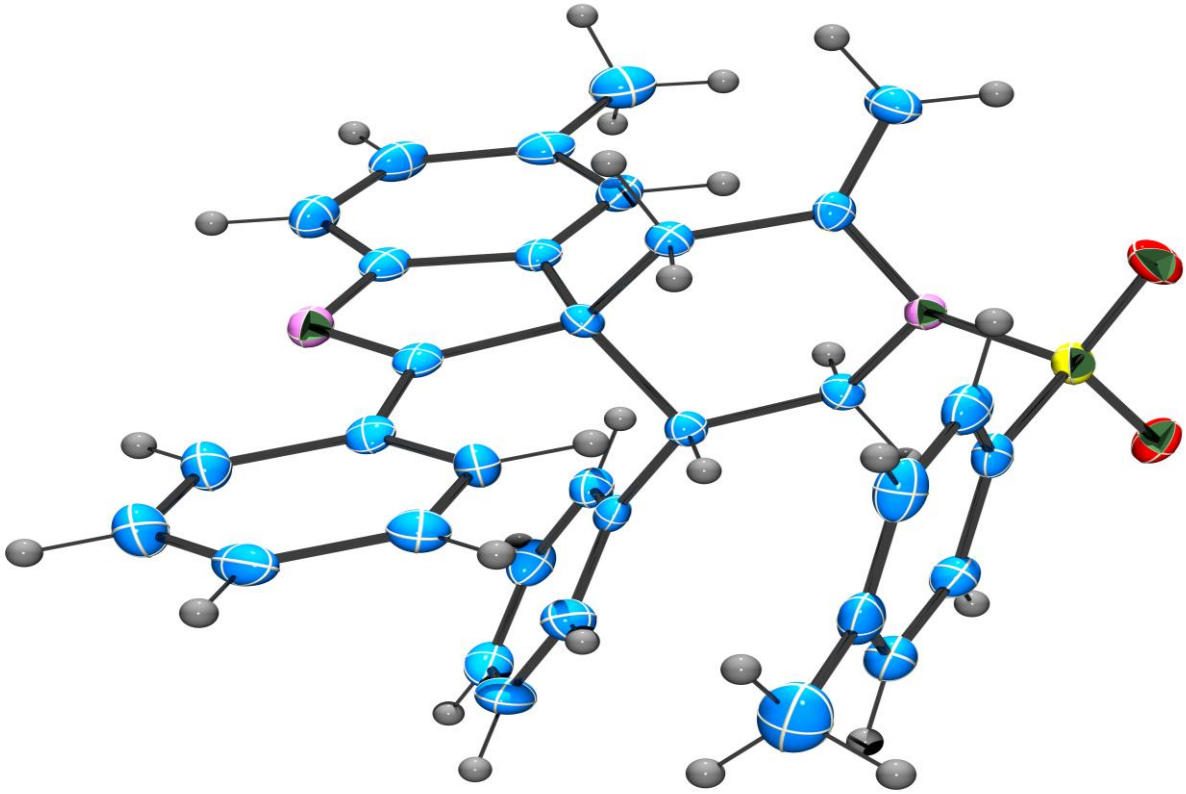


Figure S2. X-ray crystallographic structure **5f** (ORTEP view with 50% thermal ellipsoid contour probability, CCDC 1813319)

7. X-ray crystallographic data and structure refinement

Compound	**5f** (CCDC 1813319)
Formula	$C_{33}H_{30}N_2O_2S$
Formula weight	518.65
Crystal system	Monoclinic
Space group	P 1 21/n 1
T, K	100
Z	4
a, Å	7.7368(6)
b, Å	16.8658(12)
c, Å	20.2866(14)
α, deg	90
β, deg	96.461(2)
γ, deg	90
V, $Å^3$	2630.3(3)
d_{calcd}, g/cm^3	1.310
μ, mm^{-1}	0.157
θ range, deg	2.42–23.39
GOF (F^2)	1.023
R_1[b] (wR_2[c]), %	0.1936 (0.1860)

[a] [a]Mo Kα radiation, [b]$R_1 = \Sigma \| F_0 | - | F_c \| / \Sigma | F_0 |$, [c]$wR_2 = \{\Sigma[w(F_0^2 - F_c^2)^2]/\Sigma[w(F_0^2)^2]\}^{1/2}$

8. References

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9. Copies of NMR spectra

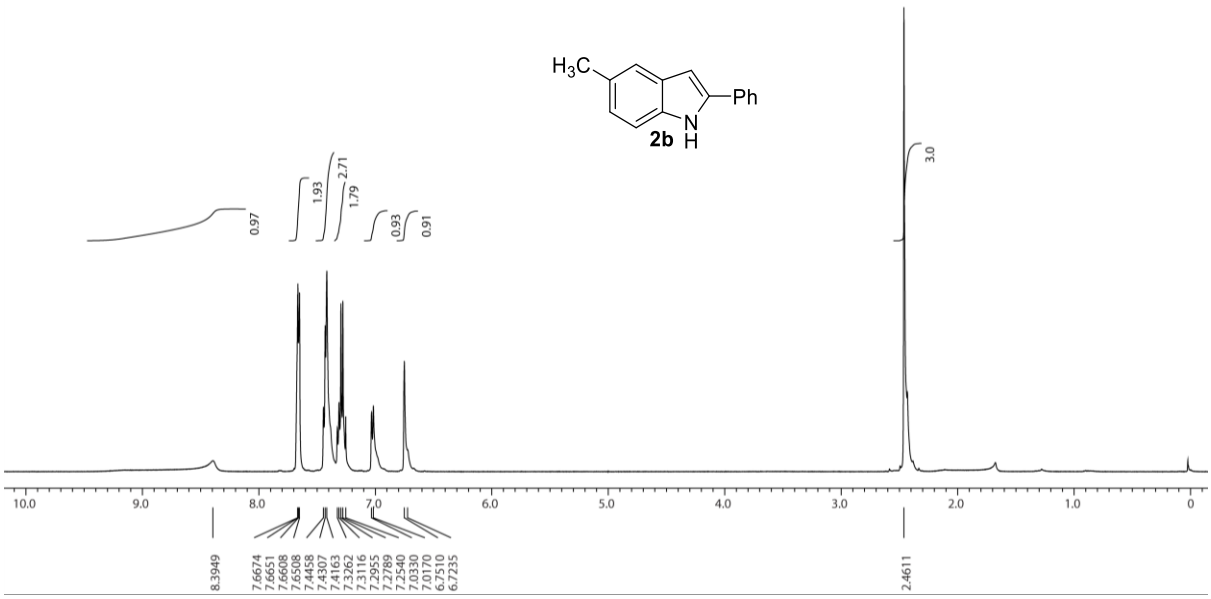


Figure S3. ^{1}H NMR of **2b** (500 MHz, $CDCl_3$/DMSO, 10:1)

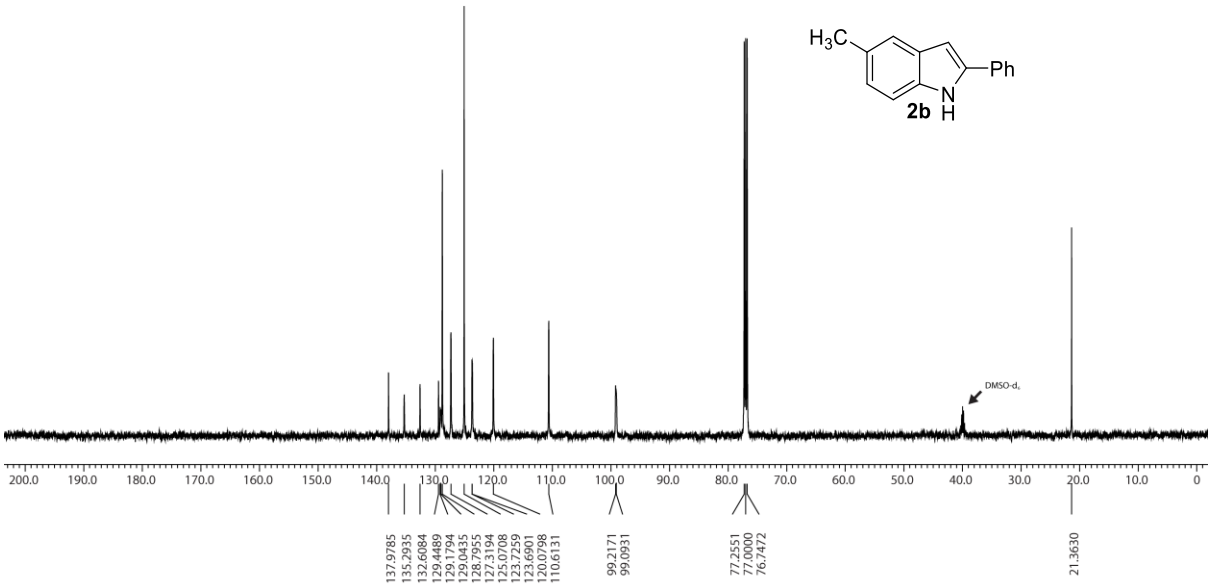


Figure S4. ^{13}C{^{1}H} NMR of **2b** (125 MHz, $CDCl_3$/DMSO, 10:1)

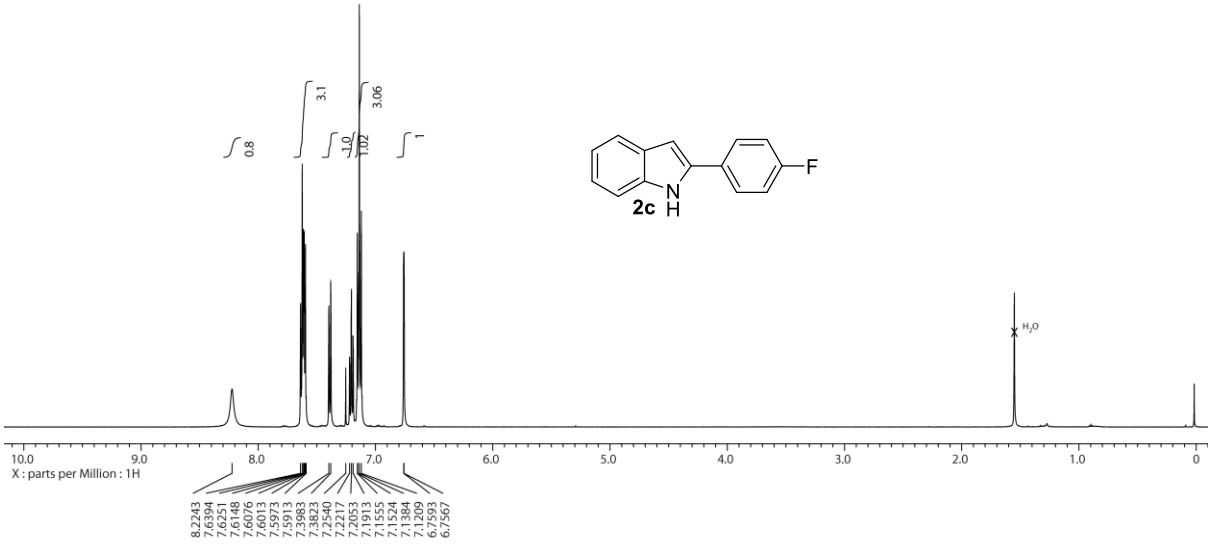


Figure S5. ^{1}H NMR of **2c** (500 MHz, $CDCl_3$)

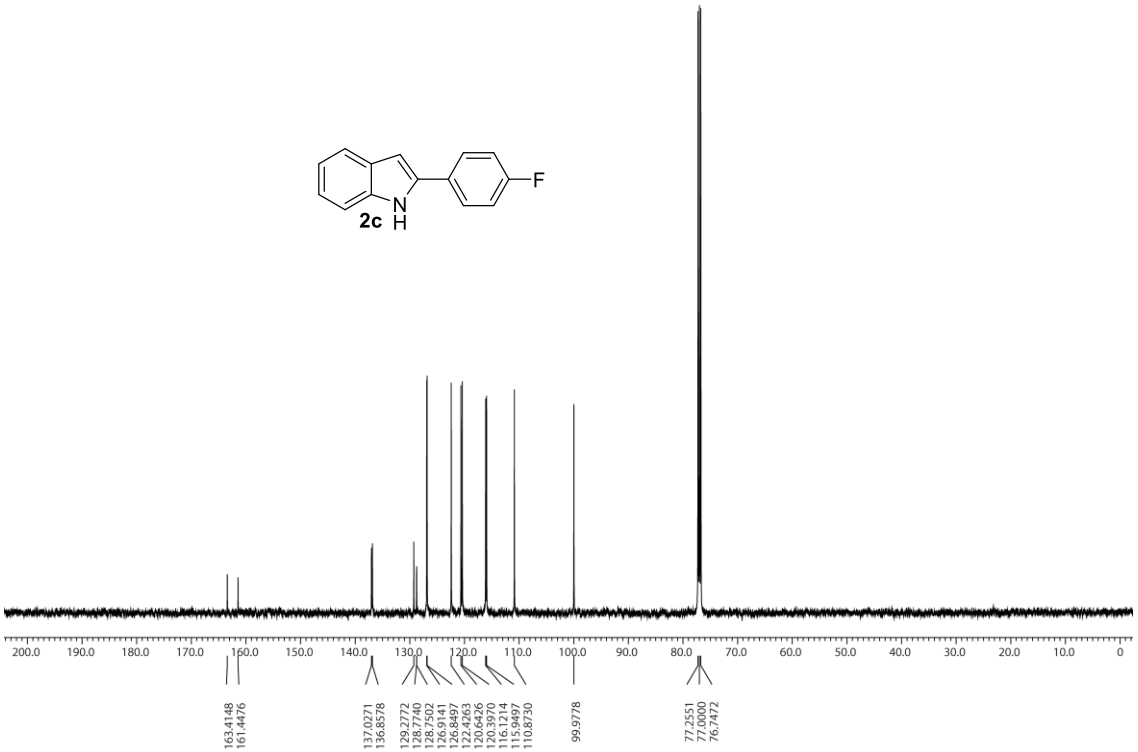


Figure S6. $^{13}C\{^{1}H\}$ NMR of **2c** (125 MHz, $CDCl_3$)

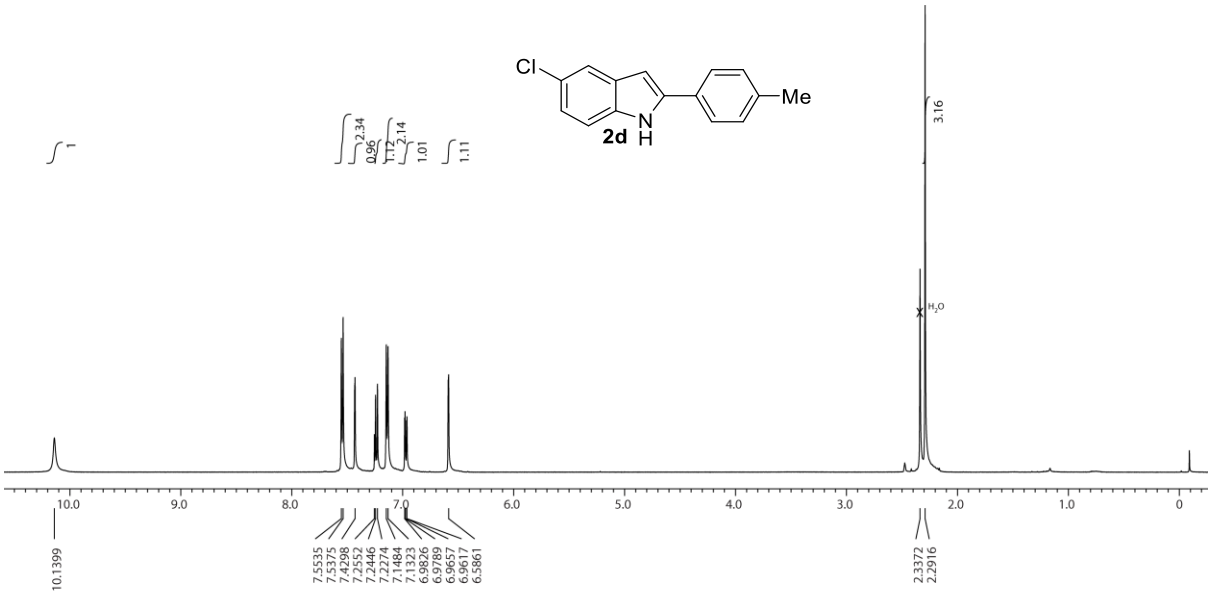


Figure S7. ^{1}H NMR of **2d** (500 MHz, $CDCl_3$/DMSO, 6:1)

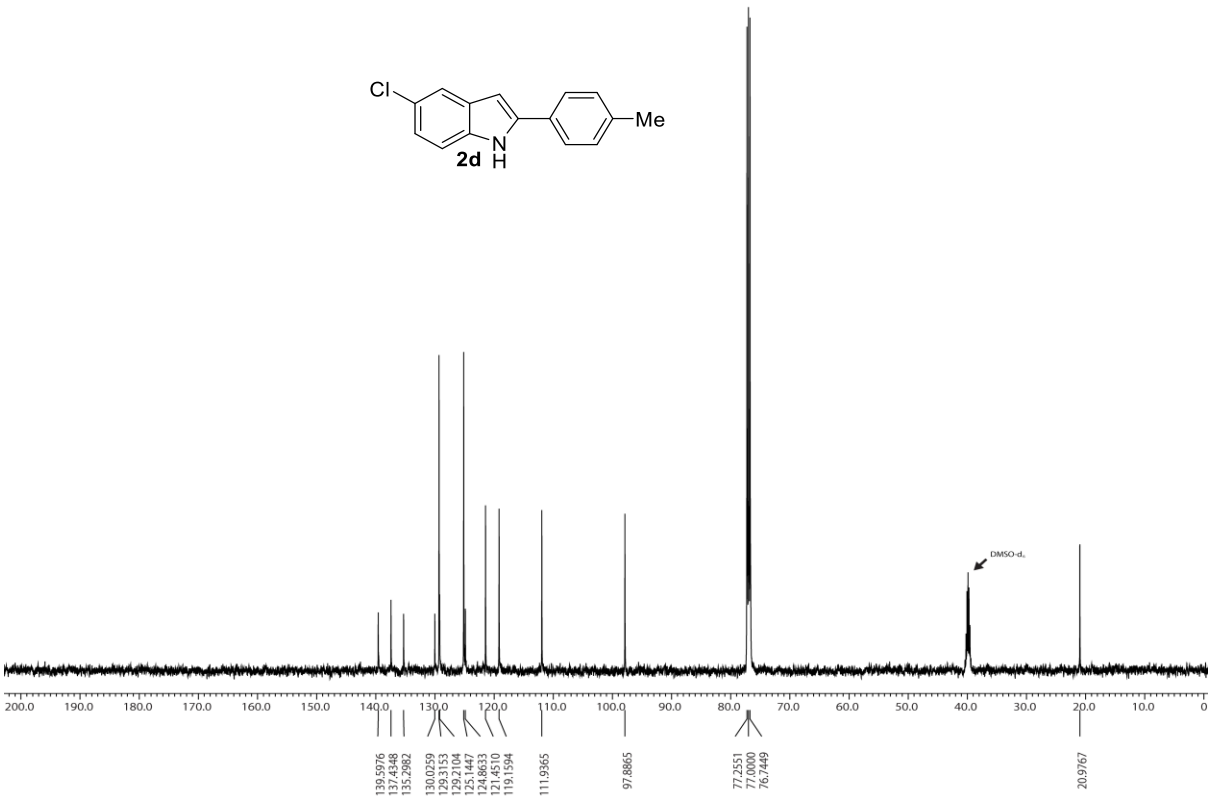


Figure S8. ^{13}C{^{1}H} NMR of **2d** (125 MHz, $CDCl_3$/DMSO, 6:1)

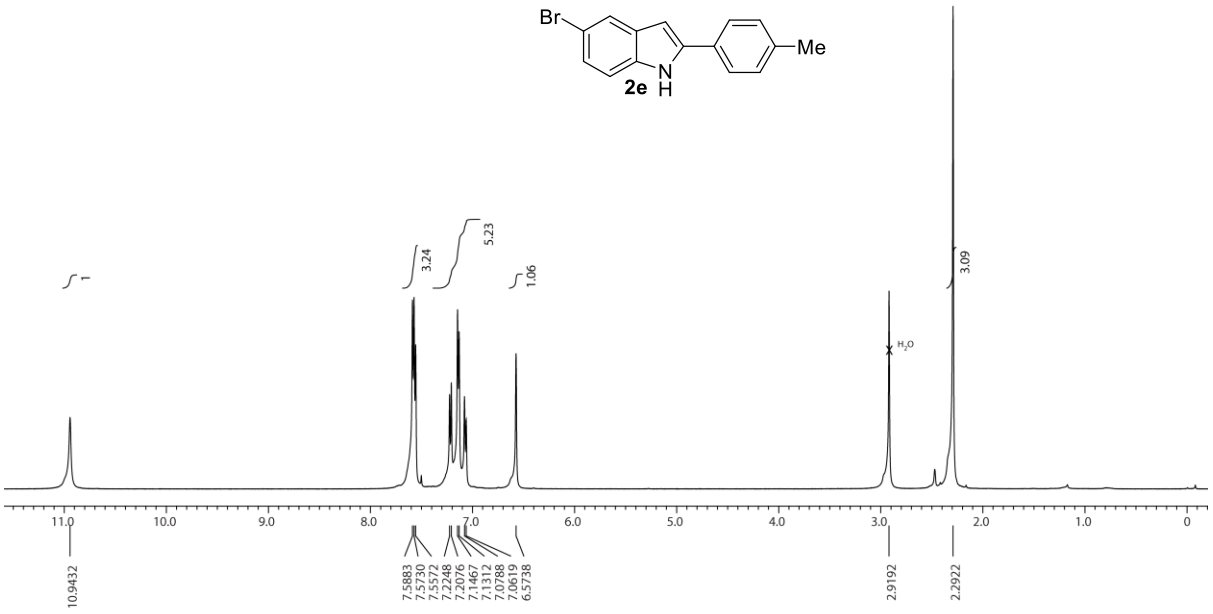


Figure S9. ^{1}H NMR of **2e** (500 MHz, $CDCl_3$/DMSO, 2:1)

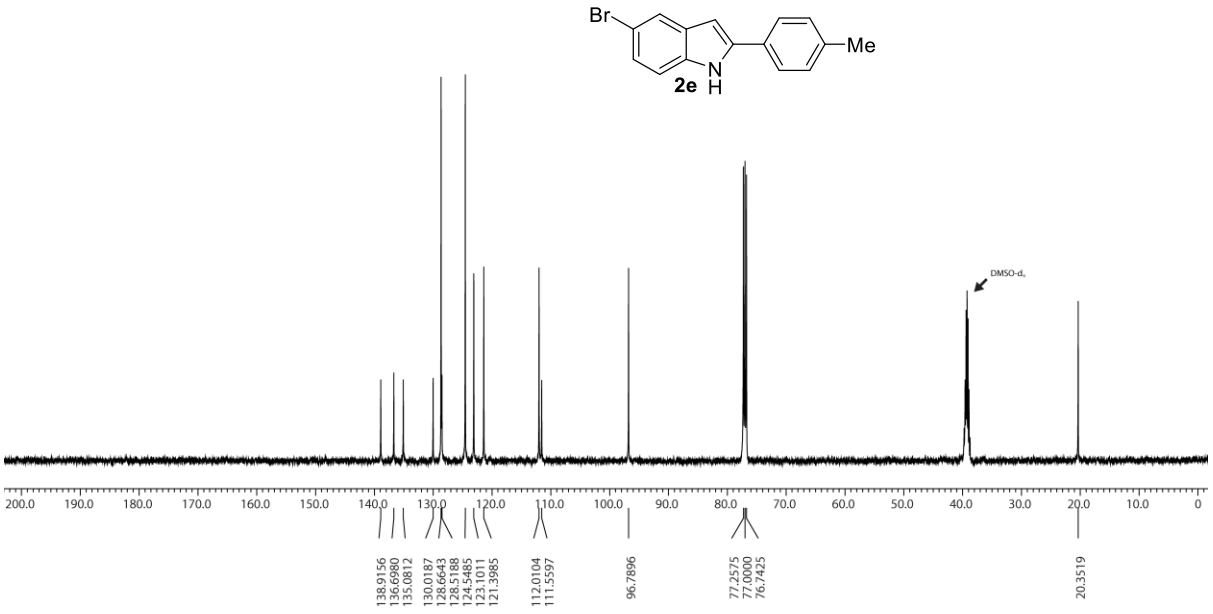


Figure S10. ^{13}C{^{1}H} NMR of **2e** (125 MHz, $CDCl_3$/DMSO, 2:1)

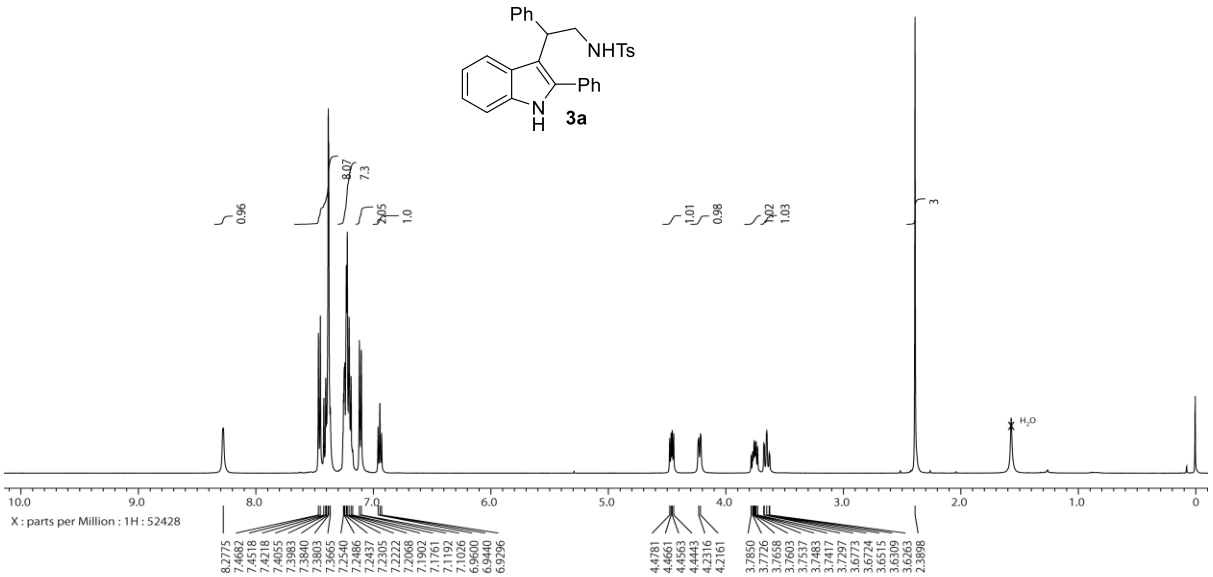


Figure S11. ^{1}H NMR of **3a** (500 MHz, $CDCl_3$)

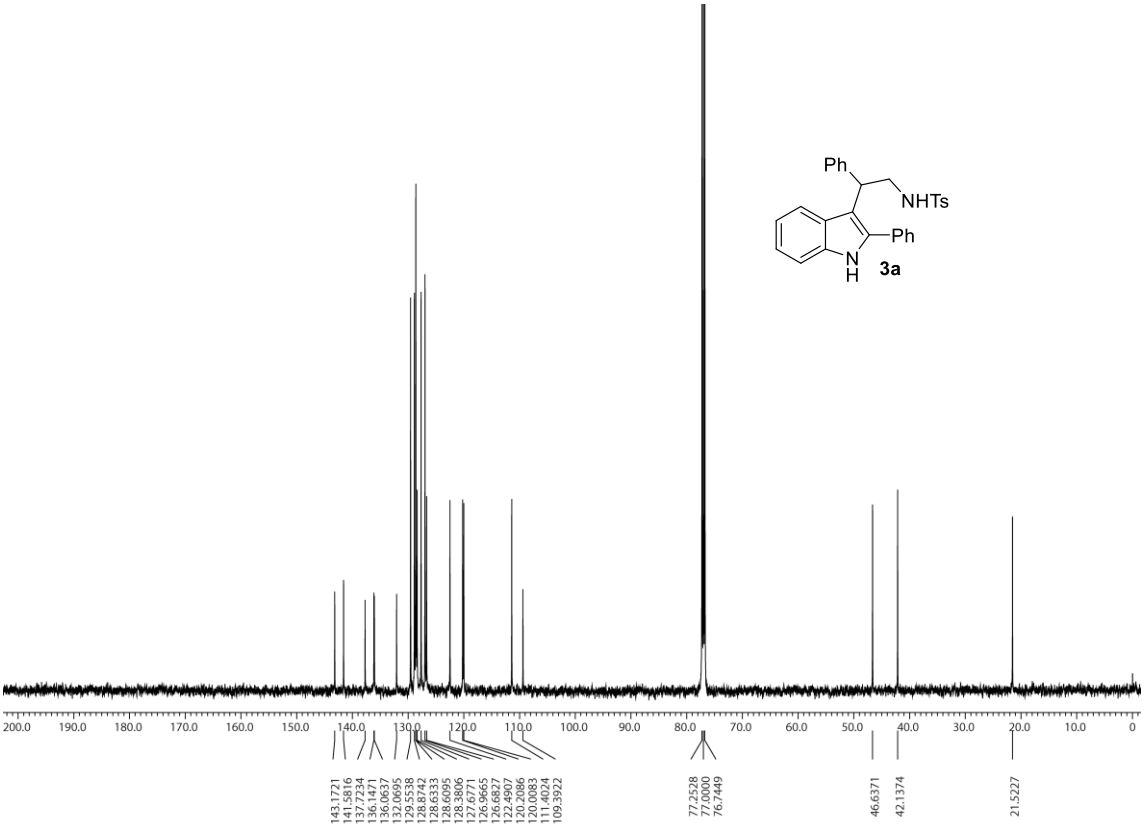


Figure S12. $^{13}C\{^{1}H\}$ NMR of **3a** (125 MHz, $CDCl_3$)

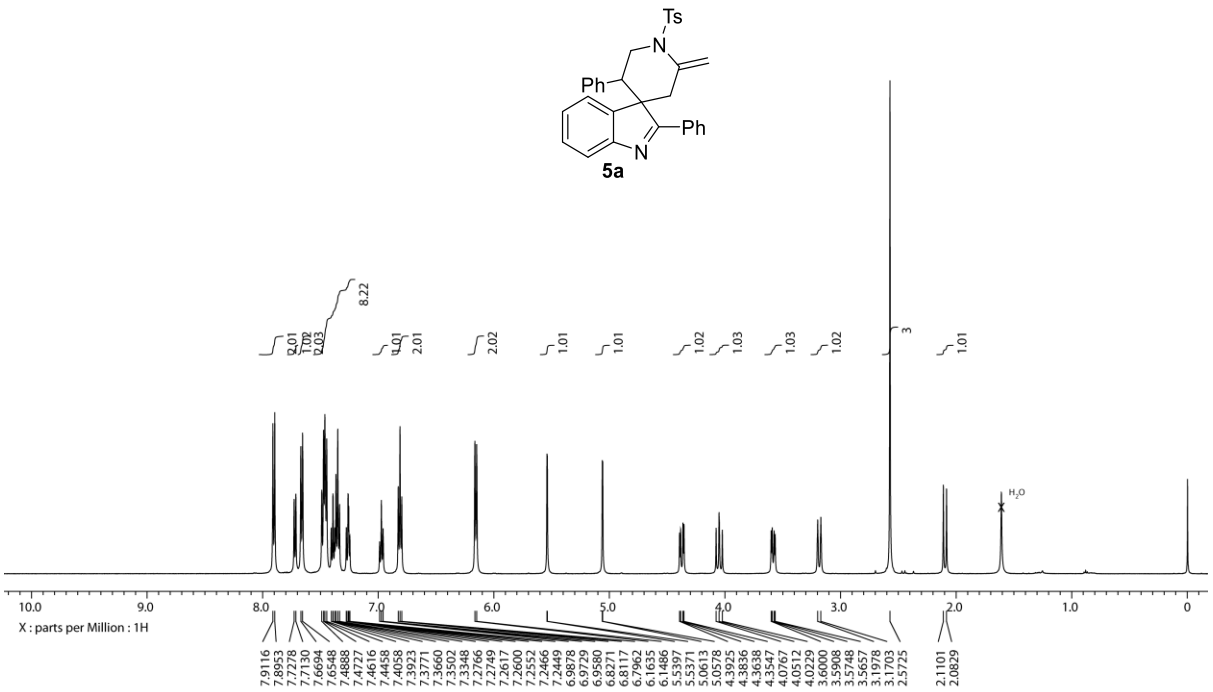


Figure S13. ^{1}H NMR of **5a** (500 MHz, $CDCl_3$)

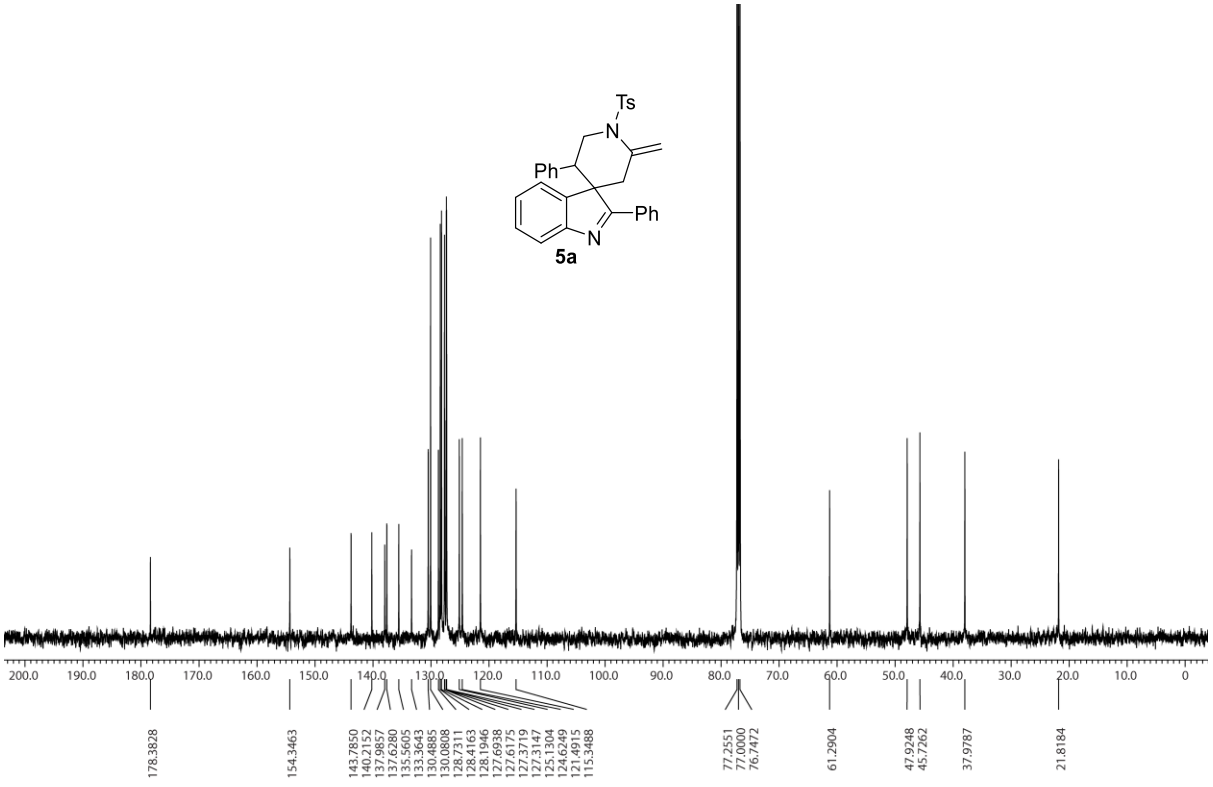


Figure S14. ^{13}C{^{1}H} NMR of **5a** (125 MHz, $CDCl_3$)

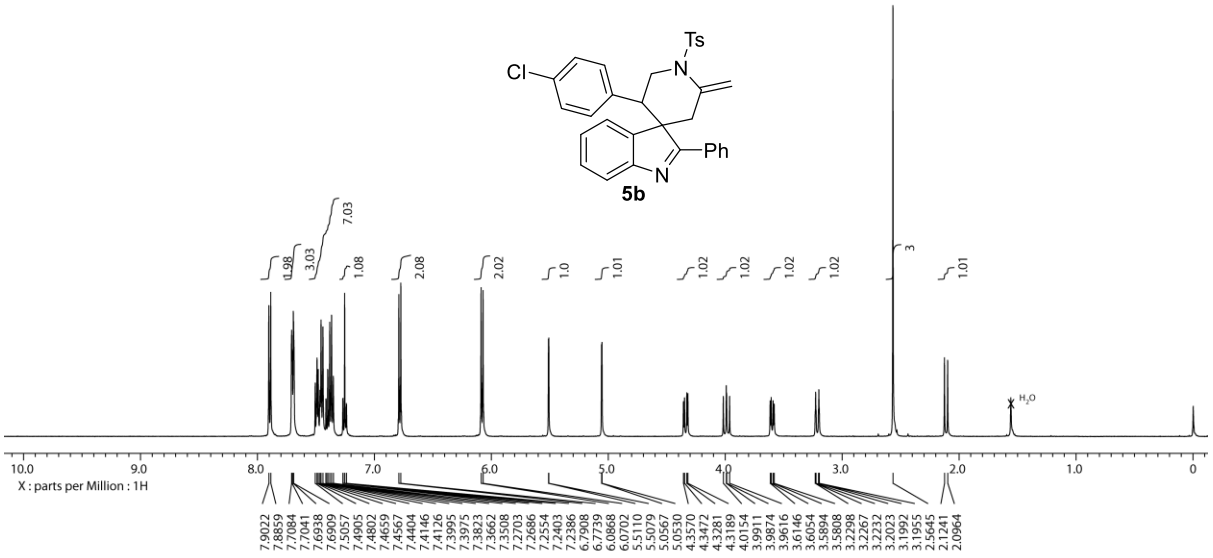


Figure S15. ^{1}H NMR of **5b** (500 MHz, $CDCl_3$)

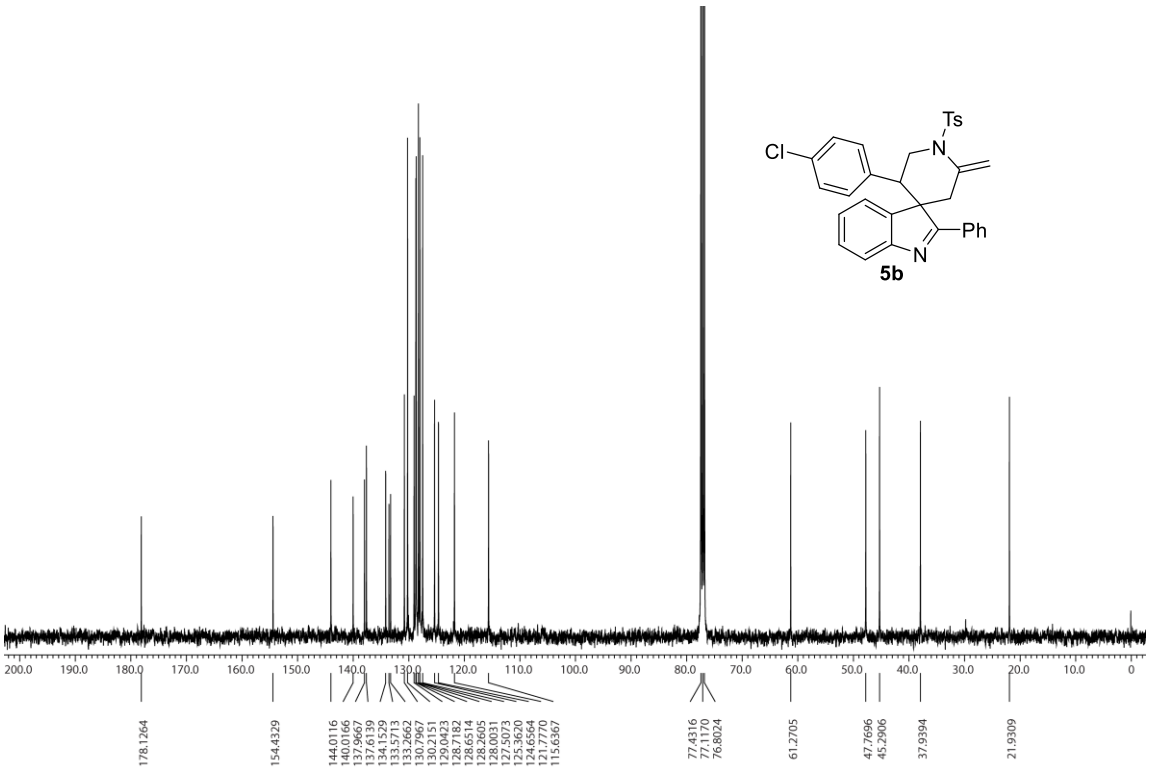


Figure S16. $^{13}C\{^{1}H\}$ NMR of **5b** (100 MHz, $CDCl_3$)

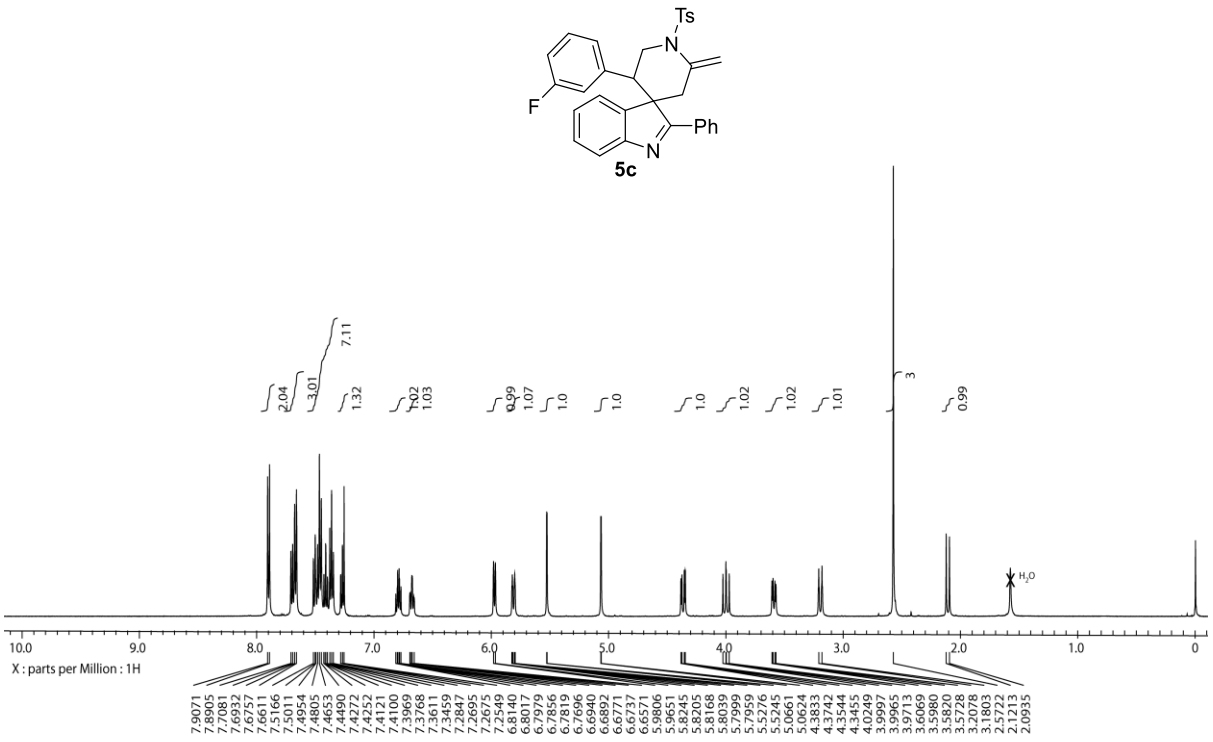


Figure S17. ^{1}H NMR of **5c** (500 MHz, $CDCl_3$)

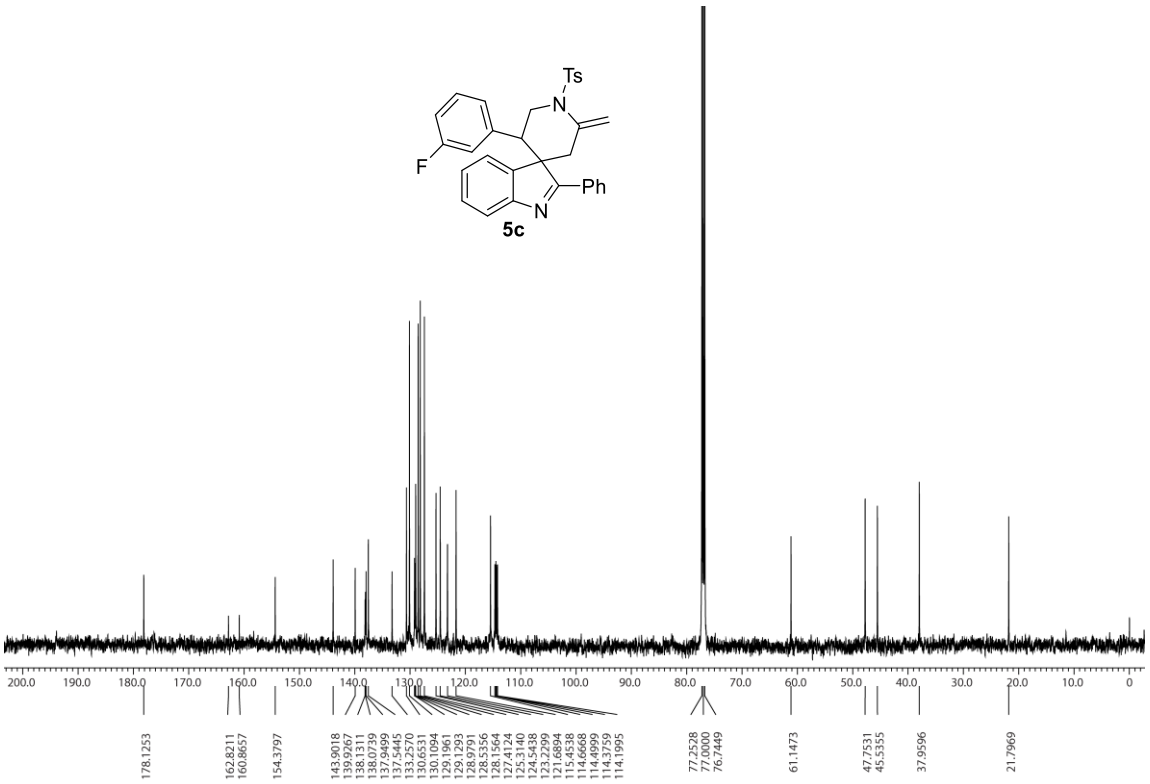


Figure S18. ^{13}C{^{1}H} NMR of **5c** (125 MHz, $CDCl_3$)

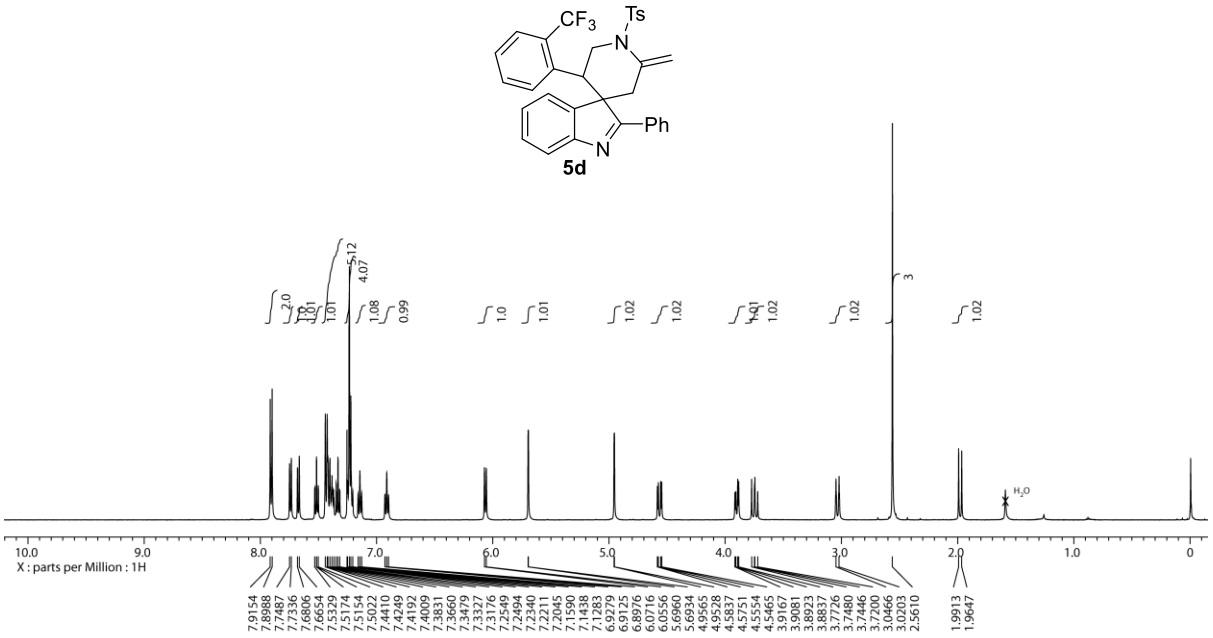


Figure S19. ^{1}H NMR of **5d** (500 MHz, $CDCl_3$)

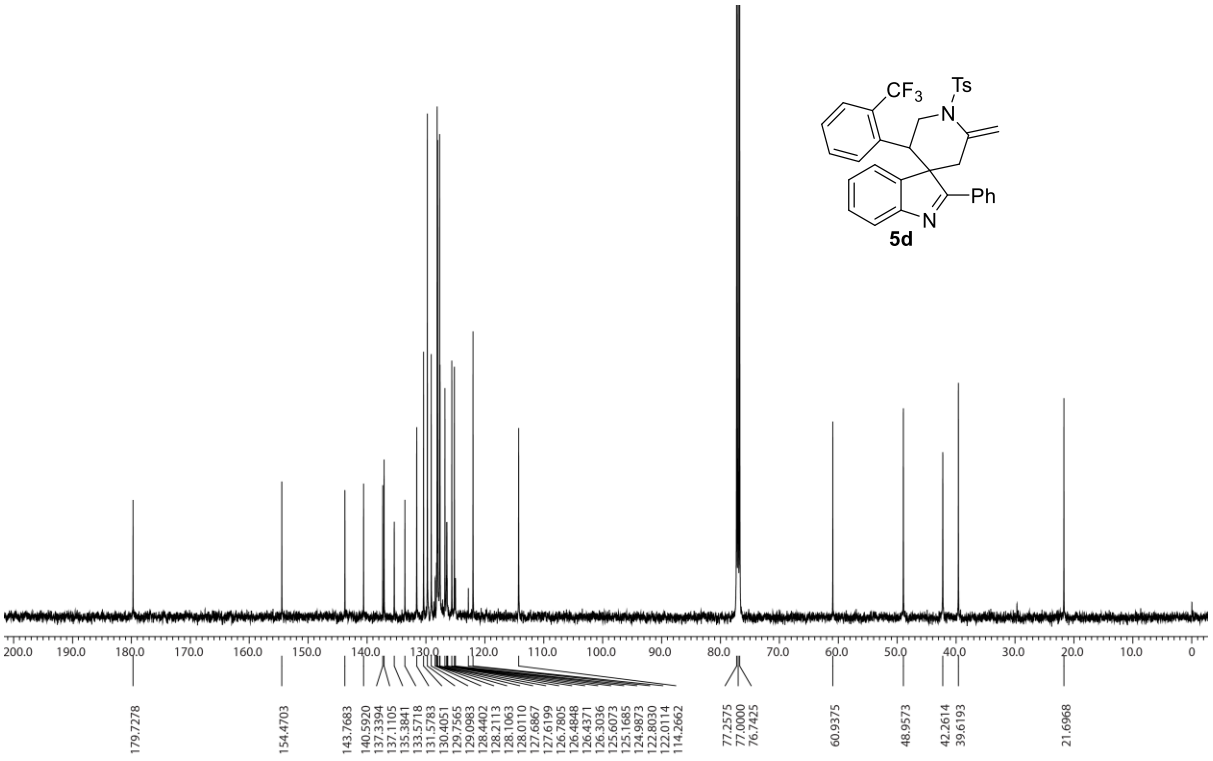


Figure S20. $^{13}C\{^{1}H\}$ NMR of **5d** (125 MHz, $CDCl_3$)

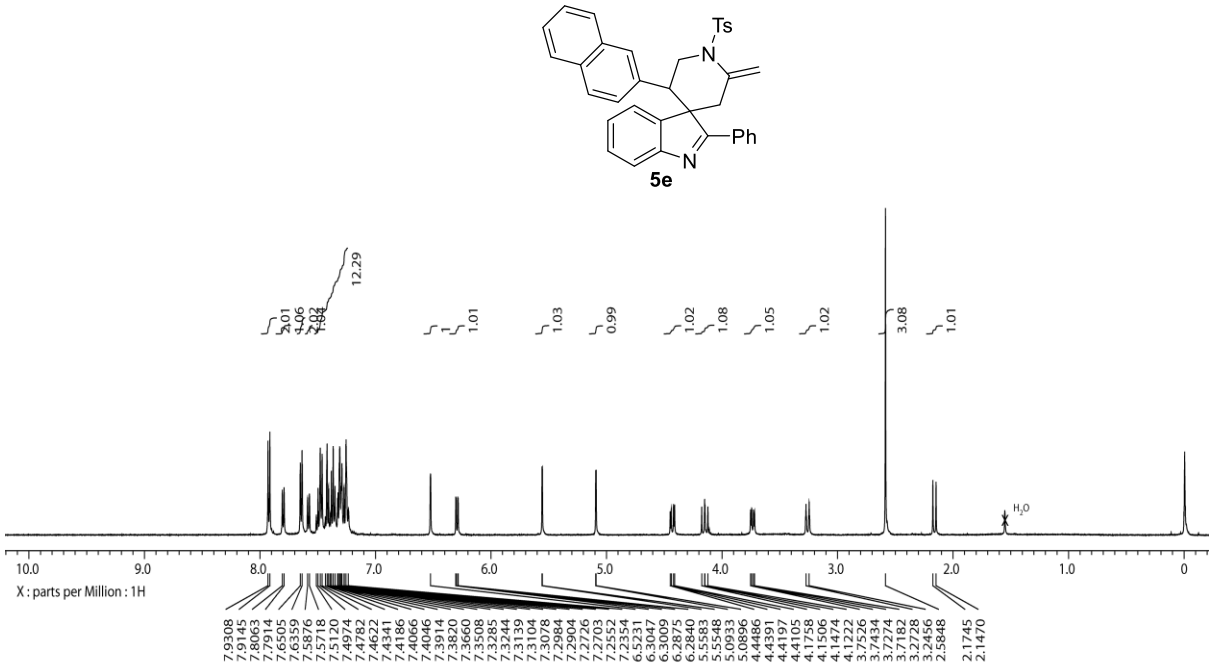


Figure S21. ^{1}H NMR of **5e** (500 MHz, $CDCl_3$)

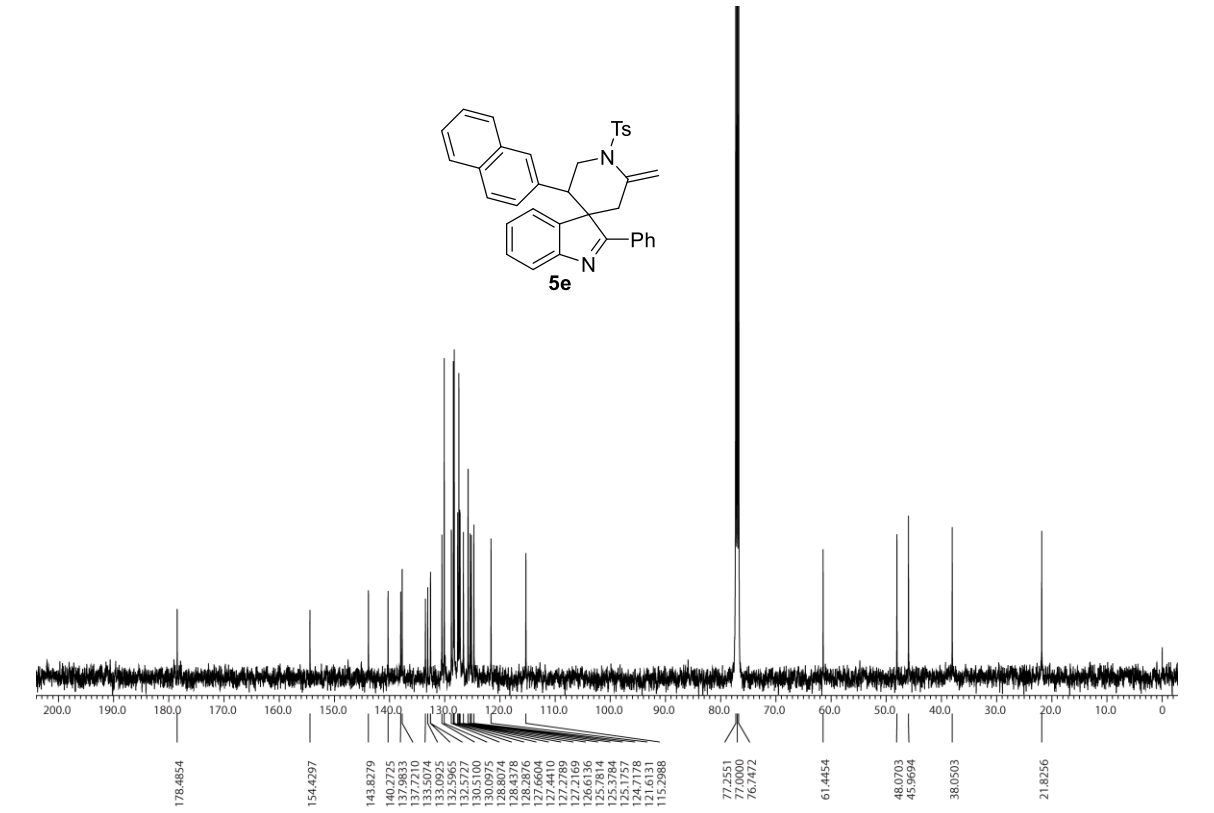


Figure S22. ^{13}C{^{1}H} NMR of **5e** (125 MHz, $CDCl_3$)

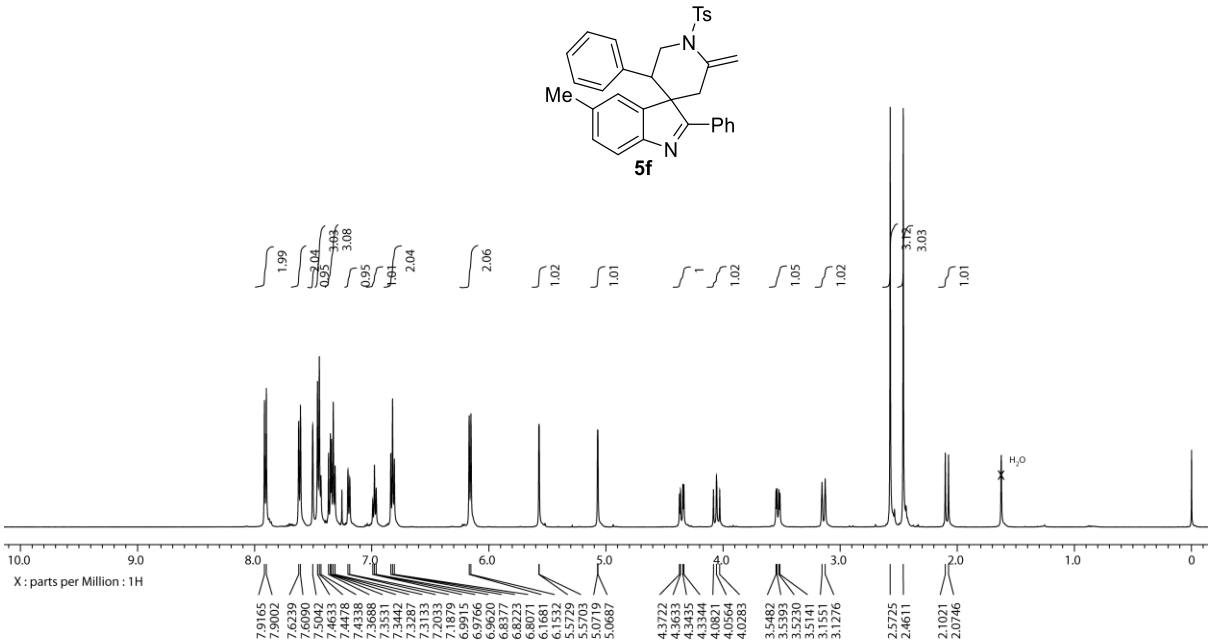


Figure S23. ^{1}H NMR of **5f** (500 MHz, $CDCl_3$)

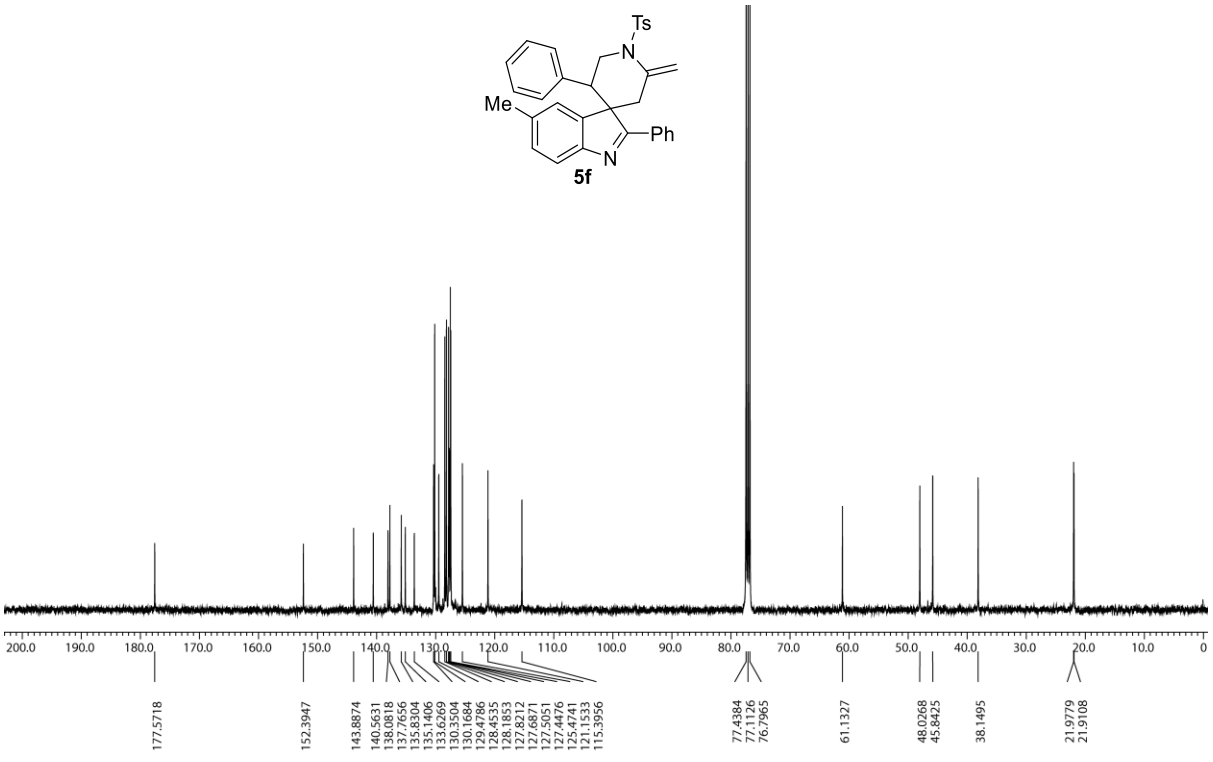


Figure S24. $^{13}C\{^{1}H\}$ NMR of **5f** (100 MHz, $CDCl_3$)

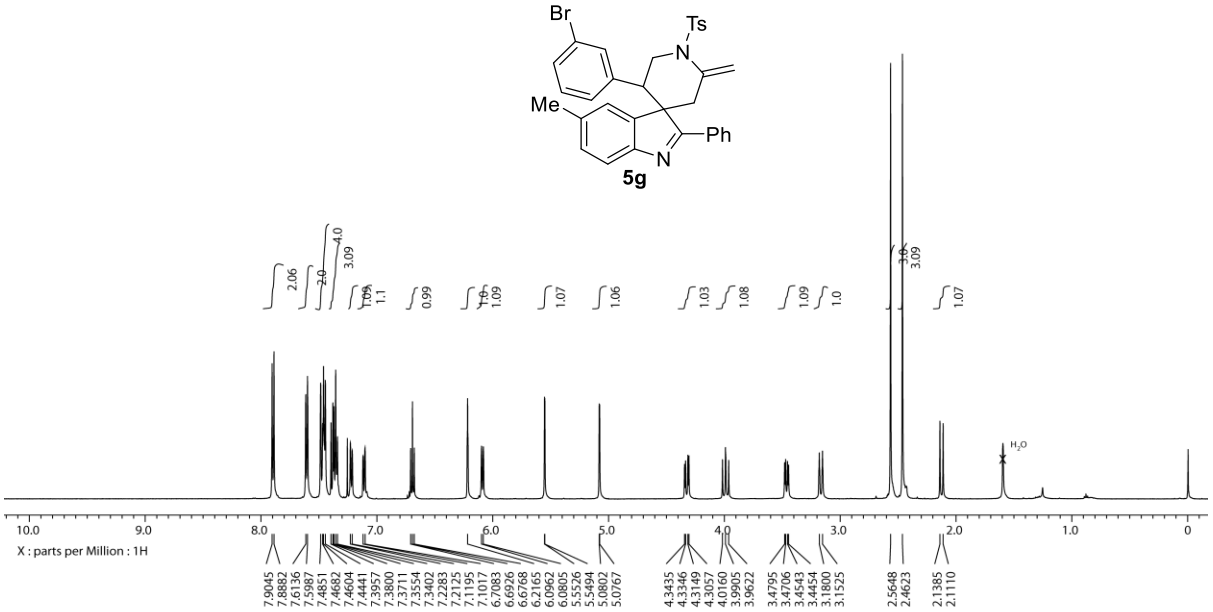


Figure S25. ^{1}H NMR of **5g** (500 MHz, $CDCl_3$)

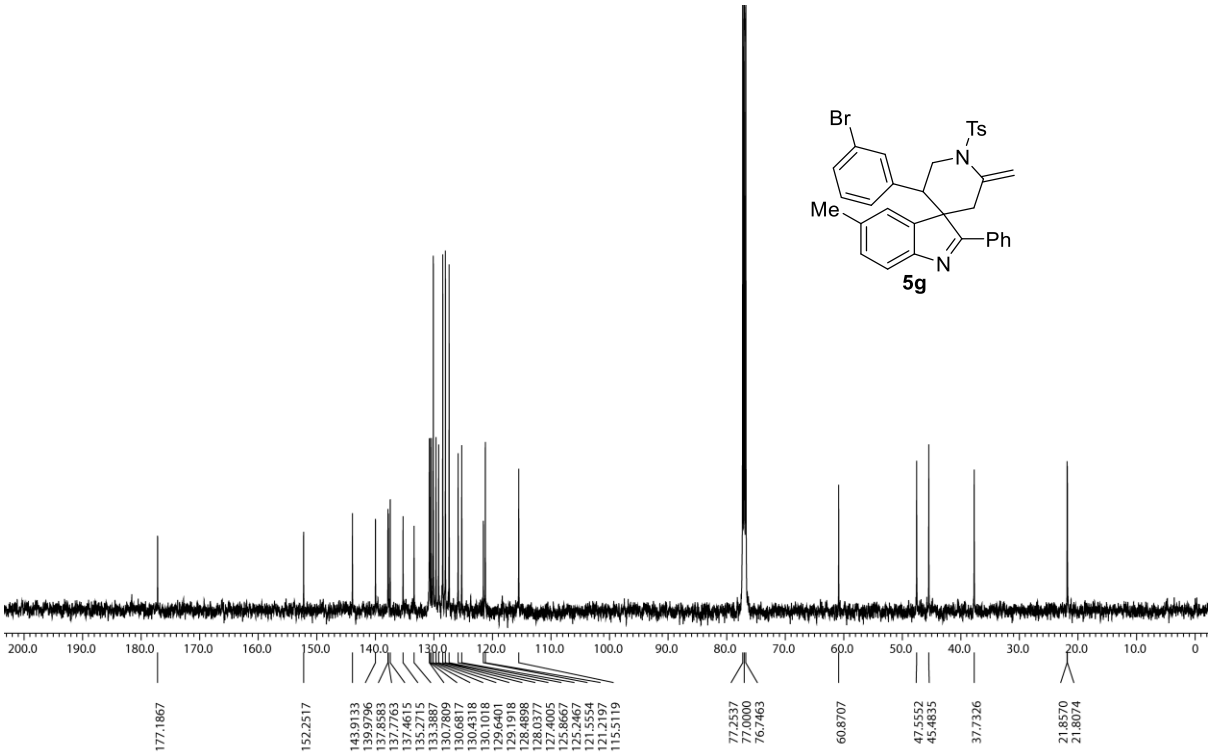


Figure S26. $^{13}C\{^{1}H\}$ NMR of **5g** (125 MHz, $CDCl_3$)

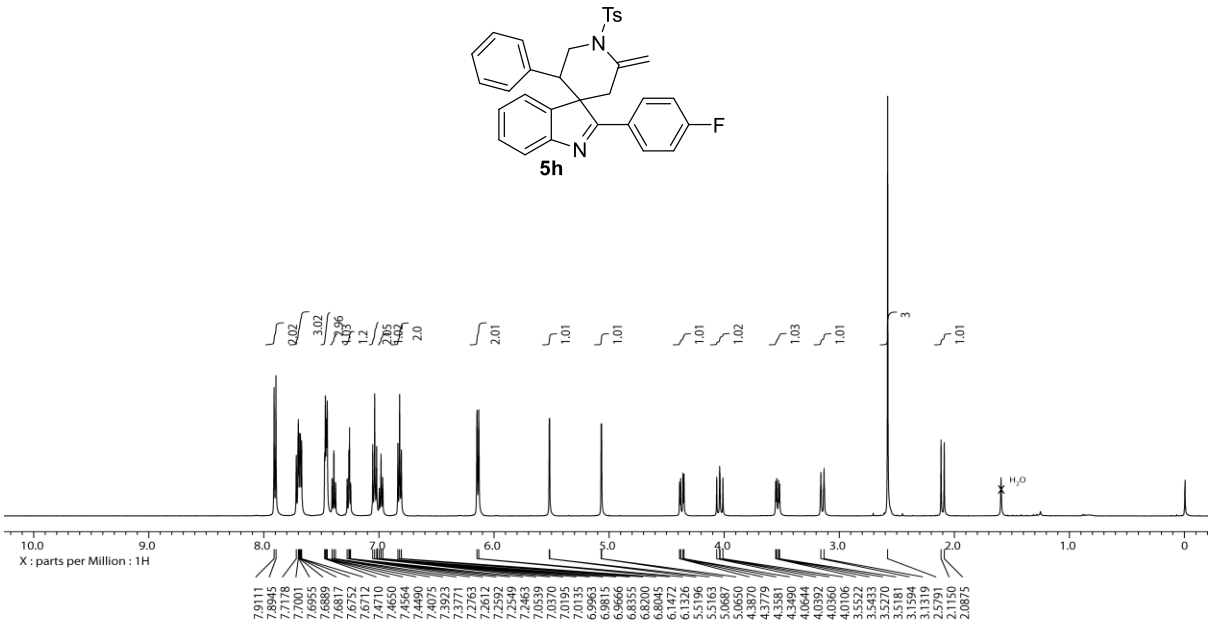


Figure S27. ^{1}H NMR of **5h** (500 MHz, $CDCl_3$)

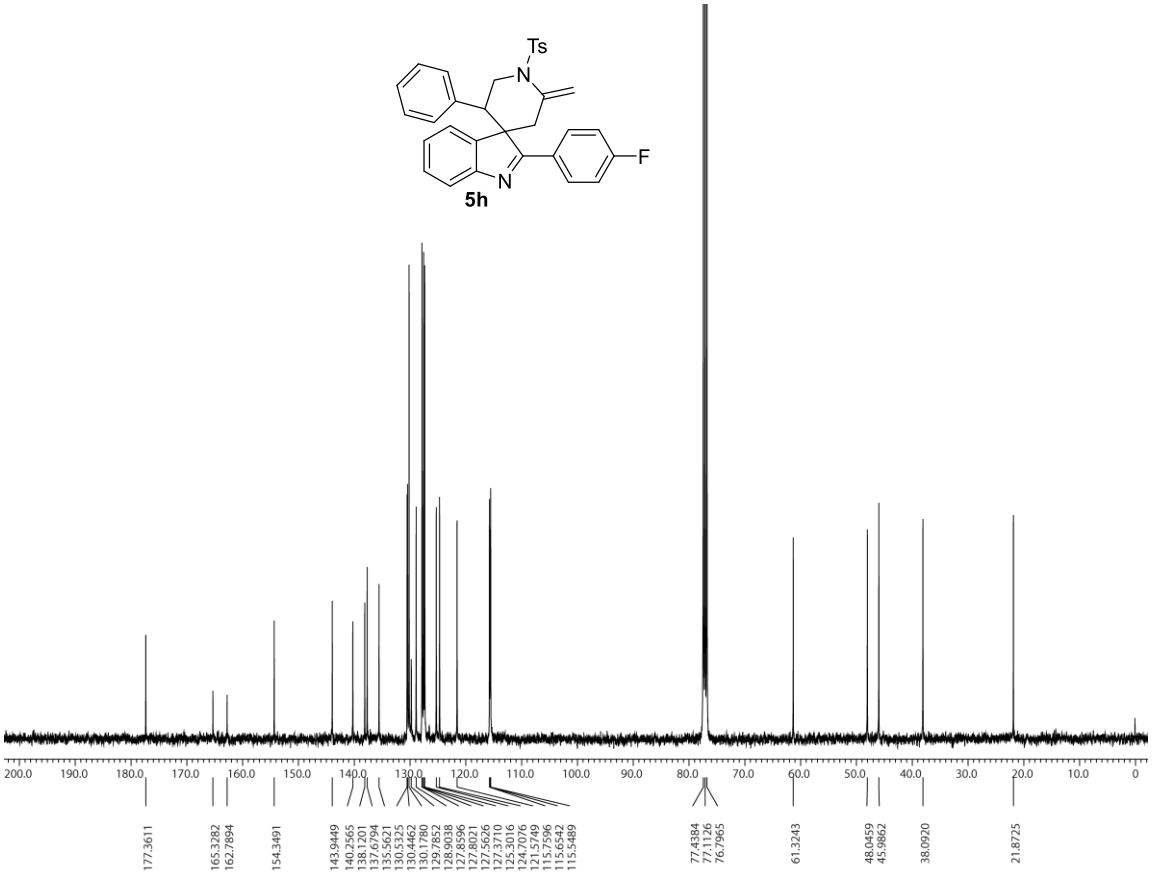


Figure S28. $^{13}C\{^{1}H\}$ NMR of **5h** (100 MHz, $CDCl_3$)

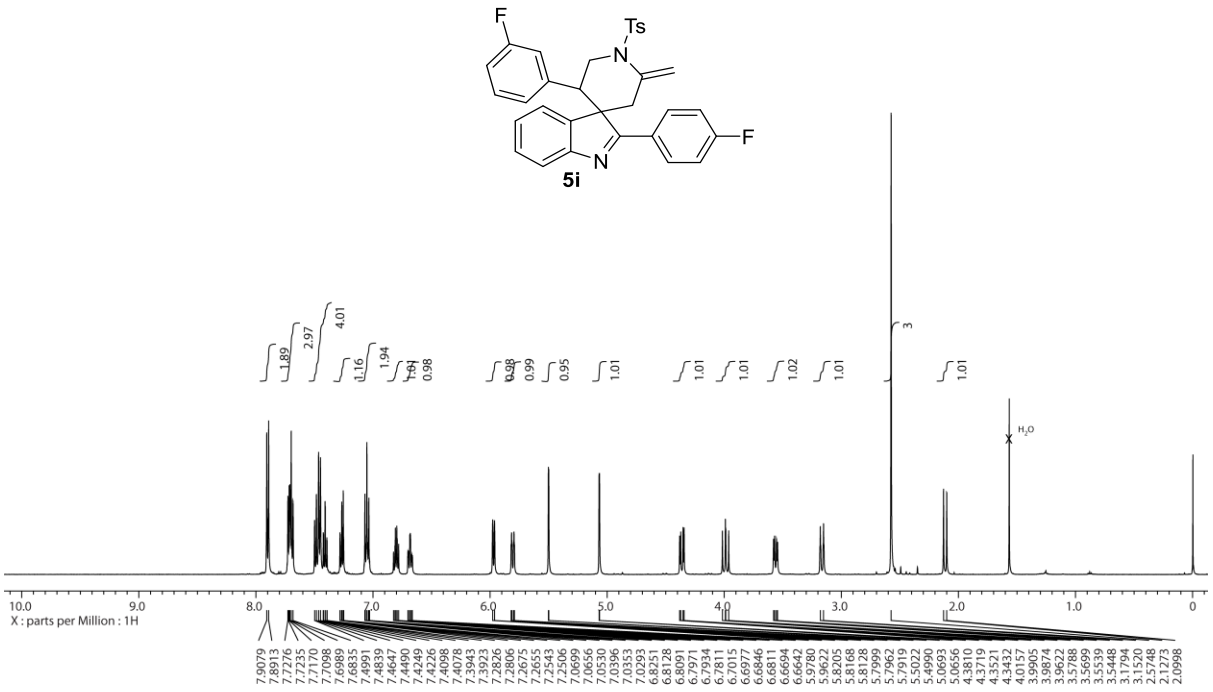


Figure S29. ^{1}H NMR of **5i** (500 MHz, $CDCl_3$)

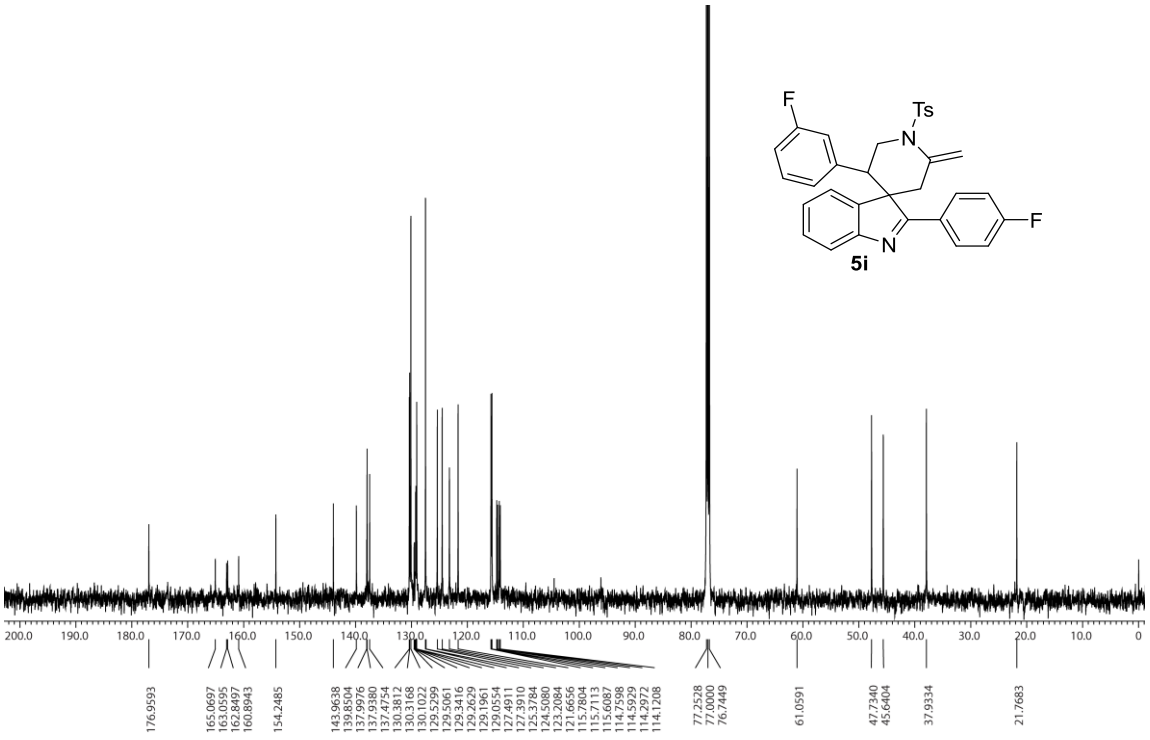


Figure S30. ^{13}C{^{1}H} NMR of **5i** (125 MHz, $CDCl_3$)

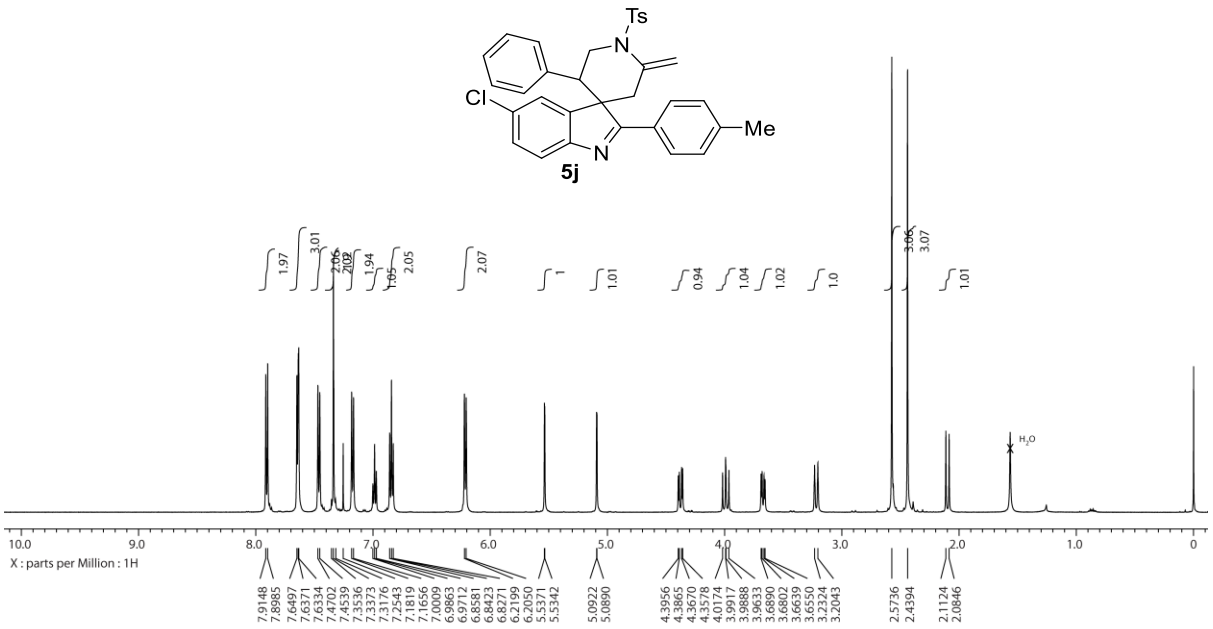


Figure S31. ^{1}H NMR of **5j** (500 MHz, $CDCl_3$)

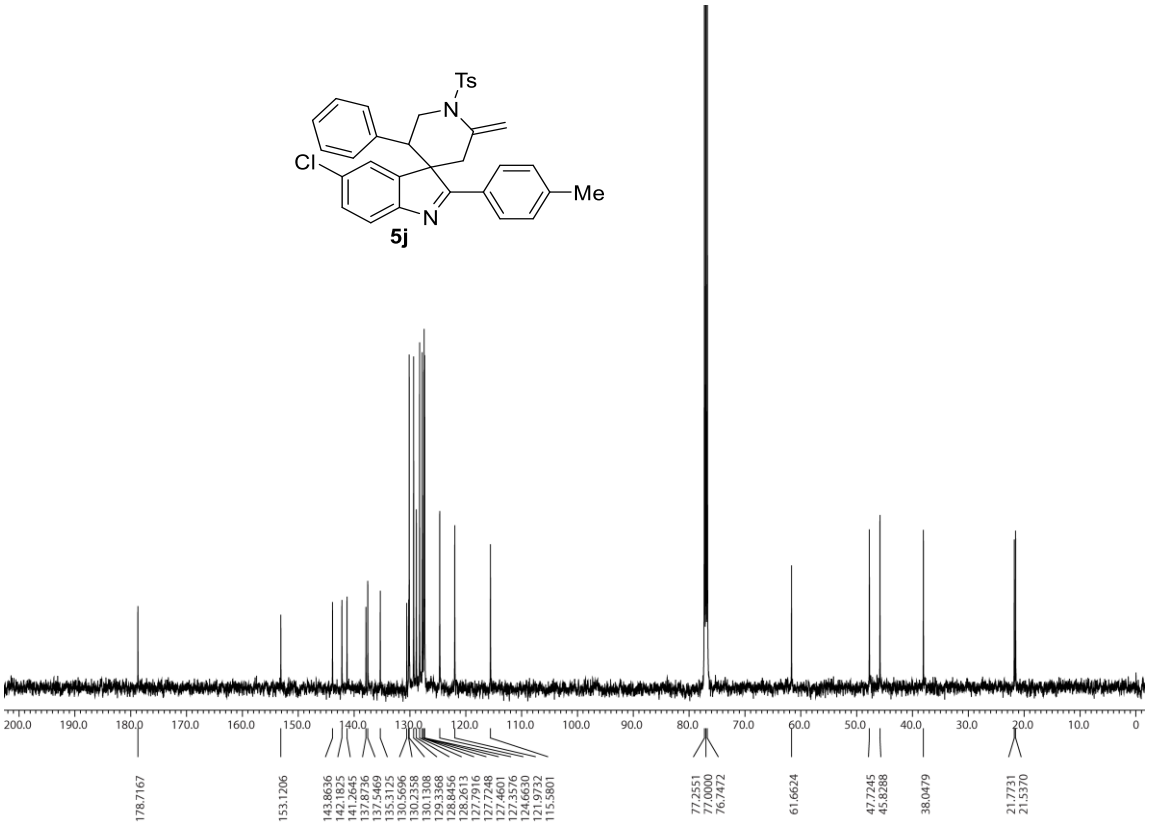


Figure S32. $^{13}C\{^{1}H\}$ NMR of **5j** (125 MHz, $CDCl_3$)

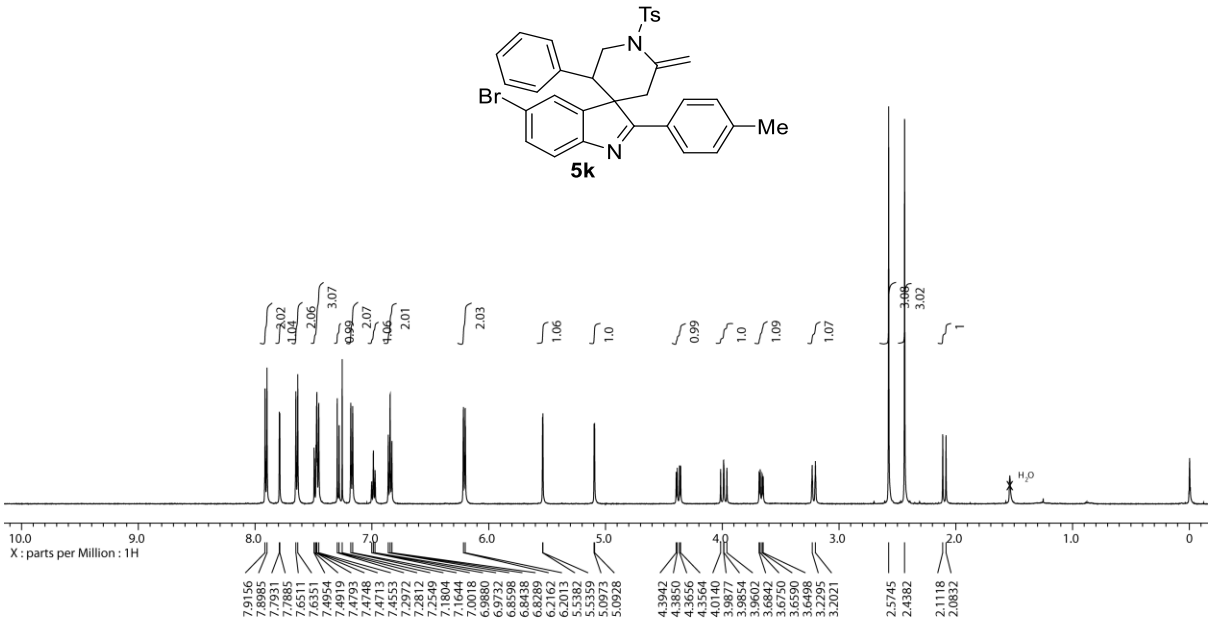


Figure S33. ^{1}H NMR of **5k** (500 MHz, $CDCl_3$)

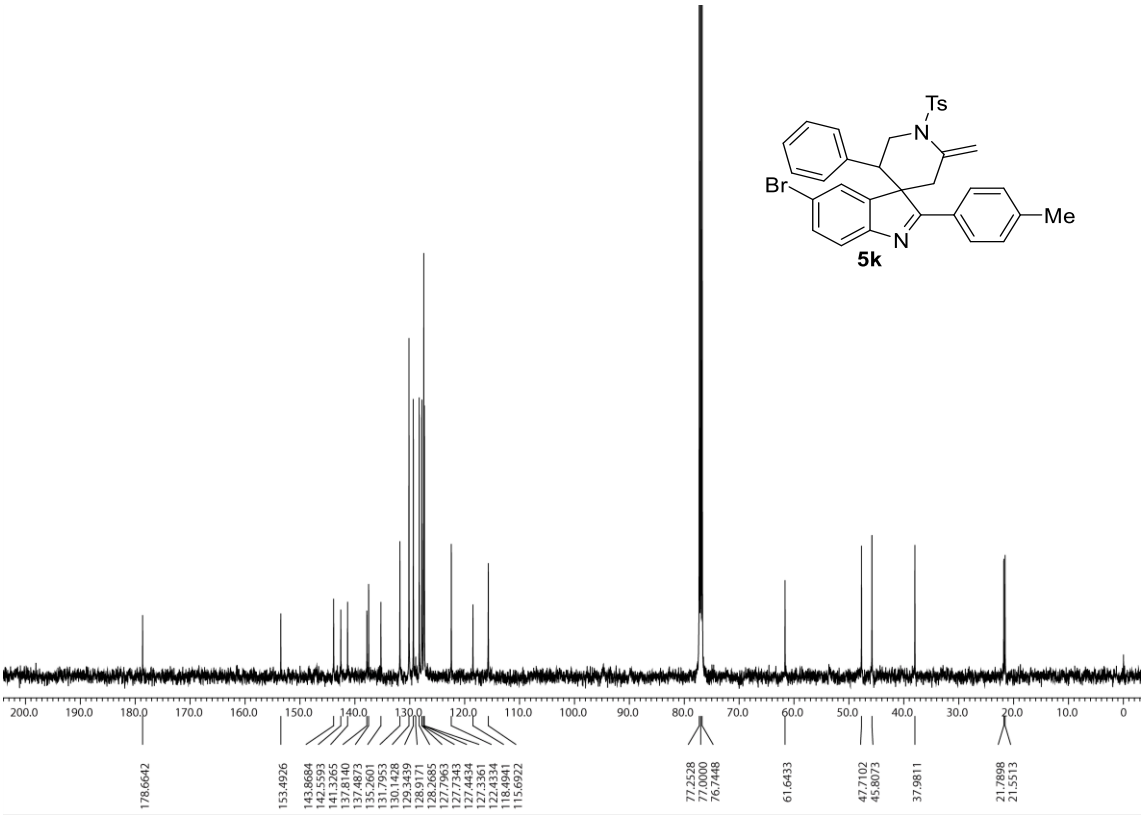


Figure S34. $^{13}C\{^{1}H\}$ NMR of **5k** (125 MHz, $CDCl_3$)

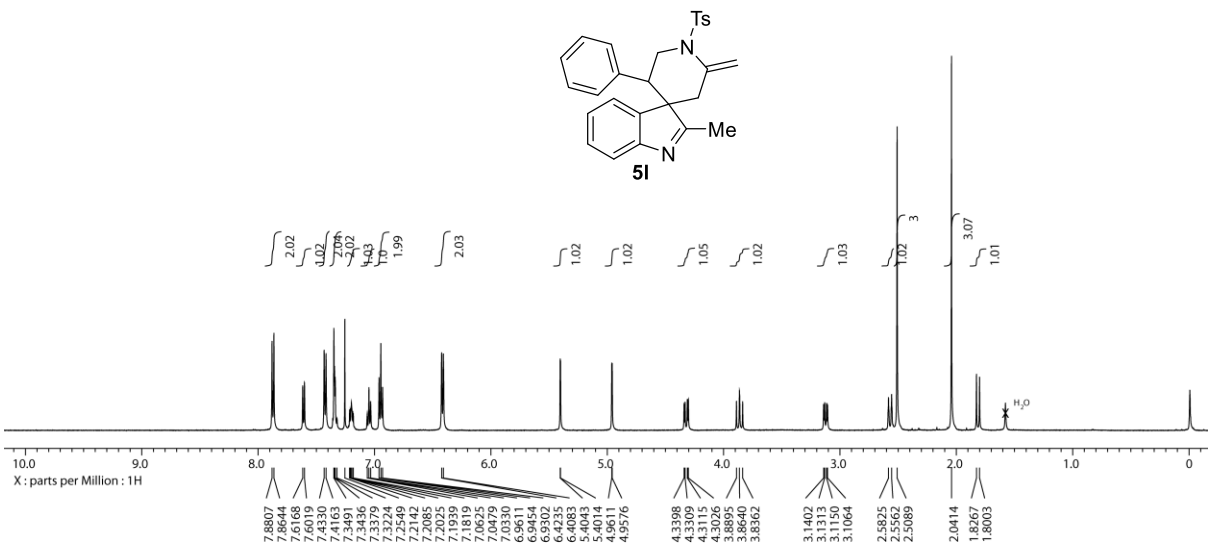


Figure S35. ^{1}H NMR of **5l** (400 MHz, $CDCl_3$)

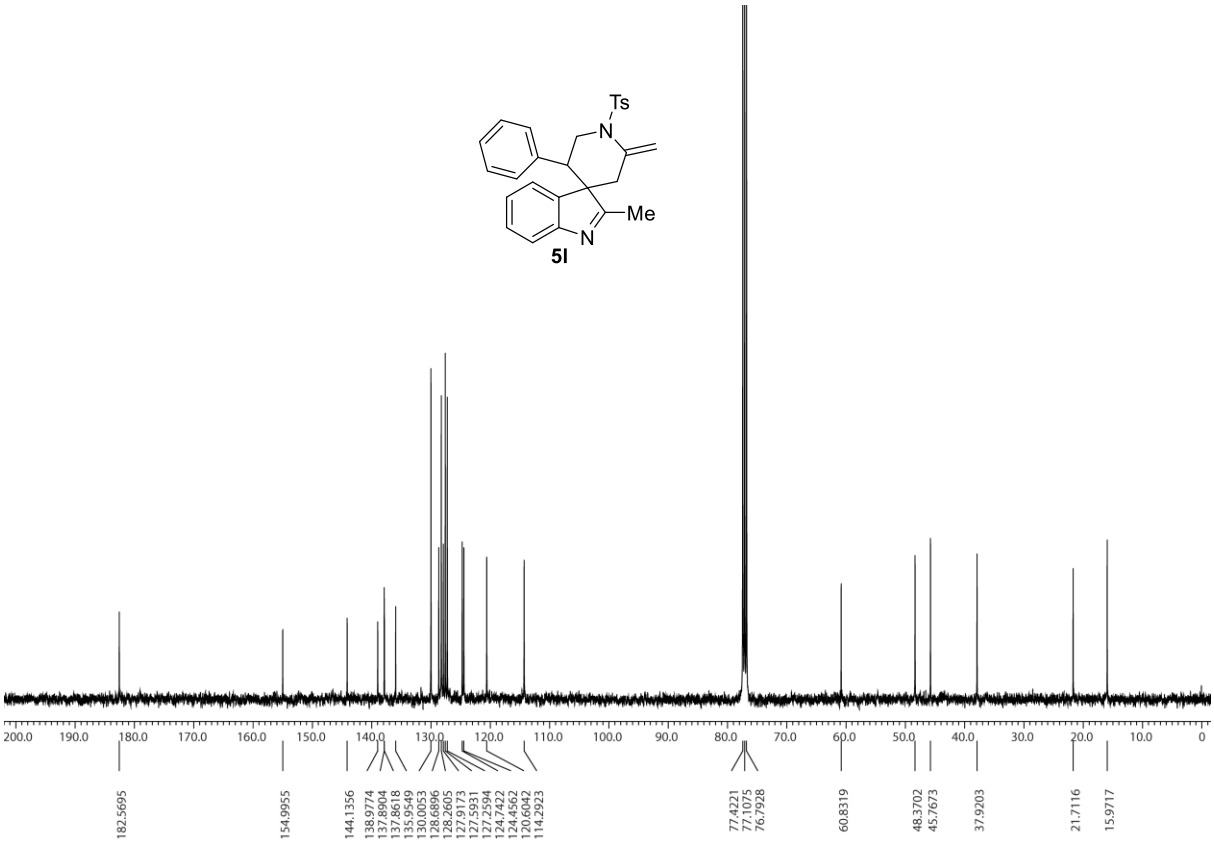


Figure S36. $^{13}C\{^{1}H\}$ NMR of **5l** (100 MHz, $CDCl_3$)

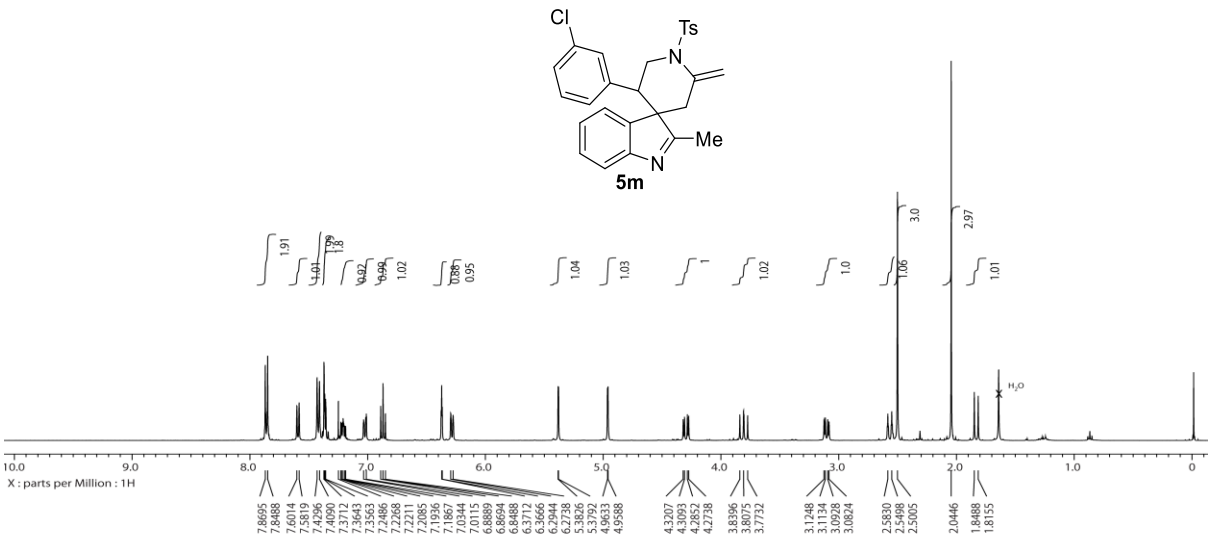


Figure S37. ^{1}H NMR of **5m** (400 MHz, $CDCl_3$)

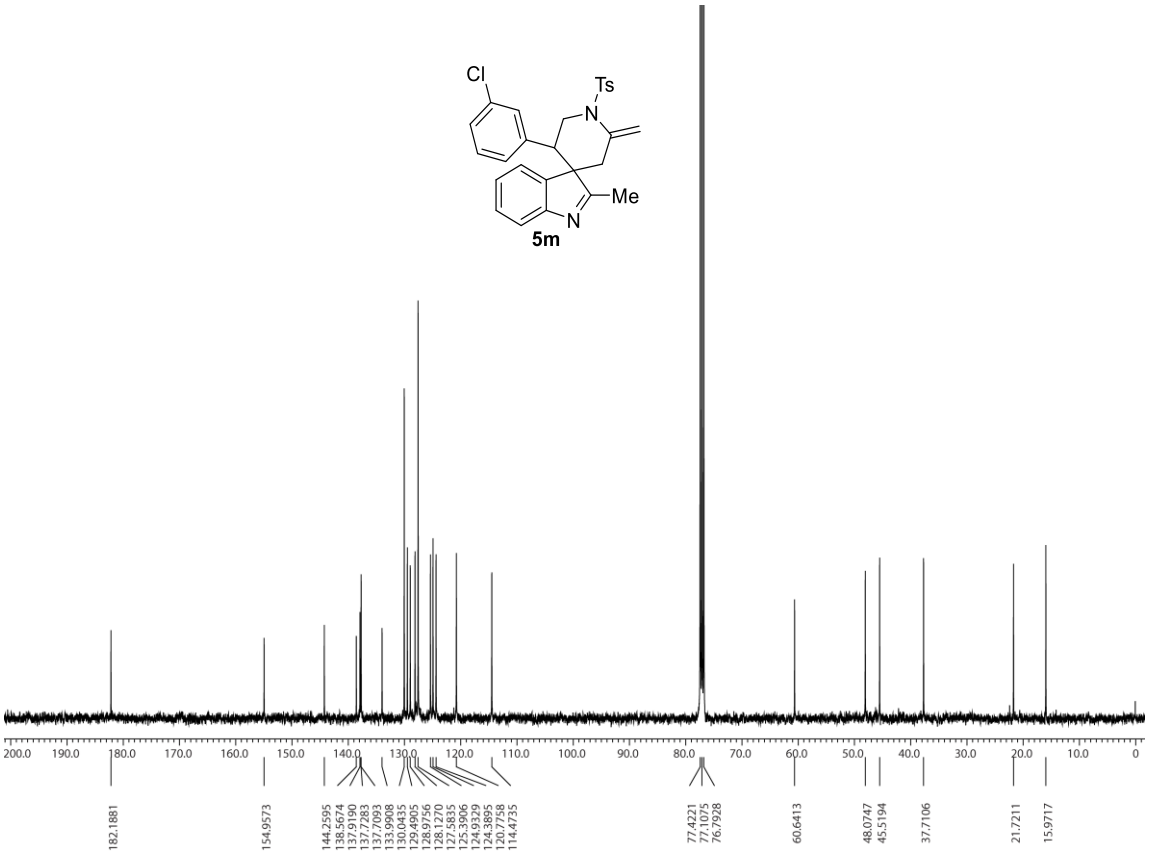


Figure S38. $^{13}C\{^{1}H\}$ NMR of **5m** (100 MHz, $CDCl_3$)

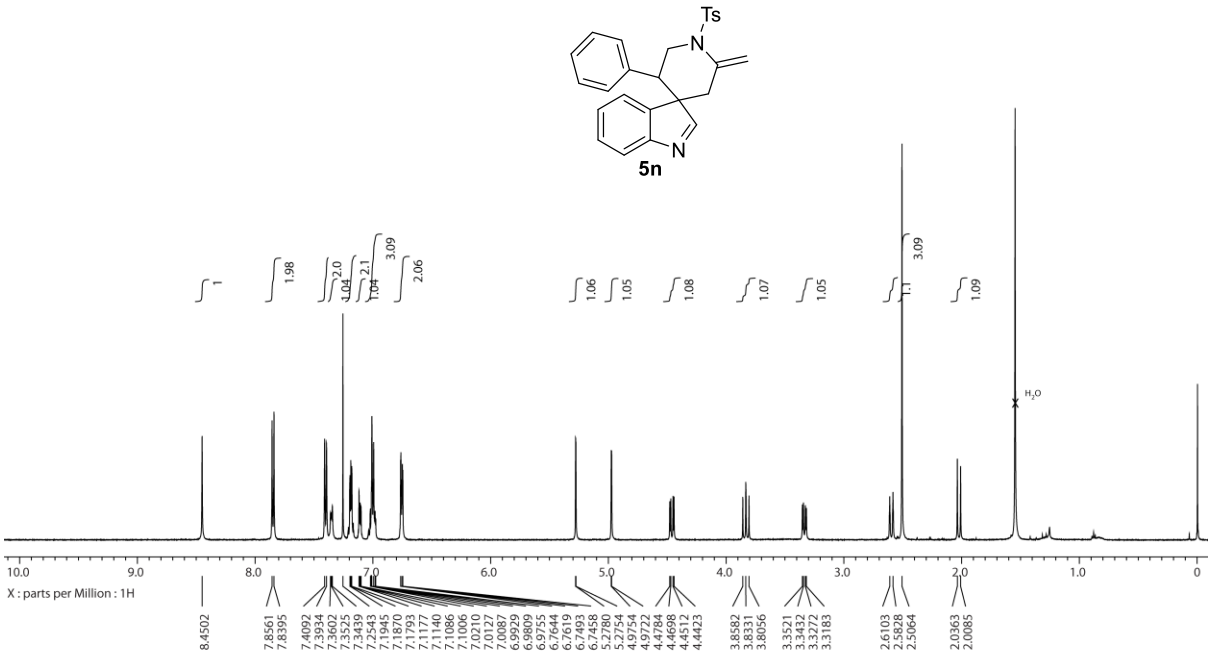


Figure S39. ^{1}H NMR of **5n** (500 MHz, $CDCl_3$)

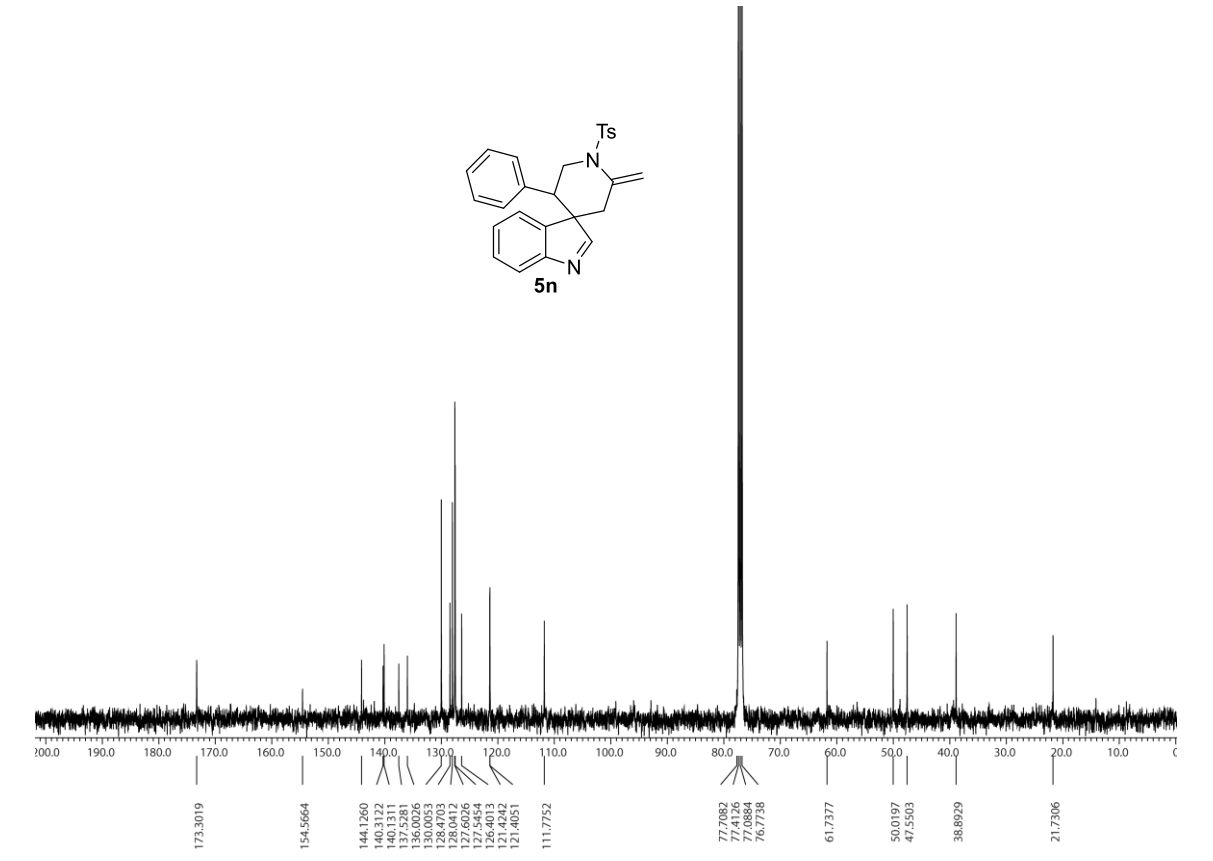


Figure S40. ^{13}C{^{1}H} NMR of **5n** (100 MHz, $CDCl_3$)

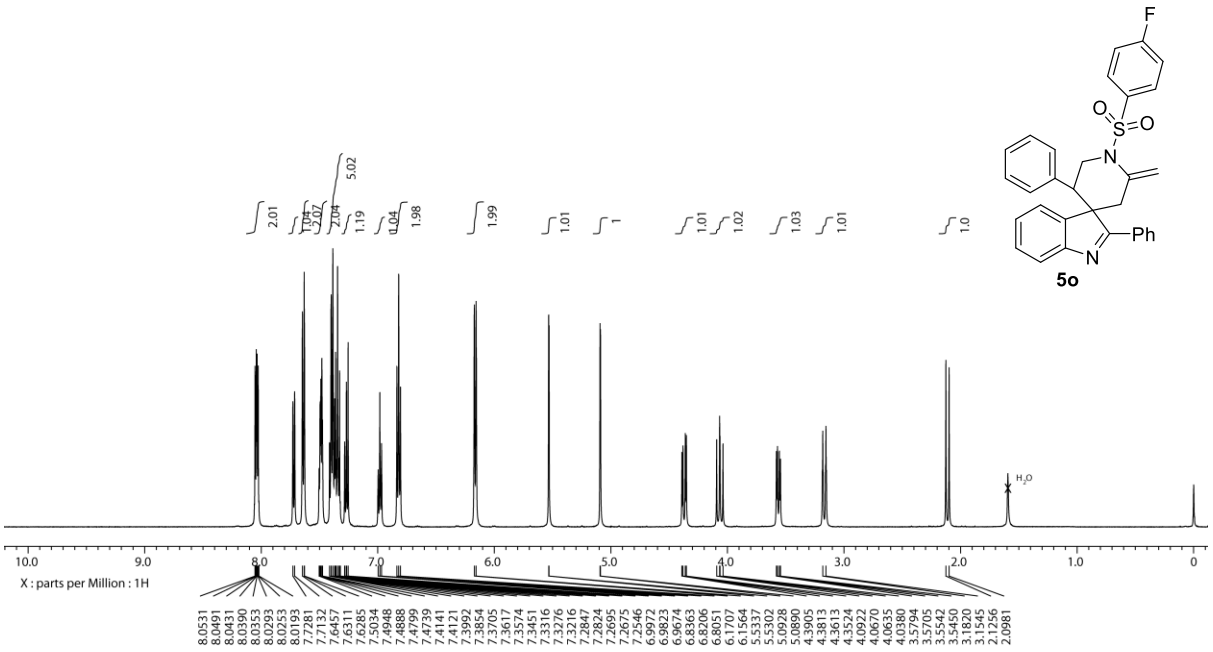


Figure S41. ^{1}H NMR of **5o** (500 MHz, $CDCl_3$)

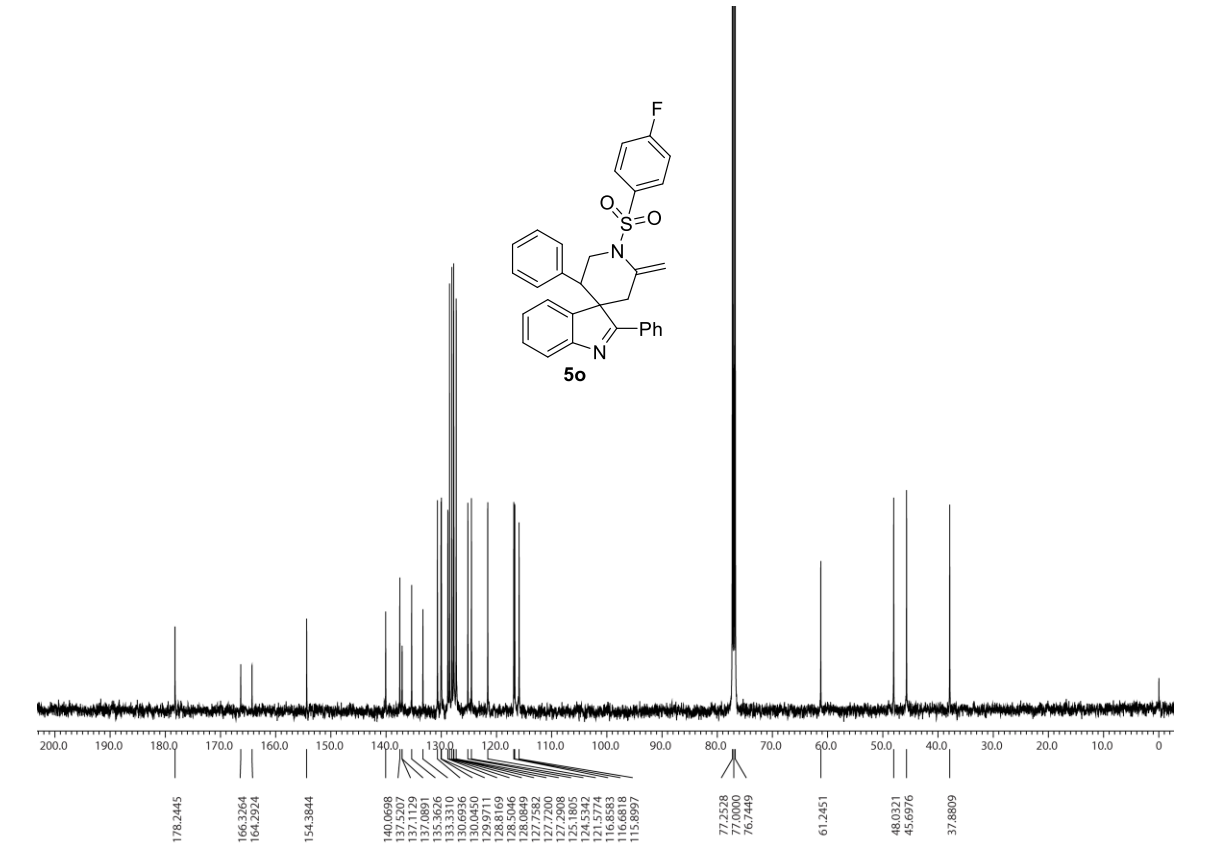


Figure S42. $^{13}C\{^{1}H\}$ NMR of **5o** (125 MHz, $CDCl_3$)

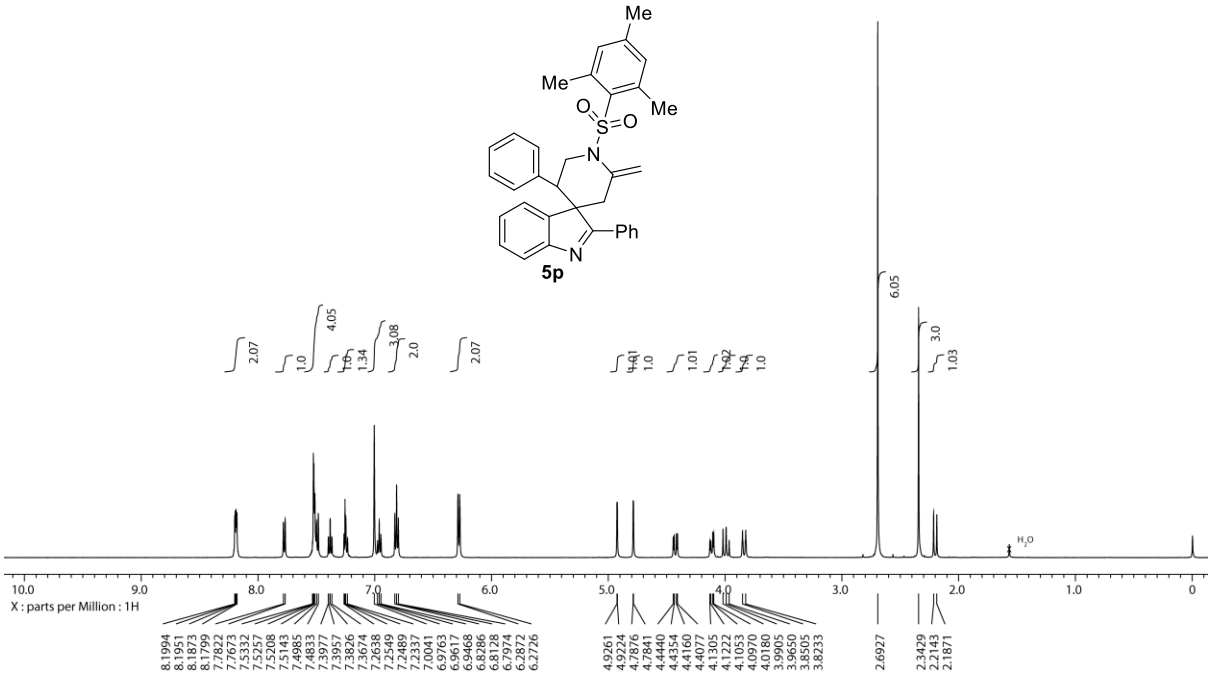


Figure S43. ^{1}H NMR of **5p** (500 MHz, $CDCl_3$)

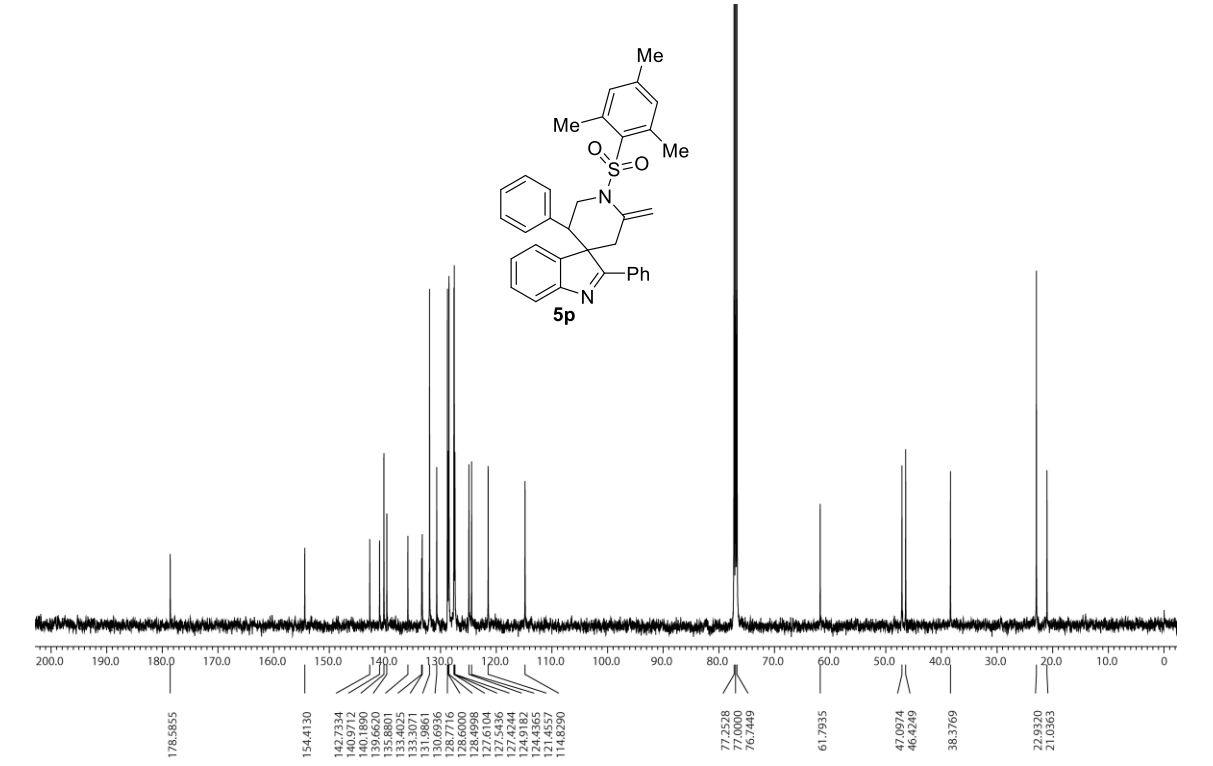


Figure S44. ^{13}C{^{1}H} NMR of **5p** (125 MHz, $CDCl_3$)

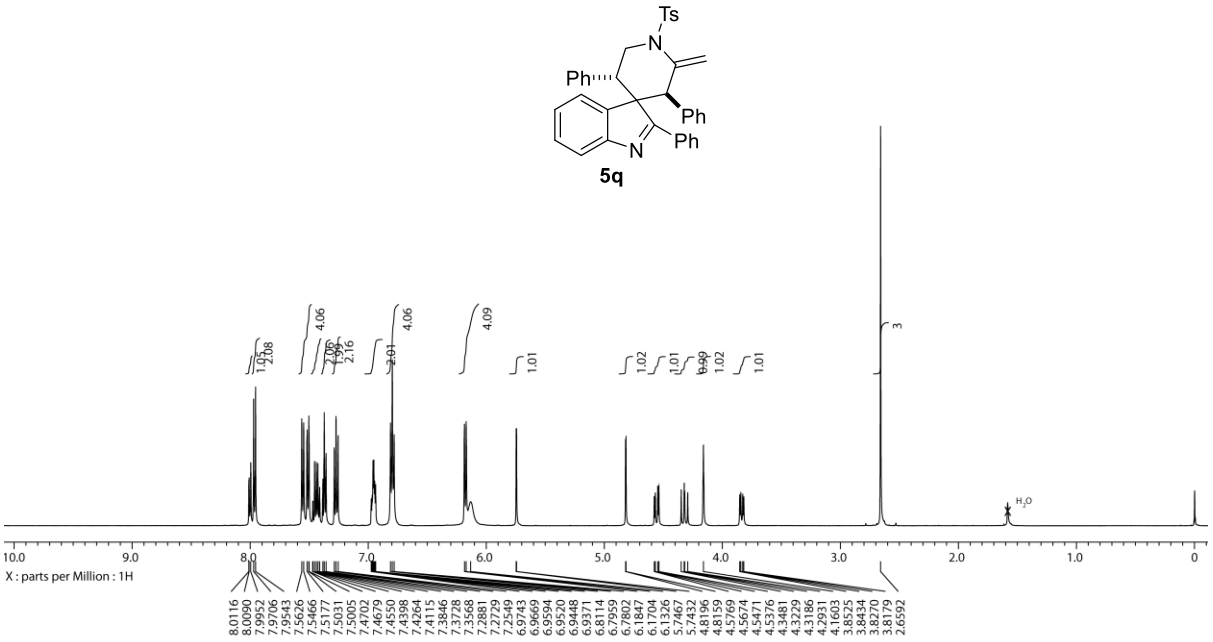


Figure S45. ^{1}H NMR of **5q** (500 MHz, $CDCl_3$)

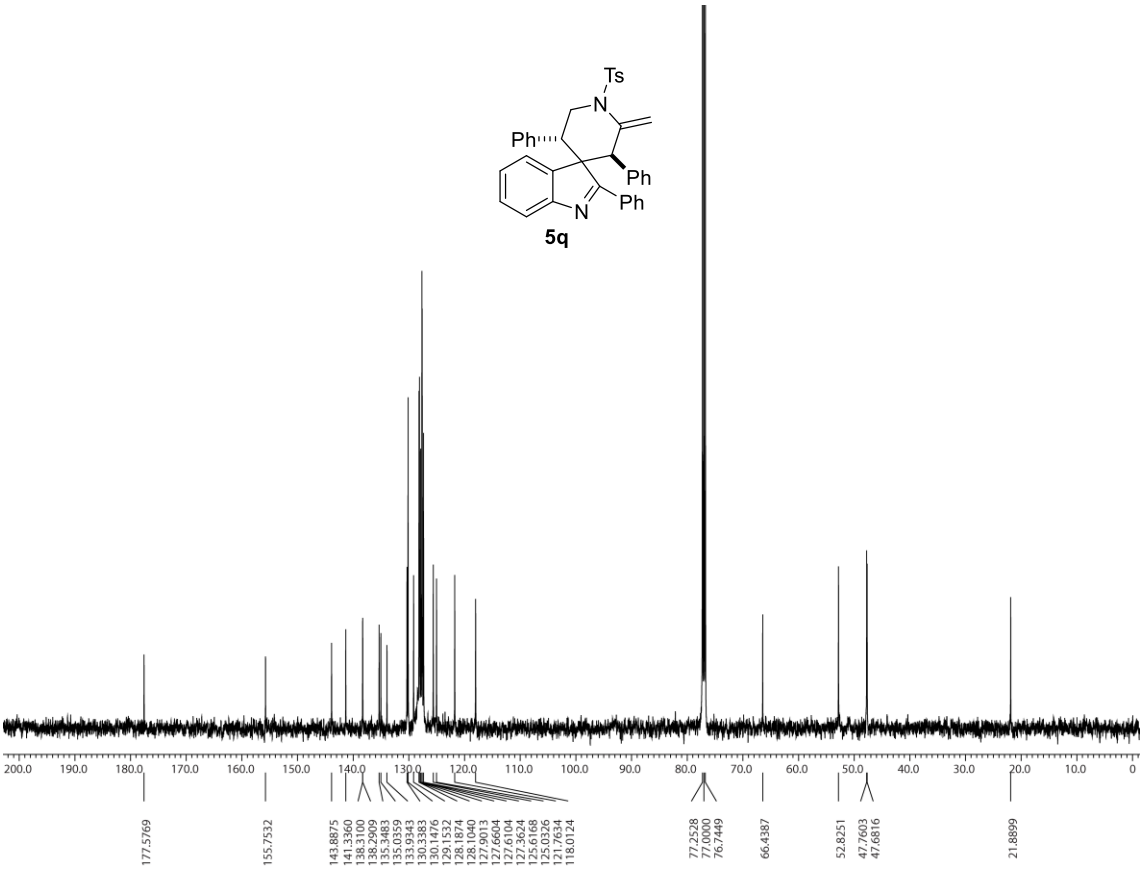
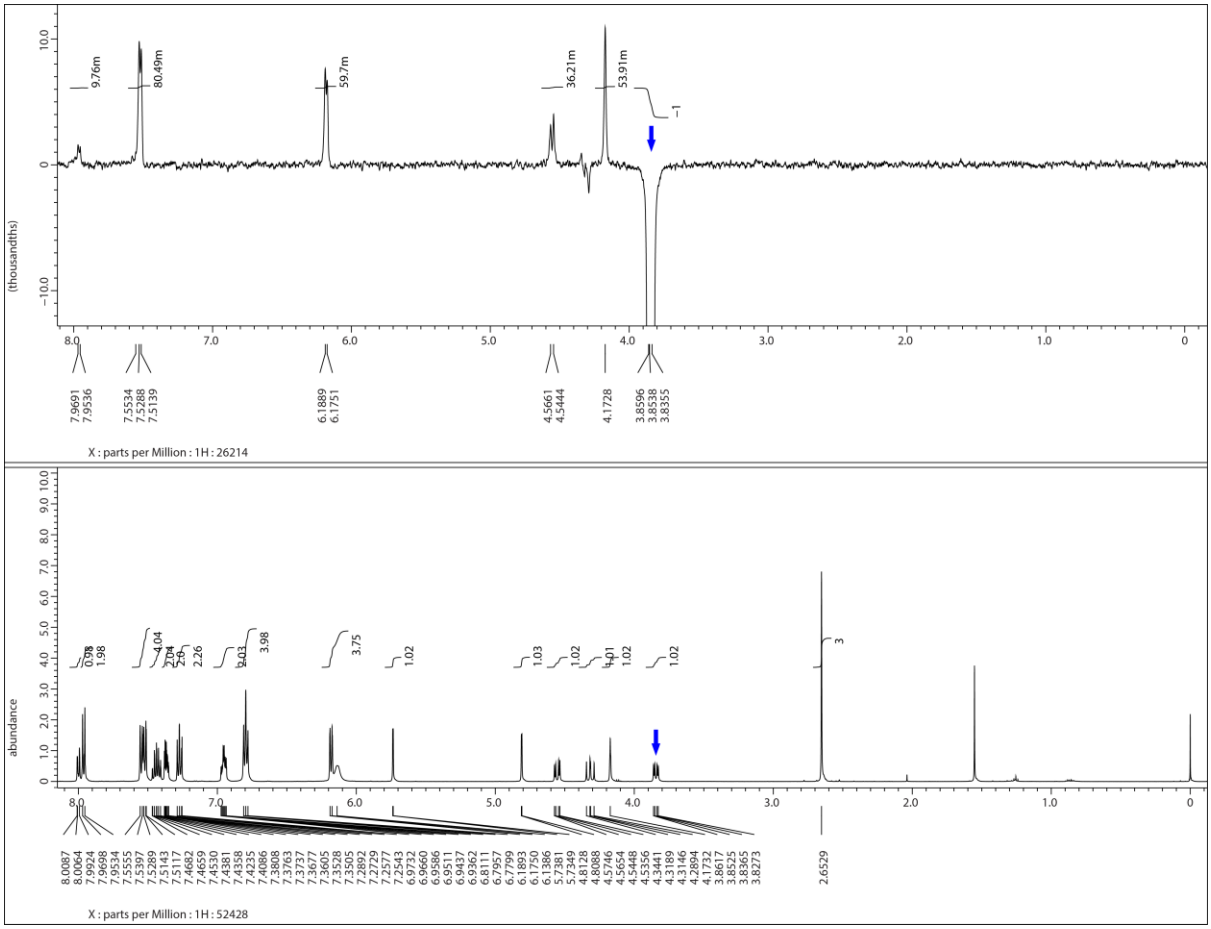


Figure S46. $^{13}C\{^{1}H\}$ NMR of **5q** (125 MHz, $CDCl_3$)



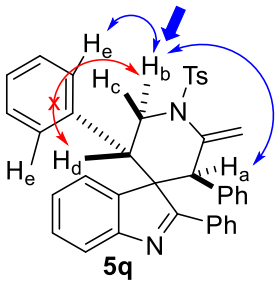
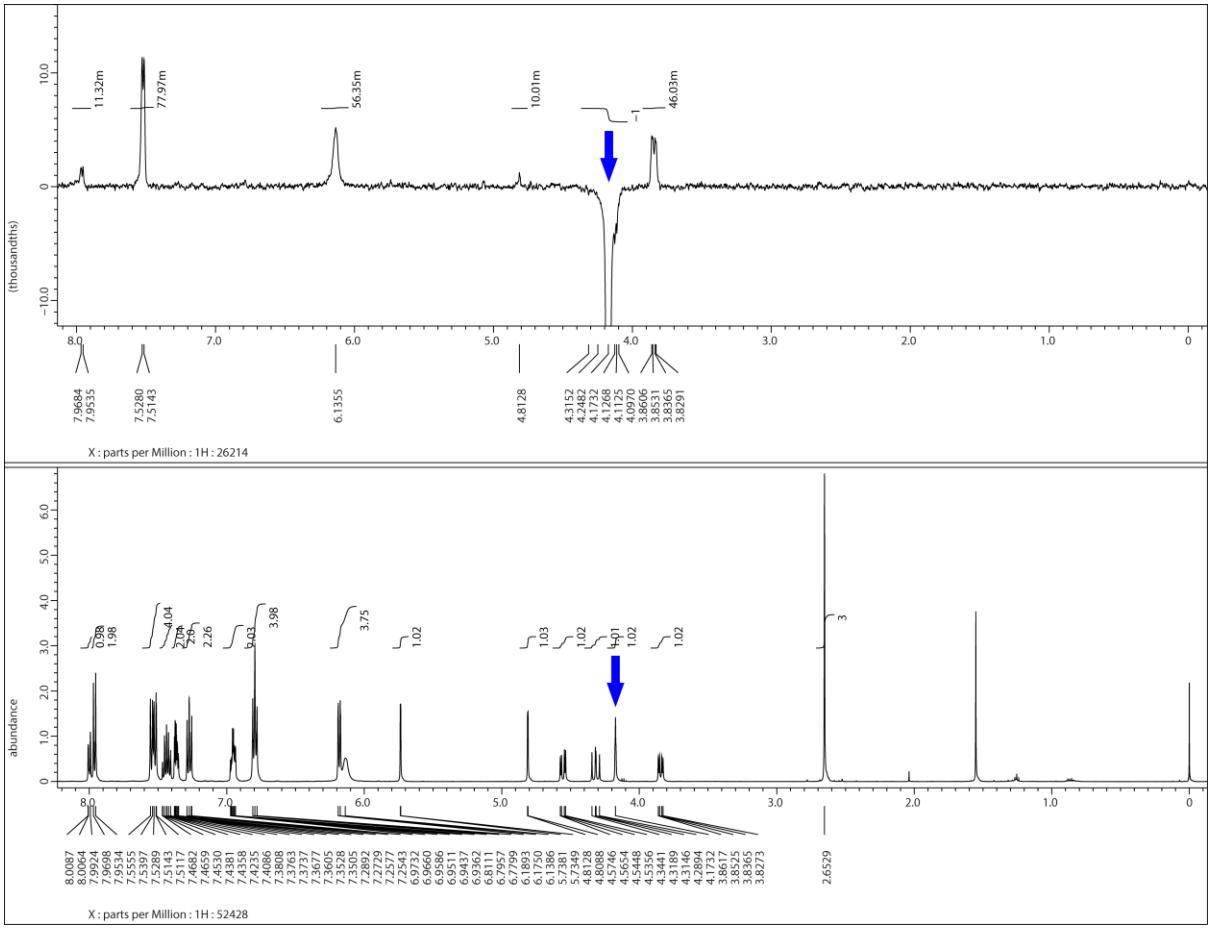


Figure S47. NOE spectrum of **5q** with irradiation of H_b at 3.83–3.85 ppm ($CDCl_3$, 500 MHz)



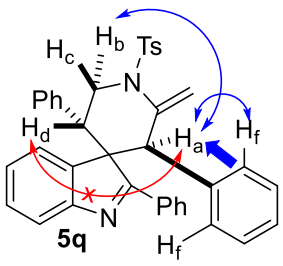


Figure S48. NOE spectrum of **5q** with irradiation of H_a at 4.17 ppm ($CDCl_3$, 500 MHz)

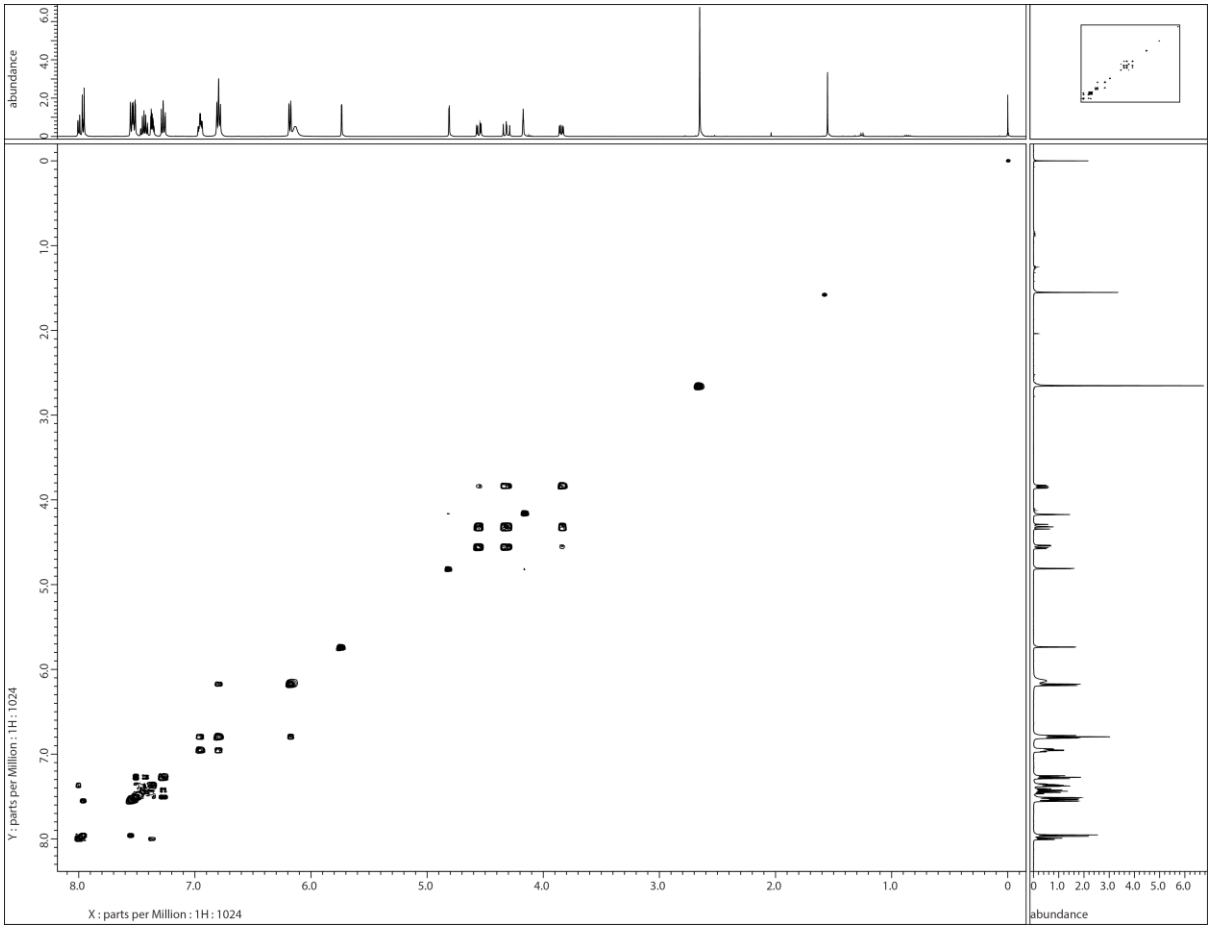


Figure S49. COSY spectrum of **5q** ($CDCl_3$, 500 MHz)

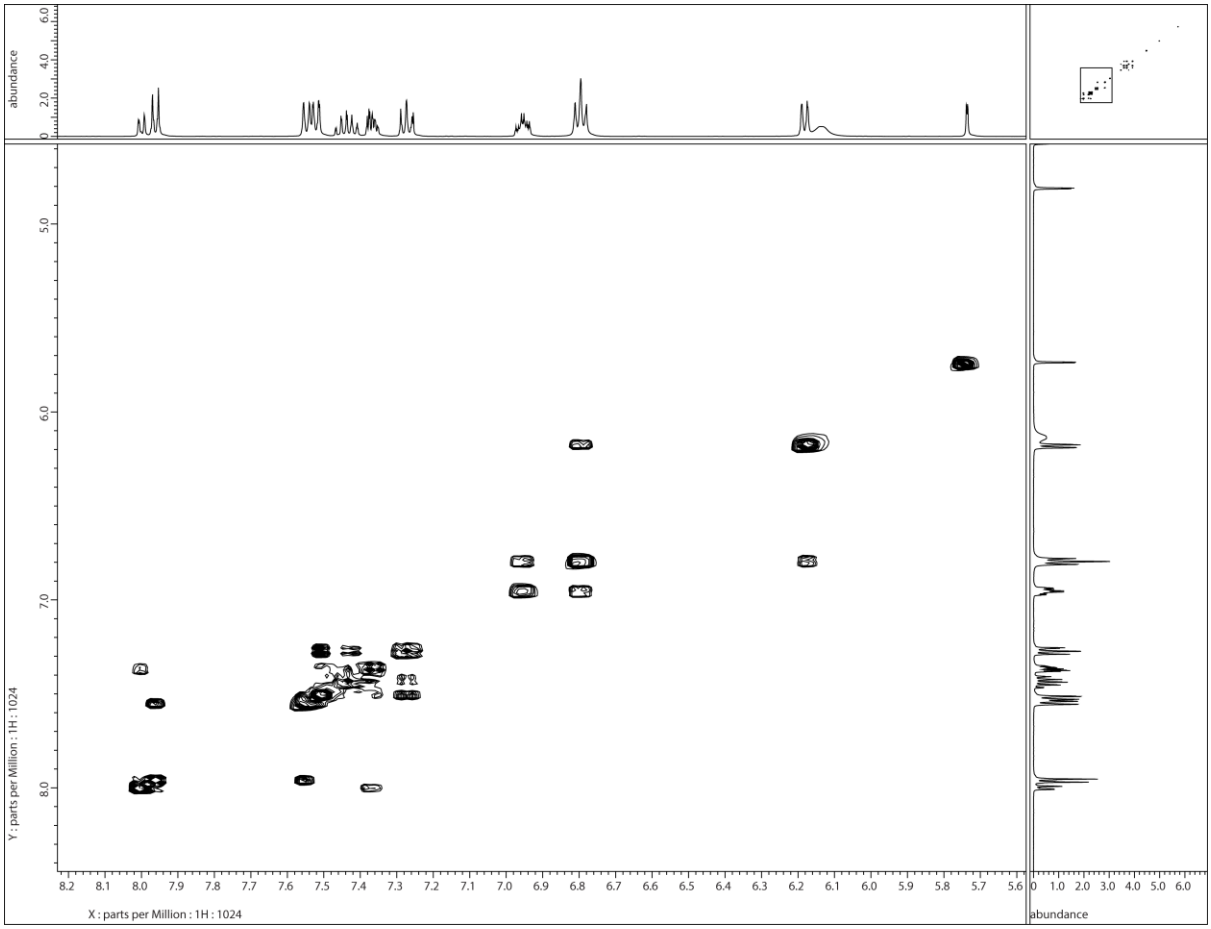


Figure S50. COSY spectrum of **5q** ($CDCl_3$, 500 MHz)

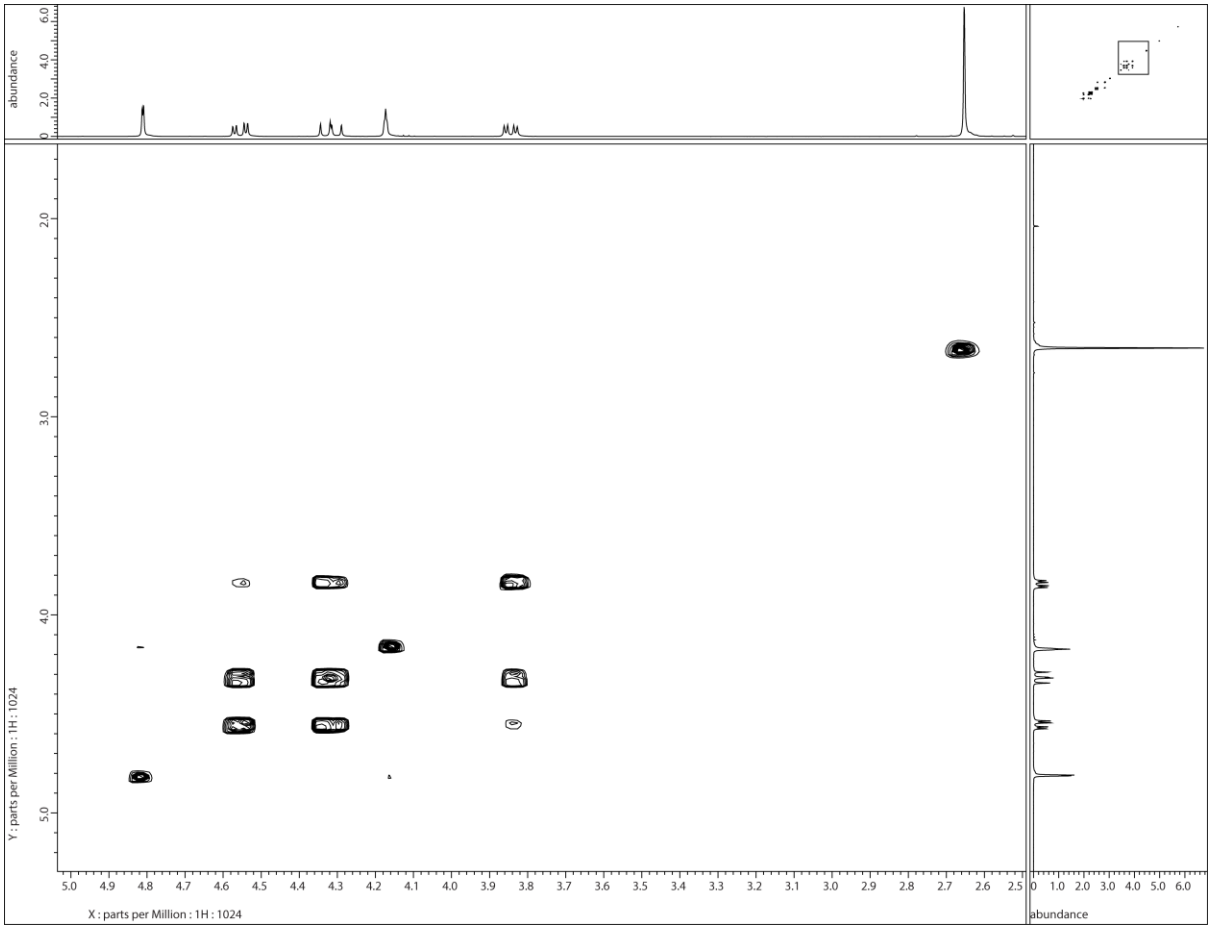


Figure S51. COSY spectrum of **5q** ($CDCl_3$, 500 MHz)

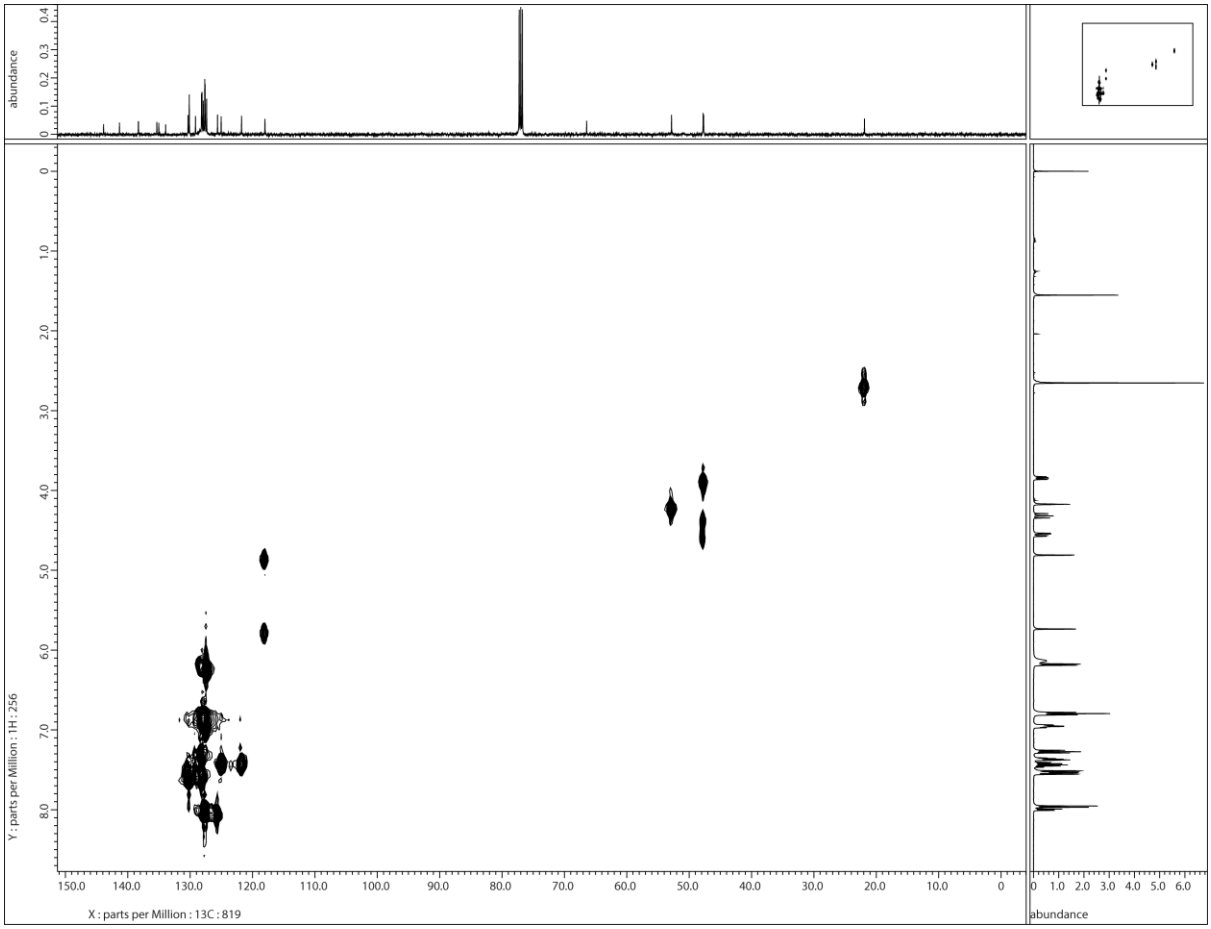


Figure S52. HETCOR spectrum of **5q** ($CDCl_3$, 125 MHz)

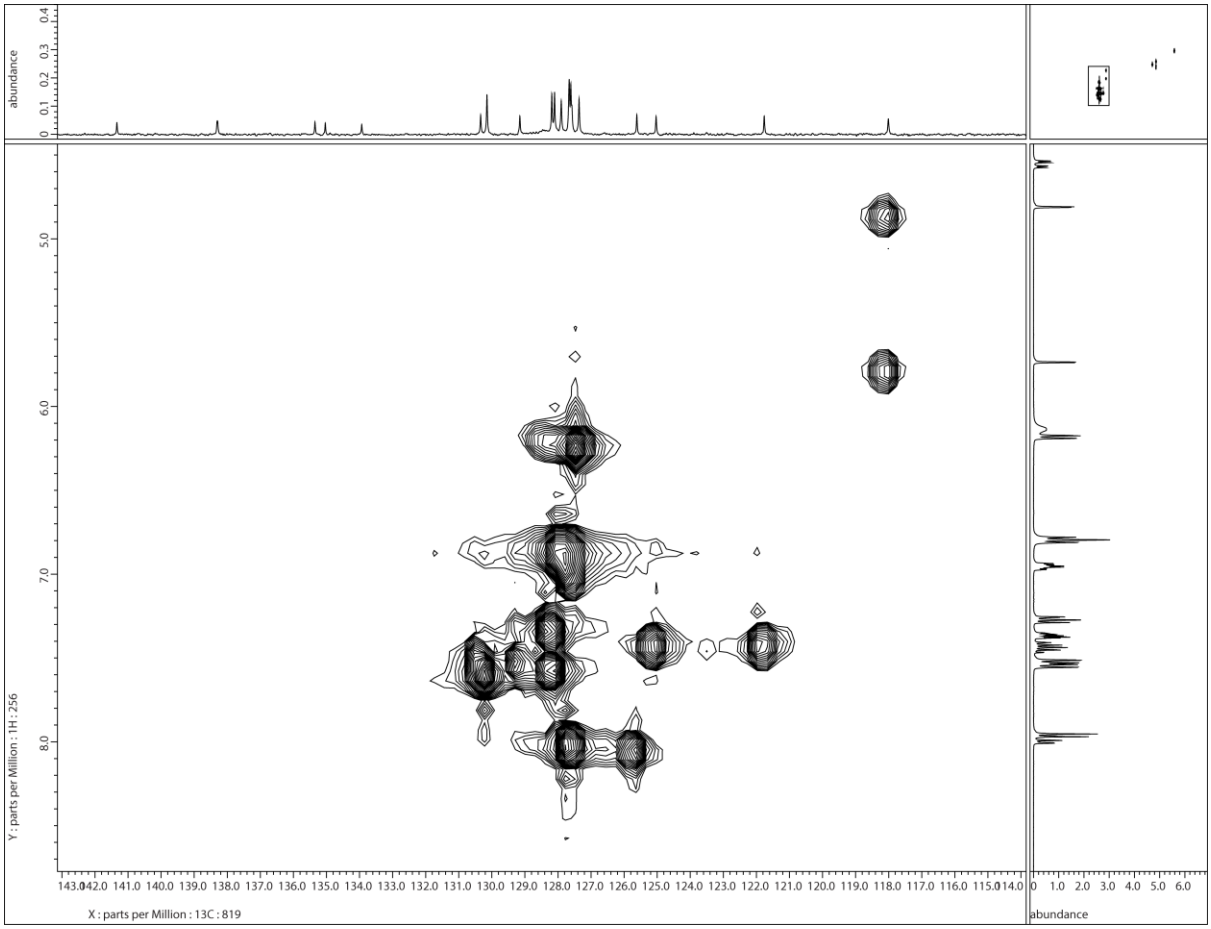


Figure S53. HETCOR spectrum of **5q** ($CDCl_3$, 125 MHz)

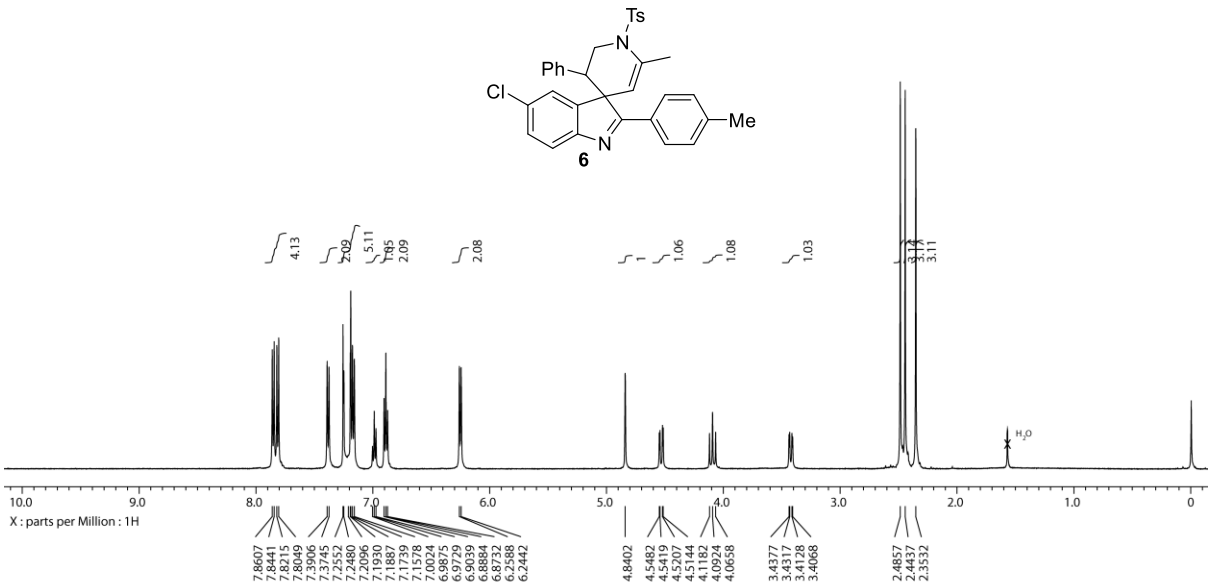


Figure S54. ^{1}H NMR of **6** (500 MHz, $CDCl_3$)

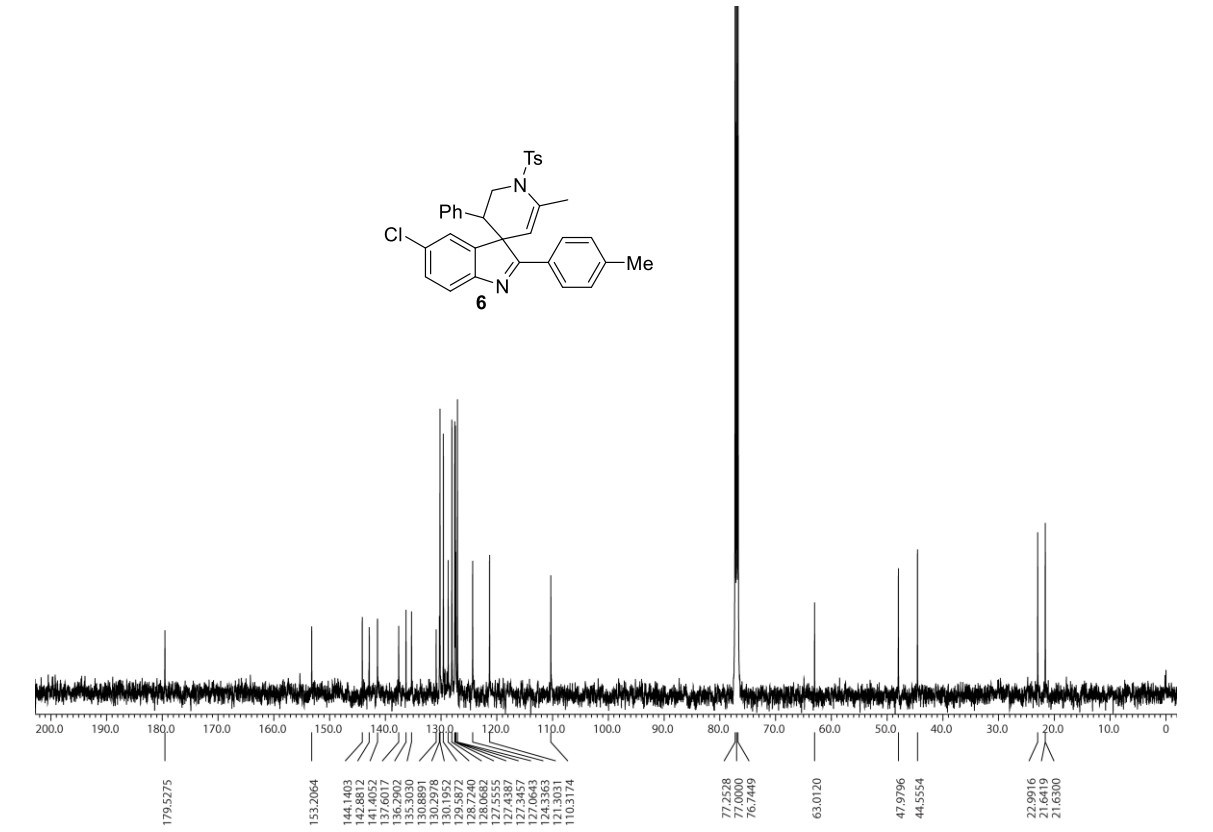


Figure S55. $^{13}C\{^{1}H\}$ NMR of **6** (125 MHz, $CDCl_3$)

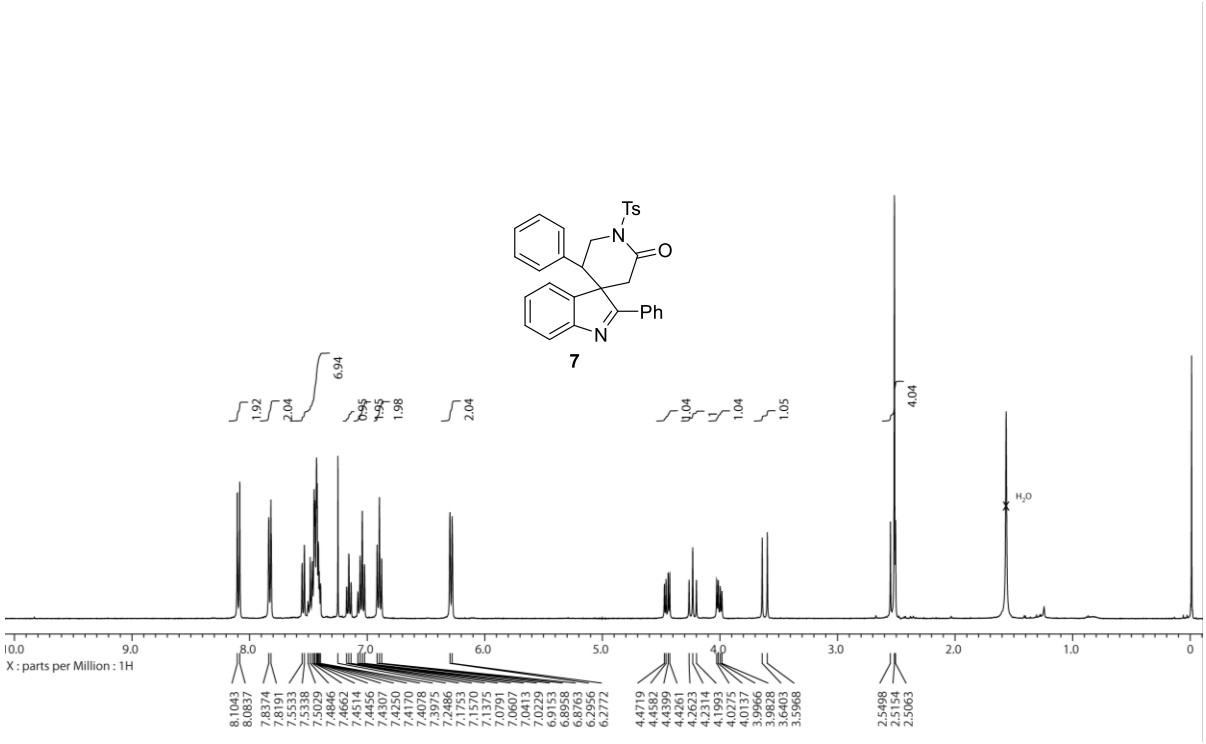


Figure S56. ^{1}H NMR of **7** (400 MHz, $CDCl_3$)

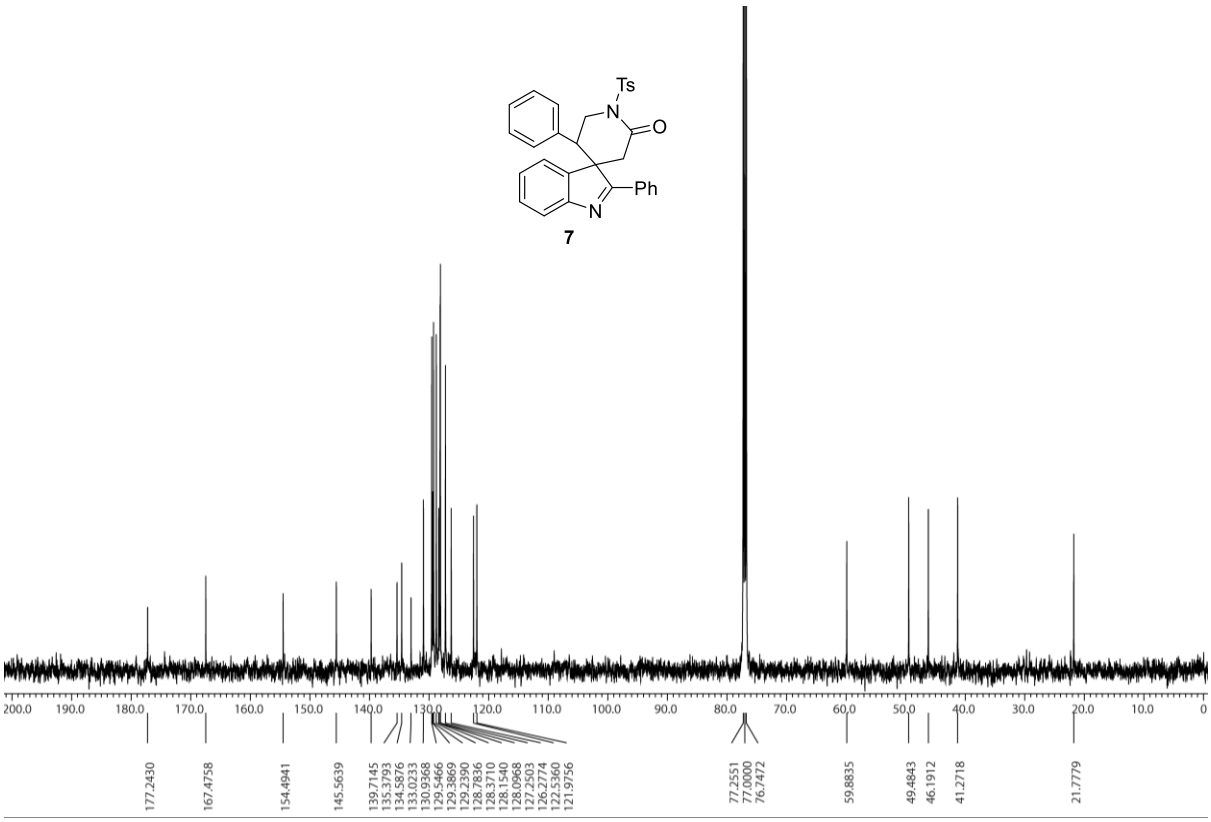


Figure S57. $^{13}C\{^{1}H\}$ NMR of **7** (125 MHz, $CDCl_3$)

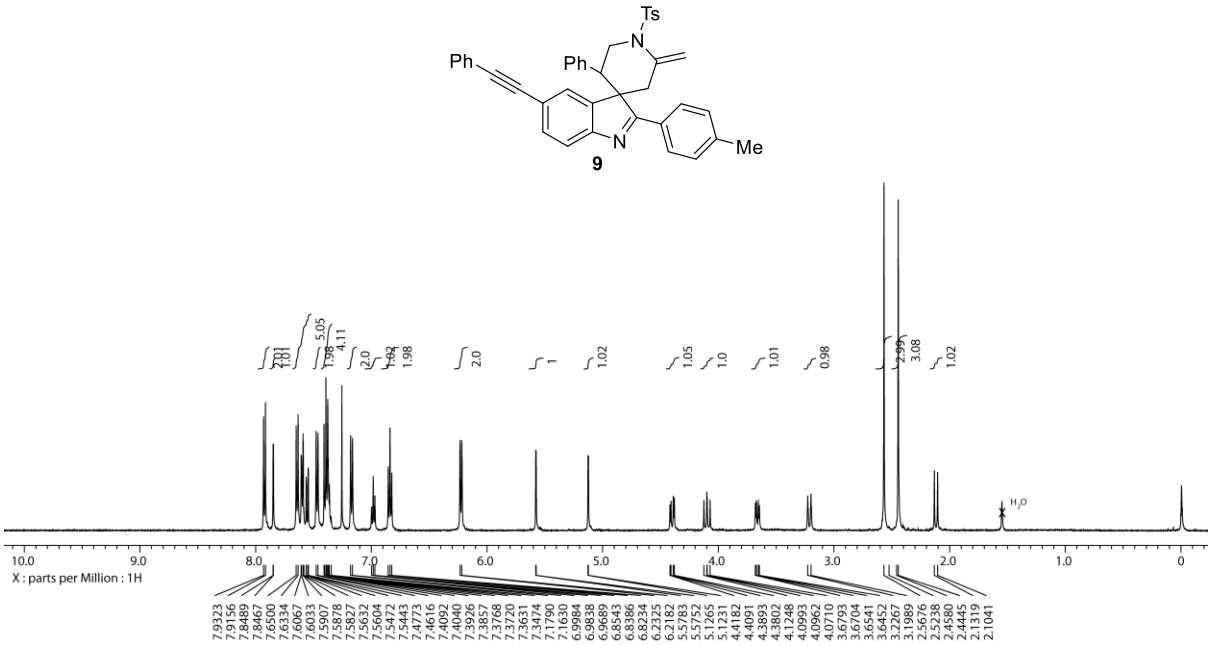


Figure S58. ^{1}H NMR of **9** (500 MHz, $CDCl_3$)

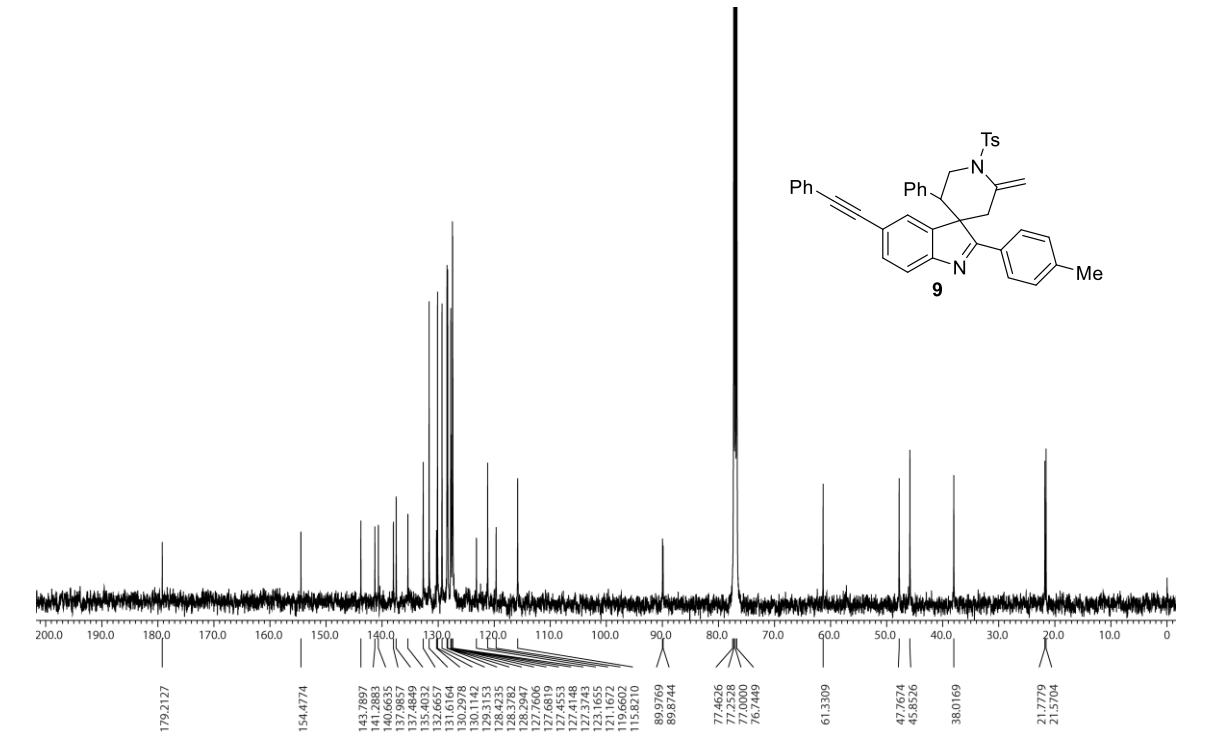
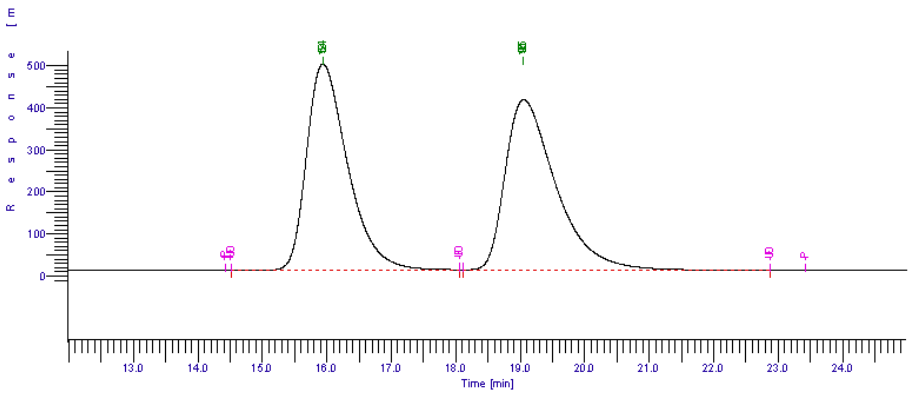


Figure S59. $^{13}C\{^{1}H\}$ NMR of **9** (125 MHz, $CDCl_3$)

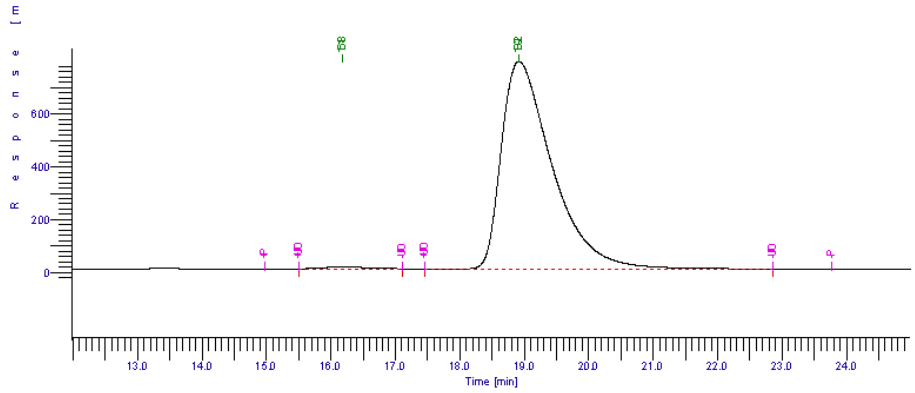
10. Selected HPLC Chromatograms



SP-8-46 rac OD-H 95-5 1 mL/min 510 psi

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	Cal. Range	Volt Range	BL	Raw Amount
1		15.937	21712071.50	492213.66	49.53	49.53			MM	21.7121
2		19.052	22119740.47	406128.07	50.47	50.47			MM	22.1197
			43831811.97	898341.73	100.00	100.00				43.8318

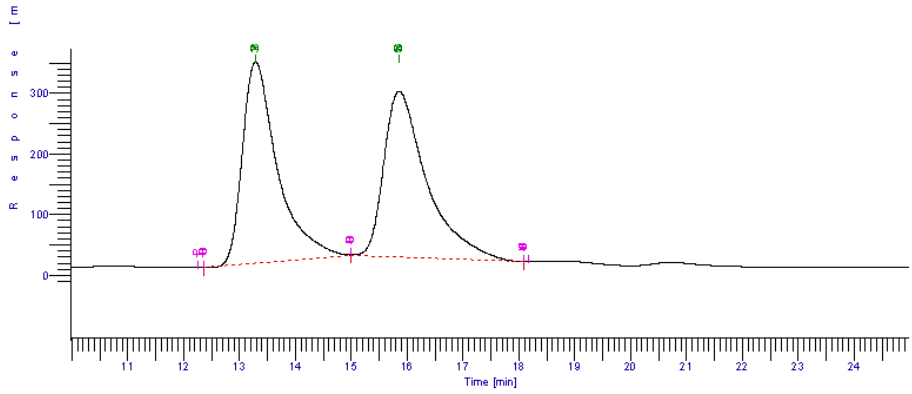
Figure S60. HPLC chromatogram of racemic **5a** (Chiralcel OD-H, hexane:isopropyl 95:5, 0% ee)



SP-8-46 chi OD-H 95-5 1 mL/min 510 psi

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	Cal. Range	Volt Range	BL	Raw Amount
1		16.175	321936.78	7293.06	0.74	0.74			MM	0.3219
2		18.915	43005795.96	788357.81	99.26	99.26			MM	43.0058
3		56.146	58.76	23.38	0.00	0.00			BB	0.0001
			43327791.50	795674.25	100.00	100.00				43.3278

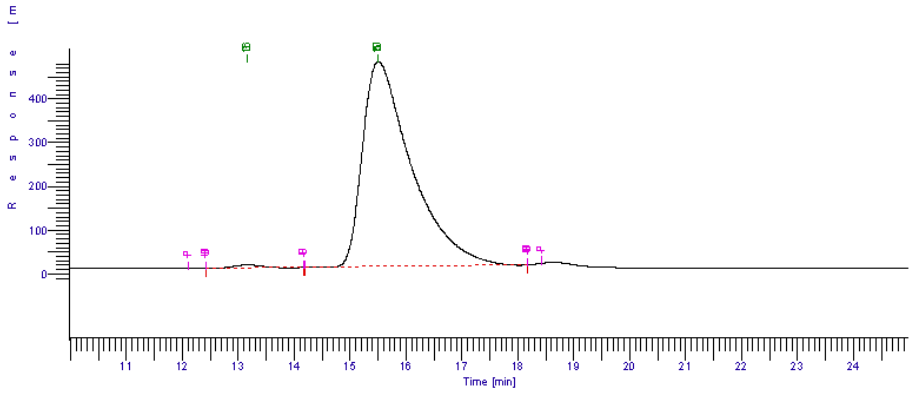
Figure S61. HPLC chromatogram of nonracemic (*S*)-**5a** (Chiralcel OD-H, hexane:isopropyl 95:5, 99% ee)



SP-8-60 racemic

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	Cal. Range	Volt Range	BL	Raw Amount
1		13.282	14443136.65	332935.64	49.78	49.78			MM	14.4431
2		15.855	14570273.66	273309.00	50.22	50.22			MM	14.5703
			29013410.31	606244.64	100.00	100.00				29.0134

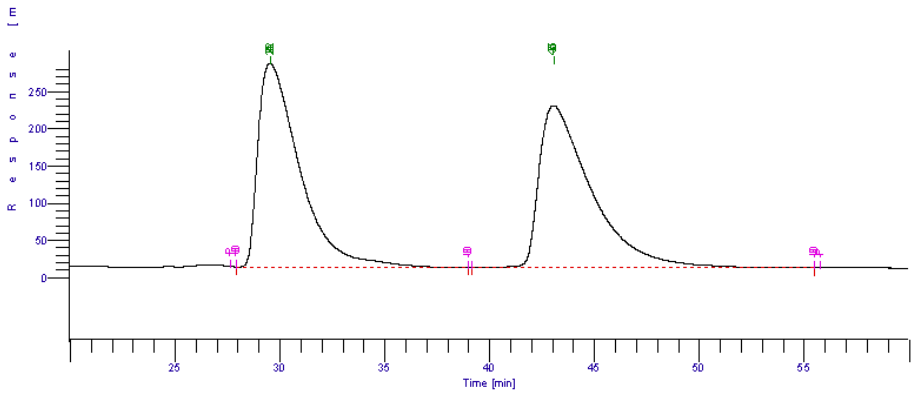
Figure S62. HPLC chromatogram of racemic **5f** (Chiralcel OD-H, hexane:isopropyl 95:5, 0% ee)



SP-8-60 chiral

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	Cal. Range	Volt Range	BL	Raw Amount
1		13.158	257253.74	7353.83	0.89	0.89			MM	0.2573
2		15.503	28555088.92	469969.15	99.11	99.11			MM	28.5551
			28812342.66	477322.97	100.00	100.00				28.8123

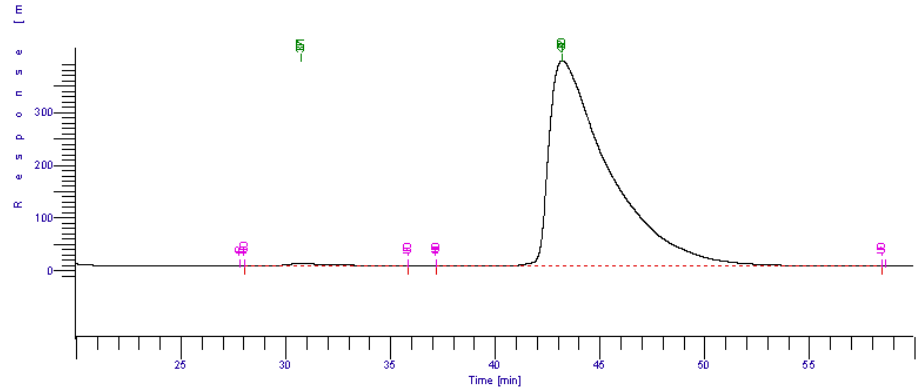
Figure S63. HPLC chromatogram of nonracemic (*S*)-**5f** (Chiralcel OD-H, hexane:isopropyl 95:5, 98% ee)



SP-8-59 rac

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	Cal. Range	Volt Range	BL	Raw Amount
1		29.522	37847598.05	274756.52	50.13	50.13			MM	37.8476
2		43.047	37650190.03	218187.22	49.87	49.87			MM	37.6502
			75497788.08	492943.74	100.00	100.00				75.4978

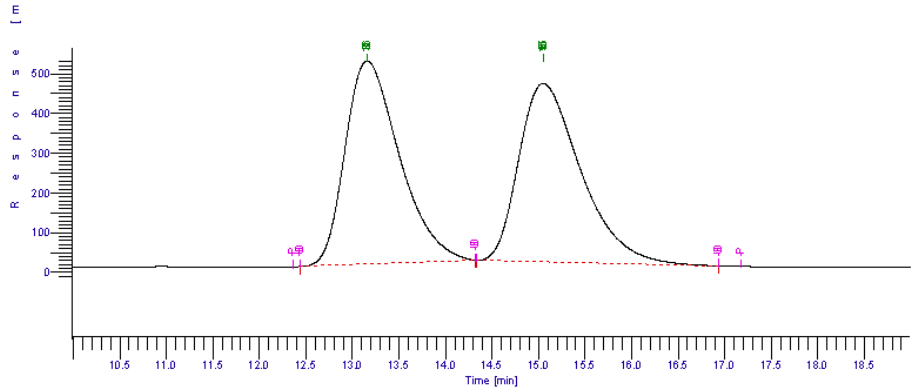
Figure S64. HPLC chromatogram of racemic **5h** (Chiralcel OD-H, hexane:isopropyl 98:2, 0% ee)



SP-8-59 chiral

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	Cal. Range	Volt Range	BL	Raw Amount
1		30.707	813618.23	4954.84	1.03	1.03			MM	0.8136
2		43.202	77816039.49	390167.45	98.97	98.97			MM	77.8160
			78629657.71	395122.29	100.00	100.00				78.6297

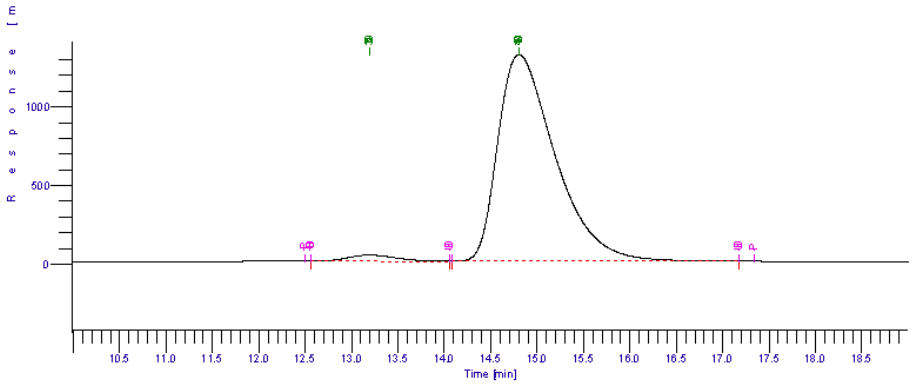
Figure S65. HPLC chromatogram of nonracemic (*S*)-**5h** (Chiralcel OD-H, hexane:isopropyl 98:2, 98% ee)



SP-8-74 racemic

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	Cal. Range	Volt Range	BL	Raw Amount
1		13.155	20779333.40	513268.79	49.95	49.95			MM	20.7793
2		15.050	20820009.21	450050.27	50.05	50.05			MM	20.8200
			41599342.60	963319.06	100.00	100.00				41.5993

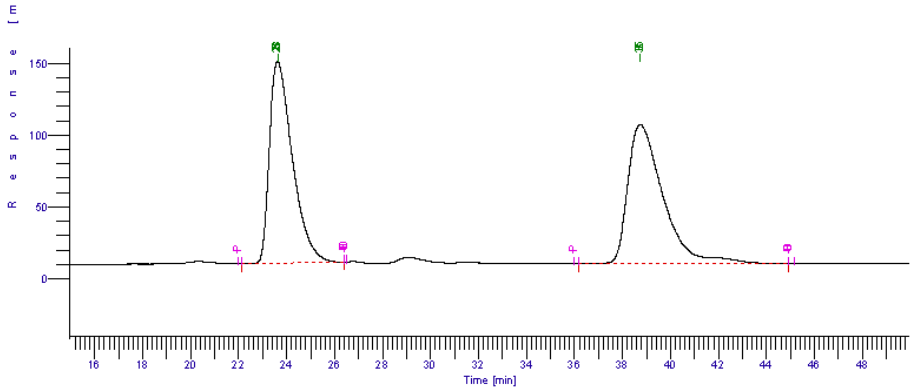
Figure S66. HPLC chromatogram of racemic **5j** (Chiralcel OD-H, hexane:isopropyl 95:5, 0% ee)



SP-8-74 chiral

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	Cal. Range	Volt Range	BL	Raw Amount
1		13.192	1391670.67	39020.23	2.40	2.40			MM	1.3917
2		14.802	56499691.55	1.32e+06	97.60	97.60			MM	56.4997
			57891362.22	1.36e+06	100.00	100.00				57.8914

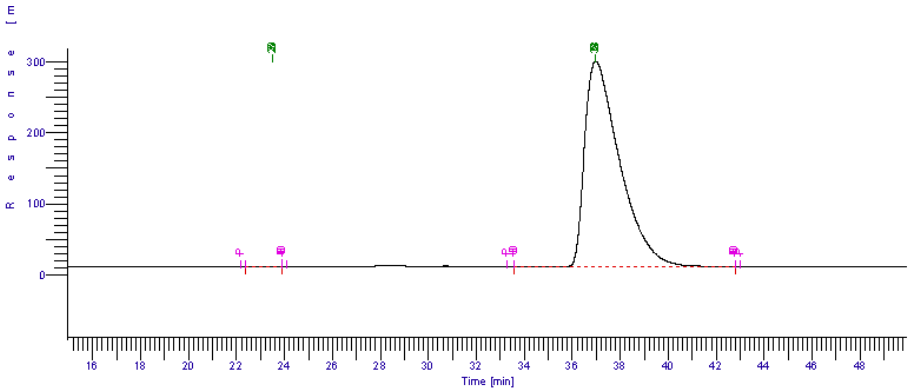
Figure S67. HPLC chromatogram of nonracemic (*S*)-**5j** (Chiralcel OD-H, hexane:isopropyl 95:5, 95% ee)



SP-8-68 racemic

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	Cal. Range	Volt Range	BL	Raw Amount
1		23.625	9409280.11	141478.34	48.64	48.64			MM	9.4093
2		38.748	9936747.21	97458.43	51.36	51.36			MM	9.9367
			19346027.31	238936.77	100.00	100.00				19.3460

Figure S68. HPLC chromatogram of racemic **5l** (Chiralcel OD-H, hexane:isopropyl 95:5, 0% ee)



SP-8-68 chiral

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	Cal. Range	Volt Range	BL	Raw Amount
1		23.498	12326.41	327.35	0.04	0.04			MM	0.0123
2		36.975	29479138.60	290534.36	99.96	99.96			MM	29.4791
3		78.521	12.99	21.36	4e-05	0.00			BB	0.0000
			29491478.00	290883.07	100.00	100.00				29.4915

Figure S69. HPLC chromatogram of nonracemic (*S*)-**5l** (Chiralcel OD-H, hexane:isopropyl 95:5, 99% ee)