Supporting information for:

Rapid synthesis of azepinoindole derivatives from tryptamine sulfonamides and bromoallyl sulfones via an acid-mediated cyclization and rearrangement

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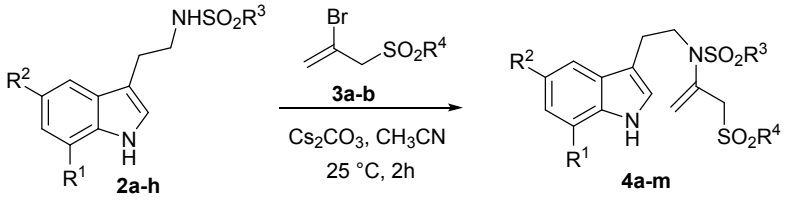
1. General Information

All ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded in $CDCl_3$ solvent at ambient temperature, chemical shift δ are given in ppm on a scale downfield from TMS, and the coupling constant *J* are in Hz. The signal patterns are indicated as follows: s, singlet; d, doublet; t, triplet; dd, doublet of doublet; m, multiplet. FTIR spectra were recorded as neat. Melting points were recorded on an electrothermal apparatus and are uncorrected. All the reagents and solvents were used without further purification unless specified otherwise. Technical grade ethyl acetate and petroleum ether used for column chromatography were distilled prior to use. Column chromatography was carried out using silica gel (60-120 mesh and 100- 200 mesh) packed in glass columns. All reactions were performed in oven-dried glassware with magnetic stirring. TLC analysis was performed on commercially prepared 60 F_{254} silica gel plates. Visualization of spots on TLC plate was accomplished with UV light (254 nm) and staining by $KMnO_4$. High-resolution mass spectra were recorded with q-TOF electrospray mass spectrometer. All purchased chemicals were used as received.

Bromoallyl sulfones **3a-b** were prepared from 2,3-dibromopropene and sodium arylsulfinates as reported earlier.[1]N-sulfonyl tryptamine derivatives **2** were prepared via the sulfonylation of corresponding amines with methanesulfonyl chloride, phenylsulfonyl chloride or p-toluenesulfonyl chloride as previously described.[2]

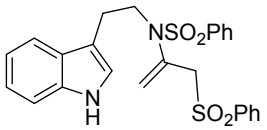
2. General procedure for the preparation of N-sulfonyl enamines 4



Cesium carbonate (815 mg, 2.50 mmol) was added to a solution of the N-arylsulfonamide **2** (1.00 mmol) and the bromoallyl sulfone **3a-b** (1.25 mmol) in acetonitrile (8 mL) at ambient temperature and stirred for 2 hours. The solvent was removed on a rotavapor, deionized water (20 mL) was added and the aqueous solution was extracted with ethyl acetate (3X 15 mL). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate and concentrated on a rotavapor. The residue on column chromatography on silica gel using petroleum ether-ethyl acetate as eluent afforded analytically pure samples of the products **4a-m**.

3. Spectroscopic data for N-sulfonyl enamines 4a-m

N-[2-(1H-indol-3-yl)ethyl]-N-[3-(phenylsulfonyl)prop-1-en-2-yl]benzenesulfonamide, **4a**



Off-white solid, 389 mg, 81%

Melting point: 120-122 ˚C.

R_f = 0.4 (40% ethyl acetate in hexanes)

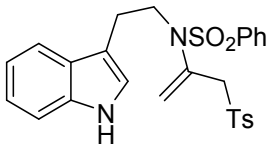
IR (KBr) ν_{max}: 3408, 2934, 1631, 1450, 1343, 1158, 963, 688, 597 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (brs, 1H), 7.94-7.92 (m, 2H), 7.70-7.68 (m, 2H), 7.67-7.64 (m, 1H), 7.58-7.55 (m, 4H), 7.47- 7.44 (m, 2H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.21-7.18 (m, 1H), 7.14-7.11 (m, 1H), 7.02 (d, *J* = 2.1 Hz, 1H), 5.63 (s, 1H), 4.93 (s, 1H), 4.22 (s, 2H), 3.58-3.55 (m, 2H), 3.07- 3.03 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 139.2, 136.5, 136.1, 135.6, 133.9, 133.0, 129.3, 128.82, 128.2, 127.9, 127.2, 122.2, 122.1, 120.4, 119.5, 118.7, 112.3, 111.2, 62.6, 51.6, 24.4.

HRMS: calcd for $C_{25}H_{25}O_4N_2S_2$ $[M+H^+]$ 481.1256; found 481.1249.

N-[2-(1H-indol-3-yl)ethyl]-N-(3-tosylprop-1-en-2-yl)benzenesulfonamide, **4b**



Light yellow solid, 390 mg 79%

Melting point: 94-96 ˚C.

R_f = 0.4 (40% ethyl acetate in hexanes).

IR (KBr) ν_{max}: 3404, 2927, 1595, 1451, 1343, 1157, 1015, 751, 520 cm^{-1}.

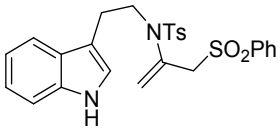
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.80 (d, *J* = 8.1 Hz, 2H), 7.70 (s, 1H), 7.57-7.55 (m, 2H), 7.47-7.43 (m, 2H), 7.36-7.33(m, 2H), 7.21-7.18 (m, 1H), 7.14-7.11 (m, 1H), 7.03 (s, 1H), 5.62 (d, *J* = 45.7 Hz, 1H), 4.92 (s, 1H), 4.19 (s, 2H), 3.57-3.54 (m, 2H), 3.05-3.02 (m, 2H), 2.41 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 145.0, 136.5, 136.2, 136.1, 135.7, 133.0, 129.9, 128.78, 128.2, 127.8, 127.2, 122.2, 122.0, 120.5, 119.4, 118.6, 112.2, 111.2, 62.6, 51.5, 24.4, 21.6.

^{13}CNMR (125 MHz, $CDCl_3$) δ 144.9, 136.5, 136.2, 136.1, 135.6, 133.0, 129.8, 128.7, 128.2, 127.8, 127.2, 122.1, 121.9, 120.4, 119.3, 118.5, 112.1, 111.1, 62.6, 51.4, 24.4, 21.5.

HRMS: calcd for $C_{26}H_{27}O_4N_2S_2$ [M+H$^+$] 495.1412; found 495.1407.

N-[2-(1H-indol-3-yl)ethyl]-4-methyl-N-[3-(phenylsulfonyl)prop-1-en-2-yl]benzenesulfonamide, **4c**



Pale yellow solid, 385 mg, 78 %

Melting point: 105-107 ˚C.

R_f = 0.4 (40% ethyl acetate in hexane)

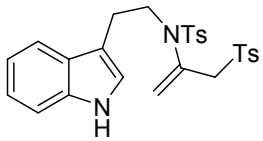
IR (KBr) ν_{max}: 3404, 2923, 1595, 1451, 1343, 1123, 1015, 744, 536 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.94-7.92 (m, 2H), 7.66-7.63 (m, 1H), 7.58-7.55 (m, 5H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.23 (d, *J* = 8.1 Hz, 2H), 7.21-7.18 (m, 1H), 7.14-7.10 (m, 1H), 7.02 (d, *J* = 2.1 Hz, 1H), 5.62 (s, 1H), 4.93 (d, *J* = 1.3 Hz, 1H), 4.23 (s, 2H), 3.54-3.51 (m, 2H), 3.05-3.01 (m, 2H), 2.39 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0, 139.2, 136.1, 135.7, 133.9, 133.4, 129.4, 129.3, 128.2, 127.9, 127.2, 122.2, 122.0, 120.1, 119.4, 118.6, 112.3, 111.2, 62.6, 51.4, 24.3, 21.5.

HRMS: calcd for $C_{26}H_{26}O_4N_2S_2$ Na [M+Na$^+$] 517.1232; found 517.1220.

N-[2-(1H-indol-3-yl)ethyl]-4-methyl-N-(3-tosylprop-1-en-2-yl)benzenesulfonamide, **4d**



Pale yellow solid, 401 mg, 79%

Melting point: 100-102 ˚C.

R_f = 0.4 (40% ethyl acetate in hexanes)

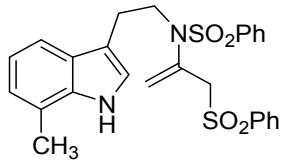
IR (KBr) ν_{max}: 3351, 2925, 1595, 1454, 1310, 1083, 916, 696, 551 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.80 (d, *J* = 8.3 Hz, 2H), 7.58-7.54 (m, 3H), 7.37-7.33 (m, 3H), 7.24-7.12 (m, 5H), 7.02 (d, *J* = 2.2 Hz, 1H), 5.62 (s, 1H), 5.30 (s, 1H), 4.93 (d, *J* = 1.1 Hz, 1H), 4.20 (s, 2H), 3.55-3.50 (m, 2H), 3.24-2.99 (m, 2H), 2.41 (s, 3H), 2.39 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.9, 143.6, 139.3, 137.3, 136.2, 135.1, 130.0, 129.8, 129.7, 127.6, 127.0, 125.7, 122.7, 119.7, 118.3, 111.6, 109.0, 64.5, 60.1, 43.6, 26.1, 21.7.

HRMS: calcd for $C_{27}H_{29}O_4N_2S_2$ [M+H$^+$] 509.1569; found 509.1596.

N-[2-(7-methyl-1H-indol-3-yl)ethyl]-N-[3-(phenylsulfonyl)prop-1-en-2-yl]benzenesulfonamide, **4e**



White solid, 375 mg, 76%

Melting point: 128-130 ˚C

R_f = 0.4 (40% ethyl acetate in hexanes)

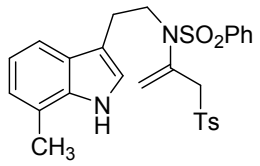
IR (KBr) ν_{max}: 3360, 2857, 1968, 1623, 1309, 1164, 958, 691cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89-7.87 (m, 3H), 7.68-7.64 (m, 3H), 7.58-7.51 (m, 3H), 7.46-7.42 (m, 2H), 7.19 (d, *J* = 6.9 Hz, 1H), 7.02-6.98 (m, 2H), 6.89 (s, 1H), 6.46 (s, 1H), 6.08 (s, 1H), 4.03 (s, 2H), 3.37-3.33 (m, 2H), 2.77-2.73 (m, 2H), 2.46 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 146.3, 139.0, 138.5, 135.7, 133.9, 132.8, 129.4, 129.2, 129.2, 128.2, 127.0, 126.1, 122.7, 121.7, 120.4, 119.8, 116.2, 112.3, 49.8, 46.8, 24.6, 16.5.

HRMS: calcd for $C_{26}H_{27}O_4N_2S_2$ [M+H$^+$] 495.1412; found 495.1411.

N-[2-(7-methyl-1H-indol-3-yl)ethyl]-N-(3-tosylprop-1-en-2-yl)benzenesulfonamide, **4f**



White solid, 402 mg, 79%

Melting point: 125-127 ˚C

R_f = 0.4 (40% ethyl acetate in hexanes)

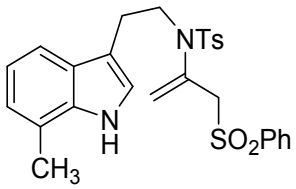
IR (KBr) ν_{max} 3384, 2916, 1631, 1336, 1235, 1158, 1085, 963, 559 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.81 (d, *J* = 8.3 Hz, 2H), 7.70-7.67 (m, 2H), 7.57-7.54 (m, 1H), 7.46-7.39 (M, 3H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.07-6.99 (m, 3H), 5.62 (s, 1H), 4.92 (d, *J* = 1.2 Hz, 1H), 4.20 (s, 2H), 3.56-3.52 (m, 2H), 3.04-3.00 (m, 2H), 2.48 (s, 3H), 2.41 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.0, 136.5, 136.3, 135.7, 133.0, 130.1, 129.9, 128.8, 128.3, 127.9, 127.0, 126.8, 122.6, 121.9, 120.4, 119.7, 116.4, 112.8, 62.7, 51.5, 24.5, 21.6, 16.6.

HRMS: calcd for $C_{27}H_{29}O_4N_2S_2$ [M+H$^+$] 509.1569; found 509.1568.

4-Methyl-N-[2-(7-methyl-1H-indol-3-yl)ethyl]-N-[3-(phenylsulfonyl)prop-1-en-2-yl]benzenesulfonamide, **4g**



White solid, 406 mg, 80%

Melting point: 183-185 ˚C

R_f = 0.4 (40% ethyl acetate in hexanes)

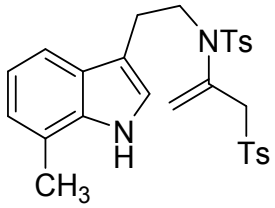
IR (KBr) ν_{max}: 3455, 2920, 1492, 1338, 1131, 1084, 964,821,786, 752, 690, 556 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89-7.87 (m, 3H), 7.68-7.64 (m, 1H), 7.58-7.52 (m, 4H), 7.23-7.18 (m, 3H), 7.03-6.99 (m, 2H), 6.91 (d, *J* = 1.9 Hz, 1H), 6.46 (s, 1H), 6.10 (s, 1H), 4.01 (s, 2H), 3.34-3.30 (m, 2H), 2.77-2.73 (m, 2H), 2.47 (s, 3H), 2.40 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 146.4, 143.7, 138.5, 135.9, 135.7, 133.9, 129.8, 129.4, 128.2, 127.1, 126.5, 126.1, 122.7, 121.7, 120.4, 119.7, 116.2, 112.4, 49.8, 46.8, 24.6, 21.5, 16.5.

HRMS: calcd for $C_{27}H_{29}O_4N_2S_2$ [M+H$^+$] 509.1569; found 509.1565

4-Methyl-N-[2-(7-methyl-1H-indol-3-yl)ethyl]-N-(3-tosylprop-1-en-2-yl)benzenesulfonamide, **4h**



White solid, 392 mg, 75%

Melting point: 167-169 ˚C

R_f = 0.4 (40% ethyl acetate in hexanes).

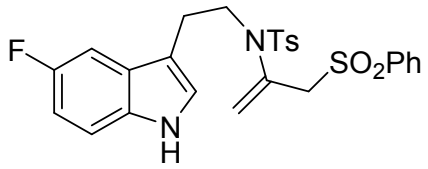
IR (KBr) ν_{max}: 3353, 2934, 1595, 1492, 1337, 1160, 959, 651, 590 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.75 (d, *J* = 8.3 Hz, 2H), 7.55 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.23 (d, *J* = 8.1 Hz, 2H), 7.19 – 7.17 (m, 1H), 7.02 – 6.99 (m, 2H), 6.91 (d, *J* = 2.2 Hz, 1H), 6.43 (s, 1H), 6.07 (s, 1H), 4.02 (s, 2H), 3.33-3.30 (m, 2H), 2.75-2.72 (m, 2H), 2.47 (s, 3H), 2.42 (s, 3H), 2.40 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 146.5, 145.0 , 143.7, 135.9, 135.7, 135.4, 130.0, 129.8, 128.2, 127.0, 126.4, 125.6, 122.6, 121.7, 120.4, 119.6, 116.1, 112.2, 49.7, 46.7, 24.5, 21.6, 21.4, 16.5.

HRMS: calcd for $C_{28}H_{30}O_4N_2S_2Na$ [M+Na^+] 545.1545; found 545.1538.

N-[2-(5-fluoro-1H-indol-3-yl)ethyl]-4-methyl-N-[3-(phenylsulfonyl)prop-1-en-2-yl]benzenesulfonamide, **4i**



White solid, 369 mg 72%

Melting point: 100-102 ˚C

R_f = 0.4 (40% ethyl acetate in hexanes)

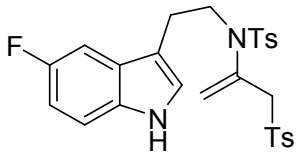
IR (KBr) ν_{max}: 3401, 2926, 1715, 1584, 754, 649, 526 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.94 (d, *J* = 7.5 Hz, 2H),7.67-7.64 (m, 1H), 7.59-7.56 (m, 4H), 7.26-7.24 (m, 3H), 7.15 (dd, *J* = 9.5, 2.1 Hz, 1H), 7.08 (s, 1H), 6.97-6.90 (m, 1H), 5.60 (s, 1H), 4.94 (s, 1H), 4.22 (s, 2H), 3.52-3.49 (m, 2H), 3.01-2.98 (m, 2H), 2.40 (s, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.7 (d, *J* = 234.8 Hz), 144.1, 139.3, 135.7, 133.9, 133.5, 132.6, 129.9, 129.5, 129.3, 128.2, 127.9, 127.65 (d, *J* = 9.5 Hz), 124.1, 120.4, 112.6 (d, *J* = 3.8 Hz), 111.8 (d, *J* = 9.6 Hz), 110.4 (d, *J* = 26.4 Hz), 103.5 (d, *J* = 23.4 Hz), 62.7, 51.3, 24.3, 21.5.

HRMS: calcd for $C_{26}H_{26}FO_4N_2S_2$ [M+H^+] 513.1318; found 513.1308.

N-[2-(5-fluoro-1H-indol-3-yl)ethyl]-4-methyl-N-(3-tosylprop-1-en-2-yl)benzenesulfonamide, **4j**



White solid, 426 mg 81%

Melting point: 147-149 ˚C

R_f = 0.4 (40% ethyl acetate in hexanes).

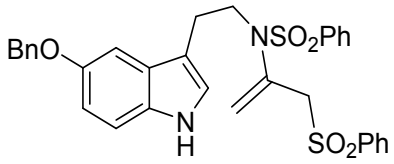
IR (KBr) ν_{max}: 3383, 2973, 1930, 1487, 1240, 1087, 797,642, 560,429 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.80 (d, *J* = 8.2 Hz, 2H), 7.59 (d, *J* = 8.2 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.27-7.24 (m, 3H), 7.14 (dd, *J* = 9.5, 2.4 Hz, 1H), 7.08 (d, *J* = 1.3 Hz, 1H), 6.93 (td, *J* = 9.0, 2.4 Hz, 1H), 5.59 (s, 1H), 4.94 (s, 1H), 4.19 (s, 2H), 3.52-3.49 (m, 2H), 2.99-2.96 (m, 2H), 2.42 (s, 3H), 2.40 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.7 (d, *J* = 234.7 Hz), 136.3, 135.8, 133.6, 132.6, 129.9, 129.5, 128.3, 127.9, 127.7 (d, *J* = 9.5 Hz), 124.0, 120.4, 112.6 (d, *J* = 4.1 Hz), 111.8 (d, *J* = 9.6 Hz), 110.4 (d, *J* = 26.4 Hz), 103.6 (d, *J* = 23.4 Hz), 62.7, 51.2, 24.3, 21.6, 21.5.

HRMS: calcd for $C_{27}H_{28}O_4FN_2S_2$ [M+H$^+$] 527.1475; found 527.1469.

N-{2-[5-(benzyloxy)-1H-indol-3-yl]ethyl}-N-[3-(phenylsulfonyl)prop-1-en-2-yl]benzenesulfonamide, **4k**



White solid, 399 mg, 68%

Melting point: 73-75 ˚C

R_f = 0.4 (40% ethyl acetate in hexanes).

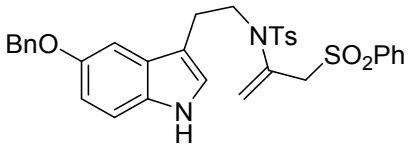
IR (KBr) ν_{max}: 3449, 2912, 1931, 1449, 1310, 1254, 1141, 1082, 672, 576 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93-7.91 (m, 2H), 7.88 (s, 1H), 7.70-7.62 (m, 4H), 7.57-7.53 (m, 4H), 7.49-7.43 (m, 5H), 7.38-7.35 (m, 2H), 7.16 (d, *J* = 2.2 Hz, 1H), 7.01 (d, *J* = 2.2 Hz, 1H), 6.94 (dd, *J* = 8.8, 2.2 Hz, 1H), 5.60 (s, 1H), 5.13 (s, 2H), 4.89 (d, *J* = 1.2 Hz, 1H), 4.20 (s, 2H), 3.57-3.53 (m, 2H), 3.05-3.01 (m, 2H),

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.2, 139.2, 137.7, 136.5, 135.7, 133.9, 133.0, 131.4, 129.3, 128.8, 128.4, 128.2, 127.8, 127.7, 127.6, 123.0, 120.6, 113.1, 112.1, 111.9, 102.0, 70.8, 62.6, 51.6, 24.6.

HRMS: calcd for $C_{32}H_{31}O_5N_2S_2$ [M+H$^+$] 587.1674; found 587.1653.

N-{2-[5-(benzyloxy)-1H-indol-3-yl]ethyl}-4-methyl-N-[3-(phenylsulfonyl)prop-1-en-2-yl]benzenesulfonamide, **4l**



White solid, 402 mg 67%

Melting point: 158-160 ˚C

R_f = 0.4 (40% ethyl acetate in hexanes)

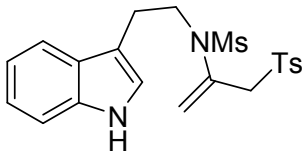
IR (KBr) ν_{max}: 3410, 2923, 1306, 1153, 1020, 807, 691 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.6 Hz, 2H), 7.87 (s, 1H), 7.66-7.62 (m, 1H), 7.57-7.53 (m, 4H), 7.48 (d, *J* = 7.5 Hz, 2H), 7.38-7.35 (m, 2H), 7.30 (d, *J* = 7.3 Hz, 1H), 7.26-7.22 (m, 3H), 7.15 (s, 1H), 7.01 (s, 1H), 6.94 (dd, *J* = 8.7, 2.0 Hz, 1H), 5.59 (s, 1H), 5.13 (s, 2H), 4.90 (s, 1H), 4.21 (s, 2H),3.54-3.50 (m, 2H), 3.03-3.00(m, 2H), 2.39 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.2, 143.9, 139.3, 137.7, 135.8, 133.9, 133.5, 131.4, 129.4, 129.3, 128.4, 128.2, 127.9, 127.7, 127.6, 123.0, 120.3, 113.1, 112.2, 111.9, 102.1, 70.8, 62.7, 51.5, 24.6, 21.5.

HRMS: calcd for $C_{33}H_{33}O_5N_2S_2$ [M+H$^+$] 601.1831; found 601.1818.

N-[2-(1H-indol-3-yl)ethyl]-N-(3-tosylprop-1-en-2-yl)methanesulfonamide, **4m**



White solid, 311 mg, 72%

Melting point: 172-175 ˚C

R_f = 0.4 (40% ethyl acetate in hexanes)

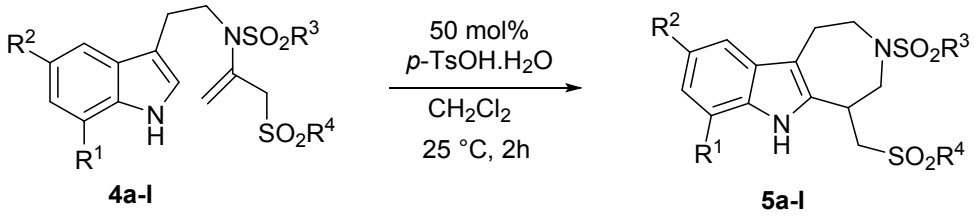
IR (KBr) ν_{max}: 3367, 2920, 1595, 1313, 1287, 1146, 1086, 742, 674, 543 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.79 (d, *J* = 8.2 Hz, 1H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.37-7.33 (m, 3H), 7.22-7.19 (m, 1H), 7.15-7.12 (m, 1H), 7.06 (d, *J* = 2.0 Hz, 1H), 5.50 (s, 1H), 5.47 (s, 1H), 4.08 (s, 2H), 3.77 – 3.74 (m, 2H), 3.11– 3.08 (m, 2H), 2.88 (s, 3H), 2.42 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 144.9, 137.1, 136.3, 129.7, 127.6, 125.7, 122.8, 119.9, 118.4, 111.5, 64.3, 59.9, 43.6, 26.4, 21.9.

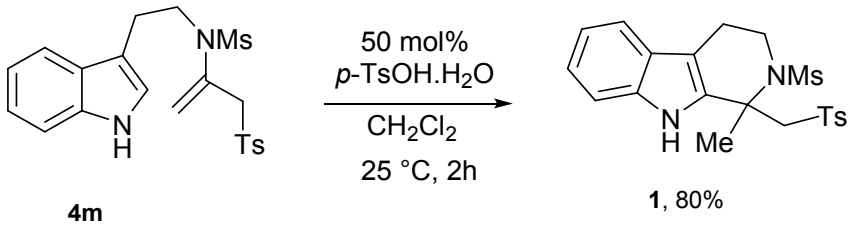
HRMS: calcd for $C_{21}H_{25}O_4N_2S_2$ [M+H$^+$] 433.1256; found 433.1252.

4. General procedure for the *p*-TsOH-mediated cyclisation of N-sulfonyl enamines 4a-m



4a-l **5a-l**

To a solution of the N-sulfonyl enamine **4a-l** (0.20 mmol) in dichloromethane (2 mL) maintained at ambient temperature *p*-TsOH.H_2O (19 mg, 0.10 mmol) was added and the reaction was stirred for 2 h at 25 °C. Silica gel was then added to the reaction mixture, the solvent was evaporated on a rotavapor and the residue was chromatographed on a silica column using petroleum ether-ethyl acetate as eluent to afford analytically pure samples of the products **5a**-**l**.

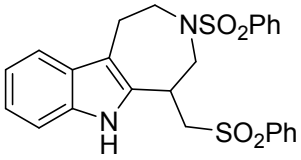


4m **1**, 80%

The N-mesyl derivative **4m** afforded the tetrahydro-β-carboline product **1** (80%) when treated under identical conditions.

5. Spectroscopic data for tetrahydroazepinoindoles 5a-l and the tetrahydro-β-carboline 1

3-(Phenylsulfonyl)-5-[(phenylsulfonyl)methyl]-1,2,3,4,5,6-hexahydroazepino[4,5-b]indole, **5a**



White solid, 84 mg, 87%

Melting point: 214-216 ˚C

R_f = 0.4 (30% ethyl acetate in hexanes).

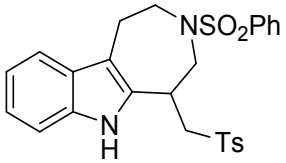
IR (KBr) ν_{max}: 34047, 2932, 1617, 1446, 1339, 1144, 992, 687, 574 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.87-7.85 (m, 2H), 7.82-7.80 (m, 2H), 7.62-7.53 (m, 4H), 7.47-7.43 (m, 2H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.32 (d, *J* = 8.1 Hz, 1H), 7.19-7.15 (m, 1H), 7.09-7.06 (m, 1H), 4.24 (dd, *J* = 13.8, 2.6 Hz, 1H), 4.18 (dt, *J* = 13.0, 3.3 Hz, 1H), 4.01 (dd, *J* = 14.4, 4.5 Hz, 1H), 3.89-3.86 (m, 1H), 3.47 (dd, *J* = 14.4, 6.8 Hz, 1H), 3.08 (dd, *J* = 13.8, 2.1 Hz, 1H), 3.03 (ddd, *J* = 15.9, 4.1, 2.1 Hz, 1H), 2.92-2.86 (m, 1H), 2.77-2.72 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 139.2, 138.6, 134.9, 134.5, 133.7, 132.9, 129.3, 129.2, 128.2, 127.6, 126.9, 122.3, 119.5, 117.9, 111.5, 110.9, 58.2, 53.2, 50.9, 34.4, 25.70.

HRMS: calcd for $C_{25}H_{25}O_4N_2S_2$ [M+H$^+$] 481.1256; found 481.1265.

3-(Phenylsulfonyl)-5-(tosylmethyl)-1,2,3,4,5,6-hexahydroazepino[4,5-b]indole, **5b**



White solid, 79 mg, 80%

Melting point: 223-225 ˚C

R_f = 0.4 (30% ethyl acetate in hexanes).

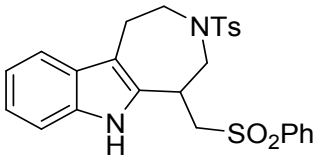
IR (KBr) ν_{max}: 3373, 2930, 1598, 1454, 1337, 1282, 1140, 744, 570 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (s, 1H), 7.81 (d, *J* = 8.6 Hz, 2H), 7.73 (d, *J* = 8.3 Hz, 2H), 7.562-7.52 (m, 3H), 7.36 (d, *J* = 7.9 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 1H), 7.23 (d, *J* = 8.1 Hz, 2H), 7.16 (t, *J* = 7.1 Hz, 1H), 7.07 (t, *J* = 7.2 Hz, 1H), 4.25 – 4.16 (m, 2H), 3.97 (dd, *J* = 14.4, 4.5 Hz, 1H), 3.86-3.85 (m, 1H), 3.45 (dd, *J* = 14.4, 6.7 Hz, 1H), 3.09 – 3.00 (m, 2H), 2.93 – 2.85 (m, 1H), 2.78-2.75 (m, 1H), 2.38 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.7, 138.6, 136.2, 134.8, 134.6, 132.8, 129.8, 129.3, 128.2, 127.6, 126.9, 122.2, 119.5, 117.8, 111.3, 110.9, 58.2, 53.2, 50.9, 34.4, 25.7, 21.5.

HRMS: calcd for $C_{26}H_{27}O_4N_2S_2$ [M+H$^+$] 495.1412; found 495.1406.

5-[(Phenylsulfonyl)methyl]-3-tosyl-1,2,3,4,5,6-hexahydroazepino[4,5-b]indole**, 5c**



White solid, 86 mg, 87%

Melting point: 221-223 ˚C

R_f = 0.4 (30% ethyl acetate in hexanes)

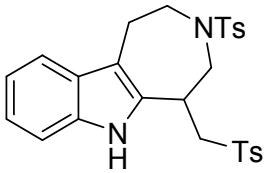
IR (KBr) ν_{max}: 3365, 2945, 1572, 1336, 1286, 1041, 901, 565 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.86 (d, *J* = 7.3 Hz, 2H), 7.68 (d, *J* = 8.3 Hz, 2H), 7.58-7.54 (m, 1H), 7.47-7.43 (m, 2H), 7.37 – 7.31 (m, 4H), 7.19-7.15 (m, 1H), 7.09-7.05 (m, 1H), 4.23 – 4.15 (m, 2H), 4.00 (dd, *J* = 14.4, 4.4 Hz, 1H), 3.88-3.85 (m, 1H), 3.47 (dd, *J* = 14.4, 6.8 Hz, 1H), 3.07-2.99 (m, 2H), 2.92 – 2.84 (m, 1H), 2.75-2.68 (m, 1H), 2.43 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.7, 139.2, 135.7, 134.9, 134.6, 133.7, 129.9, 129.2, 128.2, 127.6, 127.0, 122.3, 119.5, 117.9, 111.5, 110.9, 58.3, 53.3, 50.9, 34.4, 25.7, 21.5.

HRMS: calcd for $C_{26}H_{27}O_4N_2S_2$ $[M+H^+]$ 495.1412; found 495.1409.

3-Tosyl-5-(tosylmethyl)-1,2,3,4,5,6-hexahydroazepino[4,5-b]indole, **5d**



White solid, 91 mg, 90%

Melting point: 232-235 ˚C

R_f = 0.4 (30% ethyl acetate in hexanes).

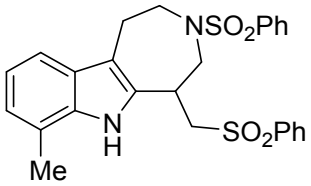
IR (KBr) ν_{max}: 34047, 2946, 1617, 1412, 1339, 1082, 992, 687, 574 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1H), 7.73 (d, *J* = 8.3 Hz, 2H), 7.68 (d, *J* = 8.3 Hz, 2H), 7.36 (d, *J* = 7.9 Hz, 1H), 7.33 – 7.29 (m, 3H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.18 – 7.14 (m, 1H), 7.09 – 7.05 (m, 1H), 4.22-4.14 (m, 2H), 3.97 (dd, *J* = 14.4, 4.4 Hz, 1H), 3.86-3.84 (m, 1H), 3.45 (dd, *J* = 14.4, 6.8 Hz, 1H), 3.06 – 2.99 (m, 2H), 2.92 – 2.84 (m, 1H), 2.75 – 2.68 (m, 1H), 2.43 (s, 3H), 2.37 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 144.7, 143.7, 136.3, 135.7, 134.8, 134.7, 129.9, 129.8, 128.2, 127.6, 127.0, 122.2, 119.5, 117.8, 111.4, 110.9, 58.3, 53.2, 50.9, 34.4, 25.7, 21.5, 21.5.

HRMS: calcd for $C_{27}H_{28}O_4N_2S_2$ Na[M+Na^+] 531.1388; found 531.1384.

7-Methyl-3-(phenylsulfonyl)-5-[(phenylsulfonyl)methyl]-1,2,3,4,5,6-hexahydroazepino[4,5-b]indole, **5e**



White solid, 80 mg, 81%

Melting point: 201-203 ˚C

R_f = 0.5 (30% ethyl acetate in hexanes).

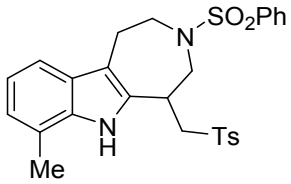
IR (KBr) ν_{max}: 3385, 2926, 1593, 1451, 1290, 1092, 724, 549 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1H), 7.87 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.82 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.61 – 7.52 (m, 4H), 7.47 – 7.43 (m, 2H), 7.21 (d, *J* = 6.8 Hz, 1H), 7.02 – 6.96 (m, 2H), 4.27 (ddd, *J* = 13.9, 3.6, 1.1 Hz, 1H), 4.19 (dt, *J* = 12.9, 3.4 Hz, 1H), 4.03 (dd, *J* = 14.3, 4.7 Hz, 1H), 3.93 – 3.89 (m, 1H), 3.46 (dd, *J* = 14.3, 6.5 Hz, 1H), 3.08 (dd, *J* = 13.9, 2.1 Hz, 1H), 3.02 (ddd, *J* = 15.9, 4.2, 2.3 Hz, 1H), 2.93 – 2.85 (m, 1H), 2.78 – 2.71 (m, 1H), 2.49 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 139.2, 138.7, 134.4, 134.3, 133.7, 132.9, 129.3, 129.1, 127.7, 127.5, 126.9, 122.8, 120.2, 119.8, 115.6, 112.0, 58.1, 53.2, 51.0, 34.4, 25.9, 16.6.

HRMS: calcd for $C_{26}H_{27}O_4N_2S_2$ [M+H^+] 495.1412; found 495.1410.

7-Methyl-3-(phenylsulfonyl)-5-(tosylmethyl)-1,2,3,4,5,6-hexahydroazepino[4,5-b]indole, **5f**



White solid, 82 mg, 81%

Melting point: 190-192 ˚C

R_f = 0.48 (30% ethyl acetate in hexanes).

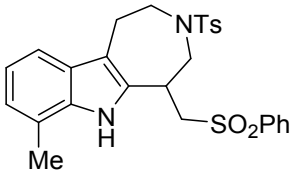
IR (KBr) ν_{max}: 3365, 2924, 1596, 1336, 1286, 1041, 901, 565 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (s, 1H), 7.81 (d, *J* = 8.7 Hz, 2H), 7.74 (d, *J* = 8.2 Hz, 2H), 7.62-7.59 (m, 1H), 7.55-7.52 (m, 2H), 7.24 – 7.20 (m, 3H), 7.00 – 6.96 (m, 2H), 4.25 (dd, *J* = 13.8, 3.0 Hz, 1H), 4.18 (dt, *J* = 13.0, 3.3 Hz, 1H), 3.99 (dd, *J* = 14.4, 4.6 Hz, 1H), 3.90 – 3.86 (m, 1H), 3.45 (dd, *J* = 14.4, 6.6 Hz, 1H), 3.08 (dd, *J* = 13.8, 1.9 Hz, 1H), 3.03 – 2.99 (m, 1H), 2.92 – 2.86 (m, 1H), 2.77 – 2.71 (m, 1H), 2.48 (s, 3H), 2.37 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 144.8, 138.7, 136.2, 134.4, 134.4, 132.8, 129.7, 129.3, 127.8, 127.5, 126.9, 122.7, 120.2, 119.8, 115.6, 111.9, 58.2, 53.2, 50.9, 34.5, 25.8, 21.5, 16.6.

HRMS: calcd for $C_{27}H_{28}O_4N_2S_2Na$ [M+Na^+] 531.1388; found 531.1385.

7-Methyl-5-[(phenylsulfonyl)methyl]-3-tosyl-1,2,3,4,5,6-hexahydroazepino[4,5-b]indole, **5g**



Melting point: 185-187 ˚C

White solid, 79 mg 78%

R_f = 0.46 (30% ethyl acetate in hexanes)

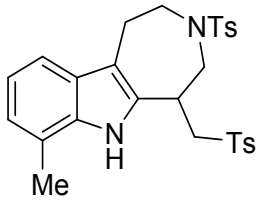
IR (KBr) ν_{max}: 3383, 2926, 1496, 1396, 1290, 1091, 814, 716, 674, 600, 546 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1H), 7.88 – 7.85 (m, 2H), 7.69 (d, *J* = 8.3 Hz, 2H), 7.57 – 7.53 (m, 1H), 7.47 – 7.43 (m, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.21 (d, *J* = 7.2 Hz, 1H), 7.02 – 6.96 (m, 2H), 4.25 (dd, *J* = 14.4, 3.1 Hz, 1H), 4.17 (dt, *J* = 6.9, 3.2 Hz, 1H), 4.03 (dd, *J* = 14.4, 4.7 Hz, 1H), 3.92 – 3.88 (m, 1H), 3.46 (dd, *J* = 14.3, 6.5 Hz, 1H), 3.07 – 2.98 (m, 2H), 2.92-2.84 (m, 1H), 2.76 – 2.67 (m, 1H), 2.48 (s, 3H), 2.43 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.7, 139.2, 135.7, 134.4, 134.3, 133.7, 129.9, 129.1, 127.8, 127.5, 127.0, 122.8, 120.2, 119.8, 115.6, 112.0, 58.2, 53.2, 50.9, 34.4, 25.9, 21.5, 16.6.

HRMS: calcd for $C_{27}H_{29}O_4N_2S_2$ [M+H^+] 509.1569; found 509.1561.

7-Methyl-3-tosyl-5-(tosylmethyl)-1,2,3,4,5,6-hexahydroazepino[4,5-b]indole, **5h**



White solid, 84 mg, 80%

Melting point: 220-222 ˚C

R_f = 0.52 (30% ethyl acetate in hexanes)

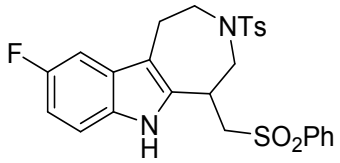
IR (KBr) ν_{max}: 3397, 2926, 1593, 1451, 1290, 1092, 724, 549.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.66 (d, *J* = 8.3 Hz, 2H), 7.62 (d, *J* = 8.3 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.17-7.13 (m, 3H), 6.94 – 6.88 (m, 2H), 4.16 (dd, *J* = 13.8, 2.7 Hz, 1H), 4.09 (dt, *J* = 13.5, 3.7 Hz, 1H), 3.91 (dd, *J* = 14.4, 4.5 Hz, 1H), 3.82 – 3.78 (m, 1H), 3.37 (dd, *J* = 14.3, 6.6 Hz, 1H), 3.00 – 2.90 (m, 2H), 2.85 – 2.77 (m, 1H), 2.68 – 2.61 (m, 1H), 2.41 (s, 4H), 2.36 (s, 4H), 2.30 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.8, 143.7, 136.3, 135.7, 134.4, 129.9, 129.7, 127.8, 127.5, 127.0, 122.7, 120.2, 119.8, 115.6, 111.9, 58.3, 53.2, 50.9, 34.5, 25.9, 21.6, 21.5, 16.6.

HRMS: calcd for $C_{28}H_{30}O_4N_2S_2Na[M+Na^+]$ 545.1545; found 545.1536.

9-fluoro-5-[(phenylsulfonyl)methyl]-3-tosyl-1,2,3,4,5,6-hexahydroazepino[4,5-b]indole, **5i**



White solid, 85 mg 83%

Melting point: 251-253 ˚C

R_f = 0.50 (30% ethyl acetate in hexanes)

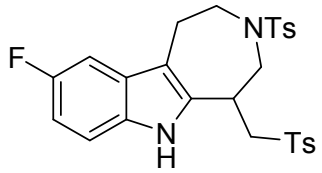
IR (KBr) ν_{max}: 3393, 2926, 1593, 1451, 1399, 1290, 1153, 1092, 680, 549 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.84 (d, *J* = 7.6 Hz, 2H), 7.68 (d, *J* = 8.1 Hz, 2H), 7.57-7.55 (m, 1H), 7.46-7.43 (m, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.22 (dd, *J* = 8.7, 4.3 Hz, 1H), 6.99 – 6.97 (m, 1H), 6.92-6.88 (m, 1H), 4.21 (m, 1H), 4.16-4.14 (d, *J* = 11.1 Hz, 2H), 3.97 (dd, *J* = 14.4, 4.2 Hz, 1H), 3.86-3.85 (m, 1H), 3.51 (dd, *J* = 14.4, 7.2 Hz, 1H), 3.05-3.02 (m, 1H), 2.92 – 2.81 (m, 2H), 2.72-2.67 (m, 1H), 2.43 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.9 (d, *J* = 235.0 Hz), 143.8, 139.2, 136.5, 135.6, 133.8, 131.3, 130.0, 129.4, 129.2, 128.7 (d, *J* = 9.5 Hz), 128.3, 127.6, 127.0, 111.7 (d, *J* = 9.8 Hz), 110.6 (d, *J* = 26.4 Hz), 103.00 (d, *J* = 23.5 Hz), 58.2, 53.2, 50.8, 34.5, 25.8, 21.6.

HRMS: calcd for $C_{26}H_{26}FO_4N_2S_2$ [M+H$^+$] 513.1318; found 513.1308.

9-Fluoro-3-tosyl-5-(tosylmethyl)-1,2,3,4,5,6-hexahydroazepino[4,5-b]indole, **5j**



White solid, 92 mg, 87%

Melting point: 251-253 ˚C

R_f = 0.51 (30% ethyl acetate in hexanes)

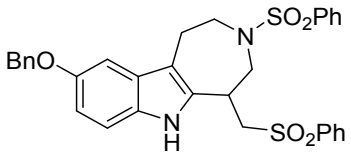
IR (KBr) ν_{max}: 3373, 2924, 1594, 1452, 1334, 1291, 1153, 1093, 1033, 905, 807, 695, 608 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.50 (s, 1H), 7.71 (d, *J* = 8.3 Hz, 2H), 7.67 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.23 – 7.21 (m, 3H), 6.98 (dd, *J* = 9.6, 2.3 Hz, 1H), 6.90 (td, *J* = 9.1, 2.4 Hz, 1H), 4.21-4.13 (m, 2H), 3.93 (dd, *J* = 14.4, 4.2 Hz, 1H), 3.84-3.82 (m, 1H), 3.48 (dd, *J* = 14.4, 7.2 Hz, 1H), 3.04 (dd, *J* = 13.8, 1.9 Hz, 1H), 2.92 – 2.81 (m, 2H), 2.73 – 2.67 (m, 1H), 2.43 (s, 3H), 2.38 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 157.9 (d, *J* = 292.3 Hz), 144.9, 143.8, 136.6, 136.2, 135.6, 131.3, 130.0, 129.8, 127.6, 127.0, 110.4 (d, *J* = 32.8 Hz), 110.4 (d, *J* = 32.8 Hz), 102.9 (d, *J* = 30.2 Hz), 58.3, 53.2, 50.8, 34.6, 25.8, 21.6(2).

HRMS: calcd for $C_{27}H_{28}O_4FN_2S_2$ [M+H$^+$] 527.1475; found 527.1468.

9-(benzyloxy)-3-(phenylsulfonyl)-5-[(phenylsulfonyl)methyl]-1,2,3,4,5,6-hexahydroazepino[4,5-b]indole**, 5k**



White solid, 81 mg 69%

Melting point: 123-125 ˚C

R_f = 0.47 (30% ethyl acetate in hexanes)

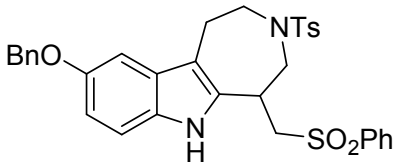
IR (KBr) ν_{max}: 3384, 2922, 1720, 1588, 1451, 1301, 1155, 1093, 801, 691, 573 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.85-7.83 (m, 2H), 7.81-7.79 (m, 2H), 7.60-7.52 (m, 4H), 7.47-7.33 (m, 7H), 7.21 (d, *J* = 8.7 Hz, 1H), 6.92 – 6.87 (m, 2H), 5.08 (s, 3H), 4.23 – 4.16 (m, 2H), 3.98 (dd, *J* = 14.4, 4.5 Hz, 1H), 3.86-3.81 (m, 1H), 3.48 (dd, *J* = 14.4, 6.9 Hz, 1H), 3.06 (d, *J* = 11.7 Hz, 1H), 2.96-2.80 (m, 3H), 2.75-2.69 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.3, 139.2, 138.6, 137.6, 133.7, 132.9, 130.2, 129.3, 129.2, 128.6, 128.5, 128.2, 127.8, 127.5 (2), 126.9, 113.0, 111.7, 111.3, 101.9, 71.0, 58.2, 53.2, 50.9, 34.5, 25.8.

HRMS: calcd for $C_{32}H_{30}O_5N_2S_2Na[M+Na^+]$ 609.1494; found 609.1476.

9-(benzyloxy)-5-[(phenylsulfonyl)methyl]-3-tosyl-1,2,3,4,5,6-hexahydroazepino[4,5-b]indole, **5l**



White solid, 84 mg 70%

Melting point: 148-150 ˚C

R_f = 0.48 (30% ethyl acetate in hexanes)

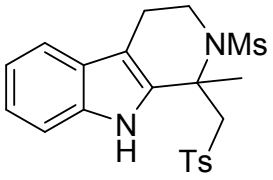
IR (KBr) ν_{max}: 3347, 2924, 1594, 1488, 1336, 1158, 811, 676 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.84 (d, *J* = 7.4 Hz, 2H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.56-7.52 (m, 1H), 7.47 – 7.36 (m, 7H), 7.33-7.30 (m, 3H), 7.21 (d, *J* = 8.7 Hz, 1H), 6.92 – 6.88 (m, 2H), 5.08 (s, 2H), 4.22 – 4.13 (m, 2H), 3.98 (dd, *J* = 14.4, 4.5 Hz, 1H), 3.84-3.81 (m, 1H), 3.48 (dd, *J* = 14.4, 6.9 Hz, 1H), 3.03 (dd, *J* = 13.7, 1.7 Hz, 1H), 2.95 – 2.79 (m, 2H), 2.72 – 2.66 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.3, 143.7, 139.2, 137.6, 135.6, 135.4, 133.7, 130.2, 129.9, 129.2, 128.6, 128.5, 127.8, 127.5, 127.5, 127.0, 113.0, 111.6, 111.3, 101.9, 71.0, 58.2, 53.2, 50.9, 34.5, 25.8, 21.5.

HRMS: calcd for $C_{33}H_{33}O_5N_2S_2$ $[M+H^+]$ 601.1831; found 601.1821.

1-Methyl-2-(methylsulfonyl)-1-(tosylmethyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole, **1**



White solid, 69 mg 80%.

Melting point: 175-178 ˚C

R_f = 0.52 (30% ethyl acetate in hexanes)

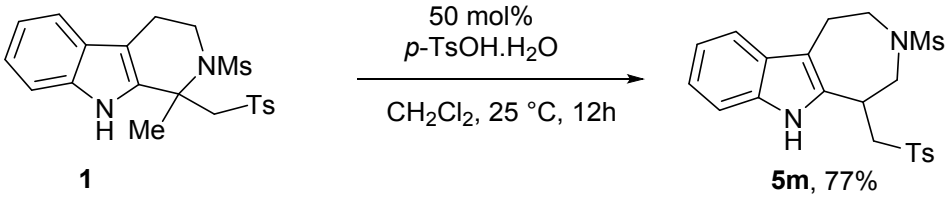
IR (KBr) ν_{max} 3368, 2989, 1594, 1459, 1209, 1145,965, 769, 672, 584 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.95 (s, 1H), 7.64 (d, *J* = 8.3 Hz, 2H), 7.45 (d, *J* = 7.9 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 1H), 7.22 – 7.16 (m, 3H), 7.13 – 7.09 (m, 1H), 4.33 (d, *J* = 14.6 Hz, 1H), 4.13 (d, *J* = 14.6 Hz, 1H),, 3.92-3.86 (m, 1H), 3.59-3.52 (m, 1H), 3.10 (s, 3H), 2.85-2.82 (m, 2H), 2.34 (s, 3H), 2.20 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$ + DMSO-d6) δ 143.7, 136.2, 136.0, 133.3, 128.4, 127.0, 125.4, 121.8, 119.1, 118.0, 110.9, 108.8, 62.4, 59.6, 43.8, 41.8, 41.7, 27.3, 21.2.

HRMS: calcd for $C_{21}H_{25}O_4N_2S_2$ [M+H$^+$] 433.1256; found 433.1254.

6. Procedure for the conversion of tetrahydro-β-carboline 1 to the tetrahydroazepinoindole 5m



To a solution of **1** (43 mg, 0.10 mmol) in dichloromethane (2 mL) maintained at ambient temperature *p*-TsOH.H_2O (10 mg, 0.05 mmol) was added and the reaction was stirred for 12 h at 25 °C. Silica gel was then added to the reaction mixture, the solvent was evaporated on a rotavapor and the residue was chromatographed on a silica column using petroleum ether-ethyl acetate as eluent to afford analytically pure sample of the product **5m** (33 mg, 77%).

3-(Methanesulfonyl)-5-(tosylmethyl)-1,2,3,4,5,6-hexahydroazepino[4,5-b]indole, **5m**

White solid, 33 mg, 77 %

Melting point: 190-192 ˚C

R_f = 0.51 (30% ethyl acetate in hexanes).

IR (KBr) ν_{max}: 3350, 2582,1682, 1471, 1354, 1185, 1042, 750, 654 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.68 (d, *J* = 8.3 Hz, 2H), 7.39 (d, *J* = 7.9 Hz, 1H), 7.34-7.32 (m, 1H), 7.21 – 7.17 (m, 3H), 7.10 – 7.07 (m, 1H), 4.20 – 4.16 (m, 1H), 4.13-4.11 (m, 1H), 3.88-3.84 (m, 2H), 3.40 (dd, *J* = 15.4, 7.9 Hz, 1H), 3.33 (dd, *J* = 13.8, 2.0 Hz, 1H,), 3.07 (ddd, *J* = 15.8, 4.1, 2.0 Hz, 1H), 3.02-2.96 (m, 1H), 2.89-2.84 (m, 4H), 2.36 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 144.9, 137.1, 136.2, 134.7, 129.7, 127.5, 125.7, 122.8, 119.9, 118.4, 111.5, 109.4, 59.9, 43.8, 43.6, 26.4, 21.8, 21.6.

HRMS: calcd for $C_{21}H_{25}O_4N_2S_2$ $[M+H^+]$ 433.1256; found 433.1264.

7. Single crystal X-ray analysis of 5e

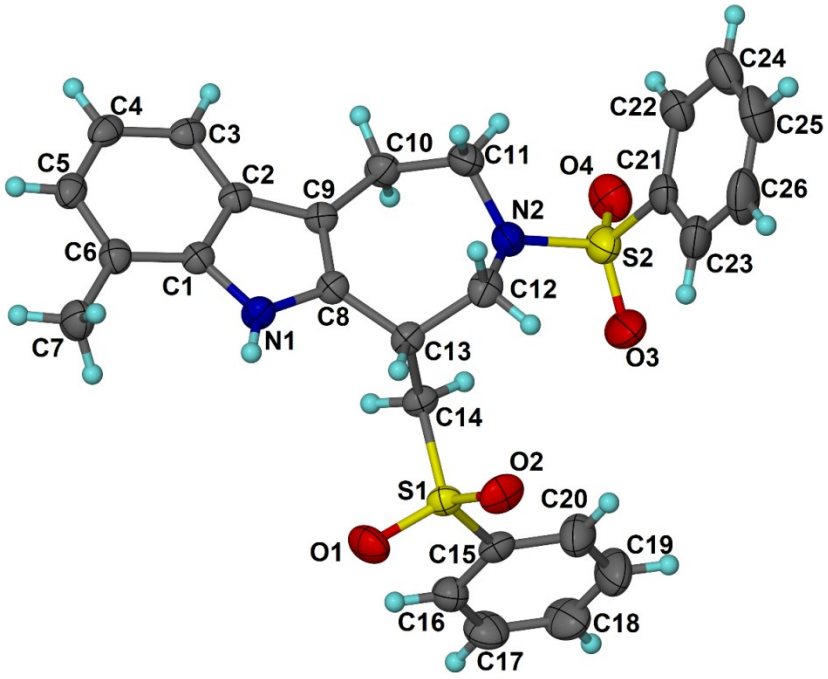


Figure 1: ORTEP diagram of **5e** with the atom-numbering. Displacement ellipsoids are drawn at the 35% probability level and H atoms are shown as small spheres of arbitrary radius. (CCDC2025452).

Table 1: Crystallographic details of **5e**.

Datablock: BE27M

```
Bond precision:  C-C = 0.0037 A          Wavelength=0.71073

Cell:           a=16.1653(14)    b=8.6116(7)         c=18.7980(16)
                alpha=90         beta=111.557(1)     gamma=90
Temperature:    293 K

                Calculated                Reported
Volume          2433.8(4)                 2433.8(4)
Space group     P 21/n                    P 21/n
Hall group      -P 2yn                    -P 2yn
Moiety formula  C26 H26 N2 O4 S2          C26 H26 N2 O4 S2
Sum formula     C26 H26 N2 O4 S2          C26 H26 N2 O4 S2
Mr              494.61                    494.61
Dx,g cm-3       1.350                     1.350
Z               4                         4
Mu (mm-1)       0.254                     0.254
F000            1040.0                    1040.0
F000'           1041.42
h,k,lmax        21,11,24                  20,11,24
Nref            5578                      5569
Tmin,Tmax       0.906,0.934               0.906,0.934
Tmin'           0.906

Correction method= # Reported T Limits: Tmin=0.906 Tmax=0.934
AbsCorr = MULTI-SCAN

Data completeness= 0.998          Theta(max)= 27.494

R(reflections)= 0.0488( 3883)     wR2(reflections)= 0.1296( 5569)

S = 1.014                 Npar= 340
```

8. Single crystal X-ray analysis of 1

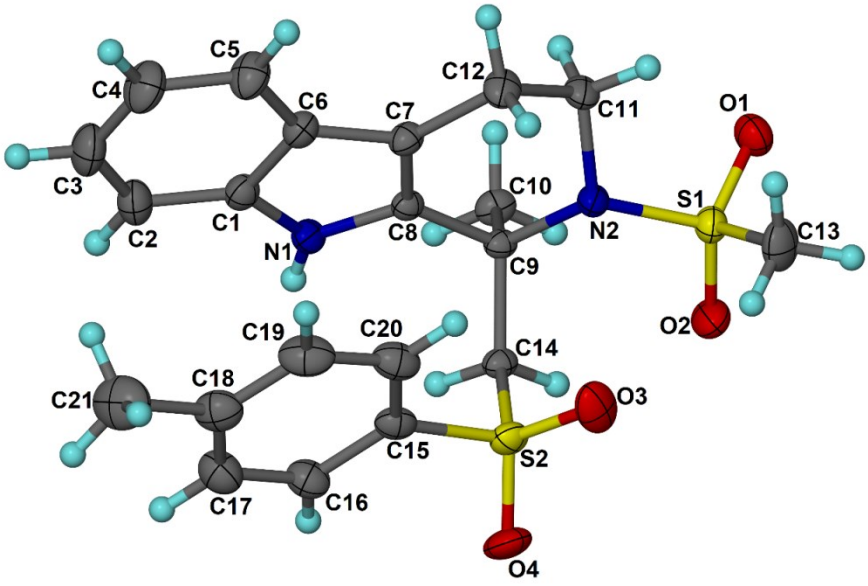


Figure 2: ORTEP diagram of **1** with the atom-numbering. Displacement ellipsoids are drawn at the 35% probability level and H atoms are shown as small spheres of arbitrary radius. (CCDC2025453).

Table 2: Crystallographic details of **1**.

Datablock: BE40M

```
Bond precision:  C-C = 0.0033 A          Wavelength=0.71073

Cell:            a=12.745(3)     b=8.2887(17)         c=20.697(4)
                 alpha=90        beta=104.665(3)      gamma=90
Temperature:     293 K

                Calculated                Reported
Volume          2115.2(8)                 2115.2(8)
Space group     P 21/n                    P 21/n
Hall group      -P 2yn                    -P 2yn
Moiety formula  C21 H24 N2 O4 S2          C21 H24 N2 O4 S2
Sum formula     C21 H24 N2 O4 S2          C21 H24 N2 O4 S2
Mr              432.54                    432.54
Dx,g cm-3       1.358                     1.358
Z               4                         4
Mu (mm-1)       0.282                     0.282
F000            912.0                     912.0
F000'           913.37
h,k,lmax        16,10,26                  16,10,26
Nref            4858                      4850
Tmin,Tmax       0.891,0.919               0.891,0.919
Tmin'           0.891

Correction method= # Reported T Limits: Tmin=0.891 Tmax=0.919
AbsCorr = MULTI-SCAN

Data completeness= 0.998          Theta(max)= 27.499

R(reflections)= 0.0524( 4496)     wR2(reflections)= 0.1333( 4850)

S = 1.152                 Npar= 269
```

9. Data collection and Structure solution details

X-ray data for **5e** (BE27) and **1** (BE40) compounds were collected at room temperature using the Bruker Smart Apex CCD diffractometer with graphite monochromated MoKα radiation (λ=0.71073Å) with ω-scan method.[3] Preliminary lattice parameters and orientation matrices were obtained from four sets of frames. Unit cell dimensions were determined using 5938 reflections for **5e** (BE27) and 9807 for **1** (BE40) compounds. Integration and scaling of intensity data were accomplished using SAINT program.[3] The structure was solved by Direct Methods using SHELXS97[4] and refinement was carried out by full-matrix least-squares technique using SHELXL97.[4] Anisotropic displacement parameters were included for all non-hydrogen atoms. All H atoms were positioned geometrically and treated as riding on their parent C atoms, with C-H distances of 0.93--0.97 Å, and with $U_{iso}(H) = 1.2U_{eq}$ (C) or $1.5U_{eq}$for methyl atoms. N bound H atoms were located from the difference Fourier map and their positions were refined. In **5e** (BE27) crystal data, the sulfoxide S and O atoms were disordered over two sites, with the major component(S1/O1/O2) refining to 0.752(14) site occupancy and minor component (S1D/O1D/O2D)to 0.248(14) site occupancy. PART and FVAR instructions were used for the disorder treatment. The anisotropic displacement parameters of the disordered atoms were restrained to be similar (SIMU instruction) and the direction of motion along the axis between these atoms was also restrained (DELU instruction).[5] **CCDC2025452 (5e)** and **CCDC-2025453 (1)** contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/.

10. References

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2. (a) Y.-S. Zhang, X.-Y. Tang and M. Shi, *Org. Chem. Front.*, 2015, **2**, 1516-1520. (b) M. E. Keiffer, K. V. Chuang and S. E. Reisman, *Chem. Sci.*, 2012, **3**, 3170-3174.

3. SMART & SAINT. Software Reference manuals. Versions 6.28a & 5.625, Bruker Analytical X-ray Systems Inc., Madison, Wisconsin, U.S.A., 2001.
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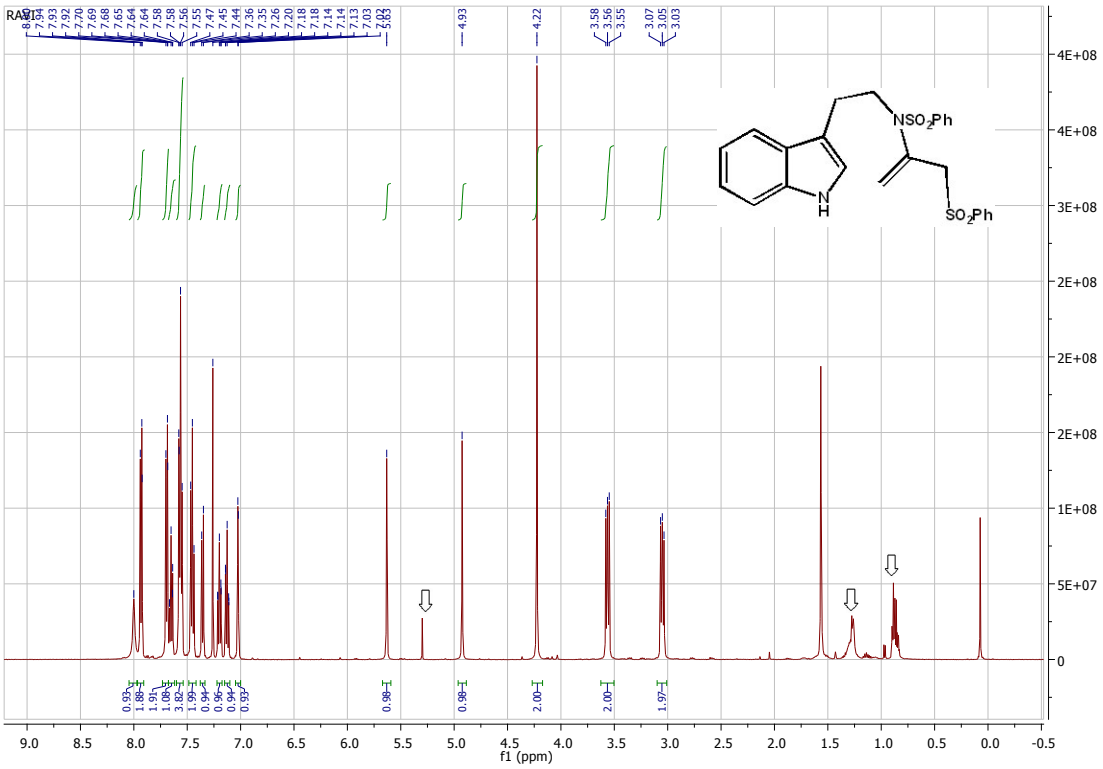
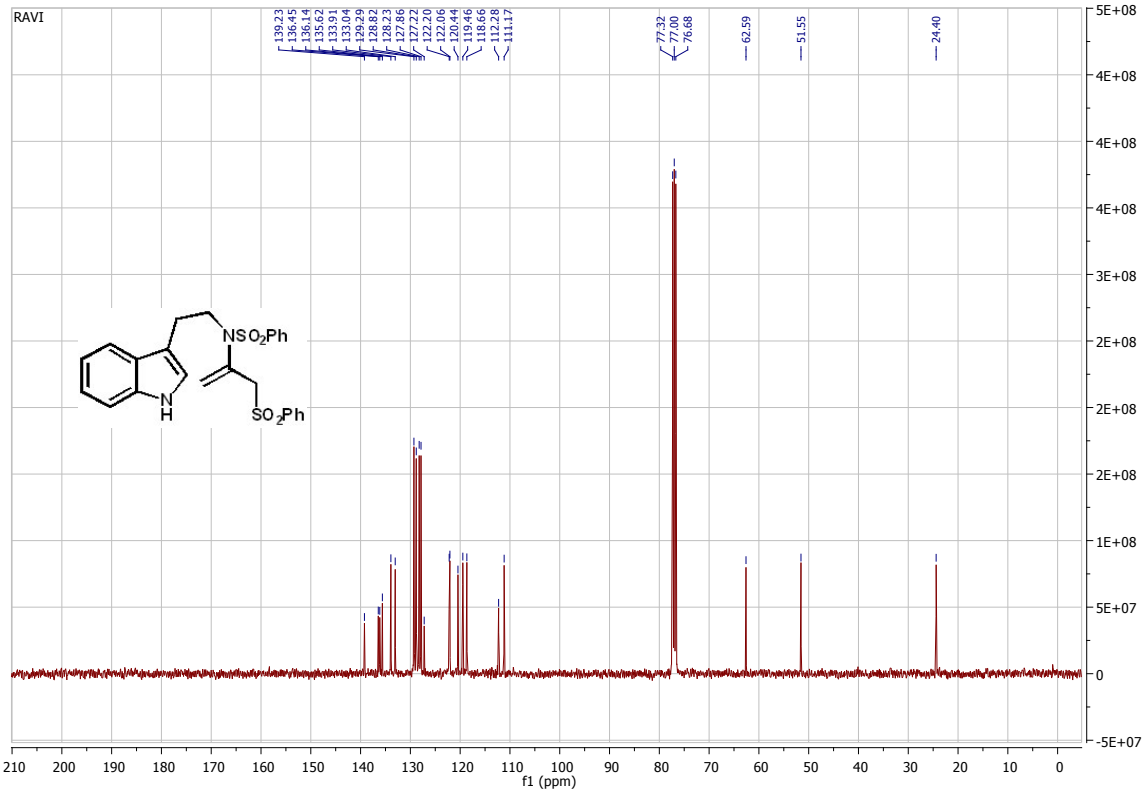
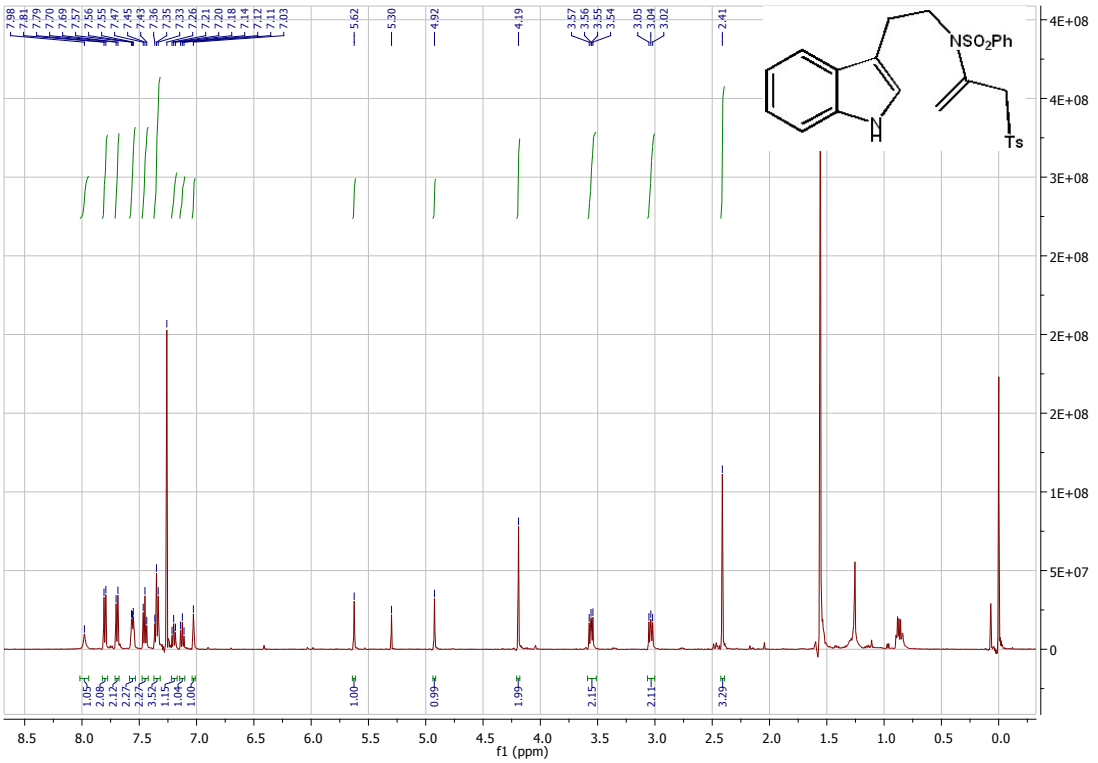
5. Muller, P, Herbst-Imer, R, Spek, A. L, Schneider, T. R, and Sawaya, M. R. Crystal Structure Refinement: A Crystallographer's Guide to SHELXL. Muller, P. Ed. 2006 Oxford University Press: Oxford, New York, pp. 57–91

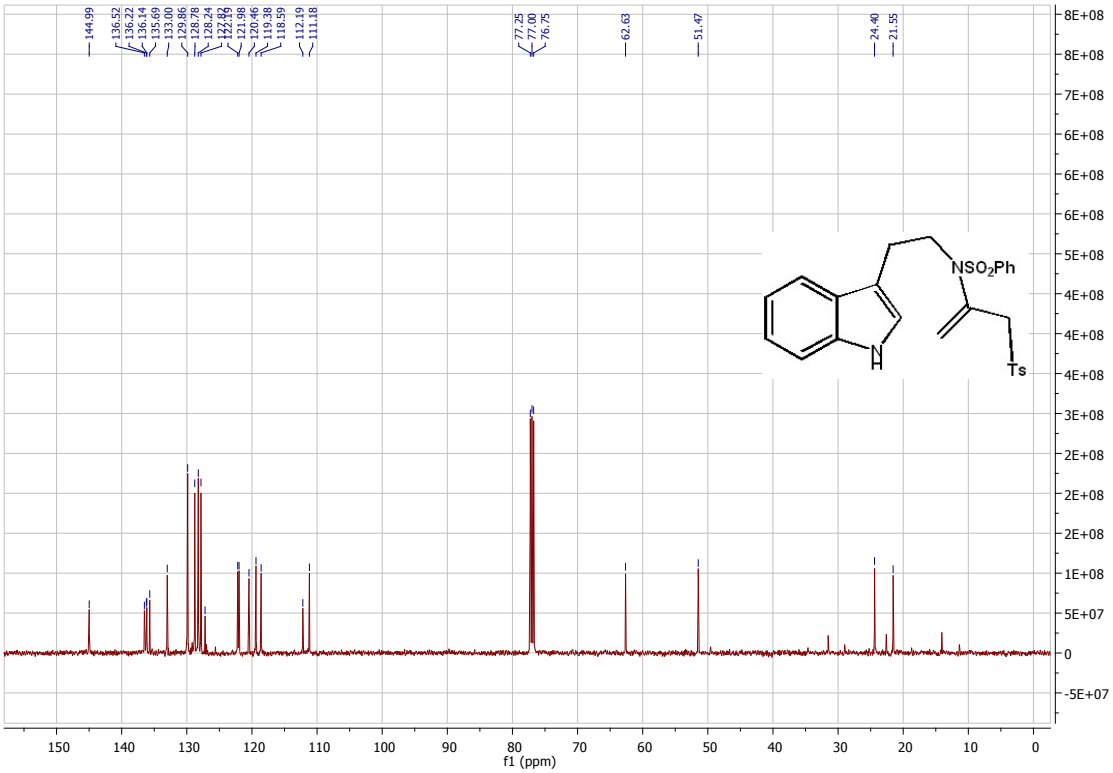
11. ^{1}H and ^{13}C NMR spectra of new compounds 4a



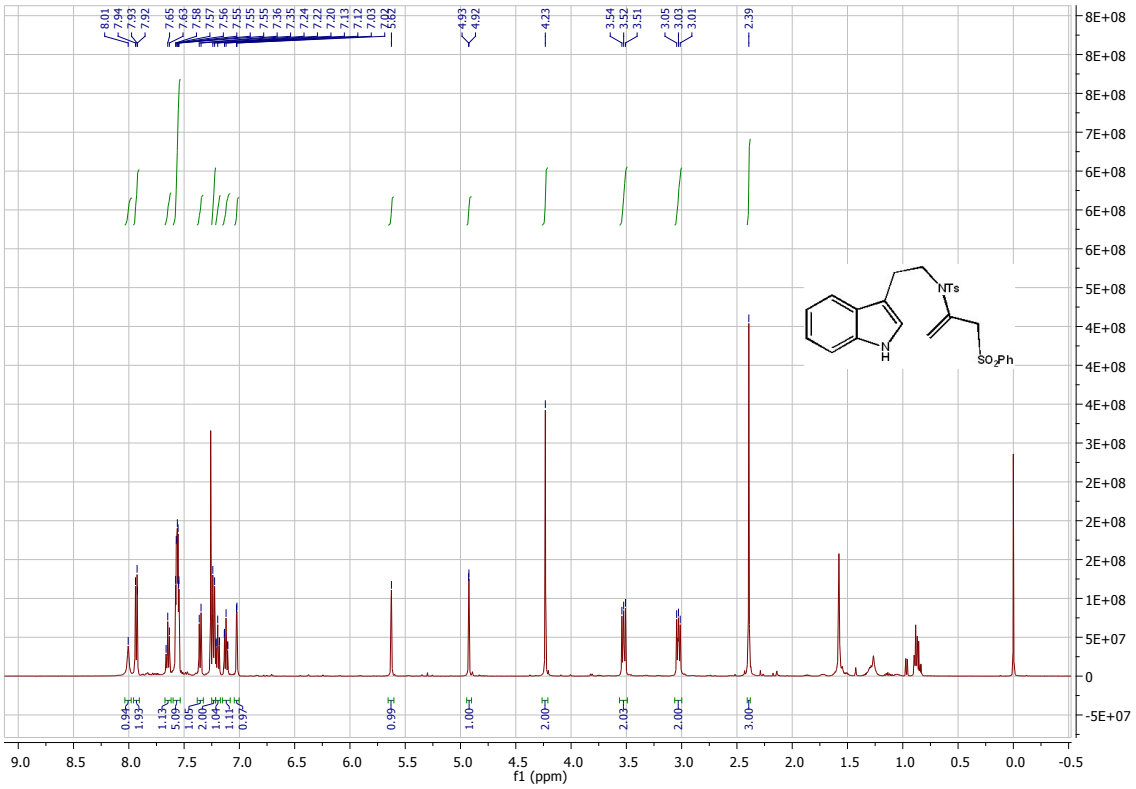


4b





4c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7.93
7.92
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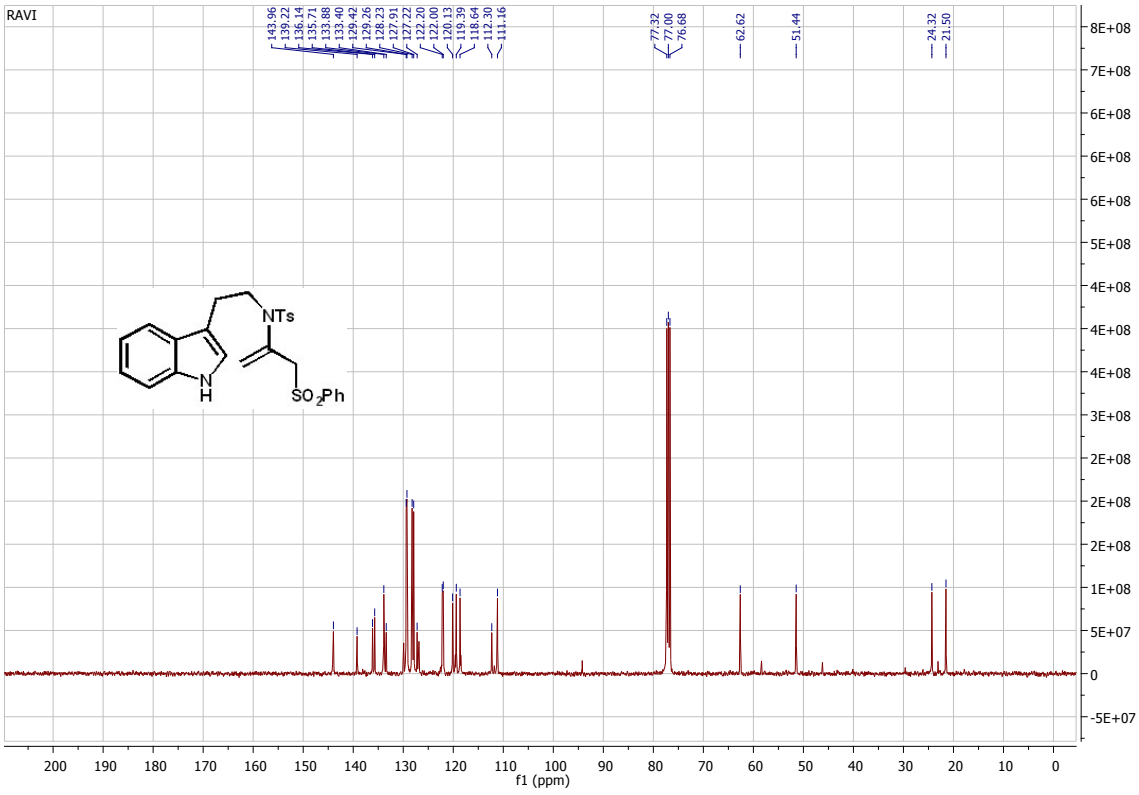
7.55
7.55
7.55
7.36
7.35
7.24
7.22
7.20
7.13
7.12
7.03
5.32
5.32
4.93
4.92
4.23
3.54
3.52
3.51
3.05
3.03
3.01
2.39
NTs
N
H
SO2Ph
0.94
1.93
1.13
5.09
1.05
2.06
1.04
1.11
0.97
0.99
1.00
2.00
2.03
2.00
3.00
f1 (ppm)


RAVI
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129.42
129.26
128.23
127.91
127.22
122.20
122.00
120.13
119.39
118.64
112.30
111.16
77.32
77.00
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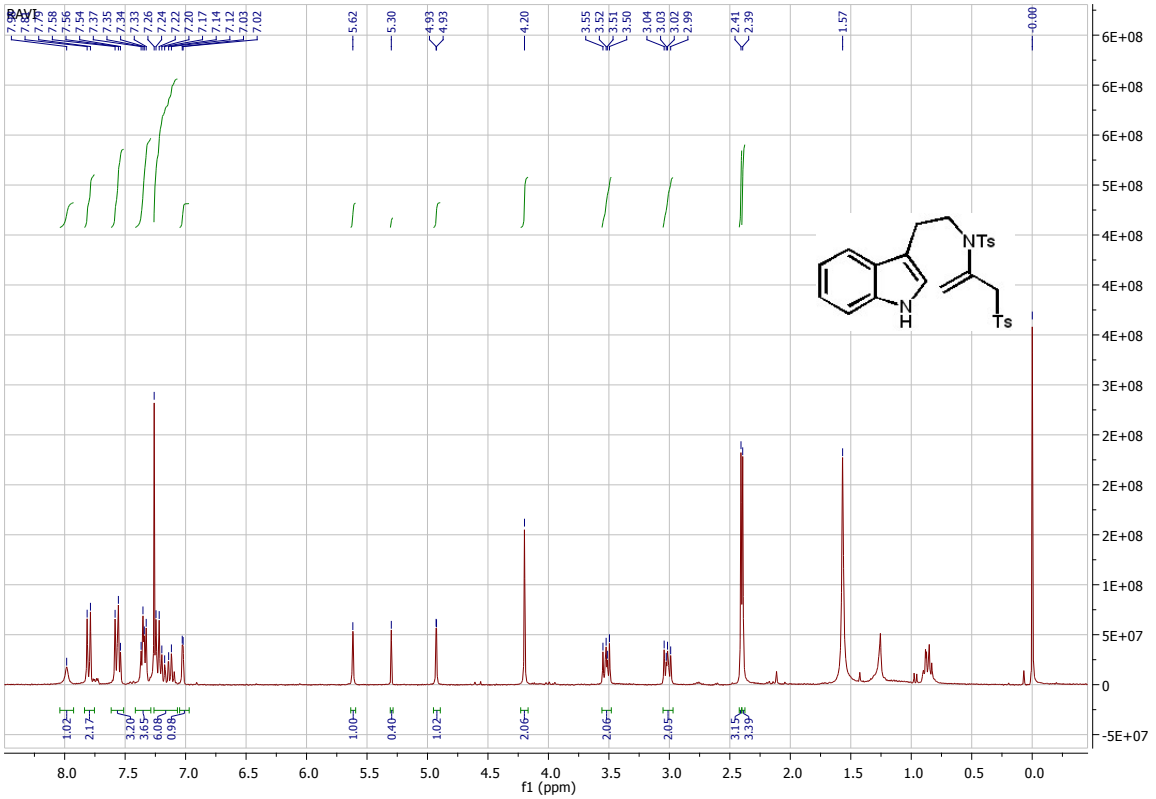
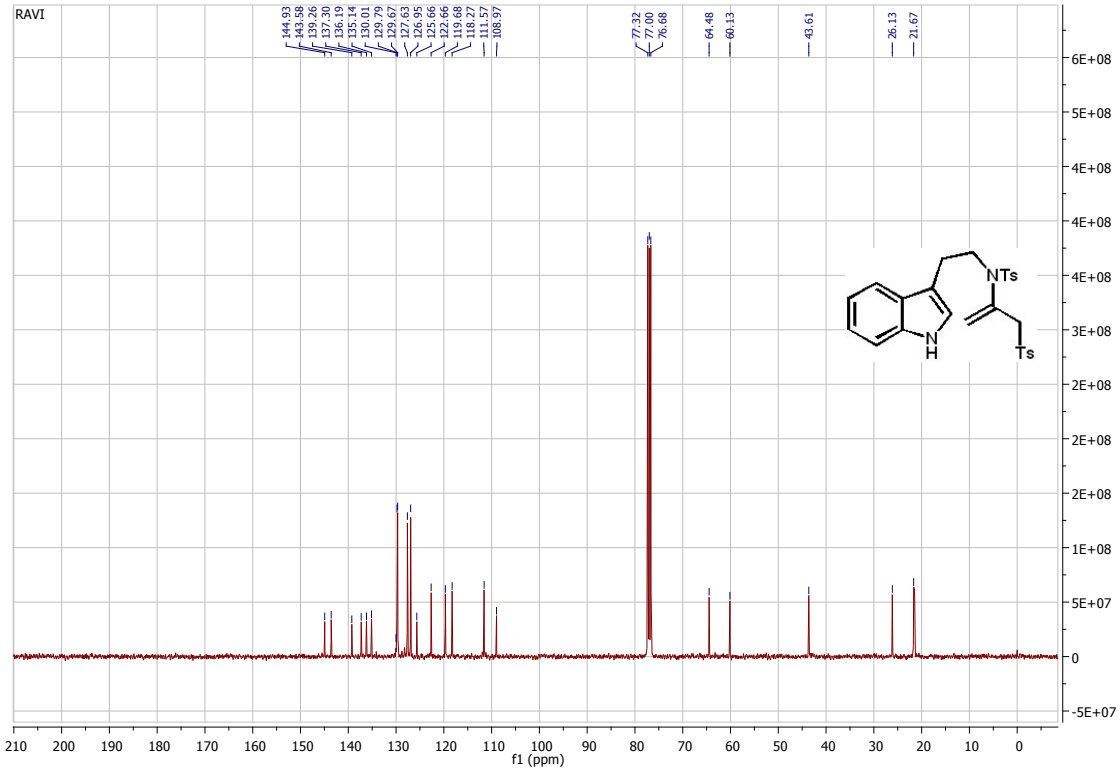
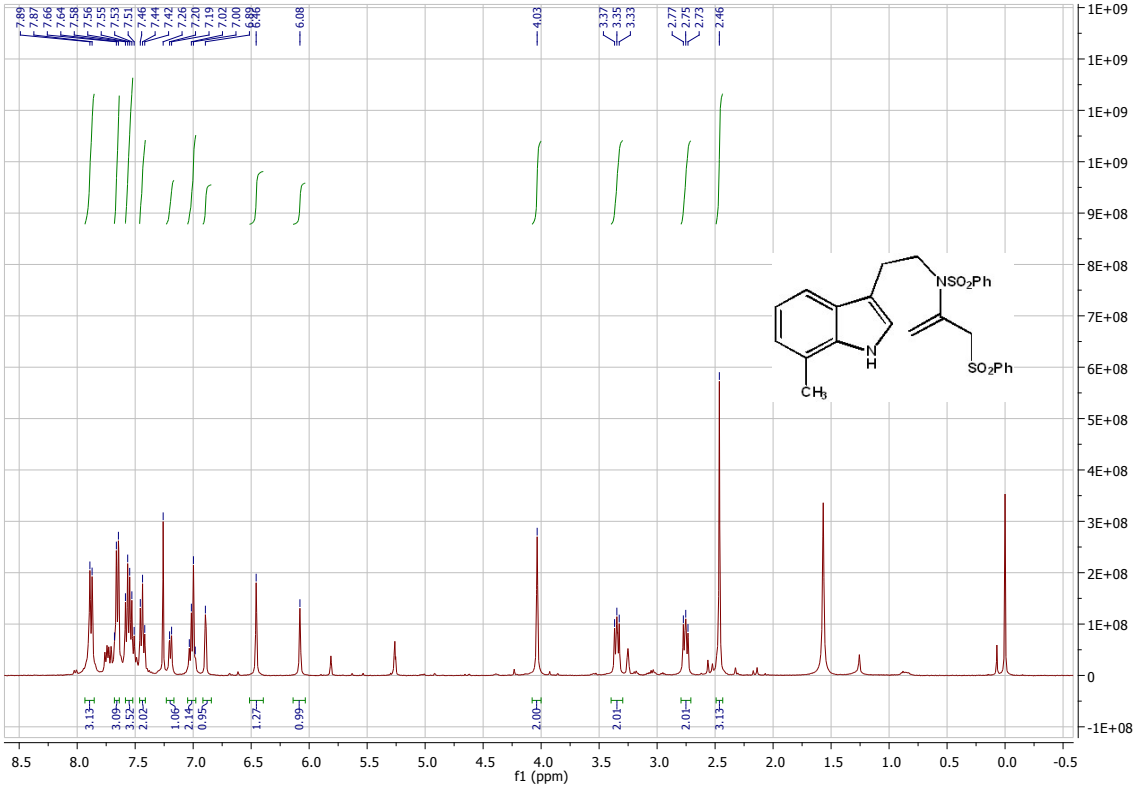
62.62
51.44
24.32
21.50
NTs
N
H
SO2Ph
f1 (ppm)

4d





4e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7.46
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6.88
6.08
4.03
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3.33
2.77
2.75
2.73
2.46
NSO2Ph
SO2Ph
N
H
CH3
3.13
3.09
3.02
2.02
1.06
2.14
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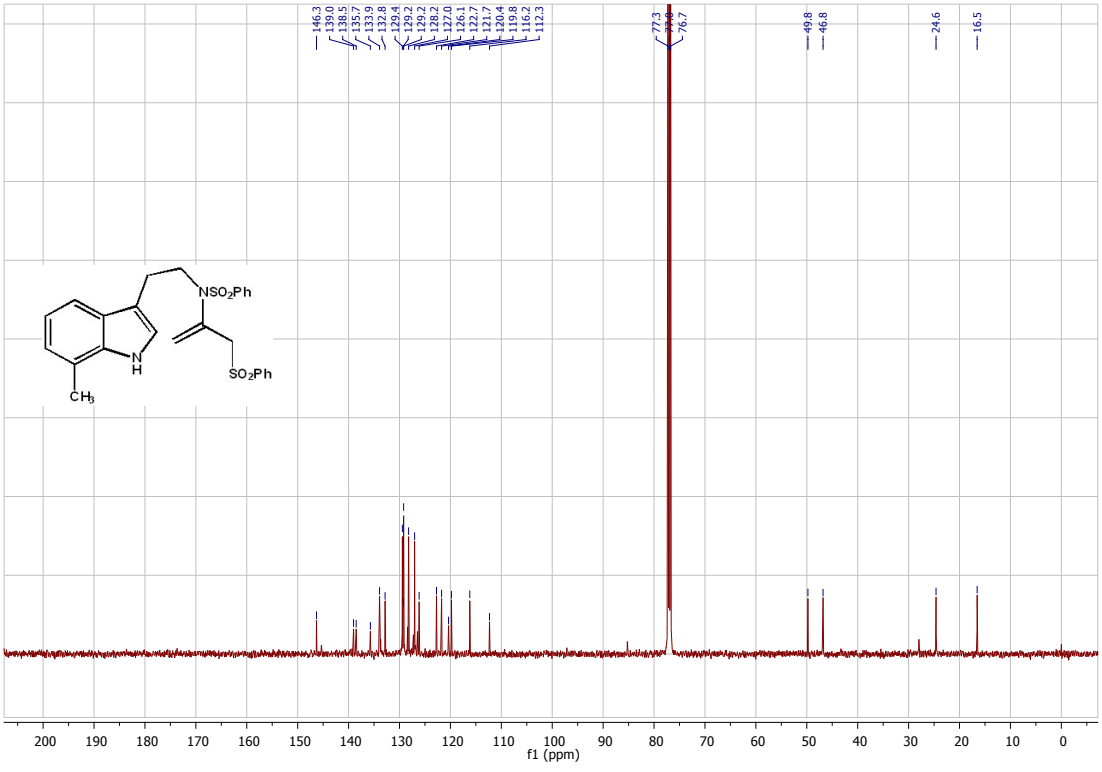
1.27
0.99
2.00
2.01
2.01
3.13
f1 (ppm)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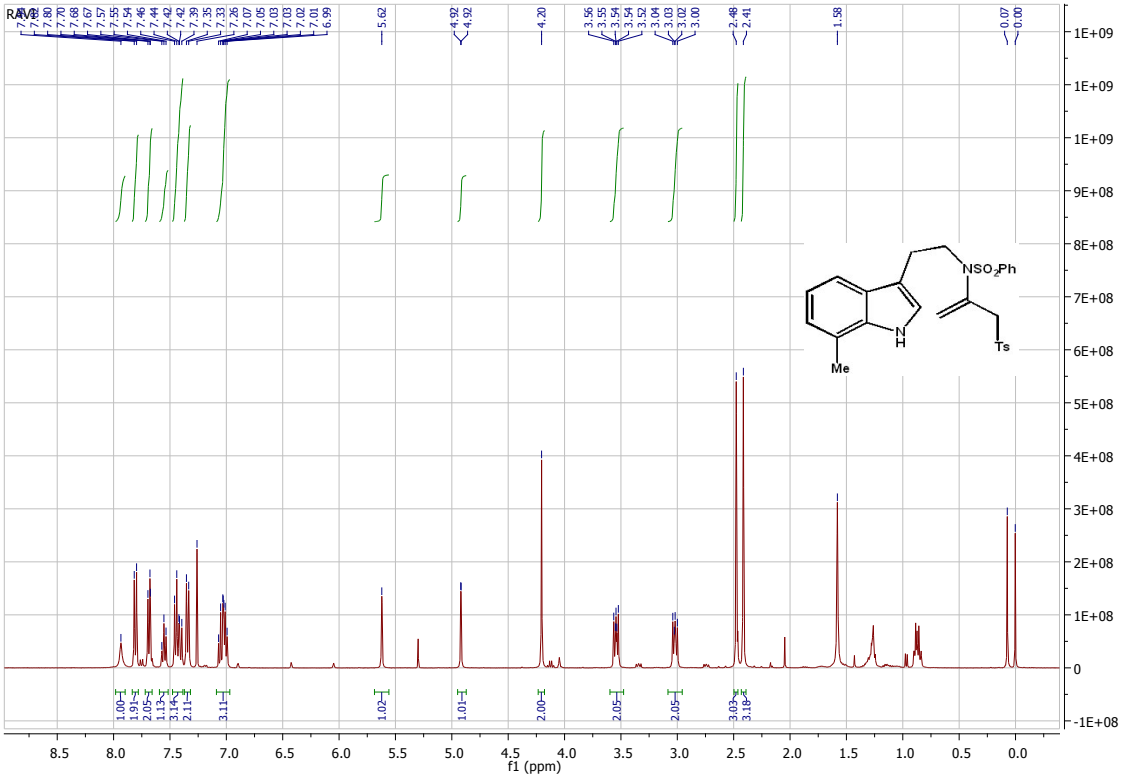
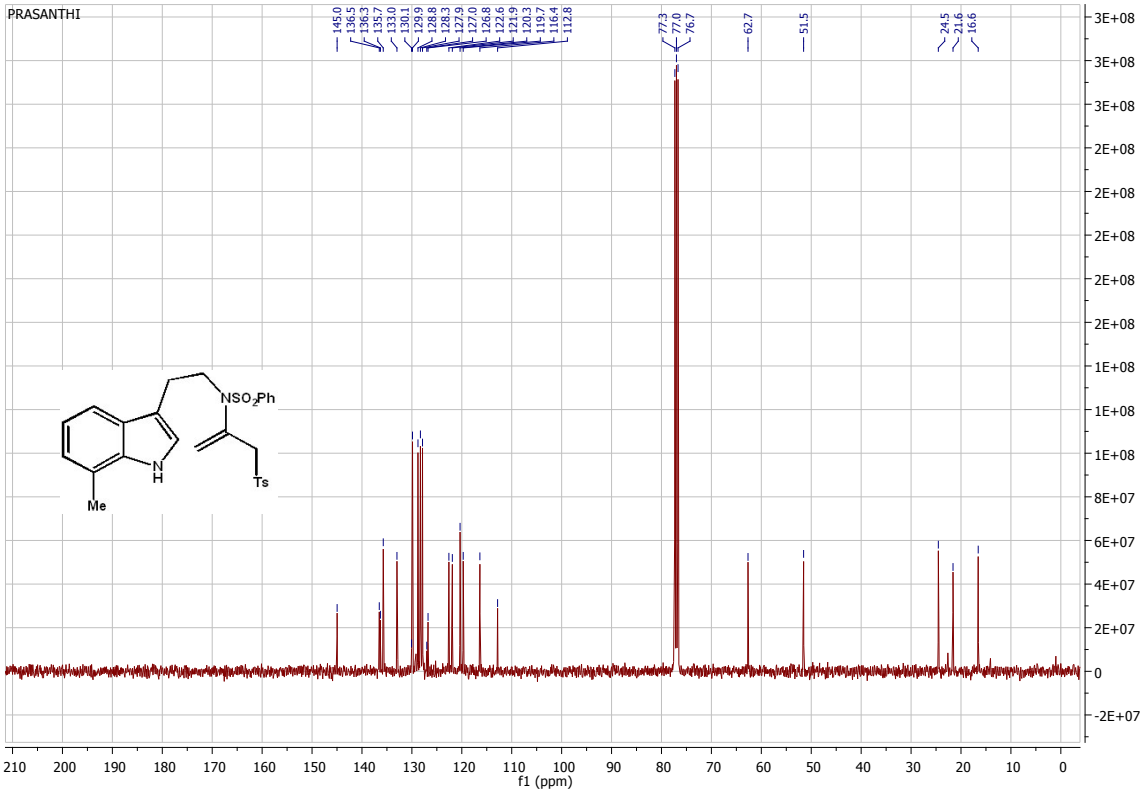
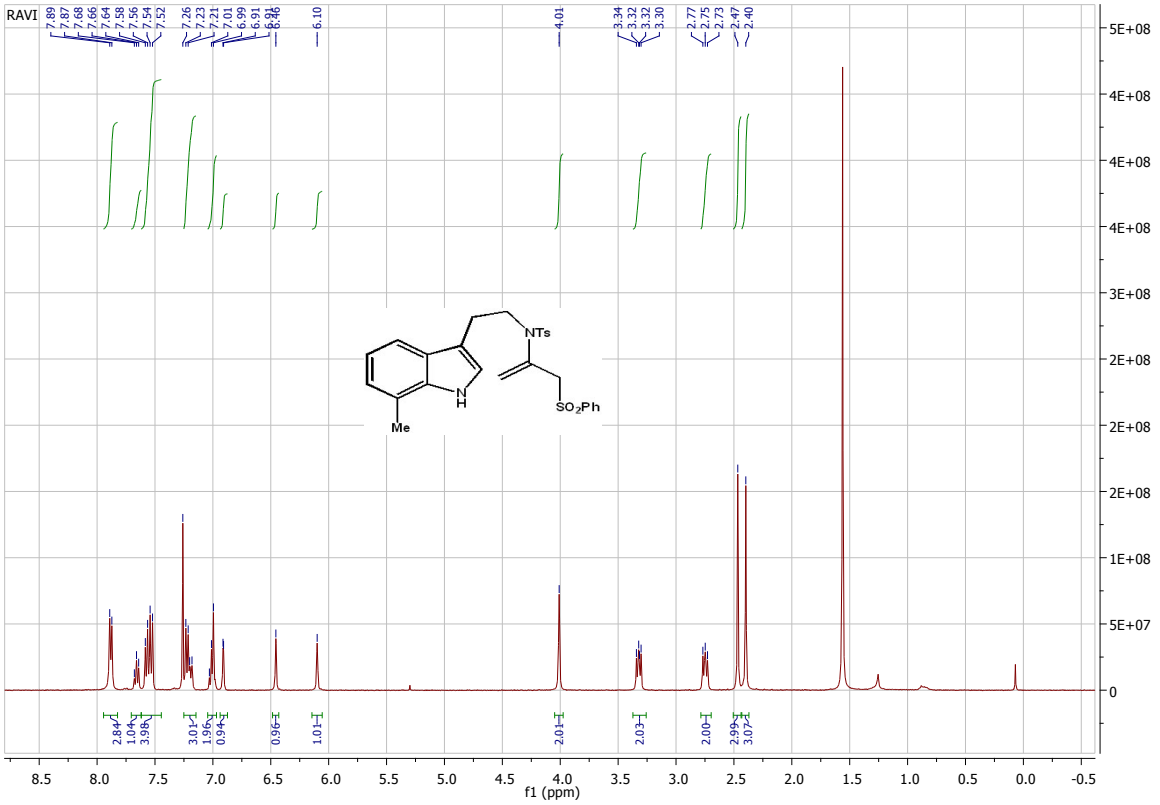
121.7
120.4
119.8
116.2
112.3
77.3
77.0
76.7
49.8
46.8
24.6
16.5
NSO2Ph
SO2Ph
N
H
CH3
f1 (ppm)

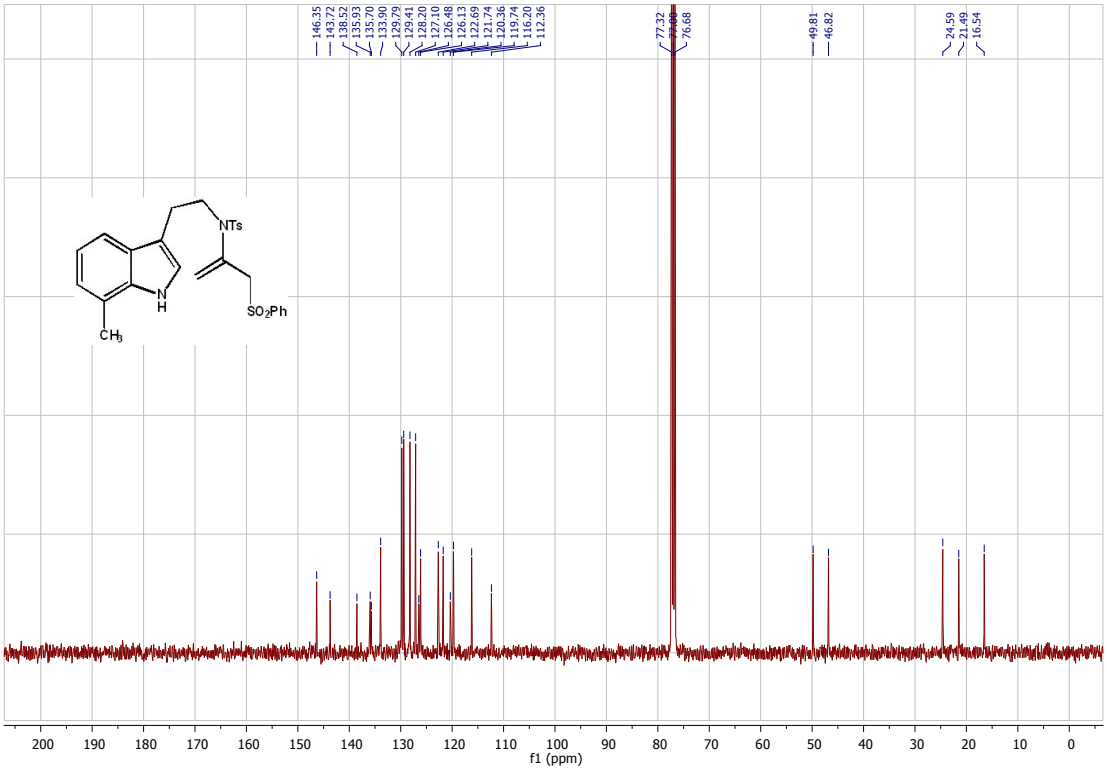
4f



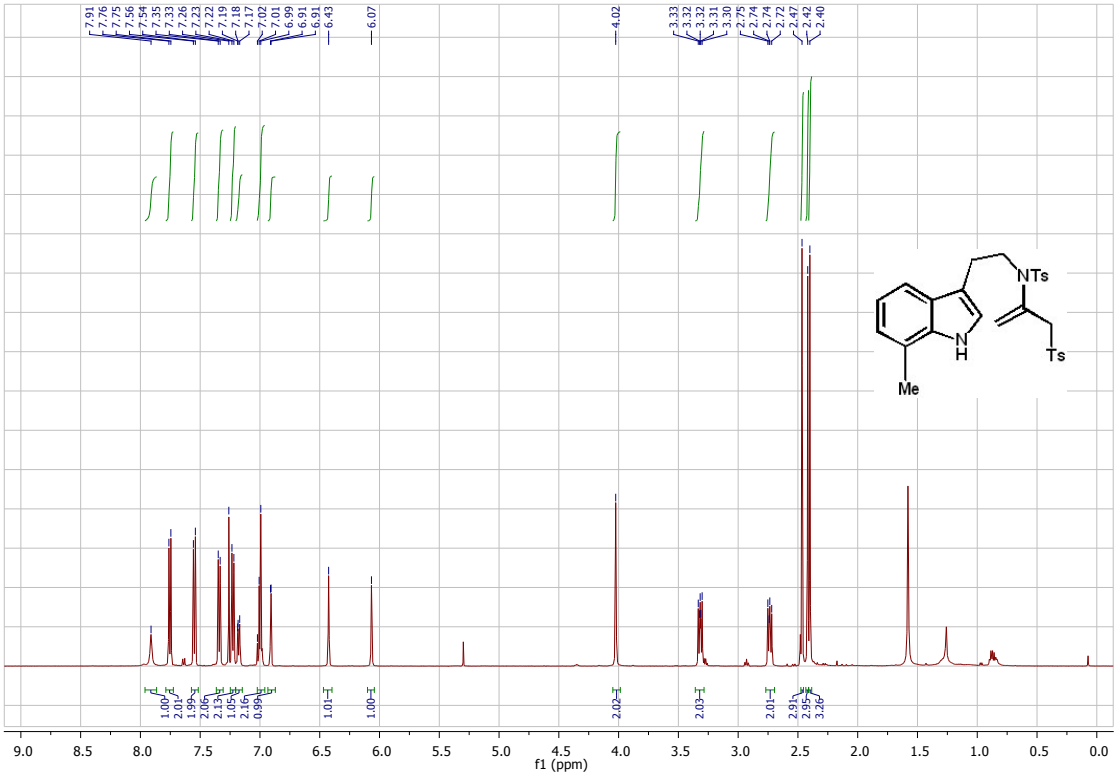


4g





4h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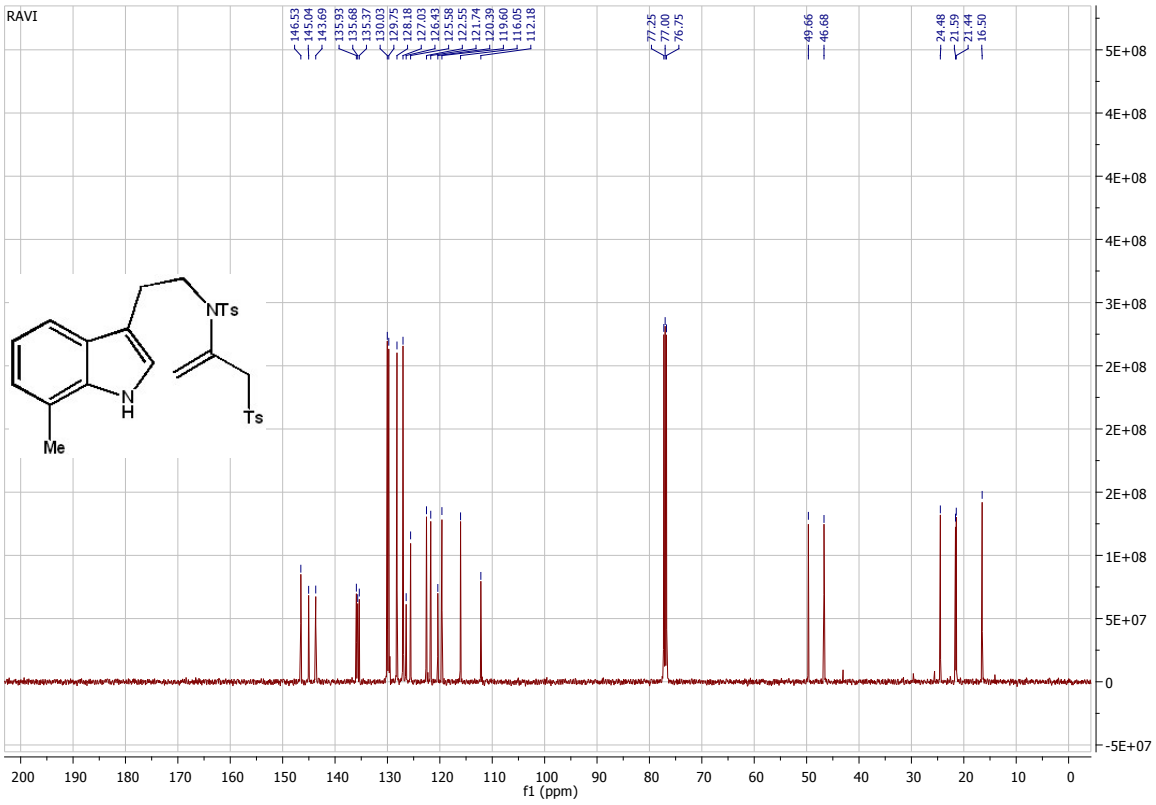
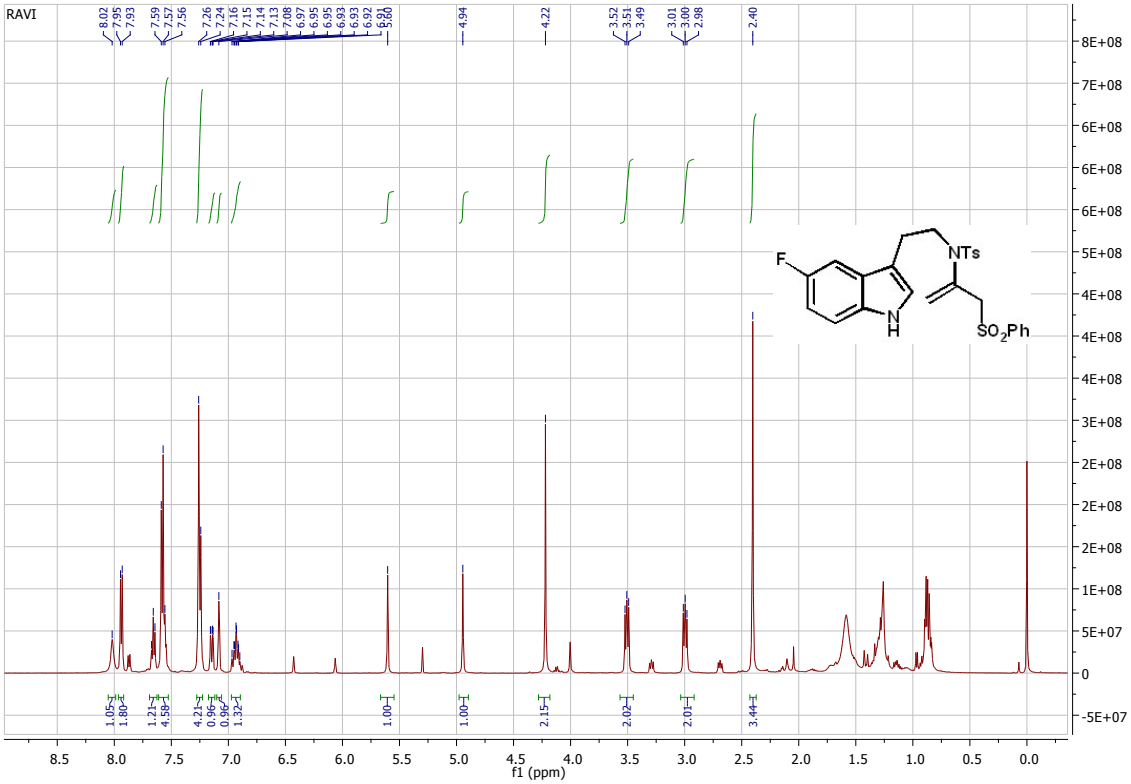
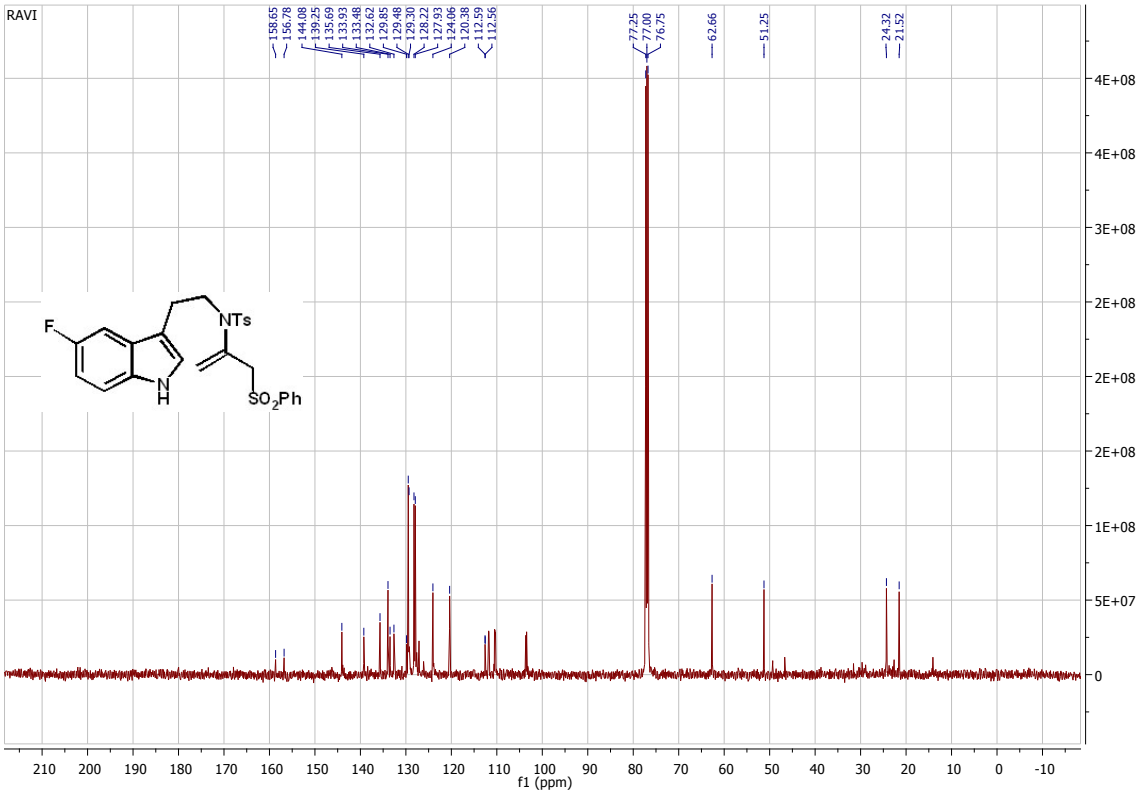
7.76
7.75
7.55
7.54
7.35
7.33
7.26
7.23
7.22
7.19
7.18
7.17
7.02
7.01
6.99
6.91
6.91
6.43
6.07
4.02
3.33
3.32
3.32
3.31
3.30
2.75
2.74
2.74
2.72
2.47
2.42
2.40
NTs
N
H
Ts
Me
1.00
2.01
1.99
2.06
2.13
1.05
2.16
0.99
1.01
1.00
2.02
2.03
2.01
2.91
2.95
3.26
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

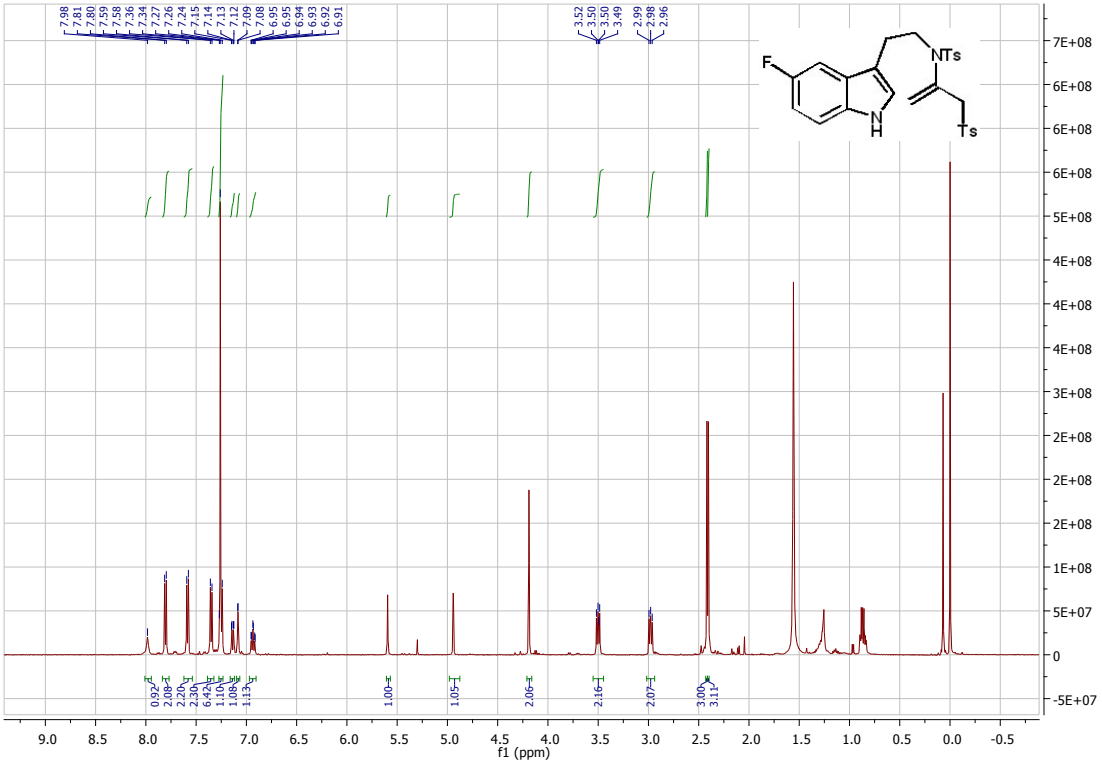

RAVI
146.53
145.04
143.69
135.93
135.68
135.37
130.03
129.75
128.18
127.03
126.43
125.58
122.55
121.74
120.39
119.60
116.05
112.18
77.25
77.00
76.75
49.66
46.68
24.48
21.59
21.44
16.50
NTs
N
H
Ts
Me
5E+08
4E+08
4E+08
4E+08
3E+08
2E+08
2E+08
2E+08
1E+08
5E+07
0
-5E+07
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

4i


RAVI
8.02
7.95
7.93
7.59
7.57
7.56
7.26
7.24
7.16
7.15
7.14
7.13
7.08
6.97
6.95
6.95
6.93
6.93
6.91
6.90
5.60
4.94
4.22
3.52
3.51
3.49
3.01
3.00
2.98
2.40
F
NTs
N
H
SO2Ph
1.05
1.80
1.21
4.58
4.21
0.96
0.96
1.32
1.00
1.00
2.15
2.02
2.01
3.44
f1 (ppm)


RAVI
158.65
156.78
144.08
139.25
135.69
133.93
133.48
132.62
129.85
129.48
129.30
128.22
127.23
124.46
120.38
112.59
112.56
77.25
77.00
76.75
62.66
51.25
24.32
21.52
F
NTs
N
H
SO2Ph
f1 (ppm)

4j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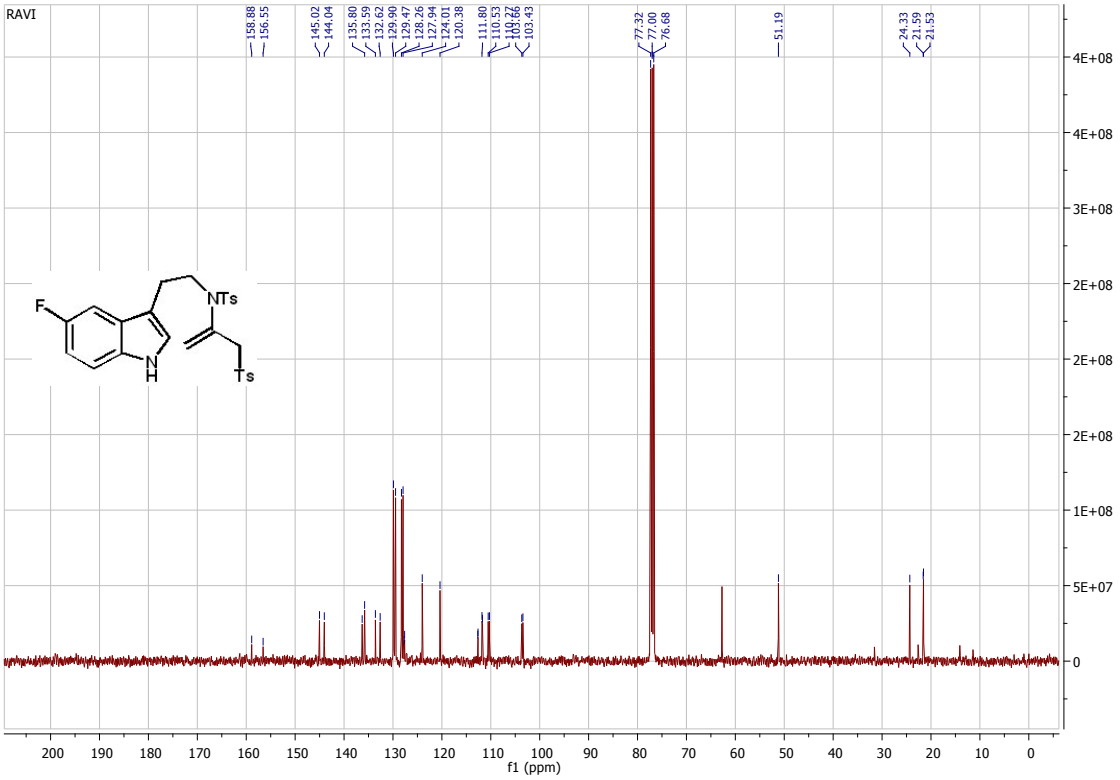
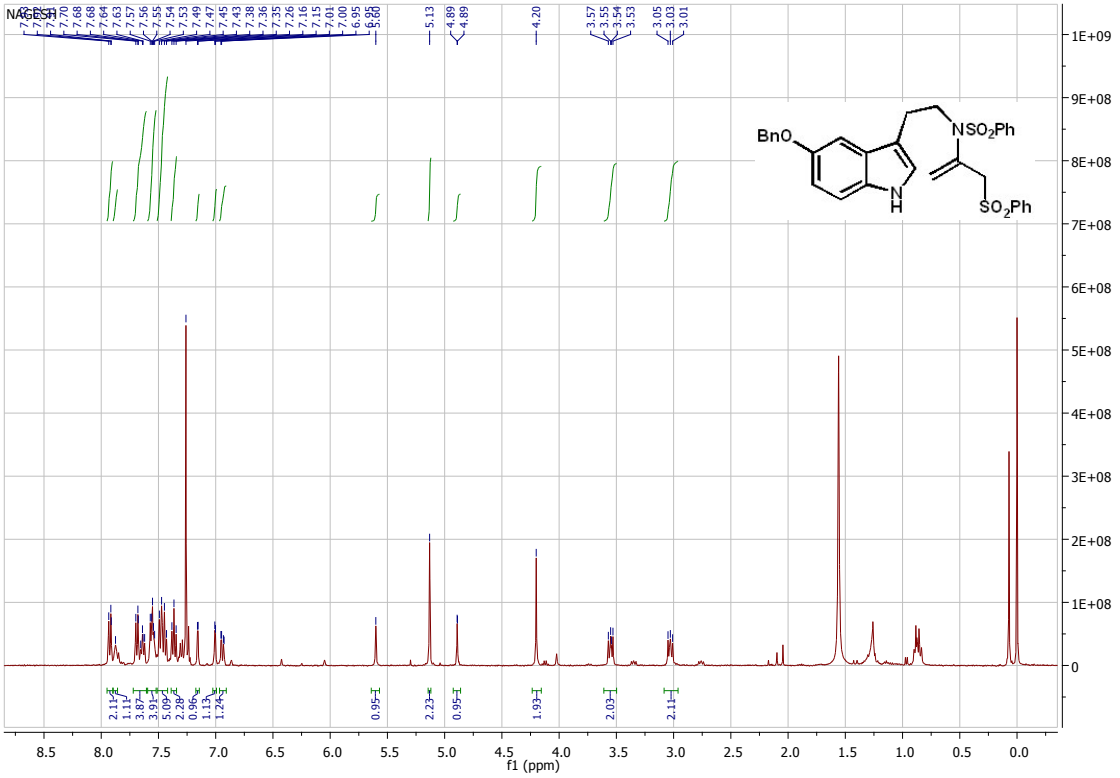
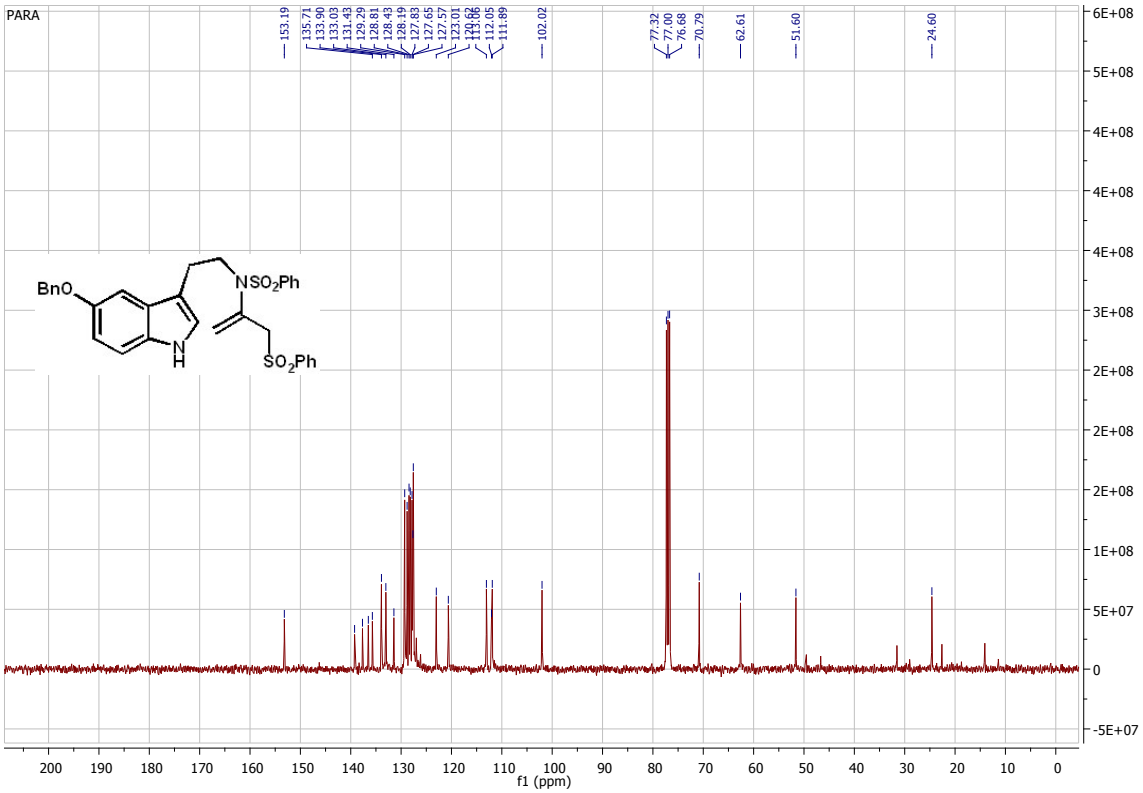
7.81
7.80
7.59
7.58
7.36
7.34
7.27
7.26
7.24
7.15
7.14
7.13
7.12
7.09
7.08
6.95
6.95
6.94
6.93
6.92
6.91
3.52
3.51
3.50
3.49
2.99
2.98
2.96
F
NTs
N
H
Ts
f1 (ppm)

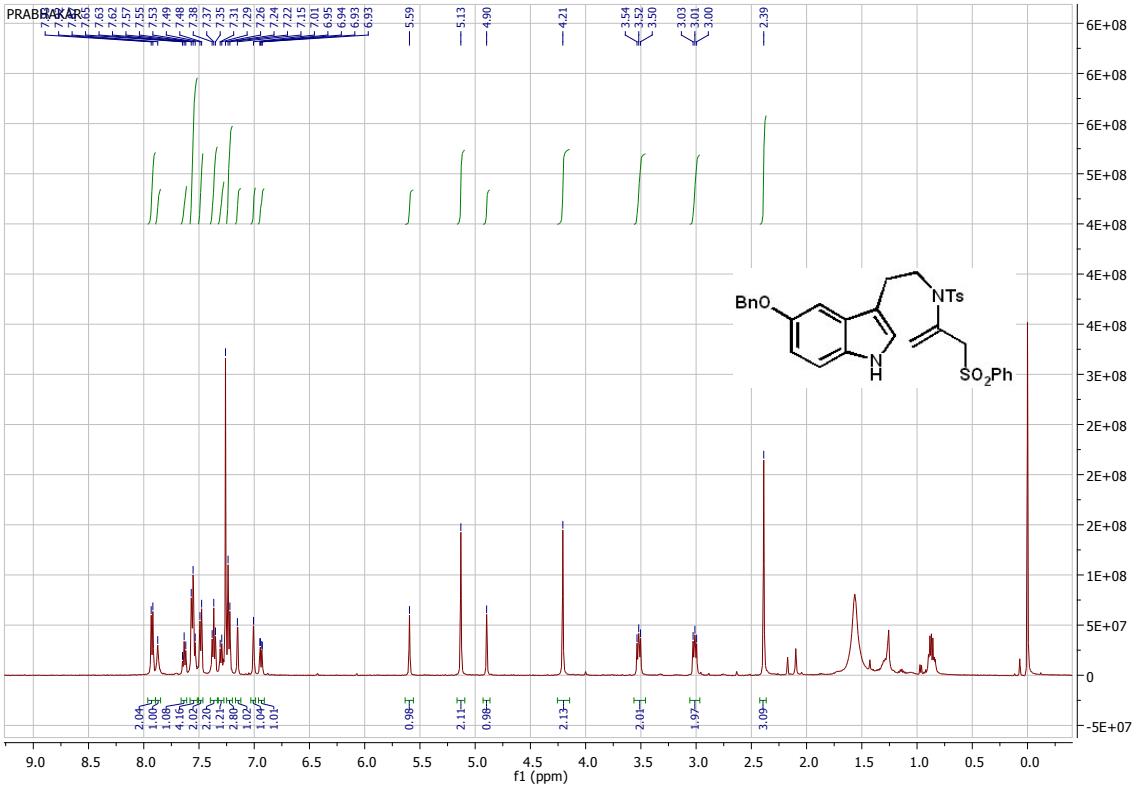

RAVI
158.88
156.55
145.02
144.04
135.80
133.59
132.62
129.90
129.47
128.26
127.94
124.01
120.38
111.80
110.53
103.77
103.66
103.43
77.32
77.00
76.68
51.19
24.33
21.59
21.53
F
NTs
N
H
Ts
f1 (ppm)

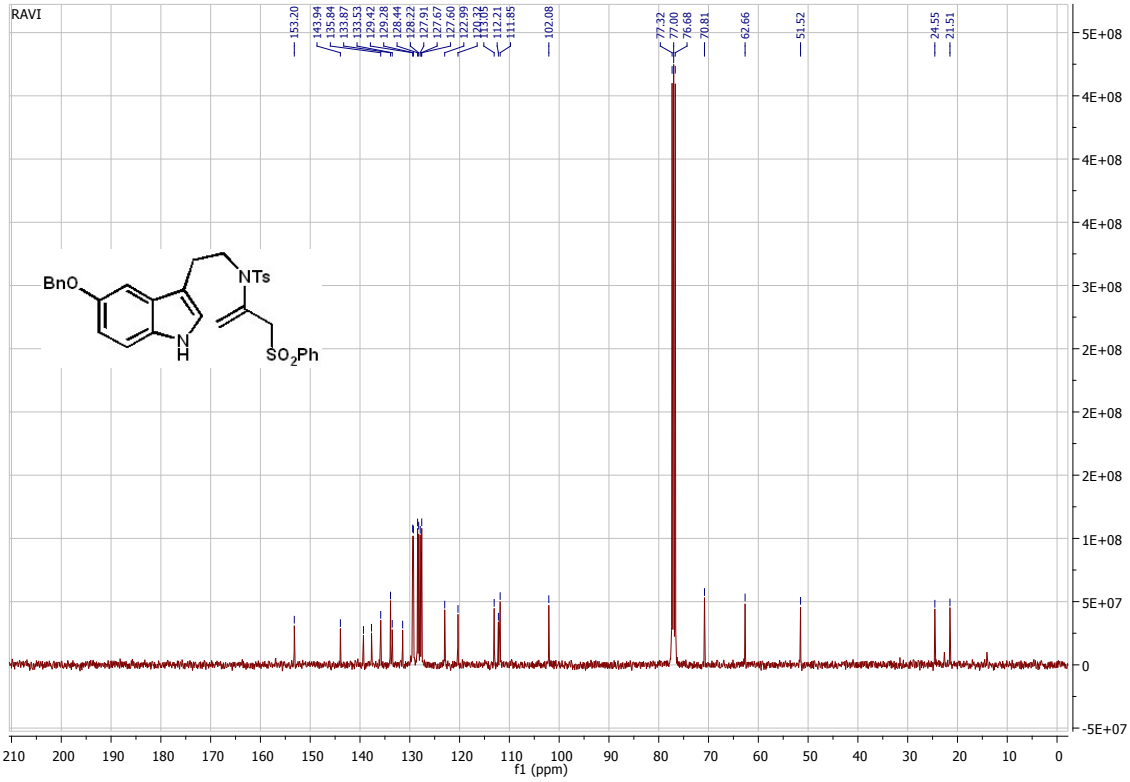
4k


NAGESH
BnO
NSO2Ph
SO2Ph
N
H
f1 (ppm)

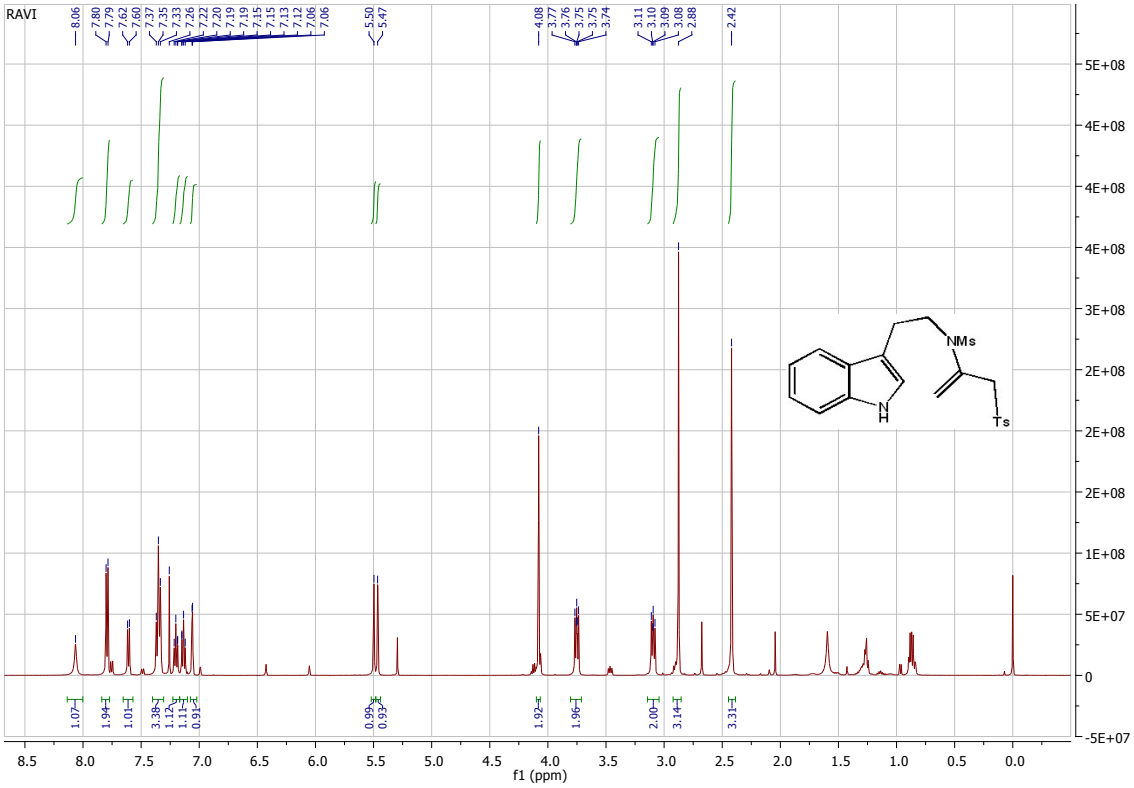

PARA
BnO
NSO2Ph
SO2Ph
N
H
f1 (ppm)

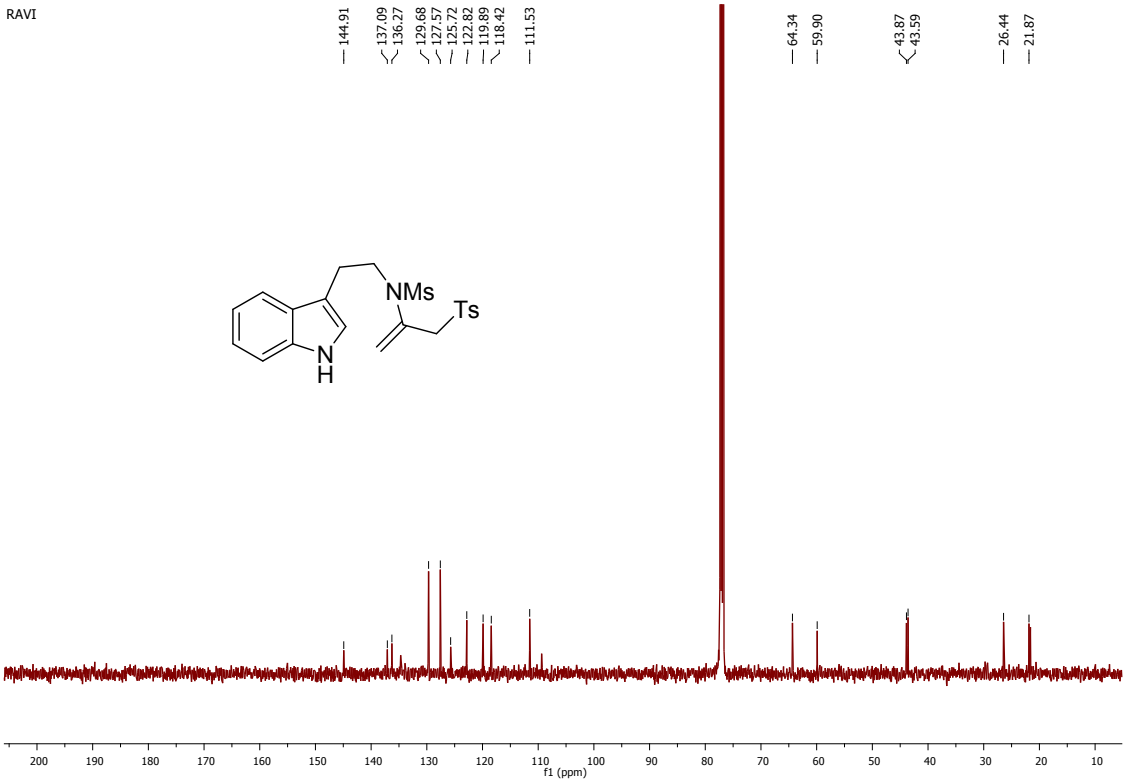
4l



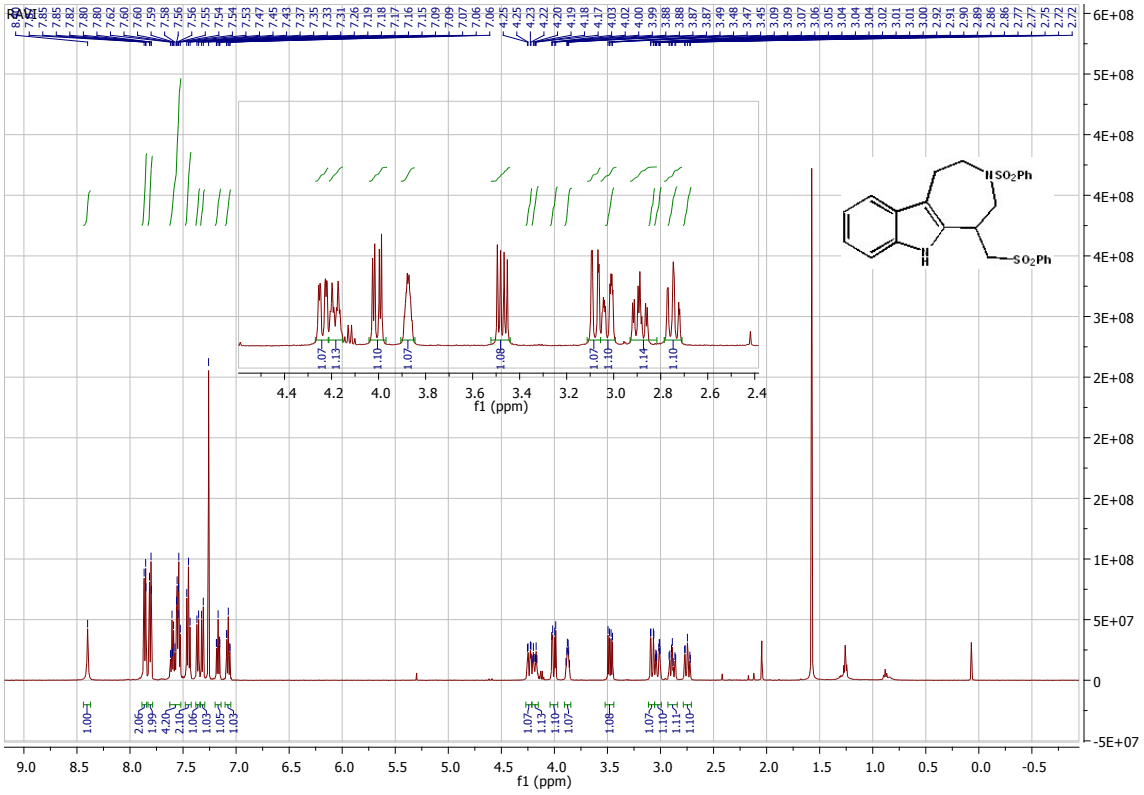


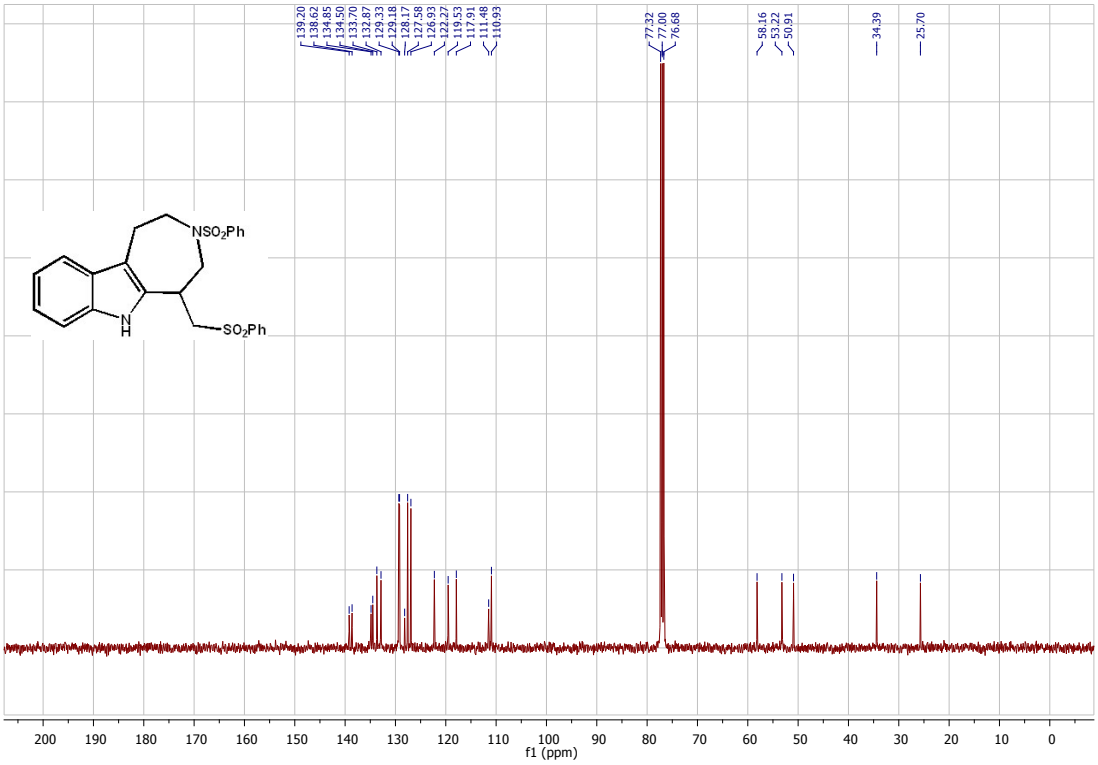
4m


RAVI
8.06
7.80
7.79
7.62
7.60
7.37
7.35
7.33
7.26
7.22
7.20
7.19
7.19
7.15
7.15
7.13
7.12
7.06
7.06
5.50
5.47
4.08
3.77
3.76
3.75
3.75
3.74
3.11
3.10
3.09
3.08
2.88
2.42
NMs
Ts
N
H
f1 (ppm)

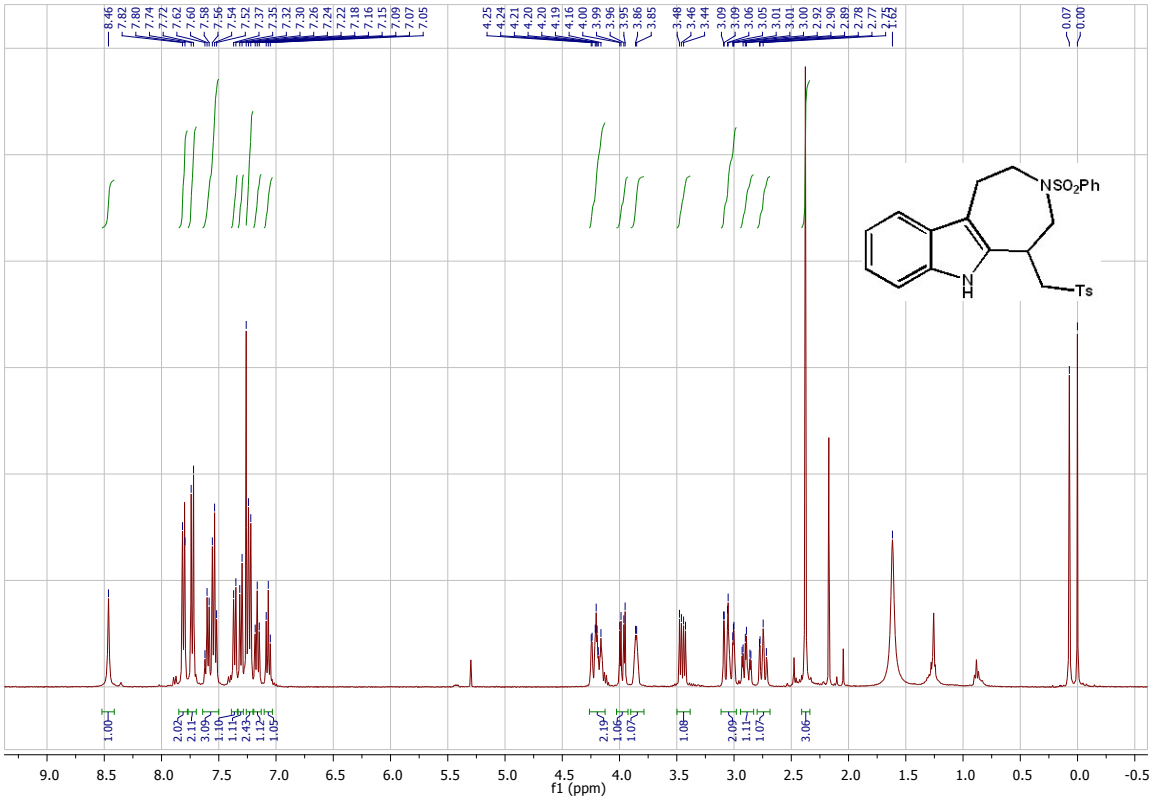

RAVI
144.91
137.09
136.27
129.68
127.57
125.72
122.82
119.89
118.42
111.53
64.34
59.90
43.87
43.59
26.44
21.87
NMs
Ts
N
H
f1 (ppm)

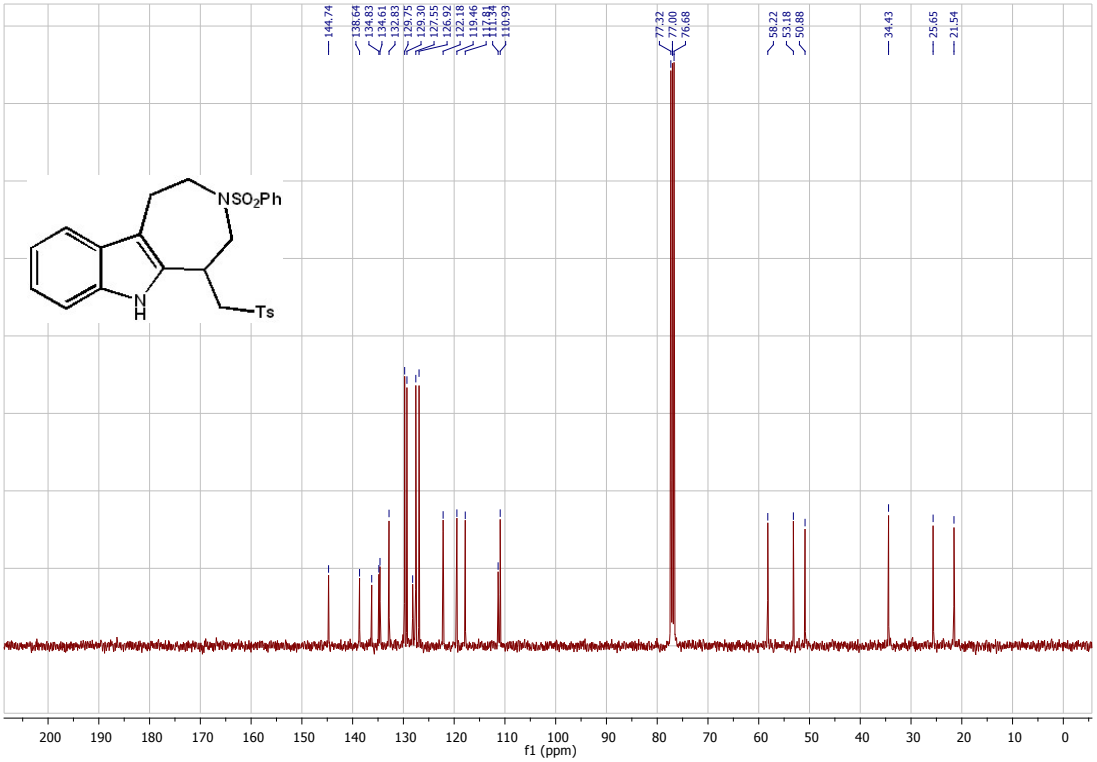
5a



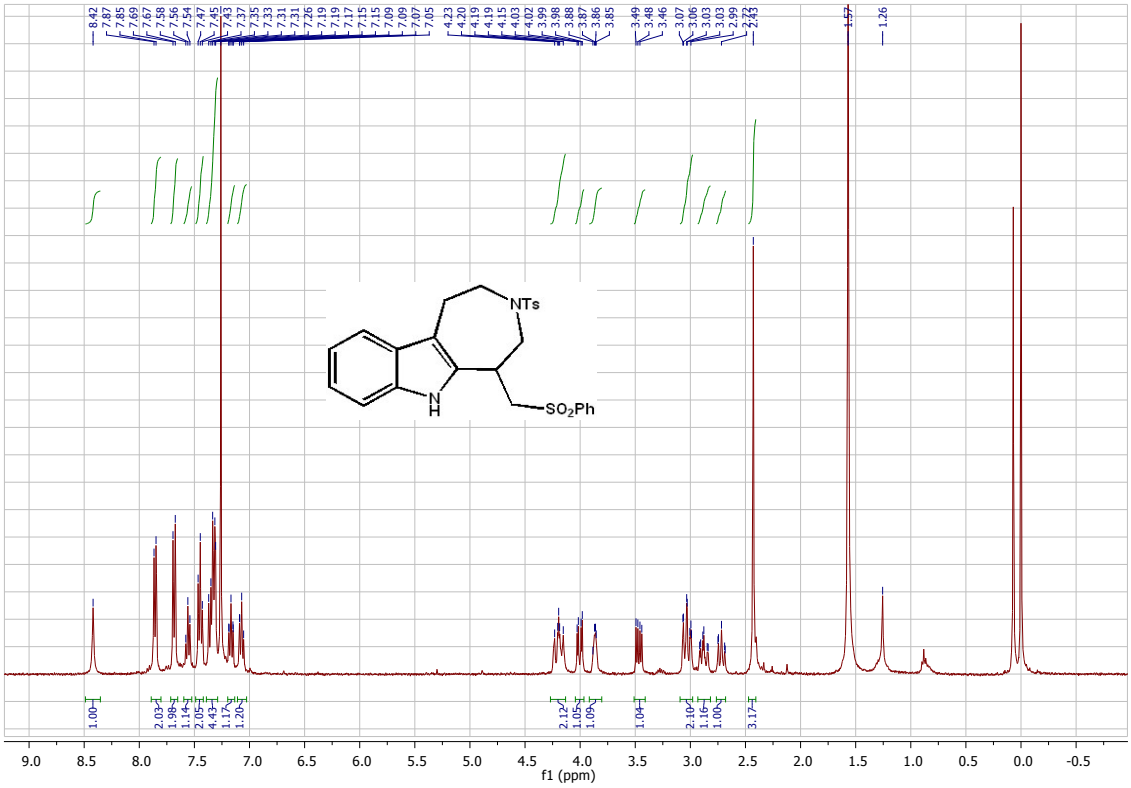


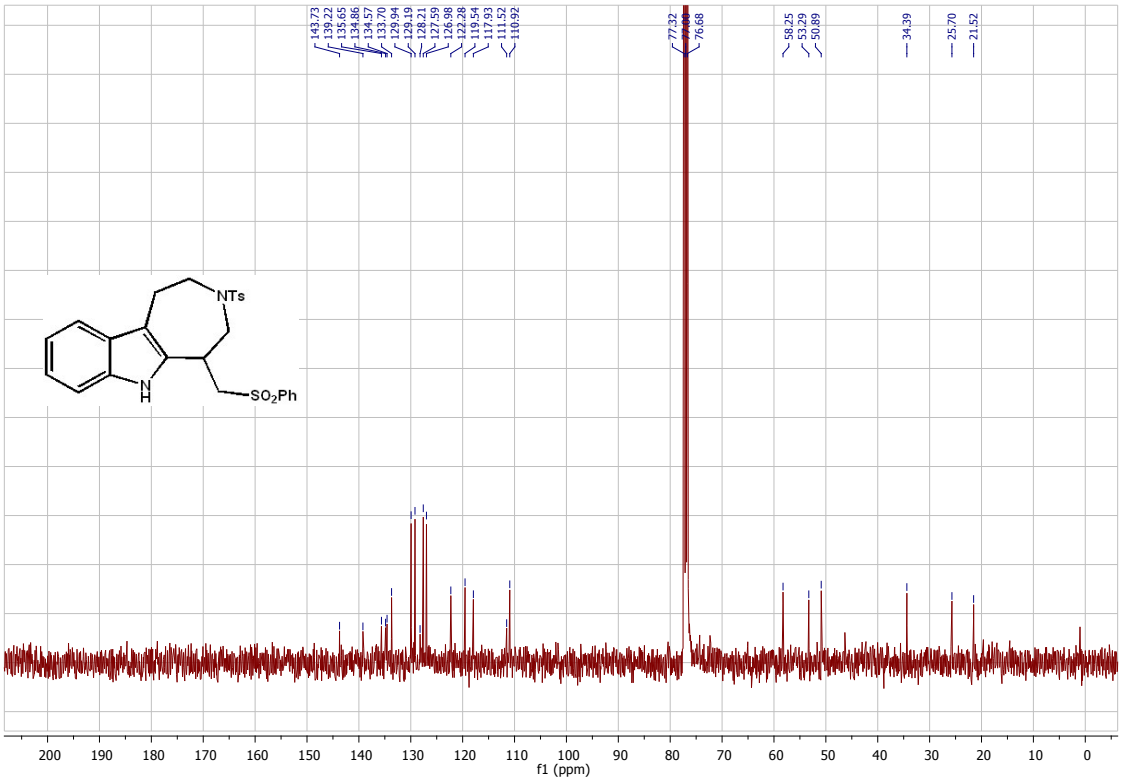
5b



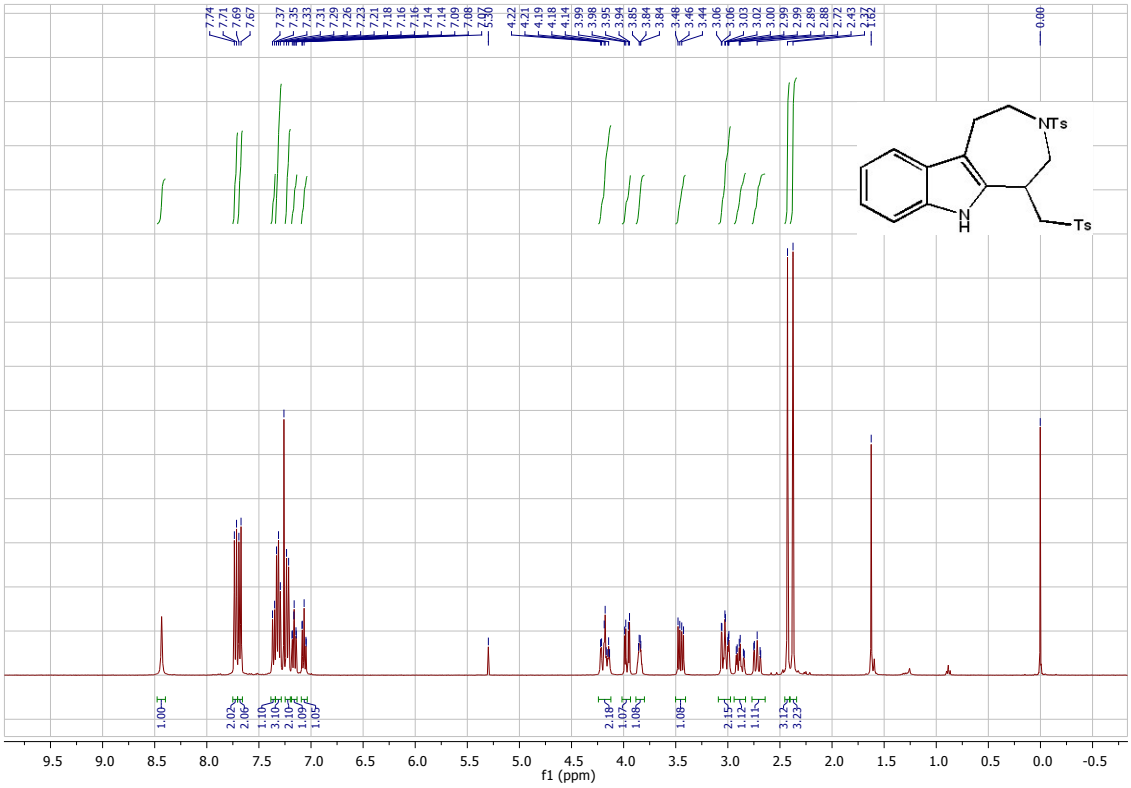


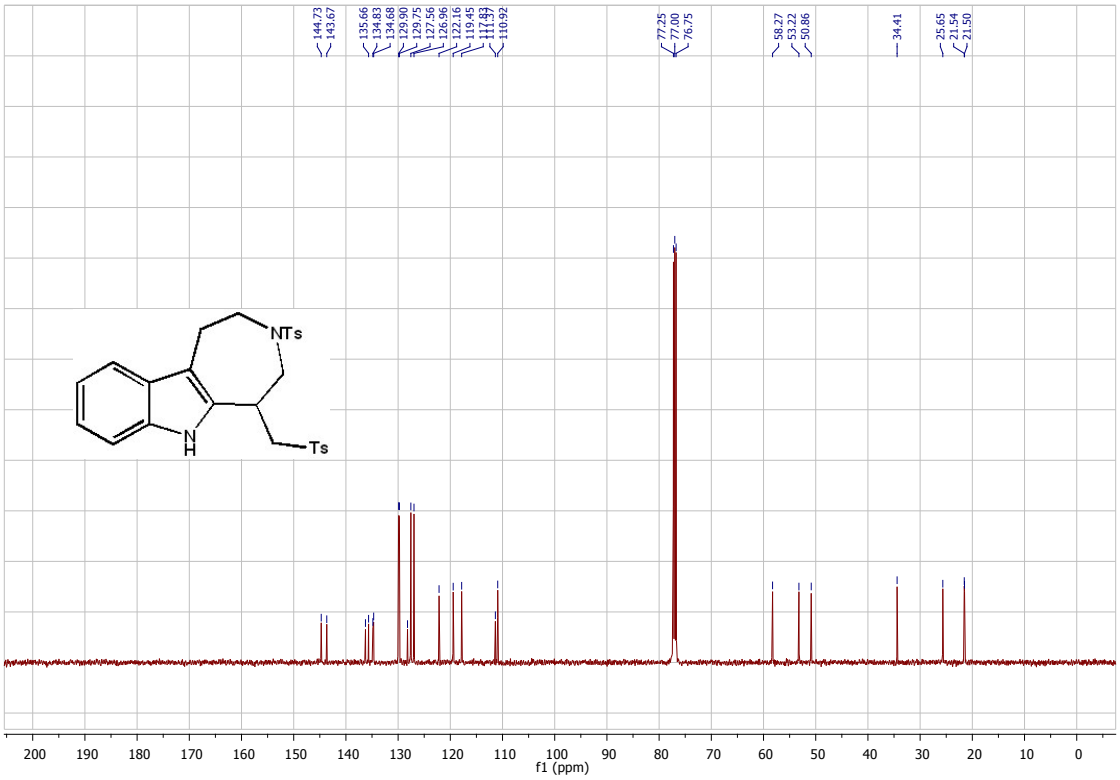
5c



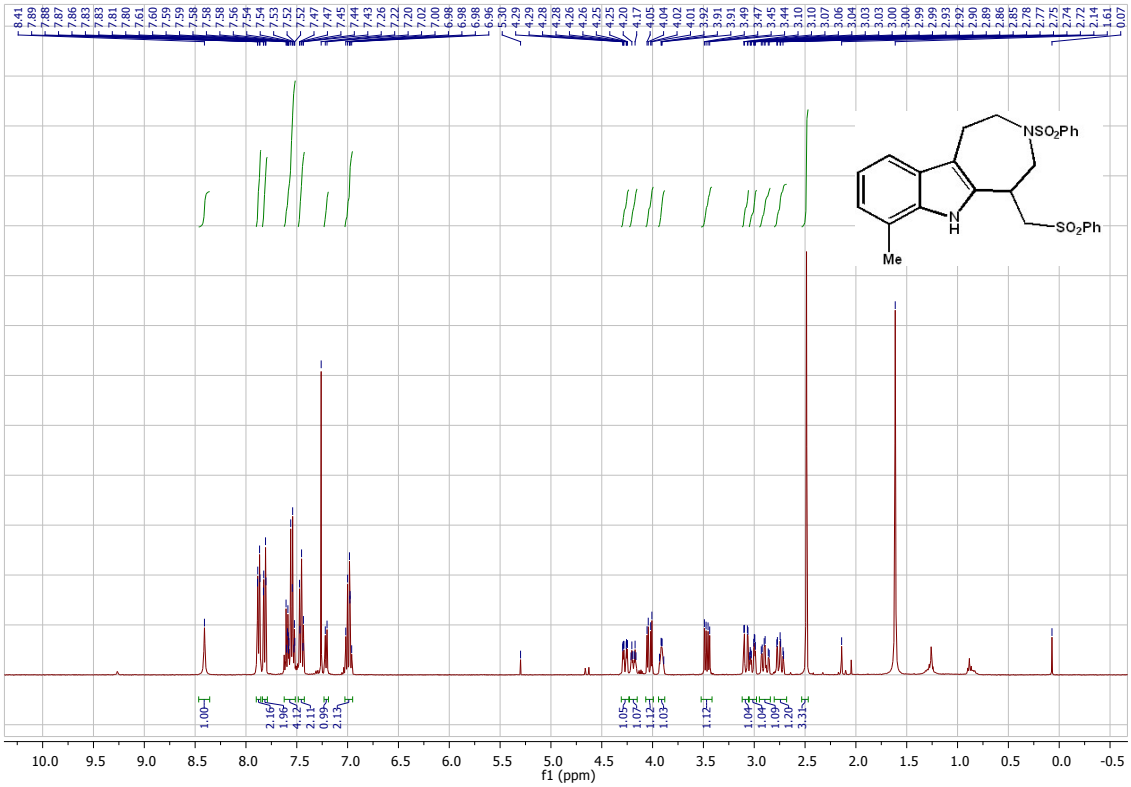


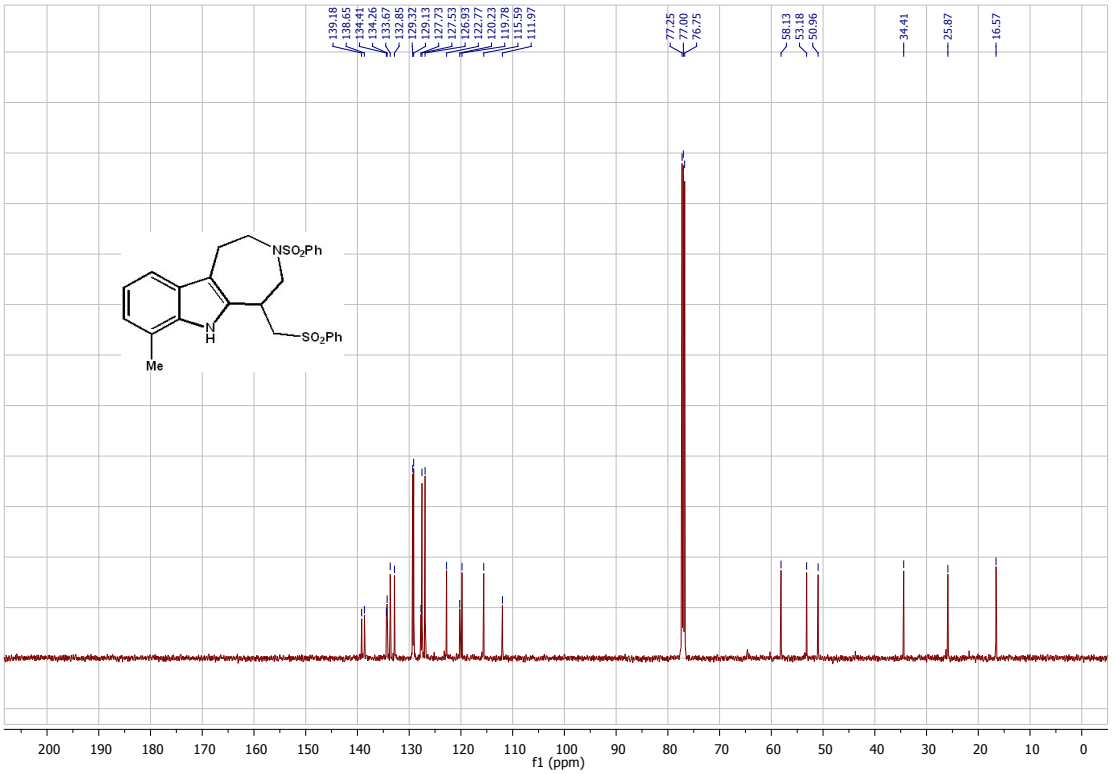
5d



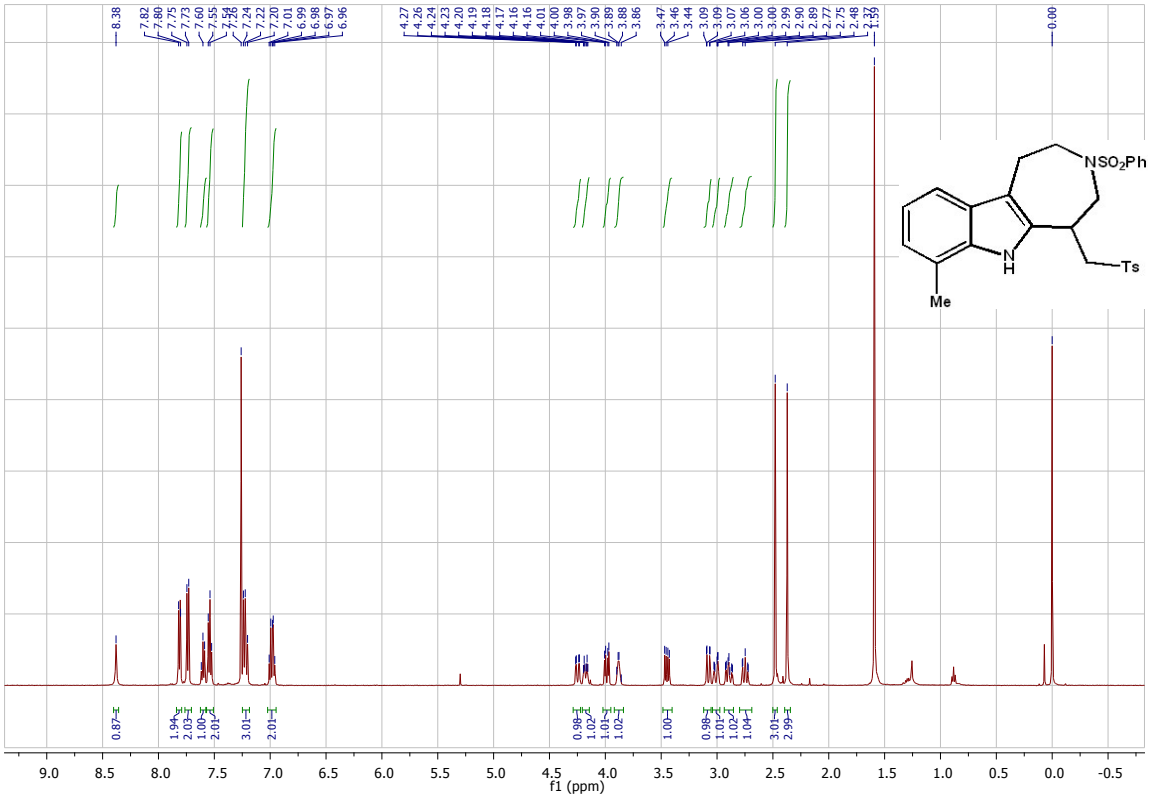


5e





5f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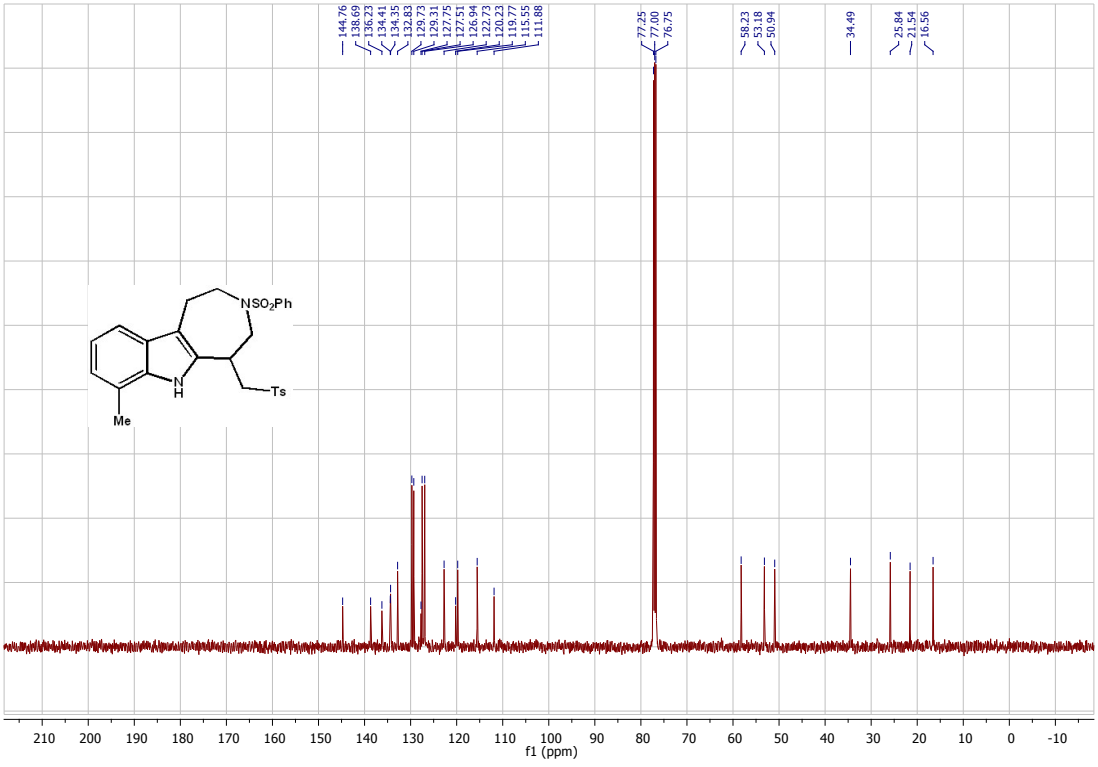
7.22
7.20
7.01
6.99
6.98
6.97
6.96
4.27
4.26
4.24
4.23
4.20
4.19
4.18
4.17
4.16
4.16
4.01
4.00
3.98
3.97
3.90
3.89
3.88
3.86
3.47
3.46
3.44
3.09
3.09
3.07
3.06
3.00
3.00
2.99
2.90
2.89
2.77
2.75
2.48
2.37
1.59
0.00
NSO2Ph
N
H
Ts
Me
0.87
1.94
2.03
1.00
2.01
3.01
2.01
0.98
1.02
1.01
1.02
1.00
0.98
1.01
1.02
1.04
3.01
2.99
f1 (ppm)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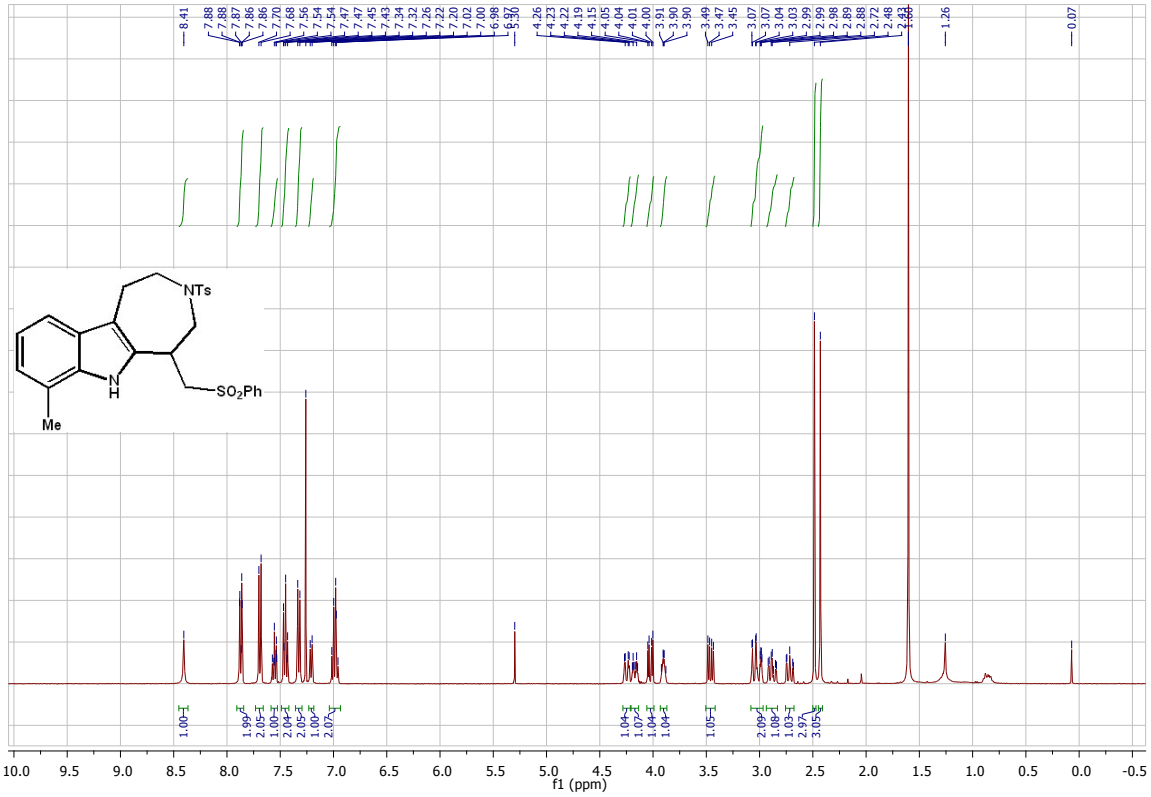
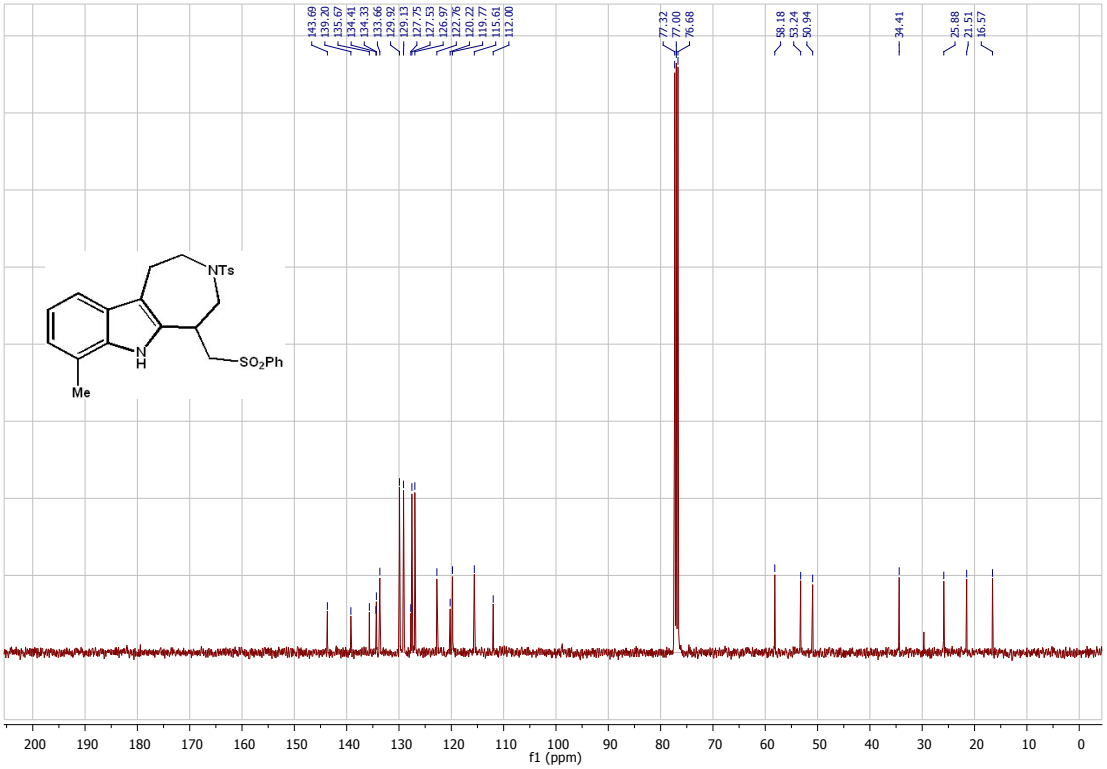
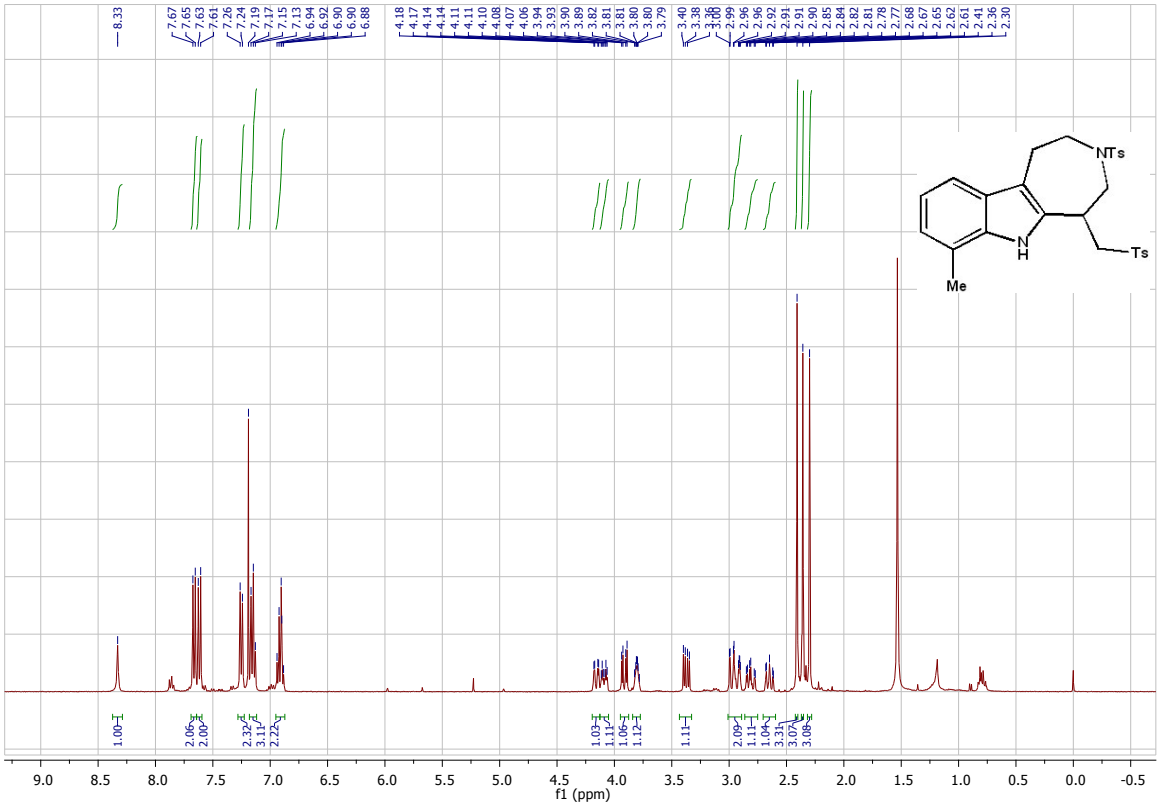
129.31
127.75
127.51
126.94
122.73
120.23
119.77
115.55
111.88
77.25
77.00
76.75
58.23
53.18
50.94
34.49
25.84
21.54
16.56
NSO2Ph
N
H
Ts
Me
f1 (ppm)

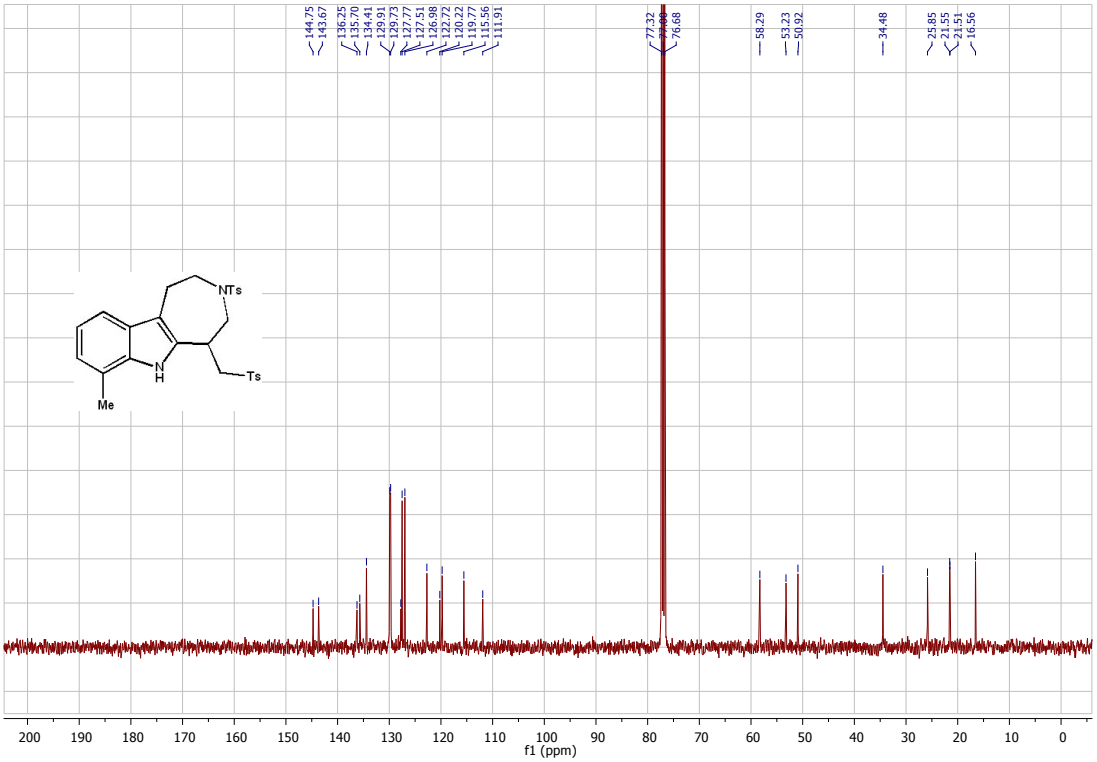
5g



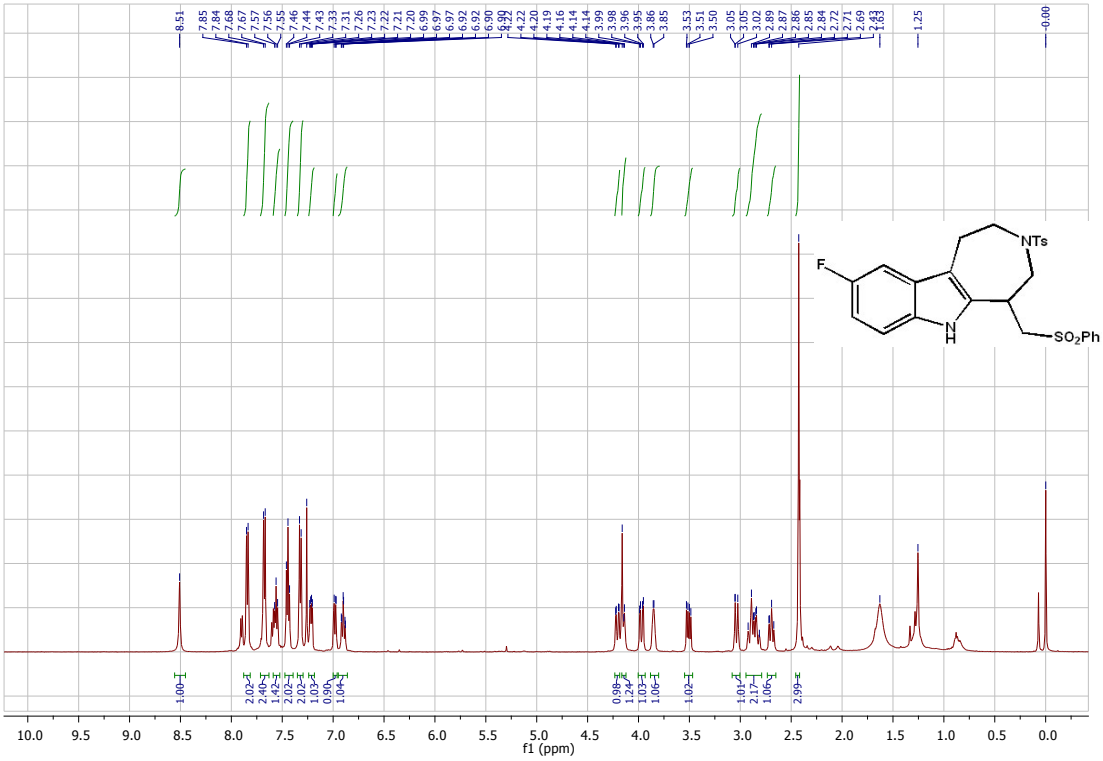


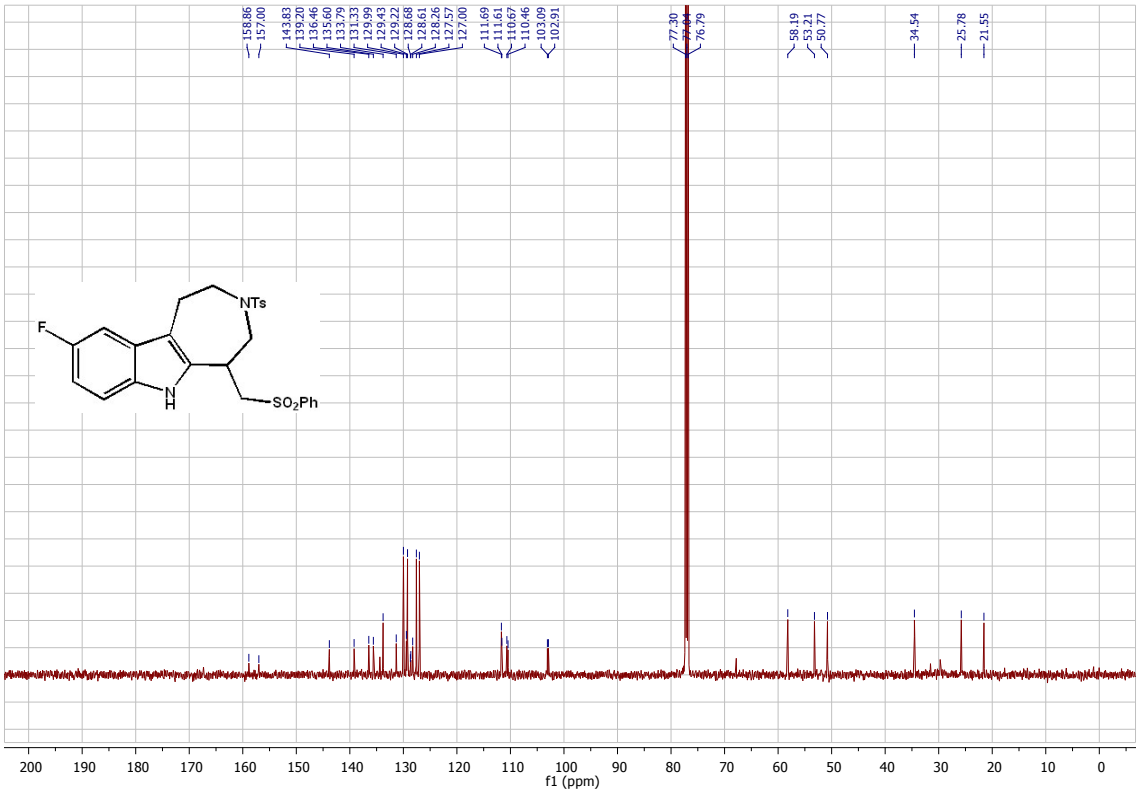
5h



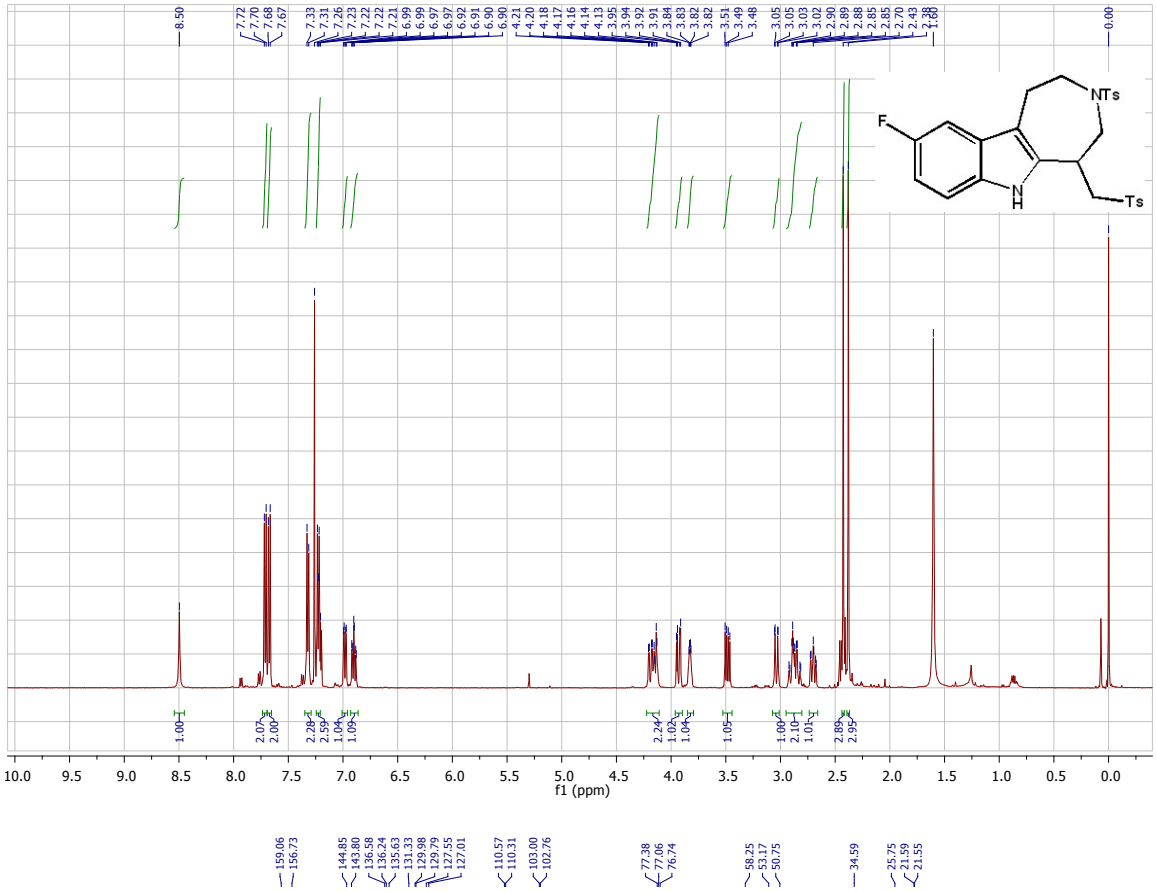


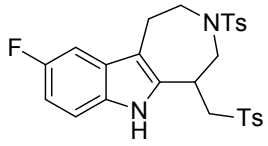
5i

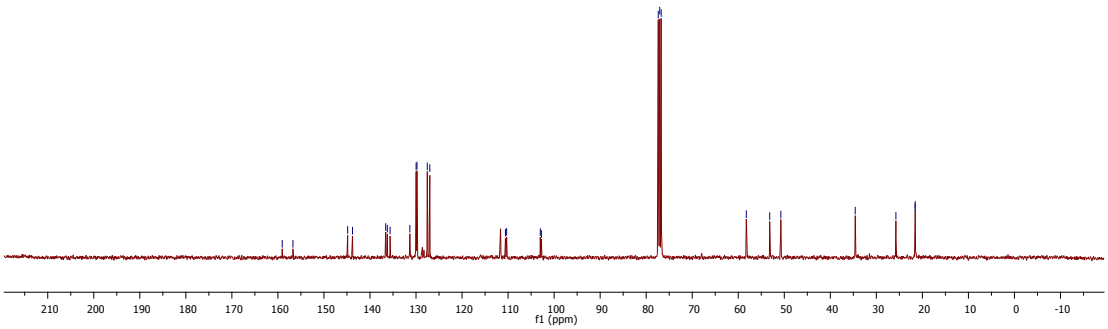




5j







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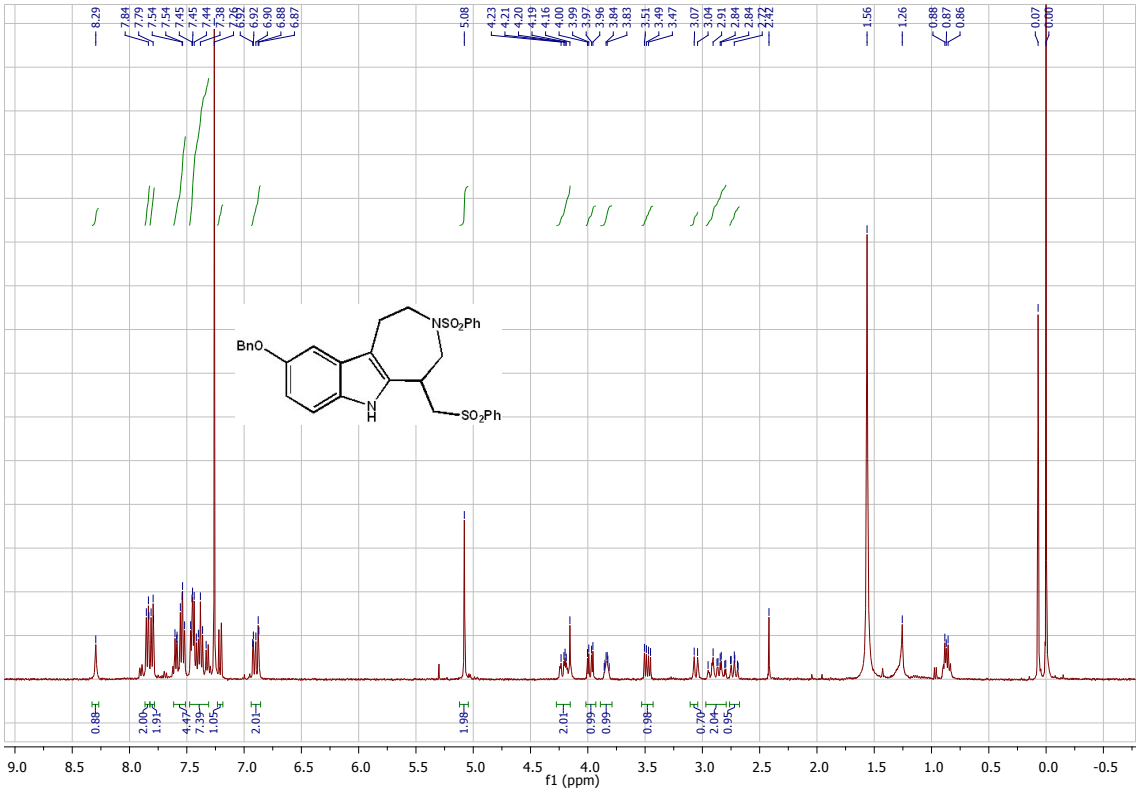
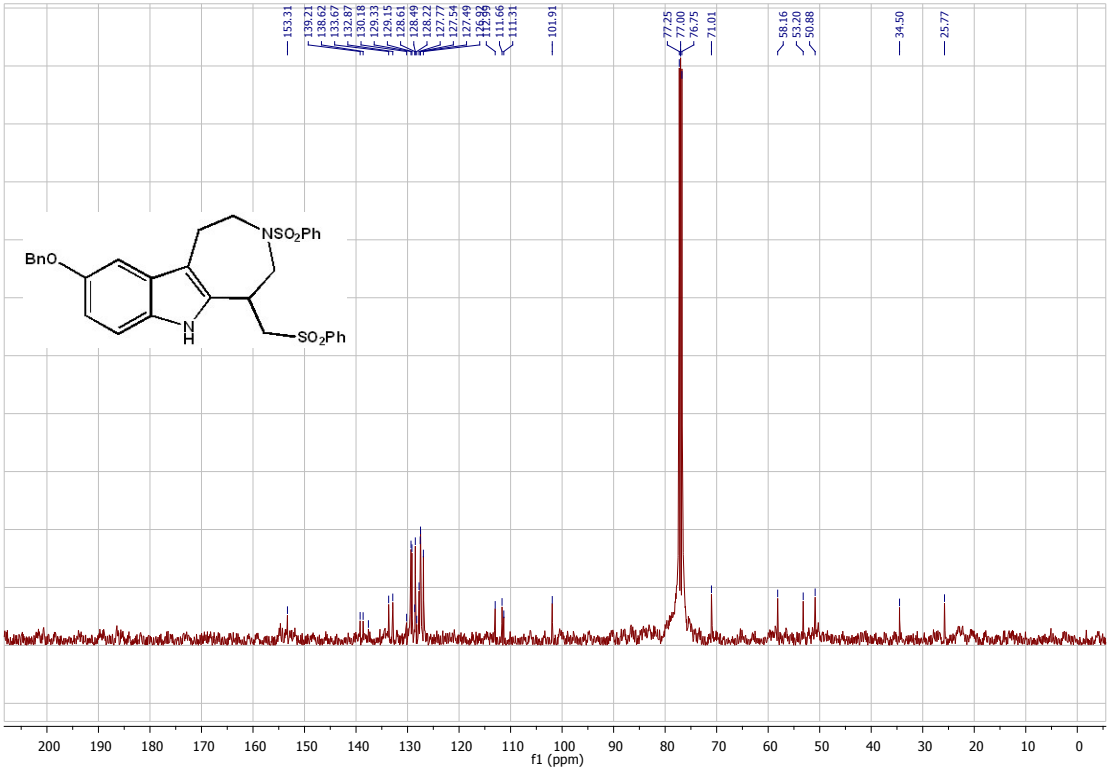
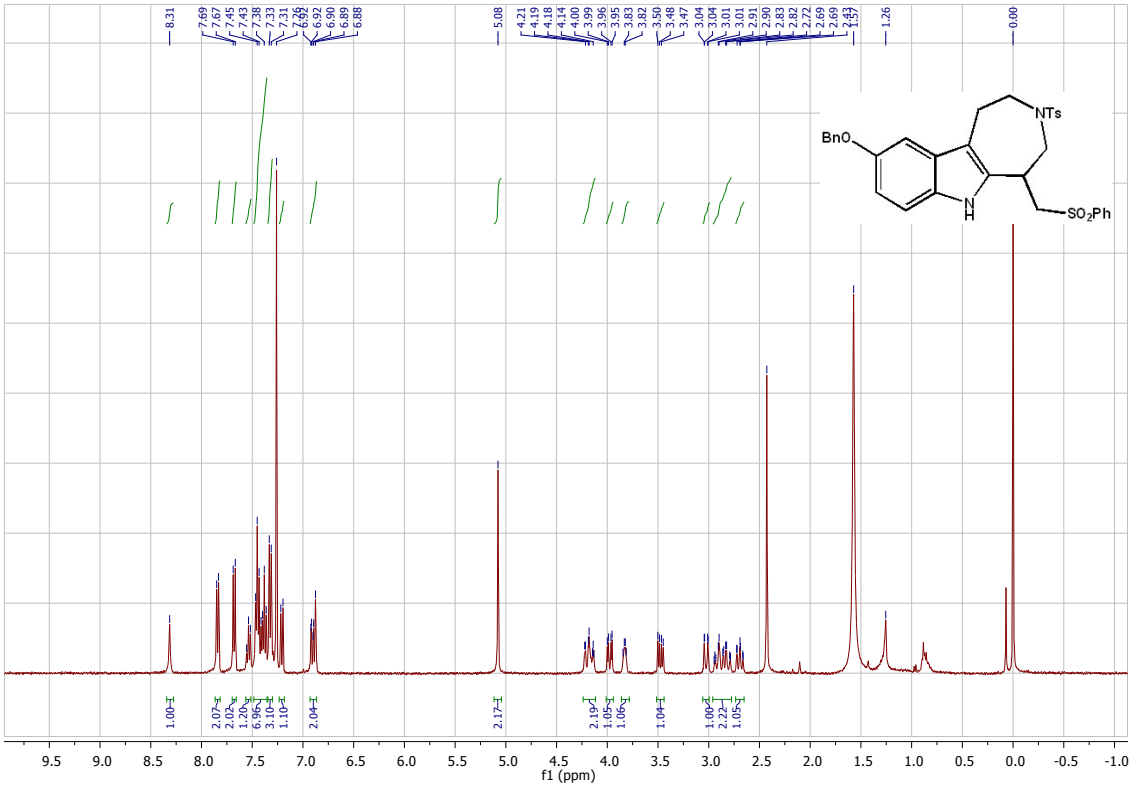




5l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5.08
4.21
4.19
4.18
4.14
4.00
3.99
3.96
3.95
3.83
3.82
3.50
3.48
3.47
3.04
3.01
3.01
2.91
2.90
2.83
2.82
2.72
2.69
2.69
1.26
0.00
BnO
NTs
N
H
SO2Ph
1.00
2.07
2.02
1.20
6.96
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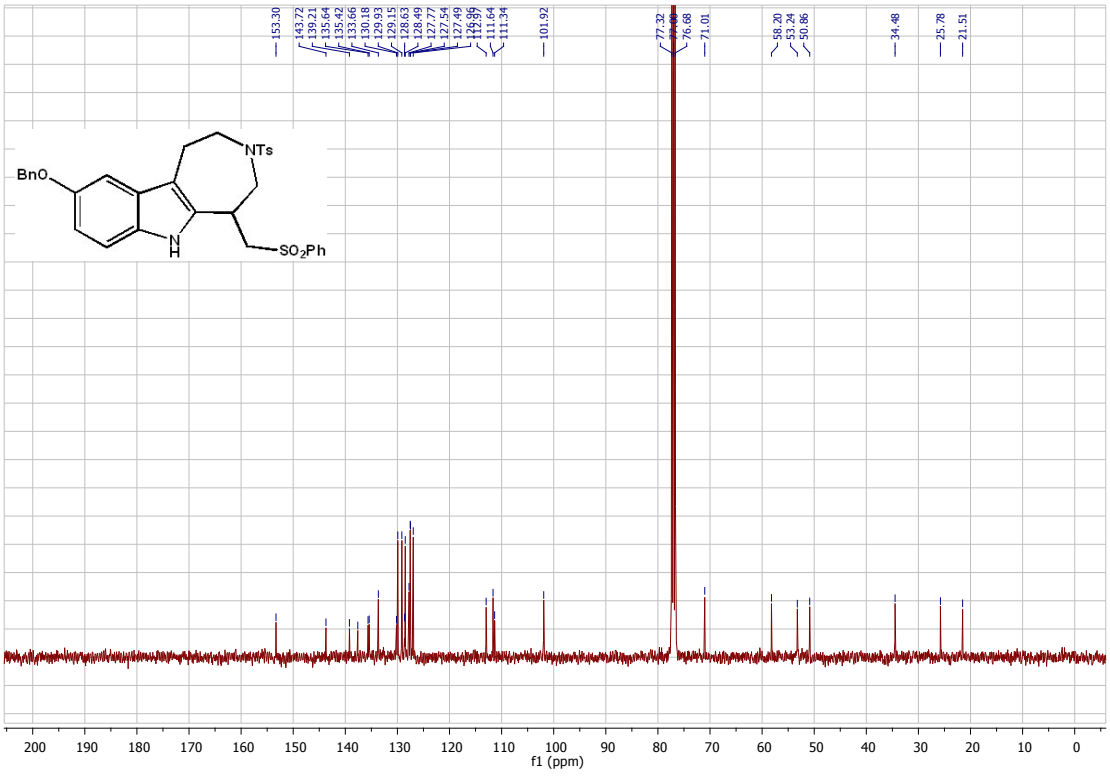
1.10
2.04
2.17
2.19
1.05
1.06
1.04
1.00
2.22
1.05
f1 (ppm)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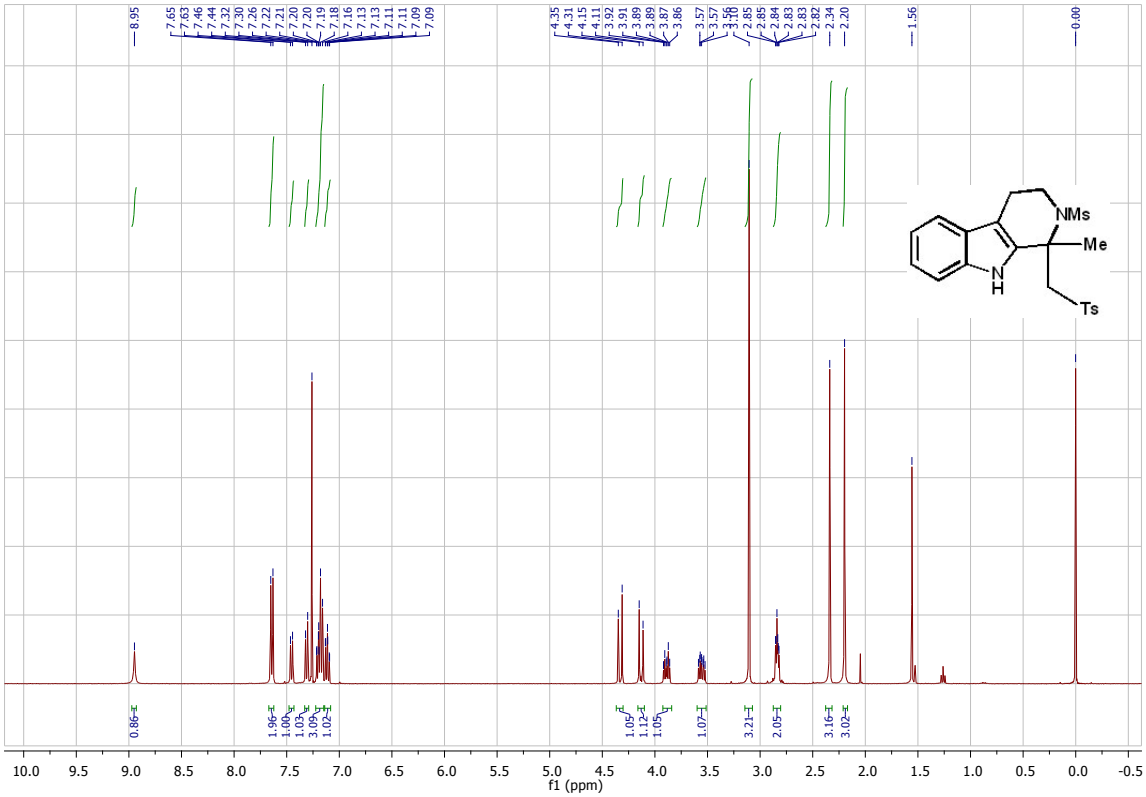
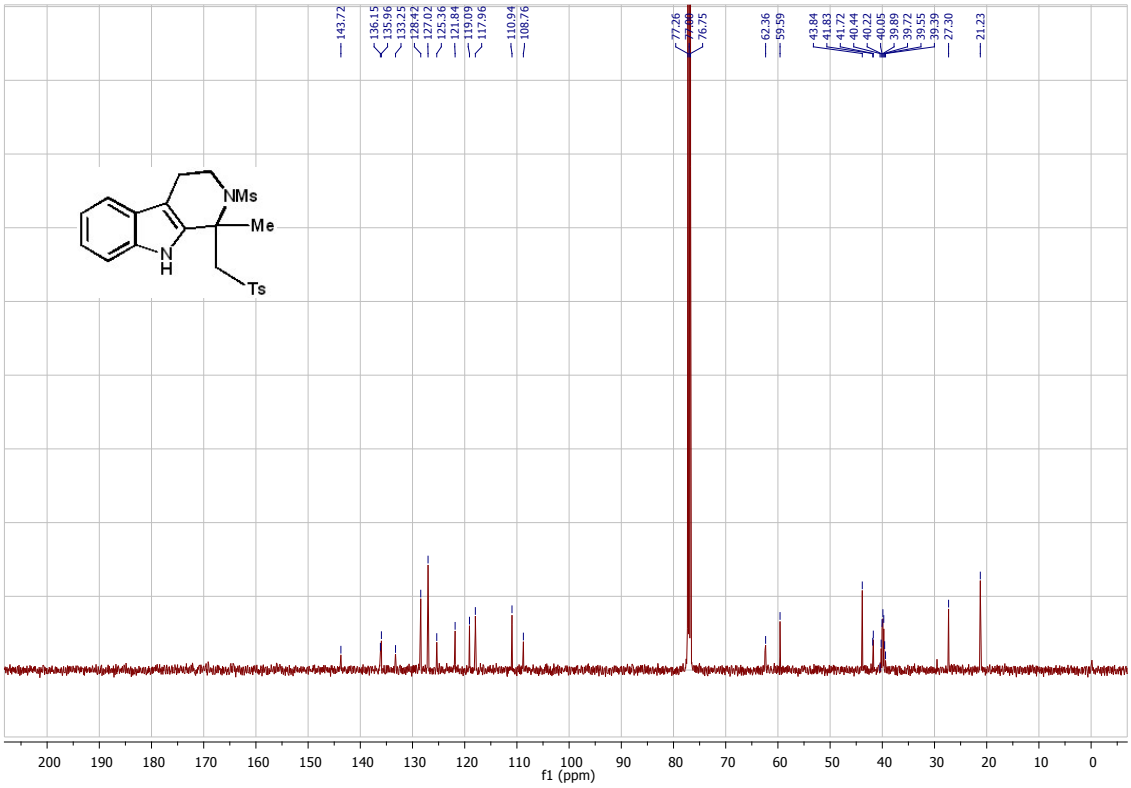
135.64
135.42
133.66
130.18
129.93
129.15
128.63
128.49
127.77
127.54
127.49
111.64
111.34
101.92
77.32
76.68
71.01
58.20
53.24
50.86
34.48
25.78
21.51
BnO
NTs
N
H
SO2Ph
f1 (ppm)

1





5m