Supporting Information

Cp*Co(III)-Catalyzed Oxidative [5+2] Annulation: Regioselective Synthesis of 2-Aminobenzoxepines via C-H/O-H Functionalization of 2-Vinylphenols with Ynamides

Xiang-Lei Han,[a] Xu-Ge Liu,[a] E Lin,[a] Yunyun Chen,[a] Zhuangzhong Chen,[c] Honggen Wang[a] and Qingjiang Li*[ab]

[a] School of Pharmaceutical Sciences, Sun Yat-sen University, Guangzhou, 510006, China

[b] State Key Laboratory of Natural and Biomimetic Drugs, Peking University, Beijing, 100191, China

[c] The First Clinical Medical College, Guangzhou University of Chinese Medicine, Guangzhou, 510405, China

E-mail: liqingj3@mail.sysu.edu.cn

Table of Contents

1. General information

The solvents used were dried by distillation over the drying agents indicated in parentheses and were transferred under argon: toluene (Na), tetrahydrofuran (Na), and acetonitrile (CaH_2). 2,2,2-Trifluoroethanol (TFE), methanol, *N*,*N*-dimethylformamide (DMF) and 1,2-dichloroethane (DCE) were purchased from Energy-chemical. Commercially available chemicals were obtained from commercial suppliers and used without further purification unless otherwise stated.

Proton (^{1}H), fluorine (^{19}F), and carbon (^{13}C) NMR spectra were recorded at 500 (or 400), 376, and 126 (or 101) MHz, respectively. The following abbreviations are used for the multiplicities: s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet, dd = doublet of doublet for proton spectra. Coupling constants (*J*) are reported in hertz (Hz).

High-resolution mass spectra (HRMS) were recorded on a Bruker VPEXII spectrometer with EI and ESI modes unless otherwise stated, and the mass analysis mode of HRMS was TOF.

Analytical thin layer chromatography was performed on Polygram SIL G/UV254 plates. Visualization was accomplished with short wave UV light, or $KMnO_4$ staining solutions followed by heating. Flash column chromatography was performed using silica gel (200-300 mesh) with solvents distilled prior to use.

No attempts were made to optimize yields for substrate preparation.

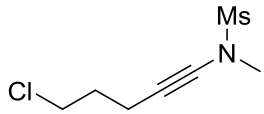
2. Preparation of the starting materials

2.1 Preparation of substrates 2c, 2e, 2f, 2g and 2h

General procedure A:

Following the method reported by Stahl,[1] $CuCl_2$ (0.2 equiv), *N*-methylmethanesulfonamide (2.5 equiv) and Na_2CO_3 (2.0 equiv) were added to a flame-dried 50 mL three-necked round-bottomed flask. The flask was purged with oxygen for 15 min and a solution of pyridine (2 equiv) in dry toluene (0.2 M) was added. A balloon filled with oxygen was connected to the flask and the stirred mixture was heated at 70 ℃. After 15 min, a solution of alkyne (10 mmol, 1 equiv) in dry toluene (0.2 M) was added dropwise. The mixture was allowed to stir at 70 ℃ for another 16 h and was then cooled to rt. The reaction mixture was concentrated under reduced pressure and the residue was purified by flash chromatography.

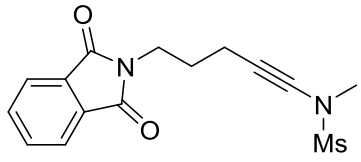
***N*-(5-Chloropent-1-yn-1-yl)-*N*-methylmethanesulfonamide (2c)**



2c

Following the general procedure A，the substrate **2c** was obtained in 38% yield (0.79 g) as a colourless liquid after column chromatography (eluent = petroleum ether/EtOAc 6:1 v/v); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 3.64 (t, *J* = 6.3 Hz, 2H), 3.16 (s, 3H), 3.03 (s, 3H), 2.48 (t, *J* = 6.9 Hz, 2H), 1.97 (p, *J* = 6.7 Hz, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 75.3, 67.4, 43.8, 39.2, 36.3, 31.6, 16.0. **HRMS (ESI-TOF):** *m/z* calculated for $C_7H_{13}ClNO_2S$ $[M+H]^+$: 210.0350, found: 210.0349.

***N*-(5-(1,3-Dioxoisoindolin-2-yl)pent-1-yn-1-yl)-*N*-methylmethanesulfonamide (2e)**

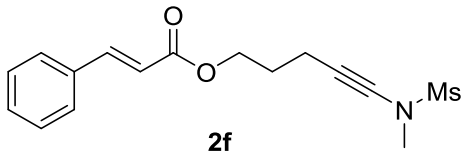


2e

Following the general procedure A，the substrate **2e** was obtained in 78% yield (2.50 g) as a white solid after column chromatography (eluent = petroleum ether/EtOAc 4:1 v/v); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.84 (dd, *J* = 5.3, 3.1 Hz, 2H), 7.72 (dd, *J* = 5.5, 3.1 Hz, 2H), 3.79 (t, *J* = 7.1 Hz, 2H) 3.12 (s, 3H), 3.08 (s, 3H), 2.36 (t, *J* = 6.9 Hz, 2H), 1.91

(p, *J* = 6.9 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 168.5, 134.1, 132.2, 123.4, 75.2, 67.9, 39.2, 37.1, 36.3, 27.8, 16.3. **HRMS (ESI-TOF):** *m/z* calculated for $C_{15}H_{17}N_2O_4S$ $[M+H]^+$: 321.0904, found: 321.0898.

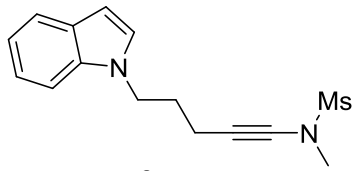
5-(*N*-Methylmethylsulfonamido)pent-4-yn-1-yl cinnamate (2f)



2f

Following the general procedure A，the substrate **2f** was obtained in 48% yield (1.54 g) as a colourless liquid after column chromatography (eluent = petroleum ether/EtOAc 4:1 v/v); **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.69 (d, *J* = 16.1 Hz, 1H), 7.53 (ddd, *J* = 6.0, 3.0, 2.1 Hz, 2H), 7.41 – 7.37 (m, 3H), 6.44 (d, *J* = 16.0 Hz, 1H), 4.30 (t, *J* = 6.3 Hz, 2H), 3.17 (s, 3H), 3.05 (s, 3H), 2.45 (t, *J* = 7.0 Hz, 2H), 1.93 (p, *J* = 6.7 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 167.1, 145.1, 134.4, 130.5, 129.1, 128.2, 118.0, 75.1, 67.9, 63.2, 39.3, 36.3, 28.2, 15.4. **HRMS (ESI-TOF):** *m/z* calculated for $C_{16}H_{20}NO_4S$ $[M+H]^+$: 322.1108, found: 322.1103.

***N*-(5-(1*H*-Indol-1-yl)pent-1-yn-1-yl)-*N*-methylmethanesulfonamide (2g)**

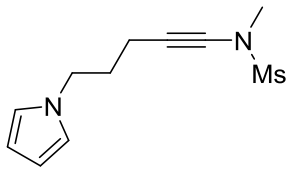


2g

Following the general procedure A，the substrate **2g** was obtained in 39% yield (1.13 g) as a colourless liquid after column chromatography (eluent = petroleum ether/EtOAc 4:1 v/v); **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.64 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.42 – 7.36 (m, 1H), 7.21 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.14 (d, *J* = 3.2 Hz, 1H), 7.11 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 1H), 6.50 (dd, *J* = 3.1, 0.9 Hz, 1H), 4.27 (t, *J* = 6.6 Hz, 2H), 3.16 (s, 3H), 3.02 (s, 3H), 2.25 (t, *J* = 6.7 Hz, 2H), 2.05 (p, *J* = 6.7 Hz, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 136.0, 128.8, 128.2, 121.6, 121.1, 119.4, 109.5, 101.3, 75.4, 67.8, 44.9, 39.2, 36.3, 29.2, 15.9. **HRMS (ESI-TOF):** *m/z* calculated for $C_{15}H_{19}N_2O_2S$ $[M+H]^+$: 291.1162, found: 291.1154.

***N*-(5-(1*H*-Pyrrol-1-yl)pent-1-yn-1-yl)-*N*-methylmethanesulfonamide (2h)**

Following the general procedure A，the substrate **2h** was obtained in 42% yield (1.00 g) as a colourless liquid after column chromatography (eluent = petroleum



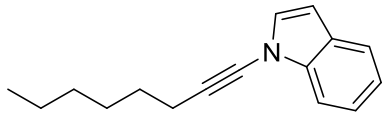
2h

ether/EtOAc 4:1 v/v); **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 6.67 (t, *J* = 2.1 Hz, 2H), 6.14 (t, *J* = 2.1 Hz, 2H), 4.01 (t, *J* = 6.7 Hz, 2H), 3.17 (s, 3H), 3.03 (s, 3H), 2.25 (t, *J* = 6.8 Hz, 2H), 1.95 (p, *J* = 6.8 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 120.7, 108.2, 75.4, 67.7, 48.0, 39.2, 36.3, 30.6, 15.7. **HRMS (ESI-TOF):** *m/z* calculated for $C_{11}H_{17}N_2O_2S$ $[M+H]^+$: 241.1005, found: 241.0997.

2.2 Representative procedure for synthesis of compound 2p:

According to the known procedure:[2] Using indole (702 mg, 6.0 mmol), K_3PO_4 (2.55 g, 12.0 mmol), $CuSO_4$ $5H_2O$ (150 mg, 0.6 mmol), 1,10-phenanthroline (216 mg, 1.2 mmol) and 1-bromooct-1-yne (1.52 g, 8.1 mmol) at 70 ℃ for 28 h. Column chromatography was replaced by filtration through a 5 cm deep x 6.5 cm diameter pad of silica gel eluting with hexane. After the solvent was removed under reduced pressure, the residue was recrystallised from hexane, isolated by filtration, and washed with ice cold hexane (20 mL) to give ynamide **2p** as a pale yellow liquid (0.77 g, 57%).

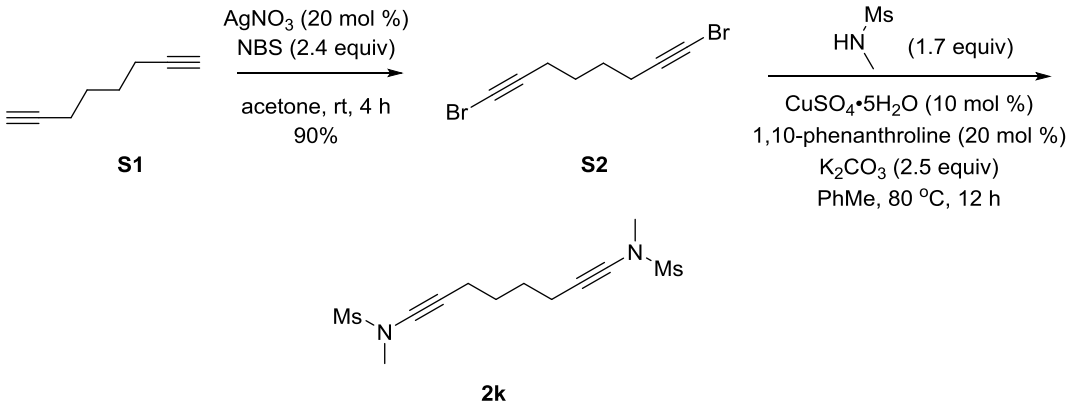
1-(Oct-1-yn-1-yl)-1*H*-indol (2p)



2p

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.60 (d, *J* = 7.8 Hz, 1H), 7.54 (d, *J* = 8.1 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.22 – 7.16 (m, 2H), 6.52 (d, *J* = 3.4 Hz, 1H), 2.48 (t, *J* = 7.0 Hz, 2H), 1.65 (p, *J* = 7.0 Hz, 2H), 1.56 – 1.46 (m, 2H), 1.36 (dq, *J* = 7.0, 3.8, 3.3 Hz, 4H), 0.93 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 138.4, 129.2, 127.6, 123.3, 121.6, 121.1, 111.2, 104.4, 72.1, 70.2, 31.5, 29.1, 28.7, 22.7, 18.6, 14.2. **HRMS (ESI-TOF):** *m/z* calculated for $C_{11}H_{17}N_2O_2S$ $[M+H]^+$: 226.1590, found: 266.1988.

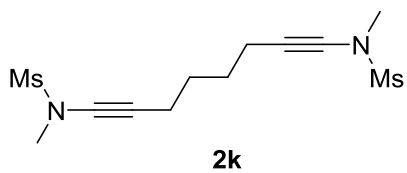
2.3 Representative procedure for synthesis of compound 2k:



To a solution of octa-1,7-diyne (**S1**) (10.0 mmol, 1.0 equiv) in acetone (30 mL) was added NBS (2.14 g, 12.0 mmol, 1.2 equiv) and $AgNO_3$ (169.9 mg, 1.0 mmol, 10 mol %), the resulting mixture was stirred under Ar at room temperature for 4 hours. After removing excess acetone, the reaction was quenched with saturated NH_4Cl solution. The organic layer was extracted with petroleum ether (30 mL x 2), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford bromoalkyne **S2** .

To a dried flask was added *N*-methymethanesulphonamide (1.11 g, 10.2 mmol, 1.7 equiv), $CuSO_4$ $5H_2O$ (150 mg, 0.6 mmol, 10 mol %), 1,10-phenanthroline (216 mg, 1.2 mmol, 20 mol %) and K_2CO_3 (2.07 g, 15.0 mmol, 2.5 equiv). The resulting mixture was subsequently treated with anhydrous toluene (25 mL) and bromoalkyne **S2** (6.0 mmol), and stirred at 80 ^oC for 16 h under Ar. After completion, the crude mixture was cooled to room temperature, filtered through Celite, and concentrated in vacuo. The resulting residue was purified by flash column chromatography on silica gel, giving the pure ynamide **2k** as a white solid (1.4 g, 44%).

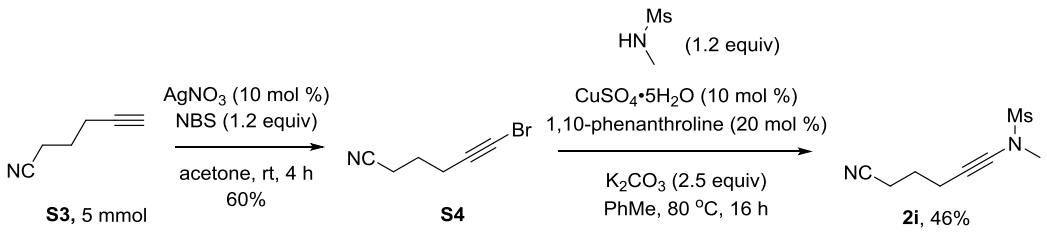
***N*,*N*'-(Octa-1,7-diyne-1,8-diyl)bis(*N*-methylmethanesulfonamide) (2k)**



2k

^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.15 (s, 6H), 3.03 (s, 6H), 2.31 (tt, *J* = 5.4, 1.9 Hz, 4H), 1.68 – 1.50 (m, 4H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 74.7, 68.7, 39.3, 36.1, 28.1, 18.1. **HRMS (ESI-TOF):** *m/z* calculated for $C_{12}H_{21}N_2O_4S_2$ $[M+H]^+$: 321.0937, found: 321.0922.

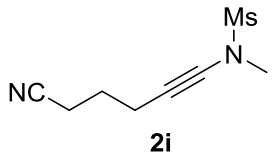
2.4 Representative procedure for synthesis of compound 2i:



To a solution of hex-5-ynenitrile (**S3**) (5.0 mmol, 1.0 equiv) in acetone (20 mL) was added NBS (1.07 g, 6.0 mmol, 1.2 equiv) and $AgNO_3$ (80.0 mg, 0.5 mmol, 10 mol %), the resulting mixture was stirred under Ar at room temperature for 4 hours. After removing excess acetone, the reaction was quenched with saturated NH_4Cl solution. The organic layer was extracted with petroleum ether (20 mL x 2), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford bromoalkyne **S4**.

To a dried flask was added *N*-methymethanesulphonamide (0.39 g, 3.6 mmol, 1.2 equiv), $CuSO_4$ $5H_2O$ (75 mg, 0.3 mmol, 10 mol %), 1,10-phenanthroline (108 mg, 0.6 mmol, 20 mol %) and K_2CO_3 (1.04 g, 7.5 mmol, 2.5 equiv). The resulting mixture was subsequently treated with anhydrous toluene (15 mL) and bromoalkyne **S4** (3.0 mmol), and stirred at 80 ^oC for 16 h under Ar. After completion, the crude mixture was cooled to room temperature, filtered through Celite, and concentrated in vacuo. The resulting residue was purified by flash column chromatography on silica gel, giving the pure ynamide **2i** as a colourless liquid (276 mg, 46%).

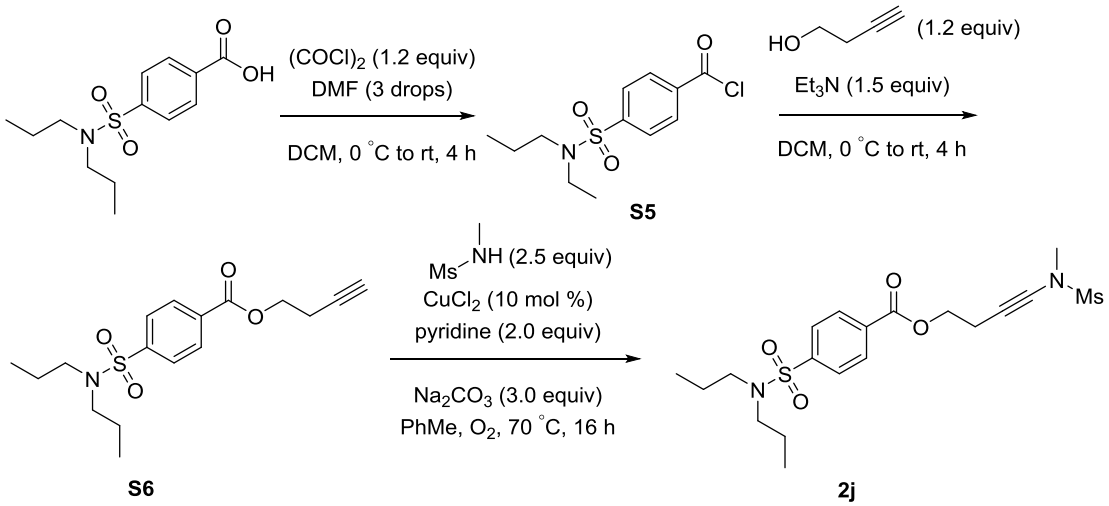
***N*-(5-Cyanopent-1-yn-1-yl)-*N*-methylmethanesulfonamide (2i)**



2i

^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.17 (s, 3H), 3.04 (s, 3H), 2.49 (td, *J* = 6.9, 1.8 Hz, 4H), 1.87 (p, *J* = 6.8 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 119.3, 76.2, 66.5, 39.1, 36.5, 24.8, 17.7, 16.3. **HRMS (ESI-TOF):** *m/z* calculated for $C_{11}H_9N_2O_2$ $[M+H]^+$: 201.0659, found: 201.0658.

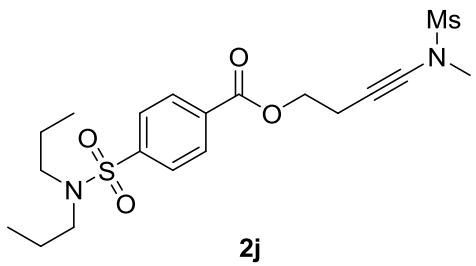
2.5 Representative procedure for synthesis of compound 2j:



To a solution of 4-(*N*,*N*-dipropylsulfamoyl)benzoic acid (10 mmol) and DMF (3 drops) in CH_2Cl_2 (30 mL) under N_2 atmosphere was dropwise added oxalyl chloride (1.0 mL, 12 mmol) at 0 ℃. After 5 min, the mixture was stirred at room temperature for 6 h, then solvent was removed under reduced pressure to give the residue **S5**. To a solution of but-3-yn-1-ol (15 mmol), Et_3N (2.08 mL, 7.5 mmol) in CH_2Cl_2 (30 mL) under N_2 atmosphere was dropwise added **S5** (dissolved in 15 mL) at 0 ℃. Then, the mixture was stirred at room temperature for 6 h. After 6 h, the reaction mixture was concentrated under reduced pressure and the residue was purified by flash chromatography to give the pure **S6** as a colourless liquid (95%).

$CuCl_2$ (0.2 equiv), *N*-methylmethanesulfonamide (2.5 equiv) and Na_2CO_3 (2.0 equiv) were added to a flame-dried 50 mL three-necked round-bottomed flask. The flask was purged with oxygen for 15 min and a solution of pyridine (2 equiv) in dry toluene (0.2 M) was added. A balloon filled with oxygen was connected to the flask and the stirred mixture was heated at 70 ℃. After 15 min, a solution of alkyne **S6** (4 mmol, 1 equiv) in dry toluene (0.2 M) was added dropwise. The mixture was allowed to stir at 70 ℃ for another 16 h and was then cooled to rt. The reaction mixture was concentrated under reduced pressure and the residue was purified by flash chromatography to afford the pure ynamide **2j** (0.75 g, 42%) as a colourless liquid.

4-(*N*-Methylmethylsulfonamido)but-3-yn-1-yl4-(*N*,*N*-dipropylsulfamoyl)benzoate (2j)

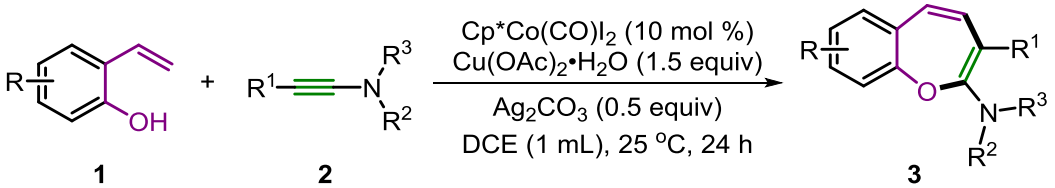


2j

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.15 (d, *J* = 8.5 Hz, 2H), 7.85 (d, *J* = 8.5 Hz, 2H), 4.42 (t, *J* = 6.7 Hz, 2H), 3.13 (s, 3H), 3.10 – 3.05 (m, 2H), 2.99 (s, 3H), 2.76 (t, *J* = 6.7 Hz, 2H), 1.52 (h, *J* = 7.4 Hz, 4H), 0.84 (t, *J* = 7.4 Hz , 6H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 165.1, 144.5, 133.3, 130.4, 127.1, 75.9, 64.8, 63.4, 49.9, 39.1, 36.4, 21.9, 19.2, 11.2. **HRMS (ESI-TOF):** *m/z* calculated for $C_{19}H_{29}N_2O_6S_2$ $[M+H]^+$: 445.1462, found: 445.1465.

3. General procedure for the synthesis of compounds 3

General Procedure B:

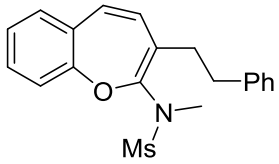


1 **2** **3**

2-Vinylphenols **1** (0.3 mmol, 1.5 equiv), [Cp*Co(CO)I_2] (9.8 mg, 10 mol%), $Cu(OAc)_2$ ·H_2O (60 mg, 1.5 equiv), Ag_2CO_3 (28 mg, 0.5 equiv), DCE (1.0 mL) and ynamides **2** (0.2 mmol) were added to a 15 mL Schlenk tube. The mixture was stirred at 25 ℃ for 24 h under air, then the reaction mixture was diluted with EtOAc (10 mL) and H_2O (10 mL). The organic layer was separated and the aqueous phase was extracted with EtOAc (3×10 mL). The combined organic layer was washed with brine (10 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford the desired products **3**.

4. Characterization of products

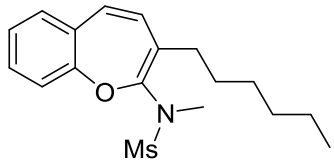
***N*-methyl-*N*-(3-phenethylbenzo[*b*]oxepin-2-yl)methanesulfonamide (3aa)**



3aa

Following the general procedure B，the product **3aa** was obtained in 72% yield (51.1 mg) as a white solid after column chromatography (eluent = petroleum ether/EtOAc 6:1 v/v); (PE/EA = 4/1, $R_F \approx 0.37$). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.29 (ddd, *J* = 7.9, 6.6, 2.5 Hz, 1H), 7.25 – 7.13 (m, 2H), 7.07 – 6.98 (m, 3H), 7.00 – 6.91 (m, 2H), 6.85 (d, *J* = 8.0 Hz, 1H), 6.81 (d, *J* = 11.3 Hz, 1H), 6.15 (d, *J* = 11.2 Hz, 1H), 3.04 (s, 3H), 2.68 (s, 2H), 2.58 (s, 2H), 2.56 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 156.9, 142.7, 141.0, 132.1, 130.8, 130.3, 130.2, 129.1, 128.9, 128.1, 125.9, 125.3, 124.6, 120.6, 38.3, 36.4, 34.7, 34.1. **HRMS (ESI-TOF):** *m/z* calculated for $C_{10}H_{22}NO_3S$ $[M+H]^+$: 356.1315, found: 356.1332.

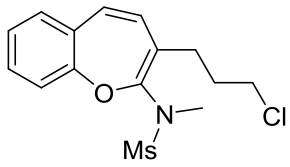
***N*-(3-Hexylbenzo[*b*]oxepin-2-yl)-*N*-methylmethanesulfonamide (3ab)**



3ab

Following the general procedure B，the product **3ab** was obtained in 70% yield (46.9 mg) as a colourless liquid after column chromatography (eluent = petroleum ether/EtOAc 6:1 v/v); (PE/EA = 6/1, $R_F \approx 0.21$). **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.33 – 7.25 (m, 1H), 7.17 – 7.10 (m, 2H), 6.96 (d, *J* = 8.1 Hz, 1H), 6.72 (d, *J* = 11.3 Hz, 1H), 6.09 (d, *J* = 11.3 Hz, 1H), 3.17 (s, 3H), 3.11 (s, 3H), 2.28 (d, *J* = 12.1 Hz, 2H), 1.42 – 1.32 (m, 2H), 1.29 – 1.16 (m, 6H), 0.83 (t, *J* = 6.8 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 157.1, 141.7, 131.5, 130.6, 130.2, 130.2, 129.4, 126.1, 125.3, 120.5, 38.5, 37.3, 31.8, 31.7, 29.1, 28.5, 22.6, 14.1. **HRMS (ESI-TOF):** *m/z* calculated for $C_{18}H_{26}NO_3S$ $[M+H]^+$: 336.1628, found: 336.1617.

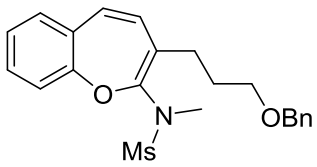
***N*-(3-(3-Chloropropyl)benzo[*b*]oxepin-2-yl)-*N*-methylmethanesulfonamide (3ac)**



3ac

Following the general procedure B，the product **3ac** was obtained in 72% yield (47.1 mg) as a colourless liquid after column chromatography (eluent = petroleum ether/EtOAc 6:1 v/v); (PE/EA = 4/1, $R_F \approx 0.30$). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.31 (dp, *J* = 8.4, 4.0 Hz, 1H), 7.15 (d, *J* = 4.5 Hz, 2H), 6.96 (d, *J* = 8.1 Hz, 1H), 6.74 (d, *J* = 11.2 Hz, 1H), 6.07 (d, *J* = 11.2 Hz, 1H), 3.46 (t, *J* = 6.5 Hz, 2H), 3.18 (s, 3H), 3.11 (s, 3H), 2.44 (s, 2H), 1.89 (p, *J* = 7.5 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 156.9, 142.6, 132.0, 130.5, 130.4, 129.5, 129.4, 125.4, 124.3, 120.6, 44.5, 38.5, 37.2, 31.4, 29.0. **HRMS (ESI-TOF):** *m/z* calculated for $C_{15}H_{19}ClNO_3S$ $[M+H]^+$: 328.0769, found: 328.0764.

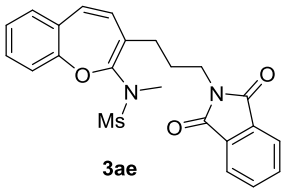
***N*-(3-(3-(benzyloxy)propyl)benzo[*b*]oxepin-2-yl)-*N*-methylmethanesulfonamide (3ad)**



3ad

Following the general procedure B，the product **3ad** was obtained in 56% yield (44.7 mg) as a colourless liquid after column chromatography (eluent = petroleum ether/EtOAc 6:1 v/v); (PE/EA = 4/1, $R_F \approx 0.29$). **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.36 – 7.25 (m, 6H), 7.14 (d, *J* = 4.0 Hz, 2H), 6.96 (d, *J* = 8.1 Hz, 1H), 6.72 (d, *J* = 11.3 Hz, 1H), 6.10 (d, *J* = 11.3 Hz, 1H), 4.44 (s, 2H), 3.43 (t, *J* = 6.4 Hz, 2H), 3.14 (s, 3H), 3.09 (s, 3H), 2.37 (s, 2H), 1.74 (q, *J* = 7.4 Hz, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 157.0, 142.0, 138.6, 131.6, 130.5, 130.28, 130.0, 129.4, 128.5, 127.8, 127.6, 125.4, 125.3, 120.6, 72.9, 69.8, 38.6, 37.2, 28.7, 28.4. **HRMS (ESI-TOF):** *m/z* calculated for $C_{22}H_{26}NO_4S$ $[M+H]^+$: 400.1577, found: 400.1583.

***N*-(3-(3-(1,3-dioxoisoindolin-2-yl)propyl)benzo[b]oxepin-2-yl)-*N*-methylmethanesulfonamide (3ae)**

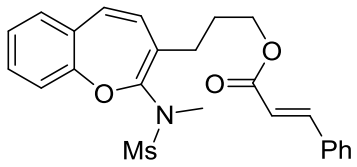


3ae

Following the general procedure B，the product **3ae** was obtained in 63% yield (55.2 mg) as a colourless liquid after column chromatography (eluent = petroleum ether/EtOAc 4:1 v/v); (PE/EA = 2/1, $R_F \approx 0.25$). **^{1}H NMR (400 MHz, $CDCl_3$)**

δ = 7.80 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.68 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.32 – 7.24 (m, 1H), 7.13 – 7.06 (m, 2H), 6.97 – 6.90 (m, 1H), 6.71 (d, *J* = 11.4 Hz, 1H), 6.08 (d, *J* = 11.2 Hz, 1H), 3.63 (t, *J* = 7.5 Hz, 2H), 3.17 (s, 3H), 3.08 (s, 3H), 2.36 (t, *J* = 6.9 Hz, 2H), 1.80 (q, *J* = 7.8 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 168.4, 156.9, 142.2, 134.0, 132.2, 131.9, 130.4, 130.3, 129.5, 129.4, 125.4, 124.7, 123.3, 120.6, 38.4, 37.8, 37.1, 29.2, 27.5. **HRMS (ESI-TOF):** *m/z* calculated for $C_{23}H_{23}N_2O_5S$ $[M+H]^+$: 439.1322, found: 439.1327.

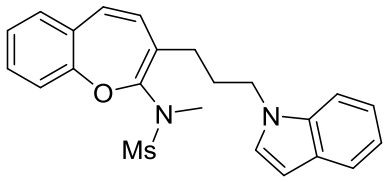
3-(2-(Dimethylamino)benzo[*b*]oxepin-3-yl)propyl cinnamate (3af)



3af

Following the general procedure B，the product **3af** was obtained in 62% yield (54.5 mg) as a white solid after column chromatography (eluent = petroleum ether/EtOAc 6:1 v/v); (PE/EA = 4/1, R_F ≈ 0.30). **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.67 (d, *J* = 16.0 Hz, 1H), 7.55 – 7.49 (m, 2H), 7.41 – 7.35 (m, 3H), 7.29 (t, *J* = 7.2 Hz, 1H), 7.13 (d, *J* = 8.4 Hz, 2H), 6.95 (d, *J* = 8.1 Hz, 1H), 6.75 (d, *J* = 11.2 Hz, 1H), 6.39 (d, *J* = 16.0 Hz, 1H), 6.10 (d, *J* = 11.3 Hz, 1H), 4.14 (t, *J* = 6.8 Hz, 2H), 3.17 (s, 3H), 3.11 (s, 3H), 2.52 – 2.40 (m, 2H), 1.83 (s, 2H) **^{13}C NMR (126 MHz, $CDCl_3$)** δ 167.1, 156.9, 144.9, 142.4, 134.5, 132.0, 130.4, 130.3, 129.6, 129.5, 129.0, 128.2, 125.4, 124.8, 120.5, 118.1, 63.9, 38.5, 37.1, 28.4, 27.7. **HRMS (ESI-TOF):** *m/z* calculated for $C_{24}H_{26}NO_5S$ $[M+H]^+$: 440.1526, found: 440.1522.

***N*-(3-(3-(1*H*-indol-1-yl)propyl)benzo[*b*]oxepin-2-yl)-*N*-methylmethanesulfonamide (3ag)**

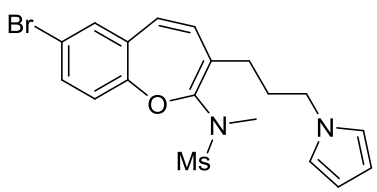


3ag

Following the general procedure B，the product **3ag** was obtained in 58% yield (47.3 mg) as a colourless liquid after column chromatography (eluent = petroleum ether/EtOAc 64:1 v/v); (PE/EA = 64/1, R_F ≈ 0.44). **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.60 (d, *J* = 7.9 Hz, 1H), 7.35 – 7.28 (m, 1H), 7.19 – 7.15 (m, 3H), 7.15 – 7.10 (m, 2H), 7.09 – 7.04 (m, 1H), 6.95 (d, *J* = 8.1

Hz, 1H), 6.74 (d, *J* = 11.3 Hz, 0H), 6.46 (d, *J* = 3.2 Hz, 1H), 6.03 (d, *J* = 11.2 Hz, 1H), 4.05 (t, *J* = 7.4 Hz, 2H), 3.05 (s, 3H), 3.01 (s, 3H), 2.33 (t, *J* = 7.9 Hz, 2H), 1.96 (s, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 156.9, 142.5, 135.9, 132.1, 130.5, 130.4, 129.5, 129.4, 128.7, 127.7, 125.5, 124.5, 121.5, 121.0, 120.7, 119.3, 109.4, 101.3, 45.7, 38.4, 36.9, 29.0, 28.9. **HRMS (ESI-TOF):** *m/z* calculated for $C_{23}H_{25}N_2O_3S$ $[M+H]^+$: 409.1580, found: 409.1573.

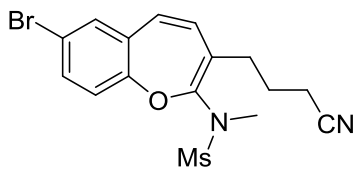
***N*-(3-(3-(1*H*-pyrrol-1-yl)propyl)-7-bromobenzo[*b*]oxepin-2-yl)-*N*-methylmethanesulfonamide (3bh)**



3bh

Following the general procedure B，the product **3bh** was obtained in 54% yield (47.1 mg) as a colourless liquid after column chromatography (eluent = petroleum ether/EtOAc 6:1 v/v); (PE/EA = 4/1, R_F ≈ 0.24). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.40 (dd, *J* = 8.6, 2.4 Hz, 1H), 7.28 (d, *J* = 2.4 Hz, 1H), 6.84 (d, *J* = 8.5 Hz, 1H), 6.64 (d, *J* = 11.4 Hz, 1H), 6.60 (t, *J* = 2.1 Hz, 2H), 6.11 (t, *J* = 2.1 Hz, 2H), 6.06 (d, *J* = 11.2 Hz, 1H), 3.84 (t, *J* = 7.1 Hz, 2H), 3.12 (s, 3H), 3.03 (s, 3H), 2.28 – 2.21 (m, 2H), 1.87 (p, *J* = 7.5 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$) δ** 155.8, 142.5, 133.0, 132.2, 131.9, 130.8, 130.6, 124.7, 122.4, 120.5, 118.2, 108.2, 49.2, 38.6, 37.0, 30.4, 28.9. **HRMS (ESI-TOF):** *m/z* calculated for $C_{19}H_{22}BrN_2O_3S$ $[M+H]^+$: 437.0529, found: 437.0533.

***N*-(7-Bromo-3-(3-cyanopropyl)benzo[*b*]oxepin-2-yl)-*N*-methylmethanesulfonamide (3bi)**

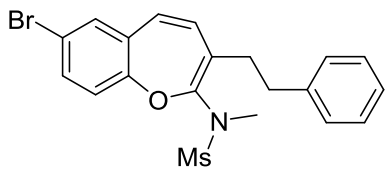


3bi

Following the general procedure B，the product **3bi** was obtained in 73% yield (57.8 mg) as a colourless liquid after column chromatography (eluent = petroleum ether/EtOAc 4:1 v/v); (PE/EA = 2/1, R_F ≈ 0.40). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.41 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.29 (d, *J* = 2.4 Hz, 1H), 6.84 (d, *J* = 8.7 Hz, 1H), 6.67 (d, *J* = 11.2 Hz, 1H), 6.09 (d, *J* = 11.2 Hz, 1H), 3.17 (s, 3H), 3.09 (s, 3H), 2.42 (t, *J* = 7.9 Hz, 2H), 2.30 (t, *J* = 7.2 Hz, 2H), 1.79 (p, *J* = 7.3 Hz,

2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 155.8, 143.3, 133.2, 132.1, 132.0, 131.0, 130.2, 123.6, 122.4, 119.4, 118.4, 38.6, 37.0, 30.5, 24.2, 16.8. **HRMS (ESI-TOF):** *m/z* calculated for $C_{16}H_{18}BrN_2O_3S$ $[M+H]^+$: 397.0216, found: 397.0203.

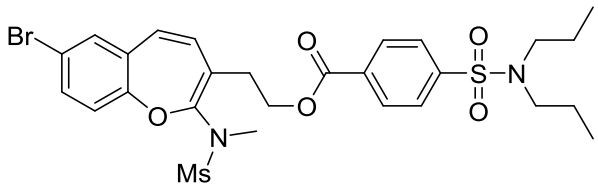
***N*-(7-Bromo-3-phenethylbenzo[*b*]oxepin-2-yl)-*N*-methylmethanesulfonamide (3ba)**



3ba

Following the general procedure B，the product **3ba** was obtained in 63% yield (54.6 mg) as a white solid after column chromatography (eluent = petroleum ether/EtOAc 6:1 v/v); (PE/EA = 4/1, R_F ≈ 0.35). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.38 (dd, *J* = 8.6, 2.4 Hz, 1H), 7.33 (d, *J* = 2.4 Hz, 1H), 7.09 – 7.04 (m, 3H), 6.97 (dd, *J* = 6.6, 3.1 Hz, 2H), 6.76 – 6.68 (m, 2H), 6.18 (d, *J* = 11.4 Hz, 1H), 3.01 (s, 3H), 2.68 (s, 2H), 2.57 (s, 5H) . **^{13}C NMR (101 MHz, $CDCl_3$)** δ 155.9, 143.1, 140.9, 132.8, 132.7, 131.6, 130.7, 128.9, 128.2, 126.1, 124.8, 122.3, 118.1, 38.4, 36.5, 34.7, 34.0. **HRMS (ESI-TOF):** *m/z* calculated for $C_{20}H_{21}BrNO_3S$ $[M+H]^+$: 434.0420, found: 434.0419.

2-(7-Bromo-2-(*N*-methylmethylsulfonamido)benzo[*b*]oxepin-3-yl)ethyl4-(*N*,*N*-dipropylsulfamoyl)benzoate (3bj)

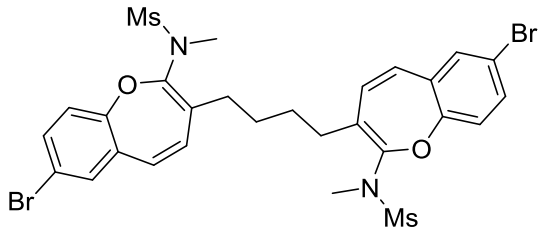


3bj

Following the general procedure B，the product **3bj** was obtained in 59% yield (75.5 mg) as a white solid after column chromatography (eluent = petroleum ether/EtOAc 3:1 v/v); (PE/EA = 2/1, R_F ≈ 0.55). **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.94 (d, *J* = 8.7 Hz, 2H), 7.80 (d, *J* = 8.6 Hz, 2H), 7.40 (dd, *J* = 8.7, 2.4 Hz, 1H), 7.21 (d, *J* = 2.4 Hz, 1H), 6.83 (d, *J* = 8.5 Hz, 1H), 6.64 (d, *J* = 11.3 Hz, 1H), 6.19 (d, *J* = 11.3 Hz, 1H), 4.39 (t, *J* = 6.9 Hz, 2H), 3.12 (s, 3H), 3.11 – 3.08 (m, 7H), 1.54 (h, *J* = 7.4 Hz, 4H), 0.86 (t, *J* = 7.4 Hz, 6H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 165.0, 155.8, 144.4, 144.1, 133.4, 133.1, 132.3, 130.8, 130.7, 130.2, 127.0, 122.3, 121.8, 118.4, 63.7, 50.0, 38.5, 37.0, 31.3, 22.0, 11.3. **HRMS (ESI-TOF):** *m/z*

calculated for $C_{27}H_{34}BrN_2O_7S_2$ $[M+H]^+$: 641.0985, found: 641.0962.

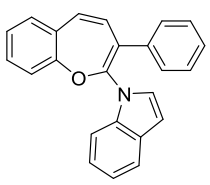
***N*,*N'*-(Butane-1,4-diylbis(7-bromobenzo[*b*]oxepine-3,2-diyl))bis(*N*-methylmethan esulfonamide) (3bk)**



3bk

Following the general procedure B，the product **3bk** was obtained in 35% yield (49.8 mg) as a white solid after column chromatography (eluent = petroleum ether/EtOAc 3:1 v/v); (PE/EA = 2/1, $R_F \approx$ 0.33). **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.39 (dd, *J* = 8.5, 2.4 Hz, 2H), 7.25 (d, *J* = 2.4 Hz, 2H), 6.82 (d, *J* = 8.5 Hz, 2H), 6.59 (d, *J* = 11.3 Hz, 2H), 6.03 (d, *J* = 11.3 Hz, 2H), 3.08 (s, 6H), 3.06 (s, 6H), 2.29 – 2.18 (m, 4H), 1.26 (q, *J* = 3.7 Hz, 4H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 156.0, 142.3, 132.9, 132.4, 131.8, 131.3, 130.3, 125.6, 122.3, 118.1, 38.6, 37.2, 31.4, 28.1. **HRMS (ESI-TOF):** *m/z* calculated for $C_{28}H_{30}Br_2N_2O_6S_2Na$ $[M+Na]^+$: 734.9804, found: 734.9797.

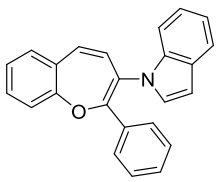
1-(3-Phenylbenzo[*b*]oxepin-2-yl)-1*H*-indole (3al)



3al

Following the general procedure B，the product **3al** was obtained in 37% yield (24.8 mg) as a pale yellow solid after column chromatography (eluent = petroleum ether/EtOAc 100:1 v/v); (PE/EA = 100/1, $R_F \approx$ 0.31). **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.66 (d, *J* = 8.2 Hz, 1H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.41 (dd, *J* = 7.2, 2.3 Hz, 1H), 7.21 (tdd, *J* = 7.6, 6.6, 1.8 Hz, 3H), 7.18 – 7.12 (m, 4H), 7.10 (d, *J* = 11.1 Hz, 1H), 6.98 (dd, *J* = 6.7, 3.1 Hz, 2H), 6.80 – 6.74 (m, 2H), 6.53 (d, *J* = 11.3 Hz, 1H), 6.35 (d, *J* = 3.4 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 154.5, 137.8, 137.0, 136.3, 130.7, 130.4, 130.3, 130.1, 129.0, 128.9, 128.7, 128.5, 127.5, 125.4, 122.9, 121.2, 121.1, 120.8, 118.9, 113.5, 104.5. **HRMS (ESI-TOF):** *m/z* calculated for $C_{24}H_{18}NO$ $[M+H]^+$: 336.1383, found: 336.1372.

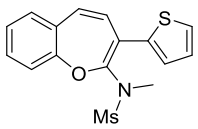
1-(2-phenylbenzo[b]oxepin-3-yl)-1*H*-indole (3al')



3al′

Following the general procedure B，the product **3al´**was obtained in 37% yield (24.8 mg) as a pale yellow solid after column chromatography (eluent = petroleum ether/EtOAc 100:1 v/v); (PE/EA = 100/1, $R_F \approx 0.30$). **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.64 – 7.58 (m, 1H), 7.42 (dd, *J* = 7.7, 2.0 Hz, 1H), 7.33 (td, *J* = 7.6, 1.9 Hz, 1H), 7.27 – 7.18 (m, 2H), 7.17 (d, *J* = 7.1 Hz, 3H), 7.16 – 7.08 (m, 4H), 7.08 (d, *J* = 11.1 Hz, 1H), 7.00 (d, J = 8.1 Hz, 1H), 6.89 (d, J = 3.2 Hz, 1H), 6.54 (d, *J* = 3.4 Hz, 1H), 6.41 (d, *J* = 11.1 Hz, 1H).**^{13}C NMR (126 MHz, $CDCl_3$)** δ 155.1, 147.2, 136.0, 133.3, 132.0, 131.3, 131.2, 129.4, 129.2, 129.1, 128.8, 128.6, 128.2, 127.9, 126.1, 125.3, 122.3, 121.4, 120.9, 120.5, 111.4, 104.1. **HRMS (ESI-TOF):** *m/z* calculated for $C_{24}H_{18}NO$ $[M+H]^+$: 336.1383, found: 336.1375.

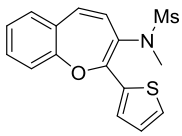
***N*-Methyl-*N*-(3-(thiophen-2-yl)benzo[*b*]oxepin-2-yl)methanesulfonamide (3am)**



3am

Following the general procedure B，the product **3am** was obtained in 43% yield (28.6 mg) as a pale yellow solid after column chromatography (eluent = petroleum ether/EtOAc 6:1 v/v); (PE/EA = 4/1, $R_F \approx 0.27$). **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.40 (td, *J* = 7.6, 1.8 Hz, 1H), 7.36 (d, *J* = 5.0 Hz, 1H), 7.34 – 7.29 (m, 1H), 7.25 – 7.22 (m, 2H), 7.12 (d, *J* = 8.1 Hz, 1H), 7.05 (dd, *J* = 5.2, 3.7 Hz, 1H), 6.99 (d, *J* = 11.3 Hz, 1H), 6.58 (d, *J* = 11.3 Hz, 1H), 3.20 (s, 3H), 3.16 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 156.6, 141.4, 137.5, 131.8, 130.6, 130.1, 129.3, 128.6, 127.7, 127.1, 126.9, 125.6, 120.7, 119. 4, 39.6, 36.7. **HRMS (ESI-TOF):** *m/z* calculated for $C_{16}H_{16}NO_3S_2$ $[M+H]^+$: 334.0556, found: 334.0560.

***N*-methyl-*N*-(2-(thiophen-2-yl)benzo[*b*]oxepin-3-yl)methanesulfonamide (3am ′)**

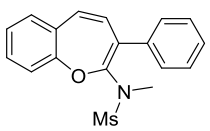


3am′

Following the general procedure B，the product **3am ´**was obtained in 22% yield (14.7 mg) as a yellow solid after column chromatography (eluent = petroleum ether/EtOAc 6:1 v/v); (PE/EA = 4/1, $R_F \approx 0.17$). **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.87 (dd, *J* = 3.8, 1.4 Hz, 1H), 7.42 (dd, *J* = 5.2, 1.4 Hz, 1H), 7.34 (td, *J* = 7.6, 1.8 Hz, 1H), 7.24 (d, *J* = 7.6 Hz, 1H), 7.20 – 7.08 (m, 3H),

6.89 (d, *J* = 11.4 Hz, 1H), 6.35 (d, *J* = 11.4 Hz, 1H), 3.12 (s, 3H), 2.94 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 155.0, 149.8, 135.7, 131.6, 131.2, 131.0, 129.5, 129.4, 129.1, 127.3, 126.3, 125.6, 124.2, 121.4, 38.2, 35.6. **HRMS (ESI-TOF):** *m/z* calculated for $C_{16}H_{16}NO_3S_2$ $[M+H]^+$: 334.0556, found: 334.0561.

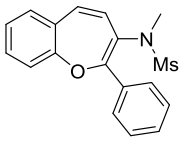
***N*-Methyl-*N*-(3-phenylbenzo[*b*]oxepin-2-yl)methanesulfonamide (3an)**



3an

Following the general procedure B，the product **3an** was obtained in 60% yield (39.3 mg) as a white solid after column chromatography (eluent = petroleum ether/EtOAc 4:1 v/v); (PE/EA = 3/1, $R_F \approx 0.47$). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.41 – 7.33 (m, 5H), 7.32 – 7.25 (m, 2H), 7.21 (td, *J* = 7.4, 1.2 Hz, 1H), 7.07 (dd, *J* = 8.1, 1.3 Hz, 1H), 6.90 (d, *J* = 11.3 Hz, 1H), 6.26 (d, *J* = 11.1 Hz, 1H), 3.01 (s, 3H), 2.70 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 155.4, 140.6, 137.2, 131.3, 130.7, 130.3, 129.8, 129.2, 129.0, 128.6, 127.9, 125.4, 124.7, 120.9, 39.8, 36.8. **HRMS (ESI-TOF):** *m/z* calculated for $C_{18}H_{18}NO_3S$ $[M+H]^+$: 328.1002, found: 328.1000.

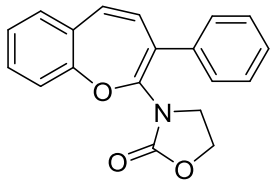
***N*-Methyl-*N*-(2-phenylbenzo[*b*]oxepin-3-yl)methanesulfonamide (3an ′)**



3an′

Following the general procedure B， the product **3an ′**was obtained in 20% yield (13.1 mg) as a white solid after column chromatography (eluent = petroleum ether/EtOAc 4:1 v/v); (PE/EA = 3/1, $R_F \approx 0.31$). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.89 – 7.82 (m, 2H), 7.46 – 7.35 (m, 3H), 7.26 (d, *J* = 14.3 Hz, 2H), 7.15 (td, *J* = 7.2, 1.3 Hz, 1H), 6.97 (d, *J* = 11.4 Hz, 1H), 6.90 – 6.85 (m, 1H), 6.34 (d, *J* = 11.3 Hz, 1H), 3.03 (s, 3H), 2.67 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 155.1, 152.7, 134.0, 132.6, 131.0, 130.9, 129.7, 128.7, 128.5, 128.5, 127.9, 127.7, 125.3, 121.3, 39.3, 37.2. **HRMS (ESI-TOF):** *m/z* calculated for $C_{18}H_{18}NO_3S$ $[M+H]^+$: 328.1002, found: 328.1028.

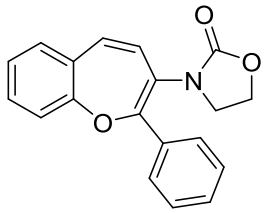
3-(3-Phenylbenzo[*b*]oxepin-2-yl)oxazolidin-2-one (3ao)



3ao

Following the general procedure B，the product **3ao** was obtained in 18% yield (11.0 mg) as a colourless liquid after column chromatography (eluent = petroleum ether/EtOAc 6:1 v/v); (PE/EA = 2/1, $R_F \approx 0.34$). **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.41 – 7.32 (m, 3H), 7.32 – 7.27 (m, 4H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.11 (d, *J* = 8.1 Hz, 1H), 6.90 (d, *J* = 11.3 Hz, 1H), 6.31 (d, *J* = 11.3 Hz, 1H), 4.26 (t, *J* = 7.9 Hz, 2H), 3.63 (t, *J* = 7.9 Hz, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 155.5, 155.4, 138.0, 136.9, 131.2, 130.8, 130.4, 129.8, 129.1, 128.8, 128.3, 128.0, 125.5, 123.1, 121.2, 62.7, 45.4. **HRMS (ESI-TOF):** *m/z* calculated for $C_{19}H_{16}NO_3$ $[M+H]^+$: 306.1125, found: 306.1127.

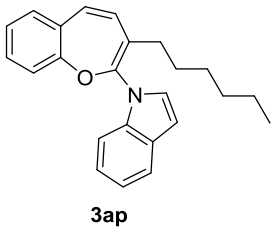
3-(2-Phenylbenzo[*b*]oxepin-3-yl)oxazolidin-2-one (3ao′)



3ao′

Following the general procedure B，the product **3ao′** was obtained in 48% yield (29.0 mg) as a pale yellow solid after column chromatography (eluent = petroleum ether/EtOAc 6:1 v/v); (PE/EA = 2/1, $R_F \approx 0.30$). **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.74 (dd, *J* = 8.1, 1.7 Hz, 2H), 7.45 – 7.34 (m, 3H), 7.28 (td, *J* = 7.2, 6.7, 1.9 Hz, 1H), 7.24 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.15 (td, *J* = 7.4, 1.1 Hz, 1H), 6.98 (d, *J* = 11.3 Hz, 1H), 6.86 (d, *J* = 8.1 Hz, 1H), 6.28 (d, *J* = 11.3 Hz, 1H), 4.30 – 4.23 (m, 2H), 3.55 – 3.48 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 157.0, 154.9, 149.0, 134.0, 132.4, 131.0, 131.0, 129.7, 129.0, 128.6, 128.1, 127.6, 125.2, 124.4, 121.0, 77.2, 62.6, 45.8. **HRMS (ESI-TOF):** *m/z* calculated for $C_{19}H_{16}NO_3$ $[M+H]^+$: 306.1125, found: 306.1123.

1-(3-Hexylbenzo[*b*]oxepin-2-yl)-1*H*-indole (3ap)

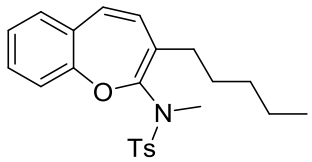


3ap

Following the general procedure B，the product **3ap** was obtained in 62% yield (42.6 mg) as a colourless liquid after column chromatography (eluent = petroleum ether/EtOAc 32:1 v/v); (PE/EA = 16/1, $R_F \approx 0.50$). **^{1}H NMR (400 MHz, $CDCl_3$)**

δ = 7.64 (dd, *J* = 6.9, 1.7 Hz, 1H), 7.34 (d, *J* = 8.1 Hz, 1H), 7.25 – 7.20 (m, 2H), 7.19 – 7.13 (m, 4H), 6.92 (d, *J* = 11.2 Hz, 1H), 6.74 (dd, *J* = 7.9, 1.4 Hz, 1H), 6.58 (d, *J* = 3.3 Hz, 1H), 6.31 (d, *J* = 11.2 Hz, 1H), 2.03 – 1.91 (m, 2H), 1.23 – 1.01 (m, 7H), 0.77 (t, *J* = 7.1 Hz, 4H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 155.7, 138.8, 136.9, 131.0, 130.5, 130.5, 129.8, 128.8, 128.5, 128.4, 125.1, 122.6, 121.7, 121.2, 120.9, 120.8, 111.9, 103.7, 31.5, 30.6, 28.9, 28.9, 22.6, 14.1. **HRMS (ESI-TOF):** *m/z* calculated for $C_{26}H_{26}NO$ $[M+H]^+$: 344.2009, found: 344.2001.

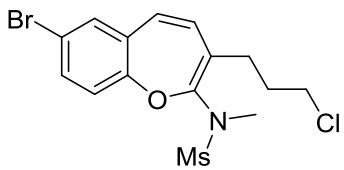
***N*,4-Dimethyl-*N*-(3-pentylbenzo[*b*]oxepin-2-yl)benzenesulfonamide (3aq)**



3aq

Following the general procedure B，the product **3aq** was obtained in 38% yield (30.2 mg) as a colourless liquid after column chromatography (eluent = petroleum ether/EtOAc 8:1 v/v); (PE/EA = 4/1, R_F ≈ 0.49). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.83 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.16 – 7.00 (m, 3H), 6.71 (d, *J* = 11.2 Hz, 1H), 6.31 (dd, *J* = 8.1, 1.9 Hz, 1H), 6.13 (d, *J* = 11.4 Hz, 1H), 3.02 (s, 3H), 2.45 (s, 3H), 2.29 (s, 2H), 1.42 (s, 2H), 1.35 – 1.20 (m, 4H), 0.86 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 156.9, 143.8, 141.5, 135.8, 131.2, 130.5, 130.2, 129.9, 129.6, 129.0, 128.6, 126.0, 124.9, 120.7, 37.2, 31.8, 31.7, 28.3, 22.6, 21.8, 14.1. **HRMS (ESI-TOF):** *m/z* calculated for $C_{23}H_{28}NO_3S$ $[M+H]^+$: 398.1784, found: 398.1788.

***N*-(7-Bromo-3-(3-chloropropyl)benzo[*b*]oxepin-2-yl)-*N*-methylmethanesulfonamide (3bc)**

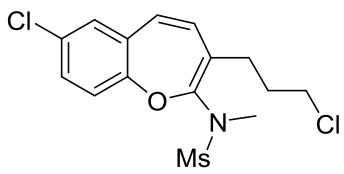


3bc

Following the general procedure B，the product **3bc** was obtained in 82% yield (66.4 mg) as a pale yellow liquid after column chromatography (eluent = petroleum ether/EtOAc 6:1 v/v); (PE/EA = 4/1, R_F ≈ 0.29). **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.40 (dd, *J* = 8.5, 3.1 Hz, 1H), 7.27 (d, *J* = 2.7 Hz, 1H), 6.84 (d, *J* = 8.6 Hz, 1H), 6.65 (d, *J* = 11.3 Hz, 1H), 6.11 (d, *J* = 11.4 Hz, 1H), 3.46 (t, *J* = 6.4 Hz, 2H), 3.16 (s, 3H), 3.08 (s, 3H), 2.43 (s, 2H), 1.87 (p, *J* = 6.9 Hz, 2H). **^{13}C**

NMR (126 MHz, $CDCl_3$) δ 155.9, 142.9, 133.1, 132.3, 131.9, 130.8, 130.7, 124.4, 122.3, 118.2, 44.4, 38.6, 37.1, 31.3, 28.9 . **HRMS (ESI-TOF):** *m/z* calculated for $C_{15}H_{18}BrClNO_3S$ $[M+H]^+$: 405.9874, found: 405.9894.

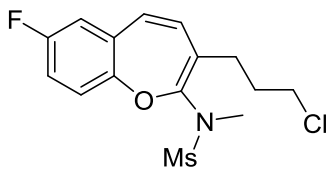
***N*-(7-Chloro-3-(3-chloropropyl)benzo[*b*]oxepin-2-yl)-*N*-methylmethanesulfonamide (3cc)**



3cc

Following the general procedure B，the product **3cc** was obtained in 58% yield (41.9 mg) as a colourless liquid after column chromatography (eluent = petroleum ether/EtOAc 6:1 v/v); (PE/EA = 4/1, R_F ≈ 0.22). **^{1}H NMR** (**400 MHz, $CDCl_3$**) δ = 7.25 (dd, *J* = 8.7, 2.6 Hz, 1H), 7.12 (d, *J* = 2.6 Hz, 1H), 6.90 (d, *J* = 8.5 Hz, 1H), 6.65 (d, *J* = 11.4 Hz, 1H), 6.11 (d, *J* = 11.4 Hz, 1H), 3.46 (t, *J* = 6.4 Hz, 2H), 3.17 (s, 3H), 3.09 (s, 3H), 2.46 (d, *J* = 21.0 Hz, 2H), 1.88 (p, *J* = 6.9 Hz, 2H). **^{13}C NMR (126 MHz, Acetone-d_6)** δ 156.8, 144.5, 133.5, 132.2, 131.7, 131.3, 131.2, 129.8, 125.3, 124.0, 45.7, 39.4, 37.9, 32.6, 30.0. **HRMS (ESI-TOF):** *m/z* calculated for $C_{15}H_{18}Cl_2NO_3S$ $[M+H]^+$: 362.0379, found: 362.0386.

***N*-(3-(3-Chloropropyl)-7-fluorobenzo[*b*]oxepin-2-yl)-*N*-methylmethanesulfonamide (3dc)**

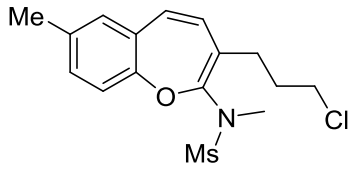


3dc

Following the general procedure B，the product **3dc** was obtained in 44% yield (30.3 mg) as a white solid after column chromatography (eluent = petroleum ether/EtOAc 6:1 v/v); (PE/EA = 4/1, R_F ≈ 0.33). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 6.99 (ddd, *J* = 8.8, 7.6, 3.0 Hz, 1H), 6.92 (dd, *J* = 8.8, 4.8 Hz, 1H), 6.84 (dd, *J* = 8.6, 3.0 Hz, 1H), 6.66 (d, *J* = 11.2 Hz, 1H), 6.12 (d, *J* = 11.2 Hz, 1H), 3.46 (t, *J* = 6.4 Hz, 2H), 3.18 (s, 3H), 3.09 (s, 3H), 2.43 (t, *J* = 7.8 Hz, 2H), 1.88 (p, *J* = 6.7 Hz, 2H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -117.83. **^{13}C NMR (101 MHz, $CDCl_3$)** δ = 159.8 (d, *J* = 243.9 Hz), 152.7 (d, *J* = 2.4 Hz), 143.1, 131.8 (d, *J* = 8.3 Hz), 130.9 (d, *J* = 2.0 Hz), 130.7, 124.2, 121.8 (d, *J* = 8.8 Hz), 116.8 (d, *J* = 23.7 Hz), 115.3 (d, *J* = 23.5 Hz), 44.4, 38.6, 37.1, 31.3, 28.9. **HRMS (ESI-TOF):** *m/z* calculated for

$C_{15}H_{17}ClFNO_3SNa$ $[M+Na]^+$: 368.0494, found: 368.0474.

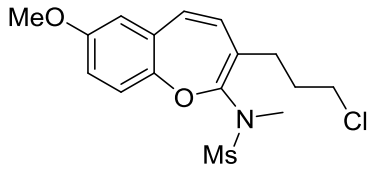
***N*-(3-(3-Chloropropyl)-7-methylbenzo[*b*]oxepin-2-yl)-*N*-methylmethanesulfonamide (3ec)**



3ec

Following the general procedure B，the product **3ec** was obtained in 54% yield (36.8 mg) as a colourless liquid after column chromatography (eluent = petroleum ether/EtOAc 6:1 v/v); (PE/EA = 6/1, $R_F \approx 0.26$). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.09 (dd, *J* = 8.2 Hz, 2.4, 1H), 6.94 (d, *J* = 2.6 Hz, 1H), 6.84 (d, *J* = 8.2 Hz, 1H), 6.69 (d, *J* = 11.4 Hz, 1H), 6.05 (d, *J* = 11.4 Hz, 1H), 3.46 (t, *J* = 6.5 Hz, 2H), 3.17 (s, 3H), 3.10 (s, 3H), 2.43 (s, 2H), 2.31 (s, 3H), 1.88 (p, *J* = 7.7, 7.0 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 154.9, 142.8, 135.0, 132.1, 131.0, 130.0, 129.8, 129.4, 124.2, 120.2, 44.5, 38.5, 37.1, 31.4, 29.0, 20.8. **H RMS (ESI-TOF):** *m/z* calculated for $C_{16}H_{21}ClNO_3S$ $[M+H]^+$: 342.0925, found: 342.0910.

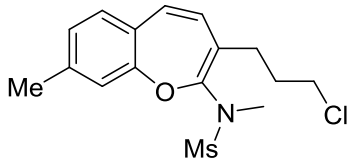
***N*-(3-(3-Chloropropyl)-7-methoxybenzo[*b*]oxepin-2-yl)-*N*-methylmethanesulfonamide (3fc)**



3fc

Following the general procedure B，the product **3fc** was obtained in 31% yield (22.1 mg) as a yellow liquid after column chromatography (eluent = petroleum ether/EtOAc 6:1 v/v); (PE/EA = 4/1, $R_F \approx 0.24$). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 6.88 (d, *J* = 8.8 Hz, 1H), 6.82 (dd, *J* = 8.9, 3.0 Hz, 1H), 6.69 (d, *J* = 11.3 Hz, 1H), 6.64 (d, *J* = 3.0 Hz, 1H), 6.08 (d, *J* = 11.3 Hz, 1H), 3.79 (s, 3H), 3.46 (t, *J* = 6.5 Hz, 2H), 3.18 (s, 3H), 3.09 (s, 3H), 2.43 (s, 2H), 1.89 (q, *J* = 7.1 Hz, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 156.9, 150.7, 143.2, 131.8, 131.0, 129.9, 124.0, 121.2, 115.8, 113.5, 55.8, 44.5, 38.5, 37.2, 31.4, 29.0. **HRMS (ESI-TOF):** *m/z* calculated for $C_{16}H_{21}ClNO_4S$ $[M+H]^+$: 358.0874, found: 358.0875.

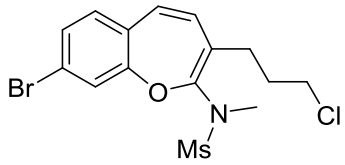
***N*-(3-(3-Chloropropyl)-8-methylbenzo[*b*]oxepin-2-yl)-*N*-methylmethanesulfonamide (3gc)**



3gc

Following the general procedure B，the product **3gc** was obtained in 68% yield (46.4 mg) as a colourless liquid after column chromatography (eluent = petroleum ether/EtOAc 6:1 v/v); (PE/EA = 4/1, $R_F \approx 0.35$). **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 7.02 (d, *J* = 7.6 Hz, 1H), 6.95 (dt, *J* = 7.8, 0.9 Hz, 1H), 6.76 (d, *J* = 1.7 Hz, 1H), 6.69 (d, *J* = 11.3 Hz, 1H), 6.00 (d, *J* = 11.3 Hz, 1H), 3.46 (t, *J* = 6.6 Hz, 2H), 3.18 (s, 3H), 3.11 (s, 3H), 2.51 – 2.36 (m, 2H), 2.34 (s, 3H), 1.92 – 1.85 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 156.9, 142.4, 141.1, 131.9, 129.2, 128.5, 127.5, 126.2, 124.3, 121.1, 44.5, 38.5, 37.2, 31.4, 29.0, 21.3. **HRMS (ESI-TOF):** *m/z* calculated for $C_{16}H_{21}ClNO_3S$ $[M+H]^+$: 342.0925, found: 342.0912.

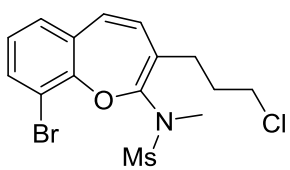
***N*-(8-Bromo-3-(3-chloropropyl)benzo[*b*]oxepin-2-yl)-*N*-methylmethanesulfonamide (3hc)**



3hc

Following the general procedure B，the product **3hc** was obtained in 78% yield (63.2 mg) as a white solid after column chromatography (eluent = petroleum ether/EtOAc 6:1 v/v); (PE/EA = 6/1, $R_F \approx 0.20$). **^{1}H NMR** (400 MHz, **$CDCl_3$**) δ = 7.28 (ddd, *J* = 8.2, 2.0, 0.8 Hz, 1H), 7.12 (d, *J* = 2.1Hz, 1H), 7.01 (d, *J* = 8.1 Hz, 1H), 6.67 (d, *J* = 11.4 Hz, 1H), 6.08 (d, *J* = 11.4 Hz, 1H), 3.46 (t, *J* = 6.2 Hz, 2H), 3.18 (s, 3H), 3.10 (s, 3H), 2.51 – 2.36 (m, 2H)., 1.88 (p, *J* = 7.0 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 157.2, 142.7, 131.1, 130.4, 130.0, 129.5, 128.7, 124.7, 124.0, 123.4, 44.4, 38.6, 37.2, 31.3, 29.0. **HRMS (ESI-TOF):** *m/z* calculated for $C_{15}H_{18}BrClNO_3S$ $[M+H]^+$: 405.9874, found: 405.9875.

***N*-(9-Bromo-3-(3-chloropropyl)benzo[*b*]oxepin-2-yl)-*N*-methylmethanesulfonamide (3ic)**

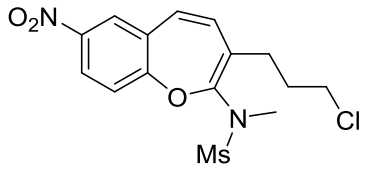


3ic

Following the general procedure B，the product **3ic** was obtained in 60% yield (48.6 mg) as a colourless liquid after column chromatography (eluent = petroleum ether/EtOAc 6:1 v/v); (PE/EA = 4/1, $R_F \approx 0.42$). **^{1}H NMR (400 MHz,**

$CDCl_3$) δ = 7.52 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.10 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.01 (t, *J* = 7.8 Hz, 1H), 6.69 (d, *J* = 11.2 Hz, 1H), 6.10 (d, *J* = 11.2 Hz, 1H), 3.50 (td, *J* = 6.4, 1.7 Hz, 2H), 3.28 (s, 3H), 3.20 (s, 3H), 2.58 (ddd, *J* = 13.8, 9.4, 6.7 Hz, 1H), 2.31 (ddd, *J* = 14.2, 9.5, 5.1 Hz, 1H), 2.10 – 1.94 (m, 1H), 1.86 (ddt, *J* = 14.2, 9.4, 6.6 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 154.3, 141.8, 134.1, 131.9, 131.7, 130.0, 129.1, 126.5, 126.2, 114.4, 44.5, 40.1, 38.2, 31.3, 29.3. **HRMS (ESI-TOF):** *m/z* calculated for $C_{15}H_{18}BrClNO_3S$ $[M+H]^+$: 405.9874, found: 405.9894.

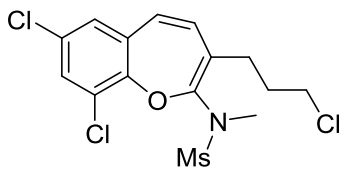
***N*-(3-(3-Chloropropyl)-7-nitrobenzo[*b*]oxepin-2-yl)-*N*-methylmethanesulfonamide (3jc)**



3jc

Following the general procedure B，the product **3jc** was obtained in 72% yield (53.6 mg) as a pale yellow solid after column chromatography (eluent = petroleum ether/EtOAc 4:1 v/v); (PE/EA = 3/1, R_F ≈ 0.28). **^{1}H NMR (500 MHz, $CDCl_3$)** δ = 8.18 (dt, *J* = 8.9, 2.1 Hz, 1H), 8.05 (s, 1H), 7.10 (dd, *J* = 8.9, 1.1 Hz, 1H), 6.76 (d, *J* = 11.3 Hz, 1H), 6.21 (d, *J* = 11.3 Hz, 1H), 3.49 (t, *J* = 6.3 Hz, 2H), 3.19 (s, 3H), 3.11 (s, 3H), 2.45 (t, *J* = 7.8 Hz, 2H), 1.89 (p, *J* = 6.6 Hz, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 161.3, 145.2, 142.4, 131.8, 131.3, 130.4, 125.6, 124.9, 124.8, 121.9, 44.4, 38.9, 37.0, 31.1, 29.0. **HRMS (ESI-TOF):** *m/z* calculated for $C_{15}H_{17}ClN_2O_5SNa$ $[M+Na]^+$: 395.0439, found: 395.0440.

***N*-(2,4-Dichloro-7-(3-chloropropyl)-5*H*-benzo[7]annulen-6-yl)-*N*-methylmethanesulfonamide (3kc)**



3kc

Following the general procedure B，the product **3kc** was obtained in 70% yield (55.3 mg) as a colourless liquid after column chromatography (eluent = petroleum ether/EtOAc 6:1 v/v); (PE/EA = 4/1, R_F ≈ 0.44). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.37 (d, *J* = 2.6 Hz, 1H), 7.05 (d, *J* = 2.6 Hz, 1H), 6.63 (d, *J* = 11.4 Hz, 1H), 6.16 (d, *J* = 11.3 Hz, 1H), 3.50 (td, *J* = 6.5, 2.0 Hz, 2H), 3.23 (s, 3H), 3.15 (s, 3H), 2.56 (ddd, *J* = 13.8, 9.4, 6.7 Hz, 1H), 2.31 (ddd, *J* = 14.2, 9.5, 5.0

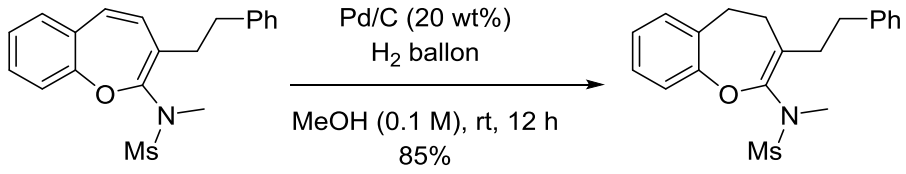
Hz, 1H), 2.00 (tt, *J* = 15.2, 6.1 Hz, 1H), 1.91 – 1.78 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 151.6, 142.4, 132.6, 131.3, 130.6, 130.6, 130.3, 127.8, 126.36, 125.7, 44.4, 39.6, 37.8, 31.2, 29.2. **HRMS (ESI-TOF):** *m/z* calculated for $C_{15}H_{17}Cl_3NO_3S$ $[M+H]^+$: 395.9989, found: 395.9981.

5. Gram-scale synthesis of compound 3ba

4-Bromo-2-vinylphenol **1b** (6.0 mmol, 1.5 equiv), [Cp*Co(CO)I_2] (195 mg, 0.4 mmol, 10 mol %), $Cu(OAc)_2$ H_2O (1.19 g, 6.0 mmol, 1.5 equiv), Ag_2CO_3 (0.55g, 2.0 mmol, 0.5 equiv), DCE (20.0 mL) and ynamide **2a** (1.19 g, 4.0 mmol, 1.0 equiv) were added to a 75 mL Schlenk tube. The mixture was stirred at room temperature for 24 h under air, then the reaction mixture was filtered through celite and washed with ethyl acetate. The solvents were removed *in vacuo* and the remaining residue was purified by flash column chromatography on silica gel to afford he desired products **3ba** as a white solid in 66% yield (1.15 g).

6. Derivatization of product 3aa, 3ba, and 3ac

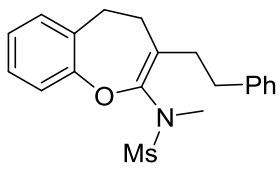
Synthesis of 5



3aa **5**

To a 15.0 mL tube charged with **3aa** (71.0 mg, 0.20 mmol), were added Pd/C (13 mg, 20 wt %) and MeOH (2.0 mL). The tube was evacuated and refilled with hydrogen ballon for three times. At room temperature, the suspension was stirred under hydrogen (approximately 1 atm) for 12 h and then filtered through a pad of Celite and concentrated. The residue was purified by flash column chromatography on silica gel (PE/EtOAc = 6/1; PE/EA = 6/1, RF = 0.4) to afford the product **5** (60.7 mg, 85%).

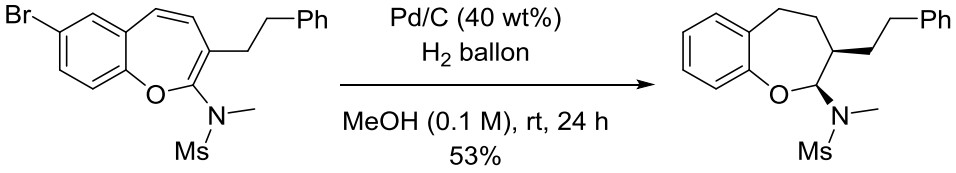
***N*-Methyl-*N*-(3-phenethyl-4,5-dihydrobenzo[*b*]oxepin-2-yl)methanesulfonamide (5)**



5

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.22 – 7.09 (m, 5H), 7.13 – 7.03 (m, 3H), 6.94 (d, *J* = 8.0 Hz, 1H), 3.20 (brs, 1H), 3.03 (s, 3H), 2.81 (s, 7H), 2.52 (brs, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 157.4, 142.8, 141.8, 134.0, 129.6, 128.7, 128.4, 127.4, 125.9, 124.8, 121.8, 119.6, 37.9, 36.3, 35.8, 34.0, 31.1, 29.5. **HRMS (ESI-TOF):** *m/z* calculated for $C_{20}H_{24}NO_3S$ $[M+H]^+$: 358.1471, found: 358.1487.

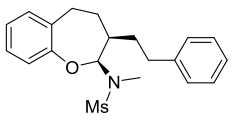
Synthesis of 6



3ba **6**

To a 15.0 mL tube charged with **3ba** (86.9.0 mg, 0.20 mmol), were added Pd/C (26 mg, 40 wt %) and MeOH (2.0 mL). The tube was evacuated and refilled with hydrogen ballon for three times. At room temperature, the suspension was stirred under hydrogen (approximately 1 atm) for 24 h and then filtered through a pad of Celite and concentrated. The residue was purified by flash column chromatography on silica gel (PE/EtOAc = 6/1; PE/EA = 6/1, RF = 0.4) to afford the product **6** (38.1 mg, 53%).

***N*-Methyl-*N*-(3-phenethyl-2,3,4,5-tetrahydrobenzo[*b*]oxepin-2-yl)methanesulfonamide (6)**

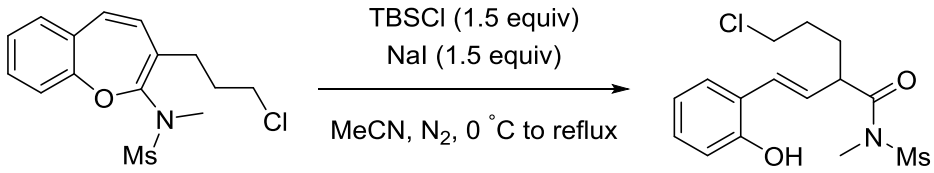


6

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.25 – 7.22 (m, 2H), 7.17 (t, *J* = 7.3 Hz, 1H), 7.09 (d, *J* = 8.1 Hz, 2H), 7.06 (d, *J* = 7.5 Hz, 1H), 7.01 (dd, *J* = 7.5, 1.5 Hz, 1H), 6.82 (t, *J* = 7.4 Hz, 1H), 6.76 (d, *J* = 8.1 Hz, 1H), 5.52 (s, 1H), 3.17 (s, 3H), 2.97 (s, 3H), 2.77 (dp, *J* = 10.5, 5.6 Hz, 1H),

2.64 (tdd, *J* = 7.9, 5.6, 2.4 Hz, 3H), 2.56 (ddd, *J* = 13.6, 8.7, 5.3, 1H), 2.00 (dq, *J* = 15.0, 7.3, 6.7 Hz, 2H), 1.88 (dq, *J* = 13.7, 7.3, 6.7 Hz, 2H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 177.6, 153.8, 140.9, 130.2, 128.5, 128.5, 127.7, 127.1, 126.2, 120.7, 115.6, 42.6, 41.8, 33.4, 33.1, 32.1, 31.6, 27.7. **HRMS (ESI-TOF):** *m/z* calculated for $C_{20}H_{25}NO_3SK$ $[M+K]^+$: 398.1187, found: 398.1193.

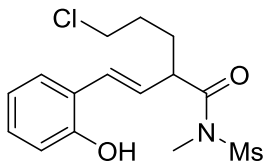
Synthesis of 7



3ac **7**, 51%

To a suspension of sodium iodide (0.6 mmol) in acetonitrile (4 mL), chlorotrimethylsilane (0.6 mmol) was added dropwise and stirred for 10 min at 0 ℃ under a N_2 atmosphere. To this suspension, a solution of **3ac** (0.4 mmol) in acetonitrile (2 mL) was added and refluxed for 6 hrs under a N_2 atmosphere.The reaction mixture was quenched with water and extracted with ethylacetate (15 mL). The orangic layer was washed with 10% sodium thiosulphate solution, brine, dried over anhydrous Na_2SO_4 and concentrated under vacuum to give the crude product. This was purified by column chromatography to afford **7** as a colorless liquid (70.4 mg, 51%).

(*E*)-5-Chloro-2-(2-hydroxystyryl)-*N*-methyl-*N*-(methylsulfonyl)pentanamide (7)

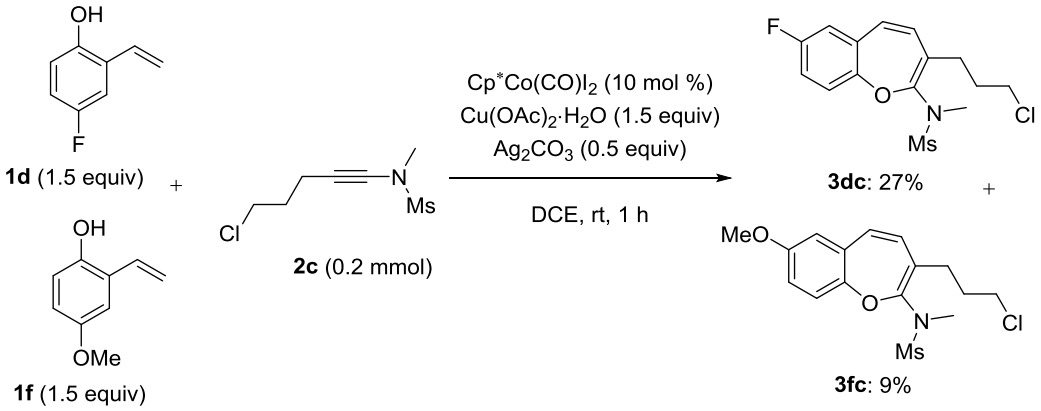


7

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.35 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.13 (td, *J* = 7.8, 1.7 Hz, 1H), 6.89 (t, *J* = 7.5 Hz, 1H), 6.83 – 6.74 (m, 2H), 6.19 (dd, *J* = 16.2, 8.9 Hz, 1H), 5.76 (s, 1H), 3.81 (dt, *J* = 9.2, 6.5 Hz, 1H), 3.55 (td, *J* = 6.4, 2.3 Hz, 2H), 3.34 (s, 3H), 3.27 (s, 3H), 1.92 – 1.74 (m, 4H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 174.9, 153.2, 129.3, 128.8, 127.4, 127.1, 123.4, 121.0, 116.1, 48.8, 44.7, 41.9, 32.8, 30.3, 30.0. **HRMS (ESI-TOF):** *m/z* calculated for $C_{15}H_{20}ClNO_4SNa$ $[M+Na]^+$: 368.0964, found: 368.0710.

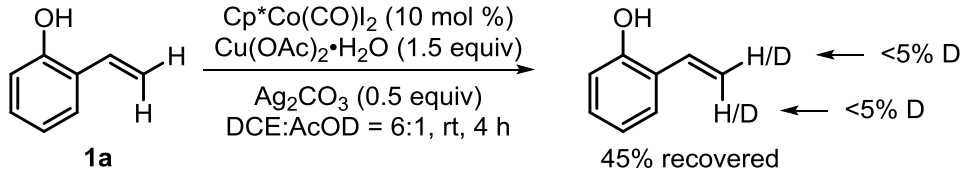
7. Mechanistic studies

7.1 Intermolecular competition experiments



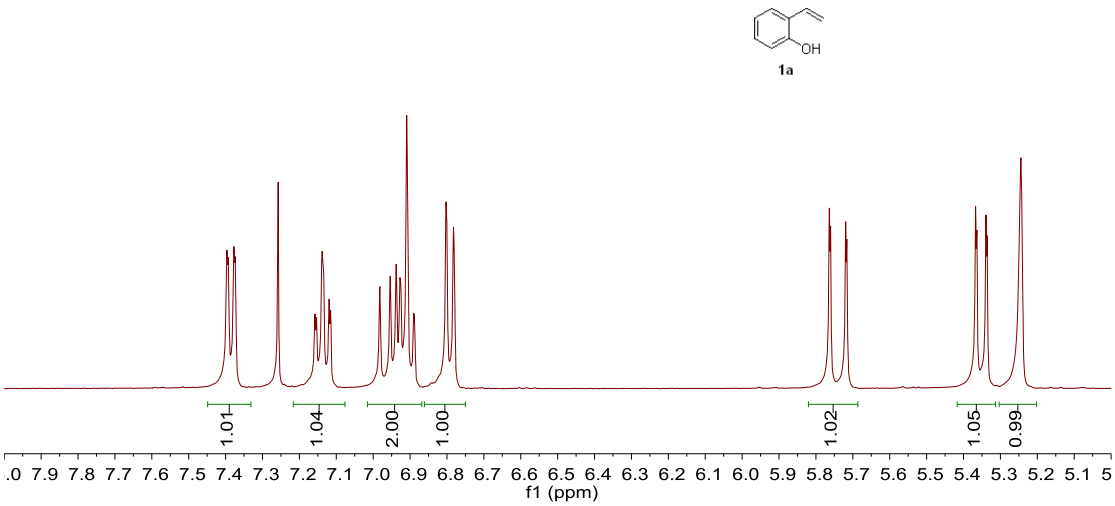
To a solution of [Cp*Co(CO)I_2] (9.8 mg, 0.02 mmol, 10 mol %), Cu(OAc)$_2$ Ꮒ$_2$O (60.0 mg, 0.30 mmol, 1.5 equiv), Ag_2CO_3 (0.55g, 0.10 mmol, 0.5 equiv),and ynamide **2c** (0.20 mmol) in DCE (1.0 mL) under air atmosphere was added a solution of **1d** and **1f** (0.30 mmol each). The mixture was stirred at 25 ℃ for 1 h under air. Then, the mixture was diluted with CH_2Cl_2 (10 mL). The mixture was filtered through a Celite pad and the Celite pad was washed with CH_2Cl_2 (3 × 10 mL). The filtrate was concentrated under reduced pressure and the crude mixture was analyzed by ^{1}H NMR. The yield of **3dc** and **3fc** was 27% and 9%, respectively.

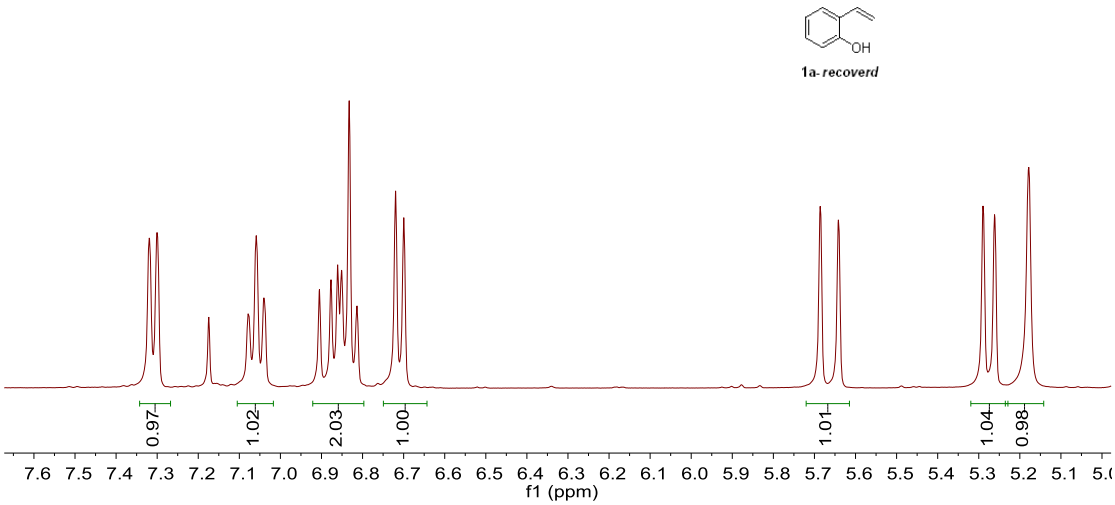
7.2 H/D scrambling experiment



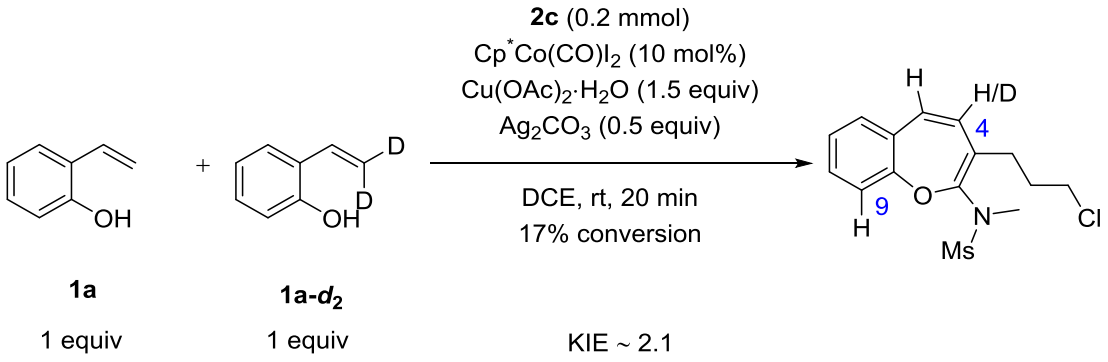
To a solution of Cp*Co(CO)I_2 (10 mg, 10 mol%), Cu(OAc)$_2$ Ꮒ$_2$O (60 mg, 1.5 equiv) and Ag_2CO_3 (28 mg, 0.5 equiv) in DCE (0.86 mL) under air atmosphere was added 2-vinylphenol **1a** (36 mg, 1.5 equiv) and AcOD (0.14 mL). After stirring for 4 h at room temperature, the solvents were removed in vacuo and the remaining residue was purified by flash column chromatography on silica gel to give **1a** and **1a**-dn (16.2

mg, 45% recovery). No deuterationon were observed for both olefinic protons based on ^{1}H-NMR.

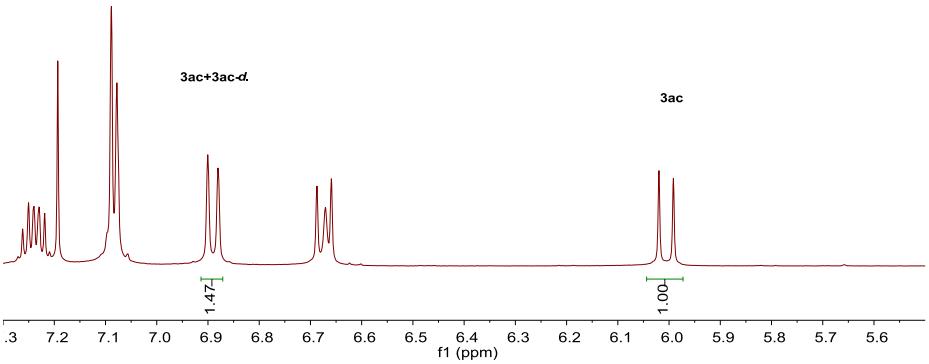




7.3 Kinetic isotopic effect



To a solution of [Cp*Co(CO)I_2] (9.8 mg, 0.02 mmol, 10 mol %) and Cu(OAc)$_2$ H_2O (60 mg, 0.30 mmol, 1.5 equiv), Ag_2CO_3 (28 mg, 0.10 mmol, 0.5 equiv) and **2c** (41.8 mg, 0.20 mmol) in DCE (1 mL) under air atmosphere was added a equimolar solution of **1a** and **1a-*d*$_2$** (0.20 mmol each). This solution was prepared by mixing 21.3 mg of **1a** and 27.1 mg of **1a-*d*$_2$** (90% deuterated). The mixture stirred at room temperature for 20 min under air. After 20 minutes the reaction mixture was diluted with DCM (10 mL) and filtered through silica (washing with ethyl acetate). The solvents were evaporated in vacuo and the remaining residue was purified by flash column chromatography on silica to remove the remaining starting material. The residue was analysed by ^{1}HNMR. The KIE value (~ 2.1) was obtained by integrating the H_4 of the 1-benzoxepine **3ac** and the H_9 of the 1-benzoxepine **3ac** and **3ac-*d***.



8. X-ray data for compounds 3aa and 3jc

8.1 X-ray data for compound 3aa

Single crystals of $C_{20}H_{21}NO_3S$ [hxl_180125] were colourless block. A suitable crystal was selected and on a **Xcalibur, Onyx, Nova** diffractometer. The crystal was kept at 100 K during data collection. Using Olex2 [1], the structure was solved with the ShelXS [2] structure solution program using Direct Methods and refined with the ShelXL [3] refinement package using Least Squares minimisation.

Crystal Data for $C_{20}H_{21}NO_3S$ (M =355.44 g/mol): monoclinic, space group P21/c (no. 14), a = 13.5862(3) Å, b = 9.9930(2) Å, c = 13.1956(3) Å, β = 94.489(2)°, V = 1786.03(7) Å3, Z = 4, T = 100 K, μ(CuKα) = 1.762 mm-1, Dcalc = 1.322 g/cm3, 6433 reflections measured (6.526° ≤ 2Θ ≤ 134.16°), 3164 unique (Rint = 0.0200, Rsigma = 0.0232) which were used in all calculations. The final R1 was 0.0343 (I > 2σ(I)) and wR2 was 0.0933 (all data).

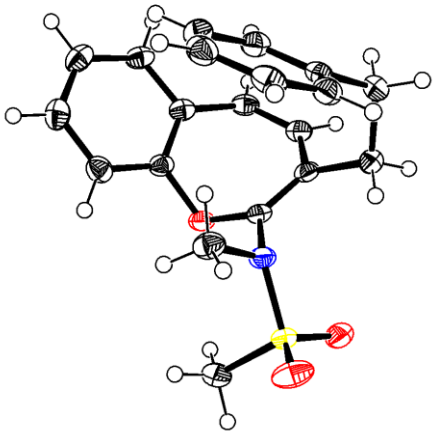


Table 1 Crystal data and structure refinement for hxl_180125.

Identification code	hxl_180125
Empirical formula	$C_{20}H_{21}NO_3S$
Formula weight	355.44

Temperature/K	100
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	13.5862(3)
b/Å	9.9930(2)
c/Å	13.1956(3)
α/°	90
β/°	94.489(2)
γ/°	90
Volume/$Å^3$	1786.03(7)
Z	4
$\rho_{calc}g/cm^3$	1.322
μ/mm^{-1}	1.762
F(000)	752.0
Crystal size/mm^3	0.3 × 0.2 × 0.1
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	6.526 to 134.16
Index ranges	$-16 \leq h \leq 14$, $-11 \leq k \leq 11$, $-12 \leq l \leq 15$
Reflections collected	6433
Independent reflections	3164 [R_{int} = 0.0200, R_{sigma} = 0.0232]
Data/restraints/parameters	3164/0/228
Goodness-of-fit on F^2	1.047
Final R indexes [I>=2σ (I)]	R_1 = 0.0343, wR_2 = 0.0920
Final R indexes [all data]	R_1 = 0.0360, wR_2 = 0.0933
Largest diff. peak/hole / e $Å^{-3}$	0.27/-0.34

Table 2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for hxl_180125. U_{eq} is defined as 1/3 of of the

trace of the orthogonalised U_{IJ} tensor.

Atom	***x***	***y***	***z***	**U(eq)**
S1	591.2(3)	262.4(4)	1638.4(3)	26.06(13)
O1	2490.4(7)	2073.2(10)	2459.5(7)	25.9(2)
O2	1097.7(8)	-433.5(12)	893.0(9)	36.3(3)
N3	1343.3(9)	335.0(13)	2682.6(9)	24.5(3)
O4	-318.1(9)	-266.1(15)	1943.8(10)	44.3(3)
C5	3079.4(11)	-183.9(15)	2565.5(10)	23.4(3)
C6	3034.5(11)	-1493.1(15)	4630.9(11)	25.8(3)
C7	4102.7(11)	239.6(16)	2481.3(11)	25.8(3)
C8	3440.5(12)	-325.4(16)	5062.3(12)	29.4(3)
C9	4033.2(11)	2343.0(15)	3477.2(11)	24.3(3)
C10	4554.9(11)	2984.1(16)	4297.3(11)	27.9(3)
C11	2192.3(11)	-2016.0(16)	5025.3(12)	29.1(3)
C12	3456.9(11)	-2150.9(15)	3730.4(12)	27.7(3)
C13	4087.8(12)	3839.2(16)	4925.5(12)	31.9(4)
C14	2558.2(12)	3521.1(15)	3912.7(12)	29.3(3)
C15	3029.8(11)	2638.0(15)	3307.0(11)	24.1(3)
C16	2344(1)	694.7(15)	2573(1)	22.5(3)
C17	4523.8(11)	1353.4(16)	2879.8(11)	26.3(3)
C18	3014.0(13)	315.1(17)	5854.0(12)	33.9(4)
C19	2171.0(13)	-211.9(17)	6233.1(12)	34.5(4)
C20	914.4(11)	831.0(18)	3606.9(12)	31.7(4)
C21	1769.6(12)	-1383.8(17)	5819.1(12)	32.8(4)
C22	387.5(14)	1910.7(18)	1204.6(14)	40.2(4)
C23	3088.5(13)	4114.6(16)	4735.8(12)	32.7(4)
C24	2934.2(11)	-1666.1(15)	2713.4(11)	26.6(3)

Table 3 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for hxl_180125. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
S1	19.5(2)	29.5(2)	28.1(2)	-3.03(14)	-5.21(14)	-0.70(13)
O1	23.9(5)	26.0(5)	26.3(5)	3.3(4)	-7.1(4)	-0.9(4)
O2	32.3(6)	43.0(7)	32.3(6)	-13.3(5)	-6.1(5)	5.6(5)
N3	19.3(6)	29.7(7)	23.9(6)	-1.4(5)	-2.7(5)	0.4(5)
O4	24.2(6)	64.3(9)	43.2(7)	0.4(6)	-4.3(5)	-14.3(6)
C5	23.1(7)	29.7(8)	16.6(6)	-2.5(5)	-2.6(5)	-0.3(6)
C6	25.1(7)	26.9(7)	24.8(7)	4.9(6)	-2.6(6)	5.1(6)
C7	22.1(7)	33.7(8)	21.4(7)	0.5(6)	0.8(5)	3.2(6)
C8	28.5(8)	31.2(8)	27.7(8)	3.8(6)	-2.2(6)	-0.4(6)
C9	23.2(7)	27.2(7)	22.1(7)	4.6(6)	-0.1(5)	-4.2(6)
C10	24.9(7)	32.4(8)	25.9(7)	4.5(6)	-2.8(6)	-6.6(6)
C11	27.9(8)	27.0(8)	31.8(8)	4.8(6)	-1.2(6)	1.1(6)
C12	26.7(7)	25.6(7)	30.5(8)	1.4(6)	-0.6(6)	4.3(6)
C13	39.3(9)	30.7(8)	25.3(7)	-1.1(6)	0.1(6)	-11.1(7)
C14	27.2(8)	25.4(8)	35.2(8)	3.0(6)	1.8(6)	0.2(6)
C15	25.4(7)	22.8(7)	23.2(7)	3.7(6)	-2.7(6)	-3.3(6)
C16	20.7(7)	26.6(7)	19.3(7)	0.7(5)	-4.2(5)	-1.4(6)
C17	19.4(7)	35.5(8)	23.7(7)	4.5(6)	1.1(5)	-0.6(6)
C18	40.4(9)	32.8(9)	27.5(8)	-1.0(6)	-3.7(7)	1.9(7)
C19	40.2(9)	37.8(9)	25.4(8)	3.1(7)	2.8(7)	11.7(7)
C20	25.5(8)	42.8(9)	26.8(8)	-1.2(7)	2.2(6)	-1.2(7)
C21	29.2(8)	38.2(9)	31.3(8)	10.6(7)	3.8(6)	5.5(7)

C22	42.1(10)	35.2(9)	40.1(9)	1.1(7)	-16.1(8)	9.1(8)
C23	40.0(9)	26.2(8)	32.6(8)	-2.0(6)	7.2(7)	-2.3(7)
C24	26.0(7)	27.0(8)	26.1(7)	-4.3(6)	-1.1(6)	1.7(6)

Table 4 Bond Lengths for hxl_180125.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
S1	O2	1.4250(12)	C7	C17	1.340(2)
S1	N3	1.6516(12)	C8	C18	1.390(2)
S1	O4	1.4302(12)	C9	C10	1.401(2)
S1	C22	1.7586(18)	C9	C15	1.396(2)
O1	C15	1.4064(17)	C9	C17	1.458(2)
O1	C16	1.4015(18)	C10	C13	1.379(2)
N3	C16	1.4245(18)	C11	C21	1.386(2)
N3	C20	1.4778(19)	C12	C24	1.546(2)
C5	C7	1.466(2)	C13	C23	1.389(2)
C5	C16	1.331(2)	C14	C15	1.381(2)
C5	C24	1.509(2)	C14	C23	1.389(2)
C6	C8	1.393(2)	C18	C19	1.389(2)
C6	C11	1.395(2)	C19	C21	1.386(3)
C6	C12	1.510(2)			

Table 5 Bond Angles for hxl_180125.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
O2	S1	N3	107.25(6)	C15	C9	C10	117.15(14)
O2	S1	O4	119.26(8)	C15	C9	C17	122.58(13)

O2	S1	C22	107.74(9)	C13	C10	C9	121.25(14)
N3	S1	C22	107.56(7)	C21	C11	C6	120.77(15)
O4	S1	N3	105.83(7)	C6	C12	C24	111.69(12)
O4	S1	C22	108.68(9)	C10	C13	C23	120.25(14)
C16	O1	C15	112.27(10)	C15	C14	C23	119.32(15)
C16	N3	S1	117.35(10)	C9	C15	O1	119.00(13)
C16	N3	C20	116.12(12)	C14	C15	O1	118.69(13)
C20	N3	S1	116.43(10)	C14	C15	C9	122.23(14)
C7	C5	C24	115.32(13)	O1	C16	N3	113.79(12)
C16	C5	C7	121.81(14)	C5	C16	O1	122.33(13)
C16	C5	C24	122.75(14)	C5	C16	N3	123.87(14)
C8	C6	C11	118.12(14)	C7	C17	C9	125.19(13)
C8	C6	C12	121.57(14)	C19	C18	C8	120.01(16)
C11	C6	C12	120.25(14)	C21	C19	C18	119.24(15)
C17	C7	C5	126.05(14)	C11	C21	C19	120.65(15)
C18	C8	C6	121.19(15)	C14	C23	C13	119.76(15)
C10	C9	C17	120.17(13)	C5	C24	C12	111.35(12)

Table 6 Torsion Angles for hxl_180125.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
S1	N3	C16	O1	79.54(13)	C12	C6	C11	C21	-176.80(13)
S1	N3	C16	C5	-99.73(15)	C15	O1	C16	N3	111.45(13)
O2	S1	N3	C16	45.03(13)	C15	O1	C16	C5	-69.27(17)
O2	S1	N3	C20	-170.81(11)	C15	C9	C10	C13	1.8(2)
O4	S1	N3	C16	173.34(11)	C15	C9	C17	C7	-32.7(2)
O4	S1	N3	C20	-42.50(13)	C15	C14	C23	C13	1.5(2)

C5	C7	C17	C9	0.4(2)	C16	O1	C15	C9	71.00(16)
C6	C8	C18	C19	0.4(2)	C16	O1	C15	C14	-112.30(15)
C6	C11	C21	C19	0.5(2)	C16	C5	C7	C17	34.9(2)
C6	C12	C24	C5	62.58(17)	C16	C5	C24	C12	-112.32(16)
C7	C5	C16	O1	2.7(2)	C17	C9	C10	C13	-174.51(14)
C7	C5	C16	N3	-178.12(12)	C17	C9	C15	O1	-7.2(2)
C7	C5	C24	C12	63.68(16)	C17	C9	C15	C14	176.25(14)
C8	C6	C11	C21	0.4(2)	C18	C19	C21	C11	-1.0(2)
C8	C6	C12	C24	-92.83(17)	C20	N3	C16	O1	-64.74(16)
C8	C18	C19	C21	0.6(2)	C20	N3	C16	C5	116.00(16)
C9	C10	C13	C23	-2.0(2)	C22	S1	N3	C16	-70.62(13)
C10	C9	C15	O1	176.57(12)	C22	S1	N3	C20	73.54(13)
C10	C9	C15	C14	0.0(2)	C23	C14	C15	O1	-178.25(13)
C10	C9	C17	C7	143.47(15)	C23	C14	C15	C9	-1.7(2)
C10	C13	C23	C14	0.3(2)	C24	C5	C7	C17	-141.13(15)
C11	C6	C8	C18	-0.9(2)	C24	C5	C16	O1	178.42(12)
C11	C6	C12	C24	84.31(17)	C24	C5	C16	N3	-2.4(2)
C12	C6	C8	C18	176.32(14)					

Table 7 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for hxl_180125.

Atom	***x***	***y***	***z***	**U(eq)**
H7	4504.61	-328.17	2109.72	31
H8	4019.39	39.59	4810.86	35
H10	5243.18	2826.78	4423.03	34
H11	1905.12	-2814.93	4746.36	35

H12A	3384.05	-3133.57	3783.19	33
H12B	4170.41	-1945.13	3741.27	33
H13	4451.13	4241.3	5490.01	38
H14	1878.05	3720.35	3767.62	35
H17	5195.45	1510.65	2764	32
H18	3299.15	1113.5	6135.95	41
H19	1872.85	225.94	6770.09	41
H20A	753.66	1782.83	3524.95	48
H20B	1392.81	712.13	4195.3	48
H20C	312.42	326.97	3713.32	48
H21	1199.18	-1757.37	6082.01	39
H22A	1016.47	2311.19	1048.46	60
H22B	99.51	2438.08	1733.33	60
H22C	-67.02	1901.38	590.12	60
H23	2768.84	4707.01	5167.66	39
H24A	3200.8	-2159.49	2144.65	32
H24B	2219.4	-1862.91	2704.51	32

8.2 X-ray data for compound 3jc

Single crystals of $C_{15}H_{17}N_2O_5ClS$ [hxl_180420] were colourless block. A suitable crystal was selected and on a **Xcalibur, Onyx, Nova** diffractometer. The crystal was kept at 100 K during data collection. Using Olex2 [1], the structure was solved with the ShelXS [2] structure solution program using Direct Methods and refined with the ShelXL [3] refinement package using Least Squares minimisation.

Crystal Data for $C_{15}H_{17}N_2O_5ClS$ (M =372.82 g/mol): monoclinic, space group $P2_1/c$ (no. 14), a = 8.5374(3) Å, b = 10.4577(3) Å, c = 18.7809(6) Å, β = 97.412(3) °, V = 1662.79(9) Å^3, Z = 4, T = 100 K, μ(CuKα) = 3.473 mm^{-1}, *Dcalc* = 1.489 g/cm^3, 6037 reflections measured (9.498° ≤ 2Θ ≤ 134.116°), 2968 unique (R_{int} = 0.0328,

R_{sigma} = 0.0334) which were used in all calculations. The final R_1 was 0.0417 (I > 2σ(I)) and wR_2 was 0.1116 (all data).

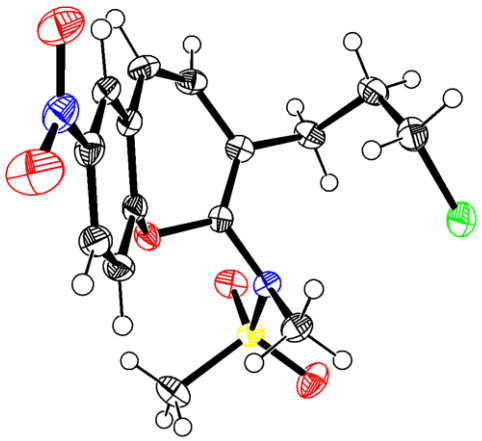


Table 1 Crystal data and structure refinement for hxl_180420.

Identification code	hxl_180420
Empirical formula	$C_{15}H_{17}N_2O_5ClS$
Formula weight	372.82
Temperature/K	100
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	8.5374(3)
b/Å	10.4577(3)
c/Å	18.7809(6)
α/°	90
β/°	97.412(3)
γ/°	90
Volume/Å^3	1662.79(9)
Z	4
ρ_{calc}g/cm^3	1.489
μ/mm^{-1}	3.473
F(000)	776.0

Crystal size/mm^3	0.3 × 0.2 × 0.1
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	9.498 to 134.116
Index ranges	-10 ≤ h ≤ 8, -12 ≤ k ≤ 12, -20 ≤ l ≤ 22
Reflections collected	6037
Independent reflections	2968 [R_{int} = 0.0328, R_{sigma} = 0.0334]
Data/restraints/parameters	2968/0/219
Goodness-of-fit on F^2	1.077
Final R indexes [I>=2σ (I)]	R_1 = 0.0417, wR_2 = 0.1093
Final R indexes [all data]	R_1 = 0.0448, wR_2 = 0.1116
Largest diff. peak/hole / e Å^{-3}	0.37/-0.34

Table 2 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for hxl_180420. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
S1	4898.5(6)	1198.5(5)	2247.5(3)	20.74(16)
Cl2	10048.7(7)	143.4(6)	2414.1(3)	37.75(19)
O1	5431.7(18)	2770.5(14)	790.3(8)	22.9(3)
O2	9446(2)	6079.7(17)	-1089.1(9)	35.5(4)
O3	4186.3(19)	162.3(15)	1823.3(9)	28.8(4)
C4	7799(3)	4207(2)	-497.5(11)	22.4(4)
N5	6405(2)	1686.2(16)	1855.8(9)	19.9(4)
O6	8819(3)	7493.6(17)	-338.9(11)	45.7(5)
N7	8803(2)	6398.6(19)	-571.0(10)	28.4(4)
O8	5492(2)	974.3(19)	2983.9(9)	37.4(4)
C9	6533(3)	4851(2)	751.4(12)	25.6(5)

C10	6994(2)	3267(2)	-156.3(11)	20.9(4)
C11	7958(3)	5418(2)	-207.7(12)	24.0(5)
C12	6248(2)	1696.9(19)	1095.6(11)	18.9(4)
C13	6770(2)	775.0(19)	696.3(12)	21.1(4)
C14	6791(3)	1979(2)	-457.0(12)	24.9(5)
C15	7401(3)	2703(2)	2226.0(12)	24.6(5)
C16	6377(3)	3627(2)	469.5(11)	21.0(4)
C17	6676(3)	895(2)	-85.5(12)	24.0(5)
C18	9244(3)	-577(2)	1011.3(13)	28.8(5)
C19	7459(3)	-453(2)	1022.6(13)	25.3(5)
C20	7341(3)	5768(2)	411.5(12)	26.9(5)
C21	3541(3)	2473(2)	2212.7(15)	34.7(6)
C22	10212(3)	382(2)	1476.2(13)	30.4(5)

Table 3 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for hxl_180420. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
S1	23.0(3)	20.6(3)	19.4(3)	1.95(18)	5.6(2)	-2.03(18)
Cl2	38.8(4)	43.6(4)	29.8(3)	8.3(2)	0.5(2)	13.0(3)
O1	23.6(8)	22.3(7)	24.1(8)	6.7(6)	7.8(6)	5.2(6)
O2	43.8(10)	37.5(9)	27.2(9)	4.5(7)	12.0(8)	-6.3(8)
O3	29.1(8)	23.7(8)	34.9(9)	-3.0(7)	9.3(7)	-7.9(6)
C4	24.4(11)	26.8(11)	16.1(10)	3.0(8)	2.7(8)	2.4(9)
N5	22.9(9)	17.4(8)	19.5(9)	0.1(7)	3.2(7)	-3.8(7)
O6	74.7(15)	22.7(9)	42.9(11)	1.1(8)	19.4(10)	-9.9(9)
N7	34.4(11)	26.8(10)	24.0(10)	6.4(8)	3.1(8)	-1.8(8)

O8	37.7(10)	51.9(11)	22.3(8)	10.4(8)	3.2(7)	-6.7(8)
C9	34.7(12)	21.7(11)	21.8(11)	2.4(8)	8.7(9)	6.9(9)
C10	20.8(10)	23.9(10)	17.5(10)	1.9(8)	0.9(8)	1.9(8)
C11	27.0(11)	22.4(10)	22.5(11)	6.9(9)	2.8(9)	0.2(9)
C12	19.3(10)	17.0(9)	20.3(10)	1.9(8)	2.2(8)	-1.9(8)
C13	20.3(10)	18.0(10)	25.6(11)	-0.9(8)	4.9(8)	-4.8(8)
C14	26.5(11)	30.4(11)	18.3(10)	-4.5(9)	4.8(9)	-3.7(9)
C15	27.1(11)	23.0(11)	23.2(11)	-3.7(8)	1.2(9)	-5.8(9)
C16	22.8(11)	20.9(10)	19.5(10)	5.3(8)	3.2(8)	3.6(8)
C17	25.0(11)	22.5(10)	24.8(11)	-7.9(8)	5.0(9)	-4.2(9)
C18	28.4(12)	27.7(11)	31.8(12)	0.8(9)	9.1(10)	4.8(9)
C19	27.1(11)	17.2(10)	32.9(12)	-1.1(9)	8.1(9)	-1.5(9)
C20	39.1(13)	18.5(10)	23.4(11)	1.2(8)	4.7(10)	5.1(9)
C21	29.1(13)	30.6(12)	46.3(15)	-3.8(11)	11.7(11)	4.7(10)
C22	26.9(12)	34.0(12)	30.9(12)	8.2(10)	6.3(10)	1.3(10)

Table 4 Bond Lengths for hxl_180420.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
S1	O3	1.4330(16)	N7	C11	1.471(3)
S1	N5	1.6435(17)	C9	C16	1.385(3)
S1	O8	1.4297(17)	C9	C20	1.384(3)
S1	C21	1.762(2)	C10	C14	1.463(3)
Cl2	C22	1.802(2)	C10	C16	1.400(3)
O1	C12	1.404(3)	C11	C20	1.386(3)
O1	C16	1.394(3)	C12	C13	1.333(3)
O2	N7	1.224(3)	C13	C17	1.466(3)

C4	C10	1.401(3)	C13	C19	1.510(3)
C4	C11	1.378(3)	C14	C17	1.341(3)
N5	C12	1.417(3)	C18	C19	1.532(3)
N5	C15	1.478(3)	C18	C22	1.505(3)
O6	N7	1.225(3)			

Table 5 Bond Angles for hxl_180420.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
O3	S1	N5	106.64(9)	C4	C11	N7	119.11(19)
O3	S1	C21	108.76(12)	C4	C11	C20	123.0(2)
N5	S1	C21	107.32(11)	C20	C11	N7	117.9(2)
O8	S1	O3	119.07(11)	O1	C12	N5	113.28(17)
O8	S1	N5	106.48(10)	C13	C12	O1	122.20(19)
O8	S1	C21	108.02(12)	C13	C12	N5	124.49(19)
C16	O1	C12	113.94(15)	C12	C13	C17	121.5(2)
C11	C4	C10	119.5(2)	C12	C13	C19	121.9(2)
C12	N5	S1	118.41(14)	C17	C13	C19	116.61(19)
C12	N5	C15	116.26(16)	C17	C14	C10	126.2(2)
C15	N5	S1	116.65(14)	O1	C16	C10	119.42(19)
O2	N7	O6	123.5(2)	C9	C16	O1	117.46(18)
O2	N7	C11	118.42(19)	C9	C16	C10	122.8(2)
O6	N7	C11	118.06(19)	C14	C17	C13	126.6(2)
C20	C9	C16	119.5(2)	C22	C18	C19	114.10(19)
C4	C10	C14	120.68(19)	C13	C19	C18	113.74(18)
C16	C10	C4	117.1(2)	C9	C20	C11	118.0(2)
C16	C10	C14	122.25(19)	C18	C22	Cl2	111.64(16)

Table 6 Torsion Angles for hxl_180420.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
S1	N5	C12	O1	80.51(19)	C11	C4	C10	C14	179.3(2)
S1	N5	C12	C13	-97.6(2)	C11	C4	C10	C16	0.4(3)
O1	C12	C13	C17	6.9(3)	C12	O1	C16	C9	-117.7(2)
O1	C12	C13	C19	-172.01(18)	C12	O1	C16	C10	68.5(2)
O2	N7	C11	C4	-5.6(3)	C12	C13	C17	C14	32.5(3)
O2	N7	C11	C20	175.0(2)	C12	C13	C19	C18	-109.6(2)
O3	S1	N5	C12	37.48(18)	C14	C10	C16	O1	-5.2(3)
O3	S1	N5	C15	-175.98(15)	C14	C10	C16	C9	-178.6(2)
C4	C10	C14	C17	150.3(2)	C15	N5	C12	O1	-66.2(2)
C4	C10	C16	O1	173.62(18)	C15	N5	C12	C13	115.8(2)
C4	C10	C16	C9	0.2(3)	C16	O1	C12	N5	110.60(19)
C4	C11	C20	C9	0.1(4)	C16	O1	C12	C13	-71.3(2)
N5	C12	C13	C17	-175.20(19)	C16	C9	C20	C11	0.5(3)
N5	C12	C13	C19	5.9(3)	C16	C10	C14	C17	-30.9(4)
O6	N7	C11	C4	174.1(2)	C17	C13	C19	C18	71.4(3)
O6	N7	C11	C20	-5.2(3)	C19	C13	C17	C14	-148.5(2)
N7	C11	C20	C9	179.4(2)	C19	C18	C22	Cl2	65.3(2)
O8	S1	N5	C12	165.60(16)	C20	C9	C16	O1	-174.2(2)
O8	S1	N5	C15	-47.87(18)	C20	C9	C16	C10	-0.6(4)
C10	C4	C11	N7	-179.88(19)	C21	S1	N5	C12	-78.92(18)
C10	C4	C11	C20	-0.6(3)	C21	S1	N5	C15	67.61(18)
C10	C14	C17	C13	-1.8(4)	C22	C18	C19	C13	66.0(3)

Table 7 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for hxl_180420.

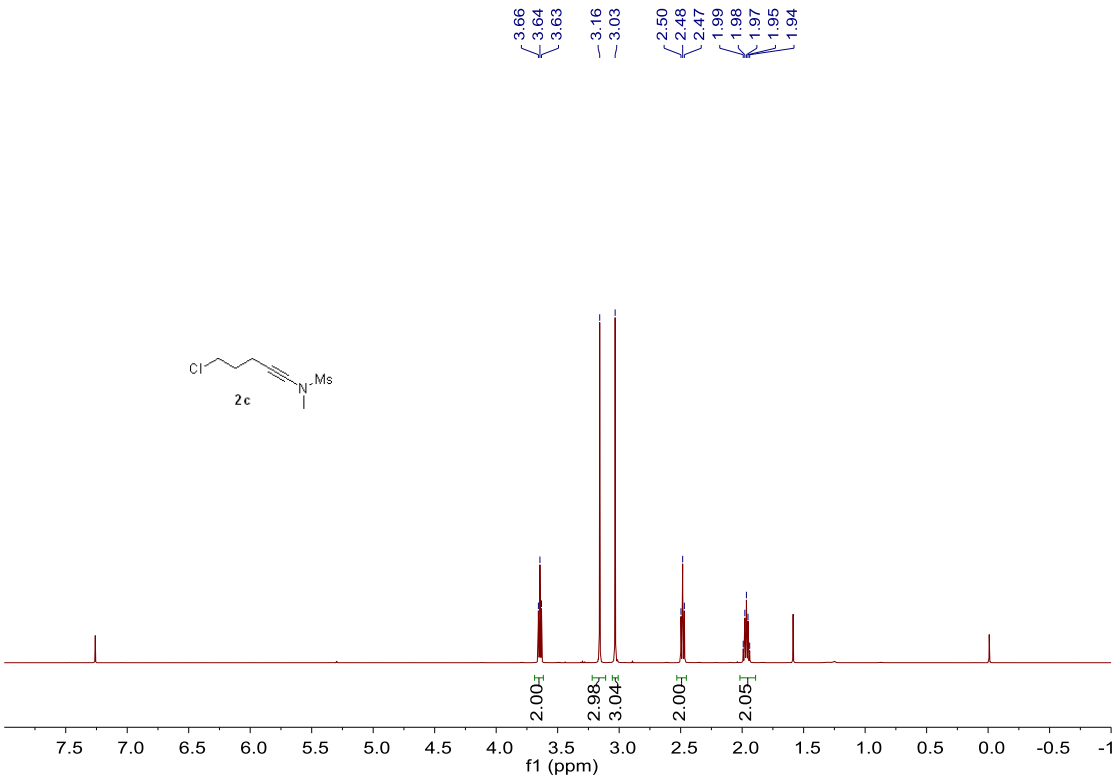
Atom	*x*	*y*	*z*	U(eq)
H4	8232.85	4010.91	-925.64	27
H9	6087.55	5060.28	1174.8	31
H14	6736.81	1901.87	-963.59	30
H15A	6795.54	3500.9	2215.73	37
H15B	8336.89	2832.48	1982.4	37
H15C	7730.41	2451.39	2725.5	37
H17	6516.46	128.56	-356.42	29
H18A	9577.37	-1448.22	1172.31	35
H18B	9470.52	-477.85	510.44	35
H19A	6924.5	-1183.67	757.86	30
H19B	7236.05	-506.25	1526.14	30
H20	7469.52	6611.48	597.16	32
H21A	3188.06	2694.2	1710.51	52
H21B	4051.23	3217.31	2461.02	52
H21C	2629.11	2216.93	2447.13	52
H22A	9850.92	1256.01	1334.3	36
H22B	11333.48	305.9	1398.94	36

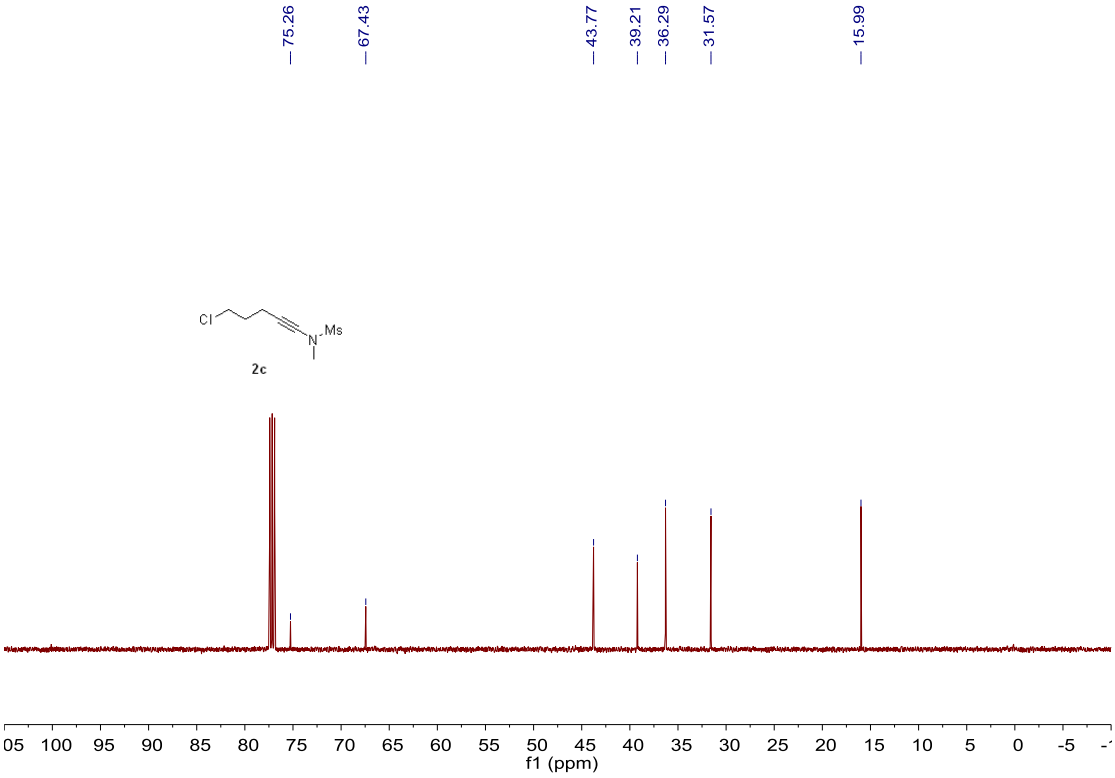
9. References

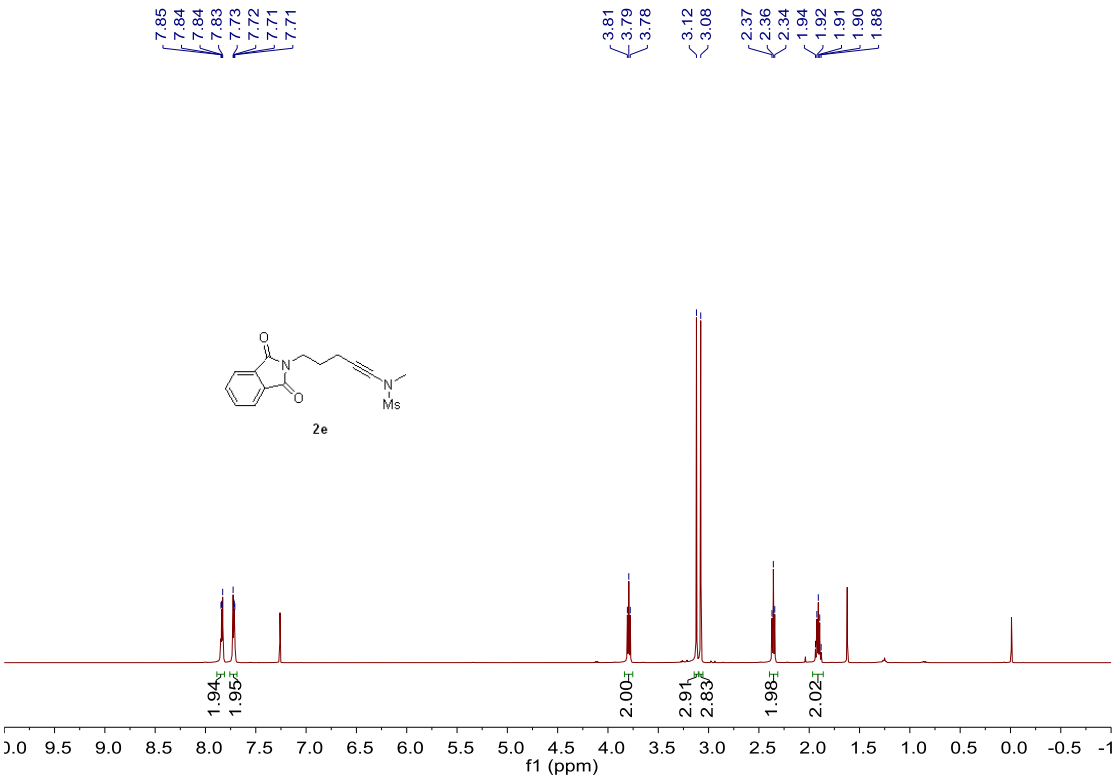
[1] T. Hamada, X. Ye and S. S. Stahl, *J. Am. Chem. Soc*., 2008, **130**, 833-835.

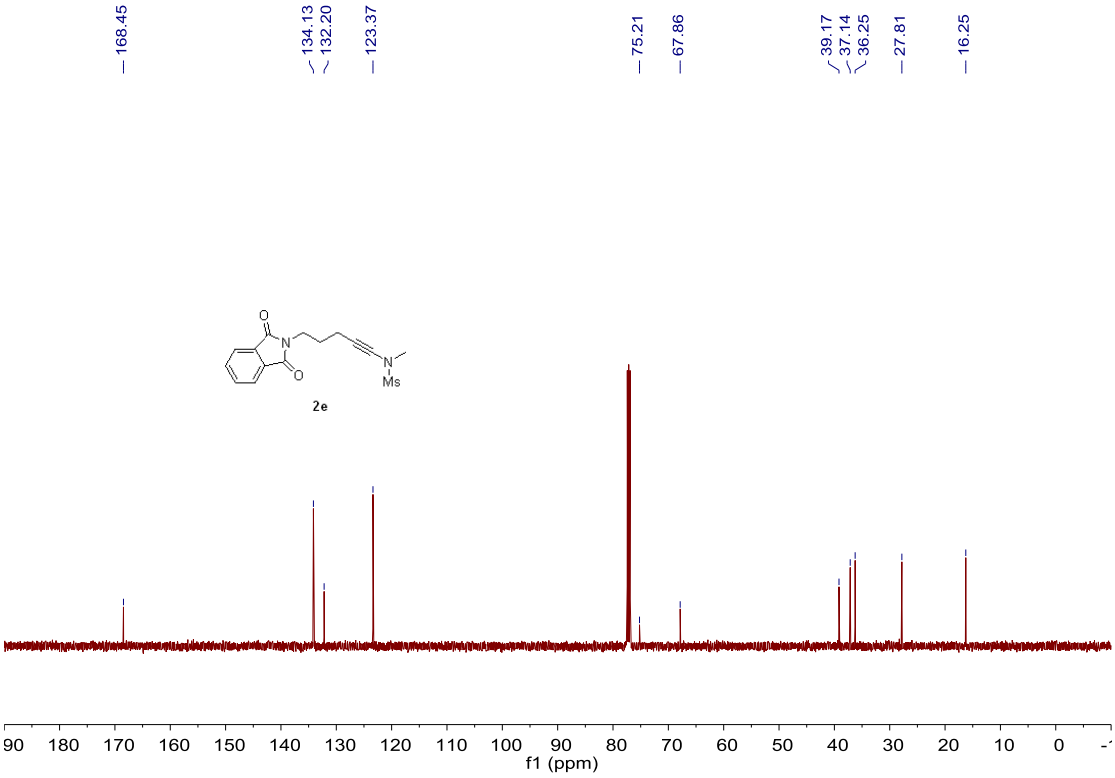
[2] A. D. Gillie, R. J. Redd and P. W. Davies, *Adv.Synth. Catal.*, 2016, **358**, 226-239.

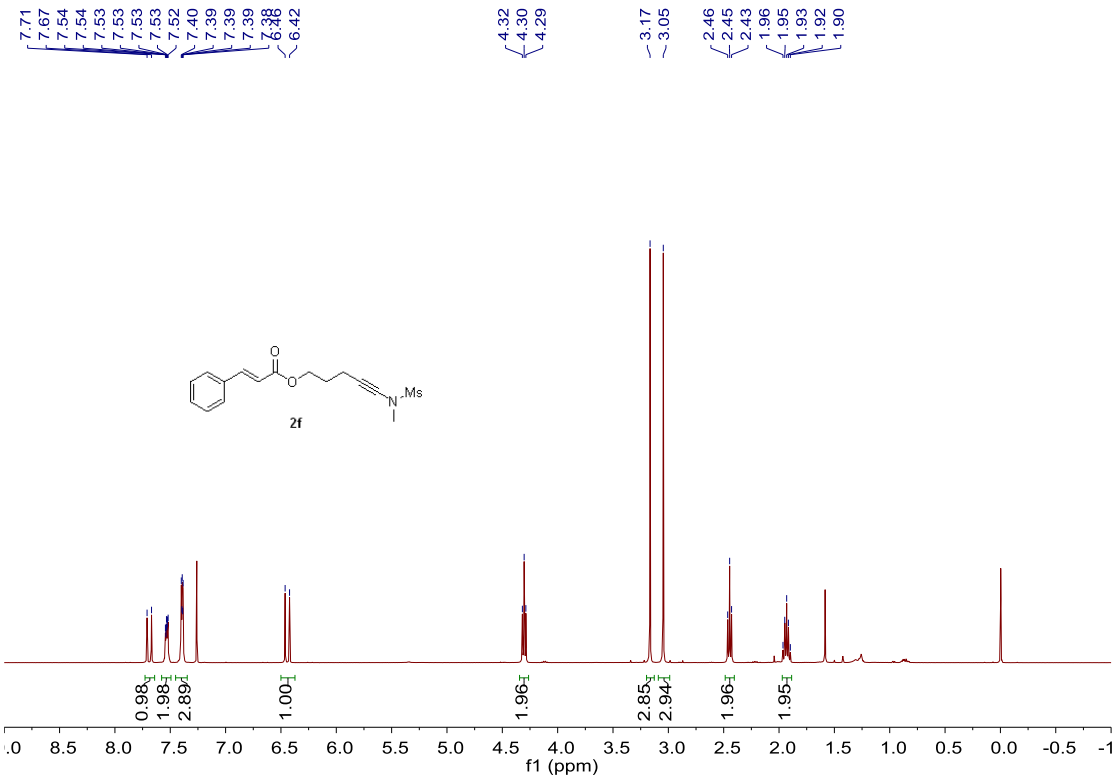
10. NMR spectrum of some starting materials and products

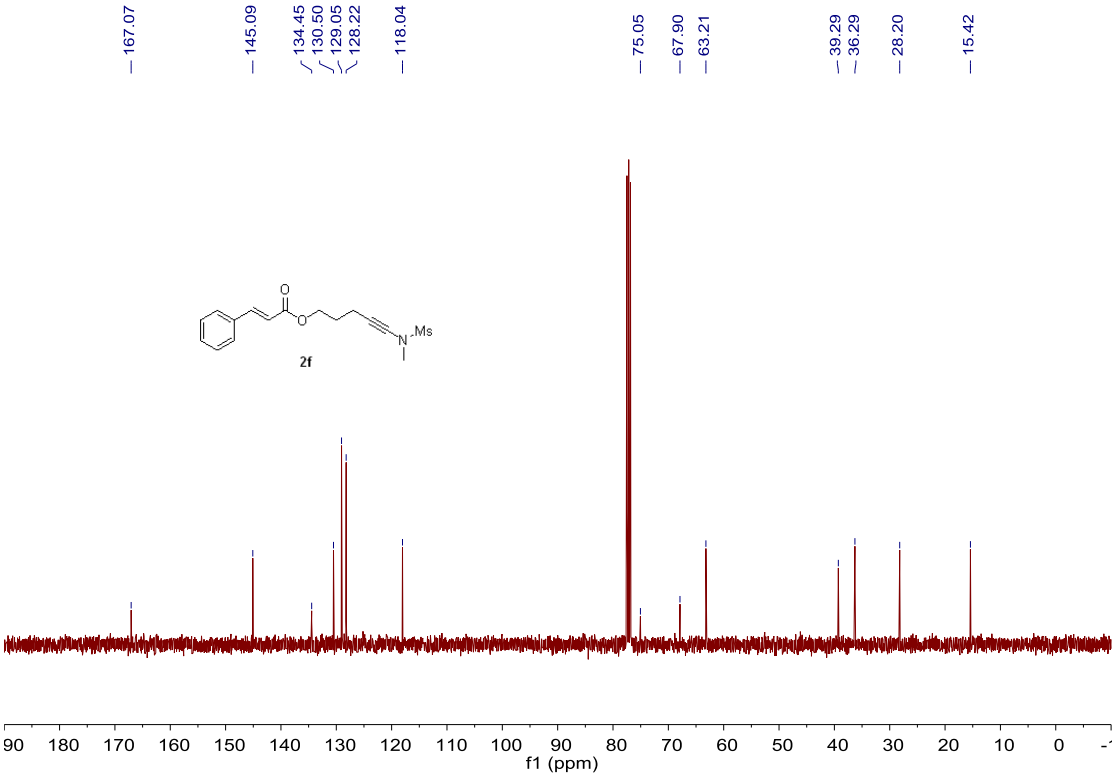

3.66
3.64
3.63
3.16
3.03
2.50
2.48
2.47
1.99
1.98
1.97
1.95
1.94
Cl
N
Ms
2c
2.00
2.98
3.04
2.00
2.05
f1 (ppm)


75.26
67.43
43.77
39.21
36.29
31.57
15.99
Cl
N
Ms
2c
f1 (ppm)

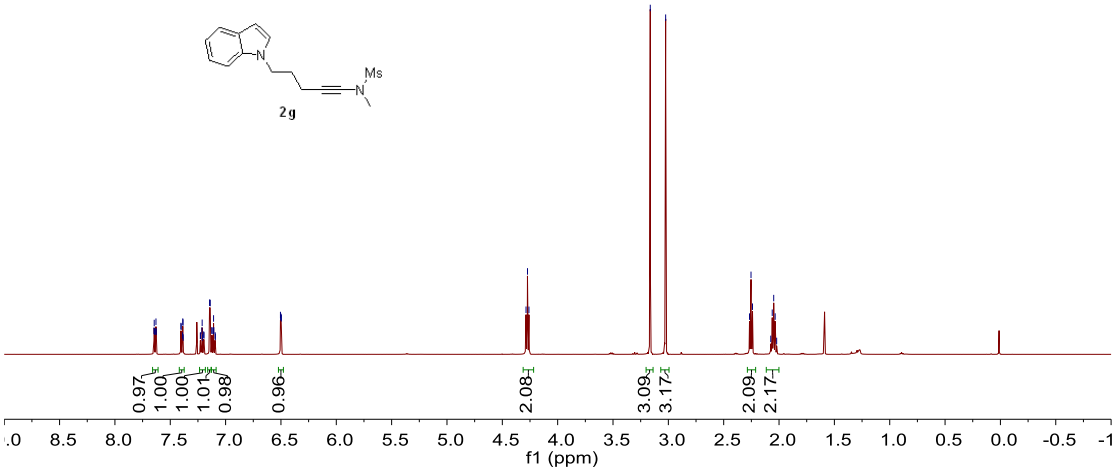

7.85
7.84
7.84
7.83
7.73
7.72
7.71
7.71
3.81
3.79
3.78
3.12
3.08
2.37
2.36
2.34
1.94
1.92
1.91
1.90
1.88
O
N
O
N
Ms
2e
1.94
1.95
2.00
2.91
2.83
1.98
2.02
f1 (ppm)


168.45
134.13
132.20
123.37
75.21
67.86
39.17
37.14
36.25
27.81
16.25
O
N
O
N
Ms
2e
f1 (ppm)

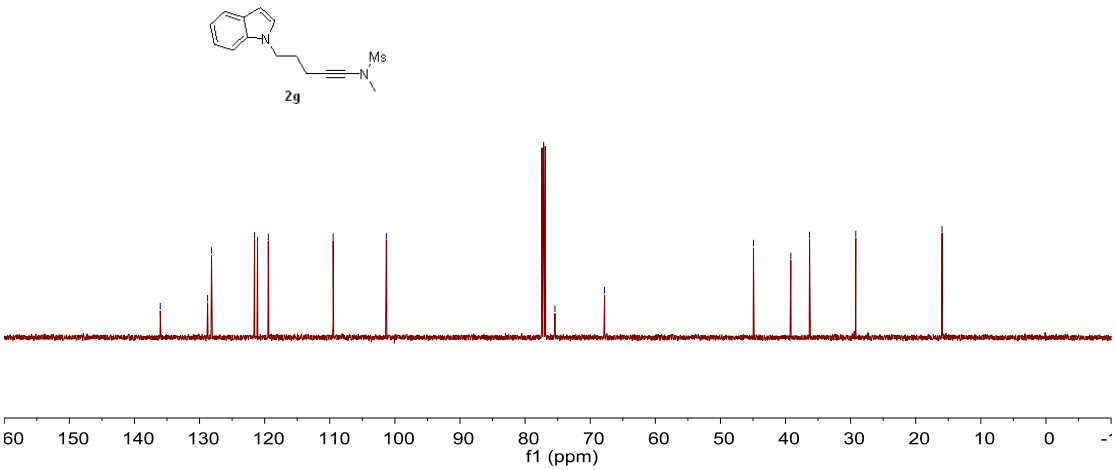

7.71
7.67
7.54
7.54
7.53
7.53
7.53
7.53
7.52
7.40
7.39
7.39
7.39
7.38
6.42
4.32
4.30
4.29
3.17
3.05
2.46
2.45
2.43
1.96
1.95
1.93
1.92
1.90
O
O
N
Ms
2f
0.98
1.98
2.89
1.00
1.96
2.85
2.94
1.96
1.95
f1 (ppm)

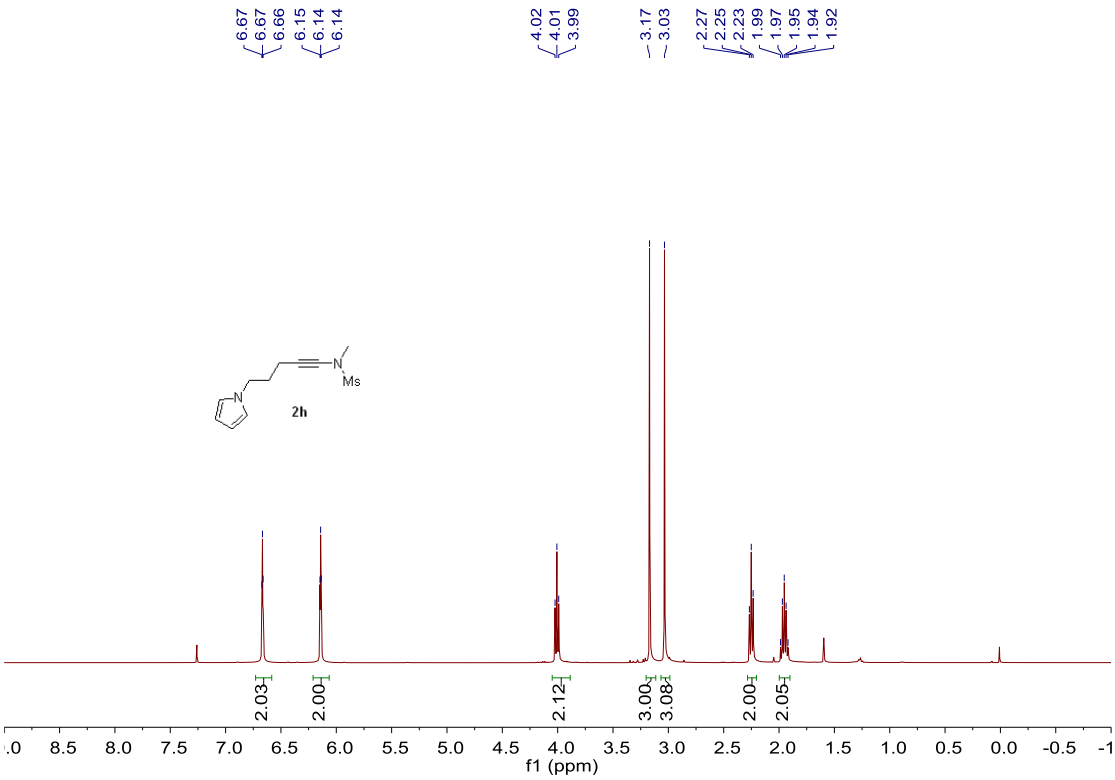

167.07
145.09
134.45
130.50
129.05
128.22
118.04
75.05
67.90
63.21
39.29
36.29
28.20
15.42
O
O
N
Ms
2f
f1 (ppm)

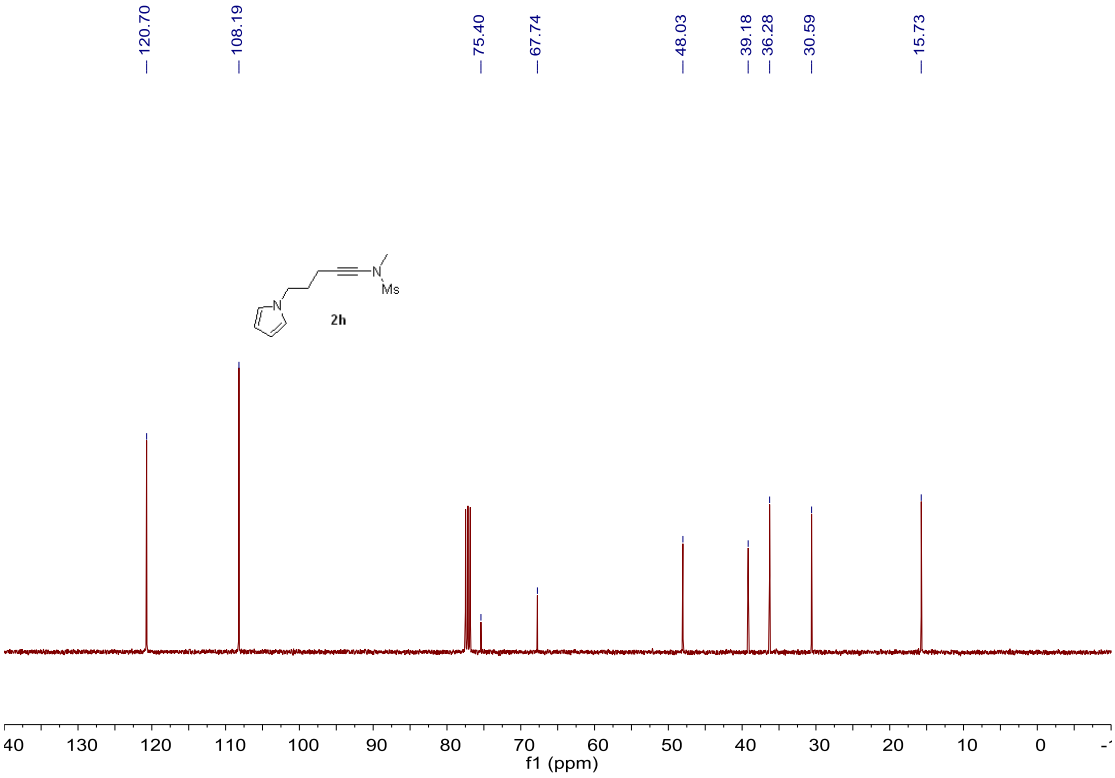

7.65
7.65
7.64
7.63
7.63
7.63
7.40
7.40
7.39
7.39
7.39
7.23
7.21
7.21
7.21
7.20
7.20
7.14
7.14
7.12
7.12
7.11
7.11
7.11
7.09
7.09
6.50
6.50
6.50
6.50
4.29
4.27
4.26
4.18
3.02
2.27
2.25
2.24
2.07
2.06
2.05
2.03
2.02

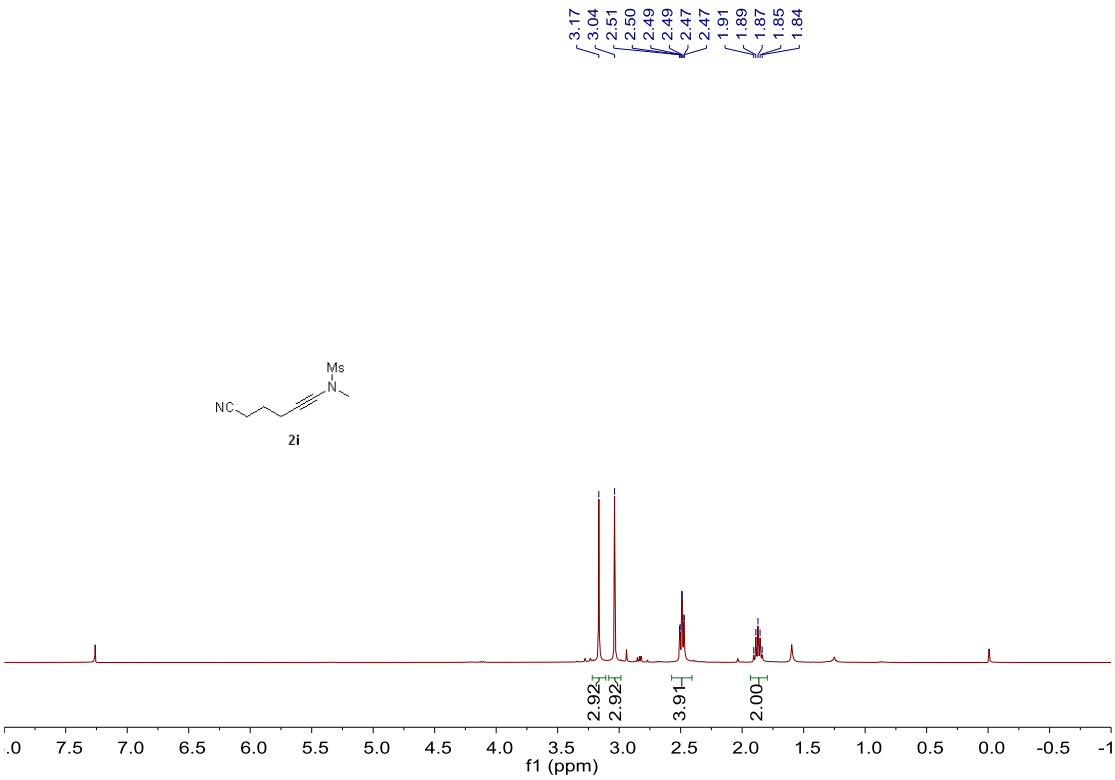

Ms
N
2g
0.97
1.00
1.01
0.98
0.96
2.08
3.09
3.17
2.09
2.17
f1 (ppm)

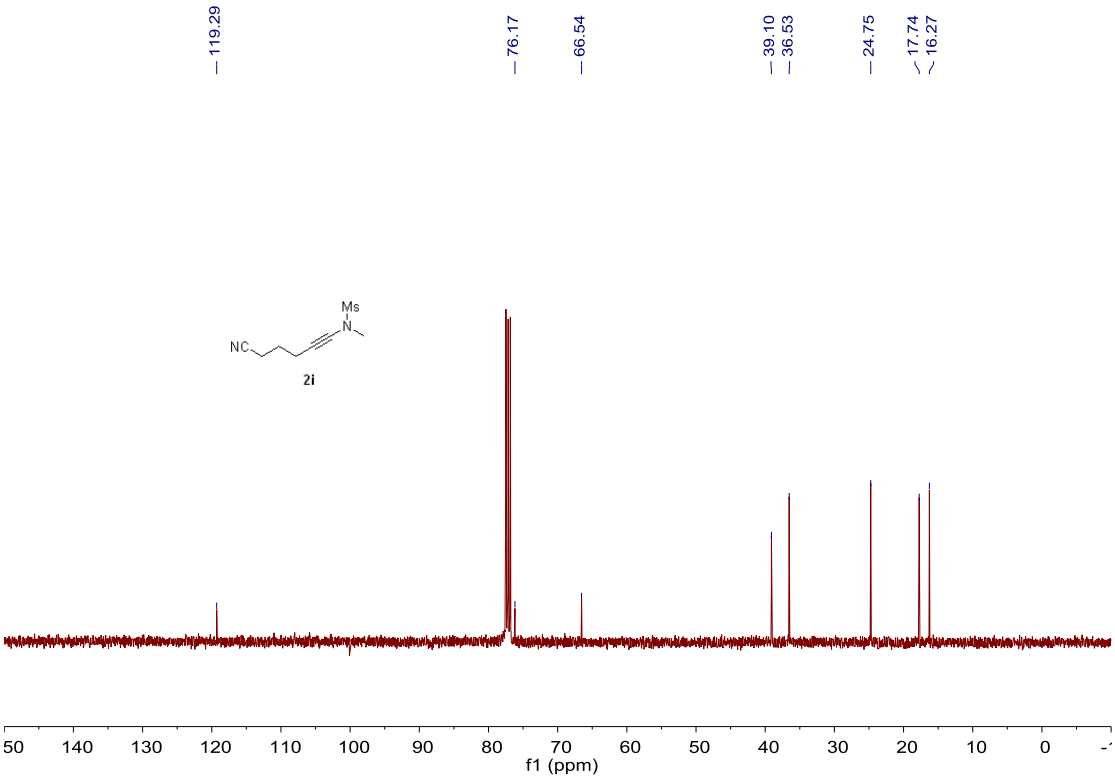

136.04
128.76
128.16
121.55
121.10
119.44
109.49
101.31
75.41
67.80
44.93
39.19
36.31
29.21
15.96

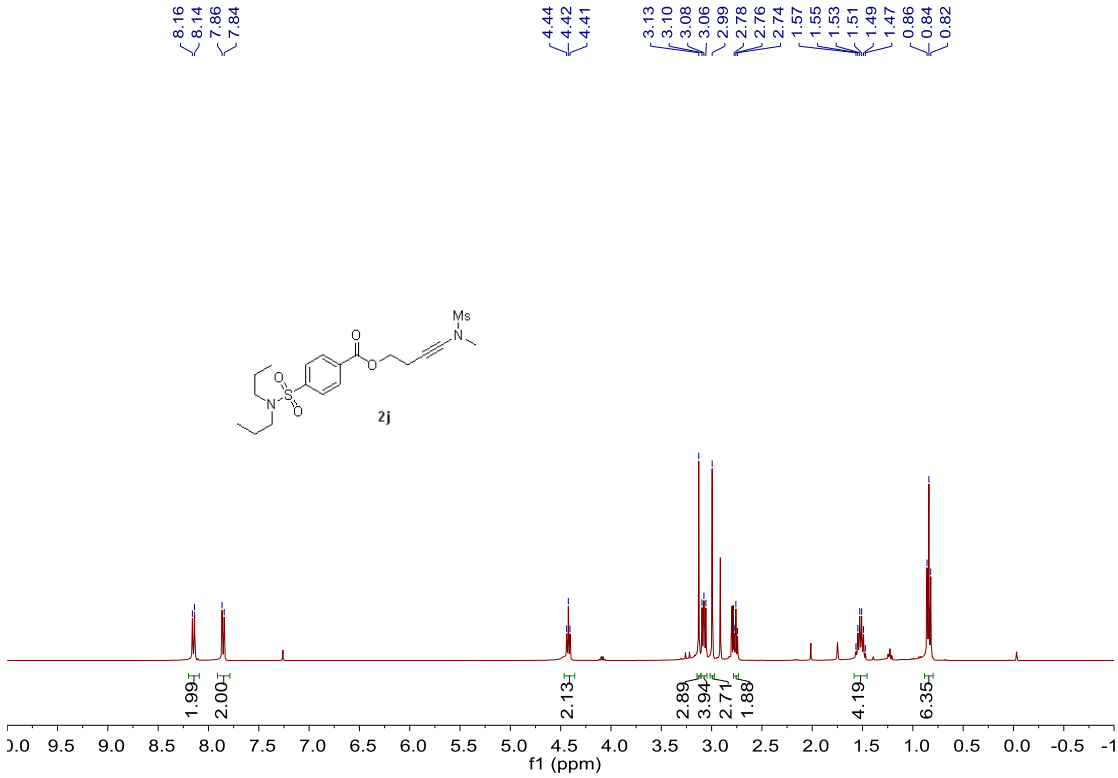

Ms
N
2g
f1 (ppm)

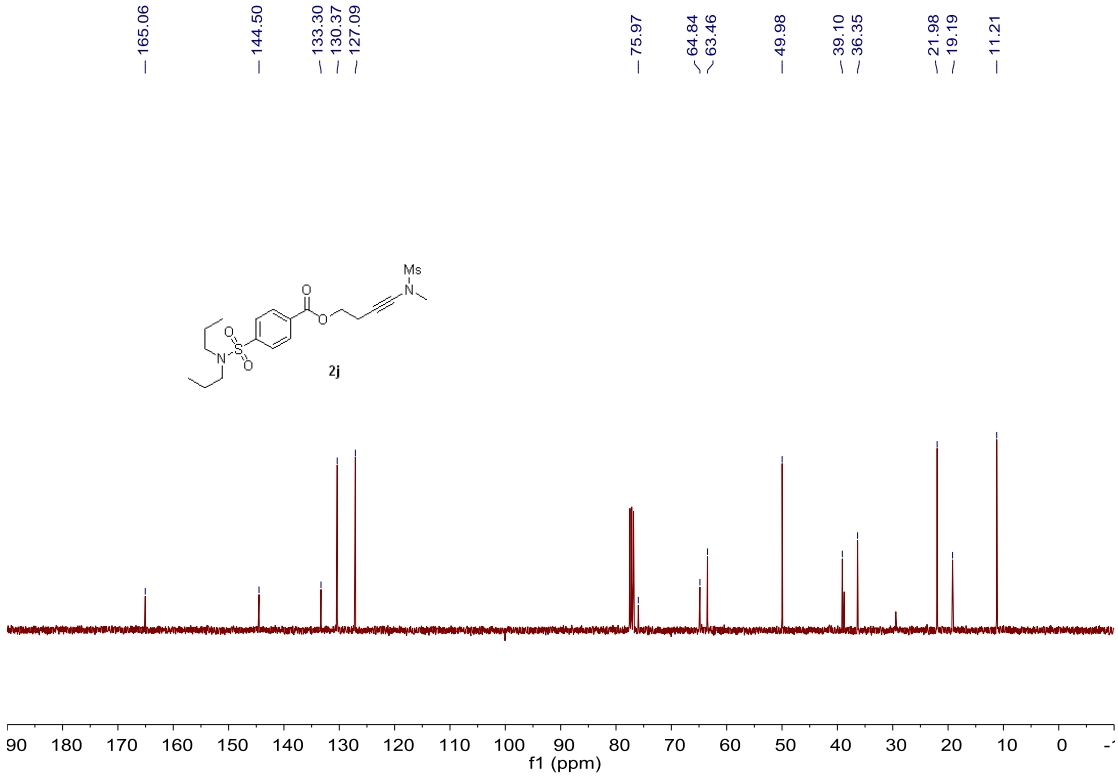

6.67
6.67
6.66
6.15
6.14
6.14
4.02
4.01
3.99
3.17
3.03
2.27
2.25
2.23
1.99
1.97
1.95
1.94
1.92
N
Ms
N
2h
2.03
2.00
2.12
3.00
3.08
2.00
2.05
f1 (ppm)

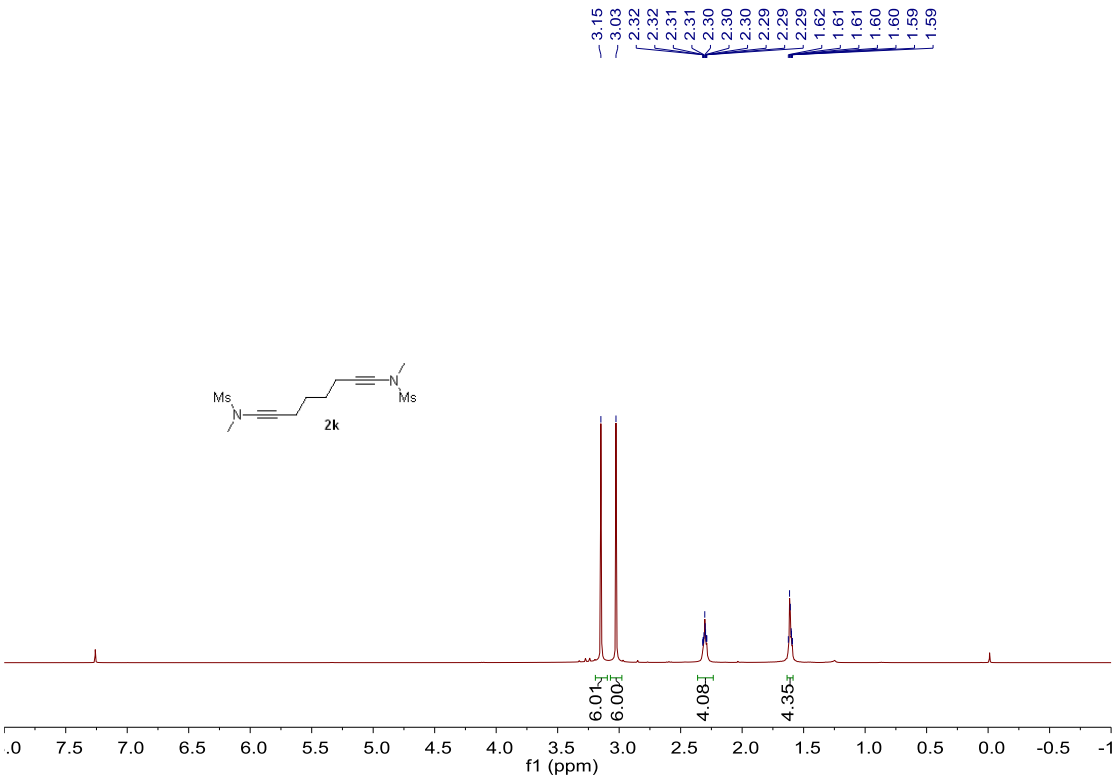

120.70
108.19
75.40
67.74
48.03
39.18
36.28
30.59
15.73
N
Ms
N
2h
f1 (ppm)

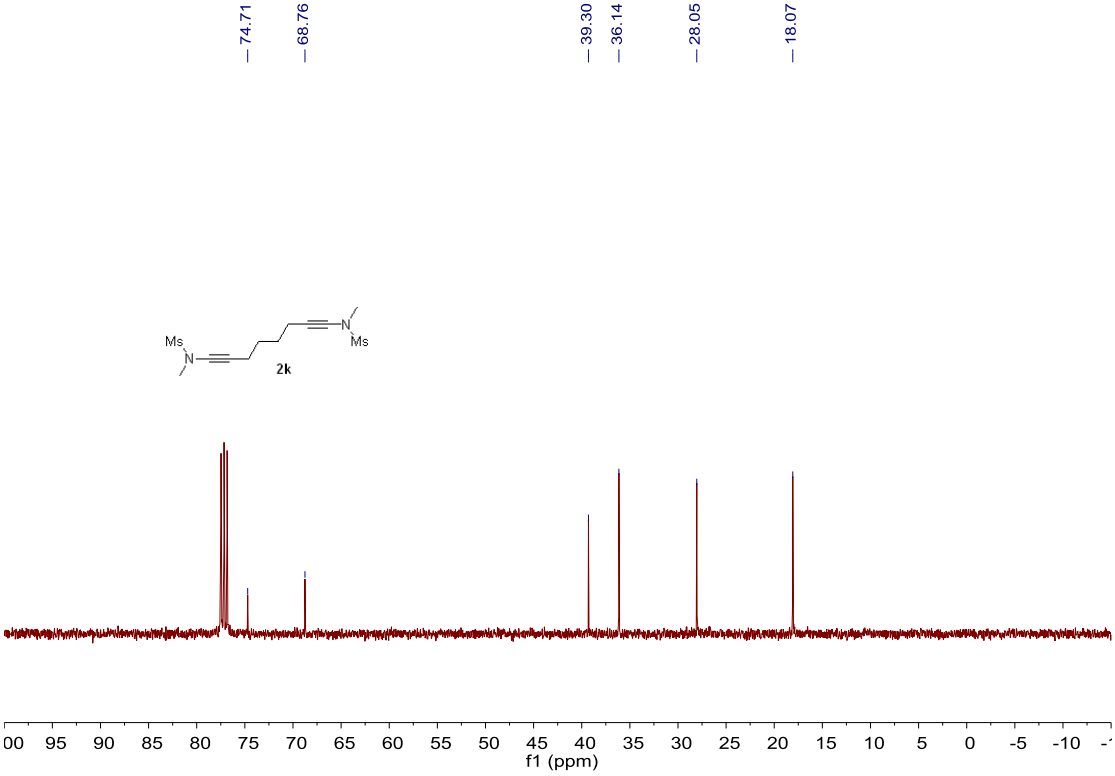

3.17
3.04
2.51
2.50
2.49
2.49
2.47
2.47
1.91
1.89
1.87
1.85
1.84
Ms
N
NC
2i
2.92
2.92
3.91
2.00
f1 (ppm)

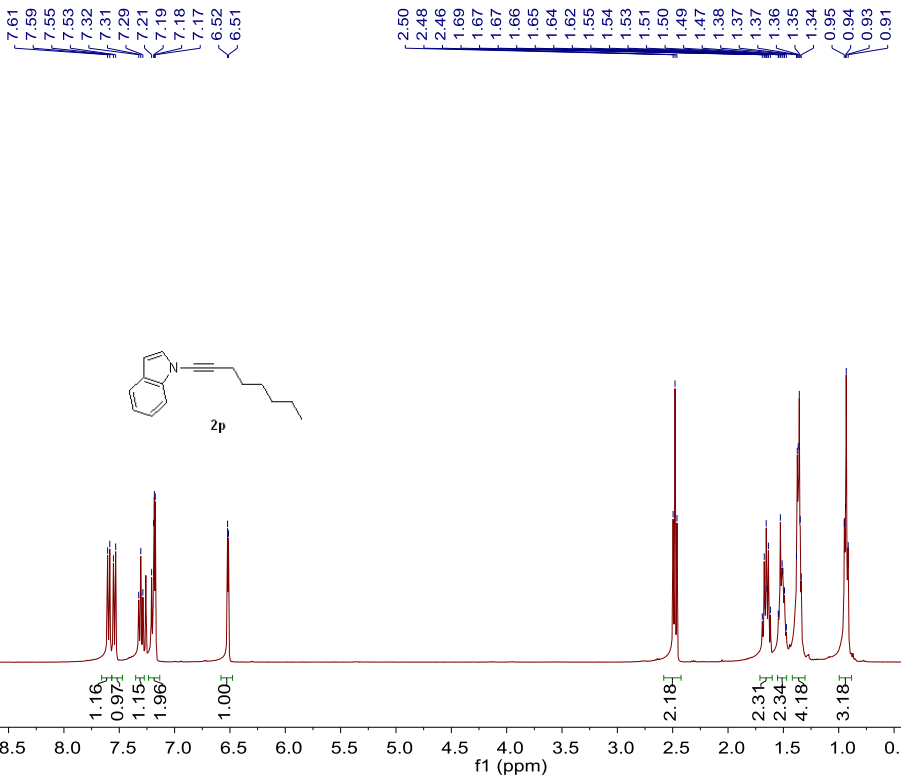

119.29
76.17
66.54
39.10
36.53
24.75
17.74
16.27
Ms
N
NC
2i
f1 (ppm)

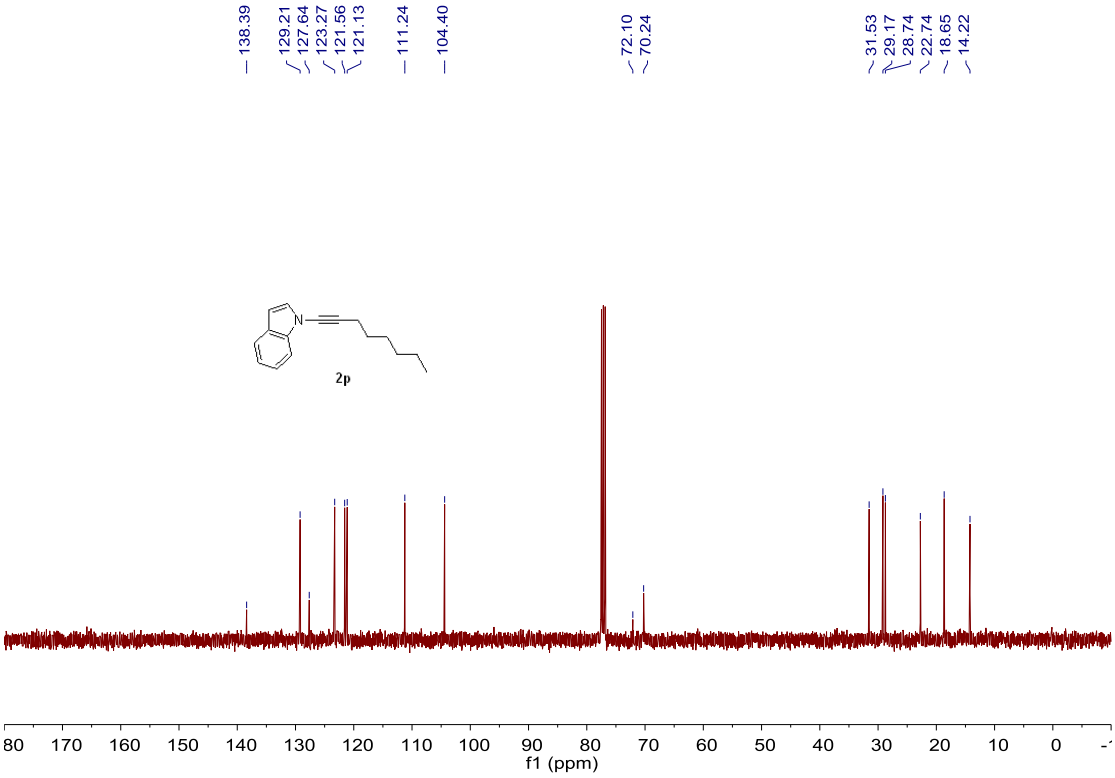

8.16
8.14
7.86
7.84
4.44
4.42
4.41
3.13
3.10
3.08
3.06
2.99
2.78
2.76
2.74
1.57
1.55
1.53
1.51
1.49
1.47
0.86
0.84
0.82
Ms
N
O
O
O
O
S
N
2j
1.99
2.00
2.13
2.89
3.94
2.71
1.88
4.19
6.35
f1 (ppm)


165.06
144.50
133.30
130.37
127.09
75.97
64.84
63.46
49.98
39.10
36.35
21.98
19.19
11.21
Ms
N
O
O
O
O
S
N
2j
f1 (ppm)

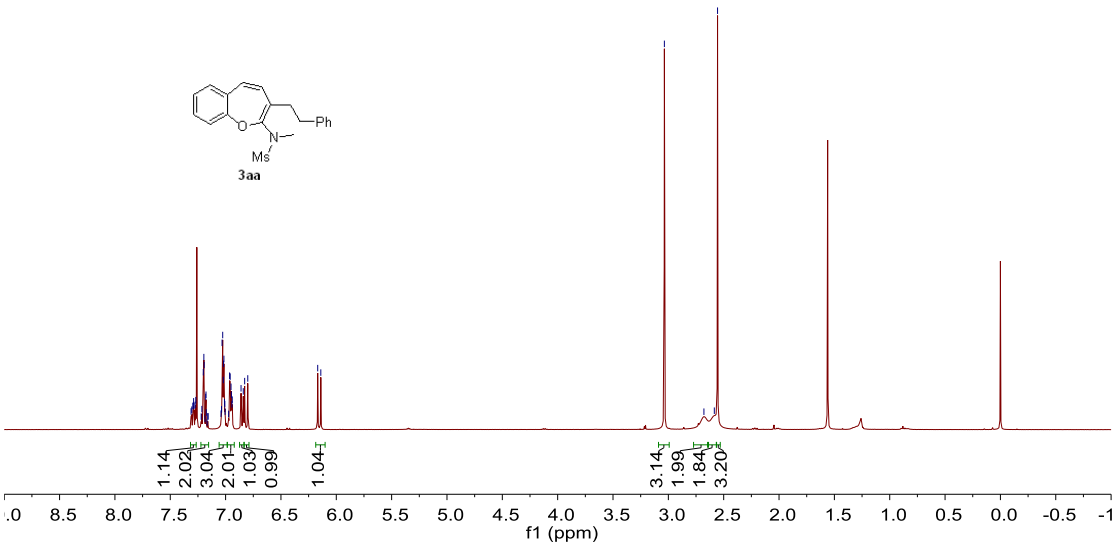

3.15
3.03
2.32
2.32
2.31
2.31
2.30
2.30
2.30
2.29
2.29
2.29
1.62
1.61
1.61
1.60
1.60
1.59
1.59
Ms
N
N
Ms
2k
6.01
6.00
4.08
4.35
f1 (ppm)


74.71
68.76
39.30
36.14
28.05
18.07
Ms
N
N
Ms
2k
f1 (ppm)

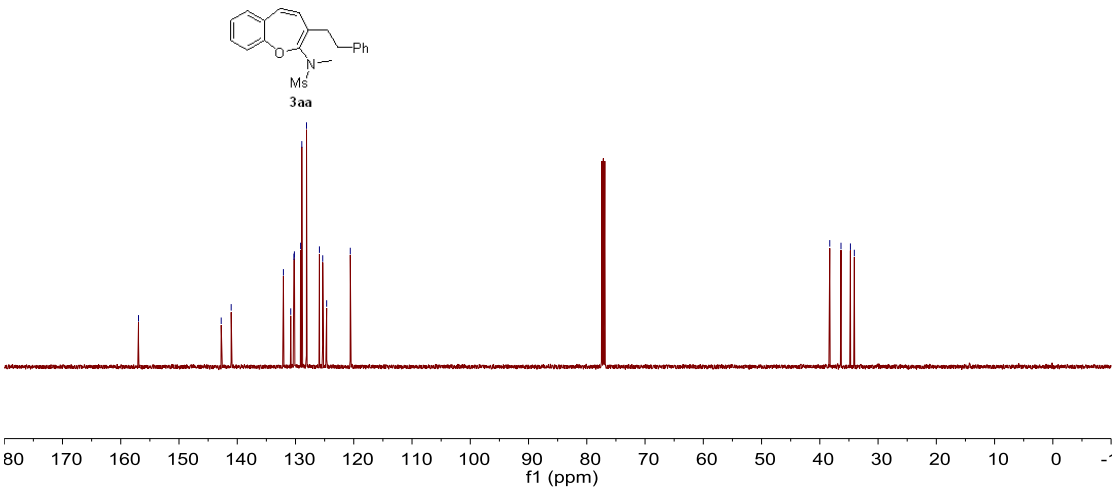

7.61
7.59
7.55
7.53
7.32
7.31
7.29
7.21
7.19
7.18
7.17
6.52
6.51
2.50
2.48
2.46
1.69
1.67
1.67
1.66
1.65
1.64
1.62
1.55
1.54
1.53
1.51
1.50
1.49
1.47
1.38
1.37
1.37
1.36
1.35
1.34
0.95
0.94
0.93
0.91
2p
1.16
0.97
1.15
1.96
1.00
2.18
2.31
2.34
4.18
3.18
f1 (ppm)

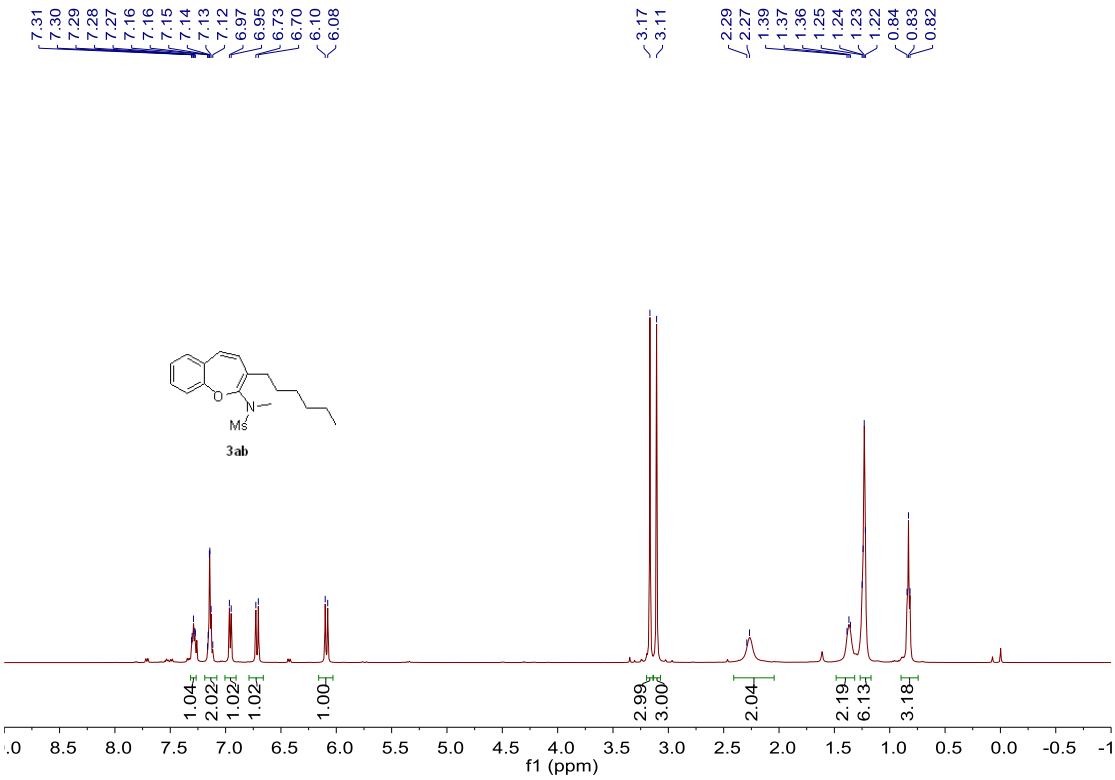

138.39
129.21
127.64
123.27
121.56
121.13
111.24
104.40
72.10
70.24
31.53
29.17
28.74
22.74
18.65
14.22
2p
f1 (ppm)

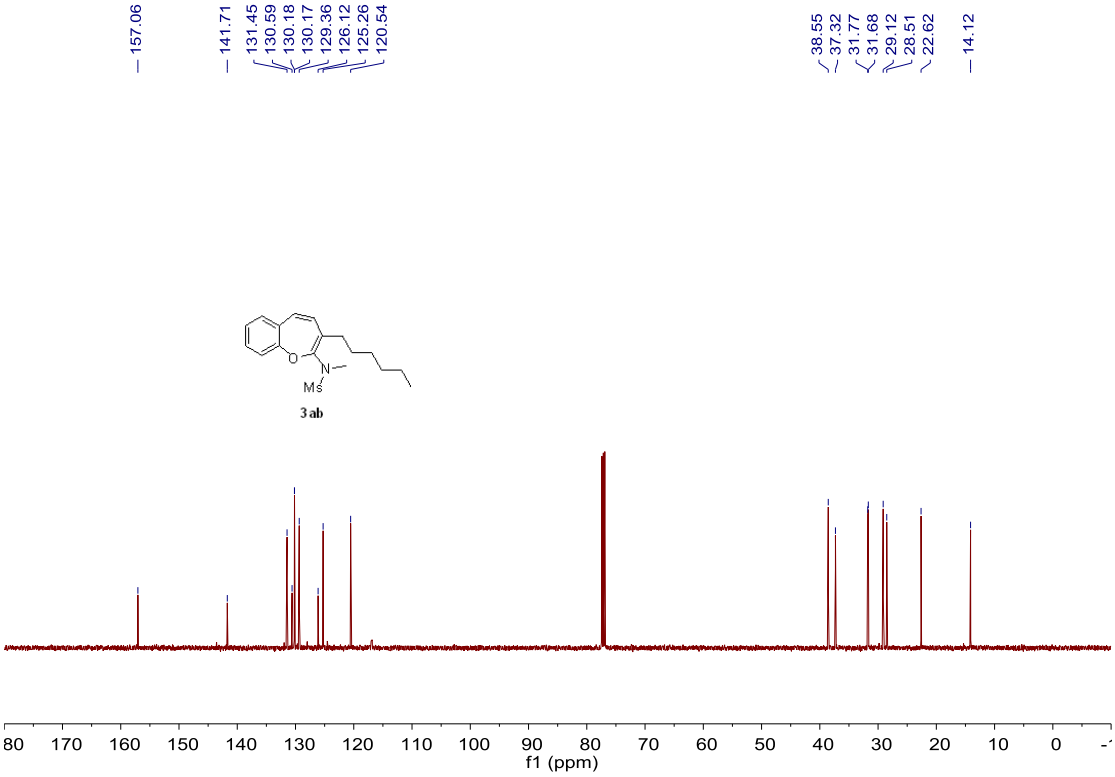

7.31
7.31
7.30
7.29
7.29
7.29
7.28
7.27
7.21
7.20
7.20
7.19
7.18
7.18
7.04
7.03
7.03
7.02
7.02
7.02
7.01
7.01
7.00
6.96
6.96
6.95
6.95
6.94
6.94
6.86
6.84
6.83
6.80
6.17
6.14
3.04
2.68
2.58
2.56

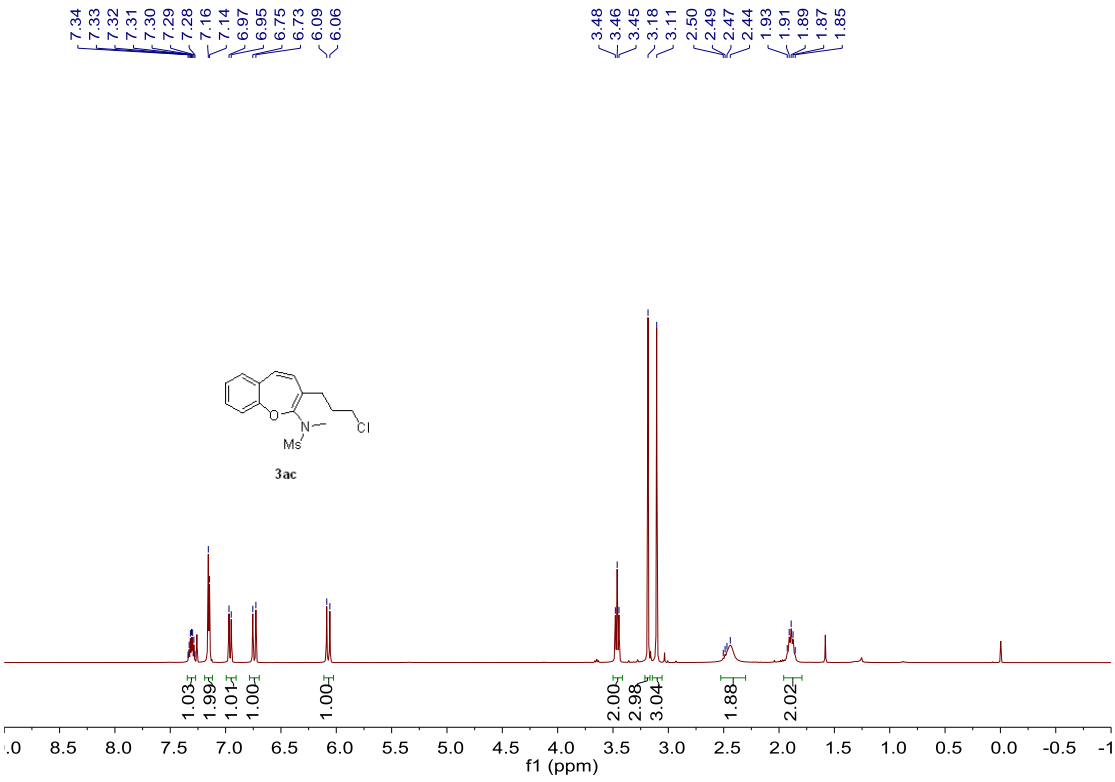

Ph
N
Ms
3aa
1.14
2.02
3.04
2.01
1.03
0.99
1.04
3.14
1.99
1.84
3.20
f1 (ppm)

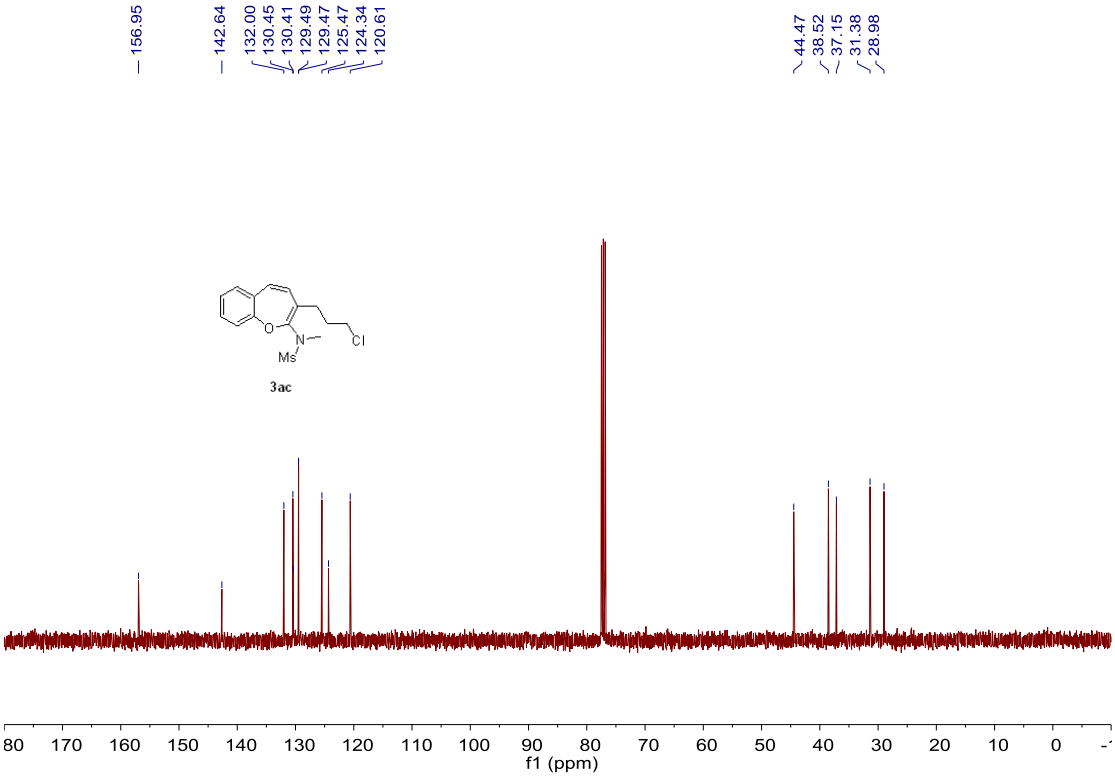

HXL-D-022-C.1.fid
156.95
142.75
141.04
132.08
130.82
130.27
130.19
129.13
128.92
128.11
125.90
125.33
124.65
120.60
38.29
36.36
34.75
34.07

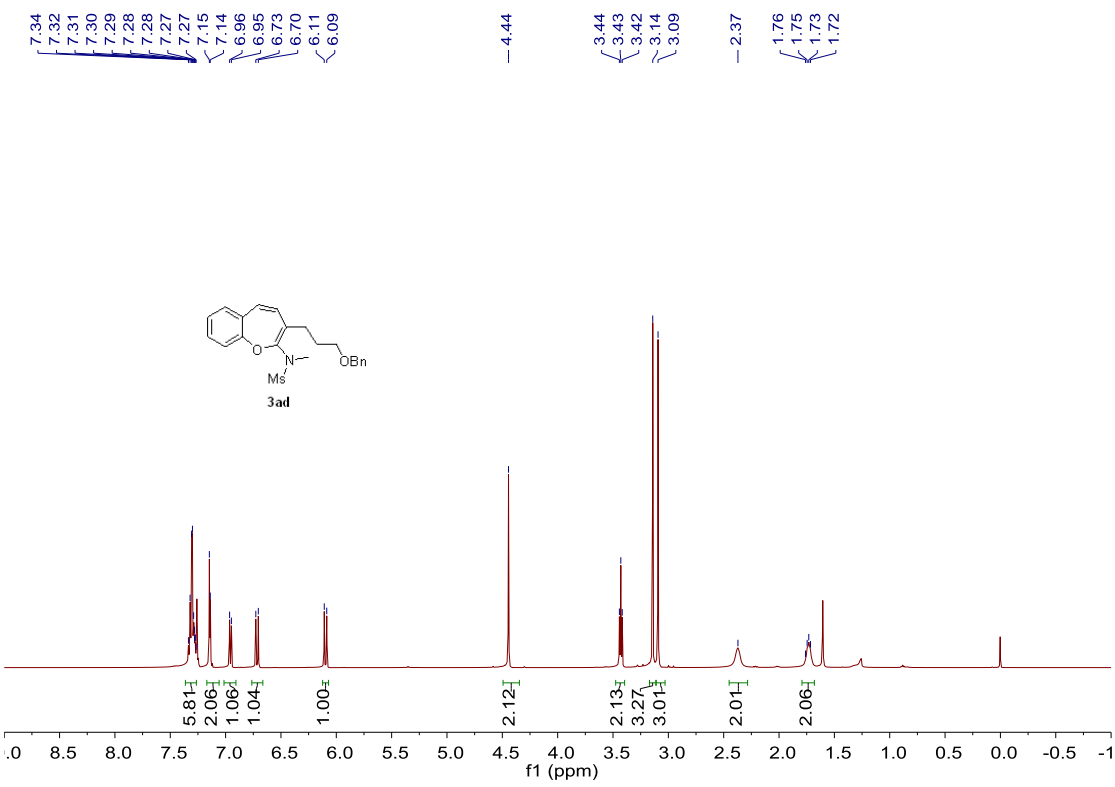

Ph
N
Ms
3aa
f1 (ppm)

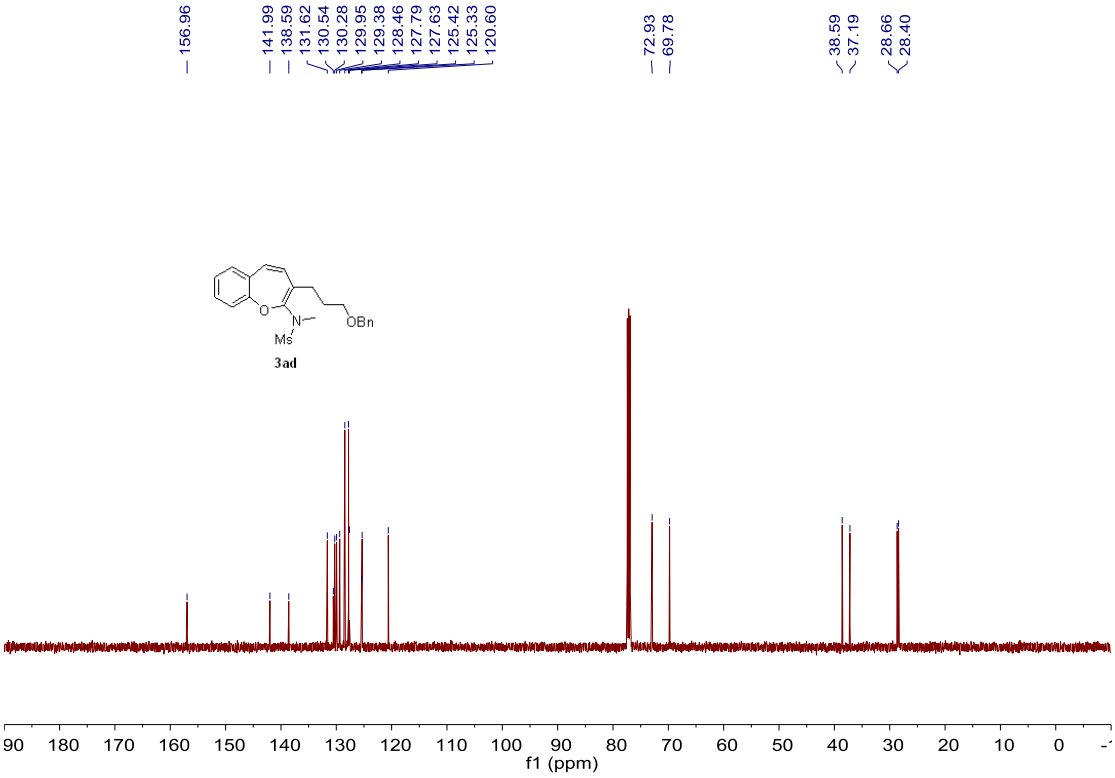

7.31
7.30
7.29
7.28
7.27
7.16
7.16
7.15
7.14
7.13
7.12
6.97
6.95
6.73
6.70
6.10
6.08
3.17
3.11
2.29
2.27
1.39
1.37
1.36
1.25
1.24
1.23
1.22
0.84
0.83
0.82
Ms
3ab
1.04
2.02
1.02
1.02
1.00
2.99
3.00
2.04
2.19
6.13
3.18
f1 (ppm)

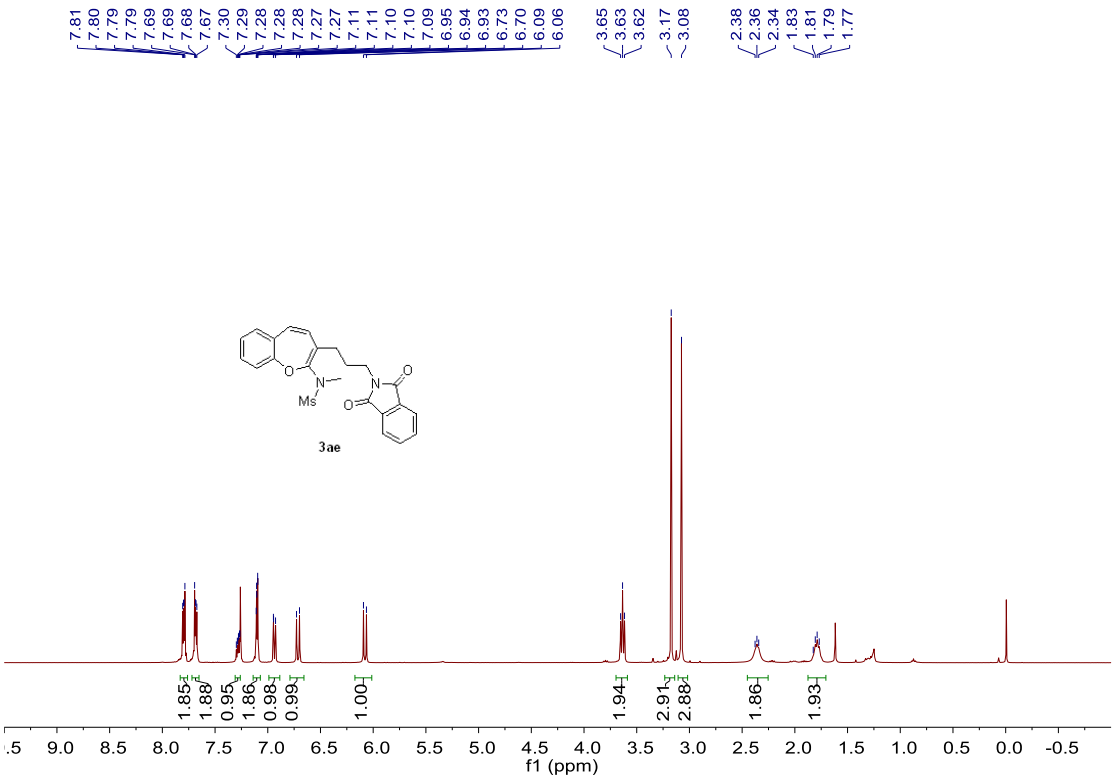

157.06
141.71
131.45
130.59
130.18
130.17
129.36
126.12
125.26
120.54
38.55
37.32
31.77
31.68
29.12
28.51
22.62
14.12
Ms
3ab
f1 (ppm)

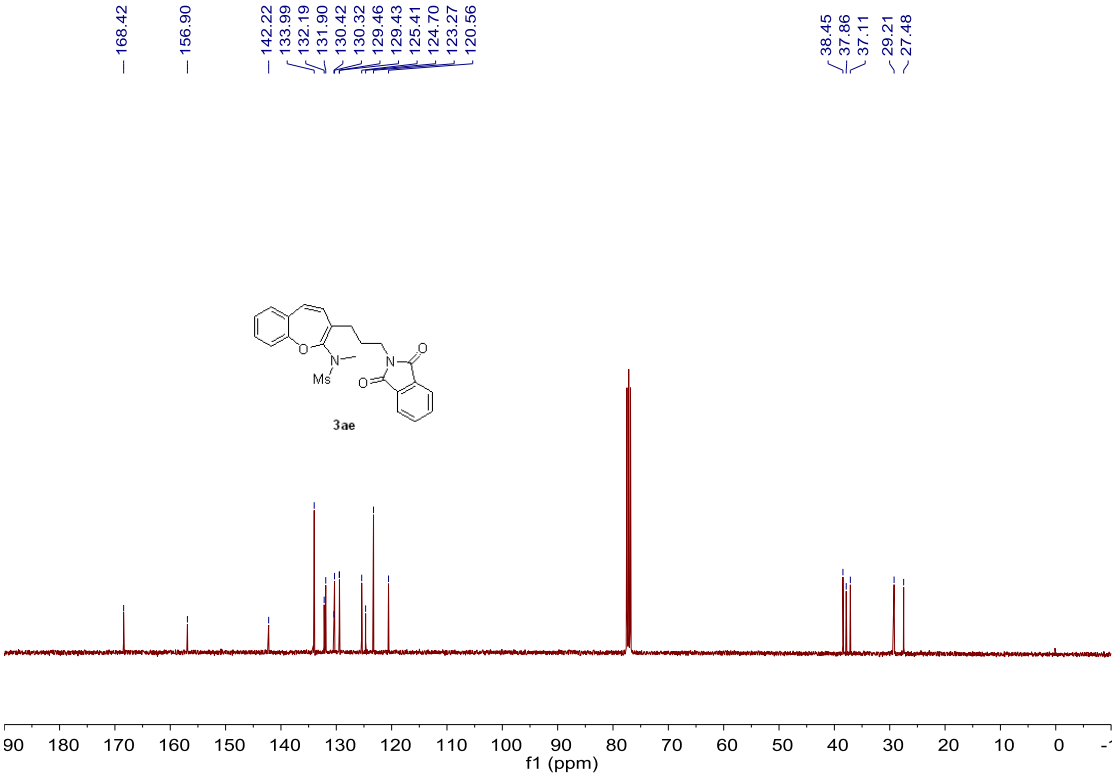

7.34
7.33
7.32
7.31
7.30
7.29
7.28
7.16
7.14
6.97
6.95
6.75
6.73
6.09
6.06
3.48
3.46
3.45
3.18
3.11
2.50
2.49
2.47
2.44
1.93
1.91
1.89
1.87
1.85
Cl
N
Ms
O
3ac
1.03
1.99
1.01
1.00
1.00
2.00
2.98
3.04
1.88
2.02
f1 (ppm)

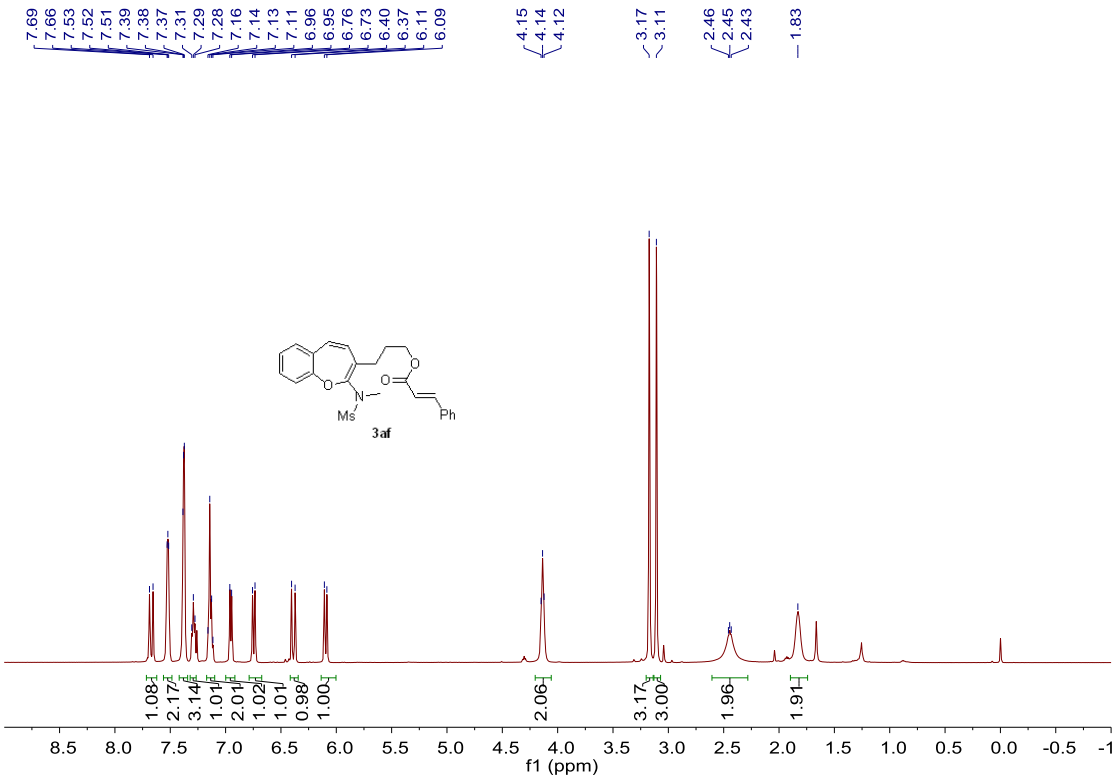

156.95
142.64
132.00
130.45
130.41
129.49
129.47
125.47
124.34
120.61
44.47
38.52
37.15
31.38
28.98
Cl
N
Ms
O
3ac
f1 (ppm)

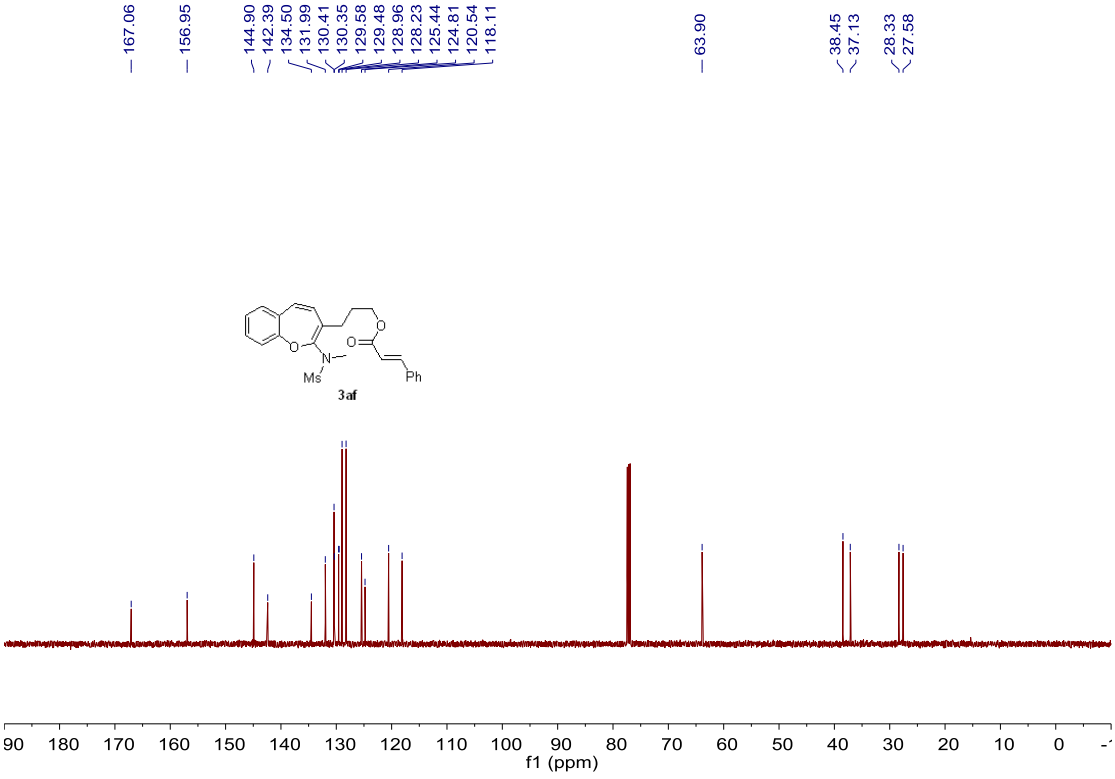

7.34
7.32
7.31
7.30
7.29
7.28
7.28
7.27
7.27
7.15
7.14
6.96
6.95
6.73
6.70
6.11
6.09
4.44
3.44
3.43
3.42
3.14
3.09
2.37
1.76
1.75
1.73
1.72
OBn
N
Ms
3ad
5.81
2.06
1.06
1.04
1.00
2.12
2.13
3.27
3.01
2.01
2.06
f1 (ppm)


156.96
141.99
138.59
131.62
130.54
130.28
129.95
129.38
128.46
127.79
127.63
125.42
125.33
120.60
72.93
69.78
38.59
37.19
28.66
28.40
OBn
N
Ms
3ad
f1 (ppm)

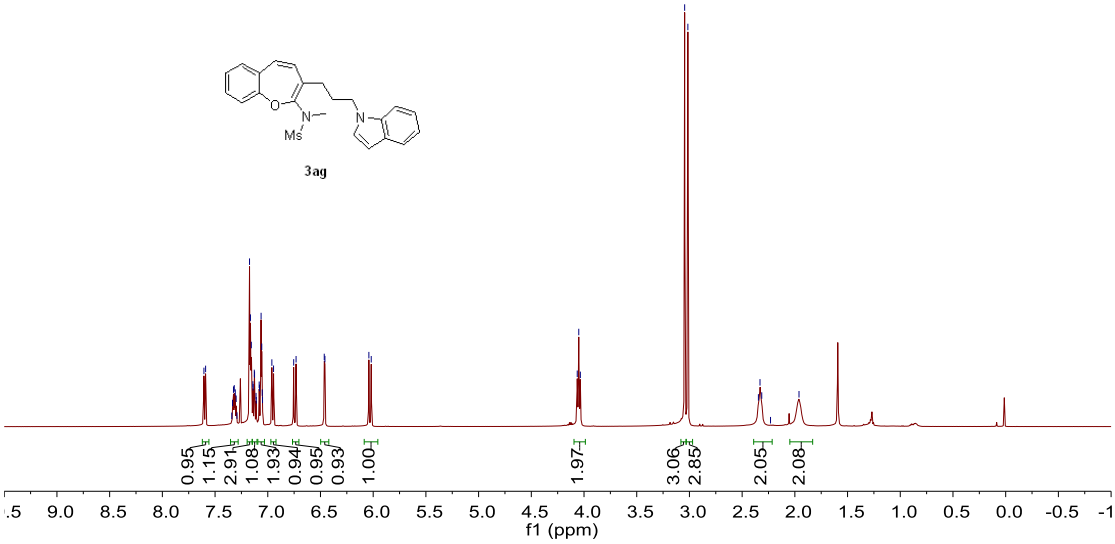

7.81
7.80
7.79
7.79
7.69
7.69
7.68
7.67
7.30
7.29
7.28
7.28
7.28
7.27
7.27
7.11
7.11
7.10
7.10
7.09
6.95
6.94
6.93
6.73
6.70
6.09
6.06
3.65
3.63
3.62
3.17
3.08
2.38
2.36
2.34
1.83
1.81
1.79
1.77
Ms
3ae
1.85
1.88
0.95
1.86
0.98
0.99
1.00
1.94
2.91
2.88
1.86
1.93
f1 (ppm)


168.42
156.90
142.22
133.99
132.19
131.90
130.42
130.32
129.46
129.43
125.41
124.70
123.27
120.56
38.45
37.86
37.11
29.21
27.48
Ms
3ae
f1 (ppm)

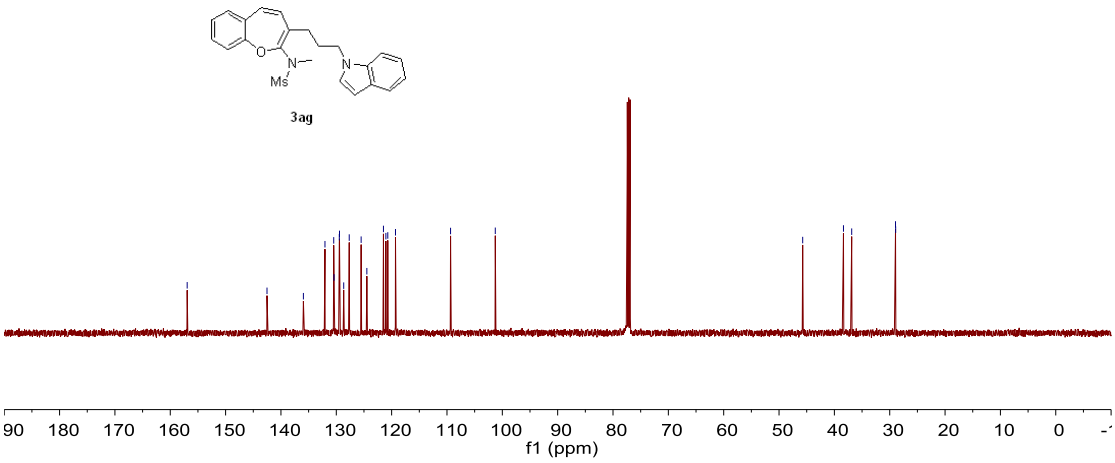

7.69
7.66
7.53
7.52
7.51
7.39
7.38
7.37
7.31
7.29
7.28
7.16
7.14
7.13
7.11
6.96
6.95
6.76
6.73
6.40
6.37
6.11
6.09
4.15
4.14
4.12
3.17
3.11
2.46
2.45
2.43
1.83
Ms
Ph
3af
1.08
2.17
3.14
1.01
2.01
1.02
1.01
0.98
1.00
2.06
3.17
3.00
1.96
1.91
f1 (ppm)

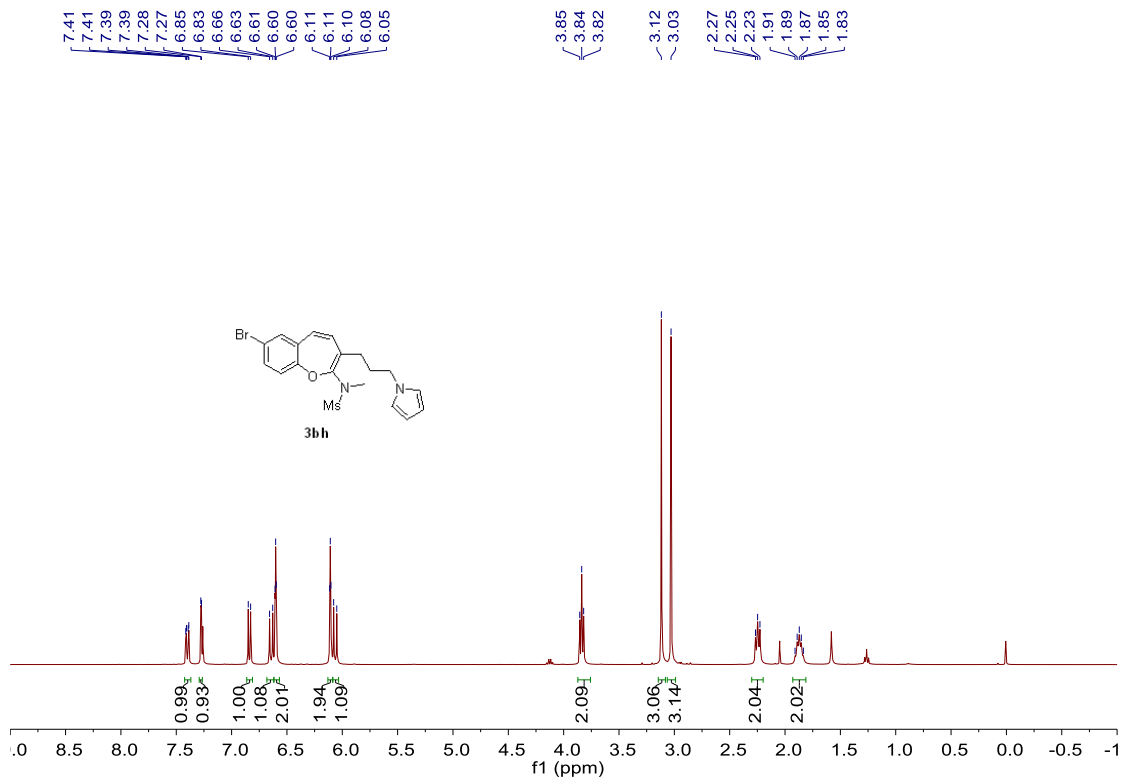

167.06
156.95
144.90
142.39
134.50
131.99
130.41
130.35
129.58
129.48
128.96
128.23
125.44
124.81
120.54
118.11
63.90
38.45
37.13
28.33
27.58
Ms
Ph
3af
f1 (ppm)

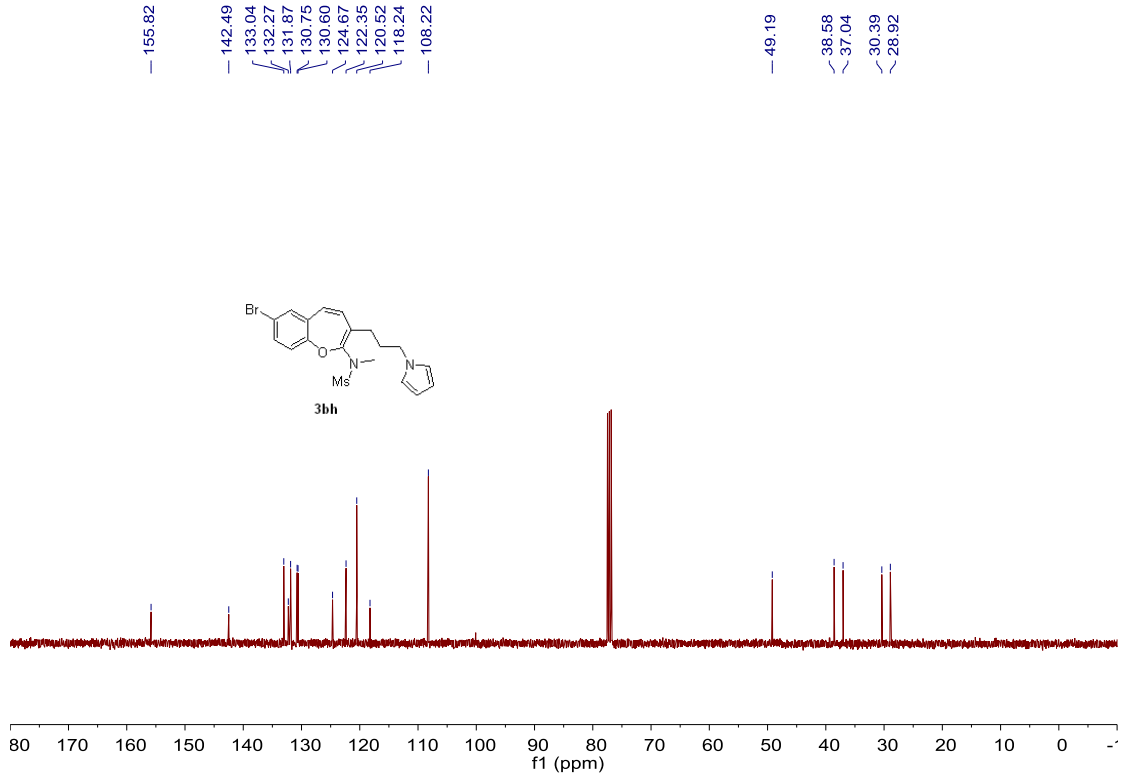

7.61
7.59
7.34
7.33
7.33
7.32
7.31
7.30
7.29
7.17
7.16
7.16
7.14
7.14
7.13
7.13
7.11
7.11
7.08
7.08
7.06
7.06
7.05
7.05
6.96
6.95
6.75
6.73
6.46
6.46
6.04
6.02
4.06
4.05
4.03
3.05
3.01
2.35
2.33
2.31
2.23
1.96

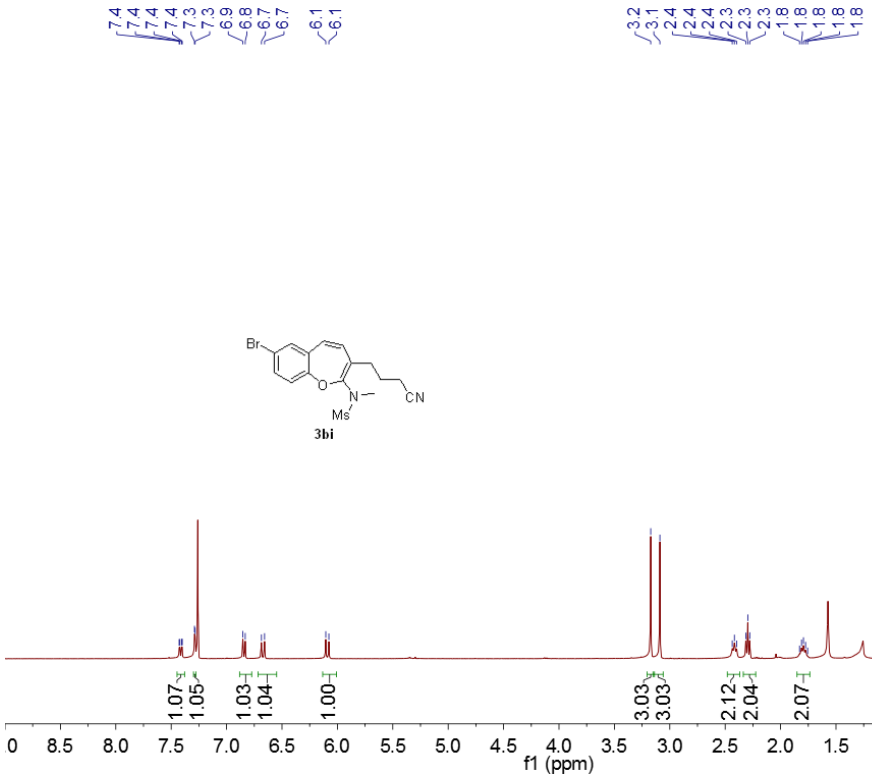

Ms
3ag
0.95
1.15
2.91
1.08
1.93
0.94
0.95
0.93
1.00
1.97
3.06
2.85
2.05
2.08
f1 (ppm)

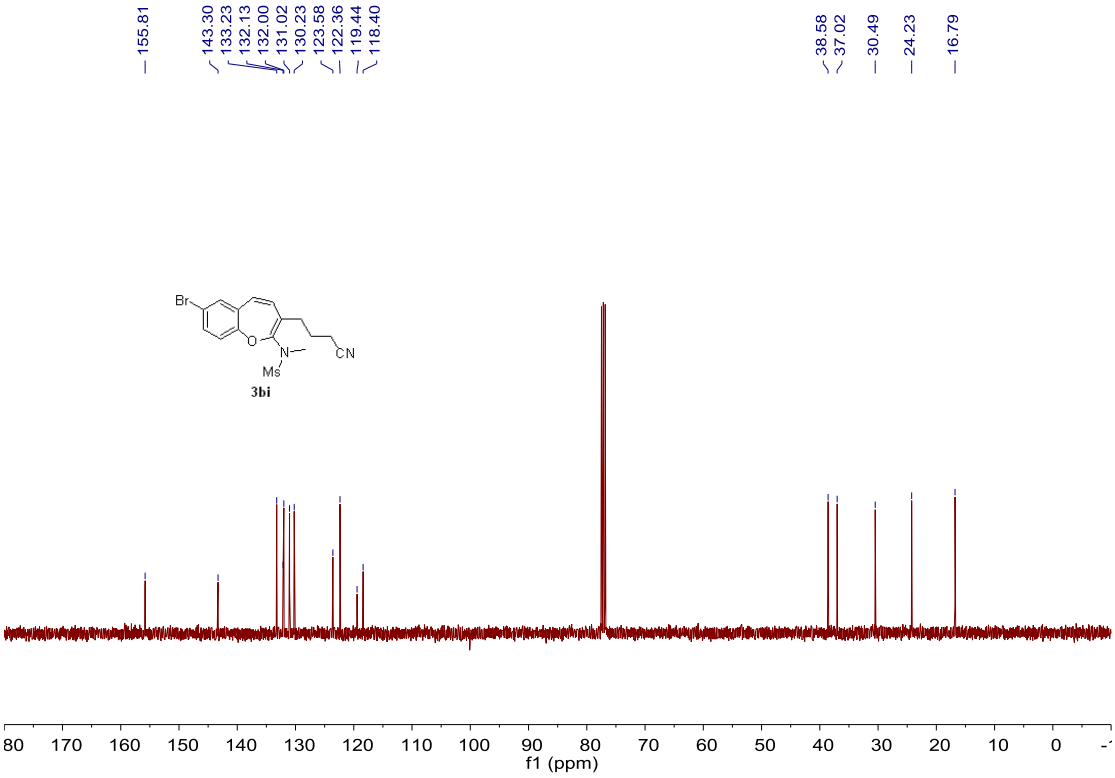

156.94
142.52
135.94
132.05
130.46
130.41
129.46
129.42
128.66
127.66
125.51
124.48
121.48
121.04
120.69
119.30
109.35
101.27
45.73
38.36
36.87
28.95
28.93

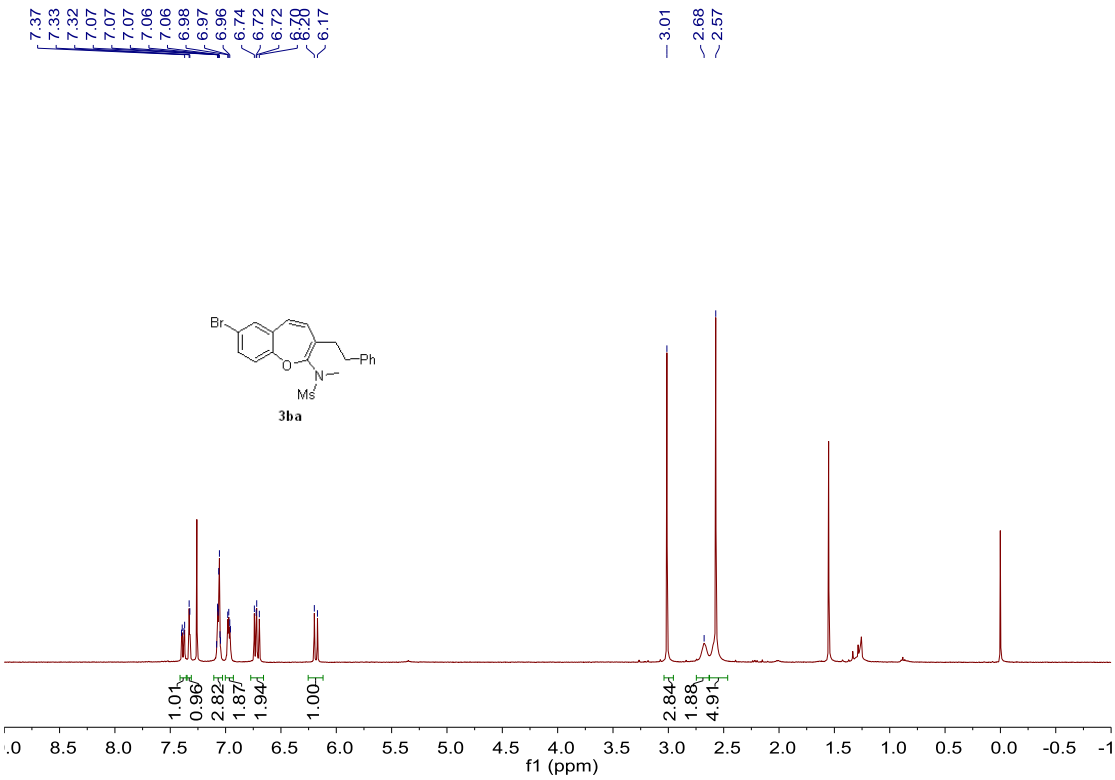

Ms
3ag
f1 (ppm)

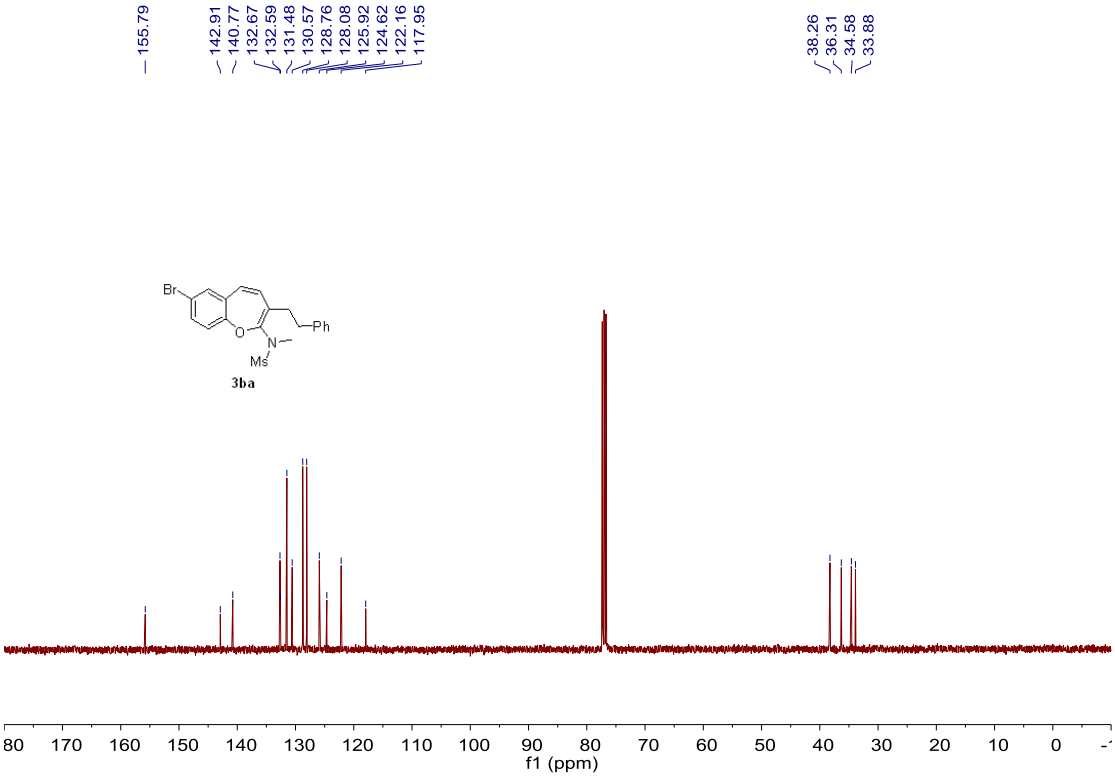

7.41
7.41
7.39
7.39
7.28
7.27
6.85
6.83
6.66
6.63
6.61
6.60
6.60
6.11
6.11
6.10
6.08
6.05
3.85
3.84
3.82
3.12
3.03
2.27
2.25
2.23
1.91
1.89
1.87
1.85
1.83
Br
O
N
Ms
N
3bh
0.99
0.93
1.00
1.08
2.01
1.94
1.09
2.09
3.06
3.14
2.04
2.02
f1 (ppm)

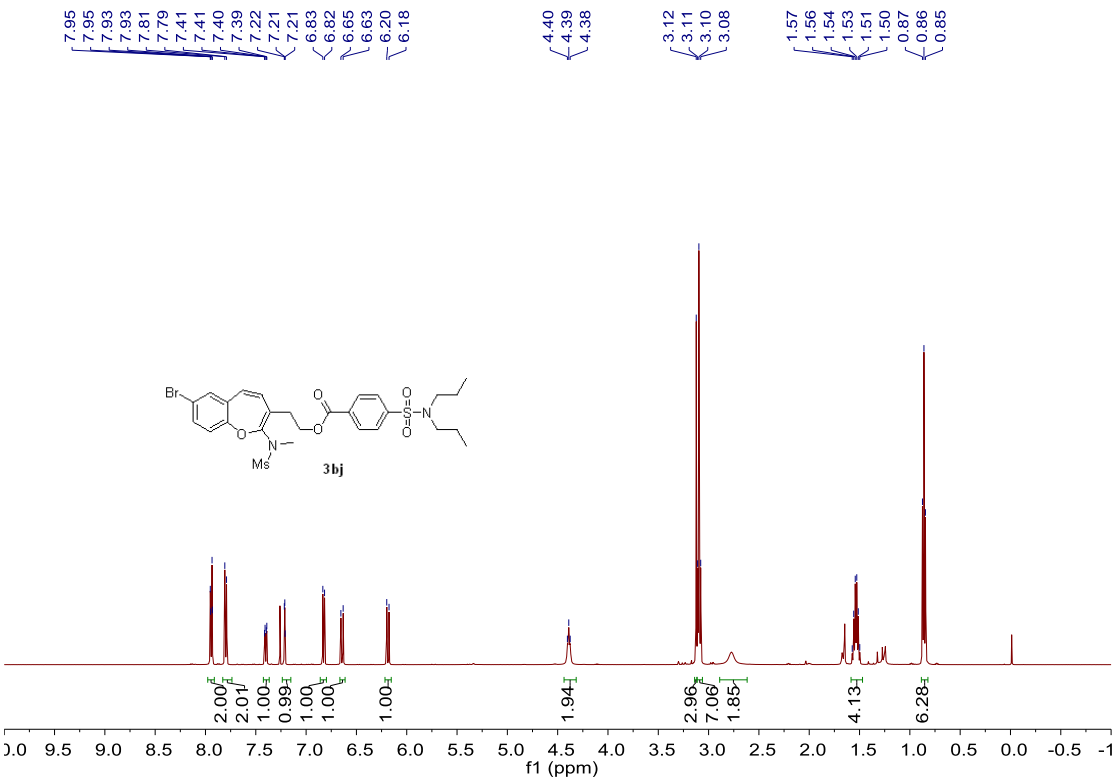

155.82
142.49
133.04
132.27
131.87
130.75
130.60
124.67
122.35
120.52
118.24
108.22
49.19
38.58
37.04
30.39
28.92
Br
O
N
Ms
N
3bh
f1 (ppm)

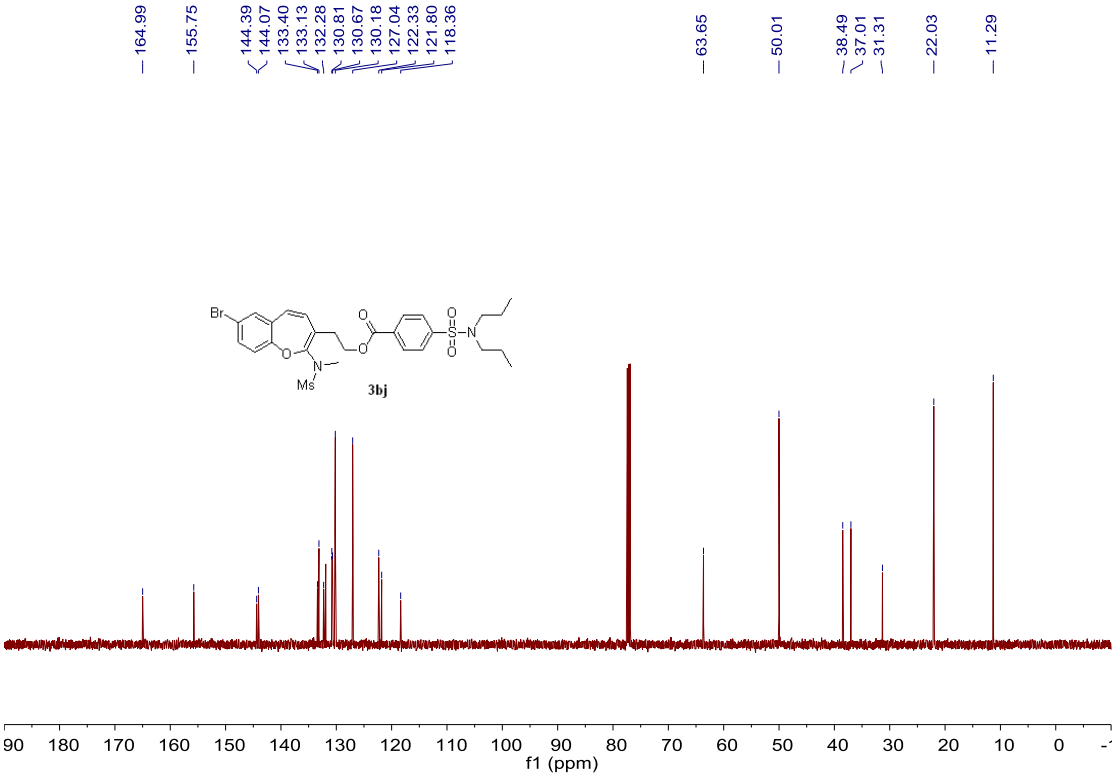

7.4
7.4
7.4
7.4
7.3
7.3
6.9
6.8
6.7
6.7
6.1
6.1
3.2
3.1
2.4
2.4
2.3
2.3
2.3
1.8
1.8
1.8
1.8
Br
O
N
Ms
CN
3bi
1.07
1.05
1.03
1.04
1.00
3.03
3.03
2.12
2.04
2.07
0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

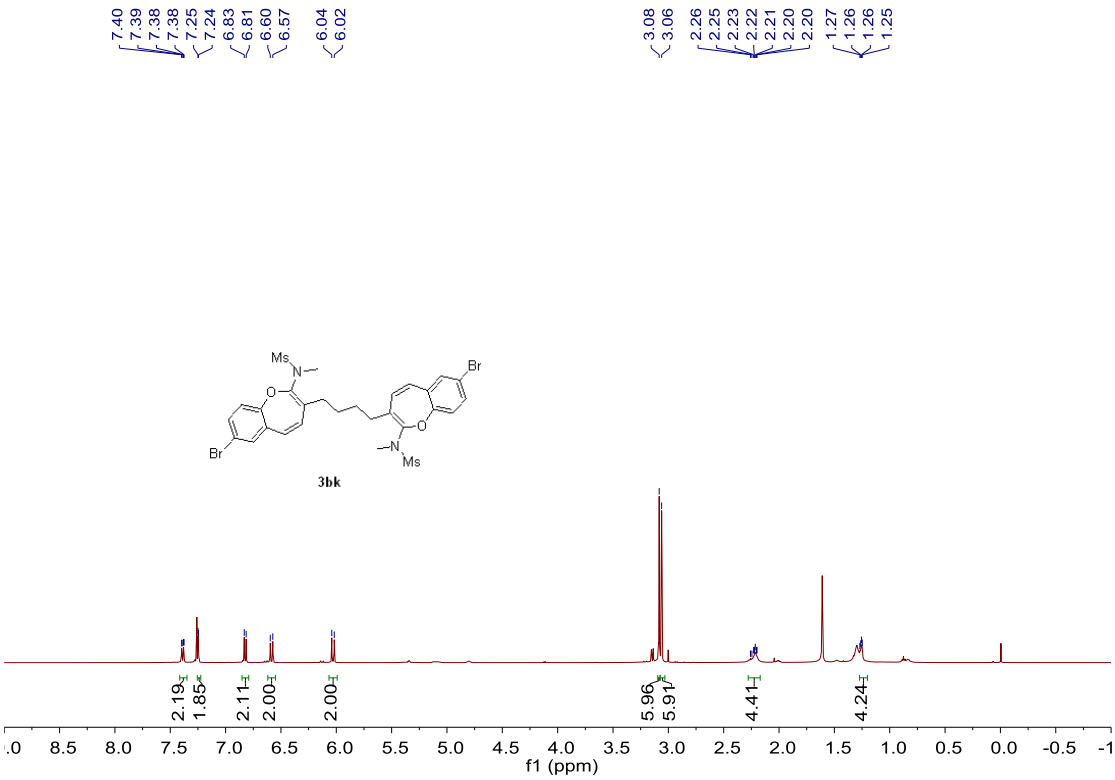

155.81
143.30
133.23
132.13
132.00
131.02
130.23
123.58
122.36
119.44
118.40
38.58
37.02
30.49
24.23
16.79
Br
O
N
Ms
CN
3bi
80 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

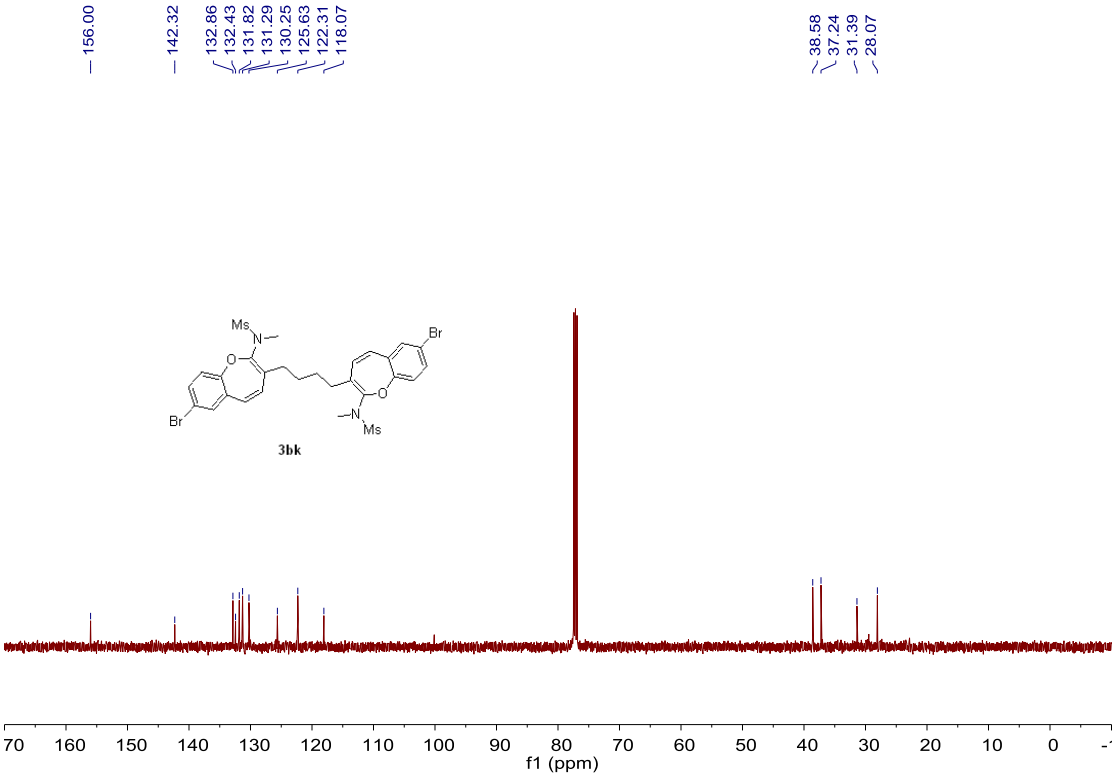

7.37
7.33
7.32
7.07
7.07
7.07
7.06
7.06
6.98
6.97
6.96
6.74
6.72
6.72
6.70
6.20
6.17
3.01
2.68
2.57
Br
Ph
N
Ms
3ba
1.01
0.96
2.82
1.87
1.94
1.00
2.84
1.88
4.91
f1 (ppm)


155.79
142.91
140.77
132.67
132.59
131.48
130.57
128.76
128.08
125.92
124.62
122.16
117.95
38.26
36.31
34.58
33.88
Br
Ph
N
Ms
3ba
f1 (ppm)

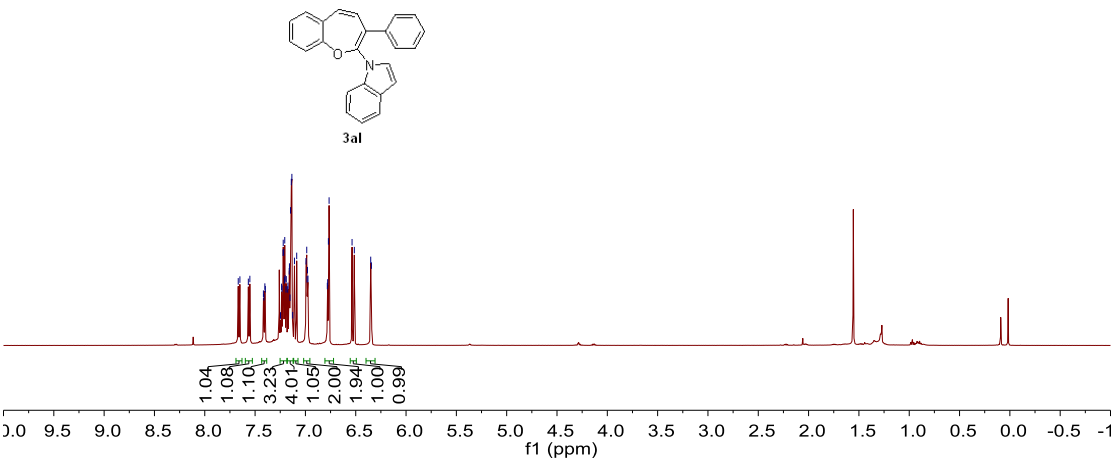

7.95
7.95
7.93
7.93
7.81
7.79
7.41
7.41
7.40
7.39
7.22
7.21
7.21
6.83
6.82
6.65
6.63
6.20
6.18
4.40
4.39
4.38
3.12
3.11
3.10
3.08
1.57
1.56
1.54
1.53
1.51
1.50
0.87
0.86
0.85
Br
O
O
O
O
S
N
N
Ms
3bj
2.00
2.01
1.00
0.99
1.00
1.00
1.00
1.94
2.96
7.06
1.85
4.13
6.28
f1 (ppm)


164.99
155.75
144.39
144.07
133.40
133.13
132.28
130.81
130.67
130.18
127.04
122.33
121.80
118.36
63.65
50.01
38.49
37.01
31.31
22.03
11.29
Br
O
O
O
O
S
N
N
Ms
3bj
f1 (ppm)

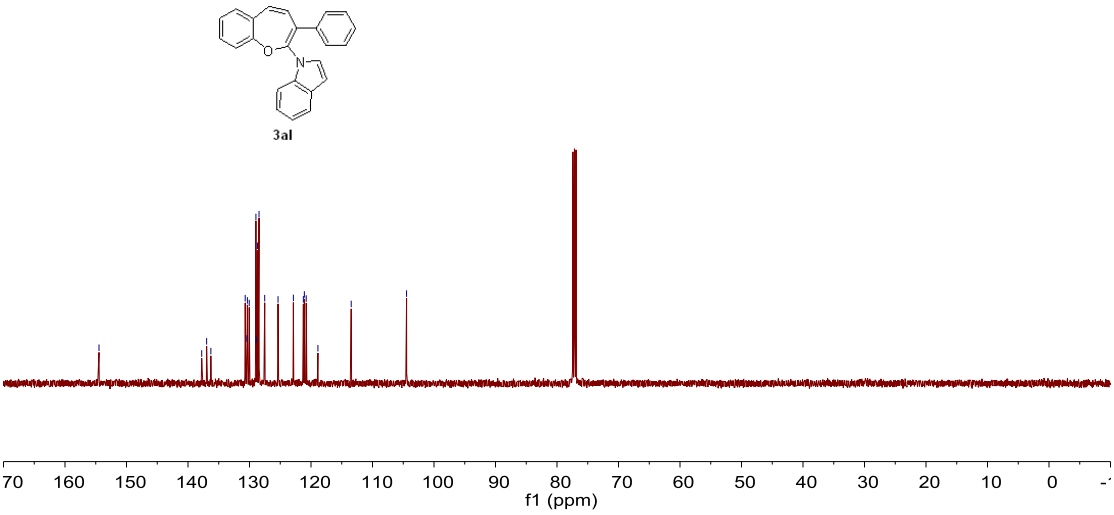

7.40
7.39
7.38
7.38
7.25
7.24
6.83
6.81
6.60
6.57
6.04
6.02
3.08
3.06
2.26
2.25
2.23
2.22
2.21
2.20
2.20
1.27
1.26
1.26
1.25
Ms
N
O
Br
Br
N
Ms
O
3bk
2.19
1.85
2.11
2.00
2.00
5.96
5.91
4.41
4.24
f1 (ppm)


156.00
142.32
132.86
132.43
131.82
131.29
130.25
125.63
122.31
118.07
38.58
37.24
31.39
28.07
Ms
N
O
Br
Br
N
Ms
O
3bk
f1 (ppm)

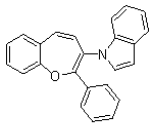

7.67
7.65
7.57
7.55
7.42
7.41
7.40
7.40
7.25
7.24
7.23
7.22
7.22
7.22
7.21
7.21
7.20
7.19
7.19
7.18
7.17
7.16
7.16
7.15
7.15
7.14
7.13
7.13
7.11
7.09
6.99
6.99
6.98
6.98
6.97
6.78
6.78
6.77
6.76
6.54
6.51
6.35
6.34


3al
1.04
1.08
1.10
3.23
4.01
1.05
2.00
1.94
1.00
0.99
f1 (ppm)

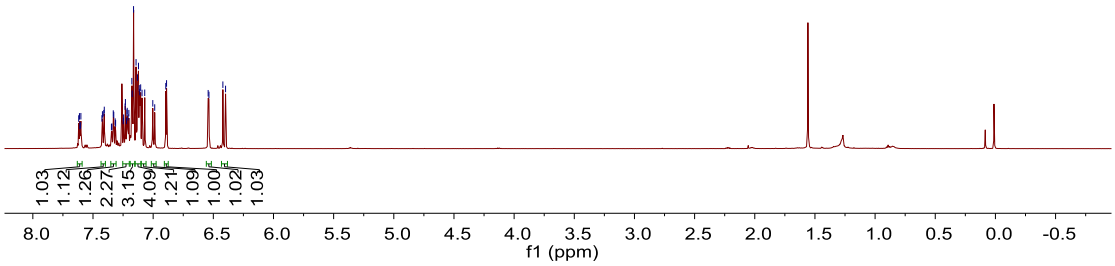

154.47
137.77
136.97
136.28
130.70
130.42
130.34
130.05
128.96
128.91
128.71
128.45
127.53
125.36
122.87
121.24
121.08
120.78
118.87
113.46
104.46


3al
f1 (ppm)

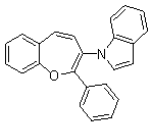

7.62
7.61
7.61
7.61
7.60
7.43
7.42
7.41
7.41
7.35
7.34
7.33
7.33
7.32
7.31
7.25
7.25
7.23
7.23
7.22
7.22
7.22
7.21
7.20
7.18
7.17
7.16
7.14
7.13
7.12
7.12
7.11
7.10
7.09
7.07
7.00
6.99
6.90
6.89
6.54
6.54
6.42
6.40



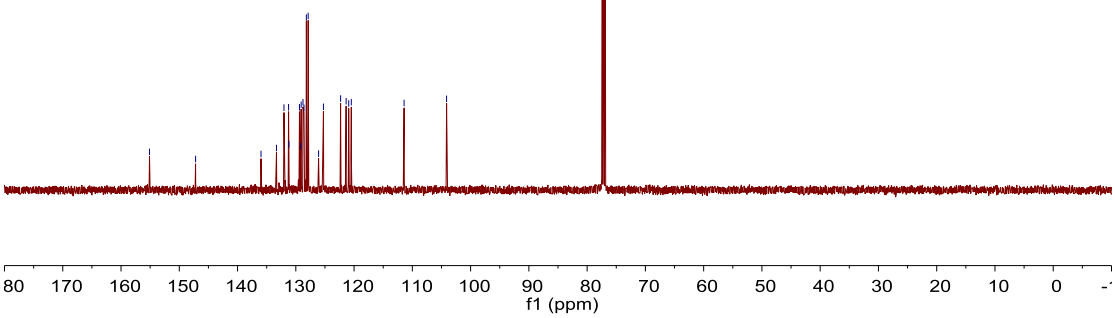
3al'

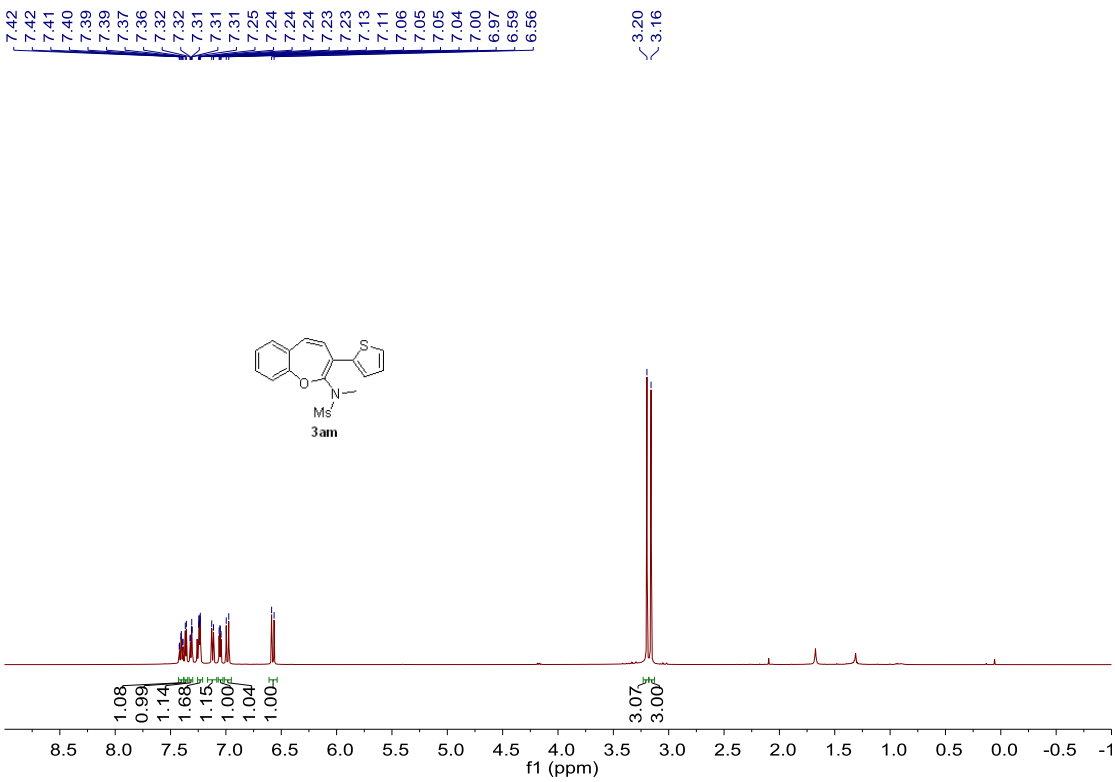

1.03
1.12
1.26
2.27
3.15
4.09
1.21
1.09
1.00
1.02
1.03
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

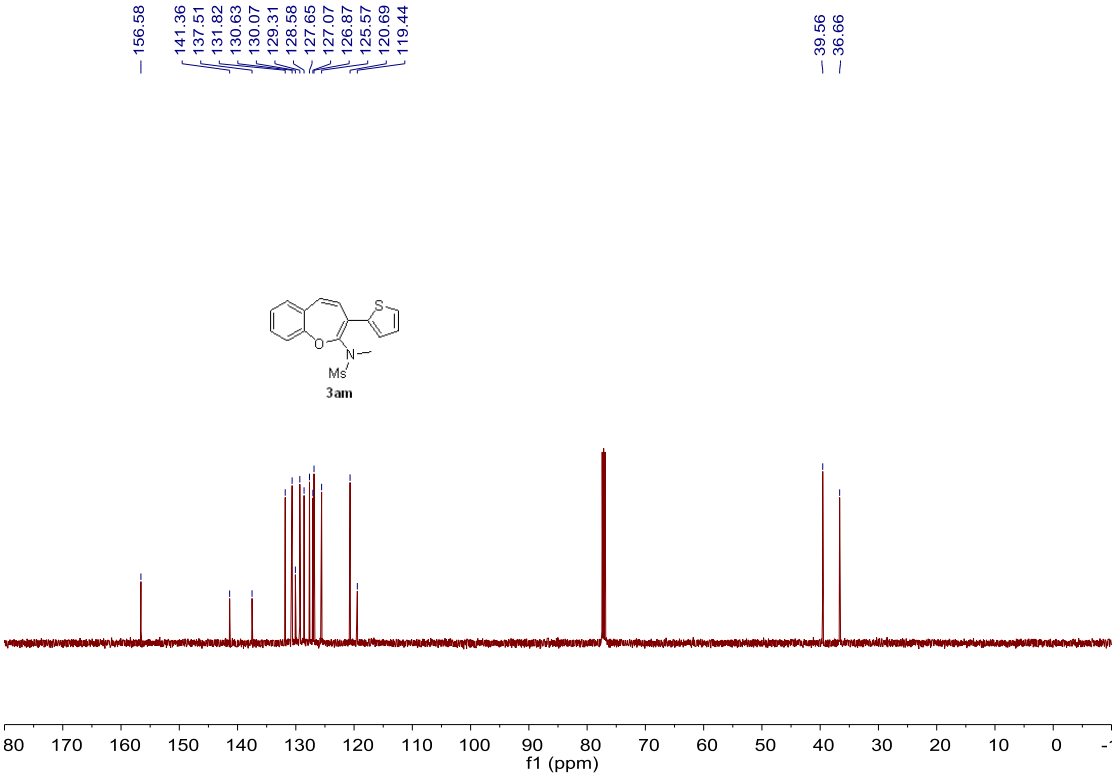

155.11
147.20
135.98
133.32
132.03
131.25
131.19
129.37
129.19
129.08
128.77
128.60
128.19
127.88
126.09
125.26
122.32
121.36
120.92
120.48
111.42
104.12



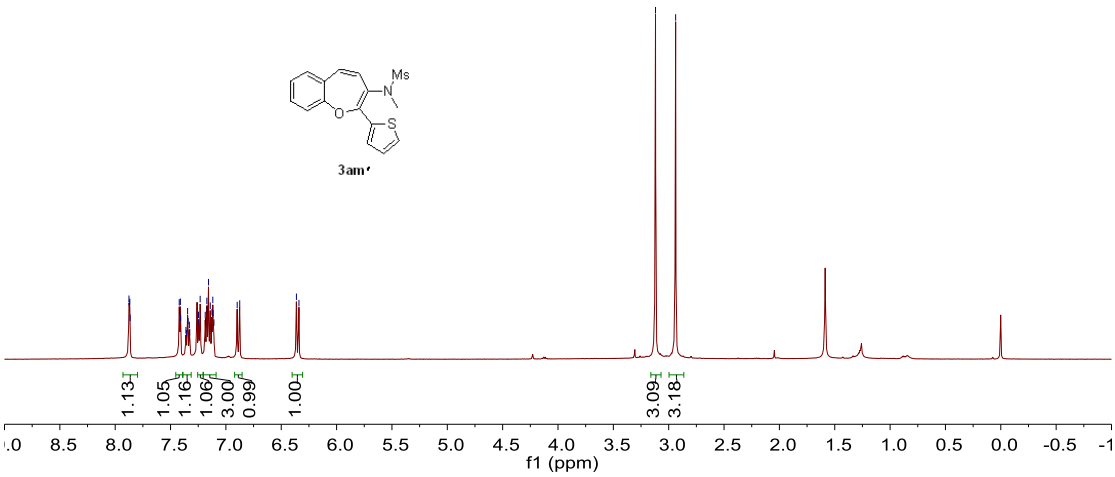
3al'


80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

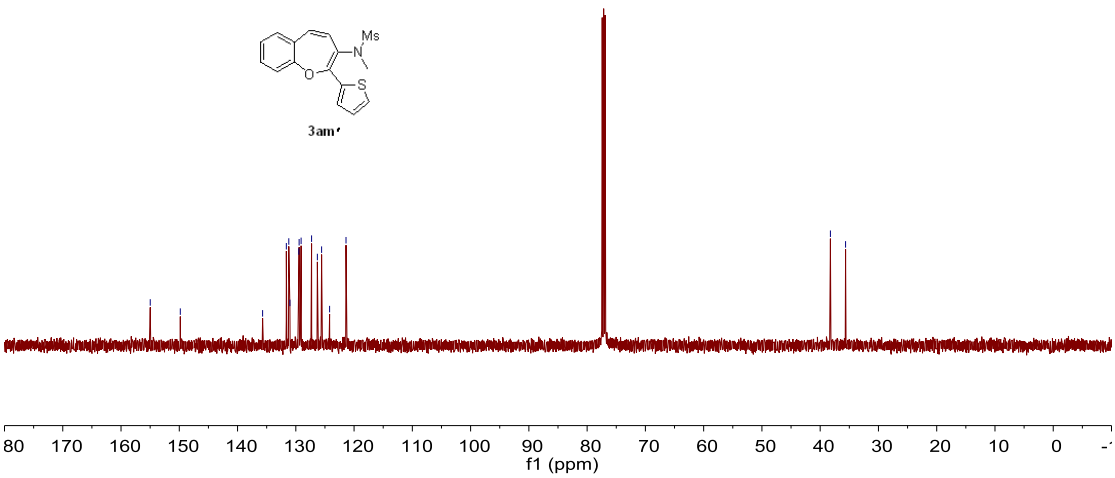

7.42
7.42
7.41
7.40
7.39
7.39
7.37
7.36
7.32
7.32
7.31
7.31
7.31
7.25
7.24
7.24
7.24
7.23
7.23
7.13
7.11
7.06
7.05
7.05
7.04
7.00
6.97
6.59
6.56
3.20
3.16
S
O
N
Ms
3am
1.08
0.99
1.14
1.68
1.15
1.00
1.04
1.00
3.07
3.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

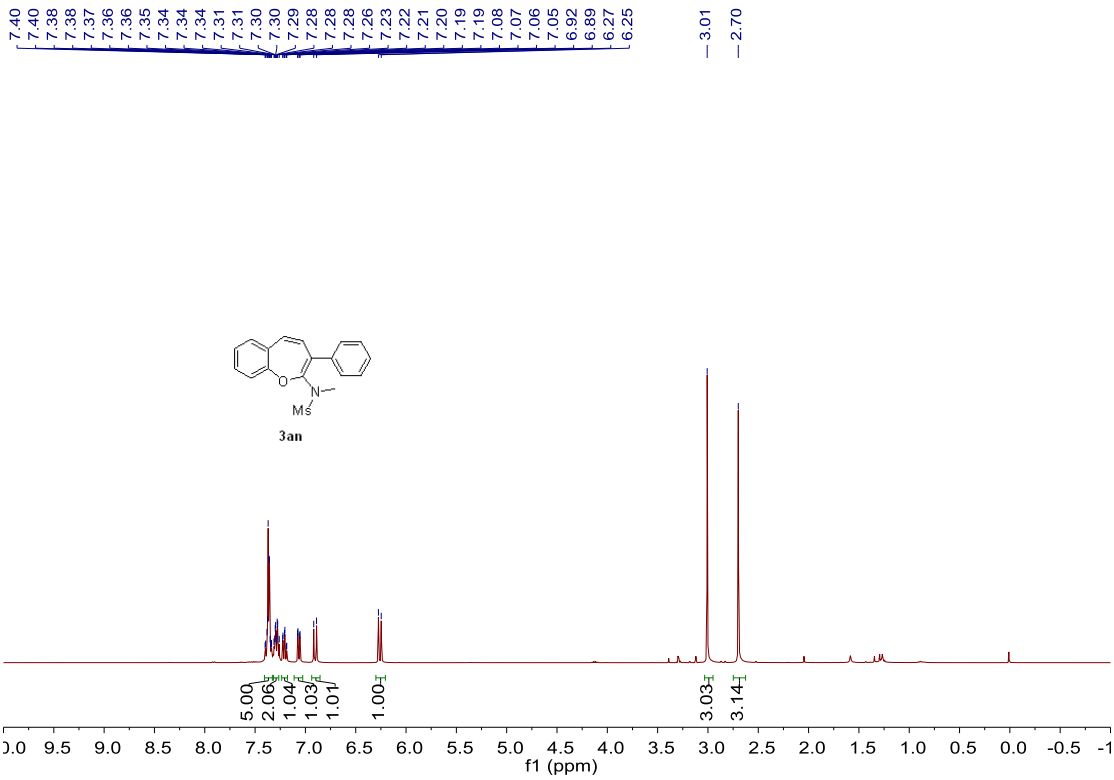

156.58
141.36
137.51
131.82
130.63
130.07
129.31
128.58
127.65
127.07
126.87
125.57
120.69
119.44
39.56
36.66
S
O
N
Ms
3am
80 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

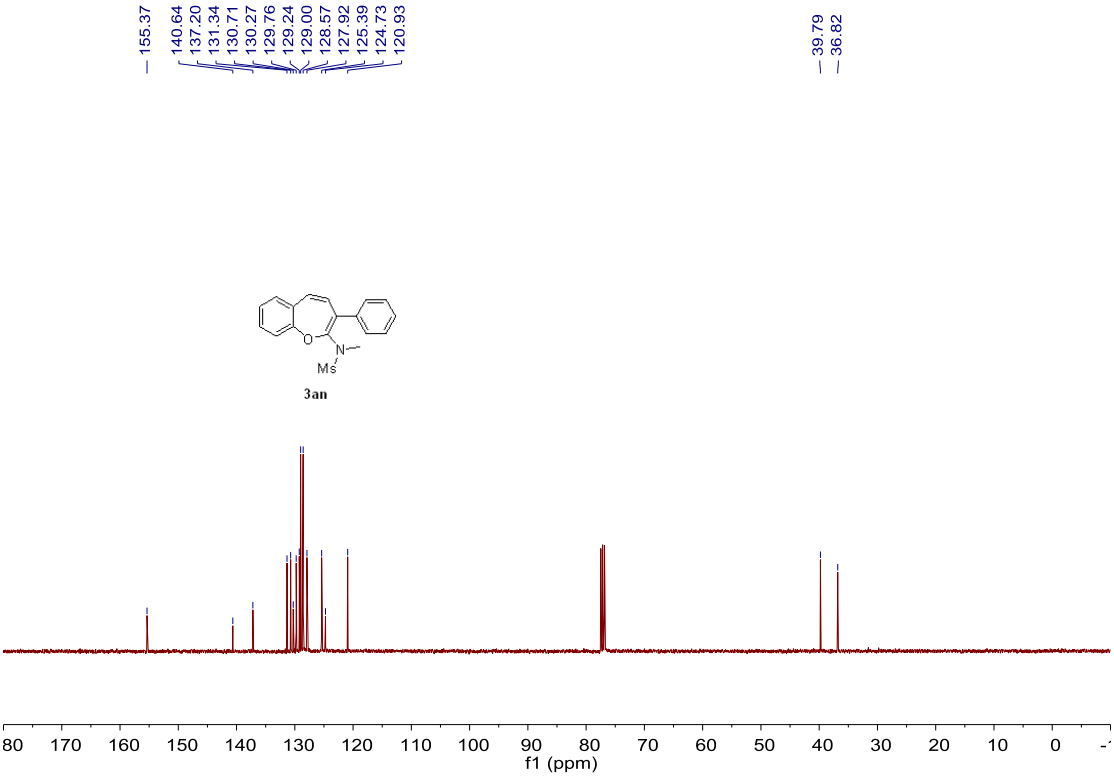

7.88
7.87
7.87
7.87
7.42
7.42
7.41
7.41
7.36
7.36
7.35
7.34
7.33
7.33
7.25
7.24
7.23
7.19
7.18
7.17
7.17
7.16
7.14
7.13
7.13
7.12
7.12
7.11
6.90
6.88
6.36
6.34
3.12
2.94


Ms
N
O
S
3am'
1.13
1.05
1.16
1.06
3.00
0.99
1.00
3.09
3.18
f1 (ppm)

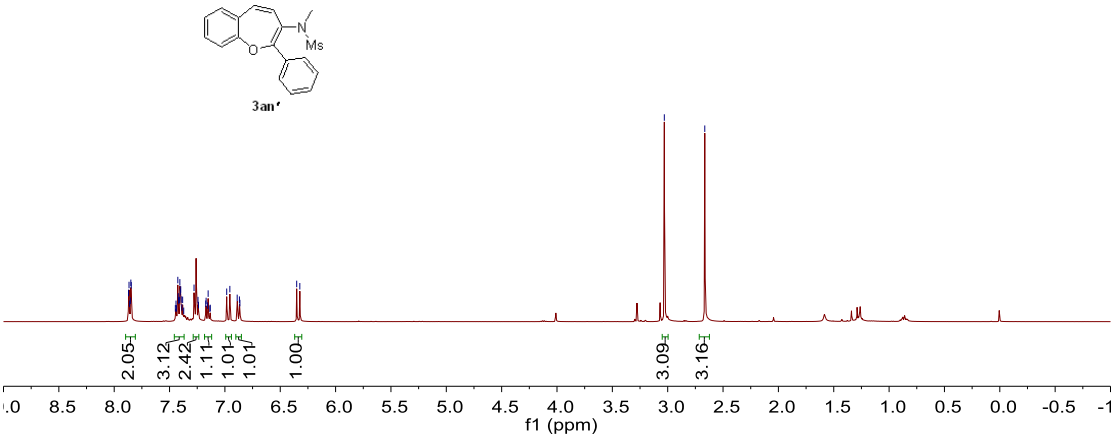

154.99
149.83
135.70
131.63
131.20
131.01
129.48
129.43
129.09
127.29
126.30
125.57
124.20
121.38
38.24
35.64


Ms
N
O
S
3am'
f1 (ppm)

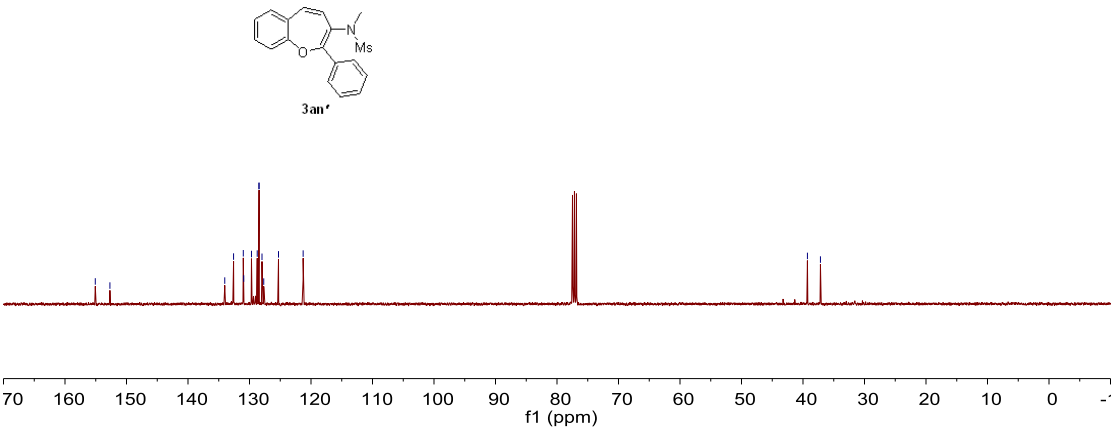

7.40
7.40
7.38
7.38
7.37
7.36
7.36
7.35
7.34
7.34
7.34
7.31
7.31
7.30
7.30
7.29
7.28
7.28
7.28
7.26
7.23
7.22
7.21
7.20
7.19
7.19
7.08
7.07
7.06
7.05
6.92
6.89
6.27
6.25
3.01
2.70
Ms
N
O
3an
5.00
2.06
1.04
1.03
1.01
1.00
3.03
3.14
f1 (ppm)

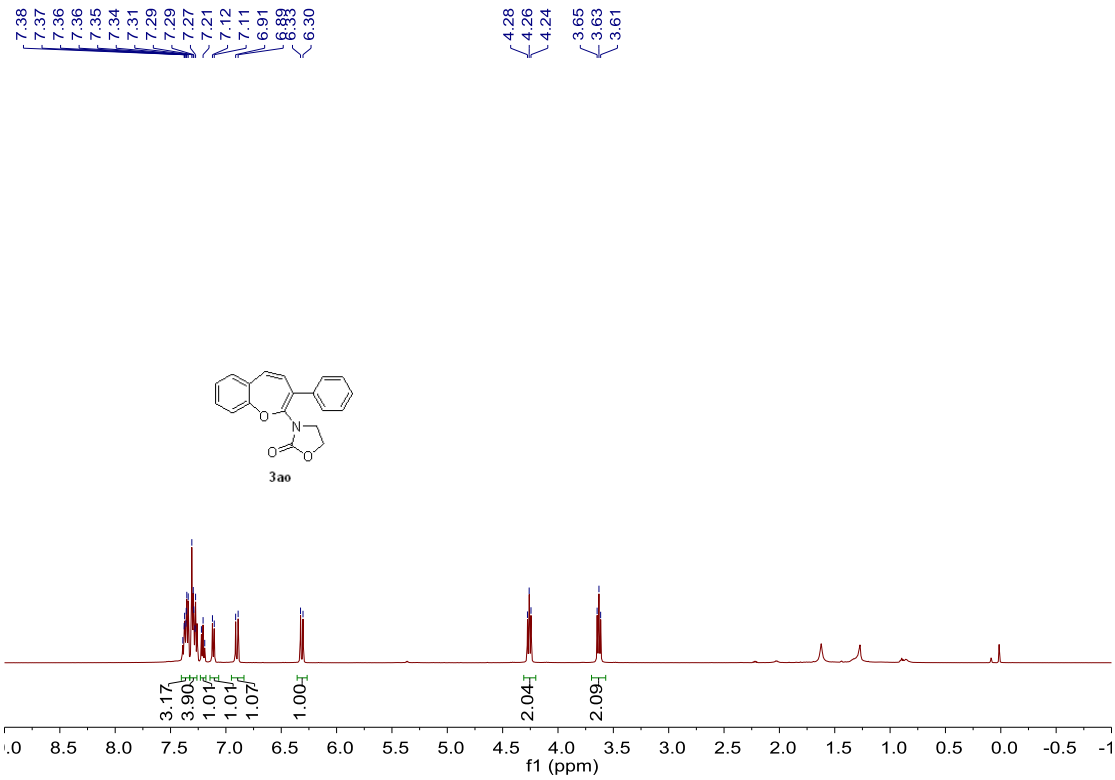

155.37
140.64
137.20
131.34
130.71
130.27
129.76
129.24
129.00
128.57
127.92
125.39
124.73
120.93
39.79
36.82
Ms
N
O
3an
f1 (ppm)

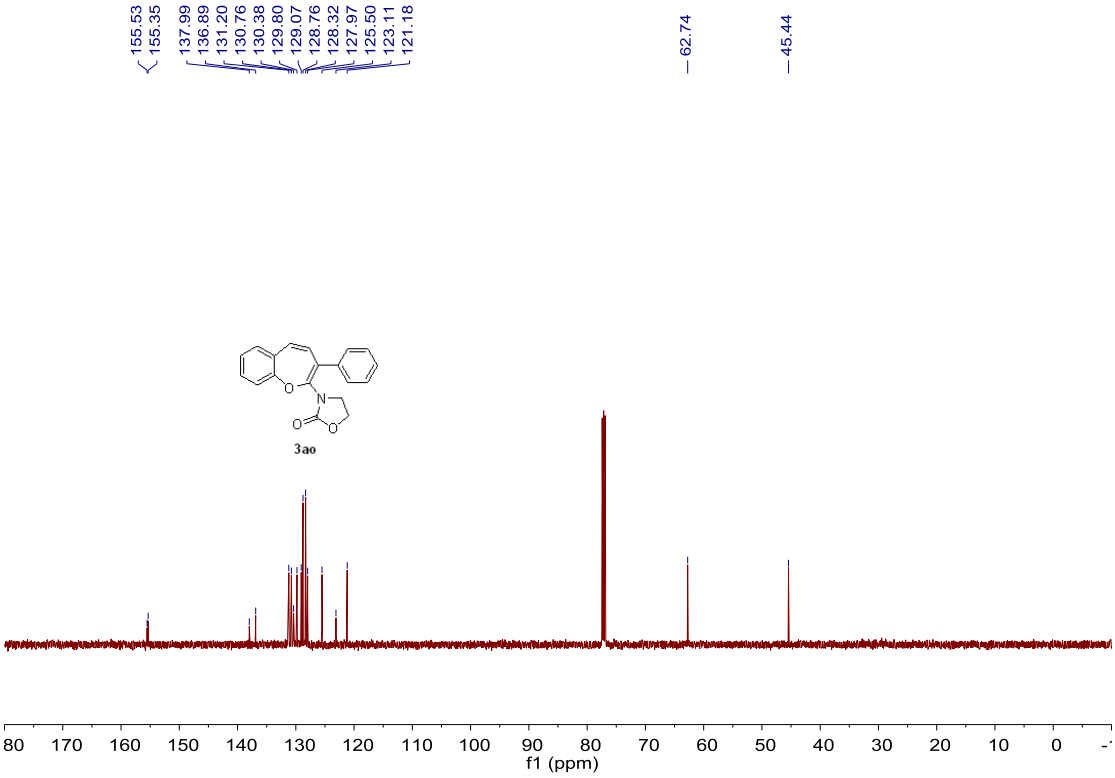

7.87
7.87
7.86
7.85
7.85
7.85
7.45
7.44
7.44
7.43
7.42
7.42
7.41
7.41
7.40
7.40
7.39
7.39
7.38
7.37
7.28
7.24
7.24
7.17
7.17
7.16
7.15
7.14
7.13
6.98
6.96
6.89
6.87
6.86
6.35
6.32
3.03
2.67


N
Ms
O
3an'
2.05
3.12
2.42
1.11
1.01
1.01
1.00
3.09
3.16
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
-0.5
f1 (ppm)

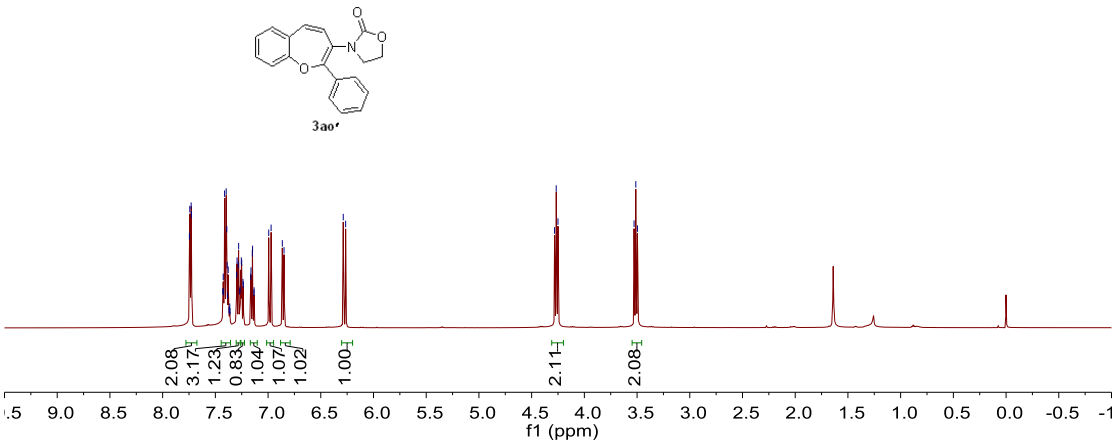

155.08
152.70
134.02
132.59
131.01
130.94
129.68
128.74
128.46
128.45
127.97
127.68
125.28
121.28
39.28
37.16


N
Ms
O
3an'
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

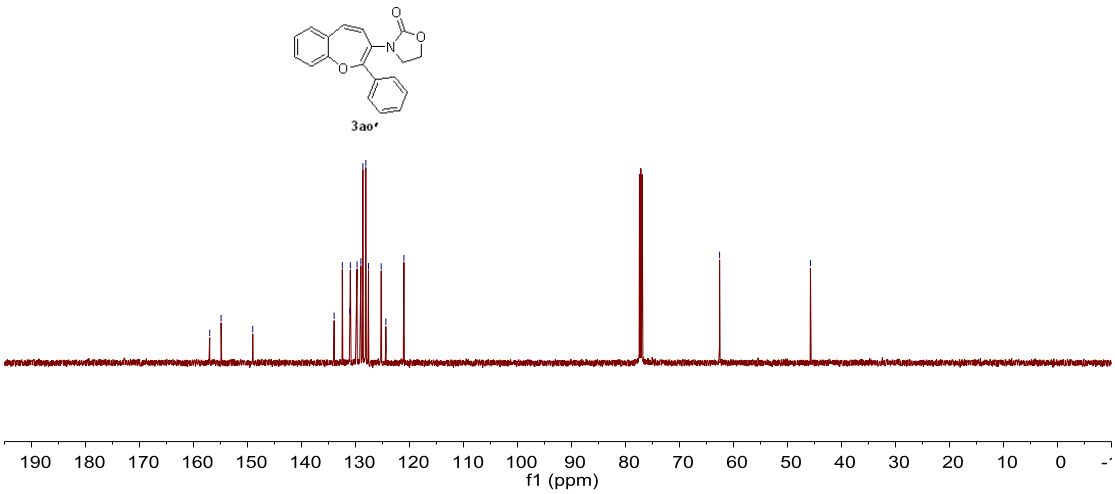

7.38
7.37
7.36
7.36
7.35
7.34
7.31
7.29
7.29
7.27
7.21
7.12
7.11
6.91
6.89
6.33
6.30
4.28
4.26
4.24
3.65
3.63
3.61
3ao
3.17
3.90
1.01
1.01
1.07
1.00
2.04
2.09
f1 (ppm)

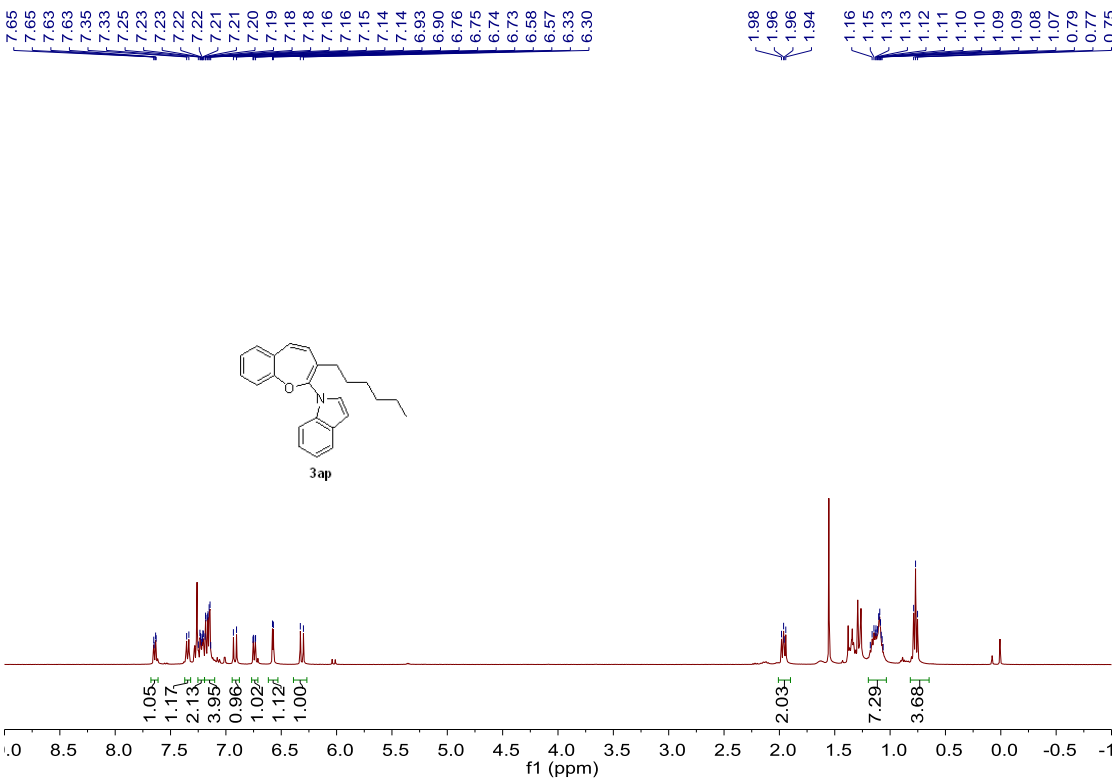

155.53
155.35
137.99
136.89
131.20
130.76
130.38
129.80
129.07
128.76
128.32
127.97
125.50
123.11
121.18
62.74
45.44
3ao
f1 (ppm)

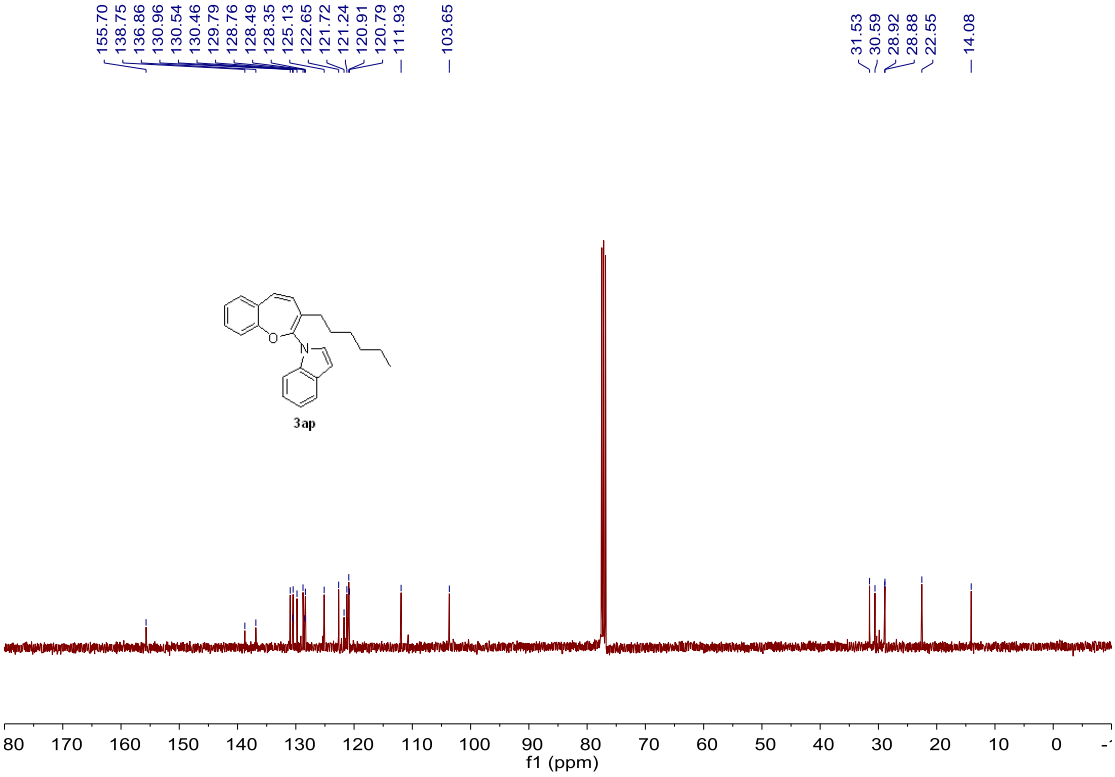

7.75
7.74
7.73
7.73
7.43
7.43
7.42
7.41
7.40
7.39
7.39
7.38
7.38
7.37
7.37
7.36
7.36
7.30
7.29
7.28
7.28
7.27
7.27
7.25
7.25
7.24
7.23
7.16
7.16
7.15
7.15
7.13
7.13
6.99
6.97
6.86
6.85
6.29
6.26
4.28
4.27
4.25
3.53
3.51
3.50

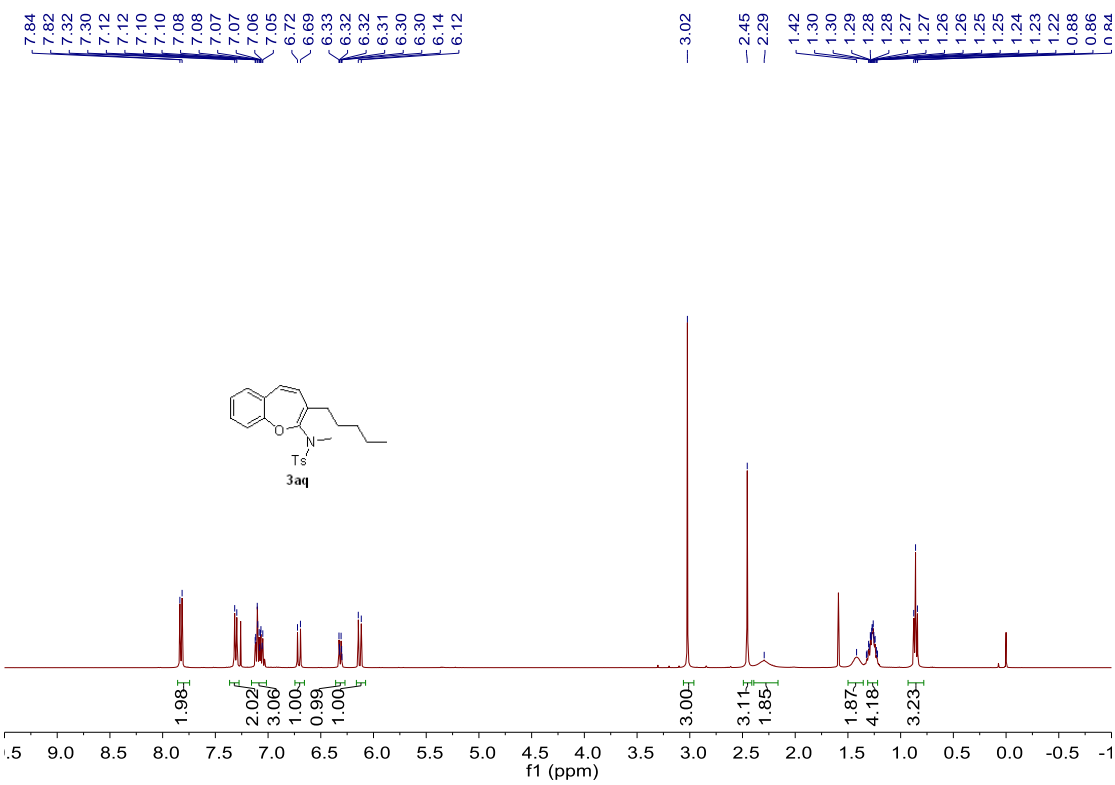

3ao'
2.08
3.17
1.23
0.83
1.04
1.07
1.02
1.00
2.11
2.08
f1 (ppm)

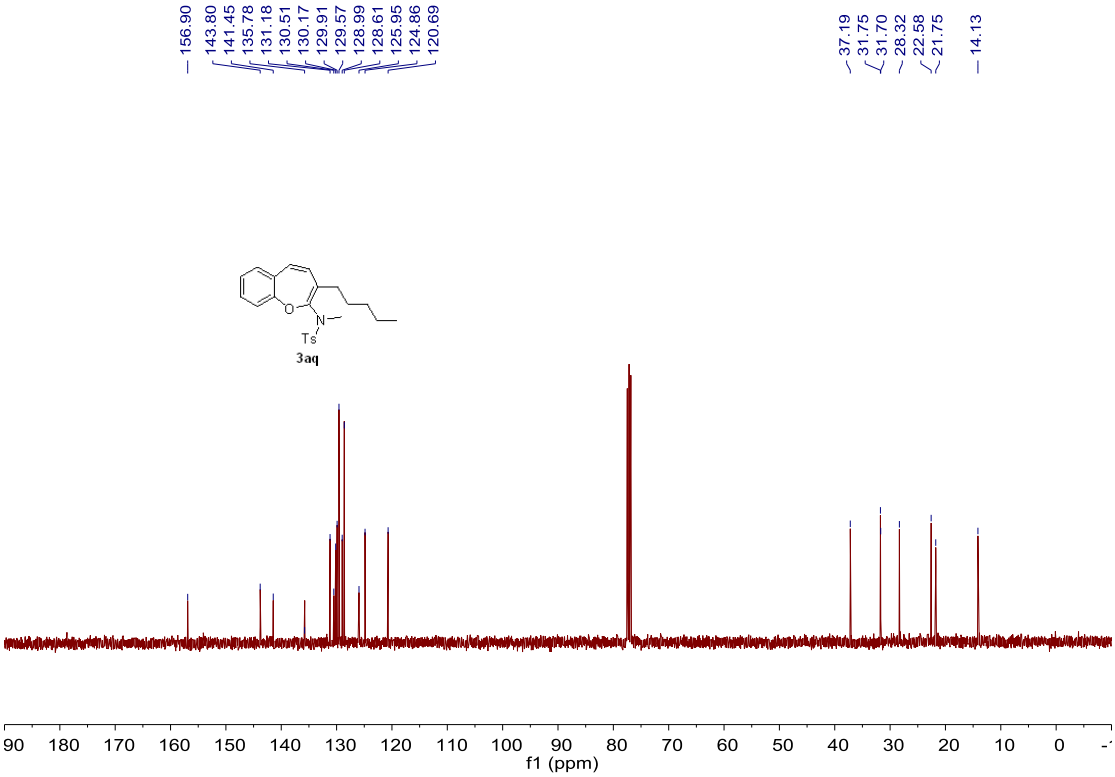

156.99
154.89
149.03
133.96
132.44
131.04
130.96
129.71
129.00
128.63
128.09
127.60
125.24
124.38
121.03
62.57
45.75

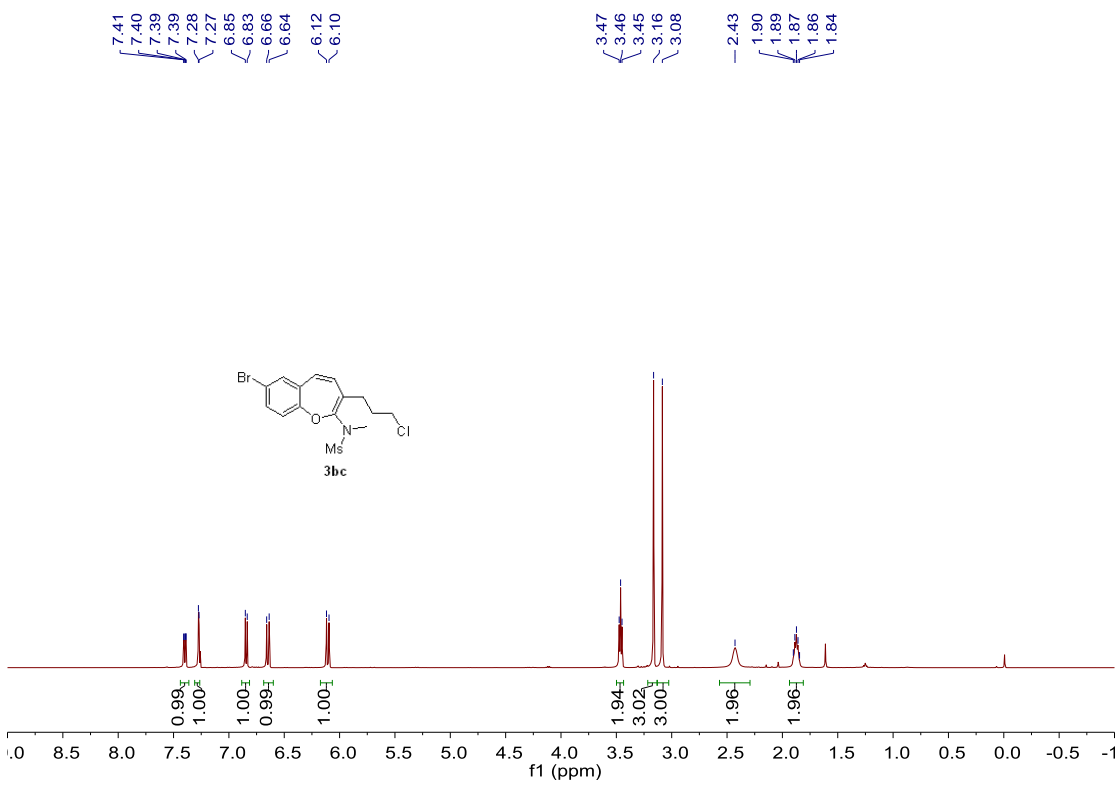

3ao'
f1 (ppm)

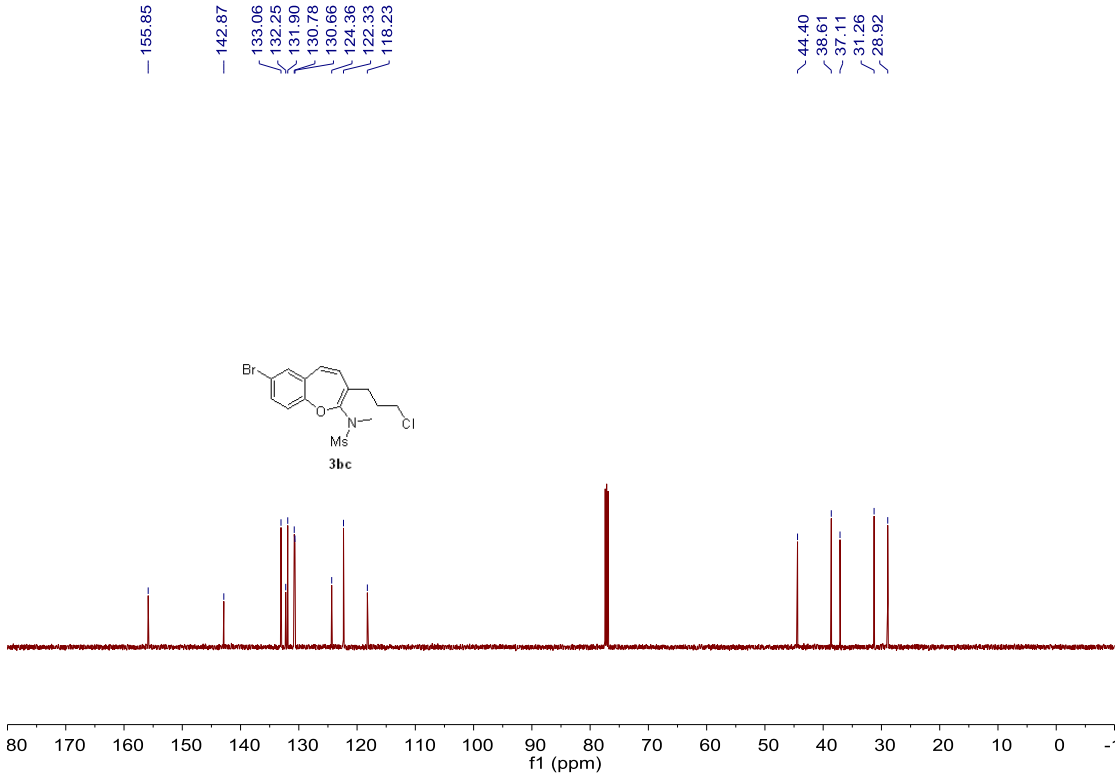

7.65
7.65
7.63
7.63
7.35
7.33
7.25
7.23
7.23
7.22
7.22
7.21
7.21
7.20
7.19
7.18
7.18
7.16
7.16
7.15
7.14
7.14
6.93
6.90
6.76
6.75
6.74
6.73
6.58
6.57
6.33
6.30
1.98
1.96
1.96
1.94
1.16
1.15
1.13
1.13
1.12
1.11
1.10
1.10
1.09
1.09
1.08
1.07
0.79
0.77
3ap
1.05
1.17
2.13
3.95
0.96
1.02
1.12
1.00
2.03
7.29
3.68
f1 (ppm)

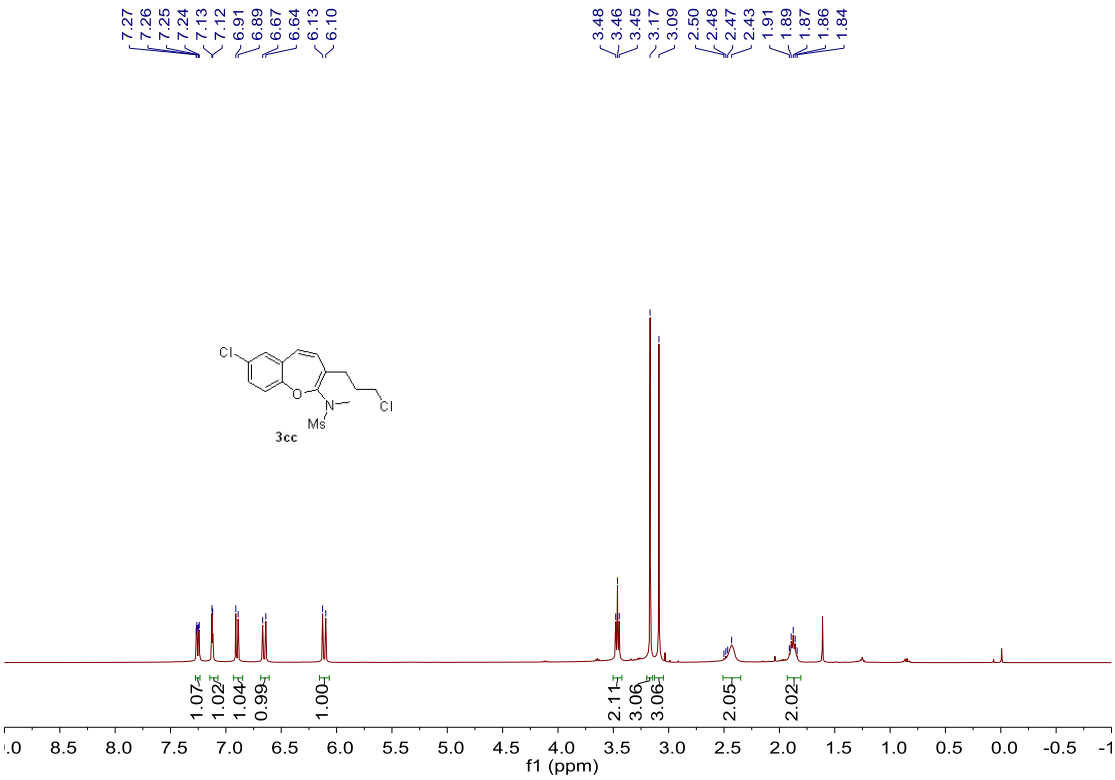

155.70
138.75
136.86
130.96
130.54
130.46
129.79
128.76
128.49
128.35
125.13
122.65
121.72
121.24
120.91
120.79
111.93
103.65
31.53
30.59
28.92
28.88
22.55
14.08
3ap
f1 (ppm)

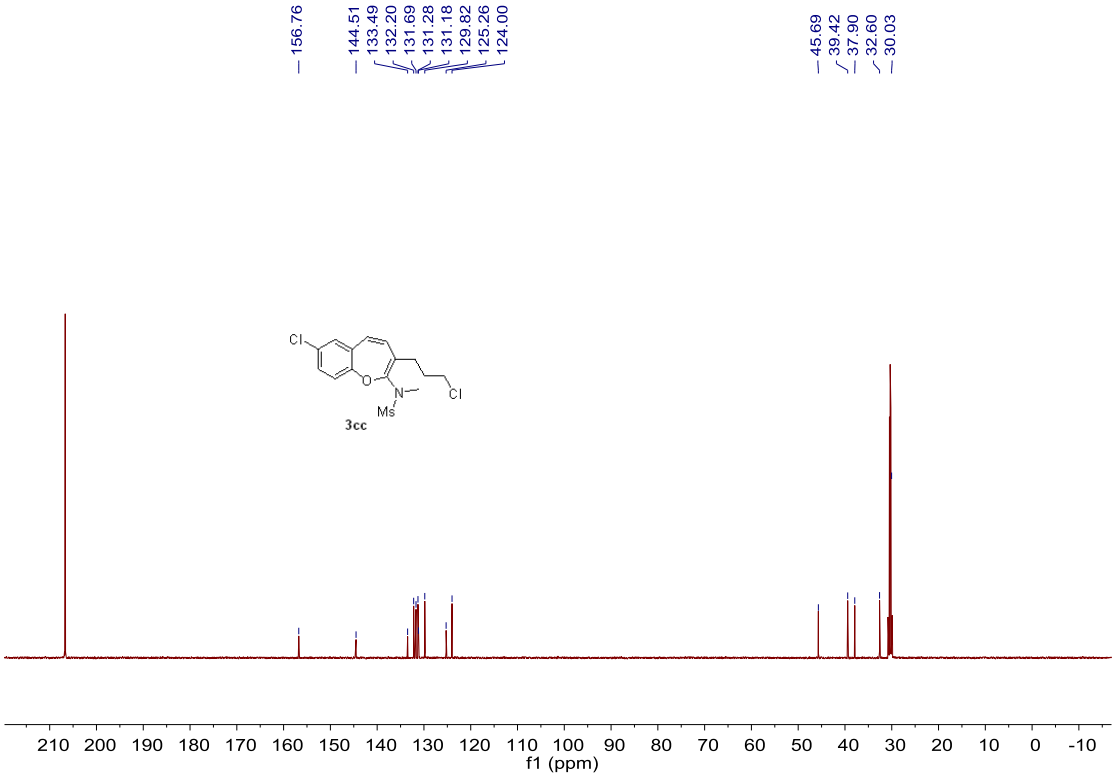

7.84
7.82
7.32
7.30
7.12
7.12
7.10
7.10
7.08
7.08
7.07
7.07
7.06
7.05
6.72
6.69
6.33
6.32
6.32
6.31
6.30
6.30
6.14
6.12
3.02
2.45
2.29
1.42
1.30
1.30
1.29
1.28
1.28
1.27
1.27
1.26
1.26
1.25
1.25
1.24
1.23
1.22
0.88
0.86
Ts
3aq
1.98
2.02
3.06
1.00
0.99
1.00
3.00
3.11
1.85
1.87
4.18
3.23
f1 (ppm)

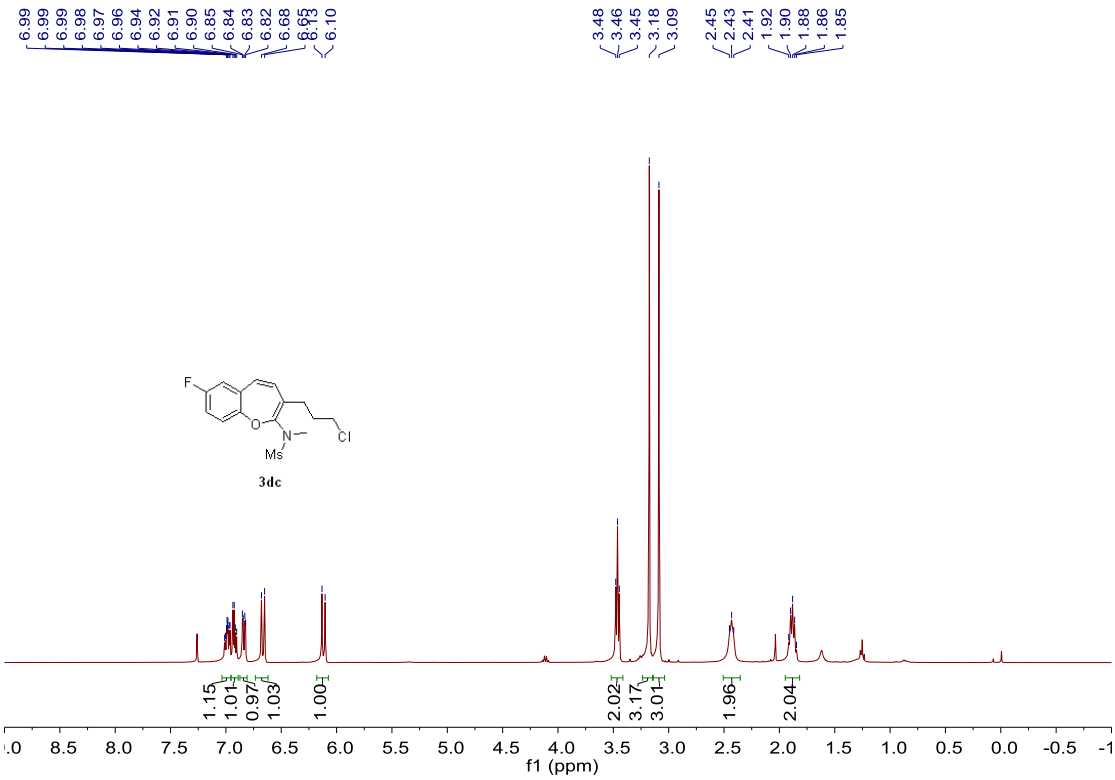

156.90
143.80
141.45
135.78
131.18
130.51
130.17
129.91
129.57
128.99
128.61
125.95
124.86
120.69
37.19
31.75
31.70
28.32
22.58
21.75
14.13
Ts
3aq
f1 (ppm)

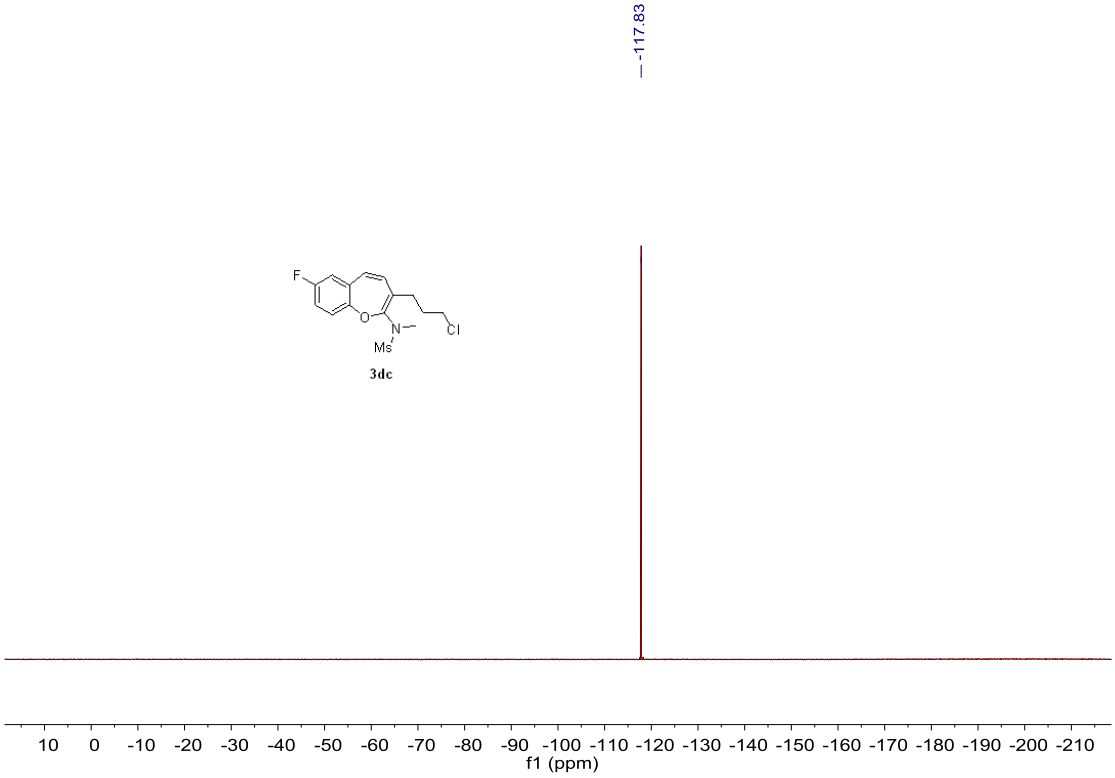

7.41
7.40
7.39
7.39
7.28
7.27
6.85
6.83
6.66
6.64
6.12
6.10
3.47
3.46
3.45
3.16
3.08
2.43
1.90
1.89
1.87
1.86
1.84
Br
O
N
Ms
Cl
3bc
0.99
1.00
1.00
0.99
1.00
1.94
3.02
3.00
1.96
1.96
f1 (ppm)

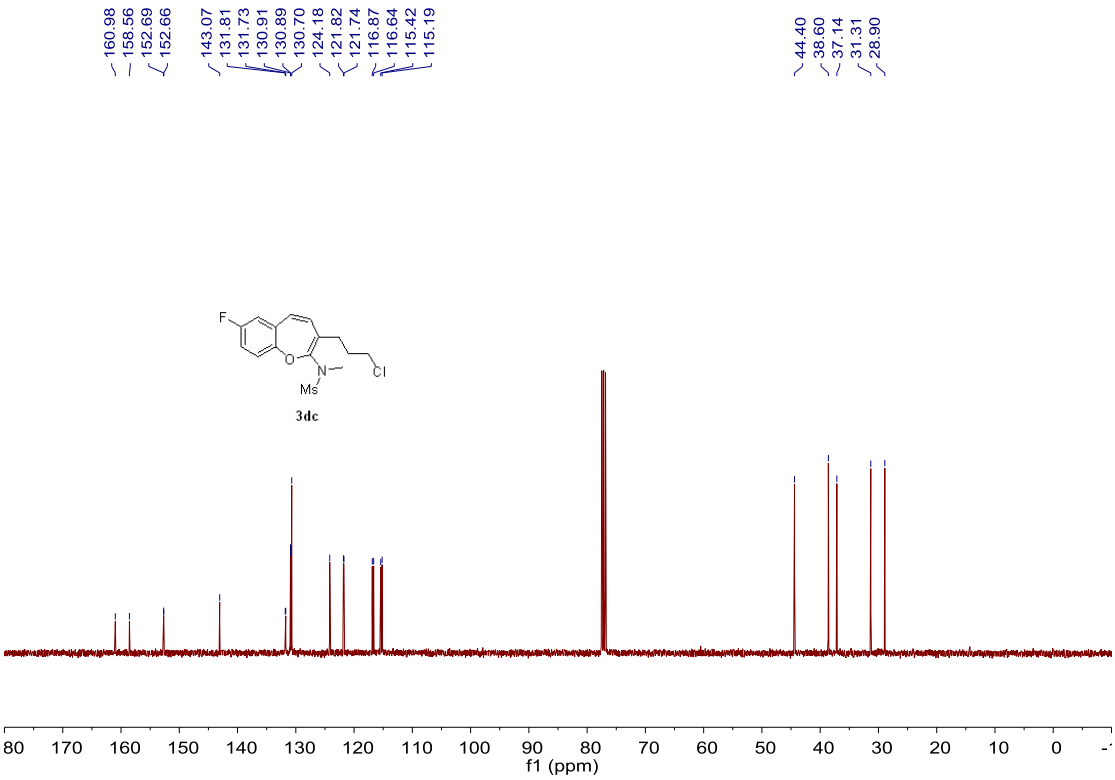

155.85
142.87
133.06
132.25
131.90
130.78
130.66
124.36
122.33
118.23
44.40
38.61
37.11
31.26
28.92
Br
O
N
Ms
Cl
3bc
f1 (ppm)

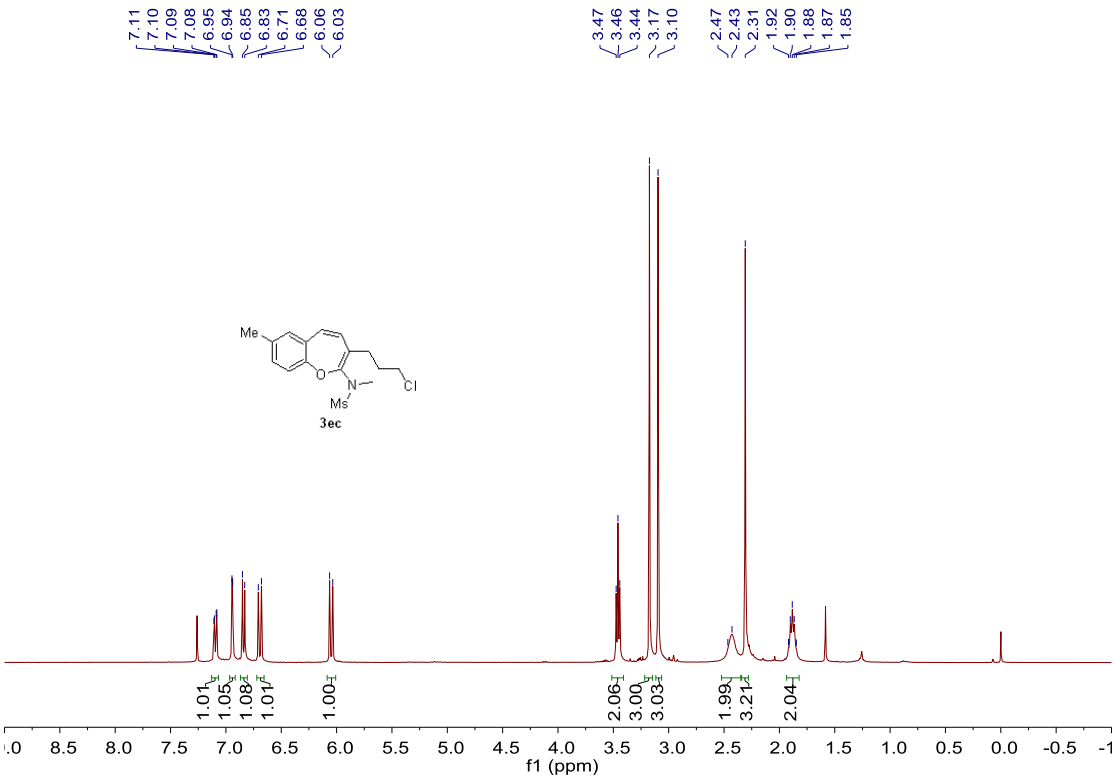

7.27
7.26
7.25
7.24
7.13
7.12
6.91
6.89
6.67
6.64
6.13
6.10
3.48
3.46
3.45
3.17
3.09
2.50
2.48
2.47
2.43
1.91
1.89
1.87
1.86
1.84
Cl
O
N
Ms
Cl
3cc
1.07
1.02
1.04
0.99
1.00
2.11
3.06
3.06
2.05
2.02
f1 (ppm)

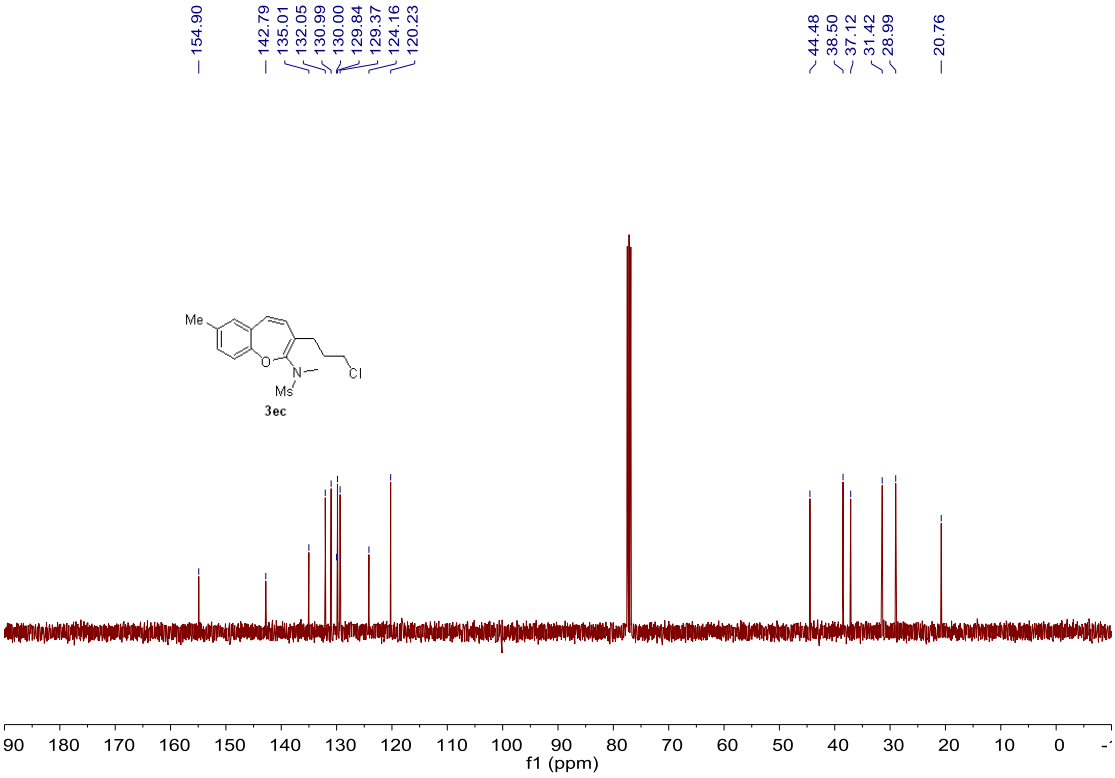

156.76
144.51
133.49
132.20
131.69
131.28
131.18
129.82
125.26
124.00
45.69
39.42
37.90
32.60
30.03
Cl
O
N
Ms
Cl
3cc
f1 (ppm)

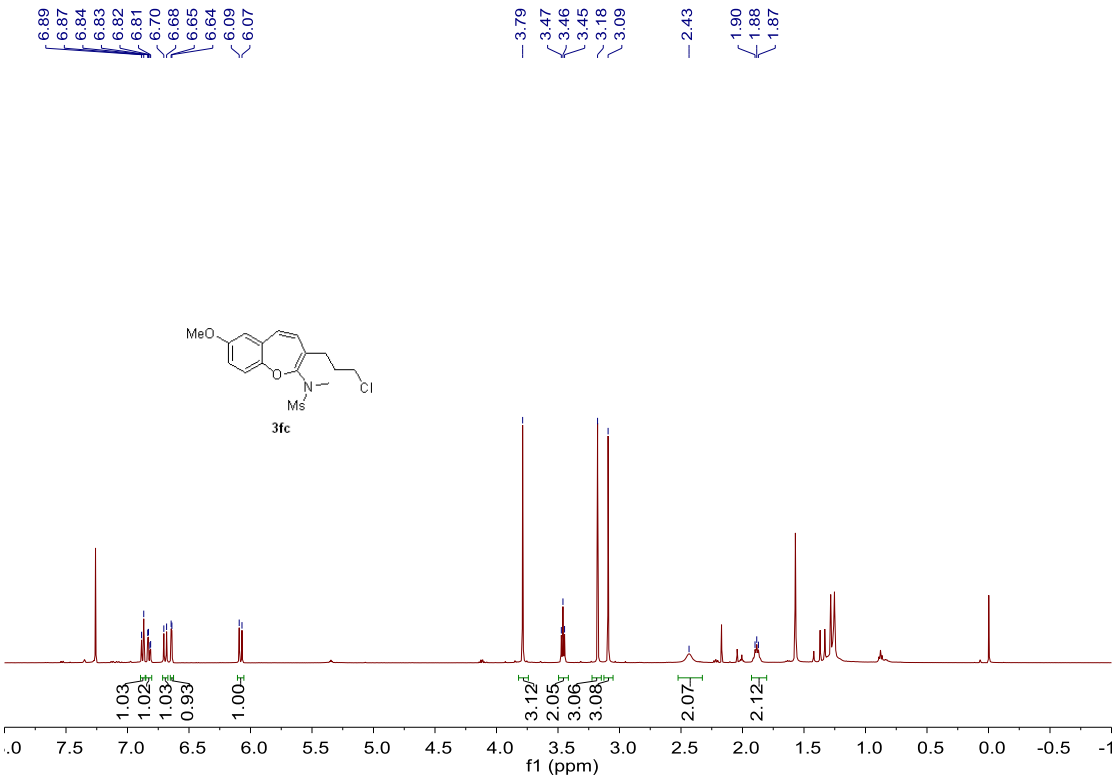

6.99
6.99
6.99
6.98
6.97
6.96
6.94
6.92
6.91
6.90
6.85
6.84
6.83
6.82
6.68
6.65
6.13
6.10
3.48
3.46
3.45
3.18
3.09
2.45
2.43
2.41
1.92
1.90
1.88
1.86
1.85
F
O
N
Ms
Cl
3dc
1.15
1.01
0.97
1.03
1.00
2.02
3.17
3.01
1.96
2.04
f1 (ppm)

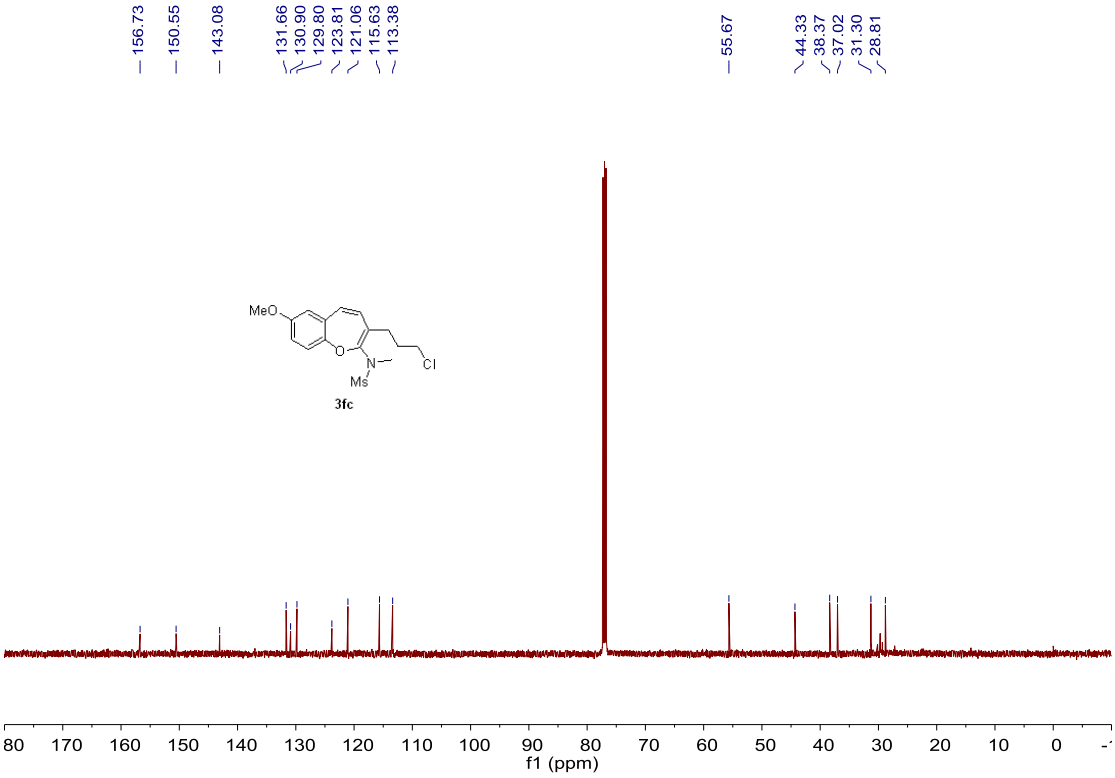

-117.83
F
O
N
Ms
Cl
3dc
f1 (ppm)

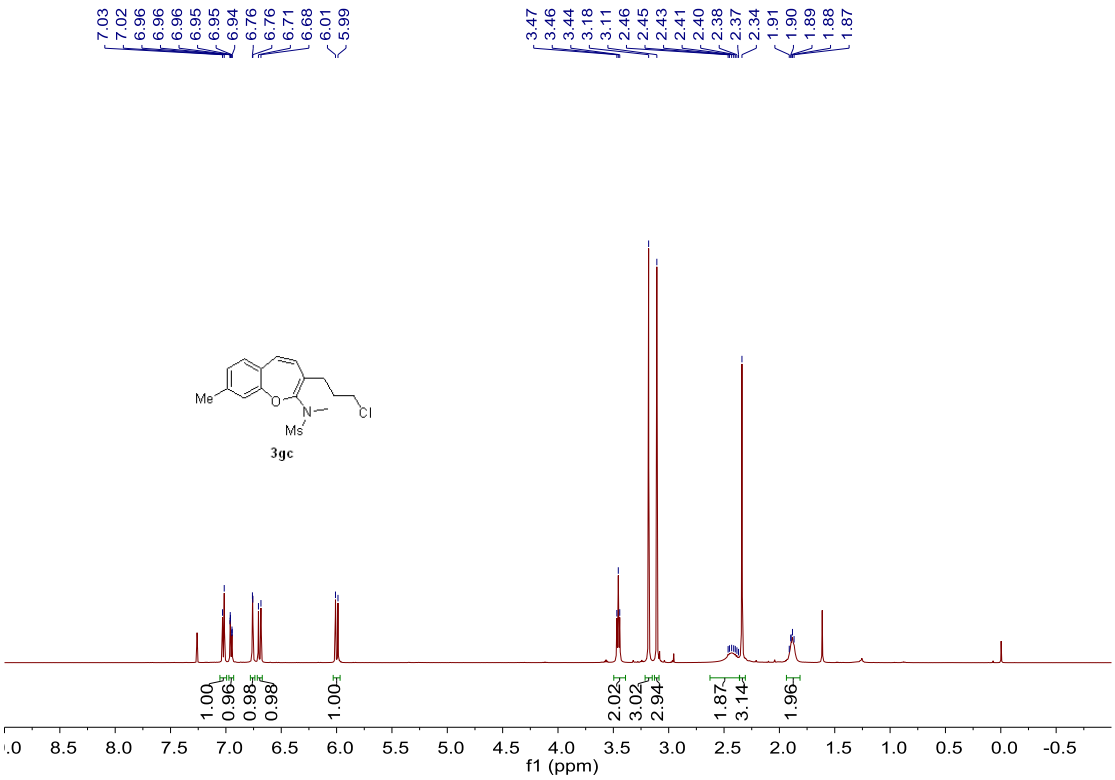

160.98
158.56
152.69
152.66
143.07
131.81
131.73
130.91
130.89
130.70
124.18
121.82
121.74
116.87
116.64
115.42
115.19
44.40
38.60
37.14
31.31
28.90
F
O
N
Ms
Cl
3dc
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

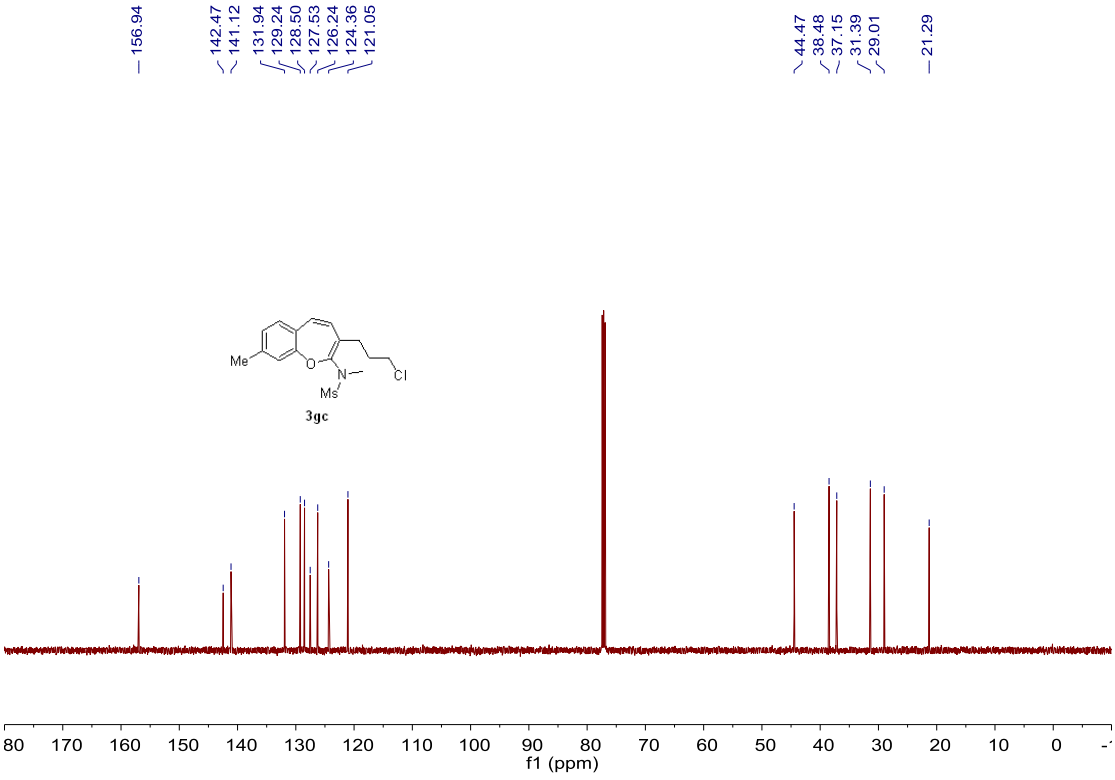

7.11
7.10
7.09
7.08
6.95
6.94
6.85
6.83
6.71
6.68
6.06
6.03
3.47
3.46
3.44
3.17
3.10
2.47
2.43
2.31
1.92
1.90
1.88
1.87
1.85
Me
O
N
Ms
Cl
3ec
1.01
1.05
1.08
1.01
1.00
2.06
3.00
3.03
1.99
3.21
2.04
f1 (ppm)

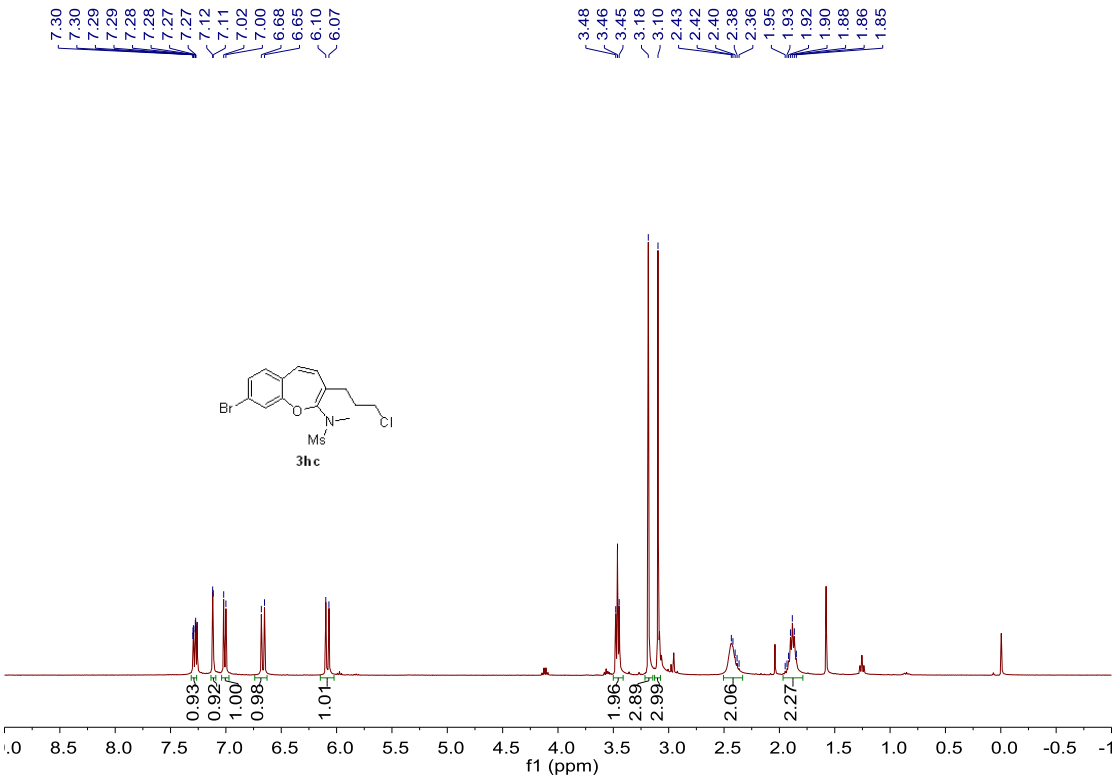

154.90
142.79
135.01
132.05
130.99
130.00
129.84
129.37
124.16
120.23
44.48
38.50
37.12
31.42
28.99
20.76
Me
O
N
Ms
Cl
3ec
f1 (ppm)

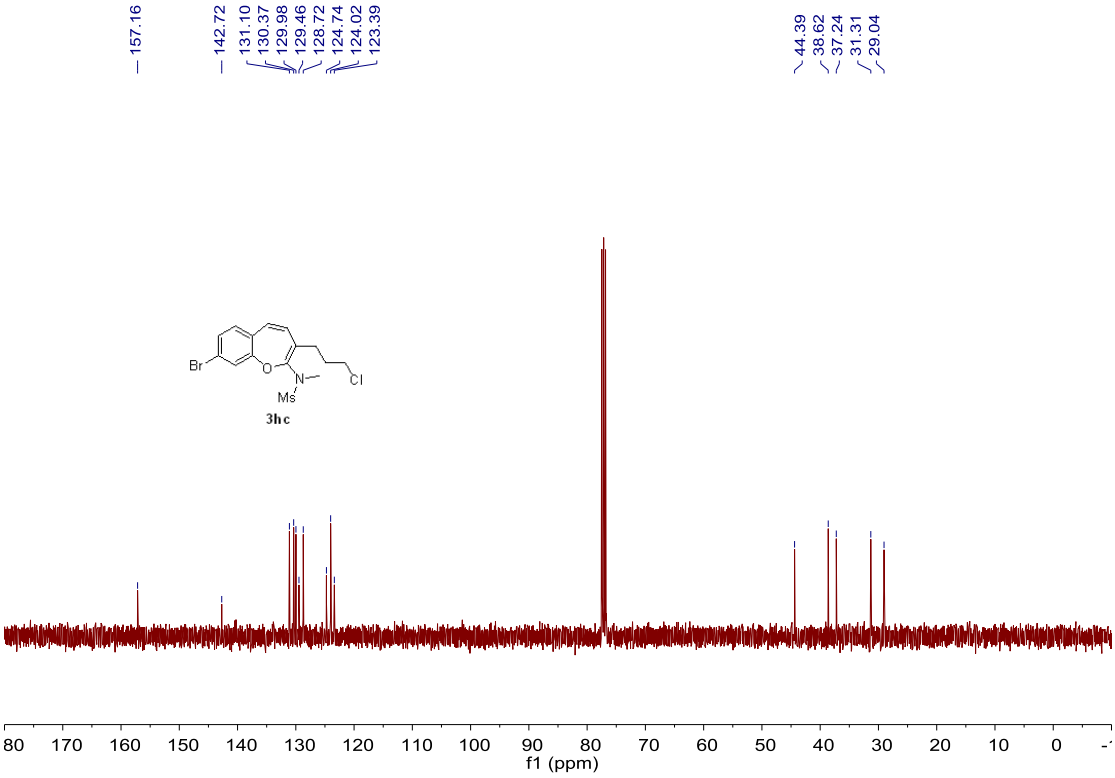

6.89
6.87
6.84
6.83
6.82
6.81
6.70
6.68
6.65
6.64
6.09
6.07
3.79
3.47
3.46
3.45
3.18
3.09
2.43
1.90
1.88
1.87
MeO
O
N
Ms
Cl
3fc
1.03
1.02
1.03
0.93
1.00
3.12
2.05
3.06
3.08
2.07
2.12
f1 (ppm)

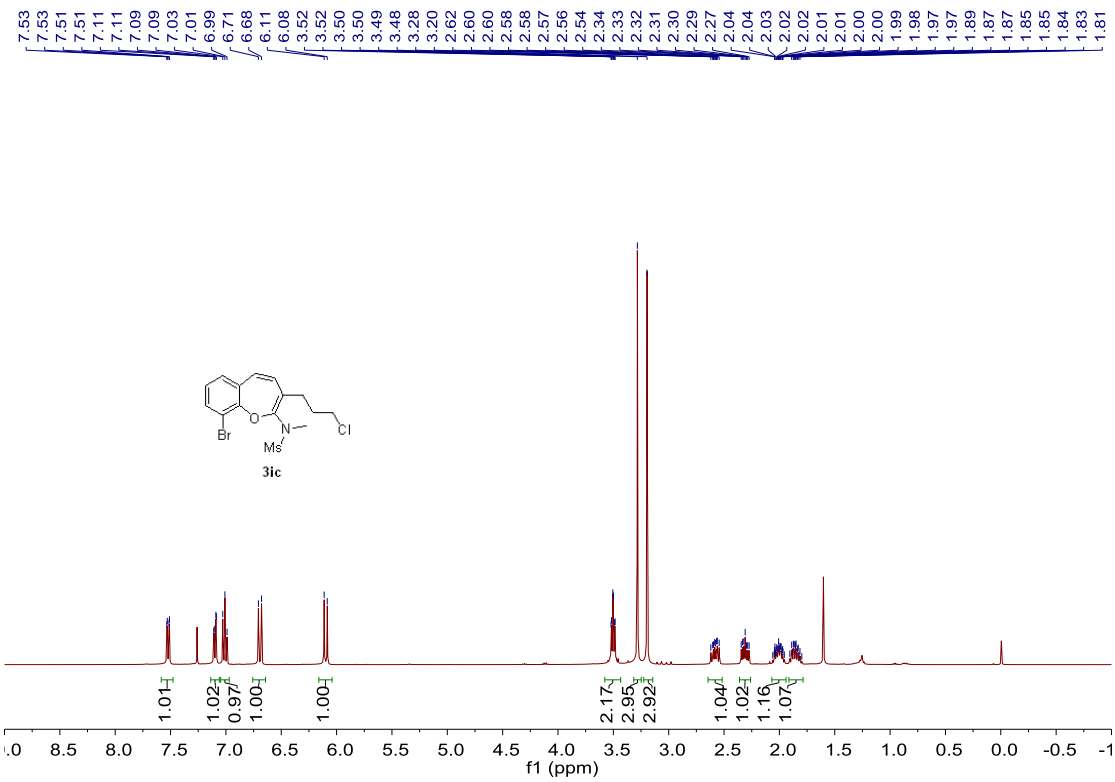

156.73
150.55
143.08
131.66
130.90
129.80
123.81
121.06
115.63
113.38
55.67
44.33
38.37
37.02
31.30
28.81
MeO
O
N
Ms
Cl
3fc
f1 (ppm)

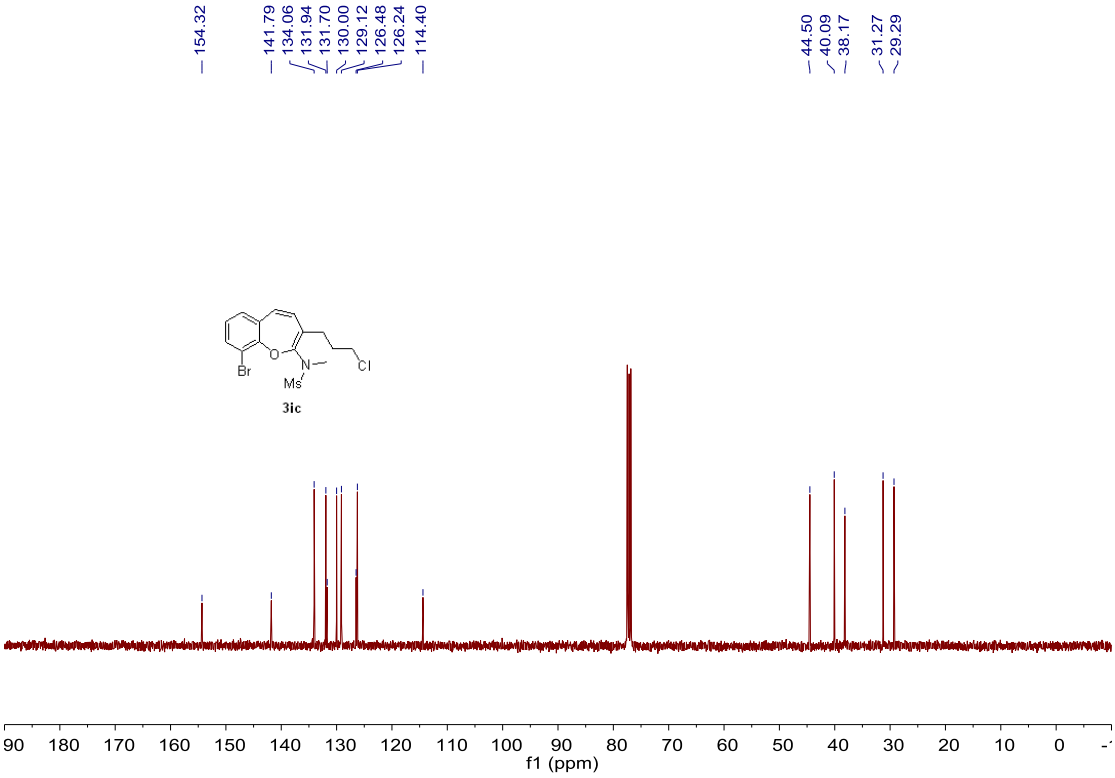

7.03
7.02
6.96
6.96
6.96
6.95
6.95
6.94
6.76
6.76
6.71
6.68
6.01
5.99
3.47
3.46
3.44
3.18
3.11
2.46
2.45
2.43
2.41
2.40
2.38
2.37
2.34
1.91
1.90
1.89
1.88
1.87
Me
O
N
Cl
Ms
3gc
1.00
0.96
0.98
0.98
1.00
2.02
3.02
2.94
1.87
3.14
1.96
f1 (ppm)

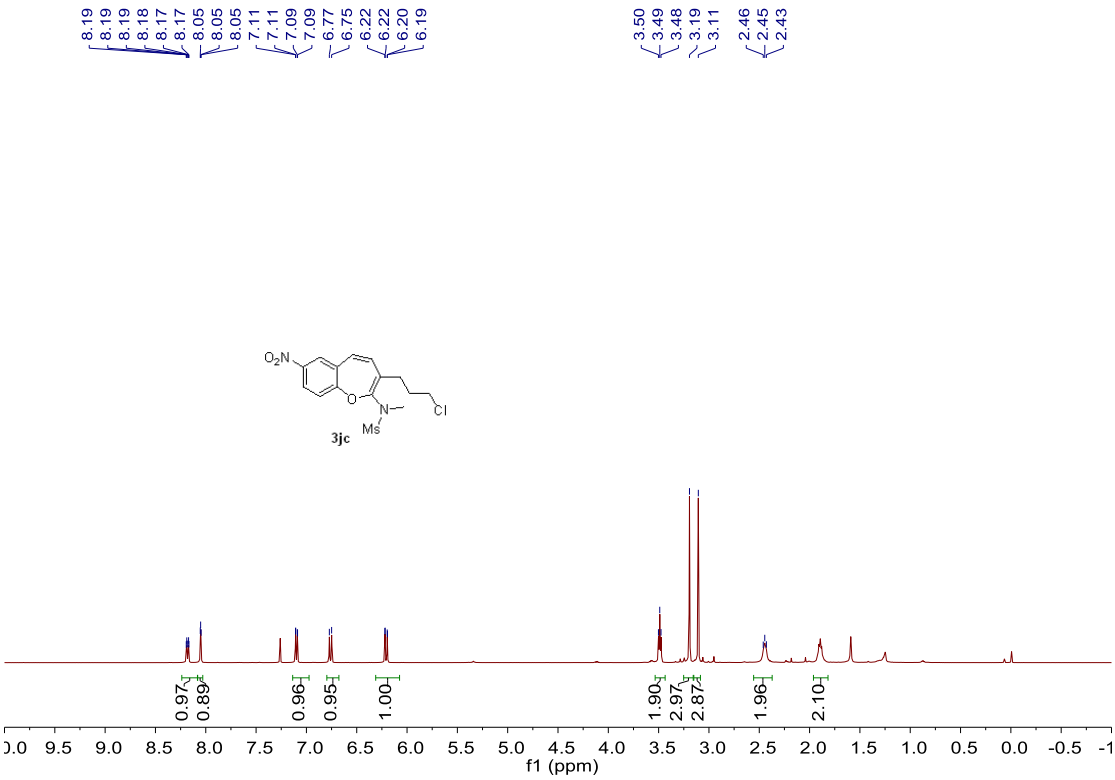

156.94
142.47
141.12
131.94
129.24
128.50
127.53
126.24
124.36
121.05
44.47
38.48
37.15
31.39
29.01
21.29
Me
O
N
Cl
Ms
3gc
f1 (ppm)

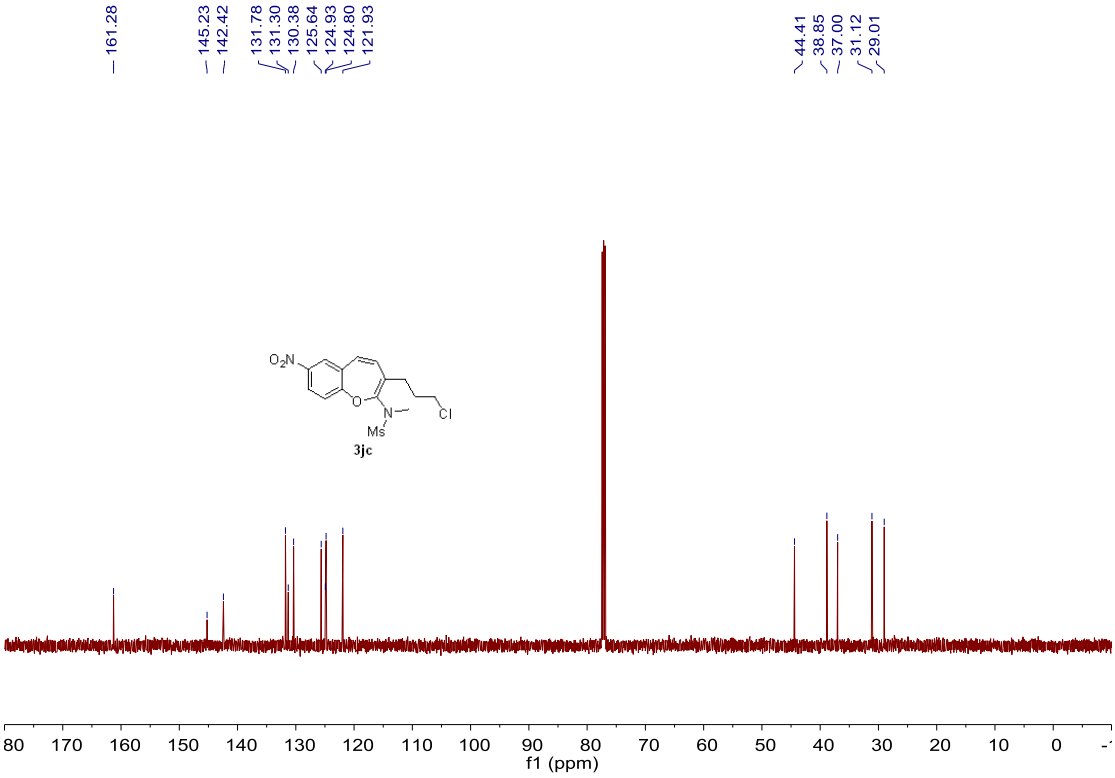

7.30
7.30
7.29
7.29
7.28
7.28
7.27
7.27
7.12
7.11
7.02
7.00
6.68
6.65
6.10
6.07
3.48
3.46
3.45
3.18
3.10
2.43
2.42
2.40
2.38
2.36
1.95
1.93
1.92
1.90
1.88
1.86
1.85
Br
O
N
Ms
Cl
3hc
0.93
0.92
1.00
0.98
1.01
1.96
2.89
2.99
2.06
2.27
f1 (ppm)

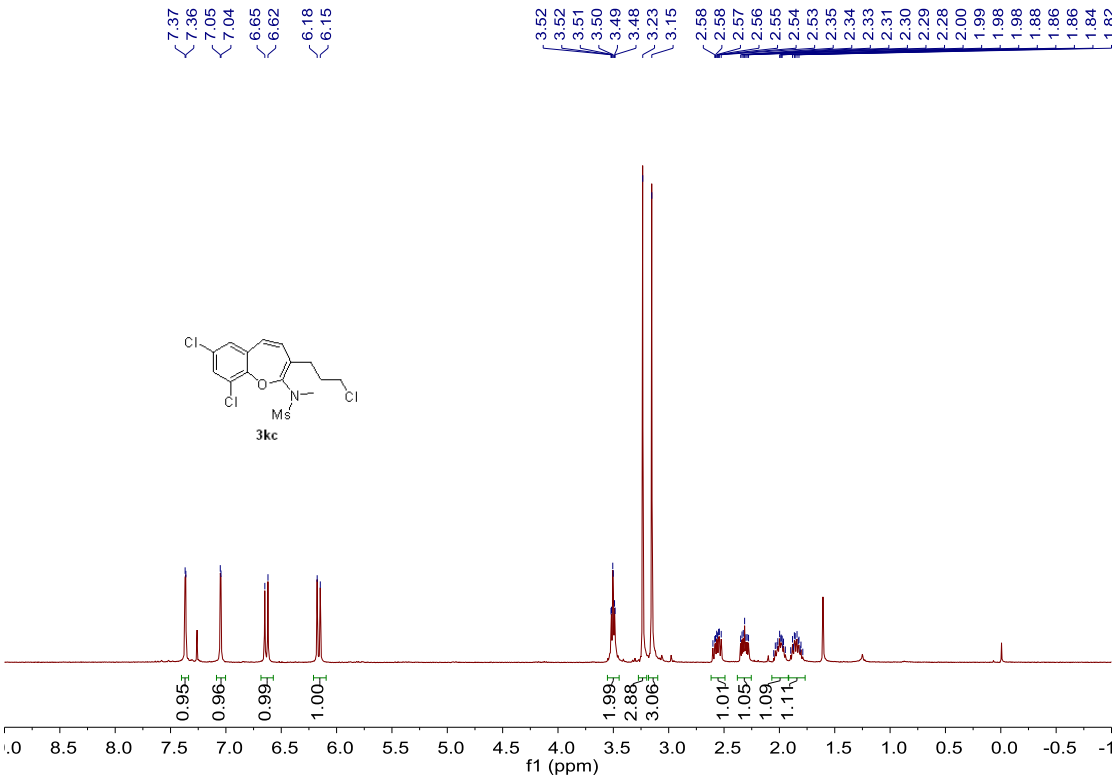

157.16
142.72
131.10
130.37
129.98
129.46
128.72
124.74
124.02
123.39
44.39
38.62
37.24
31.31
29.04
Br
O
N
Ms
Cl
3hc
f1 (ppm)

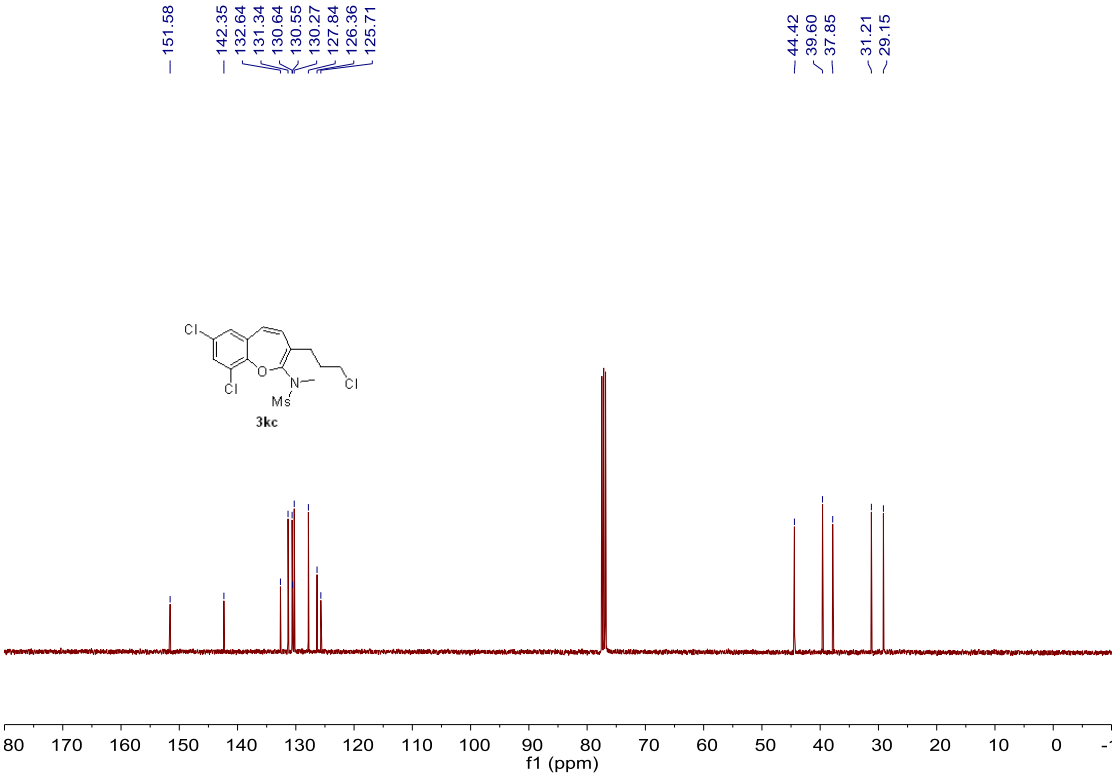

7.53 7.53 7.51 7.51 7.11 7.11 7.09 7.09 7.03 7.01 6.99 6.71 6.68 6.11 6.08 3.52 3.52 3.50 3.50 3.49 3.48 3.28 3.20 2.62 2.60 2.60 2.58 2.58 2.57 2.56 2.54 2.34 2.33 2.32 2.31 2.30 2.29 2.27 2.04 2.04 2.03 2.02 2.02 2.01 2.01 2.00 2.00 1.99 1.98 1.97 1.97 1.89 1.87 1.87 1.85 1.85 1.84 1.83 1.81
Br
O
N
Ms
Cl
3ic
1.01 1.02 0.97 1.00 1.00 2.17 2.95 2.92 1.04 1.02 1.16 1.07
f1 (ppm)

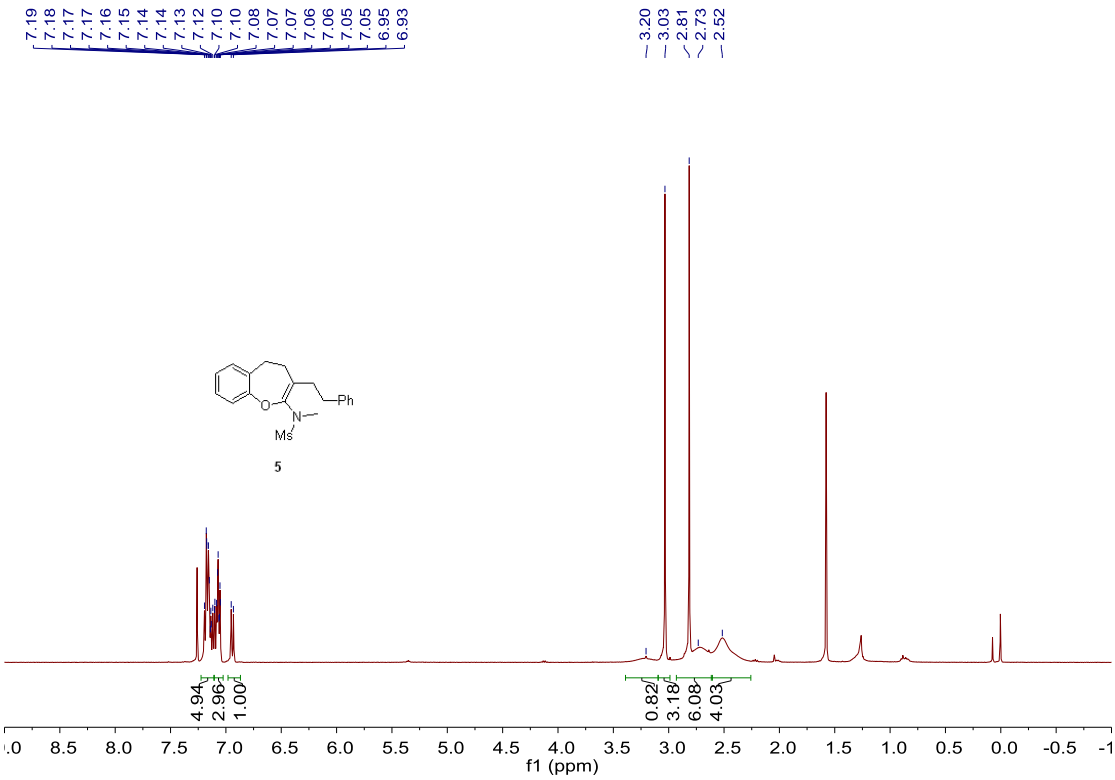

154.32 141.79 134.06 131.94 131.70 130.00 129.12 126.48 126.24 114.40
44.50 40.09 38.17 31.27 29.29
Br
O
N
Ms
Cl
3ic
f1 (ppm)

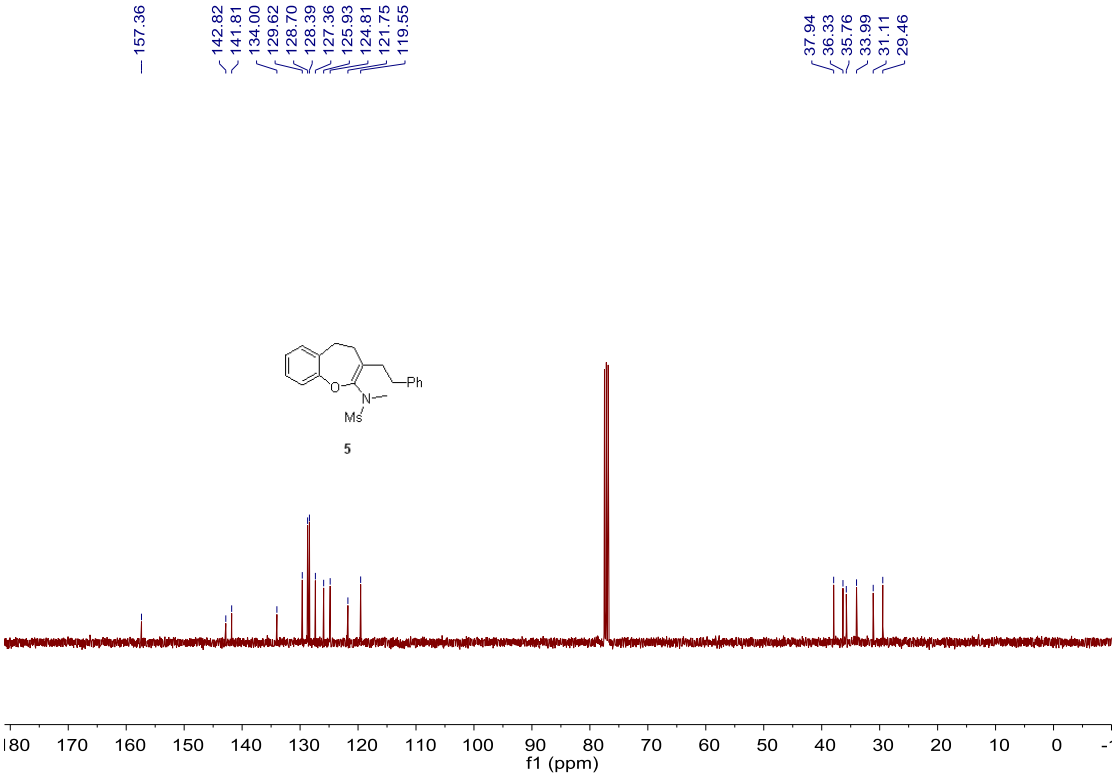

8.19
8.19
8.19
8.18
8.17
8.17
8.05
8.05
8.05
7.11
7.11
7.09
7.09
6.77
6.75
6.22
6.22
6.20
6.19
3.50
3.49
3.48
3.19
3.11
2.46
2.45
2.43
O2N
O
N
Cl
Ms
3jc
0.97
0.89
0.96
0.95
1.00
1.90
2.97
2.87
1.96
2.10
f1 (ppm)


161.28
145.23
142.42
131.78
131.30
130.38
125.64
124.93
124.80
121.93
44.41
38.85
37.00
31.12
29.01
O2N
O
N
Cl
Ms
3jc
f1 (ppm)

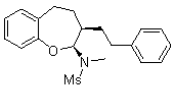

7.37
7.36
7.05
7.04
6.65
6.62
6.18
6.15
3.52
3.52
3.51
3.50
3.49
3.48
3.23
3.15
2.58
2.58
2.57
2.56
2.55
2.54
2.53
2.35
2.34
2.33
2.31
2.30
2.29
2.28
2.00
1.99
1.98
1.98
1.88
1.86
1.86
1.84
Cl
Cl
O
N
Ms
Cl
3kc
0.95
0.96
0.99
1.00
1.99
2.88
3.06
1.01
1.05
1.09
1.11
f1 (ppm)


151.58
142.35
132.64
131.34
130.64
130.55
130.27
127.84
126.36
125.71
44.42
39.60
37.85
31.21
29.15
Cl
Cl
O
N
Ms
Cl
3kc
f1 (ppm)

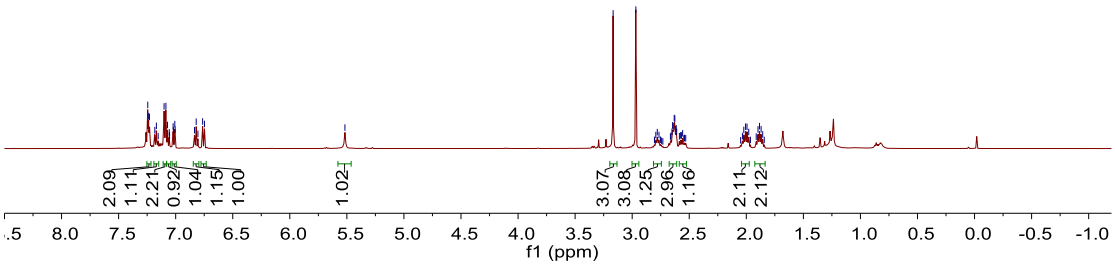

7.19
7.18
7.17
7.17
7.16
7.15
7.14
7.14
7.13
7.12
7.10
7.10
7.08
7.07
7.07
7.06
7.06
7.05
7.05
6.95
6.93
3.20
3.03
2.81
2.73
2.52
Ph
N
Ms
5
4.94
2.96
1.00
0.82
3.18
6.08
4.03
f1 (ppm)


157.36
142.82
141.81
134.00
129.62
128.70
128.39
127.36
125.93
124.81
121.75
119.55
37.94
36.33
35.76
33.99
31.11
29.46
Ph
N
Ms
5
f1 (ppm)

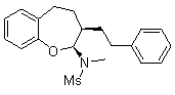

7.24 7.24 7.23 7.18 7.17 7.15 7.10 7.09 7.07 7.06 7.05 7.02 7.02 7.01 7.00 6.83 6.82 6.81 6.76 6.75 5.52 3.17 2.97 2.80 2.79 2.78 2.77 2.75 2.74 2.67 2.66 2.65 2.65 2.64 2.63 2.63 2.62 2.61 2.61 2.59 2.58 2.57 2.56 2.55 2.54 2.53 2.05 2.03 2.02 2.01 1.99 1.98 1.96 1.91 1.90 1.88 1.87 1.86 1.84


O
N
Ms

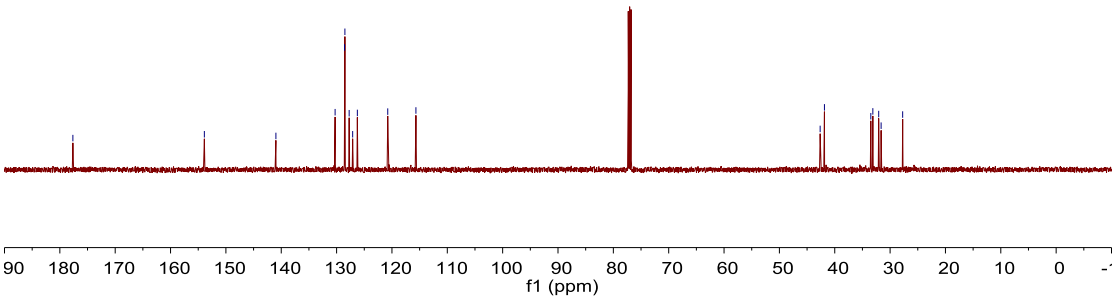
6

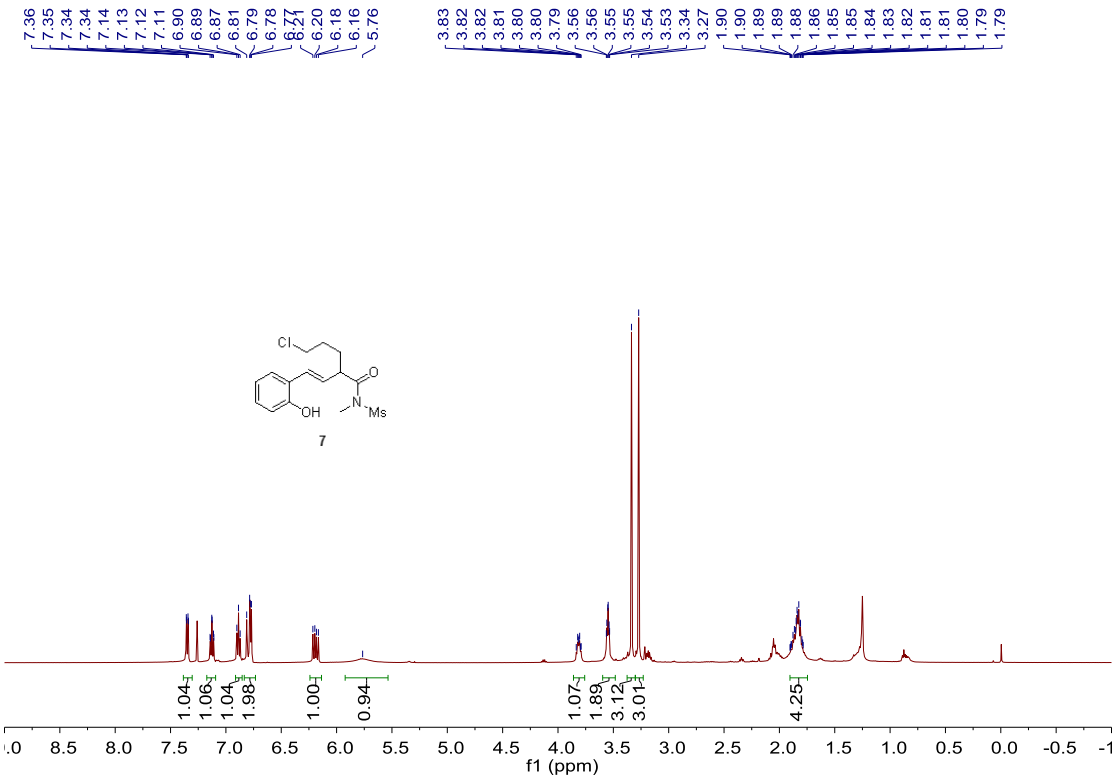

2.09 1.11 2.21 0.92 1.04 1.15 1.00 1.02 3.07 3.08 1.25 2.96 1.16 2.11 2.12
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

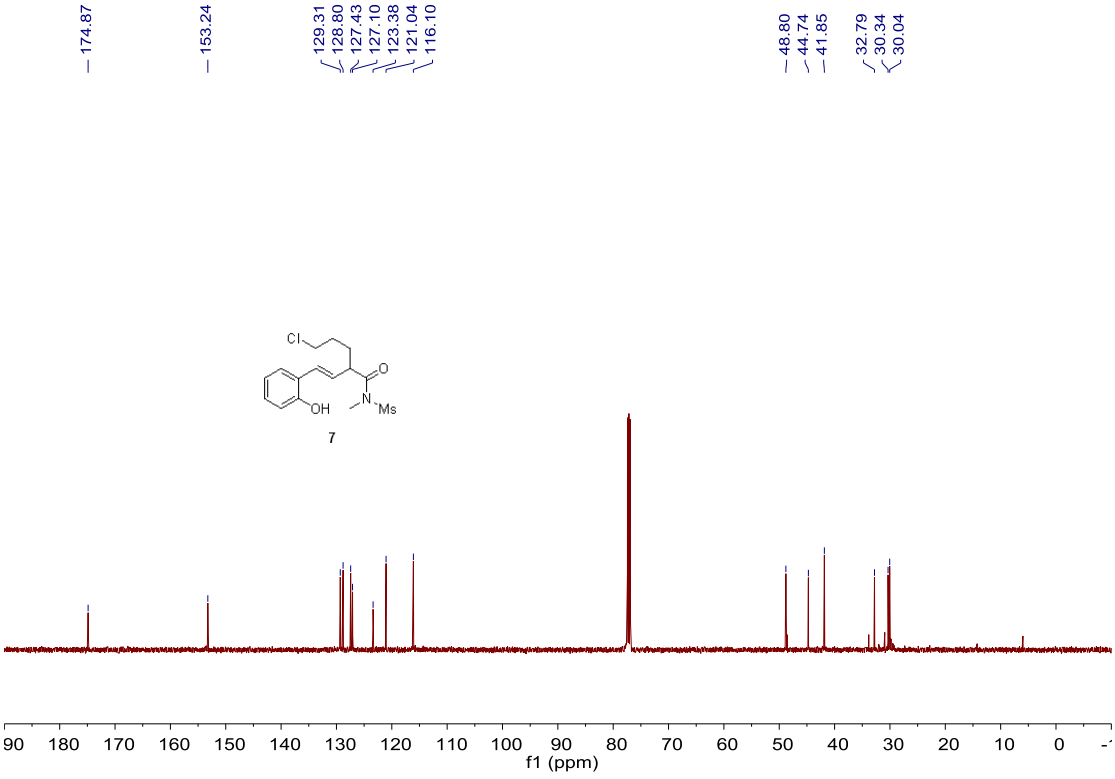

177.65 153.89 140.97 130.27 128.57 128.50 127.73 127.10 126.25 120.76 115.67 42.64 41.86 33.48 33.12 32.06 31.62 27.73


O
N
Ms

6


90 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.36
7.35
7.34
7.34
7.14
7.13
7.12
7.11
6.90
6.89
6.87
6.81
6.79
6.78
6.77
6.21
6.20
6.18
6.16
5.76
3.83
3.82
3.82
3.81
3.80
3.80
3.79
3.56
3.56
3.55
3.55
3.54
3.53
3.34
3.27
1.90
1.90
1.89
1.89
1.88
1.86
1.85
1.85
1.84
1.83
1.82
1.81
1.81
1.80
1.79
1.79
Cl
O
OH
N
Ms
7
1.04
1.06
1.04
1.98
1.00
0.94
1.07
1.89
3.12
3.01
4.25
f1 (ppm)


174.87
153.24
129.31
128.80
127.43
127.10
123.38
121.04
116.10
48.80
44.74
41.85
32.79
30.34
30.04
Cl
O
OH
N
Ms
7
f1 (ppm)