Supporting Information

Iron-Catalyzed Alkyne-Carbonyl Metathesis for the Synthesis of 6,7-Dihydro-5*H*-dibenzo[*c*,*e*]azonines

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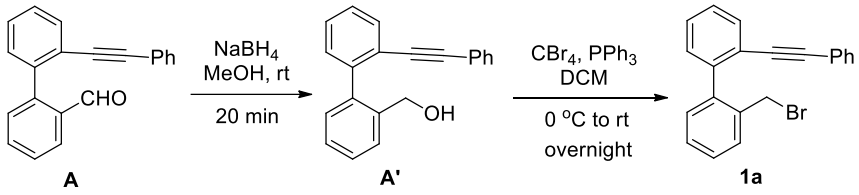
Content

General Information

^{1}H NMR spectra were recorded as solutions in $CDCl_3$ using a 400 MHz spectrometer. Chemical shifts are expressed in parts per million (ppm, δ) which are referenced to $CDCl_3$ as an internal standard (δ 7.26 ppm for all the compounds). Reported values of the coupling constants are absolute values expressed in Hz. The description of the signals should be interpreted as the following: s = singlet, d = doublet, dd = doublet of doublets, t = triplet, m = multiplet and td = triplet of doublets. ^{13}C NMR spectra were recorded as solutions in $CDCl_3$ with complete proton decoupling using 400 (75) MHz spectrometers. Chemical shifts, expressed in parts per million (ppm, δ), are referenced to $CDCl_3$ (δ = 77.0 ppm) as an internal standard. Electrospray ionization technique and TOF mass analyzer were used for HRMS. The monitoring of the reaction was done with silica gel coated aluminium sheet TLC (Merck). Solvents, reagents and chemicals were purchased from Aldrich, Alfa aeser, Merck, Spectrochem. Oven-dried glass wares were used for moisture-sensitive reactions. Reactions that required heating were performed in silicon oil bath.

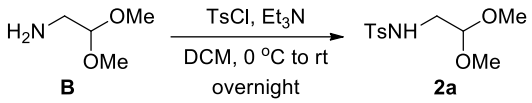
Representative Experimental Procedure for the Synthesis, and the Characterization Data of 2-(Bromomethyl)-2'-(phenylethynyl)-1,1'-biphenyl (1a)



A A' 1a

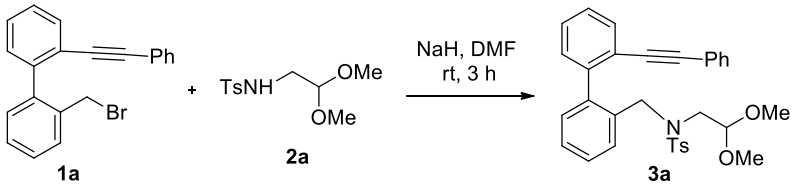
2'-(Phenylethynyl)-[1,1'-biphenyl]-2-carbaldehyde **A** (423 mg, 1.5 mmol) was taken in methanol (4.5 mL) in a 25 mL round-bottom flask. Stirring was started at room temperature and sodium borohydride (171 mg, 4.5 mmol) was added to the reaction mixture in three portions. The substrate **A** was consumed within 20 minutes (monitored by TLC). The reaction mixture was extracted with ethyl acetate and, then, washed with aqueous ammonium chloride solution. Then the organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The dried product (2'-(phenylethynyl)-[1,1'-biphenyl]-2-yl)methanol **A'** (422 mg, 1.49 mmol) was taken in a 50 mL round-bottom flask. Triphenylphosphine (585 mg, 2.23 mmol) and DCM (7 mL) were added to it. The mixture was stirred at room temperature for 10 minutes. Then, it was placed in an ice bath and tetrabromomethane (592 mg, 1.78 mmol) in DCM (4 mL) was added drop wise. After the addition was complete, the reaction was allowed to run at room temperature overnight. After the reaction was complete (monitored by TLC), the reaction mixture was concentrated and column chromatography on silica gel (60-120 mesh) was performed to purify the brominated product **1a**. The desired 2-(bromomethyl)-2'-(phenylethynyl)-1,1'-biphenyl **1a** (447 mg, 1.29 mmol), a brown liquid, was eluted with petroleum ether to get a two-step yield of 86%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 7.2 Hz, 1H), 7.62 (d, *J* = 7.2 Hz, 1H), 7.50 – 7.40 (m, 5H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.28 – 7.24 (m, 3H), 7.17 – 7.15 (m, 2H), 4.53 (d, *J* = 10.0 Hz, 1H), 4.44 (d, *J* = 10.0 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 142.7, 140.9, 136.1, 131.9, 131.5, 130.9, 130.4, 129.8, 128.4, 128.3, 128.3, 128.3, 127.8, 123.2, 123.0, 93.3, 88.6, 32.2.

Experimental Procedure for the Synthesis, and the Characterization Data of *N*-(2,2-dimethoxyethyl)-4-methylbenzen-esulfonamide (2a)



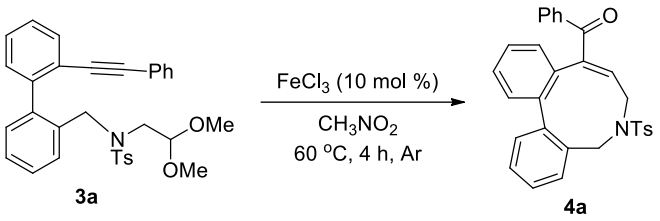
In an oven-dried 100 mL round-bottom flask, aminoacetaldehyde dimethyl acetal **B** (840 mg, 8 mmol) and triethylamine (1.617 mg, 16 mmol) were taken in DCM (16 mL) in an ice bath. Tosyl chloride (1.520 mg, 8 mmol), dissolved in DCM (10 mL) was added drop wise to the reaction vessel at 0 °C. After the addition was done, the reaction was allowed to run overnight at the room temperature. On completion of the reaction (monitored by TLC), the reaction mixture was diluted with DCM, washed with water. The combined organic layer was separated and dried over anhydrous Na_2SO_4. After evaporating the solvent and drying it, the pure product **2a** (2.05 g, 99%) was obtained as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 7.8 Hz, 2H), 7.28 (d, *J* = 7.8 Hz, 2H), 4.30 (t, *J* = 6.6 Hz, 1H), 3.28 (s, 6H), 3.00 (d, *J* = 6.4 Hz, 2H), 2.39 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 143.6, 136.9, 129.8, 127.1, 102.6, 54.6, 44.6, 21.6.

Representative Experimental Procedure for the Synthesis, and the Characterization Data of *N*-(2,2-dimethoxyethyl)-4-methyl-*N*-((2'-(phenylethynyl)-[1,1'-biphenyl]-2-yl)methyl)benzenesulfonamide (3a)



NaH (13.2 mg, 0.55 mmol) was taken in DMF (1.5 mL) in a 25 mL round-bottom flask fitted under Ar balloon. Substrate **2a** (129 mg, 0.5 mmol) dissolved in DMF (3 mL) was added to the reaction flask kept at stirring. After 15 minutes, substrate **1a** (173 mg, 0.5 mmol) dissolved in DMF (4 mL) was added drop wise for 5 minutes. The reaction mixture was stirred at room temperature for 3 hours under Ar atmosphere. The reaction was complete after 3 hours (monitored by TLC). The reaction mixture was extracted with ethyl acetate and, then, washed with water. The organic layer was separated and dried over anhydrous Na_2SO_4. The crude product obtained after evaporating the solvent under reduced pressure was purified by silica gel column chromatography (60-120 mesh). The desired product eluted with ethyl acetate/ petroleum ether (1:5 v/v) to furnish the dark yellow semi-solid compound **3a** (194 mg, 74%) as the substrate for the alkyne-aldehyde metathesis reaction. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 – 7.53 (m, 4H), 7.38 (td, *J* = 7.6, 1.6 Hz, 1H), 7.32 (td, *J* = 7.6, 1.2 Hz, 1H), 7.24 – 7.12 (m, 8H), 7.04 (td, *J* = 8.6, 2.6 Hz, 1H), 6.93 (dd, *J* = 9.2, 2.8 Hz, 1H), 4.61 (d, *J* = 16.0 Hz, 1H), 4.23 – 4.16 (m, 2H), 3.20 – 3.14 (m, 1H), 3.05 (d, *J* = 4.4 Hz, 6H), 3.02 – 2.98 (m, 1H), 2.36 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 143.1, 143.0, 140.2, 138.5, 137.3, 134.9, 131.6, 131.4, 131.3, 130.1, 129.8, 129.8, 129.5, 129.2, 129.1, 128.1, 128.0, 128.0, 127.4, 127.4, 127.3, 126.9, 123.5, 120.0, 103.0, 93.3, 87.9, 54.0, 50.1, 49.5, 21.6. HRMS (ESI): calcd for $C_{32}H_{32}NO_4S$ [M+H] 526.2052; found 526.2047.

Representative Experimental Procedure for the Synthesis, and Characterization Data of (*E*)-phenyl(6-tosyl-6,7-dihydro-5*H*-dibenzo[*c*,*e*]azonin-9-yl)methanone (4a)



In an oven-dried 10 mL round-bottom flask, *N*-(2,2-dimethoxyethyl)-4-methyl-N-((2'-(phenylethynyl)-[1,1'-biphenyl]-2-yl)methyl)benzenesulfonamide (**3a**, 105 mg, 0.2 mmol) and $FeCl_3$ (3.3 mg, 0.02 mmol) were added to nitromethane (2 mL) fitted under an Ar balloon. The mixture was stirred at 60 °C for 4 h until the reaction was complete (monitored by TLC). Then, the solvent was evaporated and the crude reaction mixture was purified by silica gel column chromatography (100−200 mesh). A solvent mixture of ethyl acetate/petroleum ether (15:85 v/v) was used to elute the desired product **4a** (68 mg, 71%) as a pale yellow semi-solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, *J* = 7.6 Hz, 1H), 7.64 (dd, *J* = 10.2, 1.8 Hz, 2H), 7.46 – 7.34 (m, 5H), 7.28 – 7.20 (m, 5H), 7.15 (td, *J* = 7.6, 1.2 Hz, 1H), 6.92 (dd, *J* = 7.2, 4.8 Hz, 3H), 6.22 (dd, *J* = 10.2, 6.2 Hz, 1H), 4.78 (d, *J* = 13.8 Hz, 1H), 4.13 (dd, *J* = 13.8, 5.8 Hz, 1H), 3.48 (d, *J* = 14.0 Hz, 1H), 3.17 – 3.11 (m, 1H), 2.38 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 195.5, 143.6, 141.5, 140.5, 137.0, 136.7, 136.6, 135.1, 132.2, 130.9, 130.0, 129.7, 129.6, 129.2, 128.6, 128.4, 128.1, 128.0, 127.8, 127.0, 52.1, 48.2, 21.6. HRMS (ESI): calcd for $C_{30}H_{26}NO_3S$ [M+H] 480.1633; found 480.1634.

(*E*)-*p*-Tolyl(6-tosyl-6,7-dihydro-5*H*-dibenzo[*c*,*e*]azonin-9-yl)methanone (4b)

N-(2,2-Dimethoxyethyl)-4-methyl-*N*-((2'-(*p*-tolylethynyl)-[1,1'-biphenyl]-2-yl)methyl)benzenesulfonamide (**3b**, 108 mg, 0.2 mmol) and $FeCl_3$ (3.3 mg, 0.02 mmol) in nitromethane (2 mL) were treated similarly to the procedure for the synthesis of **4a**. A solvent mixture of ethyl acetate/petroleum ether (15:85 v/v) was used to elute the desired product **4b** (71 mg, 72%) as a colorless semi-solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, *J* = 7.6 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.47 – 7.36 (m, 4H), 7.27 – 7.25 (m, 3H), 7.17 – 7.14 (m, 1H), 7.03 (d, *J* = 8.0 Hz, 2H), 6.91 (d, *J* = 7.6 Hz, 1H), 6.85 (d, *J* = 8.0 Hz, 2H), 6.20 (dd, *J* = 10.2, 6.2 Hz, 1H), 4.79 (d, *J* = 14.0 Hz, 1H), 4.14 (dd, *J* = 13.8, 5.8 Hz, 1H), 3.49 (d, *J* = 14.0 Hz, 1H), 3.14 (t, *J* = 12.0 Hz, 1H), 2.39 (s, 3H), 2.35 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 195.2, 144.2, 143.6, 143.1, 141.6, 140.5, 136.7, 135.9, 135.5, 135.3, 134.3, 130.9, 130.0, 130.0, 129.8, 129.3, 128.9, 128.6, 128.4, 128.2, 128.0, 127.8, 127.1, 77.5, 52.2, 48.3, 21.7, 21.6. HRMS (ESI): calcd for $C_{31}H_{28}NO_3S$ [M+H] 494.1790; found 494.1795.

(*E*)-(4-Methoxyphenyl)(6-tosyl-6,7-dihydro-5*H*-dibenzo[*c*,*e*]azonin-9-yl)methanone (4c)

N-(2,2-Dimethoxyethyl)-*N*-((2'-((4-methoxyphenyl)ethynyl)-[1,1'-biphenyl]-2-yl)methyl)-4-methylbenzenesulfonamide (**3c**, 111 mg, 0.2 mmol) and $FeCl_3$ (3.3 mg, 0.02 mmol) in nitromethane (2 mL) were treated similarly to the procedure for the synthesis of **4a**. A solvent mixture of ethyl acetate/petroleum ether (20:80 v/v) was used to elute the desired product **4c** (77 mg, 76%) as a colorless semi-solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, *J* = 7.6 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.46 – 7.34 (m, 4H), 7.26 – 7.23 (m, 3H), 7.12 (td, *J* = 7.6, 1.2 Hz, 1H), 6.95 – 6.87 (m, 3H), 6.70 – 6.67 (m, 2H), 6.15 (dd, *J* = 10.4, 6.4 Hz, 1H), 4.78 (d, *J* = 14.0 Hz, 1H), 4.13 (dd, *J* = 14.0, 6.0 Hz, 1H), 3.81 (s, 3H), 3.48 (d, *J* = 14.0 Hz, 1H), 3.16 – 3.10 (m, 1H), 2.38 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 194.0, 163.2, 143.6, 141.6, 140.4, 136.7, 135.5, 135.3, 134.5, 132.3, 130.9, 130.0, 129.8, 129.4, 129.3,

128.5, 128.4, 128.1, 127.9, 127.7, 127.0, 113.4, 55.5, 52.2, 48.2, 21.6. HRMS (ESI): calcd for $C_{31}H_{28}NO_4S$ [M+H] 510.1739; found 510.1732.

(*E*)-(4-Fluorophenyl)(6-tosyl-6,7-dihydro-5*H*-dibenzo[*c*,*e*]azonin-9-yl)methanone (4d)

N-(2,2-Dimethoxyethyl)-*N*-((2'-((4-fluorophenyl)ethynyl)-[1,1'-biphenyl]-2-yl)methyl)-4-methylbenzenesulfonamide (**3d**, 109 mg, 0.2 mmol) and $FeCl_3$ (3.3 mg, 0.02 mmol) in nitromethane (2 mL) were treated similarly to the procedure for the synthesis of **4a**. A solvent mixture of ethyl acetate/petroleum ether (15:75 v/v) was used to elute the desired product **4d** (50 mg, 50%) as a yellow semi-solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, *J* = 7.6 Hz, 1H), 7.66 (d, *J* = 7.6 Hz, 2H), 7.48 – 7.37 (m, 4H), 7.27 (d, *J* = 7.2 Hz, 3H), 7.15 (t, *J* = 7.6, 1H), 6.97 – 6.88 (m, 5H), 6.19 (dd, *J* = 10.0, 6.4 Hz, 1H), 4.80 (d, *J* = 14.0 Hz, 1H), 4.14 (dd, *J* = 13.6, 5.6 Hz, 1H), 3.50 (d, *J* = 14.0 Hz, 1H), 3.17 (t, *J* = 11.6 Hz, 1H), 2.40 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 193.9, 166.7, 164.2, 144.0, 143.7, 141.7, 140.5, 136.8, 136.0, 135.6, 135.0, 133.2, 133.1, 132.5, 132.4, 131.1, 130.0, 129.8, 129.4, 128.7, 128.5, 128.2, 128.1, 127.9, 127.1, 115.4, 115.2, 52.2, 48.2, 21.6. HRMS (ESI): calcd for $C_{30}H_{25}FNO_3S$ [M+H] 498.1539; found 498.1539.

(*E*)-(12-Methyl-6-tosyl-6,7-dihydro-5*H*-dibenzo[*c*,*e*]azonin-9-yl)(phenyl)methanone (4e)

N-(2,2-Dimethoxyethyl)-4-methyl-*N*-((5'-methyl-2'-(phenylethynyl)-[1,1'-biphenyl]-2-yl)methyl)benzenesulfonamide (**3e**, 108 mg, 0.2 mmol) and $FeCl_3$ (3.3 mg, 0.02 mmol) in nitromethane (2 mL) were treated similarly to the procedure for the synthesis of **4a**. A solvent mixture of ethyl acetate/petroleum ether (15:85 v/v) was used to elute the desired product **4e** (66 mg, 67%) as a colorless semi-solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.46 – 7.40 (m, 2H), 7.27 – 7.20 (m, 6H), 7.15 (t, *J* = 7.4 Hz, 1H), 7.09 (s, 1H), 6.93 – 6.90 (m, 3H), 6.21 (dd, *J* = 10.4, 6.4 Hz, 1H), 4.80 (d, *J* = 14.4 Hz, 1H), 4.15 (dd, *J* = 14.0, 6.4 Hz, 1H), 3.50 (d, *J* = 14.0 Hz, 1H), 3.21 – 3.18 (m, 1H), 2.39 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 195.6, 144.1, 143.5, 141.6, 140.4, 137.8, 137.1, 136.8, 136.7, 135.4, 132.2, 131.3, 130.9, 130.0, 129.6, 129.4, 129.3, 129.2, 128.5, 128.3, 128.1, 128.1, 127.0, 52.1, 48.2, 21.6, 21.3. HRMS (ESI): calcd for $C_{31}H_{28}NO_3S$ [M+H] 494.1790; found 494.1787.

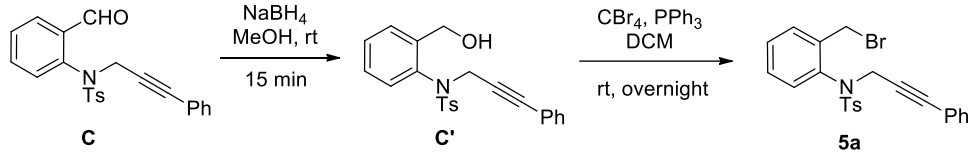
(*E*)-(12-Fluoro-6-tosyl-6,7-dihydro-5*H*-dibenzo[*c*,*e*]azonin-9-yl)(phenyl)methanone (4f)

N-(2,2-Dimethoxyethyl)-*N*-((5'-fluoro-2'-(phenylethynyl)-[1,1'-biphenyl]-2-yl)methyl)-4-methylbenzenesulfonamide (**3f**, 109 mg, 0.2 mmol) and $FeCl_3$ (3.3 mg, 0.02 mmol) in nitromethane (2 mL) were treated similarly to the procedure for the synthesis of **4a**. A solvent mixture of ethyl acetate/petroleum ether (12:88 v/v) was used to elute the desired product **4f** (45 mg, 45%) as a pale yellow semi-solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, *J* = 7.6 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.48 – 7.40 (m, 2H), 7.32 (dd, *J* = 8.6, 5.8 Hz, 1H), 7.27 (d, *J* = 8.0 Hz, 2H), 7.22 (t, *J* = 7.8 Hz, 2H), 7.18 – 7.11 (m, 2H), 7.00 (dd, *J* = 9.0, 2.6 Hz, 1H), 6.92 – 6.89 (m, 3H), 6.24 (dd, *J* = 10.0, 6.4 Hz, 1H), 4.77 (d, *J* = 13.2 Hz, 1H), 4.18 – 4.10 (m, 1H), 3.47 (d, *J* = 14.0 Hz, 1H), 3.16 – 3.10 (m, 1H), 2.39 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 195.4, 163.2, 161.0, 143.7, 142.6, 142.5, 140.4, 137.4, 136.8, 136.4, 135.2, 132.4, 131.5, 131.4, 131.1, 130.0, 129.6, 129.0, 128.8, 128.3, 128.2, 127.0, 123.2, 122.9, 122.7, 122.6, 115.9, 115.7, 115.0, 114.8, 52.1, 48.3, 21.6. HRMS (ESI): calcd for $C_{30}H_{25}FNO_3S$ [M+H] 498.1539; found 498.1530.

(*E*)-(12-Methyl-6-tosyl-6,7-dihydro-5*H*-dibenzo[*c*,*e*]azonin-9-yl)(2,4,5-trimethylphenyl)methanone (4g)

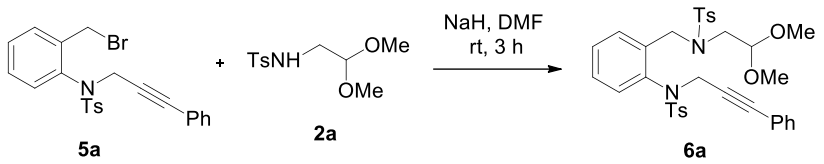
N-(2,2-Dimethoxyethyl)-4-methyl-*N*-((5'-methyl-2'-((2,4,5-trimethylphenyl)ethynyl)-[1,1'-biphenyl]-2-yl)methyl)benzenesulfonamide (**3g**, 116 mg, 0.2 mmol) and $FeCl_3$ (3.3 mg, 0.02 mmol) in nitromethane (2 mL) were treated similarly to the procedure for the synthesis of **4a**. A solvent mixture of ethyl acetate/petroleum ether (10:90 v/v) was used to elute the desired product **4g** (46 mg, 43%) as a brown semi-solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, *J* = 7.6 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.26 – 7.22 (m, 5H), 7.15 – 7.10 (m, 2H), 7.03 (d, *J* = 7.6 Hz, 1H), 6.87 (s, 1H), 6.22 (dd, *J* = 10.4, 6.4 Hz, 1H), 4.73 (d, *J* = 14.0 Hz, 1H), 4.12 (dd, *J* = 13.6, 6.4 Hz, 1H), 3.44 (d, *J* = 14.0 Hz, 1H), 3.19 – 3.13 (m, 1H), 2.39 (d, *J* = 2.0 Hz, 6H), 2.19 (s, 3H), 2.09 (s, 3H), 1.97 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 198.2, 146.3, 143.5, 141.8, 140.8, 140.1, 138.9, 137.8, 136.9, 135.6, 135.4, 133.1, 132.1, 132.1, 130.7, 129.9, 129.8, 129.7, 129.5, 129.4, 129.3, 129.2, 128.8, 128.5, 128.5, 128.2, 127.9, 127.1, 52.2, 48.5, 21.6, 21.4, 19.6, 19.1, 19.0. HRMS (ESI): calcd for $C_{34}H_{34}NO_3S$ [M+H] 536.2259; found 536.2263.

Experimental Procedure for the Synthesis, and the Characterization Data of *N*-(2-(bromomethyl)phenyl)-4-methyl-*N*-(3-phenylprop-2-yn-1-yl)benzenesulfonamide (5a)



N-(2-formylphenyl)-4-methyl-*N*-(3-phenylprop-2-yn-1-yl)benzenesulfonamide **C** (390 mg, 1 mmol) was taken in methanol (4 mL) in a 25 mL round-bottom flask. Stirring was started at room temperature and sodium borohydride (114 mg, 3 mmol) was added to the reaction mixture in three portions. The substrate **C** was consumed within 15 minutes (monitored by TLC). The reaction mixture was extracted with ethyl acetate and, then, washed with aqueous ammonium chloride solution. Then the organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The dried product *N*-(2-(hydroxymethyl)phenyl)-4-methyl-*N*-(3-phenylprop-2-yn-1-yl)benzenesulfonamide **C'** (374 mg, 0.95 mmol) was taken in a 50 mL round-bottom flask. Triphenylphosphine (375 mg, 1.43 mmol) and DCM (5 mL) were added to it. The mixture was stirred at room temperature for 10 minutes. Then, it was placed in an ice bath and tetrabromomethane (379 mg, 1.14 mmol) in DCM (3 mL) was added drop wise. After the addition was complete, the reaction was allowed to run at room temperature overnight. After the reaction was complete (monitored by TLC), the reaction mixture was concentrated and column chromatography on silica gel (60-120 mesh) was performed to purify the brominated product **5a**. The desired *N*-(2-(bromomethyl)phenyl)-4-methyl-*N*-(3-phenylprop-2-yn-1-yl)benzenesulfonamide **5a** (335 mg, 0.74 mmol), a colorless solid, was eluted with a solvent mixture of ethyl acetate/petroleum ether (5:95 v/v) to get a two-step yield of 74%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 7.2 Hz, 2H), 7.56 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.35 (td, *J* = 7.4, 1.4 Hz, 1H), 7.30 – 7.25 (m, 4H), 7.22 (s, 1H), 7.18 (td, *J* = 8.2, 1.8 Hz, 3H), 6.96 (dd, *J* = 8.0, 1.2 Hz, 1H), 5.13 – 4.98 (m, 2H), 4.54 – 4.45 (m, 2H), 2.38 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 144.0, 139.5, 138.0, 135.9, 131.8, 131.6, 129.6, 129.5, 129.4, 129.0, 128.7, 128.6, 128.3, 122.4, 85.9, 83.5, 42.1, 29.9, 21.7.

Experimental Procedure for the Synthesis, and the Characterization Data of *N*-(2,2-dimethoxyethyl)-4-methyl-*N*-(2-(4-methyl-*N*-(3-phenylprop-2-yn-1-yl)phenylsulfonamido)benzyl)benzenesulfonamide (6a)



NaH (13.2 mg, 0.55 mmol) was taken in DMF (1.5 mL) in a 25 mL round-bottom flask fitted under Ar balloon. Substrate **2a** (129 mg, 0.5 mmol) dissolved in DMF (3 mL) was added to the reaction flask kept at stirring. After 15 minutes, substrate **5a** (227 mg, 0.5 mmol) dissolved in DMF (4 mL) was added drop wise for 5 minutes. The reaction mixture was stirred at room temperature for 3 hours under Ar atmosphere. The reaction was complete after 3 hours (monitored by TLC). The reaction mixture was extracted with ethyl acetate and, then, washed with water. The organic layer was separated and dried over anhydrous Na_2SO_4. The crude product obtained after evaporating the solvent under reduced pressure was purified by silica gel column chromatography (60-120 mesh). The desired product eluted with ethyl acetate/ petroleum ether (1:3 v/v) to furnish the colorless solid compound **6a** (278 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 – 7.68 (m, 3H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.36 (td, *J* = 7.6, 1.2 Hz, 1H), 7.29 – 7.26 (m, 4H), 7.22 (d, *J* = 10.8 Hz, 3H), 7.17 – 7.16 (m, 1H), 7.15 – 7.14 (m, 1H), 7.11 (td, *J* = 7.6, 1.4 Hz, 1H), 6.84 (dd, *J* = 8.0, 1.2 Hz, 1H), 4.80 (d, *J* = 18.0 Hz, 1H), 4.70 (d, *J* = 3.2 Hz, 2H), 4.40 – 4.34 (m, 2H), 3.30 – 3.25 (m, 2H), 3.21 (s, 3H), 3.09 (s, 3H), 2.42 (s, 3H), 2.38 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 143.9, 143.5, 139.0, 137.4, 136.8, 135.8, 131.6, 129.8, 129.7, 129.4, 129.2, 128.6, 128.6, 128.5, 128.3, 127.5, 127.3, 122.3, 103.3, 85.7, 83.4, 54.5, 54.3, 51.1, 49.7, 42.2, 21.6. HRMS (ESI): calcd for $C_{34}H_{37}N_2O_6S_2$ [M+H] 633.2093; found 633.2101.

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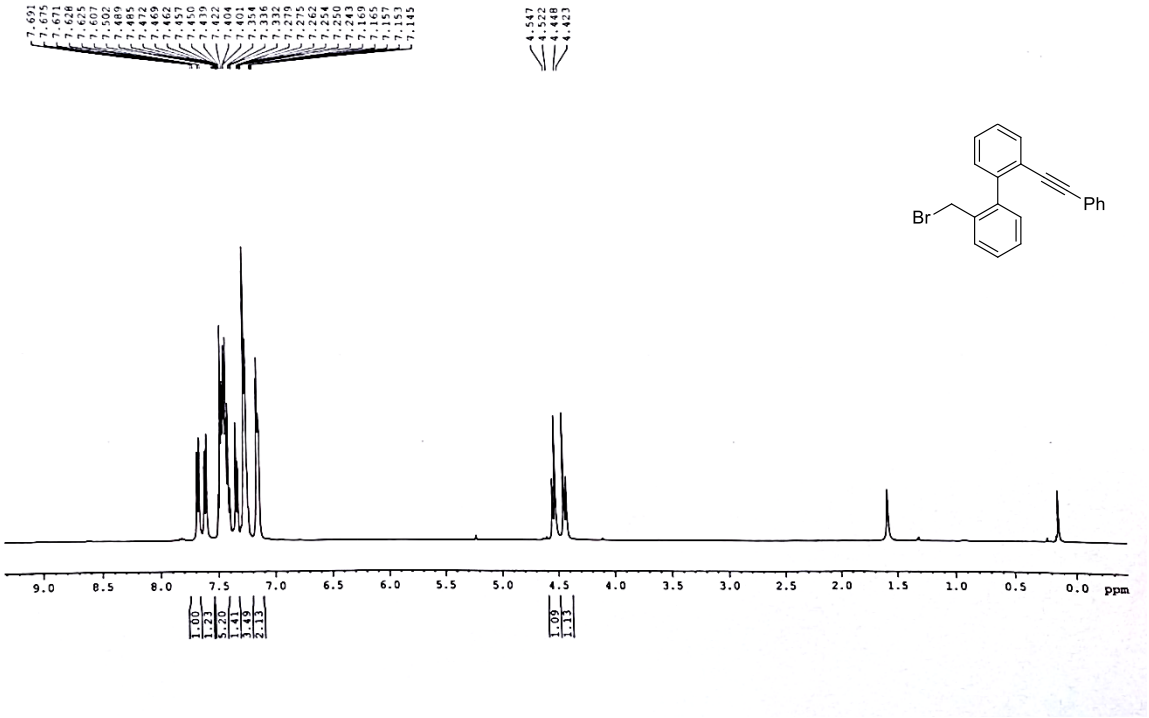
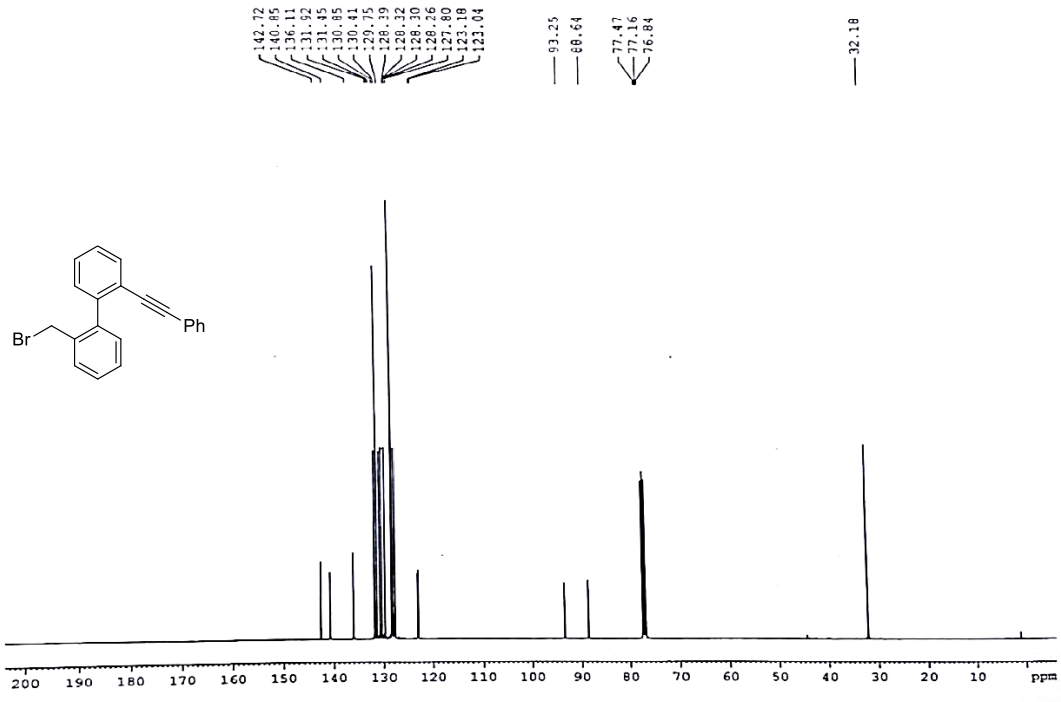
^{1}H AND ^{13}C NMR SPECTRA OF THE RELEVANT COMPOUNDS

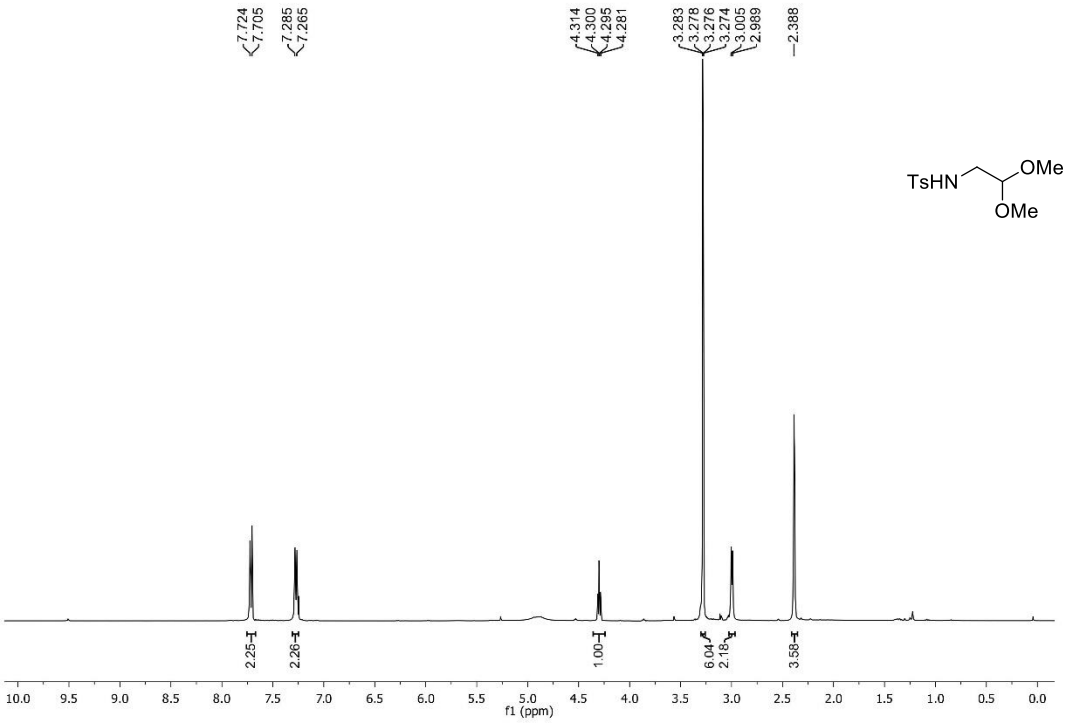
^{1}H NMR (400 MHz, $CDCl_3$) of compound 1a



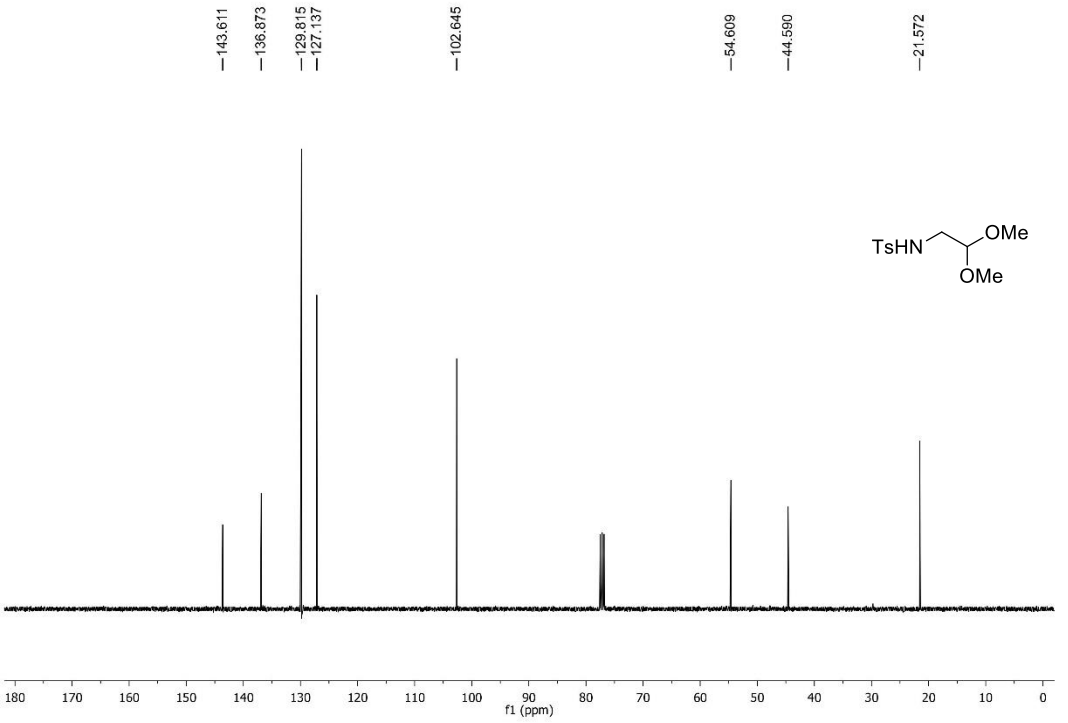
^{13}C NMR (100 MHz, $CDCl_3$) of compound 1a



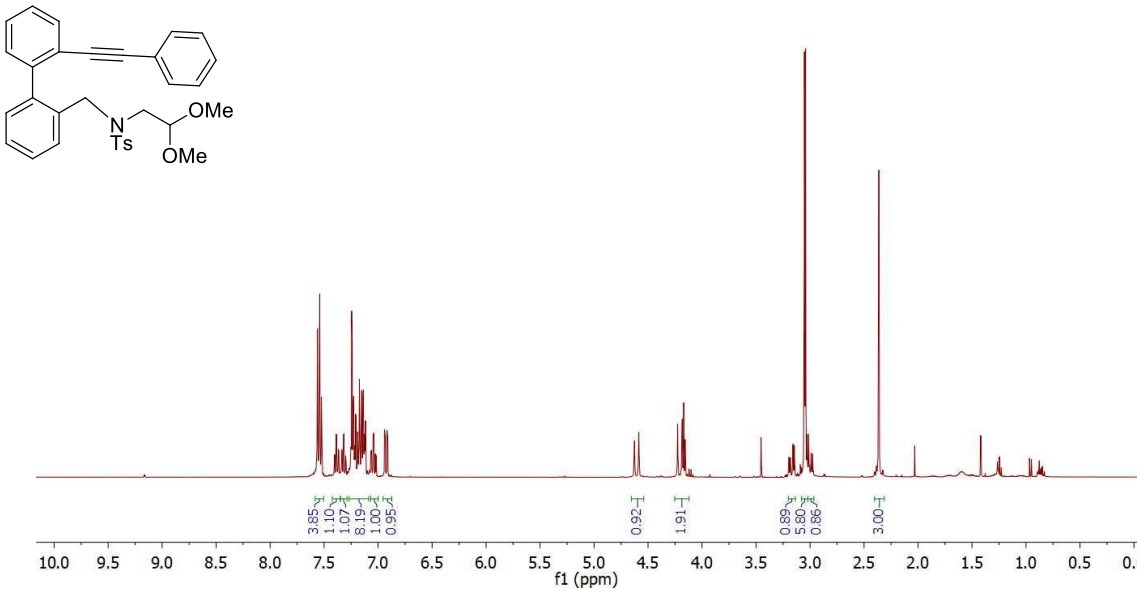
^{1}H NMR (400 MHz, $CDCl_3$) of compound 2a



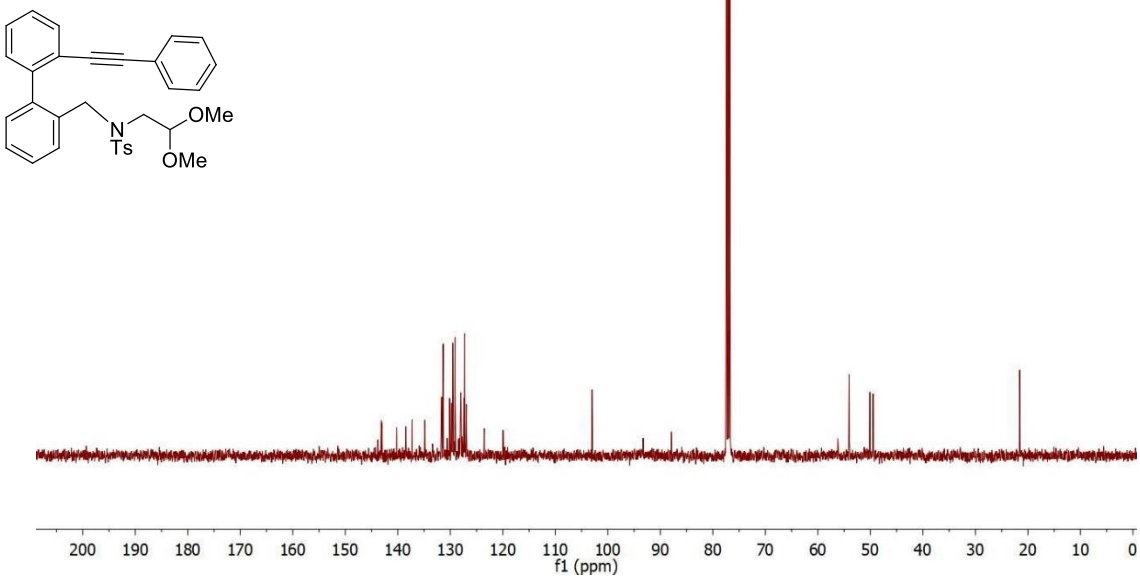
^{13}C NMR (100 MHz, $CDCl_3$) of compound 2a



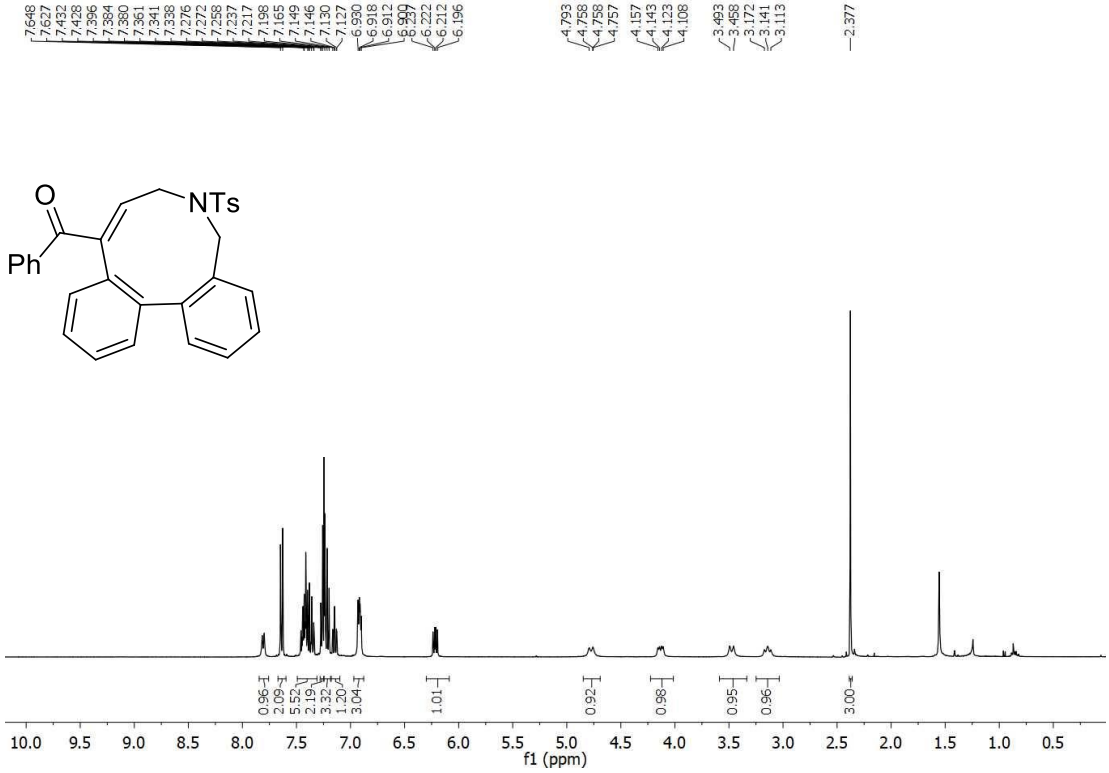
^{1}H NMR (400 MHz, $CDCl_3$) of compound 3a



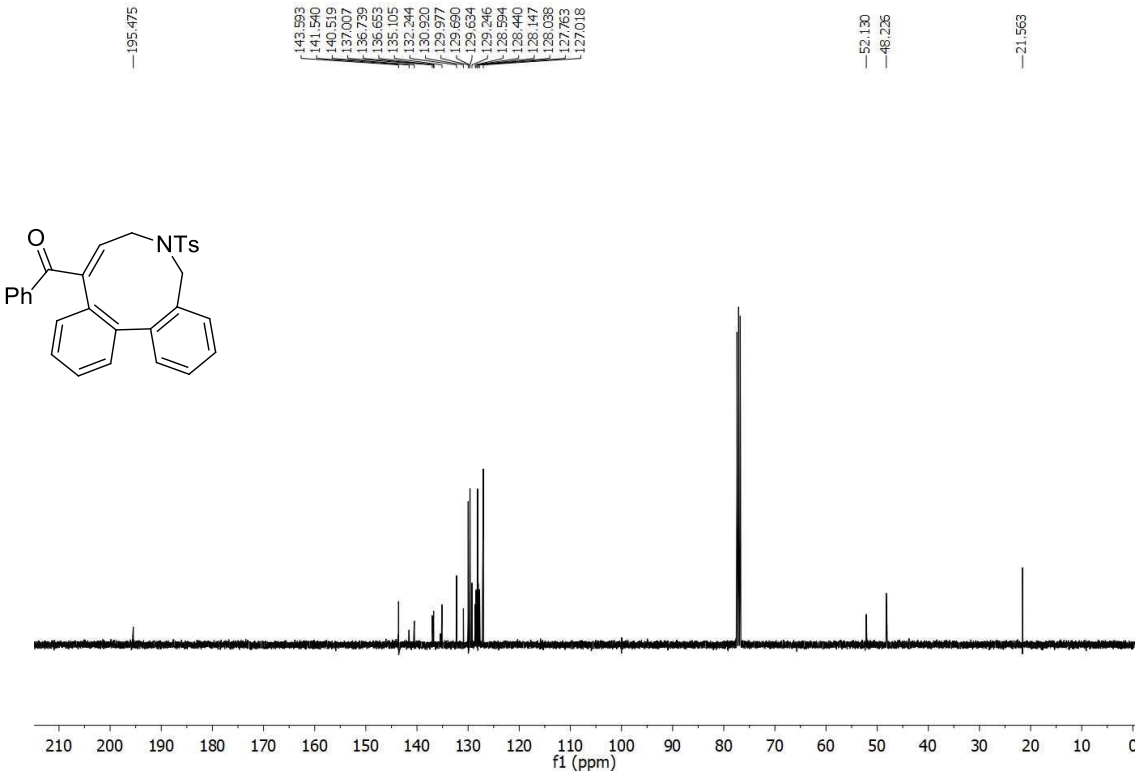
^{13}C NMR (100 MHz, $CDCl_3$) of compound 3a



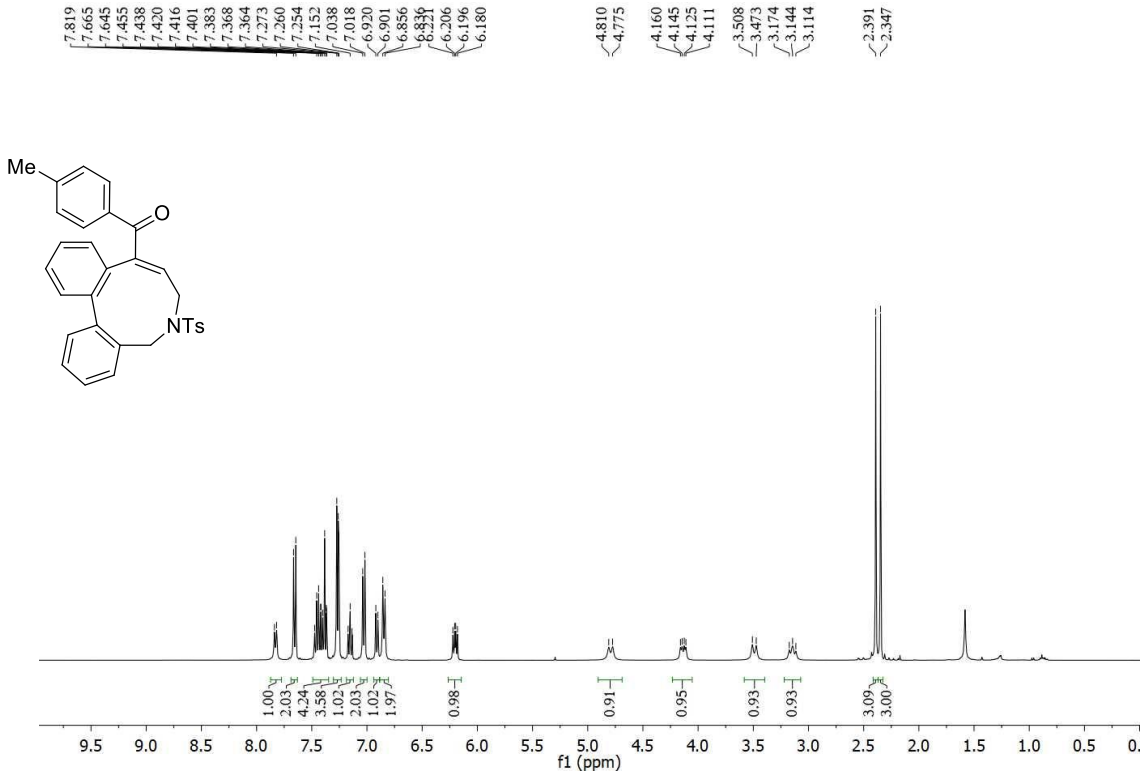
^{1}H NMR (400 MHz, $CDCl_3$) of compound 4a



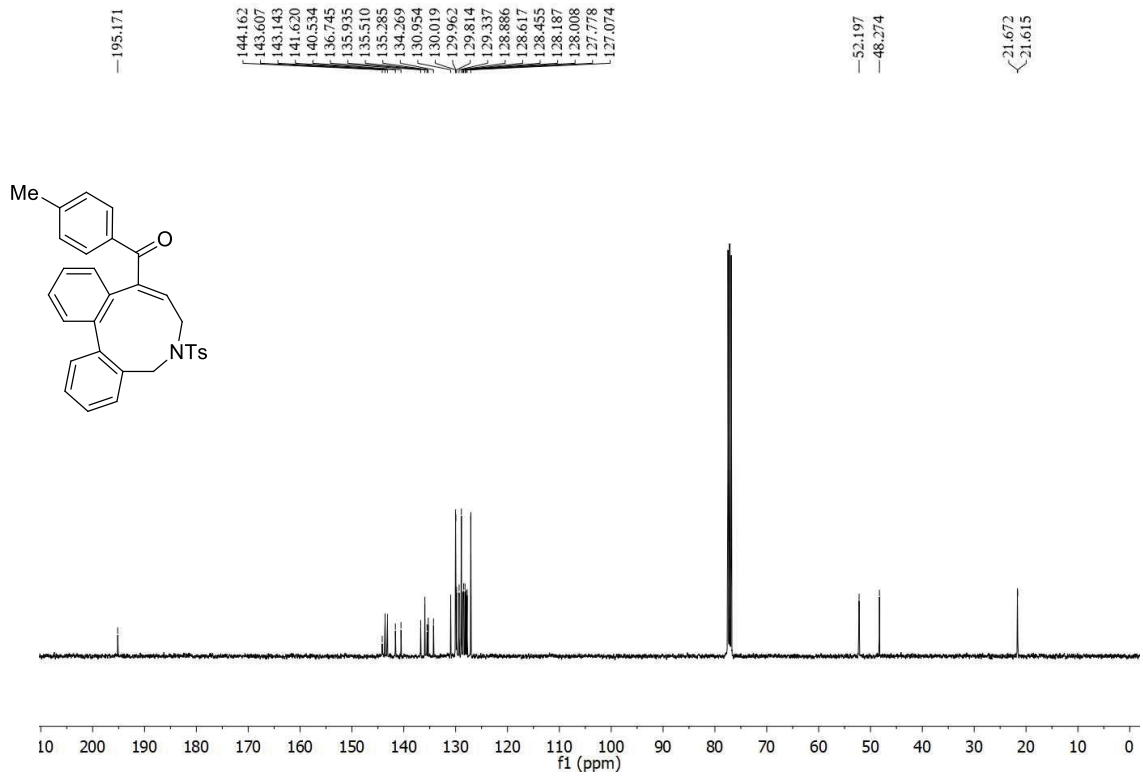
^{13}C NMR (100 MHz, $CDCl_3$) of compound 4a



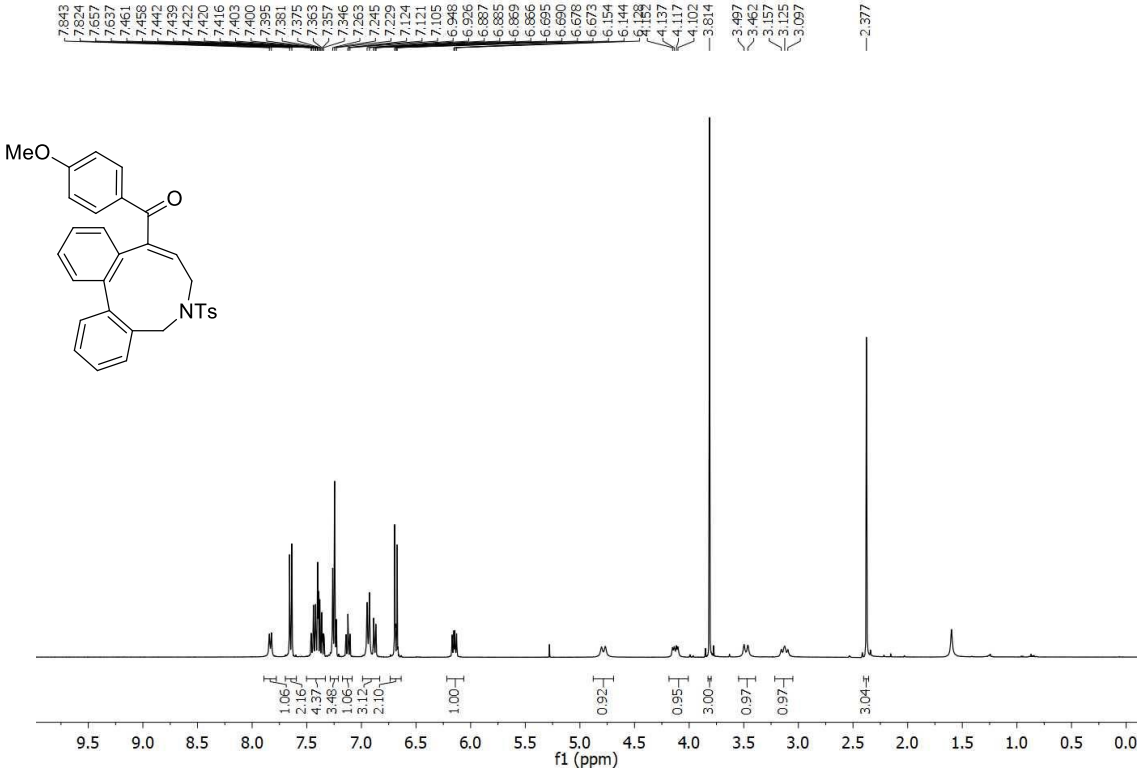
^{1}H NMR (400 MHz, $CDCl_3$) of compound 4b



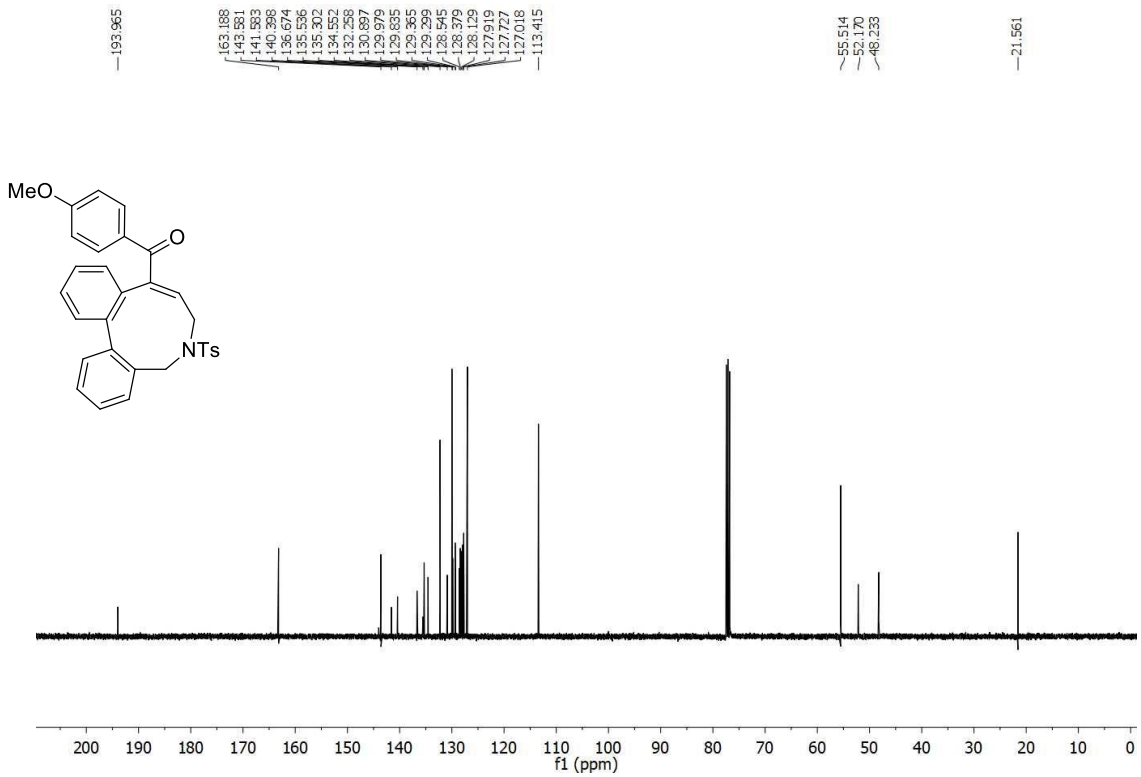
^{13}C NMR (100 MHz, $CDCl_3$) of compound 4b



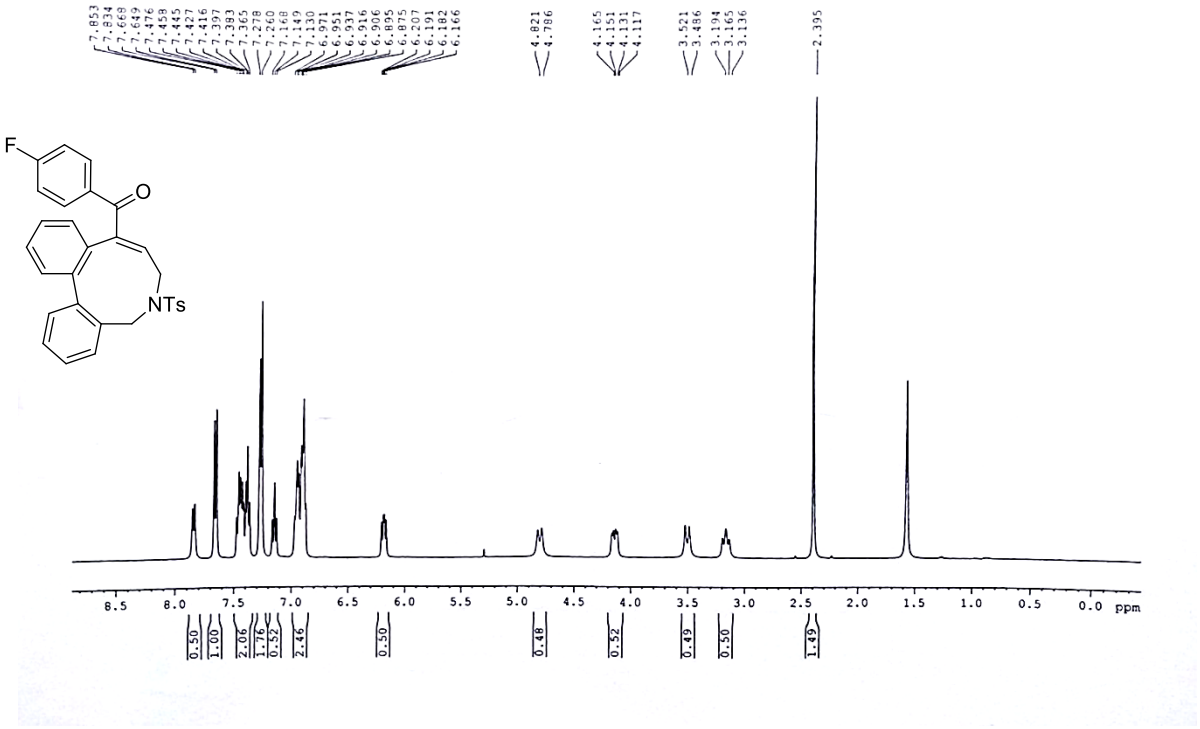
^{1}H NMR (400 MHz, $CDCl_3$) of compound 4c



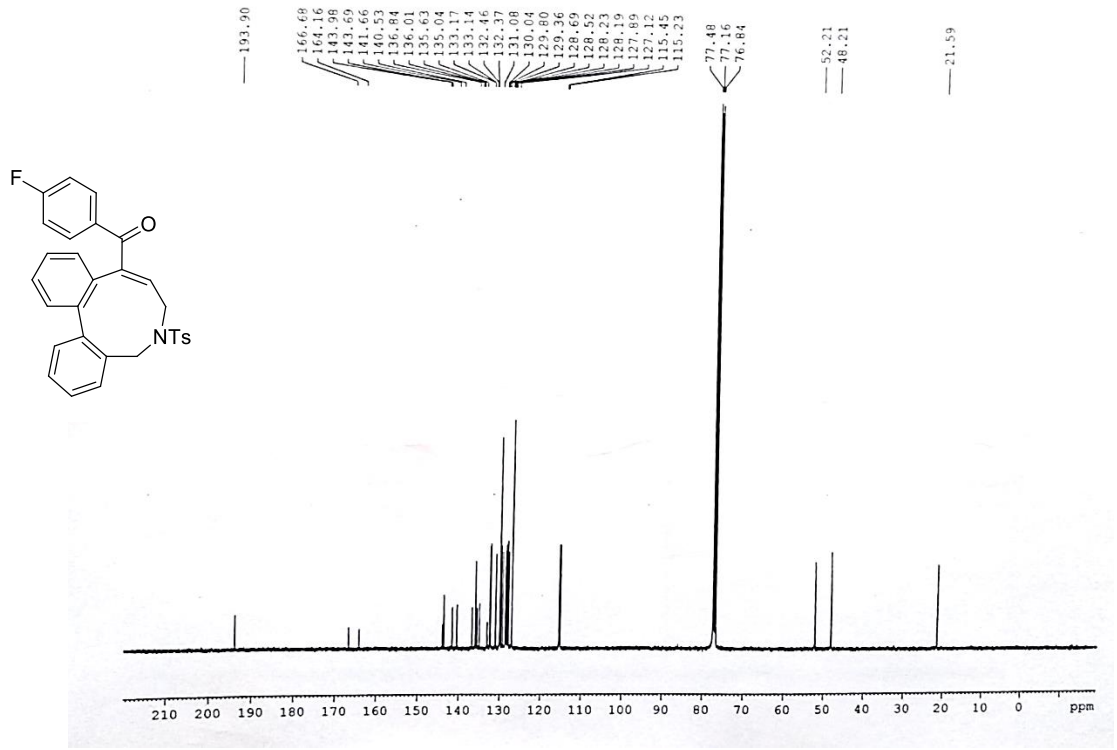
^{13}C NMR (100 MHz, $CDCl_3$) of compound 4c



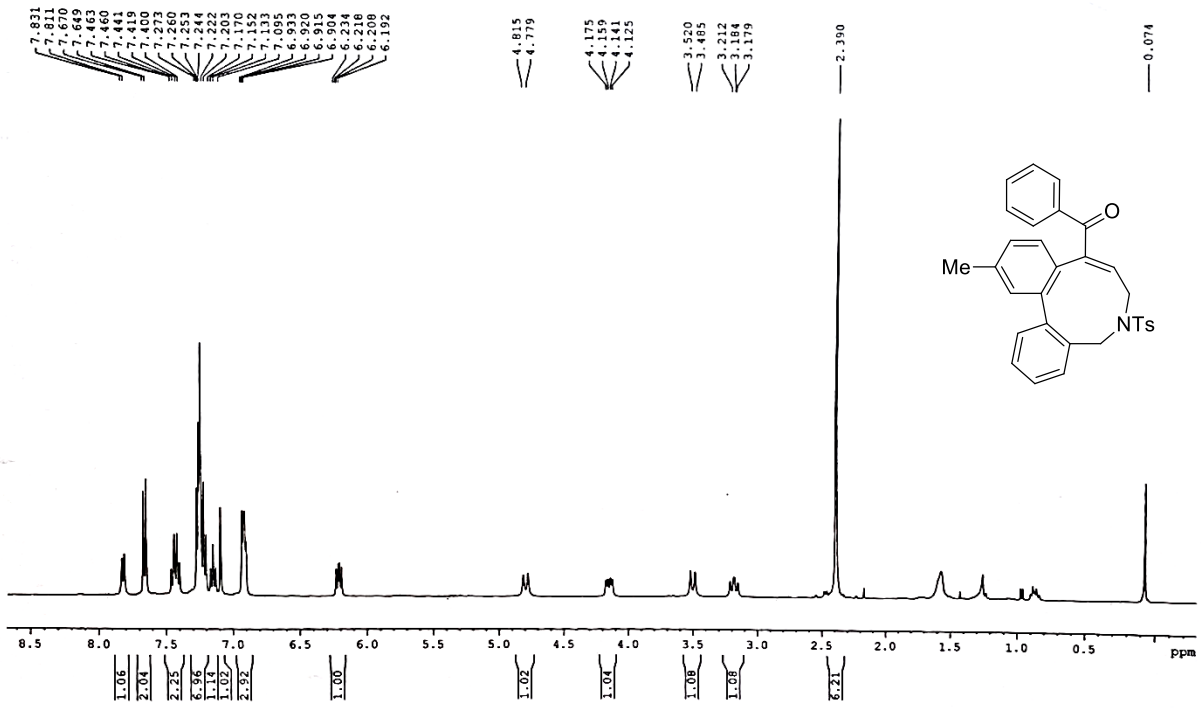
^{1}H NMR (400 MHz, $CDCl_3$) of compound 4d



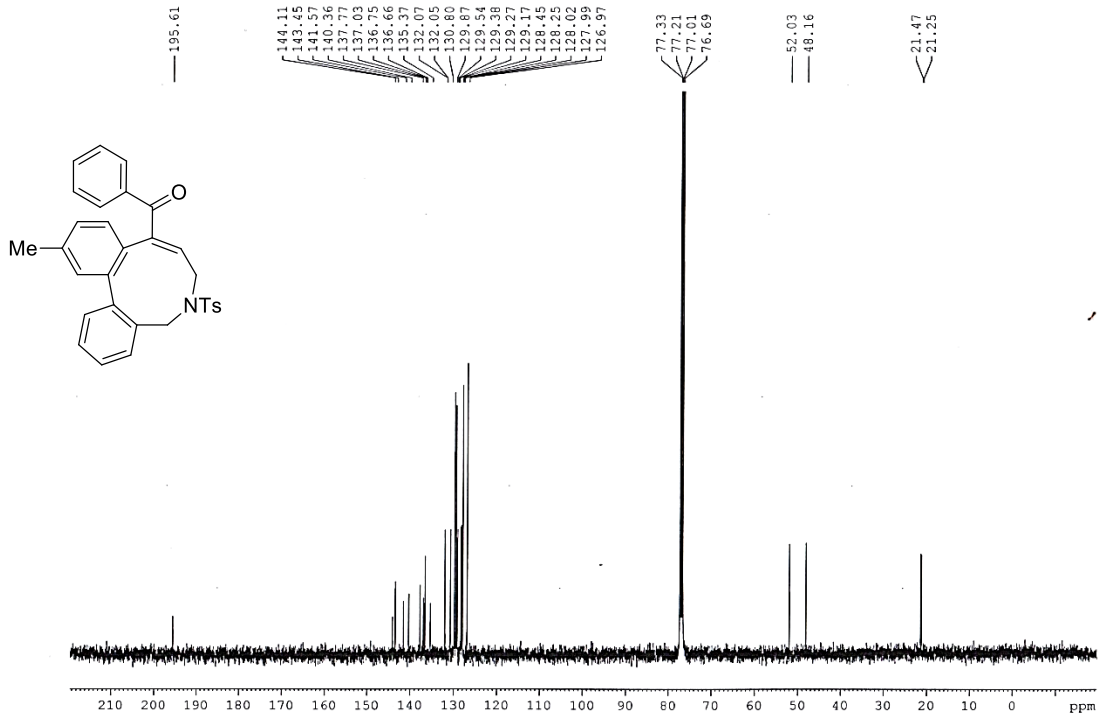
^{13}C NMR (100 MHz, $CDCl_3$) of compound 4d



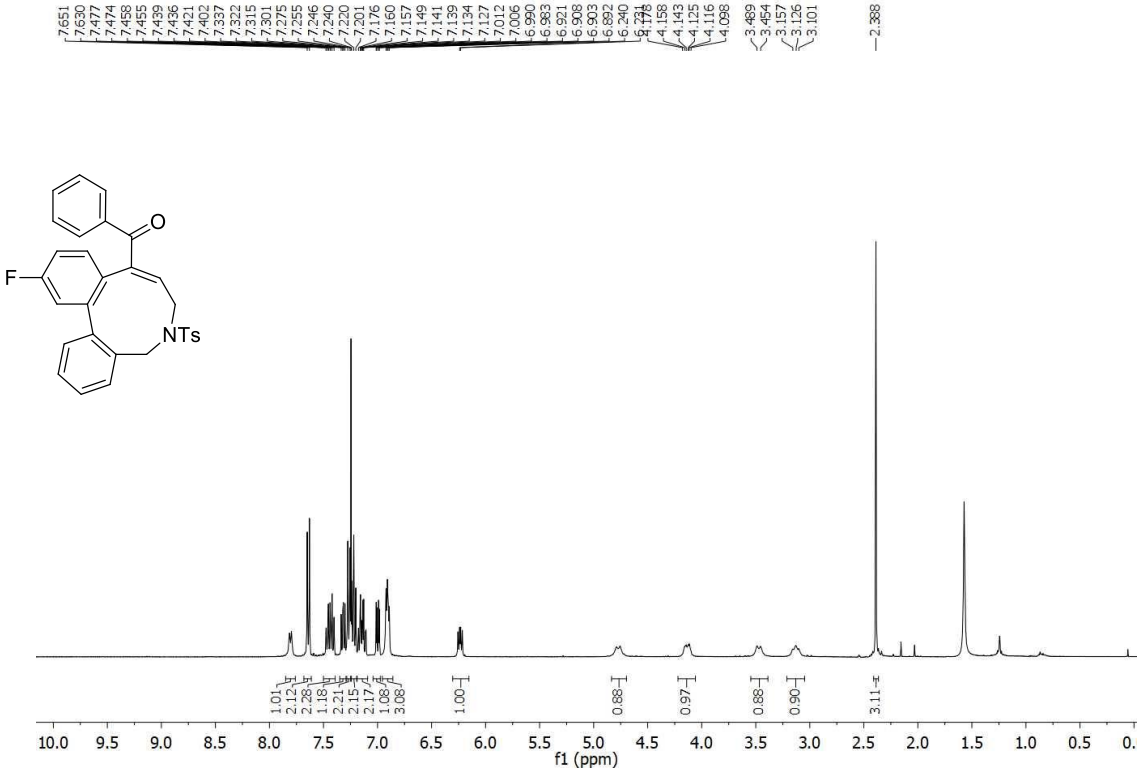
^{1}H NMR (400 MHz, $CDCl_3$) of compound 4e



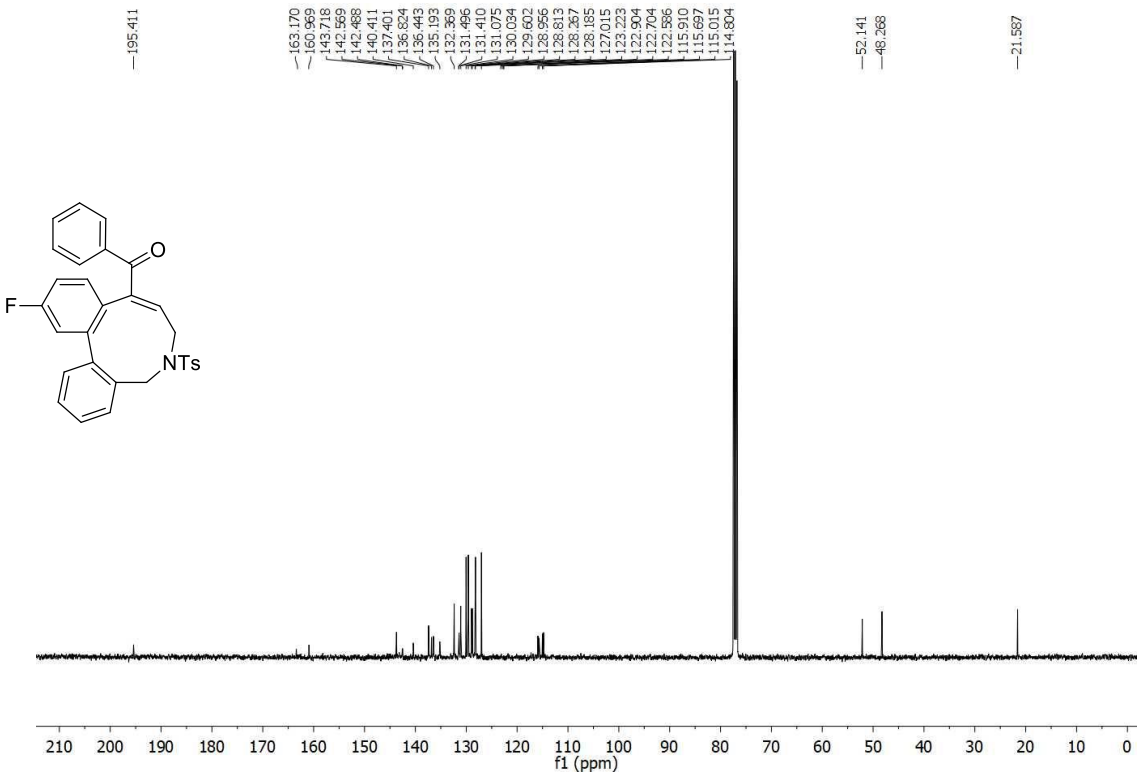
^{13}C NMR (100 MHz, $CDCl_3$) of compound 4e



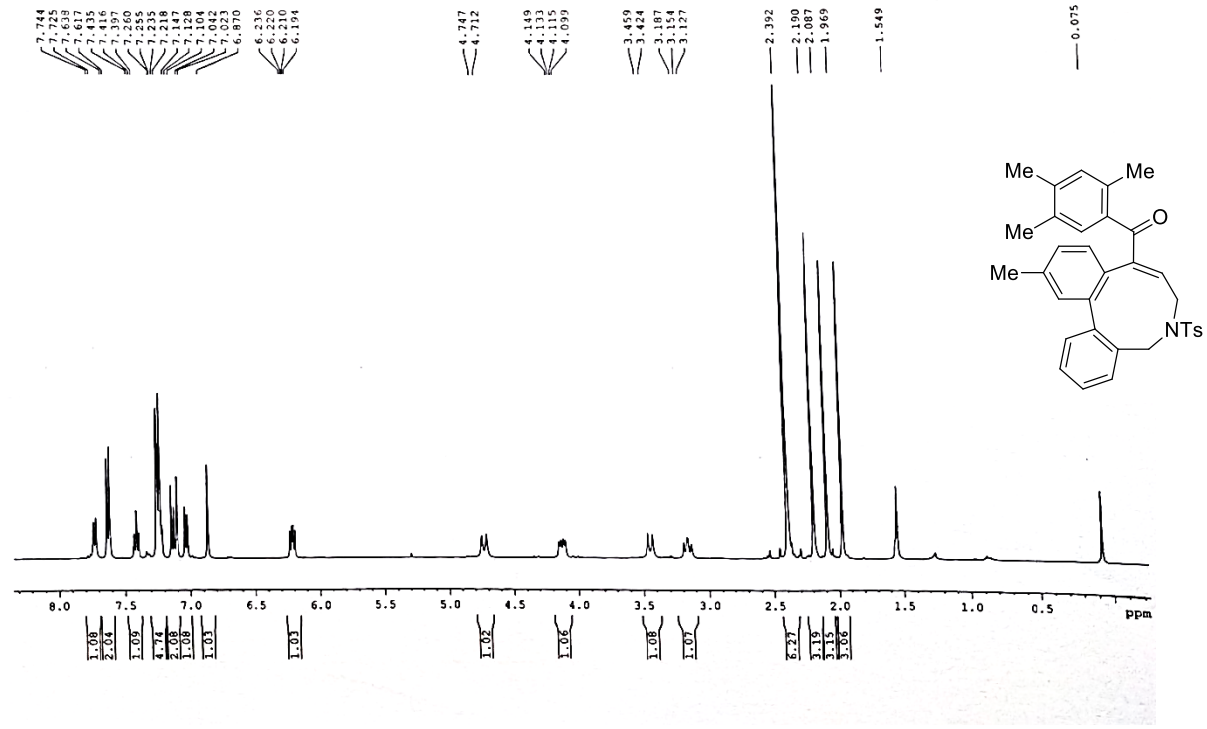
^{1}H NMR (400 MHz, $CDCl_3$) of compound 4f



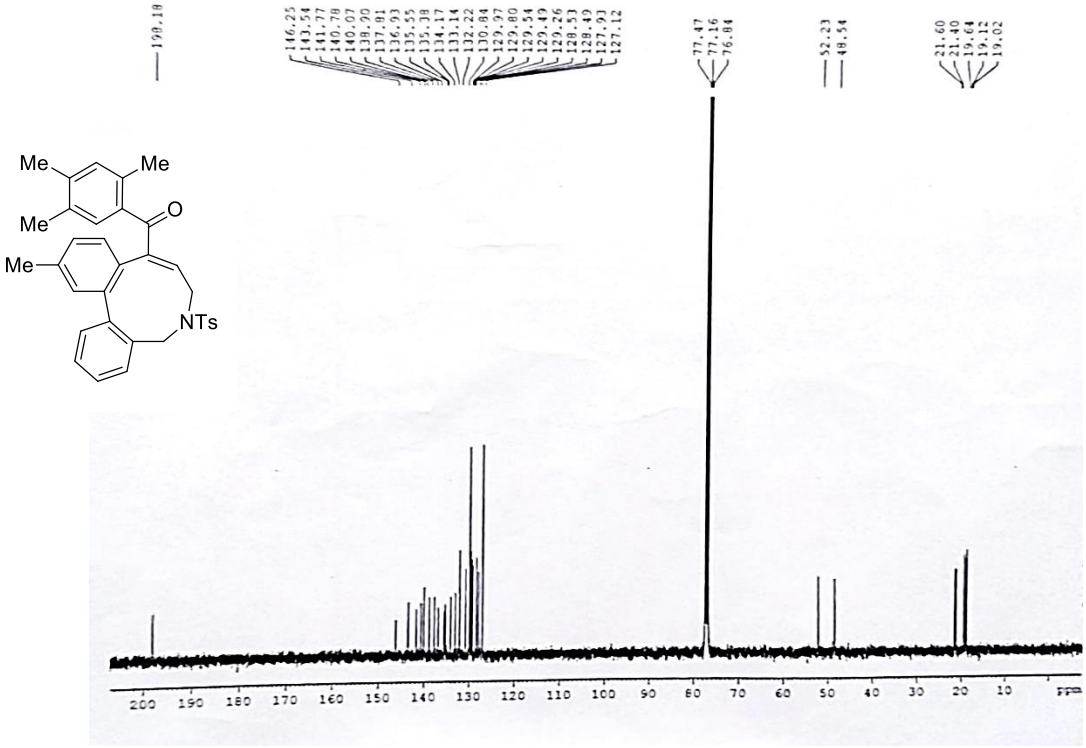
^{13}C NMR (100 MHz, $CDCl_3$) of compound 4f



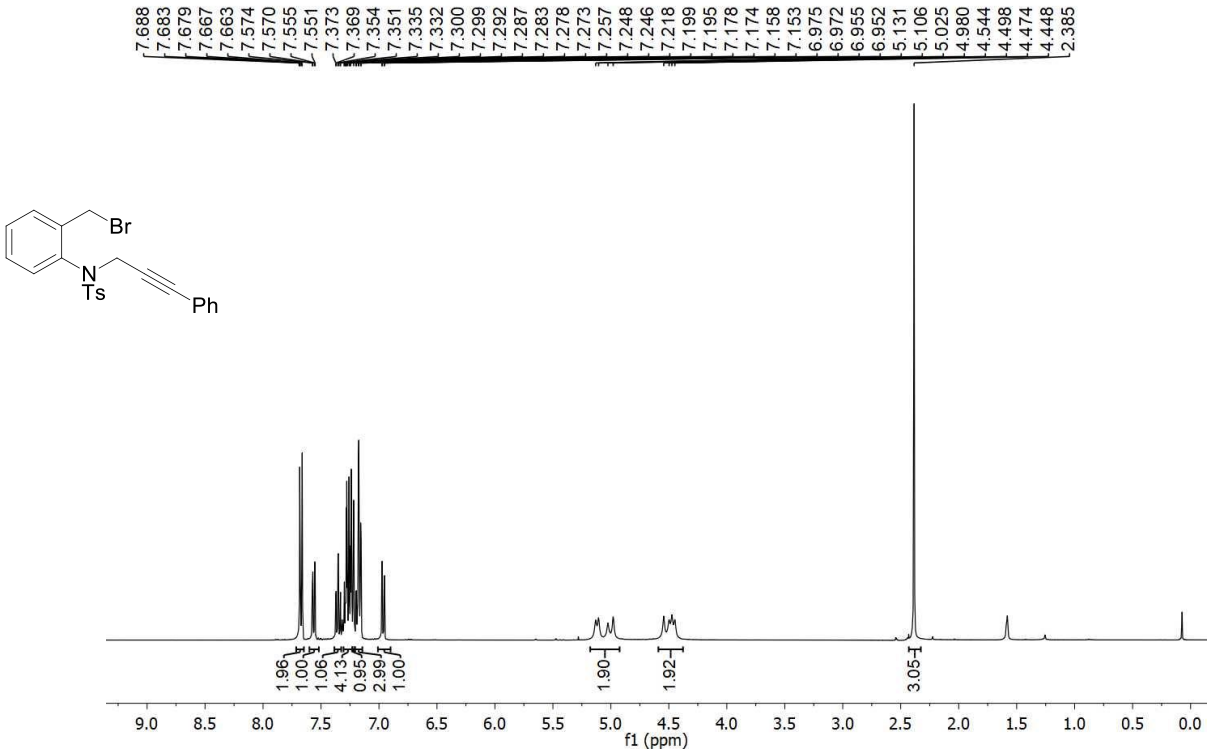
^{1}H NMR (400 MHz, $CDCl_3$) of compound 4g



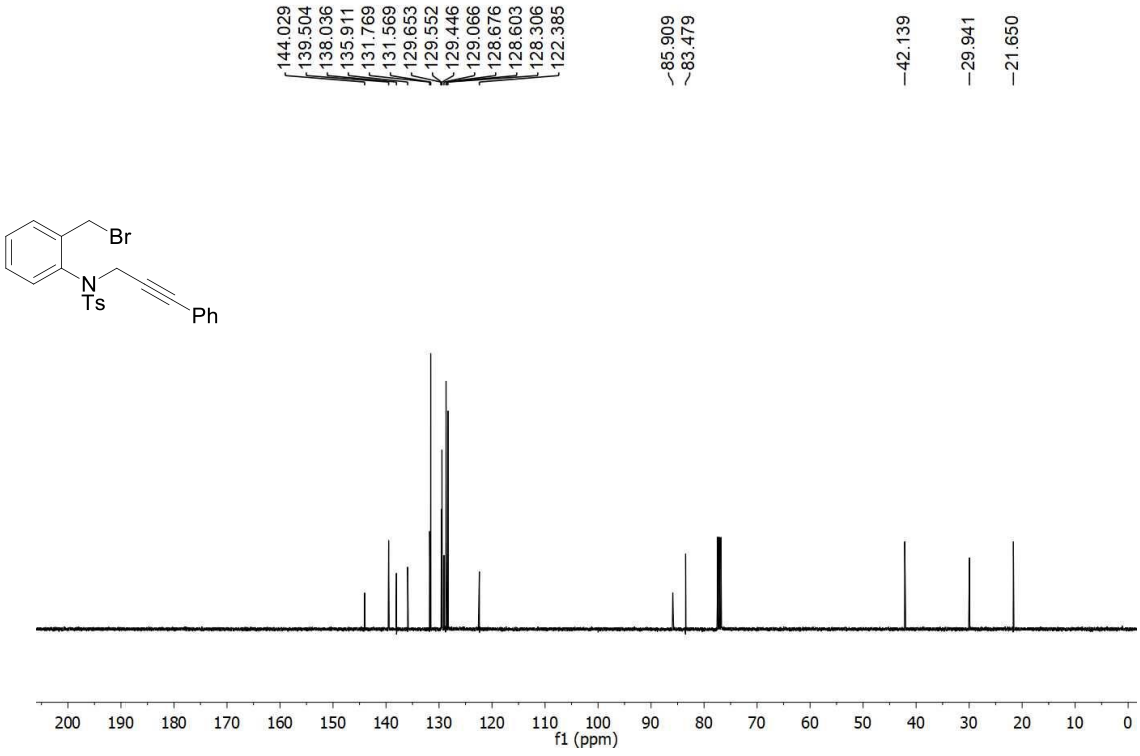
^{13}C NMR (100 MHz, $CDCl_3$) of compound 4g



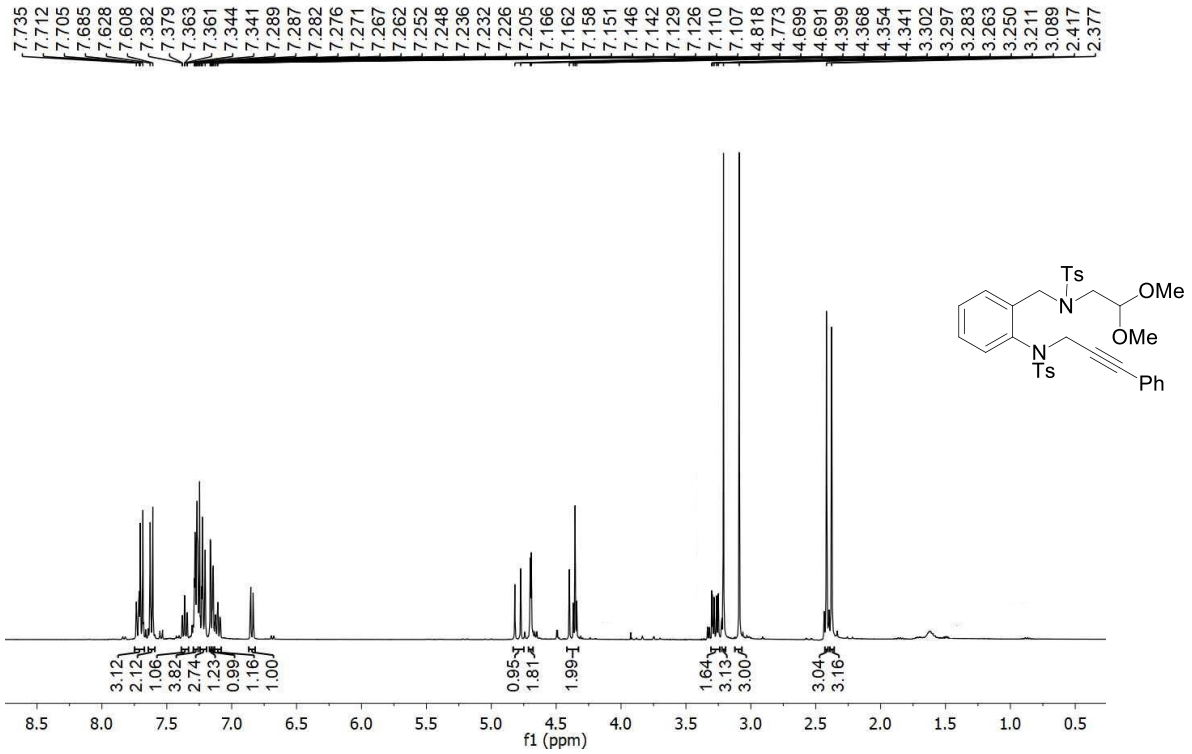
^{1}H NMR (400 MHz, $CDCl_3$) of compound 5a



^{13}C NMR (100 MHz, $CDCl_3$) of compound 5a



^{1}H NMR (400 MHz, $CDCl_3$) of compound 6a



^{13}C NMR (100 MHz, $CDCl_3$) of compound 6a