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Supporting Information

Alkyne Activation in the Diversity Oriented Synthesis of sp^2-Rich Scaffolds: A Biased Library Approach for Targeting Polynucleotides (DNA/RNA)

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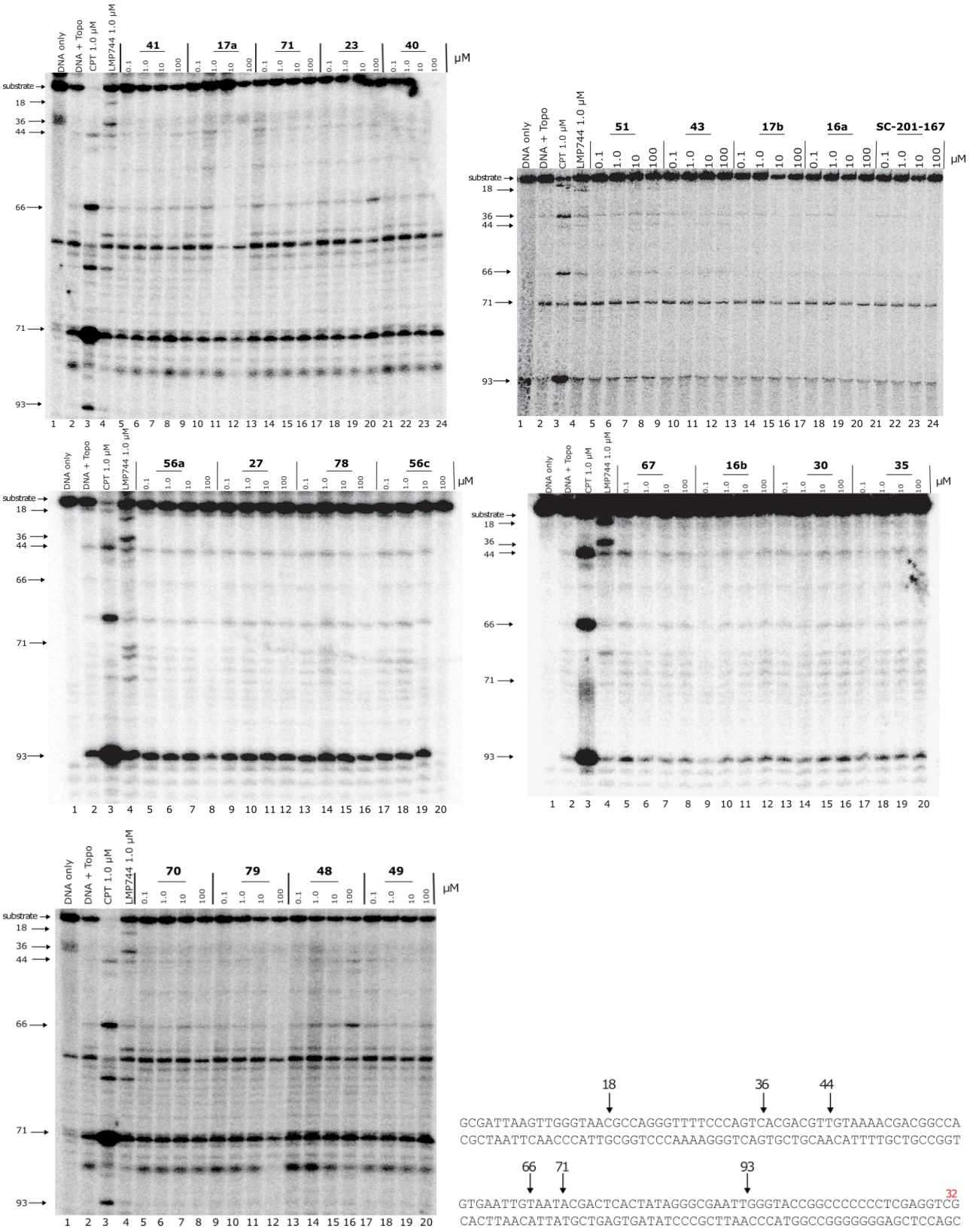
Top1-mediated DNA cleavage assay

DNA cleavage assays were performed as previously reported.[1]



The arrows and numbers at left of the gel images indicate the cleavage site positions. LMP744 is the positive non-camptothecin indenoisoquinoline control. Sequence of the 3'-[^{32}P]-labeled 117-bp DNA (labeled Guanine in red) with the indicated TOP1 cleavage site positions is shown at the bottom right.

PC3 cell viability assays

Routine cell culture: PC3 prostate cancer cell lines were cultured in DMEM (containing 10% fetal calf serum and penicillin-streptomycin). Cells were grown at 37 °C with 5 % CO_2 and passaged when 80-90% confluent 4 times before use. Cells were harvested by trypsin treatment (5 min) then quenched with an equal volume of serum containing media and the cell suspension then centrifuged at 200 xg for 5 min and the pellet resuspended in 5 mL of media. Cells were exposed to Trypan blue (excludes dead cells) and counted with a haemocytometer. Before treatment with drug compounds, cells were plated at 2,500 cells/well in 96 well plates and incubated at 37 °C with 5 % CO_2 in a humidified incubator for 24 h. Drug stock solutions (50 or 10 mM) were diluted x 1000 in media to a final concentration of either 50 µM or 10 µM with a DMSO vehicle concentration of 0.1%. Compounds were then serially diluted in media (containing 0.1% DMSO) to give 8 final concentrations, all at 0.1% DMSO. Cell culture supernatants were aspirated and replaced with drug containing media. Drug treatments were performed in duplicate wells, while potential plate layout-specific variation in cell growth was accounted for by addition of a vehicle control (0.1% DMSO). An untreated control (media only) was included in each assay. Cells were then incubated with drug compounds at 37 °C with 5 % CO_2 in a humidified incubator for 72 h prior to assay. Cell media were diluted with CellTitre AQueous One Solution to produce a final concentration of 317 µg/mL. Cell culture supernatants were then aspirated from wells and replaced with 100 µL of CellTitre solution. Triplicate cell-free control wells containing only CellTitre solution were also included in each assay. Cells were then incubated at 37 °C with 5 % CO_2 in a humidified incubator for 1 h at which time absorbance was read at 490 nm with a microplate reader. When analysing data, background absorbance (taken from cell-free control wells) was subtracted from each reading. To determine percentage inhibition of cell viability, absorbance readings for each drug treatment were expressed as a fraction of the vehicle control (0.1% DMSO) readings. For each drug concentration the mean (± SEM) is calculated and a sigmoidal curved is fitted to the data and used to calculate the IC_{50} of each compound.

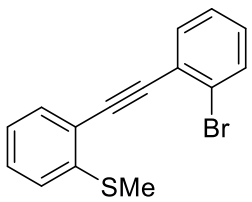
General Experimental Information

All reactions were performed under an inert atmosphere of anhydrous N_2(g), unless otherwise stated. Solvents used for various reactions were dried using a commercial solvent purification system. DCE and THF were purchased in an anhydrous form and stored under N_2(g). Solvents used in reaction extractions and chromatography and all other reagents were used as supplied by commercial vendors without further purifications or drying. All glassware used was dried by heating with a heat gun under high vacuum. Hexanes with a boiling point range of 40–60 ºC was used in chromatography. Flash column chromatography was performed on either 40–60 or 20–40 micron silica gel. ^{1}H NMR spectra were recorded at 400 MHz. ^{13}C NMR spectra were recorded at 101 MHz, for selected compounds the number of attached hydrogens to each carbon atom was determined using Distortionless Enhancement by Polarization Transfer with detection of quaternary carbons (DEPTQ-135), as indicated. All chemical shifts were calibrated using residual non-deuterated solvent (e.g. chloroform) as an internal reference and are reported in parts per million (δ) relative to trimethylsilane (δ = 0). Thin layer chromatography (TLC) was performed using 0.25 mm thick plates pre-coated with Merck Kieselgel 60 F254 silica gel, and visualised using UV light (254 nm and 365 nm). Liquid chromatography mass spectrometry (LCMS) was performed using either APCI or ESI LCMS. Each method used 254 nm detector and a reverse phase C8(2) 5 µ 50 × 4.6 mm 100A column. The column temperature was 30 °C and the injection volume, 2 µL. The eluent system used was solvent A (H_2O with 0.1% formic acid) and solvent B (MeCN with 0.1% formic acid). LCMS (ESI) method: the gradient starts from [95 % solvent A / 5 % solvent B] for 1 minute, reaches [100% solvent B] over 1.5 min, maintained for 1.3 min, and then changed to [95 % solvent A / 5 % solvent B] over 1.2 min. LCMS (APCI) method: the gradient starts from [95 % solvent A / 5 % solvent B] for 1 min, reaches [100% solvent B] over 1.9 min, maintained for 2 min, and then changed to [95 % solvent A / 5 % solvent B] over 1.0 min. Analytical HPLC was performed on an Agilent 1260 Infinity Analytical HPLC with a G1312B 1260 binary pump and G4212B 1260 DAD detector. The column used was a Zorbax Eclipse Plus C18 Rapid Resolution 4.6 x 100 mm, 3.5 micron. The eluent system used was [Solvent A: H_2O with 0.1% Formic Acid; Solvent B: MeCN with 0.1% Formic Acid]. All the samples were analyzed using a 'PP gradient method', in which the gradient increases from [95 % solvent A / 5 % solvent B] to [100 % solvent B] over 9 min and maintained at [100 % solvent B] for 1 min with flow rate of 1.0 mL/min. High resolution mass spectra (HRMS) were recorded on both a time-of-flight mass spectrometer fitted with either an electrospray (ESI) ion or atmospheric pressure chemical ionization (APCI) source, the capillary voltage was 4000 V or on an exactive mass spectrometer fitted with an ASAP ion source.

The following materials were prepared according to literature procedures: **12a**,**b**,[2] **20**,[3] **21**-**22**,[2] **31**-**32**,[4] **33**-**34**,[2] **44**-**45**,[2] **46b**, [2] **50**, [2] **58**,[5] **59**[6].

Experimental Procedures and Characterization Data

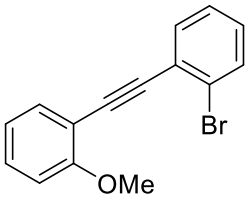
(2-((2-Bromophenyl)ethynyl)phenyl)(methyl)sulfane (13a):



Compound **13a** was synthesised according to General Procedure A. The crude product obtained was purified by flash column chromatography (49:1 hexanes:EtOAc, R_f = 0.3) to yield **13a** (577 mg, 100%) as a yellow oil. ^{1}H NMR (400 MHz,$CDCl_3$) δ 7.62 (dt, *J* = 7.5, 1.2 Hz, 2H), 7.57 – 7.53 (m, 1H), 7.36-7.28 (m, 2H), 7.22 – 7.16 (m, 2H), 7.13 (td, *J* = 7.5, 1.2 Hz, 1H), 2.52 (s, 3H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 142.0 (C), 133.7 (CH), 132.9 (CH), 132.6 (CH), 129.6 (CH), 129.3 (CH), 127.1 (CH), 125.6 (C), 125.5 (C), 124.43 (CH),

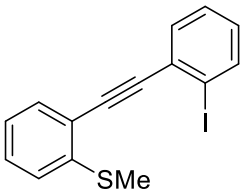
124.41 (CH), 121.2 (C), 94.3 (C), 91.5 (C), 15.4 (CH_3). LCMS (API-ES) *m/z* (%): 4.2 min, 304.9. HPLC: PP gradient method, t_R = 7.7 min, 97.9 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{15}H_{12}BrS^+$ $[M + H]^+$ 302.9838, found 302.9831. The spectroscopic data are consistent with those previously reported in the literature.[7]

1-Bromo-2-((2-methoxyphenyl)ethynyl)benzene (13b):



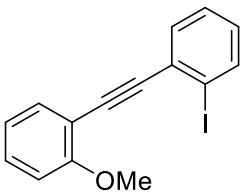
Compound **13b** was synthesised according to General Procedure A. The crude product (2.80 g) was purified by flash column chromatography (100% hexanes, R_f = 0 → 4:1 hexanes:EtOAc, R_f = 0.7) to yield the title compound (2.35 g, 96%) as a bright orange oil. ^{1}H NMR (400 MHz,$CDCl_3$) δ 7.60 (app td, *J* = 7.8, 1.4, 2H), 7.55 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.33 (ddd, *J* = 8.4, 7.5, 1.7 Hz, 1H), 7.30-7.26 (td, *J* = 7.6, 1.3 Hz, 1H), 7.16 (ddd, *J* = 8.0, 7.5, 1.7 Hz, 1H), 6.95 (td, *J* = 7.5, 1.0 Hz, 1H), 6.92 (d, *J* = 8.4 Hz, 1H), 3.93 (s, 3H). HPLC: PP gradient method, t_R = 7.6 min, 90.8 % purity at 254 nm. HR-APCI calcd for $C_{15}H_{12}BrO$ $[M + H]^+$ 287.0066 and 289.0047, found 287.0065 and 289.0044. The spectroscopic data are consistent with those previously reported in the literature.[8]

(2-((2-Iodophenyl)ethynyl)phenyl)(methyl)sulfane (14a):



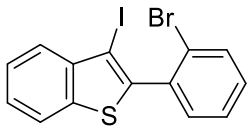
Compound **14a** was synthesised according to General Procedure A. The crude product obtained (brown oil, 1.38 g) was purified by flash column chromatography (50:1 hexanes:EtOAc, R_f = 0.25) to yield **14a** (227 mg, 64%) as a light purple oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.58 (td, *J* = 7.5, 1.7 Hz, 2H), 7.34 (td, *J* = 7.6, 1.2 Hz, 1H), 7.33 (ddd, *J* = 8.0, 7.4, 1.5 Hz, 1H), 7.20 (d, *J* = 7.3 Hz, 1H), 7.13 (td, *J* = 7.5, 1.2 Hz, 1H), 7.04 – 6.99 (m, 1H), 2.53 (s, 3H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 142.0 (C), 138.9 (CH), 133.0 (CH), 132.9 (CH), 130.0 (C), 129.6 (CH), 129.3 (CH), 127.9 (CH), 124.5 (CH), 124.4 (CH), 121.2 (C), 100.7 (C), 97.6 (C), 90.6 (C), 15.4 (CH_3). LCMS (APCI) *m/z* (%): *t* = 4.8 min, 351.0 (100, $M + H^+$). HPLC: PP gradient method, t_R = 7.1 min, 95.7 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{15}H_{12}IS^+$ $[M + H]^+$ 350.9699, found 350.9695. The spectroscopic data are consistent with those previously reported in the literature.[9]

1-Iodo-2-((2-methoxyphenyl)ethynyl)benzene (14b):



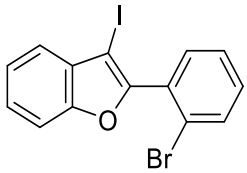
Compound **14b** was synthesised according to General Procedure A. The crude product obtained (14.12 g, red oil) was purified by flash column chromatography (49:1 hexanes:EtOAc, R_f = 0.33) to yield the title product (3.89 g, 91%) as an orange oil. ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.3 Hz, 2H), 7.62 – 7.53 (m, 2H), 7.36 – 7.29 (m, 2H), 7.06 – 7.03 (m, 1H), 7.02 – 6.93 (m, 2H), 6.92 (d, *J* = 8.4 Hz, 1H), 3.93 (s, 3H). LCMS (APCI) *m/z* (%): *t* = 4.4 min, 335.0 (100, M + H^+). HPLC: PP gradient method, t_R = 6.7 min, 92.8 % purity at 254 nm. The spectroscopic data are consistent with those previously reported in the literature.[10]

2-(2-Bromophenyl)-3-iodobenzo[*b*]thiophene (15a):



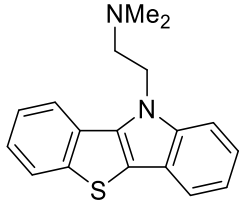
Compound **15a** was synthesised according to General Procedure D. **15a** (705 mg, 95%) was obtained as a yellow oil and directly used in the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 7.9, 1.1 Hz, 2H), 7.73 (dd, *J* = 8.2, 0.9 Hz, 1H), 7.50 (ddd, *J* = 7.2, 4.6, 1.1 Hz, 1H), 7.46-7.41 (m, 3H), 7.35 (ddd, *J* = 8.0, 6.0, 3.2 Hz, 1H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 141.8 (C), 141.0 (C), 139.5 (C), 136.1 (C), 133.2 (CH), 132.7 (CH), 130.9 (CH), 127.4 (CH), 126.2 (CH), 125.9 (CH), 125.6 (CH), 124.7 (C), 122.4 (CH), 83.7 (C). HPLC: PP gradient method, t_R = 8.4 min, 92.6 % purity at 254 nm. HR-APCI (*m/z*) calcd for $C_{14}H_8BrIS^+$ $[M]^+$ 413.8569, found 413.8561. The spectroscopic data are consistent with those previously reported in the literature.[11]

2-(2-Bromophenyl)-3-iodobenzofuran (15b):



Compound **15b** was synthesised according to General Procedure D. The crude product obtained was purified by flash column chromatography (9:1 hexanes:CH_2Cl_2, R_f = 0.33) to yield **15b** (2.54 g, 78%) as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.57 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.52 (dd, *J* = 7.3, 0.9 Hz, 1H), 7.49 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.45 (td, *J* = 7.6, 1.2 Hz, 1H), 7.43-7.34 (m, 3H). LCMS (ESI) *m/z* (%): *t* = 4.6 min, 271.0 (100, M-I^-) and 272.9 (70, M-I^-). HPLC: PP gradient method, t_R = 8.2 min, 96.4 % purity at 254 nm. HR-APCI calcd for $C_{14}H_8BrIO$ $[M]^+$ 397.8798 and 399.8778, found 397.8791 and 399.8771. The spectroscopic data are consistent with those previously reported in the literature.[9]

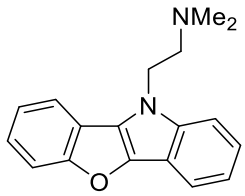
2-(10*H*-Benzo[4,5]thieno[3,2-*b*]indol-10-yl)-*N*,*N*-dimethylethan-1-amine (16a):



Compound **16a** was synthesised according to General UCC Procedure. The crude product (83 mg, yellow solid) obtained was purified by flash column chromatography (99:1 CH_2Cl_2:MeOH, R_f = 0.3) to yield **16a** (25 mg, 29%) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.0 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H),

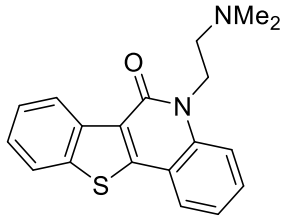
7.78 (d, *J* = 7.9 Hz, 1H), 7.54 – 7.47 (m, 1H), 7.46 (ddd, *J* = 8.1, 7.2, 1.1 Hz, 2H), 7.37 (ddd, *J* = 8.3, 7.2, 1.1 Hz, 2H), 7.23 (ddd, *J* = 7.9, 7.1, 0.9 Hz, 1H), 4.69 (app d, *J* = 8.0 Hz, 2H), 2.80 (app d, *J* = 8.0 Hz, 2H), 2.41 (s, 6H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 143.3 (C), 141.5 (C), 137.4 (C), 127.0 (C), 124.8 (CH), 124.5 (CH), 124.0 (CH), 123.2 (CH), 121.9 (C), 119.8 (CH), 119.7 (CH), 119.6 (CH), 115.7 (C), 109.9 (CH), 58.9 (CH_2), 46.2 (CH_3), 43.8 (CH_2). LCMS (ESI) *m/z* (%): *t* = 2.6 min, 295.1 (100, M + H^+). HPLC: PP gradient method, t_R = 5.2 min, 98.2 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{18}H_{19}N_2S^+$ $[M + H]^+$ 295.1263, found 295.1272.

2-(10*H*-Benzofuro[3,2-*b*]indol-10-yl)-*N*,*N*-dimethylethan-1-amine (16b):



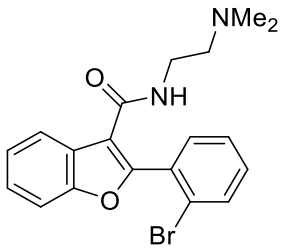
Compound **16b** was synthesised according to General UCC Procedure. The crude product was purified by flash column chromatography (10:5:1 hexanes:CH_2Cl_2:Et_3N, R_f = 0.35) to yield **16b** (86 mg, 42%) as a transparent oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (ddd, *J* = 7.9, 1.2, 0.8 Hz, 1H), 7.78-7.75 (m, 1H), 7.65-7.63 (m, 1H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.36-7.29 (m, 3H), 7.22 (ddd, *J* = 8.0, 7.1, 0.9 Hz, 1H), 4.54 (t, *J* = 7.6 Hz, 2H), 2.81 (t, *J* = 7.6 Hz, 2H), 2.37 (s, 6H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 159.3 (C), 142.5 (C), 139.7 (C), 126.8 (C), 123.9 (CH), 122.8 (CH), 122.6 (CH), 119.7 (CH), 118.9 (C), 117.6 (CH), 117.5 (CH), 113.8 (C), 112.9 (CH), 110.1 (CH), 59.0, 46.1, 44.0. LCMS (ESI) *m/z* (%): *t* = 3.1 min, 278.9 (100, M + H^+), 279.9 (20, M + H^+). HPLC: PP gradient method, t_R = 5.5 min, 98.0 % purity at 254 nm. HR-ESI calcd for $C_{18}H_{19}N_2O$ $[M + H]^+$ 279.1492, found 279.1487.

5-(2-(Dimethylamino)ethyl)benzo[4,5]thieno[3,2-*c*]quinolin-6(5*H*)-one (17a):



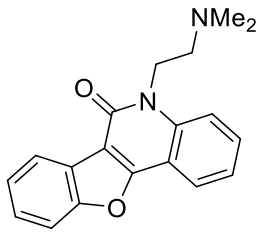
Compound **17a** was synthesised according to General PdCC[1] Procedure. The crude product (182 mg) was purified by flash column chromatography (3:1 Et_2O:MeOH, R_f = 0.35) to yield **17a** (25 mg, 43%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.88 – 7.82 (m, 2H), 7.60 – 7.42 (m, 4H), 7.30 – 7.24 (m, 1H), 4.60 – 4.52 (m, 2H), 2.72 – 2.64 (m, 2H), 2.42 (s, 6H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 158.7 (C), 147.7 (C), 137.9 (C), 137.3 (C), 137.2 (C), 130.5 (CH), 126.2 (CH), 125.8 (CH), 125.7 (CH), 125.4 (CH), 123.5 (C), 122.4 (CH), 122.0 (CH), 118.0 (C), 115.1 (CH), 56.3 (CH_2), 46.0 (CH_3), 40.7 (CH_2). LCMS (ESI) m/z (%): *t* = 4.7 min, 323.1. HPLC: PP gradient method, t_R = 5.5 min, 90.8 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{19}H_{19}N_2OS^+$ $[M + H]^+$ 323.1213, found 323.1221.

2-(2-Bromophenyl)-*N*-(2-(dimethylamino)ethyl)benzofuran-3-carboxamide:



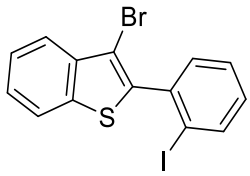
14b (100 mg, 251 µmol), $Pd(OAc)_2$ (5.6 mg, 25 µmol), PPh_3 (98.6 mg, 376 µmol), DMD (331 mg, 3.76 mmol, 0.41 mL), Et_3N (51 mg, 501 µmol, 47 µL), CuI (4.8 mg, 25 µmol) and dry NMP (2.5 mL) was added to a 10 mL dry RBF accordingly. The RBF was degassed and backfilled with CO(g) for three times, the reaction mixture was then heated at 80 °C for 18 h. After heating, the mixture was cooled down to rt, diluted with saturated $NaHCO_3$ solution (25 mL) and extracted with EtOAc (2 x 15 mL). The combined organic extracts were washed with H_2O (2 x 20 mL), and brine (2 x 20 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product obtained (light yellow oil) was purified by flash column chromatography (100% EtOAc → 9:1 EtOAc:MeOH, R_f = 0.2) to yield **2-(2-bromophenyl)-*N*-(2-(dimethylamino)ethyl)benzofuran-3-carboxamide** (62 mg, 64%) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 – 8.13 (m, 1H), 7.75 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.58 (dd, *J* = 7.4, 1.9 Hz, 1H), 7.57 – 7.48 (m, 1H), 7.47 (td, *J* = 7.5, 1.3 Hz, 1H), 7.44 – 7.34 (m, 3H), 6.40 (br s, 1H), 3.41 (td, *J* = 6.0, 4.8 Hz, 2H), 2.36 (t, *J* = 5.9 Hz, 2H), 2.07 (s, 6H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 163.1 (C), 154.6 (C), 154.4 (C), 133.5 (CH), 132.7 (CH), 131.8 (CH), 131.4 (C), 127.7 (CH), 126.8 (C), 125.5 (CH), 124.5 (C), 124.1 (CH), 122.4 (CH), 115.2 (C), 111.4 (CH), 57.1 (CH_2), 44.8 (CH_3), 36.6 (CH_2). LCMS (ESI) *m/z* (%): *t* = 2.3 min, 387.1 (100, M + H^+) and 389.1 (100, M + H^+). HPLC: PP gradient method, t_R = 5.2 min, 94.8 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{19}H_{20}BrN_2O_2^+$ $[M + H]^+$ 387.0703, found 387.0711.

5-(2-(Dimethylamino)ethyl)benzofuro[3,2-*c*]quinolin-6(5*H*)-one (17b):



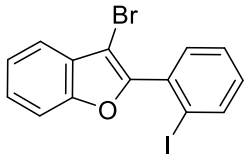
In a dry RBF, **2-(2-bromophenyl)-*N*-(2-(dimethylamino)ethyl)benzofuran-3-carboxamide** (60 mg, 155 µmol) was dissolved in *n*-butanol (0.8 mL) and K_3PO_4 (132 mg, 620 µmol, 4.0 equiv.), ethylene glycol (104 µL, 1.86 mmol, 12 equiv.), TMD (288 mg, 2.48 mmol, 0.37 mL), and CuI (11.8 mg, 62 µmol), were added accordingly. The RBF was degassed and backfilled with N_2(g) for three times, the reaction mixture was then heated at 90 °C for 15 h. After heating, the reaction mixture was cooled down to rt and diluted with EtOAc (20 mL). The combined organic layer was washed with H_2O (2 x 15 mL) and brine (2 x 15 mL), then dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product (44 mg) obtained was purified by flash column chromatography (10:1 EtOAc:MeOH, R_f = 0.1) to yield **16b** (34 mg, 72%) as a transparent oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (dd, *J* = 6.0, 2.3 Hz, 1H), 8.20 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.69 – 7.60 (m, 2H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.51 – 7.39 (m, 2H), 7.38 (ddd, *J* = 8.0, 7.1, 1.0 Hz, 1H), 4.59 (br t, *J* = 7.8 Hz, 2H), 2.69 (br t, *J* = 7.9 Hz, 2H), 2.43 (s, 6H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 159.6 (C), 157.6 (C), 155.6 (C), 138.8 (C), 131.0 (CH), 126.3 (CH), 124.7 (C), 124.6 (CH), 122.7 (CH), 122.5 (CH), 122.4 (CH), 115.2 (CH), 113.2 (C), 111.5 (CH), 110.3 (C), 56.5 (CH_2), 46.0 (CH_3), 40.7 (CH_2). LCMS (ESI) *m/z* (%): *t* = 3.06 min, 307.2 (100, M + H^+). HPLC: PP gradient method, t_R = 5.1 min, 99.2 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{19}H_{19}N_2O_2^+$ $[M + H]^+$ 307.1441, found 307.1447.

3-Bromo-2-(2-iodophenyl)benzo[*b*]thiophene (18a):



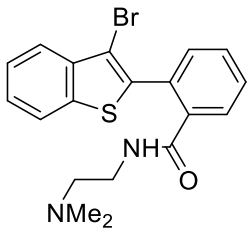
$CuBr_2$ (899 mg, 4.03 mmol, 3.0 equiv.) was added to a stirred solution of **14a** (470 mg, 1.34 mmol) in dry DCE (7 mL) under N_2(g) atmosphere. The reaction was heated at 45 ºC for 15 h. On completion, the reaction mixture was quenched with saturated $Na_2S_2O_3$ solution (35 mL), and extracted with CH_2Cl_2 (2 x 25 mL). The combined organic extracts were washed with H_2O (2 x 40 mL) and brine (2 x 40 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product obtained (pale yellow solid, 550 mg) was purified by flash column chromatography (40:1 hexanes:CH_2Cl_2, R_f = 0.55) to yield **18a** (453 mg, 81%) as a white crystal. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.88 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.84 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.51 (ddd, *J* = 8.0, 7.2, 1.2 Hz, 1H), 7.48 – 7.40 (m, 3H), 7.16 (ddd, *J* = 8.0, 7.0, 2.1 Hz, 1H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 140.6 (C), 139.5 (CH), 138.5 (C), 138.4 (C), 138.0 (C), 131.7 (CH), 130.8 (CH), 128.2 (CH), 125.9 (CH), 125.4 (CH), 123.9 (CH), 122.5 (CH), 108.6 (CH), 100.4 (C). LCMS (ESI) *m/z* (%): *t* = 4.9 min, 413.9 (100, M + H^+). HPLC: PP gradient method, t_R = 7.4 min, 97.0 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{14}H_9BrIS^+$ $[M + H]^+$ 414.8648, found 414.8634. mp 134–136 °C.

3-Bromo-2-(2-iodophenyl)benzofuran (18b):



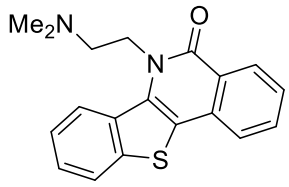
14b (407 mg, 1.22 mmol) was dissolved in anhydrous DCE (6.5 mL), followed by addition of *N*-methylpyrrolidin-2-one hydrotribromide (MPHT) (575 mg, 1.31 mmol). The orange solution was heated at 45 °C over a period of 69 h. On completion, the mixture was cooled down to rt, diluted with saturated $Na_2S_2O_3$ solution (30 mL) and extracted with CH_2Cl_2 (2 x 25 mL). The combined organic extracts were washed with H_2O (2 x 50 mL) and brine (2 x 50 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product obtained (light yellow oil, 630 mg) was purified by flash column chromatography (25:1 hexanes:CH_2Cl_2, R_f = 0.6) to yield **18b** (202 mg, 42%) as a transparent oil. ^{1}H NMR (401 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.61 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.59 – 7.50 (m, 2H), 7.48 (td, *J* = 7.5, 1.2 Hz, 1H), 7.46 – 7.33 (m, 2H), 7.19 (ddd, *J* = 8.0, 7.3, 1.8 Hz, 1H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 153.8 (C), 153.4 (C), 139.9 (CH), 134.8 (C), 132.4 (CH), 131.4 (CH), 128.4 (C), 128.0 (CH), 125.9 (CH), 123.7 (CH), 120.2 (CH), 111.8 (CH), 98.3 (C), 97.0 (C). LCMS (APCI) *m/z* (%): *t* = 4.7 min, 399.9 (100, M + H^+). HPLC: PP gradient method, t_R = 7.1 min, 99.8 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{14}H_9BrIO^+$ $[M + H]^+$ 398.8876, found 398.8882.

2-(3-Bromobenzo[*b*]thiophen-2-yl)-*N*-(2-(dimethylamino)ethyl)benzamide:



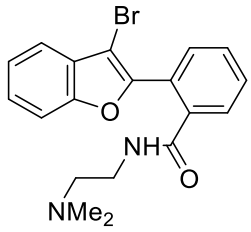
18a (250 mg, 602 µmol), $Pd(OAc)_2$ (20 mg, 90 µmol), PPh_3 (237 mg, 903 µmol), DMD (796 mg, 9.03 mmol, 0.97 mL), Et_3N (122 mg, 1.2 mmol, 0.11 mL), CuI (11 mg, 60 µmol) and dry NMP (4.5 mL) was added to a 25 mL dry RBF accordingly. The RBF was degassed and backfilled with CO(g) for three times, the reaction mixture was then heated at 90 °C for 19 h. After heating, the mixture was cooled down to rt, diluted with saturated NH_4Cl solution (25 mL) and extracted with EtOAc (2 x 25 mL). The combined organic extracts were washed with H_2O (2 x 25 mL), and brine (2 x 25 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product (463 mg, orange oil) obtained was purified by flash column chromatography (9:1 EtOAc:MeOH, R_f = 0.2) to yield **2-(3-bromobenzo[*b*]thiophen-2-yl)-*N*-(2-(dimethylamino)ethyl)benzamide** (192 mg, 79%) as a transparent oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.89 (m, 1H), 7.85 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.82 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.58 – 7.40 (m, 5H), 6.37 (br s, 1H), 3.23 (td, *J* = 5.9, 4.7 Hz, 2H), 2.03 (t, *J* = 5.9 Hz, 2H), 1.70 (s, 6H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 167.7 (C), 138.8 (C), 138.4 (C), 137.0 (C), 136.9 (C), 132.0 (CH), 130.4 (C), 130.3 (CH), 129.7 (CH), 129.6 (CH), 125.9 (CH), 125.5 (CH), 123.8 (CH), 122.4 (CH), 108.5 (C), 56.9 (CH_2), 44.5 (CH_3), 37.4 (CH_2). LCMS (ESI) *m/z* (%): *t* = 3.1 min, 403.0 (100, M + H^+). HPLC: PP gradient method, t_R = 5.0 min, 98.1 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{19}H_{20}N_2BrOS^+$ $[M + H]^+$ 403.0474, found 403.0482.

6-(2-(Dimethylamino)ethyl)benzo[4,5]thieno[3,2-*c*]isoquinolin-5(6*H*)-one (19a):



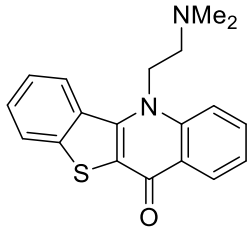
In a dry RBF, **2-(3-bromobenzo[*b*]thiophen-2-yl)-*N*-(2-(dimethylamino)ethyl)benzamide** (73 mg, 181 µmol) was dissolved in *n*-butanol (0.9 mL) and K_3PO_4 (154 mg, 724 µmol), ethylene glycol (121 µL, 2.17 mmol), TMD(337 mg, 2.9 mmol, 0.43 mL), and CuI (14 mg, 72 µmol) were added accordingly. The RBF was degassed and backfilled with N_2(g) for three times, the reaction mixture was then heated at 90 °C for 22 h. After heating, the reaction mixture was cooled down to rt and diluted with EtOAc (20 mL). The combined organic extracts were washed with H_2O (2 x 15 mL) and brine (2 x 15 mL), then dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product (47 mg) obtained was purified by flash column chromatography (94:5:1 EtOAc:Et_3N:MeOH, R_f = 0.15) to yield **19a** (61 mg, 80%) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, *J* = 8.0 Hz, 1H), 8.29 (d, *J* = 8.3 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.68 (d, *J* = 4.5 Hz, 2H), 7.54-7.49 (m, 1H), 7.47 (ddd, *J* = 8.5, 7.1, 1.4 Hz, 1H), 7.41 (td, *J* = 7.6, 7.1, 1.1 Hz, 2H), 4.81 (t, *J* = 8.0 Hz, 2H), 2.81 (t, *J* = 8.1 Hz, 2H), 2.43 (s, 6H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 162.5 (C), 138.6 (C), 133.0 (C), 132.8 (CH), 132.4 (C), 130.8 (C), 129.1 (CH), 127.6 (CH), 125.8 (CH), 125.4 (CH), 124.0 (C), 123.9 (CH), 123.5 (CH), 123.2 (CH), 117.9 (C), 57.0 (CH_2), 46.1 (CH_3), 43.5 (CH_2). LCMS (ESI) *m/z* (%): *t* = 3.1 min, 323.1 (100, M + H^+). HPLC: PP gradient method, t_R = 4.9 min, 95.5 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{19}H_{19}N_2OS^+$ $[M + H]^+$ 323.1213, found 323.1220.

2-(3-Bromobenzofuran-2-yl)-*N*-(2-(dimethylamino)ethyl)benzamide:



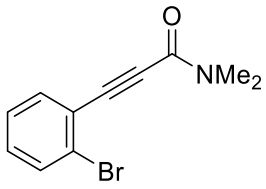
17b (125 mg, 313 µmol), $Pd(OAc)_2$ (11 mg, 47 µmol), PPh_3 (123 mg, 470 µmol), DMD (414 mg, 4.7 mmol, 0.51 mL), Et_3N (63 mg, 627 µmol, 57 µL) and dry NMP (2 mL) was added to a 25 mL dry RBF accordingly. The RBF was degassed and backfilled with CO(g) for three times, the reaction mixture was then heated at 90 °C for 20 h. After heating, the mixture was cooled down to rt, diluted with saturated $NaHCO_3$ solution (25 mL) and extracted with EtOAc (2 x 25 mL). The combined organic extracts were washed with H_2O (2 x 25 mL), and brine (2 x 25 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product (270 mg, orange oil) obtained was purified by flash column chromatography (10:1 EtOAc:MeOH, R_f = 0.15) to yield the title product (91 mg, 75%) as a light yellow oil. ^{1}H NMR (401 MHz, $CDCl_3$) δ 7.85 – 7.77 (m, 1H), 7.79 – 7.71 (m, 1H), 7.61 – 7.51 (m, 3H), 7.49 (dd, *J* = 7.6, 2.2 Hz, 1H), 7.36 (td, *J* = 7.3, 1.7 Hz, 1H), 7.33 (td, *J* = 7.3, 1.3 Hz, 1H), 6.36 (s, 1H), 3.32 (dd, *J* = 10.7, 5.9 Hz, 2H), 2.10 (t, *J* = 5.9 Hz, 3H), 1.85 (s, 6H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 168.5 (C), 154.0 (C), 150.7 (C), 137.0 (C), 130.9 (CH), 130.12 (CH), 130.11 (CH), 129.3 (CH), 128.8 (C), 126.7 (C), 125.9 (CH), 123.8 (CH), 120.2 (CH), 111.7 (CH), 96.7 (C), 57.2 (CH_2), 44.6 (CH_3), 37.3 (CH_2). LCMS (ESI) *m/z* (%): *t* = 3.2 min, 389.1 (100, M + H^+). HPLC: PP gradient method, t_R = 4.84 min, 95.1 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{19}H_{20}BrN_2O_2$ $[M + H]^+$ 387.0703, found 387.0712.

5-(2-(Dimethylamino)ethyl)benzo[4,5]thieno[3,2-*b*]quinolin-11(5*H*)-one (23):



Compound **23** was synthesised according to General UCC Procedure. The crude product (91 mg, bright yellow oil) obtained was purified by flash column chromatography (24:1 EtOAc:Et_3N, R_f = 0.35) to yield **23** (23 mg, 36%) as a pale orange solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (dd, *J* = 8.2, 1.8 Hz, 1H), 8.48 (dd, *J* = 8.3, 1.6 Hz, 1H), 8.00 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.84 – 7.71 (m, 2H), 7.63 – 7.50 (m, 2H), 7.45 (ddd, *J* = 7.9, 6.6, 1.2 Hz, 1H), 4.92 (t, *J* = 8.2 Hz, 2H), 3.05 (br t, *J* = 7.9 Hz, 2H), 2.50 (s, 6H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 173.4 (C), 142.5 (C), 142.0 (C), 141.4 (C), 132.8 (CH), 130.6 (C), 127.9 (CH), 126.8 (CH), 125.3 (CH), 125.1 (CH), 124.8 (CH), 123.5 (C), 123.1 (C), 123.0 (CH), 115.1 (CH), 57.37 (CH_2), 48.0 (CH_2), 46.2 (CH_3). LCMS (ESI) *m/z* (%): *t* = 2.7 min, 323.1 (100, M + H^+). HPLC: PP gradient method, t_R = 4.3 min, 96.2 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{19}H_{19}N_2OS^+$ $[M + H]^+$ 323.1213, found 323.1216. mp 177–179 °C.

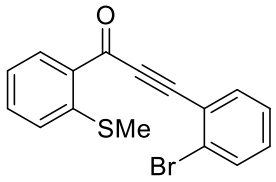
3-(2-Bromophenyl)-*N*,*N*-dimethylpropiolamide (24):



n-BuLi (3.15 mL, 7.88 mmol) was added dropwise to a stirred solution of **33**[2] (1.09 mL, 8.73 mmol) in dry THF (44 mL) at –78 °C under N_2(g) atmosphere. The solution was left to stir at –78 °C for 30 min, followed by dropwise addition of dimethylcarbamoyl chloride (0.88 mL, 9.60 mmol). The reaction mixture was then left at stirring at –78 °C for 5 min, then raised to rt. The dark brown suspension was quenched with saturated NH_4Cl solution and extracted with Et_2O (2 x 75 mL). The combined organic extracts were washed with H_2O (2 x 100 mL) and brine (2 x 100 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product (2.01 g) was obtained as a brown oil and purified by flash column chromatography (2:1 hexanes:EtOAc , R_f = 0.3) to yield **24** (1.47 g, 74%) as a pink solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62

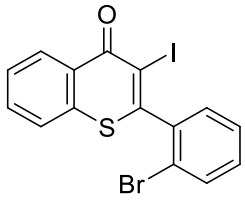
(dd, *J* = 7.5, 1.9 Hz, 1H), 7.61 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.26 (td, *J* = 7.8, 1.8 Hz, 1H), 3.36 (s, 3H), 3.04 (s, 3H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 154.1 (C), 134.5 (CH), 132.5 (CH), 131.1 (CH), 127.2 (CH), 125.9 (C), 122.9 (C), 87.7 (C), 85.4 (C), 38.3 (CH_3), 34.1 (CH_3). LCMS (ESI) *m/z* (%): *t* = 3.6 min, 253.9 (100, M + H^+), 255.9 (80, M + H^+). HPLC: PP gradient method, t_R = 5.6 min, 98.8 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{11}H_{11}BrNO^+$ $[M + H]^+$ 252.0019, found 252.0022. mp 70–74 °C.

3-(2-Bromophenyl)-1-(2-(methylthio)phenyl)prop-2-yn-1-one (25):



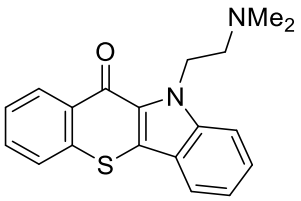
n-BuLi (0.64 mL, 1.6 mmol, 2.5 M in hexanes) was added dropwise to a stirred solution of **11a** (400 mg, 1.6 mmol) in dry THF (8 mL) at –78 °C under N_2(g) atmosphere. The solution was left to stir at –78 °C for 15 min, followed by addition of a solution of **24** (353 mg, 1.4 mmol) in dry THF (2 mL). The reaction was left to stir at –78 °C for 1 h, then raised to rt and quenched with saturated NH_4Cl solution (40 mL) and extracted with Et_2O (2 x 25 mL). The combined organic extracts were washed with H_2O (2 x 40 mL) and brine (2 x 40 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product (544 mg, brown oil) obtained was purified by flash column chromatography (19:1 hexanes:EtOAc, R_f = 0.25) to yield **25** (330 mg, 71%) as a bright yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.66 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.62 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.52 (ddd, *J* = 8.2, 7.2, 1.6 Hz, 1H), 7.37 – 7.20 (m, 4H), 2.44 (s, 3H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 177.4 (C), 145.0 (C), 135.3 (CH), 135.2 (CH), 133.5 (CH), 132.9 (C), 132.8 (CH), 131.8 (CH), 127.4 (CH), 126.7 (C), 124.2 (CH), 123.4 (CH), 122.9 (C), 90.6 (C), 90.3 (C), 15.5 (CH_3). LCMS (APCI) *m/z* (%): *t* = 3.4 min, 331.0 (25, M + H^+), 354.9 (100, M+Na^+). HPLC: PP gradient method, t_R = 7.2 min, 90.8 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{16}H_{12}BrOS^+$ $[M + H]^+$ 330.9787, found 330.9780. mp 96–100 °C.

2-(2-Bromophenyl)-3-iodo-4*H*-thiochromen-4-one (26):



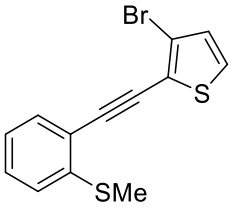
25 (140 mg, 423 µmol) was dissolved in anhydrous CH_3CN (4 mL) in a dry RBF, followed by slow addition of a solution of ICl (103 mg, 634 µmol) in anhydrous CH_3CN (0.9 mL) to the stirred solution. The reaction was left to stir at rt for 26 h in the dark. On completion, the reaction mixture was quenched with saturated $Na_2S_2O_3$ solution (30 mL) and extracted with EtOAc (2 x 20 mL). The combined organic extracts was washed with H_2O (2 x 30 mL) and with brine (2 x 30 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product (185 mg) obtained was purified by flash column chromatography (2:1 hexanes:toluene, R_f = 0.2) to yield **26** (97 mg, 52%) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (dd, *J* = 8.7, 1.5 Hz, 1H), 7.72 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.71 – 7.57 (m, 3H), 7.48 (td, *J* = 7.5, 1.2 Hz, 1H), 7.39 (ddd, *J* = 8.1, 7.5, 1.8 Hz, 1H), 7.32 (dd, *J* = 7.6, 1.7 Hz, 1H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 176.2 (C), 153.2 (C), 141.2 (C), 137.5 (C), 133.6 (CH), 132.2 (CH), 131.5 (CH), 130.24 (CH), 130.16 (CH), 128.7 (CH), 128.1 (CH), 127.5 (C), 125.6 (CH), 122.3 (C), 105.1 (C). LCMS (APCI) *m/z* (%): *t* = 3.4 min, 443.9 (25, M + H^+), 466.9 (100, M+Na^+). HPLC: PP gradient method, t_R = 7.0 min, 95.0 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{15}H_9BrIOS^+$ $[M + H]^+$ 442.8597, found 442.8597. mp 200–202 °C.

10-(2-(Dimethylamino)ethyl)thiochromeno[3,2-*b*]indol-11(10*H*)-one (27):



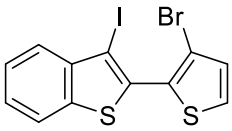
Compound **27** was synthesised according to General UCC Procedure. The crude product (51 mg) was purified by flash column chromatography (97:3 EtOAc:Et_3N, R_f = 0.25) to yield **27** (38 mg, 78%) as a bright yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.86 (dt, *J* = 8.1, 1.0 Hz, 1H), 7.76 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.66 – 7.50 (m, 4H), 7.28 (td, *J* = 8.1, 1.4 Hz, 1H), 5.04 (br t, *J* = 7.6 Hz, 2H), 2.79 (br t, *J* = 7.6 Hz, 2H), 2.41 (s, 6H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 173.3 (C), 139.6 (C), 136.0 (C), 132.7 (C), 130.7 (CH), 129.0 (CH), 128.1 (CH), 127.7 (C), 126.9 (CH), 126.0 (CH), 123.0 (C), 120.9 (CH), 120.7 (C), 119.4 (C), 110.9 (CH), 59.6 (CH_2), 46.1 (CH_3), 44.0 (CH_2). LCMS (ESI) *m/z* (%): *t* = 2.5 min, 323.1 (100, M + H^+). HPLC: PP gradient method, t_R = 5.5 min, 97.8 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{19}H_{19}N_2OS^+$ $[M + H]^+$ 323.1213, found 323.1221.

3-Bromo-2-((2-(methylthio)phenyl)ethynyl)thiophene (28):



Compound **28** was synthesised according to General Procedure A. The crude product (2.83 g) obtained was purified by flash column chromatography (100% hexanes → 17:3 hexanes:EtOAc, R_f = 0.45) to yield **28** (1.23 g, 58%) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (ddd, *J* = 7.7, 1.5, 0.4 Hz, 1H), 7.33 (ddd, *J* = 8.0, 7.4, 1.5 Hz, 1H), 7.25 (d, *J* = 5.4 Hz, 1H), 7.20 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.12 (td, *J* = 7.5, 1.2 Hz, 1H), 7.01 (d, *J* = 5.4 Hz, 1H), 2.53 (s, 3H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 141.8 (C), 132.5 (CH), 130.3 (CH), 129.3 (CH), 127.5 (CH), 124.5 (CH), 124.4 (CH), 120.8 (C), 120.8 (C), 116.3 (C), 94.5 (C), 87.2 (C), 15.3 (CH_3). HPLC: PP gradient method, t_R = 7.8 min, 97.1 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{13}H_{10}BrS_2^+$ $[M + H]^+$ 308.9402, found 308.9398.

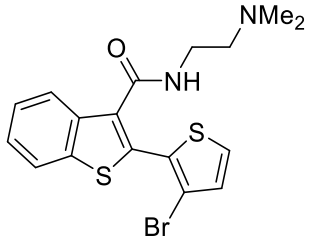
2-(3-Bromothiophen-2-yl)-3-iodobenzo[*b*]thiophene (29):



Compound **29** was synthesised according to General Procedure D. **29** (1.44 g, 97%) was obtained as a grey amorphous solid and directly used in the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (app tdd, *J* = 7.9, 1.4, 0.7, 2H), 7.51-7.47 (m, 1H), 7.48 (d, *J* = 5.4 Hz, 1H), 7.44 (ddd, *J* = 7.8, 7.2, 1.4, 1H), 7.13 (d, *J* = 5.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.1 (C), 140.1 (C), 133.4 (C), 131.0 (CH),

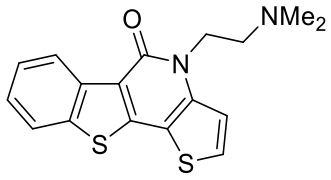
128.4 (CH), 126.6 (CH), 126.3 (CH), 125.7 (CH), 122.3 (CH), 113.5 (C), 86.3 (C). One quaternary carbon is overlapping at 113.5 ppm. HPLC: PP gradient method, t_R = 8.5 min, 99.3 % purity at 254 nm. HR-APCI calcd for $C_{12}H_6BrIS_2$ $[M]^+$ 419.8133, found 419.8129.

2-(3-Bromothiophen-2-yl)-*N*-(2-(dimethylamino)ethyl)benzo[*b*]thiophene-3-carboxamide:



29 (100 mg, 0.24 mmol), $Pd(OAc)_2$ (5.3 mg, 0.024 mmol), PPh_3 (94 mg, 0.36 mmol), DMD (80 µL, 0.71 mmol), Et_3N (70 µL, 0.47 mmol) and dry DMF (2.5 mL) was added to a Schlenk tube. The tube was degassed and backfilled with CO(g) for three times, the reaction mixture was then heated at 80 ºC for 17 h. On completion, the reaction mixture was cooled down to rt and extracted with EtOAc (2 x 15 mL). The combined organic extracts were washed with H_2O (3 x 40 mL), saturated NH_4Cl solution (40 mL) and brine (2 x 40 mL), then dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product (165 mg) obtained was purified by flash column chromatography (4:1 MeOH:EtOAc, R_f = 0.17). **2-(3-Bromothiophen-2-yl)-*N*-(2-(dimethylamino)ethyl)benzo[*b*]thiophene-3-carboxamide** (51 mg, 52%) was obtained as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.80 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.45 (d, *J* = 5.4 Hz, 1H), 7.46-7.38 (m, 2H), 7.09 (d, *J* = 5.4, 1H), 6.41 (s, 1H), 3.39 (dd, *J* = 10.8, 5.9 Hz, 2H), 2.28 (t, *J* = 6.0 Hz, 2H), 2.05 (s, 6H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 163.7 (C), 139.8 (C), 138.2 (C), 133.4 (C), 132.5 (C), 131.3 (CH), 129.5 (C), 128.4 (CH), 125.8 (CH), 125.3 (CH), 125.0 (CH), 121.7 (CH), 113.4 (C), 57.1 (CH_2), 44.9 (CH_3), 37.0 (CH_2). LCMS (ESI) *m/z* (%): *t* = 3.9 min, 408.8 (100, M + H^+), 410.9 (80, M + H^+). HPLC: PP gradient method, t_R = 5.42 min, 97.0 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{17}H_{18}BrN_2OS_2^+$ $[M + H]^+$ 409.0038, found 409.0044.

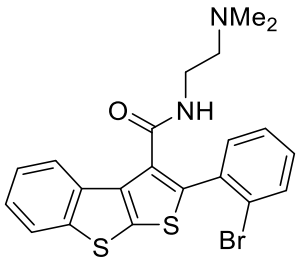
4-(2-(Dimethylamino)ethyl)benzo[4,5]thieno[2,3-*d*]thieno[3,2-*b*]pyridin-5(4*H*)-one (30):



In a dry RBF, **2-(3-bromothiophen-2-yl)-*N*-(2-(dimethylamino)ethyl)benzo[*b*]thiophene-3-carboxamide** (50 mg, 0.12 mmol) was dissolved in *n*-butanol (0.6 mL) and CuI (9.3 mg, 50 µmol), K_3PO_4 (104 mg, 0.49 mmol), ethylene glycol (80 µL, 1.47 mmol), and TMD (40 µL, 0.24 mmol) were added sequentially. The RBF was degassed and backfilled with N_2(g) for three times, the reaction mixture was then heated at 90 °C for 17 h. After heating, the reaction mixture was cooled down to rt and diluted with EtOAc (15 mL). The organic extract was washed with H_2O (2 x 20 mL) and brine (2 x 20 mL), then dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product (40 mg) obtained was then purified by flash column chromatography (3:1 EtOAc:MeOH, R_f = 0.33). **30** (33 mg, 83%) was obtained as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.55 (d, *J* = 5.4 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.19 (d, *J* = 5.5 Hz, 1H), 4.49 (t, *J* = 7.7 Hz, 2H), 2.72 (t, *J* = 7.7 Hz, 2H), 2.40 (s, 6H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 158.5 (C), 143.7 (C), 141.7 (C), 137.0 (C), 128.2 (CH), 125.87 (CH), 125.86 (CH), 125.3 (CH), 122.2 (CH), 120.9 (C), 117.2 (CH), 114.5 (C), 57.0 (CH_2), 45.9 (CH_3), 43.3 (CH_2). One quaternary carbon is overlapping at 137.0 ppm. LCMS (ESI) *m/z* (%): *t* = 4.0 min,

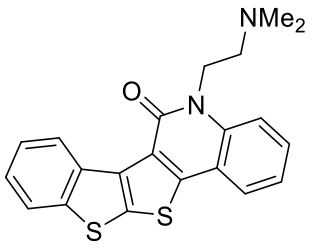
328.9 (100, M + H^+). HPLC: PP gradient method, t_R = 5.5 min, 95.3 % at 254 nm. HR-ESI (*m/z*) calcd for $C_{17}H_{17}N_2OS_2^+$ $[M + H]^+$ 329.0777, found 329.0788.

2-(2-Bromophenyl)-*N*-(2-(dimethylamino)ethyl)benzo[*b*]thieno[3,2-*d*]thiophene-3-carboxamide:



34[2] (95 mg, 0.20 mmol), $Pd(OAc)_2$ (4.5 mg, 20 µmol), PPh_3 (79 mg, 0.30 mmol), DMD (0.34 mL, 3.2 mmol), Et_3N (60 µL, 0.40 mmol) and dry DMF (2.0 mL) were added to a 25 mL dry RBF. The RBF was degassed and backfilled with CO(g) for three times, the reaction mixture was then heated at 80 °C for 17 h. On completion, the reaction mixture was cooled down to rt, diluted with H_2O (25 mL) and extracted with EtOAc (2 x 20 mL). The combined organic extracts were washed with saturated NH_4Cl solution (25 mL), H_2O (3 x 40 mL) and brine (2 x 30 mL). The organic extract was then dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product (142 mg) obtained was then purified by flash column chromatography (100% EtOAc → 7:3 EtOAc:MeOH, R_f = 0.45) to yield **2-(2-bromophenyl)-*N*-(2-(dimethylamino)ethyl)benzo[*b*]thieno[3,2-*d*]thiophene-3-carboxamide** (56 mg, 60%) as a pale brown amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.80 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.69 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.52 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.43-7.33 (m, 3H), 7.30 (td, *J* = 7.7, 1.8 Hz, 1H), 6.39 (s, 1H), 3.35 (dd, *J* = 11.0, 5.8 Hz, 2H), 2.18 (t, *J* = 6.0 Hz, 2H), 2.02 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.1 (C), 143.6 (C), 143.2 (C), 139.2 (C), 138.4 (C), 134.3 (C), 133.1 (CH), 133.0 (CH), 132.7 (C), 130.7 (CH), 130.5 (C), 127.6 (CH), 125.2 (C), 124.8 (C), 124.8 (CH), 123.7 (CH), 122.9 (CH), 57.0 (CH_2), 44.8 (CH_3), 37.1 (CH_2). LCMS (ESI) *m/z* (%): *t* = 4.0 min, 460.8 (100, M + H^+), 462.8 (20, M + H^+). HPLC: PP gradient method, t_R = 6.0 min, 99.3 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{21}H_{20}BrN_2OS_2^+$ $[M + H]^+$ 459.0195, found 459.0205.

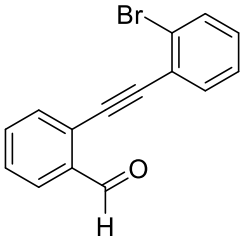
5-(2-(Dimethylamino)ethyl)benzo[4',5']thieno[3',2':4,5]thieno[3,2-*c*]quinolin-6(5*H*)-one (35):



In a dry RBF, **2-(2-bromophenyl)-*N*-(2-(dimethylamino)ethyl)benzo[*b*]thieno[3,2-*d*]thiophene-3-carboxamide** (50 mg, 0.11 mmol) was dissolved in *n*-butanol (0.55 mL) and CuI (8.3 mg, 40 µmol), K_3PO_4 (92 mg, 0.44 mmol), ethylene glycol (70 µL, 1.31 mmol), and TMD(30 µL, 0.22 mmol) were added sequentially. The RBF was degassed and backfilled with N_2(g) for three times, the reaction mixture was then heated at 90 °C for 20 h. The reaction mixture was cooled down to rt and extracted with EtOAc (2 x 10 mL). The combined organic extracts were washed with H_2O (2 x 10 mL) and brine (2 x 10 mL), then dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product (43 mg) obtained was purified by flash column chromatography (100 % EtOAc → 3:1 EtOAc:MeOH, R_f = 0.33) to yield **35** (39 mg, 95%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.61 (ddd, *J* = 8.2, 1.2, 0.6 Hz, 1H), 7.81 (app t, *J* = 7.3 Hz, 2H), 7.54-7.49 (m, 3H), 7.39 (ddd, *J* = 8.1, 7.1, 1.2 Hz, 1H), 7.29-7.25 (m, 1H), 4.59 (app t, *J* = 7.8 Hz, 2H), 2.75-2.71 (app t, *J* = 7.9 Hz, 2H), 2.45 (s, 6H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 158.4 (C), 149.3 (C), 143.6 (C), 139.7 (C), 137.5 (C), 136.6 (C), 133.4 (C), 129.7 (CH), 126.6 (CH), 125.1 (CH), 124.9 (CH),

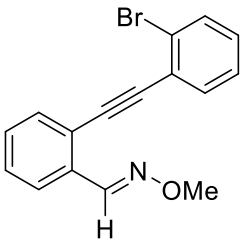
124.85 (C), 124.0 (CH), 122.6 (CH), 122.6 (CH), 118.7 (C), 115.2 (CH), 56.2 (CH_2), 46.0 (CH_3), 41.2 (CH_2). LCMS (API-ES) *m/z* (%): *t* = 4.2 min, 378.9 (100, M + H^+). HPLC: PP gradient method, t_R = 6.5 min, 99.8 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{21}H_{19}N_2OS_2^+$ $[M + H]^+$ 379.0933, found 379.0945.

2-((2-Bromophenyl)ethynyl)benzaldehyde (37):



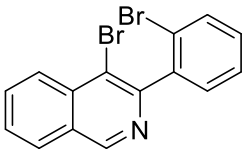
Compound **37** was synthesised according to General Procedure A. The crude product (839 mg) obtained was purified by flash column chromatography (3:1 hexanes:CH_2Cl_2, R_f = 0.25) to yield **37** (678 mg, 92%) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.76 (d, *J* = 0.8 Hz, 1H), 7.97 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.70 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.64 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.63 – 7.57 (m, 2H), 7.51 – 7.46 (td, *J* = 7.6, 1.1 Hz, 1H), 7.33 (td, *J* = 7.6, 1.3 Hz, 1H), 7.23 (td, *J* = 7.5, 1.7 Hz, 1H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 192.1 (CH), 136.3 (C), 133.9 (CH), 133.6 (CH), 133.5 (CH), 132.8 (CH), 130.3 (CH), 129.2 (CH), 127.33 (CH), 127.31 (CH), 126.6 (C), 125.9 (C), 124.8 (C), 94.8 (C), 89.5 (C). LCMS (ESI) *m/z* (%): *t* = 3.6 min, 285.0 (100, M + H^+). HPLC: PP gradient method, t_R = 7.04 min, 95.3 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{15}H_{10}BrO^+$ $[M + H]^+$ 284.9910, found 284.9907. mp 66–68 °C. The spectroscopic data are consistent with those previously reported in the literature.[12]

(*E*)-2-((2-Bromophenyl)ethynyl)benzaldehyde *O*-methyl oxime (38a):



O-Methylhydroxylamine hydrochloride (776 mg, 9.29 mmol) was slowly added to a stirred solution of **37** (530 mg, 1.86 mmol) in pyridine (3 mL) and EtOH (6 mL). The reaction mixture was left to stir at rt overnight. On completion, the reaction mixture was diluted with H_2O (20 mL) and extracted with CH_2Cl_2 (2 x 25 mL). The combined organic extracts were washed with H_2O (2 x 30 mL) and with brine (2 x 30 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product (824 mg) obtained was purified by flash column chromatography (2:1 hexanes:CH_2Cl_2, R_f = 0.45) to yield **38a** (546 mg, 94%) as a clear yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 7.98 – 7.90 (m, 1H), 7.63 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.62 – 7.54 (m, 2H), 7.38 – 7.34 (m, 2H), 7.31 (td, *J* = 7.6, 1.2 Hz, 1H), 7.20 (ddd, *J* = 8.0, 7.5, 1.7 Hz, 1H), 4.01 (s, 3H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 147.5 (CH), 133.7 (C), 133.4 (CH), 132.73 (CH), 132.66 (CH), 129.8 (CH), 129.5 (CH), 129.0 (CH), 127.2 (CH), 125.9 (C), 125.3 (CH), 125.2 (C), 122.7 (C), 93.4 (C), 91.0 (C), 62.3 (CH_3). LCMS (ESI) *m/z* (%): *t* = 5.0 min, 314.0 (100, M + H^+). HPLC: PP gradient method, t_R = 8.0 min, 96.4 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{16}H_{13}BrNO^+$ $[M + H]^+$ 314.0175, found 314.0170.

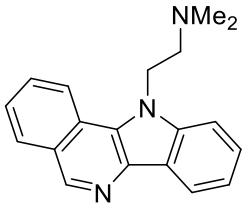
4-Bromo-3-(2-bromophenyl)isoquinoline (39a) and **4-bromo-3-(2-bromophenyl)isoquinolin-1-ol (39b):**



$CuBr_2$ (448 mg, 2.01 mmol, 2 equiv.) was added slowly to a stirred solution of **38a** (315 mg, 1.0 mmol) in dry dimethylacetamide (5 mL) under N_2(g) atmosphere. The reaction was heated at 100 ºC for 17 h. After heating, the mixture was quenched with saturated NH_4Cl solution (35 mL) and extracted with EtOAc (3 x 30 mL). The combined organic extracts were washed with H_2O (2 x 80 mL) and with brine (2 x 80 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product (327 mg, brown oil) obtained was purified by flash column chromatography (3:1 hexanes:CH_2Cl_2, R_f = 0.1 → 1:1 hexanes:CH_2Cl_2, R_f = 0.2, → 2:3 hexanes:CH_2Cl_2, R_f = 0.7) to yield **39a** (122 mg, 34%) as a clear yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.26 (s, 1H), 8.32 (dd, *J* = 8.5, 0.9 Hz, 1H), 8.06 (dt, *J* = 8.1, 1.0 Hz, 1H), 7.88 (ddd, *J* = 8.4, 6.9, 1.3 Hz, 1H), 7.78 – 7.68 (m, 2H), 7.50 – 7.38 (m, 2H), 7.32 (ddd, *J* = 8.1, 7.0, 2.2 Hz, 1H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 152.4 (C), 151.2 (CH), 142.0 (C), 135.7 (C), 132.9 (CH), 132.2 (CH), 130.9 (CH), 130.0 (CH), 129.0 (C), 128.5 (CH), 128.0 (CH), 127.5 (CH), 126.9 (CH), 123.1 (C), 121.3 (C), 120.0 (C). LCMS (ESI) *m/z* (%): *t* = 5.6 min, 363.8 (100, M + H^+). HPLC: PP gradient method, t_R = 6.6 min, 96.6 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{15}H_{10}Br_2N^+$ [M + H]$^+$ 361.9175, found 361.9176.

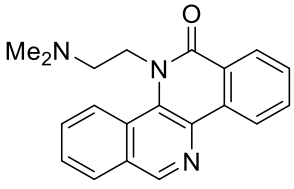
Byproduct **4-bromo-3-(2-bromophenyl)isoquinolin-1-ol 39b** (167 mg, 44%) was also obtained as an off-white solid. ^{1}H NMR (400 MHz, Methanol-*d4*) δ 8.88 (br s, 1H), 8.32 (d, *J* = 8.5 Hz, 1H), 7.99 (d, *J* = 8.3 Hz, 1H), 7.88 (t, *J* = 7.5 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 2H), 7.59 (s, 1H), 7.48 (t, *J* = 7.6 Hz, 2H). LCMS (ESI) *m/z* (%): *t* = 3.5 min, 377.8 (100, M+H^+). HPLC: PP gradient method, t_R = 5.8 min, 98.3 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{15}H_{10}Br_2NO^+$ [M + H]$^+$ 377.9124, found 377.9123.

2-(11*H*-indolo[3,2-*c*]isoquinolin-11-yl)-*N*,*N*-dimethylethan-1-amine (40):



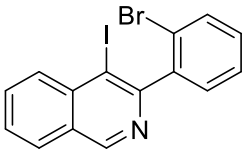
Compound **40** was synthesised according to General UCC Procedure. The crude product (68 mg, brown oil) obtained was purified by flash column chromatography (99:1 EtOAc:Et_3N, R_f = 0.2) to yield **40** (23 mg, 53%) as a light green oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.12 (s, 1H), 8.48 (d, *J* = 8.6 Hz, 1H), 8.45 (d, *J* = 7.8 Hz, 1H), 8.18 (d, *J* = 8.0 Hz, 1H), 7.83 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 1H), 7.64 (ddd, *J* = 8.0, 6.9, 1.0 Hz, 1H), 7.63 – 7.51 (m, 2H), 7.39 (ddd, *J* = 7.9, 6.4, 1.6 Hz, 1H), 4.86 (br t, *J* = 8.1 Hz, 2H), 2.87 (br t, *J* = 8.1 Hz, 2H), 2.44 (s, 6H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 145.9 (CH), 140.0 (C), 135.1 (C), 130.1 (CH), 129.7 (CH), 127.7 (C), 127.0 (C), 126.2 (CH), 125.6 (CH), 124.5 (C), 122.9 (C), 120.8 (CH), 120.6 (CH), 120.2 (CH), 109.0 (CH), 58.3 (CH_2), 46.2 (CH_3), 44.4 (CH_2). LCMS (ESI) *m/z* (%): *t* = 3.3 min, 290.1 (100, M + H^+). HPLC: PP gradient method, t_R = 3.5 min, 96.7 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{19}H_{20}N_3^+$ [M + H]$^+$ 290.1652, found 290.1659.

5-(2-(Dimethylamino)ethyl)dibenzo[*c*,*h*][1,5]naphthyridin-6(5*H*)-one (41):



Compound **41** was synthesised according to General PdCC[1] Procedure. The crude product (111 mg) was purified by flash column chromatography (9:1 EtOAc:MeOH, R_f = 0.2) to yield **41** (23 mg, 44%) as a beige oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 8.91 (d, *J* = 8.2 Hz, 1H), 8.52 (d, *J* = 8.8 Hz, 1H), 8.48 (d, *J* = 8.0 Hz, 1H), 8.08 (d, *J* = 8.1 Hz, 1H), 7.85 (ddd, *J* = 8.3, 7.1, 1.4 Hz, 1H), 7.80 (ddd, *J* = 8.6, 6.9, 1.5 Hz, 1H), 7.68 (ddd, *J* = 8.0, 6.0, 1.0 Hz, 2H), 7.66 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 2H), 4.73 (t, *J* = 7.3 Hz, 2H), 3.02 (t, *J* = 7.3 Hz, 2H), 2.33 (s, 6H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 164.3 (C), 148.0 (CH), 135.7 (C), 133.1 (CH), 132.3 (C), 130.2 (CH), 130.1 (C), 129.5 (C), 129.2 (CH), 128.9 (CH), 127.9 (CH), 127.5 (CH), 127.1 (C), 126.0 (C), 124.2 (CH), 124.1 (CH), 57.6 (CH_2), 48.8 (CH_2), 45.8 (CH_3). LCMS (ESI) *m/z* (%): *t* = 2.6 min, 318.2 (100, M + H^+). HPLC: PP gradient method, t_R = 4.9 min, 95.4 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{20}H_{20}N_3O^+$ $[M + H]^+$ 318.1601, found 318.1604.

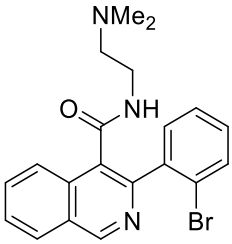
3-(2-Bromophenyl)-4-iodoisoquinoline (42):



In a dry RBF, **37** (350 mg, 1.23 mmol) was dissolved in anhydrous DCE (6 mL), followed by addition of anhydrous $MgSO_4$ (443 mg, 3.68 mmol) and *tert*-butylamine (898 mg, 12.27 mmol, 1.29 mL). The reaction mixture was left to stir at 45 ºC for 1 d. After heating, the reaction mixture was cooled down to rt, diluted with CH_2Cl_2 (20 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to yield **38b** (417 mg) as an orange oil. **38b** was unstable and used in situ in the next step. Rapid analysis of **38b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.00 (s, 1H), 8.14 – 8.09 (m, 1H), 7.64 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.62 – 7.55 (m, 2H), 7.42 – 7.36 (m, 2H), 7.32 (td, *J* = 7.6, 1.2 Hz, 1H), 7.21 (ddd, *J* = 8.1, 7.5, 1.7 Hz, 1H), 1.34 (s, 9H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 154.3 (CH), 138.2 (C), 133.5 (CH), 132.8 (CH), 132.6 (CH), 129.9 (CH), 129.8 (CH), 129.2 (CH), 127.3 (CH), 126.2 (CH), 125.5 (C), 125.4 (C), 123.6 (C), 93.1 (C), 91.5 (C), 30.1 (CH_3).

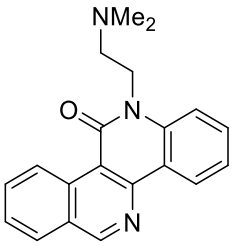
Oven-dried 4Å powdered molecular sieves was added to **38b** (265 mg, 779 µmol) and NaOAc (192 mg, 2.34 mmol) in a dry RBF, followed by addition of dry CH_2Cl_2 (15 mL) under N_2(g) atmosphere. A solution of ICl (253 mg, 1.56 mmol) and in dry CH_2Cl_2 (7.5 mL) was added slowly over 10 min to the stirred suspension, and reaction was left to stir at 0 °C for 4 h in the dark. The reaction mixture was filtered through Celite®. The organic extract was washed with saturated $Na_2S_2O_3$ solution (2 x 30 mL), H_2O (2 x 30 mL) and brine (20 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product obtained (406 mg, brown oil) was purified by flash column chromatography (19:1 toluene:EtOAc, R_f = 0.2) to yield **42** (164 mg, 51% from **37**) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.21 (d, *J* = 0.7 Hz, 1H), 8.20 (dd, *J* = 8.5, 0.9 Hz, 1H), 8.00 (dt, *J* = 8.1, 1.0 Hz, 1H), 7.85 (ddd, *J* = 8.4, 6.9, 1.3 Hz, 1H), 7.75 – 7.70 (m, 2H), 7.46 (td, *J* = 7.5, 1.2 Hz, 1H), 7.38 (dd, *J* = 7.6, 1.9 Hz, 1H), 7.33 (ddd, *J* = 8.0, 7.3, 1.8 Hz, 1H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 157.0 (C), 152.2 (CH), 144.8 (C), 138.3 (C), 132.8 (CH), 132.5 (CH), 132.1 (CH), 130.9 (CH), 130.0 (CH), 128.6 (CH), 128.4 (C), 128.2 (CH), 127.5 (CH), 123.1 (C), 100.0 (C). LCMS (ESI) *m/z* (%): *t* = 5.6 min, 411.7 (100, M + H^+). HPLC: PP gradient method, t_R = 6.48 min, 82.6 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{15}H_{10}BrIN^+$ $[M + H]^+$ 409.9036 and 411.9016, found 409.9043 and 411.9023. mp 164–166 °C.

3-(2-Bromophenyl)-*N*-(2-(dimethylamino)ethyl)isoquinoline-4-carboxamide:



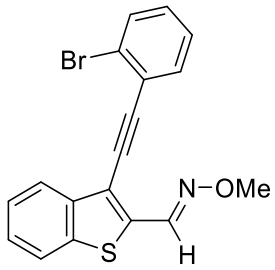
42 (75 mg, 183 µmol), $Pd(OAc)_2$ (4.1 mg, 18 µmol), PPh_3 (72 mg, 274 µmol), DMD (242 mg, 2.74 mmol, 0.30 mL), Et_3N (37 mg, 366 µmol, 33 µL) and dry NMP (1.8 mL) was added to a 10 mL dry RBF accordingly. The RBF was degassed and backfilled with CO(g) for three times, the reaction mixture was then heated at 90 °C for 47 h. After heating, the mixture was cooled down to rt, diluted with saturated $NaHCO_3$ solution (25 mL) and extracted with EtOAc (2 x 15 mL). The combined organic extracts were washed with H_2O (2 x 20 mL), and brine (2 x 20 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product (138 mg) was purified by flash column chromatography (49:1 EtOAc:Et_3N, R_f = 0.15) to yield **3-(2-bromophenyl)-*N*-(2-(dimethylamino)ethyl)isoquinoline-4-carboxamide** (53 mg, 73%) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$ δ 9.34 (d, *J* = 0.9 Hz, 1H), 8.12 (dq, *J* = 8.5, 0.9 Hz, 1H), 8.05 (dt, *J* = 8.2, 1.1 Hz, 1H), 7.79 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.69 (dtd, *J* = 8.1, 3.5, 1.1 Hz, 2H), 7.46 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.38 (td, *J* = 7.5, 1.2 Hz, 1H), 7.29 (ddd, *J* = 8.0, 7.4, 1.8 Hz, 1H), 6.48 (br s, 1H), 3.37 (t, *J* = 7.0 Hz, 1H), 3.25 (br q, *J* = 5.3, 4.7 Hz, 2H), 2.36 (t, *J* = 8.1 Hz, 1H), 2.06 (s, 6H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 167.0 (C), 153.0 (CH), 149.3 (C), 140.7 (C), 133.5 (C), 132.9 (CH), 131.7 (CH), 131.3 (CH), 130.0 (CH), 128.1 (CH), 127.99 (C), 127.96 (CH), 127.62 (C), 127.59 (CH), 125.1 (CH), 123.2 (C), 57.1 (CH_2), 45.0 (CH_3), 37.1 (CH_2). LCMS (ESI) *m/z* (%): *t* = 2.0 min, 398.1 (100, M + H^+). HPLC: PP gradient method, t_R = 3.3 min, 79.2 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{20}H_{21}BrN_3O^+$ $[M + H]^+$ 398.0863, found 398.0869.

12-(2-(Dimethylamino)ethyl)dibenzo[*c*,*h*][1,6]naphthyridin-11(12*H*)-one (43):



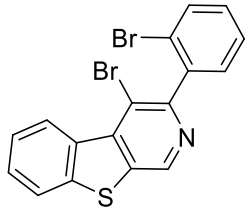
In a dry RBF, **3-(2-bromophenyl)-*N*-(2-(dimethylamino)ethyl)isoquinoline-4-carboxamide** (34 mg, 85 µmol) was dissolved in *n*-butanol (0.8 mL) and K_3PO_4 (72 mg, 341 µmol), ethylene glycol (57 µL, 1.02 mmol), TMD(159 mg, 1.37 mmol, 0.2 mL), and CuI (6.5 mg, 34 µmol), were added accordingly. The RBF was degassed and backfilled with N_2(g) for three times, the reaction mixture was then heated at 80 °C for 18 h. After heating, the reaction mixture was cooled down to rt, diluted with water (20 mL) and extracted with EtOAc (3 x 20 mL). The combined organic extracts were washed with H_2O (2 x 15 mL) and brine (2 x 15 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product (29 mg) obtained was purified by flash column chromatography (19:1 EtOAc:MeOH, R_f = 0.1) to yield **43** (16.4 mg, 61%) as an off-white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.08 (d, *J* = 9.0 Hz, 1H), 9.50 (d, *J* = 0.8 Hz, 1H), 9.09 (dd, *J* = 8.1, 1.6 Hz, 1H), 8.09 (d, *J* = 8.1 Hz, 1H), 7.94 (ddd, *J* = 8.6, 7.0, 1.5 Hz, 1H), 7.73 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 1H), 7.67 (ddd, *J* = 8.6, 7.1, 1.6 Hz, 1H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.41 (ddd, *J* = 8.1, 7.1, 1.0 Hz, 1H), 4.64 (br t, *J* = 7.9 Hz, 2H), 2.76 (br t, *J* = 7.9 Hz, 2H), 2.47 (s, 6H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 162.4 (C), 157.7 (CH), 147.7 (C), 138.1 (C), 134.5 (C), 132.9 (CH), 131.3 (CH), 128.7 (CH), 128.2 (C), 127.8 (CH), 127.3 (CH), 126.6 (CH), 122.6 (CH), 121.1 (C), 114.1 (CH), 113.2 (C), 56.1 (CH_2), 46.0 (CH_3), 41.3 (CH_2). LCMS (ESI) m/z (%): *t* = 2.3 min, 318.2 (100, M + H^+). HPLC: PP gradient method, t_R = 5.1 min, 95.8 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{20}H_{20}N_3O^+$ $[M + H]^+$ 318.1601, found 318.1613.

3-((2-Bromophenyl)ethynyl)benzo[*b*]thiophene-2-carbaldehyde *O*-methyl oxime (46a):



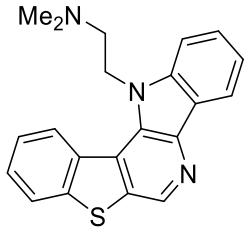
O-Methylhydroxylamine hydrochloride (284 mg, 3.4 mmol) was slowly added to a stirred solution of **45** (232 mg, 680 µmol) in pyridine (3 mL) and EtOH (6 mL). The reaction mixture was left to stir at rt overnight. On completion, the reaction mixture was diluted with H_2O (25 mL) and extracted with CH_2Cl_2 (2 x 25 mL). The combined organic extracts were washed with H_2O (2 x 25 mL) and brine (2 x 25 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product (500 mg) obtained was purified by flash column chromatography (10:1 hexanes: EtOAc, R_f = 0.45) to yield **46a** (247 mg, 99%) as a yellow solid. **46a** appears as a pair of *E*/*Z* isomers in ^{1}H NMR, ^{13}C NMR, LCMS and analytical HPLC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (s, 1H), 8.37 (s, 1H), 8.19 – 8.12 (m, 1H), 8.12 – 8.03 (m, 1H), 7.89 – 7.81 (m, 1H), 7.83 – 7.75 (m, 1H), 7.71 – 7.60 (m, 4H), 7.51 – 7.41 (m, 4H), 7.38 – 7.34 (m, 2H), 7.26 – 7.21 (m, 2H), 4.17 (s, 3H), 4.04 (s, 3H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 143.7 (CH), 141.2 (C), 140.2(CH), 139.32 (C), 139.29 (C), 138.5 (C), 137.7 (C), 133.7 (C), 133.54 (CH), 133.50 (CH), 132.8 (CH), 132.7 (CH), 130.04 (CH), 130.00 (CH), 127.4 (CH), 127.3(CH), 127.0 (CH), 126.8 (CH), 125.64 (C), 125.63 (C), 125.34 (CH), 125.30 (CH), 125.08 (C), 125.06 (C), 124.1 (CH), 123.7 (CH), 122.6 (CH), 122.4 (CH), 121.0 (C), 119.9 (C), 96.1 (C), 95.8 (C), 86.5 (C), 86.0 (C), 63.0 (CH_3), 62.8 (CH_3). LCMS (ESI) *m/z* (%): *t* = 7.8 min, 371.8 (40, M + H^+). HPLC: PP gradient method, t_R = 8.8 and 8.9 min, 95.1 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{18}H_{13}BrNOS^+$ $[M + H]^+$ 369.9896, found 369.9896.

4-Bromo-3-(2-bromophenyl)benzo[4,5]thieno[2,3-*c*]pyridine (47):



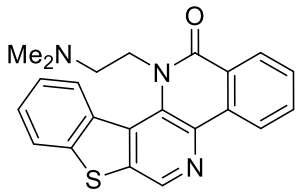
$CuBr_2$ (205 mg, 918 µmol) was added slowly to a stirred solution **46a** (170 mg, 392 µmol) in DMA (3 mL) under N_2(g) atmosphere. The reaction was heated at 100 ºC for 7 h. After heating, the mixture was quenched with saturated NH_4Cl solution (15 mL) and extracted with EtOAc (3 x 15 mL). The combined organic extracts were washed with H_2O (2 x 25 mL) and brine (2 x 25 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product (163 mg) obtained was purified by flash column chromatography (100 % CH_2Cl_2, R_f = 0.4) to **47** (62 mg, 32%) as a brown foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.30 (dd, *J* = 8.3, 1.3 Hz, 1H), 9.15 (s, 1H), 7.99 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.73 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.69 (ddd, *J* = 8.1, 7.2, 1.3 Hz, 1H), 7.60 (ddd, *J* = 8.3, 7.2, 1.2 Hz, 1H), 7.47 (ddd, *J* = 7.6, 7.2, 1.1 Hz, 1H), 7.42 (dd, *J* = 7.9, 2.0 Hz, 1H), 7.34 (ddd, *J* = 8.1, 7.2, 2.0 Hz, 1H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 154.4 (C), 142.7 (CH), 142.0 (C), 141.6 (C), 140.1 (C), 136.8 (C), 134.2 (C), 132.9 (CH), 130.9 (CH), 130.1 (CH), 129.5 (CH), 127.6 (CH), 127.1 (CH), 124.8 (CH), 123.4 (CH), 123.3 (C), 116.2 (C). LCMS (ESI) *m/z* (%): *t* = 4.3 min, 417.9 (50, M + H^+) and 419.9 (100, M + H^+). HPLC: PP gradient method, t_R = 7.6 min, 97.1 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{17}H_{10}Br_2NS^+$ $[M + H]^+$ 417.8895, found 417.8903.

2-(12*H*-Benzo[4',5']thieno[3',2':4,5]pyrido[3,2-*b*]indol-12-yl)-*N*,*N*-dimethylethan-1-amine (48):



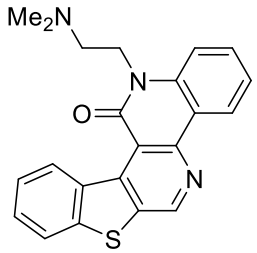
Compound **48** was synthesised according to General UCC Procedure. The crude product (44 mg) obtained was purified by flash column chromatography (100% EtOAc, R_f = 0.2) to yield **48** (13 mg, 35%) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (s, 1H), 8.74 – 8.66 (m, 1H), 8.43 (d, *J* = 7.8 Hz, 1H), 8.05 – 7.98 (m, 1H), 7.67 – 7.55 (m, 4H), 7.41 (ddd, *J* = 7.9, 6.7, 1.3 Hz, 1H), 4.93 (br t, *J* = 7.9 Hz, 2H), 2.84 (br t, *J* = 7.9 Hz, 2H), 2.32 (s, 6H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 142.0 (C), 140.9 (C), 139.4 (C), 137.4 (CH), 134.1 (C), 133.1 (C), 131.1 (C), 127.6 (CH), 127.3 (CH), 126.6 (C), 126.2 (CH), 125.0 (CH), 123.9 (C), 123.8 (CH), 121.2 (CH), 120.5 (CH), 110.4 (CH), 58.4 (CH_2), 46.0 (CH_3), 45.9 (CH_2). LCMS (ESI) *m/z* (%): *t* = 2.6 min, 346.1 (60, M + H^+). HPLC: PP gradient method, t_R = 4.5 min, 94.2 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{21}H_{20}N_3S^+$ $[M + H]^+$ 346.1372, found 346.1379.

12-(2-(Dimethylamino)ethyl)benzo[*c*]benzo[4,5]thieno[2,3-*h*][1,5]naphthyridin-13(12*H*)-one (49):



Compound **49** was synthesised according to General PdCC[1] Procedure. The crude product (121 mg) was purified by two flash column chromatography (4:1 EtOAc:CH_2Cl_2, R_f = 0.25; 3:1 EtOAc:CH_2Cl_2, R_f = 0.2) to yield **49** (20 mg, 44%) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (s, 1H), 8.82 (dd, , *J* = 8.1, 1.1 Hz, 1H), 8.49 (dd, *J* = 8.0, 1.4 Hz, 1H), 8.20 (d, *J* = 7.5 Hz, 1H), 7.97 (dd, *J* = 6.4, 2.3 Hz, 1H), 7.84 (ddd, *J* = 8.2, 7.2, 1.4 Hz, 1H), 7.66 (ddd, *J* = 8.2, 7.2, 1.2 Hz, 1H), 7.61 – 7.54 (m, 2H), 4.68 (br s, 2H), 2.25 (t, *J* = 6.5 Hz, 2H), 1.88 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.6 (C), 141.1 (C), 139.3 (CH), 136. 8 (C), 135.4 (C), 135.1 (C), 133.3 (CH), 132.8 (C), 131.0 (C), 130.4 (C), 129.2 (CH), 128.4 (CH), 128.3 (CH), 127.0 (CH), 126.7 (C), 125.0 (CH), 123.8 (CH), 123.5 (CH), 57.2 (CH_2), 49.1 (CH_2), 45.3 (CH_3). LCMS (ESI) *m/z* (%): *t* = 3.9 min, 374.0 (100, M + H^+). HPLC: PP gradient method, t_R = 5.6 min, 95.5 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{22}H_{20}N_3OS^+$ $[M + H]^+$ 374.1322, found 374.1322.

13-(2-(Dimethylamino)ethyl)benzo[*h*]benzo[4,5]thieno[2,3-*c*][1,6]naphthyridin-12(13*H*)-one (51):

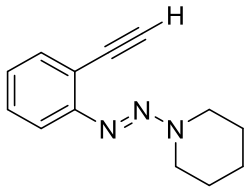


50[2] (42 mg, 90 µmol), $Pd(OAc)_2$ (2.0 mg, 9 µmol), PPh_3 (35 mg, 135 µmol), DMD (119 mg, 1.35 mmol, 0.15 mL), Et_3N (18 mg, 180 µmol, 16 µL) and dry NMP (1 mL) was added to a 10 mL dry RBF. The RBF was degassed and backfilled with CO(g) for three times, the reaction mixture was then heated at 90 °C for 28 h. On completion, the reaction mixture was cooled down to rt, diluted with H_2O (15 mL) and extracted with

EtOAc (2 x 20 mL). The combined organic extracts were washed with saturated $NaHCO_3$ solution (30 mL), H_2O (2 x 30 mL) and brine (2 x 30 mL). Dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure, the crude product (85 mg) was purified by flash column chromatography (49:1 EtOAc:Et_3N, R_f = 0.15) to yield the **3-(2-bromophenyl)-*N*-(2-(dimethylamino)ethyl)benzo[4,5]thieno [2,3-*c*]pyridine-4-carboxamide** (27 mg) as a cloudy white oil containing impurity but was directly used in the next step without further purification. LCMS (ESI) *m/z* (%): *t* = 2.3 min, 454.1 (100, M + H^+). HPLC: PP gradient method, t_R = 4.41 min, 81 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{22}H_{21}BrN_3OS^+$ $[M + H]^+$ 454.0583, found 454.0585.

In a dry RBF, **3-(2-bromophenyl)-*N*-(2-(dimethylamino)ethyl)benzo[4,5]thieno[2,3-*c*]pyridine-4-carboxamide** (20 mg, 44 µmol) was dissolved in *n*-butanol (0.4 mL) and K_3PO_4 (37 mg, 176 µmol), ethylene glycol (30 µL, 528 µmol, 12 equiv.), TMD (0.1 mL), and CuI (3.3 mg, 18 µmol), were added accordingly. The RBF was degassed and backfilled with N_2(g) for three times, the reaction mixture was then heated at 80 °C for 15 h. After heating, the reaction mixture was cooled down rt, diluted with H_2O (15 mL) and extracted with EtOAc (3 x 15 mL). The combined organic extracts were washed with H_2O (2 x 30 mL) and brine (2 x 30 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product (32 mg) obtained was purified by flash column chromatography (19:1 EtOAc:MeOH, R_f = 0.2) to yield **51**(10 mg, 40% from **50**) as an off-white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.93 – 9.88 (m, 1H), 9.42 (s, 1H), 9.04 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.99 – 7.94 (m, 1H), 7.68 – 7.57 (m, 3H), 7.53 (d, *J* = 8.5 Hz, 1H), 7.40 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1H), 4.6 (br t, *J* = 7.8 Hz, 2H), 2.84 – 2.72 (br t, *J* = 7.8 Hz, 2H), 2.48 (s, 6H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 161.5 (C), 148.7 (CH), 148.1 (C), 142.3 (C), 141.0 (C), 137.7 (C), 136.7 (C), 134.6 (C), 132.1 (CH), 131.1 (CH), 129.1 (CH), 126.5 (CH), 124.8 (CH), 122.8 (CH), 121.5 (C), 117.6 (C), 114.1 (CH), 56.0 (CH_2), 46.0 (CH_3), 41.6 (CH_2). LCMS (ESI) *m/z* (%): *t* = 2.5 min, 374.1 (100, M + H^+). HPLC: PP gradient method, t_R = 5.8 min, 98.8 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{22}H_{20}N_3OS^+$ $[M + H]^+$ 374.1322, found 374.1336. mp 186–188 °C.

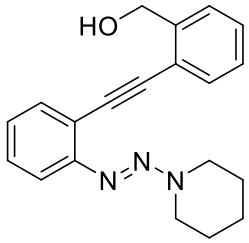
(*E*)-1-((2-Ethynylphenyl)diazenyl)piperidine (53):



Compound **53** was synthesised according to General Procedure C from **(*E*)-1-((2-iodophenyl)diazenyl) piperidine**, the synthesis of which has been reported in our previous work.[13] Intermediate **1-((2-((trimethylsilyl)ethynyl)phenyl)diazenyl)piperidine** (2.3 g, quant.) was obtained as an orange oil after purified by flash column chromatography (49:1 hexanes:EtOAc, R_f = 0.2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (ddd, *J* = 0.4, 1.5, 7.6 Hz, 1H), 7.42 (dd, *J* = 0.8, 8.2 Hz, 1H), 7.25 (ddd, *J* = 1.5, 7.3, 8.2 Hz, 1H), 7.06 (dt, *J* = 1.2, 7.6 Hz, 1H), 3.85 (br s, 4H), 1.72 (br s, 6H), 0.25 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.2, 133.0, 129.0, 124.9, 118.0, 116.7, 103.2, 98.2 24.3, 0.0. HR-ESI (*m/z*) calcd for $C_{16}H_{24}N_3Si^+$ $[M + H]^+$ 286.1734, found 286.1725.

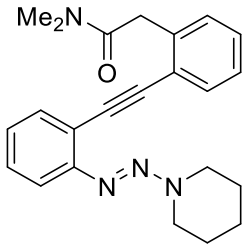
53 (1.6 g, 90% from **52**) was obtained as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (dd, *J* = 1.4, 7.7 Hz, 1H), 7.43 (dd, *J* = 0.8, 8.2 Hz, 1H), 7.29 (ddd, *J* = 1.5, 7.4, 8.2 Hz, 1H), 7.08 (dt, *J* = 1.2, 7.5 Hz, 1H), 3.84 (br s, 4H), 3.27 (s, 1H), 1.72 (br s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.5, 133.6, 129.4, 125.0, 117.1, 116.9, 81.9, 81.0, 24.4.). LCMS (ESI) *m/z*: 214.2 $[M + H]^+$. HR-ESI (*m/z*) calcd for $C_{13}H_{16}N_3^+$ $[M + H]^+$ 214.1339, found 214.1337.

(*E*)-(2-((2-(Piperidin-1-yldiazenyl)phenyl)ethynyl)phenyl)methanol (55a):



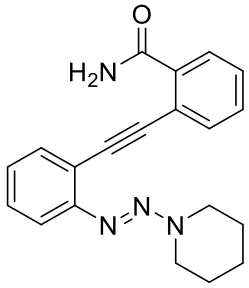
Compound **55a** was synthesised according to General Procedure B. The crude product obtained was purified by flash column chromatography (2:1 hexanes:EtOAc, R_f = 0.45) to yield **55a** (789 mg, 96%) as a pale orange oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.56 (m, 2H), 7.48 (dd, *J* = 0.8, 8.2 Hz, 1H), 7.36 – 7.39 (m, 1H), 7.28 – 7.33 (m, 3H), 7.13 (dt, *J* = 1.2, 7.6 Hz, 1H), 4.85 (d, *J* = 7.0 Hz, 2H), 3.88 (brs, 2H), 3.12 (t, *J* = 7.0 Hz, 1H), 1.72 (br s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.2, 143.0, 132.9, 131.9, 129.3, 128.3, 127.6, 127.5, 125.1, 122.3, 117.5, 117.3, 93.0, 91.1, 64.5, 25.4, 24.2. LCMS (ESI) *m/z*: 320.1 $[M + H]^+$. HR-ESI (*m/z*) calcd for $C_{20}H_{22}N_3O$ $[M + H]^+$ 320.1757, found 320.1757.

(*E*)-*N*,*N*-Dimethyl-2-(2-((2-(piperidin-1-yldiazenyl)phenyl)ethynyl)phenyl)acetamide (55b):



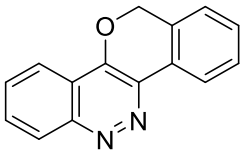
Compound **55b** was synthesised according to General Procedure B. The crude product obtained was purified by flash column chromatography (1:1 hexanes:EtOAc) to yield **55b** (464 mg, 62%) as a brown oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (t, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 8.2 Hz, 1H), 7.39 (d, *J* = 7.7 Hz, 1H), 7.26 – 7.30 (m, 2H), 7.23 (t, *J* = 7.4 Hz, 1H), 7.12 (t, *J* = 7.4 Hz, 1H), 4.09 (s, 2H), 3.85 (br s, 4H), 2.95 (s, 3H), 2.94 (s, 3H), 1.71 (br s, 6H). HR-ESI (*m/z*) calcd for $C_{23}H_{26}N_4ONa^+$ $[M + Na]^+$ 397.1999, found 397.1980.

(*E*)-2-((2-(Piperidin-1-yldiazenyl)phenyl)ethynyl)benzamide (55c):



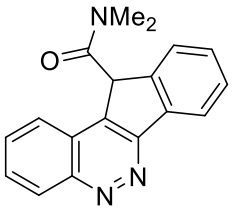
Compound **55c** was synthesised according to General Procedure B. The crude product obtained was purified by flash column chromatography (1:1 hexanes:EtOAc) to yield **55c** (1.03 g, 42%) as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (br s, 1H), 8.25 (m, 1H), 7.62 (m, 1H), 7.55 (dd, *J* = 1.2, 7.7 Hz, 1H), 7.42 – 7.50 (m, 3H), 7.34 (ddd, *J* = 1.5, 7.3, 8.2 Hz, 1H), 7.15 (dt, *J* = 1.2, 7.6 Hz, 1H), 5.85 (br s, 1H), 3.84 (br s, 4H), 1.72 (br s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 152.4, 133.43, 133.38, 132.8, 131.1, 130.9, 130.0, 128.5, 125.3, 120.9, 117.3, 116.8, 95.1, 92.0, 24.2. HR-ESI (*m/z*) calcd for $C_{20}H_{21}N_4O^+$ $[M + H]^+$ 333.1710, found 333.1711.

12*H*-Isochromeno[4,3-*c*]cinnoline (56a):



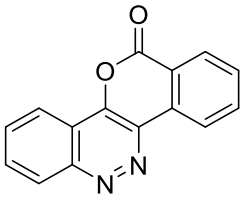
55a (350 mg, 1.09 mmol) was dissolved in CH_2Cl_2 (10 mL), followed by addition of HCl (2.74 mL, 1 M in Et_2O) solution. The reaction mixture was left to stir at rt for 1 h. On completion, the reaction was quenched by saturated $NaHCO_3$ solution (10 mL), and extracted with CH_2Cl_2 (2 x 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product obtained was purified by flash column chromatography (4:1 hexanes:EtOAc, , R_f = 0.25) to yield **56a** (226 mg, 88%) as a pale orange solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, *J* = 5.2 Hz, 1H), 8.42 (d, *J* = 5.7 Hz, 1H), 8.12 (d, *J* = 5.6 Hz, 1H), 7.76 (t, *J* = 5.5 Hz, 1H), 7.66 (t, *J* = 5.3 Hz, 1H), 7.51 (t, *J* = 5.0 Hz, 1H), 7.41 (t, *J* = 5.0 Hz, 1H), 7.17 (d, *J* = 5.0 Hz, 1H), 5.52 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.3, 148.0, 137.5, 130.4, 129.9, 129.61, 129.57, 129.4, 129.2, 128.5, 124.2, 123.0, 120.8, 117.9, 69.1. LCMS (ESI) *m/z*: 235.1 $[M + H]^+$. HR-ESI (*m/z*) calcd for $C_{15}H_{11}N_2O^+$ $[M + H]^+$ 235.0866, found 235.0851. mp 165–167 °C.

***N*,*N*-Dimethyl-11*H*-indeno[1,2-*c*]cinnoline-11-carboxamide (56b):**



55b (374 mg, 1 mmol) was dissolved in CH_2Cl_2 (10 mL) at 0 ºC, followed by addition of $MeSO_3H$ (5 mmol). The reaction mixture was left to stir at rt for 72 h. On completion, the mixture was quenched by saturated $NaHCO_3$ solution (10 mL) and extracted with CH_2Cl_2 (2 x 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product obtained was purified by flash column chromatography (3:1 hexanes:EtOAc) to yield **56b** (234 mg, 81%) as a yellow amorphous solid. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 10.52 (d, *J* = 8.5 Hz, 1H), 8.56 (d, *J* = 8.3 Hz, 1H), 8.01 (d, *J* = 8.6 Hz, 1H), 7.76 – 7.79 (m, 2H), 7.68 – 7.74 (m, 2H), 7.50 (dd, *J* = 7.2, 8.2 Hz, 1H), 7.37 (s, 1H), 3.16 (s, 6H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 172.3, 149.6, 146.4, 132.6, 129.5, 129.2, 128.2, 127.4, 125.84, 125.79, 125.5, 125.4, 124.5, 111.4, 43.4. HR-ESI (*m/z*) calcd for $C_{18}H_{15}N_3ONa^+$ $[M + Na]^+$ 312.1107, found 312.1094.

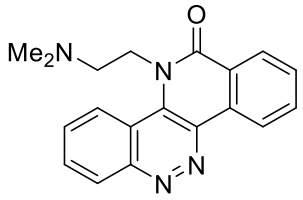
Isoquinolino[4,3-*c*]cinnolin-12(11*H*)-one (56c):



55c (900 mg, 2.71 mmol) was dissolved in CH_2Cl_2 (10 mL) at 0 °C, followed by addition of $MeSO_3H$ (906 mg, 9.22 mmol). The reaction mixture was allowed to warm to rt and left to stir for 72 h. After this time, saturated $NaHCO_3$ solution (15 mL) was added, followed by another 0.5 h stirring and extraction with CH_2Cl_2 (2 × 15 mL). The combined organic extracts were dried over $MgSO_4$, filtered through a silica plug, and evaporated *in vacuo* to afford the title compound as a bright yellow solid (524 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 – 8.53 (m, 1H), 8.32 – 8.34 (m, 1H), 8.25 – 8.28 (m, 1H), 7.85 – 7.94 (m, 3H), 7.43 – 7.50 (m,

2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 157.8, 151.3, 135.5, 134.5, 133.6, 131.5, 130.7, 130.4, 129.9, 128.6, 127.2, 123.8, 122.2, 120.6. LCMS (ESI) *m/z*: 249.1 $[M + H]^+$. HR-ESI (*m/z*) calcd for $C_{15}H_9N_2O_2^+$ $[M + H]^+$ 249.0659, found 249.0660. mp 273–274 °C.

11-(2-(Dimethylamino)ethyl)isoquinolino[4,3-*c*]cinnolin-12(11*H*)-one (56d):

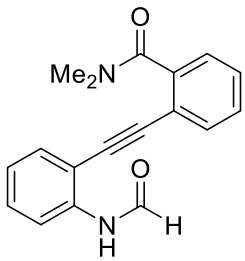


Compound **55d** was synthesised according to General Procedure B. The crude product obtained was purified by flash column chromatography (19:1 hexanes:EtOAc → 9:1 hexanes:EtOAc) to yield **55d** (1.08 g, 91%) which was directly used in the next step without characterisation.

55d (235 mg, 680 µmol) and tetraethylammonium chloride (224 mg, 1.35 mmol) were dissolved in CH_2Cl_2 (5 mL) at rt, followed by addition of $MeSO_3H$ (1 M in CH_2Cl_2, 2.03 mL). The reaction mixture was left to stir at rt for 2 h, then quenched with H_2O (10 mL) and extracted with CH_2Cl_2 (3 x 5 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated under reduced pressure to yield **57**.

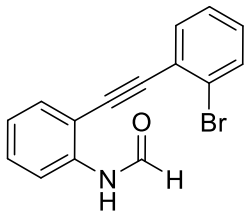
57 (100 mg, 0.33 mmol) was dissolved in CH_3CN (2 mL), followed by addition of DMD (148 mg, 1.67 mmol). The reaction mixture was heated at 120 °C in the microwave for 1 h. After heating, the mixture was cooled down to rt, concentrated and purified by flash column chromatography (9:1 $CHCl_3$:MeOH, R_f = 0.25) to yield **56d** (101 mg, 95% from **55d**) as a beige amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.20 (dd, *J* = 0.6, 8.2 Hz, 1H), 8.56 – 8.62 (m, 2H), 8.42 (ddd, *J* = 0.5, 1.3, 8.0 Hz, 1H), 7.76 – 7.91 (m, 3H), 7.69 (ddd, *J* = 1.2, 7.2, 8.1 Hz, 1H), 4.68 (t, *J* = 7.2 Hz, 2H), 3.00 (t, *J* = 7.2 Hz, 2H), 2.36 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 150.1, 133.6, 131.2, 130.4, 129.92, 129.88, 127.8, 123.9, 123.6, 115.8, 57.2, 47.4, 45.9. LCMS (ESI) *m/z*: 319.1 $[M + H]^+$. HR-ESI (*m/z*) calcd for $C_{19}H_{19}N_4O^+$ $[M + H]^+$ 319.1553, found 319.1556. mp 179–183 °C. The spectroscopic data are consistent with those previously reported in the literature.[14]

2-((2-Formamidophenyl)ethynyl)-*N*,*N*-dimethylbenzamide (60a):



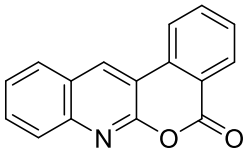
Compound **60a** was synthesised according to General Procedure A. The crude product (466 mg, brown oil) obtained was purified by flash column chromatography (10:1 CH_2Cl_2:EtOAc, R_f = 0.2) to yield **60a** (337 mg, 67%) an orange oil. ^{1}H NMR (401 MHz, $CDCl_3$) δ 9.02 (s, 1H), 8.71 (d, *J* = 2.0 Hz, 1H), 8.55 (dd, *J* = 8.4, 1.1 Hz, 1H), 7.62 (dd, *J* = 6.7, 1.8 Hz, 1H), 7.45 (dd, *J* = 7.8, 1.5 Hz, 2H), 7.46 – 7.34 (m, 4H), 7.37 – 7.27 (m, 2H), 7.06 (td, *J* = 7.6, 1.2 Hz, 1H), 3.13 (s, 3H), 2.92 (s, 3H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 171.1 (C), 160.7 (CH), 140.3 (C), 138.4 (C), 132.2 (CH), 131.1 (CH), 130.1 (CH), 129.5 (CH), 128.4 (CH), 126.3 (CH), 123.4 (CH), 120.9 (C) 119.9 (CH), 111.4 (C), 93.9 (C), 89.2 (C), 39.4 (CH_3), 35.4 (CH_3). LCMS (ESI) *m/z* (%): *t* = 2.8 min, 293.1 (100, $M + H^+$). HPLC: PP gradient method, t_R = 5.0 min, 97.8 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{18}H_{17}N_2O_2^+$ $[M + H]^+$ 293.1285, found 293.1294.

***N*-(2-((2-Bromophenyl)ethynyl)phenyl)formamide (60b):**



Compound **60b** was synthesised according to General Procedure A. The crude product (1.86 g) obtained was purified by flash column chromatography twice (4:1 hexanes:EtOAc, R_f = 0.2; 1:1 hexanes:CH_2Cl_2) to yield **60b** (711 mg, 66%) as a grey amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (d, *J* = 11.2 Hz, 1H), 8.51 (d, *J* = 1.7 Hz, 1H), 8.48 (d, *J* = 8.0 Hz, 1H), 8.43 (br s, 1H), 8.32 (br s, 1H), 7.66-7.63 (m, 2H), 7.61-7.56 (app td, *J* = 8.4, 1.6 Hz, 3H), 7.53 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.41-7.27 (m, 5H), 7.26-7.20 (m, 2H), 7.16 (d, *J* = 8.2 Hz, 1H), 7.12 (td, *J* = 7.6, 1.1 Hz, 1H). This compound appears as a pair of rotamers (ratio = 0.36 : 1) in the ^{1}H NMR spectrum. LCMS (ESI) *m/z* (%): *t* = 3.6 min, 299.8 (60, M + H^+), 301.8 (50, M + H^+). HPLC: PP gradient method, t_R = 6.9 min, 97.9 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{15}H_{11}BrNO^+$ [M + H]$^+$ 300.0019, found 300.0008.

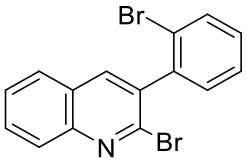
5*H*-Isochromeno[3,4-*b*]quinolin-5-one (67):



60a (100 mg, 342 µmol) was dissolved in dry CH_2Cl_2 (5 mL) in a dry RBF. The RBF was degassed and backfilled with N_2(g) for three times. Burgess reagent (122.3 mg, 513 µmol) was added under N_2(g) atmosphere, the reaction mixture was left to stir at rt for 22 h. After this time, the reaction was heated at reflux for 3 h, then cooled down to rt and dilutaed with CH_2Cl_2 (20 mL). The organic extract was washed with H_2O (2 x 20 mL), dried over $MgSO_4$, filtered concentrated to about 5 mL in volume. **61a** obtained obtained in the organic phase was directly used without isolation as *o*-alkynylaryl isocyanides are usually quite unstable.[15]

$MeSO_3H$ (32.9 mg, 0.22 mL, 342 µmol) was added slowly to a stirred solution of **61a** in CH_2Cl_2 (5 mL) under N_2(g) atmosphere. The reaction mixture was left to stir at rt for 14 h. On completion, the reaction mixture was diluted with H_2O (25 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic extracts were washed dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product (brown oil) was purified by flash column chromatography (7:3 hexanes:EtOAc) to yield **63** (18 mg, 21% from **60a**) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (s, 1H), 8.44 (dd, *J* = 8.0, 1.4 Hz, 1H), 8.27 (d, *J* = 8.0 Hz, 1H), 8.06 (d, *J* = 8.5 Hz, 1H), 7.96 (d, *J* = 8.1 Hz, 1H), 7.89 (ddd, *J* = 8.1, 7.3, 1.4 Hz, 1H), 7.78 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.65 (ddd, *J* = 8.1, 7.3, 1.0 Hz, 1H), 7.58 (ddd, *J* = 7.9, 6.8, 0.9 Hz, 1H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 160.6 (C), 155.0 (C), 146.8 (C), 135.3 (CH), 133.5 (C), 132.9 (CH), 131.6 (CH), 131.2 (CH), 130.0 (CH), 128.6 (CH), 128.1 (CH), 126.7 (CH), 126.6 (C), 122.3 (CH), 121.8 (C), 113.9 (C). LCMS (ESI) m/z (%): *t* = 3.6 min, 248.1 (100, M + H^+). HPLC: PP gradient method, t_R = 5.0 min, 96.1% purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{16}H_{10}NO_2^+$ [M + H]$^+$ 248.0706, found 248.0705. The spectroscopic data are consistent with those previously reported in the literature.[16]

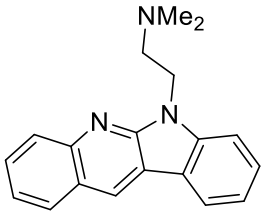
2-Bromo-3-(2-bromophenyl)quinoline (69):



60b (200 mg, 0.67 mmol) and DIPEA (0.75 mL, 5.33 mmol,) were dissolved in CH_2Cl_2 (4.5 mL), followed by dropwise addition of $POCl_3$ (96 µL) under N_2(g) atmosphere at –78 °C. The reaction mixture was left to stir at 0 °C for 2 h. On completion, reaction mixture was diluted with CH_2Cl_2 (15 mL) and washed with saturated $NaHCO_3$(aq) solution (2 x 15 mL). The organic extract was dried over anhydrous $MgSO_4$, filtered and concentrated to about 5 mL in volume. **61b** obtained in the organic phase was directly used without isolation as *o*-alkynylaryl isocyanides are usually quite unstable.[15]

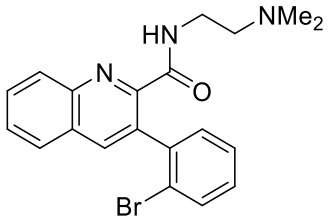
TBAB (644 mg, 2.00 mmol) was added slowly to a stirred solution of **61b** in CH_2Cl_2 (12 mL) under N_2(g) atmosphere. The reaction mixture was left to stir at rt for 17 h. On completion, the reaction mixture was concentrated under reduced pressure, diluted with H_2O (50 mL) and extracted with EtOAc (2 x 50 mL). The combined organic extracts were washed with H_2O (2 x 75 mL) and brine (2 x 50 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product (415 mg) was purified by flash column chromatography (2:1 CH_2Cl_2:hexanes, R_f = 0.4) to yield **69** (173 mg, 72% from **60b**) as an off-white amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.6 Hz, 1H), 8.02 (s, 1H), 7.84 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.78 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H), 7.72 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.62 (ddd, *J* = 8.1, 7.0, 1.2 Hz, 1H), 7.44 (ddd, *J* = 7.5, 7.0, 1.4 Hz, 1H), 7.36-7.32 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.9 (C), 143.0 (C), 140.0 (C), 138.4 (CH), 136.5 (C), 132.9 (CH), 131.4 (CH), 130.8 (CH), 130.2 (CH), 128.6 (CH), 127.9 (CH), 127.6 (CH), 127.5 (CH), 127.0 (C), 124.1 (C). LCMS (ESI) *m/z* (%): *t* = 3.7 min, 363.8 (100, M + H$^+$), 365.8 (50, M + H$^+$). HPLC: PP gradient method, t_R = 7.3 min, 90.4 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{15}H_{10}Br_2N^+$ [M + H]$^+$ 363.9155; found 363.9167.

2-(6*H*-Indolo[2,3-*b*]quinolin-6-yl)-*N*,*N*-dimethylethan-1-amine (70):



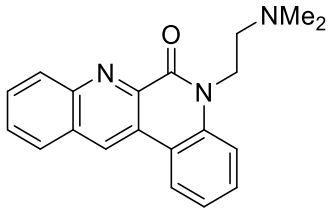
Compound **70** was synthesised according to General UCC Procedure.. The crude product (76 mg) obtained was purified by flash column chromatography (4:1 EtOAc:MeOH, R_f = 0.33) to yield **70** (31 mg, 52%) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 1H), 8.16 (d, *J* = 7.7 Hz, 1H), 8.12 (d, *J* = 8.6 Hz, 1H), 8.01 (d, *J* = 8.2 Hz, 1H), 7.71 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H), 7.61-7.52 (m, 2H), 7.46 (ddd, *J* = 8.0, 6.9, 1.1 Hz, 1H), 7.31 (t, *J* = 8.0 Hz, 1H), 4.72 (t, *J* = 7.2 Hz, 2H), 2.94 (app br s, 2H), 2.47 (s, 6H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 152.6 (C), 147.0 (C), 142.3 (C), 128.9 (CH), 128.6 (CH), 128.2 (CH), 127.9 (CH), 127.4 (CH), 124.4 (C), 123.1 (CH), 121.7 (CH), 120.8 (C), 120.1 (CH), 118.3 (CH), 109.1 (C), 57.2 (CH_2), 45.9 (CH_3), 39.9 (CH_2). LCMS (ESI) *m/z* (%): *t* = 3.0 min, 290.1 (100, M + H$^+$), 291.1 (20, M + H$^+$). HPLC: PP gradient method, t_R = 5.3 min, 96.6 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{19}H_{19}N_3^+$ [M + H]$^+$ 290.1652, found 290.1656.

3-(2-Bromophenyl)-*N*-(2-(dimethylamino)ethyl)quinoline-2-carboxamide:



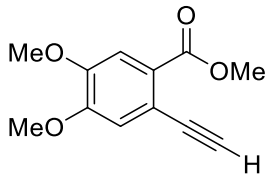
68 (99 mg, 0.27 mmol), $Pd(OAc)_2$ (6.1 mg, 27 µmmol), PPh_3 (107 mg, 0.41 mmol), DMD (0.45 mL, 4.1 mmol), Et_3N (50 µL, 0.55 mmol) and dry NMP (2 mL) were added to a 25 mL dry RBF. The RBF was degassed and backfilled with CO(g) for three times, and then heated at 80 °C for 40 h. On completion, the reaction mixture was cooled down to rt and extracted with EtOAc (2 x 15 mL). The combined organic extracts were washed with H_2O (3 x 50 mL), saturated NH_4Cl solution (2 x 50 mL), and brine (2 x 50 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product (182 mg) obtained was purified by flash column chromatography (100 % EtOAc, R_f = 0 → 2:1 EtOAc:MeOH, R_f = 0.4). The title compound (63 mg, 58%) was obtained as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (br s, 1H), 8.20 (d, *J* = 8.5 Hz, 1H), 8.06 (s, 1H), 7.87 (d, *J* = 8.5 Hz, 1H), 7.80 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.67-7.63 (m, 2H), 7.42 (td, *J* = 7.5, 1.2 Hz, 1H), 7.36 (dd, *J* = 7.6, 1.9 Hz, 1H), 7.29 – 7.23 (m, 1H), 3.59-3.51 (m, 2H), 2.60 (t, *J* = 6.1 Hz, 2H), 2.34 (s, 6H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 164.9 (C), 148.8 (C), 146.0 (C), 141.3 (C), 139.2, 134.2 (C), 132.2 (CH), 130.4 (CH), 130.1 (CH), 129.8 (CH), 129.0 (CH), 128.6 (C), 128.4 (CH), 127.7 (CH), 127.3 (CH), 123.5 (C), 58.4 (CH_2), 45.5 (CH_3), 37.3 (CH_2). LCMS (ESI) *m/z* (%): *t* = 3.2 min, 399.9 (100, M + H^+), 400.9 (20, M + H^+). HPLC: PP gradient method, t_R = 5.3 min, 92.5 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{20}H_{21}BrN_3O^+$ [M + H]$^+$ 398.0863, found 398.0871.

5-(2-(Dimethylamino)ethyl)dibenzo[*b,f*][1,7]naphthyridin-6(5*H*)-one (71):



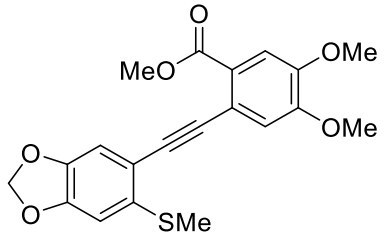
3-(2-Bromophenyl)-*N*-(2-(dimethylamino)ethyl)quinoline-2-carboxamide (34 mg, 85 µmol) was dissolved in *n*-butanol (0.85 mL) in a dry RBF, and CuI (6.5 mg, 34 µmol), K_3PO_4 (72 mg, 0.34 mmol), ethylene glycol (57 µL, 1.02 mmol), and TMD(30 µL, 0.17 mmol) were added sequentially. The RBF was degassed and backfilled with N_2(g) for three times, the reaction mixture was heated at 80 °C for 22 h. After heating, the reaction mixture was cooled down to rt, diluted with H_2O (15 mL) and extracted with EtOAc (2 x 15 mL). The combined organic extracts were washed with H_2O (2 x 20 mL) and brine (2 x 20 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product (29 mg) obtained was purified by flash column chromatography (100 % EtOAc → 100 % MeOH, R_f = 0.5) to yield **69** (15 mg, 56%) as a transparent oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (s, 1H), 8.45 (d, *J* = 8.6 Hz, 1H), 8.37 (dd, *J* = 8.0, 1.4 Hz, 1H), 8.00 (d, *J* = 8.2 Hz, 1H), 7.80 (ddd, *J* = 8.5, 6.8, 1.4 Hz, 1H), 7.67 (ddd, *J* = 8.1, 6.8, 1.1 Hz, 1H), 7.58 (ddd, *J* = 8.5, 7.2, 1.4 Hz, 1H), 7.49 (d, *J* = 7.9 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 4.60 (app t, *J* = 7.6 Hz, 2H), 2.75 (app t, *J* = 7.8 Hz, 2H), 2.42 (s, 6H). ^{13}C DEPT-Q NMR (101 MHz, $CDCl_3$) δ 160.2 (C), 148.6 (C), 142.0 (C), 136.9 (C), 131.2 (CH), 130.7 (CH), 130.4 (CH), 130.2 (CH), 129.3 (C), 128.8 (CH), 127.8 (CH), 126.5 (C), 123.9 (CH), 123.0 (CH), 118.5 (C), 115.4 (CH), 56.1 (CH_2), 46.1 (CH_3), 41.7 (CH_2). LCMS (ESI) *m/z* (%): *t* = 3.1 min, 318.0 (100, M + H^+), 319.0 (20, M + H^+). HPLC: PP gradient method, t_R = 4.7 min, 94.6 % purity at 254 nm. HR-ESI (*m/z*) calcd for $C_{20}H_{20}N_3O^+$ [M + H]$^+$ 318.1601, found 318.1610.

Methyl 2-ethynyl-4,5-dimethoxybenzoate (73):



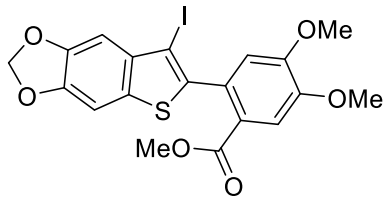
Compound **73** was synthesised according to General Procedure C. **73** (1.05 g, 93%) was obtained as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (s, 1H), 7.00 (s, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.87 (s, 3H), 3.31 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 151.5, 148.9, 125.1, 116.6, 116.3, 112.6, 82.3, 80.9, 56.1, 56.0, 52.0. LCMS (ESI) *m/z* : 221.1 $[M + H]^+$. HR-ESI (*m/z*) calcd for $C_{12}H_{13}O_4^+$ $[M + H]^+$ 221.0808, found 221.0808.

Methyl 4,5-dimethoxy-2-((6-(methylthio)benzo[*d*][1,3]dioxol-5-yl)ethynyl)benzoate (74):



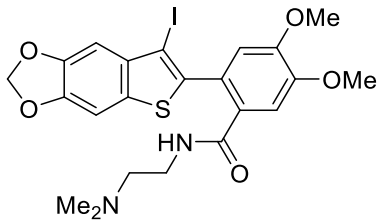
72 (250 mg, 850 µmol) was dissolved in Et_3N (2 mL) and DMF (2 mL) in a dry RBF, followed by addition of $Pd(PPh_3)_2Cl_2$ (18 mg, 26 µmol) and CuI (13 mg, 68 µmol). The RBF was then degassed and backfilled with N_2(g) for three times. Finally, **73** (225 mg, 1.02 mmol) was slowly added under N_2(g) atmosphere over a period of 2 h. The reaction was left to stir at rt for 16 h. On completion, the reaction mixture was filtered through Celite®, rinsed with EtOAc (40 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product obtained was purified by flash column chromatography (4:1 hexanes:EtOAc) to yield **74** (291 mg, 89%) as a pale oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.10 (s, 1H), 7.01 (s, 1H), 6.75 (s, 1H), 5.98 (s, 2H), 3.95 (s, 3H), 3.94 (s, 6H), 2.49 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.0, 139.1, 128.7, 127.0, 117.6, 96.7, 52.6, 45.6, 24.4. LCMS (ESI) *m/z*: 387.0 $[M + H]^+$. HR-ESI (*m/z*) calcd for $C_{20}H_{19}O_6S^+$ $[M + H]^+$ 387.0897, found 387.0901. mp 184.2 − 184.9 °C.

Methyl 2-(7-iodothieno[2',3':4,5]benzo[1,2-*d*][1,3]dioxol-6-yl)-4,5-dimethoxybenzoate (75):



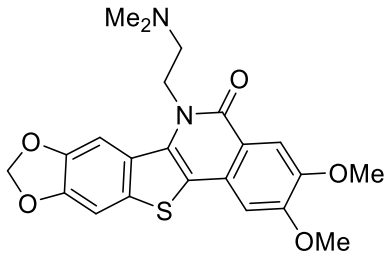
Compound **75** was synthesised according to General Procedure D. The crude product obtained was purified by flash column chromatography (3:1 hexanes:EtOAc) to yield **75** (414 mg, 94%) as a pale brown amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.18 (s, 1H), 7.16 (s, 1H), 6.04 (s, 1H), 3.99 (s, 3H), 3.92 (s, 3H), 3.65 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 151.3, 149.0, 147.5, 147.3, 140.6, 135.9, 132.6, 129.6, 123.6, 114.8, 113.0, 105.0, 101.6, 101.2, 81.4, 56.22, 56.16, 52.2. LCMS (ESI) *m/z*: 498.9 $[M + H]^+$. HR-ESI (*m/z*) calcd for $C_{19}H_{16}O_6SI^+$ $[M + H]^+$ 498.9707, found 498.9699.

***N*-(2-(Dimethylamino)ethyl)-2-(7-iodothieno[2',3':4,5]benzo[1,2-*d*][1,3]dioxol-6-yl)-4,5-dimethoxybenzamide (76):**



75 (200 mg, 0.40 mmol) was dissolved in DMSO (8 mL), followed by addition of KOH (2 M, 4 mL). The reaction mixture was left to stir at rt for 16 h. After stirring, the solution was acidified to pH 3 (using 1M HCl) and extracted with EtOAc (3 x 10 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to afford the carboxylic acid. The acid was dissolved in dry CH_2Cl_2 (10 mL) and cooled to 0 °C, followed by addition of DMF (2 drops) and oxalyl chloride (102 mg, 0.80 mmol). The solution was left to stir at rt for 3 h. After this time the reaction mixture was concentrated under reduced pressure, then redissolved in dry CH_2Cl_2 (10 mL) followed by addition of *N*,*N*-dimethylethylenediamine (106 mg, 1.2 mmol). The reaction mixture was left to stir at rt for 2 h. On completion, the mixture was quenched with H_2O (20 mL) and extracted with CH_2Cl_2 (2 x 15 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to afford **76** as a pale brown amorphous solid (205 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (s, 1H), 7.19 (s, 1H), 7.15 (s, 1H), 6.77 (s, 1H), 6.29 (br s, 1H), 6.04 (s, 2H), 3.95 (s, 3H), 3.88 (s, 3H), 3.15 – 3.19 (m, 2H), 1.98 (t, *J* = 5.9 Hz, 2H), 1.65 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 148.9, 148.5, 146.7, 146.7, 138.3, 135.2, 132.3, 128.0, 127.2, 123.9, 113.3, 111.3, 104.1, 100.7, 100.2, 82.1, 55.6, 55.2, 55.1, 43.4, 36.3. LCMS (ESI) *m/z*: 555.1 $[M + H]^+$. HR-ESI (*m/z*) calcd for $C_{22}H_{24}N_2O_5SI^+$ $[M + H]^+$ 555.0445, found 555.0448.

6-(2-(Dimethylamino)ethyl)-2,3-dimethoxy-[1,3]dioxolo[4'',5'':4',5']benzo[1',2':4,5]thieno[3,2-*c*]isoquinolin-5(6*H*)-one (77):



A sealed tube containing **76** (200 mg, 360 µmol), $Pd_2(dba)_3$ (8 mg, 8.7 µmol), Xantphos (10 mg, 17 µmol) and Cs_2CO_3 (353 mg, 1.1 mmol) in 1,4-dioxane (3 mL) was heated to 120 °C for 16 h. After heating, the reaction mixture was cooled to rt, filtered and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography (1:9 MeOH:$CHCl_3$) to yield **77** as a pale brown solid (78 mg, 51%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.75 (s, 1H), 7.17 (s, 1H), 6.85 (s, 1H), 6.07 (s, 2H), 4.47 (t, *J* = 8.0 Hz, 2H), 4.03 (s, 3H), 4.00 (s, 3H), 2.79 (t, *J* = 8.0 Hz, 2H), 2.42 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.7, 153.7, 149.3, 147.6, 147.0, 132.1, 132.0, 127.7, 124.8, 117.1, 116.3, 108.9, 102.8, 102.6, 102.4, 101.9, 57.1, 56.23, 56.17, 45.9, 43.2. LCMS (ESI) *m/z*: 427.0 $[M + H]^+$. HR-ESI (*m/z*) calcd for $C_{22}H_{23}N_2O_5S^+$ $[M + H]^+$ 427.1322, found 427.1328. mp 263.8 − 266.9 °C.

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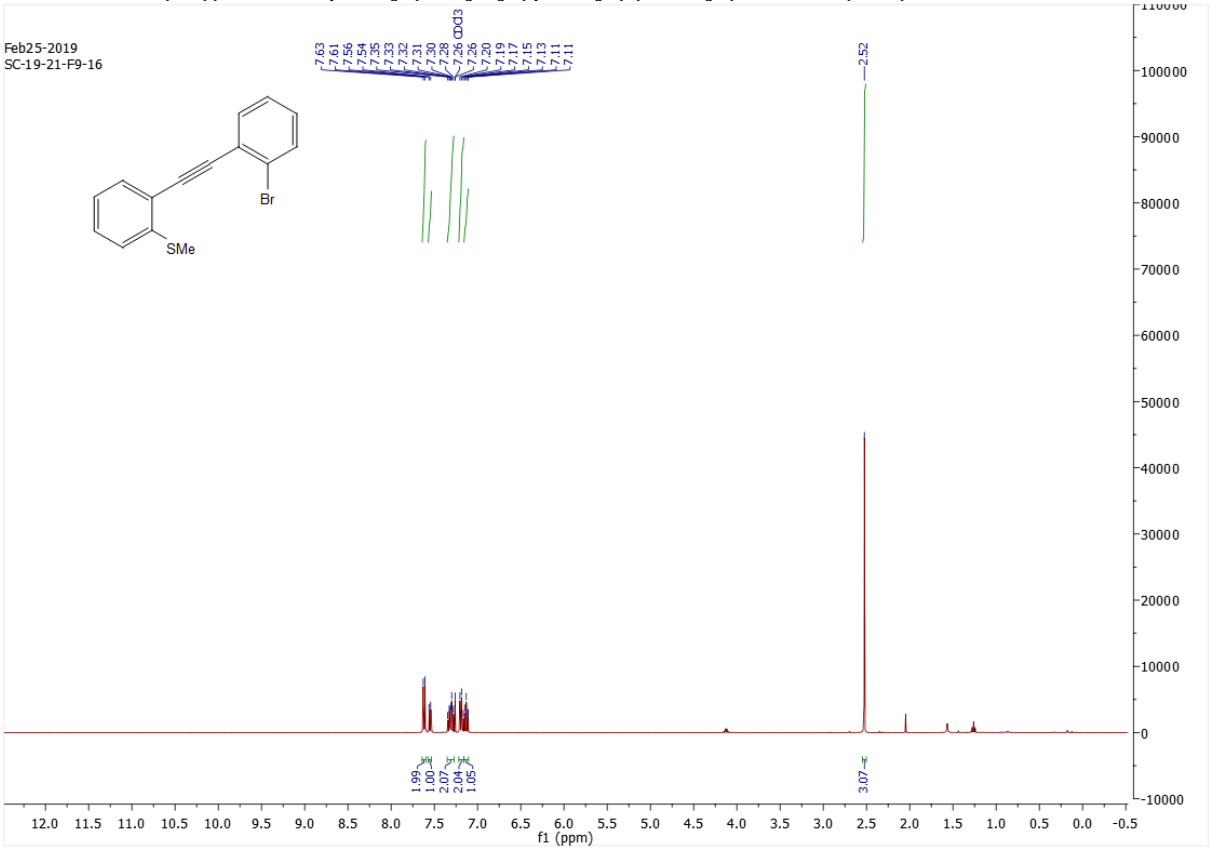
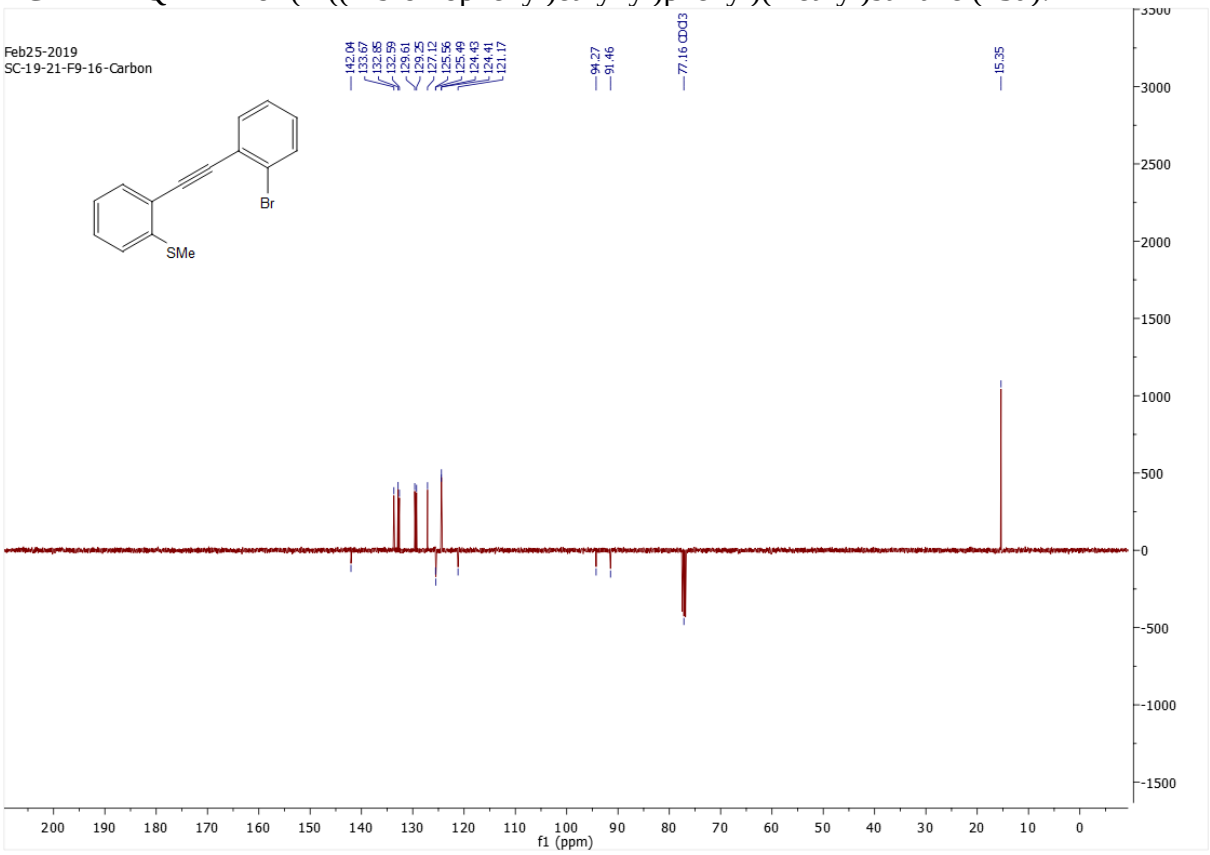
NMR spectra of the synthesized compounds

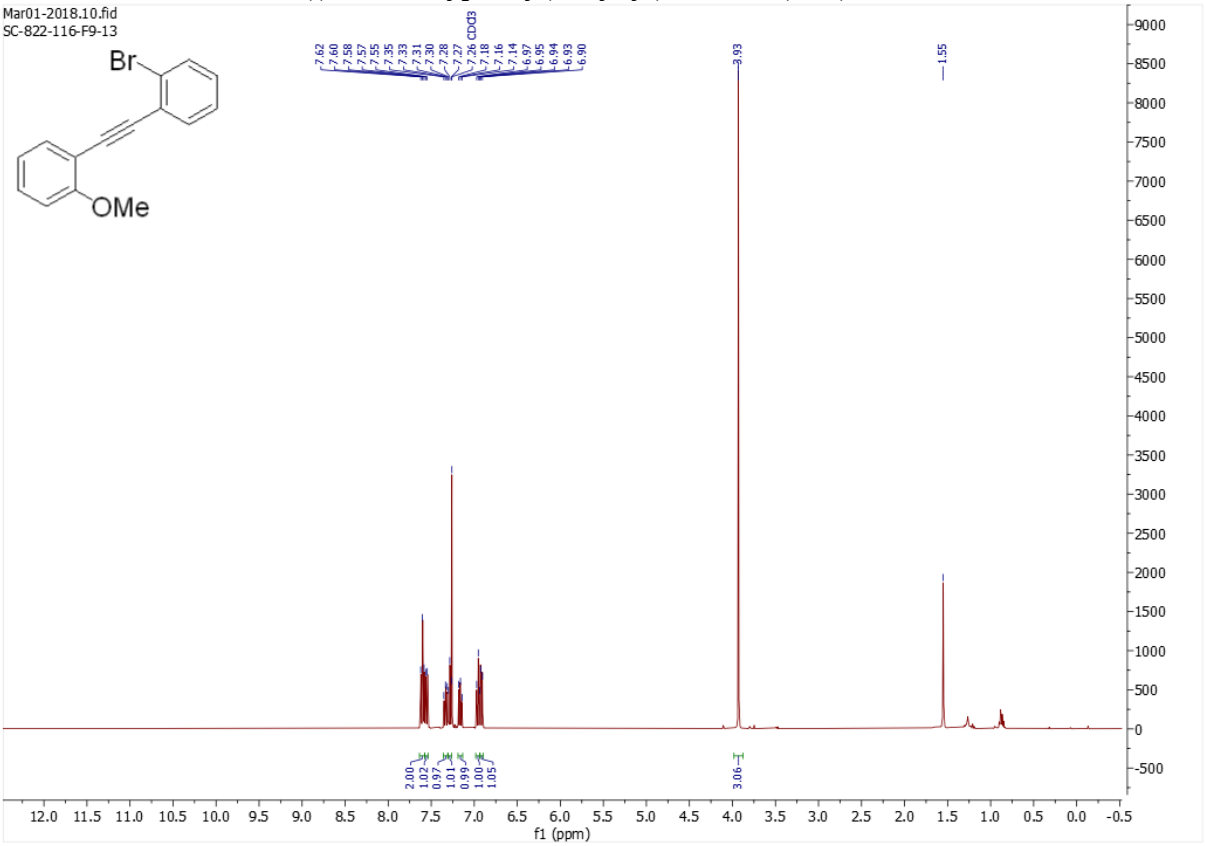
^{1}H NMR of (2-((2-bromophenyl)ethynyl)phenyl)(methyl)sulfane (**13a**):



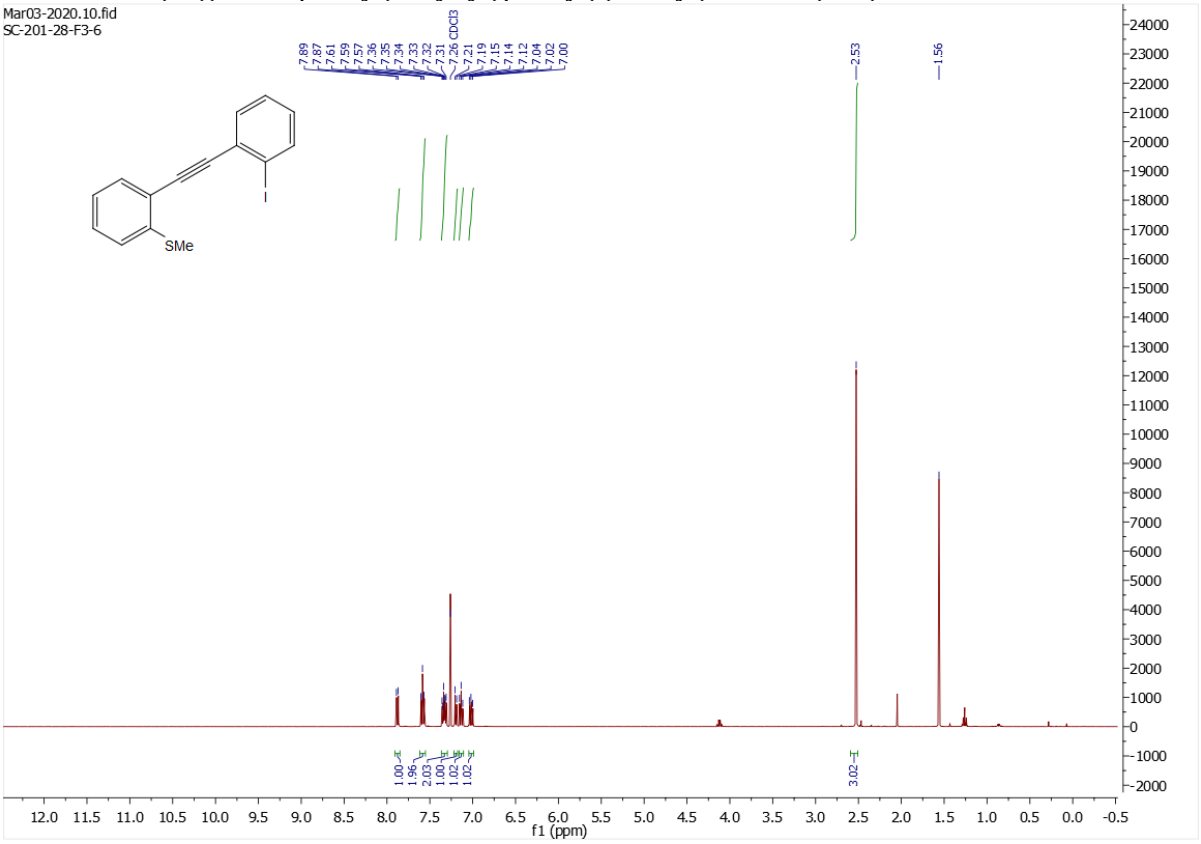
^{13}C DEPT-Q NMR of (2-((2-bromophenyl)ethynyl)phenyl)(methyl)sulfane (**13a**):



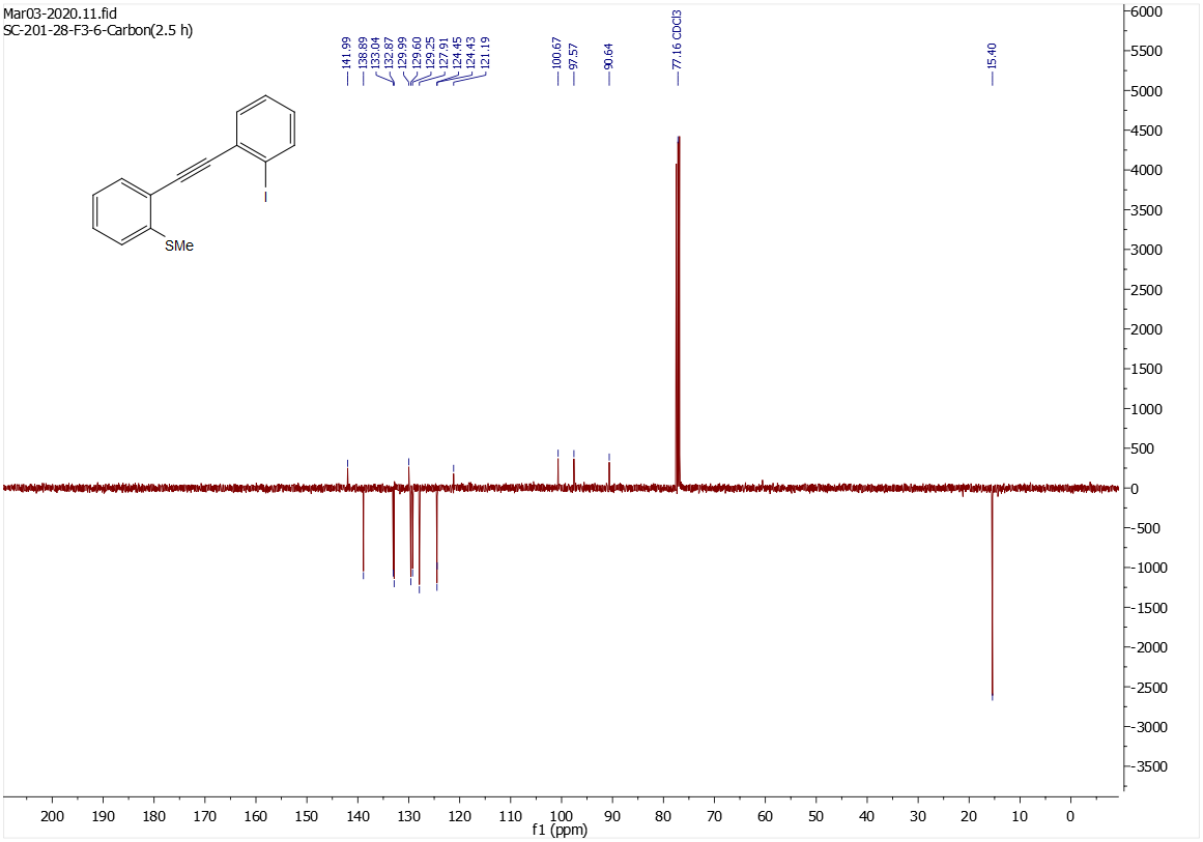
^{1}H NMR of 1-bromo-2-((2-methoxyphenyl)ethynyl)benzene (**13b**):



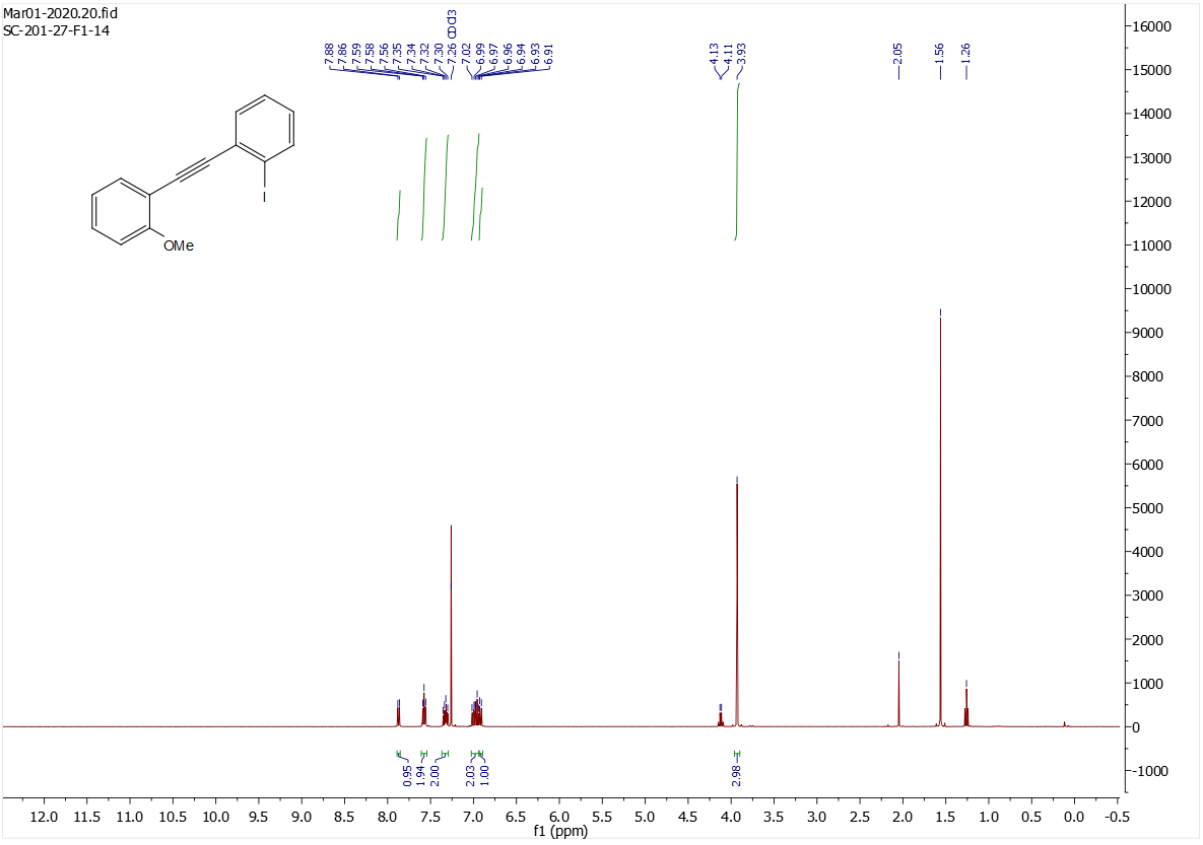
^{1}H NMR of (2-((2-iodophenyl)ethynyl)phenyl)(methyl)sulfane (**14a**):



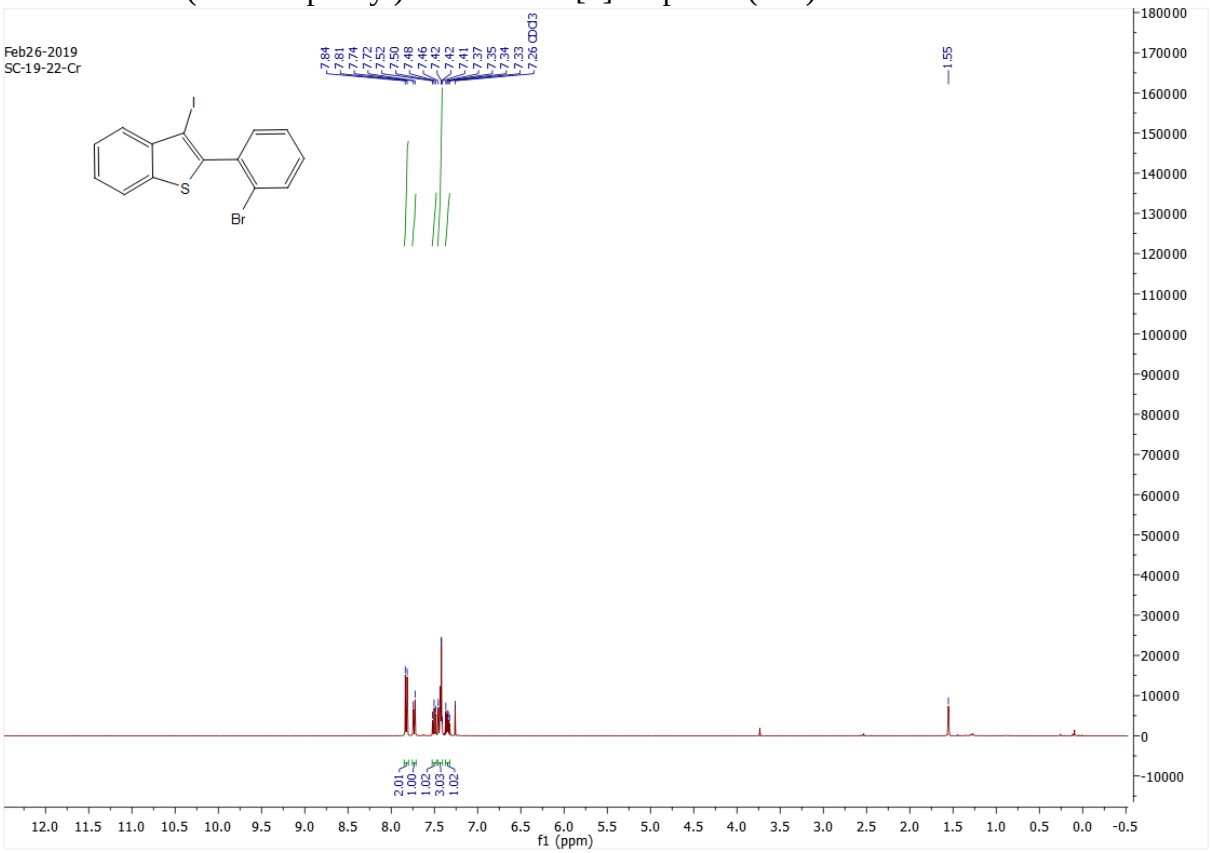
^{13}C DEPT-Q NMR of (2-((2-iodophenyl)ethynyl)phenyl)(methyl)sulfane (**14a**):



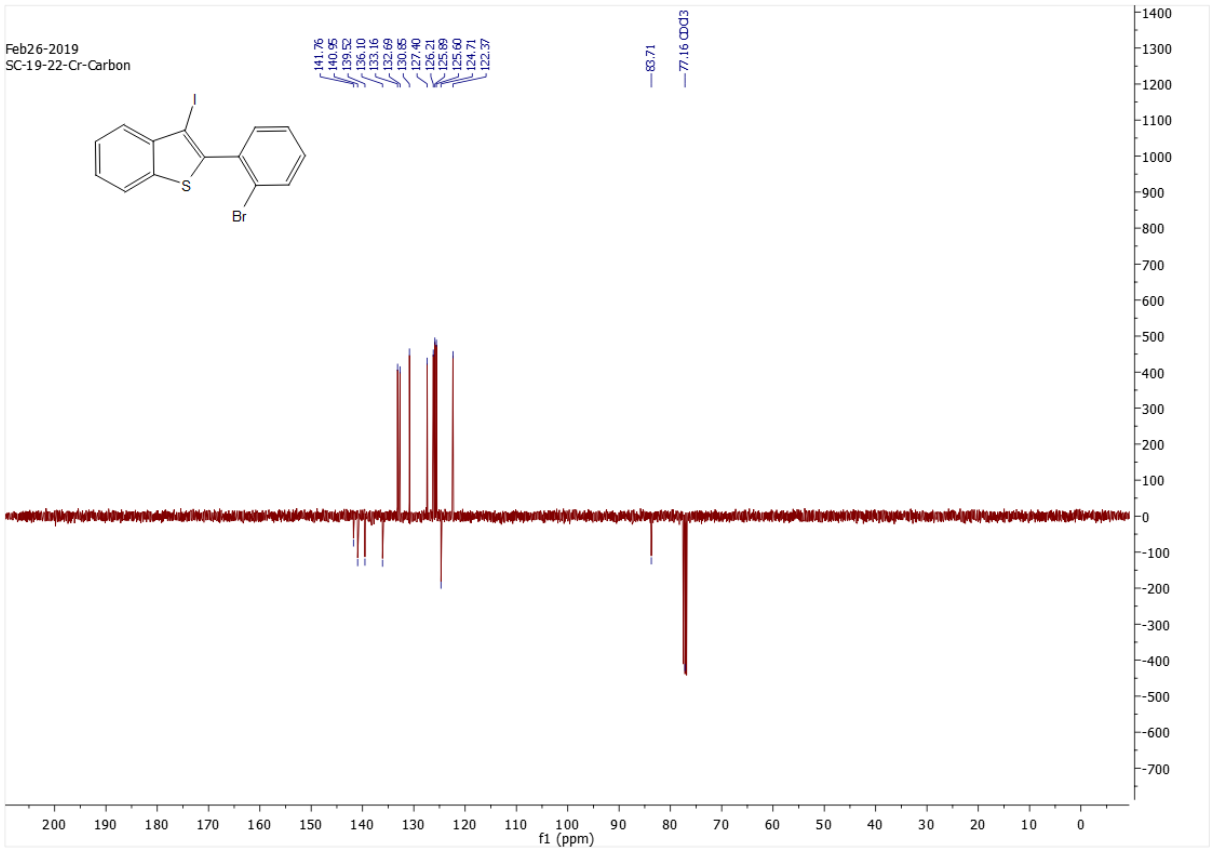
^{1}H NMR of 1-Iodo-2-((2-methoxyphenyl)ethynyl)benzene (**14b**):



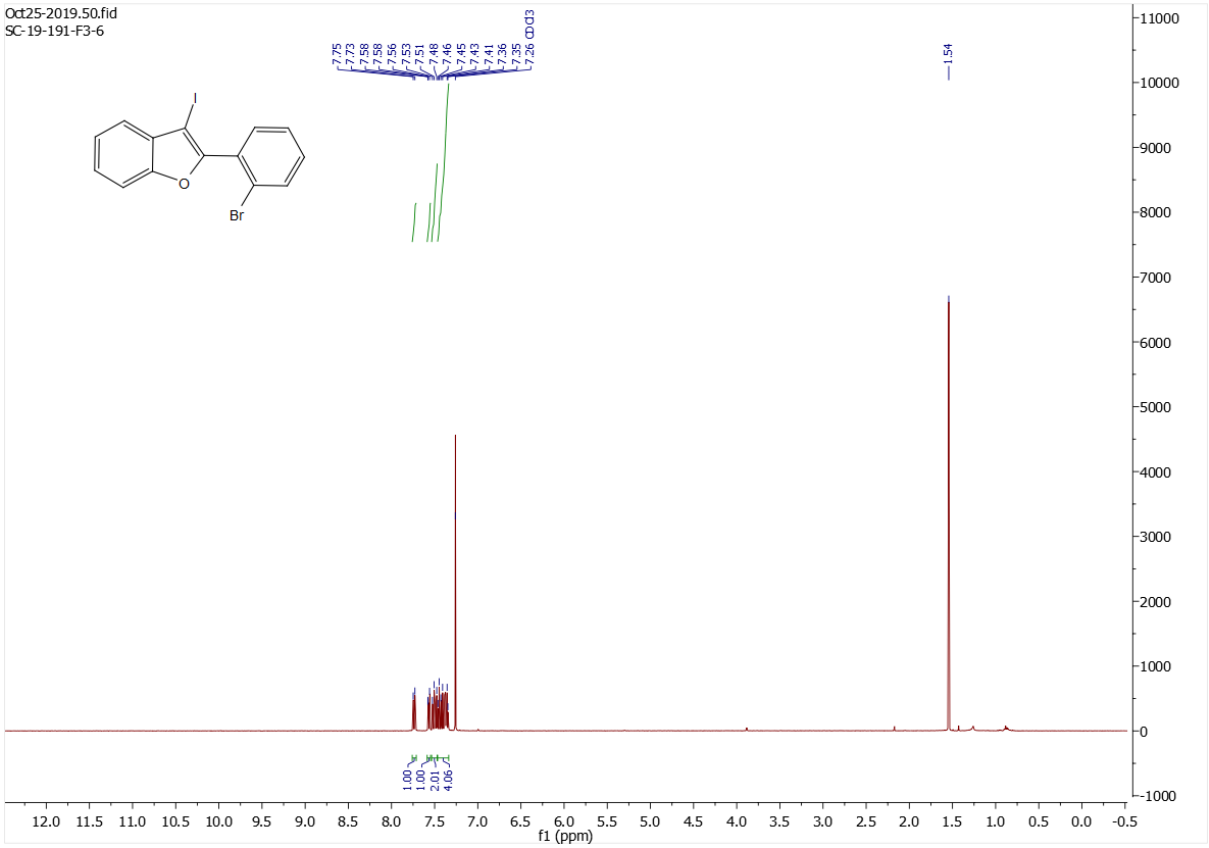
^{1}H NMR of 2-(2-bromophenyl)-3-iodobenzo[*b*]thiophene (**15a**):



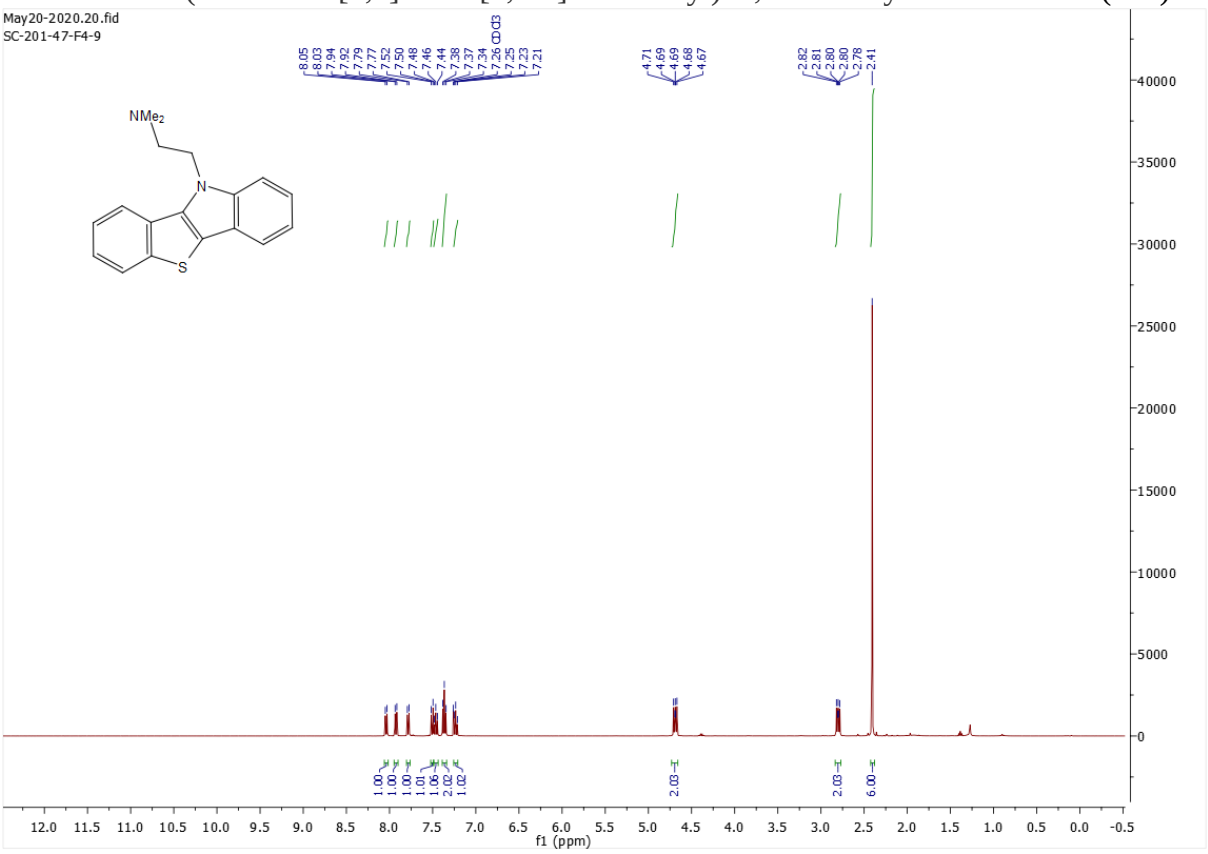
^{13}C DEPT-Q NMR of 2-(2-bromophenyl)-3-iodobenzo[*b*]thiophene (**15a**):



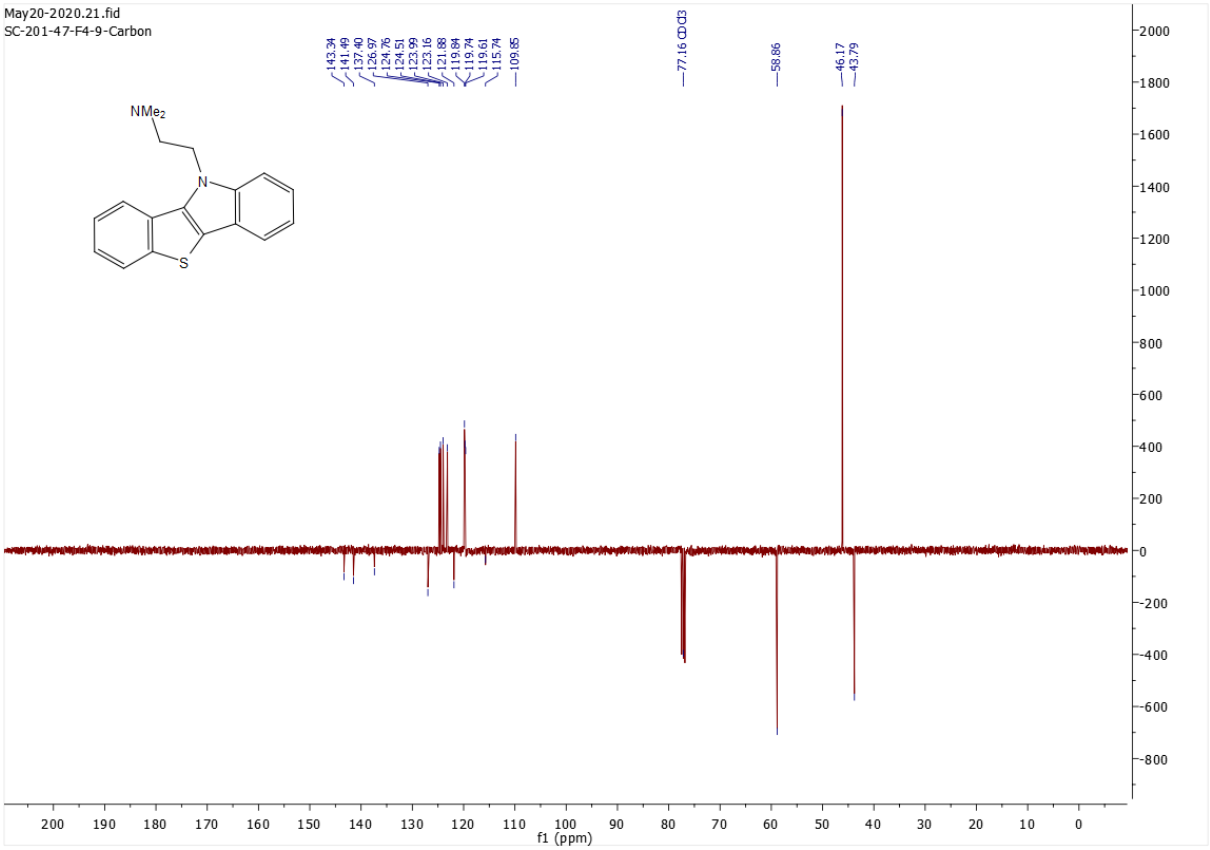
^{1}H NMR of 2-(2-bromophenyl)-3-iodobenzofuran (**15b**):



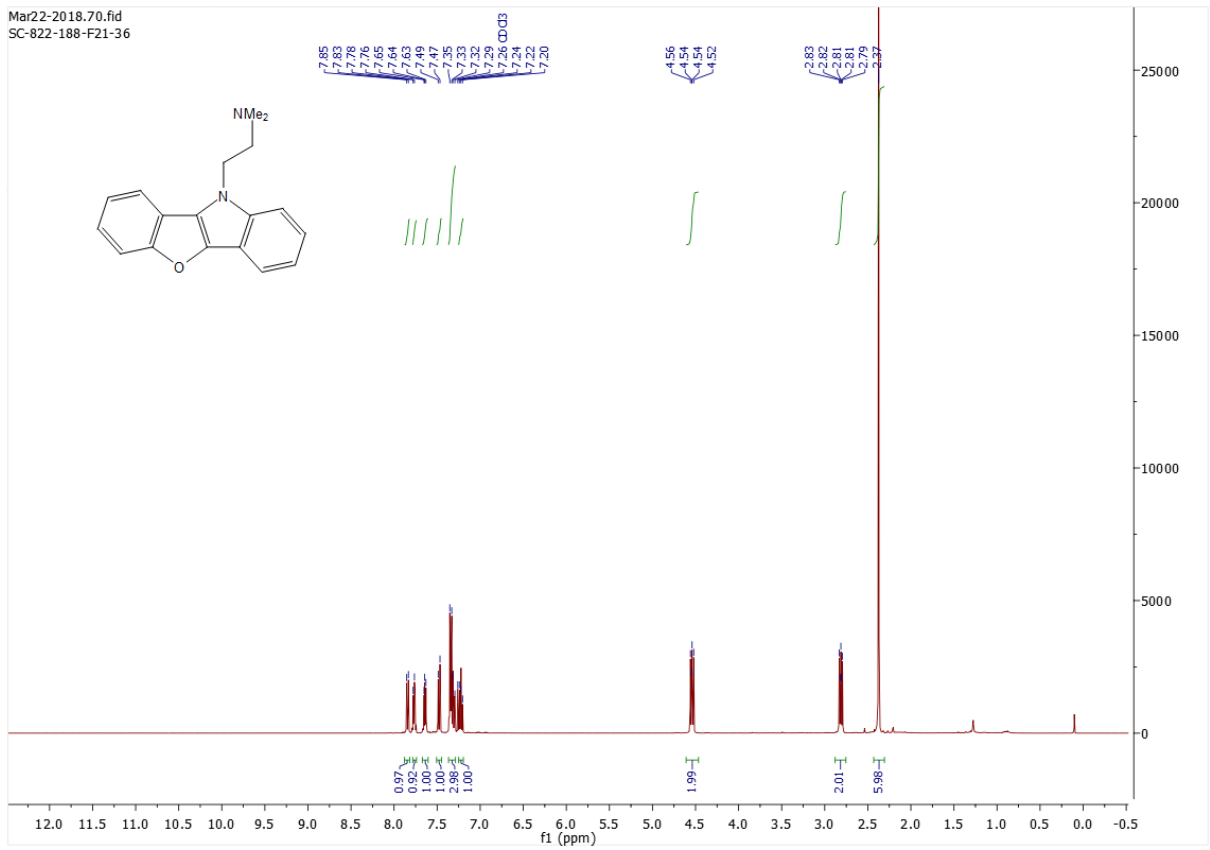
^{1}H NMR of 2-(10*H*-benzo[4,5]thieno[3,2-*b*]indol-10-yl)-*N*,*N*-dimethylethan-1-amine (**16a**):



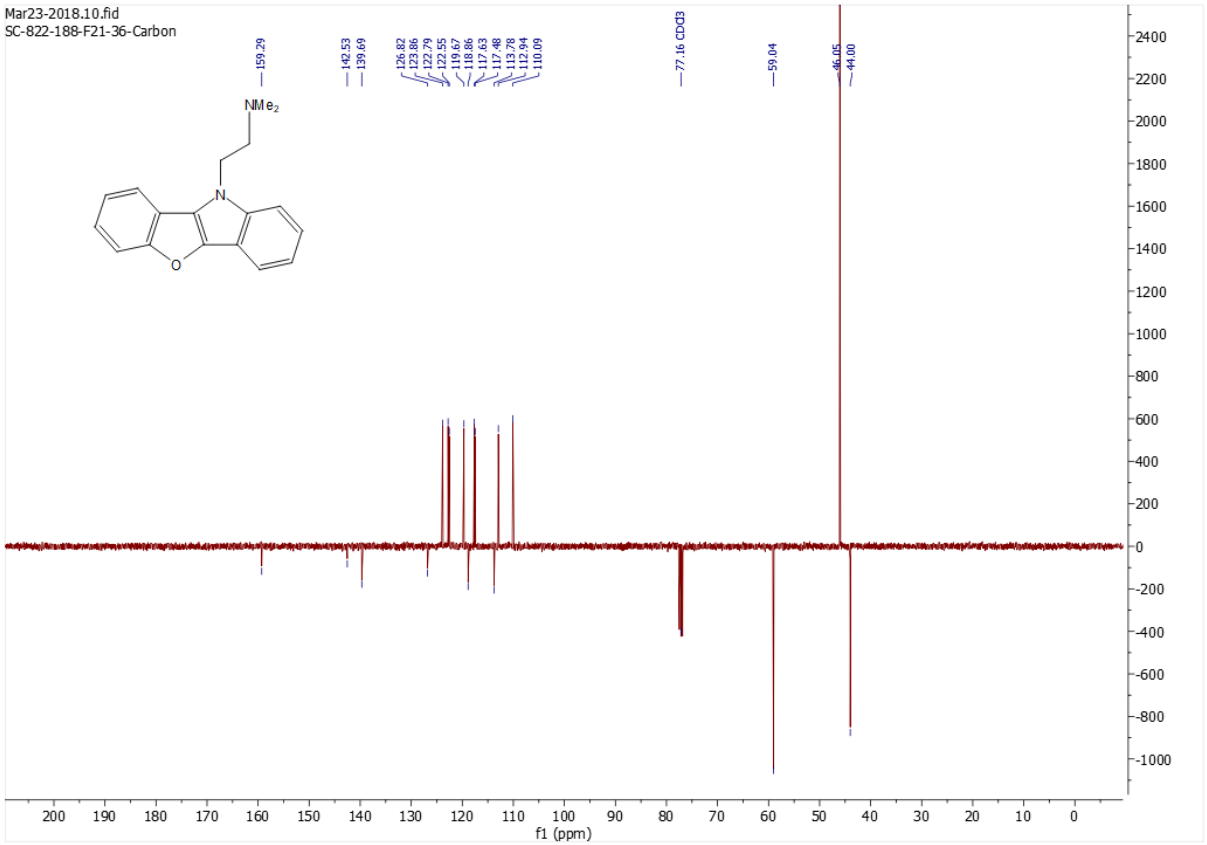
^{13}C DEPT-Q NMR of 2-(10*H*-benzo[4,5]thieno[3,2-*b*]indol-10-yl)-*N*,*N*-dimethylethan-1-amine (**16a**):



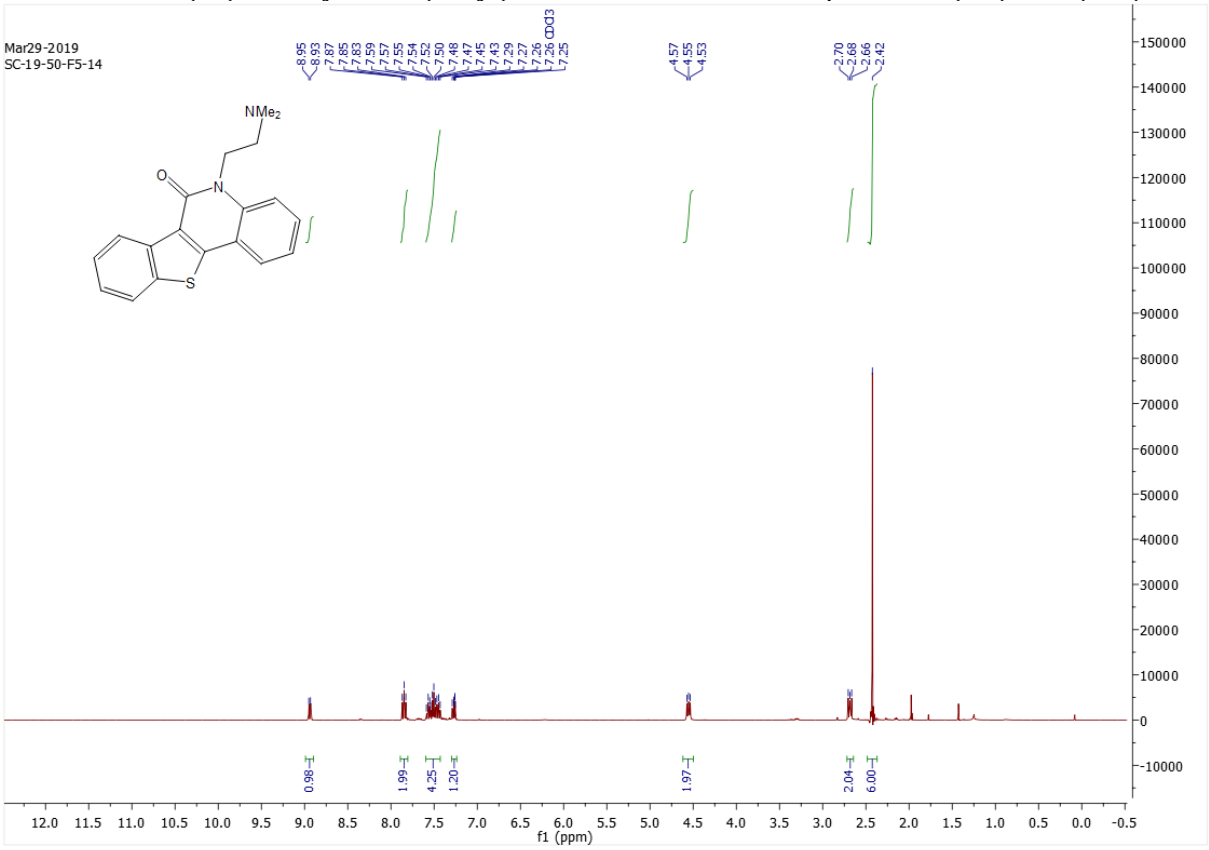
^{1}H NMR of 2-(10*H*-benzofuro[3,2-*b*]indol-10-yl)-*N*,*N*-dimethylethan-1-amine (**16b**):



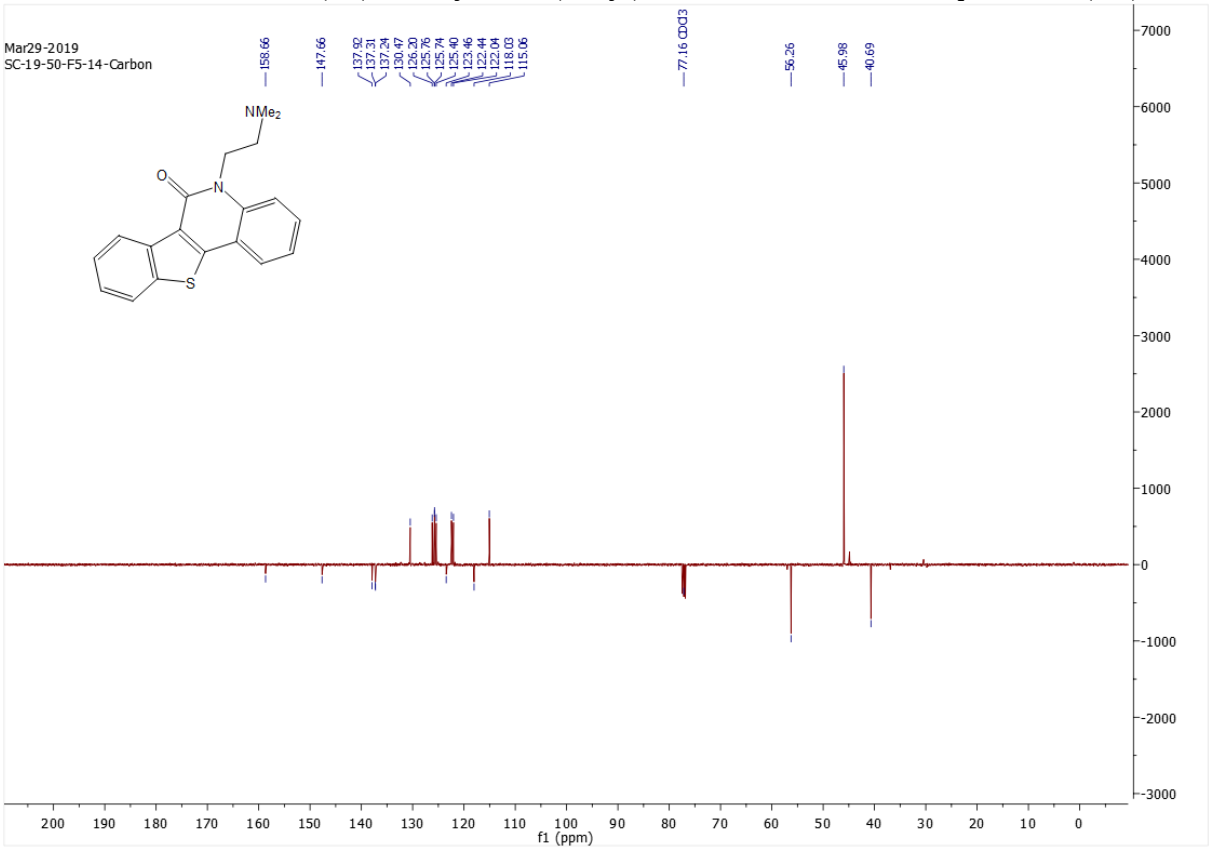
^{13}C DEPT-Q NMR of 2-(10*H*-benzofuro[3,2-*b*]indol-10-yl)-*N*,*N*-dimethylethan-1-amine (**16b**):



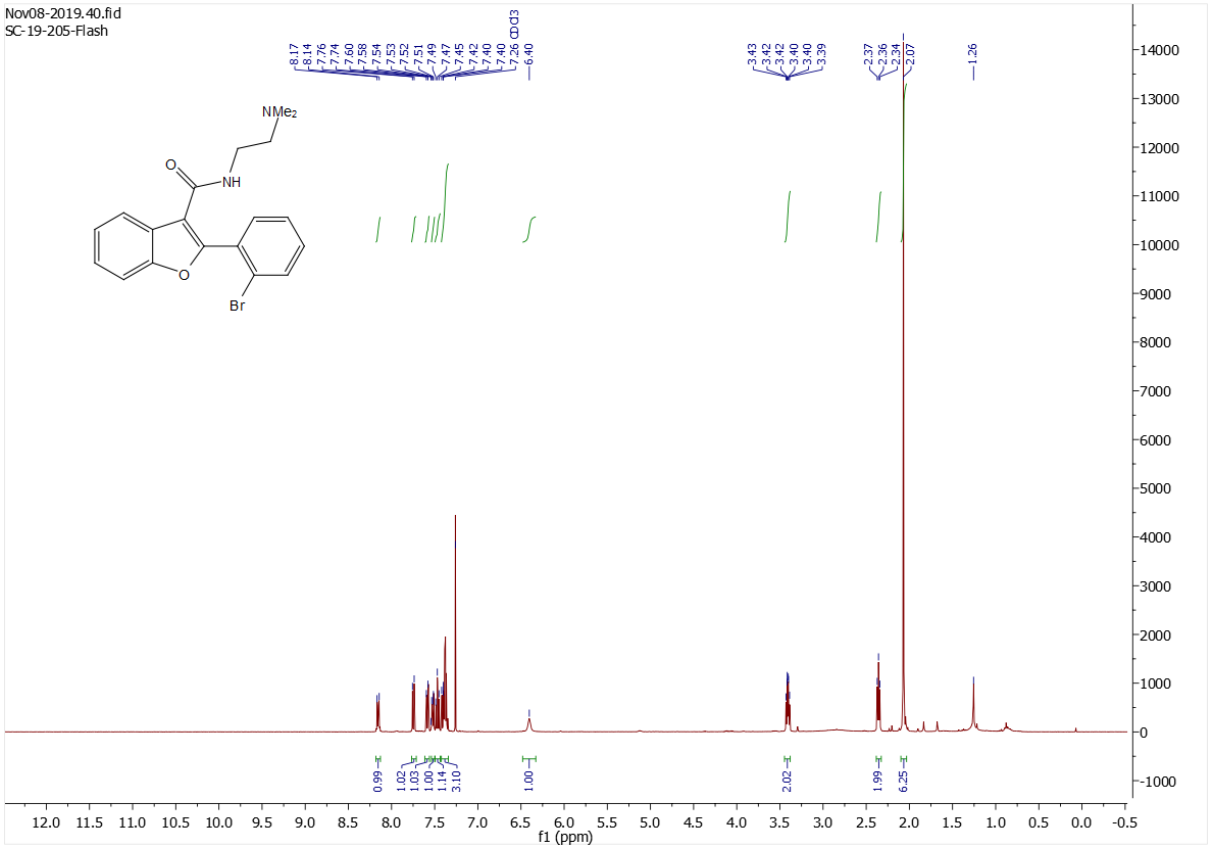
^{1}H NMR of 5-(2-(dimethylamino)ethyl)benzo[4,5]thieno[3,2-*c*]quinolin-6(5*H*)-one (**17a**):



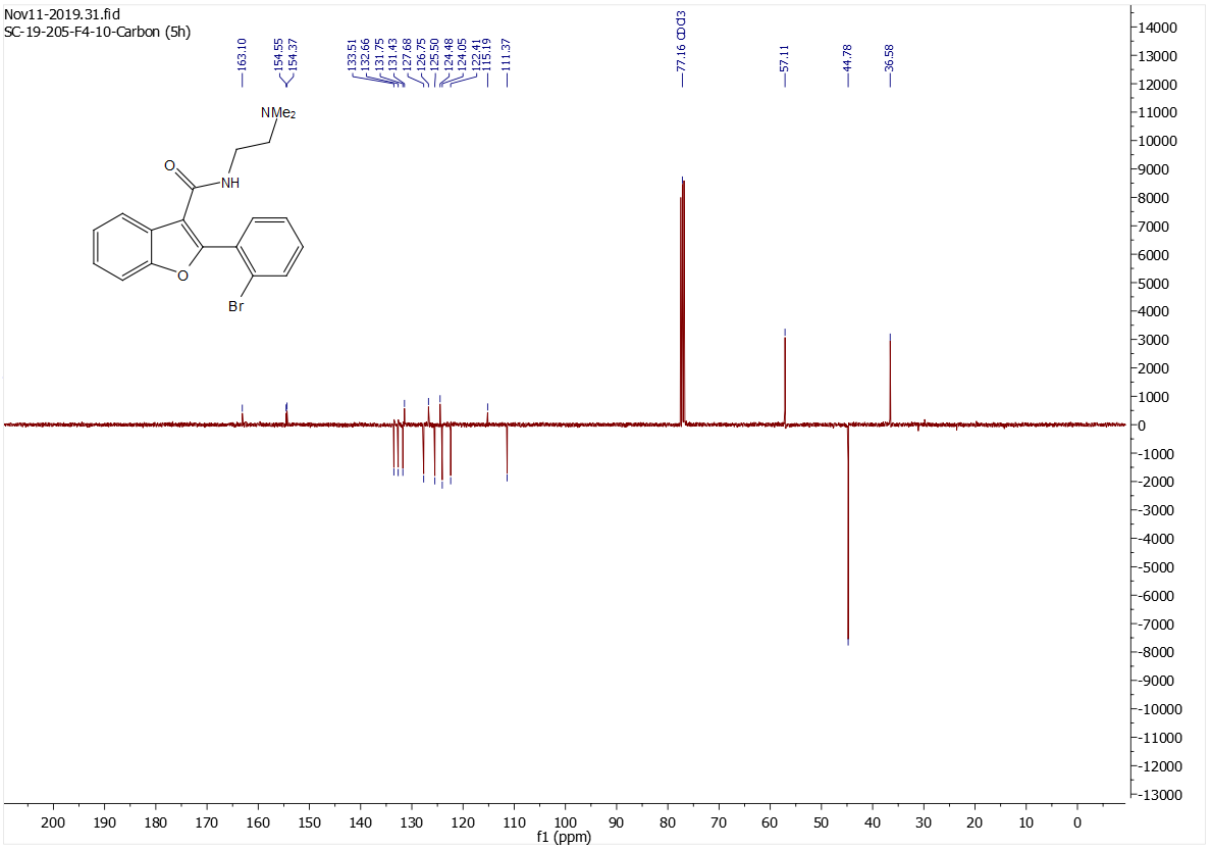
^{13}C DEPT-Q NMR of 5-(2-(dimethylamino)ethyl)benzo[4,5]thieno[3,2-*c*]quinolin-6(5*H*)-one (**17a**):



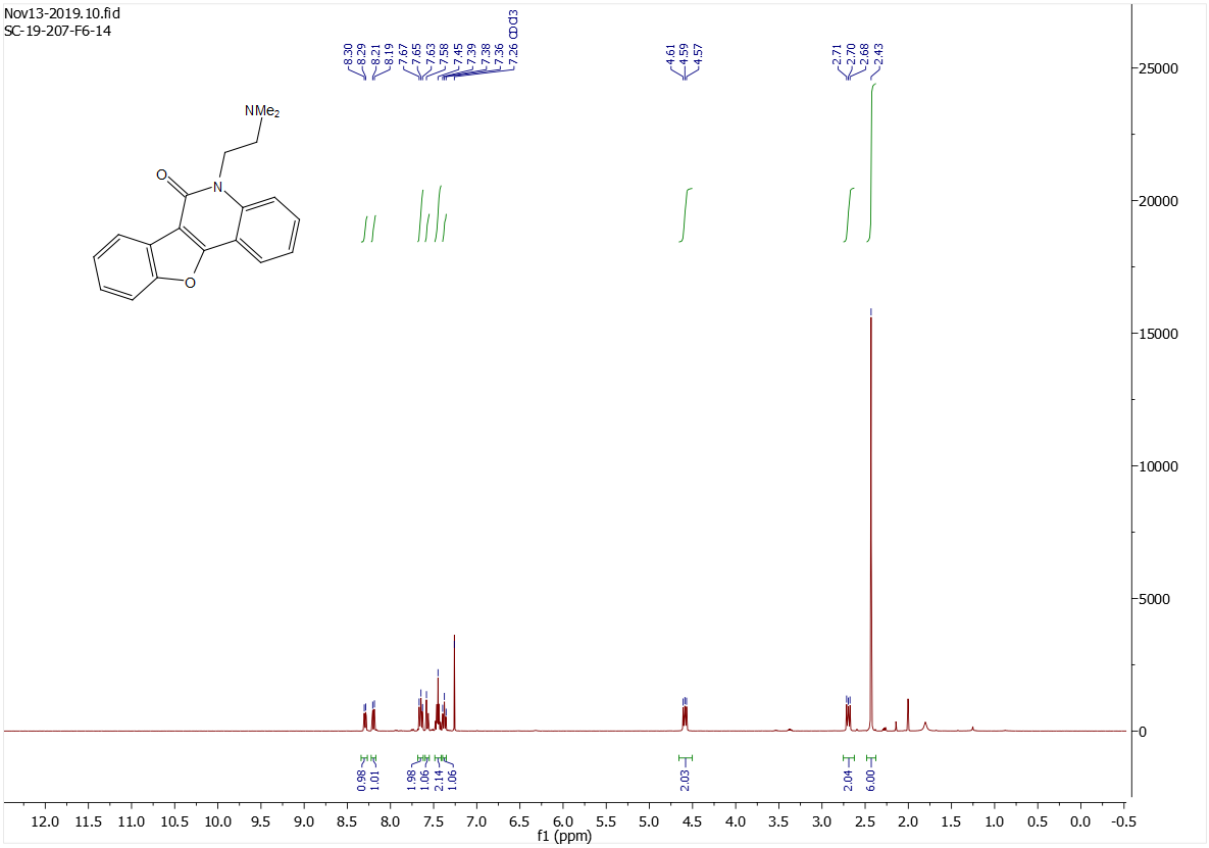
^{1}H NMR of 2-(2-bromophenyl)-*N*-(2-(dimethylamino)ethyl)benzofuran-3-carboxamide:



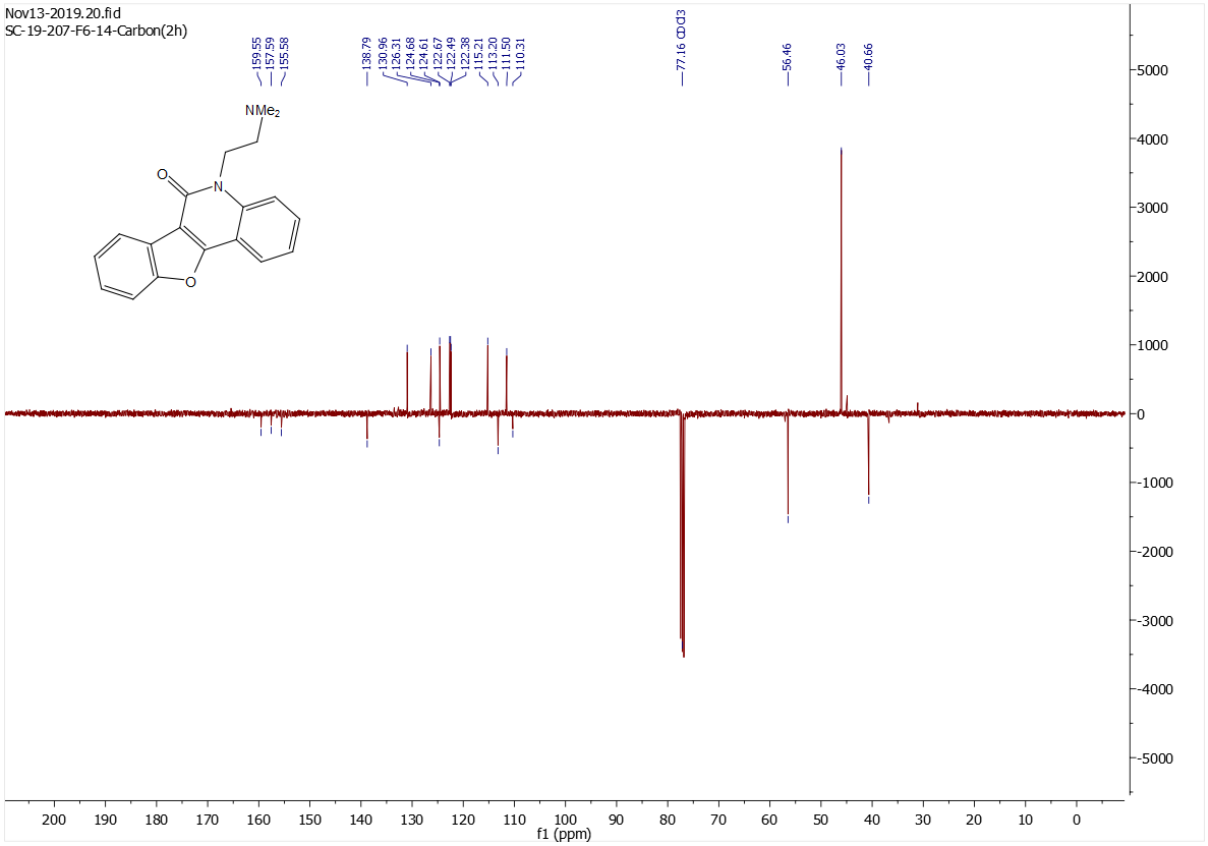
^{13}C DEPT-Q NMR of 2-(2-bromophenyl)-*N*-(2-(dimethylamino)ethyl)benzofuran-3-carboxamide:



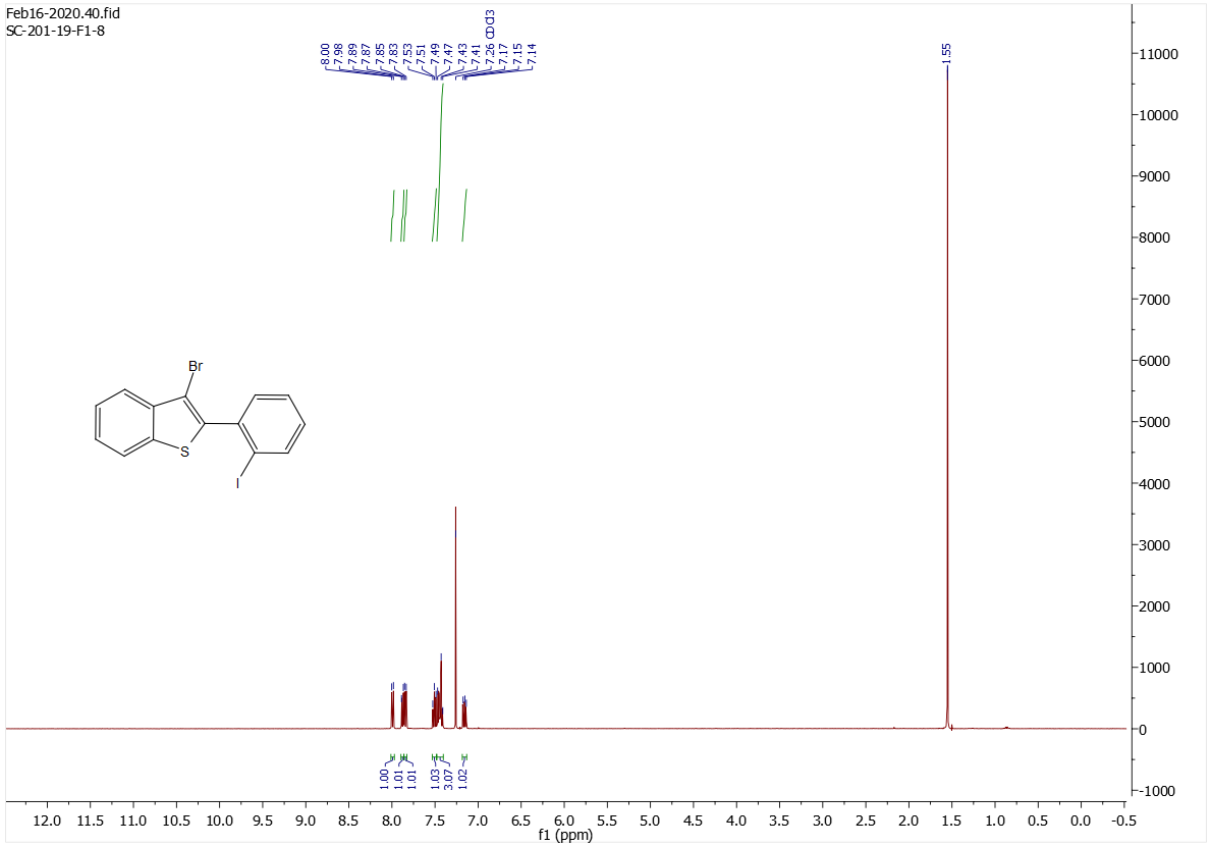
^{1}H NMR of 5-(2-(dimethylamino)ethyl)benzofuro[3,2-*c*]quinolin-6(5*H*)-one (**17b**):



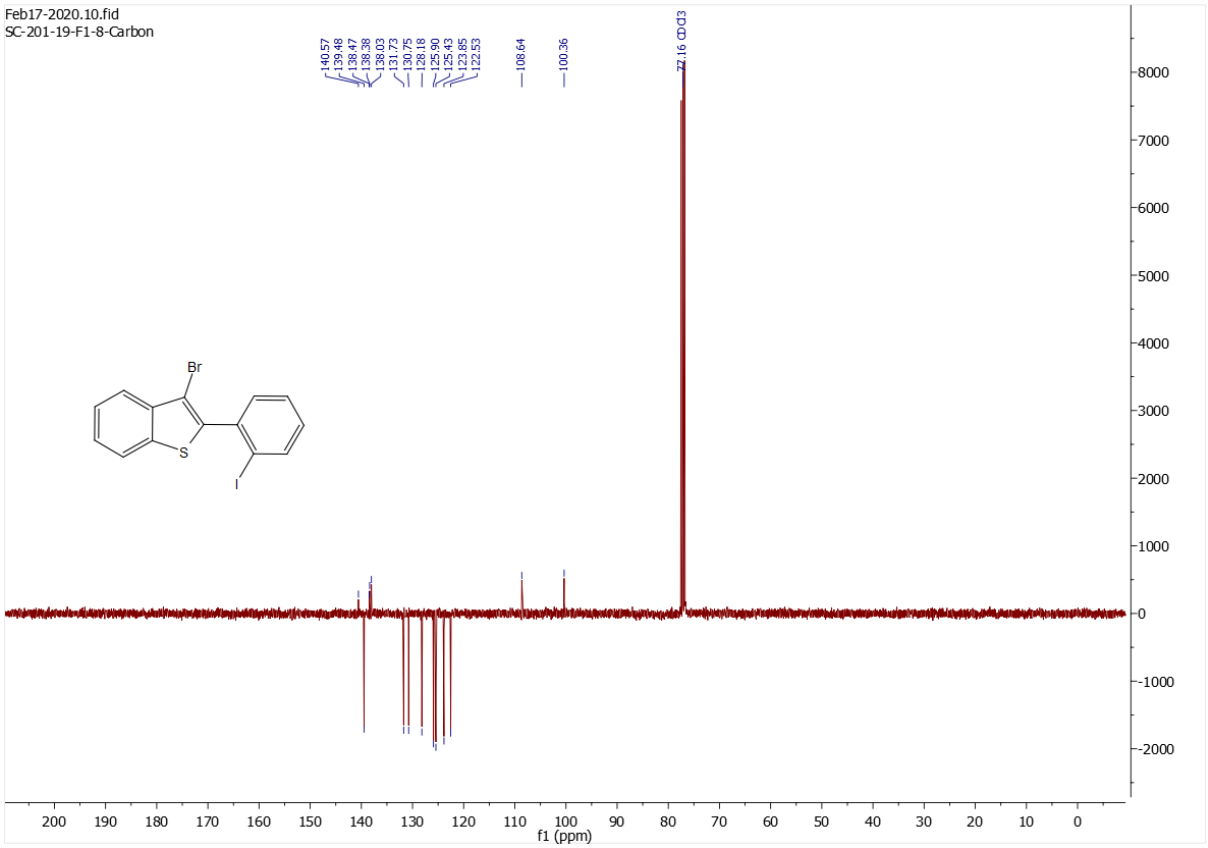
^{13}C DEPT-Q NMR of 5-(2-(dimethylamino)ethyl)benzofuro[3,2-*c*]quinolin-6(5*H*)-one (**17b**):



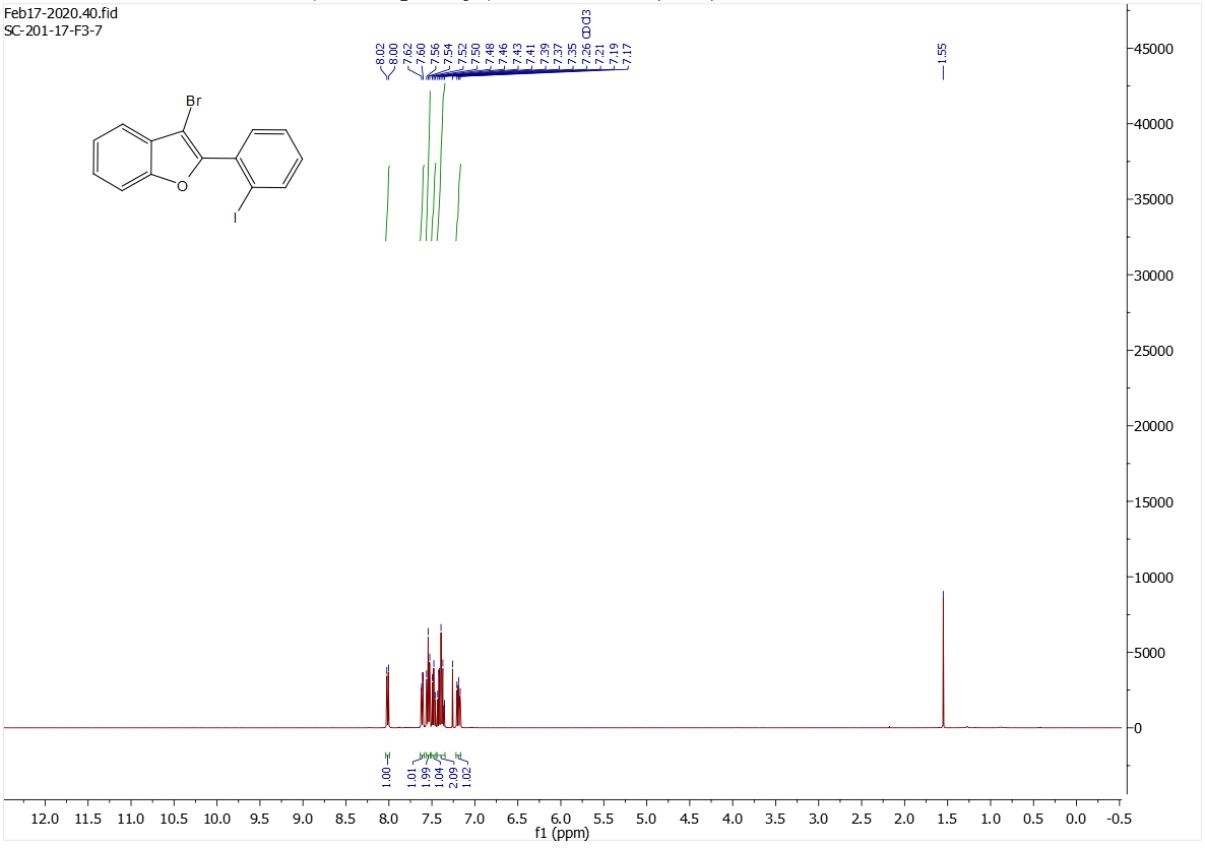
^{1}H NMR of 3-bromo-2-(2-iodophenyl)benzo[*b*]thiophene (**18a**):



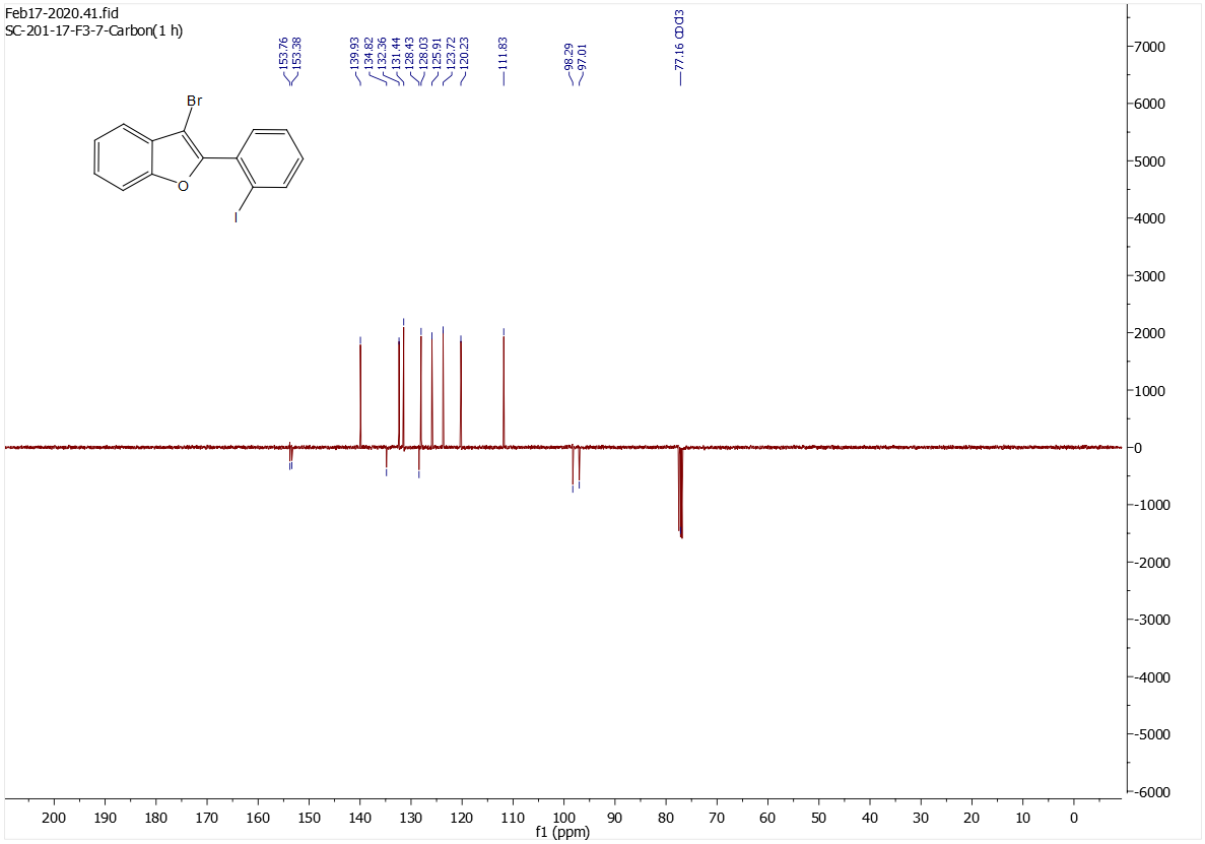
^{13}C DEPT-Q NMR of 3-bromo-2-(2-iodophenyl)benzo[*b*]thiophene (**18a**):



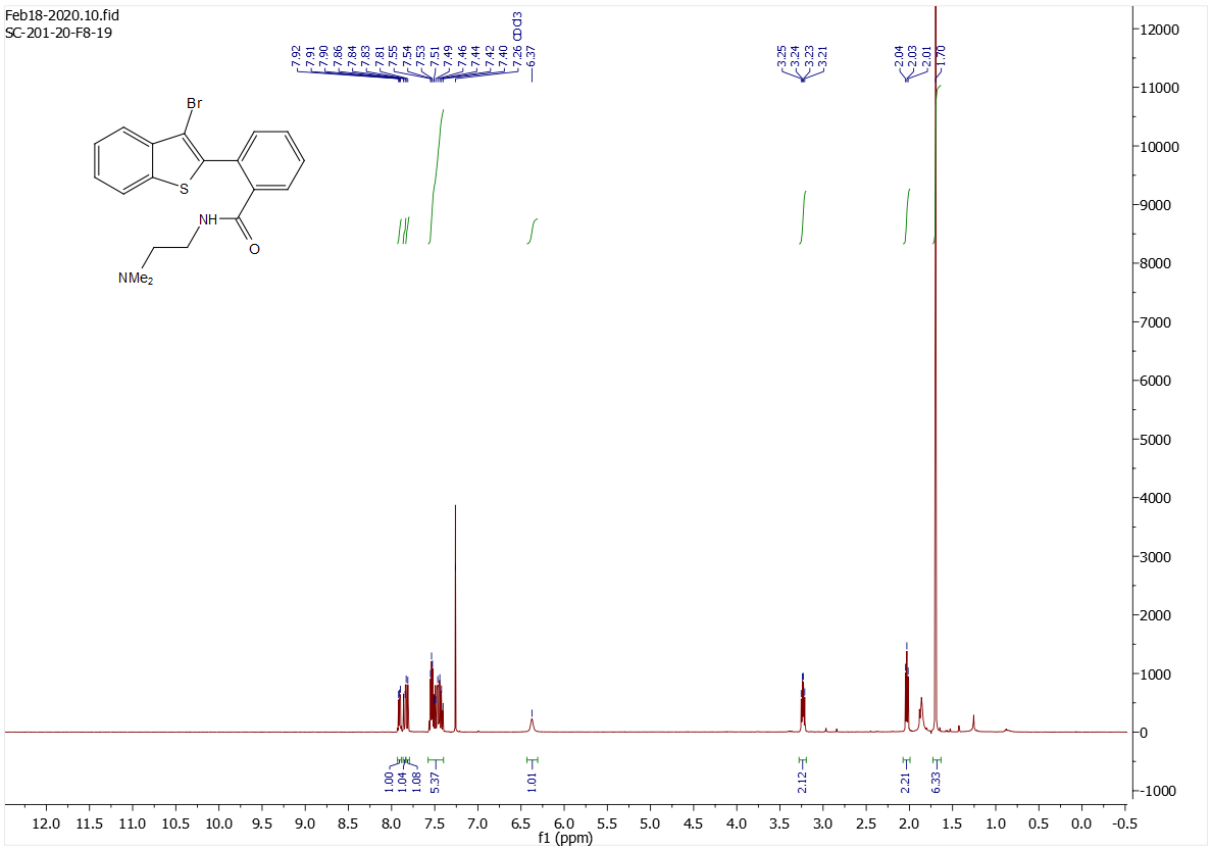
^{1}H NMR of 3-bromo-2-(2-iodophenyl)benzofuran (**18b**):



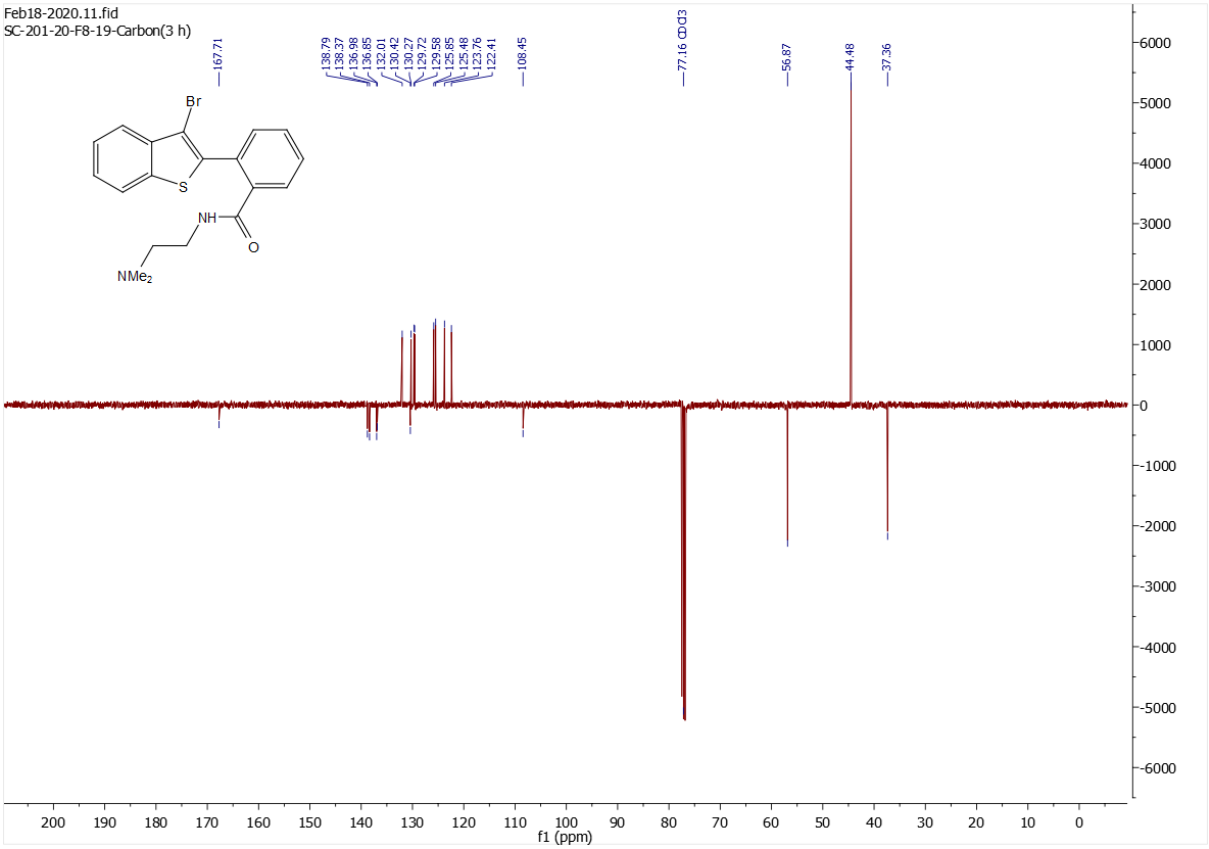
^{13}C DEPT-Q NMR of 3-bromo-2-(2-iodophenyl)benzofuran (**18b**):



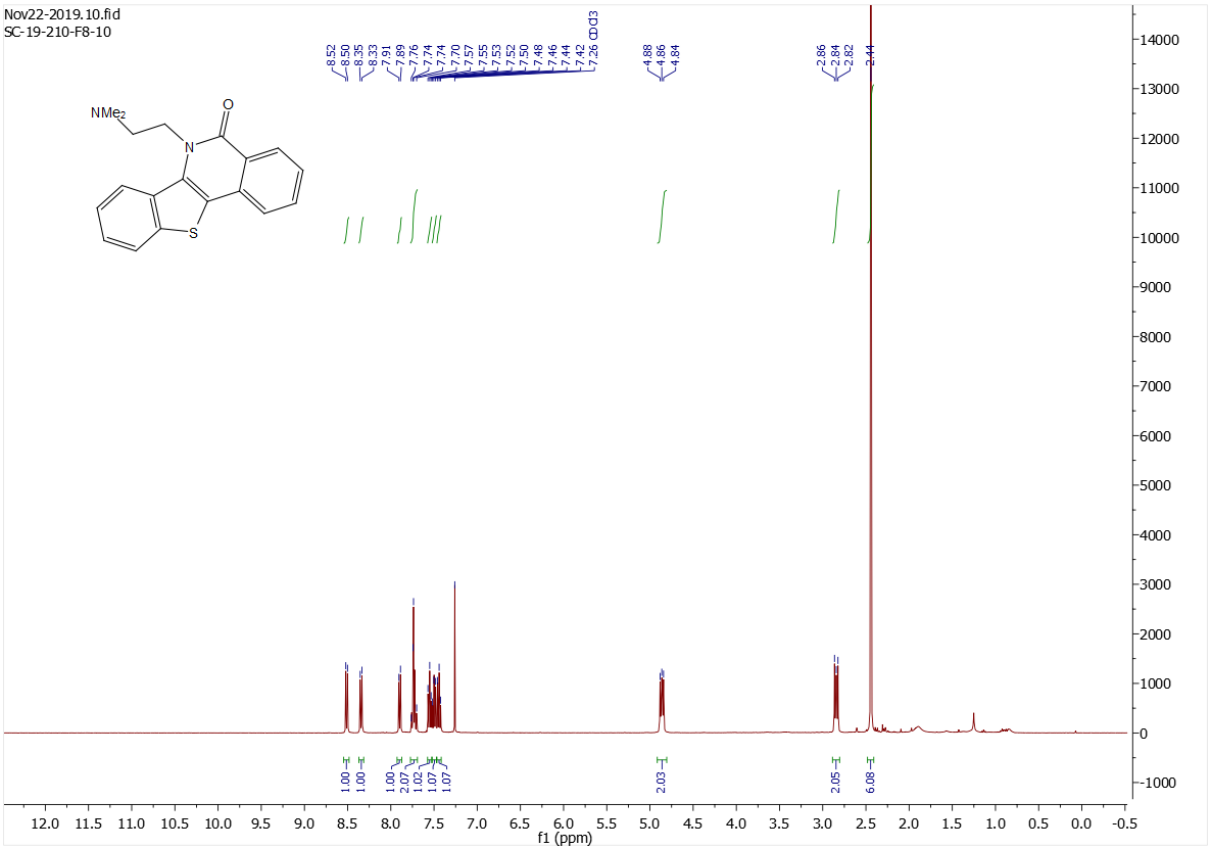
^{1}H NMR of 2-(3-Bromobenzo[*b*]thiophen-2-yl)-*N*-(2-(dimethylamino)ethyl)benzamide:



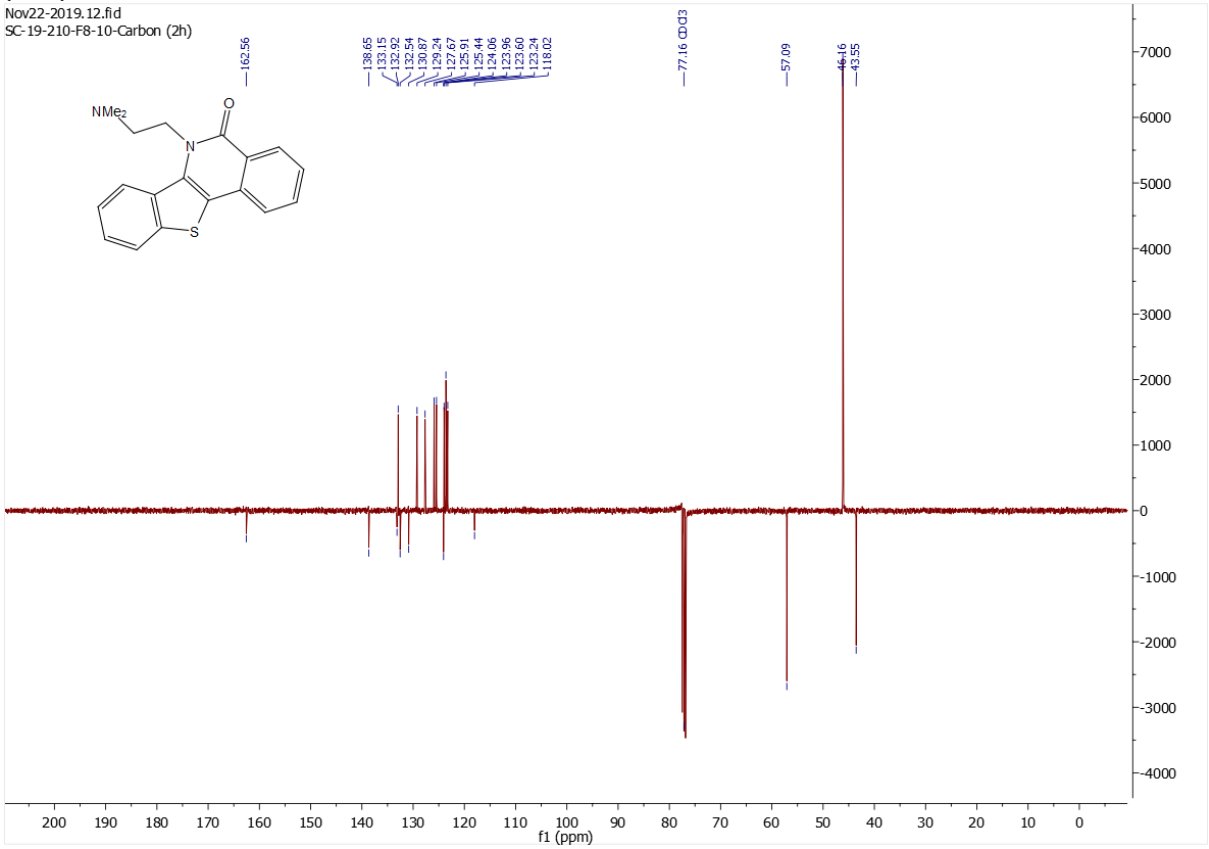
^{13}C DEPT-Q NMR of 2-(3-Bromobenzo[*b*]thiophen-2-yl)-*N*-(2-(dimethylamino)ethyl)benzamide:



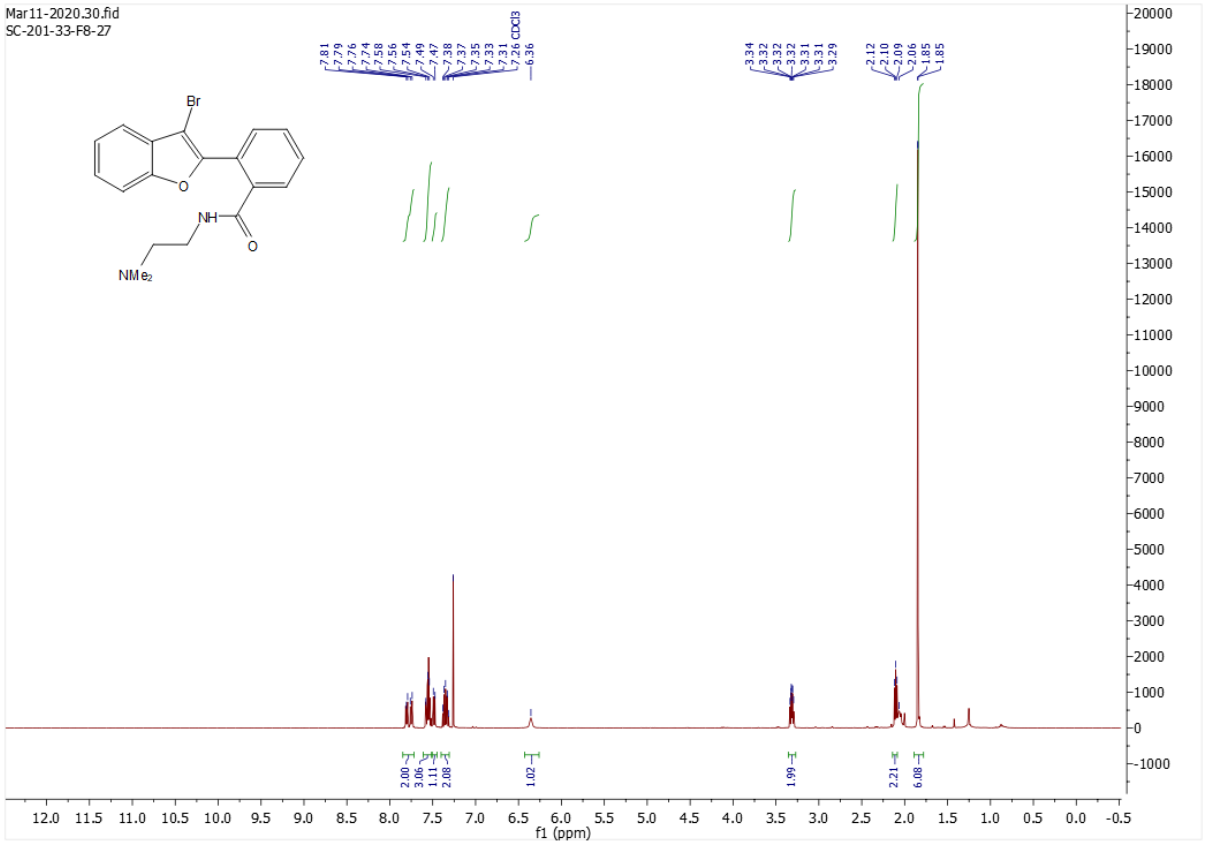
^{1}H NMR of 6-(2-(dimethylamino)ethyl)benzo[4,5]thieno[3,2-*c*]isoquinolin-5(6*H*)-one (**19a**):



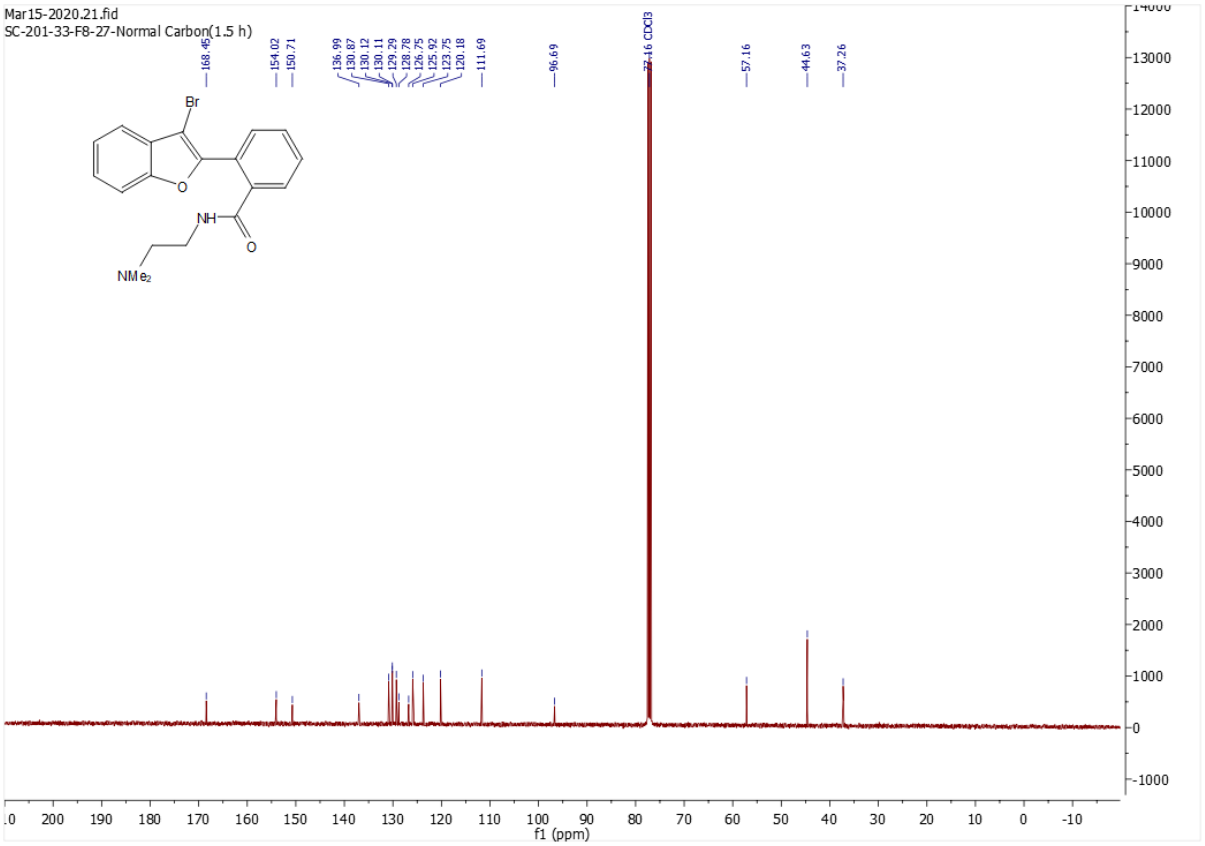
^{13}C DEPT-Q NMR of 6-(2-(dimethylamino)ethyl)benzo[4,5]thieno[3,2-*c*]isoquinolin-5(6*H*)-one (**19a**):



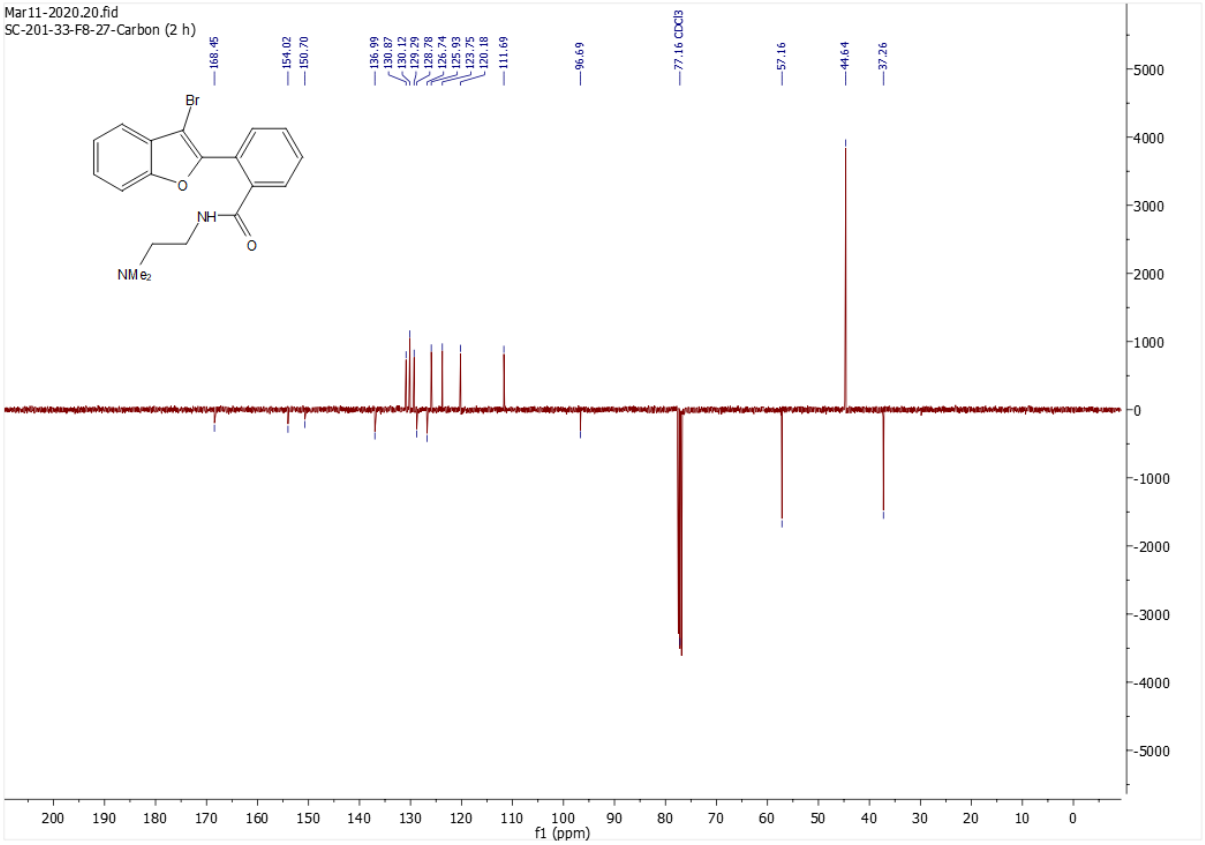
^{1}H NMR of 2-(3-bromobenzofuran-2-yl)-*N*-(2-(dimethylamino)ethyl)benzamide:



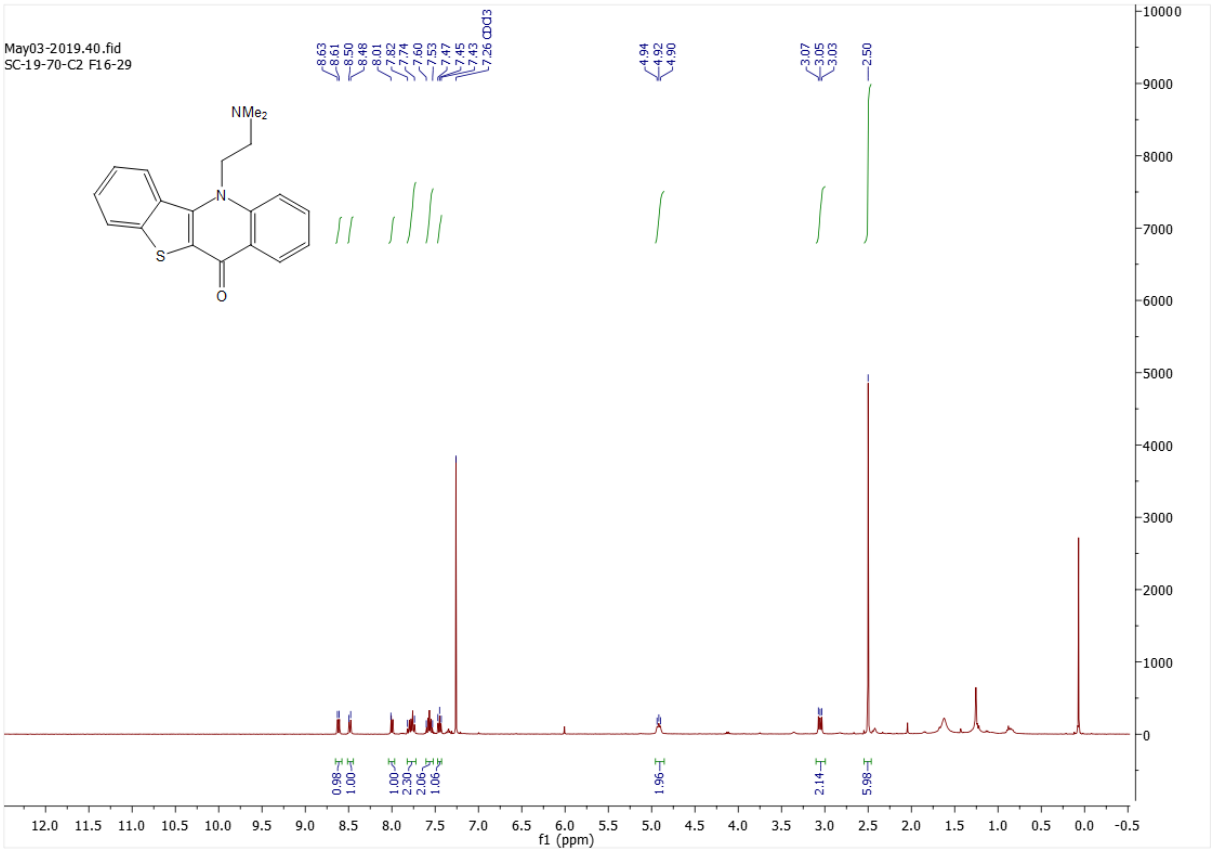
^{13}C NMR of 2-(3-bromobenzofuran-2-yl)-*N*-(2-(dimethylamino)ethyl)benzamide:



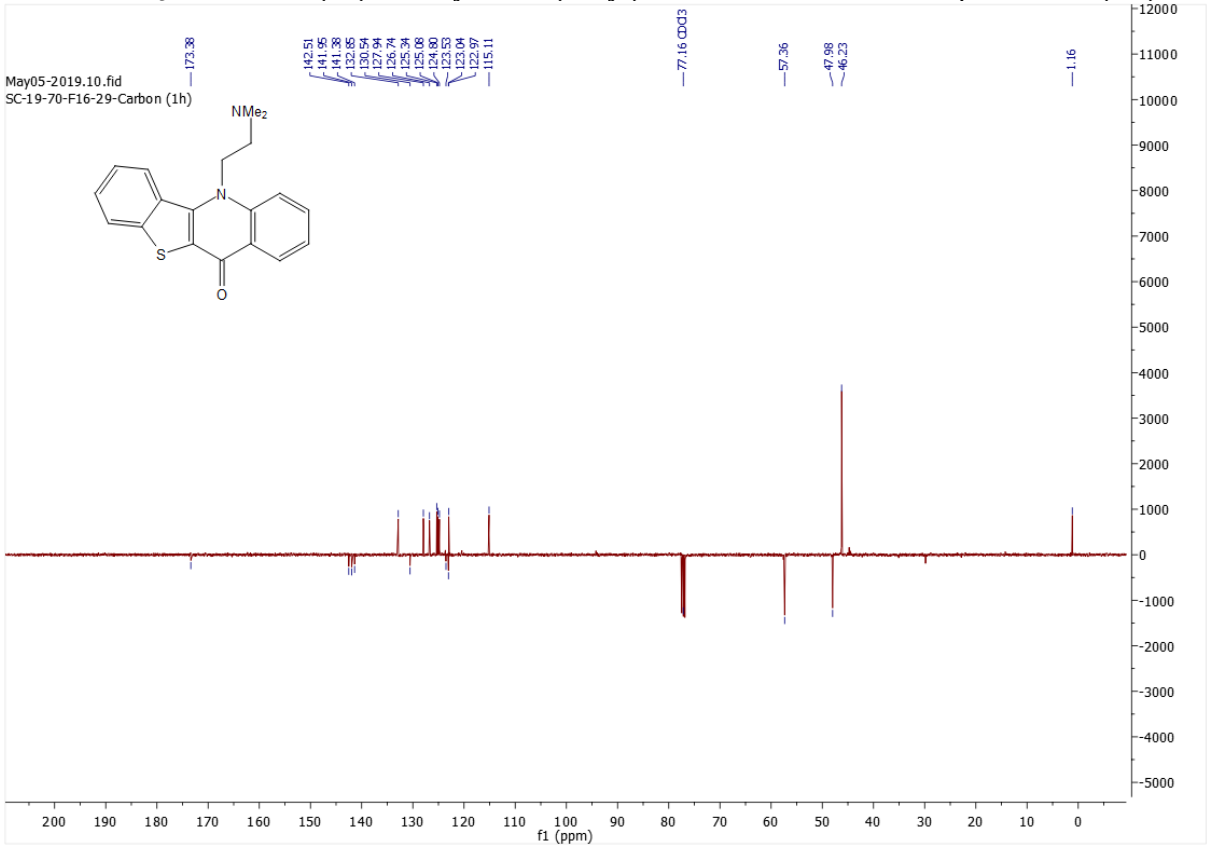
^{13}C DEPT-Q NMR of 2-(3-bromobenzofuran-2-yl)-*N*-(2-(dimethylamino)ethyl)benzamide:



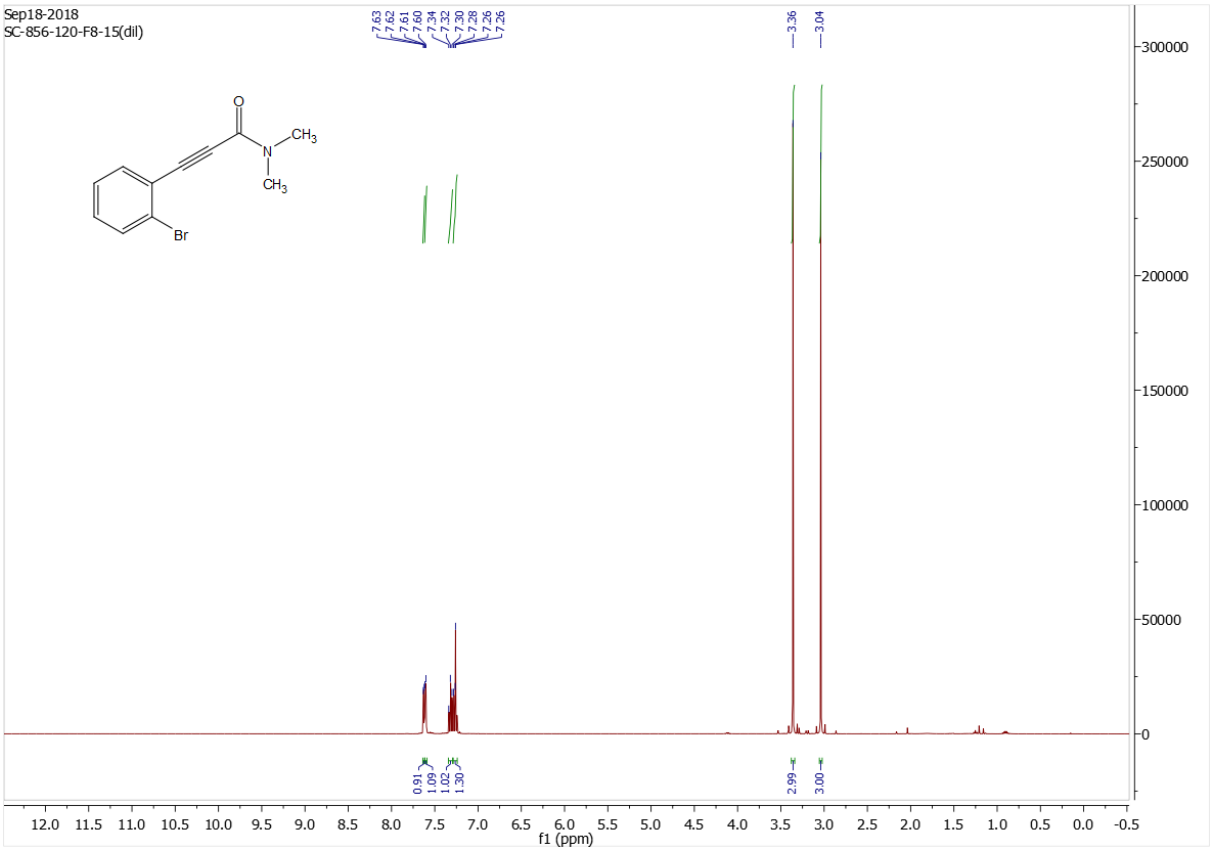
^{1}H NMR of 5-(2-(dimethylamino)ethyl)benzo[4,5]thieno[3,2-*b*]quinolin-11(5*H*)-one (**23**):



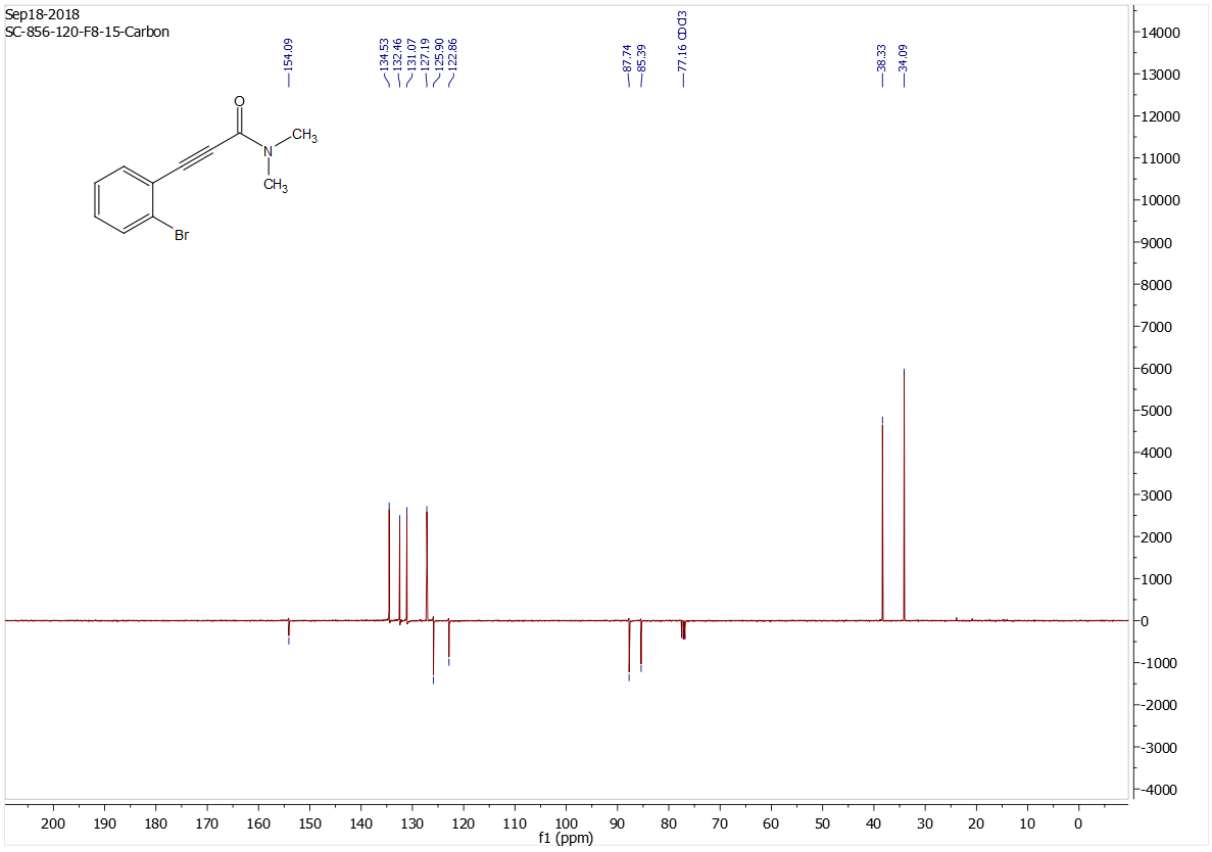
^{13}C DEPT-Q NMR of 5-(2-(dimethylamino)ethyl)benzo[4,5]thieno[3,2-*b*]quinolin-11(5*H*)-one (**23**):



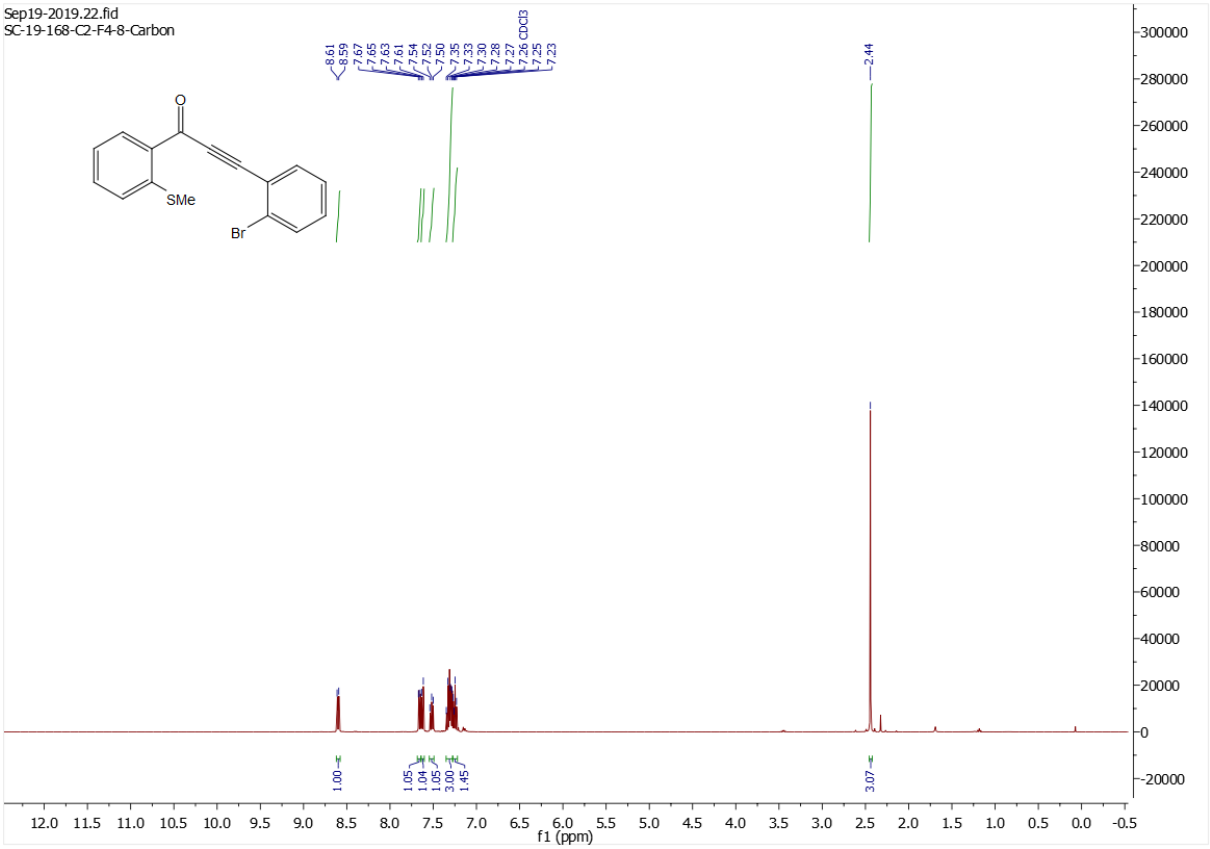
^{1}H NMR of 3-(2-bromophenyl)-*N*,*N*-dimethylpropiolamide (**24**):



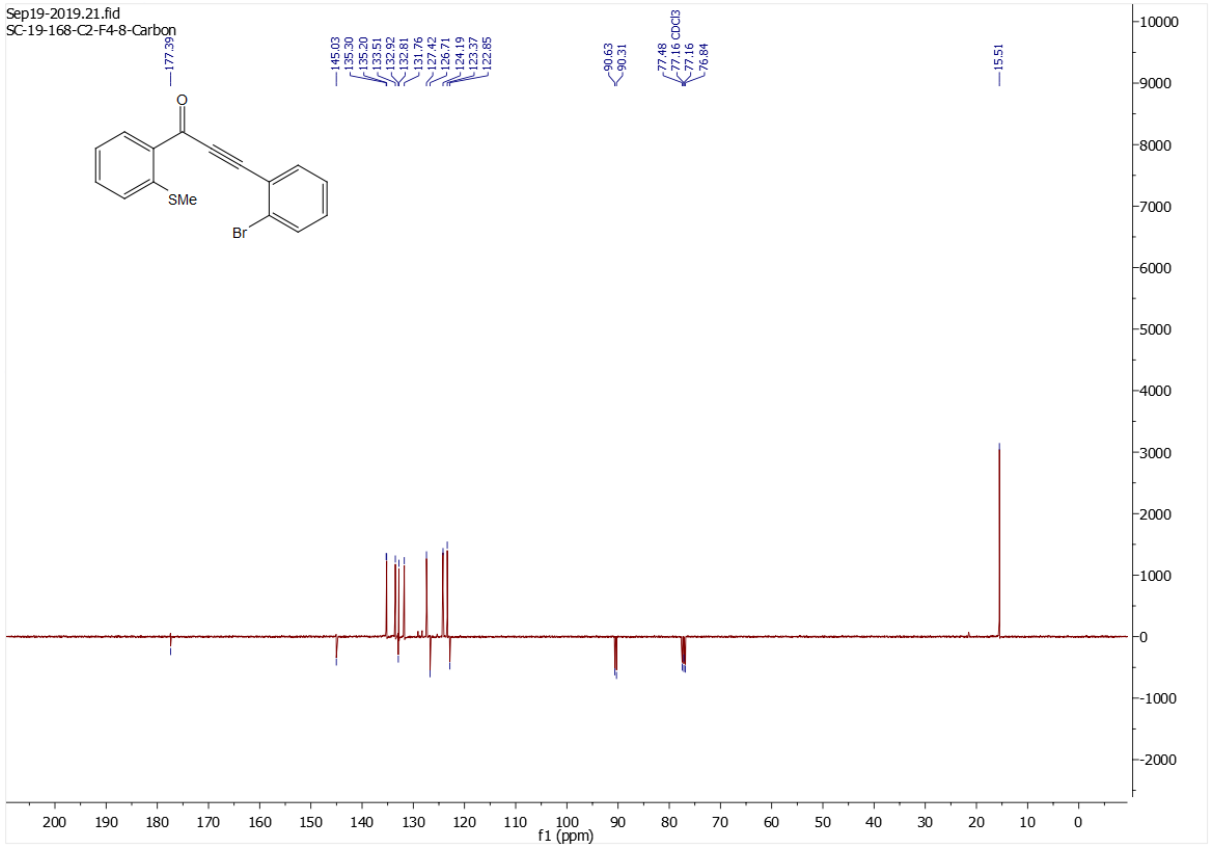
^{13}C DEPT-Q NMR of 3-(2-bromophenyl)-*N*,*N*-dimethylpropiolamide (**24**):



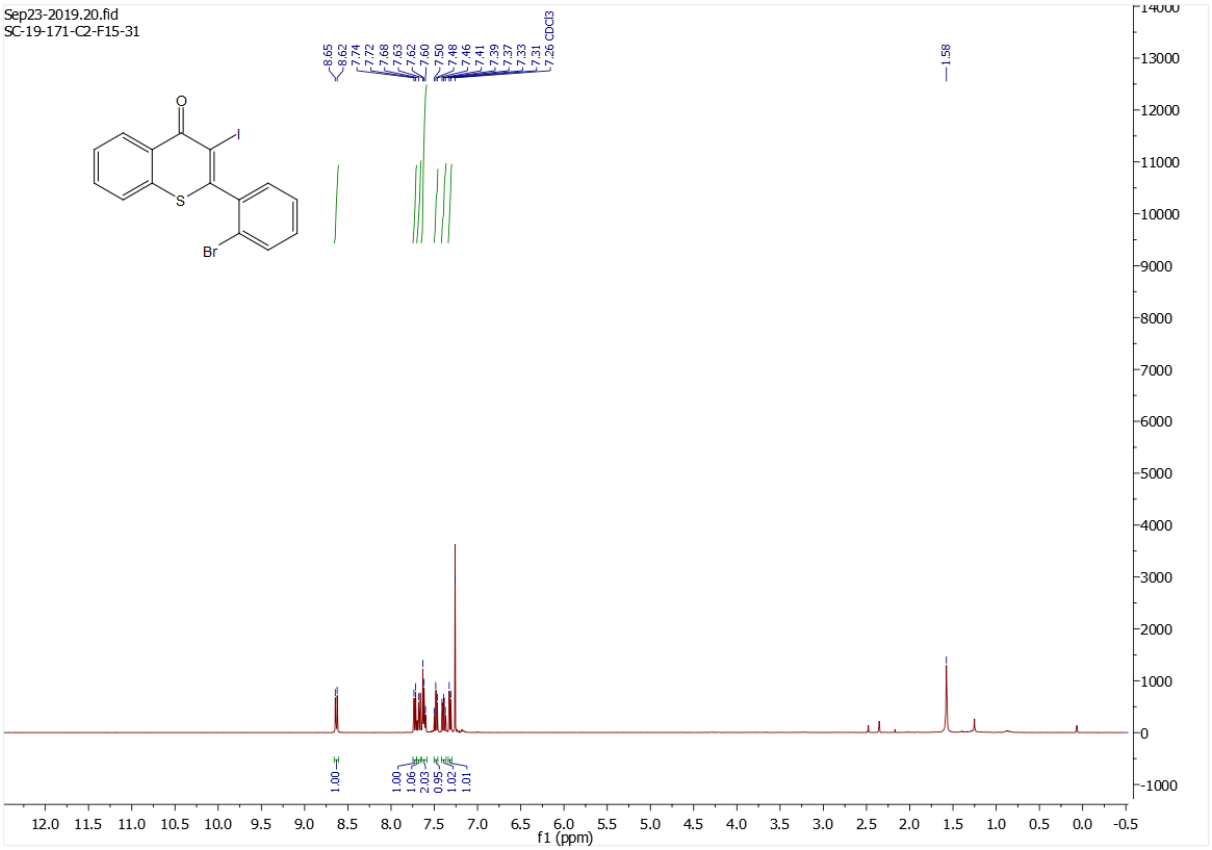
^{1}H NMR of 3-(2-bromophenyl)-1-(2-(methylthio)phenyl)prop-2-yn-1-one (**25**):



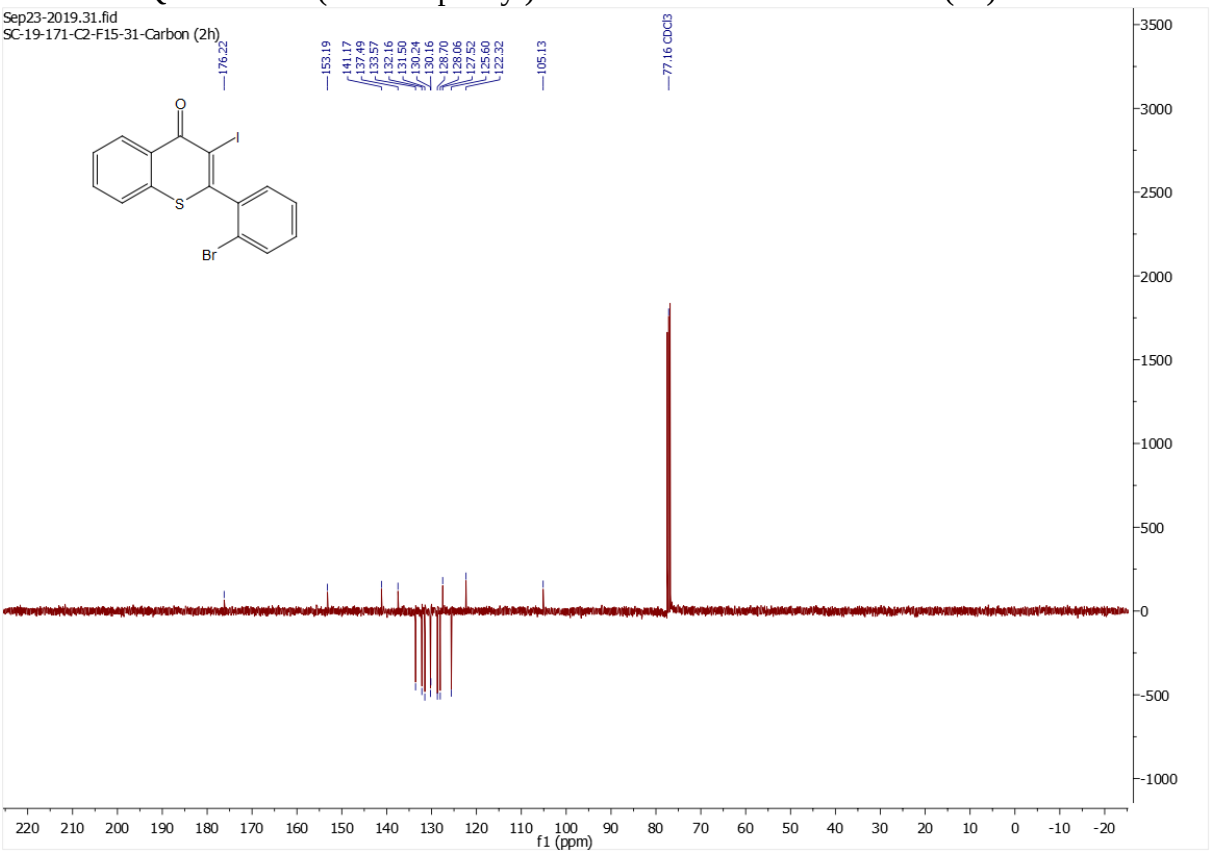
^{13}C DEPT-Q NMR of 3-(2-bromophenyl)-1-(2-(methylthio)phenyl)prop-2-yn-1-one (**25**):



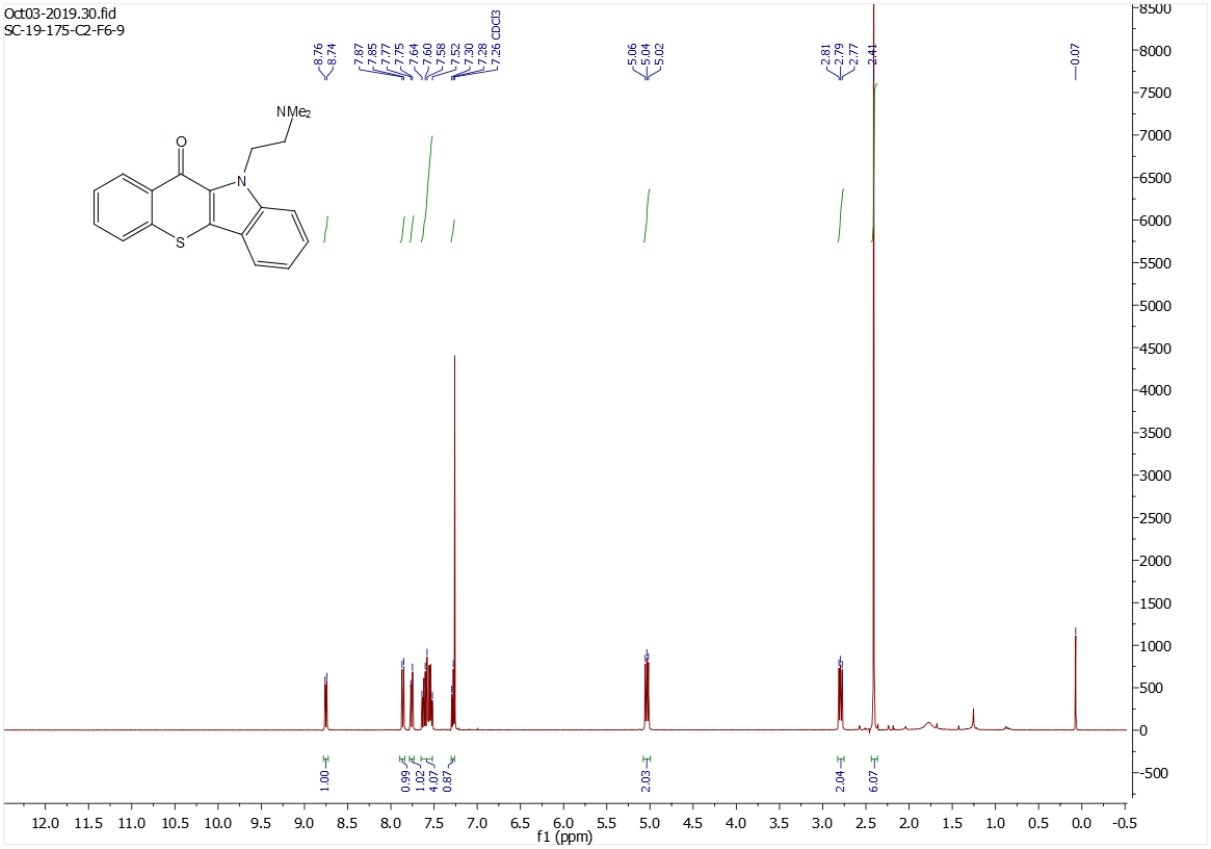
^{1}H NMR of 2-(2-bromophenyl)-3-iodo-4*H*-thiochromen-4-one (**26**):



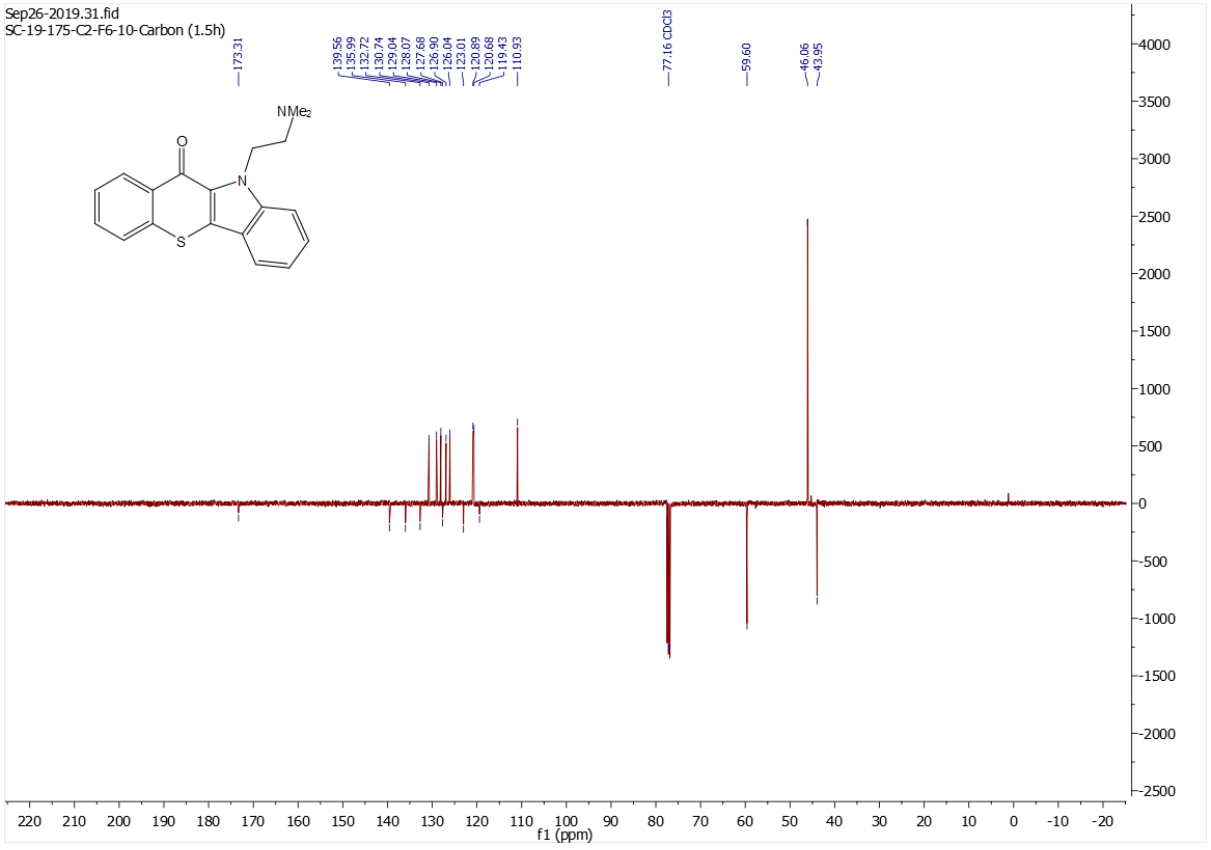
^{13}C DEPT-Q NMR of 2-(2-bromophenyl)-3-iodo-4*H*-thiochromen-4-one (**26**):



^{1}H NMR of 10-(2-(dimethylamino)ethyl)thiochromeno[3,2-*b*]indol-11(10*H*)-one (**27**):

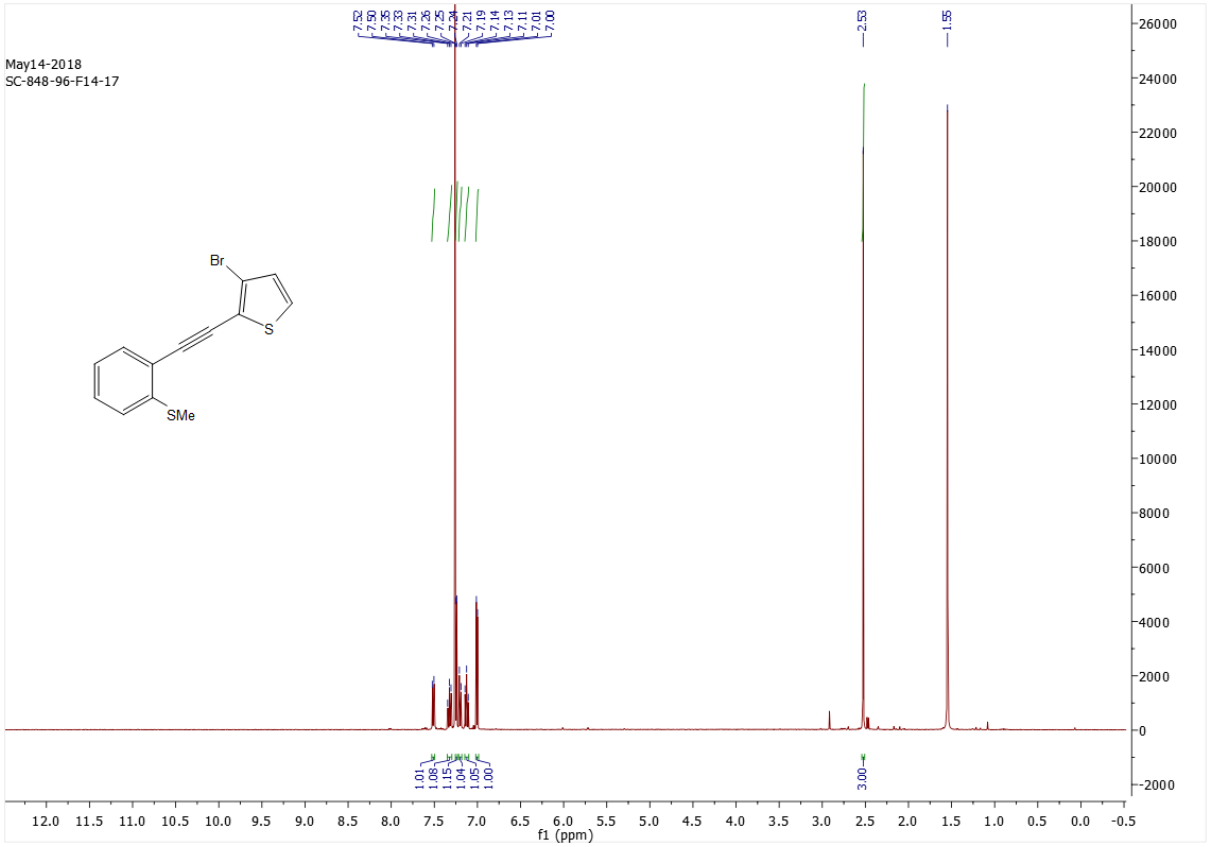


^{13}C DEPT-Q NMR of 10-(2-(dimethylamino)ethyl)thiochromeno[3,2-*b*]indol-11(10*H*)-one (**27**):

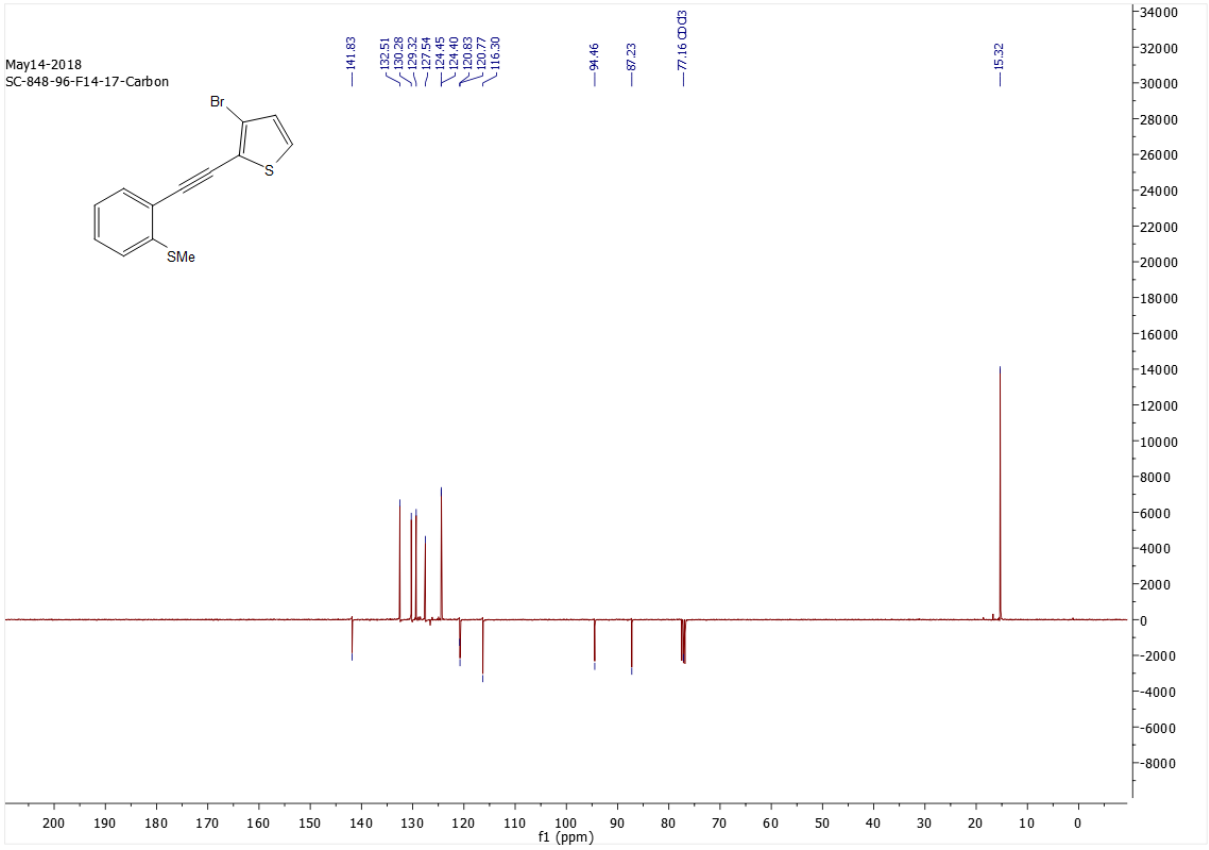


x

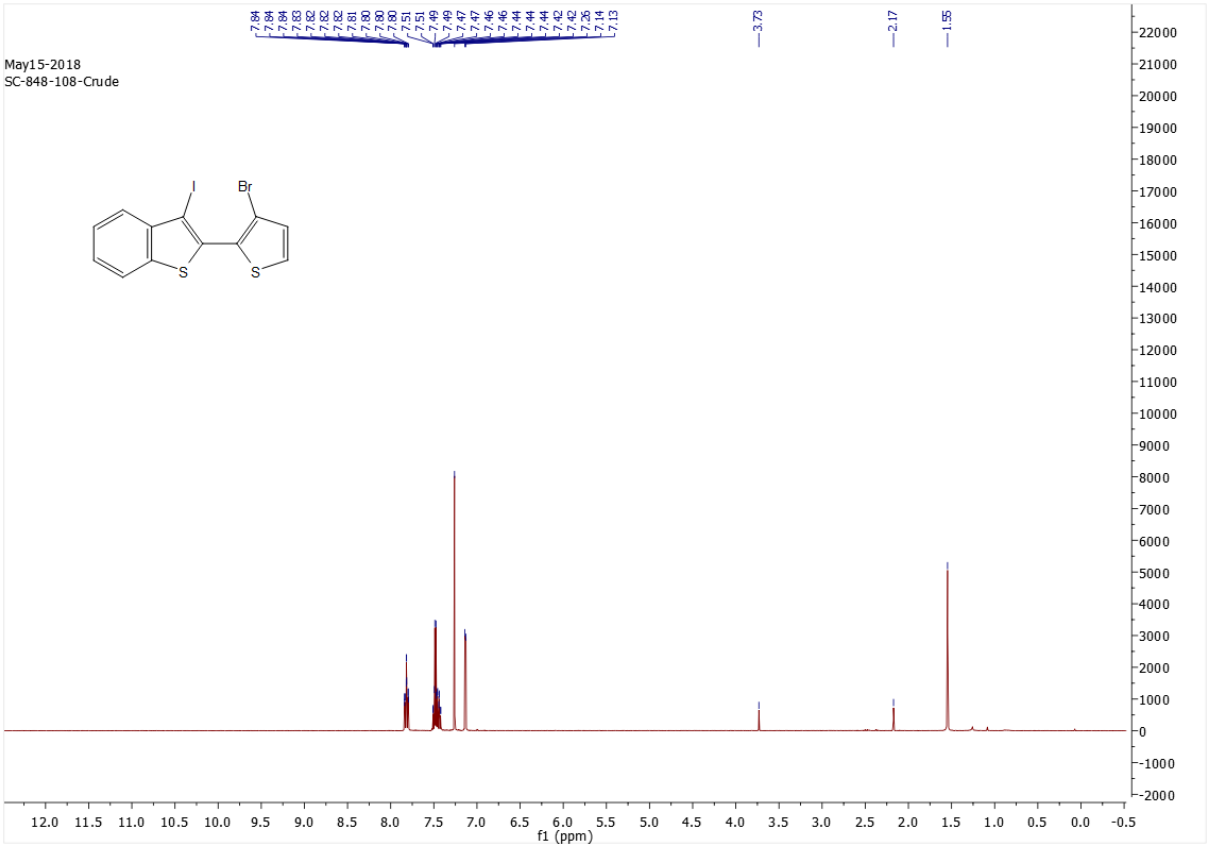
^{1}H NMR of 3-bromo-2-((2-(methylthio)phenyl)ethynyl)thiophene (**28**):



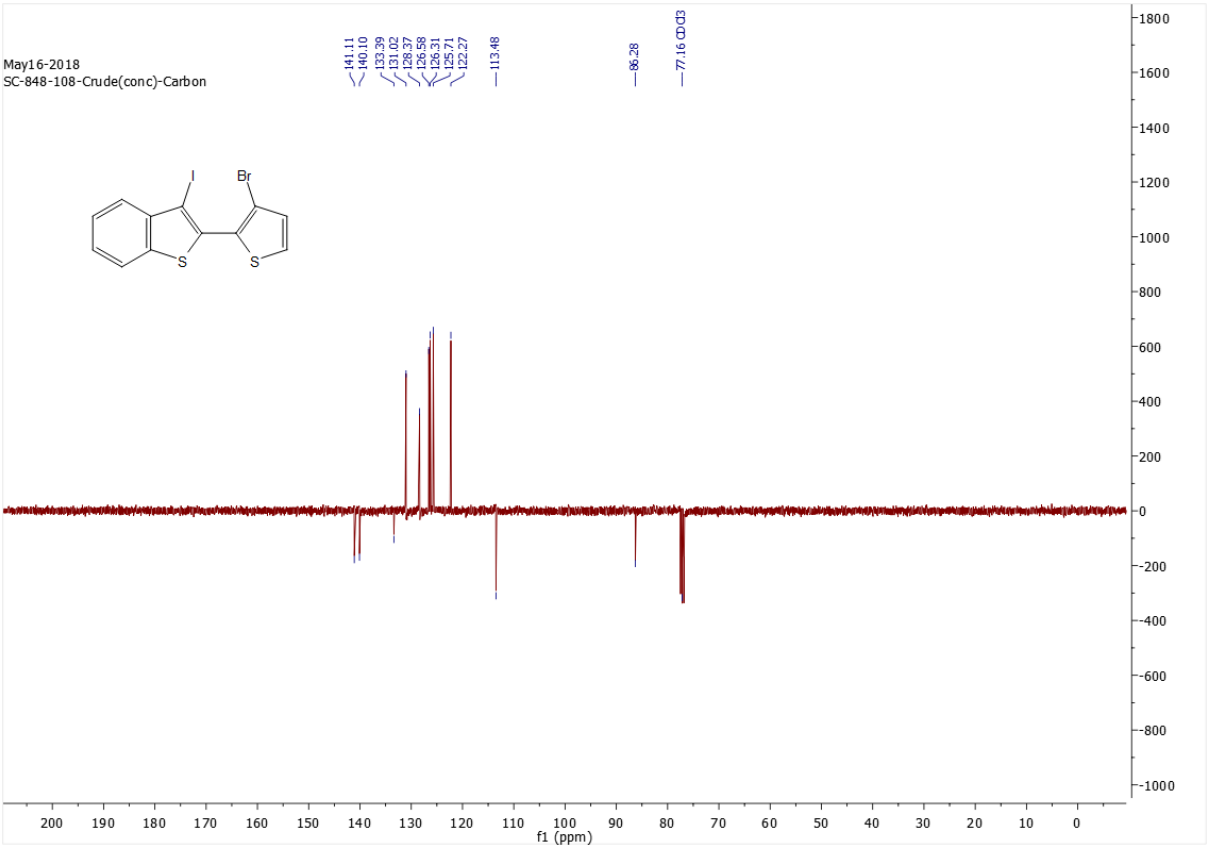
^{13}C DEPT-Q NMR of 3-bromo-2-((2-(methylthio)phenyl)ethynyl)thiophene (**28**):



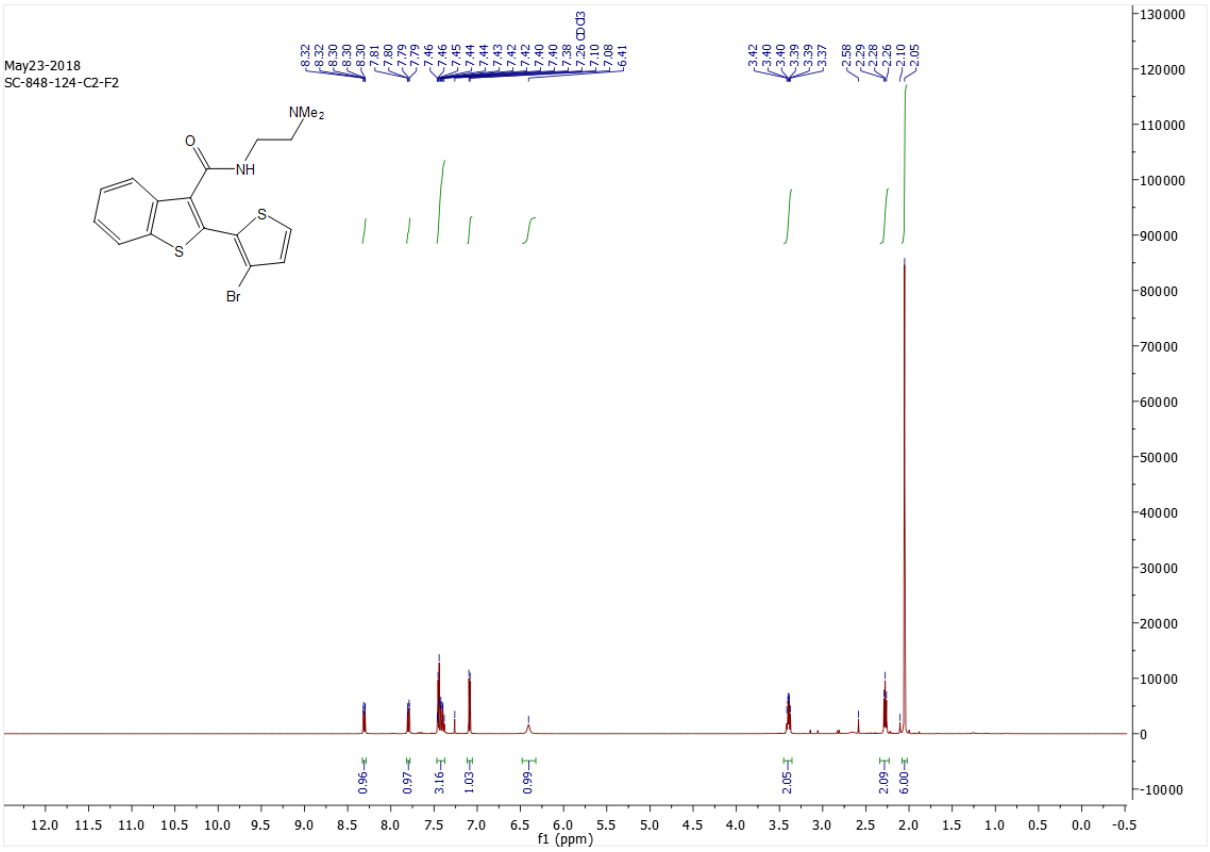
^{1}H NMR of 2-(3-bromothiophen-2-yl)-3-iodobenzo[*b*]thiophene (**29**):



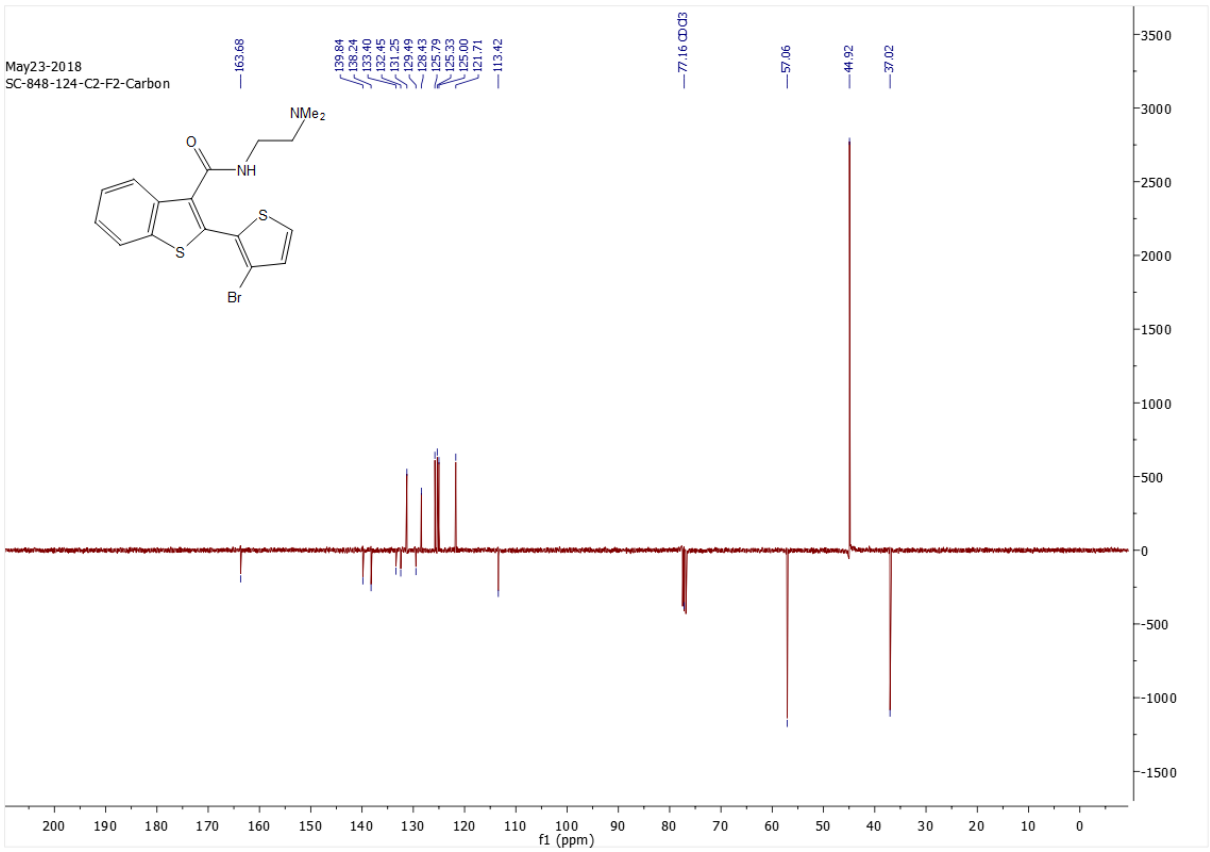
^{13}C DEPT-Q NMR of 2-(3-bromothiophen-2-yl)-3-iodobenzo[*b*]thiophene (**29**):



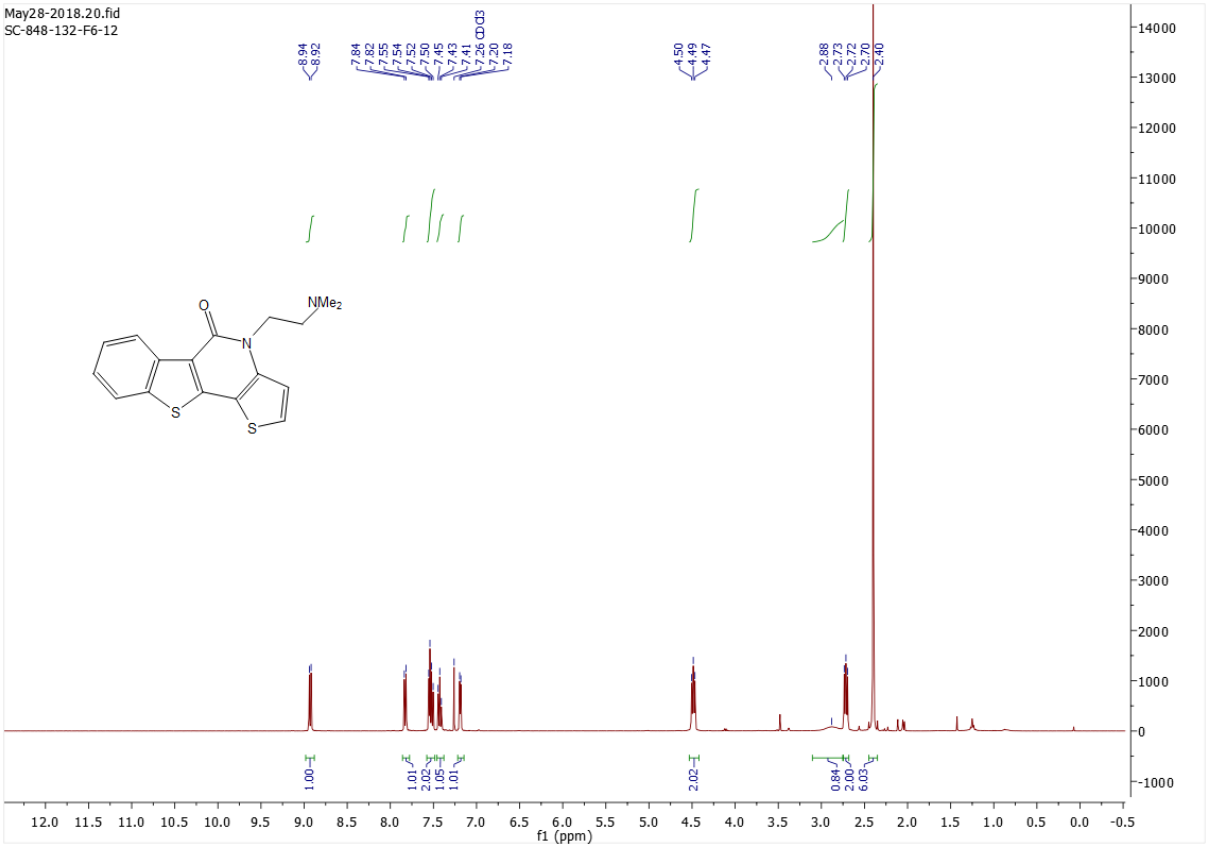
^{1}H NMR of 2-(3-bromothiophen-2-yl)-*N*-(2-(dimethylamino)ethyl)benzo[*b*]thiophene-3-carboxamide:



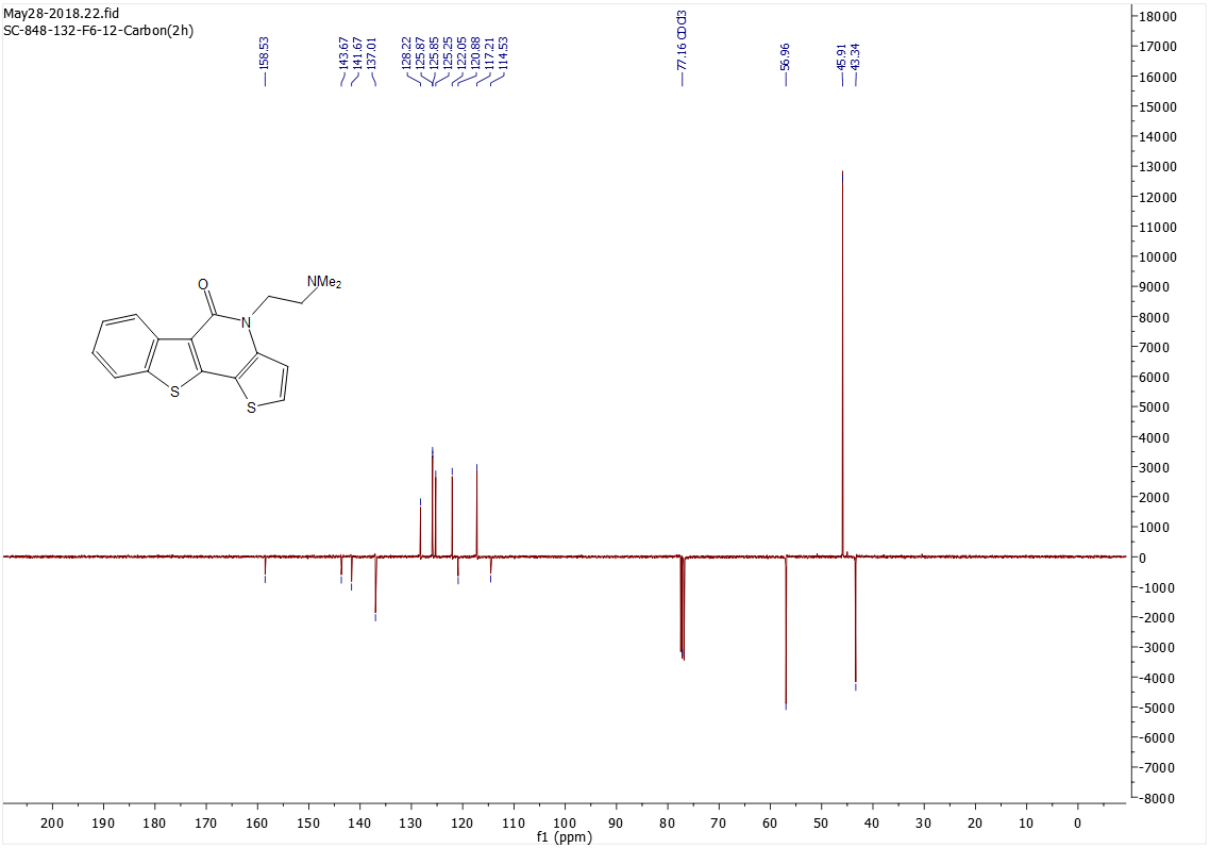
^{13}C DEPT-Q NMR of 2-(3-bromothiophen-2-yl)-*N*-(2-(dimethylamino)ethyl)benzo[*b*]thiophene-3-carboxamide:



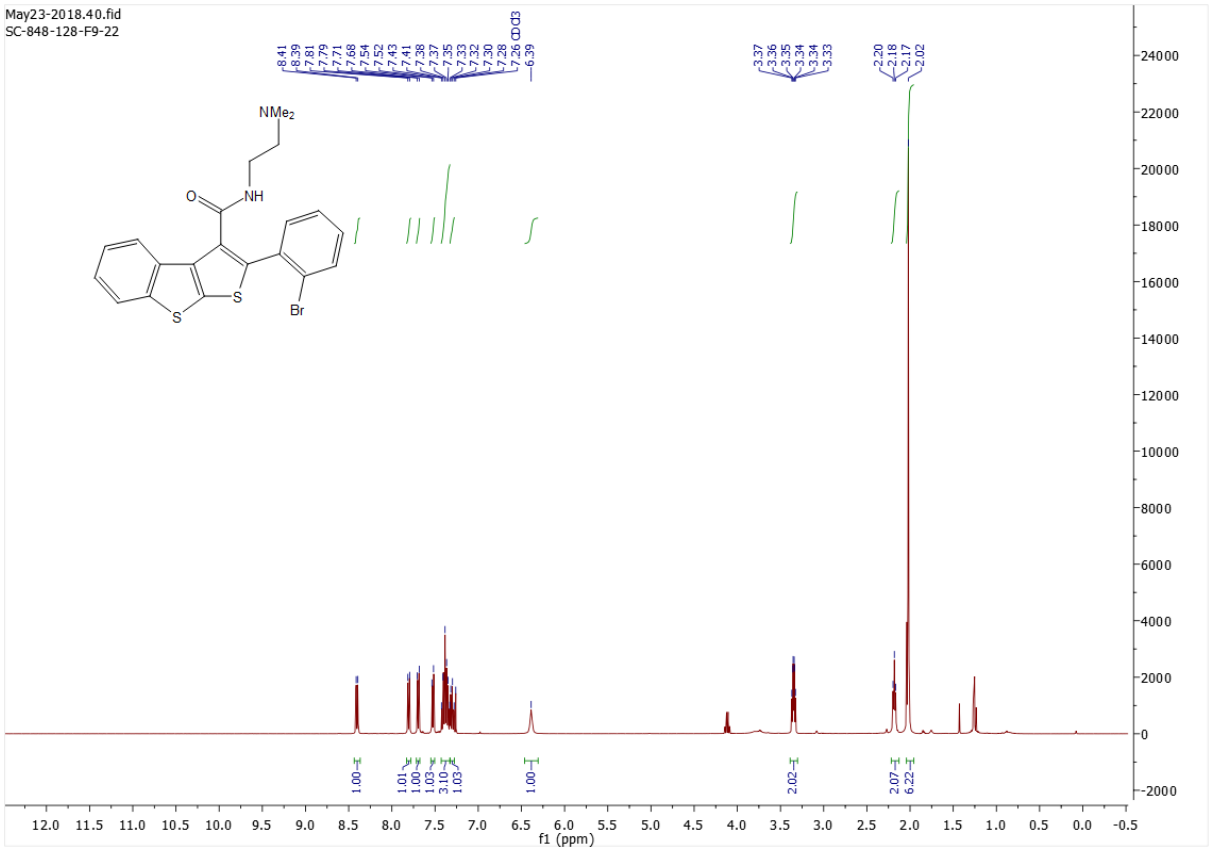
^{1}H NMR of 4-(2-(dimethylamino)ethyl)benzo[4,5]thieno[2,3-*d*]thieno[3,2-*b*]pyridin-5(4*H*)-one (**30**):



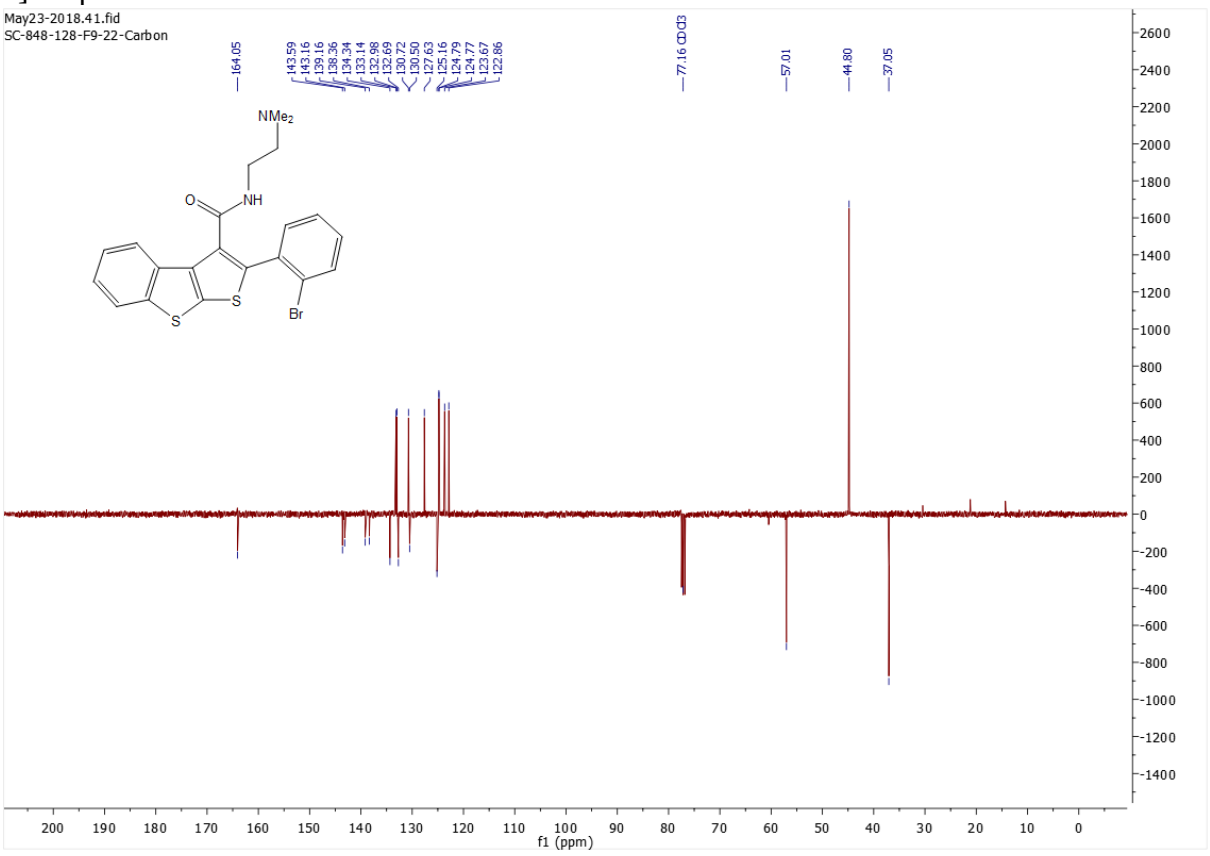
^{13}C DEPT-Q NMR of 4-(2-(dimethylamino)ethyl)benzo[4,5]thieno[2,3-*d*]thieno[3,2-*b*]pyridin-5(4*H*)-one (**30**):



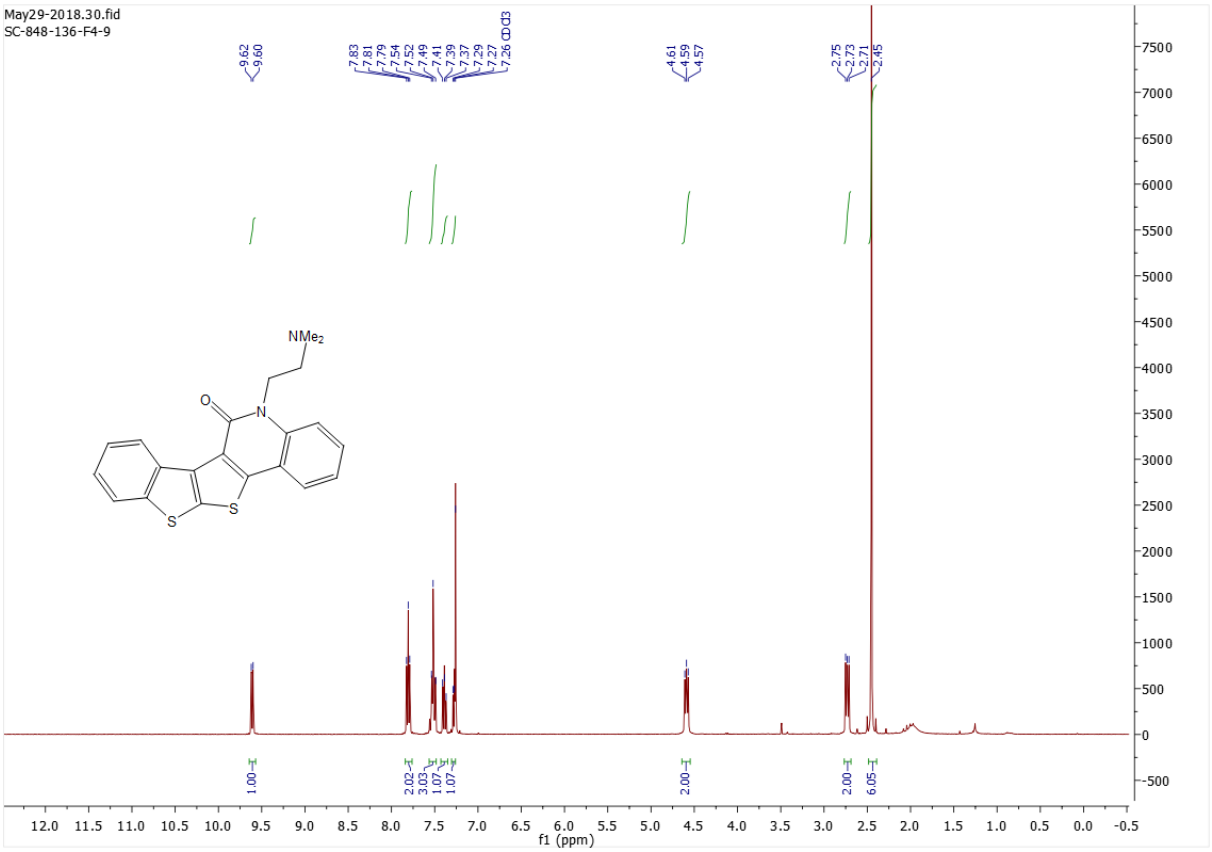
^{1}H NMR of 2-(2-bromophenyl)-*N*-(2-(dimethylamino)ethyl)benzo[*b*]thieno[3,2-*d*]thiophene-3-carboxamide:



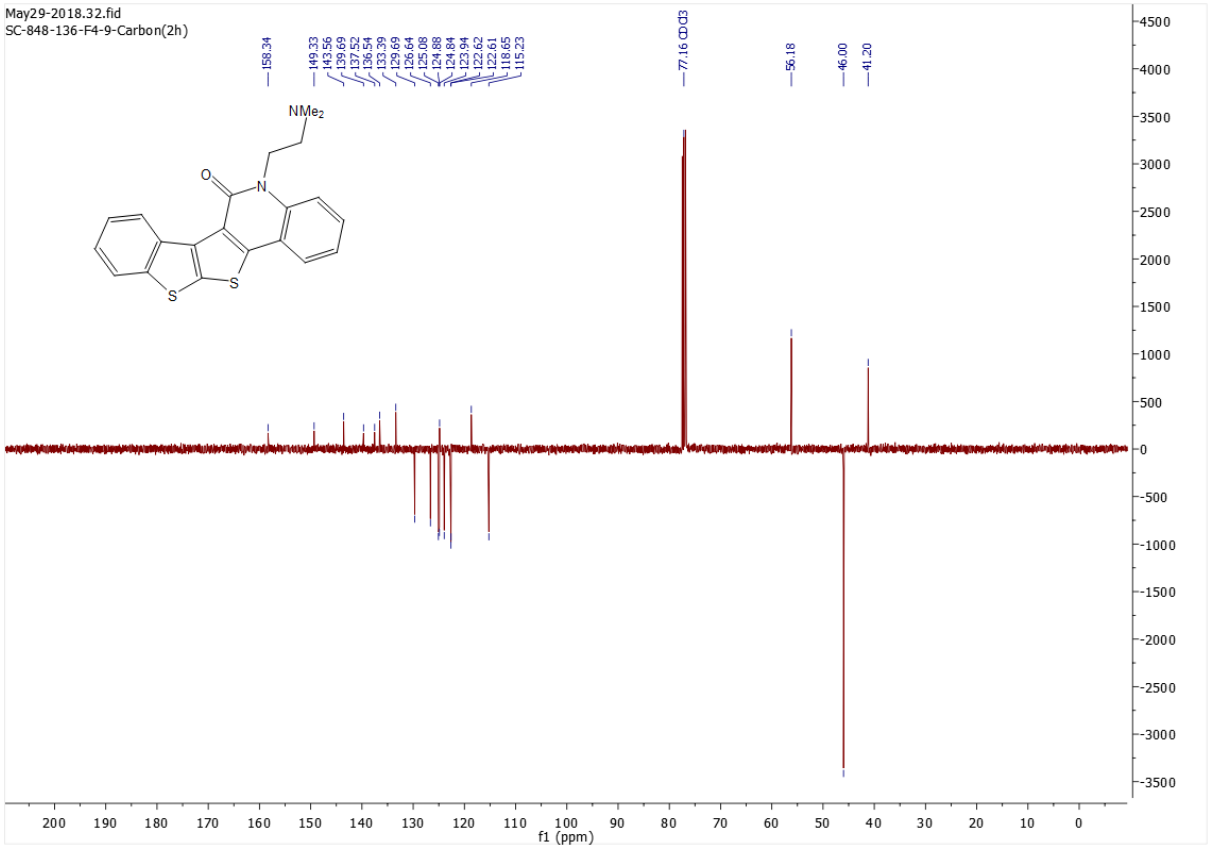
^{13}C DEPT-Q NMR of 2-(2-bromophenyl)-*N*-(2-(dimethylamino)ethyl)benzo[*b*]thieno[3,2-*d*]thiophene-3-carboxamide:



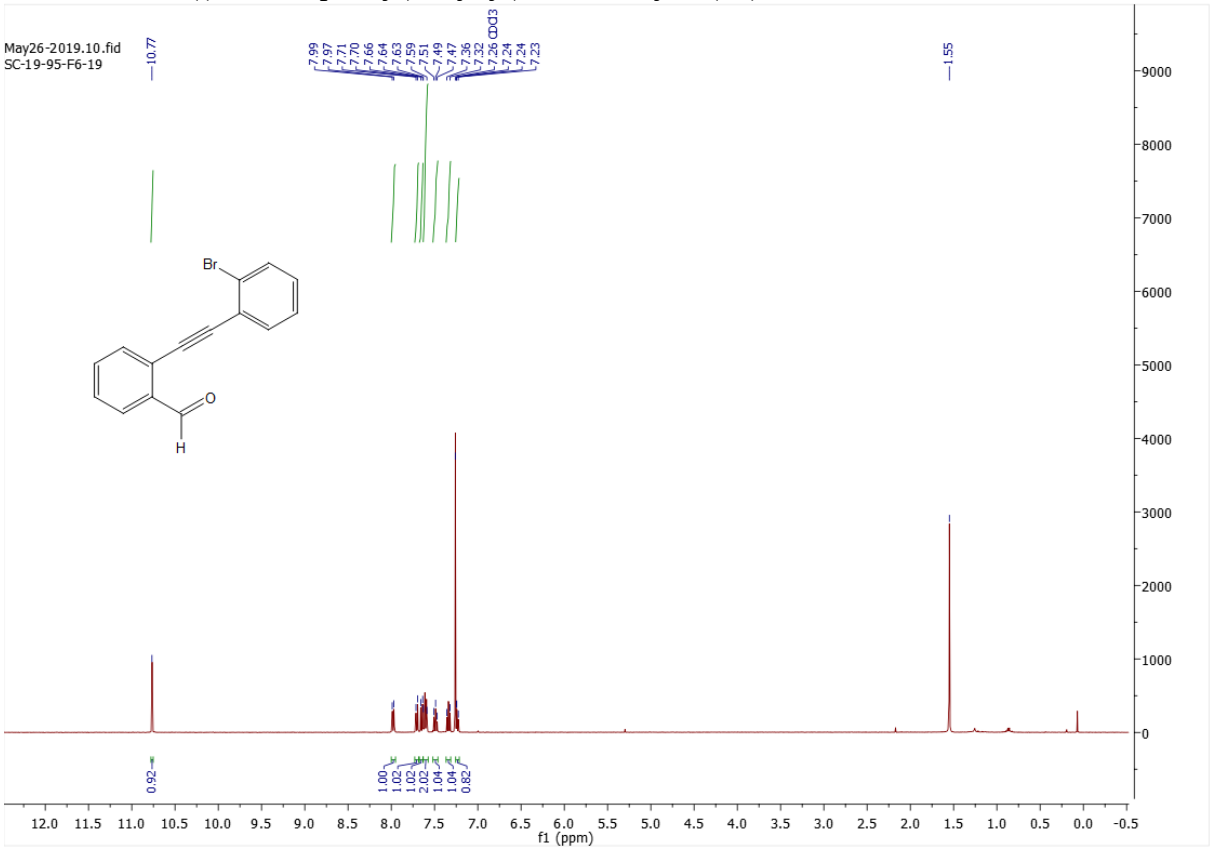
^{1}H NMR of 5-(2-(dimethylamino)ethyl)benzo[4',5']thieno[3',2':4,5]thieno[3,2-*c*]quinolin-6(5*H*)-one (**35**):



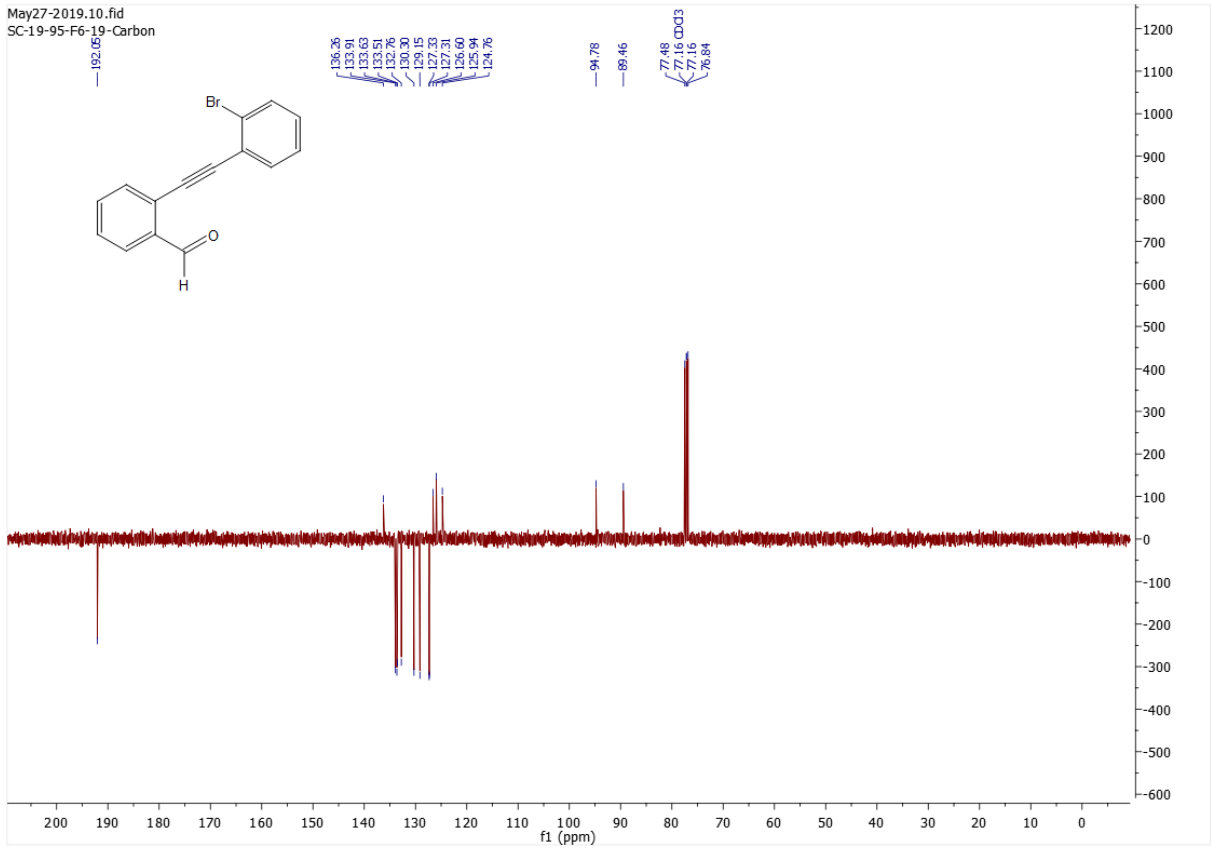
^{13}C DEPT-Q NMR of 5-(2-(dimethylamino)ethyl)benzo[4',5']thieno[3',2':4,5]thieno[3,2-*c*]quinolin-6(5*H*)-one (**35**):



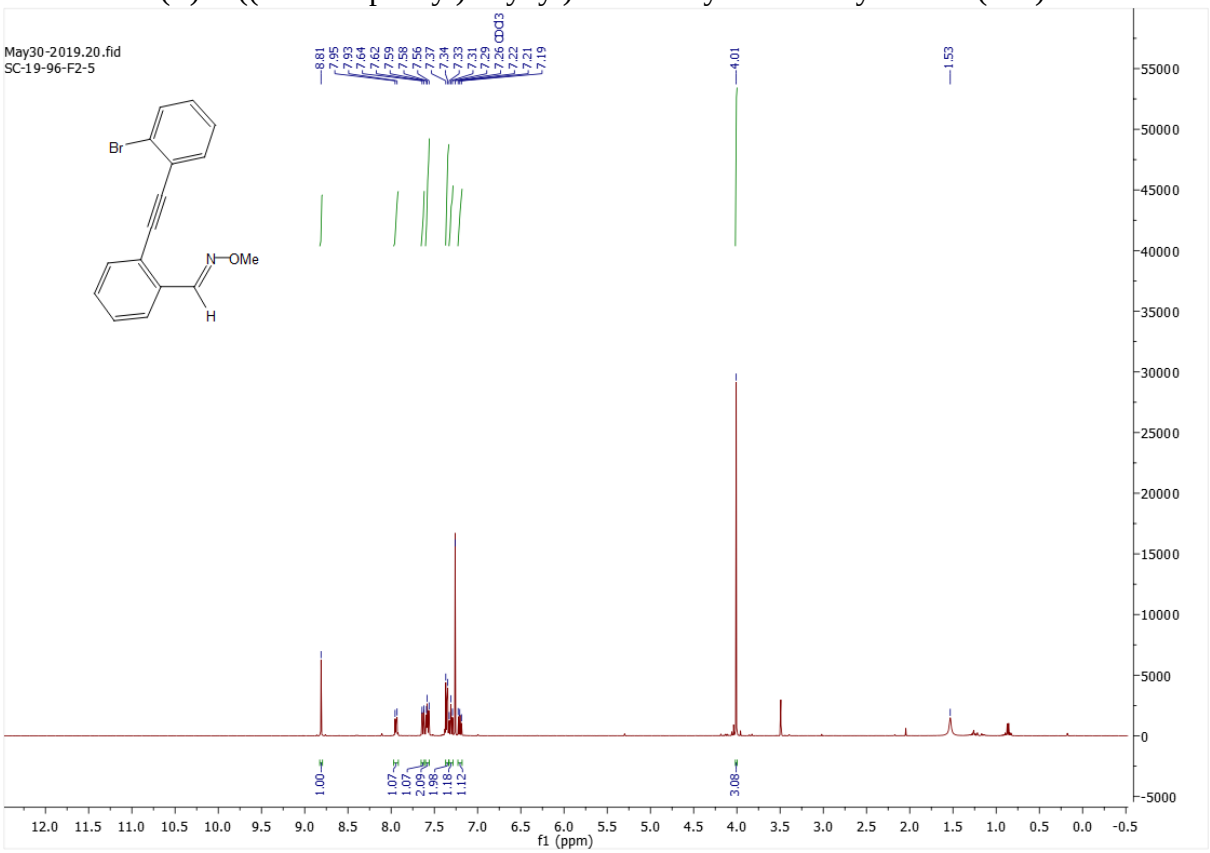
^{1}H NMR of 2-((2-bromophenyl)ethynyl)benzaldehyde (**37**):



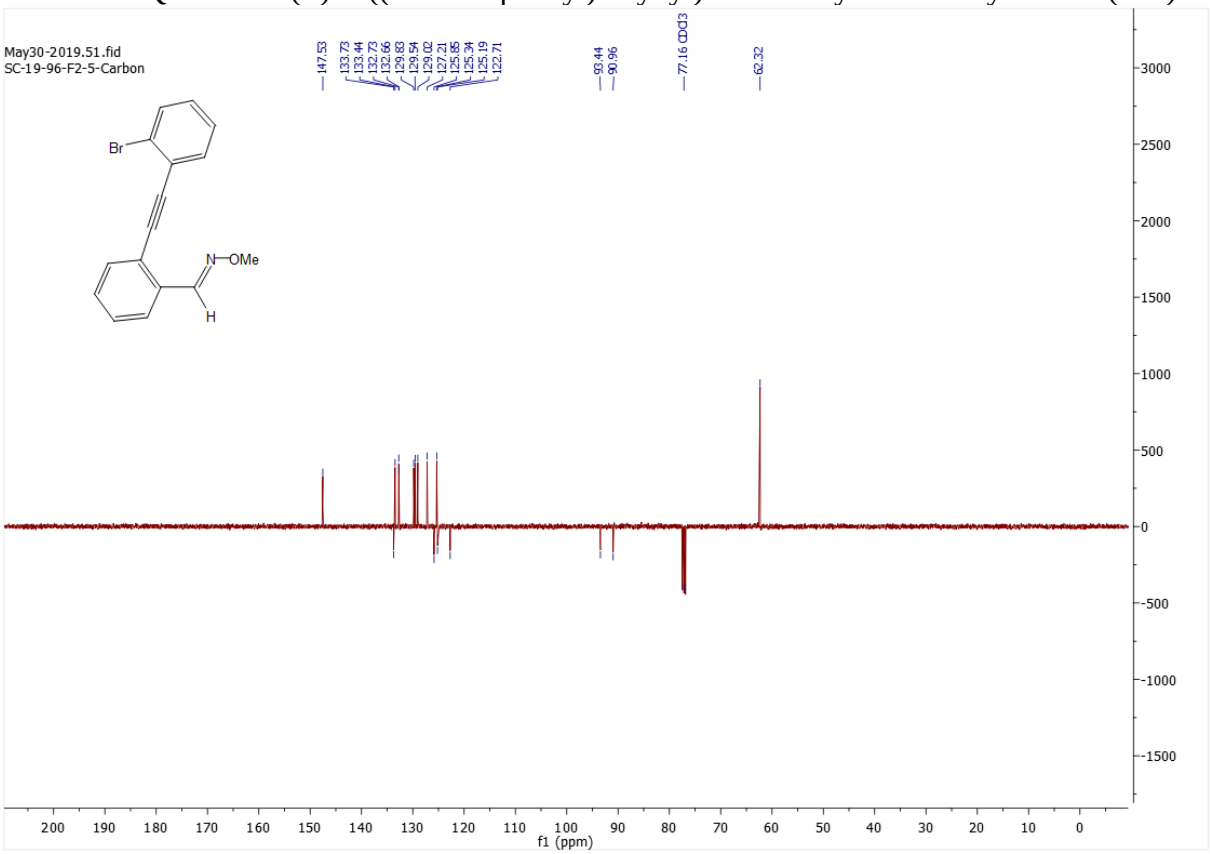
^{13}C DEPT-Q NMR of 2-((2-bromophenyl)ethynyl)benzaldehyde (**37**):



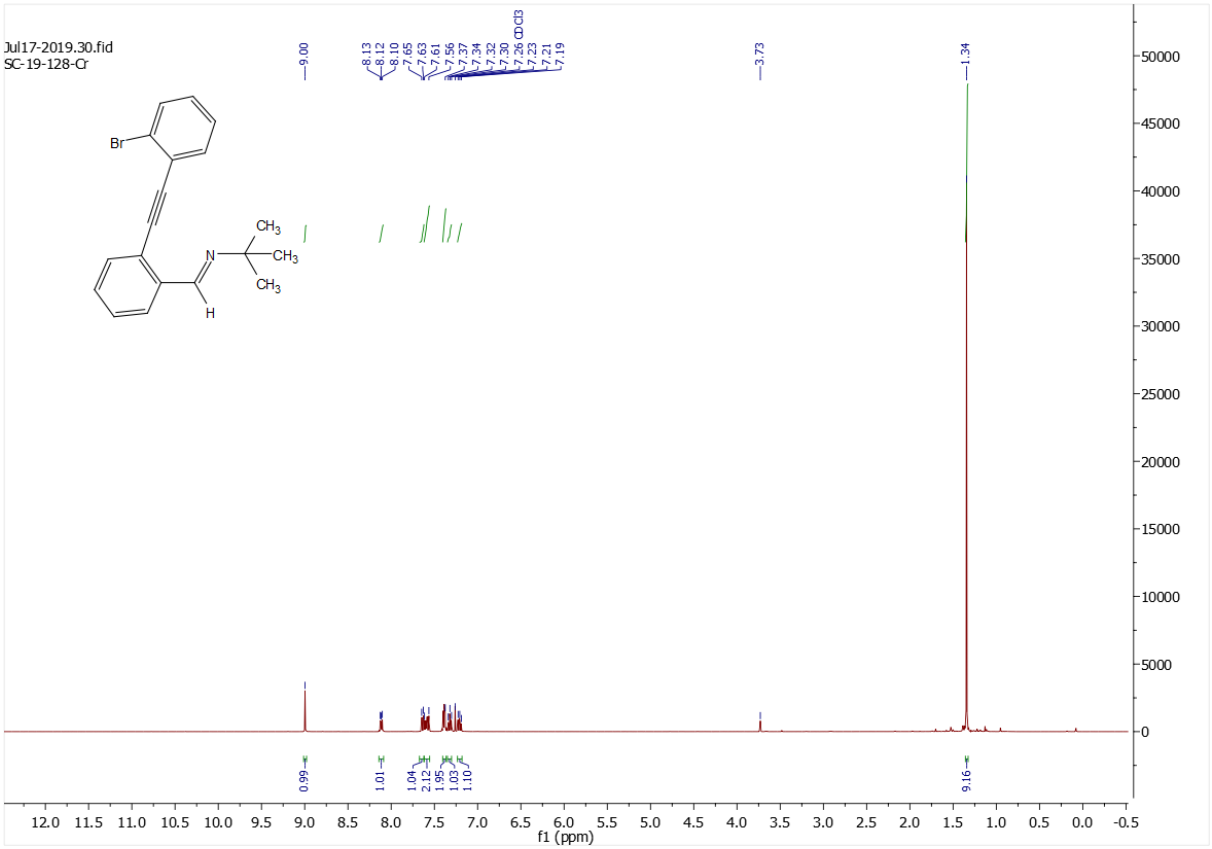
^{1}H NMR of (*E*)-2-((2-bromophenyl)ethynyl)benzaldehyde *O*-methyl oxime (**38a**):



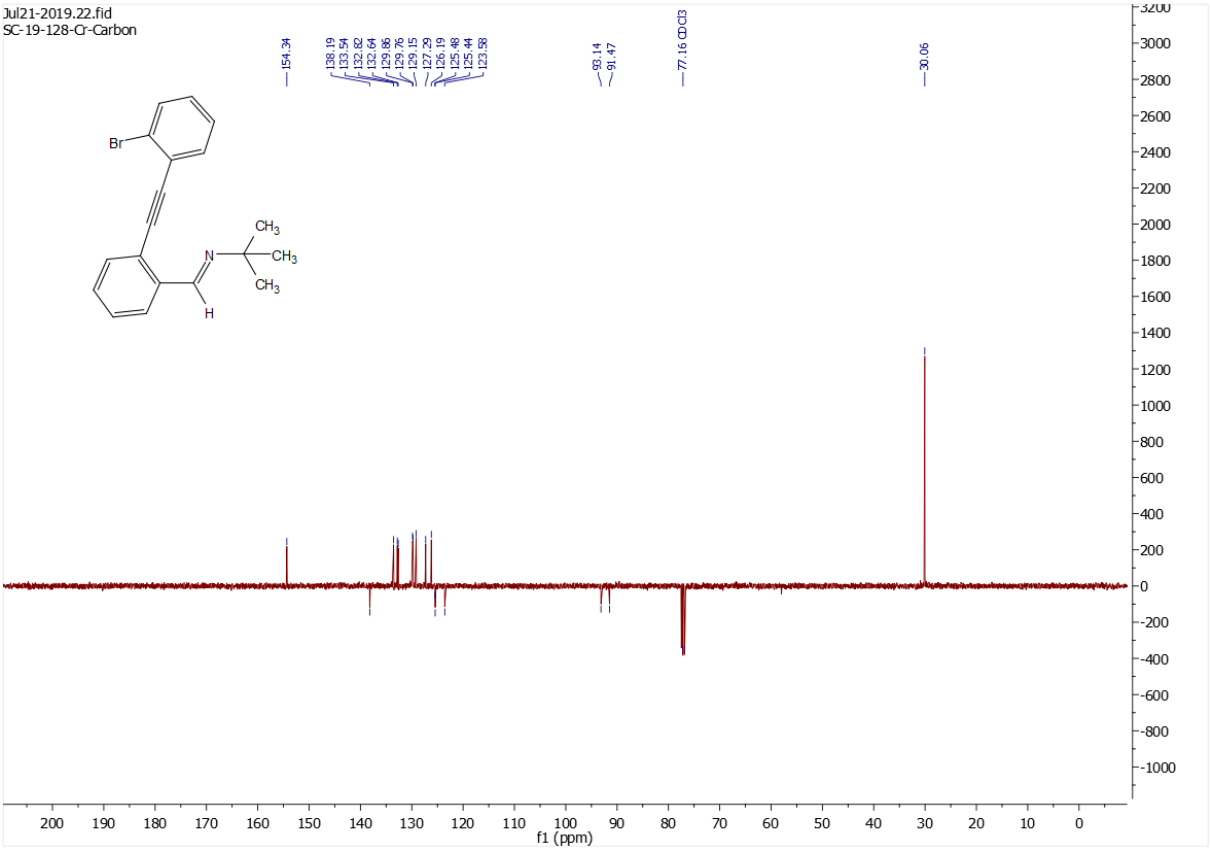
^{13}C DEPT-Q NMR of (*E*)-2-((2-bromophenyl)ethynyl)benzaldehyde *O*-methyl oxime (**38a**):



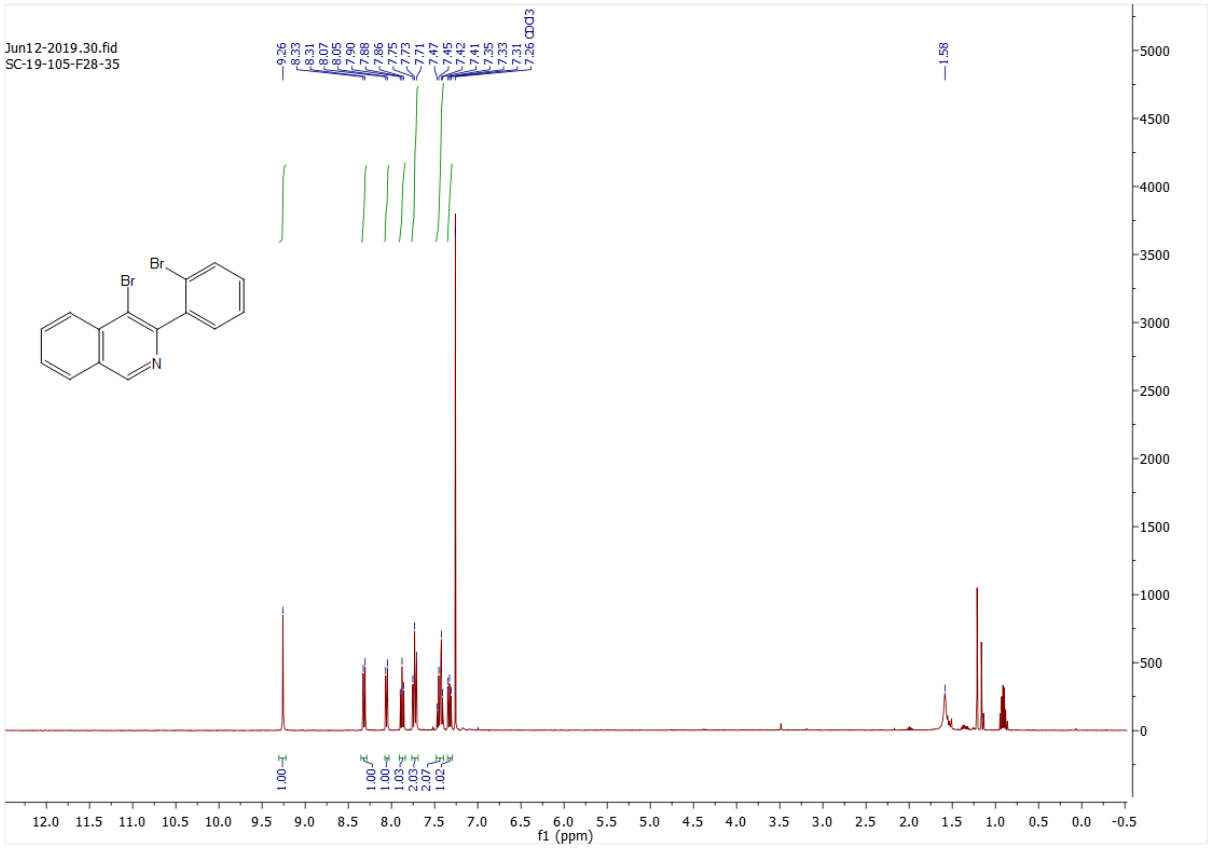
^{1}H NMR of (*E*)-1-(2-((2-Bromophenyl)ethynyl)phenyl)-*N*-(*tert*-butyl)methanimine (**38b**):



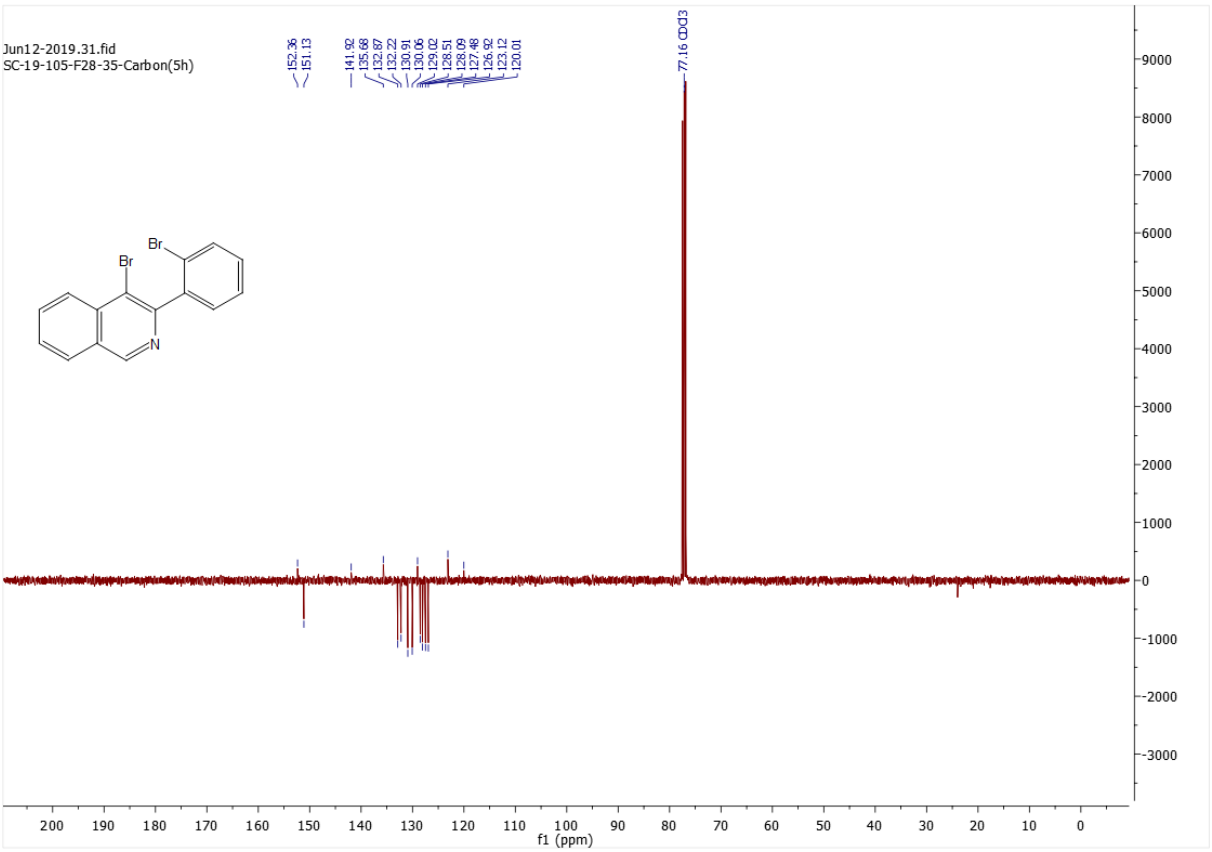
^{13}C DEPT-Q NMR of (*E*)-1-(2-((2-Bromophenyl)ethynyl)phenyl)-*N*-(*tert*-butyl)methanimine (**38b**):



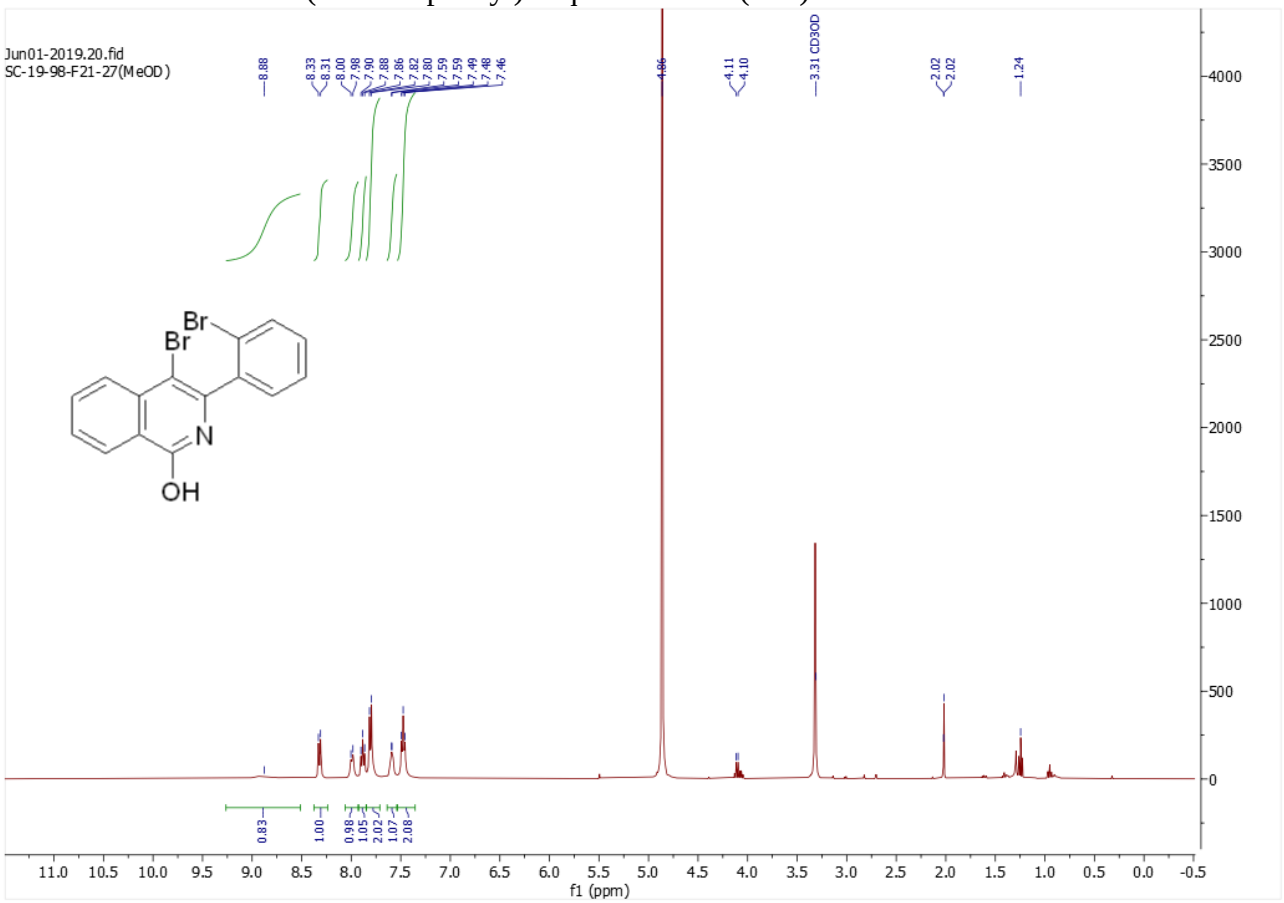
^{1}H NMR of 4-bromo-3-(2-bromophenyl)isoquinoline (**39a**):



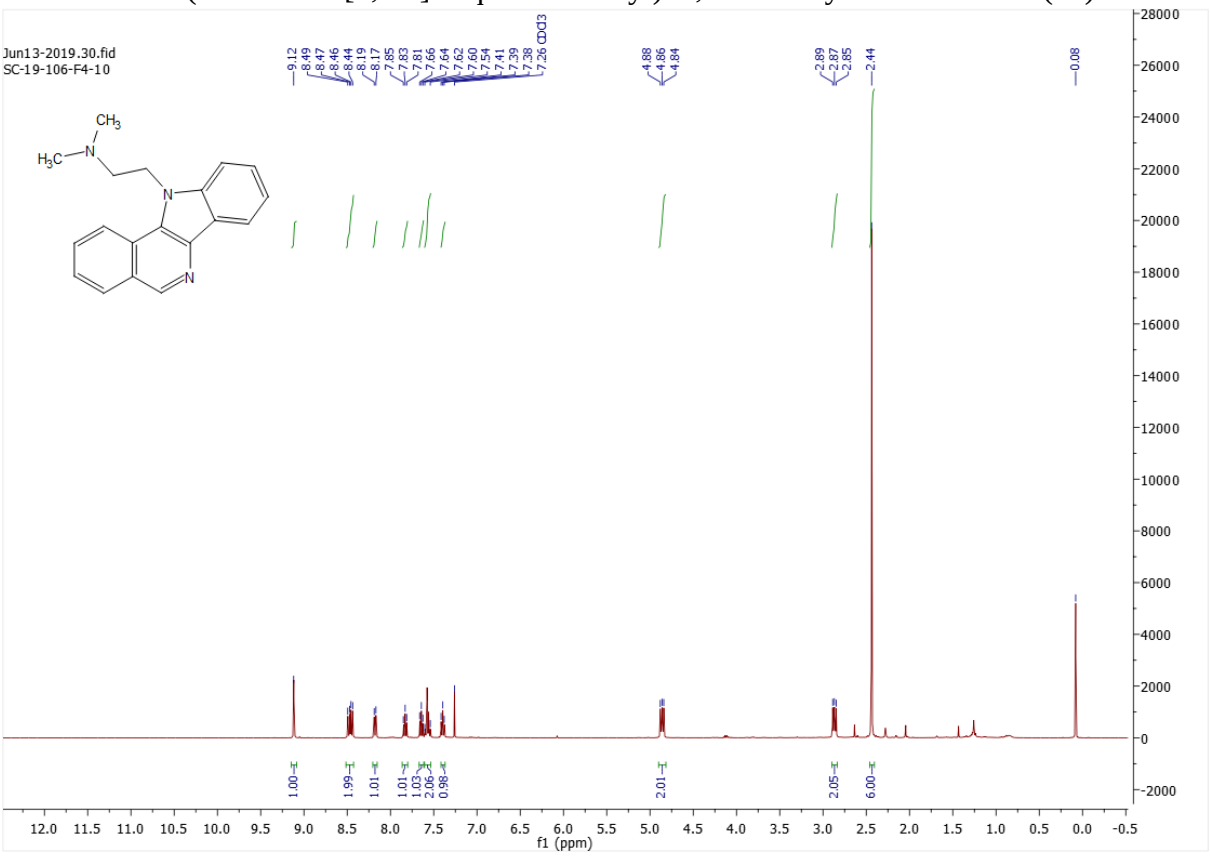
^{13}C DEPT-Q NMR of 4-bromo-3-(2-bromophenyl)isoquinoline (**39a**):



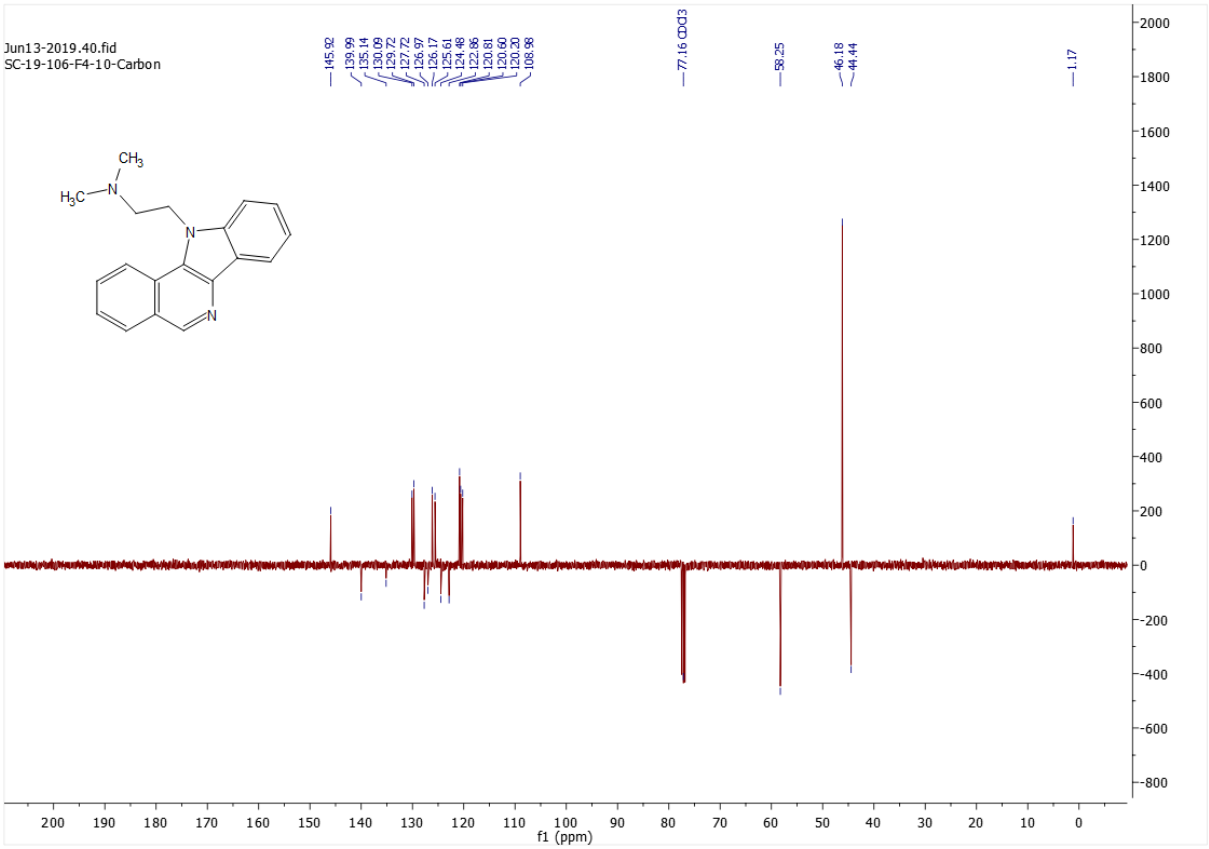
^{1}H NMR of 4-bromo-3-(2-bromophenyl)isoquinolin-1-ol (**39b**):



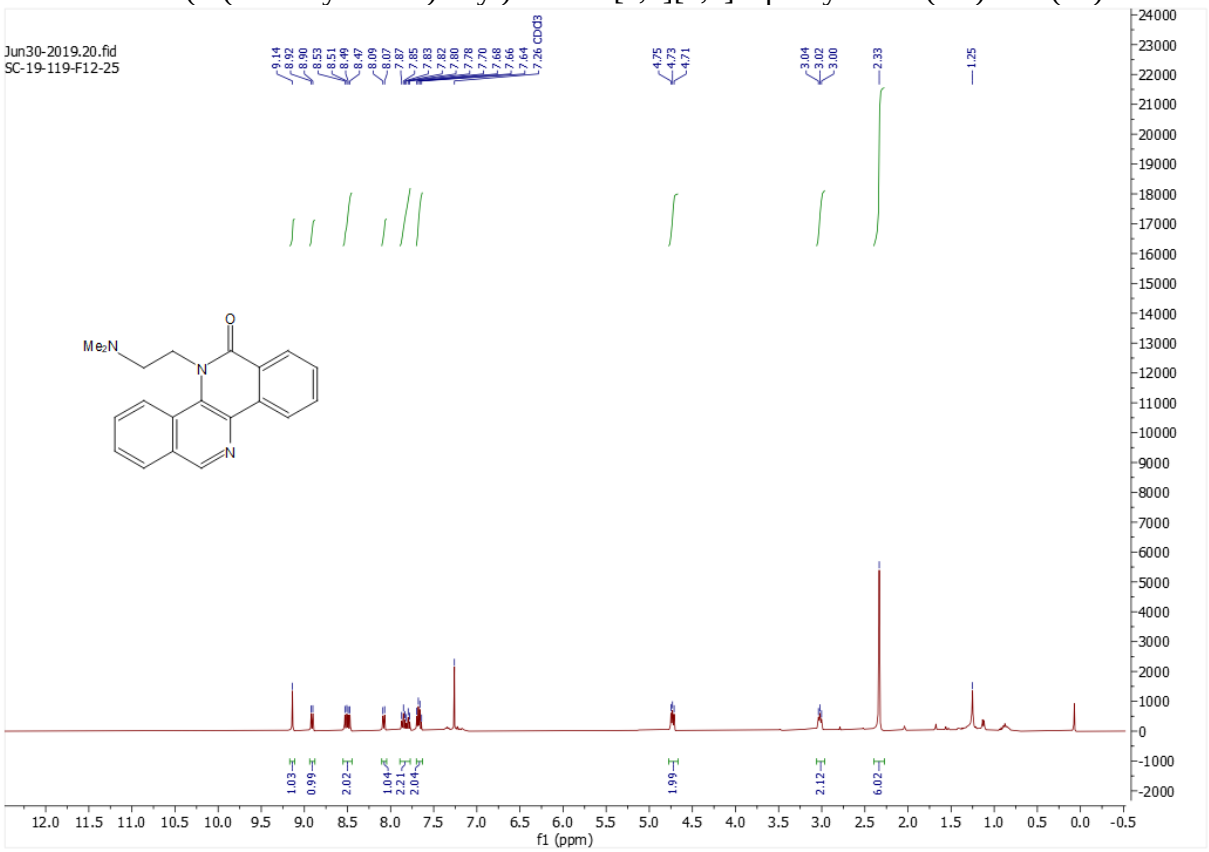
^{1}H NMR of 2-(11*H*-indolo[3,2-*c*]isoquinolin-11-yl)-*N*,*N*-dimethylethan-1-amine (**40**):



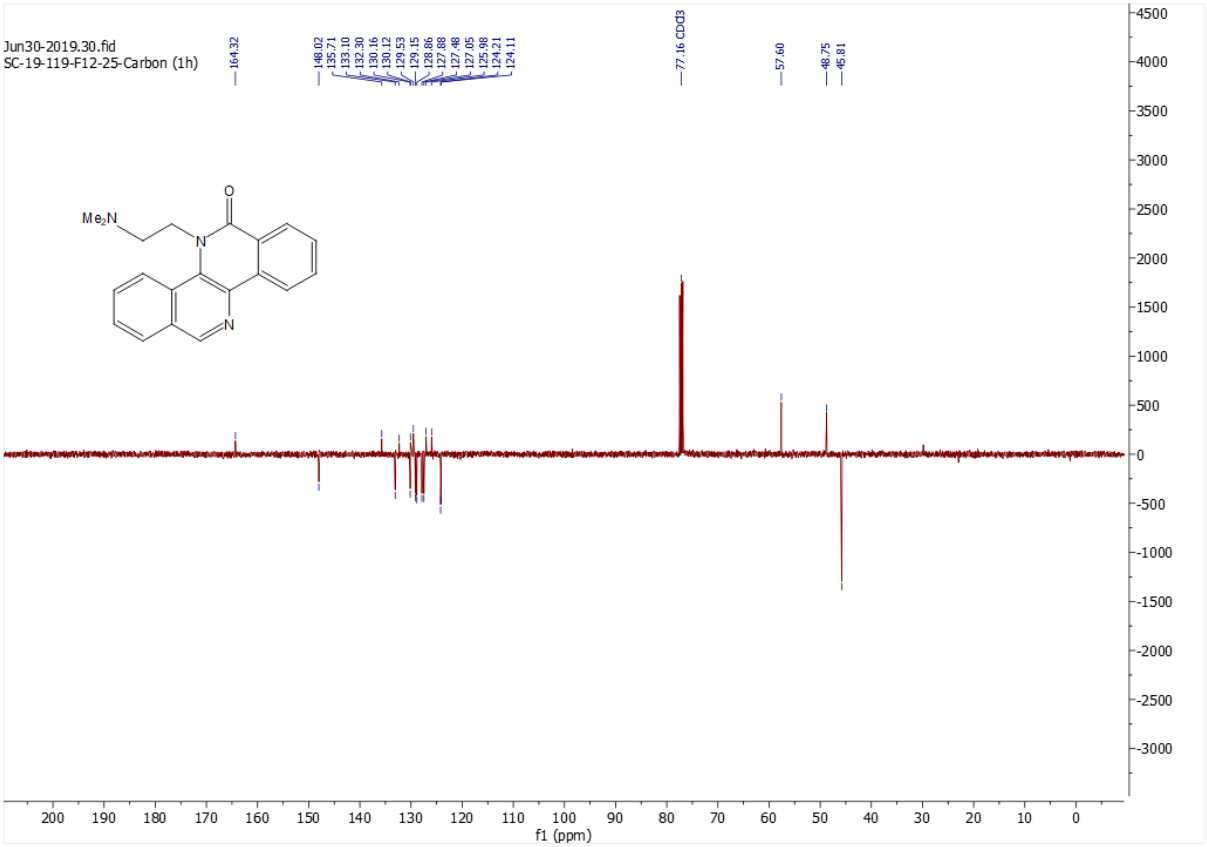
^{13}C DEPT-Q NMR of 2-(11*H*-indolo[3,2-*c*]isoquinolin-11-yl)-*N*,*N*-dimethylethan-1-amine (**40**):



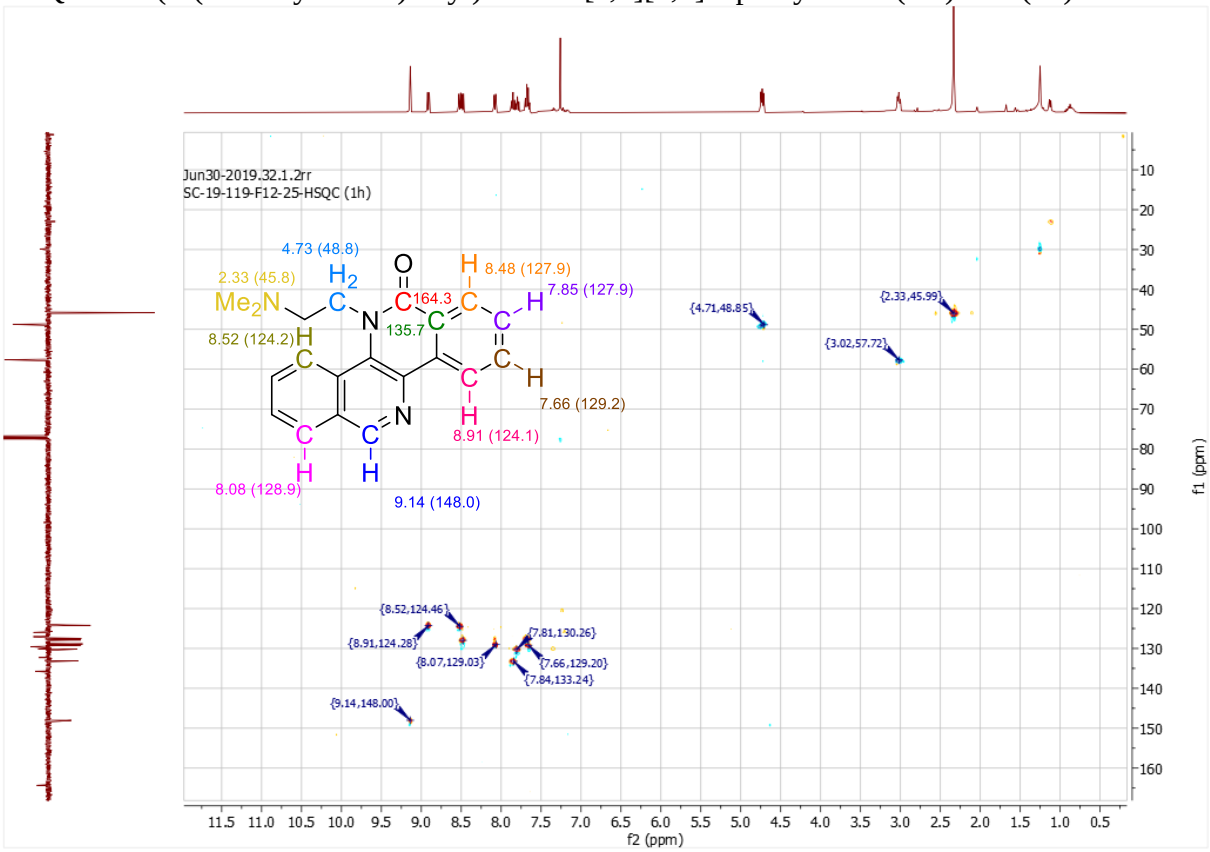
^{1}H NMR of 5-(2-(dimethylamino)ethyl)dibenzo[*c*,*h*][1,5]naphthyridin-6(5*H*)-one (**41**):



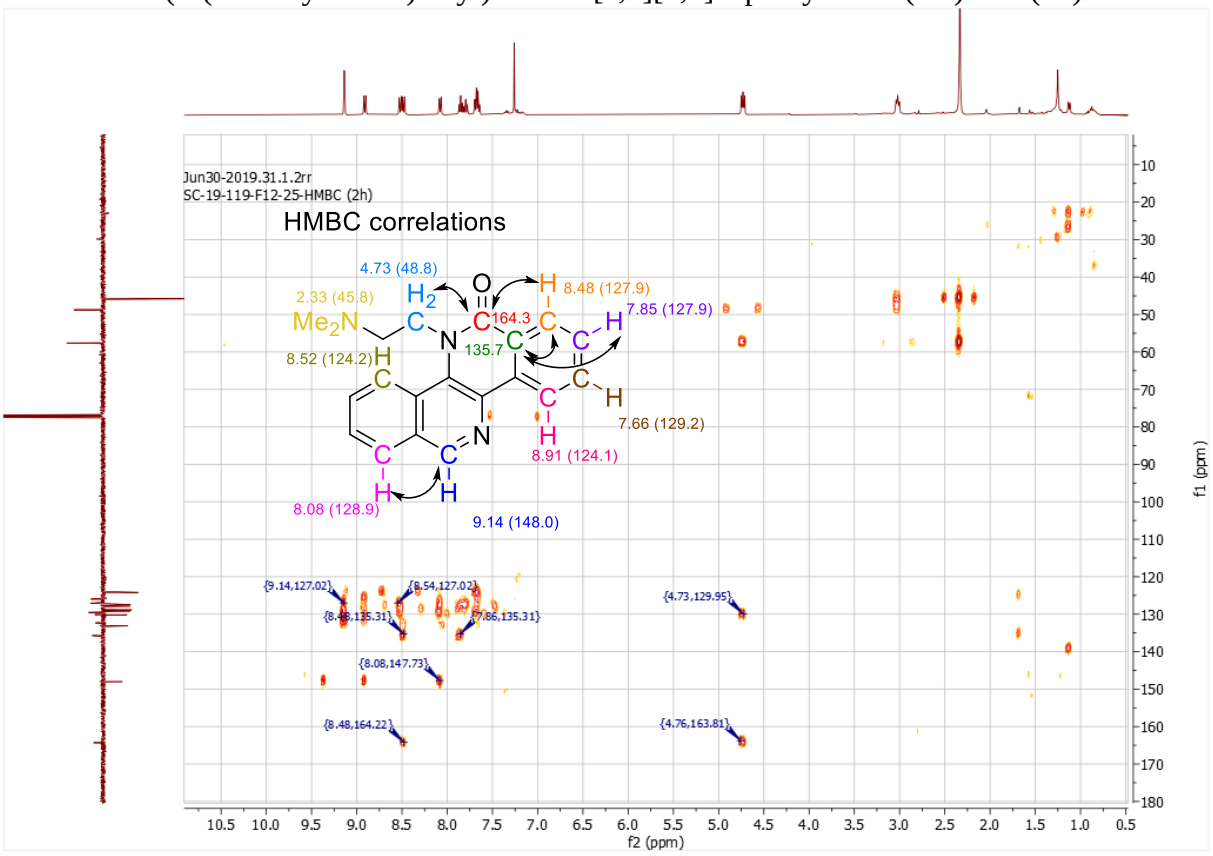
^{13}C DEPT-Q NMR of 5-(2-(dimethylamino)ethyl)dibenzo[*c*,*h*][1,5]naphthyridin-6(5*H*)-one (**41**):



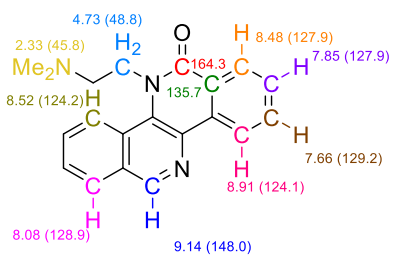
HSQC of 5-(2-(dimethylamino)ethyl)dibenzo[*c*,*h*][1,5]naphthyridin-6(5*H*)-one (**41**):

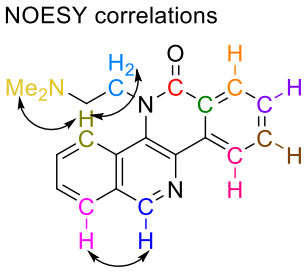


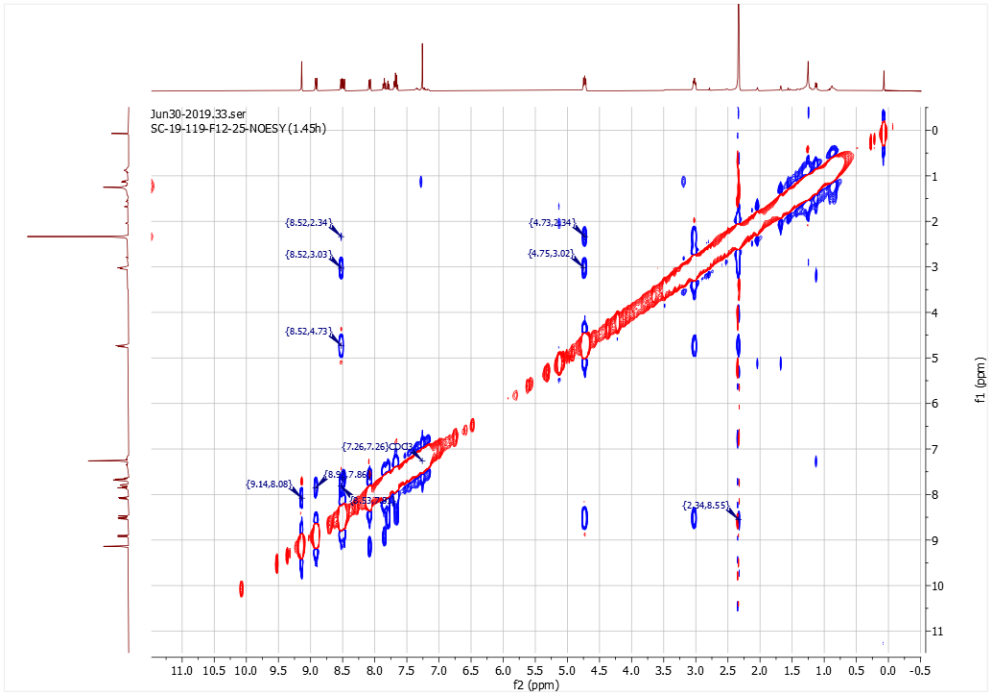
HMBC of 5-(2-(dimethylamino)ethyl)dibenzo[*c*,*h*][1,5]naphthyridin-6(5*H*)-one (**41**):

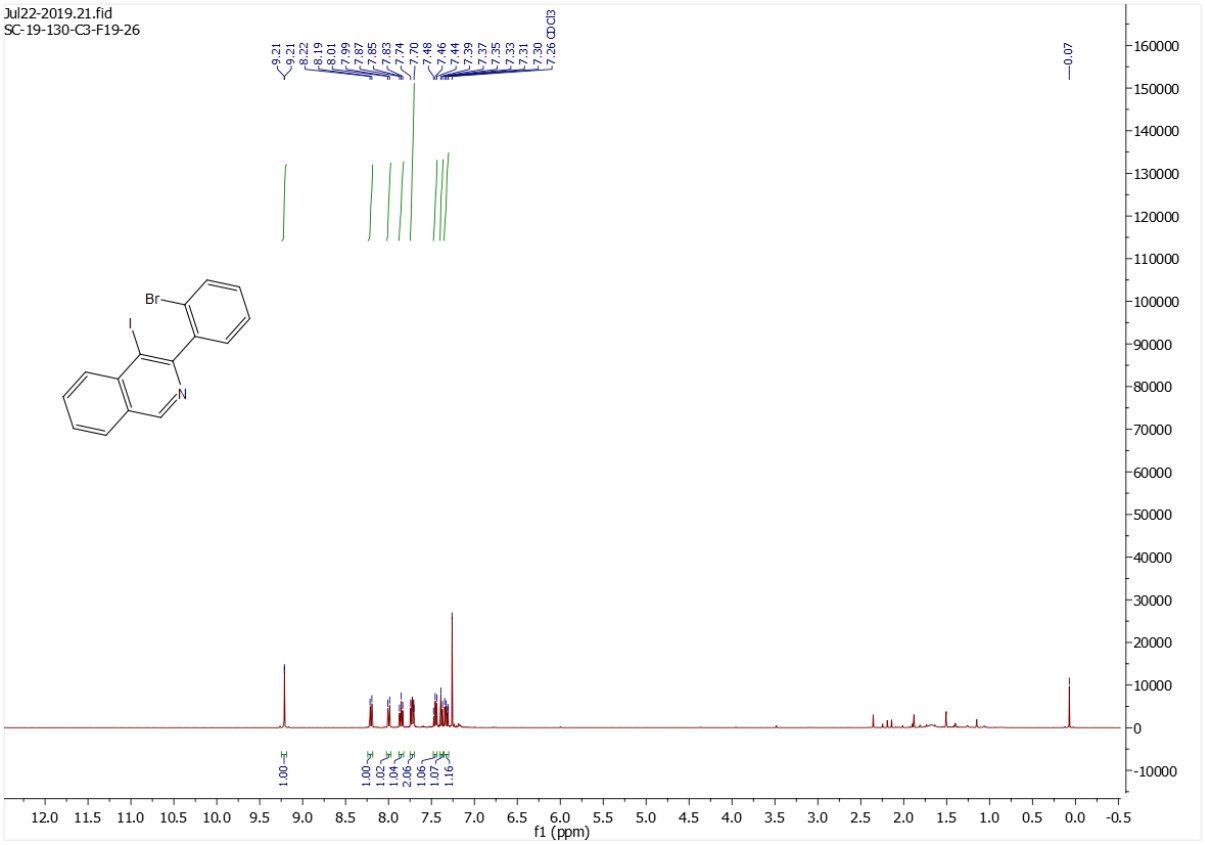


NOESY of 5-(2-(dimethylamino)ethyl)dibenzo[*c*,*h*][1,5]naphthyridin-6(5*H*)-one (**41**):

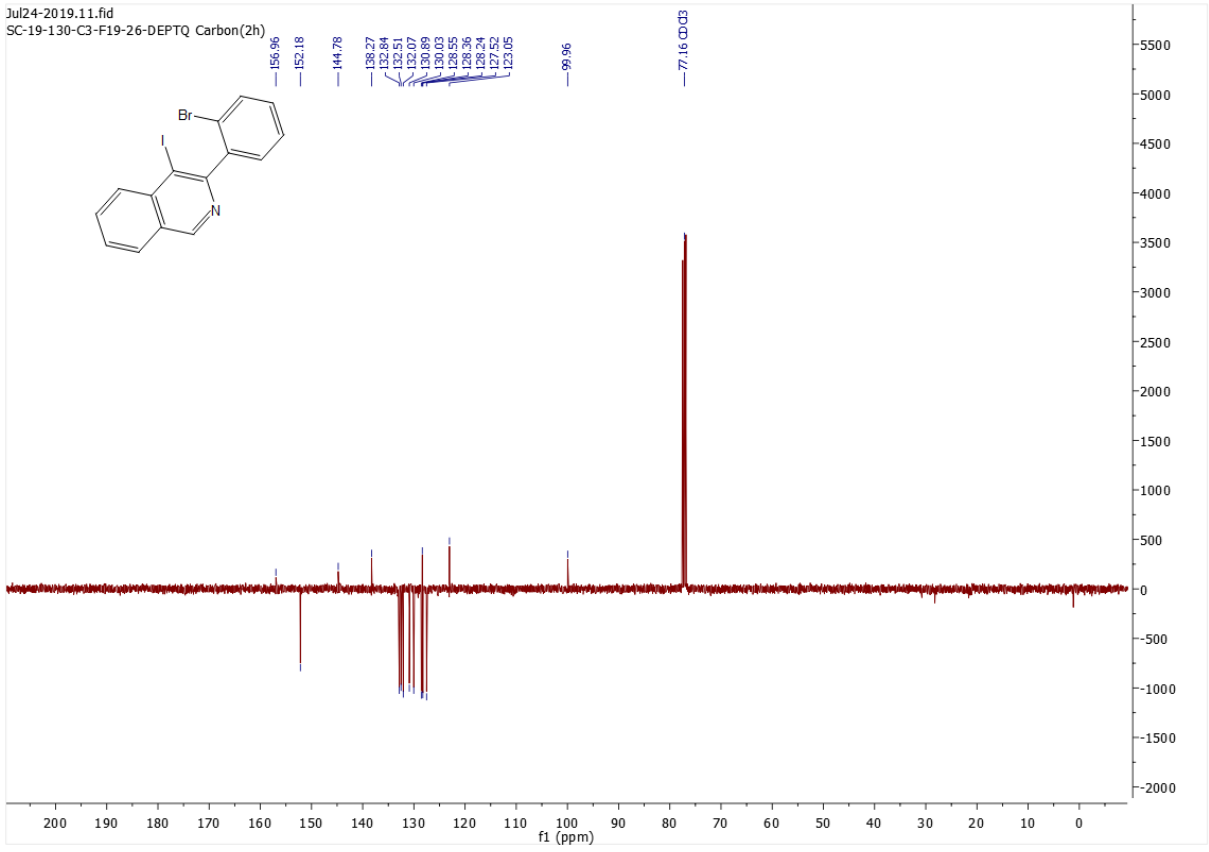




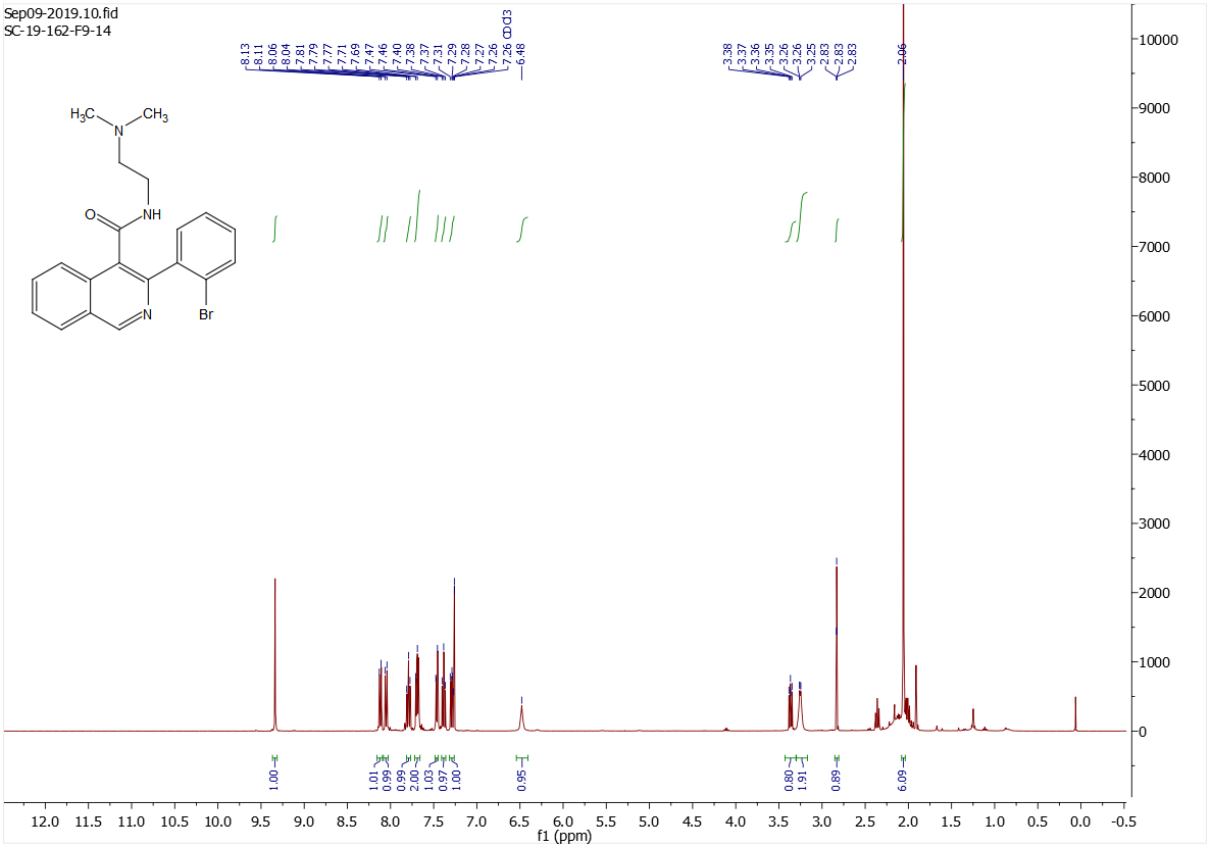




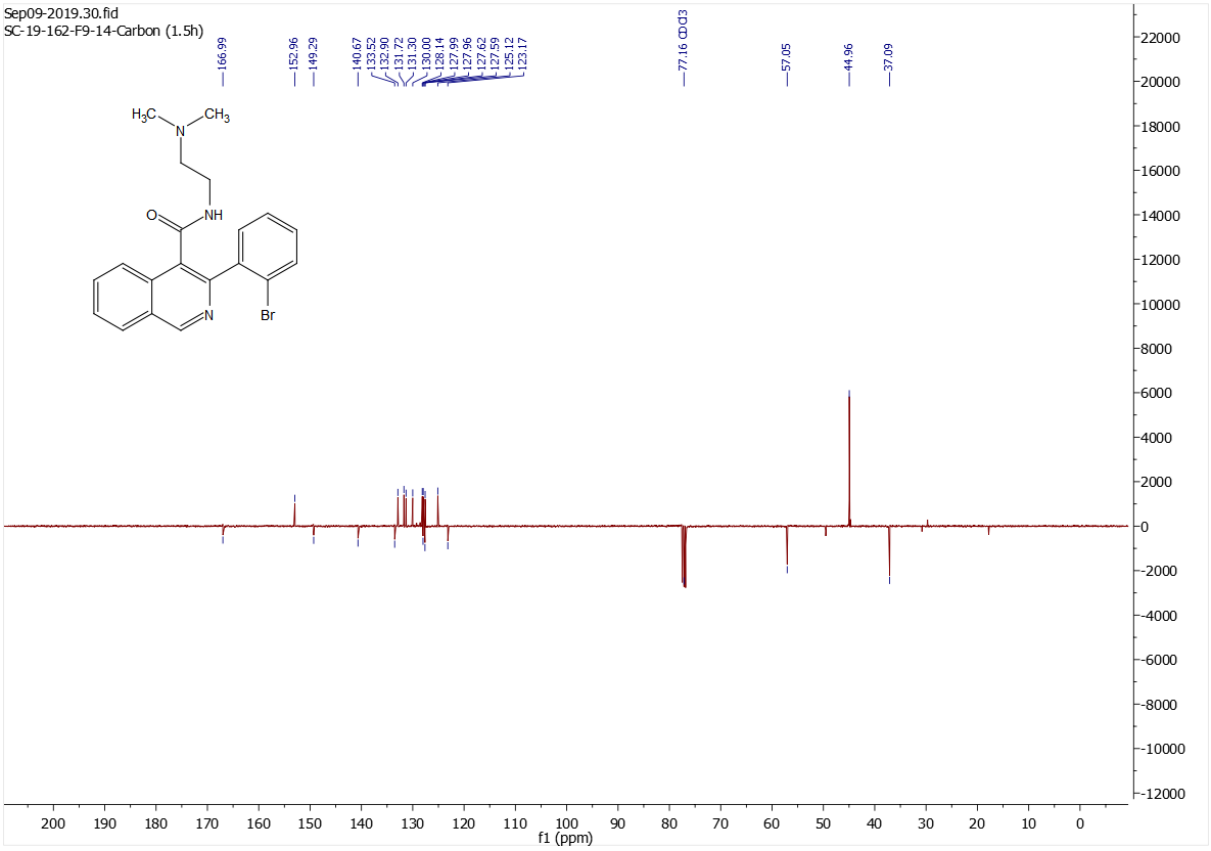
^{13}C DEPT-Q NMR of 3-(2-bromophenyl)-4-iodoisoquinoline (**42**):



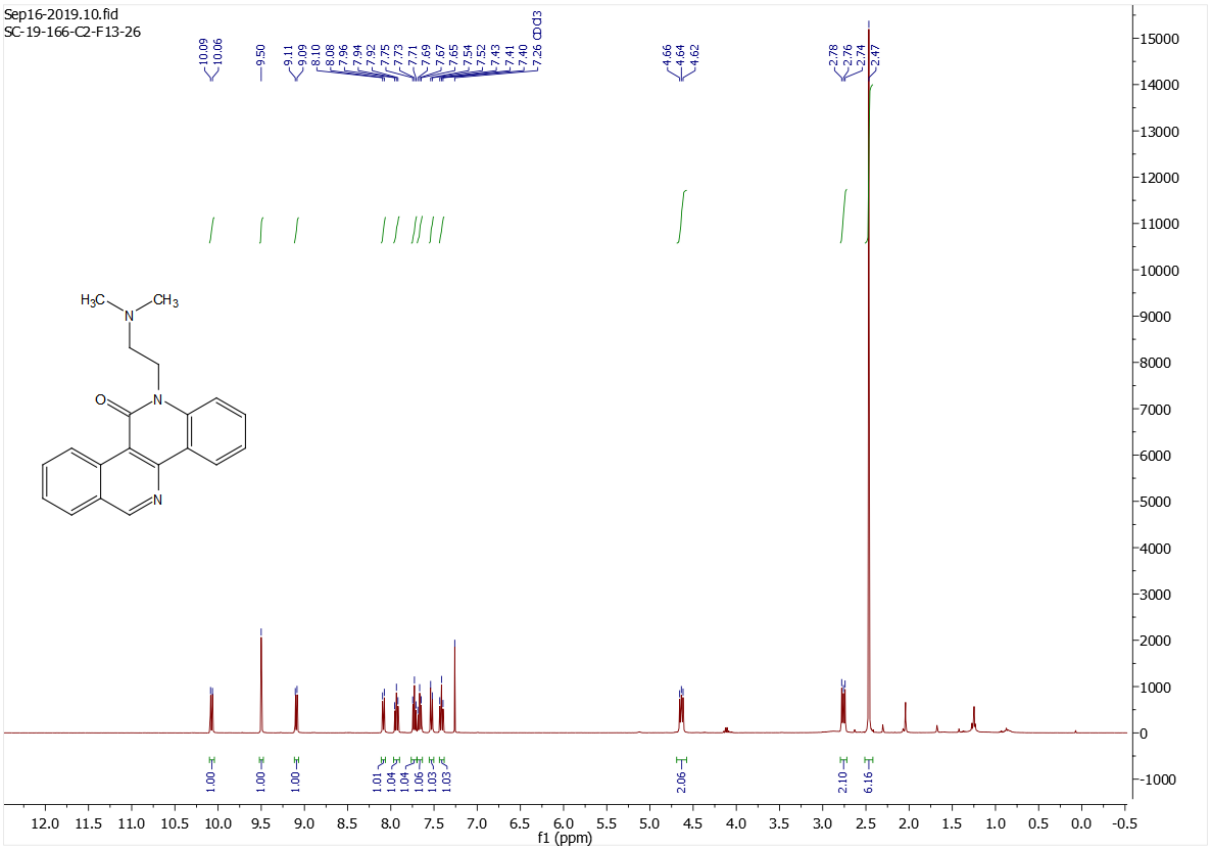
^{1}H NMR of 3-(2-bromophenyl)-*N*-(2-(dimethylamino)ethyl)isoquinoline-4-carboxamide:



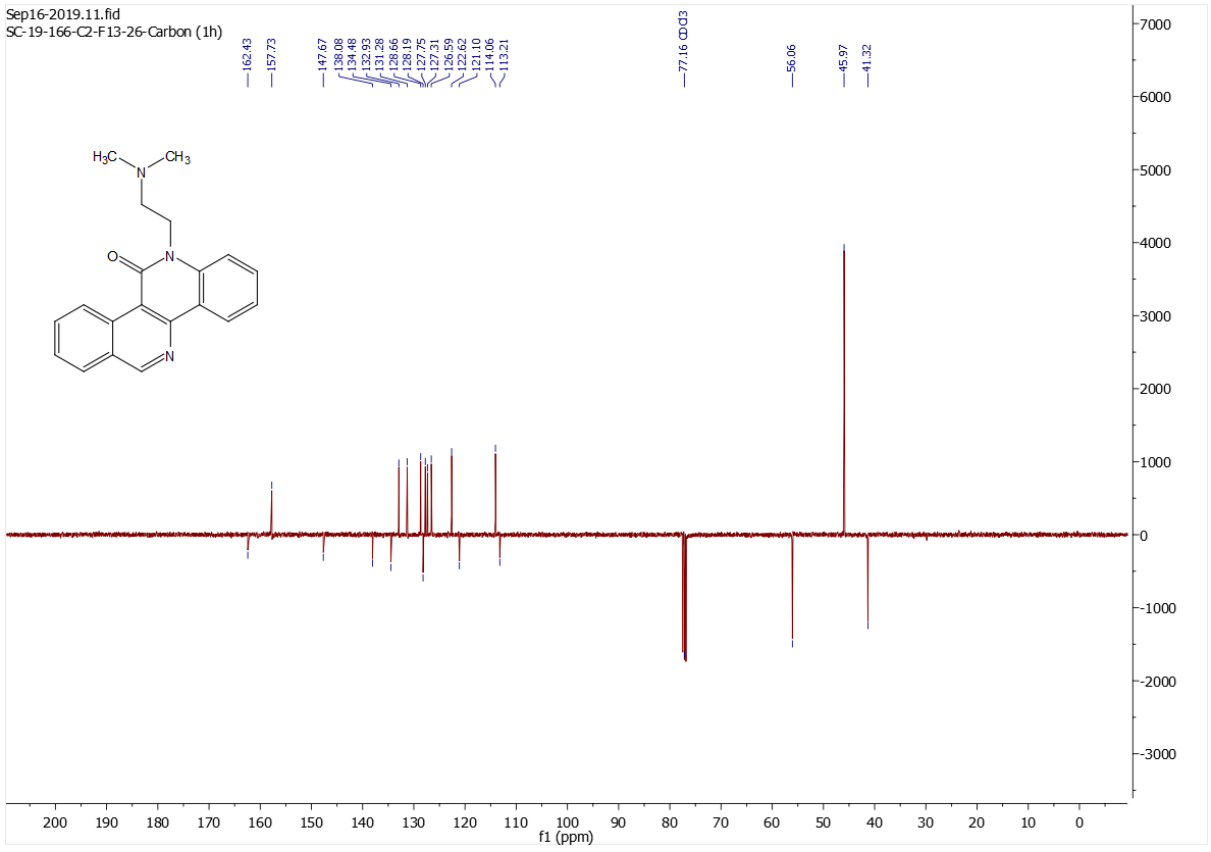
^{13}C DEPT-Q NMR of 3-(2-bromophenyl)-*N*-(2-(dimethylamino)ethyl)isoquinoline-4-carboxamide:



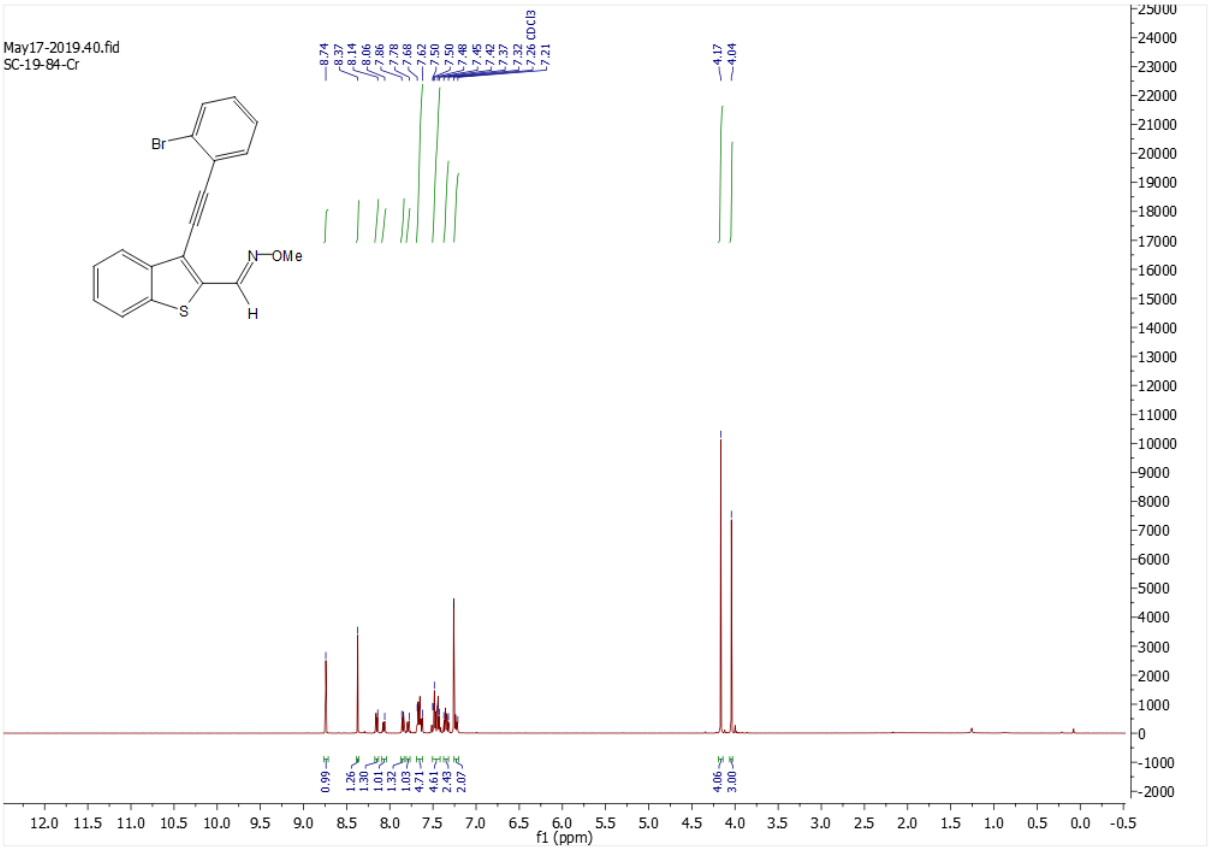
^{1}H NMR of 12-(2-(dimethylamino)ethyl)dibenzo[*c*,*h*][1,6]naphthyridin-11(12*H*)-one (**43**):



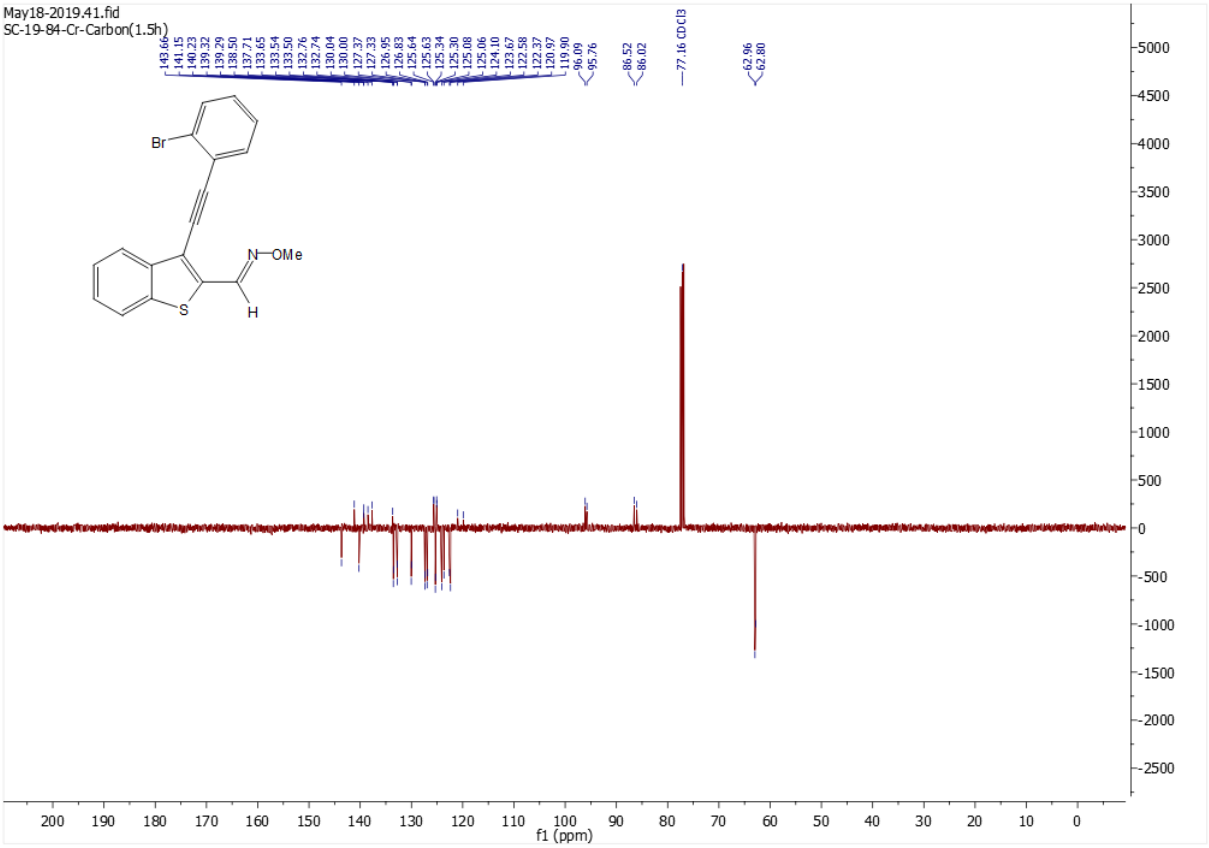
^{13}C DEPT-Q NMR of 12-(2-(dimethylamino)ethyl)dibenzo[*c*,*h*][1,6]naphthyridin-11(12*H*)-one (**43**):



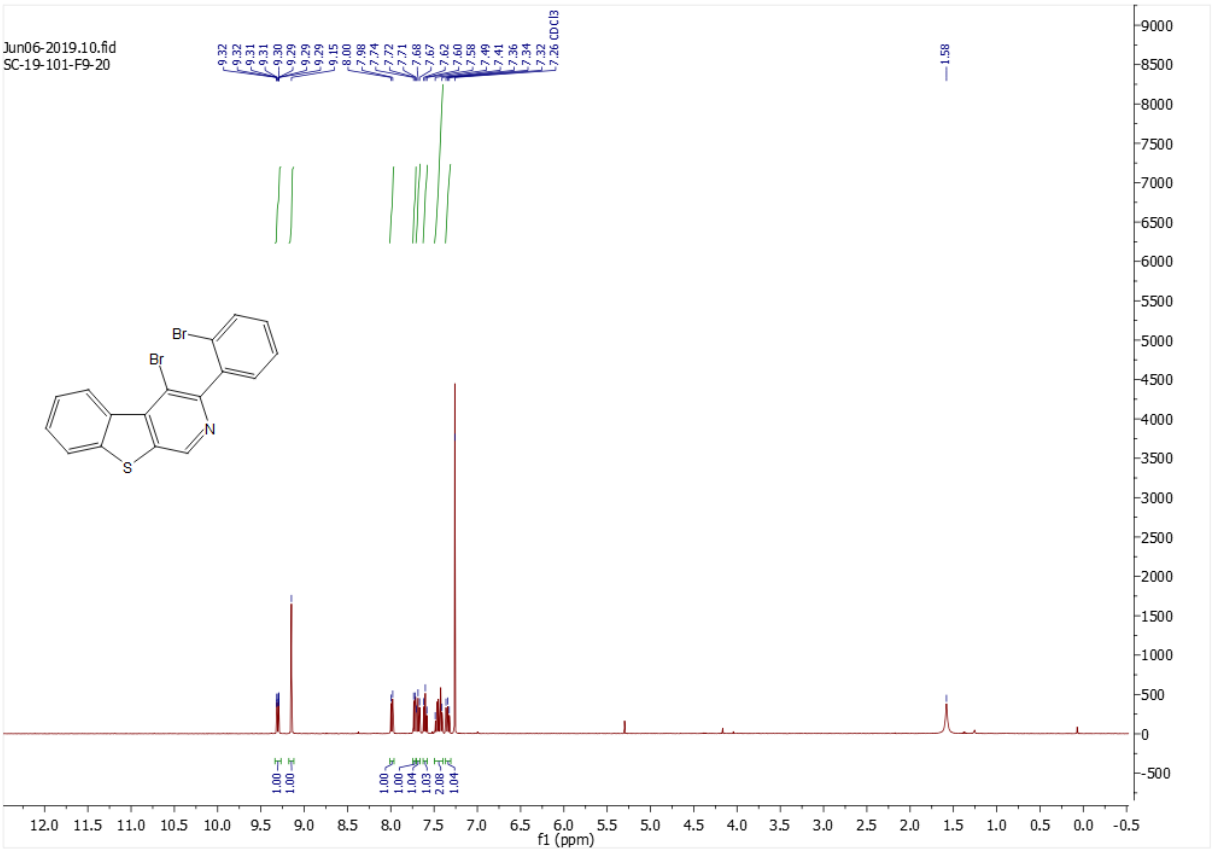
^{1}H NMR of 3-((2-bromophenyl)ethynyl)benzo[*b*]thiophene-2-carbaldehyde *O*-methyl oxime (**46a**):



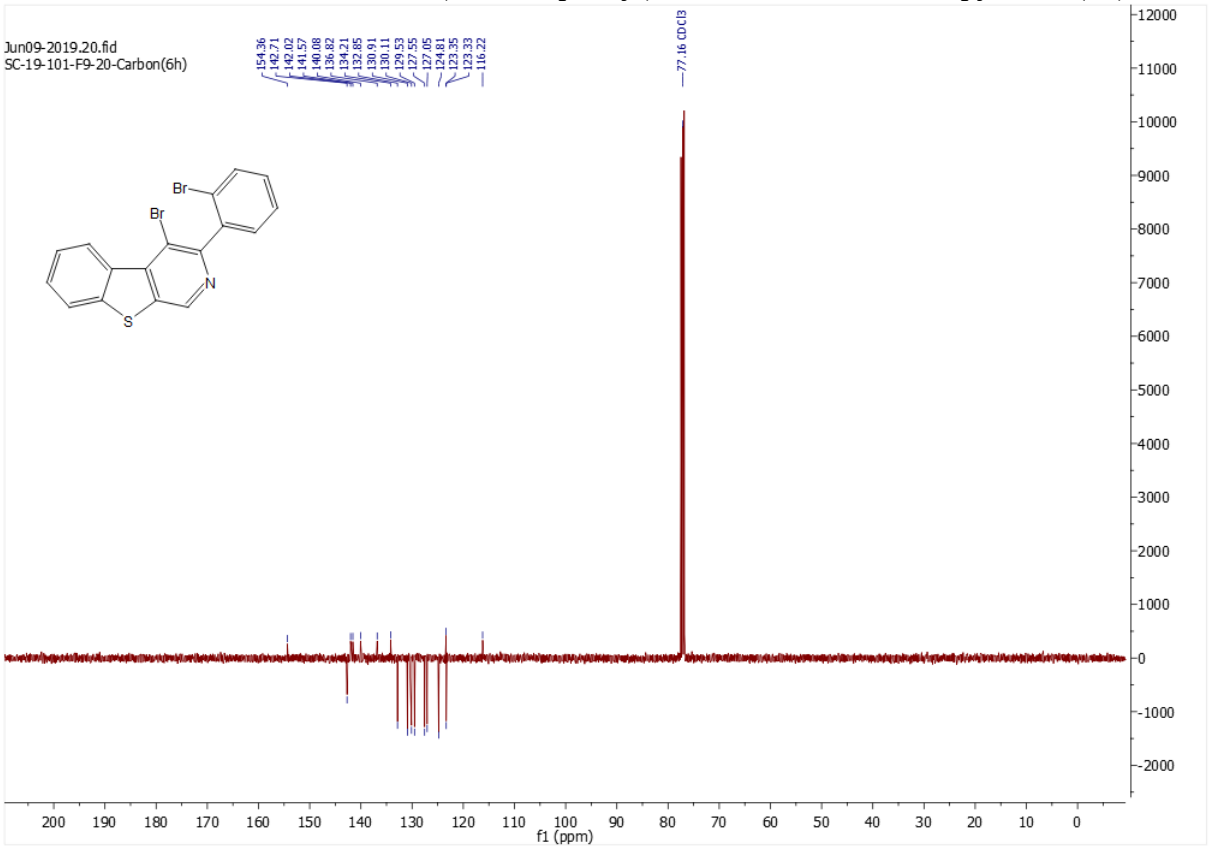
^{13}C DEPT-Q NMR of 3-((2-bromophenyl)ethynyl)benzo[*b*]thiophene-2-carbaldehyde *O*-methyl oxime (**46a**):



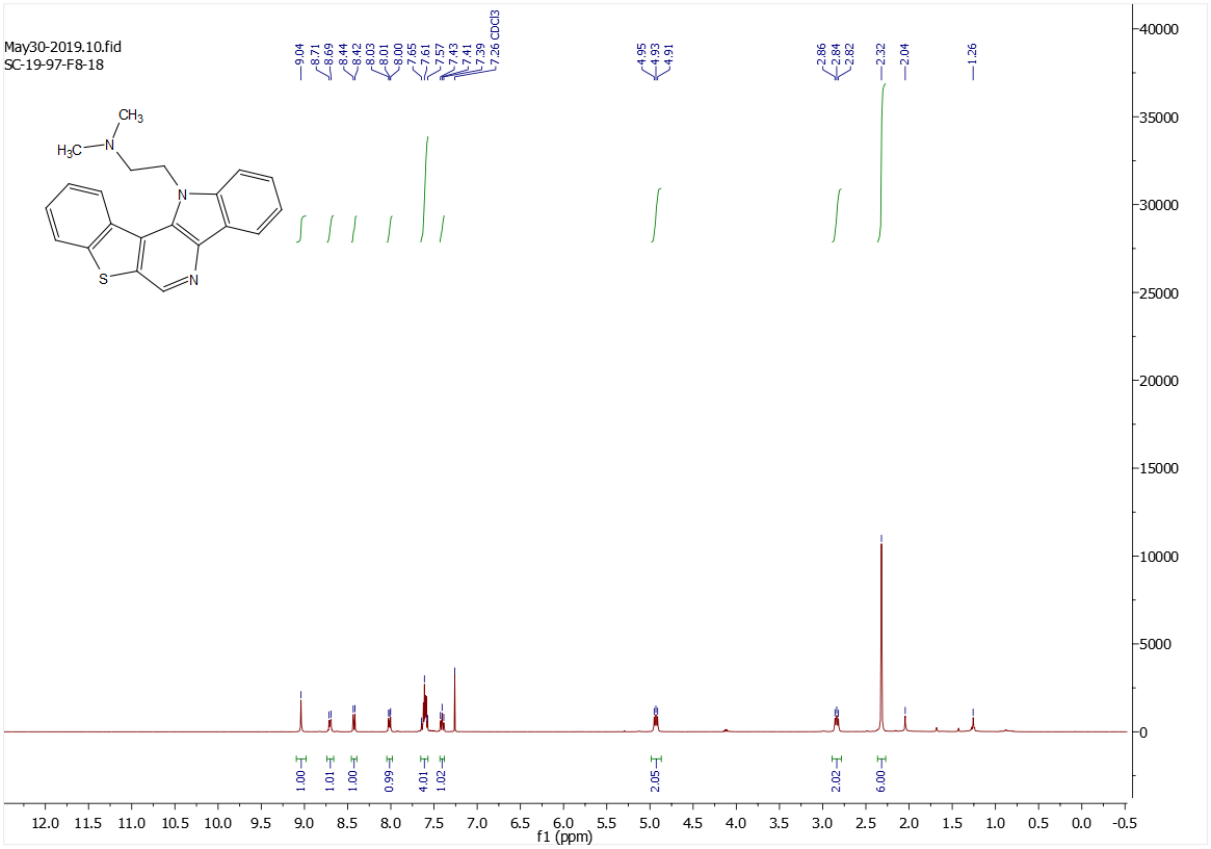
^{1}H NMR of 4-bromo-3-(2-bromophenyl)benzo[4,5]thieno[2,3-*c*]pyridine (**47**):



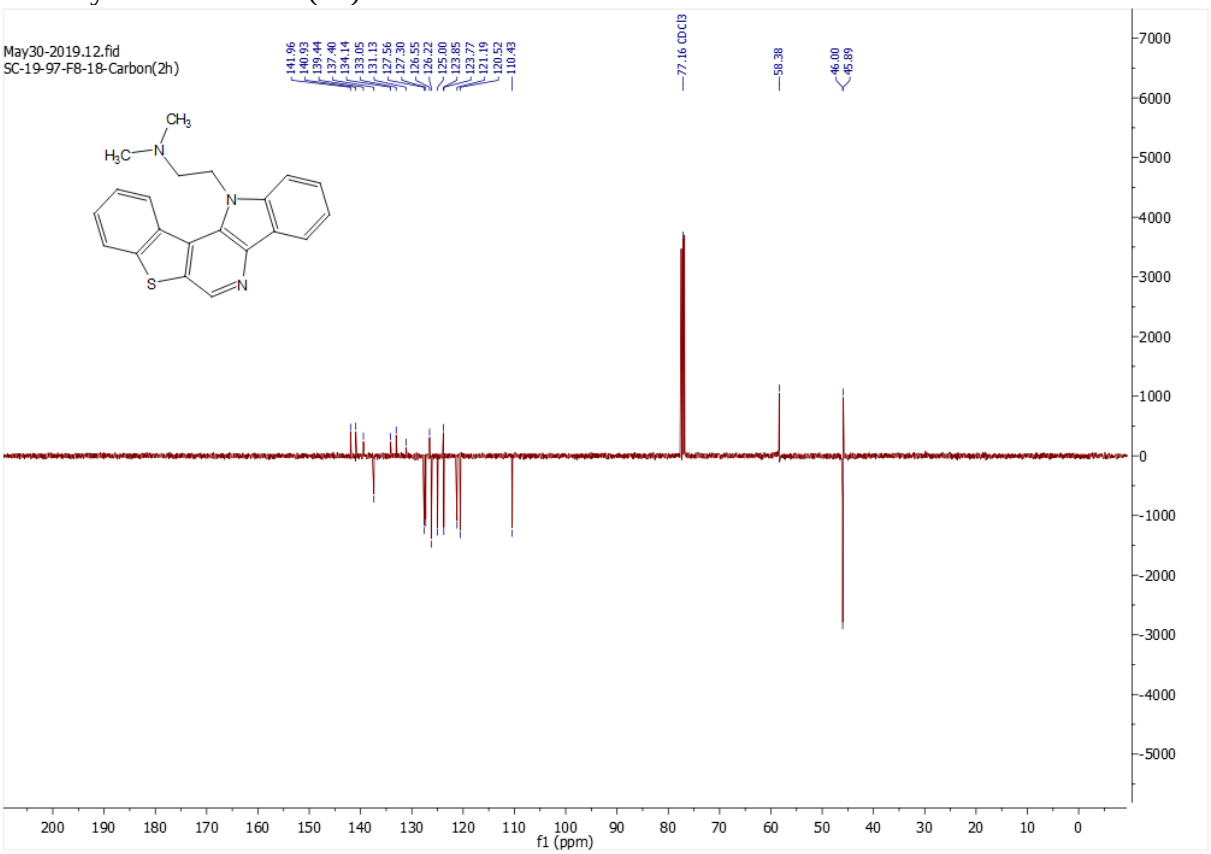
^{13}C DEPT-Q NMR of 4-bromo-3-(2-bromophenyl)benzo[4,5]thieno[2,3-*c*]pyridine (**47**):



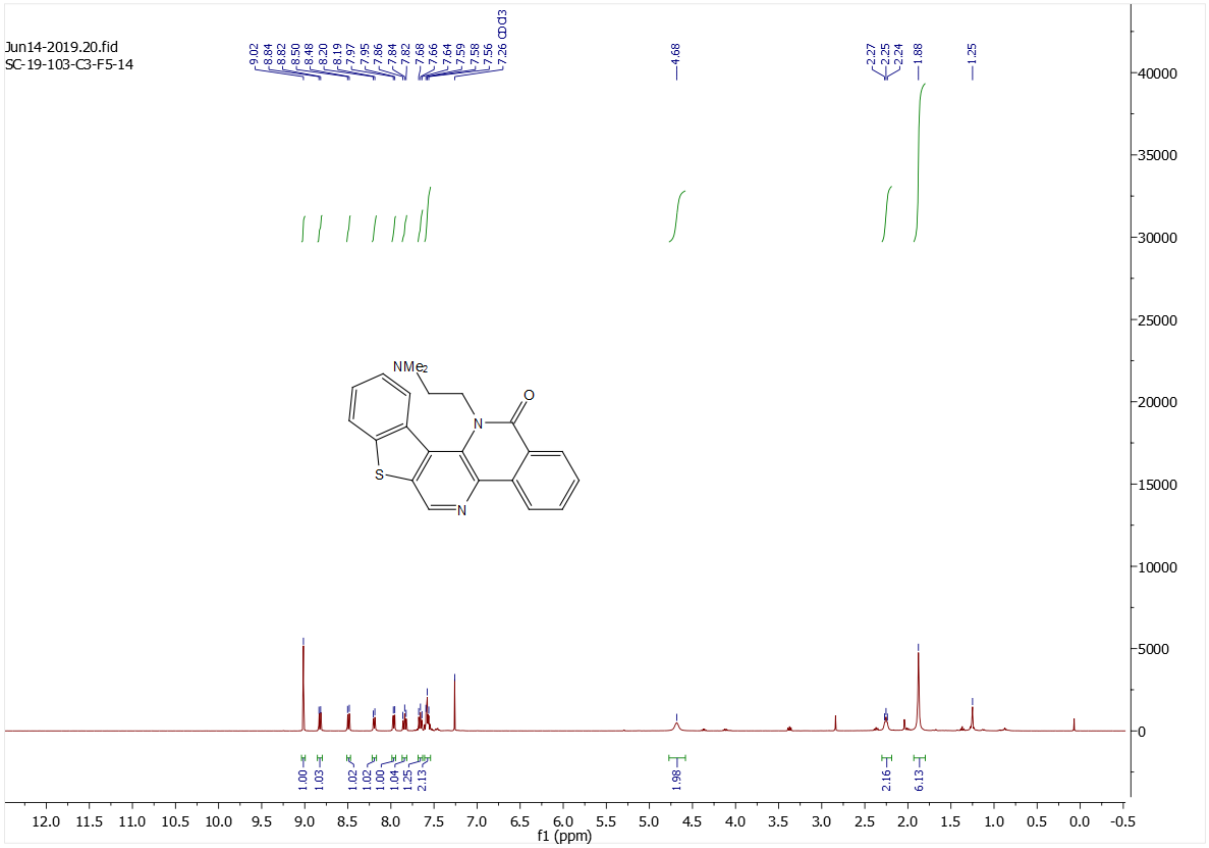
^{1}H NMR of 2-(12*H*-benzo[4',5']thieno[3',2':4,5]pyrido[3,2-*b*]indol-12-yl)-*N*,*N*-dimethylethan-1-amine (**48**):



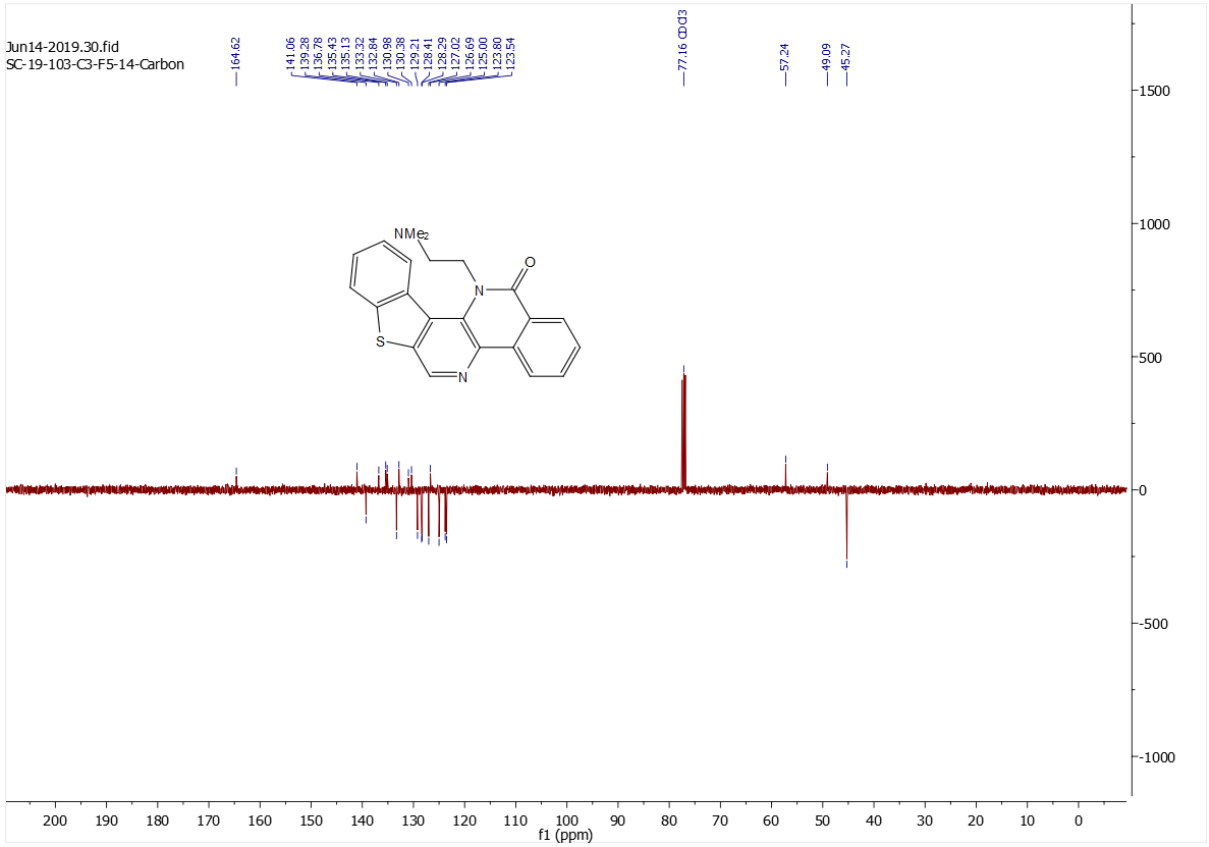
^{13}C DEPT-Q NMR of 2-(12*H*-benzo[4',5']thieno[3',2':4,5]pyrido[3,2-*b*]indol-12-yl)-*N*,*N*-dimethylethan-1-amine (**48**):



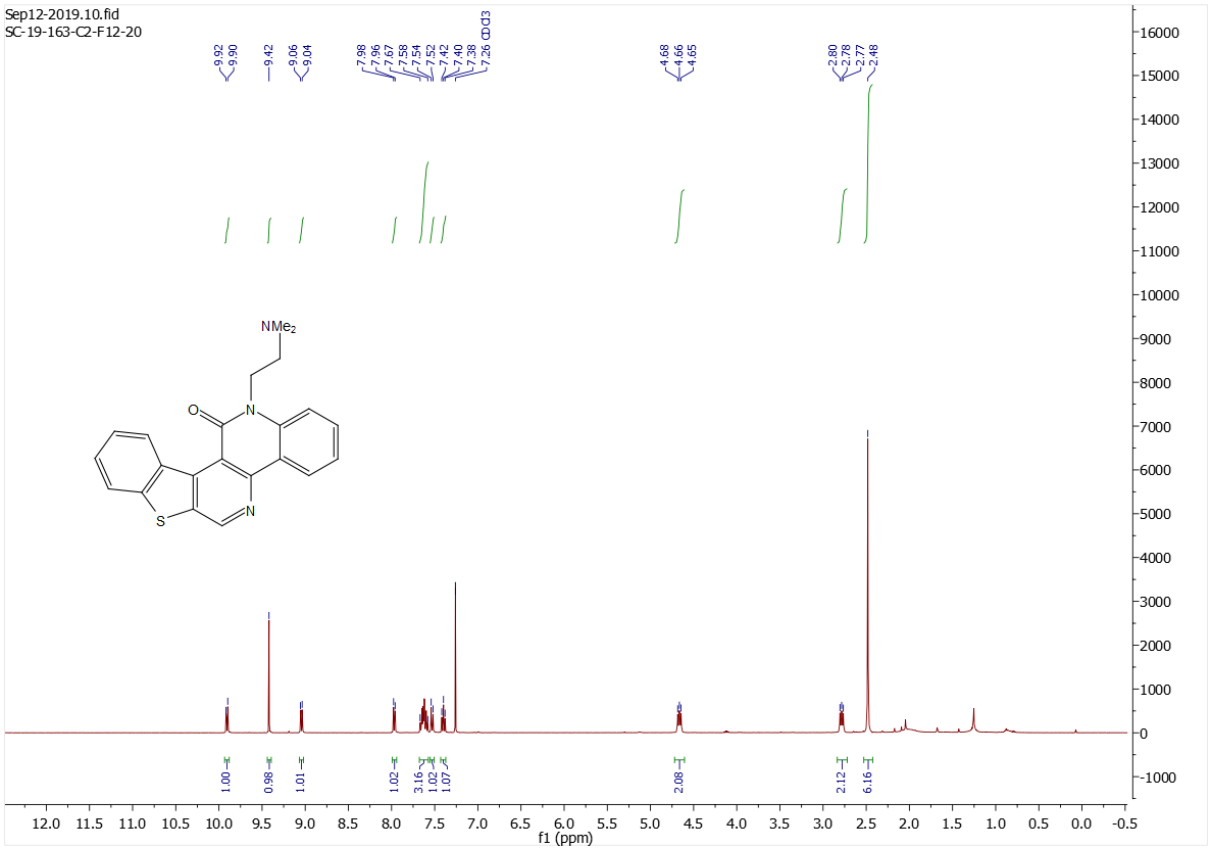
^{1}H NMR of 12-(2-(dimethylamino)ethyl)benzo[*c*]benzo[4,5]thieno[2,3-*h*][1,5]naphthyridin-13(12*H*)-one (**49**):



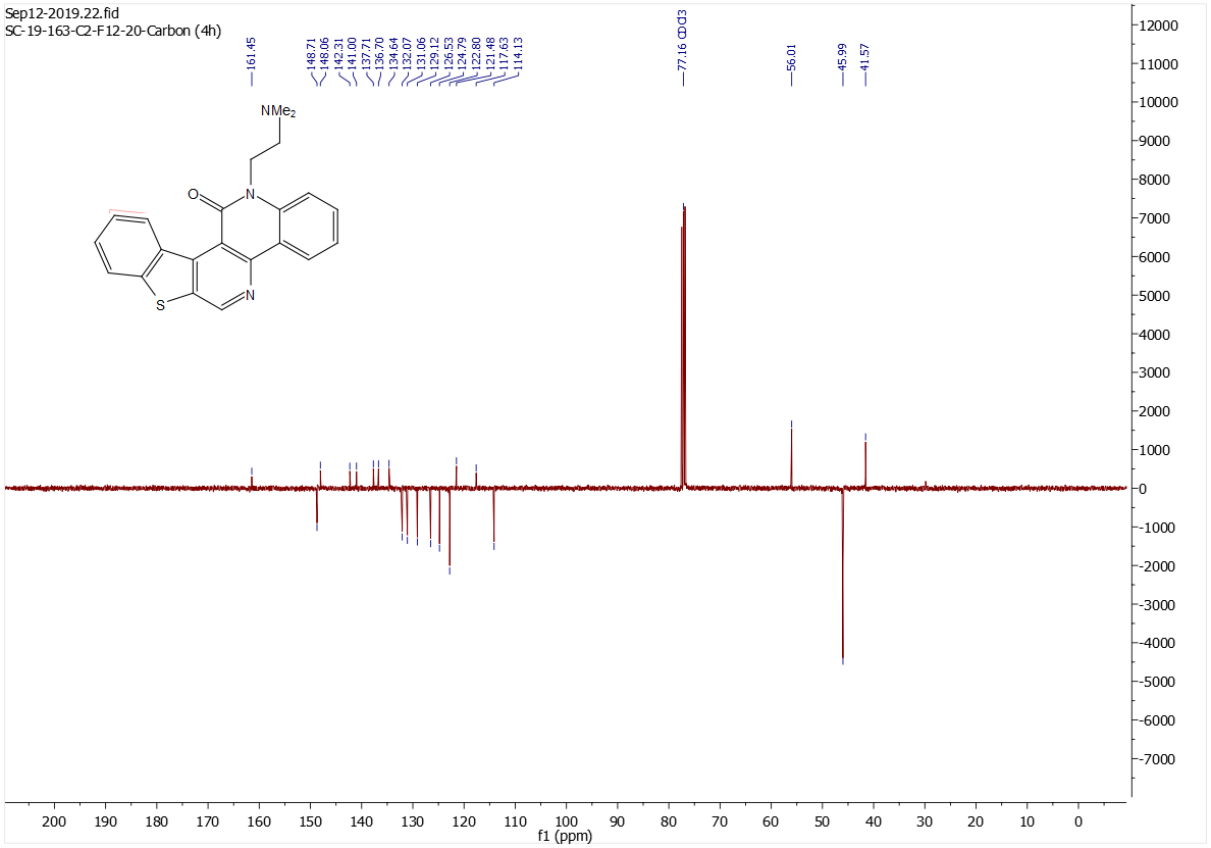
^{13}C DEPT-Q NMR of 12-(2-(dimethylamino)ethyl)benzo[*c*]benzo[4,5]thieno[2,3-*h*][1,5]naphthyridin-13(12*H*)-one (**49**):



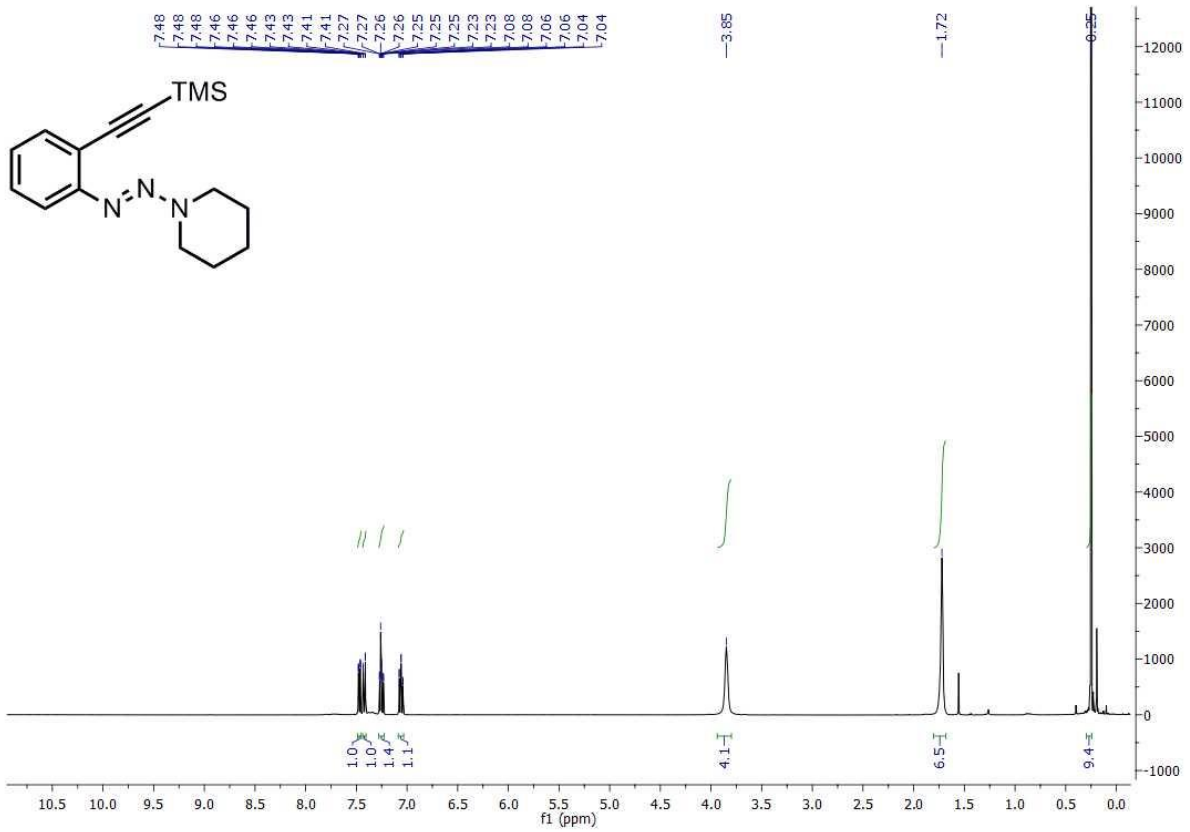
^{1}H NMR of 13-(2-(dimethylamino)ethyl)benzo[*h*]benzo[4,5]thieno[2,3-*c*][1,6]naphthyridin-12(13*H*)-one (**51**):



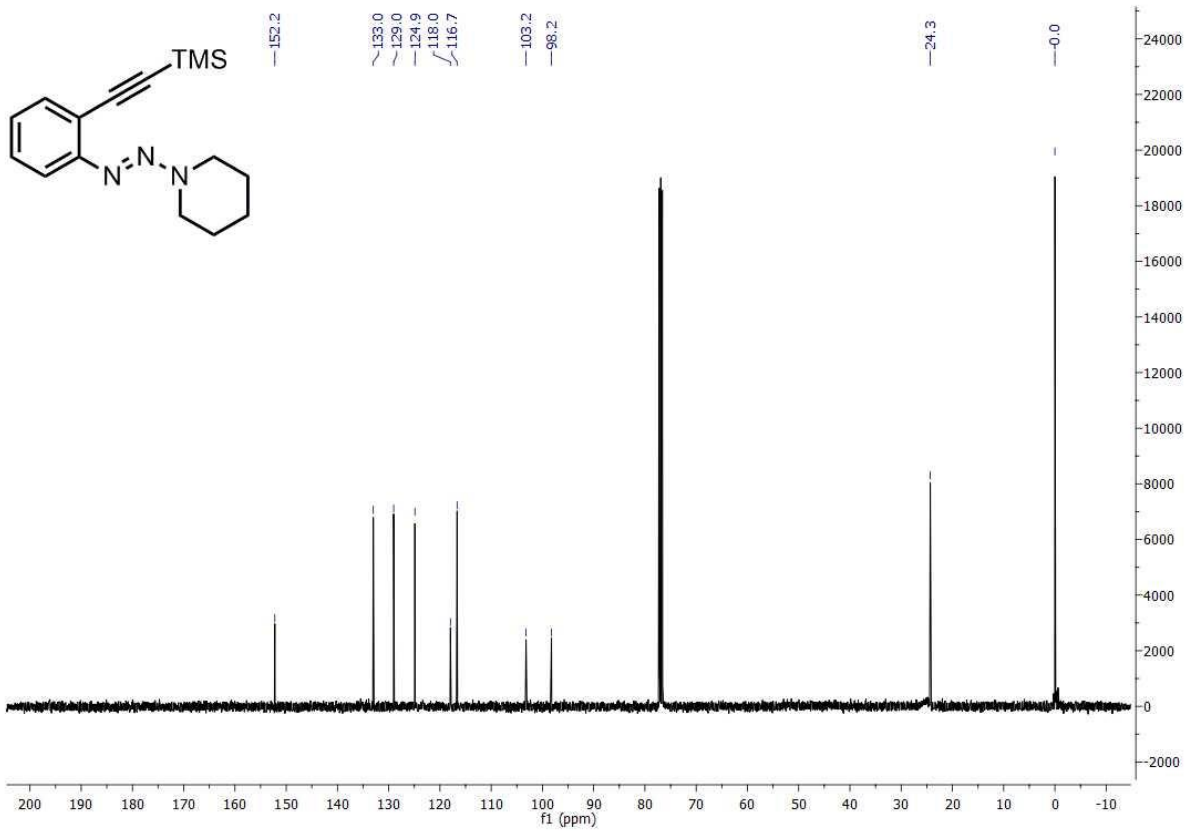
^{13}C DEPT-Q NMR of 13-(2-(dimethylamino)ethyl)benzo[*h*]benzo[4,5]thieno[2,3-*c*][1,6]naphthyridin-12(13*H*)-one (**51**):



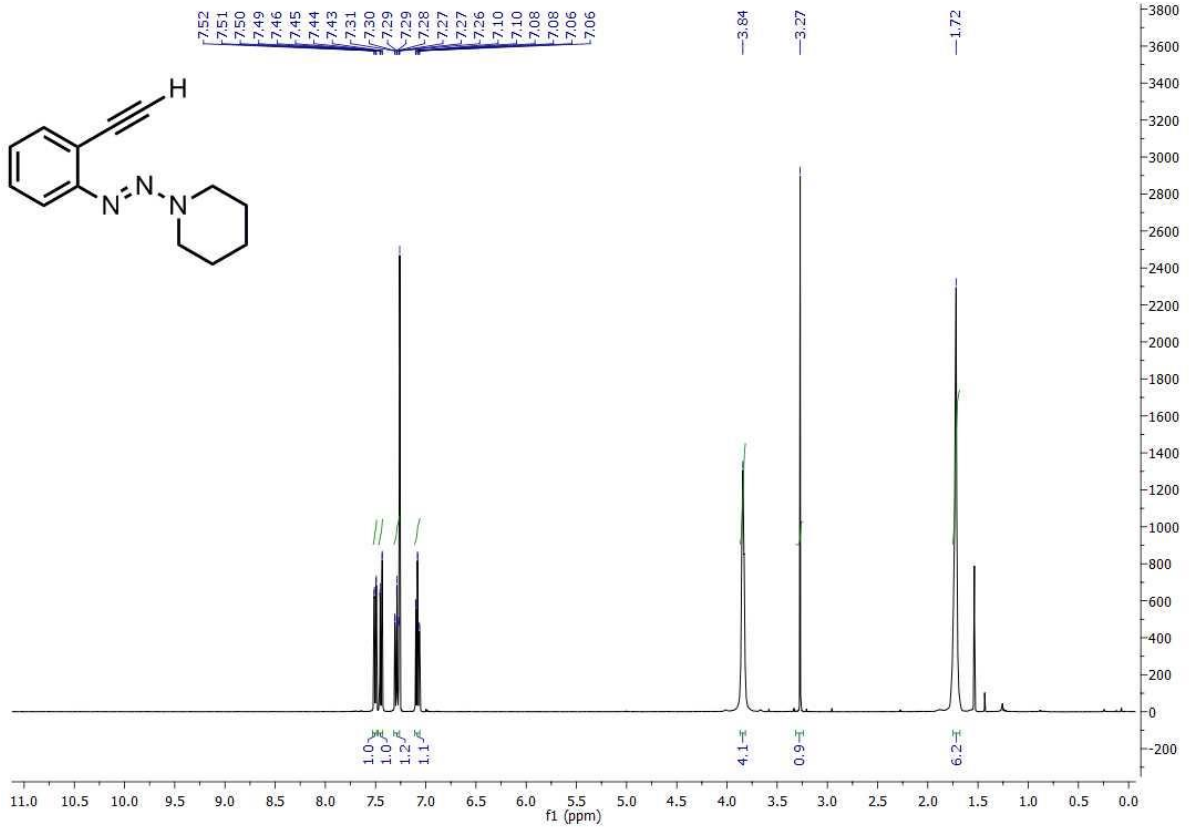
^{1}H NMR of (*E*)-1-((2-((trimethylsilyl)ethynyl)phenyl)diazenyl)piperidine:



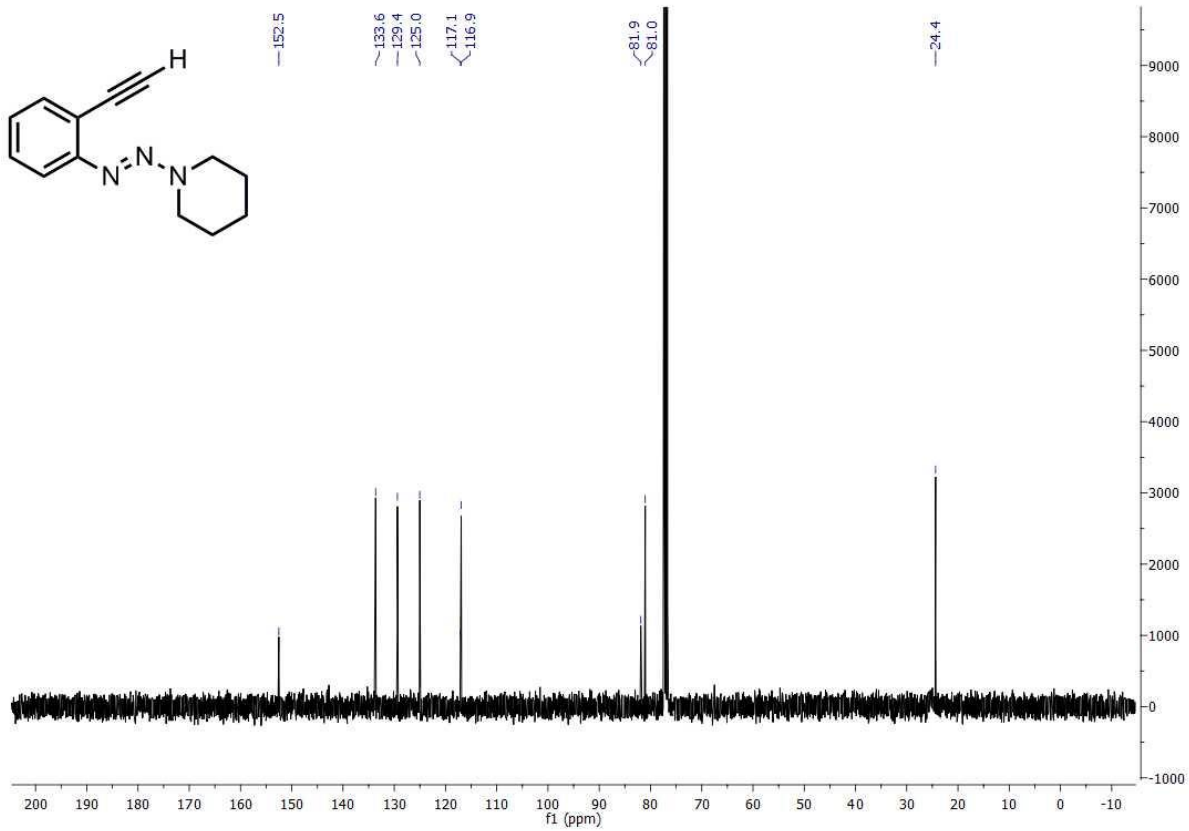
^{13}C NMR of (*E*)-1-((2-((trimethylsilyl)ethynyl)phenyl)diazenyl)piperidine:



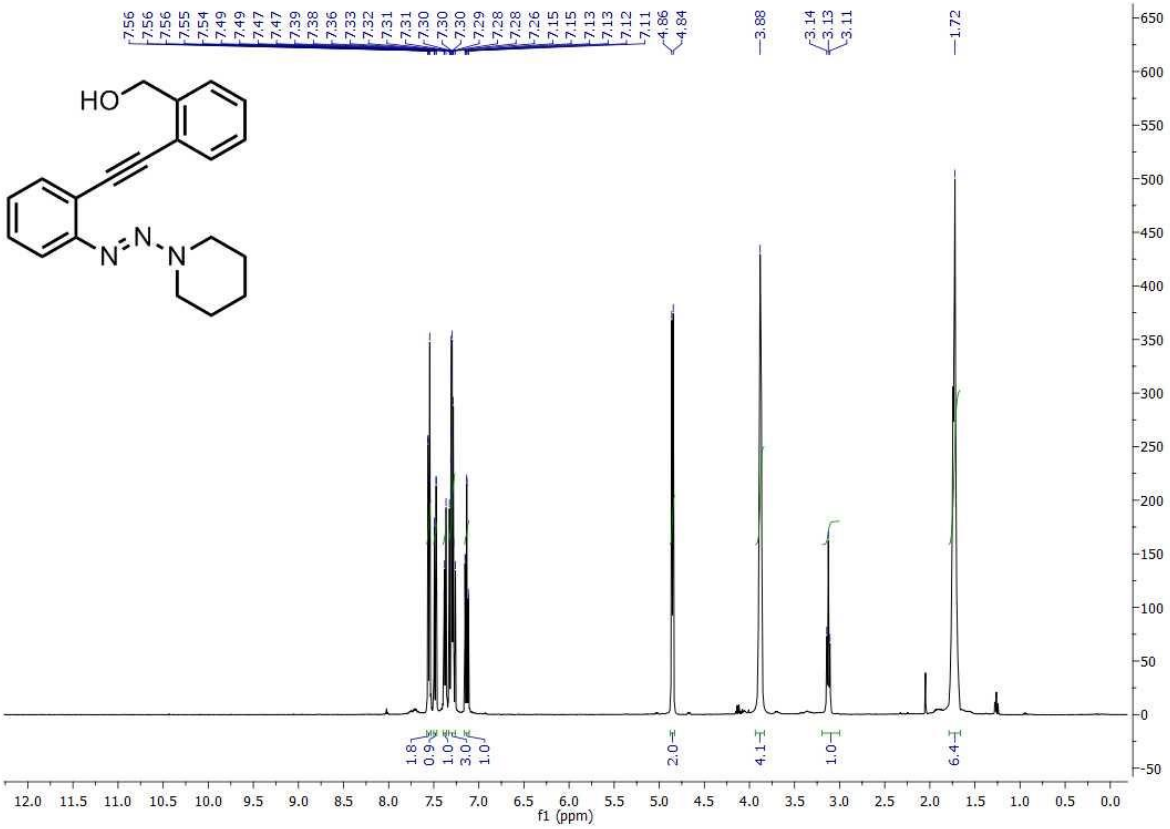
^{1}H NMR of (*E*)-1-((2-ethynylphenyl)diazenyl)piperidine (**53**):



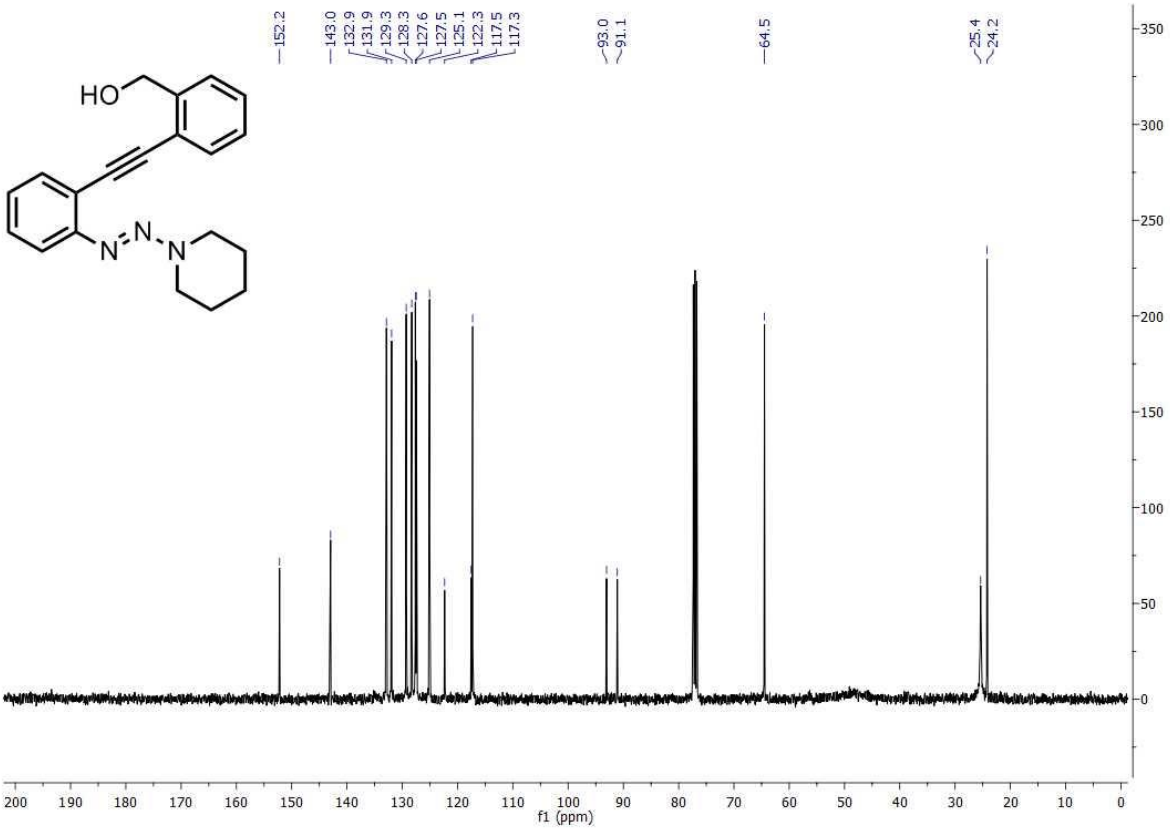
^{13}C NMR of (*E*)-1-((2-ethynylphenyl)diazenyl)piperidine (**53**):



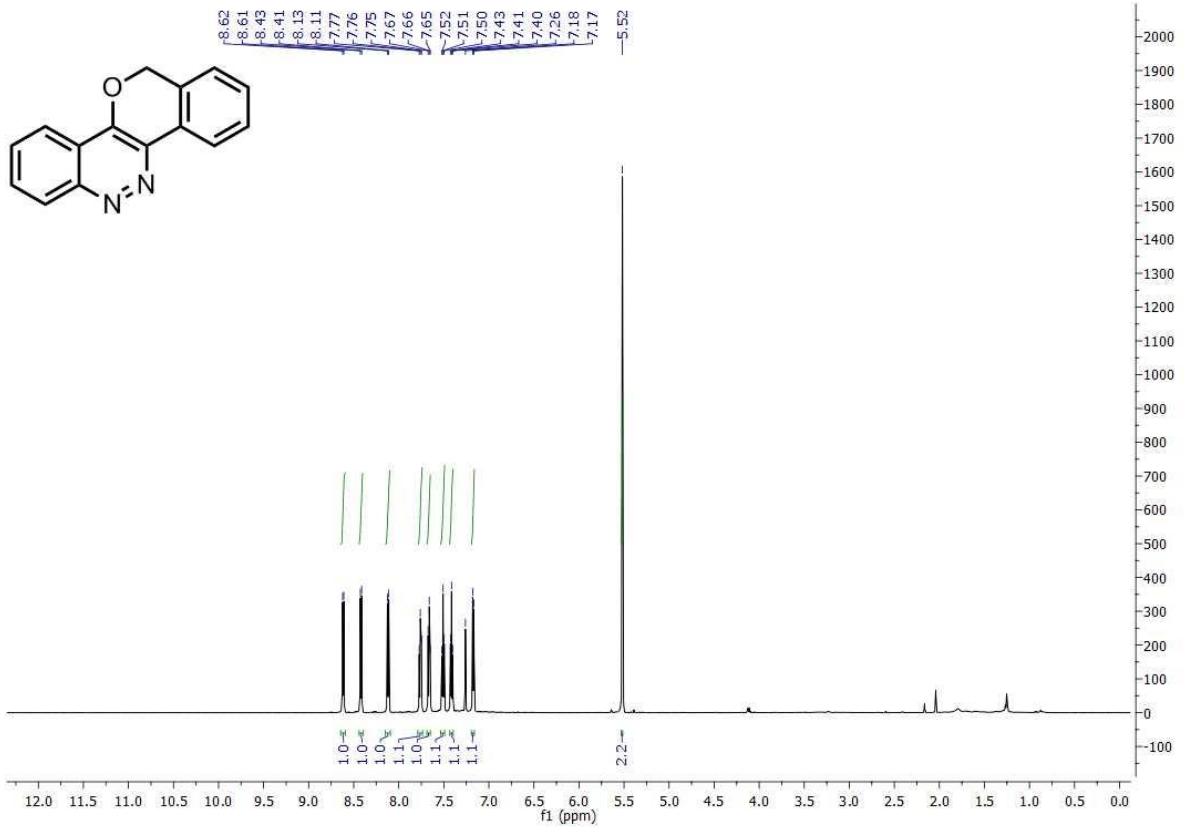
^{1}H NMR of (*E*)-(2-((2-(piperidin-1-yldiazenyl)phenyl)ethynyl)phenyl)methanol (**55a**):



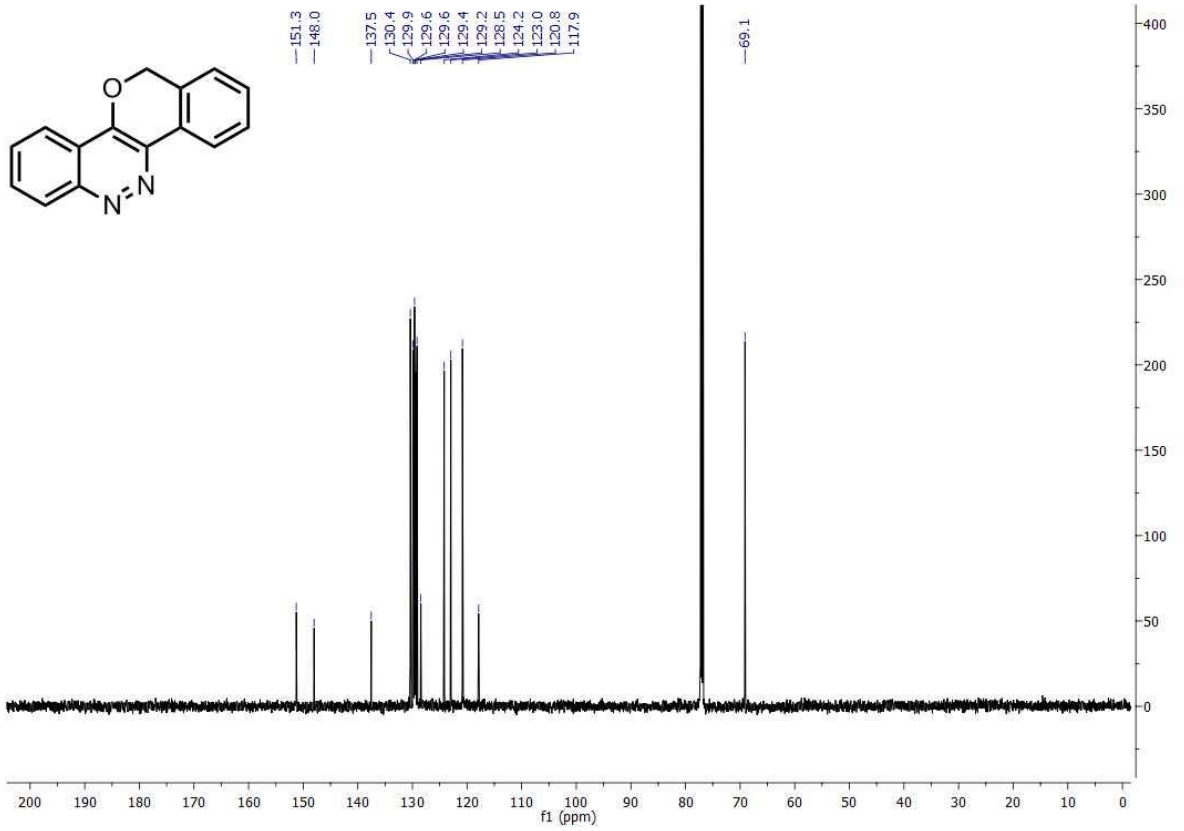
^{13}C NMR of (*E*)-(2-((2-(piperidin-1-yldiazenyl)phenyl)ethynyl)phenyl)methanol (**55a**):



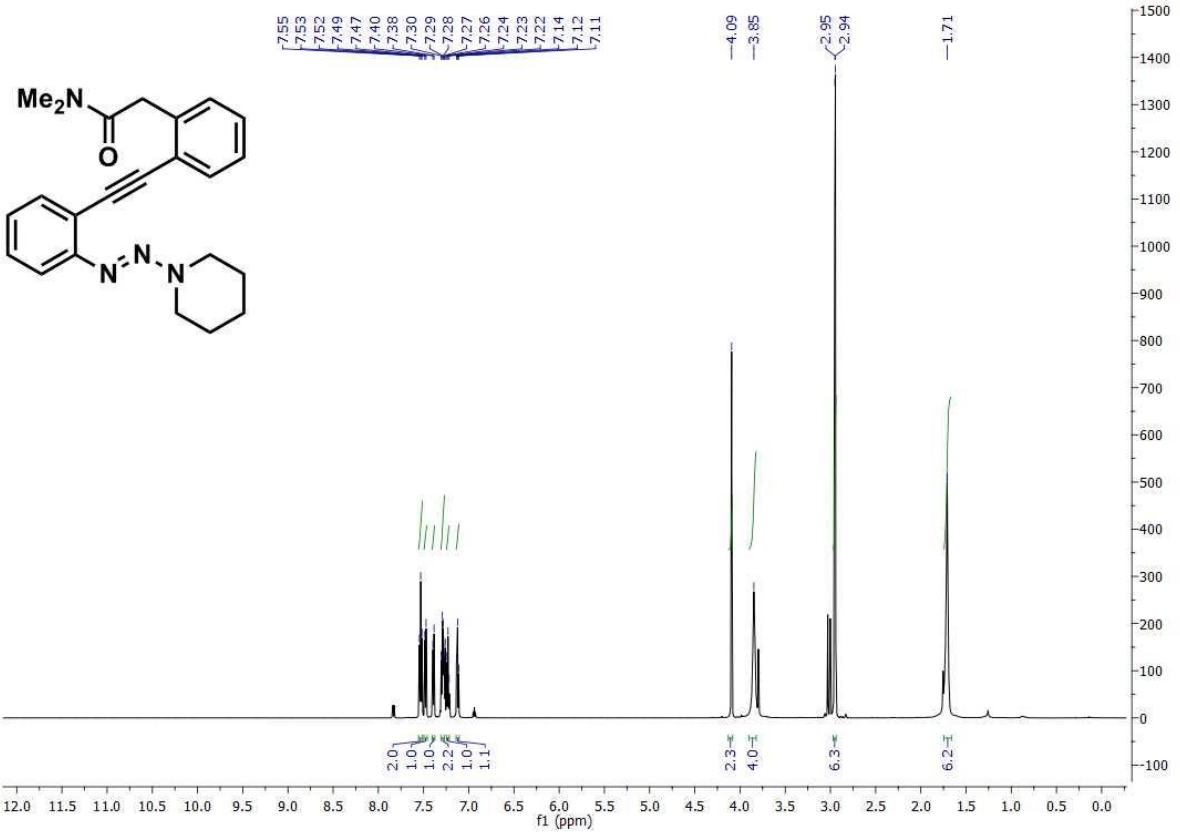
^{1}H NMR of 12*H*-isochromeno[4,3-*c*]cinnoline (**56a**):



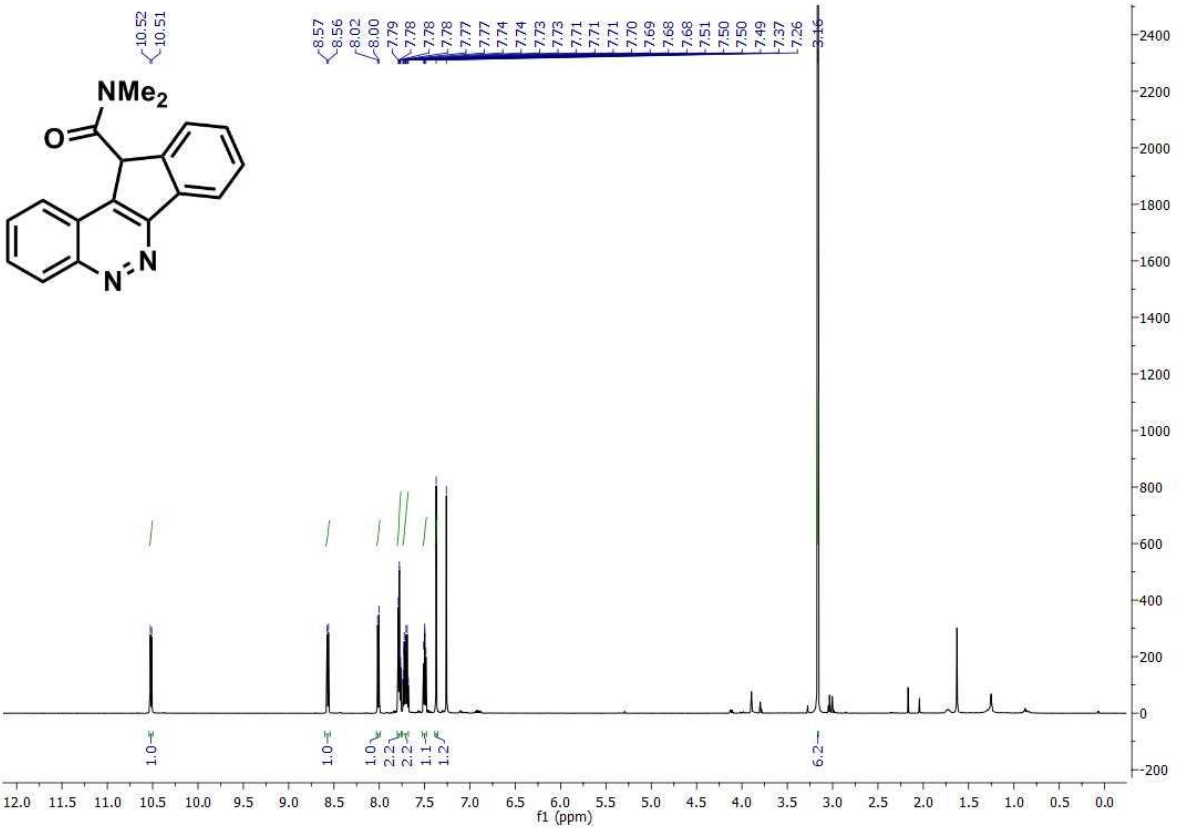
^{13}C NMR of 12*H*-isochromeno[4,3-*c*]cinnoline (**56a**):



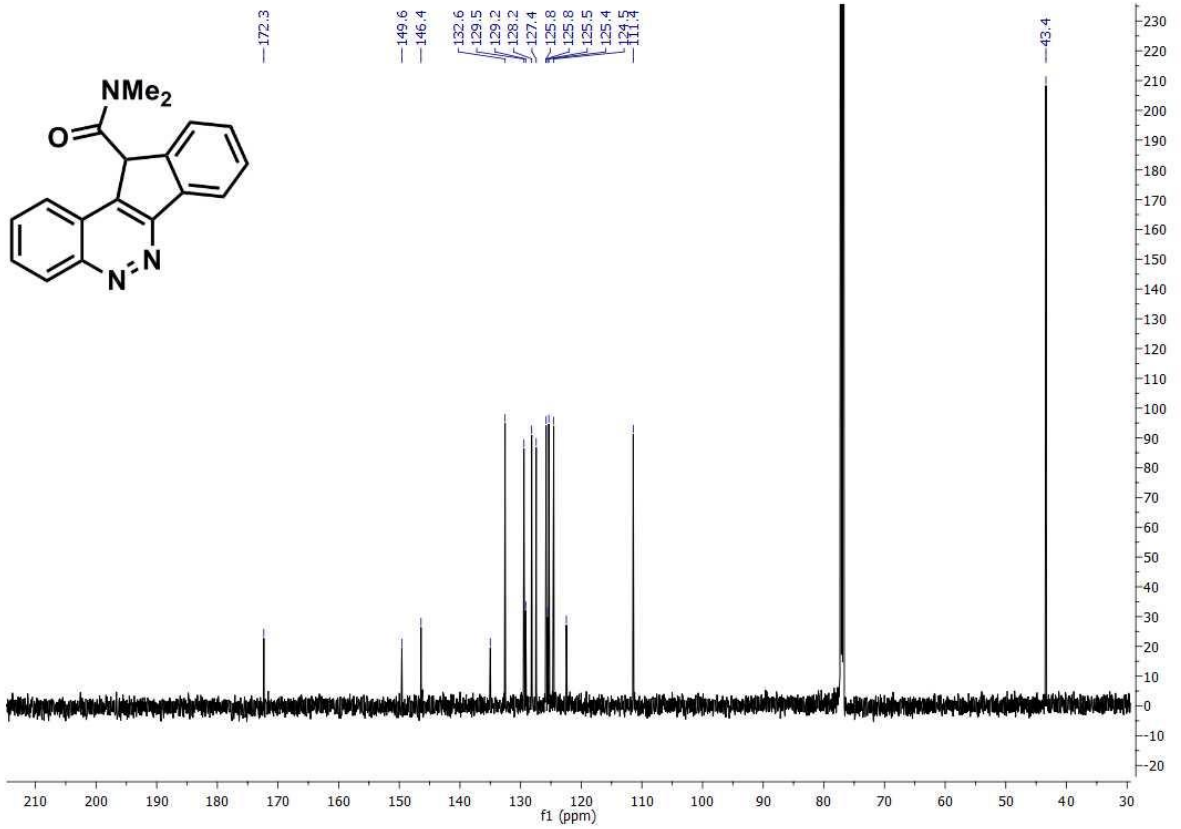
^{1}H NMR of (*E*)-*N*,*N*-dimethyl-2-(2-((2-(piperidin-1-yldiazenyl)phenyl)ethynyl)phenyl)acetamide (**55b**):



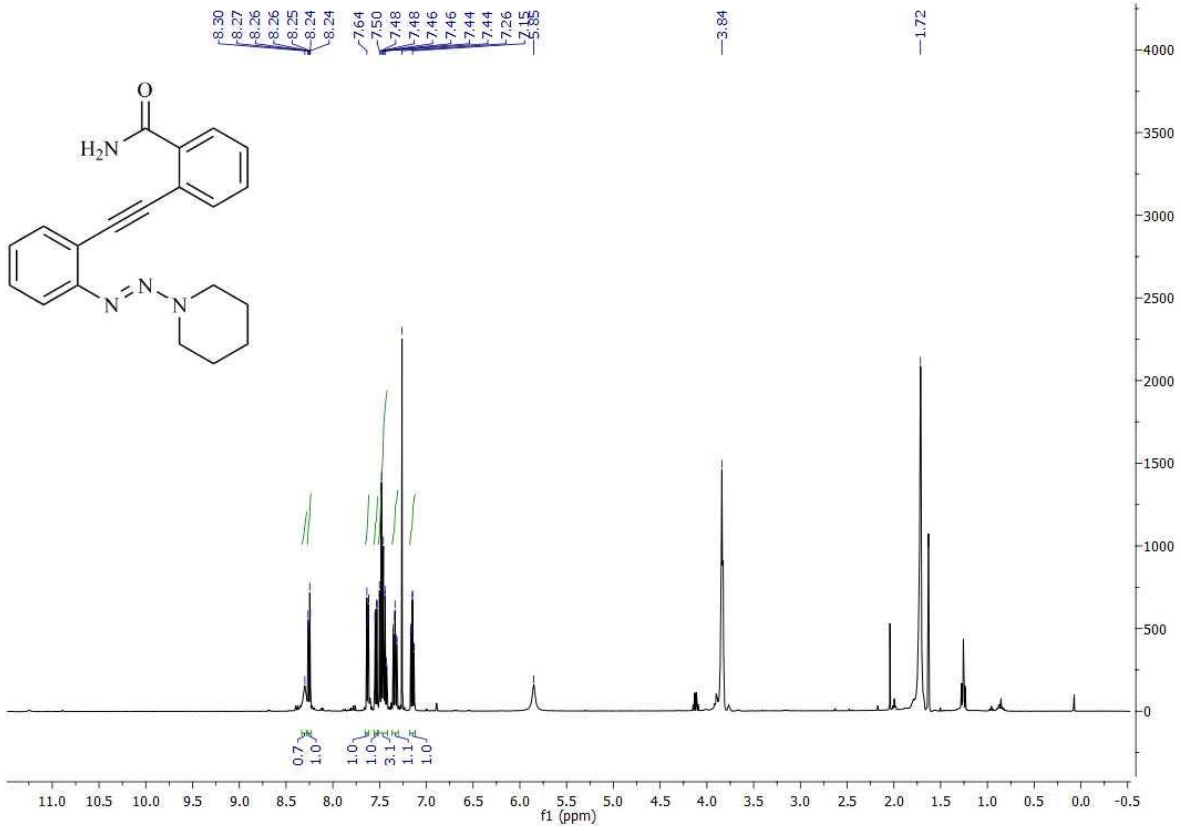
^{1}H NMR of *N*,*N*-dimethyl-11*H*-indeno[1,2-*c*]cinnoline-11-carboxamide (**56b**):



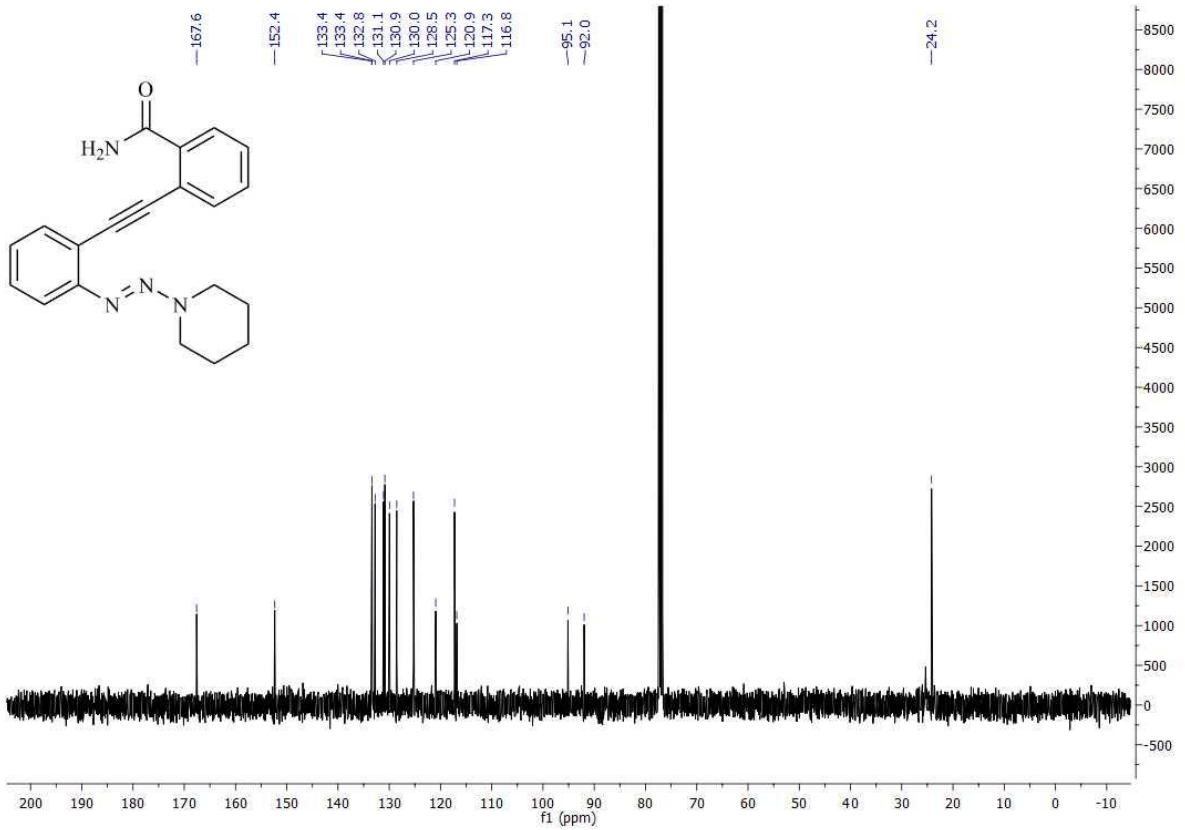
^{13}C NMR of *N*,*N*-dimethyl-11*H*-indeno[1,2-*c*]cinnoline-11-carboxamide (**56b**):



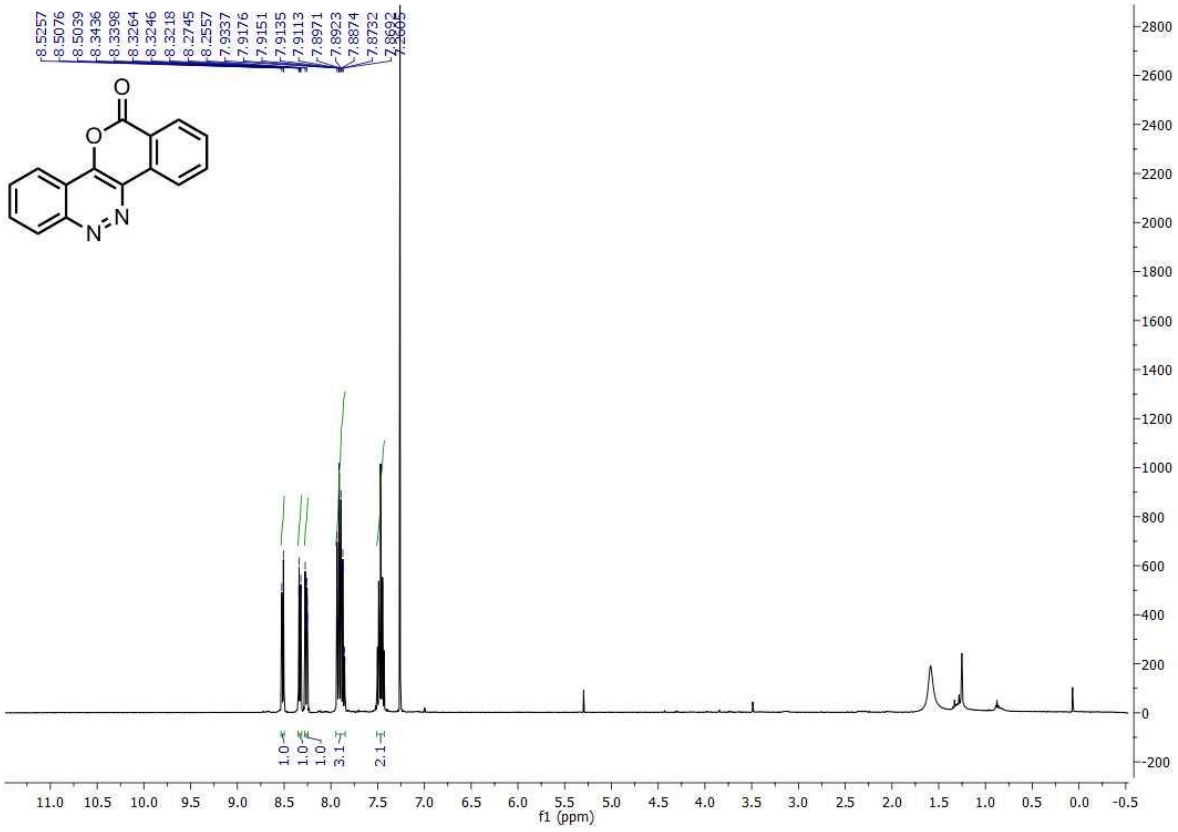
^{1}H NMR of (*E*)-2-((2-(piperidin-1-yldiazenyl)phenyl)ethynyl)benzamide (**55c**):



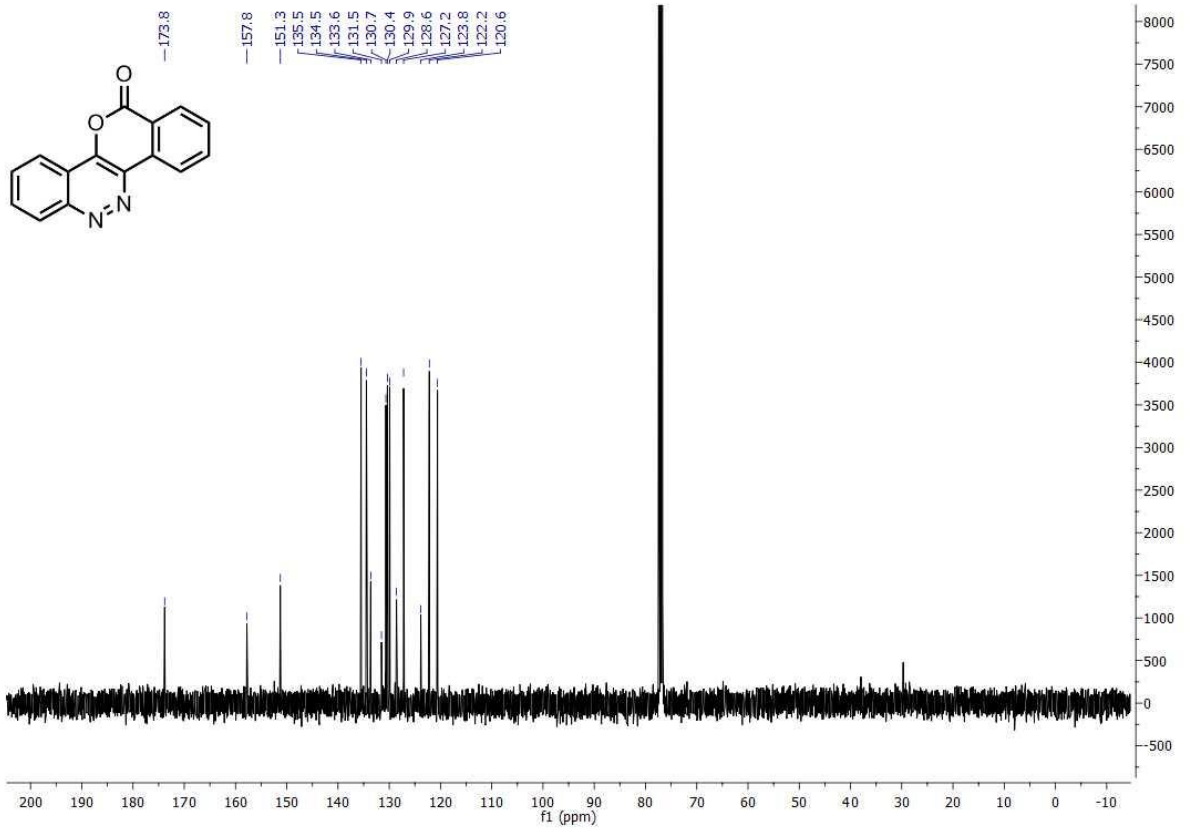
^{13}C NMR of (*E*)-2-((2-(piperidin-1-yldiazenyl)phenyl)ethynyl)benzamide (**55c**):



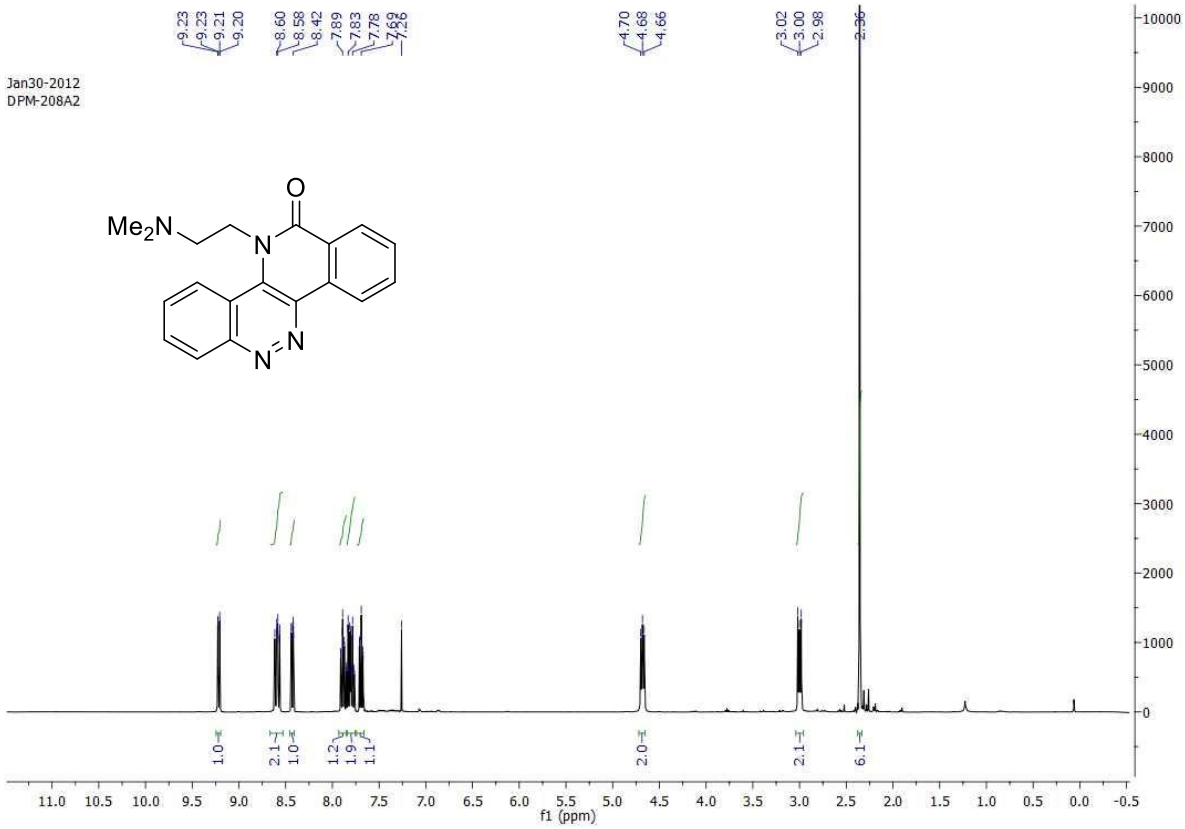
^{1}H NMR of isoquinolino[4,3-*c*]cinnolin-12(11*H*)-one (**56c**):



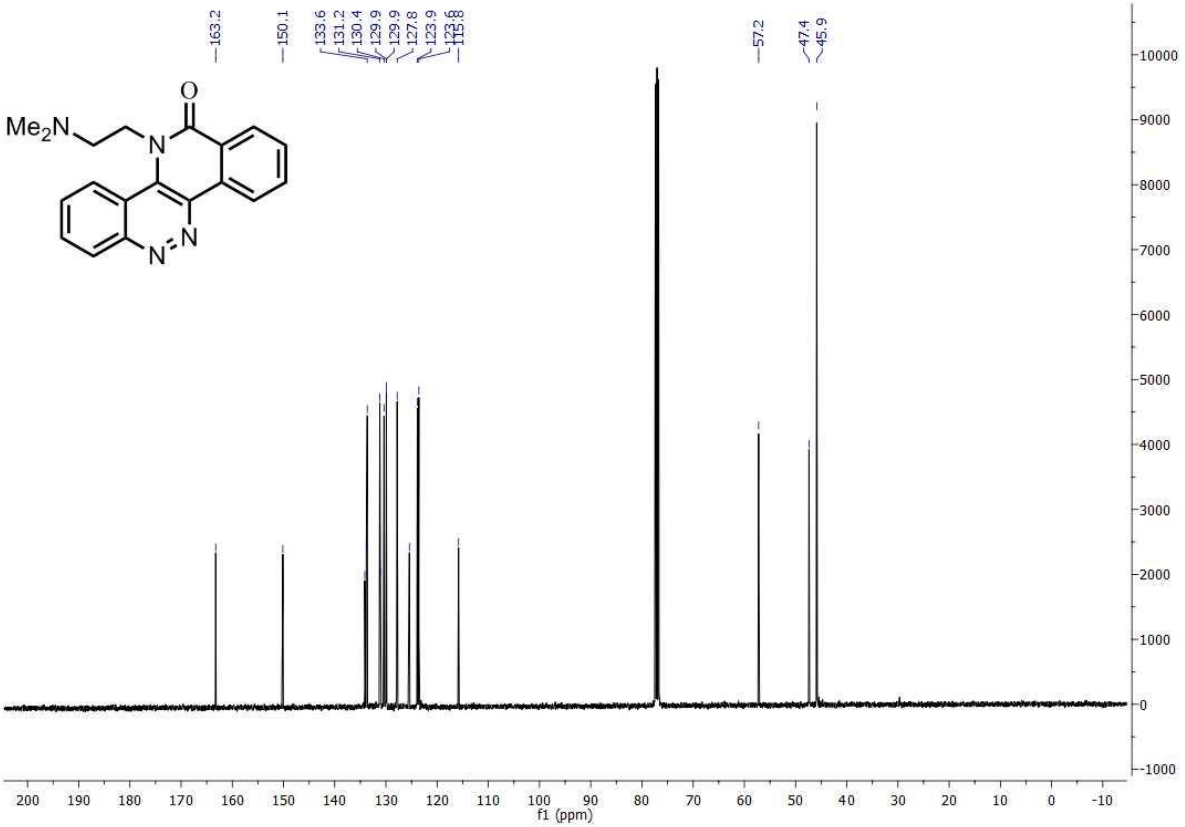
^{13}C NMR of isoquinolino[4,3-*c*]cinnolin-12(11*H*)-one (**56c**):



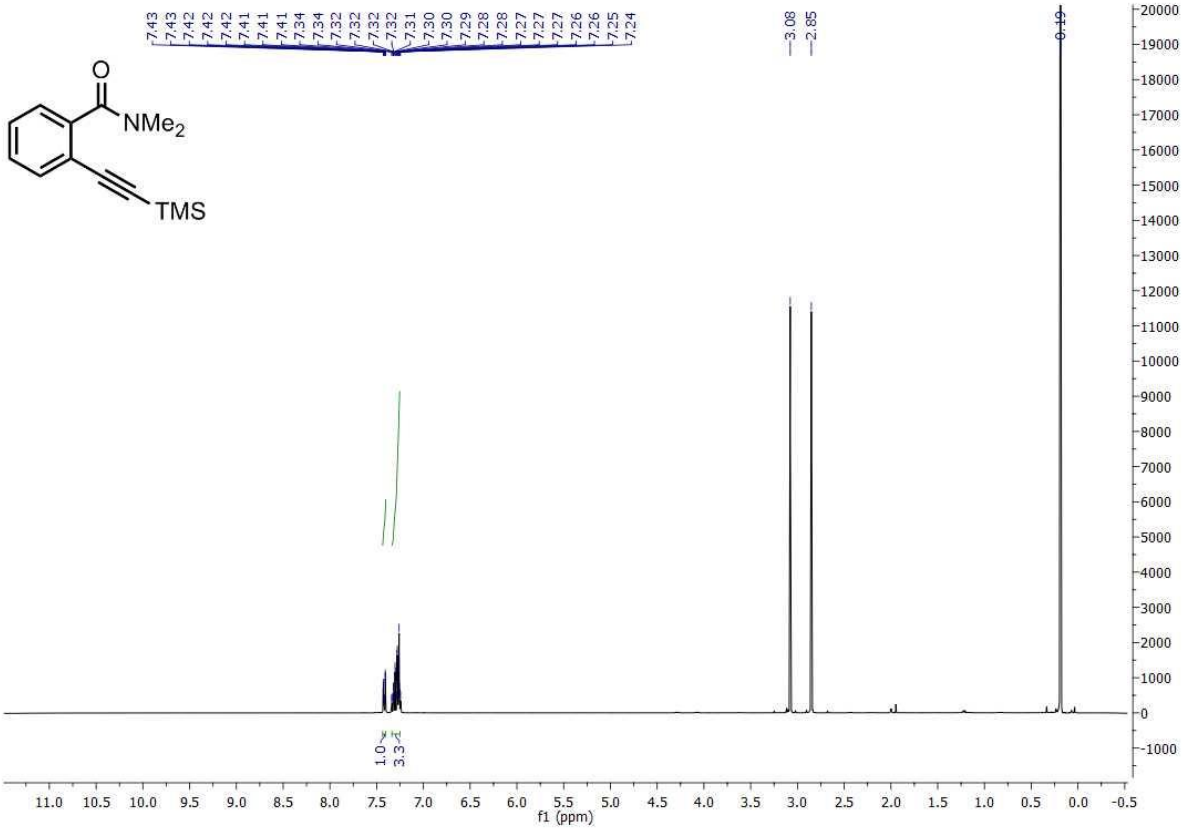
^{1}H NMR of 11-(2-(dimethylamino)ethyl)isoquinolino[4,3-*c*]cinnolin-12(11*H*)-one (**56d**):



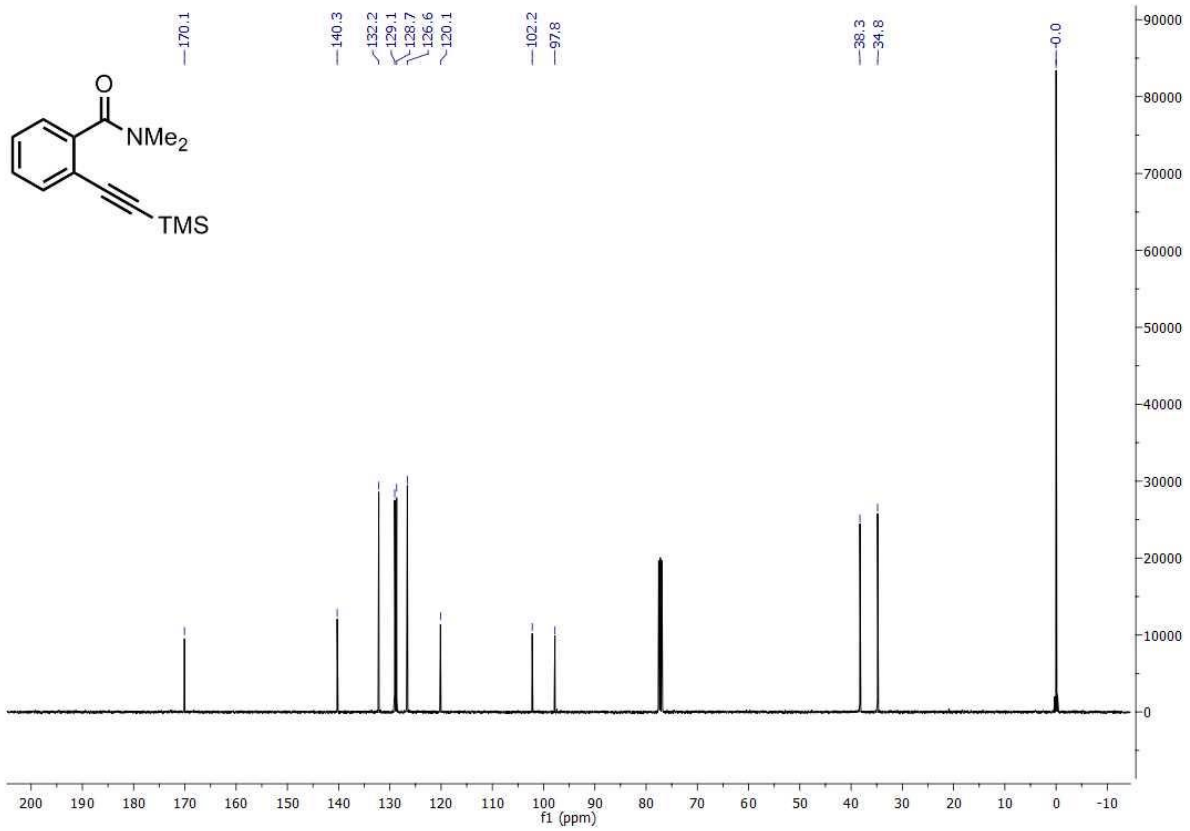
^{13}CNMR of 11-(2-(dimethylamino)ethyl)isoquinolino[4,3-*c*]cinnolin-12(11*H*)-one (**56d**):



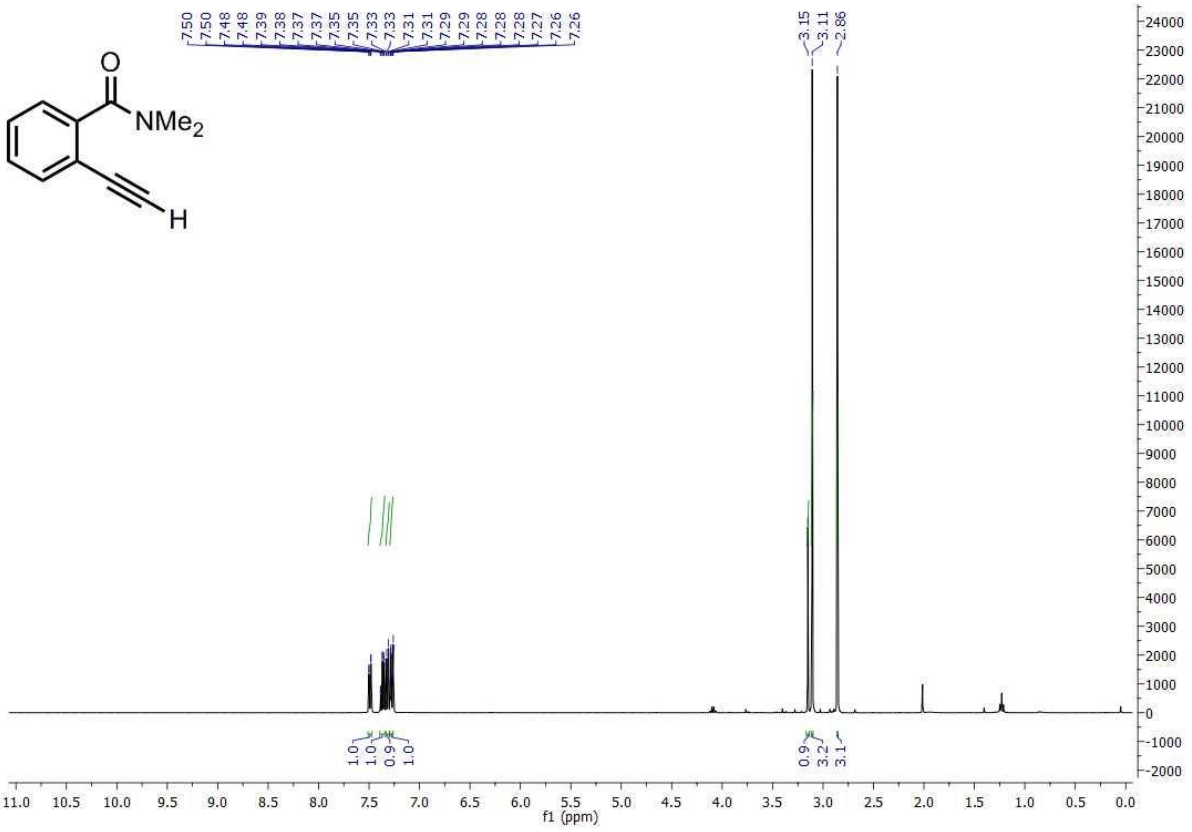
^{1}H NMR of *N*,*N*-dimethyl-2-((trimethylsilyl)ethynyl)benzamide:



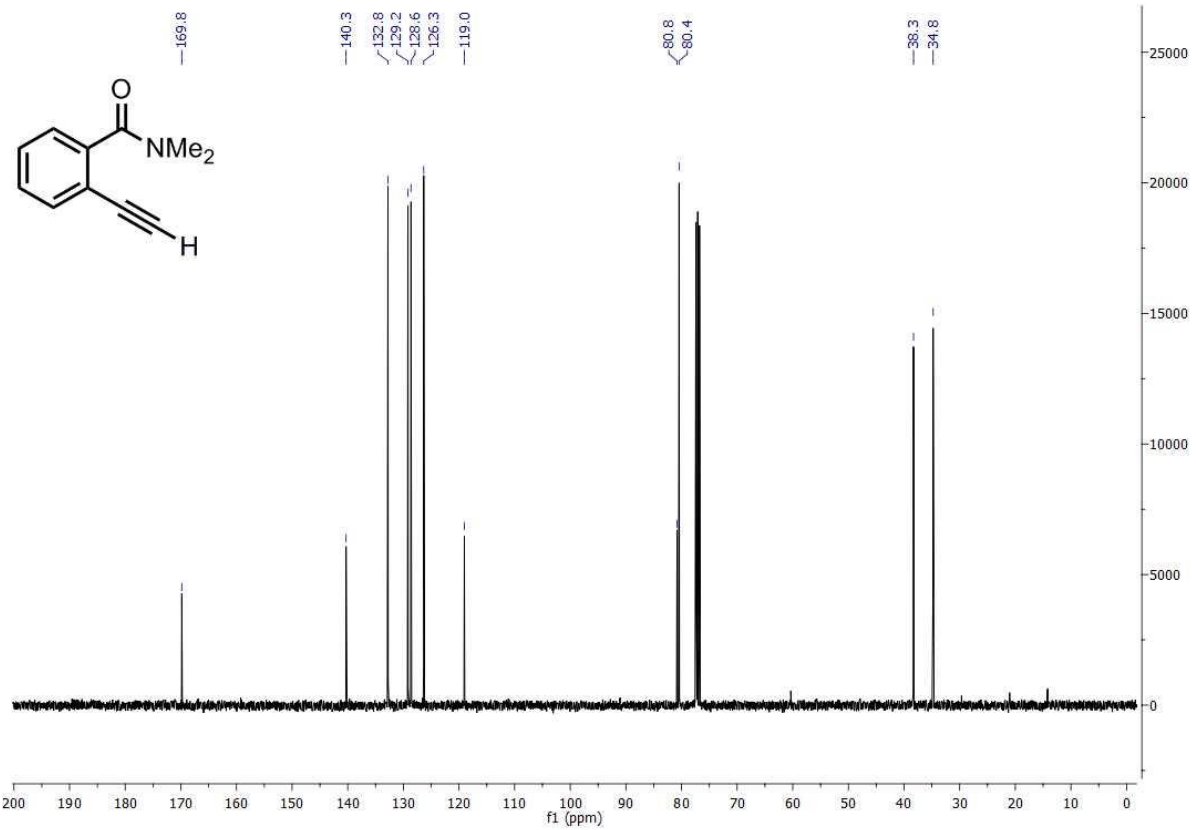
^{13}C NMR of *N*,*N*-dimethyl-2-((trimethylsilyl)ethynyl)benzamide:



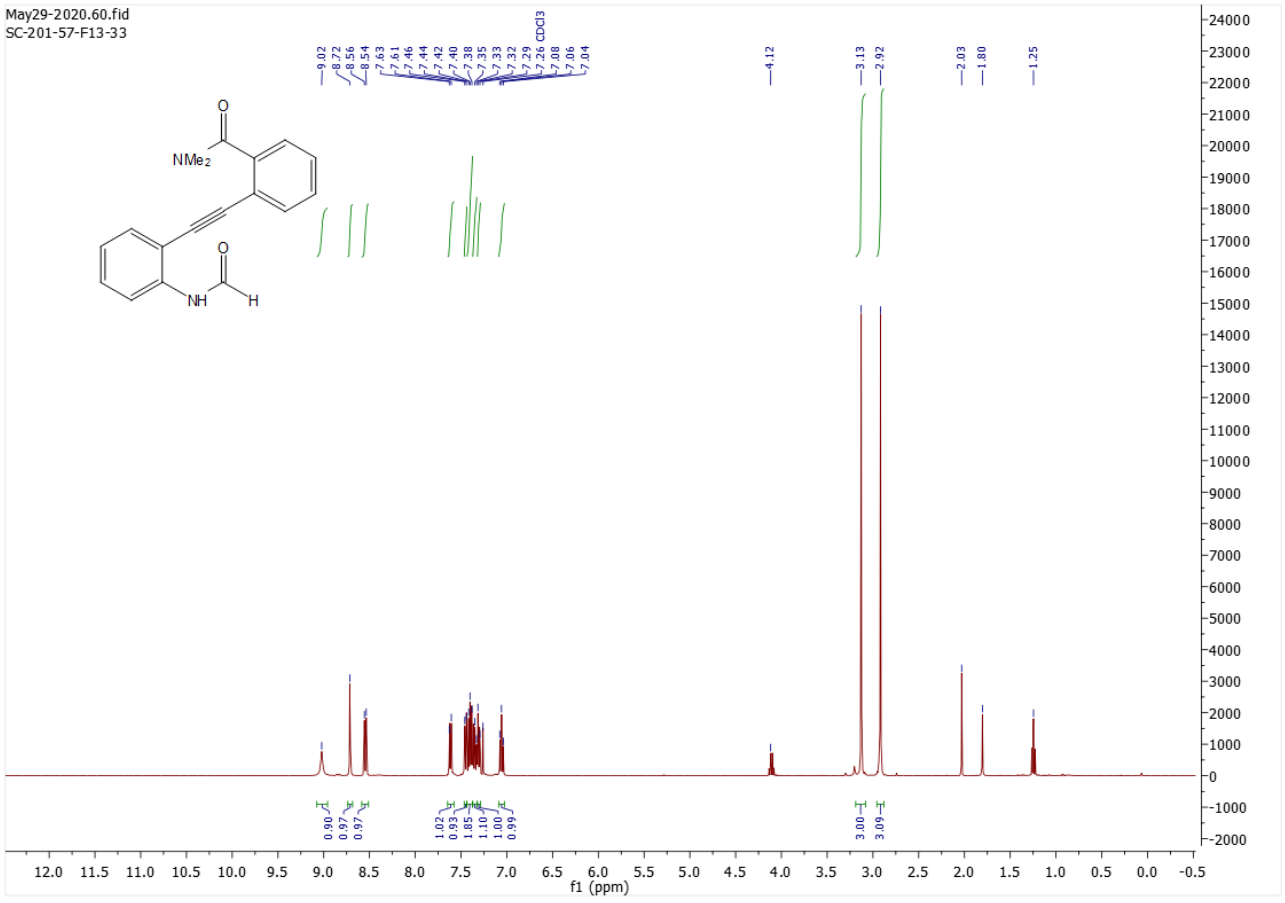
^{1}H NMR of *N*,*N*-dimethyl-2-(ethynyl)benzamide (**33**):



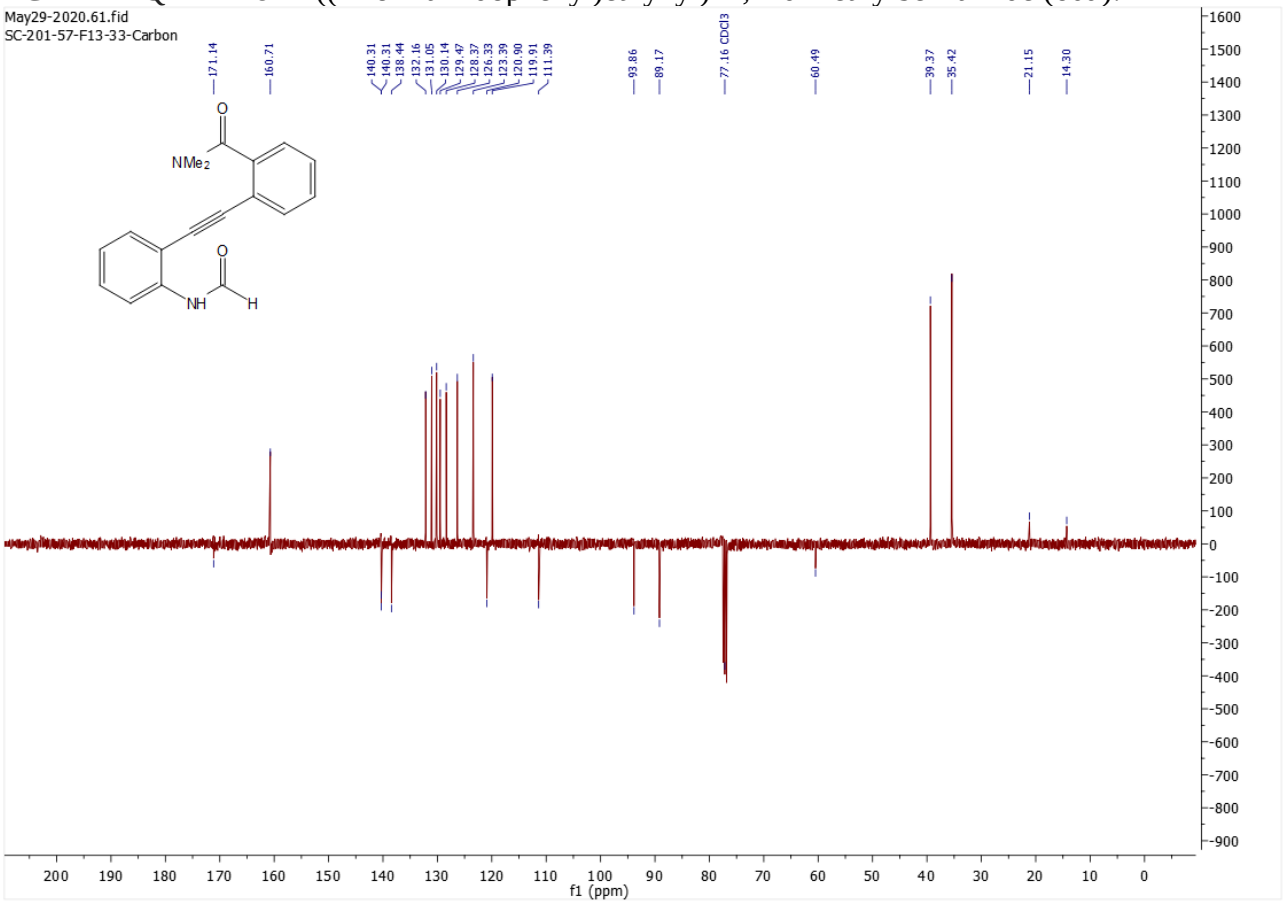
^{13}C NMR of *N*,*N*-dimethyl-2-(ethynyl)benzamide (**33**):



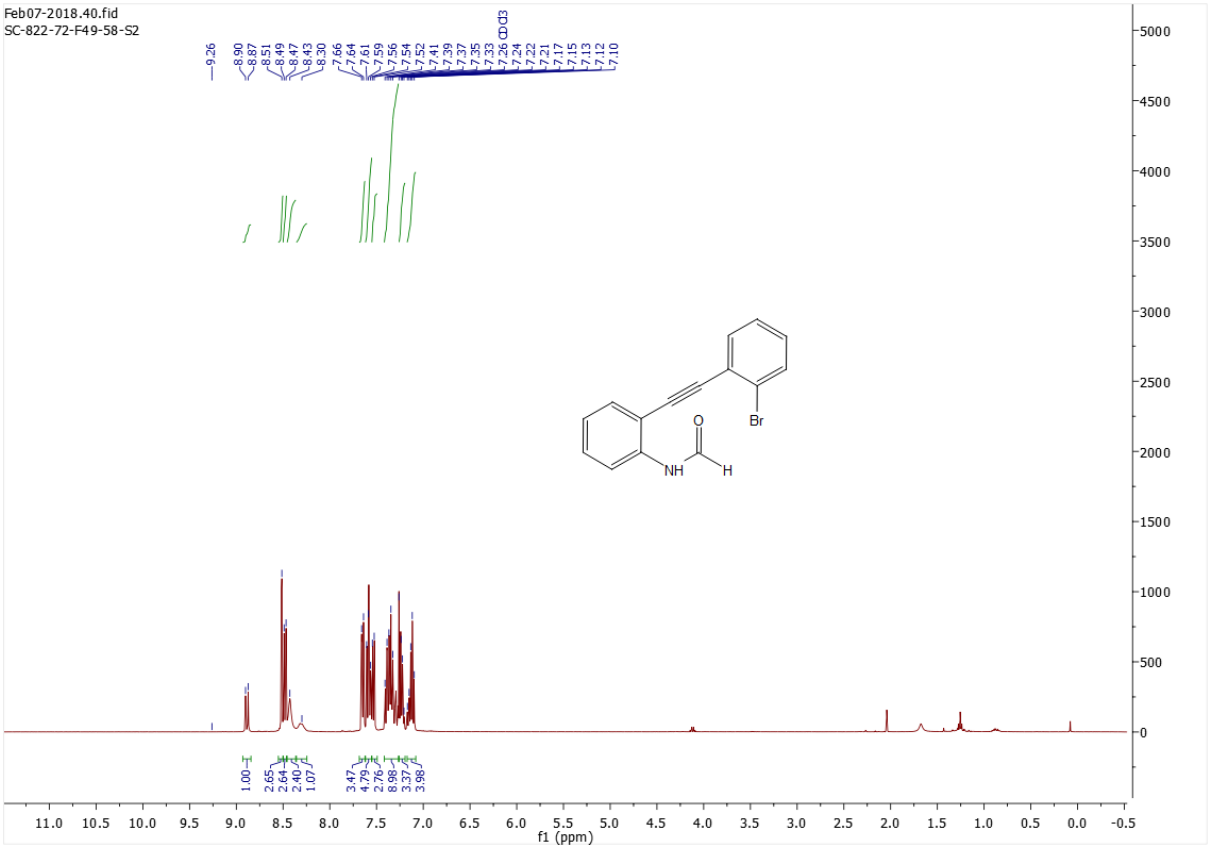
^{1}H NMR of 2-((2-formamidophenyl)ethynyl)-*N*,*N*-dimethylbenzamide (**60a**):



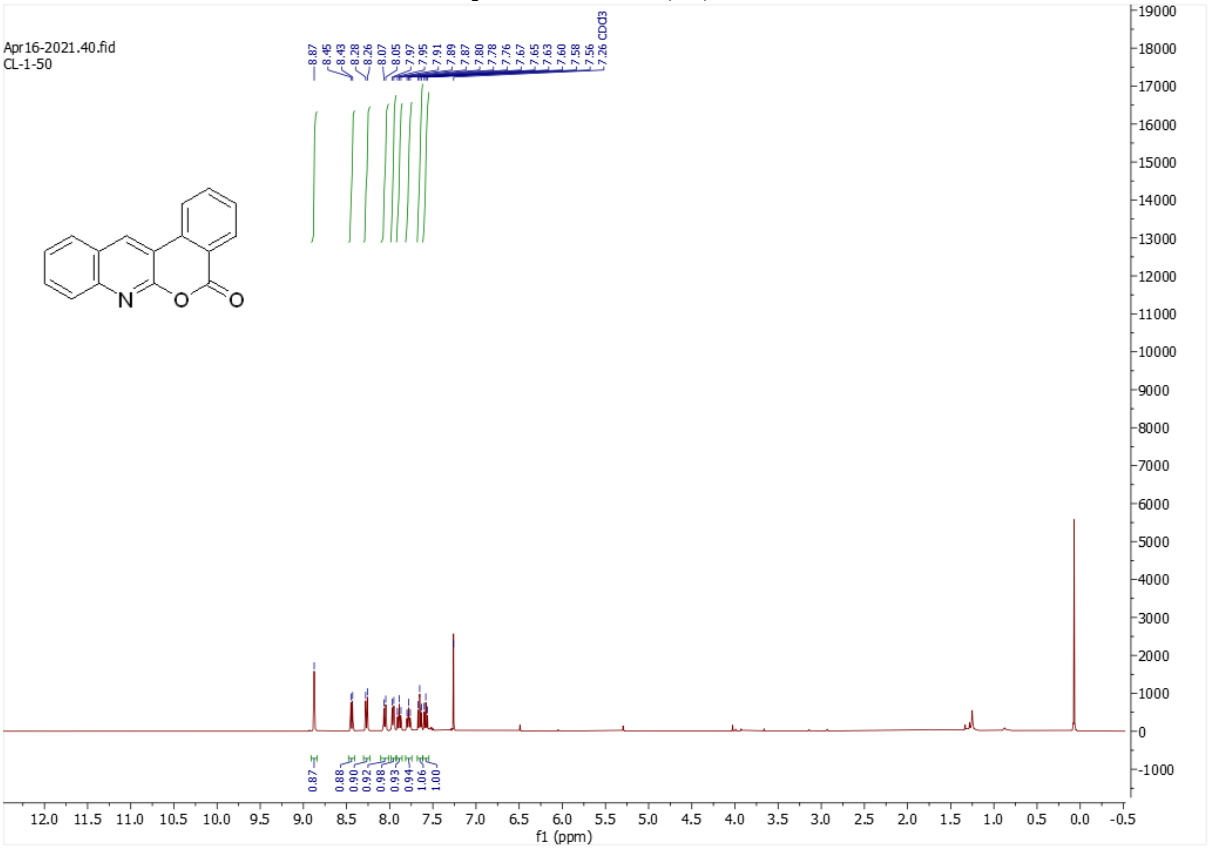
^{13}C DEPT-Q NMR of 2-((2-formamidophenyl)ethynyl)-*N*,*N*-dimethylbenzamide (**60a**):



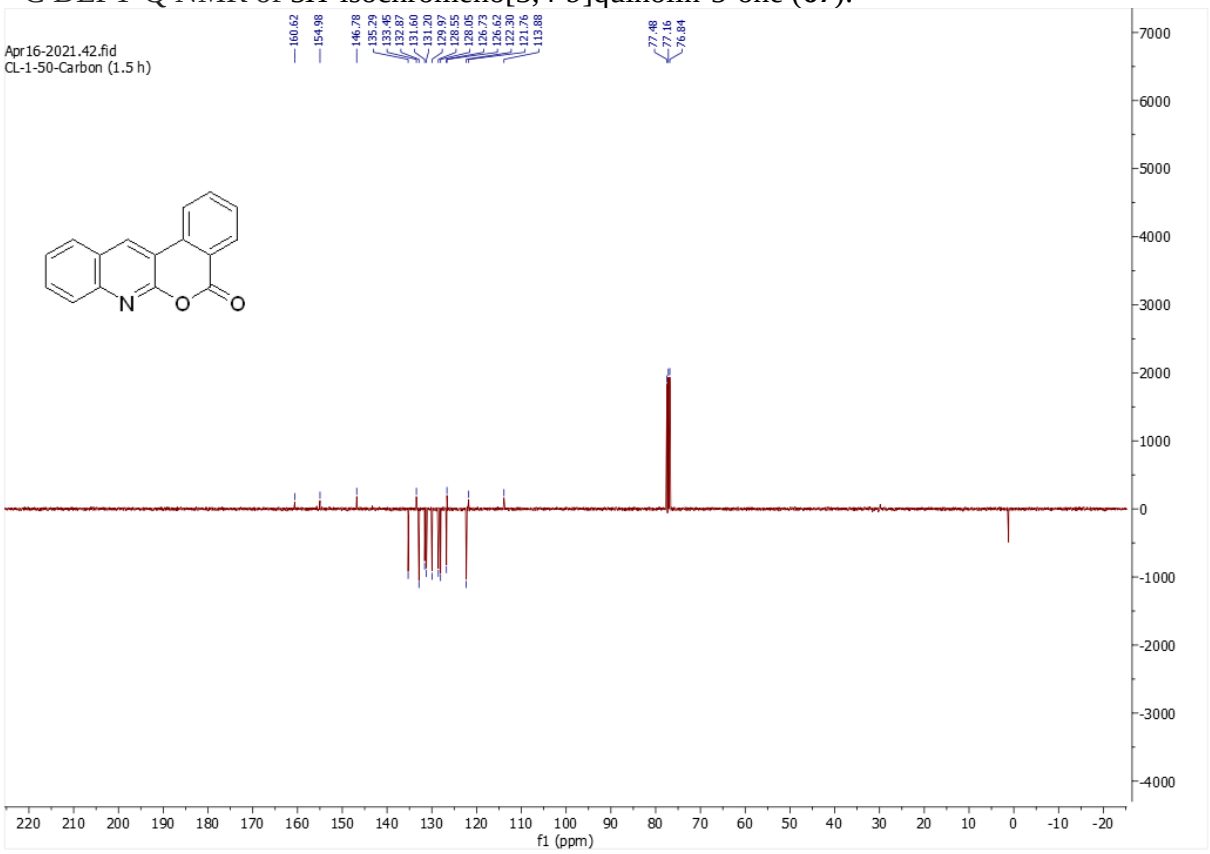
^{1}H NMR of *N*-(2-((2-bromophenyl)ethynyl)phenyl)formamide (**60b**):



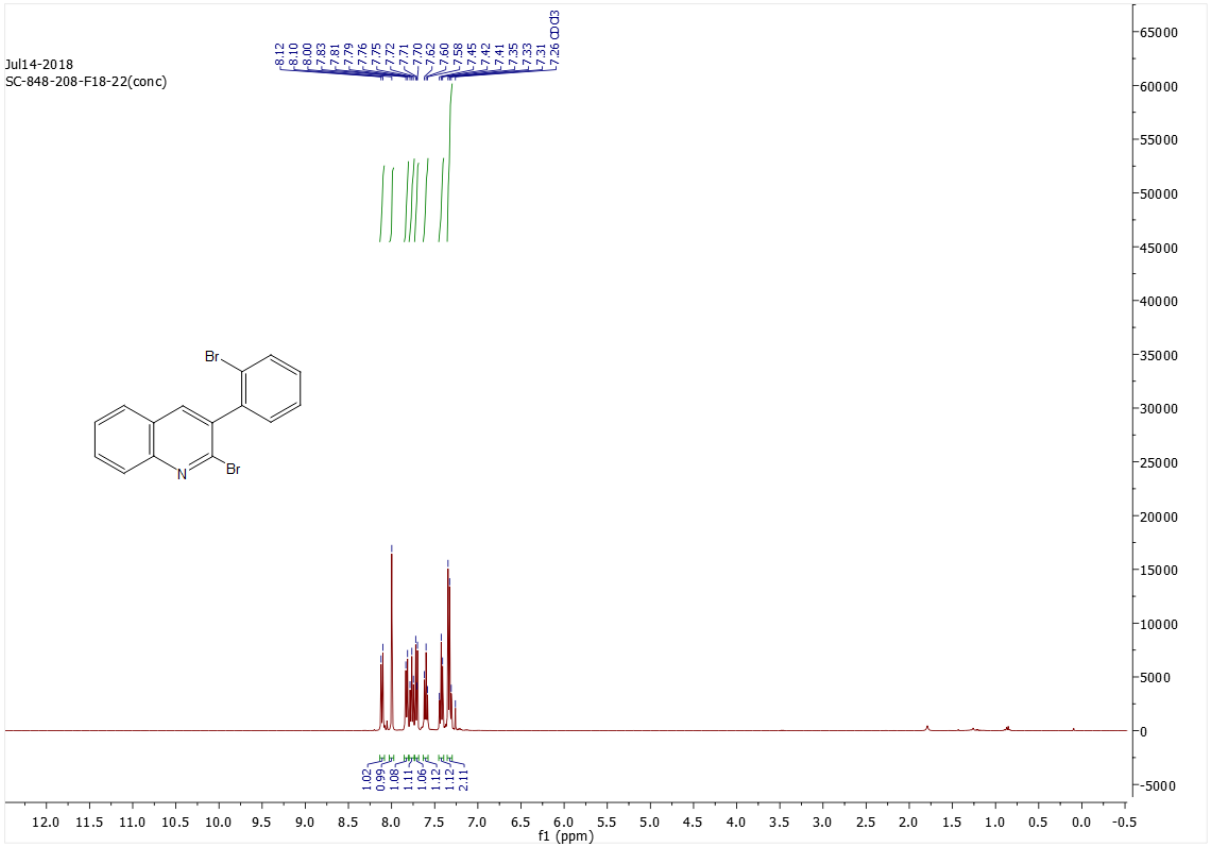
^{1}H NMR of 5*H*-isochromeno[3,4-*b*]quinolin-5-one (**67**):



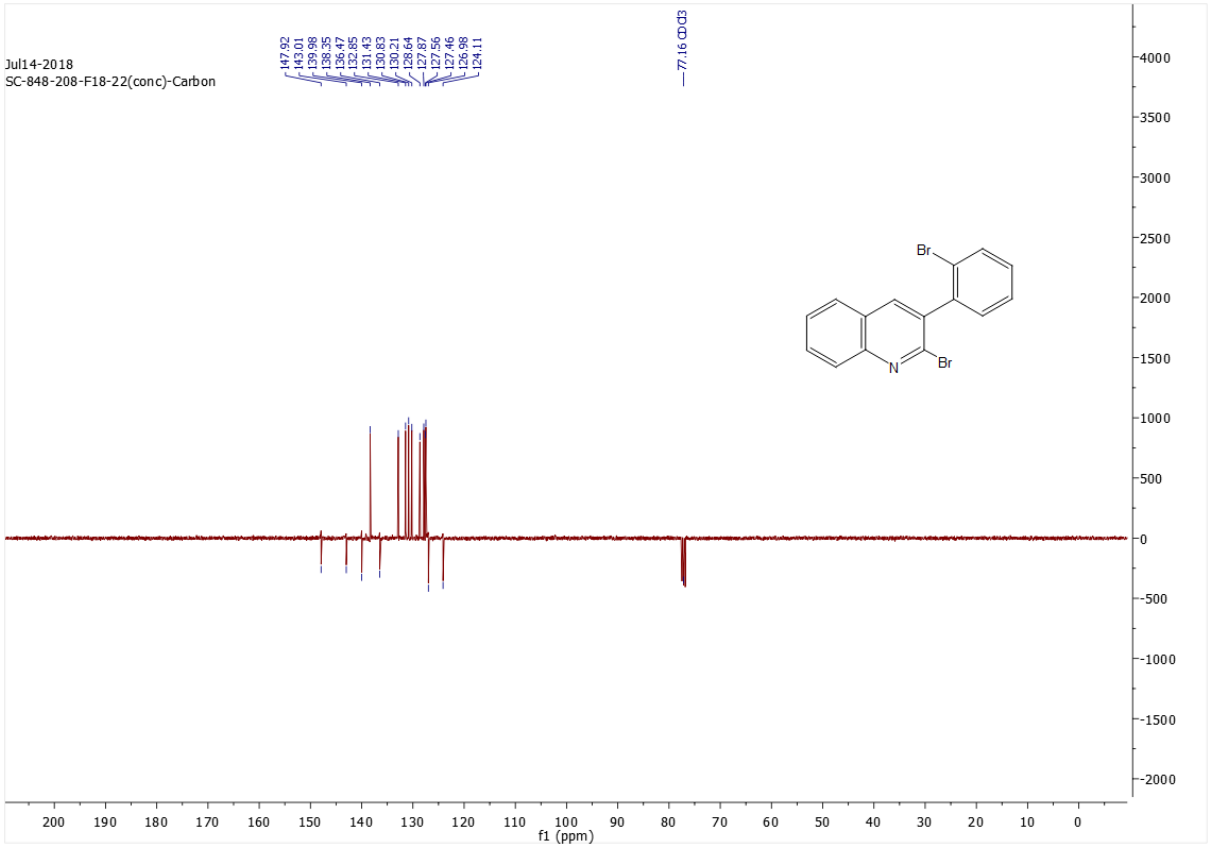
^{13}C DEPT-Q NMR of 5*H*-isochromeno[3,4-*b*]quinolin-5-one (**67**):



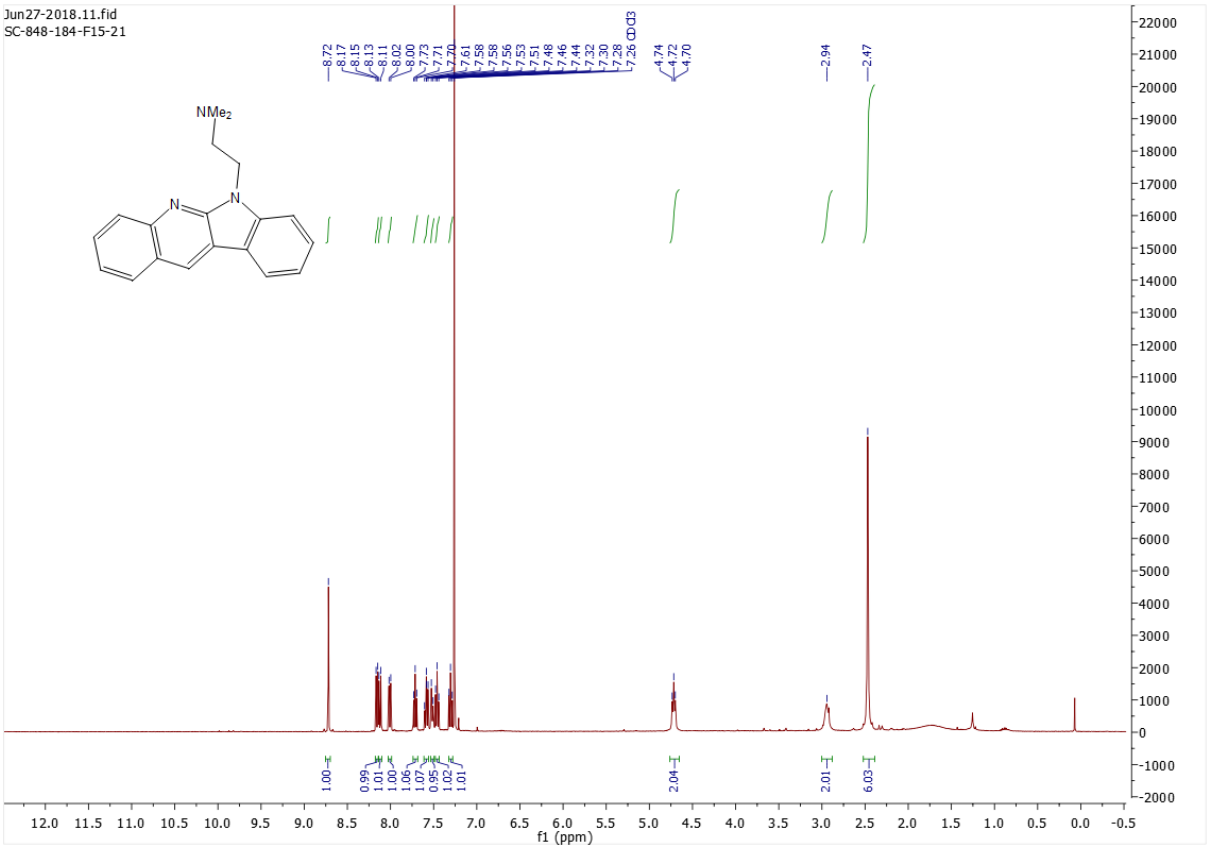
^{1}H NMR of 2-bromo-3-(2-bromophenyl)quinoline (**69**):



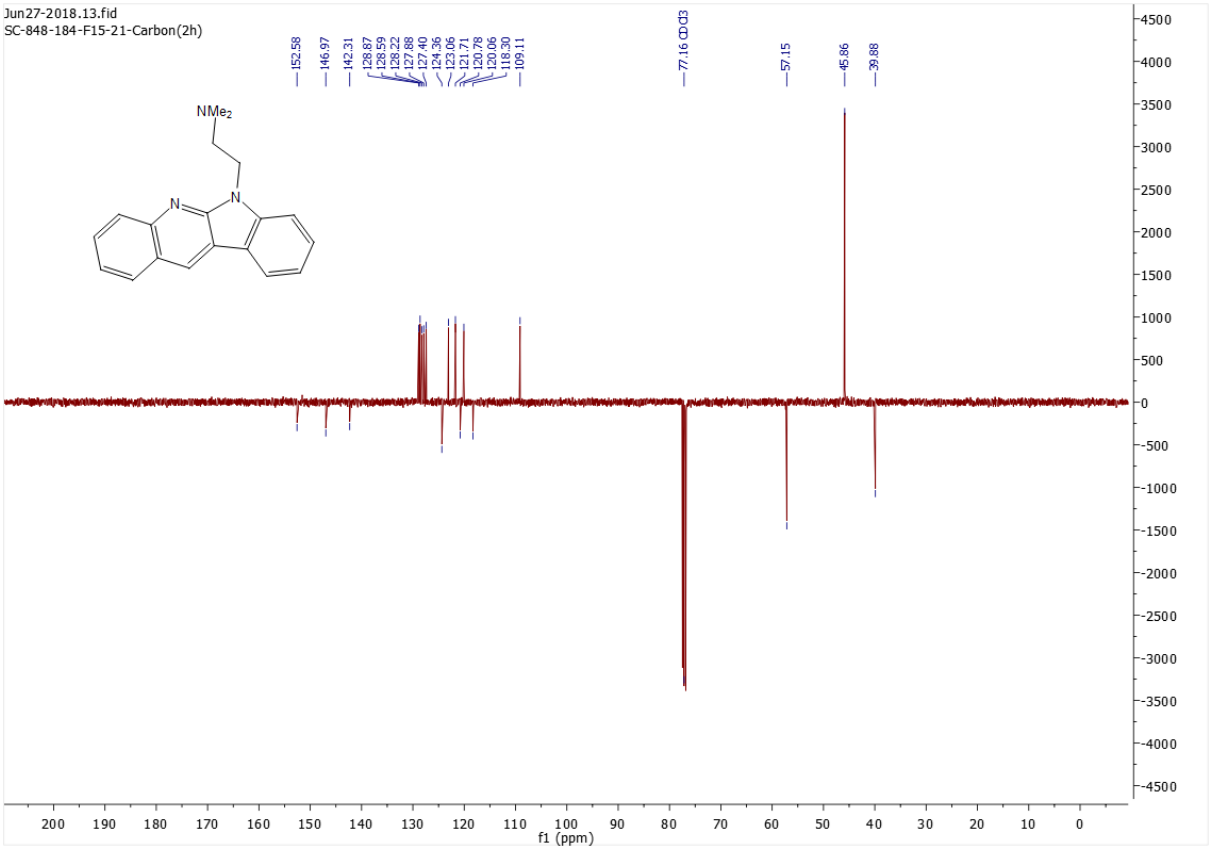
^{13}C DEPT-Q NMR of 2-bromo-3-(2-bromophenyl)quinoline (**69**):



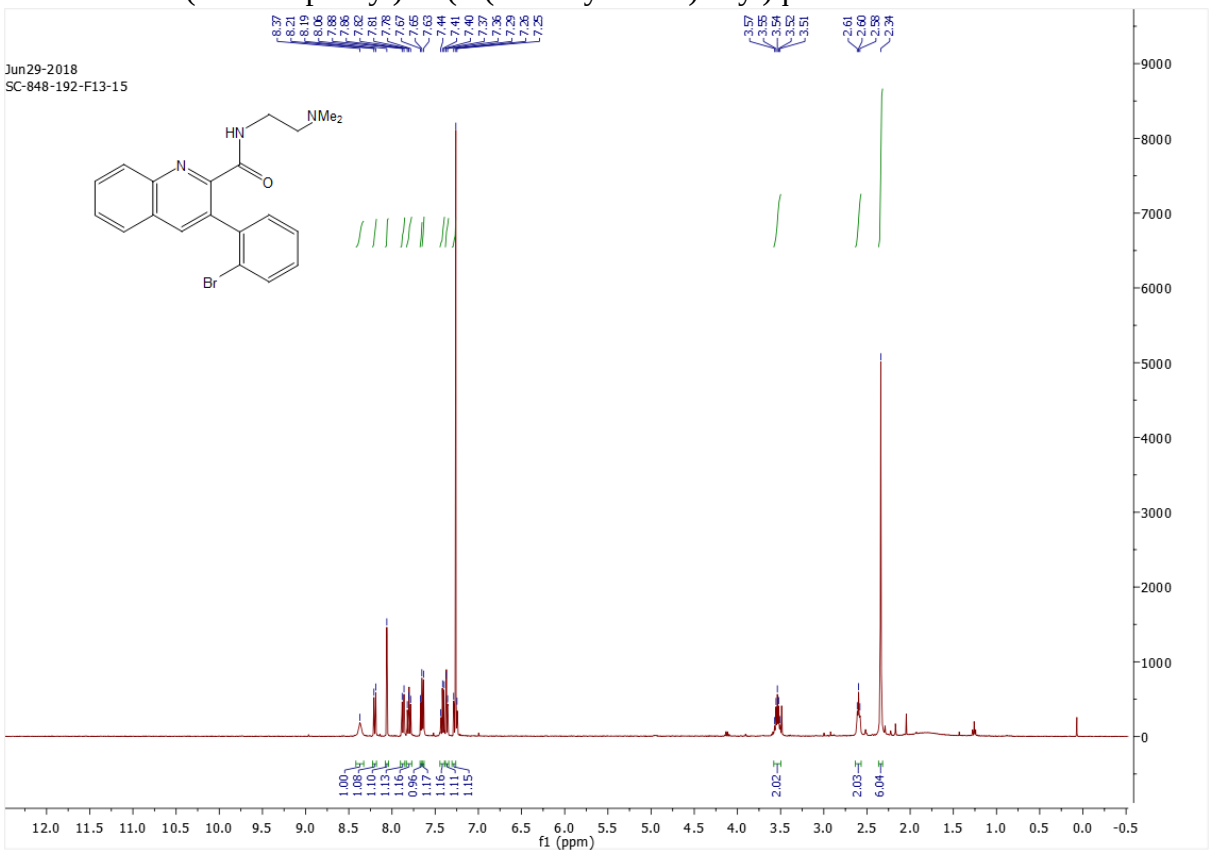
^{1}H NMR of 2-(6*H*-indolo[2,3-*b*]quinolin-6-yl)-*N*,*N*-dimethylethan-1-amine (**70**):



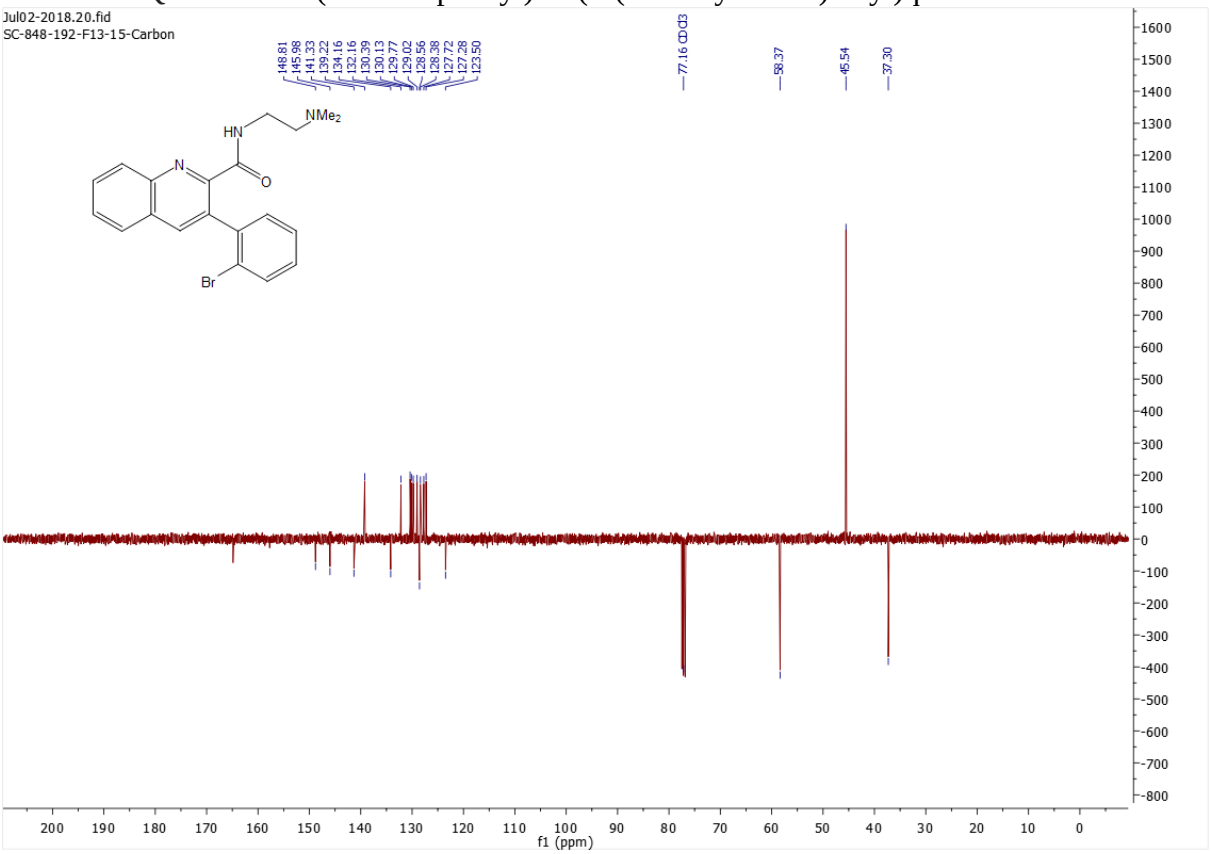
^{13}C DEPT-Q NMR of 2-(6*H*-indolo[2,3-*b*]quinolin-6-yl)-*N*,*N*-dimethylethan-1-amine (**70**):



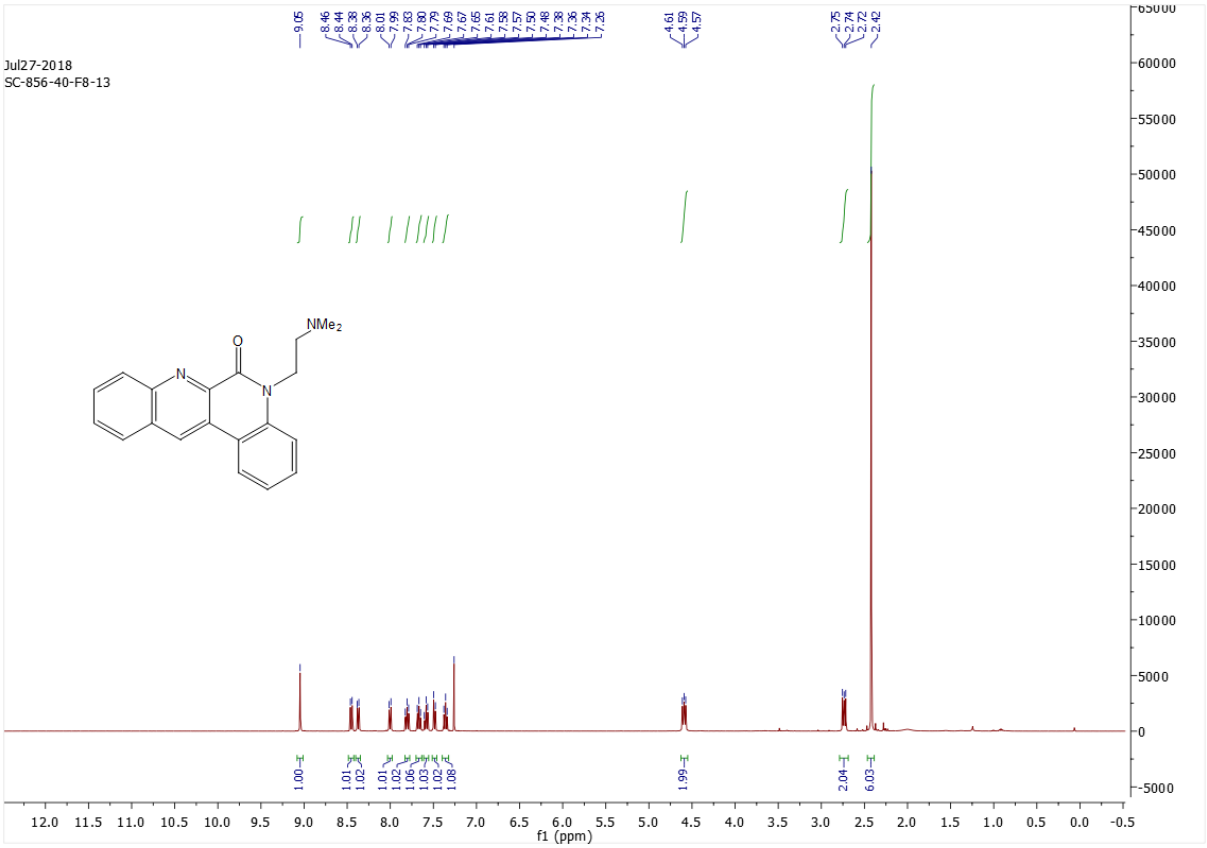
^{1}H NMR of 3-(2-bromophenyl)-*N*-(2-(dimethylamino)ethyl)quinoline-2-carboxamide:



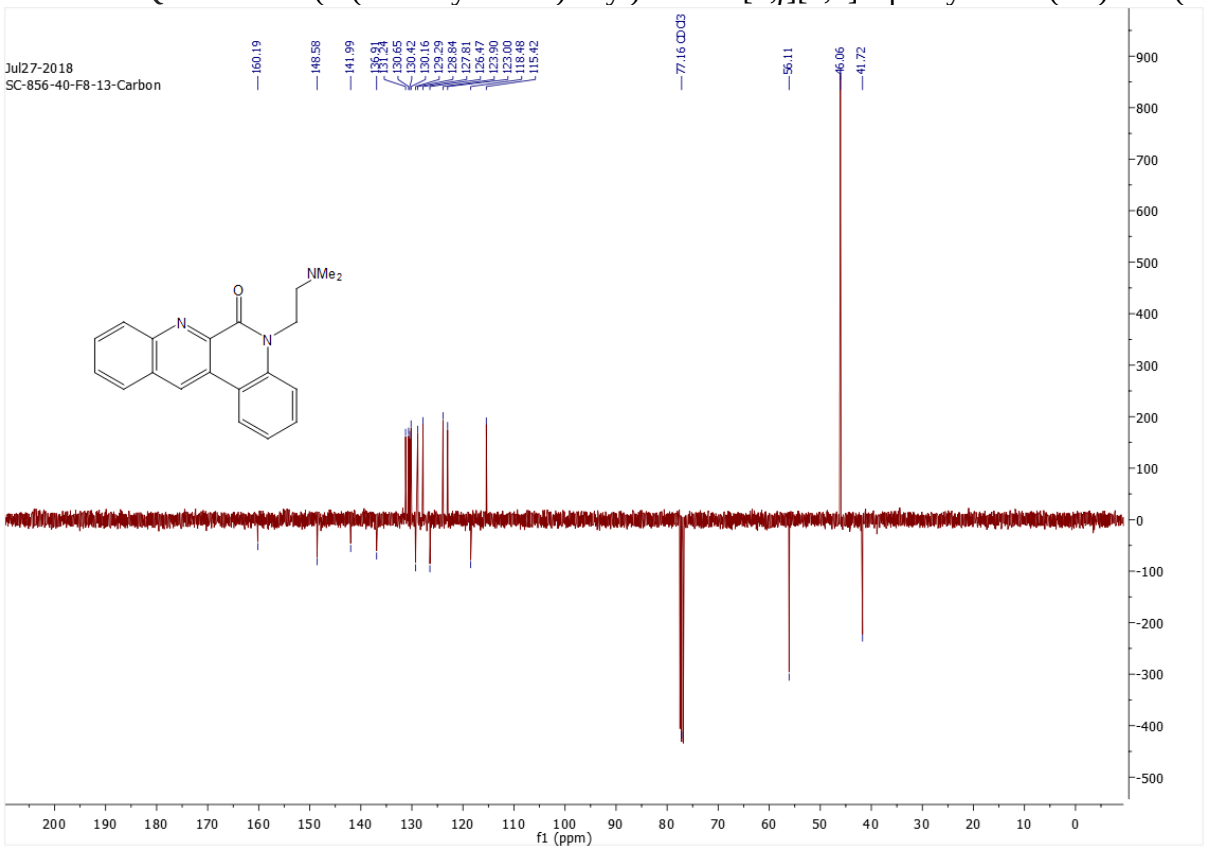
^{13}C DEPT-Q NMR of 3-(2-bromophenyl)-*N*-(2-(dimethylamino)ethyl)quinoline-2-carboxamide:



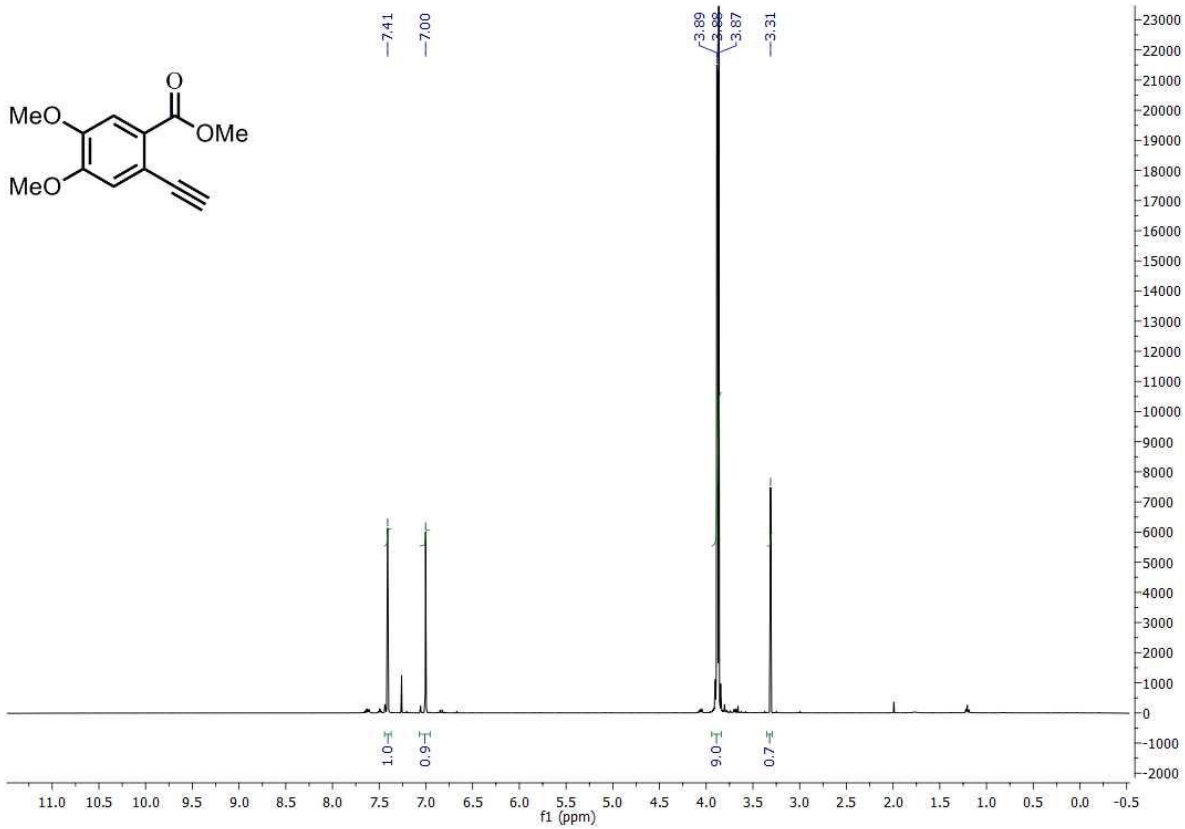
^{1}H NMR of 5-(2-(dimethylamino)ethyl)dibenzo[*b*,*f*][1,7]naphthyridin-6(5*H*)-one (**71**):



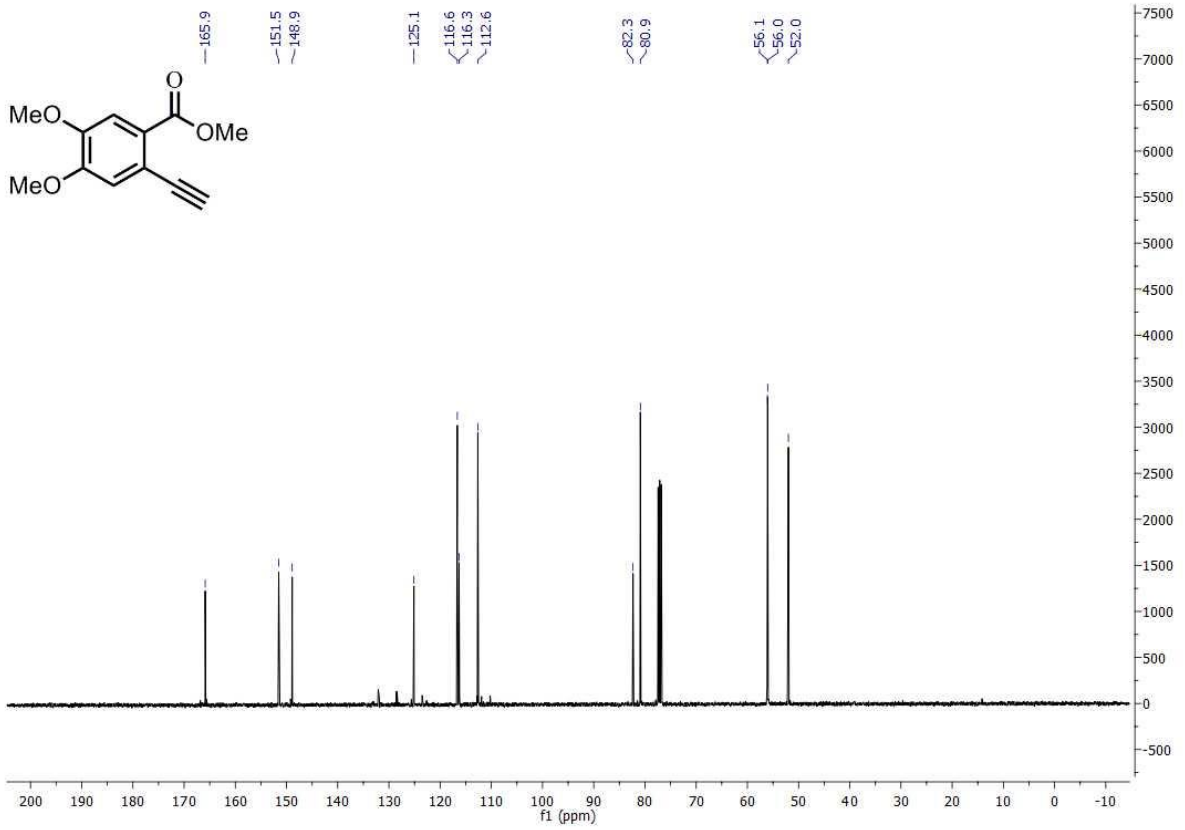
^{13}C DEPT-Q NMR of 5-(2-(dimethylamino)ethyl)dibenzo[*b*,*f*][1,7]naphthyridin-6(5*H*)-one (**71**):



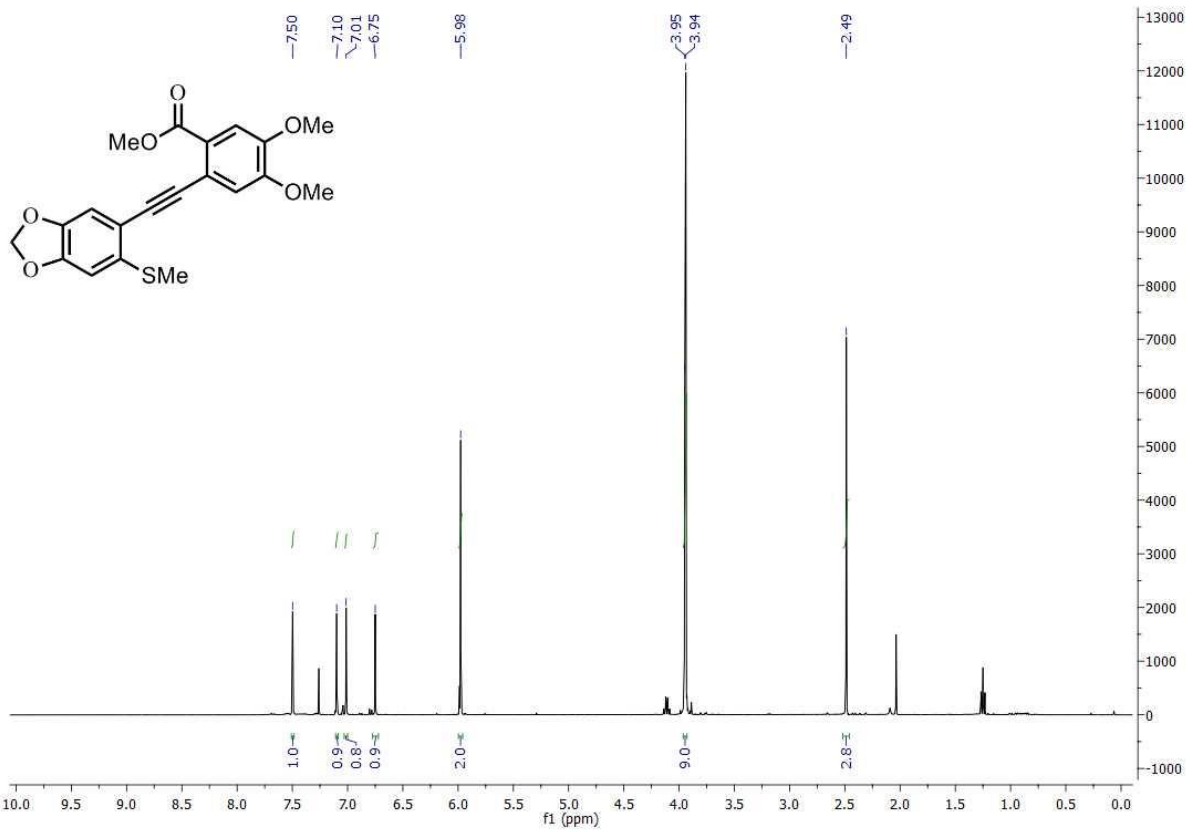
^{1}H NMR of methyl 2-ethynyl-4,5-dimethoxybenzoate (**73**):



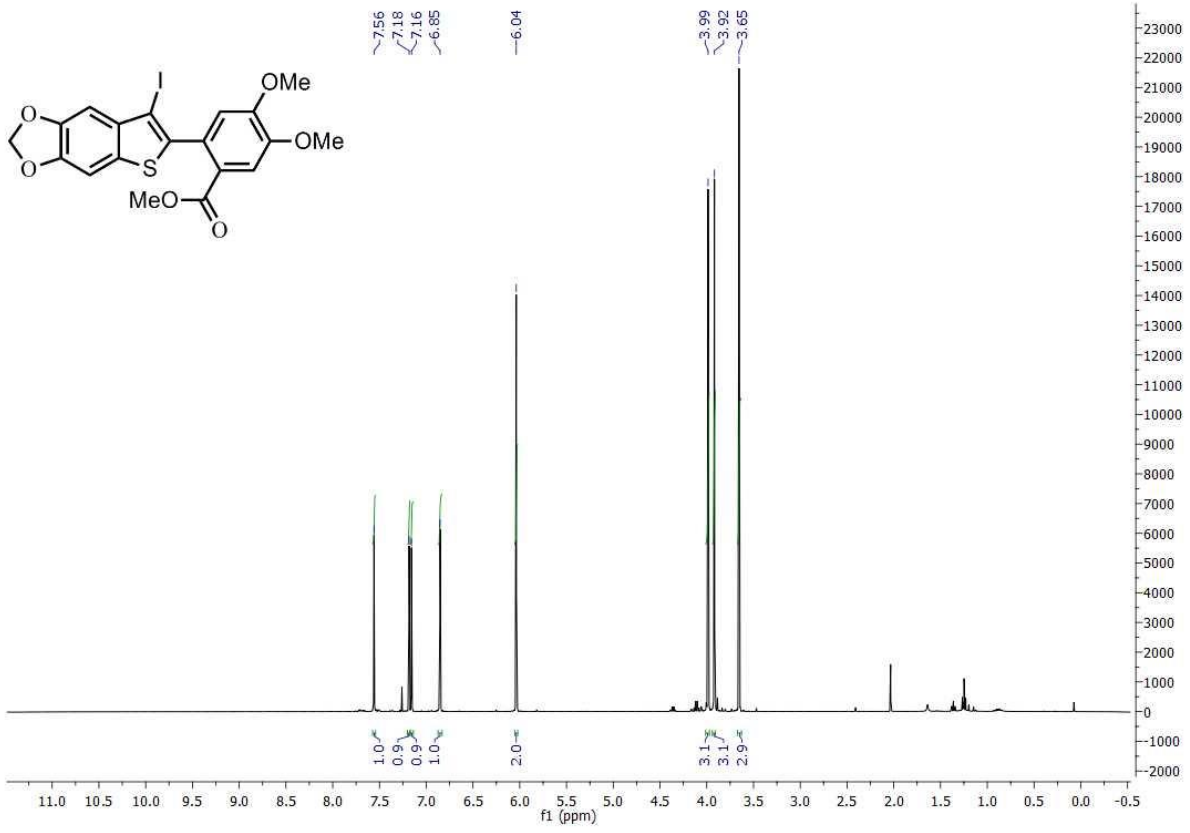
^{13}C NMR of methyl 2-ethynyl-4,5-dimethoxybenzoate (**73**):



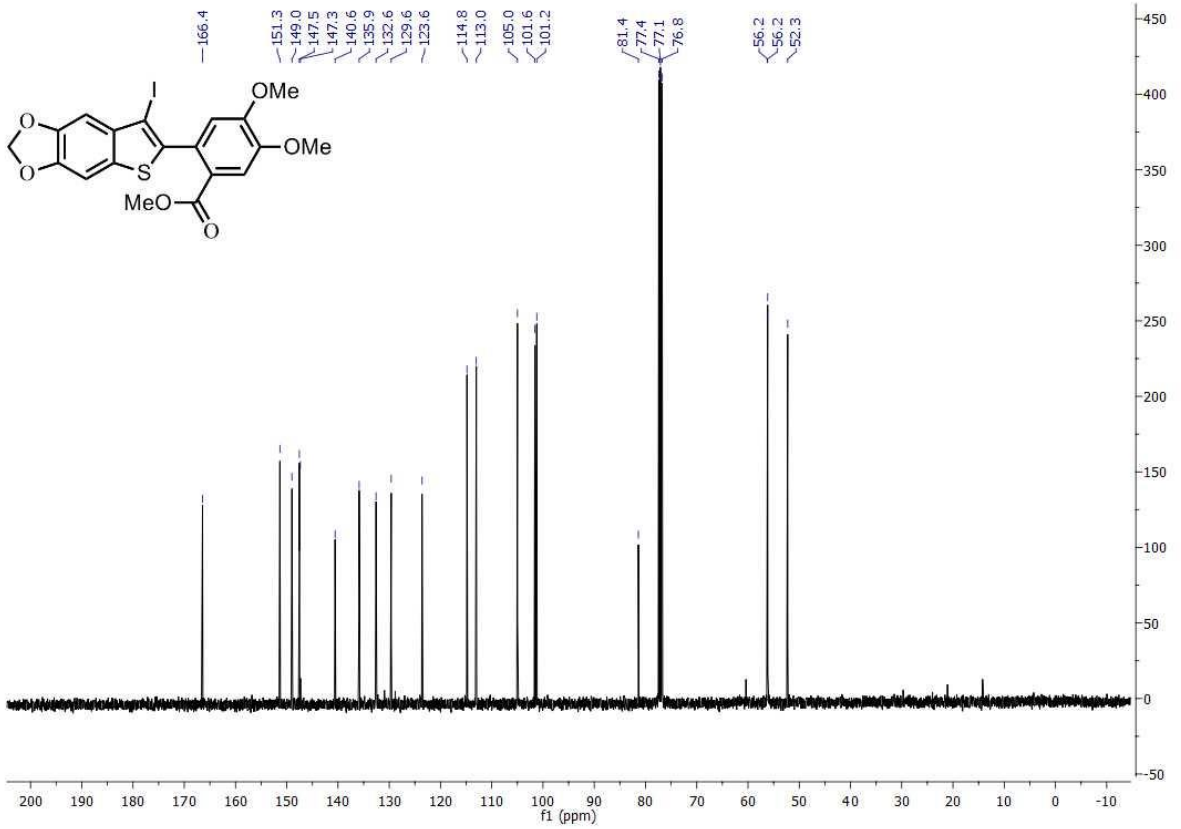
^{1}H NMR of methyl 4,5-dimethoxy-2-((6-(methylthio)benzo[*d*][1,3]dioxol-5-yl)ethynyl)benzoate (**74**):



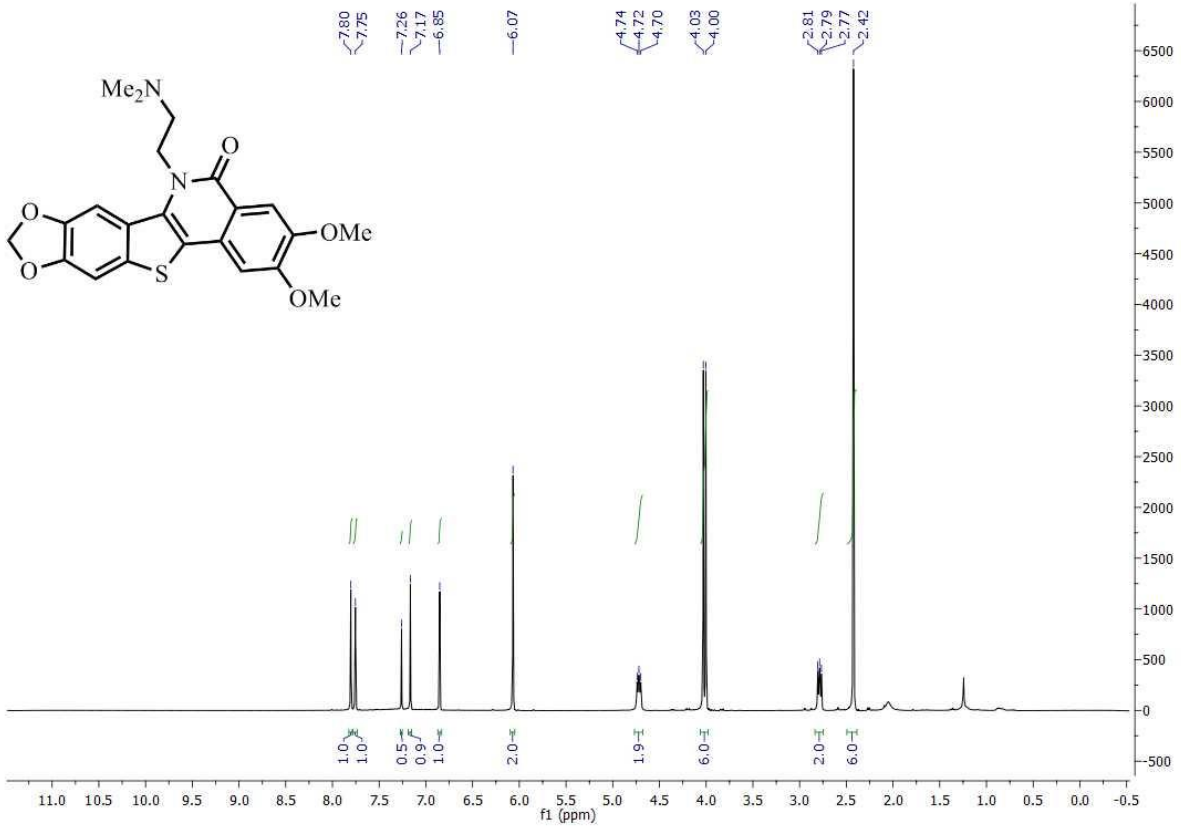
^{1}H NMR of methyl 2-(7-iodothieno[2',3':4,5]benzo[1,2-*d*][1,3]dioxol-6-yl)-4,5-dimethoxybenzoate (**75**):



^{13}C NMR of methyl 2-(7-iodothieno[2',3':4,5]benzo[1,2-*d*][1,3]dioxol-6-yl)-4,5-dimethoxybenzoate (**75**):



^{1}H NMR of 6-(2-(dimethylamino)ethyl)-2,3-dimethoxy-[1,3]dioxolo[4",5":4',5']benzo[1',2':4,5]thieno[3,2-*c*]isoquinolin-5(6*H*)-one (**77**):



^{13}C NMR of 6-(2-(dimethylamino)ethyl)-2,3-dimethoxy-[1,3]dioxolo[4'',5'':4',5']benzo[1',2':4,5]thieno[3,2-*c*]isoquinolin-5(6*H*)-one (**77**):