Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

SUPPORTING INFORMATION

Synthesis of *5H*-chromeno[3,4-*c*]pyridine derivatives through ruthenium-catalyzed [2+2+2] cycloaddition

William Parisot,[a] Steve Huvelle,[a] Mansour Haddad,[a] Guillaume Lefèvre,[a] Phannarath Phansavath,[a] Virginie Ratovelomanana-Vidal [a]*

[a] PSL University, Chimie ParisTech, CNRS, Institute of Chemistry for Life and Health Sciences, CSB2D Team, 11 Rue Pierre et Marie Curie, 75005 Paris, France

e-mail : virginie.vidal@chimieparistech.psl.eu

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I. General informations

General Methods: Unless otherwise stated, all reactions were carried out under argon. Thin-layer chromatography was performed on silica gel 60 F254 on aluminum plates (Merck). Visualization was accomplished using UV light (λ = 254 or 365 nm) or by staining in basic KMnO4, p-anisaldehyde or phosphomolybdic acid solution followed by heating. Flash chromatography was performed under positive air pressure using silica gel (40-63 µm) from VWR Chemical.

Instrumentation and Data Acquisition: Proton (^{1}H), carbon (^{13}C) and fluorine (^{19}F) nuclear magnetic resonance spectra were recorded on Bruker AV400 instrument, using non deuterated chloroform (^{1}H NMR : δ = 7.26 ppm) as an internal chemical shift reference for Proton (^{1}H) and (^{13}C NMR : δ = 77.16 ppm) relative to the centre line of the triplet as an internal chemical shift reference for Carbon (^{13}C). Melting points (M. p.) were determined on a Köfler melting point apparatus. High resolution mass spectrometric (HRMS) analyses were measured on Q-Tof 6545LTQ-Orbitrap (Agilent) by ESI or APCI. Low resolution mass spectrometric (LRMS) analyses were measured on DSQII (ThermoScientific) by DEP.

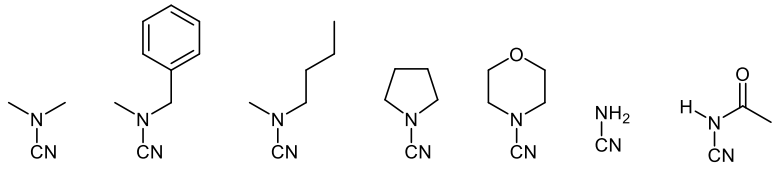
Data Reporting: The presentation of ^{1}H NMR spectroscopic data: magnet strength, analysis solvent, chemical shift (*δ*, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint. = quintuplet, sext. = sextuplet sept. = septuplet, m = multiplet, b = broad, app. = apparent), *J*-coupling constants (Hz), and integration. The regioisomeric ratio was determined by integration of ^{1}H-NMR signals. The response factor of both regioisomers was assumed to be equal in each case. For regioisomeric ratios greater than 90:10 only the major isomer is depicted in the following NMR characterizations. HRMS were given for the mixture of regioisomers of *5H*-chromeno[3,4-*c*]pyridines and *5H*-chromeno[4,3-*c*]pyridines.

Materials: All reagents were purchased in the highest purity grade available from Acros Organics, Sigma-Aldrich, Tokyo Chemical Industry, Alfa Aesar and Fluorochem. They were used without further purification unless otherwise specified. Argon and liquid nitrogen were provided from Air liquid. Anhydrous solvents were freshly distilled before use or obtained from solvent purificator Pure Solv^{TM}. Petroleum ether, pentane, ethyl acetate, dichloromethane and diethyl ether were used as received. Anhydrous 2-methyltetrahydrofuran was obtained by distillation over sodium in the presence of benzophenone under argon prior to use.

Safety Notice: Cyanamides are volatile and toxic. Propargyl bromide is toxic and carcinogenic. Iodophenols reagents are known to be harmful. All these reagents must be handled under a fume hood and with gloves.

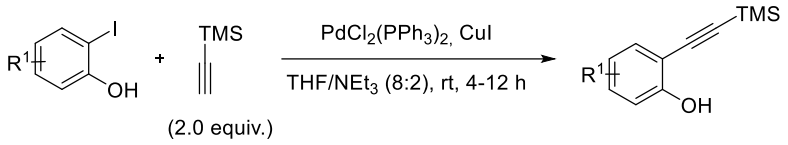
II. Cyanamide syntheses

Dimethylcyanamide **2a**, pyrrolidine carbonitrile **2d**, cyanamide **2f** and 4-morpholinecarbonitrile **2e** were purchased from commercial sources. Cyanamides **2b**, **2c** and **2g** were prepared according to reported procedures.[1,2]



III. General procedures

1. Sonogashira coupling (general procedure A)

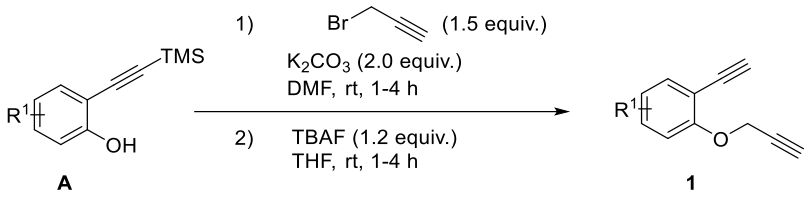


In a 100 mL round bottom flask was suspended $PdCl_2(PPh_3)_2$ (255 mg, 0.36 mmol, 0.02 equiv.) and CuI (139 mg, 0.73 mmol, 0.04 equiv.) in 26 mL of THF/NEt_3 (8:2). Under argon, a solution of 2-iodophenol (4.00 g, 18.2 mmol, 1.0 equiv.) and trimethylsilyl acetylene (5.03 mL, 36.4 mmol, 2.0 equiv.) in 26 mL of THF/NEt_3 (8:2) was added, the solution turns to black. The resulting mixture was stirred overnight at room temperature. A saturated aqueous solution of NH_4Cl (30 mL) was added and the aqueous layer was extracted with EtOAc (3 x 30 mL). The combined organic layers were dried over $MgSO_4$, filtered, and the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, cyclohexane/EtOAc ; 100:0 to 95:5) affording 2-((trimethylsilyl)ethynyl)phenol as a yellow oil (3.36 g, 17.6 mmol, 97%).

[1] Auvinet, A-L.; Ez-Zoubir, M.; Vitale, M. R.; Brown, J. A.; Michelet, V.; Ratovelomanana-Vidal, V.; *ChemSusChem*, 2012, **5**, 1888.

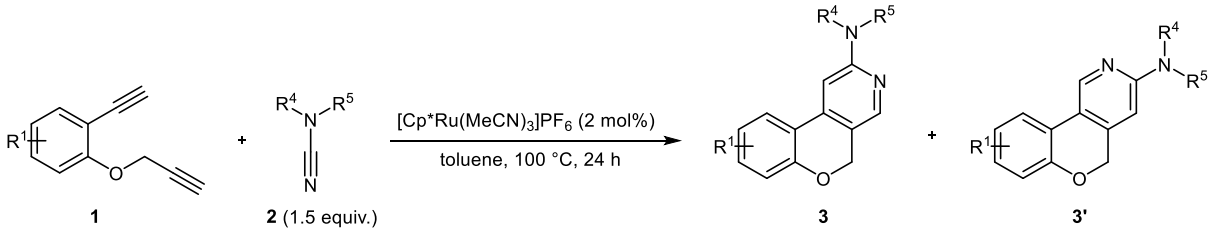
[2] Shirota, F. N.; Nagasawa, H. T.; Kwon, C. H., Demaster E. G.; *Drug Metab. Dispos.,* 1984, **12**, 337.

2. Ether formation and alkyne deprotection (general procedure B)



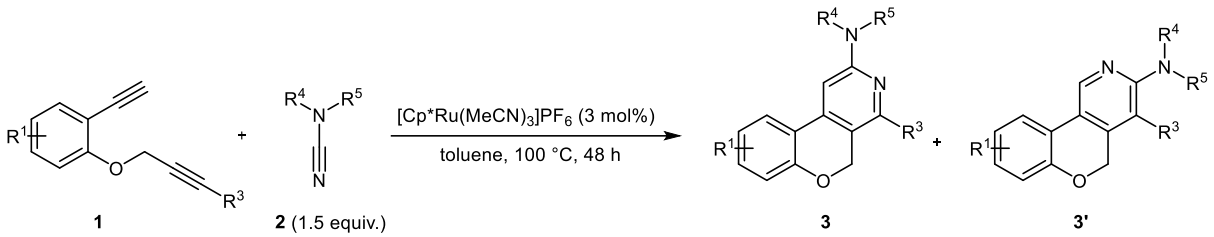
In a 100 mL round bottom flask 2-((trimethylsilyl)ethynyl)phenol (3.36 g, 17.6 mmol, 1.0 equiv.), and K_2CO_3 (4.88 g, 35.3 mmol, 2.0 equiv.) were mixed in 50 mL of anhydrous DMF at room temperature. Under argon, propargyl bromide (80 % in toluene) (2.93 mL, 26.4 mmol, 1.5 equiv.) was added and the brownish mixture was stirred 4 h at room temperature. When the reaction was complete (NMR monitoring), 20 mL of water was added. The resulting solution was extracted with Et_2O (3 x 20 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$ and the filtrate was concentrated under reduced pressure. The residue was dissolved in 50 mL of THF and tetrabutylammonium fluoride (5.52 g, 21.1 mmol, 1.2 equiv.) was added, the solution turns to black. The solution was stirred 1 h at room temperature, then water (20 mL) was added. The resulting solution was extracted with DCM (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, cyclohexane/EtOAc ; 95:5) affording **1a** as a pale-yellow solid (2.31 g, 14.8 mmol, 84%).

3. [2+2+2] Cycloaddition method (general procedure C)



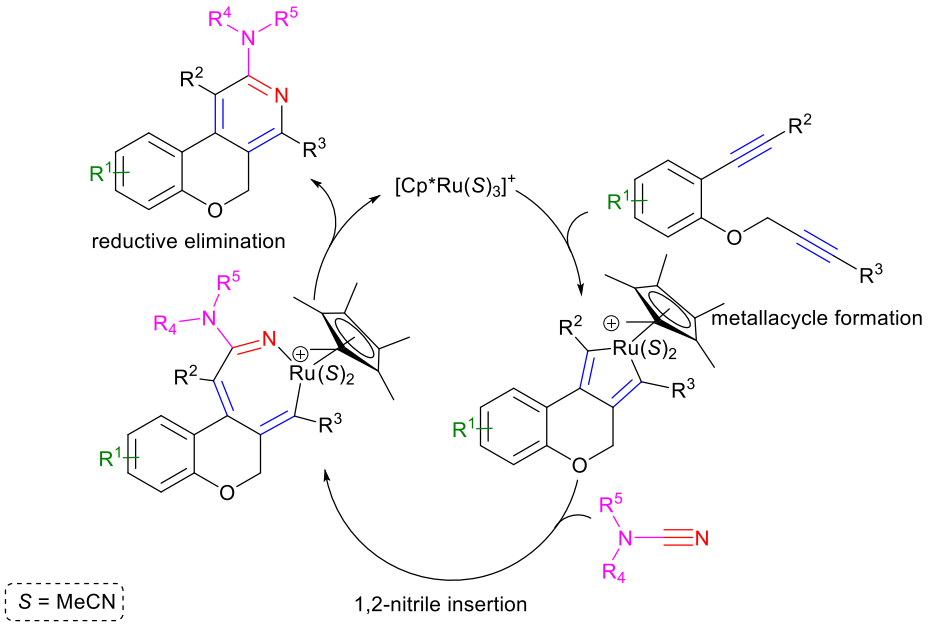
A sealed tube was charged with $[Cp^*Ru(MeCN)_3]PF_6$ (6.5 mg, $1.28x10^{-2}$ mmol, 0.02 equiv.) and dimethylcyanamide **2a** (76 µL, 0.96 mmol, 1.5 equiv.) was added. Under argon a solution of diyne **1a** (100 mg, 0.64 mmol, 1.0 equiv.) in 1.8 mL of anhydrous toluene was added. The tube was sealed, and the reaction mixture was stirred vigorously at 100 °C for 24 h. When the reaction was complete, the solvent was removed under reduced pressure. The residue was purified by flash column chromatography (SiO_2, petroleum ether/EtOAc ; 80:20), then the excess of cyanamide was distilled off with a Kugelrohr distillation apparatus, affording a mixture of **3aa** and **3aa'** as a pale-brown oil (121 mg, 535 µmol, 84%).

4. [2+2+2] Cycloaddition method (general procedure D)



A sealed tube was charged with $[Cp^*Ru(MeCN)_3]PF_6$ (9.7 mg, 1.92x10^{-2} mmol, 0.03 equiv.) and 4-morpholinecarbonitrile **2e** (97 µL, 0.96 mmol, 1.5 equiv.) was added. Under argon a solution of diyne **1a** (100 mg, 0.64 mmol, 1.0 equiv.) in 1.8 mL of anhydrous toluene was added. The tube was sealed, and the reaction mixture was stirred vigorously at 100 °C for 48 h. When the reaction was complete, the solvent was removed under reduced pressure. The residue was purified by flash column chromatography (SiO_2, petroleum ether/EtOAc ; 80:20 to 70:30), then the excess of cyanamide was distilled off with a Kugelrohr distillation apparatus, affording a mixture of **3ae** and **3ae'** as a pale-brown oil (148 mg, 552 µmol, 86%).

Proposed mechanism[3]



[3] Roglans, A.; Pla-Quintana, A.; Solà, M. ; *Chem. Rev.*, 2021, **121**, 1894.

IV. Optimization

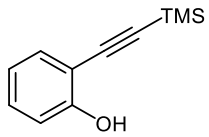
Entry	Catalyst (mol %)	Solvent	T°C	Conv. (%)	Yield (%)	Ratio
1	$[Cp^*RuCl]_4$ (2 mol%)	Toluene	100	100	43	>99/1
2	$[Cp^*Ru(MeCN)_3]PF_6$ (5 mol%)	Toluene	100	100	83	96/4
3	Cp*Ru(cod)Cl (5 mol%)	Toluene	100	92	37	>99/1
4	$[Rh(cod)Cl]_2$ (5 mol%)	Toluene	100	100	0	ND
5	$RuCl_3.nH_2O$ (5 mol%)	Toluene	100	58	33	92/8
6	$[Ir(cod)Cl]_2$ (5 mol%)	Toluene	100	100	0	ND
7	$In(OTf)_3$ (5 mol%)	Toluene	100	0	0	ND
8	$Fe(acac)_3$ (5 mol%)	Toluene	100	0	0	ND
9	$FeSO_4$ (5 mol%)	Toluene	100	0	0	ND
10	$CpCo(CO)_2$ (5 mol%)	Toluene	100	26	21	76/24
11	$[Cp_2Ni]$ (5 mol%), Xantphos (10 mol%), Cs_2CO_3 (1.00 equiv.)	Toluene	100	0	0	ND
12	$[Cp^*Ru(MeCN)_3]PF_6$ (2 mol%)	Toluene	100	100	84	96/4
13	$[Cp^*Ru(MeCN)_3]PF_6$ (2 mol%)	DCE	80	54	40	97/3
14	$[Cp^*Ru(MeCN)_3]PF_6$ (2 mol%)	DCM	50	43	26	97/3
15	$[Cp^*Ru(MeCN)_3]PF_6$ (2 mol%)	EtOH	80	10	9	92/8
16	$[Cp^*Ru(MeCN)_3]PF_6$ (2 mol%)	MeTHF	80	71	61	96/4
17	$[Cp^*Ru(MeCN)_3]PF_6$ (1 mol%)	Toluene	100	62	61	96/4
18	$[Cp^*Ru(MeCN)_3]PF_6$ (2 mol%)	Toluene	90	95	77	96/4

Table 1 : Optimization table

V. Characterization

1. Characterization of 2-((trimethylsilyl)ethynyl)phenol derivatives

2-((trimethylsilyl)ethynyl)phenol (A1)



A1
Chemical Formula: $C_{11}H_{14}OSi$

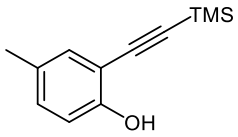
Prepared according to the general procedure **A** using 2-iodophenol (4.00 g, 18.2 mmol, 1.0 equiv.). After flash column chromatography (cyclohexane/EtOAc ; 100:0 to 95:5), the expected product was obtained as a yellow oil (3.36 g, 17.6 mmol, 97%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.27-7.22 (m, 1H), 6.94 (dd, *J* = 8.3, 0.8 Hz, 1H), 6.85 (td, *J* = 7.6, 1.1 Hz, 1H), 5.84 (s, 1H), 0.29 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.2, 131.7, 130.8, 120.4, 114.7, 109.6, 102.5, 99.1, 0.1 (3C).

LRMS (EI): Calculated for $C_{11}H_{14}OSi$ $[M\text{-}CH_3]^+$: 175 (100) found 175 (100).

4-methyl-2-((trimethylsilyl)ethynyl)phenol (A2)



A2
Chemical Formula: $C_{12}H_{16}OSi$

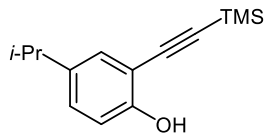
Prepared according to the general procedure **A** using 2-iodo-4-methylphenol (1.65 g, 7.05 mmol, 1.0 equiv.). After flash column chromatography (cyclohexane/EtOAc ; 100:0 to 95:5), the expected product was obtained as a yellow oil (1.40 g, 6.85 mmol, 97%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, *J* = 2.1 Hz, 1H), 7.02 (dd, *J* = 8.4, 2.2 Hz, 1H), 6.84 (d, *J* = 8.4, Hz, 1H), 5.69 (s, 1H), 2.24 (s, 3H), 0.28 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.1, 131.8, 131.6, 129.5, 114.4, 109.2, 102.0, 99.4, 20.4, 0.1 (3C).

LRMS (EI): Calculated for $C_{12}H_{16}OSi$ $[M\text{-}CH_3]^+$: 189 (100) found 189 (100).

4-isopropyl-2-((trimethylsilyl)ethynyl)phenol (A3)



A3
Chemical Formula: $C_{14}H_{20}OSi$

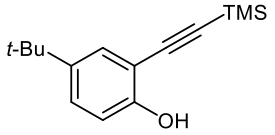
Prepared according to the general procedure **A** using 2-iodo-4-isopropylphenol (5.80 g, 22.1 mmol, 1.0 equiv.). After flash column chromatography (cyclohexane/EtOAc ; 98:2), the expected product was obtained as a yellow oil (3.72 g, 16.0 mmol, 72%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 2.3 Hz, 1H), 7.08 (dd, *J* = 8.5, 2.3 Hz, 1H), 6.88 (d, *J* = 8.5 Hz, 1H), 5.81 (s, 1H), 2.80 (sept., *J* = 6.9 Hz, 1H), 1.28 (app. s, 3H), 1.27 (app. s, 3H), 0.29 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.3, 140.6, 129.2, 129.1, 114.6, 109.2, 101.6, 99.7, 33.3, 24.1 (2C), 0.1 (3C).

LRMS (EI): Calculated for $C_{14}H_{20}OSi$ $[M\text{-}CH_3]^+$: 217 (100) found 217 (100).

4-(*tert*-butyl)-2-((trimethylsilyl)ethynyl)phenol (A4)



A4
Chemical Formula: $C_{15}H_{22}OSi$

Prepared according to the general procedure **A** using 4-(*tert*-butyl)-2-iodophenol (2.90 g, 10.5 mmol, 1.0 equiv.). After flash column chromatography (cyclohexane/EtOAc ; 98:2 to 95:5), the expected product was obtained a white solid (2.15 g, 8.72 mmol, 83%).

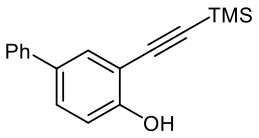
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 2.4 Hz, 1H), 7.27 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.87 (d, *J* = 8.6 Hz, 1H), 5.68 (s, 1H), 1.27 (s, 9H), 0.28 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.0, 143.1, 128.3, 128.1, 114.2, 108.8, 101.8, 99.7, 34.2, 31.5 (3C), 0.2 (3C).

M.p. : 71-73 °C

LRMS (EI): Calculated for $C_{15}H_{22}OSi$ $[M\text{-}CH_3]^+$: 231 (100) found 231 (100).

3-((trimethylsilyl)ethynyl)-[1,1'-biphenyl]-4-ol (A5)



A5
Chemical Formula: $C_{17}H_{18}OSi$

Prepared according to the general procedure **A** using 3-iodo-[1,1'-biphenyl]-4-ol (7.50 g, 25.3 mmol, 1.0 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 98:2), the expected product was obtained as yellow solid (3.40 g, 12.8 mmol, 51%).

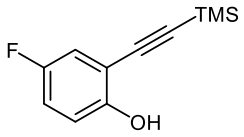
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 2.3 Hz, 1H), 7.58-7.55 (m, 2H), 7.52 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.46-7.43 (m, 2H), 7.38-7.33 (m, 1H), 7.07 (d, *J* = 8.5 Hz, 1H), 5.97 (s, 1H), 0.37 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.6, 140.1, 133.7, 130.2, 129.6, 128.9 (2C), 127.1, 126.7 (2C), 115.1, 110.0, 102.6, 99.1, 0.1 (3C).

M.p. : 98-100 °C

LRMS (EI): Calculated for $C_{17}H_{18}OSi$ $[M-CH_3]^+$: 251 (100) found 251 (100).

4-fluoro-2-((trimethylsilyl)ethynyl)phenol (A6)



A6
Chemical Formula: $C_{11}H_{13}FOSi$

Prepared according to the general procedure **A** using 2-iodo-4-fluorophenol (4.20 g, 17.6 mmol, 1.0 equiv.). After flash column chromatography (cyclohexane/EtOAc ; 100:0 to 98:2), the expected product was obtained as a yellow oil (3.21 g, 15.4 mmol, 87%).

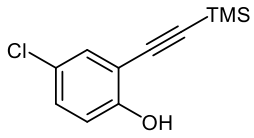
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (dd, *J* = 8.5, 3.0 Hz, 1H), 6.97-6.92 (m, 1H), 6.89-6.86 (m, 1H), 5.76 (s, 1H), 0.29 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.1 (d, *J* = 232.3 Hz), 153.5, 117.7 (d, *J* = 31.3 Hz), 117.5 (d, *J* = 33.3 Hz), 115.7 (d, *J* = 9.1 Hz), 110.2 (d, *J* = 9.1 Hz), 103.3, 9.1 (d, *J* = 2.0 Hz), 0.1 (3C).

^{19}F NMR (376.5 MHz, CDCl3) δ = -123.8.

LRMS (EI): Calculated for $C_{11}H_{13}FOSi$ $[M-CH_3]^+$: 193 (100) found 193 (100).

4-chloro-2-((trimethylsilyl)ethynyl)phenol (A7)



A7
Chemical Formula: $C_{11}H_{13}ClOSi$

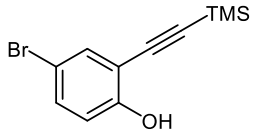
Prepared according to the general procedure **A** using 2-iodo-4-chlorophenol (3.98 g, 15.6 mmol, 1.0 equiv.). After flash column chromatography (petroleum ether/DCM ; 90:10), the expected product was obtained as a yellow oil (3.14 g, 13.9 mmol, 89%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 2.6 Hz, 1H), 7.19 (dd, *J* = 8.8, 2.6 Hz, 1H), 6.87 (d, *J* = 8.8 Hz, 1H), 5.78 (s, 1H), 0.28 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.8, 131.0, 130.8, 125.0, 116.0, 111.1, 103.9, 97.7, 0.1 (3C).

LRMS (EI): Calculated for $C_{11}H_{13}ClOSi$ $[M\text{-}CH_3]^+$: 209 (100), 211 (32) found 209 (100), 211 (48).

4-bromo-2-((trimethylsilyl)ethynyl)phenol (A8)



A8
Chemical Formula: $C_{11}H_{13}BrOSi$

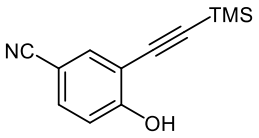
Prepared according to the general procedure **A** using 2-iodo-4-bromophenol (4.90 g, 16.4 mmol, 1.0 equiv.). After flash column chromatography (cyclohexane/EtOAc ; 96:4 to 95:5), the expected product was obtained as a yellow oil (4.12 g, 15.3 mmol, 93%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 2.4 Hz, 1H), 7.32 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.82 (d, *J* = 8.8 Hz, 1H), 5.83 (s, 1H), 0.28 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.3, 133.9, 133.6, 116.5, 111.9, 111.7, 104.0, 97.5, 0.0 (3C).

LRMS (EI): Calculated for $C_{11}H_{13}BrOSi$ $[M\text{-}CH_3]^+$: 253 (100), 255 (97) found 253 (100), 255 (97).

4-hydroxy-3-((trimethylsilyl)ethynyl)benzonitrile (A9)



A9
Chemical Formula: $C_{12}H_{13}NOSi$

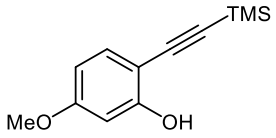
Prepared according to the general procedure **A** using 4-hydroxy-3-iodobenzonitrile (3.50 g, 14.3 mmol, 1.0 equiv.). After flash column chromatography (petroleum ether/DCM ; 70:30 to 60:40), the expected product was obtained as a white solid (2.02 g, 9.38 mmol, 66%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 1.9 Hz, 1H), 7.49 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.00 (d, *J* = 8.6 Hz, 1H), 6.50 (s, 1H), 0.28 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.4, 136.1, 134.2, 118.3, 116.0, 111.4, 105.0, 104.1, 96.4, 0.2 (3C).

LRMS (EI): Calculated for $C_{12}H_{13}NOSi$ $[M\text{-}CH_3]^+$: 200 (100) found 200 (100).

5-methoxy-2-((trimethylsilyl)ethynyl)phenol (A10)



A10
Chemical Formula: $C_{12}H_{16}O_2Si$

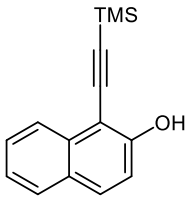
Prepared according to the general procedure **A** using 2-iodo-5-methoxyphenol (3.20 g, 12.8 mmol, 1.0 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 98:2), the expected product was obtained as a yellow oil (2.38 g, 10.8 mmol, 84%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.6 Hz, 1H), 6.50 (d, *J* = 2.4 Hz, 1H), 6.43 (dd, *J* = 8.6, 2.5 Hz, 1H), 5.91 (s, 1H), 3.78 (s, 3H), 0.28 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8, 158.7, 132.5, 107.3, 102.0, 101.0, 100.0, 99.3, 55.4, 0.2 (3C).

LRMS (EI): Calculated for $C_{12}H_{16}O_2Si$ $[M\text{-}CH_3]^+$: 205 (100) found 205 (100).

1-((trimethylsilyl)ethynyl)naphthalen-2-ol (A11)



A11
Chemical Formula: $C_{15}H_{16}OSi$

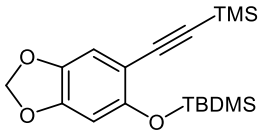
Prepared according to the general procedure **A** using 1-iodonaphthalen-2-ol (4.00 g, 14.8 mmol, 1.0 equiv.). After flash column chromatography (petroleum ether/DCM ; 80:20), the expected product was obtained as a yellow oil (562 mg, 2.34 mmol, 16%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.3 Hz, 1H), 7.78-7.74 (m, 2H), 7.58-7.54 (m, 1H), 7.40-7.36 (m, 1H), 7.21 (d, *J* = 9.0 Hz, 1H), 6.24 (s, 1H), 0.39 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.9, 133.7, 131.0, 128.5, 128.4, 127.6, 125.0, 124.2, 116.3, 107.5, 102.9, 97.6, 0.3 (3C).

HRMS (ESI): Calculated for $C_{15}H_{16}OSi$ $[M+H]^+$: 241.1043 (100) found 241.1039 (100).

***tert*-butyldimethyl((6-((trimethylsilyl)ethynyl)benzo[d][1,3]dioxol-5-yl)oxy)silane (A12)**



A12
Chemical Formula: $C_{18}H_{28}O_3Si_2$

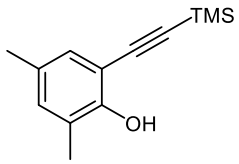
Prepared according to the general procedure **A** using *tert*-butyl ((6-iodobenzo[d][1,3]dioxol-5-yl)oxy)dimethylsilane (5.00 g, 13.2 mmol, 1.0 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 98:2), the expected product was obtained as an orange oil (3.11 g, 8.92 mmol, 68%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (s, 1H), 6.34 (s, 1H), 5.90 (s, 2H), 1.03 (s, 9H), 0.23 (s, 6H), 0.22 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.0, 148.8, 141.6, 111.9, 107.3, 102.7, 101.9, 101.6, 96.2, 25.9 (3C), 18.4, 0.2 (3C), -4.2 (2C).

LRMS (Cl/NH_3): Calculated for $C_{18}H_{28}O_3Si_2$ $[M+H]^+$: 349 (100) found 349 (100).

2,4-dimethyl-6-((trimethylsilyl)ethynyl)phenol (A13)



A13

Chemical Formula: $C_{13}H_{18}OSi$

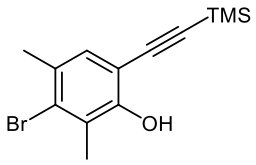
Prepared according to the general procedure **A** using 2-iodo-4,6-dimethylphenol (3.00 g, 12.1 mmol, 1.0 equiv.). After flash column chromatography (petroleum ether/DCM ; 95:5 to 80:20), the expected product was obtained as a yellow oil (2.58 g, 11.8 mmol, 97%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (s, 1H), 6.94 (s, 1H), 5.84 (s, 1H), 2.27 (s, 3H), 2.24 (s, 3H), 0.33 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.3, 133.0, 129.0, 128.9, 123.6, 108.6, 101.5, 99.9, 20.3, 15.9, 0.1 (3C).

LRMS (Cl/NH_3): Calculated for $C_{13}H_{18}OSi$ $[M+H]^+$: 219 (100) found 219 (100).

3-bromo-2,4-dimethyl-6-((trimethylsilyl)ethynyl)phenol (A14)



A14

Chemical Formula: $C_{13}H_{17}BrOSi$

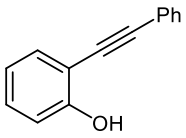
Prepared according to a modification of the general procedure **A** using 3-bromo-6-iodo-2,4-dimethylphenol (3.00 g, 9.17 mmol, 1.0 equiv.), ethynyltrimethylsilane (5.08 mL, 36.7 mmol, 4.0 equiv.), the reaction was refluxed in THF/Et_3N (8/2) for 6 hours. After flash column chromatography (cyclohexane/EtOAc ; 95:5), the expected product was obtained as a yellow oil (2.58 g, 8.68 mmol, 95%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.71 (s, 1H), 5.83 (s, 1H), 2.52 (s, 3H), 2.36 (s, 3H), 0.32 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.9, 140.5, 140.0, 117.8, 114.1, 109.0, 106.0, 98.1, 24.4, 22.4, 0.1 (3C).

LRMS (Cl/NH_3): Calculated for $C_{13}H_{17}BrOSi$ $[M+H]^+$: 297 (100), 299 (97) found 297 (100), 299 (97).

2-(phenylethynyl)phenol (A15)



A15
Chemical Formula: $C_{14}H_{10}O$

Prepared according to a modification of the general procedure **A** using 2-iodophenol (5.00 g, 22.7 mmol, 1.0 equiv.) and phenylacetylene (4.99 mL, 45.5 mmol, 2.0 equiv.). After flash column chromatography (petroleum ether/DCM ; 99.5:0.5 to 98:2), the expected product was obtained as a yellow solid (1.62 g, 8.34 mmol, 37%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57-7.55 (m, 2H), 7.45 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.40-7.37 (m, 3H), 7.31-7.27 (m, 1H), 7.01 (dd, *J* = 8.3, 0.8 Hz, 1H), 6.93 (dt, *J* = 7.6, 1.1 Hz, 1H), 5.90 (s, 1H).

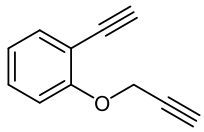
^{13}C NMR (101 MHz, $CDCl_3$) δ 156.6, 131.8, 131.7 (2C), 130.6, 128.9, 128.6 (2C), 122.5, 120.6, 114.9, 109.7, 96.5, 83.2.

M.p. : 71-73 °C

LRMS (EI): Calculated for $C_{14}H_{10}O$ $[M+H]^+$: 195 (100) found 195 (100).

2. Characterization of 1-ethynyl-2-(prop-2-yn-1-yloxy)benzene derivatives

1-ethynyl-2-(prop-2-yn-1-yloxy)benzene (1a)



1a
Chemical Formula: $C_{11}H_8O$

Prepared according to the general procedure **B** using **A1** (3.36 g, 17.6 mmol, 1.0 equiv.). After flash column chromatography (cyclohexane/EtOAc ; 95:5), the expected product was obtained as a pale-yellow solid (2.31 g, 14.8 mmol, 84%).

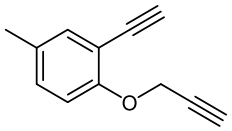
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.34 (ddd, *J* = 8.5, 7.5, 1.7 Hz, 1H), 7.06 (dd, *J* = 8.4, 0.7 Hz, 1H), 6.97 (td, *J* = 7.5, 1.0 Hz, 1H), 4.80 (d, *J* = 2.4 Hz, 2H), 3.31 (s, 1H), 2.53 (t, *J* = 2.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.7, 134.4, 130.2, 121.6, 112.9, 112.2, 81.6, 79.8, 78.3, 76.2, 56.6.

M.p. = 47-49 °C

HRMS (ESI): Calculated for $C_{11}H_8O$ $[M+H]^+$: 157.0648 (100) found 157.0648 (100).

2-ethynyl-4-methyl-1-(prop-2-yn-1-yloxy)benzene (1b)



1b
Chemical Formula: $C_{12}H_{10}O$

Prepared according to the general procedure **B** using **A2** (1.40 g, 6.85 mmol, 1.0 equiv.). After flash column chromatography (cyclohexane/EtOAc ; 95:5), the expected product was obtained as a pale-yellow solid (793 mg, 4.66 mmol, 68%).

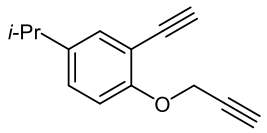
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 2.1 Hz, 1H), 7.11 (dd, *J* = 8.4, 2.2 Hz, 1H), 6.94 (d, *J* = 8.5 Hz, 1H), 4.77 (d, *J* = 2.4 Hz, 2H), 3.28 (s, 1H), 2.51 (t, *J* = 2.4 Hz, 1H), 2.27 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.6, 134.7, 131.0, 130.7, 113.1, 111.9, 81.3, 80.0, 78.5, 76.0, 56.7, 20.4.

M.p. = 60-62 °C

HRMS (ESI): Calculated for $C_{12}H_{10}O$ $[M+H]^+$: 171.0804 (100) found 171.0805 (100).

2-ethynyl-4-isopropyl-1-(prop-2-yn-1-yloxy)benzene (1c)



1c
Chemical Formula: $C_{14}H_{14}O$

Prepared according to the general procedure **B** using **A3** (2.00 g, 8.61 mmol, 1.0 equiv.). After flash column chromatography (cyclohexane/EtOAc ; 95:5), the expected product was obtained as white fluffy needles (1.36 g, 6.86 mmol, 80%).

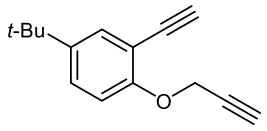
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 2.4 Hz, 1H), 7.17 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.97 (d, *J* = 8.6 Hz, 1H), 4.76 (d, *J* = 2.4 Hz, 2H), 3.30 (s, 1H), 2.84 (sept., *J* = 6.9 Hz, 1H), 2.52 (t, *J* = 2.4 Hz, 1H), 1.22 (app. s, 3H), 1.21 (app. s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.7, 141.9, 132.1, 128.1, 112.9, 111.7, 81.1, 80.2, 78.5, 75.9, 56.6, 33.1, 24.0 (2C).

M.p. = 96-98 °C

HRMS (ESI): Calculated for $C_{14}H_{14}O$ $[M+H]^+$: 199.1117 (100) found 199.1121 (100).

4-(*tert*-butyl)-2-ethynyl-1-(prop-2-yn-1-yloxy)benzene (1d)



1d
Chemical Formula: $C_{15}H_{16}O$

Prepared according to the general procedure **B** using **A4** (4.10 g, 16.6 mmol, 1.0 equiv.). After flash column chromatography (cyclohexane/EtOAc ; 95:5), the expected product was obtained as a pale-yellow solid (2.95 g, 13.9 mmol, 84%).

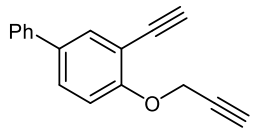
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 2.5 Hz, 1H), 7.34 (dd, *J* = 8.8, 2.6 Hz, 1H), 6.98 (d, *J* = 8.8 Hz, 1H), 4.77 (d, *J* = 2.4 Hz, 2H), 3.29 (s, 1H), 2.52 (t, *J* = 2.4 Hz, 1H), 1.29 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.5, 144.3, 131.4, 127.1, 112.6, 111.4, 81.0, 80.4, 78.6, 76.0, 56.6, 34.2, 31.4 (3C).

M.p. = 58-60 °C

HRMS (ESI): Calculated for $C_{15}H_{16}O$ $[M+H]^+$: 213.1274 (100) found 213.1277 (100).

3-ethynyl-4-(prop-2-yn-1-yloxy)-1,1'-biphenyl (1e)



1e
Chemical Formula: $C_{17}H_{12}O$

Prepared according to the general procedure **B** using **A5** (2.00 g, 7.51 mmol, 1.0 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 95:5 to 90:10), the expected product was obtained as a white solid (1.32 g, 5.68 mmol, 76%).

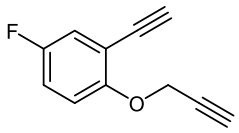
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 2.4 Hz, 1H), 7.57-7.53 (m, 3H), 7.45-7.41 (m, 2H), 7.36-7.32 (m, 1H), 7.13 (d, *J* = 8.6 Hz, 1H), 4.85 (d, *J* = 2.4 Hz, 2H), 3.35 (s, 1H), 2.56 (t, *J* = 2.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1, 139.8, 134.8, 133.0, 128.9 (2C), 128.8, 127.3, 126.9 (2C), 113.2, 112.5, 81.7, 79.8, 78.3, 76.3, 56.7.

M.p. = 101-103 °C

HRMS (ESI): Calculated for $C_{17}H_{12}O$ $[M+H]^+$: 233.0961 (100) found 233.0964 (100).

2-ethynyl-4-fluoro-1-(prop-2-yn-1-yloxy)benzene (1f)



1f
Chemical Formula: $C_{11}H_7FO$

Prepared according to the general procedure **B** using **A6** (1.50 g, 7.20 mmol, 1.0 equiv.). After flash column chromatography (cyclohexane/EtOAc ; 95:5), the expected product was obtained as a pale-brown solid (859 mg, 4.93 mmol, 68%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (dd, *J* = 8.4, 2.9 Hz, 1H), 7.03-6.95 (m, 2H), 4.74 (d, *J* = 2.4 Hz, 2H), 3.33 (s, 1H), 2.53 (t, *J* = 2.4 Hz, 1H).

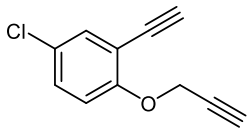
^{13}C NMR (101 MHz, $CDCl_3$) δ 155.7, 154.0 (d, *J* = 237.4 Hz), 120.5 (d, *J* = 24.7 Hz), 116.7 (d, *J* = 23.2 Hz), 114.6 (d, *J* = 8.6 Hz), 113.5 (d, *J* = 9.6 Hz), 82.7, 78.7 (d, *J* = 2.2 Hz), 78.1, 76.3, 57.2.

^{19}F NMR (376.5 MHz, CDCl3) δ = -122.0.

M.p. = 51-53 °C

HRMS (ESI): Calculated for $C_{11}H_7FO$ $[M+H]^+$: 175.0554 (100) found 175.0556 (100).

2-ethynyl-4-chloro-1-(prop-2-yn-1-yloxy)benzene (1g)



1g
Chemical Formula: $C_{11}H_7ClO$

Prepared according to the general procedure **B** using **A7** (3.15 g, 14.0 mmol, 1.0 equiv.). After flash column chromatography (petroleum ether/DCM ; 80:20), the expected product was obtained as white fluffy needles (2.18 g, 11.4 mmol, 81%).

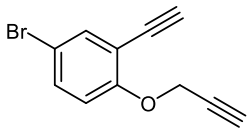
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 2.6 Hz, 1H), 7.27 (dd, *J* = 8.9, 2.6 Hz, 1H), 6.97 (d, *J* = 8.9 Hz, 1H), 4.77 (d, *J* = 2.4 Hz, 2H), 3.33 (s, 1H), 2.53 (t, *J* = 2.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.3, 133.8, 130.0, 126.4, 114.3, 113.8, 82.8, 78.5, 77.9, 76.6, 56.9.

M.p. = 80-82 °C

HRMS (ESI): Calculated for $C_{11}H_7ClO$ $[M+H]^+$: 191.0258 (100), 193.0229 (32) found 191.0260 (100), 193.0230 (32).

2-ethynyl-4-bromo-1-(prop-2-yn-1-yloxy)benzene (1h)



1h
Chemical Formula: $C_{11}H_7BrO$

Prepared according to the general procedure **B** using **A8** (2.15 g, 7.99 mmol, 1.0 equiv.). After flash column chromatography (petroleum ether/DCM ; 90:10 to 85:15), the expected product was obtained as a pale-yellow solid (747 mg, 3.18 mmol, 40%).

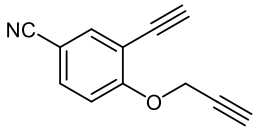
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 2.5 Hz, 1H), 7.41 (dd, *J* = 8.9, 2.5 Hz, 1H), 6.92 (d, *J* = 8.9 Hz, 1H), 4.77 (d, *J* = 2.4 Hz, 2H), 3.33 (s, 1H), 2.54 (t, *J* = 2.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.8, 136.7, 132.9, 114.6, 114.3, 113.4, 82.9, 78.4, 77.8, 76.6, 56.8.

M.p. = 75-77 °C

HRMS (ESI): Calculated for $C_{11}H_7BrO$ $[M+H]^+$: 234.9753 (100), 236.9733 (97) found 234.9756 (100), 236.9735 (97).

3-ethynyl-4-(prop-2-yn-1-yloxy)benzonitrile (1i)



1i
Chemical Formula: $C_{12}H_7NO$

Prepared according to the general procedure **B** using **A9** (1.91 g, 8.87 mmol, 1.0 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 95:5), the expected product was obtained as white fluffy needles (1.36 g, 7.51 mmol, 85%).

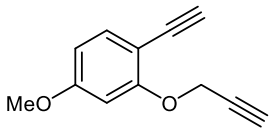
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 2.1 Hz, 1H), 7.59 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.10 (d, *J* = 8.7 Hz, 1H), 4.83 (d, *J* = 2.4 Hz, 2H), 3.37 (s, 1H), 2.58 (t, *J* = 2.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.3, 137.7, 133.9, 117.9, 113.4, 112.9, 105.0, 83.6, 77.2, 76.8, 76.7, 56.5.

M.p. = 123-125 °C

HRMS (ESI): Calculated for $C_{12}H_7NO$ $[M+H]^+$: 182.0600 (100) found 182.0602 (100).

1-ethynyl-4-methoxy-2-(prop-2-yn-1-yloxy)benzene (1j)



1j
Chemical Formula: $C_{12}H_{10}O_2$

Prepared according to the general procedure **B** using **A10** (2.30 g, 10.4 mmol, 1.0 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 98:2 to 95:5), the expected product was obtained as a yellow oil (1.17 g, 6.28 mmol, 60%).

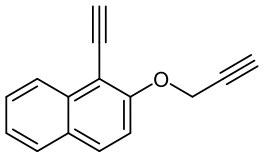
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.5 Hz, 1H), 6.59 (d, *J* = 2.4 Hz, 1H), 6.46 (dd, *J* = 8.5, 2.4 Hz, 1H), 4.75 (d, *J* = 2.4 Hz, 2H), 3.78 (s, 3H), 3.22 (s, 1H) 2.54 (t, *J* = 2.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.2, 159.8, 135.0, 106.1, 104.4, 100.3, 80.1, 79.9, 78.1, 76.3, 56.5, 55.5.

M.p. = 88-90 °C

HRMS (ESI): Calculated for $C_{12}H_{10}O_2$ $[M+H]^+$: 187.0754 (100) found 187.0756 (100).

1-ethynyl-2-(prop-2-yn-1-yloxy)naphthalene (1k)



1k
Chemical Formula: $C_{15}H_{10}O$

Prepared according to the general procedure **B** using **A11** (828 mg, 3.44 mmol, 1.0 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 99:1), the expected product was obtained as a pale-yellow solid (428 mg, 2.07 mmol, 60%).

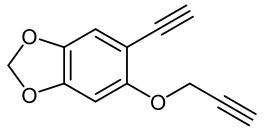
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (dd, *J* = 8.5, 0.8 Hz, 1H), 7.84 (d, *J* = 9.1 Hz, 1H), 7.80 (d, *J* = 8.2 Hz, 1H), 7.59-7.55 (m, 1H), 7.44-7.40 (m, 1H), 7.37 (d, *J* = 9.1 Hz, 1H), 4.94 (d, *J* = 2.4 Hz, 2H), 3.77 (s, 1H), 2.55 (t, *J* = 2.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.0, 134.8, 130.5, 129.1, 128.2, 127.7, 125.4, 124.9, 114.7, 106.8, 87.1, 78.6, 78.0, 76.3, 57.4.

M.p. = 70-72 °C

HRMS (ESI): Calculated for $C_{15}H_{10}O$ $[M+H]^+$: 207.0804 (100) found 207.0808 (100).

5-ethynyl-6-(prop-2-yn-1-yloxy)benzo[d][1,3]dioxole (1l)



1l
Chemical Formula: $C_{12}H_8O_3$

In a 50 mL round bottom flask **A12** (710 mg, 2.04 mmol, 1.0 equiv.), was dissolved in 10 mL of methanol and K_2CO_3 (844 mg, 6.11 mmol, 3.0 equiv.) was added, the mixture turns to brown. The suspension was stirred 6 h at room temperature, then filtrated. The resulting solution was concentrated under reduced pressure. The residue was dissolved in 13 mL of anhydrous DMF and stirred 5 minutes with K_2CO_3 (564 mg, 4.08 mmol, 2.0 equiv.). Under argon, propargyl bromide (80 mol% in toluene) (328 µL, 3.06 mmol, 1.5 equiv.) was added and the solution was stirred overnight at room temperature, then water (20 mL) was added. The resulting solution was extracted with DCM (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered, and the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, petroleum ether/EtOAc ; 98:2 to 95:5) affording **1l** as an orange solid (310 mg, 1.55 mmol, 76%).

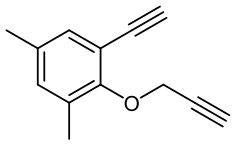
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86 (s, 1H), 6.65 (s, 1H), 5.94 (s, 2H), 4.71 (d, *J* = 2.4 Hz, 2H), 3.22 (s, 1H), 2.53 (t, *J* = 2.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.3, 149.0, 142.0, 112.4, 104.4, 101.9, 97.6, 80.4, 79.9, 78.4, 76.3, 57.8.

M.p. = 117-119 °C

HRMS (ESI): Calculated for $C_{12}H_8O_3$ $[M+H]^+$: 201.0546 (100) found 201.0545 (100).

1-ethynyl-3,5-dimethyl-2-(prop-2-yn-1-yloxy)benzene (1m)



1m

Chemical Formula: $C_{13}H_{12}O$

Prepared according to the general procedure **B** using **A13** (2.50 g, 11.4 mmol, 1.0 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 98:2), the expected product was obtained as pale-yellow solid (1.48 g, 8.03 mmol, 70%).

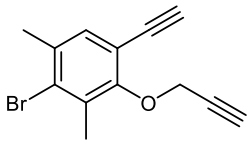
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (s, 1H), 6.99 (s, 1H), 4.82 (d, *J* = 2.4 Hz, 2H), 3.30 (s, 1H), 2.48 (t, *J* = 2.4 Hz, 1H), 2.31 (s, 3H), 2.25 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.8, 133.5, 132.8, 132.1, 131.8, 115.3, 81.7, 80.2, 79.4, 75.1, 60.3, 20.4, 16.5.

M.p. = 106-108 °C

HRMS (ESI): Calculated for $C_{13}H_{12}O$ $[M+H]^+$: 185.0961 (100) found 185.0963 (100).

2-bromo-5-ethynyl-1,3-dimethyl-4-(prop-2-yn-1-yloxy)benzene (1n)



1n

Chemical Formula: $C_{13}H_{11}BrO$

Prepared according to the general procedure **B** using **A14** (800 mg, 2.69 mmol, 1.0 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 98:2 to 95:5), the expected product was obtained as pale-yellow solid (471 mg, 1.79 mmol, 66%).

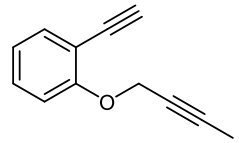
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (s, 1H), 4.76 (d, *J* = 2.4 Hz, 2H), 3.52 (s, 1H), 2.58 (s, 3H), 2.53 (t, *J* = 2.4 Hz, 1H), 2.44 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.7, 142.5, 139.9, 119.7, 112.6, 111.3, 85.8, 78.5, 78.2, 76.3, 56.7, 25.0, 22.4.

M.p. = 109-111 °C

HRMS (ESI): Calculated for $C_{13}H_{11}BrO$ $[M+H]^+$: 263.0066 (100), 265.0046 (97) found 263.0068 (100), 265.0048 (97).

1-(but-2-yn-1-yloxy)-2-ethynylbenzene (1o)



1o

Chemical Formula: $C_{12}H_{10}O$

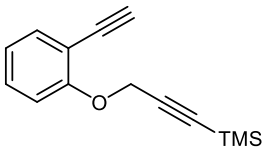
Prepared according to a modification of the general procedure **B** using **A1** (2.00 g, 10.5 mmol, 1.00 equiv.) and 1-bromo-2-butyne (1.38 mL, 15.8 mmol, 1.50 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 98:2 to 95:5), the expected product was obtained as yellow oil (1.42 g, 8.34 mmol, 79%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.32-7.28 (m, 1H), 7.02 (d, *J* = 8.4 Hz, 1H), 6.92 (app. t, *J* = 7.5 Hz, 1H), 4.74 (q, *J* = 2.2 Hz, 2H), 3.30 (s, 1H), 1.82 (t, *J* = 2.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 134.2, 130.0, 121.0, 112.6, 111.8, 84.2, 81.4, 79.9, 73.8, 57.0, 3.7.

HRMS (ESI): Calculated for $C_{12}H_{10}O$ $[M+H]^+$: 171.0804 (100) found 171.0806 (100).

(3-(2-ethynylphenoxy)prop-1-yn-1-yl)trimethylsilane (1p)



1p

Chemical Formula: $C_{14}H_{16}OSi$

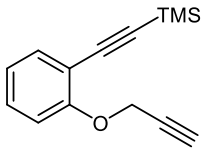
In a 100 mL round bottom flask 2-((trimethylsilyl)ethynyl)phenol (1.00 g, 5.25 mmol, 1.0 equiv.), was dissolved in 13 mL of THF and tetrabutylammonium fluoride monohydrate (1.81 g, 6.31 mmol, 1.2 equiv.) was added, the solution turns to black. The solution was stirred 1 h at room temperature, then water (20 mL) was added. The resulting solution was extracted with Et_2O (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. The residue was dissolved in 13 mL of anhydrous DMF and stirred 5 minutes with K_2CO_3 (1.50 g, 10.5 mmol, 2.0 equiv.). Under argon, 3-(trimethylsilyl)propargyl bromide (1.12 mL, 7.88 mmol, 1.5 equiv.) was added and the solution was stirred 2 h at room temperature. Water (20 mL) was added, and the resulting solution was extracted with DCM (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered, and the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, petroleum ether/DCM ; 95:5 to 90:10) affording **1p** as a yellow oil (830 mg, 3.63 mmol, 69%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.33-7.28 (m, 1H), 7.06 (dd, *J* = 8.3, 0.5 Hz, 1H), 6.94 (td, *J* = 7.6, 0.9 Hz, 1H), 4.78 (s, 2H), 3.30 (s, 1H), 0.16 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 134.3, 130.0, 121.4, 113.3, 112.1, 99.9, 93.4, 81.5, 79.9, 57.5, 0.3 (3C).

HRMS (ESI): Calculated for $C_{14}H_{16}OSi$ $[M+H]^+$: 229.1043 (100) found 229.1046 (100).

Trimethyl((2-(prop-2-yn-1-yloxy)phenyl)ethynyl)silane (1q)



1q
Chemical Formula: $C_{14}H_{16}OSi$

Prepared according to a modification the general procedure **B** using **A1** (700 mg, 3.68 mmol, 1.0 equiv.), without the deprotection step. After flash column chromatography (petroleum ether/EtOAc ; 98:2), the expected product was obtained as white crystal (577 mg, 2.53 mmol, 69%).

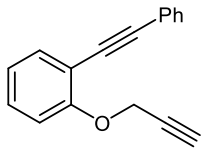
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.30-7.26 (m, 1H), 7.00 (dd, *J* = 8.3, 0.7 Hz, 1H), 6.93 (dt, *J* = 7.5, 1.0 Hz, 1H), 4.76 (d, *J* = 2.4 Hz, 2H), 2.54 (t, *J* = 2.4 Hz, 1H), 0.28 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.5, 134.2, 129.8, 121.5, 113.4 (2C), 101.0, 99.0, 78.5, 76.0, 56.7, 0.1 (3C).

M.p. = 48-50 °C

HRMS (ESI): Calculated for $C_{14}H_{16}OSi$ $[M+H]^+$: 229.1043 (100) found 229.1045 (100).

1-(phenylethynyl)-2-(prop-2-yn-1-yloxy)benzene (1r)



1r
Chemical Formula: $C_{17}H_{12}O$

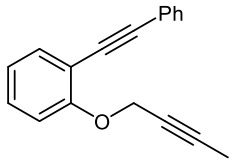
Prepared according to a modification the general procedure **B** using **A15** (750 mg, 3.86 mmol, 1.0 equiv.), without the deprotection step. After flash column chromatography (petroleum ether/EtOAc ; 98:2 to 95:5), the expected product was obtained as a yellow oil (801 mg, 3.45 mmol, 89%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61-7.58 (m, 2H), 7.56 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.39-7.31 (m, 4H), 7.08 (dd, *J* = 8.2, 0.4 Hz, 1H), 7.02 (dt, *J* = 7.5, 0.9 Hz, 1H), 4.83 (d, *J* = 2.4 Hz, 2H), 2.56 (t, *J* = 2.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1, 133.7, 131.7 (2C), 129.6, 128.4 (2C), 128.3, 123.6, 121.7, 113.5, 113.3, 93.9, 85.6, 78.5, 76.0, 56.7.

HRMS (ESI): Calculated for $C_{17}H_{12}O$ $[M+H]^+$: 233.0961 (100) found 233.0966 (100).

1-(but-2-yn-1-yloxy)-2-(phenylethynyl)benzene (1s)



1s

Chemical Formula: $C_{18}H_{14}O$

Prepared according to a modification of the general procedure **B** using **A15** (750 mg, 3.86 mmol, 1.0 equiv.) and 1-bromo-2-butyne (507 µL, 5.79 mmol, 1.5 equiv.), without the deprotection step. After flash column chromatography (petroleum ether/EtOAc ; 98:2 to 95:5), the expected product was obtained as white solid (850 mg, 3.45 mmol, 89%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60-7.57 (m, 2H), 7.52 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.38-7.30 (m, 4H), 7.08 (dd, *J* = 8.4, 0.7 Hz, 1H), 6.99 (dt, *J* = 7.5, 1.0 Hz, 1H), 4.79 (q, *J* = 2.3 Hz, 2H), 1.87 (t, *J* = 2.4 Hz, 3H).

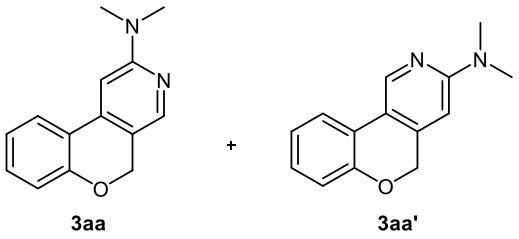
^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3, 133.6, 131.7 (2C), 129.5, 128.3 (2C), 128.1, 123.7, 121.2, 113.3, 113.1, 93.6, 85.7, 84.1, 74.1, 57.2, 3.8.

M.p. = 68-70 °C

HRMS (ESI): Calculated for $C_{18}H_{14}O$ $[M+H]^+$: 247.1117 (100) found 247.1120 (100).

3. Characterization of *5H*-chromeno[3,4-*c*]pyridines derivatives

N,N-dimethyl-*5H*-chromeno[3,4-*c*]pyridin-2-amine (3aa) and *N,N*-dimethyl-*5H*-chromeno[4,3-*c*]pyridin-3-amine (3aa')



3aa **3aa'**

Chemical Formula: $C_{14}H_{14}N_2O$

Prepared according to the general procedure **C** using **1a** (100 mg, 640 µmol, 1.0 equiv.) and dimethylcyanamide **2a** (76 µL, 960 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 80:20), the expected product was obtained as a pale-brown oil (121 mg, 535 µmol, 84%). Regioisomeric ratio (**3aa**/**3aa'**) : (96:4).

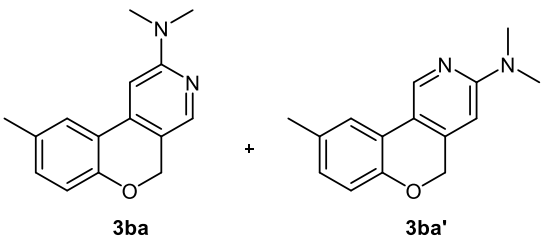
^{1}H NMR (3aa) (400 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.75 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.33-7.28 (m, 1H), 7.06 (dt, *J* = 7.6, 1.1 Hz, 1H), 7.00 (dd, *J* = 8.2, 1.0 Hz, 1H), 6.75 (s, 1H), 5.04 (s, 2H), 3.15 (s, 6H).

^{13}C NMR (3aa) (101 MHz, $CDCl_3$) δ 159.6, 155.6, 143.3, 138.2, 130.6, 123.5, 121.6, 121.3, 117.5, 114.3, 97.2, 65.8, 38.0 (2C).

^{1}H NMR (3aa') (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 7.67 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.17-7.13 (m, 1H), 7.03 (dt, *J* = 7.6, 1.2 Hz, 1H), 6.95 (dd, *J* = 8.0, 1.1 Hz, 1H), 6.27 (s, 1H), 5.02 (s, 2H), 3.13 (s, 6H).

HRMS (ESI): Calculated for $C_{14}H_{14}N_2O$ $[M+H]^+$: 191.0258 (100) found 191.0260 (100).

N,N-9-trimethyl-*5H*-chromeno[3,4-*c*]pyridin-2-amine (3ba) and *N,N*-9-trimethyl-*5H*-chromeno[4,3-*c*]pyridin-3-amine (3ba')



3ba **3ba'**

Chemical Formula: $C_{15}H_{16}N_2O$

Prepared according to the general procedure **C** using **1b** (100 mg, 587 µmol, 1.0 equiv.) and dimethylcyanamide **2a** (69 µL, 881 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc : 90:10 to 80:20), the expected product was obtained as a yellow solid (123 mg, 512 µmol, 87%). Regioisomeric ratio (**3ba**/**3ba'**) : (96:4).

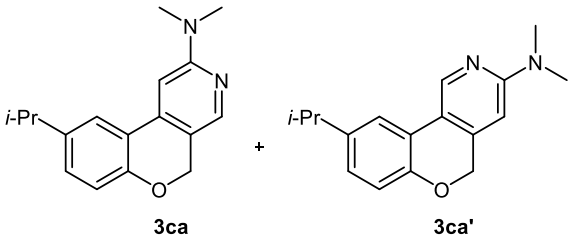
^{1}H NMR (3ba) (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.53 (d, *J* = 1.4 Hz, 1H), 7.11 (dd, *J* = 8.2, 1.9 Hz, 1H), 6.90 (d, *J* = 8.2 Hz, 1H), 6.74 (s, 1H), 5.00 (s, 2H), 3.16 (s, 6H), 2.37 (s, 3H).

^{13}C NMR (3ba) (101 MHz, $CDCl_3$) δ 160.1, 153.9, 143.6, 139.0, 131.9, 131.4, 124.1, 121.4, 117.7, 115.0, 97.7, 66.3, 38.6 (2C), 21.0.

M.p. = 117-119 °C

HRMS (ESI): Calculated for $C_{15}H_{16}N_2O$ $[M+H]^+$: 241.1335 (100) found 241.1338 (100).

9-isopropyl-*N,N*-dimethyl-*5H*-chromeno[3,4-*c*]pyridin-2-amine (3ca) and 9-isopropyl-*N,N*-dimethyl-*5H*-chromeno[4,3-*c*]pyridin-3-amine (3ca')



3ca **3ca'**

Chemical Formula: $C_{17}H_{20}N_2O$

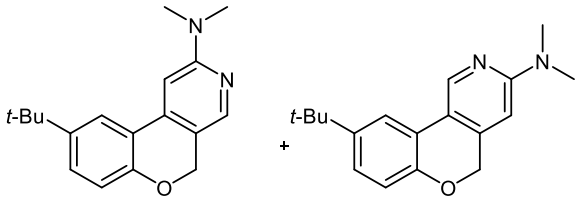
Prepared according to the general procedure **C** using **1c** (100 mg, 504 µmol, 1.0 equiv.) and dimethylcyanamide **2a** (61 µL, 757 µmol, 1.5 equiv.). After flash column chromatography (cyclohexane/EtOAc ; 90:10 to 80:20), the expected product was obtained as a yellow oil (110 mg, 410 µmol, 81%). Regioisomeric ratio (**3ca**/**3ca'**) : (95:5).

^{1}H NMR (3ca) (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 0.7 Hz, 1H), 7.56 (d, *J* = 2.2 Hz, 1H), 7.18 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 6.74 (s, 1H), 5.00 (s, 2H), 3.15 (s, 6H), 2.94 (sept., *J* = 6.9 HZ, 1H), 1.30 (app. s, 3H), 1.28 (app. s, 3H).

^{13}C NMR (3ca) (101 MHz, $CDCl_3$) δ 160.1, 154.1, 143.7, 142.5, 139.0, 129.0, 121.6, 121.3, 117.7, 115.0, 97.6, 66.3, 38.5 (2C), 33.8, 24.3 (2C).

HRMS (ESI): Calculated for $C_{17}H_{20}N_2O$ $[M+H]^+$: 269.1648 (100) found 269.1651 (100).

9-(*tert*-butyl)-*N,N*-dimethyl-*5H*-chromeno[3,4-*c*]pyridin-2-amine (3da) and 9-(*tert*-butyl)-*N,N*-dimethyl-*5H*-chromeno[4,3-*c*]pyridin-3-amine (3da')



3da **3da'**

Chemical Formula: $C_{18}H_{22}N_2O$

Prepared according to the general procedure **C** using **1d** (100 mg, 471 µmol, 1.0 equiv.) and dimethylcyanamide **2a** (56 µL, 707 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 90:10), the expected product was obtained as a yellow solid (118 mg, 418 µmol, 89%) ; NMR yield using mesitylene as an internal standard : 93%. Regioisomeric ratio (**3da**/**3da'**) : (96:4).

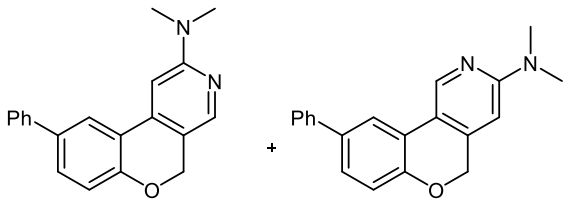
^{1}H NMR (3da) (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 0.6 Hz, 1H), 7.72 (d, *J* = 2.4 Hz, 1H), 7.35 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.95 (d, *J* = 8.6 Hz, 1H), 6.75 (s, 1H), 5.01 (s, 2H), 3.16 (s, 6H), 1.38 (s, 9H).

^{13}C NMR (3da) (101 MHz, $CDCl_3$) δ 160.1, 153.8, 144.7, 143.7, 139.1, 128.4, 120.9, 120.1, 117.4, 115.0, 97.5, 66.3, 38.5 (2C), 34.5, 31.6 (3C).

M.p. = 135-137 °C

HRMS (ESI): Calculated for $C_{18}H_{22}N_2O$ $[M+H]^+$: 283.1805 (100) found 283.1807 (100).

***N,N*-dimethyl-9-phenyl-*5H*-chromeno[3,4-*c*]pyridin-2-amine (3ea) and *N,N*-dimethyl-9-phenyl-*5H*-chromeno[4,3-*c*]pyridin-3-amine (3ea')**



3ea **3ea'**

Chemical Formula: $C_{20}H_{18}N_2O$

Prepared according to the general procedure **D** using **1e** (100 mg, 430 µmol, 1.0 equiv.) and dimethylcyanamide **2a** (51 µL, 646 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 85:15), the expected product was obtained as a pale-yellow solid (114 mg, 377 µmol, 88%). Regioisomeric ratio (**3ea**/**3ea'**) : (94:6).

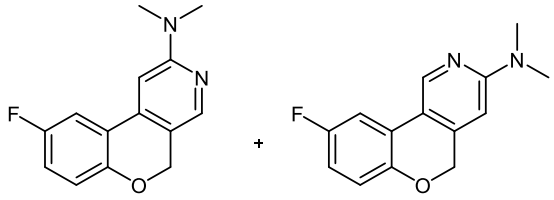
^{1}H NMR (3ea) (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 0.6 Hz, 1H), 7.92 (d, *J* = 2.2 Hz, 1H), 7.63-7.60 (m, 2H), 7.52 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.49-7.45 (m, 2H), 7.39-7.35 (m, 1H), 7.08 (d, *J* = 8.4 Hz, 1H), 6.79 (s, 1H), 5.07 (s, 2H), 3.16 (s, 6H).

^{13}C NMR (3ea) (101 MHz, $CDCl_3$) δ 160.1, 155.5, 143.8, 140.8, 138.6, 135.4, 129.9, 128.9 (2C), 127.2, 127.0 (2C), 122.5, 121.9, 118.3, 114.7, 97.6, 66.4, 38.5 (2C).

M.p. = 145-147 °C

HRMS (ESI): Calculated for $C_{20}H_{18}N_2O$ $[M+H]^+$: 303.1492 (100) found 303.1494 (100).

9-fluoro-*N,N*-dimethyl-*5H*-chromeno[3,4-*c*]pyridin-2-amine (3fa) and 9-fluoro-*N,N*-dimethyl-*5H*-chromeno[4,3-*c*]pyridin-3-amine (3fa')



3fa **3fa'**

Chemical Formula: $C_{14}H_{13}FN_2O$

Prepared according to the general procedure **C** using **1f** (100 mg, 574 µmol, 1.0 equiv.) and dimethylcyanamide **2a** (70 µL, 861 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 90:10 to 80:20), the expected product was obtained as a yellow solid (107 mg, 438 µmol, 76%). Regioisomeric ratio (**3fa**/**3fa'**) : (91:9).

^{1}H NMR (3fa) (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 0.6 Hz, 1H), 7.38 (dd, *J* = 9.0, 2.9 Hz, 1H), 7.00-6.91 (m, 2H), 6.61 (s, 1H), 4.98 (s, 2H), 3.12 (s, 6H).

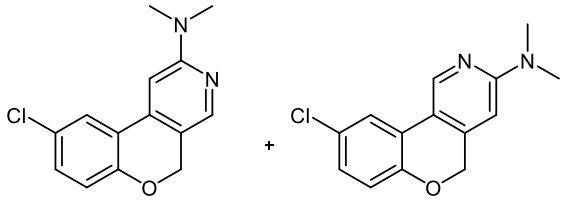
^{13}C NMR (3fa) (101 MHz, $CDCl_3$) δ 160.0, 158.0 (d, *J* = 240.4 Hz), 152.0, 143.9, 138.0, 122.8 (d, *J* = 8.1 Hz), 119.0 (d, *J* = 7.1 Hz), 117.6 (d, *J* = 23.2 Hz), 114.5, 109.9 (d, *J* = 24.2 Hz), 97.7, 66.3, 38.4 (2C).

^{19}F NMR (376.5 MHz, CDCl3) δ = -121.0.

M.p. = 105-107 °C

HRMS (ESI): Calculated for $C_{14}H_{13}FN_2O$ $[M+H]^+$: 245.1085 (100) found 245.1090 (100).

9-chloro-*N,N*-dimethyl-*5H*-chromeno[3,4-*c*]pyridin-2-amine (3ga) and 9-chloro-*N,N*-dimethyl-*5H*-chromeno[4,3-*c*]pyridin-3-amine (3ga')



3ga **3ga'**

Chemical Formula: $C_{14}H_{13}ClN_2O$

Prepared according to the general procedure **C** using **1g** (100 mg, 525 µmol, 1.0 equiv.) and dimethylcyanamide **2a** (62 µL, 787 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 85:15), the expected product was obtained as a pale-yellow solid (95 mg, 364 µmol, 69%). Regioisomeric ratio (**3ga**/**3ga'**) : (91:9).

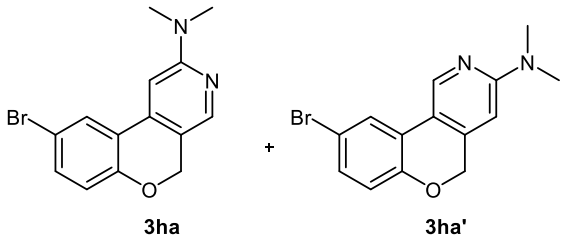
^{1}H NMR (3ga) (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 0.6 Hz, 1H), 7.63 (d, *J* = 2.5 Hz, 1H), 7.19 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.89 (d, *J* = 8.7 Hz, 1H), 6.60 (s, 1H), 4.98 (s, 2H), 3.11 (s, 6H).

^{13}C NMR (3ga) (101 MHz, $CDCl_3$) δ 159.9, 154.5, 143.9, 137.5, 130.6, 127.0, 123.6, 123.0, 119.3, 114.1, 97.5, 66.3, 38.4 (2C).

M.p. = 151-153 °C

HRMS (ESI): Calculated for $C_{14}H_{13}ClN_2O$ $[M+H]^+$: 261.0789 (100), 263.0760 (32) found 261.0792 (100), 263.0764 (32).

9-bromo-*N,N*-dimethyl-*5H*-chromeno[3,4-*c*]pyridin-2-amine (3ha) and 9-bromo-*N,N*-dimethyl-*5H*-chromeno[4,3-*c*]pyridin-3-amine (3ha')



3ha **3ha'**

Chemical Formula: $C_{14}H_{13}BrN_2O$

Prepared according to the general procedure **C** using **1h** (100 mg, 425 µmol, 1.0 equiv.) and dimethylcyanamide **2a** (50 µL, 638 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 85:15), the expected product was obtained as a pale-yellow solid (101 mg, 331 µmol, 78%). Regioisomeric ratio (**3ha**/**3ha'**) : (94:6).

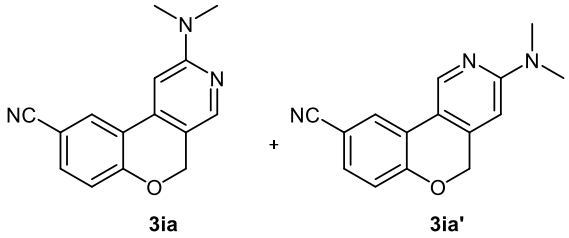
^{1}H NMR (3ha) (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 0.5 Hz, 1H), 7.78 (d, *J* = 2.4 Hz, 1H), 7.34 (dd, *J* = 8.7, 2.4 Hz, 1H), 6.85 (d, *J* = 8.7 Hz, 1H), 6.61 (s, 1H), 4.99 (s, 2H), 3.12 (s, 6H).

^{13}C NMR (3ha) (101 MHz, $CDCl_3$) δ 159.9, 155.0, 143.9, 137.4, 133.6, 126.5, 123.6, 119.7, 114.3, 114.1, 97.6, 66.3, 38.4 (2C).

M.p. = 143-145 °C

HRMS (ESI): Calculated for $C_{14}H_{13}BrN_2O$ $[M+H]^+$: 305.0284 (100), 307.0264 (97) found 305.0288 (100), 307.0268 (97).

2-(dimethylamino)-*5H*-chromeno[3,4-*c*]pyridine-9-carbonitrile (3ia) and 3-(dimethylamino)-*5H*-chromeno[4,3-*c*]pyridine-9-carbonitrile (3ia')



3ia **3ia'**

Chemical Formula: $C_{15}H_{13}N_3O$

Prepared according to the general procedure **D** using **1i** (100 mg, 552 µmol, 1.0 equiv.) and dimethylcyanamide **2a** (65 µL, 828 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/DCM/EtOAc ; 60:25:15), the expected product was obtained as a white solid (108 mg, 430 µmol, 78%). Regioisomeric ratio (**3ia**/**3ia'**) : (91:9).

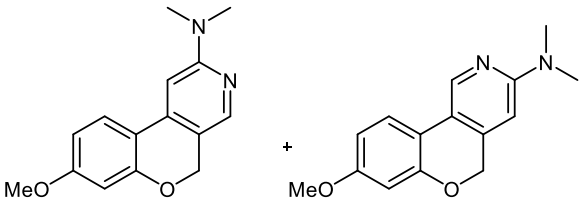
^{1}H NMR (3ia) (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 2.0 Hz, 1H), 8.01 (d, *J* = 0.7 Hz, 1H), 7.54 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.04 (d, *J* = 8.5 Hz, 1H), 6.66 (s, 1H), 5.11 (s, 2H), 3.16 (s, 6H).

^{13}C NMR (3ia) (101 MHz, $CDCl_3$) δ 160.1, 159.4, 144.3, 136.5, 134.4, 128.4, 122.6, 119.2, 119.0, 113.3, 105.5, 97.5, 66.7, 38.5 (2C).

M.p. = 185-187 °C

HRMS (ESI): Calculated for $C_{15}H_{13}N_3O$ $[M+H]^+$: 252.1131 (100) found 252.1134 (100).

8-methoxy-*N,N*-dimethyl-*5H*-chromeno[3,4-*c*]pyridin-2-amine (3ja) and 8-methoxy-*N,N*-dimethyl-*5H*-chromeno[4,3-*c*]pyridin-3-amine (3ja')



3ja **3ja'**

Chemical Formula: $C_{15}H_{16}N_2O_2$

Prepared according to the general procedure **C** using **1j** (100 mg, 537 µmol, 1.0 equiv.) and dimethylcyanamide **2a** (65 µL, 805 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 90:10 to 70:30), the expected product was obtained as a yellow solid (79 mg, 308 µmol, 57%). Regioisomeric ratio (**3ja**/**3ja'**) : (97:3).

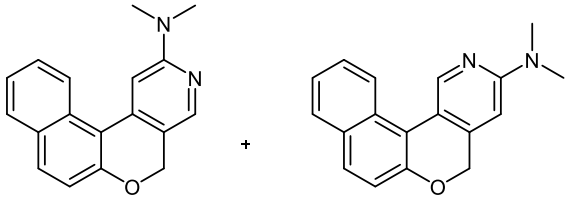
^{1}H NMR (3ja) (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.61 (d, *J* = 8.6 Hz, 1H), 6.61-6.58 (m, 2H), 6.51 (d, *J* = 2.5 Hz, 1H), 5.00 (s, 2H), 3.78 (s, 3H), 3.10 (s, 6H).

^{13}C NMR (3ja) (101 MHz, $CDCl_3$) δ 162.1, 160.0, 157.3, 143.4, 138.8, 124.8, 114.5, 113.8, 109.1, 102.3, 96.8, 66.5, 55.4, 38.4 (2C).

M.p. = 133-135 °C

HRMS (ESI): Calculated for $C_{15}H_{16}N_2O_2$ $[M+H]^+$: 257.1285 (100) found 257.1288 (100).

***N,N*-dimethyl-*5H*-benzo[5,6]chromeno[3,4-*c*]pyridin-2-amine (3ka) and *N,N*-dimethyl-*5H*-benzo[5,6]chromeno[4,3-*c*]pyridin-3-amine (3ka')**



3ka **3ka'**

Chemical Formula: $C_{18}H_{16}N_2O$

Prepared according to the general procedure **D** using **1k** (100 mg, 485 µmol, 1.0 equiv.) and dimethylcyanamide **2a** (57 µL, 727 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/DCM/EtOAc ; 70:20:10), the expected product was obtained as a yellow solid (90 mg, 326 µmol, 67%). Regioisomeric ratio (**3ka**/**3ka'**) : (89:11).

^{1}H NMR (3ka) (400 MHz, $CDCl_3$) δ 8.59 (d, *J* = 8.5 Hz, 1H), 8.14 (d, *J* = 0.4 Hz, 1H), 7.85 (dd, *J* = 8.0, 0.4 Hz, 1H), 7.77 (d, *J* = 8.8 Hz, 1H), 7.59-7.54 (m, 1H), 7.45-7.41 (m, 1H), 7.22 (d, *J* = 8.8 Hz, 1H), 7.12 (s, 1H), 4.98 (s, 2H), 3.15 (s, 6H).

^{13}C NMR (3ka) (101 MHz, $CDCl_3$) δ 159.9, 155.8, 144.0, 138.6, 131.6, 130.7, 130.6, 129.2, 127.3, 124.4, 124.1, 118.7, 116.4, 116.2, 102.4, 66.9, 38.5 (2C).

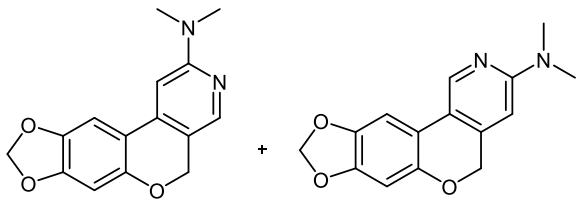
^{1}H NMR (3ka') (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.51 (d, *J* = 8.5 Hz, 1H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.66 (d, *J* = 8.8 Hz, 1H), 7.52-7.48 (m, 1H), 7.42-7.38 (m, 1H), 7.21 (d, *J* = 8.8 Hz, 1H), 6.44 (d, *J* = 0.6 Hz, 1H), 4.96 (s, 2H), 3.18 (s, 6H).

^{13}C NMR (3ka') (101 MHz, $CDCl_3$) δ 158.2, 152.8, 145.6, 143.5, 130.9, 129.9, 128.9, 128.4, 126.8, 125.0, 124.1, 118.2, 116.5, 115.1, 101.5, 68.8, 38.3 (2C).

M.p. = 134-136 °C

HRMS (ESI): Calculated for $C_{18}H_{16}N_2O$ $[M+H]^+$: 277.1335 (100) found 277.1338 (100).

***N,N*-dimethyl-*5H*-[1,3]dioxolo[4',5':6,7]chromeno[3,4-*c*]pyridin-2-amine (3la) and *N,N*-dimethyl-*5H*-[1,3]dioxolo[4',5':6,7]chromeno[4,3-*c*]pyridin-3-amine (3la')**



3la **3la'**

Chemical Formula: $C_{15}H_{14}N_2O_3$

Prepared according to the general procedure **C** using **1l** (100 mg, 499 µmol, 1.0 equiv.) and dimethylcyanamide **2a** (61 µL, 749 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 90:10 to 60:40), the expected product was obtained as a yellow solid (100 mg, 370 µmol, 74%). Regioisomeric ratio (**3la**/**3la'**) : (98:2).

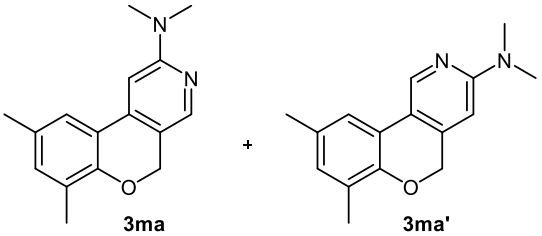
^{1}H NMR (3la) (400 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.13 (s, 1H), 6.52 (s, 1H), 6.52 (s, 1H), 5.95 (s, 2H), 4.95 (s, 2H), 3.11 (s, 6H).

^{13}C NMR (3la) (101 MHz, $CDCl_3$) δ 160.1, 152.1, 149.8, 143.4, 143.1, 139.1, 114.4, 113.9, 102.6, 101.6, 99.6, 96.9, 66.6, 38.5 (2C).

M.p. = 166-168 °C

HRMS (ESI): Calculated for $C_{15}H_{14}N_2O_3$ $[M+H]^+$: 271.1077 (100) found 271.1078 (100).

***N,N*,7,9-tetramethyl-*5H*-chromeno[3,4-*c*]pyridin-2-amine (3ma) and *N,N*,7,9-tetramethyl-*5H*-chromeno[4,3-*c*]pyridin-3-amine (3ma')**



3ma **3ma'**

Chemical Formula: $C_{16}H_{18}N_2O$

Prepared according to the general procedure **C** using **1m** (100 mg, 543 µmol, 1.0 equiv.) and dimethylcyanamide **2a** (64 µL, 814 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 90:10), the expected product was obtained as a yellow solid (113 mg, 444 µmol, 82%). Regioisomeric ratio (**3ma**/**3ma'**) : (96:4).

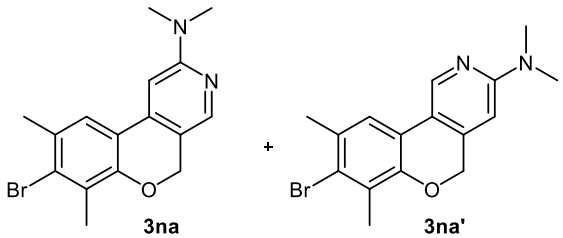
^{1}H NMR (3ma) (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 0.5 Hz, 1H), 7.37 (d, *J* = 1.2 Hz, 1H), 6.98 (s, 1H), 6.70 (s, 1H), 4.99 (s, 2H), 3.13 (s, 6H), 3.33 (s, 3H), 2.24 (s, 3H).

^{13}C NMR (3ma) (101 MHz, $CDCl_3$) δ 160.0, 152.0, 143.4, 139.2, 133.2, 130.4, 126.8, 121.5, 120.8, 115.0, 97.8, 66.1, 38.4 (2C), 20.8, 15.9.

M.p. = 143-145 °C

HRMS (ESI): Calculated for $C_{16}H_{18}N_2O$ $[M+H]^+$: 255.1492 (100) found 255.1496 (100).

8-bromo-*N,N*,7,9-tetramethyl-*5H*-chromeno[3,4-*c*]pyridin-2-amine (3na) and 8-bromo-*N,N*,7,9-tetramethyl-*5H*-chromeno[4,3-*c*]pyridin-3-amine (3na')



3na **3na'**

Chemical Formula: $C_{16}H_{17}BrN_2O$

Prepared according to a modification of the general procedure **C** using **1n** (100 mg, 380 µmol, 1.0 equiv.), dimethylcyanamide **2a** (46 µL, 570 µmol, 1.5 equiv.), $[Cp^*Ru(MeCN)_3]PF_6$ (9.6 mg, 19 µmol, 0.05 equiv.), the reaction was heated to 100°C in toluene for 64 hours. After flash column chromatography (petroleum ether/EtOAc ; 98:2 to 90:10), the expected product was obtained as a white solid (37 mg, 111 µmol, 29%). Regioisomeric ratio (**3na**/**3na'**) : (59:41).

^{1}H NMR (3na) (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 0.3 Hz, 1H), 6.85 (s, 1H), 6.72 (s, 1H), 4.83 (s, 2H), 3.12 (s, 6H), 2.79 (s, 3H), 2.42 (s, 3H).

^{13}C NMR (3na) (101 MHz, $CDCl_3$) δ 159.7, 156.1, 143.8, 140.7, 139.1, 136.0, 122.5, 122.0, 117.4, 116.5, 103.0, 66.7, 38.5 (2C), 24.6, 23.6.

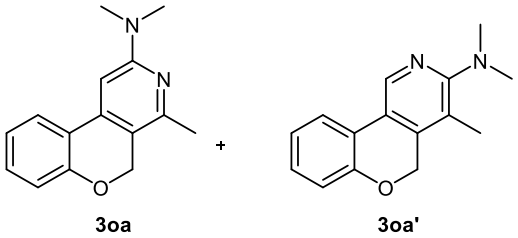
^{1}H NMR (3na') (400 MHz, $CDCl_3$) δ 8.48 (s, 1H), 6.81 (s, 1H), 6.35 (d, *J* = 0.5 Hz 1H), 4.82 (s, 2H), 3.14 (s, 6H), 2.73 (s, 3H), 2.40 (s, 3H).

^{13}C NMR (3na') (101 MHz, $CDCl_3$) δ 159.7, 153.9, 146.1, 143.6, 137.5, 133.9, 122.6, 121.4, 116.8, 115.3, 101.1, 68.8, 38.3 (2C), 24.4, 23.8.

M.p. = 162-164 °C

HRMS (ESI): Calculated for $C_{16}H_{17}BrN_2O$ $[M+H]^+$: 333.0597 (100), 335.0577 (97) found 333.0600 (100), 335.0580 (97).

N,N,4-trimethyl-*5H*-chromeno[3,4-*c*]pyridin-2-amine (3oa) and *N,N*,4-trimethyl-*5H*-chromeno[4,3-*c*]pyridin-3-amine (3oa')



3oa **3oa'**

Chemical Formula: $C_{15}H_{16}N_2O$

Prepared according to a modification of the general procedure **C** using **1o** (100 mg, 587 µmol, 1.0 equiv.) and dimethylcyanamide **2a** (71 µL, 881 µmol, 1.5 equiv.), the reaction was heated to 100 °C for five days. After flash column chromatography (petroleum ether/EtOAc ; 95:5 to 80:20), the expected product was obtained as a yellow solid (73 mg, 304 µmol, 52%). Regioisomeric ratio (**3oa**/**3oa'**) : (>99:1).

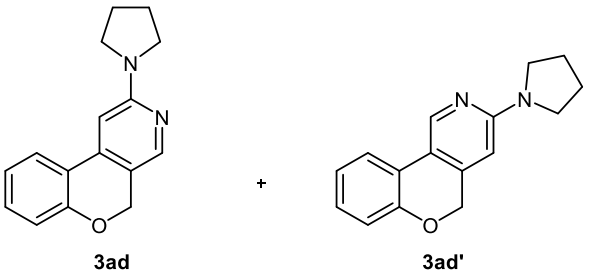
^{1}H NMR (3oa) (400 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.30-7.25 (m, 1H), 7.02 (dt, *J* = 7.5, 1.1 Hz, 1H), 6.98 (dd, *J* = 8.1, 1.1 Hz, 1H), 6.61 (s, 1H), 5.08 (s, 2H), 3.12 (s, 6H), 2.38 (s, 3H).

^{13}C NMR (3oa) (101 MHz, $CDCl_3$) δ 159.0, 155.7, 151.4, 138.6, 130.7, 124.0, 122.0, 121.9, 117.6, 112.6, 95.5, 65.4, 38.2 (2C), 21.6.

M.p. = 85-87 °C

HRMS (ESI): Calculated for $C_{15}H_{16}N_2O$ $[M+H]^+$: 241.1335 (100) found 241.1338 (100).

2-(pyrrolidin-1-yl)-*5H*-chromeno[3,4-*c*]pyridine (3ad) and 3-(pyrrolidin-1-yl)-*5H*-chromeno[4,3-*c*]pyridine (3ad')



3ad + **3ad'**

Chemical Formula: $C_{16}H_{16}N_2O$

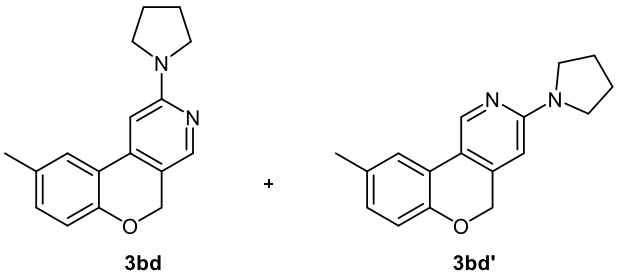
Prepared according to the general procedure **C** using **1a** (100 mg, 640 µmol, 1.0 equiv.) and pyrrolidine carbonitrile **2d** (97 µL, 960 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc : 80:20 to 60:40), the expected product was obtained as a yellow oil (127 mg, 503 µmol, 79%). Regioisomeric ratio (**3ad**/**3ad'**) : (96:4).

^{1}H NMR (3ad) (400 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.71 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.29-7.25 (m, 1H), 7.02 (dt, *J* = 7.6, 1.1 Hz, 1H), 6.97 (dd, *J* = 8.1, 1.0 Hz, 1H), 6.53 (s, 1H), 5.00 (s, 2H), 3.47 (t, *J* = 6.6 Hz, 4H), 1.99 (m, 4H).

^{13}C NMR (3ad) (101 MHz, $CDCl_3$) δ 157.9, 156.0, 143.9, 138.4, 130.9, 123.8, 121.9, 121.6, 117.8, 114.3, 98.2, 66.2, 46.9 (2C), 25.6 (2C).

HRMS (ESI): Calculated for $C_{16}H_{16}N_2O$ $[M+H]^+$: 253.1335 (100), found 253.1336 (100).

9-methyl-2-(pyrrolidin-1-yl)-*5H*-chromeno[3,4-*c*]pyridine (3bd) and 9-methyl-3-(pyrrolidin-1-yl)-*5H*-chromeno[4,3-*c*]pyridine (3bd')



3bd + **3bd'**

Chemical Formula: $C_{17}H_{18}N_2O$

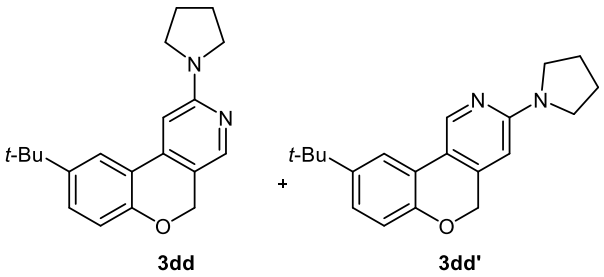
Prepared according to the general procedure **C** using **1b** (100 mg, 587 µmol, 1.0 equiv.) and pyrrolidine carbonitrile **2d** (89 µL, 881 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc : 80:20 to 70:30), the expected product was obtained as brown oil (134 mg, 503 µmol, 86%). Regioisomeric ratio (**3bd**/**3bd'**) : (96:4).

^{1}H NMR (3bd) (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.52 (d, *J* = 1.6 Hz, 1H), 7.10 (dd, *J* = 8.2, 1.8 Hz, 1H), 6.89 (d, *J* = 8.2 Hz, 1H), 6.56 (s, 1H), 4.99 (s, 2H), 3.52 (t, *J* = 6.6 Hz, 4H), 2.36 (s, 3H), 2.03 (m, 4H).

^{13}C NMR (3bd) (101 MHz, $CDCl_3$) δ 158.0, 153.9, 144.0, 138.7, 131.8, 131.3, 124.1, 121.4, 117.7, 114.6, 98.2, 66.4, 47.0 (2C), 25.7 (2C), 21.0.

HRMS (ESI): Calculated for $C_{17}H_{18}N_2O$ $[M+H]^+$: 267.1492 (100) found 267.1494 (100).

9-(*tert*-butyl)-2-(pyrrolidin-1-yl)-*5H*-chromeno[3,4-*c*]pyridine (3dd) and 9-(*tert*-butyl)-2-(pyrrolidin-1-yl)-*5H*-chromeno[4,3-*c*]pyridine (3dd')



Chemical Formula: $C_{20}H_{24}N_2O$

Prepared according to the general procedure **C** using **1d** (100 mg, 471 µmol, 1.0 equiv.) and pyrrolidine carbonitrile **2d** (72 µL, 707 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 75:15), the expected product was obtained as a yellow solid (112 mg, 363 µmol, 77%). Regioisomeric ratio (**3dd**/**3dd'**) : (94:6).

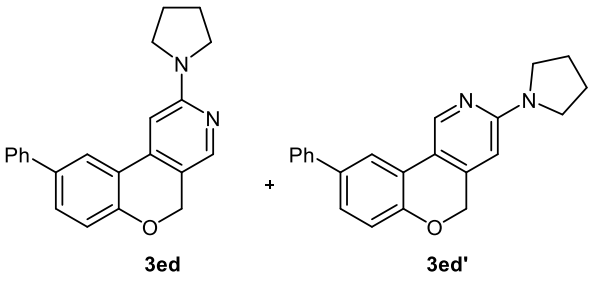
^{1}H NMR (3dd) (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 0.6 Hz, 1H), 7.71 (d, *J* = 2.4 Hz, 1H), 7.34 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.93 (d, *J* = 8.6 Hz, 1H), 6.58 (s, 1H), 5.00 (s, 2H), 3.55-3.52 (m, 4H), 2.04-2.01 (m, 4H), 1.37 (s, 9H).

^{13}C NMR (3dd) (101 MHz, $CDCl_3$) δ 158.0, 153.8, 144.7, 143.9, 138.9, 128.3, 120.9, 120.1, 117.4, 114.6, 98.0, 66.3, 47.0 (2C) , 34.5, 31.6 (3C), 25.6 (2C).

M.p. = 162-164 °C

HRMS (ESI): Calculated for $C_{20}H_{24}N_2O$ $[M+H]^+$: 309.1961 (100) found 309.1964 (100).

9-phenyl-2-(pyrrolidin-1-yl)-*5H*-chromeno[3,4-*c*]pyridine (3ed) and 9-phenyl-3-(pyrrolidine-1-yl)-*5H*-chromeno[4,3-*c*]pyridine (3ed')



3ed + **3ed'**

Chemical Formula: $C_{22}H_{20}N_2O$

Prepared according to the general procedure **D** using **1e** (100 mg, 431 µmol, 1.0 equiv.) and pyrrolidine carbonitrile **2d** (65 µL, 646 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 90:10 to 80:20), the expected product was obtained as a brown solid (100 mg, 304 µmol, 71%). Regioisomeric ratio (**3ed**/**3ed'**) : (92:8).

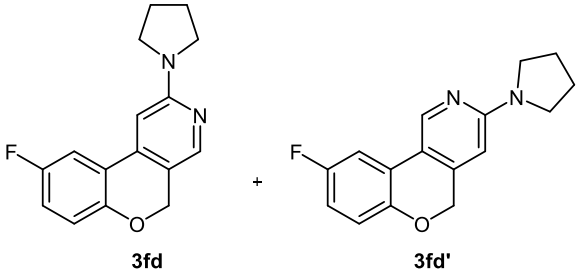
^{1}H NMR (3ed) (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.92 (d, *J* = 2.2 Hz, 1H), 7.62-7.60 (m, 2H), 7.51 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.48-7.44 (m, 2H), 7.38-7.34 (m, 1H), 7.07 (d, *J* = 8.4 Hz, 1H), 6.62 (s, 1H), 5.06 (s, 2H), 3.53 (m, 4H), 2.05-2.01 (m, 4H).

^{13}C NMR (3ed) (101 MHz, $CDCl_3$) δ 158.0, 155.6, 144.0, 140.8, 138.4, 135.3, 129.8, 128.9 (2C), 127.1, 127.0 (2C), 122.5, 121.8, 118.2, 114.3, 98.2, 66.5, 47.0 (2C), 25.6 (2C).

M.p. = 137-139 °C

HRMS (ESI): Calculated for $C_{22}H_{20}N_2O$ $[M+H]^+$: 329.1648 (100) found 329.1651 (100).

9-fluoro-2-(pyrrolidin-1-yl)-*5H*-chromeno[3,4-*c*]pyridine (3fd) and 9-fluoro-3-(pyrrolidin-1-yl)-*5H*-chromeno[4,3-*c*]pyridine (3fd')



3fd + **3fd'**

Chemical Formula: $C_{16}H_{15}FN_2O$

Prepared according to the general procedure **C** using **1f** (100 mg, 574 µmol, 1.0 equiv.) and pyrrolidine carbonitrile **2d** (87 µL, 861 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 90:10 to 75:25), the expected product was obtained as a brown solid (129 mg, 477 µmol, 83%). Regioisomeric ratio (**3fd**/**3fd'**) : (94:6).

^{1}H NMR (3fd) (400 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.35 (dd, *J* = 9.0, 2.9 Hz, 1H), 6.98-6.89 (m, 2H), 6.42 (s, 1H), 4.96 (s, 2H), 3.47 (m, 4H), 2.00 (m, 4H).

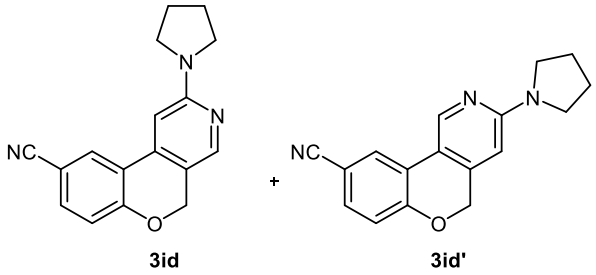
^{13}C NMR (3fd) (101 MHz, $CDCl_3$) δ 158.0 (d, *J* = 240.4 Hz), 157.9, 152.0, 144.1, 137.7, 122.7 (d, *J* = 8.9 Hz), 119.0 (d, *J* = 8.1 Hz), 117.5 (d, *J* = 24.2 Hz), 114.1, 109.9 (d, *J* = 24.2 Hz), 98.3, 66.4, 46.9 (2C), 25.6 (2C).

^{19}F NMR (376.5 MHz, CDCl3) δ = -121.4.

M.p. = 99-101 °C

HRMS (ESI): Calculated for $C_{16}H_{15}FN_2O$ $[M+H]^+$: 245.1085 (100) found 245.1090 (100).

2-(pyrrolidin-1-yl)-*5H*-chromeno[3,4-*c*]pyridine-9-carbonitrile (3id) and 3-(pyrrolidin-1-yl)-*5H*-chromeno[4,3-*c*]pyridine-9-carbonitrile (3id')



3id **3id'**

Chemical Formula: $C_{17}H_{15}N_3O$

Prepared according to the general procedure **D** using **1i** (100 mg, 552 µmol, 1.0 equiv.) and pyrrolidine carbonitrile **2d** (84 µL, 828 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 80:20), the expected product was obtained as a yellow solid (118 mg, 425 µmol, 77%). Regioisomeric ratio (**3id**/**3id'**) : (93:7).

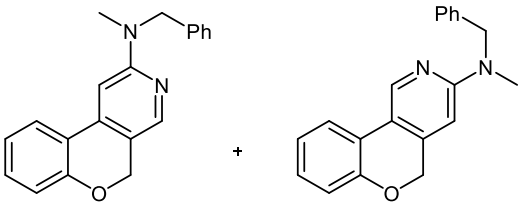
^{1}H NMR (3id) (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 2.0 Hz, 1H), 7.95 (d, *J* = 0.6 Hz, 1H), 7.51 (dd, *J* = 8.5, 2.0 Hz, 1H), 6.99 (d, *J* = 8.5 Hz, 1H), 6.47 (s, 1H), 5.08 (s, 2H), 3.50 (m, 4H), 2.05-2.01 (m, 4H).

^{13}C NMR (3id) (101 MHz, $CDCl_3$) δ 159.3, 157.9, 144.5, 136.2, 134.3, 128.4, 122.4, 119.1, 119.0, 112.9, 105.3, 98.1, 66.7, 47.0 (2C), 25.6 (2C).

M.p. = 160-162 °C

HRMS (ESI): Calculated for $C_{17}H_{15}N_3O$ $[M+H]^+$: 278.1288 (100) found 278.1294 (100).

***N*-benzyl-*N*-methyl-*5H*-chromeno[3,4-*c*]pyridin-2-amine (3ab) and *N*-benzyl-*N*-methyl-*5H*-chromeno[4,3-*c*]pyridin-3-amine (3ab')**



3ab **3ab'**

Chemical Formula: $C_{20}H_{18}N_2O$

Prepared according to the general procedure **C** using **1a** (100 mg, 640 µmol, 1.0 equiv.) and *N*-benzyl-*N*-methylcyanamide **2b** (140 mg, 960 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc : 95:5 to 90:10), the expected product was obtained as a yellow solid (165 mg, 546 µmol, 85%). Regioisomeric ratio (**3ab**/**3ab'**) : (96:4).

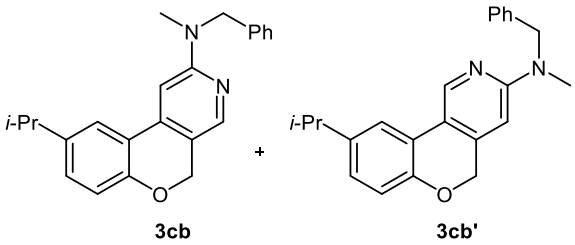
^{1}H NMR (3ba) (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.64 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.31-7.20 (m, 6H), 7.02-6.97 (m, 2H), 6.73 (s, 1H), 5.01 (s, 2H), 4.84 (s, 2H), 3.10 (s, 3H).

^{13}C NMR (3ba') (101 MHz, $CDCl_3$) δ 159.6, 156.0, 143.9, 138.9, 138.8, 131.1, 128.7 (2C), 127.1 (2C), 127.0, 123.9, 122.0, 121.6, 117.9, 115.1, 97.5, 66.2, 53.5, 36.5.

M.p. : 104-106 °C

HRMS (ESI): Calculated for $C_{20}H_{18}N_2O$ $[M+H]^+$: 303.1492 (100) found 303.1495 (100).

***N*-benzyl-9-isopropyl-*N*-methyl-*5H*-chromeno[3,4-*c*]pyridin-2-amine (3cb) and *N*-benzyl-9-isopropyl-*N*-methyl-*5H*-chromeno[4,3-*c*]pyridin-3-amine (3cb')**



3cb **3cb'**

Chemical Formula: $C_{23}H_{24}N_2O$

Prepared according to the general procedure **D** using **1c** (100 mg, 504 µmol, 1.0 equiv.) and *N*-benzyl-*N*-methylcyanamide **2b** (111 mg, 757 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 95:5 to 90:10), the expected product was obtained as a yellow solid (75 mg, 218 µmol, 43%). Regioisomeric ratio (**3cb**/**3cb'**) : (92:8).

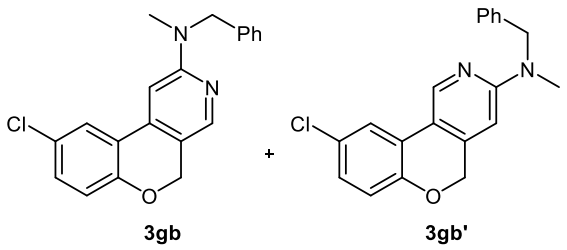
^{1}H NMR (3cb) (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 0.5 Hz, 1H), 7.50 (d, *J* = 2.2 Hz, 1H), 7.34-7.23 (m, 5H), 7.18 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 6.78 (s, 1H), 5.02 (s, 2H), 4.89 (s, 2H) 3.15 (s, 3H), 2.93 (sept., *J* = 6.9 Hz, 1H), 1.29 (app. s, 3H), 1.27 (app. s, 3H).

^{13}C NMR (3cb) (101 MHz, $CDCl_3$) δ 159.6, 154.1, 143.8, 142.5, 139.2, 138.9, 129.1, 128.7 (2C), 127.2 (2C), 127.0, 121.5, 121.3, 117.7, 115.4, 97.5, 66.3, 53.5, 36.6, 33.7, 24.3 (2C).

M.p. = 110-112 °C

HRMS (ESI): Calculated for $C_{23}H_{24}N_2O$ $[M+H]^+$: 345.1961 (100) found 345.1962 (100).

***N*-benzyl-9-chloro-*N*-methyl-*5H*-chromeno[3,4-*c*]pyridin-2-amine (3gb) and *N*-benzyl-9-chloro-*N*-methyl-*5H*-chromeno[4,3-*c*]pyridin-3-amine (3gb')**



3gb **3gb'**

Chemical Formula: $C_{20}H_{17}ClN_2O$

Prepared according to the general procedure **C** using **1g** (100 mg, 525 µmol, 1.0 equiv.) and *N*-benzyl-*N*-methylcyanamide **2b** (115 mg, 787 µmol, 1.0 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 95:5), the expected product was obtained as a white solid (131 mg, 389 µmol, 74%). Regioisomeric ratio (**3gb**/**3gb'**) : (93:7).

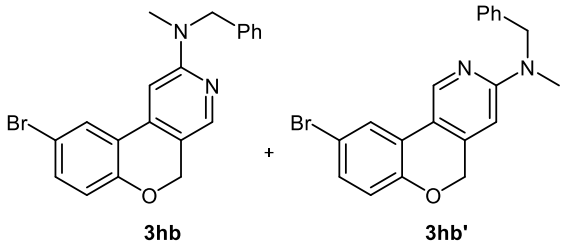
^{1}H NMR (3gb) (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 0.5 Hz, 1H), 7.57 (d, *J* = 2.5 Hz, 1H), 7.28-7.16 (m, 6H), 6.87 (d, *J* = 8.7 Hz, 1H), 6.63 (s, 1H), 4.97 (s, 2H), 4.83 (s, 2H), 3.07 (s, 3H).

^{13}C NMR (3gb) (101 MHz, $CDCl_3$) δ 159.6, 154.5, 144.1, 138.6, 137.8, 130.7, 128.7 (2C), 127.2 (2C), 127.1, 127.0, 123.6, 123.0, 119.3, 114.6, 97.4, 66.3, 53.3, 36.4.

M.p. = 142-144 °C

HRMS (ESI): Calculated for $C_{20}H_{17}ClN_2O$ $[M+H]^+$: 337.1102 (100), 339.1073 (32) found 337.1106 (100), 339.1081 (32).

***N*-benzyl-9-bromo-*N*-methyl-*5H*-chromeno[3,4-*c*]pyridin-2-amine (3hb) and *N*-benzyl-9-bromo-*N*-methyl-*5H*-chromeno[4,3-*c*]pyridin-3-amine (3hb')**



3hb **3hb'**

Chemical Formula: $C_{20}H_{17}BrN_2O$

Prepared according to the general procedure **C** using **1h** (100 mg, 425 µmol, 1.0 equiv.) and *N*-benzyl-*N*-methylcyanamide **2b** (93 mg, 638 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 97:3 to 95:5), the expected product was obtained as a pale-yellow solid (131 mg, 344 µmol, 81%). Regioisomeric ratio (**3hb**/**3hb'**) : (94:6).

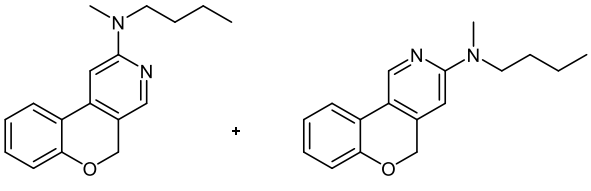
^{1}H NMR (3hb) (400 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.70 (d, *J* = 2.4 Hz, 1H), 7.30-7.18 (m, 6H), 6.81 (d, *J* = 8.7 Hz, 1H), 6.61 (s, 1H), 4.96 (s, 2H), 4.82 (s, 2H), 3.05 (s, 3H).

^{13}C NMR (3hb) (101 MHz, $CDCl_3$) δ 159.5, 155.0, 144.1, 138.6, 137.6, 133.6, 128.6 (2C), 127.2, 127.1 (2C), 126.5, 123.5, 119.7, 114.5, 114.3, 97.3, 66.3, 53.3, 36.4.

M.p. = 148-150 °C

HRMS (ESI): Calculated for $C_{20}H_{17}BrN_2O$ $[M+H]^+$: 381.0597 (100), 381.0577 (97) found 381.0599 (100), 381.0579 (97).

***N*-butyl-*N*-methyl-*5H*-chromeno[3,4-*c*]pyridin-2-amine (3ac) and *N*-butyl-*N*-methyl-*5H*-chromeno[4,3-*c*]pyridin-3-amine (3ac')**



3ac **3ac'**

Chemical Formula: $C_{17}H_{20}N_2O$

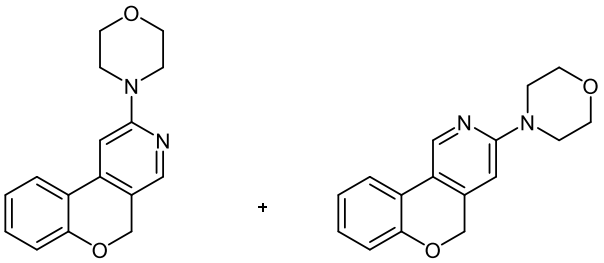
Prepared according to the general procedure **D** using **1a** (100 mg, 640 µmol, 1.0 equiv.) and *N*-butyl-*N*-methylcyanamide **2c** (108 mg, 960 µmol, 1.0 equiv.). After flash column chromatography (petroleum ether/EtOAc : 98:2 to 95:5), the expected product was obtained as a pale-brown oil (111 mg, 414 µmol, 65%). Regioisomeric ratio (**3ac**/**3ac'**) : (95:5).

^{1}H NMR (3ac) (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.72 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.31-7.27 (m, 1H), 7.04 (dt, *J* = 7.6, 1.1 Hz, 1H), 7.00 (dd, *J* = 8.1, 1.0 Hz, 1H), 6.70 (s, 1H), 5.02 (s, 2H), 3.56 (t, *J* = 7.4 Hz, 2H), 3.09 (s, 3H), 1.65-1.57 (m, 2H), 1.37 (s, *J* = 7.7 Hz, 2H), 0.97 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (3ac) (101 MHz, $CDCl_3$) δ 159.2, 156.0, 143.7, 138.5, 130.9, 123.7, 121.9, 121.7, 117.8, 114.3, 97.3, 66.2, 50.1, 36.5, 29.5, 20.3, 14.1.

HRMS (ESI): Calculated for $C_{17}H_{20}N_2O$ $[M+H]^+$: 303.1492 (100), found 303.1493 (100).

2-morpholino-*5H*-chromeno[3,4-*c*]pyridine (3ae) and 3-morpholino-*5H*-chromeno[4,3-*c*]pyridine (3ae')



3ae **3ae'**

Chemical Formula: $C_{16}H_{16}N_2O_2$

Prepared according to the general procedure **D** using **1a** (100 mg, 640 µmol, 1.0 equiv.) and 4-morpholinecarbonitrile **2e** (97 µL, 960 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc : 80:20 to 70:30), the expected product was obtained as a brown solid (148 mg, 552 µmol, 86%). Regioisomeric ratio (**3ae**/**3ae'**) : (93:7).

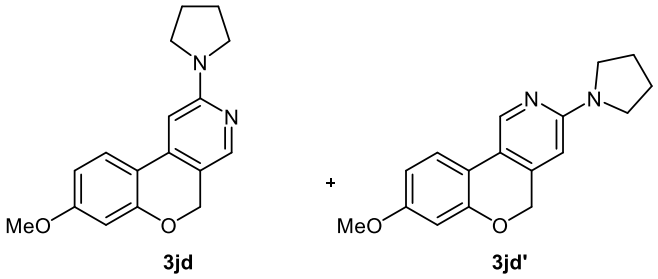
^{1}H NMR (3ae) (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 0.6 Hz, 1H), 7.71 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.32-7.28 (m, 1H), 7.05 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.00 (dd, *J* = 8.2, 1.1 Hz, 1H), 6.86 (s, 1H), 5.04 (s, 2H), 3.84 (m, 4H), 3.55 (m, 4H).

^{13}C NMR (3ae) (101 MHz, $CDCl_3$) δ 160.4, 155.9, 143.8, 139.2, 131.3, 123.8, 122.1, 121.4, 118.0, 117.0, 99.0, 66.8 (2C), 66.0, 46.0 (2C).

M.p. = 104-106 °C

HRMS (ESI): Calculated for $C_{16}H_{16}N_2O_2$ $[M+H]^+$: 269.1285 (100) found 269.1288 (100).

8-methoxy-2-(pyrrolidin-1-yl)-*5H*-chromeno[3,4-*c*]pyridine (3jd) and 8-methoxy-3-(pyrrolidin-1-yl)-*5H*-chromeno[4,3-*c*]pyridine (3jd')



Chemical Formula: $C_{17}H_{18}N_2O_2$

Prepared according to the general procedure **D** using **1j** (100 mg, 537 µmol, 1.0 equiv.) and morpholine carbonitrile **2d** (82 µL, 805 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc : 80:20 to 50:50), the expected product was obtained as a brown solid (104 mg, 368 µmol, 68%). Regioisomeric ratio (**3jd**/**3jd'**) : (97:3).

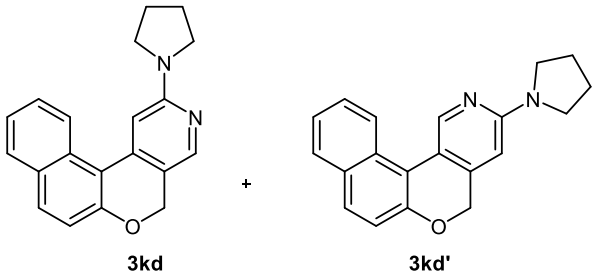
^{1}H NMR (3jd) (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 0.6 Hz, 1H), 7.61 (d, *J* = 8.6 Hz, 1H), 6.59 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.51 (d, *J* = 2.5 Hz, 1H), 6.45 (s, 1H), 4.99 (s, 2H), 3.79 (s, 3H), 3.47 (m, 4H), 1.99 (m, 4H).

^{13}C NMR (3jd) (101 MHz, $CDCl_3$) δ 162.1, 157.9, 157.4, 143.7, 138.6, 124.9, 114.5, 113.5, 109.1, 102.3, 97.3, 66.6, 55.5, 46.9 (2C), 25.6 (2C).

M.p. = 142-144 °C

HRMS (ESI): Calculated for $C_{17}H_{18}N_2O_2$ $[M+H]^+$: 283.1441 (100) found 283.1447 (100).

2-(pyrrolidin-1-yl)-*5H*-benzo[5,6]chromeno[3,4-*c*]pyridine (3kd) and 3-(pyrrolidin-1-yl)-*5H*-benzo[5,6]chromeno[4,3-*c*]pyridine (3kd')



Chemical Formula: $C_{20}H_{18}N_2O$

Prepared according to the general procedure **D** using **1k** (100 mg, 485 µmol, 1.0 equiv.) and pyrrolidine carbonitrile **2d** (74 µL, 728 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 90:10 to 80:20), the expected product was obtained as a yellow solid (79 mg, 261 µmol, 54%). Regioisomeric ratio (**3kd**/**3kd'**) : (89:11).

^{1}H NMR (3kd) (400 MHz, $CDCl_3$) δ 8.61 (d, *J* = 8.5 Hz, 1H), 8.11 (s, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 8.8 Hz, 1H), 7.58-7.54 (m, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.21 (d, *J* = 8.8 Hz, 1H), 6.96 (s, 1H), 4.97 (s, 2H), 3.53 (m, 4H), 2.06-2.02 (m, 4H).

^{13}C NMR (3kd) (101 MHz, $CDCl_3$) δ 157.8, 155.8, 144.2, 138.3, 131.5, 130.7, 130.5, 129.1, 127.3, 124.4, 124.1, 118.7, 116.3, 115.8, 103.0, 67.0, 47.0 (2C), 25.6 (2C).

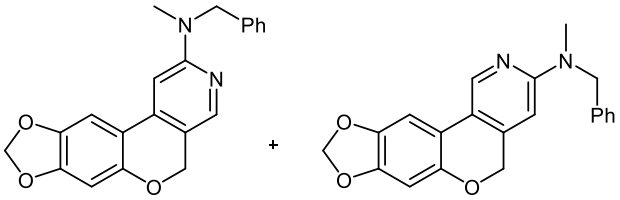
^{1}H NMR (3kd') (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.51 (d, *J* = 8.5 Hz, 1H), 7.82 (d, *J* = 7.6 Hz, 1H), 7.65 (d, *J* = 8.8 Hz, 1H), 7.52-7.47 (m, 1H), 7.41-7.37 (m, 1H), 7.20 (d, *J* = 8.8 Hz, 1H), 6.29 (s, 1H), 4.95 (s, 2H), 3.55 (m, 4H), 2.08-2.04 (m, 4H).

^{13}C NMR (3kd') (101 MHz, $CDCl_3$) δ 156.2, 152.6, 145.9, 143.3, 130.9, 129.9, 128.9, 128.3, 126.7, 125.0, 124.1, 118.2, 116.6, 114.8, 102.2, 68.7, 47.0 (2C), 25.7 (2C).

M.p. = 118-120 °C

HRMS (ESI): Calculated for $C_{20}H_{18}N_2O$ $[M+H]^+$: 303.1492 (100) found 303.1494 (100).

***N*-benzyl-*N*-methyl-*5H*-[1,3]dioxolo[4',5':6,7]chromeno[3,4-*c*]pyridin-2-amine (3lb) and 3-(benzyl(methyl)amino)-*5H*-[1,3]dioxolo[4',5':6,7]chromeno[4,3-*c*]pyridin-9-ylium (3lb')**



3lb **3lb'**

Chemical Formula: $C_{21}H_{18}N_2O_3$

Prepared according to the general procedure **D** using **1l** (100 mg, 499 µmol, 1.0 equiv.) and *N*-benzyl-*N*-methylcyanamide **2b** (110 mg, 749 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 95:5 to 90:10), the expected product was obtained as a yellow solid (142 mg, 410 µmol, 82%). Regioisomeric ratio (**3lb**/**3lb'**) : (97:3).

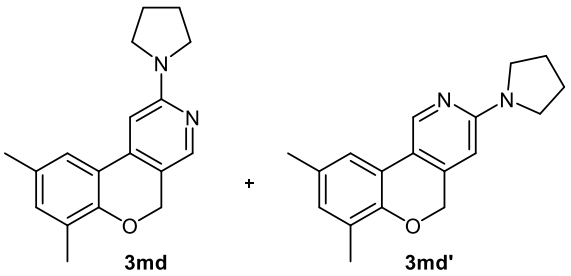
^{1}H NMR (3lb) (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 0.5 Hz, 1H), 7.32-7.20 (m, 5H), 7.03 (s, 1H), 6.52 (s, 1H), 6.49 (s, 1H), 5.90 (s, 2H), 4.93 (s, 2H), 4.82 (s, 2H), 3.07 (s, 3H).

^{13}C NMR (3lb) (101 MHz, $CDCl_3$) δ 159.6, 152.0, 149.8, 143.6, 143.1, 139.3, 138.8, 128.6 (2C), 127.1 (2C), 127.0, 114.3, 114.2, 102.6, 101.6, 99.6, 96.7, 66.6, 53.4, 36.5.

M.p. = 172-174 °C

HRMS (ESI): Calculated for $C_{21}H_{18}N_2O_3$ $[M+H]^+$: 347.1390 (100) found 347.1395 (100).

7,9-dimethyl-2-(pyrrolidin-1-yl)-*5H*-chromeno[3,4-*c*]pyridine (3md) and 7,9-dimethyl-3-(pyrrolidin-1-yl)-*5H*-chromeno[4,3-*c*]pyridine (3md')



Chemical Formula: $C_{18}H_{20}N_2O$

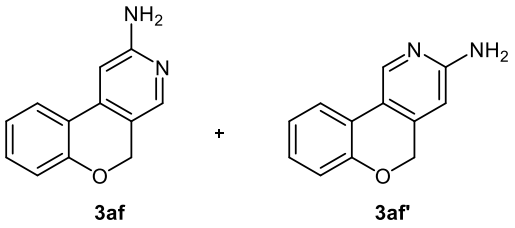
Prepared according to the general procedure **C** using **1m** (100 mg, 543 µmol, 1.0 equiv.) and pyrrolidine carbonitrile **2d** (83 µL, 814 µmol, 1.5 equiv.). After flash column chromatography (petroleum ether/EtOAc ; 90:10 to 80:20), the expected product was obtained as a brown solid (118 mg, 421 µmol, 78%). Regioisomeric ratio (**3md**/**3md'**) : (96:4).

^{1}H NMR (3md) (400 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.35 (s, 1H), 6.96 (s, 1H), 6.52 (s, 1H), 4.97 (s, 2H), 3.49 (m, 4H), 2.31 (s, 3H), 2.22 (s, 3H), 2.01-1.98 (m, 4H).

^{13}C NMR (3md) (101 MHz, $CDCl_3$) δ 157.9, 152.0, 143.6, 138.9, 133.0, 130.3, 126.7, 121.5, 120.7, 114.6, 98.3, 66.1, 46.8 (2C), 25.5 (2C), 20.7, 15.9.

HRMS (ESI): $[M+H]^+$ Calculated for $C_{18}H_{20}N_2O$: 281.1648 (100) found 281.1653 (100).

***5H*-chromeno[3,4-*c*]pyridin-2-amine (af) and *5H*-chromeno[4,3-*c*]pyridin-3-amine (af')**



Chemical Formula: $C_{12}H_{10}N_2O$

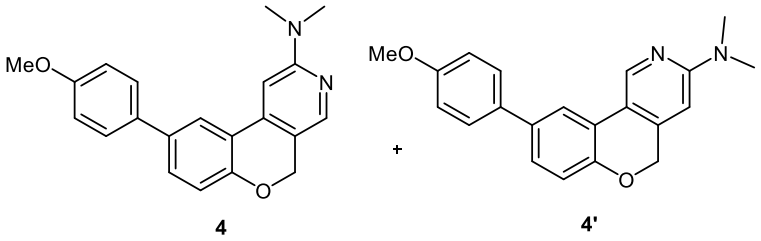
Prepared according to a modification of the general procedure **C** using **1a** (100 mg, 640 µmol, 1.0 equiv.), cyanamide **2f** (40 mg, 960 µmol, 1.5 equiv.), $[Cp^*Ru(MeCN)_3]PF_6$ (16.1 mg, 32 µmol, 0.05 equiv.), the reaction was refluxed in anhydrous MeTHF for 5 days. After flash column chromatography (Al_2O_3, petroleum ether/EtOAc/Et_3N ; 49:49:2 to 29:69:2), the expected product was obtained as a brown solid (43 mg, 217 µmol, 34%). Regioisomeric ratio (**3af**/**3af'**) : (88:12).

^{1}H NMR (3af) (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.67 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.34 (m, 1H), 7.06 (dt, *J* = 7.6, 1.2 Hz, 1H),7.00 (dd, *J* = 8.2, 1.0 Hz, 1H), 6.76 (s, 1H), 5.04 (s, 2H), 4.52 (bs, 2H).

^{13}C NMR (3af) (101 MHz, $CDCl_3$) δ 158.9, 156.0, 143.8, 139.7, 131.6, 124.0, 122.3, 121.0, 118.0, 117.4, 100.6, 66.2.

HRMS (ESI): $[M+H]^+$ Calculated for $C_{12}H_{10}N_2O$: 199.0866 (100) found 199.0868 (100).

9-(4-methoxyphenyl)-N,N-dimethyl-*5H*-chromeno[3,4-*c*]pyridin-2-amine (4) and 9-(4-methoxyphenyl)-*N,N*-dimethyl-*5H*-chromeno[4,3-*c*]pyridin-3-amine (4')



Chemical Formula: $C_{21}H_{20}N_2O_2$

Compound **3ha** (100 mg, 330 µmol, 1.0 equiv.), 4-methoxyphenyl boronic acid (74.8 mg, 490 µmol, 1.5 equiv.), K_2CO_3 (90.7 mg, 660 µmol, 2.0 equiv.), palladium acetate (3.7 mg, 16.4 µmol, 0.05 equiv.) and CataCXium A (12.9 mg, 36.1 µmol, 0.11 equiv.) were mixed in 3.3 mL of anhydrous DMF, the solution turns to brown. The resulting mixture was stirred overnight at 100 °C under argon. The mixture was diluted with DCM and washed successively with a saturated aqueous solution of $NaHCO_3$ (10 mL) and brine (10 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, petroleum ether/EtOAc ; 80:20 to 60:40) to afford the product as a white solid (97 mg, 292 µmol, 89%). Regioisomeric ratio (**4**/**4'**) : (94:6).

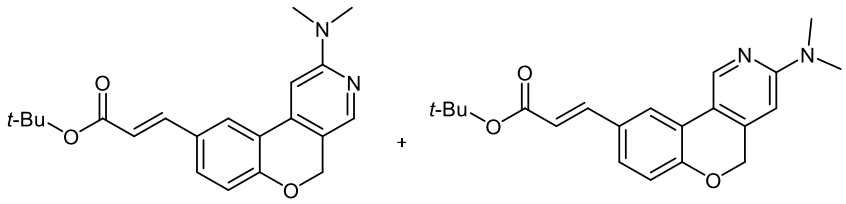
^{1}H NMR (4) (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.86 (d, *J* = 2.2 Hz, 1H), 7.54-7.52 (m, 2H), 7.46 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.05 (d, *J* = 8.4 Hz, 1H), 7.00-6.98 (m, 2H), 6.78 (s, 1H), 5.06 (s, 2H), 3.85 (s, 3H), 3.15 (s, 6H).

^{13}C NMR (4) (101 MHz, $CDCl_3$) δ 160.1, 159.1, 155.1, 143.8, 138.7, 135.0, 133.4, 129.5, 128.0 (2C), 122.0, 121.8, 118.2, 114.7, 114.3 (2C), 97.6, 66.4, 55.4, 38.5 (2C).

M.p. = 106-108 °C

HRMS (ESI): Calculated for $C_{21}H_{20}N_2O_2$ $[M+H]^+$: 333.1598 (100) found 333.1602 (100).

***Tert*-butyl (E)-3-(2-(dimethylamino)-*5H*-chromeno[3,4-*c*]pyridin-9-yl)acrylate (5) and *tert*-butyl (E)-3-(3-(dimethylamino)-*5H*-chromeno[4,3-*c*]pyridin-9-yl)acrylate (5')**



5 **5'**

Chemical Formula: $C_{21}H_{24}N_2O_3$

Compound **3ha** (100 mg, 330 µmol, 1.0 equiv.), tri(o-tolyl)phosphine (7.98 mg, 26.2 µmol, 0.08 equiv.), palladium(II) acetate (1.47 mg, 6.55 µmol, 0.02 equiv.), were mixed in 3.3 mL of an anhydrous mixture of DMF/Et_3N (10/1). Under argon, *t*-butyl-acrylate (238 µL, 1.64 mmol, 5.0 equiv.) was added, the solution turns to brown. The resulting mixture was stirred overnight at 100 °C under argon. The mixture was diluted with DCM and washed successively with a saturated aqueous solution of NH_4Cl (10 mL), water (10 mL) and brine (10 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, petroleum ether/EtOAc ; 80:20 to 70:30) to afford the product as a pale-yellow solid (107 mg, 304 µmol, 92%). Regioisomeric ratio (**5**/**5'**) : (94:6).

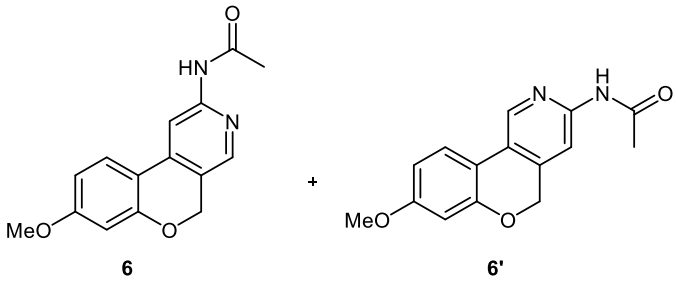
^{1}H NMR (5) (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 0.6 Hz, 1H), 7.86 (d, *J* = 2.1 Hz, 1H), 7.60 (d, *J* = 16.0 Hz, 1H), 7.46 (dd, *J* = 8.5, 2.1 Hz, 1H), 6.99 (d, *J* = 8.5 Hz, 1H), 6.73 (s, 1H), 6.33 (d, *J* = 16.0 Hz, 1H), 5.07 (s, 2H), 3.17 (s, 6H), 1.55 (s, 9H).

^{13}C NMR (5) (101 MHz, $CDCl_3$) δ 166.6, 160.2, 157.6, 144.0, 143.1, 138.0, 130.6, 128.8, 123.8, 121.9, 118.9, 118.6, 114.2, 97.6, 80.6, 66.5, 38.6 (2C), 28.4 (3C).

M.p. = 157-159 °C

HRMS (ESI): Calculated for $C_{21}H_{24}N_2O_3$ $[M+H]^+$: 353.1860 (100), 297.1234 (82) found 353.1863 (100), 297.1236 (82).

***N*-(8-methoxy-*5H*-chromeno[3,4-*c*]pyridin-2-yl)acetamide (6) and *N*-(8-methoxy-*5H*-chromeno[4,3-*c*]pyridin-3-yl)acetamide (6')**



6 **6'**

Chemical Formula: $C_{15}H_{14}N_2O_3$

Prepared according to a modification of the general procedure **C** using **1j** (950 mg, 5.09 mmol, 1.0 equiv.) and *N*-cyanoacetamide (428 mg, 7.64 mmol, 1.5 equiv.), the reaction was heated to 80°C in MeTHF for 24 hours. After flash column chromatography (DCM/EtOAc ; 100:0 to 70:30), the expected product was obtained as a yellow solid (1.13 g, 4.18 mmol, 82%). Regioisomeric ratio (**6**/**6'**) : (80:20). **6** was isolated after a second flash column chromatography (DCM/EtOAc ; 100:0 to 70:30), the expected product was obtained as a yellow solid (797 mg, 2.95 mmol, 58%)

^{1}H NMR (6) (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.43 (s, 1H), 8.01 (s, 1H), 7.75 (d, *J* = 8.7 Hz, 1H), 6.65 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.52 (d, *J* = 2.5 Hz, 1H), 5.08 (s, 2H), 3.82 (s, 3H), 2.22 (s, 3H).

^{13}C NMR (6) (101 MHz, $CDCl_3$) δ 169.0, 163.0, 157.2, 152.2, 143.2, 140.5, 126.0, 121.3, 113.7, 109.5, 105.6, 102.4, 66.2, 55.6, 24.9.

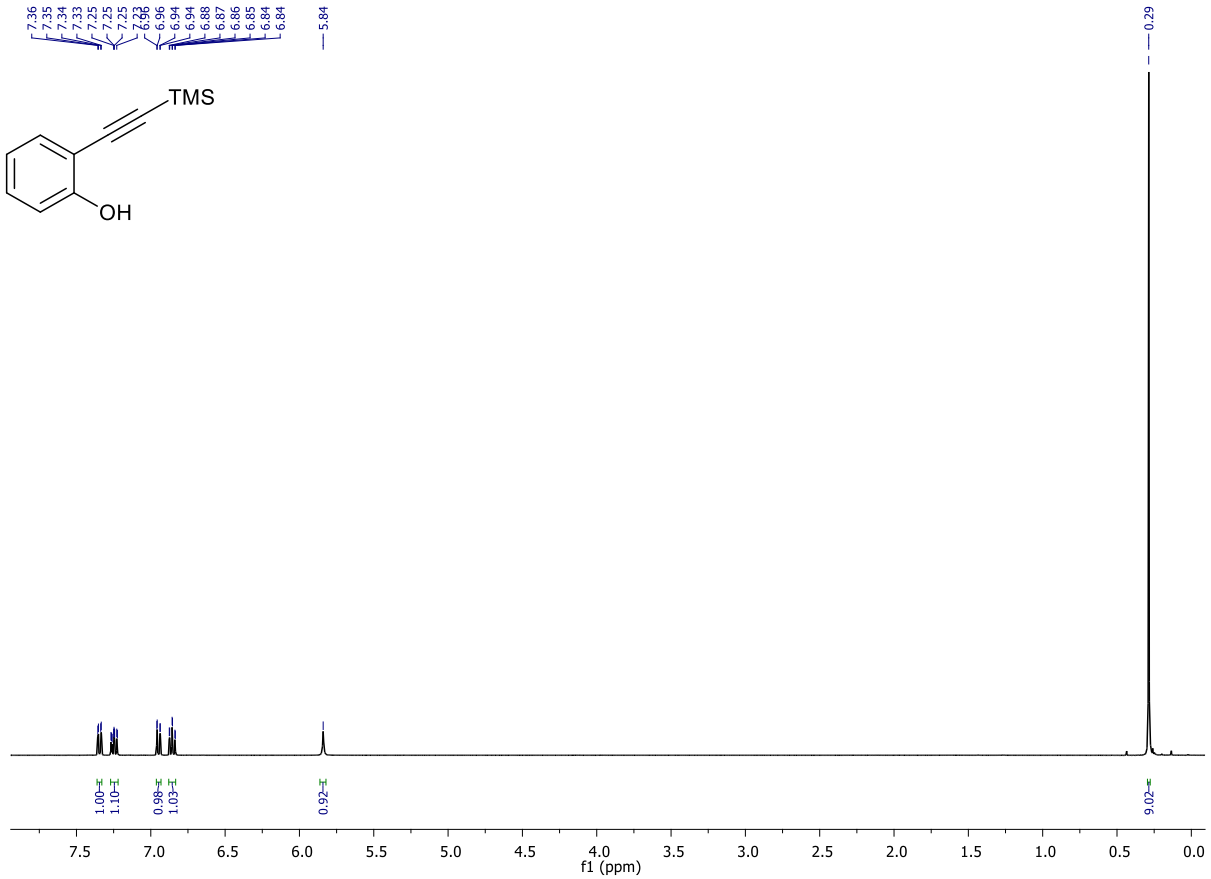
^{1}H NMR (6') (400 MHz, $CDCl_3$) δ 8.49 (s, 1H), 8.16 (s, 1H), 8.02 (s, 1H), 7.61 (d, *J* = 8.6 Hz, 1H), 6.64 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.54 (d, *J* = 2.5 Hz, 1H), 5.1 (s, 2H), 3.82 (s, 3H), 2.22 (s, 3H).

^{13}C NMR (6') (101 MHz, $CDCl_3$) δ 168.7, 161.4, 155.7, 150.0, 141.0, 140.7, 123.4, 122.9, 113.1, 109.4, 109.3, 102.7, 67.9, 55.6, 24.9.

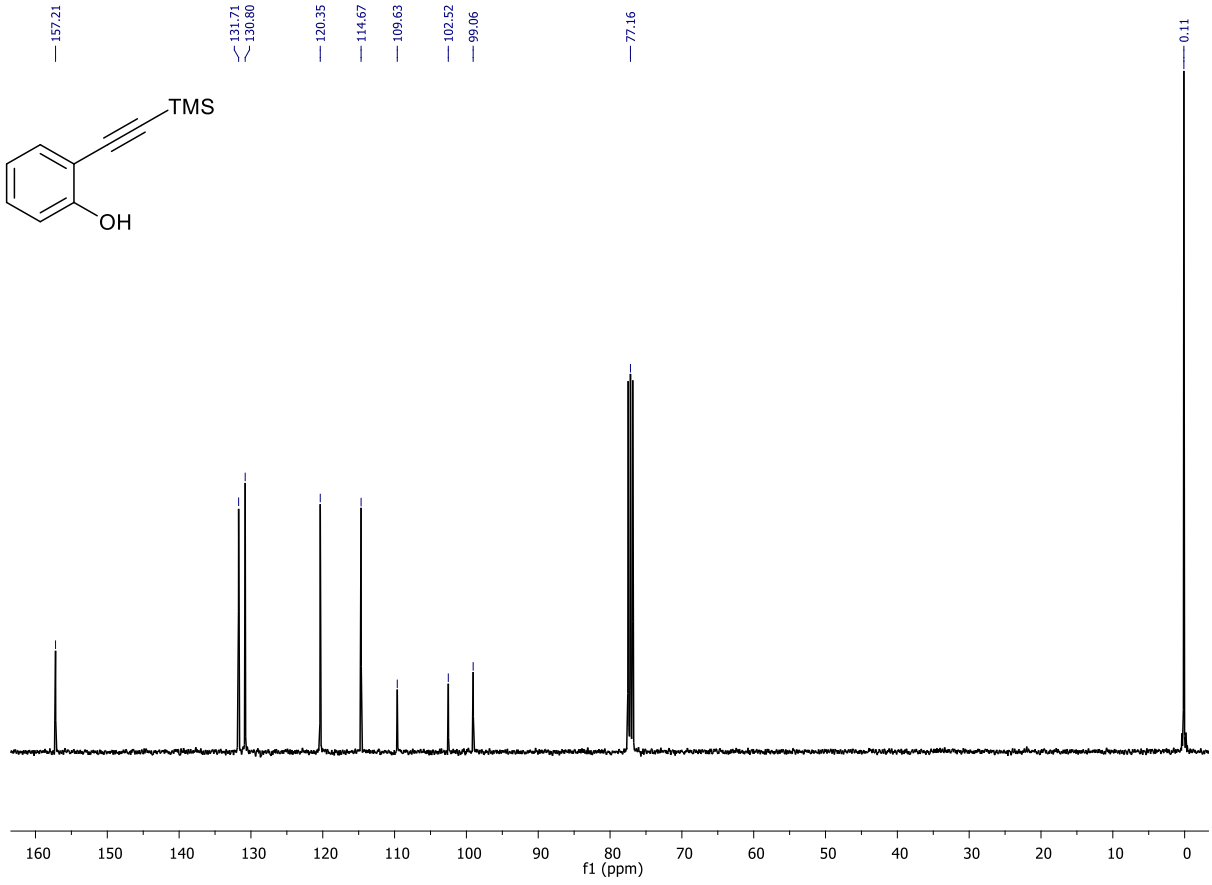
M.p. = 220-222 °C

HRMS (ESI): Calculated for $C_{15}H_{14}N_2O_3$ $[M+H]^+$: 271.1077 (100) found 271.1082 (100).

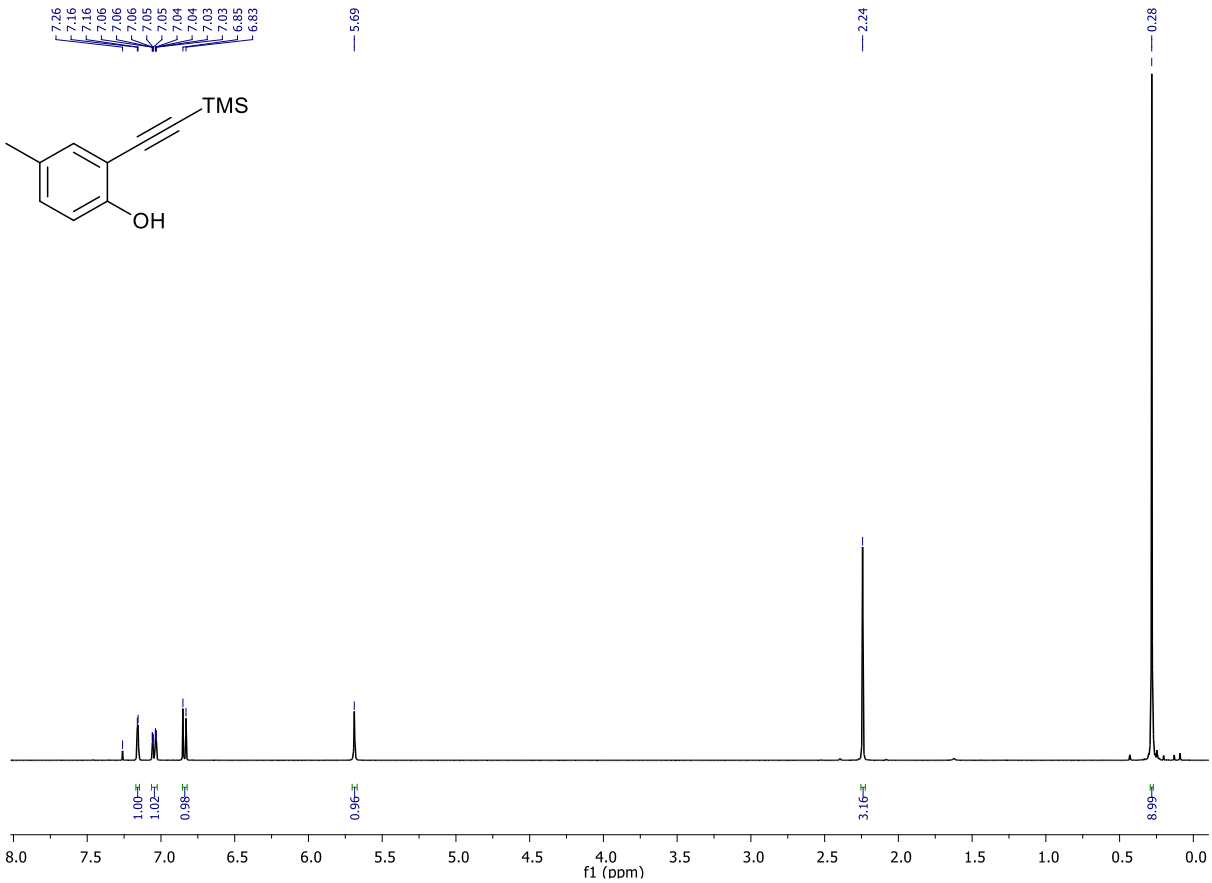
VI. NMR spectra



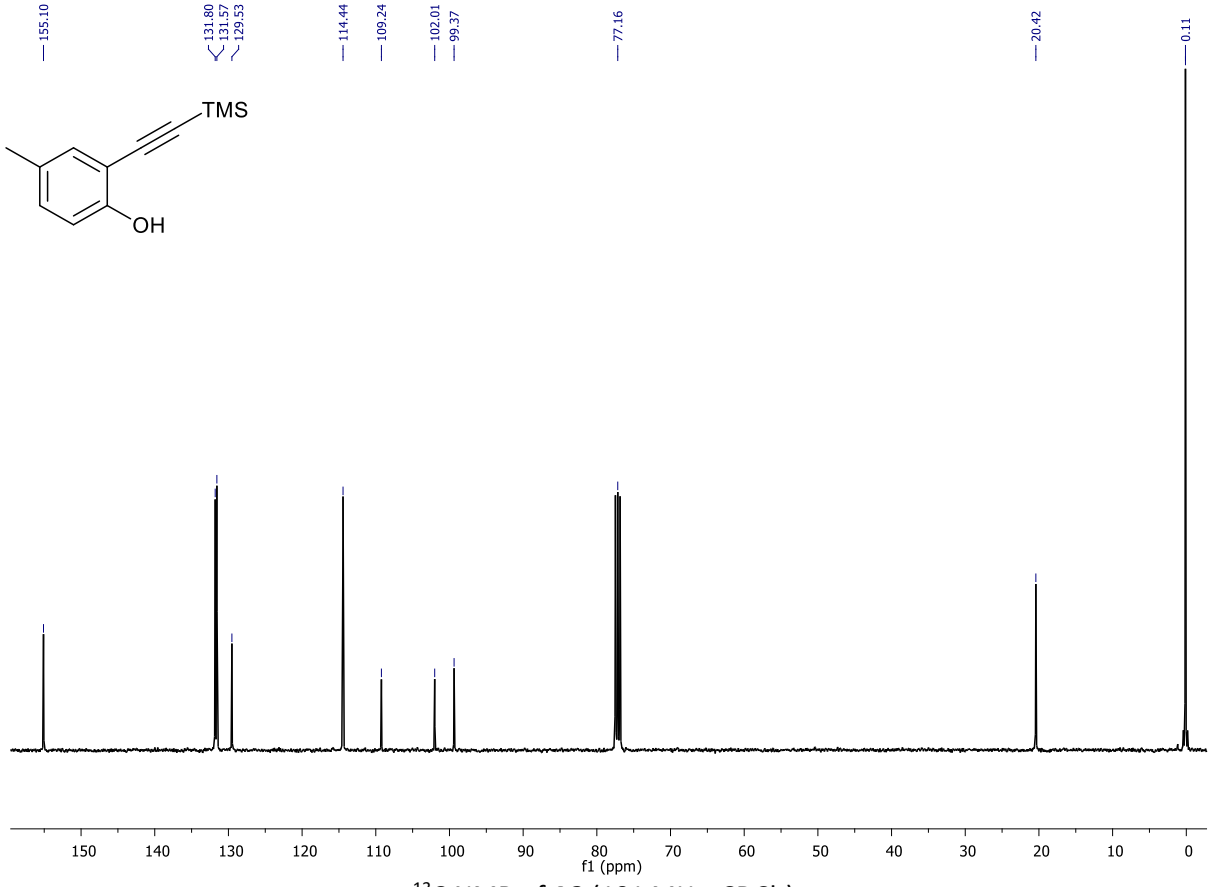
^{1}H NMR of **A1** (400 MHz, $CDCl_3$)



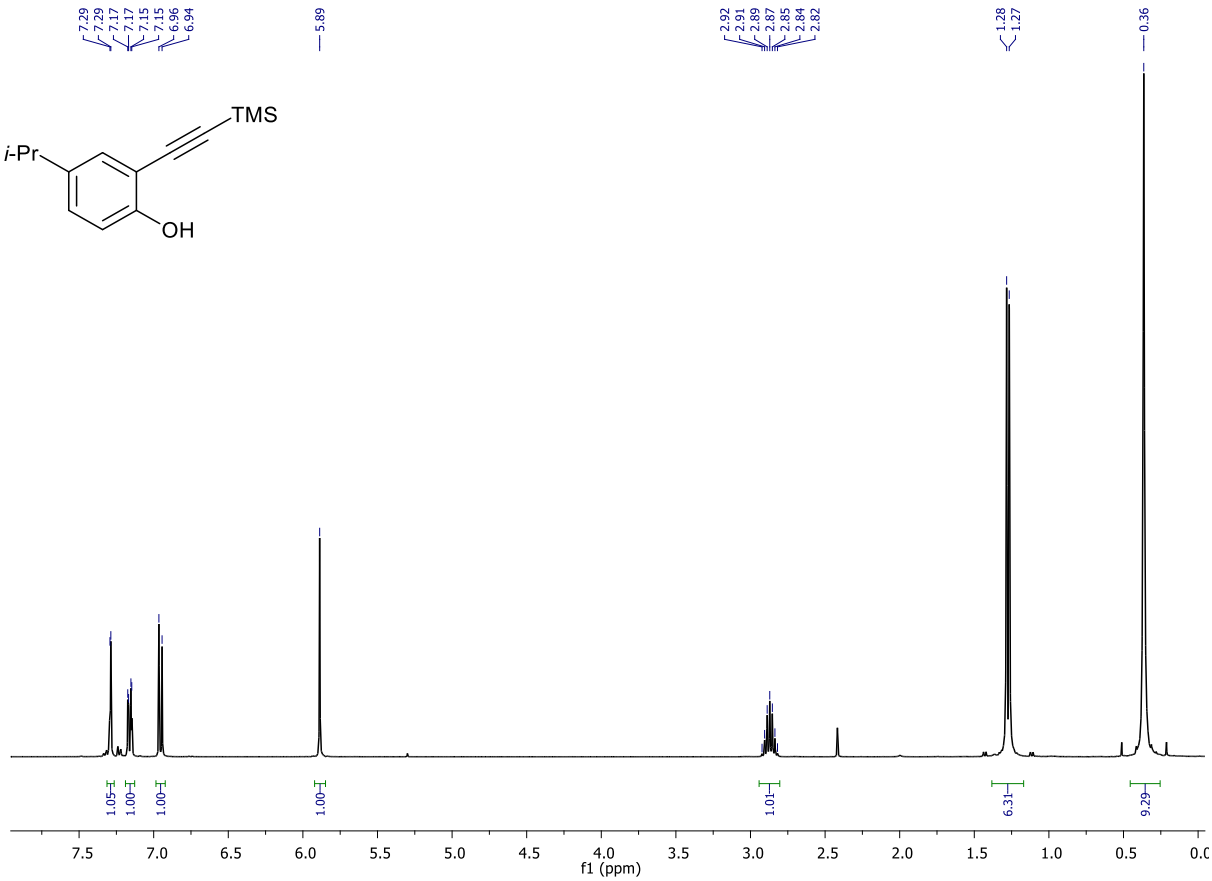
^{13}C NMR of **A1** (101 MHz, $CDCl_3$)



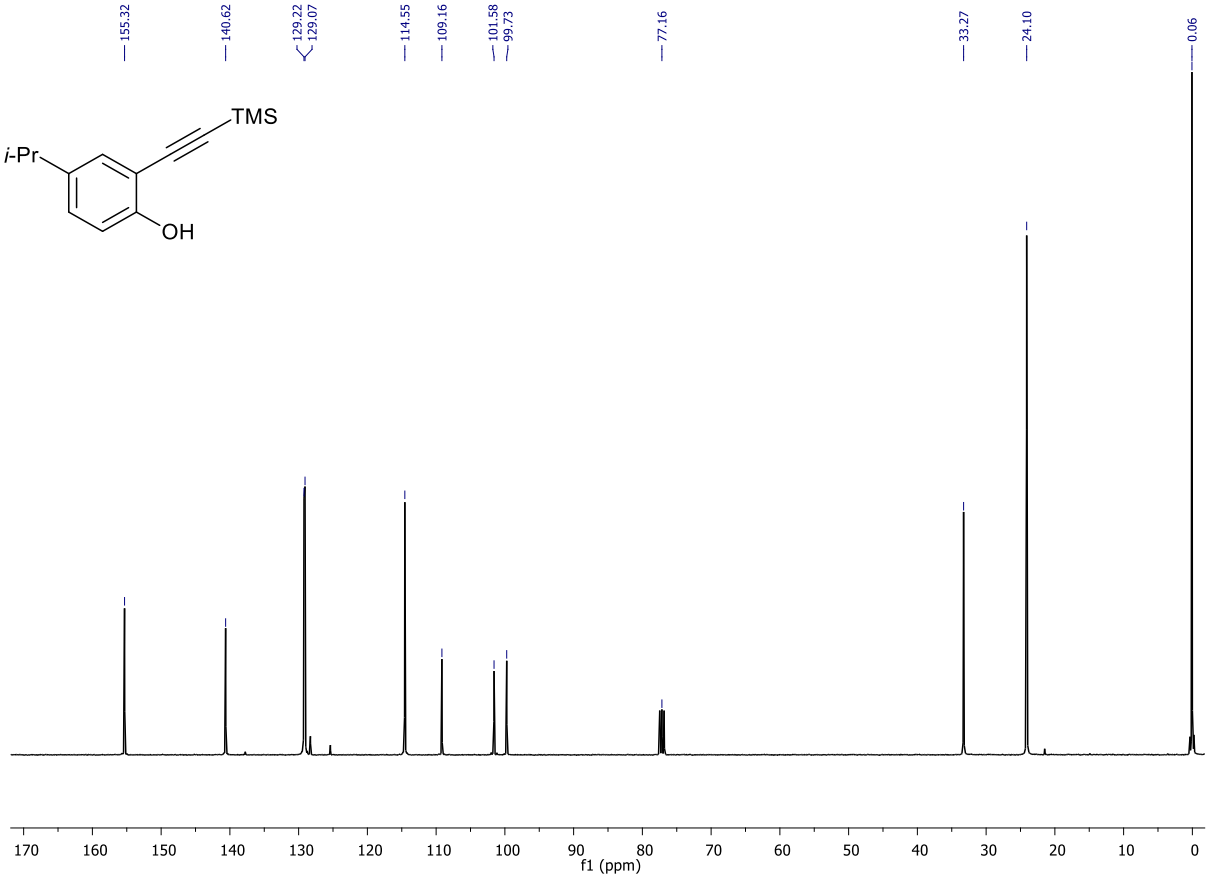
^{1}H NMR of **A2** (400 MHz, $CDCl_3$)



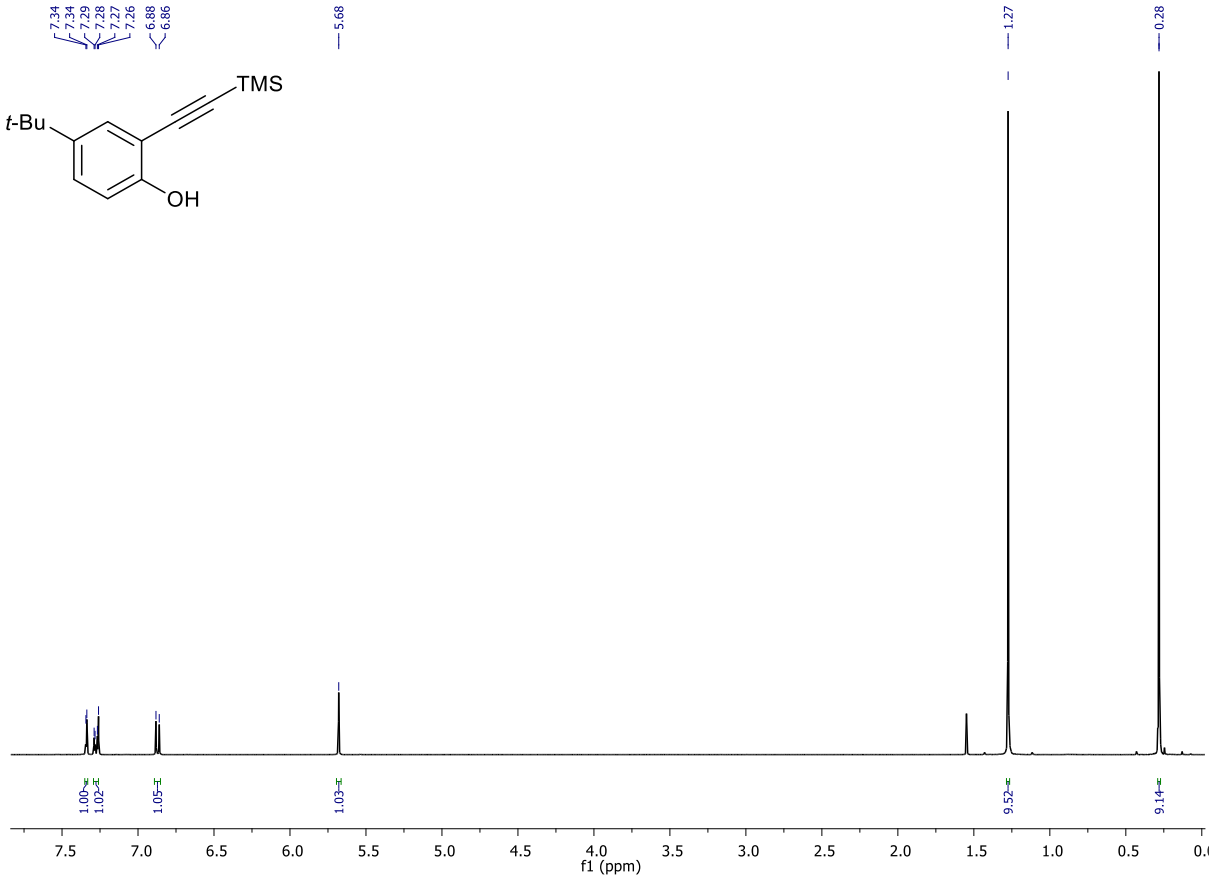
^{13}C NMR of **A2** (101 MHz, $CDCl_3$)



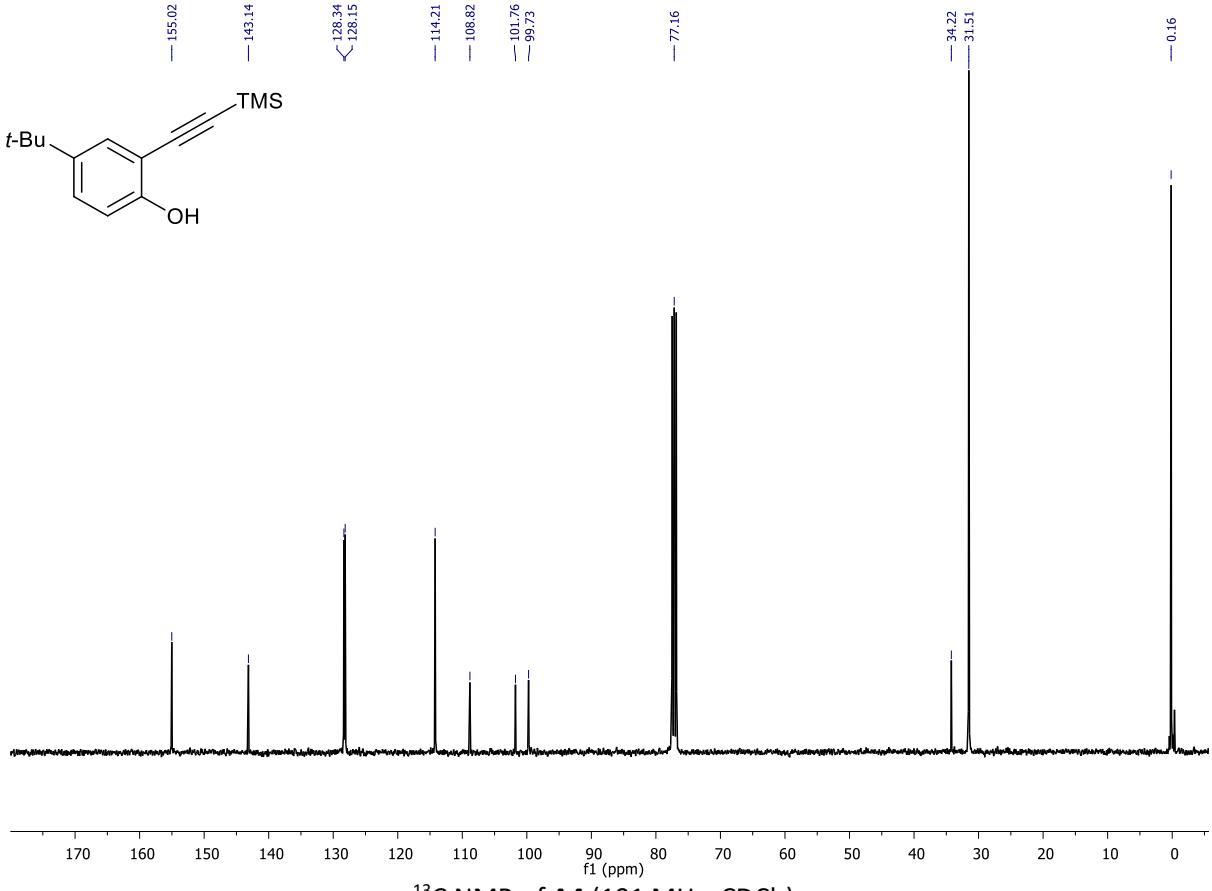
^{1}H NMR of **A3** (400 MHz, $CDCl_3$)



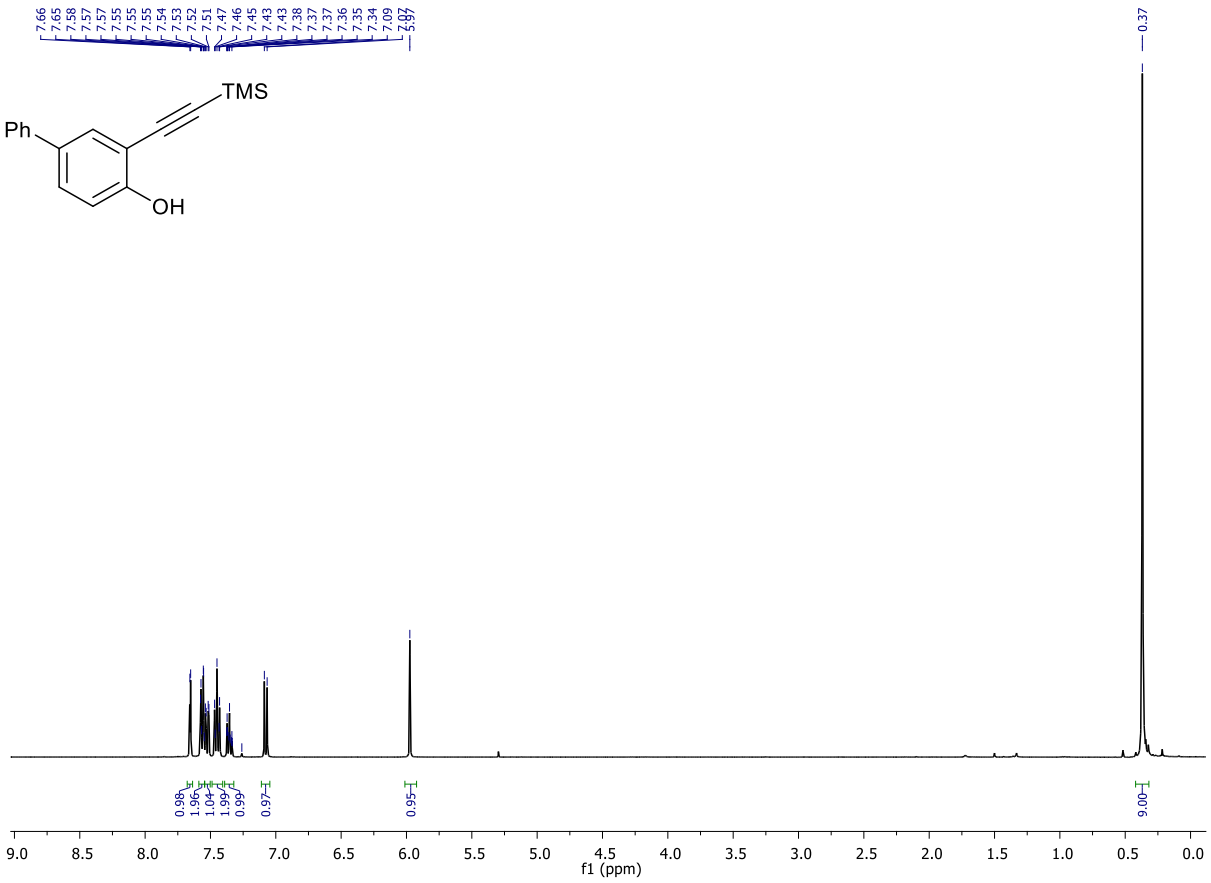
^{13}C NMR of **A3** (101 MHz, $CDCl_3$)



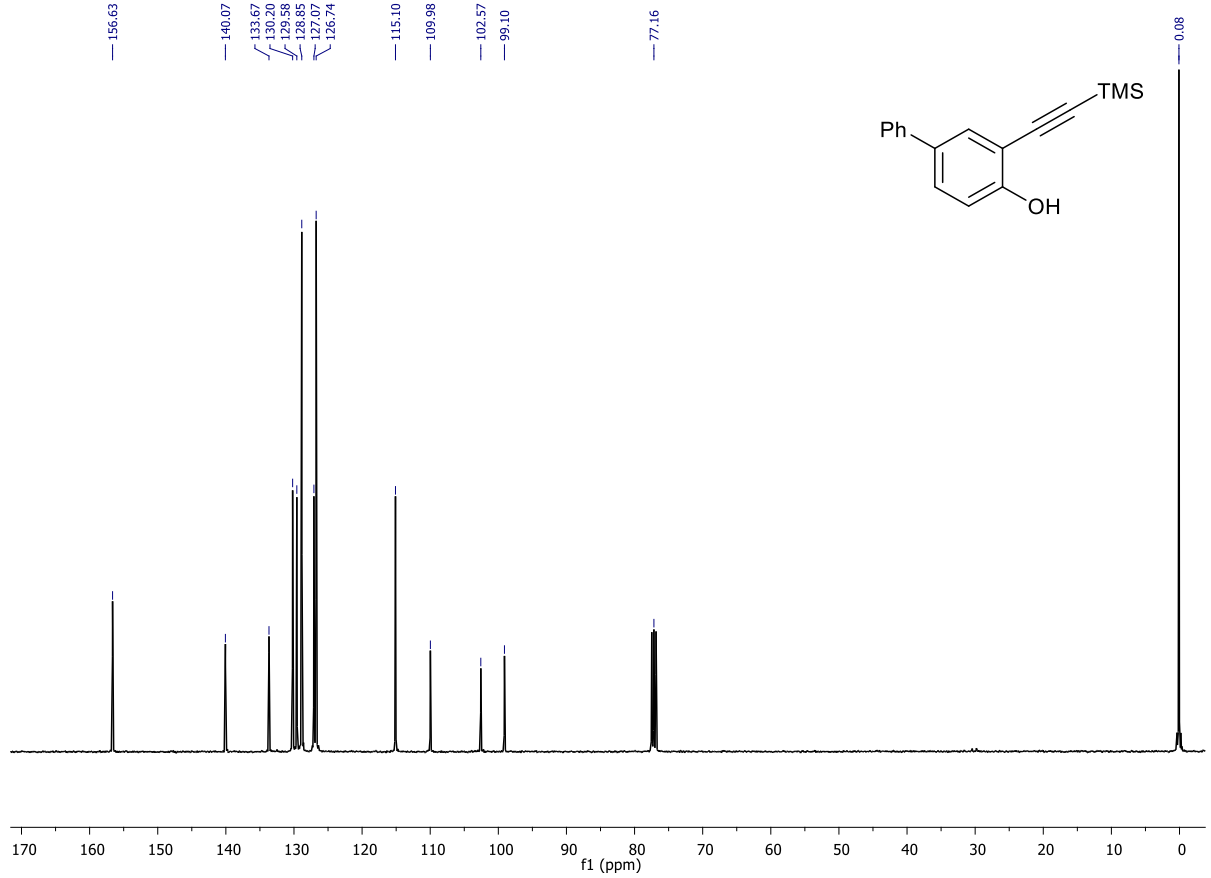
^{1}H NMR of **A4** (400 MHz, $CDCl_3$)



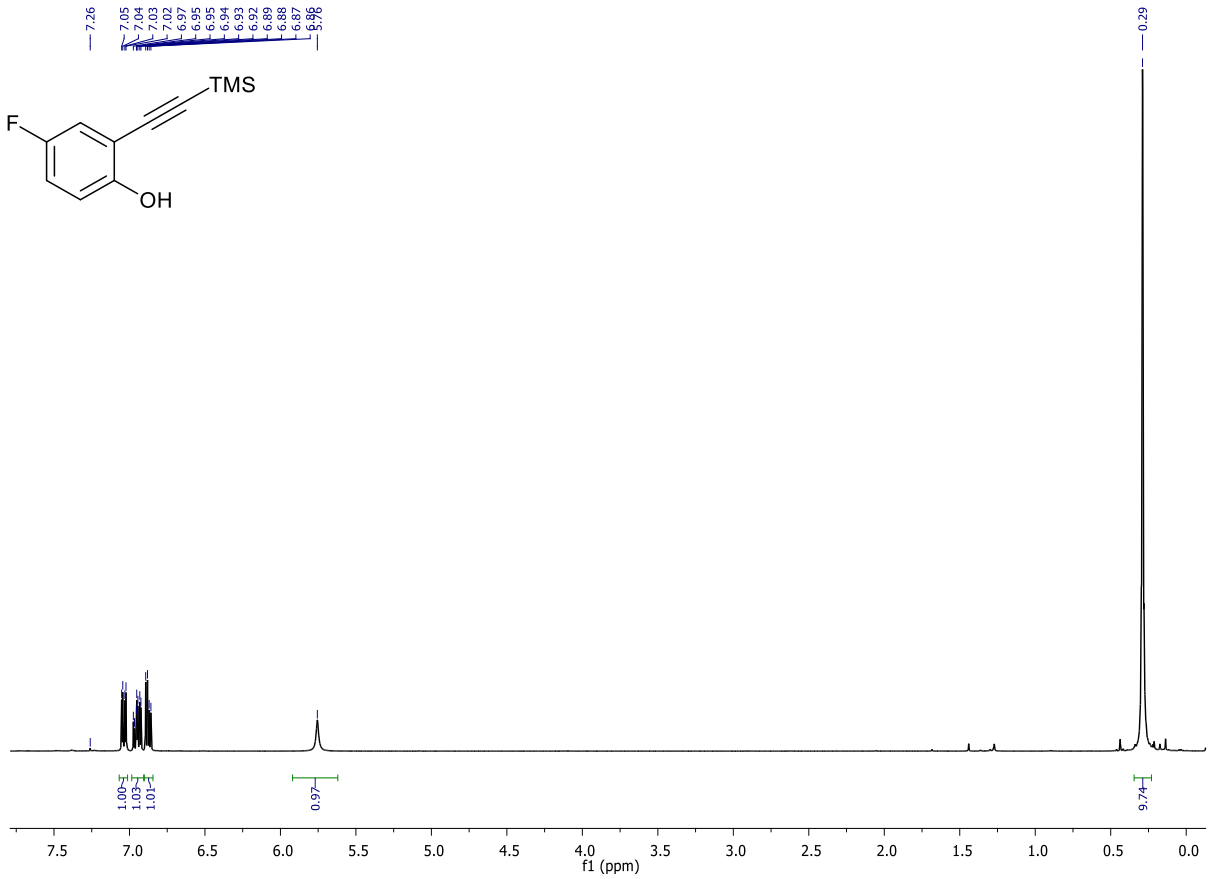
^{13}C NMR of **A4** (101 MHz, $CDCl_3$)



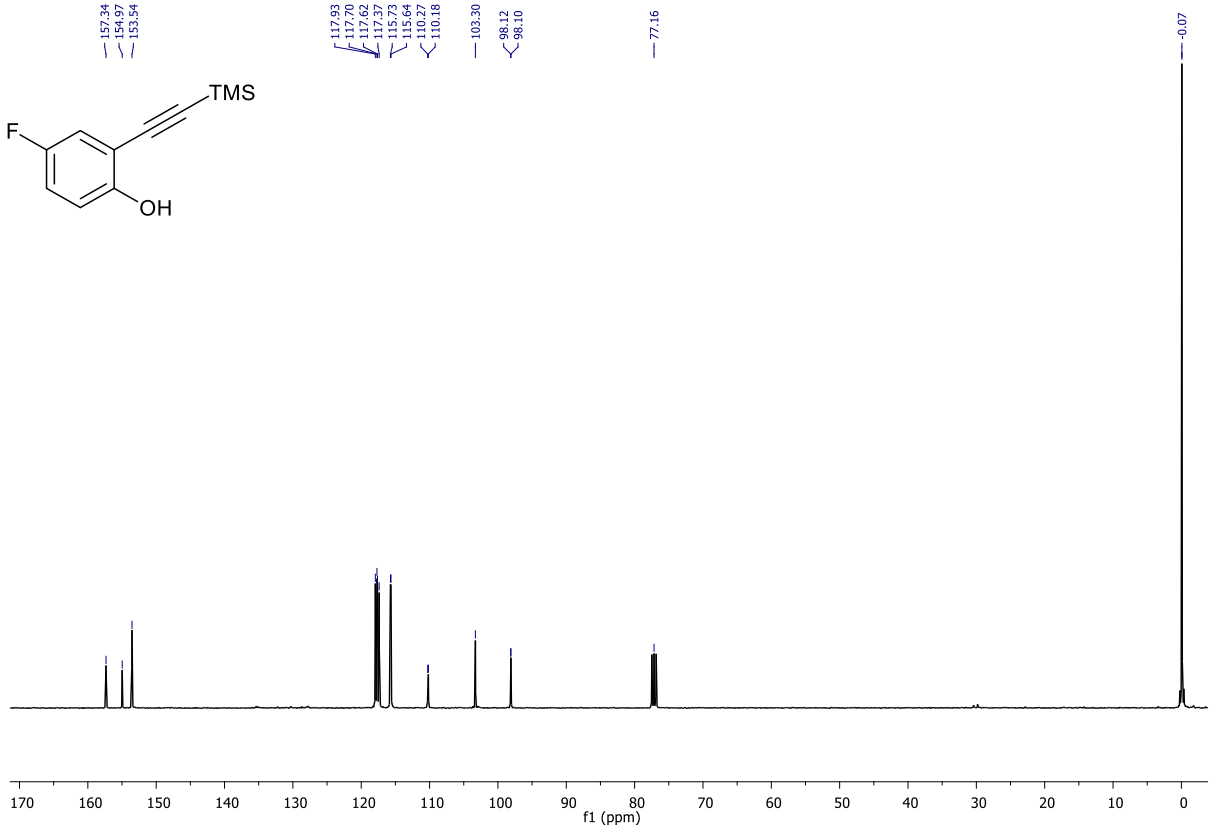
^{1}H NMR of **A5** (400 MHz, $CDCl_3$)



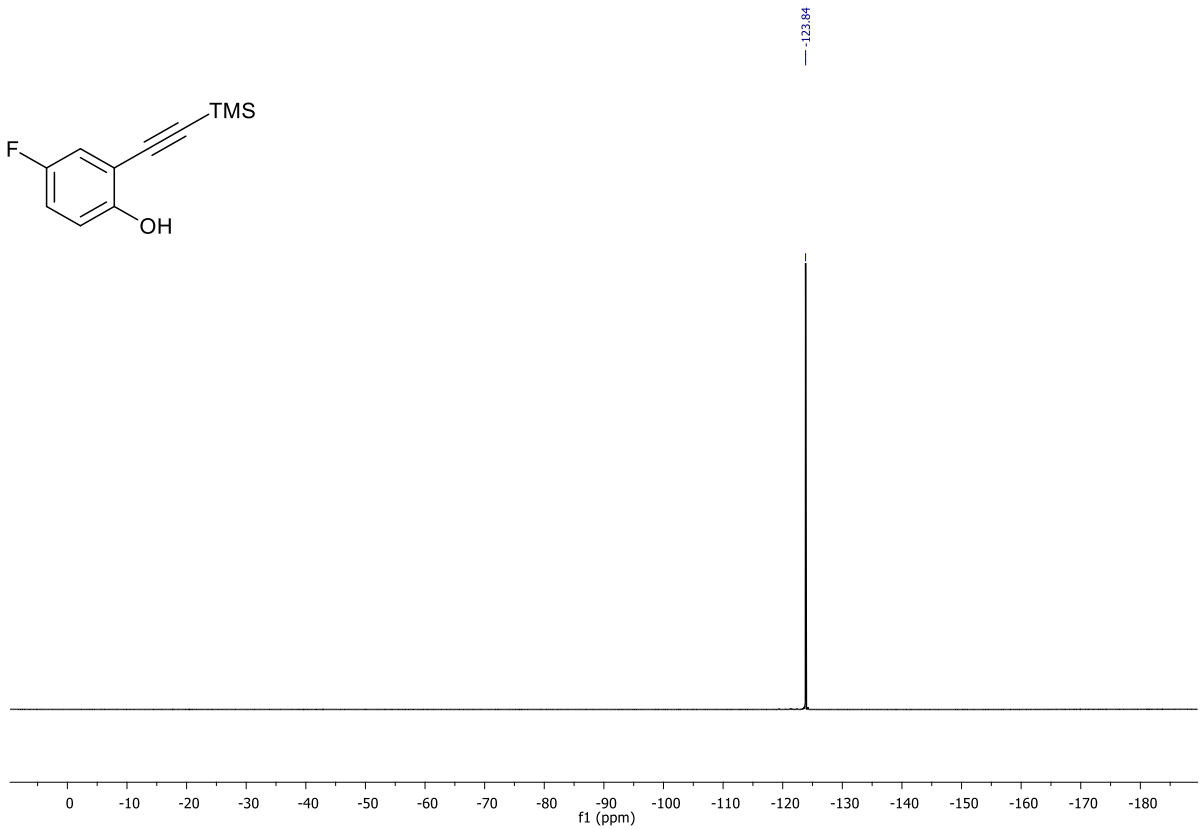
^{13}C NMR of **A5** (101 MHz, $CDCl_3$)



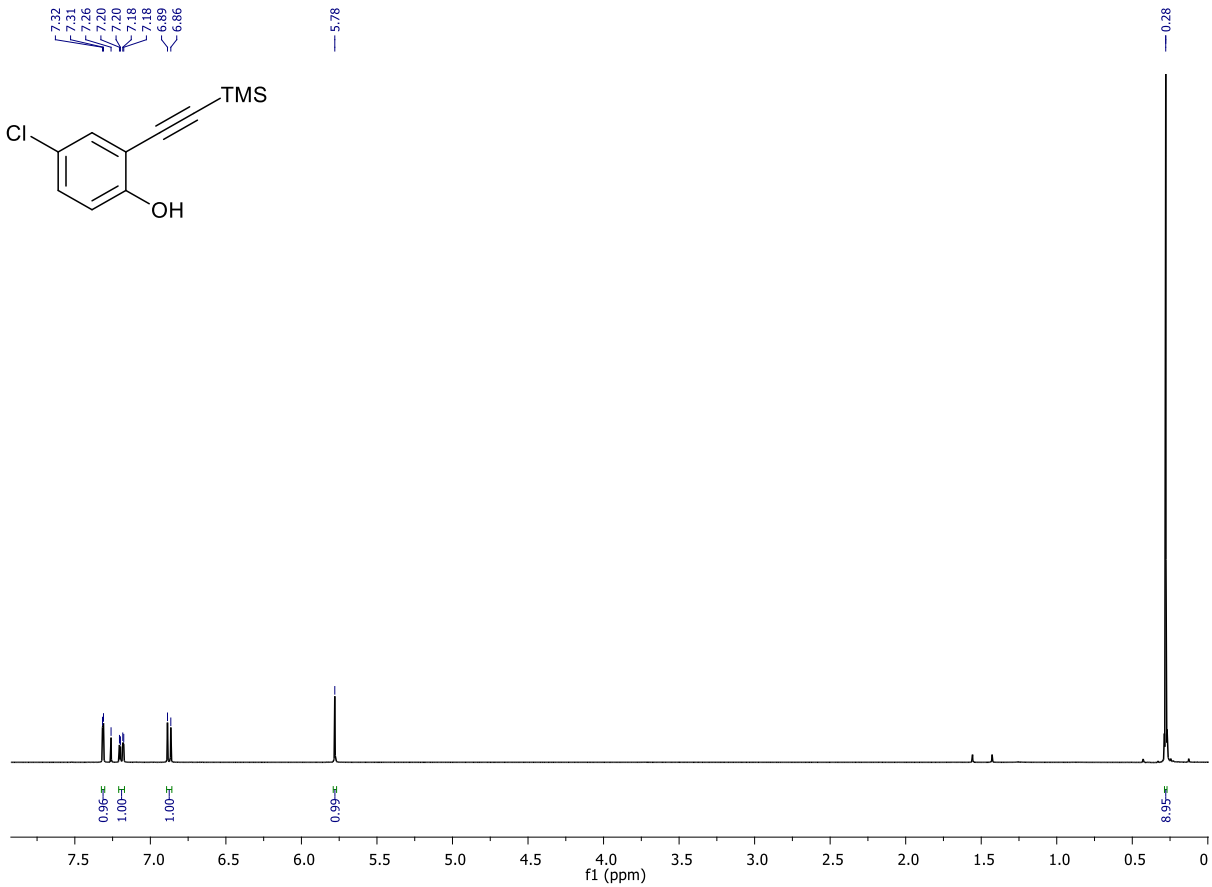
^{1}H NMR of **A6** (400 MHz, $CDCl_3$)



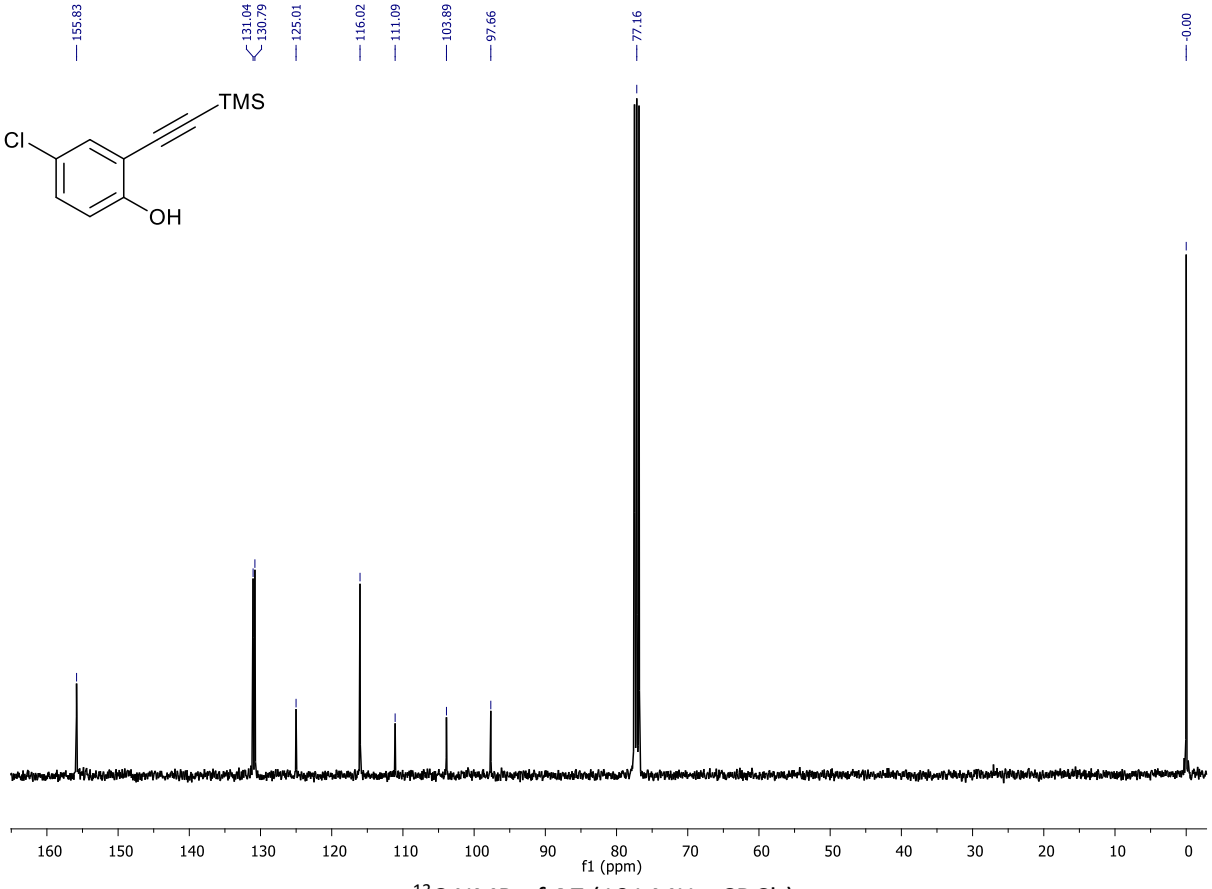
^{13}C NMR of **A6** (101 MHz, $CDCl_3$)



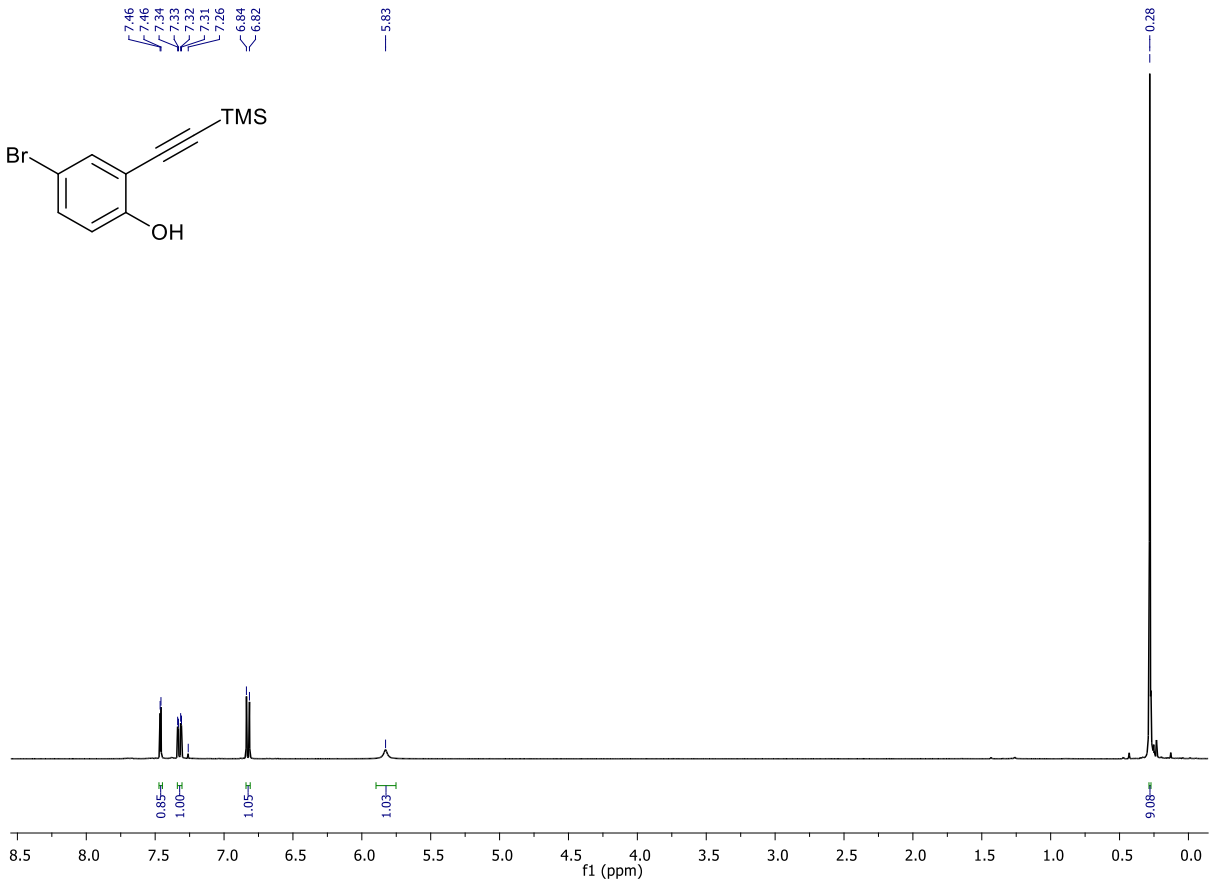
^{19}F NMR of **A6** (376.5 MHz, $CDCl_3$)



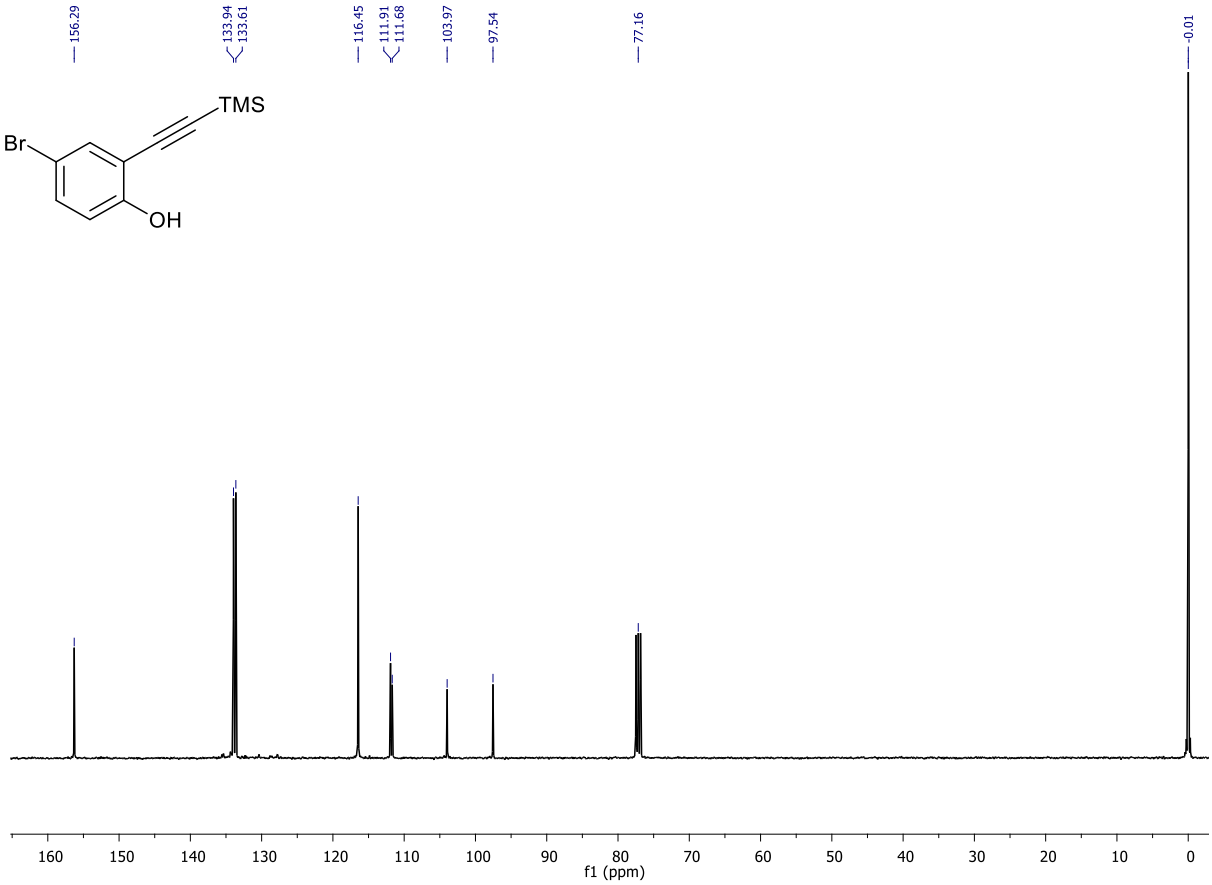
^{1}H NMR of **A7** (400 MHz, $CDCl_3$)



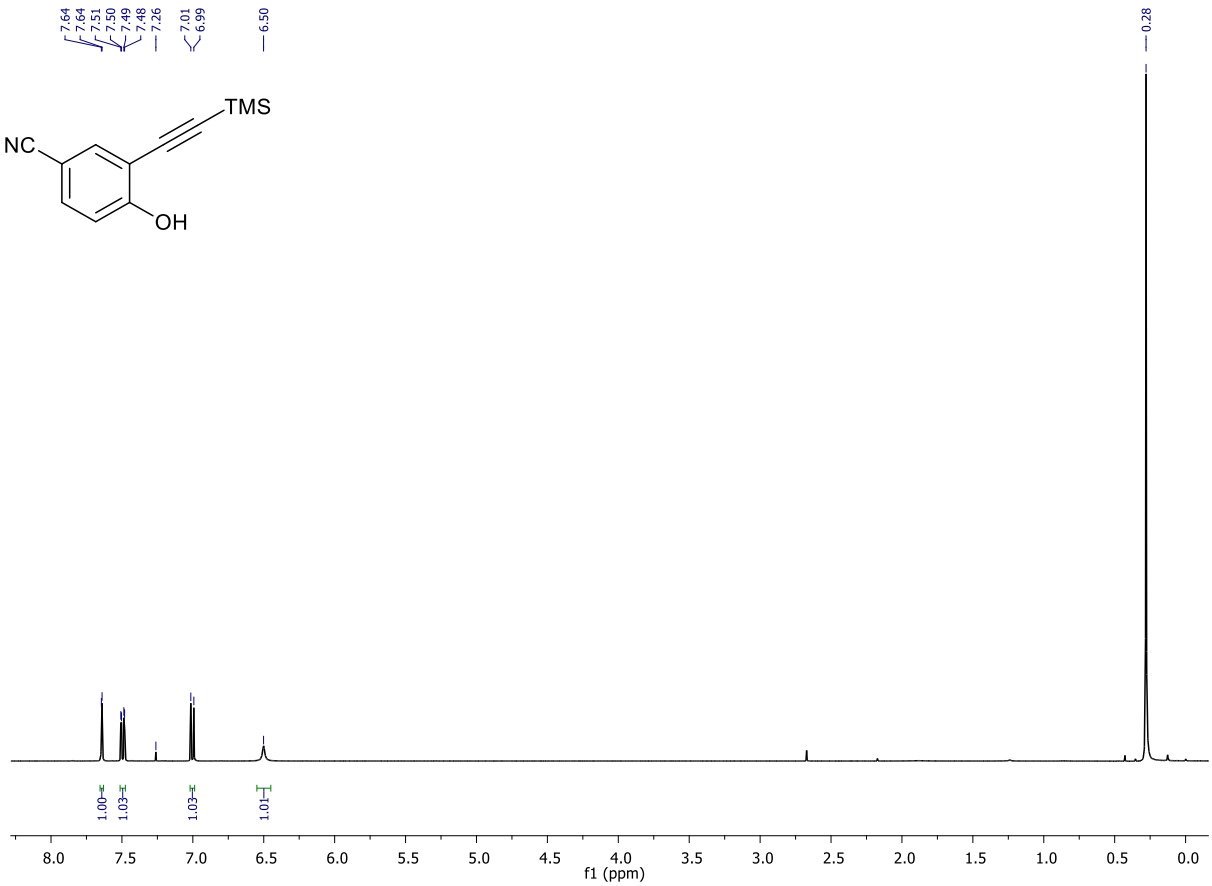
^{13}C NMR of **A7** (101 MHz, $CDCl_3$)



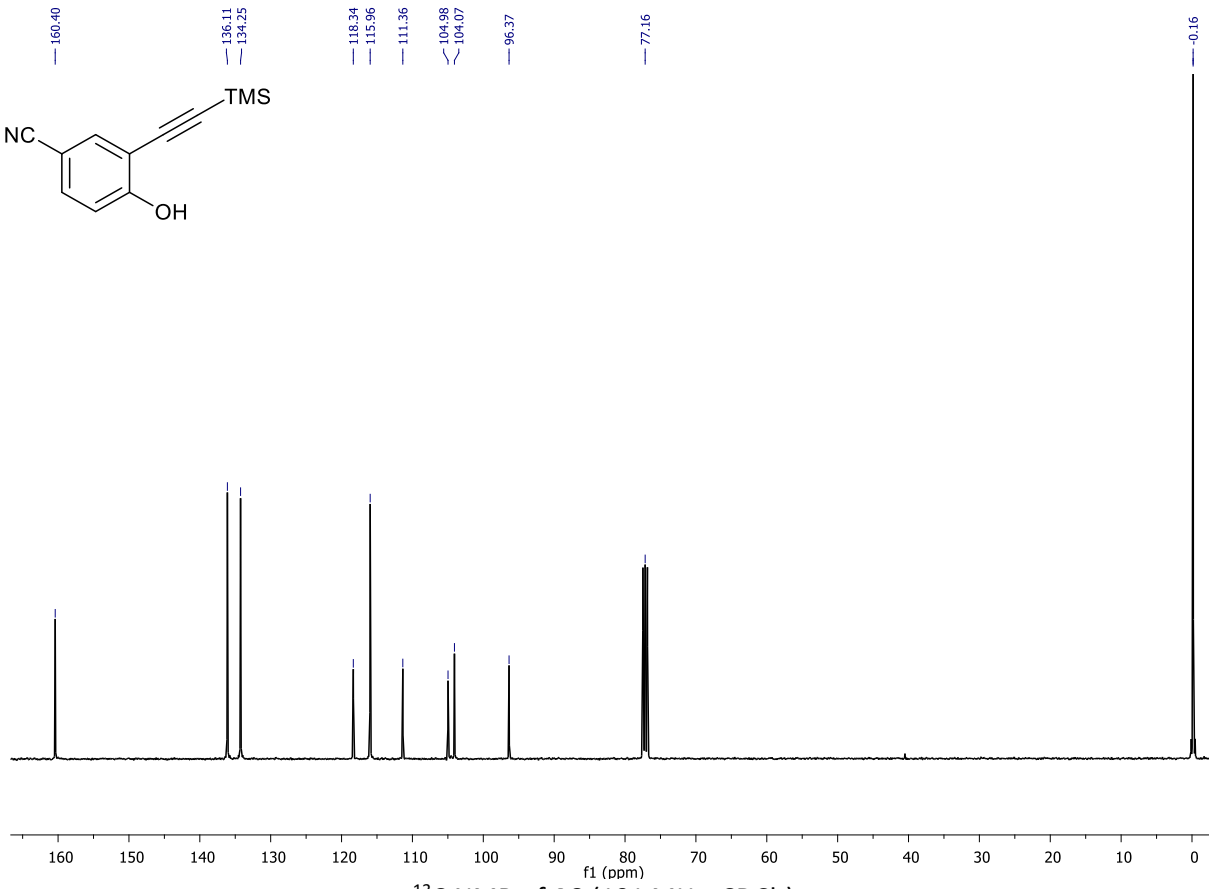
^{1}H NMR of **A8** (400 MHz, $CDCl_3$)



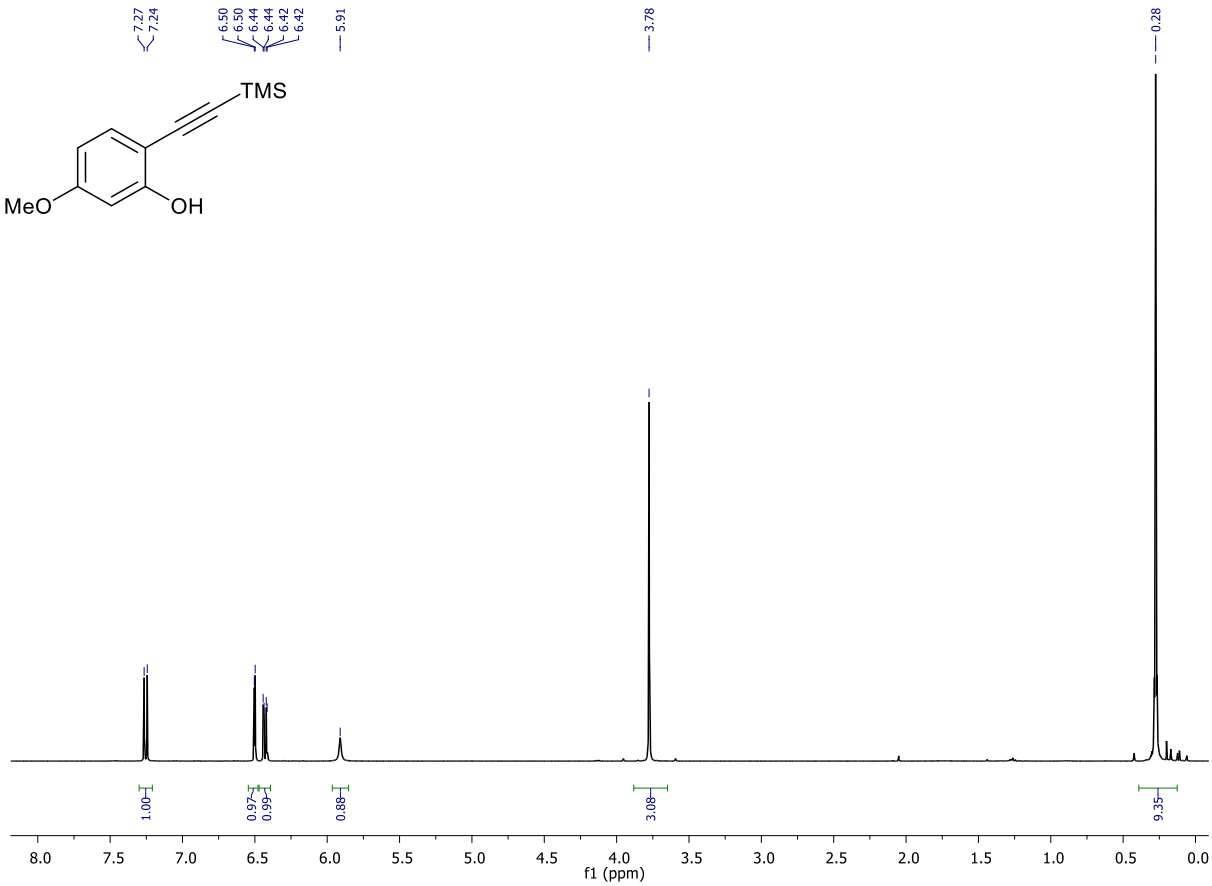
^{13}C NMR of **A8** (101 MHz, $CDCl_3$)



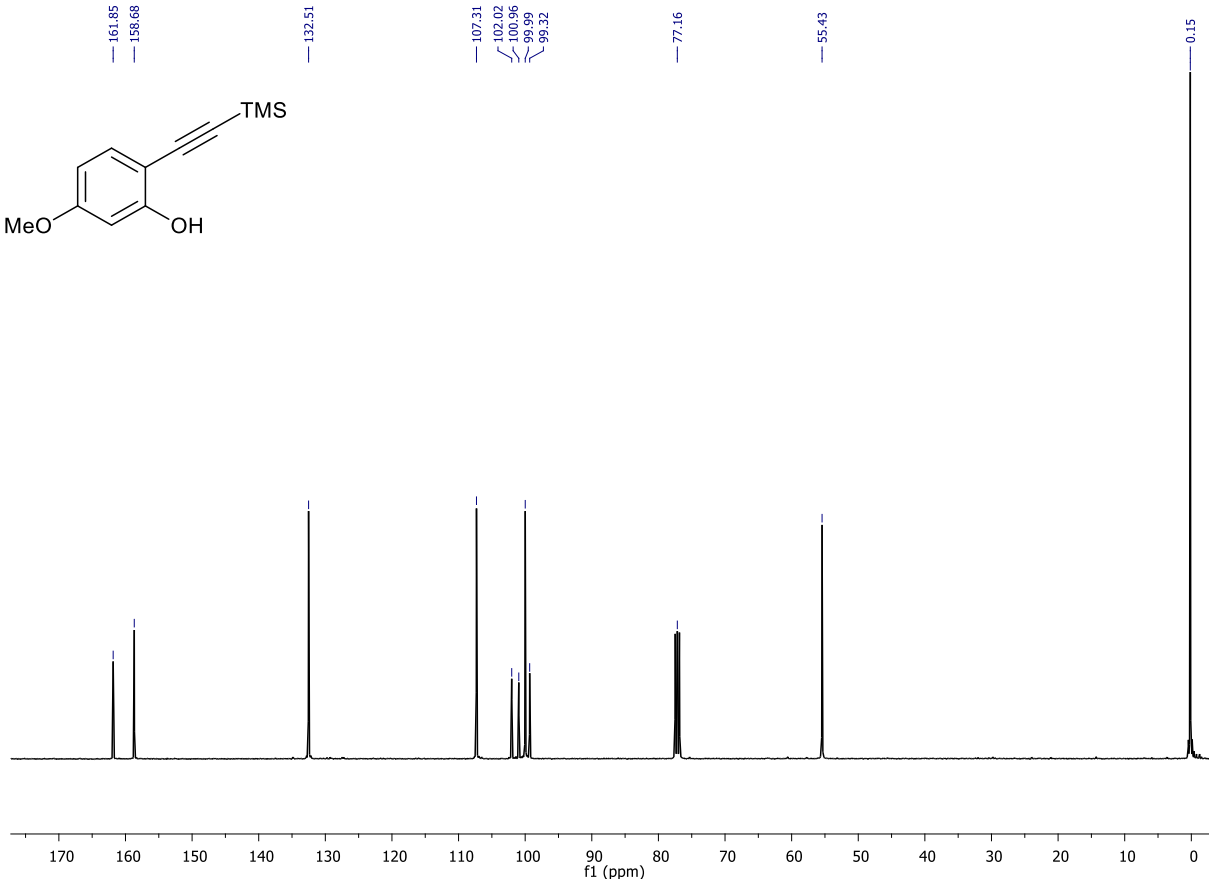
^{1}H NMR of **A9** (400 MHz, $CDCl_3$)



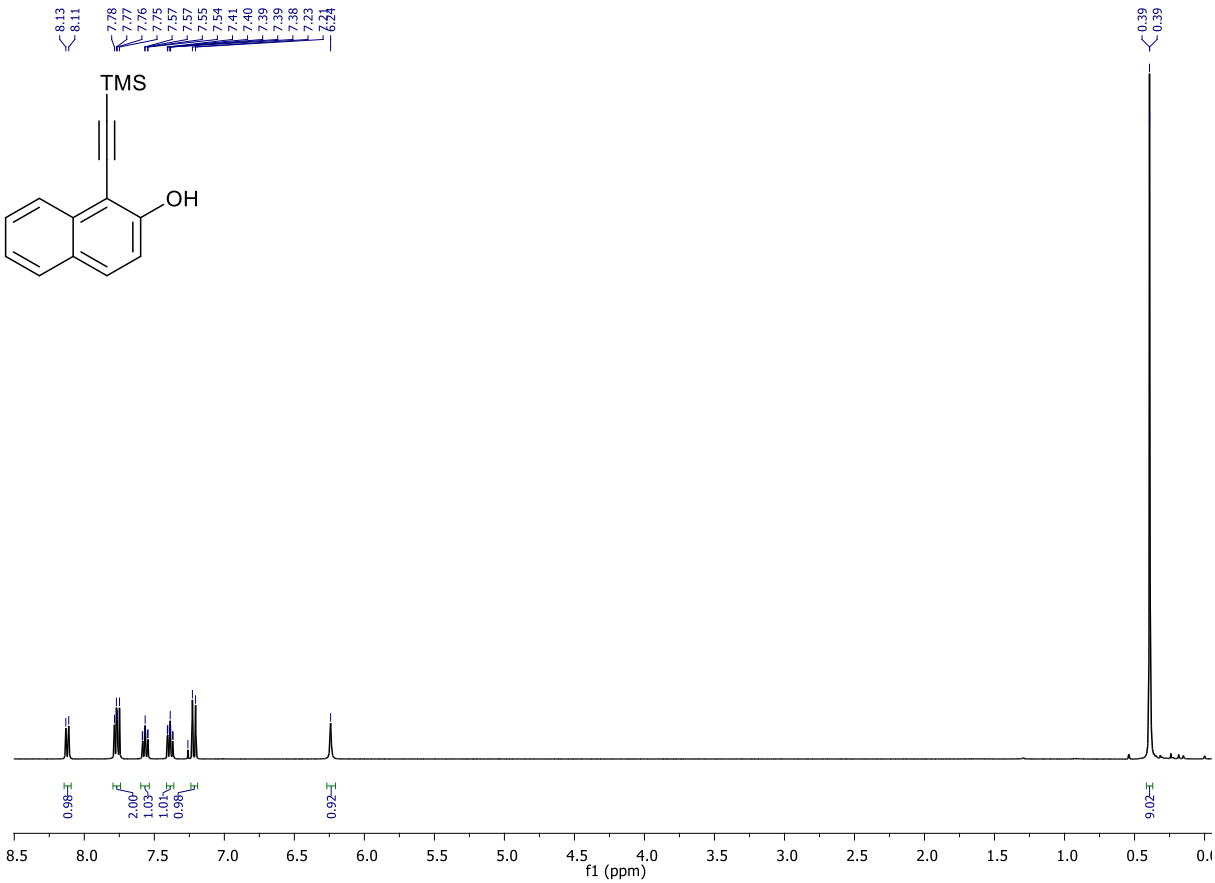
^{13}C NMR of **A9** (101 MHz, $CDCl_3$)



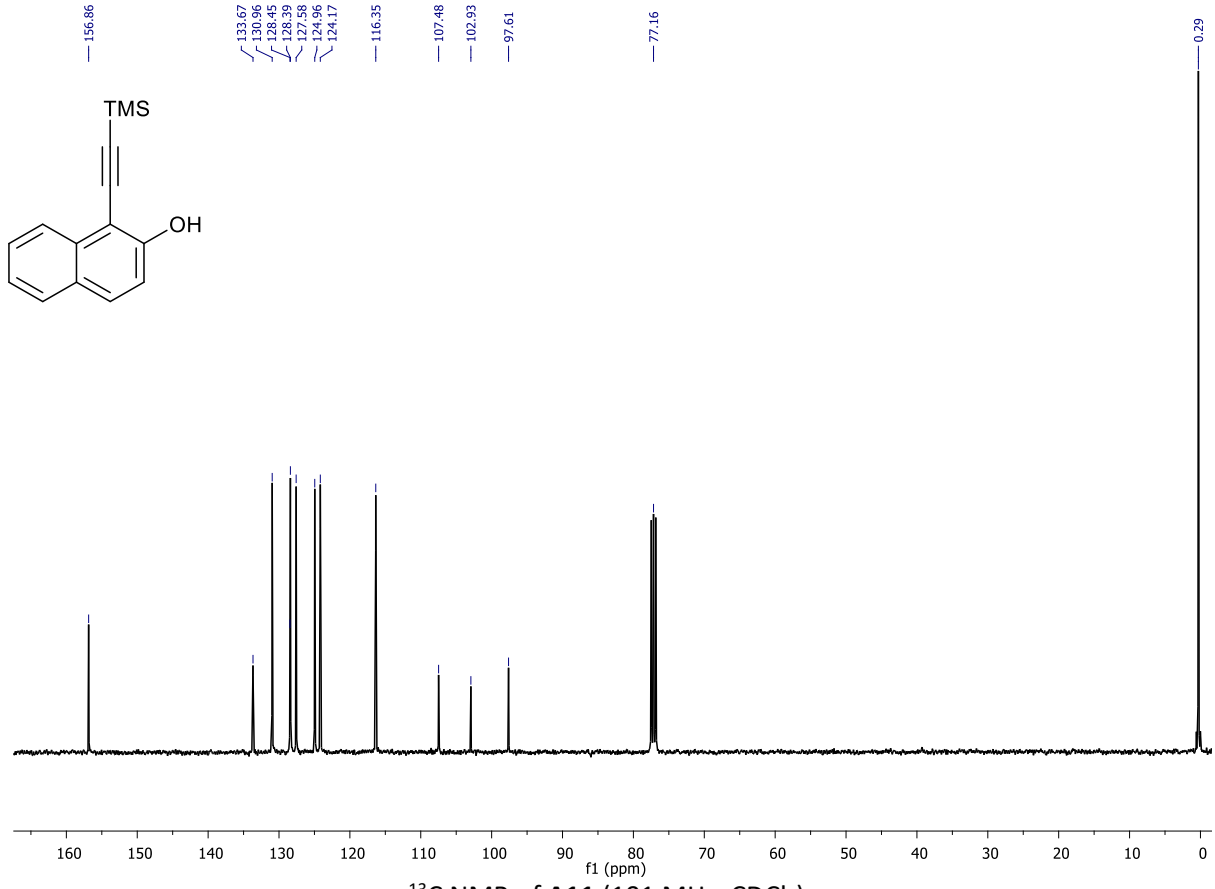
^{1}H NMR of **A10** (400 MHz, $CDCl_3$)



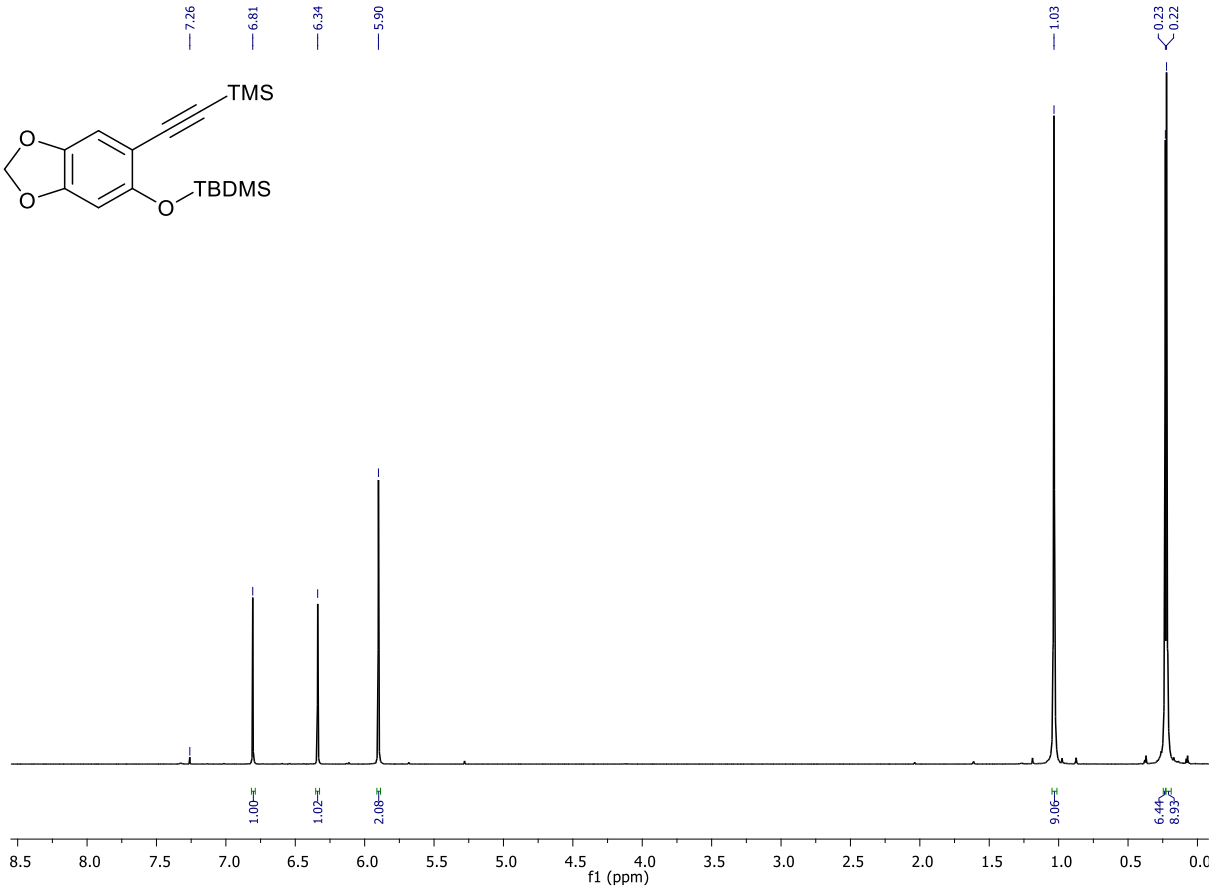
^{13}C NMR of **A10** (101 MHz, $CDCl_3$)



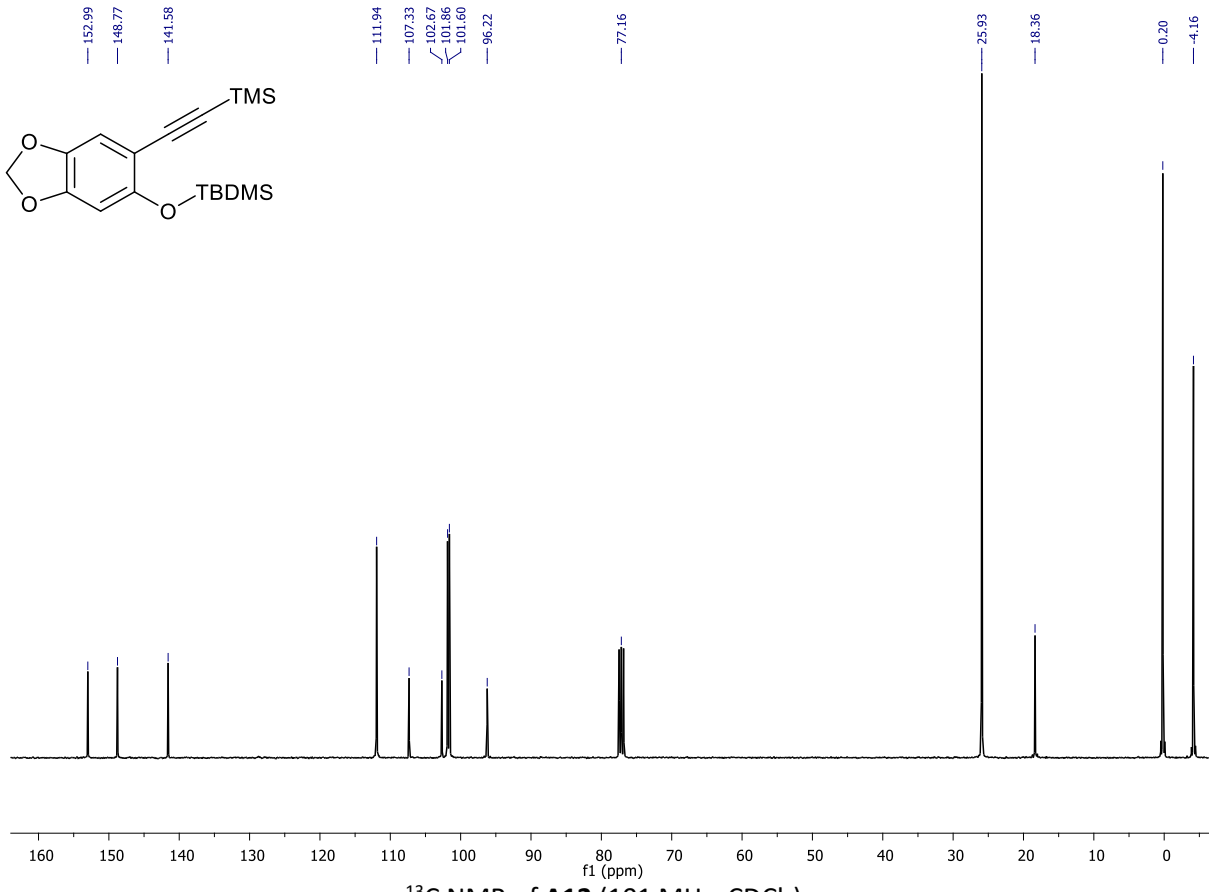
^{1}H NMR of **A11** (400 MHz, $CDCl_3$)



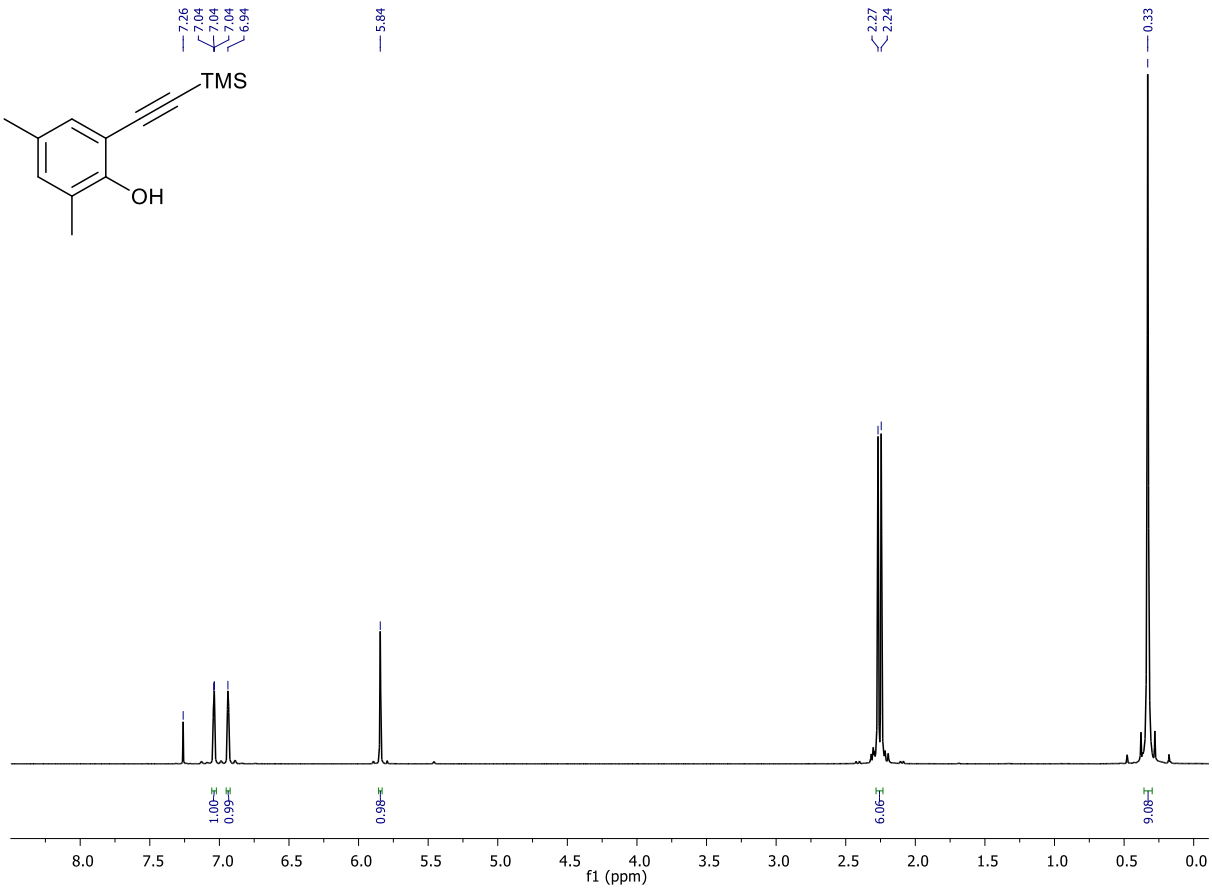
^{13}C NMR of **A11** (101 MHz, $CDCl_3$)



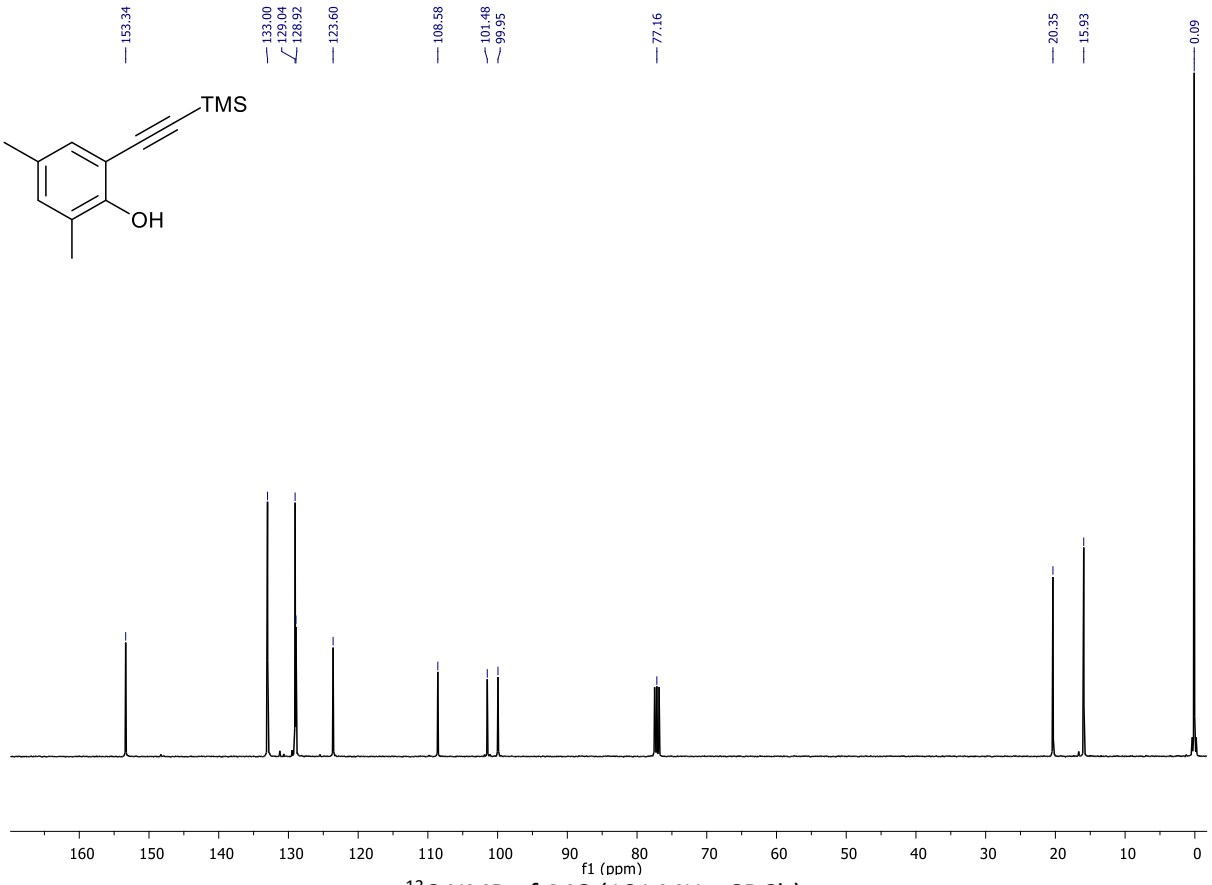
^{1}H NMR of **A12** (400 MHz, $CDCl_3$)



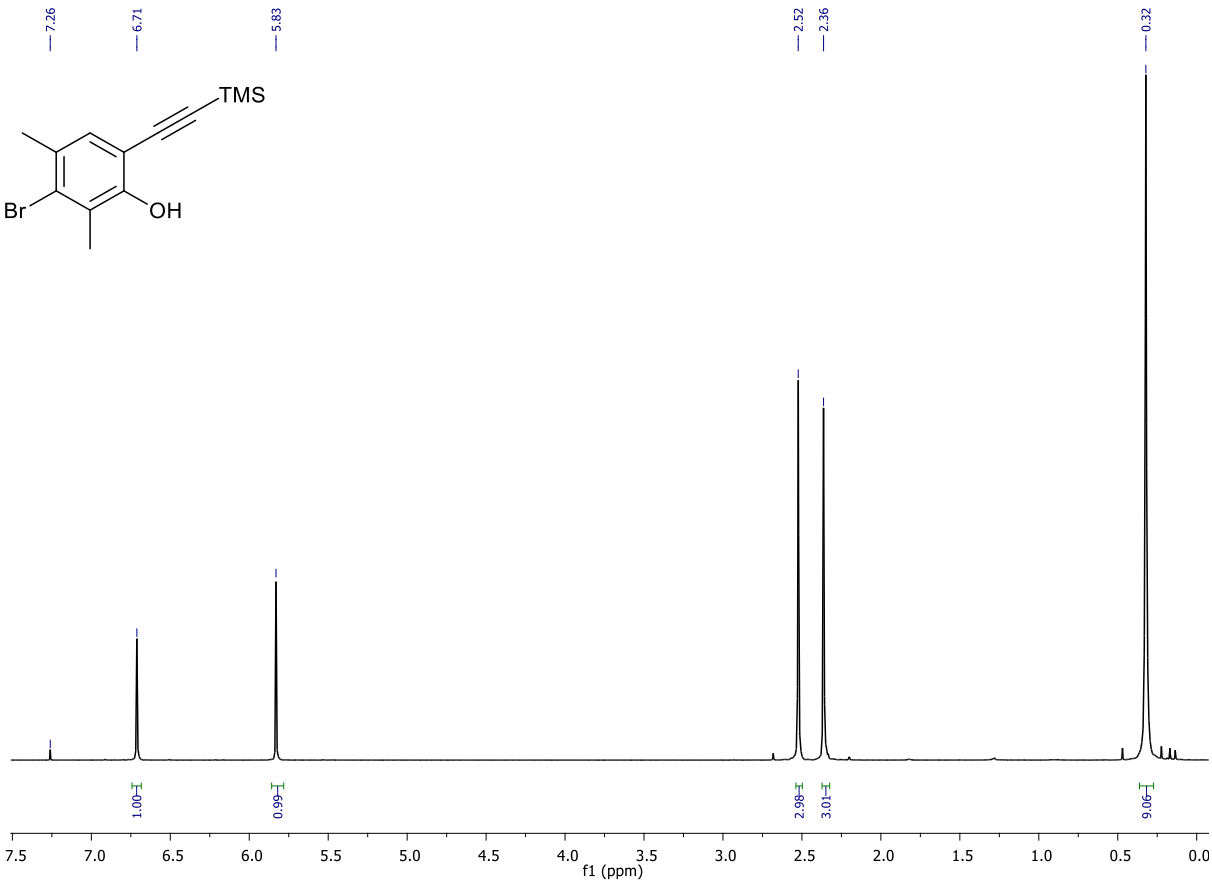
^{13}C NMR of **A12** (101 MHz, $CDCl_3$)



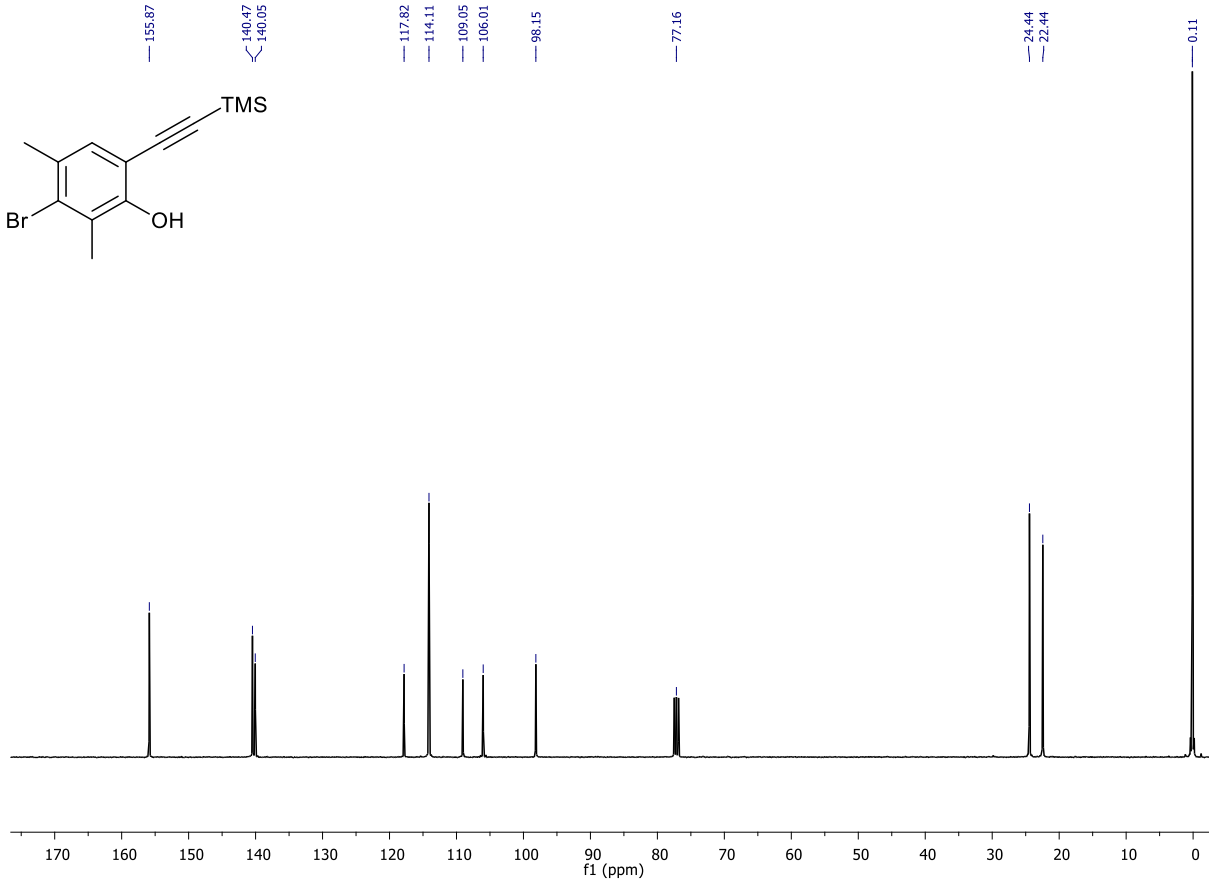
^{1}H NMR of **A13** (400 MHz, $CDCl_3$)



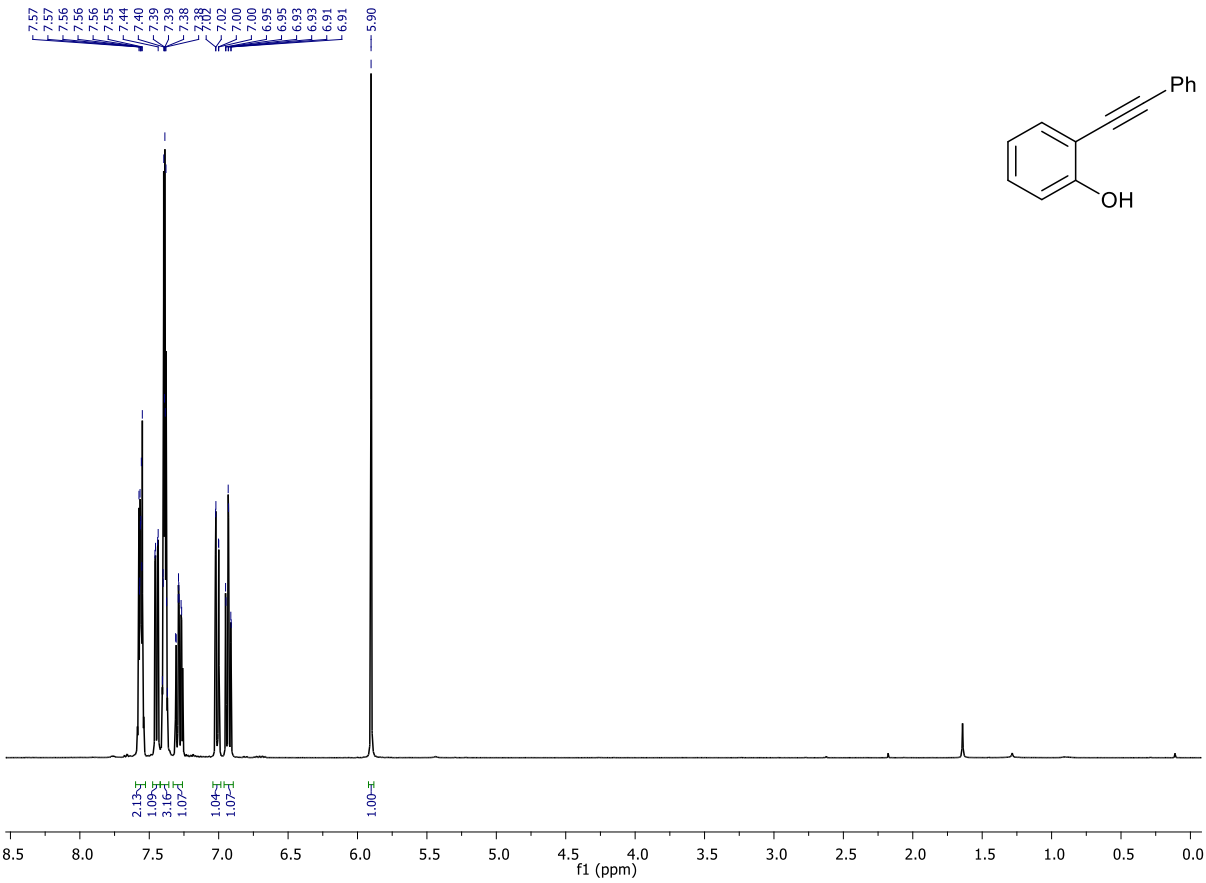
^{13}C NMR of **A13** (101 MHz, $CDCl_3$)



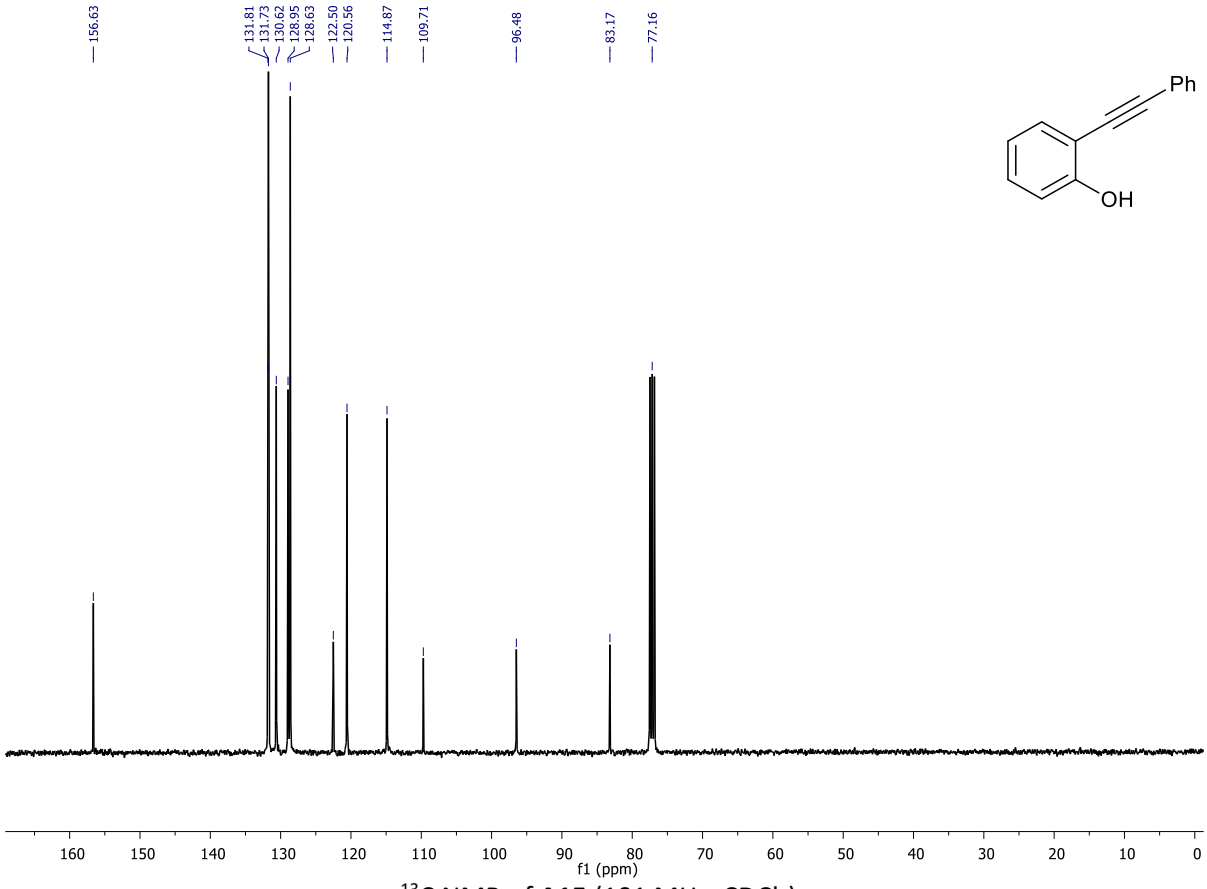
^{1}H NMR of **A14** (400 MHz, $CDCl_3$)



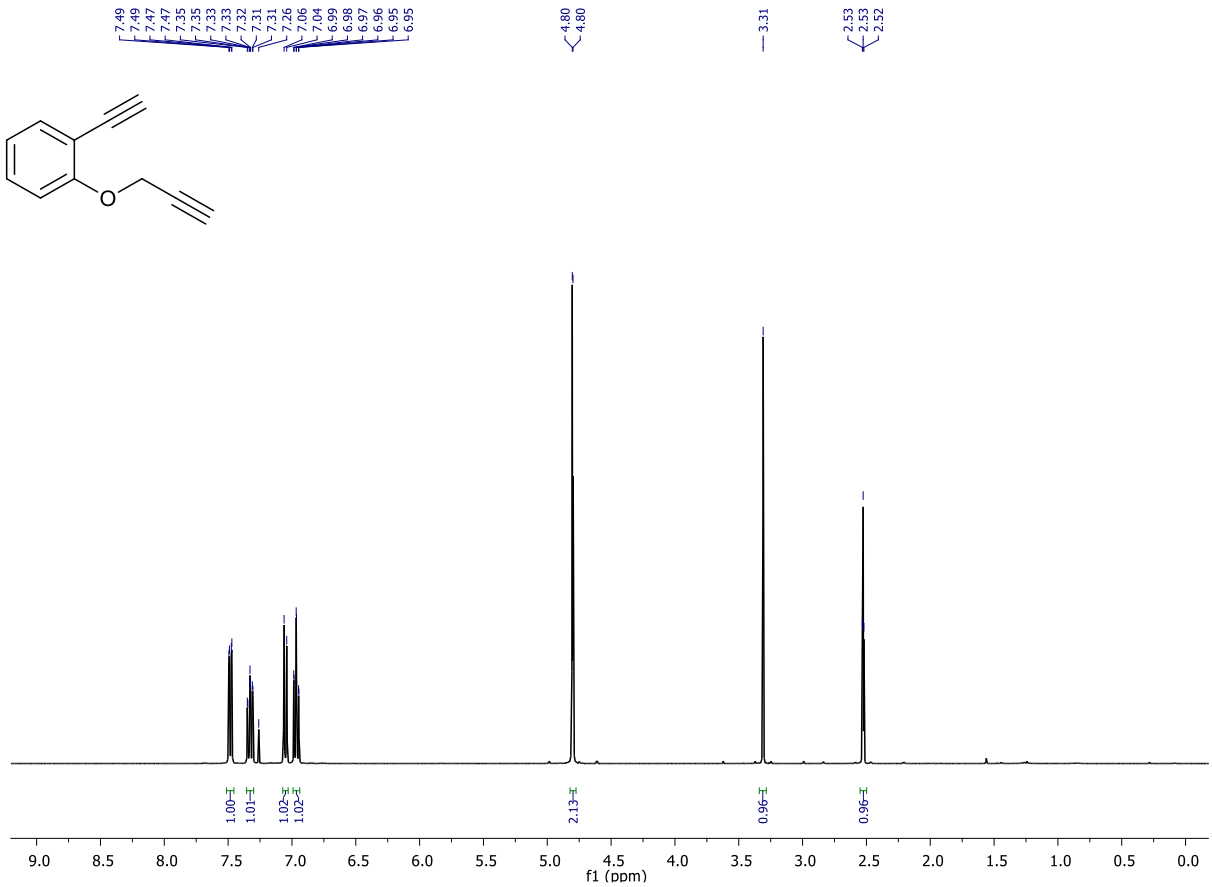
^{13}C NMR of **A14** (101 MHz, $CDCl_3$)



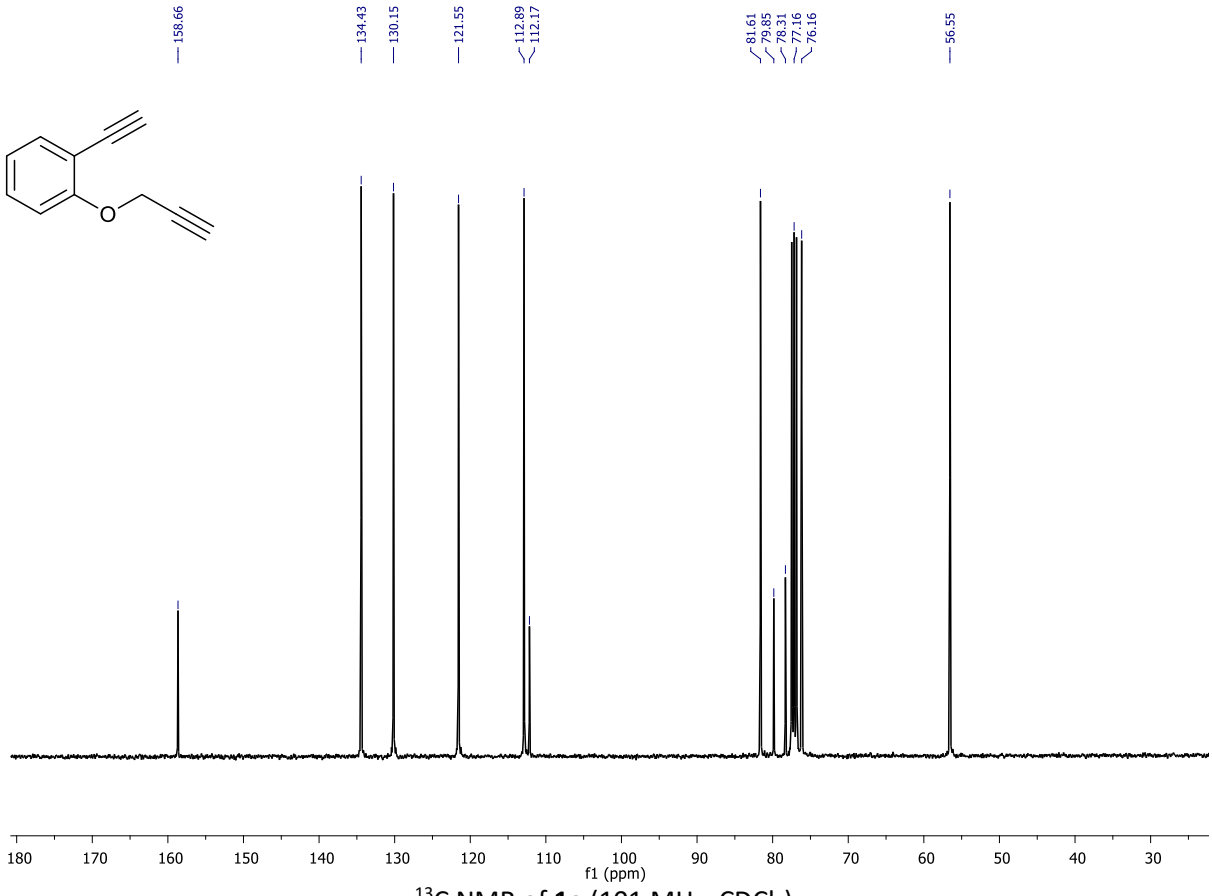
^{1}H NMR of **A15** (400 MHz, $CDCl_3$)



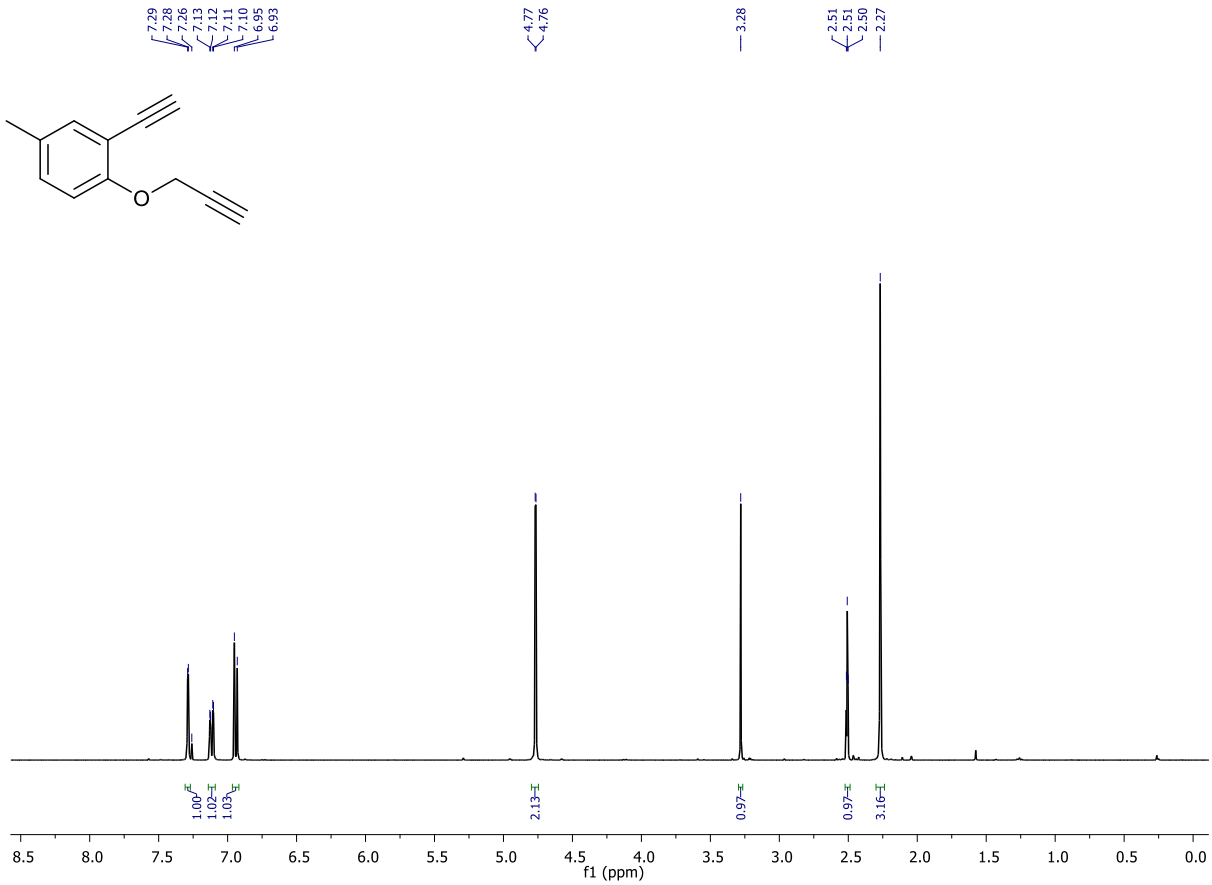
^{13}C NMR of **A15** (101 MHz, $CDCl_3$)



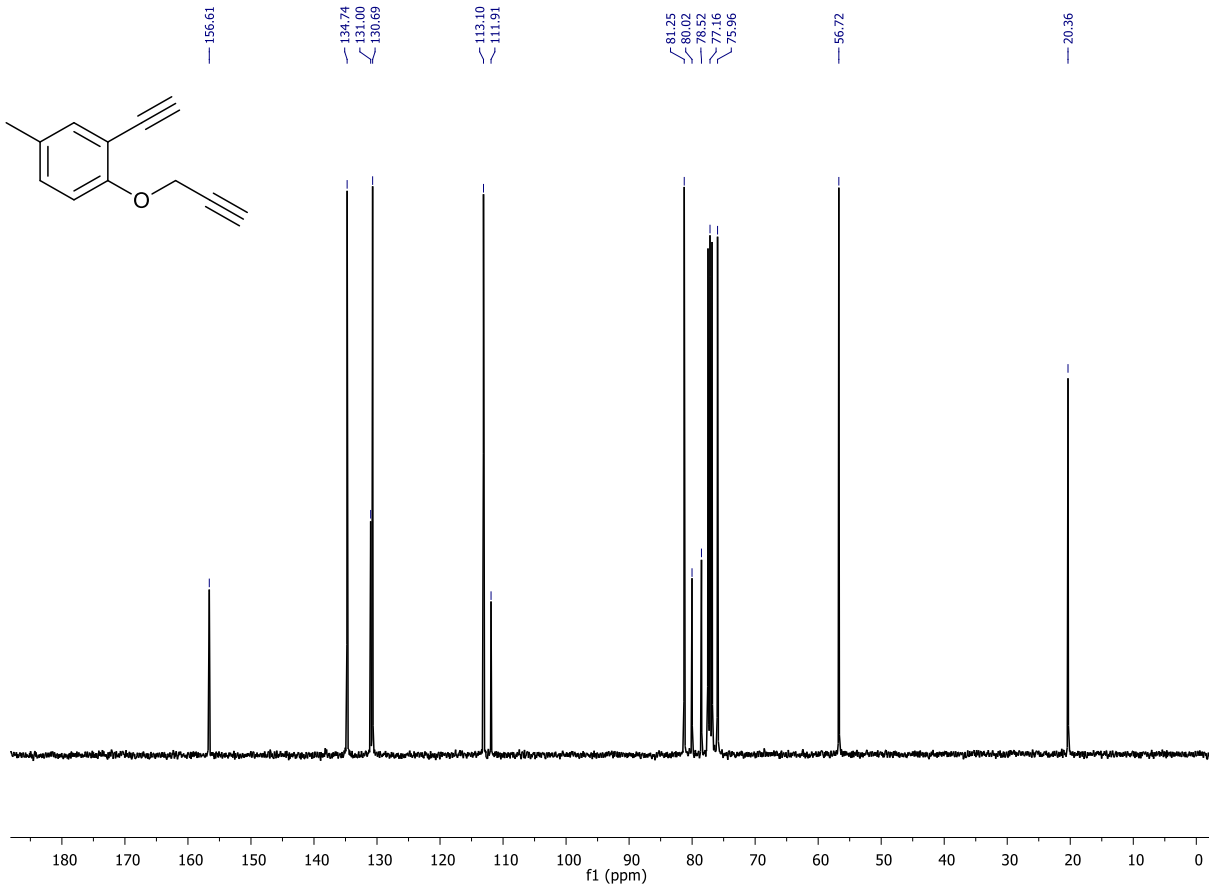
^{1}H NMR of **1a** (400 MHz, $CDCl_3$)



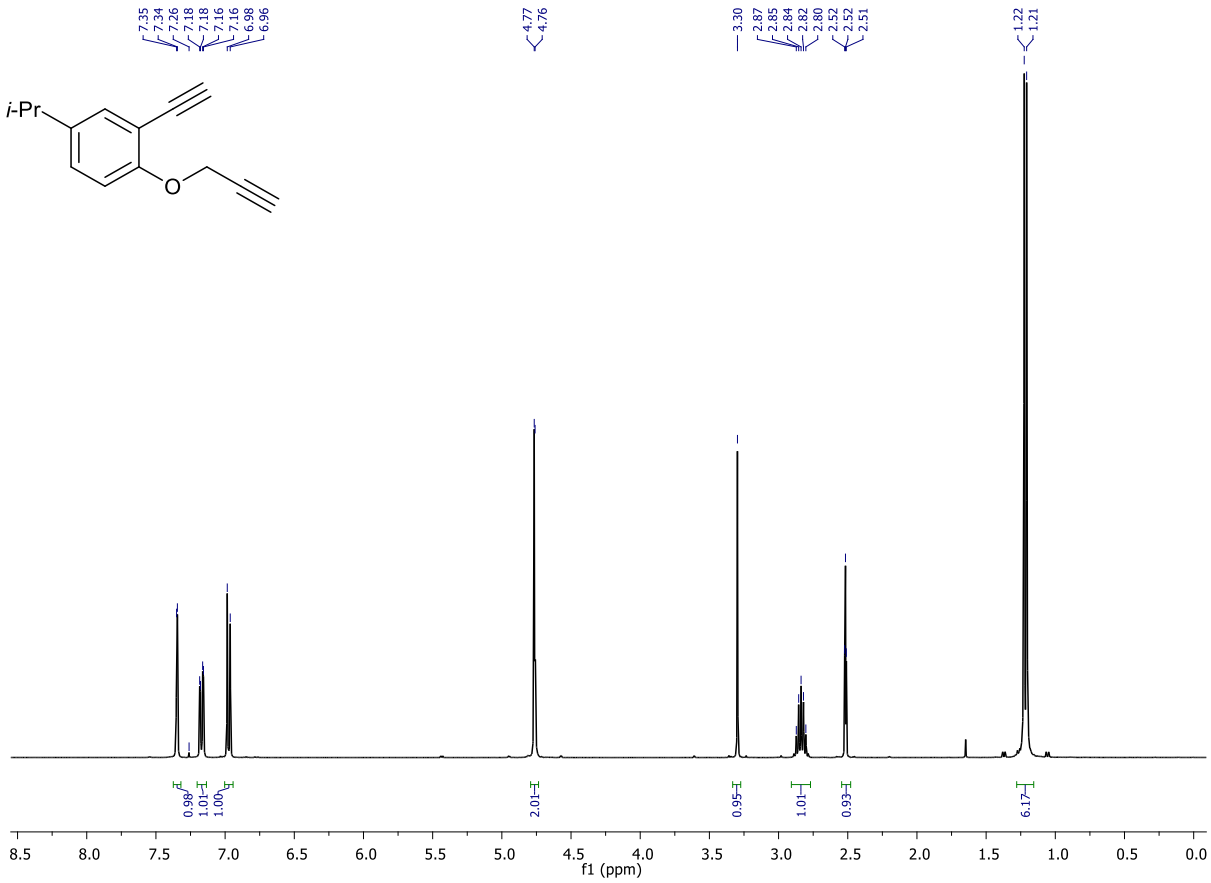
^{13}C NMR of **1a** (101 MHz, $CDCl_3$)



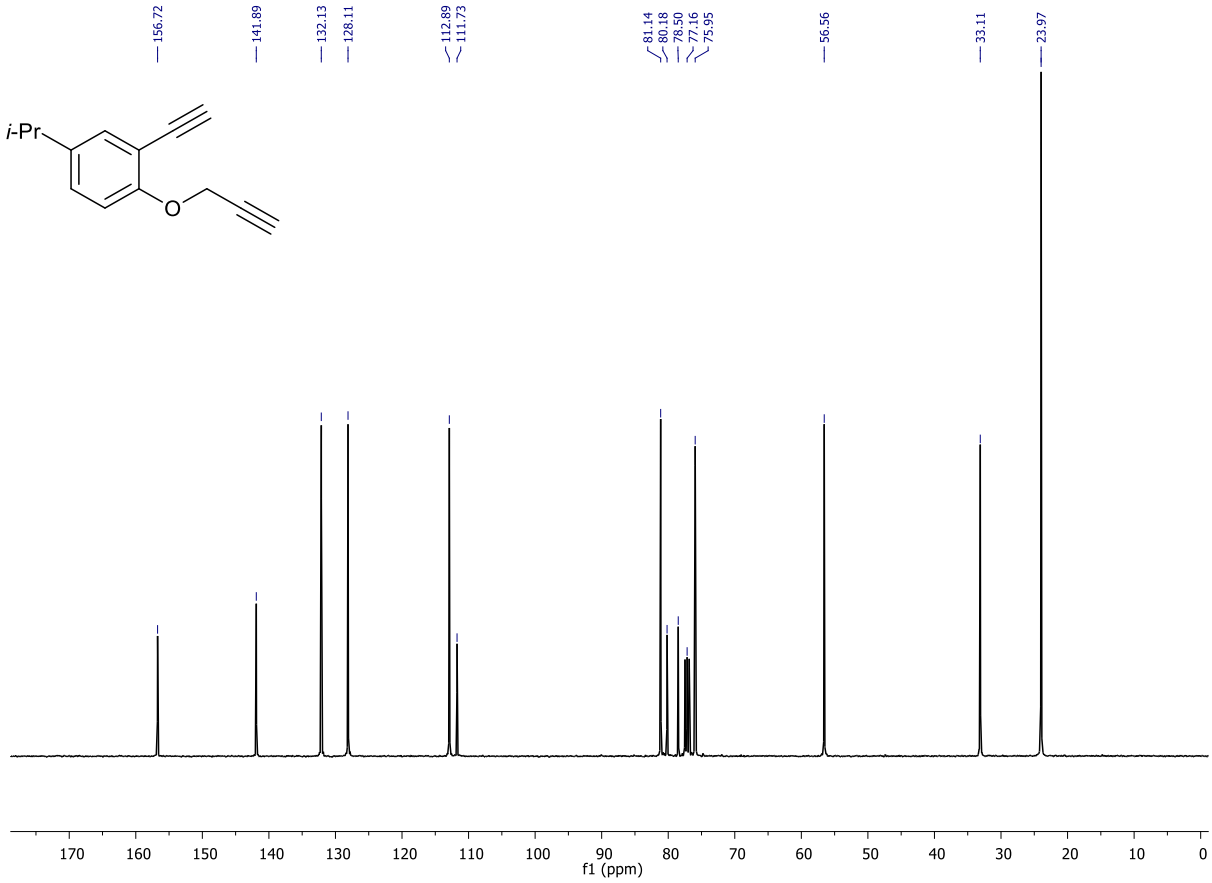
^{1}H NMR of **1b** (400 MHz, $CDCl_3$)



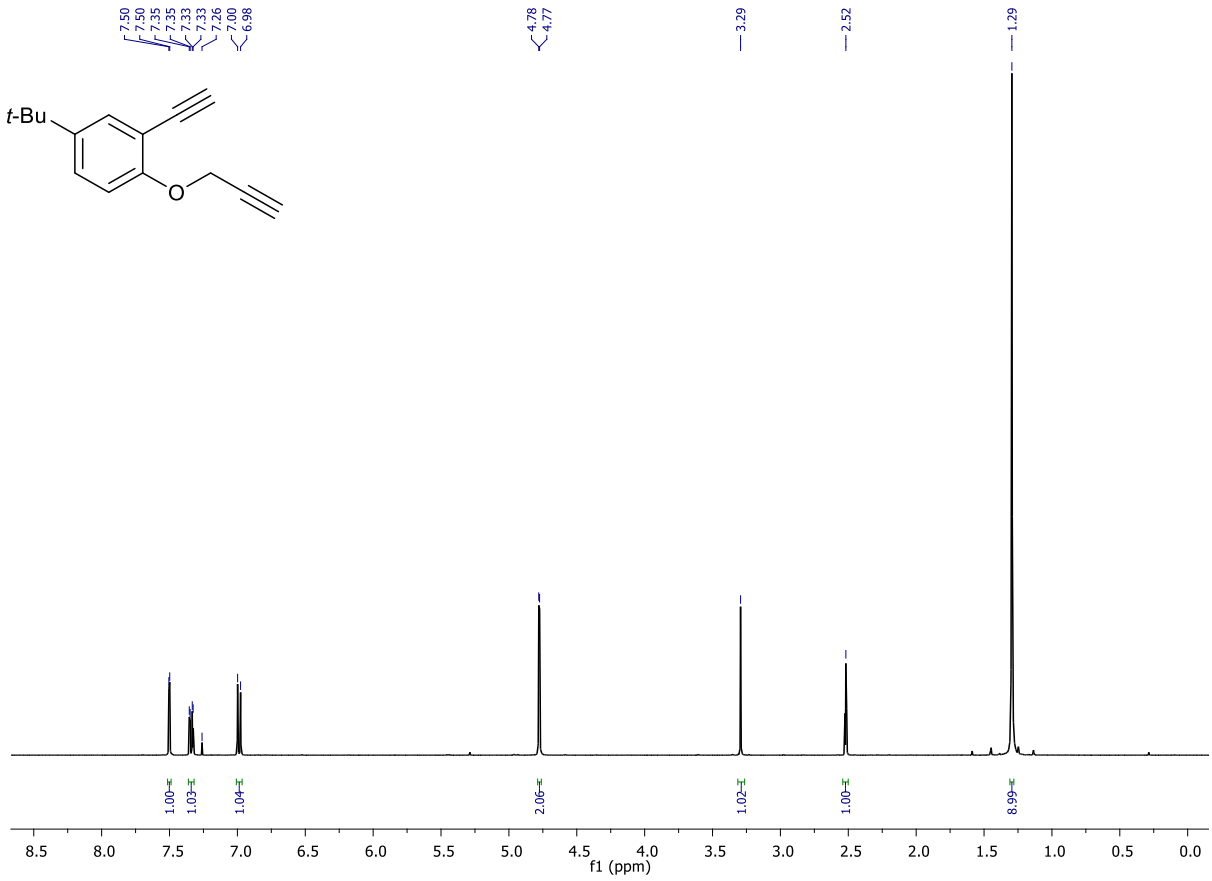
^{13}C NMR of **1b** (101 MHz, $CDCl_3$)



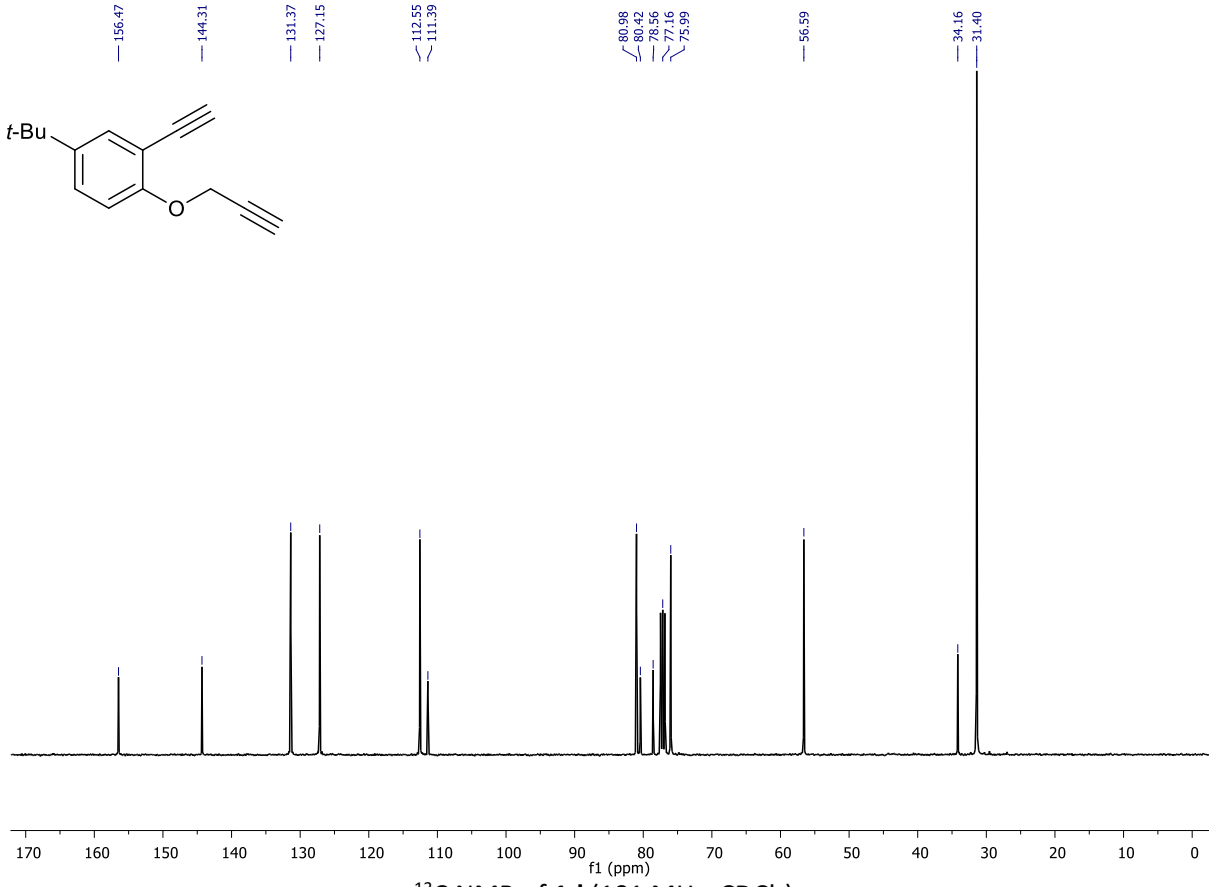
^{1}H NMR of **1c** (400 MHz, $CDCl_3$)



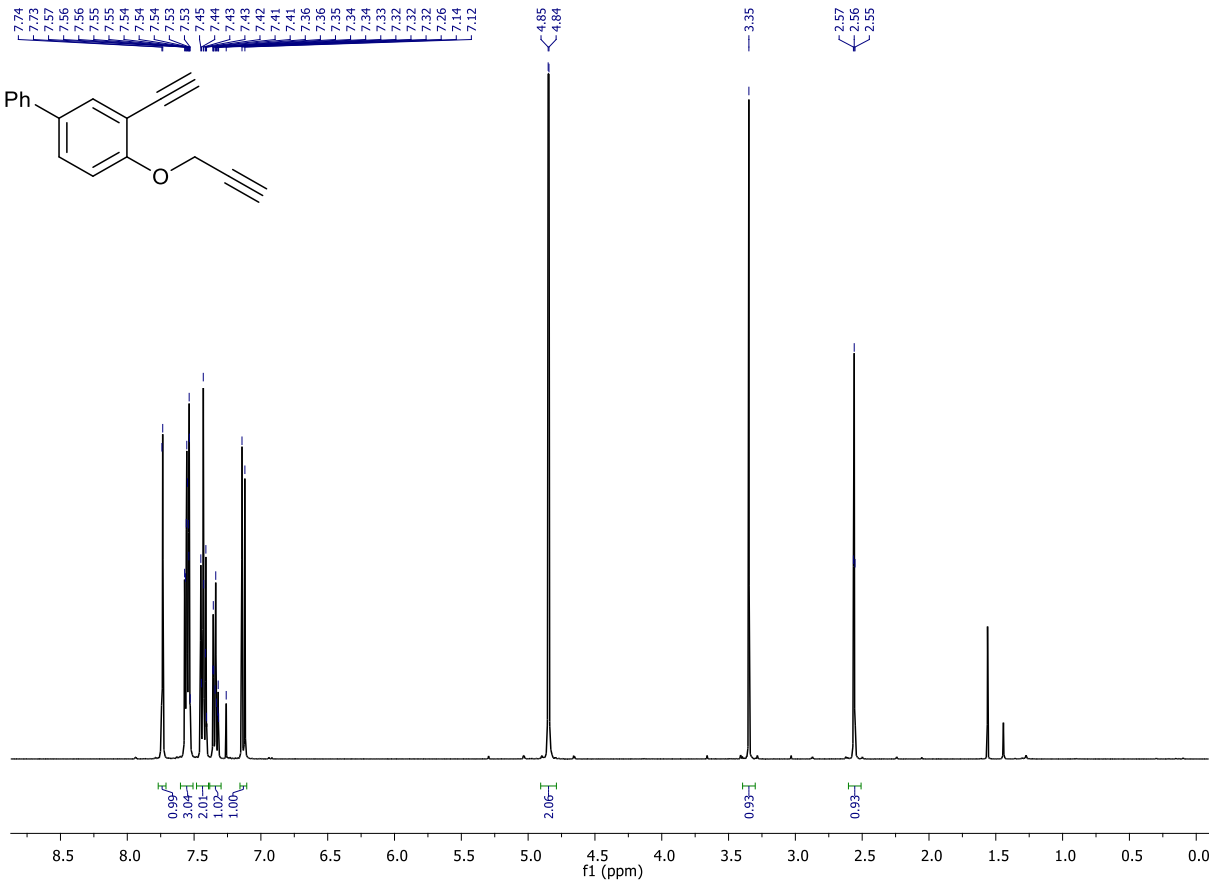
^{13}C NMR of **1c** (101 MHz, $CDCl_3$)



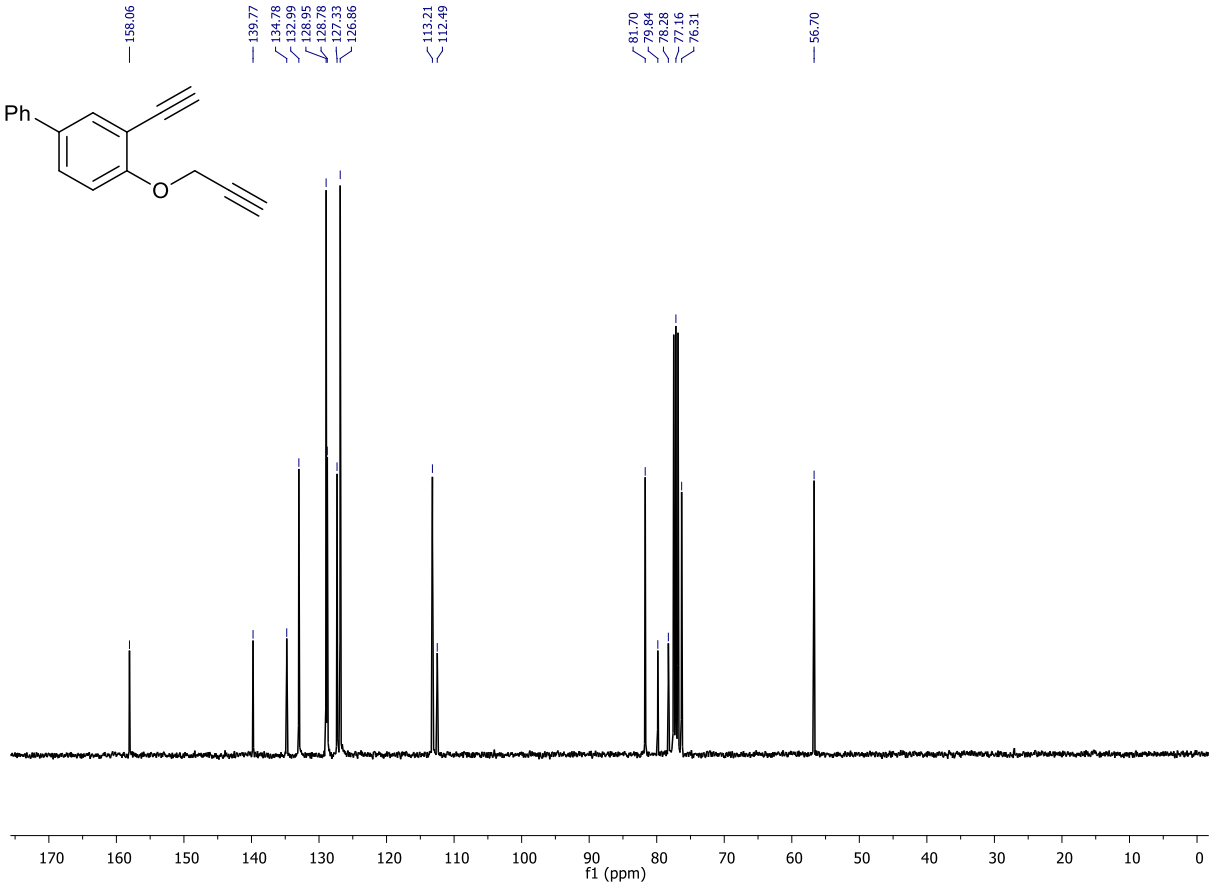
^{1}H NMR of **1d** (400 MHz, $CDCl_3$)



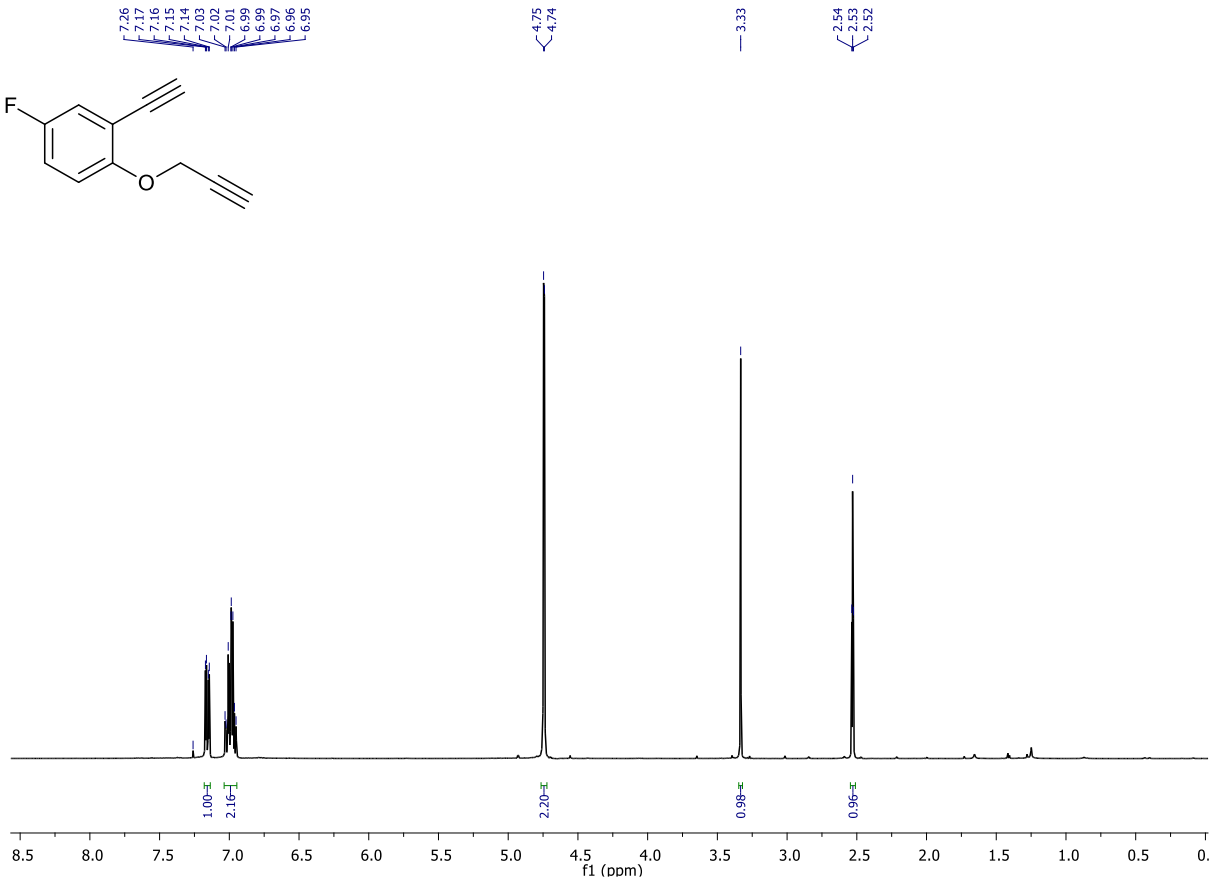
^{13}C NMR of **1d** (101 MHz, $CDCl_3$)



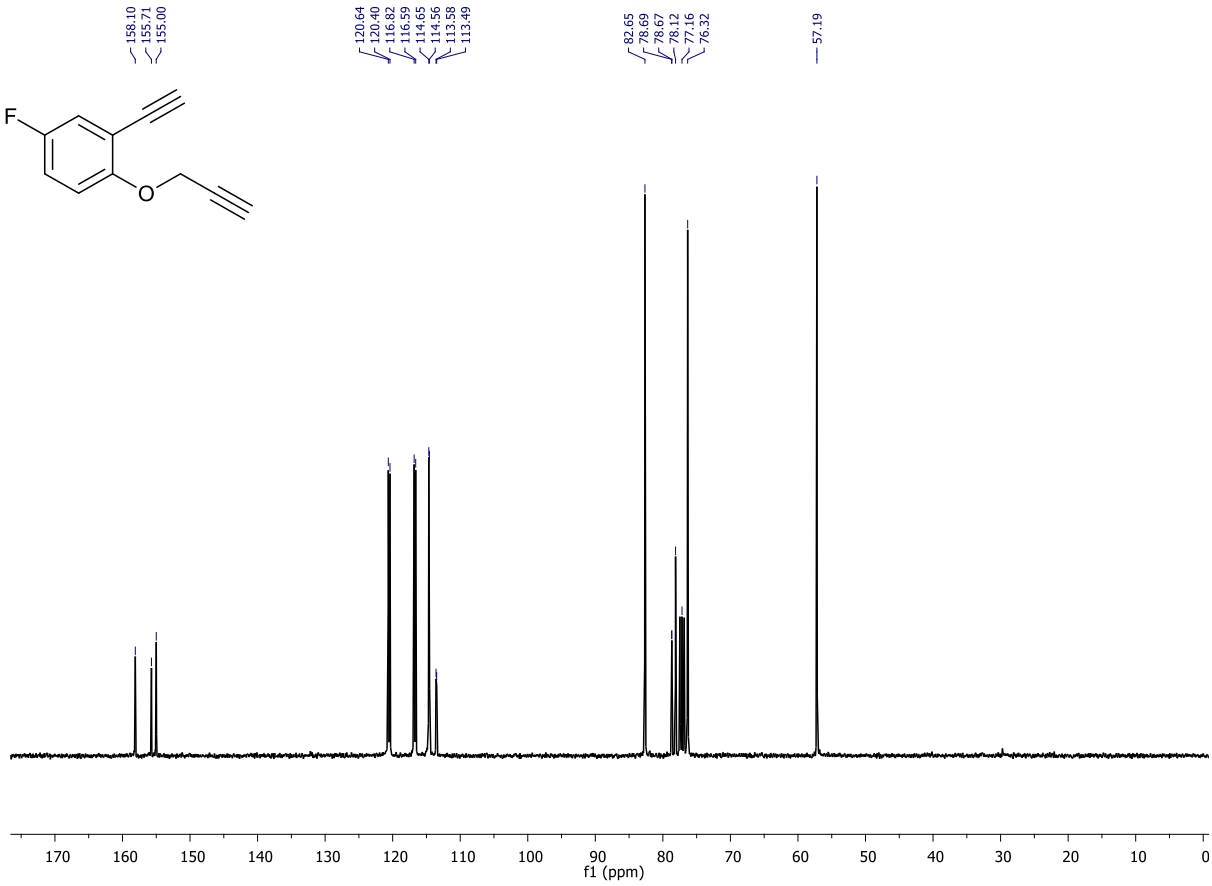
^{1}H NMR of **1e** (400 MHz, $CDCl_3$)



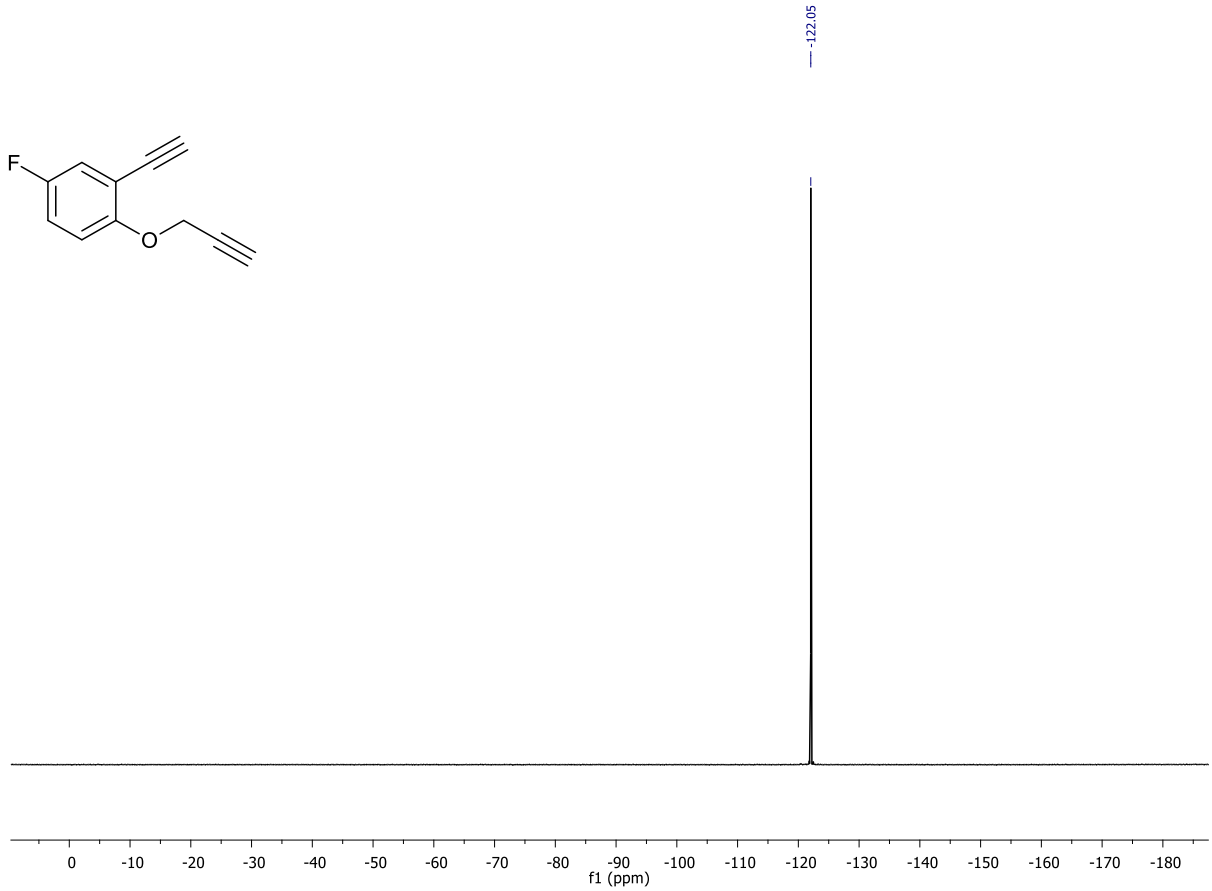
^{13}C NMR of **1e** (101 MHz, $CDCl_3$)



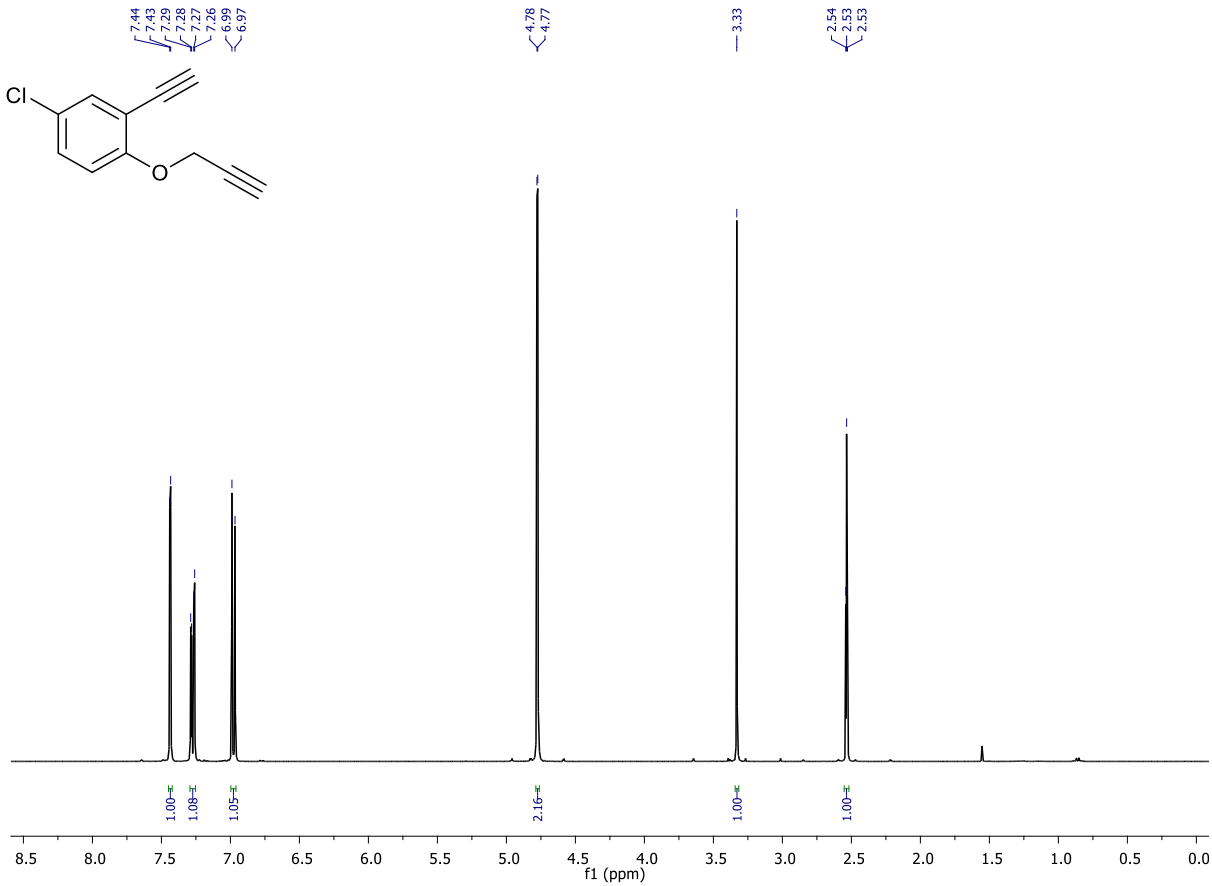
^{1}H NMR of **1f** (400 MHz, $CDCl_3$)



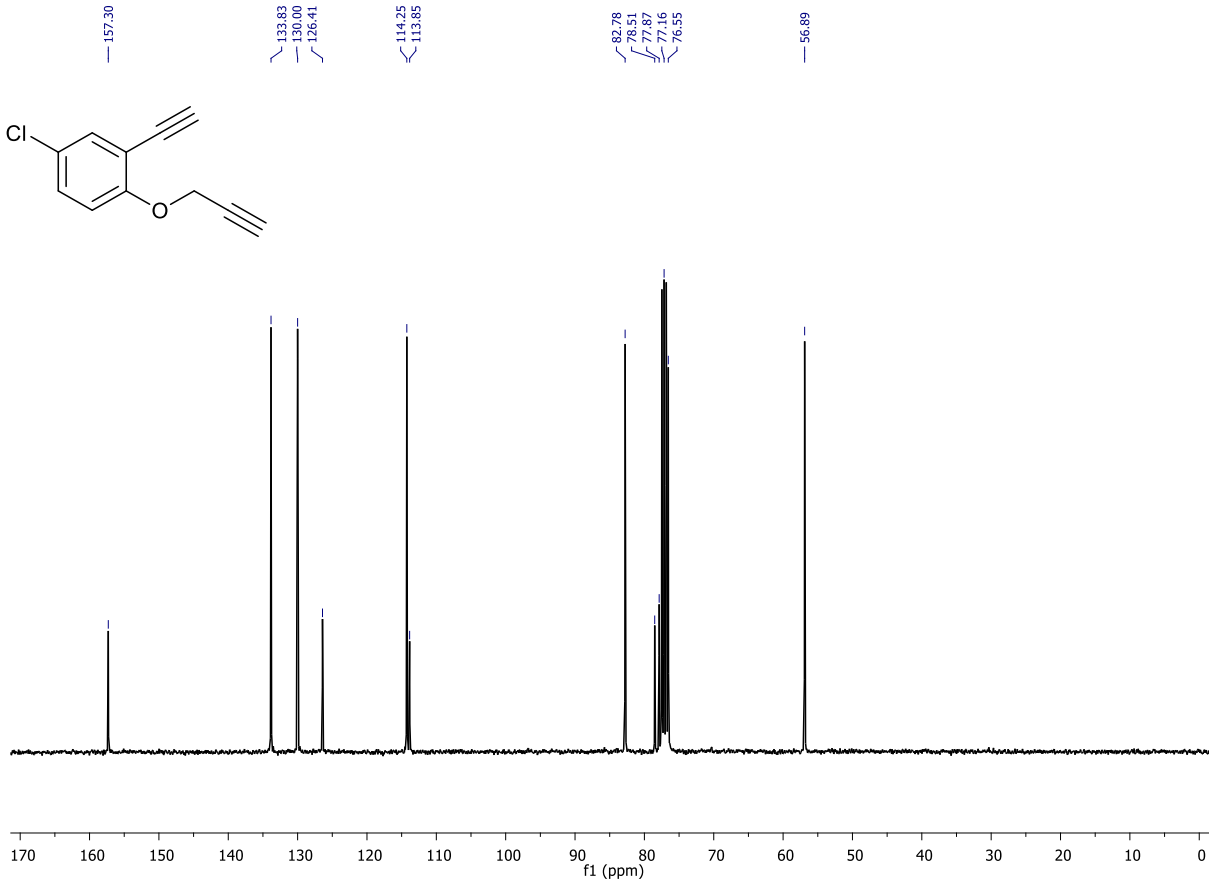
^{13}C NMR of **1f** (101 MHz, $CDCl_3$)



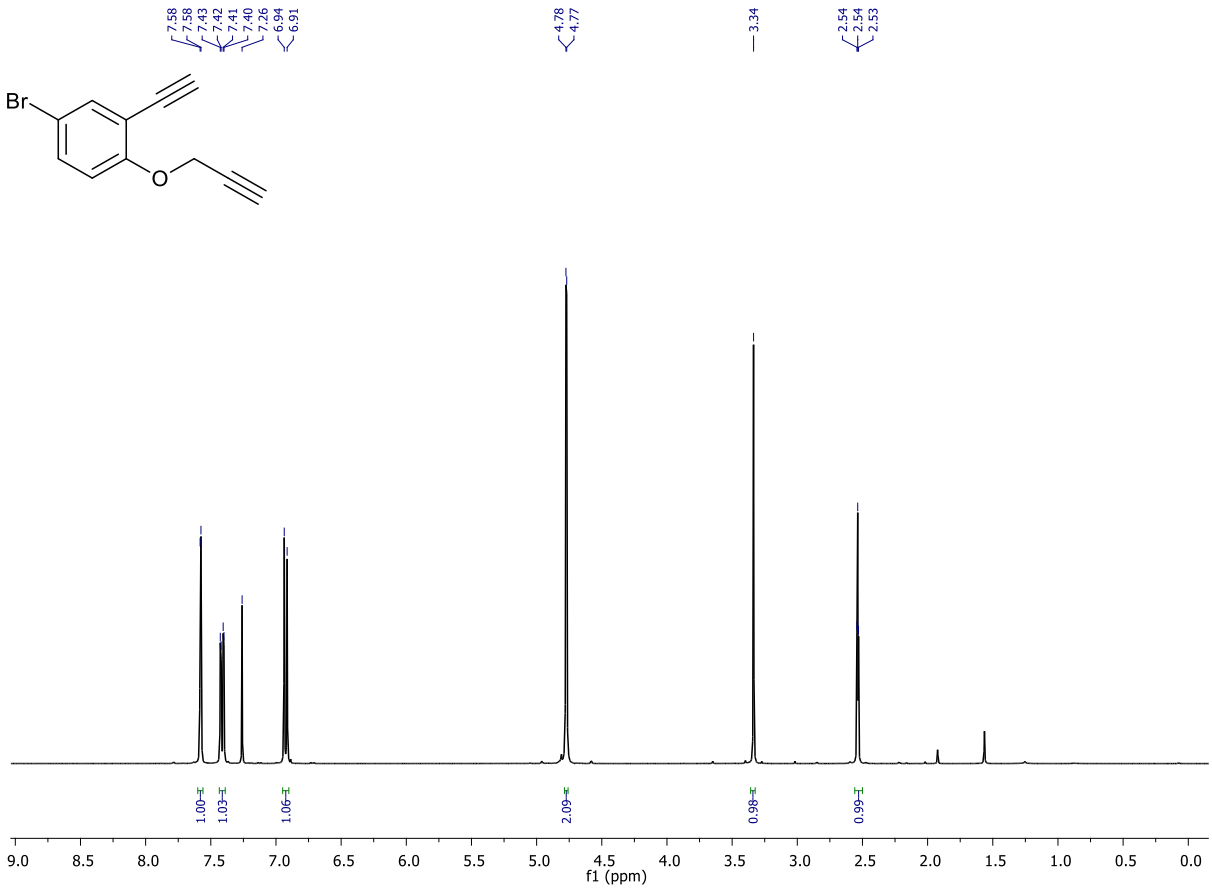
^{19}F NMR of **1f** (376.5 MHz, $CDCl_3$)



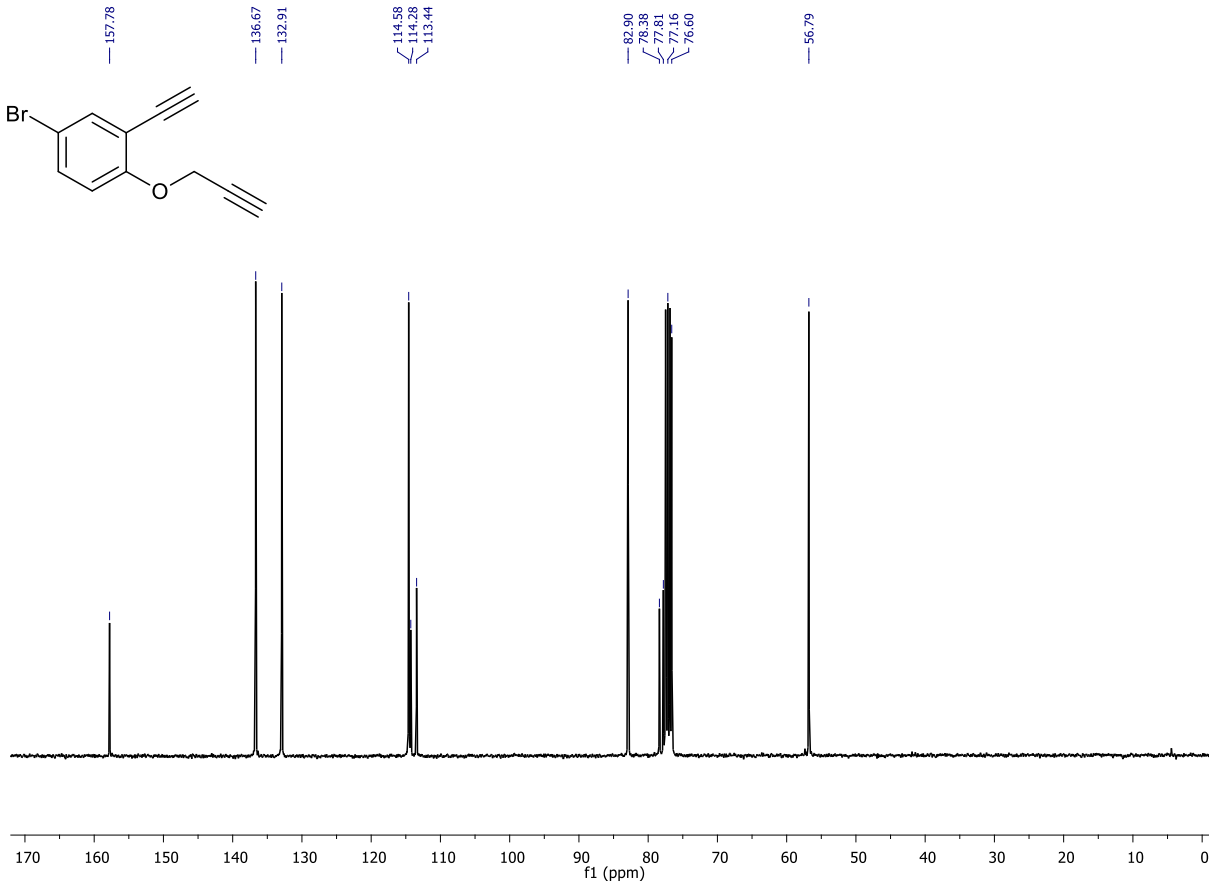
^{1}H NMR of **1g** (400 MHz, $CDCl_3$)



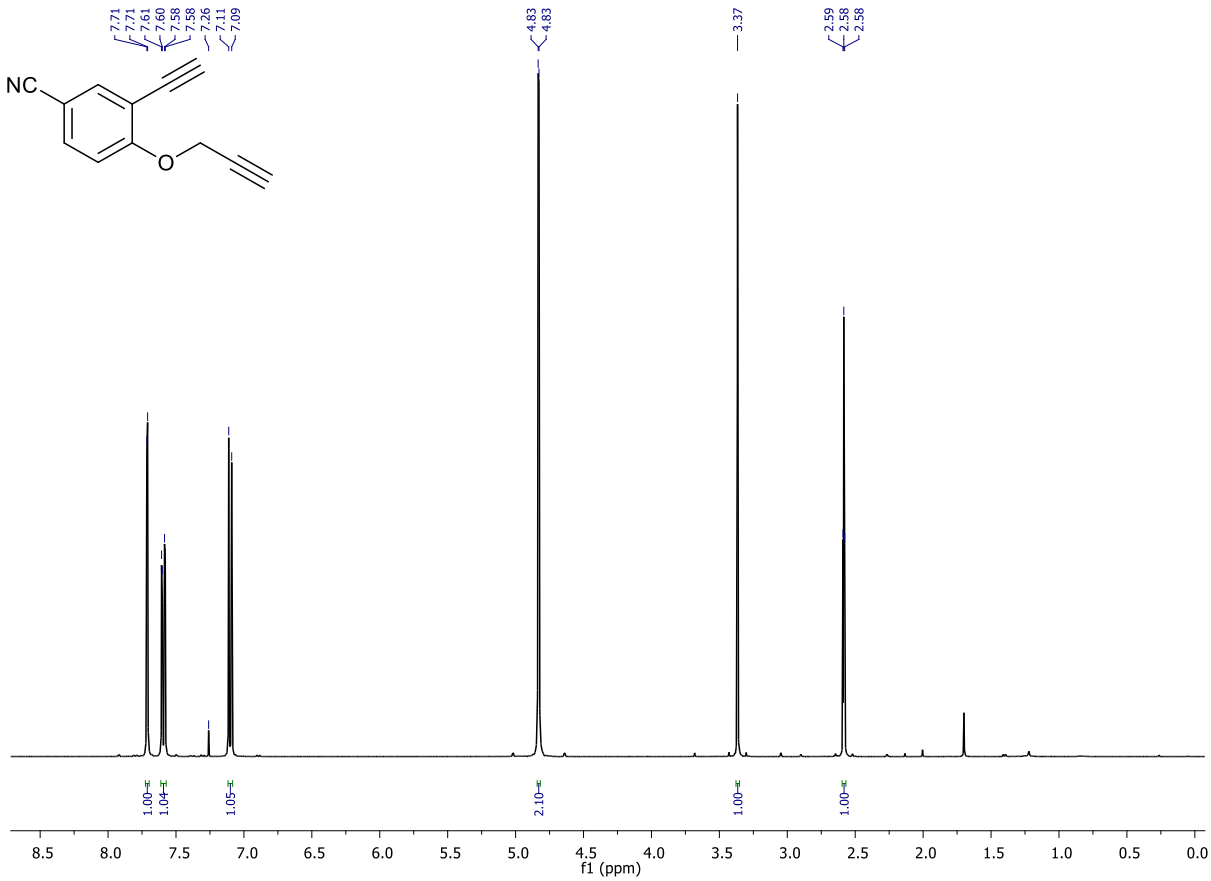
^{13}C NMR of **1g** (101 MHz, $CDCl_3$)



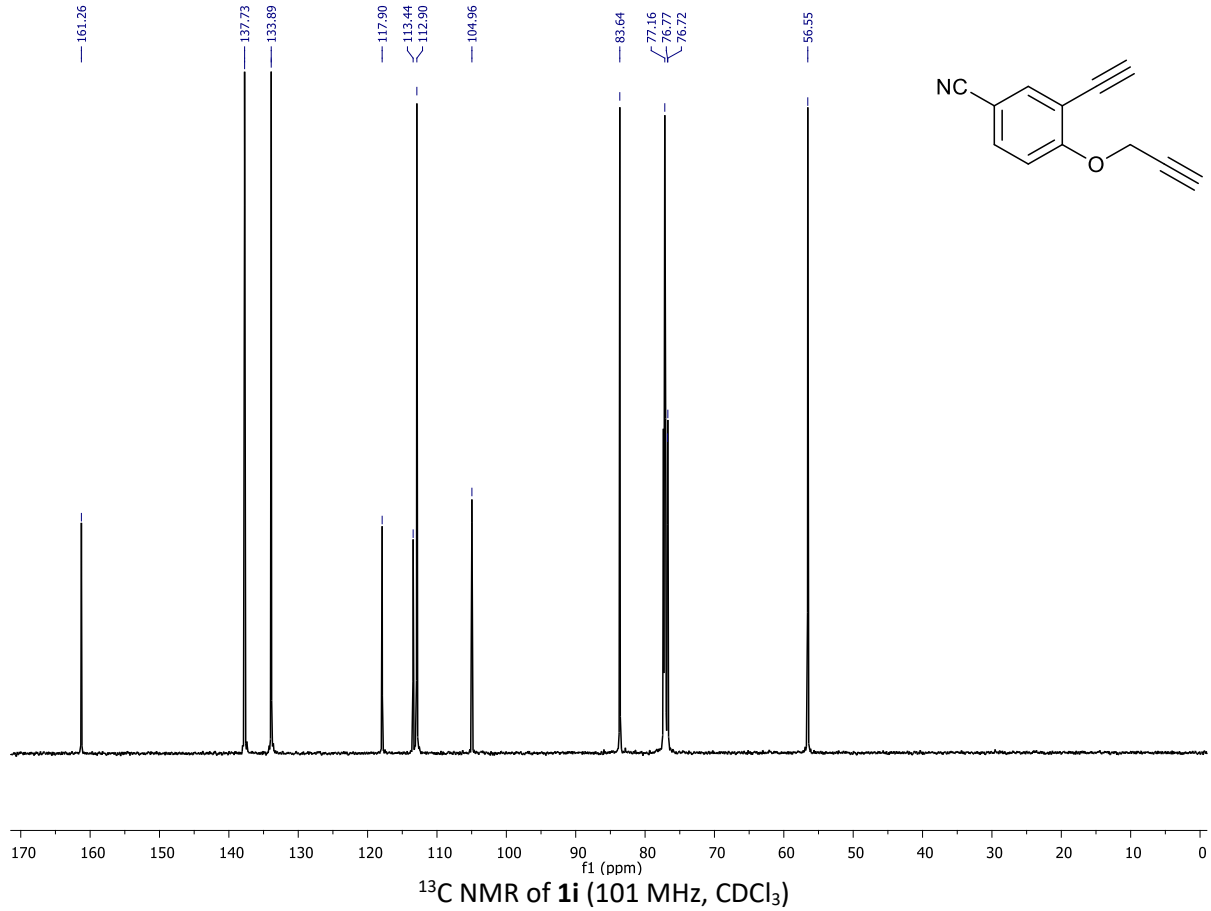
^{1}H NMR of **1h** (400 MHz, $CDCl_3$)



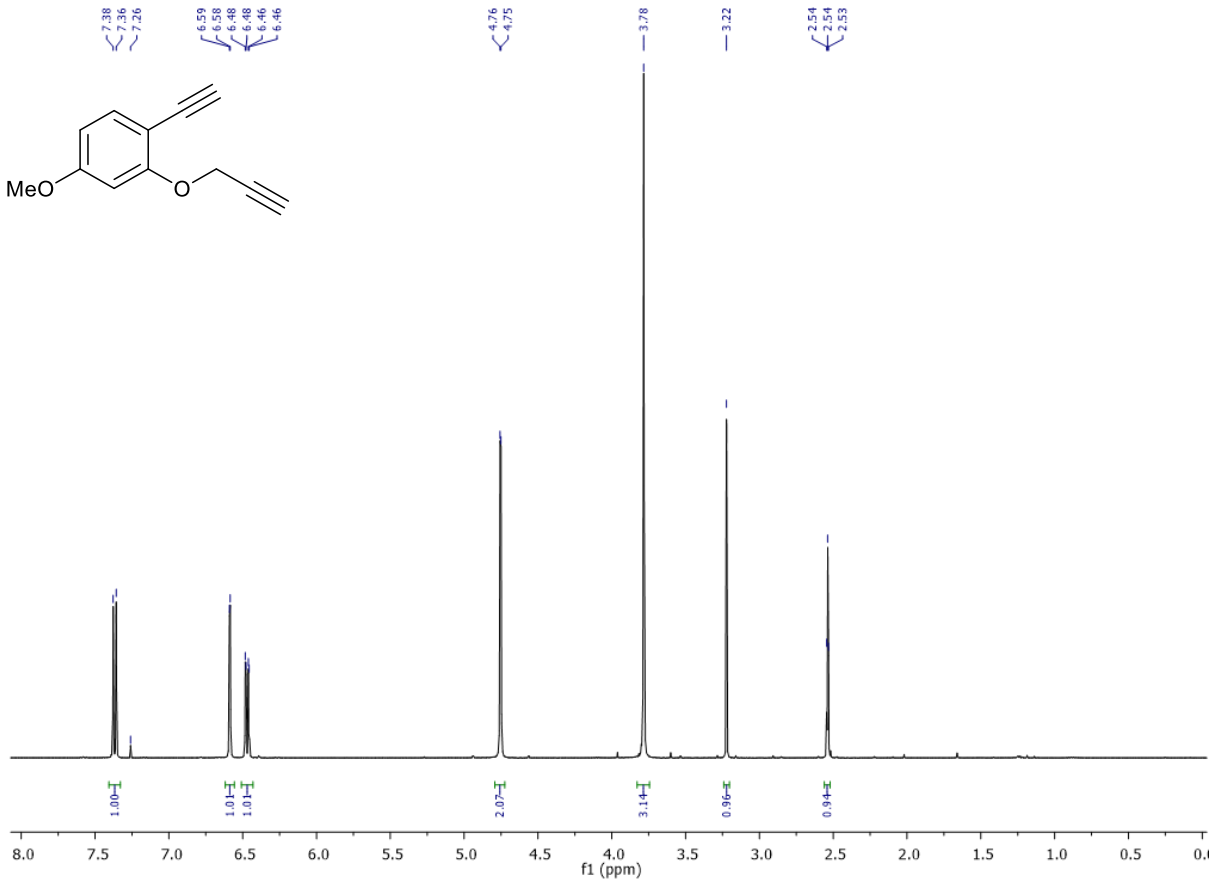
^{13}C NMR of **1h** (101 MHz, $CDCl_3$)



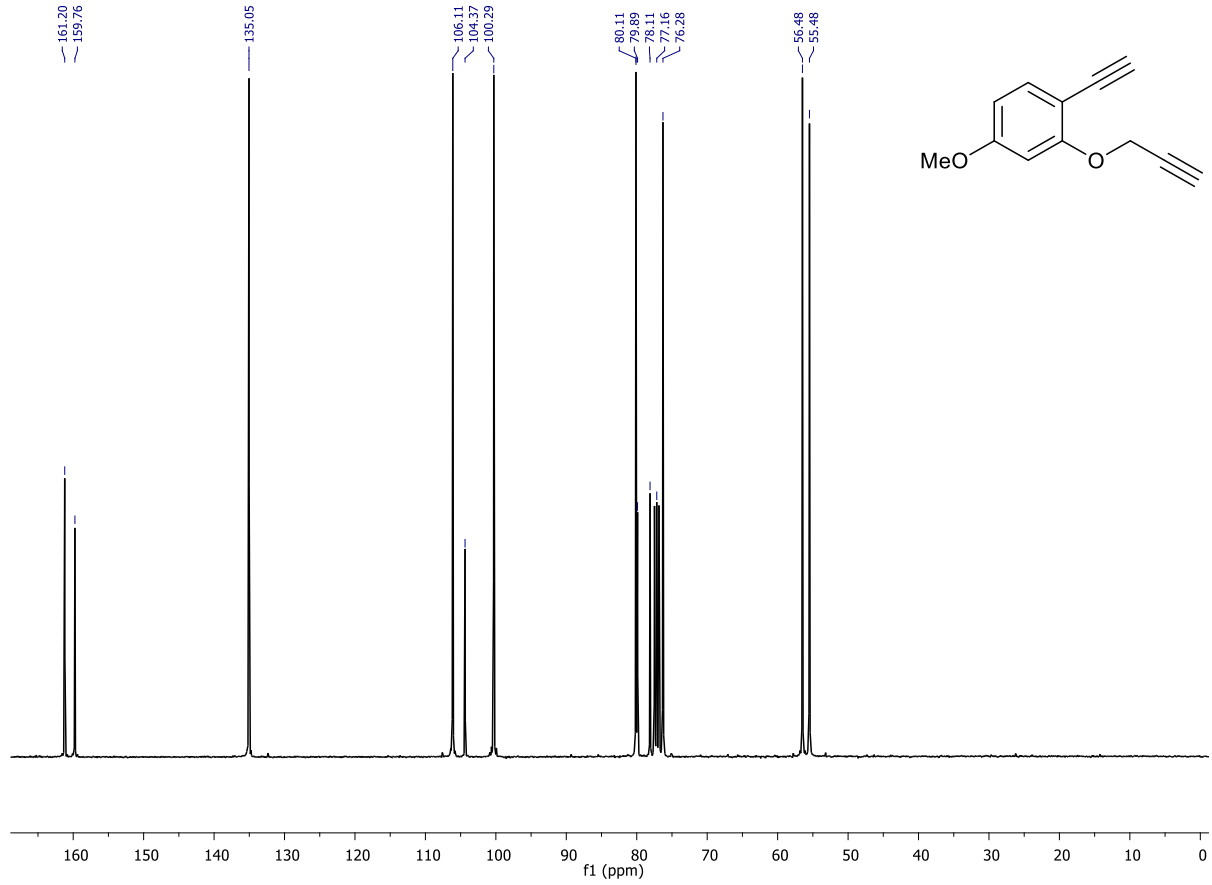
^{1}H NMR of **1i** (400 MHz, $CDCl_3$)



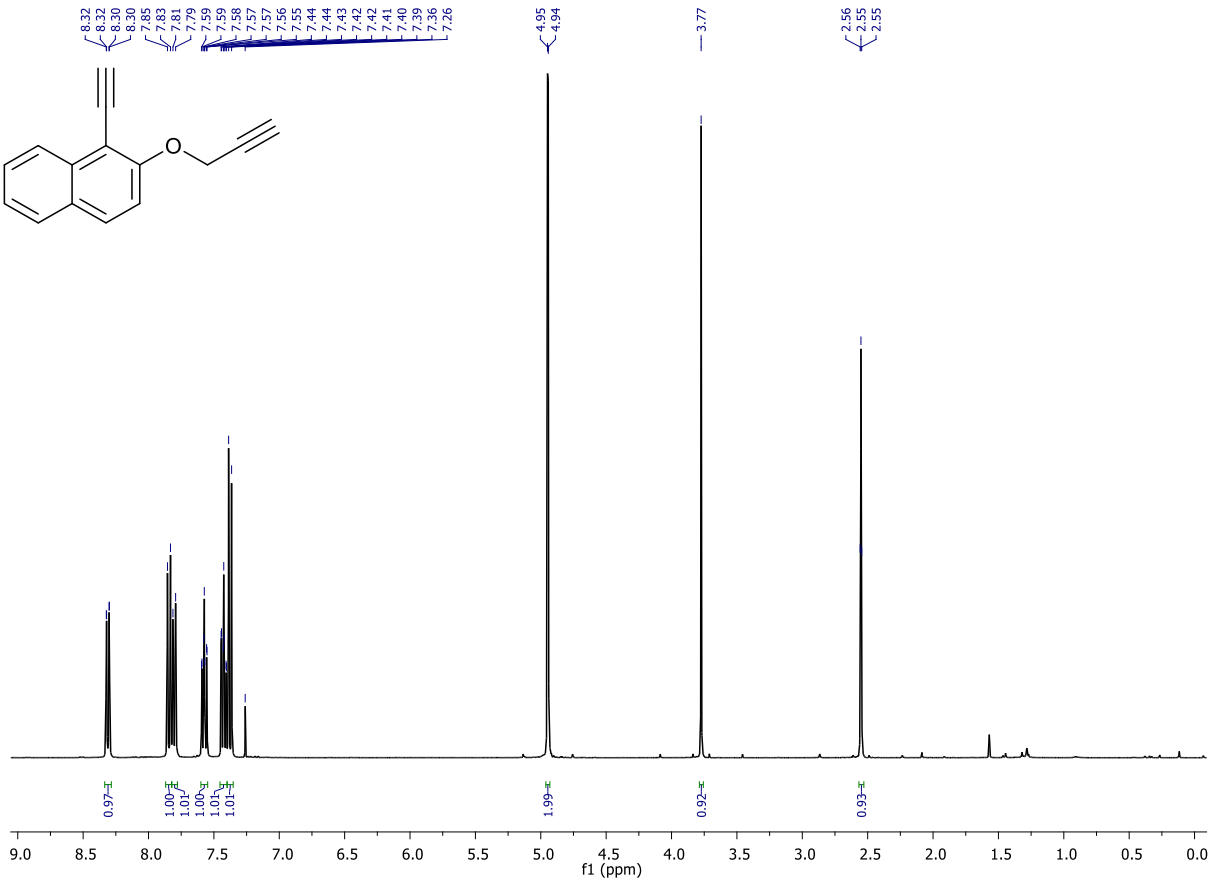
^{13}C NMR of **1i** (101 MHz, $CDCl_3$)



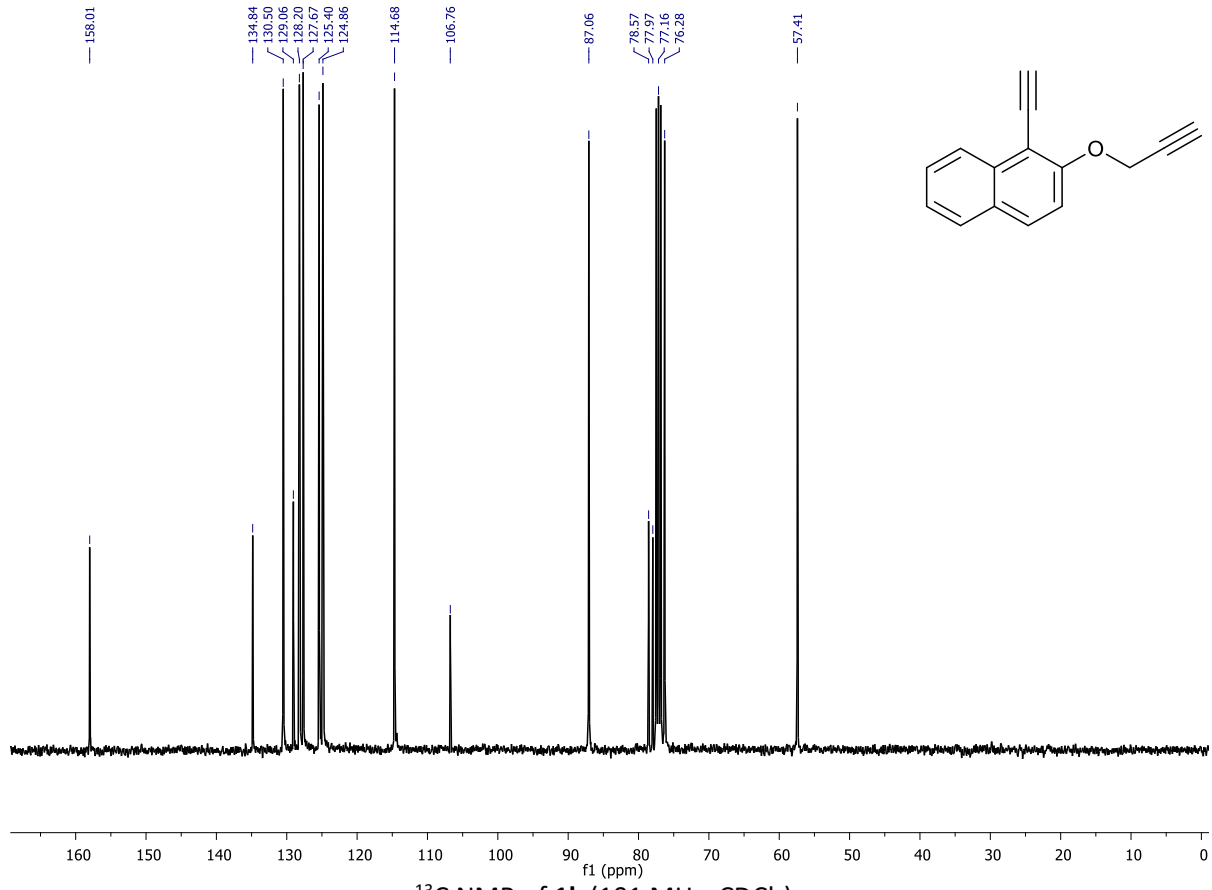
^{1}H NMR of **1j** (400 MHz, $CDCl_3$)



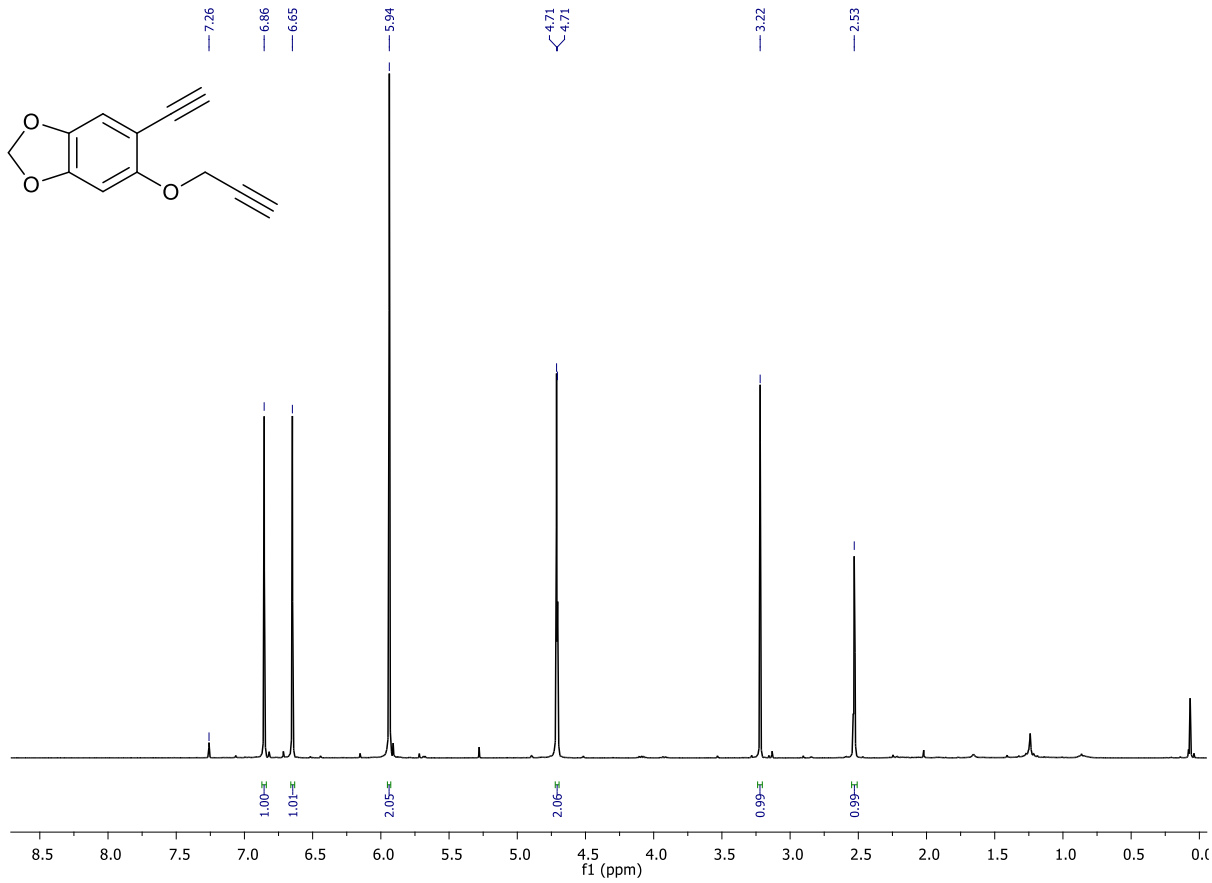
^{13}C NMR of **1j** (101 MHz, $CDCl_3$)



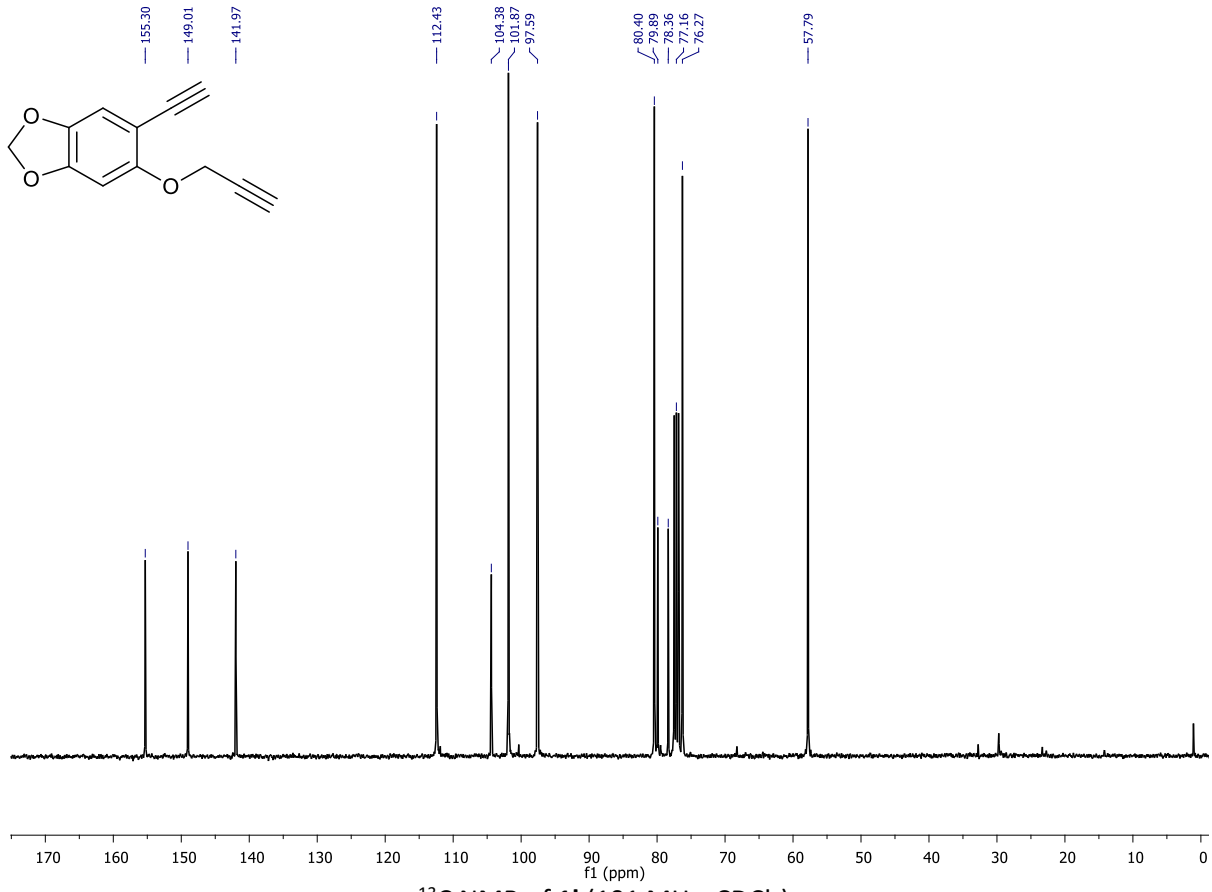
^{1}H NMR of **1k** (400 MHz, $CDCl_3$)



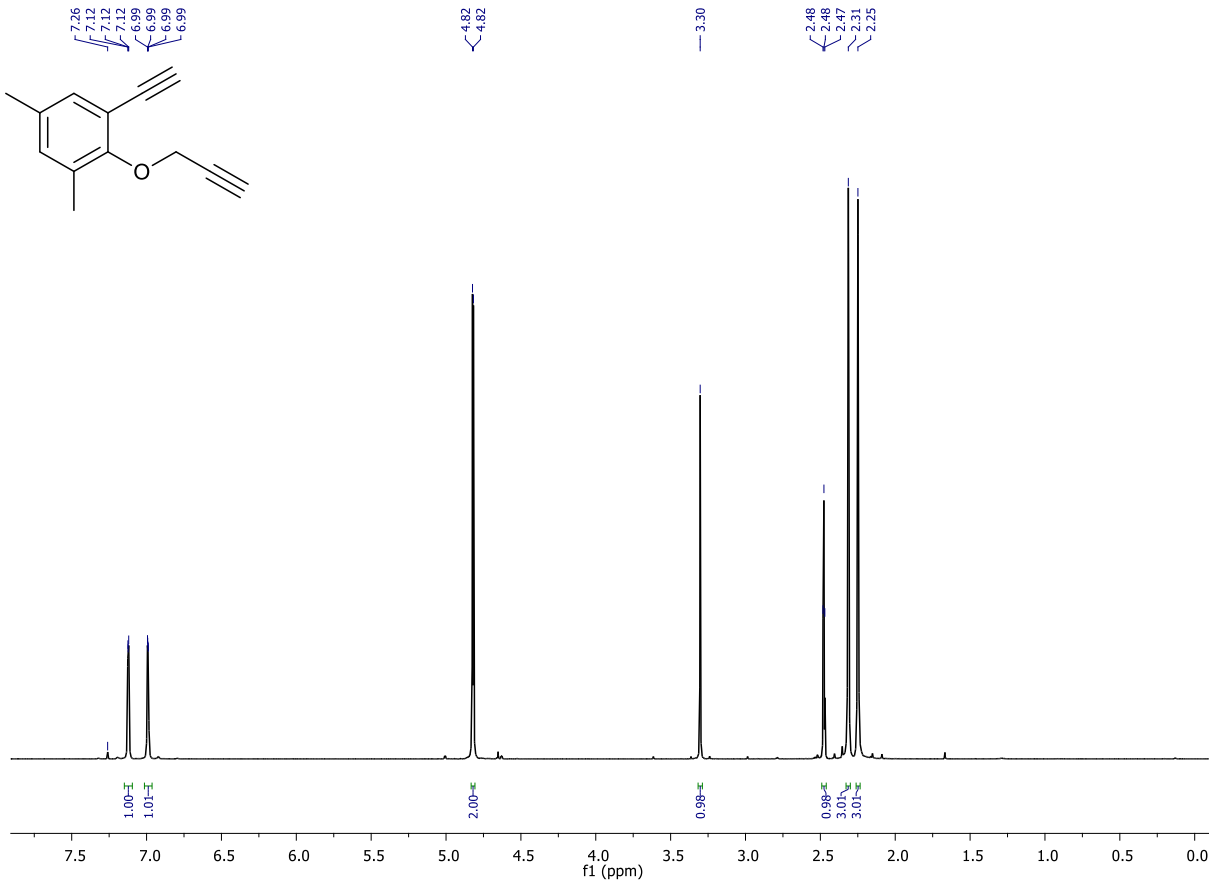
^{13}C NMR of **1k** (101 MHz, $CDCl_3$)



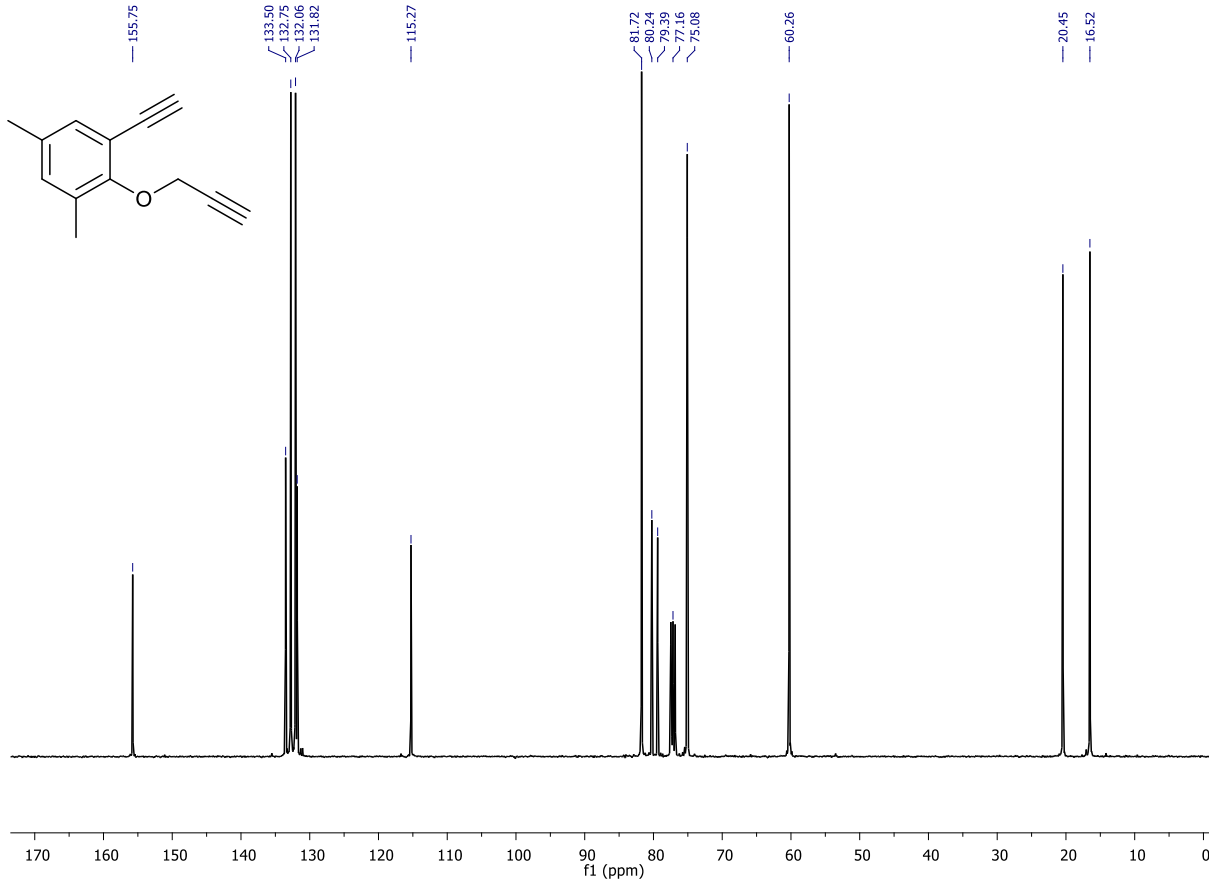
^{1}H NMR of **1l** (400 MHz, $CDCl_3$)



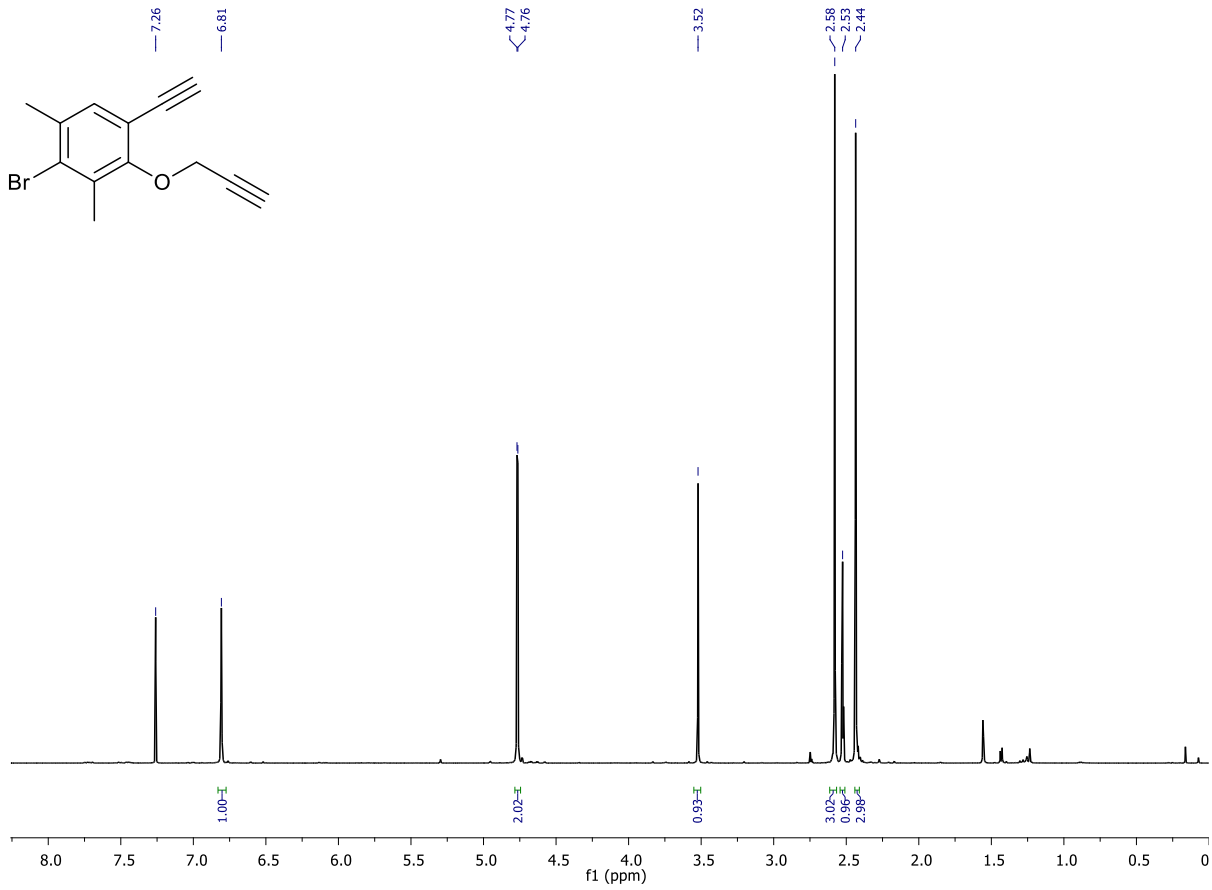
^{13}C NMR of **1l** (101 MHz, $CDCl_3$)



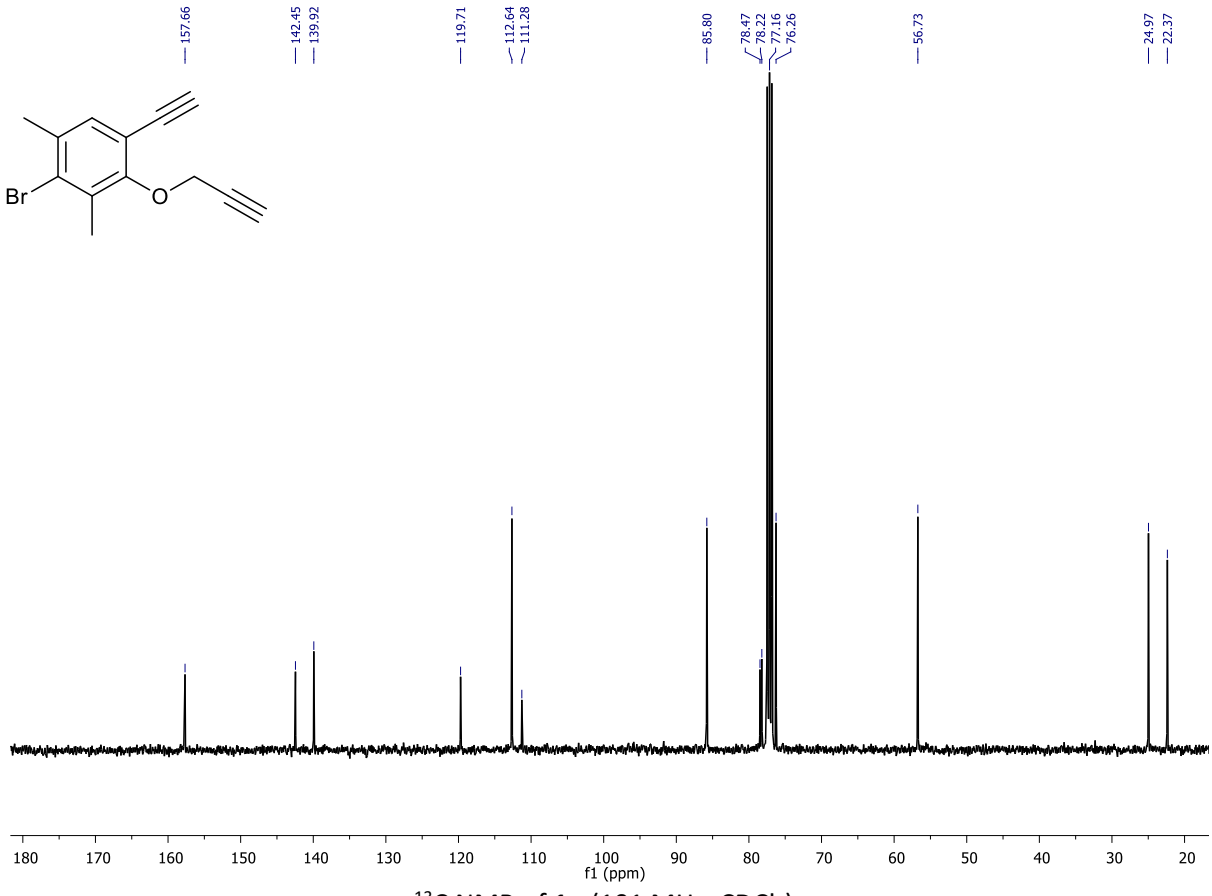
^{1}H NMR of **1m** (400 MHz, $CDCl_3$)



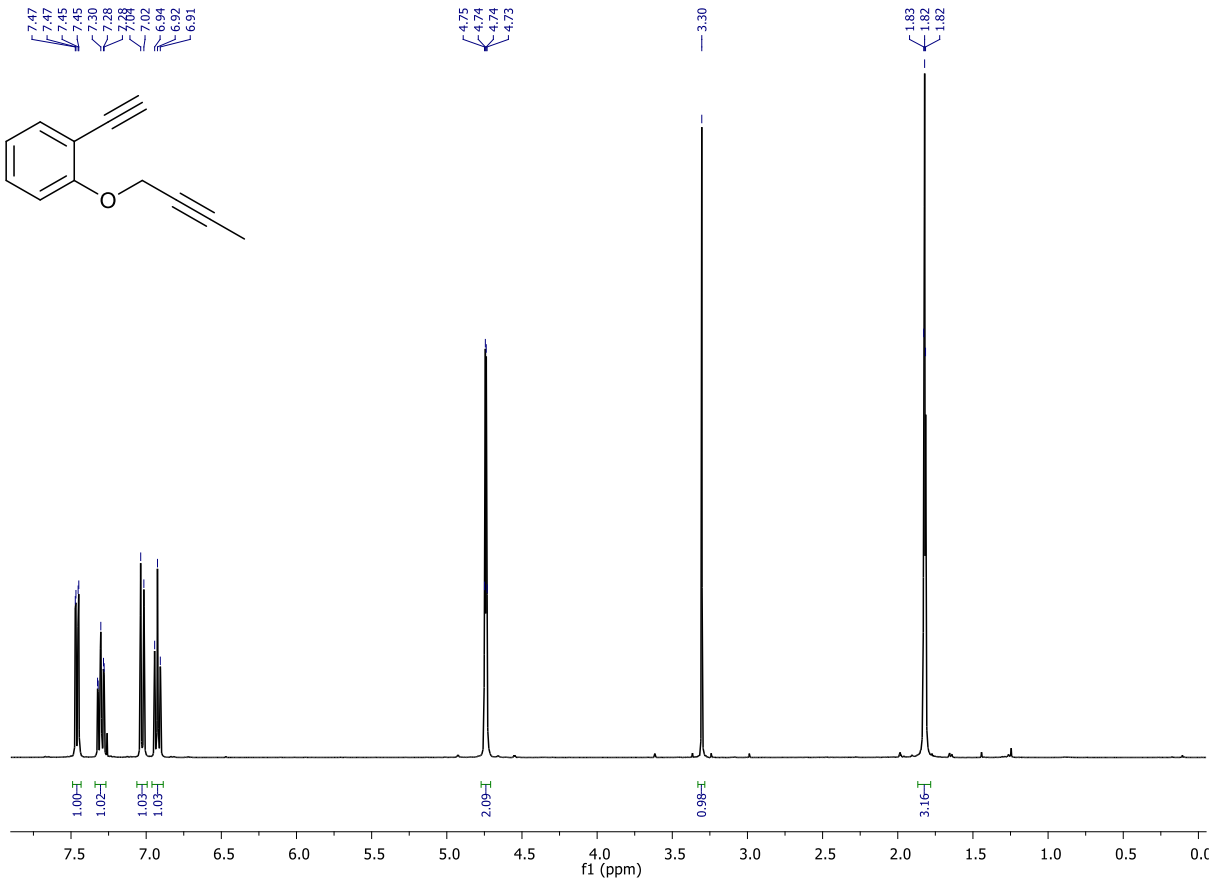
^{13}C NMR of **1m** (101 MHz, $CDCl_3$)



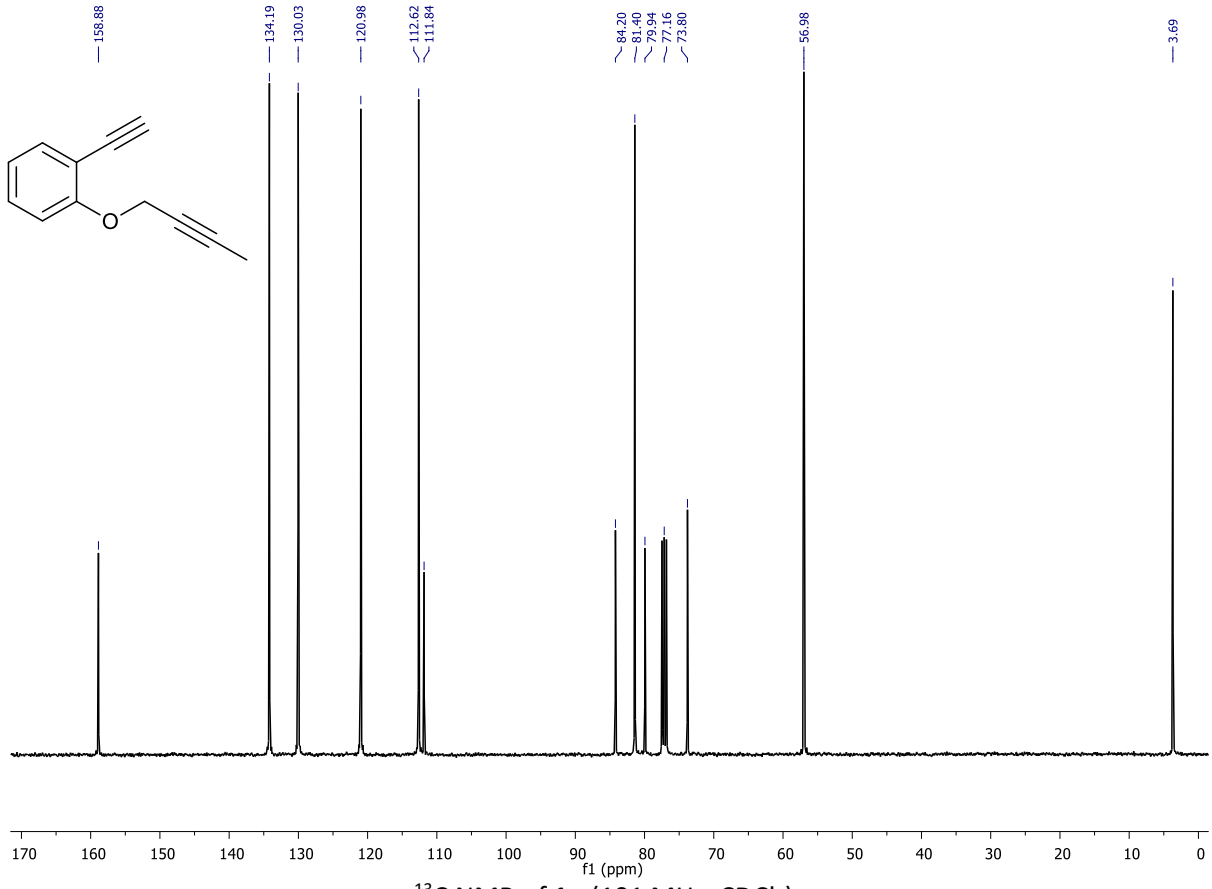
^{1}H NMR of **1n** (400 MHz, $CDCl_3$)



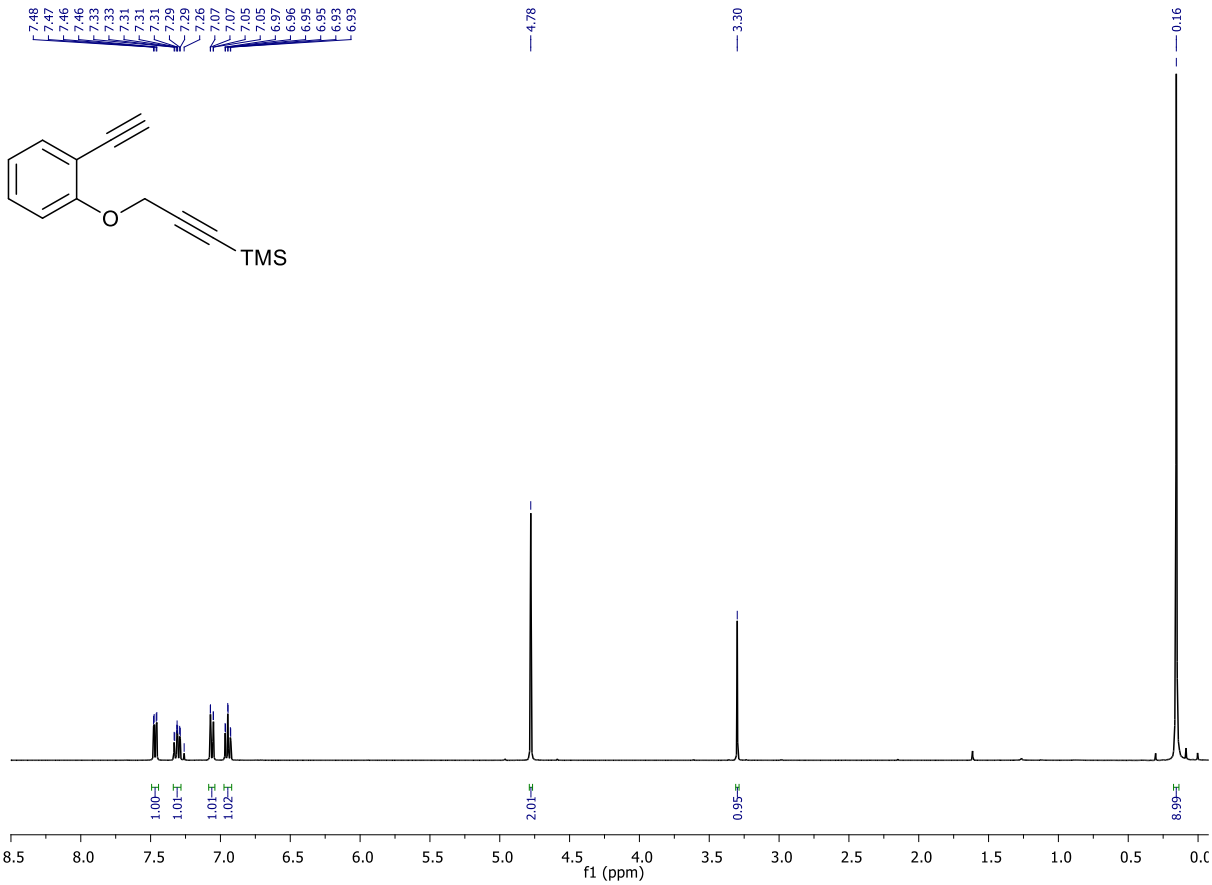
^{13}C NMR of **1n** (101 MHz, $CDCl_3$)



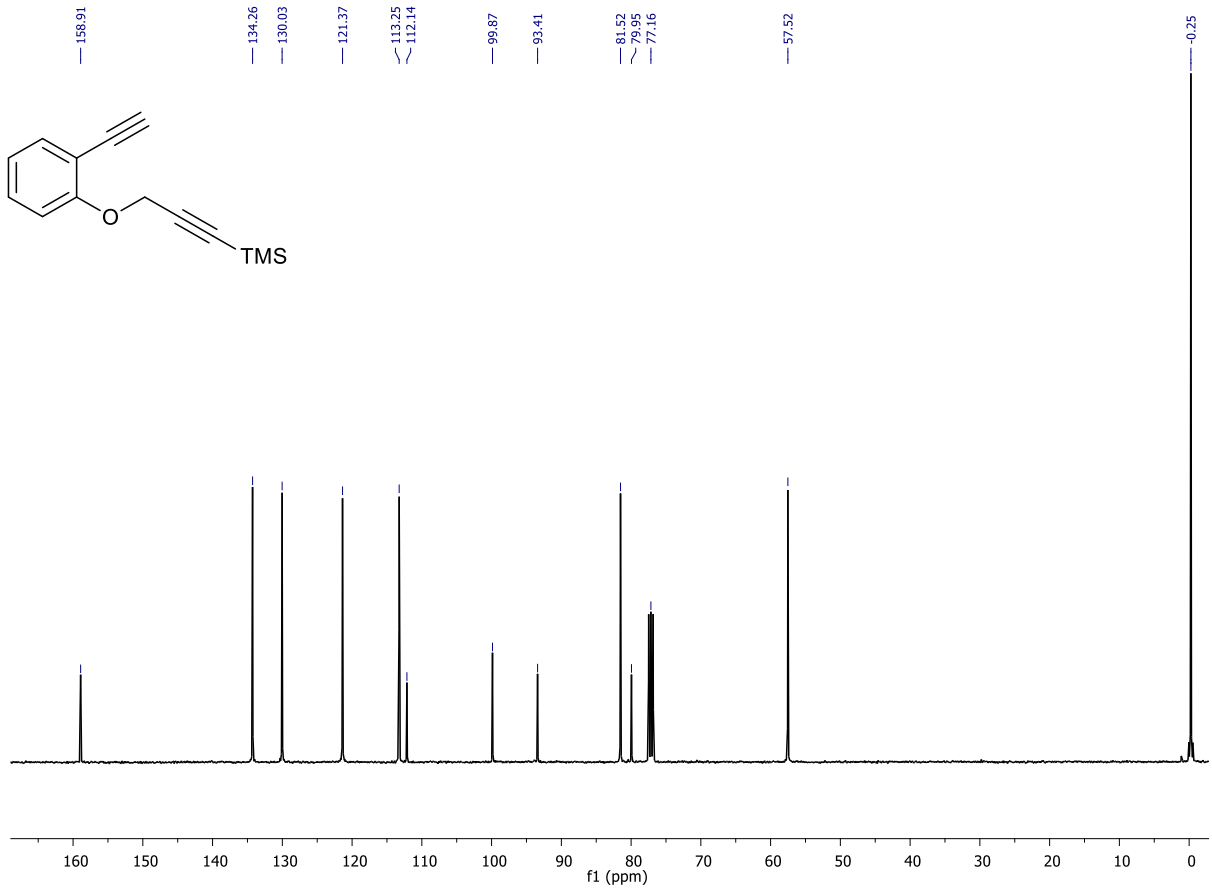
^{1}H NMR of **1o** (400 MHz, $CDCl_3$)



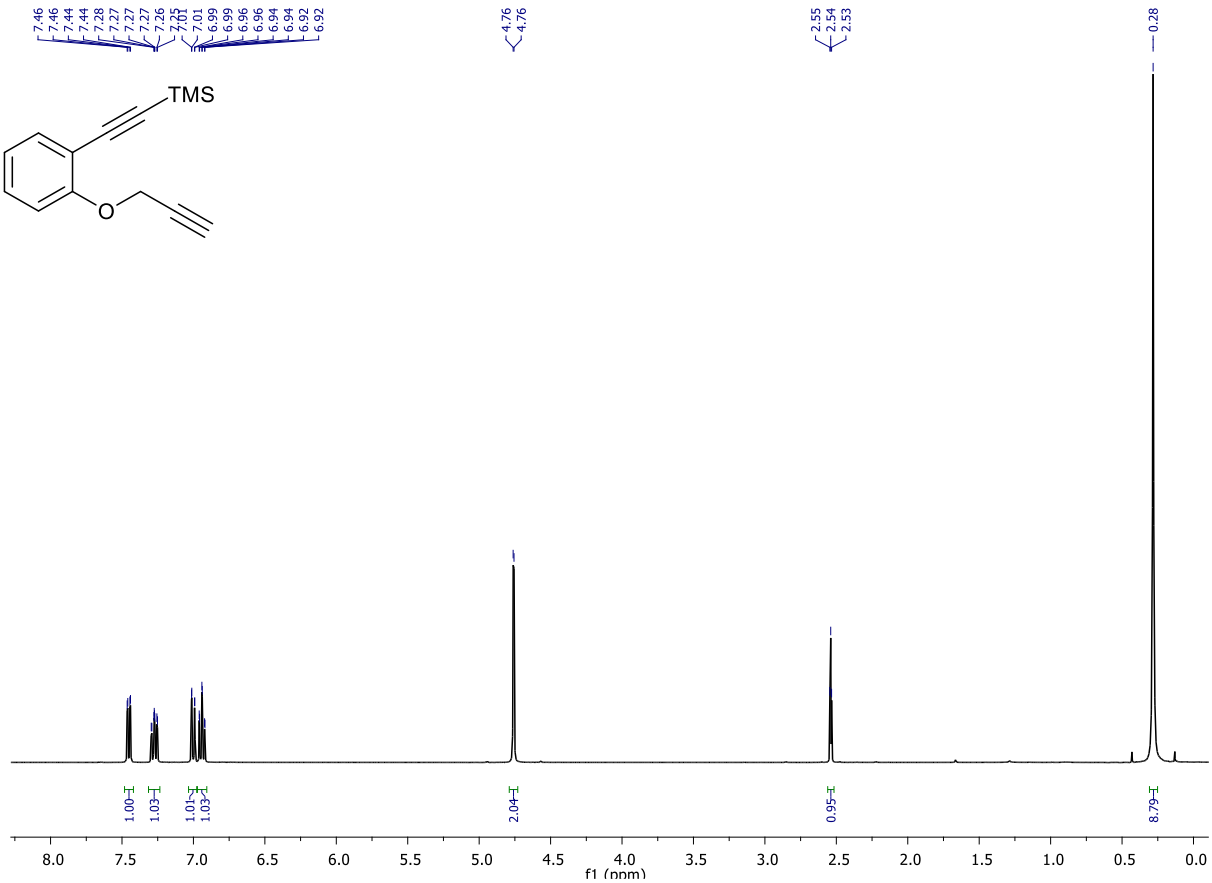
^{13}C NMR of **1o** (101 MHz, $CDCl_3$)



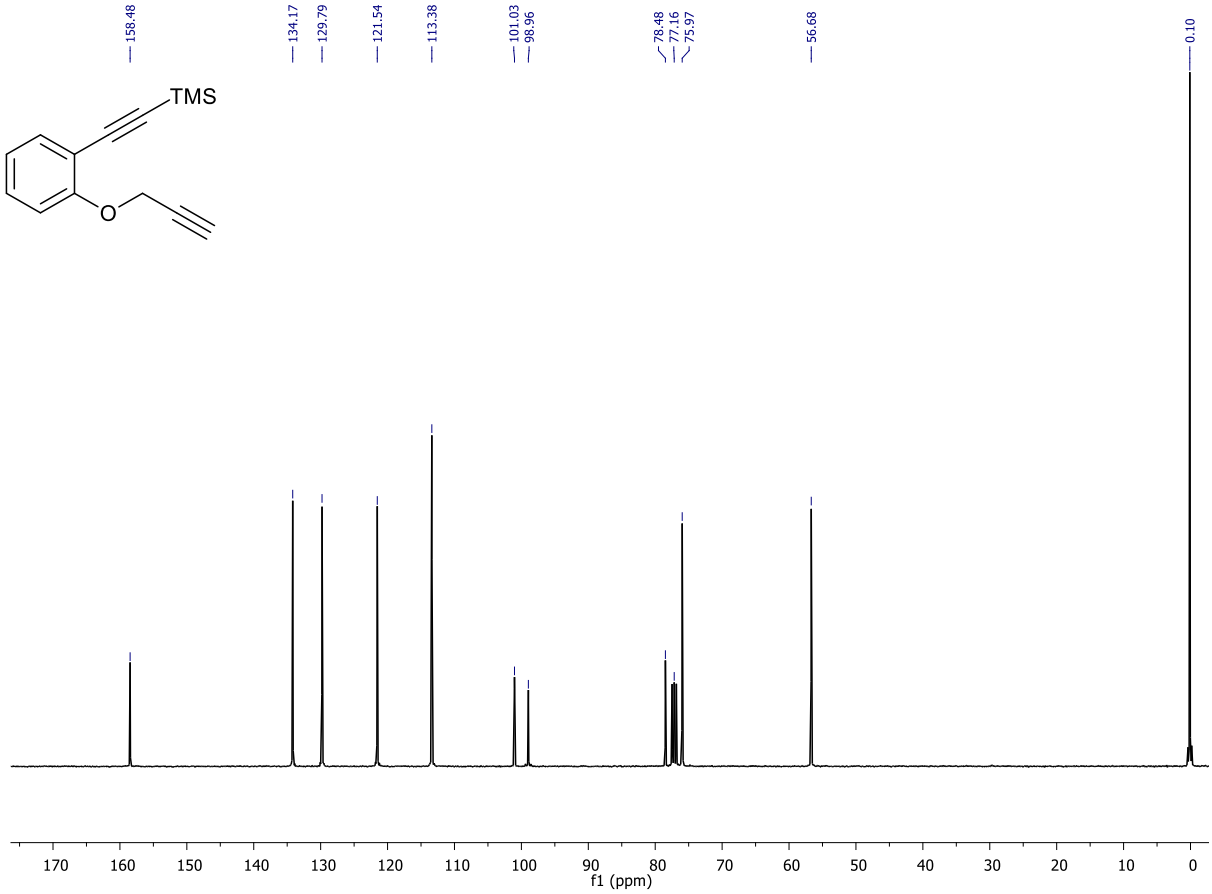
^{1}H NMR of **1p** (400 MHz, $CDCl_3$)



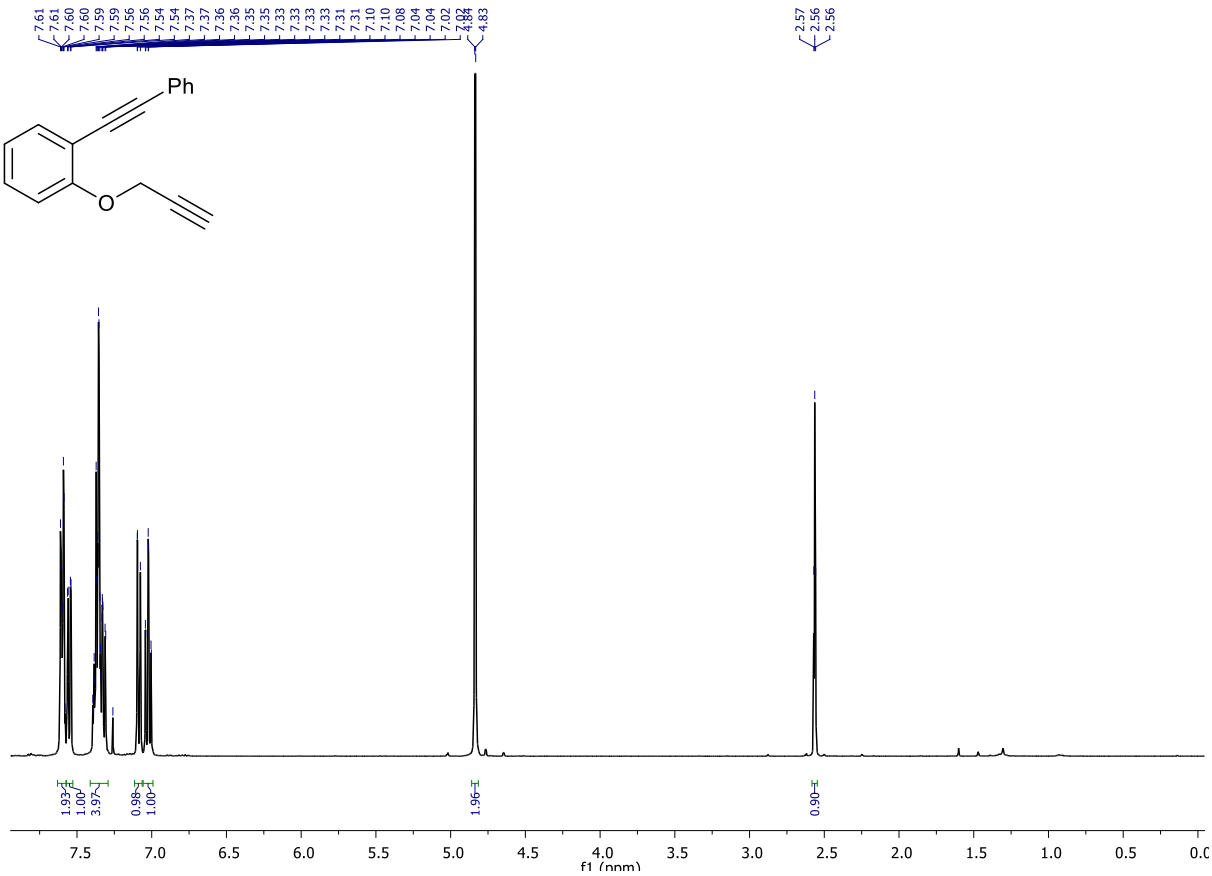
^{13}C NMR of **1p** (101 MHz, $CDCl_3$)



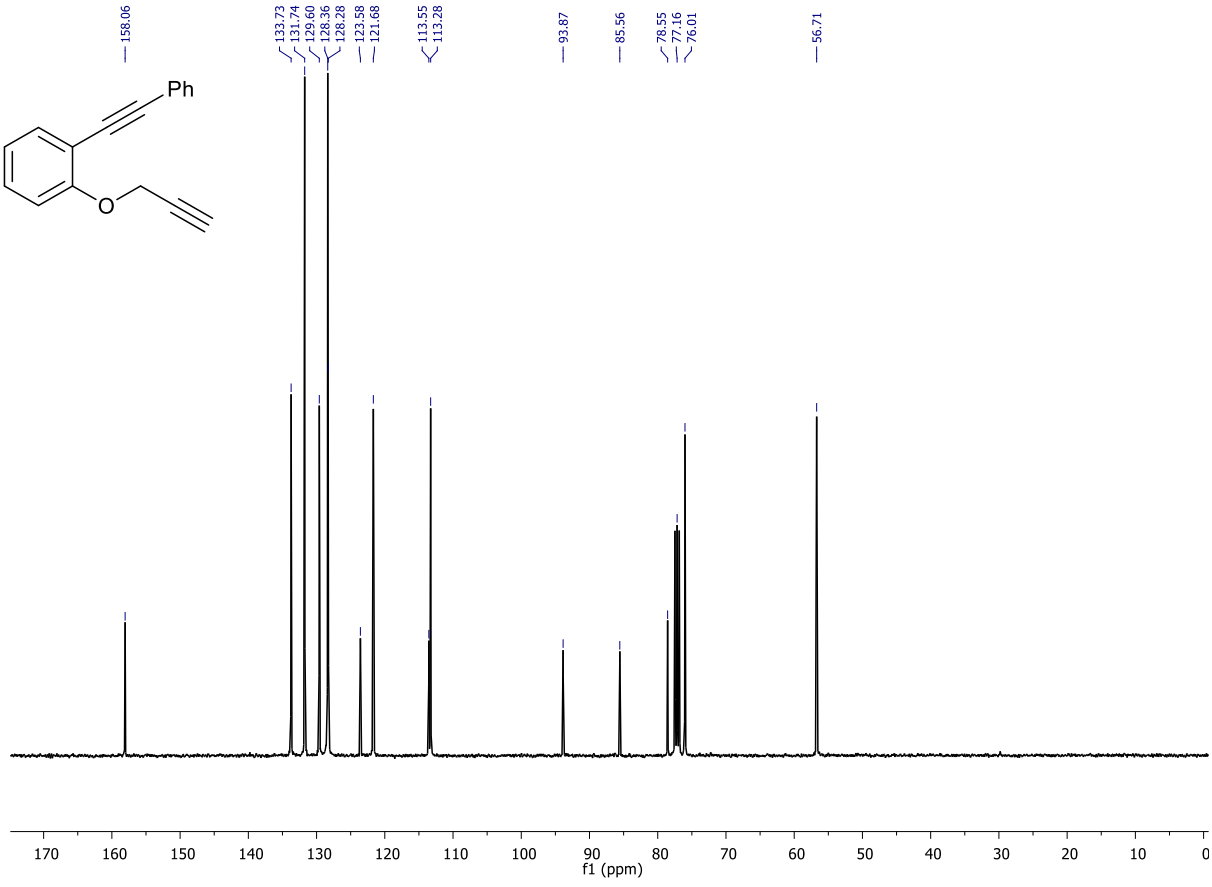
^{1}H NMR of **1q** (400 MHz, $CDCl_3$)



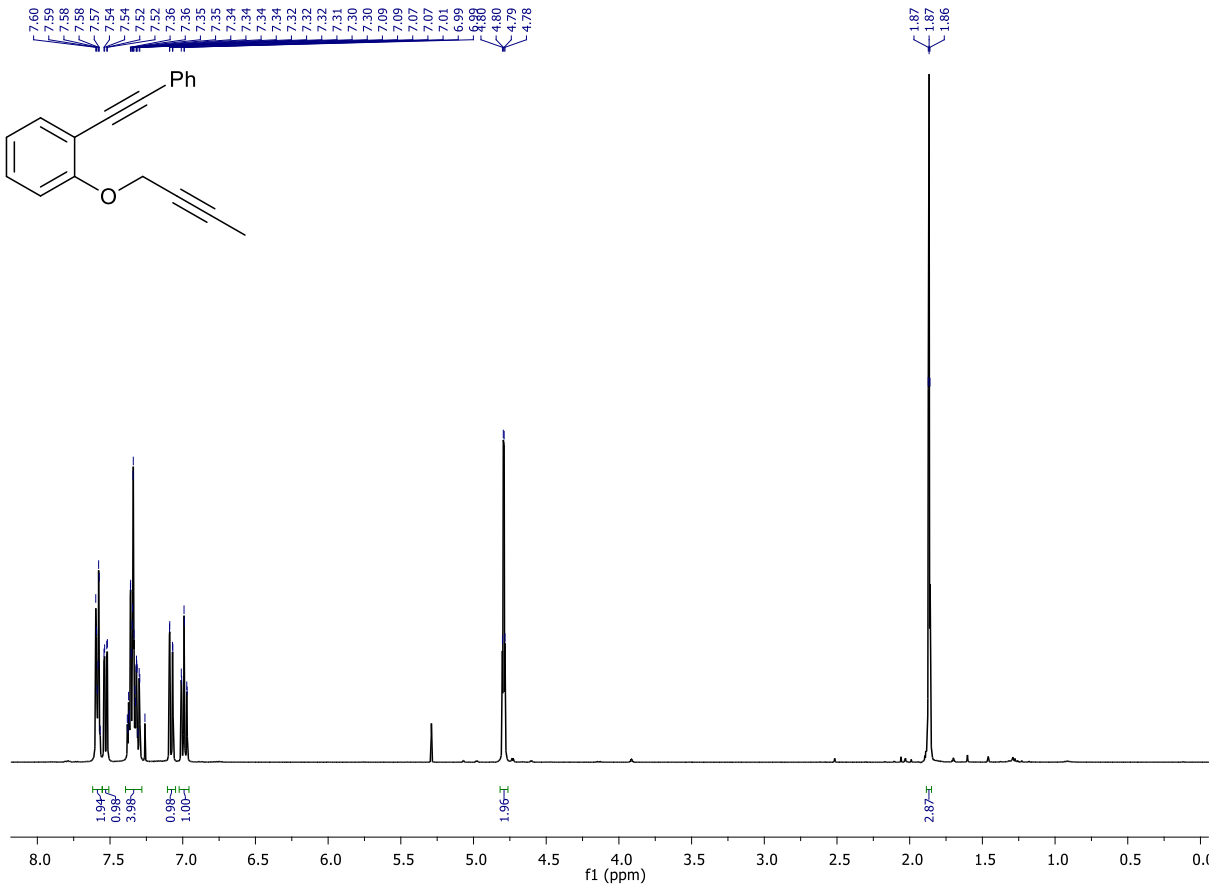
^{13}C NMR of **1q** (101 MHz, $CDCl_3$)



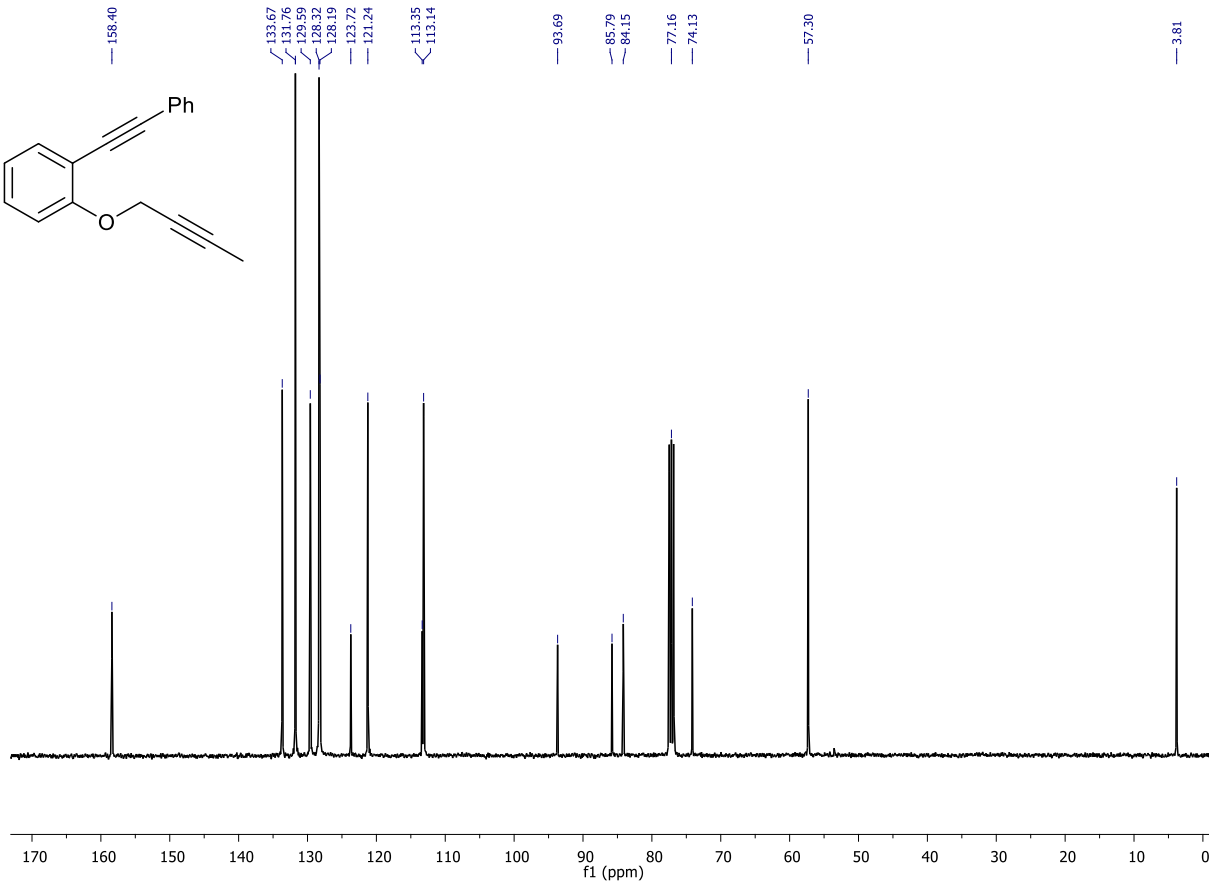
^{1}H NMR of **1r** (400 MHz, $CDCl_3$)



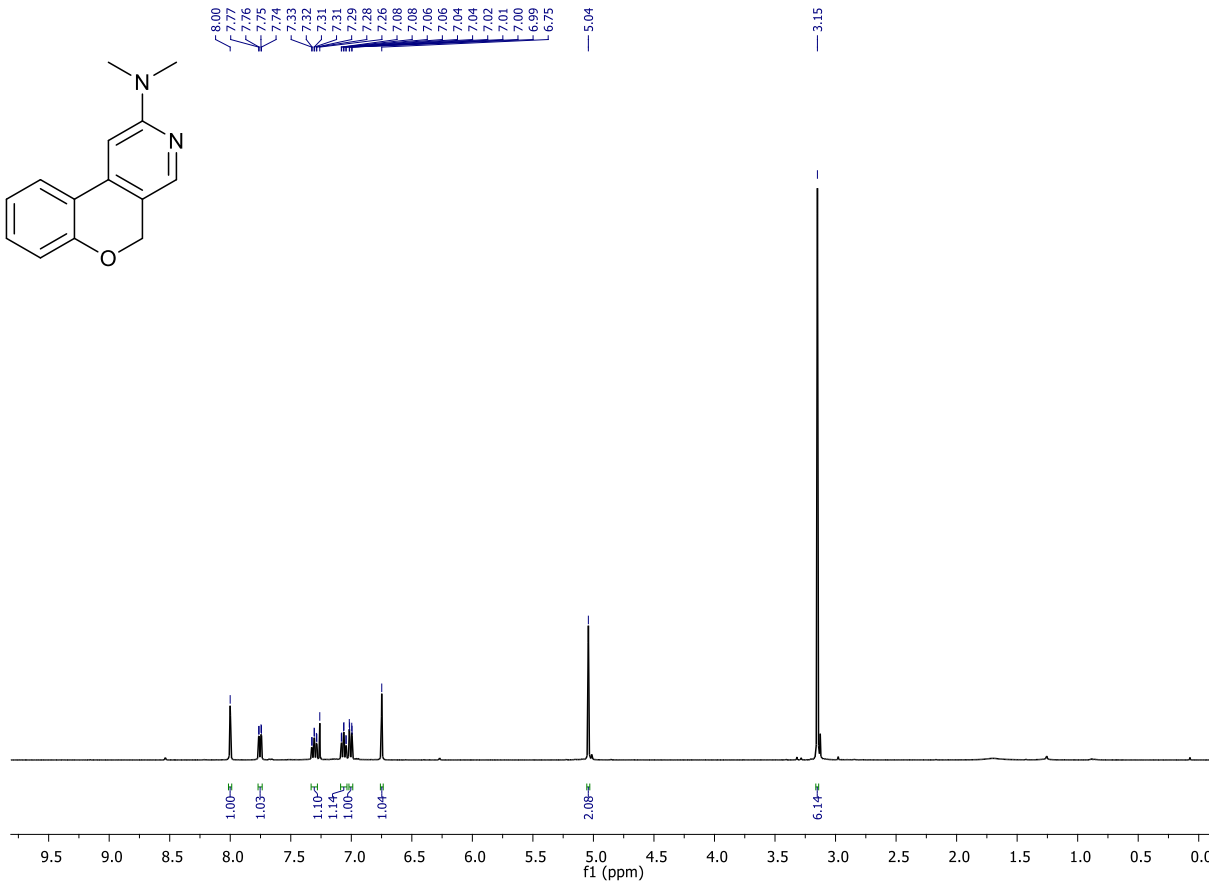
^{13}C NMR of **1r** (101 MHz, $CDCl_3$)



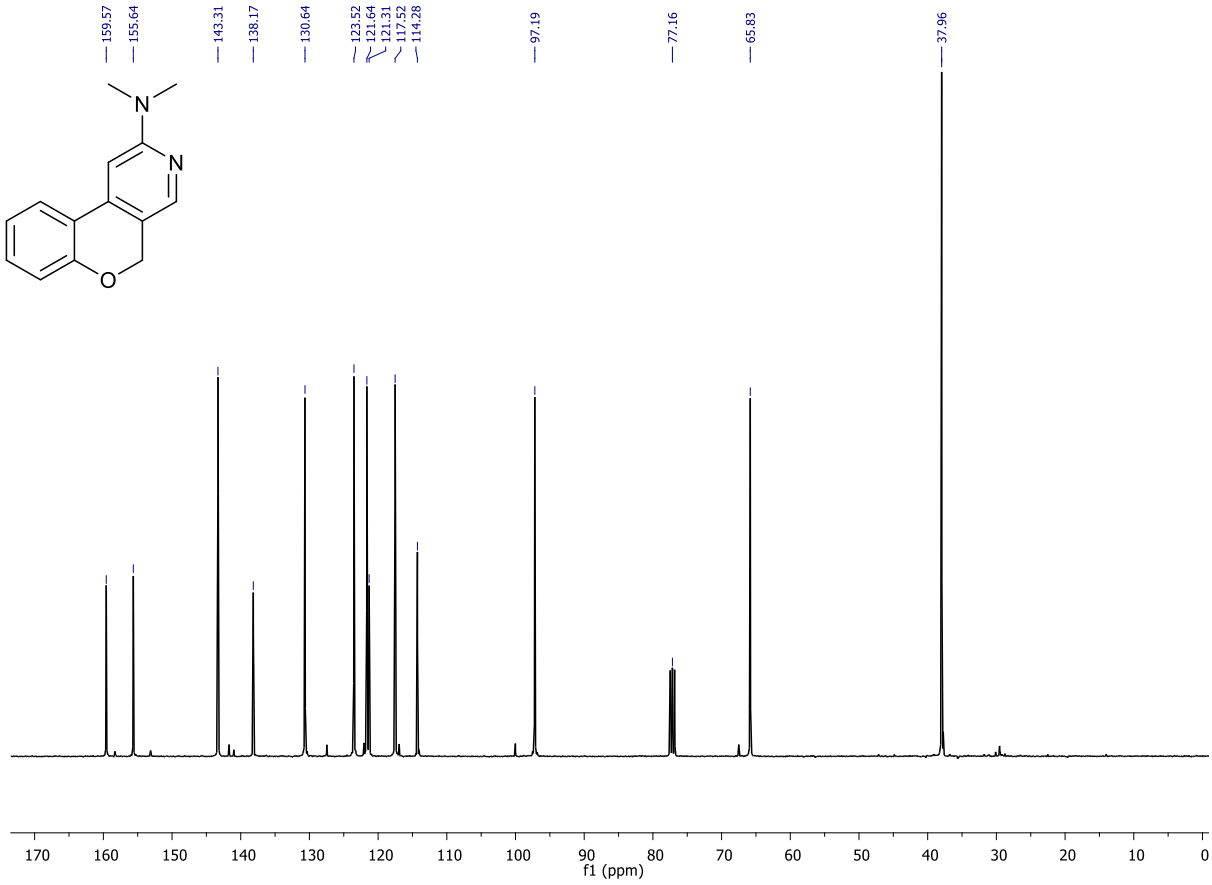
^{1}H NMR of **1s** (400 MHz, $CDCl_3$)



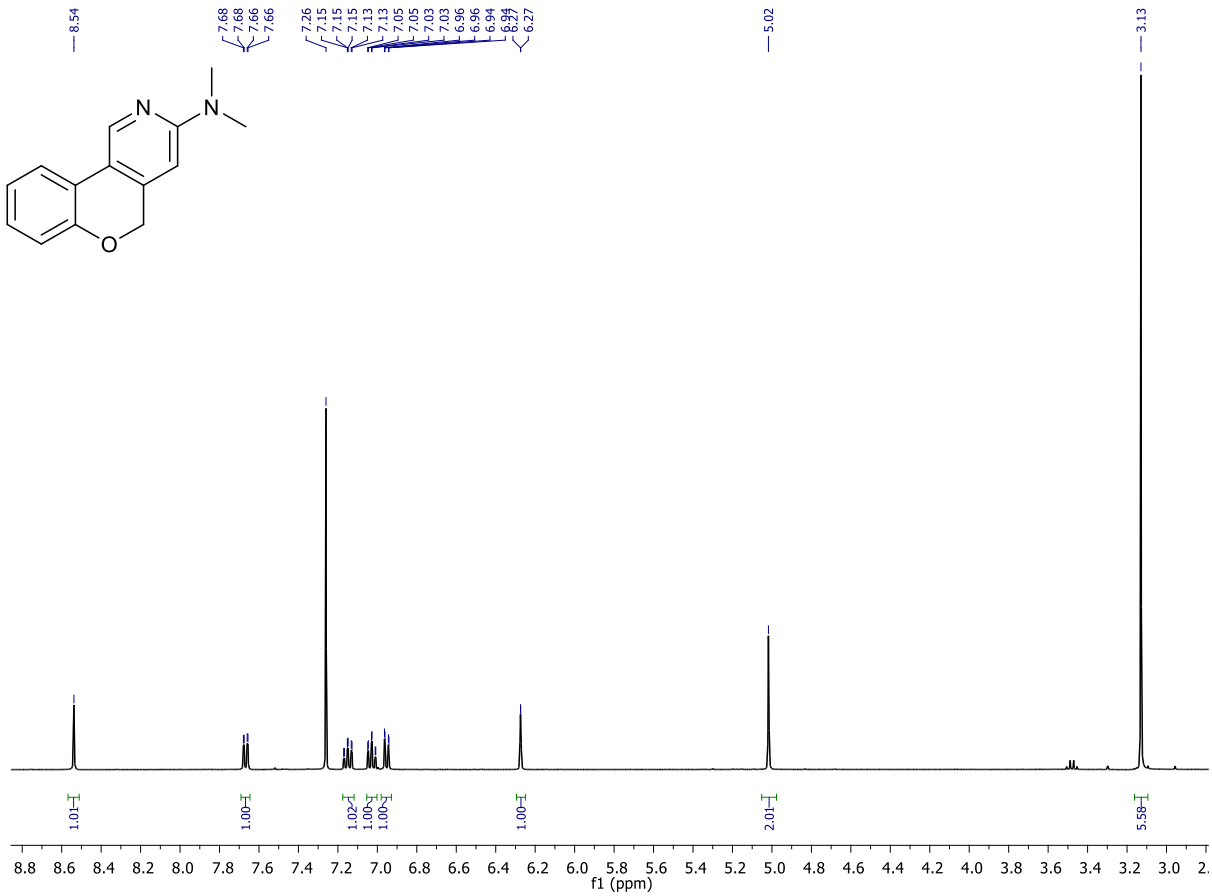
^{13}C NMR of **1s** (101 MHz, $CDCl_3$)



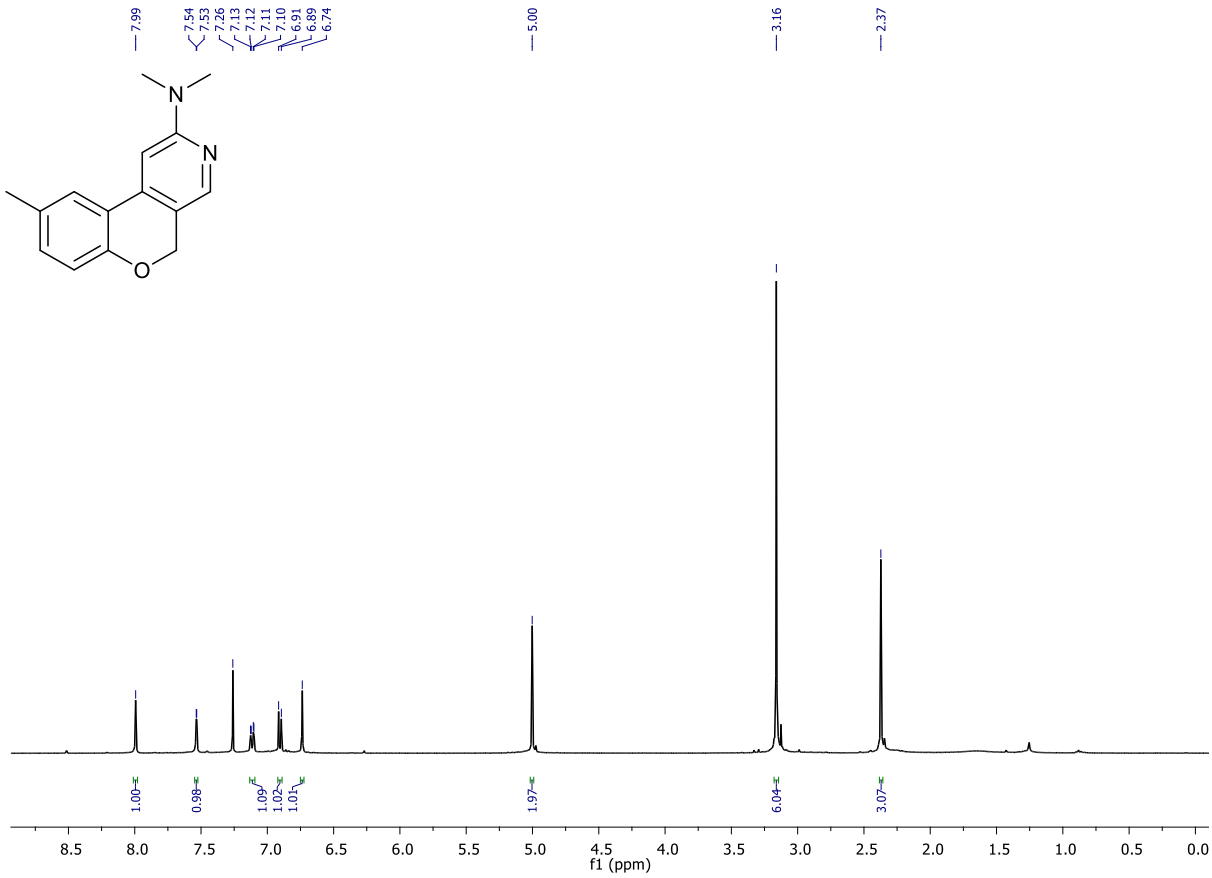
^{1}H NMR of **3aa** (400 MHz, $CDCl_3$)



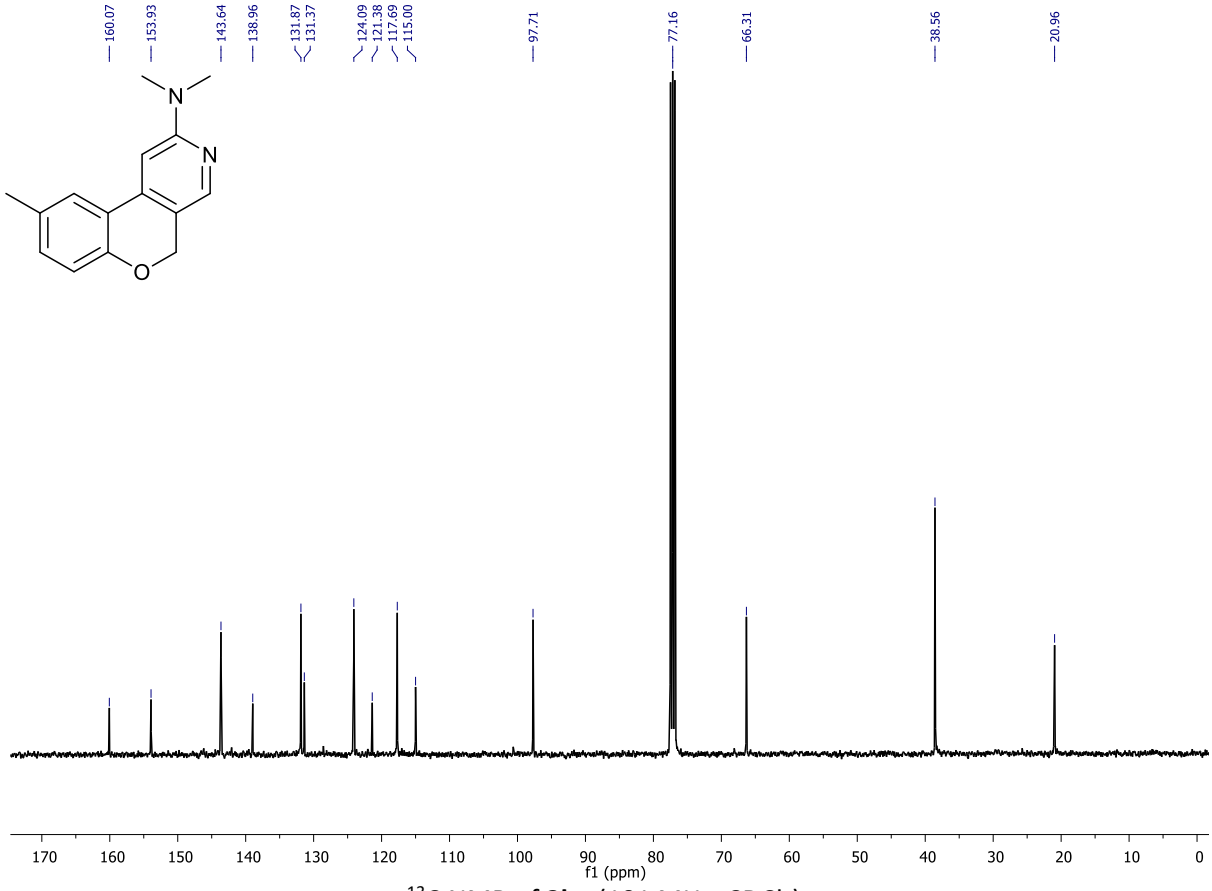
^{13}C NMR of **3aa** (101 MHz, $CDCl_3$)



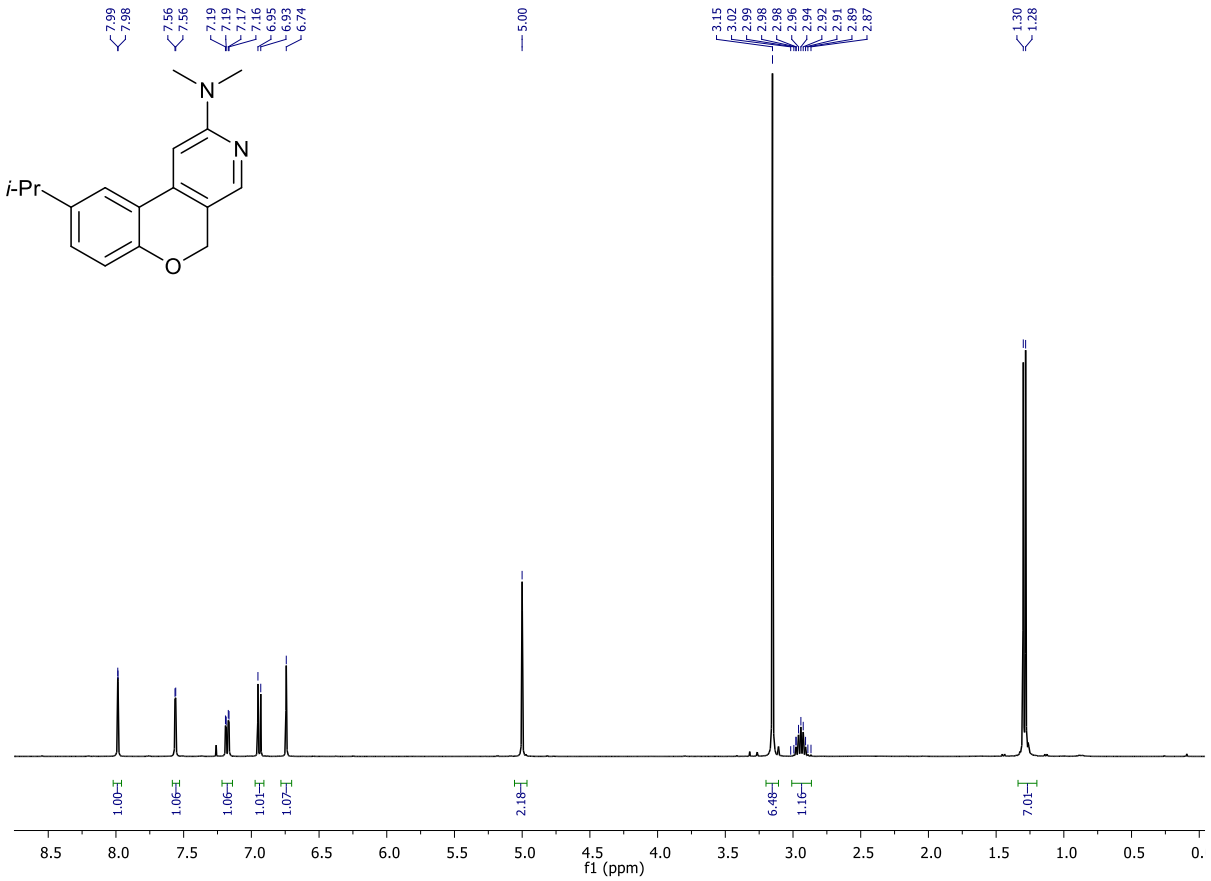
^{1}H NMR of **3aa'** (400 MHz, $CDCl_3$)



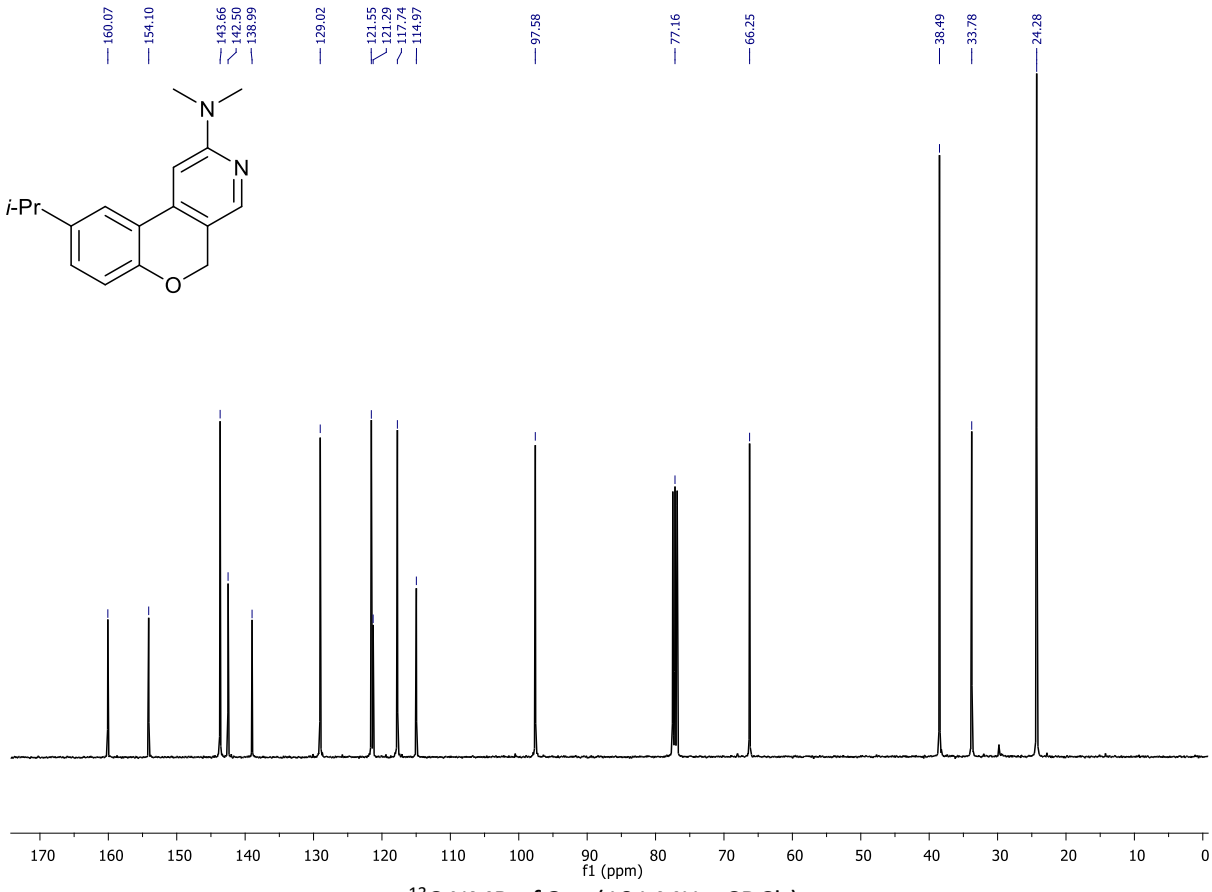
^{1}H NMR of **3ba** (400 MHz, $CDCl_3$)



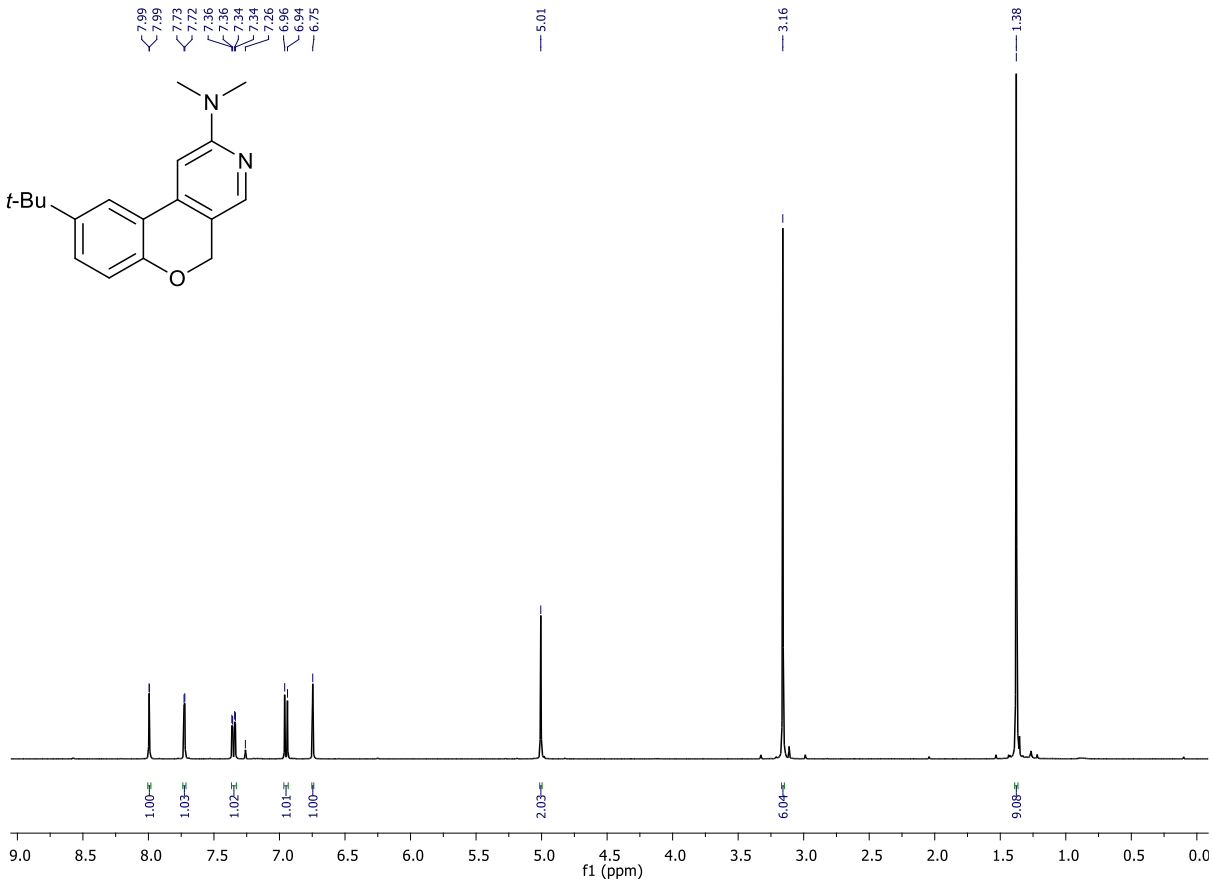
^{13}C NMR of **3ba** (101 MHz, $CDCl_3$)



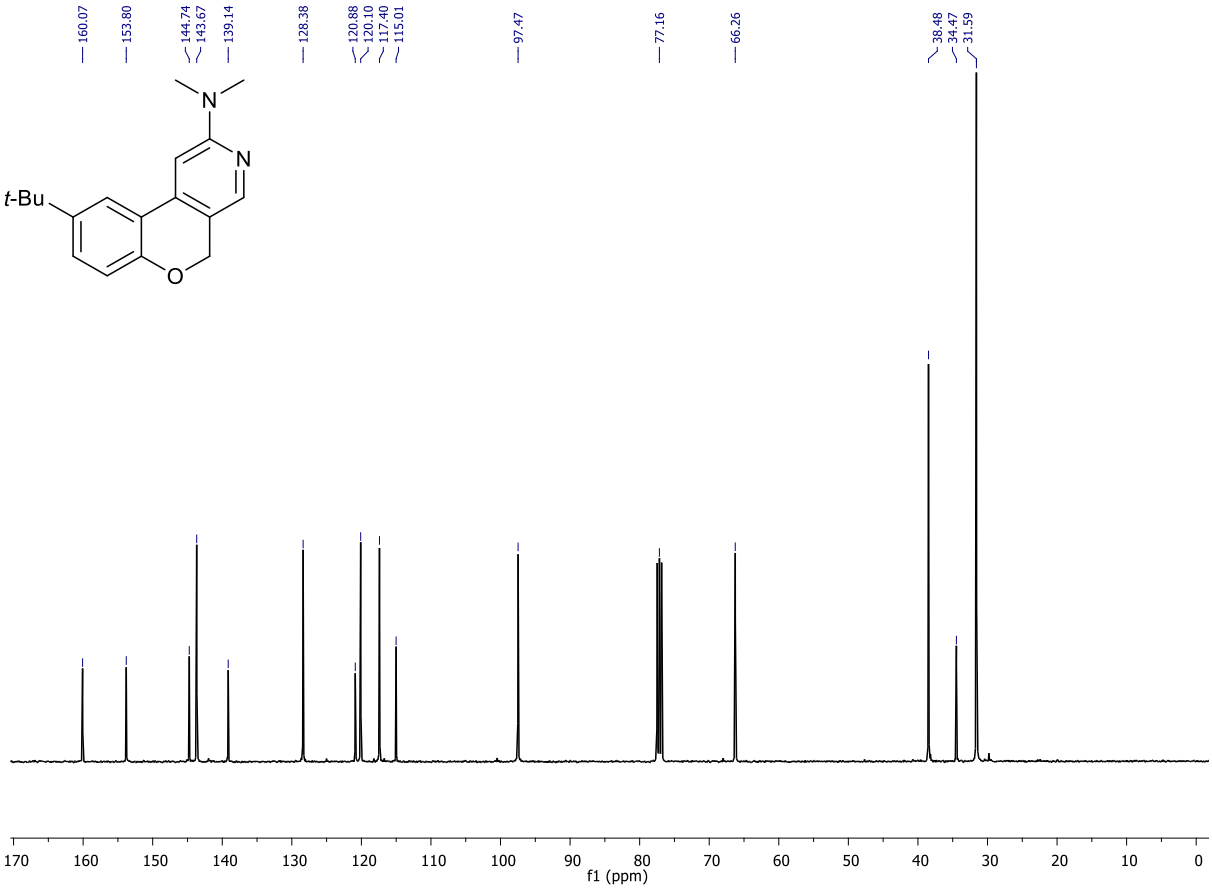
^{1}H NMR of **3ca** (400 MHz, $CDCl_3$)



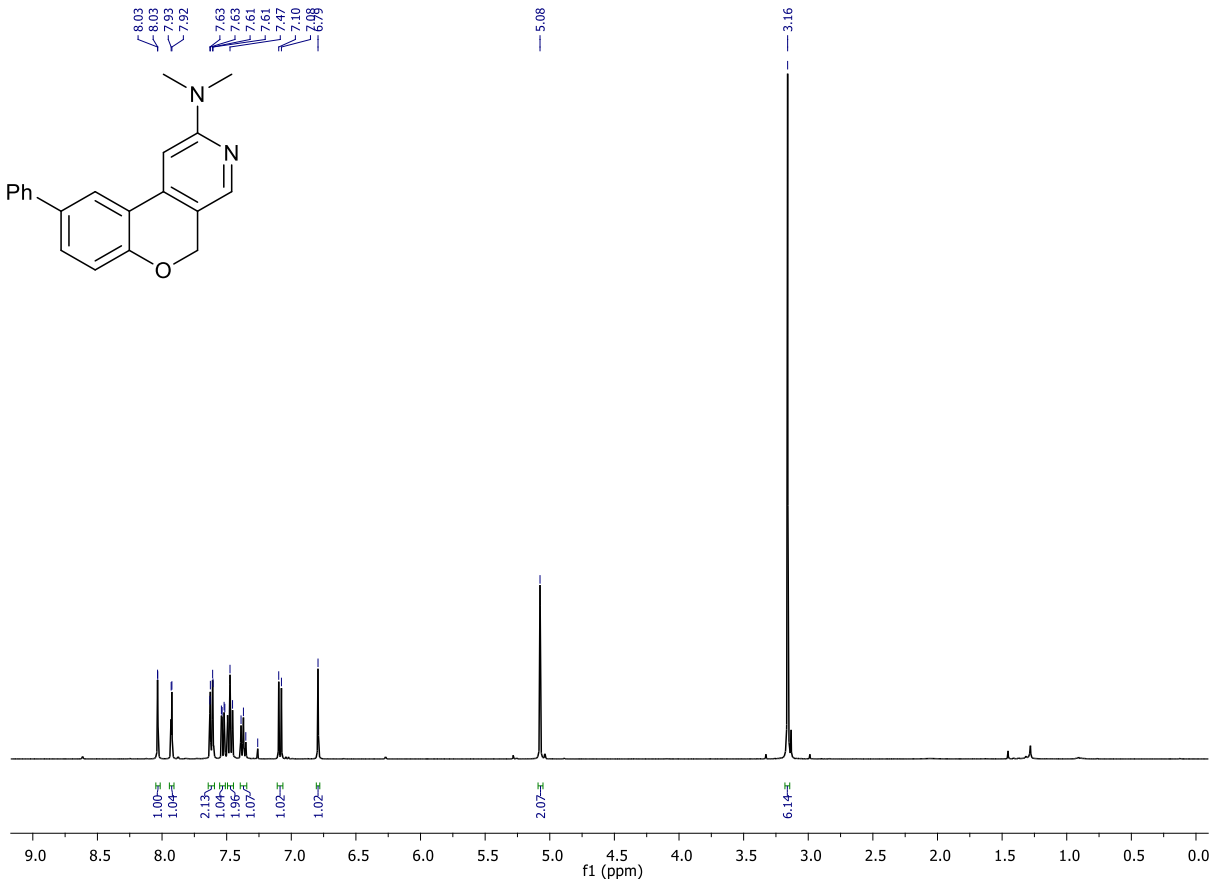
^{13}C NMR of **3ca** (101 MHz, $CDCl_3$)



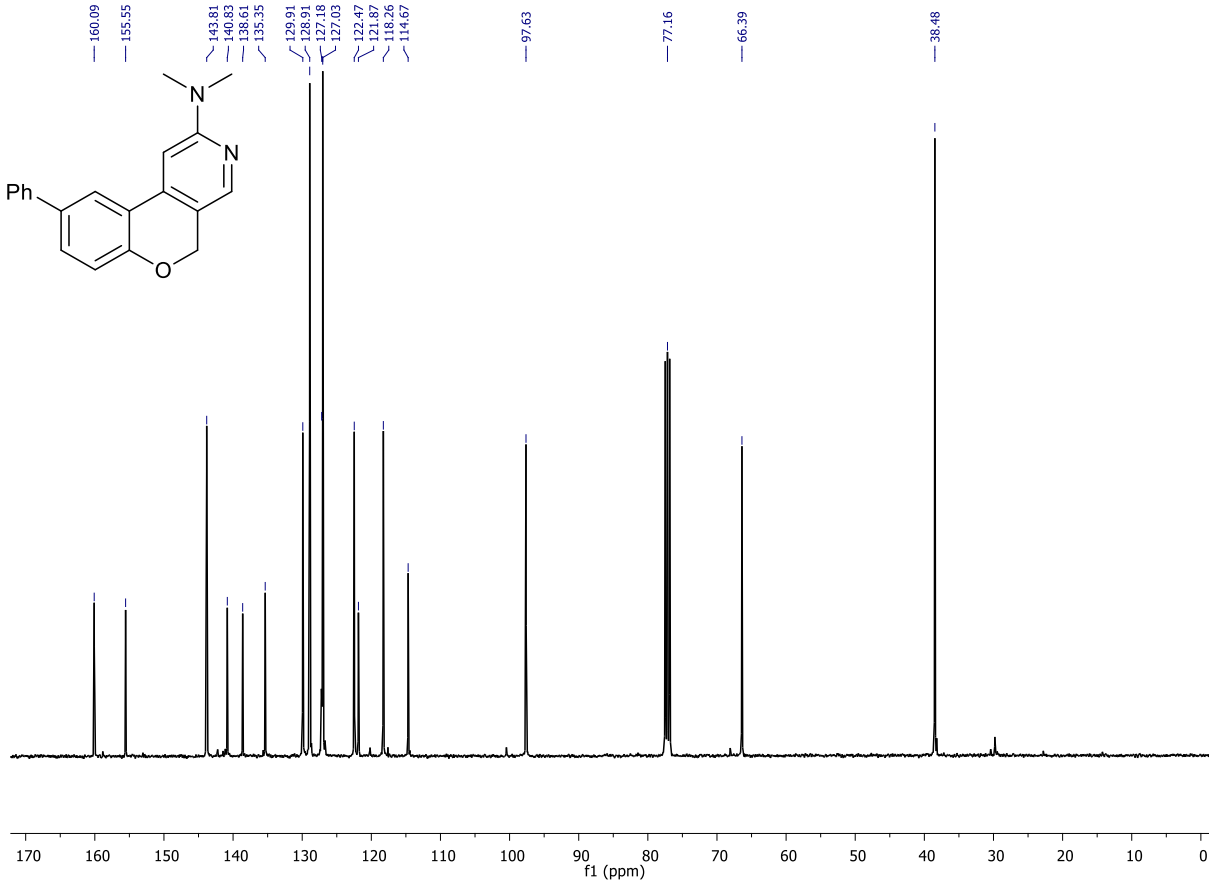
^{1}H NMR of **3da** (400 MHz, $CDCl_3$)



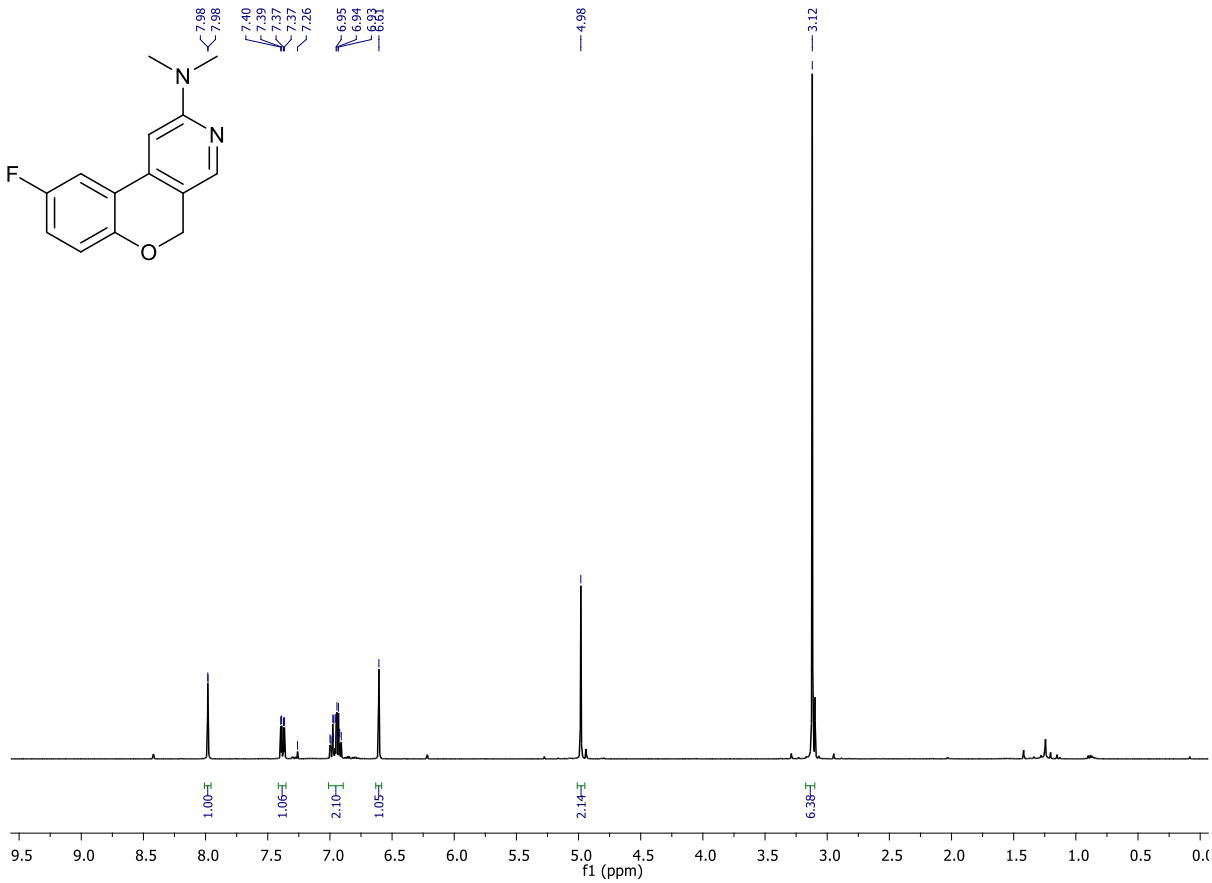
^{13}C NMR of **3da** (101 MHz, $CDCl_3$)



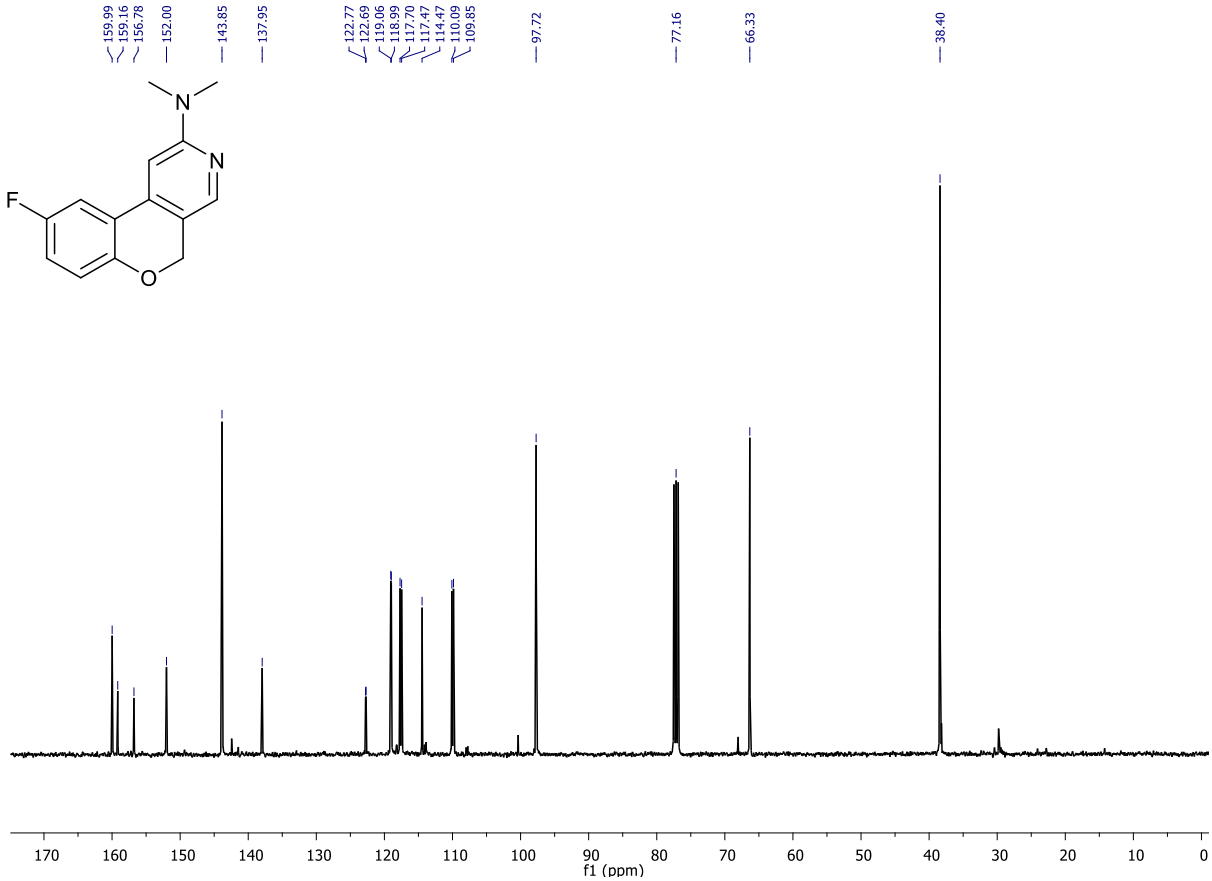
^{1}H NMR of **3ea** (400 MHz, $CDCl_3$)



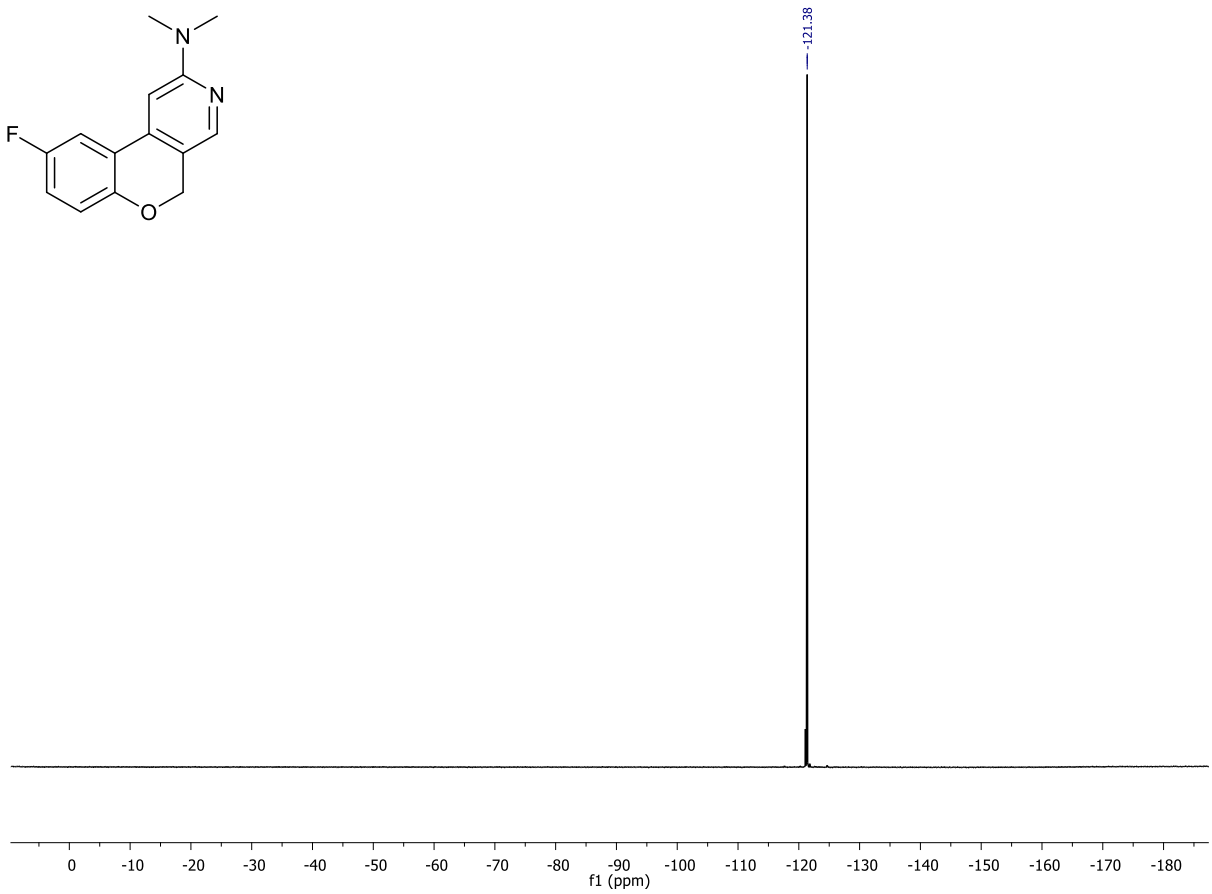
^{13}C NMR of **3ea** (101 MHz, $CDCl_3$)



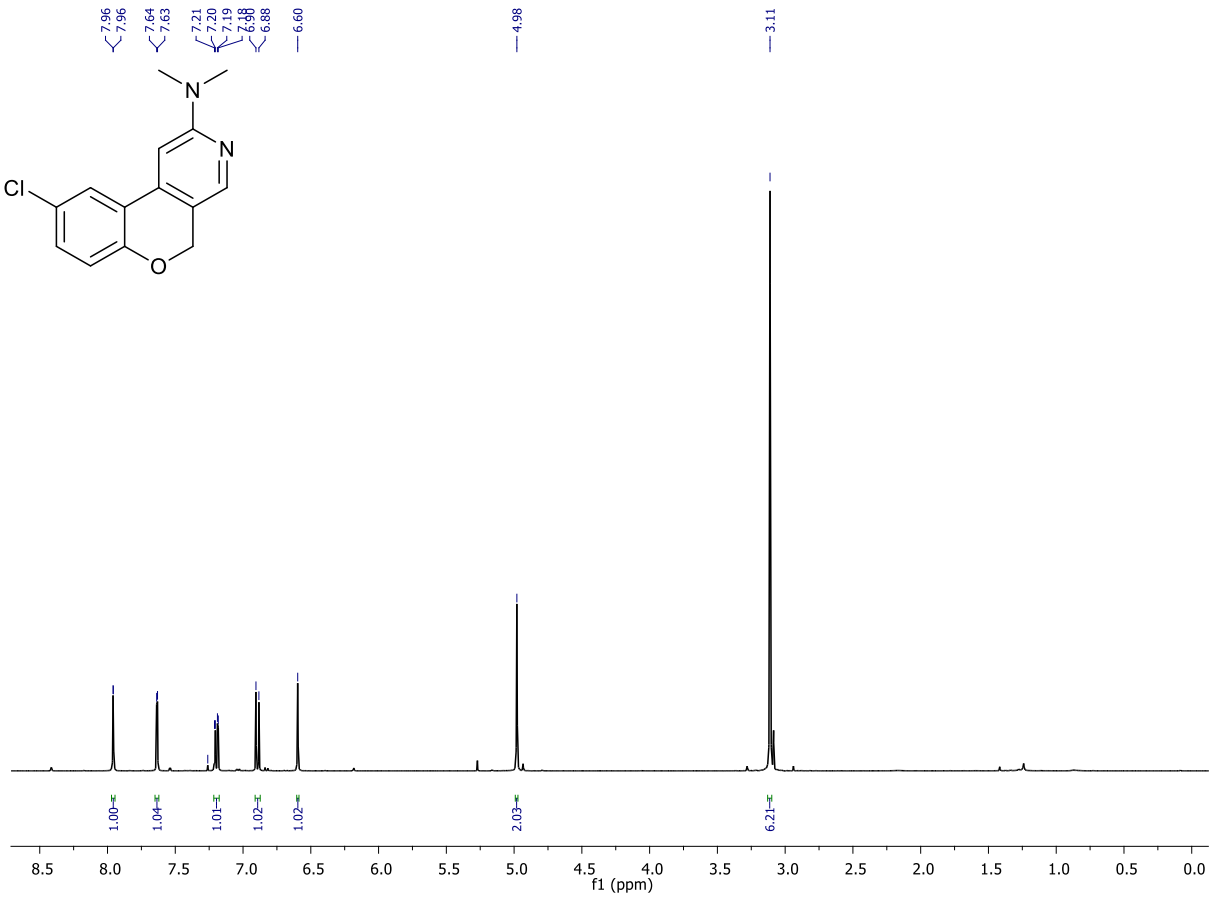
^{1}H NMR of **3fa** (400 MHz, $CDCl_3$)



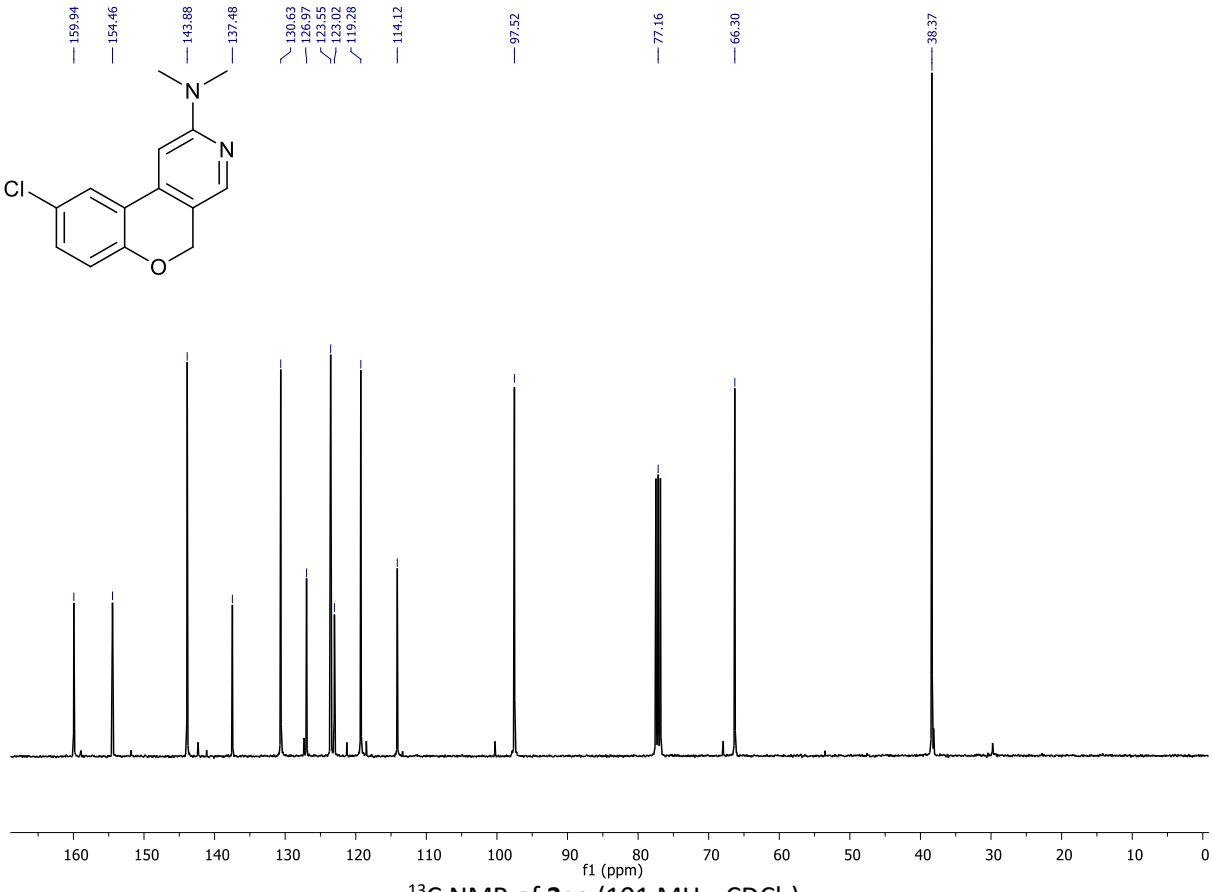
^{13}C NMR of **3fa** (101 MHz, $CDCl_3$)



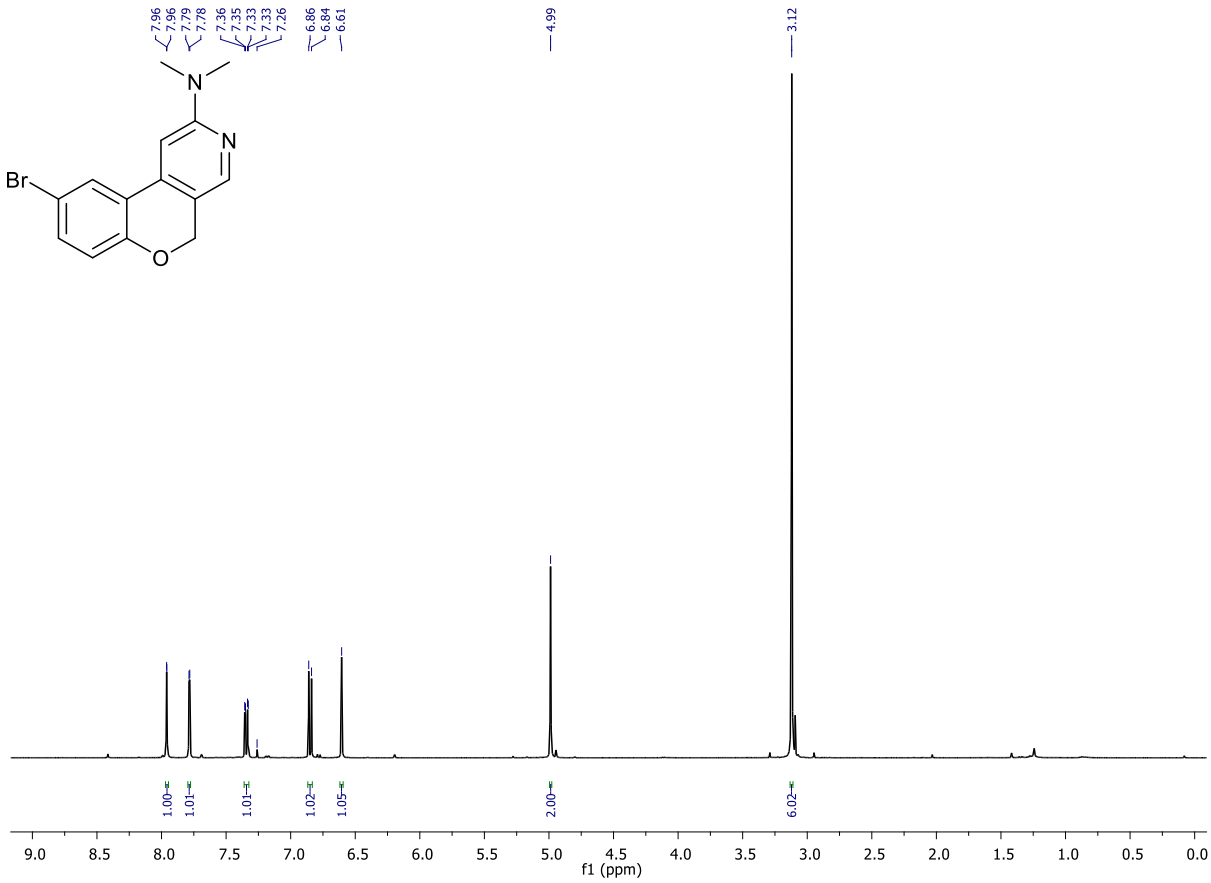
^{19}F NMR of **3fa** (376.5 MHz, $CDCl_3$)



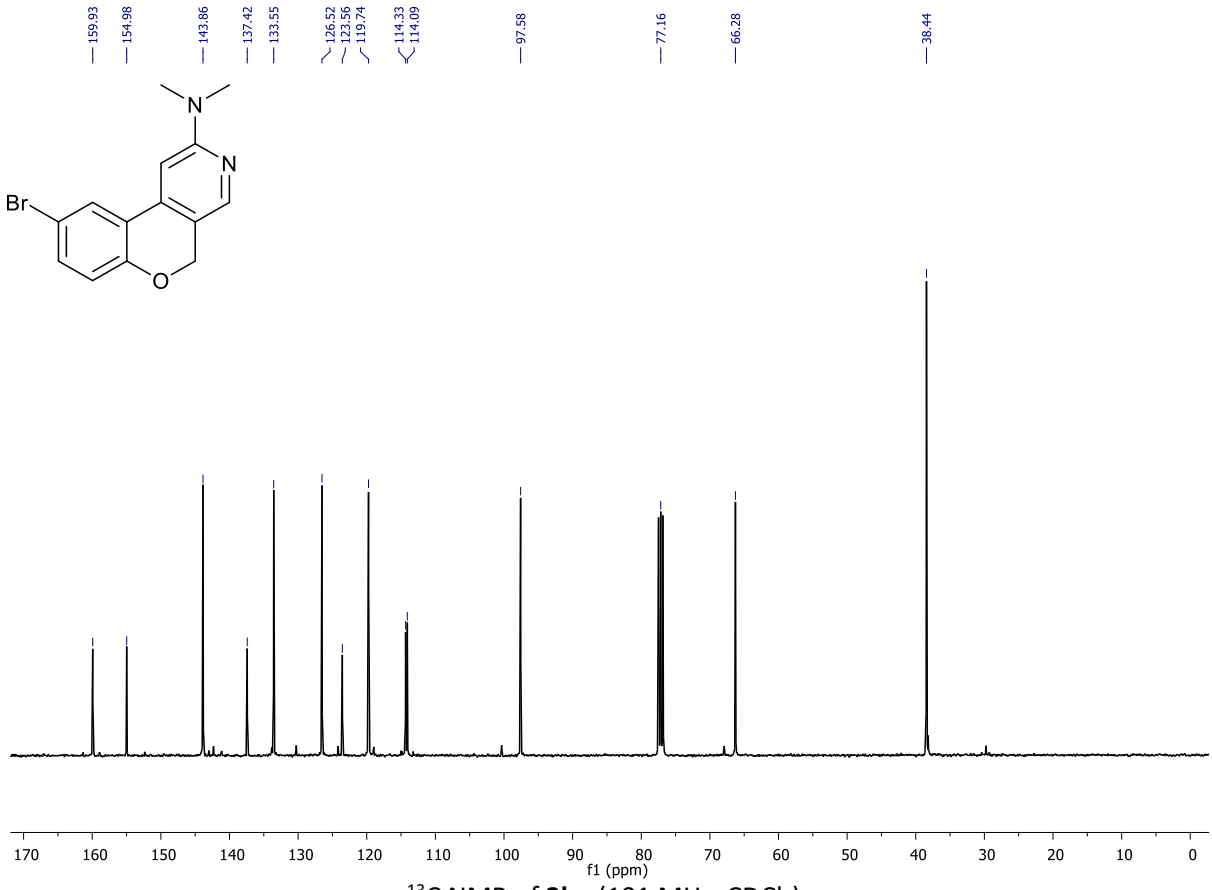
^{1}H NMR of **3ga** (400 MHz, $CDCl_3$)



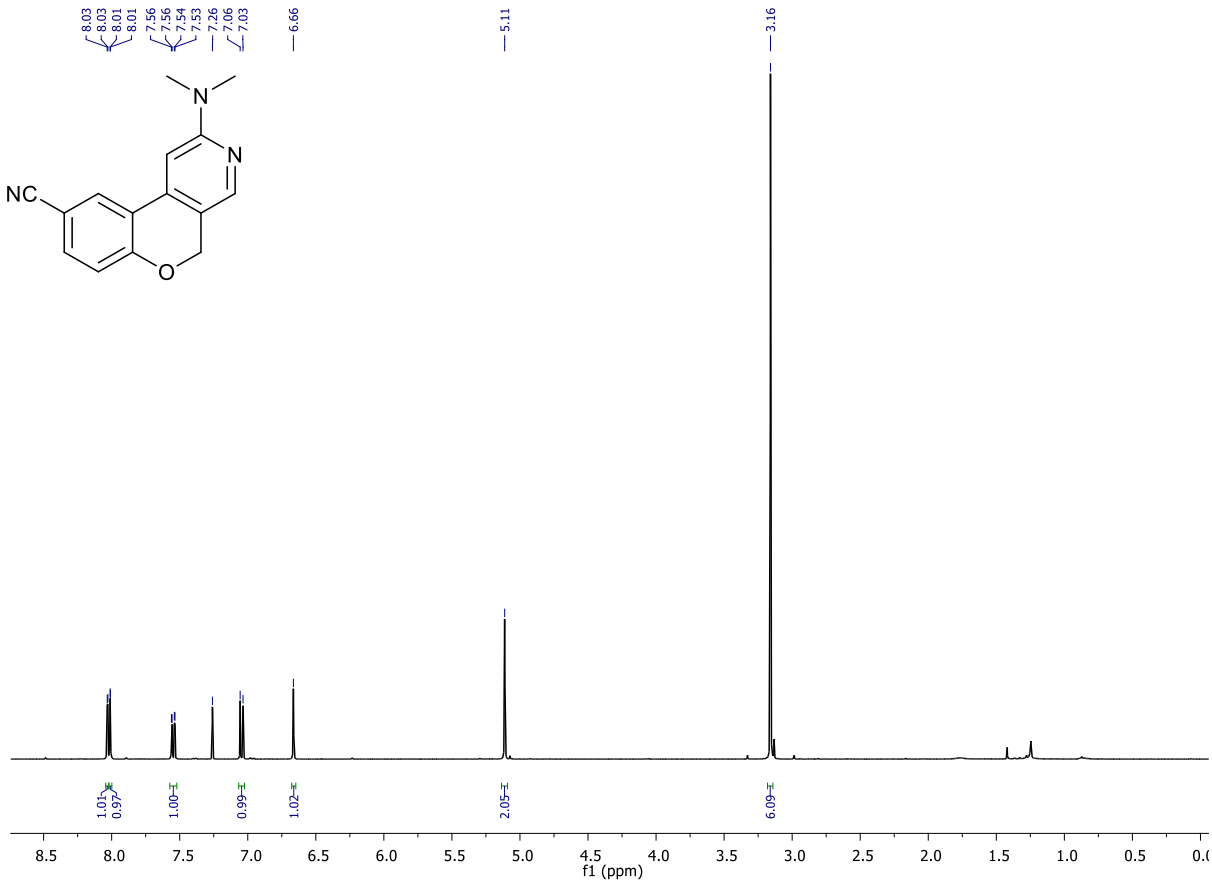
^{13}C NMR of **3ga** (101 MHz, $CDCl_3$)



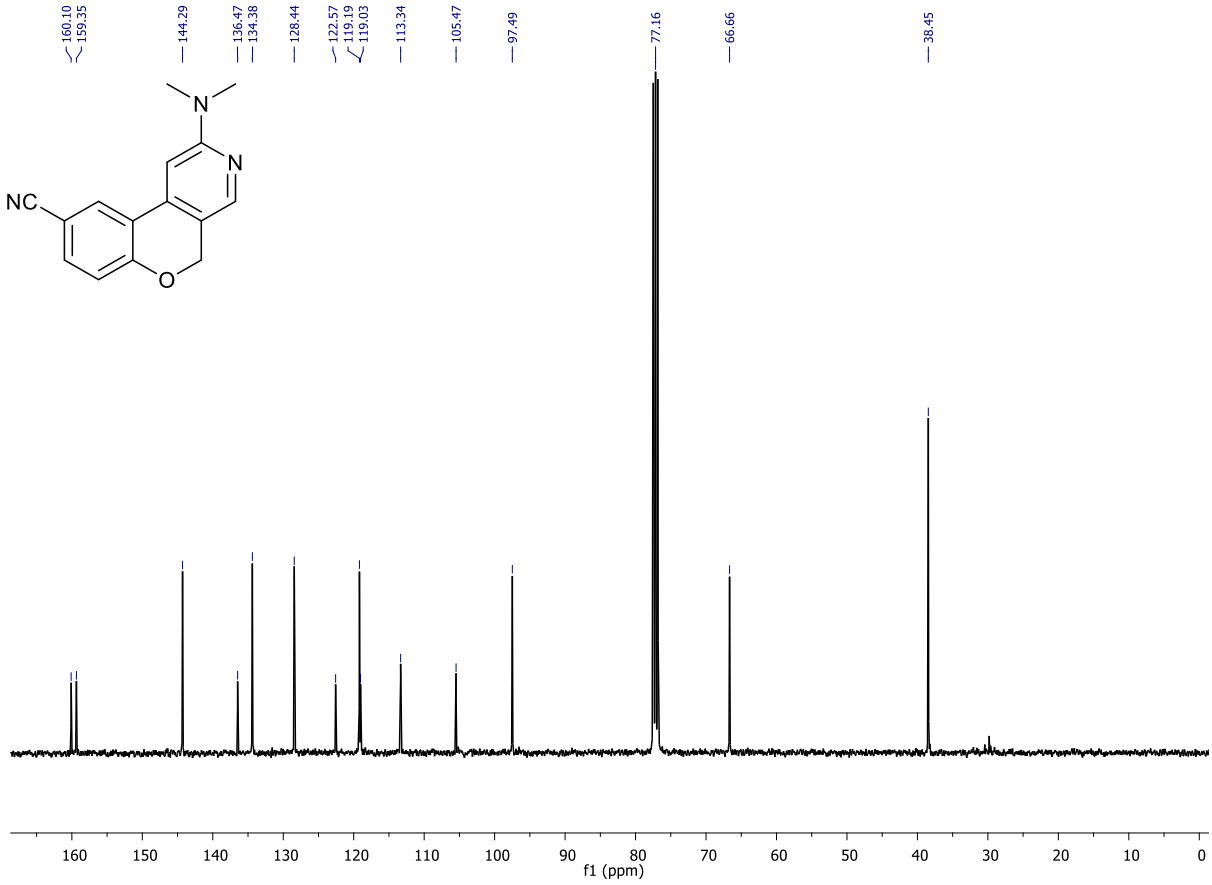
^{1}H NMR of **3ha** (400 MHz, $CDCl_3$)



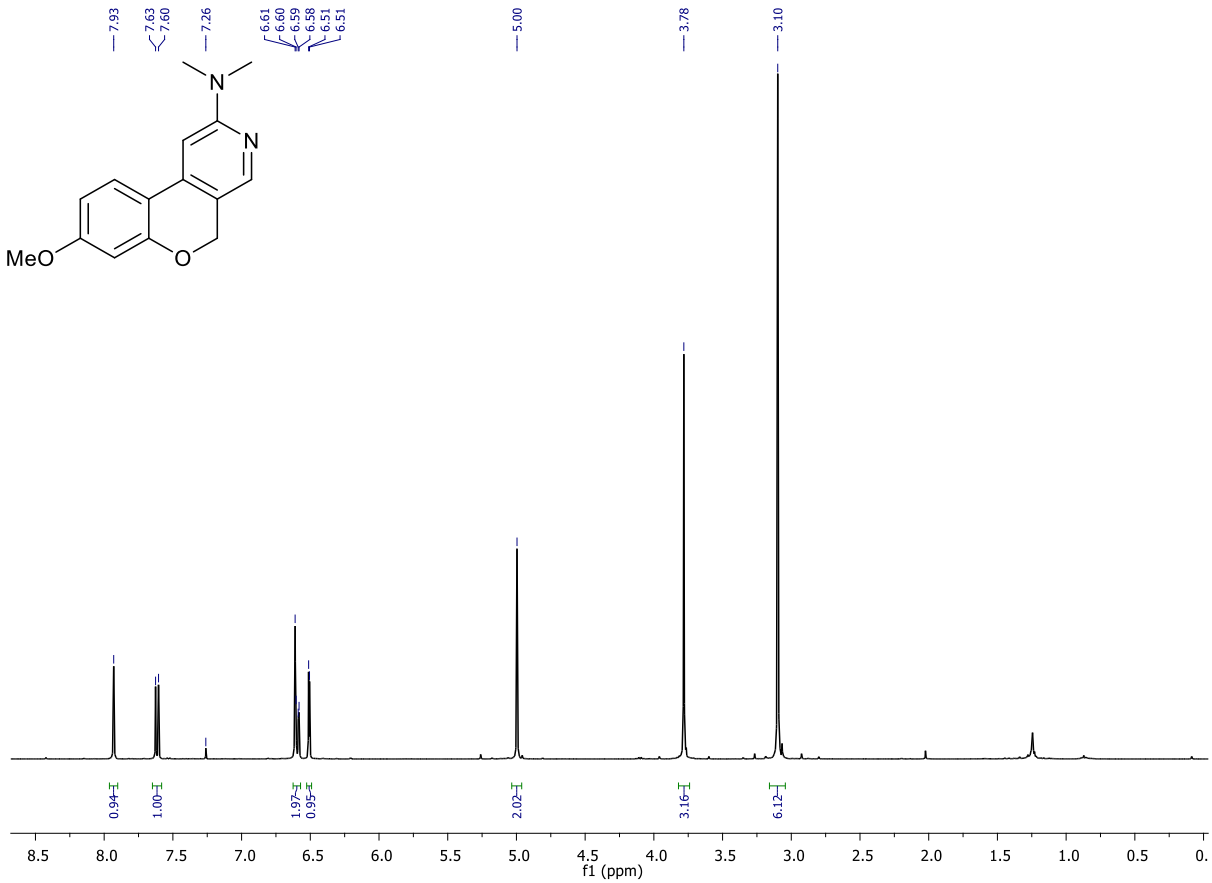
^{13}C NMR of **3ha** (101 MHz, $CDCl_3$)



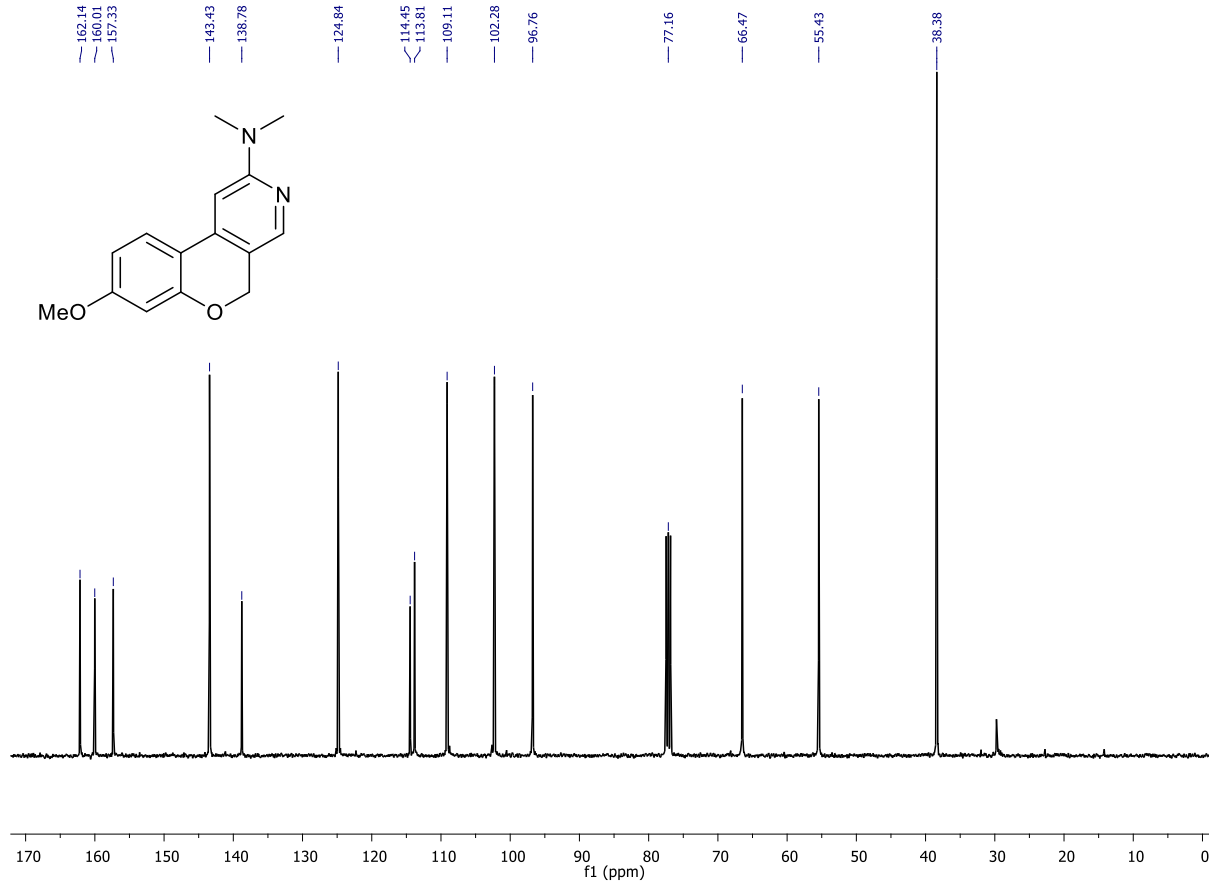
^{1}H NMR of **3ia** (400 MHz, $CDCl_3$)



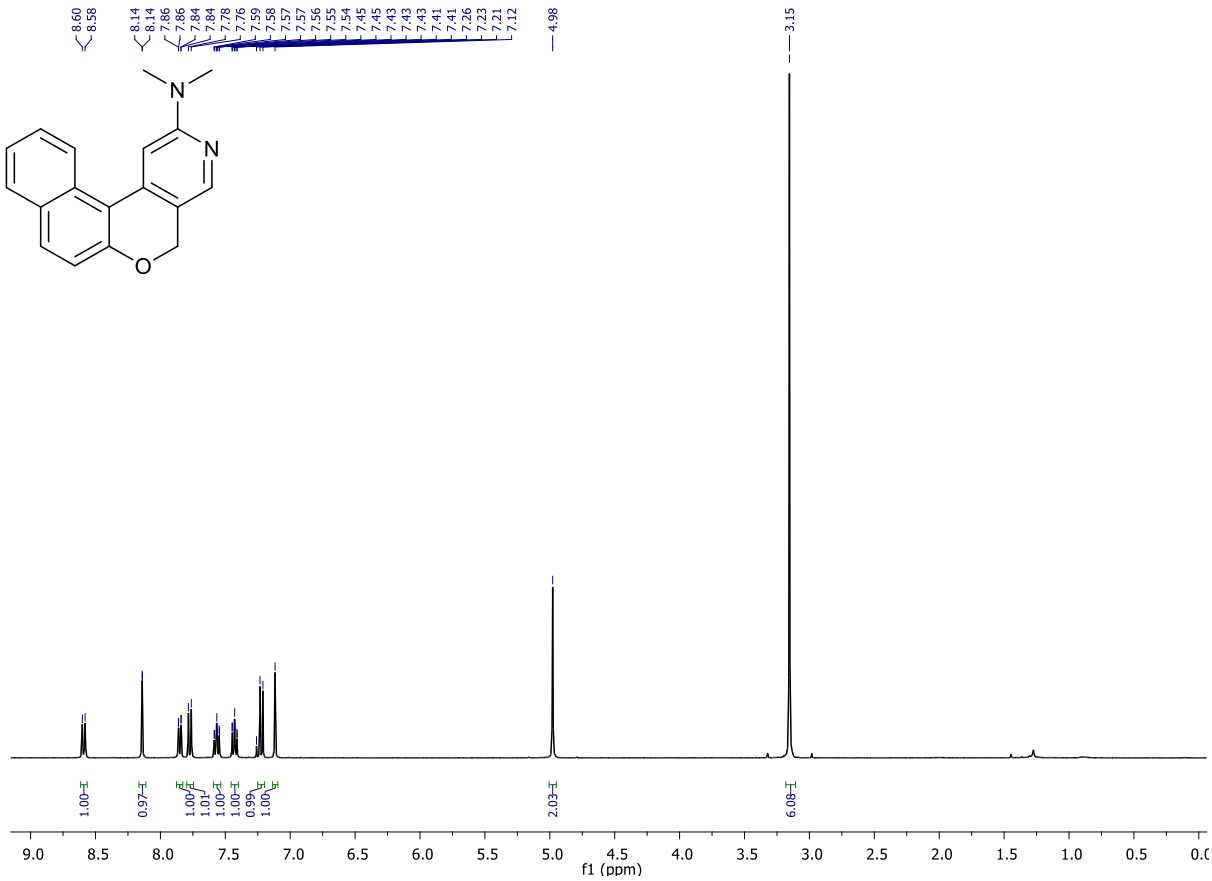
^{13}C NMR of **3ia** (101 MHz, $CDCl_3$)



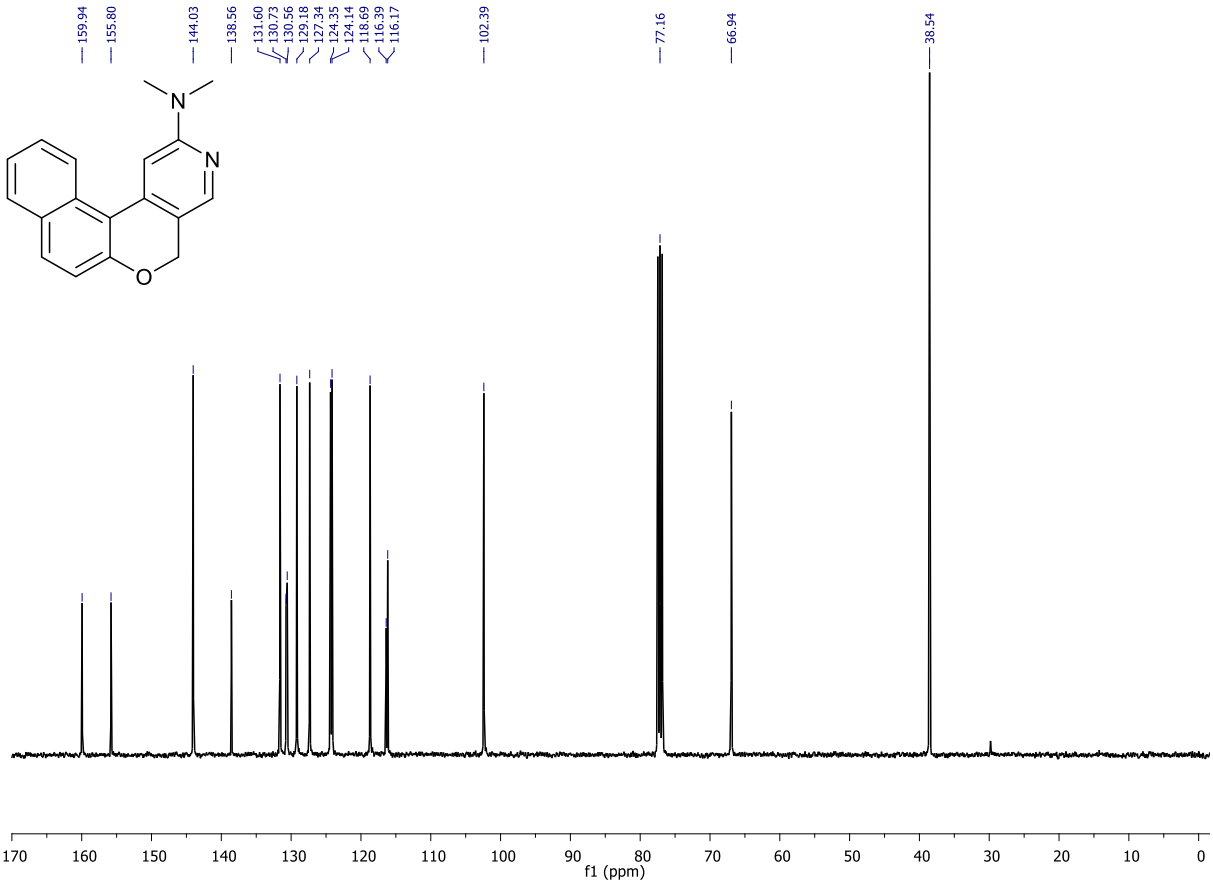
^{1}H NMR of **3ja** (400 MHz, $CDCl_3$)



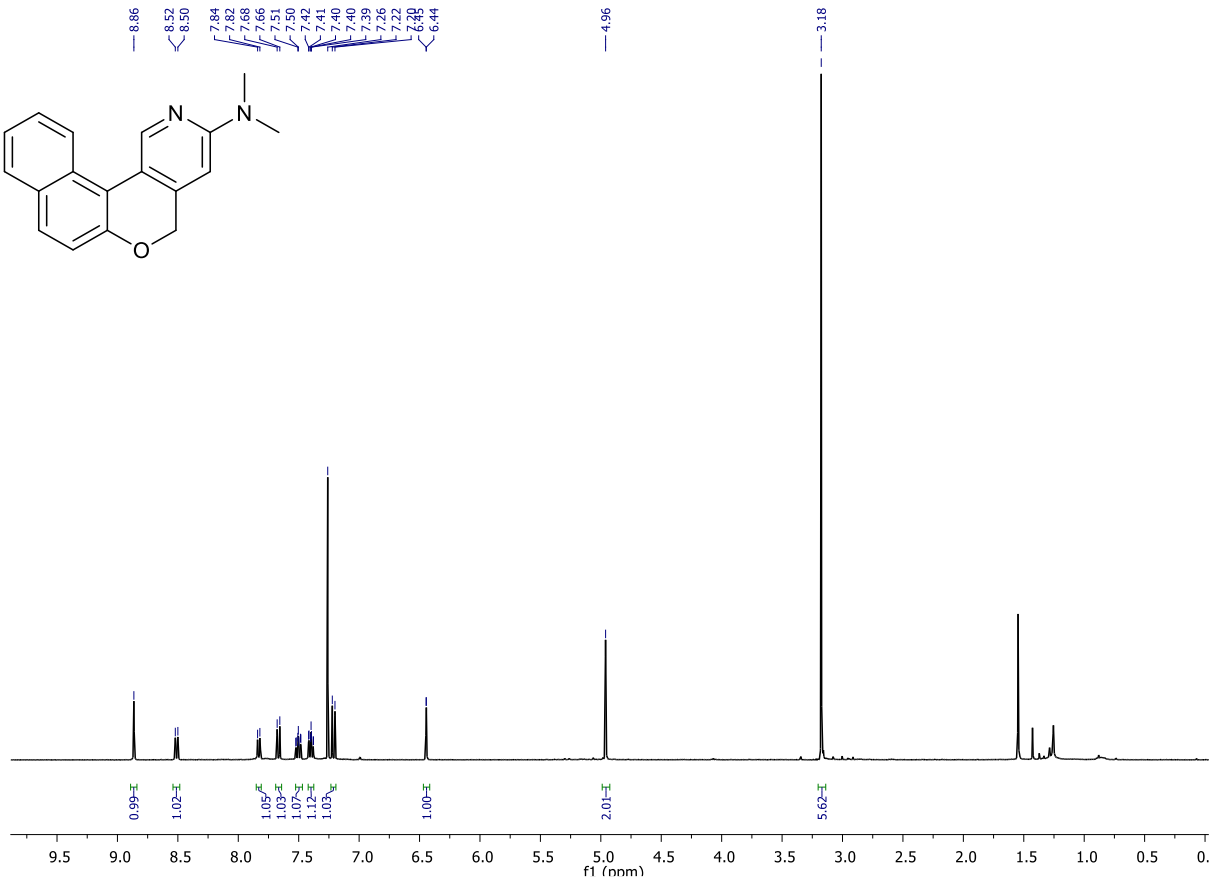
^{13}C NMR of **3ja** (101 MHz, $CDCl_3$)



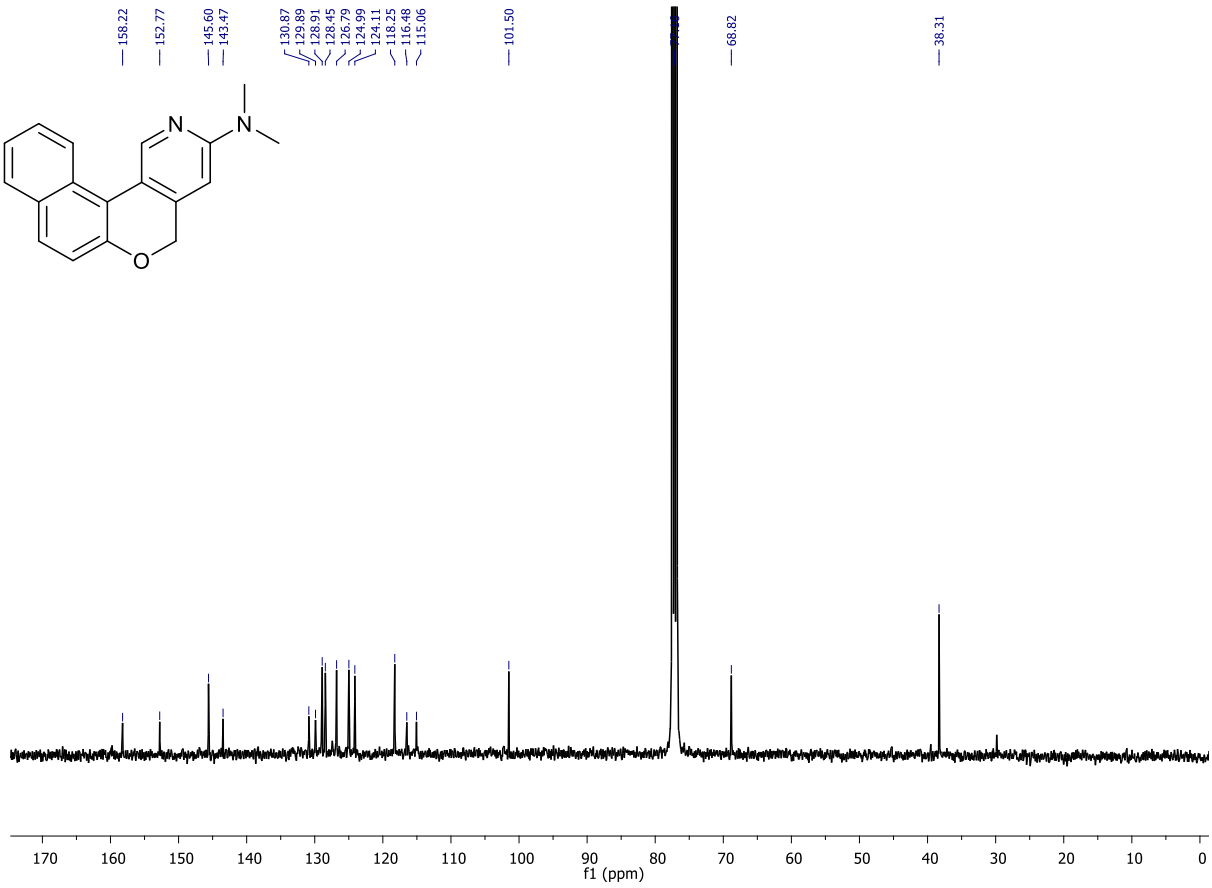
^{1}H NMR of **3ka** (400 MHz, $CDCl_3$)



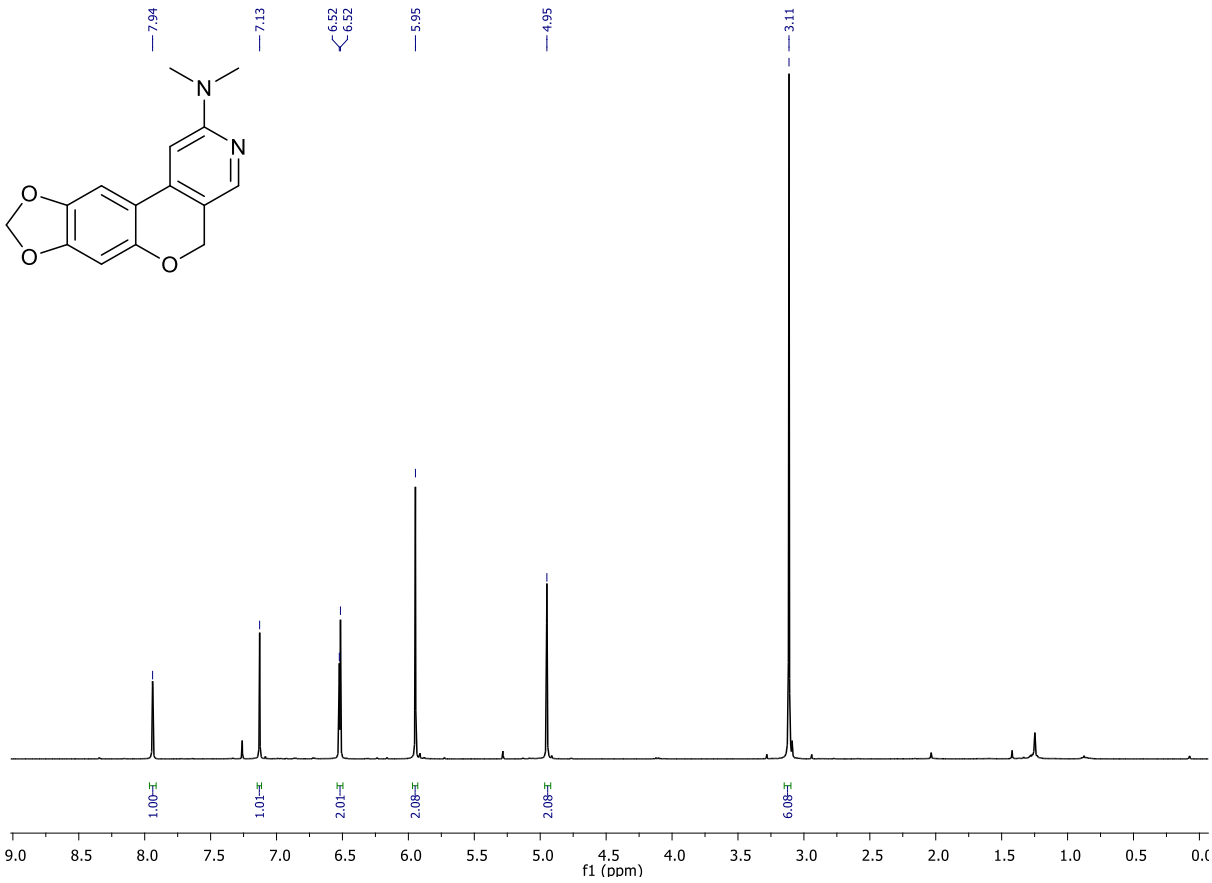
^{13}C NMR of **3ka** (101 MHz, $CDCl_3$)



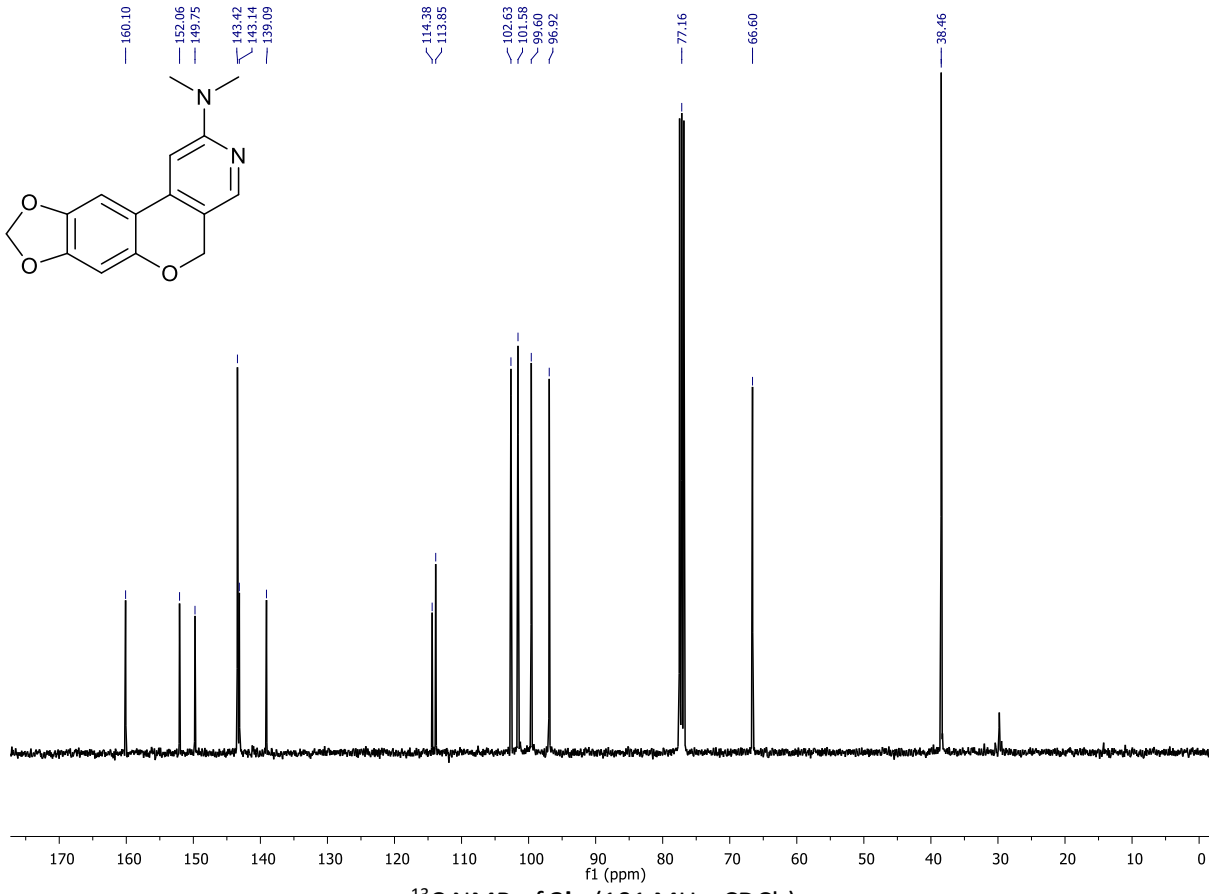
^{1}H NMR of **3ka'** (400 MHz, $CDCl_3$)



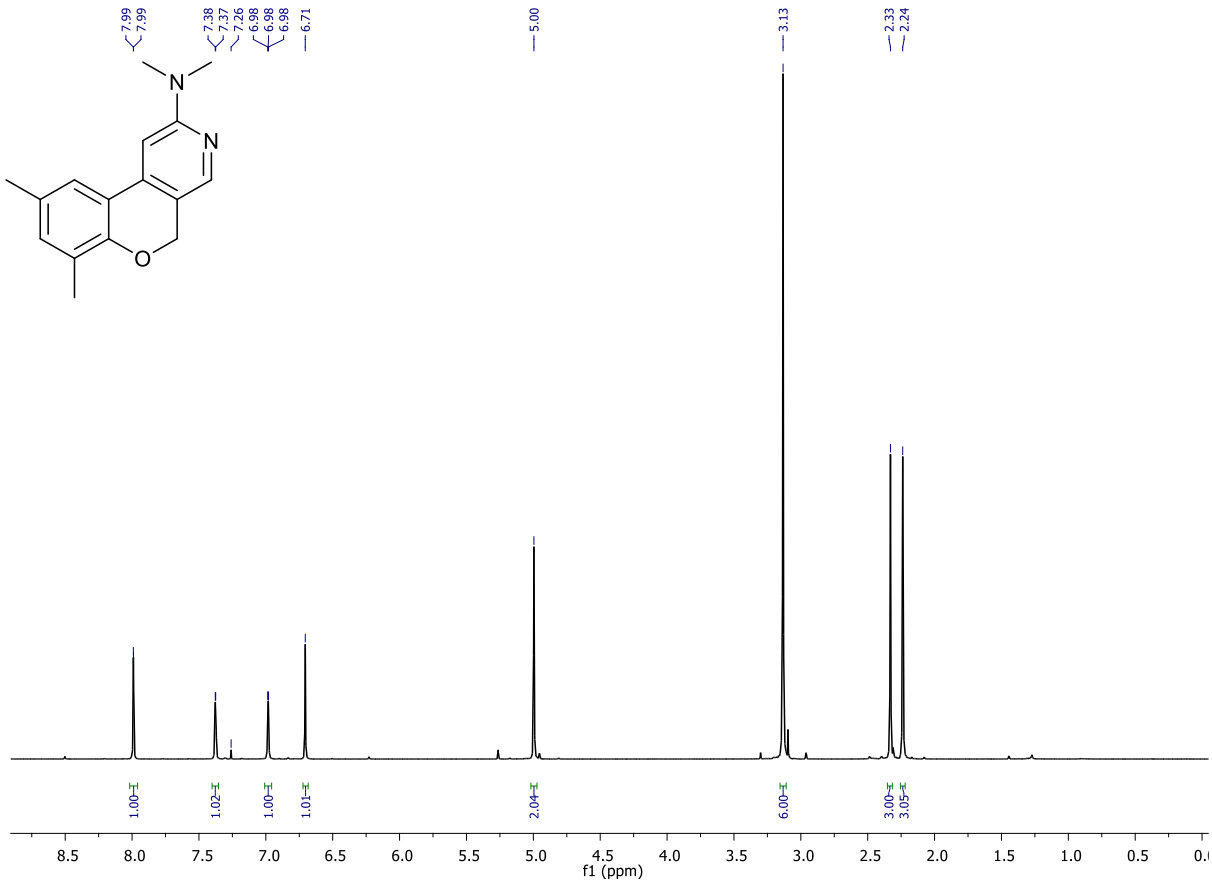
^{13}C NMR of **3ka'** (101 MHz, $CDCl_3$)



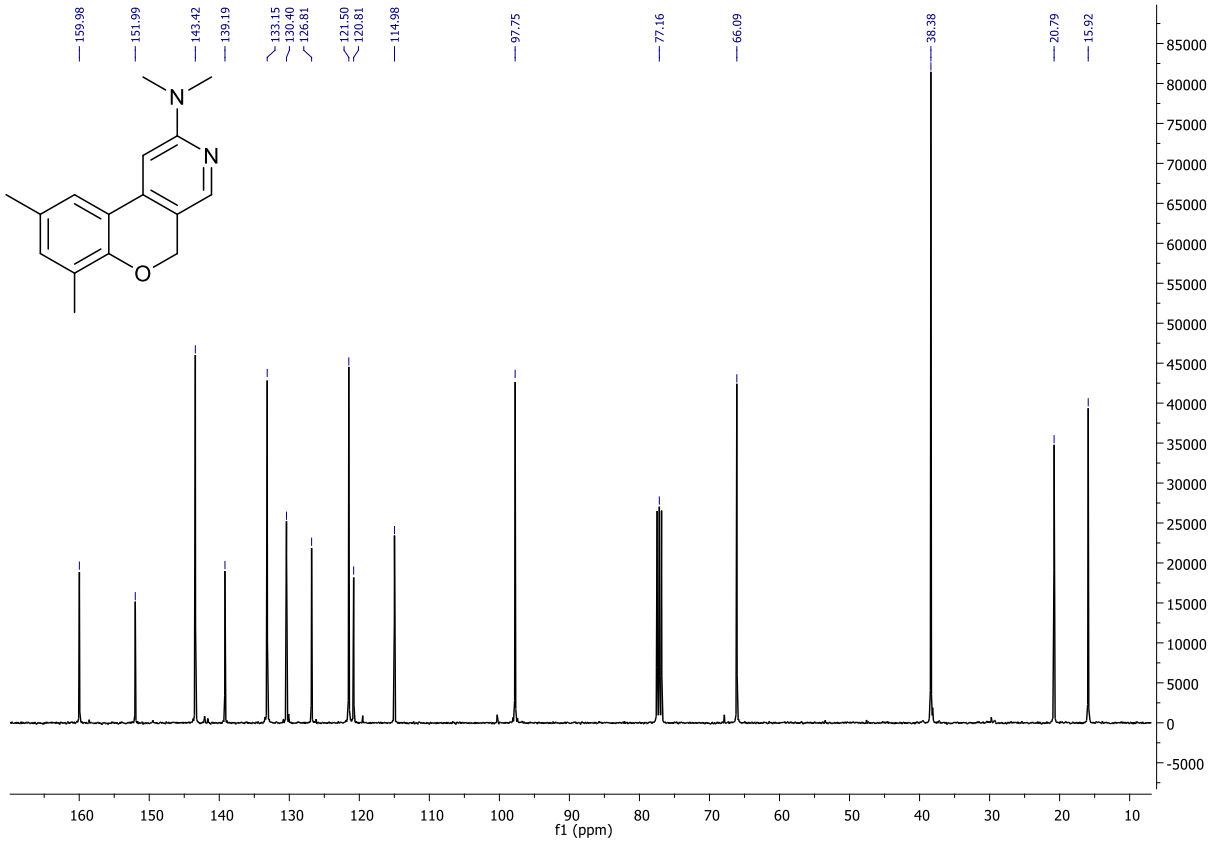
^{1}H NMR of **3la** (400 MHz, $CDCl_3$)



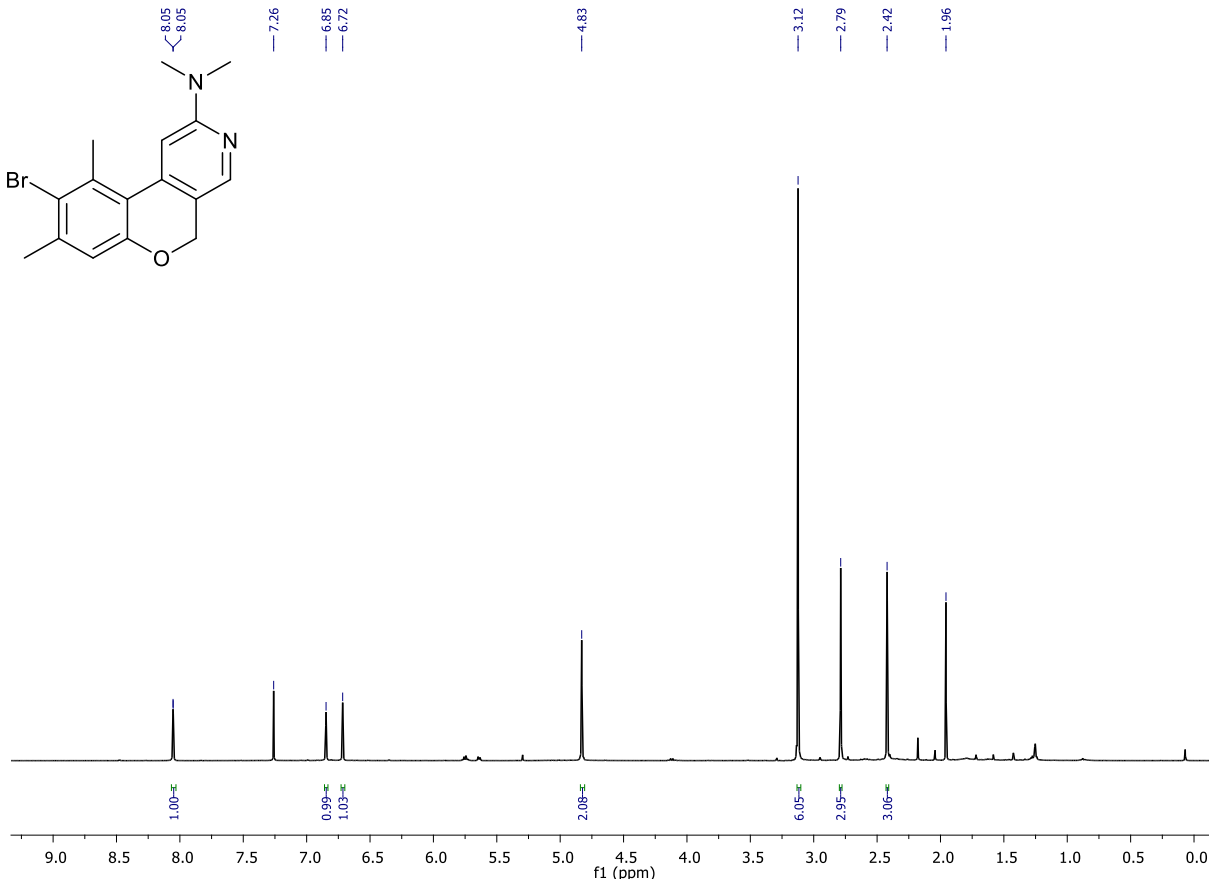
^{13}C NMR of **3la** (101 MHz, $CDCl_3$)



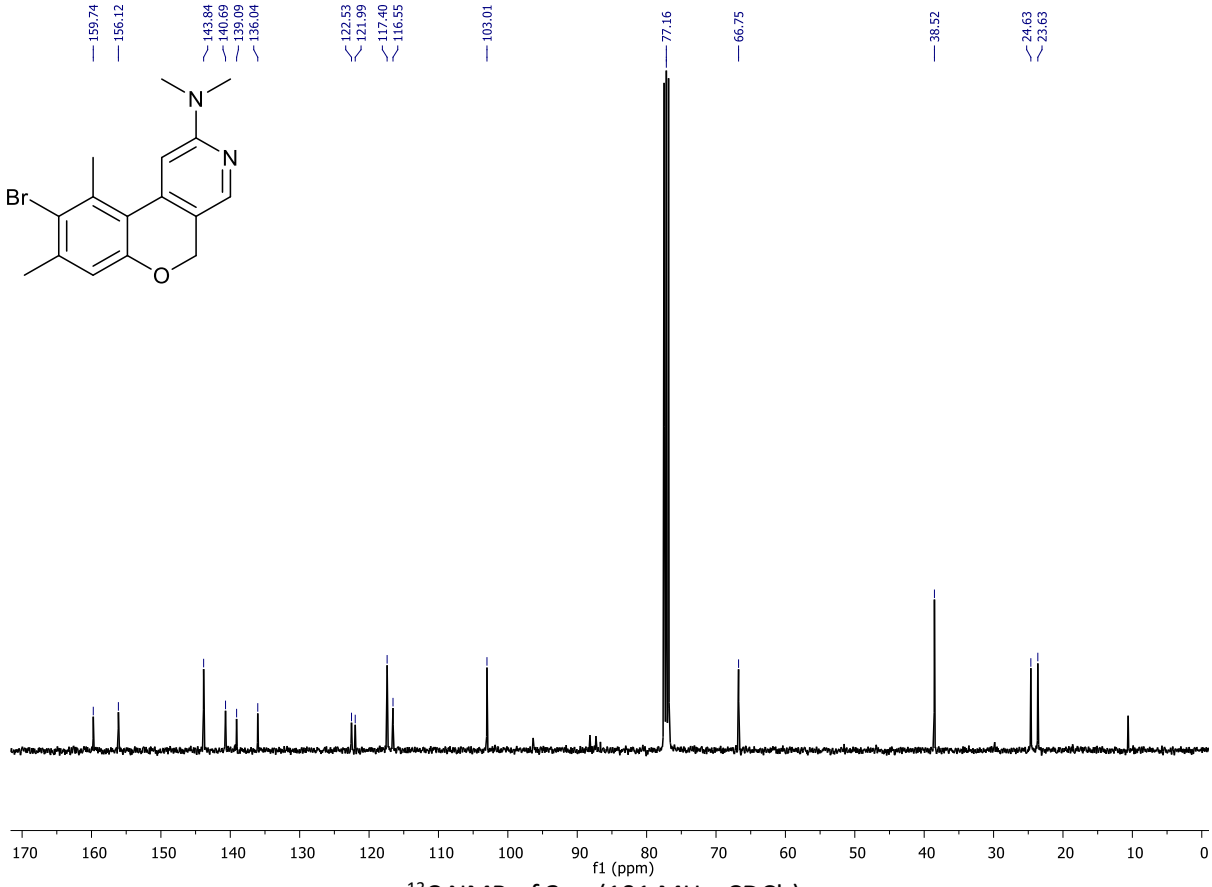
^{1}H NMR of **3ma** (400 MHz, $CDCl_3$)



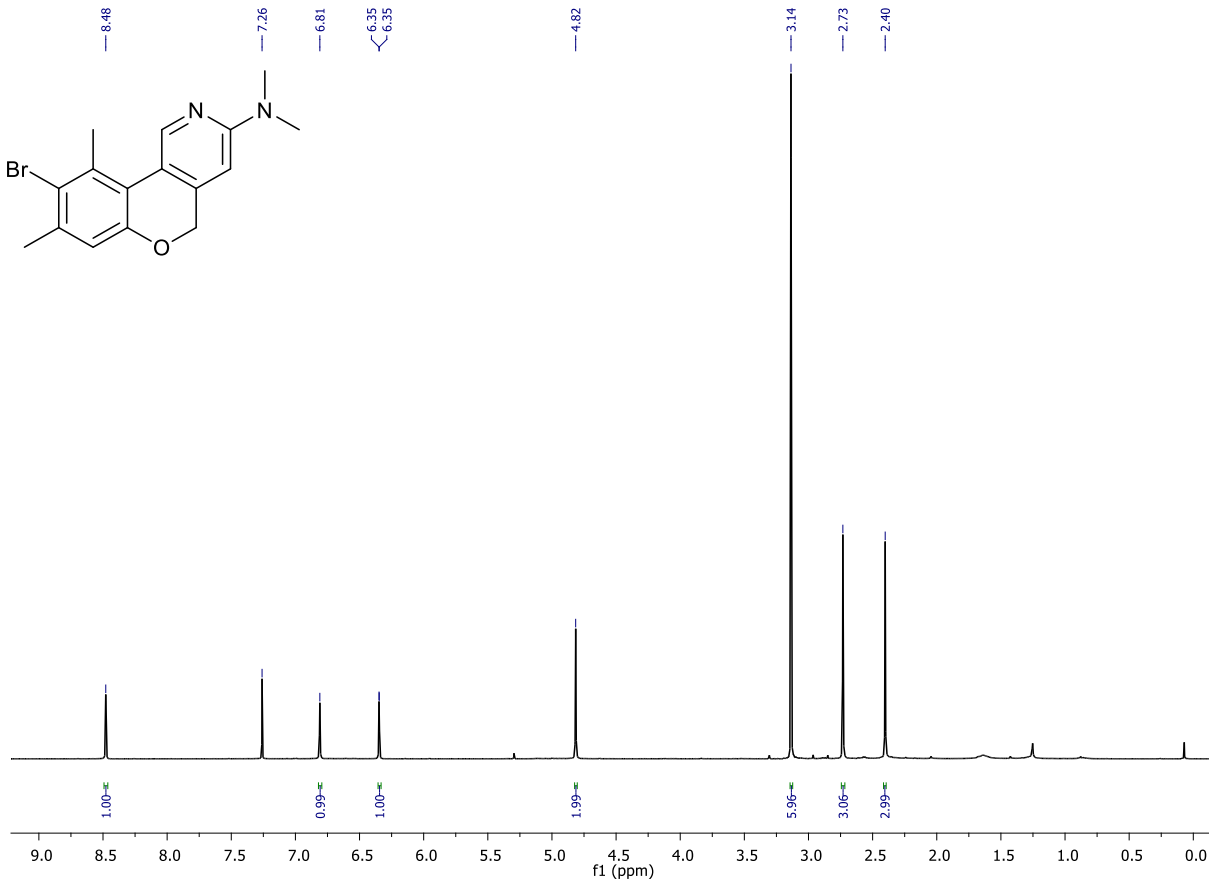
^{13}C NMR of **3ma** (101 MHz, $CDCl_3$)



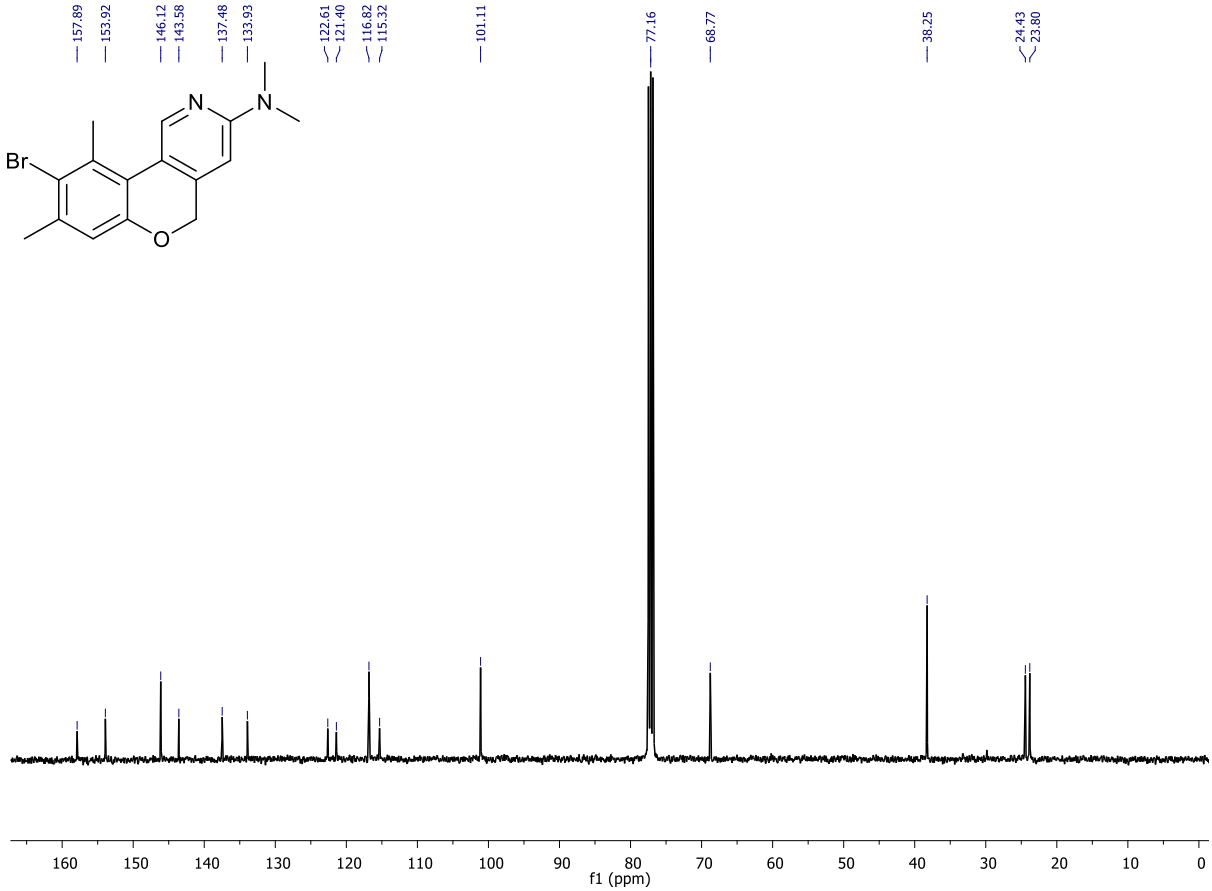
^{1}H NMR of **3na** (400 MHz, $CDCl_3$)



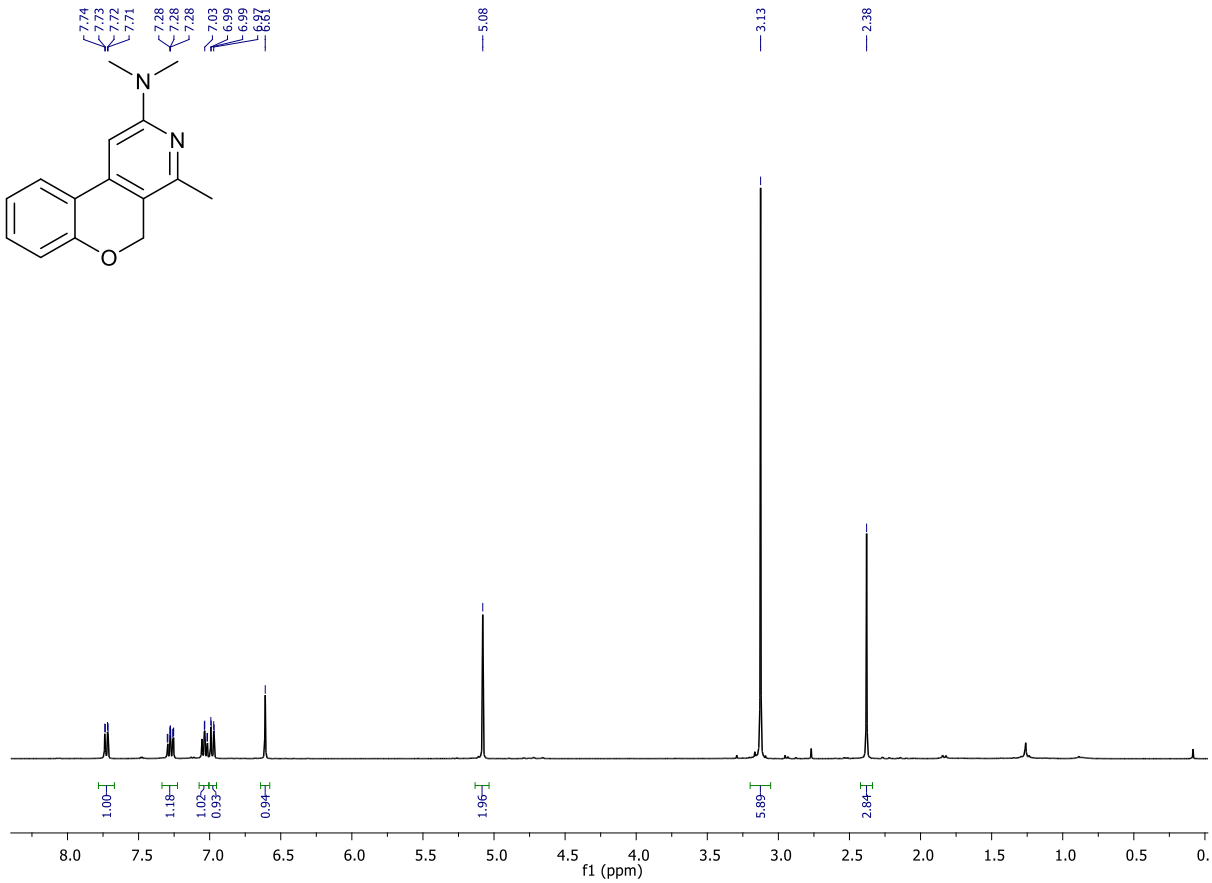
^{13}C NMR of **3na** (101 MHz, $CDCl_3$)



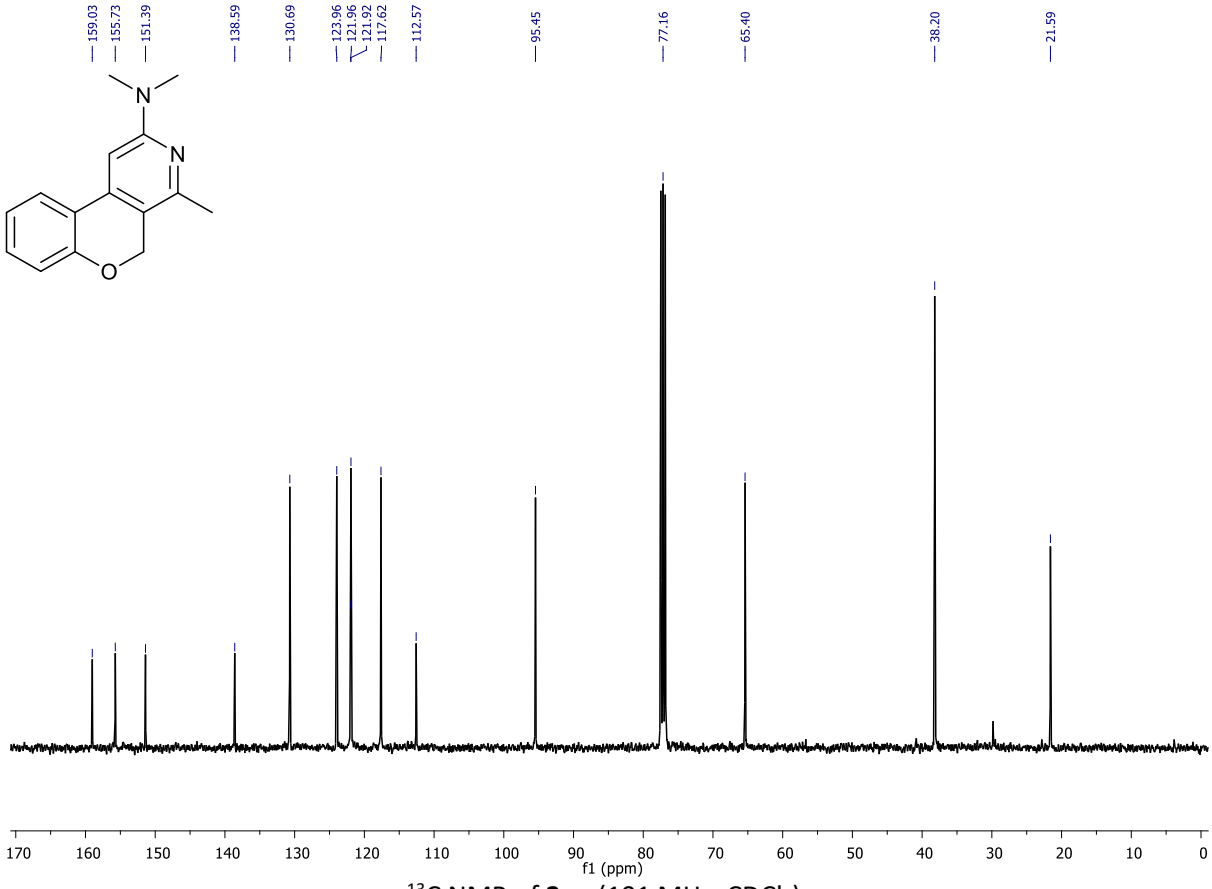
^{1}H NMR of **3na'** (400 MHz, $CDCl_3$)



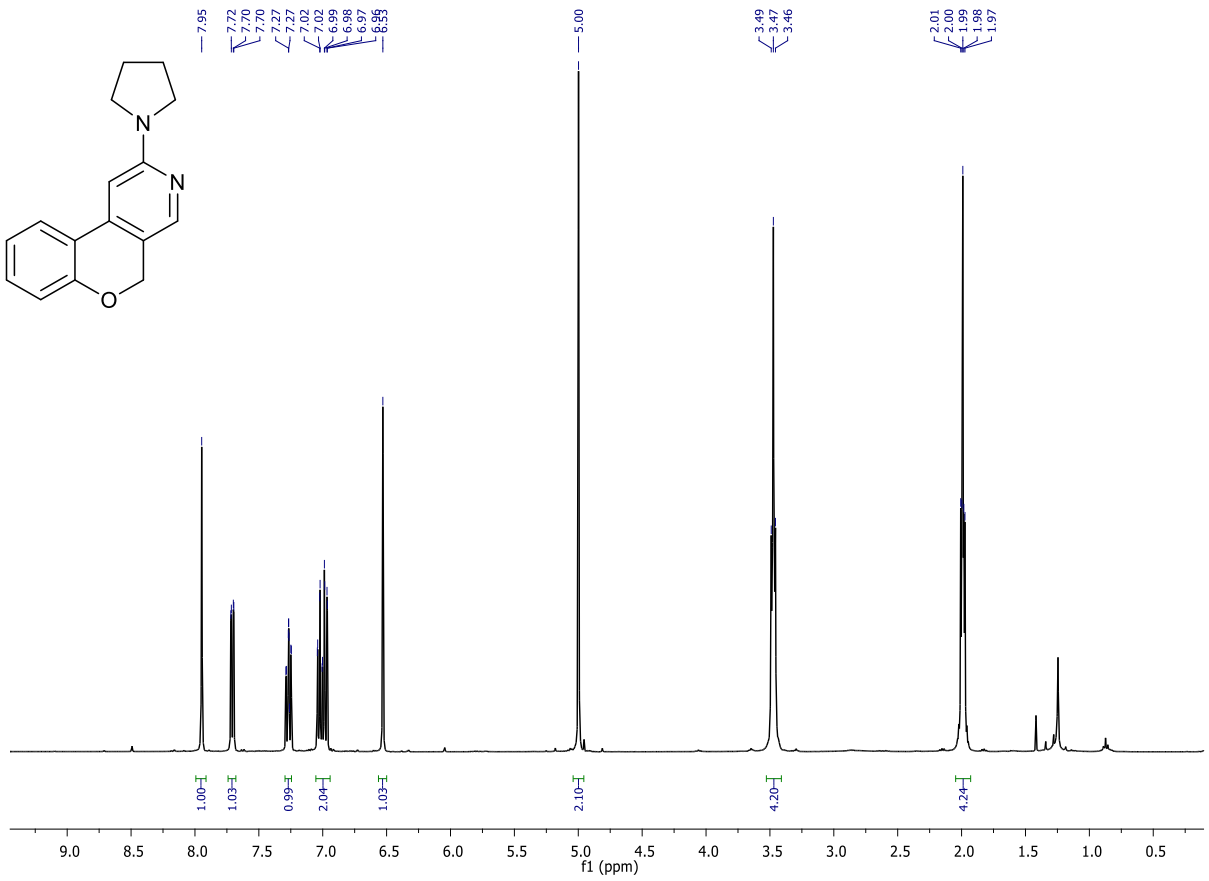
^{13}C NMR of **3na'** (101 MHz, $CDCl_3$)



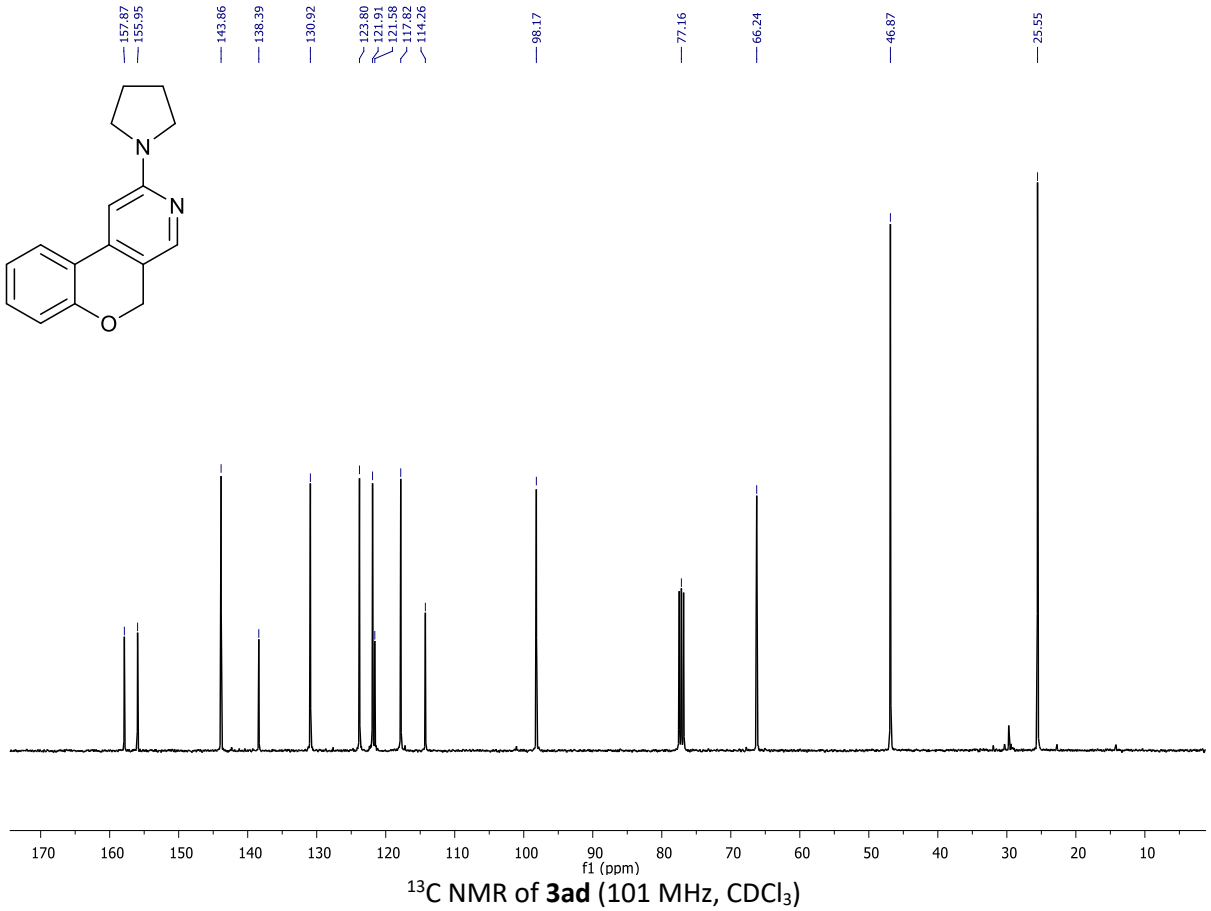
^{1}H NMR of **3oa** (400 MHz, $CDCl_3$)



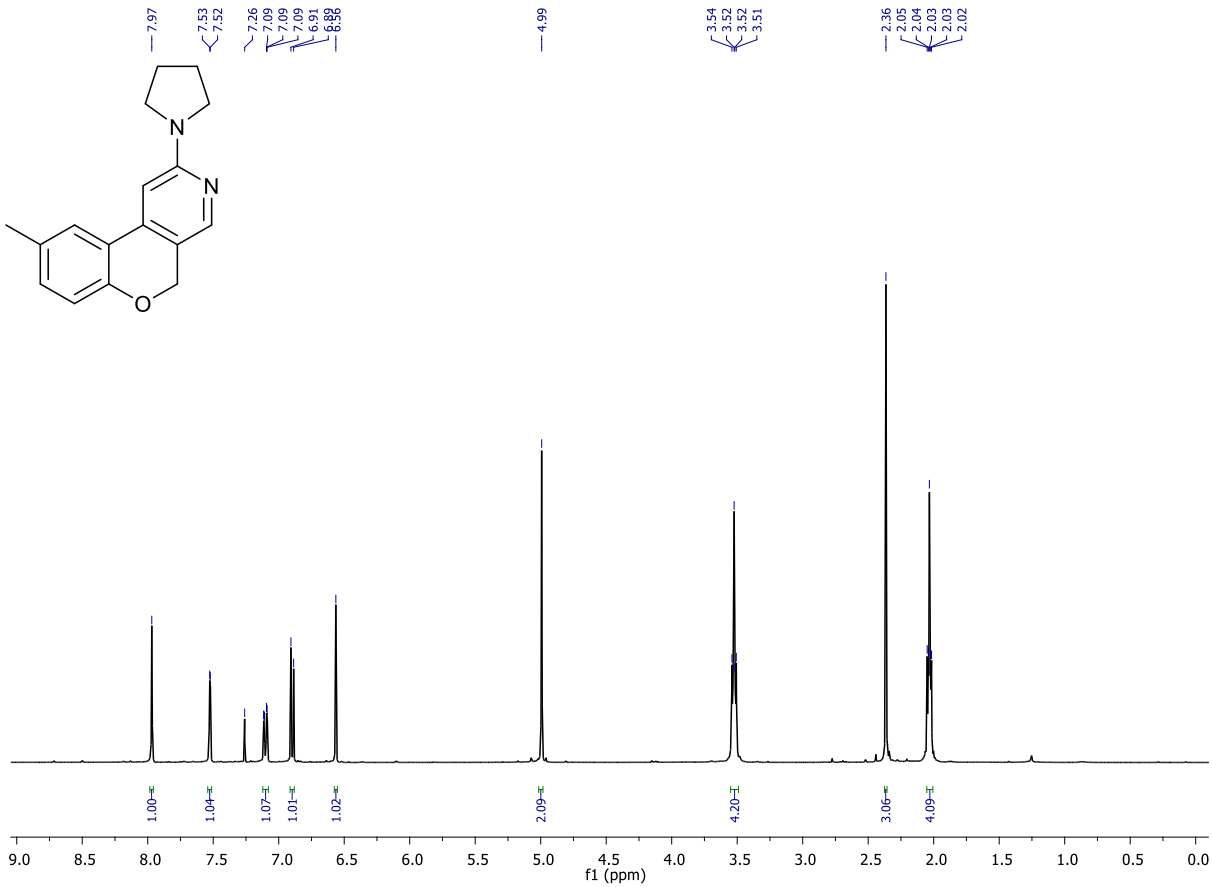
^{13}C NMR of **3oa** (101 MHz, $CDCl_3$)



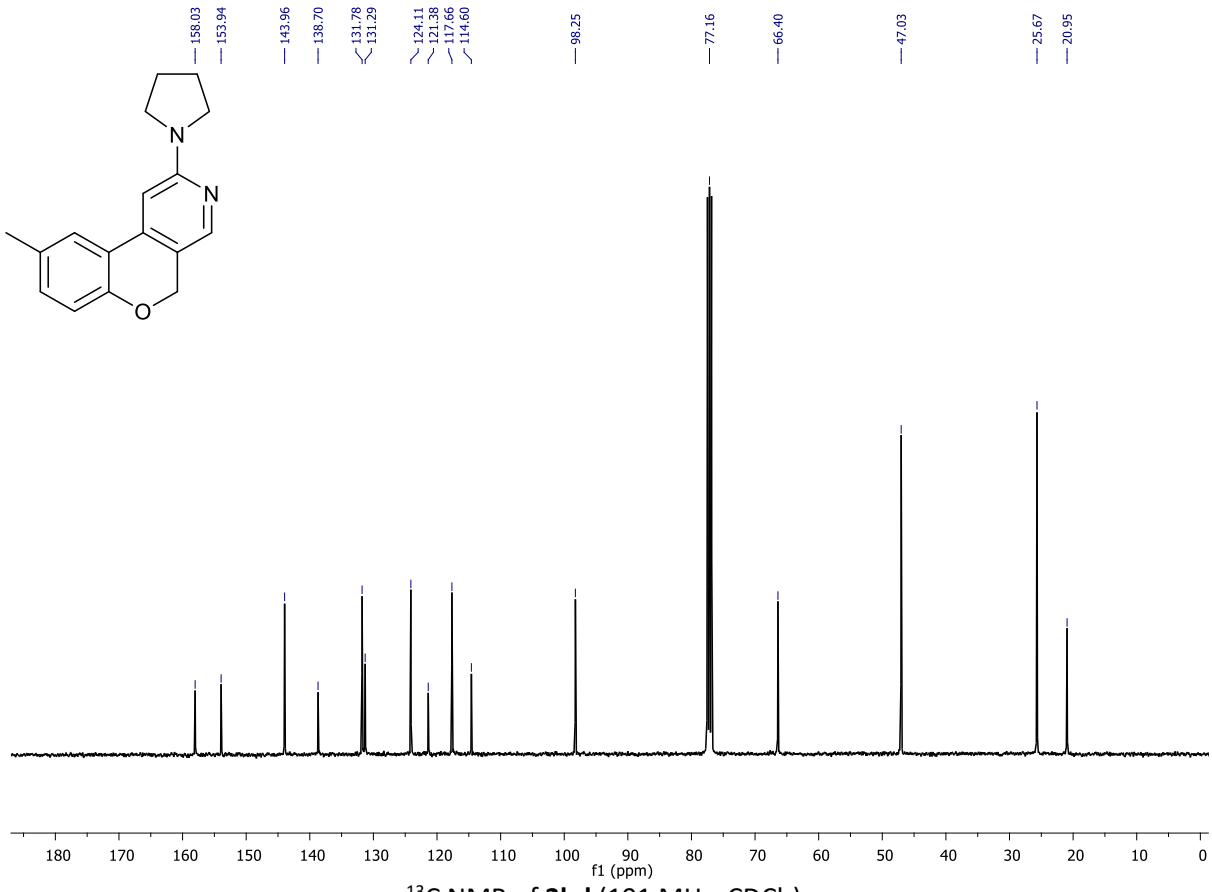
^{1}H NMR of **3ad** (400 MHz, $CDCl_3$)



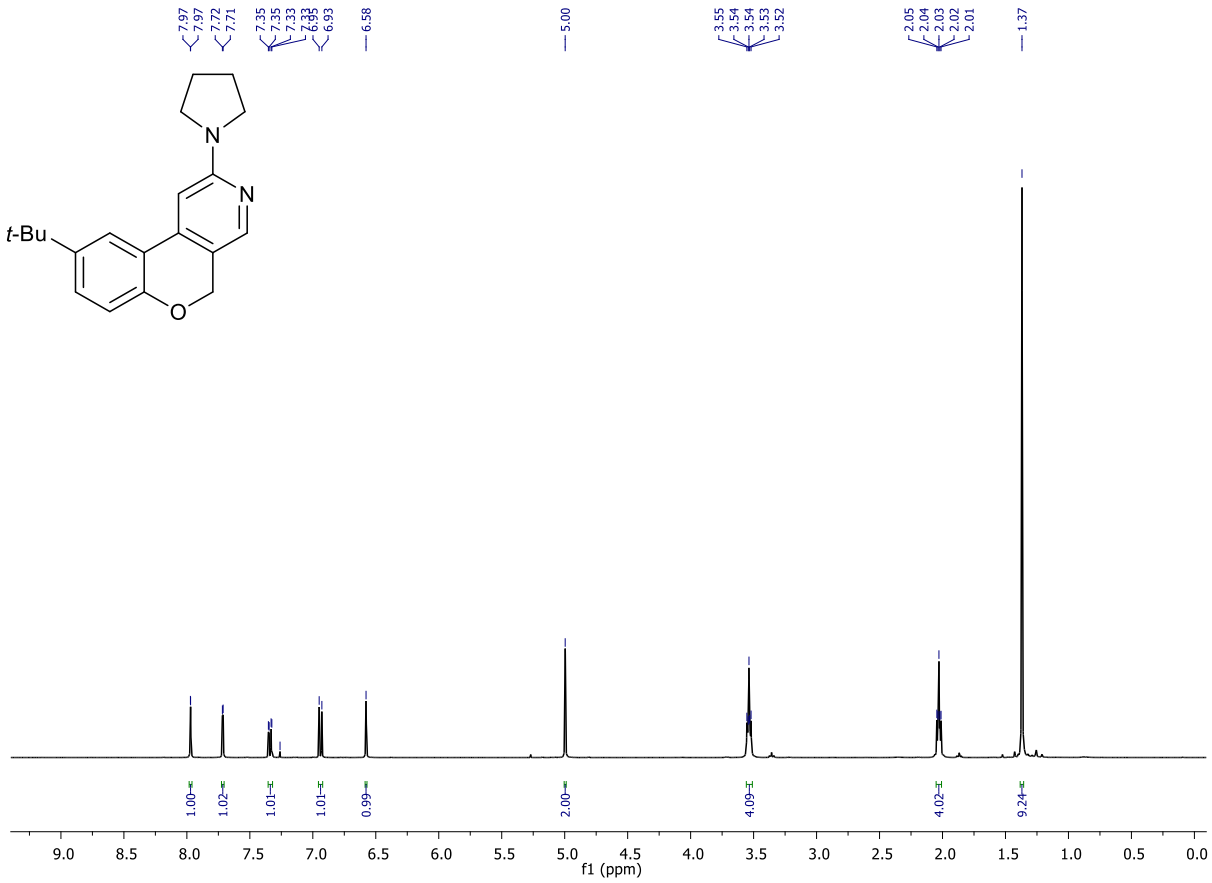
^{13}C NMR of **3ad** (101 MHz, $CDCl_3$)



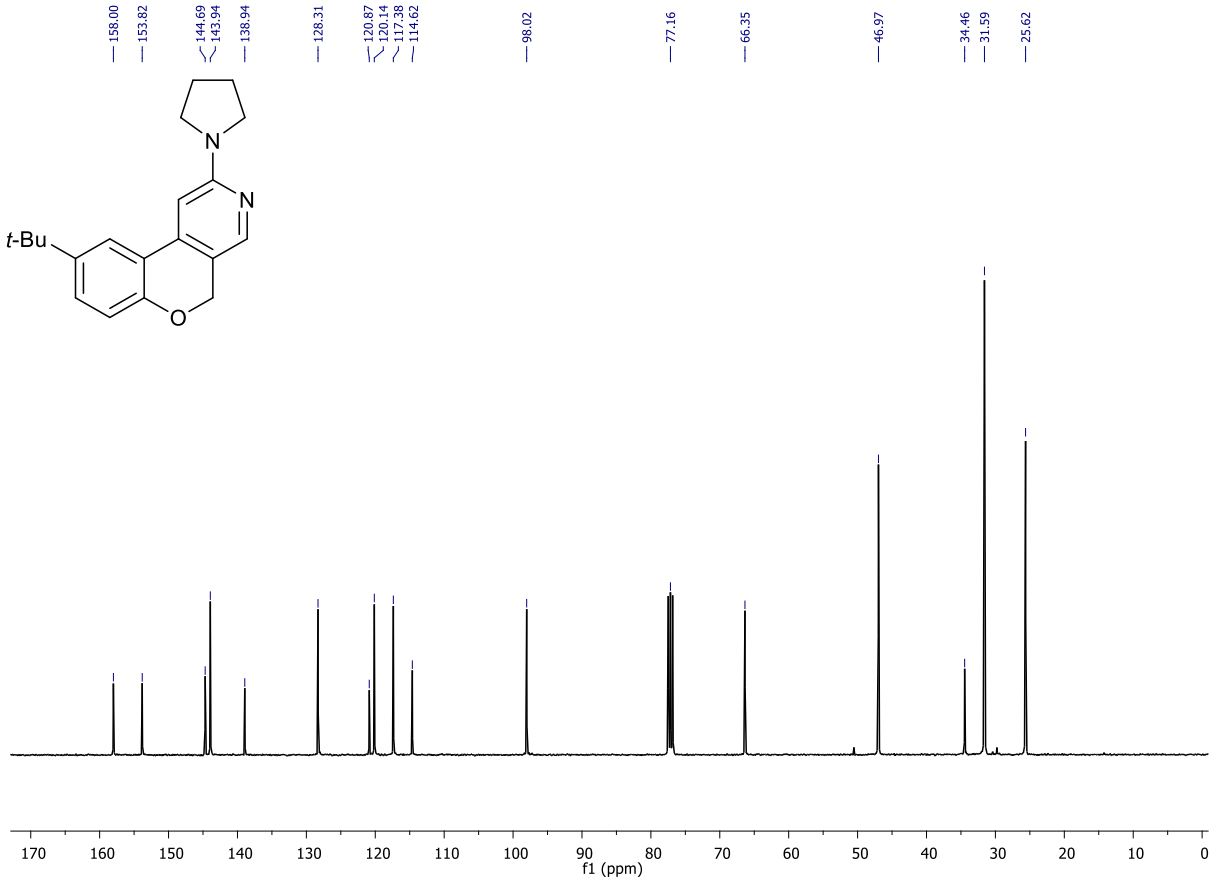
^{1}H NMR of **3bd** (400 MHz, $CDCl_3$)



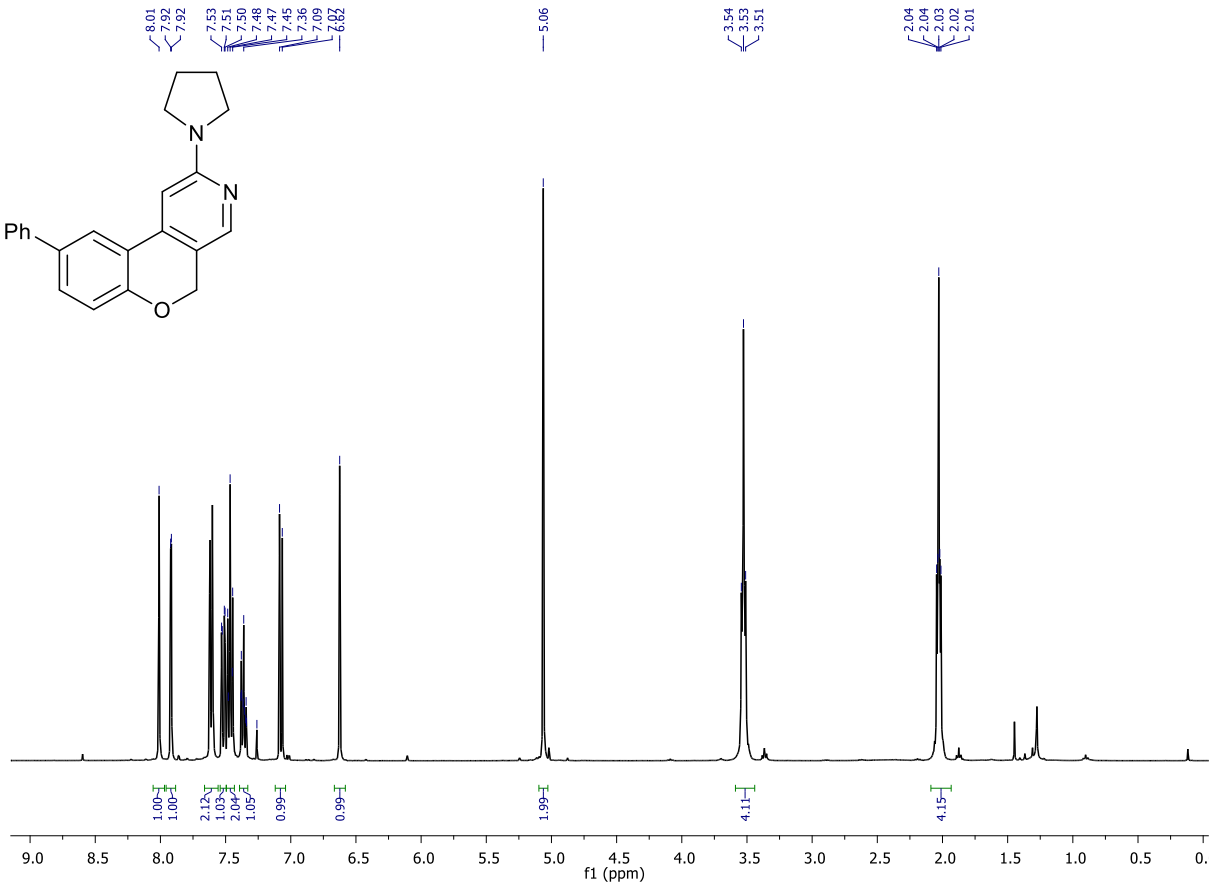
^{13}C NMR of **3bd** (101 MHz, $CDCl_3$)



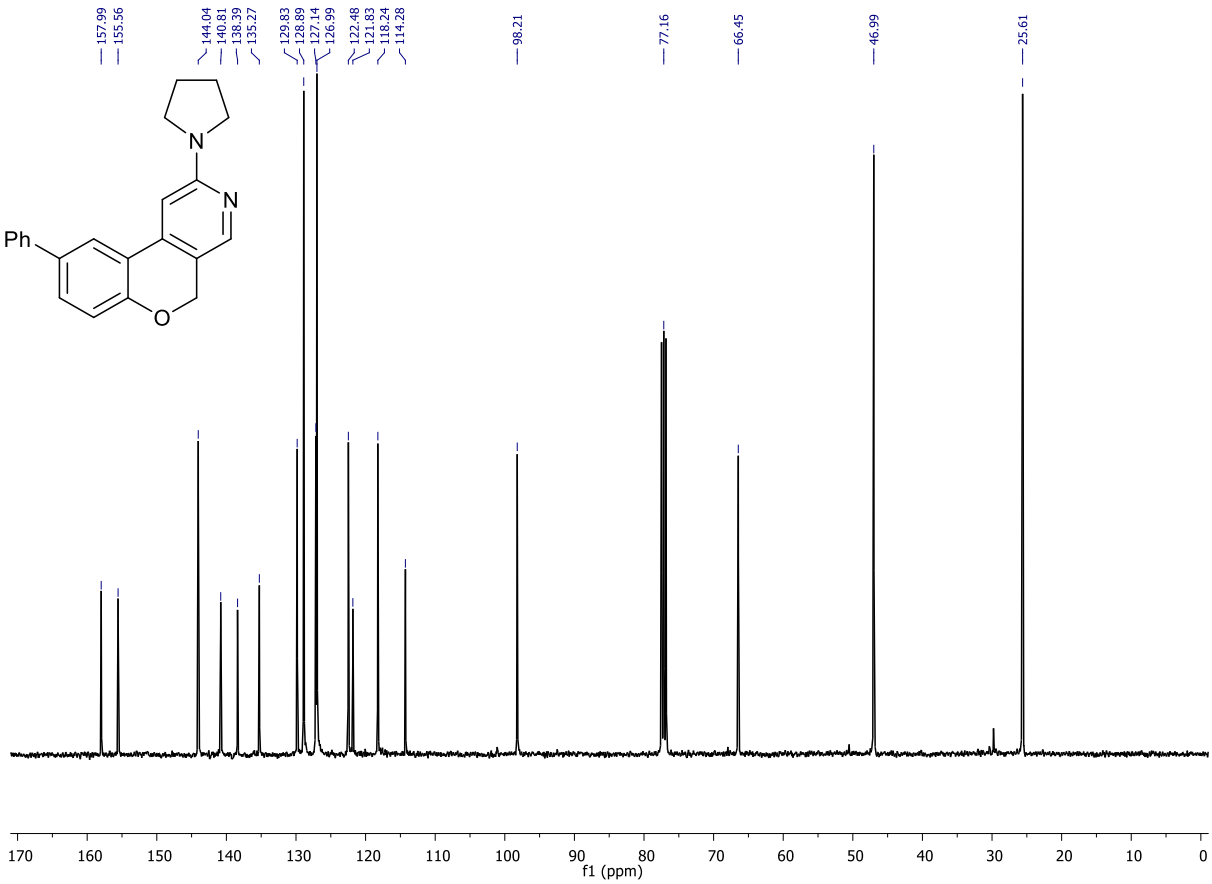
^{1}H NMR of **3dd** (400 MHz, $CDCl_3$)



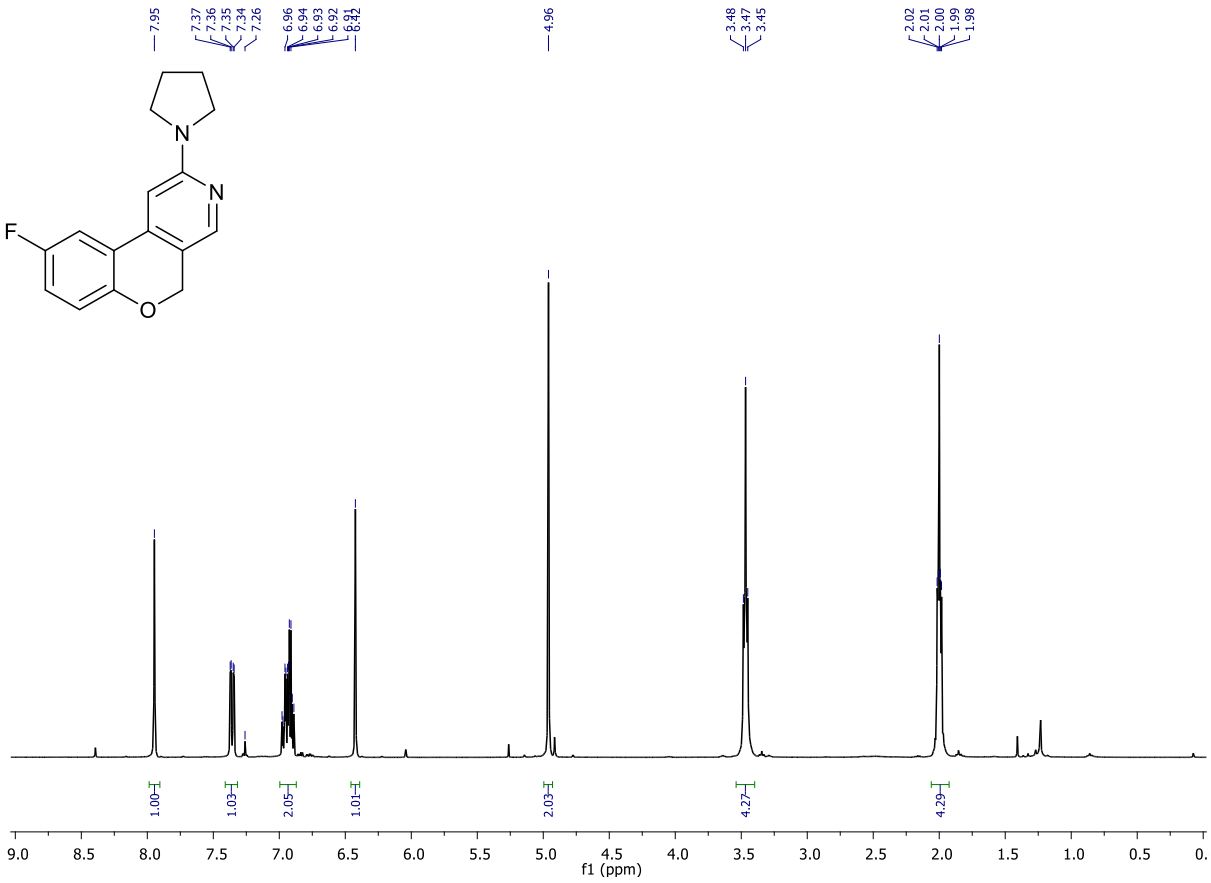
^{13}C NMR of **3dd** (101 MHz, $CDCl_3$)



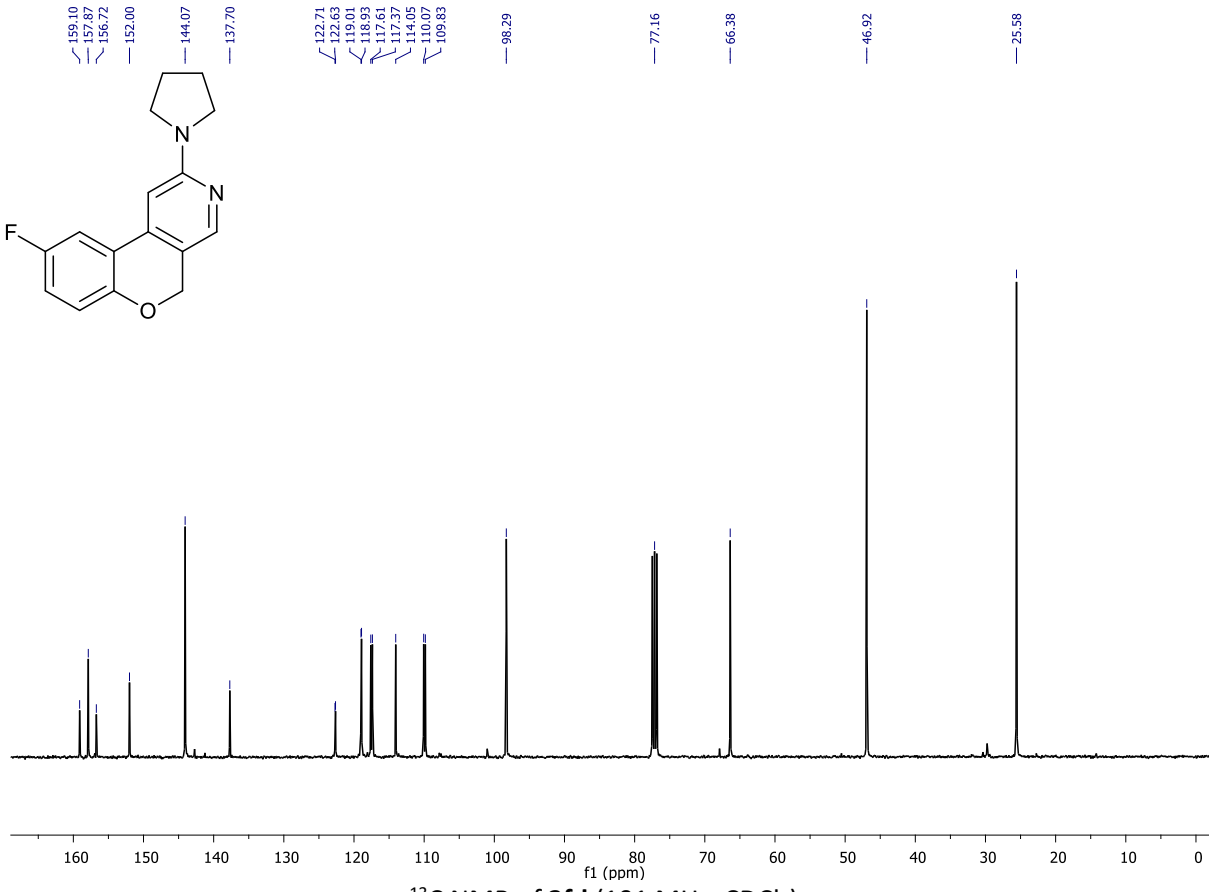
^{1}H NMR of **3ed** (400 MHz, $CDCl_3$)



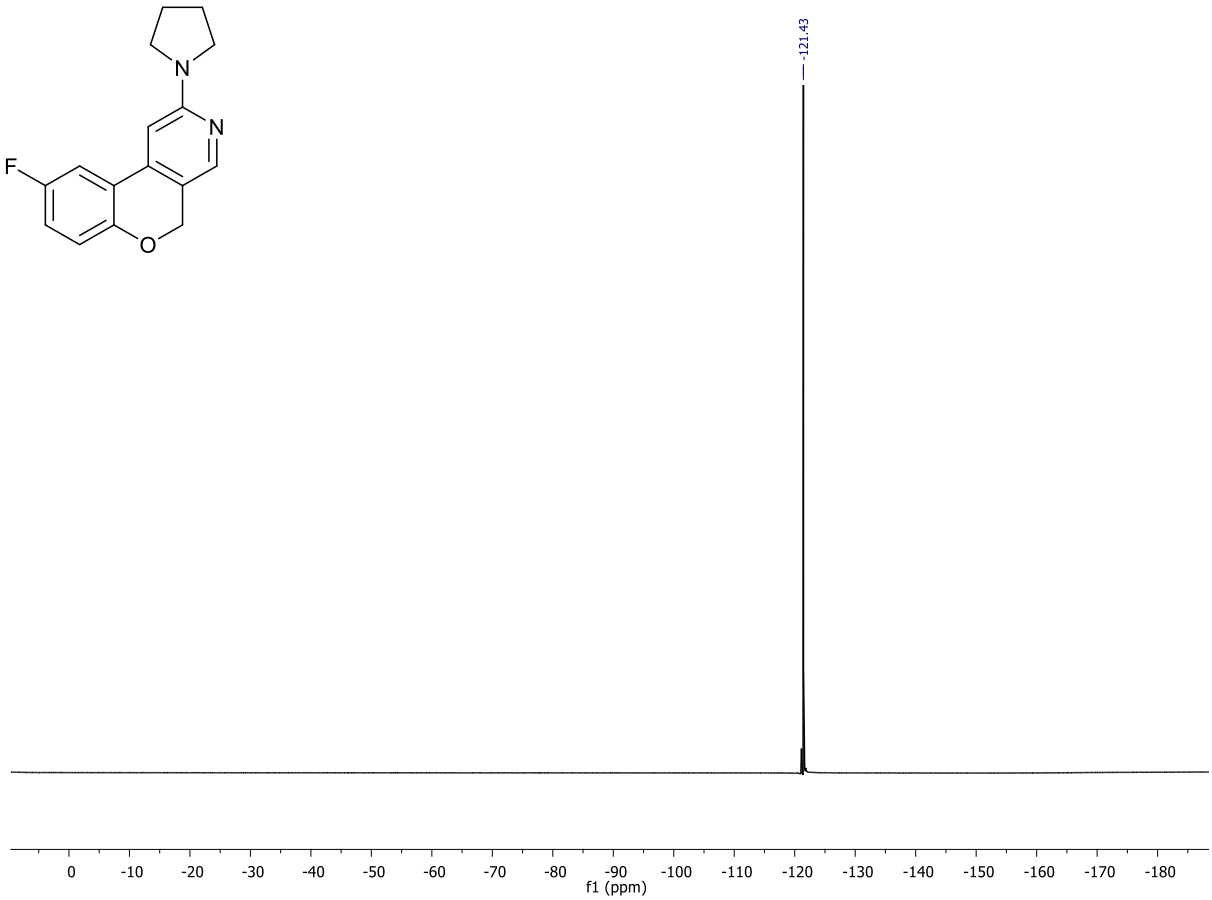
^{13}C NMR of **3ed** (101 MHz, $CDCl_3$)



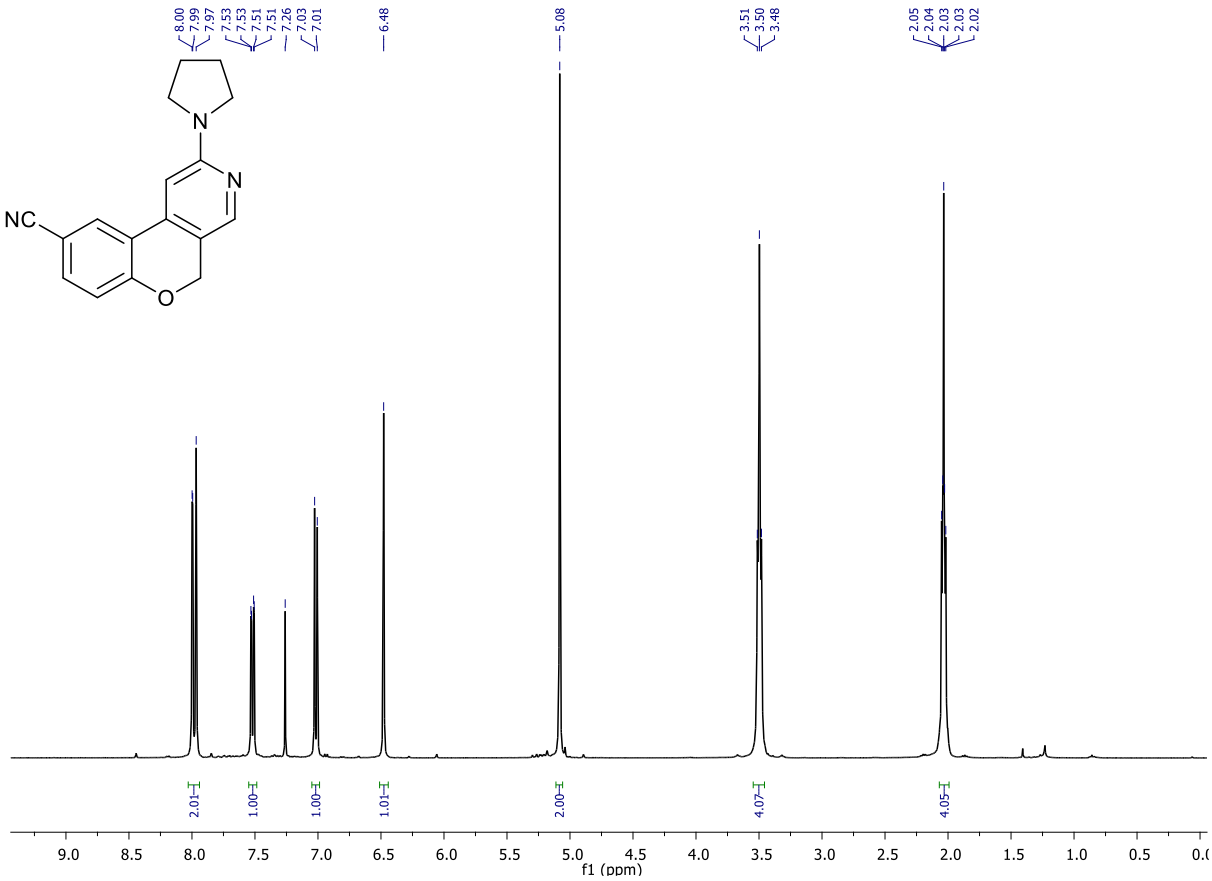
^{1}H NMR of **3fd** (400 MHz, $CDCl_3$)



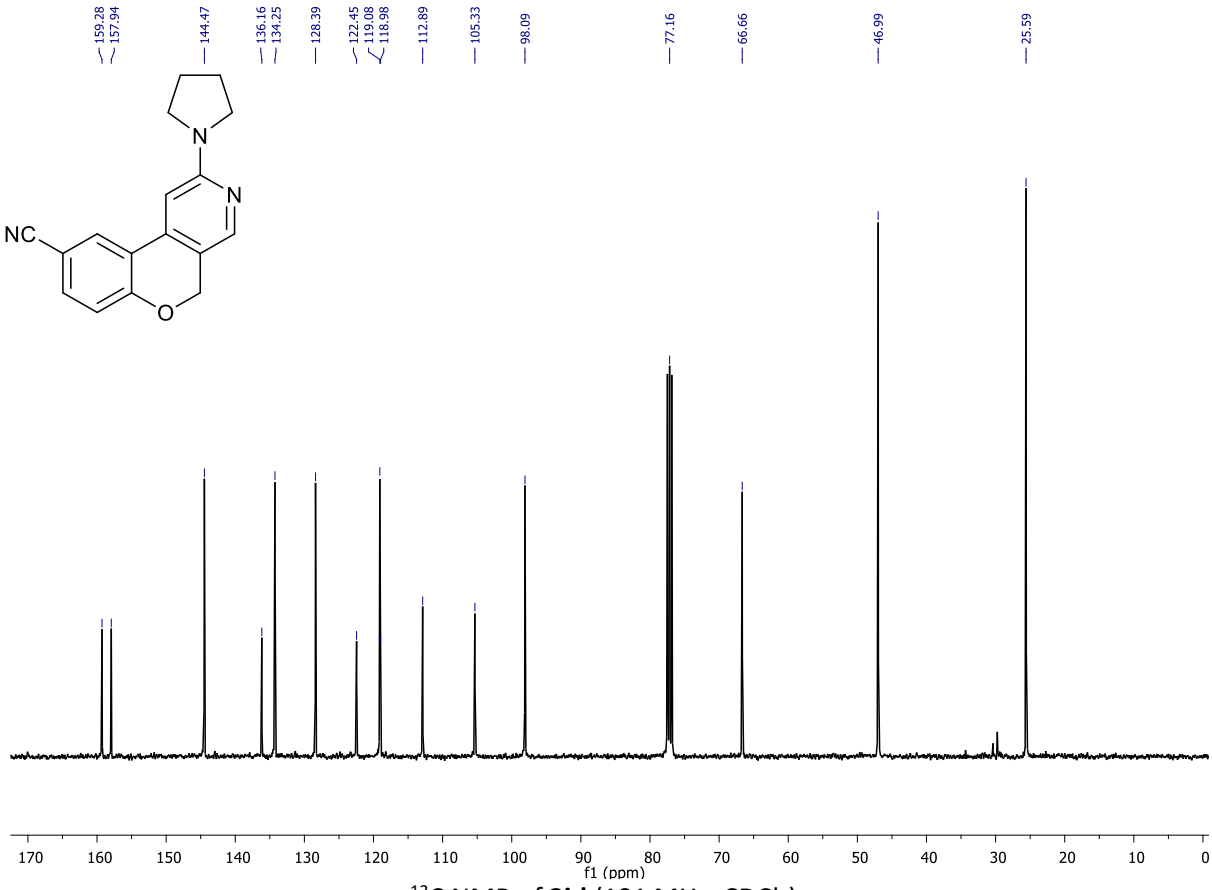
^{13}C NMR of **3fd** (101 MHz, $CDCl_3$)



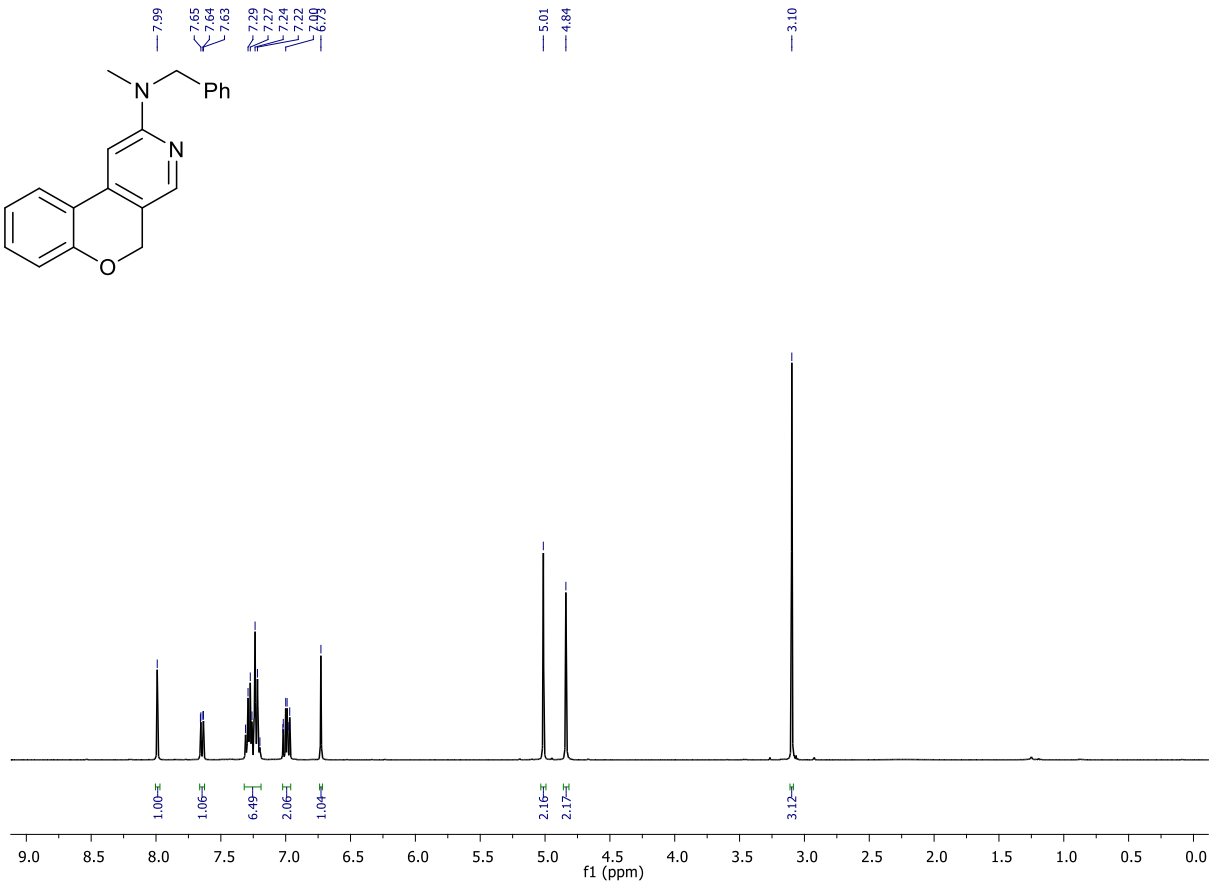
^{19}F NMR of **3fd** (376.5 MHz, $CDCl_3$)



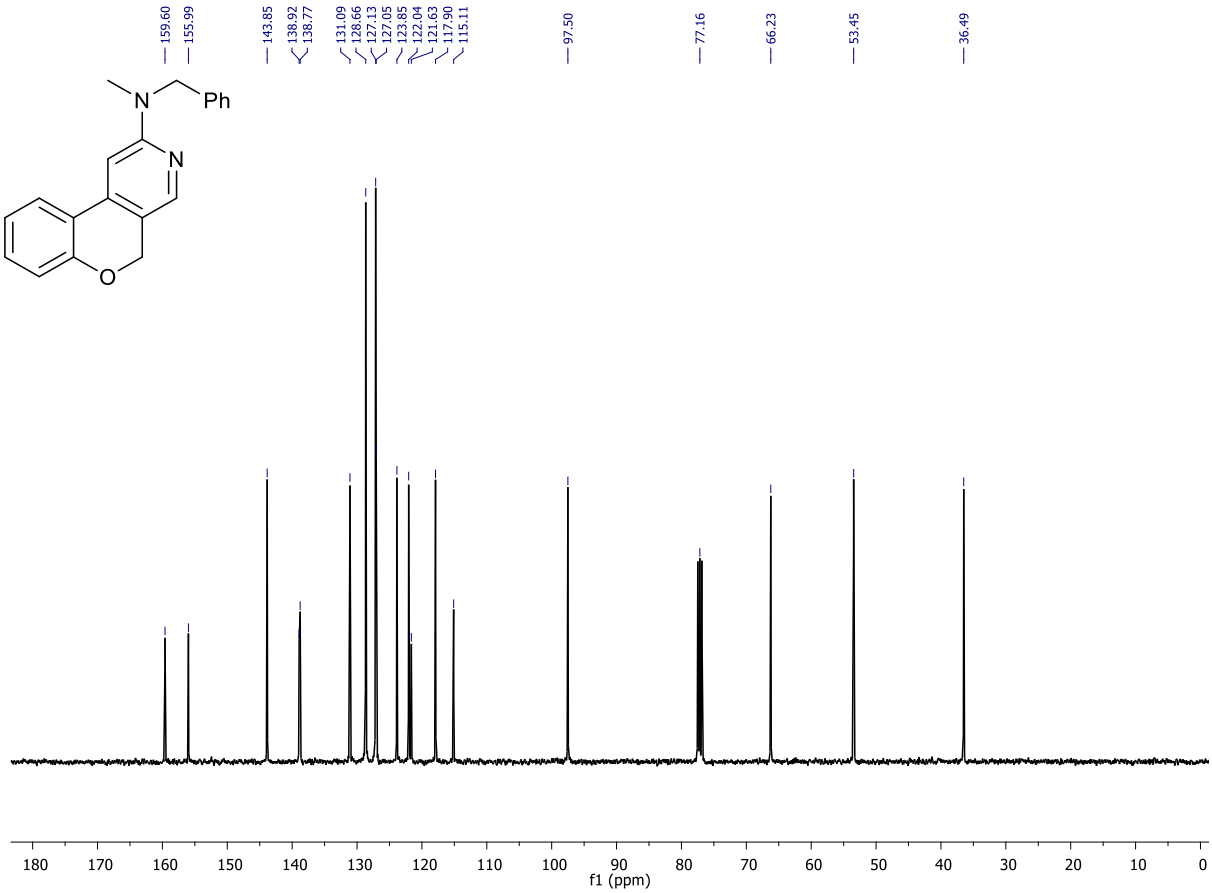
^{1}H NMR of **3id** (400 MHz, $CDCl_3$)



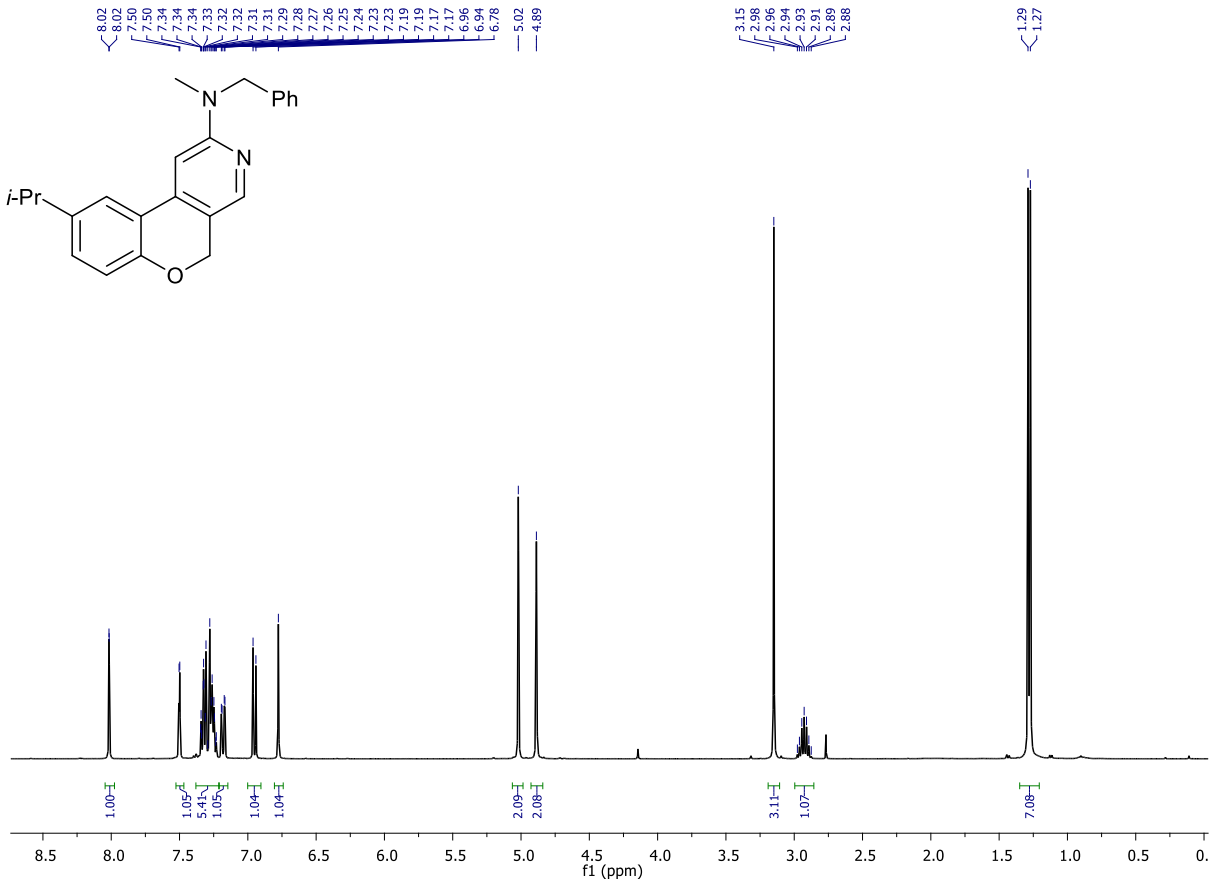
^{13}C NMR of **3id** (101 MHz, $CDCl_3$)



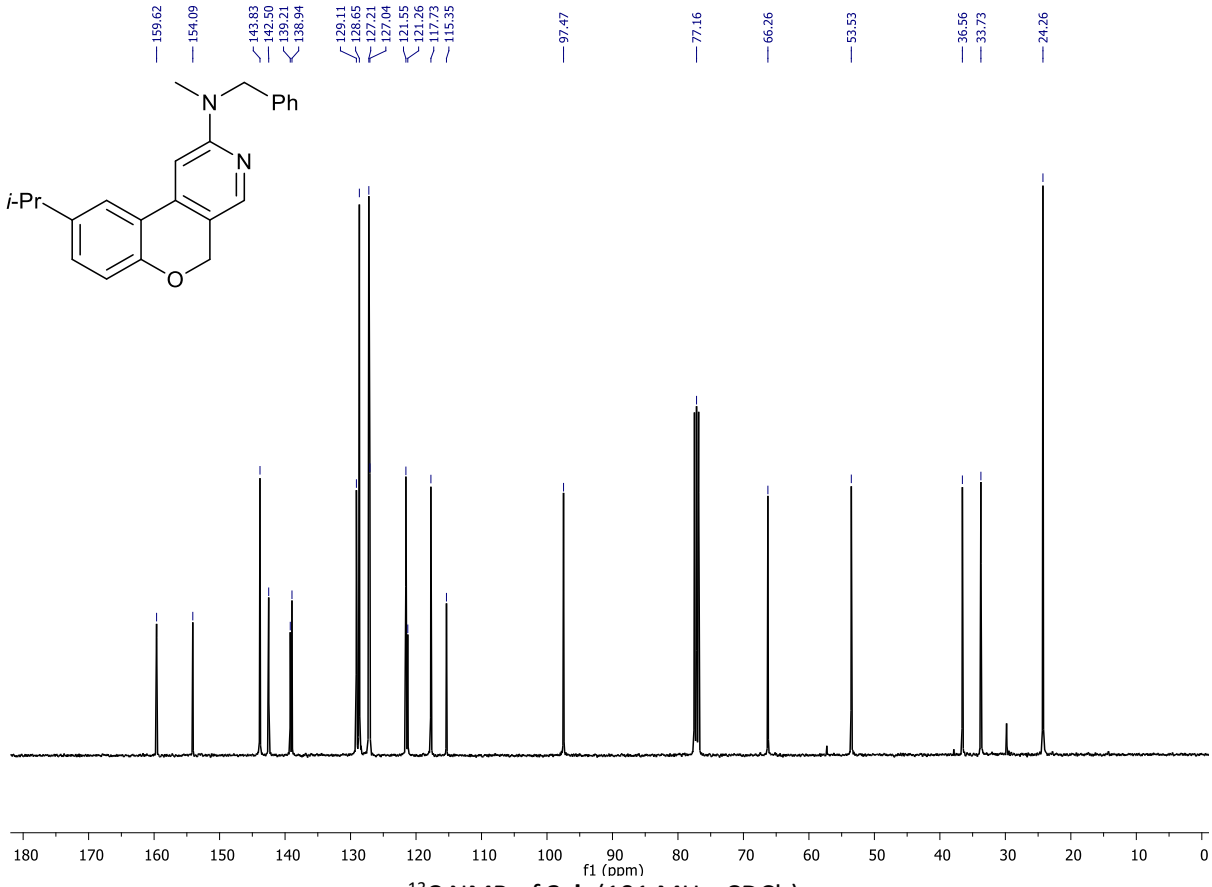
^{1}H NMR of **3ab** (400 MHz, $CDCl_3$)



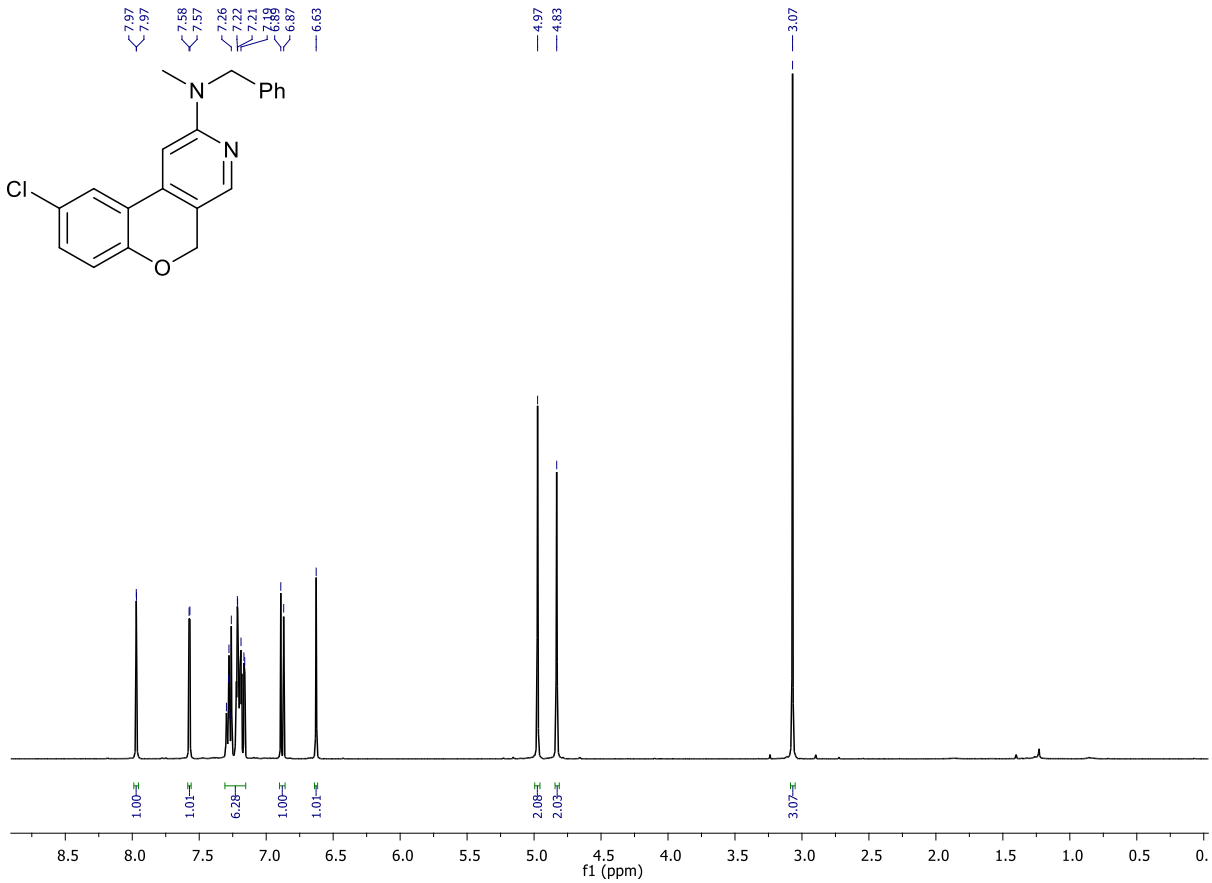
^{13}C NMR of **3ab** (101 MHz, $CDCl_3$)



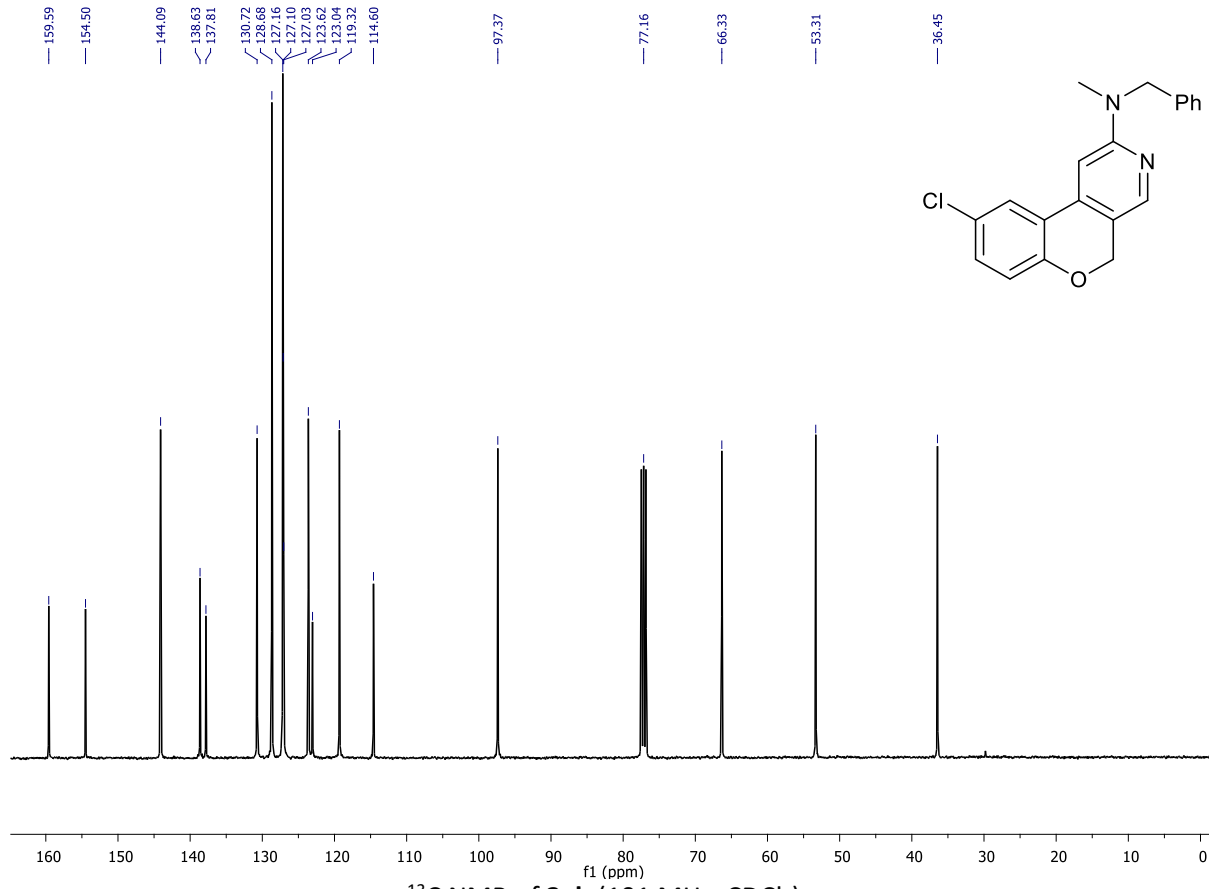
^{1}H NMR of **3cb** (400 MHz, $CDCl_3$)



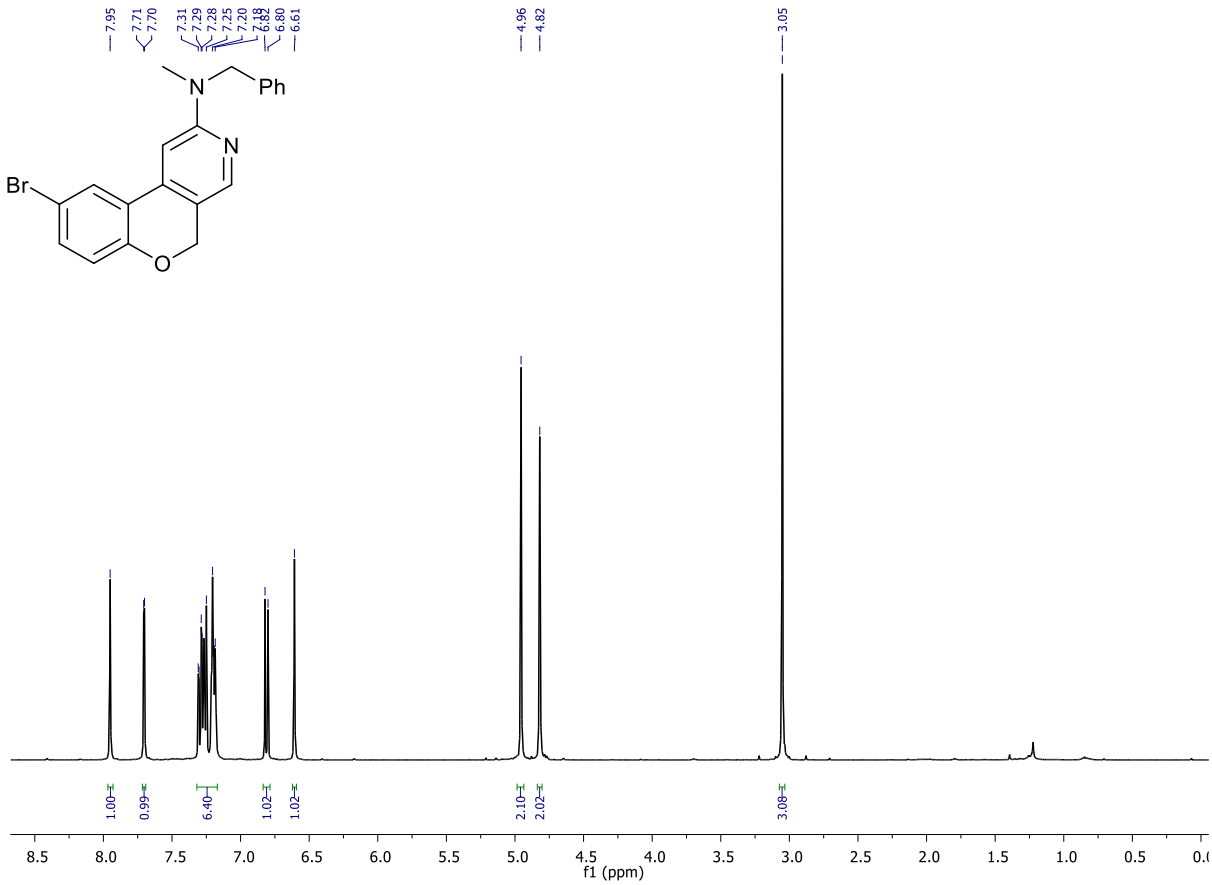
^{13}C NMR of **3cb** (101 MHz, $CDCl_3$)



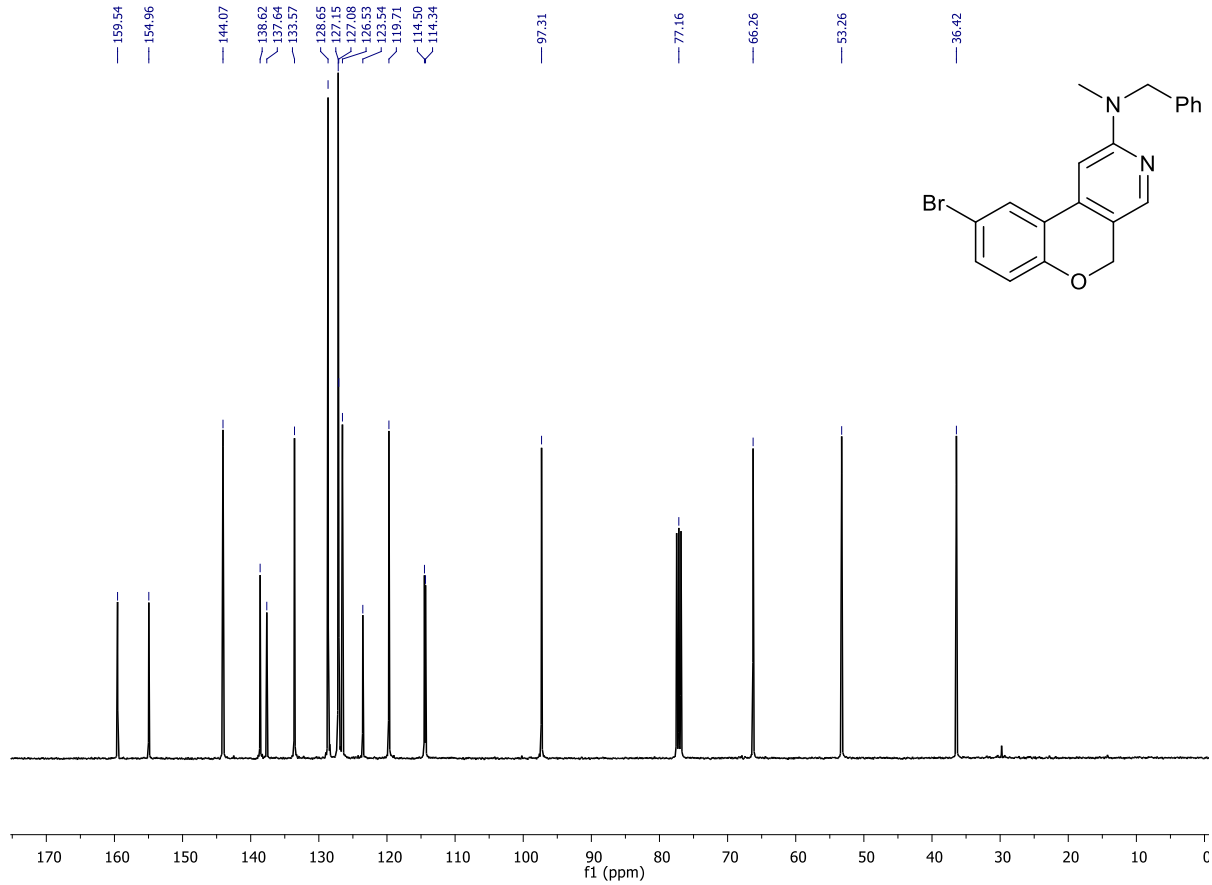
^{1}H NMR of **3gb** (400 MHz, $CDCl_3$)



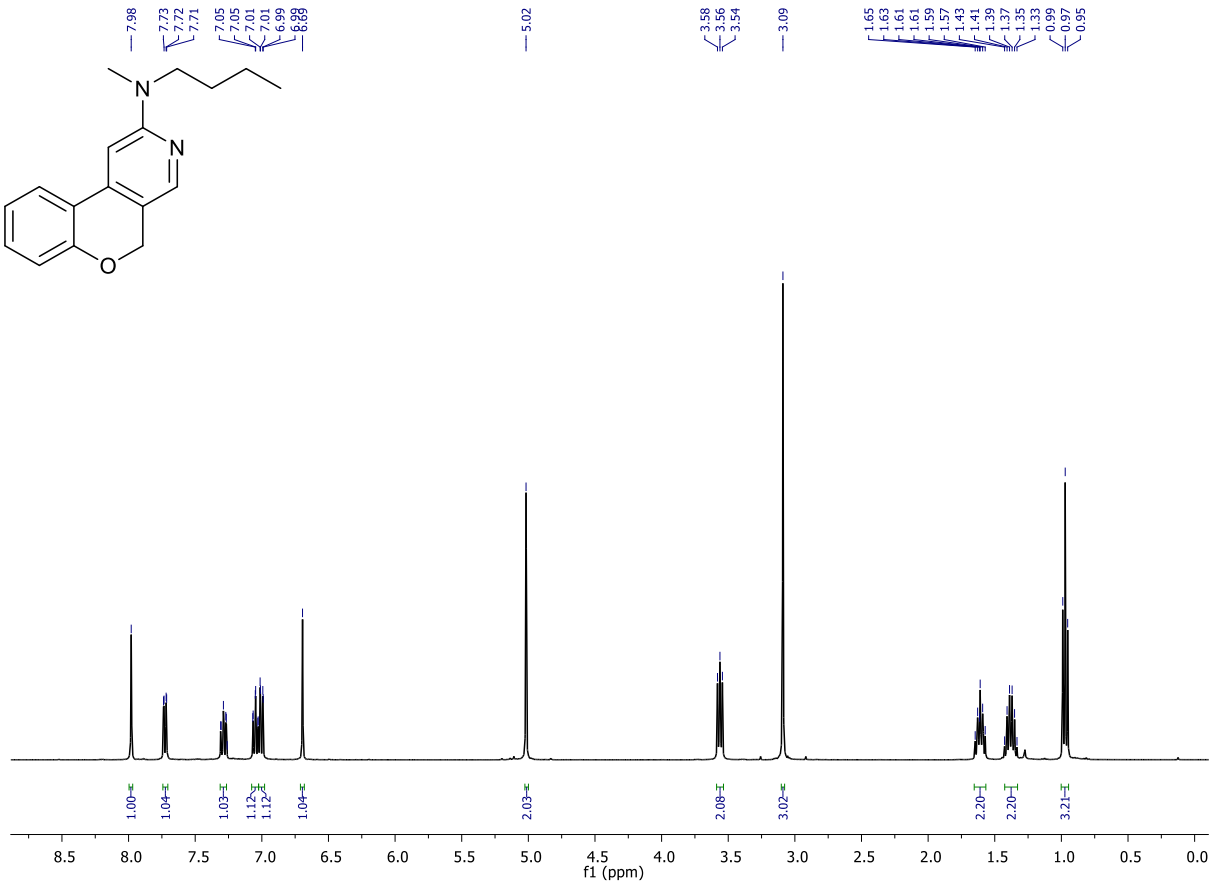
^{13}C NMR of **3gb** (101 MHz, $CDCl_3$)



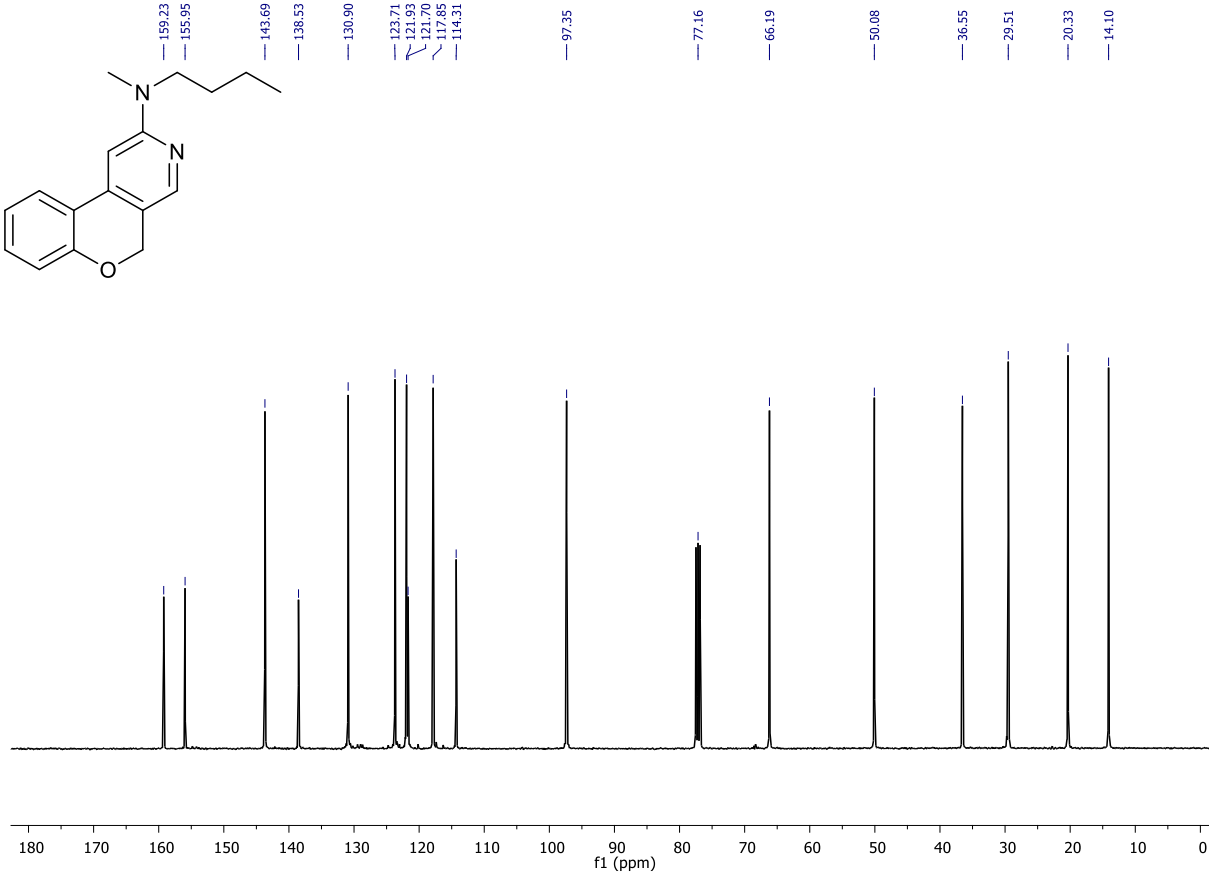
^{1}H NMR of **3hb** (400 MHz, $CDCl_3$)



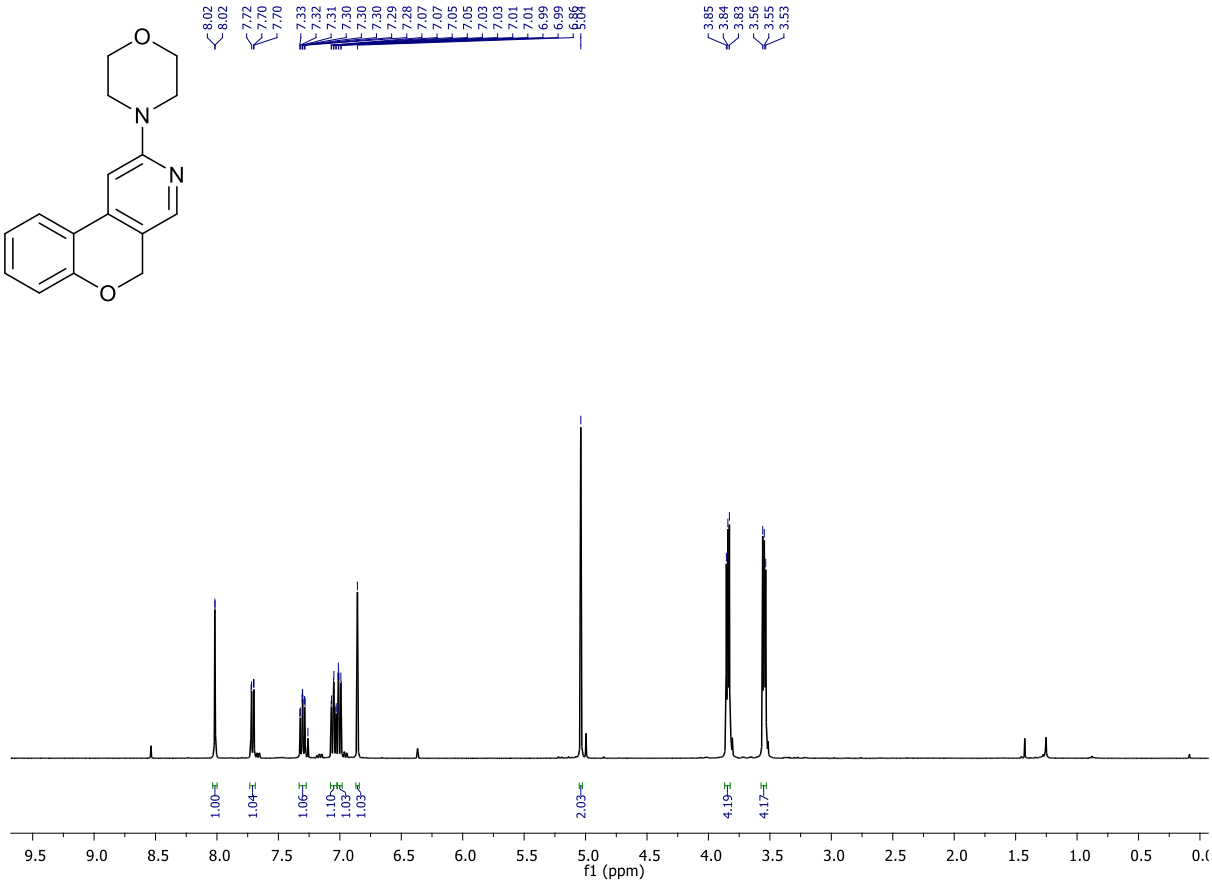
^{13}C NMR of **3hb** (101 MHz, $CDCl_3$)



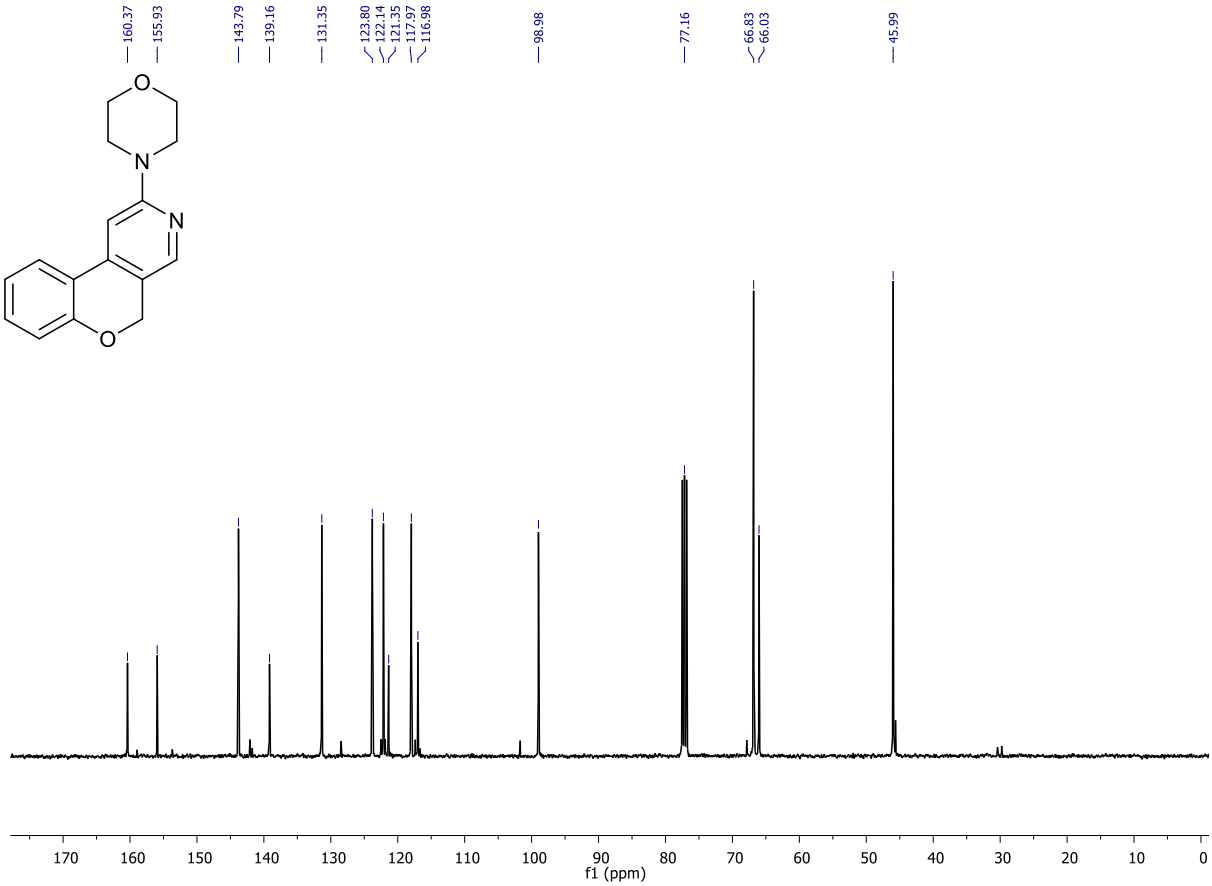
^{1}H NMR of **3ac** (400 MHz, $CDCl_3$)



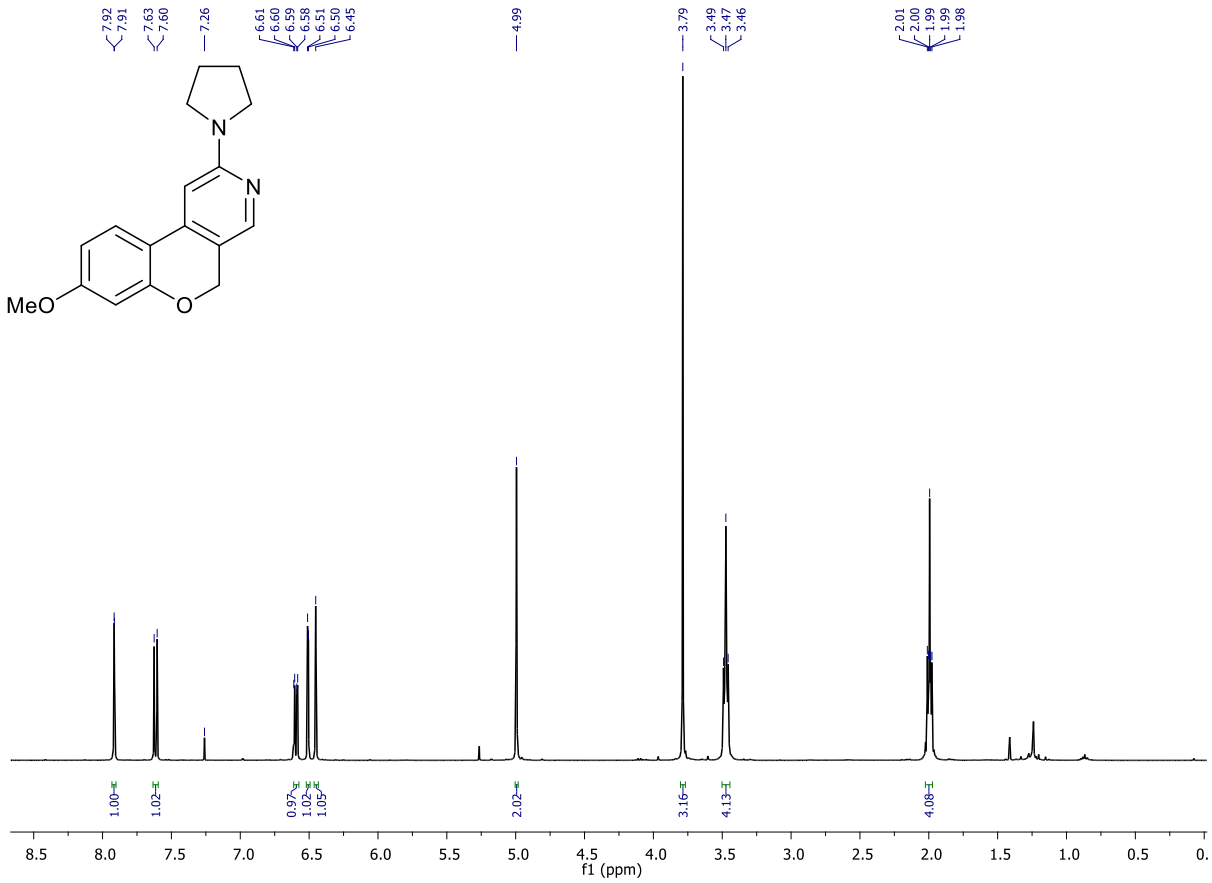
^{13}C NMR of **3ac** (101 MHz, $CDCl_3$)



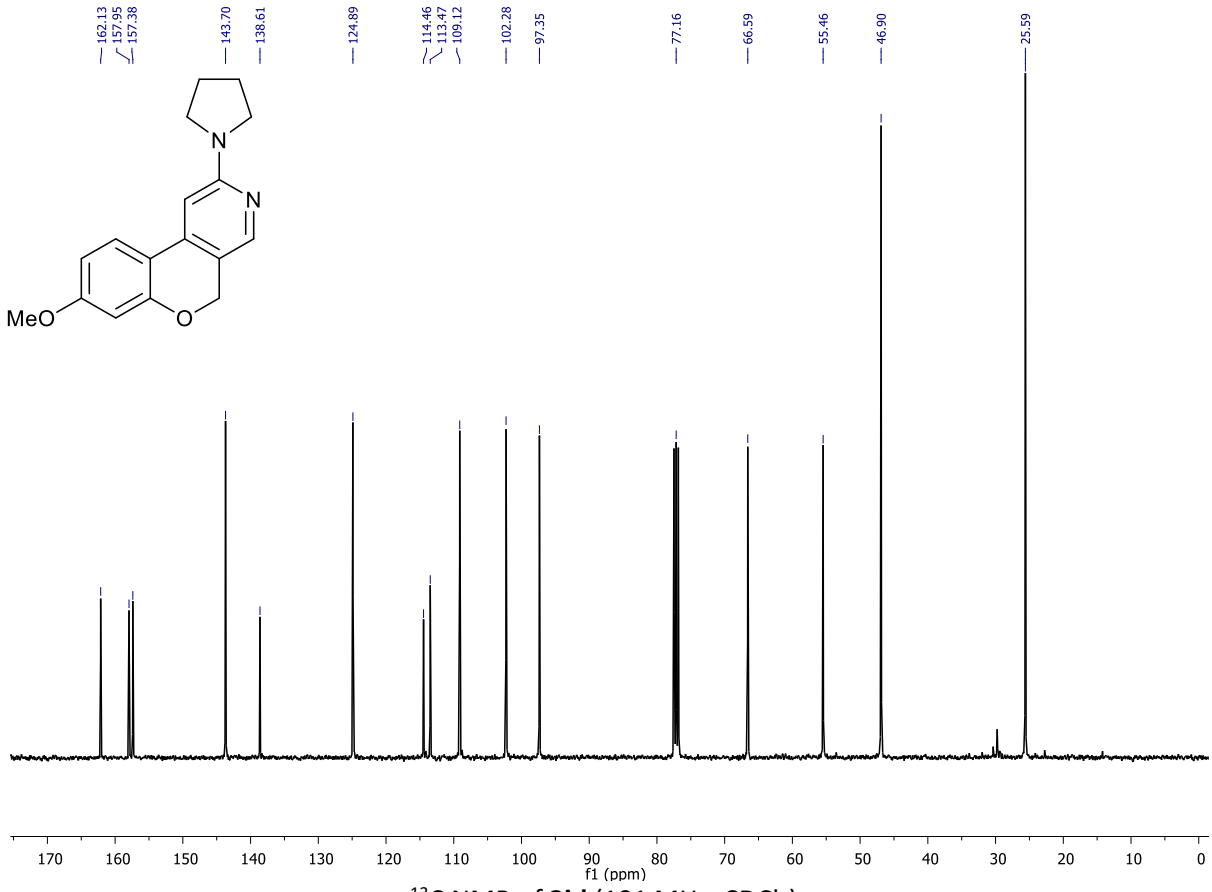
^{1}H NMR of **3ae** (400 MHz, $CDCl_3$)



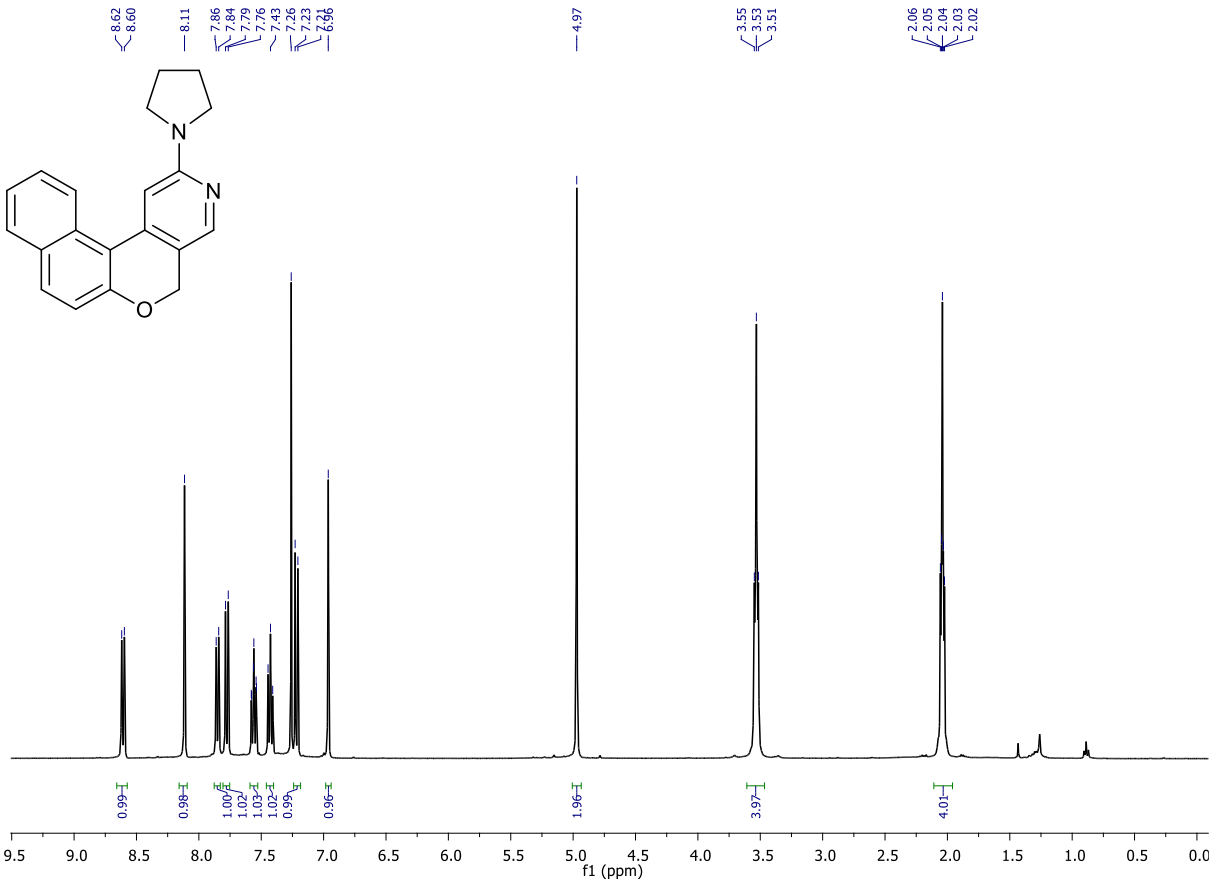
^{13}C NMR of **3ae** (101 MHz, $CDCl_3$)



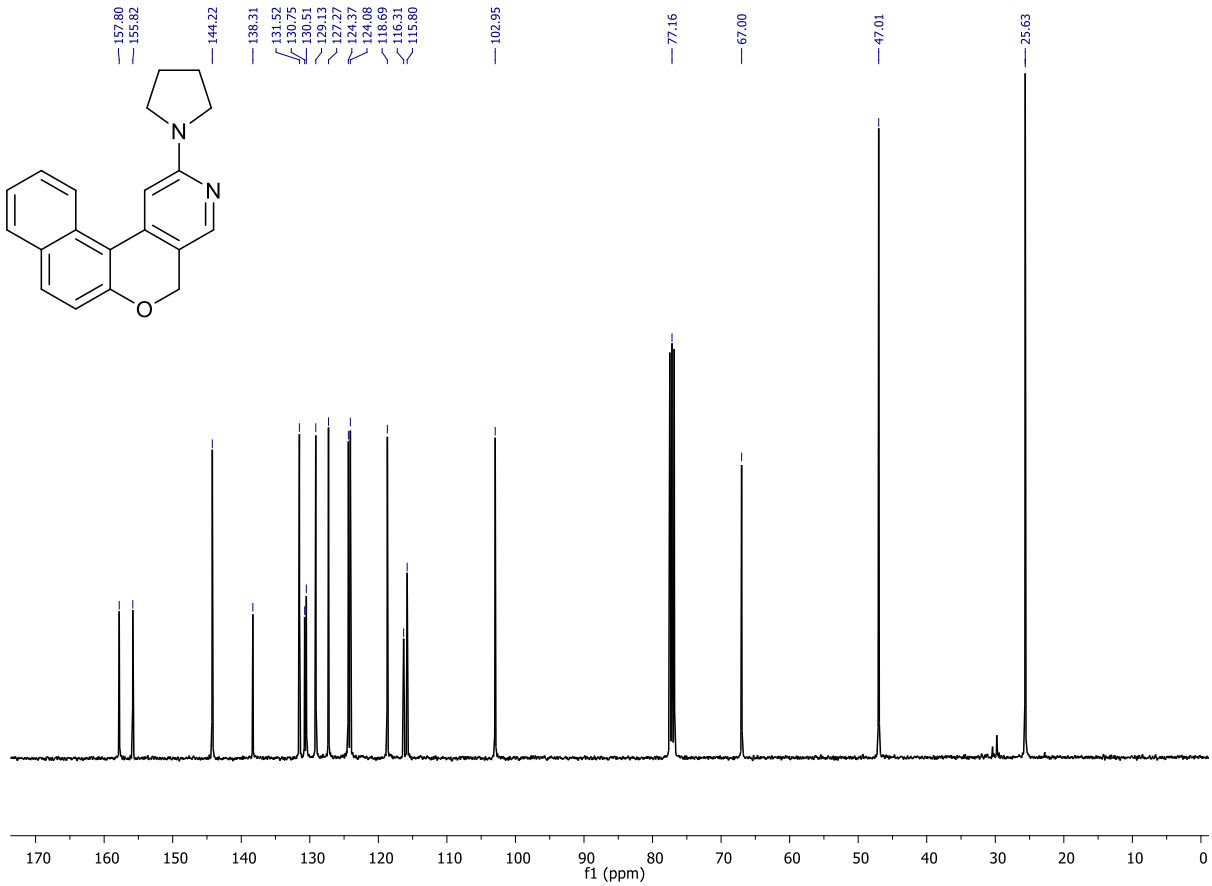
^{1}H NMR of **3jd** (400 MHz, $CDCl_3$)



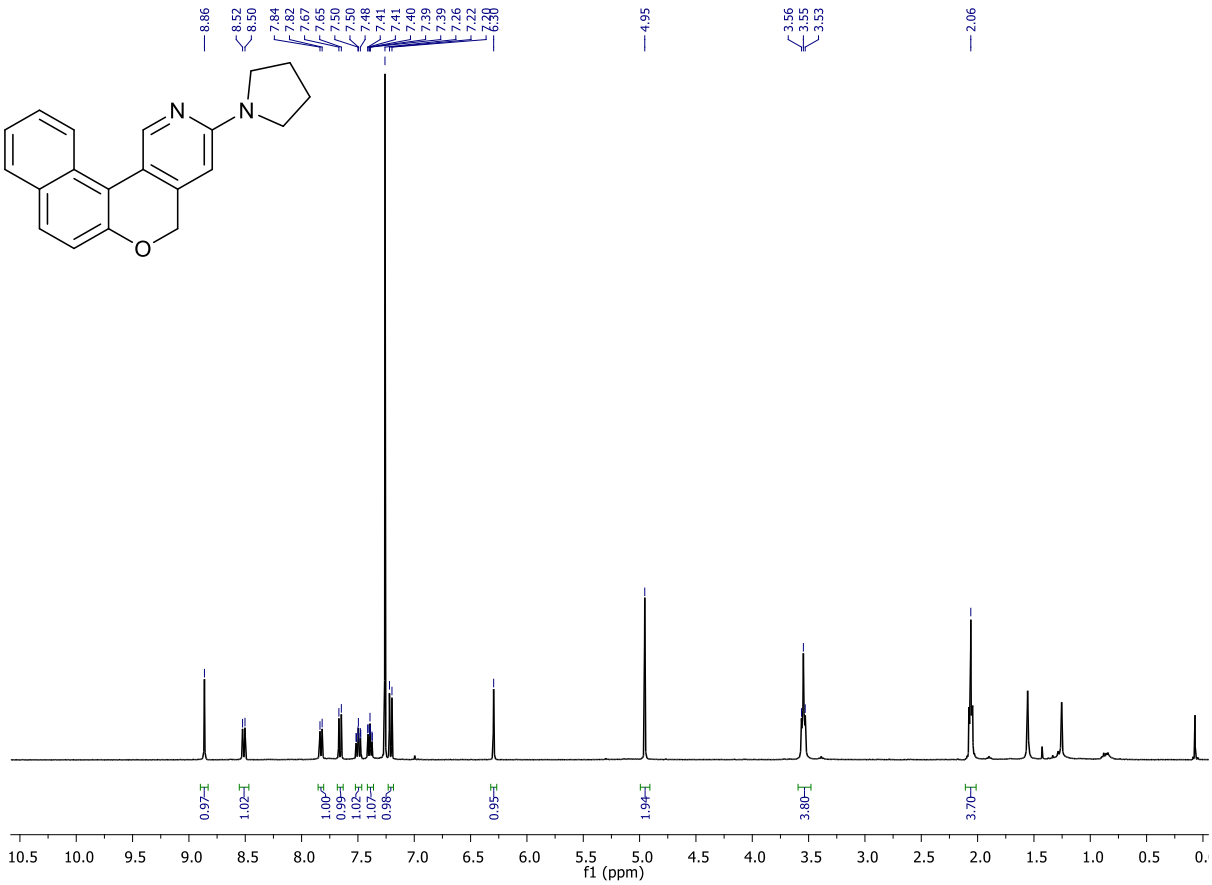
^{13}C NMR of **3jd** (101 MHz, $CDCl_3$)



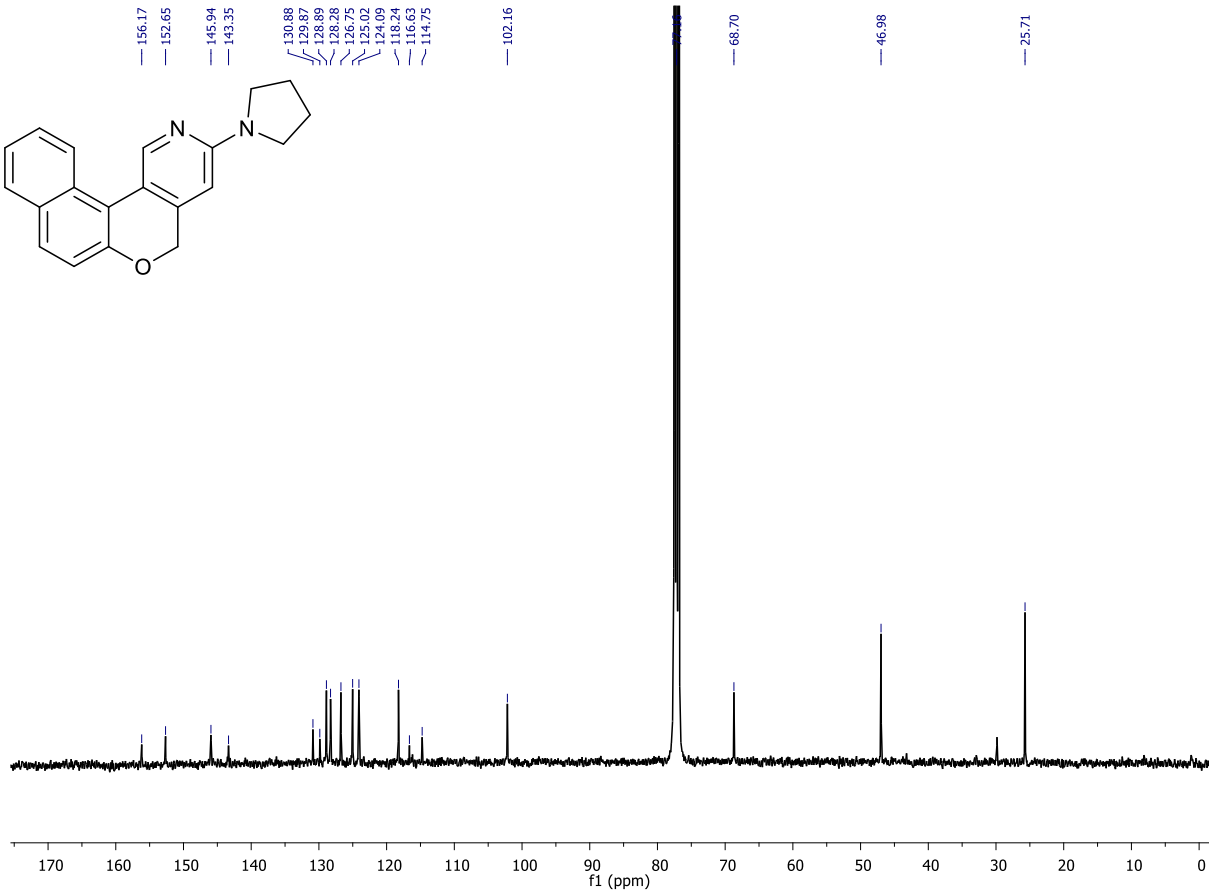
^{1}H NMR of **3kd** (400 MHz, $CDCl_3$)



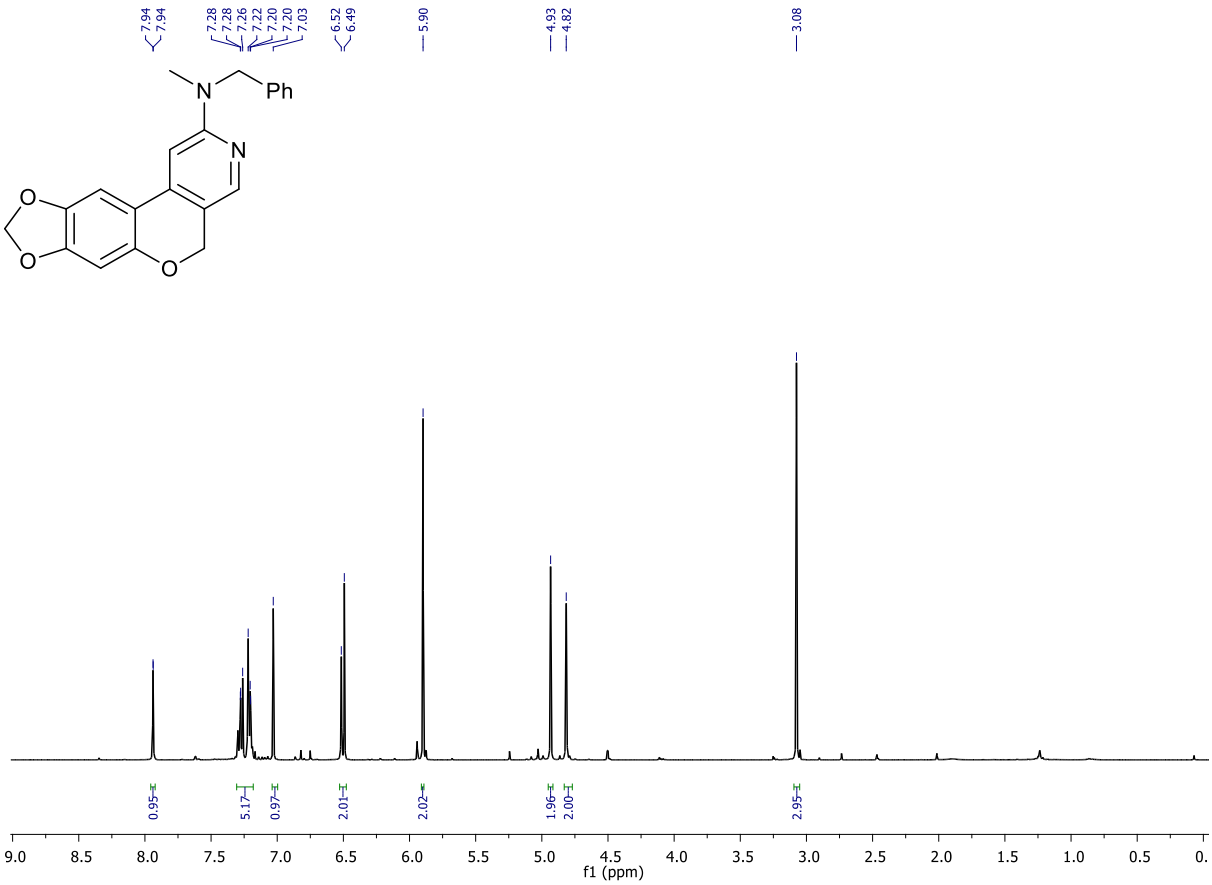
^{13}C NMR of **3kd** (101 MHz, $CDCl_3$)



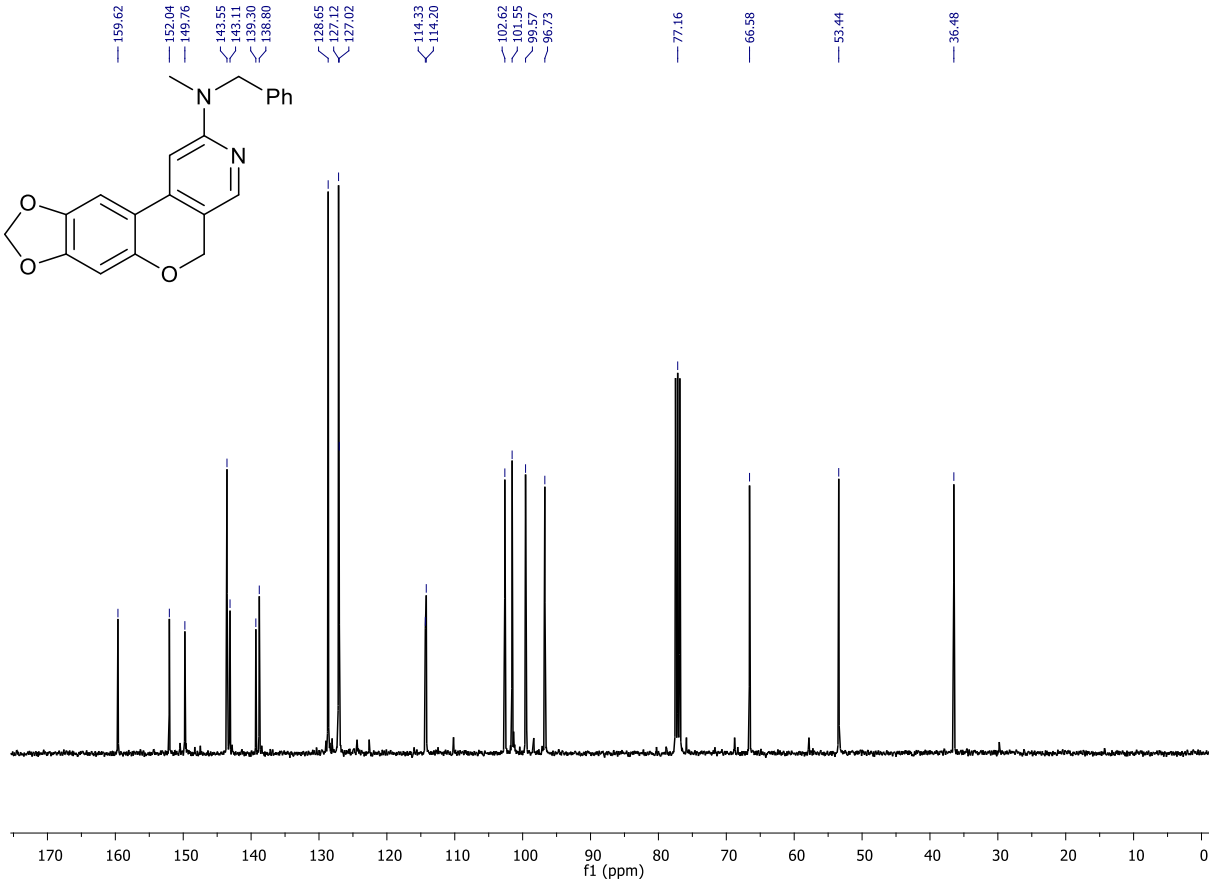
^{1}H NMR of **3kd'** (400 MHz, $CDCl_3$)



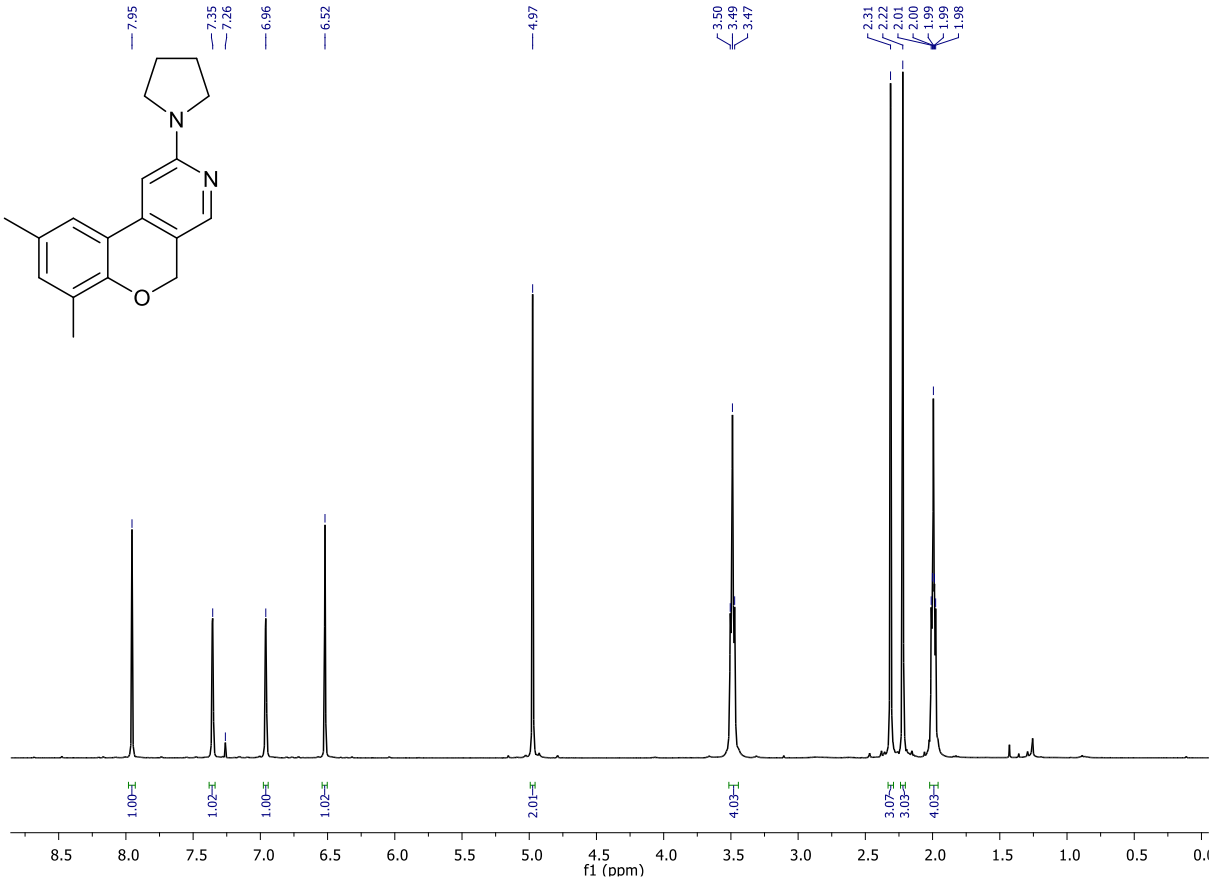
^{13}C NMR of **3kd'** (101 MHz, $CDCl_3$)



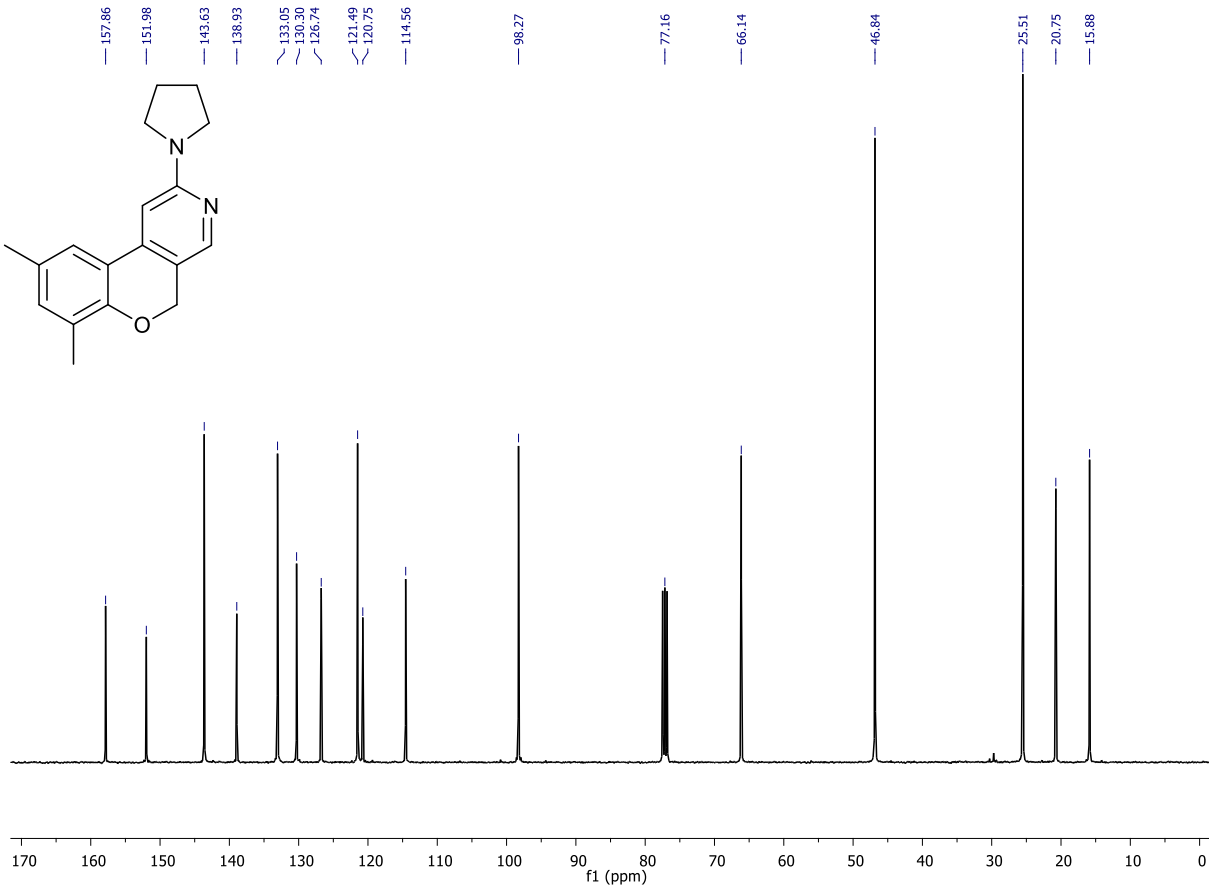
^{1}H NMR of **3lb** (400 MHz, $CDCl_3$)



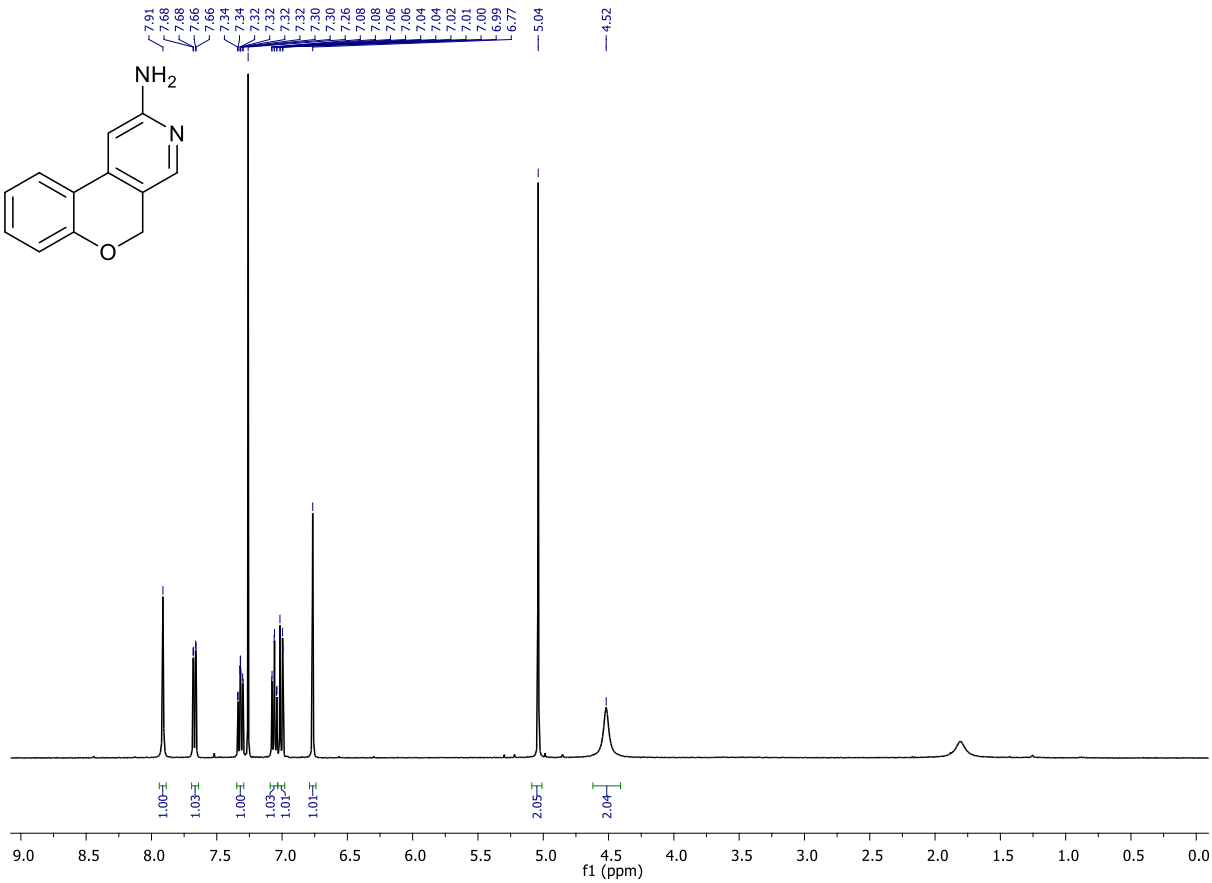
^{13}C NMR of **3lb** (101 MHz, $CDCl_3$)



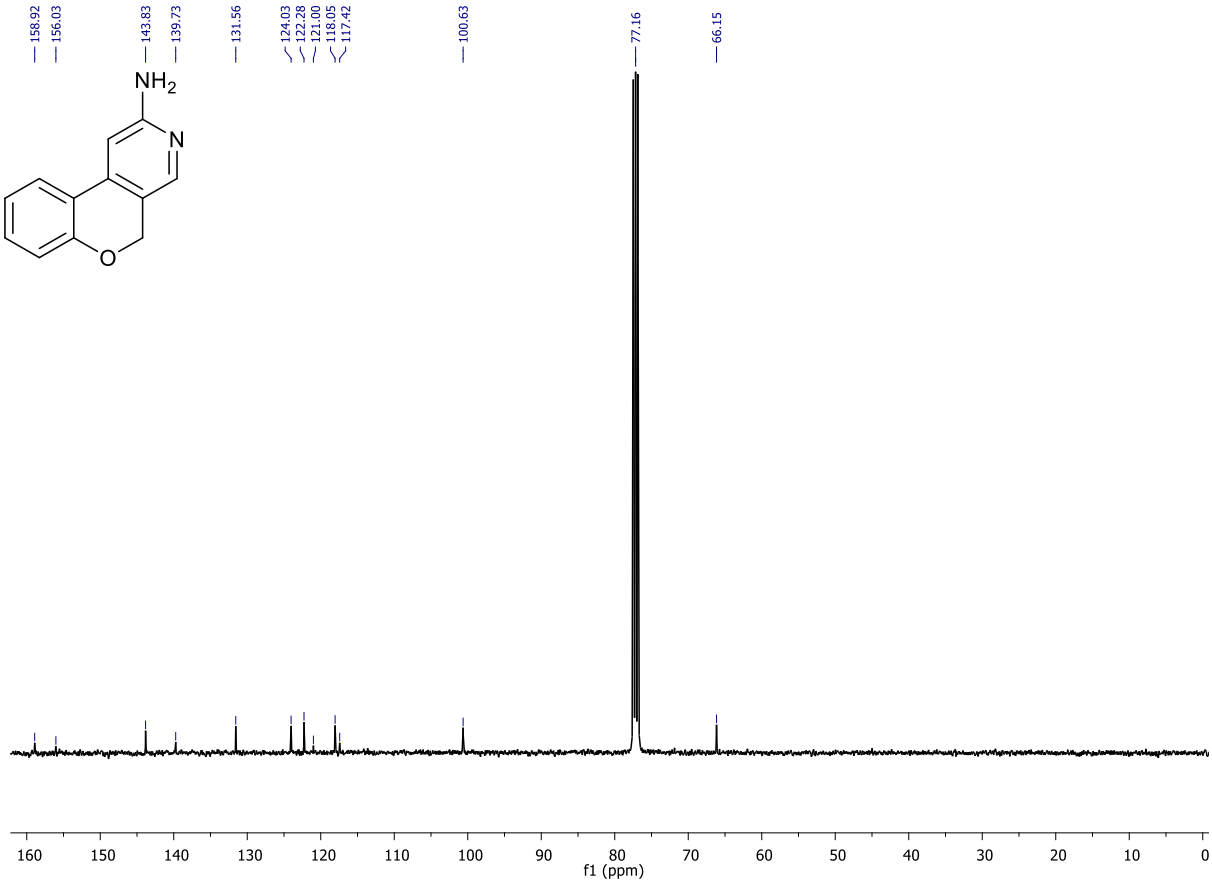
^{1}H NMR of **3md** (400 MHz, $CDCl_3$)



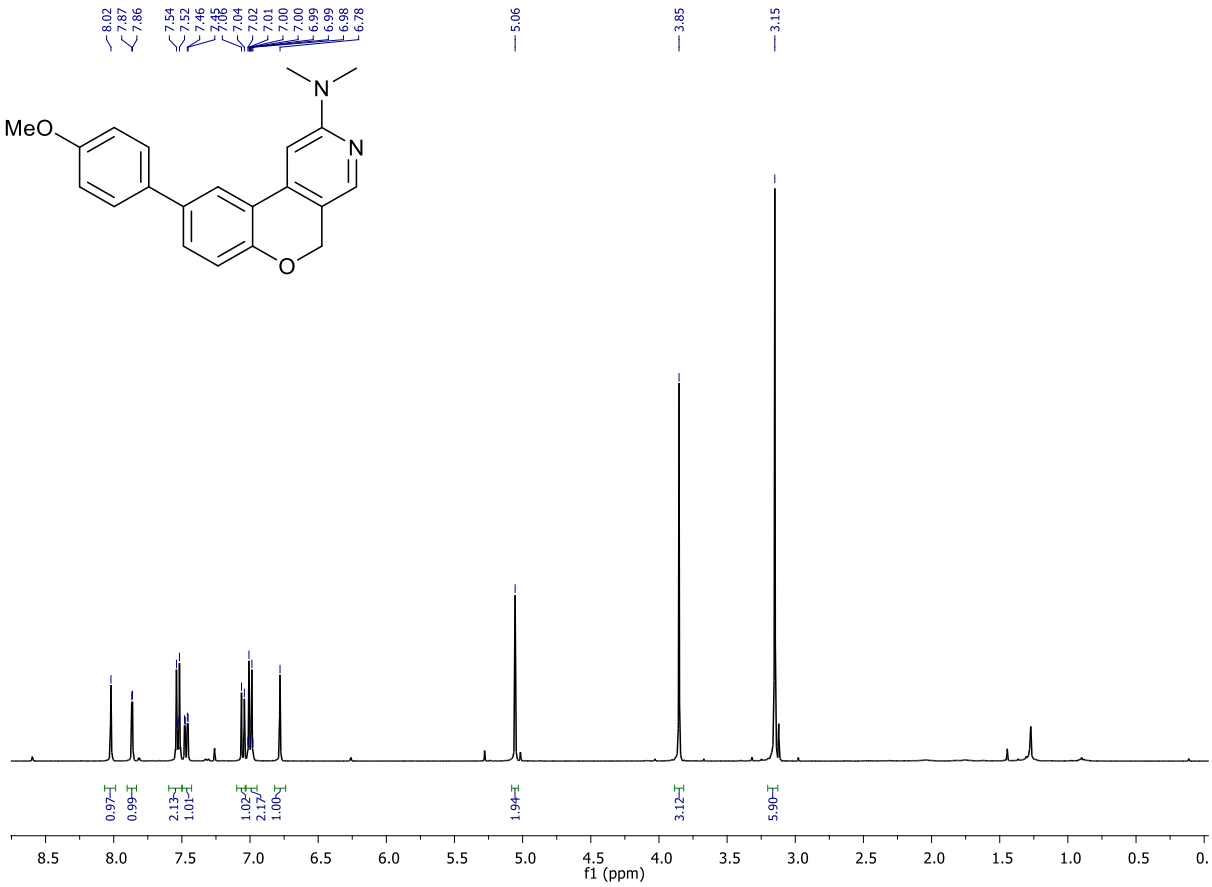
^{13}C NMR of **3md** (101 MHz, $CDCl_3$)



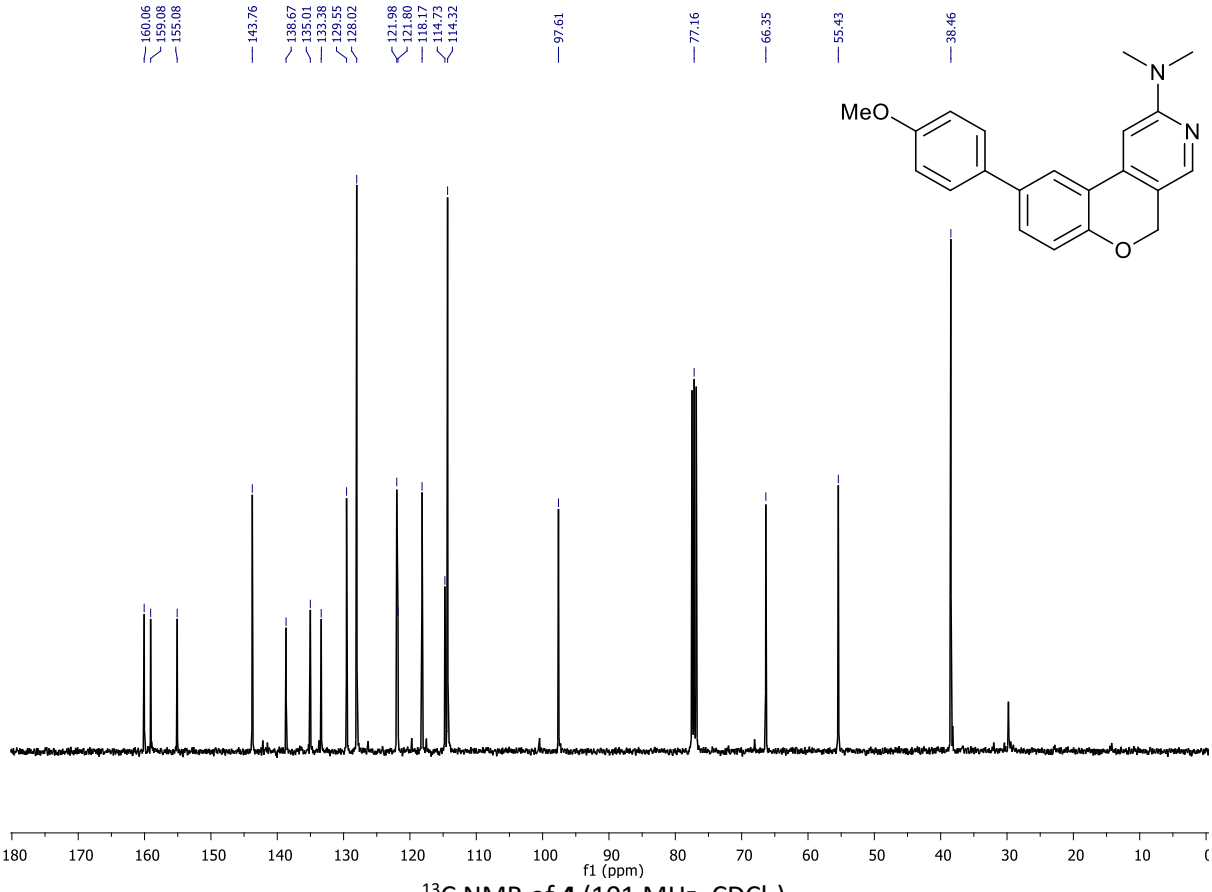
^{1}H NMR of **3af** (400 MHz, $CDCl_3$)



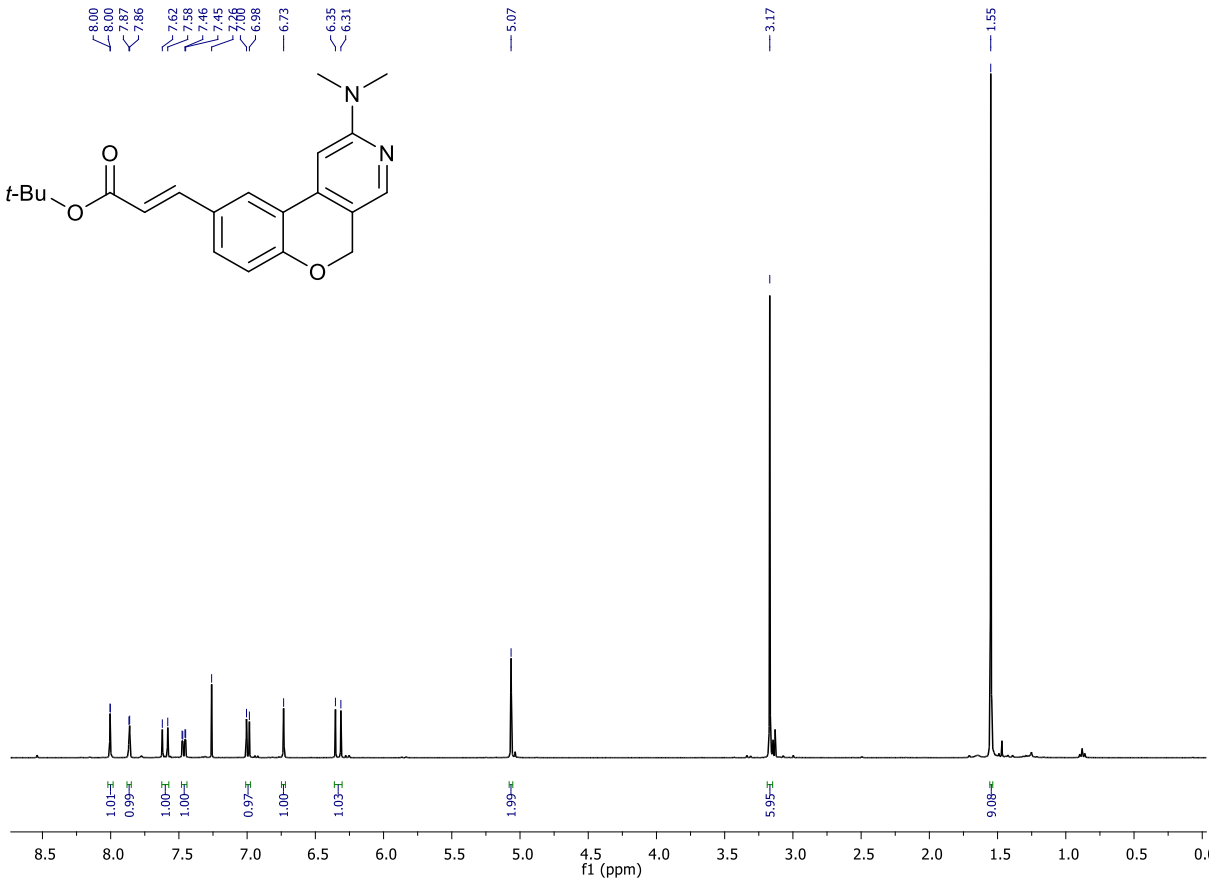
^{13}C NMR of **3af** (101 MHz, $CDCl_3$)



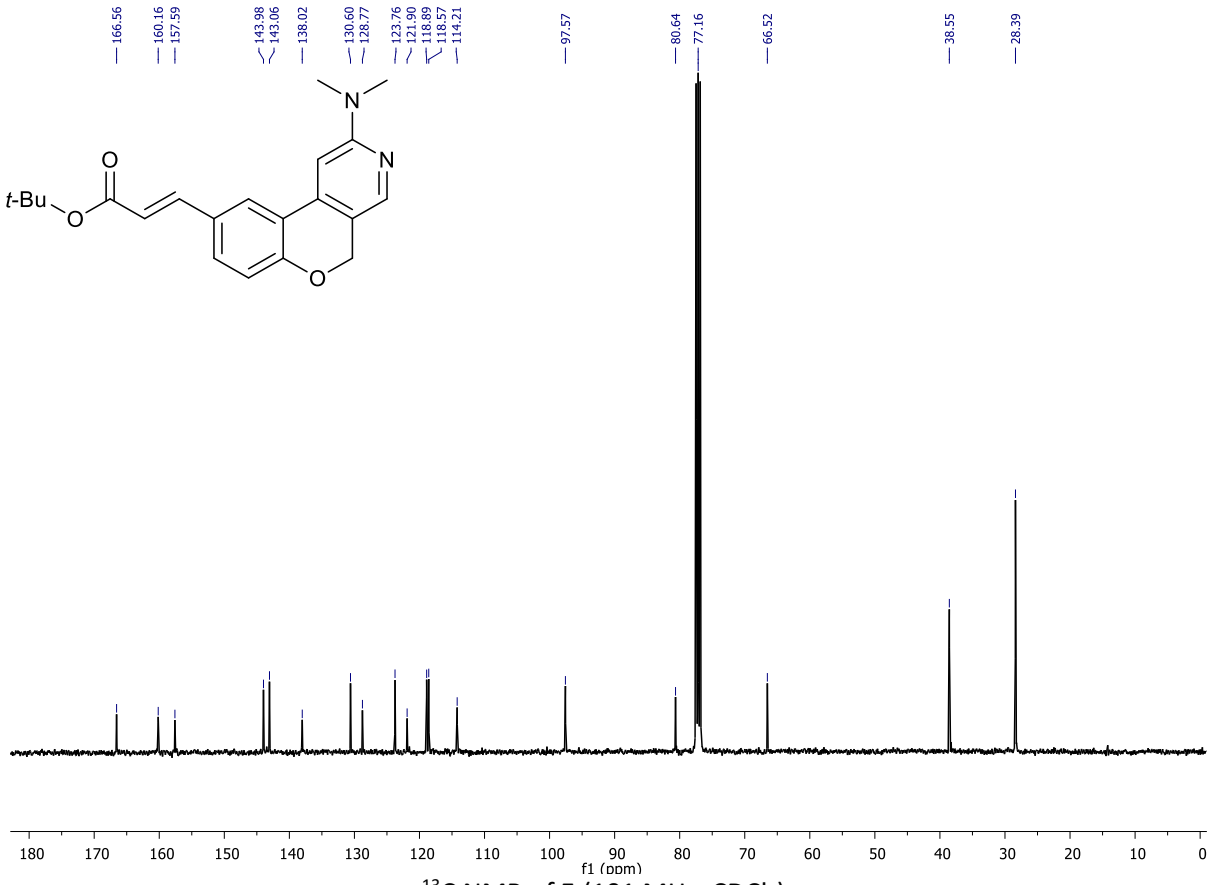
^{1}H NMR of **4** (400 MHz, $CDCl_3$)



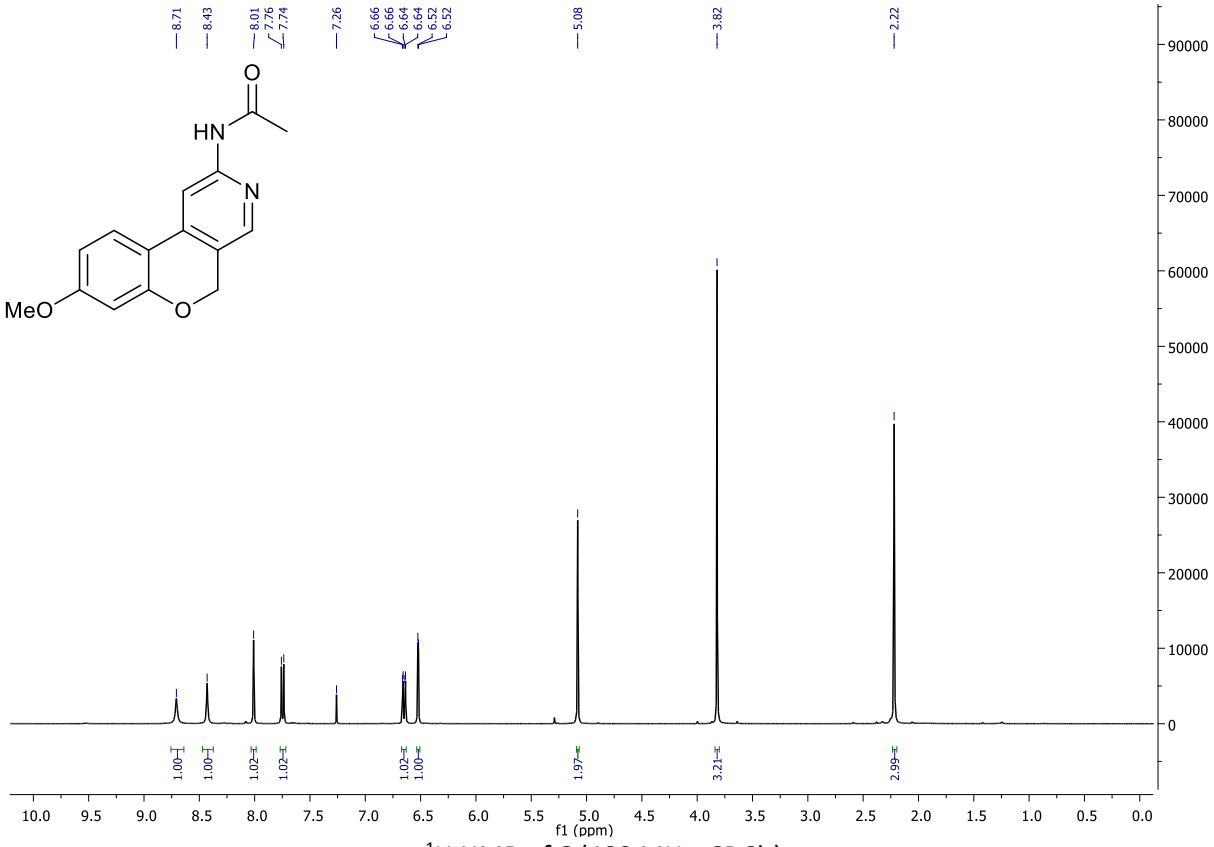
^{13}C NMR of **4** (101 MHz, $CDCl_3$)



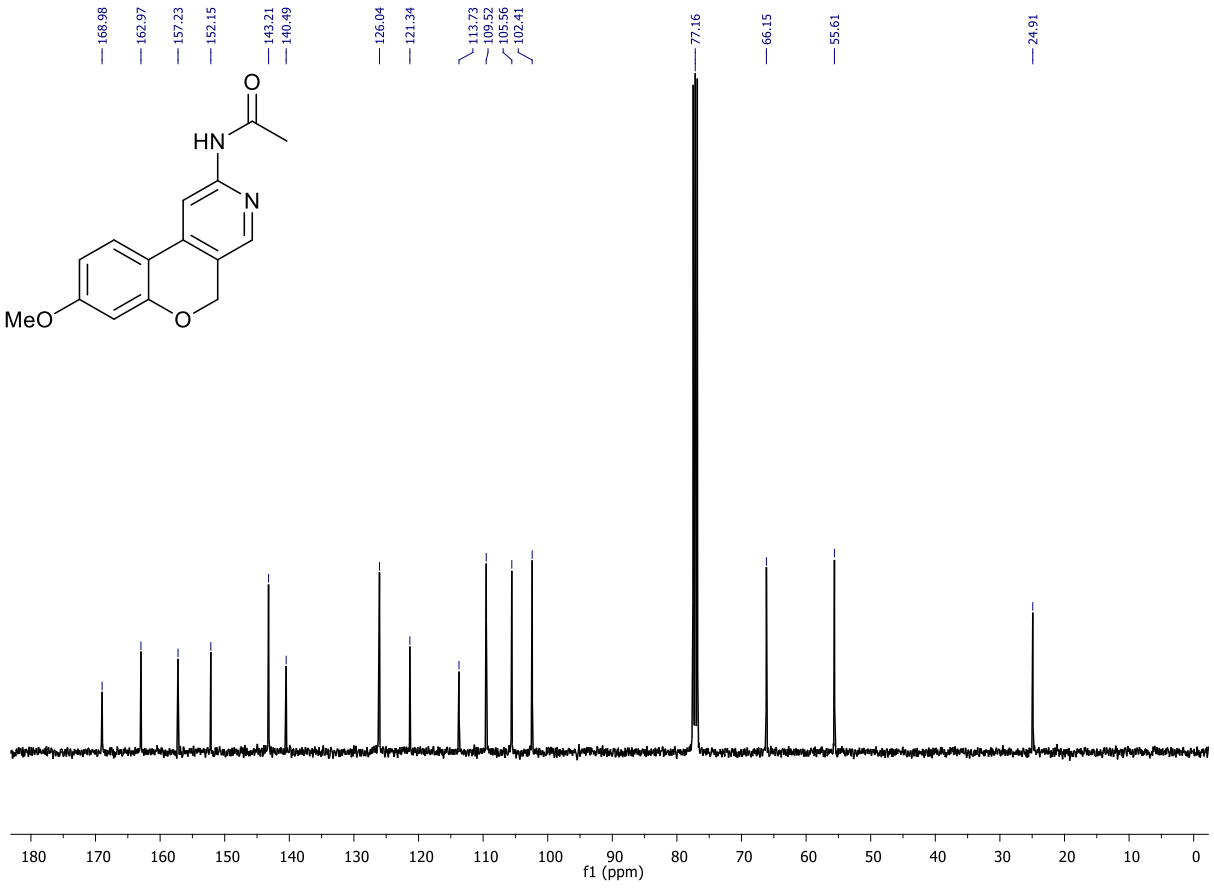
^{1}H NMR of **5** (400 MHz, $CDCl_3$)



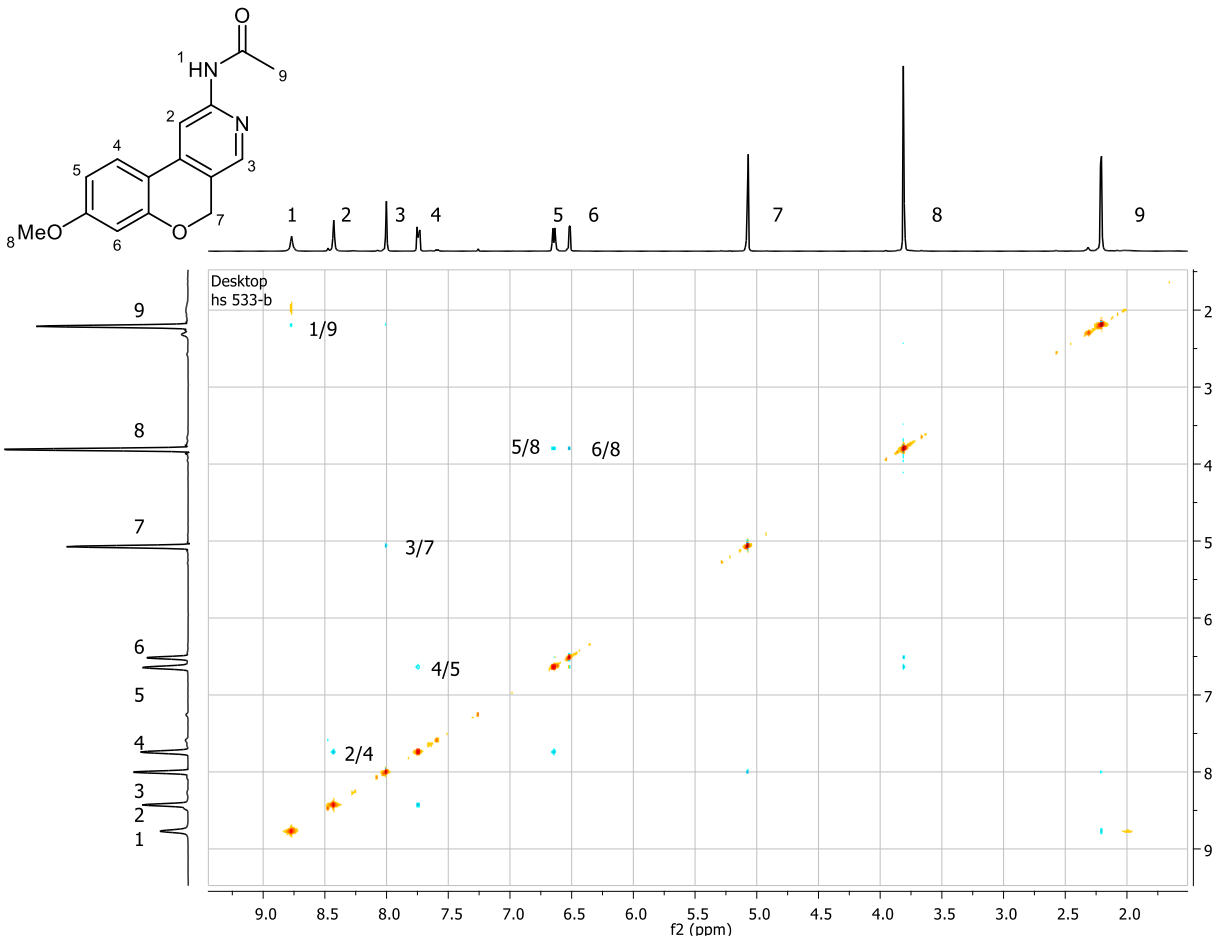
^{13}C NMR of **5** (101 MHz, $CDCl_3$)



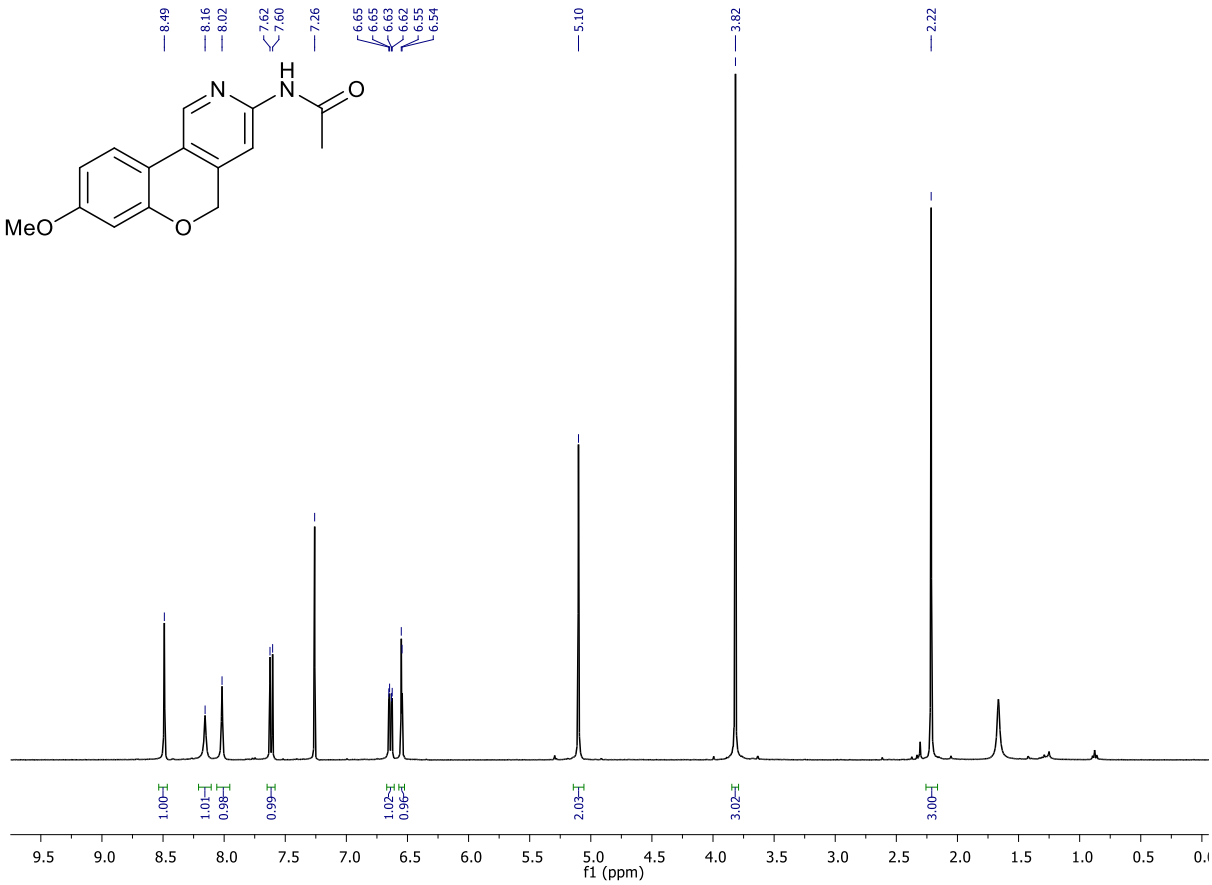
^{1}H NMR of **6** (400 MHz, $CDCl_3$)



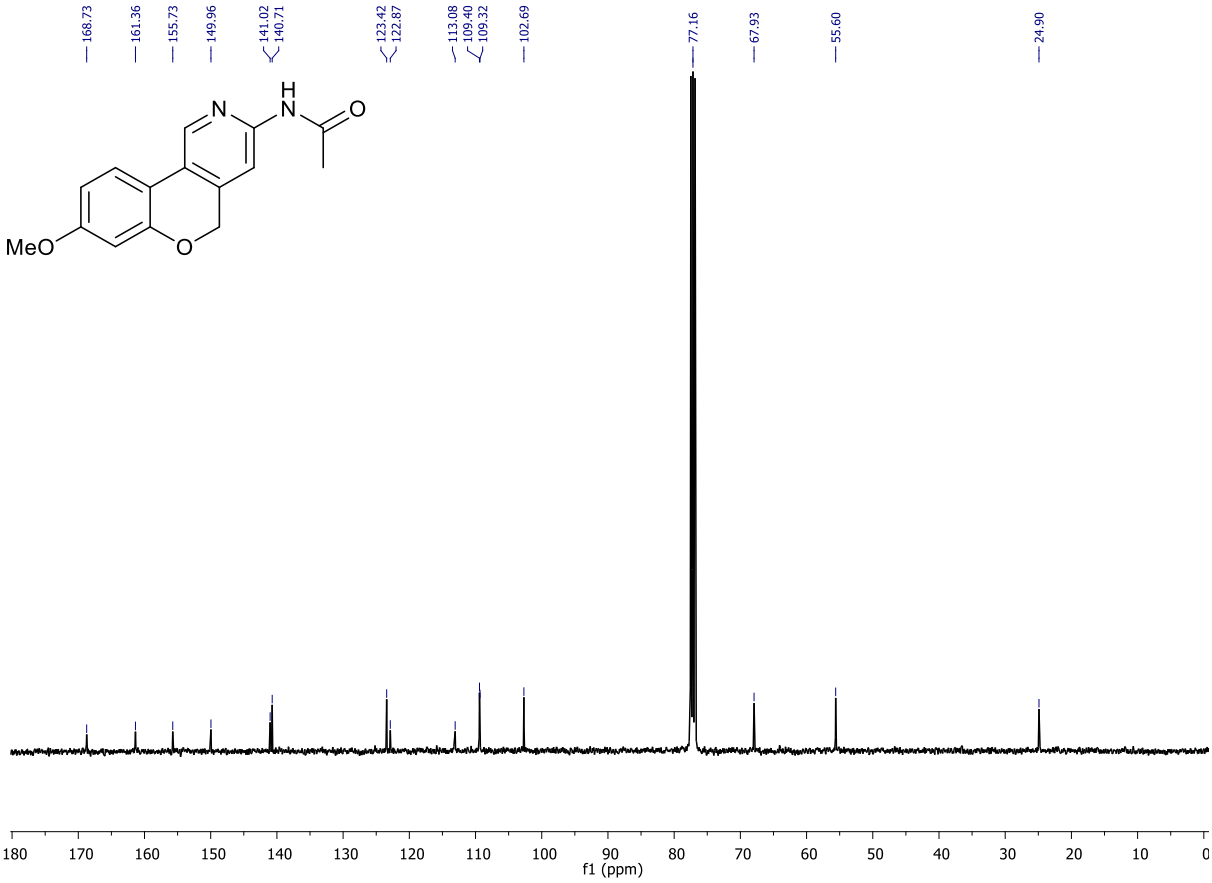
^{13}C NMR of **6** (101 MHz, $CDCl_3$)



NOESY of **6** (500 MHz, $CDCl_3$)



^{1}H NMR of **6'** (400 MHz, $CDCl_3$)



^{13}C NMR of **6'** (101 MHz, $CDCl_3$)

VII. X-Ray crystallographic data for compound 3aa

A saturated solution of 10 mg of compound **3aa** in CH_2Cl_2 was introduced into a 1 mL vial. This vial was then placed in a 10 mL vial already containing 2 mL of hexane and the system was closed. The vapour diffusion was let to happen at room temperature for 2 weeks, leading to long-needle crystals.

1. X-Ray crystal structure determination

For **3aa** a single crystal was selected, mounted, and transferred into a cold nitrogen gas stream. Intensity data was collected with a Bruker Kappa-APEX2 system using micro-source Cu-Kα radiation. Unit-cell parameters determination, data collection strategy, integration and absorption correction were carried out with the Bruker APEX2 suite of programs. The structure was solved with SHELXT and refined anisotropically by full-matrix least-squares methods with SHELXL using WinGX. Absolute structure couldn't be reliably determined by anomalous scattering effects analysis. The structure was deposited at the Cambridge Crystallographic Data Centre with number CCDC 2192543 and can be obtained free of charge via www.ccdc.cam.ac.uk.

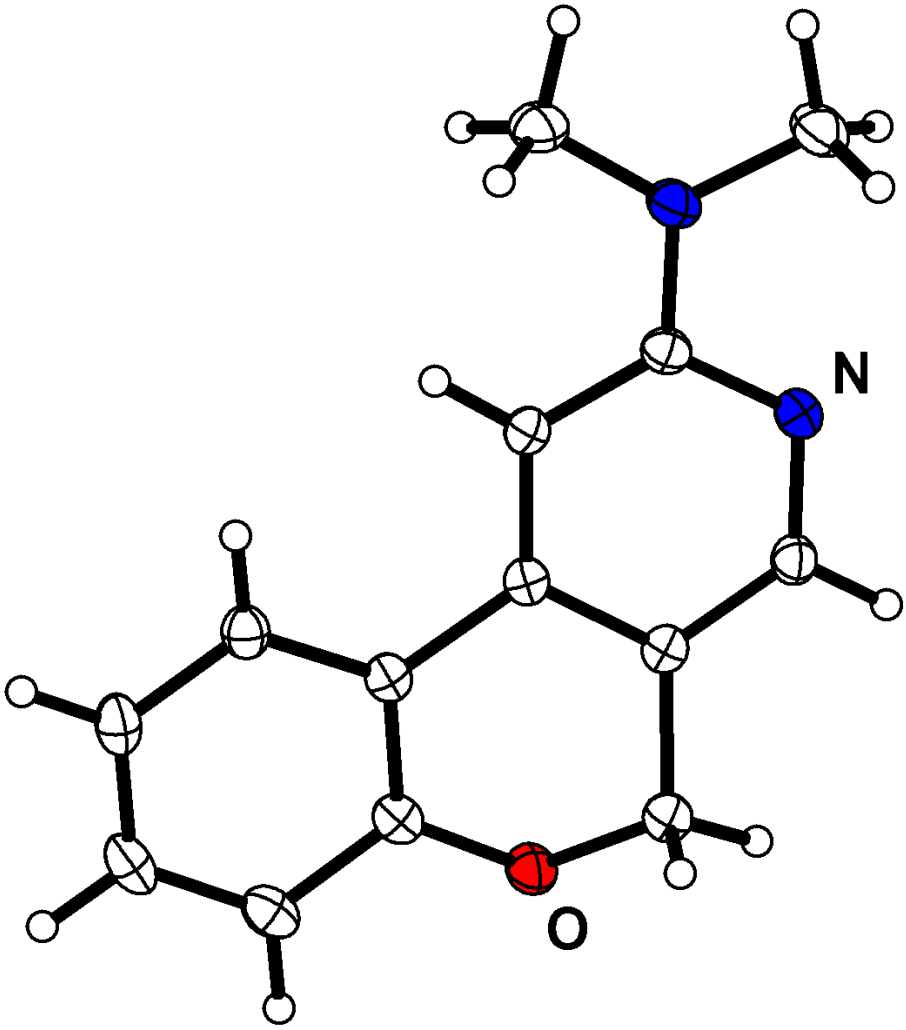


Figure 1 : Crystal structure representation of **3aa**.

Ellipsoids are drawn with 30% probability. All hydrogen atoms are omitted for the sake of clarity.

2. Crystal data for 3aa

Orthorhombic P n a 21, a = 18.0753(4) Å, b = 6.5874(1) Å, c = 9.4903(2) Å, α = β = γ = 90°, V = 1130.00(4) Å3, Z = 4, pale yellow plate 0.4 × 0.2 × 0.02 mm3, μ = 0.679 mm-1, min / max transmission = 0.55 / 0.75, T= 200(1) K, λ = 1.54178 Å, θ range = 4.90° to 66.58°, 7941 reflections measured, 1985 independent, Rint = 0.0258, completeness = 1.000, 156 parameters, 1 restraints, Flack x = 0.3(2), final R indices R1 [I>2σ(I)] = 0.0297 and wR2 (all data) = 0.0831, GOF on F2 = 1.068, largest difference peak / hole = 0.15 / -0.12 e·Å-3.