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Electronic Supplementary Information

for

Simple and Scalable Electrochemical Synthesis of 2,1-Benzisoxazoles and Quinoline *N*-Oxides

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1. General information

All reagents were used in analytical grades. Solvents were purified by standard methods. For electrochemical reactions, lead and glassy carbon electrodes were used.

NMR spectra: ^{1}H NMR and ^{13}C NMR spectra were recorded at 25 °C by using a Bruker Avance III HD 300 (300 MHz, 5 mm BBFO-SmartProbe with z gradient and ATM, SampleXPress 60 sample changer, Analytische Messtechnik, Karlsruhe, Germany). Chemical shifts (δ) are reported in parts per million (ppm) relative to traces of $CHCl_3$ (7.26 ppm for ^{1}H NMR and 77.0 ppm for ^{13}C NMR) or DMSO (2.52 ppm for ^{1}H NMR and 40.0 ppm for ^{13}C NMR) in the corresponding deuterated solvent. Multiplicity of the signals is also indicated in brackets (s = singlet, d = doublet, t = triplet, q = quartet, quin = quintuplet, m = multiplet).

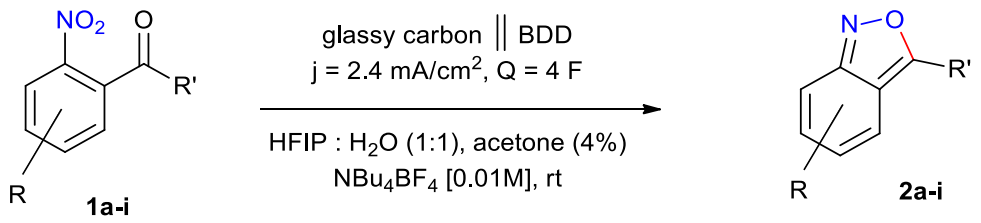
Mass Spectrometry: Mass spectra and high resolution mass spectra were obtained by using a QTof Ultima 3 (Waters, Milford, Massachusetts) apparatus employing ESI^{+}.

Gas chromatography was performed with a Shimadzu GC-2010 (Shimadzu, Japan) using a HP 5 column (Agilent Technologies, USA; length: 30 m, inner diameter: 0.25 mm, film: 0.25 µm, carrier gas: hydrogen). GC-MS measurements were carried out with a Shimadzu GC-2010 (Shimadzu, Japan) using a Zebron ZB-5MSi column (Phenomenex, USA; length: 30 m, inner diameter: 0.25 mm, film: 0.25 µm, carrier gas: helium) combined with a GCMS-QP2010.

Column chromatography was performed on silica gel 60 M (0.040-0.063 mm, Macherey-Nagel GmbH & Co, Düren, Germany) with a maximum pressure of 1.2 bar. As eluents mixtures of cyclohexane and ethyl acetate were used. Silica gel 60 sheets on aluminum (F254, Merck, Darmstadt, Germany) were used for thin layer chromatography.

Melting points were determined with a Melting Point Apparatus B-545 (Büchi, Flawil, Switzerland) and were uncorrected. The heating rate was 3°C/min.

2. General procedure for the electrosynthesis of 2,1-benzisoxazoles (2)



Screening cell (beaker-type cell, 5 mL)

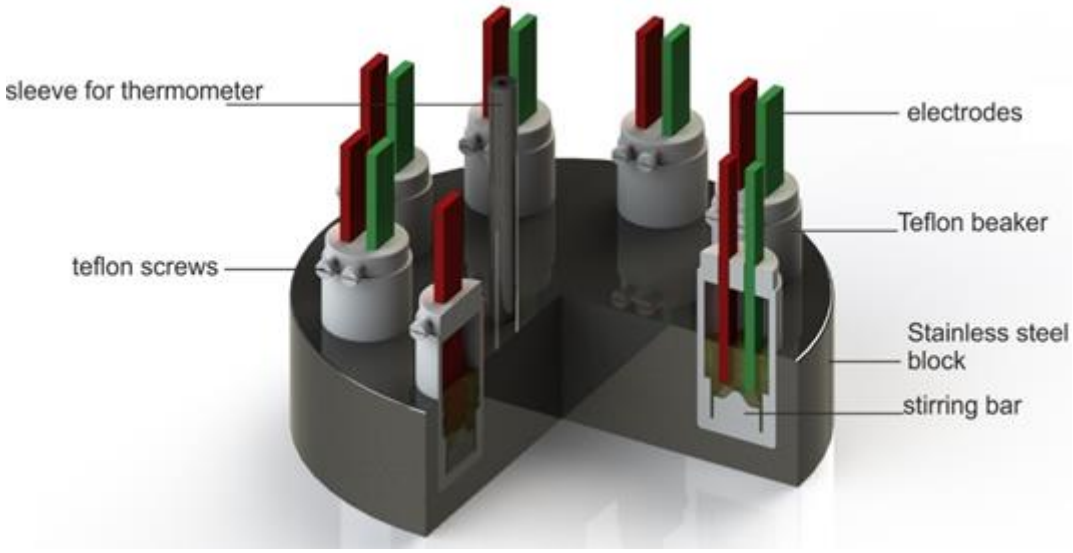


Figure S1. Schematic view of undivided screening cells of 5 mL in a screening arrangement.

For electrolysis in smaller scales, the screening cell array (Figure S1) was used, a detailed description of which was published recently.[1] In addition, the screening set-up is also commercially available as IKA Screenings System, IKA-Werke GmbH & Co. KG, Staufen, Germany. Set-ups with electrodes in a parallel orientation were conducted in a 5 mL teflon cells (Figure S1). Dimensions of glassy carbon and BDD electrodes were 7.0 x 1.0 x 0.3 cm. Using a 5 mL reaction mixture, electrodes immersed 1.65 cm into solution and had upon immersion into the electrolyte an active surface of 1.65 cm^2 (1 cm x 1.65 cm).

HFIP (2.4 mL), water (2.4 mL), acetone (0.2 mL), NBu_4BF_4 (16.4 mg, 0.05 mmol), and 2-nitrobenzaldehydes **1** (0.1 mmol) were added to the cell. A constant current electrolysis with a current density of 2.4 mA/cm^2 (I = 4 mA) was performed at room temperature. After application of 48 C (4F) the electrolysis was stopped.

[1] C. Gütz, B. Klöckner and S. R. Waldvogel, *Org. Process Res. Dev.*, 2016, **20**, 26.

Beaker-type cell (25 mL)

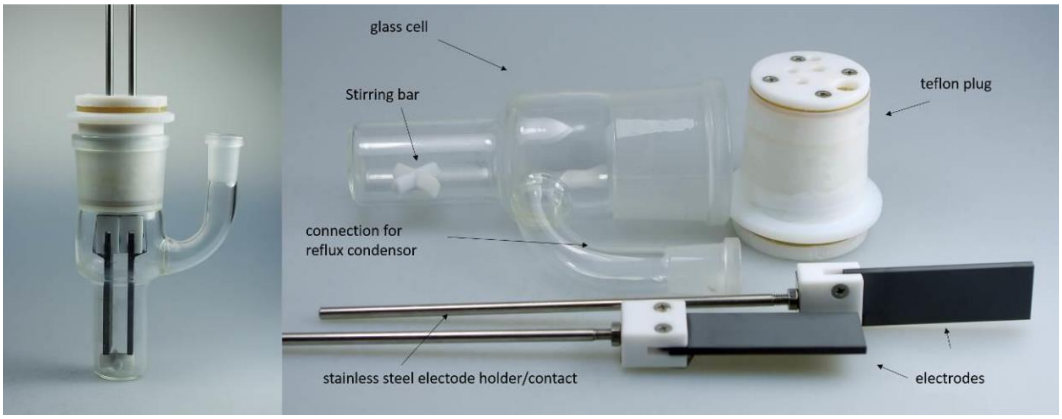


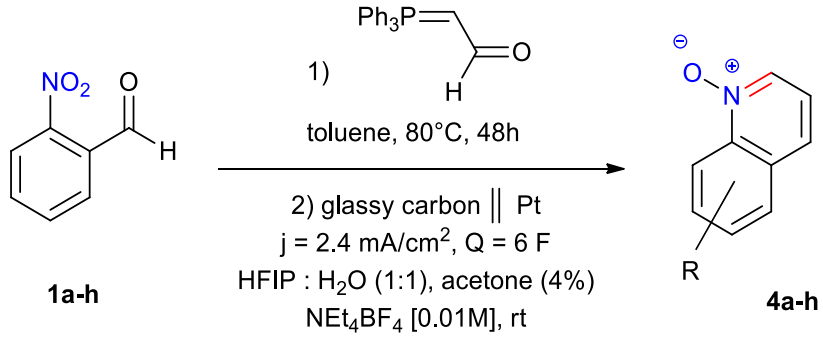
Figure S2. View of undivided Beaker-type cell of 25 mL.

The beaker-type cell (25 mL, figure S2) consists of a simple glass beaker with or without cooling jacket and closed by a teflon plug. The cap allows precise arrangement of the electrodes. Dimensions of glassy carbon and BDD electrodes were 7.0 x 2.0 x 0.2 cm. The electrodes had upon immersion into the electrolyte an active surface of 7 cm^2 (2 x 3.5 cm).

Into an undivided beaker-type screening electrolysis cell equipped with a glassy carbon anode and a BDD cathode, HFIP (12 mL), water (12 mL), acetone (1 mL), NBu_4BF_4 (82.3 mg, 0.25 mmol), and 2-nitrobenzaldehydes **1** (0.5 mmol) were added. A constant current electrolysis with a current density of 2.4 mA/cm^2 (I = 17 mA) was performed at room temperature. After application of 193 C (4F) the electrolysis was stopped.

The mixture was then transferred into a separation funnel, whereby AcOEt (50 mL) and water (50 mL) were added. The aqueous layer was again extracted with AcOEt (50 mL), the combined organic fractions were washed with brine (50 mL) and dried over $MgSO_4$. The solution was concentrated under reduced pressure and the crude was purified under flash column chromatography to afford the corresponding 2,1-benzisoxazoles **2**.

3. General procedure for the electrosynthesis of quinolines *N*-oxides (4) from 2-nitrobenzaldehydes (1)



2-Nitrocinnamaldehyde **3a** was commercial. 2-nitrocinnamaldehydes **3b-h** were directly obtained from the corresponding 2-nitrobenzaldehydes **1b-h.** Compounds **1b-h** (1.5 mmol) were dissolved in toluene (15 mL), and (triphenylphosphoranylidene)acetaldehyde (472 mg, 1.55 mmol) was added to the solution. The mixture was heated at 80°C during 48h, whereupon the solvent was evaporated under reduced pressure. The product was purified under flash column chromatography to afford the corresponding 2-nitrocinnamaldehydes **3b-h.** (See products **4b-h** for purification details).

The electrolysis of **3a-h** was carried out with glassy carbon and Pt electrodes in a Beaker-type cell (25 mL, see section 2 for a detailed picture) closed by a teflon plug. Dimensions of the glassy carbon electrode were 7.0 x 2.0 x 0.2 cm. The dimensions of the Pt layer were 4.0 x 2.0 cm. Both electrodes had upon immersion into the electrolyte an active surface of 7 cm^2 (2 x 3.5 cm).

Into an undivided beaker-type screening electrolysis cell equipped with a glassy carbon anode and a Pt cathode, HFIP (12 mL), water (12 mL), acetone (1 mL), NEt_4BF_4 (54.3 mg, 0.25 mmol), and 2-nitrocinnamaldehydes **3** (0.5 mmol) were added. A constant current electrolysis with a current density of 2.4 mA/cm^2 (I = 17 mA) was performed at room temperature. After application of 290C (6F) the electrolysis was stopped.

The mixture was then transferred into a separation funnel, whereby AcOEt (50 mL) and water (50 mL) were added. The aqueous layer was again extracted with AcOEt (2 x 20 mL), the combined organic fractions were washed with brine (50 mL) and dried over $MgSO_4$. The solution was concentrated under reduced pressure and the crude was purified under flash column chromatography to afford the corresponding quinoline *N*-oxides **4**.

4. Scale-up of compounds 2c and 4a

The scale-up of **1c** was carried out with glassy carbon and BDD electrodes in a 1L Erlenmeyer flask closed by a teflon plug, which allowed precise arrangement of the electrodes (Figure S3). Dimensions of glassy carbon and BDD electrodes were 14 x 3.5 x 0.3 cm. The electrodes had upon immersion into the electrolyte an active surface of 17.5 cm^2 (3.5 x 5 cm).



Figure S3. 1L Erlenmeyer flask with the Teflon plug and the electrodes.

HFIP (288 mL), water (288 mL), acetone (24 mL), NBu_4BF_4 (1.97 g, 6 mmol), and compound **1c** (12 mmol, 2.84 g) were added. A constant current electrolysis with a current density of 2.4 mA/cm^2 (I = 42 mA) was performed at room temperature. After application of 4631C (4F) the electrolysis was stopped.

The mixture was then transferred into a separation funnel, whereby AcOEt (250 mL) and water (250 mL) were added. The aqueous layer was again extracted with AcOEt (2 x 100 mL), the combined organic fractions were washed with brine (100 mL) and dried over $MgSO_4$. The solution was concentrated under reduced pressure and the crude was purified under flash column chromatography (cyclohexane/EtOAc = 5:1 to 3:1) to afford the corresponding 2,1-benzisoxazol **2c** with a 55% yield (1.18 g).

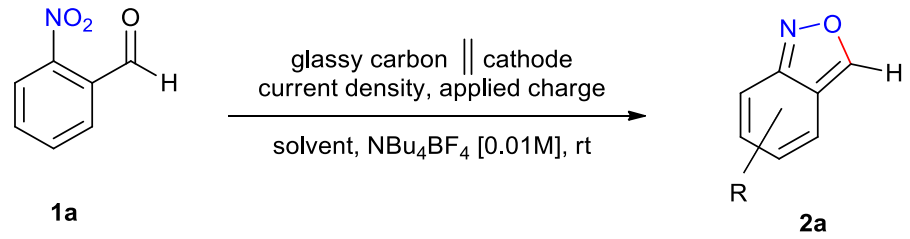
The scale-up of **3a** was carried out with glassy carbon and Pt electrodes in a 250 mL Erlenmeyer flask closed by a teflon plug, which allowed precise arrangement of the electrodes. Dimensions of the glassy carbon electrode were 7.0 x 2.0 x 0.2 cm. The dimensions of the Pt layer were 4.0 x 2.0 cm. Both electrodes had upon immersion into the electrolyte an active surface of 7 cm^2 (2 x 3.5 cm).

A 250 mL Erlenmeyer flask was equipped with a glassy carbon anode and a Pt cathode, HFIP (96 mL), water (96 mL), acetone (8 mL), NEt_4BF_4 (434 mg, 2 mmol), and 2-nitrocinnamaldehyde **3a** (5 mmol, 885 mg) were added. A constant current electrolysis with a current density of 2.4 mA/cm^2 (I = 17 mA) was performed at room temperature. After application of 3136C (6.5F) the electrolysis was stopped.

The mixture was then transferred into a separation funnel, whereby AcOEt (100 mL) and water (100 mL) were added. The aqueous layer was again extracted with AcOEt (2 x 50 mL), the combined organic fractions were washed with brine (100 mL) and dried over $MgSO_4$. The solution was concentrated under reduced pressure and the crude was purified under flash column chromatography (EtOAc to EtOAc 9:1 MeOH) to afford the corresponding quinoline *N*-oxide **4a** with a 38% yield (272 mg).

5. Data from the synthesis optimization of 2,1-benzisoxazole 2a

All the experiments carried out for the optimization of the reaction of **2a** are included in Table S1.



1a **2a**

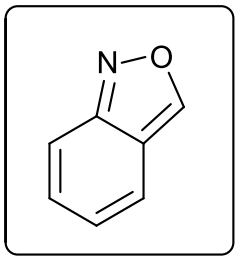
Entry	curr. density (mA/cm^2)	Charge, F	Solvent	Cathode	Yield (%)
1	2.4	4	EtOH:H_2O 1:1	BDD	25
2	6.5	4	EtOH:H_2O 1:1	BDD	15
3	4.1	4	EtOH:H_2O 1:1	BDD	23
4	0.6	4	EtOH:H_2O 1:1	BDD	26
5	4.1	4	EtOH	BDD	5
6	2.4	4	MeOH:H_2O 1:1	BDD	31
7	2.4	4	MeCN:H_2O 1:1	BDD	<5
8	2.4	4	DMF:H_2O 1:1	BDD	17
9	2.4	4	THF:H_2O 1:1	BDD	19
10	2.4	4	iPrOH:H_2O 1:1	BDD	21
11	2.4	4	EtOH:H_2O 1:1	Leaded Bronze	10
12	2.4	4	HFiP:H_2O 1:3	BDD	42
13	2.4	4	HFiP:H_2O 3:1	BDD	17
14	2.4	4	HFiP:H_2O 1:9	BDD	25
15	2.4	4	H_2O	BDD	0
16	2.4	4	AcOH:H_2O 1:9	BDD	8
17	2.4	4	HFiP:H_2O 1:2	BDD	43
18	2.4	4	HFiP:H_2O 2:1	BDD	41
19	2.4	4	HFiP:H_2O 1:1	BDD	53
20	2.4	3	HFiP:H_2O 1:1	BDD	23
21	2.4	5	HFiP:H_2O 1:1	BDD	51
22	2.4	6	HFiP:H_2O 1:1	BDD	42
23	2.4	7	HFiP:H_2O 1:1	BDD	35
24	2.4	4	HFiP:H_2O 1:1	BDD	23
25	2.4	4	HFiP:H_2O 1:1	BDD	38
26	2.4	4	HFiP:H_2O 1:1	Pt	41
27	2.4	4	HFiP:H_2O 1:1	Leaded Bronze	26
28	2.4	4	HFiP:H_2O 1:1	BDD	5*
29	2.4	8	HFiP:H_2O 1:1	BDD	31
30	2.4	4	HFiP:H_2O 1:1	BDD	21**
31	2.4	4	HFiP:H_2O 1:1	BDD	14
32	2.4	4	AcOH:H_2O 1:1	BDD	26

* BDD was also used as anode
** At 50°C

Table S1. Experiments for the optimization of the synthesis of compound **2a.**

6. Characterization of 2,1-benzisoxazoles (2) and quinoline *N*-oxides (4).

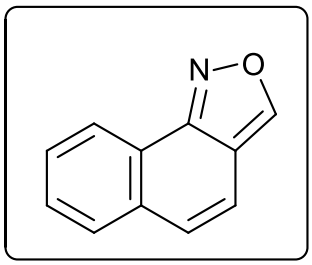
Benzo[*c*]isoxazole (2a)



Pale yellow oil. Purified by flash column chromatography (toluene 100%). Yield: 70% (25.2 mg).

^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.14 (d, *J* = 1.0 Hz, 1H), 7.64 (dq, *J* = 9.0 and 1.0 Hz, 1H), 7.58 (dt, *J* = 9.0 and 1.0 Hz, 1H), 7.32 (ddd, *J* = 9.0, 6.2 and 1.0 Hz, 1H), 7.02 (dd, *J* = 9.0 and 6.2 Hz, 1H). Data is in agreement with the literature.[2]

Naphtho[1,2-*c*]isoxazole (2b)



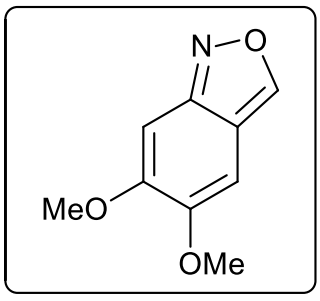
Brown oil. Purified by flash column chromatography (cyclohexane/EtOAc = 20:1). Yield: 70% (59.1 mg).

^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.96 (s, 1H), 8.57-8.51 (m, 1H), 7.75-7.68 (m, 1H), 7.66-7.55 (m, 2H), 7.32 (d, *J* = 9.2 Hz, 1H), 7.24 (d, *J* = 9.2 Hz, 1H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 155.23 (C), 153.23 (CH), 133.74 (C), 129.67 (CH), 128.50 (CH), 127.79 (CH), 127.20 (CH), 124.09 (CH), 121.94 (C), 116.20 (C), 116.09 (CH).

HRMS (ESI): calculated for $C_{11}H_8NO$ $(M + H)^+$:170.0600; found: 170.0598.

5,6-Dimethoxybenzo[*c*]isoxazole (2c)



Pale yellow solid (m.p. = 112-114 °C). Purified by flash column chromatography (cyclohexane/EtOAc = 5:1 to 3:1). Yield: 59% (53.0 mg). Upon scale-up (see page S7), yield: 55% (1.18 g).

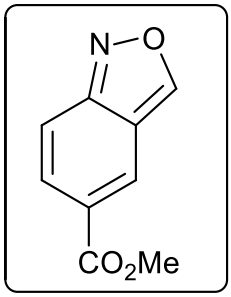
^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.82 (s, 1H), 6.80 (s, 1H), 6.66 (s, 1H), 3.98 (s, 3H), 3.92 (s, 3H)

^{13}C NMR ($CDCl_3$, 75 MHz): δ 155.16 (C), 154.43 (C), 151.71 (CH), 149.90 (C), 114.03 (C), 93.91 (CH), 91.05 (CH), 56.20 (CH_3), 55.97 (CH_3).

HRMS (ESI): calculated for $C_9H_{10}NO_3$ $(M + H)^+$: 180.0655; found: 180.0650.

[2] B. H. Kim, Y. M. Jun, Y. R. Choi, D. B. Lee, W. Baik, *Heterocycles*, **1998**, *48*, 749.

Methyl benzo[*c*]isoxazole-5-carboxylate (2d)



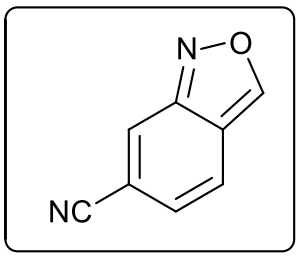
Pale brown solid (m.p. = 118-119 °C). Purified by flash column chromatography (toluene to toluene/acetone = 10:1). Yield: 76% (68.0 mg).

^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.32 (s, 1H), 8.44 (s, 1H), 7.88 (d, *J* = 9.3 Hz, 1H), 7.65 (d, *J* = 9.3 Hz, 1H), 3.94 (s, 3H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.99 (C), 157.52 (CH), 156.20 (C), 130.12 (CH), 126.93 (C), 124.83 (CH), 117.80 (C), 115.17 (CH), 52.45 (CH_3).

HRMS (ESI): calculated for $C_9H_8NO_3$ $(M + H)^+$: 178.0499; found: 178.0497.

Benzo[*c*]isoxazole-6-carbonitrile (2e)



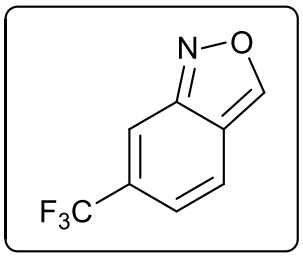
Pale yellow solid (m.p. = 130-131 °C). Purified by flash column chromatography (toluene to toluene/acetone = 50:1). Yield: 62% (44.6 mg).

^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.40 (d, *J* = 0.9 Hz, 1H), 8.15 (t, *J* = 1.2 Hz, 1H), 7.77 (dt, J = 0.9 and 9.3 Hz, 1H), 7.41 (dd, *J* = 1.2 and 9.3 Hz, 1H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 157.46 (CH), 154.77 (C), 130.26 (CH), 128.82 (CH), 118.12 (C), 117.11 (CH), 108.95 (C).

HRMS (ESI): calculated for $C_8H_5N_2O$ $(M + H)^+$: 145.0396; found: 145.0396.

6-(Trifluoromethyl)benzo[*c*]isoxazole (2f)



Yellow oil. Purified by flash column chromatography (toluene 100%). Yield: 41% (38.5 mg).

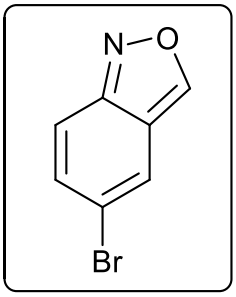
^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.27 (d, *J* = 0.9 Hz, 1H), 8.01 (quint, *J* = 1.2 Hz, 1H), 7.74 (dt, *J* = 9.2 and 0.9 Hz, 1H), 7.17 (dd, *J* = 9.2 and 1.2 Hz, 1H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 155.64 (CH), 154.81 (C), 132.98 (q, *J* = 32 Hz, C), 123.80 (q, *J* = 271 Hz, CF_3), 121.65 (CH), 120.23 (q, *J* = 2.8 Hz, CH), 118.44 (C), 114.21 (q, *J* = 5.5 Hz, CH).

^{19}F NMR ($CDCl_3$, 282 MHz): δ -64.31 (CF_3).

HRMS (ESI): calculated for $C_8H_5F_3NO$ $(M + H)^+$: 188.0318; found: 188.0321.

5-Bromobenzo[*c*]isoxazole (2g)



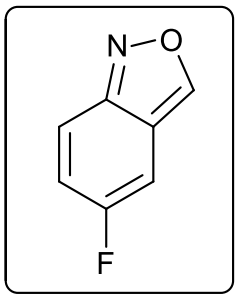
Pale brown solid (m.p. = 95-96 °C). Purified by flash column chromatography (Toluene). Yield: 45% (43.8 mg).

^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.11 (d, *J* = 0.9 Hz, 1H), 7.79-7.77 (m, 1H), 7.54 (dt, *J* = 0.9 and 9.5 Hz, 1H), 7.35 (dd, *J* = 1.6 and 9.5 Hz, 1H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 154.52 (C), 153.90 (CH), 134.86 (CH), 121.44 (CH), 119.24 (C), 118.15 (C), 116.82 (CH).

HRMS (ESI): calculated for $C_7H_5{}^{79}BrNO$ $(M + H)^+$: 197.9549; found: 197.9550.

5-Fluorobenzo[*c*]isoxazole (2h)



Yellow solid (m.p. = 45-47 °C). Purified by flash column chromatography (Toluene). Yield: 44% (30.2 mg).

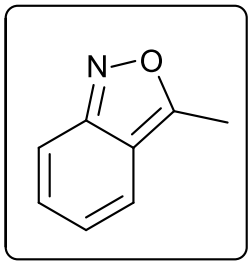
^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.10 (s, 1H), 7.65 (qt, *J* = 4.6 and 2.0 Hz, 1H), 7.19-7.09 (m, 2H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.93 (d, *J* = 247 Hz, CF), 154.50 (d, *J* = 11 Hz, CH), 154.35 (d, *J* = 11 Hz, C), 124.21 (d, *J* = 31 Hz, C), 117.76 (d, *J* = 10 Hz, CH), 117.36 (d, *J* = 12 Hz, C), 100.84 (d, *J* = 25 Hz, CH).

^{19}F NMR ($CDCl_3$, 282 MHz): δ - 116.52 (CF).

HRMS (ESI): calculated for C_7H_5FNO $(M + H)^+$: 138.0350; found: 138.0351.

3-Methylbenzo[*c*]isoxazole (2i)



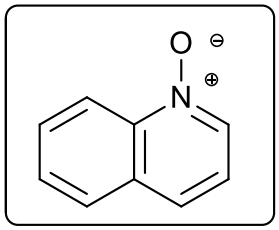
Pale yellow oil. Purified by flash column chromatography (cyclohexane/AcOEt = 8:1 to 6:1). Yield: 60% (40.1 mg)

^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.50 (d, *J* = 9.2 Hz, 1H), 7.42 (d, *J* = 8.8 Hz, 1H), 7.29-7.21 (m, 1H), 6.91 (dd, *J* = 8.8 and 6.3 Hz, 1H), 2.78 (s, 3H).

^{13}C NMR ($CDCl_3$, 75 MHz): 165.64 (C), 157.00 (C), 130.76 (CH), 122.73 (CH), 119.81 (CH), 115.59 (C), 114.81 (CH), 11.94 (CH_3).

HRMS (ESI): calculated for C_8H_8NO $(M + H)^+$: 134.0600; found:134.0602.

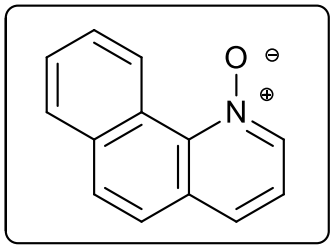
Quinoline 1-oxide (4a)



Brown solid. Purified by flash column chromatography (AcOEt to AcOEt/MeOH = 9:1). Yield: 44% (32 mg). Upon scale-up (see page S8), yield was 38% (272 mg).

^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.74 (d, *J* = 8.8 Hz, 1H), 8.53 (d, *J* = 6.0 Hz, 1 H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.80-7.73 (m, 2H), 7.67-7.61 (m, 1H), 7.32-7.26 (m, 1H). Data is in agreement with literature.[3]

Benzo[*h*]quinoline 1-oxide (4b)



3b was purified by flash column chromatography (cyclohexane/AcOEt = 3:1).

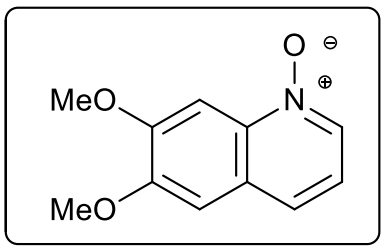
Brown solid (m.p. = 112-113 °C). Purified by flash column chromatography (AcOEt 100%). Yield: 38% (37 mg).

^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.87-10.79 (m, 1H), 8.67 (d, *J* = 6.2 Hz, 1H), 7.96-7.88 (m, 1H), 7.87-7.71 (m, 4H), 7.67-7.59 (m, 1H), 7.39 (t, *J* = 7.6 Hz, 1H).

^{13}C NMR ($CDCl_3$, 75 MHz): 139.31 (CH), 138.40 (C), 134.08 (C), 131.22 (C), 130.61 (CH), 129.10 (CH), 128.31 (CH), 128.05 (CH), 127.75 (CH), 126.10 (CH), 125.95 (C), 124.97 (CH), 121.23 (CH).

HRMS (ESI): calculated for $C_{13}H_{10}NO$ $(M + H)^+$: 196.0757; found: 196.0756.

6,7-Dimethoxyquinoline 1-oxide (4c)



3c was purified by flash column chromatography (cyclohexane/AcOEt = 2:1).

Brown solid (m.p. = 118-120 °C). Purified by flash column chromatography (AcOEt to AcOEt/MeOH = 9:1). Yield: 31% (32 mg).

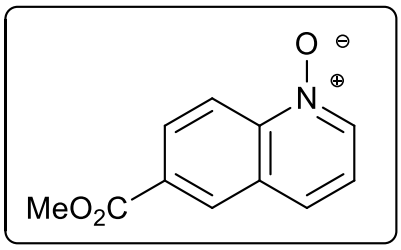
^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.40 (d, *J* = 6.0 Hz, 1H), 8.07 (s, 1H), 7.59 (d, *J* = 8.1 Hz, 1H), 7.15 (dd, *J* = 6.0 and 8.1 Hz, 1H), 7.07 (s, 1H), 4.06 (s, 3H), 4.00 (s, 3H)

^{13}C NMR ($CDCl_3$, 75 MHz): δ 153.52 (C), 151.24 (C), 137.72 (C), 134.30 (CH), 126.18 (C), 124.80 (CH), 119.13 (CH), 105.50 (CH), 98.95 (CH), 56.62 (CH_3), 56.21 (CH_3).

HRMS (ESI): calculated for $C_{11}H_{12}NO_3$ $(M + H)^+$: 206.0812; found: 206.0811.

[3] Y. Ding, W. Zhao, W. Song, Z. Zhang, B. Ma, *Green Chem.*, **2011**, *13*, 1486-1489.

6-(Methoxycarbonyl)quinoline-1-oxide (4d)



3d was purified by flash column chromatography (cyclohexane/AcOEt = 5:1).

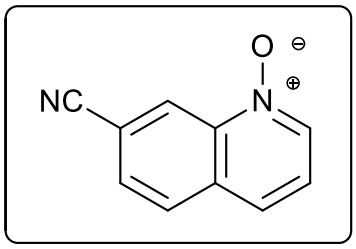
Brown solid (m.p. = 134-136 °C). Purified by flash column chromatography (AcOEt to AcOEt/MeOH = 9:1). Yield: 44% (44 mg).

^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.77 (d, *J* = 9.1 Hz, 1H), 8.64-8.55 (m, 2H), 8.31 (dd, *J* = 1.7 and 9.1 Hz, 1H), 7.84 (d, *J* = 8.3 Hz, 1H), 7.37 (dd, *J* = 6.2 and 8.3 Hz, 1H), 4.00 (s, 3H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.70 (C), 143.13 (C), 137.18 (CH), 130.95 (CH), 130.45 (C), 129.91 (CH), 126.88 (CH), 121.87 (CH), 120.34 (CH), 52.70 (CH_3).

HRMS (ESI): calculated for $C_{11}H_{10}NO_3$ $(M + H)^+$: 204.0655; found: 204.0657.

7-Cyanoquinoline-1-oxide (4e)



3e was purified by flash column chromatography (cyclohexane/AcOEt = 3:1).

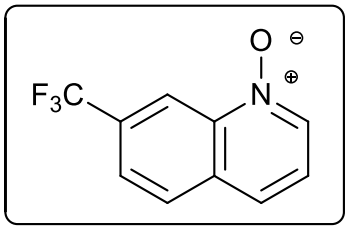
Brown solid (m.p. = 188-190 °C) Purified by flash column chromatography (AcOEt to AcOEt/MeOH = 9:1). Yield: 29% (25 mg).

^{1}H NMR (DMSO, 300 MHz): δ 8.77 (d, *J* = 1.2 Hz, 1H), 8.74 (d, *J* = 6.0 Hz, 1H), 8.63 (d, *J* = 9.0 Hz, 1H), 8.10 (dd, *J* = 9.0 and 1.2 Hz, 1H), 8.02 (d, *J* = 8.2 Hz, 1H), 7.62 (dd, *J* = 6.0 and 8.2 Hz, 1H).

^{13}C NMR (DMSO, 75 MHz): δ 142.30 (C), 138.12 (CH), 135.74 (CH), 131.44 (CH), 130.32 (C), 125.66 (CH), 124.23 (CH), 121.05 (CH), 118.41 (C), 111.99 (C).

HRMS (ESI): calculated for $C_{10}H_7N_2O$ $(M + H)^+$: 171.0553; found: 171.0556.

7-(Trifluoromethyl)quinoline-1-oxide (4f)



3f was purified by flash column chromatography (cyclohexane/AcOEt = 6:1).

Dark brown solid (m.p. = 46-48 °C). Purified by flash column chromatography (AcOEt to AcOEt/MeOH = 9:1). Yield: 32% (34 mg).

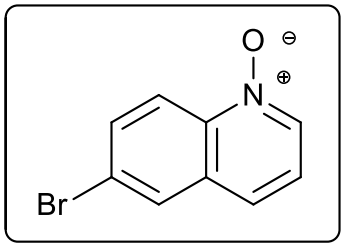
^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.07 (s, 1H), 8.59 (d, *J* = 5.9 Hz, 1H), 8.01 (d, *J* = 8.5 Hz, 1H), 7.80 (m, 2H), 7.43 (dd, *J* = 5.9 and 8.5 Hz, 1H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 141.02 (C), 136.47 (CH), 132.22 (q, *J* = 33 Hz, C), 132.00 (C), 129.52 (CH), 125.32 (CH), 124.68 (q, *J* = 3 Hz, CH), 123.43 (q, *J* = 273 Hz, CF_3) 123.15 (CH), 118.20 (q, *J* = 5 Hz, CH).

^{19}F NMR ($CDCl_3$, 282 MHz): δ -63.94 (CF_3).

HRMS (ESI): calculated for $C_{10}H_7NOF_3$ $(M + H)^+$: 214.0474; found: 214.0472.

6-Bromoquinoline-1-oxide (4g)



3g was purified by flash column chromatography (cyclohexane/AcOEt = 6:1).

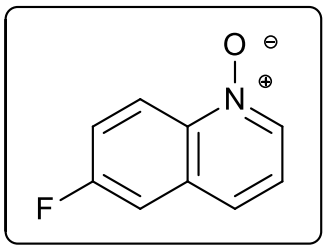
Dark brown solid (m.p. = 128-129 °C). Purified by flash column chromatography (AcOEt to AcOEt/MeOH = 9:1). Yield: 31% (35 mg).

^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.62 (d, *J* = 9.2 Hz, 1H), 8.52 (d, *J* = 6.0 Hz, 1H), 8.05 (d, *J* = 2.0 Hz, 1H), 7.83 (dd, *J* = 9.2 and 2.0 Hz, 1H), 7.65 (d, *J* = 8.3 Hz, 1H), 7.33 (dd, *J* = 6.0 and 8.3 Hz, 1H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 140.39 (C), 135.85 (CH), 133.82 (CH), 131.62 (C), 130.12 (CH), 124.77 (CH), 123.32 (C), 122.22 (CH), 121.79 (CH).

HRMS (ESI): calculated for $C_9H_7NO^{79}Br$ $(M + H)^+$: 223.9706; found: 223.9709.

6-Fluorooquinoline-1-oxide (4h)



3h was purified by flash column chromatography (cyclohexane/AcOEt = 5:1).

Brown solid (m.p. = 102-104 °C). Purified by flash column chromatography (AcOEt to AcOEt/MeOH = 9:1). Yield: 34% (28 mg).

^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.76 (dd, *J* = 10.3 and 5.2 Hz, 1H), 8.47 (d, *J* = 6.0 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.55-7.44 (m, 2H), 7.31 (dd, *J* = 8.4 and 6.0 Hz, 1H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 161.82 (d, *J* = 255 Hz, CF), 138.63 (C), 135.03 (CH), 131.62 (d, *J* = 10 Hz, C), 125.17 (d, *J* = 5 Hz, CH) 122.90 (d, *J* = 10 Hz, CH), 122.20 (CH), 120.35 (d, *J* = 26 Hz, CH), 111.55 (d, *J* = 22 Hz, CH).

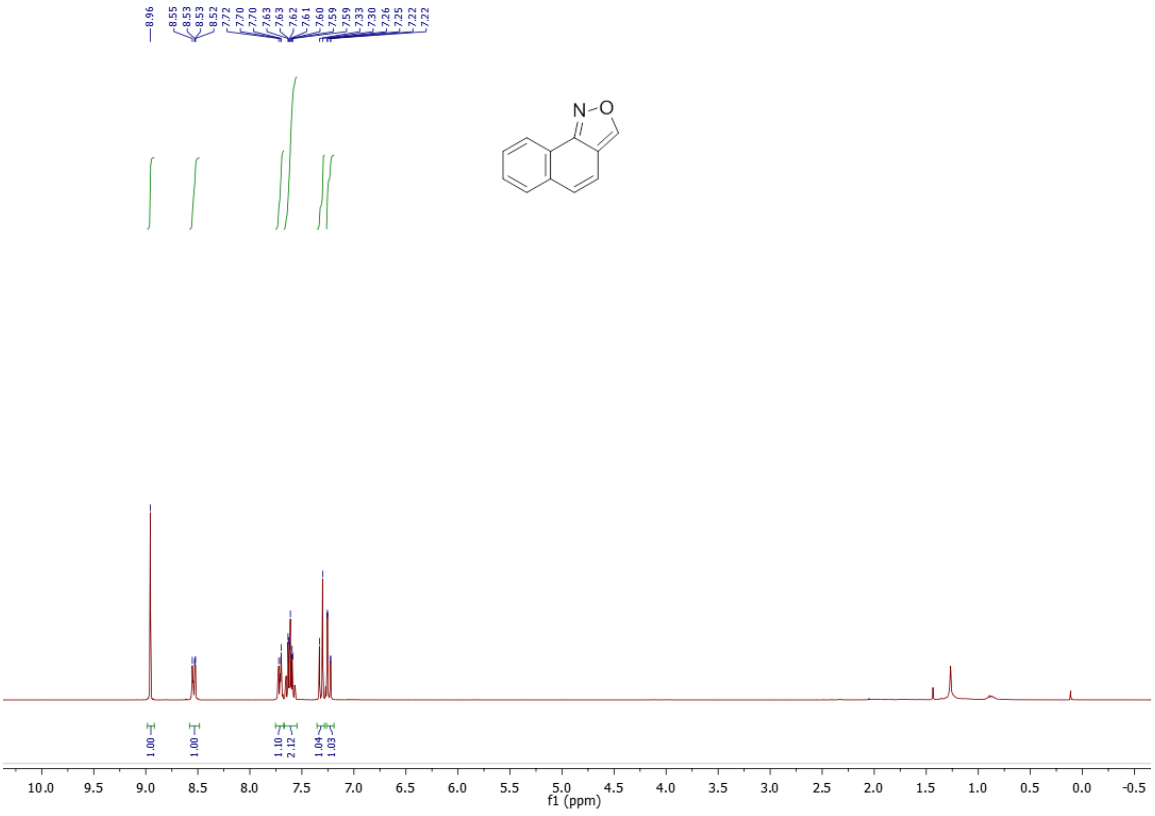
^{19}F NMR ($CDCl_3$, 282 MHz): δ -110.97 (CF).

HRMS (ESI): calculated for C_9H_7NOF $(M + H)^+$: 164.0506; found: 164.0507.

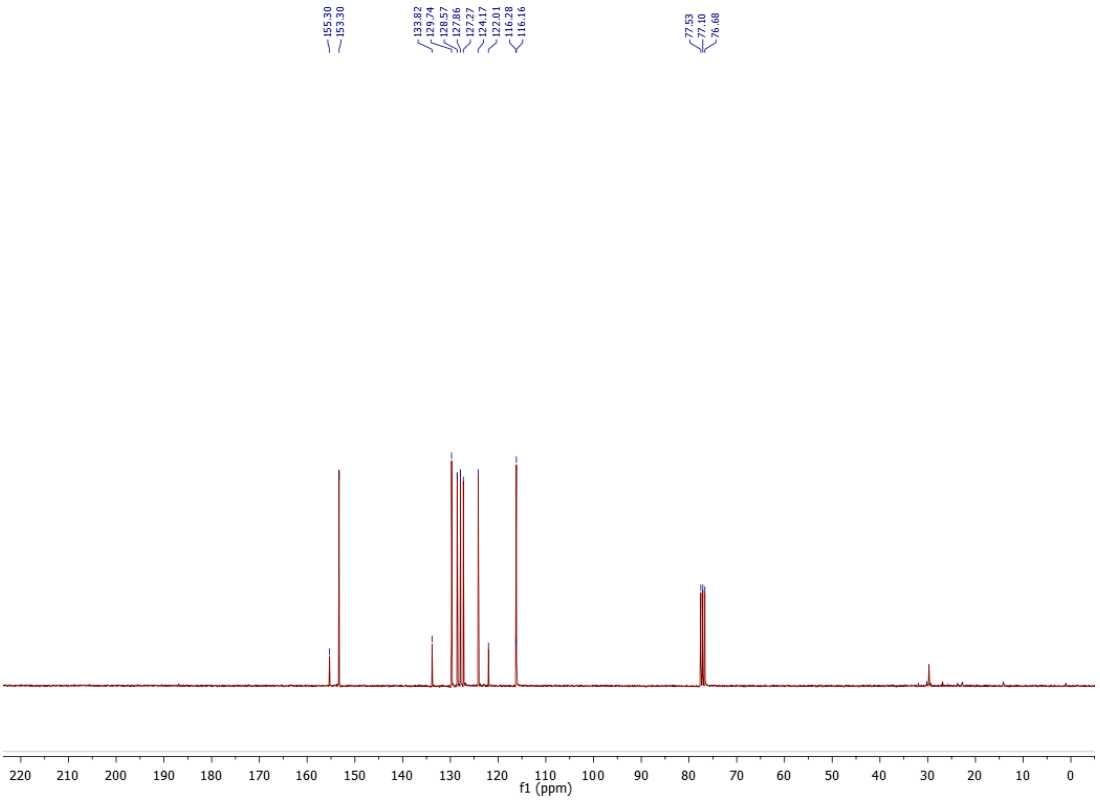
6. NMR spectra of 2,1-benzisoxazoles (2) and quinoline *N*-oxides (4)

Naphtho[1,2-*c*]isoxazole (2b)

(^{1}H NMR, $CDCl_3$, 300 MHz)

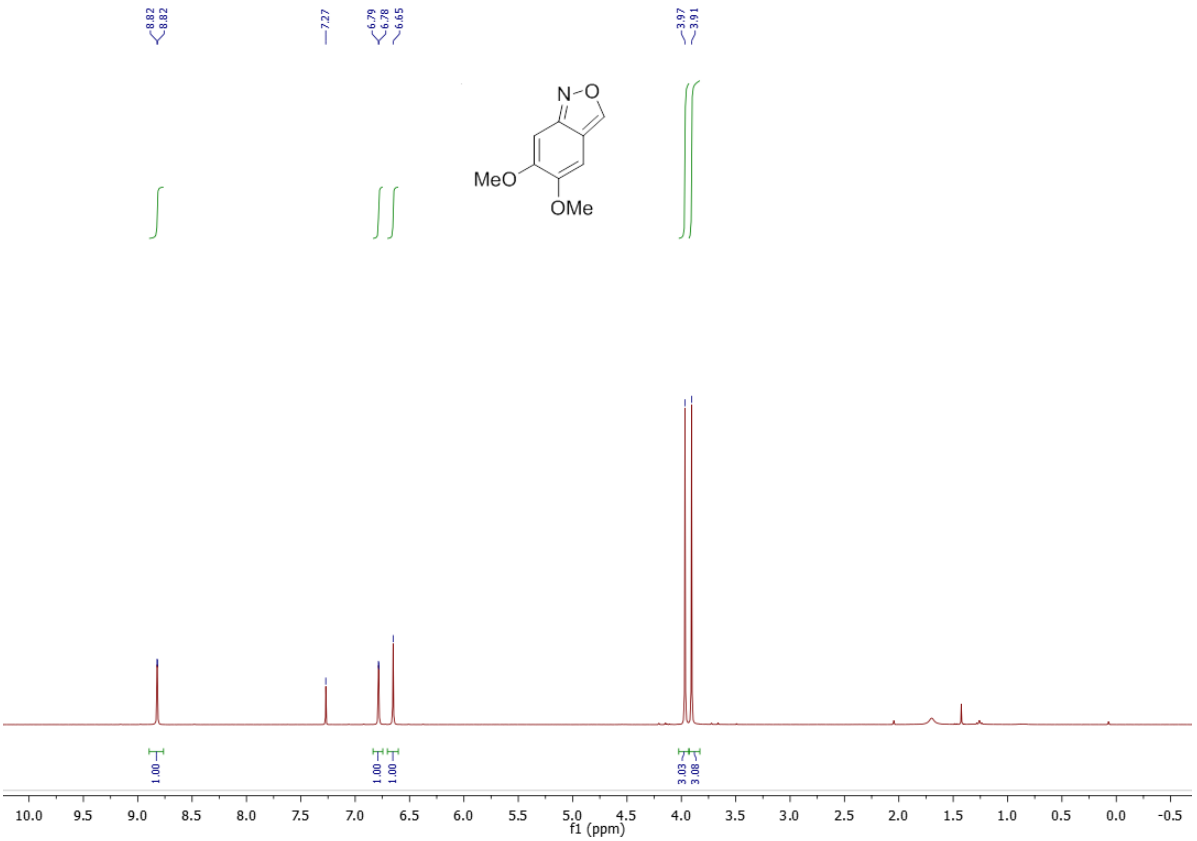


(^{13}C NMR, $CDCl_3$, 75 MHz)

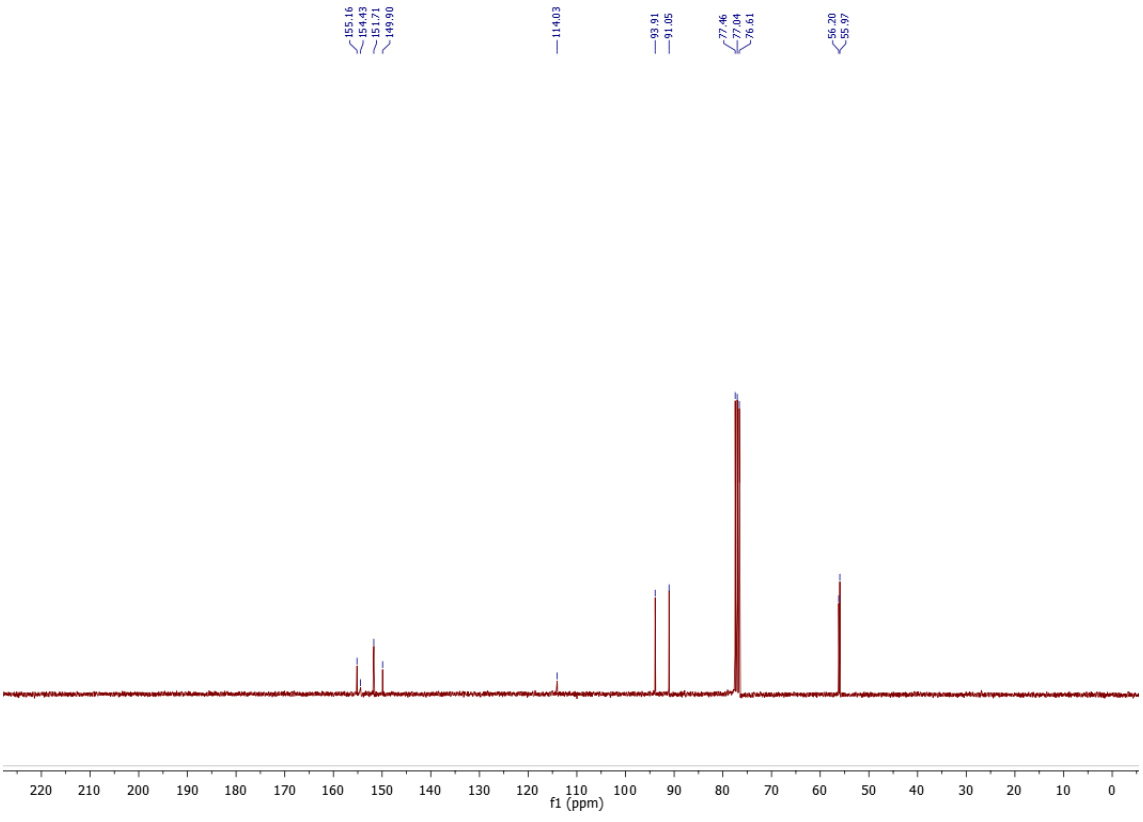


5,6-Dimethoxybenzo[*c*]isoxazole (2c)

(^{1}H NMR, $CDCl_3$, 300 MHz)

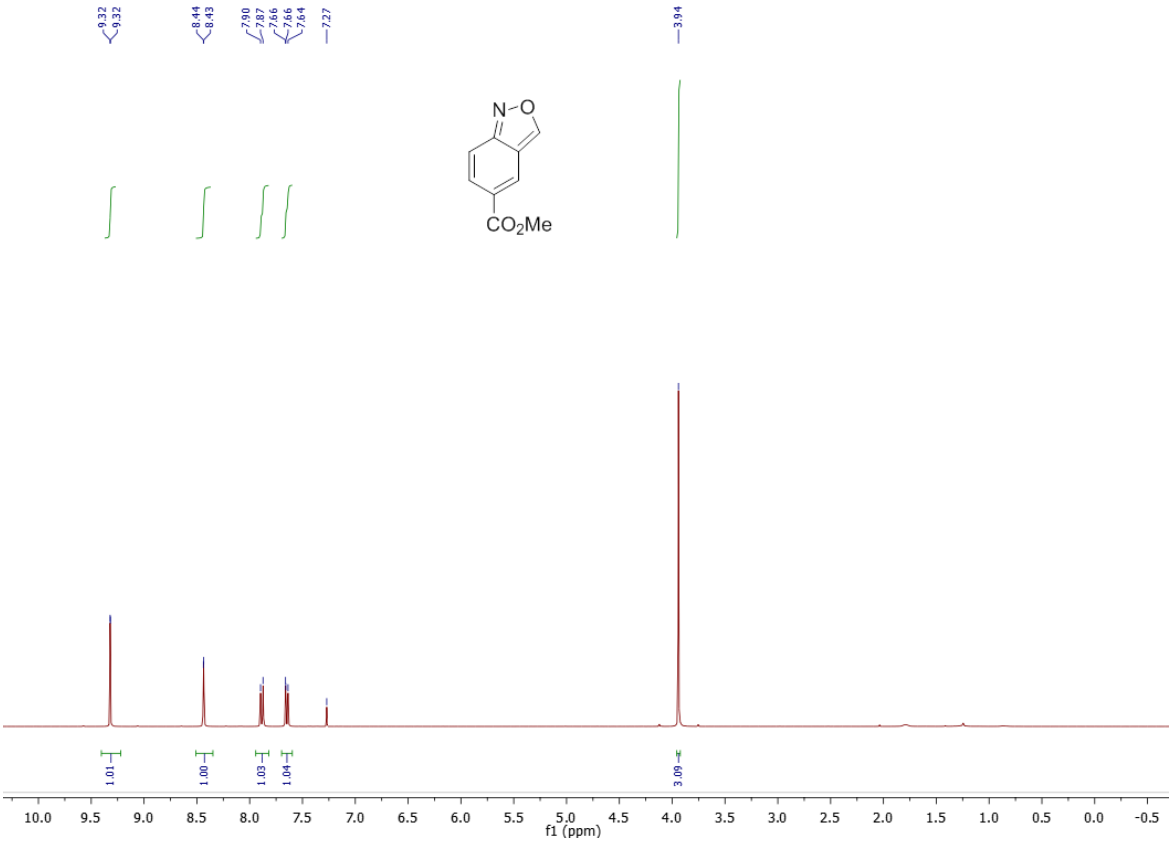


(^{13}C NMR, $CDCl_3$, 75 MHz)

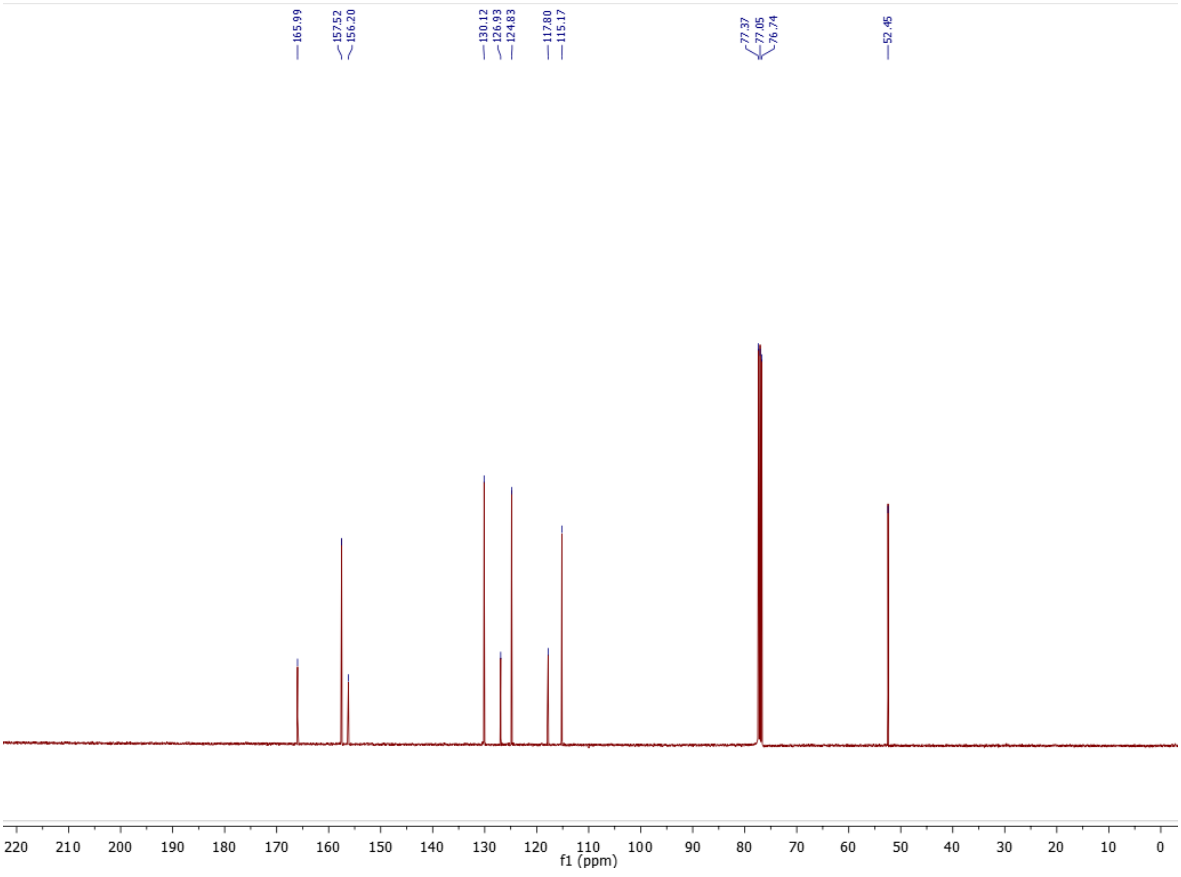


Methyl benzo[*c*]isoxazole-5-carboxylate (2d)

(^{1}H NMR, $CDCl_3$, 300 MHz)

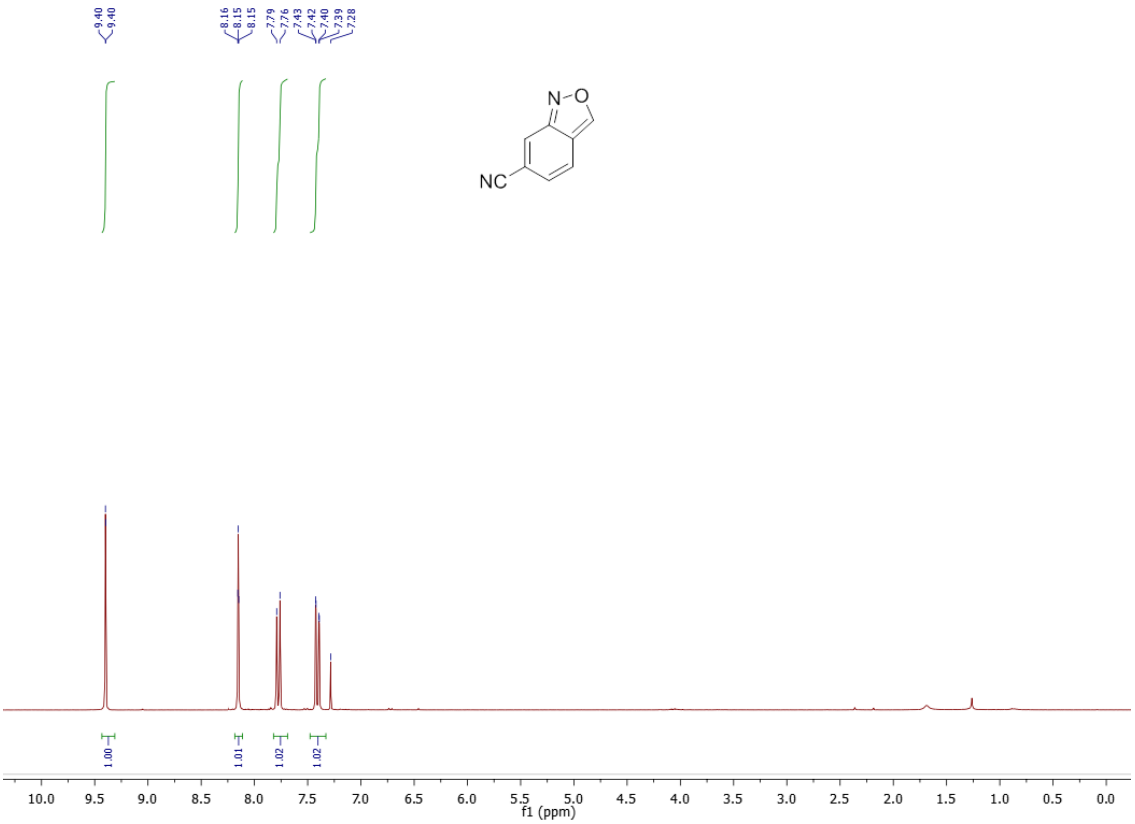


(^{13}C NMR, $CDCl_3$, 75 MHz)

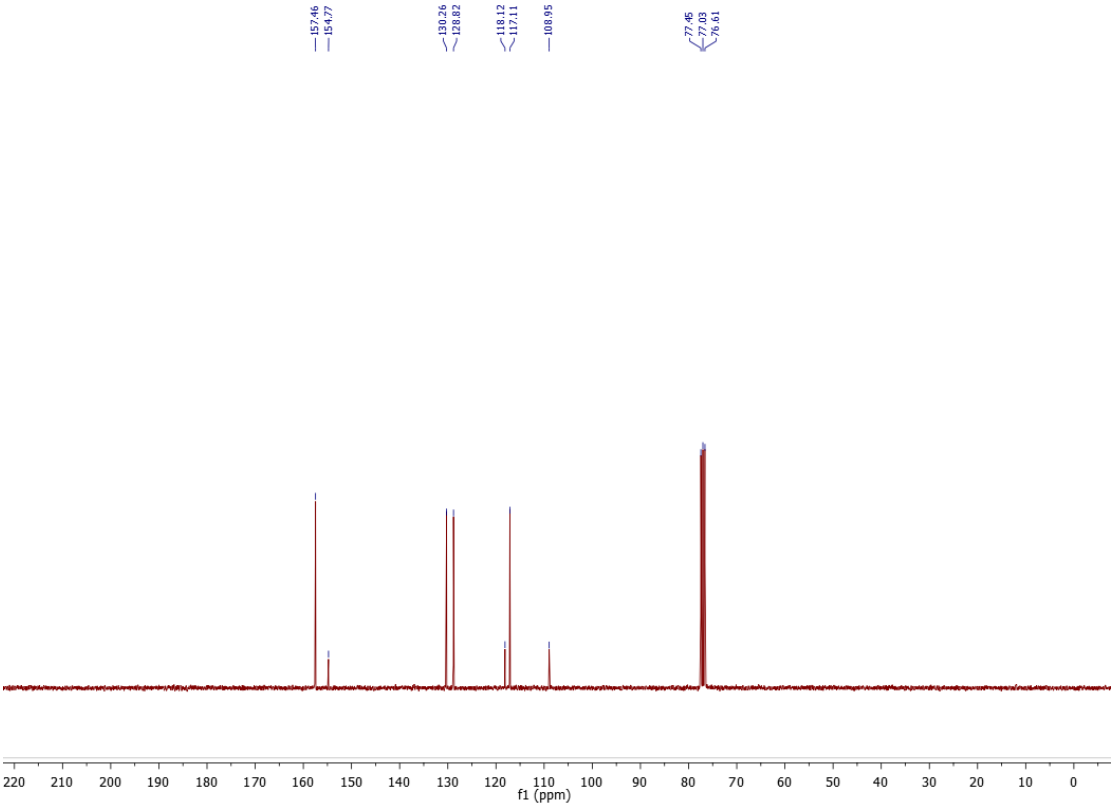


Benzo[*c*]isoxazole-6-carbonitrile (2e)

(^{1}H NMR, $CDCl_3$, 300 MHz)

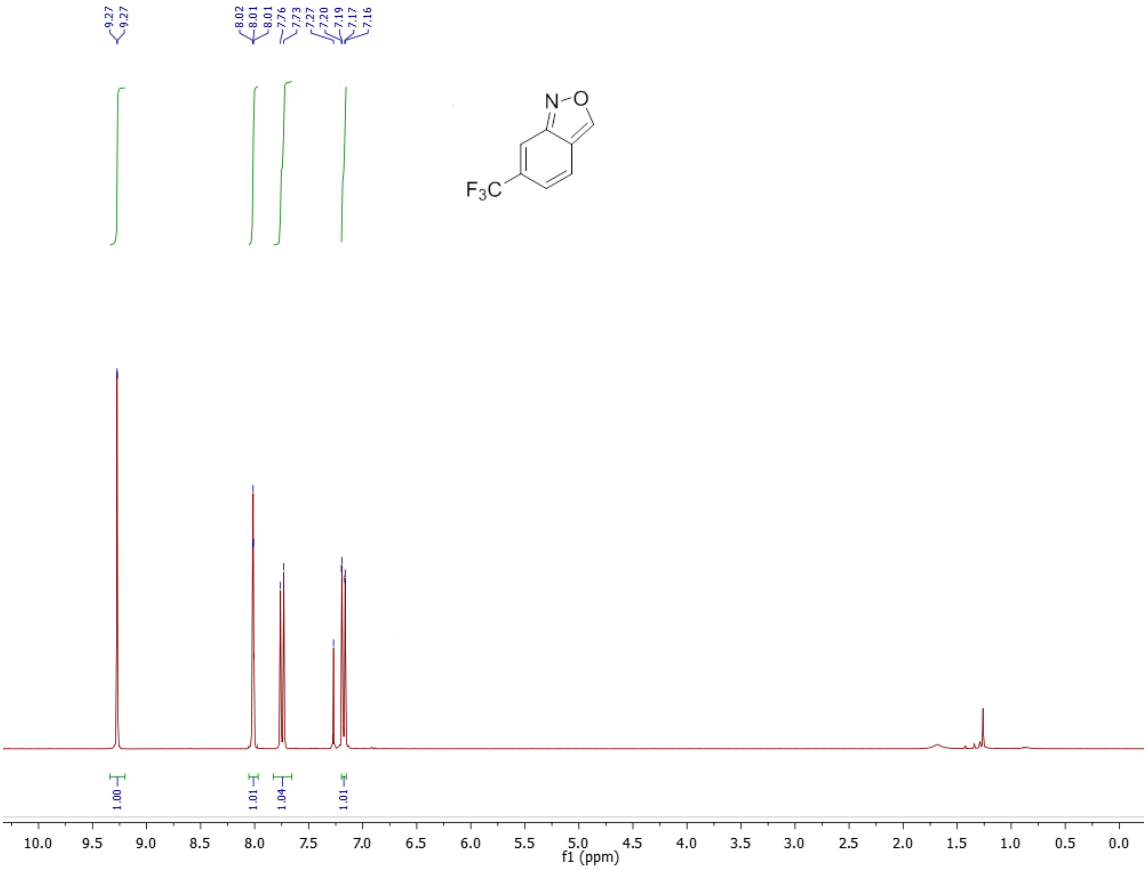


(^{13}C NMR, $CDCl_3$, 75 MHz)

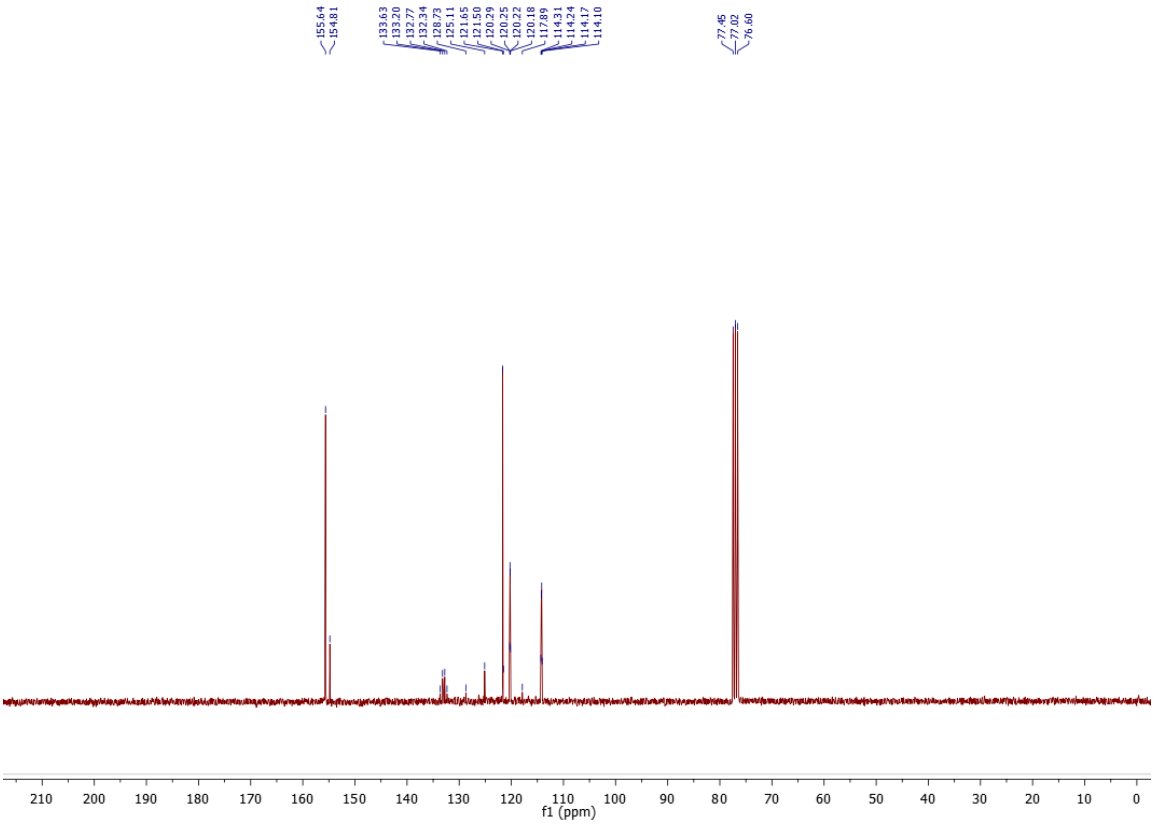


6-(Trifluoromethyl)benzo[*c*]isoxazole (2f)

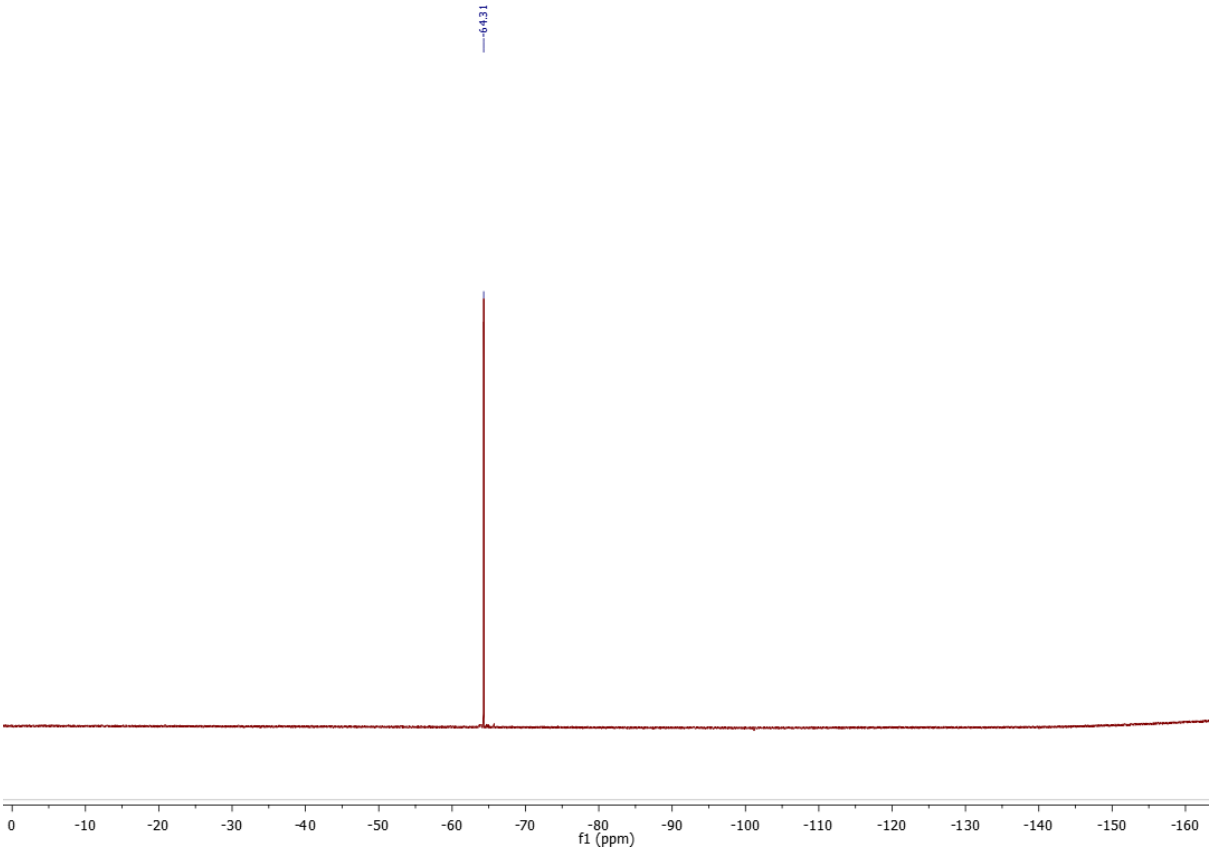
(^{1}H NMR, $CDCl_3$, 300 MHz)



(^{13}C NMR, $CDCl_3$, 75 MHz)

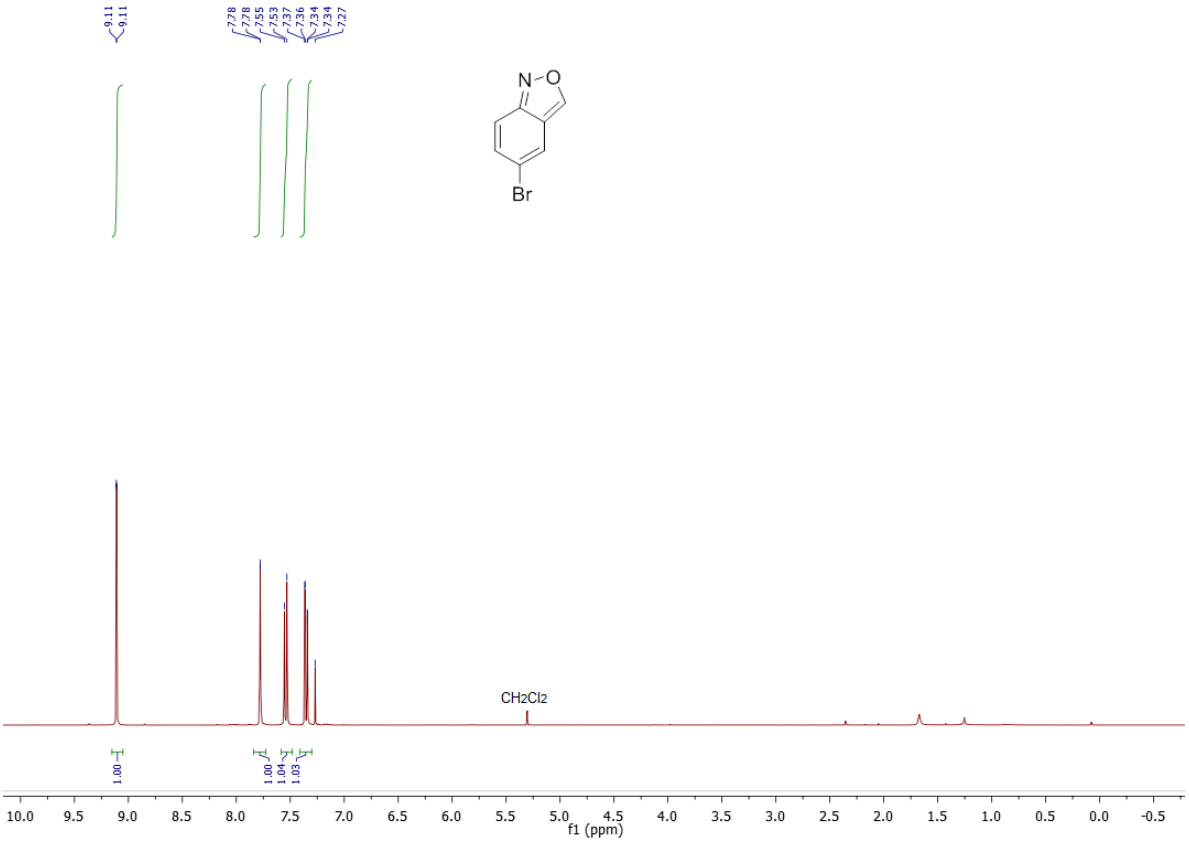


(^{19}F NMR, $CDCl_3$, 282 MHz)

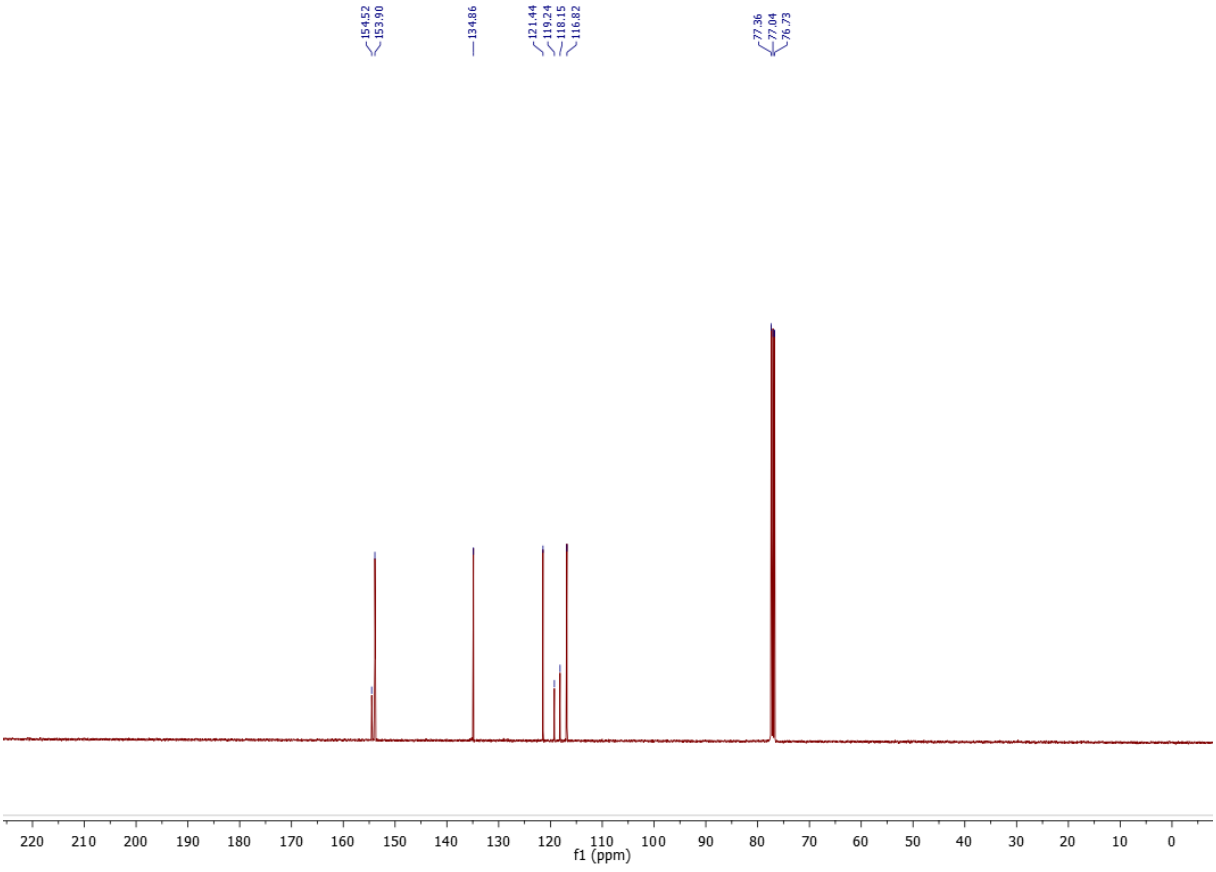


5-Bromobenzo[*c*]isoxazole (2g)

(^{1}H NMR, $CDCl_3$, 300 MHz)

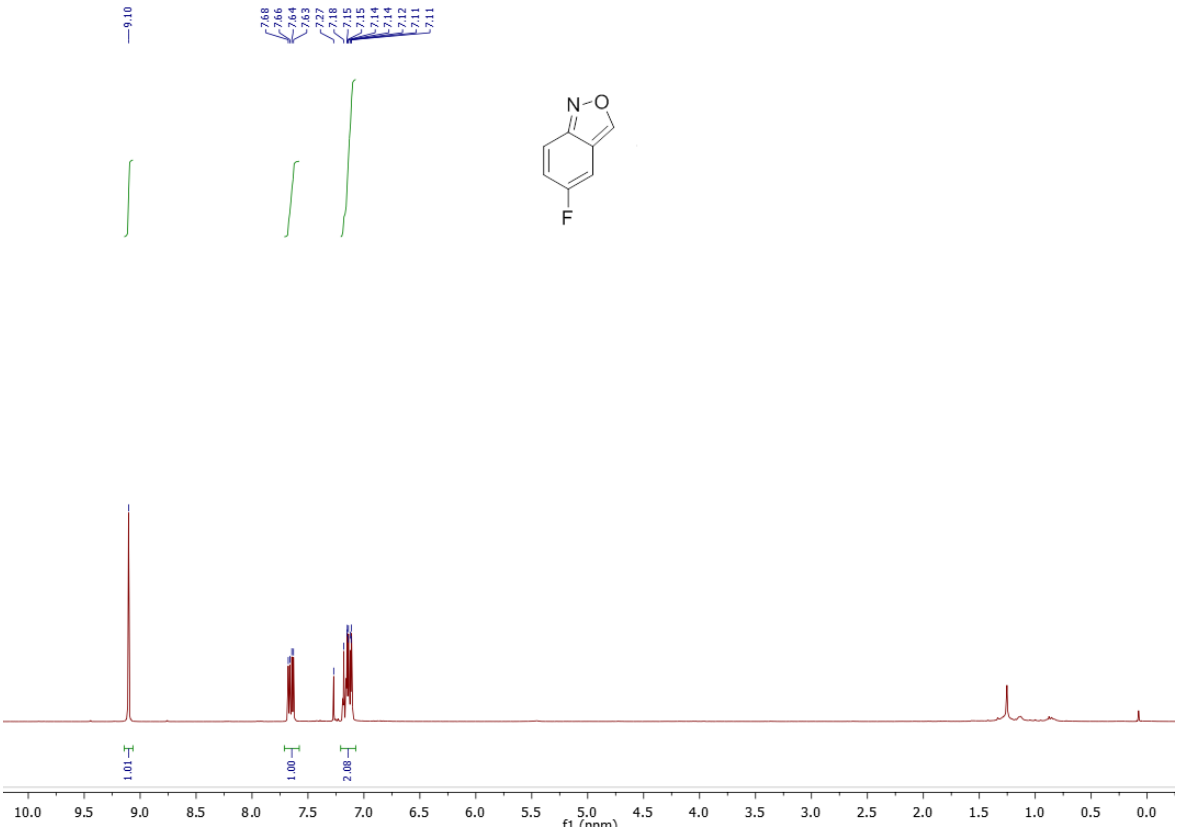


(^{13}C NMR, $CDCl_3$, 75 MHz)

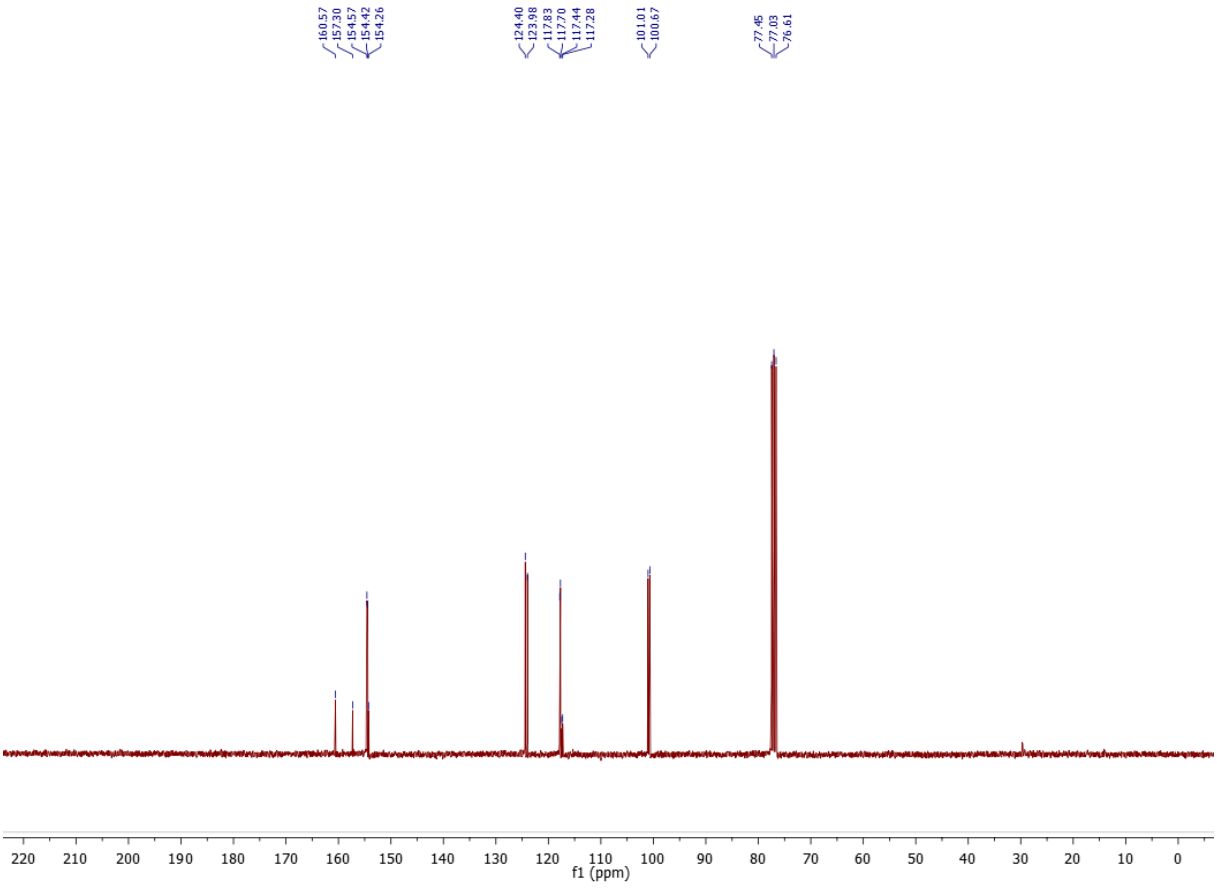


5-Fluorobenzo[*c*]isoxazole (2h)

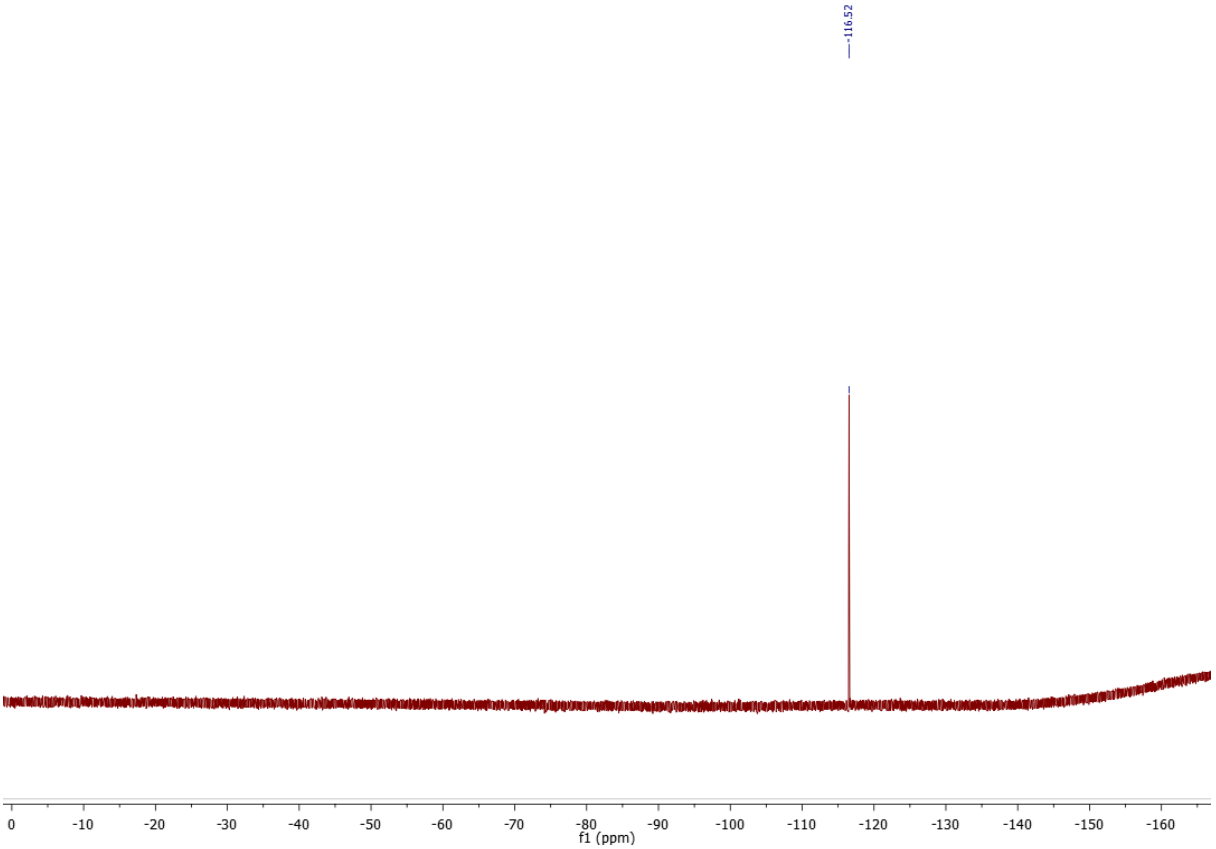
(^{1}H NMR, $CDCl_3$, 300 MHz)



(^{13}C NMR, $CDCl_3$, 75 MHz)

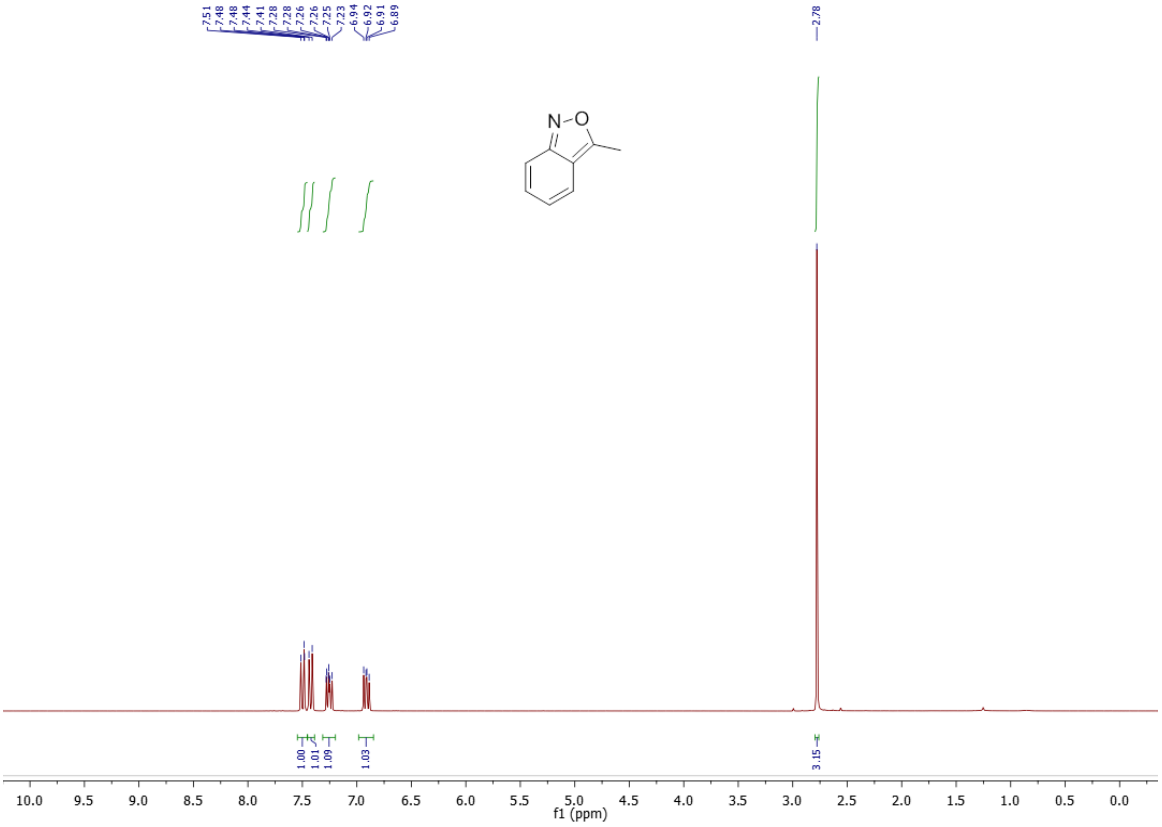


(^{19}F NMR, $CDCl_3$, 282 MHz)

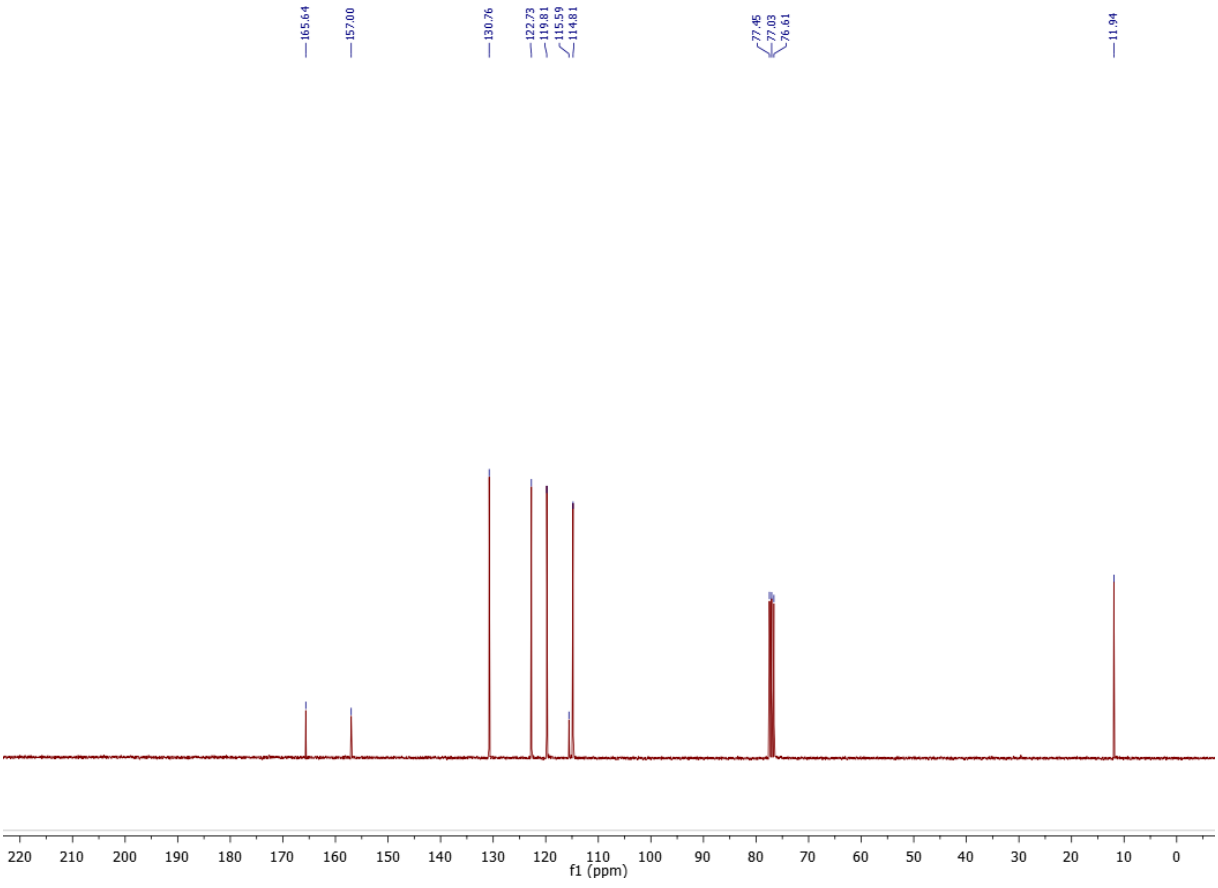


3-Methylbenzo[*c*]isoxazole (2i)

(^{1}H NMR, $CDCl_3$, 300 MHz)

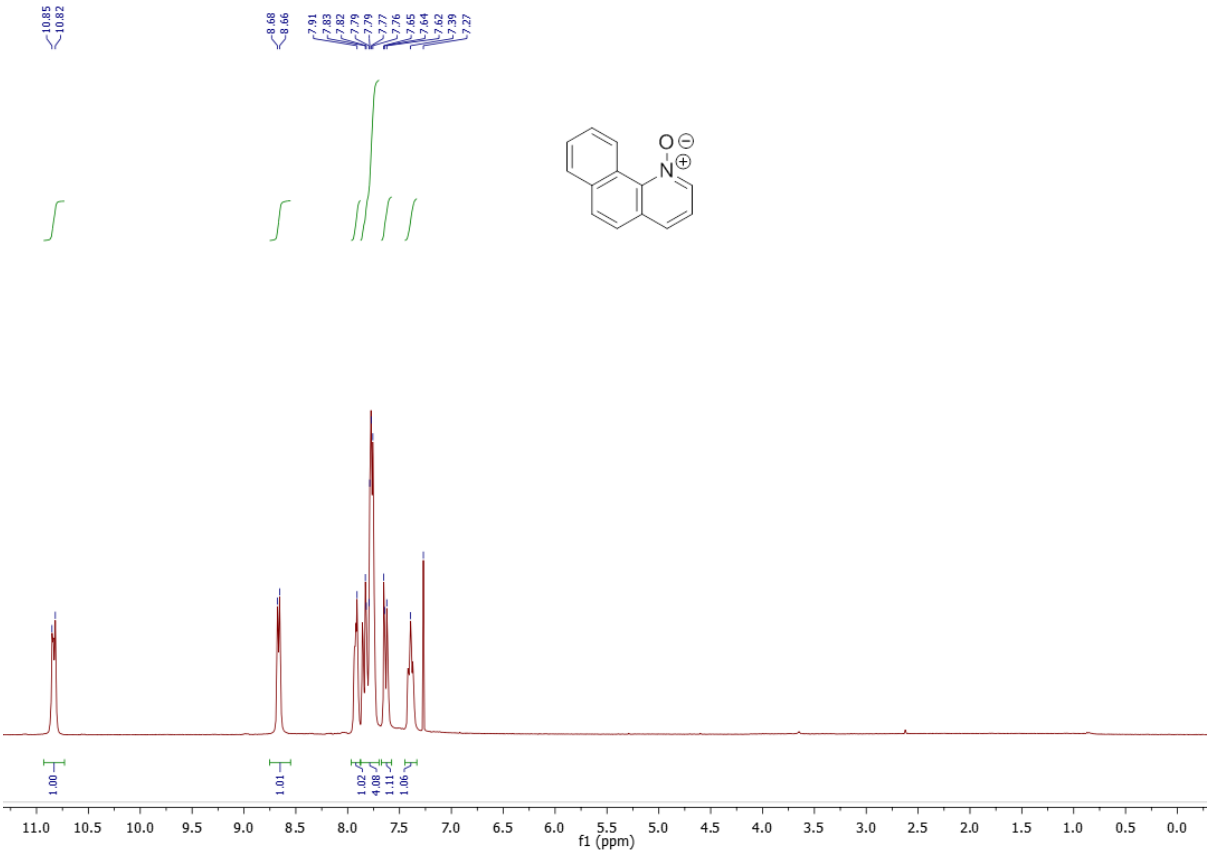


(^{13}C NMR, $CDCl_3$, 75 MHz)

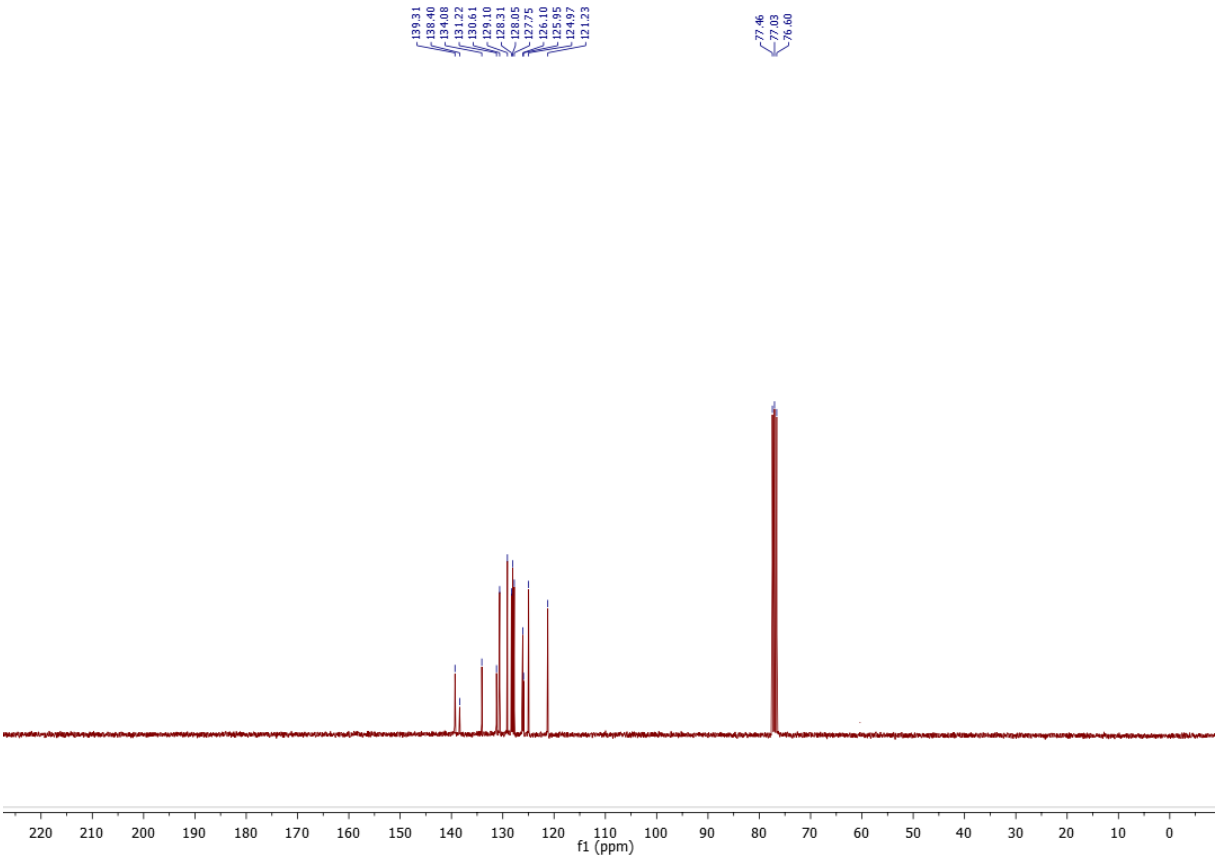


Benzo[*h*]quinoline 1-oxide (4b)

(^{1}H NMR, $CDCl_3$, 300 MHz)

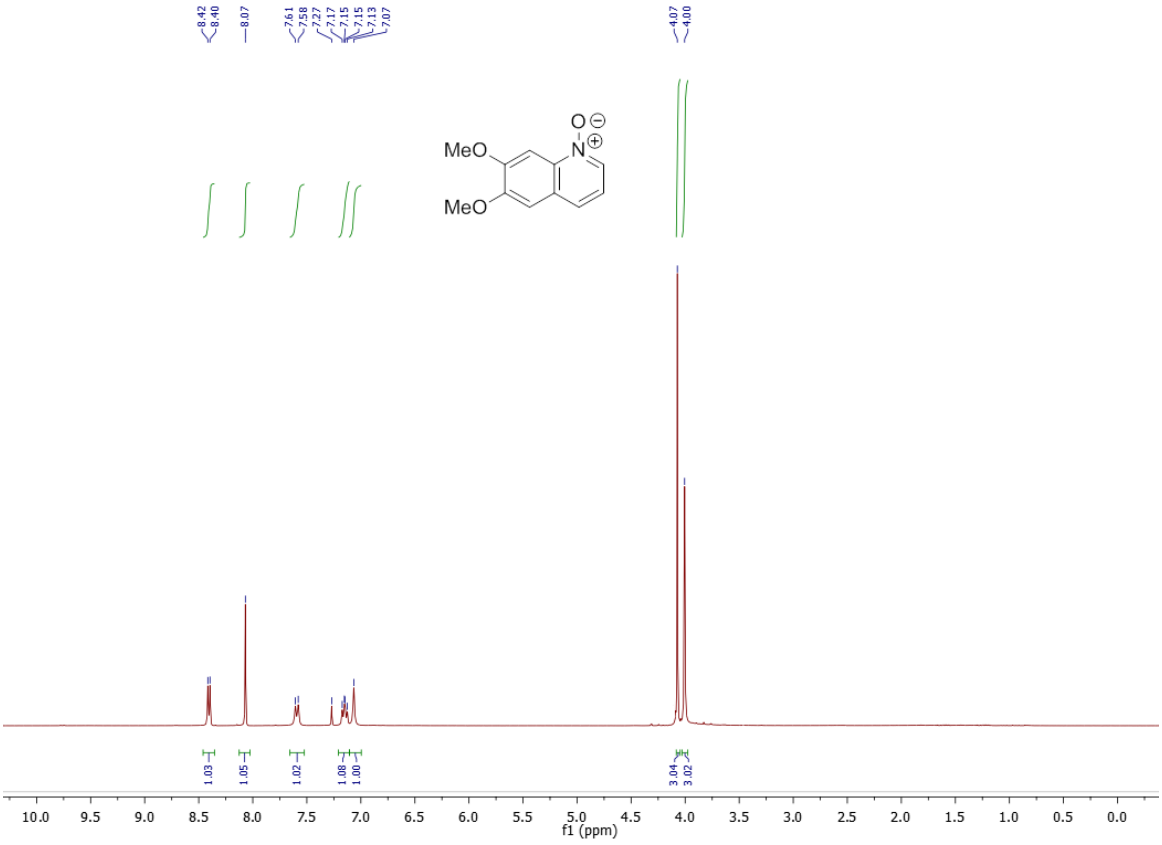


(^{13}C NMR, $CDCl_3$, 75 MHz)

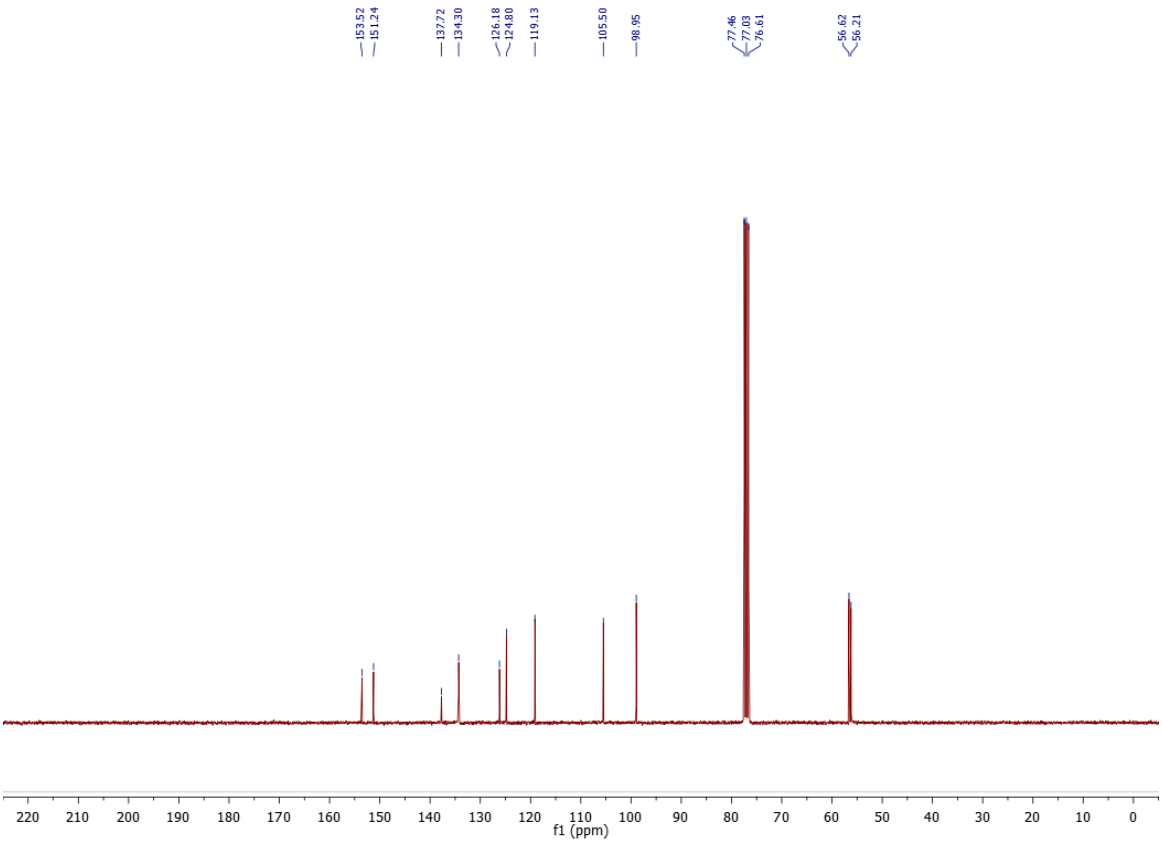


6,7-Dimethoxyquinoline 1-oxide (4c)

(^{1}H NMR, $CDCl_3$, 300 MHz)

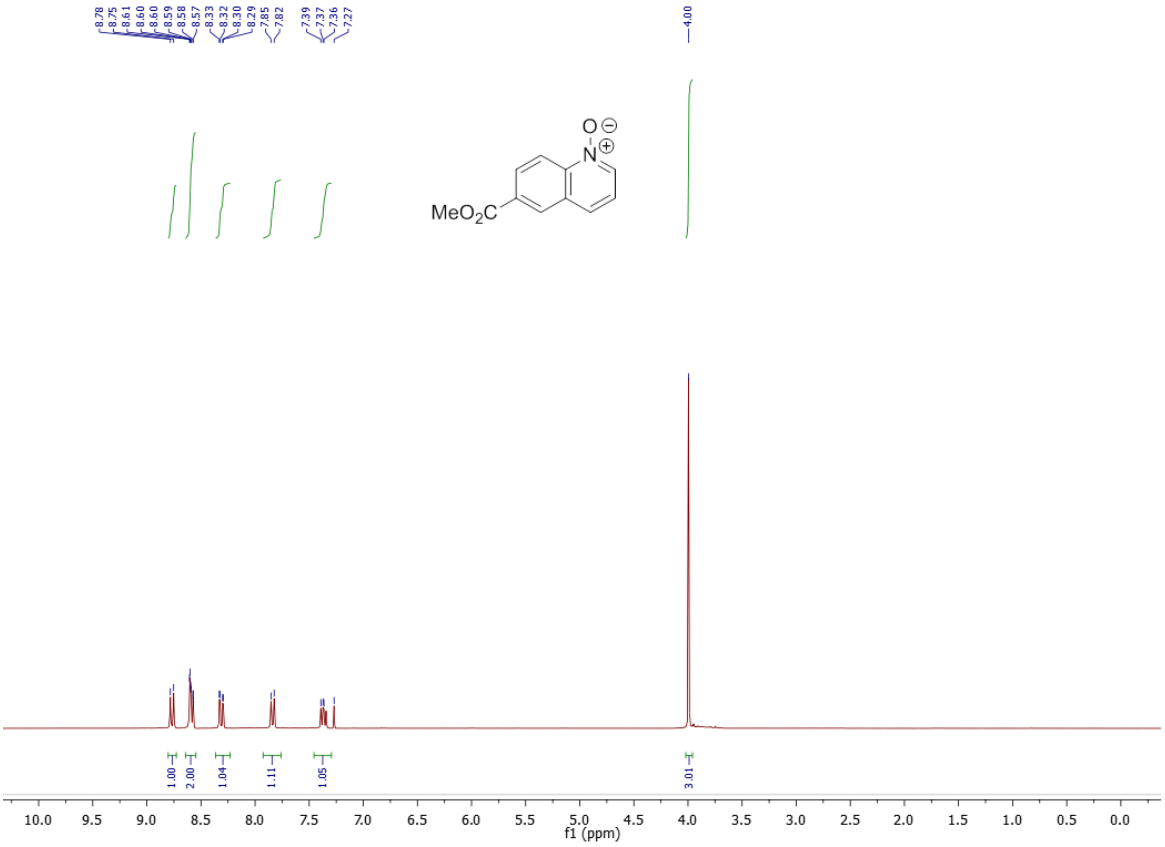


(^{13}C NMR, $CDCl_3$, 75 MHz)

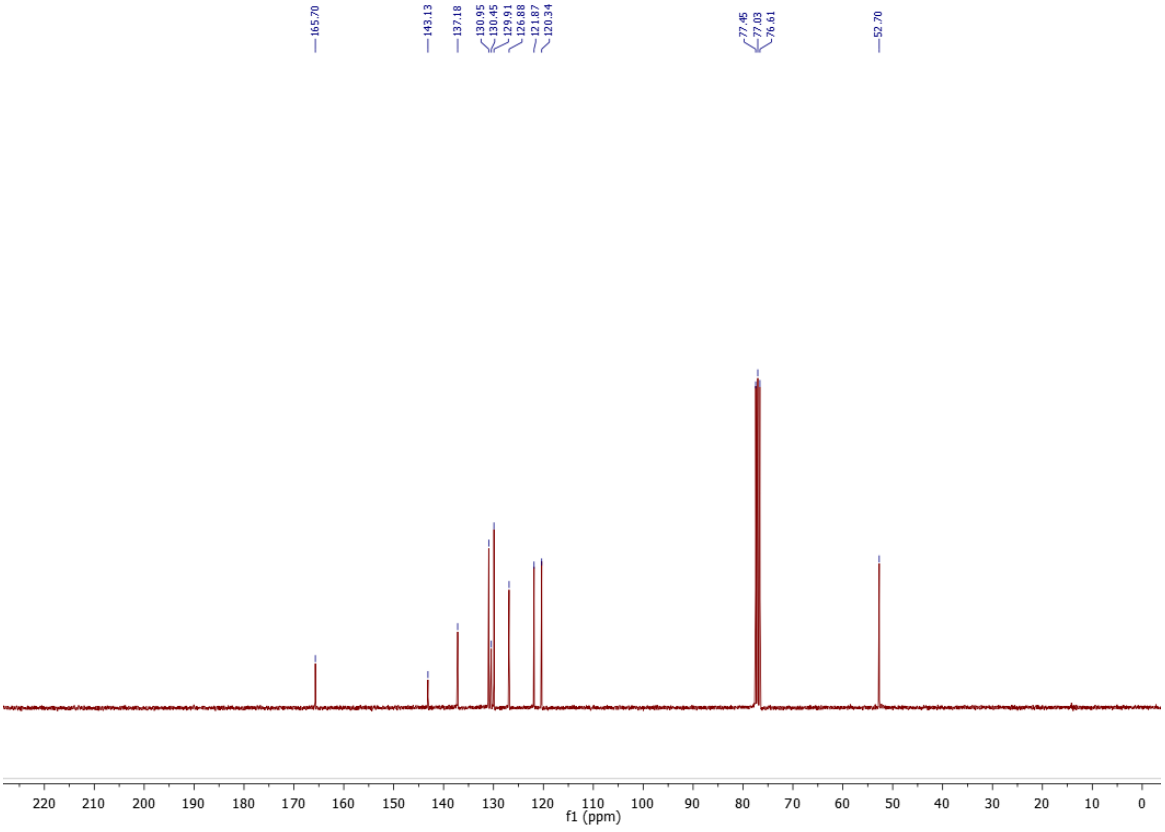


6-(Methoxycarbonyl)quinoline-1-oxide (4d)

(^{1}H NMR, $CDCl_3$, 300 MHz)

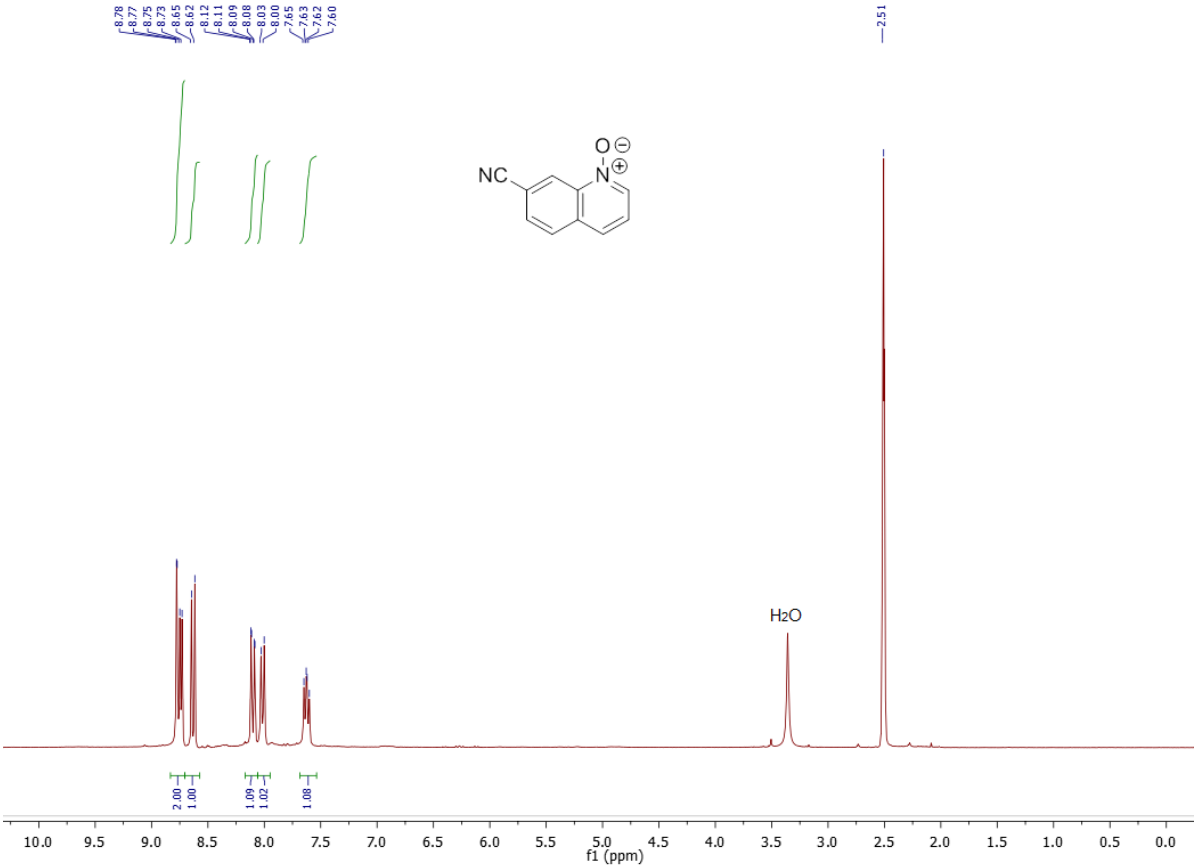


(^{13}C NMR, $CDCl_3$, 75 MHz)

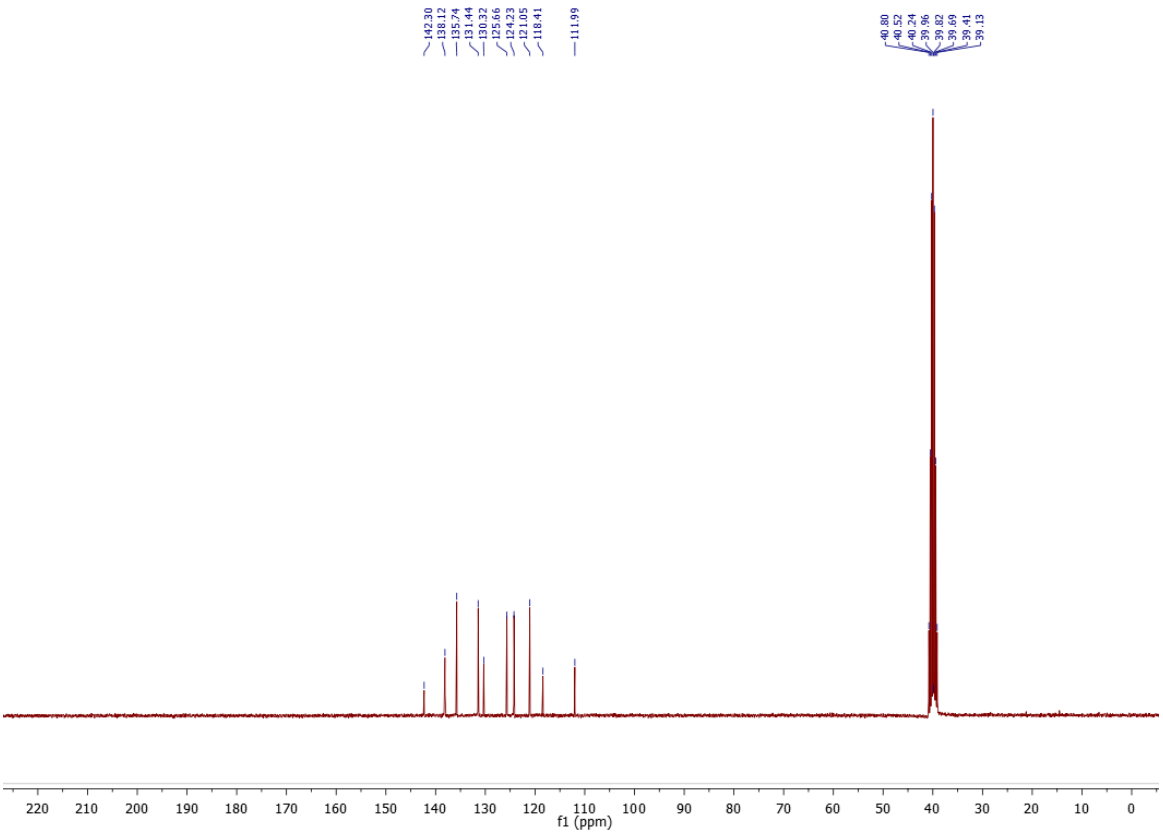


7-Cyanoquinoline-1-oxide (4e)

(^{1}H NMR, DMSO, 300 MHz)

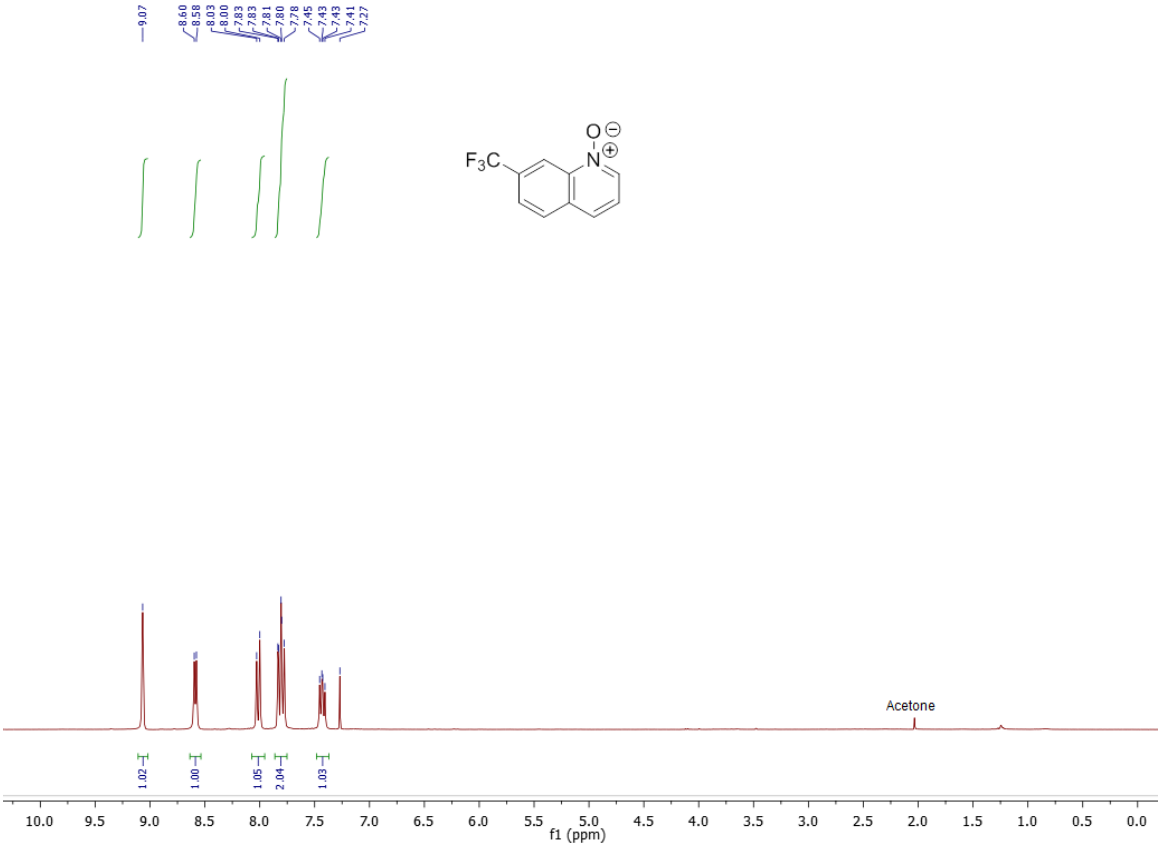


(^{13}C NMR, DMSO, 75 MHz)

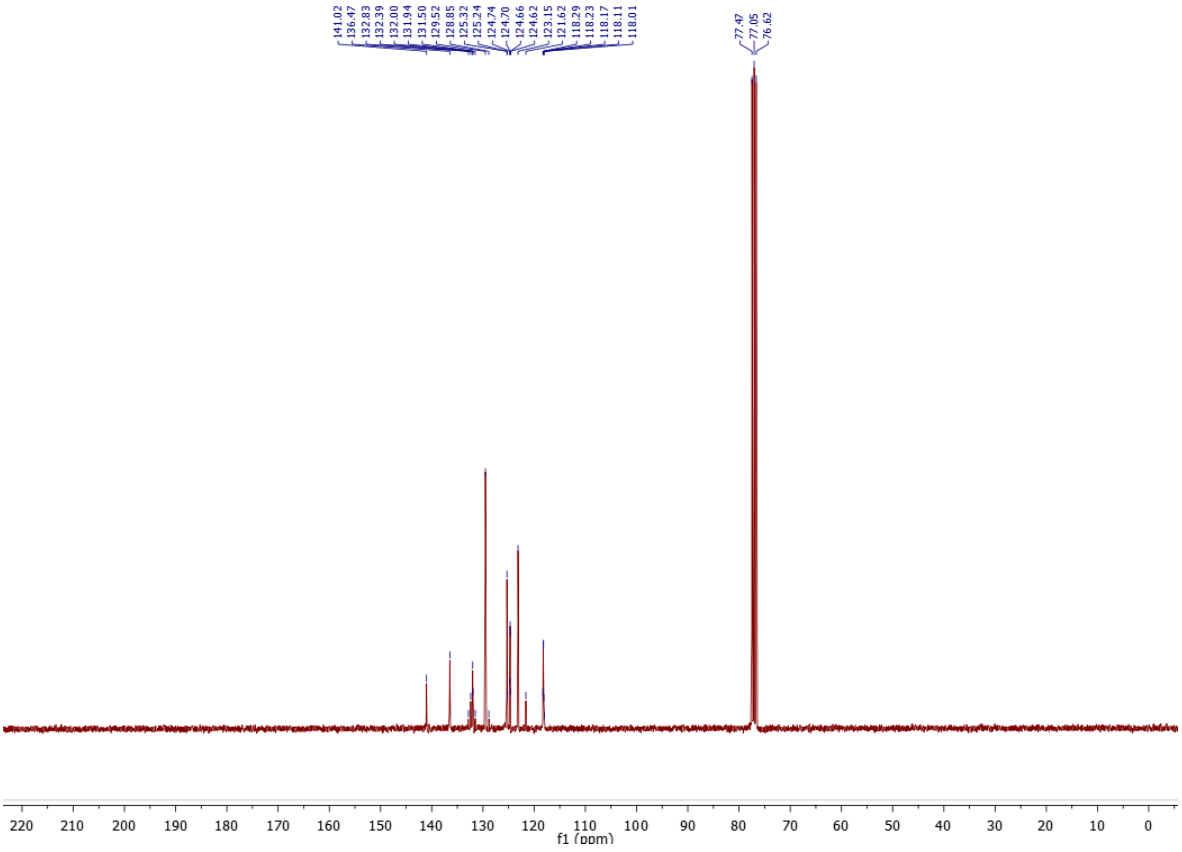


7-(trifluoromethyl)quinoline-1-oxide (4f)

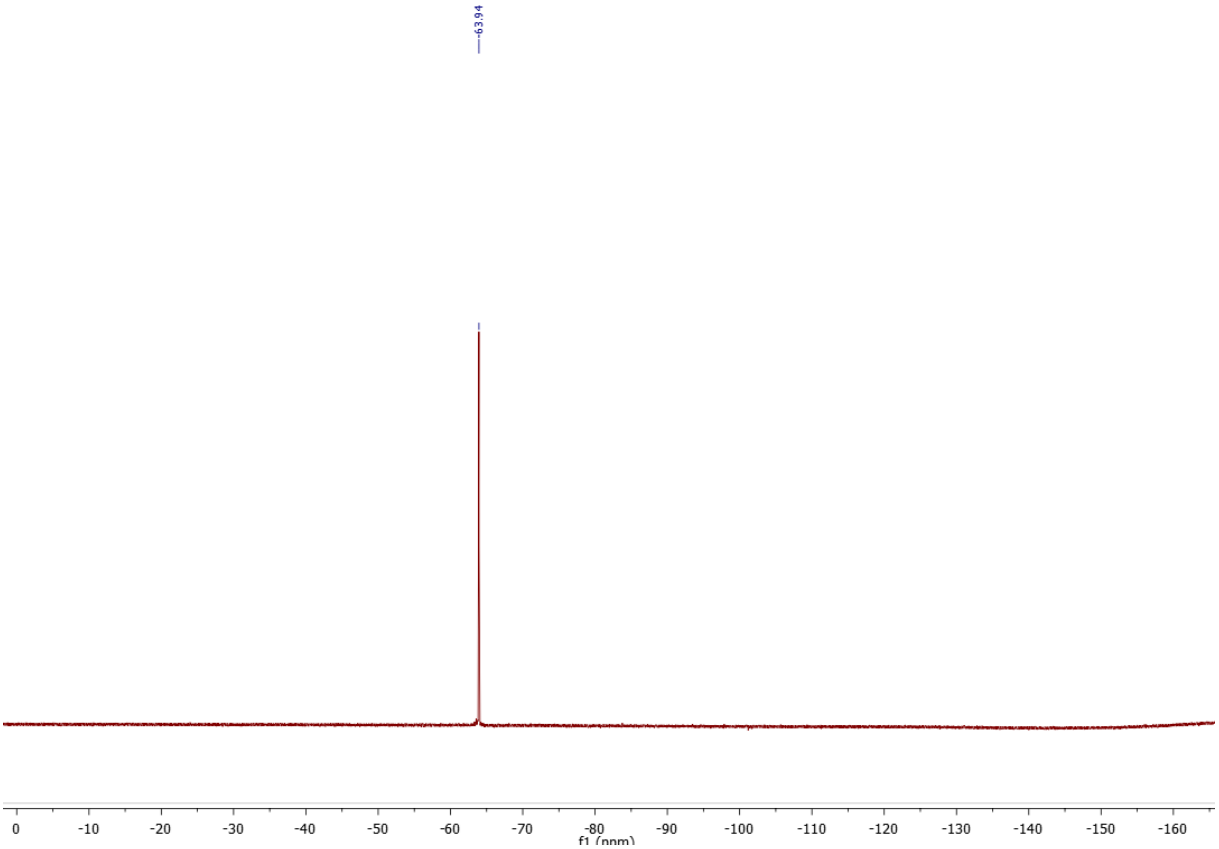
(^{1}H NMR, $CDCl_3$, 300 MHz)



(^{13}C NMR, $CDCl_3$, 75 MHz)

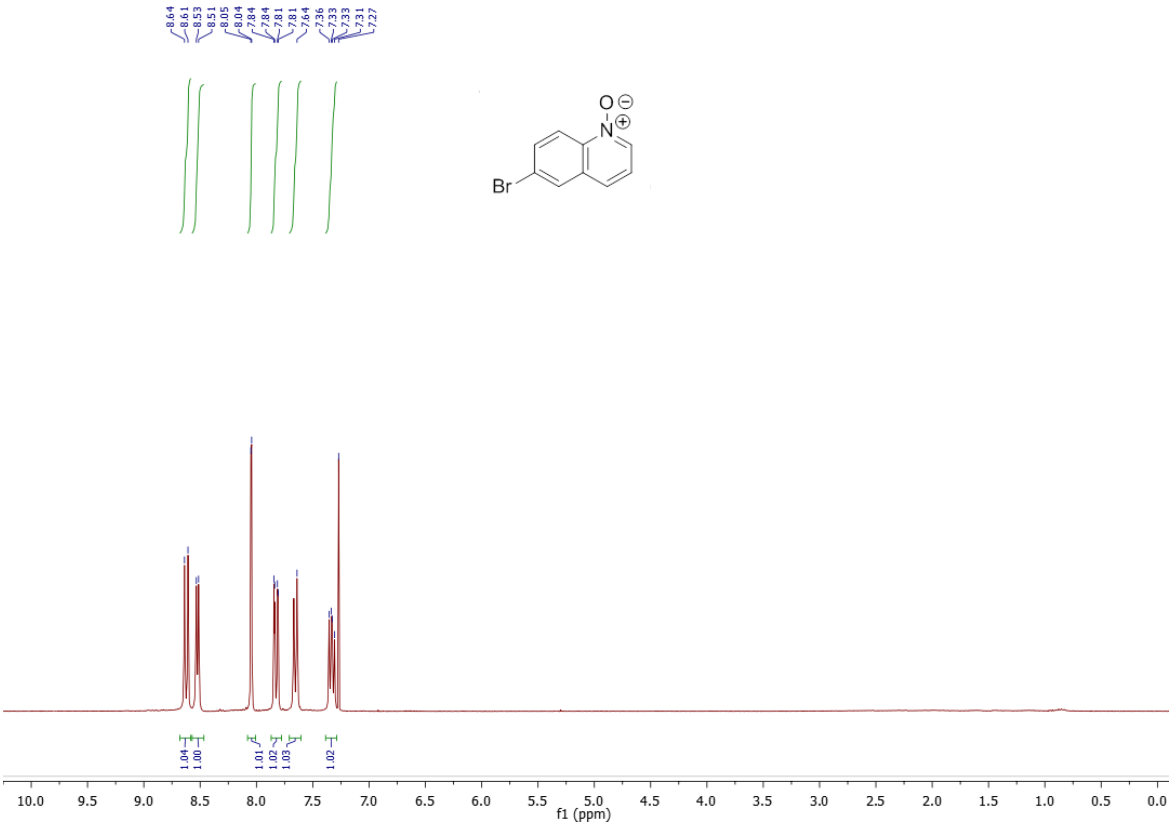


(^{19}F NMR, $CDCl_3$, 282 MHz)

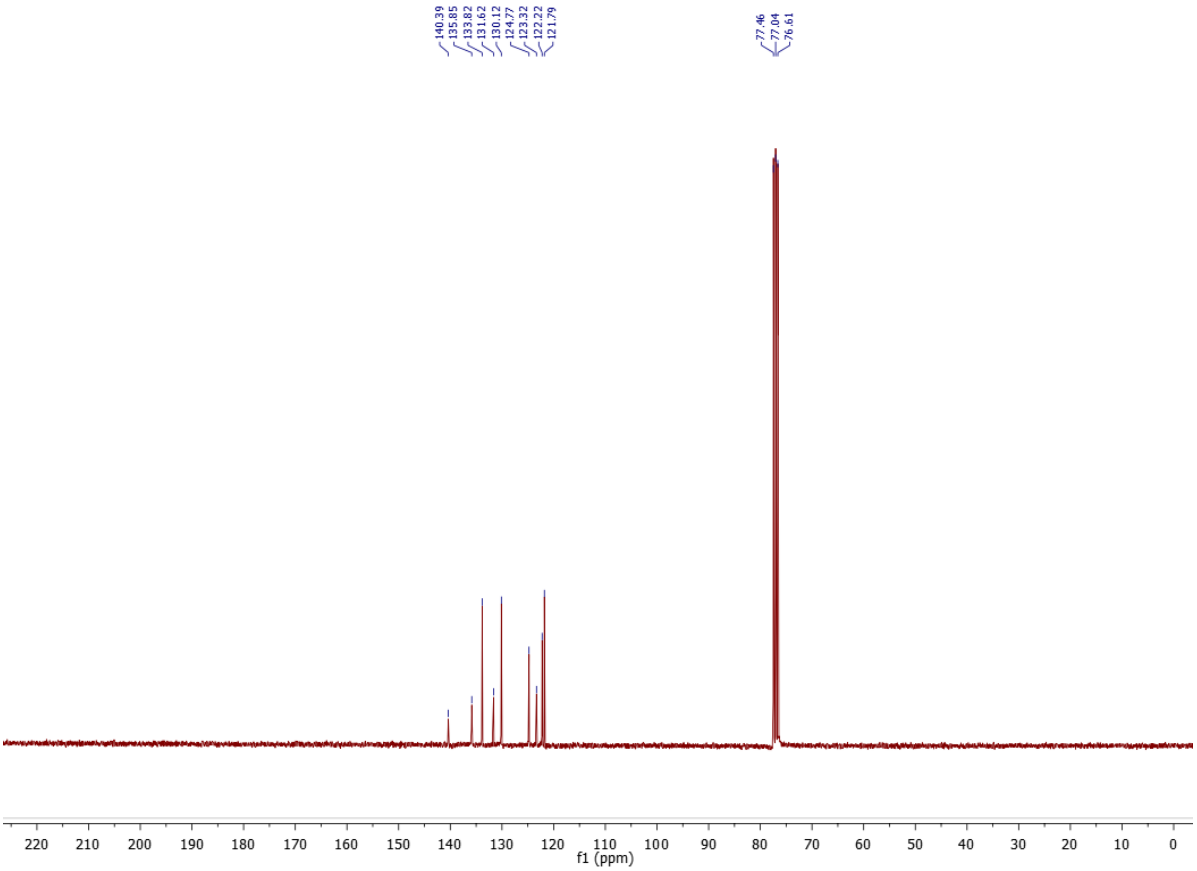


6-Bromoquinoline-1-oxide (4g)

(^{1}H NMR, $CDCl_3$, 300 MHz)

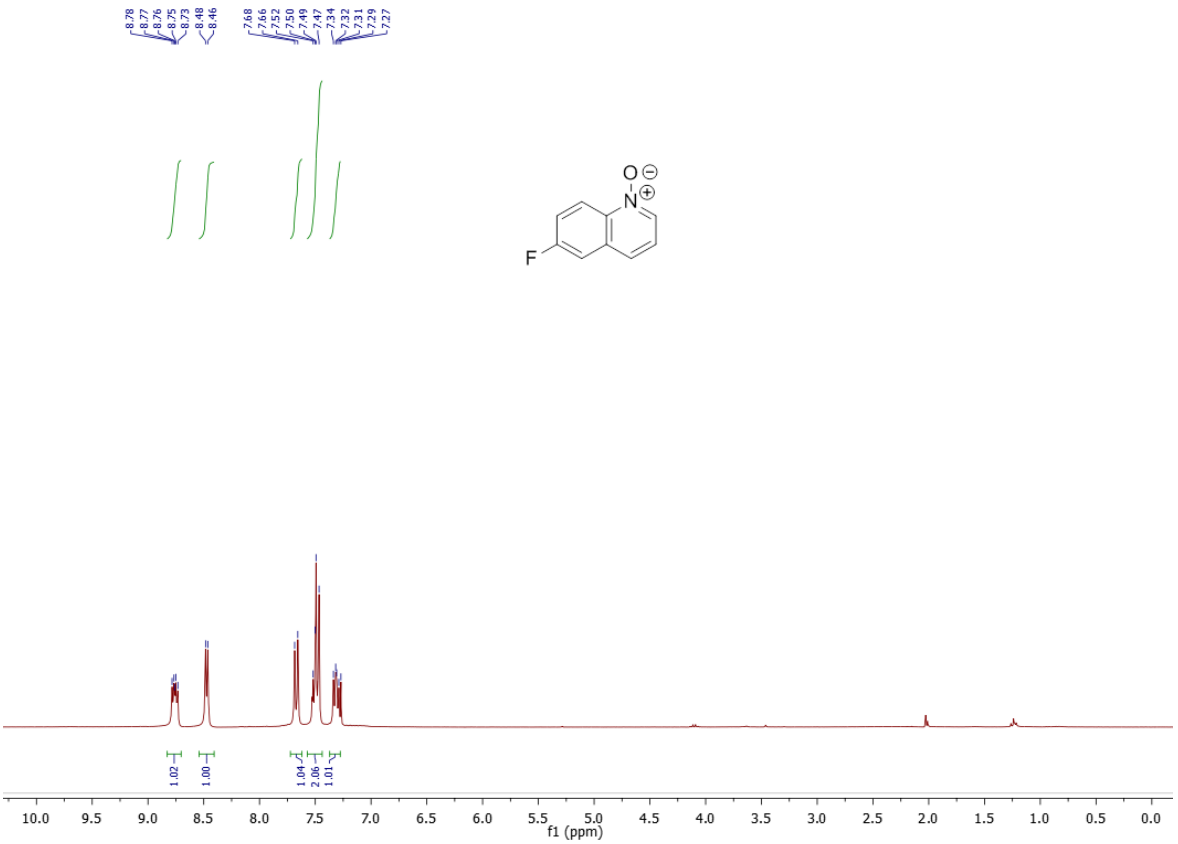


(^{13}C NMR, $CDCl_3$, 75 MHz)

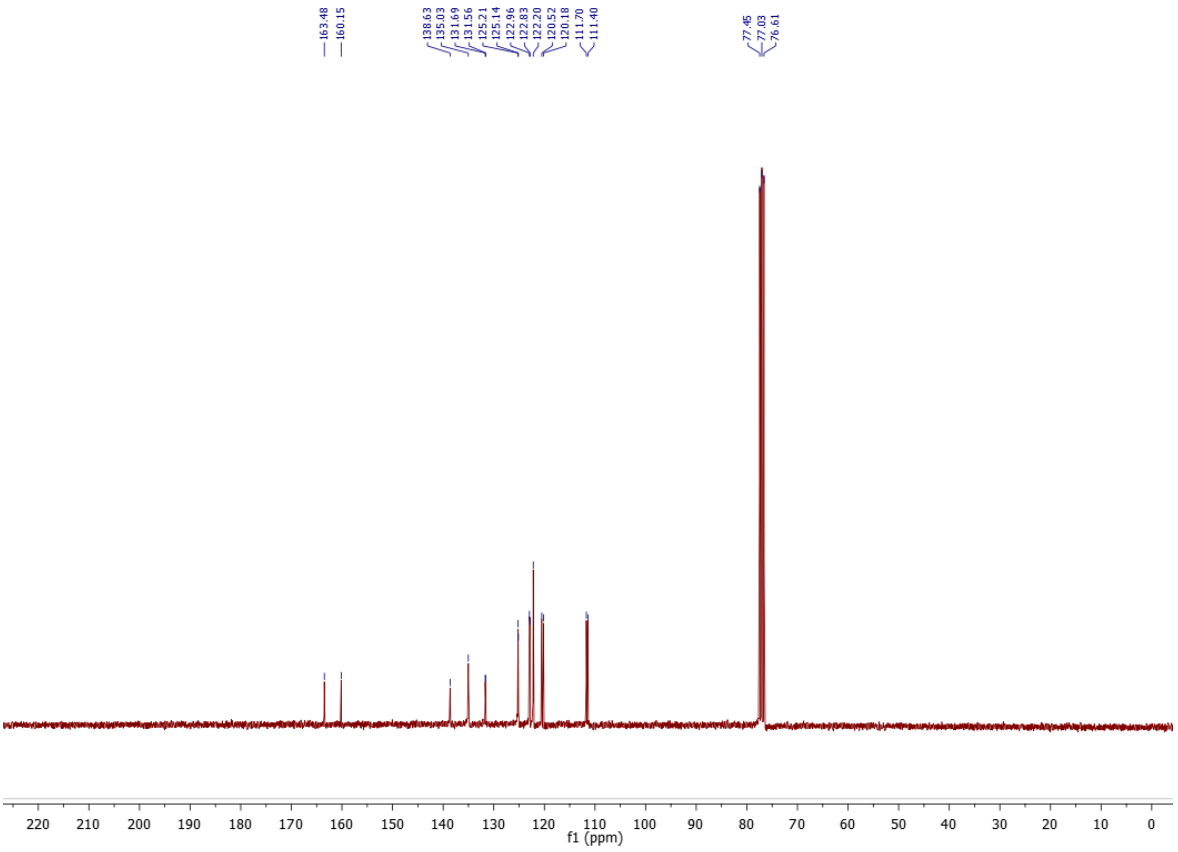


6-Fluoroquinoline-1-oxide (4h)

(^{1}H NMR, $CDCl_3$, 300 MHz)



(^{13}C NMR, $CDCl_3$, 75 MHz)



(^{19}F NMR, $CDCl_3$, 282 MHz)

