Single Electron Transfer from Dimsyl Anion in the Alkylation of Phenols

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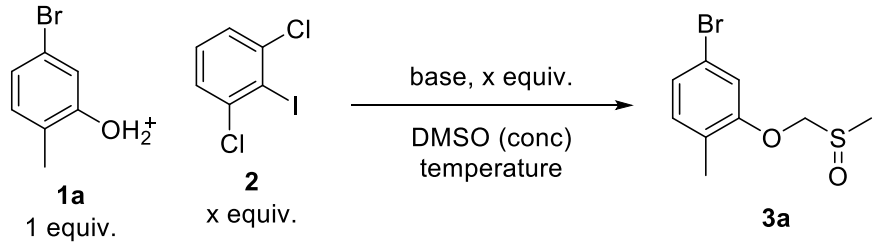
1. Full Optimization

Table S1. Optimization of the reaction conditions



Entry	Iodoarene (equiv)	DMSO conc. (M)	Base (equiv)	Temp (°C)	t (h)	conversion of sm	% yield
1	2 (1.1)	0.1	K_2CO_3 (2.2)	135	16	92	67 (58[i])
2	2 (1.1)	0.1	K_2CO_3 (2.2)	160	16	100	54
3	2 (1.1)	0.1	K_2CO_3 (2.2)	110	16	100	37
4	2 (1.1)	0.1	K_2CO_3 (2.2)	70	16	38	<5
5	2 (1.1)	0.1	K_2CO_3 (2.2)	135	66	100	57
6	2 (1.1)	0.1	K_2CO_3 (2.2)	r.t.	32	100	0
7	2 (1.1)	0.1	none	135	16	degradation	0
8	2 (1.1)	0.1	Na_2CO_3 (2.2)	135	16	100	trace
9	2 (1.1)	0.1	Cs_2CO_3 (2.2)	135	16	100	54
10	2 (1.1)	0.1	Cs_2CO_3 (2.2)	70	16	70	32
11	2 (1.1)	0.1	K_2CO_3 (1.1)	135	16	100	79
12	2 (1.1)	0.1	K_2CO_3 (3.3)	135	16	>95%	31
13	2 (1.1)	0.1	K_2CO_3 (0.5)	135	16	Recovered 80% phenol	0
14	2 (1.5)	0.1	K_2CO_3 (2.2)	135	16	100	96 (70[i])
15	2 (0.5)	0.1	K_2CO_3 (2.2)	135	16	>95	32
16	none	0.1	K_2CO_3 (2.2)	135	16	94	0
17	1-chloro-2-iodobenzene (1.5)	0.1	K_2CO_3 (2.2)	135	16	Degradation of phenol, recovered arene	0

18	Iodobenzene (1.5)	0.1	K_2CO_3 (2.2)	135	16	Degradation of phenol, recovered haloarene	0
19	Trichlorobenzene (1.5)	0.1	K_2CO_3 (2.2)	135	16	Degradation of phenol, recovered haloarene	0
20	2 (1.5)	0.5	K_2CO_3 (2.2)	135	16	100	26
21	2 (1.5)	0.2	K_2CO_3 (2.2)	135	16	100	0
22	2 (1.5)	0.05	K_2CO_3 (2.2)	135	16	100	84
23	2 (1.5)	0.025	K_2CO_3 (2.2)	135	16	100	62
24	2 (1.1)	0.1	K_2CO_3 (2.2)	135	6	84	30
25	2 (1.5)	0.1	KO*t*Bu (3)	135	16	decomposition	6
26	2 (1.5)	0.1	KO*t*Bu (0.75)	135	16	100	35
27[a]	2 (1.5)	0.1	K_2CO_3 (2.2)	135	16	degradation	0
28[b]	2 (1.5)	0.1	K_2CO_3 (2.2)	135	16	100	64
29[c]	2 (1.5)	0.1	K_2CO_3 (2.2)	135	16	100	44
30[d]	2 (1.5)	0.1	K_2CO_3 (2.2)	135	16	100	79
31[e]	2 (1.5)	0.1	K_2CO_3 (2.2)	135	16	100	60
32[f]	2 (1.5)	0.1	K_2CO_3 (2.2)	r.t.	16	Recovered 22% phenol, 88% haloarene	0
33[g]	2 (1.5)	0.1	K_2CO_3 (2.2)	r.t.	16	Recovered 25% phenol	0
34[h]	2 (1.5)	0.1	K_2CO_3 (1.1)	135	16	Recovered 11% BHT	trace

All yields are by comparison to an NMR standard (phenyltrimethylsilane) unless otherwise noted.

[i] = isolated yield. [a] reaction run with 2 equivalents of TEMPO. [b] solvent 50:50 toluene:DMSO. [c] reaction degassed and run under Ar atmosphere. [d] reaction run on 0.5g of phenol. [e] reaction run on 1g of phenol. [f] reaction run at r.t. irradiated under blue LED for 16h WITHOUT degassing solvent. [g] reaction run at r.t. irradiated under blue LED for 16h with DEGASSED solvent under Ar. [h] reaction run with 2 equivalents of BHT.

2. 2,2',6,6'-tetrachloro-1,1'-biphenyl Byproduct

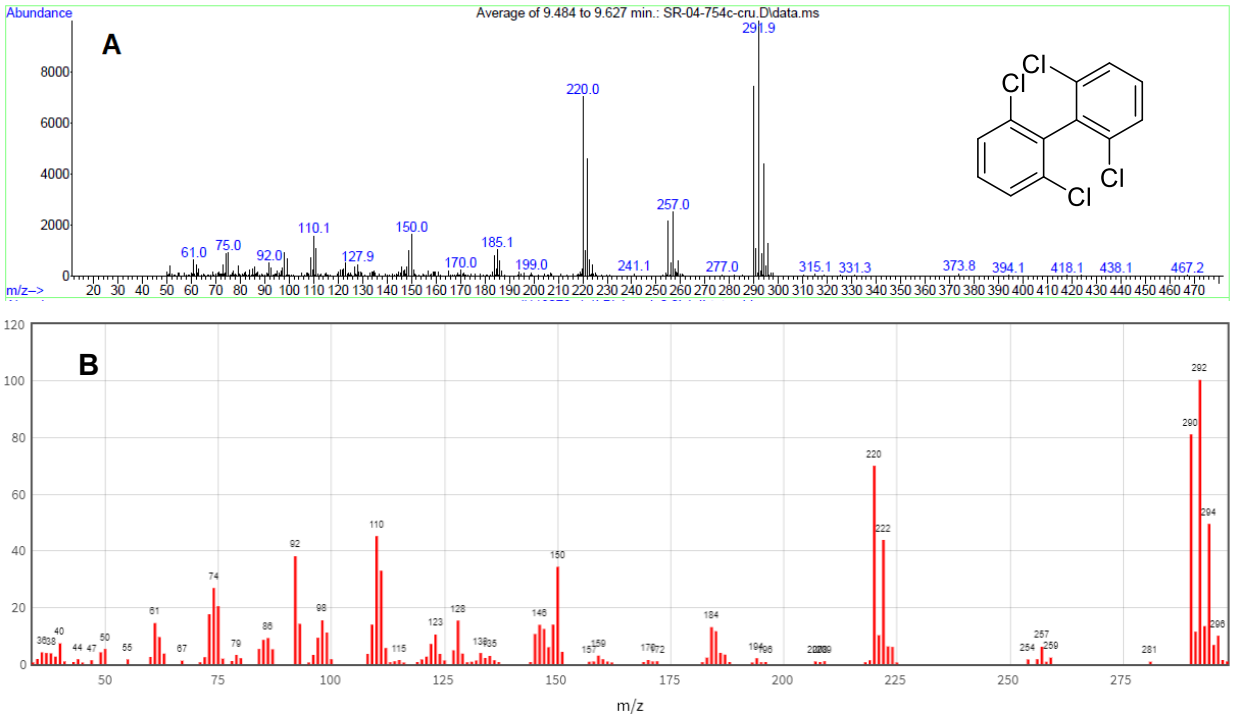


Figure S1. A) Fragmentation pattern for byproduct observed in most of the scope reactions. B) NIST Mass Spectral Database Webbook EI mass spectrum for 2,2',6,6'-tetrachloro-1,1'-biphenyl. Online record can be found at https://webbook.nist.gov/cgi/inchi/InChI%3D1S/C12H6Cl4/c13-7-3-1-4-8(14)11(7)12-9(15)5-2-6-10(12)16/h1-6H.

3. Solvent Screen for Sulfoxide Scope

Table S2.

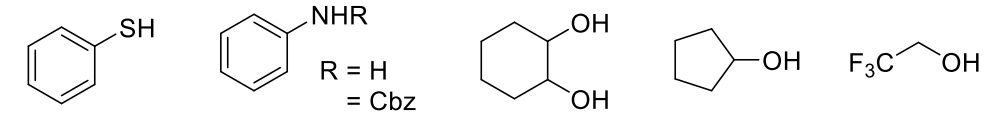
Cosolvent (vol, mL)	Sulfoxide (vol, mL)	Yield (%)[a]
None	Phenyl methyl sulfoxide (3)	<15 [b]
Benzene (1.5)	Dimethyl sulfoxide (1.5)	65
Benzene (1.5)	Phenyl methyl sulfoxide (1.5)	<15
Toluene (1.5)	Phenyl methyl sulfoxide (1.5)	Trace
o-xylene (1.5)	Phenyl methyl sulfoxide (1.5)	Trace
Mesitylene (1.5)	Phenyl methyl sulfoxide (1.5)	Trace
None	Diethyl sulfoxide (3)	Complex mixture
Benzene (1.5)	Diethyl sulfoxide (1.5)	Trace

[a] NMR Yield with phenyltrimethylsilane.

[b] Product inseparable from phenyl methyl sulfoxide starting material

4. Unsuccessful Substrates

Other Nucleophiles:



Phenols:

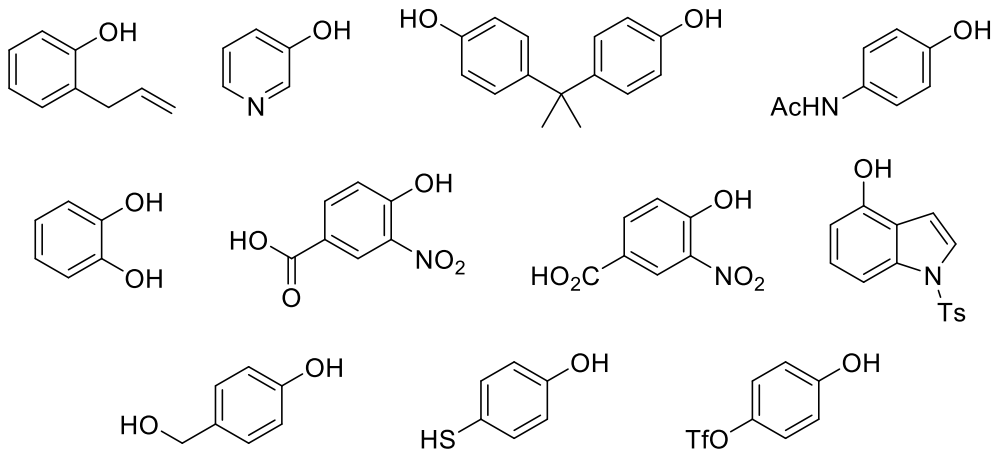


Figure S2. Substrates attempted under standard reaction conditions that resulted in <15% of product or recovery/degradation of starting material.

5. Isomerization of 2-propenylphenol Under Standard Conditions

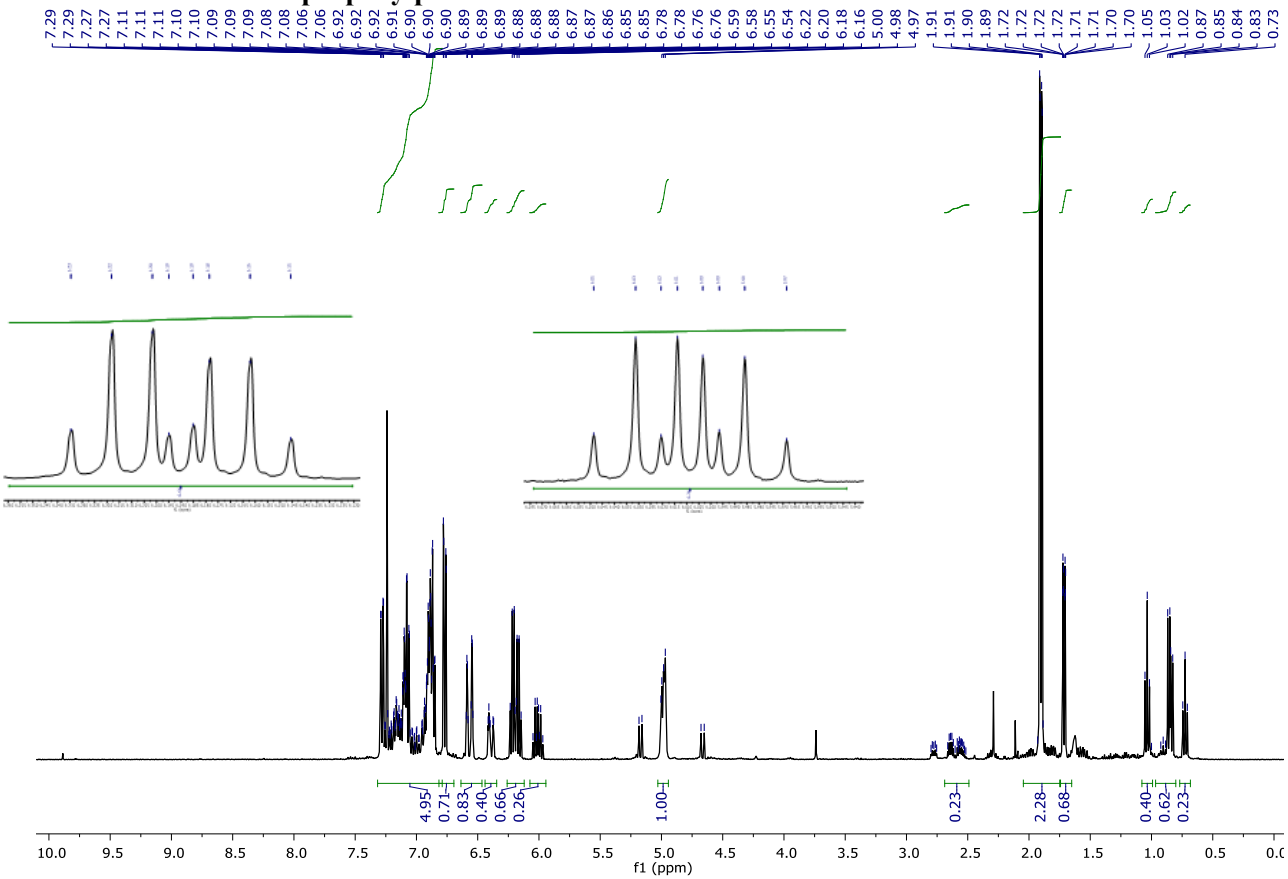


Figure S3. ^{1}H NMR spectrum of starting material **1q.**

The insert regions within the above spectrum detail the peaks used to calculate ratio of *E:Z* olefins in the parent phenol substrate. These peaks represent the same proton in the *E* and *Z* configurations (left and right respectively). Raw integration of each region was expressed as a percentage of the total giving a ratio of 72:28 *E:Z*.

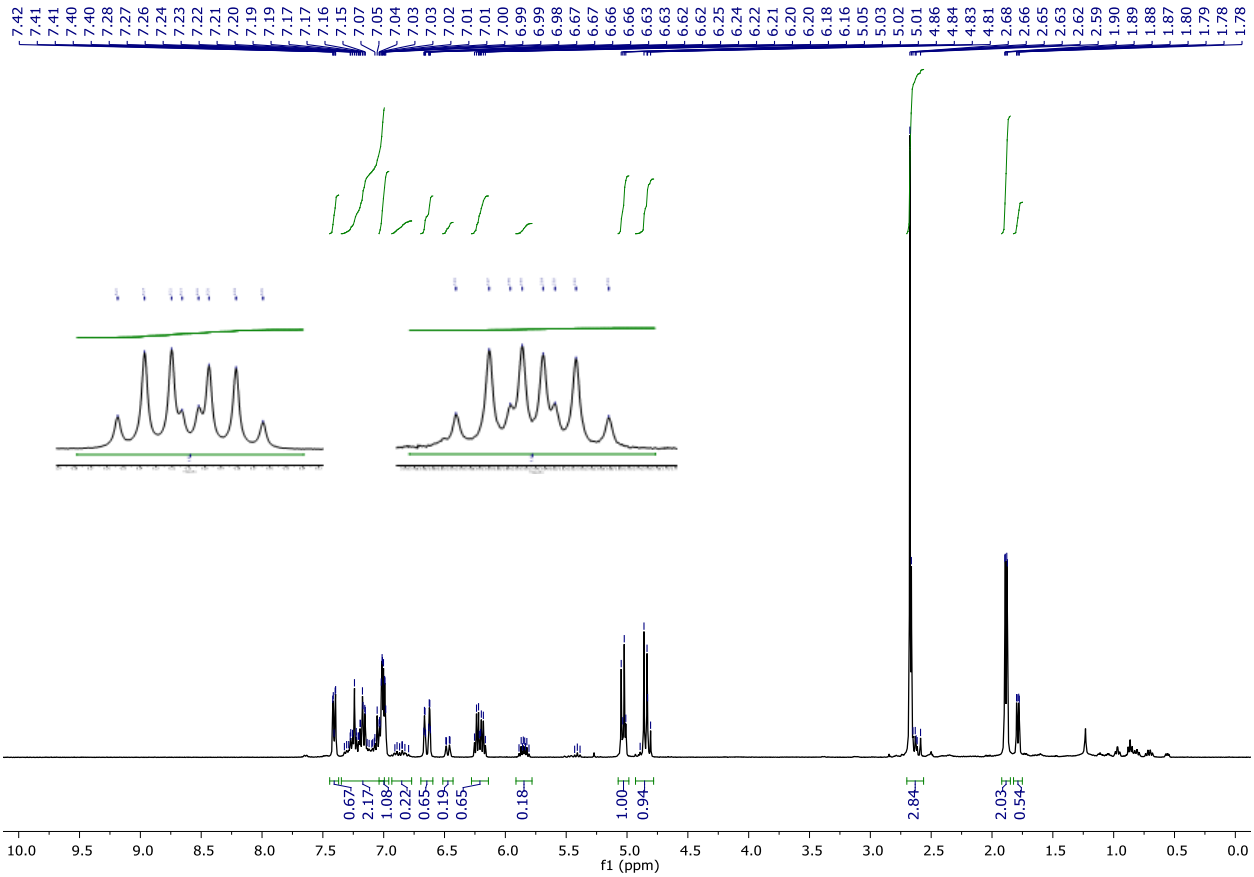


Figure S4. ^{1}H NMR spectrum of product **3q**.

The insert regions within the above spectrum detail the peaks used to calculate ratio of *E:Z* olefins in the alkylated phenol product **3q**. These peaks represent the same proton in the *E* and *Z* configurations (left and right respectively). Raw integration of each region was expressed as a percentage of the total giving a ratio of 78:22 *E:Z*.

6. Kinetic Isotope Effect (KIE) Competition Experiments

Deuterium-labeling experiments were performed as per GP1 with either pure DMSO-d6 or a 1:1 mixture of DMSO:DMSO-d6 as solvent. KIE data was obtained by analyzing the ratio between deuterated and proteated products following isolation of product (see ^{1}H NMR spectrum below). Most notably, it was observed that the deuterium incorporation in the reaction with 1:1 DMSO:DMSO-d6 was asymmetrical with respect to the α-sulfoxide positions (10% and 24% deuterium incorporation at the etheric position, and 32% deuterium incorporation at the terminal position). This data suggests that any KIE's obtained with this method will be unreliable due to facile deuterium-protium exchange at the α-sulfoxide positions.

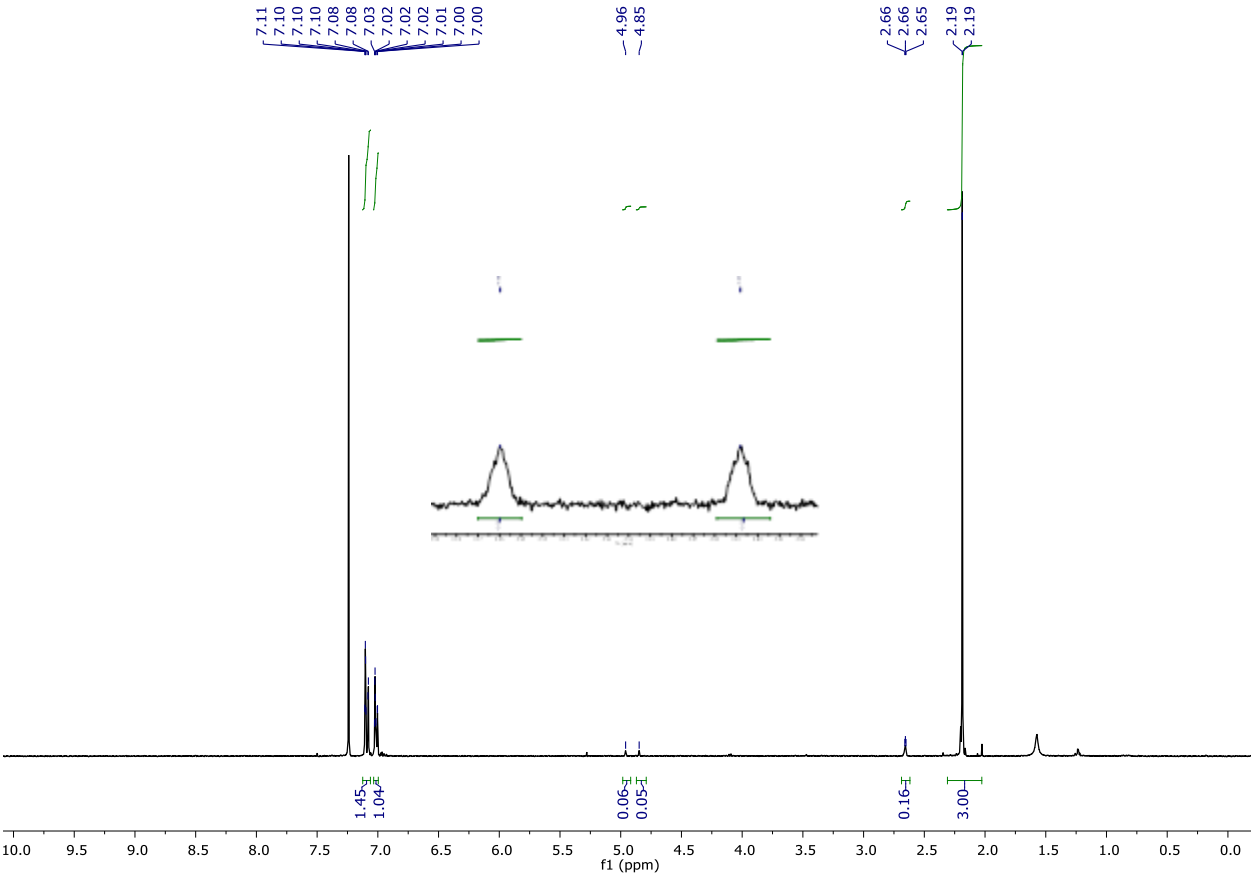


Figure S5. ^{1}H NMR spectrum of product **d-3a**

The insert region within the above spectrum details two peaks used to calculate ratio of etheric α-sulfoxide deuterium incorporation in product **d-3a**. The singlet at 2.66 was also used to calculate terminal α-sulfoxide deuterium incorporation. Solvent used for this experiment was 100% DMSO-d6.

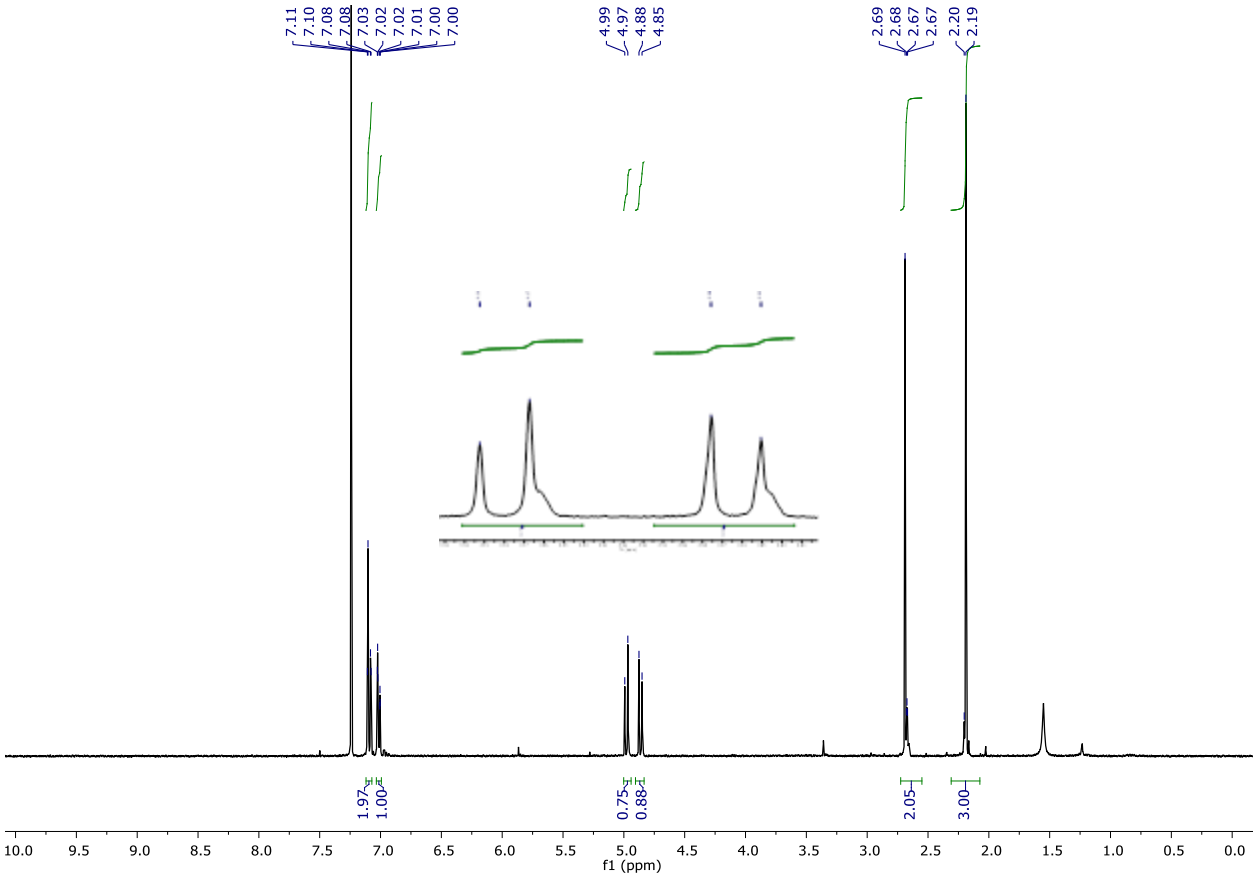
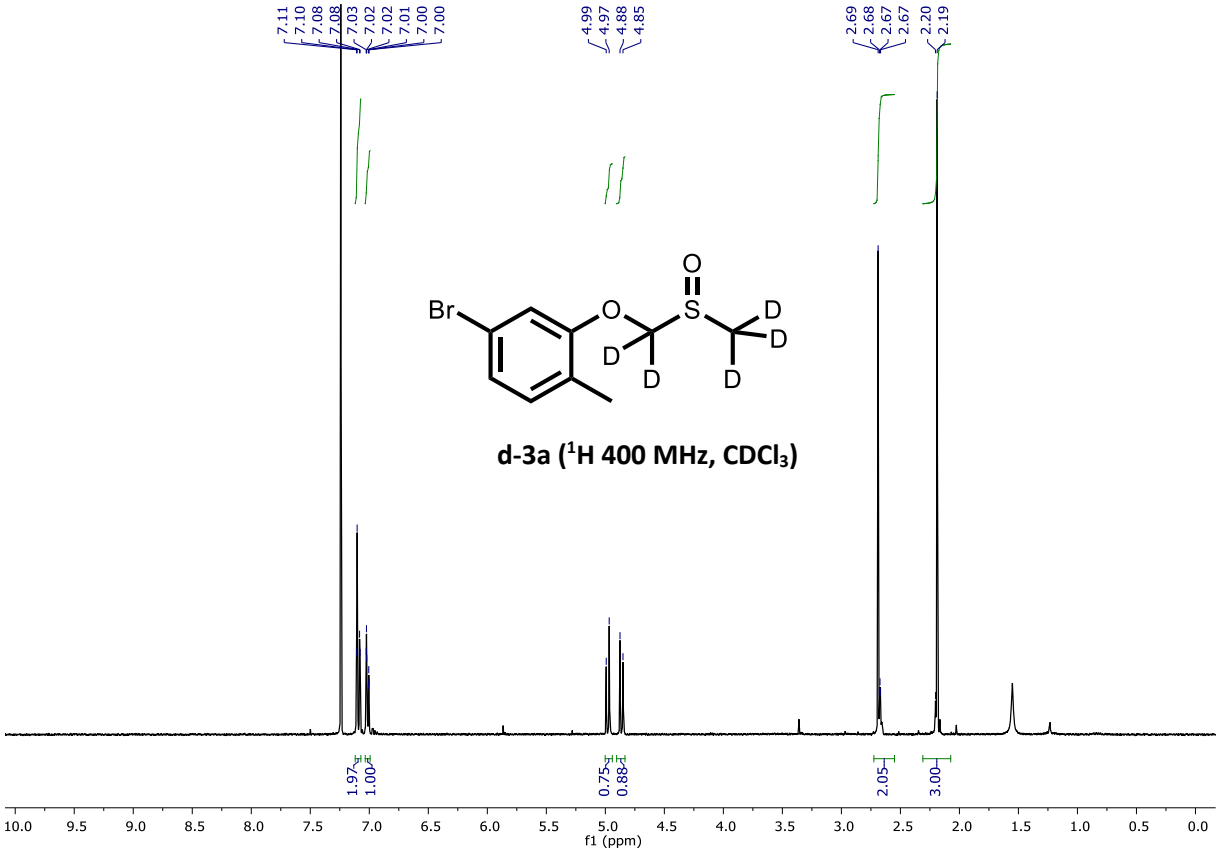


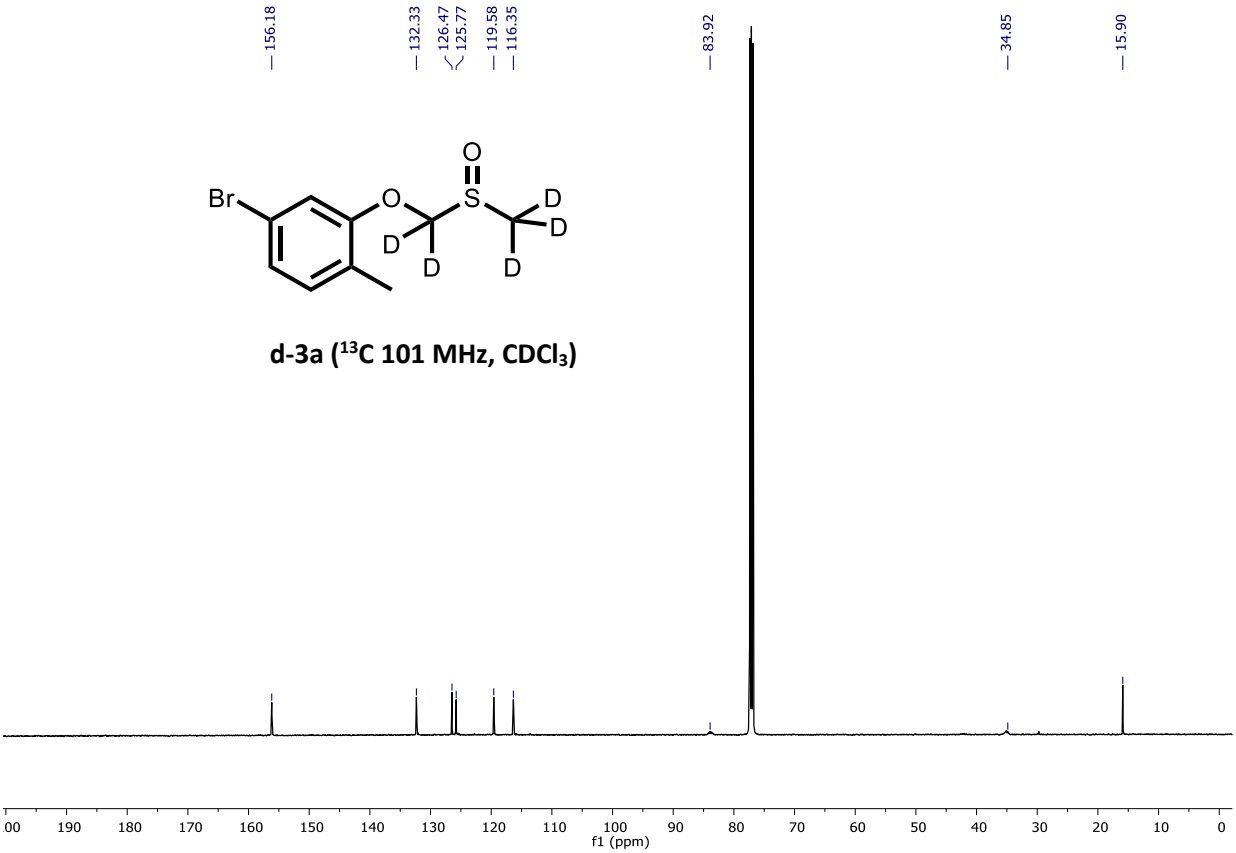
Figure S6. ^{1}H NMR spectrum of mixed deuterated product **3a** and **d-3a**

The insert region within the above spectrum details two peaks used to calculate ratio of etheric α-sulfoxide deuterium incorporation in product **d-3a**. The large singlet at 2.66 was also used to calculate terminal α-sulfoxide deuterium incorporation. Solvent used for this experiment was 1:1 DMSO:DMSO-d6.

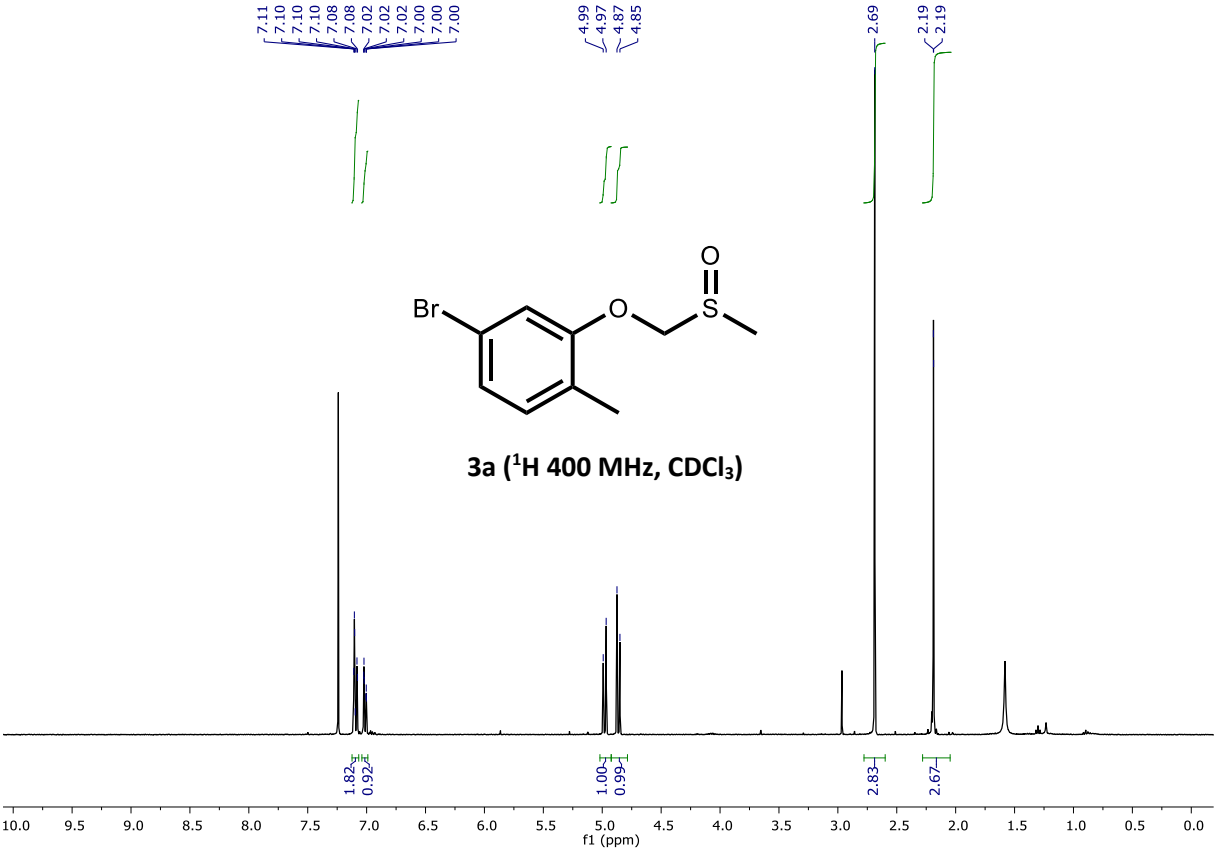
7. NMR Spectra



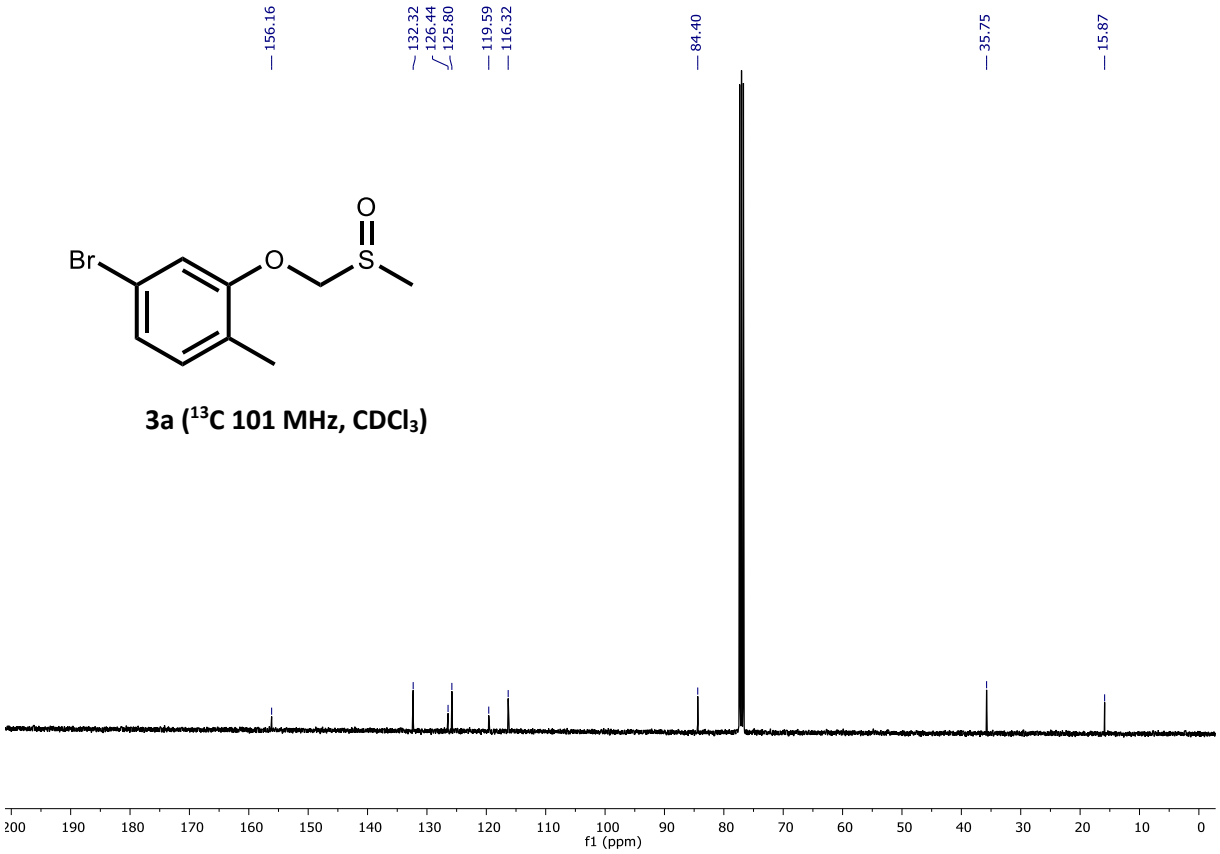
d-3a (^{1}H 400 MHz, $CDCl_3$)



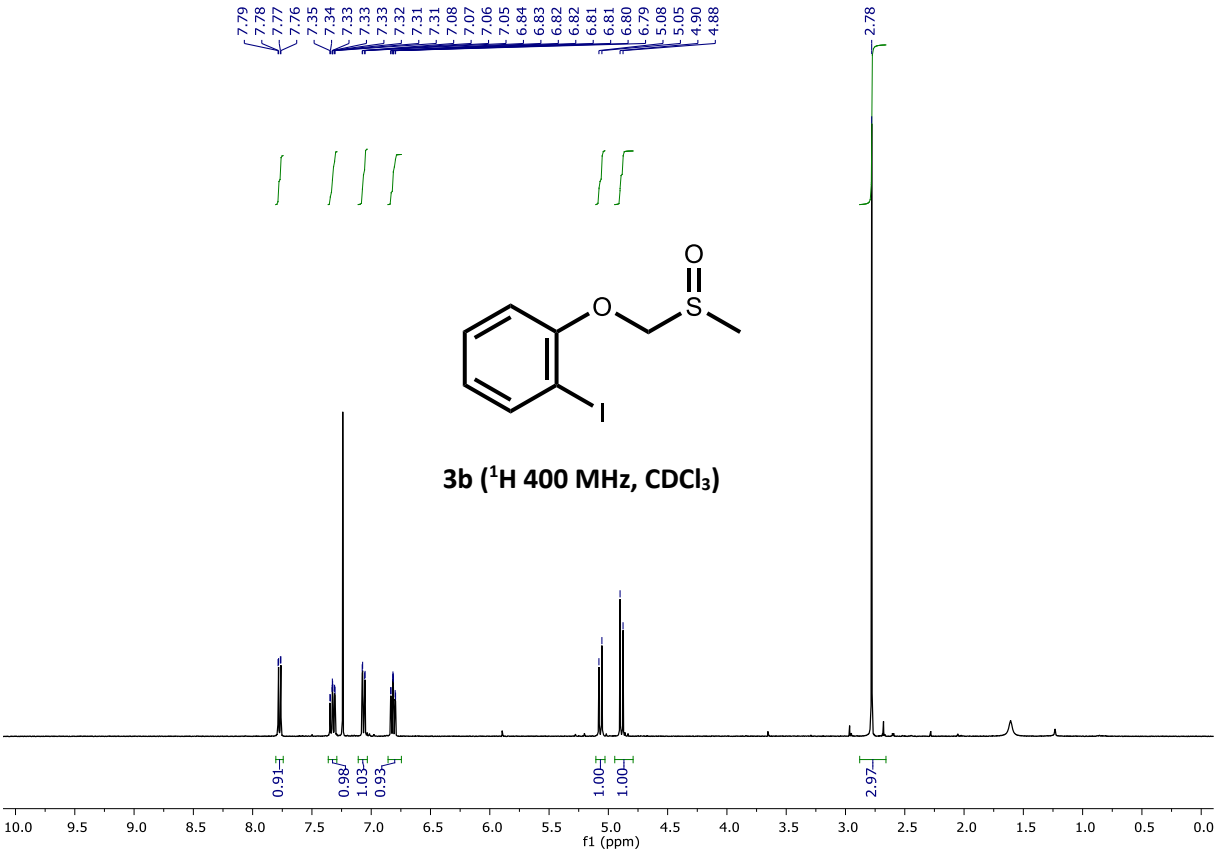
d-3a (^{13}C 101 MHz, $CDCl_3$)



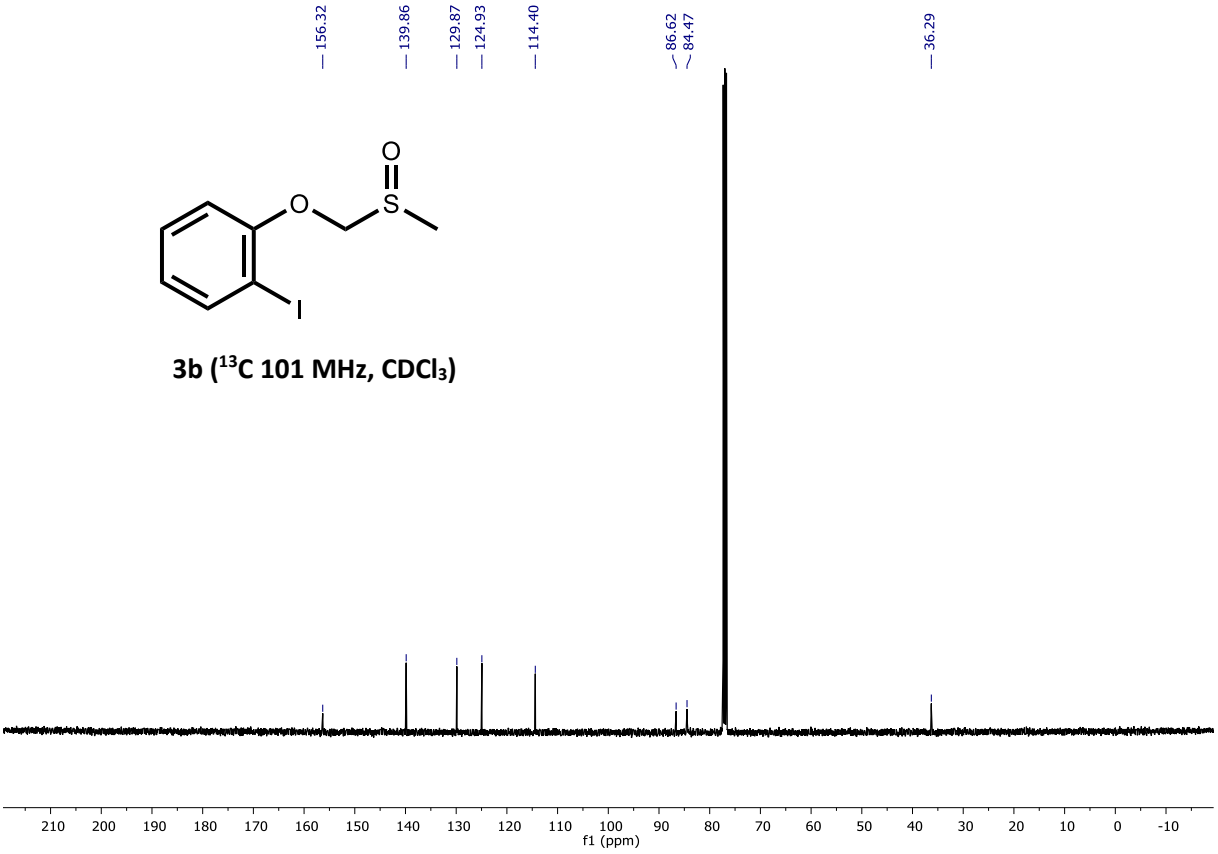
3a (^{1}H 400 MHz, $CDCl_3$)



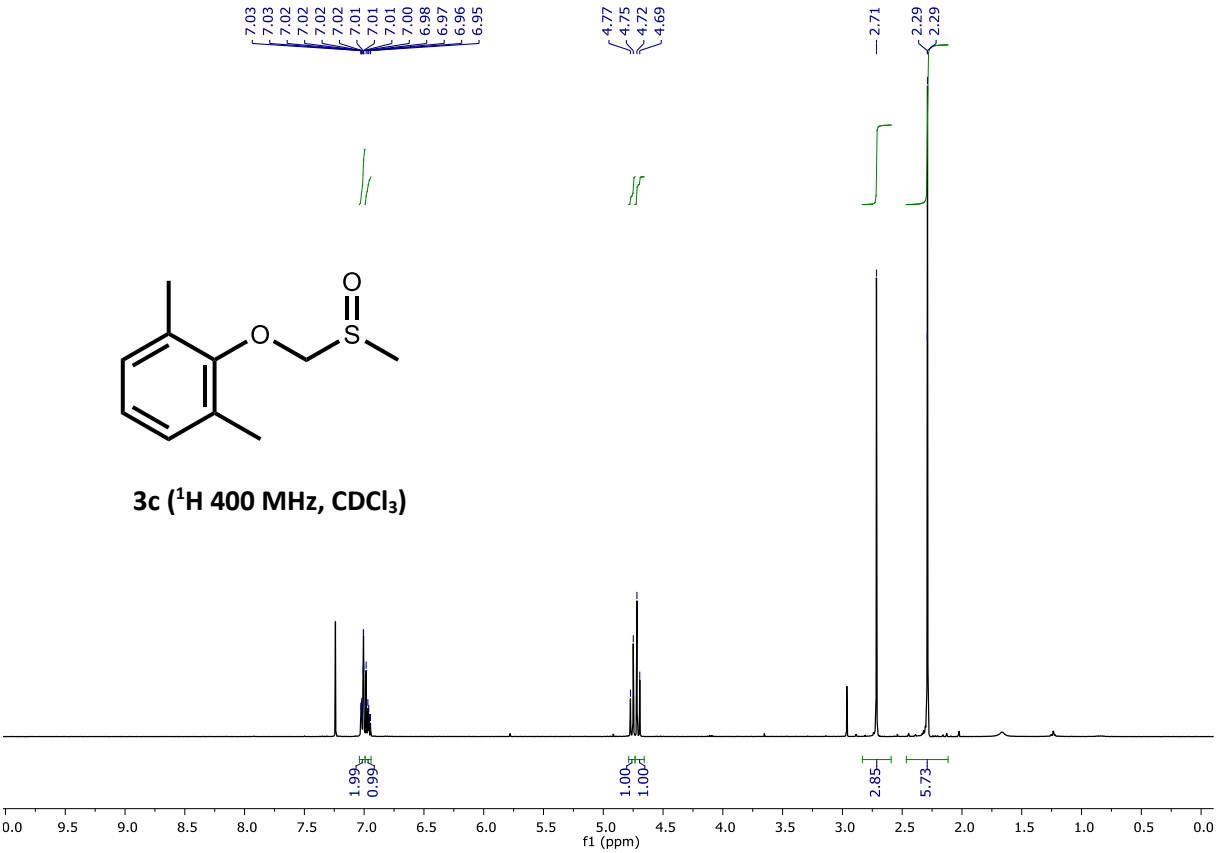
3a (^{13}C 101 MHz, $CDCl_3$)



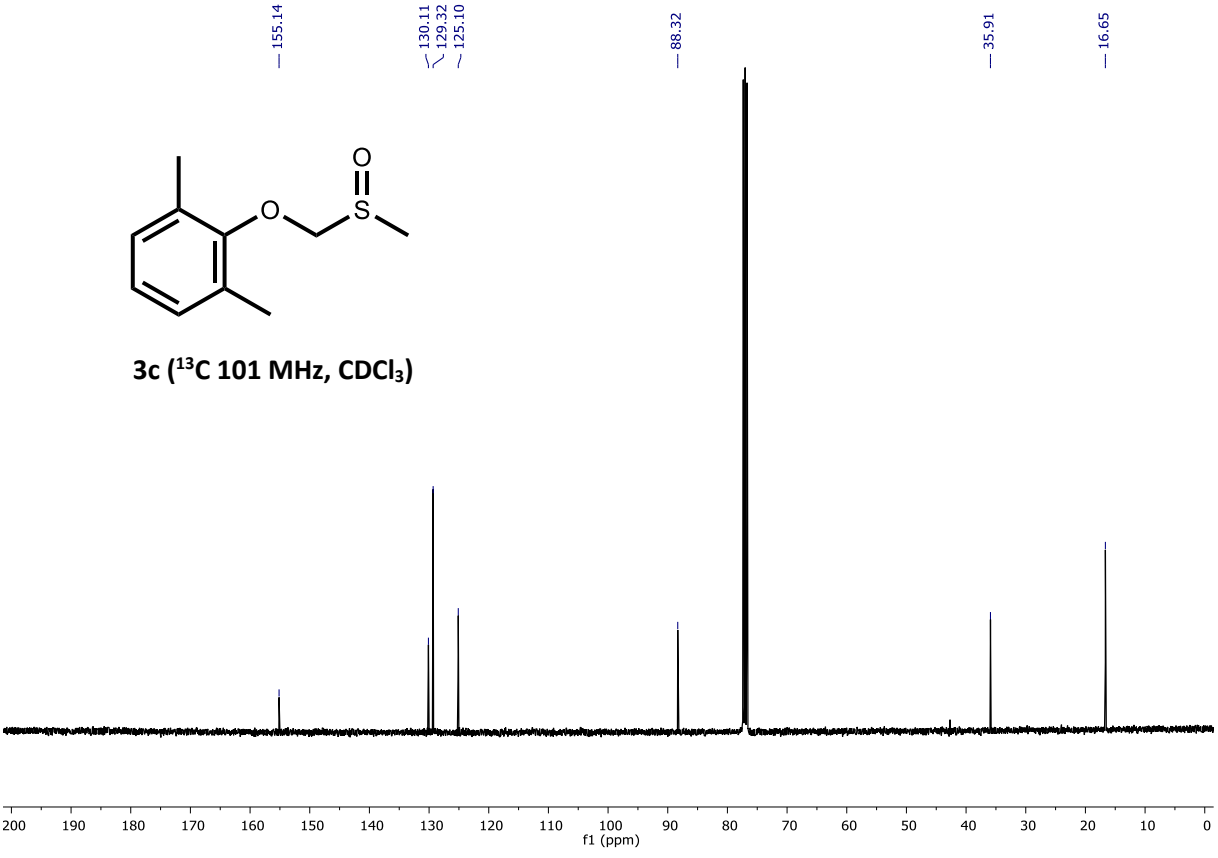
3b (^{1}H 400 MHz, $CDCl_3$)



3b (^{13}C 101 MHz, $CDCl_3$)



3c (^{1}H 400 MHz, $CDCl_3$)



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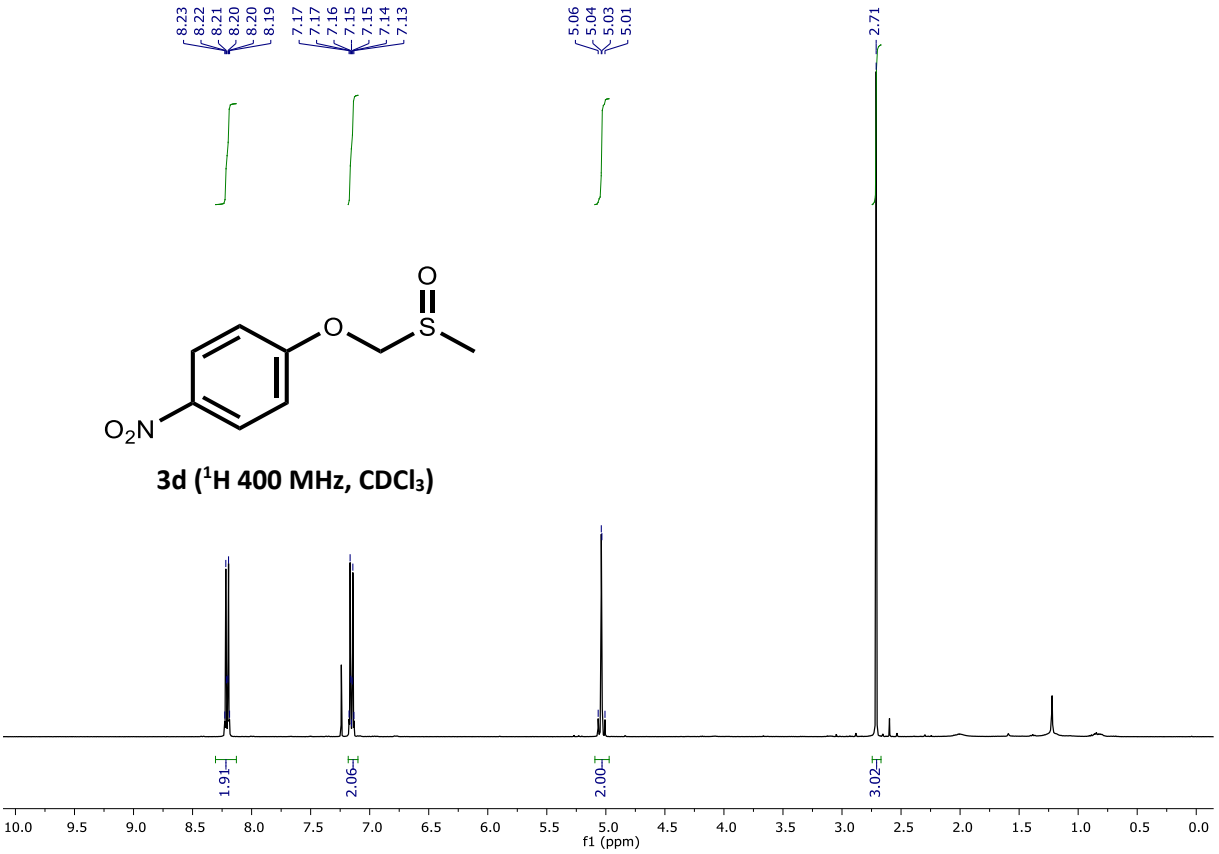

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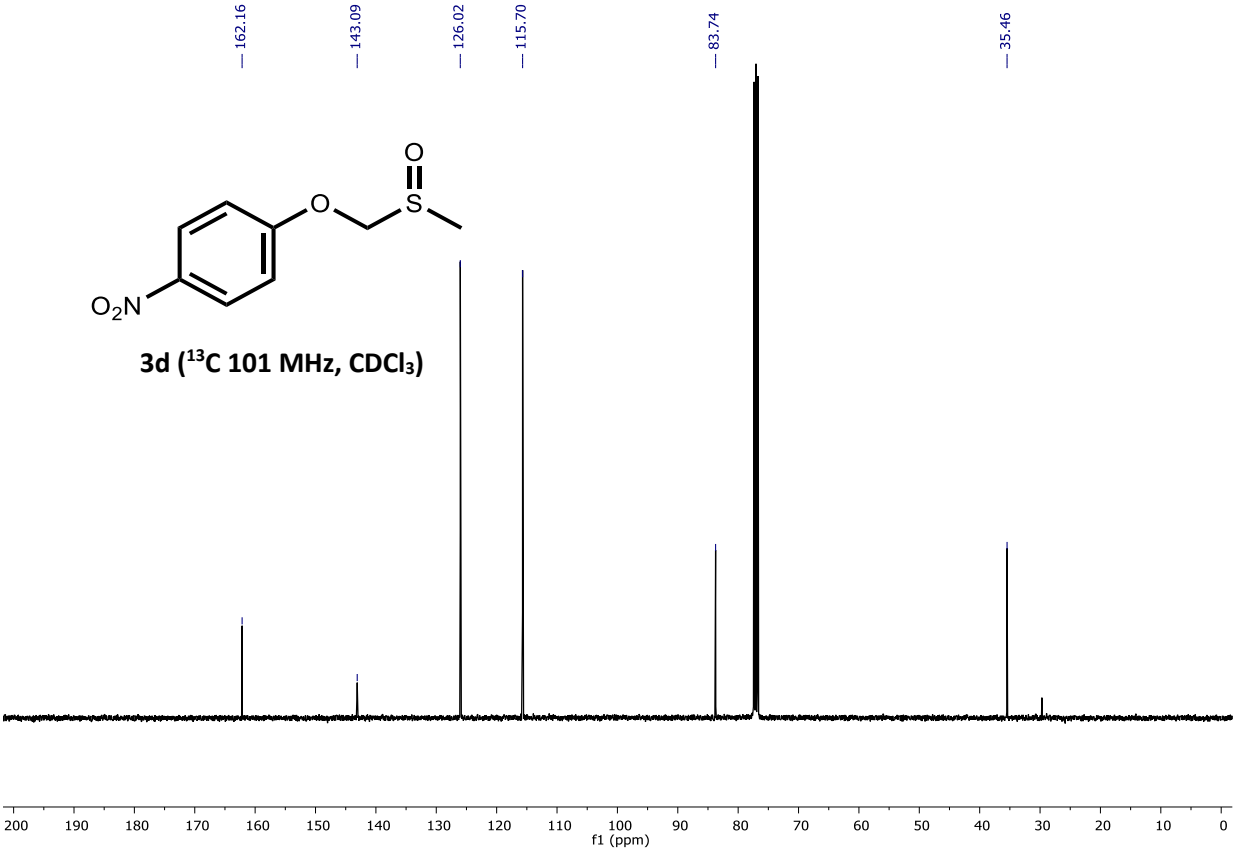

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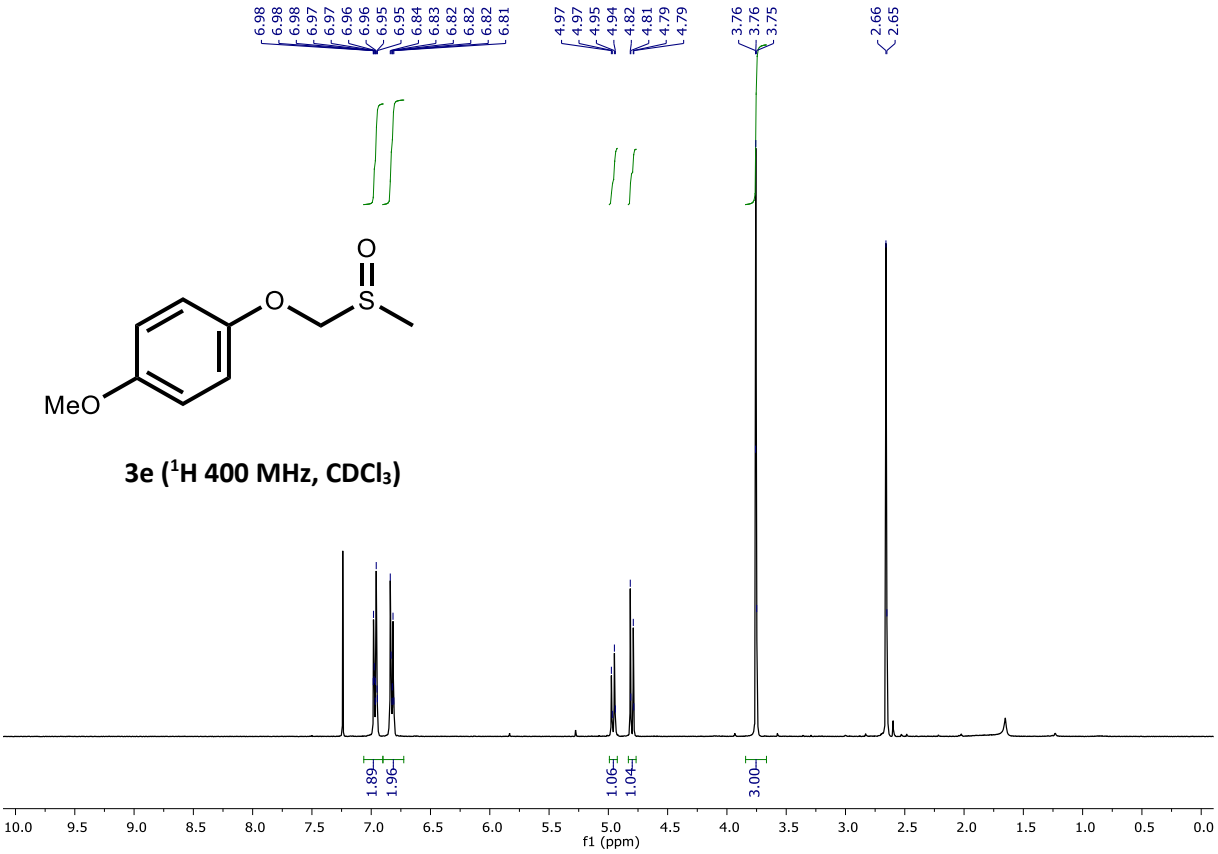

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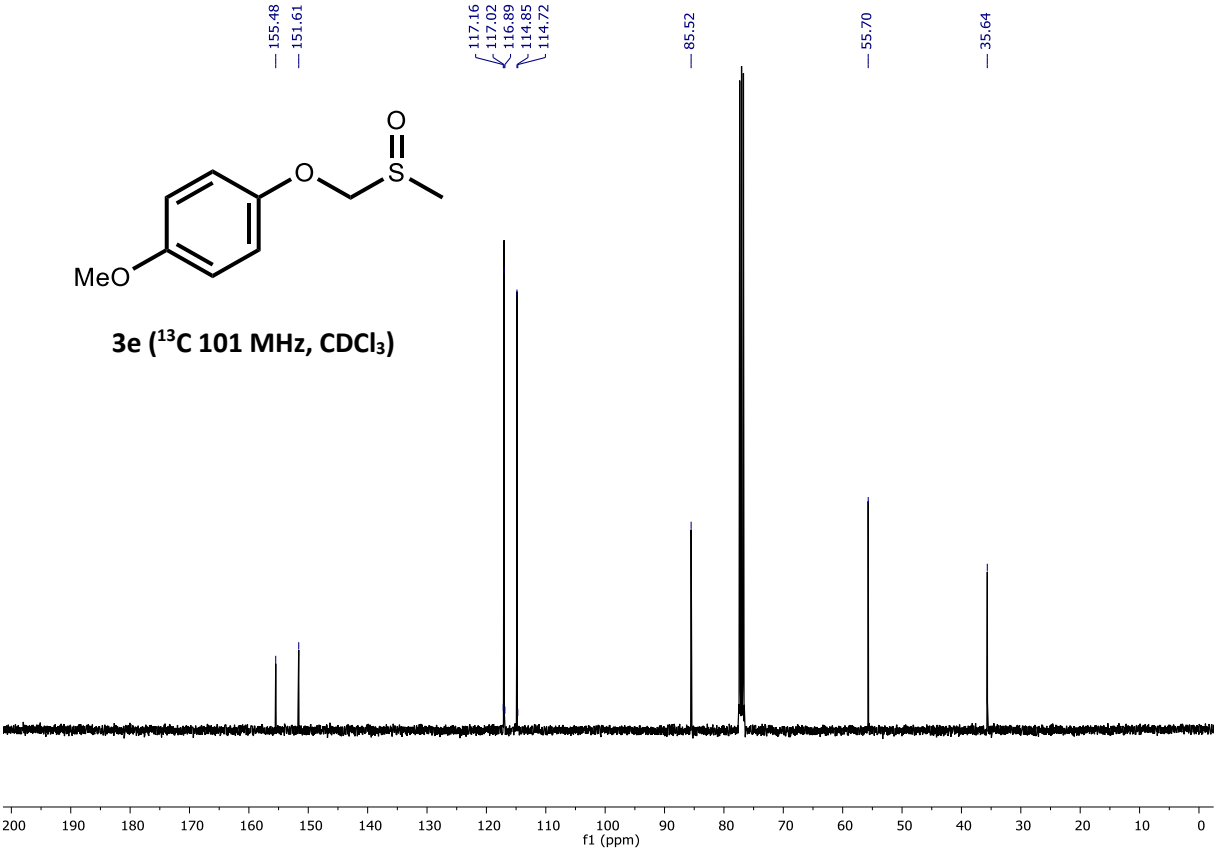

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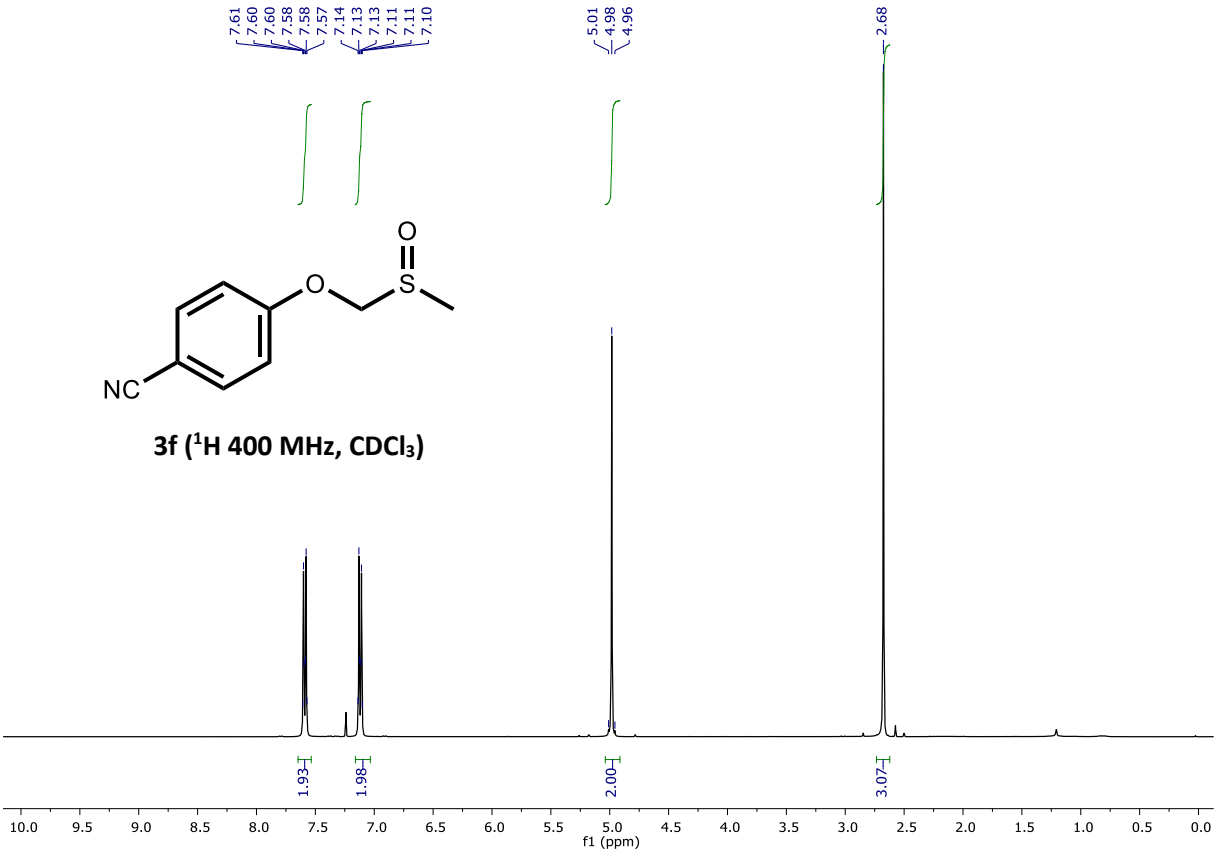

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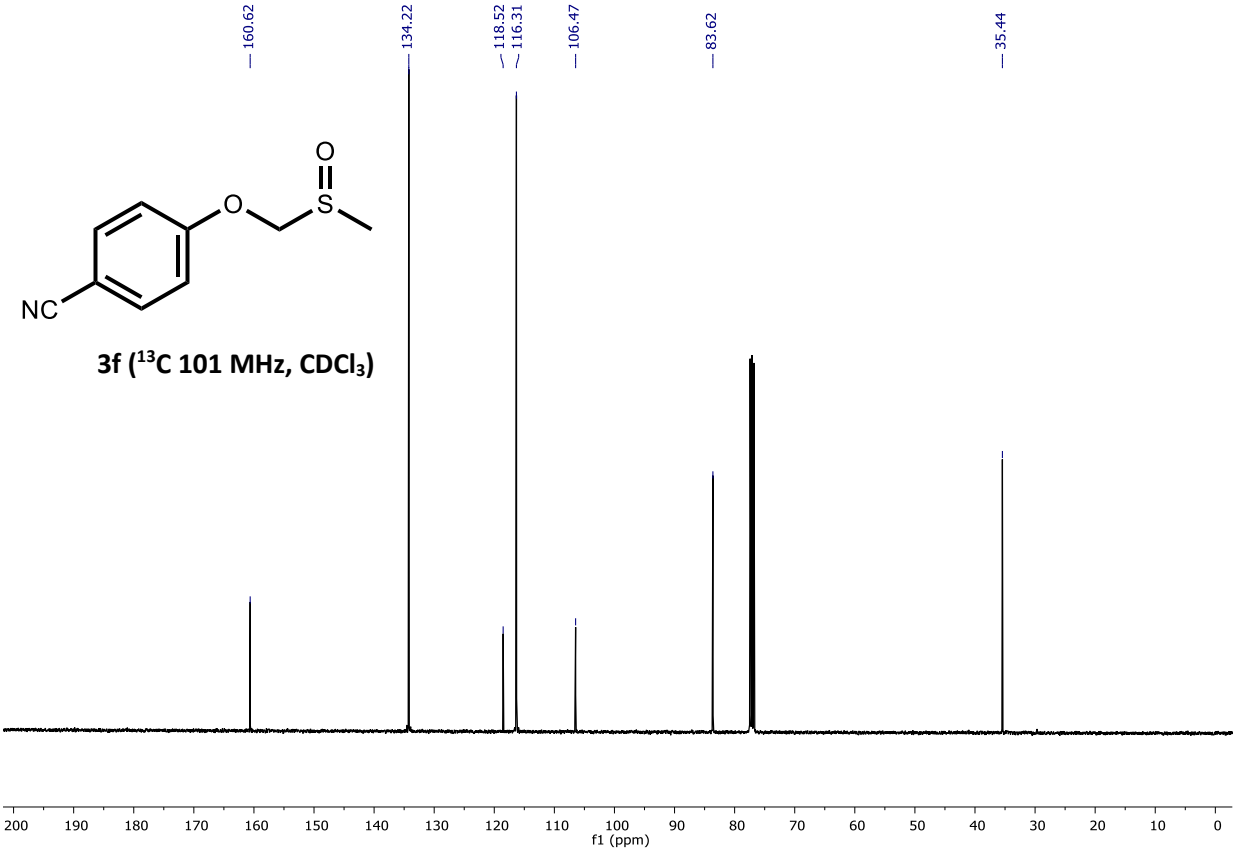

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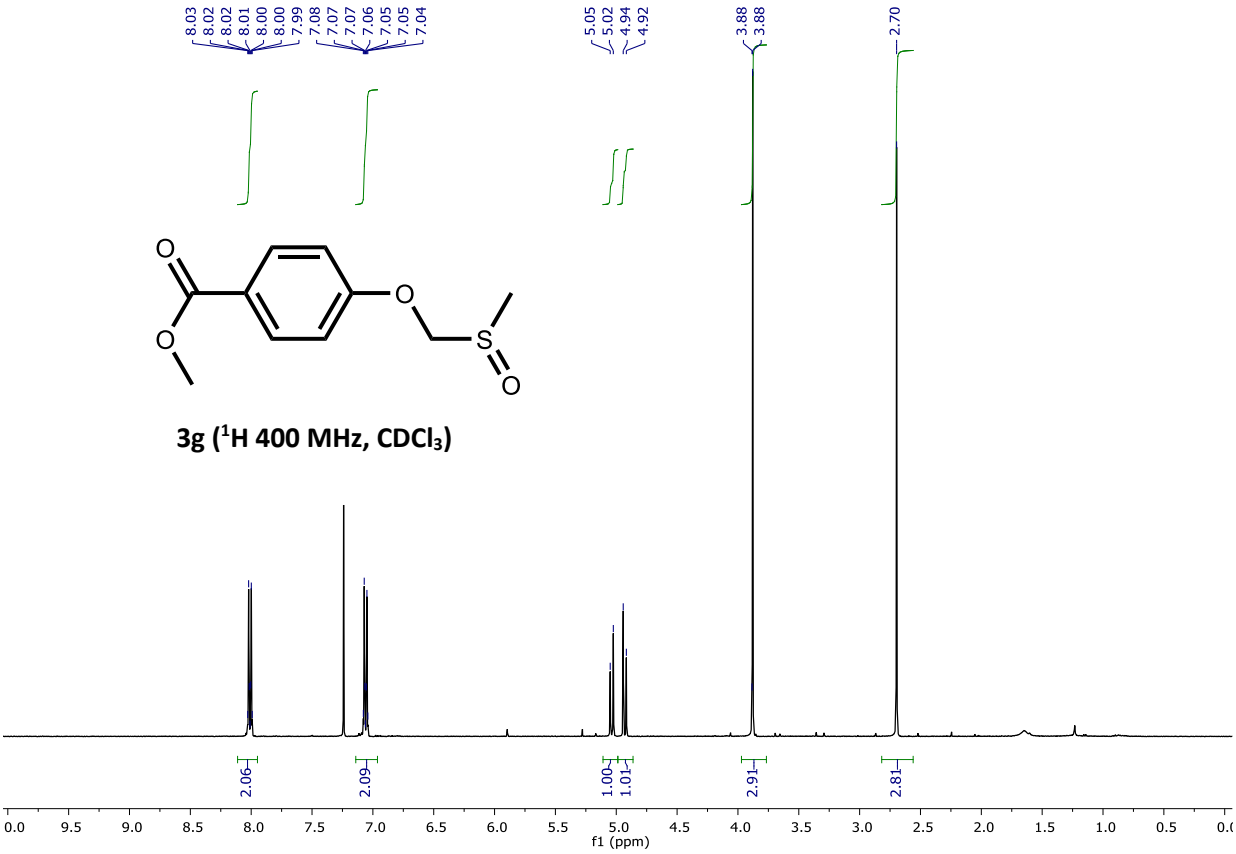

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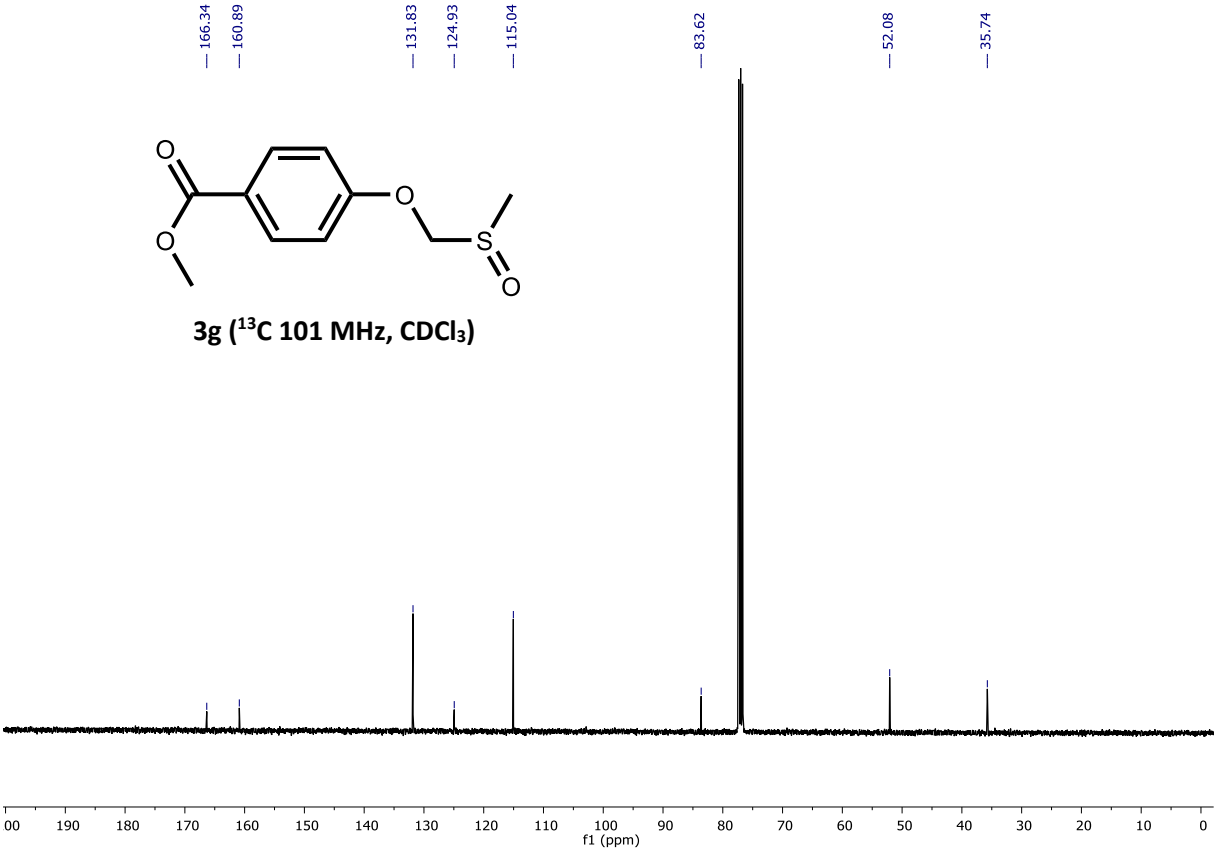

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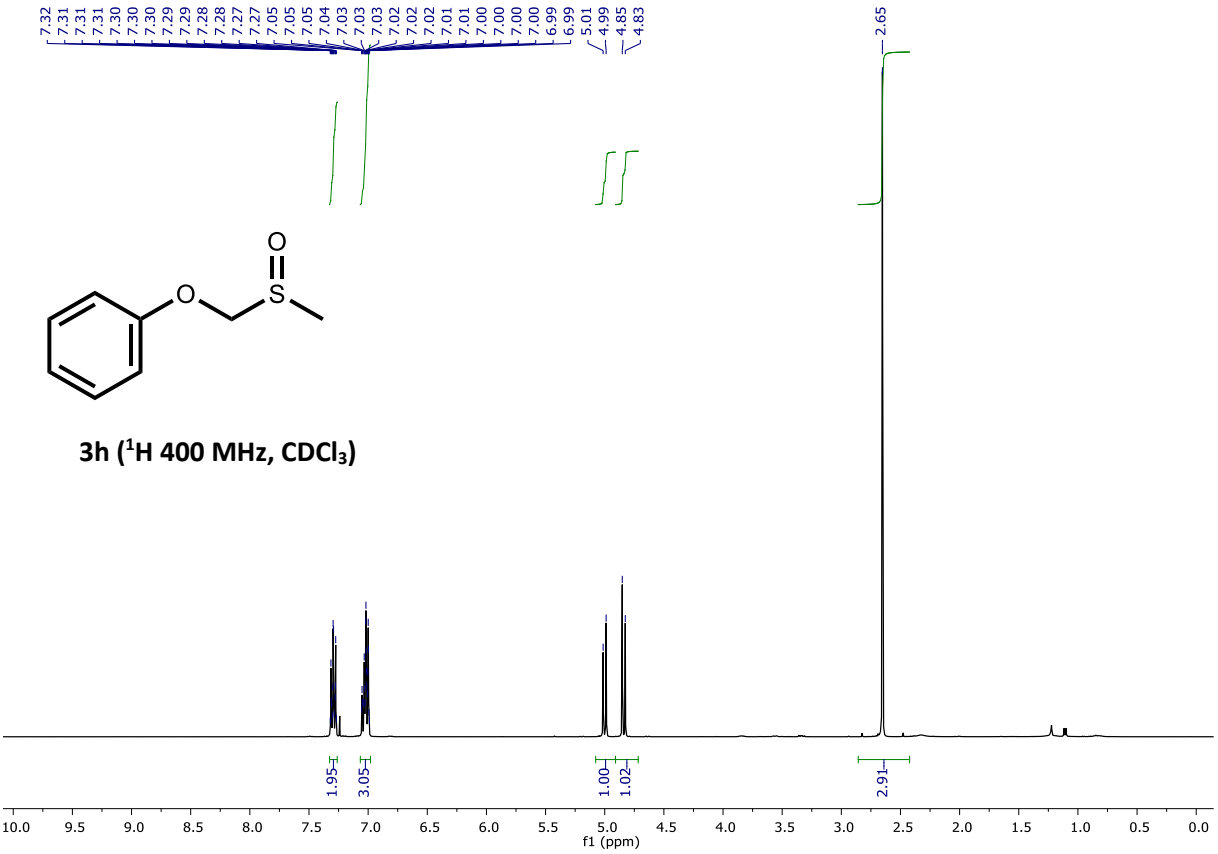

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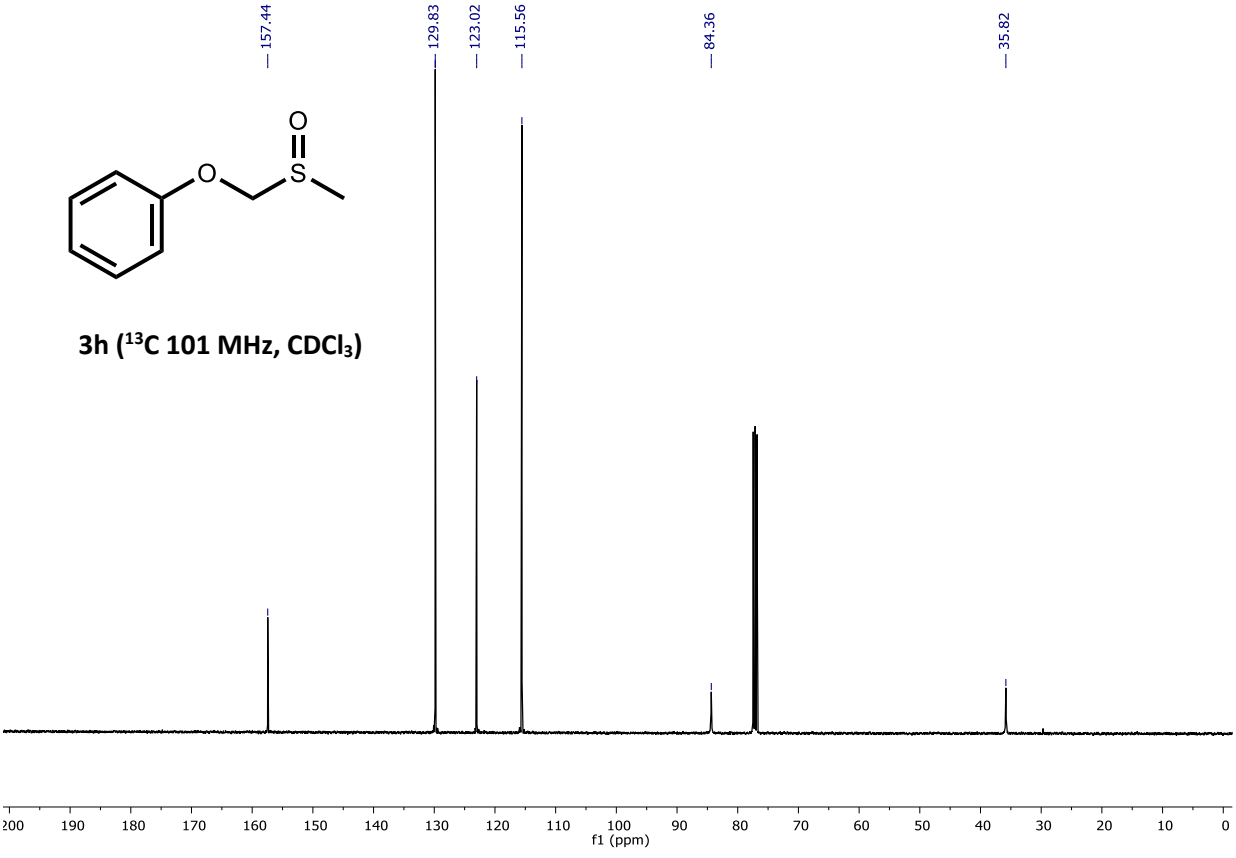

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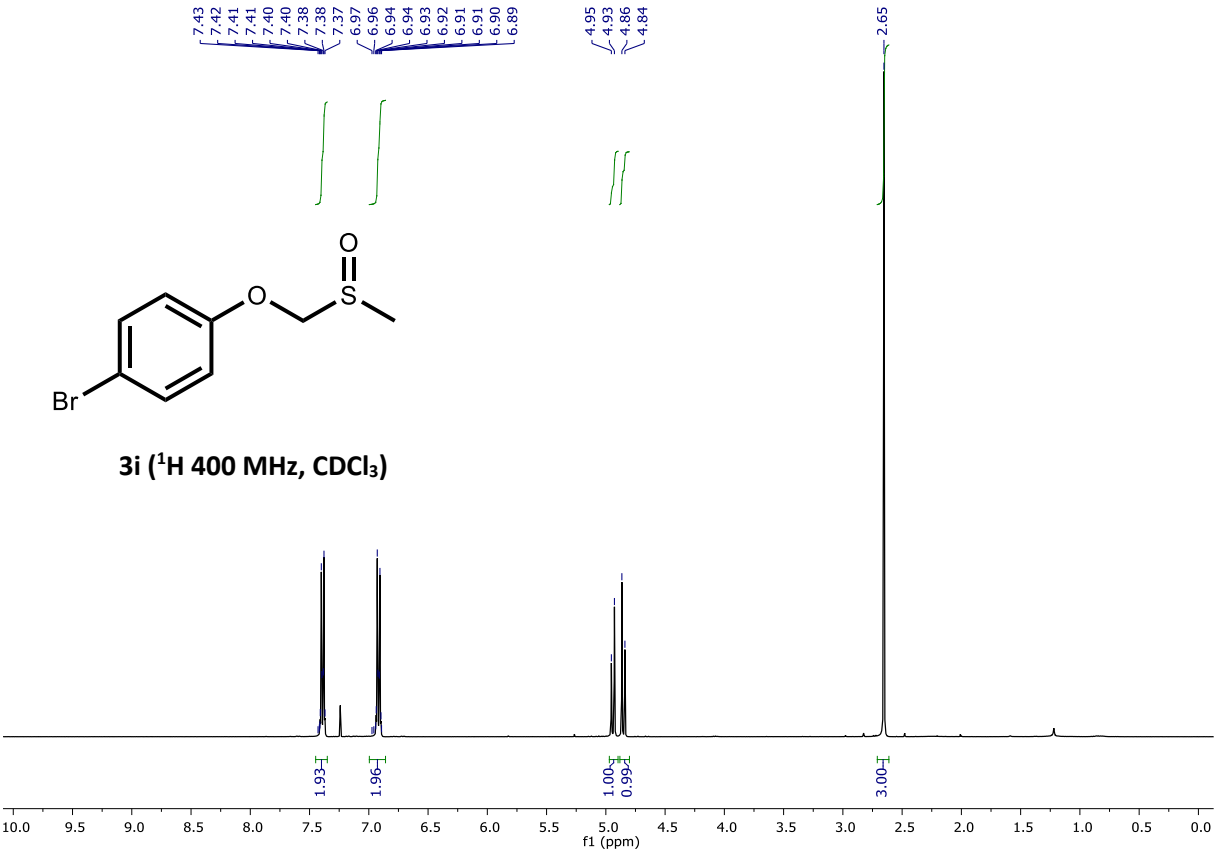

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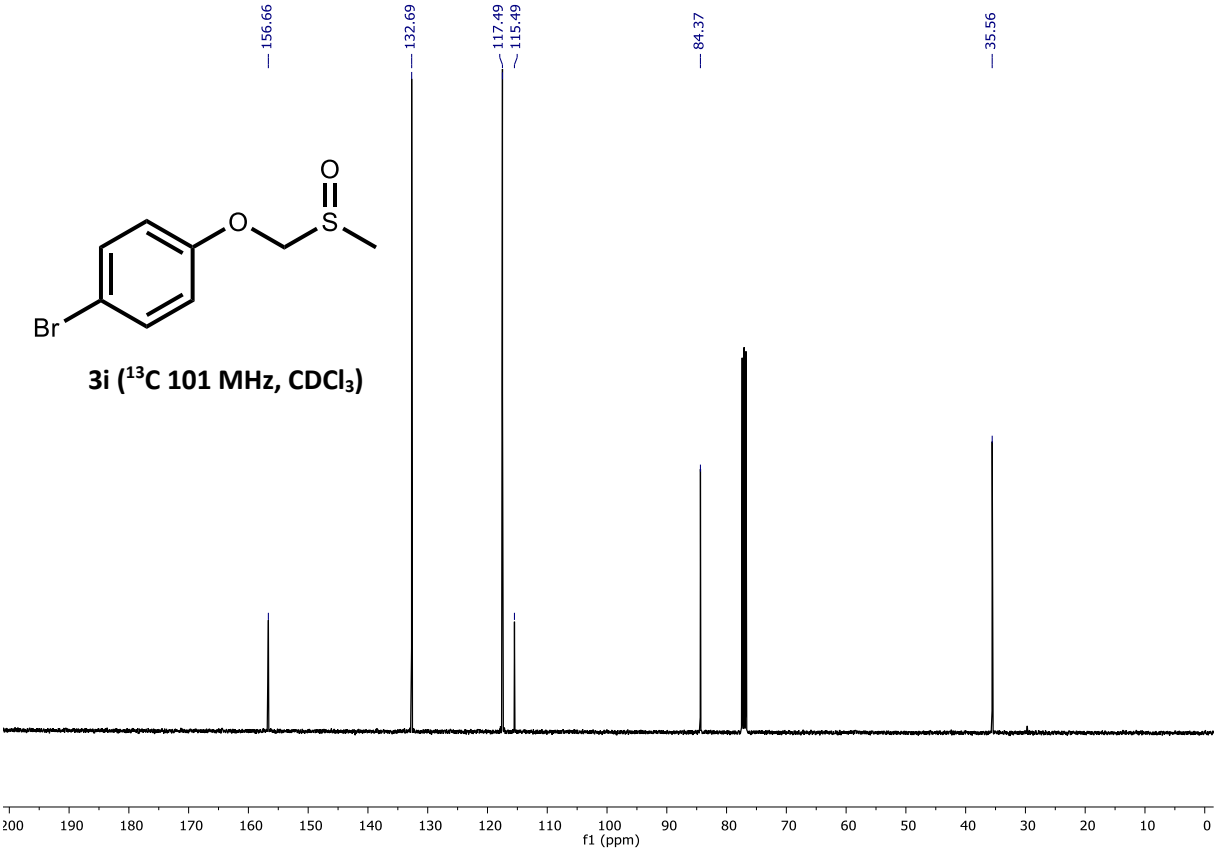

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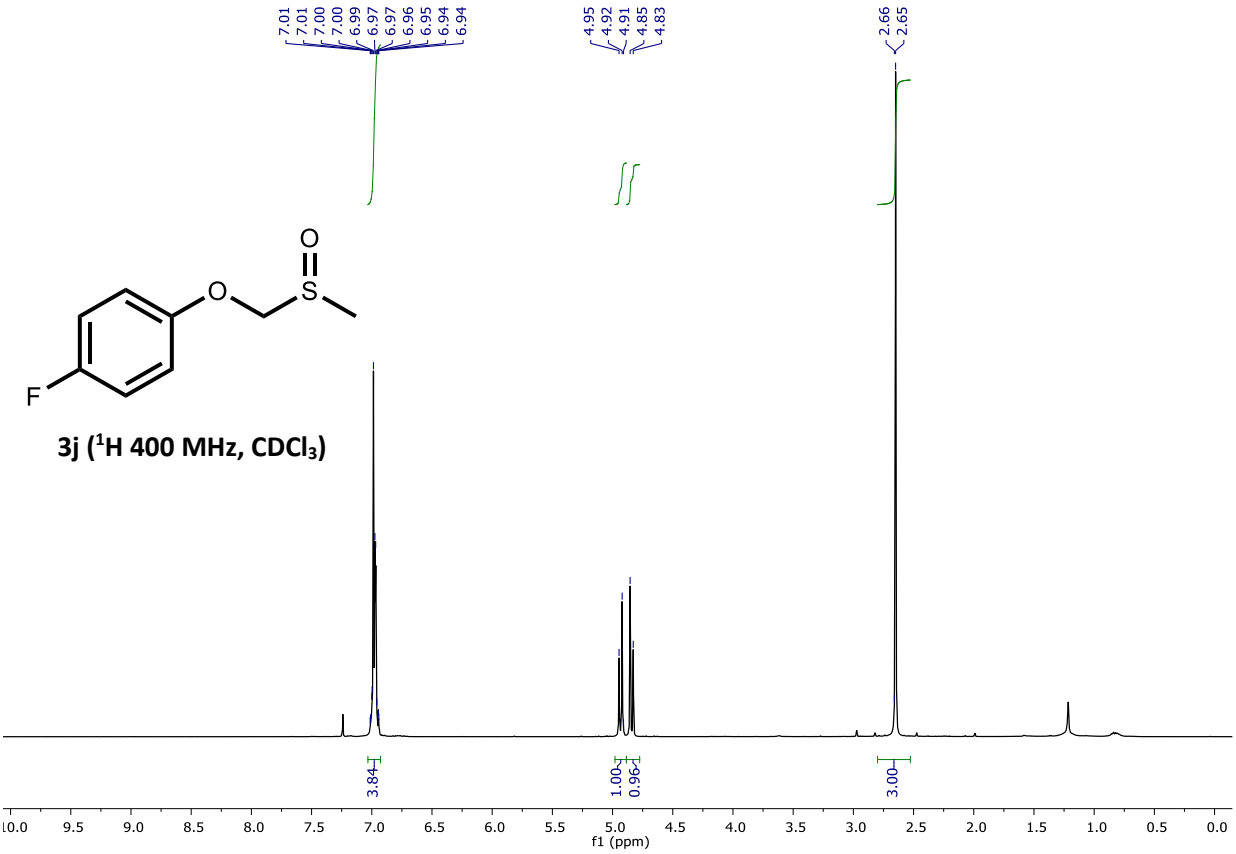

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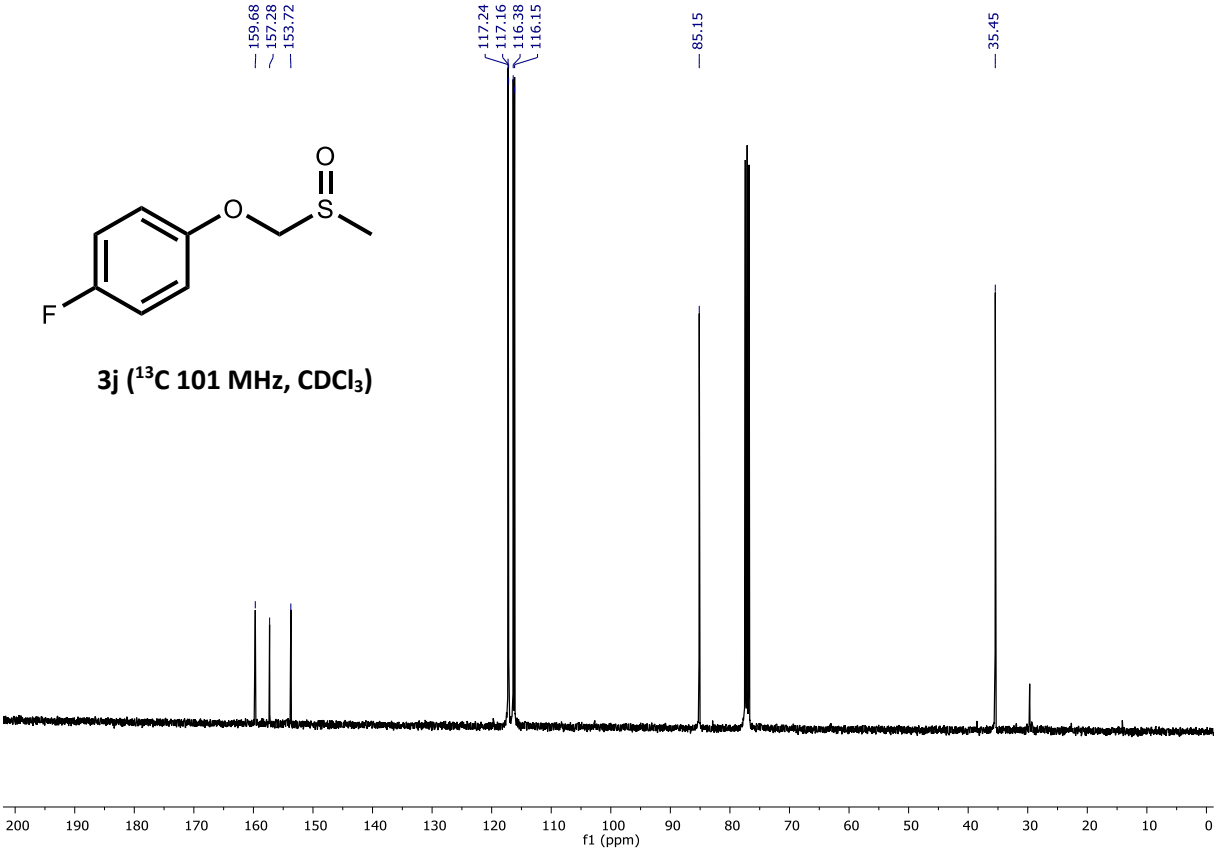

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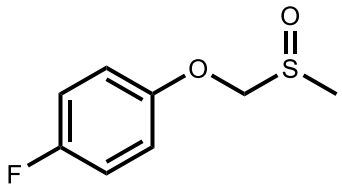
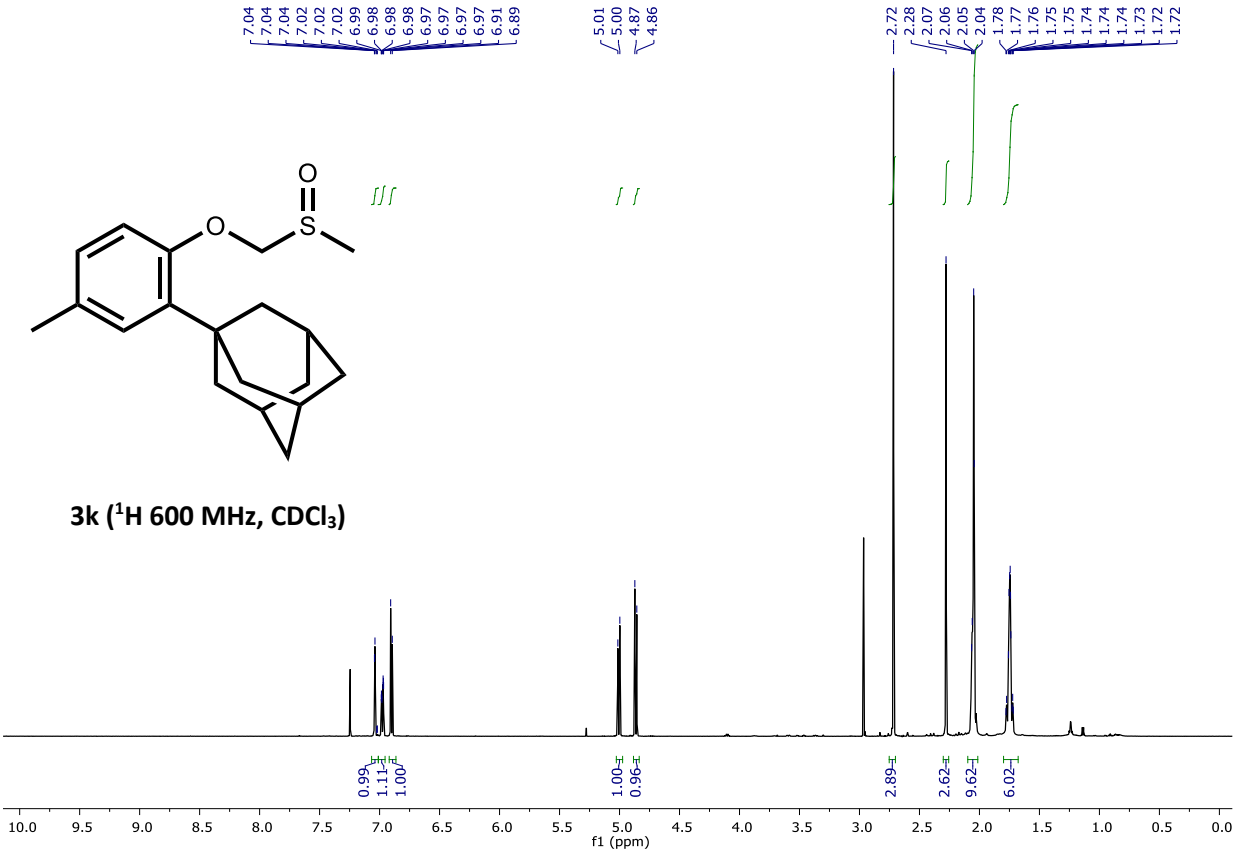


3j (^{19}F 377 MHz, $CDCl_3$)



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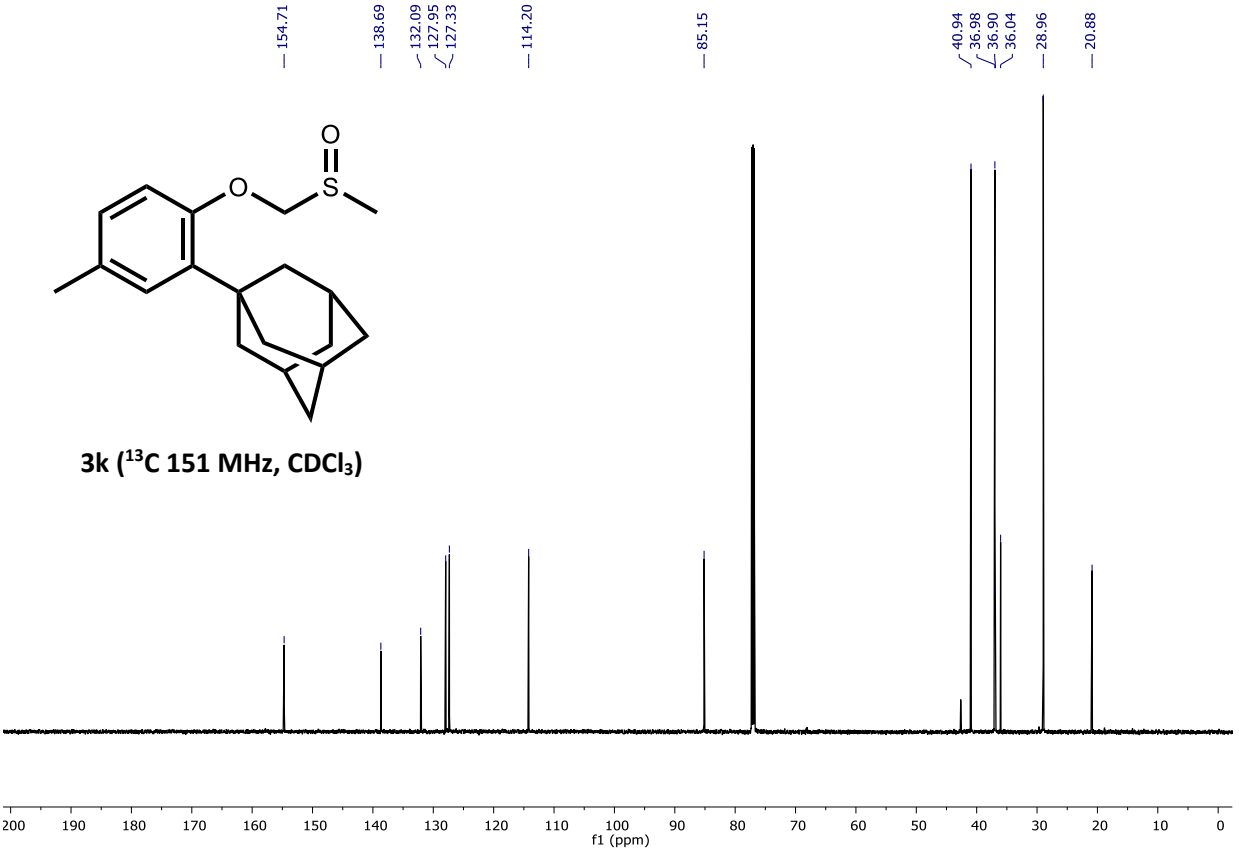

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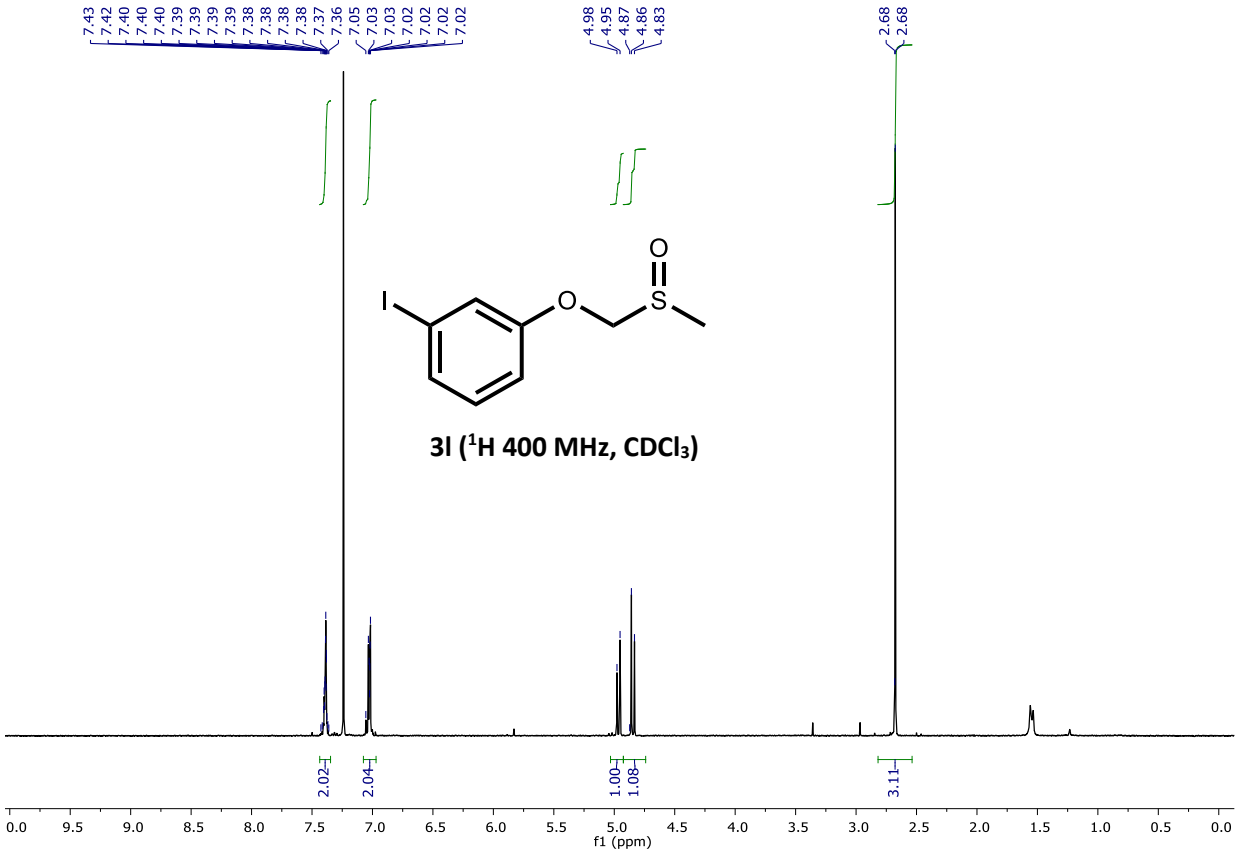

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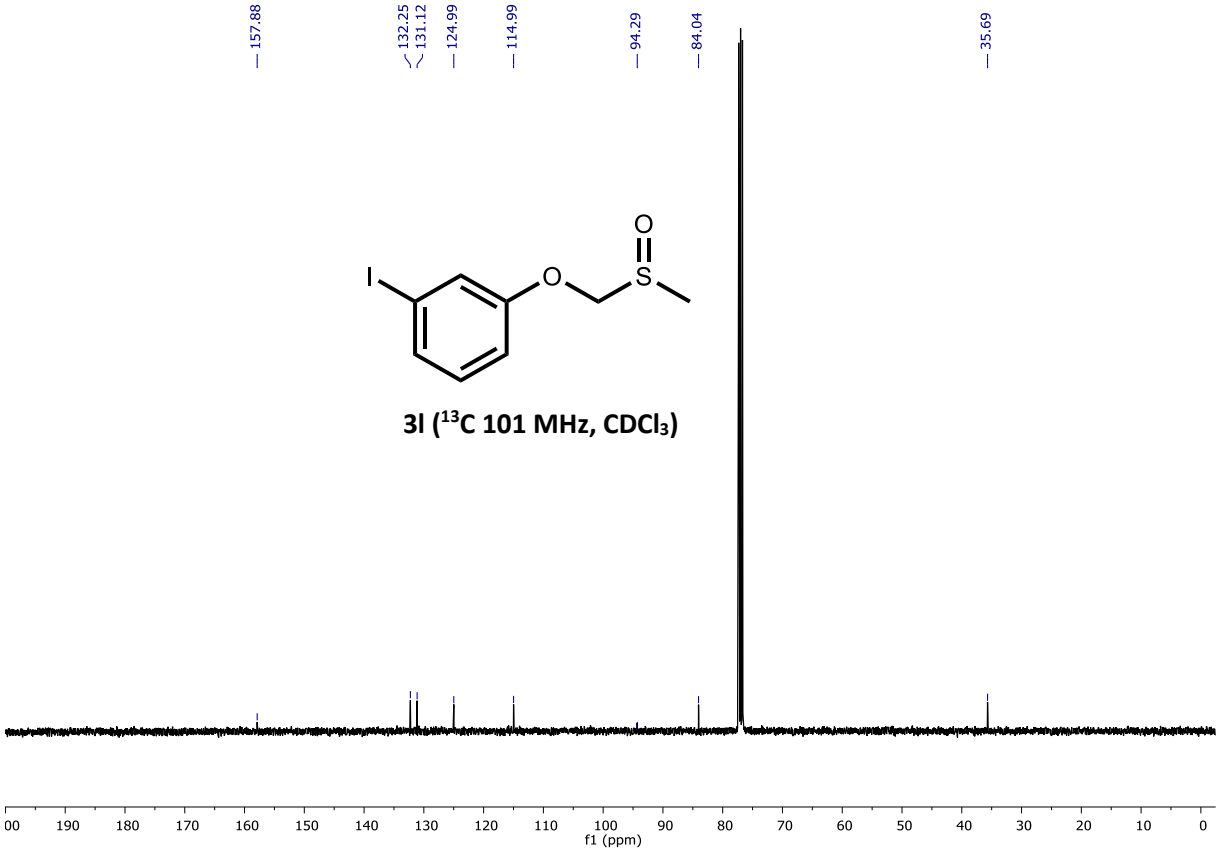

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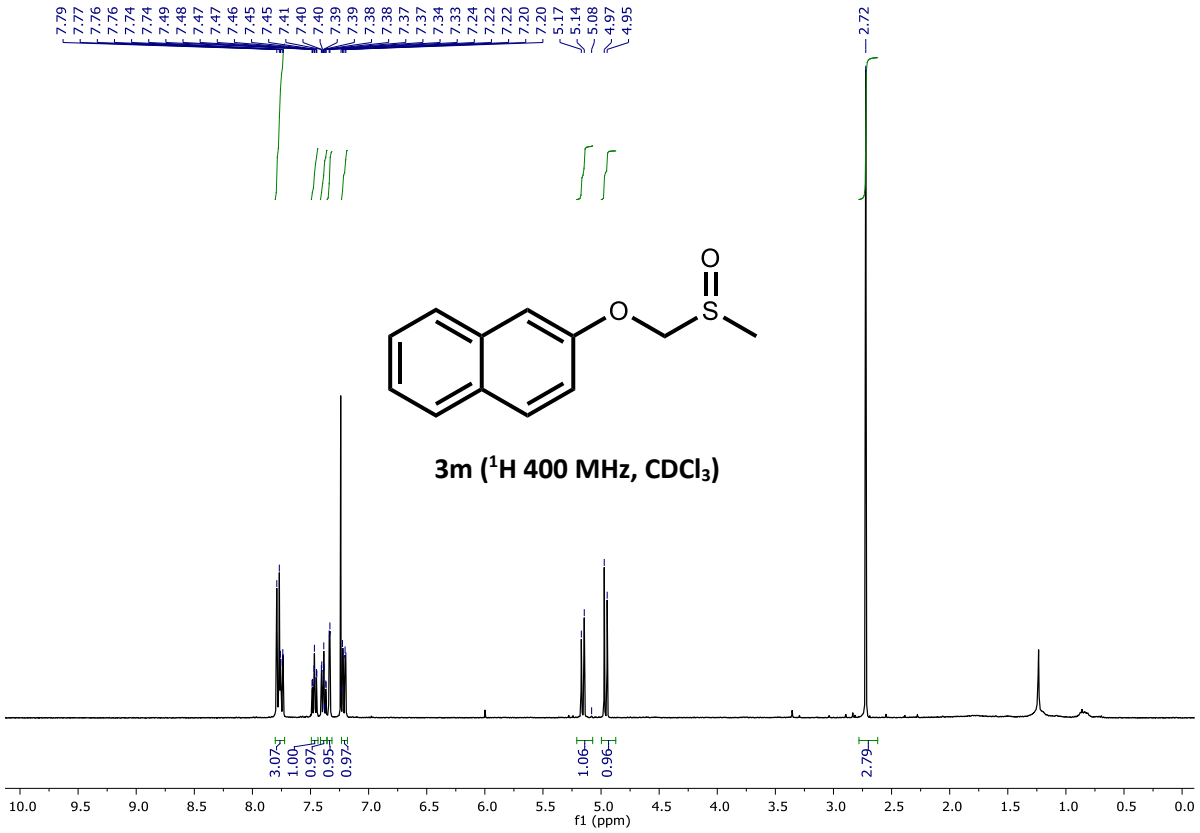

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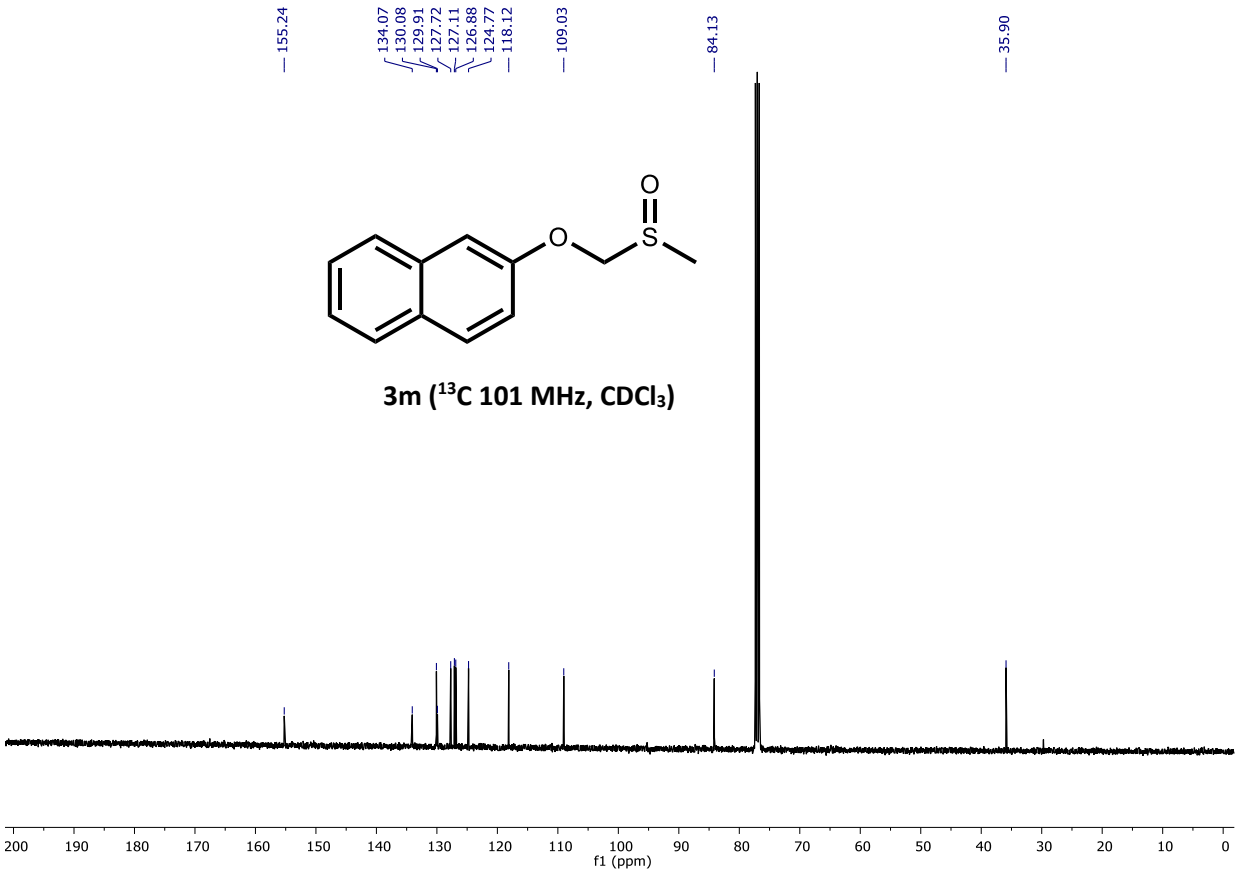

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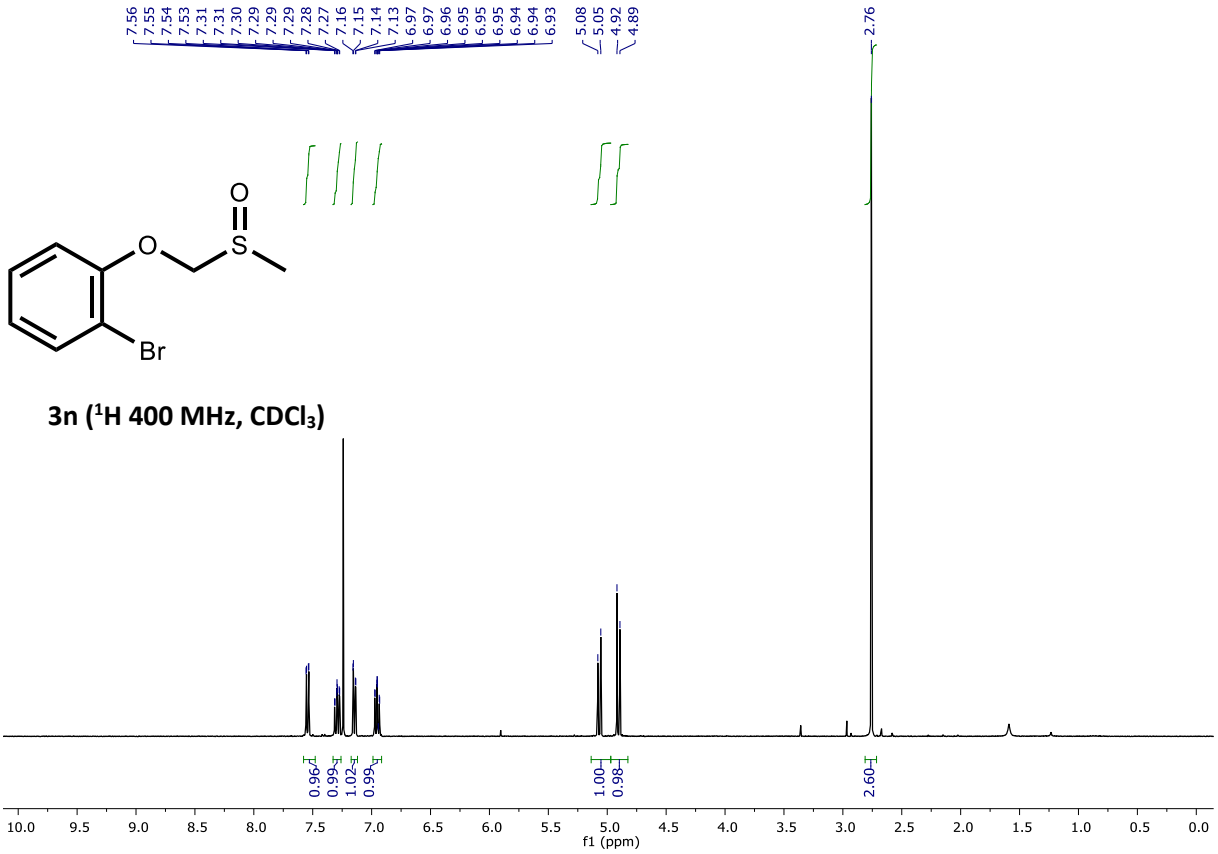
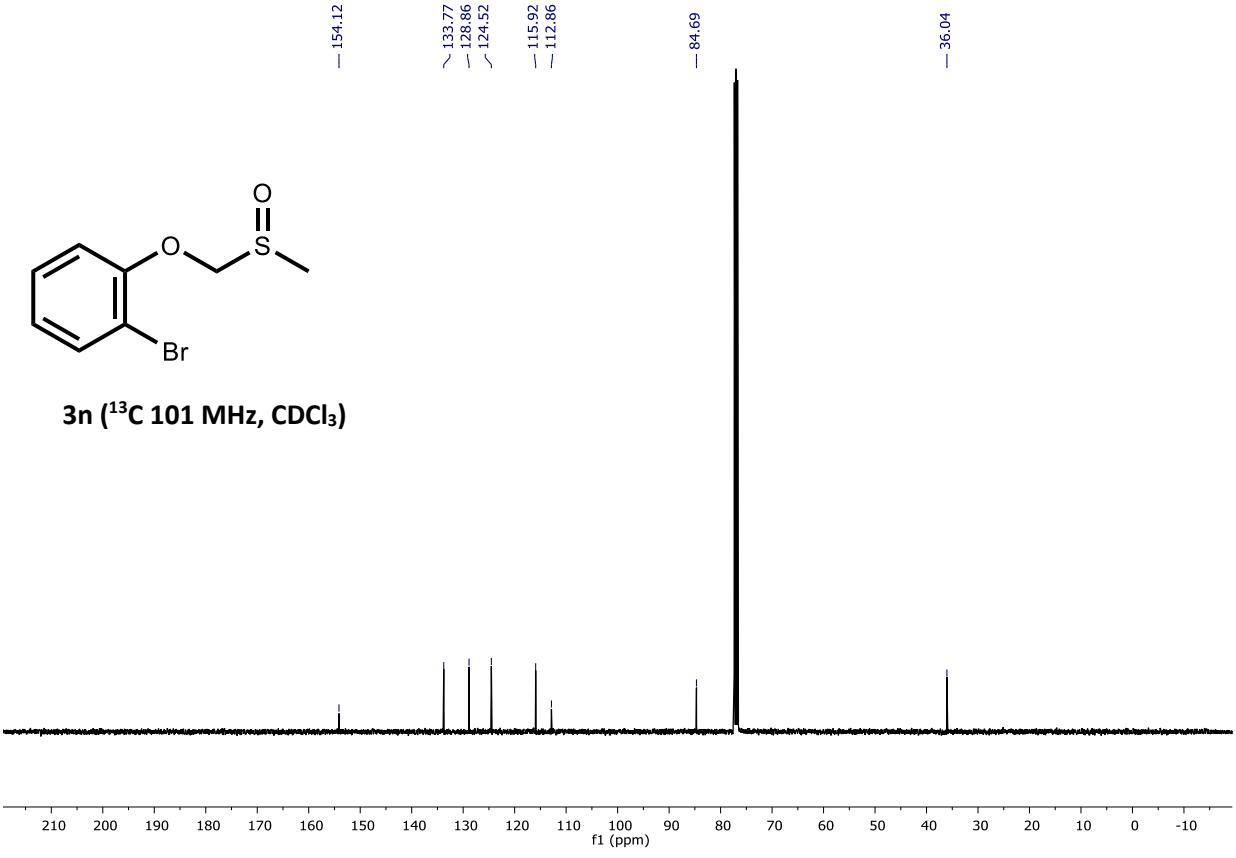
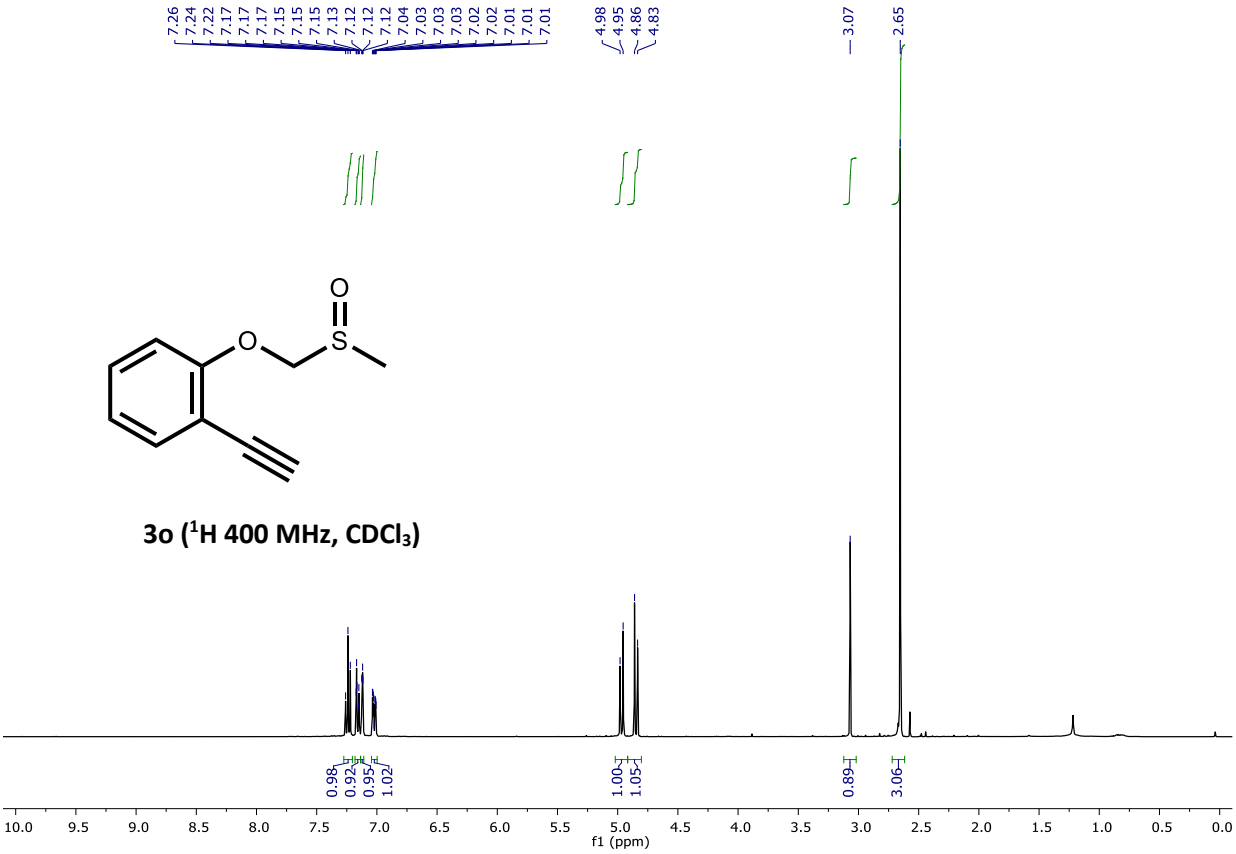


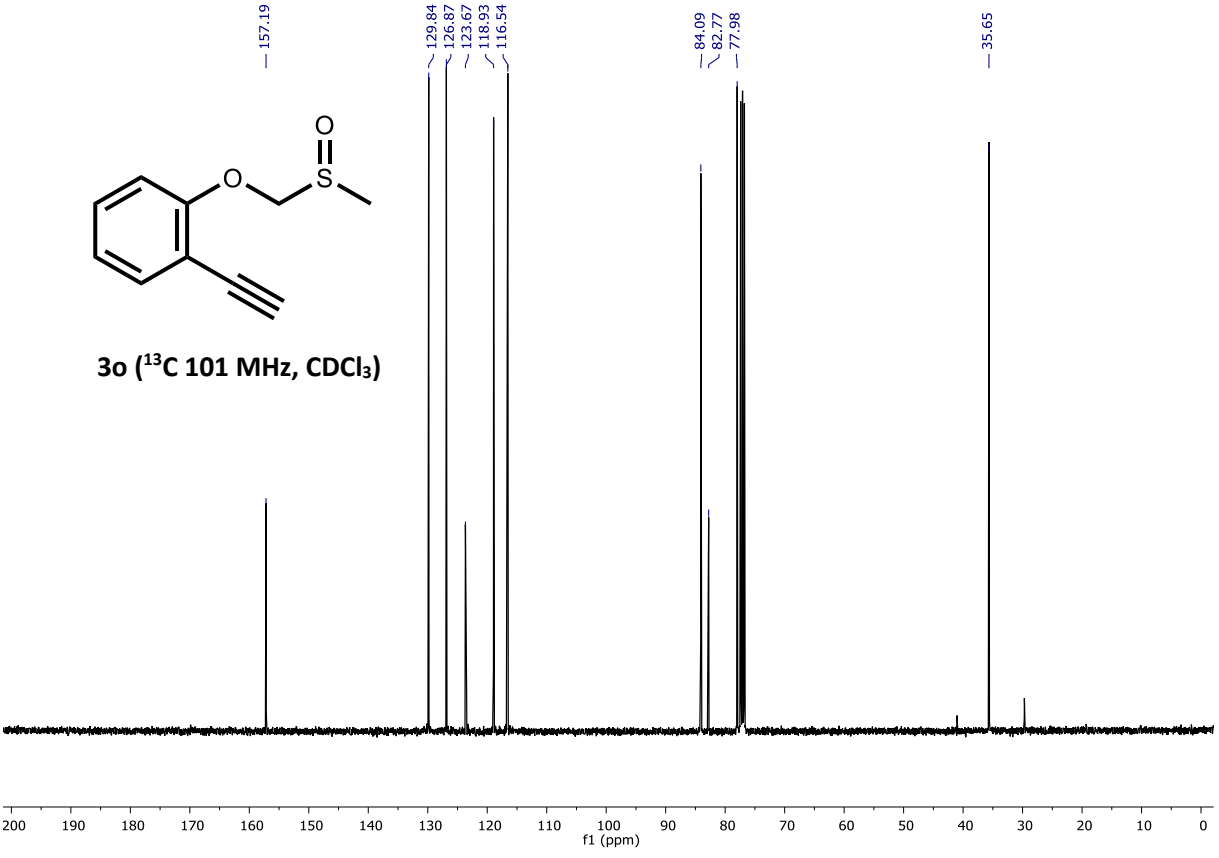
3n (^{1}H 400 MHz, $CDCl_3$)



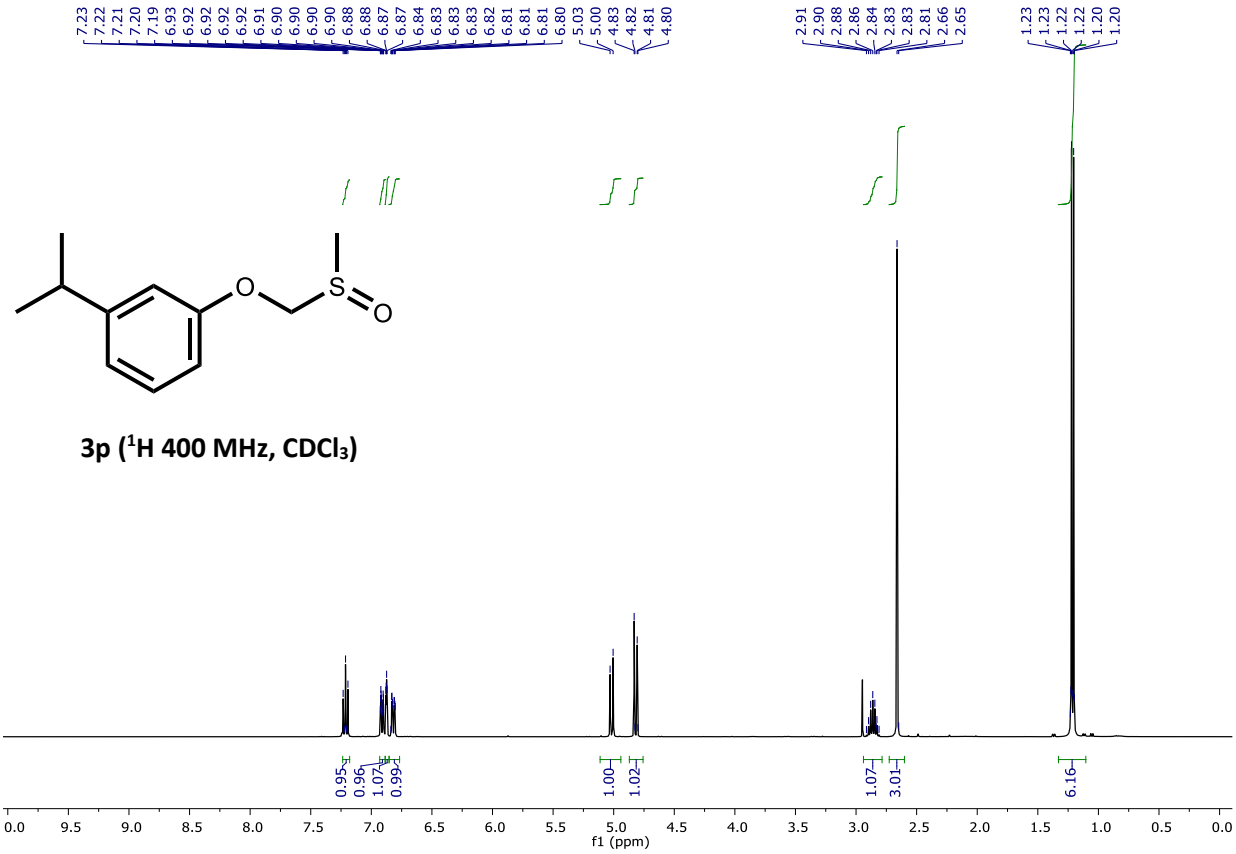
3n (^{13}C 101 MHz, $CDCl_3$)



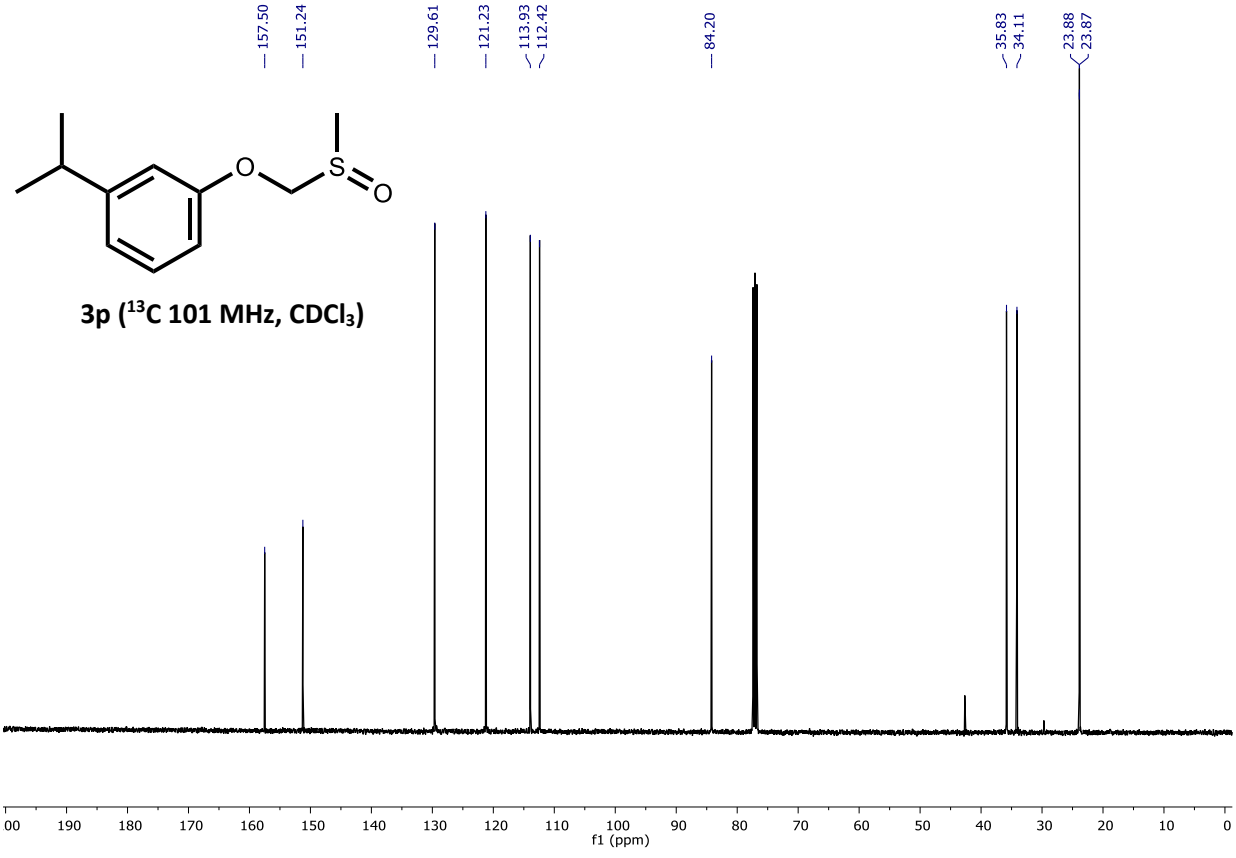
3o (^{1}H 400 MHz, $CDCl_3$)



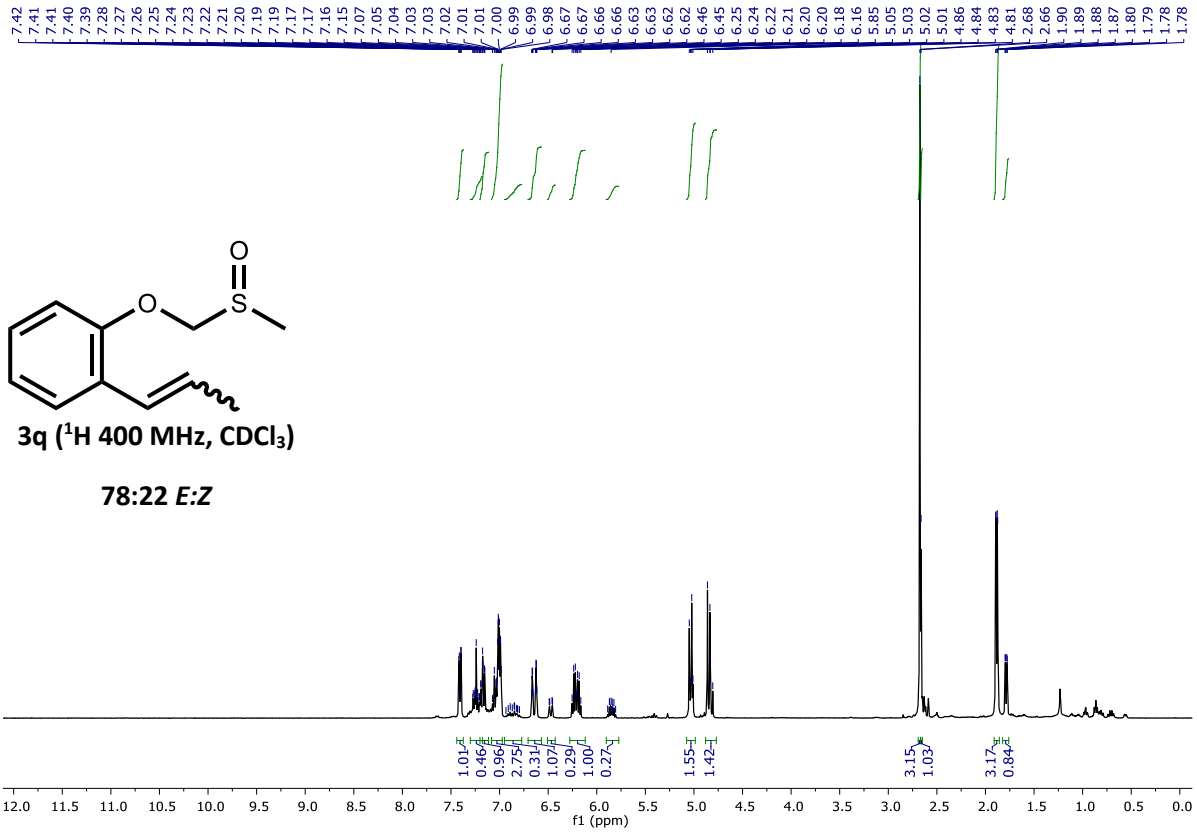
3o (^{13}C 101 MHz, $CDCl_3$)



3p (^{1}H 400 MHz, $CDCl_3$)

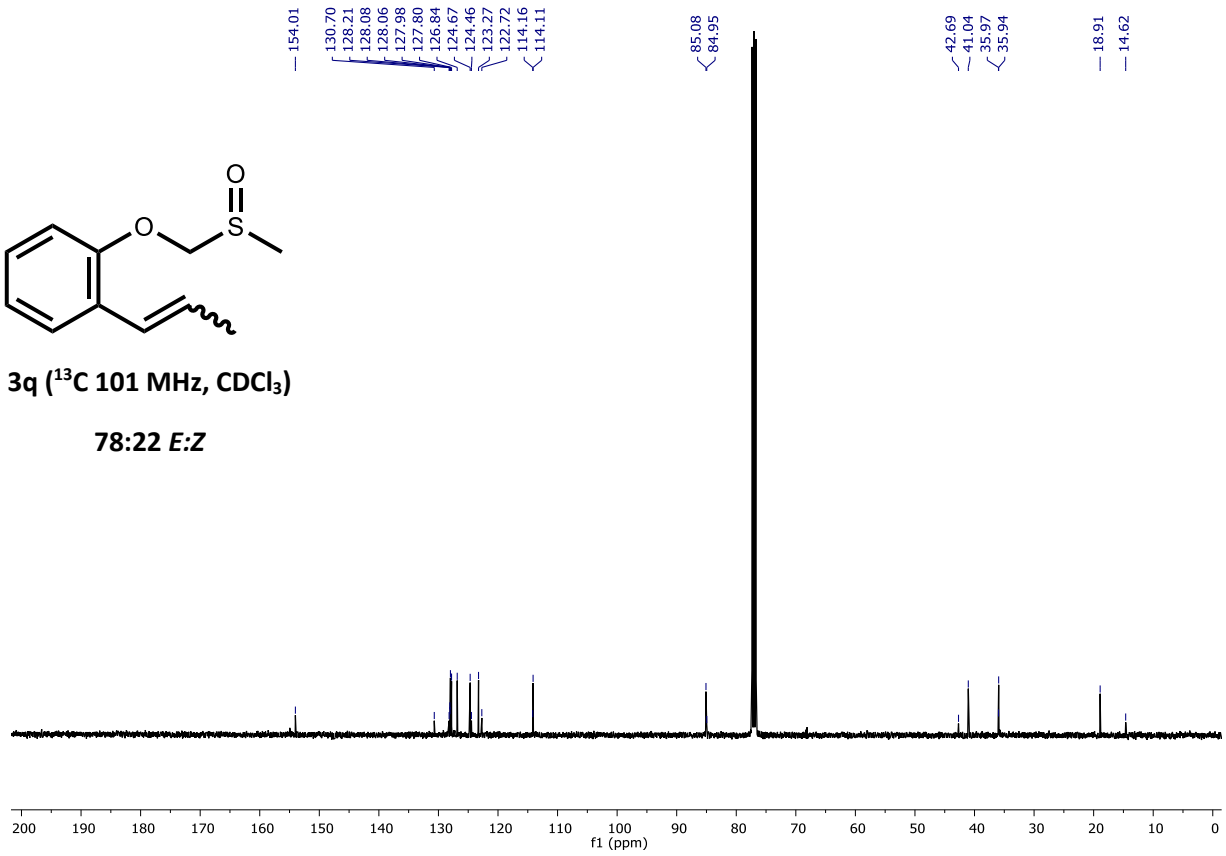


3p (^{13}C 101 MHz, $CDCl_3$)



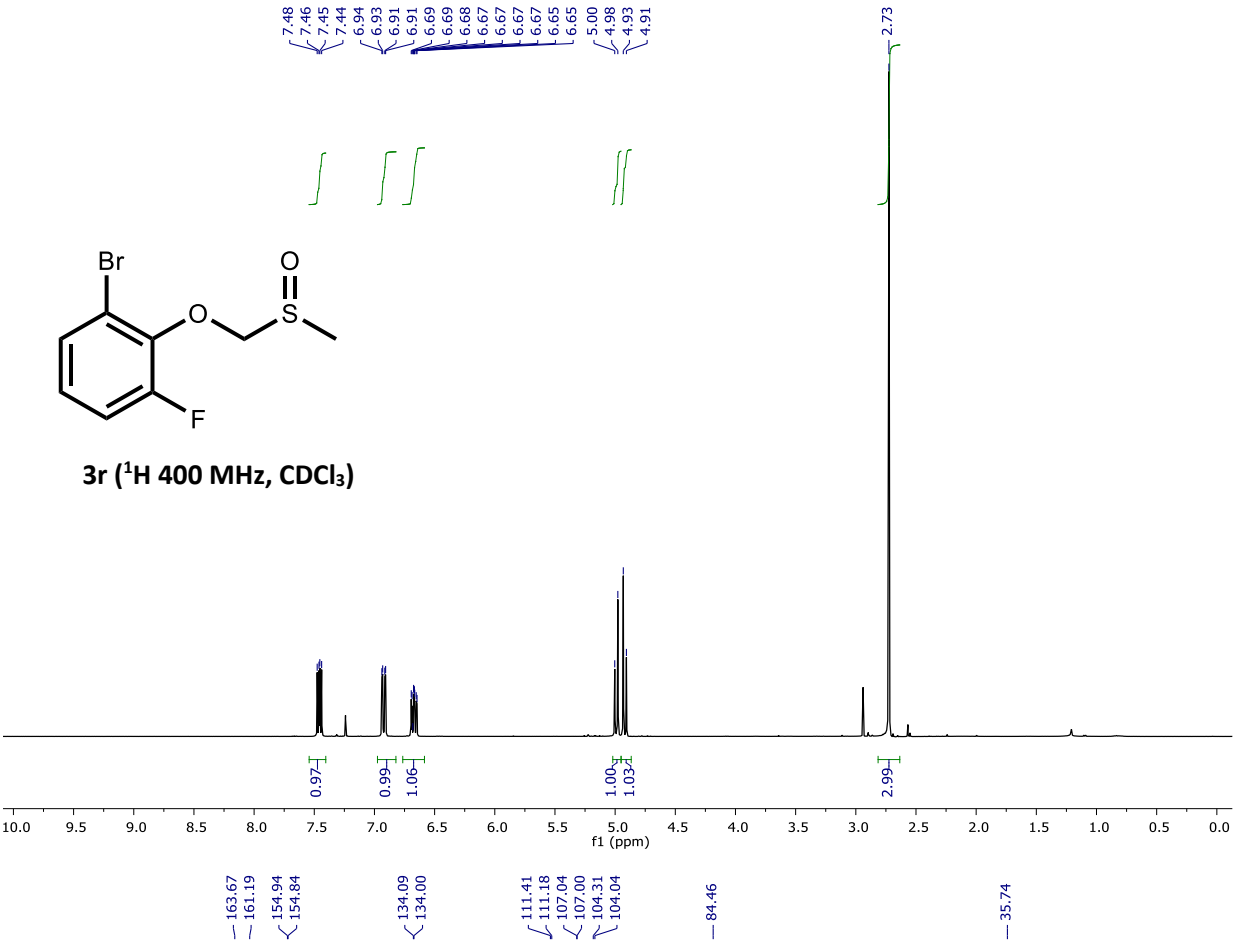
3q (^{1}H 400 MHz, $CDCl_3$)

78:22 *E:Z*

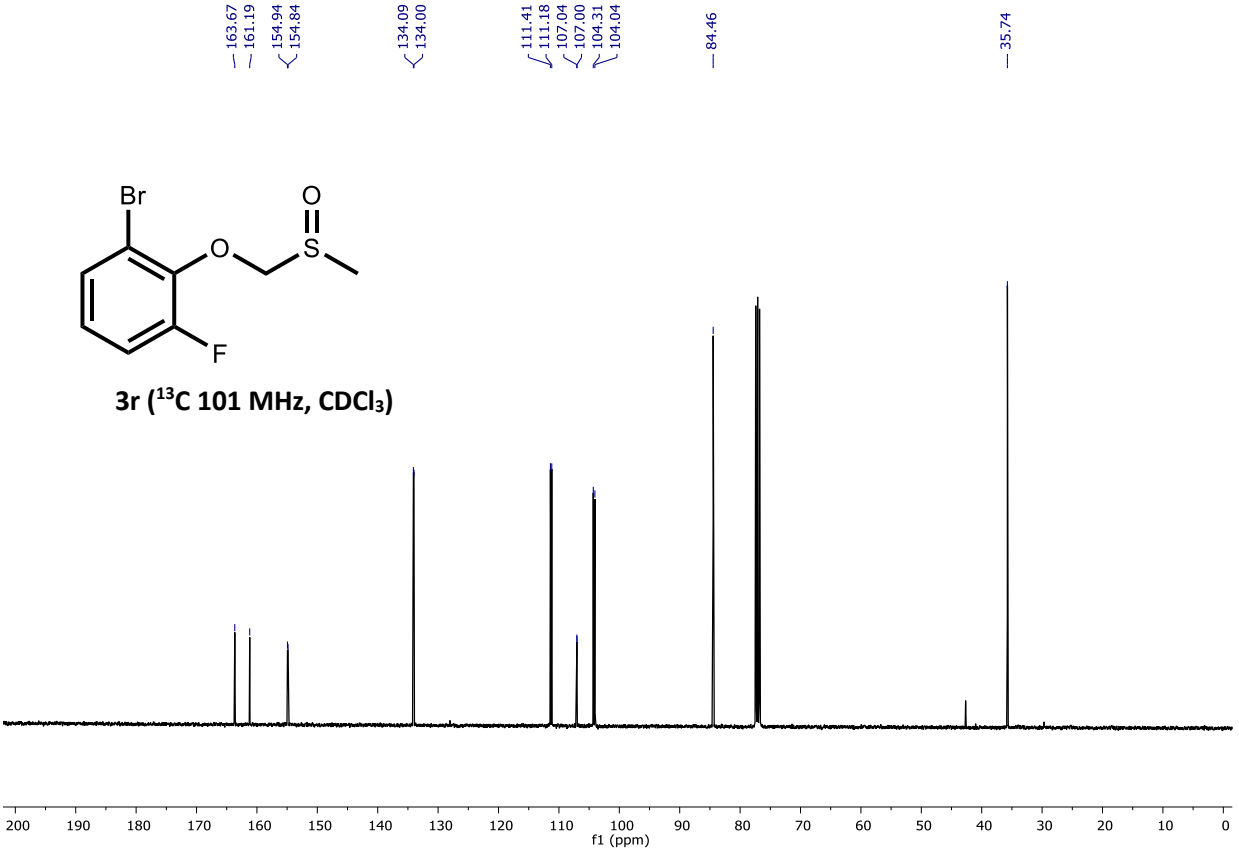


3q (^{13}C 101 MHz, $CDCl_3$)

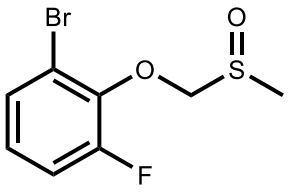
78:22 *E:Z*



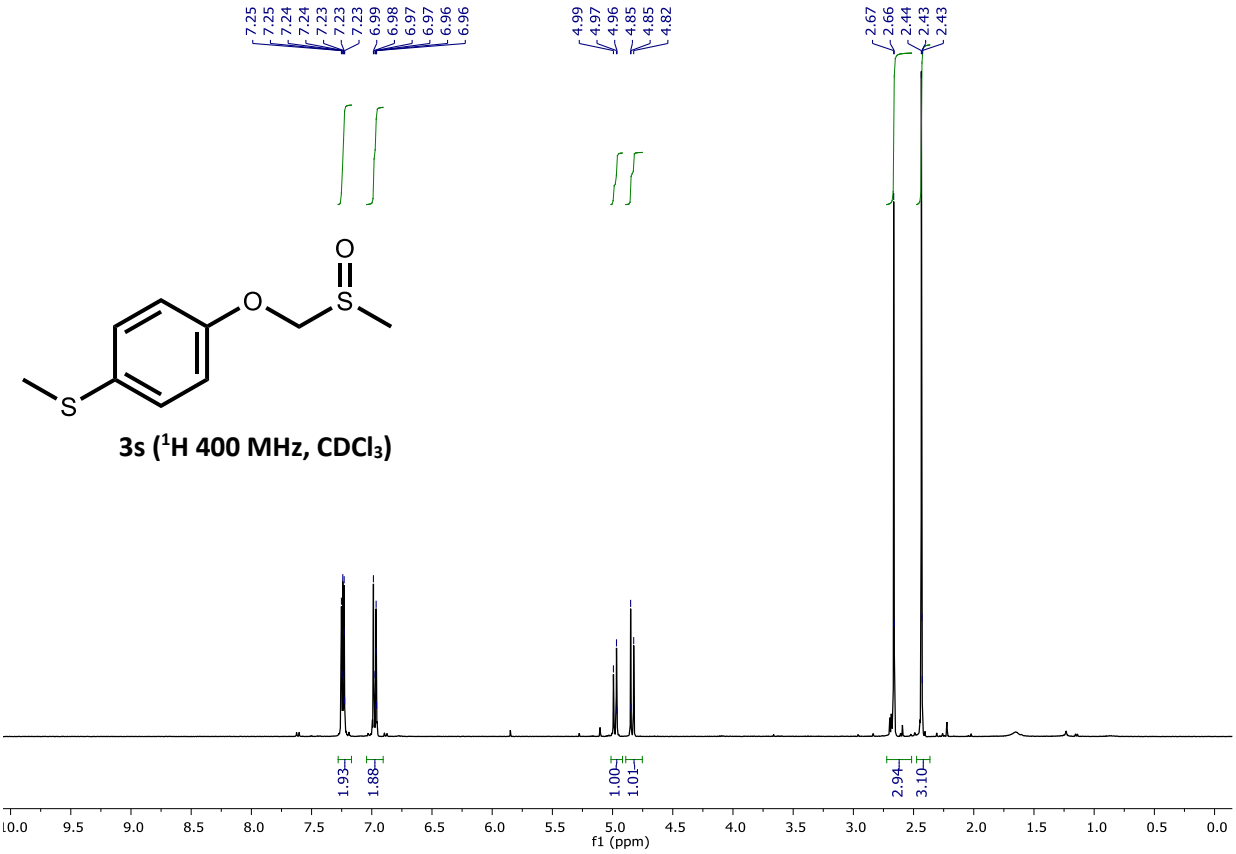
3r (^{1}H 400 MHz, $CDCl_3$)



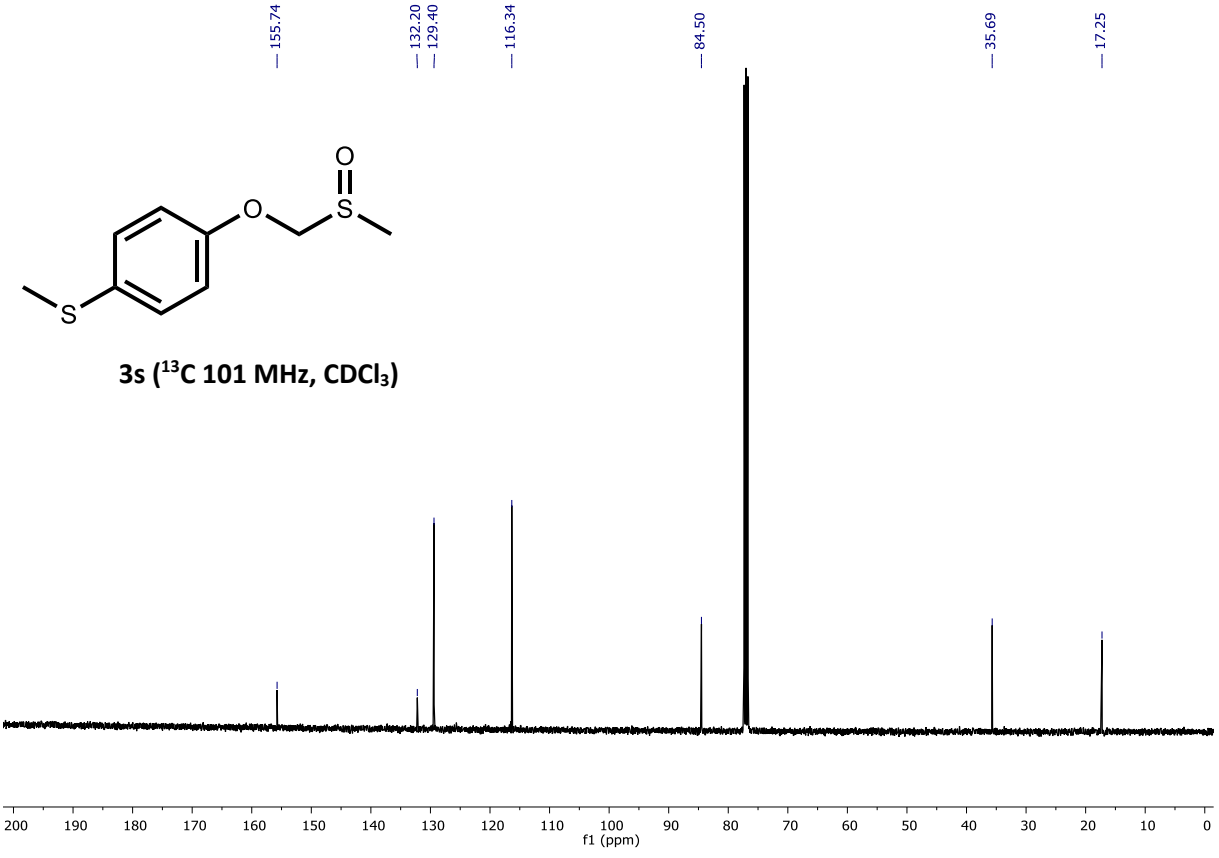
3r (^{13}C 101 MHz, $CDCl_3$)



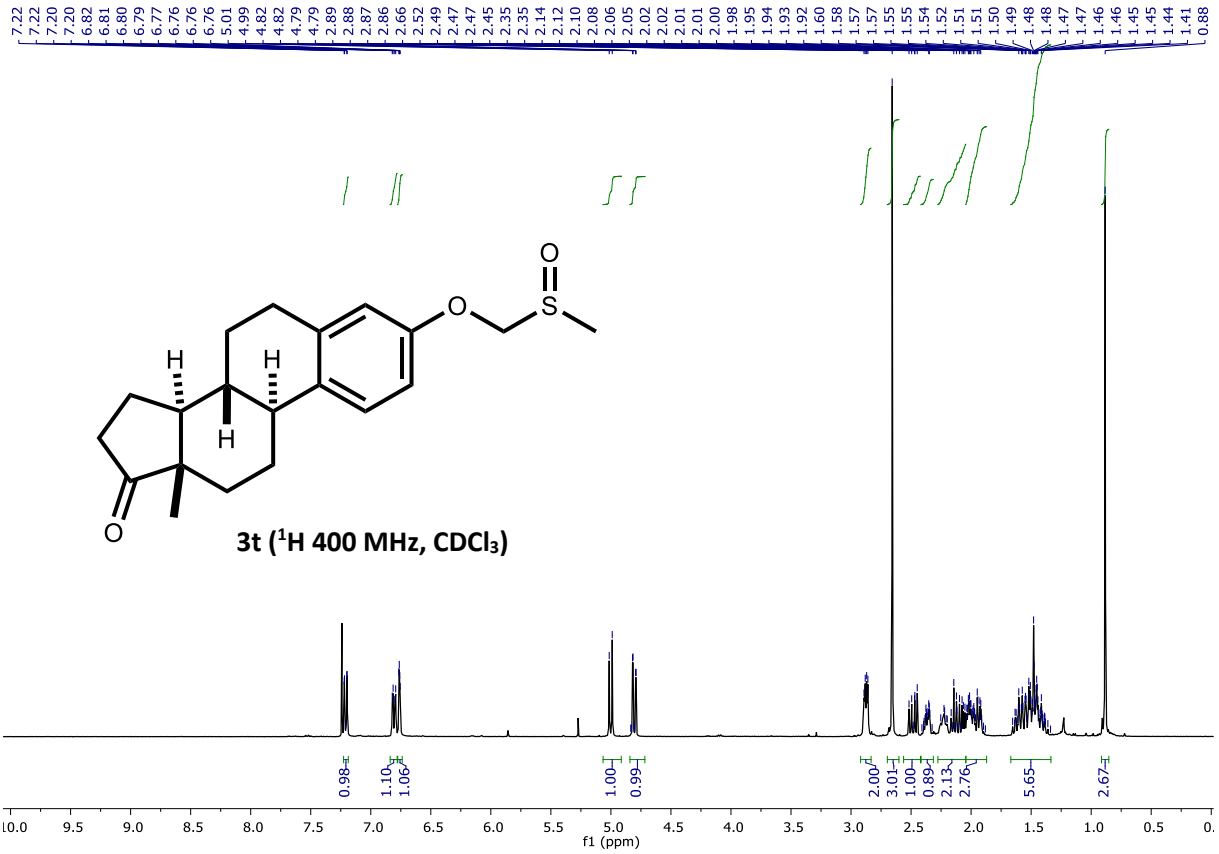
3r (^{19}F 377 MHz, $CDCl_3$)



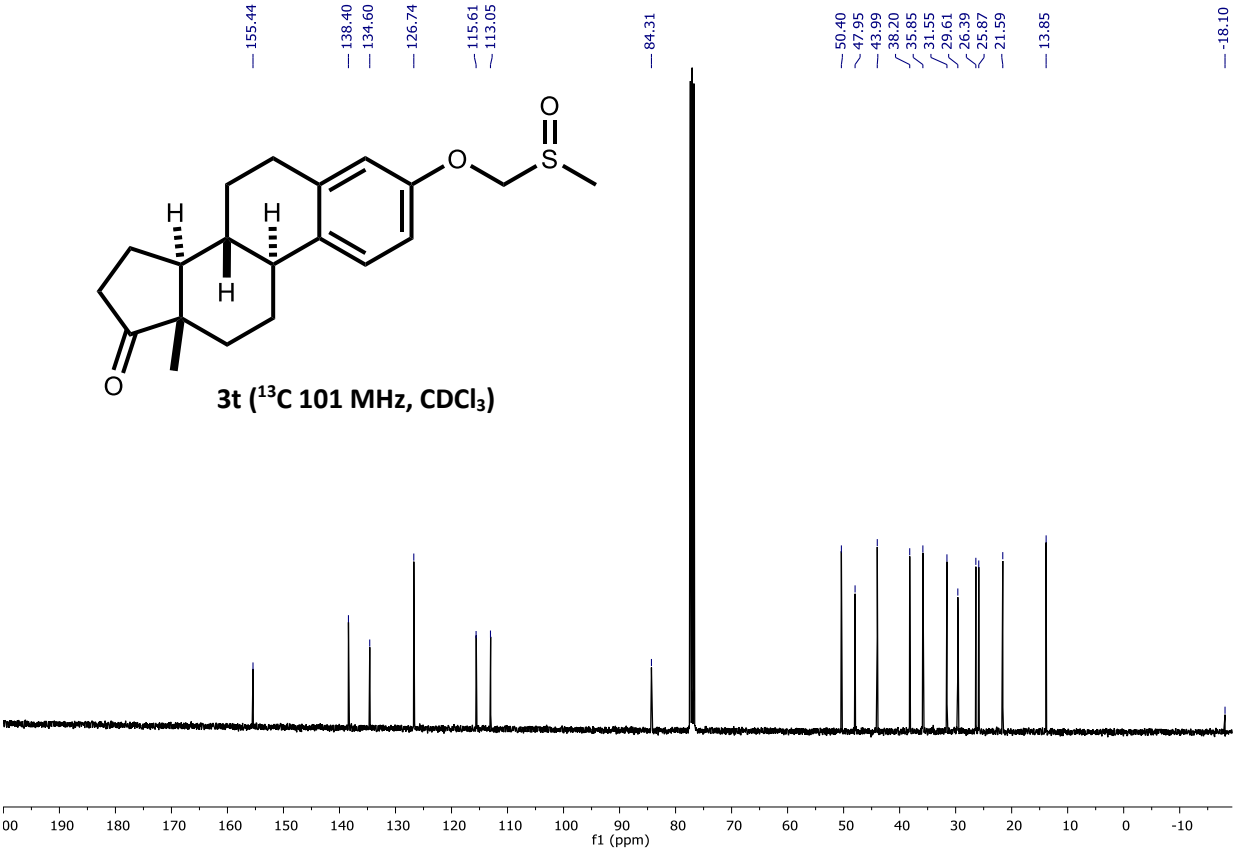
3s (^{1}H 400 MHz, $CDCl_3$)



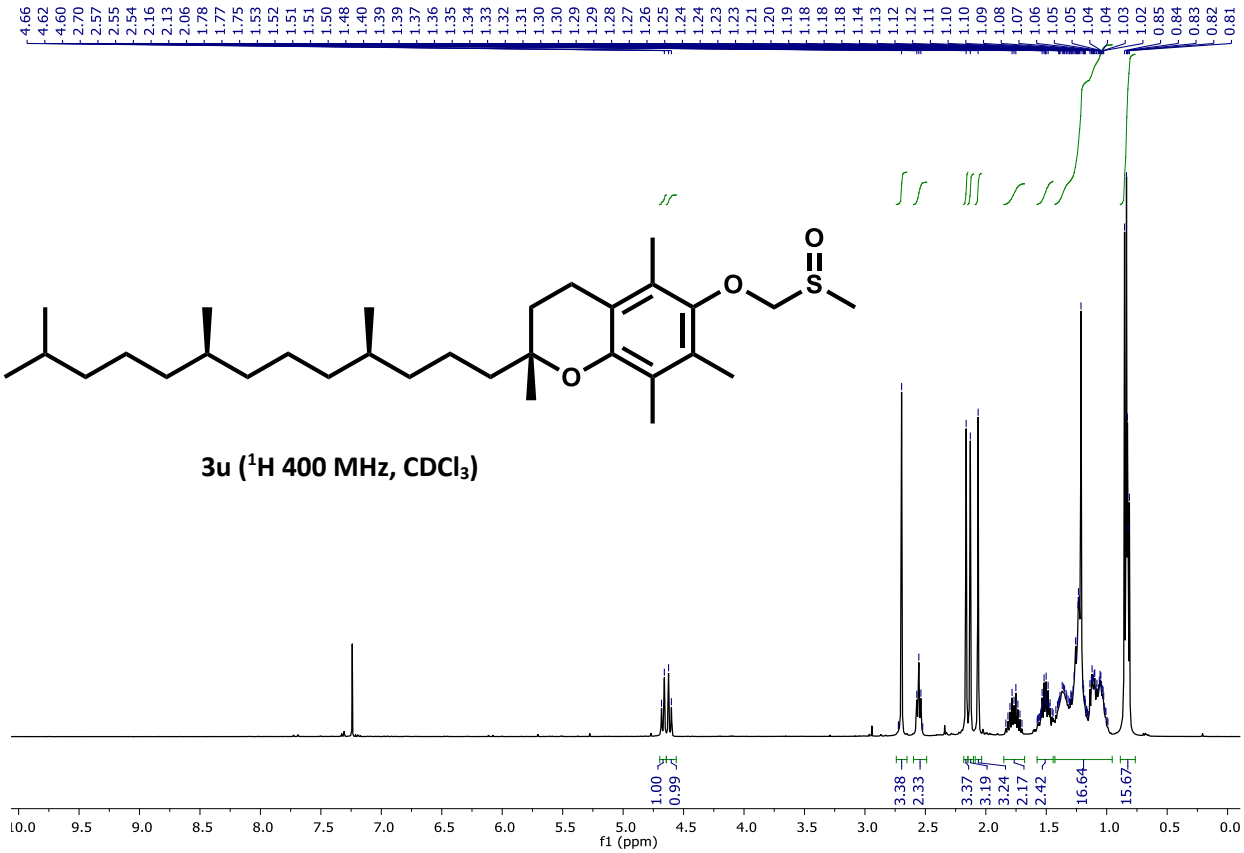
3s (^{13}C 101 MHz, $CDCl_3$)



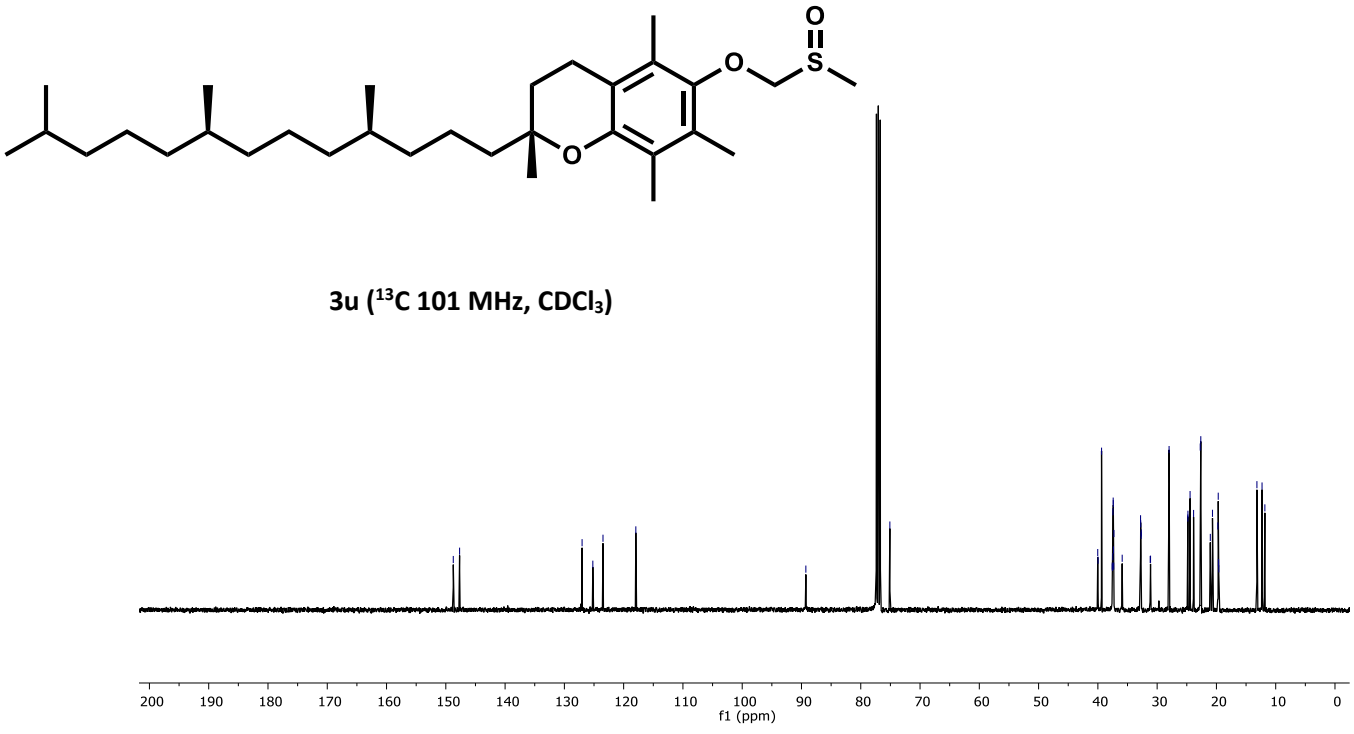
3t (^{1}H 400 MHz, $CDCl_3$)



3t (^{13}C 101 MHz, $CDCl_3$)



3u (^{1}H 400 MHz, $CDCl_3$)



3u (^{13}C 101 MHz, $CDCl_3$)