Supporting Information

Synthesis and Spectroscopic Properties of Fluorinated Coumarin Lysine Derivatives

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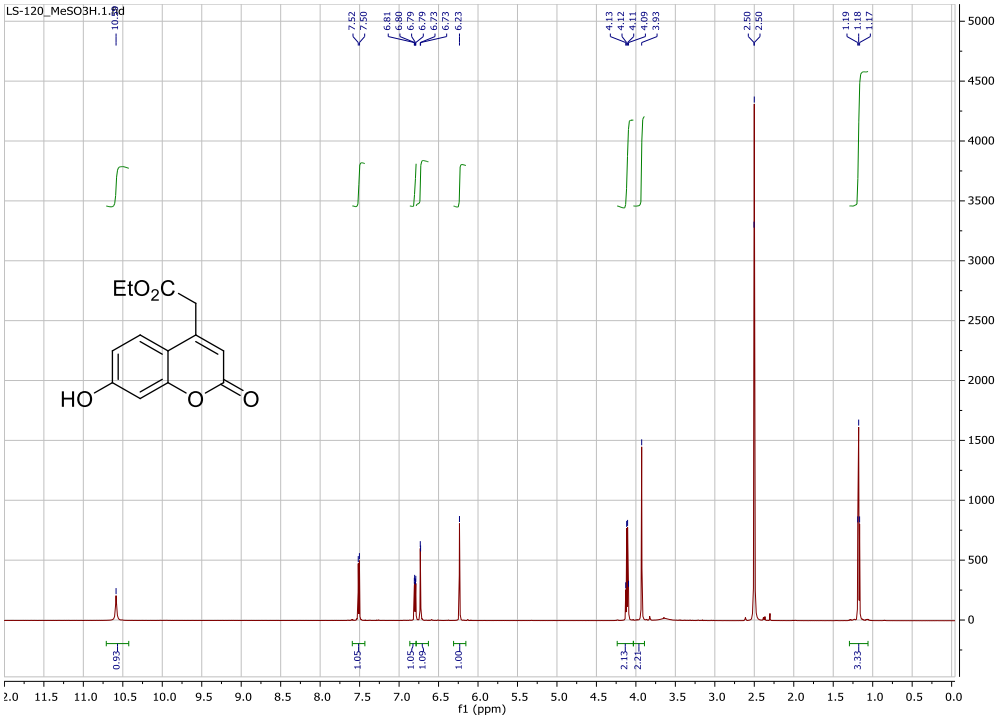
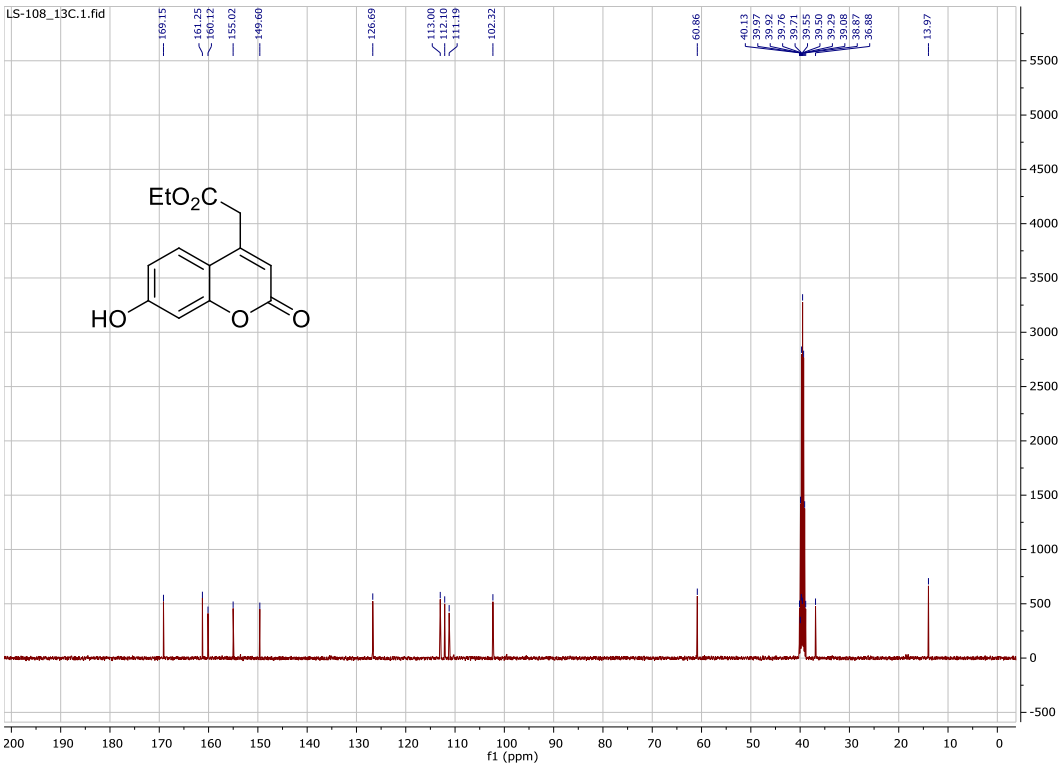
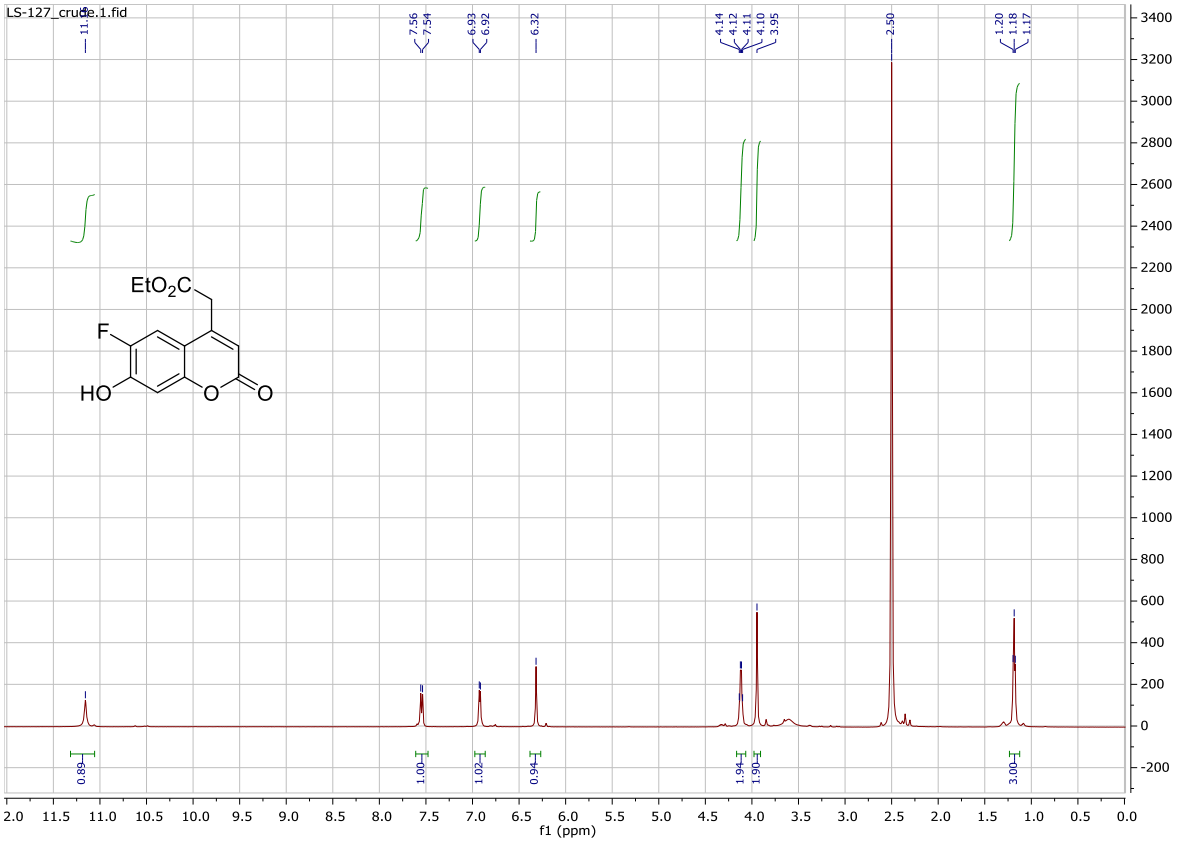
^{1}H NMR (600 MHz, DMSO-d_6) of 8a



^{13}C NMR (100 MHz, DMSO-d_6) of 8a



^{1}H NMR (600 MHz, DMSO-d_6) of 8b



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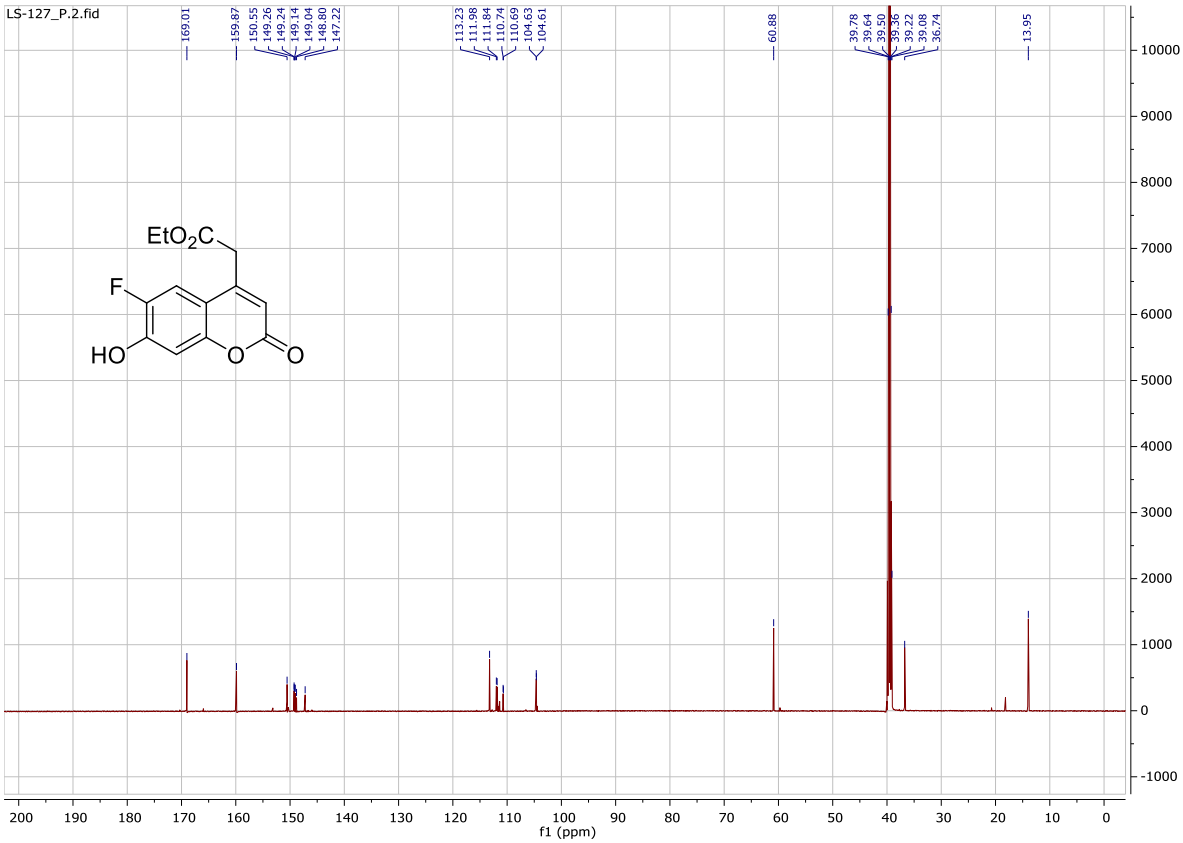
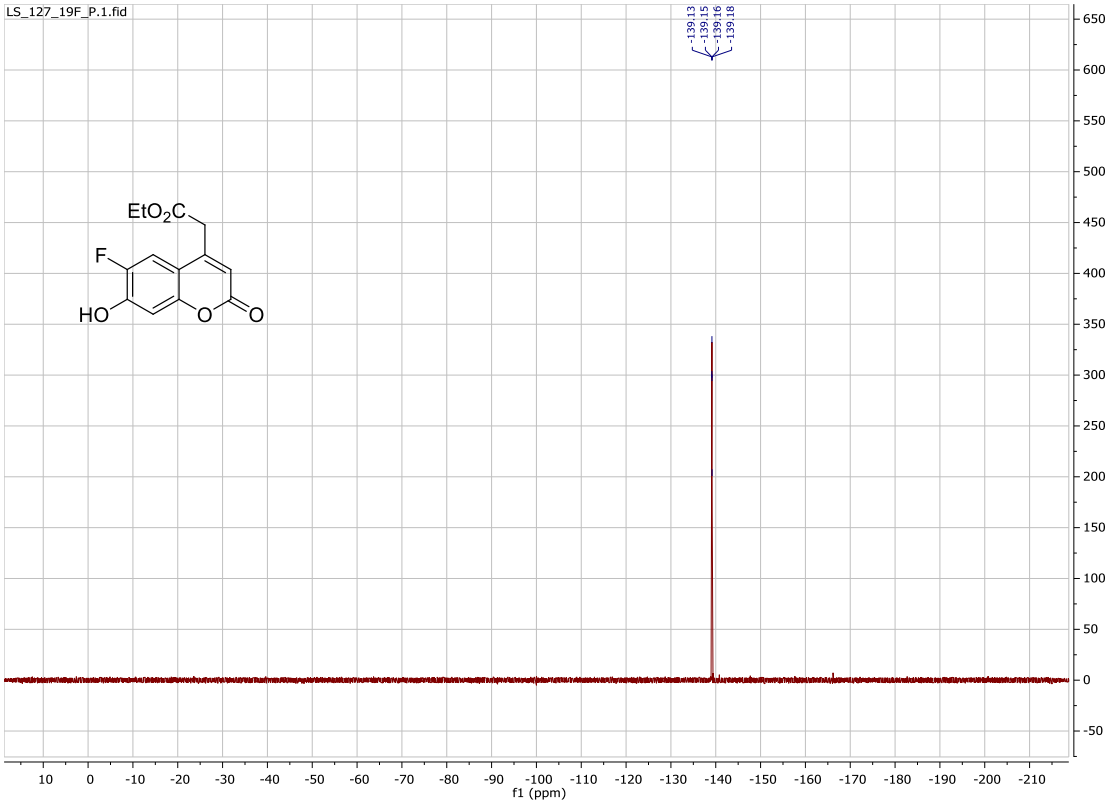


^{19}F NMR (376 MHz, DMSO-d_6) of 8b



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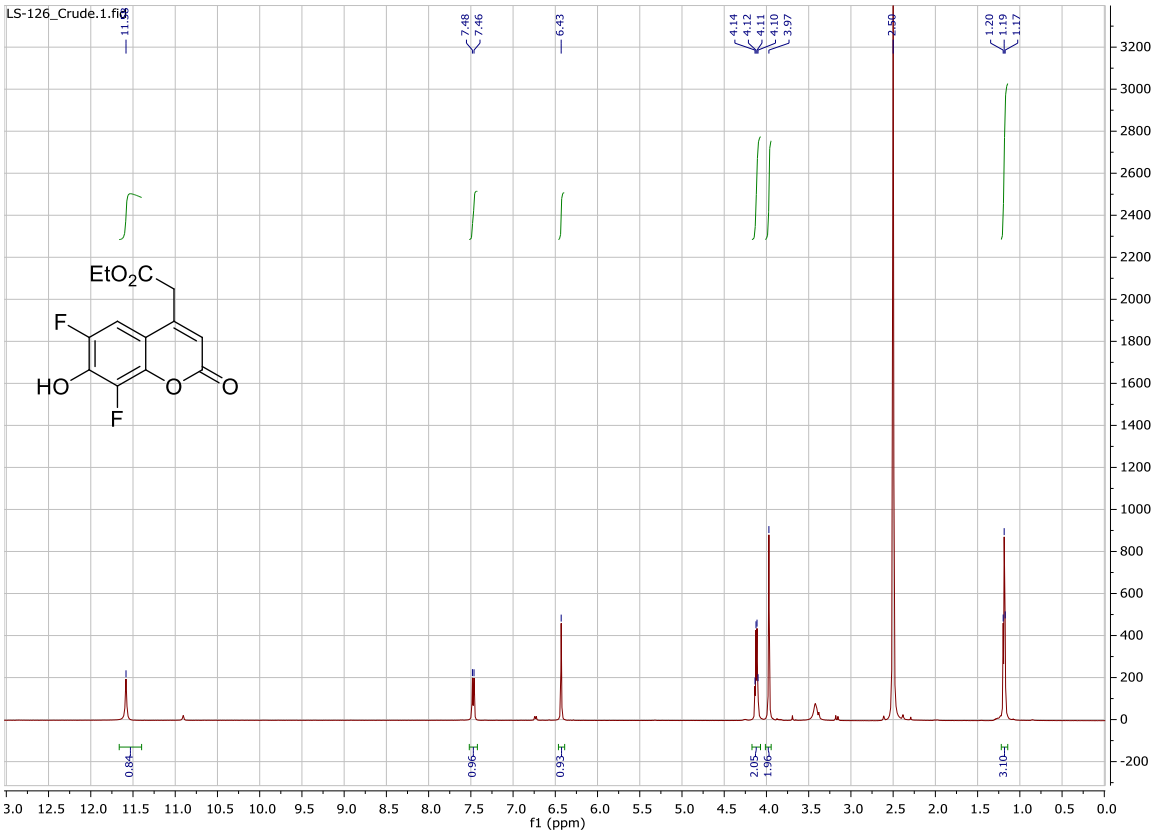

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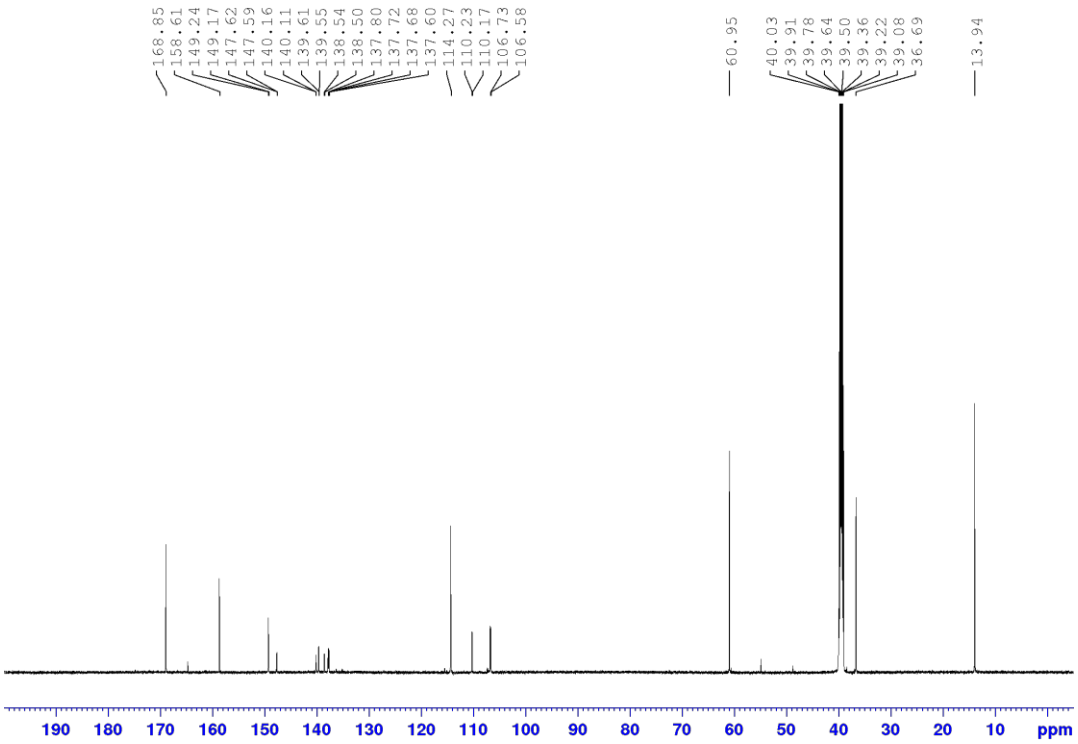

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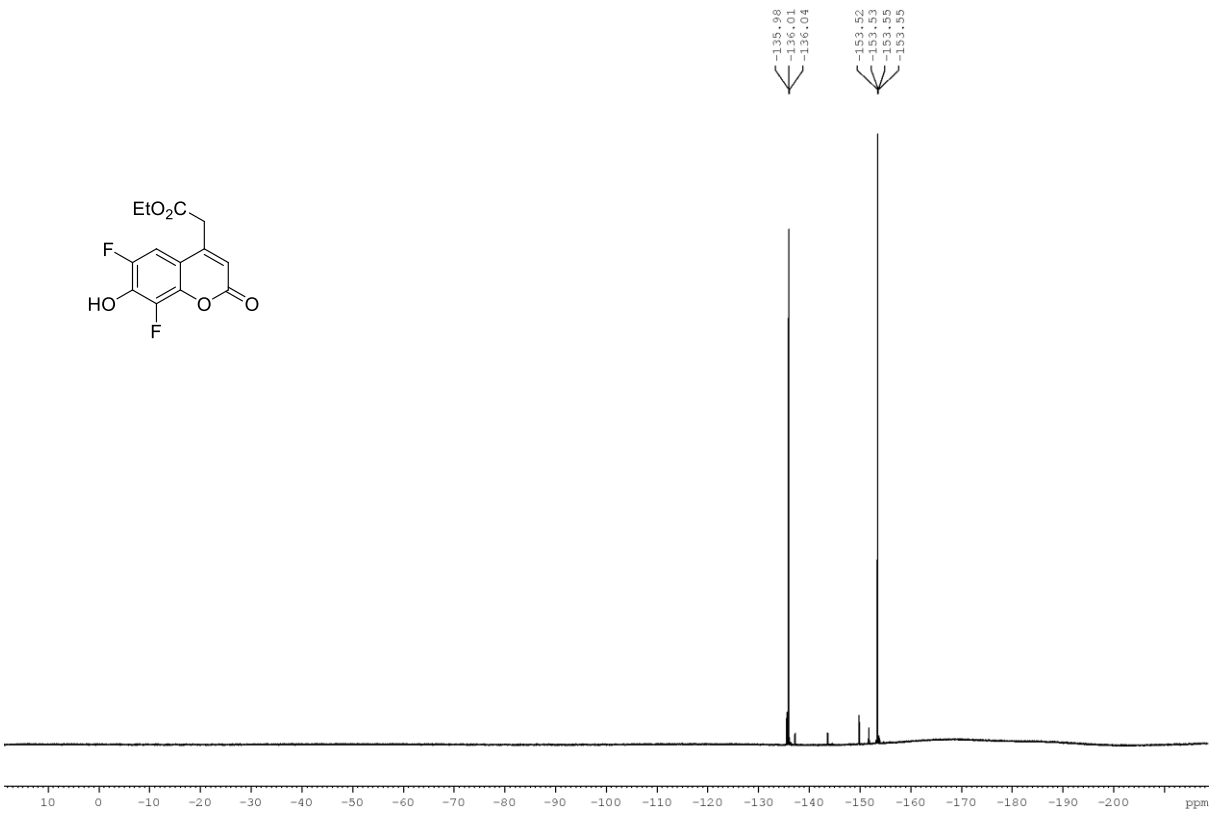

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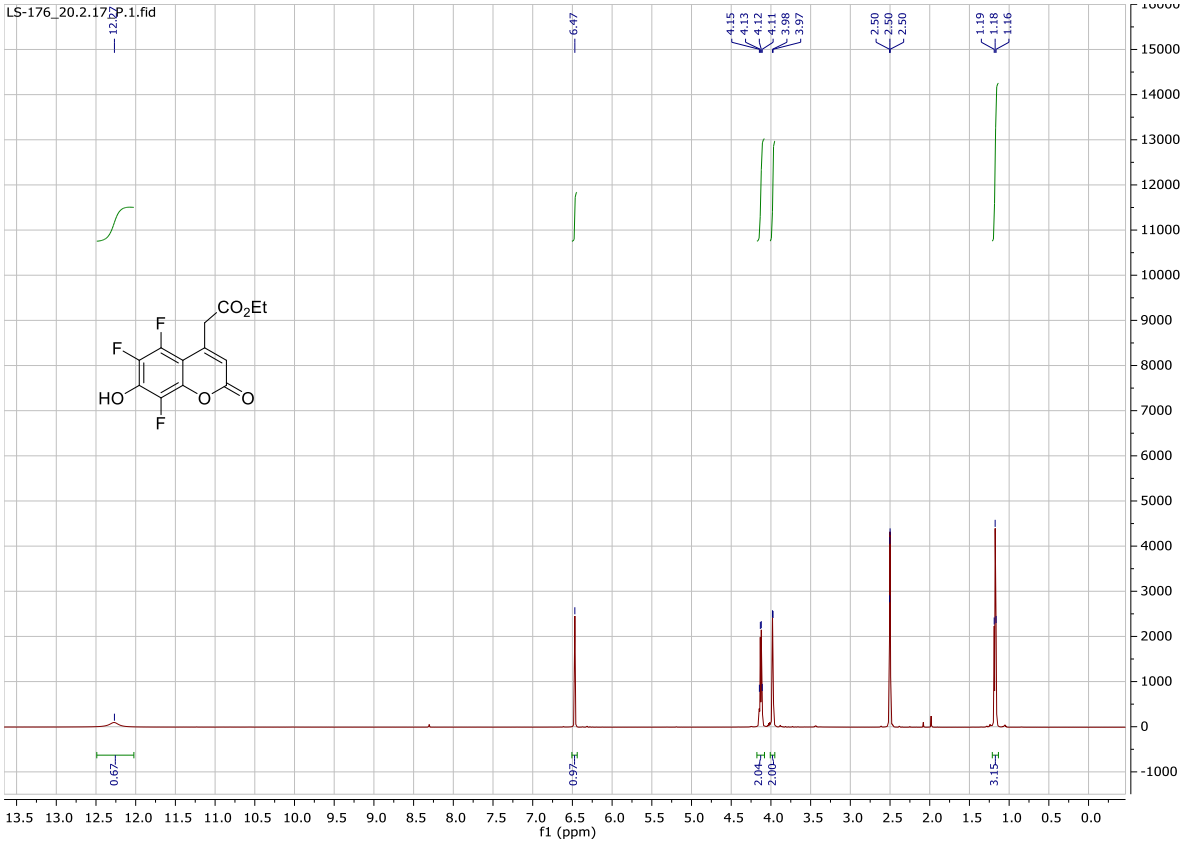
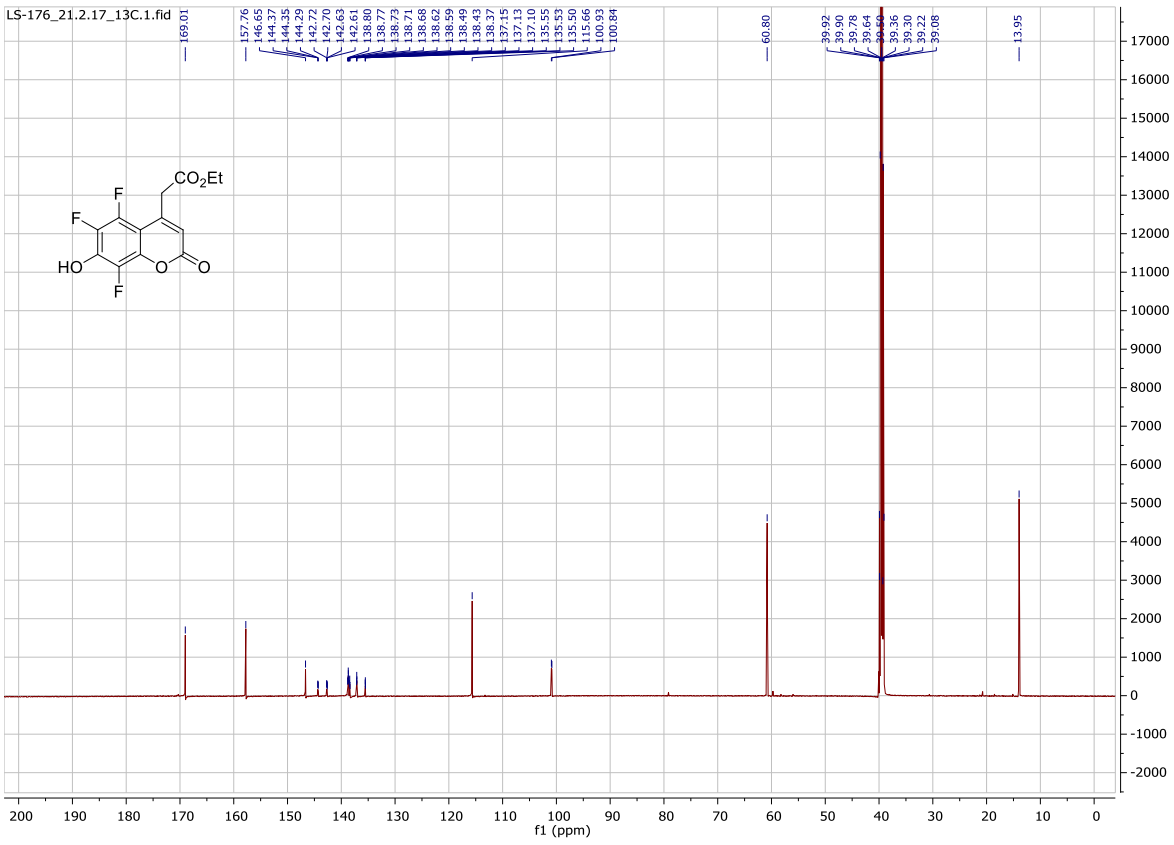


^{13}C NMR (151 MHz, DMSO-d_6) of 8d



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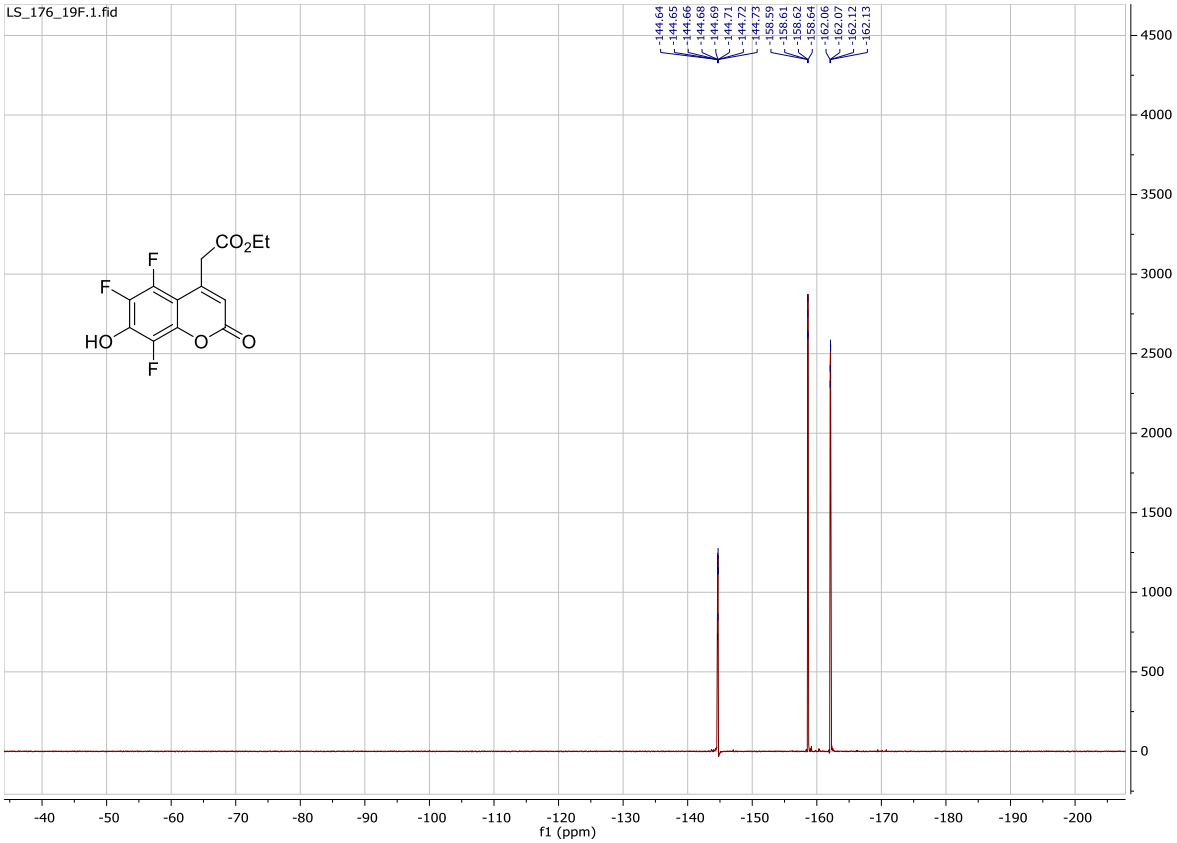
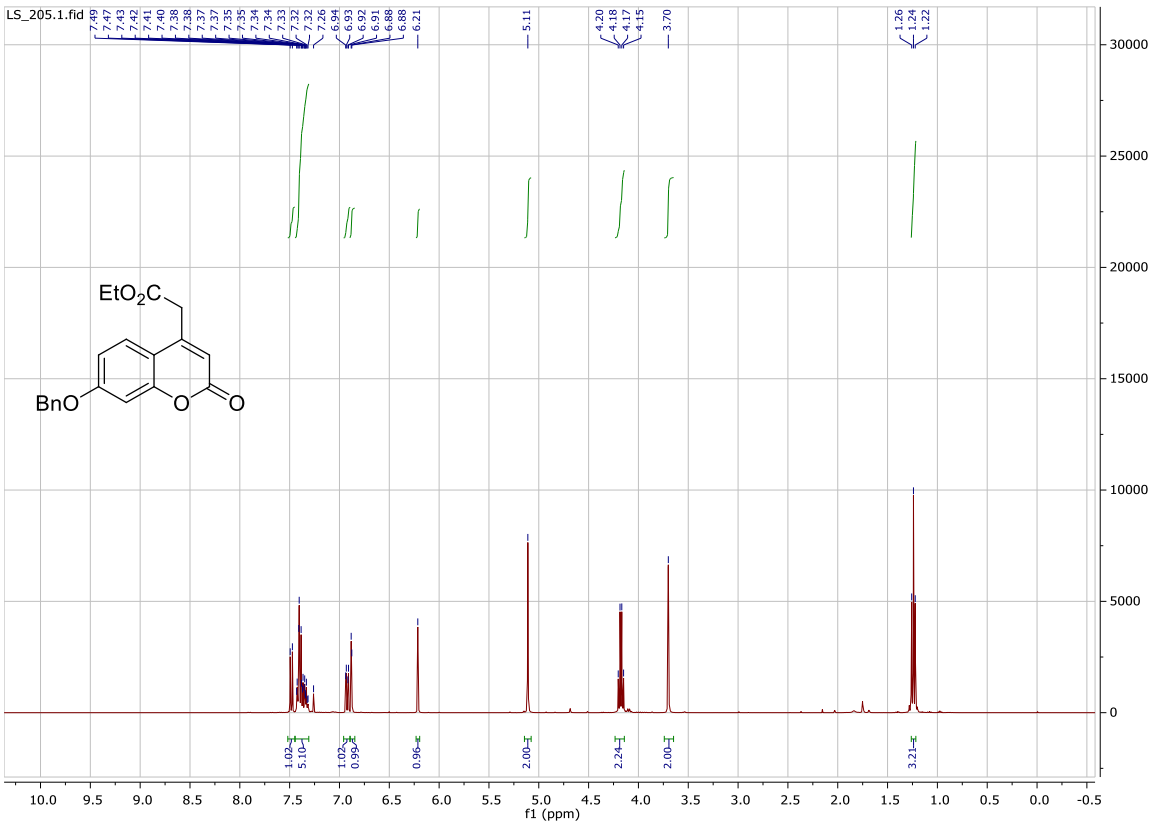


^{1}H NMR (400 MHz, $CDCl_3$) of 9a



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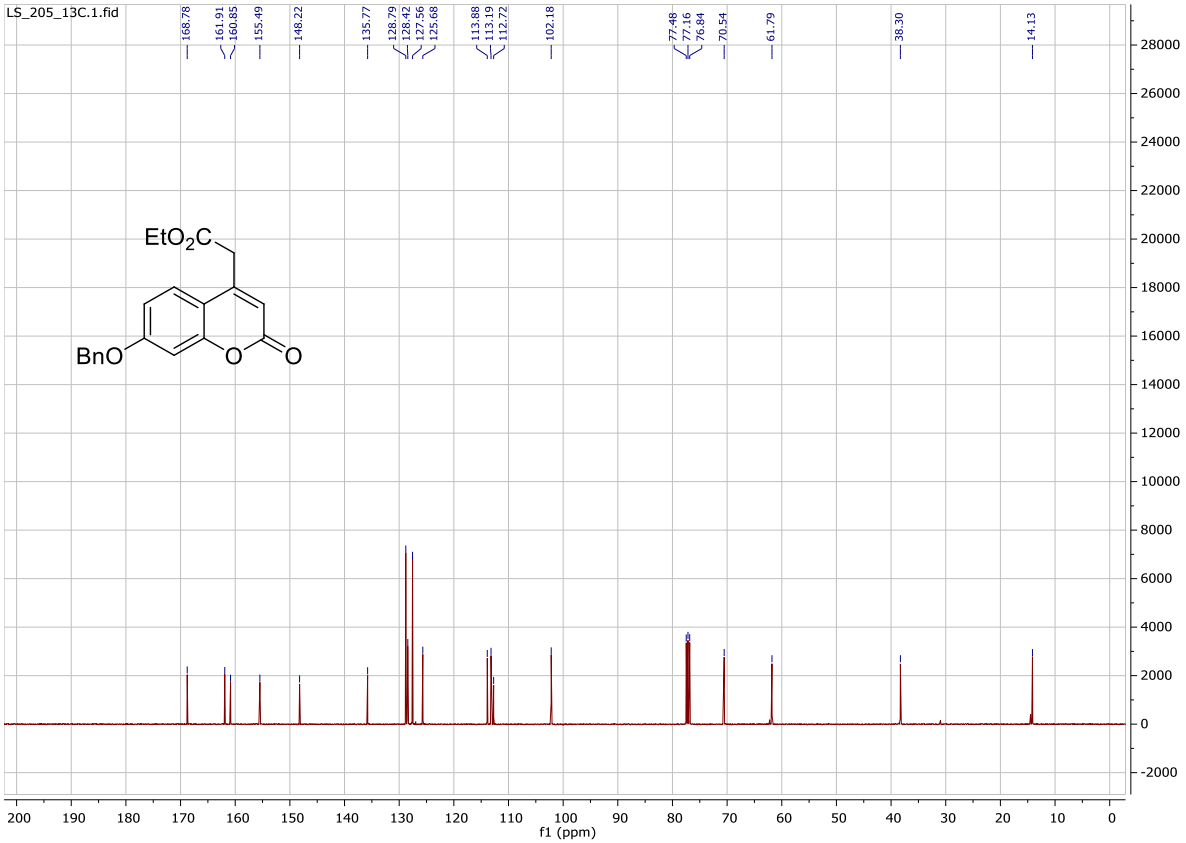

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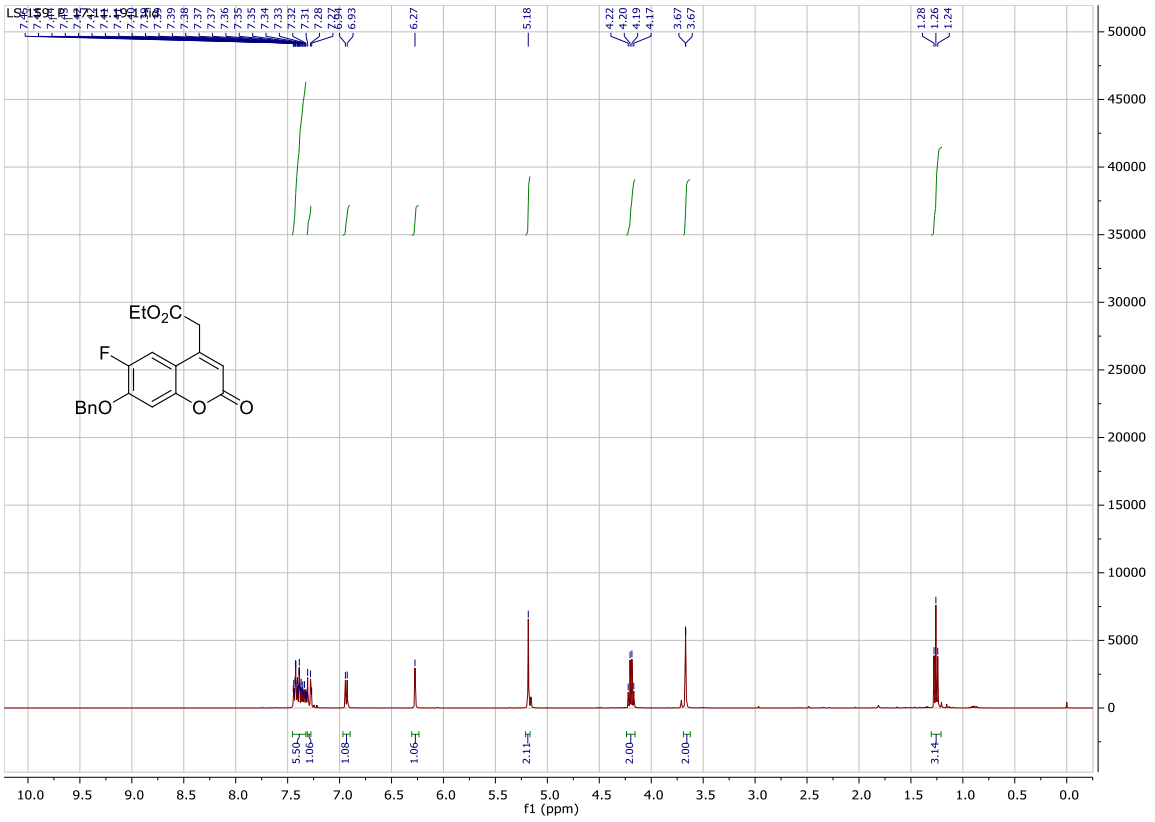

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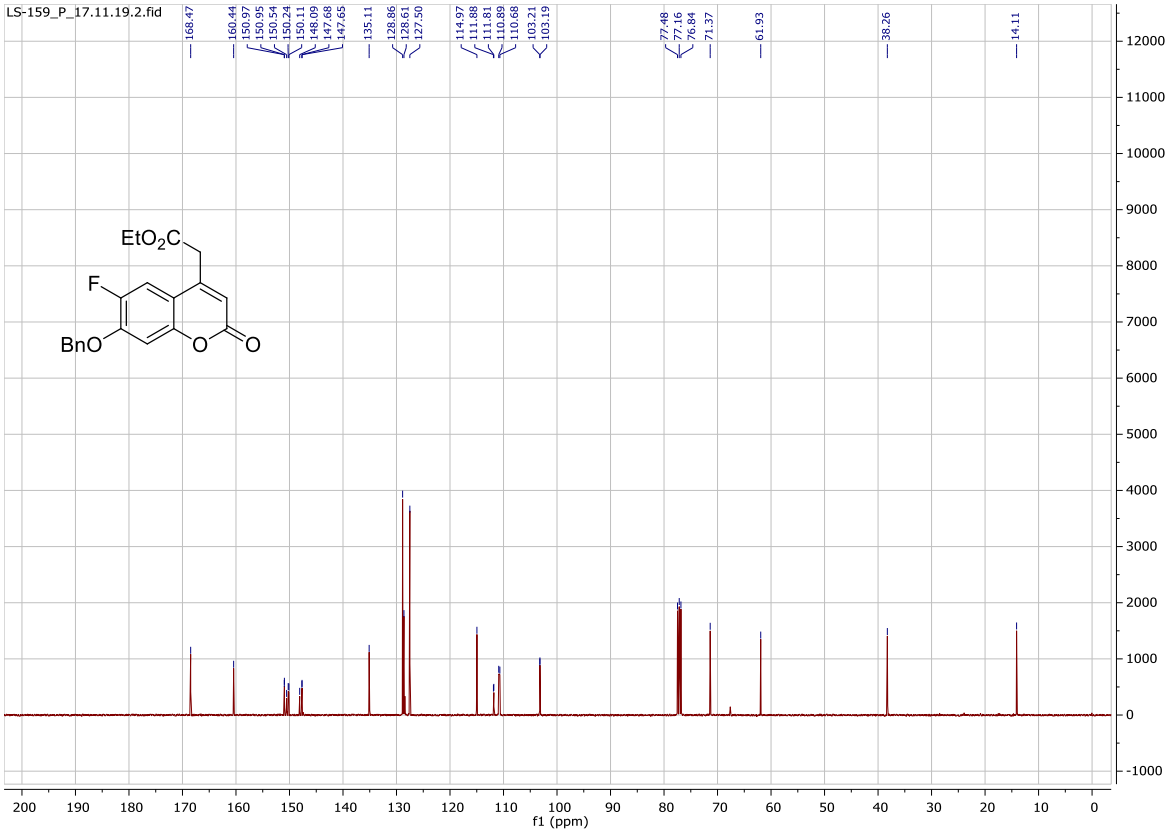

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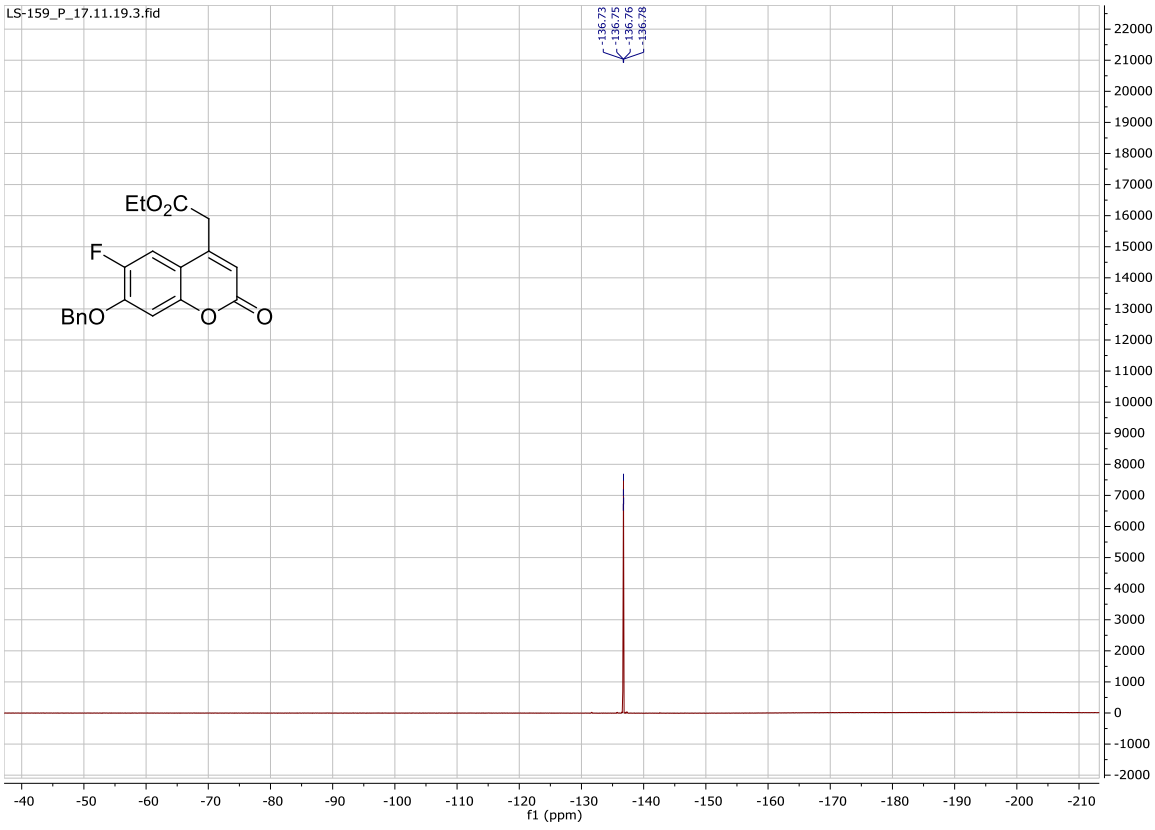

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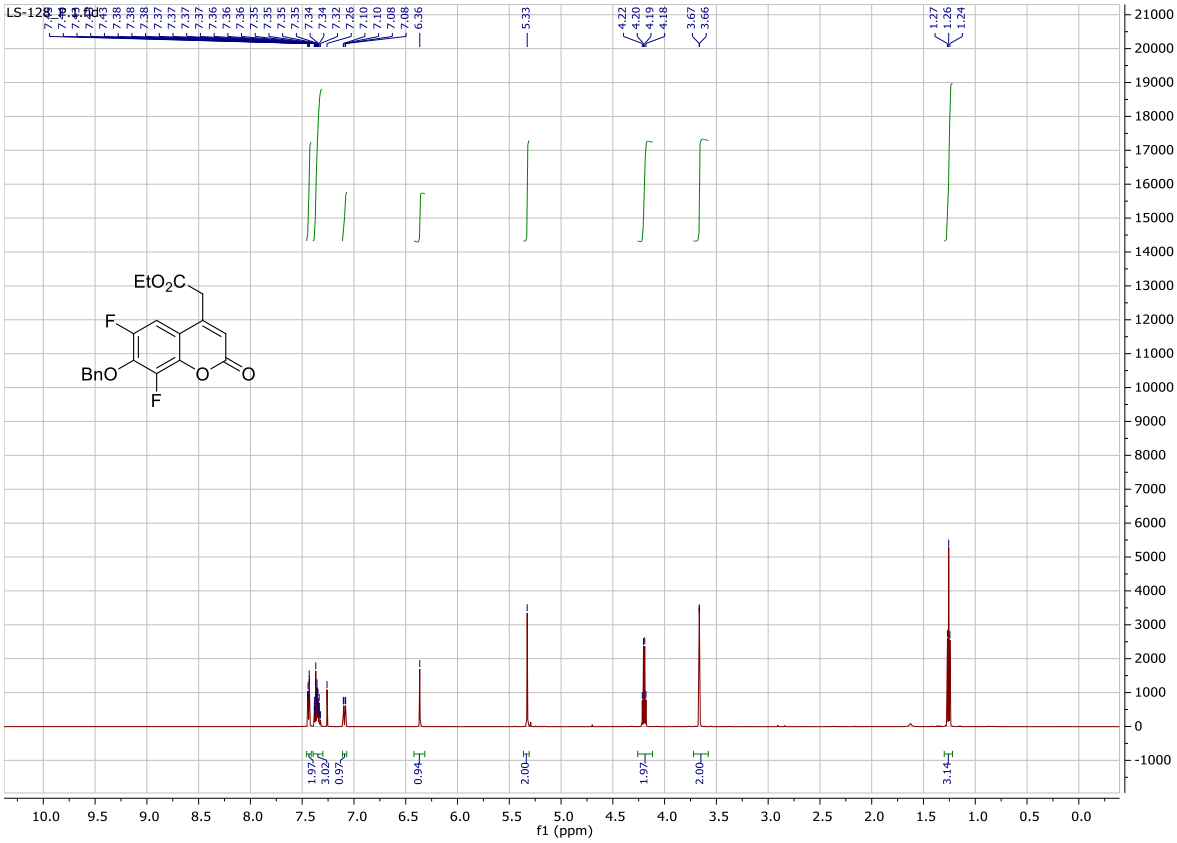

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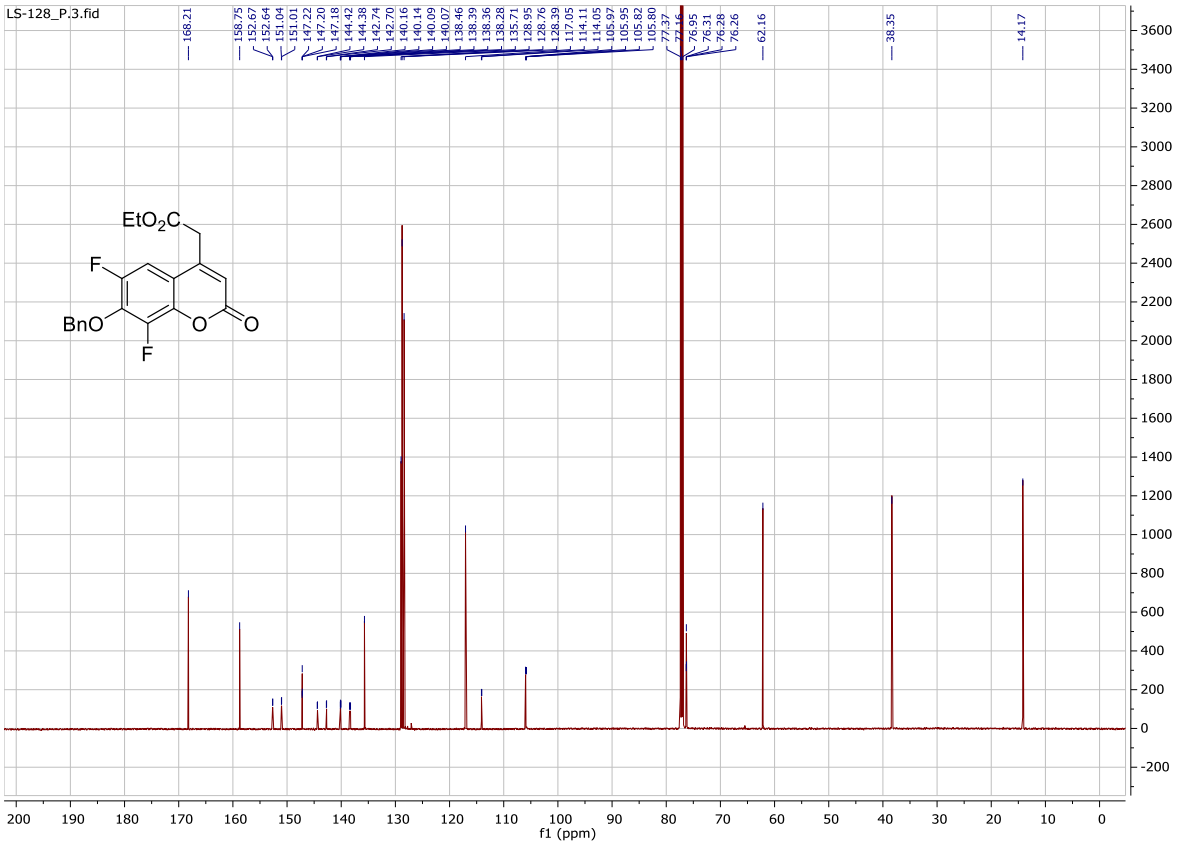

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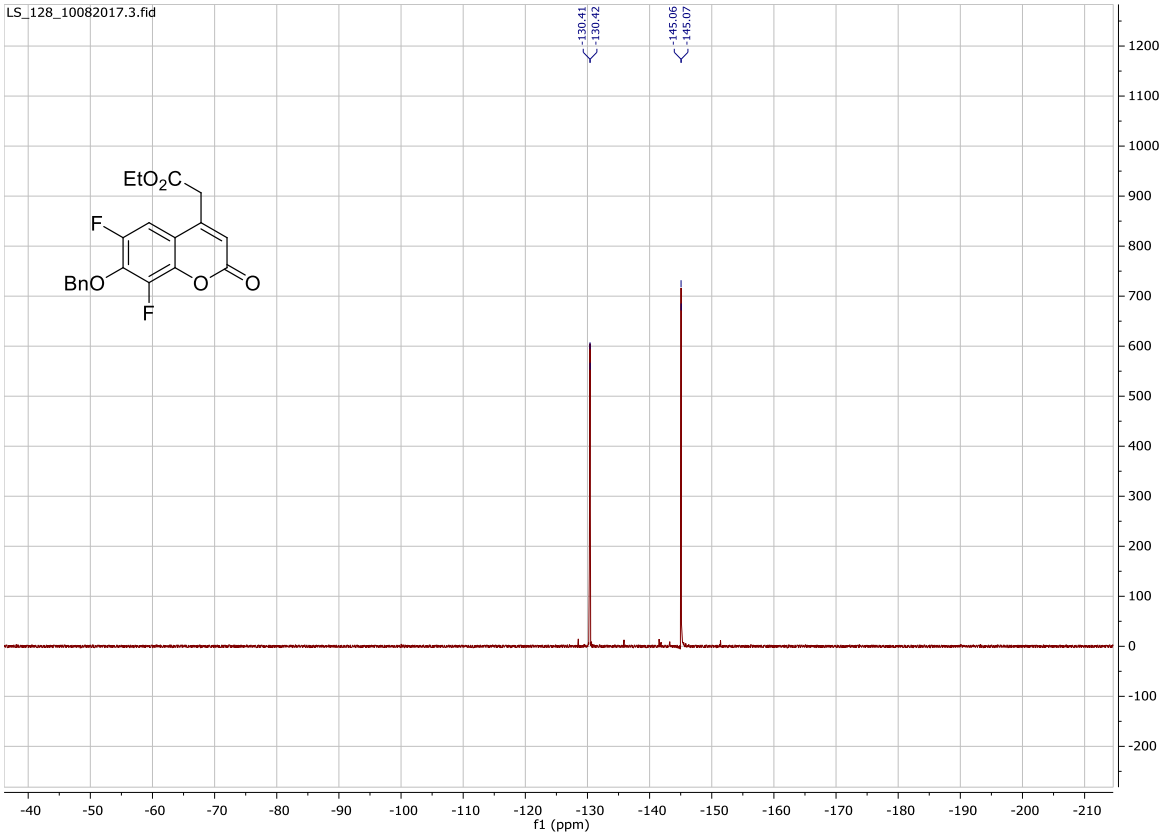

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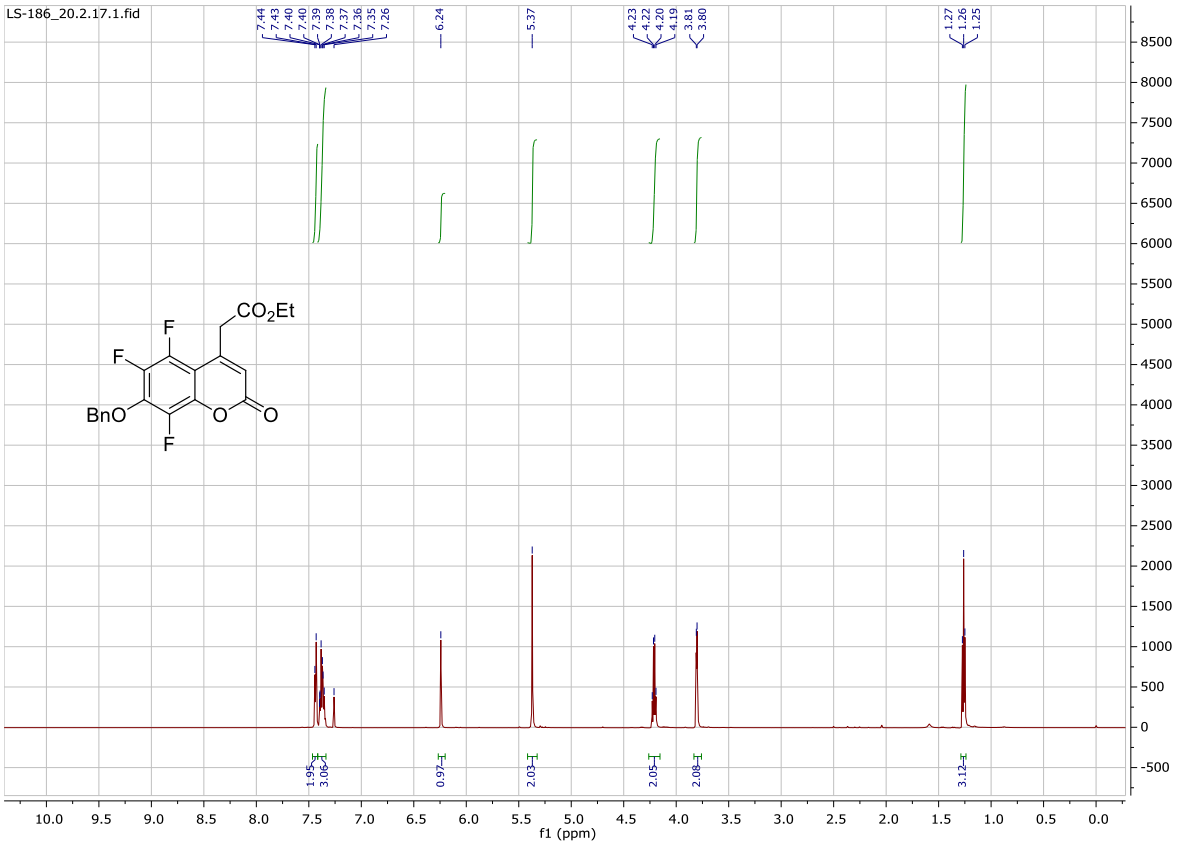

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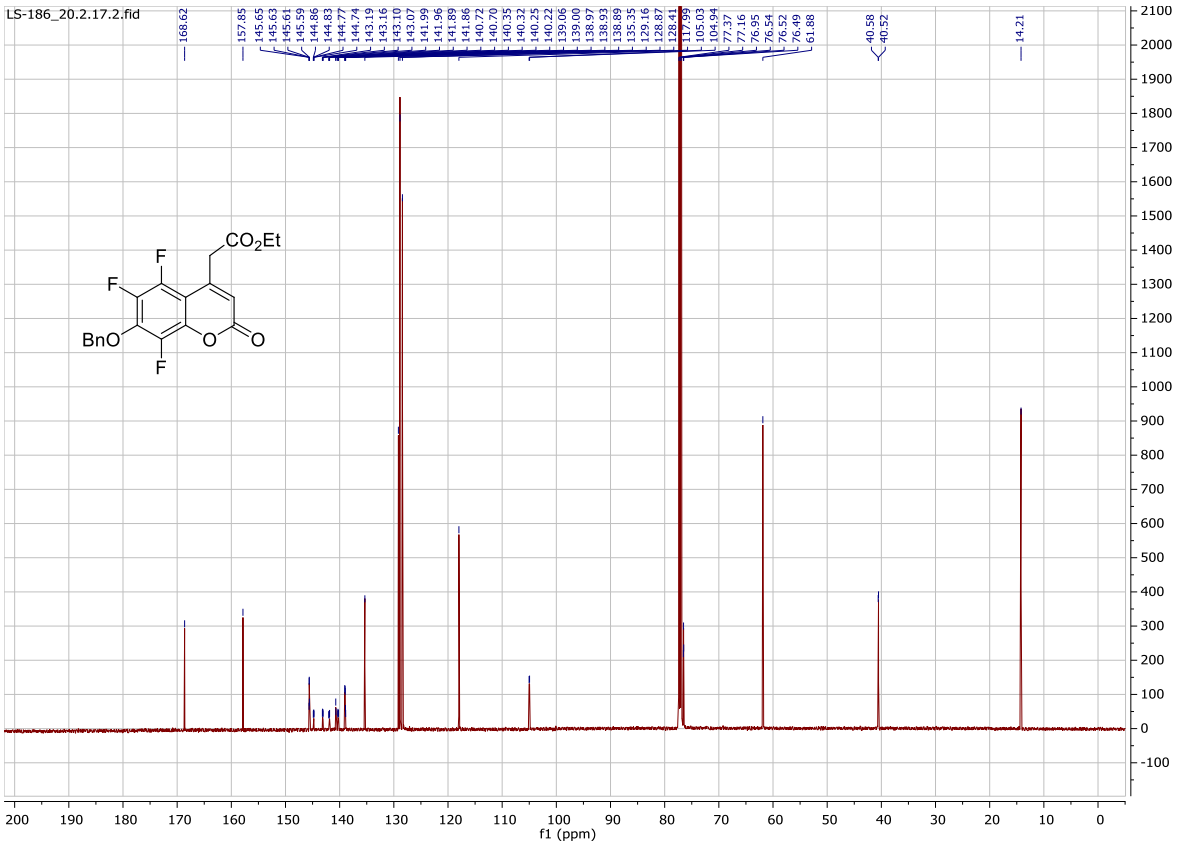

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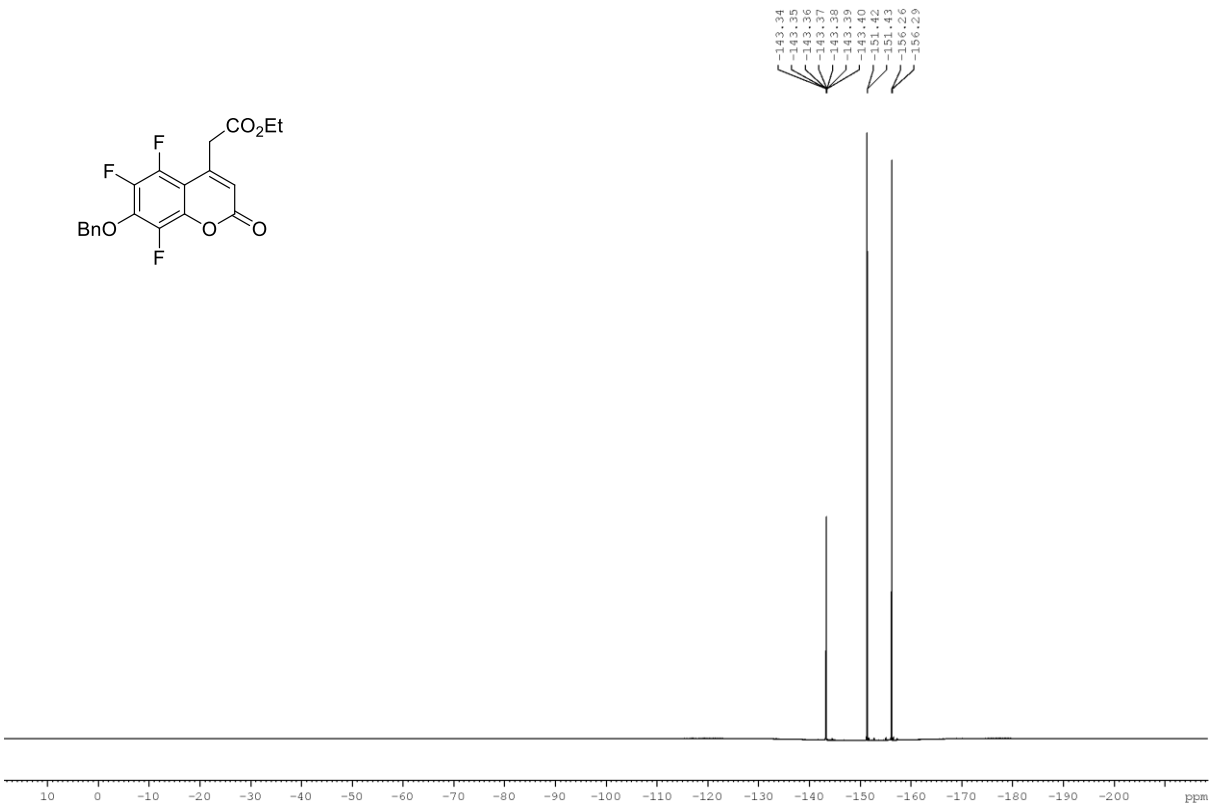

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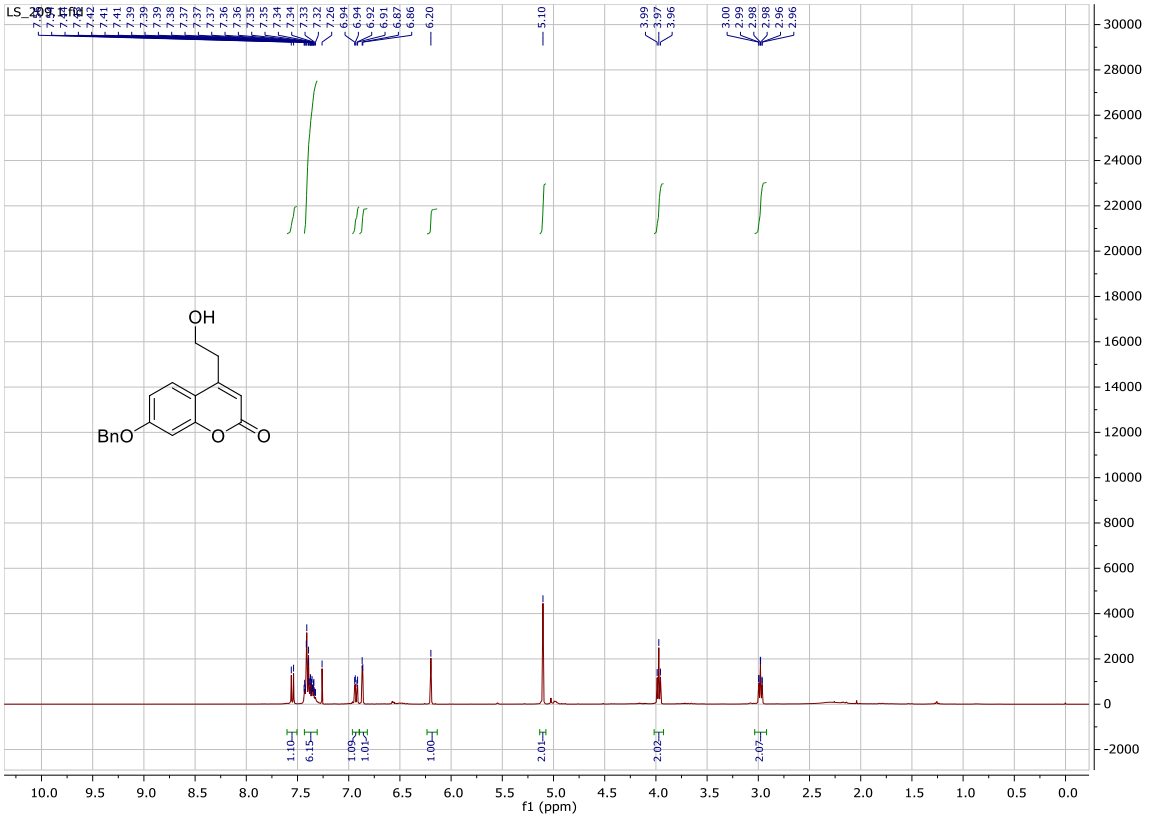

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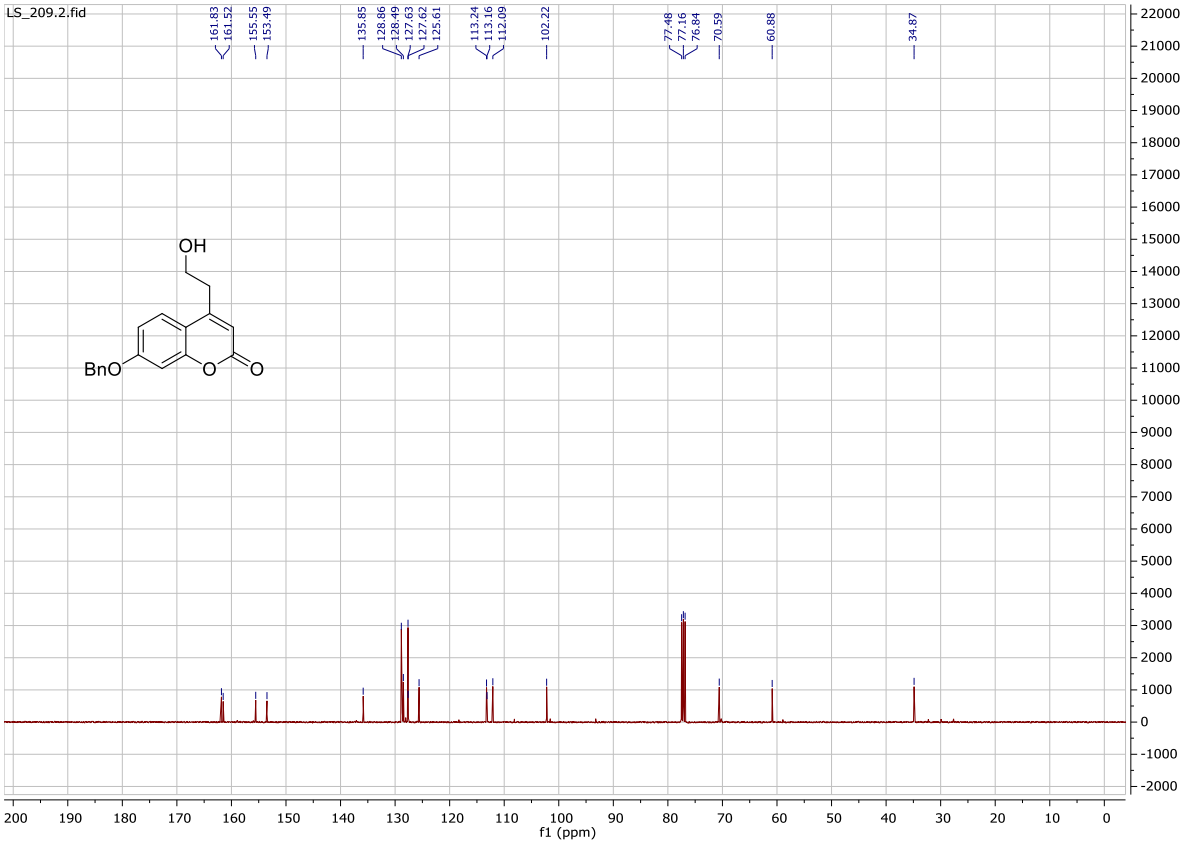

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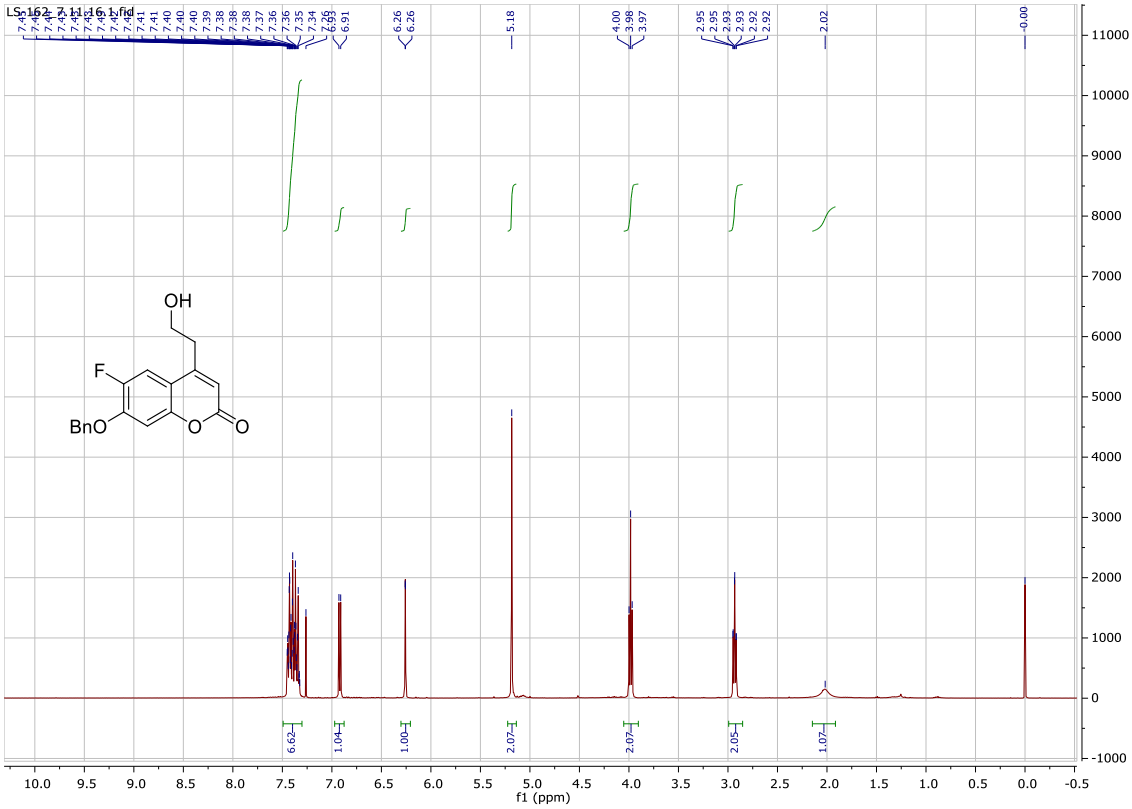

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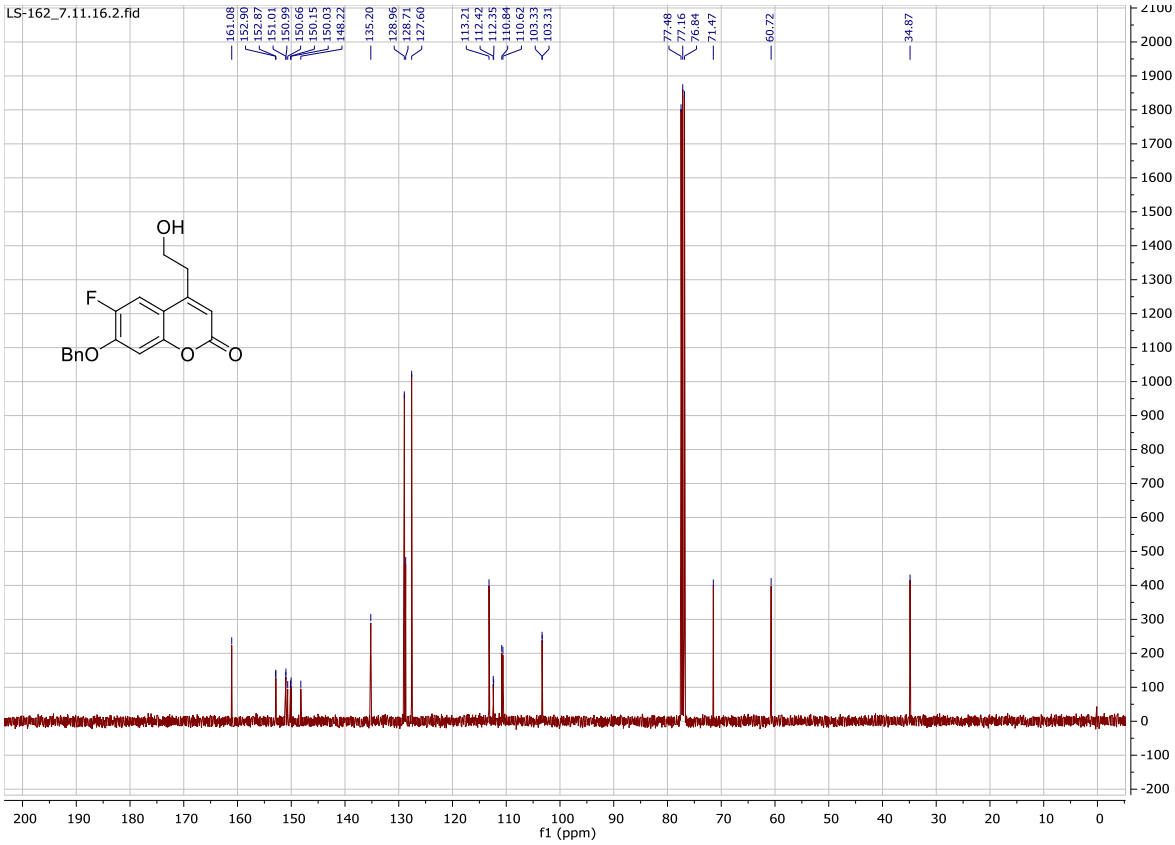

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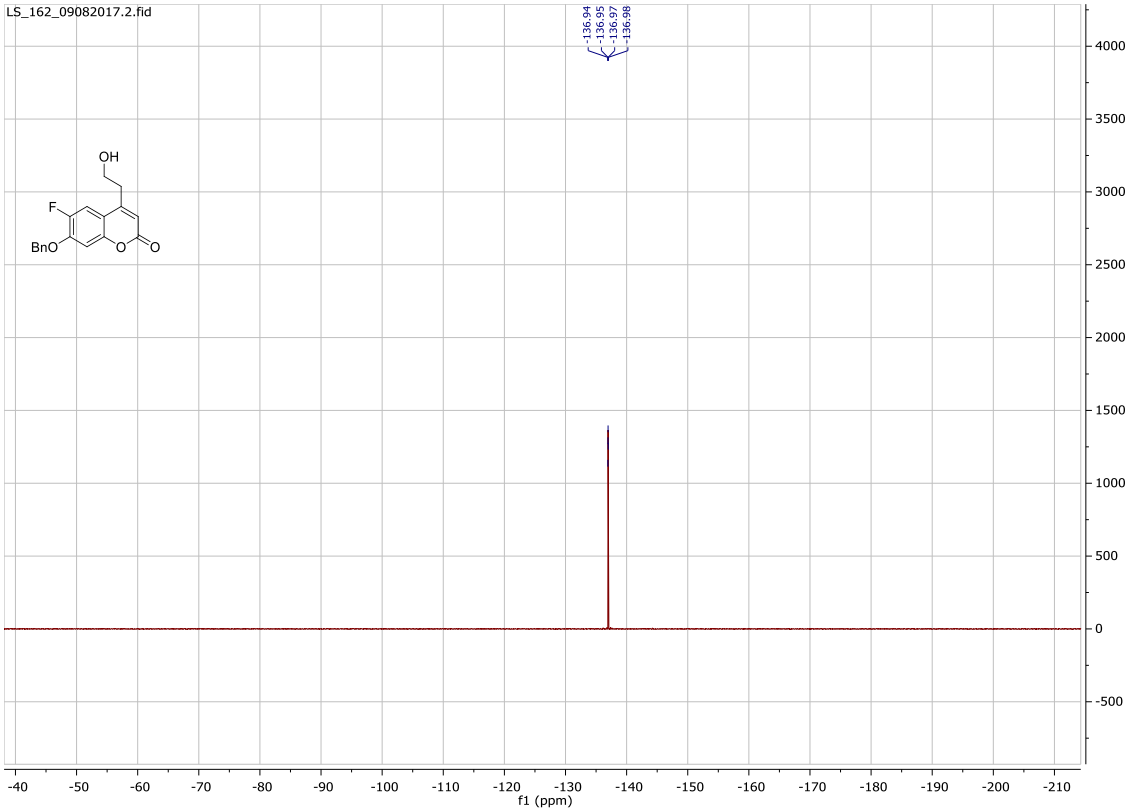

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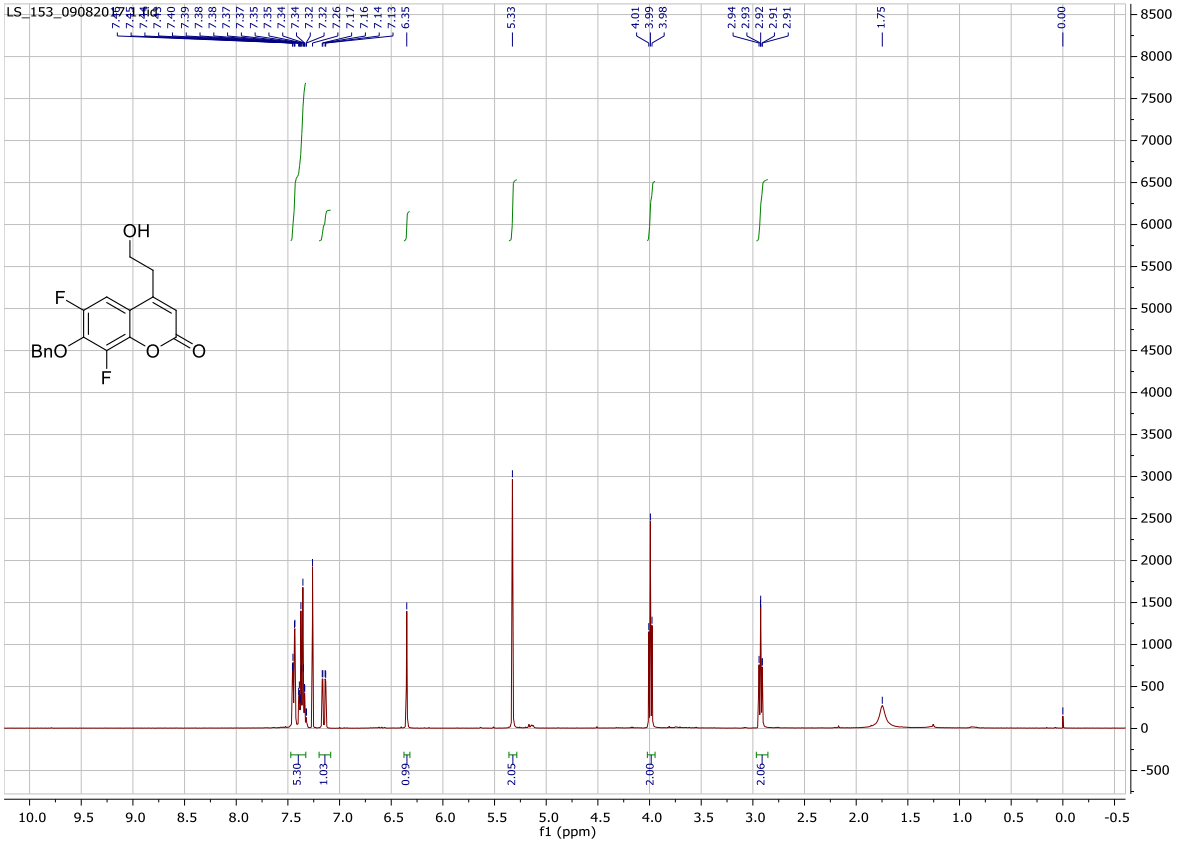

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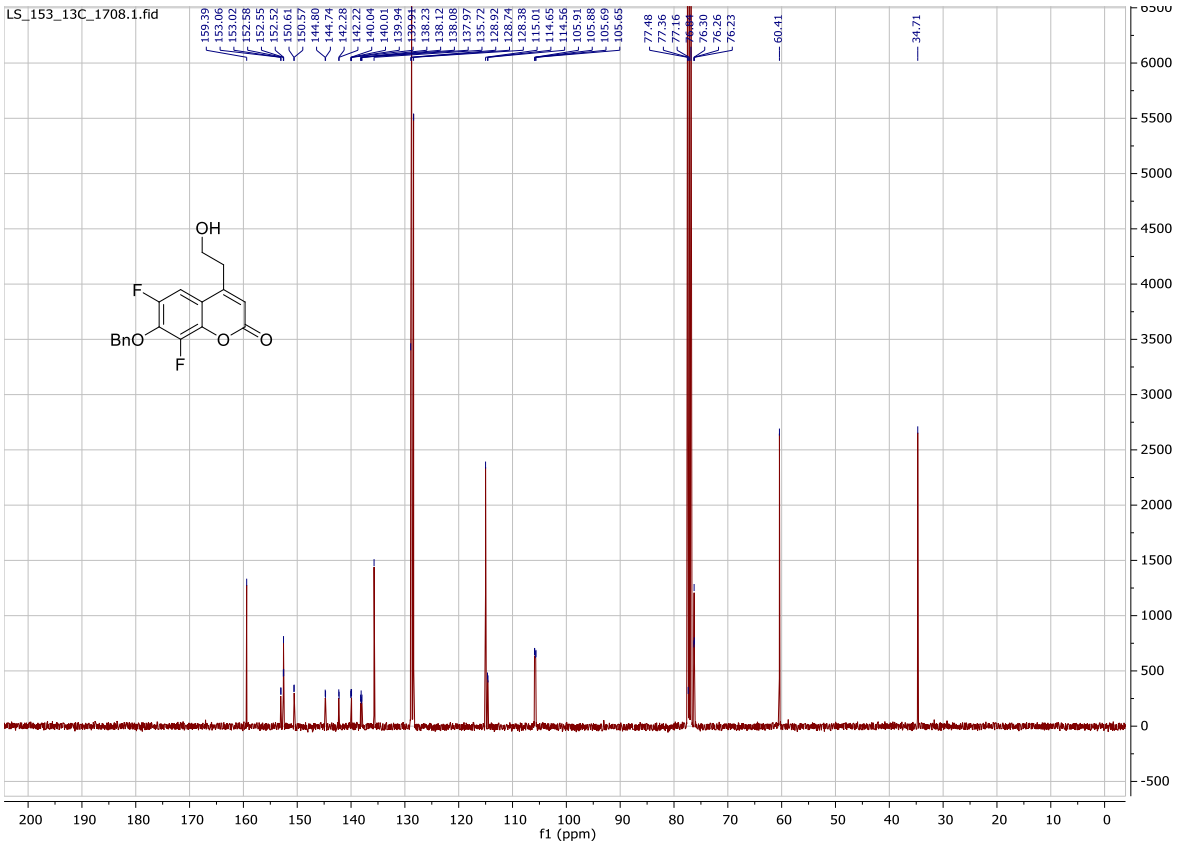

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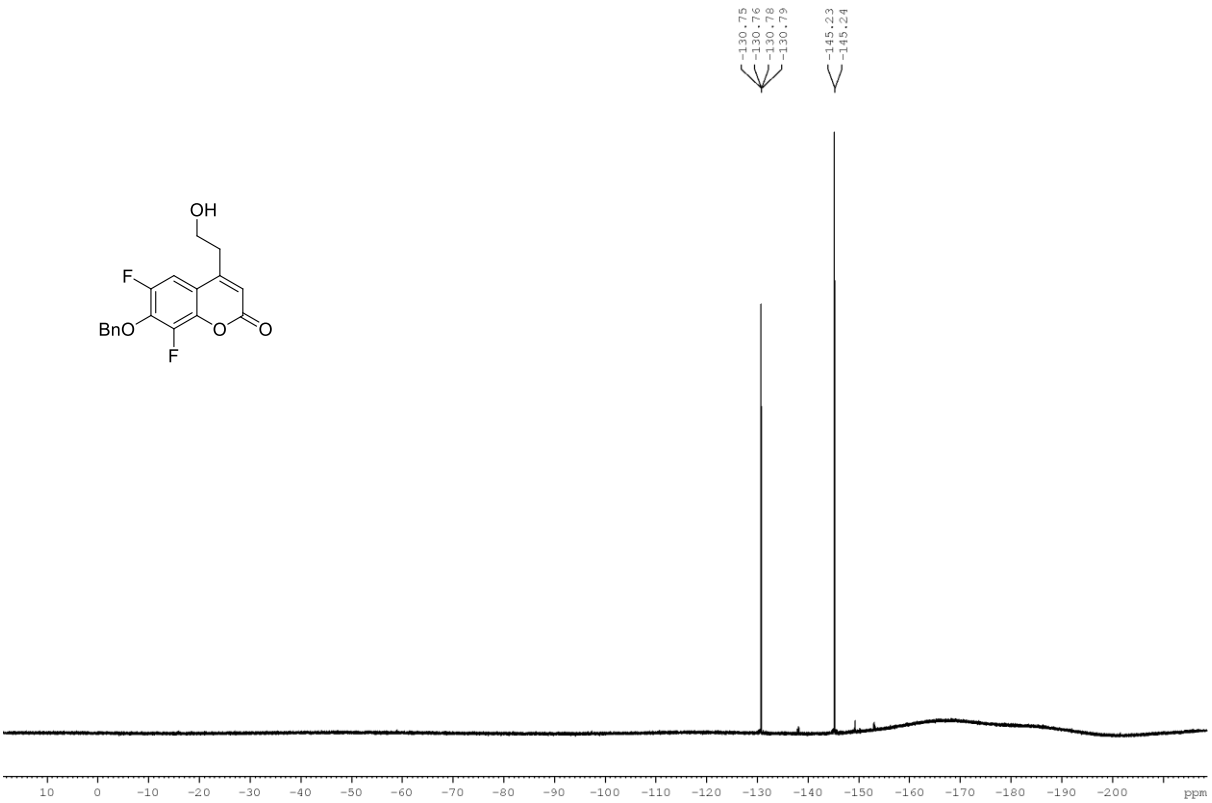
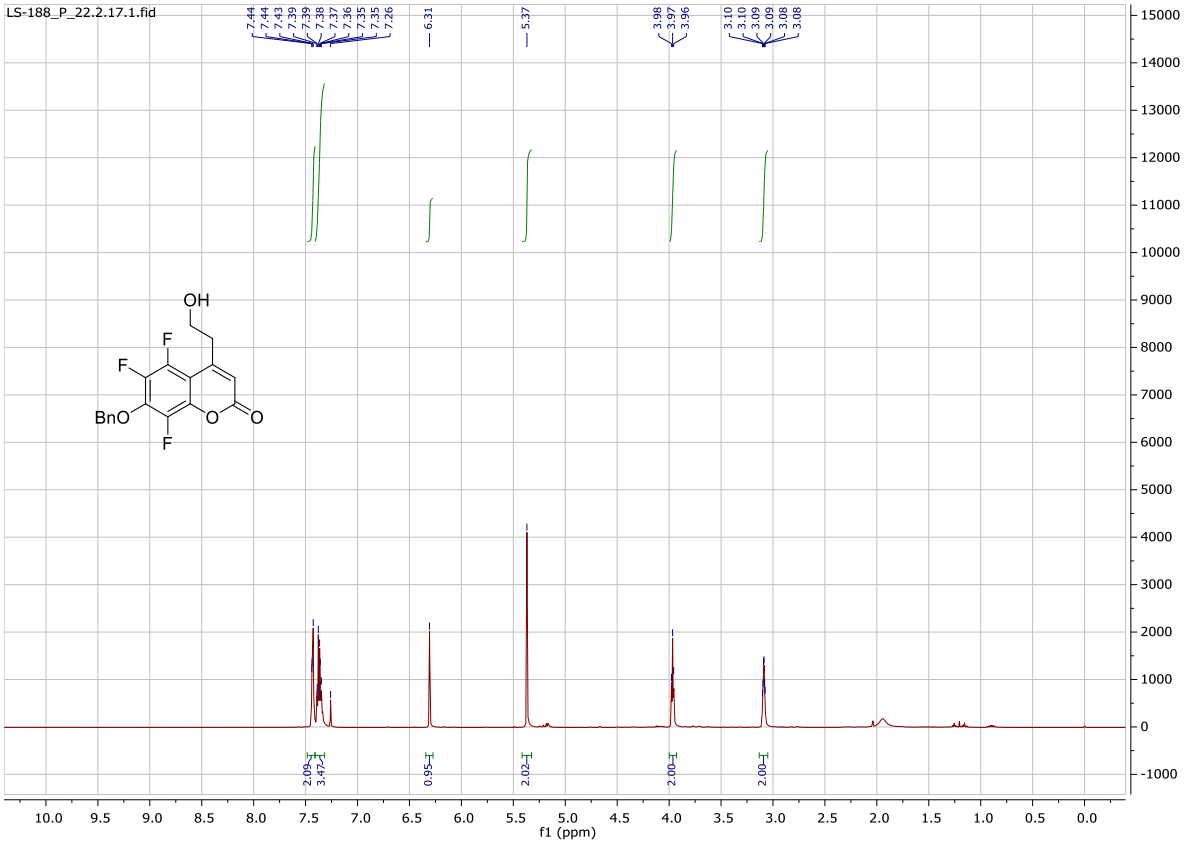
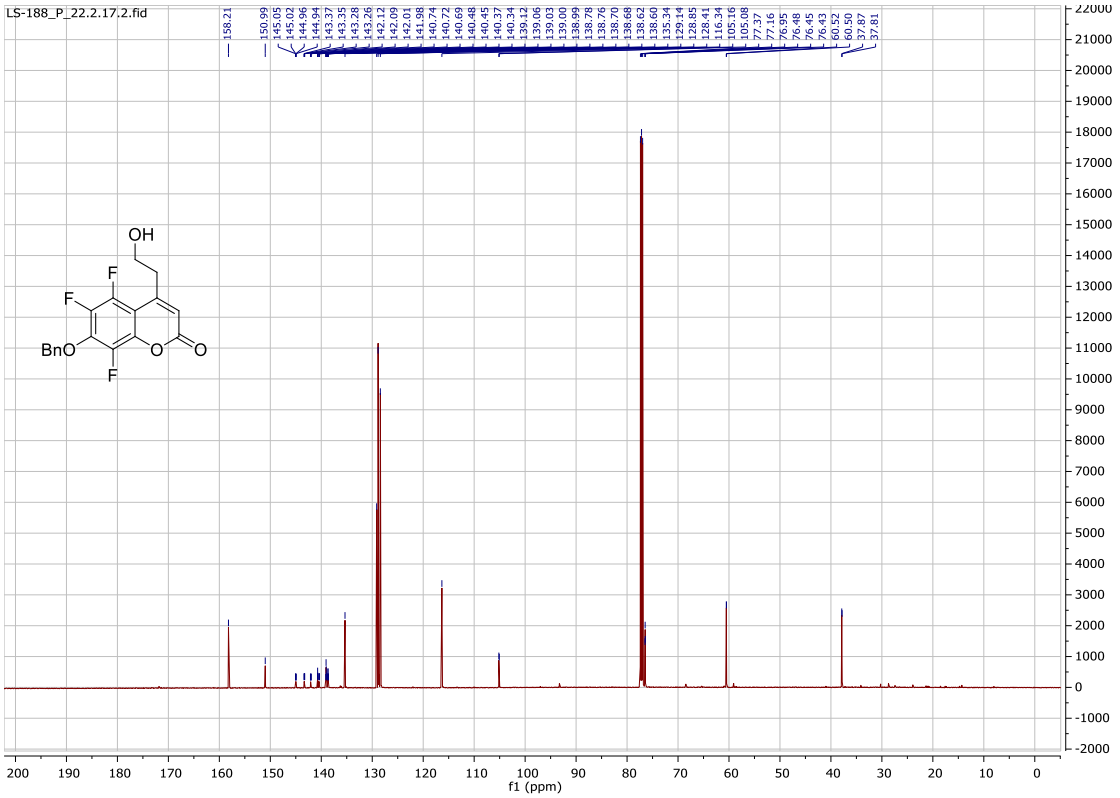


^{1}H NMR (600 MHz, $CDCl_3$) of 11d



^{13}C NMR (151 MHz, $CDCl_3$) of 11d



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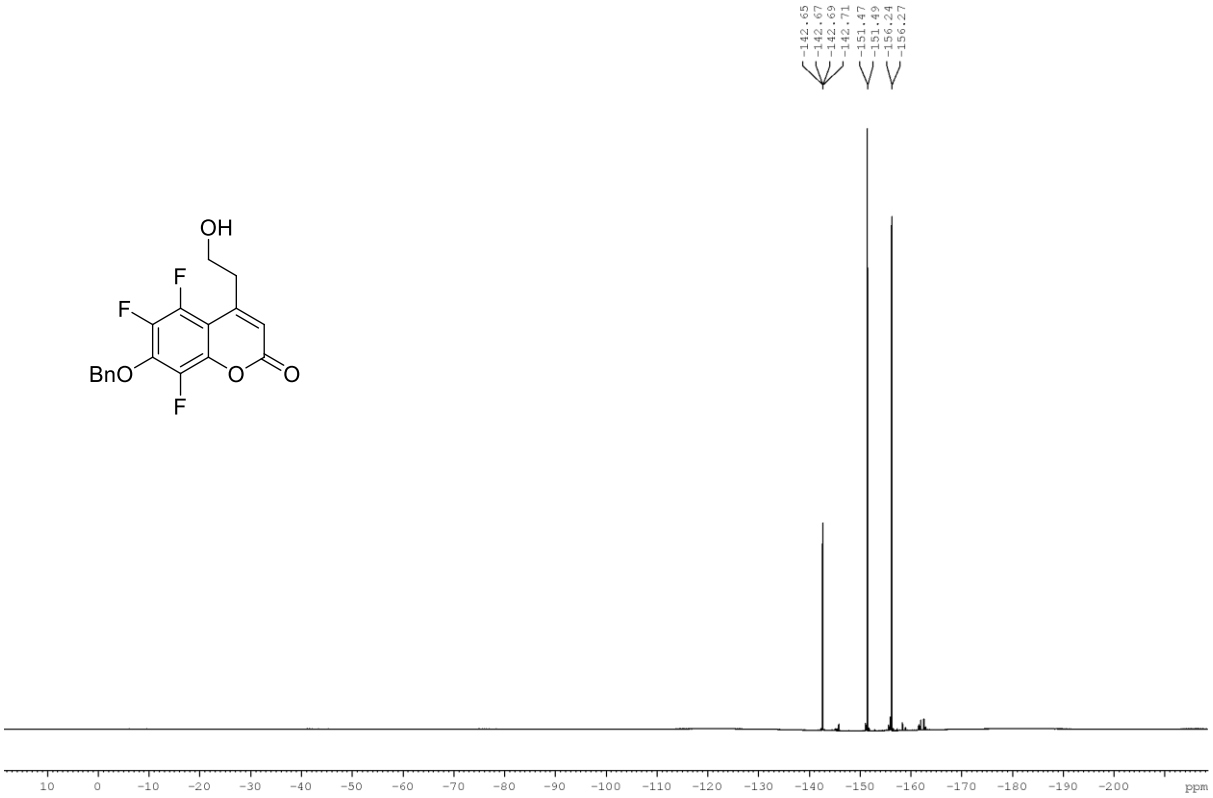

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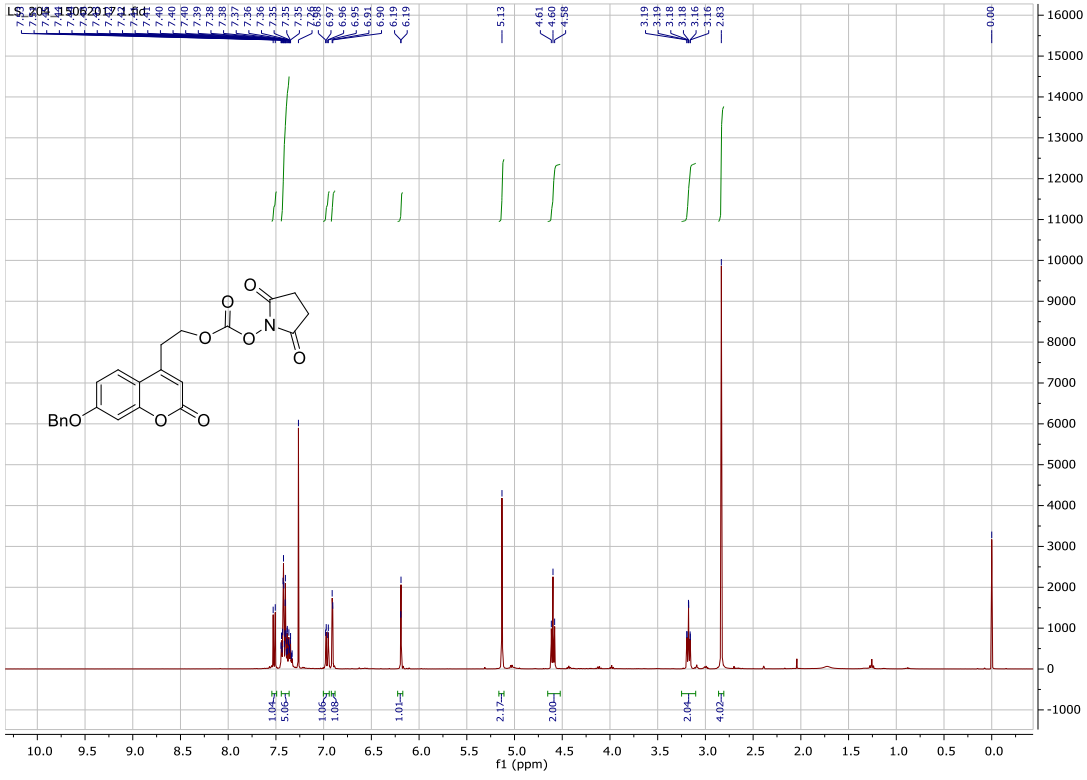

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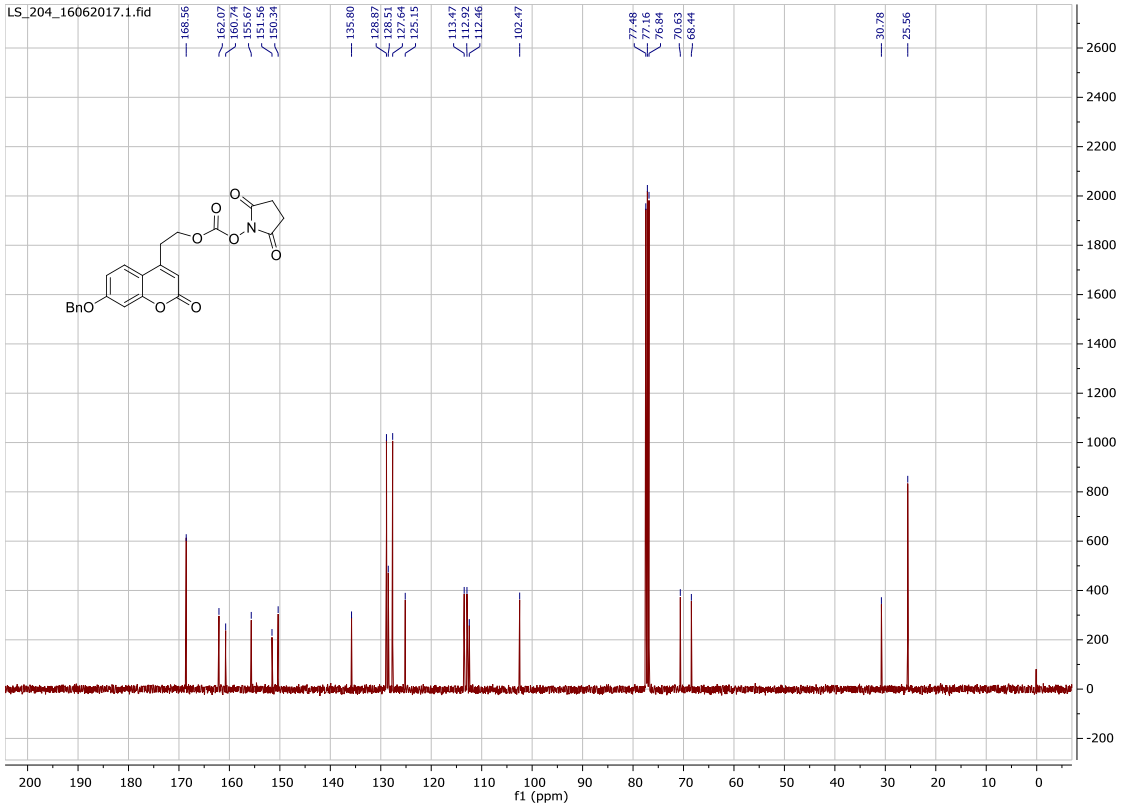

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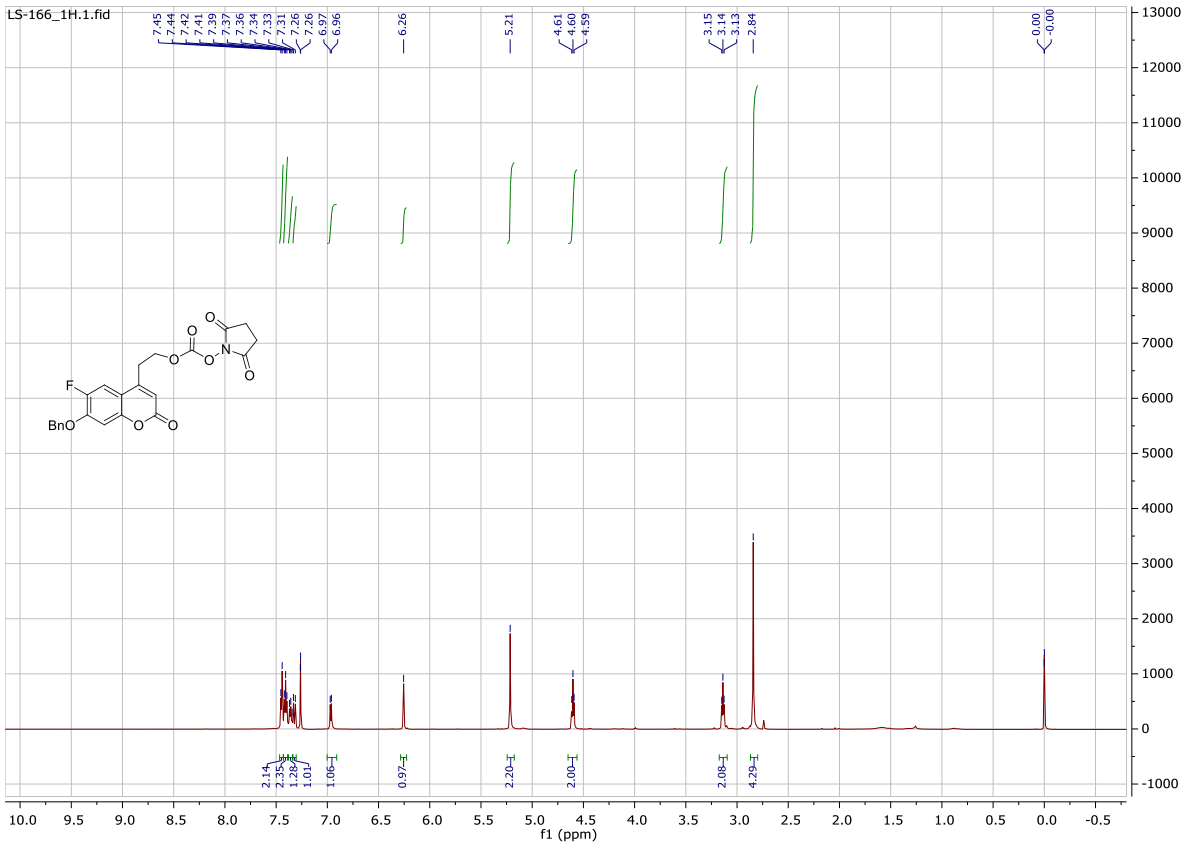

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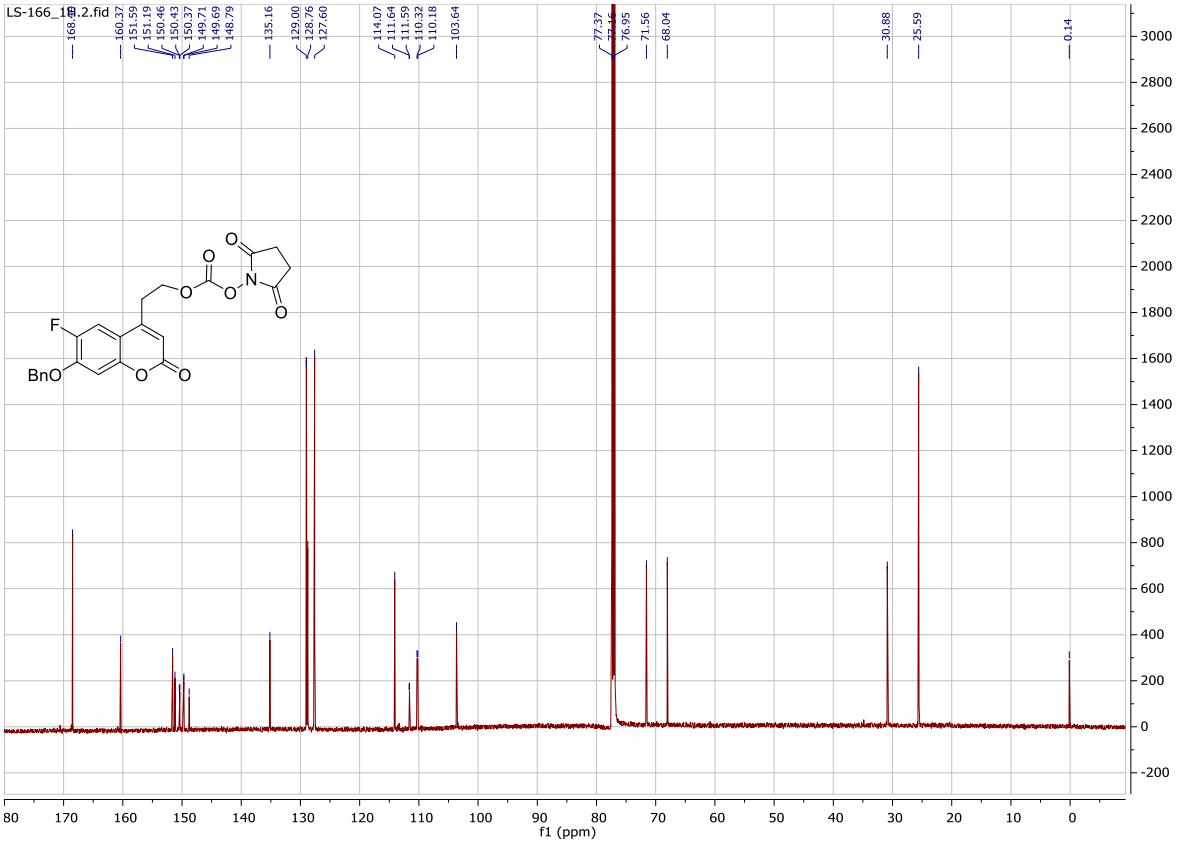

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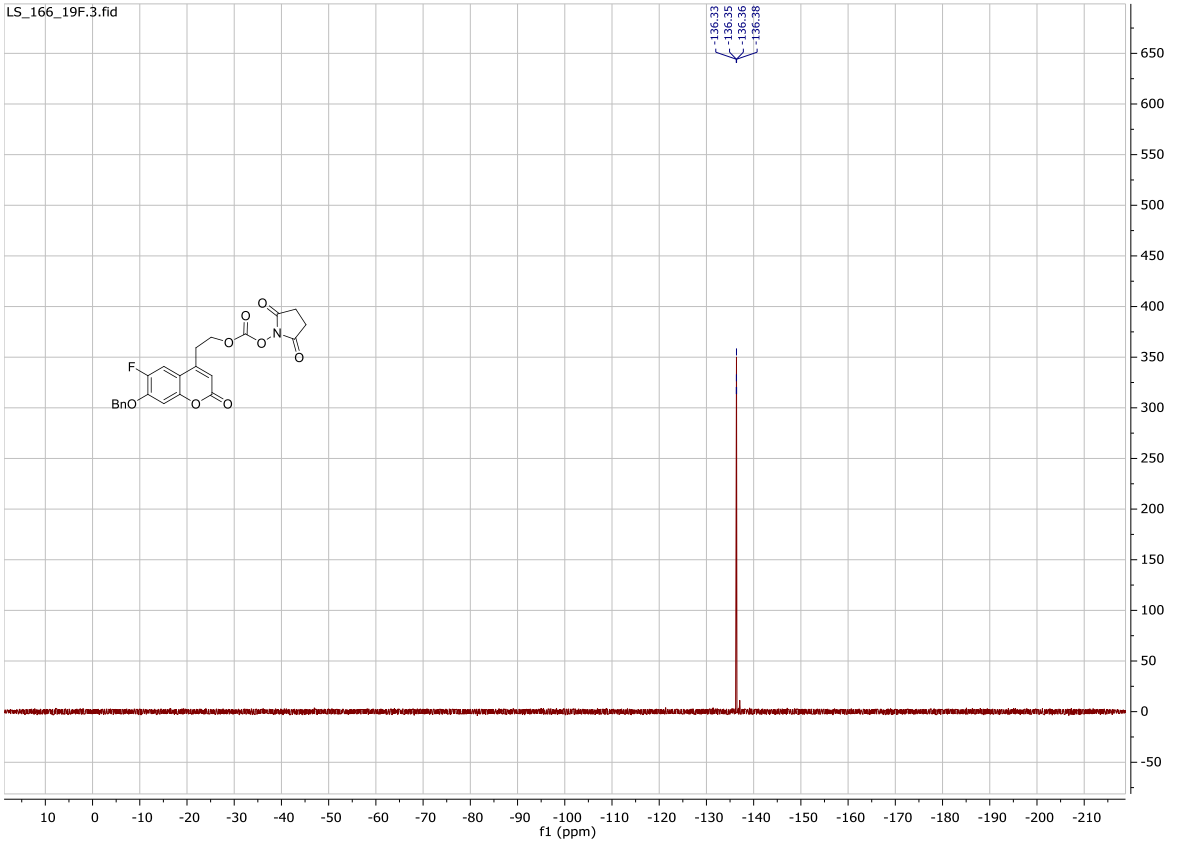

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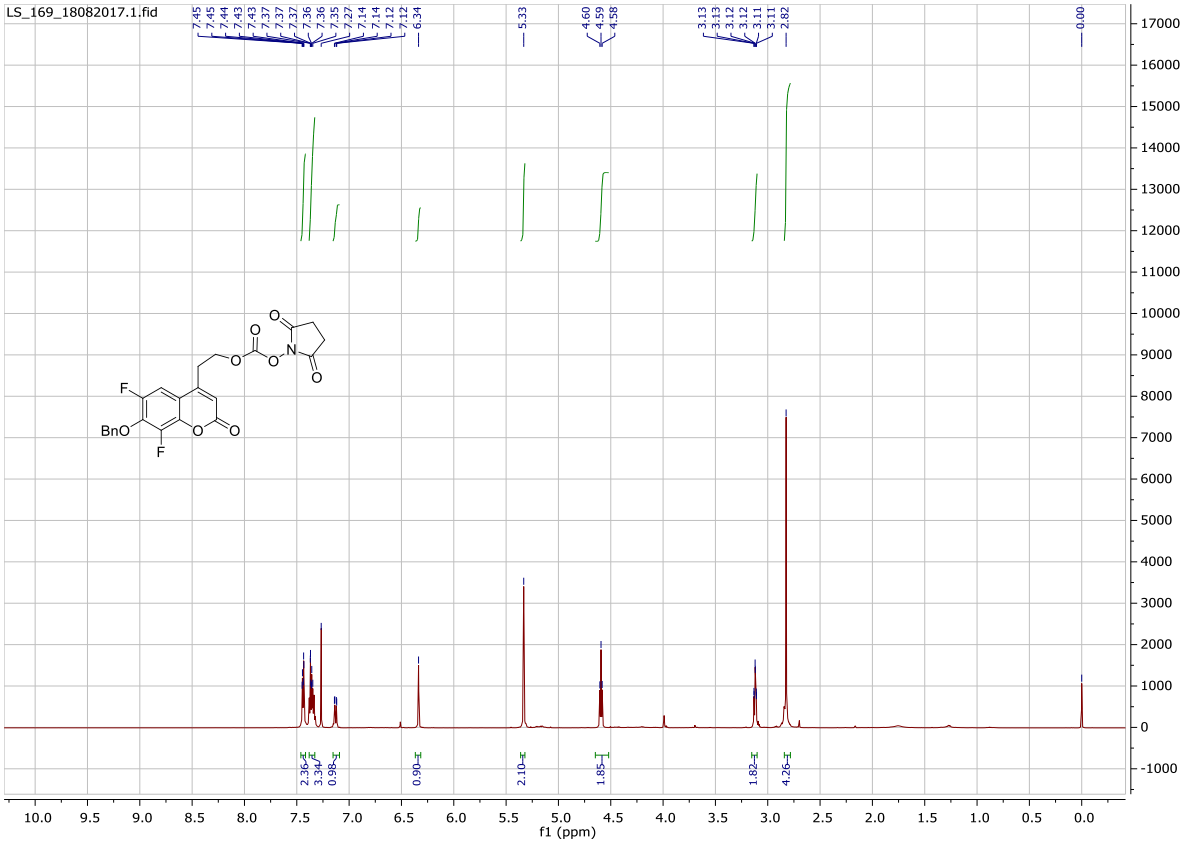

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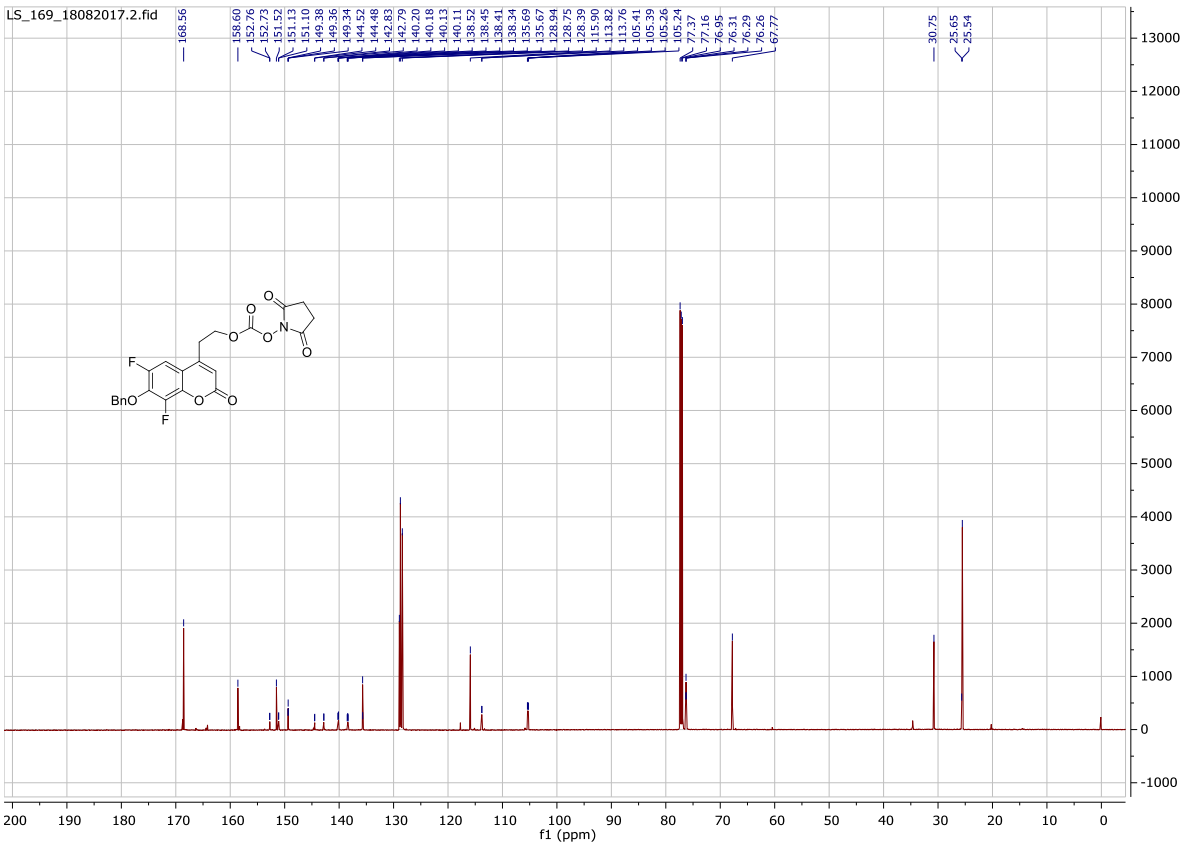

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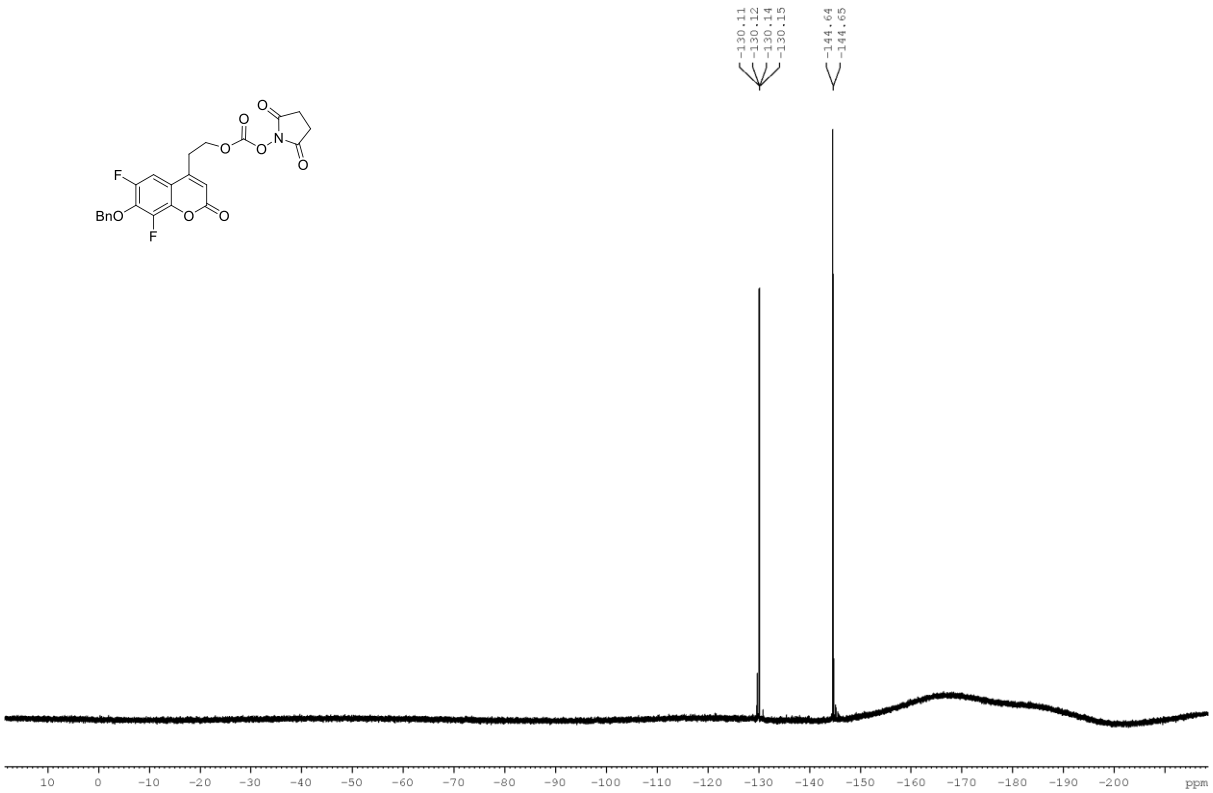

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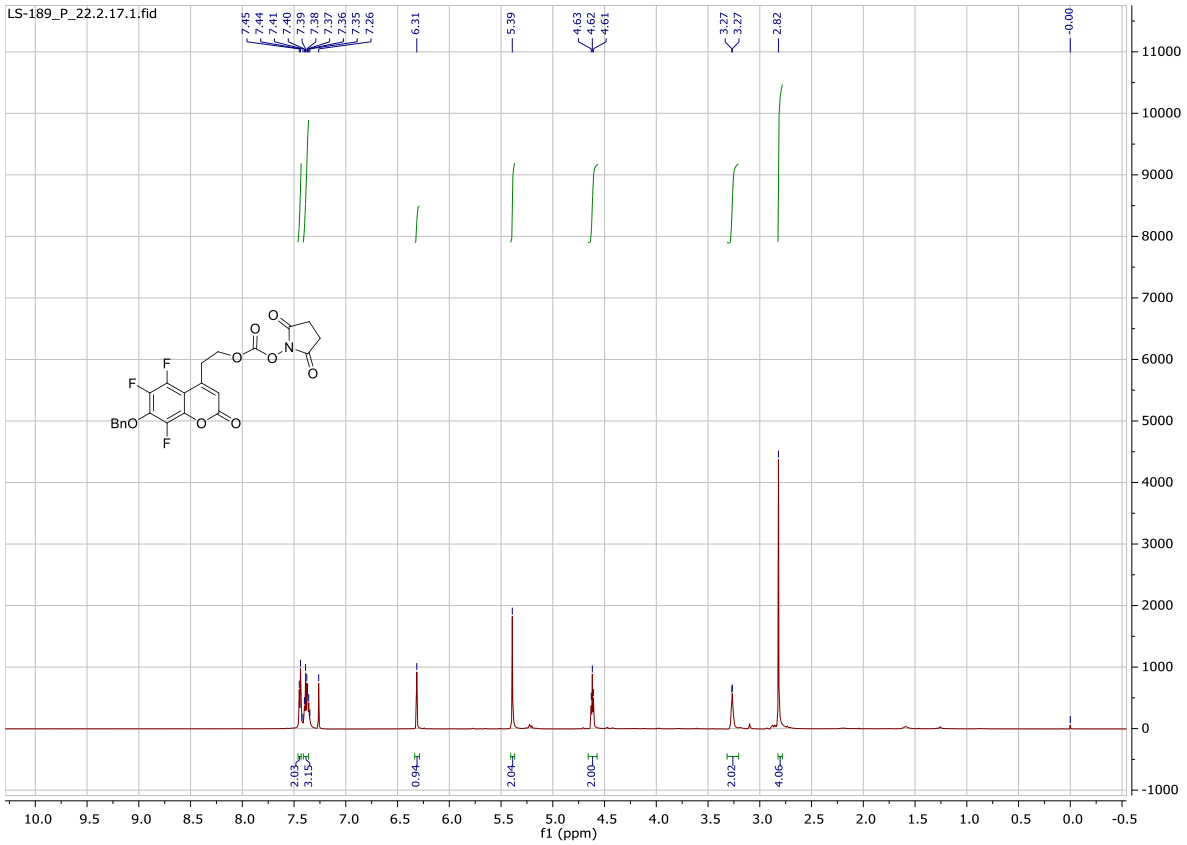

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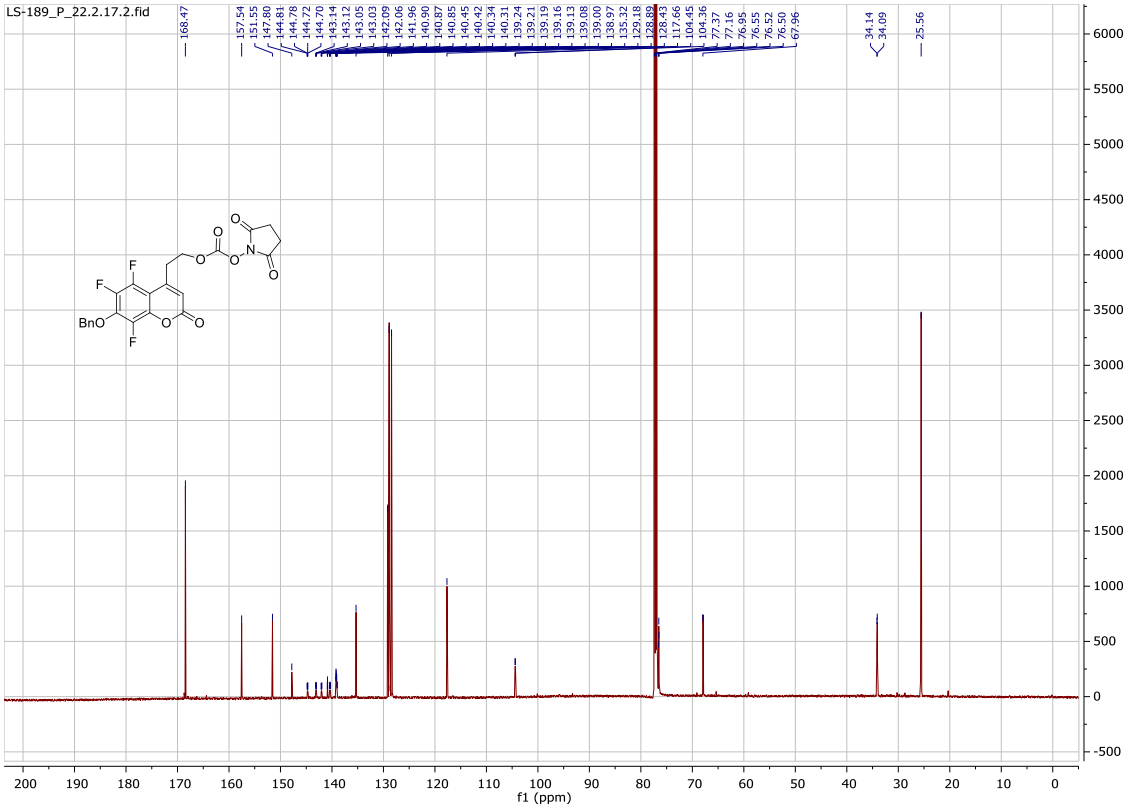

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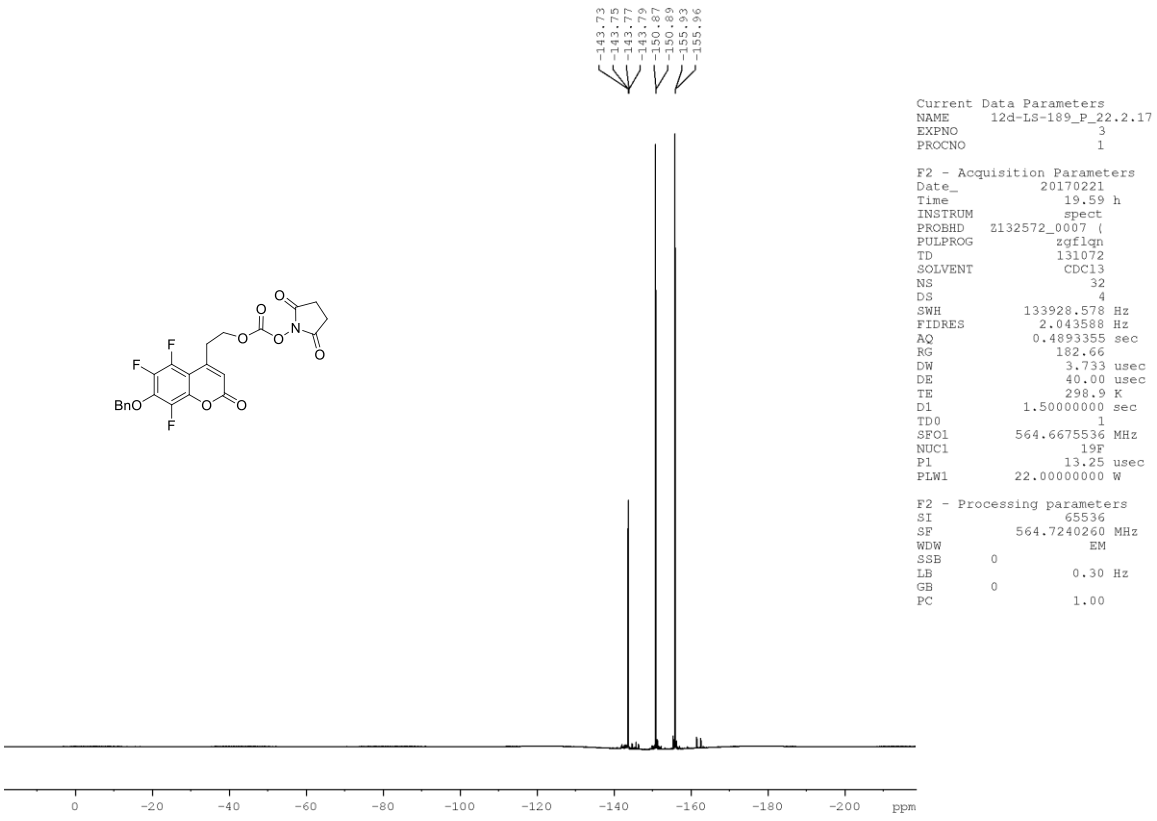


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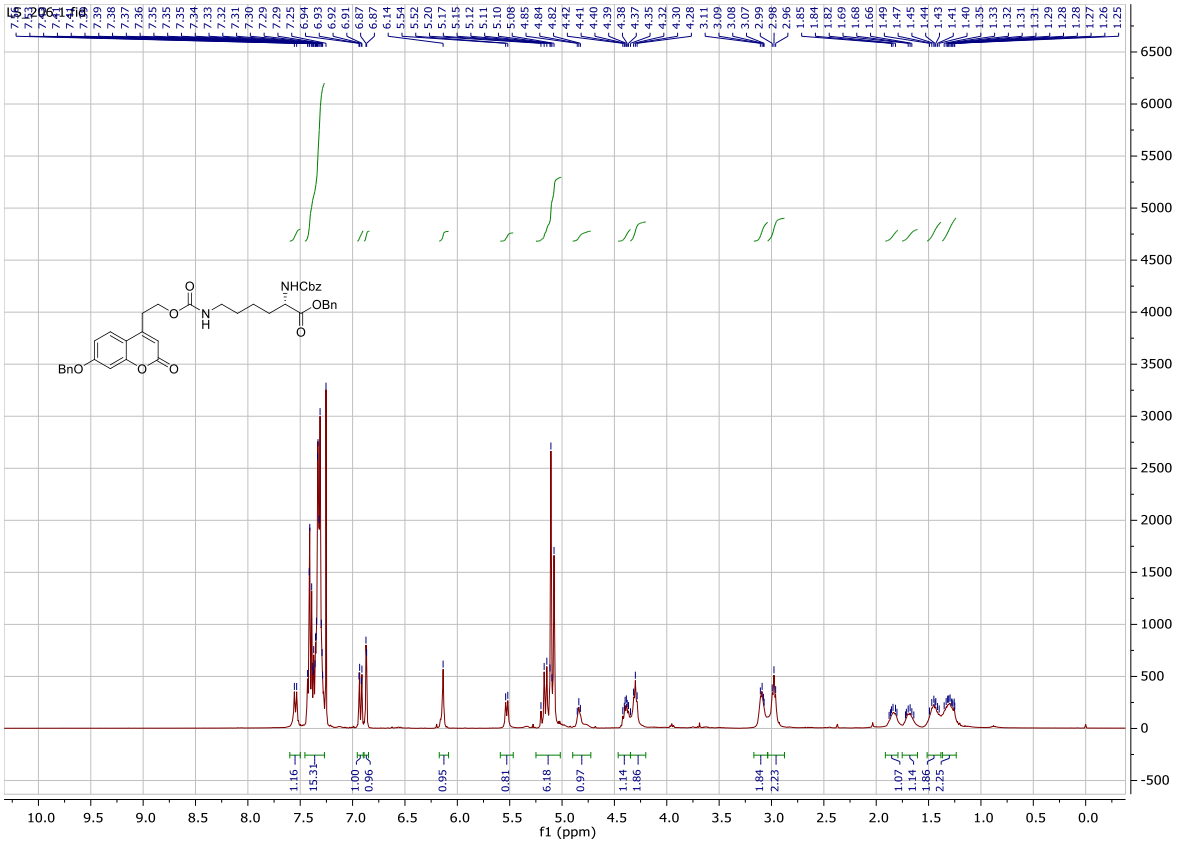

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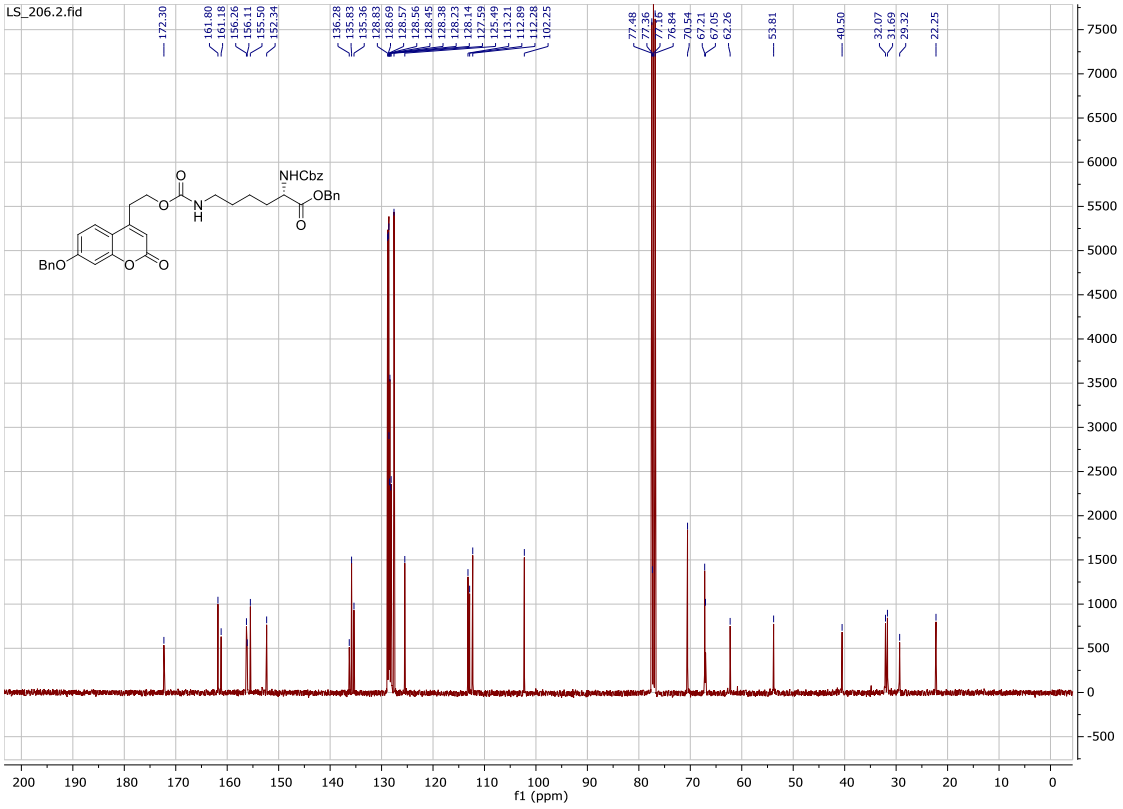

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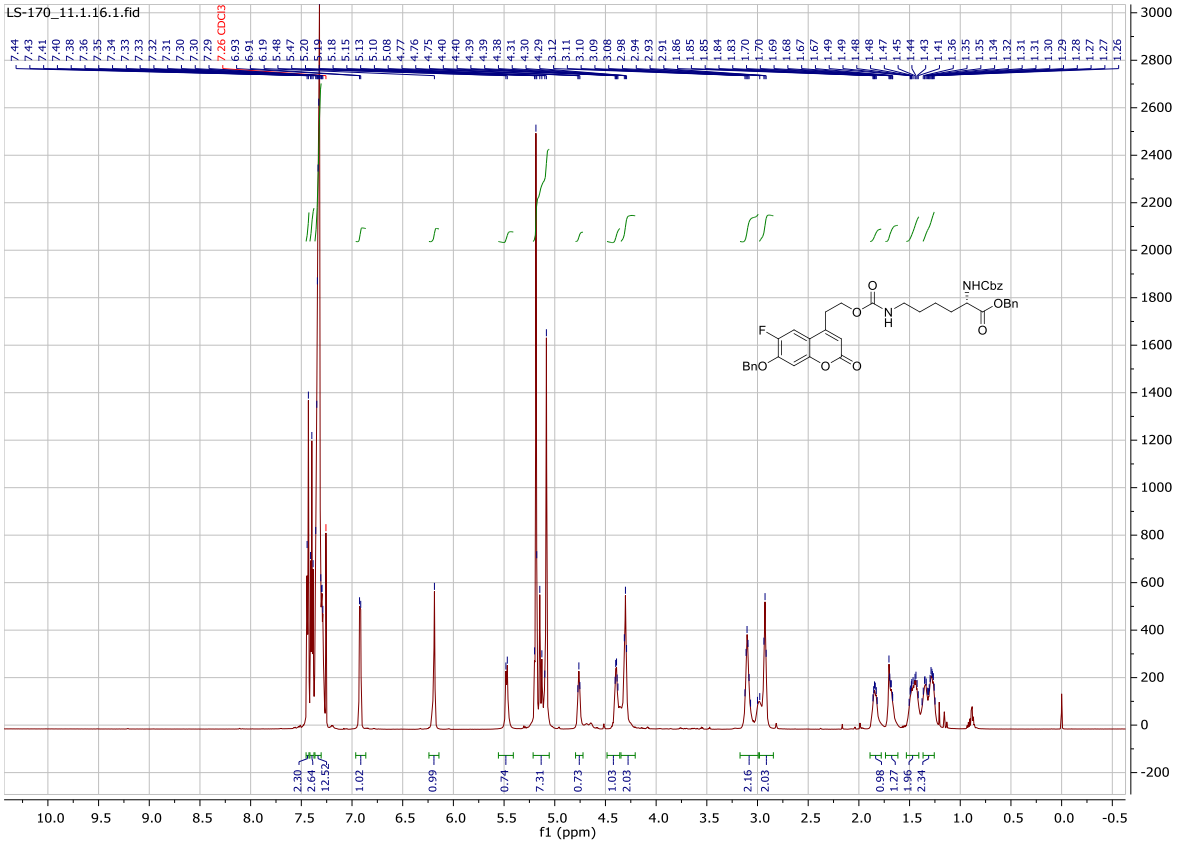

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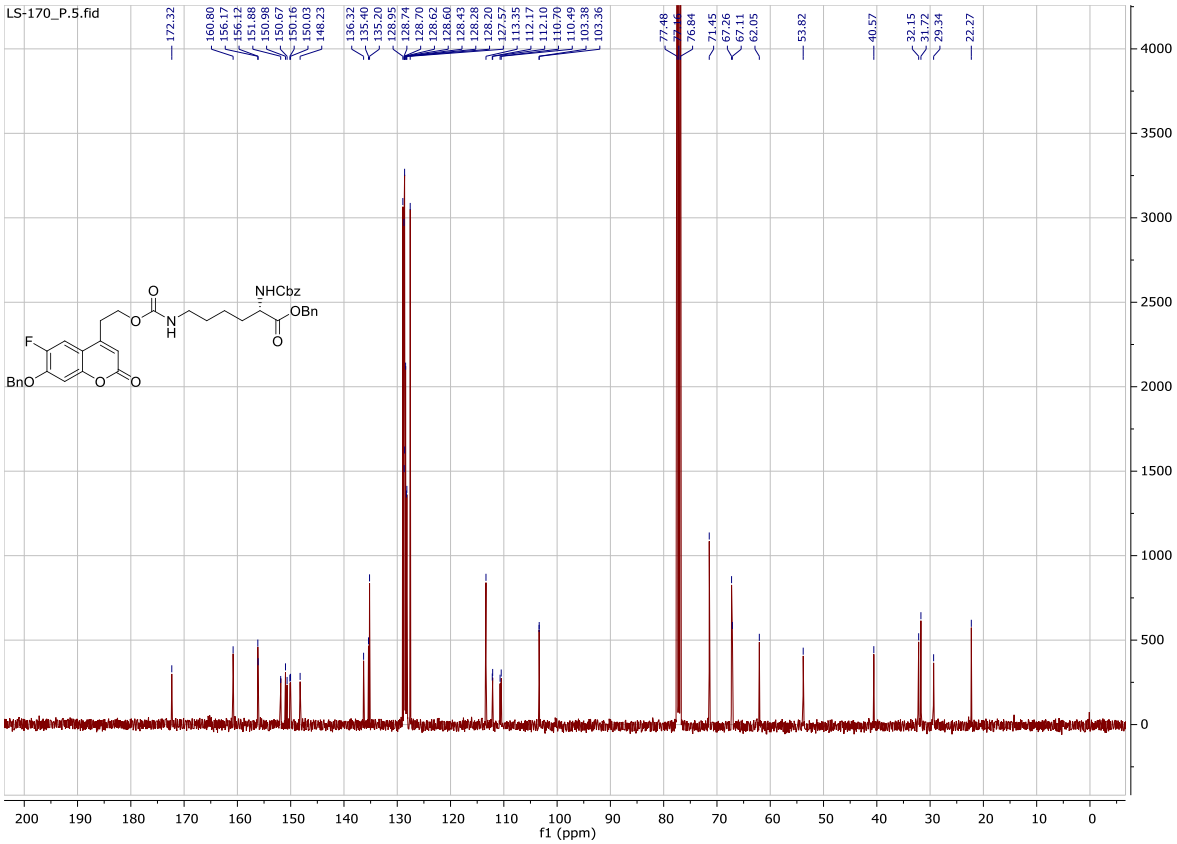

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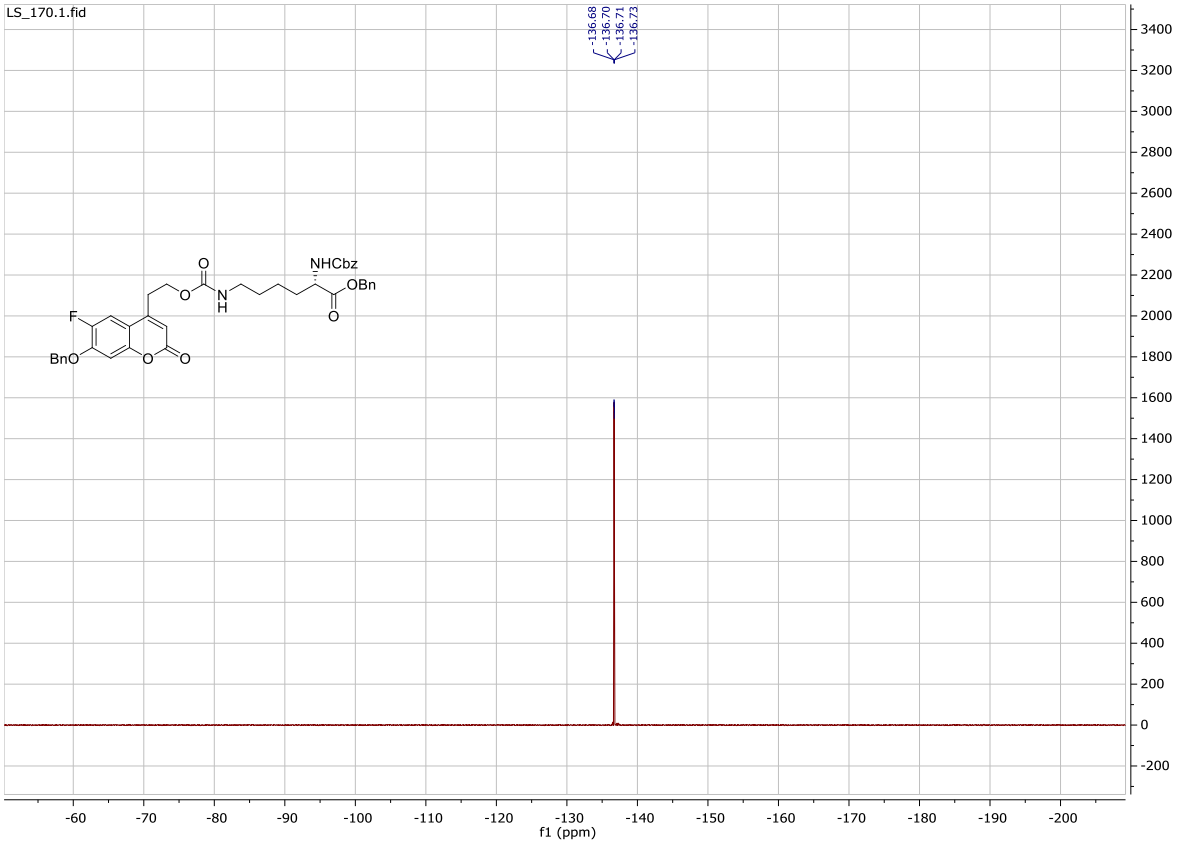

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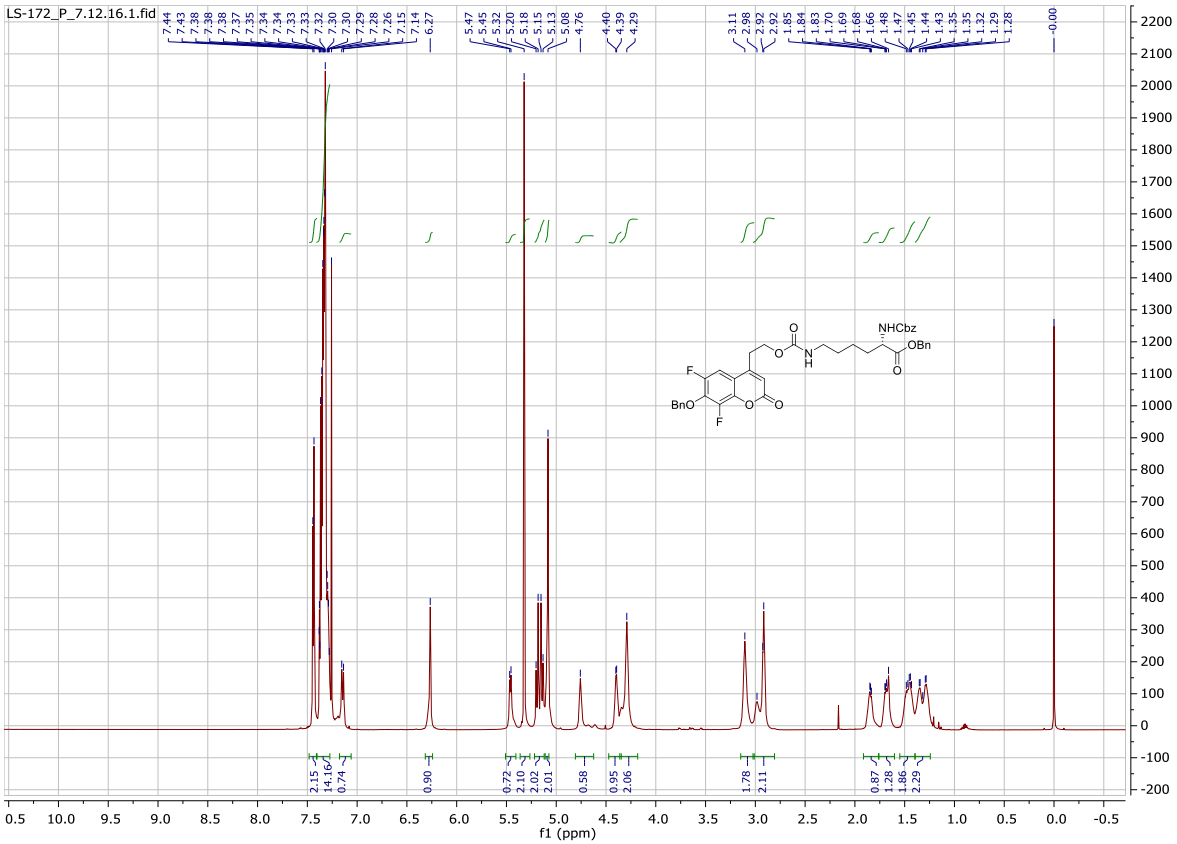
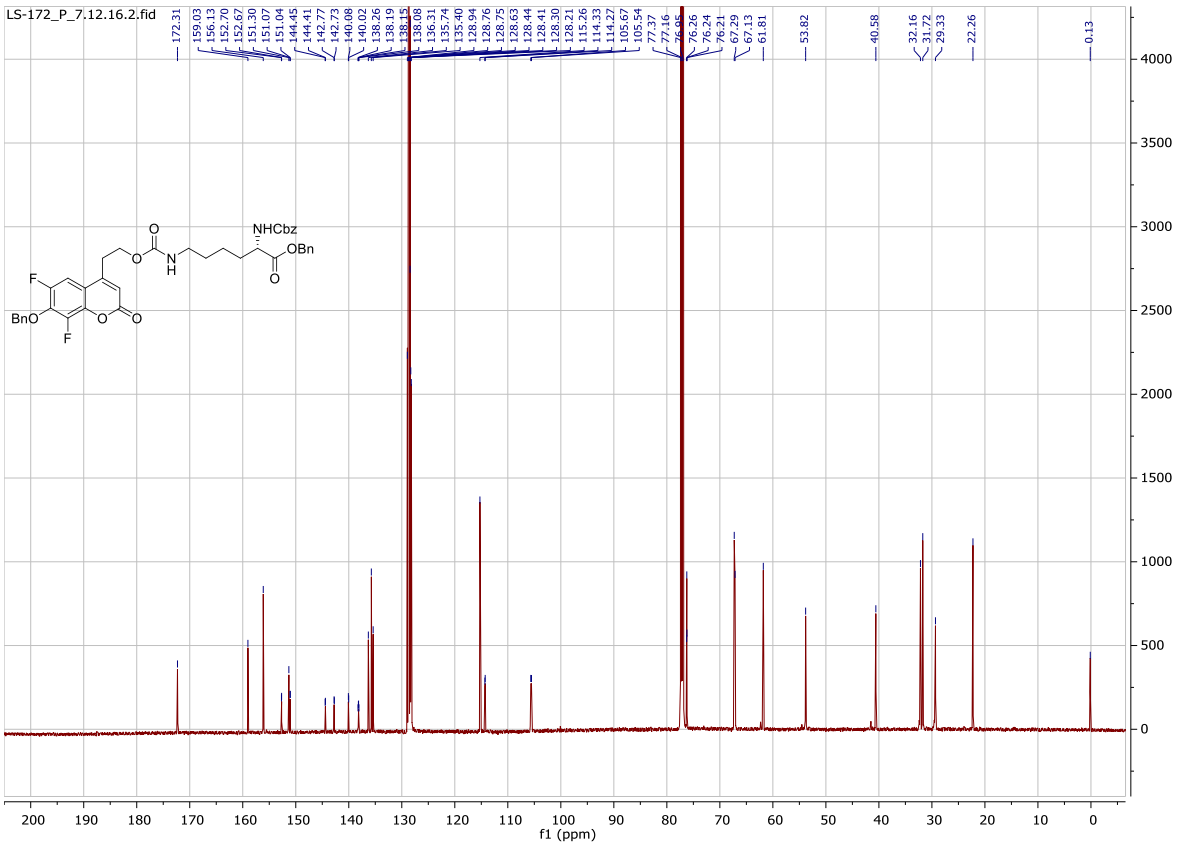
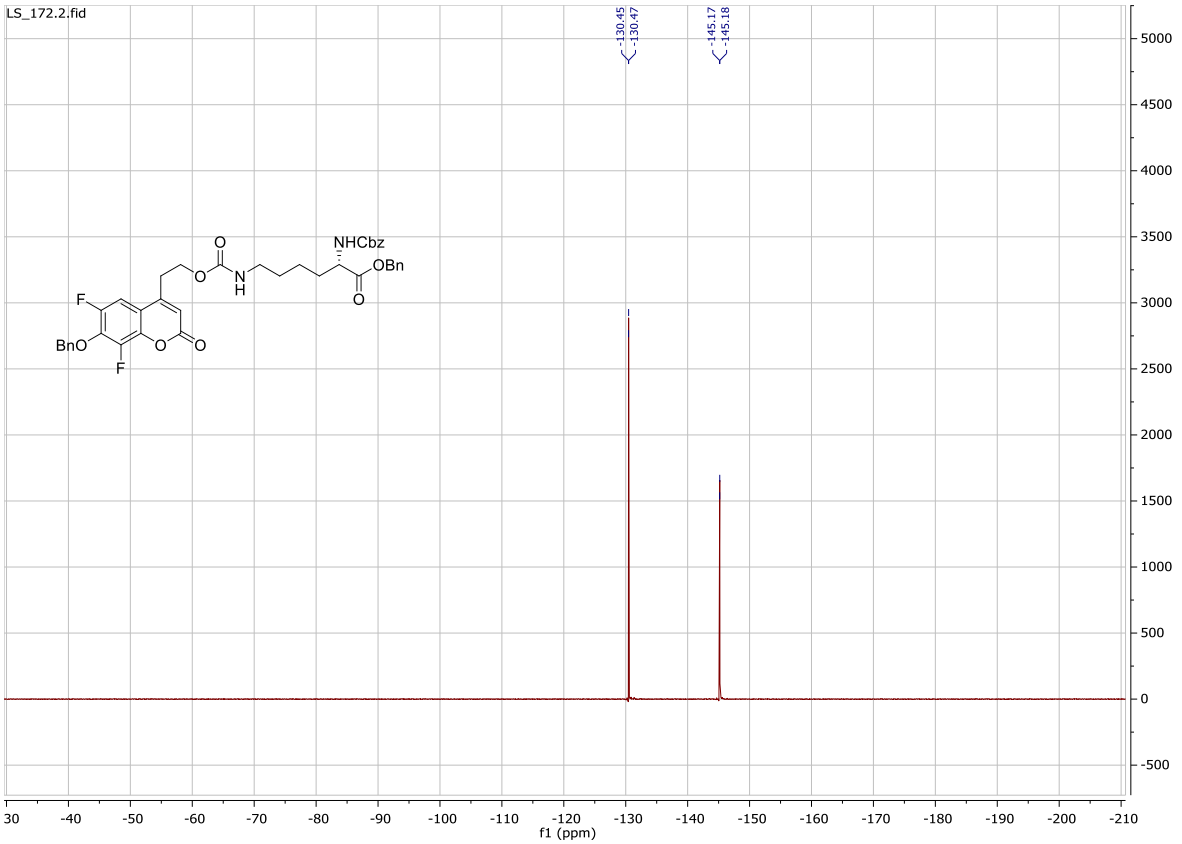


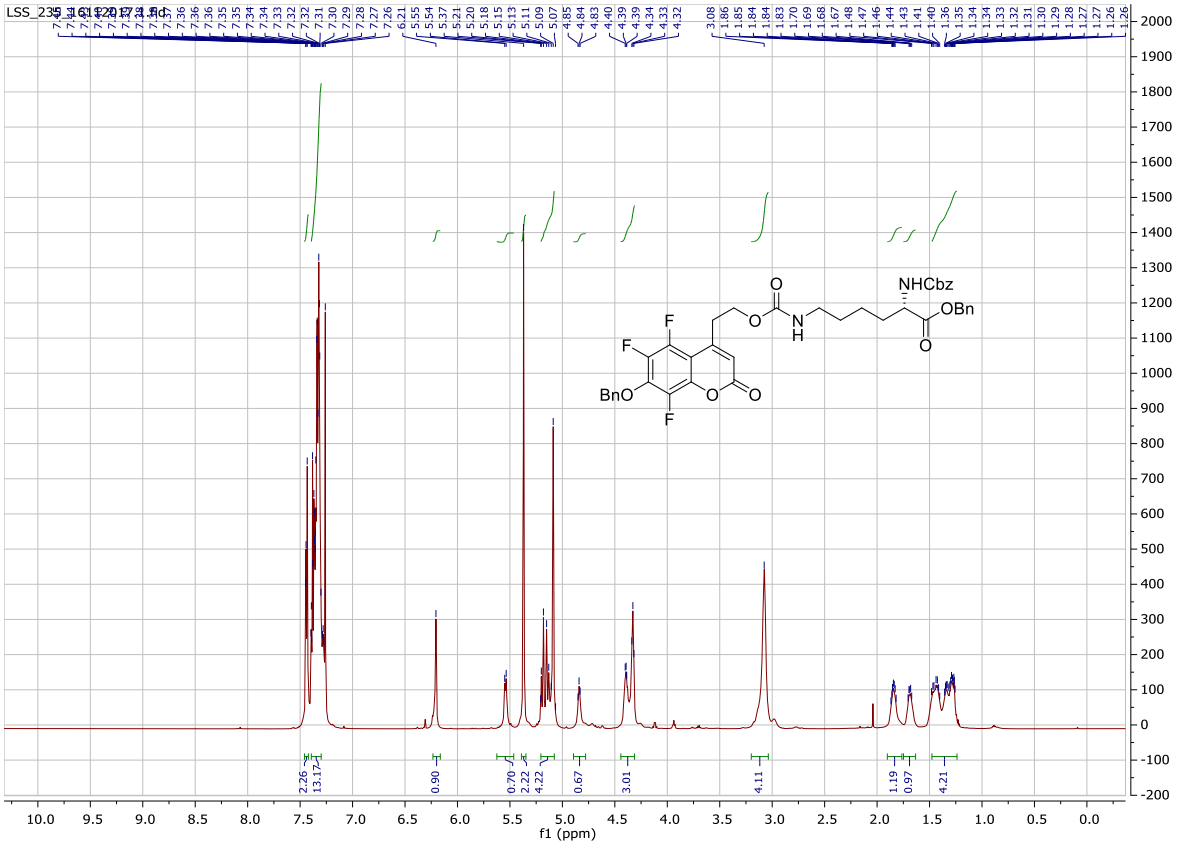
^{13}C NMR (151 MHz, $CDCl_3$) of 14c



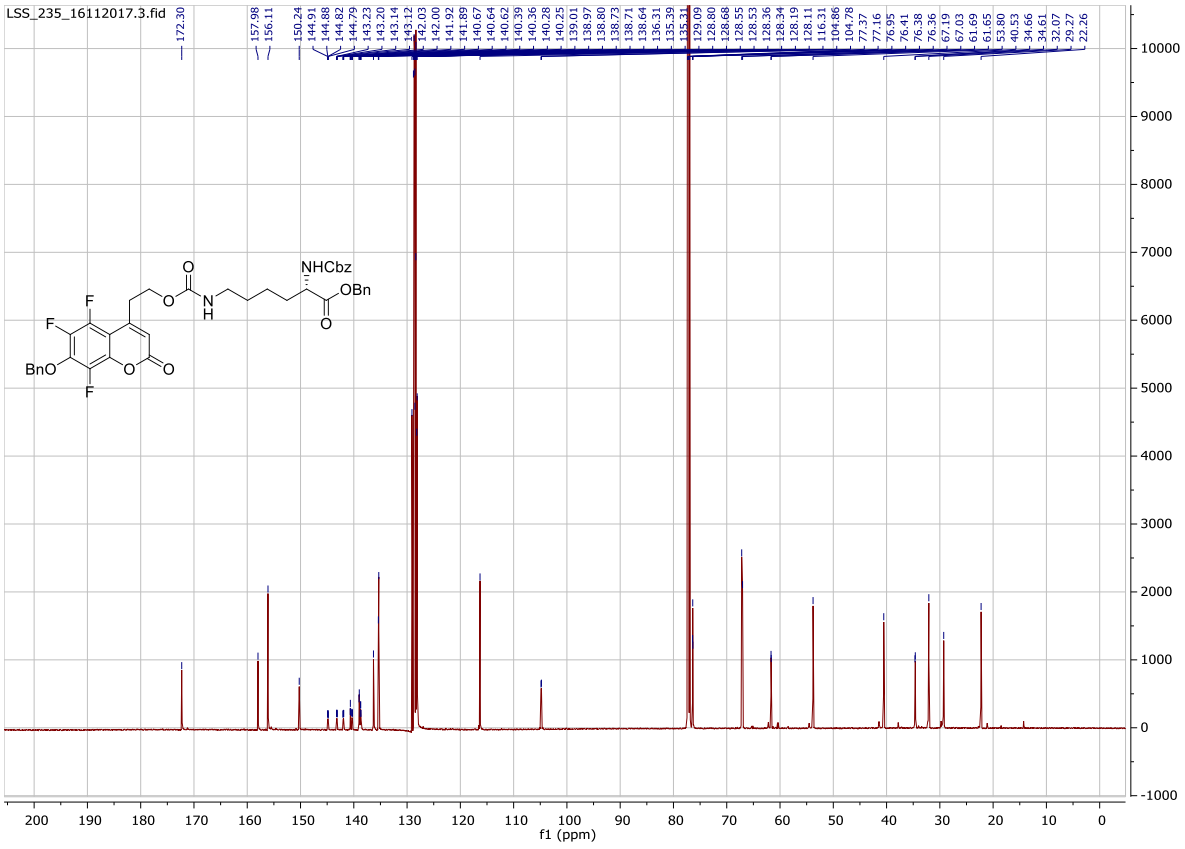
^{19}F NMR (376 MHz, $CDCl_3$) of 14c

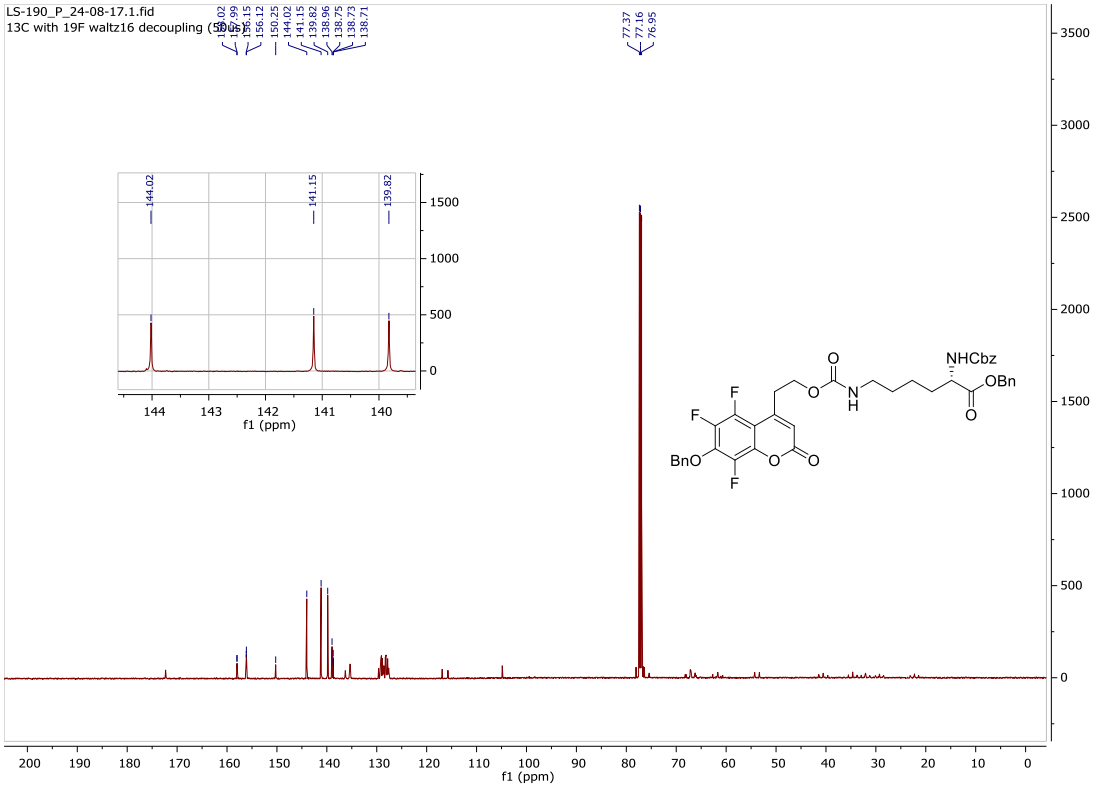


^{1}H NMR (600 MHz, $CDCl_3$) of 14d

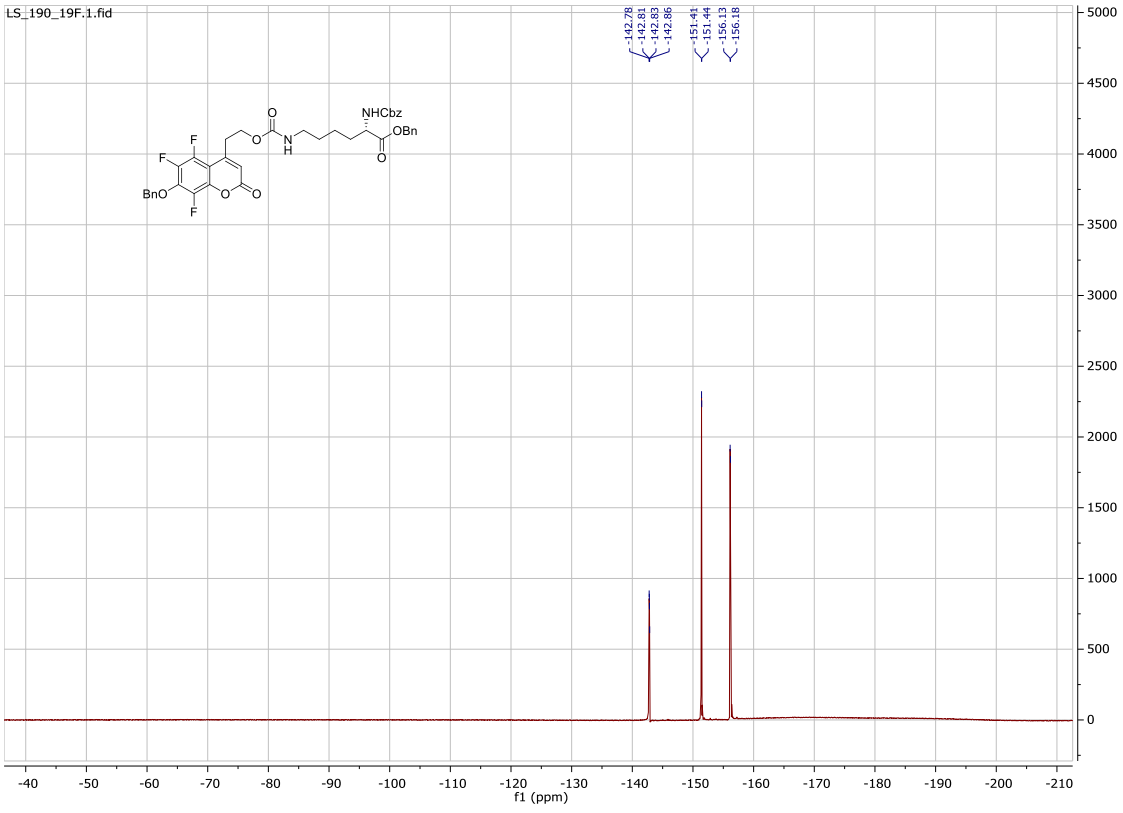


^{13}C NMR (151 MHz, $CDCl_3$) of 14d

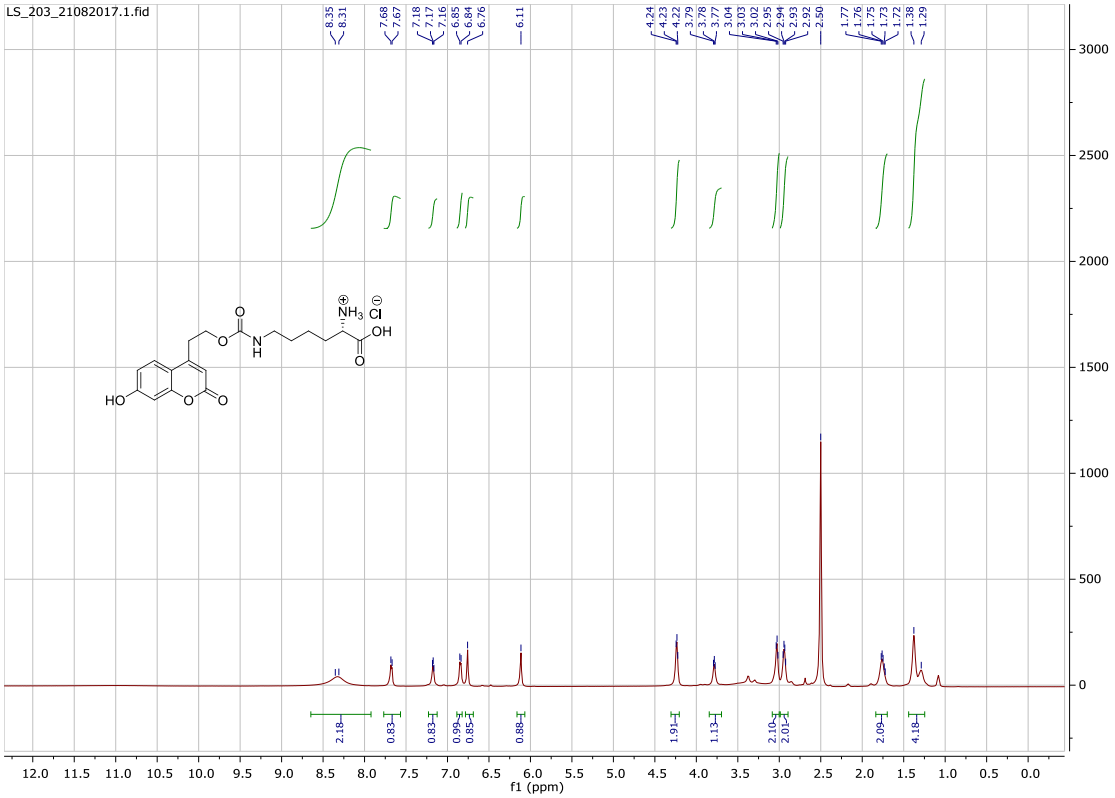




^{19}F NMR (376 MHz, $CDCl_3$) of 14d



^{1}H NMR (600 MHz, DMSO-d_6) of 1



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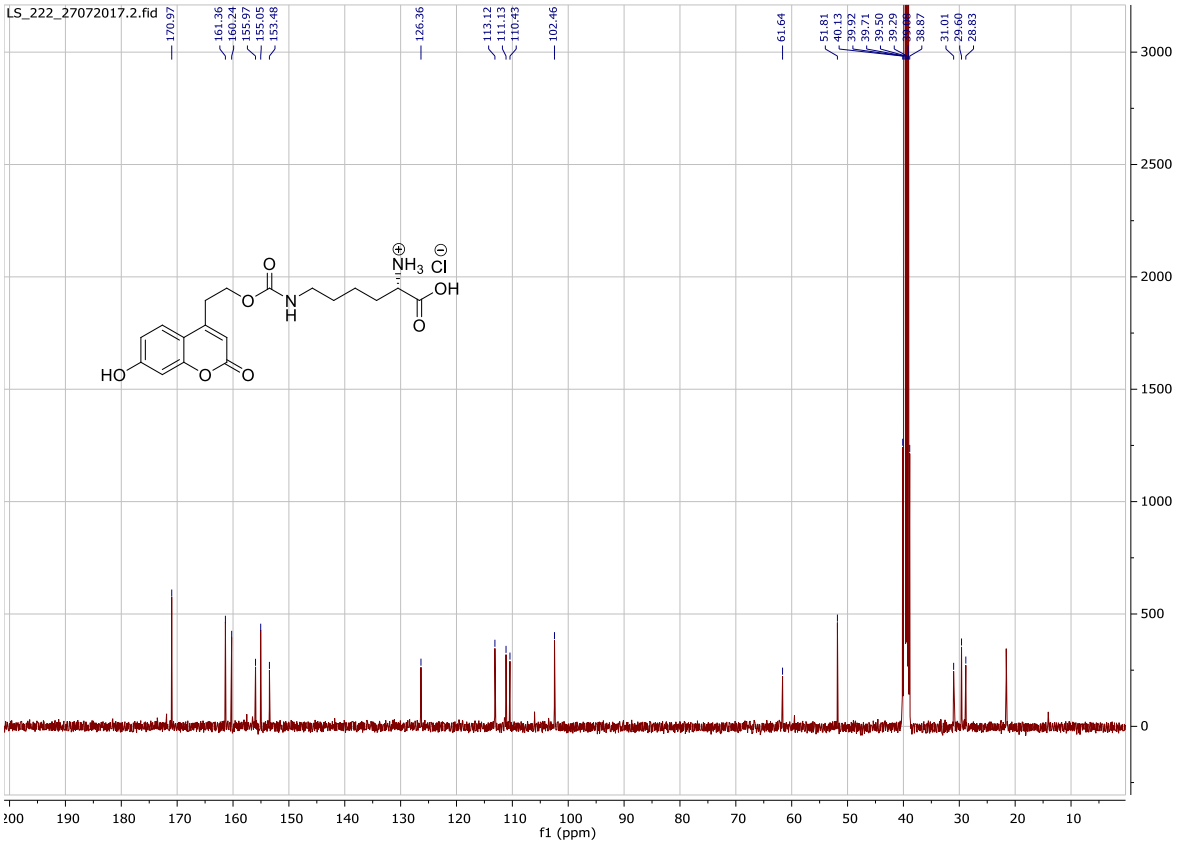
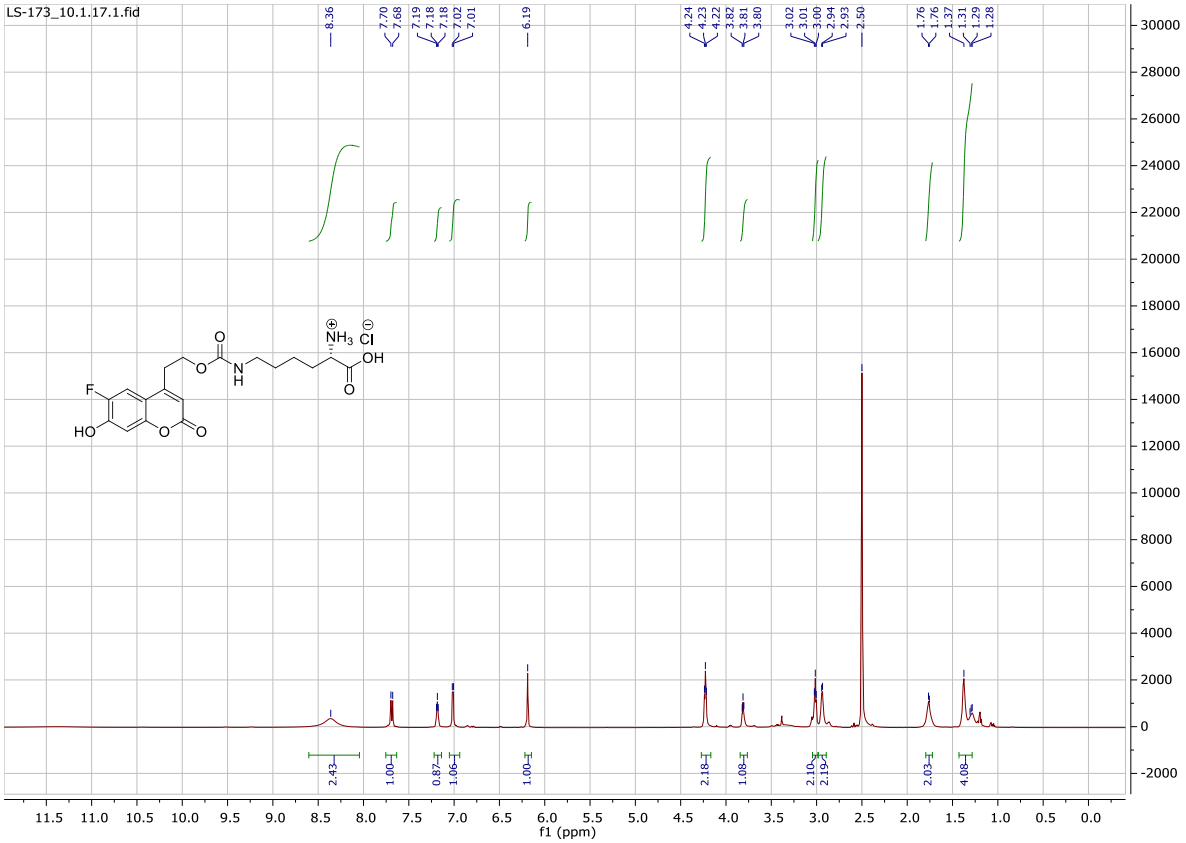
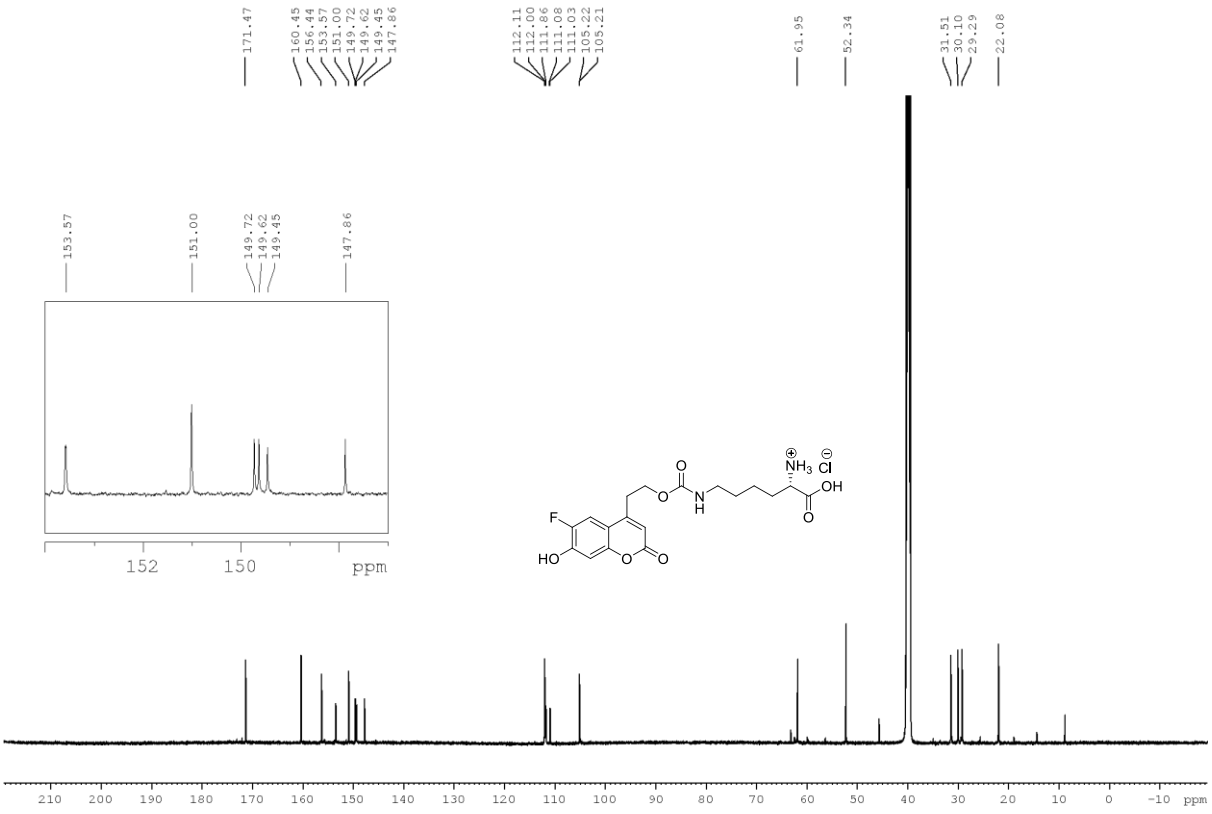


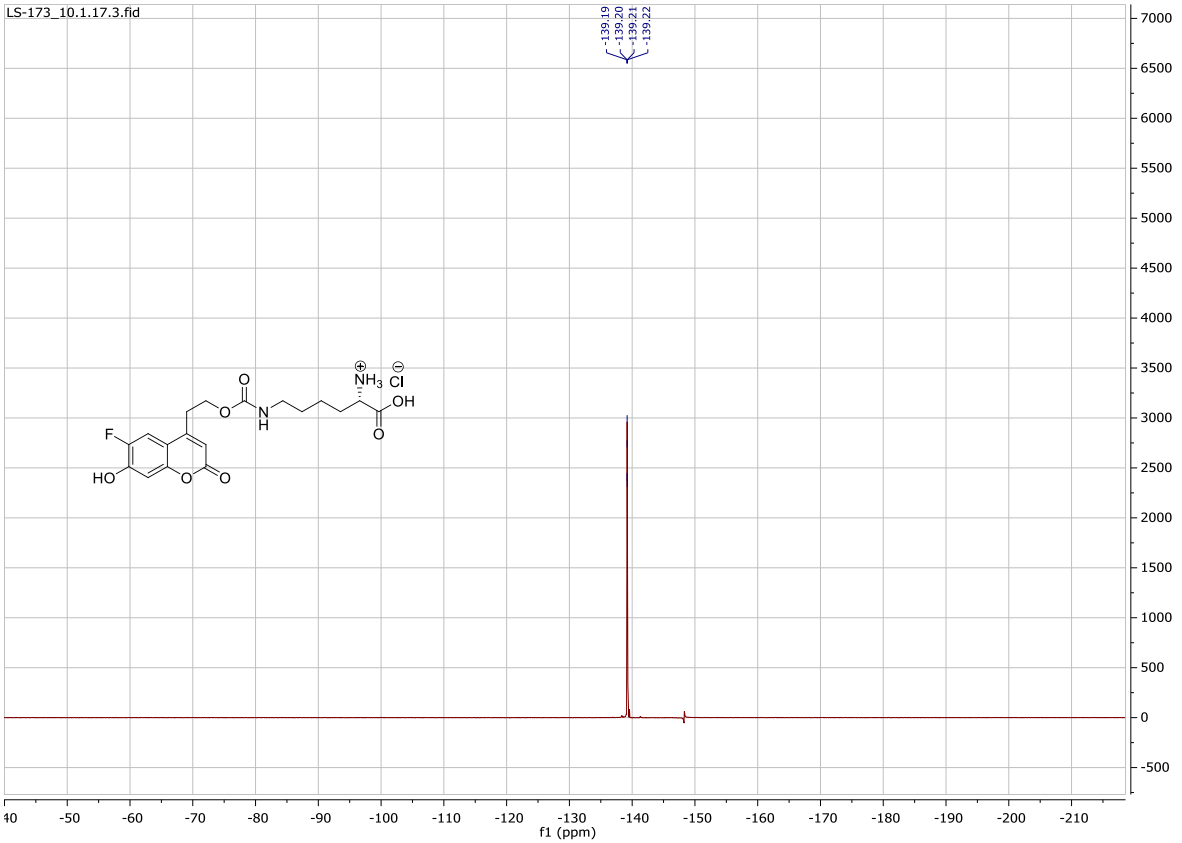
^{1}H NMR (600 MHz, DMSO-d_6) of 4



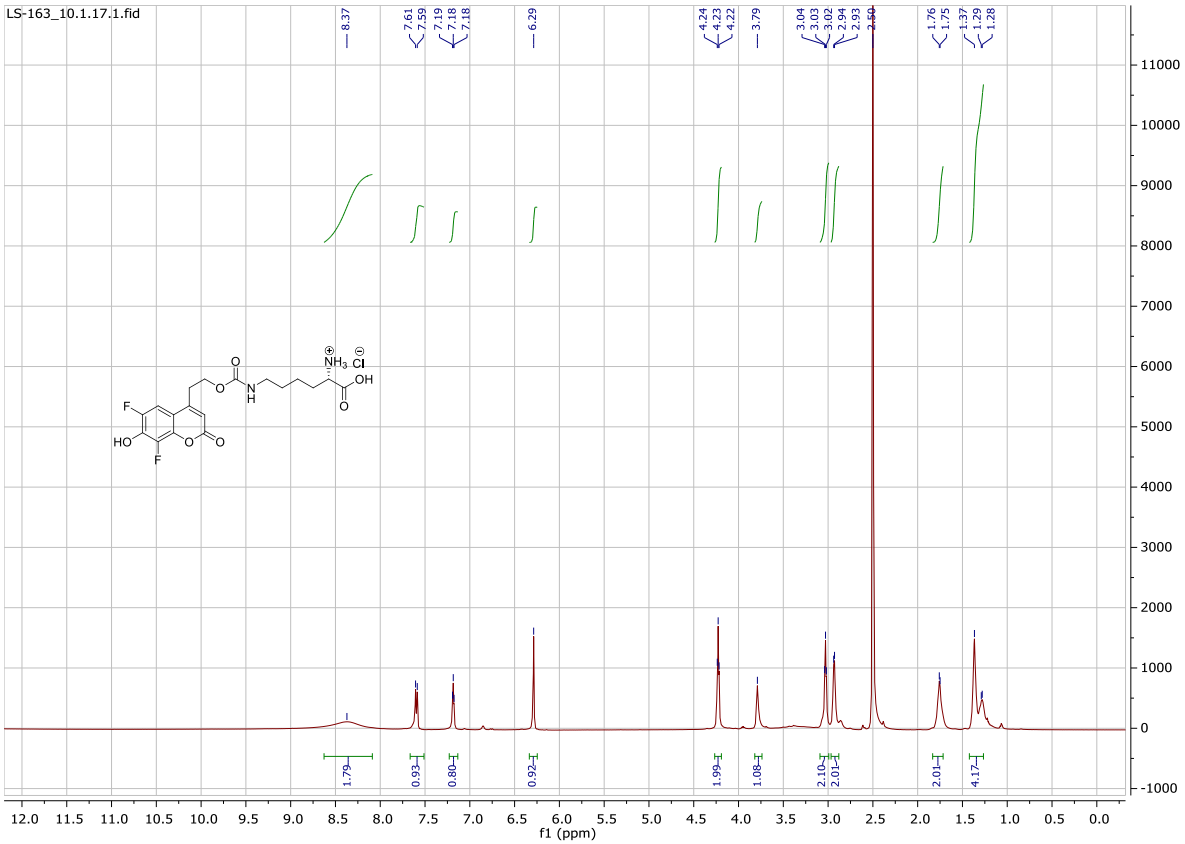
^{13}C NMR (151 MHz, DMSO-d_6) of 4



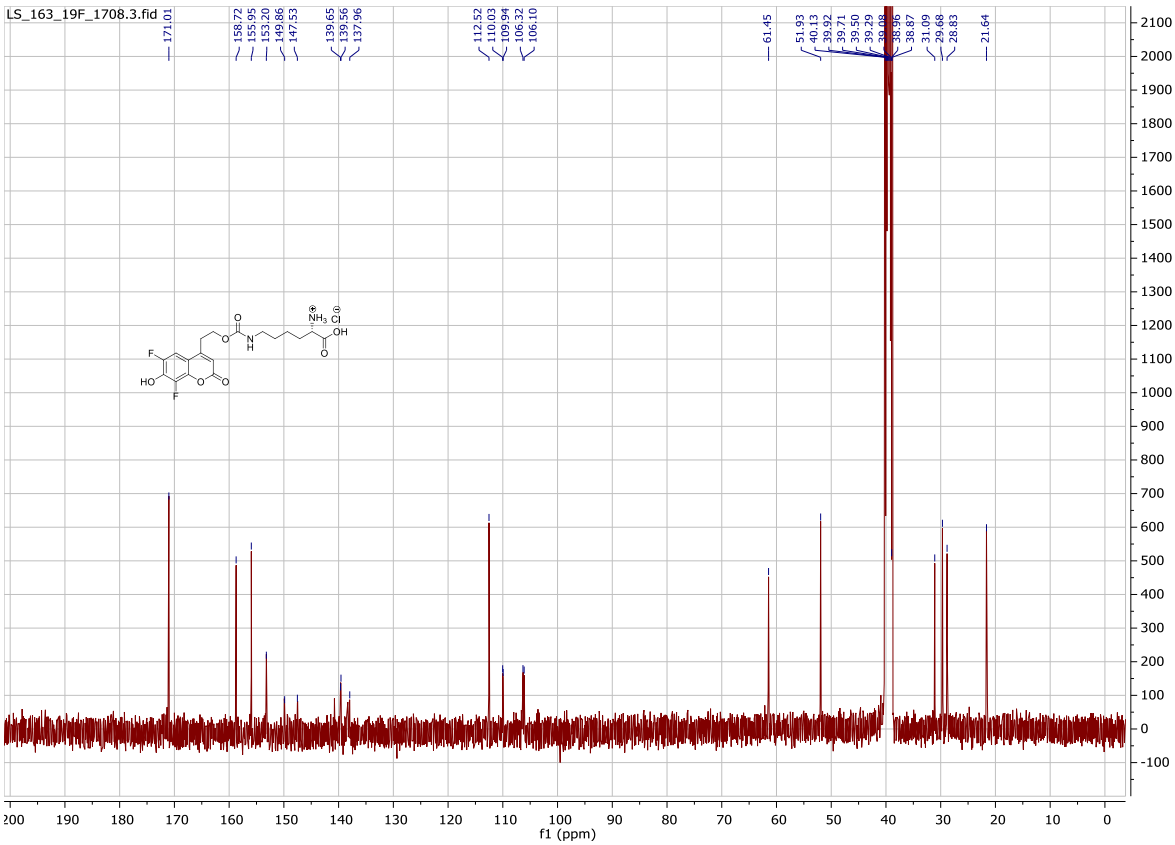
^{19}F NMR (565 MHz, $CDCl_3$) of 4



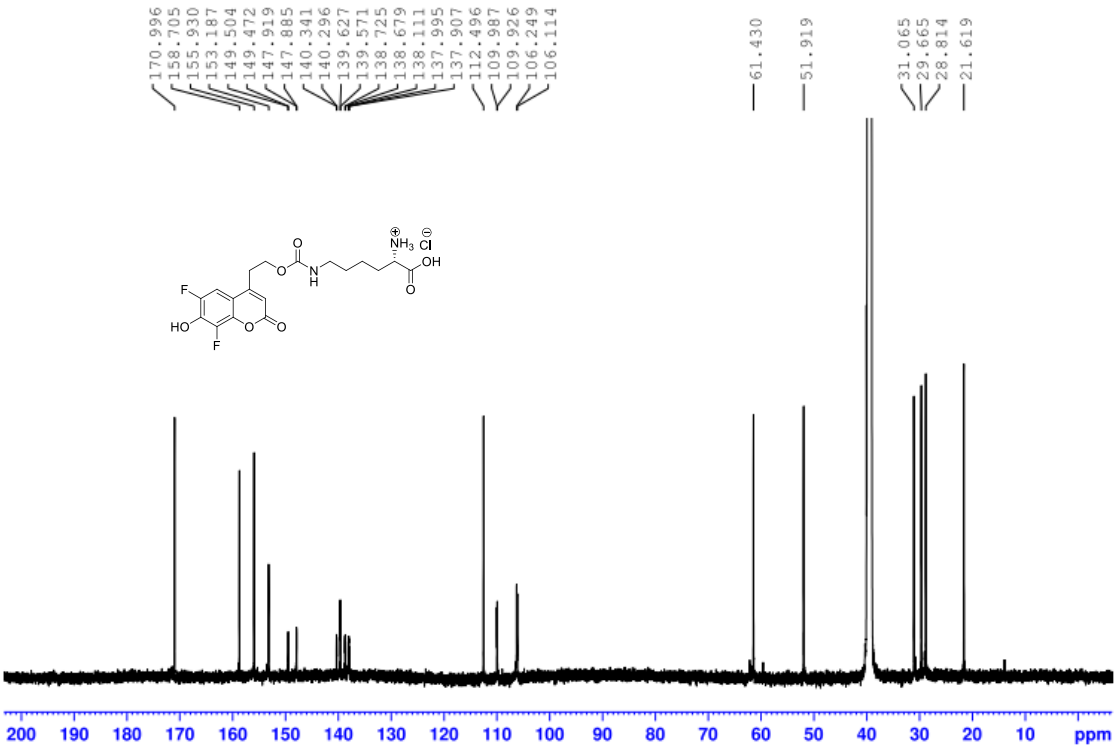
^{1}H NMR (600 MHz, DMSO-d_6) of 5

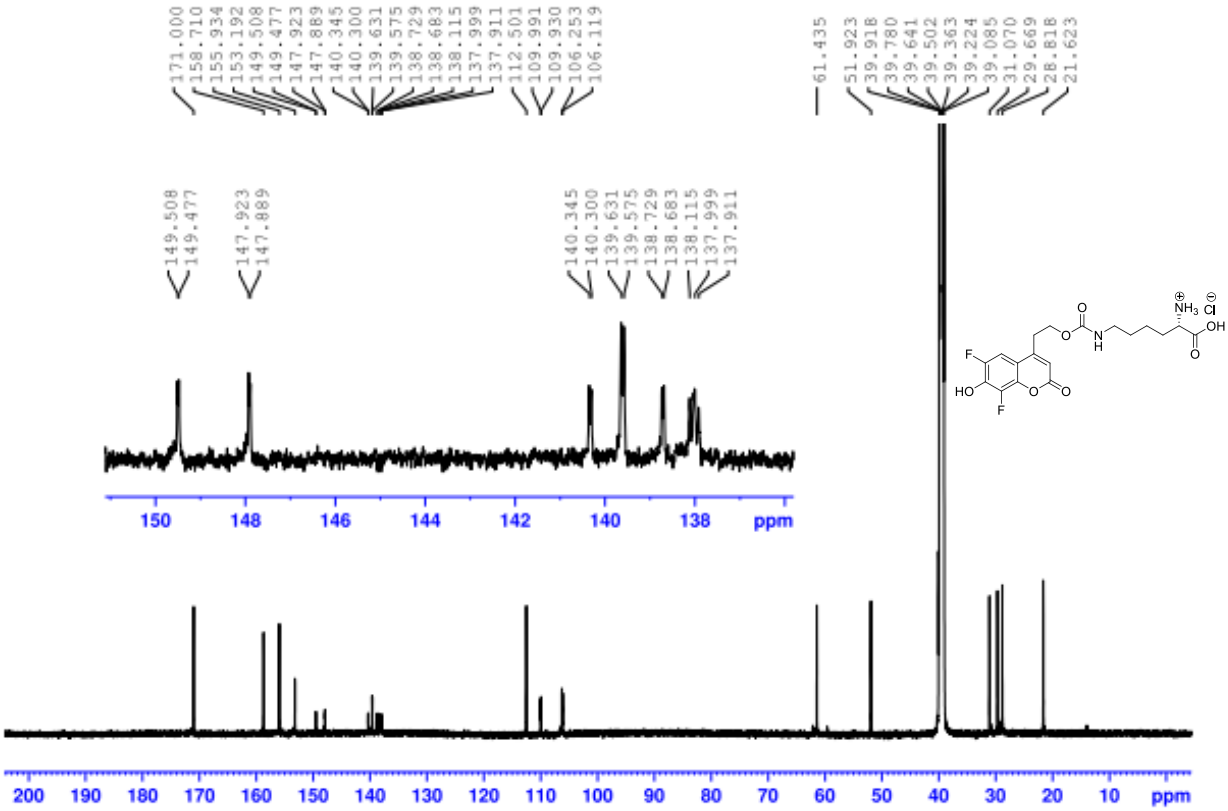


^{13}C NMR (100 MHz, DMSO-d_6) of 5

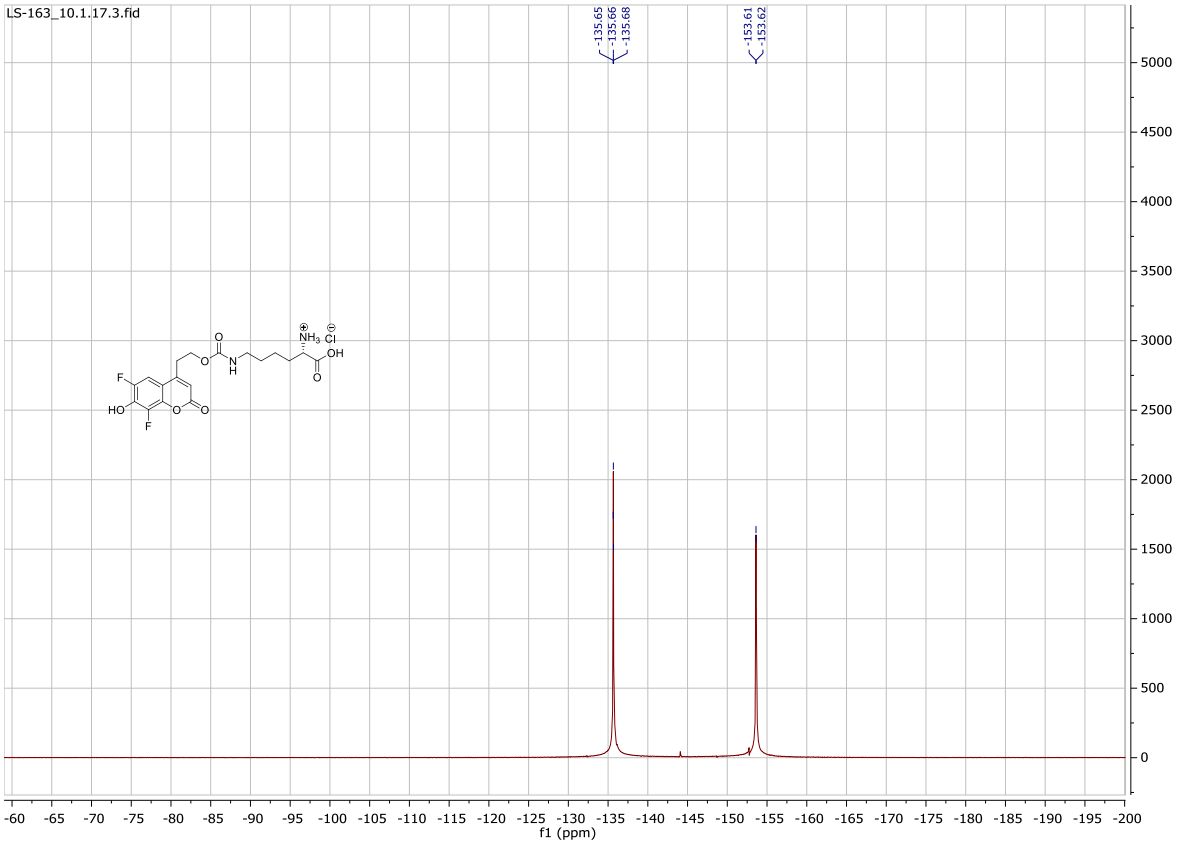


^{13}C NMR (151 MHz, DMSO-d_6) of 5

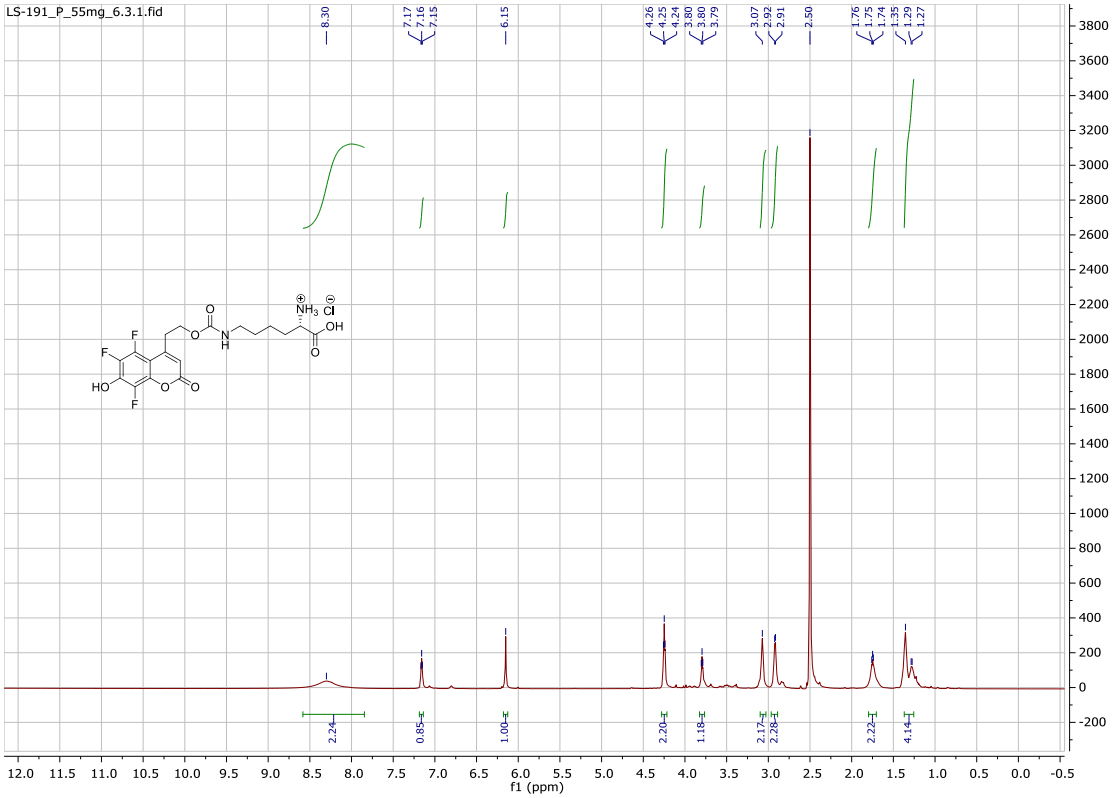




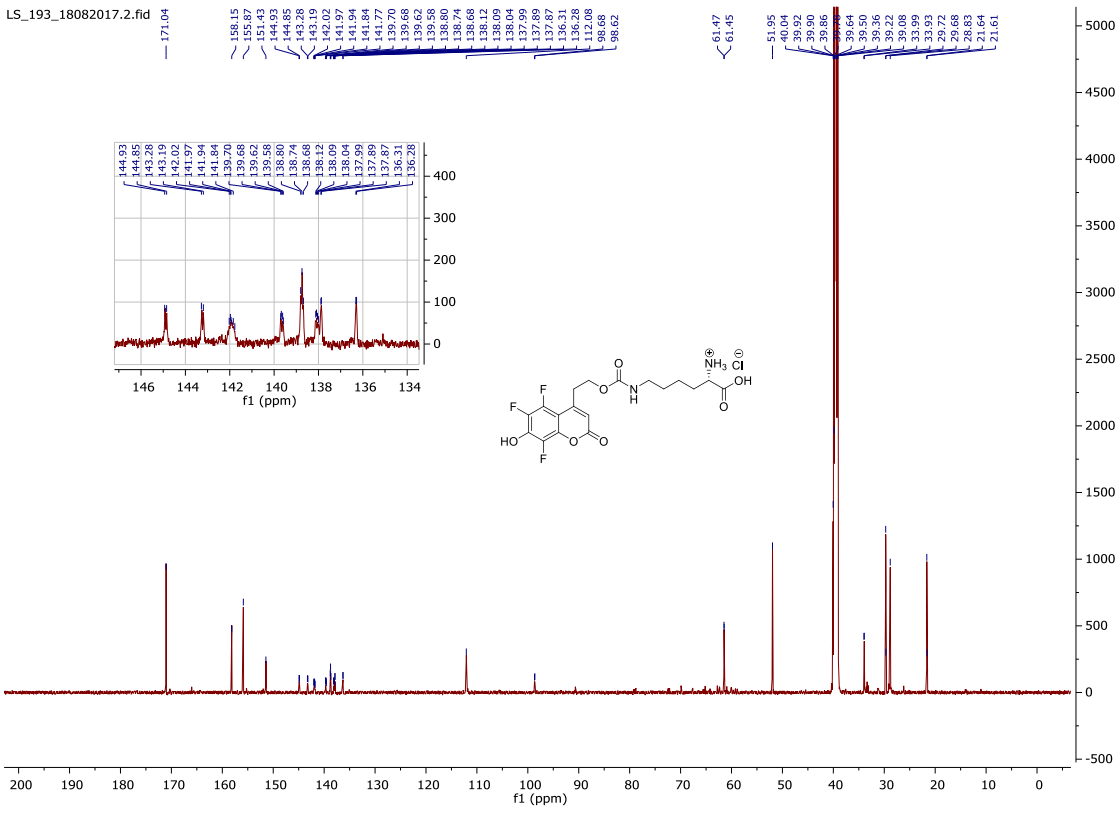
^{19}F NMR (565 MHz, $CDCl_3$) of 5

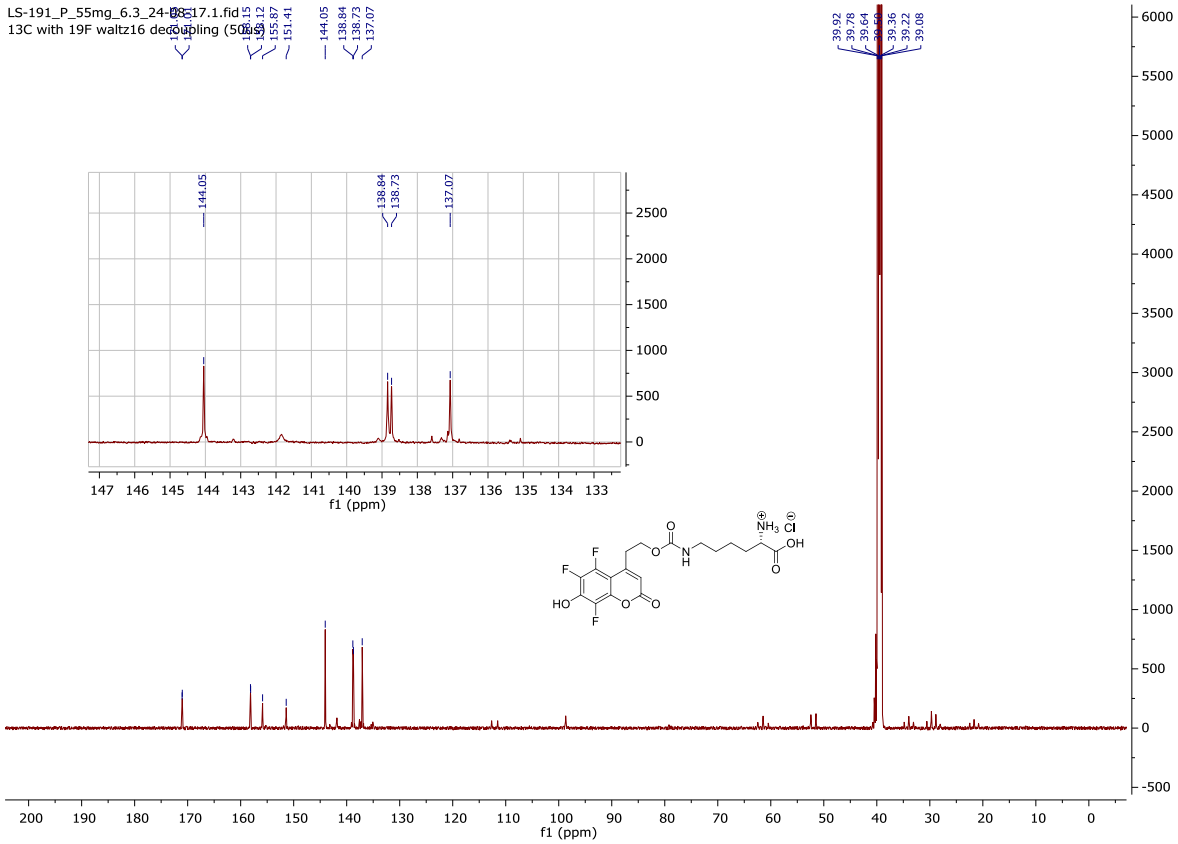


^{1}H NMR (600 MHz, DMSO-d_6) of 6



^{13}C NMR (151 MHz, DMSO-d_6) of 6

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13C with 19F waltz16 decoupling (50.3
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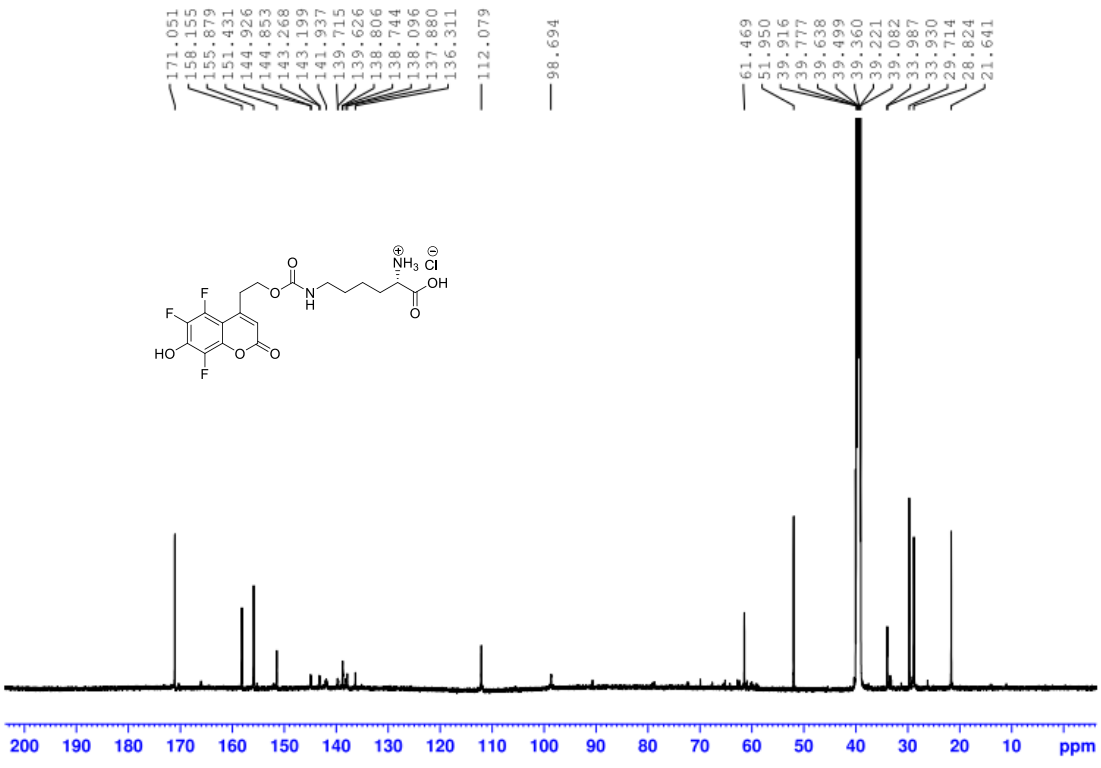
138.84
138.73
137.07
39.92
39.78
39.64
39.36
39.22
39.08
f1 (ppm)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158.155
155.879
151.431
144.926
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139.715
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138.744
138.096
137.880
136.311
112.079
98.694
61.469
51.950
39.916
39.777
39.638
39.499
39.360
39.221
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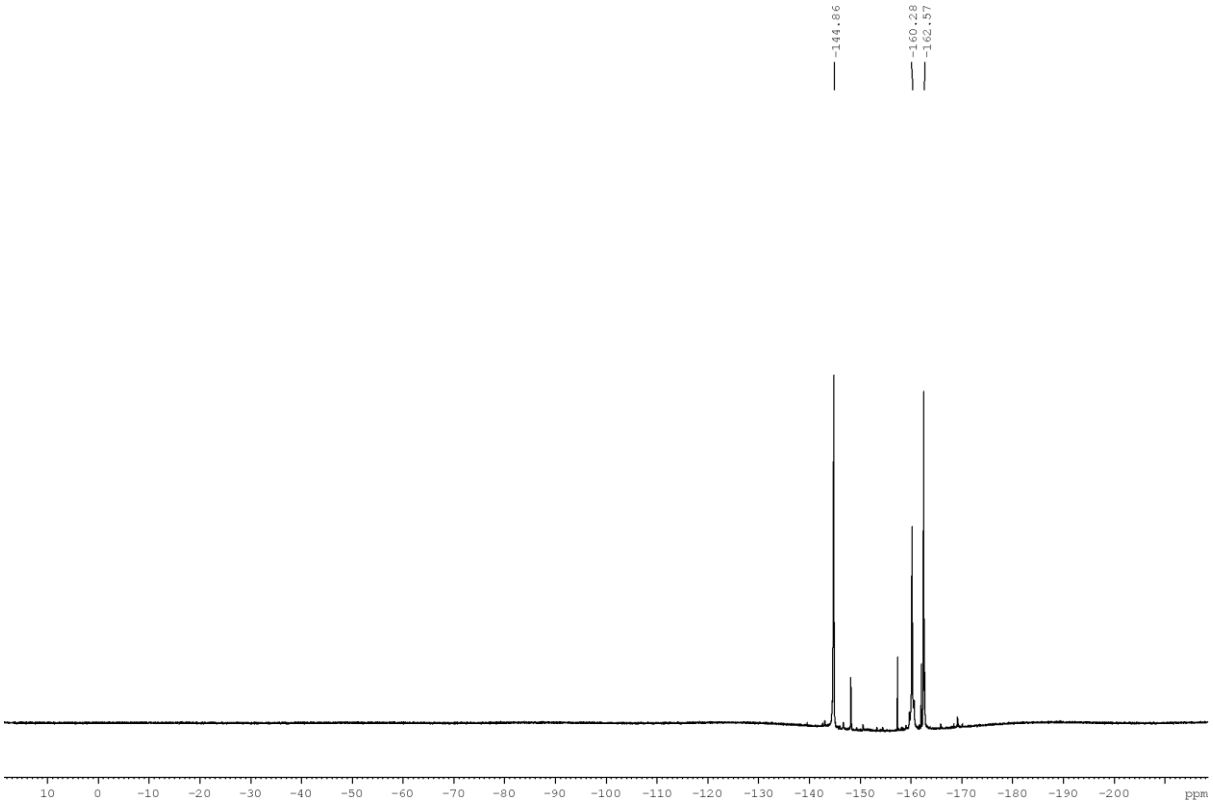
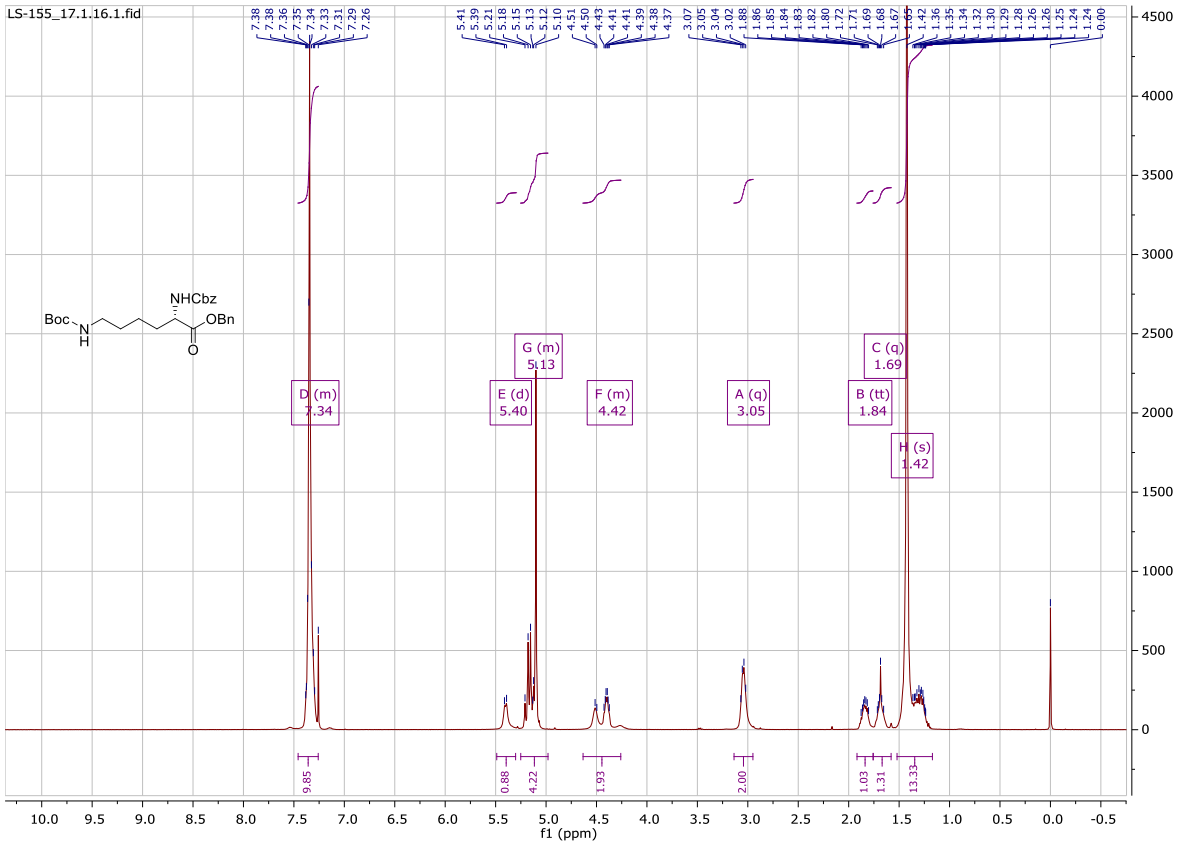
33.987
33.930
29.714
28.824
21.641
ppm

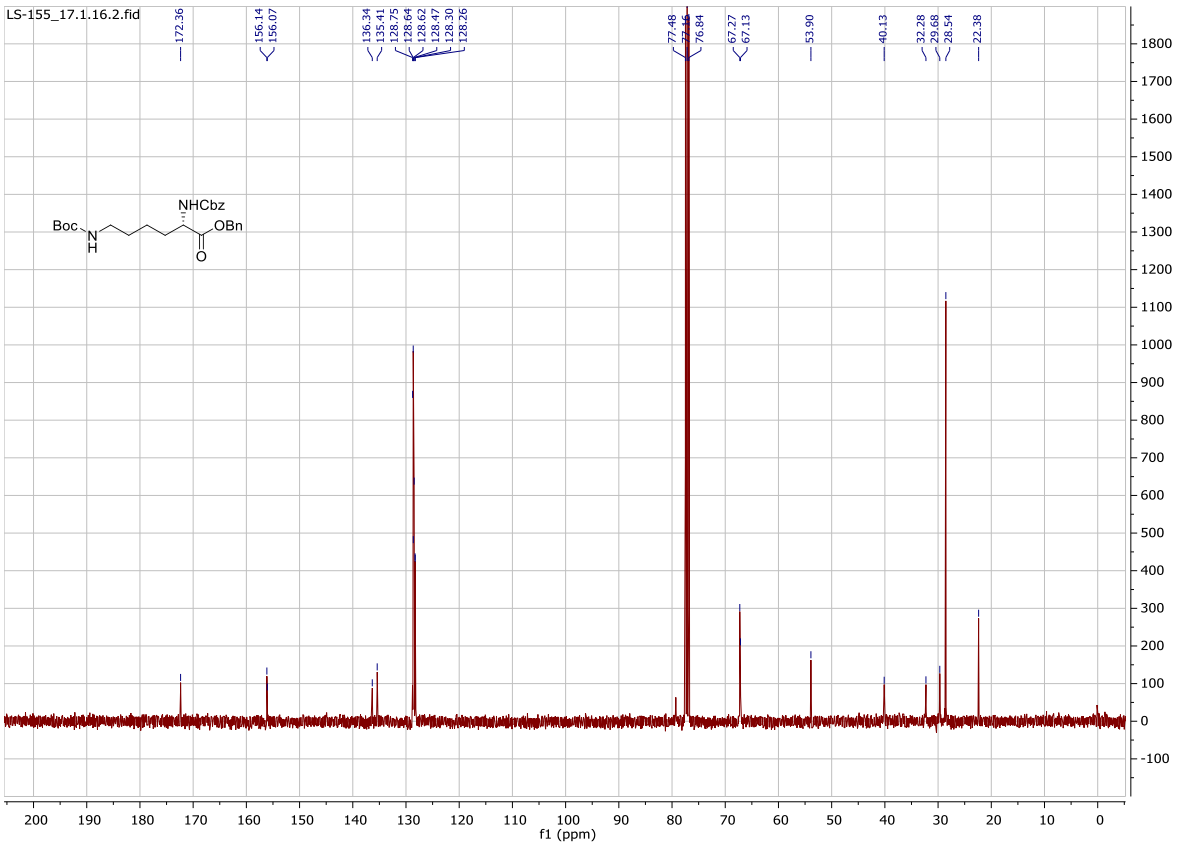
^{19}F NMR (376 MHz, $CDCl_3$) of 6



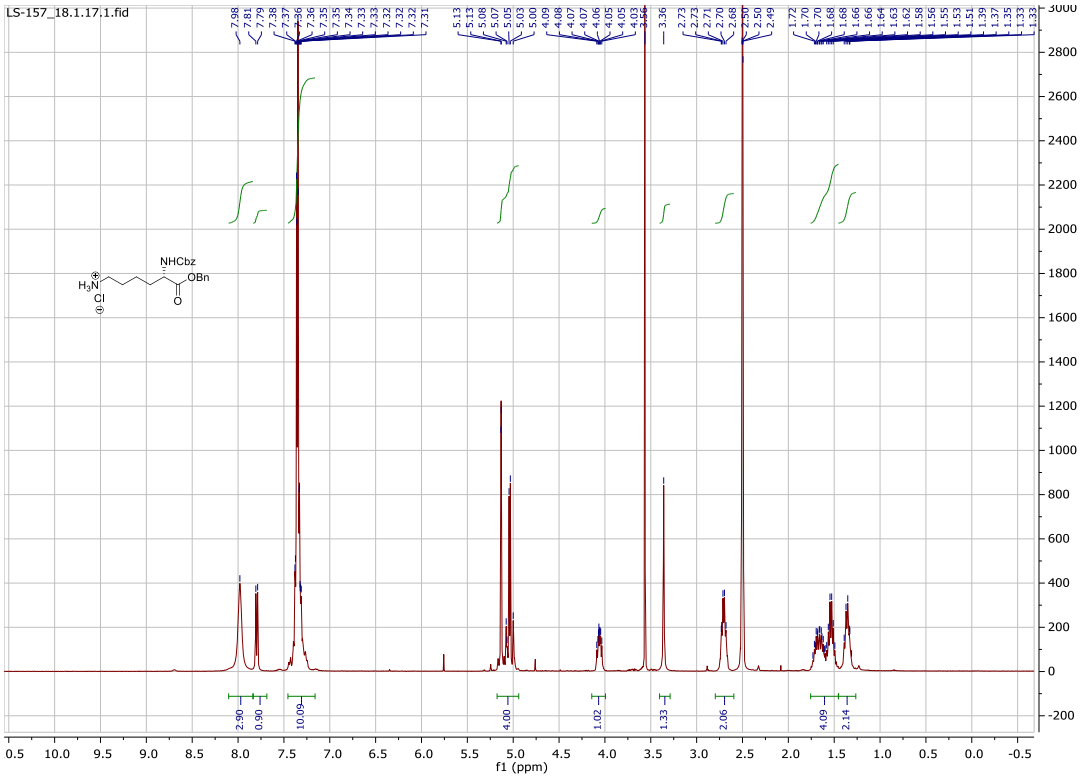
^{1}H NMR (400 MHz, $CDCl_3$) of 16



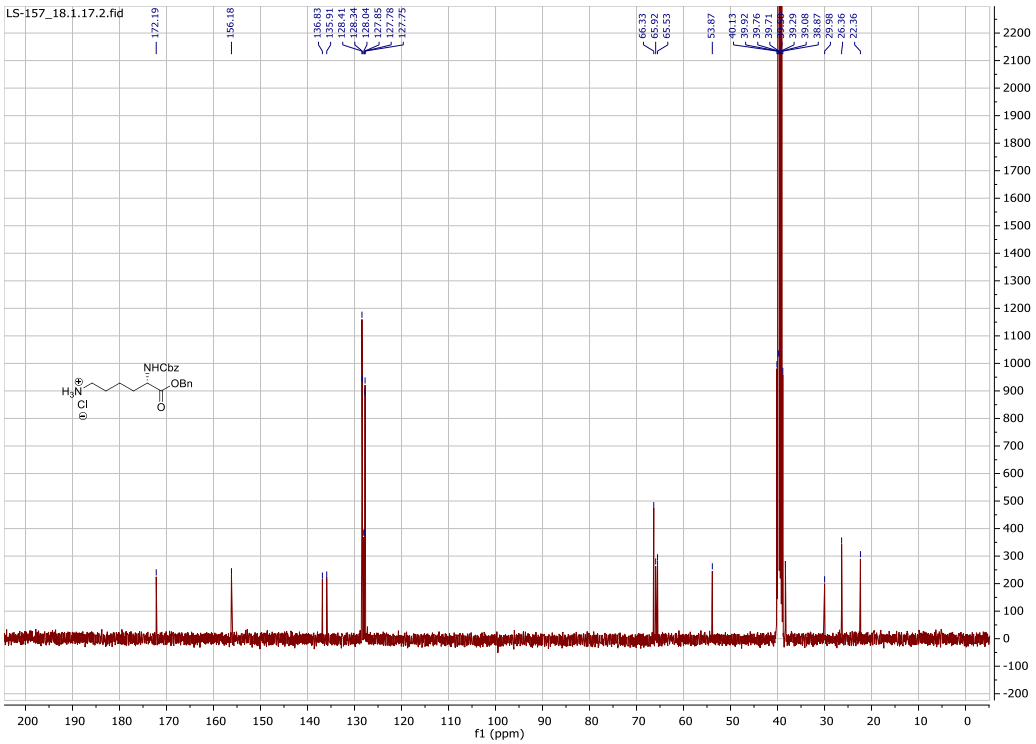
^{13}C NMR (100 MHz, DMSO-d_6) of 16



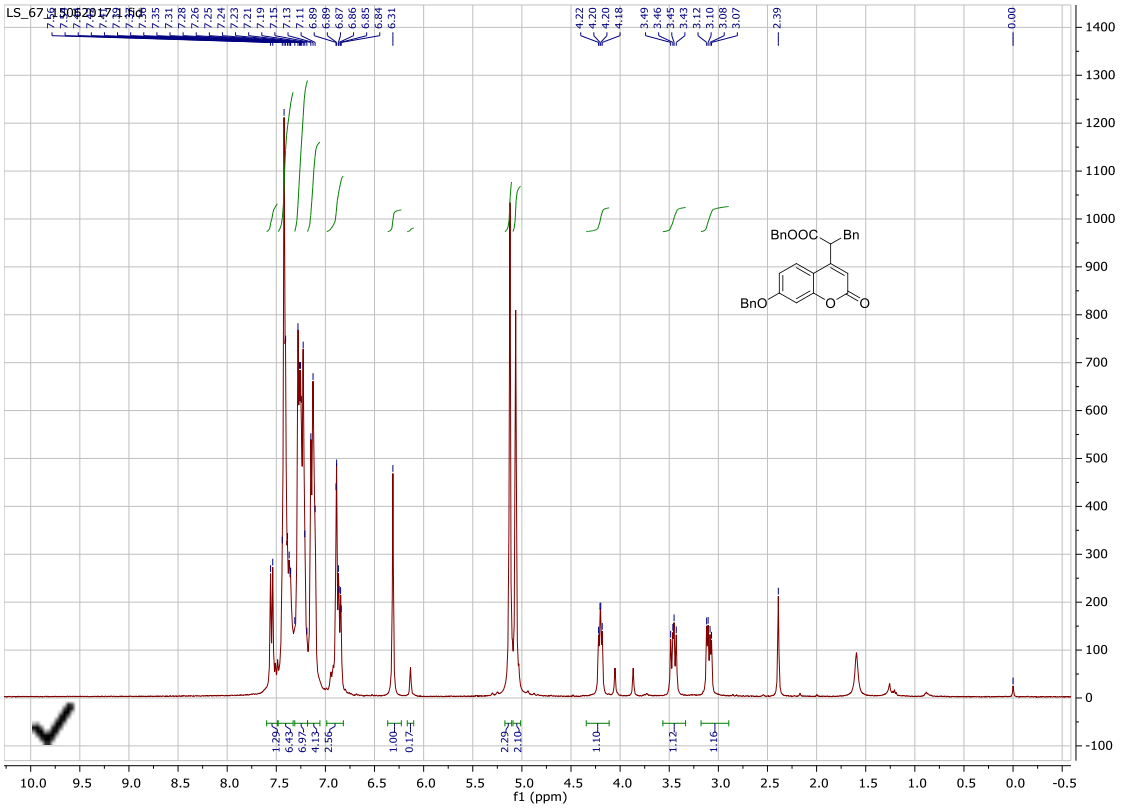
^{1}H NMR (400 MHz, $CDCl_3$) of 13



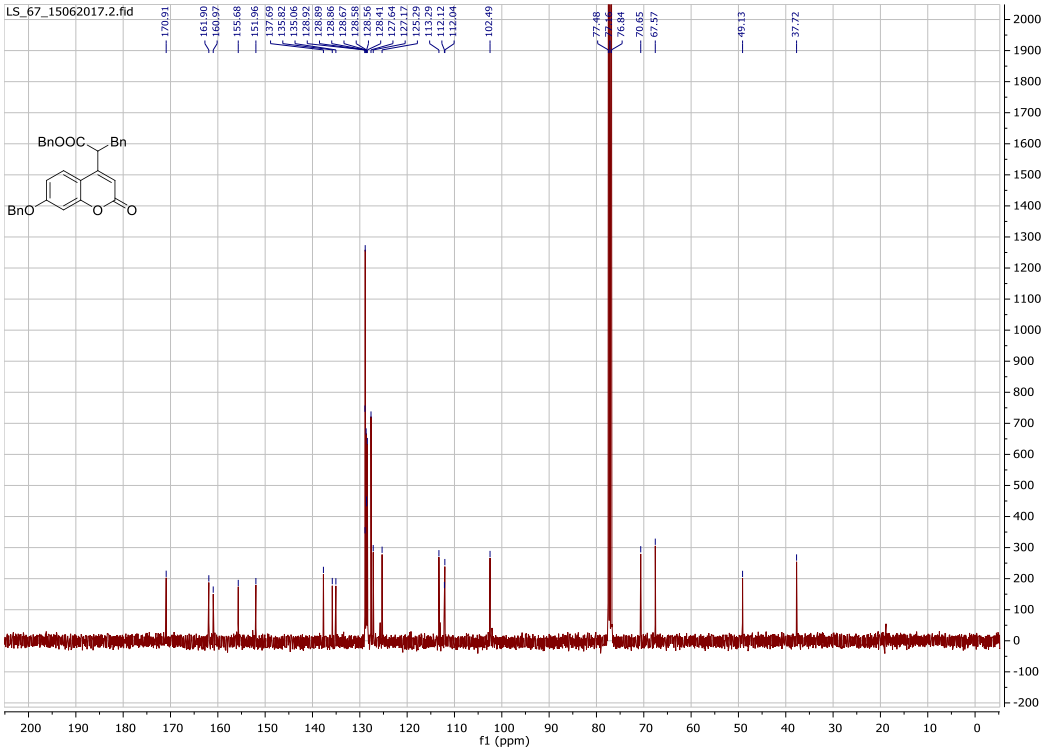
^{13}C NMR (400 MHz, $CDCl_3$) of 13



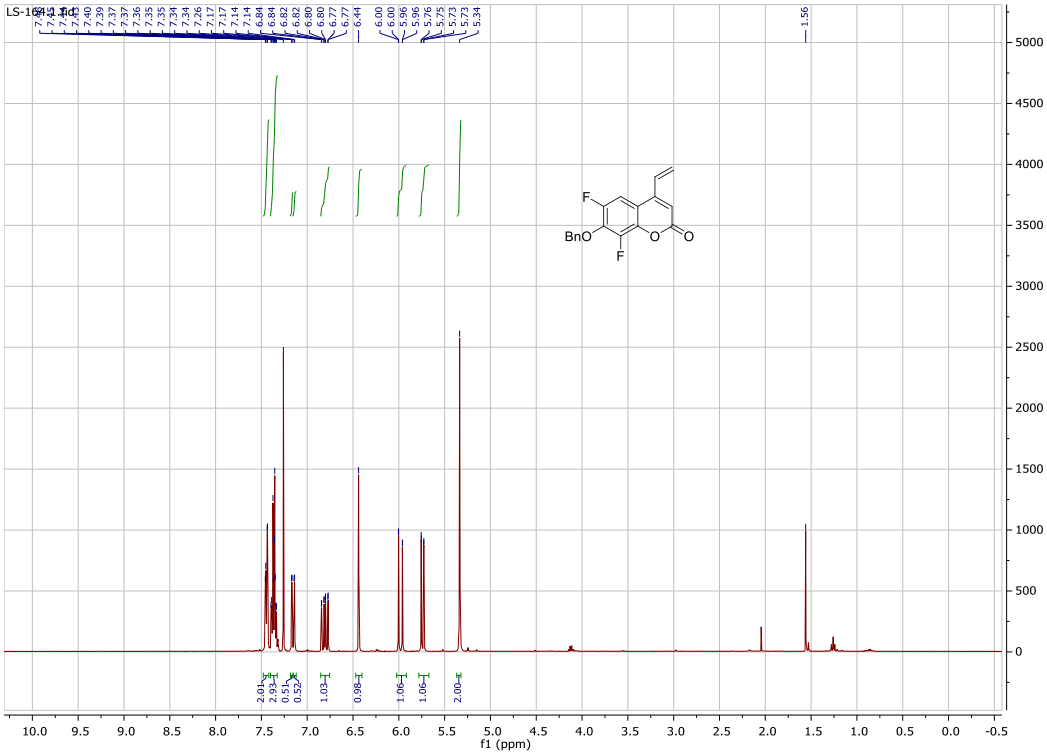
^{1}H NMR (400 MHz, $CDCl_3$) of over-benzylation by-product



^{13}C NMR (400 MHz, $CDCl_3$) of over-benzylation by-product



^{1}H NMR (400 MHz, $CDCl_3$) of elimination by-product



2. Spectroscopic Studies

UV-vis absorbance spectra were recorded on a Shimadzu UV-3101PC instrument with a compound concentration of 10 μM in KCl–HCl, citric acid–Na_2HPO_4, trizma HCl–trizma base and Na_2CO_3–$NaHCO_3$ buffer solutions. Emission spectra and lifetimes were obtained with a HORIBA Jobin Yvon Fluorolog TCSPC instrument; the absorbance in the emission wavelength range was lower than 0.1 in all measurements. The steady-state emission spectra were obtained by excitation at 320 and 360 nm, while decays were measured using LEDs at 278 and 370 nm. The quantum yields were determined relative to quinine sulfate in 0.5 M H_2SO_4 (Φ_f = 0.546). Emission decays were monitored at 460 nm, and the lifetimes were analyzed using the Tcspcfit software package.[1] Solutions of the compounds in respective buffer were prepared from stock solutions in DMSO, giving a residual stock solvent concentration of ≤0.1%.

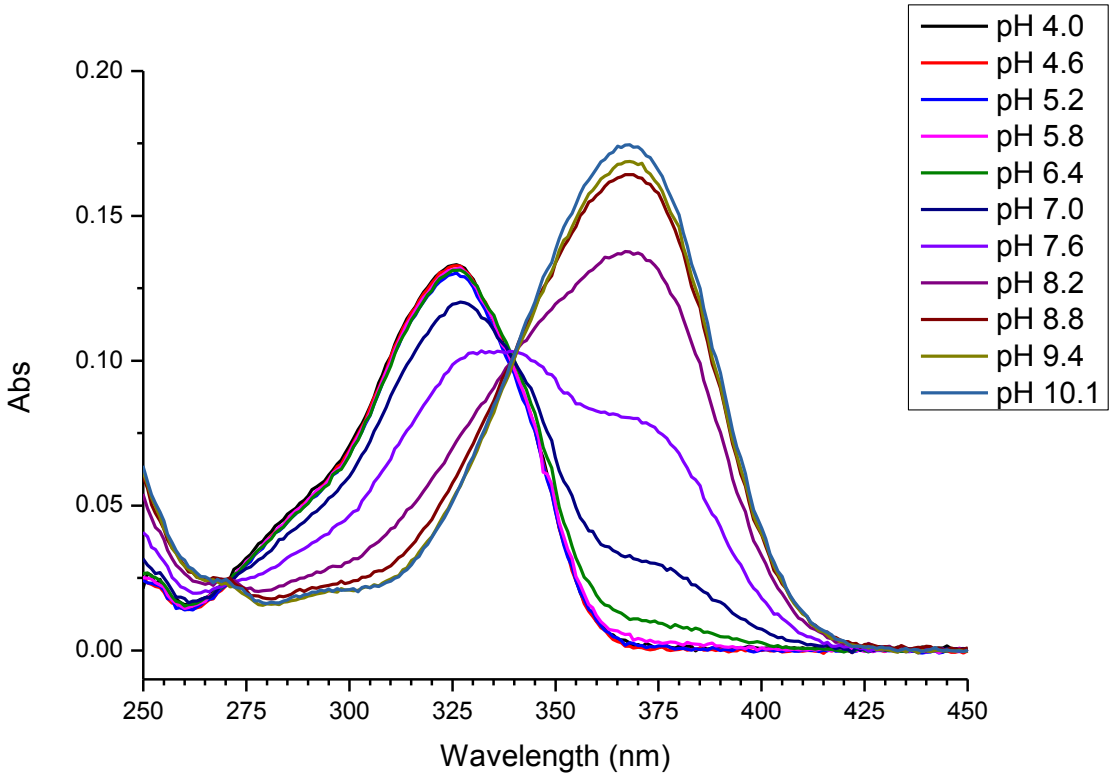


Figure S1. Absorbance of compound **1** (10 μM) at various pH:s.

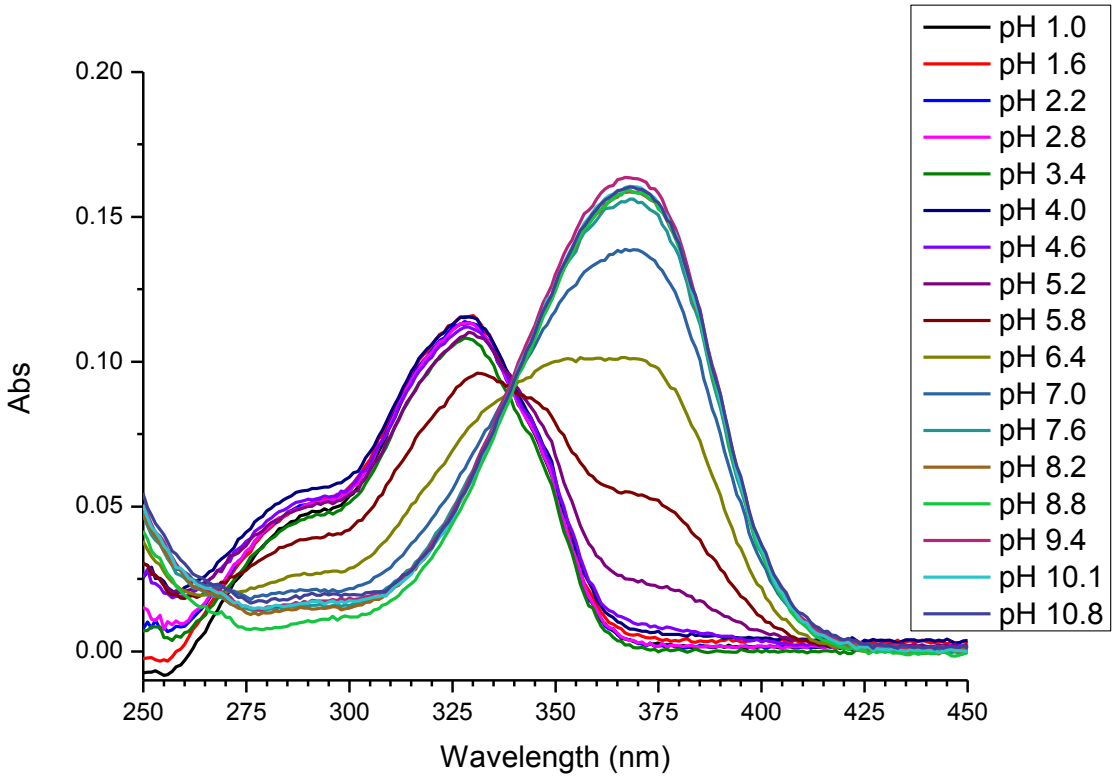


Figure S2. Absorbance of compound **4** (10 μM) at various pH:s.

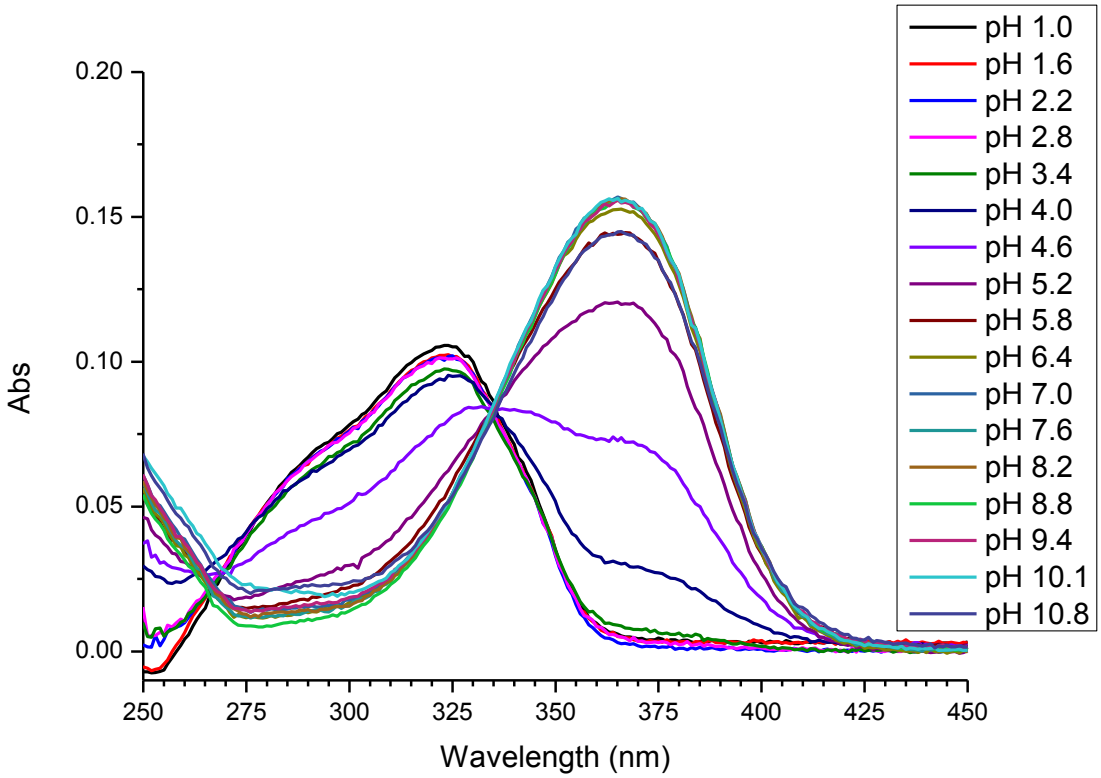


Figure S3. Absorbance of compound **5** (10 μM) at various pH:s.

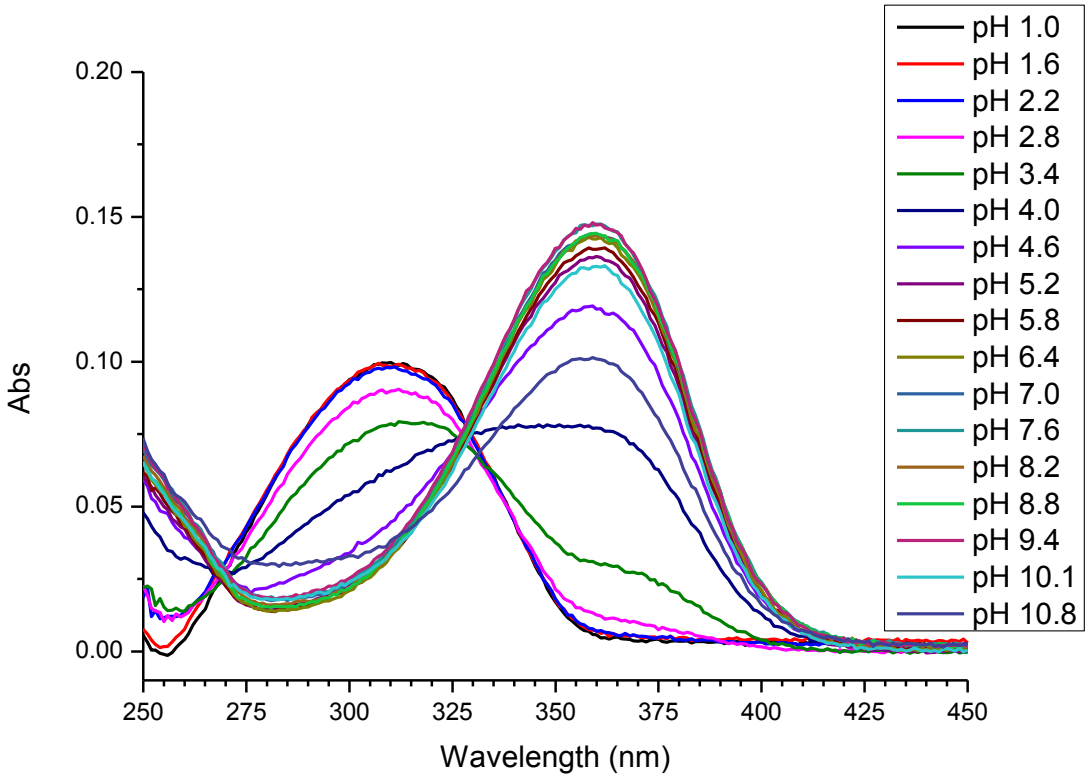


Figure S4. Absorbance of compound **6** (10 μM) at various pH:s.

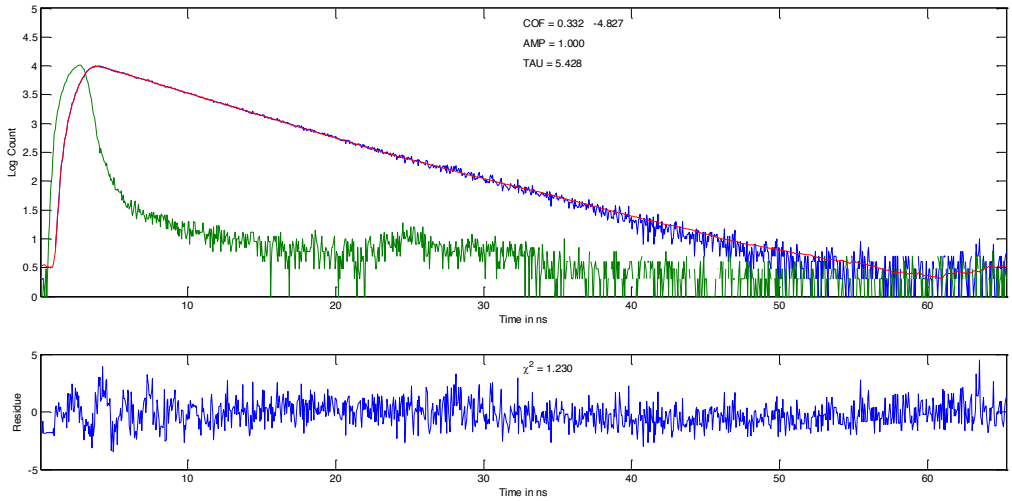


Figure S5. Fluorescence lifetime decay with fit for compound **1** (pH 10.1, ex 370 nm).

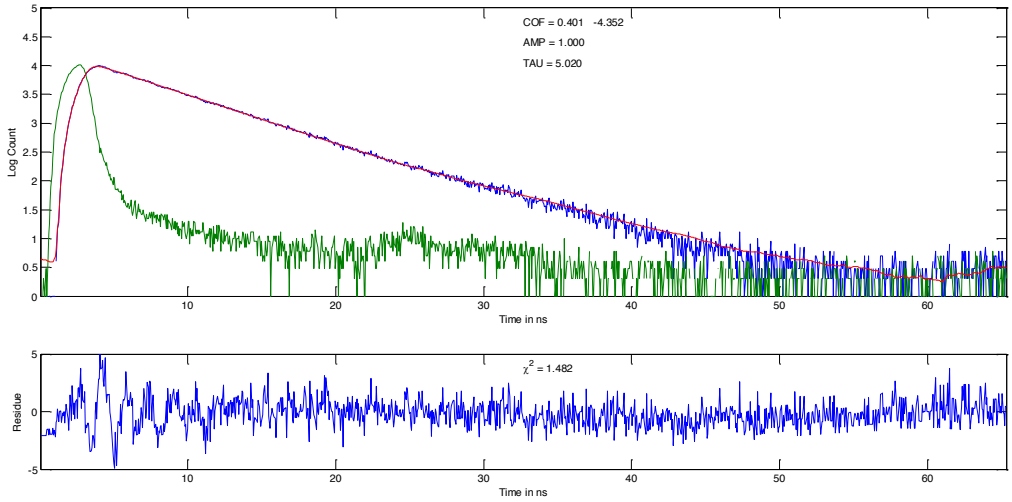


Figure S6. Fluorescence lifetime decay with fit for compound **4** (pH 10.1, ex 370 nm).

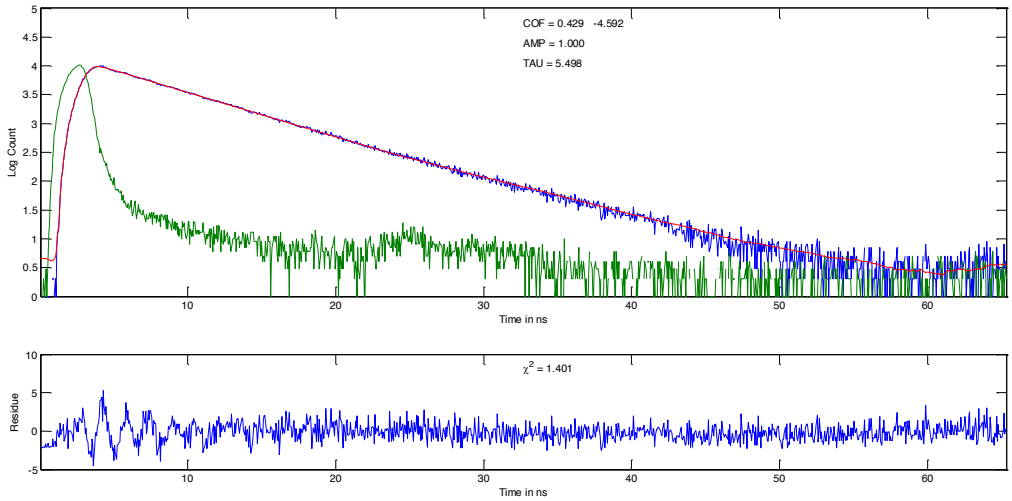


Figure S7. Fluorescence lifetime decay with fit for compound **5** (pH 10.1, ex 370 nm).

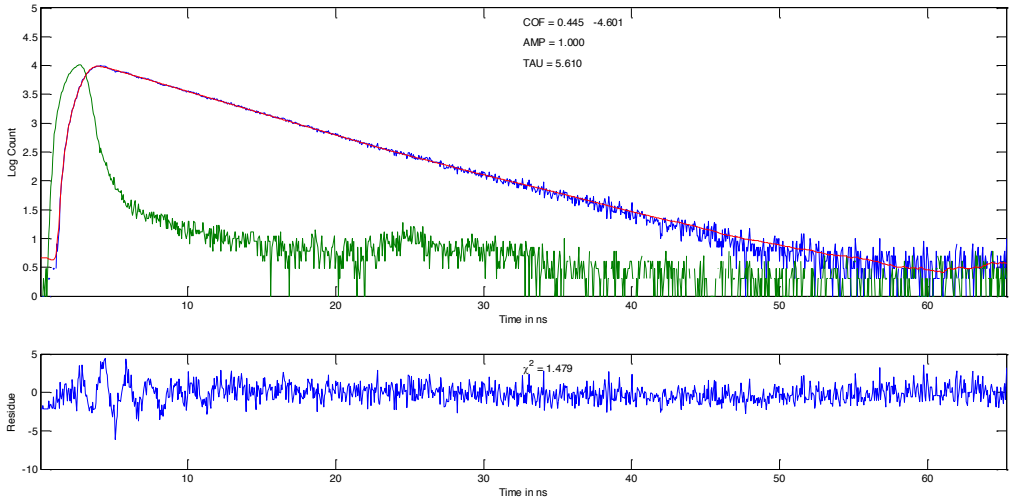


Figure S8. Fluorescence lifetime decay with fit for compound **6** (pH 10.1, ex 370 nm).

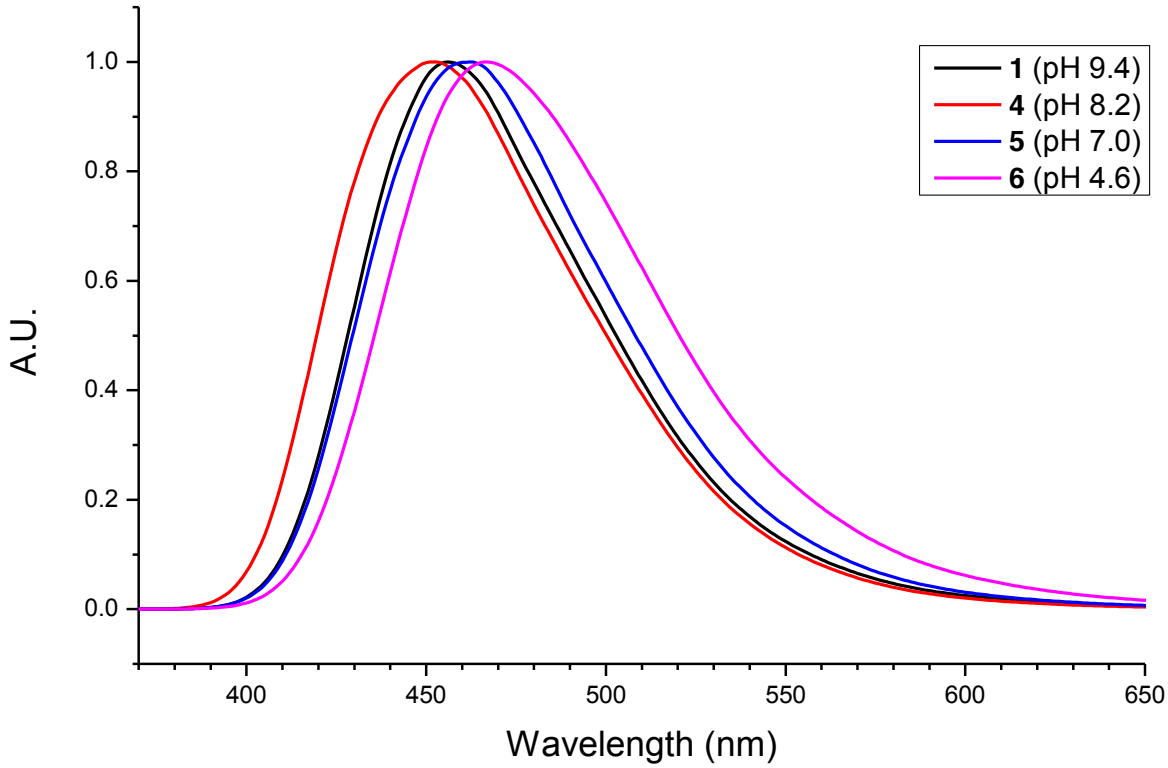


Figure S9. Smoothed and normalized emission spectra of compounds **1** and **4-6** (ex 360)

Scheme S1. Benzylation of coumarin

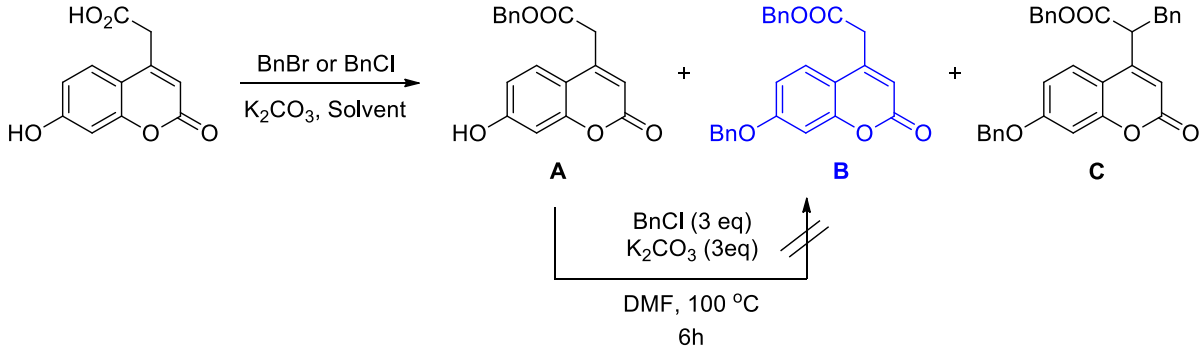
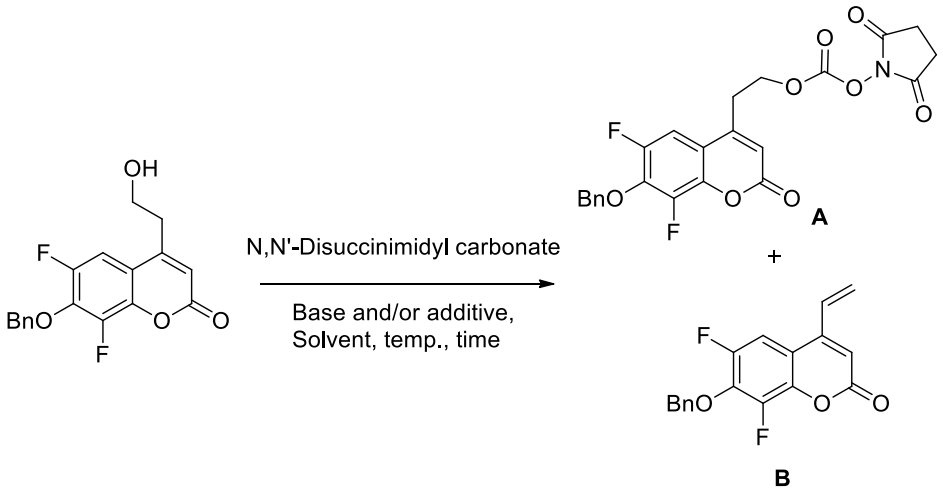


Table S1. Reaction screening conditions for benzylation of coumarin

Entry	BnBr/BnCl (eq.)	K_2CO_3 (eq.)	Solvent	Temp./time	Product (A:B:C)
1	BnBr(2.5)	3	DMF	RT/2h	C+Trace A
2	BnBr (2)	2.1	DMF	RT/2h	C+Trace A

3	BnBr (2)	2.1	Acetone	RT/9h	Trace A
4	BnBr (2)	2.1	Acetone	Reflux/24h	A and C
5	BnBr (2)	2.1	Triglyme	RT/9h	Trace A
6	BnBr (2)	2.1	Triglyme	70 ºC/24h	A and C
7	BnBr (2)	2.1	Toluene	RT/9h	No reaction
8	BnBr (2)	2.1	Toluene	70 ºC/24h	No reaction
9	BnCl(2.0)	2.1	DMF	RT/14h	Trace A
10	BnCl(2.0)	2.1	DMF	50 ºC/1.5h	20:0:0
11	BnCl(2.0)	2.1	DMF	60 ºC/3.5h	40:0:0
12	BnCl(2.0)	2.1	DMF	80 ºC/2.5h	100:0:0
13	BnCl(4.0)	4.2	DMF	80 ºC/16h	100:0:0
14	BnCl(3.0)	3	DMF	100 ºC/6h	100:0:0

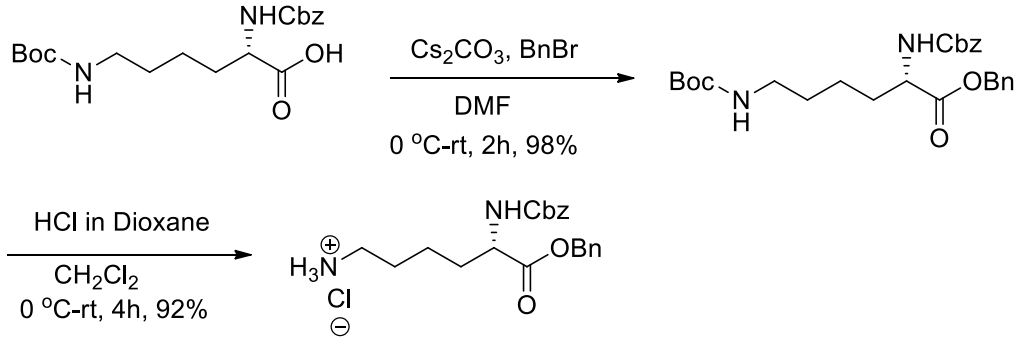
Table S2. Optimization for difluoro coumarin carbonate synthesis



Entry	Base and/or additive (eq.)	Solvent	Temp/time	A:B based on crude NMR	Yield
1	Et_3N (1.1 equiv.)	MeCN	0 ºC-rt/1h	SM+A+B	nd
2	DIPEA (1.1 equiv.)	CH_2Cl_2	0 ºC-rt/12h	0:100	nd
3	Et_3N (1.0 equiv.)	CH_2Cl_2	rt/1.5h	87:13	nd
4	DIPEA (1.0 equiv.)	CH_2Cl_2	0 ºC-rt/3h	68:32	nd

	+ DMAP (0.1 equiv.)				
5	DIPEA (1.0 equiv.) + DMAP (0.1 equiv.)	CH_2Cl_2	0 ºC-rt/3h	35:65	nd
6	DMAP (0.5 equiv.)	CH_2Cl_2	rt/15min.	95:5	nd
7	DMAP (0.2+0.2 equiv.)	CH_2Cl_2	0 ºC-rt/30min	97:3	nd
8	DMAP (total 0.15 equiv. in 2 portions)	CH_2Cl_2	0 ºC-rt/42h	100:0	Quant.
9	DMAP (0.15 equiv.)	CH_2Cl_2	0 ºC-rt/15h	100:0	Quant.

nd: yield not determined



Scheme S2. Synthesis of CBz and benzyl protected lysine hydrochloride

References

(1) J. Enderlein, R. Erdmann, *Optics Communications* **1997**, *134*, 371.