

# Supporting Information

## MediaChrom: discovering a class of pyrazinoindolone based polarity-sensitive dyes

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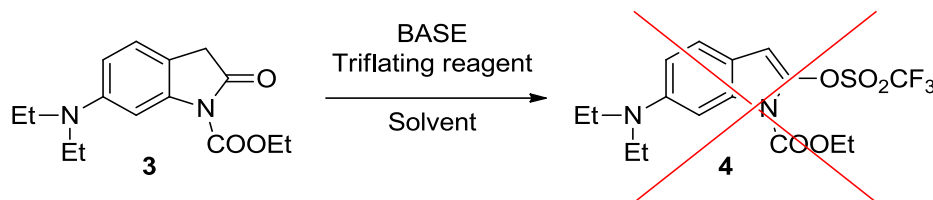
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## Attempts to obtain 2-trifluoromethanesulfonylindole derivative 4.

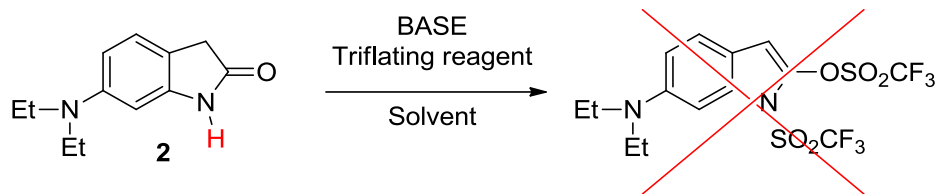
We tried different reaction conditions in order to introduce the triflate group in the position 2 of the indolinone **3** but any reaction gave the desired product (see the following table):



Entry	Base (Eq.)	Triflating agent (Eq.)	Solvent	T (°C)	Main product(s)
1	DIPEA (1.3)	Tf <sub>2</sub> O (1.5)	CH <sub>2</sub> Cl <sub>2</sub>	0 °C	Blue dimer
2	DIPEA (1.5)	Tf <sub>2</sub> O (1.3)	CH <sub>2</sub> Cl <sub>2</sub>	-78 °C	Blue dimer
3	DIPEA (1.5) then KHMDS (1.0)	PhNTf <sub>2</sub> (1.3)	CH <sub>2</sub> Cl <sub>2</sub>	-78 °C	<b>3</b>
4	KHMDS (1.25)	PhNTf <sub>2</sub> (1.25) then Tf <sub>2</sub> O (1.0)	THF	-78 °C	Blue polymer
5	/	Tf <sub>2</sub> O (1.1)	CH <sub>2</sub> Cl <sub>2</sub>	0 °C	<b>3</b> + Blue dimer
6	DTBMP (1.5)	Tf <sub>2</sub> O (1.2)	DCE	0 °C	Blue polymer

Firstly, we tried the strategy already developed in our laboratory for analogous substrates, by using DIPEA (pK<sub>a</sub> = 11) as base and Tf<sub>2</sub>O as triflating reagent (entries 1-2).<sup>1</sup> The reaction led to the formation of an unidentified blue product, in both tested conditions, *i.e.*, by changing the molar ratio between base and Tf<sub>2</sub>O and decreasing the reaction temperature. The blue product is probably a dimer with a similar-indigo structure. On the basis of these results and literature findings, we can argue that the diethylamino function at the position 6 of indole nucleus increases the reactivity of indoles, especially activating the position 3. To overcome this drawback we tried a milder triflating reagent, such as PhNTf<sub>2</sub>, in the presence of the same base. However under these conditions no product was obtained (entry 3), and the starting material was recovered unreacted even after the addition of a stronger base, such as KHMDS (pK<sub>a</sub> = 28).<sup>2</sup> The direct use of a strong base together with the mild triflating reagent (entry 4) did not lead to any reaction product, whereas a subsequent addition of Tf<sub>2</sub>O led to the formation of an unidentified dark-blue dimerization/polymerization product. On the basis of these data we concluded that the use of the mild triflating reagent (PhNTf<sub>2</sub>) always leads to the recovery of the starting material, regardless of strength of the base used. Conversely, the use of the strong triflating agent Tf<sub>2</sub>O, leads always to the formation of unidentified blue dimers/polymers depending of the strength of the base used. As further attempt, we performed the reaction in the presence of the strong triflating reagent without the base (entry 5), and in this case we recovered the starting material beside traces of dimerization product. Finally, the use of an even weaker base such as DTBMP (pK<sub>a</sub> ≈ 6)<sup>3</sup> with Tf<sub>2</sub>O at 0 °C resulted in the isolation of a dark-blue polymerization product (entry 6).

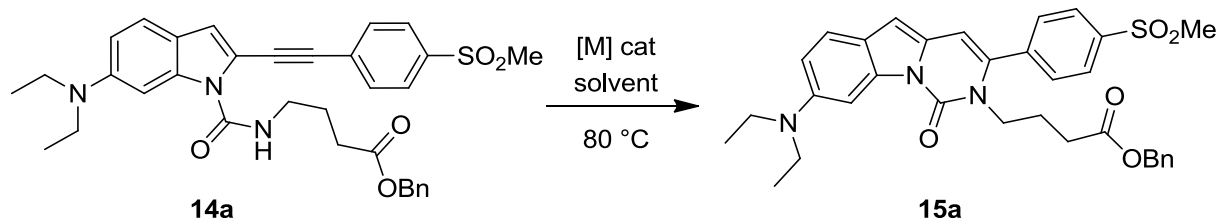
Therefore, we planned an alternative strategy involving a double triflation of the 6-(diethylamino)indolin-2-one. This path seemed to be feasible taking advantage from the absence of deactivating group on the nitrogen of indolinone and the chance to modulate the strength of the base and of the triflating reagent. The results are shown in following table:



Entry	Base (Eq.)	Triflating agent (Eq.)	Solvent	T (°C)	Main product(s)
1	TEA (2.3)	Tf <sub>2</sub> O (2.2)	THF	rt	Blue polymer
2	DTBMP (3.0)	Tf <sub>2</sub> O (3.0)	CH <sub>2</sub> Cl <sub>2</sub>	0 °C	Blue polymer
3	DIPEA (3.0)	PhNTf <sub>2</sub> (3.0)	CH <sub>2</sub> Cl <sub>2</sub>	0 °C	<b>2</b>

In the presence of TEA (pK<sub>a</sub> = 10.6, entry 1) or DTBMP (pK<sub>a</sub> ≈ 6, entry 2) and Tf<sub>2</sub>O we obtained only the polymerization product. Conversely, with DIPEA (pK<sub>a</sub> = 11, entry 3) and PhNTf<sub>2</sub> we only recovered the starting material, as in all previous cases in which the mild triflating reagent was used.

#### Study on the Au-catalyzed cycloisomerization.



Under a nitrogen atmosphere, to a solution of **14a** (0.10 mmol) in the proper solvent (3.5 mL, see table below) the catalyst (0.005 mmol) was added. The reaction mixture was heated at 80 °C for the time reported in the table below. The reaction mixture was evaporated to dryness and the crude was purified by flash chromatography over a silica gel column

Cat.	Solv.	Time (h)	Yield (%)
AuCIPPh <sub>3</sub> (5 mol%), AgOTf (5 mol%)	Toluene	24	- <sup>a</sup>
AgOTf (10 mol%)	DCE	24	- <sup>a</sup>
PPh <sub>3</sub> AuNTf <sub>2</sub> (5 mol%)	DCE	24	- <sup>a</sup>
IPrAuSbF <sub>6</sub> (5 mol%)	DCE	6	53

<sup>a</sup> The starting material was almost quantitatively recovered.

**Table S1:** Changes in dipole moments of MediaChrom **15a-f**.

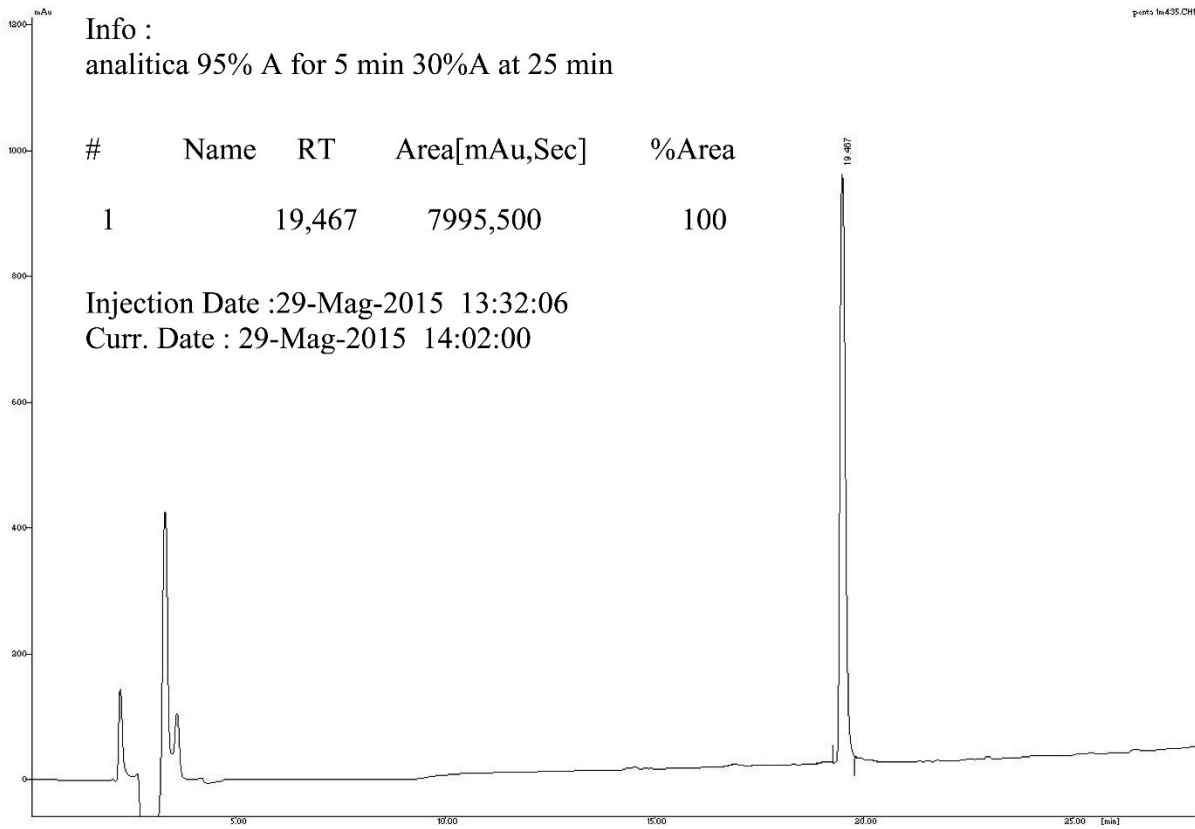
<b>MediaChrom</b>	$\mu^* - \mu$ (Debye)
<b>15a</b>	13.0
<b>15b</b>	-
<b>15c</b>	13.3
<b>15d</b>	13.4
<b>15e</b>	13.0
<b>15f</b>	13.4

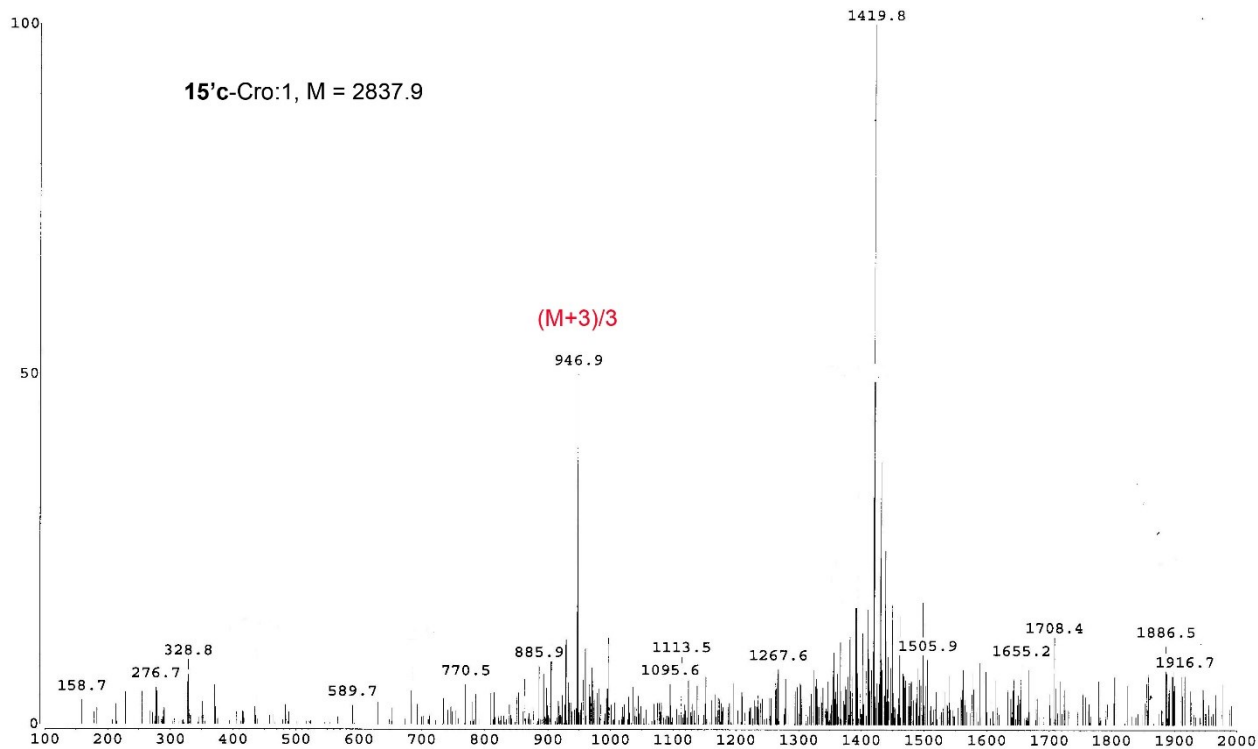
**Table S2:** Comparison between fluorescent emission peaks of MediaChrom **15c** and **15'c**.<sup>a</sup>

<b>Solvent</b>	<b>MediaChrom 15c (benzyl ester)</b>	<b>MediaChrom 15'c (carboxyl free)</b>
hexane	490 nm	487 nm
<i>n</i> -octanol	525 nm	520 nm
ethanol	540 nm	537 nm
DMF	565 nm	563 nm

<sup>a</sup> excitation wavelength: 393 nm

**Chromatogram and Mass spectra of 15’c-Cro:1: M = 2837.9. ESI-MS m/z (%): 1419.8 [(M + 2)/2]<sup>+</sup> (100), 946.9 [(M + 3)/3]<sup>+</sup>.**





## References

- <sup>1</sup> Rossi, E.; Abbiati, G.; Canevari, V.; Celentano, G.; Magri, E. *Synthesis* **2006**, 2, 299–304.
- <sup>2</sup> Prandi, C.; Ferrali, A.; Guarna, A.; Venturello, P.; Occhiato, E. G. *J. Org. Chem.* **2004**, 69, 7705–7709.
- <sup>3</sup> Conway, S. C.; Gribble, G. W. *Synt. Comm.* **1992**, 22, 2987–2995.

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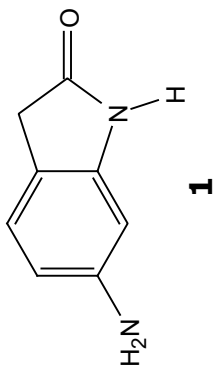
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6.75

6.09  
6.08  
6.07  
6.06

4.98

3.21



S7

H<sub>2</sub>O

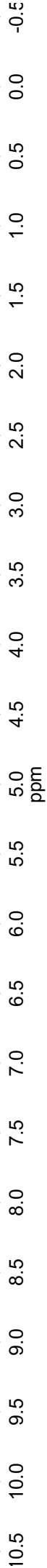
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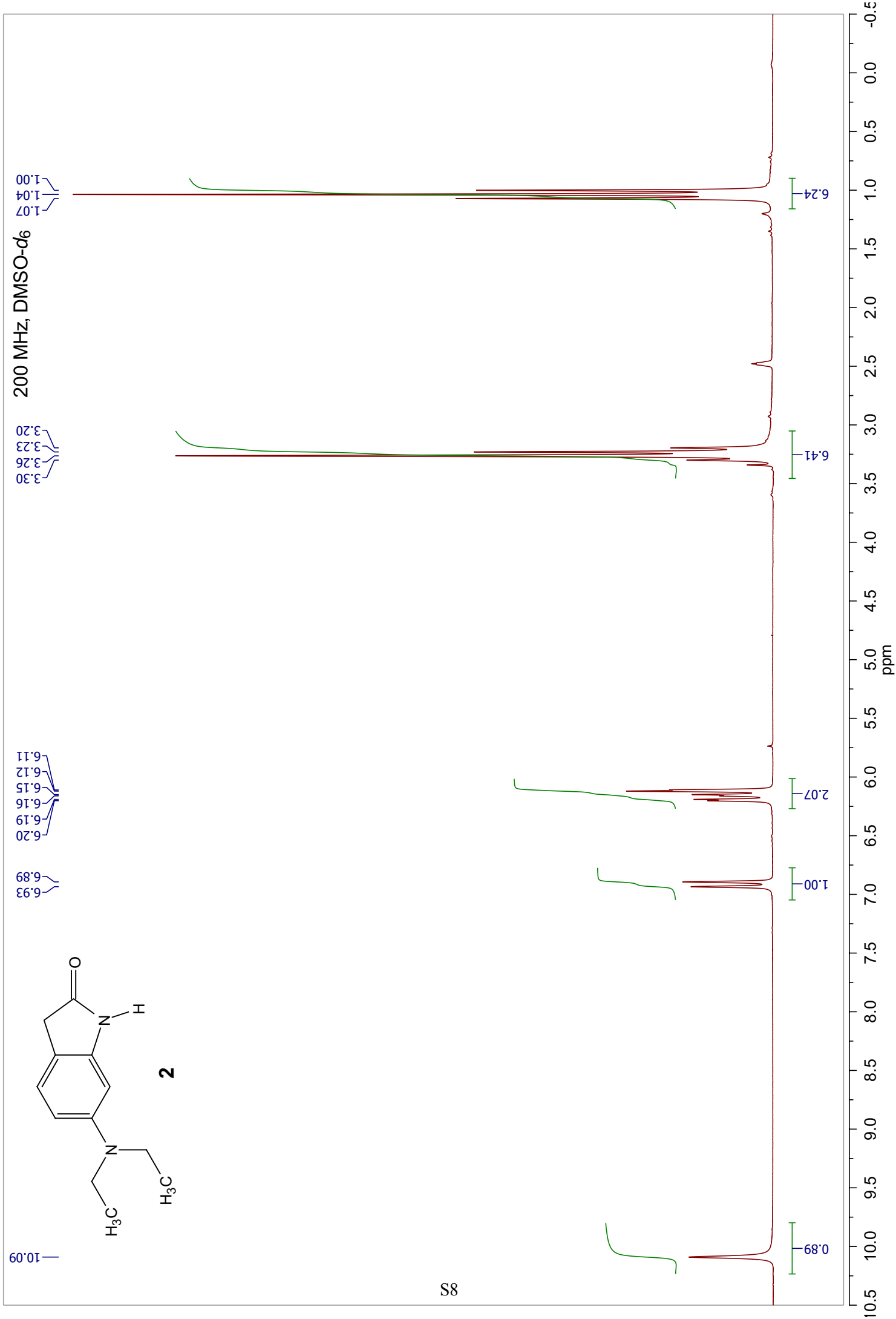
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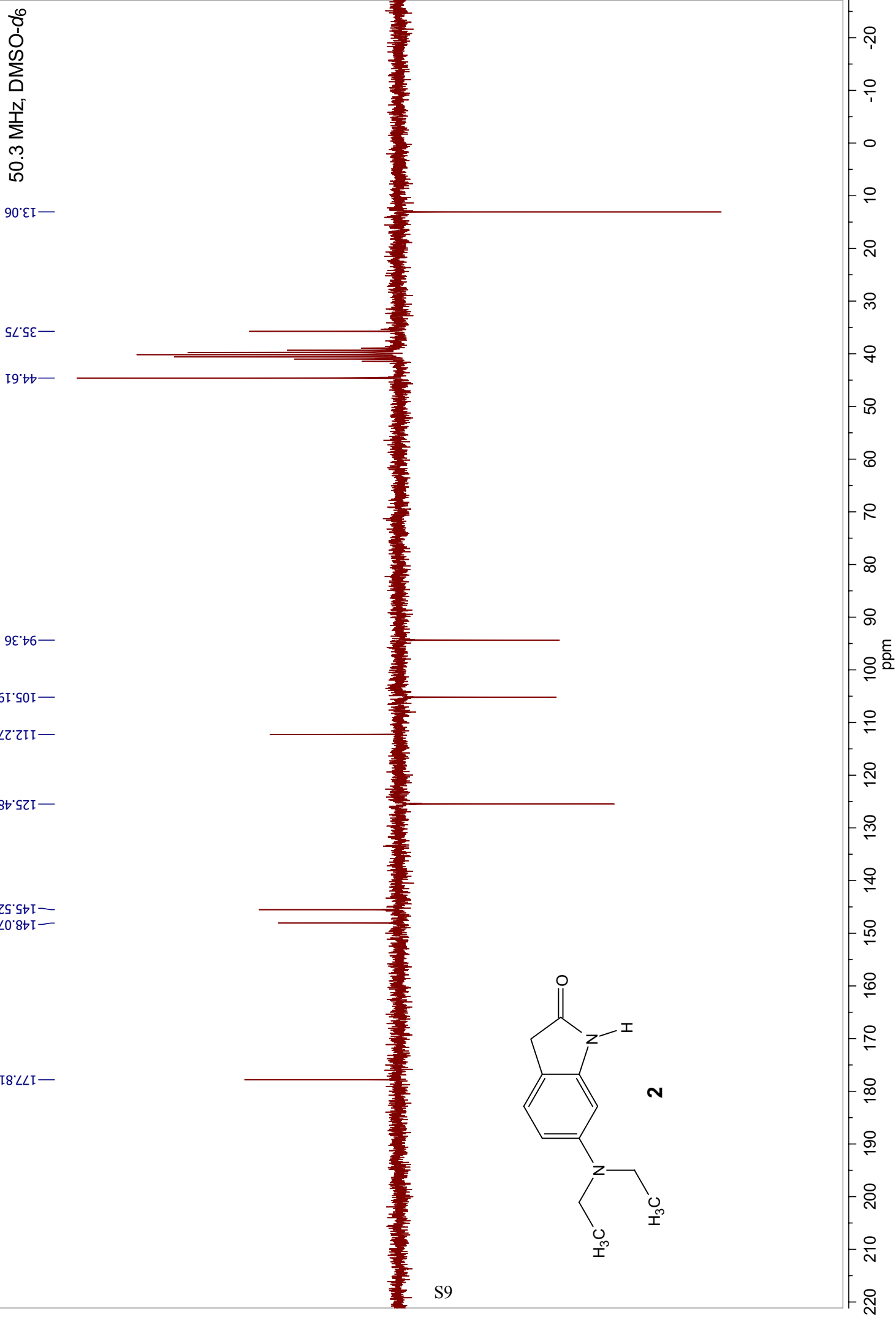
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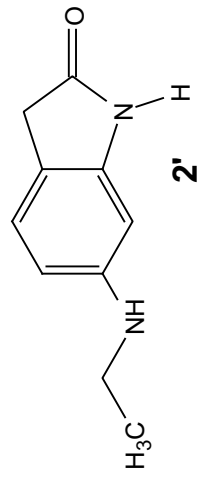
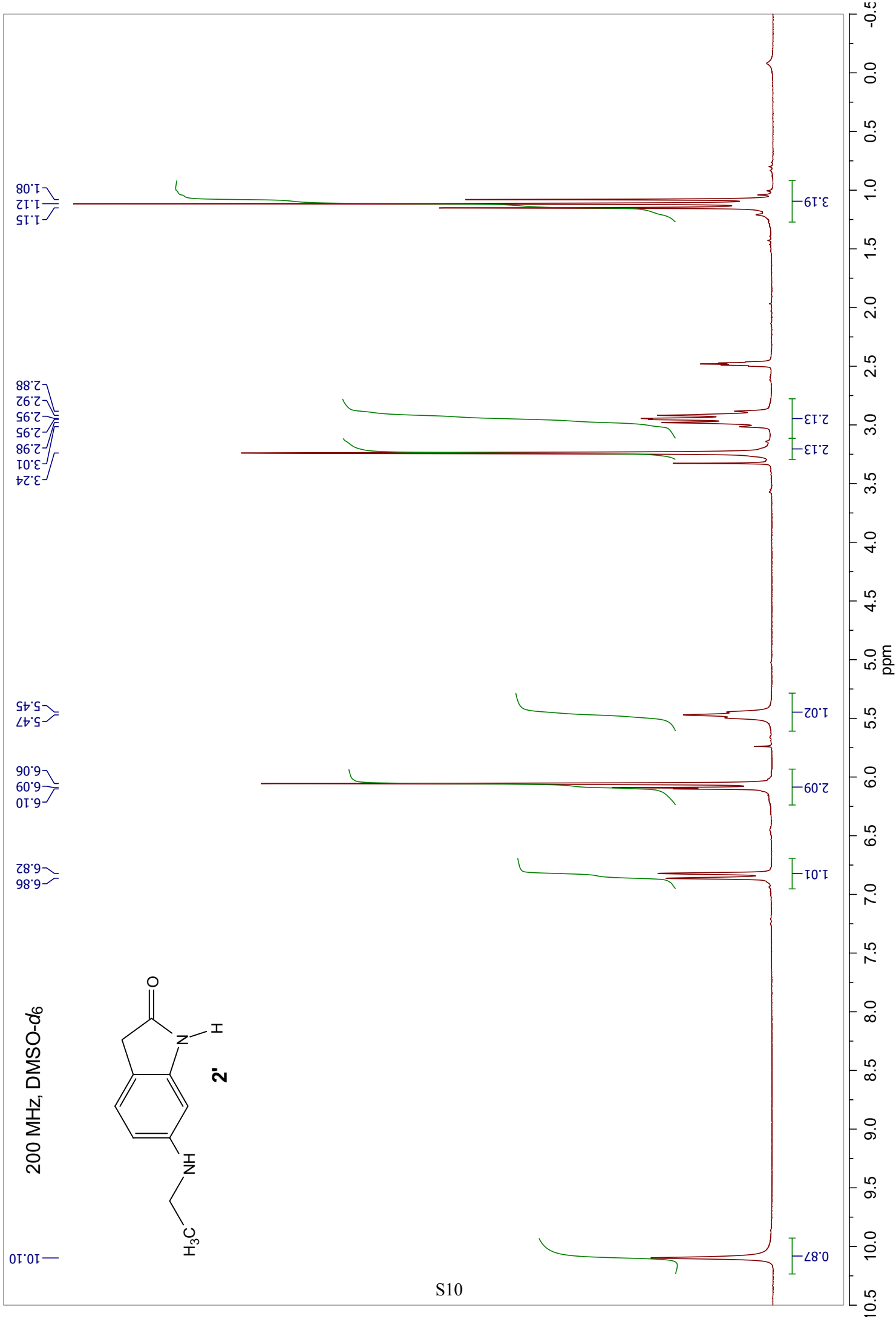
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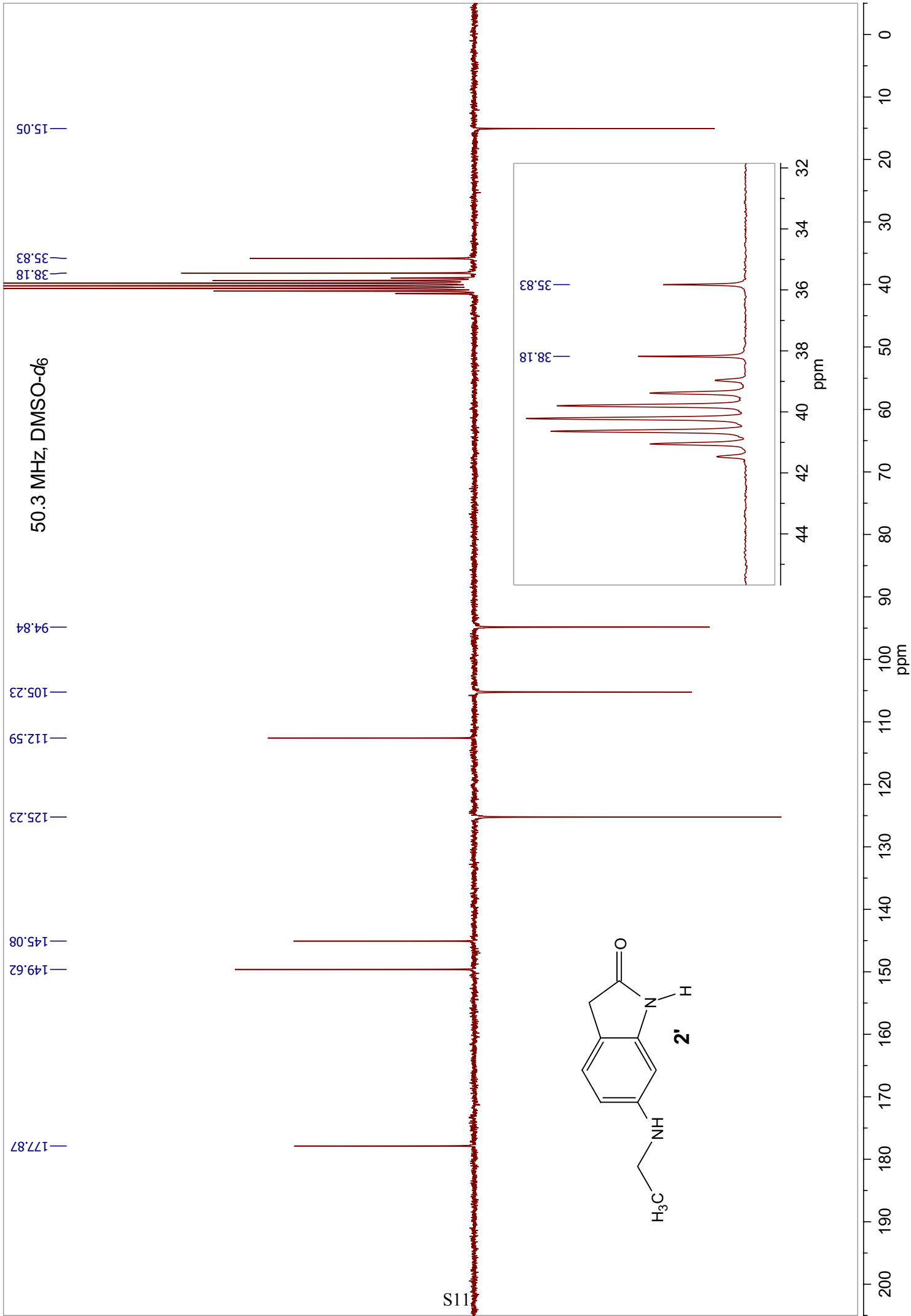








200 MHz, DMSO-d<sub>6</sub>



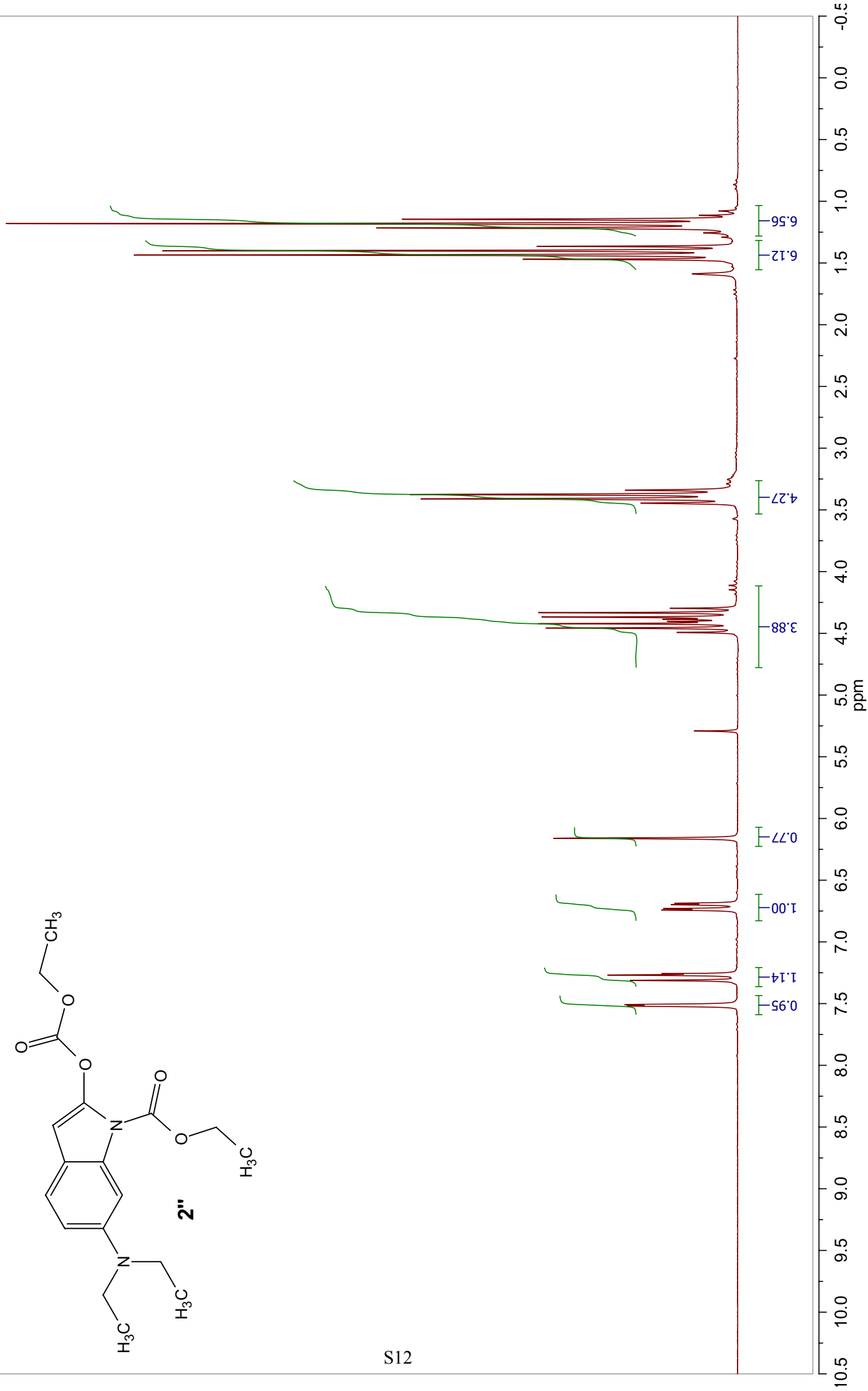
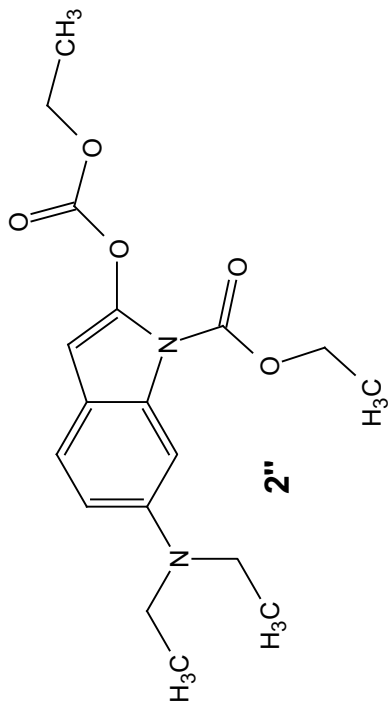
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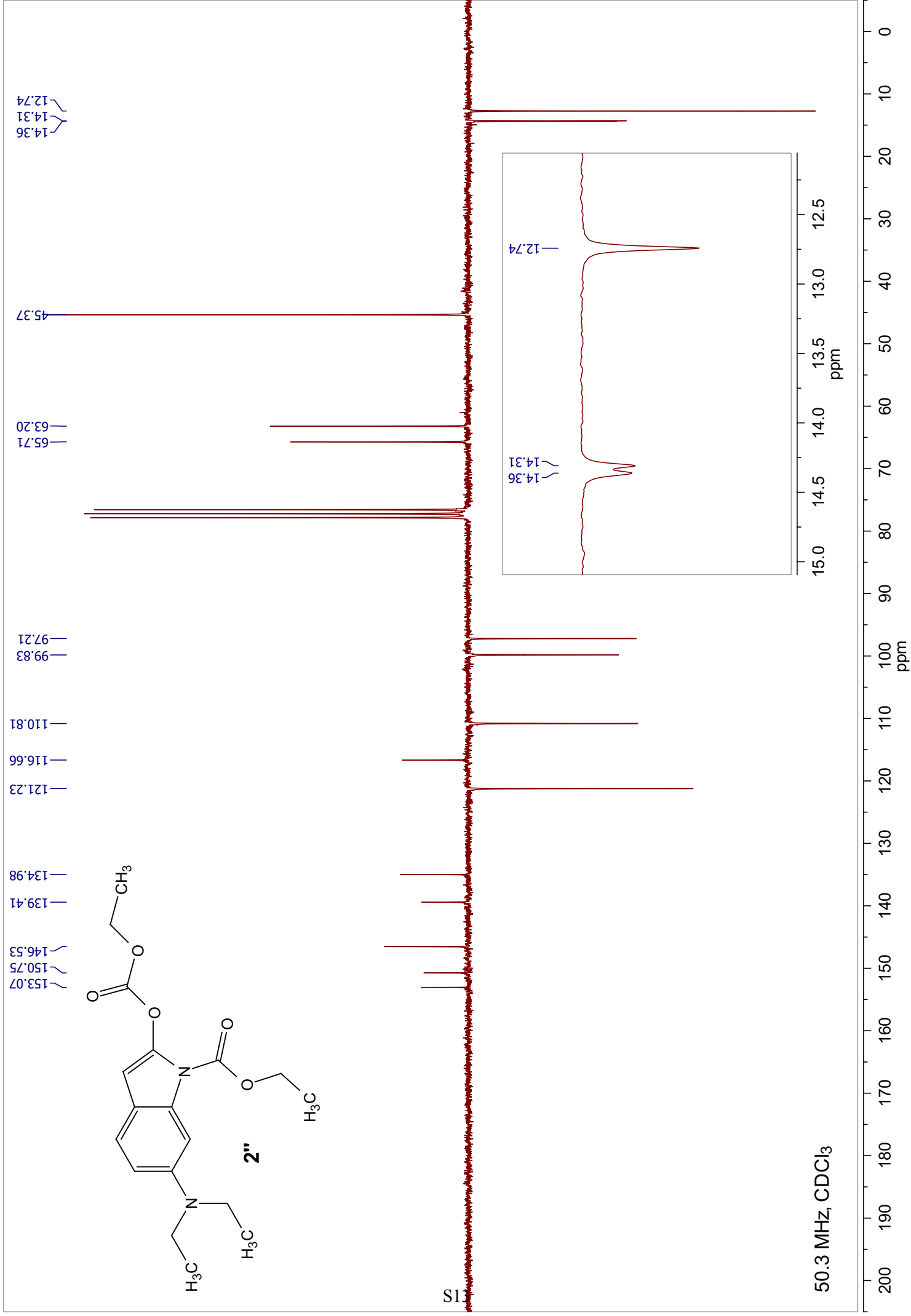
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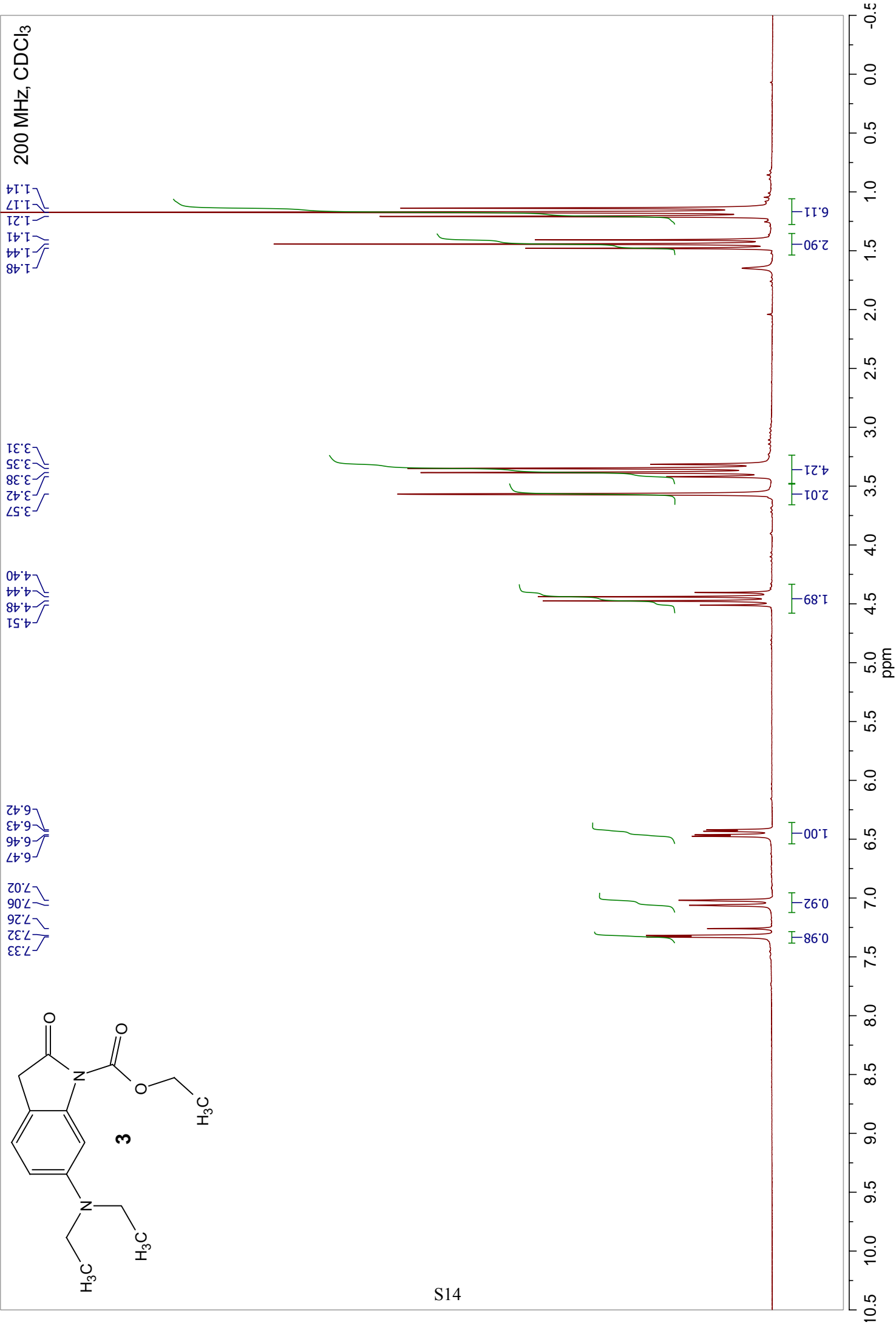
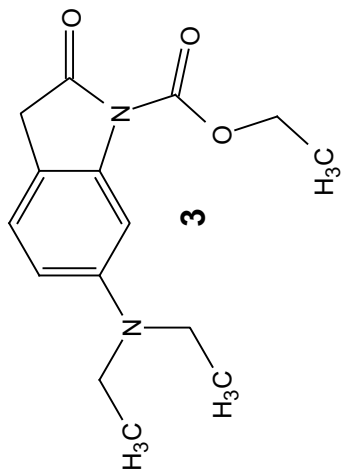
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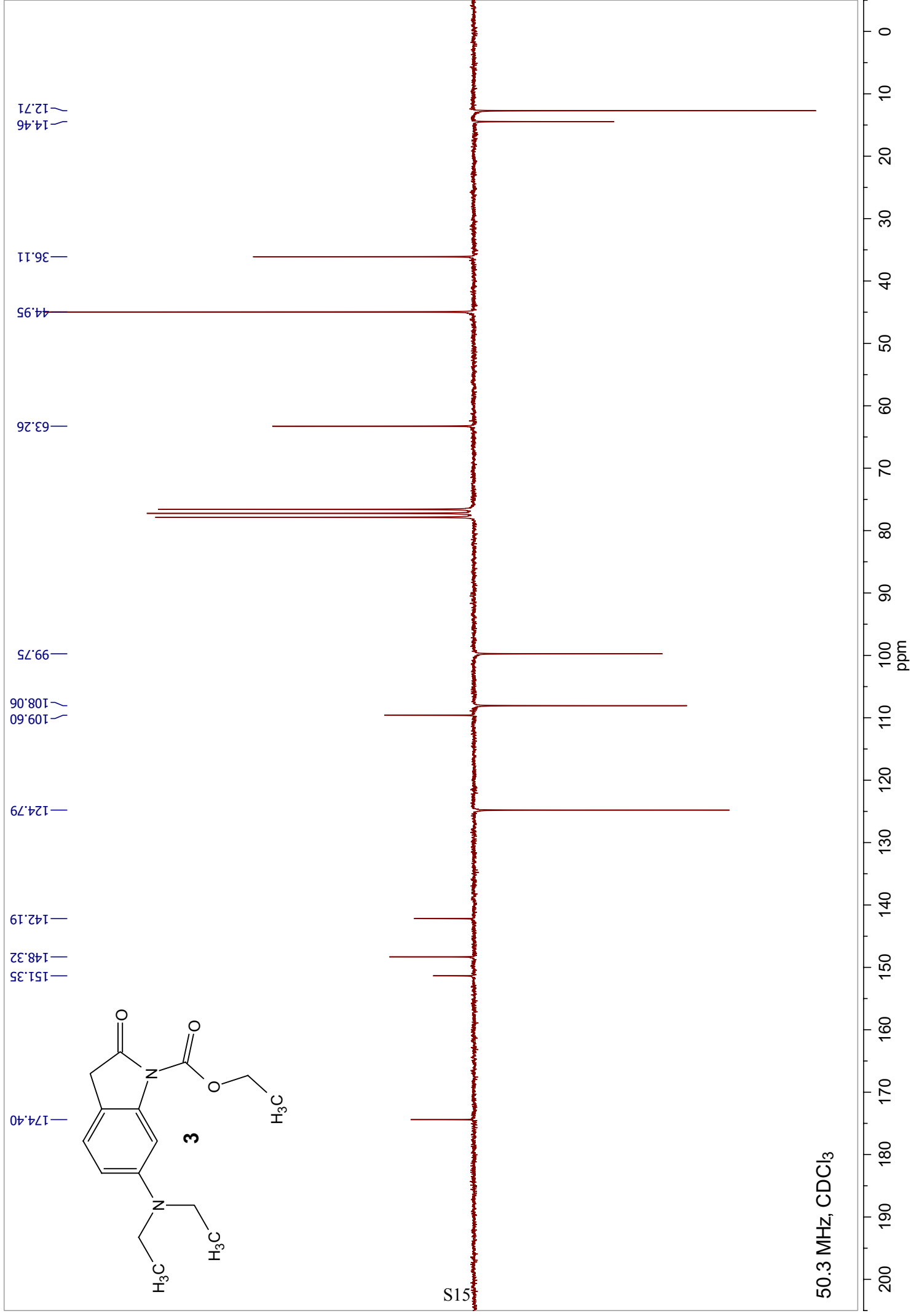
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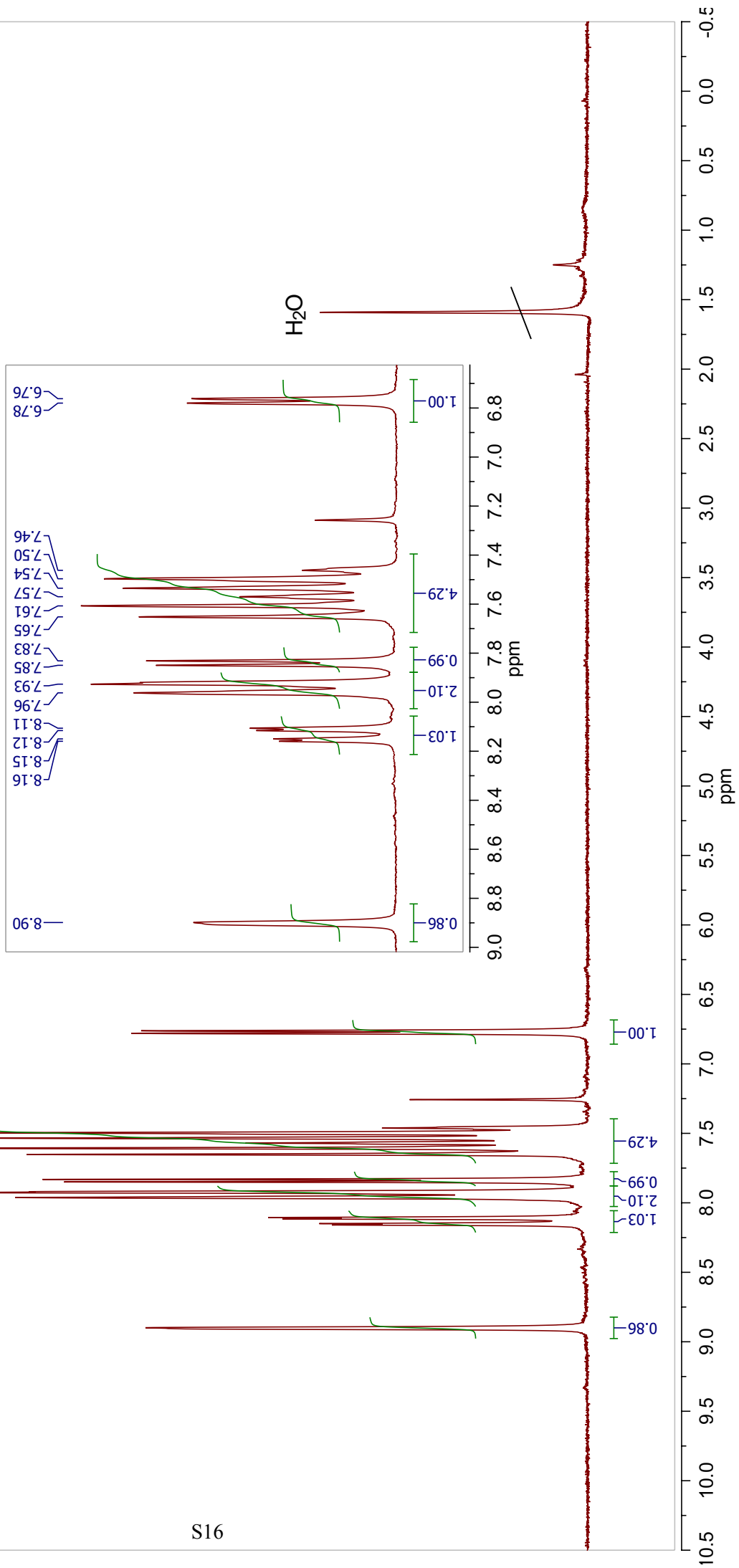
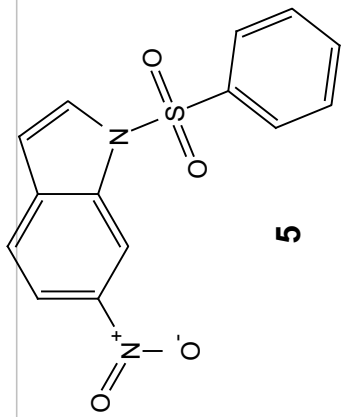
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7.52





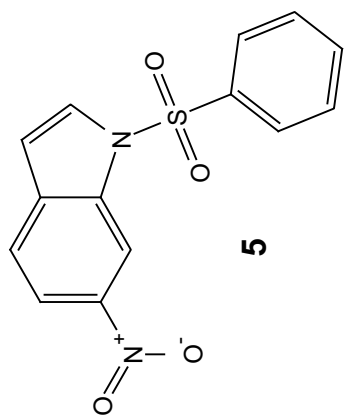
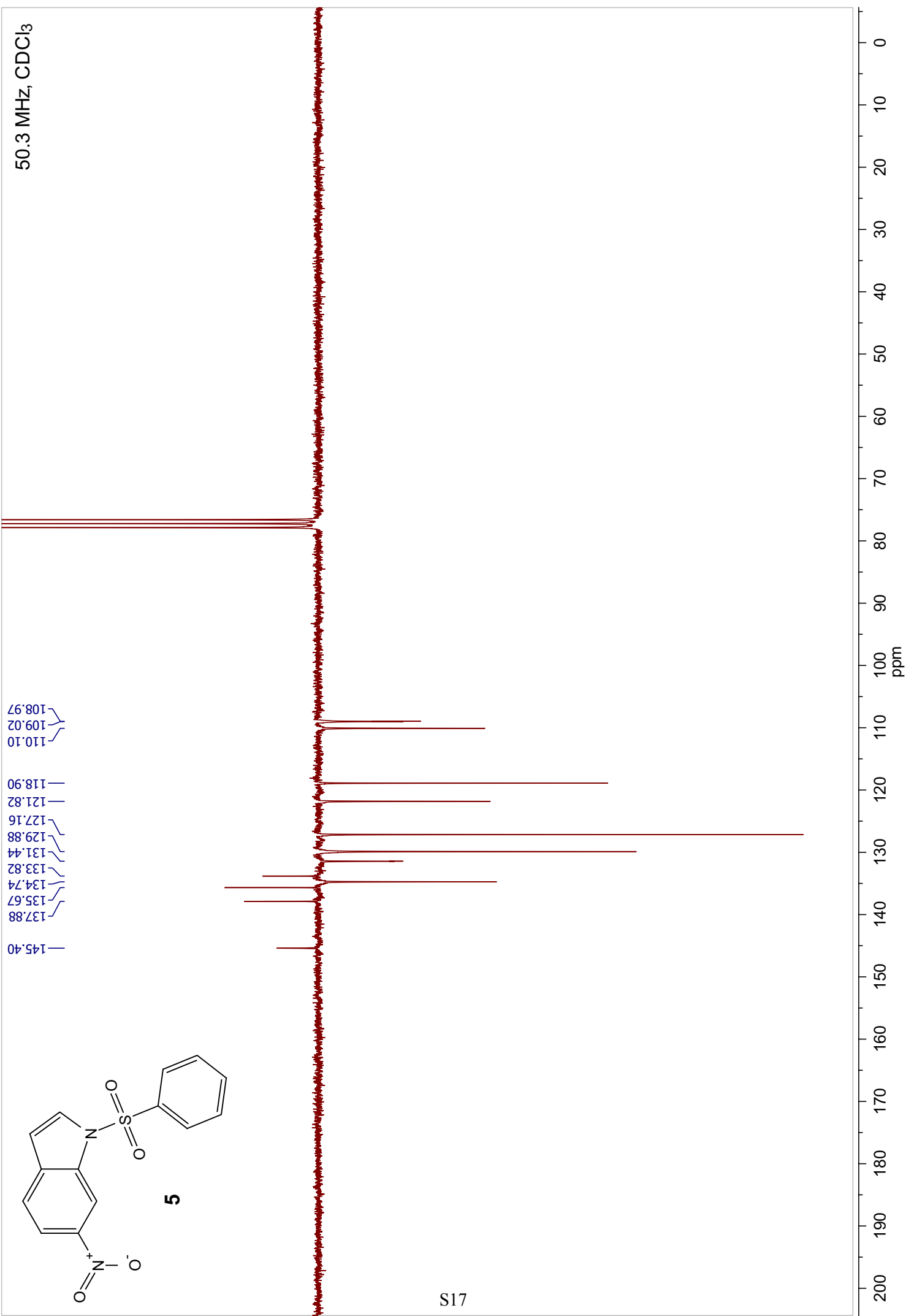




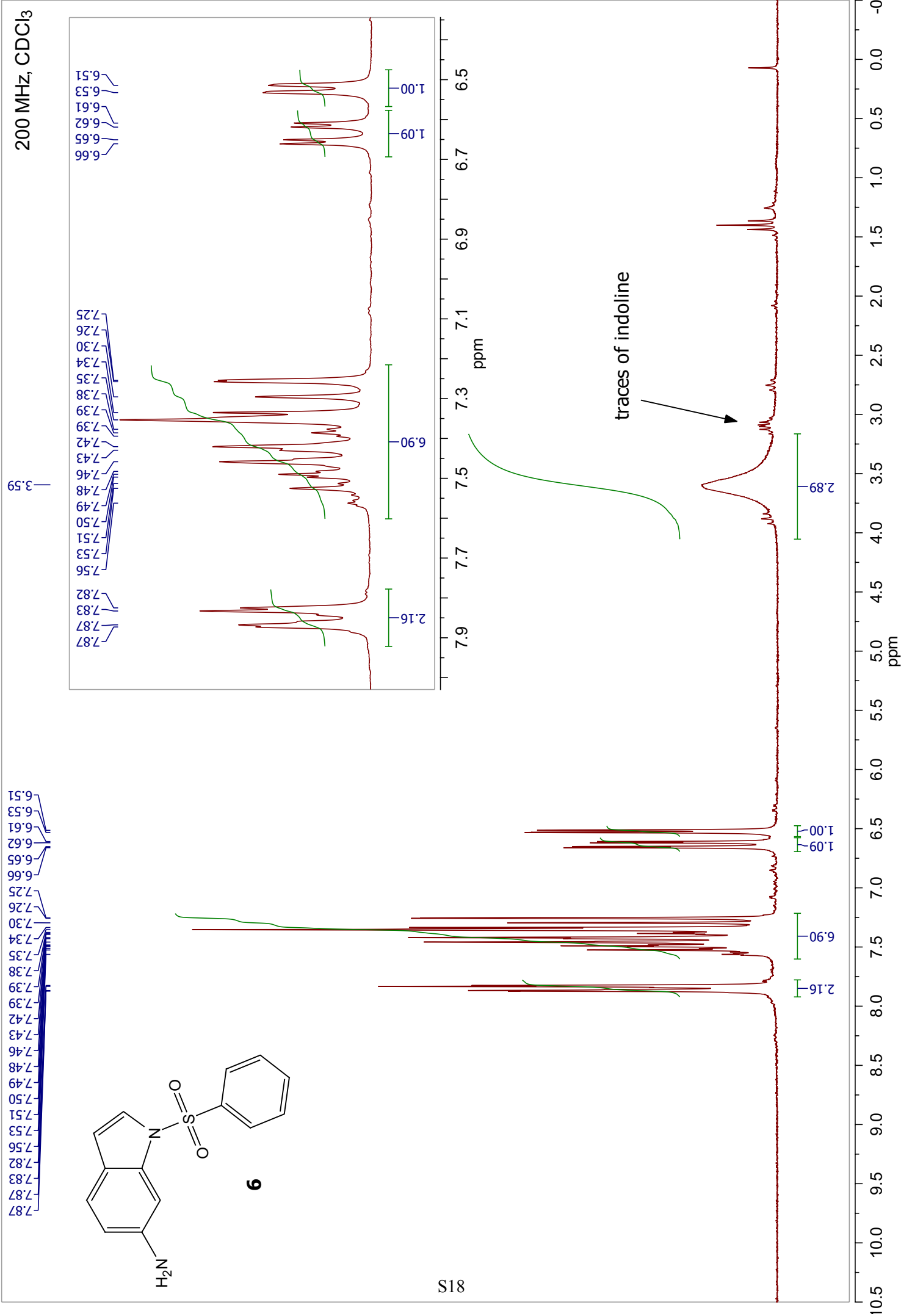




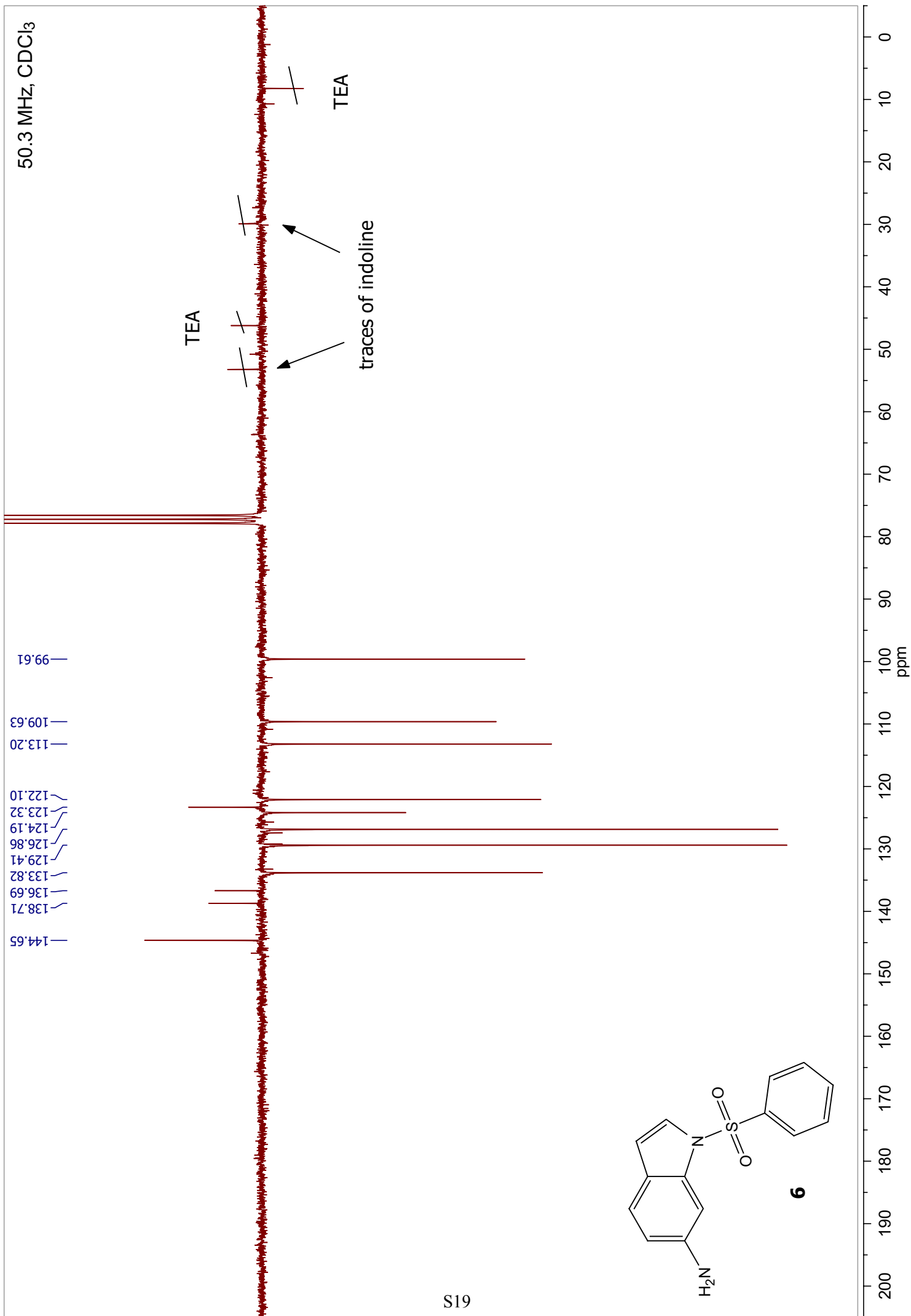
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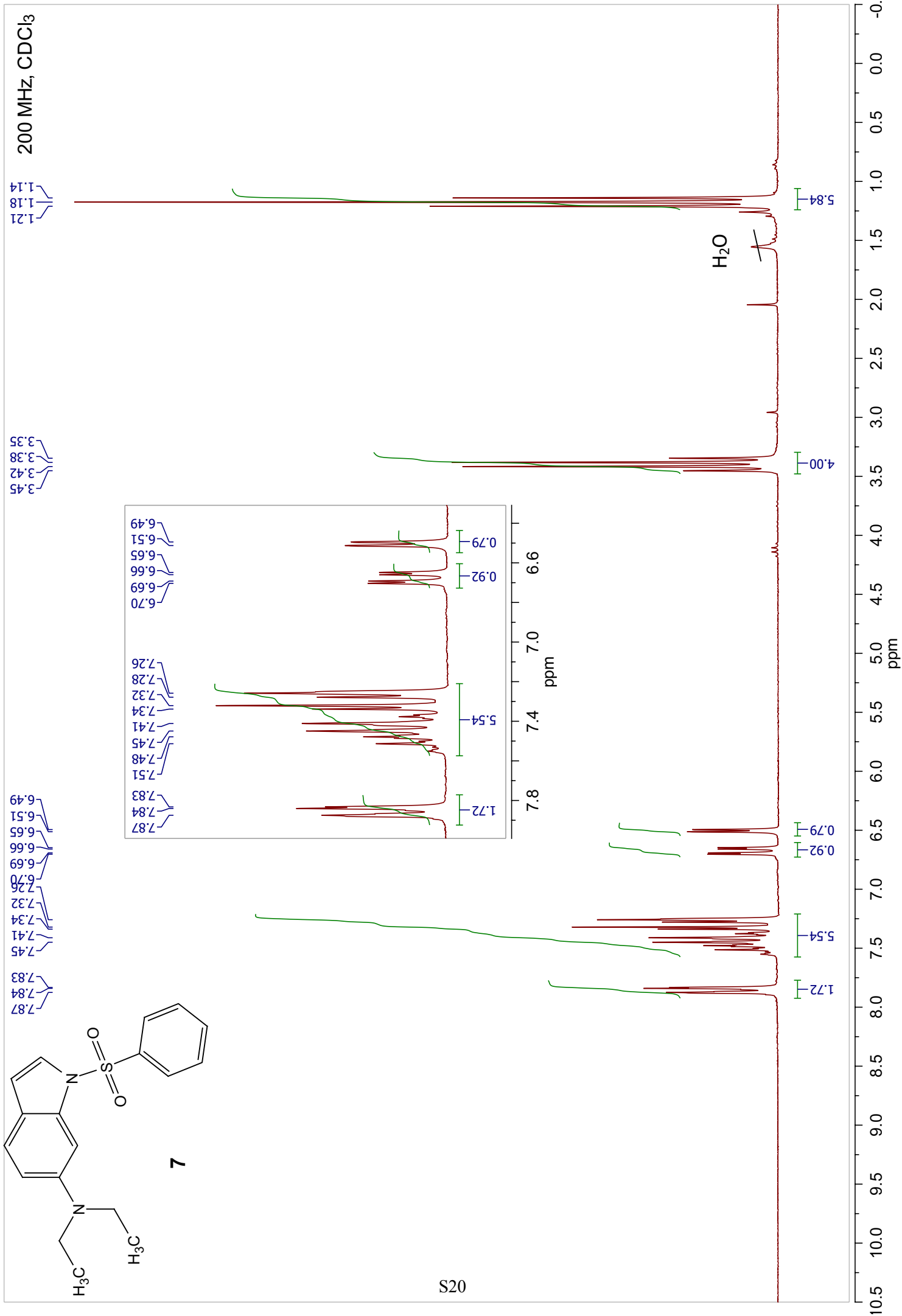


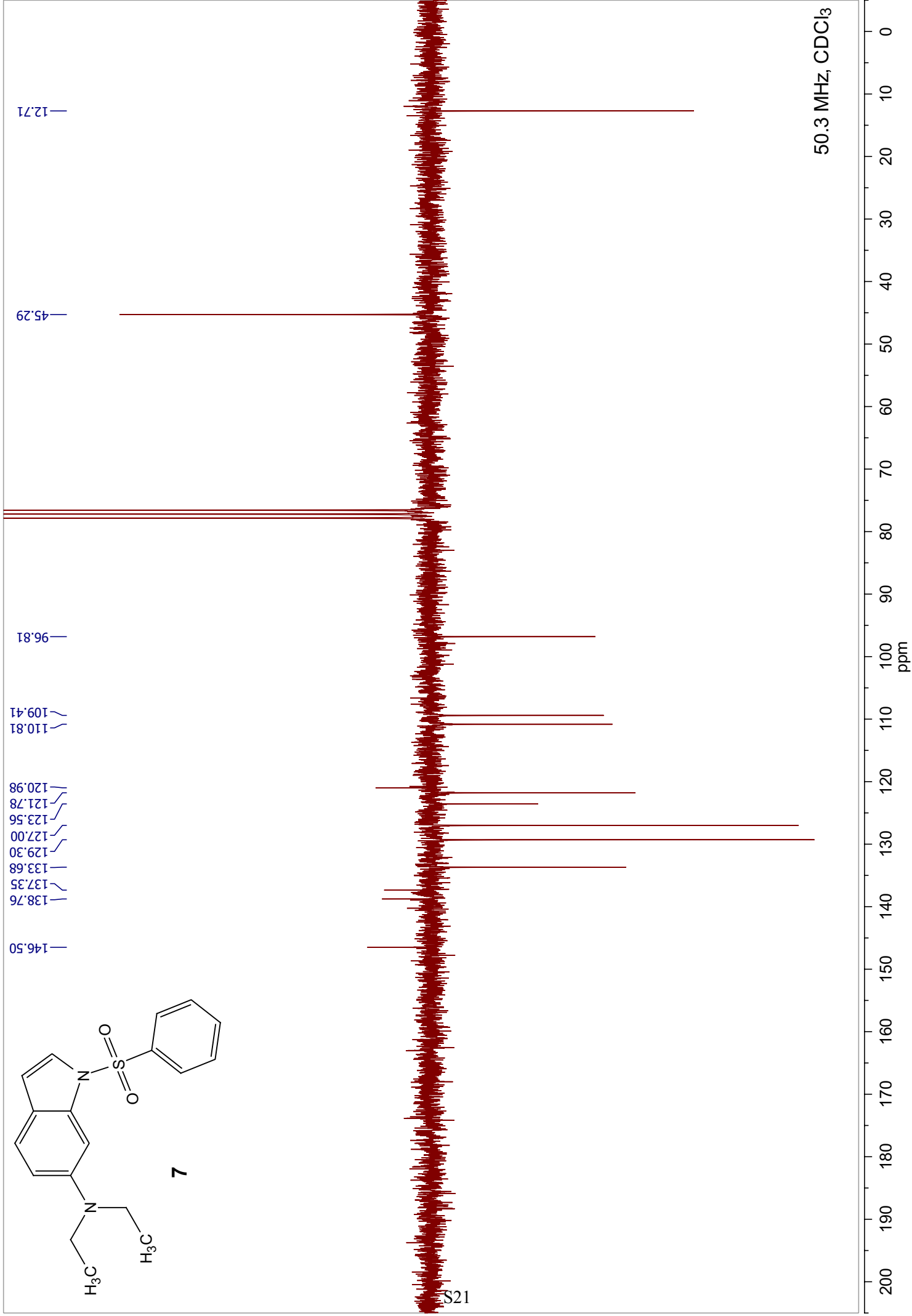
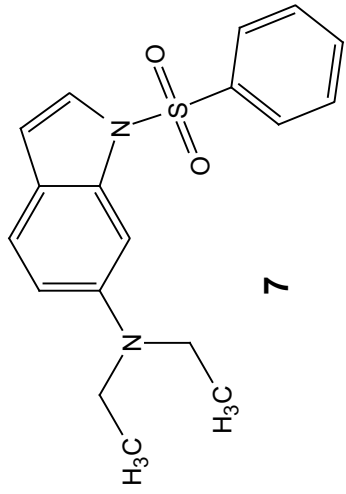
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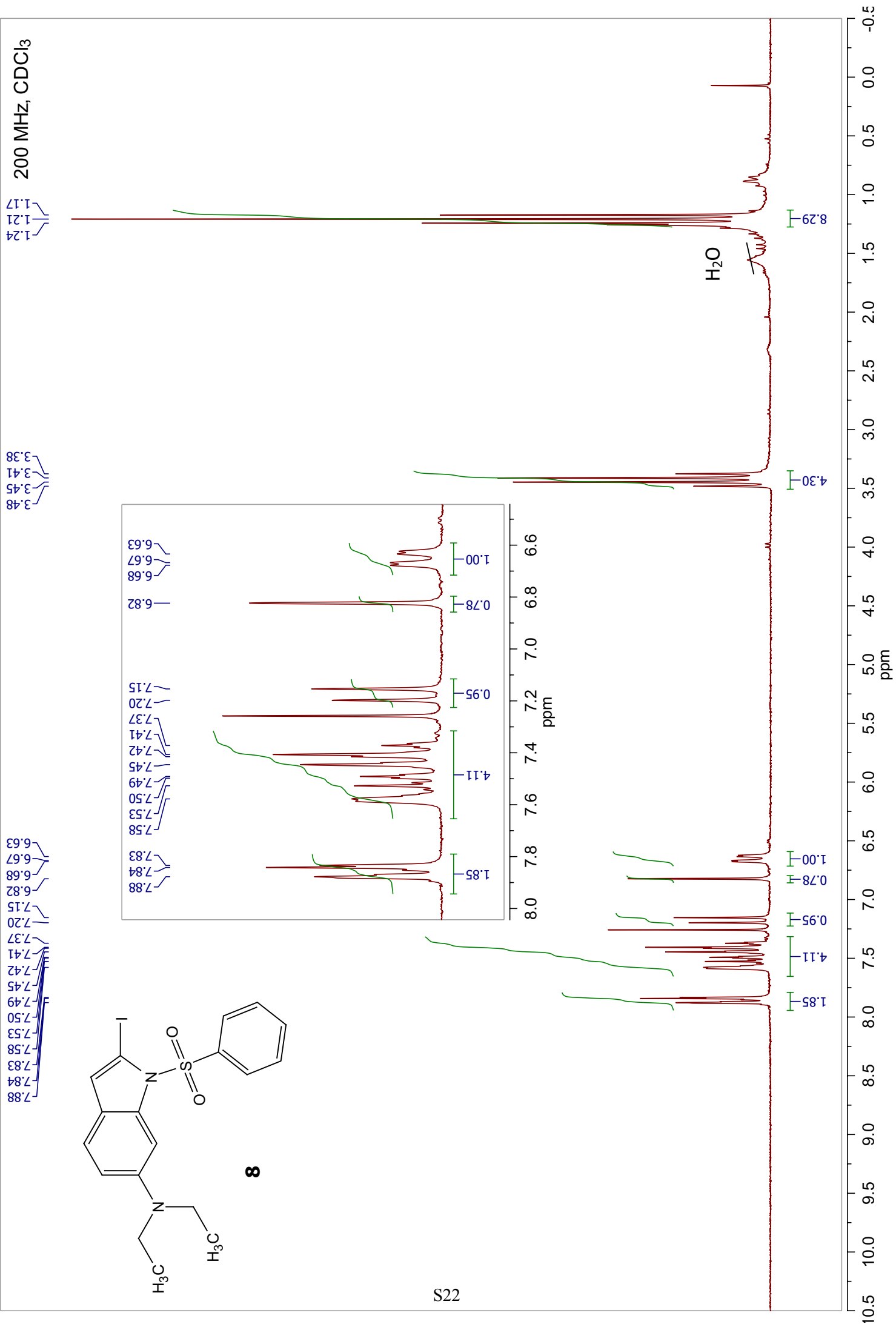


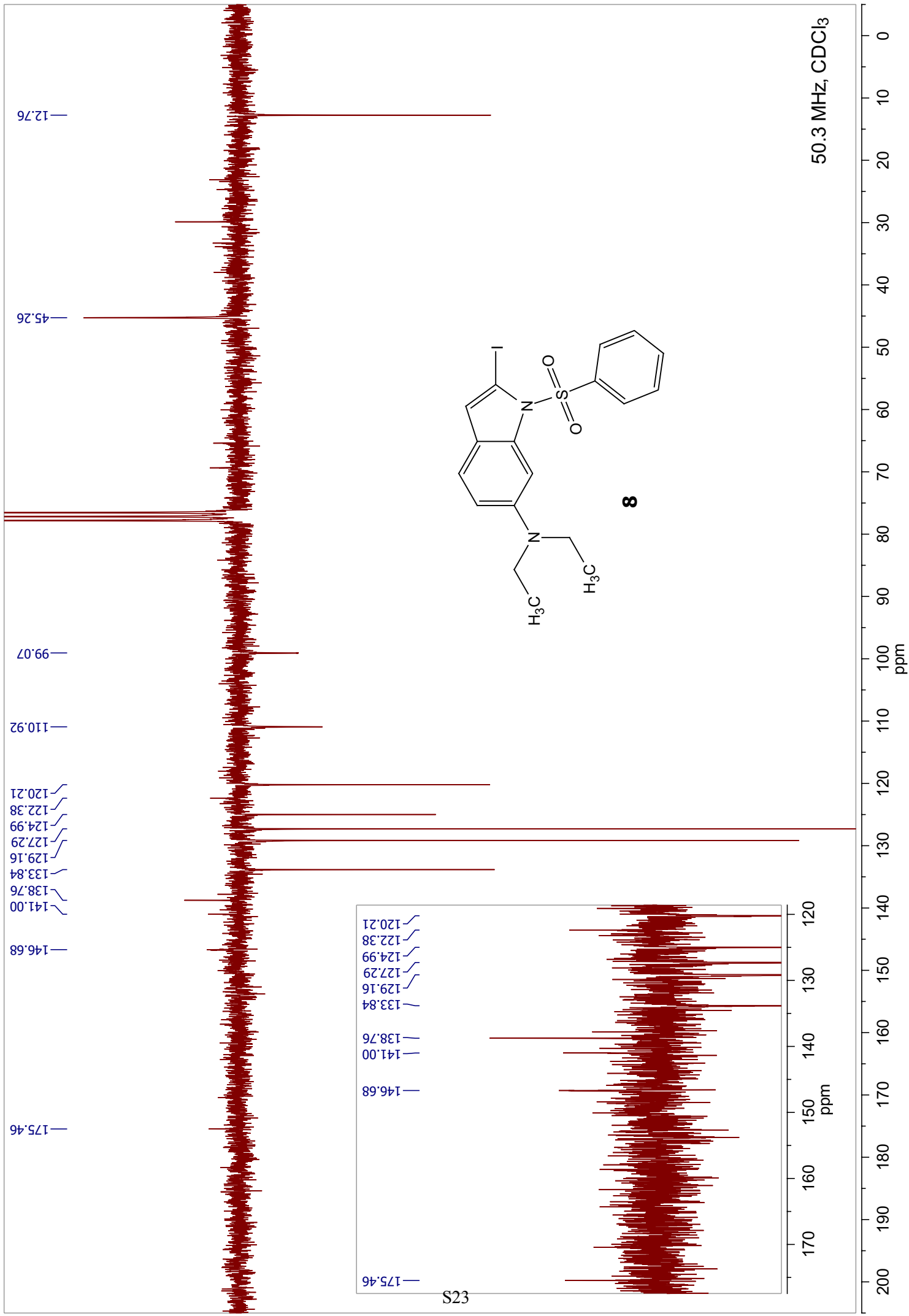
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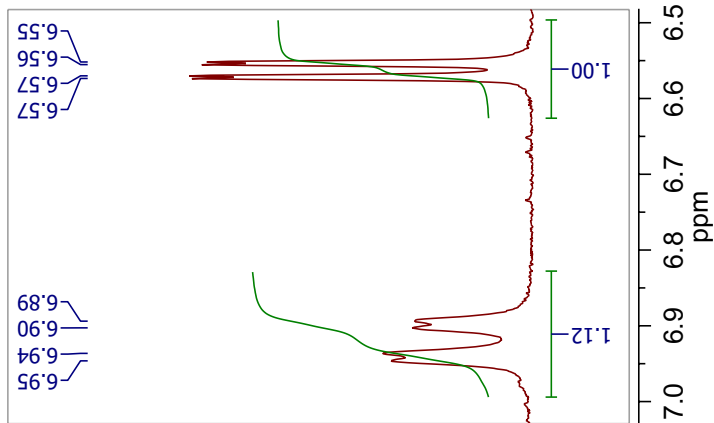
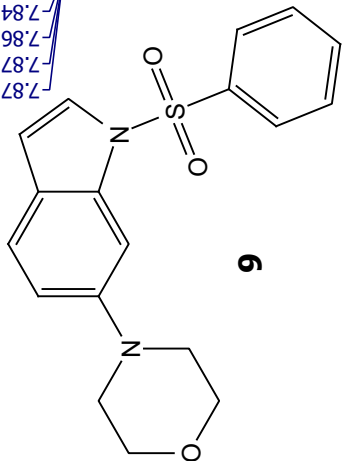


200 MHz, CDCl<sub>3</sub>

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3.17

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7.84  
7.83  
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7.42  
6.95  
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7.87  
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7.83  
7.83



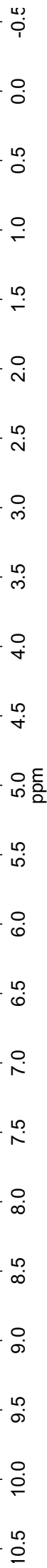
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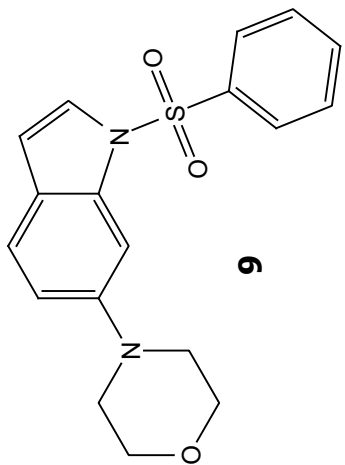
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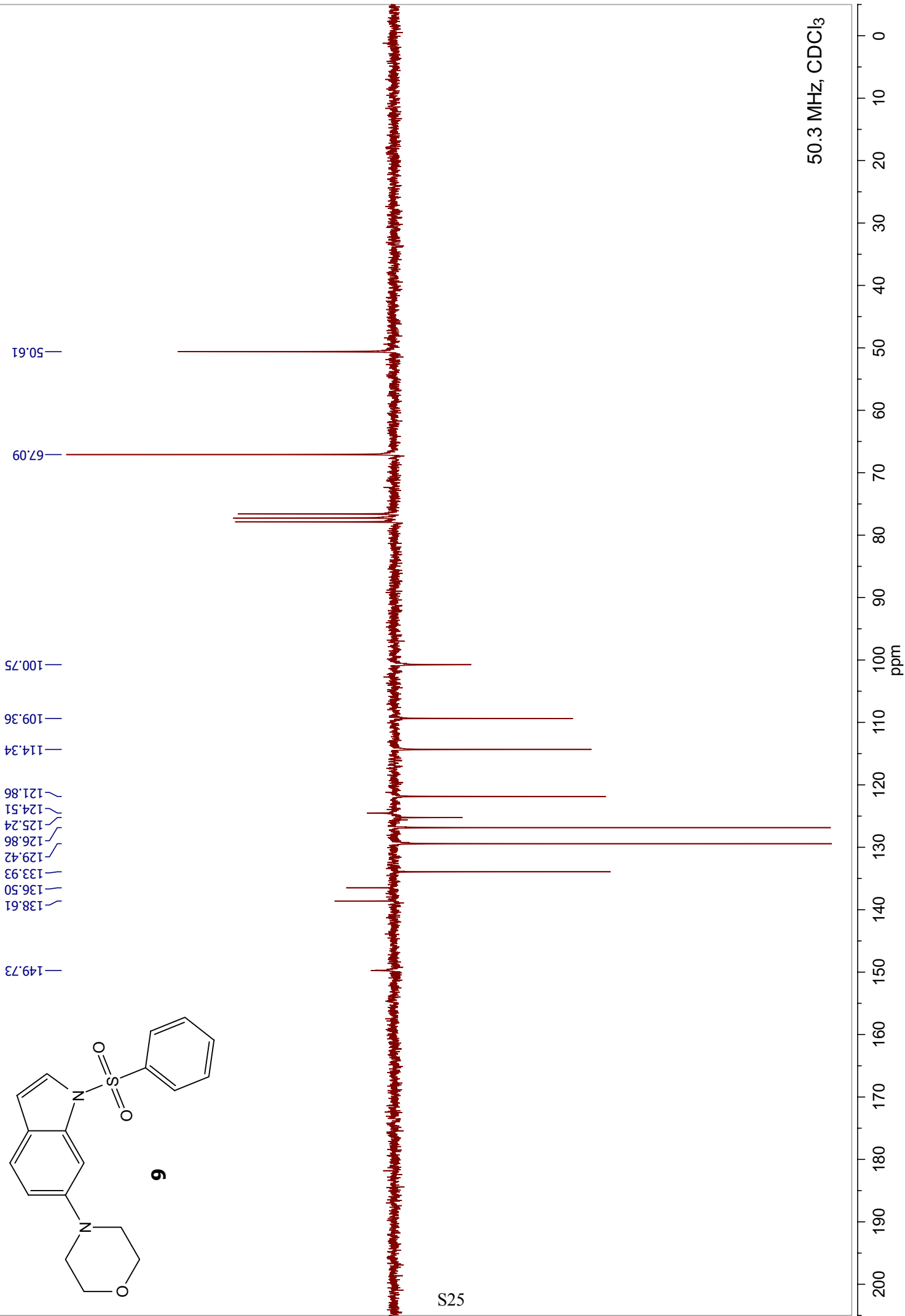
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S25



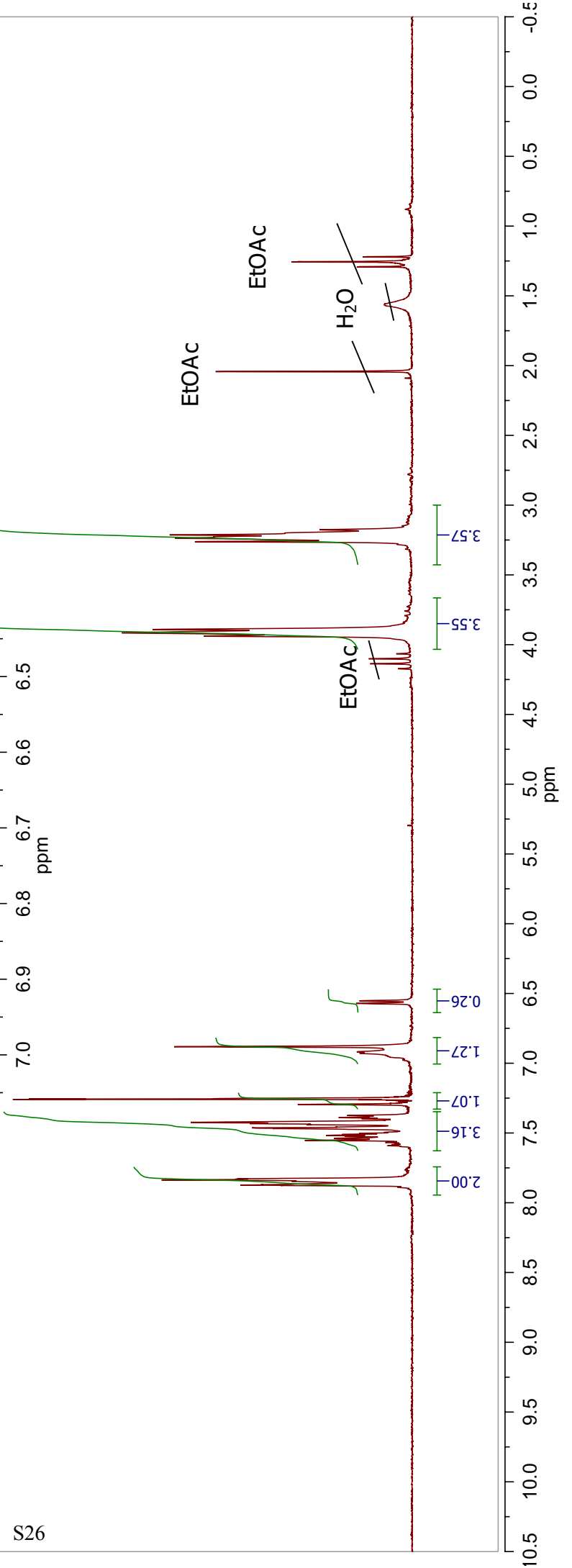
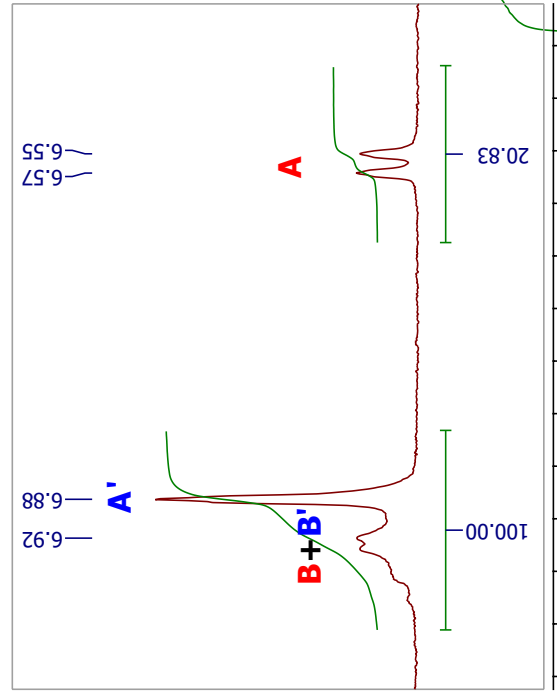
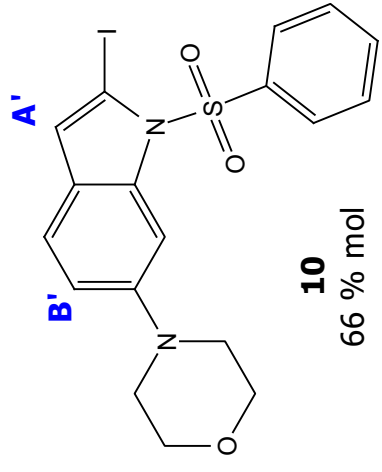
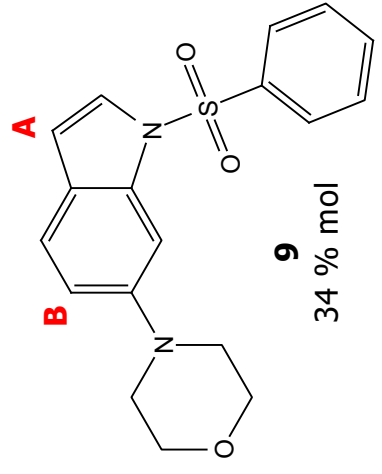
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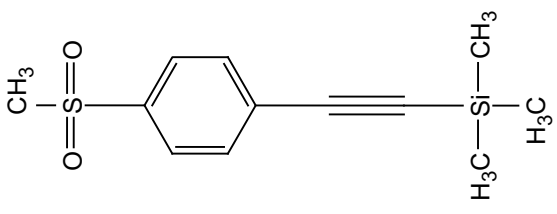
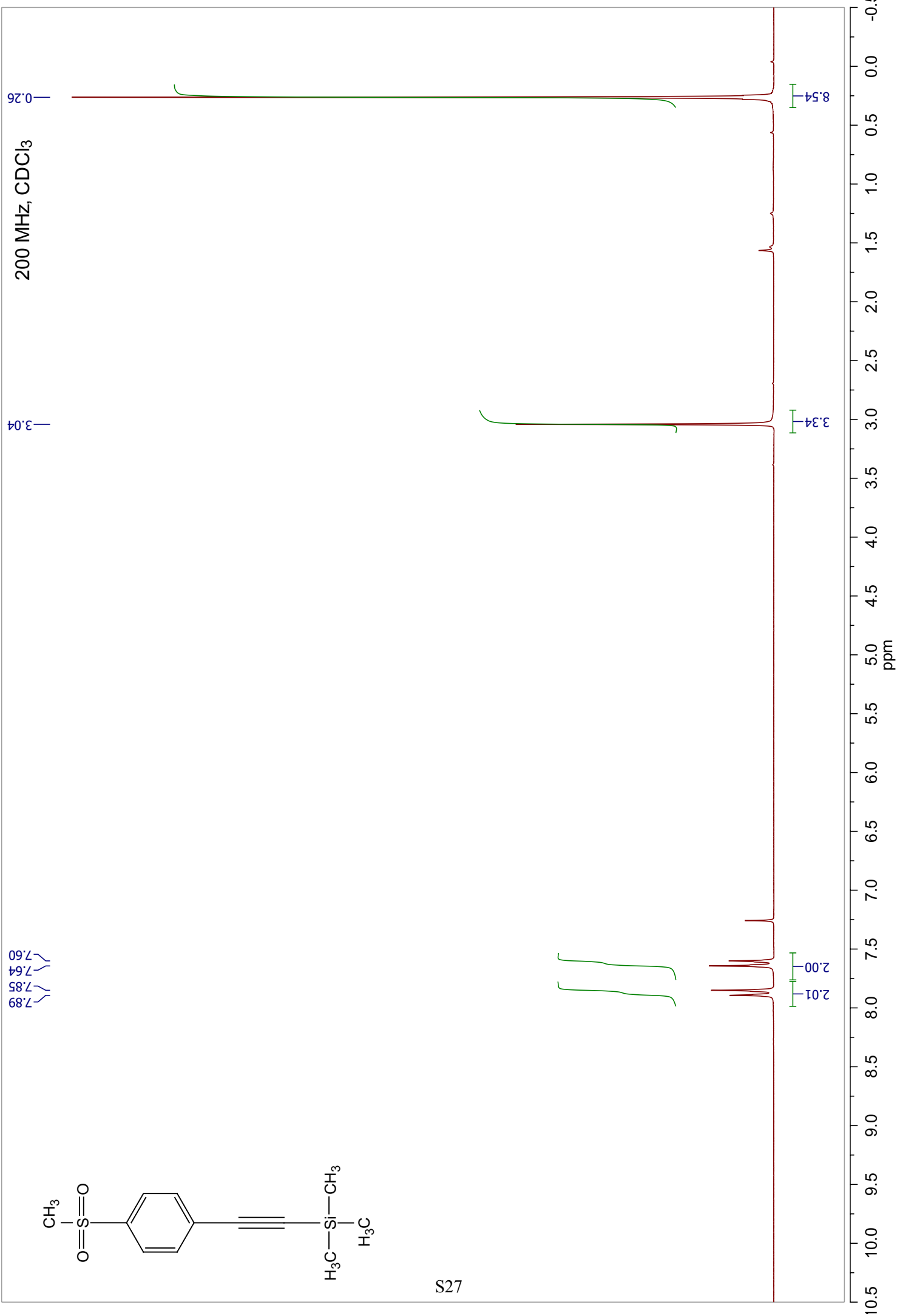
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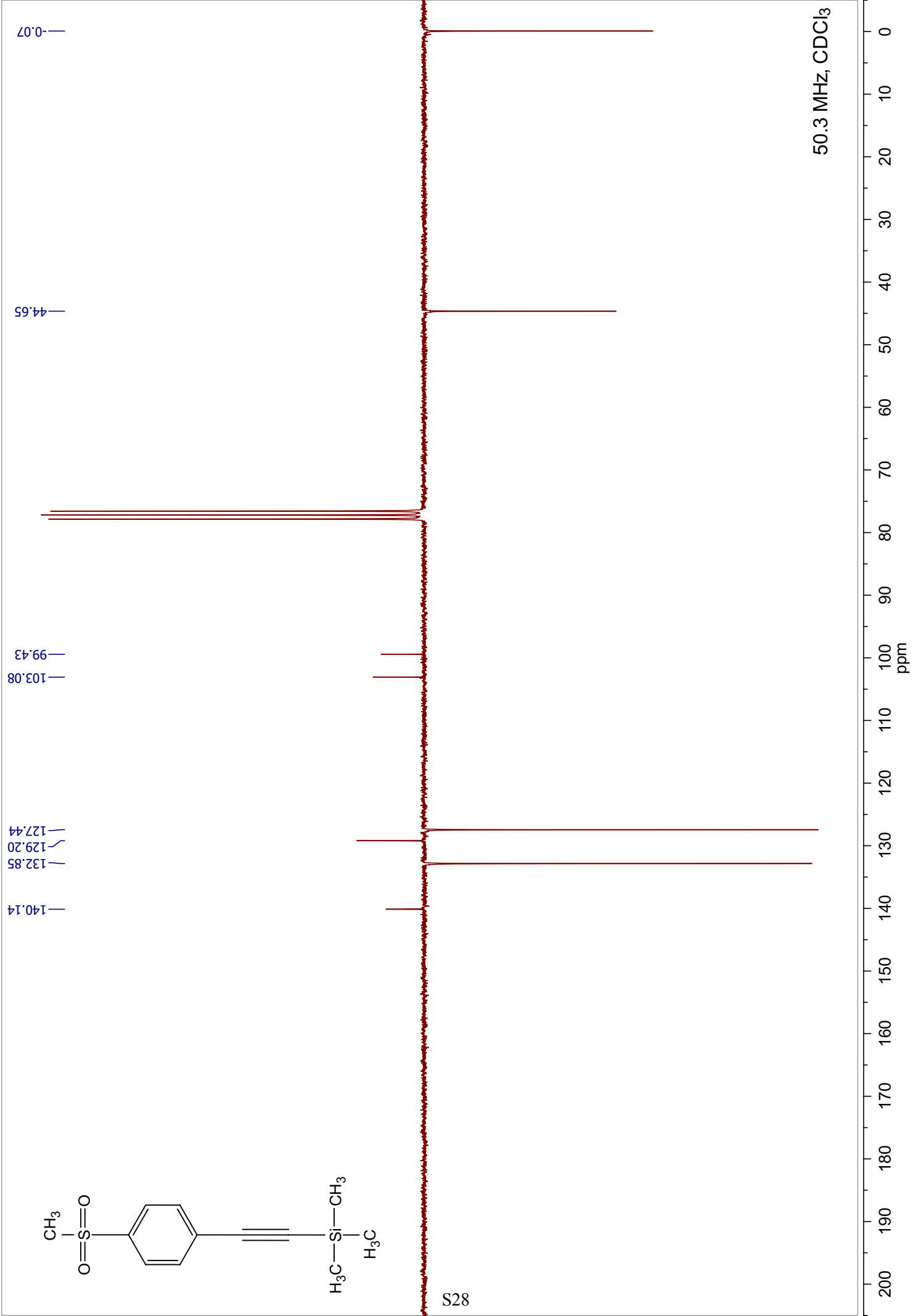
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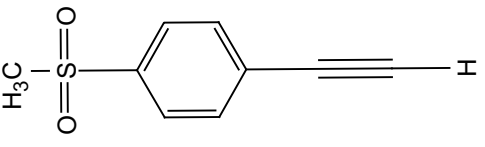


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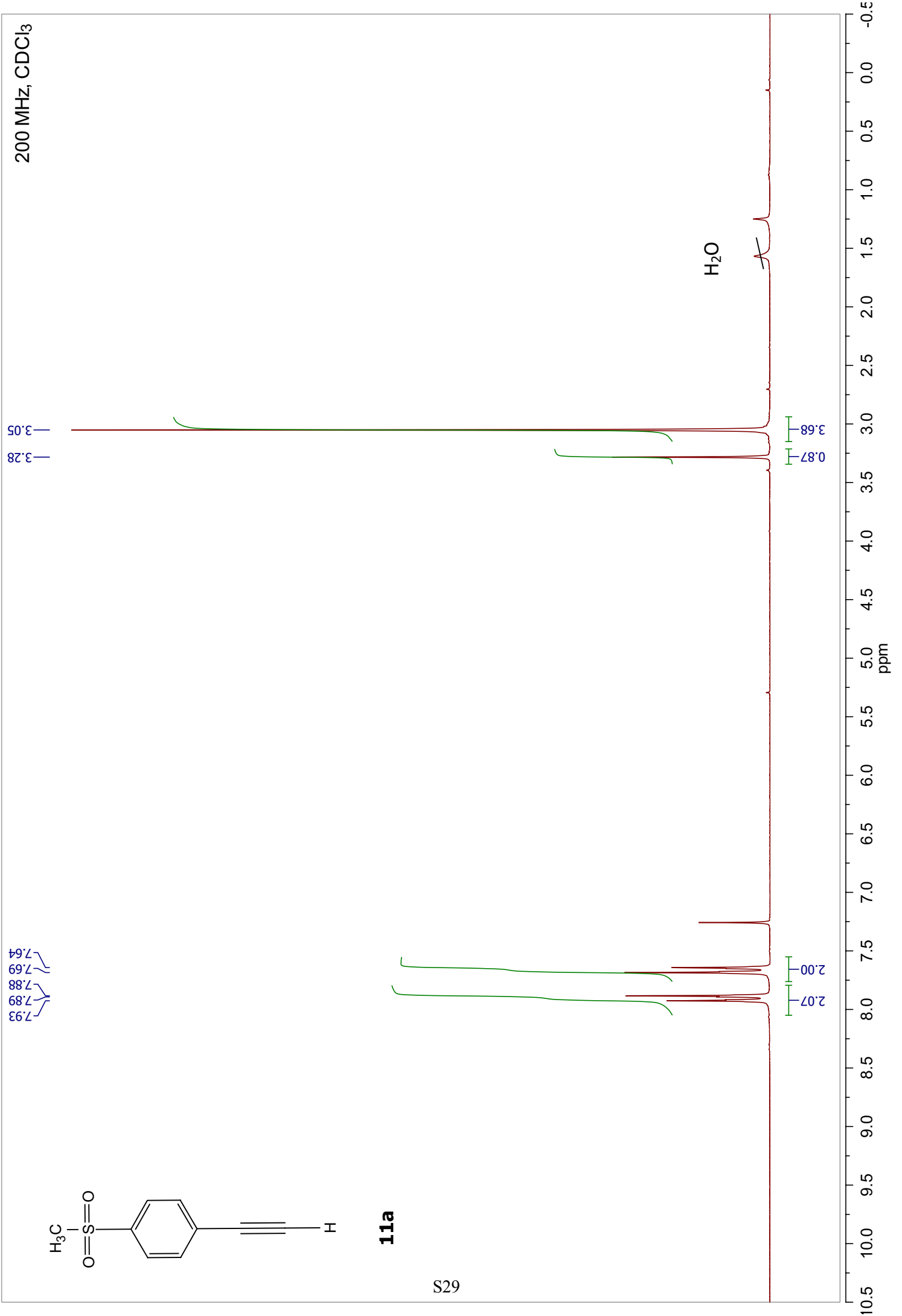


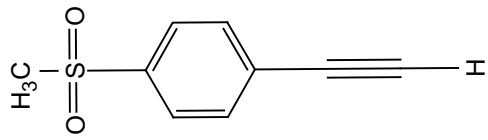
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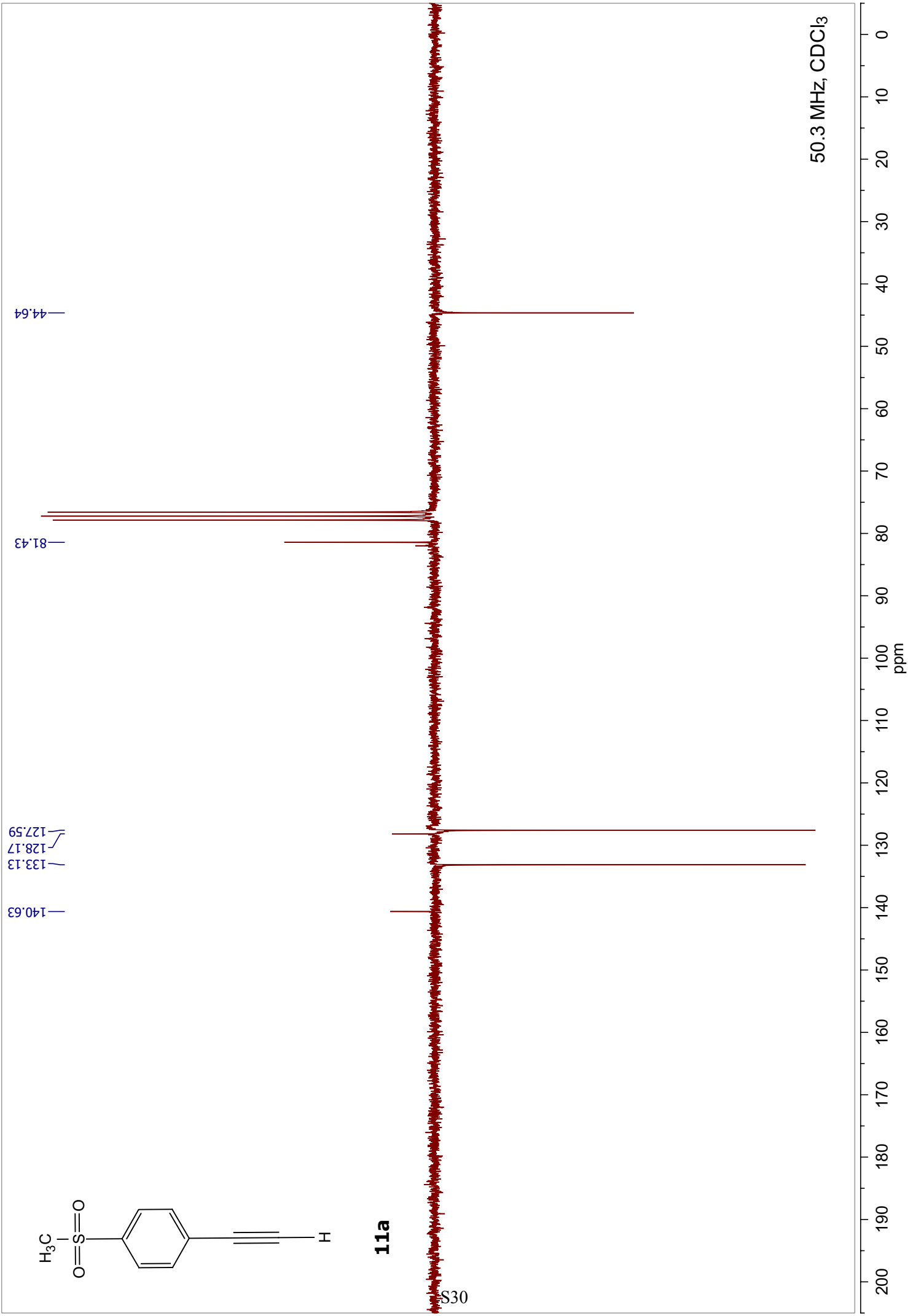
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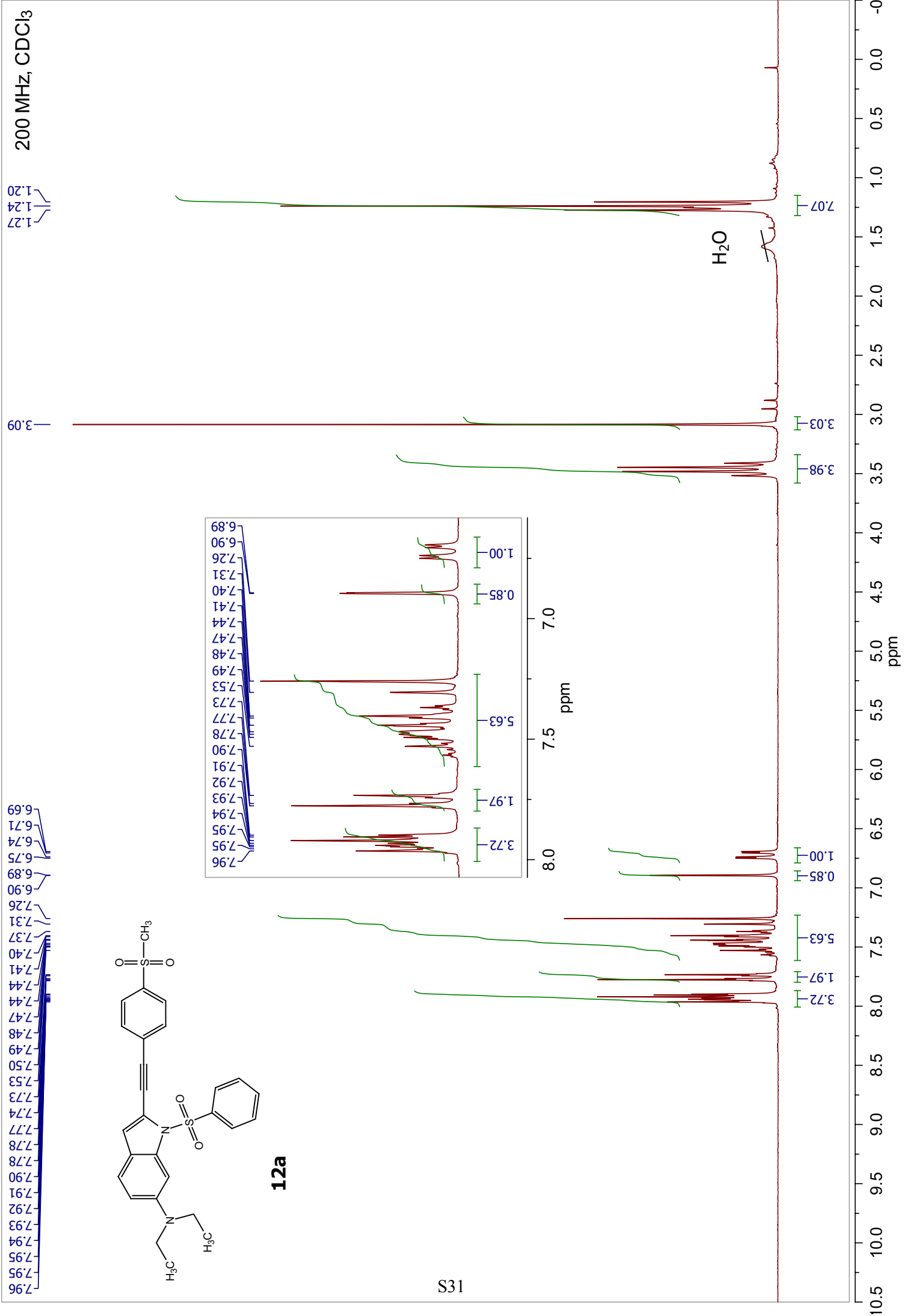
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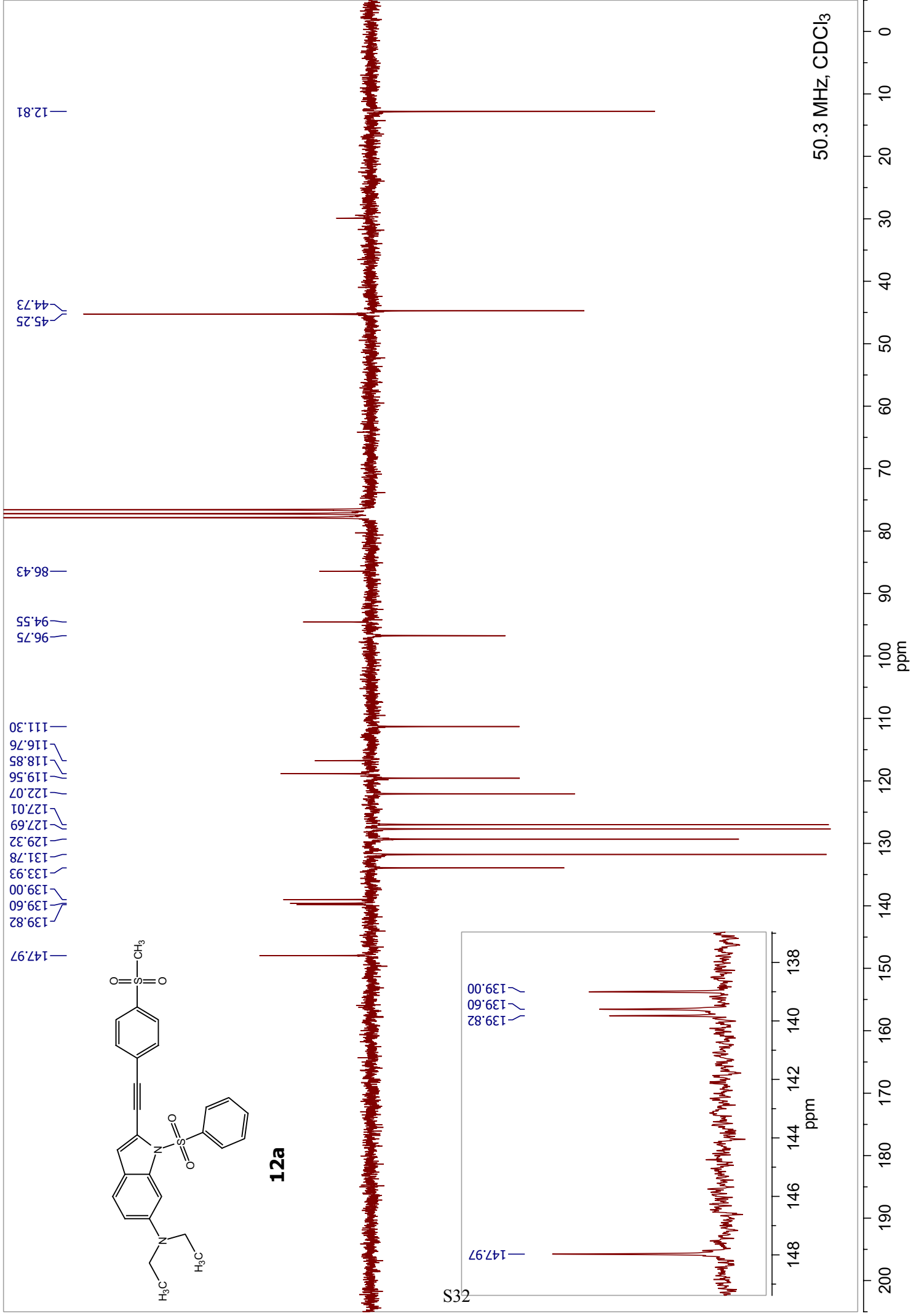




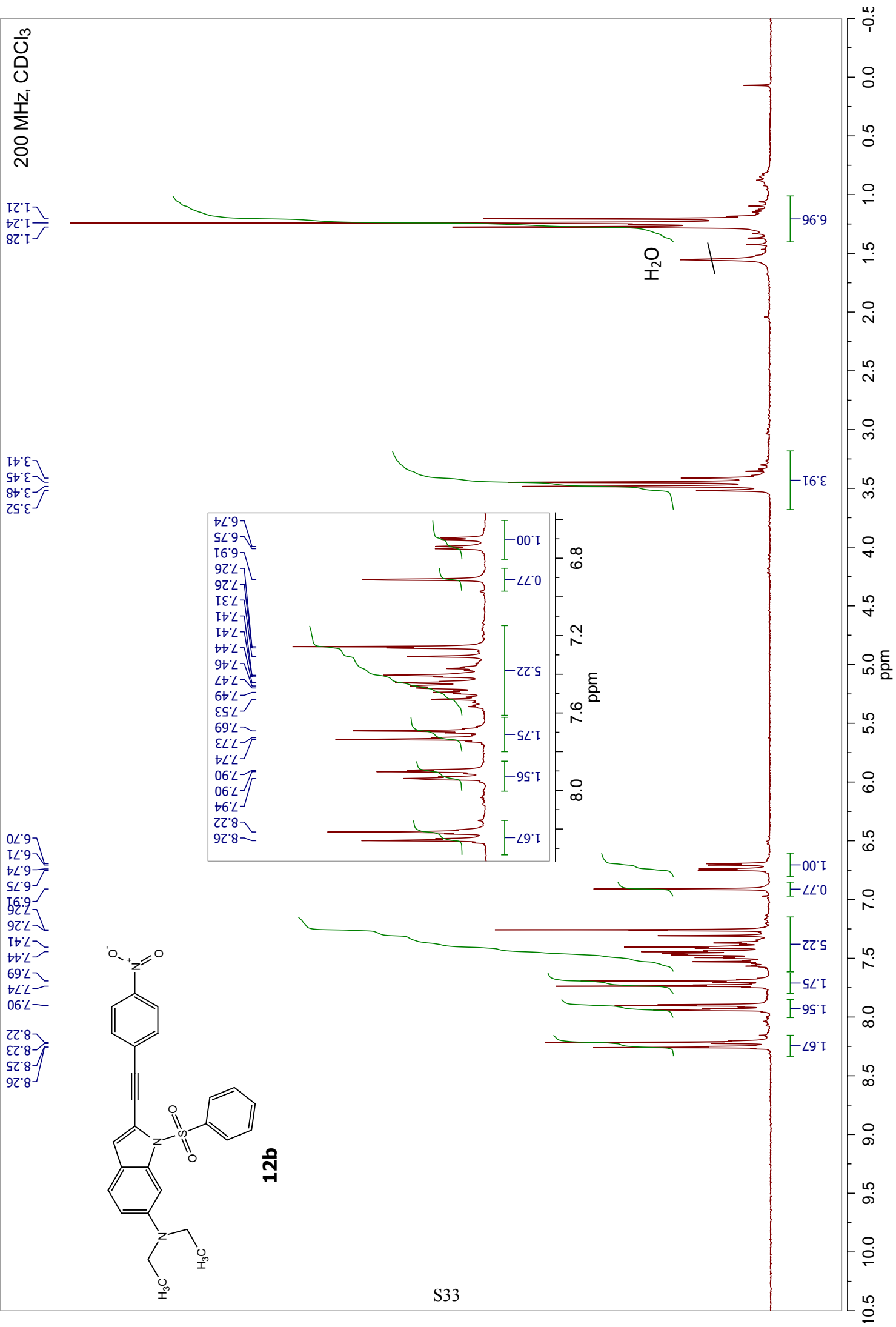
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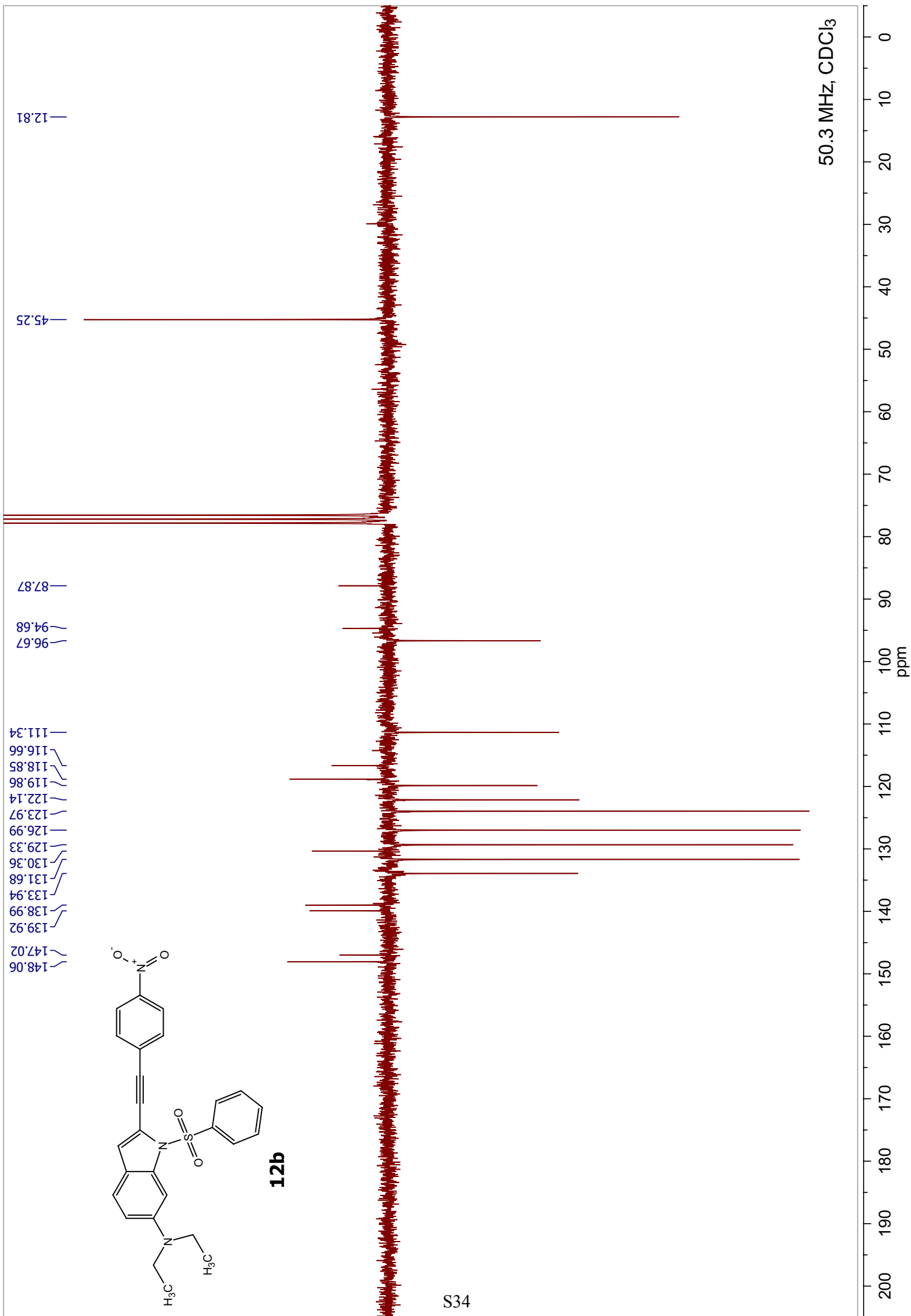










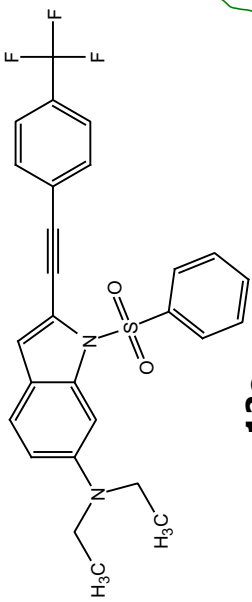
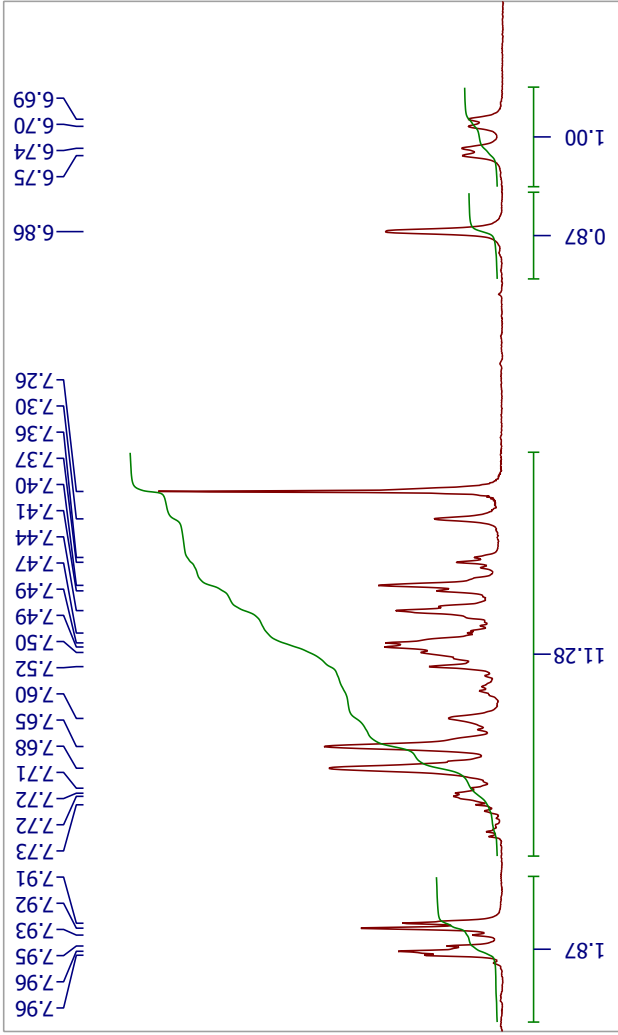


200 MHz, CDCl<sub>3</sub>

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1.21

3.52  
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3.45  
3.41

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7.96  
7.95  
7.93  
7.92  
7.91  
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S35

H<sub>2</sub>O

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4.08

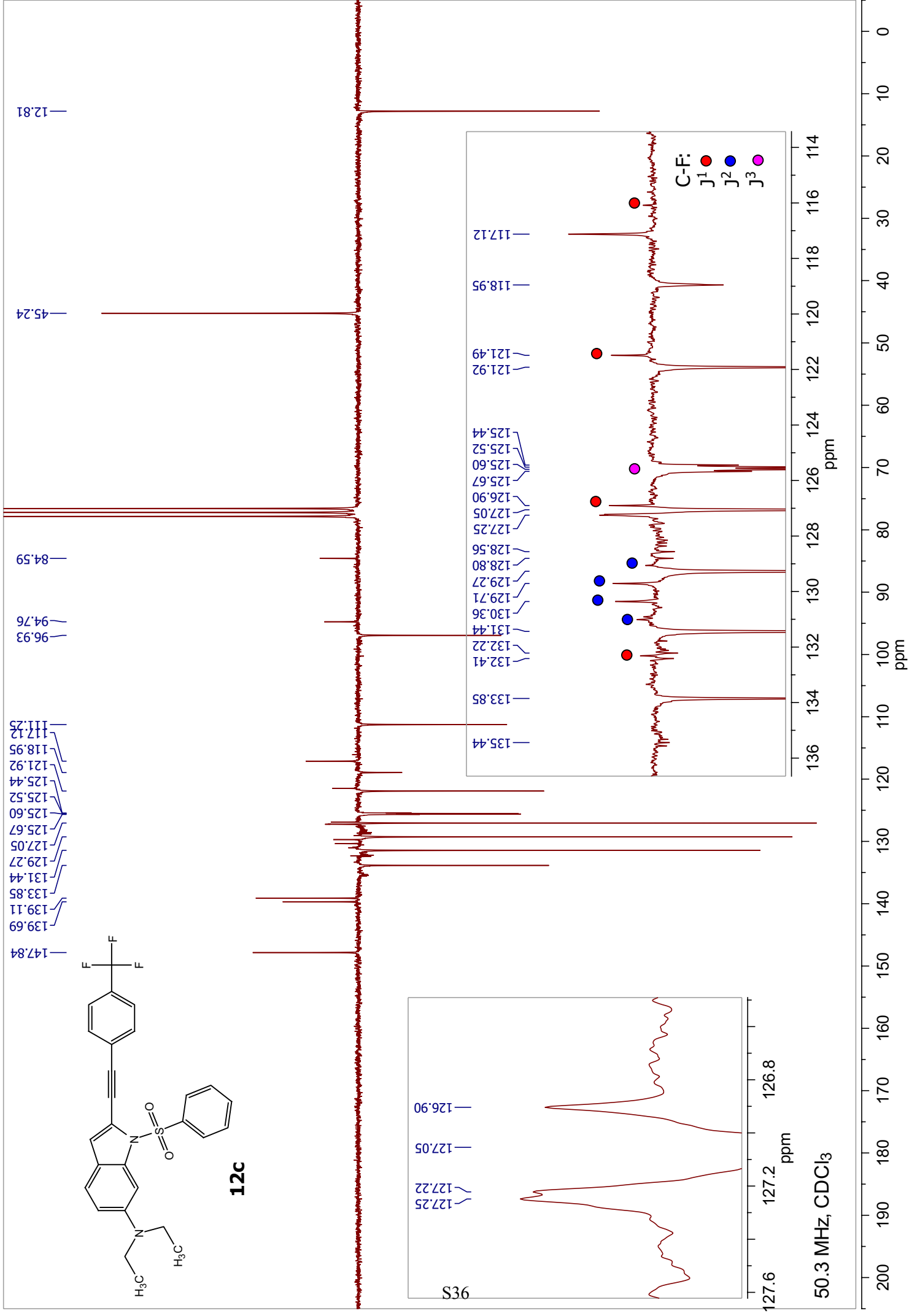
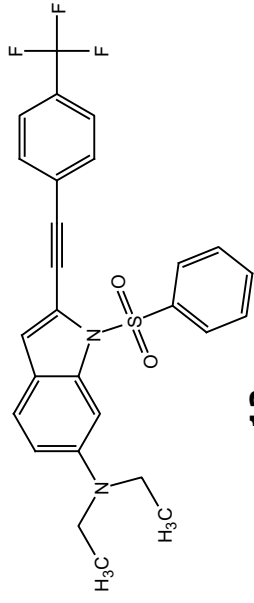
1.00  
0.87

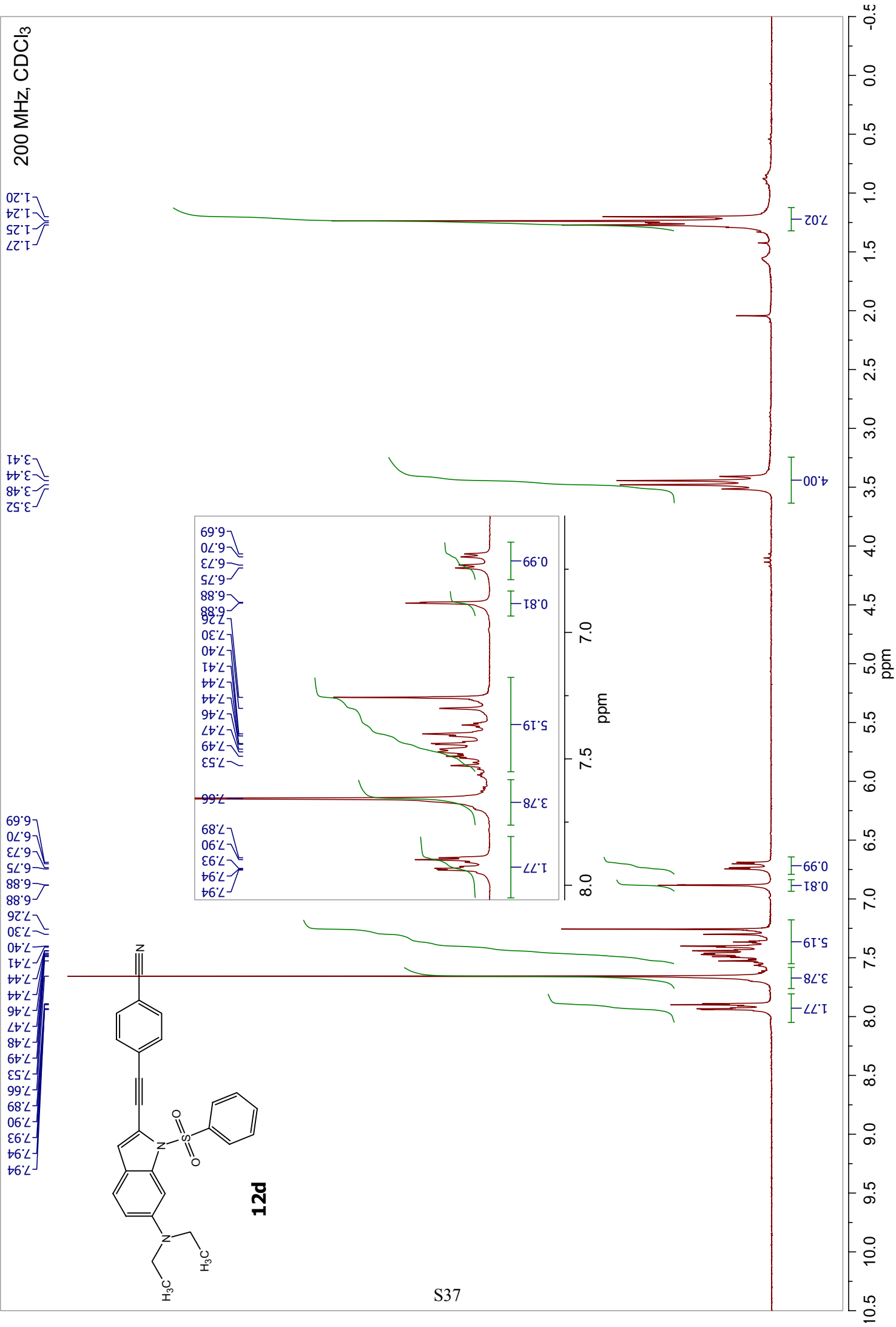
11.28

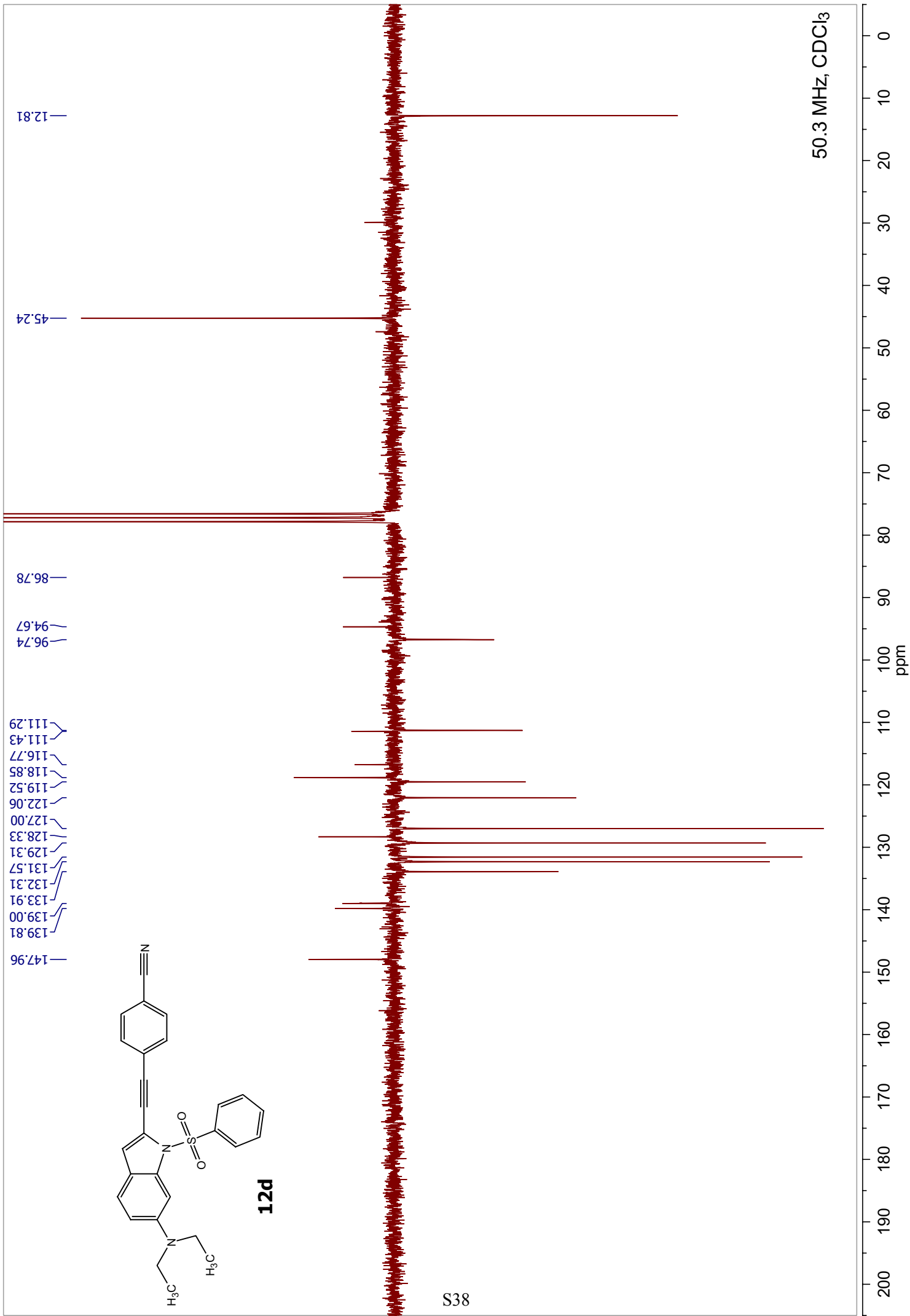
1.87

10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5

ppm





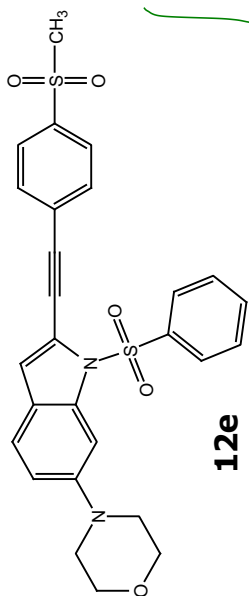
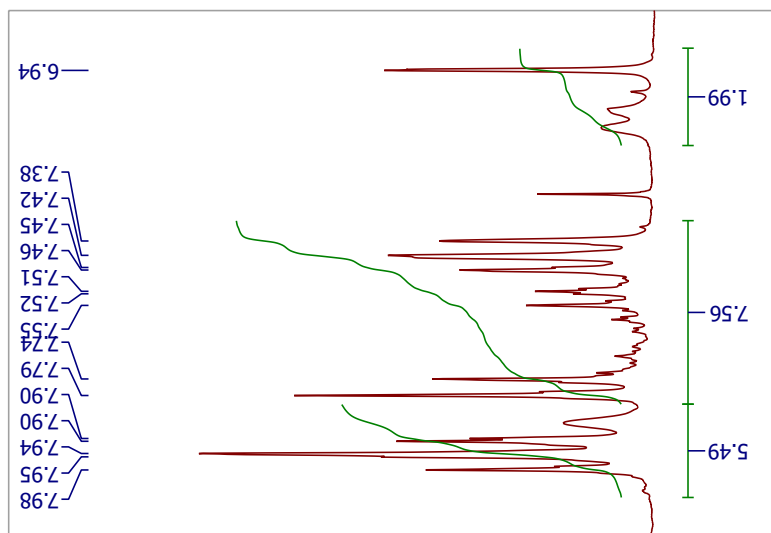


200 MHz, CDCl<sub>3</sub>

3.34  
3.32  
3.29  
3.09

3.99  
3.97  
3.95

7.98  
7.97  
7.95  
7.94  
7.90  
7.90  
7.86  
7.79  
7.78  
7.75  
7.74  
7.55  
7.52  
7.51  
7.46  
7.45  
7.42  
7.38  
6.94



grease

3.53  
4.00

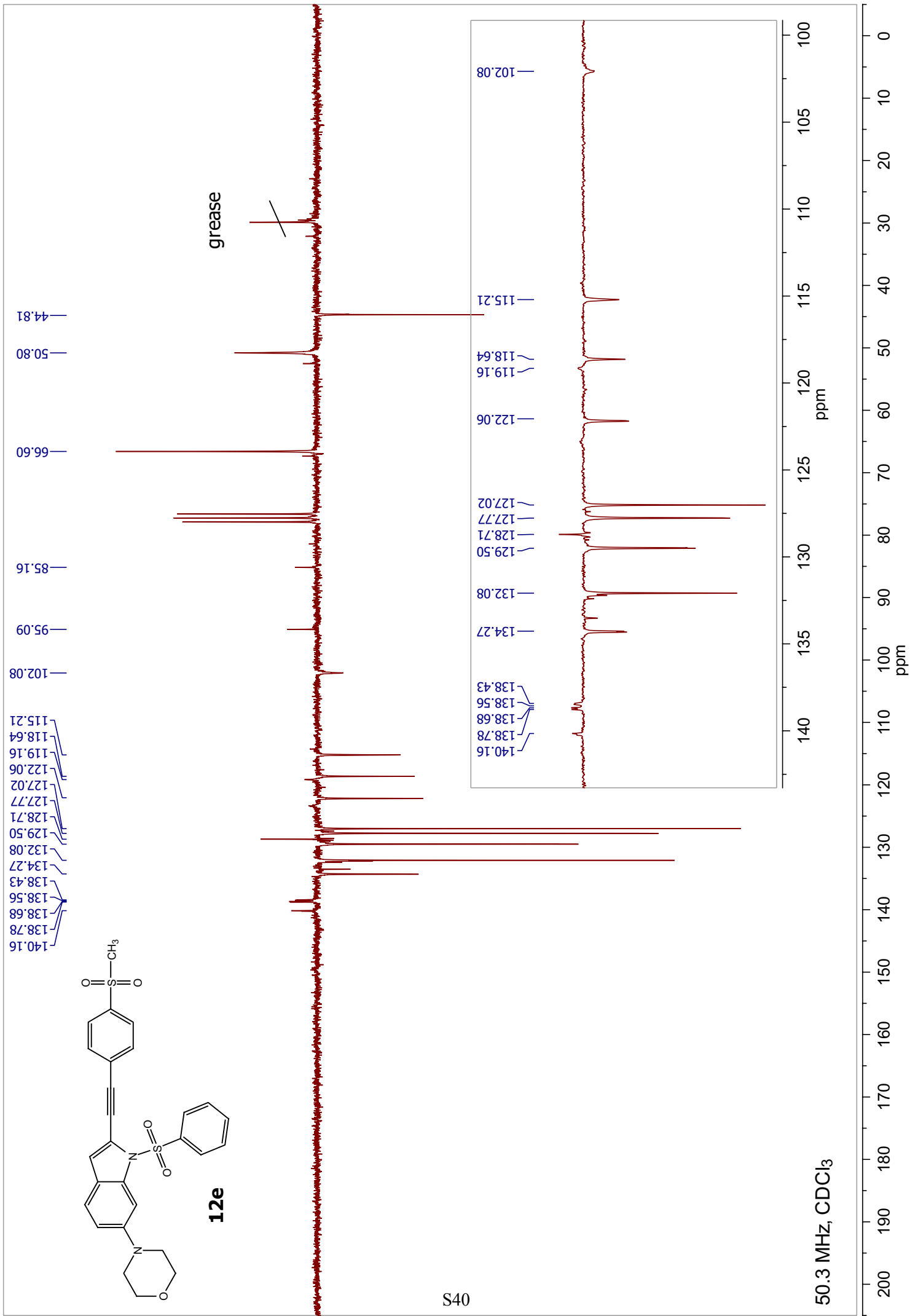
3.94

1.99

7.56

5.49

10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 ppm



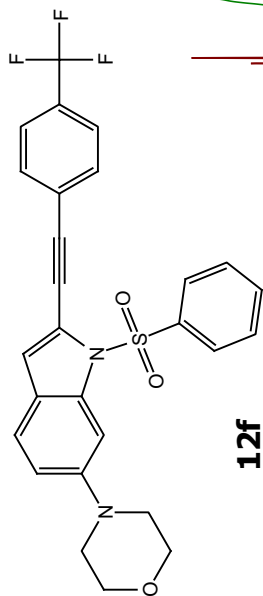


200 MHz, CDCl<sub>3</sub>

3.30  
3.28  
3.26

3.95  
3.92  
3.90

6.90  
6.94  
6.95  
6.99  
7.00  
7.35  
7.38  
7.39  
7.41  
7.45  
7.50  
7.54  
7.58  
7.61  
7.66  
7.69  
7.73  
7.78  
7.91  
7.91  
7.95



grease

4.38

4.33

2.00

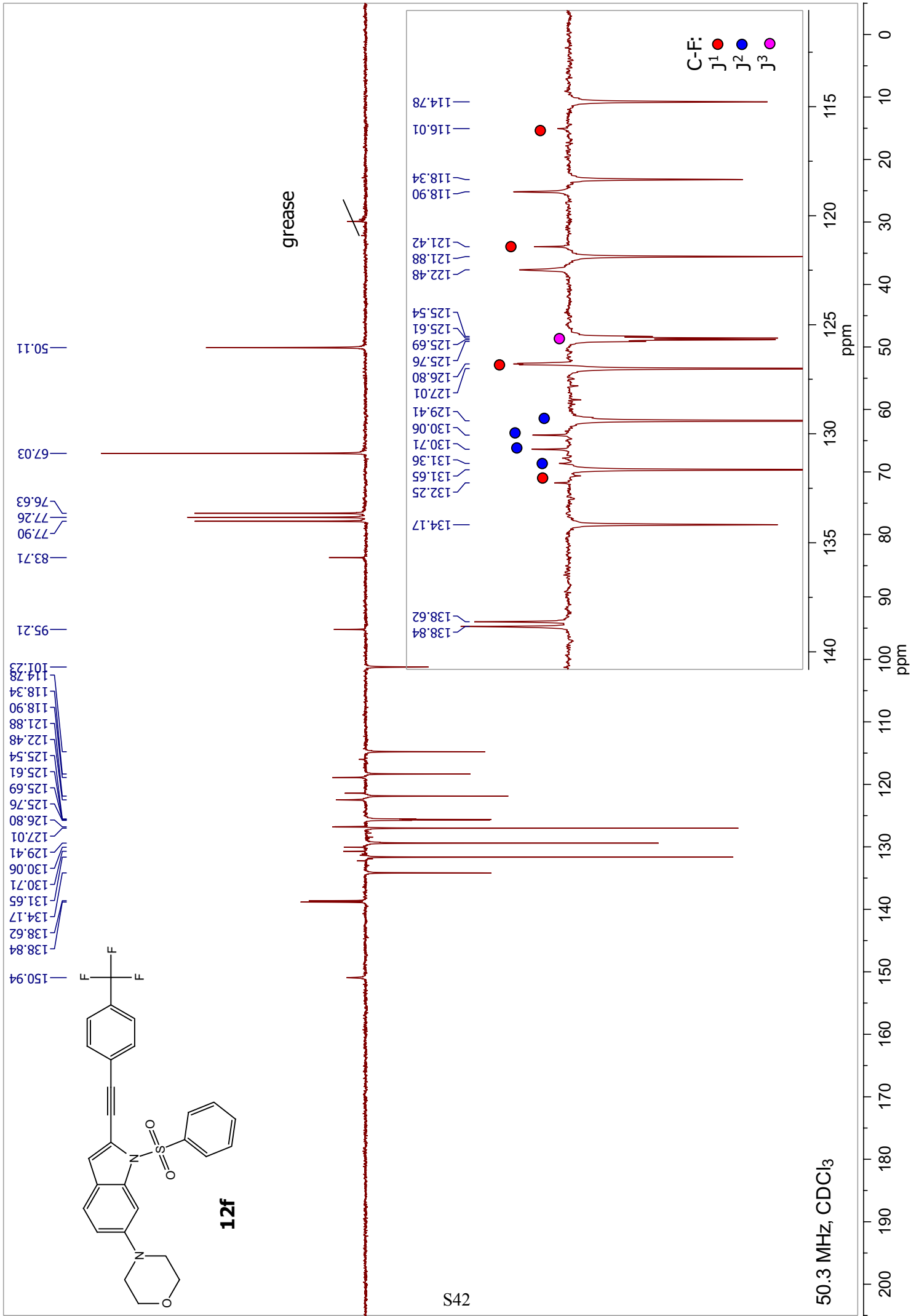
8.71

1.16

2.05

10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5

ppm

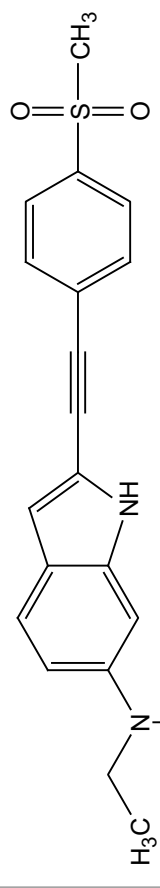


200 MHz, CDCl<sub>3</sub>

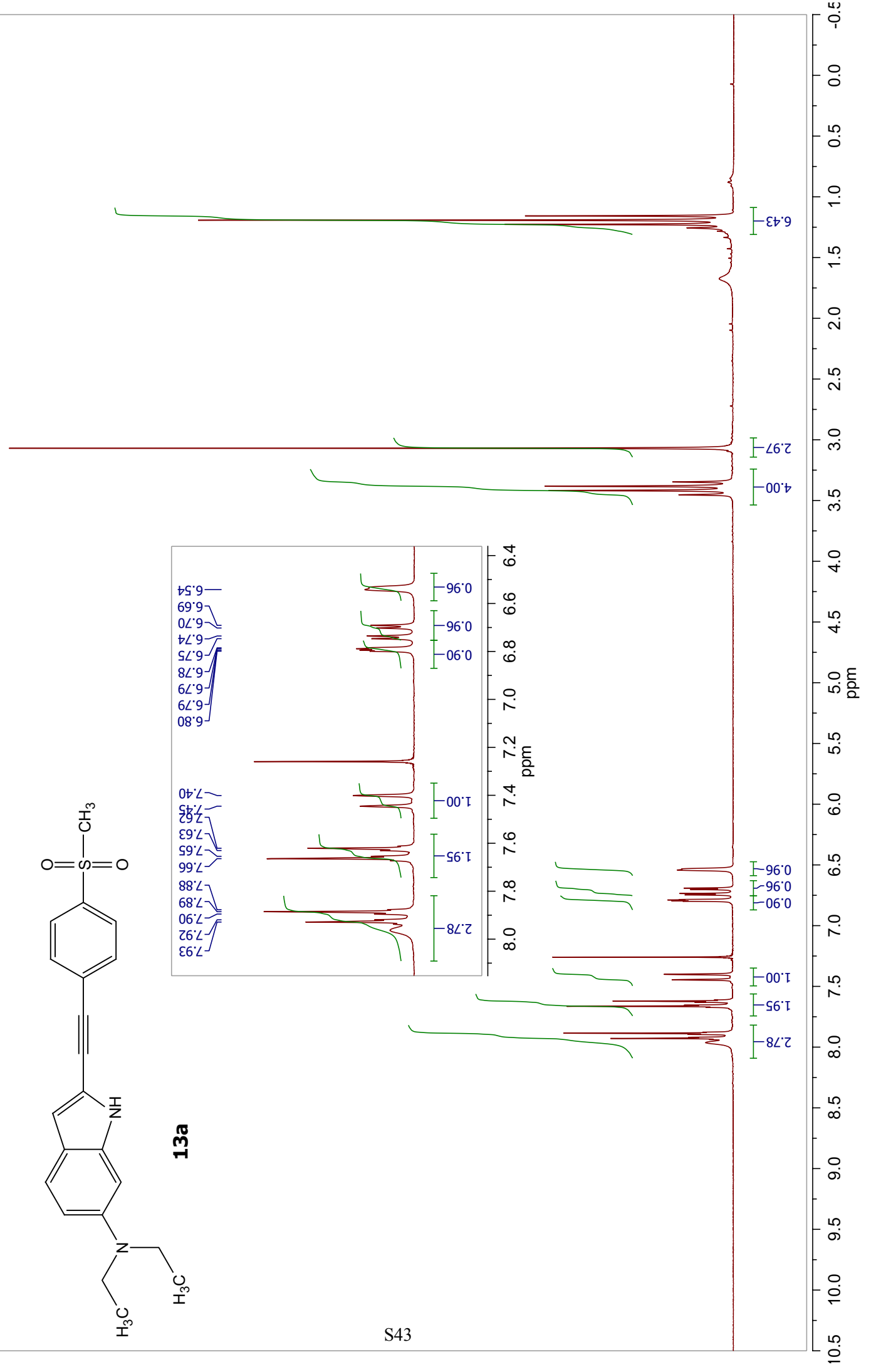
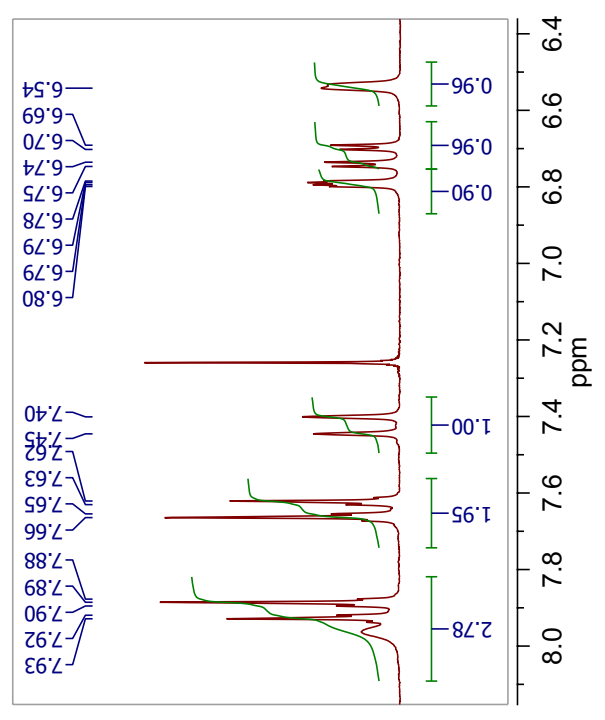
1.26  
1.23  
1.19  
1.16

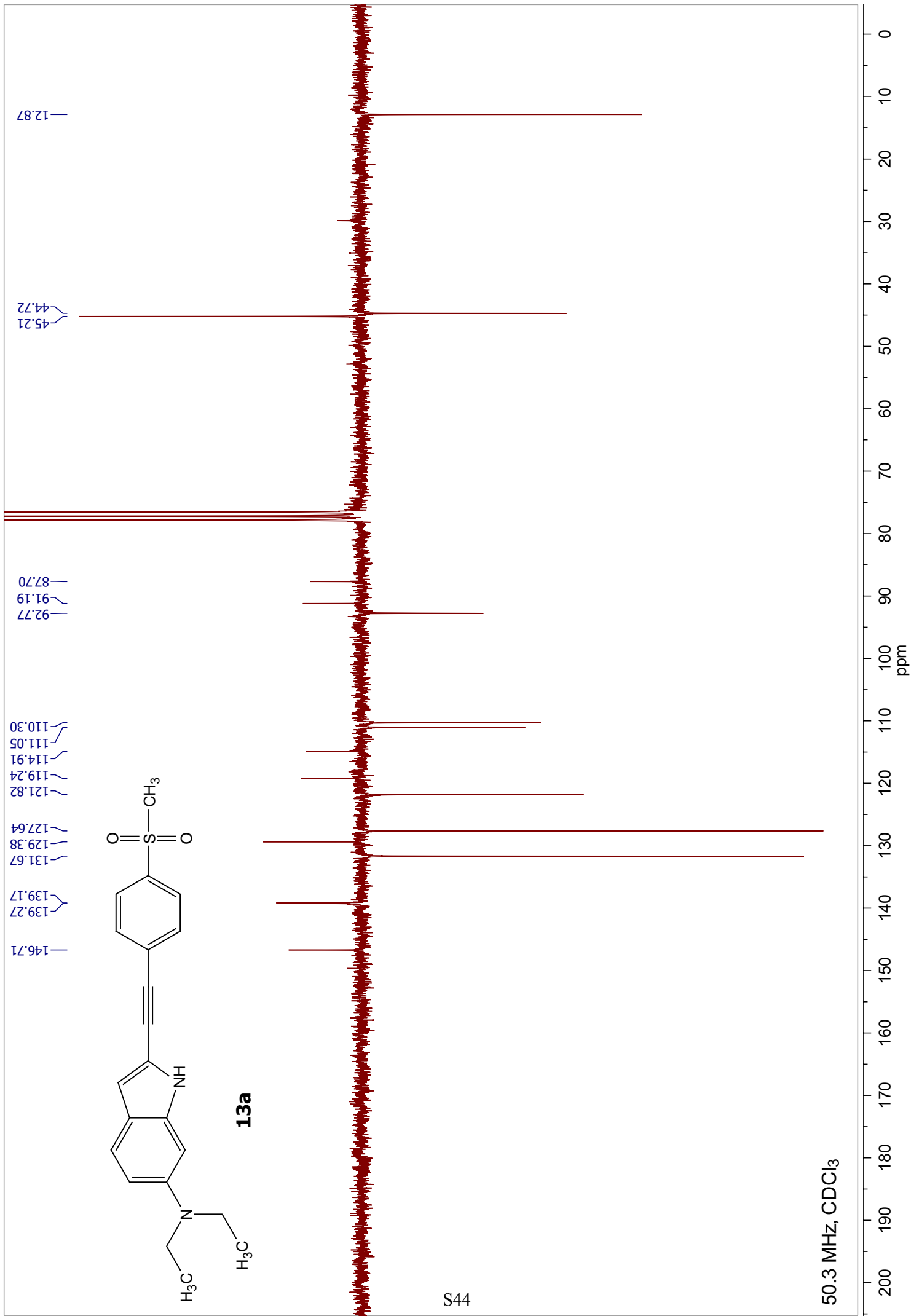
3.45  
3.42  
3.38  
3.35  
3.07

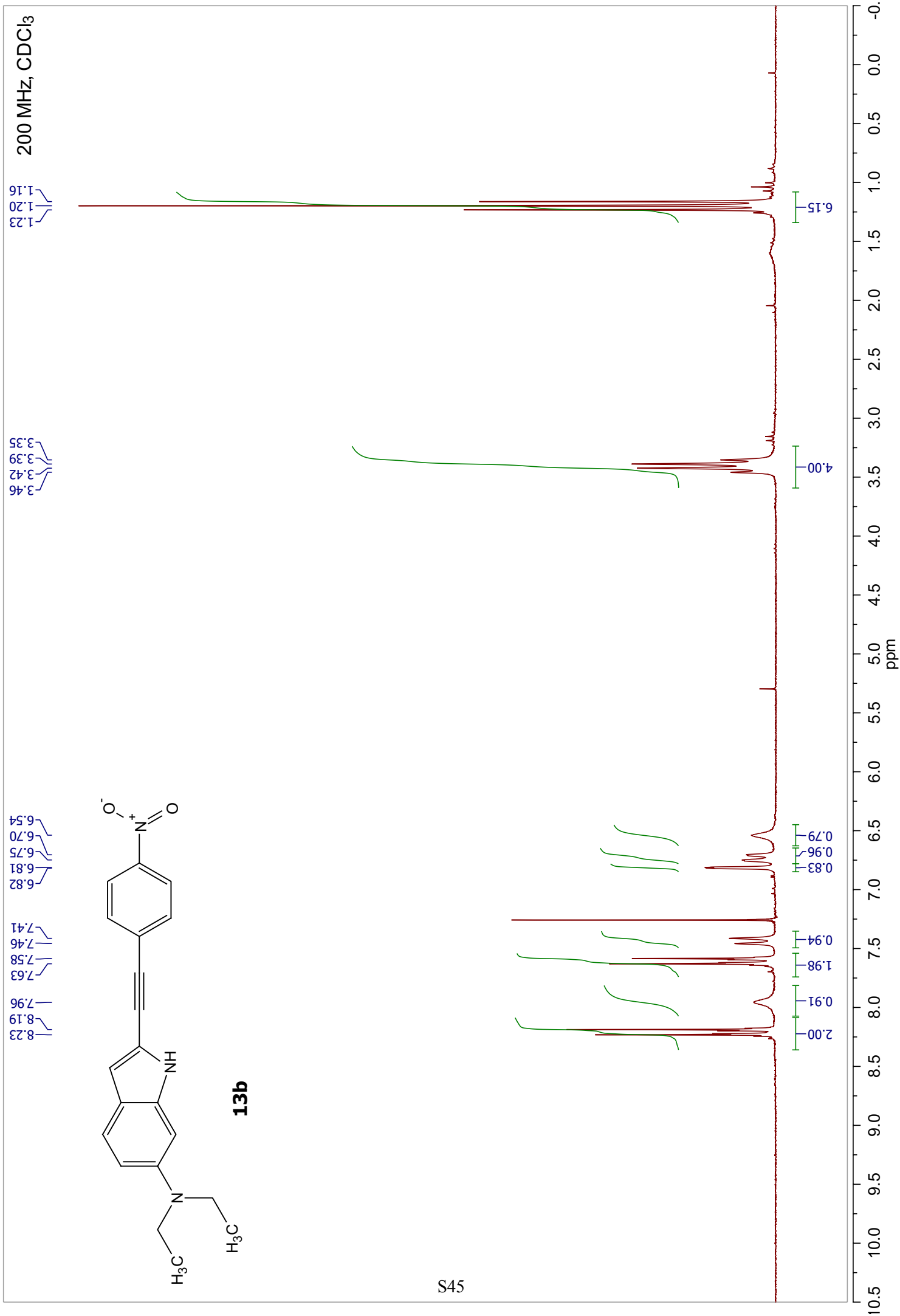
7.96  
7.94  
7.93  
7.92  
7.90  
7.89  
7.88  
7.67  
7.66  
7.65  
7.63  
7.62  
7.61  
7.45  
7.40  
6.80  
6.79  
6.79  
6.78  
6.75  
6.74  
6.70  
6.69  
6.54

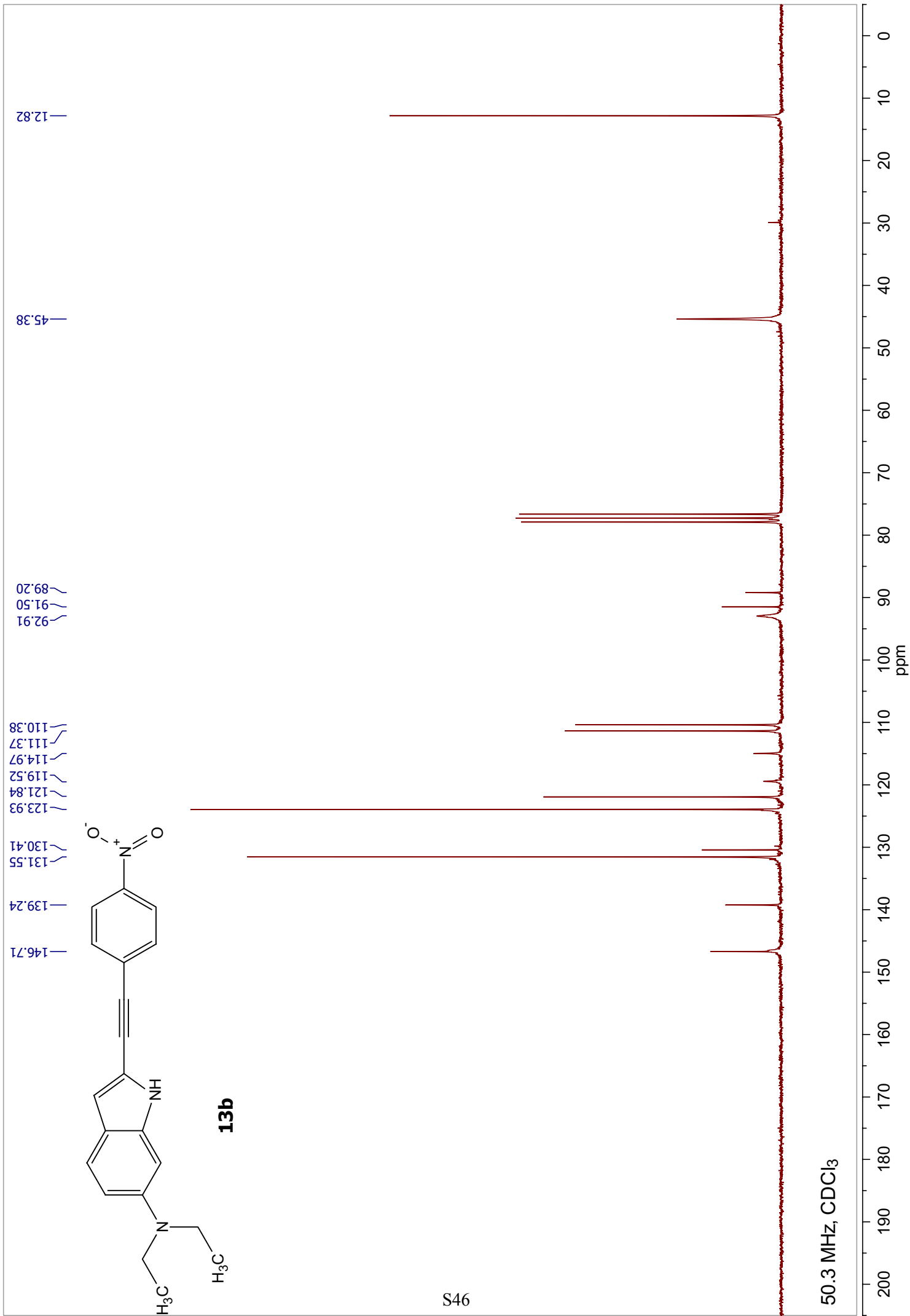


**13a**







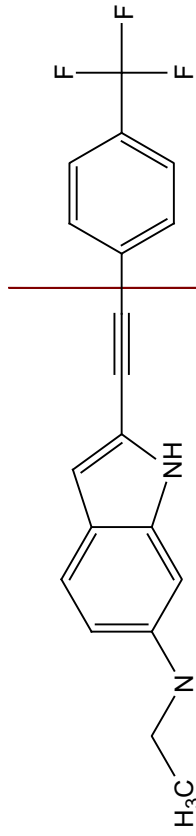


200 MHz, CDCl<sub>3</sub>

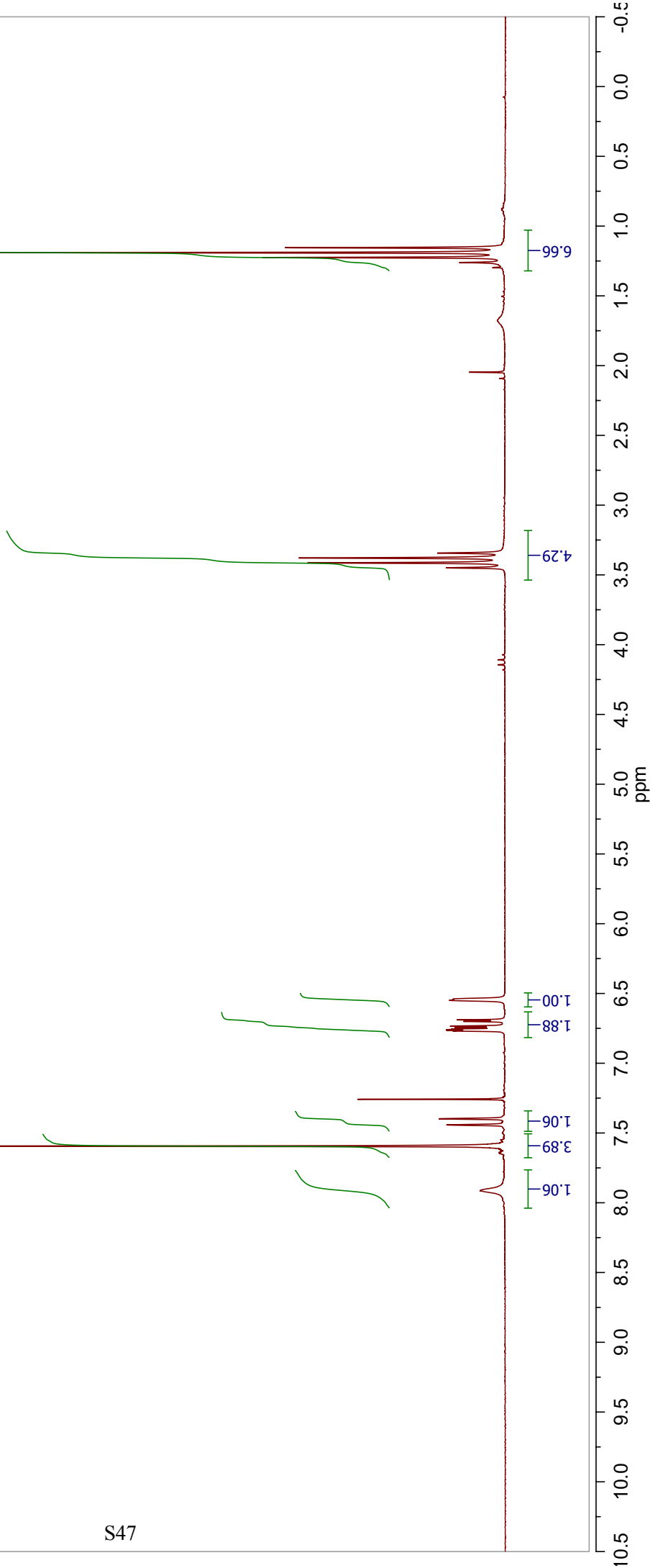
1.23  
1.19  
1.16

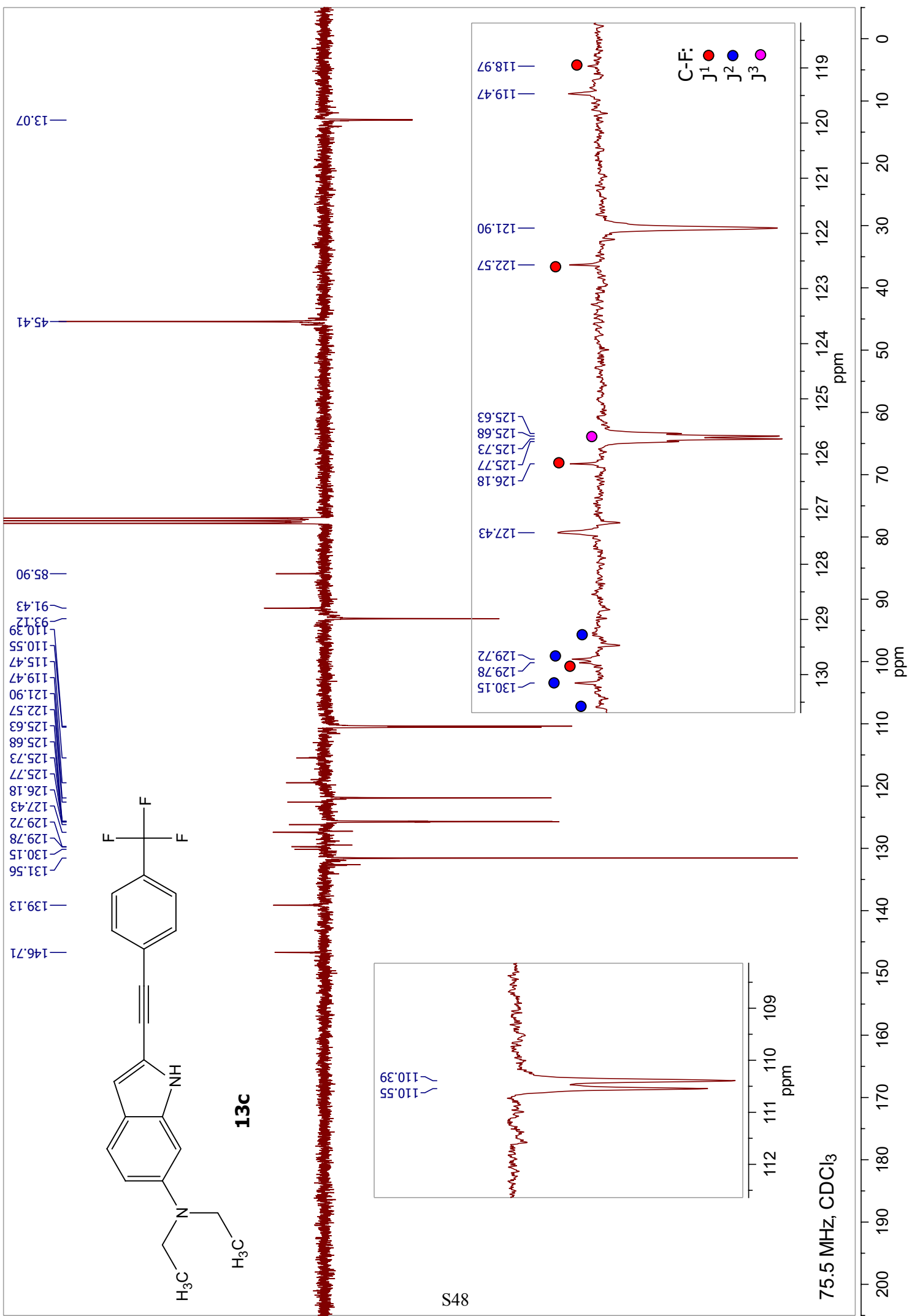
3.45  
3.41  
3.38  
3.34

7.91  
7.59  
7.44  
7.40  
7.26  
6.77  
6.77  
6.76  
6.76  
6.74  
6.73  
6.70  
6.69  
6.55

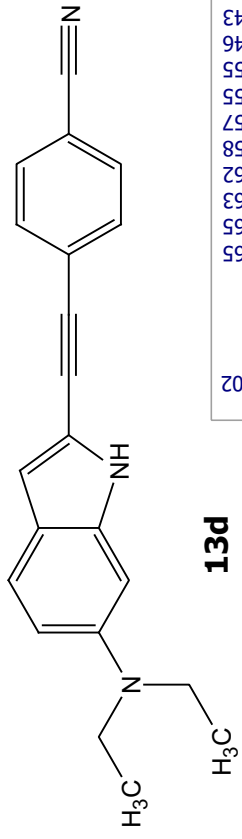


**13c**





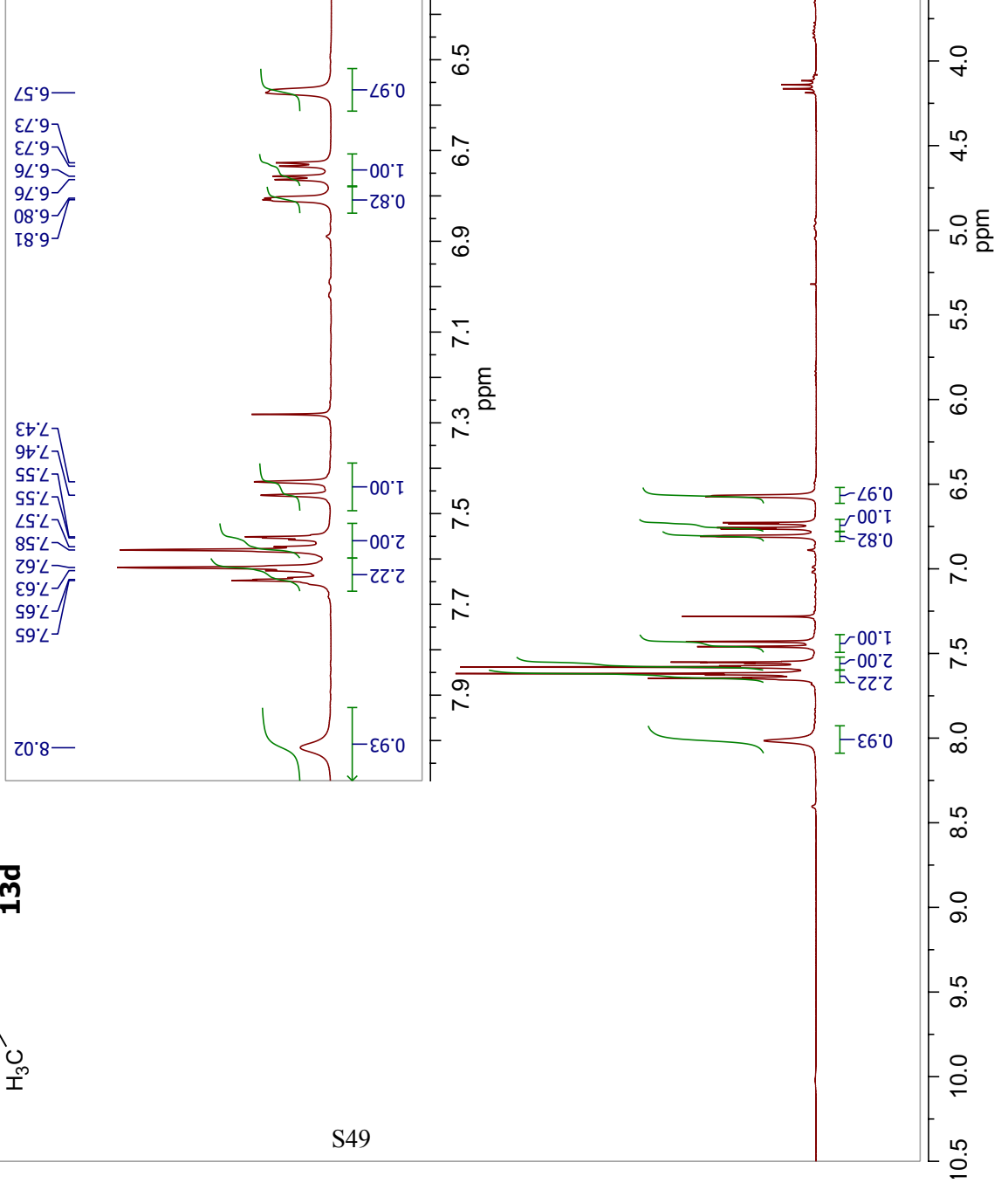


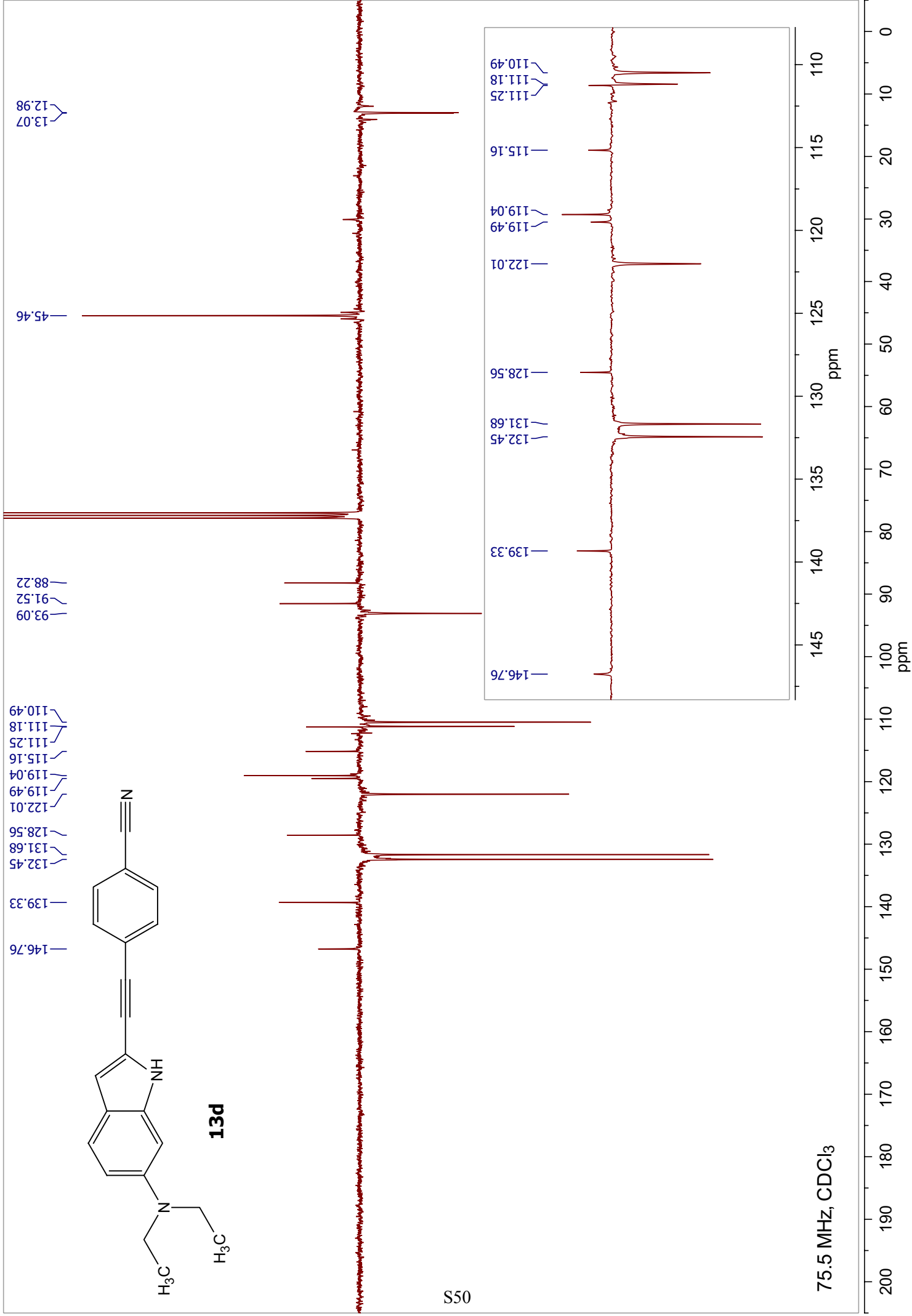
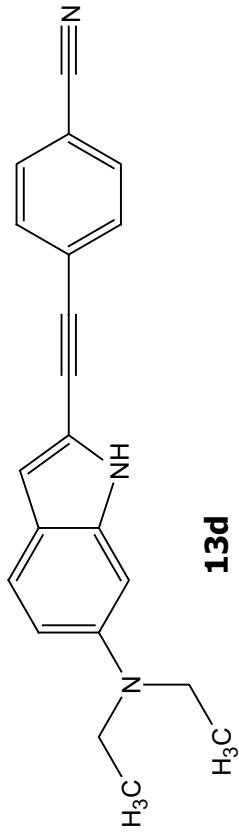


1.19  
1.21  
1.24

3.39  
3.41  
3.43  
3.46

6.57  
6.73  
6.73  
6.76  
6.76  
6.80  
6.81  
7.43  
7.55  
7.58  
7.65  
7.65  
7.62  
7.63  
7.65  
7.65  
7.62  
7.58  
7.57  
7.55  
7.55  
7.46  
7.43

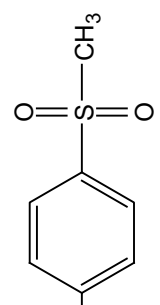




200 MHz, DMSO-d<sub>6</sub>

3.77  
3.75  
3.72  
3.25  
3.10  
3.08  
3.06

7.98  
7.93  
7.78  
7.74  
7.43  
6.89  
6.88  
6.85  
6.84  
6.78  
6.73



**13e**

11.48

S51

H<sub>2</sub>O

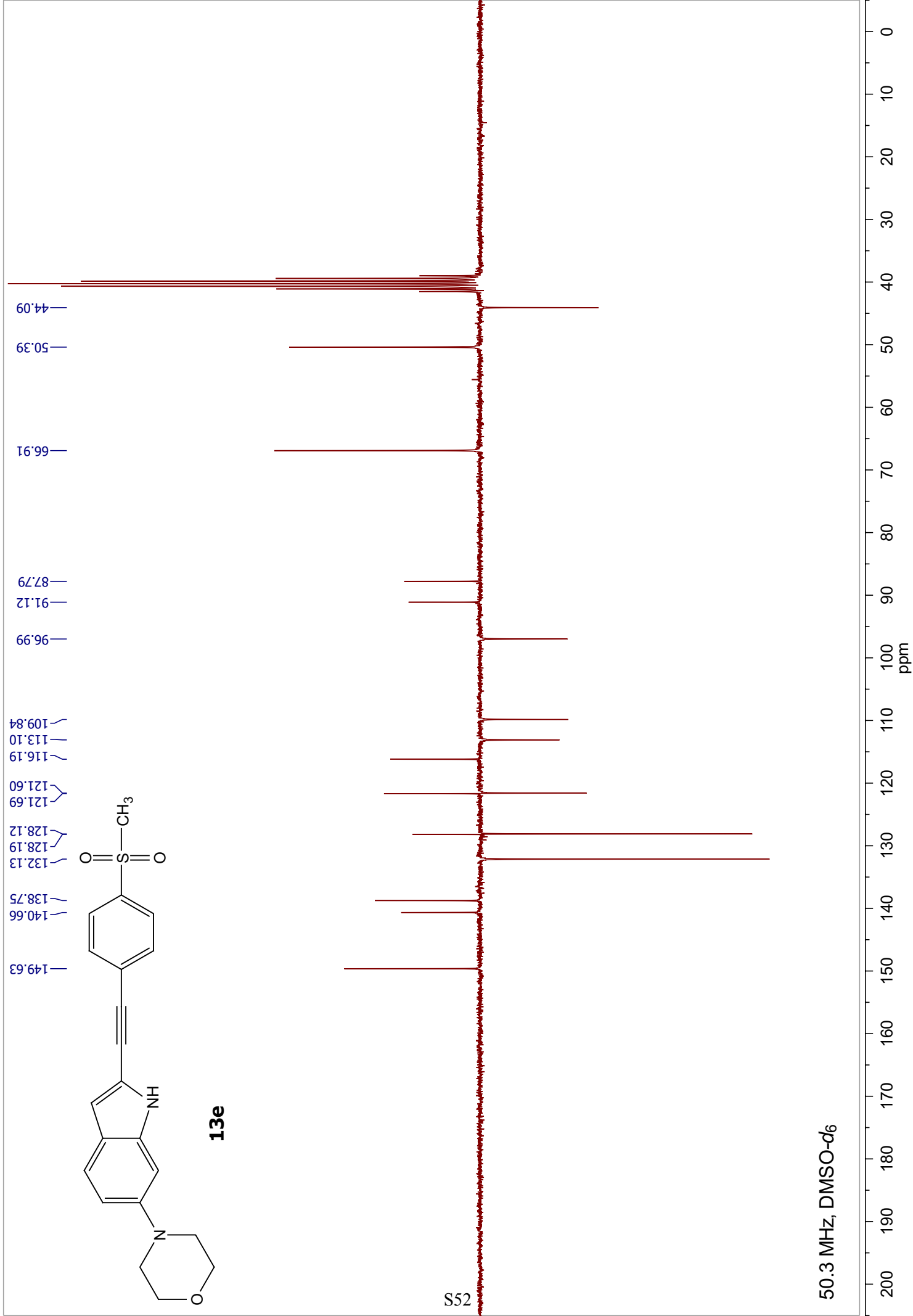
CH<sub>2</sub>Cl<sub>2</sub>

4.10  
3.01  
4.00

2.91  
1.16  
2.03  
1.98

0.71

12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5  
ppm

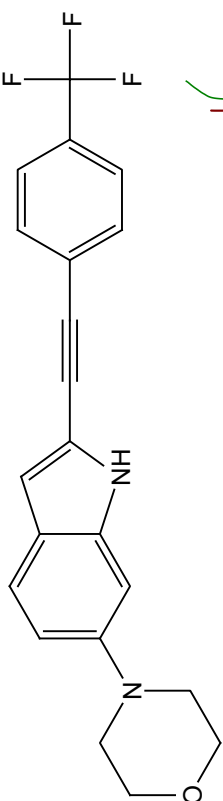


200 MHz, DMSO-*d*<sub>6</sub>

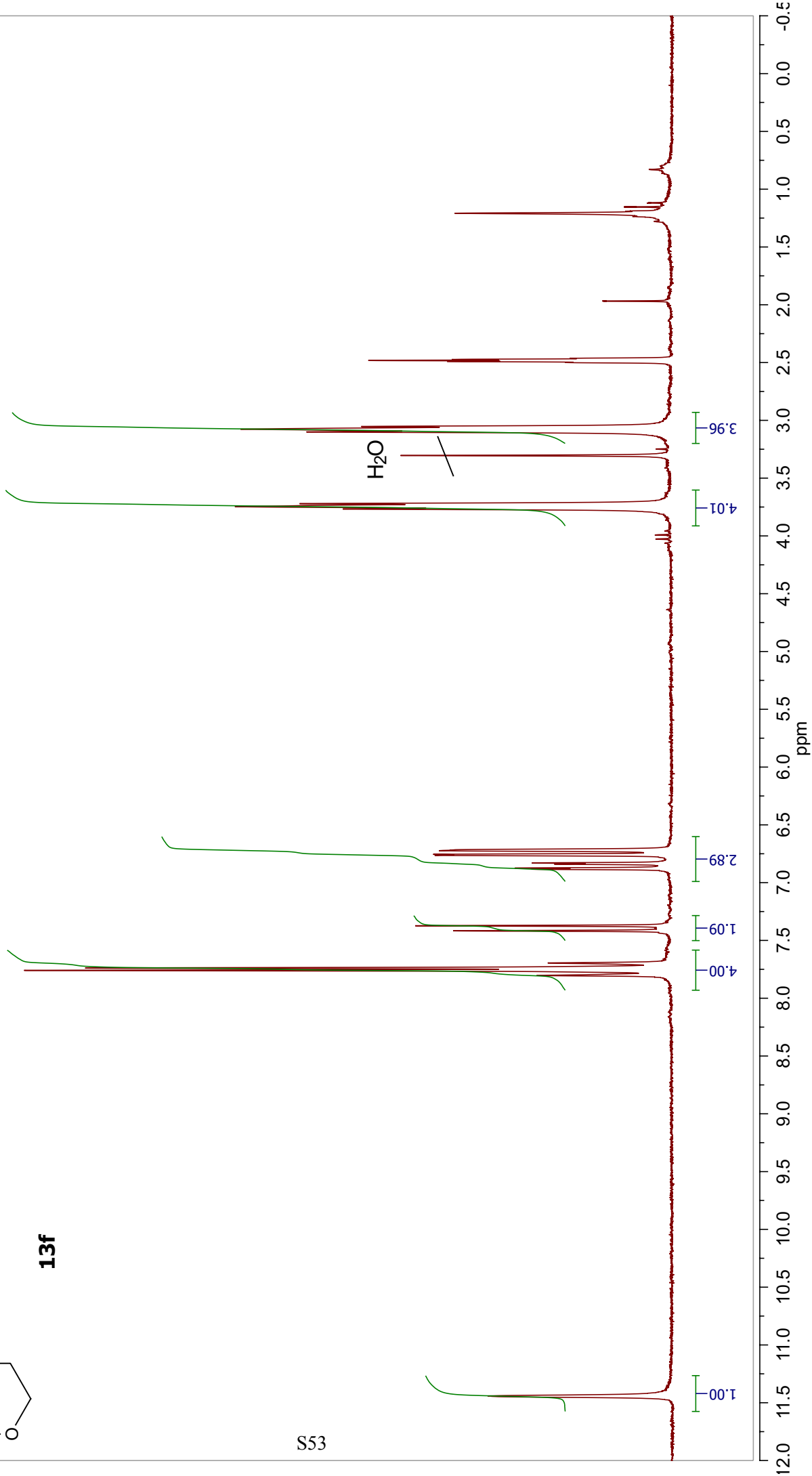
3.77  
3.75  
3.72

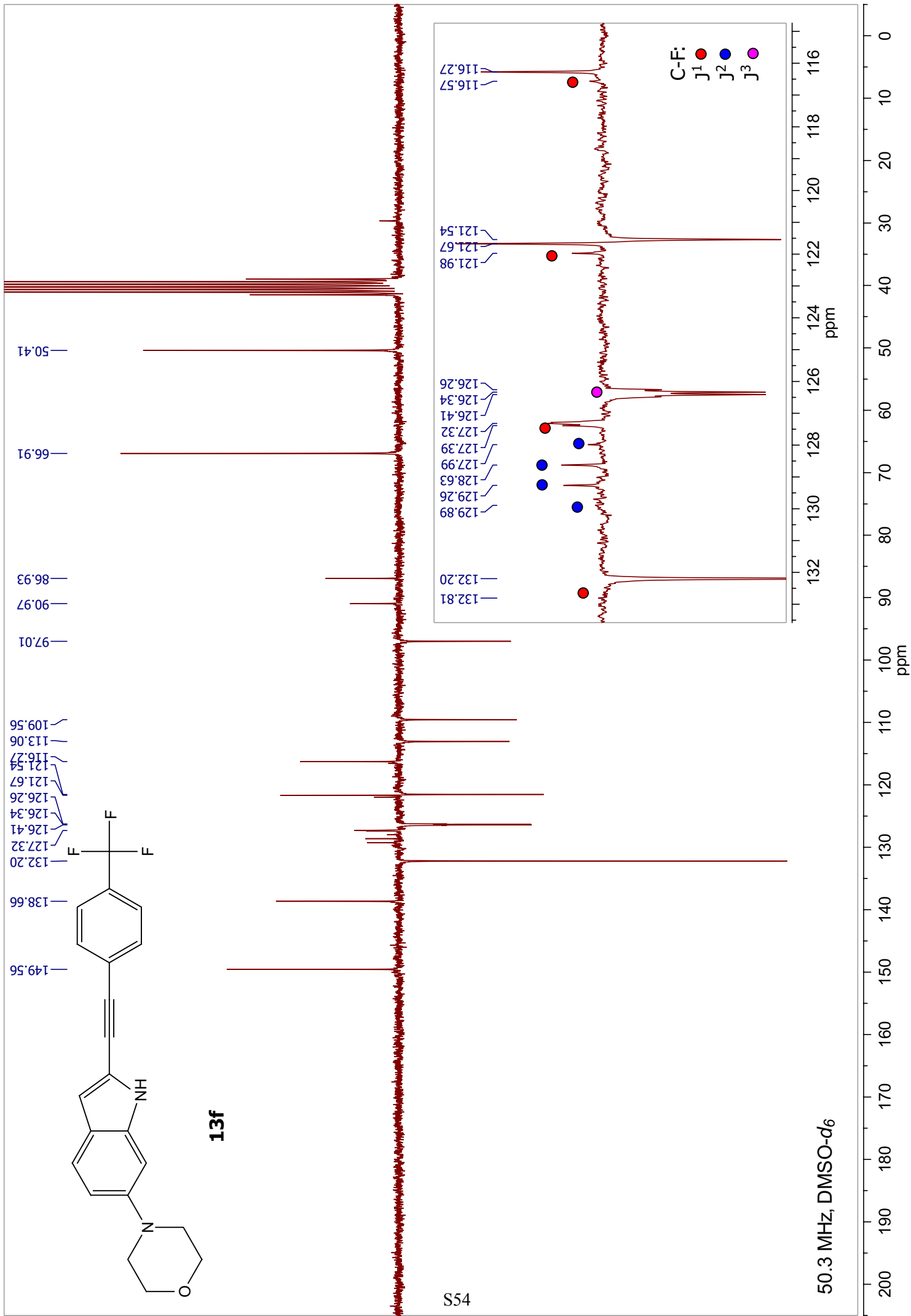
7.80  
7.76  
7.74  
7.70  
7.42  
7.37  
6.88  
6.87  
6.84  
6.83  
6.76  
6.76  
6.72

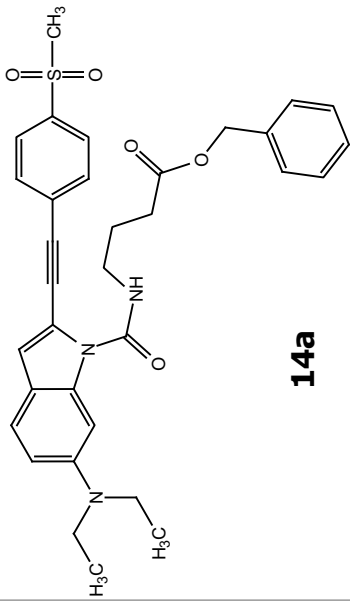
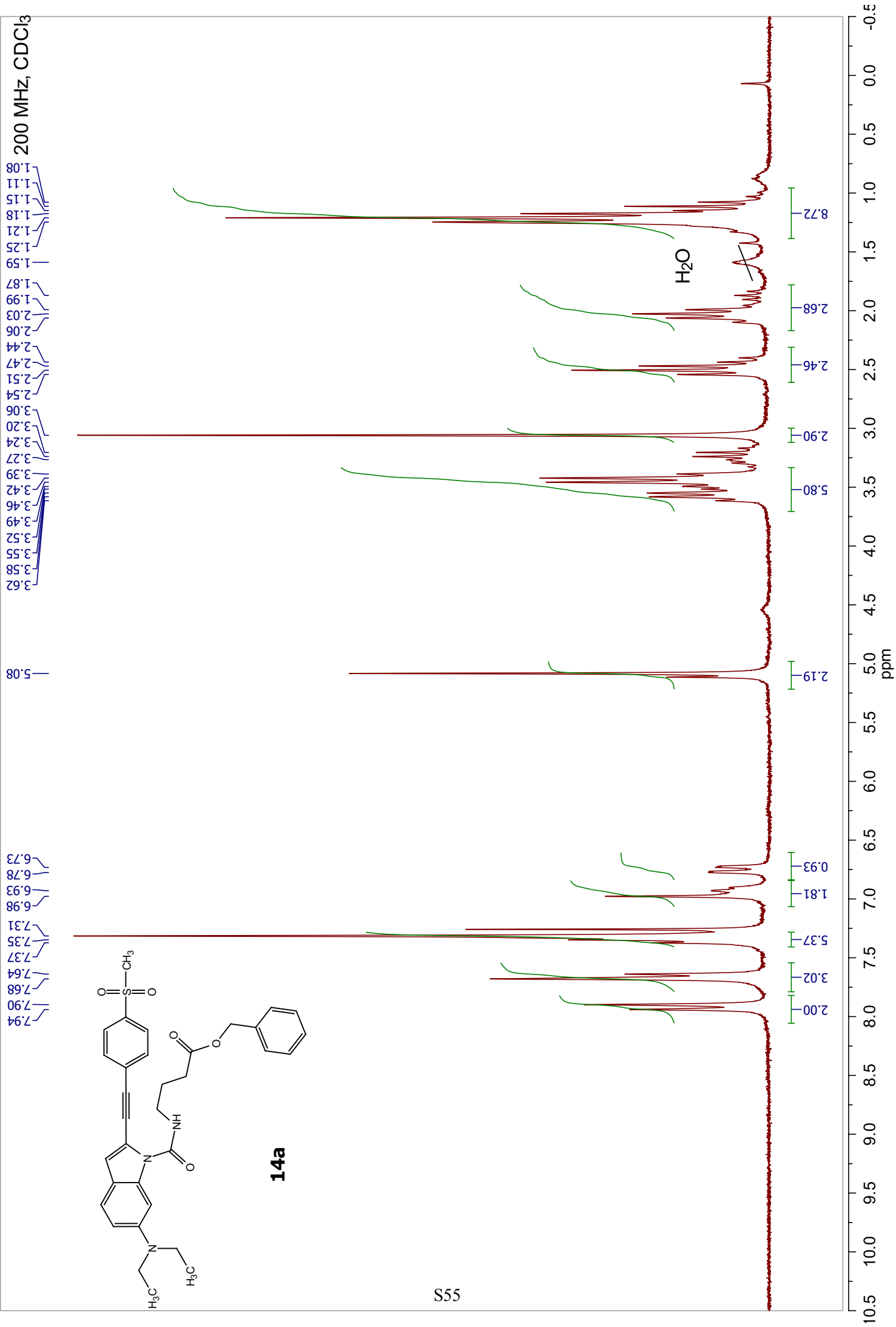
11.44

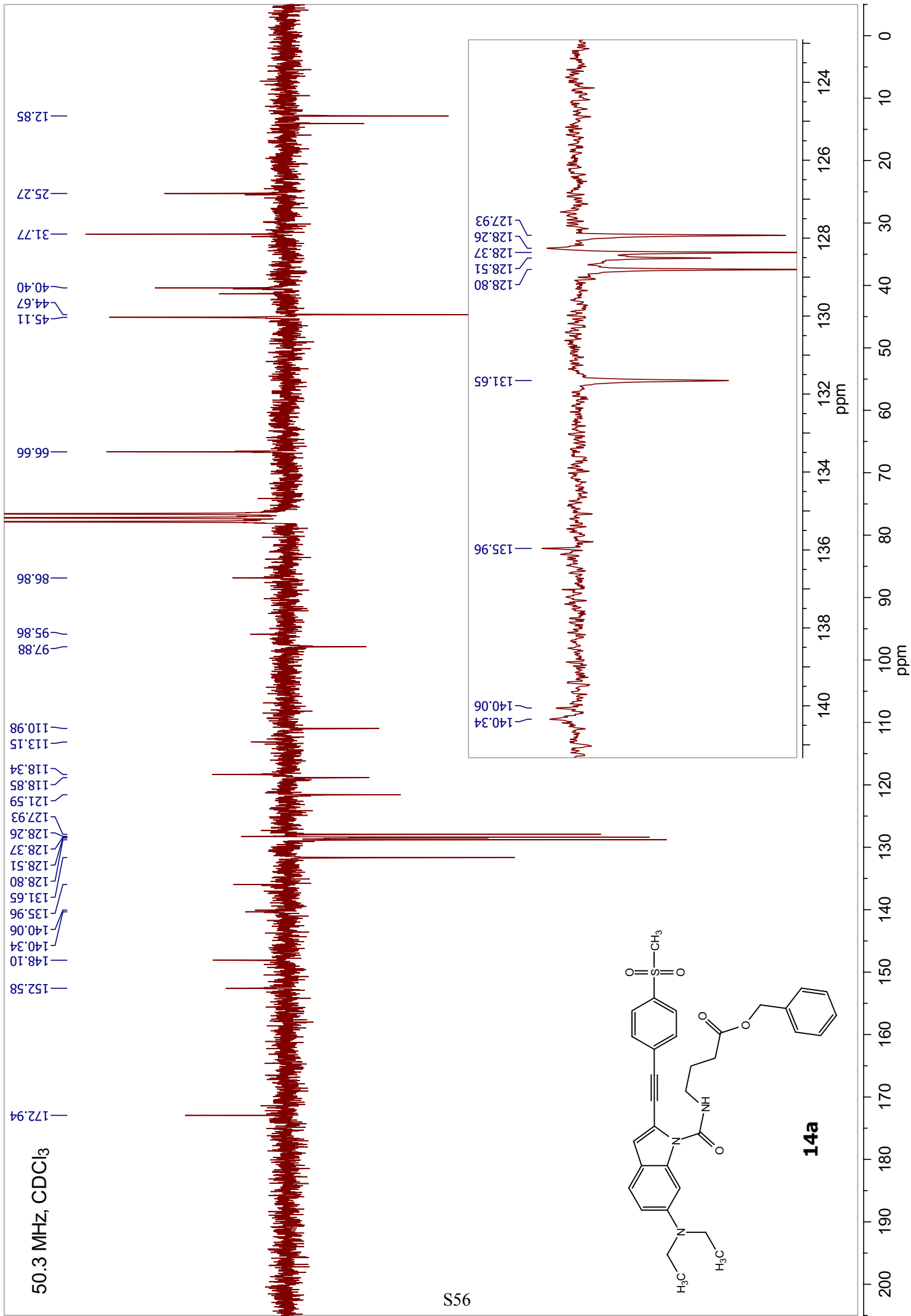


**13f**

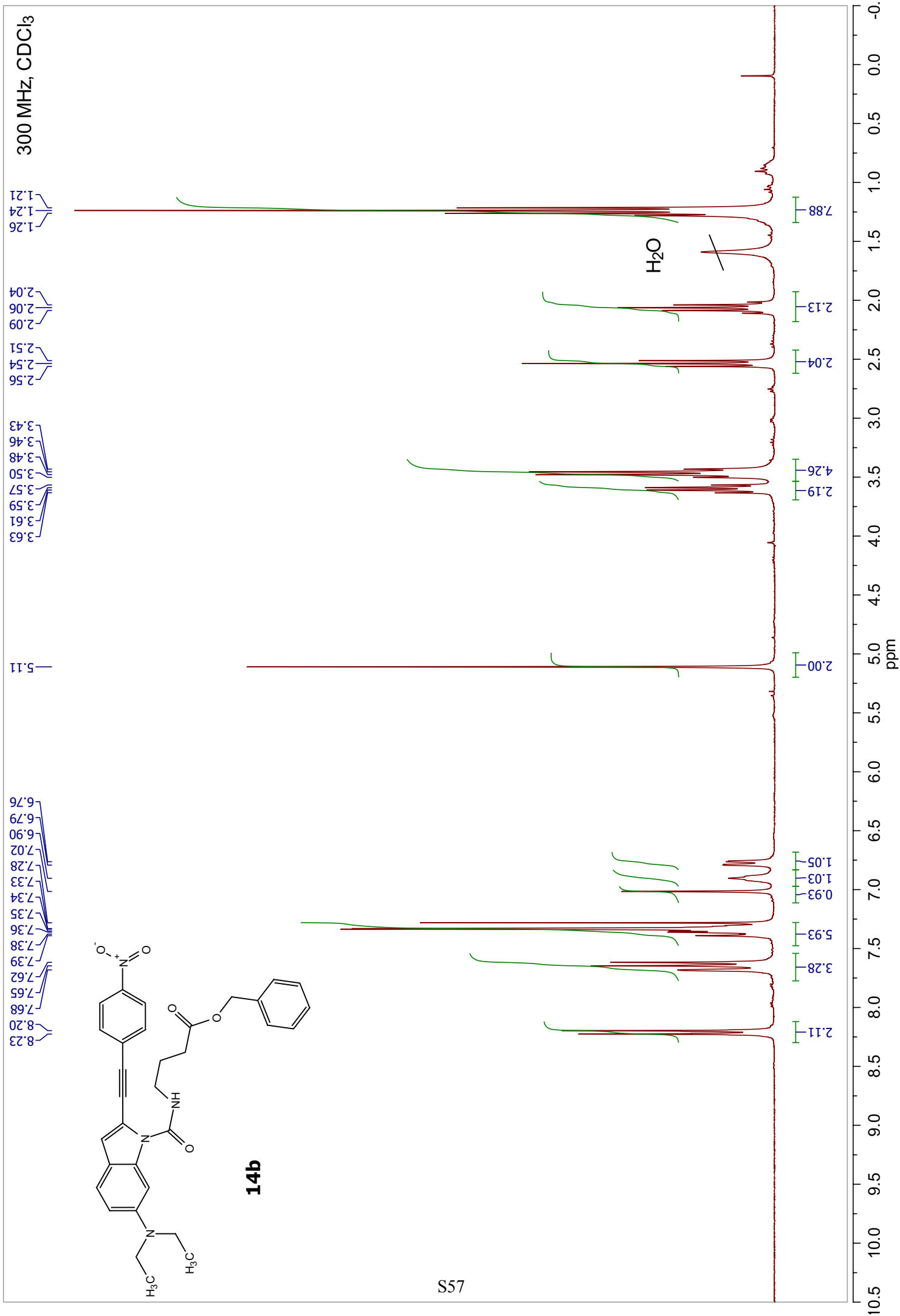


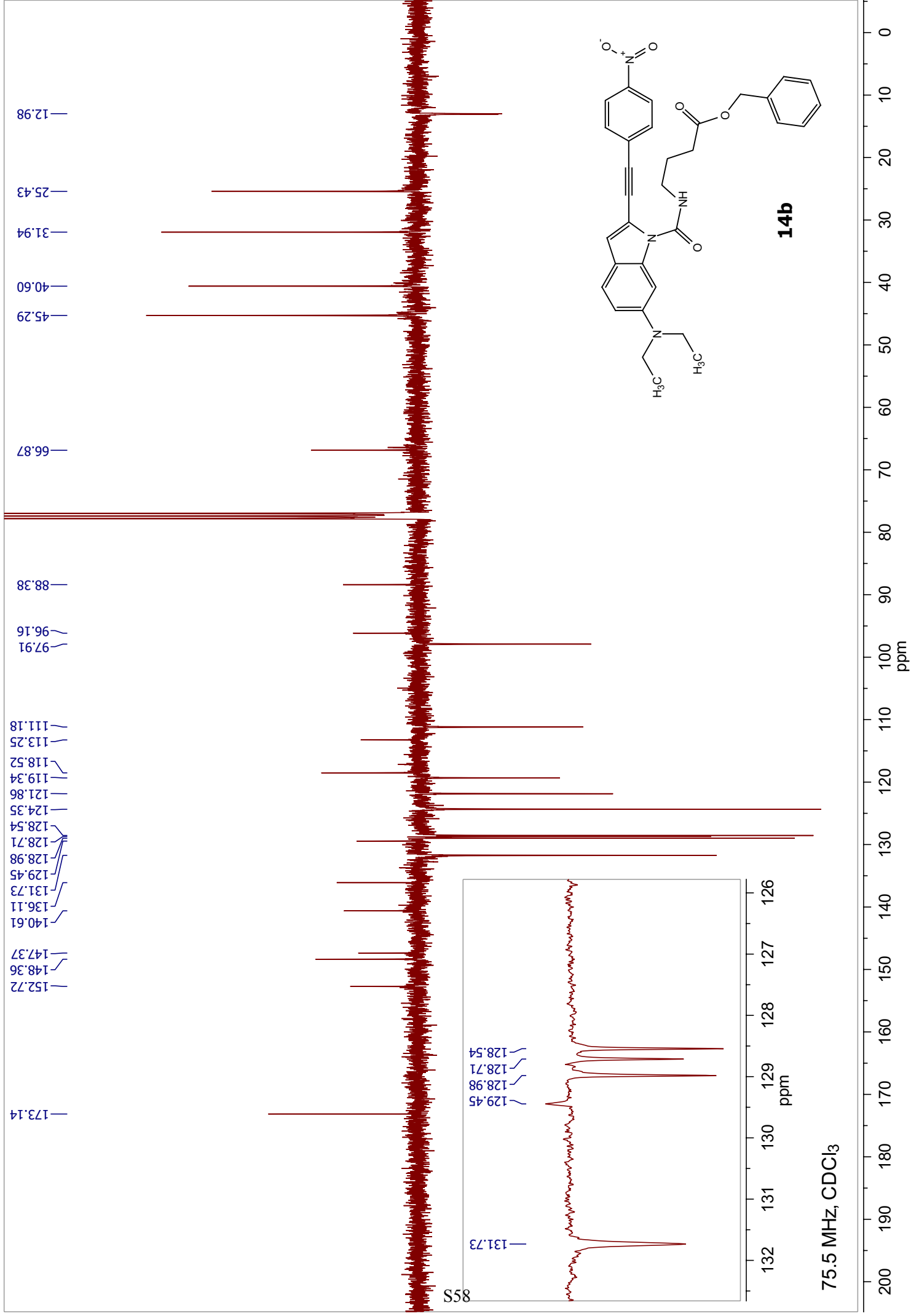


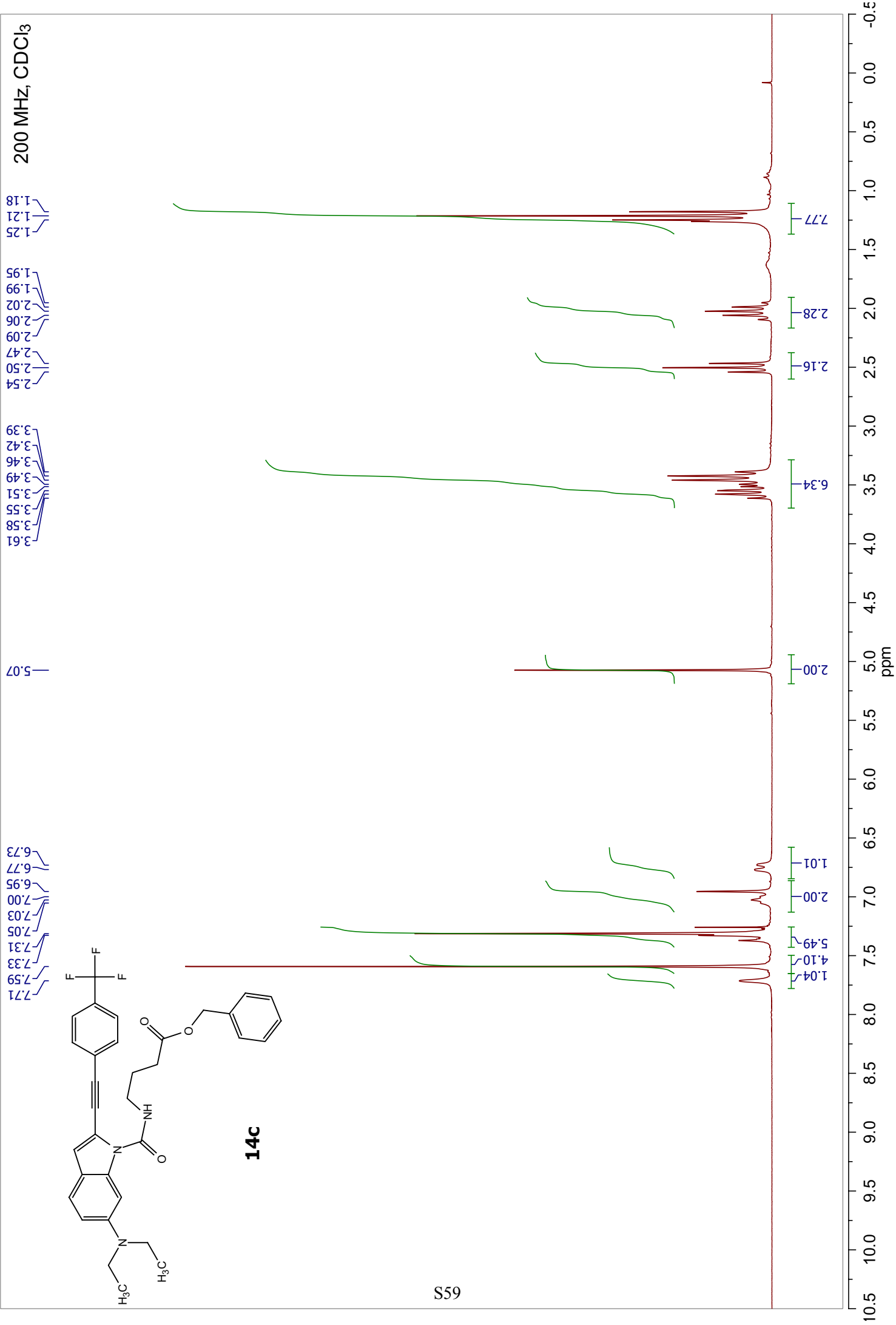
**14a**200 MHz,  $\text{CDCl}_3$ 7.94  
7.90  
7.68  
7.64  
7.37  
7.35  
7.31  
6.98  
6.93  
6.78  
6.73  
3.62  
3.58  
3.55  
3.52  
3.49  
3.46  
3.42  
3.39  
3.27  
3.24  
3.20  
3.06  
2.54  
2.51  
2.47  
2.44  
2.06  
2.03  
1.99  
1.87  
1.59  
1.25  
1.21  
1.18  
1.15  
1.11  
1.0810.5  
10.0  
9.5  
9.0  
8.5  
8.0  
7.5  
7.0  
6.5  
6.0  
5.5  
5.0  
4.5  
4.0  
3.5  
3.0  
2.5  
2.0  
1.5  
1.0  
0.5  
0.0  
-0.5  
ppm

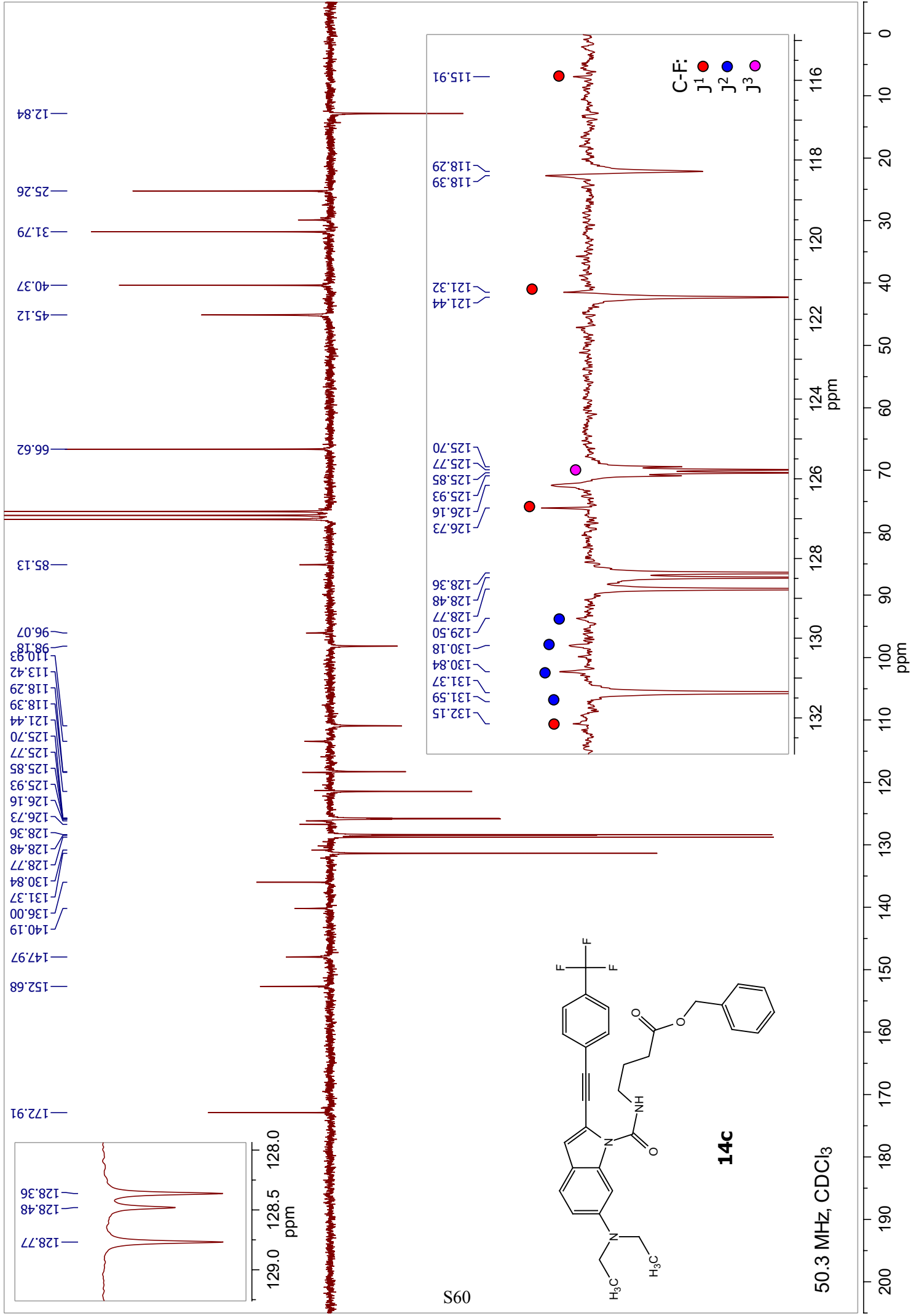


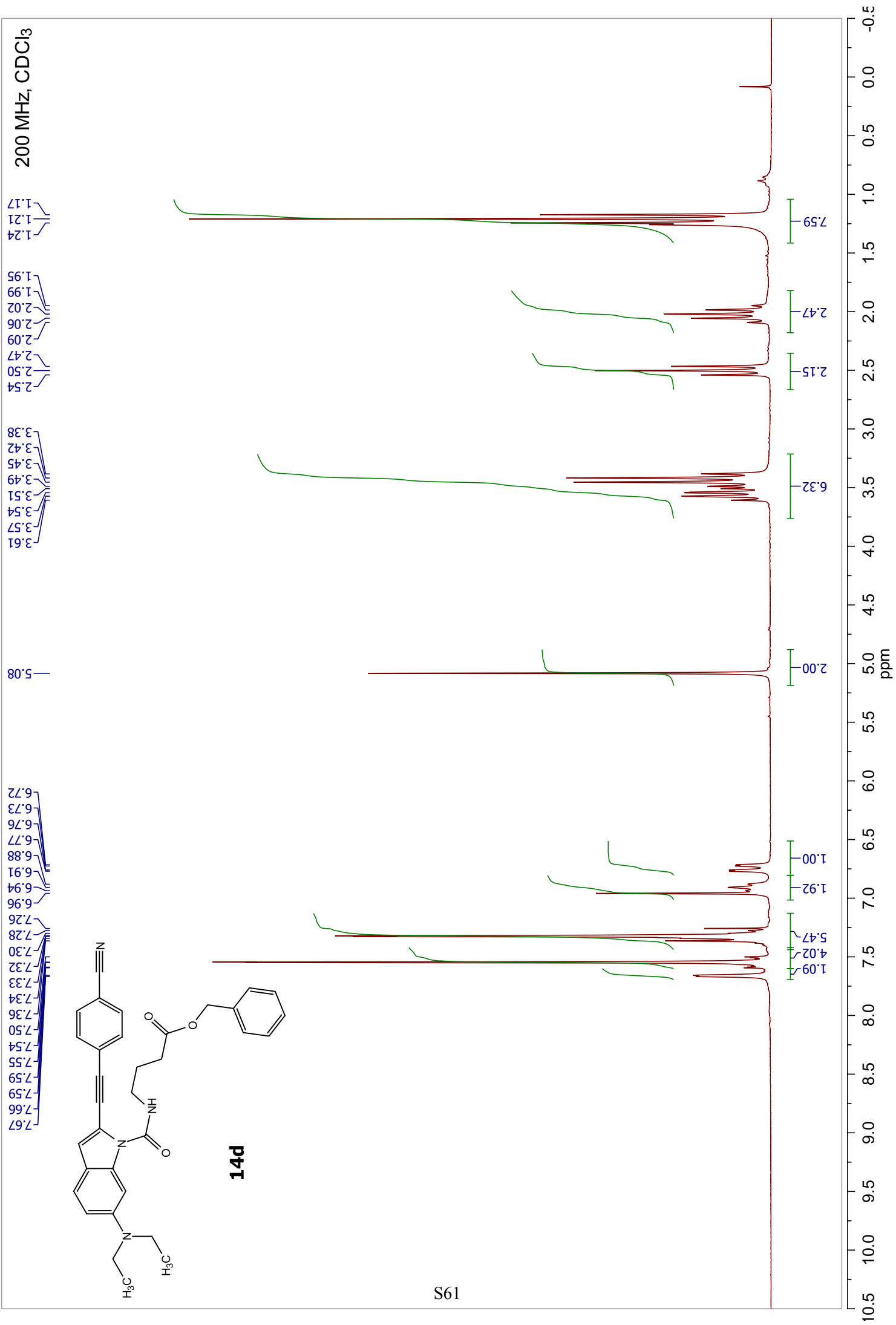


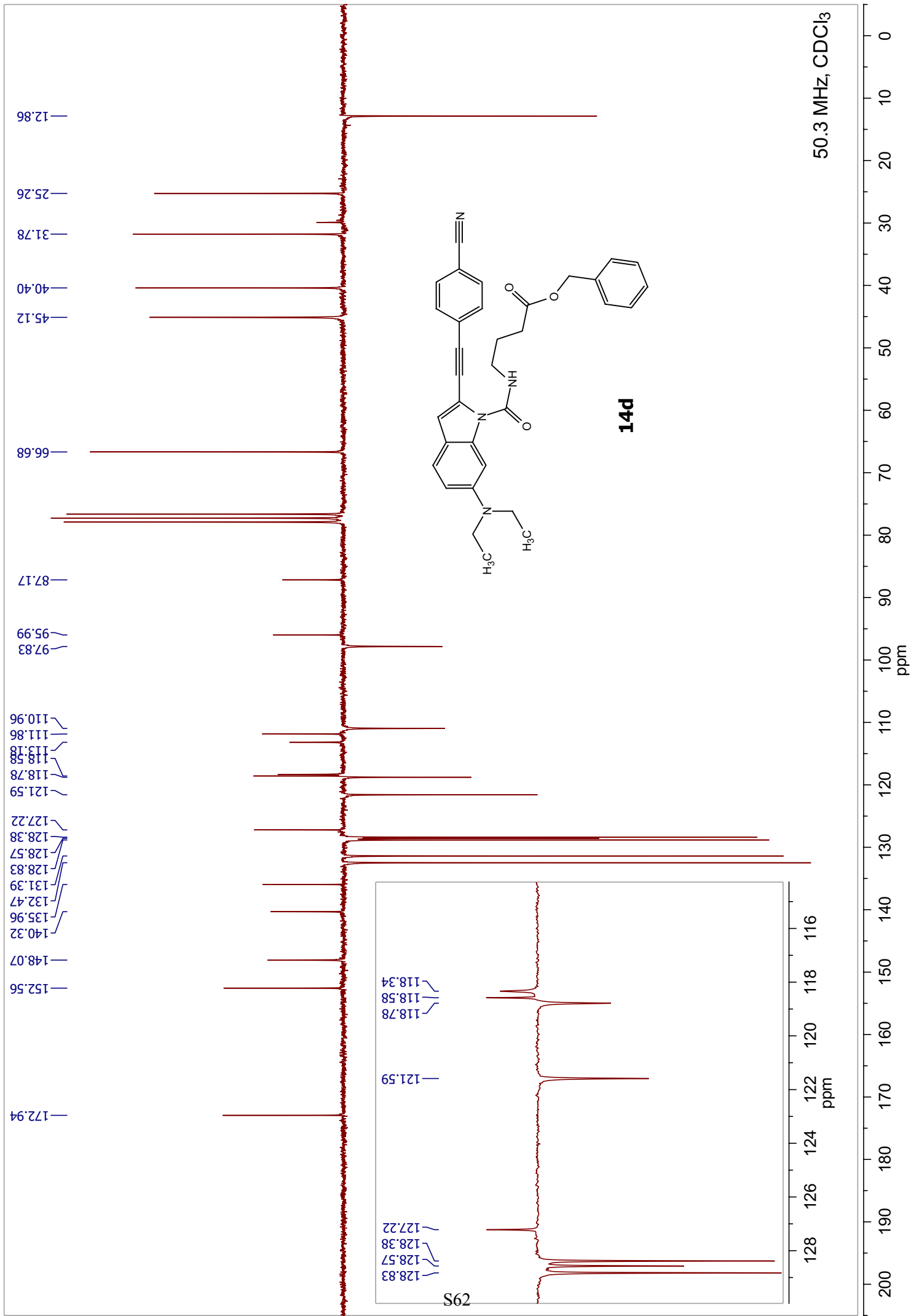










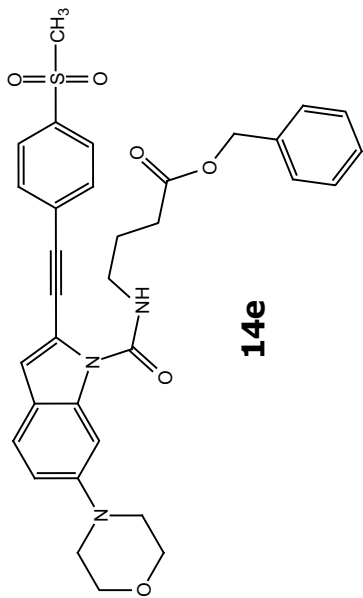


200 MHz, CDCl<sub>3</sub>

1.95  
1.99  
2.03  
2.06  
2.10  
2.47  
2.51  
2.54  
3.06  
3.24  
3.26  
3.29  
3.52  
3.55  
3.58  
3.62  
3.87  
3.90  
3.92

5.08

6.97  
6.99  
7.01  
7.31  
7.42  
7.47  
7.66  
7.71  
7.91  
7.96



2.35

2.16

3.48

4.17

2.18

4.16

2.00

2.98

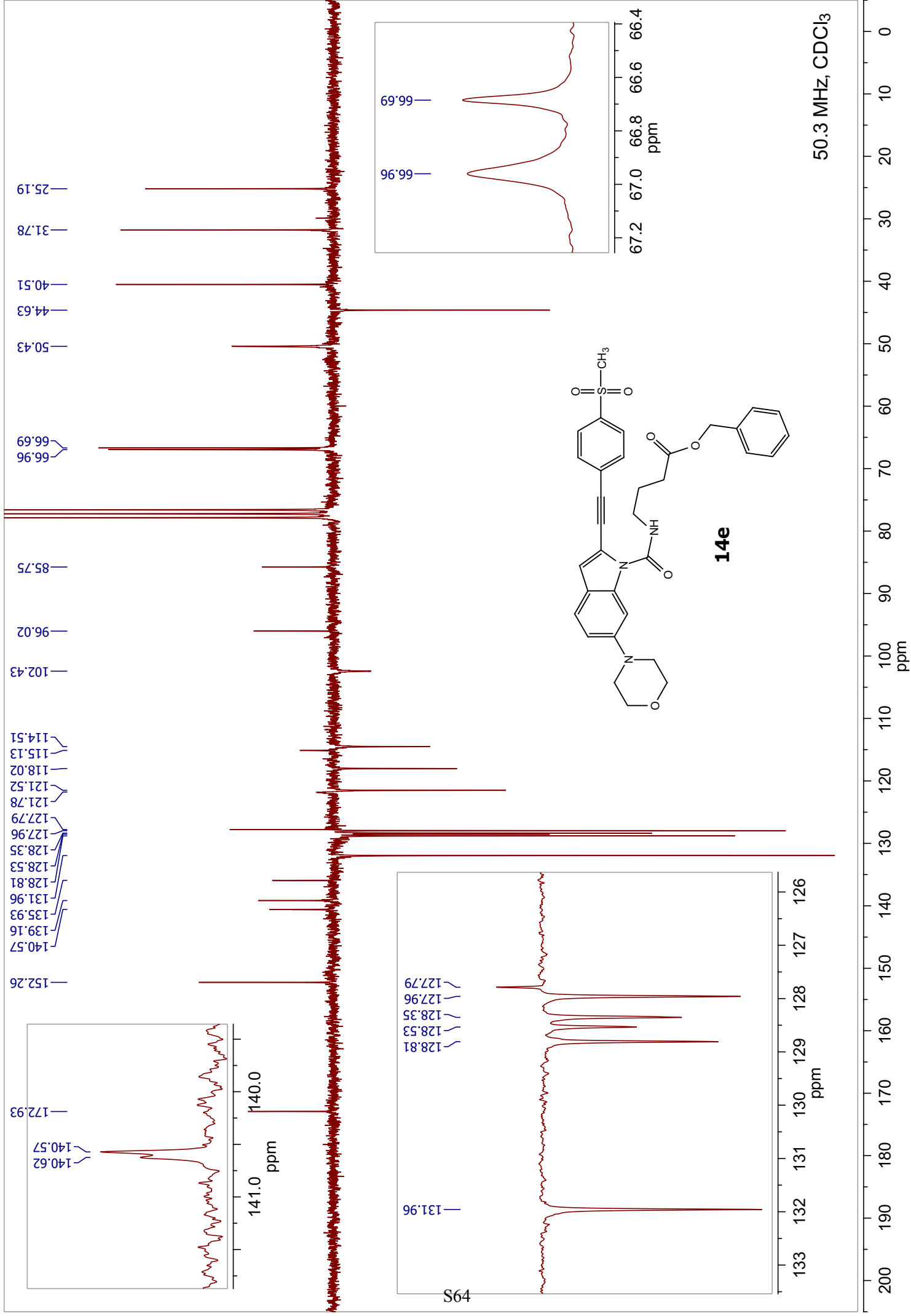
4.77

1.17

2.19

3.18

10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 ppm





200 MHz, CDCl<sub>3</sub>

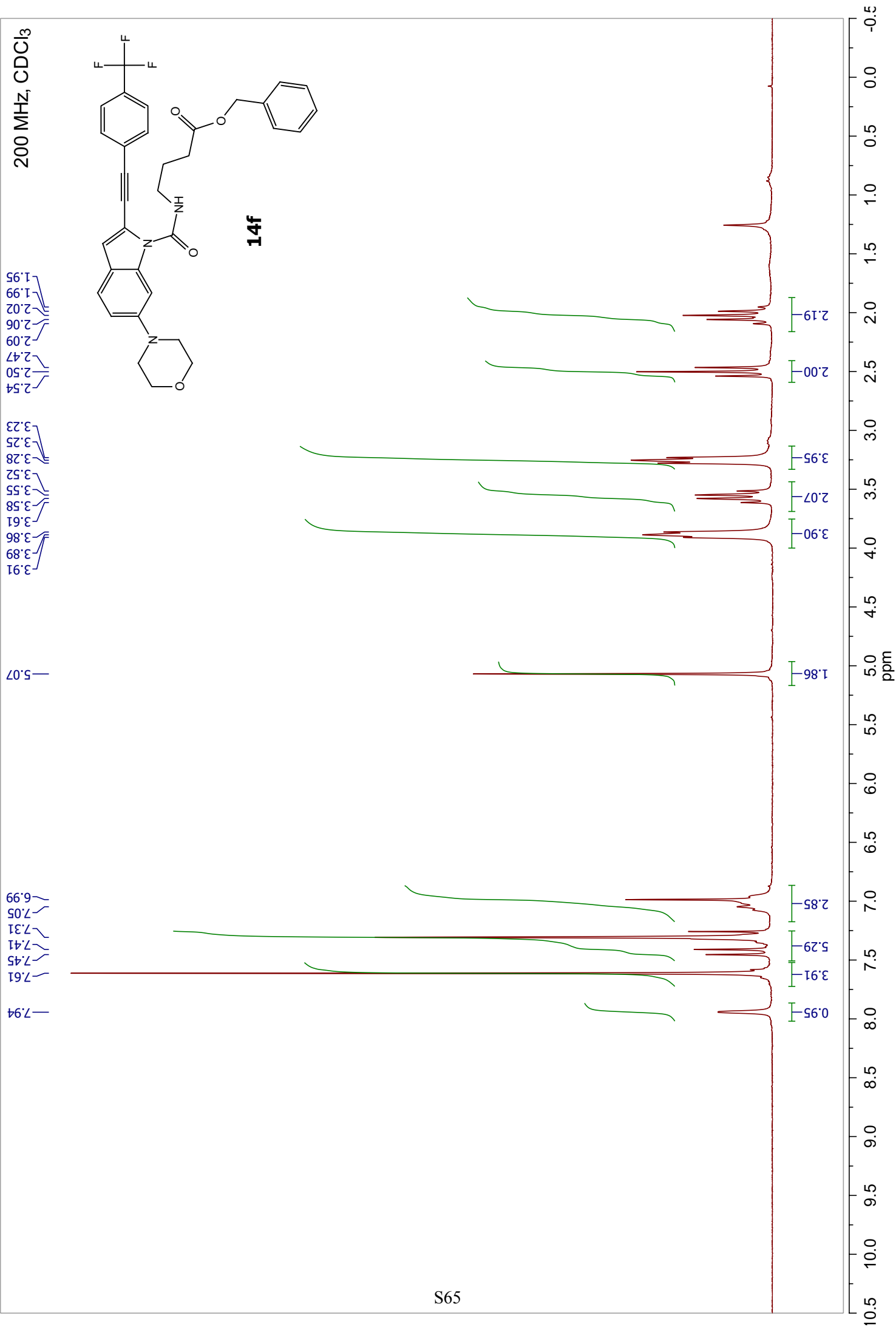
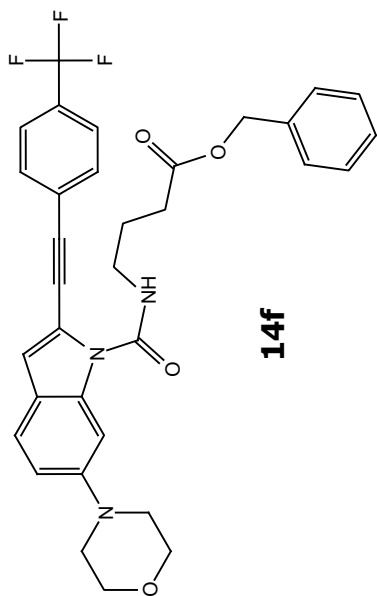
1.95  
1.99  
2.02  
2.06  
2.09  
2.47  
2.50  
2.54

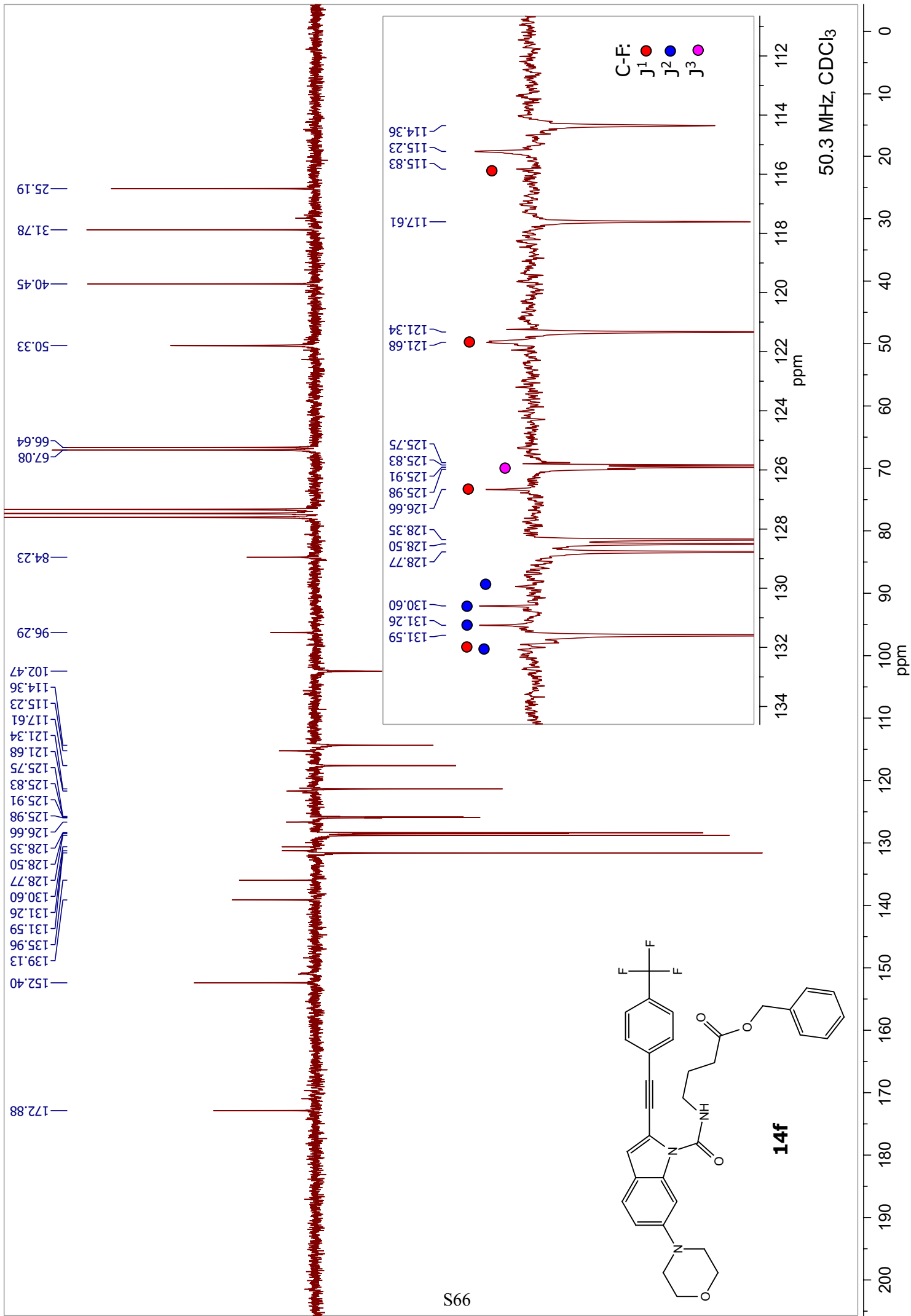
3.23  
3.25  
3.28  
3.52  
3.55  
3.58  
3.61  
3.86  
3.89  
3.91

5.07

6.99  
7.05  
7.31  
7.41  
7.45  
7.61

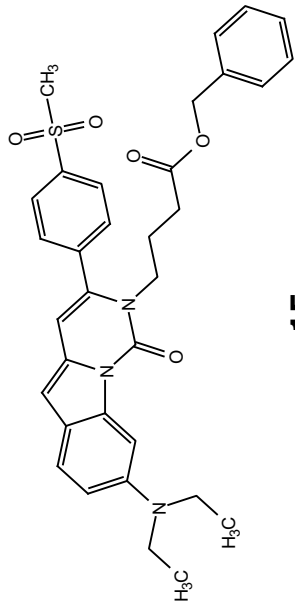
7.94



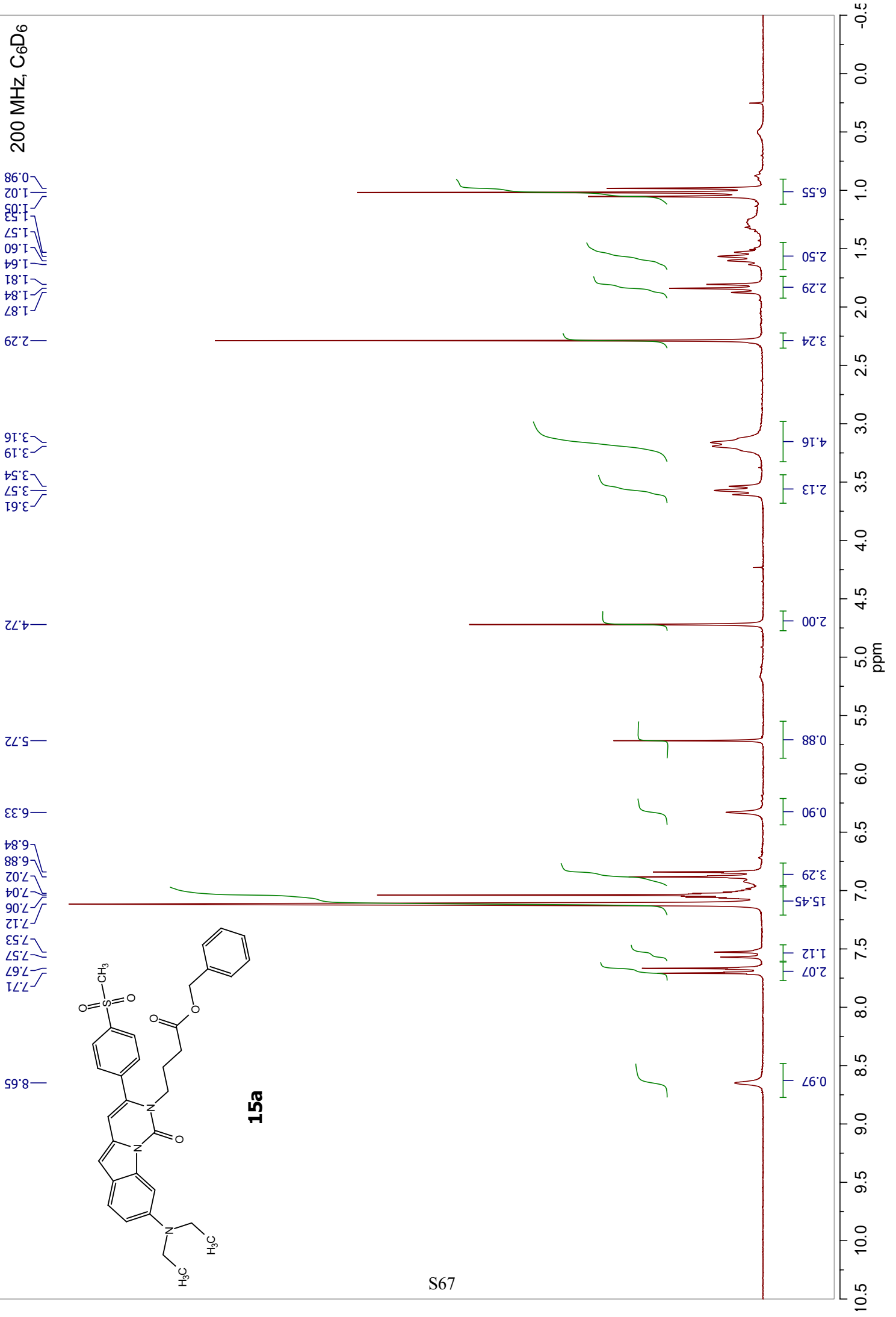


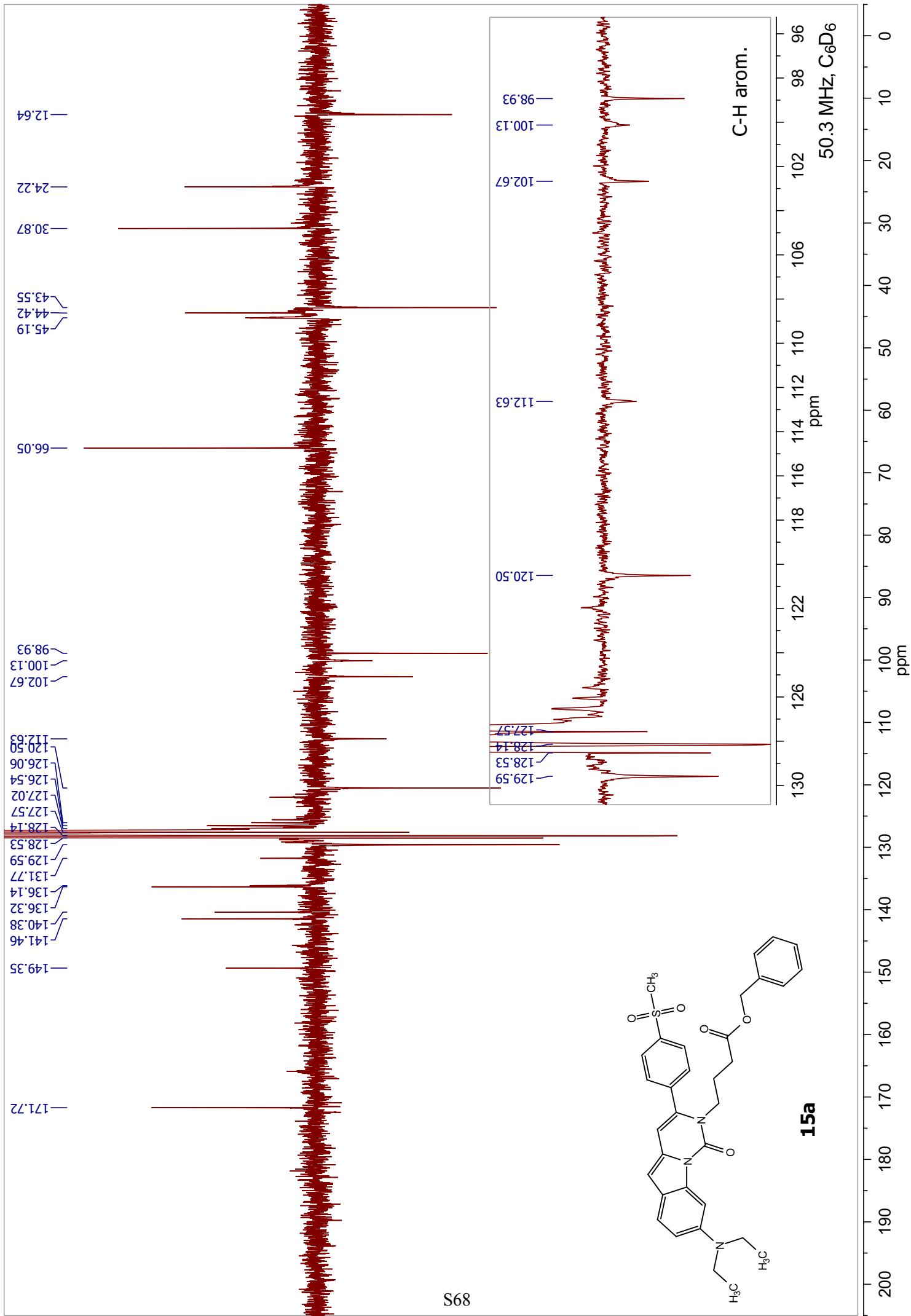
200 MHz, C<sub>6</sub>D<sub>6</sub>

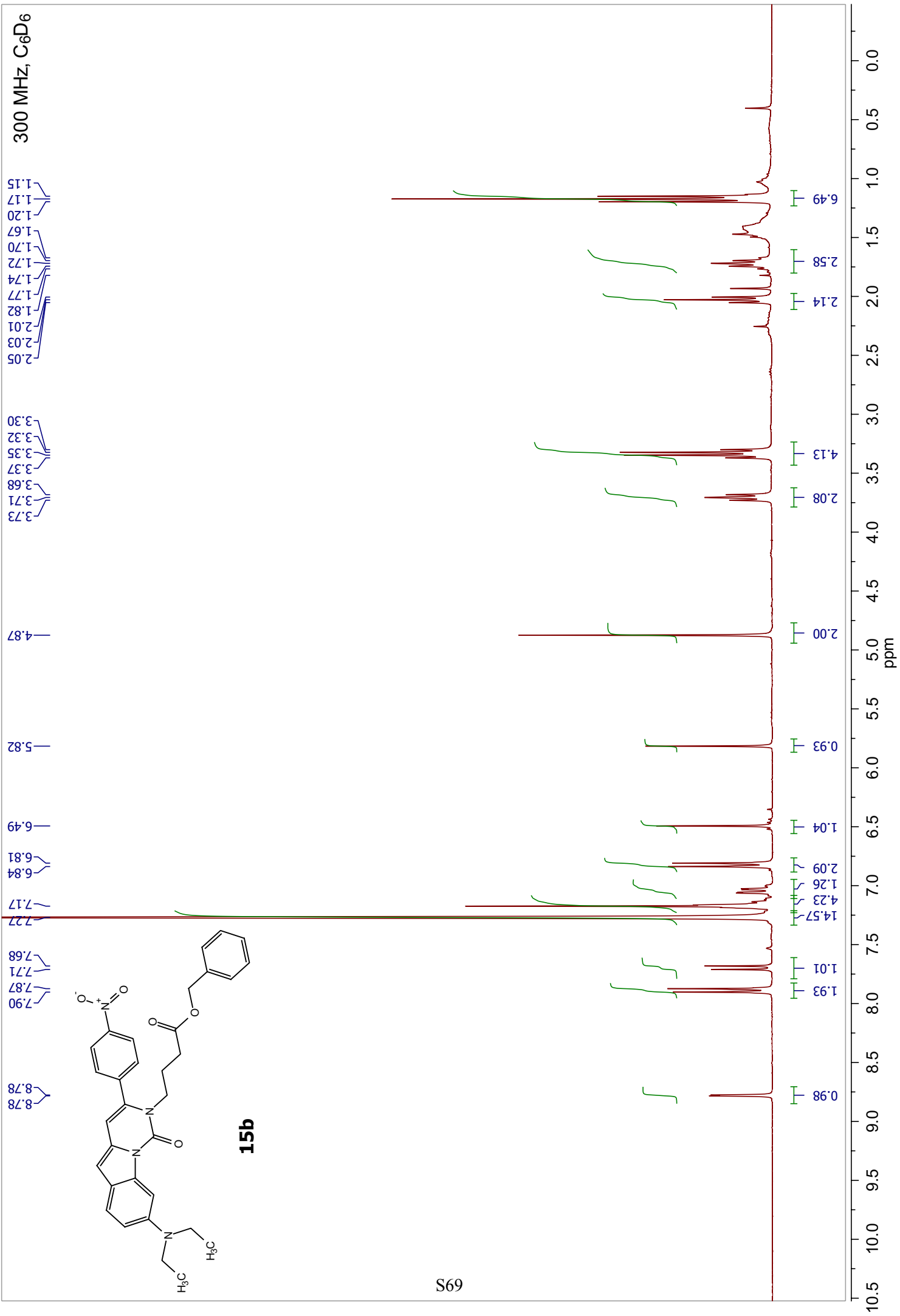
0.98  
1.02  
1.53  
1.57  
1.60  
1.64  
1.81  
1.84  
1.87  
2.29  
3.16  
3.19  
3.54  
3.57  
3.61  
4.72  
5.72  
6.33  
6.84  
6.88  
7.02  
7.04  
7.06  
7.12  
7.53  
7.57  
7.67  
7.71  
8.65

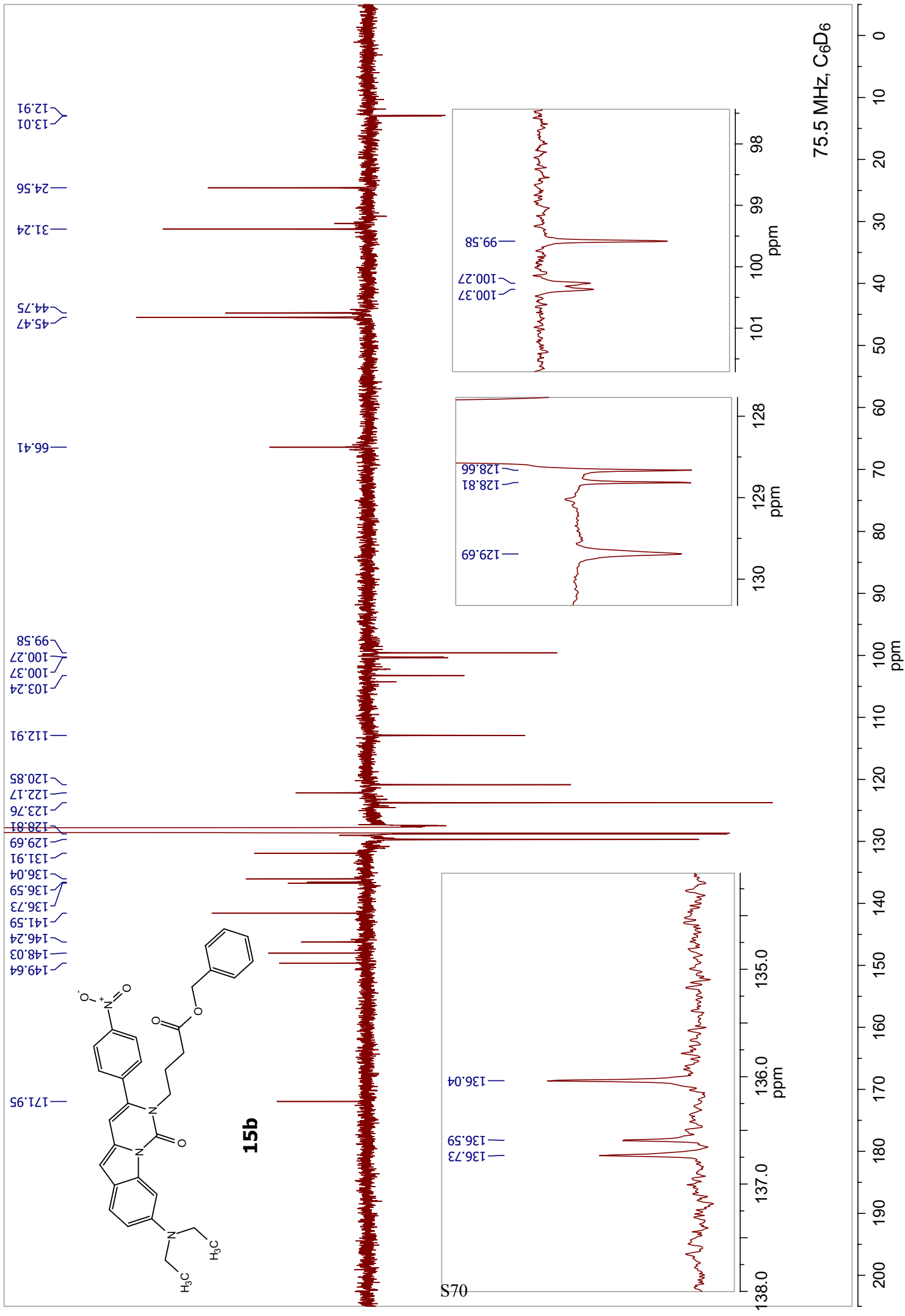


**15a**









300 MHz, C<sub>6</sub>D<sub>6</sub>

1.15  
1.20  
1.17  
1.73  
1.75  
1.78  
1.98  
2.01  
2.03  
3.30  
3.33  
3.35  
3.37  
3.71  
3.73  
3.75

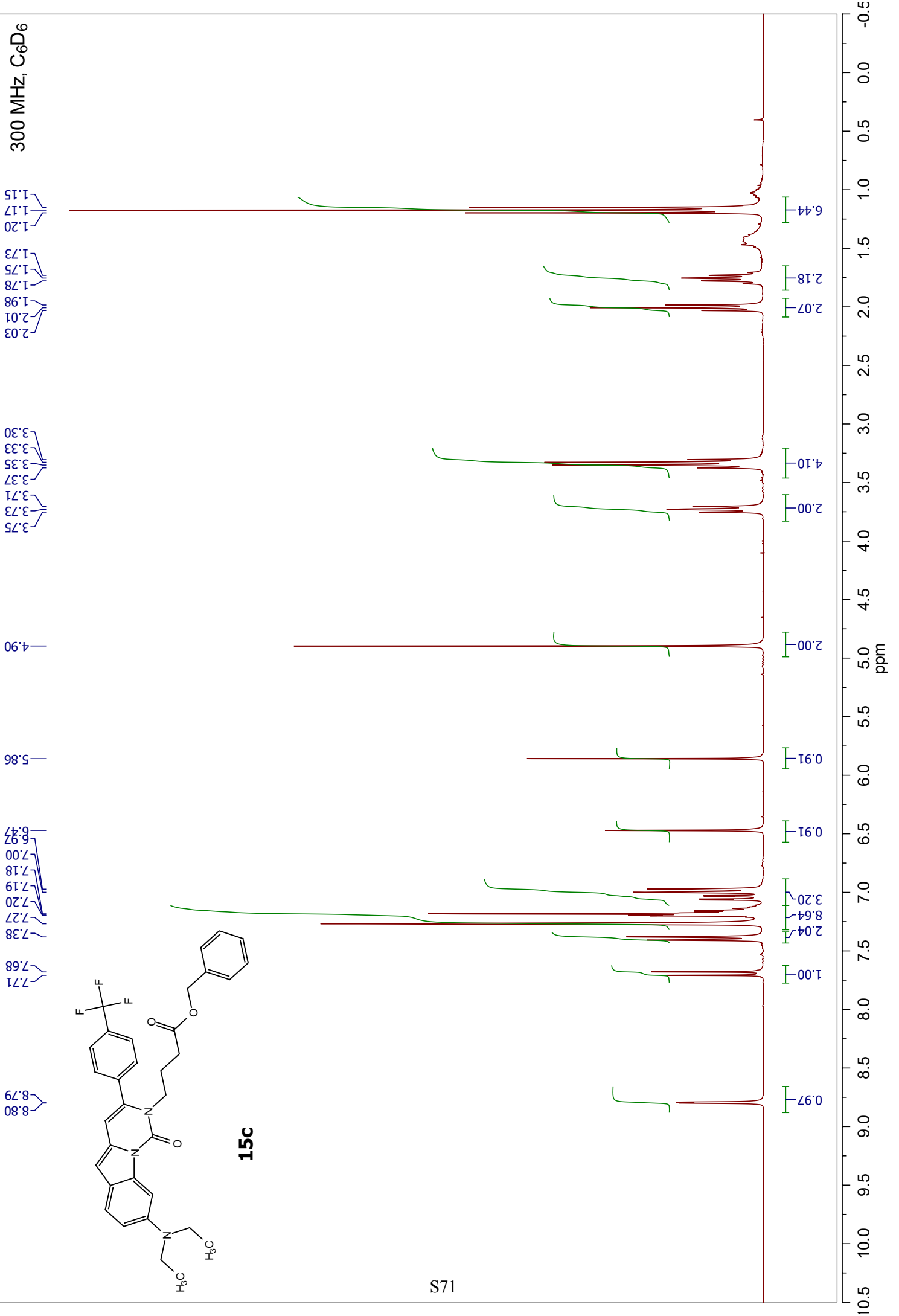
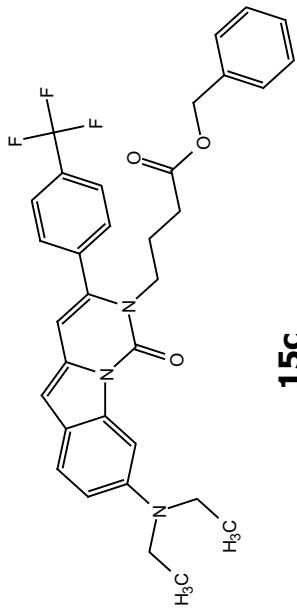
4.90

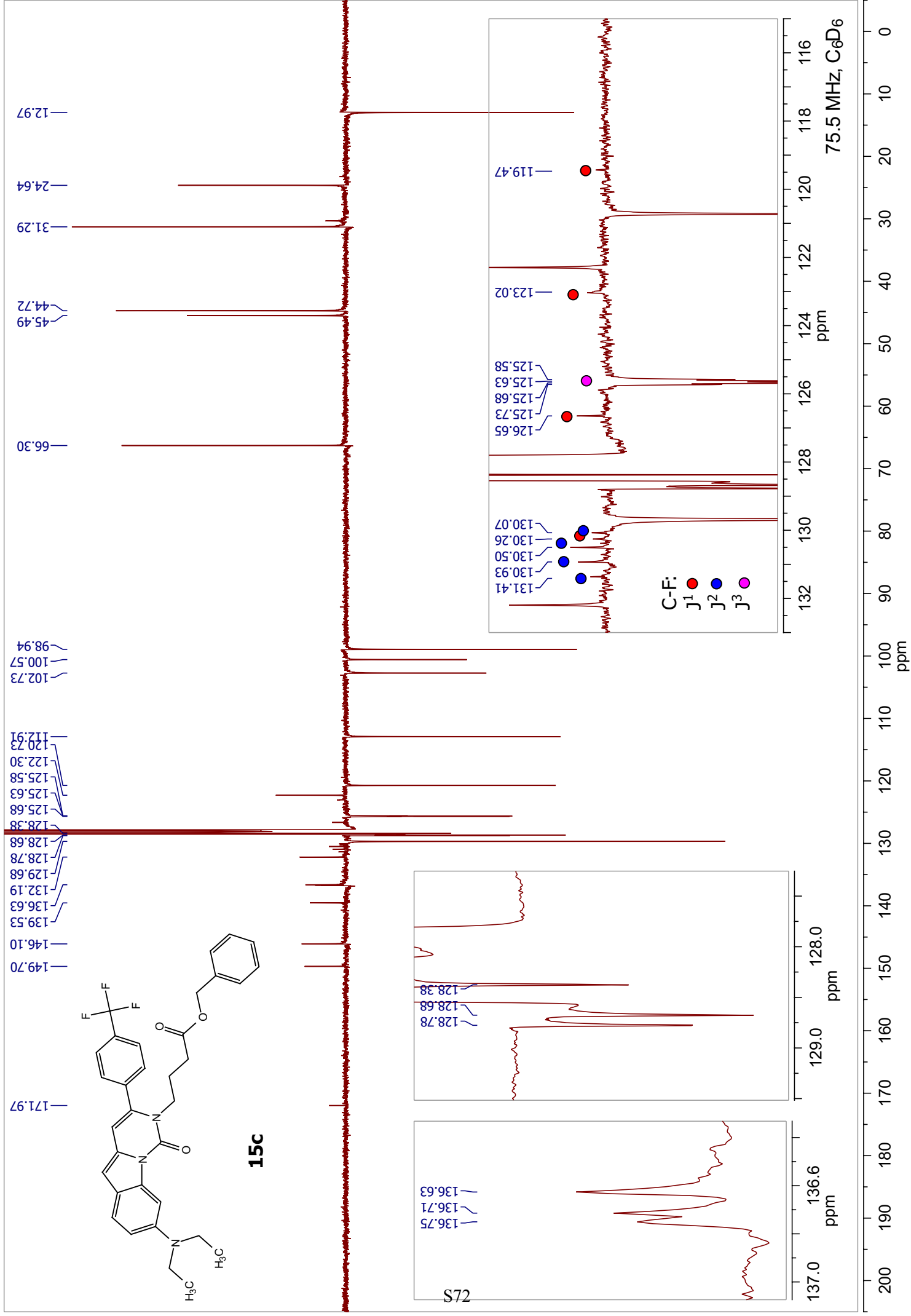
5.86

6.47  
6.97  
7.00  
7.18  
7.19  
7.20  
7.27  
7.38

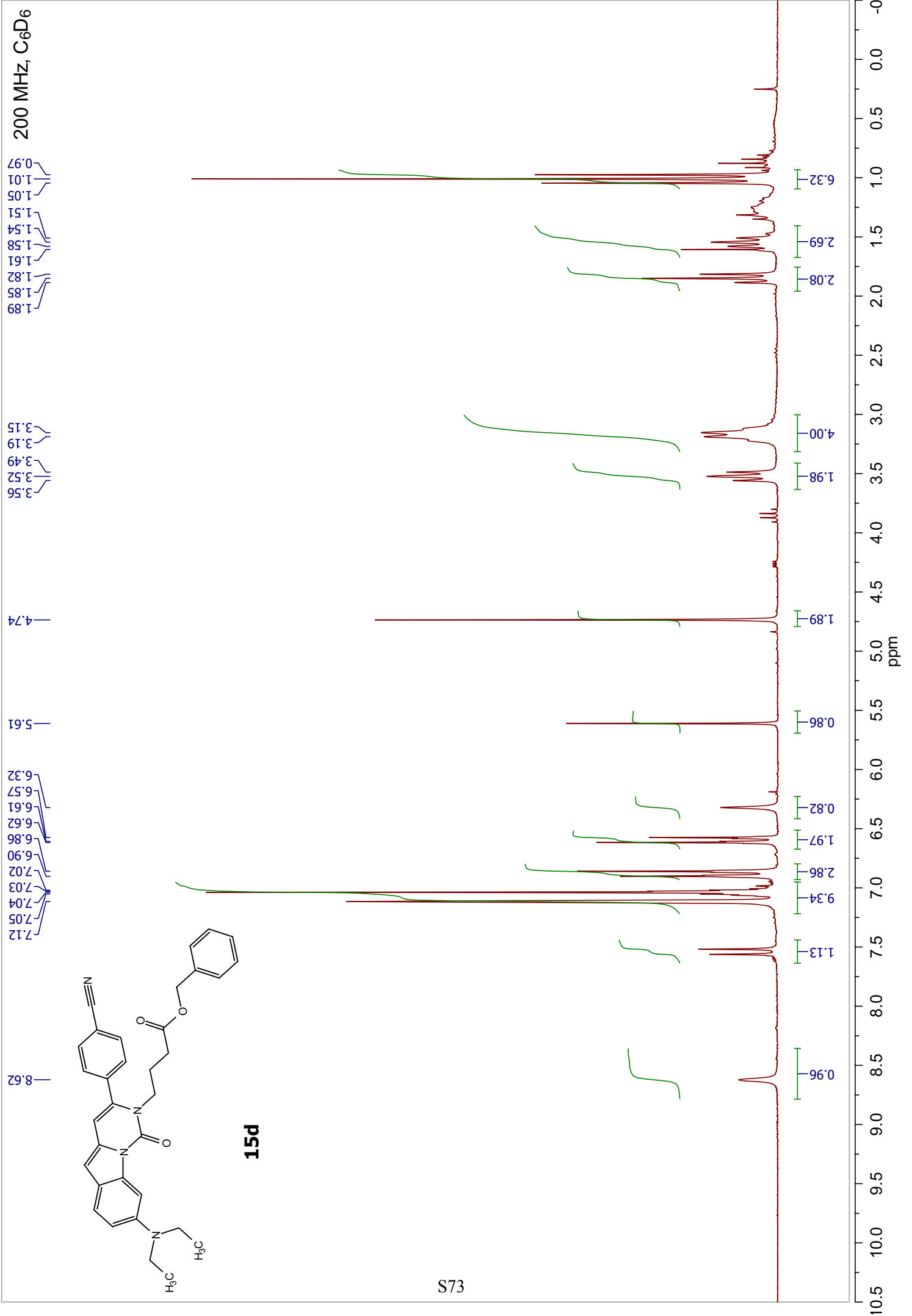
7.68  
7.71

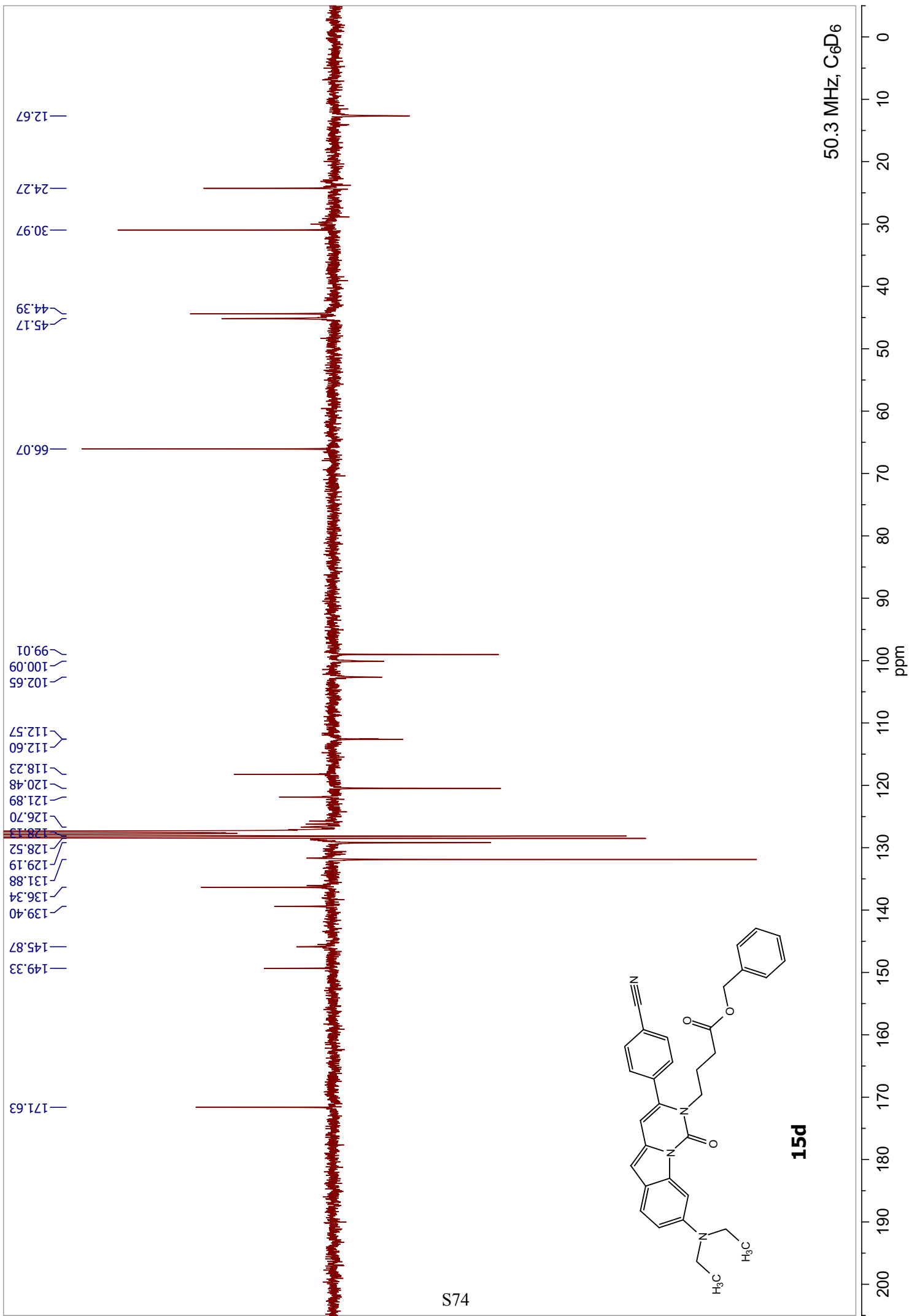
8.79  
8.80





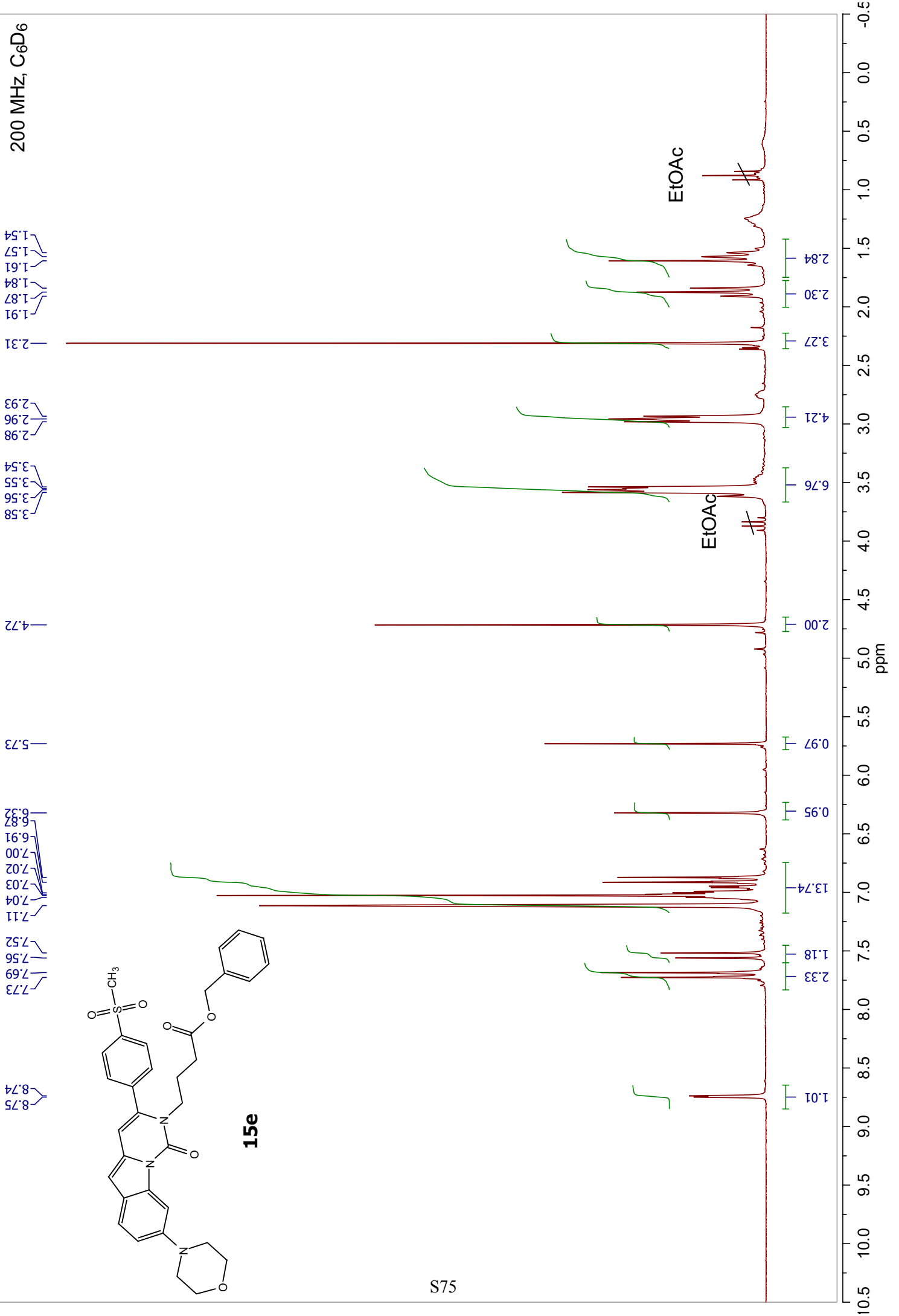
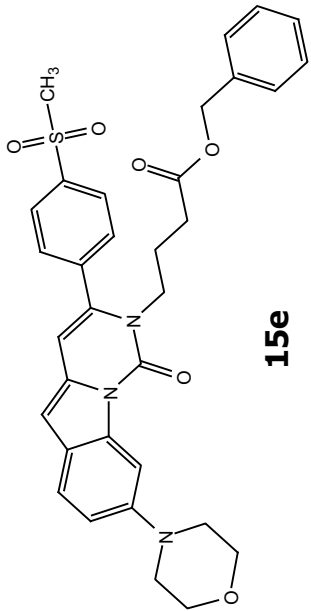


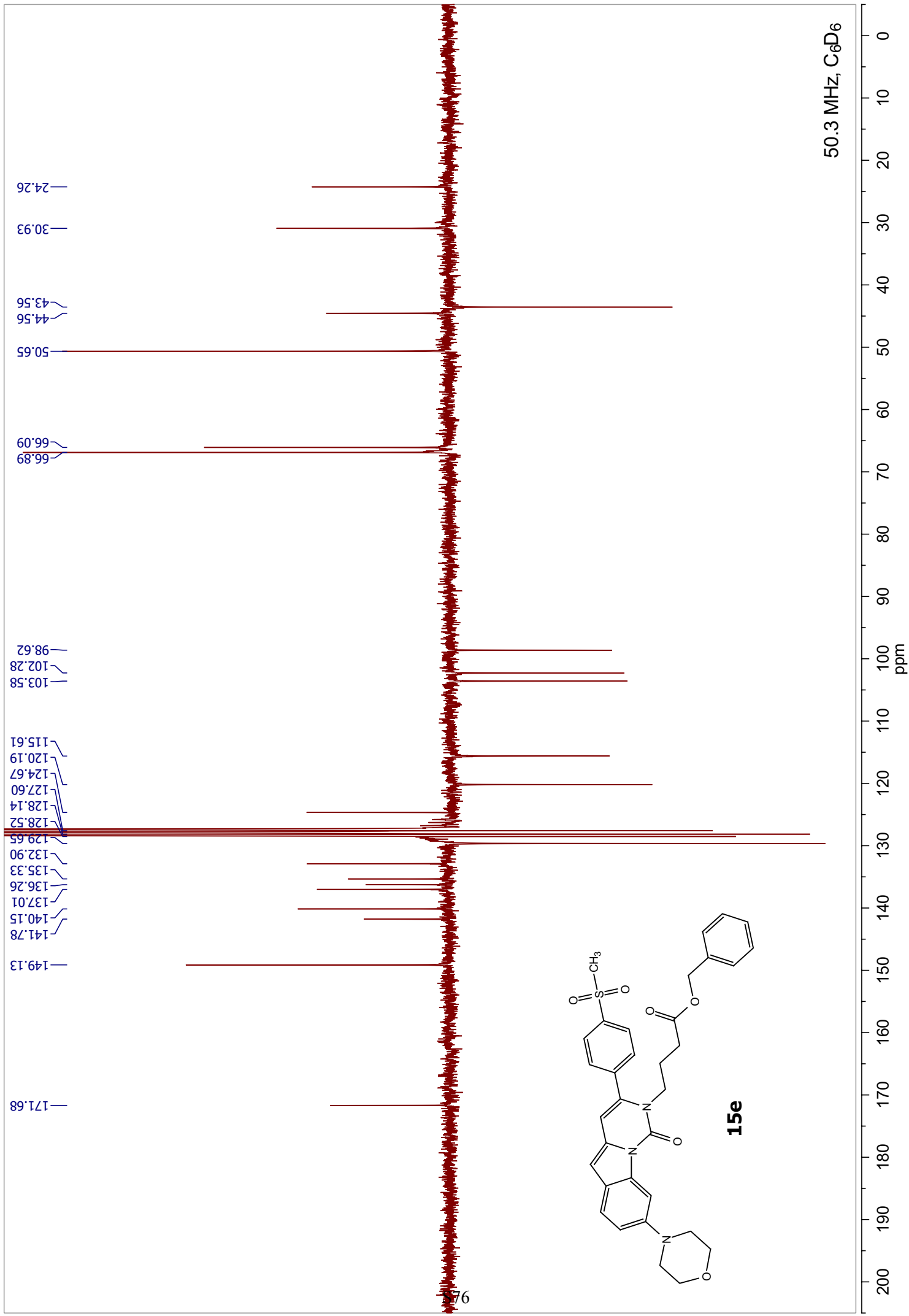




200 MHz, C<sub>6</sub>D<sub>6</sub>

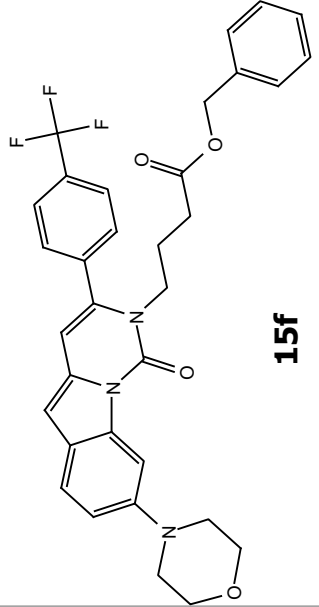
1.54  
1.57  
1.61  
1.84  
1.87  
1.91  
2.31  
2.93  
2.96  
2.98  
3.54  
3.55  
3.56  
3.58  
4.72  
5.73  
6.87  
6.91  
7.00  
7.02  
7.03  
7.04  
7.11  
7.52  
7.56  
7.69  
7.73  
8.74  
8.75





200 MHz, C<sub>6</sub>D<sub>6</sub>

1.52  
1.56  
1.59  
1.61  
1.63  
1.66  
1.84  
1.88  
1.91  
2.93  
2.96  
2.98  
3.54  
3.56  
3.57  
3.59  
4.73  
5.70  
6.31  
6.81  
6.85  
6.95  
6.96  
6.99  
7.01  
7.02  
7.03  
7.04  
7.12  
7.23  
7.27  
7.52  
7.57  
8.75  
8.76



S77

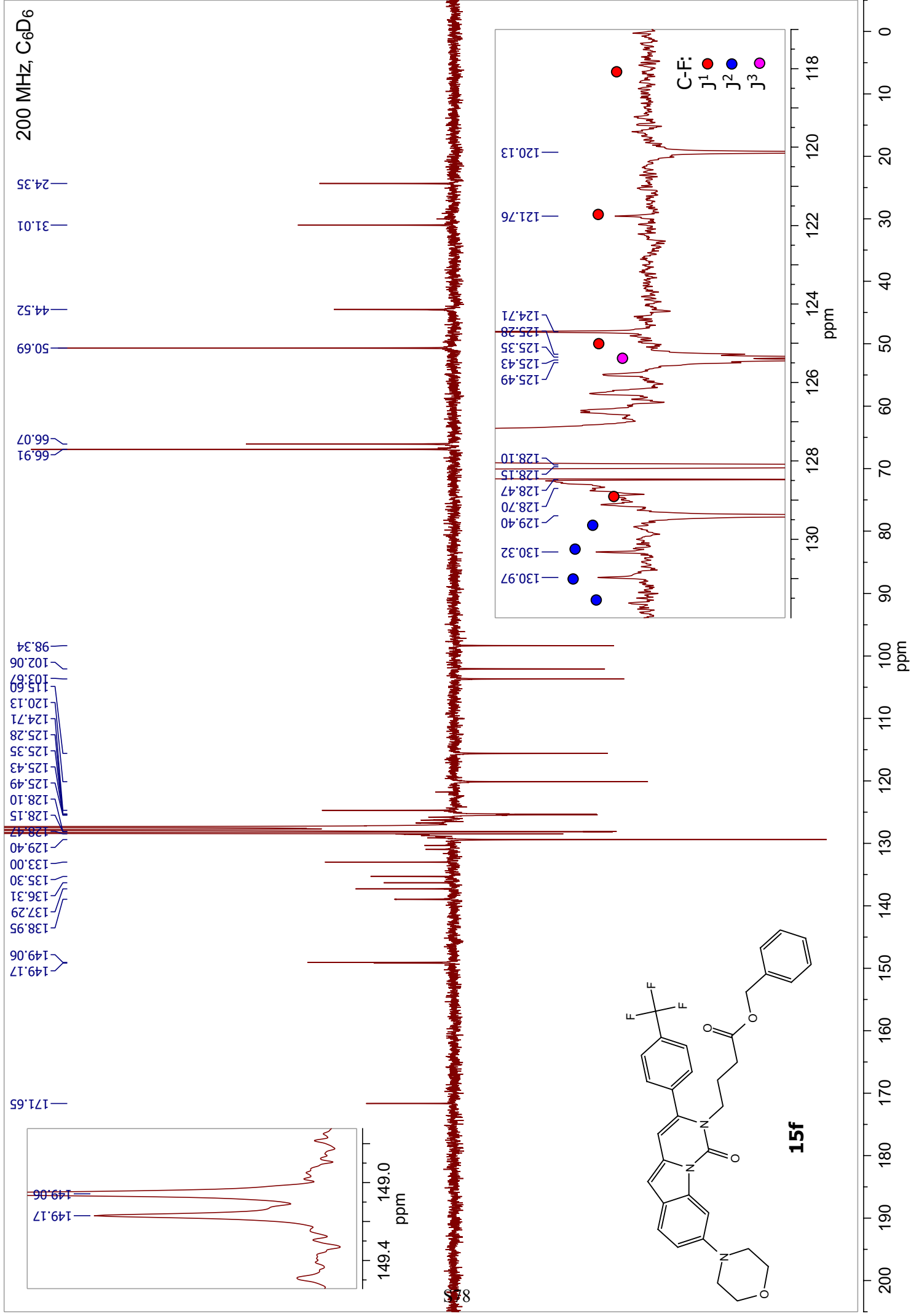
EtoAc

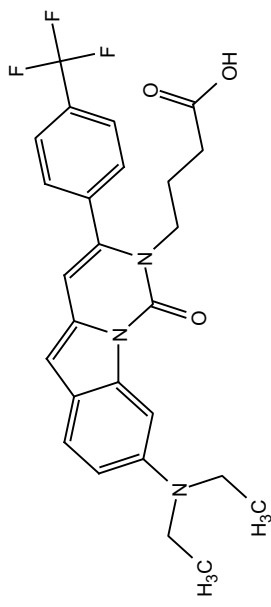
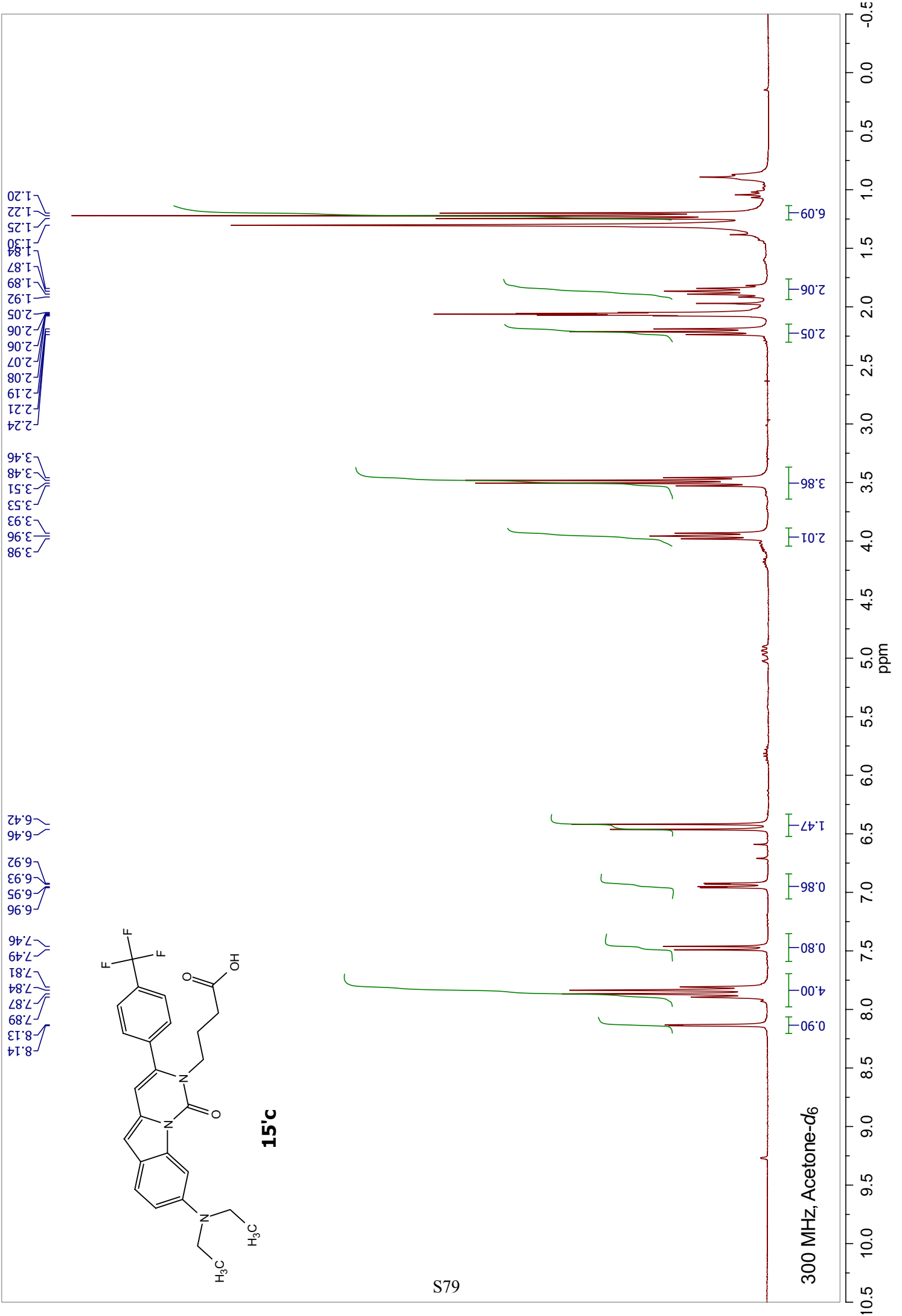
EtoAc

EtoAc

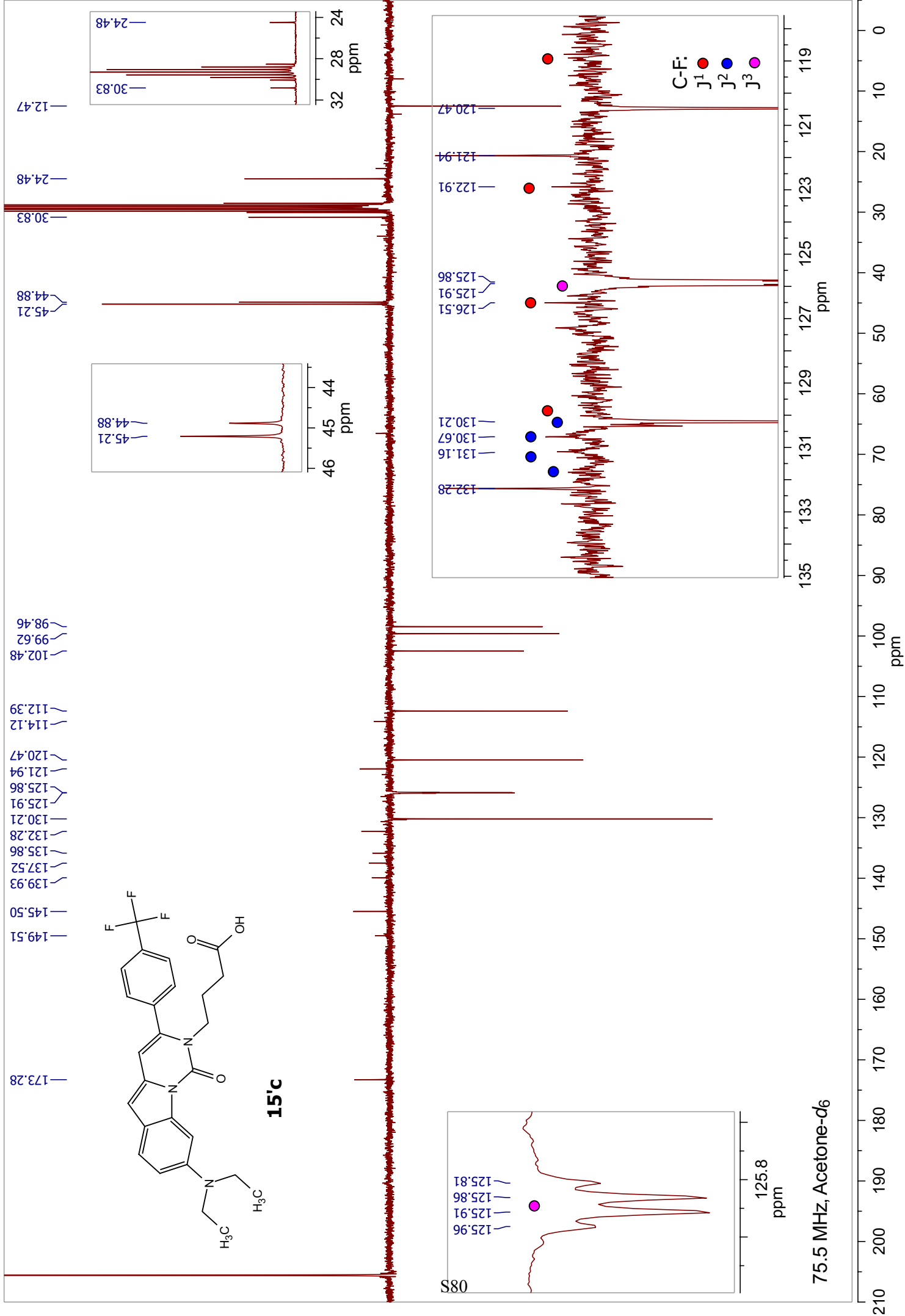
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5  
ppm

2.83  
2.31  
6.68  
2.16  
1.00  
1.01  
2.33  
5.90  
4.94  
2.46  
1.12  
1.03



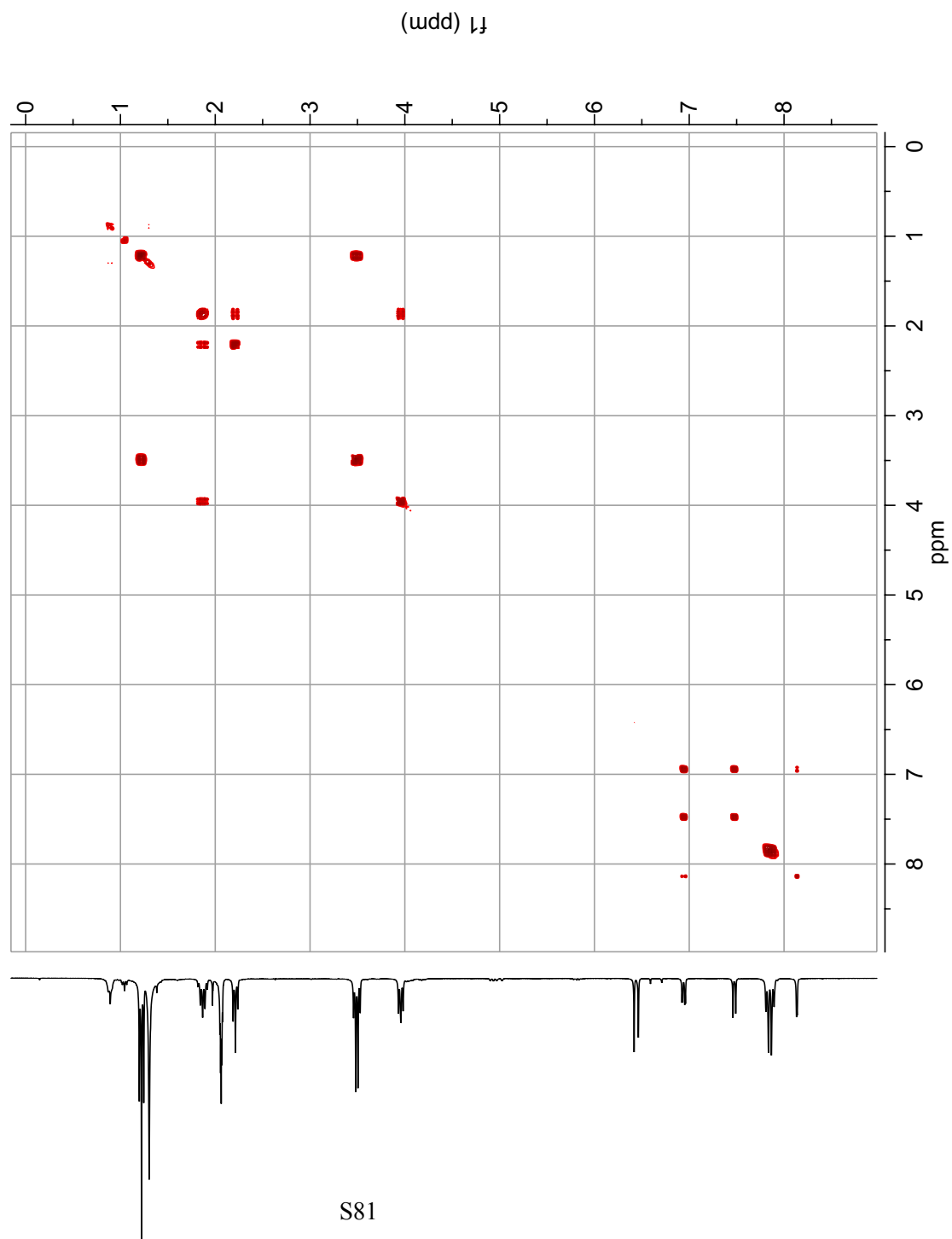
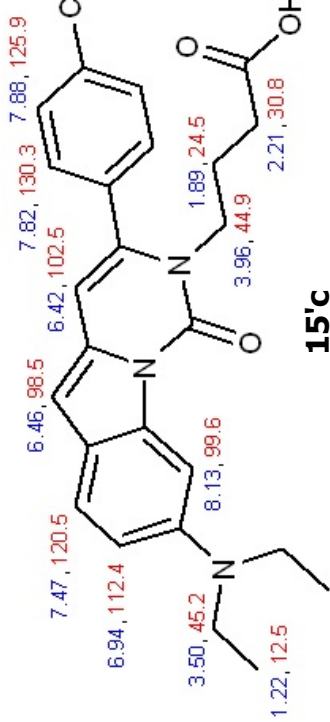


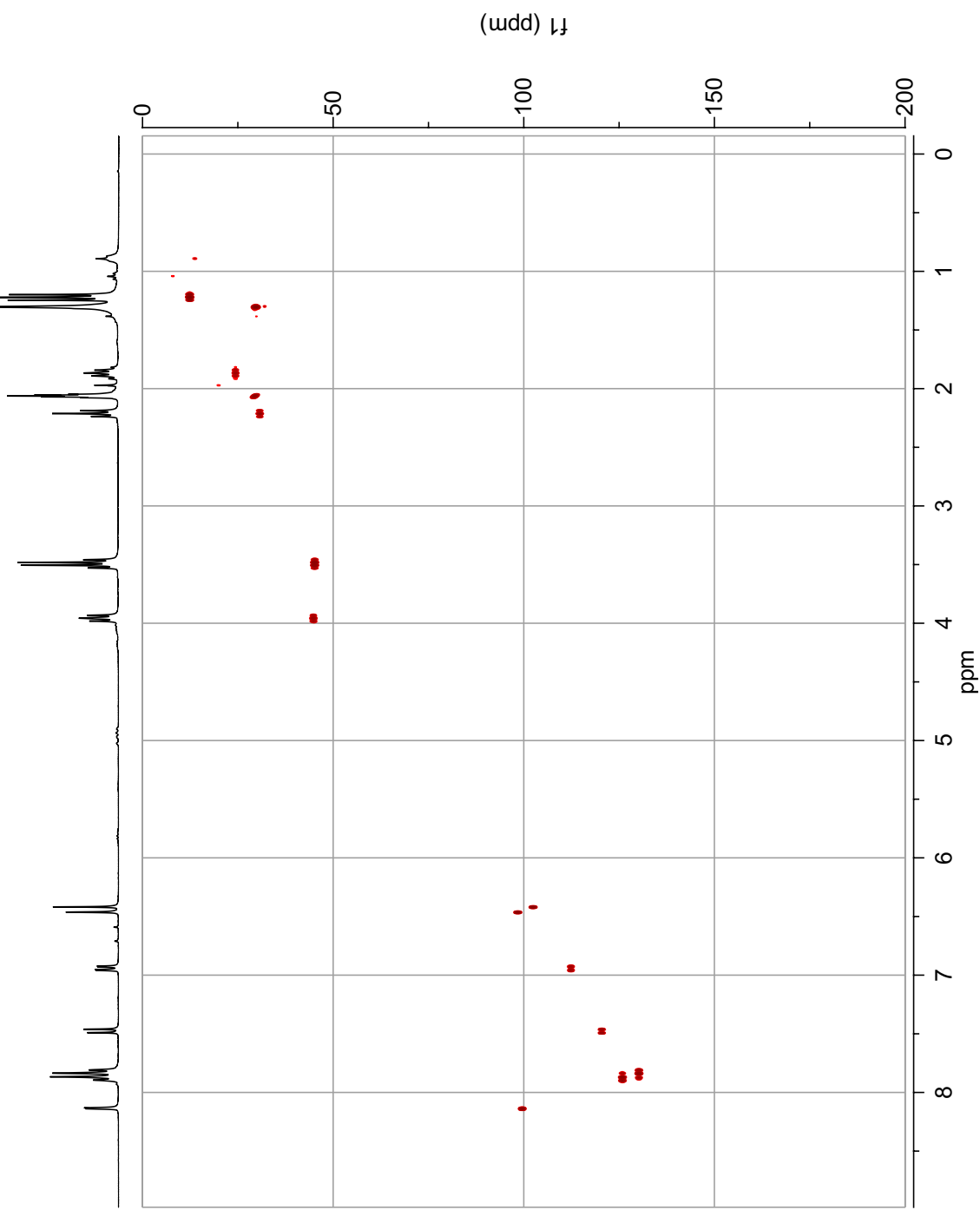
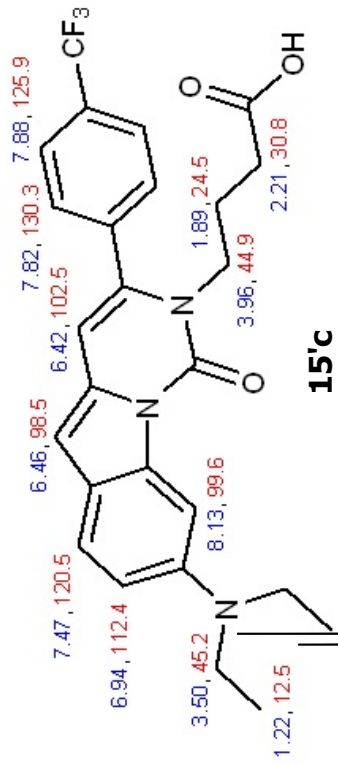
15c

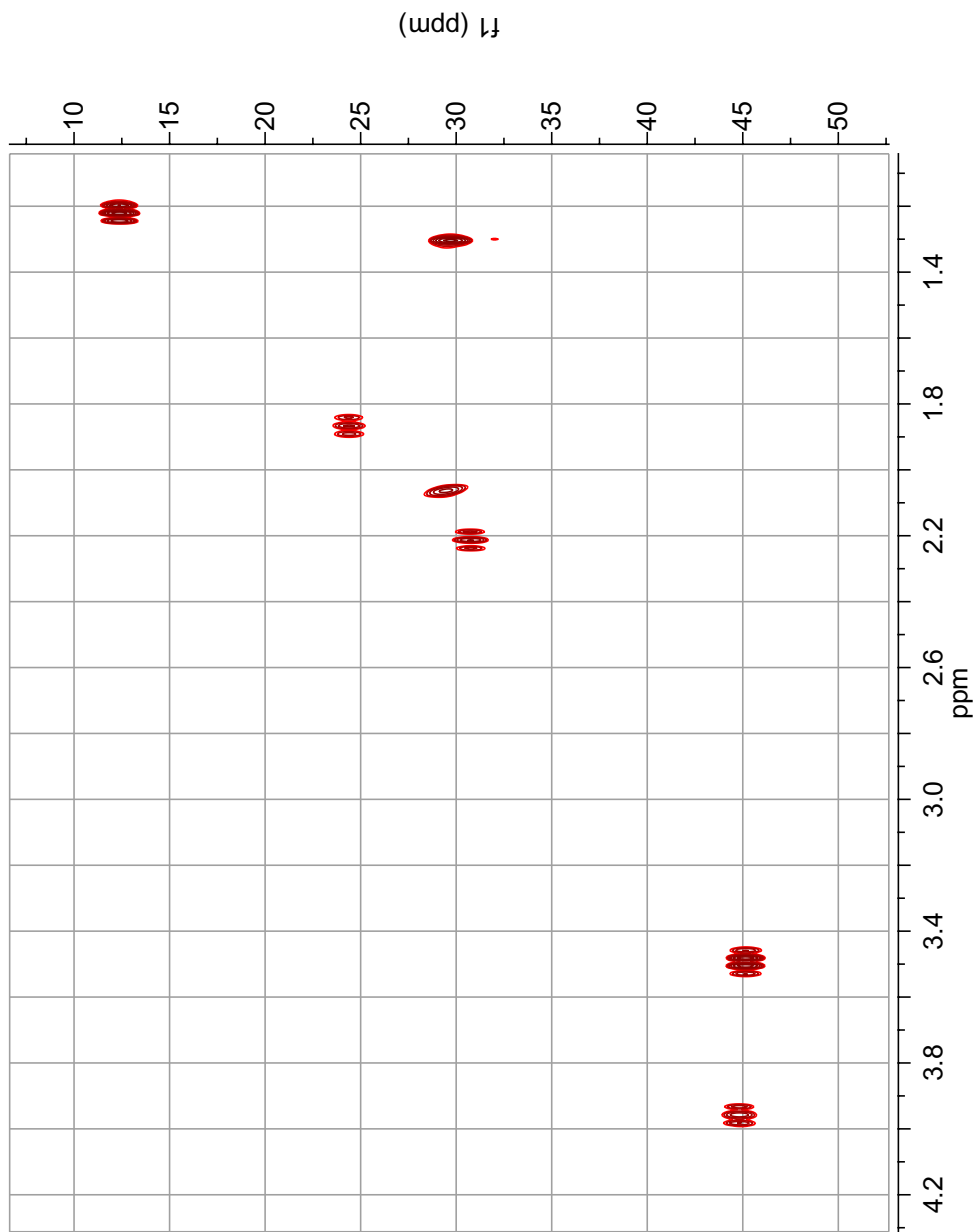
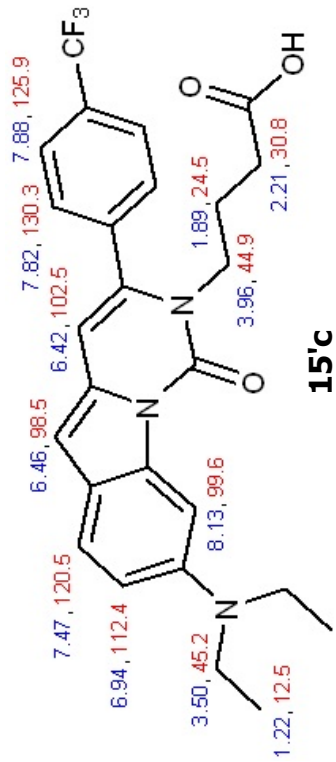




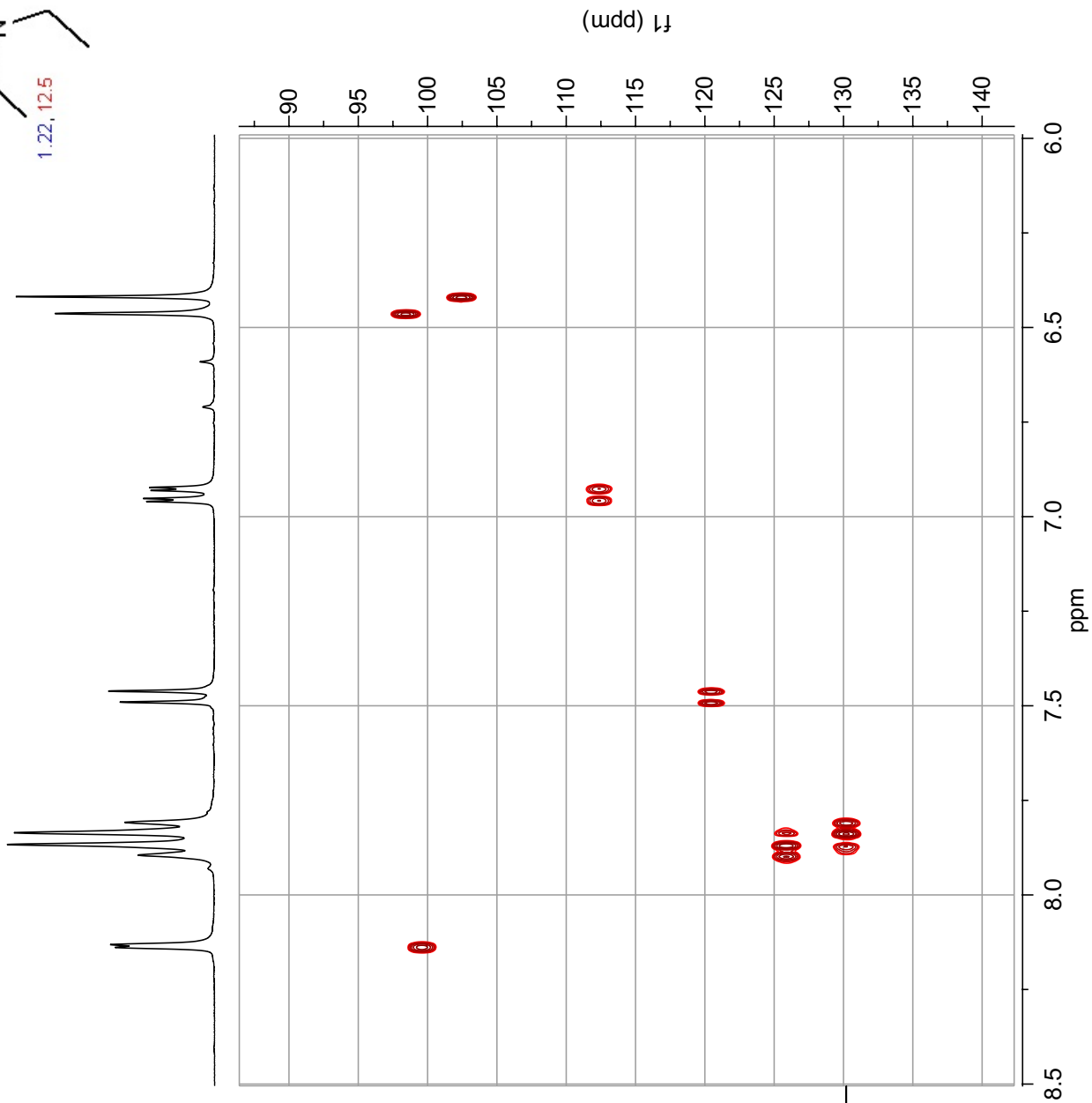
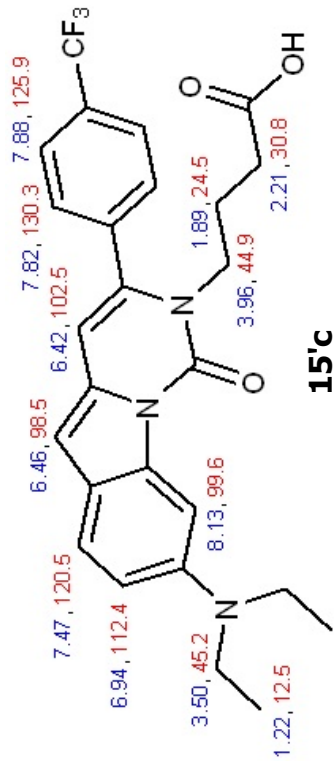
COSY, acetone-*d*<sub>6</sub>



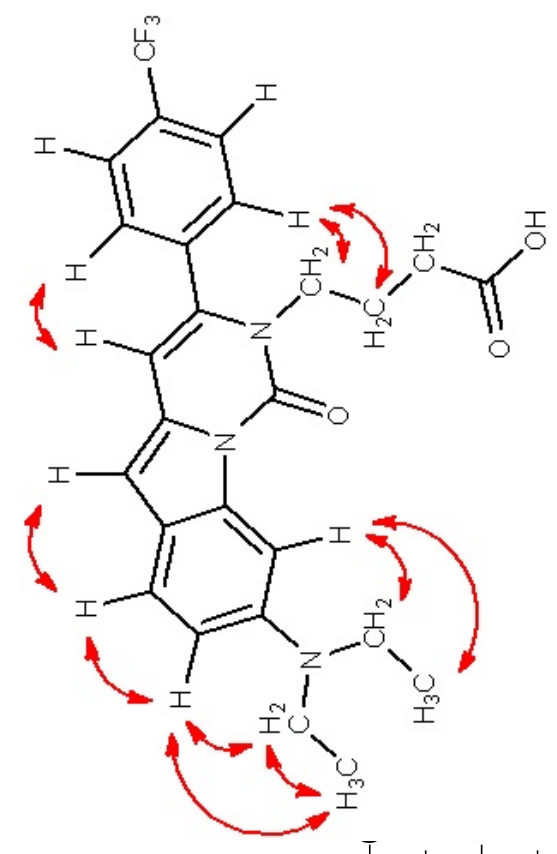




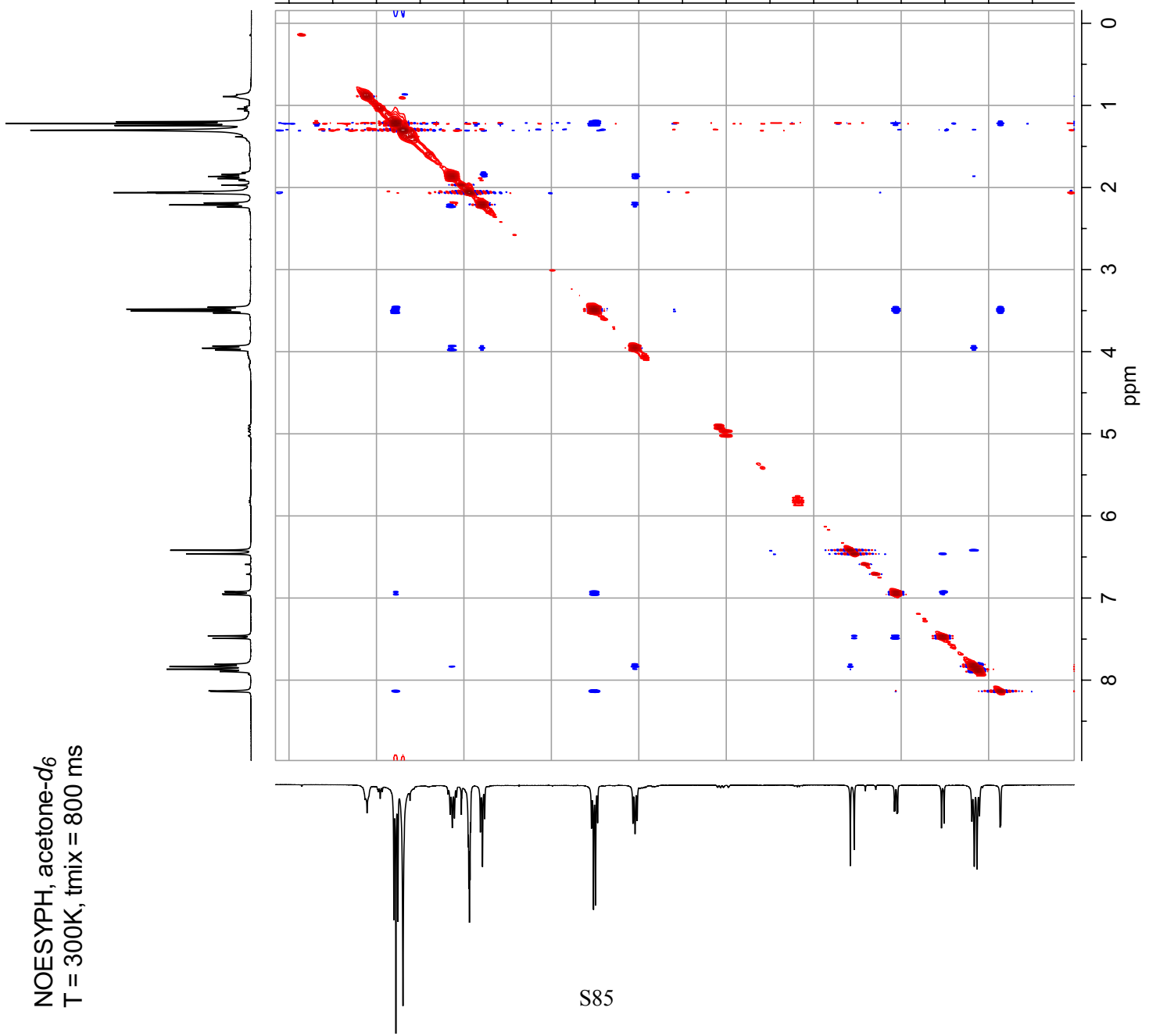
HSQC, acetone-*d*<sub>6</sub>



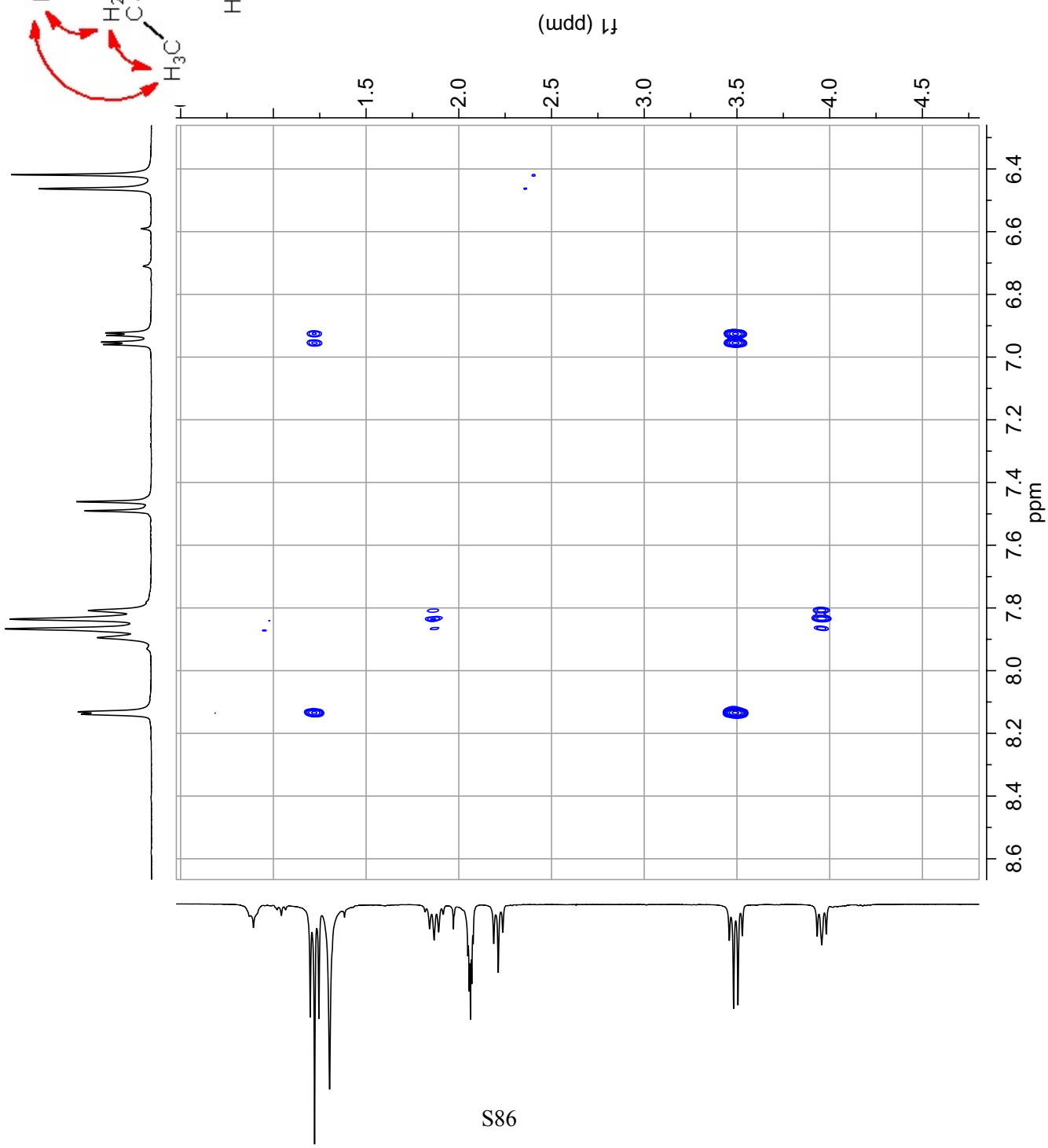
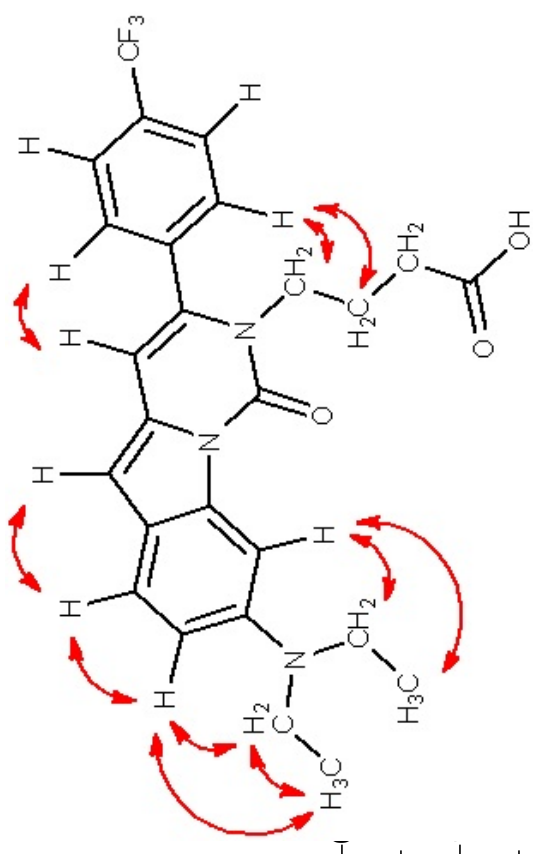
NOESYPH, acetone- $d_6$   
T = 300K, t<sub>mix</sub> = 800 ms



15°C



NOESYPH, acetone- $d_6$   
T = 300K, t<sub>mix</sub> = 800 ms



NOESYPH, acetone- $d_6$   
T = 300K, t<sub>mix</sub> = 800 ms

