Novel chemoenzymatic oxidation of amines into oximes based on hydrolase-catalyzed peracid formation

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SUPPORTING INFORMATION (page 1 of 67 pages)

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1. Structures of oximes synthesized in this study

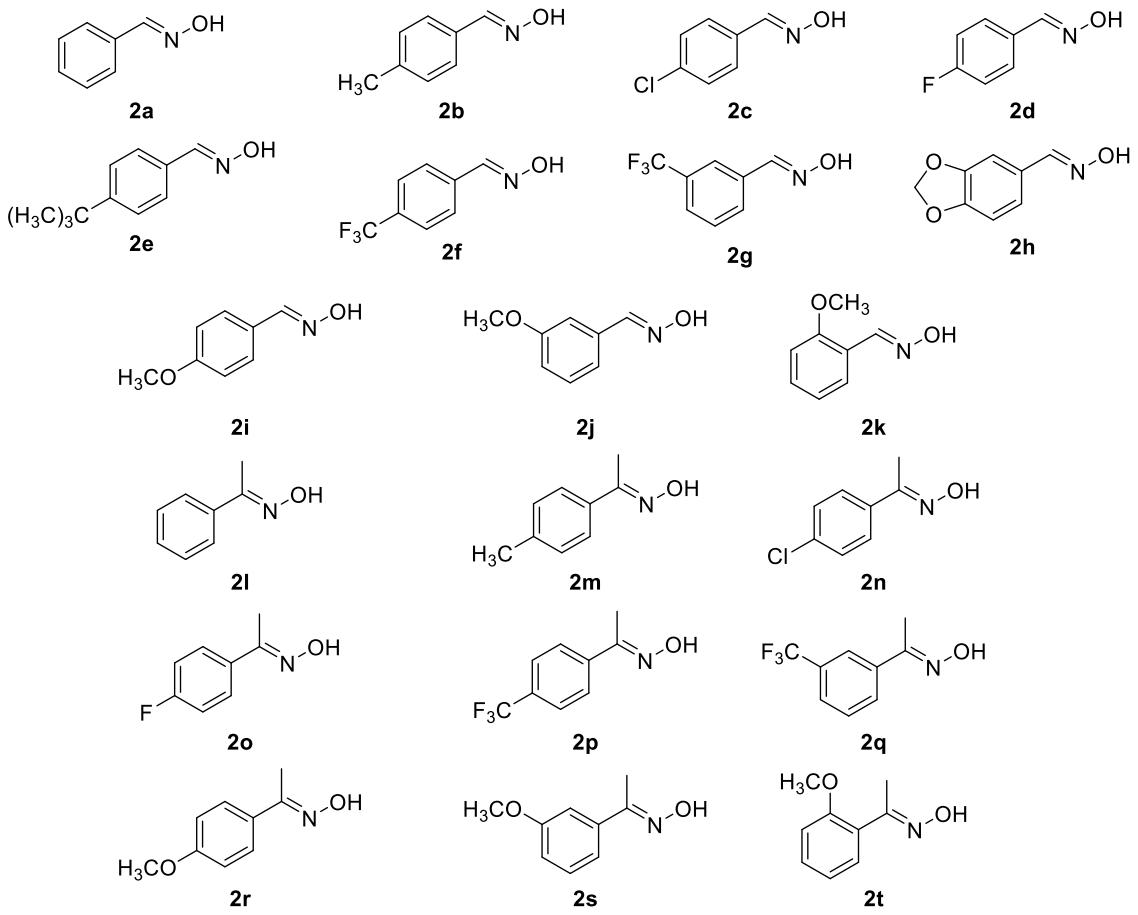


Figure S1. Oximes **2a-t** obtained in this study starting from the corresponding benzylamines (**1a-t**) through a chemoenzymatic oxidative strategy using CAL-B.

2. **GC analyses**

Gas chromatography (GC) analyses were performed on a Hewlett Packard 6890 Series chromatograph equipped with flame ionization detector (FID). A HP-1 column (30 m × 0,32 mm × 0.25 μm) was used. The temperature program was as follows: 90 ºC for 3 min, slope 10 ºC/min until 180 ºC, and then slope 40 ºC/min until 300 ºC.

Table S1. Retention times in GC analyses for starting benzylamines **1a-t** and synthesized oximes **2a-t**.

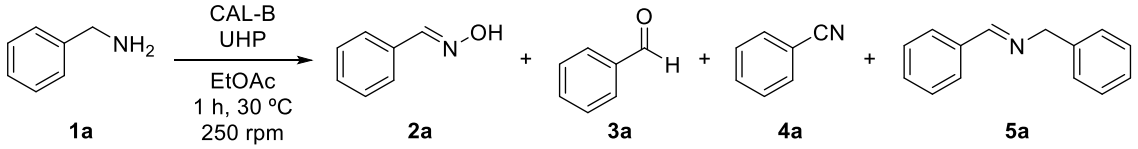
Compound	Amine 1a-t (min)	Oxime 2a-t (min)
a	2.7	4.8
b	3.8	5.2
c	5.0	7.3
d	2.7	4.7
e	6.9	9.3
f	3.0	5.1
g	3.0	5.2
h	6.0	9.6
i	5.7	8.2
j	5.4	8.1
k	5.4	8.2
l	4.7	7.0
m	4.2	7.8
n	5.4	8.8
o	3.1	6.2
p	3.4	6.6
q	3.3	6.5
r	6.2	8.7
s	6.1	9.5
t	5.7	8.6

3. Optimization of the reaction conditions for the oxidation of benzylamine (1a) into (*E*)-benzaldehyde oxime (2a)

The study of the chemoenzymatic oxidative processes was performed using GC analysis as stated in sections 2 and 3 of the Supporting Information. Two independent chemoenzymatic systems were studied.

3.1. Using ethyl acetate (EtOAc) as both solvent and peracid precursor

Table S2. Chemoenzymatic oxidation of benzylamine (**1a**) using EtOAc, the UHP complex as and CAL-B after 1 h at 30 ºC and 250 rpm.



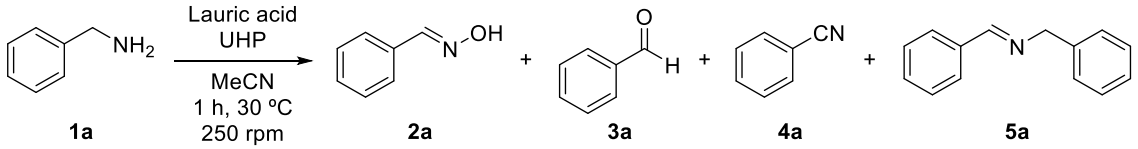
Entry	[**1a**] (mM)	UHP (eq)	CAL-B[a]	**2a** (%)[b]	**3a** (%)[b]	**4a** (%)[b]	**5a** (%)[b]
1	250	1.1	50	67	<1	<1	8
2	**250**	**2**	**50**	**90**	**<1**	**<1**	**8**
3	250	2	100	90	<1	<1	8
4	**250**	**2**	**25**	**90**	**<1**	**<1**	**8**
5	250	2	10	70	<1	<1	8
6	**500**	**2**	**25**	**88**	**<1**	**<1**	**8**
7	1000	2	25	57	<1	<1	8
8	2000	2	25	54	<1	<1	8

[a] Amount of CAL-B (weight in mg) per mmol of amine **1a**.

[b] Percentage of products calculated by GC analyses.

3.2. Using lauric acid as peracid precursor and acetonitrile (MeCN) as solvent

Table S3. Chemoenzymatic oxidation of benzylamine (**1a**, 125 mM) using lauric acid, the UHP complex as and CAL-B in acetonitrile after 1 h at 30 ºC and 250 rpm.



Entry	Lauric acid (eq)	UHP (eq)	CAL-B[a]	time (min)	**2a** (%)[b]	**3a** (%)[b]	**4a** (%)[b]	**5a** (%)[b]
1	1.1	1.1	50	120	88	<1	<1	9
2	0.5	1.1	50	360	68	<1	<1	6
3	1.1	1.1	10	360	78	<1	<1	6
4	1.1	0.5	50	360	72	<1	<1	5

[a] Amount of CAL-B (weight in mg) per mmol of amine **1a**.

[b] Percentage of products calculated by GC analyses.

4. Environmental assessment using the EATOS tool

E-factor calculations (Figures S2 and S3) were performed using the EATOS (v. 1.1) software tool. Both protocols were treated as proceeding to the corresponding conversions, hence all losses in yield apart from compounds **3a**, **4a**, and **5a** are accounted for as 'unknown by-products'. The work-up protocols have been taking into account for their comparison without the flash chromatography as it was assumed to be the same for both methodologies. The Excel file used for these calculations is also available as ESI material.

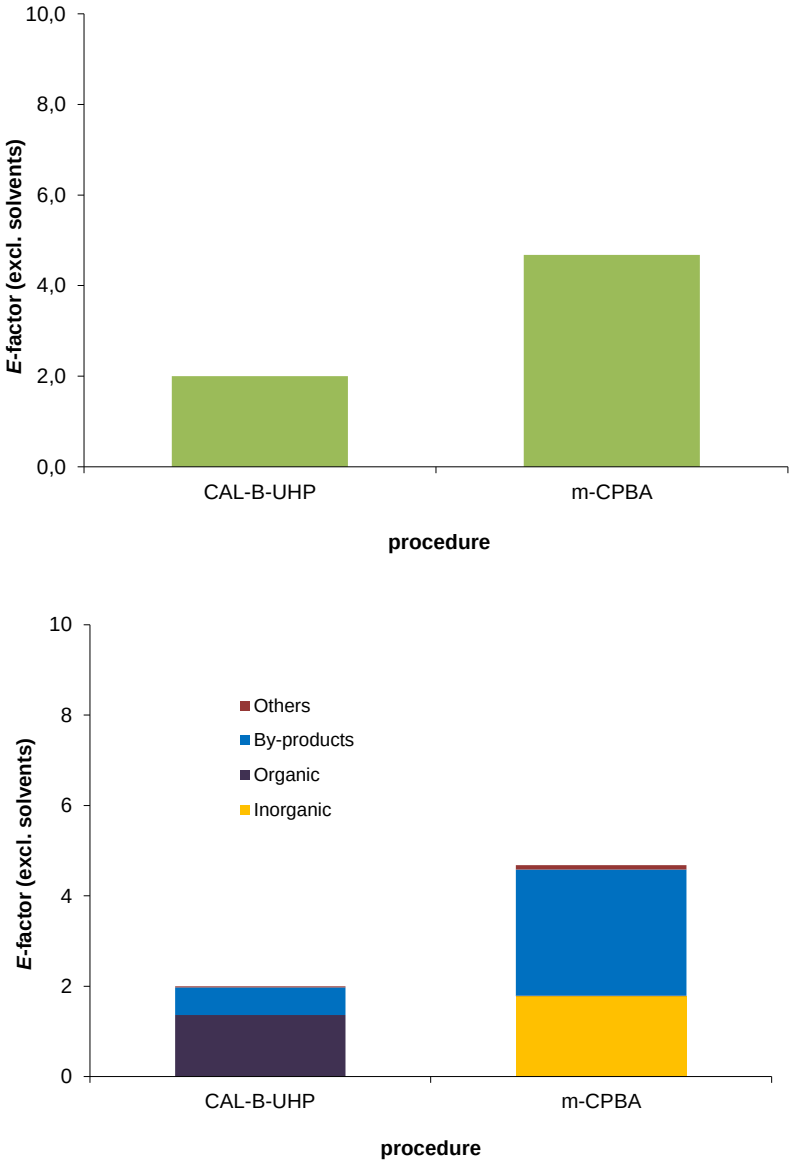


Figure S2. Contribution to *E*-factor (excluding solvents) for each procedure to oxidise benzylamine (**1a**) to (*E*)-benzaldehyde oxime (**2a**).

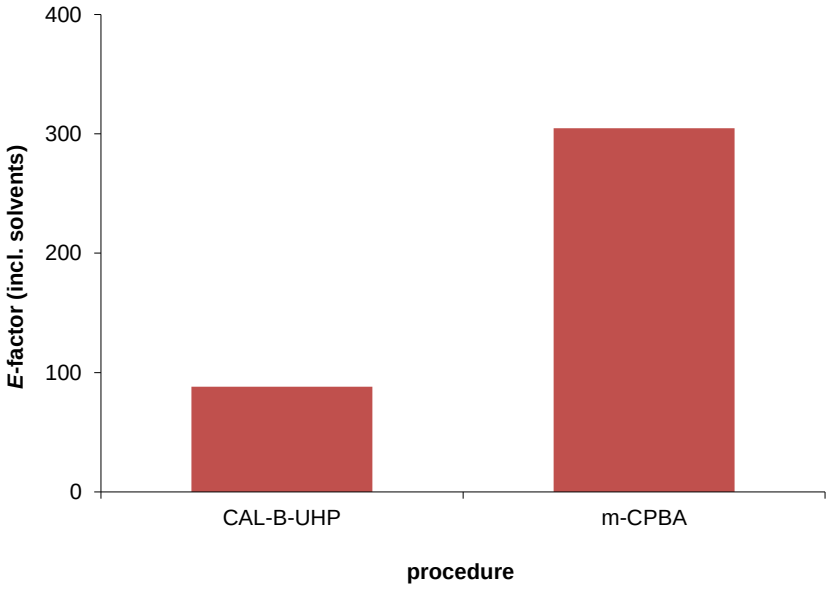
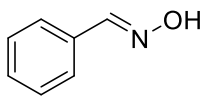


Figure S3. *E*-factor (including solvents) for each procedure to oxidise benzylamine (**1a**) to (*E*)-benzaldehyde oxime (**2a**).

5. NMR spectra



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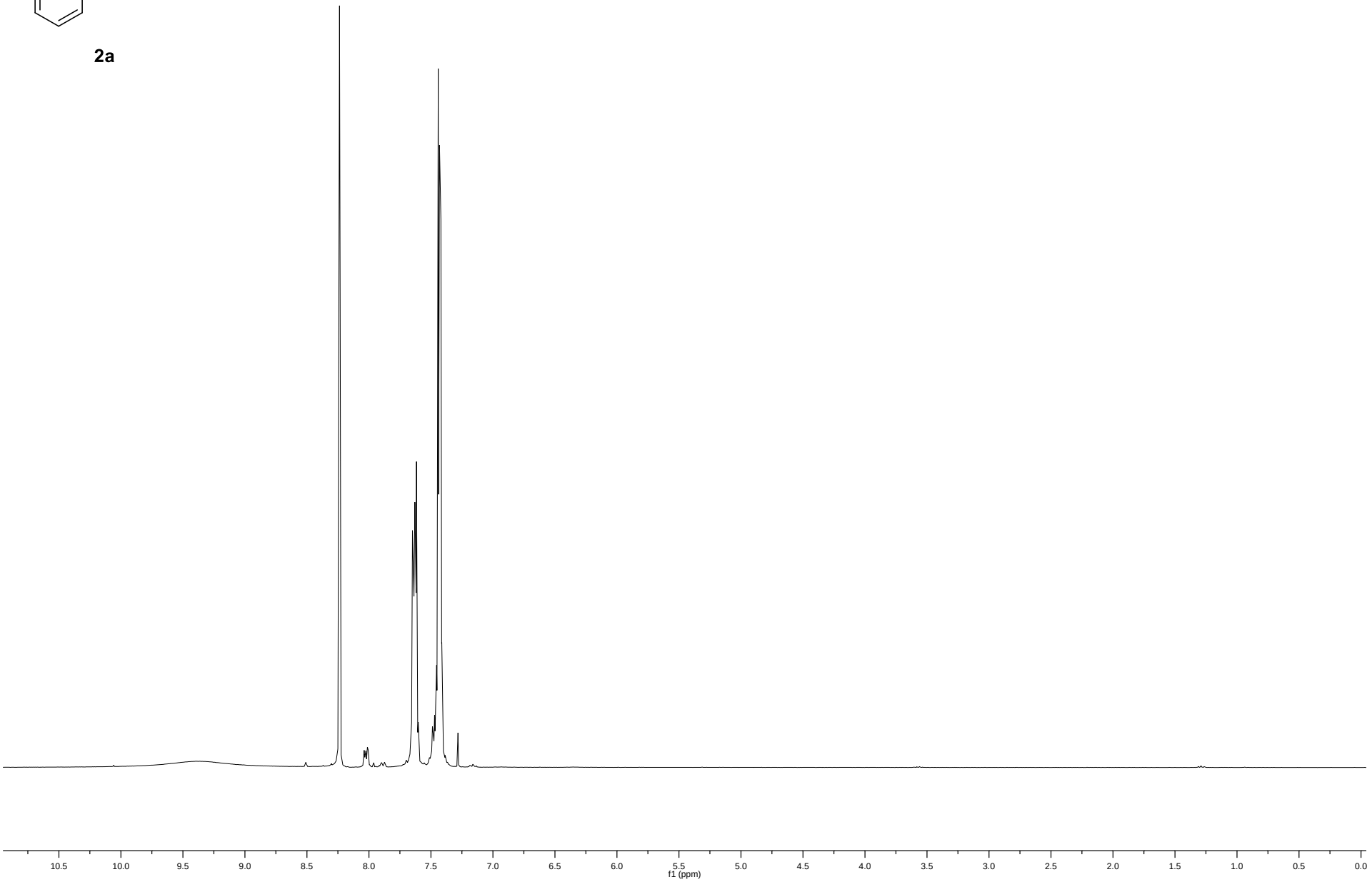

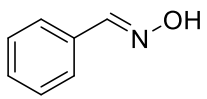
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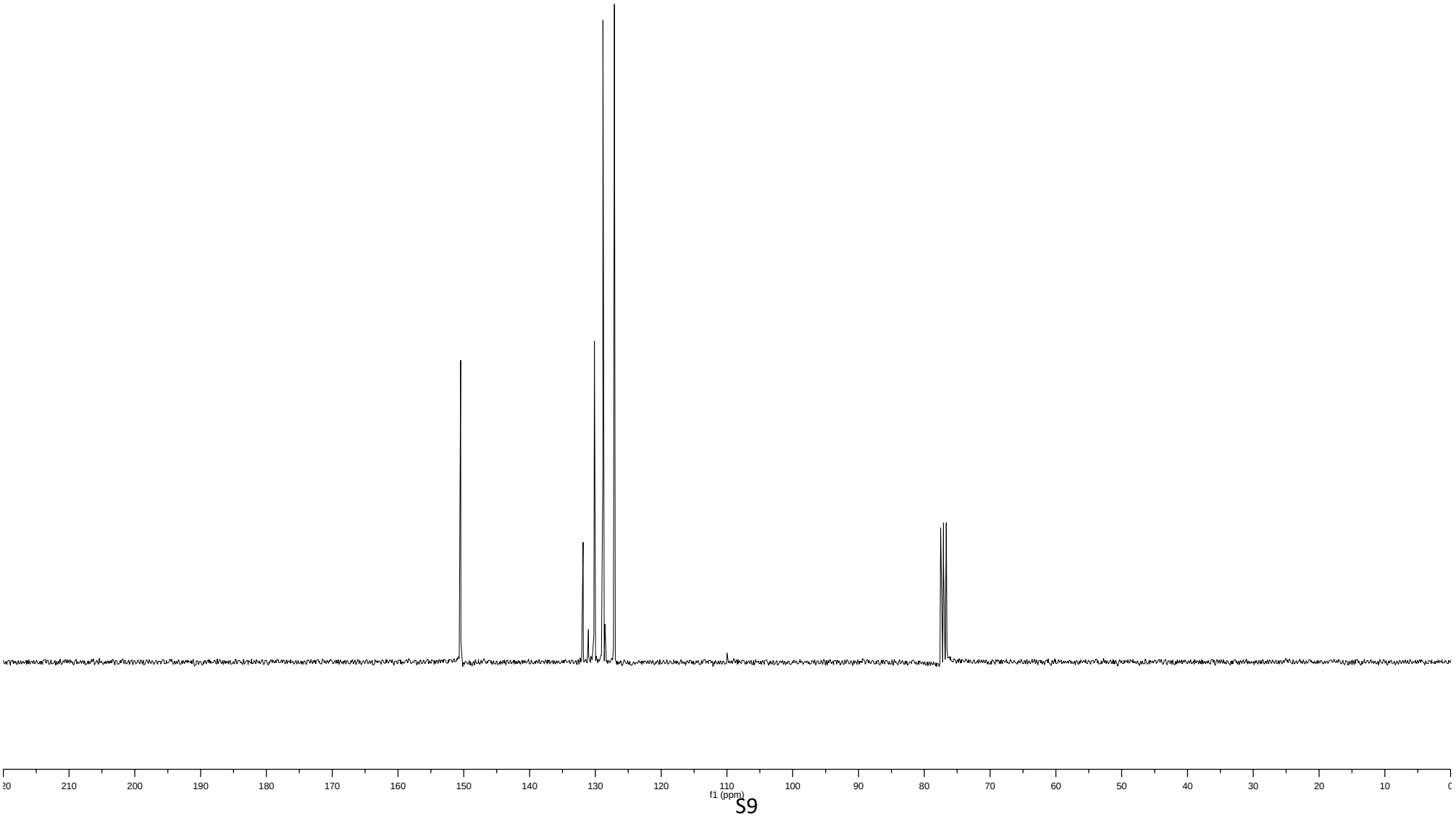
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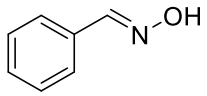

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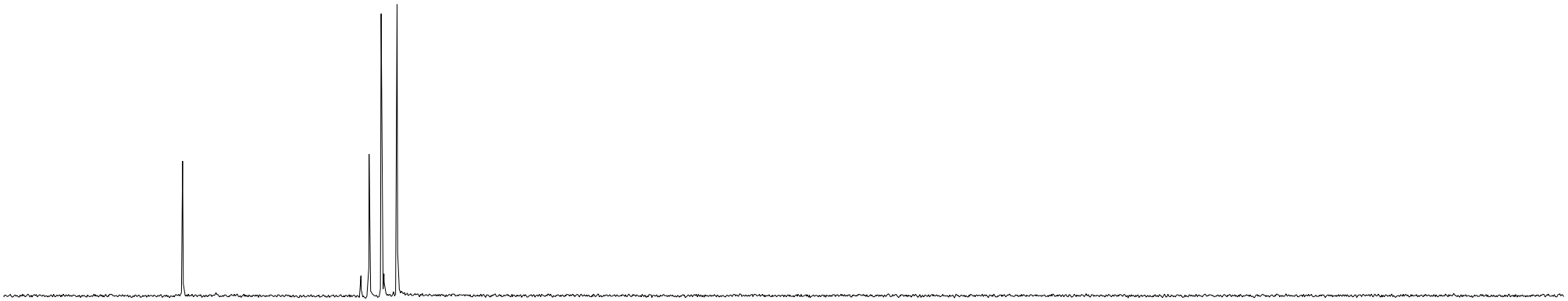

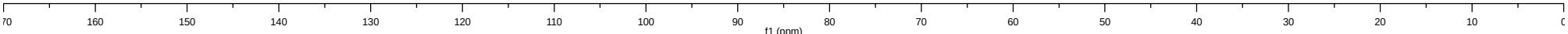

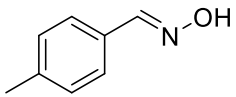

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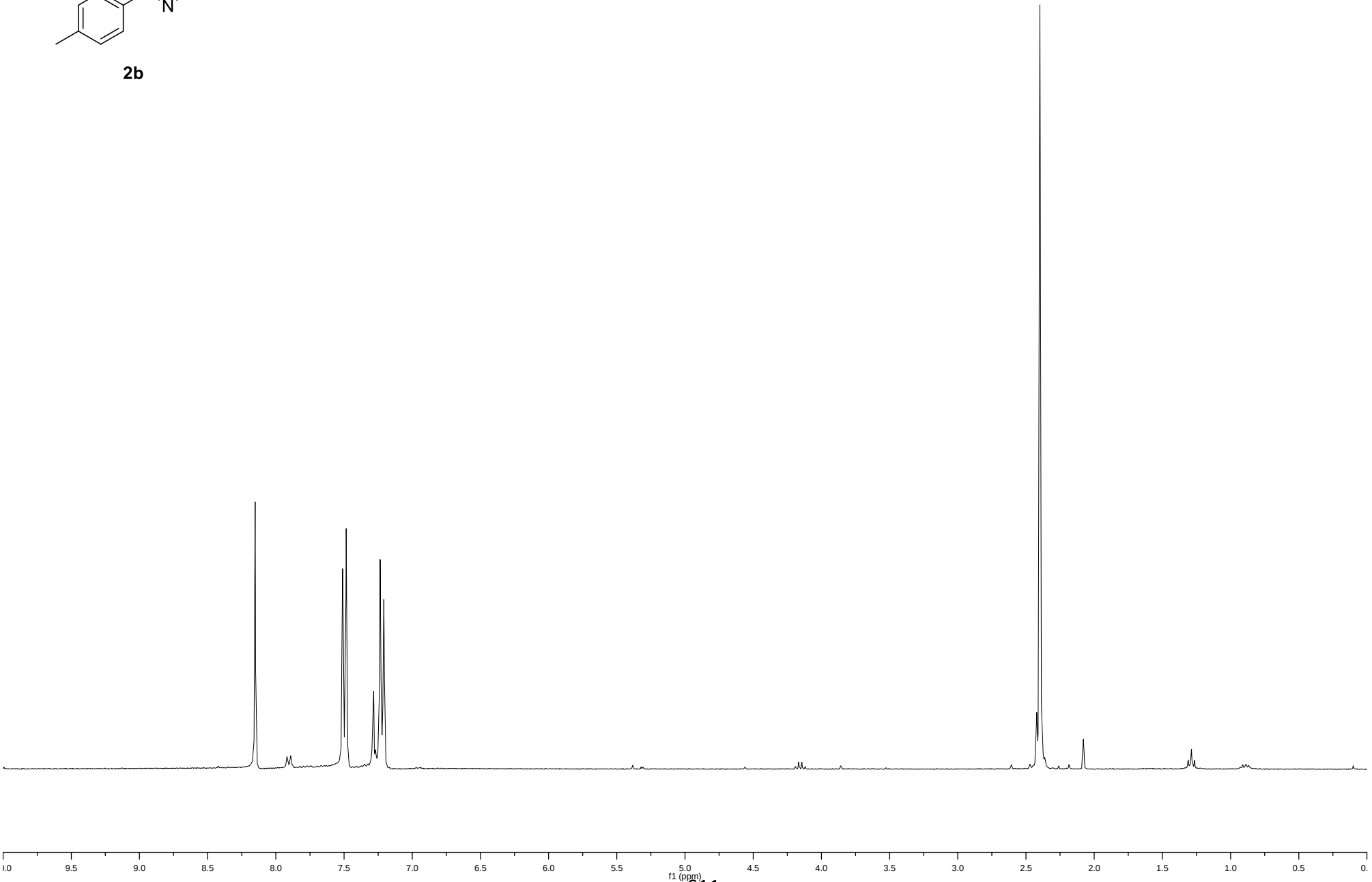

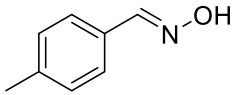
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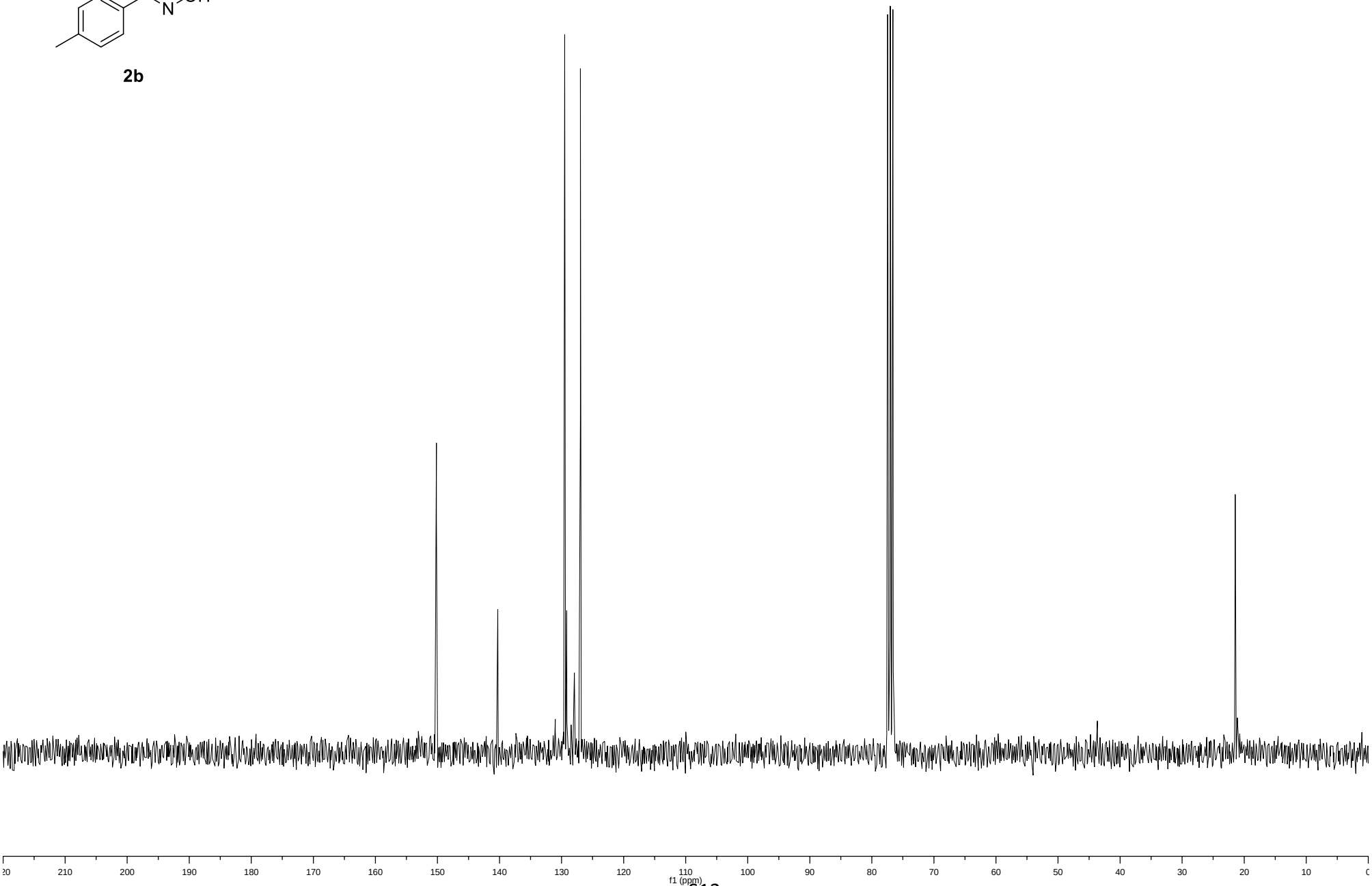
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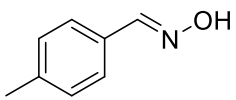
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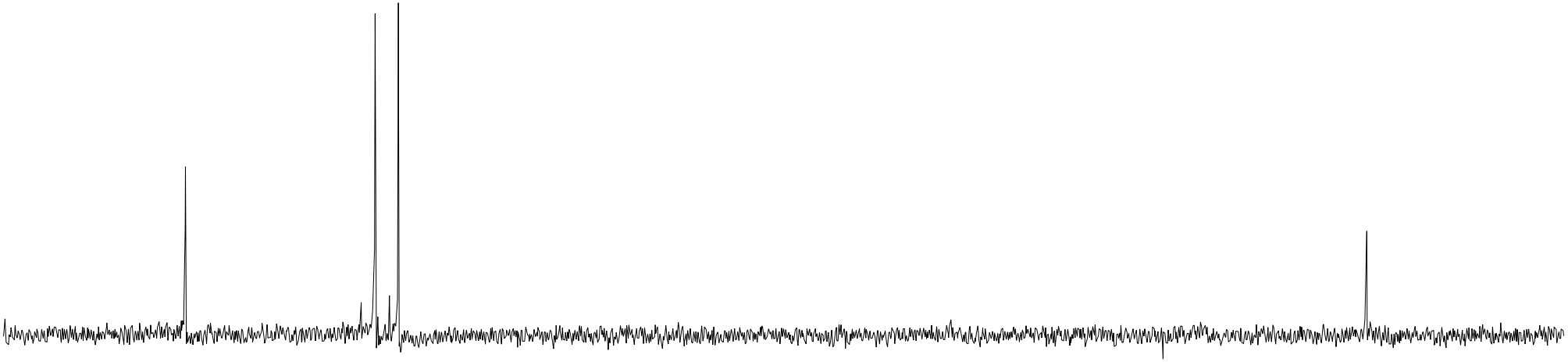

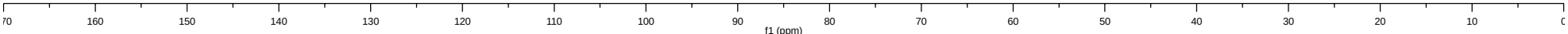
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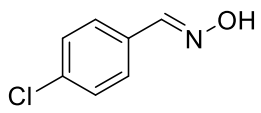

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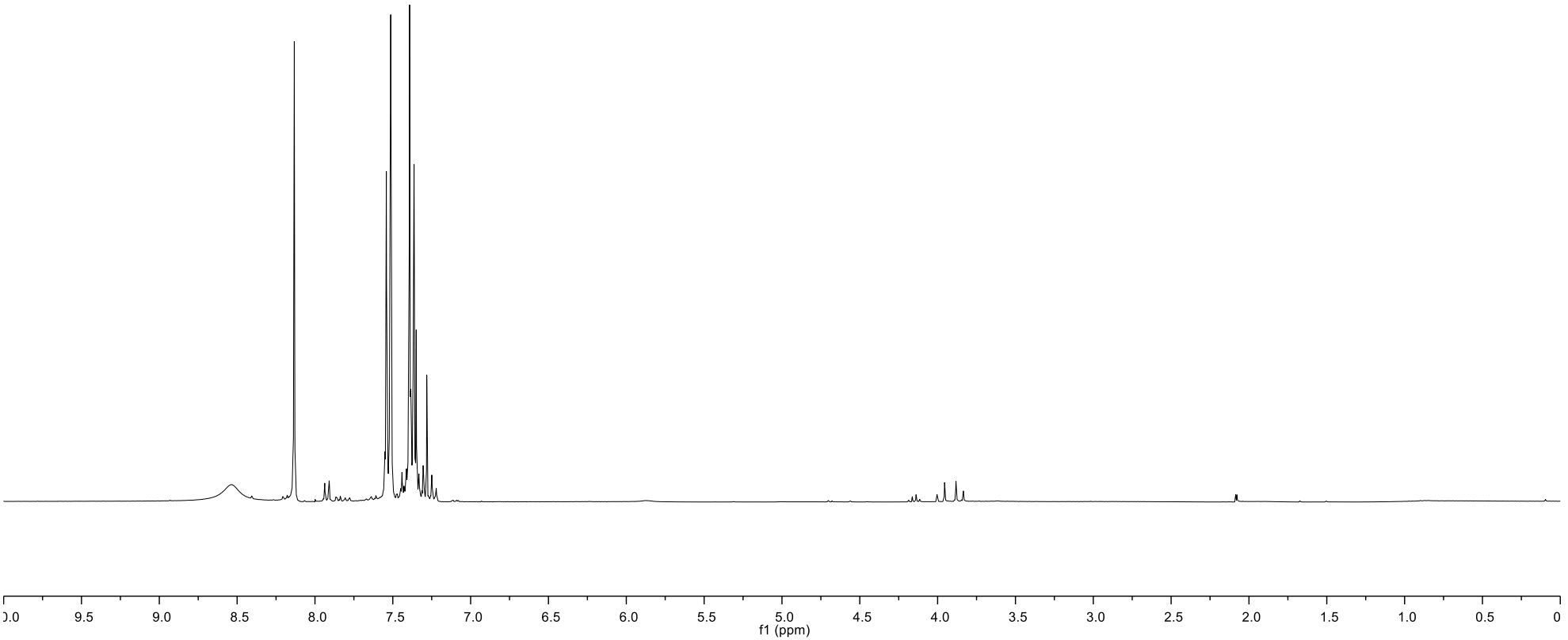

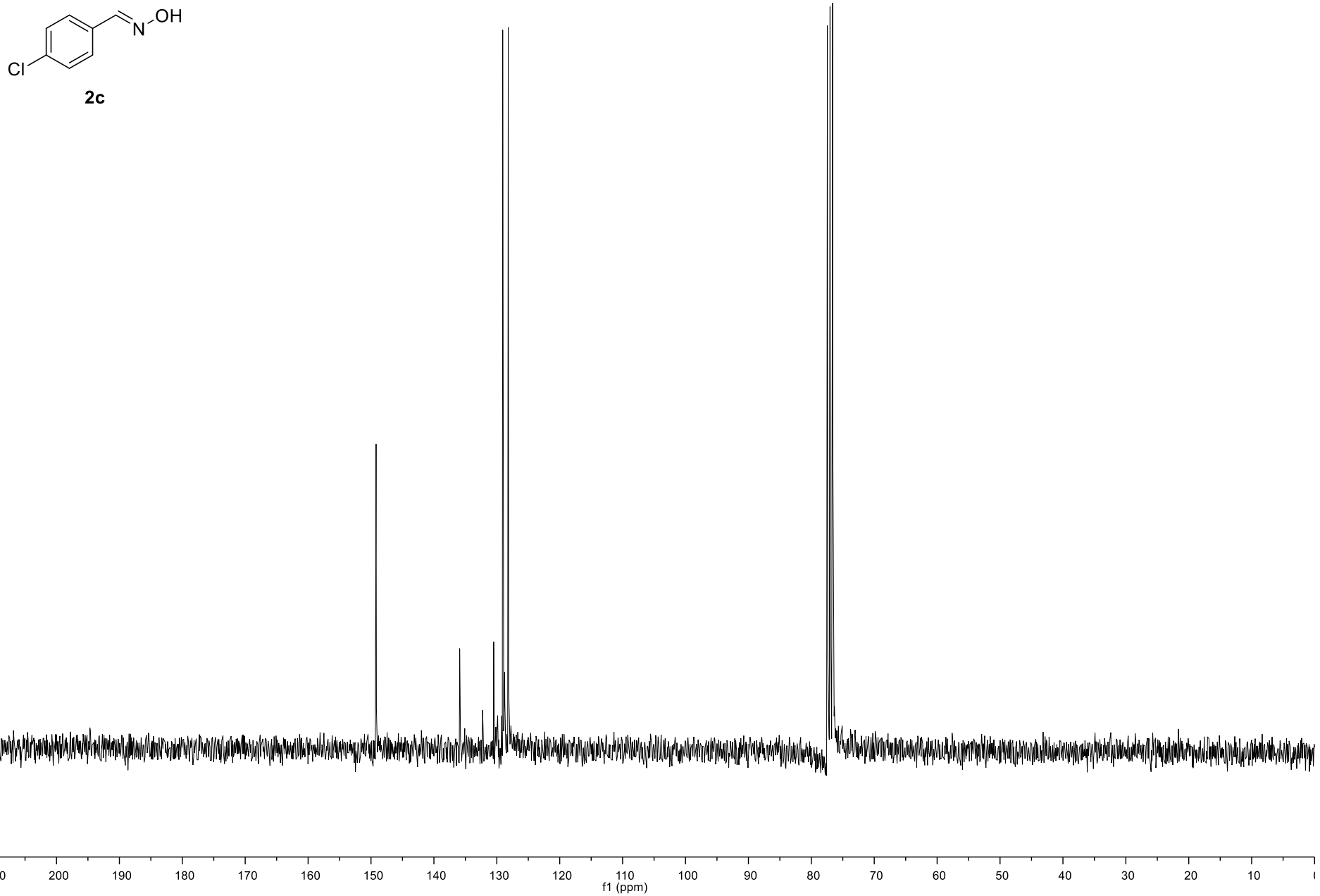
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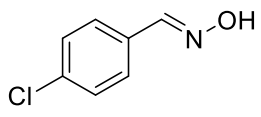
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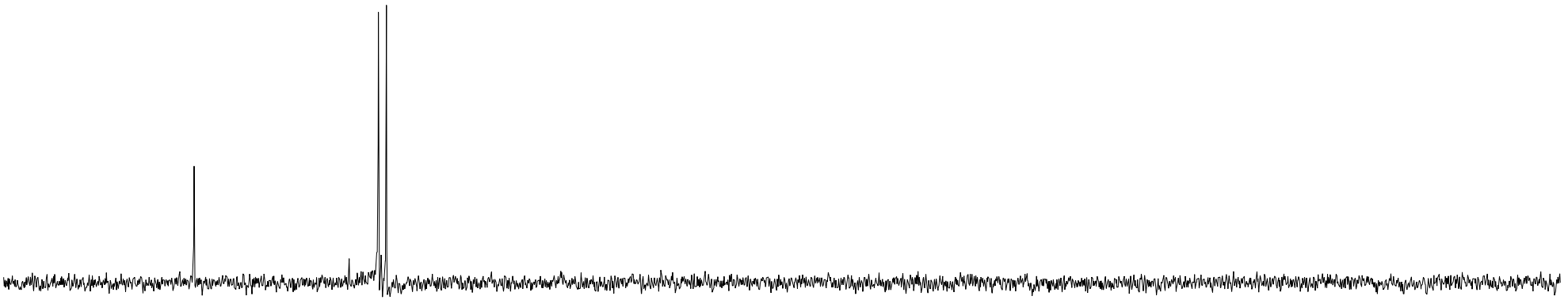

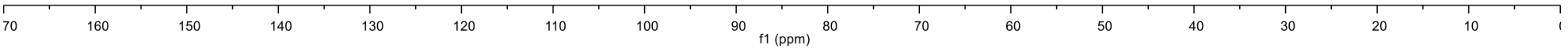
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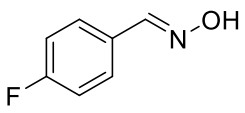

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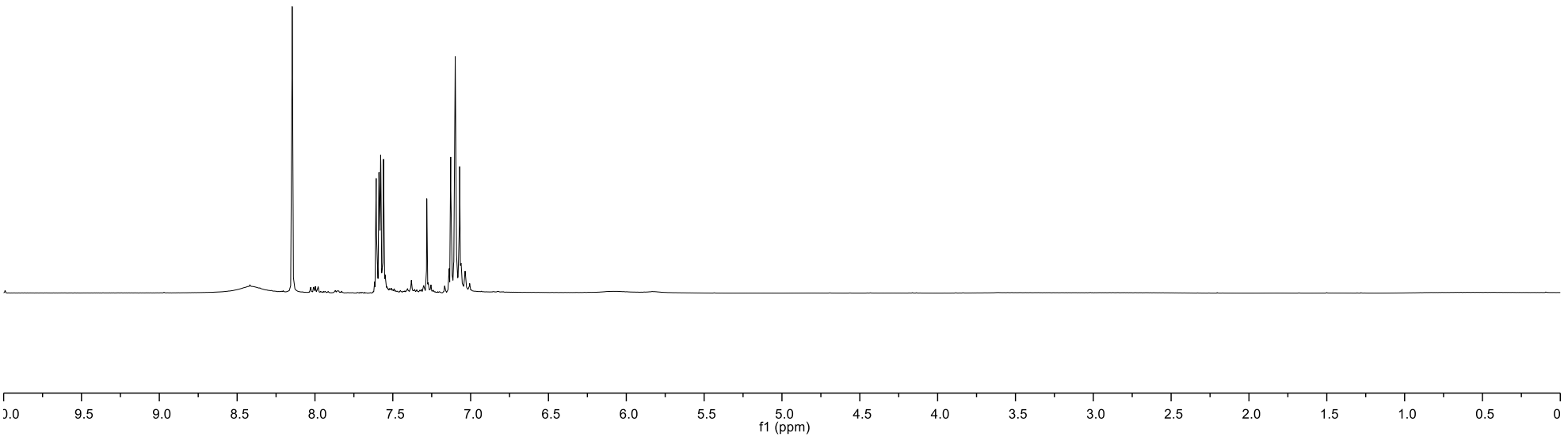

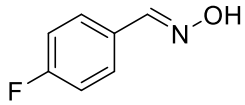
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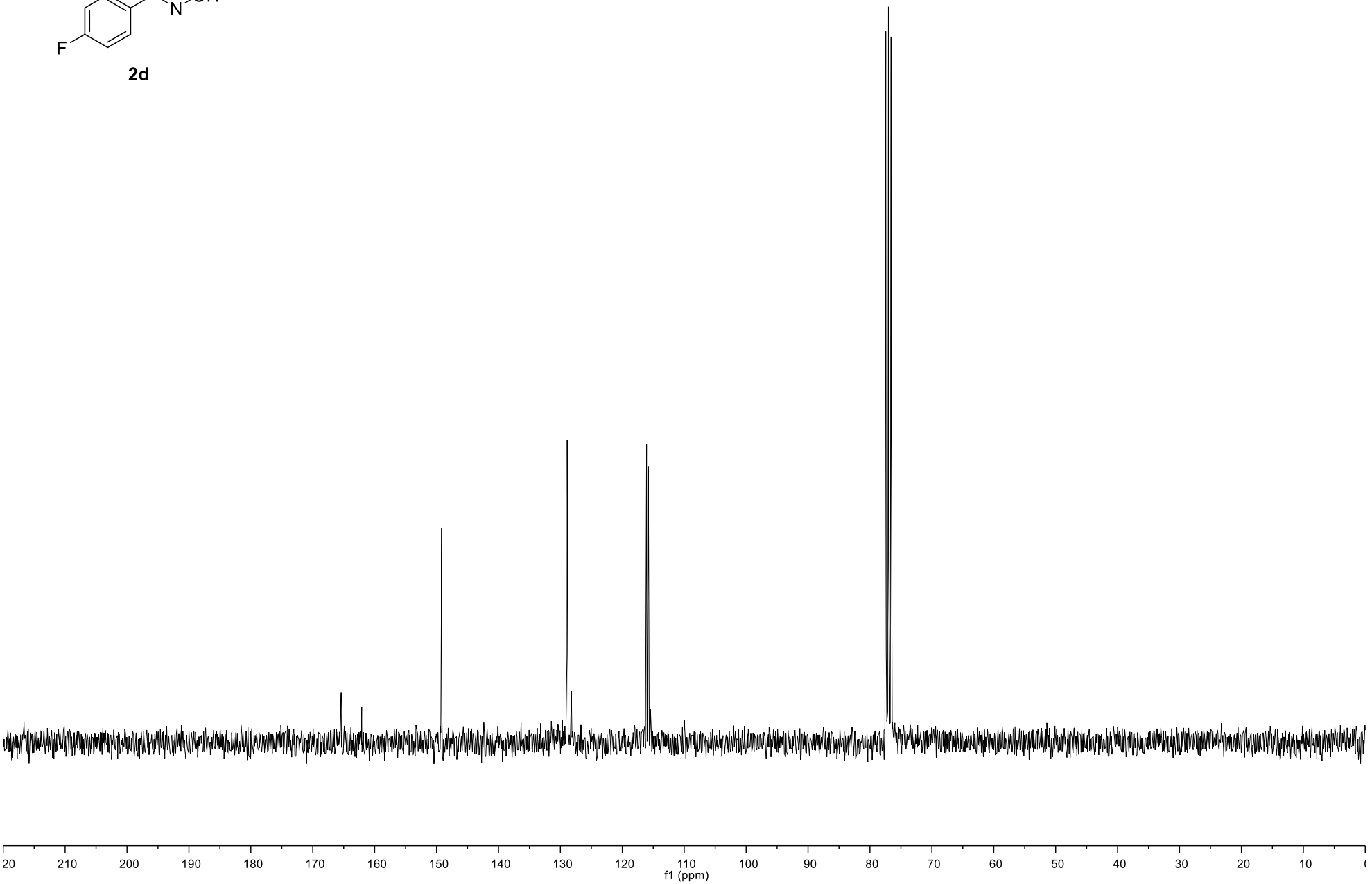
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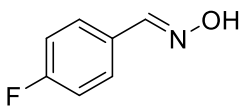
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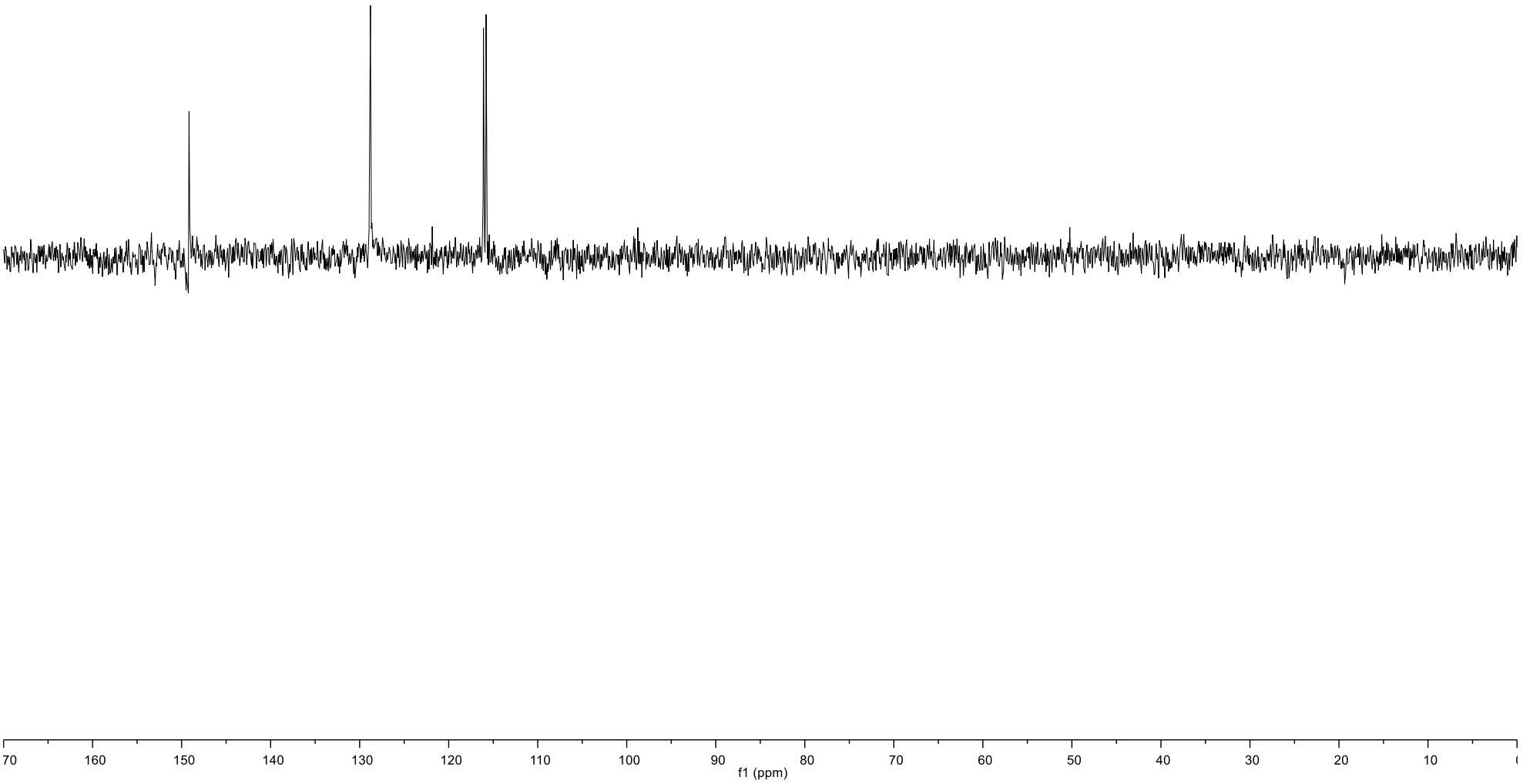
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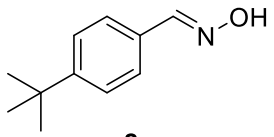

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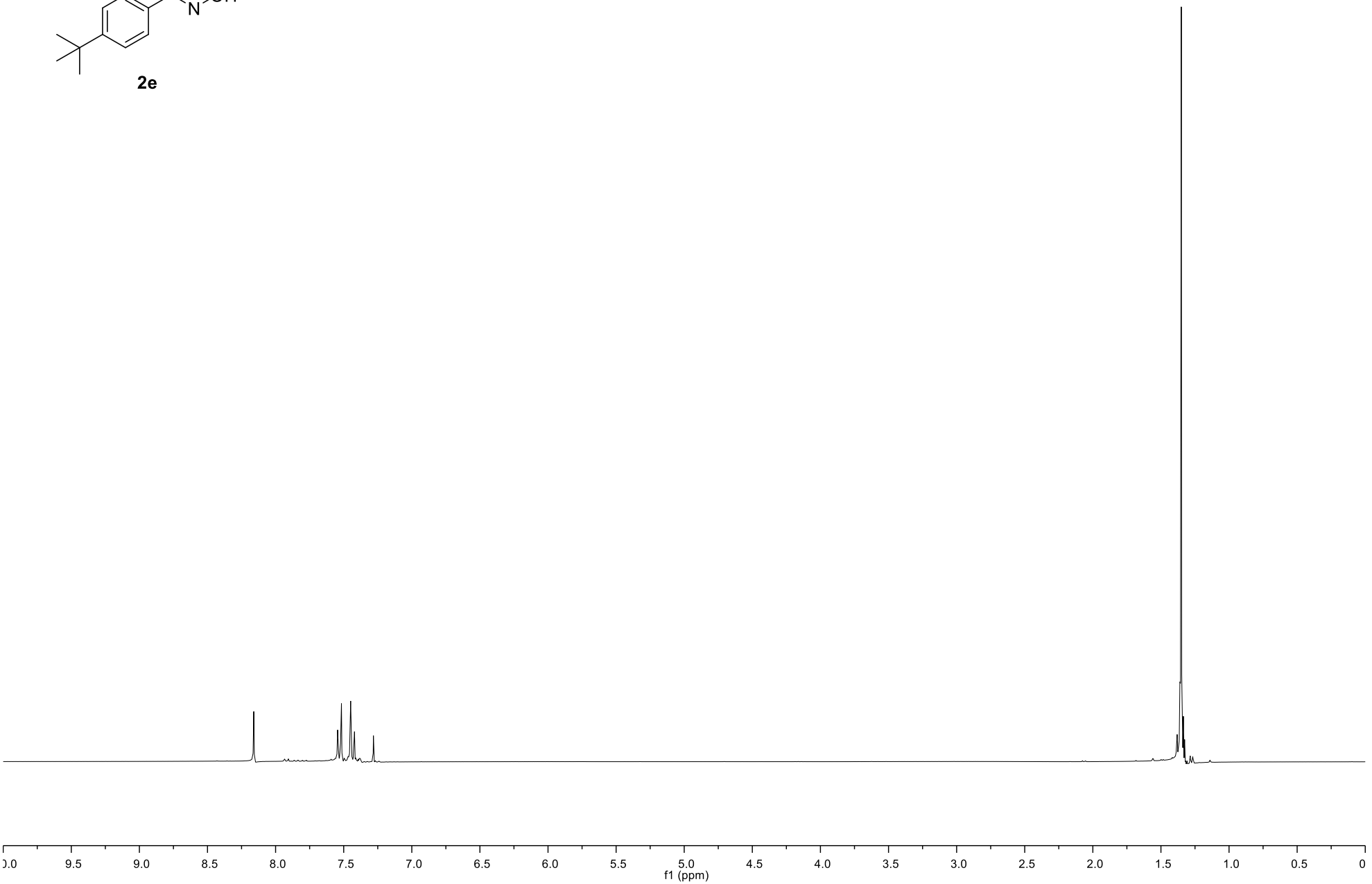

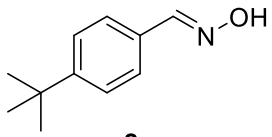
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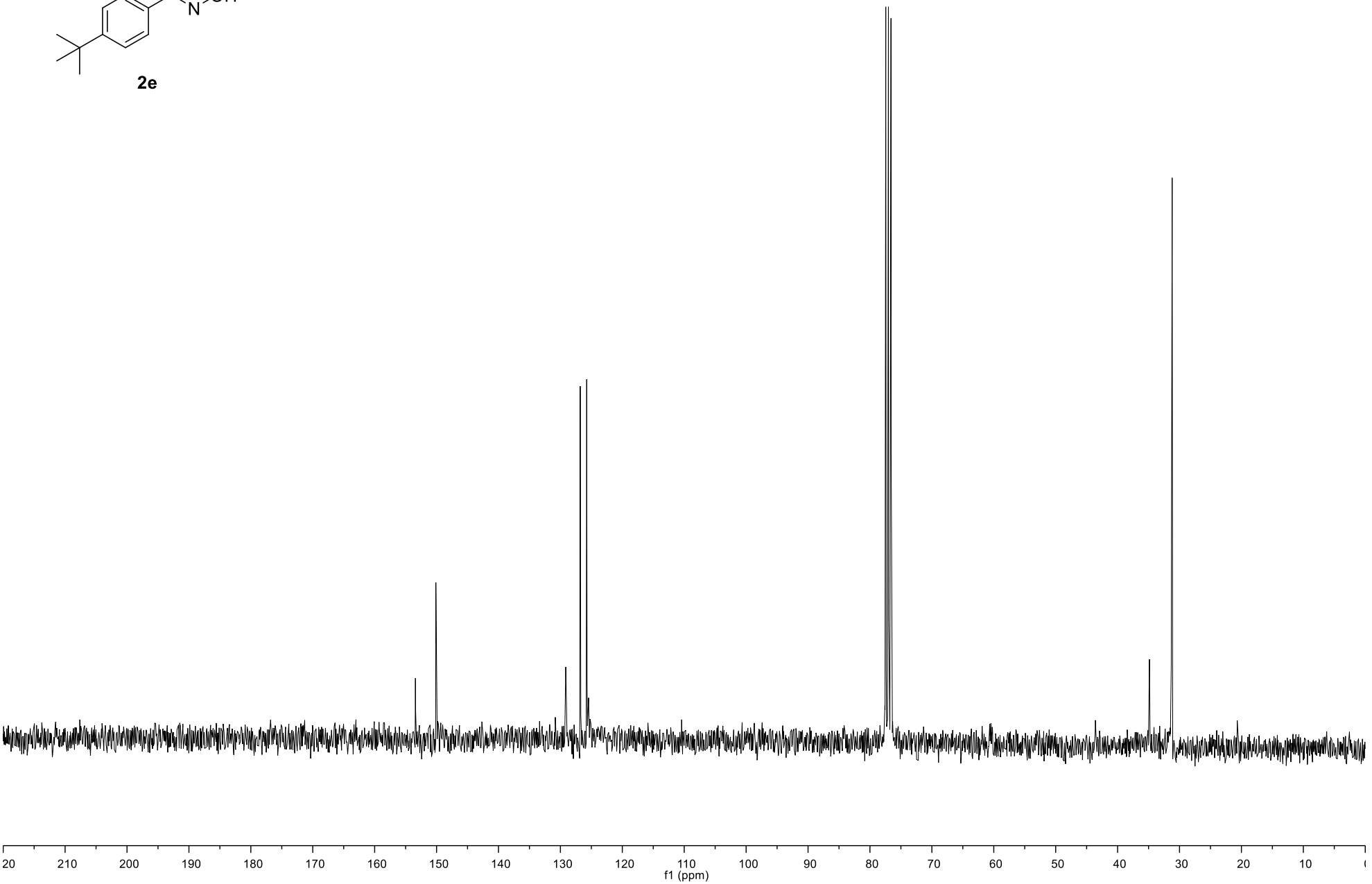
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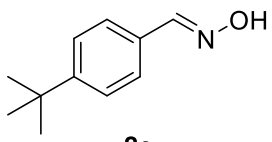

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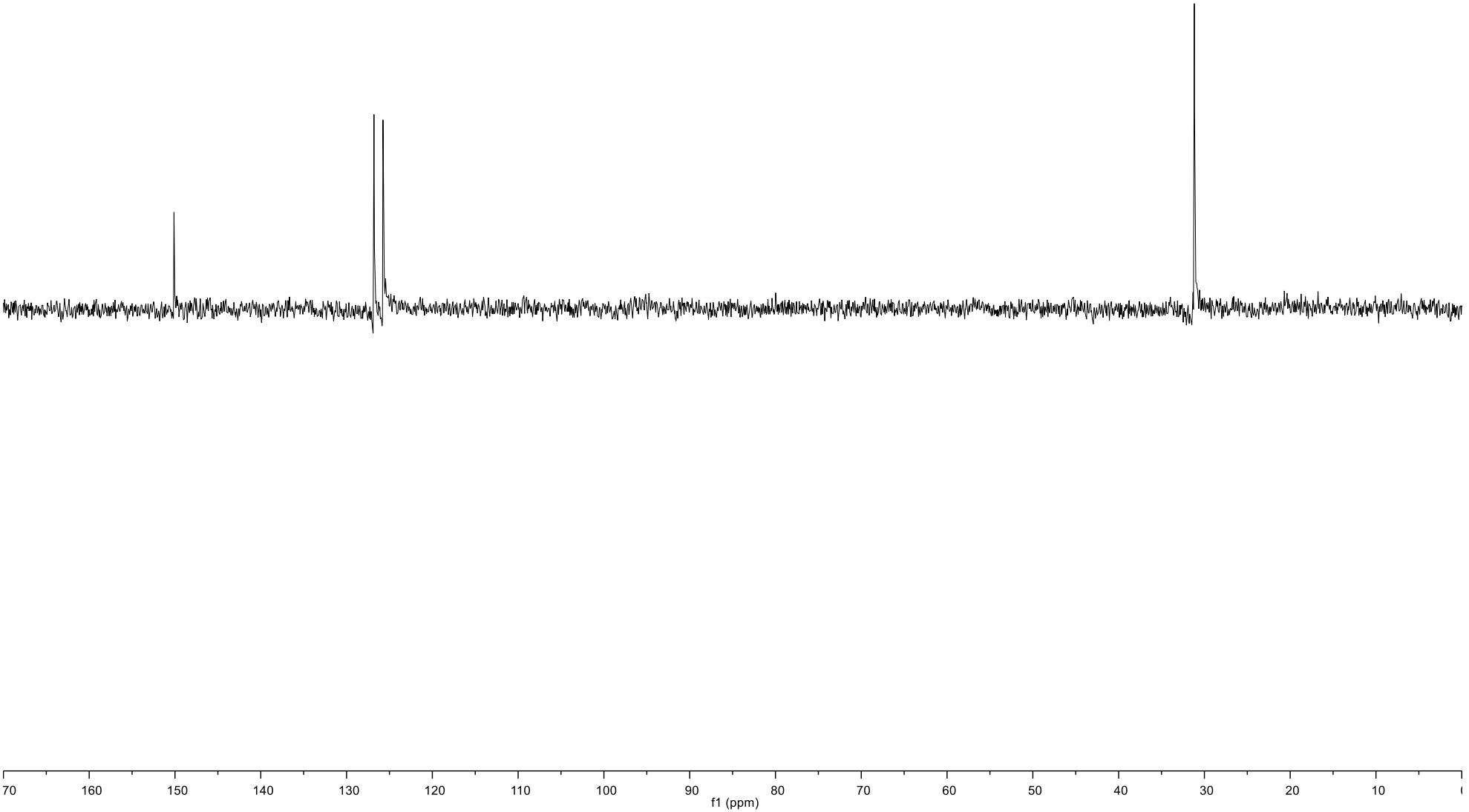

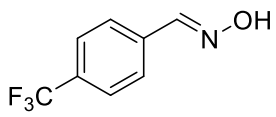
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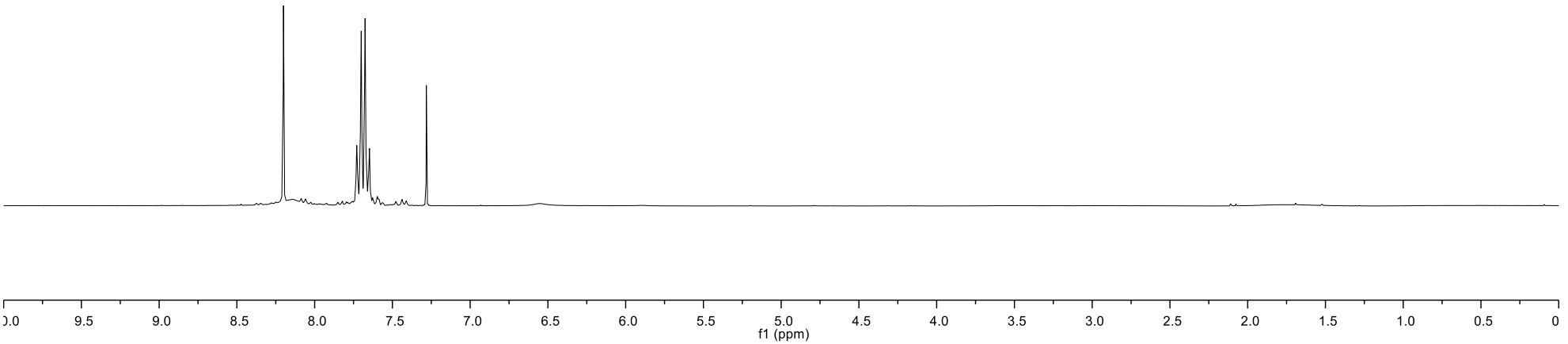
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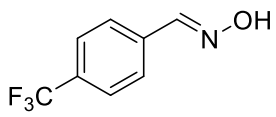
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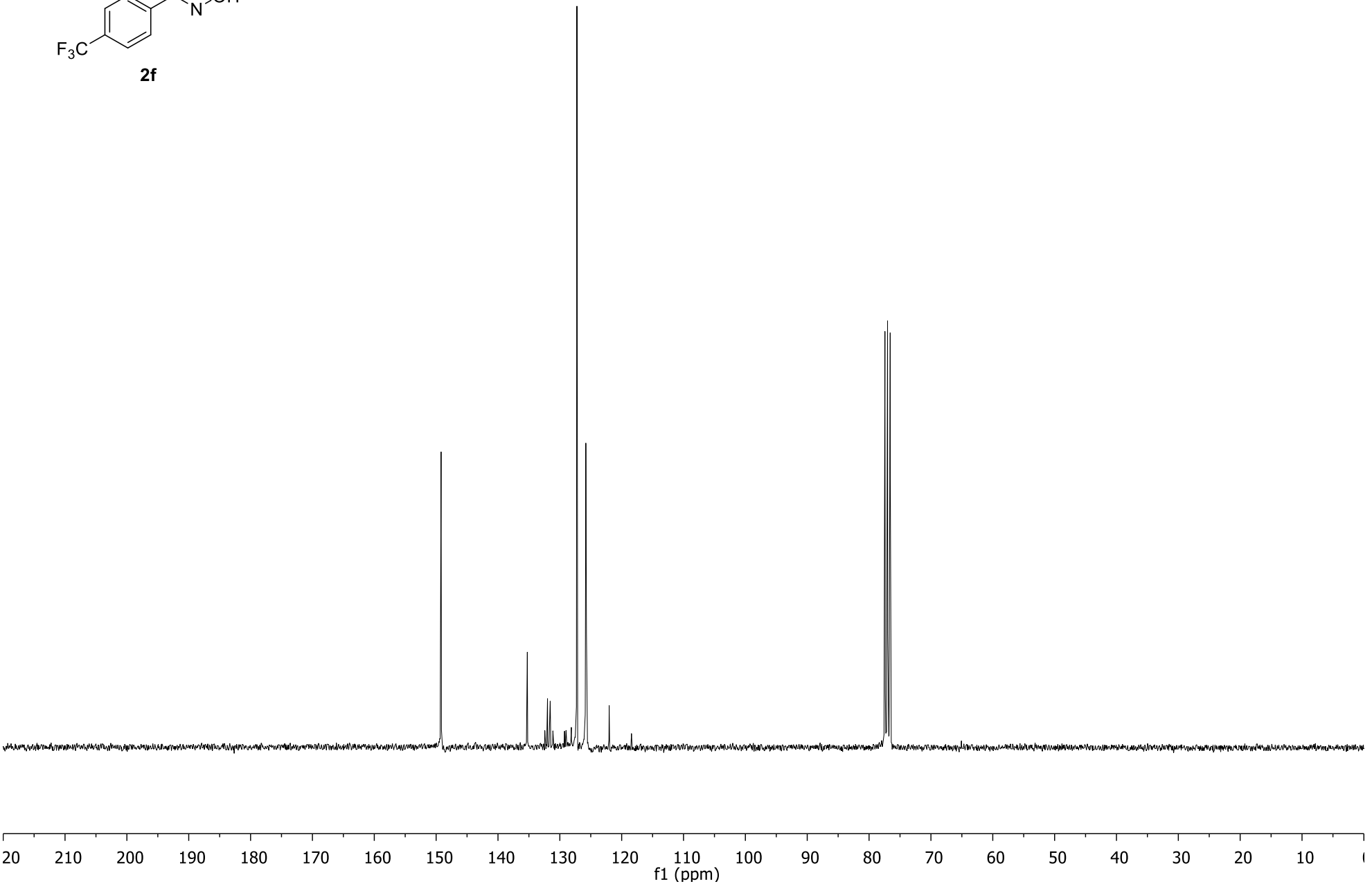
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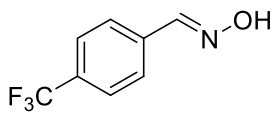
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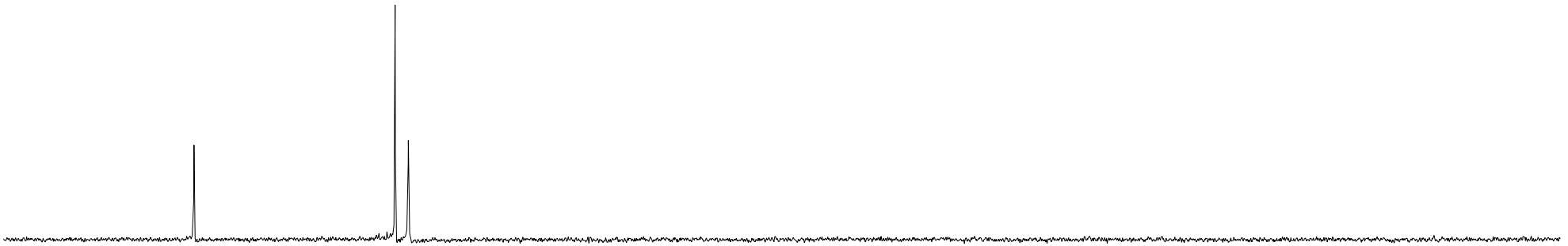
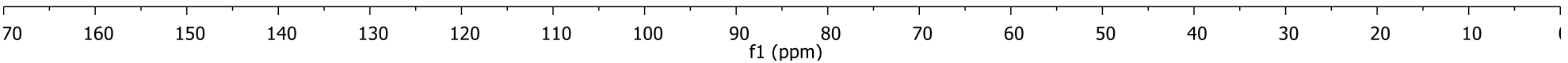
F3C

2f

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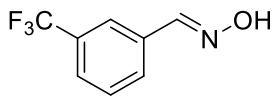
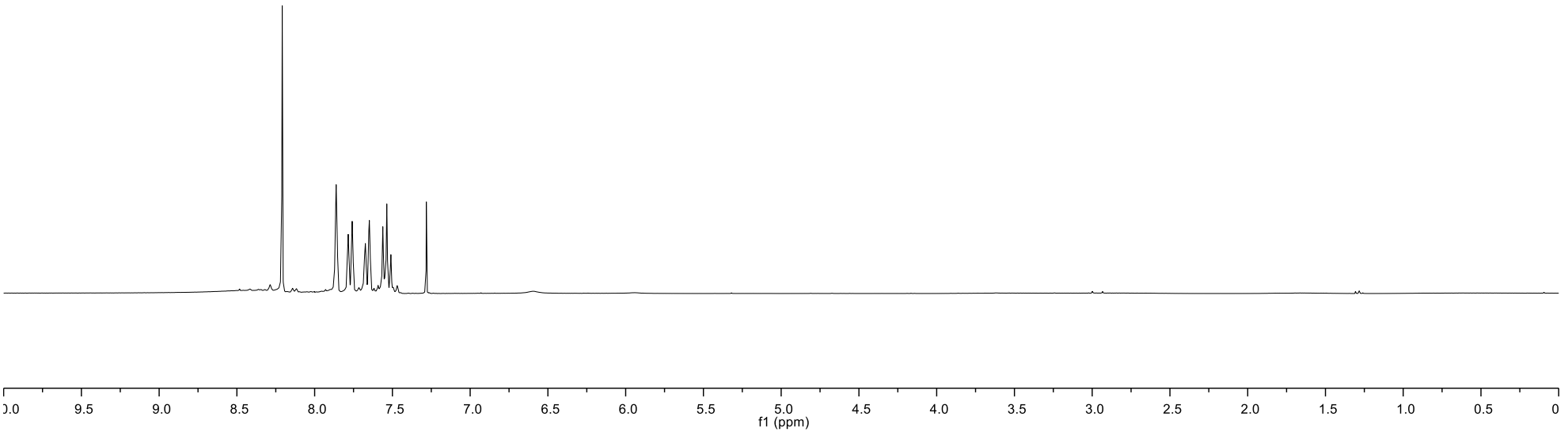

F3C
N
OH

2g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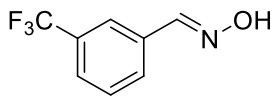
f1 (ppm)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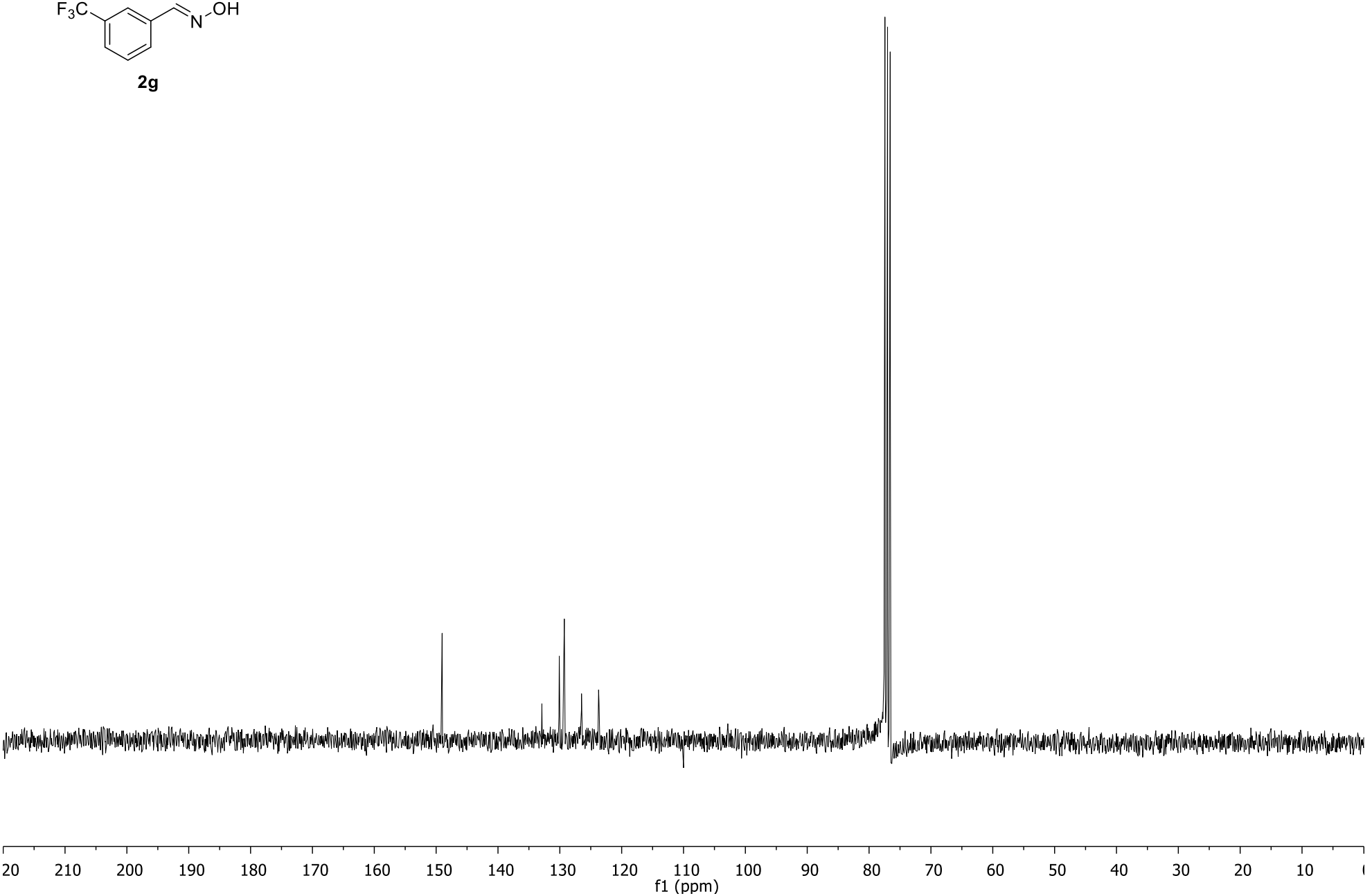
OH

2g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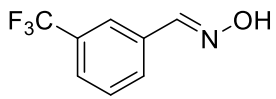
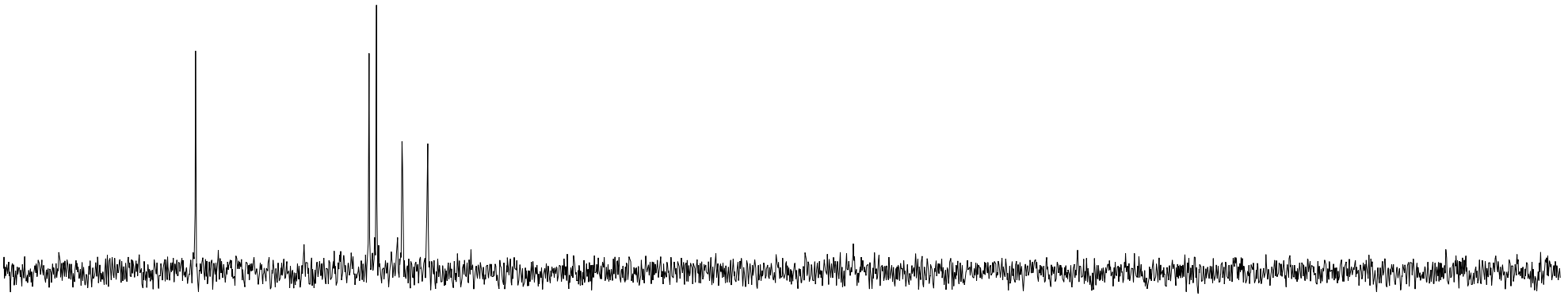
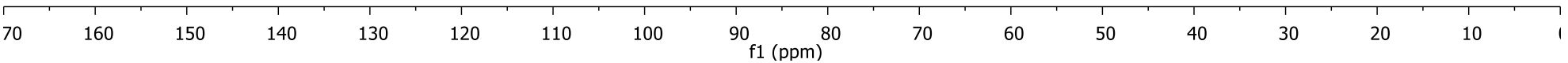
f1 (ppm)


F3C
N
OH

2g

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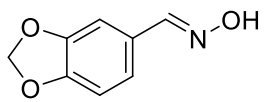
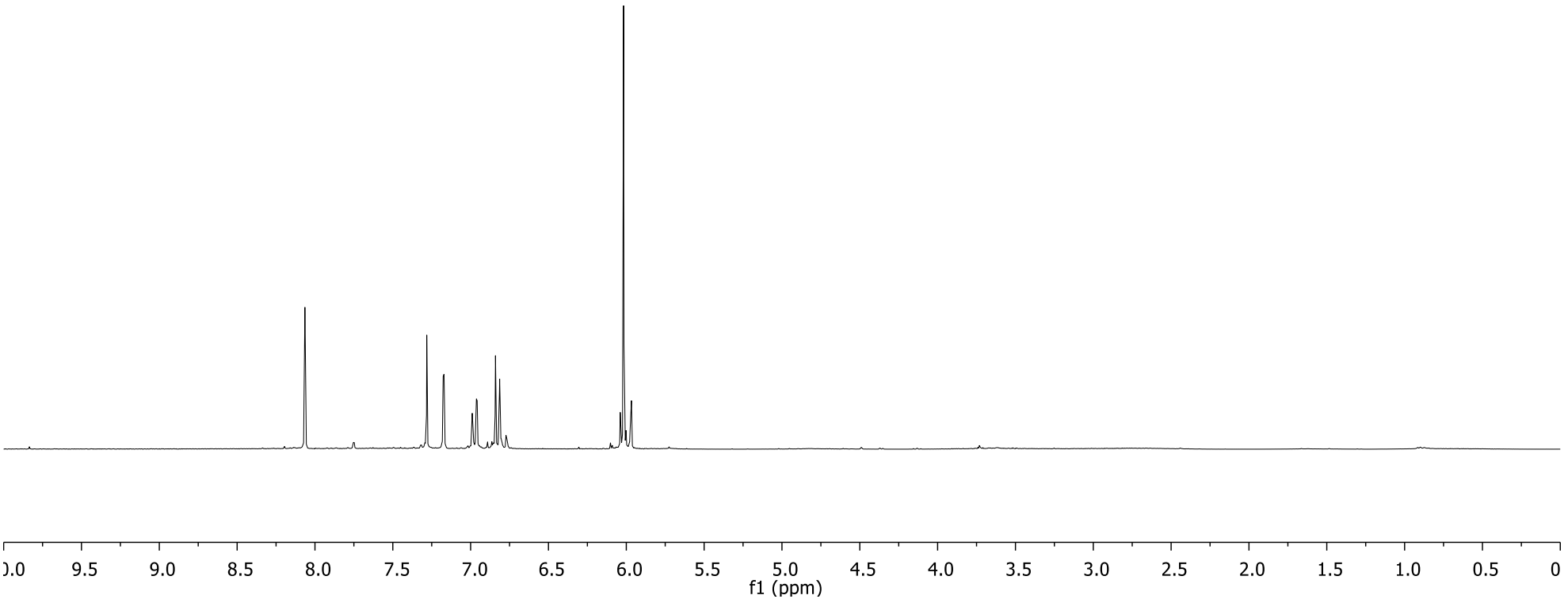

O
O
N
OH

2h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4.0
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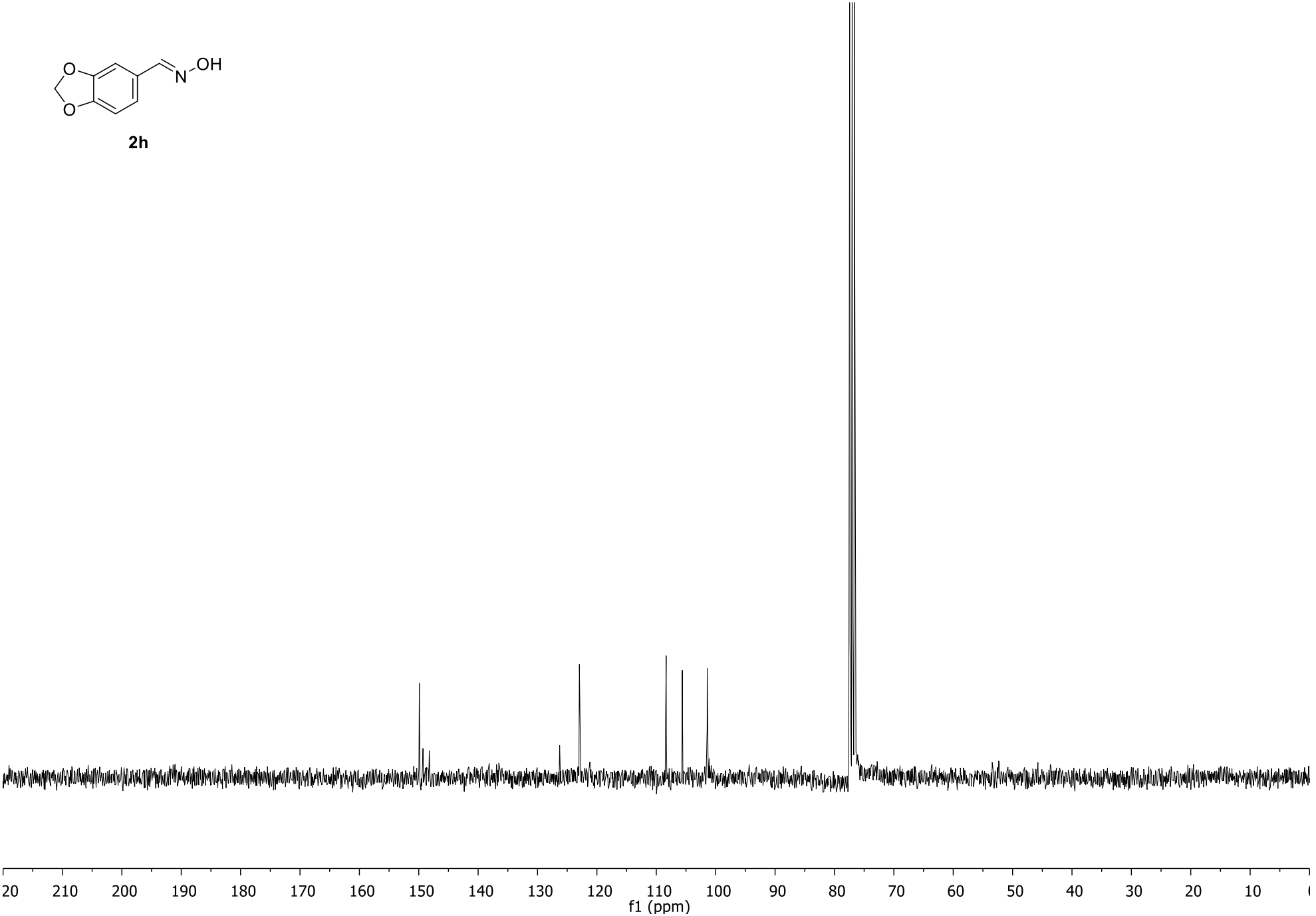
2.0
1.5
1.0
0.5
0
f1 (ppm)

O
O
N
OH

2h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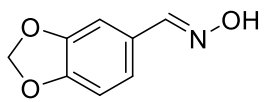
f1 (ppm)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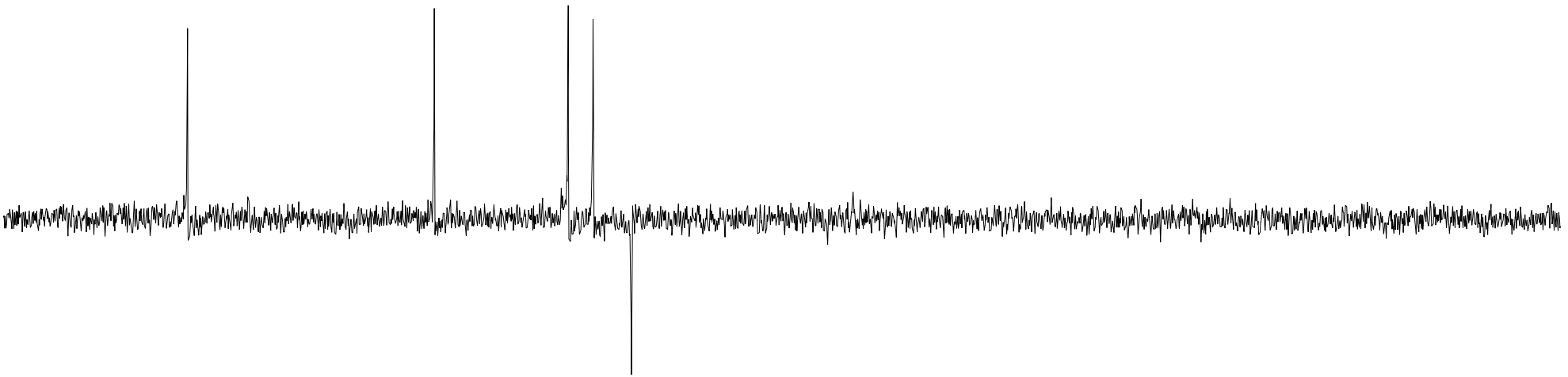
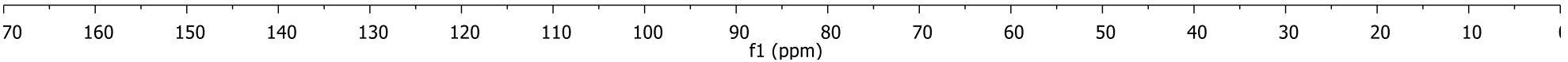
O
N
OH

2h

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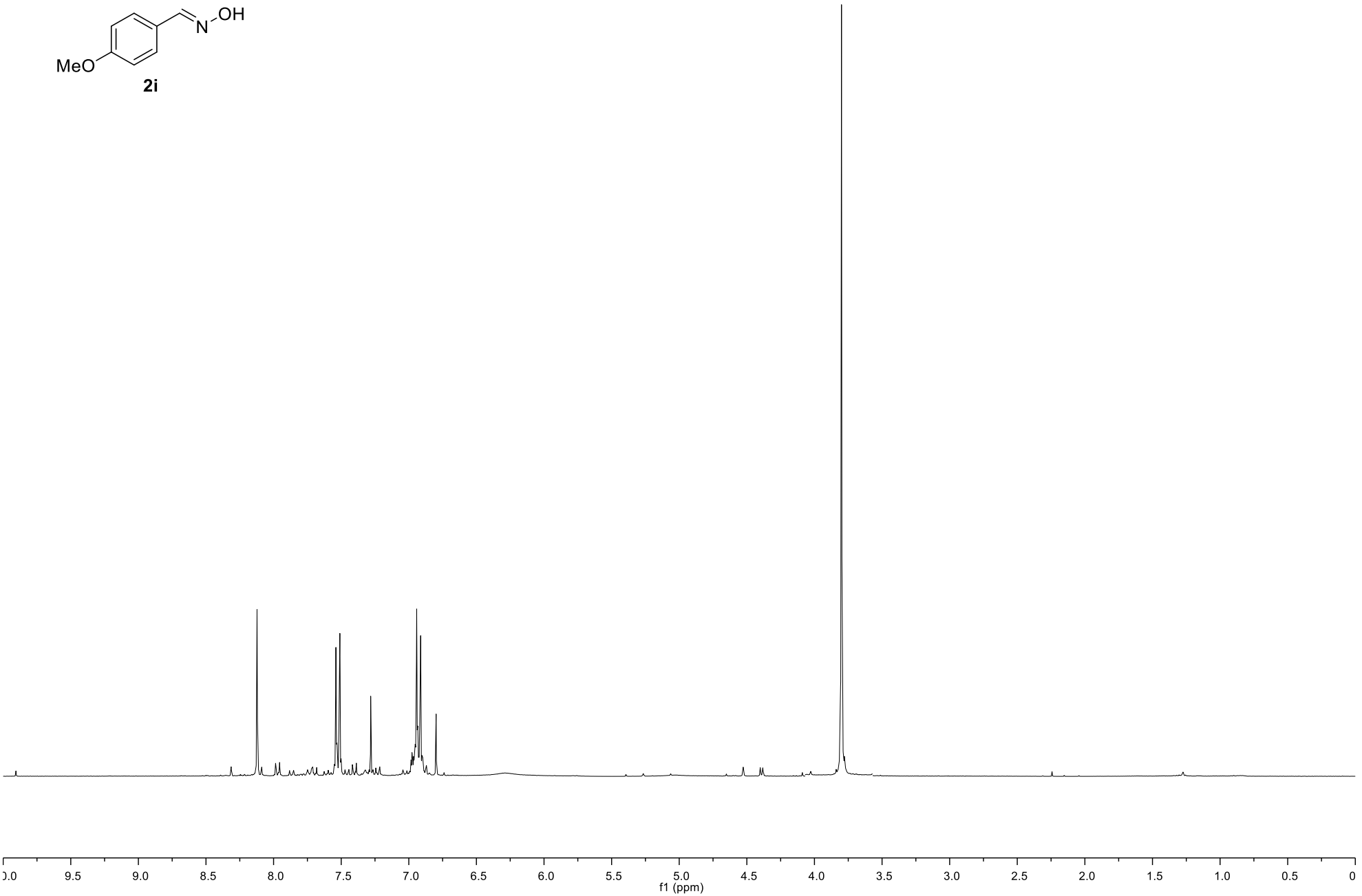
30
20
10
f1 (ppm)

MeO
N
OH

2i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4.0
3.5
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2.5
2.0
1.5
1.0
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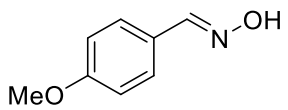
f1 (ppm)


MeO
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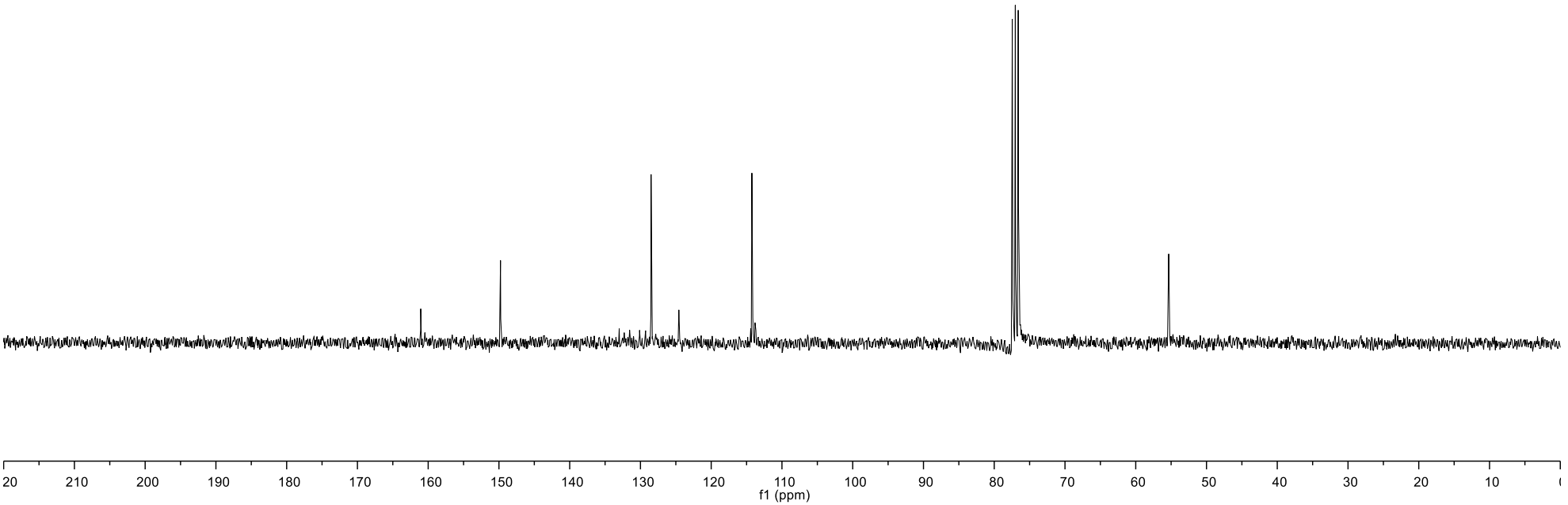
OH

2i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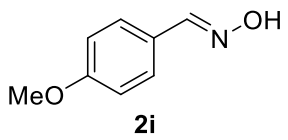
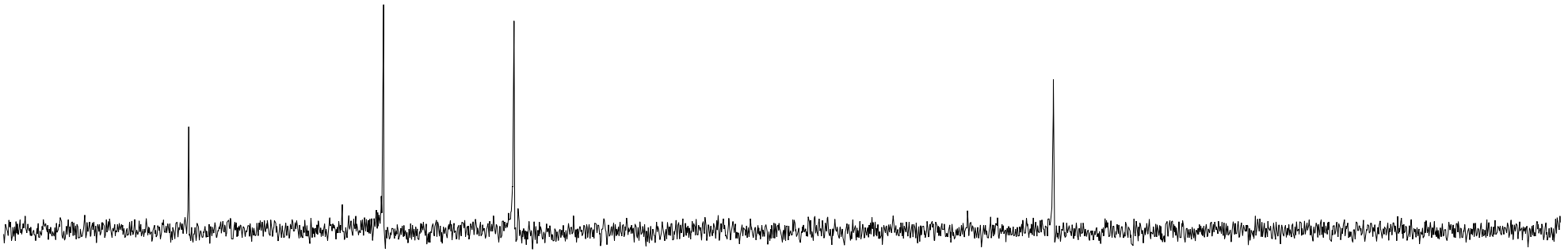
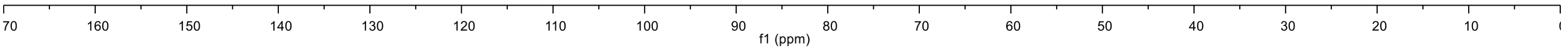
f1 (ppm)


N
OH
MeO

2i

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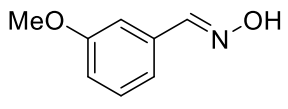
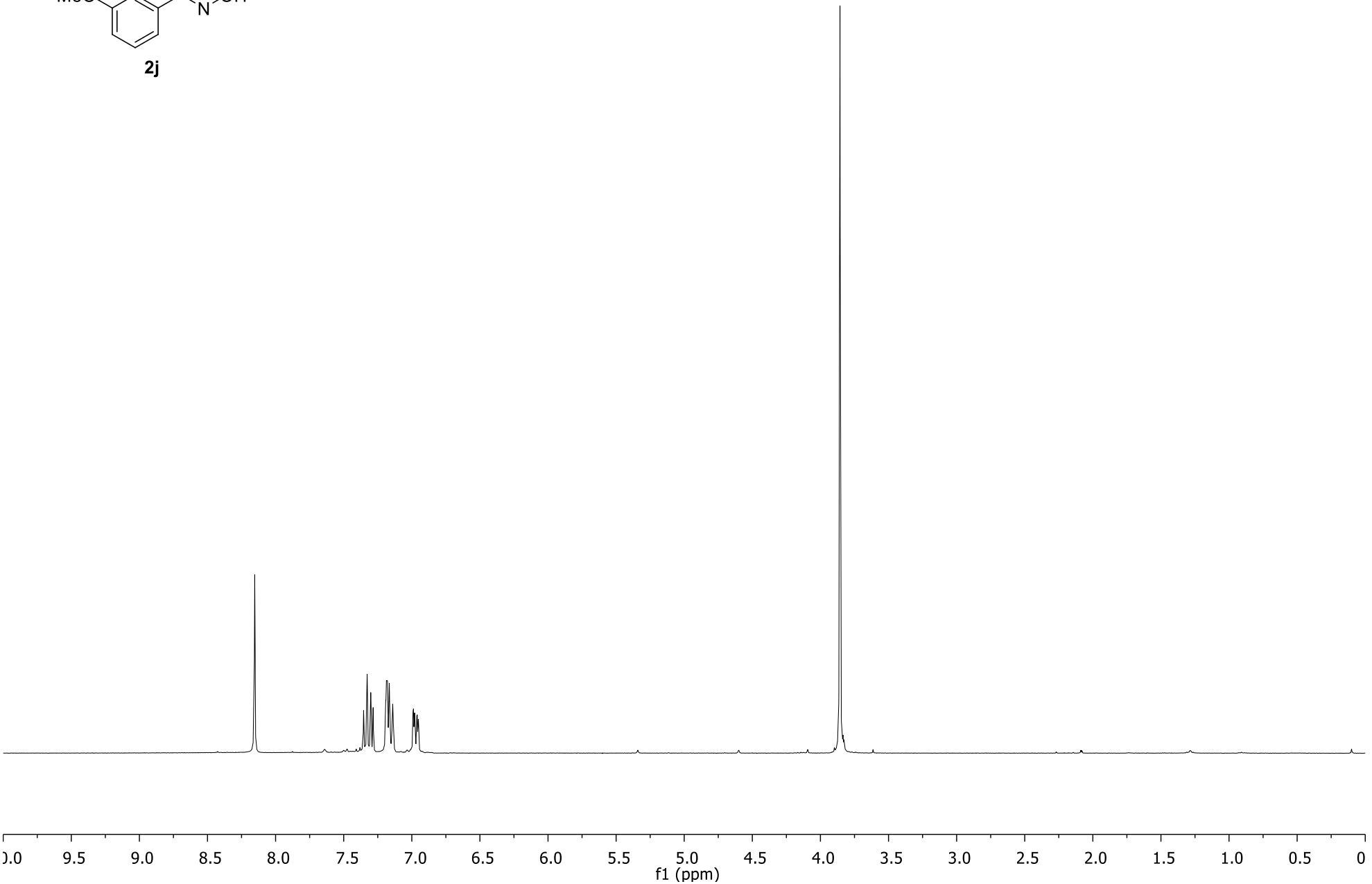

MeO
N
OH

2j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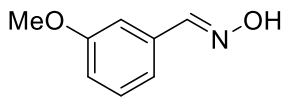
f1 (ppm)


MeO
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OH

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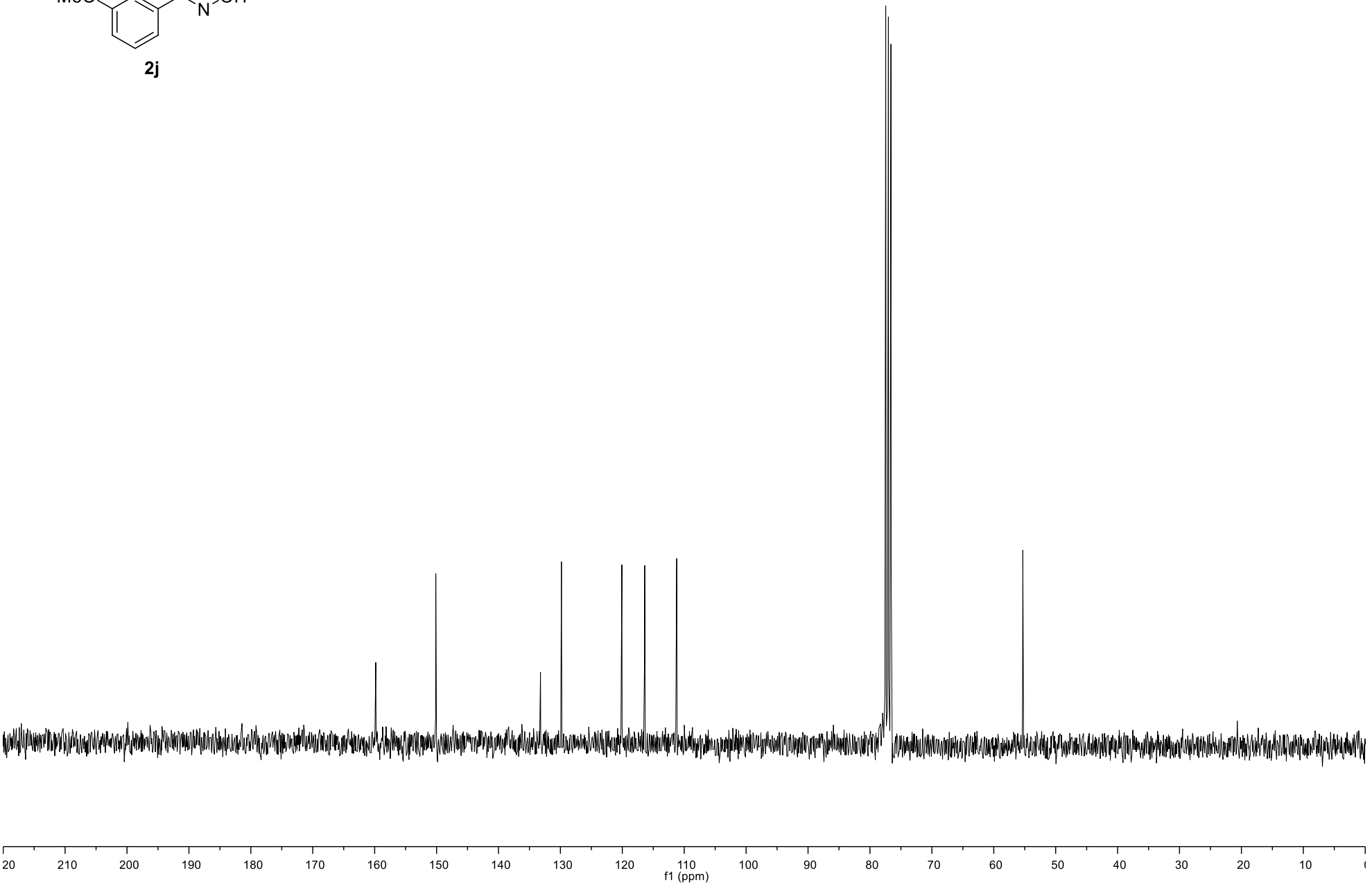
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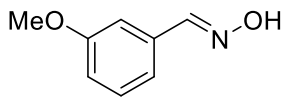
f1 (ppm)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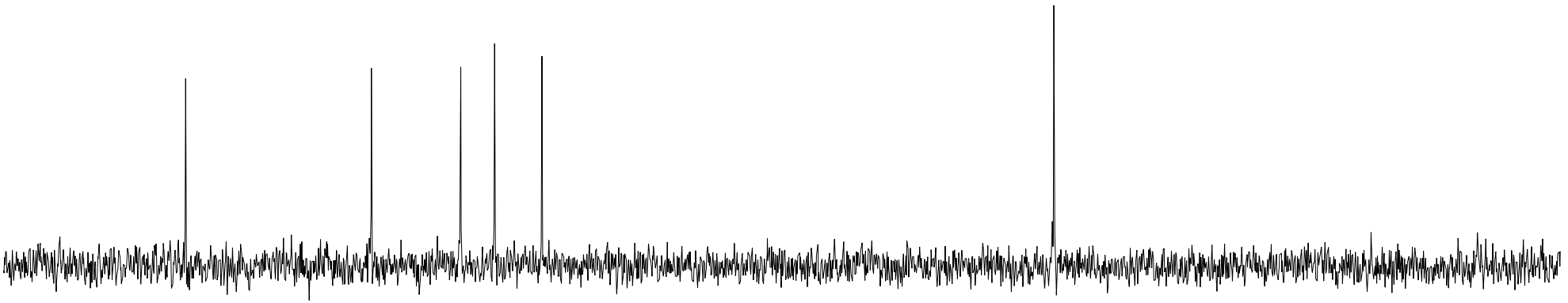
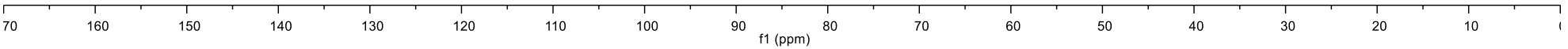
N
OH

2j

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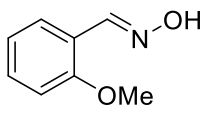
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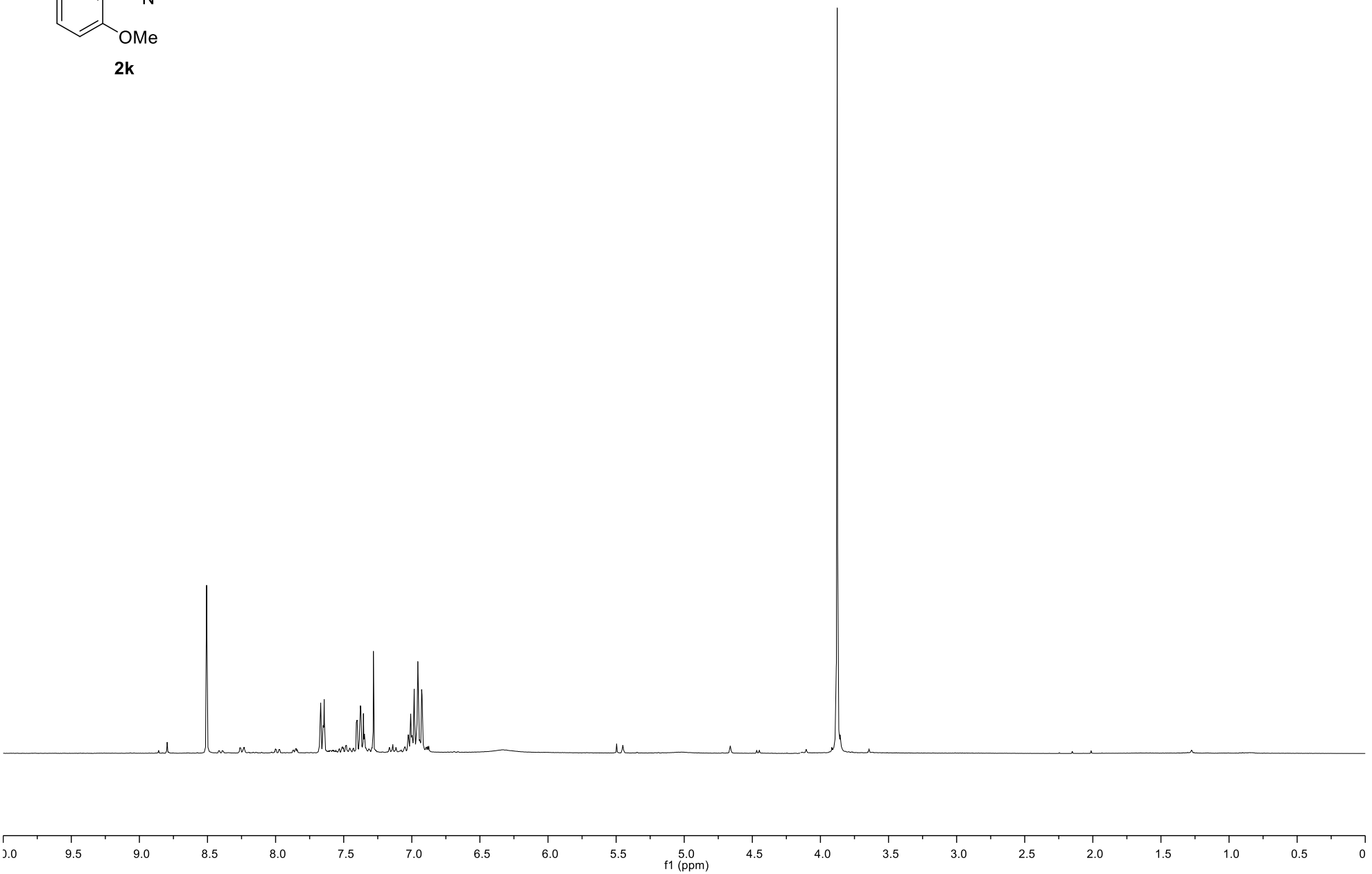
OH
OMe

2k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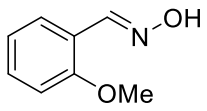
f1 (ppm)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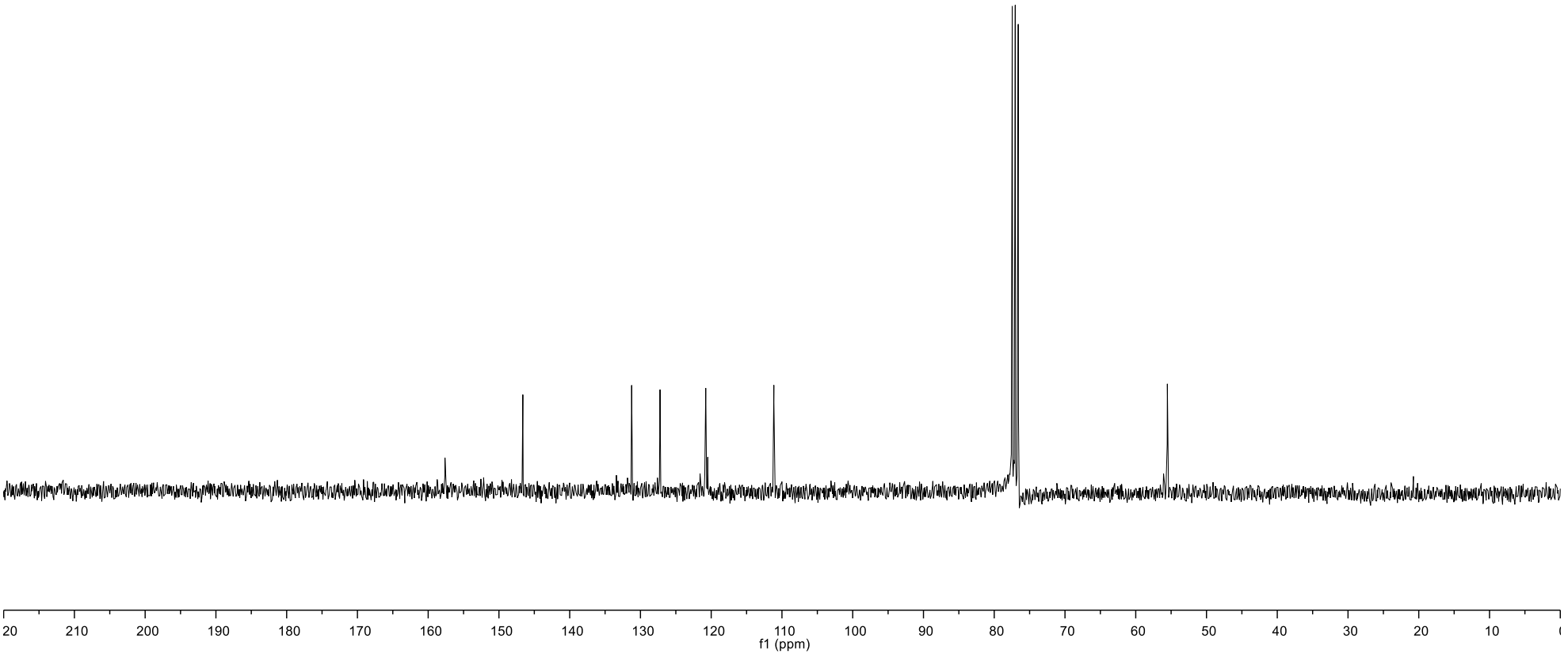
OH
OMe

2k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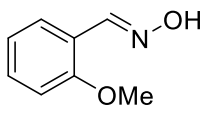
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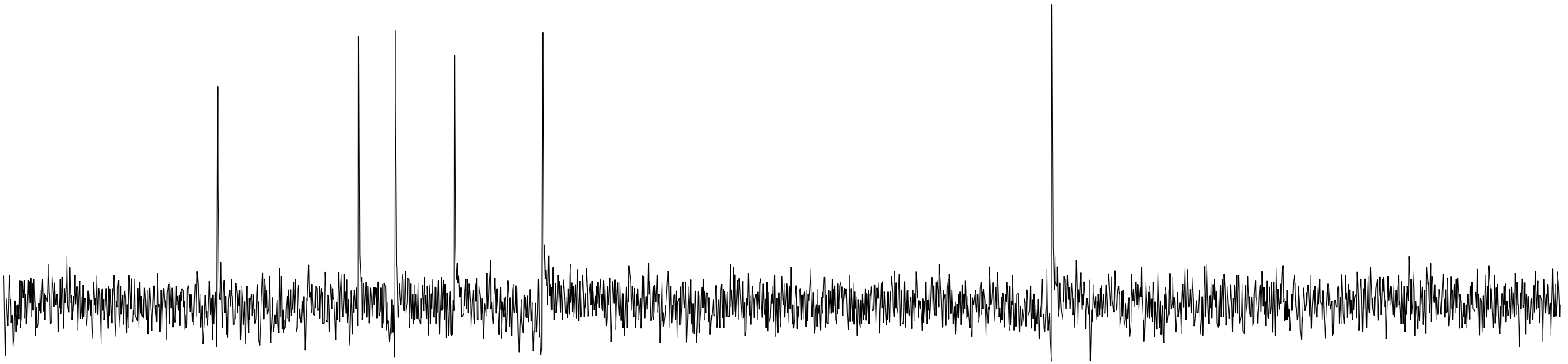
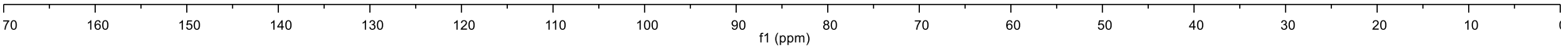
OH
OMe

2k

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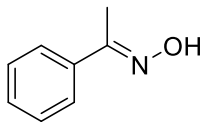

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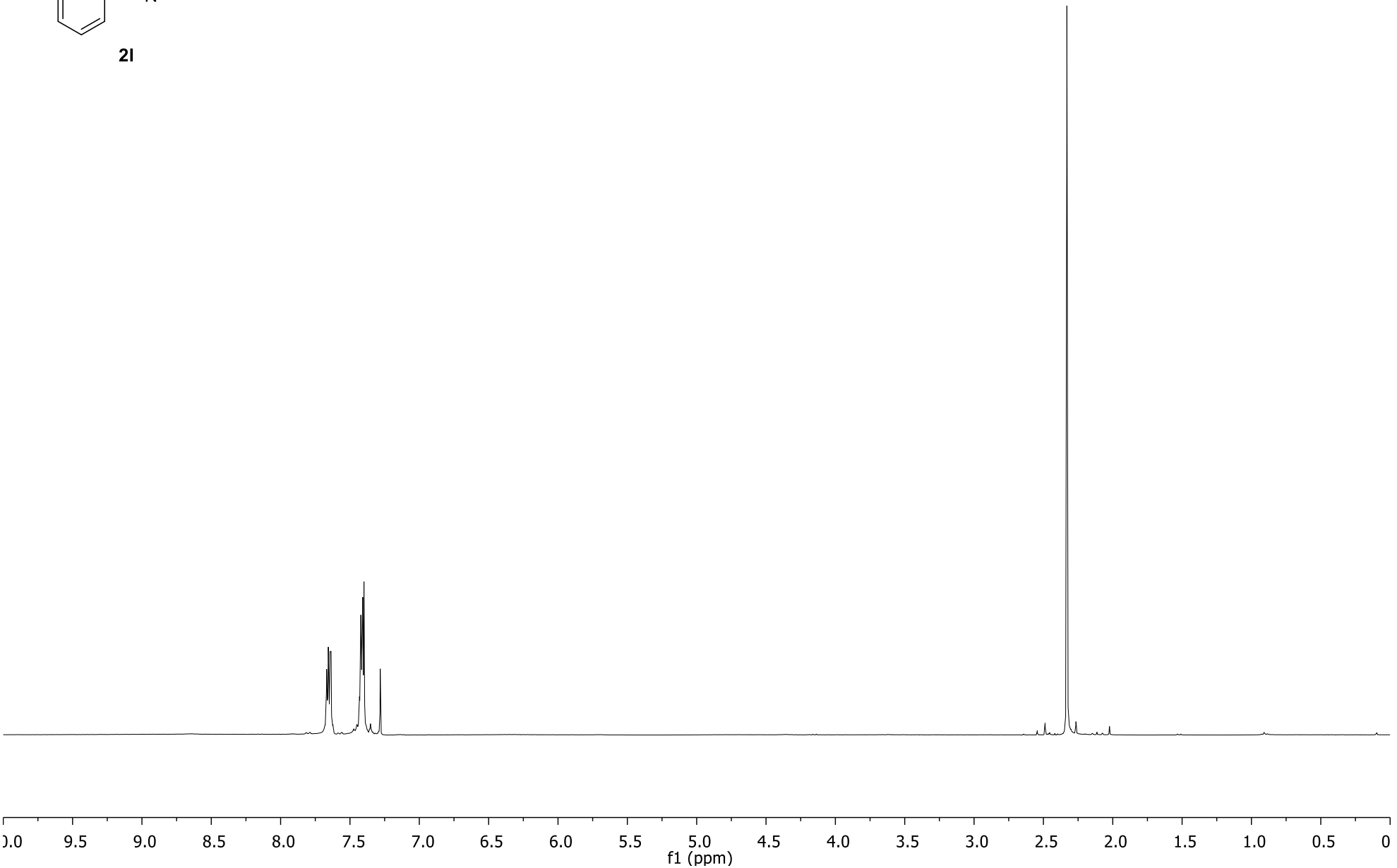

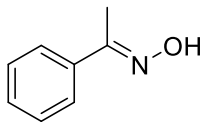
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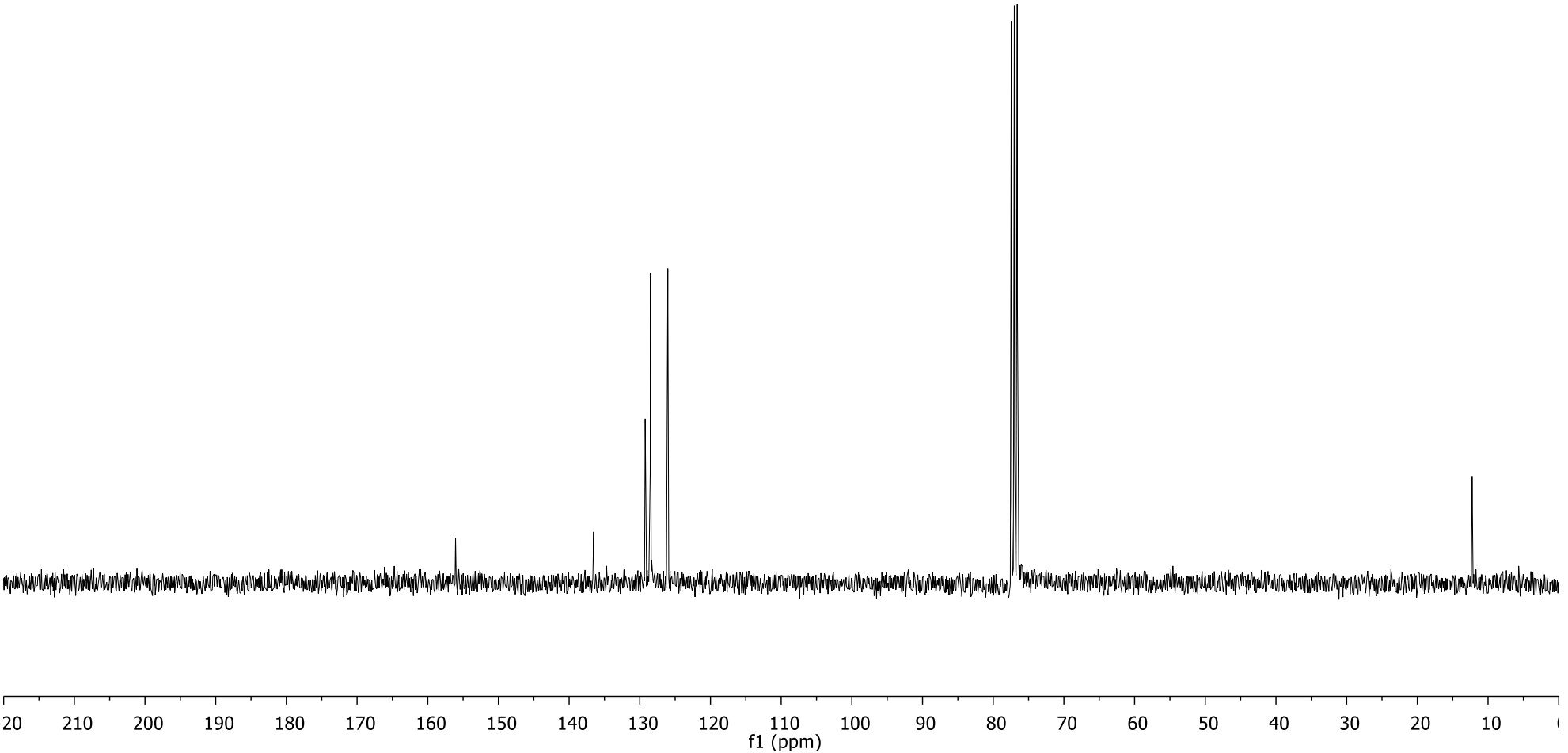
2l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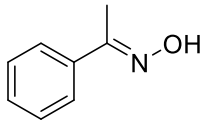

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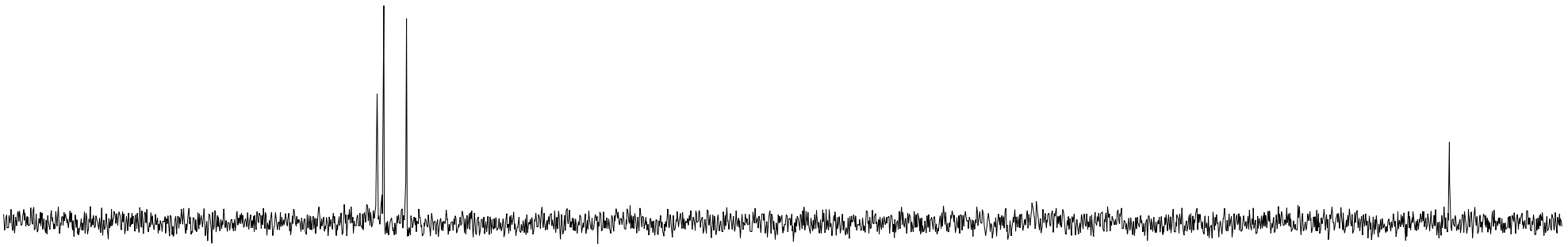

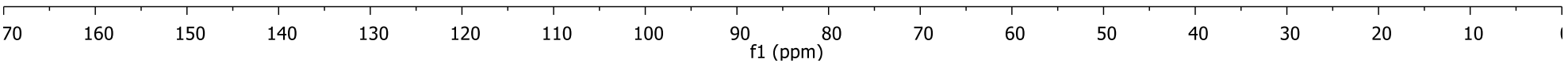

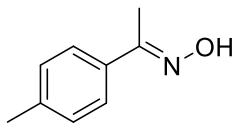

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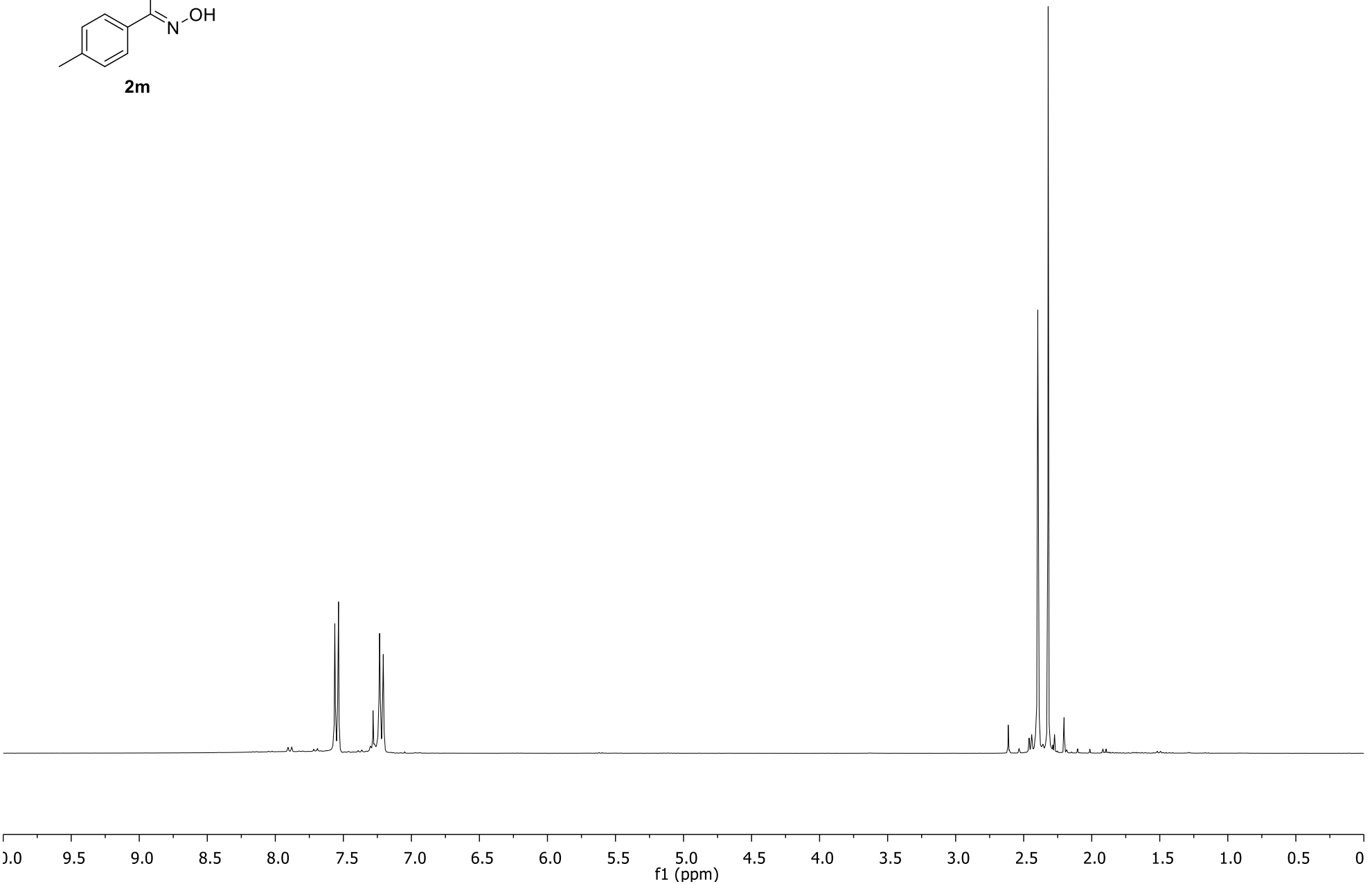

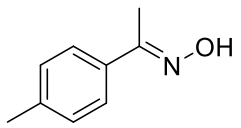
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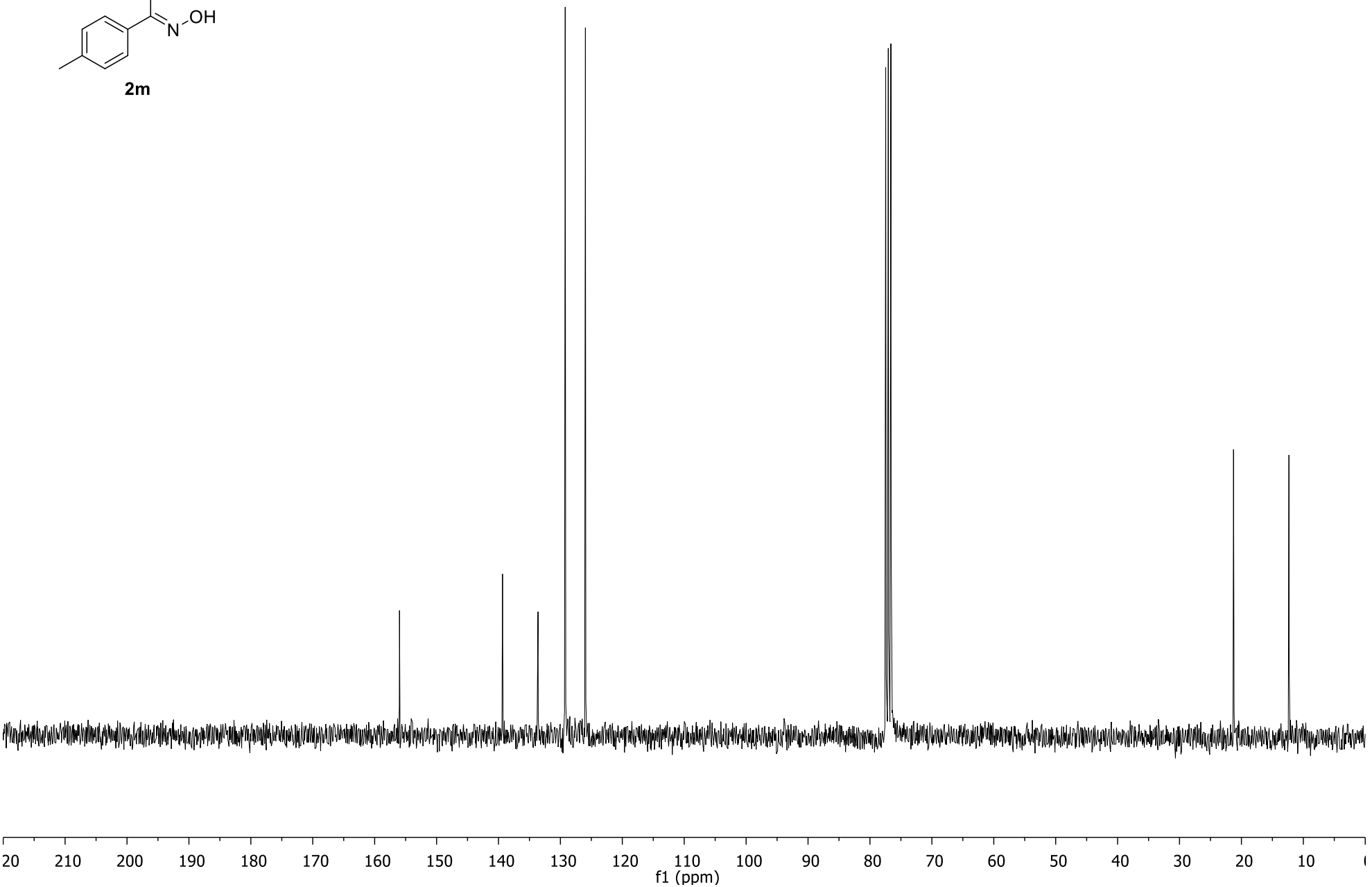
OH

2m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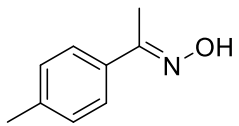
f1 (ppm)



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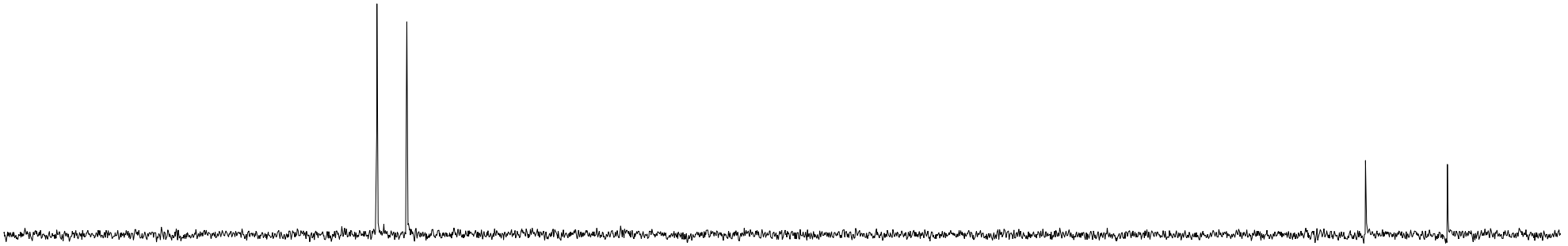
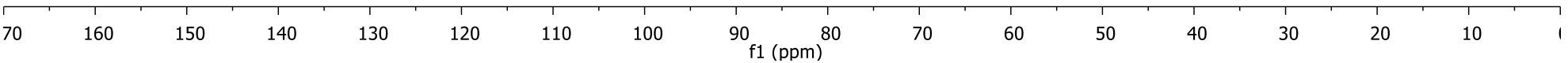
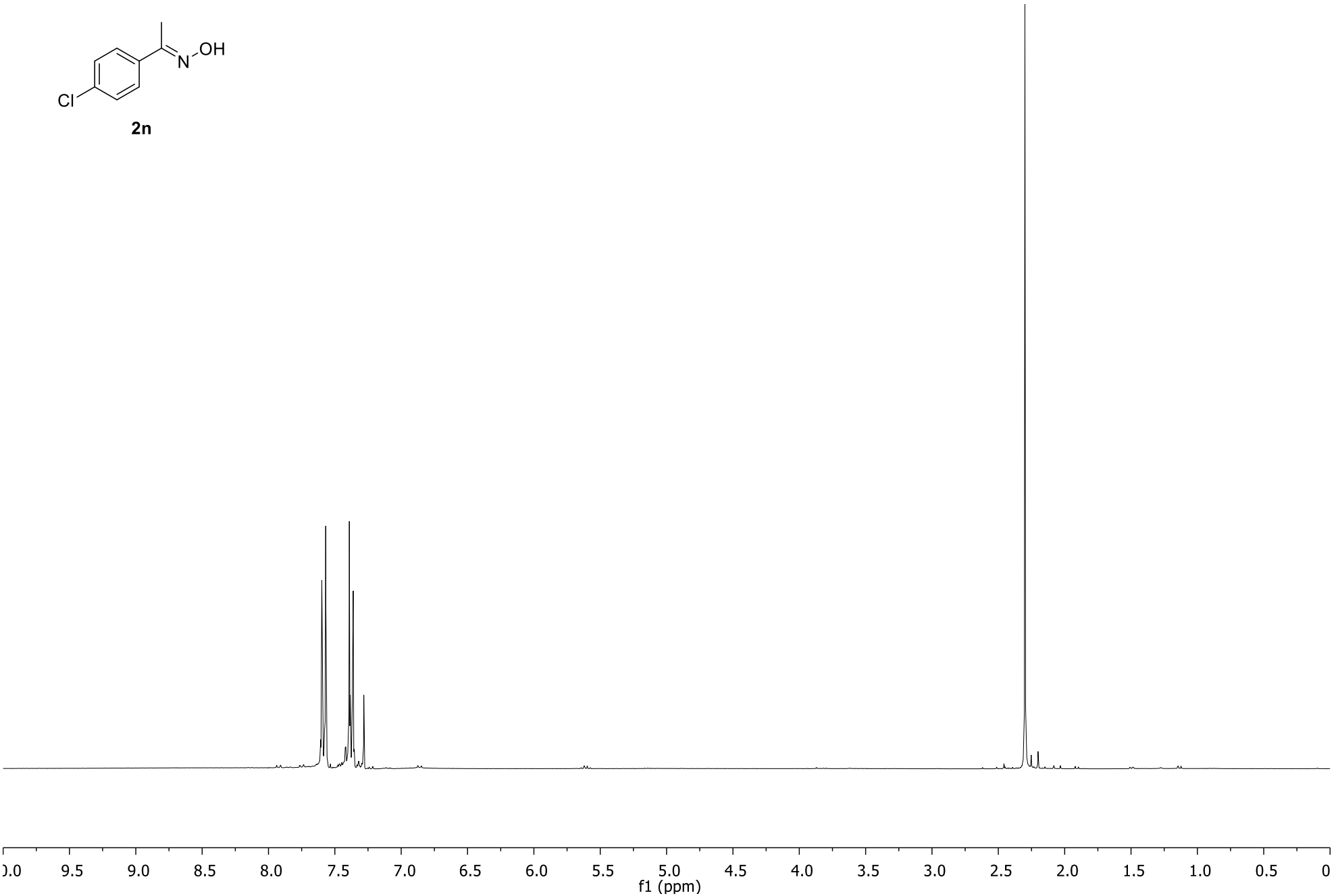




N
OH
Cl

2n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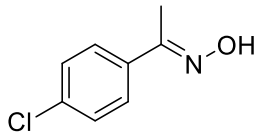
f1 (ppm)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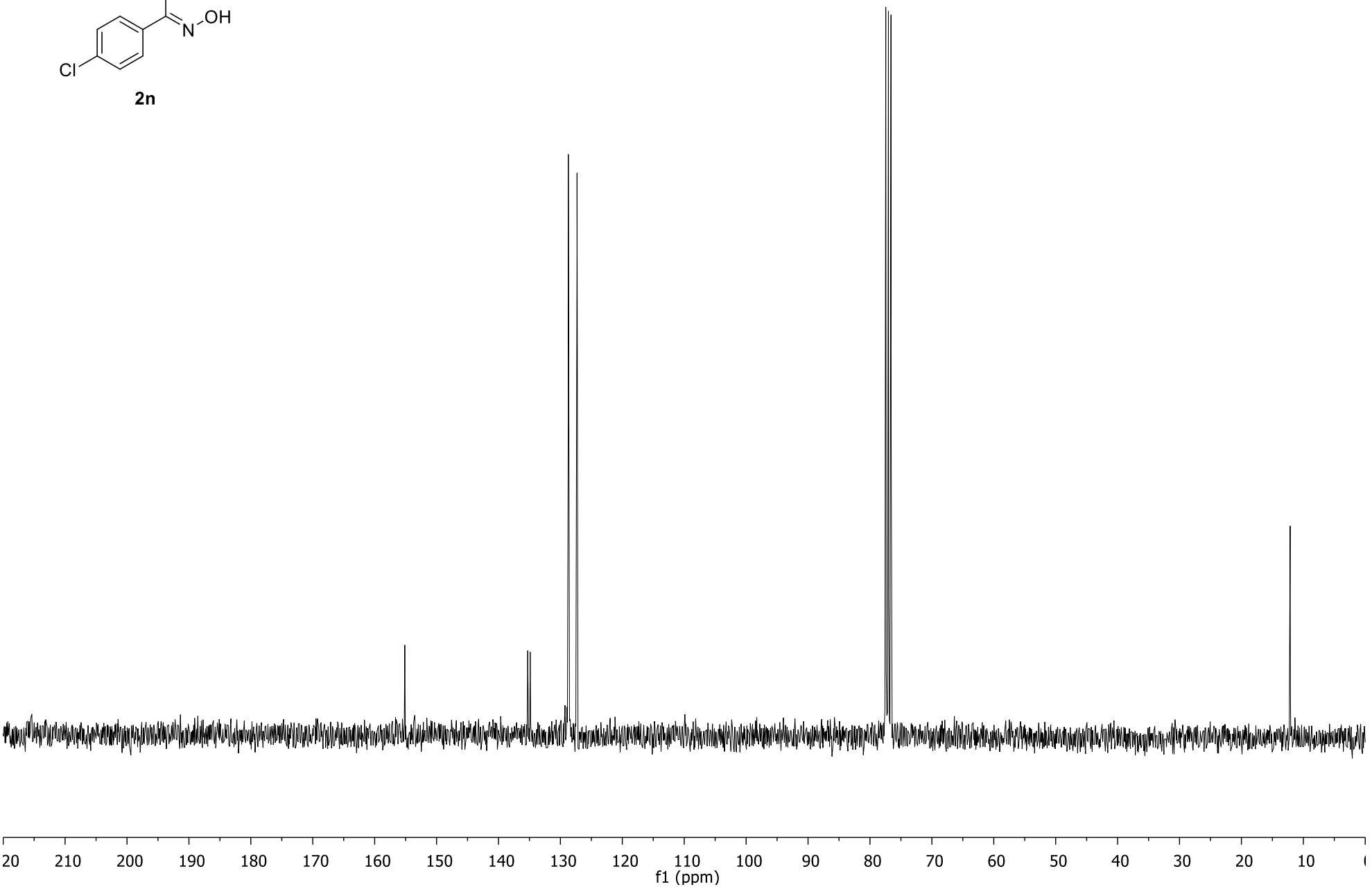
OH
Cl

2n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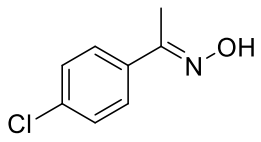
f1 (ppm)


N
OH
Cl

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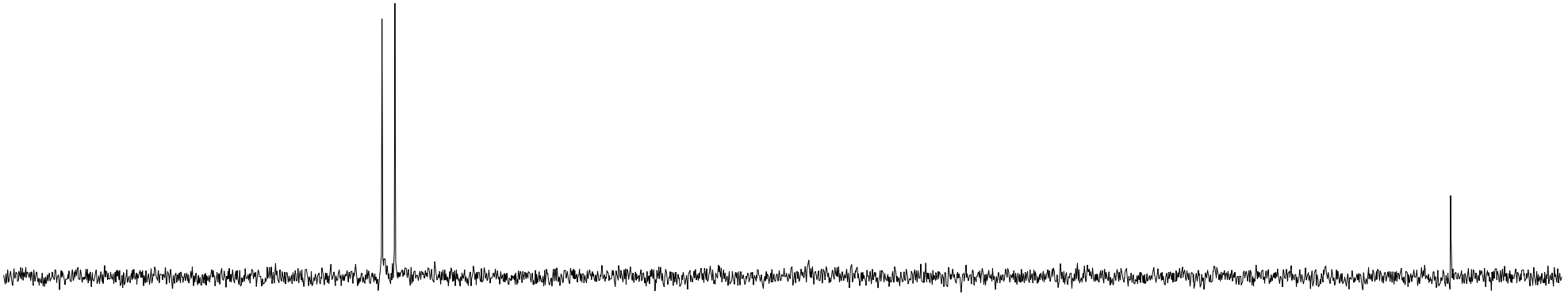

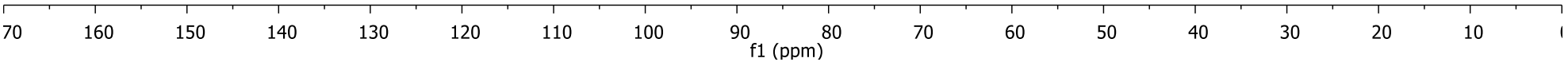
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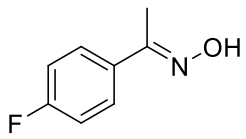
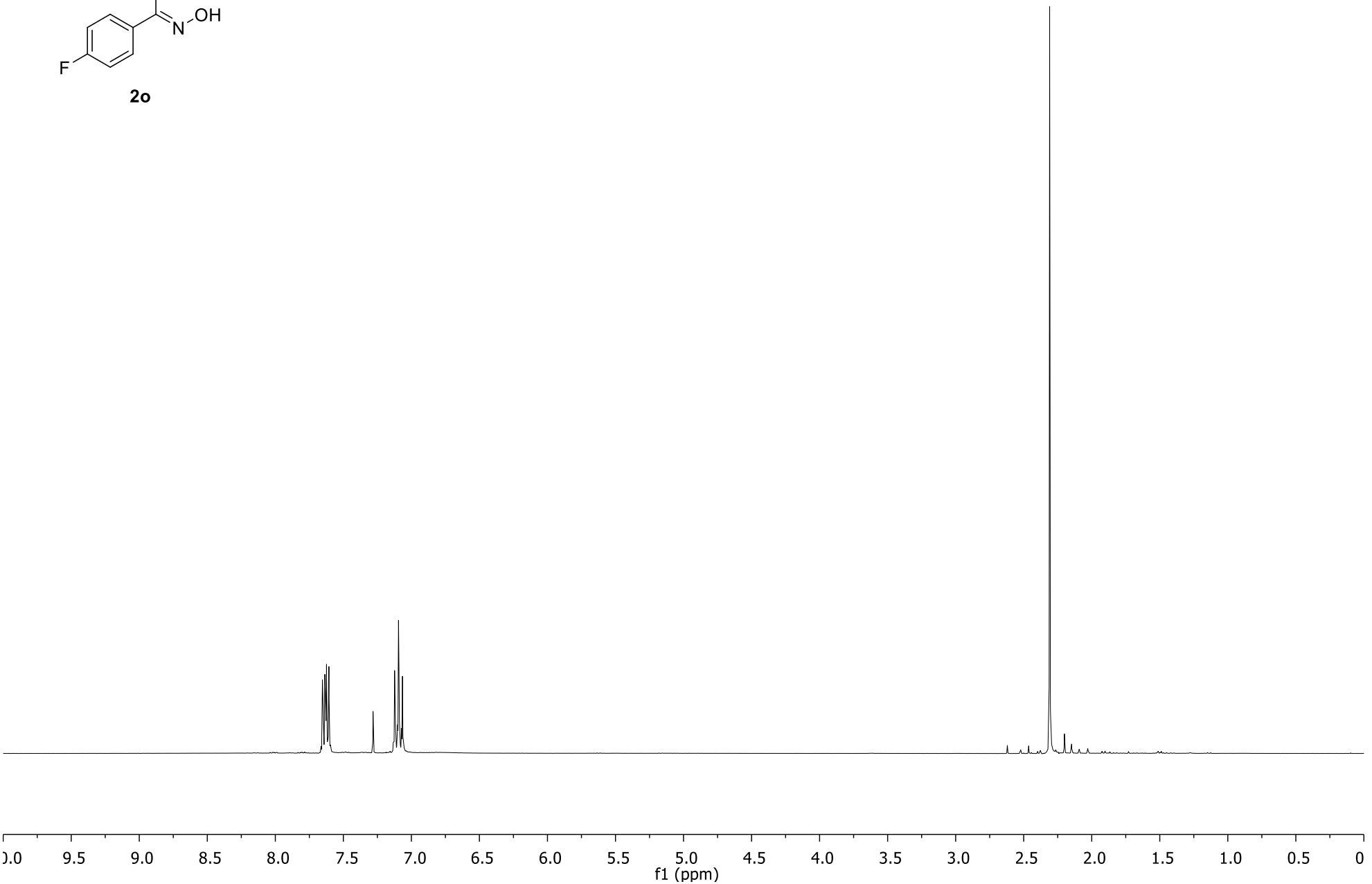
f1 (ppm)


N
OH
F

2o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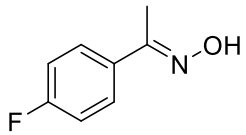
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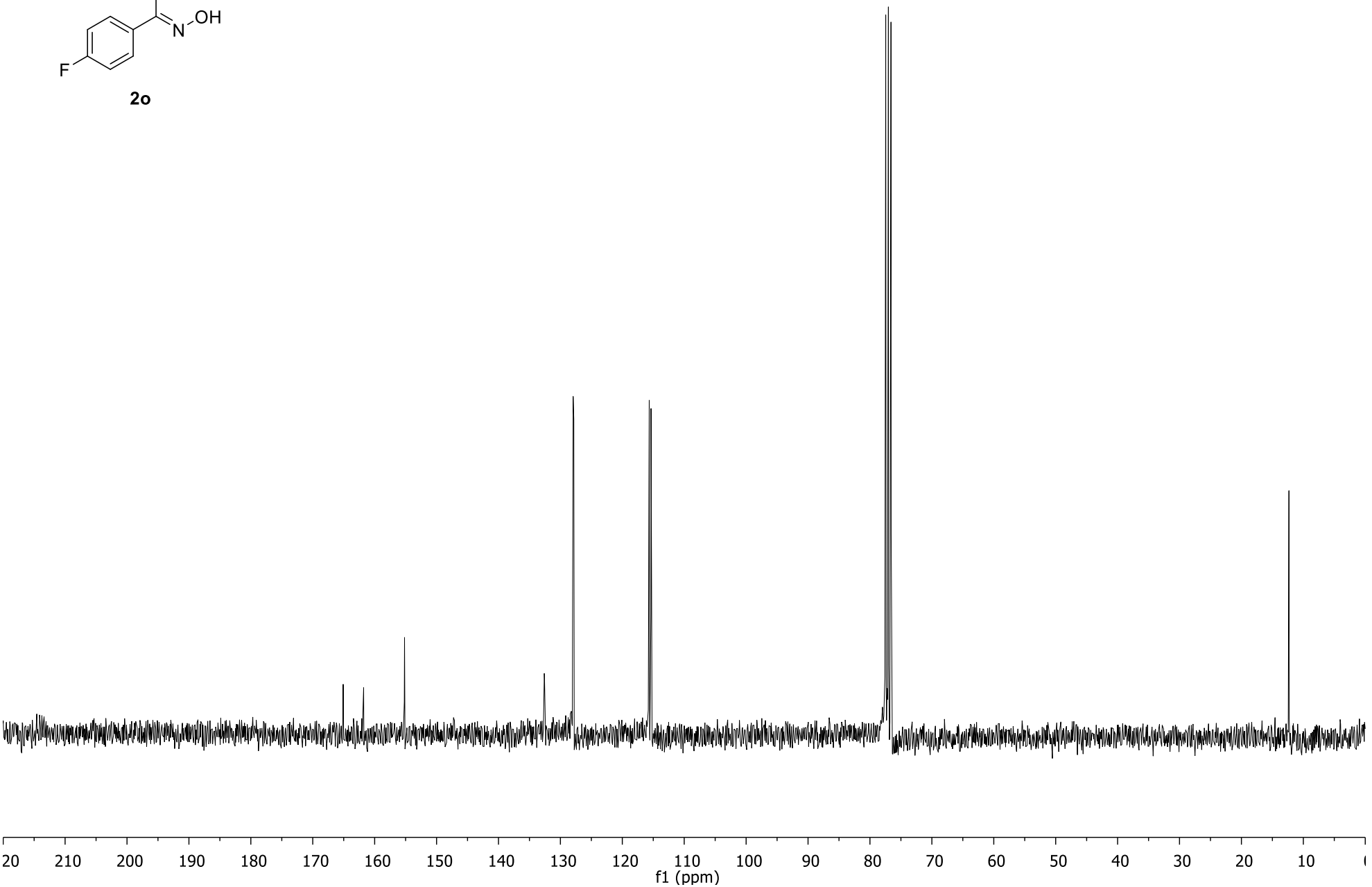
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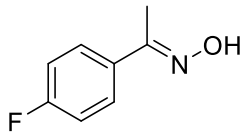
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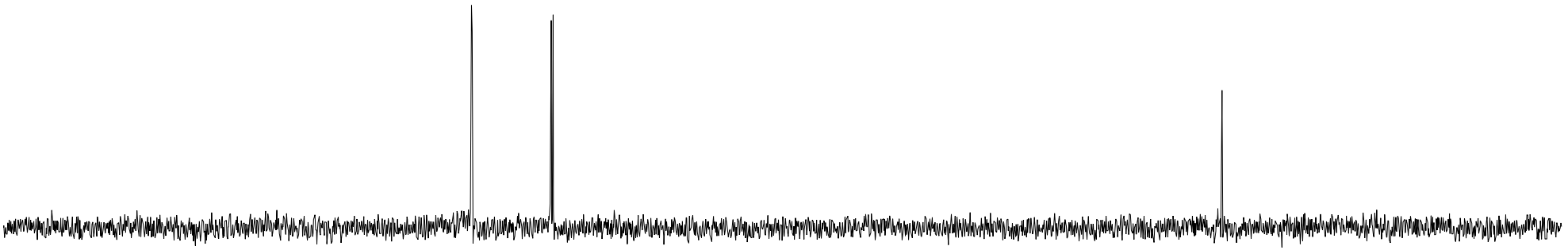

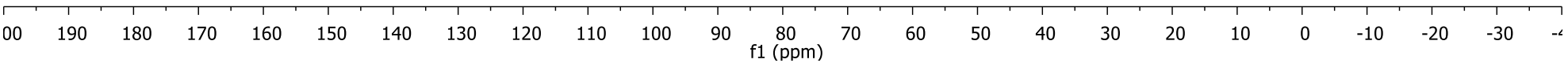
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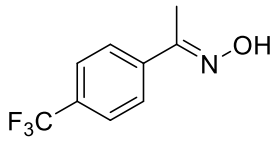
f1 (ppm)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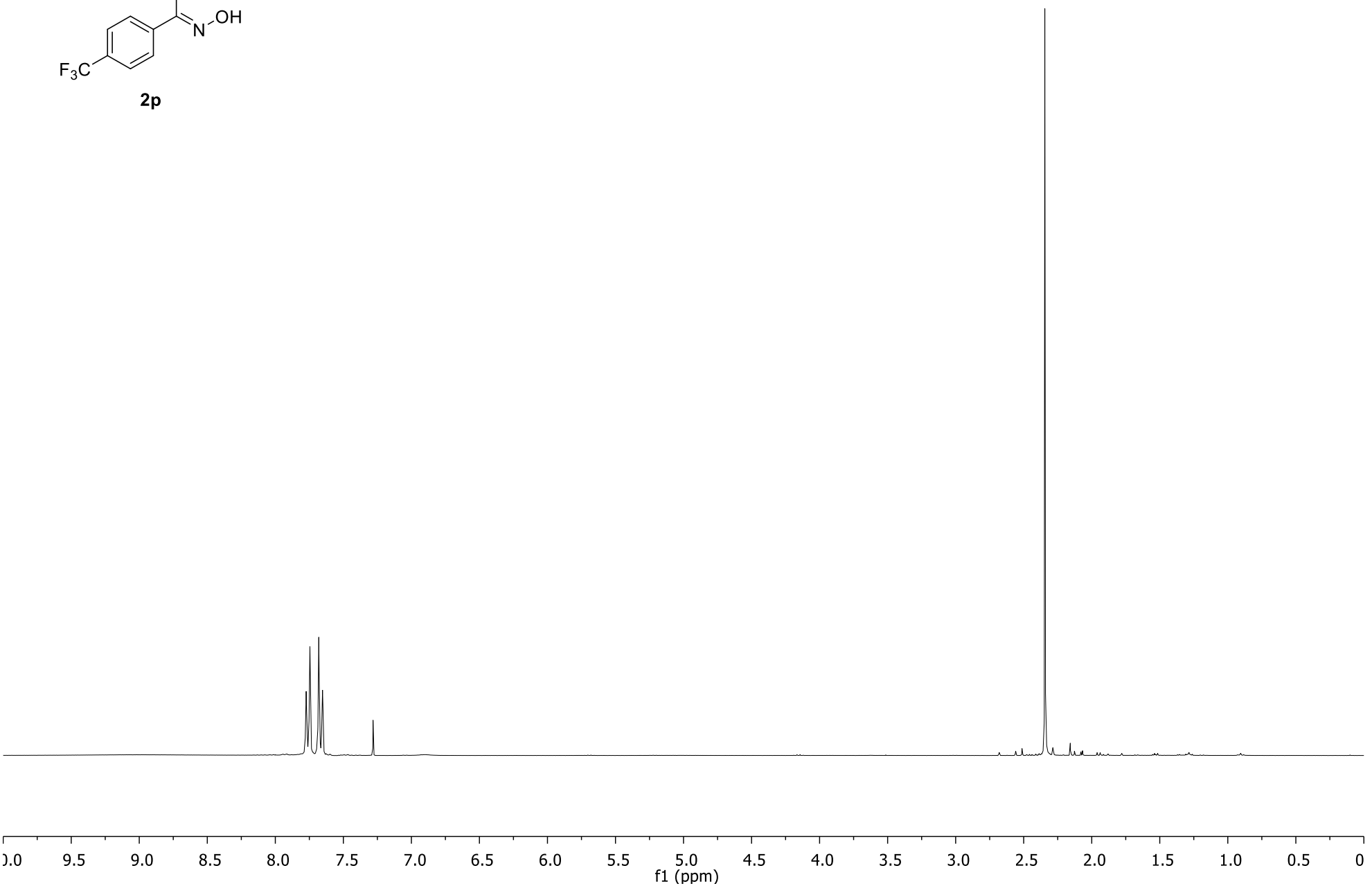
OH
F3C

2p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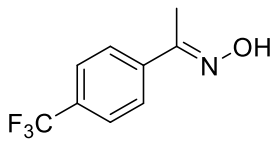
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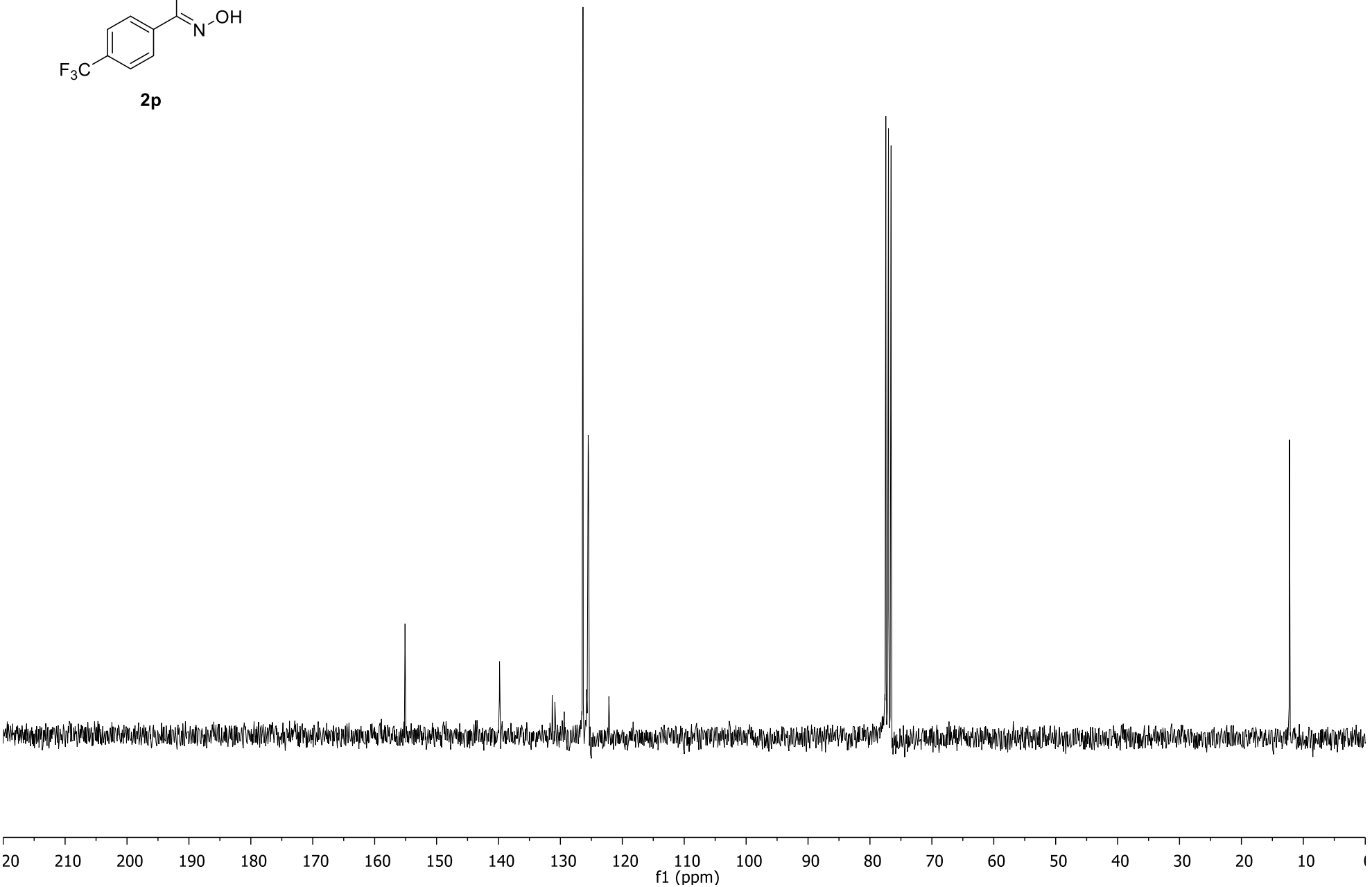
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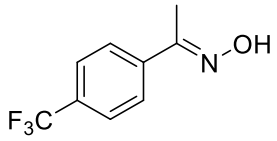
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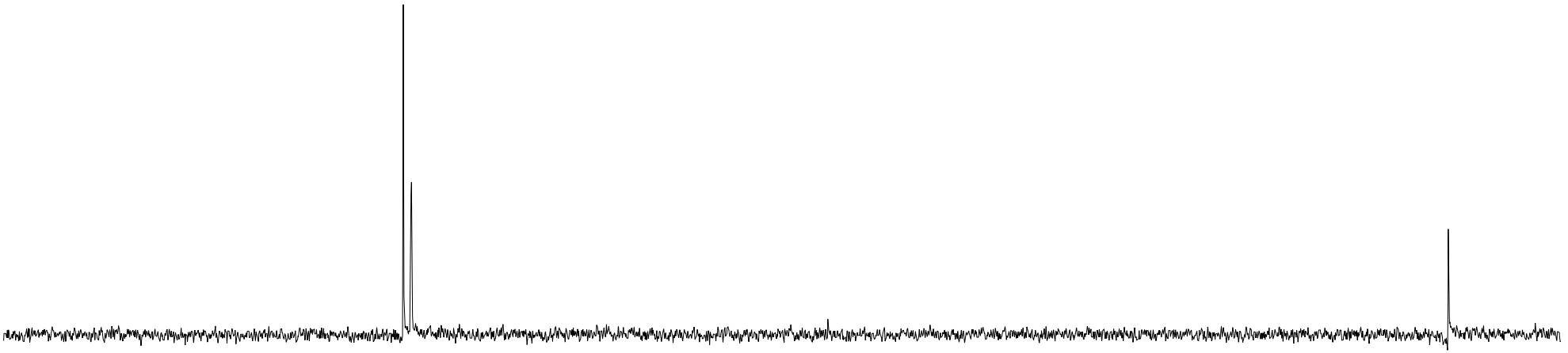
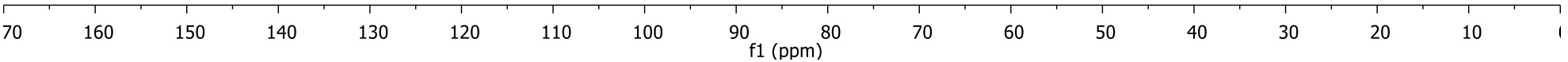
2p

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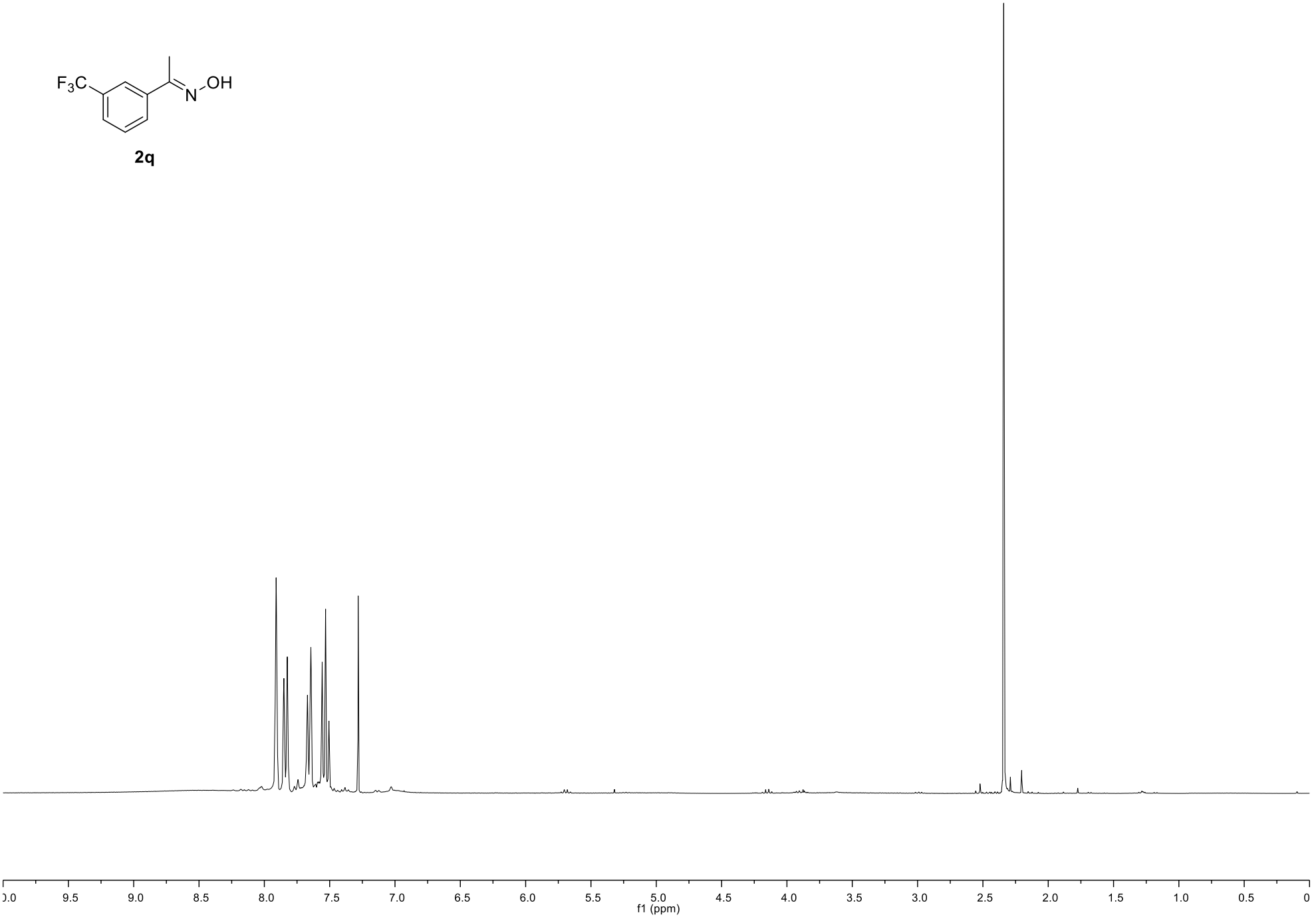
f1 (ppm)

F3C
N
OH

2q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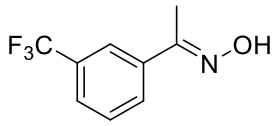
f1 (ppm)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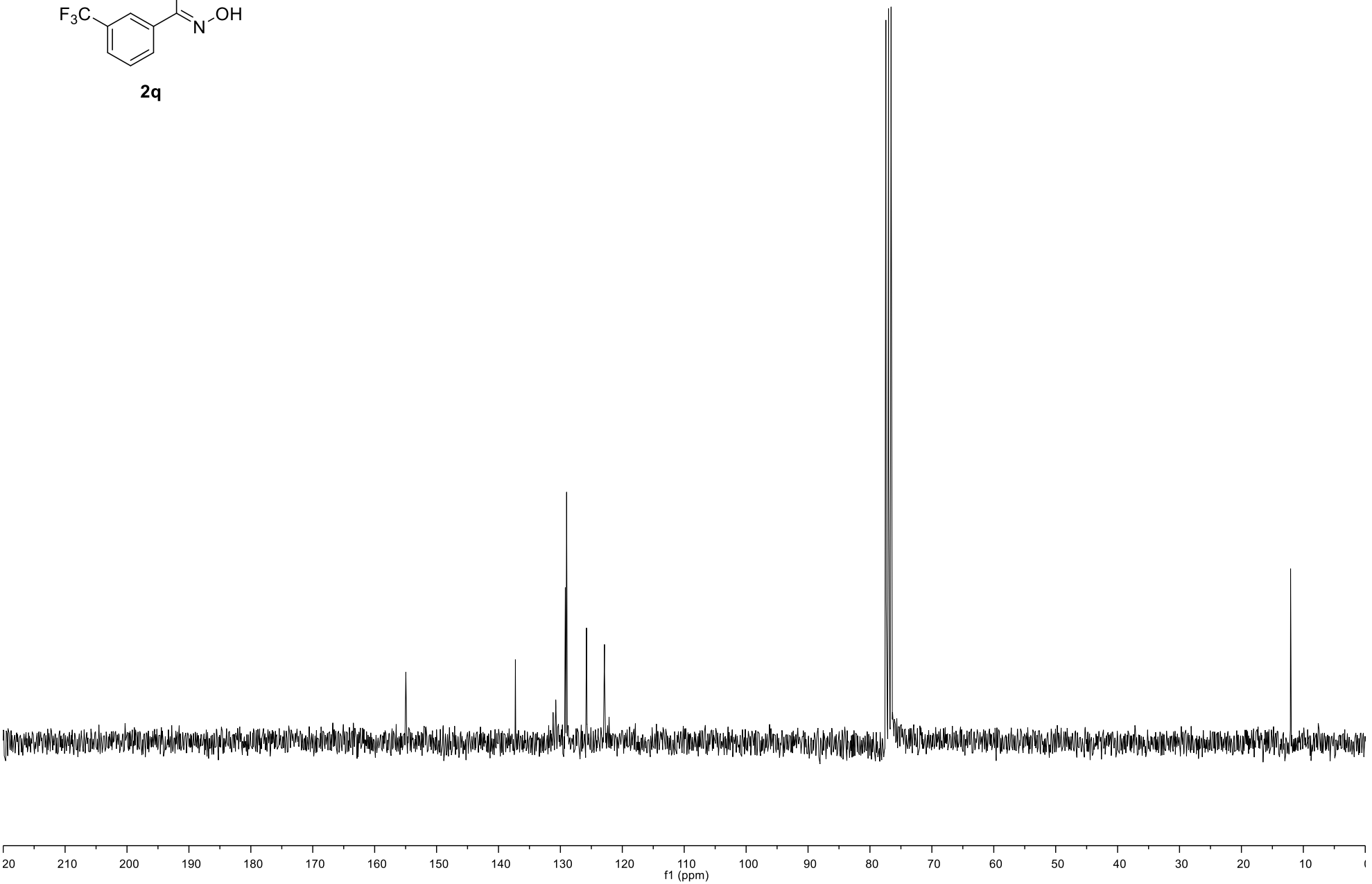
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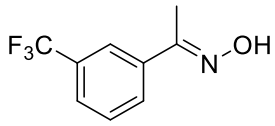
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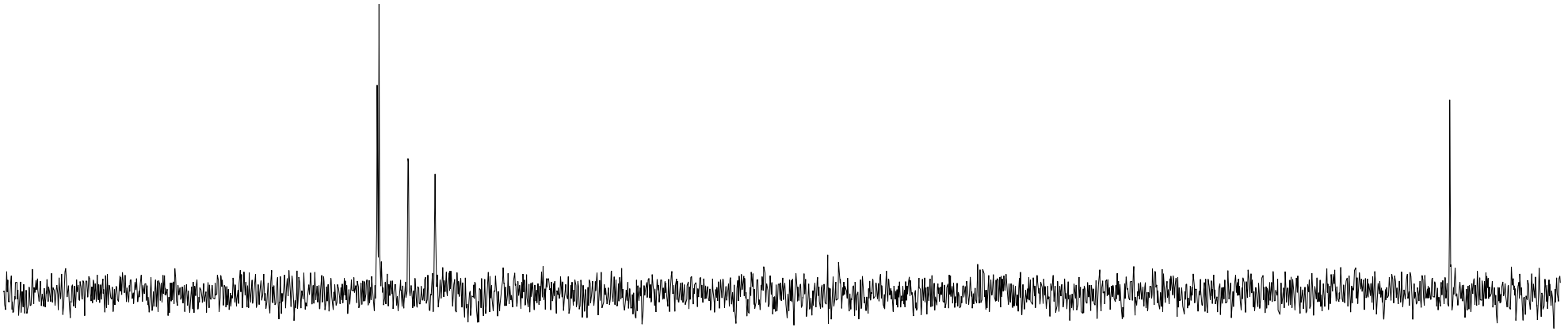

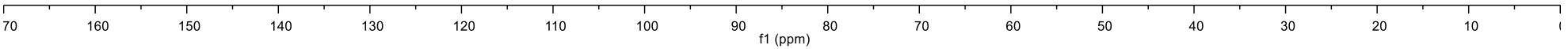
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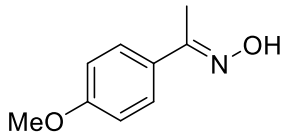
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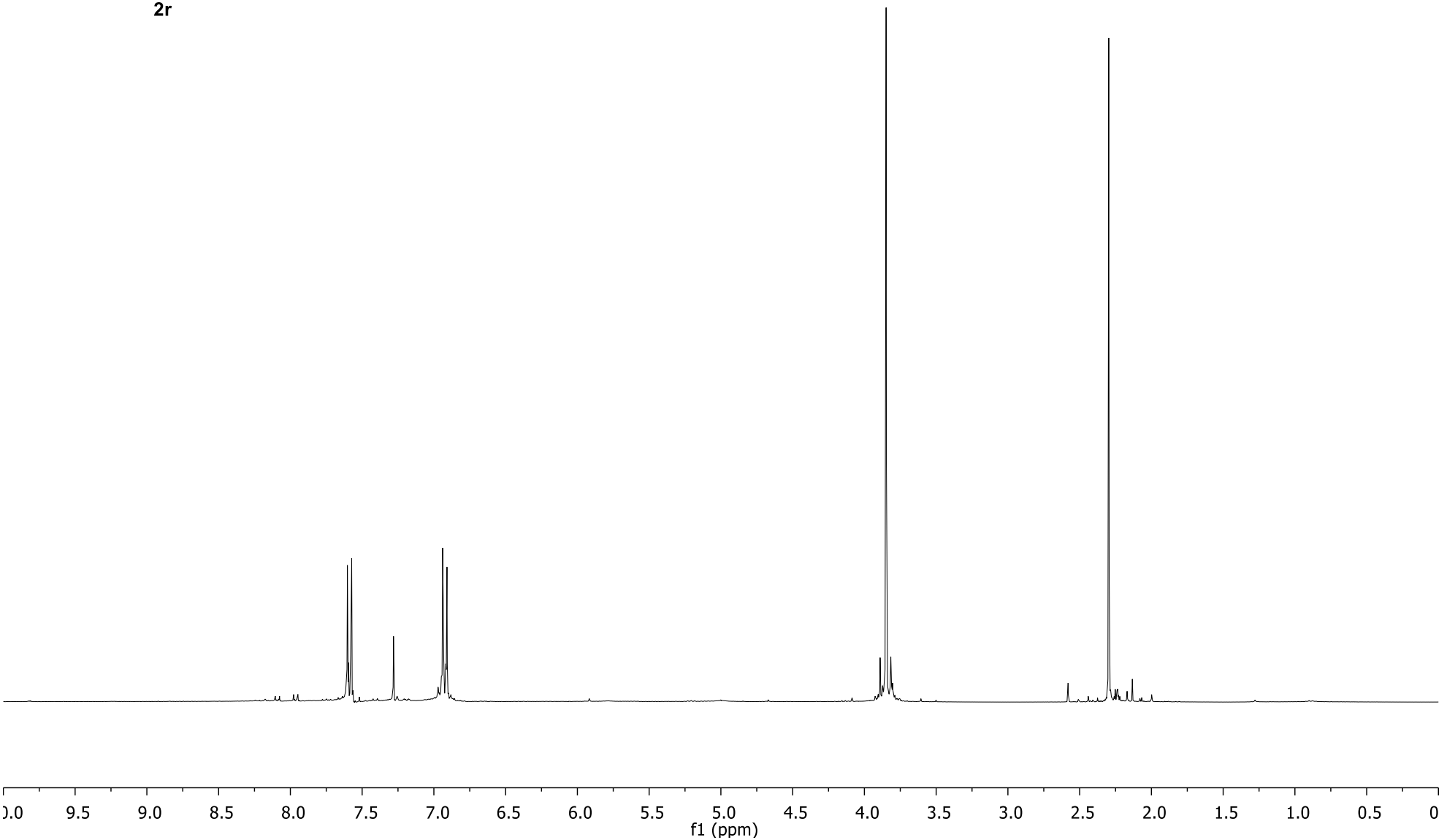
OH

2r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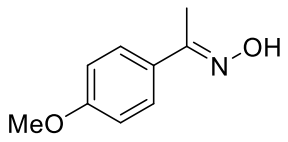
f1 (ppm)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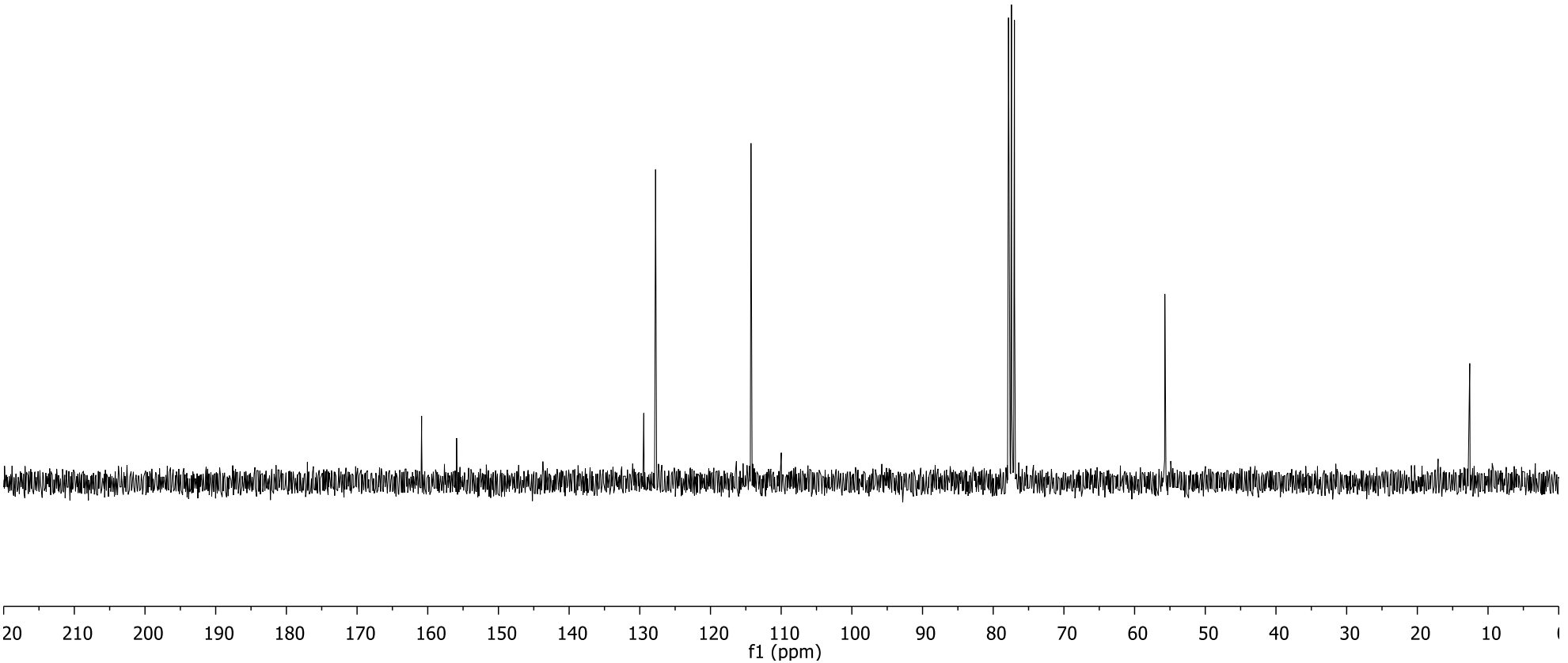
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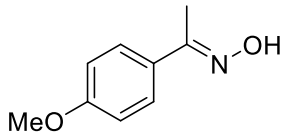
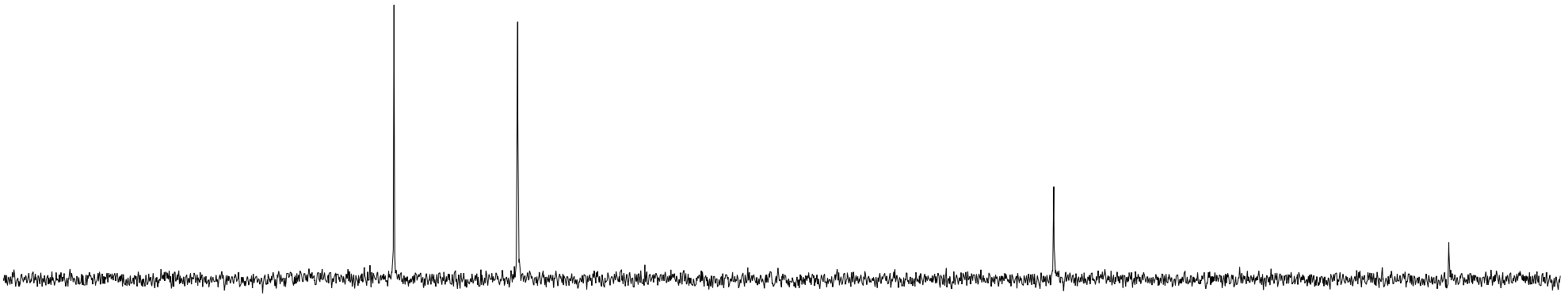
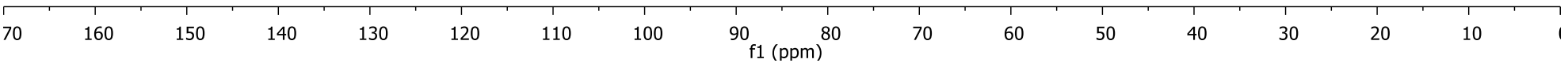

OH
N
MeO

2r

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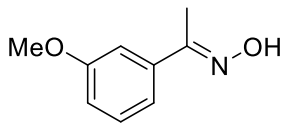
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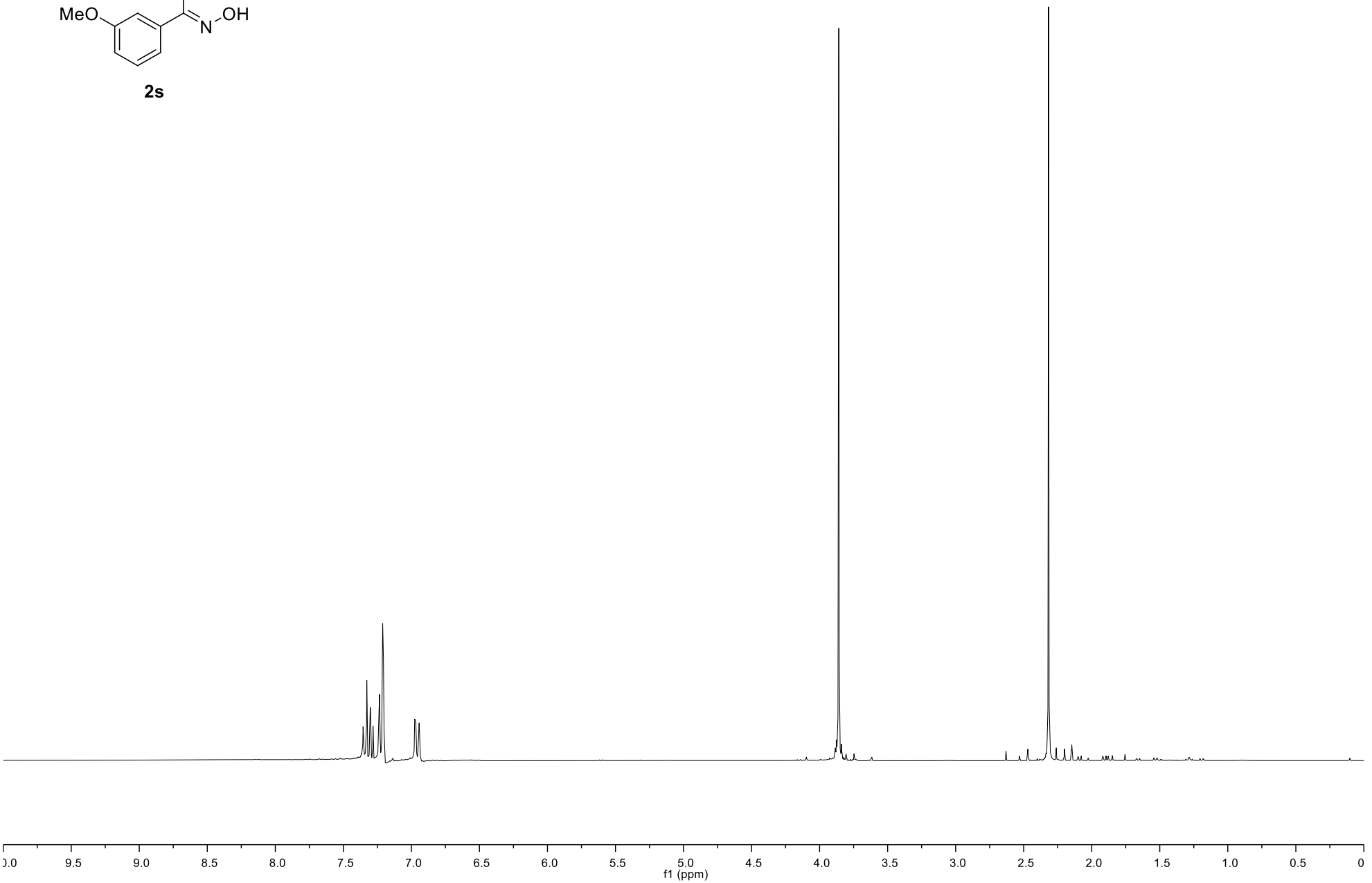
OH

2s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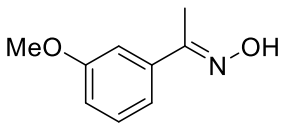
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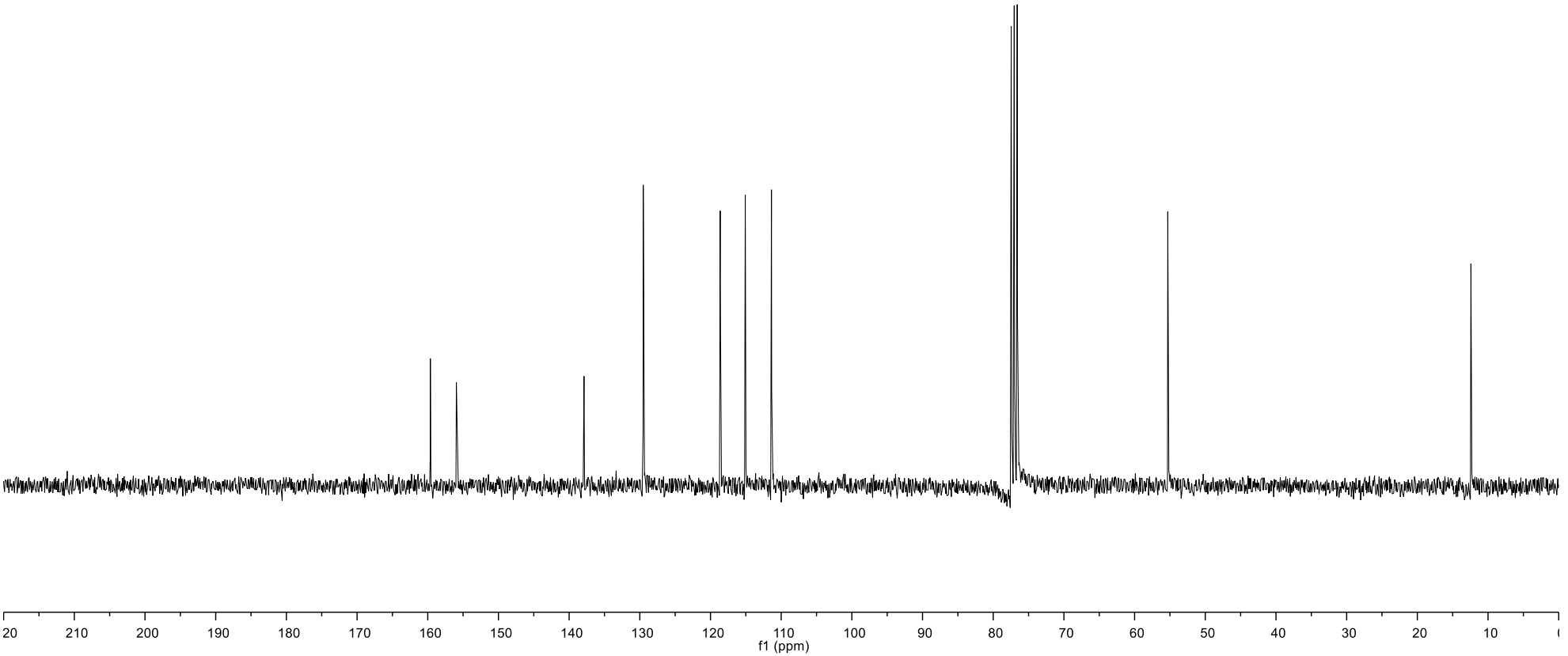
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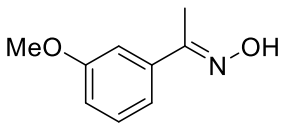
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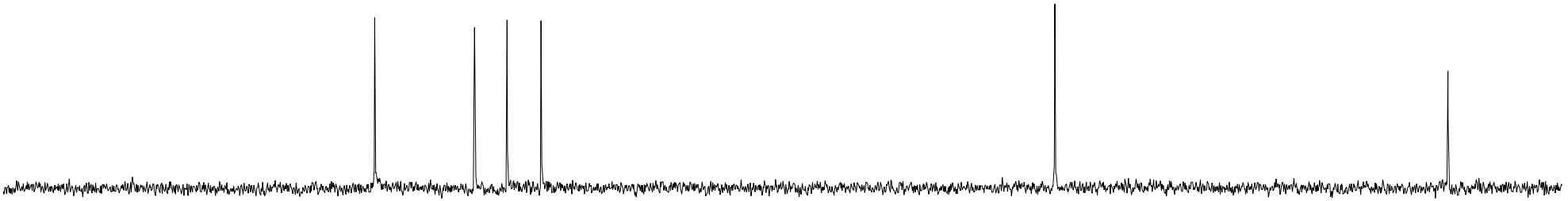

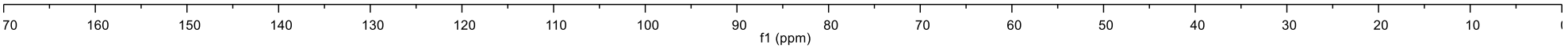
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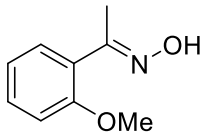
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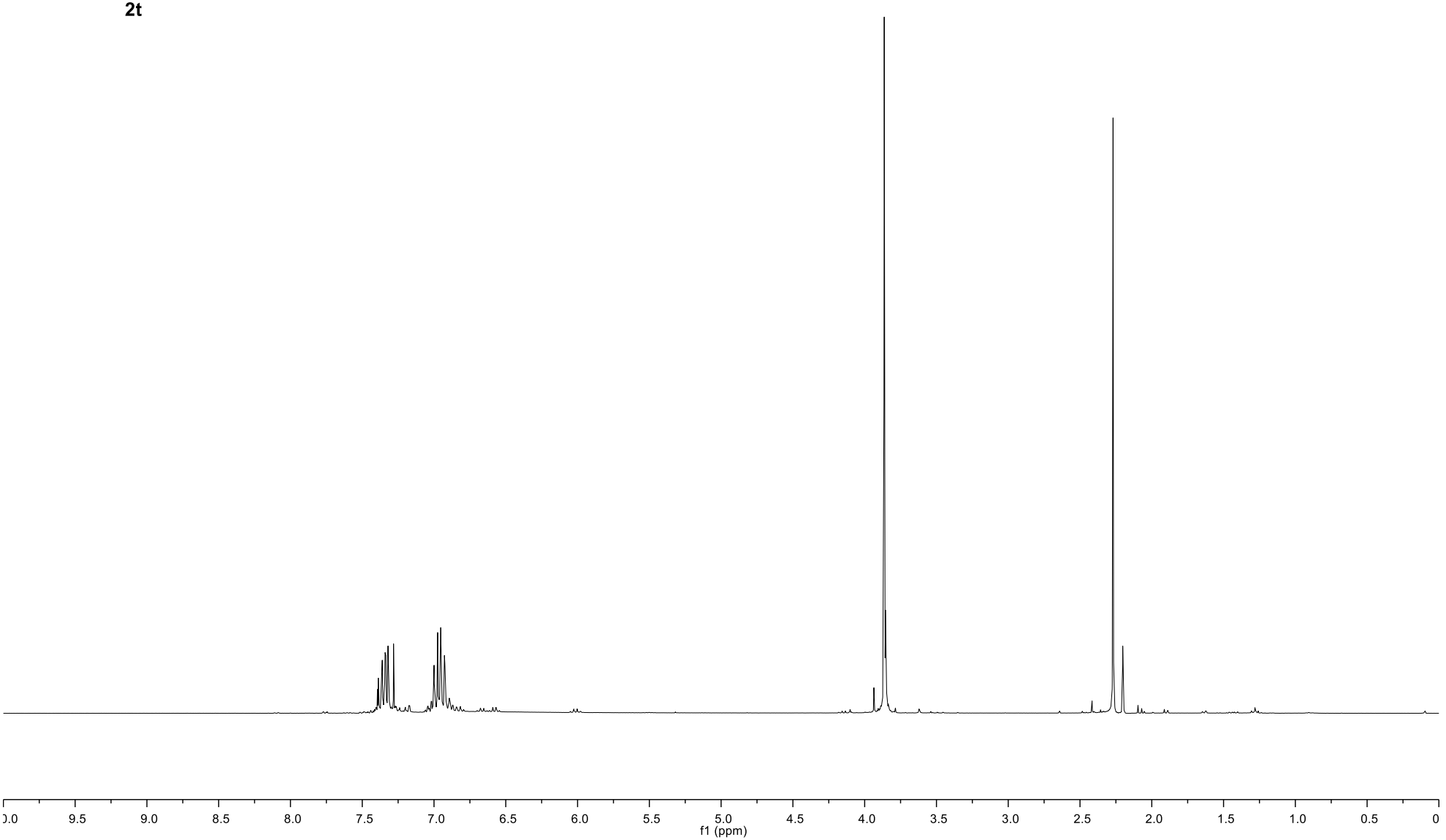
OH
OMe

2t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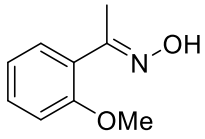
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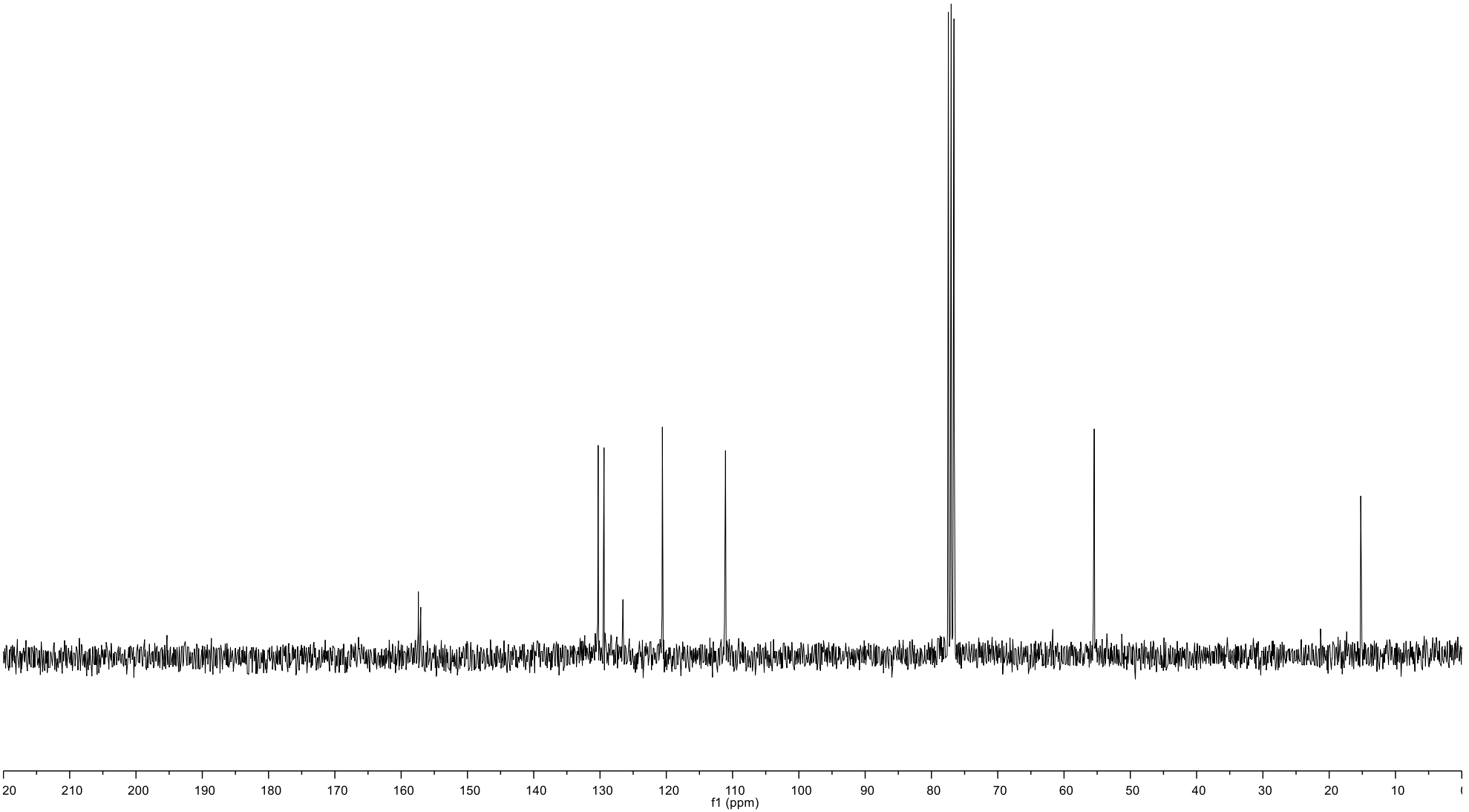
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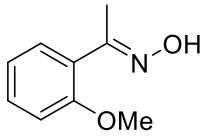
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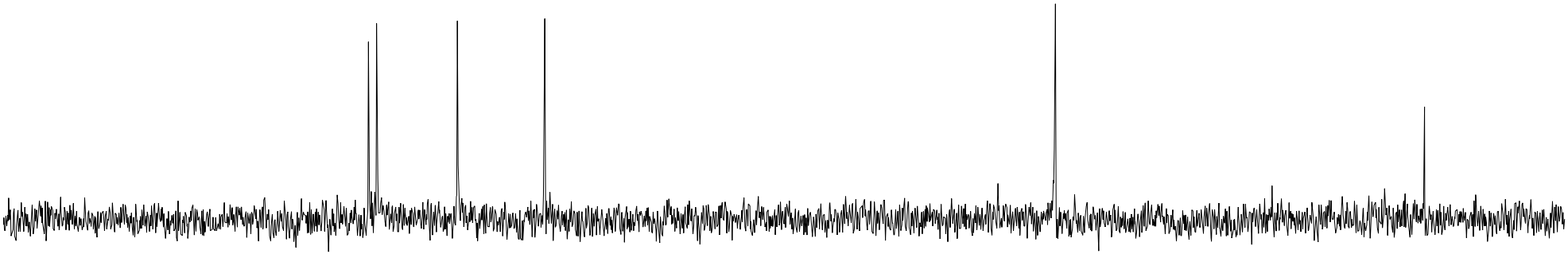

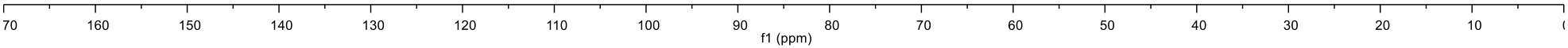
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