Trifluoromethyl Ketones from Enolizable Carboxylic Acids via Enediolate Trifluoroacetylation/Decarboxylation

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Supporting Information

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General. Compounds **2-16** were prepared according to the general procedure on 10.0 mmol scale and in the yields listed in Tables 1 and 2. ^{1}H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, in $CDCl_3$ unless indicated otherwise. Melting points are uncorrected. IR spectra were recorded neat.

References for known compounds:

Compounds **2**, **4**, **12** and **13**: Reeves, J. T.; Gallou, F.; Song, J. J.; Tan, Z.; Lee, H.; Yee, N. K.; Senanayake, C. H. *Tetrahedron Lett.* **2007**, *48*, 189-192.

Compound **3**: Yang, D.; Wong, M.-K.; Wang, X.-C.; Tang, Y.-C. *J. Am. Chem. Soc.* **1998**, *120*, 6611-6612.

Compound **5**: Greif, D.; Riedel, D.; Feindt, A.; Pulst, M. *J. Prakt. Chem.* **1995**, *337*, 34-37.

Compound **8**: Linderman, R. J.; Graves, D. M. *J. Org. Chem.* **1989**, *54*, 661-668.

Compounds **9** and **15**: Qiu, W.; Shen, Y. *J. Fluorine Chem.* **1988**, *38*, 249-256.

Compound **14**: Hornyak, G.; Fetter, J.; Nemeth, G.; Poszavacz, L.; Simig, G. *J. Fluorine Chem.* **1997**, *84*, 49-51.

Compound **16**: Kimura, M.; Tominaga, T.; Kitazume, T. *J. Fluorine Chem.* **2005**, *126*, 135-139.

General procedure for conversion of carboxylic acids to trifluoromethyl ketones. 2,2,2-Trifluoro-1-indan-2-yl-ethanone (11). To a solution of indane-2-carboxylic acid (1.62 g, 10.0 mmol) in THF (20 mL) at -20 °C was added dropwise LDA (14.7 mL, 22.0 mmol, 1.5 M in cyclohexane) over 10 min. The temperature of the reaction mixture was allowed to rise to 10 °C during the addition of LDA. The reaction mixture was then aged at 20 °C for 4 h. In a separate flask, a solution of ethyl trifluoroacetate (3.6 mL, 30.0 mmol) and THF (10 mL) was cooled to -65 °C. The enediolate solution was added dropwise via cannula to the ethyl trifluoroacetate solution. Upon completion of the addition, the reaction mixture was aged for 15 min at -65 °C and then quenched with 6 N HCl (20 mL) [Caution: CO_2 is evolved during the quench]. The reaction mixture is diluted with EtOAc (10 mL), the layers are separated, and the organic phase dried over $MgSO_4$, filtered and concentrated. Column chromatography on SiO_2 (hexanes) gave **11** (1.48 g, 69% yield) as a colorless oil.

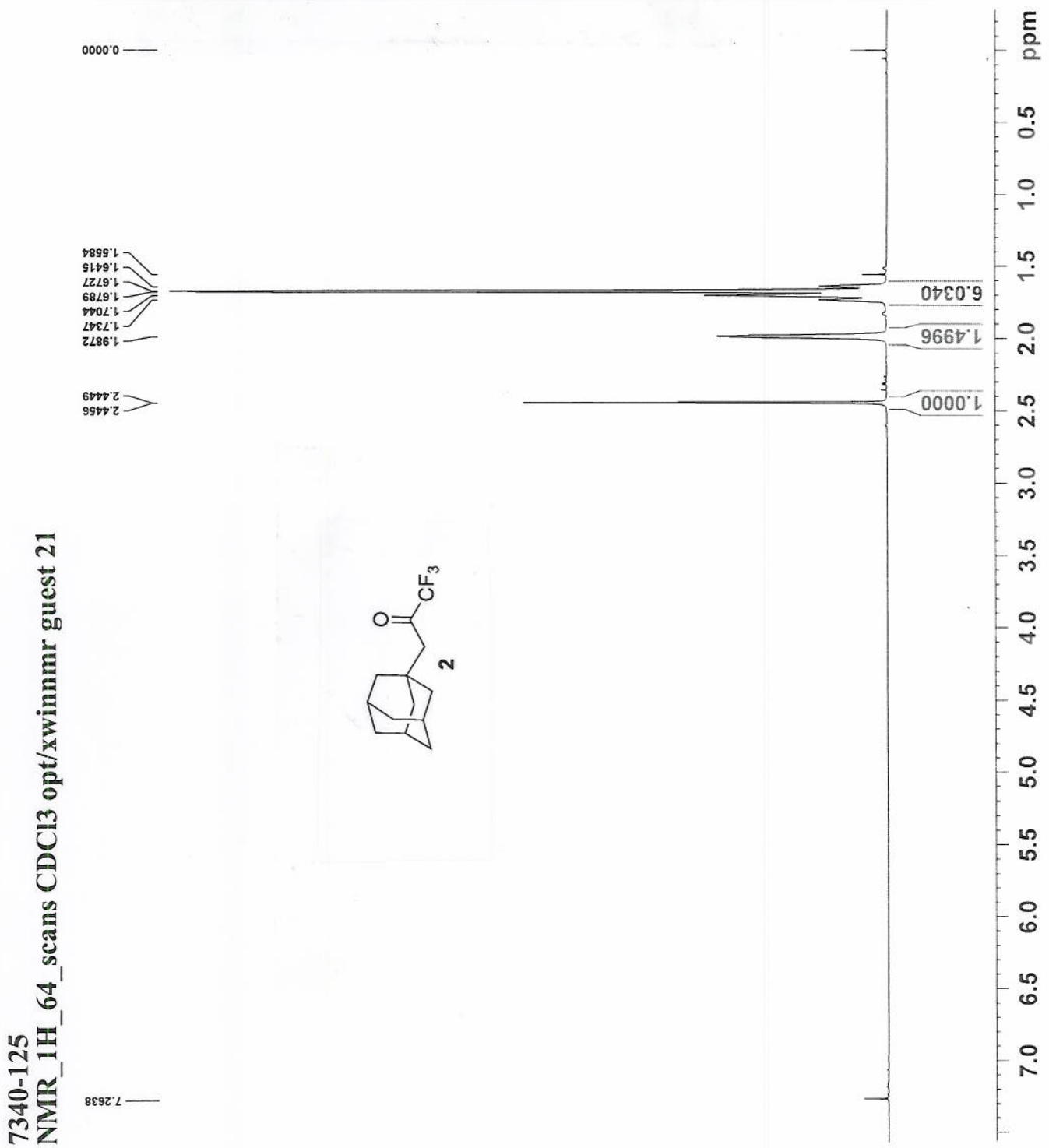
Data for 6,7,10 & 11:

1,1,1-Trifluoro-12-phenoxydodecan-2-one (6). White solid; mp 61-63 °C; IR 2916, 2852, 1755, 1603, 1587, 1497, 1473, 1246, 1149 cm^{-1}; ^1H NMR δ 7.21-7.14 (m, 2 H), 6.85-6.79 (m, 3 H), 3.86 (t, J = 6.6 Hz, 2 H), 2.60 (t, J = 7.2 Hz, 2 H), 1.72-1.65 (m, 2 H), 1.59-1.50 (m, 2 H), 1.40-1.33 (m, 2 H), 1.26-1.18 (m, 10 H); ^{13}C NMR δ 191.6 (q, J = 35 Hz), 159.2, 129.4, 120.5, 115.6 (q, J = 291 Hz), 114.5, 67.8, 36.4, 29.5, 29.4, 29.3, 29.2, 28.7, 26.1, 22.4; Anal. calcd for $C_{18}H_{25}F_3O_2$: C, 65.44; H, 7.63. Found: C, 65.70; H, 7.78.

13-(*tert*-butyldimethylsilyloxy)-1,1,1-trifluorotridecan-2-one (7). Colorless oil; IR 2932, 1760, 1472, 1140 cm^{-1}; ^1H NMR δ 3.55 (t, J = 8.0 Hz, 2 H), 2.65 (t, J = 8.0 Hz, 2 H), 1.66-1.59 (m, 2 H), 1.48-1.43 (m, 2 H), 1.31-1.20 (m, 14 H), 0.85 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR δ 191.6 (q, J = 35 Hz), 115.6 (q, J = 291 Hz), 63.3, 36.4, 32.9, 29.5, 29.43, 29.38, 29.3, 29.1, 28.7, 26.0, 25.8, 22.4, 18.4, -5.3; Anal. calcd for $C_{19}H_{37}F_3O_2Si$: C, 59.65; H, 9.75. Found: C, 59.78; H, 9.69.

1-Cyclododecyl-2,2,2-trifluoroethanone (10). Colorless oil; IR 2959, 2865, 1756, 1471, 1203, 1143 cm^{-1}; ^1H NMR δ 3.10-3.04 (m, 1 H), 1.74-1.60 (m, 4 H), 1.47-1.28 (m, 18 H); ^{13}C NMR δ 195.3 (q, J = 32 Hz), 115.8 (q, J = 321 Hz), 42.2, 29.7, 23.5, 23.44, 23.40, 23.3, 22.3; Anal. calcd for $C_{14}H_{23}F_3O$: C, 63.61; H, 8.77. Found: C, 63.80; H, 8.65.

2,2,2-Trifluoro-1-indan-2-yl-ethanone (11). Colorless oil; IR 3028, 2955, 2859, 1755, 1486, 1450, 1205, 1115 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.24-7.14 (m, 4 H), 3.80 (p, J = 8.7 Hz, 1 H), 3.34-3.23 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.7 (q, J = 34 Hz), 140.2, 126.9, 124.3, 115.9 (q, J = 290 Hz), 45.5, 34.9; Anal. calcd for $C_{11}H_9F_3O$: C, 61.68; H, 4.24. Found: C, 61.39; H, 4.13.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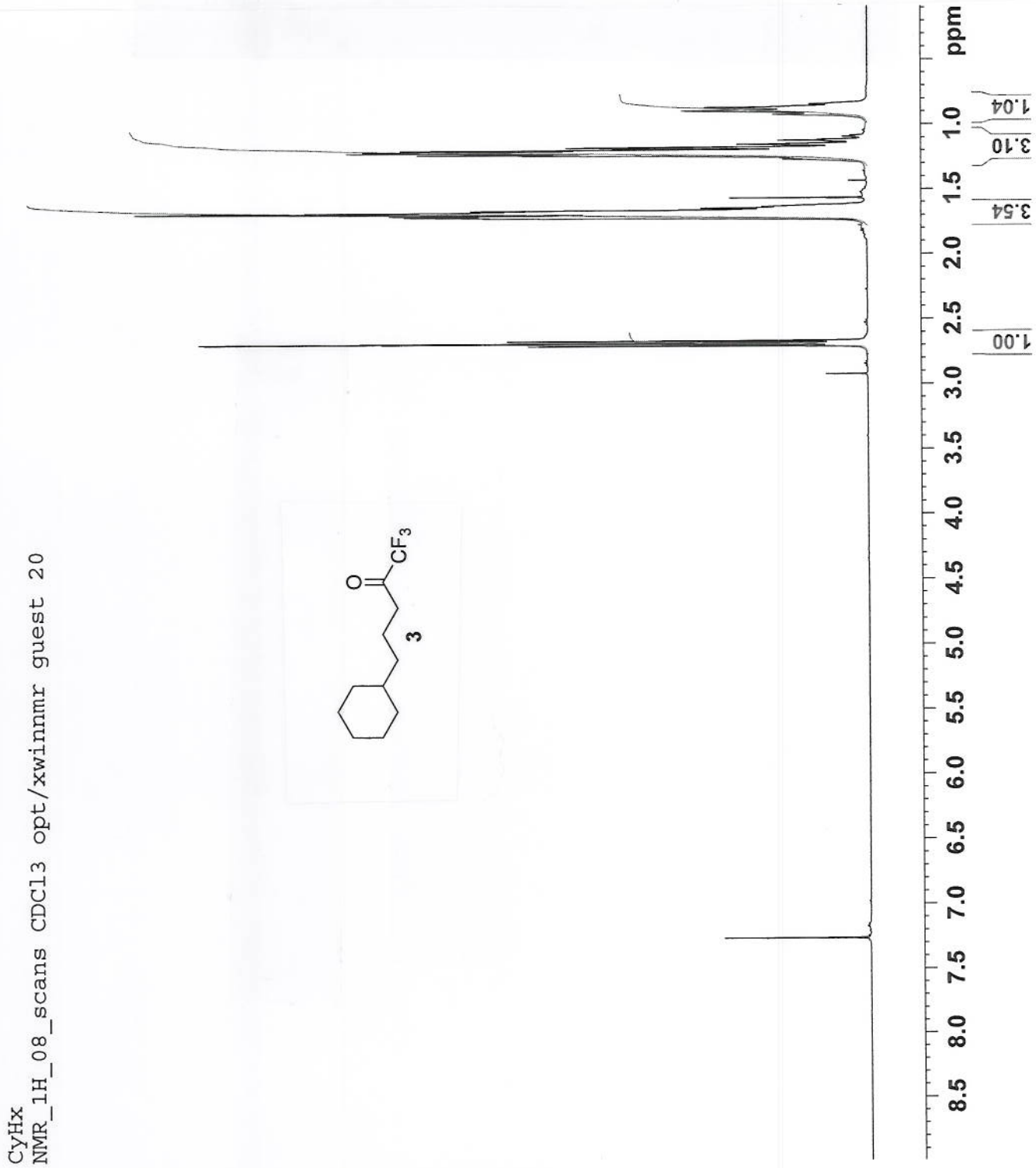
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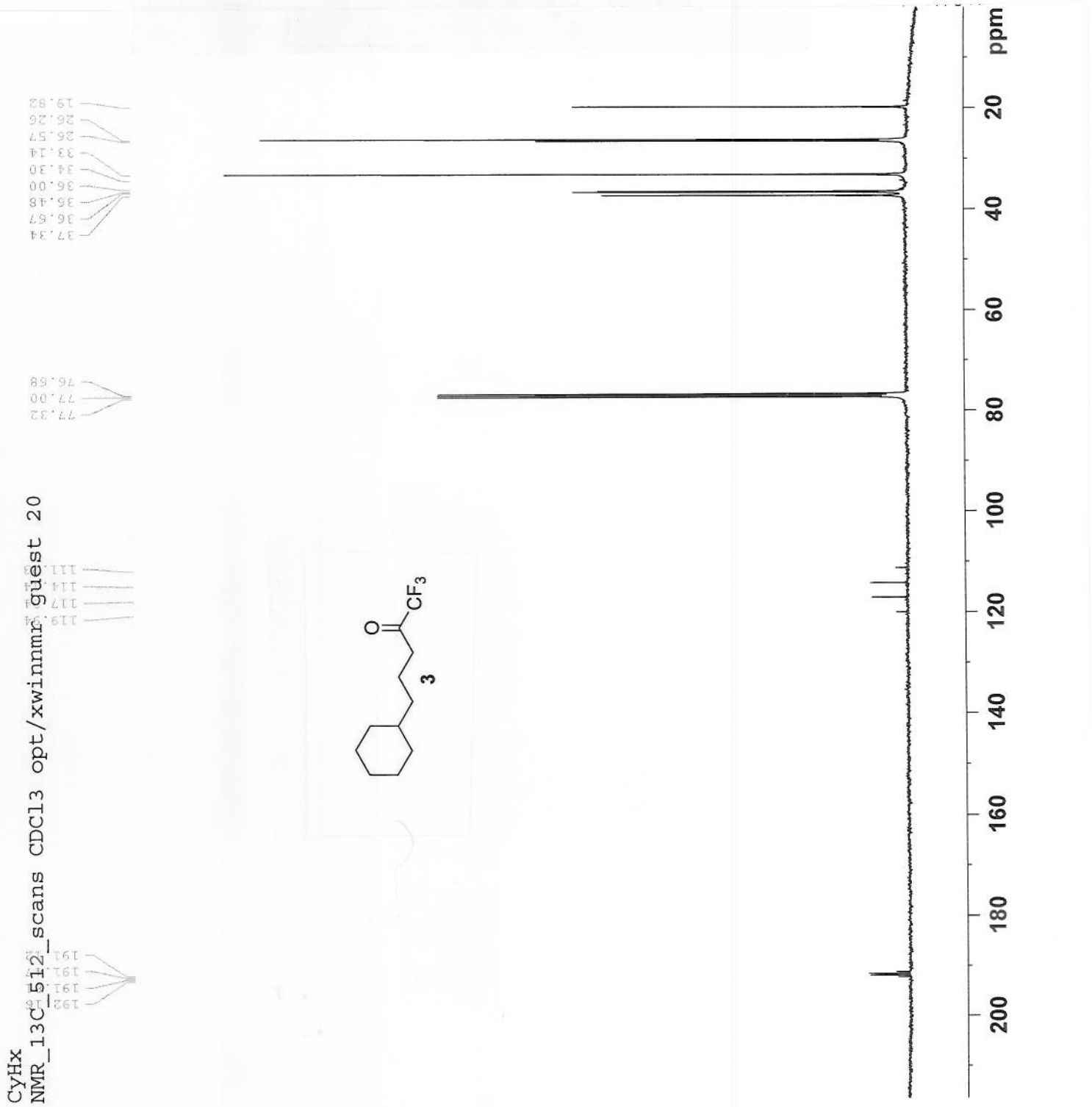
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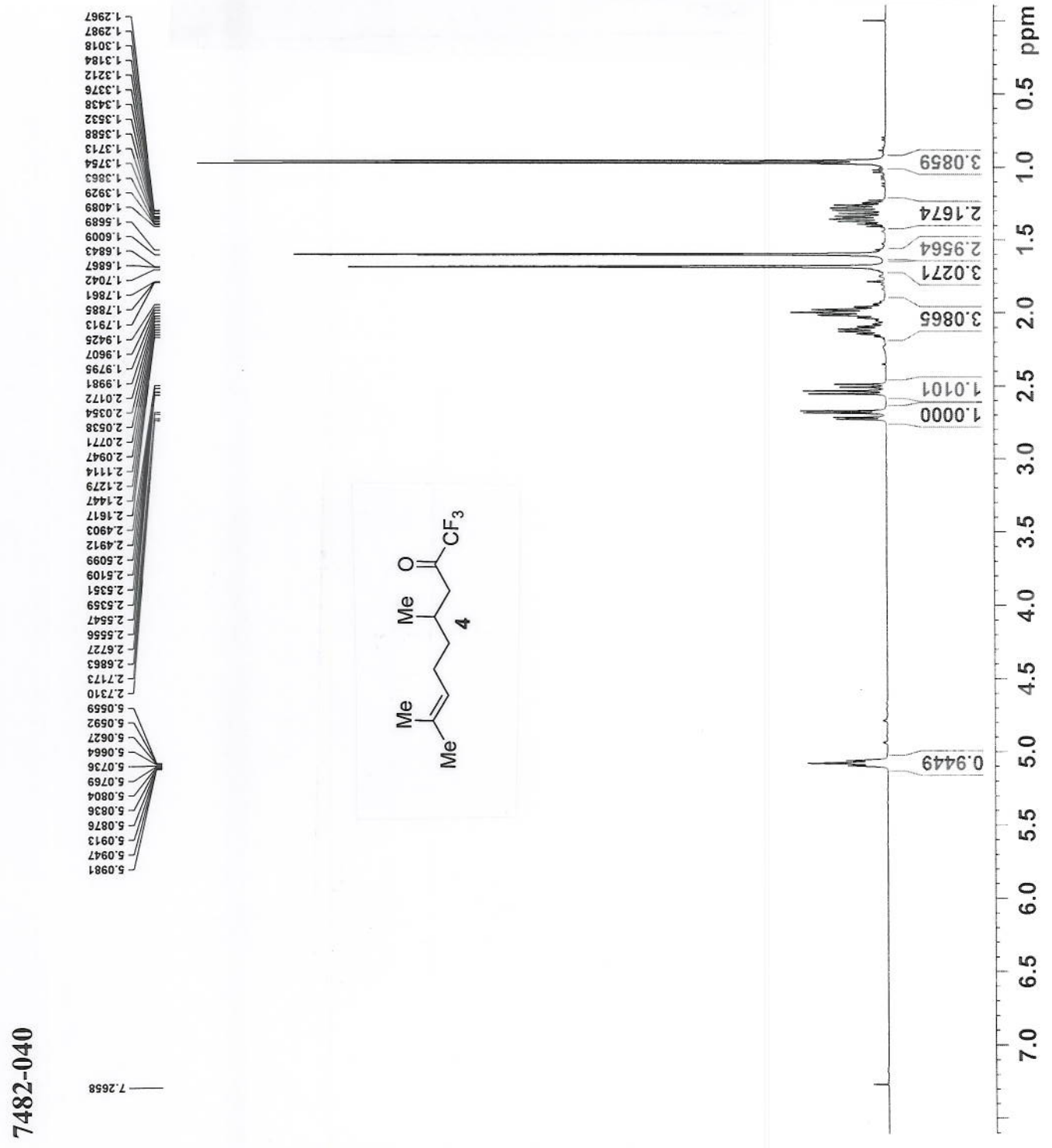
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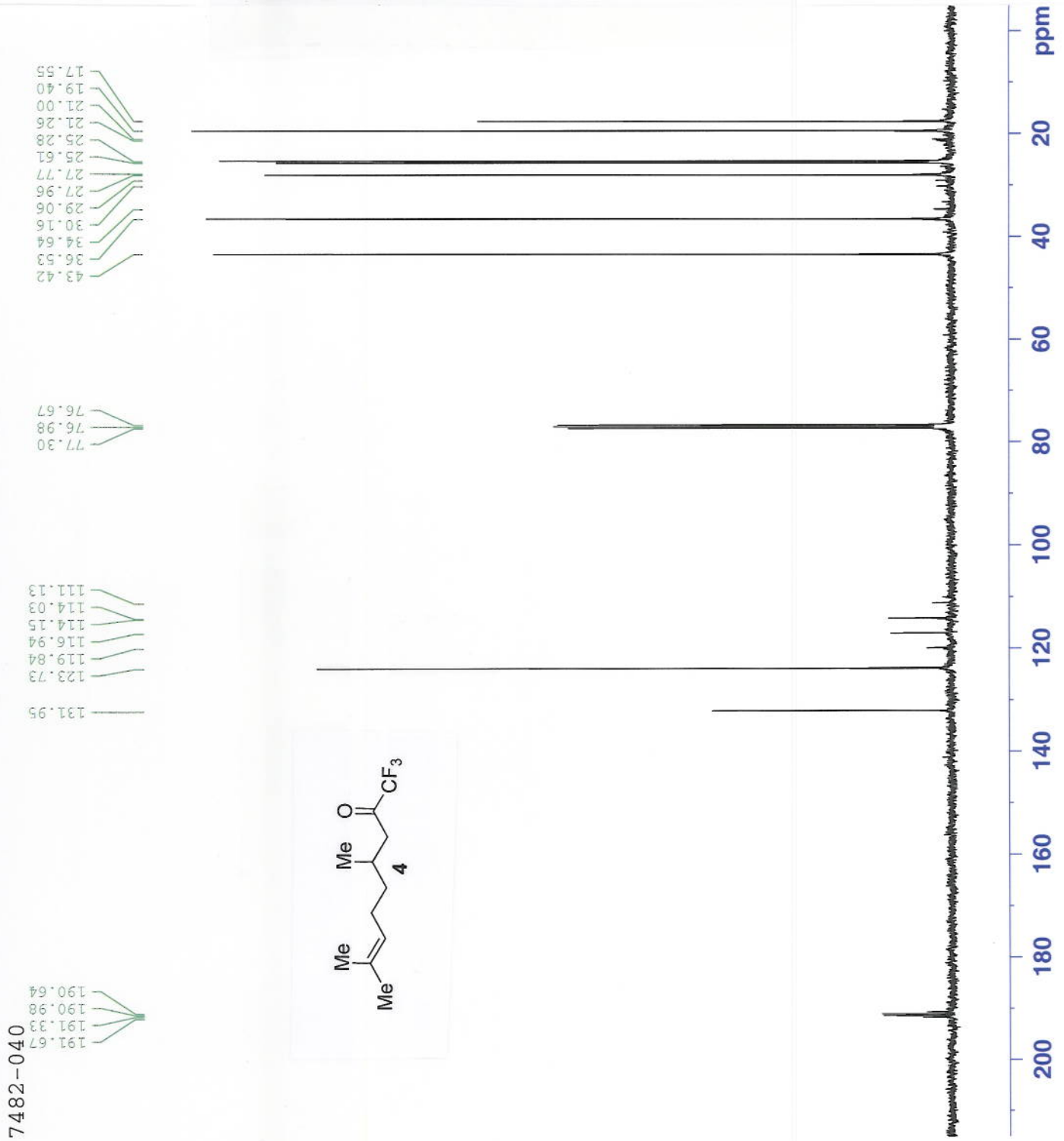
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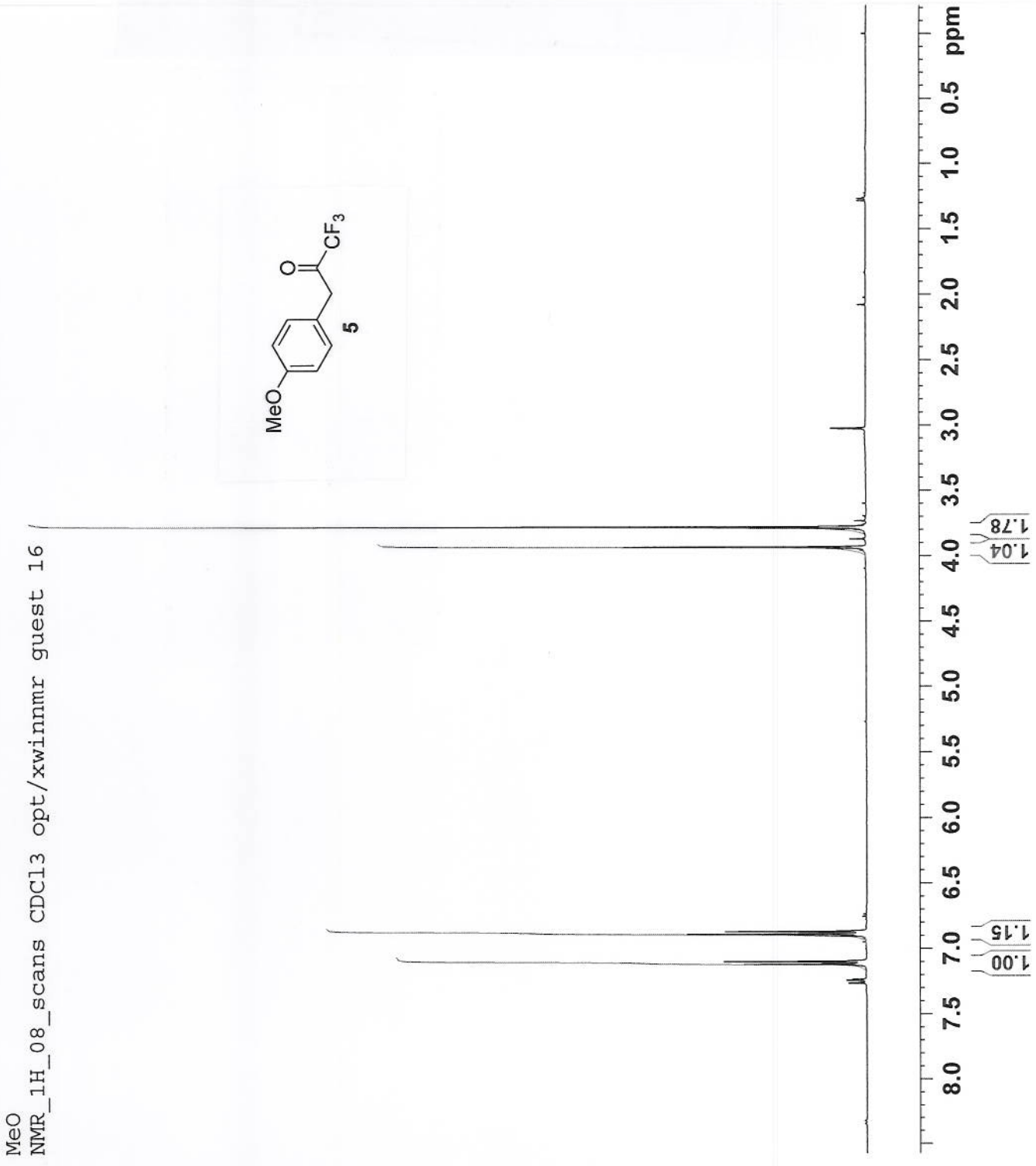
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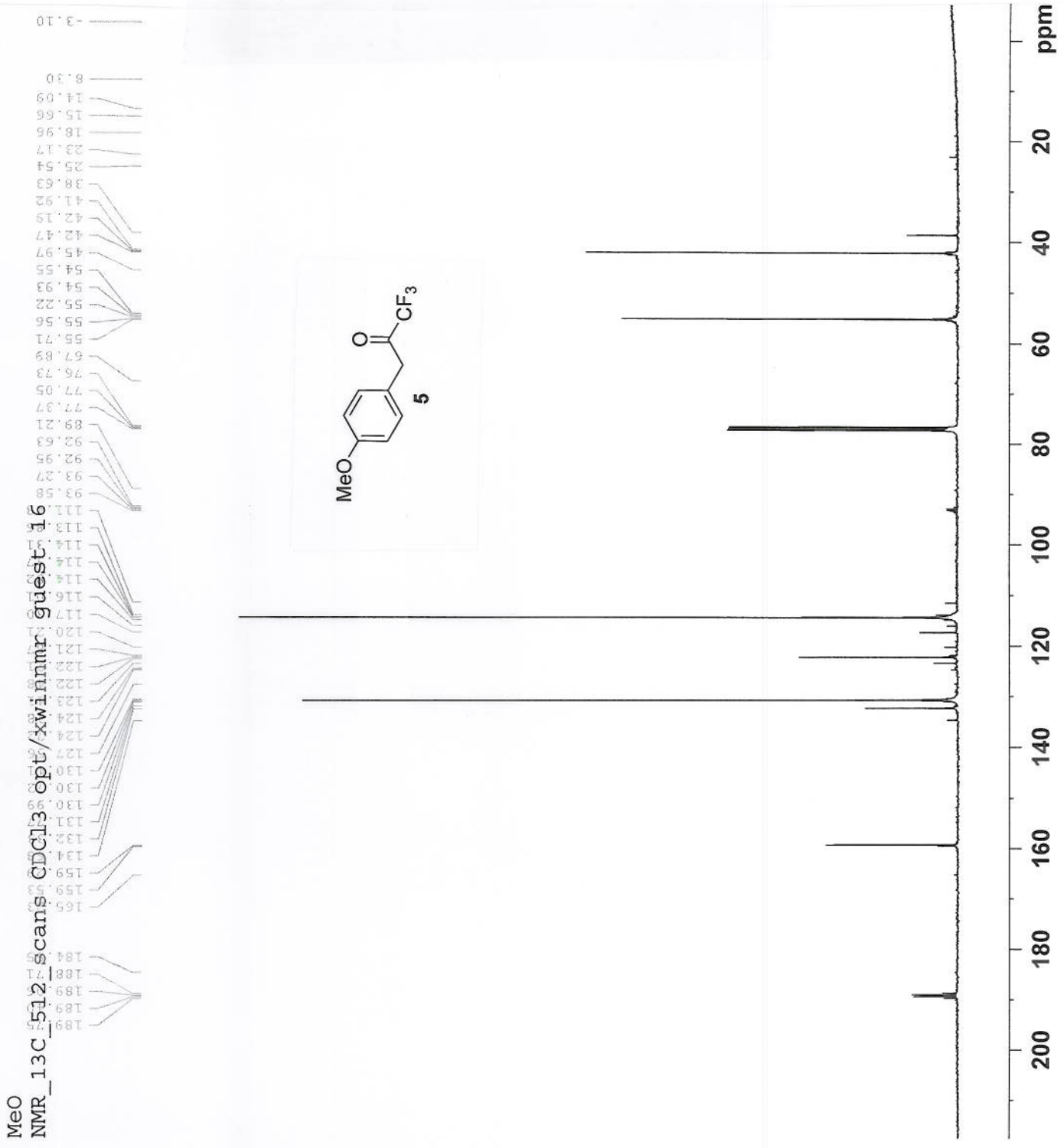
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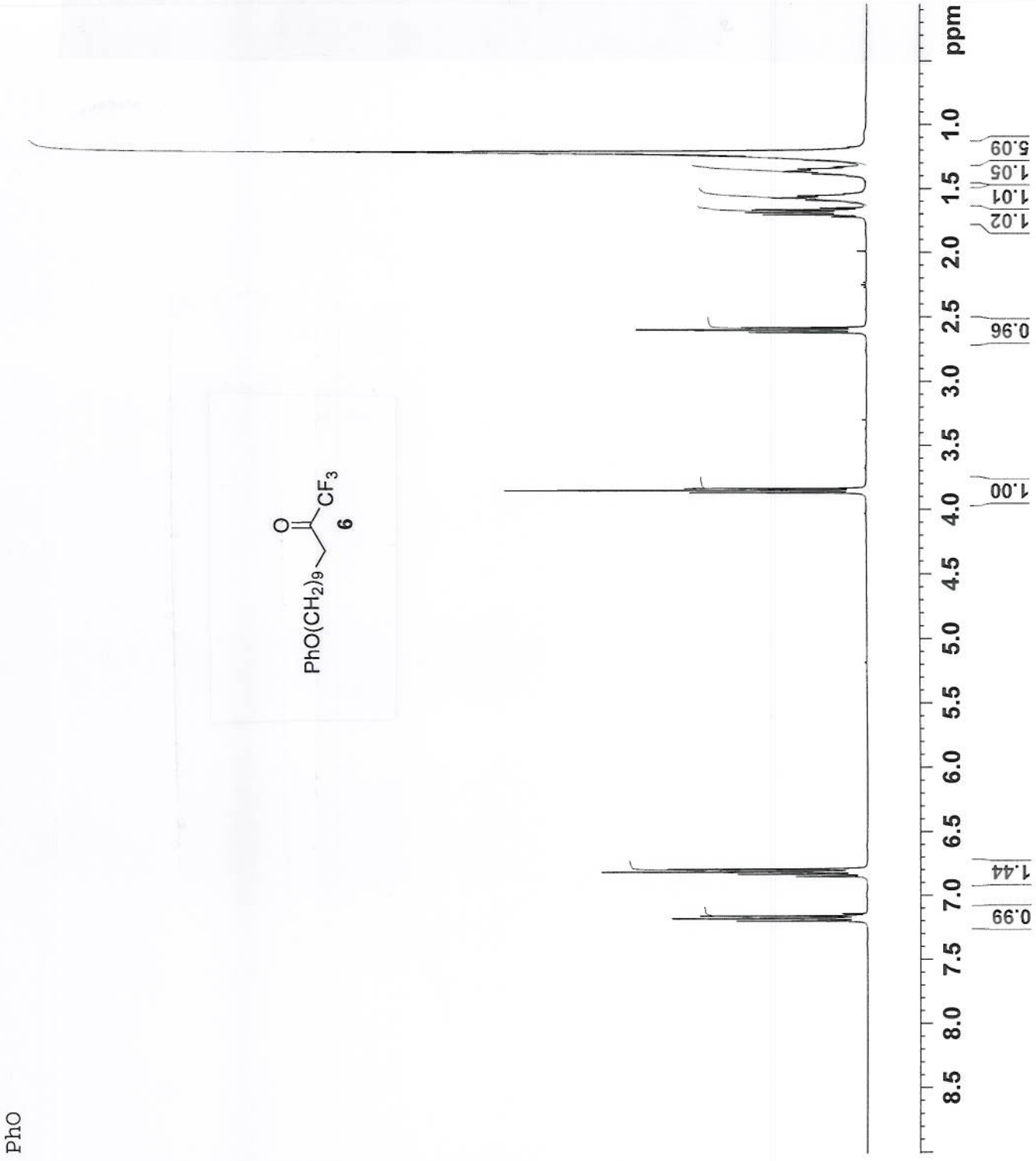
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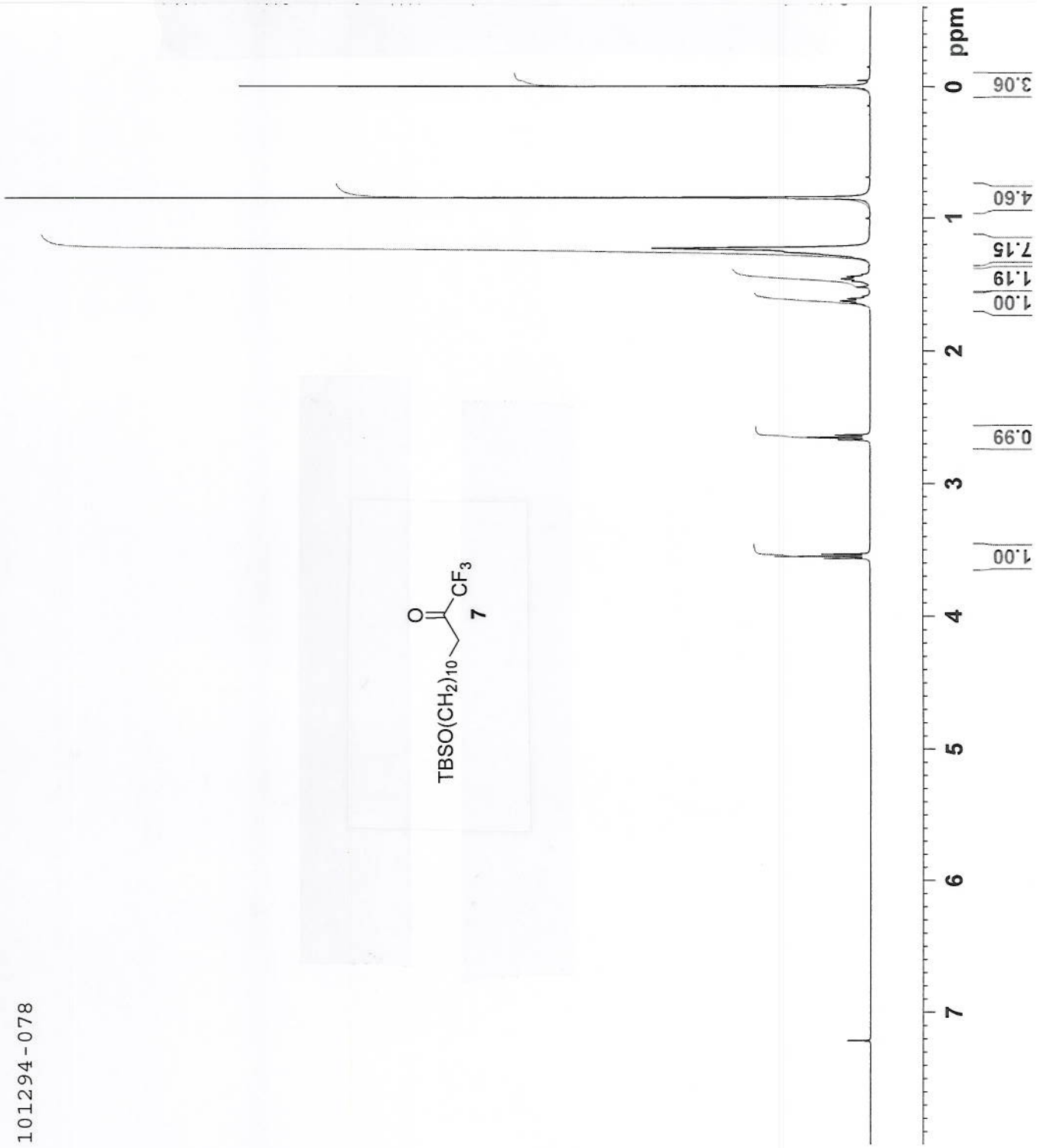
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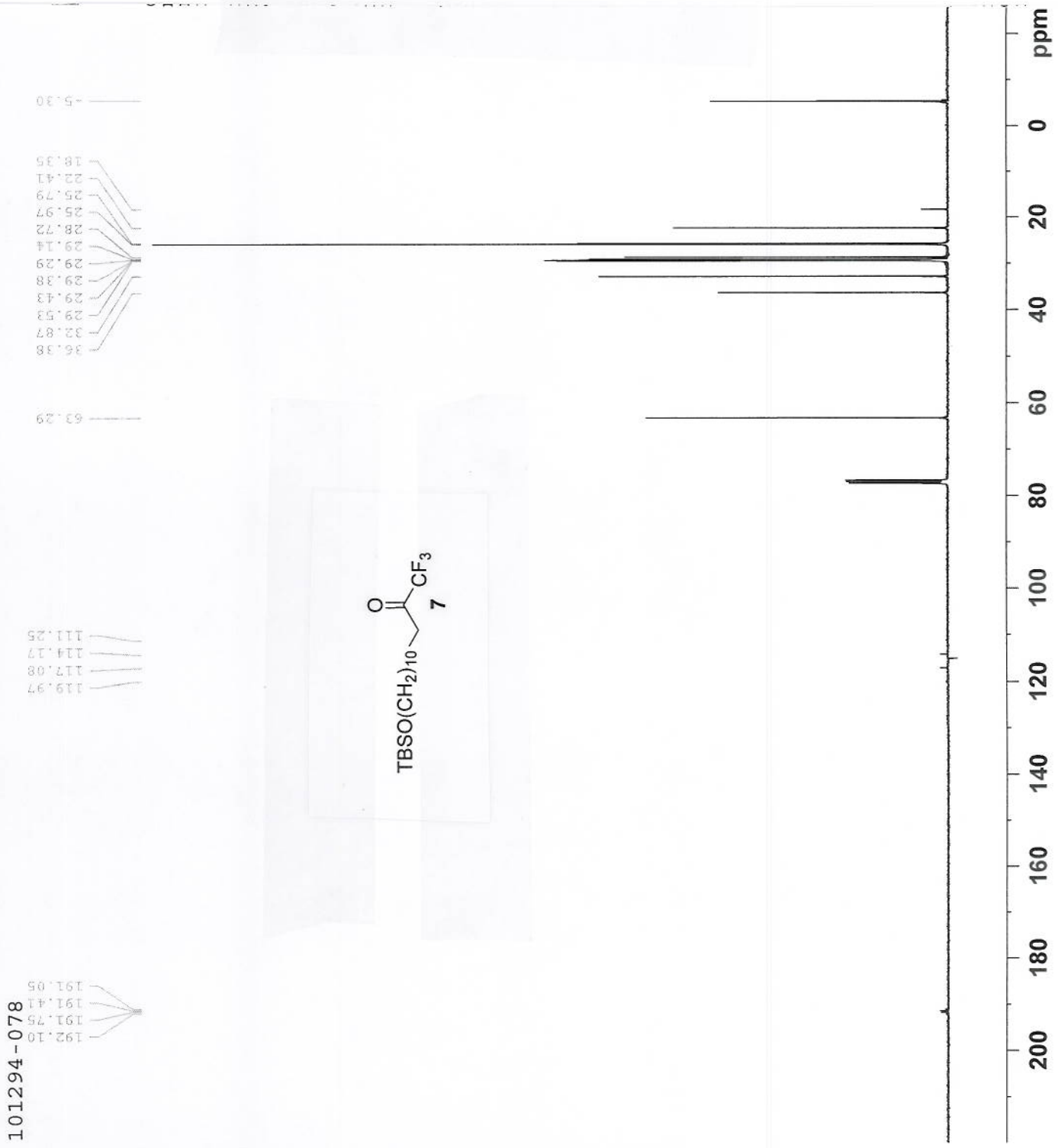
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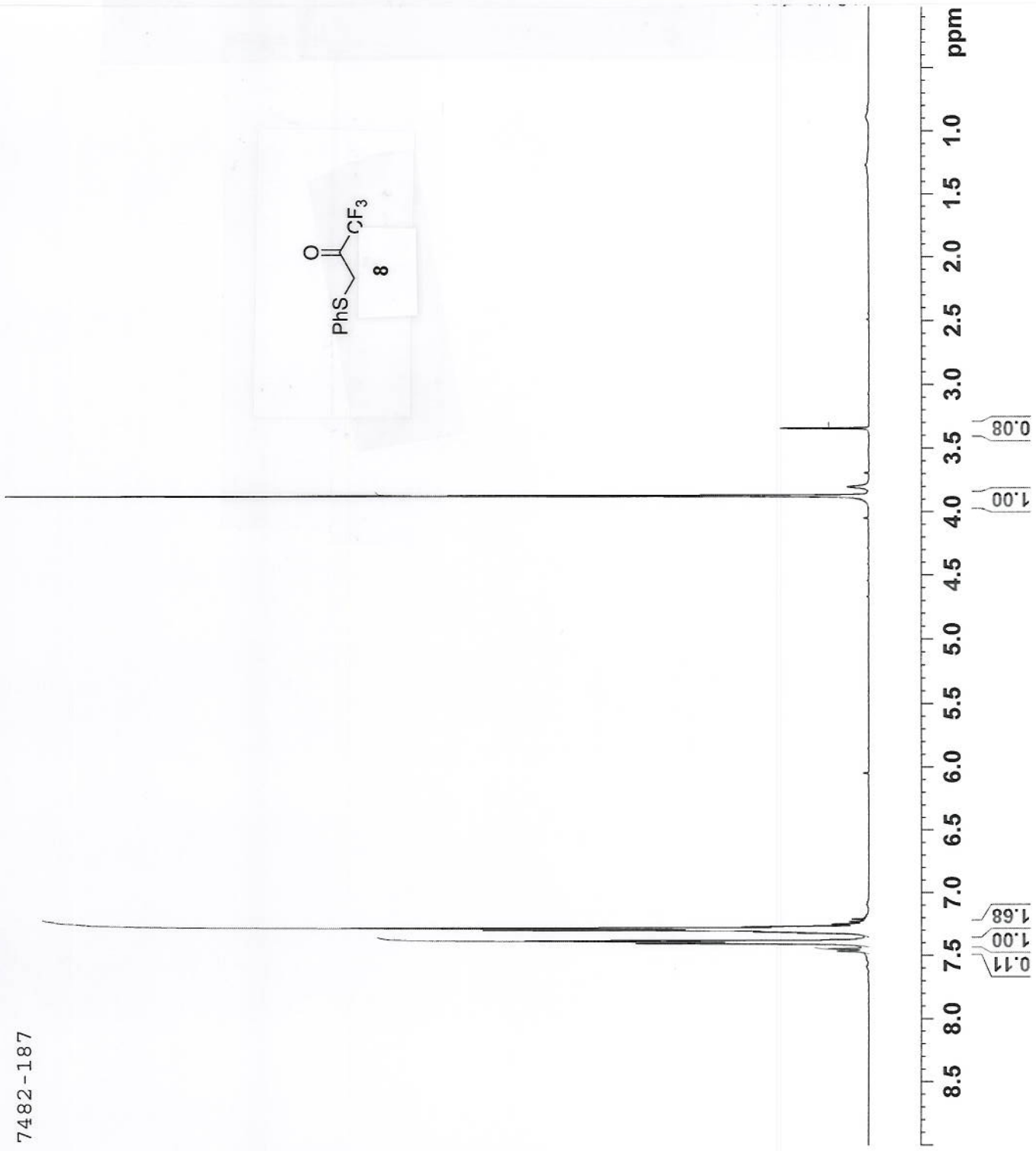
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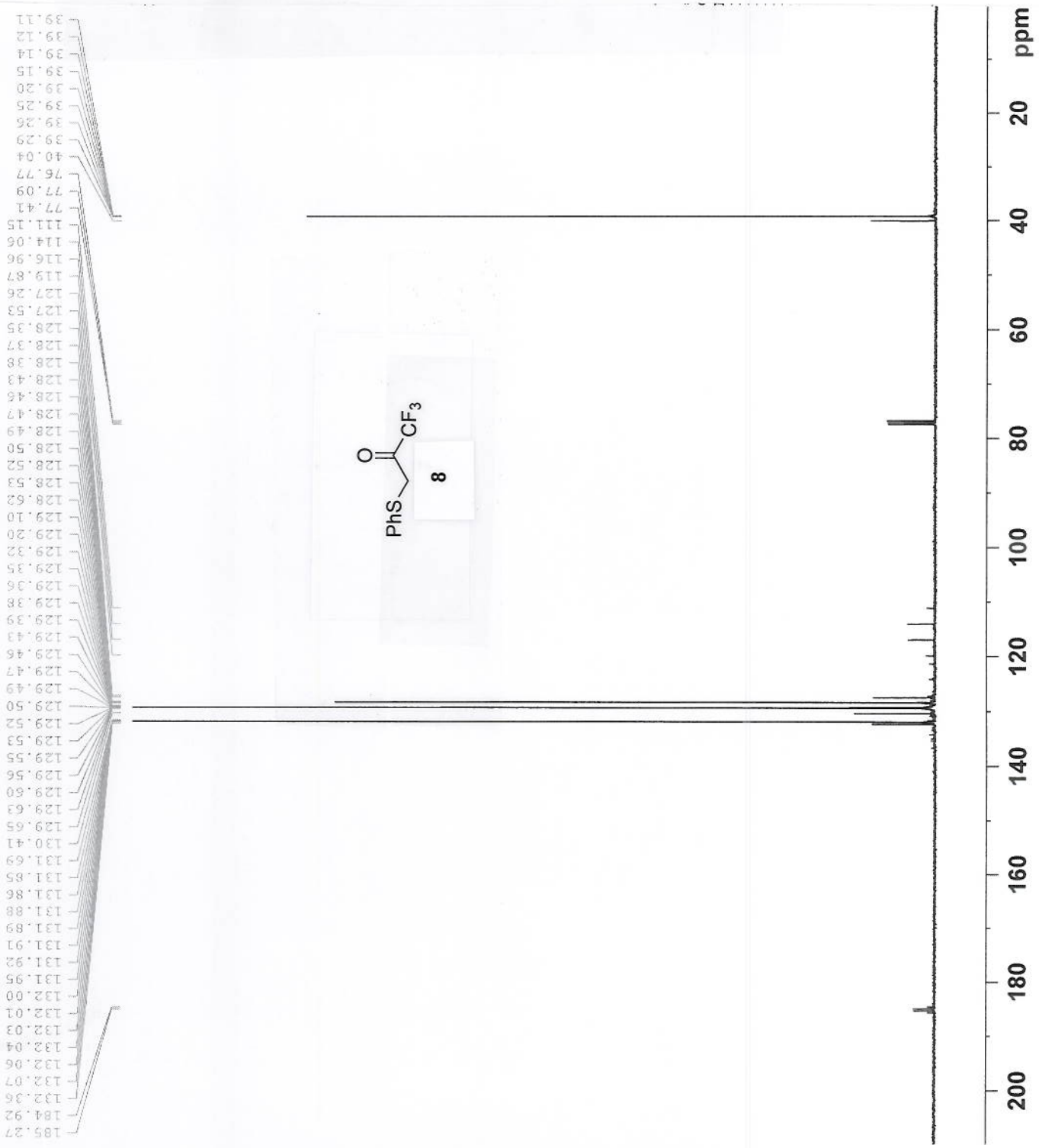
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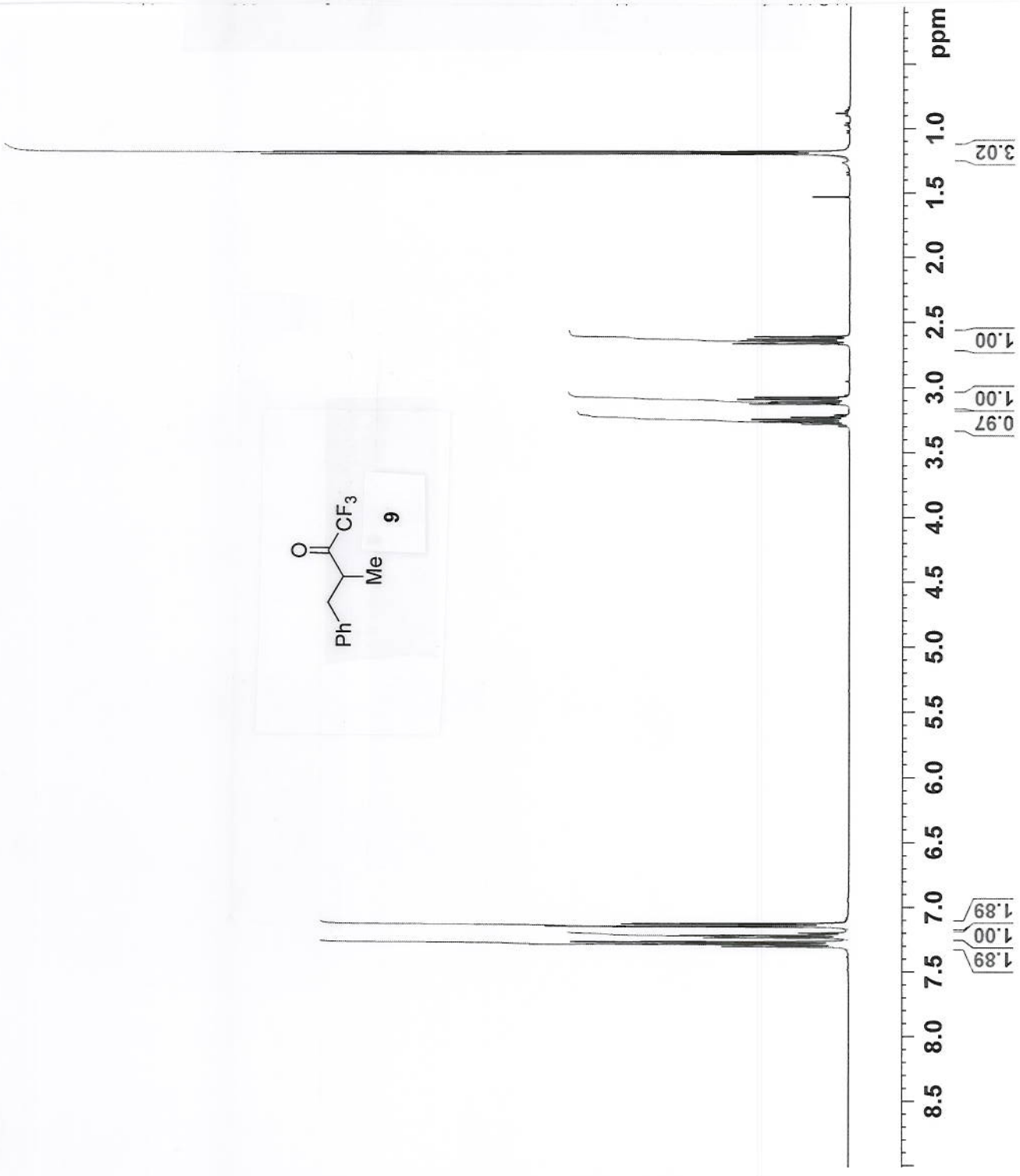
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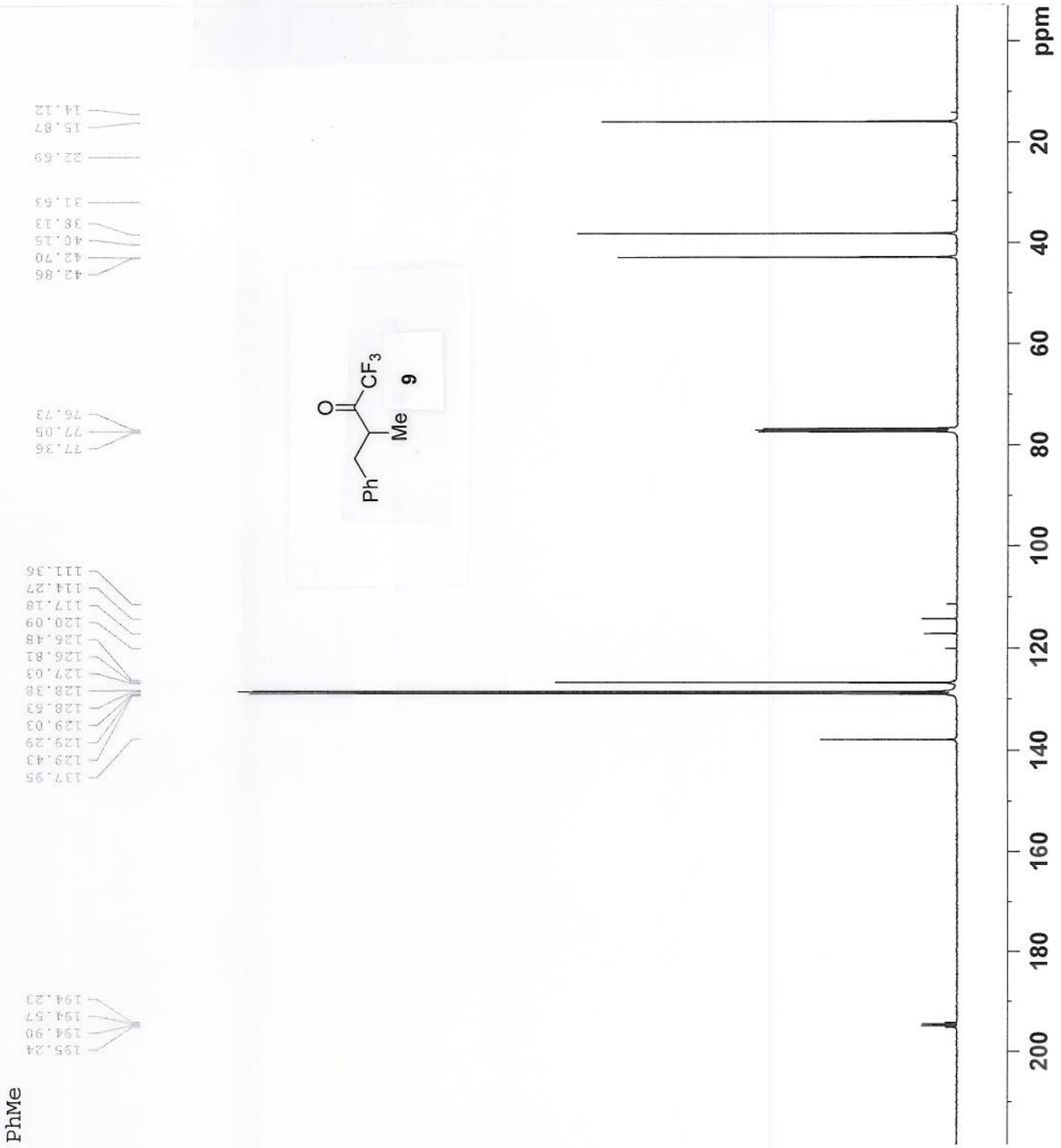
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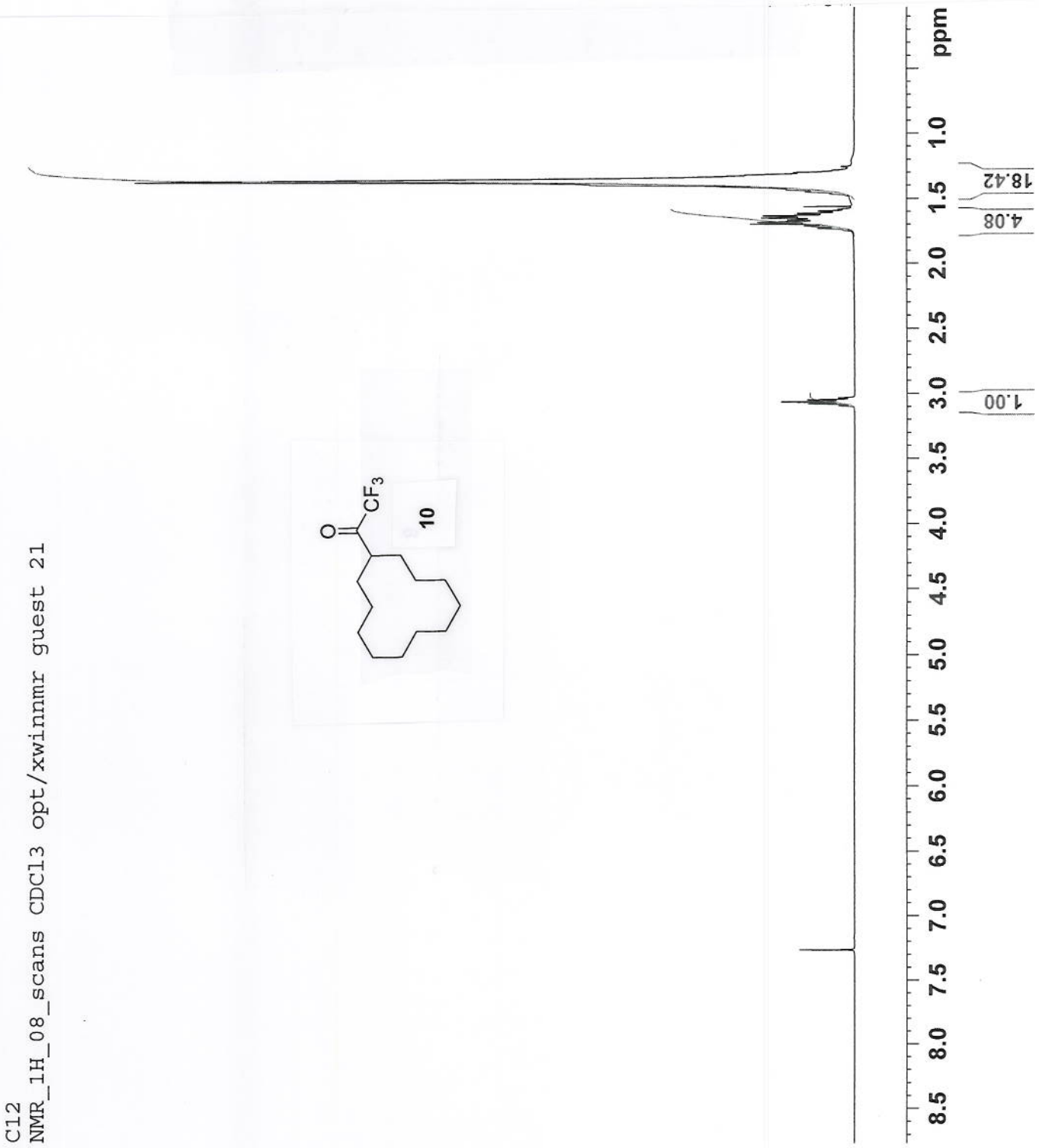
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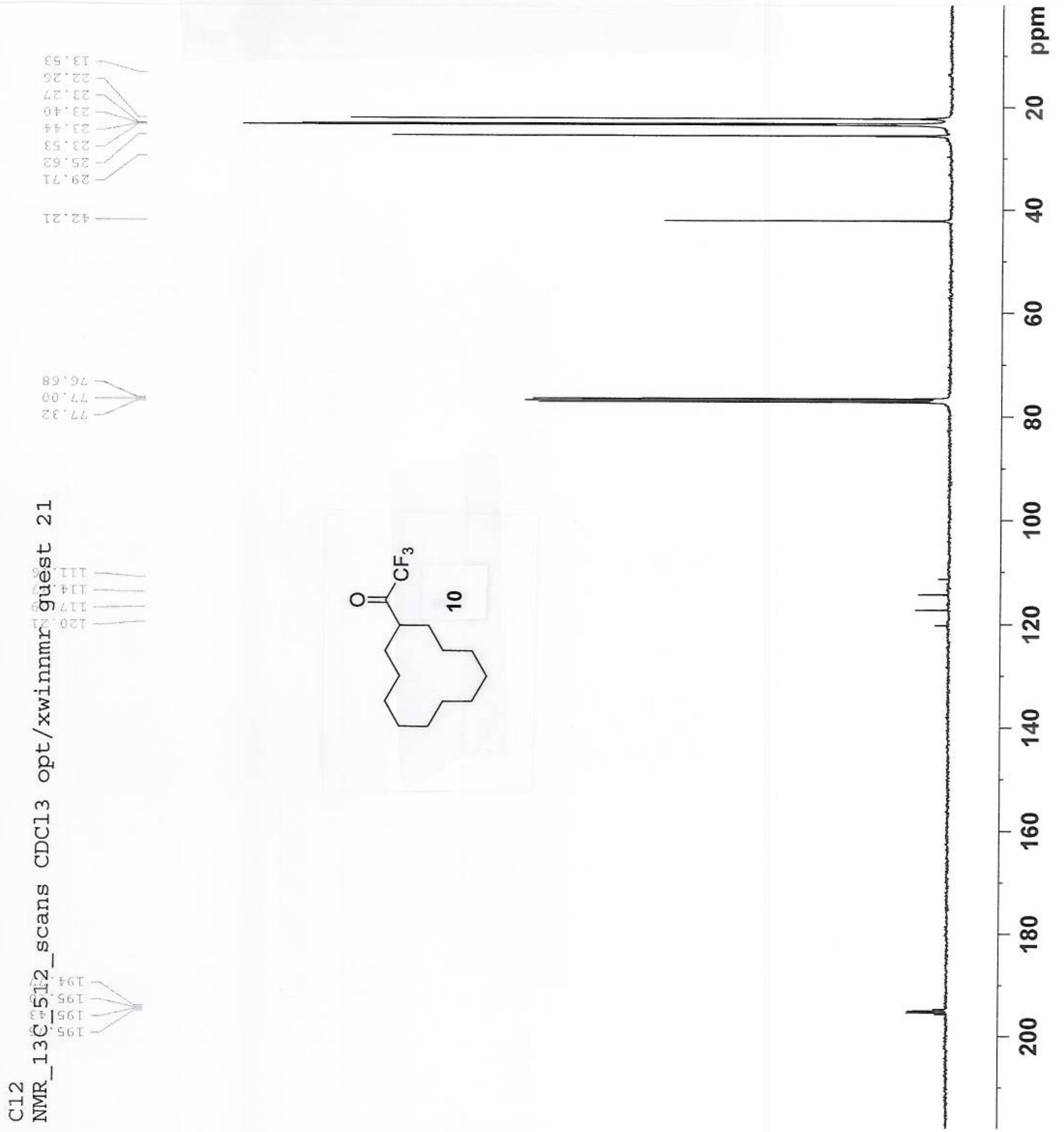
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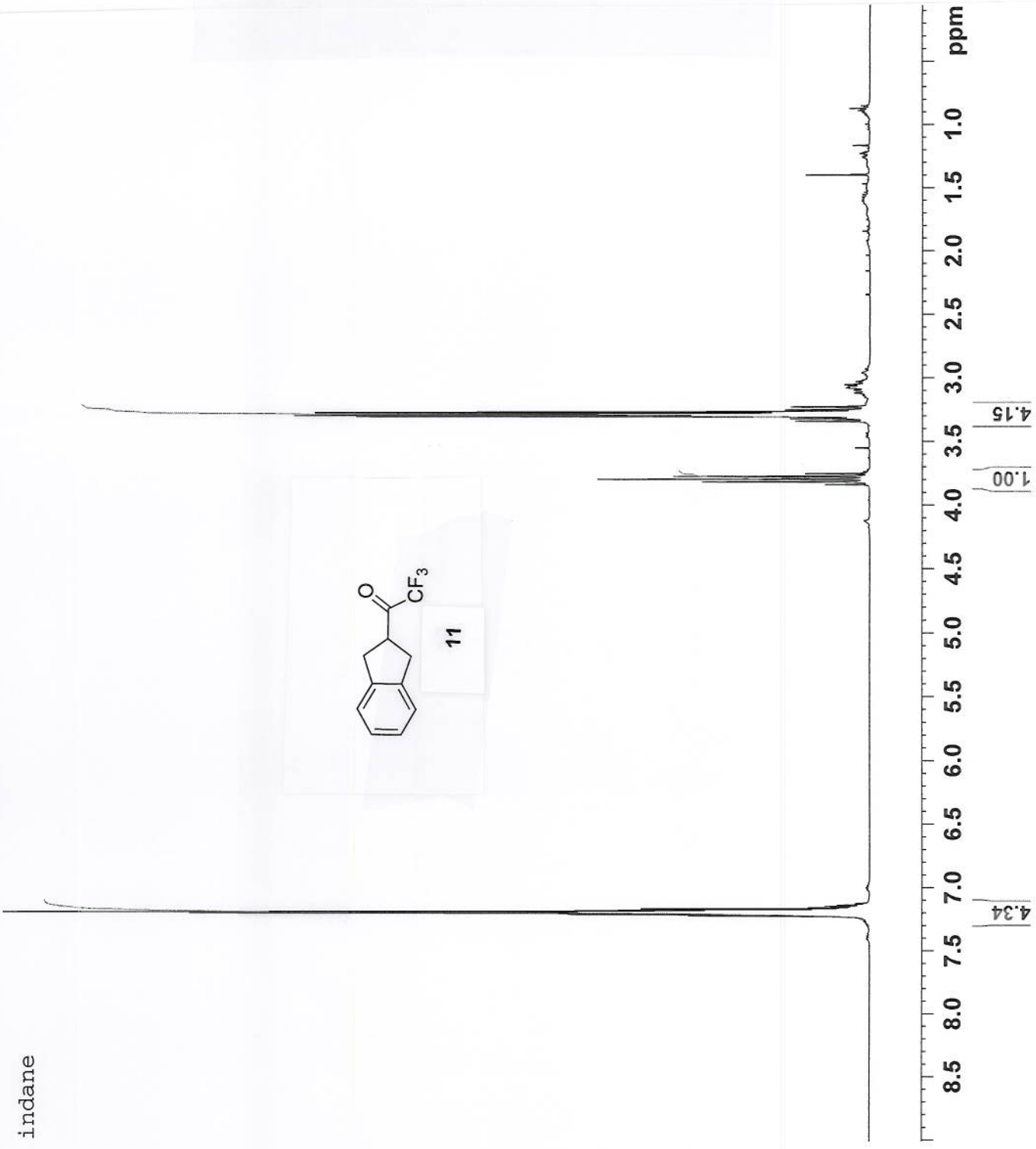
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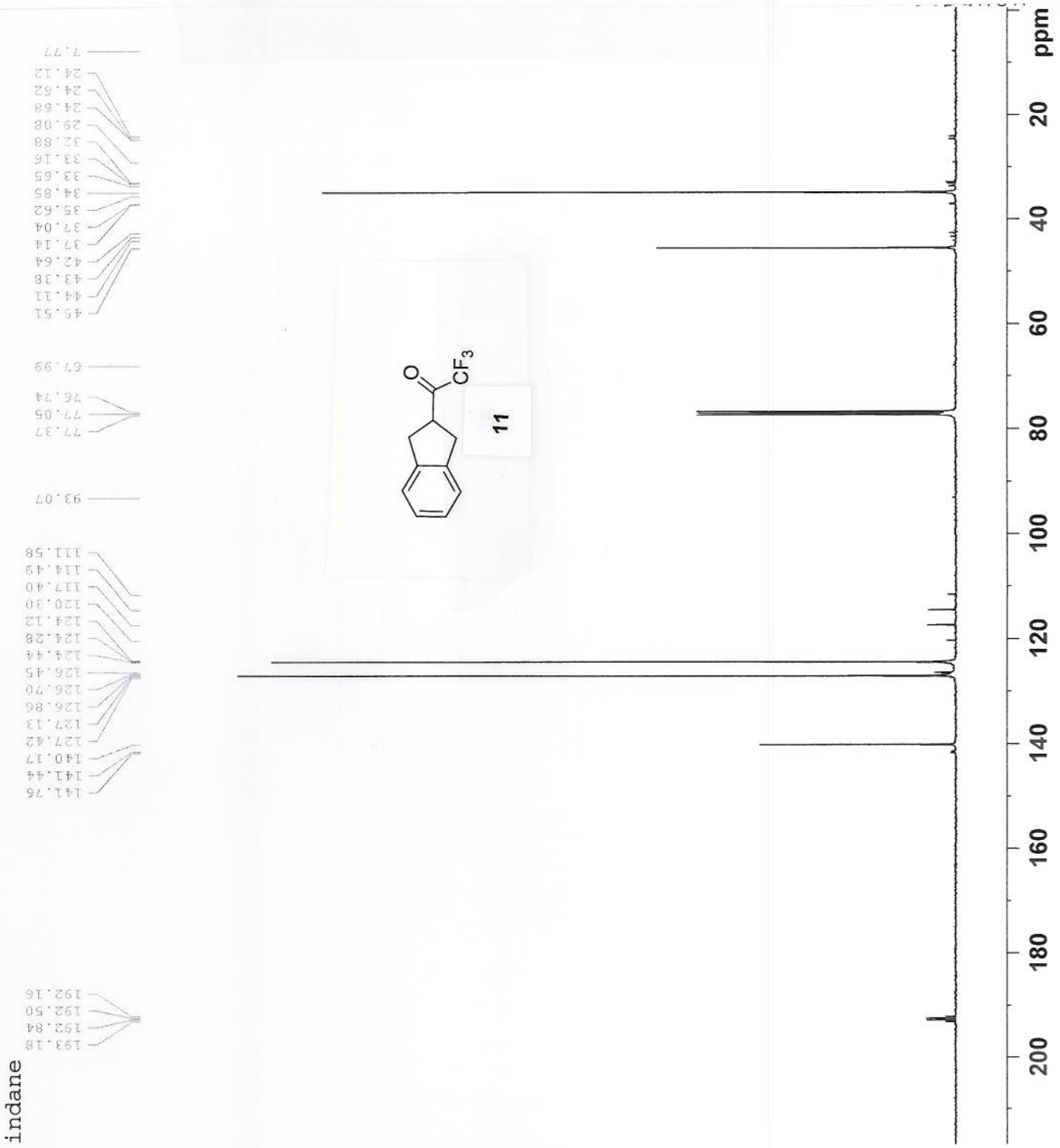
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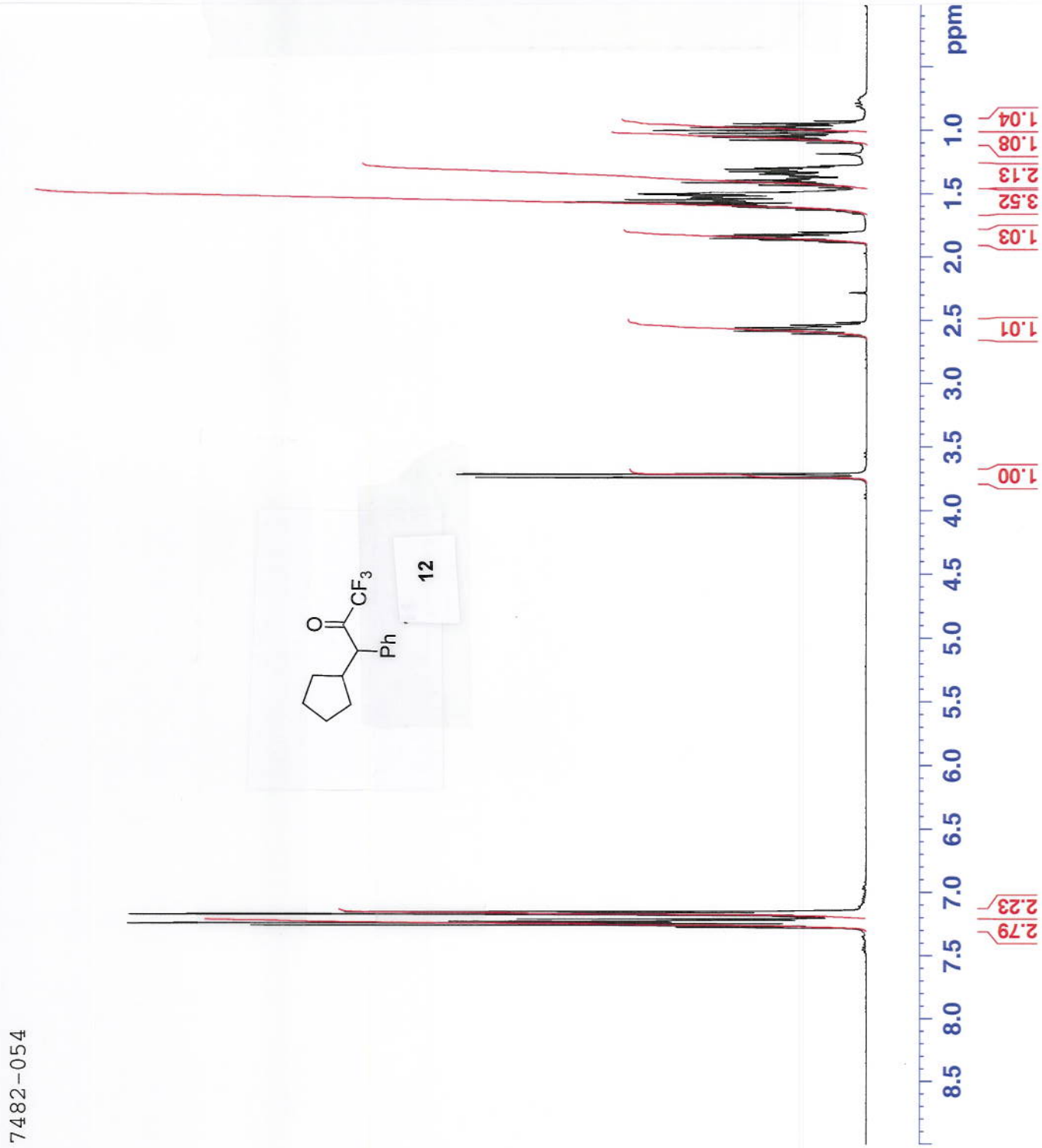
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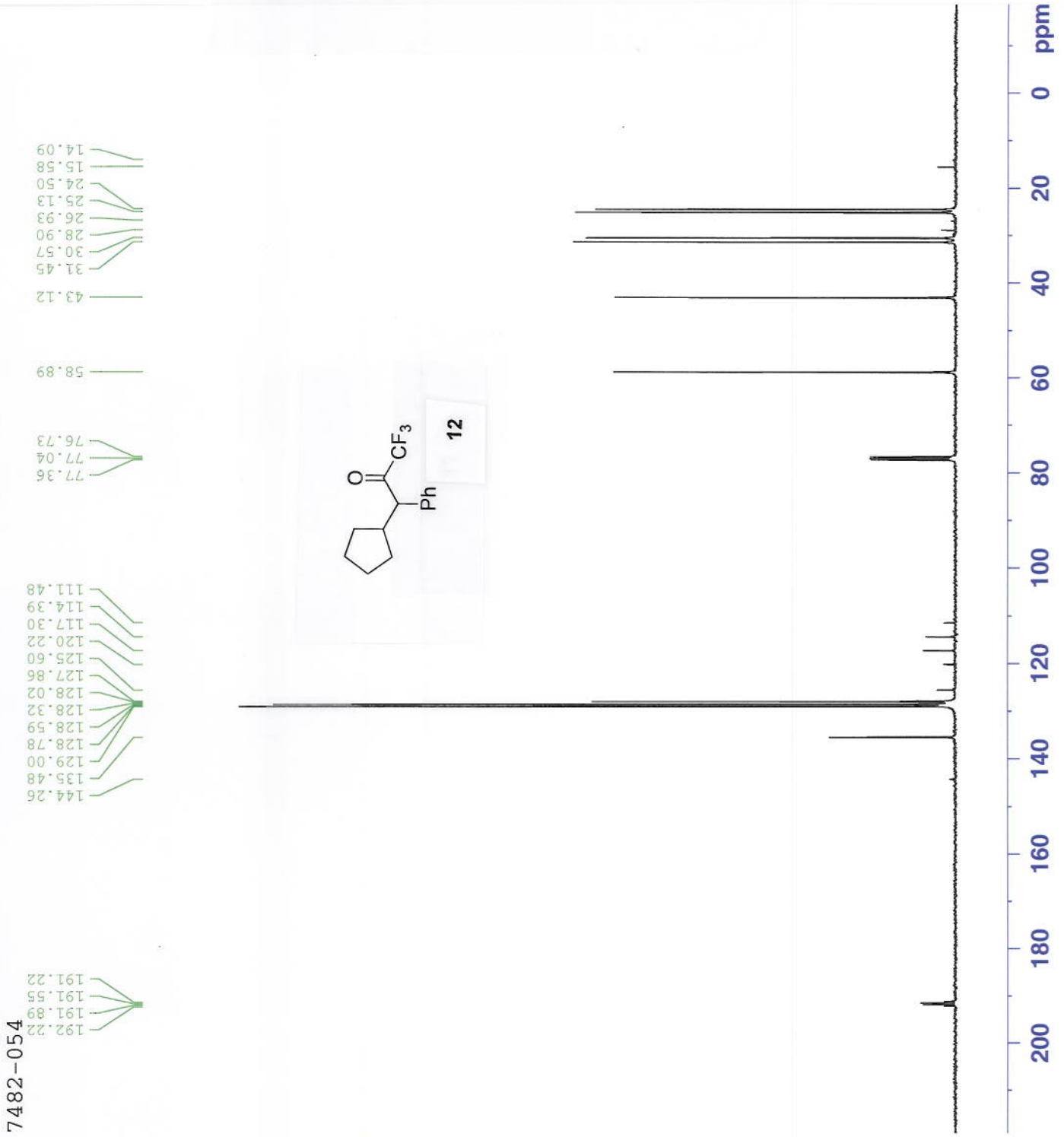
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180
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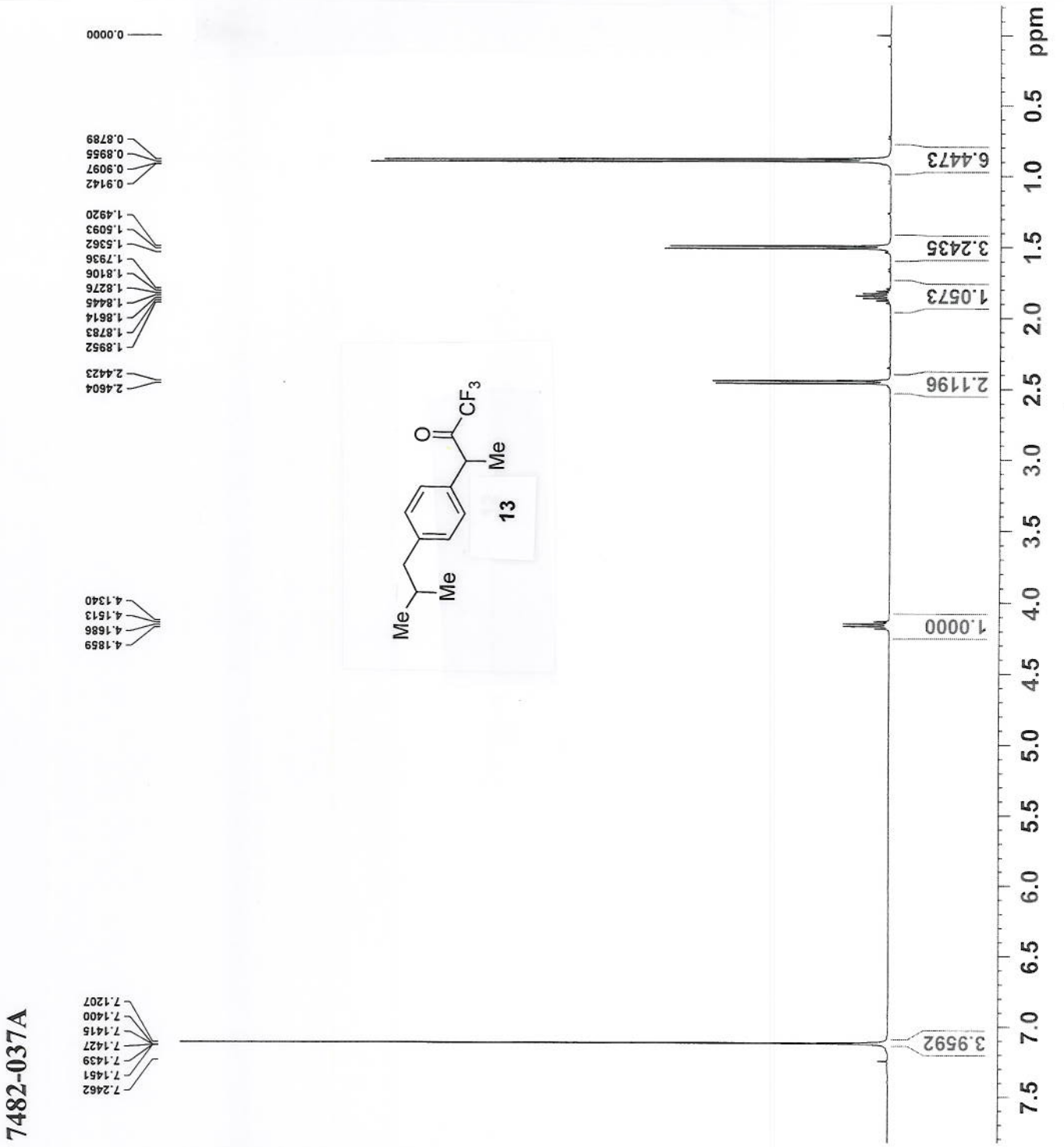
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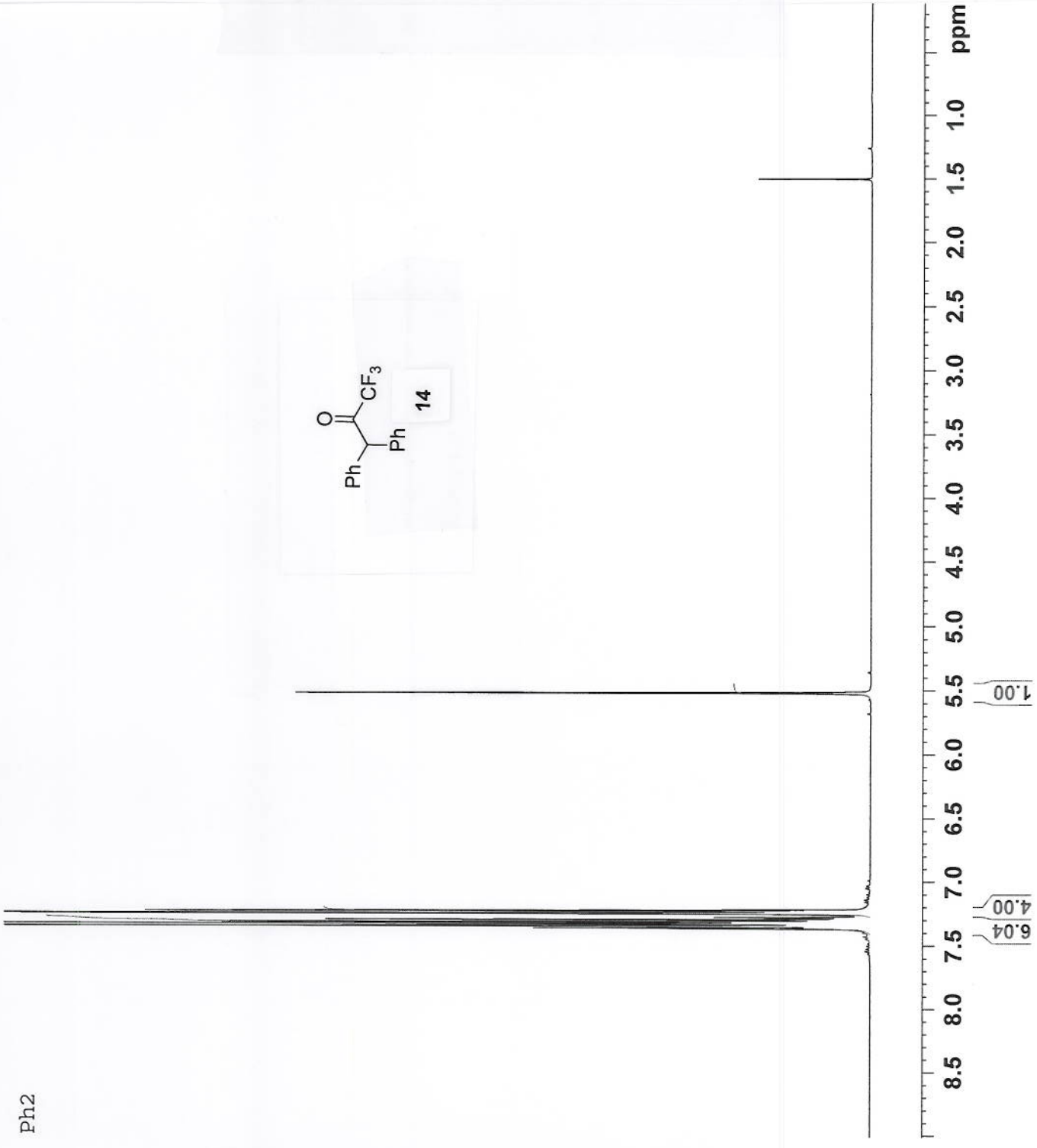
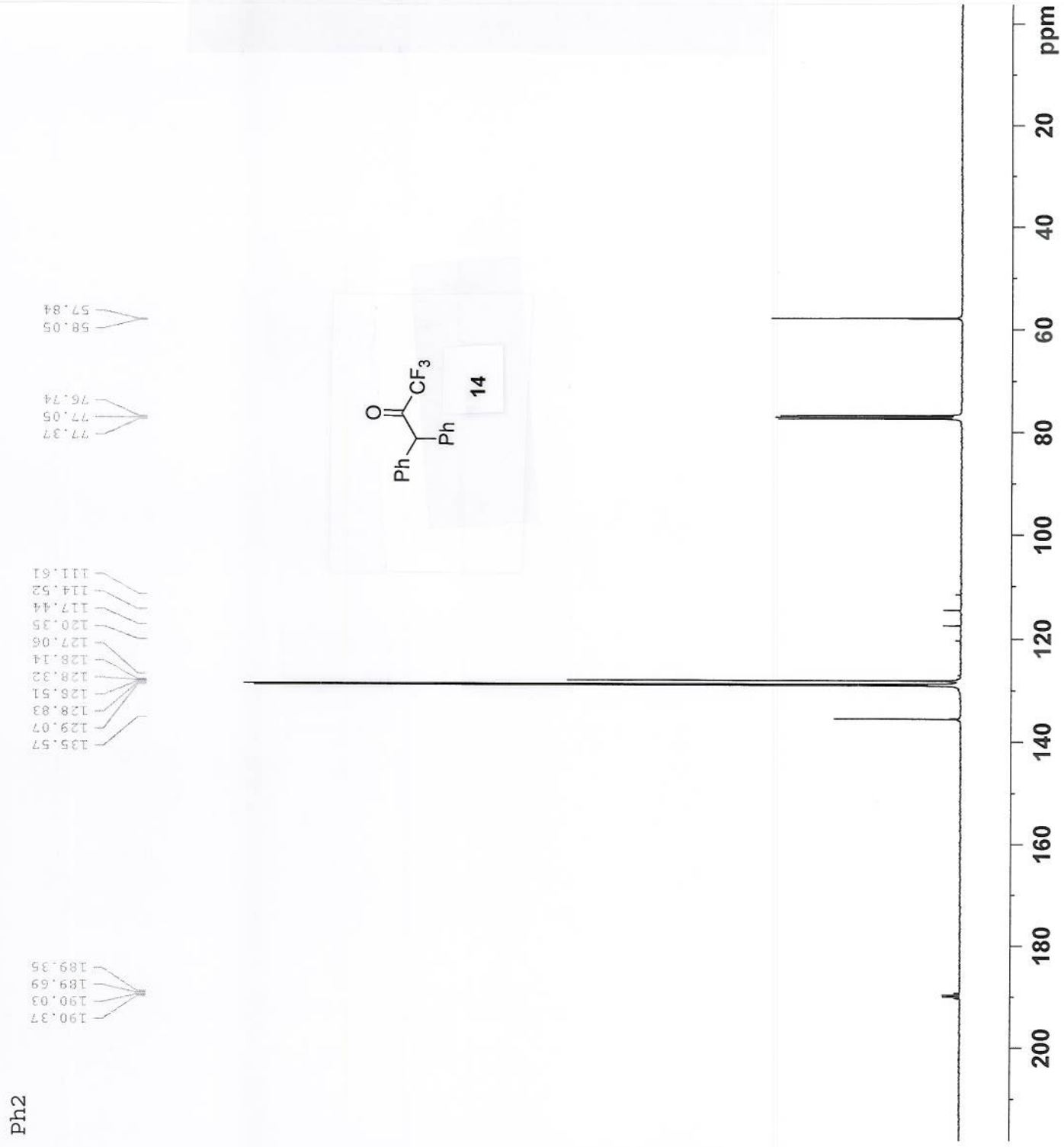
1.7936
1.8106
1.8276
1.8445
1.8614
1.8783
1.8952
2.4423
2.4604
4.1340
4.1513
4.1686
4.1859
7.1207
7.1400
7.1415
7.1427
7.1439
7.1451
7.2462
6.4473
3.2435
1.0573
2.1196
1.0000
3.9592
ppm
13
CF3
O
Me
Me
Me


7482-037A
191.61
191.94
192.27
192.60
141.66
133.96
129.85
127.73
120.28
117.36
114.45
111.54
76.70
77.01
77.33
45.00
46.87
30.16
22.32
17.90
Me
Me
O
CF3
Me
13
ppm
200
180
160
140
120
100
80
60
40
20


Ph2
O
CF3
Ph
Ph
14
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
ppm
6.04
4.00
1.00


Ph2
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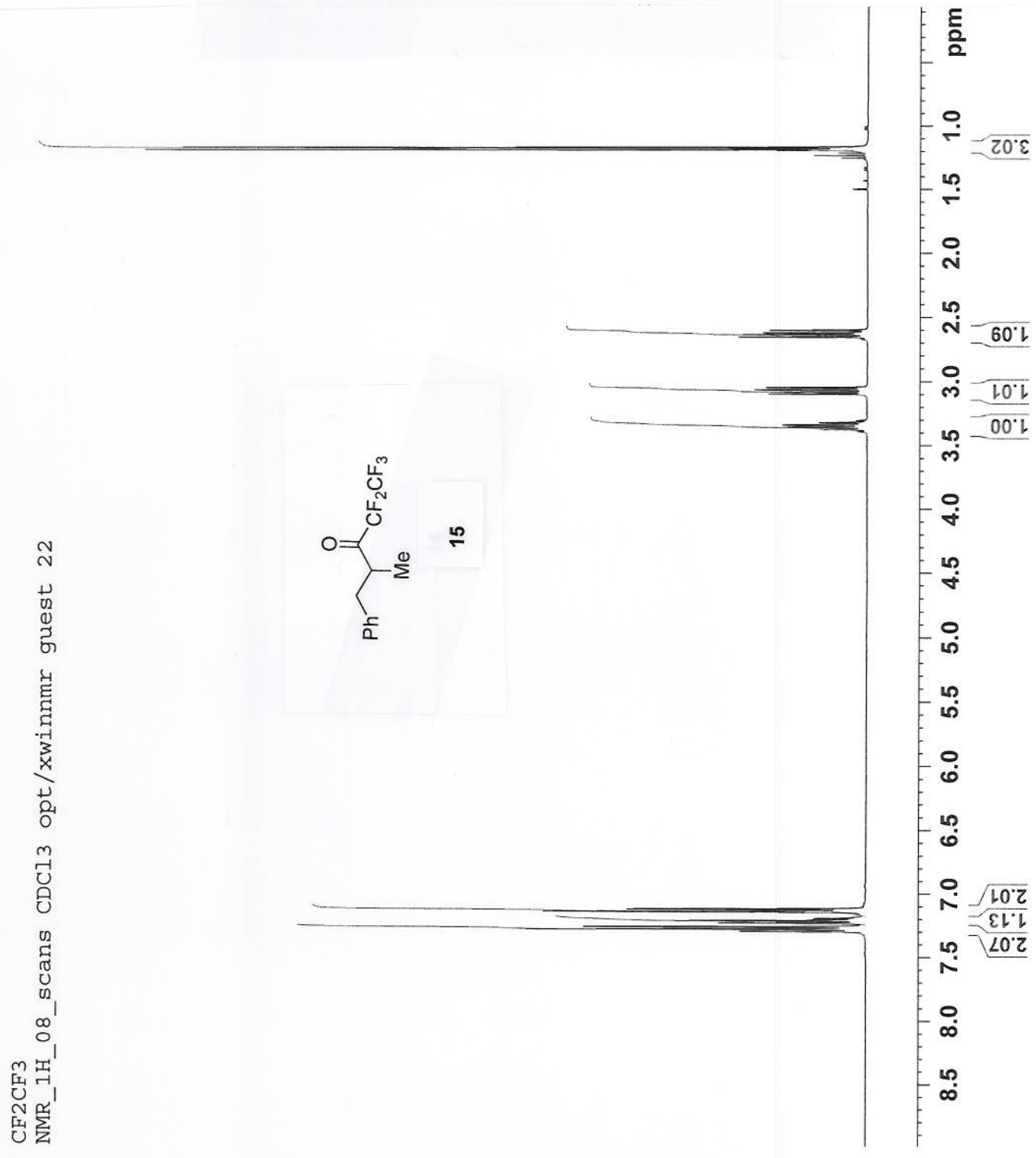
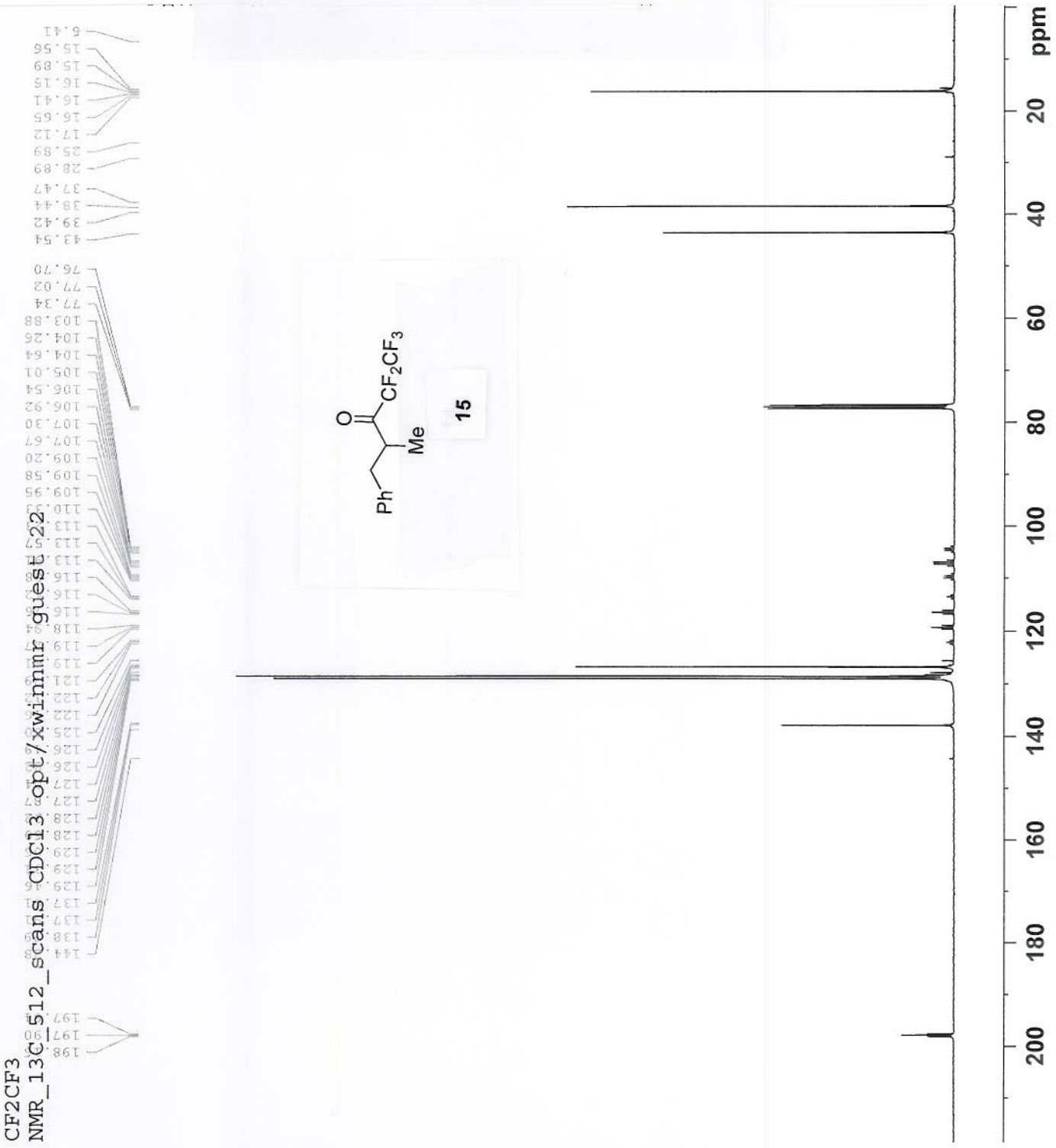
190.03
189.69
189.35
135.57
129.07
128.83
128.51
128.32
128.14
127.06
120.35
117.44
114.52
111.61
77.37
77.05
76.74
58.05
57.84
O
CF3
Ph
Ph
14
200
180
160
140
120
100
80
60
40
20
ppm


CF2CF3
NMR_1H_08_scans CDCl3 opt/xwinnmr guest 22
O
CF_2CF_3
Me
Ph
15
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 ppm
2.07
1.13
2.01
1.00
1.01
1.09
3.02


CF2CF3
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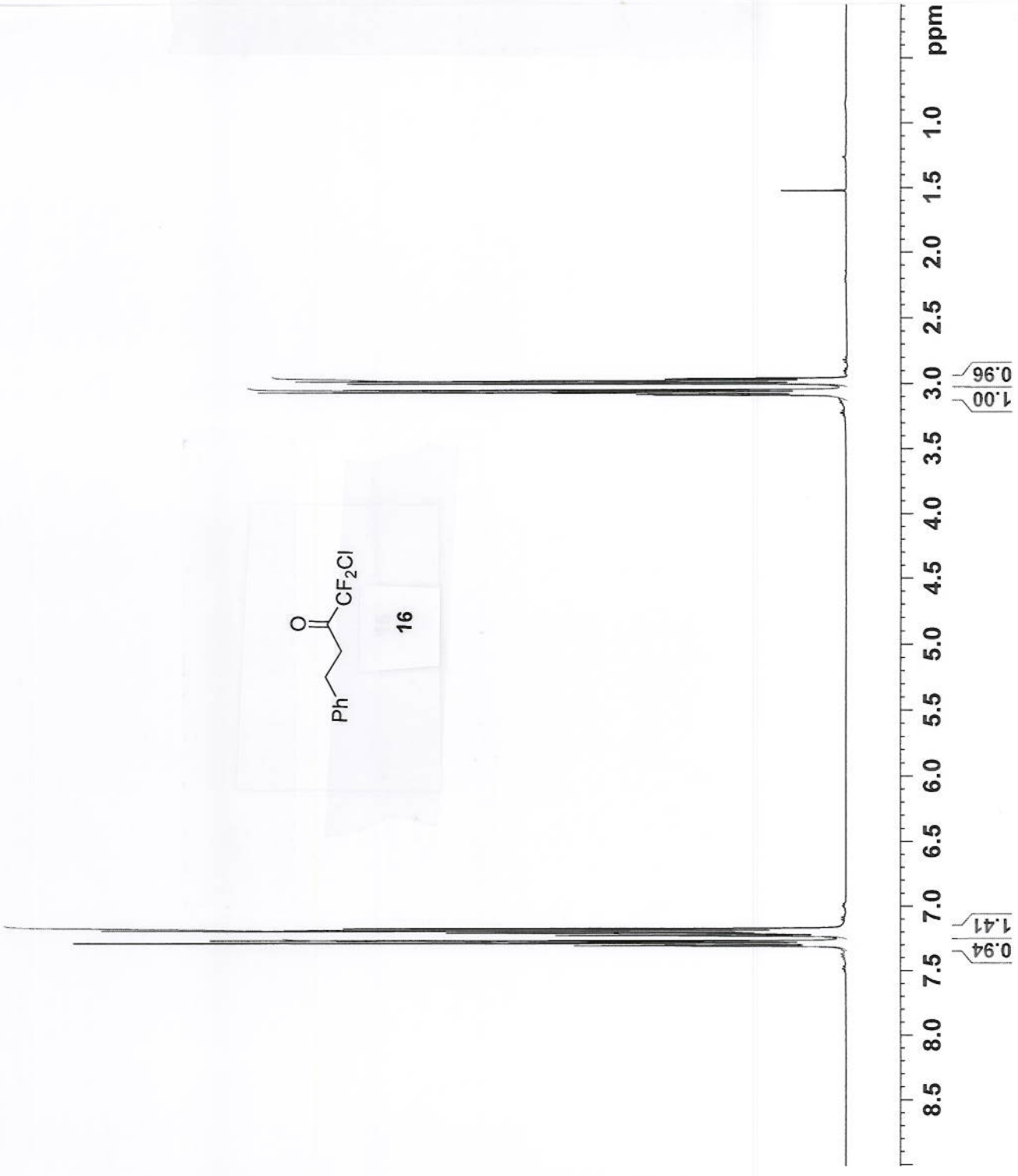
CF2CF3
Me
Ph
15
ppm
200
180
160
140
120
100
80
60
40
20


CF2Cl
O
CF2Cl
Ph
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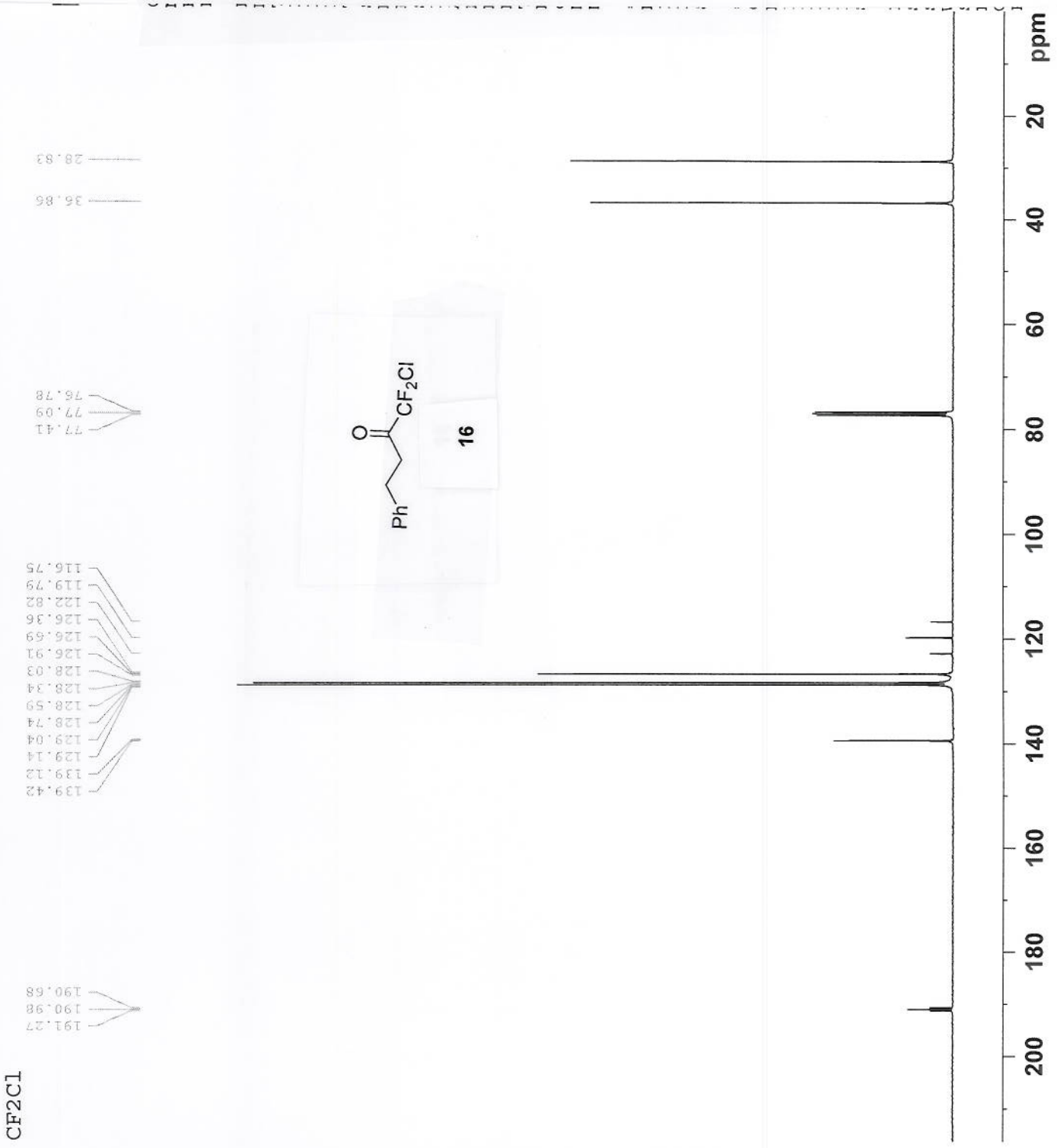
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.94
1.41
1.00
0.96


CF2Cl
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190.68
139.42
139.12
129.14
129.04
128.74
128.59
128.34
128.03
126.91
126.69
126.36
122.82
119.79
116.75
77.41
77.09
76.78
36.86
28.83
O
CF2Cl
Ph
16
ppm
200
180
160
140
120
100
80
60
40
20