Synthesis of the core of the fungal metabolite benesudon – use of oxidative decarboxylation

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SUPPORTING INFORMATION

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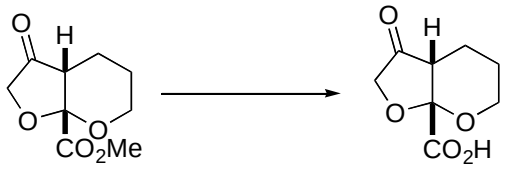
3-Oxohexahydrofuro[2,3-b]pyran-7a-carboxylic Acid (17).



16 **17**

$(Bu_3Sn)_2O$ (0.97 mL, 1.94 mmol) was added to a solution of **16** (96 mg, 0.48 mmol) in dry PhH (7.5 mL), and the solution was refluxed under N_2 for 5 h. The solvent was evaporated and EtOAc (10 mL) was added to the residue. The EtOAc solution was extracted with saturated aqueous $NaHCO_3$ solution (2 x 10 mL), and the aqueous extract was acidified (pH 1, pH paper) with ice-cold hydrochloric acid (2 N) and extracted with EtOAc (4 x 5 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated. The resulting crude acid (**17**) should be used immediately, without further purification. If hydrolysis is continued for 4-5 h more, then the acid becomes first pink and then dark, and the overall yield of **18** after the oxidation is low. The acid was an oil and had: FTIR (CH_2Cl_2, cast) 3500-2500, 1766 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.43-1.54 (m, 2 H), 1.90-2.01 (m, 1 H), 2.16-2.26 (m, 1 H), 2.89 (dd, J = 6.3, 3.4 Hz, 1 H), 1 H), 3.70-3.77 (m, 1 H), 3.94-4.02 (m, 1 H), 4.27 (AB q, $\Delta\nu_{AB}$ = 25.2 Hz, J = 16.6 Hz, 2 H), 5.75 (br s, 1 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 19.9 (t), 21.0 (t), 47.0 (d), 65.0 (t), 70.5 (t), 101.8 (s), 169.5 (s), 210.5 (s); exact mass (HR electrospray) m/z calcd for $C_8H_{11}O_5$ (M + H) 187.0601, found 187.0603.

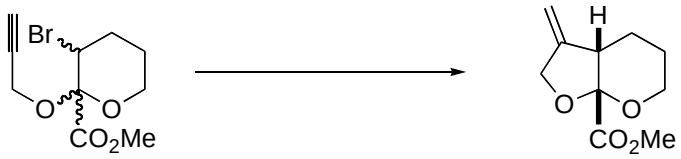
3-Bromo-2-(prop-2-ynyloxy)tetrahydropyran-2-carboxylic Acid Methyl Ester (14).

12 **14**

One isomer of **14** was an oil and had: FTIR (CH_2Cl_2, cast) 3286, 2126, 1755, cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.68-1.76 (m, 1 H), 1.86-2.00 (m, 1 H), 2.10-2.18 (m, 1 H), 2.36 (dq, *J* = 12.8, 4.1 Hz, 1 H), 2.45 (t, *J* = 2.5 Hz, 1 H), 3.76-3.83 [m, 4 H, including a singlet (3 H) at δ 3.80], 3.87 (dq, *J* = 12.4, 2.8 Hz, 1 H), 4.26 (dd, *J* = 12.4, 4.4 Hz, 1 H), 4.45 (d AB q, $\Delta\nu_{AB}$ = 108.4 Hz, *J* = 15.6, 2.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 26.9 (t), 29.2 (t), 48.4 (d), 52.2 (t), 52.9 (q), 61.9 (t), 74.3 (d), 79.6 (s), 98.9 (s), 167.3 (s); exact mass (HR electrospray) *m/z* calcd for $C_{10}H_{13}{}^{79}BrNaO_4$ (M + Na) 298.9889, found 298.9886.

The other isomer of **14** was an oil and had: FTIR (CH_2Cl_2, cast) 3282, 2124, 1761 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.38-1.44 (m, 1 H), 1.97-2.05 (m, 1 H), 2.15-2.26 (m, 1 H), 2.44 (t, *J* = 2.4 Hz, 1 H), 2.45-2.54 (m, 1 H), 3.75-3.83 [m, 4 H, including a s (3 H) at δ 3.80], 3.89-3.96 (m, 1 H), 4.13 (d AB q, $\Delta\nu_{AB}$ = 91.5 Hz, *J* = 15.4, 2.5 Hz, 2 H), 4.38 (t, *J* = 3.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 18.9 (t), 26.9 (t), 48.9 (d), 52.1 (t), 52.7 (q), 62.2 (t), 74.7 (d), 78.4 (s), 98.0 (s), 167.2 (s); exact mass (HR electrospray) *m/z* calcd for $C_{10}H_{13}{}^{79}BrNaO_4$ (M + Na) 298.9889, found 298.9890.

3-Methylenehexahydrofuro[2,3-*b*]pyran-7a-carboxylic Acid Methyl Ester (15).

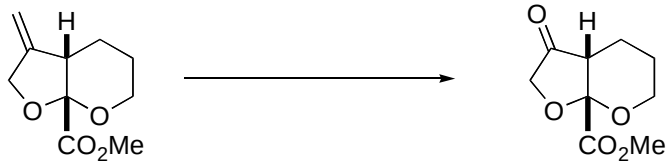


14 **15**

Compound **15** was an oil and had: FTIR (CH_2Cl_2, cast) 1742 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.29-1.41 (m, 1 H), 1.63-1.76 (m, 1 H), 1.93-2.07 (m, 2 H), 3.03-3.08 (m, 1 H), 3.59-3.66 (m, 1 H), 3.80 (s, 3 H), 3.84-3.90 (m, 1 H), 4.55-4.65 (m, 2 H), 4.97 (q, *J* = 2.6 Hz, 1 H), 5.04 (q, *J* = 2.2 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125.7

MHz) δ 19.7 (t), 22.2 (t), 43.0 (d), 52.6 (q), 64.5 (t), 71.3 (t), 103.3 (s), 104.6 (t), 146.4 (s), 168.7 (s); exact mass *m/z* calcd for $C_{10}H_{14}O_4$ 198.0892, found 198.0890.

3-Oxohexahydrofuro[2,3-*b*]pyran-7a-carboxylic Acid Methyl Ester (16).



15 **16**

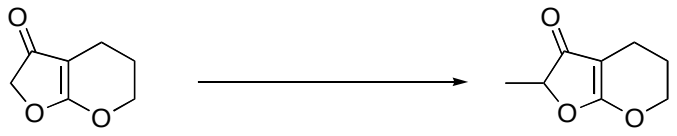
Compound **16** was an oil and had: FTIR (CH_2Cl_2, cast) 1765, 1742 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.40-1.50 (m, 2 H), 1.86-1.98 (m, 1 H), 2.19-2.28 (m, 1 H), 2.91 (dd, *J* = 6.1, 2.7 Hz, 1 H), 1 H), 3.54-3.65 (m, 1 H), 3.87 (s, 3 H), 3.90-3.98 (m, 1 H), 4.23 (AB q, $\Delta\nu_{AB}$ = 19.8 Hz, *J* = 16.6 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 19.9 (t), 21.0 (t), 47.6 (d), 53.0 (q), 64.9 (t), 70.4 (t), 102.4 (s), 167.6 (s), 211.1 (s); exact mass (HR electrospray) *m/z* calcd for $C_9H_{12}NaO_5$ (M + Na) 223.5770, found 223.0581.

5,6-Dihydro-4*H*-furo[2,3-b]pyran-3-one (6).

17 **6**

Compound **6** had: mp 60-62 °C; FTIR (CH_2Cl_2, cast) 1705, 1600 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.91-1.99 (m, 2H), 2.33 (t, *J* = 6.2 Hz, 2H), 4.47 (apparent t, *J* = 5.1 Hz, 2H), 4.52 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.5 (t), 21.2 (t), 71.5 (t), 74.2 (t), 88.9 (s), 182.8 (s), 194.1 (s); exact mass *m/z* calcd for $C_7H_8O_3$ 140.0474, found 140.0473.

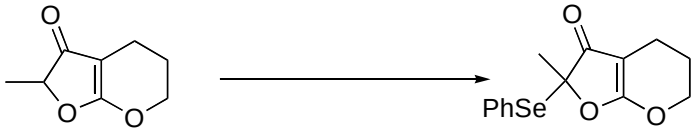
2-Methyl-5,6-dihydro-4*H*-furo[2,3-b]pyran-3-one (18).



6 **18**

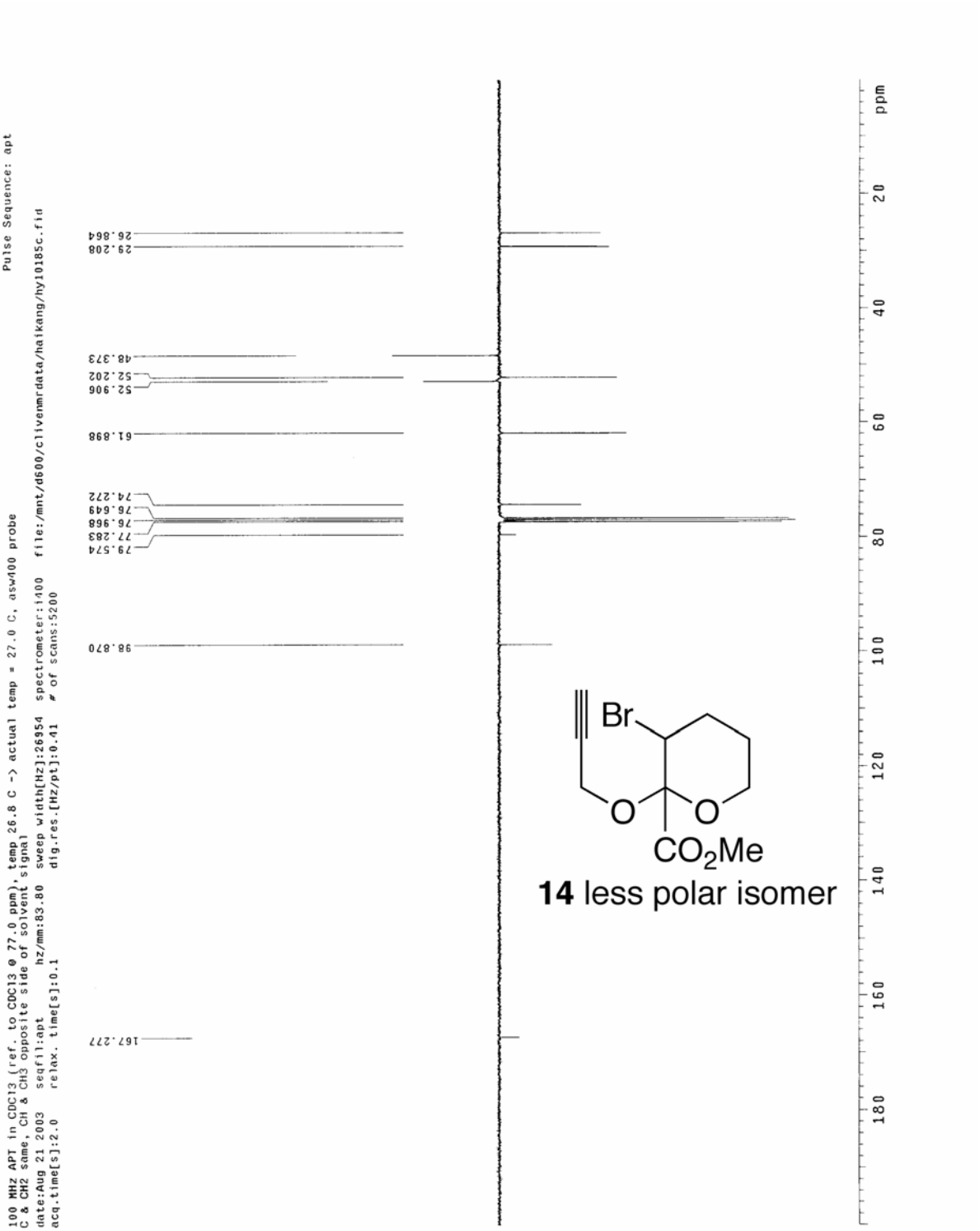
Compound **18** was an oil and had: FTIR (CH_2Cl_2, cast) 1699, 1598 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.49 (d, *J* = 7.1 Hz, 3H), 1.94 (apparent pentet, *J* = 6.3 Hz, 2H), 2.32 (dt, *J* = 6.3, 3.2 Hz, 2H), 4.45 (dt, *J* = 5.2, 1.0 Hz, 2H), 4.59 (q, *J* = 7.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.6 (t), 16.3 (q), 21.3 (t), 71.4 (t), 82.5 (d), 87.5 (s), 181.4 (s), 196.9 (s); exact mass *m/z* calcd for $C_8H_{10}O_3$ 154.0630, found 154.0630.

2-Methyl-2-phenylselenyl-5,6-dihydro-4*H*-furo[2,3-b]pyran-3-one (19).



18 **19**

Compound **19** was a white solid and had: FTIR (CH_2Cl_2, cast) 1706, 1601 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.40-1.51 (m, 1H), 1.69-1.84 (m containing a singlet, 5H in all), 2.06-2.14 (m, 1H), 4.06-4.12 (m, 1H), 4.24-4.20 (m, 1H), 7.28 (t, *J* = 7.5 Hz, 2H), 7.37 (tt, *J* = 5.1, 1.2 Hz, 1H), 7.63-7.68 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.3 (t), 21.1 (t), 21.9 (q), 71.4 (t), 88.0 (s), 91.9 (s), 125.4 (s), 128.7 (d), 129.4 (d), 137.5 (d), 179.0 (s), 194.1 (s); exact mass *m/z* calcd for $C_{14}H_{14}O_3{}^{80}Se$ 310.0108, found 310.0109.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C & CH2 same, CH & CH3 opposite side of solvent signal
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acq.time[s]:2.0 relax. time[s]:0.1 dig.res.[Hz/pt]:0.41 # of scans:5200
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29.208
48.373
52.202
52.906
61.898
74.272
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76.968
77.283
79.574
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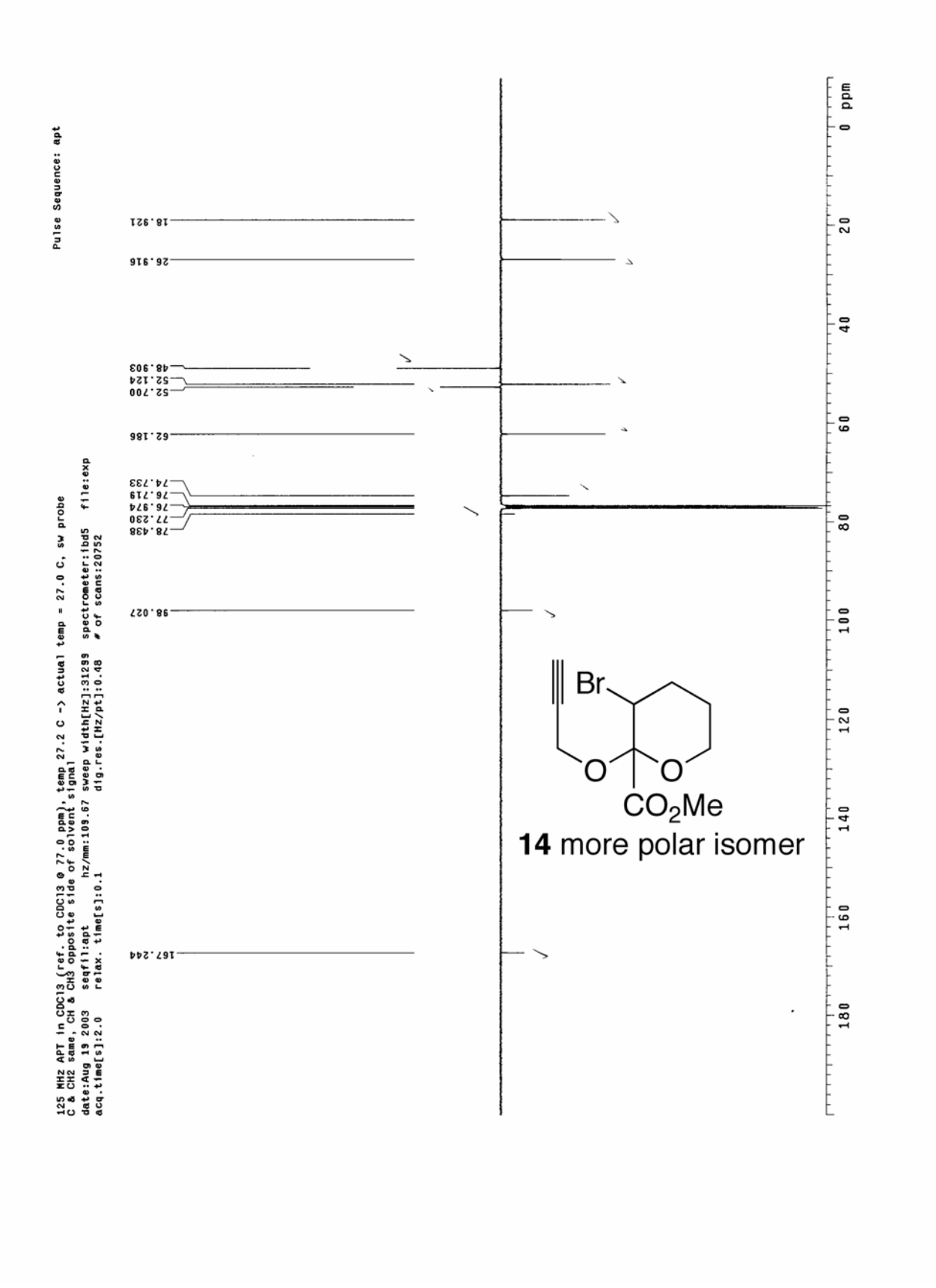
167.277
ppm
Br
O
O
CO2Me
14 less polar isomer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48.903
52.124
52.700
62.186
74.733
76.719
76.974
77.230
78.438
98.027
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20
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100
120
140
160
180
Br
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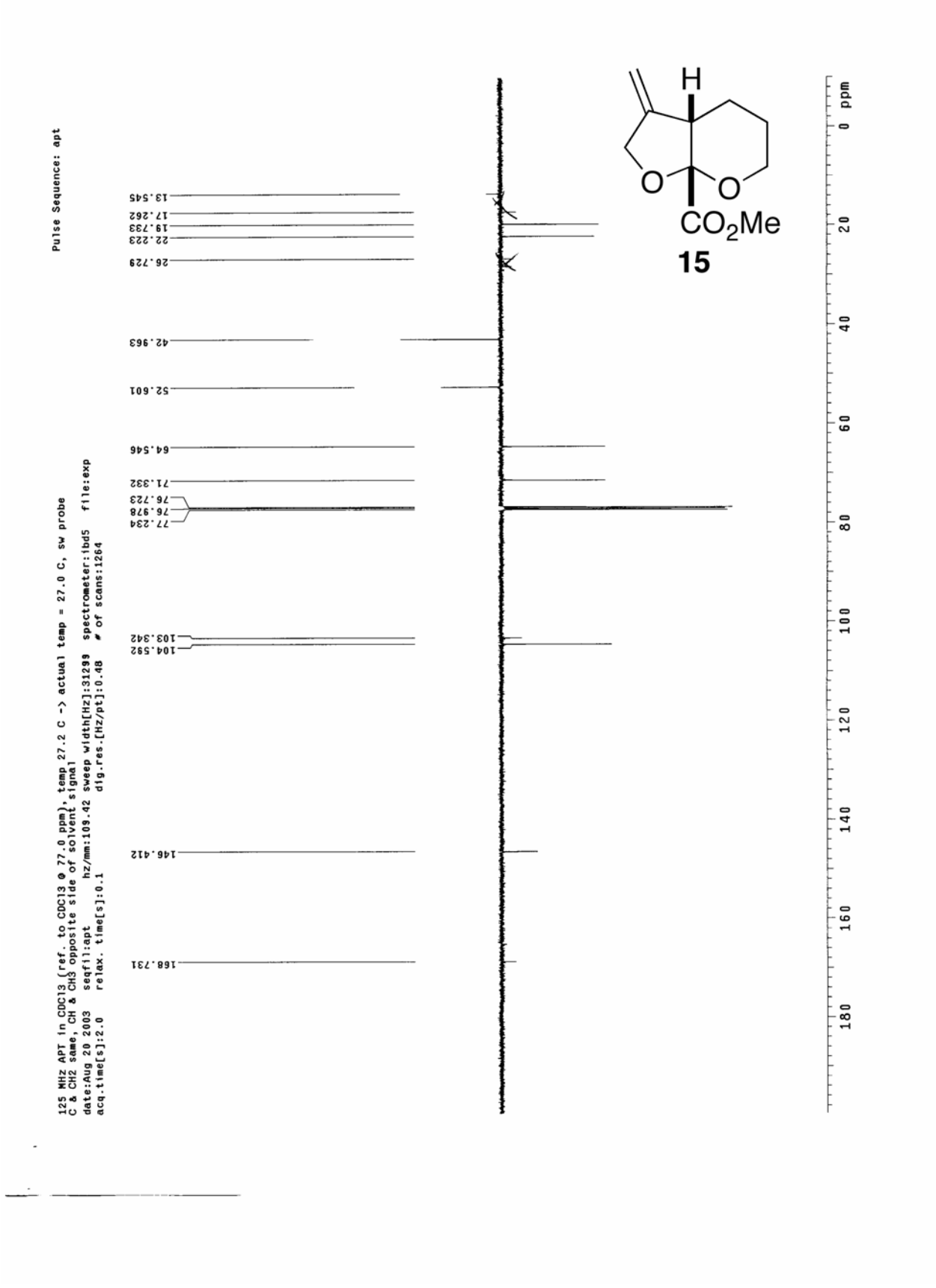
O
CO2Me
14 more polar isomer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C & CH2 same, CH & CH3 opposite side of solvent signal
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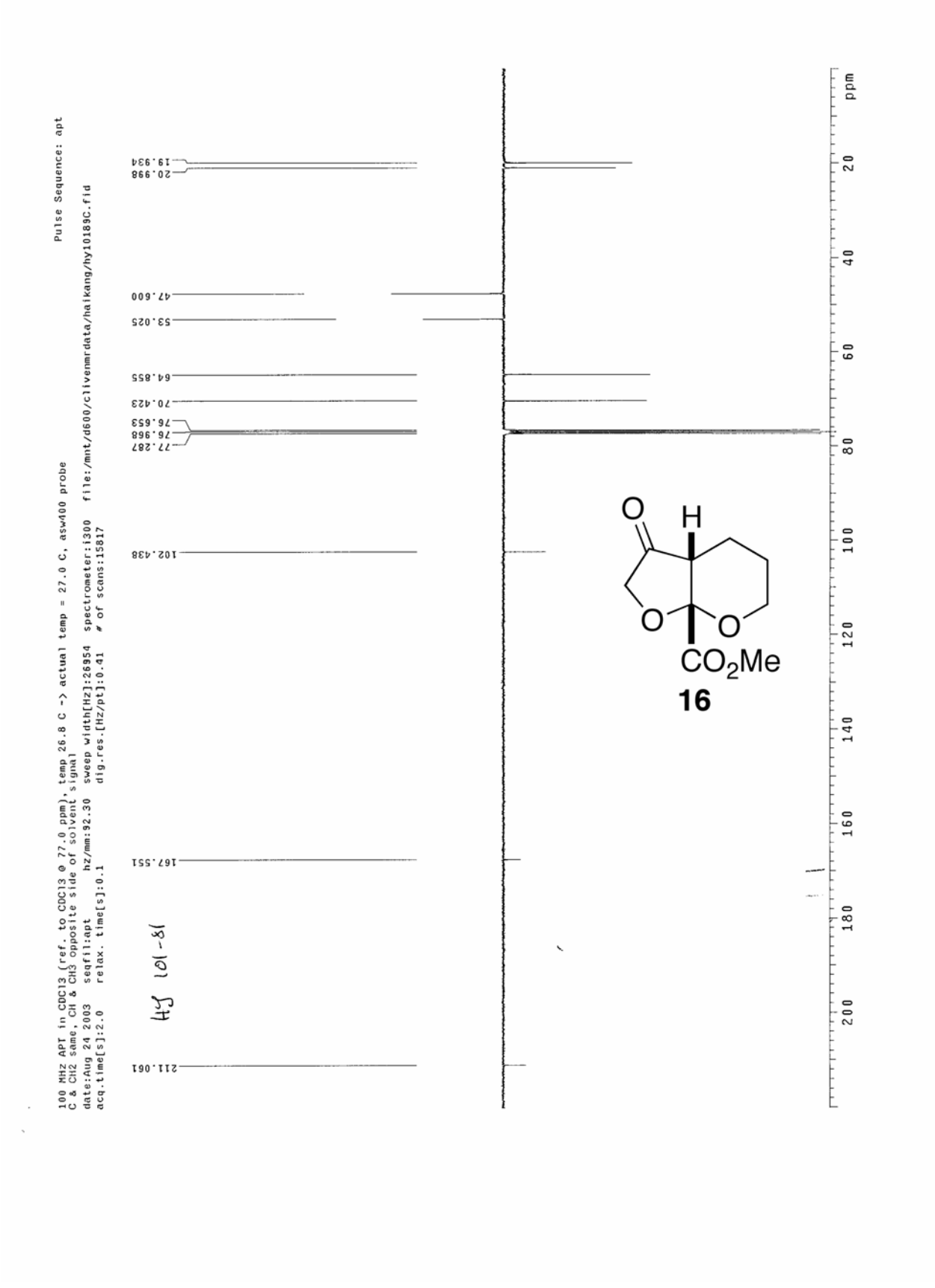
13.545
17.262
19.733
22.223
26.729
42.963
52.601
64.546
71.332
76.723
76.978
77.234
103.342
104.592
146.412
168.731
H
O
O
CO2Me
15
0 ppm
20
40
60
80
100
120
140
160
180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C & CH2 same, CH & CH3 opposite side of solvent signal
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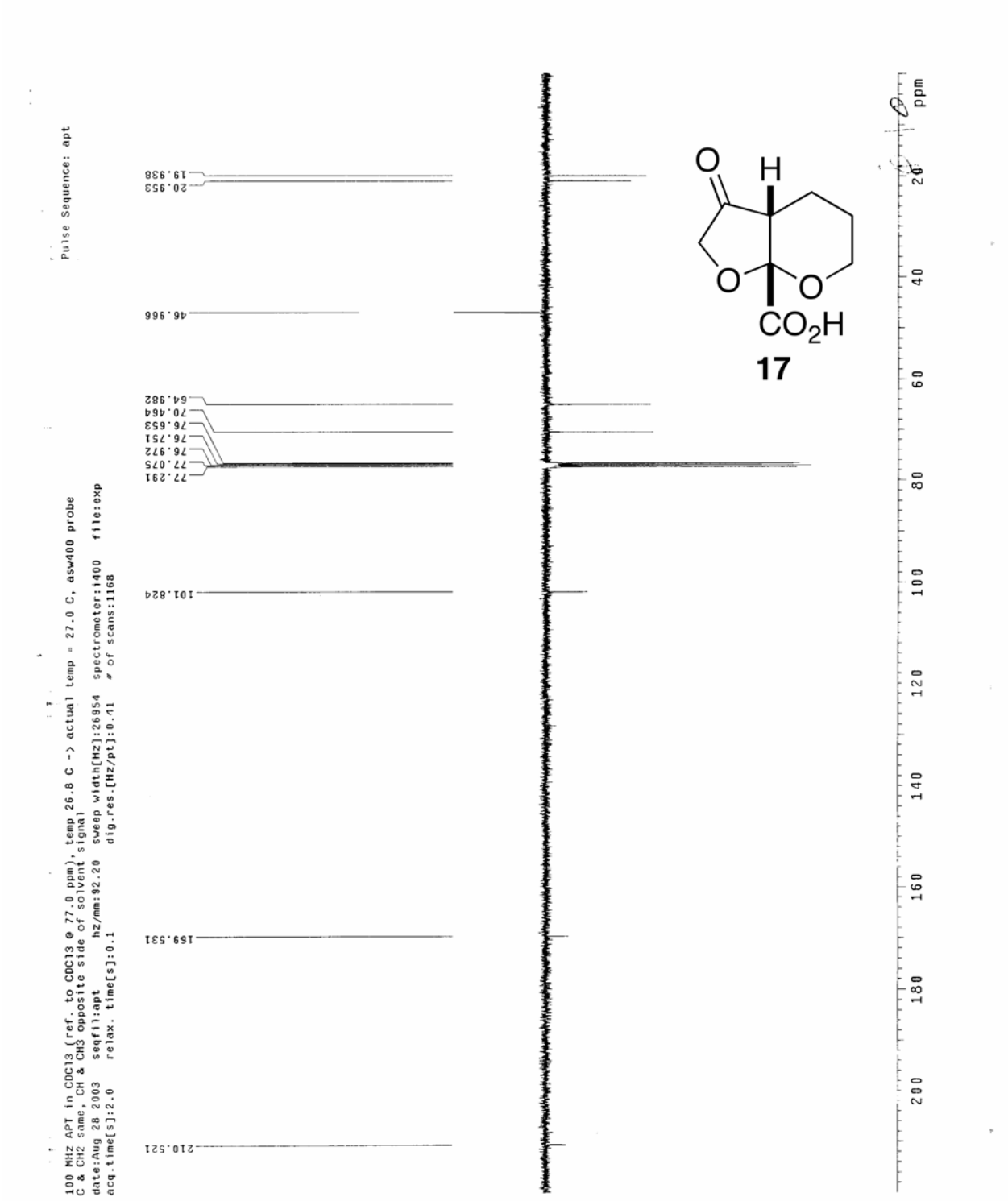
77.287
76.968
76.653
70.423
64.855
53.025
47.600
20.998
19.934
ppm
O
H
O
O
CO2Me
16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46.966
64.982
70.464
76.653
76.751
76.972
77.075
77.291
101.824
169.531
210.521
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O
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CO2H
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ppm
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80
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140
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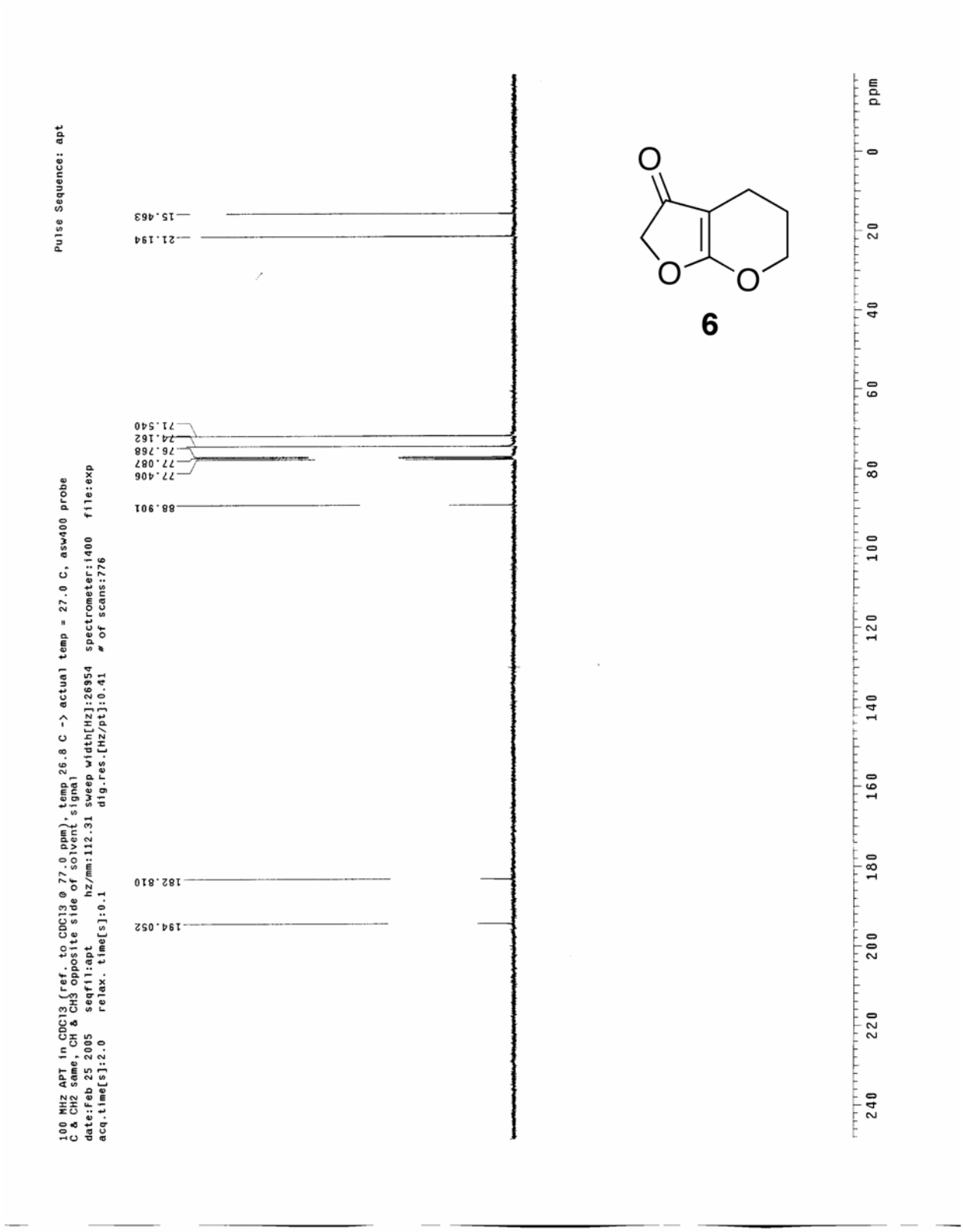
180
200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C & CH2 same, CH & CH3 opposite side of solvent signal
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21.194
71.540
74.162
76.768
77.087
77.406
88.901
182.810
194.052
O
O
O
6
ppm
0
20
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60
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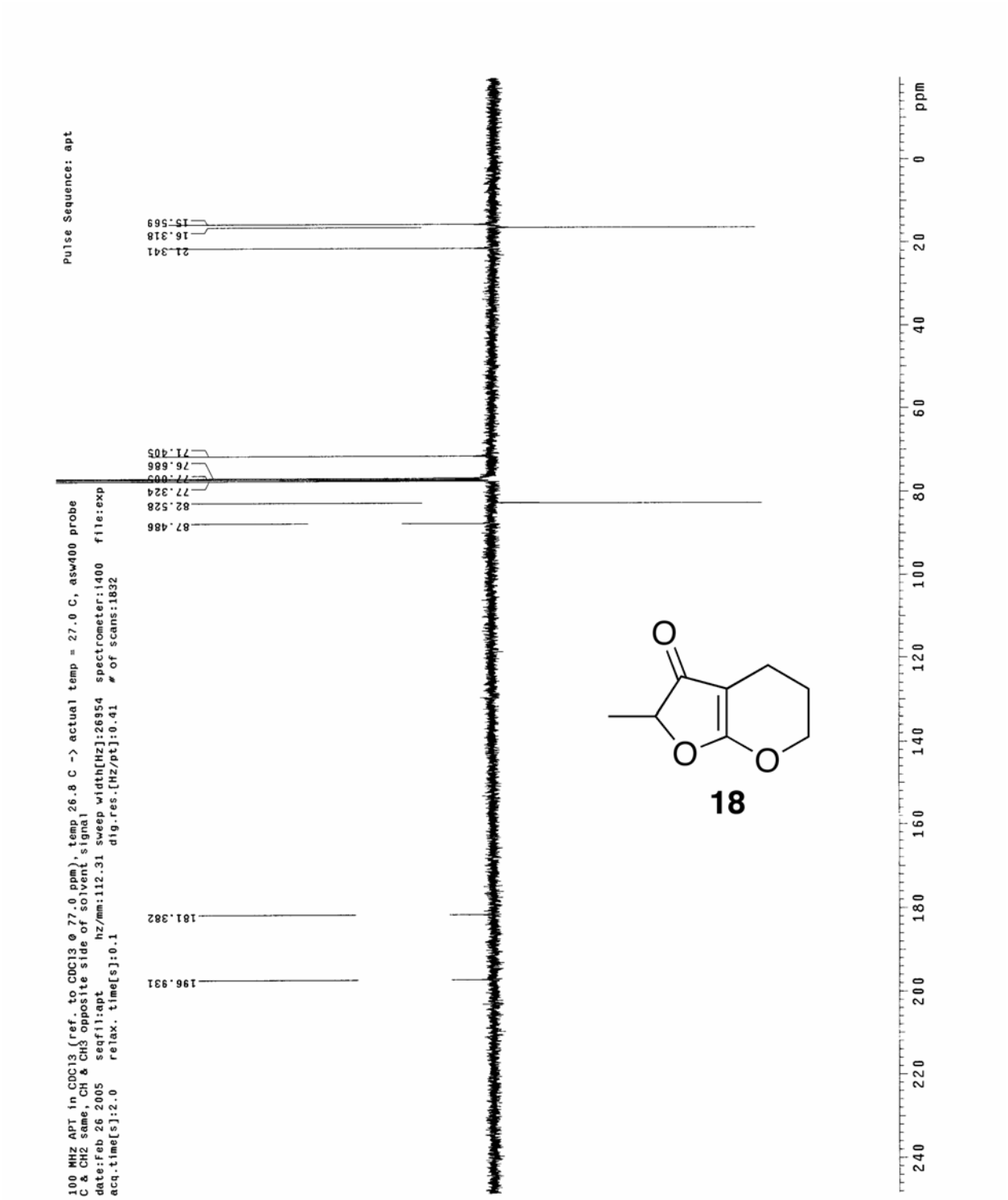
100
120
140
160
180
200
220
240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C & CH2 same, CH & CH3 opposite side of solvent signal
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16.318
21.341
71.405
76.686
77.005
77.324
82.528
87.486
181.382
196.931
ppm
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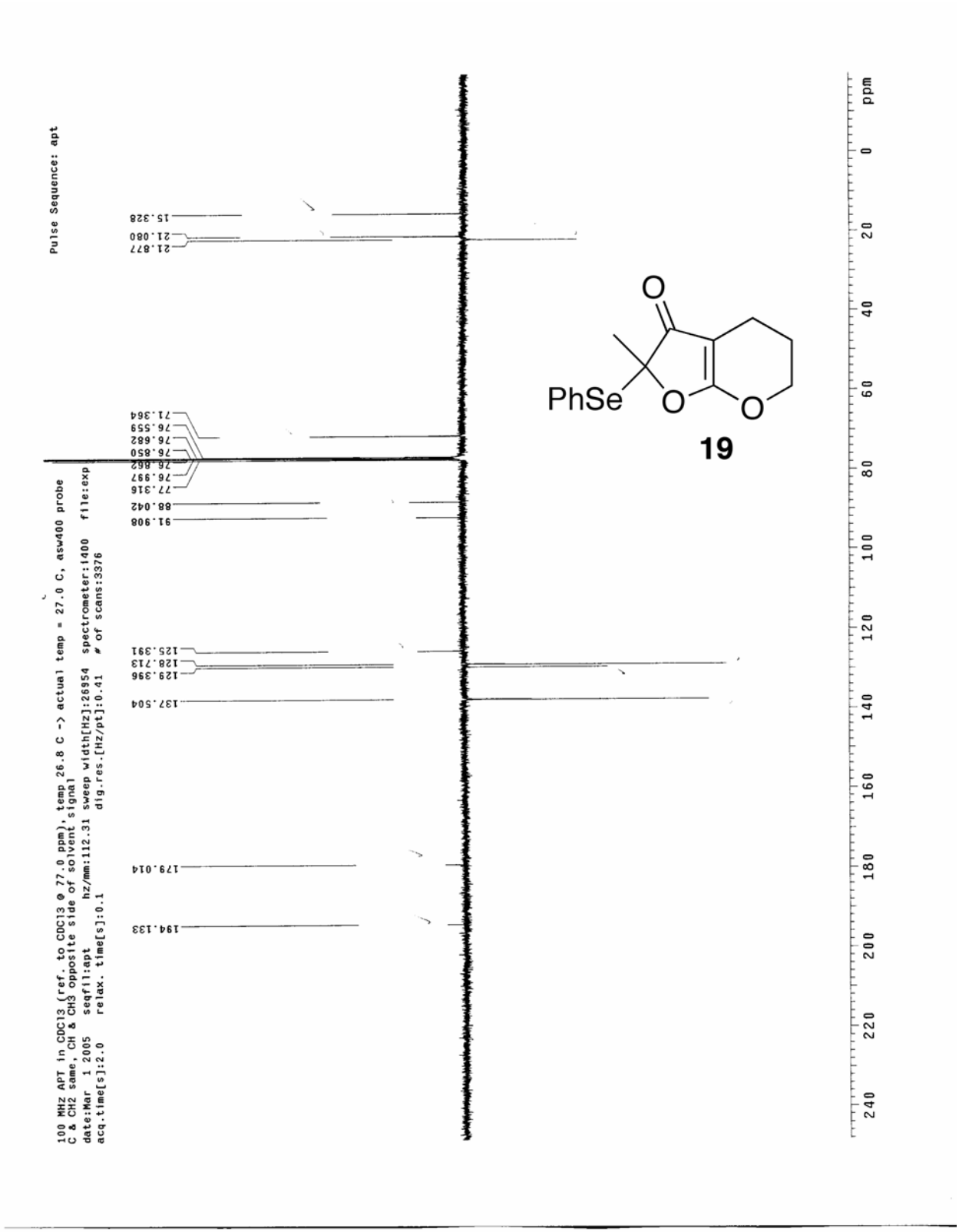
20
40
60
80
100
120
140
160
180
200
220
240
O
O
O
18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C & CH2 same, CH & CH3 opposite side of solvent signal
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21.080
21.877
71.364
76.559
76.682
76.850
76.862
76.997
77.316
88.042
91.908
125.391
128.713
129.396
137.504
179.014
194.133
PhSe
O
O
O
19
ppm
0
20
40
60
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100
120
140
160
180
200
220
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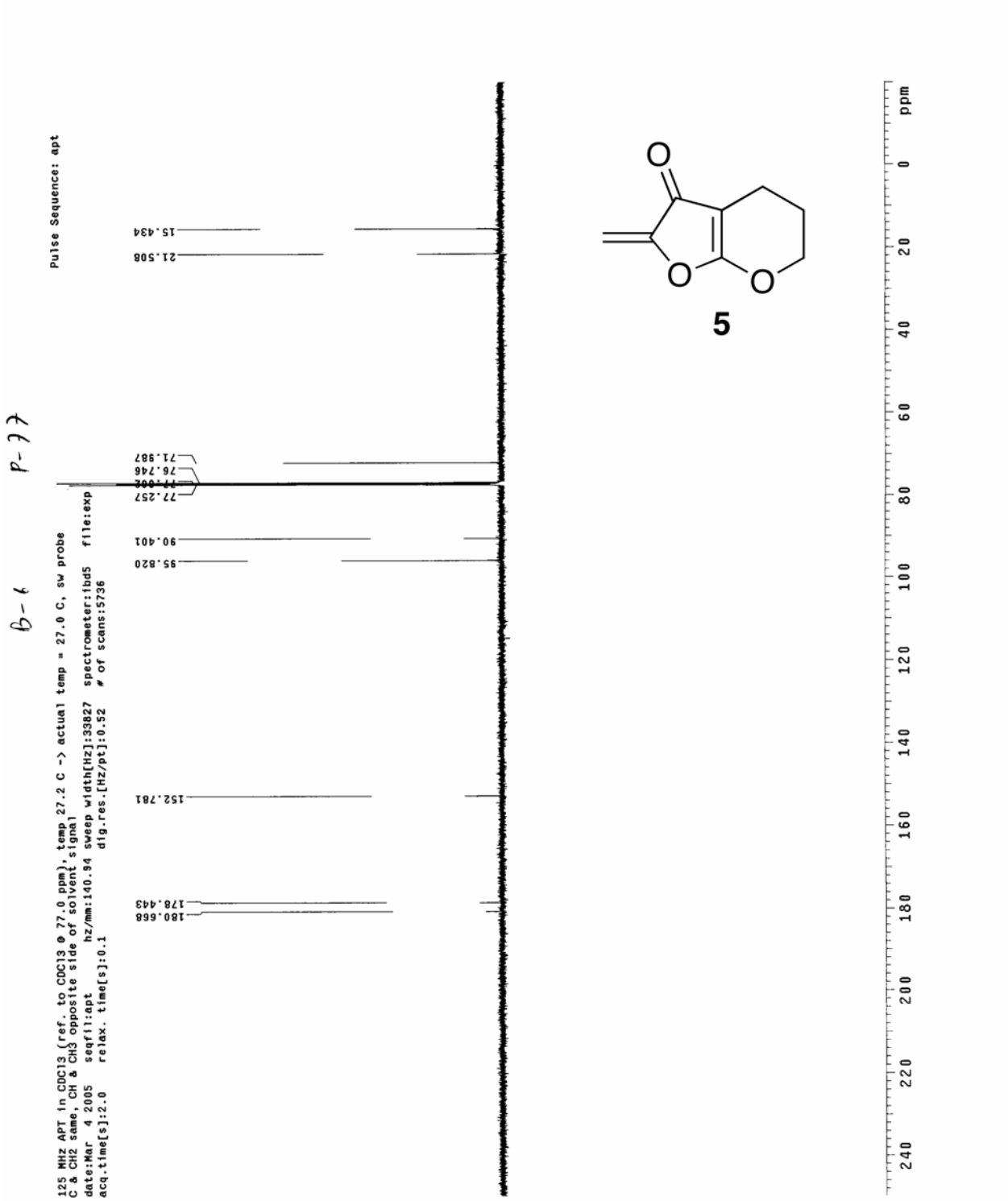
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C & CH2 same, CH & CH3 opposite side of solvent signal
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21.508
71.987
76.746
77.257
90.401
95.820
152.781
178.443
180.668
O
O
O
5
ppm
0
20
40
60
80
100
120
140
160
180
200
220
240