Electronic Supplementary Information (ESI)

An enantiospecific route towards taiwaniaquinoids. First synthesis of (-)-taiwaniaquinone H and (-)-dichroanone

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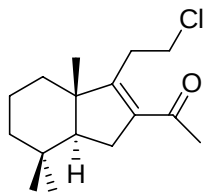
Experimental Section

Treatment of 13 with $BF_3.Et_2O$.

$BF_3.Et_2O$ (45%, 0.3 mL, 2.36 mmol) was added at 0 ºC to a stirred solution of **13** (160 mg, 0.64 mmol) in CH_2Cl_2 (10 mL) and the cooling bath was removed. After stirring for 5h at room temperature, satd aq $NaHCO_3$ (1 mL) was added slowly at 0ºC, and the solvent was removed in vacuum and the mixture was extracted with ether (2 x 15 mL). The organic phase was washed with water, brine, dried over Na_2SO_4 and concentrated to give the unaltered starting material **13** (152 mg) as a yellow oil.

Treatment of 13 with $SOCl_2$.



18

Thionyl chloride (mL) was added to a solution of **13** (176 mg, 0.70 mmol) and pyridine (1mL) in dry CH_2Cl_2 (10 mL) at -78 ºC and the reaction mixture was warmed to -58ºC for 45 min, and stirred for 10 min, at which time TLC showed no starting material. Then the reaction mixture was poured into ice and extracted with ether (3 x 10 mL). The combined organic phase was washed with 2N HCl (3 x 8 mL), water and brine, dried (Na_2SO_4) and the solvent was evaporated to give a crude product which was chromatographed on silica gel (5% ether/hexanes) to give 113 mg (60%) of **18** as a yellow syrup. $[\alpha]_D^{25}$ = +33.6 (c 0.75, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.88 (s, 3H), 0.92 (s, 3H), 0.98 (s, 3H), 1.13 (ddd, *J* = 13.8, 13.8, 4.6 Hz, 1H), 1.31 (ddd, *J* = 13.5, 13.5, 4.1 Hz, 1H), 145-1.55 (m, 2H), 1.58-1.65 (m, 1H), 1.66-1.77 (m, 3H), 2.21 (s, 3H), 2.38 (d, *J* = 8.9 Hz, 1H), 2.48 (ddd, *J* = 16.1, 10.1, 8.9 Hz, 1H), 3.04 (m, 1H), 3.51 (ddd, *J* = 10.1, 10.1, 6.0 Hz, 1H), 3.68 (ddd, *J* = 10.1, 10.1, 5.6 Hz, 1H). ^{3}C NMR ($CDCl_3$, 125 MHz) δ: 16.9 (CH_3), 19.7 (CH_2), 21.3 (CH_3), 29.9 (CH_3), 30.8 (CH_2), 31.0 (CH_2), 32.94 (CH_3), 32.92 (C), 34.4 (CH_2),

41.4 (CH_2), 42.5 (CH_2), 49.9 (C), 57.6 (CH), 137.0 (C), 163.1 (C), 198.8 (C); IR (cm^{-1}) ν: 1684, 1603, 1560, 1450, 1294, 1274, 1201, 1057, 1003, 860; HRMS [FAB, $(M + Na)^+$] m/z: calcd for $C_{16}H_{25}OClNa$ 291.1492, found: 291.1501.

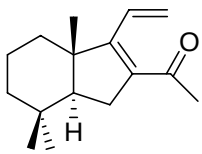
Treatment of 13 with $POCl_3$.

Phosphorous oxychloride (0.2 mL) was added to a solution of **13** (141 mg, 0.56 mmol) and pyridine (1 mL) in dry CH_2Cl_2 (8 mL) at -78 ºC and the reaction mixture was warmed to -59ºC for 35 min, and stirred for 3h, at which time TLC showed no starting material. Then, the reaction mixture was poured into ice and extracted with ether (3 x 10 mL). The combined organic phase was washed with 2N HCl (3 x 8 mL), water and brine, dried (Na_2SO_4) and the solvent was evaporated to give a crude product which was chromatographed on silica gel (7% ether/hexanes) to give 26 mg (20%) of **17** and 53 mg (35%) of **18**.

Treatment of 13 with conc. HCl.

Conc. HCl (0.1 mL) was added to a solution of **13** (250 mg, 1 mmol) in CH_2Cl_2 (10 mL) and the reaction mixture was stairred at room temperature for 1h , at which time TLC showed no **13**. Then the mixture was diluted with ether (25 mL) washed with water, satd aq $NaHCO_3$ (2 x 5 mL) and brine. The organic phase was dried over Na_2SO_4 and concentrated to give 260 mg (97%) of **18**.

1-((3aS,7aS)-3a,7,7-Trimethyl-3-vinyl-3a,4,5,6,7,7a-hexahydro-1H-inden-2-yl)ethanone (17).

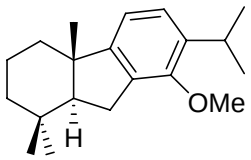


17

To a solution of **13** (0.2 g, 0 .8 mmol) in 1,4-dioxane (7 mL) was added 3 drops of conc. H_2SO_4 and the reaction mixture was stirred at room temperature for 4 h at which time TLC showed no starting material. Then water (3 mL) was slowly added to quench the reaction and the solvent was removed in vacuum, and the mixture was diluted with ether (20 mL), washed with water (3 x 6 mL), brine (2 x 5 mL), dried

over anhydrous Na_2SO_4 to give a crude product which was purified by flash chromatography on silica gel (5% ether/hexane, 2.5 cm x 18 cm) to give 135 mg of **17** (73%) as a colourless oil. $[\alpha]_D^{25}$ = -59.5 (c 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.90 (s, 3H), 0.97 (s, 3H), 1.04 (s, 3H), 1.12 (ddd, *J* = 13.6, 13.6, 4.5 Hz, 1H), 1.43 (m, 1H), 1.46 (ddd, *J* = 12.8, 12.8, 4.1 Hz, 1H), 1.52 (dd, *J* = 11.8, 6.7 Hz, 1H), 1.60 (m, 1H), 1.73 (qt, *J* = 13.7, 3.9 Hz, 1H), 1.98 (dt, *J* = 12.3, 3.4 Hz, 1H), 2.24 (s, 3H), 2.36 (dd, *J* = 15.1, 11.8 Hz, 1H), 2.42 (dd, *J* = 15.1, 6.7 Hz, 1H), 5.32 (d, *J* = 11.8 Hz, 1H), 5.57 (d, *J* = 18.2 Hz, 1H), 6.94 (dd, *J* = 18.2, 11.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 17.7 (CH_3), 19.9 (CH_2), 21.3 (CH_3), 30.3 (C), 30.9 (CH_2), 32.9 (CH_3), 33.0 (C), 35.9 (CH_2), 40.9 (CH_2), 50.0 (C), 57.3 (CH), 120.1 (CH_2), 130.7 (CH), 137.7 (C), 159.9 (C), 199.8 (C); IR (cm^{-1}) ν: 1669, 1545, 1459, 1355, 1232, 1208, 1114, 1078, 1011, 972, 912; HRMS [FAB, $(M + Na)^+$] m/z: calcd for $C_{16}H_{24}ONa$ 255.1725, found: 255.1737.

(4aS, 9aS)-7-Isopropyl-8-methoxy-1, 1, 4a-trimethyl-2, 3, 4, 4a, 9, 9a-hexahydro-1H-fluorene (22).

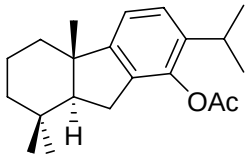


22

K_2CO_3 (360 mg, 2.61 mmol) and MeI (710 mg, 5.0 mmol) was added to a solution of **10** (281 mg, 1.03 mmol) in acetone (25 mL) and the mixture was stirred under reflux for 17 h. The mixture, cooled at room temperature, was filtered and the solvent was removed under vacuum. The crude residue was diluted with ether (30 mL)- water (10 mL) and the phases were shaken and separated. The organic phase was washed with brine (15 mL) and dried under anhydrous Na_2SO_4. After evaporating the solvent, compound **22** (285 mg, 97%) was obtained as a colourless syrup.$[\alpha]_D^{25}$ = -35.5 (c 2.4, $CHCl_3$); 1H NMR ($CDCl_3$, 500 MHz) δ(ppm): 0.98 (s, 3H), 1.06 (s, 6H), 1.19 (ddd, *J*= 13.6, 13.6, 4.2 Hz, 1H), 1.20 (d, *J*= 6.9 Hz, 3H), 1.25 (d, *J*= 6.9 Hz, 3H), 1.46 (ddd, *J*= 12.8, 12.8, 3.9 Hz, 1H), 1.54 (dt, *J*= 13.4, 3.1 Hz, 1H), 1.67 (m, 1H), 1.71 (bd, *J*= 12.5, 6.1 Hz, 1H), 1.83 (qt, *J*= 13.6, 3.9 Hz, 1H), 2.05 (dt, *J*= 12.4, 3.9 Hz, 1H), 2.66 (dd, *J*= 14.3, 12.5 Hz, 1H), 2.82 (dd, *J*=

14.3, 6.1 Hz, 1H), 3.01 (h, *J*= 6.9 Hz, 1H), 3.83 (s, 3H), 6.77 (d, *J*= 7.6Hz, 1H), 7.02 (d, *J*= 7.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 20.0 (CH_2), 21.0 (CH_3), 21.7 (CH_3), 23.7 (CH_3), 23.9 (CH_3), 26.8 (CH_2), 27.1 (CH), 33.0 (C), 33.2 (CH_3), 35.8 (CH_2), 41.6 (CH_2), 45.5 (C), 60.0 (CH_3), 60.4 (CH), 115.5 (CH), 124.5 (CH), 132.9 (C), 138.0 (C), 154.2 (C), 155.5 (C). IR (cm^{-1}) ν: 1474, 1458, 1420, 1341, 1249, 1200, 1096, 1059, 1024, 818; HRMS [FAB, $(M + Na)^+$] m/z: calcd for $C_{20}H_{30}ONa$ 309.2194, found: 309.2183.

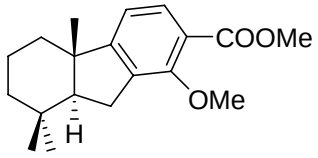
(4bS, 8aS)-2-Isopropyl-4b,8,8- trimethyl-5, 6, 7, 8a, 9-hexahydro-4bH- fluoren-1-yl acetate (28).



28

To a solution of phenol **10** (220 mg, 0.80 mmol) in pyridine (7 mL) was added acetic anhydride (5 mL) and the solution was stirred at room temperature for 1 h. Then water was added at 0ºC to quench the reaction and stirred for 10 min and ether (30 mL) was added. The organic phase was washed with water (10 mL), 2N HCl (4 x 10 mL), satd aq $NaHCO_3$ (6 x 10 mL), brine and dried over anhydrous Na_2SO_4. The solvent was evaporated under vacuum, affording pure acetate **28** (246 mg, 98%). $[\alpha]_D^{25}$ = -33.3 (c 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.95 (s, 3H), 1.02 (s, 3H), 1.05 (s, 3H), 1.19 (d, *J* = 6.9 Hz, 3H), 1.21 (d, *J* = 6.9 Hz, 3H), 1.47 (ddd, *J* = 13.6, 13.6, 3.9 Hz, 1H), 1.52 (dt, *J* = 13.3, 4.1 Hz, 1H), 1.65 (m, 1H), 1.73 (bd, *J* = 10.8, 8.2 Hz, 1H), 1.82 (qt, *J* = 13.6, 3.9 Hz, 1H), 2.04 (dt, *J* = 12.3, 3.4 Hz, 1H), 2.34 (s, 3H), 2.49 (d, *J* = 10.8 Hz, 1H), 2.51 (d, *J* = 8.2 Hz, 1H), 2.99 (h, *J* = 6.9 Hz, 1H), 6.90 (d, *J* = 7.7 Hz, 1H), 7.10 (d, *J* = 7.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 20.0 (CH_2), 20.8 (CH_3), 21.0 (CH_3), 21.8 (CH_3), 23.3 (CH), 23.4 (CH_3), 26.9 (CH_2), 27.5 (CH), 33.0 (C), 33.2 (CH_3), 35.7 (CH_2), 41.6 (CH_2), 46.1 (C), 59.9 (CH), 118.1 (CH), 124.7 (CH), 134.1(C), 137.3 (C), 144.8 (C), 155.0 (C), 168.9 (C); IR (cm^{-1}) ν: 1764, 1459, 1368, 1213, 1178, 1012, 901, 822, 758. HRMS [FAB, $(M + Na)^+$] m/z: calcd for $C_{21}H_{30}O_2Na$ 337.2143, found: 337,2136.

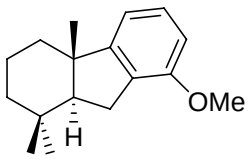
(4bS,8aS) Methyl 1-Methoxy -4b,8,8-trimethyl-5,6,7,8,8a,9-hexahydro-4bH-fluoren-2-carboxylate (33).



33

K_2CO_3 (436 mg, 3.57 mmol) and MeI (0.27 mL, 3.57 mmol) was added to a solution of **20** (320 mg, 1.19 mmol) in acetone (25 mL) and the mixture was stirred under reflux for 8 h, at which time TLC showed no starting material. Following the same work-up described for ester **22**, compound **33** (329 mg, 98%) was obtained as a colourless oil. $[\alpha]_D^{25}$ = -25.2 (c 2.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.91 (s, 3H), 0.97 (s, 3H), 0.97 (s, 3H), 1.12 (ddd, *J* = 13.7, 13,7, 4.3 Hz, 1H), 1.37 (ddd, *J* = 12.7, 12.7, 3.9 Hz, 1H), 1.47 (dt, *J* = 13.4, 3.1 Hz, 1H), 1.61 (m, 1H), 1.61 (dd, *J* = 12.6, 6.1 Hz, 1H), 1.75 (qt, *J* = 13.5, 3.9 Hz, 1H),1.97 (dt, *J* = 12.4, 3.1 Hz, 1H), 2.55 (dd, *J* = 14.6, 12.6 Hz, 1H), 2.78 (dd, *J* = 14.6, 6.1 Hz, 1H), 3.81 (s, 3H), 6.75 (d, *J* = 7.7 Hz, 1H), 7.56 (d, *J* = 7.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 19.9 (CH_2), 21.1 (CH_3), 21.4 (CH_3), 26.7 (CH_2), 33.17 (CH_3), 33.18 (C), 35.4 (CH_2), 41.5 (CH_2), 46.3 (C), 52.0 (CH), 59.8 (OCH_3), 61.2 (OCH_3), 115.6 (CH), 121.7 (C), 130.5 (CH), 135.2 (C), 156.6 (C), 162.7 (C), 167.1 (C); IR (cm^{-1}) ν: 1726, 1604,1458, 1288. HRMS [FAB, $(M + Na)^+$] m/z: calcd for $C_{19}H_{26}O_3Na$ 325.1780, found: 325.1793.

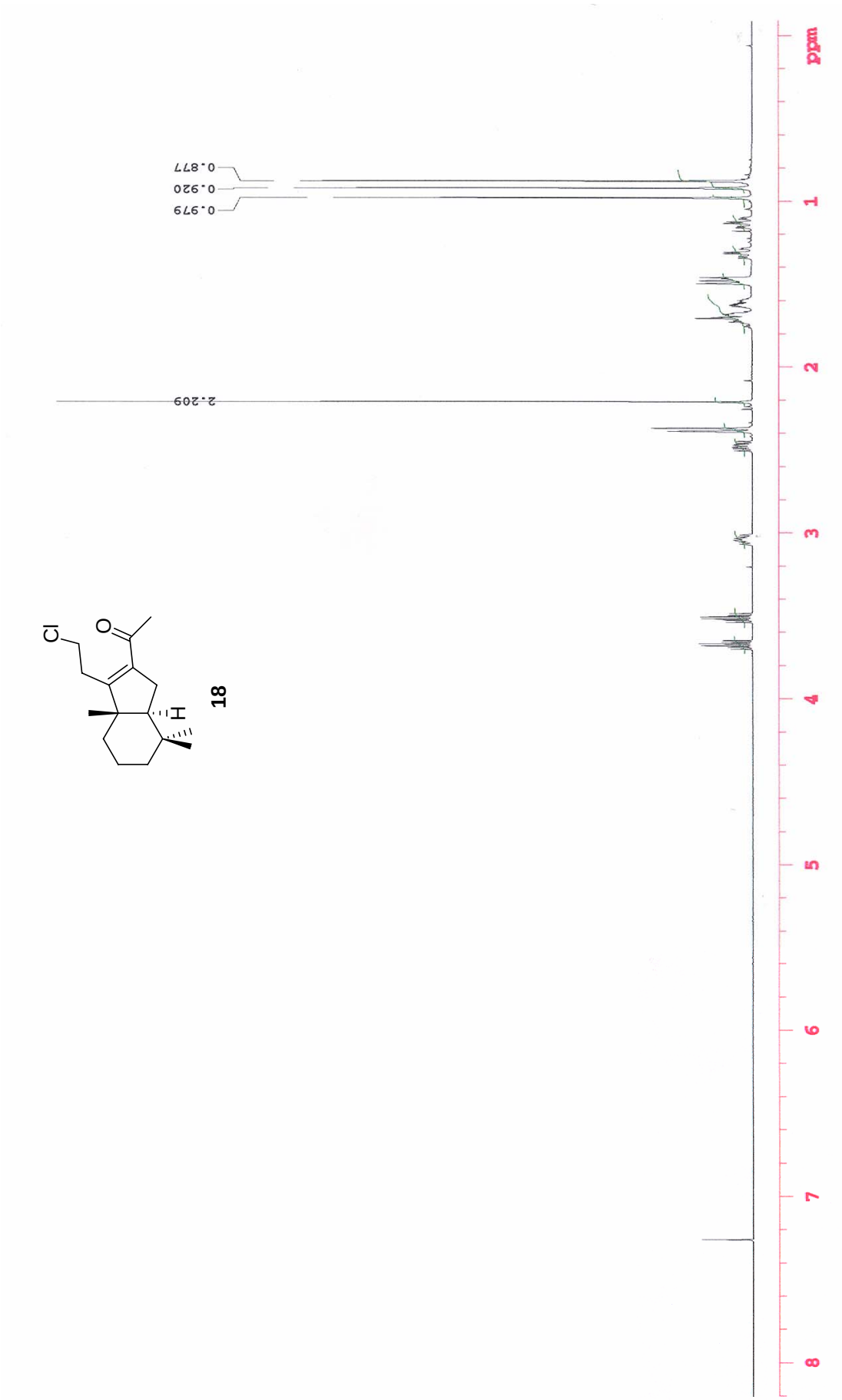
(4aS)-8-Methoxy-1,1,4a-trimethyl-2, 3, 4, 4a,9,9a-hexahydro-1H-fluorene (37).



37

K_2CO_3 (234 mg, 1.69 mmoles, 3 eq.) and MeI (0.24 g, 1.41 mmoles, 3eq.) was added to a solution of phenol **36** (130 mg, 0.56 mmol) in acetone (10 mL) and the mixture was stirred under reflux for 6 h. After cooling at room temperature, the mixture was filtered and the solvent evaporated. Following the same work-up described for ester **22**,

compound **37** (132 mg, 96%) was isolated as a yellow syrup; $[\alpha]_D^{25}$ = -19.3 (c 1.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.89 (s, 3H), 0.96 (s, 3H), 0.97 (s, 3H), 1.12 (ddd, *J* = 13.4, 13.4, 4.3 Hz, 1H), 1.38 (ddd, *J* = 12.8, 12.8, 4.2 Hz, 1H), 1.46 (dt, *J* = 13.4, 2.8 Hz, 1H), 1.59 (bd, *J* = 12.9 Hz, 1H), 1.62 (dd, *J* = 12.4, 6.3 Hz,1H), 1.76 (qt, *J* = 13.9, 3.9 Hz, 1H), 1.97 (dt, *J* = 12.4, 2.8 Hz, 1H), 2.45 (bd, *J* = 14.6, 12.4 Hz, 1H), 2.70 (dd, *J* = 14.6, 6.3 Hz, 1H), 3.78 (s, 3H), 6.59 (d, *J* = 8.2 Hz, 1H), 6.61 (d, *J* = 7.3 Hz, 1H), 7.07 (dd, *J* = 8.2, 7.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 19.0 (CH_2), 20.0 (CH_3), 20.4 (CH_3), 24.9 (CH_2), 32.0 (C), 32.2 (CH_3), 34.7 (CH_2), 40.6 (CH_2), 45.1 (C), 54.2 (OCH_3), 58.9 (CH), 106.8 (CH), 112.0 (CH), 126.6 (CH), 128.4 (C), 154.9 (C), 156.5 (C). IR (cm^{-1}) ν: 3000, 2954, 2954, 2926, 2850, 1605, 1583, 1478, 1268, 1070, 1038, 785; HRMS [FAB, $(M + Na)^+$] m/z: calcd for $C_{17}H_{24}ONa$ 267.1725, found: 267.1738.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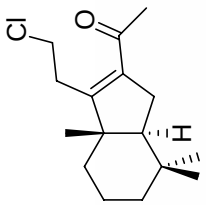
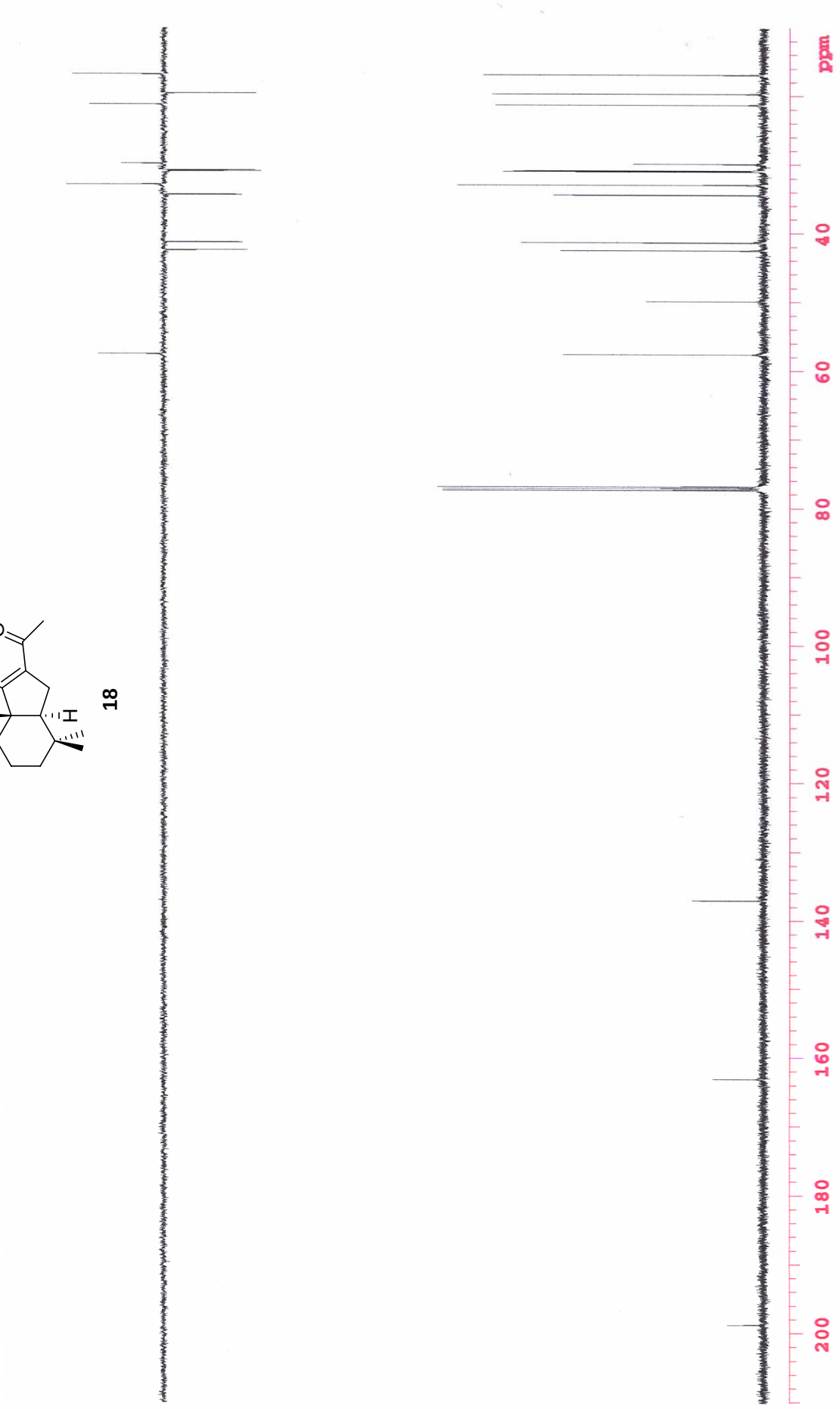
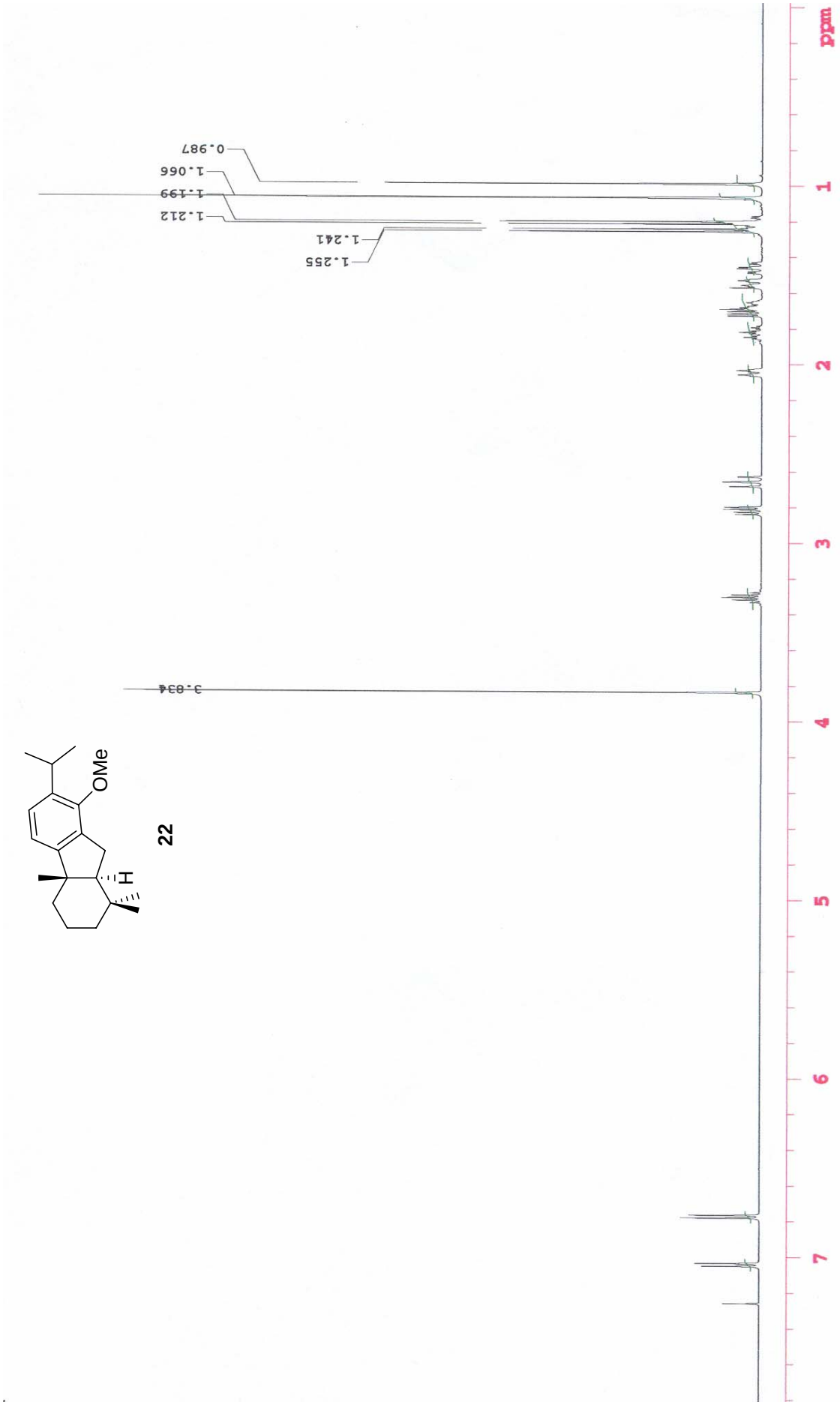


18

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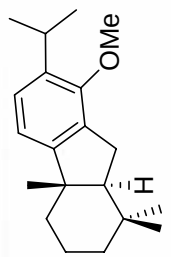

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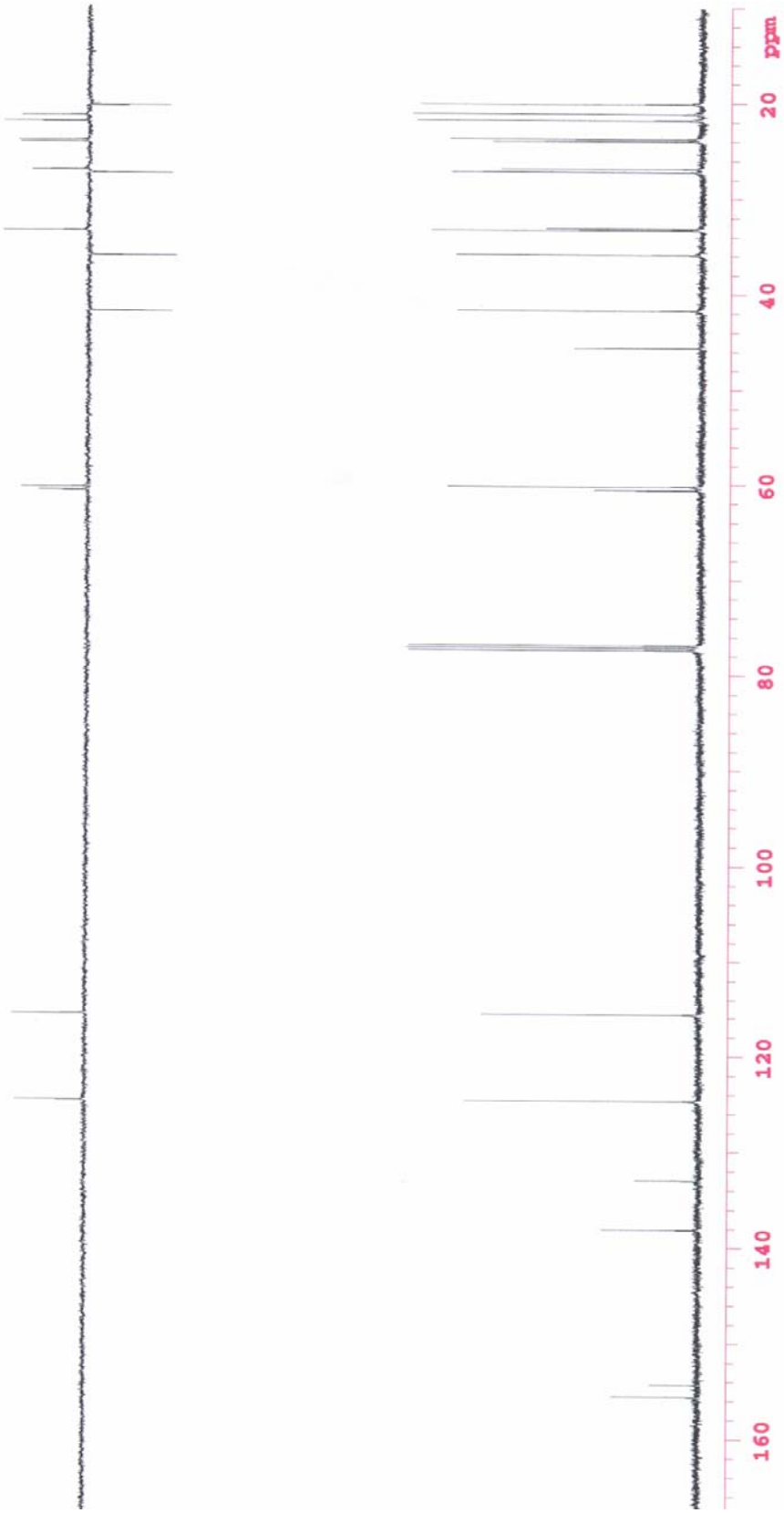

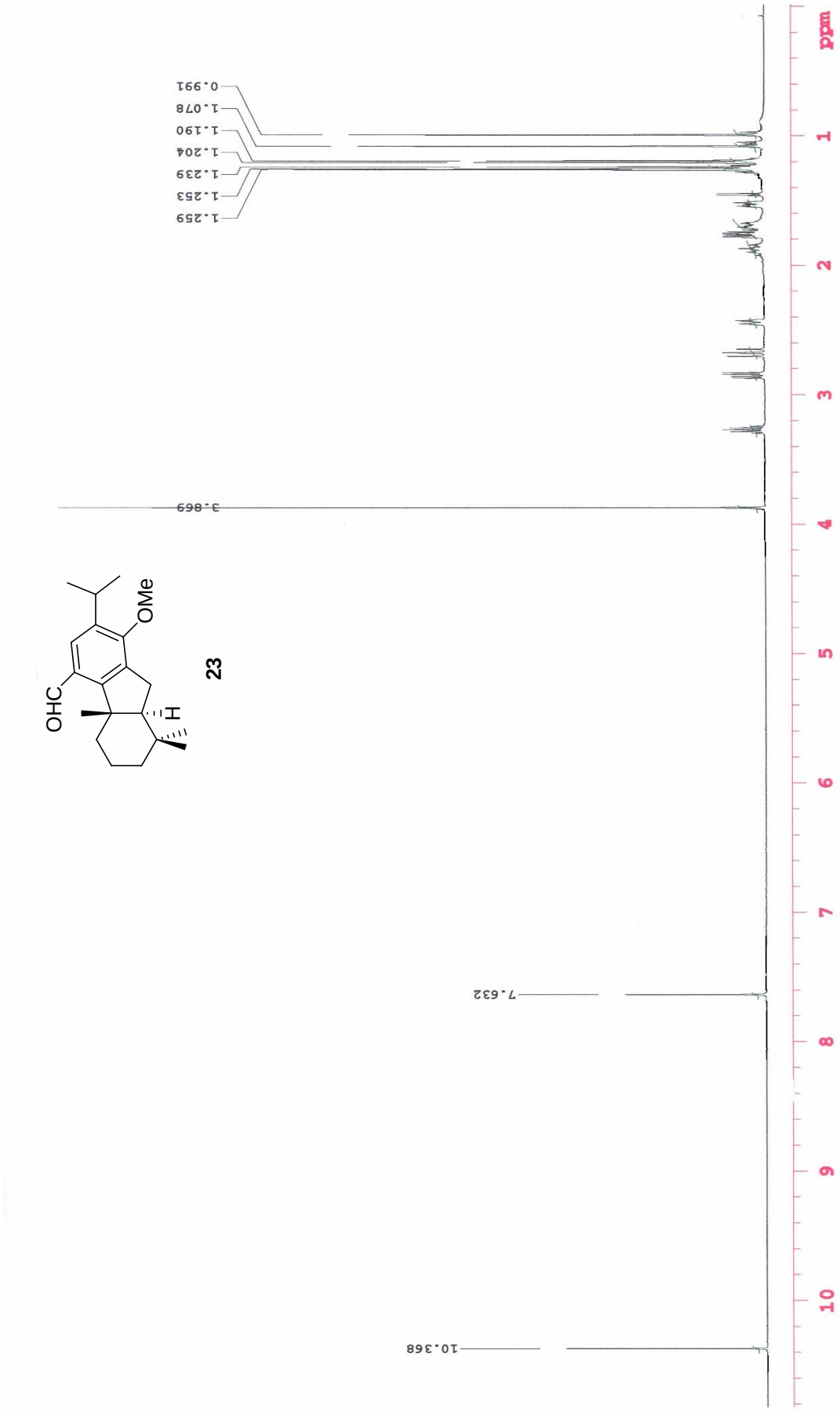
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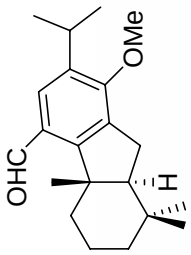

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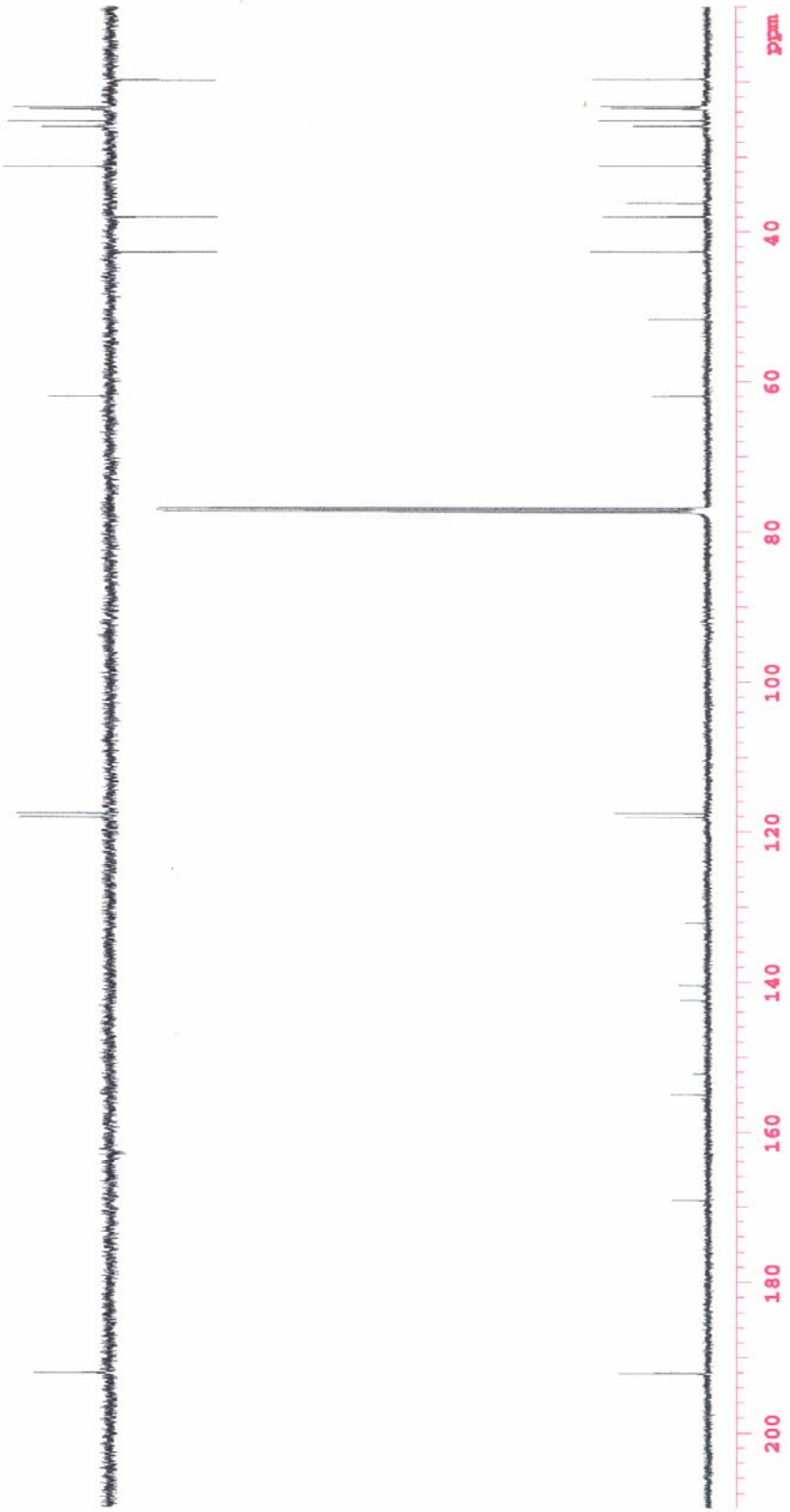

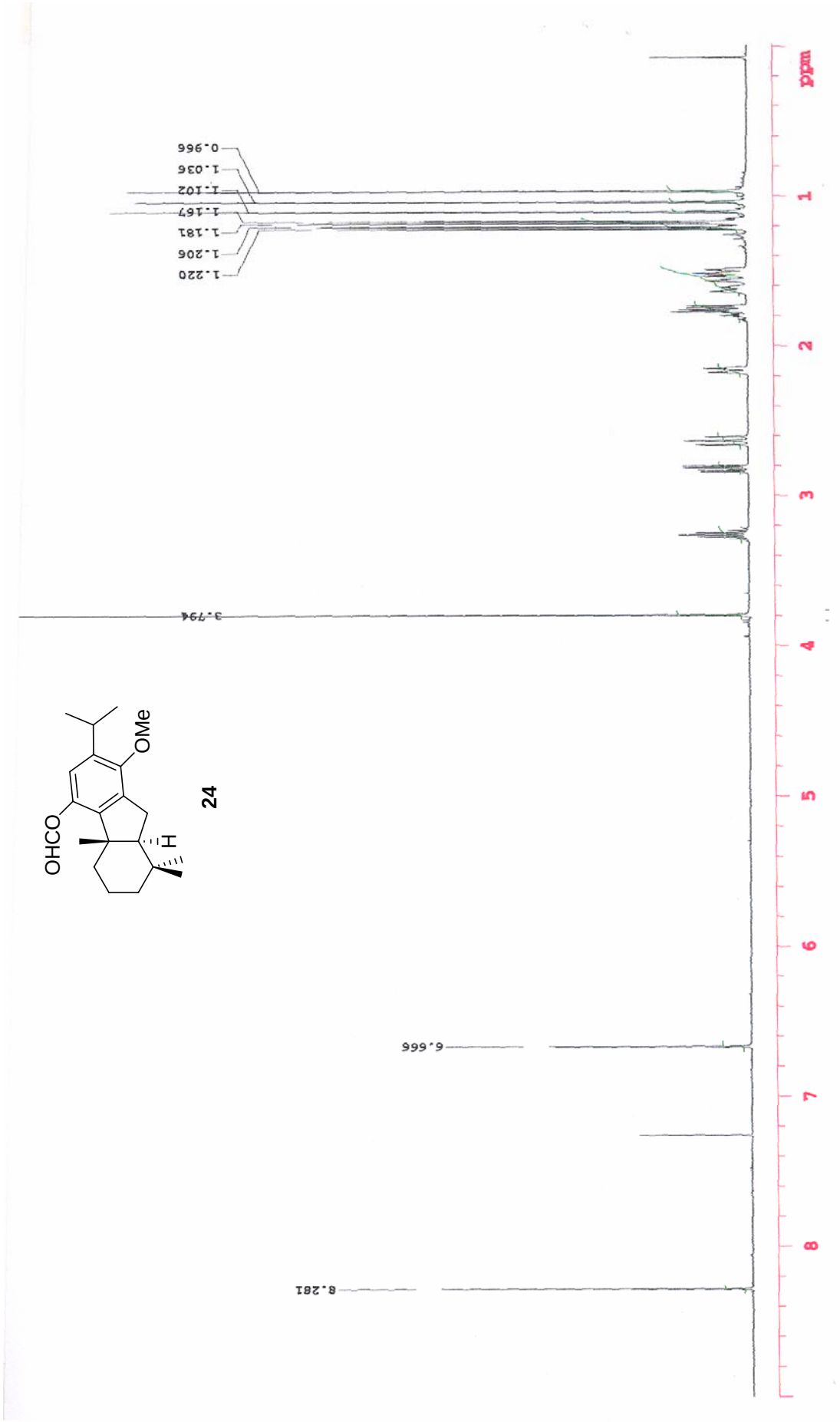
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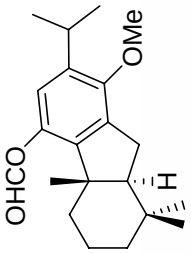

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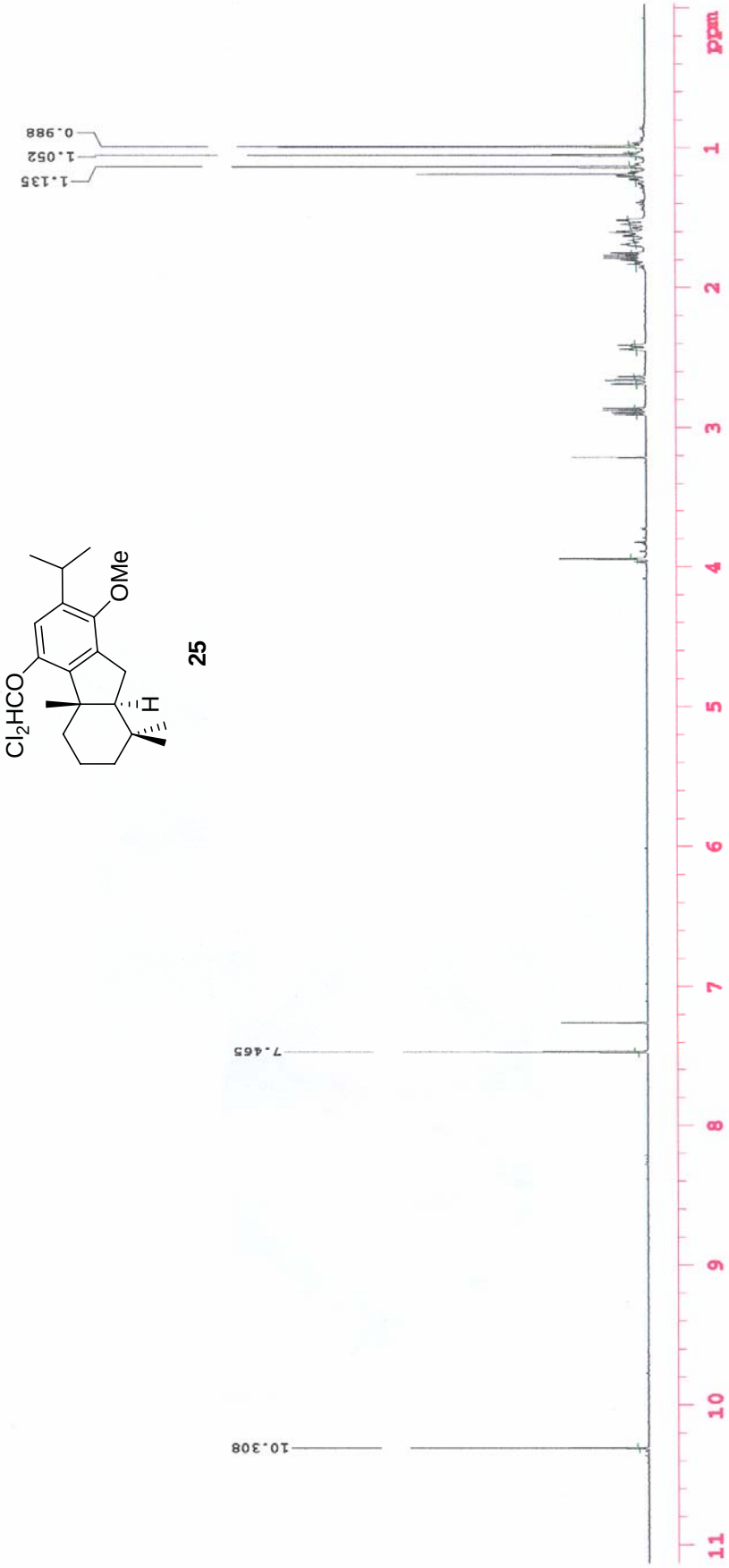
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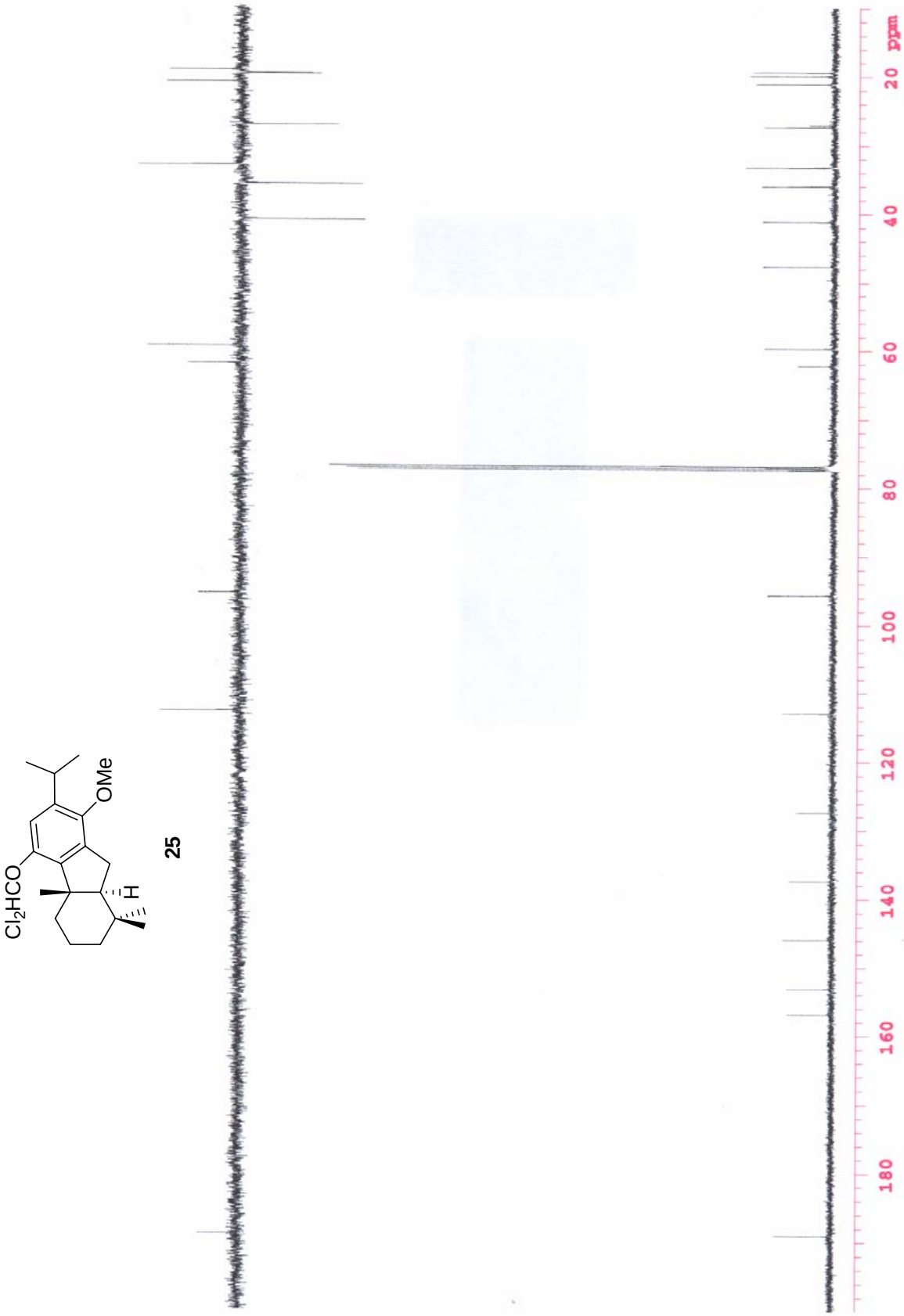
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ppm
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140
160
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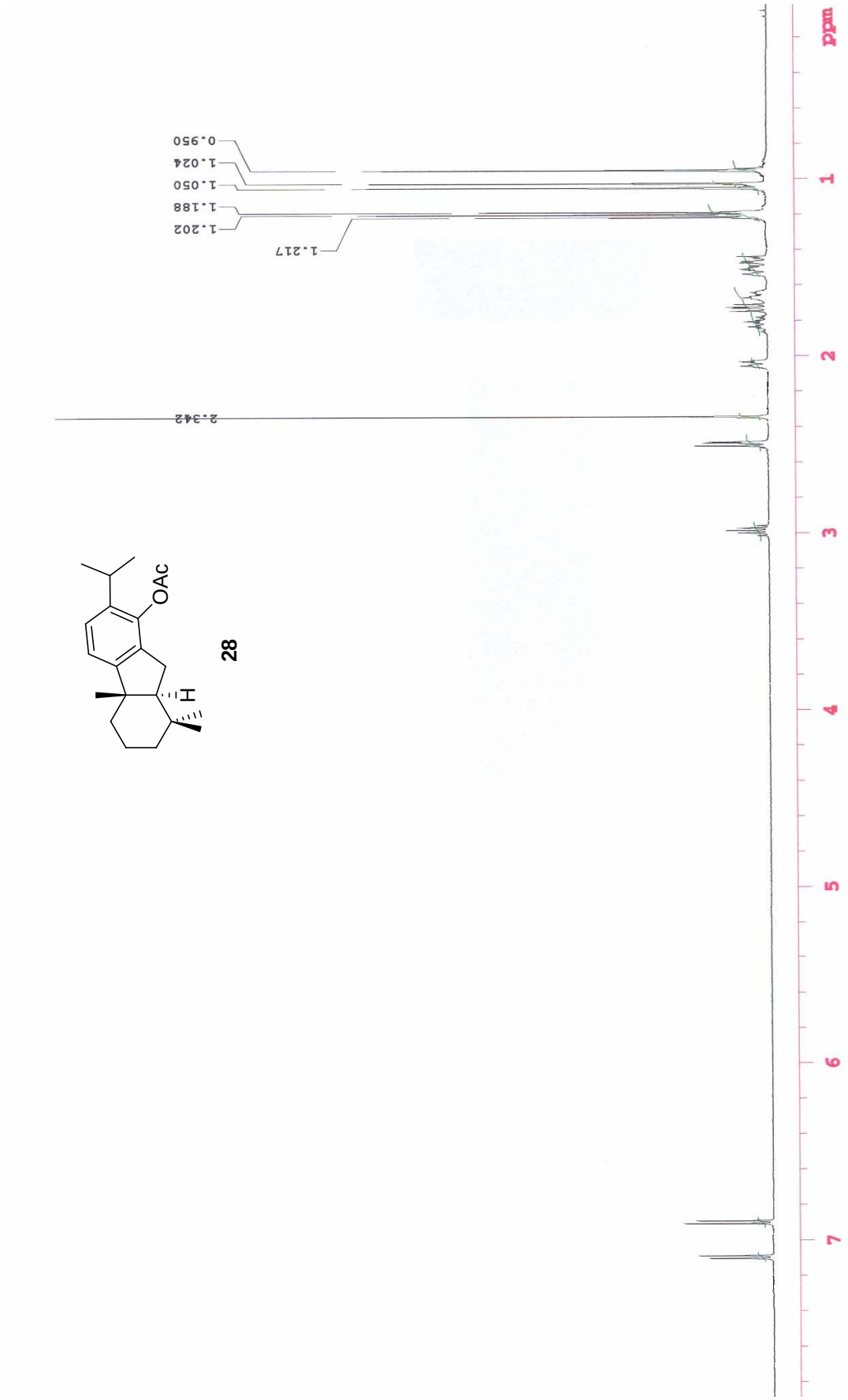
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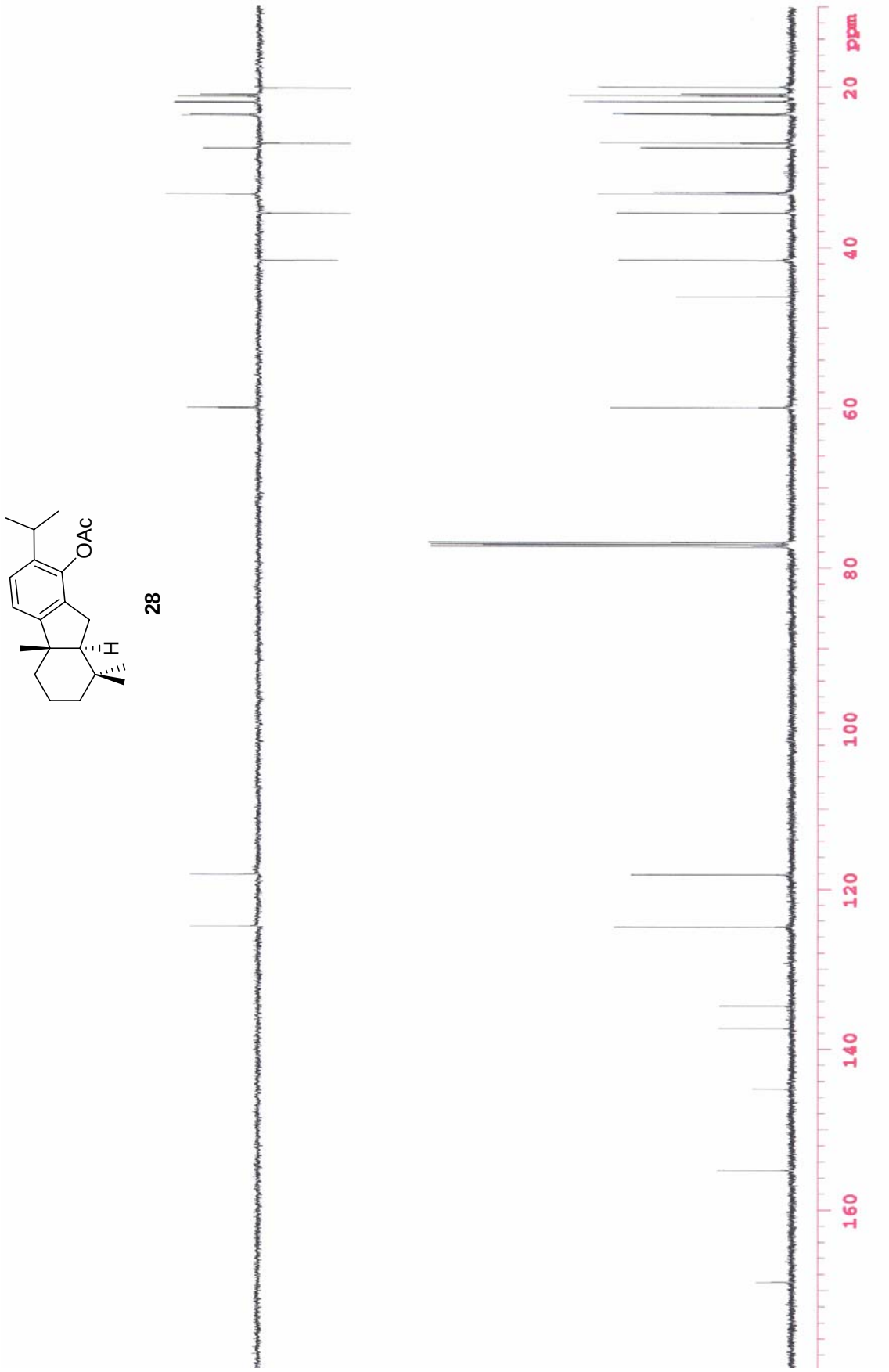
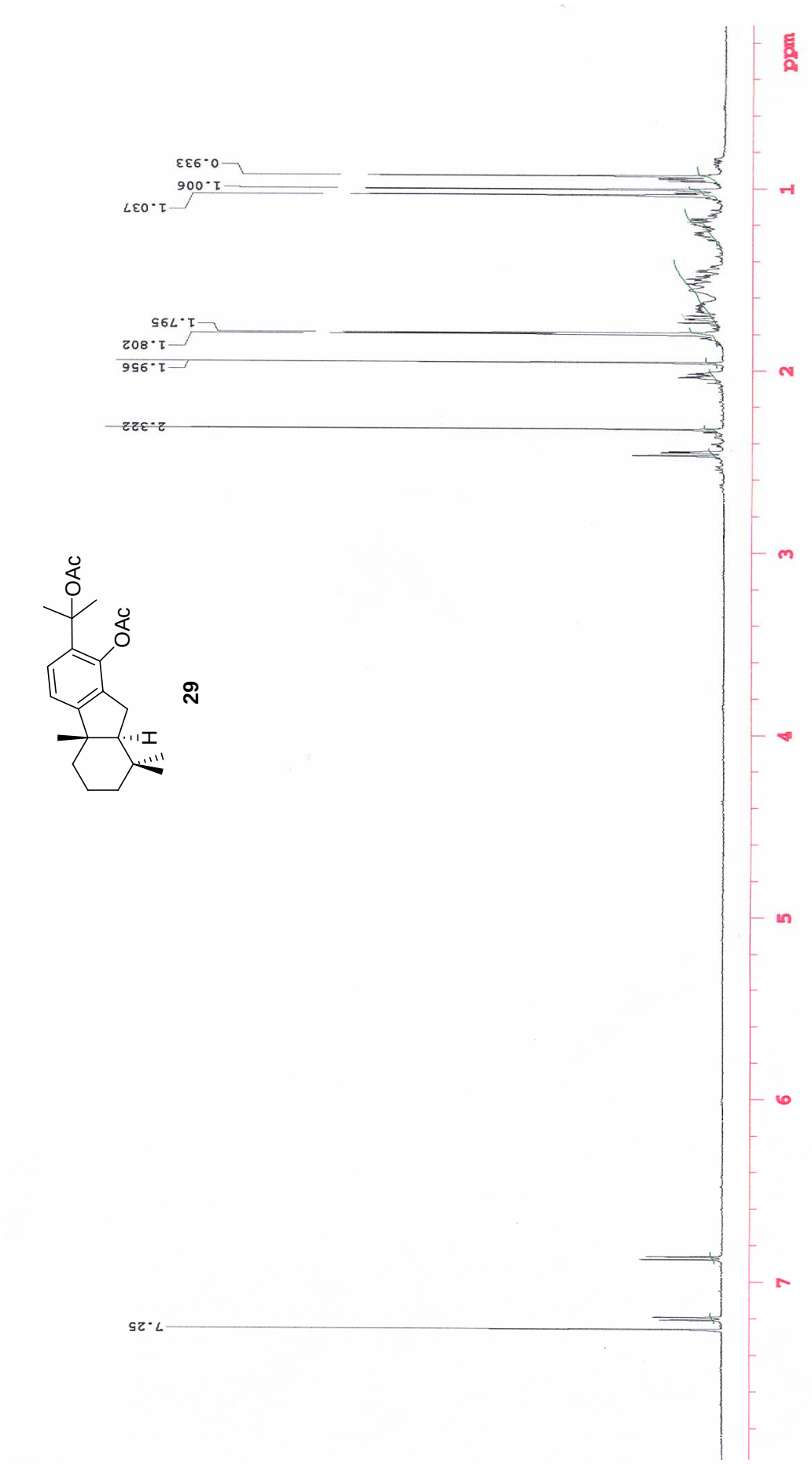
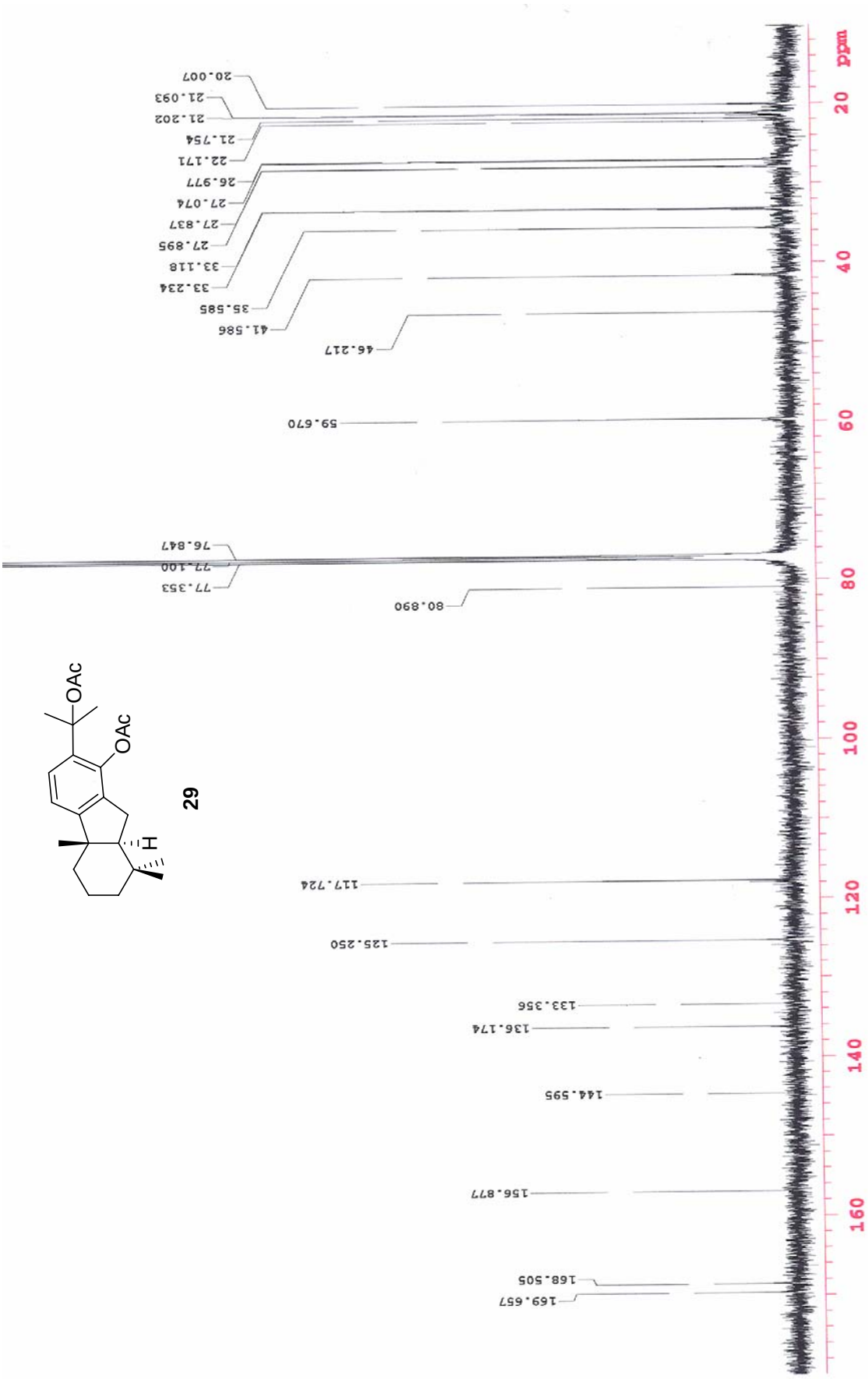
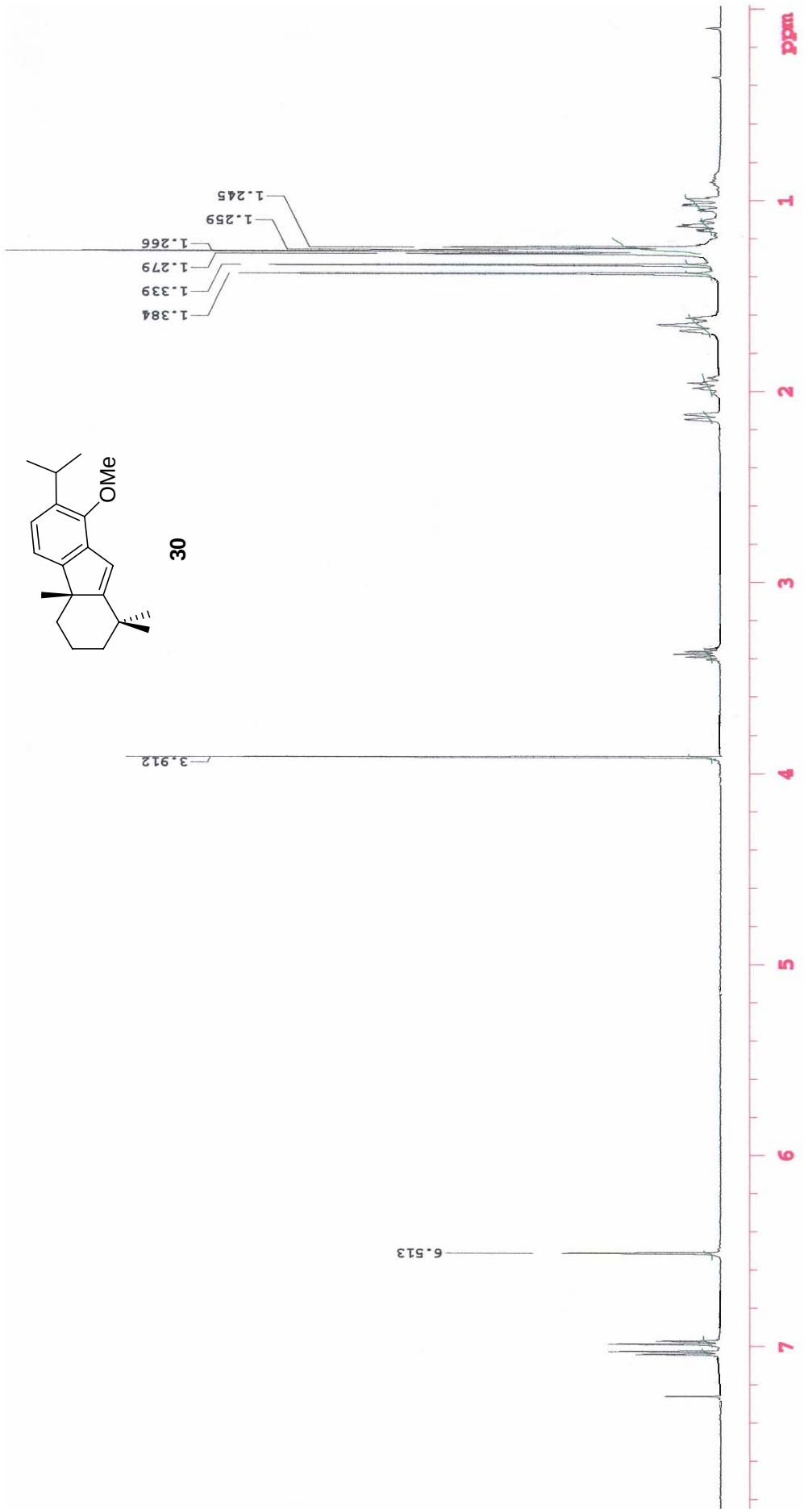
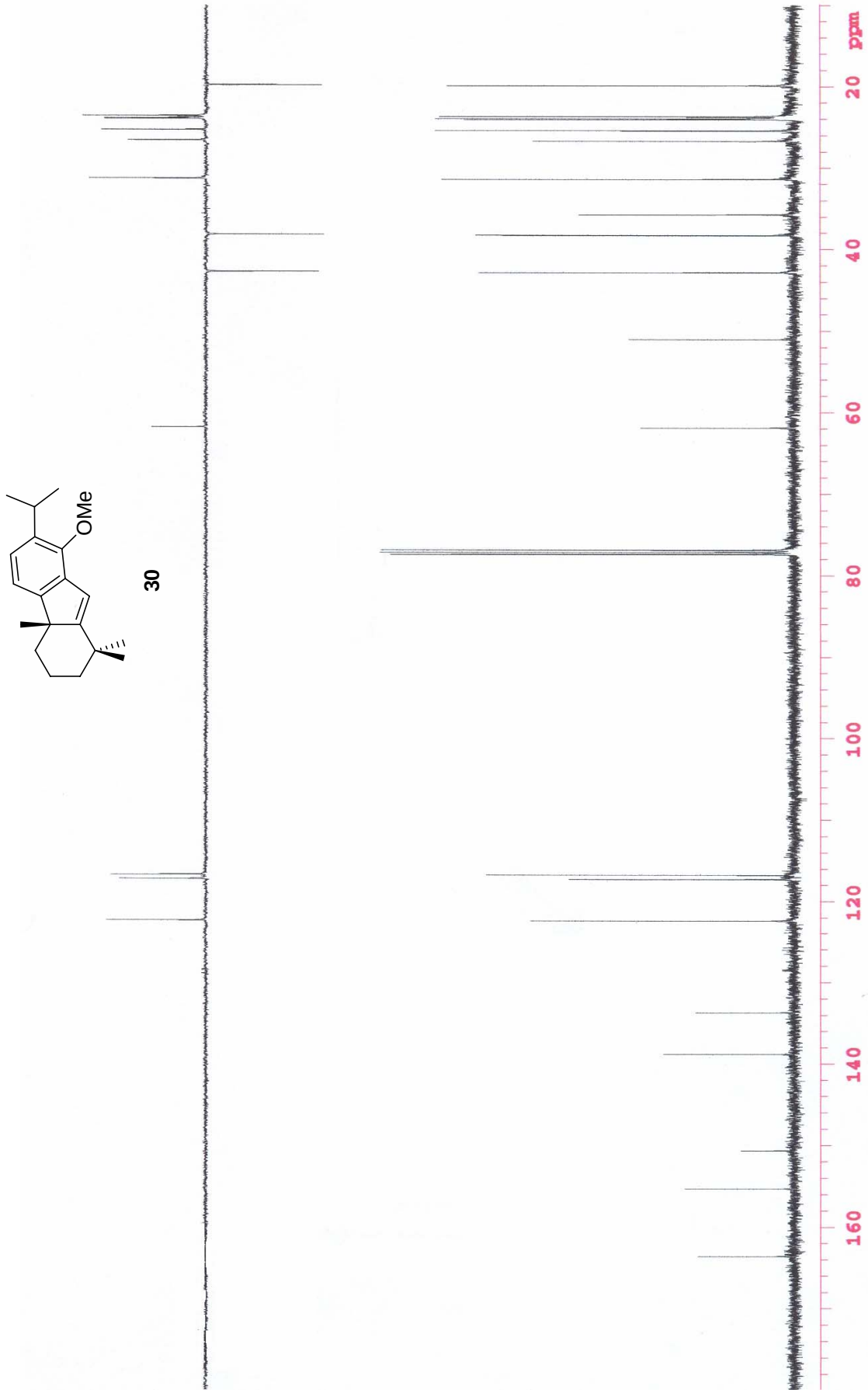
ppm
1
2
3
4
5
6
7

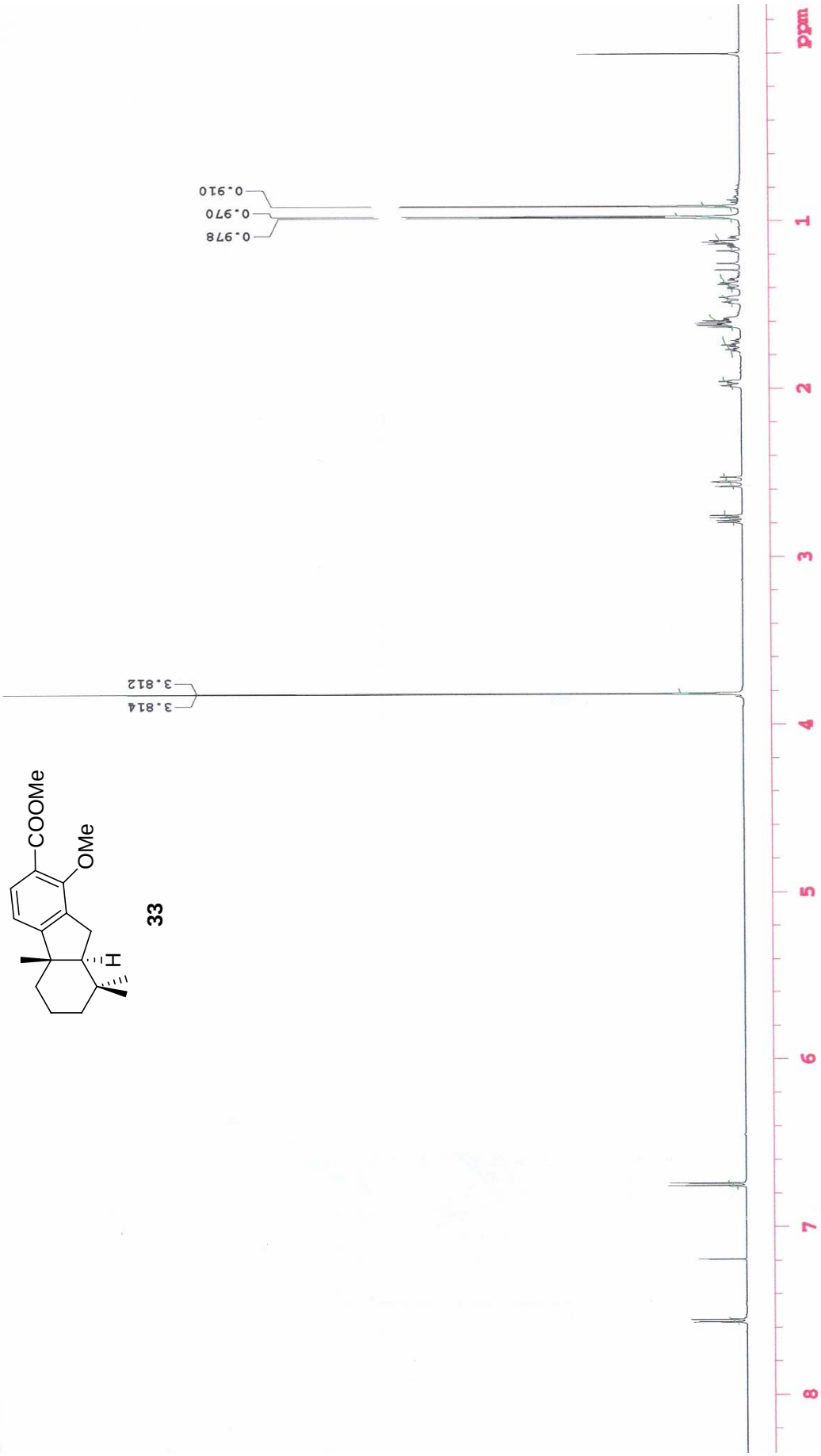

OAc
H
28
ppm
20
40
60
80
100
120
140
160

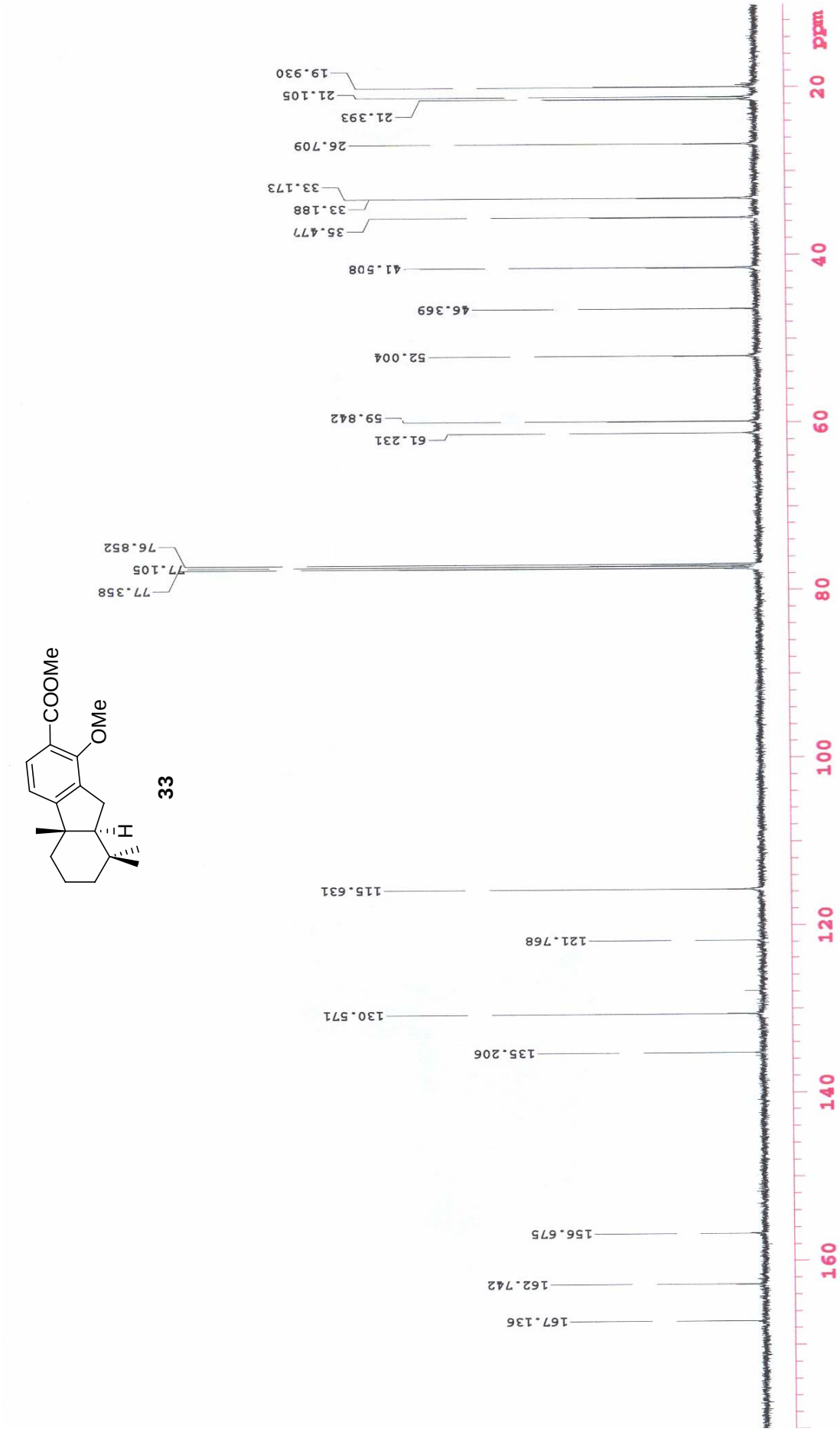

OAc
OAc
H
29
7.25
2.322
1.956
1.802
1.795
1.037
1.006
0.933
ppm
7
6
5
4
3
2
1

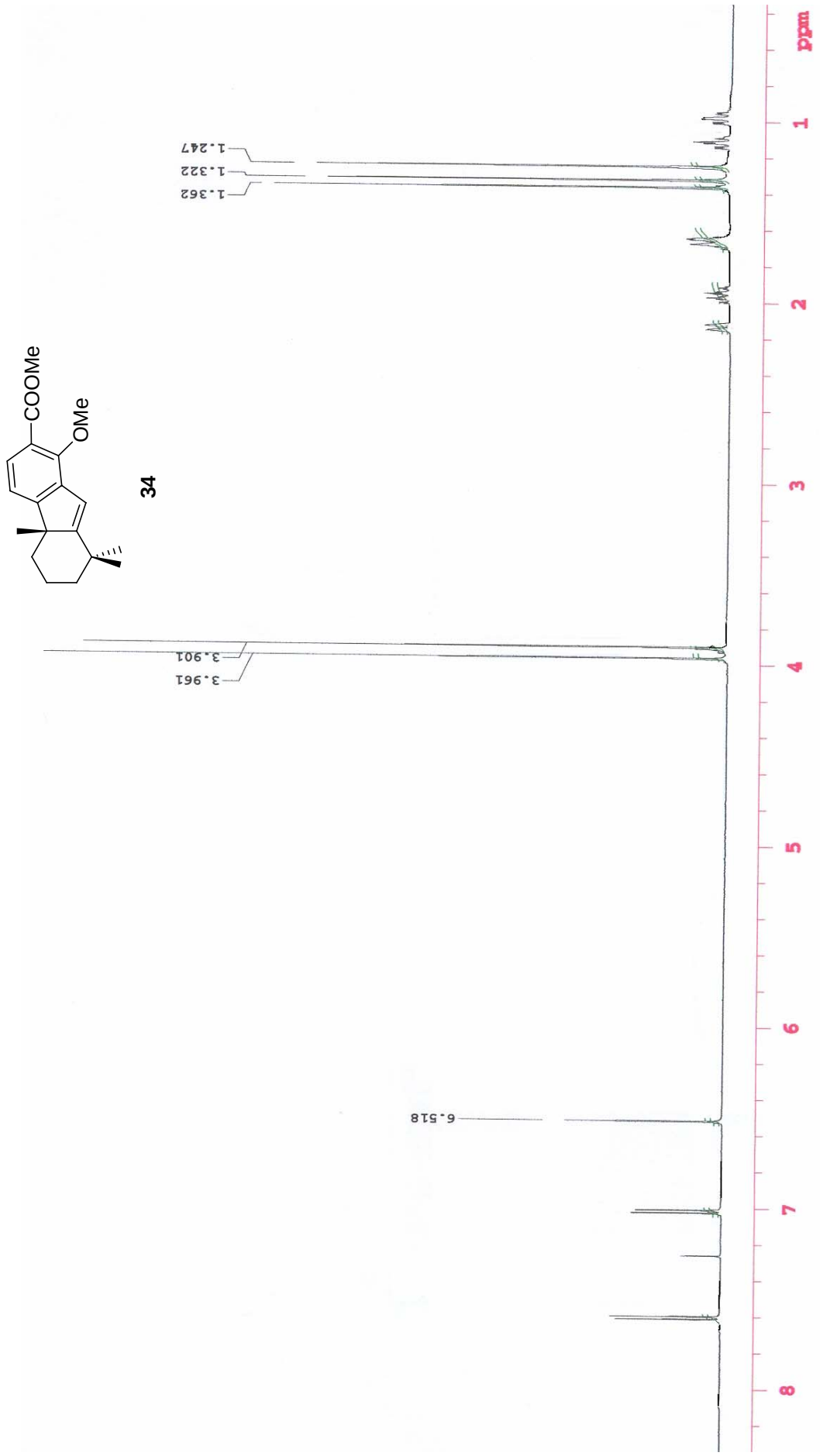

169.657
168.505
156.877
144.595
136.174
133.356
125.250
117.724
80.890
77.353
77.100
76.847
59.670
46.217
41.586
35.585
33.234
33.118
27.895
27.837
27.074
26.977
22.171
21.754
21.202
21.093
20.007
ppm
20
40
60
80
100
120
140
160
OAc
OAc
H
29

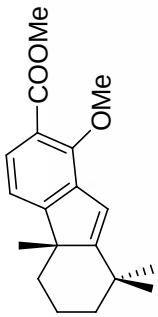

ppm
7
6
5
4
3
2
1
6.513
3.912
1.384
1.339
1.279
1.266
1.259
1.245
30
OMe


OMe
30
ppm
20
40
60
80
100
120
140
160

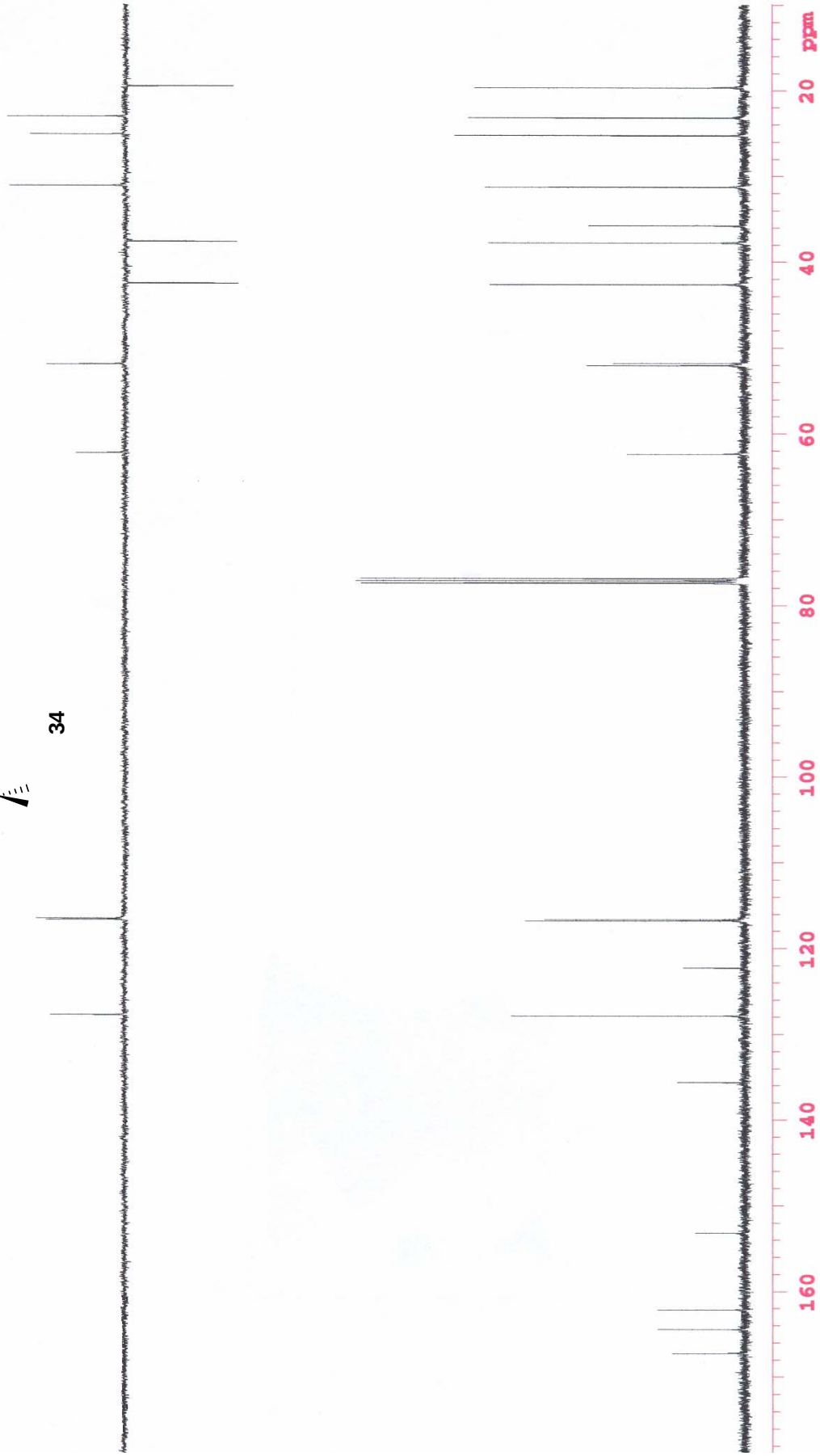

COOMe
OMe
H
33
3.814
3.812
0.978
0.970
0.910
ppm
1
2
3
4
5
6
7
8

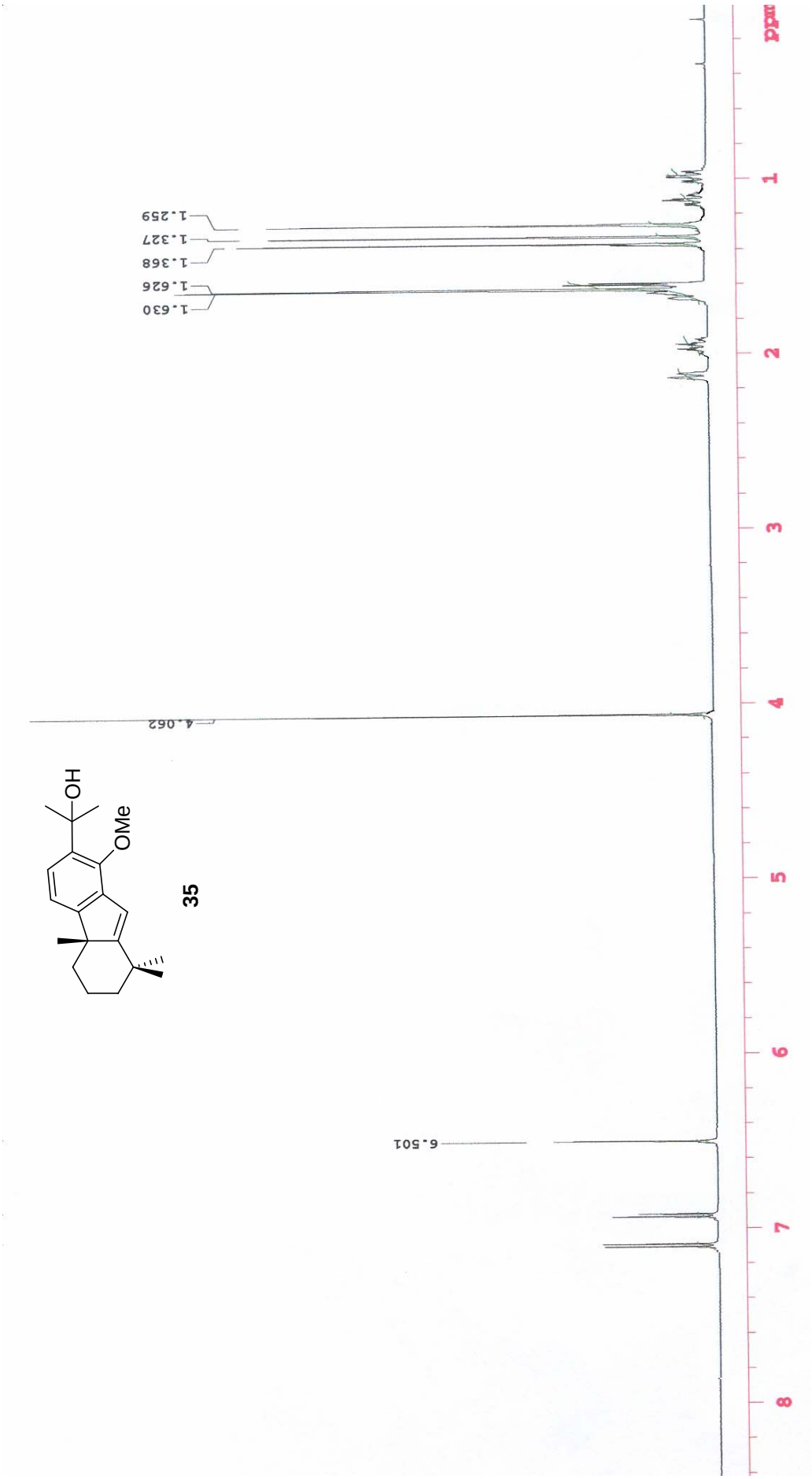

ppm
20
40
60
80
100
120
140
160
19.930
21.105
21.393
26.709
33.173
33.188
35.477
41.508
46.369
52.004
59.842
61.231
76.852
77.105
77.358
115.631
121.768
130.571
135.206
156.675
162.742
167.136
COOMe
OMe
H
33


COOMe
OMe
34
1.247
1.322
1.362
3.901
3.961
6.518
ppm
1
2
3
4
5
6
7
8

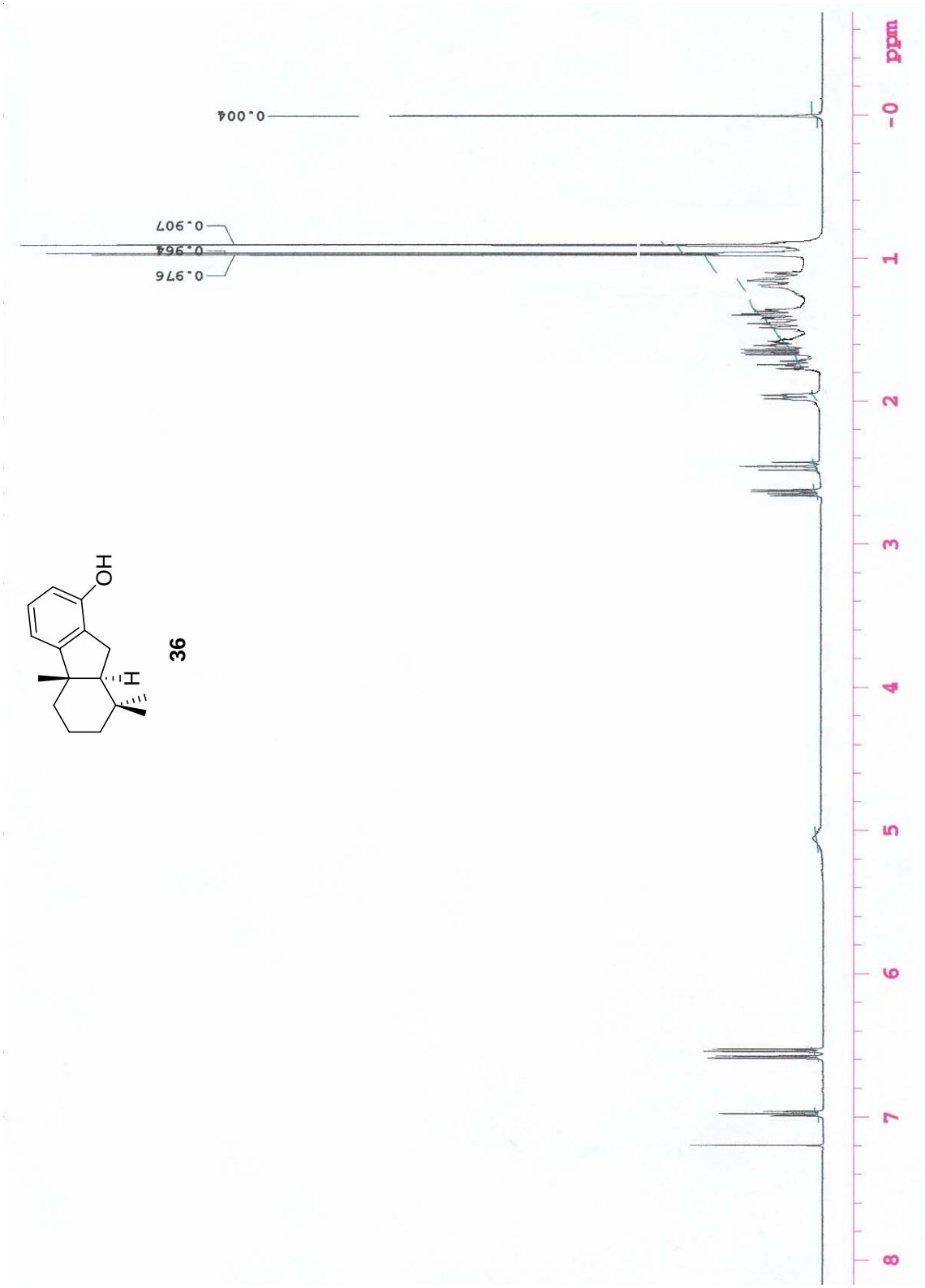


34

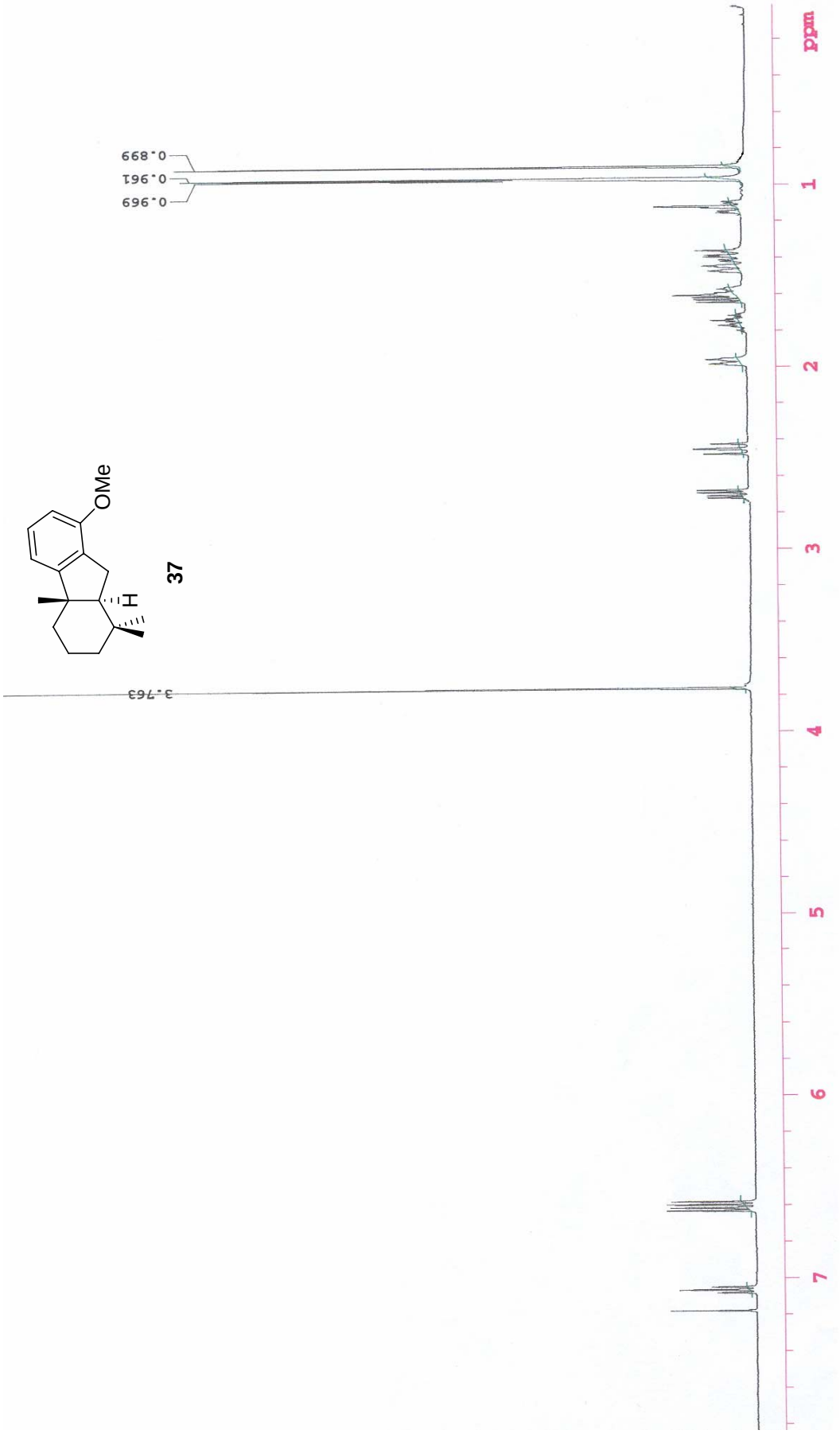


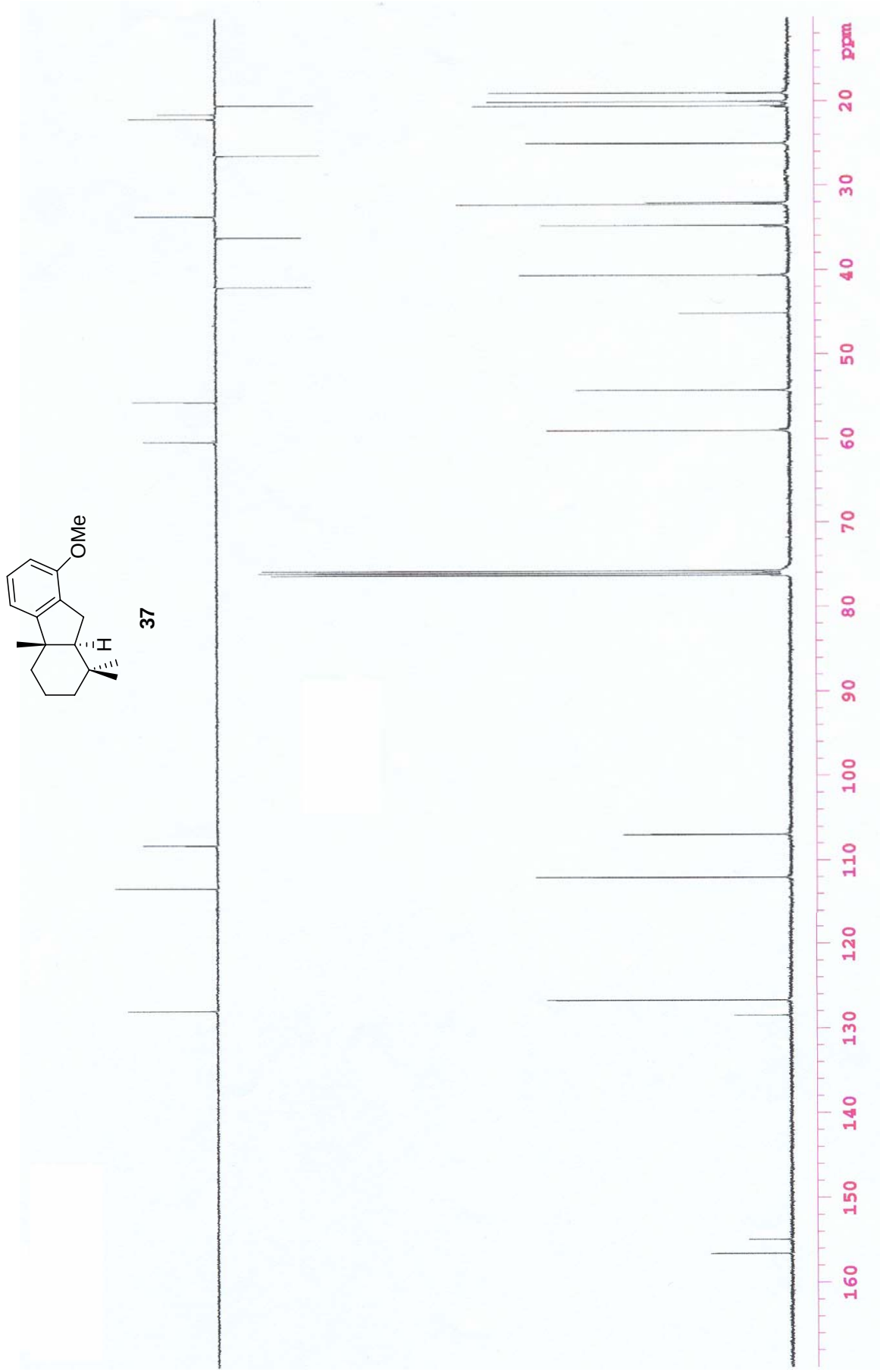

OH
OMe
35
4.062
1.630
1.626
1.368
1.327
1.259
6.501
ppm
1
2
3
4
5
6
7
8

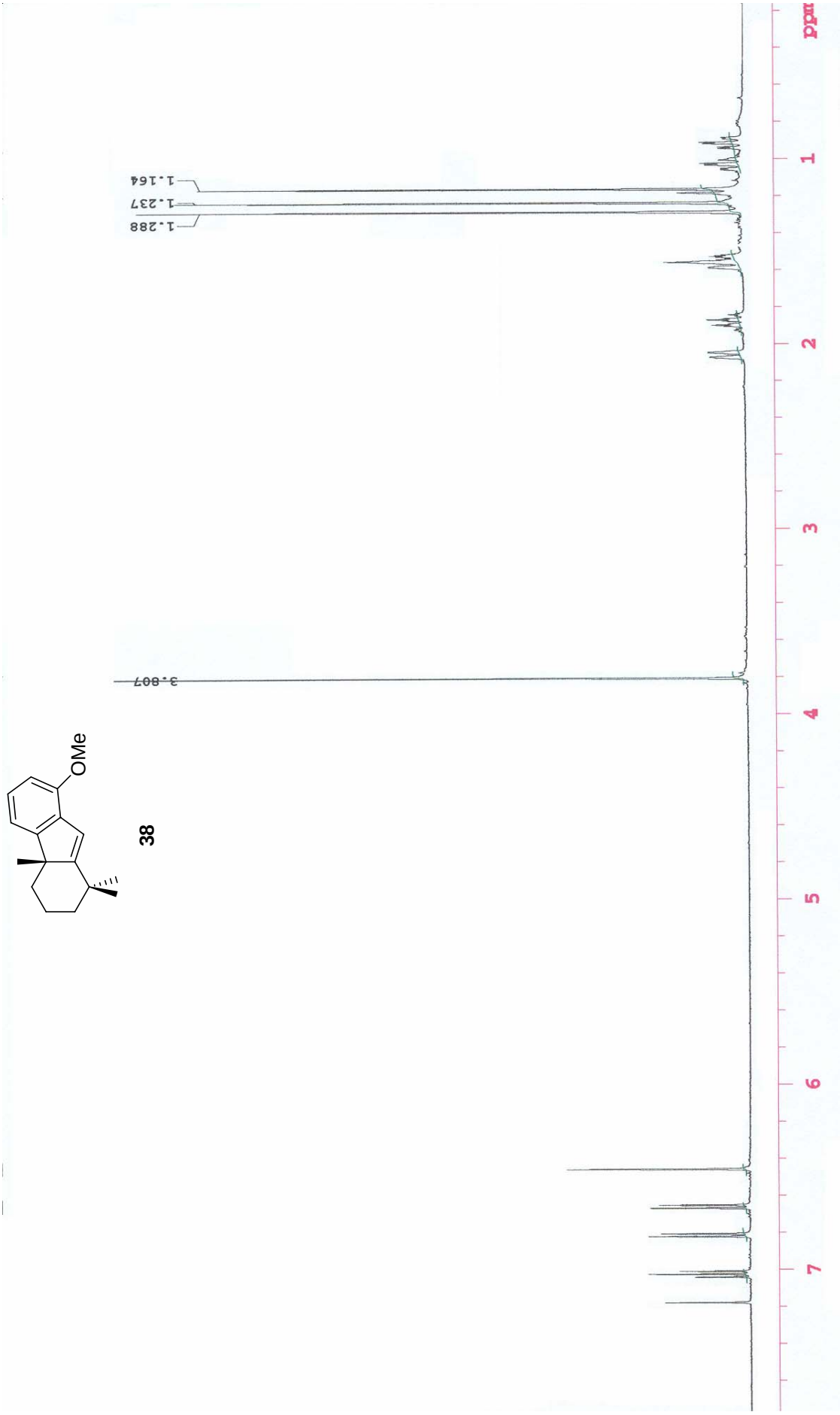

OH
OMe
35
ppm
20
40
60
80
100
120
140
160

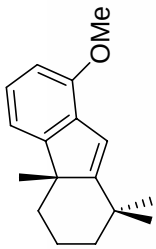

OH
H
36
0.976
0.964
0.907
0.004
ppm
-0
1
2
3
4
5
6
7
8


OH
H
36
ppm
20
40
60
80
100
120
140
160

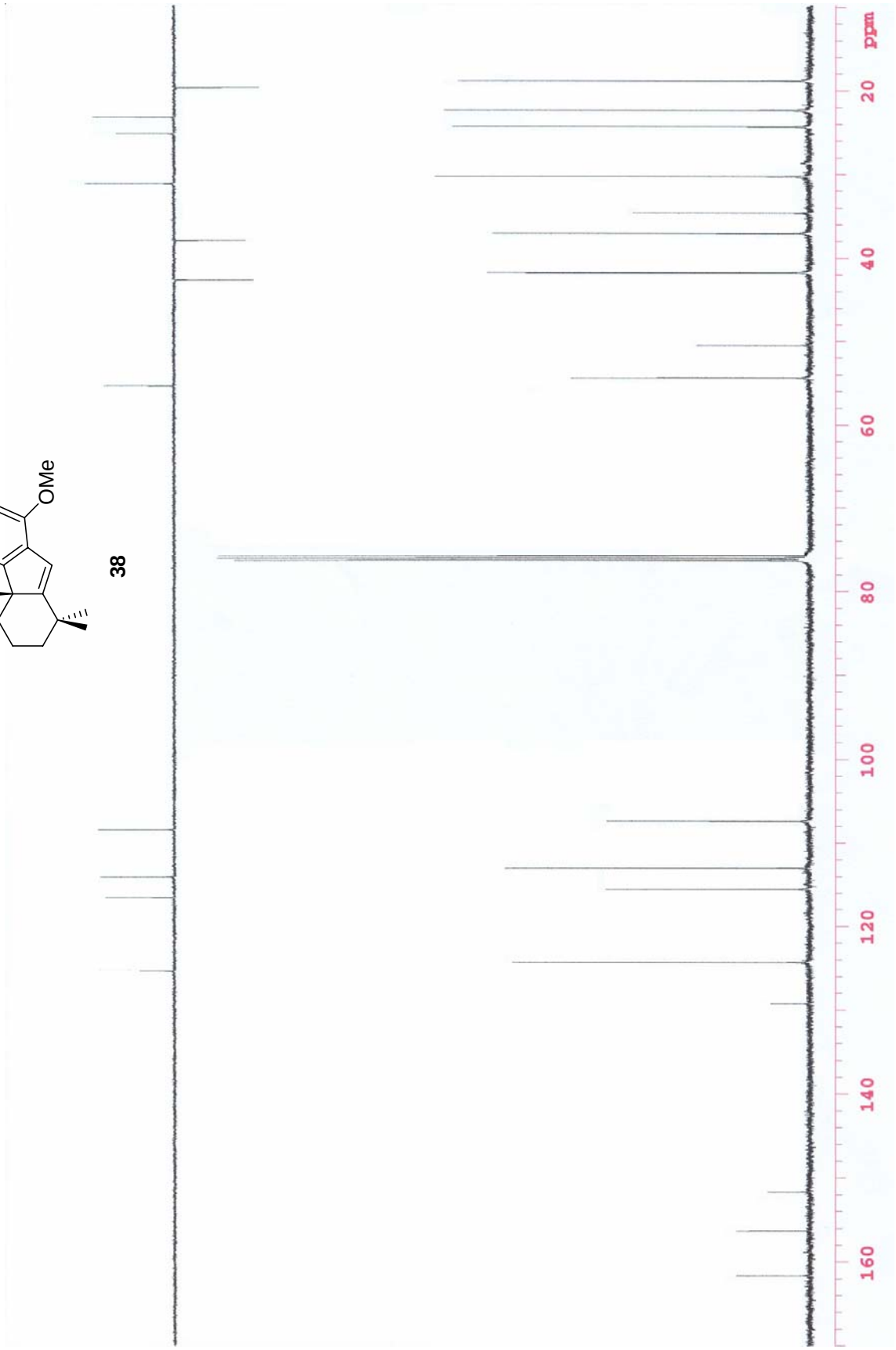

OMe
H
37
0.969
0.961
0.899
3.763
ppm
1
2
3
4
5
6
7

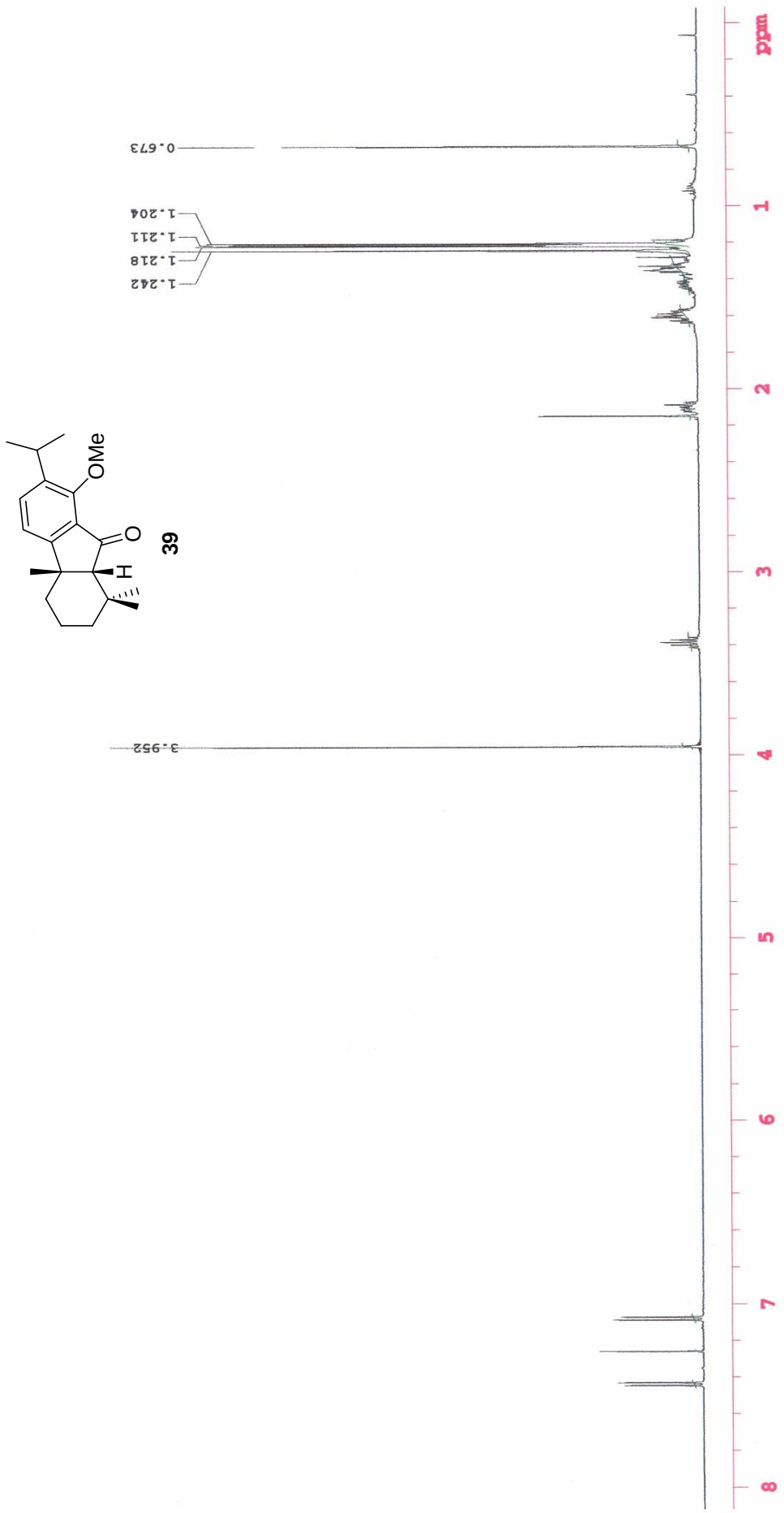

OMe
H
37
ppm
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160

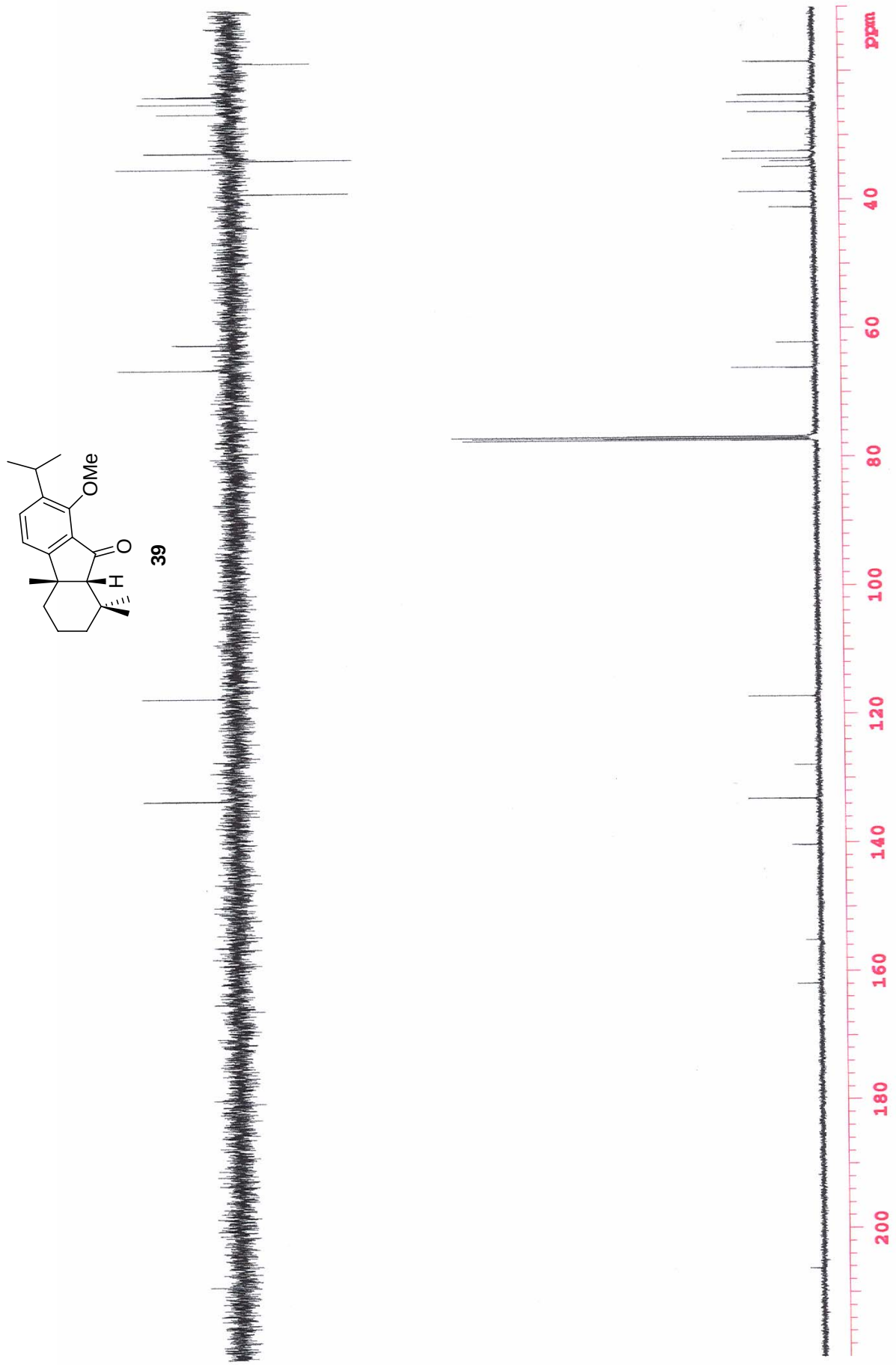

OMe
38
3.807
1.288
1.237
1.164
ppm
1
2
3
4
5
6
7

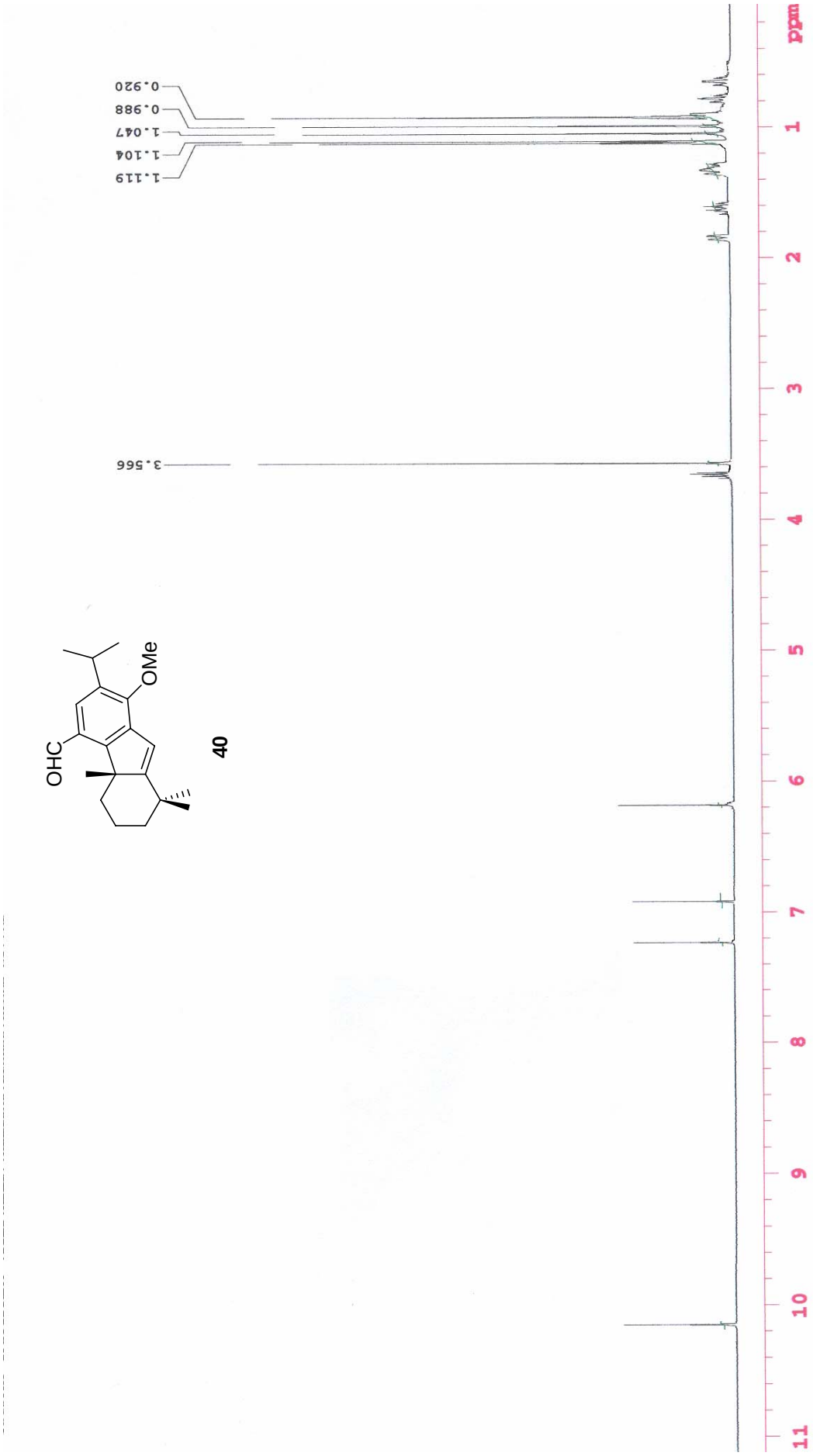


38

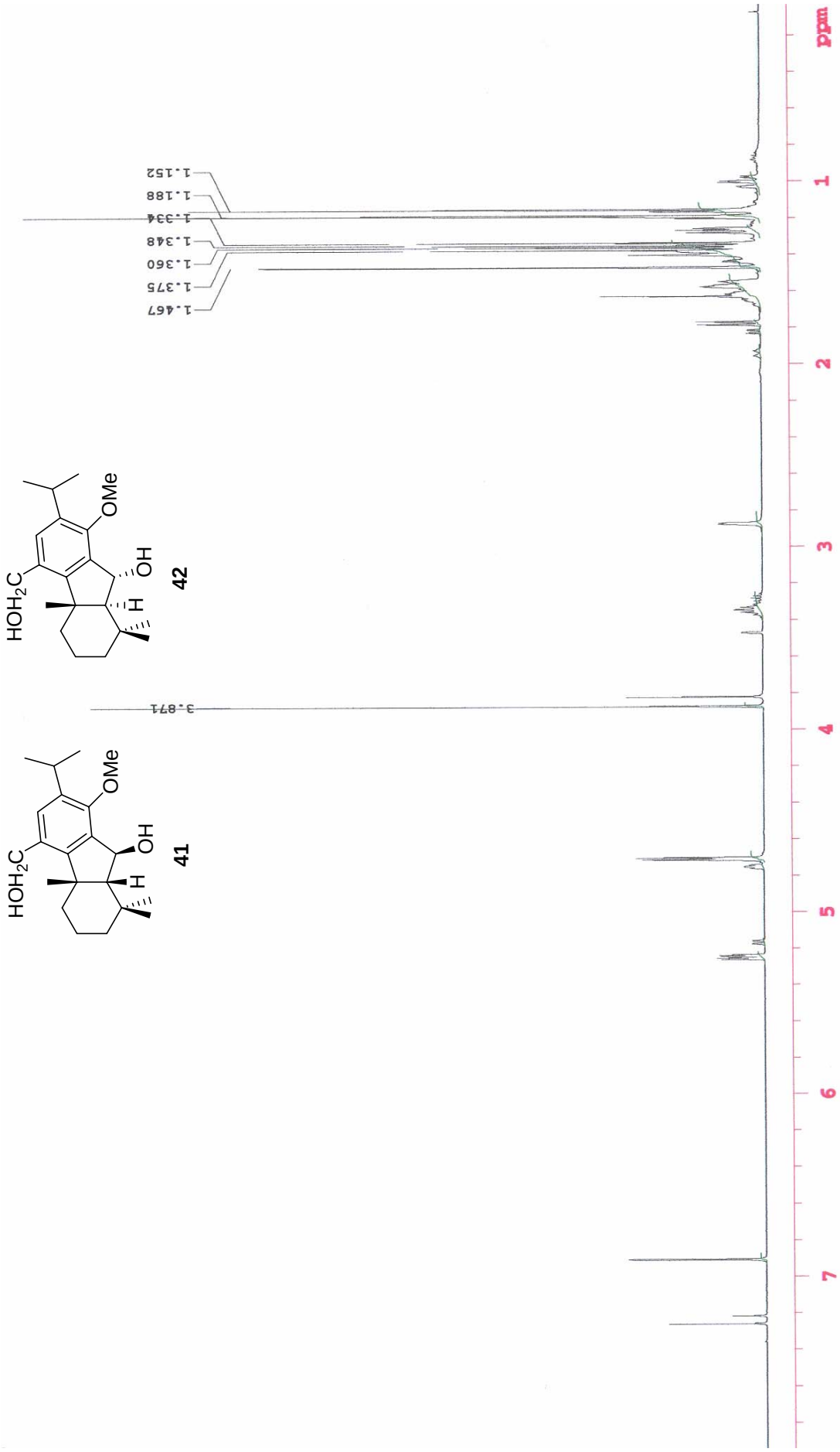


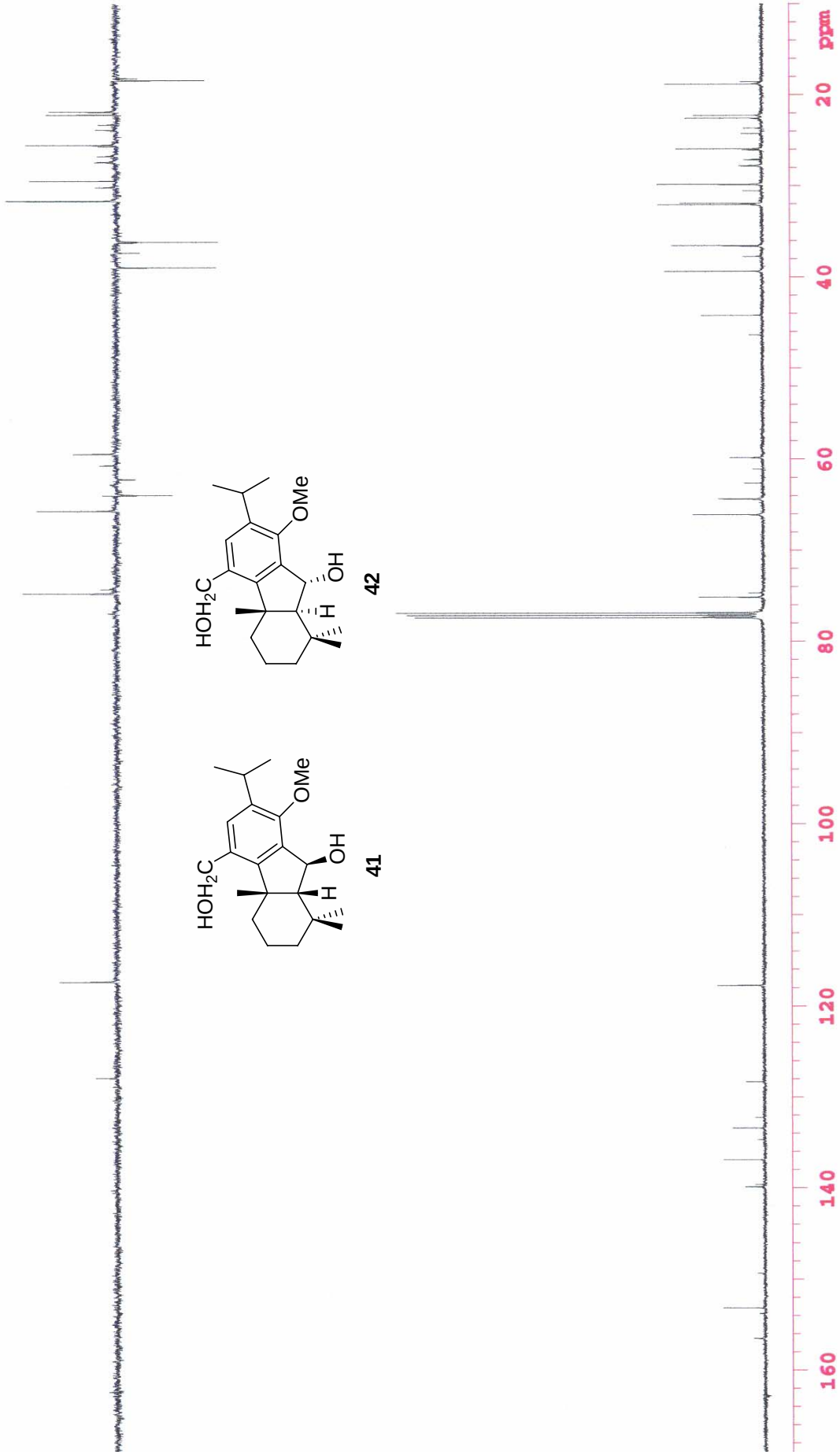

OMe
O
H
39
0.673
1.204
1.211
1.218
1.242
3.952
ppm
1
2
3
4
5
6
7
8

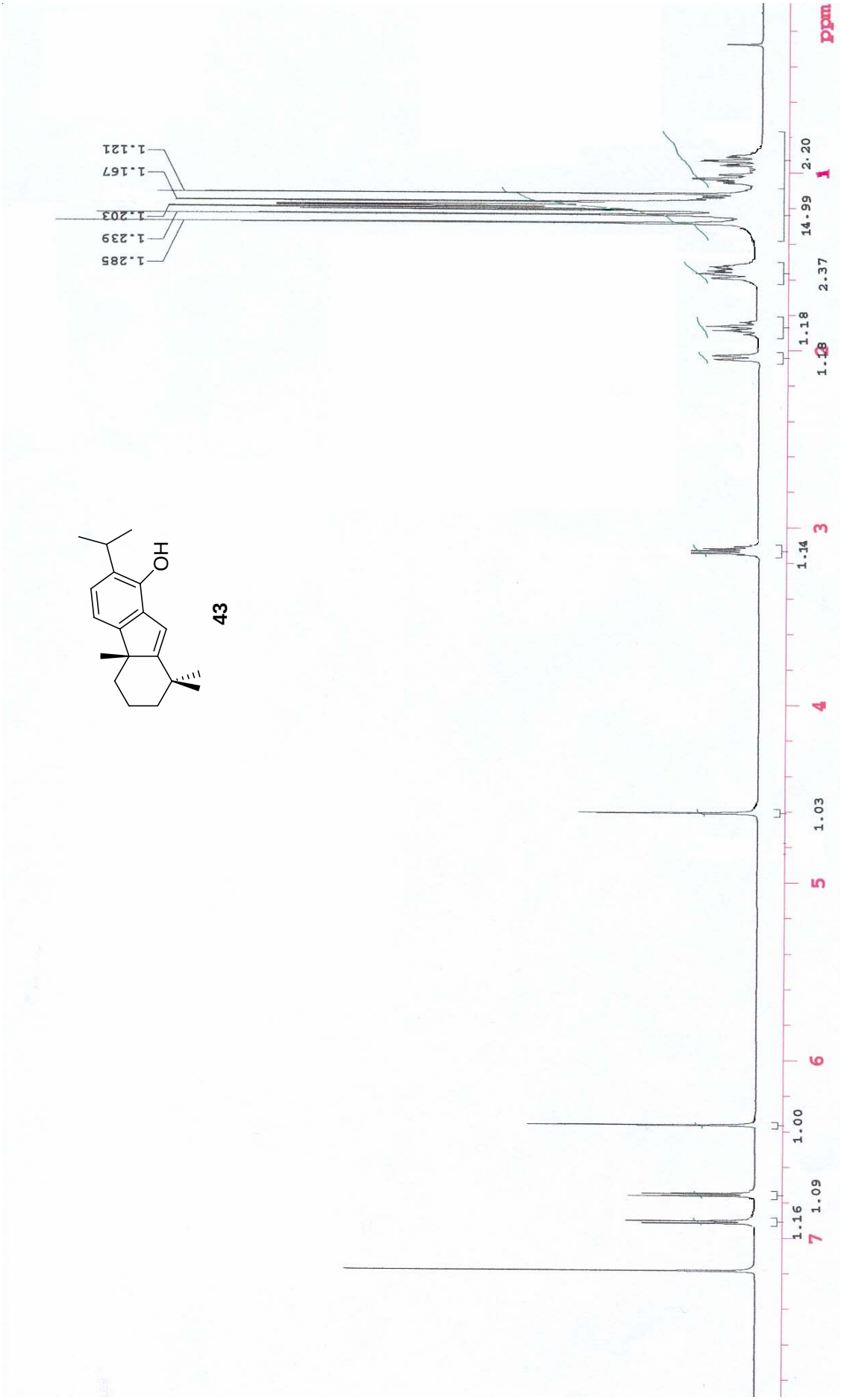

OMe
O
H
39
ppm
40
60
80
100
120
140
160
180
200

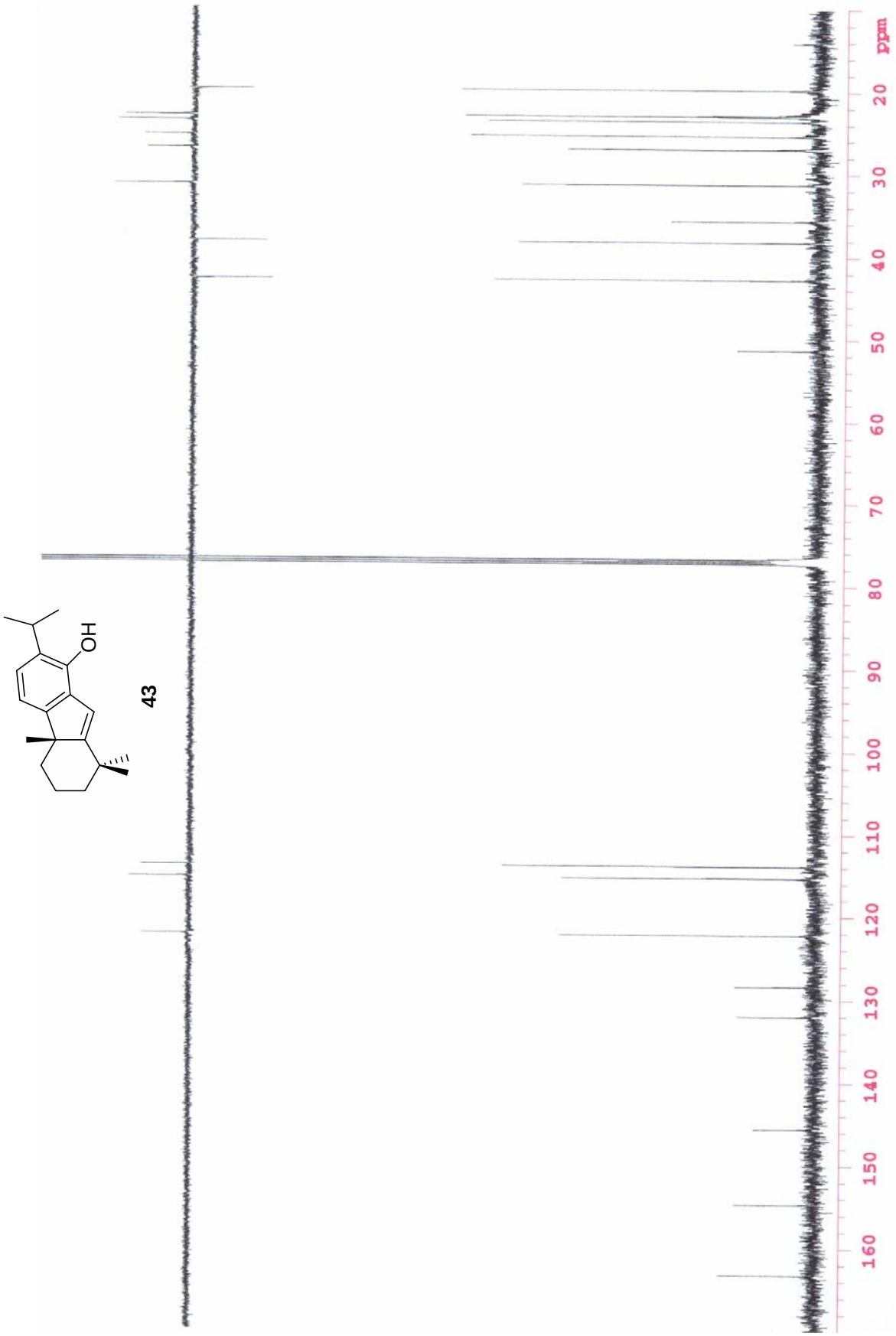

OHC
OMe
40
3.566
1.119
1.104
1.047
0.988
0.920
ppm
1
2
3
4
5
6
7
8
9
10
11

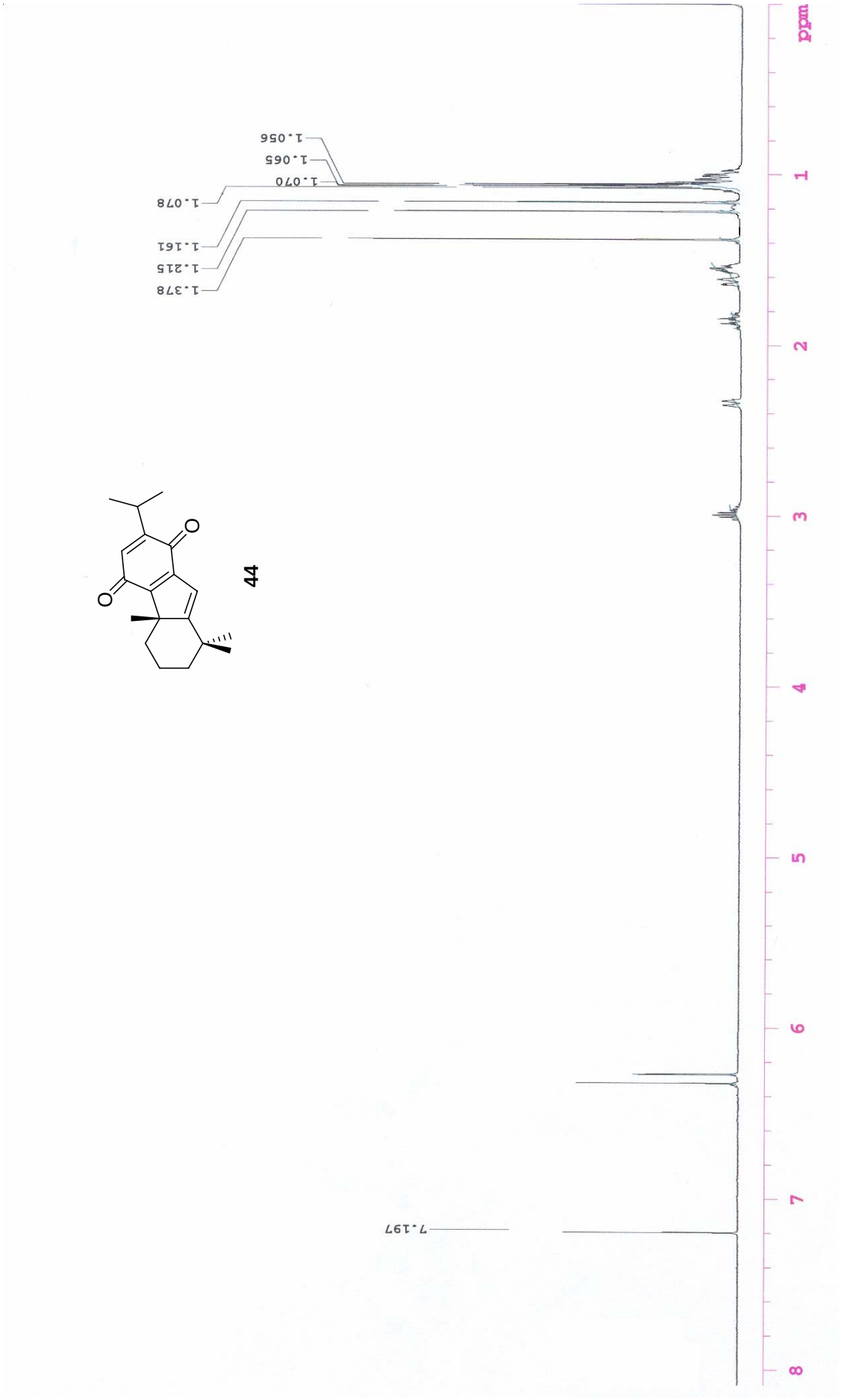

OHC
OMe
40
ppm
40
60
80
100
120
140
160
180
200

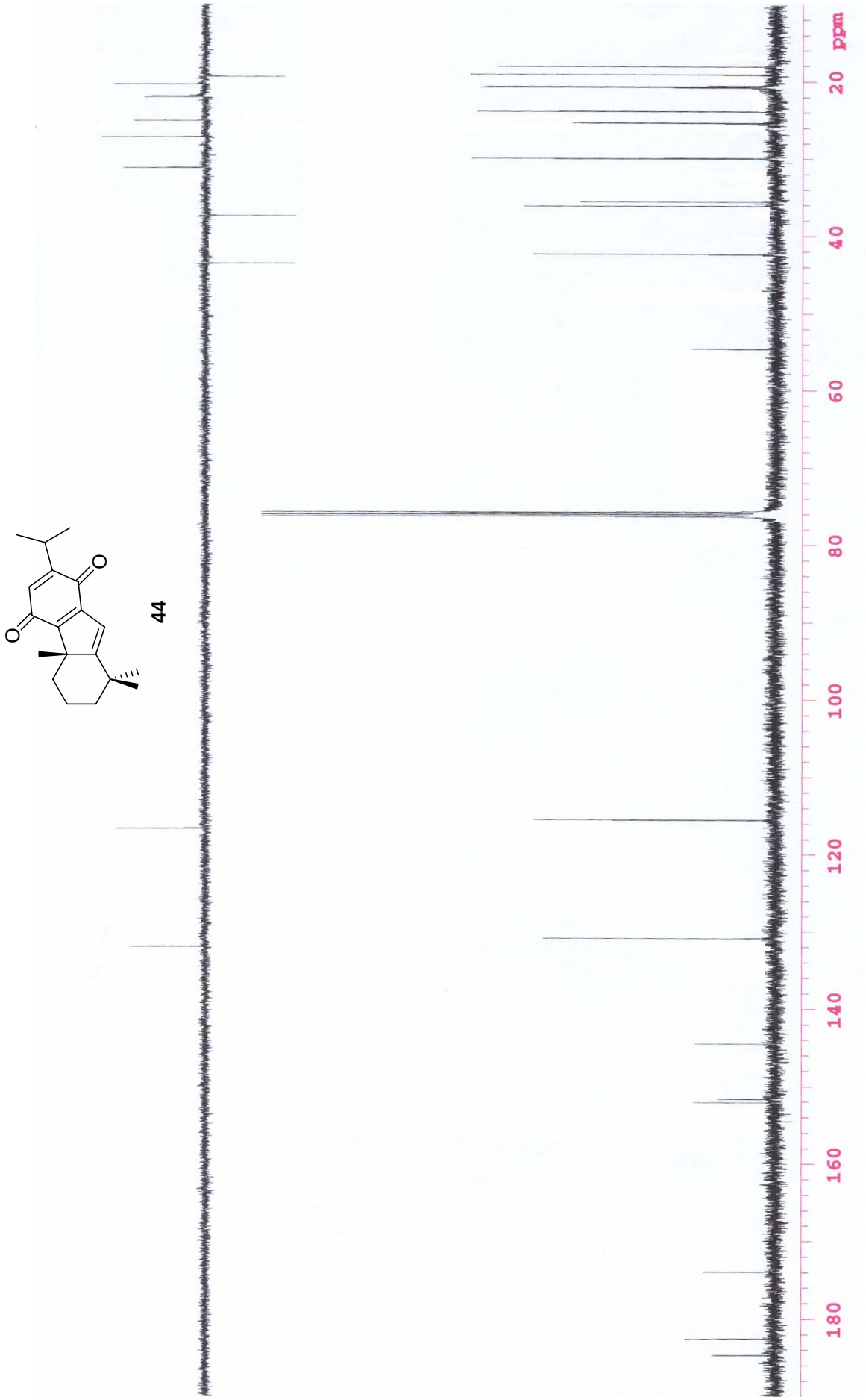

ppm
1
2
3
4
5
6
7
1.467
1.375
1.360
1.348
1.334
1.188
1.152
3.871
HOH2C
OMe
OH
H
41
HOH2C
OMe
OH
H
42

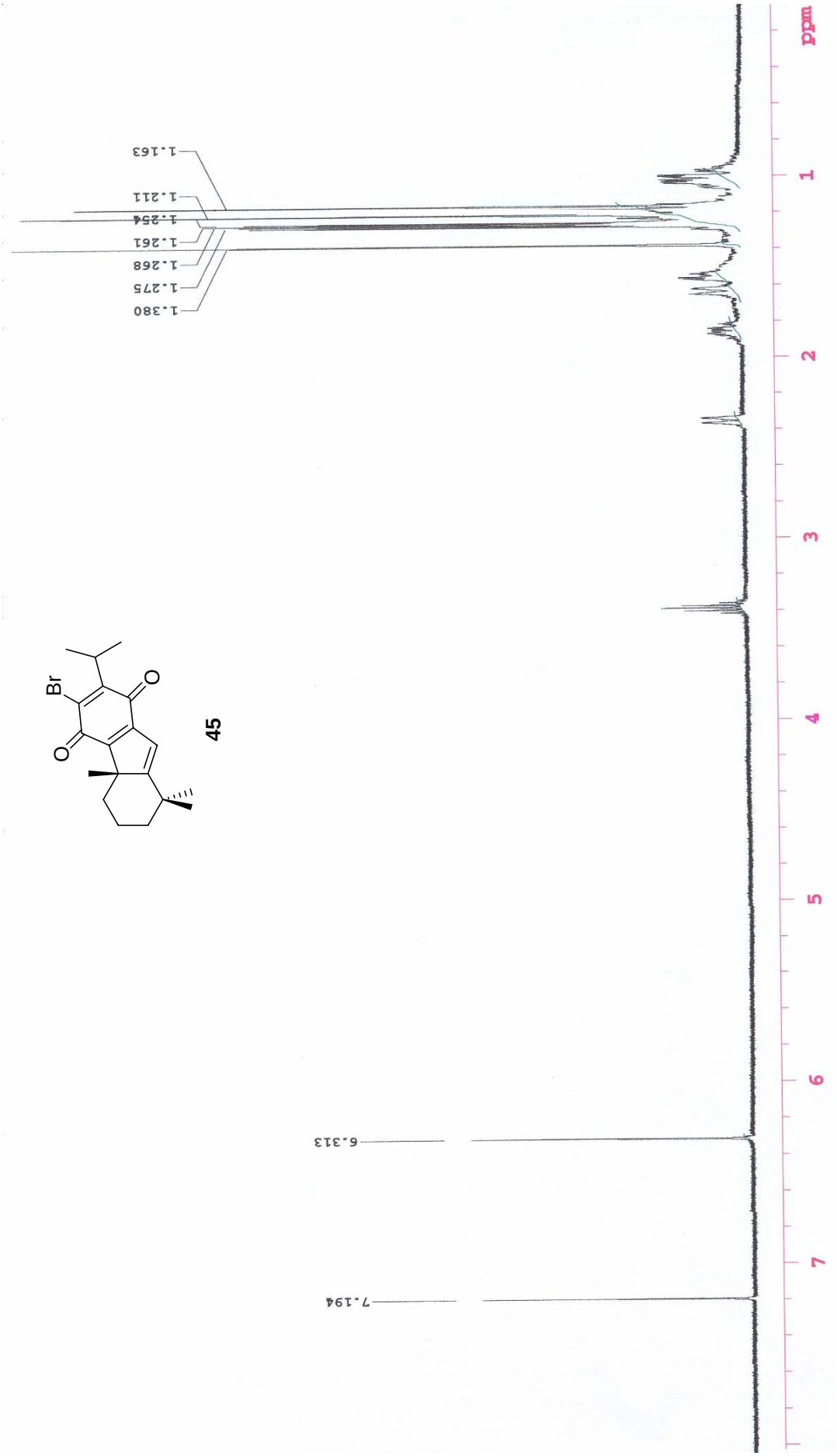

HOH2C
OMe
OH
H
41
HOH2C
OMe
OH
H
42
ppm
20
40
60
80
100
120
140
160

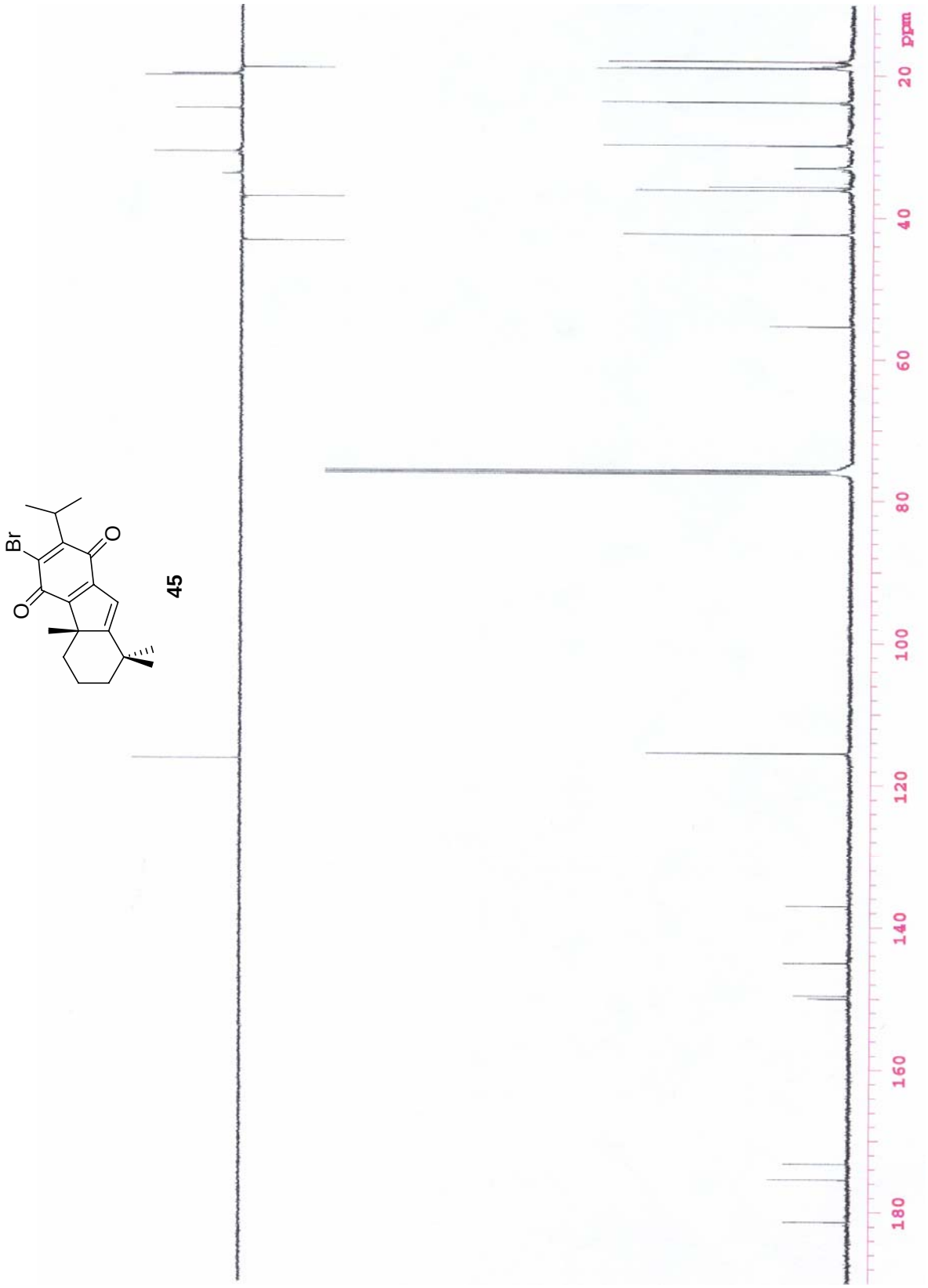

OH
43
1.285
1.239
1.203
1.167
1.121
14.99
2.20
2.37
1.18
1.18
1.14
1.03
1.00
1.09
1.16
ppm
1
2
3
4
5
6
7


OH
43
ppm
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160


44
1.378
1.215
1.161
1.078
1.070
1.065
1.056
7.197
ppm
1
2
3
4
5
6
7
8


44
ppm
20
40
60
80
100
120
140
160
180


Br
O
O
45
1.380
1.275
1.268
1.261
1.254
1.211
1.163
6.313
7.194
ppm
1
2
3
4
5
6
7


Br
O
O
45
ppm
20
40
60
80
100
120
140
160
180