Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supplementary Information for

Enantioselective total synthesis and biological evaluation of (−)-solanacol

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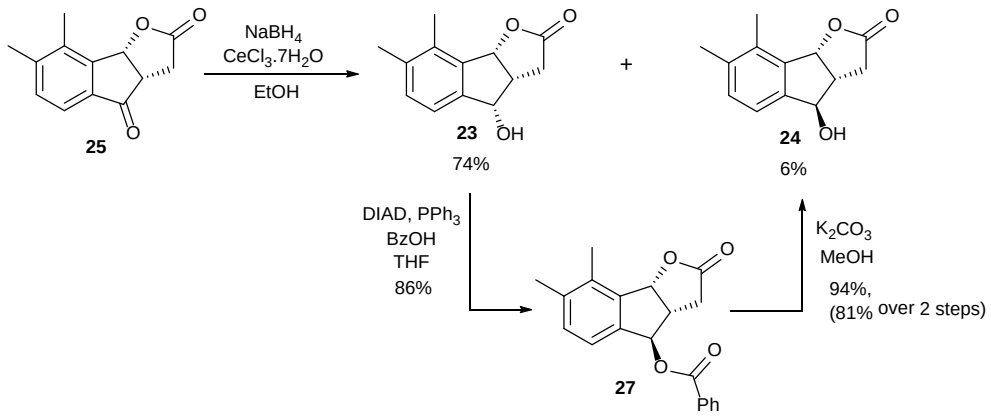
Conversion of ketone 25 into alcohol 24



Plant based assays

Seed Germination Assays

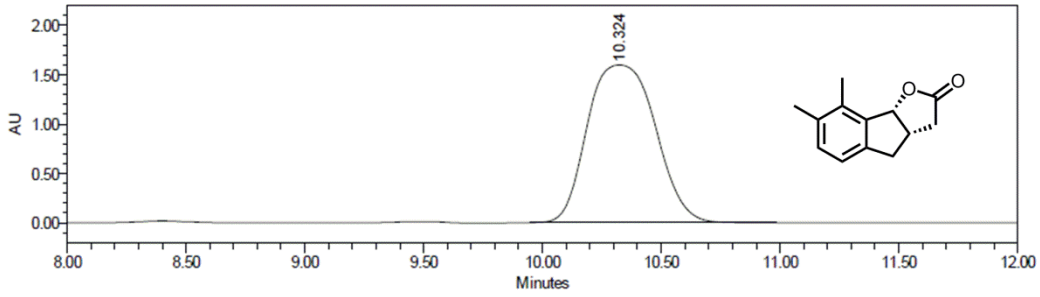
Orobanche minor seed (collected from Auckland, New Zealand) were surface sterilised in 70% ethanol, 0.05% triton X-100 for 10 minutes, followed by a rinse in 100% ethanol, and allowed to dry. Seed were then spread on 6 mm glass fibre filter disks, placed on damp filter paper in a petri dish and incubated at 24° C in the dark for 7 days for preconditioning. Filter disks were then briefly dried on filter paper, transferred to the wells of a 96-well plate and 20 µL of GR24 and Solanacol at varying concentrations in 2% DMSO were added. Each concentration was tested on triplicate filter disks containing 21-40 individual seed. After 6 days incubation, germination was scored from photographs of each filter disk.

DSF method

DSF experiments were performed on a LightCycler 480 (Roche) using excitation and emission wavelengths of 498 and 640 nm, respectively. Sypro Tangerine (Ex/Em: 490/640 nm) was used as the reporter dye. Samples were heat-denatured using a linear 25 to 95 ºC gradient at a rate of 1.3 ºC per minute. Protein unfolding was monitored by detecting changes in Sypro Tangerine fluorescence. The inflection point of the fluorescence vs temperature curves was identified by plotting the first derivative over temperature using the "Tm calling" function of the LightCycler 480 Software, and the minima were referred to as the melting temperatures.

Final reaction mixtures were prepared in triplicate in 384-well white microplates, by mixing 19.5 µL of 10 µM DAD2 containing Sypro Tangerine 20× in 20 mM Tris.HCl pH8.0, 150 mM NaCl buffer, and 0.5 µL of 10 mM GR24 or Solanacol in DMSO. Reactions were incubated for 30 minutes at room temperature in the absence of light before analysis.

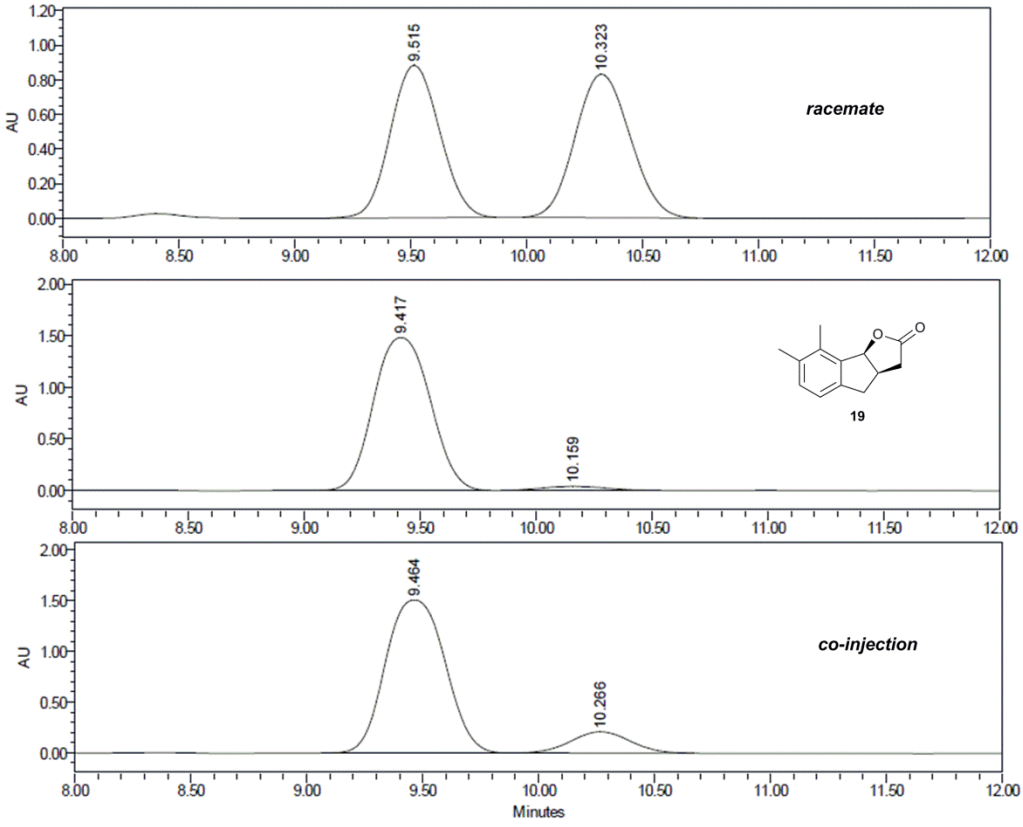
Enantioselective HPLC traces



Peak Results

	RT	Area	Height	% Area	Baseline Start (min)	Baseline End (min)	Channel	Wavelength
1	10.32	31787092	1597440	100.00	9.95	10.98	W2996	215.0nm

Column: RegisPack; Solvent: *iso*-propanol:hexane 1:9; Flow rate: 0.7 mL/min.



Peak Results

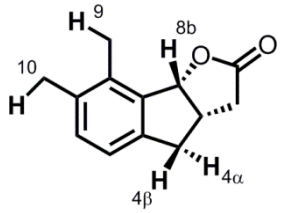
	RT	Area	Height	% Area	Baseline Start (min)	Baseline End (min)	Channel	Wavelength
1	9.42	25192185	1486939	97.14	9.02	9.80	W2996	215.0nm
2	10.16	741334	39312	2.86	9.88	10.52	W2996	215.0nm

Column: RegisPack; Solvent: *iso*-propanol:hexane 1:9; Flow rate: 0.7 mL/min.

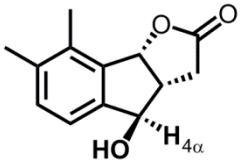
Computational details

Bond dissociation energies

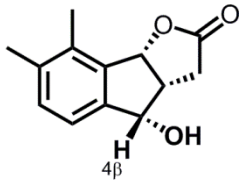
Bond dissociation energies (BDEs) were calculated using the ω-B97M-V functional, def2-TZVPPD basis set combination.[1] A recent comparative study of over 200 functionals that included more than one million data points demonstrated that ω-B97M-V outcompeted other functionals across a range of reaction types, including BDE calculations.[2] BDE was defined as [*E*(benzylic radical) + *E*(H atom)] – *E*(starting material), or [*E*(benzylic radical) + *E*(water)] – *E*[(starting material) + *E*(hydroxyl radical)].



Position	BDE (kJ/mol)
4α	-
4β	399
8b	421
9	405
10	408



BDE (kJ/mol)
372
-
-
-
-

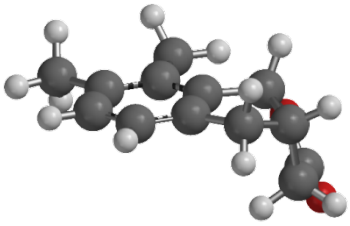


BDE (kJ/mol)
-
374
-
-
-

Cartesian co-ordinates

Compound **18**

ω-B97M-V / def2-TZVPPD (gas phase)

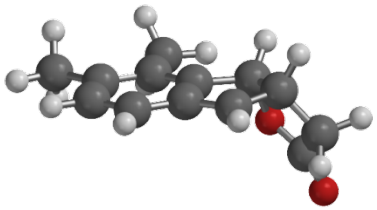


H	0.479618	-2.633315	-1.988540
C	0.323557	-1.614549	-1.650135
C	-0.068023	1.053046	-0.793097
C	-0.268458	-1.350911	-0.425814
C	0.725272	-0.541065	-2.436738
C	0.538560	0.781791	-2.032865
C	-0.448995	-0.031948	-0.005779
H	1.200735	-0.729002	-3.394216

C	-0.805078	-2.319869	0.589695
H	-0.161768	-3.192295	0.740271
H	-1.784055	-2.705929	0.281351
C	-0.932900	-1.462569	1.852232
H	-1.764773	-1.765480	2.491131
C	-1.094458	-0.012009	1.351918
C	0.351007	-1.351278	2.664314
H	1.228512	-1.578027	2.047890
H	0.399318	-1.992552	3.543375
C	-0.283571	2.467171	-0.350391
H	0.665656	3.004897	-0.257841
H	-0.778943	2.524110	0.616279
H	-0.881826	3.023274	-1.079559
C	0.987827	1.906131	-2.913910
H	1.709049	2.555954	-2.407778
H	0.153776	2.549711	-3.212892
H	1.459089	1.531726	-3.823545
H	-2.127660	0.343541	1.332581
O	-0.410976	0.832670	2.300249
C	0.445410	0.101254	3.064072
O	1.144098	0.605522	3.897744

Desired benzylic radical

ω-B97M-V / def2-TZVPPD (gas phase)

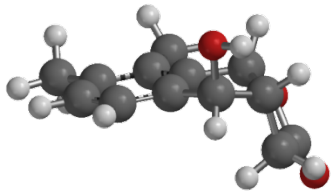


C	0.319780	-0.060877	-0.007704
C	-0.411833	-0.146430	2.645878
C	0.213352	1.135777	0.672938
C	0.054439	-1.314662	0.606187
C	-0.320259	-1.344241	1.962044
C	-0.153923	1.090673	2.038588
C	0.230924	-2.351491	-0.318668
C	0.698418	-1.820192	-1.635485
C	0.642410	-0.279402	-1.452973
O	-0.444580	0.197876	-2.280075
C	-0.992697	-0.794790	-3.025198
C	-0.222459	-2.079738	-2.824445
C	0.457193	2.449342	-0.002041
C	-0.278873	2.354985	2.826700
O	-1.935980	-0.606754	-3.741798
H	1.541789	0.236936	-1.795073

H	1.720090	-2.152698	-1.854661
H	-0.696750	-0.153278	3.693238
H	-0.529931	-2.284611	2.458411
H	0.089243	-3.405629	-0.119951
H	0.328456	-2.287312	-3.746158
H	-0.917645	-2.906252	-2.676629
H	1.284300	2.996028	0.462794
H	0.680529	2.328225	-1.061147
H	-0.420779	3.098373	0.068513
H	0.661482	2.916591	2.852115
H	-0.570993	2.152265	3.857785
H	-1.025703	3.031285	2.396817

Compound **22**

ω-B97M-V / def2-TZVPPD (gas phase)

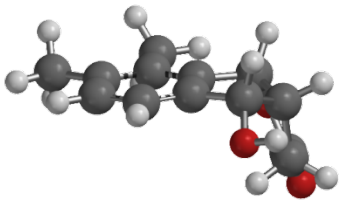


H	0.573850	-2.527840	-1.981322
C	0.424356	-1.506011	-1.651384
C	0.015822	1.168543	-0.811809
C	-0.160503	-1.229582	-0.427923
C	0.818651	-0.436787	-2.446181
C	0.623782	0.887961	-2.049144
C	-0.357829	0.087251	-0.016778
H	1.290207	-0.626639	-3.404984
C	-0.716968	-2.196903	0.573357
H	-0.065672	-3.069287	0.730081
C	-0.832944	-1.341008	1.839226
H	-1.667259	-1.662483	2.467893
C	-1.002196	0.108496	1.341406
C	0.452771	-1.234169	2.646101
H	1.327876	-1.474508	2.031053
H	0.499342	-1.866618	3.531605
C	-0.211585	2.584692	-0.382274
H	0.732224	3.133506	-0.300754
H	-0.701668	2.644639	0.586986
H	-0.821321	3.126925	-1.112280
C	1.064118	2.007994	-2.939720
H	1.779763	2.667431	-2.438318
H	0.223959	2.641641	-3.242132
H	1.537820	1.630295	-3.846547
H	-2.033563	0.463932	1.325215
O	-0.307096	0.952155	2.282758

C	0.559217	0.221721	3.034694
O	1.272662	0.724860	3.856137
O	-1.990327	-2.612158	0.089856
H	-2.327490	-3.268048	0.715180

Compound **23**

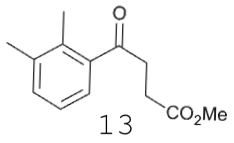
ω-B97M-V / def2-TZVPPD (gas phase)



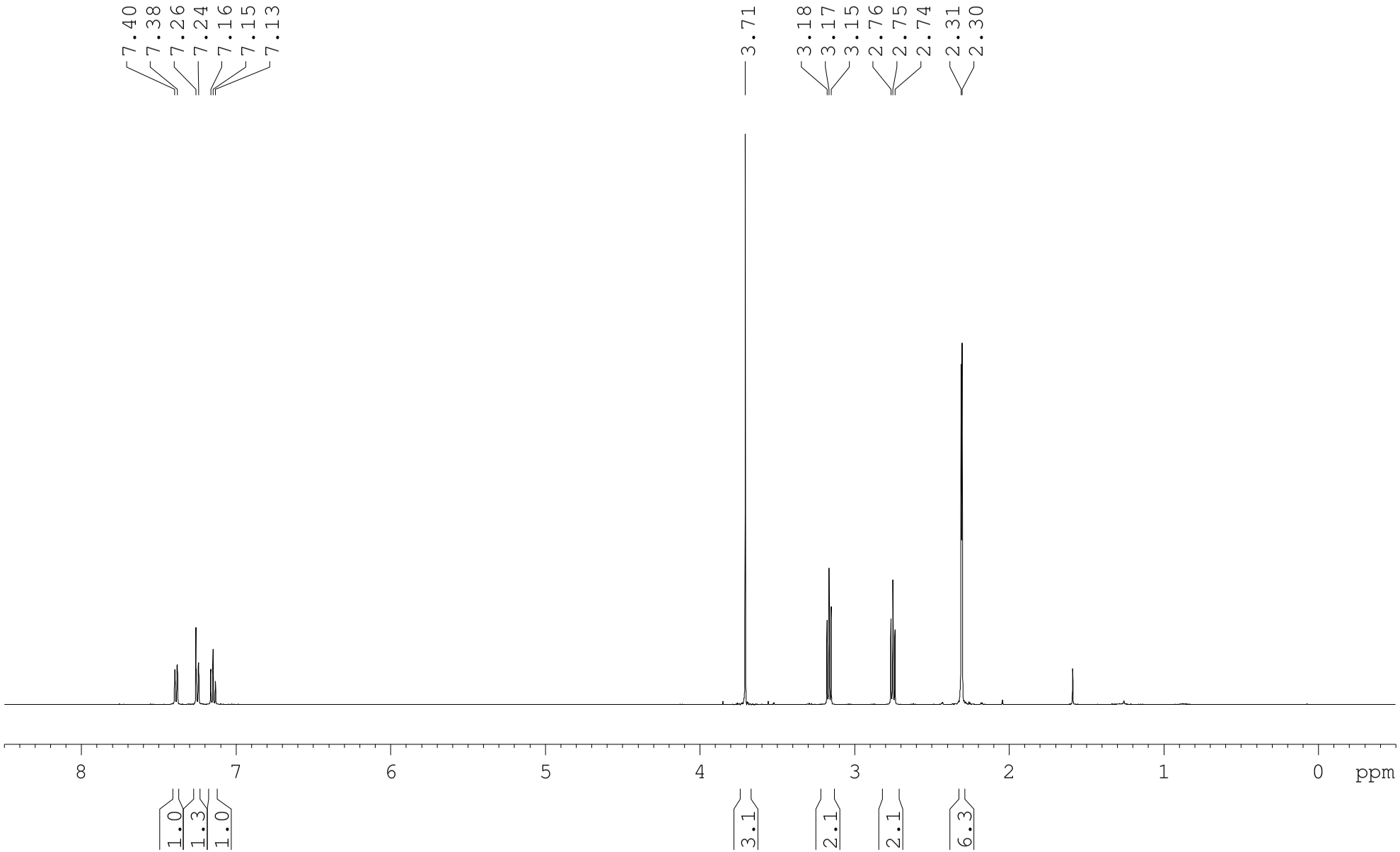
H	0.507142	-2.506908	-1.970185
C	0.337970	-1.481684	-1.664156
C	-0.076029	1.198970	-0.839351
C	-0.269515	-1.196224	-0.453534
C	0.743285	-0.415071	-2.456542
C	0.542433	0.912364	-2.069573
C	-0.460468	0.120950	-0.044054
H	1.232755	-0.608959	-3.405683
C	-0.804213	-2.165072	0.554748
H	-1.800434	-2.519670	0.247424
C	-0.934612	-1.302461	1.823122
H	-1.767604	-1.607340	2.461218
C	-1.094000	0.147316	1.319124
C	0.357153	-1.202979	2.620811
H	1.219120	-1.468307	2.001043
H	0.401968	-1.832008	3.508556
C	-0.293685	2.617041	-0.411234
H	0.655393	3.153388	-0.310318
H	-0.800730	2.681852	0.549040
H	-0.882187	3.168785	-1.151510
C	0.994881	2.027938	-2.959982
H	1.708498	2.686384	-2.454361
H	0.160515	2.664047	-3.273424
H	1.476267	1.644982	-3.860603
H	-2.124865	0.508634	1.313470
O	-0.388040	0.989844	2.250232
C	0.474197	0.251100	3.004064
O	1.191231	0.754332	3.822305
O	0.075625	-3.269332	0.671120
H	-0.382051	-3.951910	1.178232

References

1. N. Mardirossian and M. Head-Gordon, *The Journal of Chemical Physics*, 2016, **144**, 214110.
2. N. Mardirossian and M. Head-Gordon, *Mol. Phys.*, 2017, **115**, 2315-2372.


O
CO2Me

13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7.16
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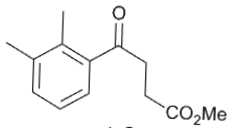
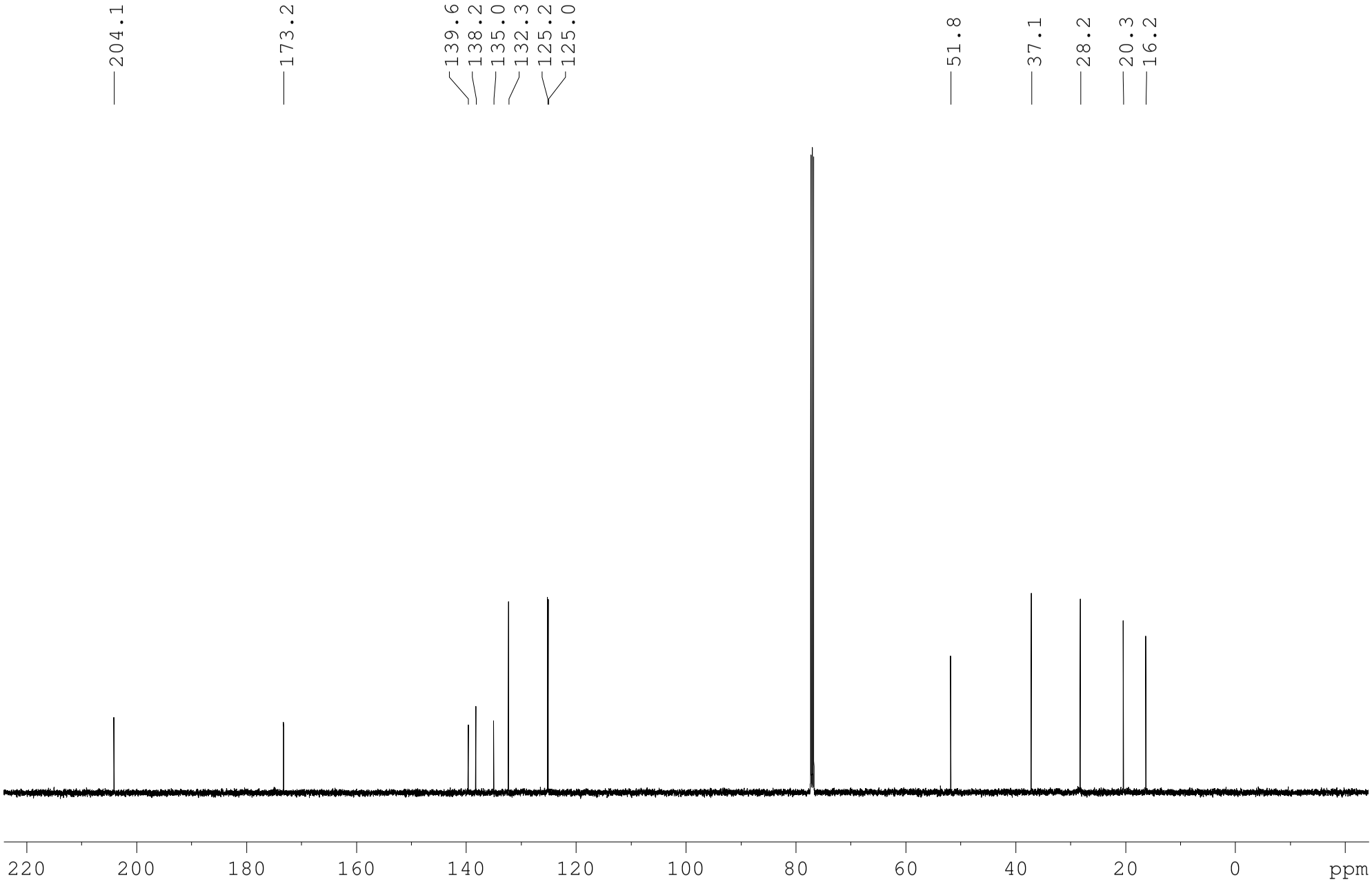
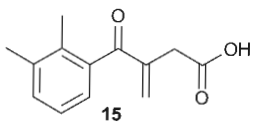
7.13
3.71
3.18
3.17
3.15
2.76
2.75
2.74
2.31
2.30
8
7
6
5
4
3
2
1
0
ppm
1.0
1.3
1.0
3.1
2.1
2.1
6.3


O
CO2Me

13


204.1
173.2
139.6
138.2
135.0
132.3
125.2
125.0
51.8
37.1
28.2
20.3
16.2
220
200
180
160
140
120
100
80
60
40
20
0
ppm



12.33

7.28
7.26
7.17
7.16
7.14
7.07
7.06

6.17

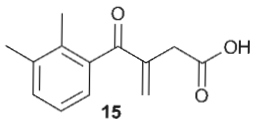
5.60

3.39

2.27
2.11

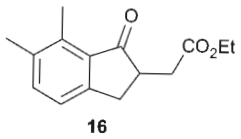
13 12 11 10 9 8 7 6 5 4 3 2 1 0 ppm

1.0 1.0 1.1 1.0 1.0 1.0 2.2 3.1 3.0

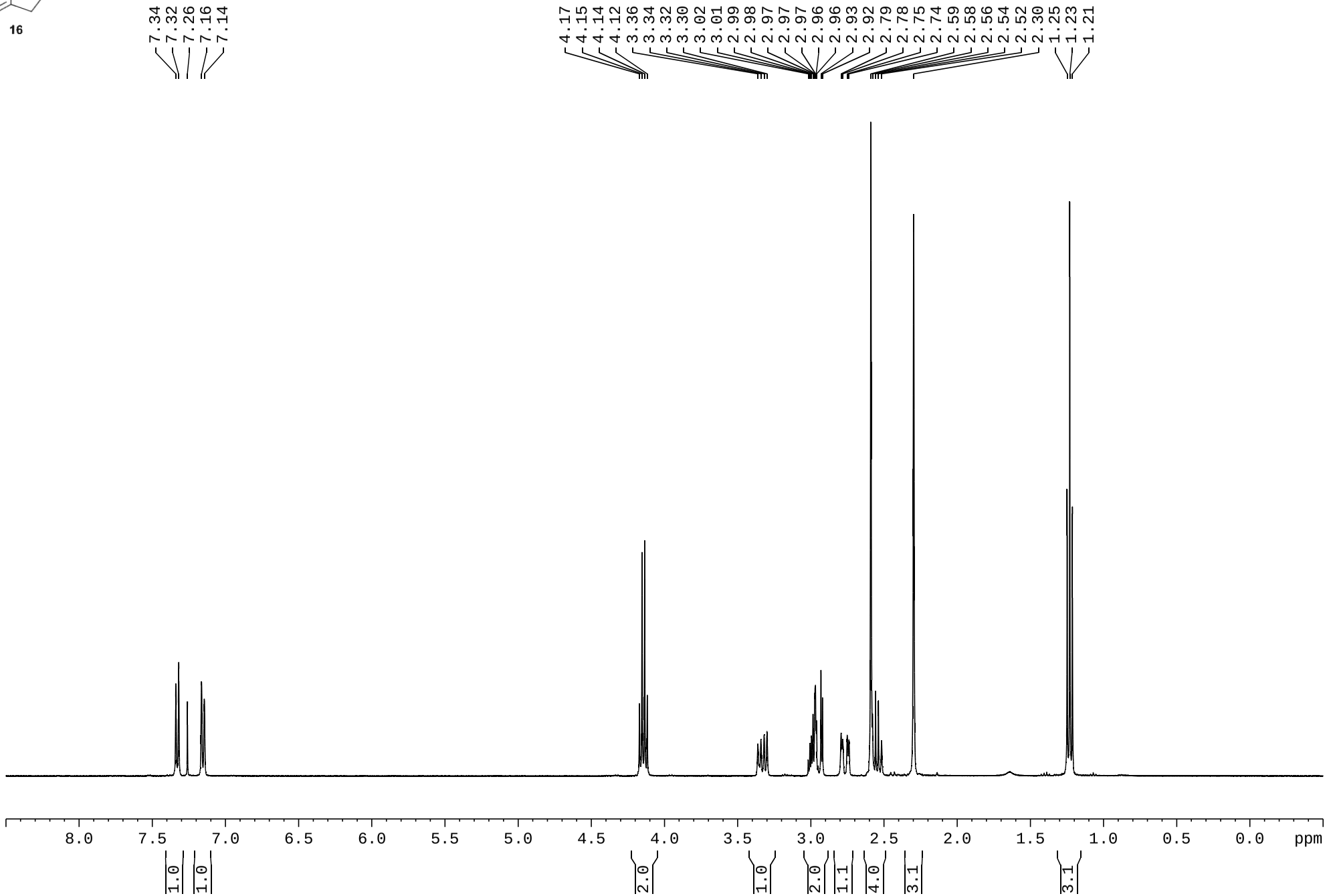


199.3
171.9
143.2
138.9
137.3
133.7
132.4
131.0
125.1
124.9
36.2
19.6
16.0

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


O
CO2Et

16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7.16
7.14
4.17
4.15
4.14
4.12
3.36
3.34
3.32
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3.02
3.01
2.99
2.98
2.97
2.97
2.97
2.96
2.96
2.93
2.92
2.79
2.78
2.75
2.74
2.59
2.58
2.56
2.54
2.52
2.30
1.25
1.23
1.21
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
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ppm
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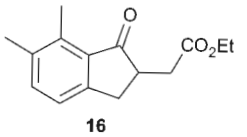
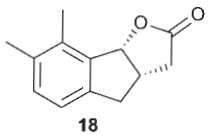
2.0
1.0
2.0
1.1
4.0
3.1
3.1



16

208.0
172.4
151.8
137.6
136.5
136.1
133.8
123.4
60.8
44.5
35.6
32.1
19.1
14.3
13.8

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm



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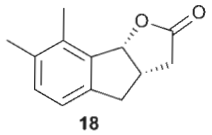
7.13
7.00
6.98
5.97
5.96
3.38
3.37
3.37
3.36
3.35
3.34
3.32
3.31
3.30
3.28
3.27
3.25
2.94
2.93
2.91
2.89
2.87
2.86
2.84
2.83
2.46
2.45
2.42
2.41
2.33
2.28

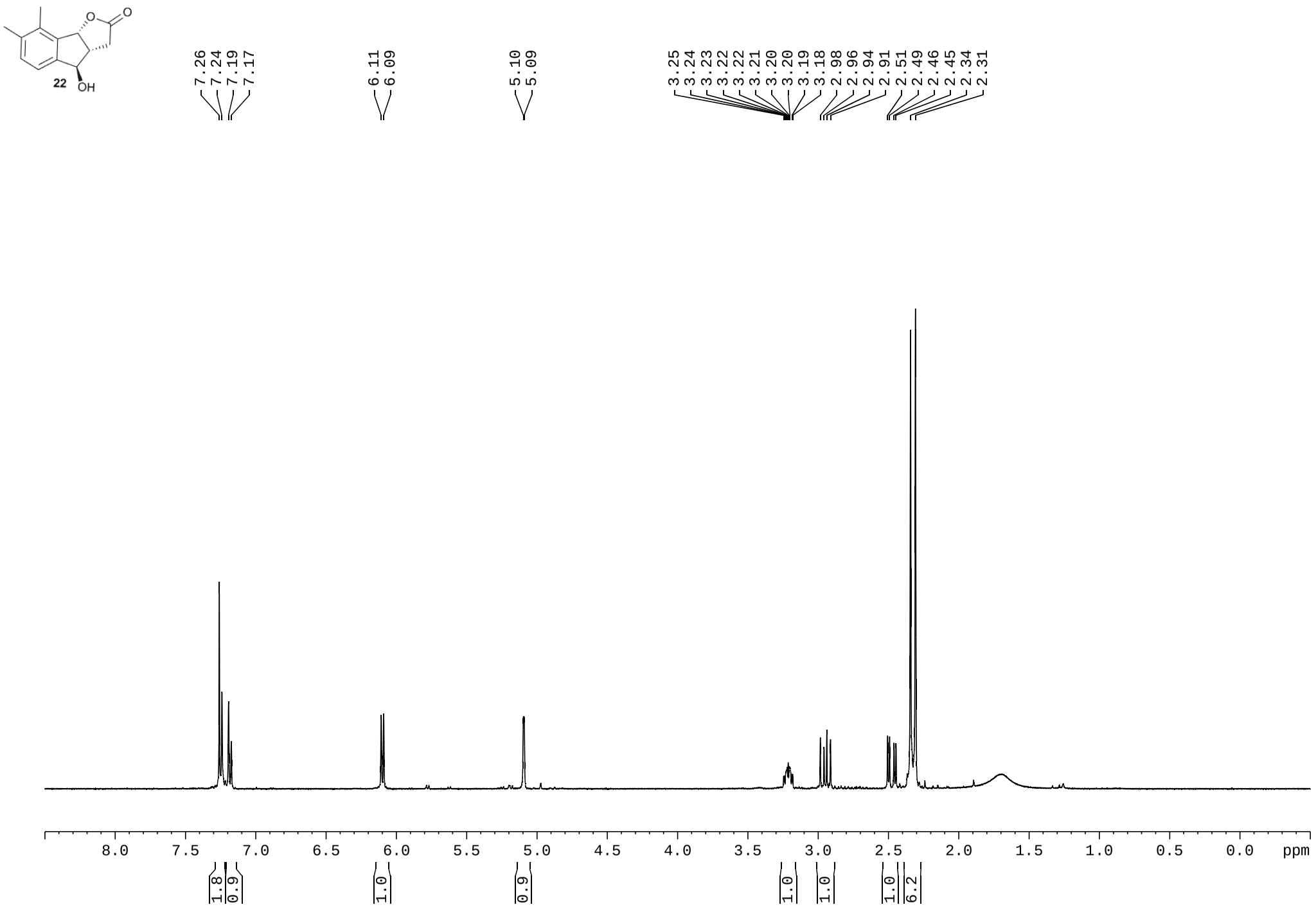
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

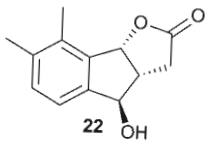
1.1
1.0
1.0
2.1
1.0
1.1
1.0
3.1
3.1



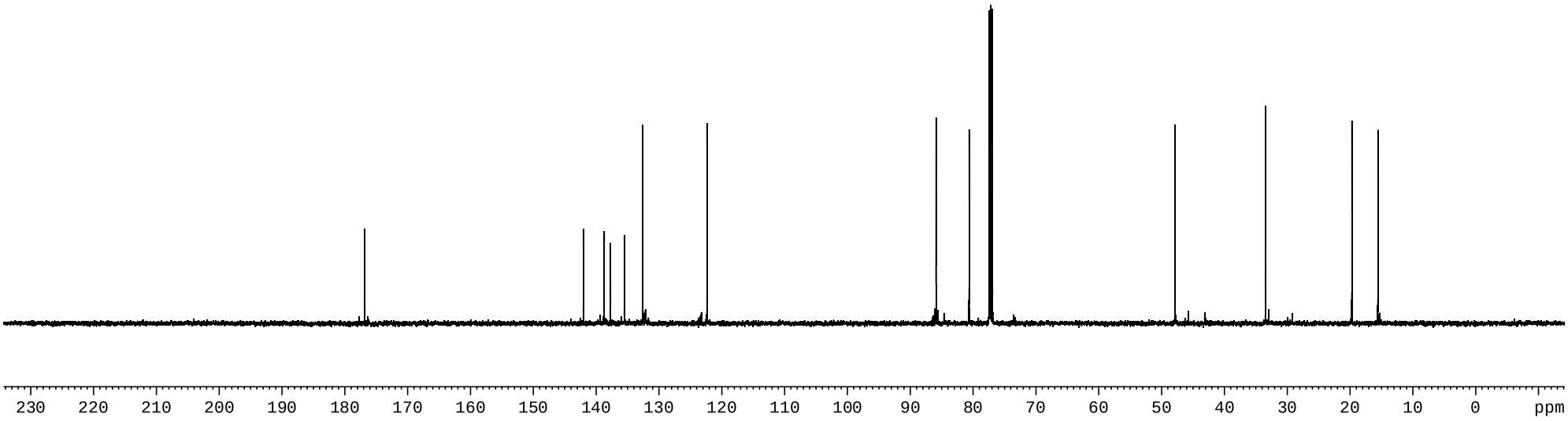
177.2
140.3
137.8
135.9
135.3
131.9
122.3
87.7
38.2
37.2
36.1
19.5
15.7

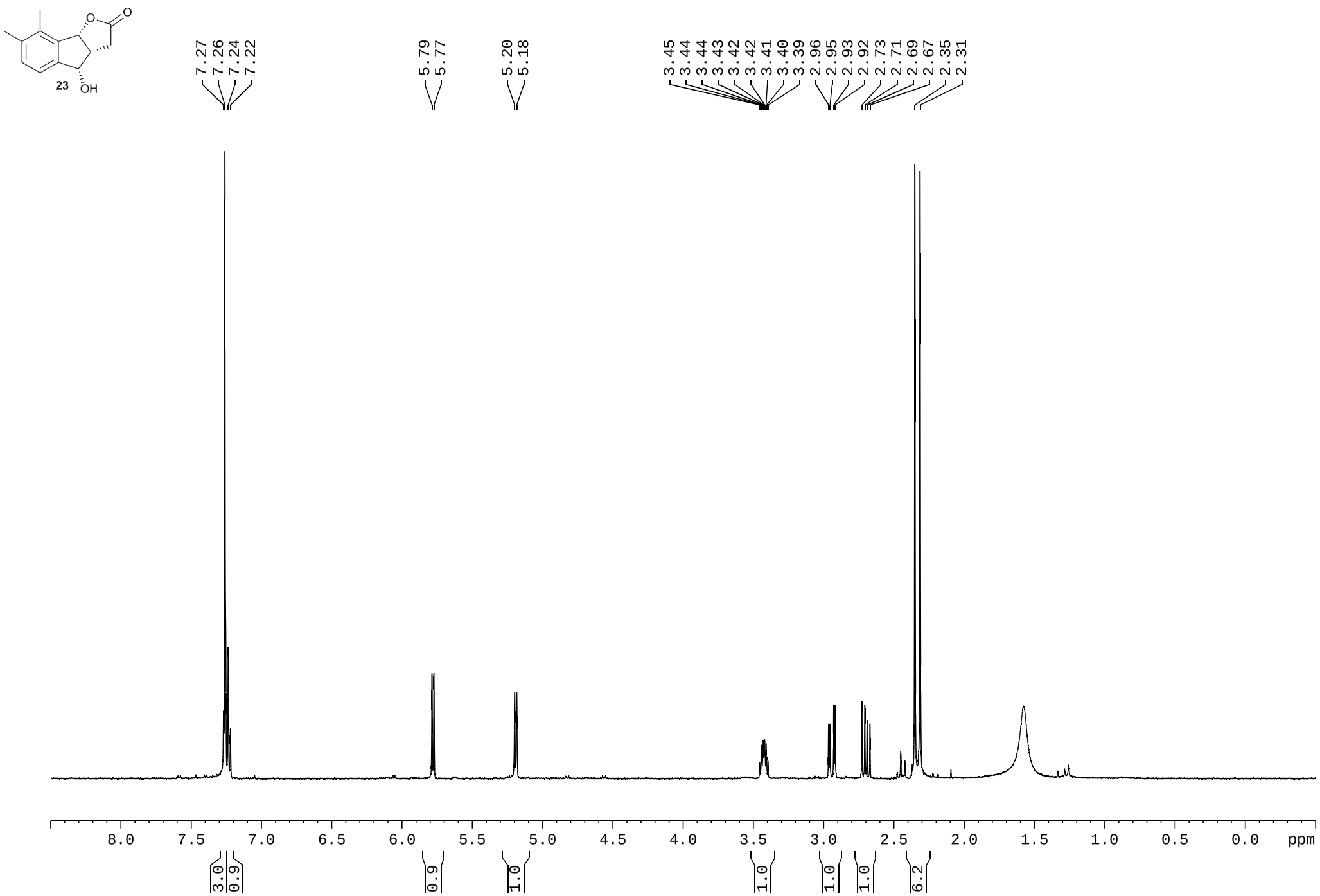
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

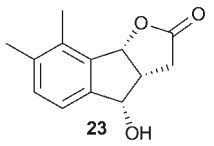

22
OH
7.26
7.24
7.19
7.17
6.11
6.09
5.10
5.09
3.25
3.24
3.23
3.22
3.22
3.21
3.20
3.20
3.19
3.18
2.98
2.96
2.94
2.91
2.51
2.49
2.46
2.45
2.34
2.31
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.8
0.9
1.0
0.9
1.0
1.0
1.0
6.2



176.8
142.0
138.7
137.7
135.5
132.6
122.3
85.9
80.6
47.8
33.4
19.7
15.5

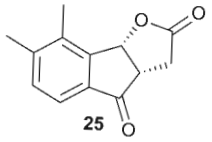



23
OH
7.27
7.26
7.24
7.22
5.79
5.77
5.20
5.18
3.45
3.44
3.44
3.43
3.42
3.42
3.41
3.40
3.39
2.96
2.95
2.93
2.92
2.73
2.71
2.69
2.67
2.35
2.31
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
3.0
0.9
0.9
1.0
1.0
1.0
1.0
6.2



177.4
142.4
138.5
137.5
135.4
132.6
122.4
84.5
73.7
43.2
29.2
19.7
15.7

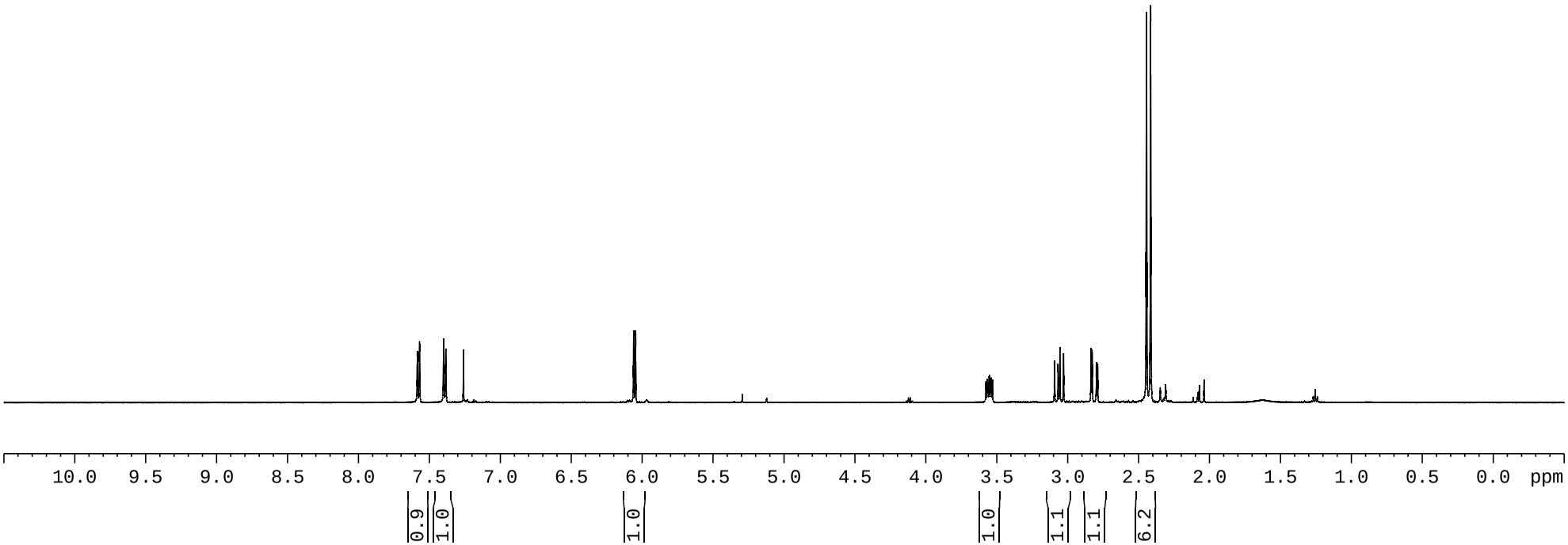
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

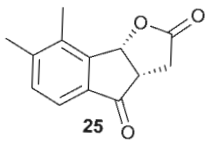


7.58
7.57
7.40
7.38
7.26

6.06
6.05

3.58
3.57
3.56
3.55
3.55
3.54
3.54
3.53
3.09
3.07
3.05
3.03
2.84
2.83
2.80
2.79
2.44
2.41

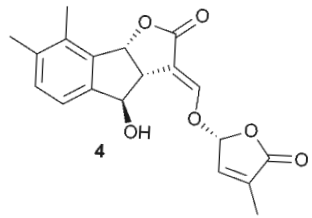




202.6
175.1
148.9
146.5
136.5
134.4
133.3
121.8
78.8
46.2
31.3
20.5
15.1

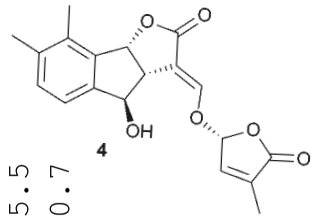
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

Solanacol


OH
4

7.54
7.53
7.23
7.22
7.16
7.14
6.99
6.99
6.99
6.98
6.98
6.22
6.22
6.21
6.21
6.21
6.14
6.12
5.23
3.80
3.80
3.80
3.79
3.79
3.78
2.35
2.29
2.04
2.03
2.03
8
7
6
5
4
3
2
1
0
ppm
1.0
1.0
1.0
1.0
1.0
1.0
1.0
3.0
3.0
3.0

Solanacol



170.8
170.1
151.6
141.7
140.9
138.6
138.0
136.0
135.3
132.6
122.3
110.5
100.6
84.0
79.8
50.3
19.5
15.5
10.7