Δ-keto-acid /hydroxy-lactone isomerization in some lichen depsides, depsidones and diphenyl ethers

Philippe Uriac,*[a] Solenn Ferron, [a] Philippe Jehan,[b] Thierry Roisnel,[a] and Sophie Tomasi [a]

a. Univ Rennes, CNRS, ISCR (Institut des Sciences Chimiques de Rennes) -UMR 6226, Rennes, France.

b. Univ Rennes, CNRS, ScanMAT UAR 2025, CRMPO (Centre Régional de Mesures Physiques de l'Ouest), F-35000 Rennes, France.

SUPPORTING INFORMATION

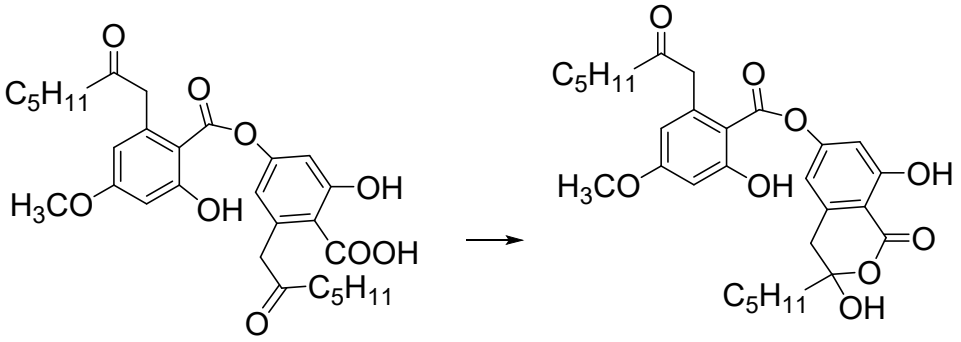
References

1 S. Huneck and I. Yoshimura, *Identification of Lichen Substances*, Springer Berlin Heidelberg, Berlin, Heidelberg, 1996.
2 S. Ferron, P. Jéhan, X. Guillory and P. Uriac, *Phytochemistry*, 2022, **198**, 113139.
3 M. Millot, S. Tomasi, S. Sinbandhit and J. Boustie, *Phytochemistry Letters*, 2008, **1**, 139–143.
4 M. Millot.; S.Tomasi; K. Articus; Rouaud, I.; A. Bernard; J. Boustie *J. Nat. Prod.* **2007**, *70* (2), 316–318.

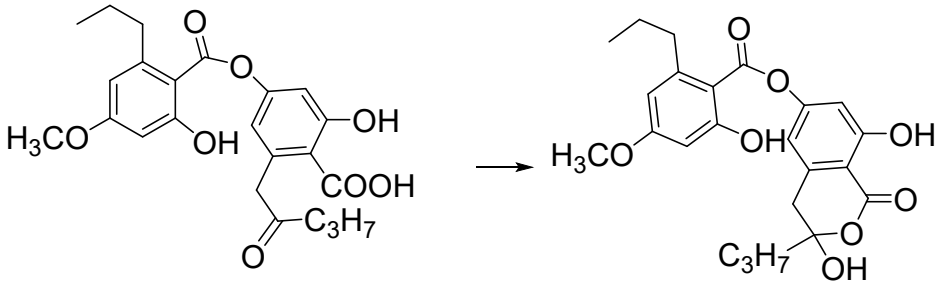
S1. Structure of other lichen specialized metabolites concerned by the study.

On the left the structure proposed in Hüneck and on the right the corrected structure according to the 2H-1''' ^{1}H NMR value and this study.

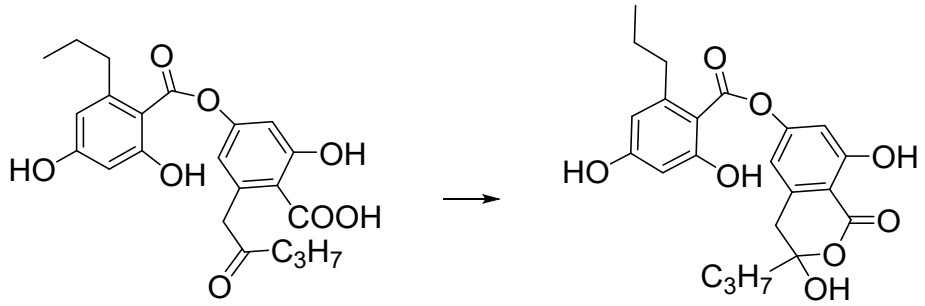
Compound with OH-2': hydroxy-lactone isomer



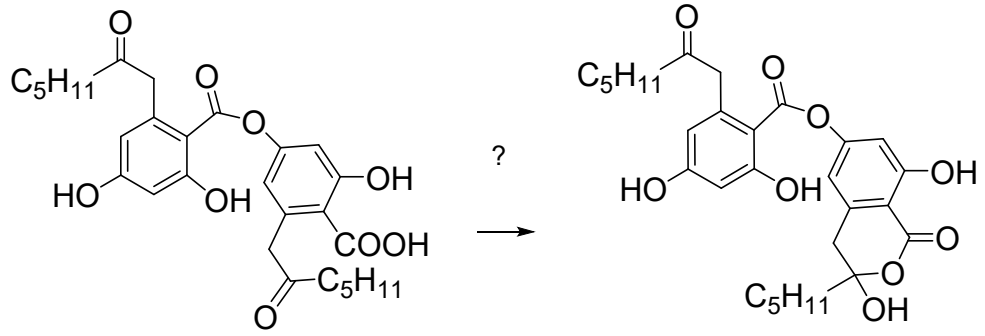
microphyllinic acid/ no data



oxostenosporic acid/ 3.22 ppm

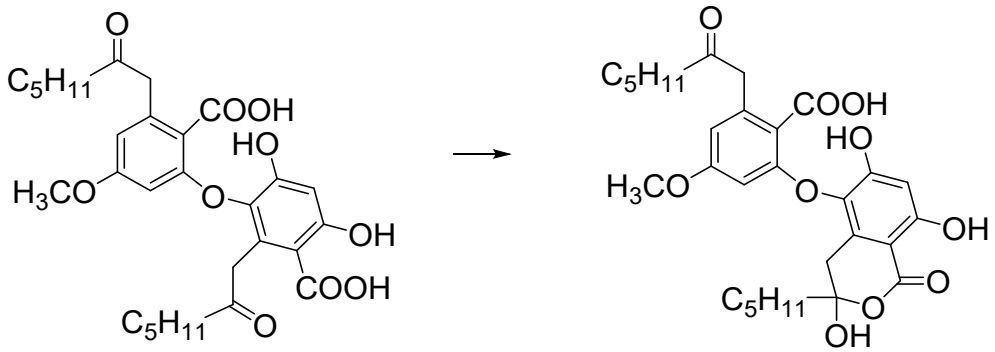


4-*O*-demethylglomellic acid/ 3.40 ppm

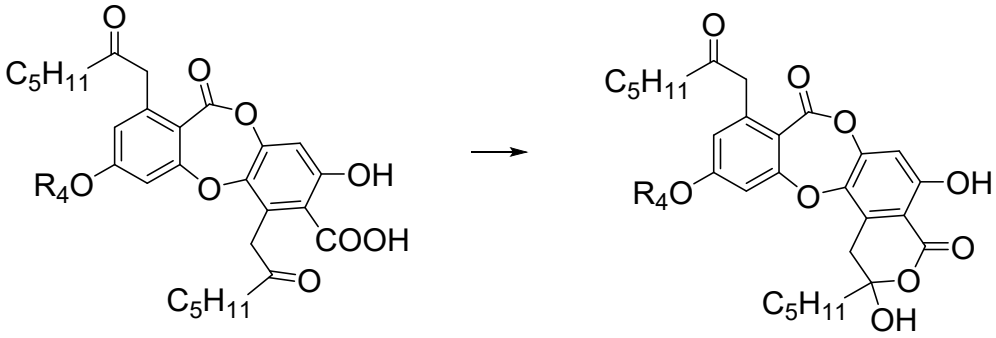


4-*O*-demethylmicrophyllinic acid/ 4.05 ppm

To check

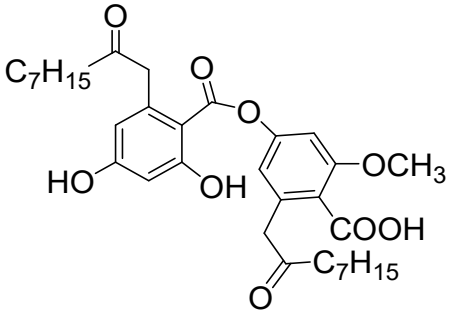


β-alectoronic acid/3.15 ppm

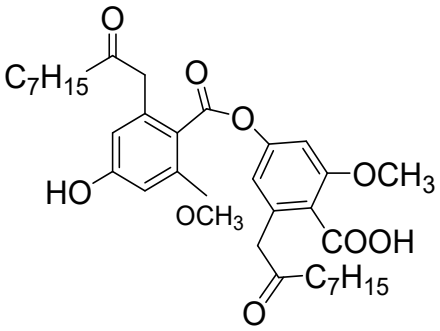


glomellonic acid/3.52 ppm

Compound with OCH_3-2': δ-keto-acid isomer



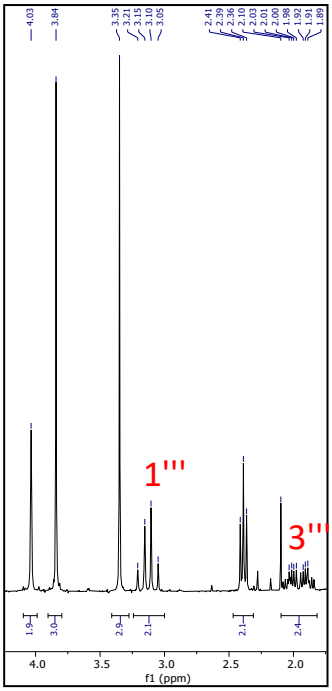
2'-*O*-methylsuperphyllinic acid/ no data



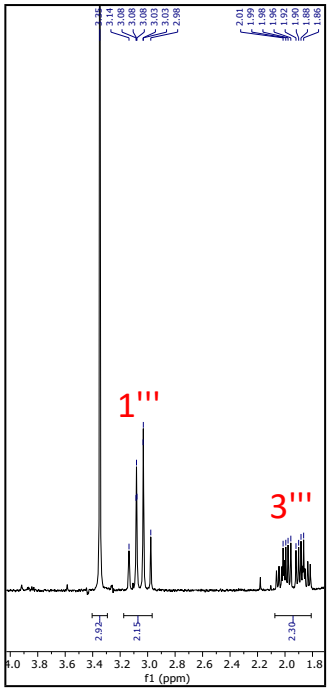
glaucophaeic acid/ no data

S2. ^{1}H NMR data concerning CH_2-**1‘’’** and CH_2-**3‘’’** of **hl** and **ka** isomers

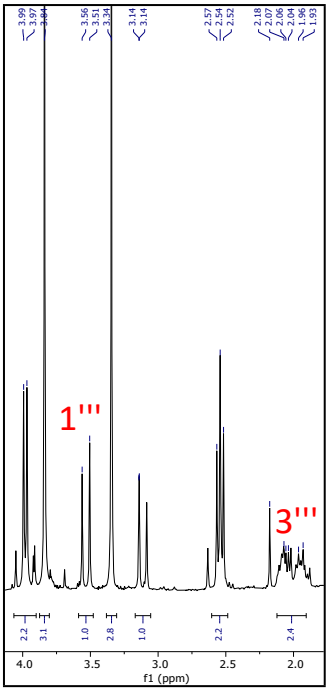
Methoxy-lactones **hl**



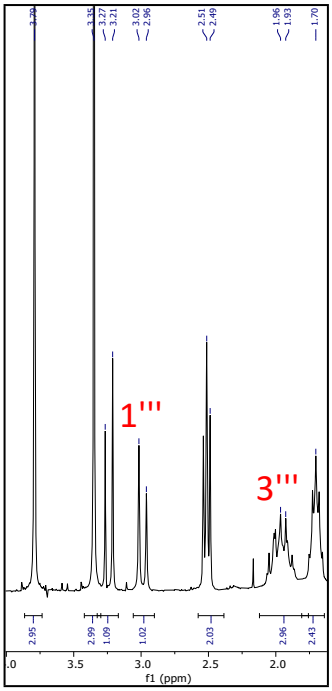
2‘’’-*O*-methylglomellic acid **10**



Compound **13’**

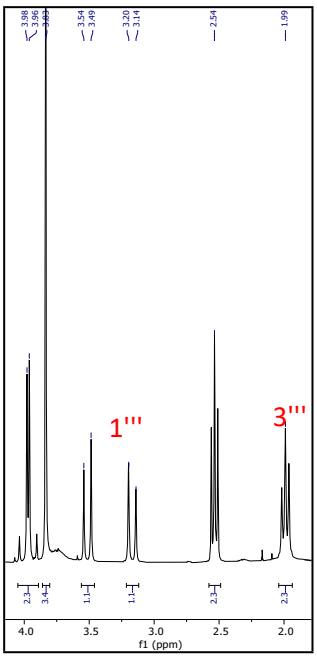


2‘’’-*O*-methyl-α-collatolic acid **11**

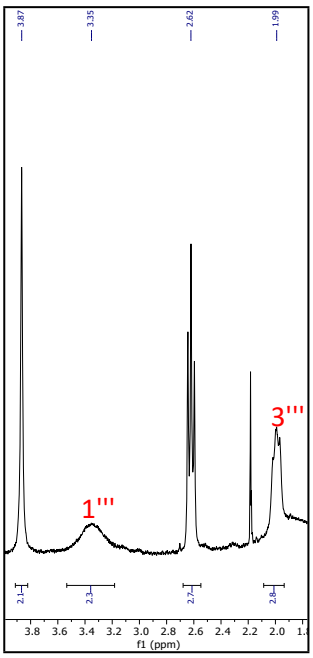


2‘’’-*O*-methyl-β-collatolic acid **12**

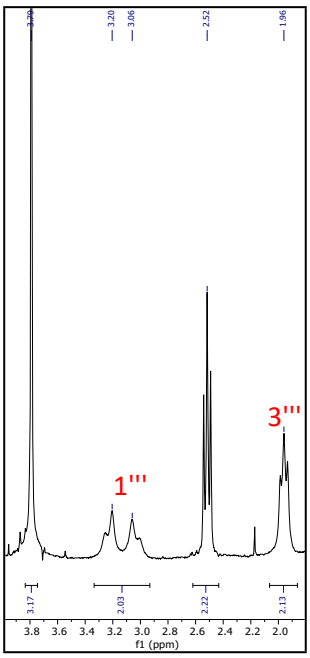
Hydroxy-lactones **hl**



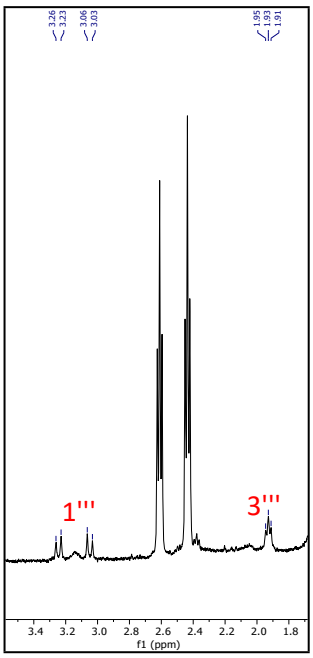
α-collatolic **5**



α-alectoronic **6**

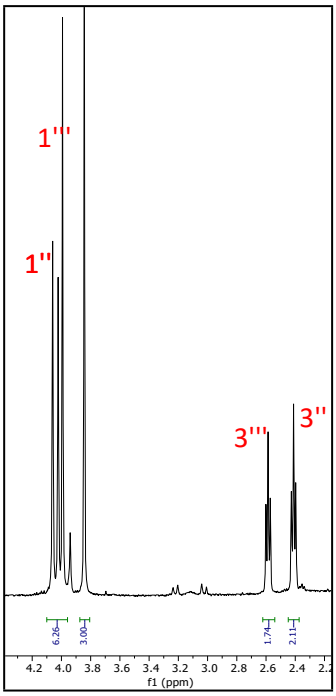


β-collatolic **7**

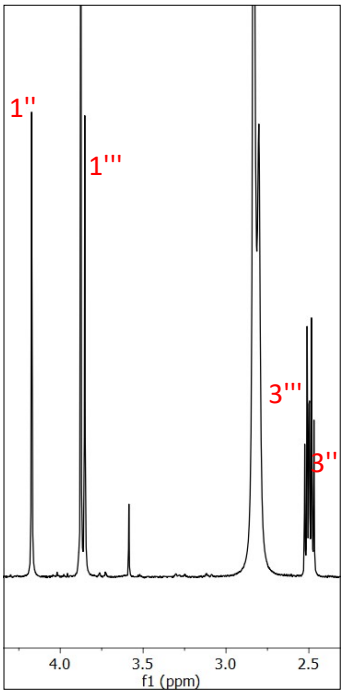


2'-*O*-methylisomicrophyllinic **2hl** (idem **3hl**)

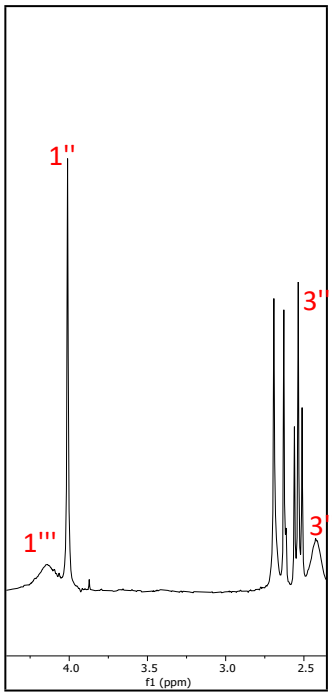
δ-keto-acides ka



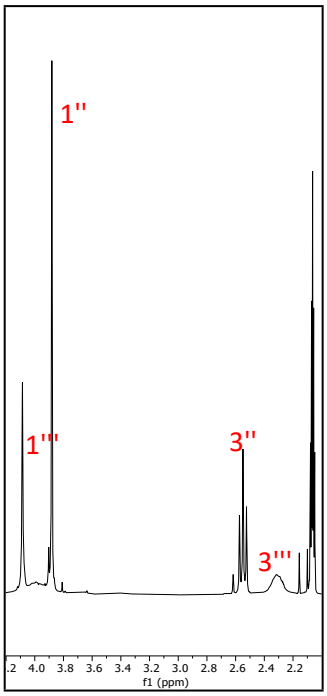
2'-*O*-methylsuperphyllinic acid **3**



Arthoniaic acid **4**

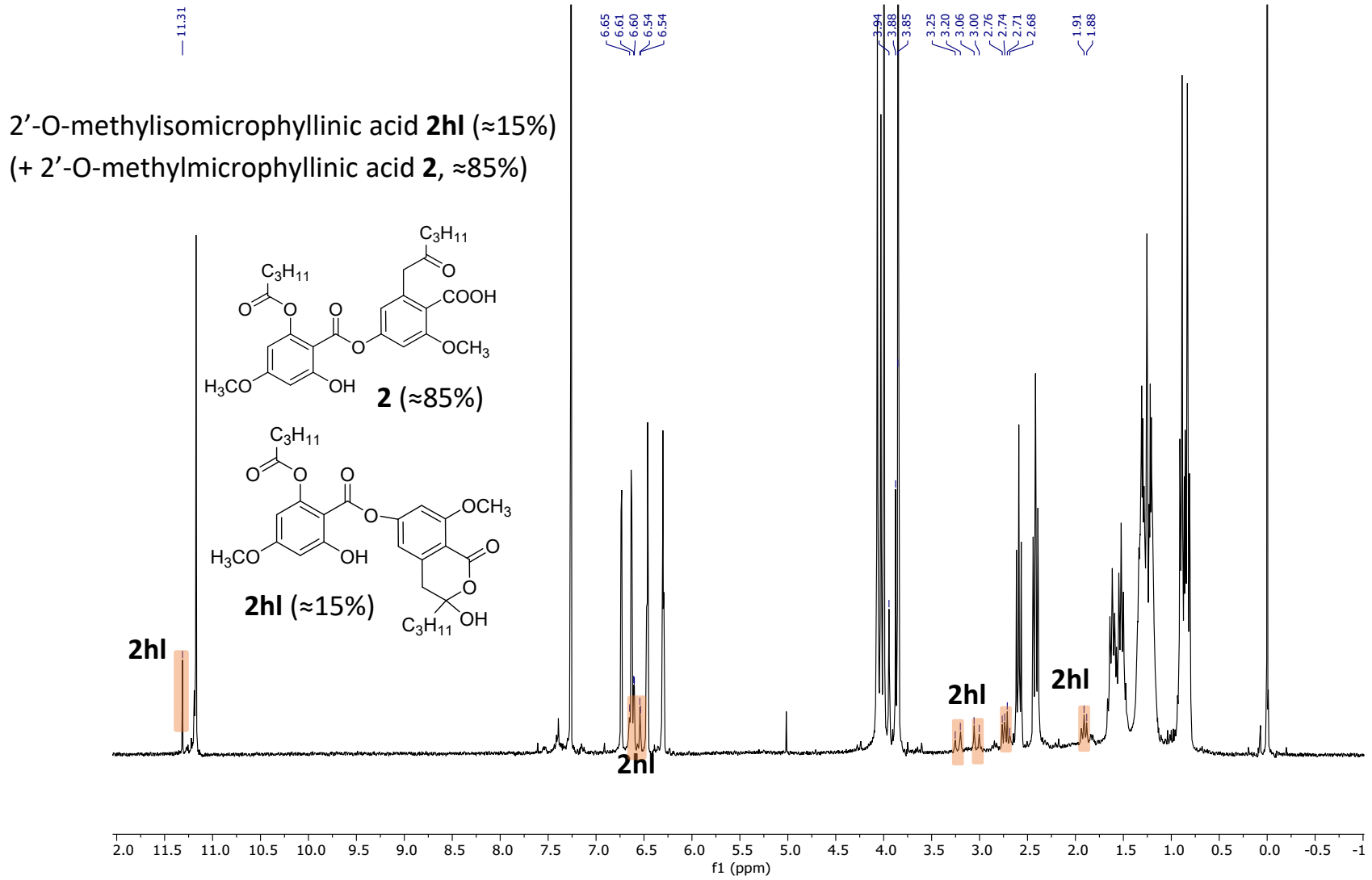


α-isoalectoronic **6ka**



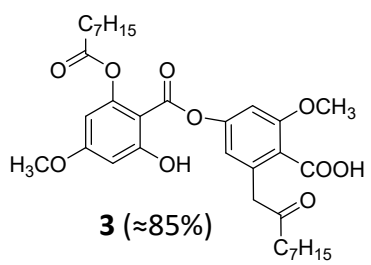
α-isocollatolic **5ka**

S3. NMR spectra of **2hl** (+ **2** major), **3hl** (+ **3** major), **5ka**, **6ka**, **9, 10**, **11**, **12**, and **13'**

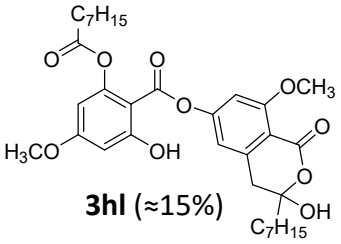


2’-*O*-methylisosuperphyllinic acid **3hl** (≈15%)

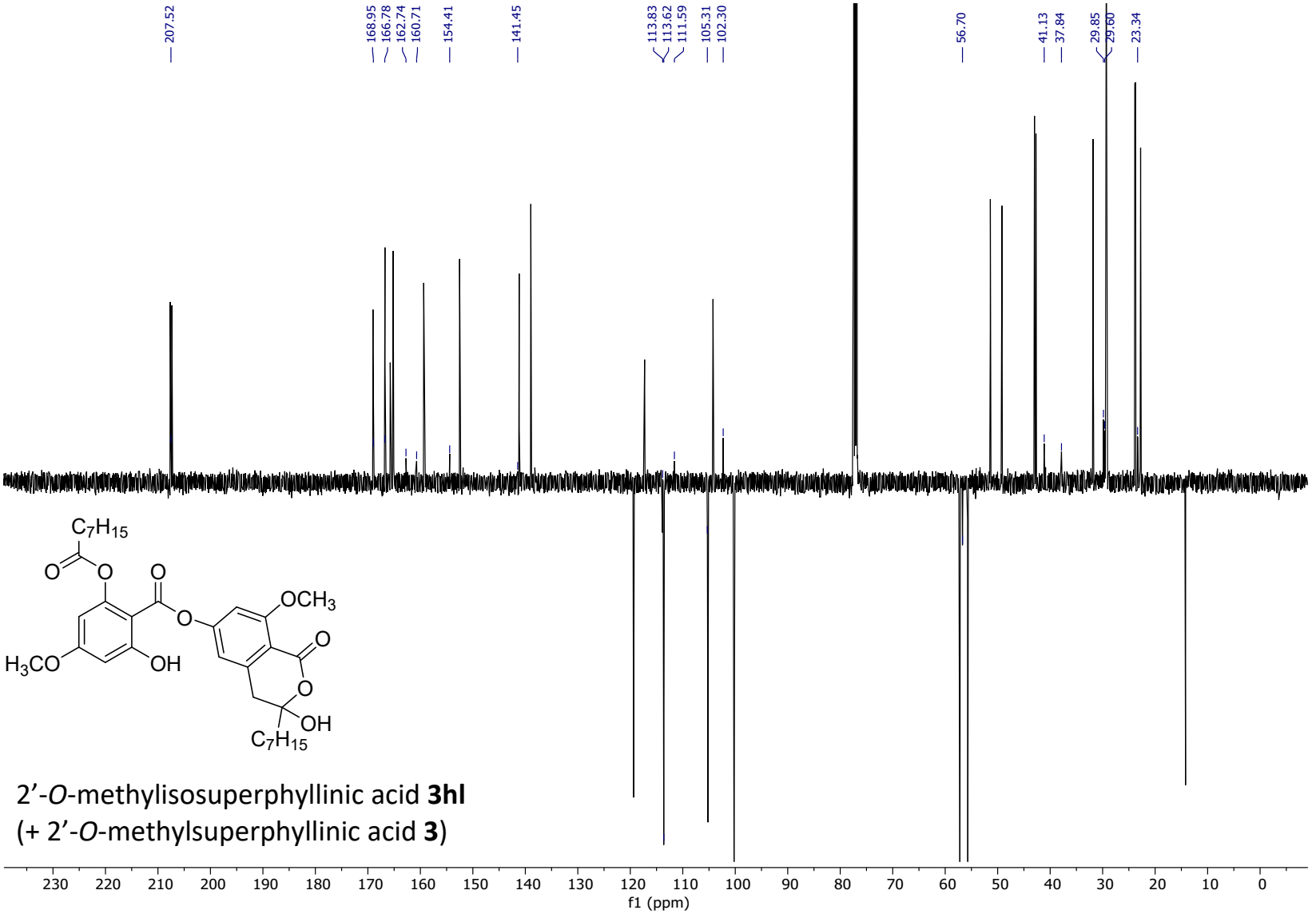
(+ 2’-*O*-methylsuperphyllinic acid **3**, ≈85%)



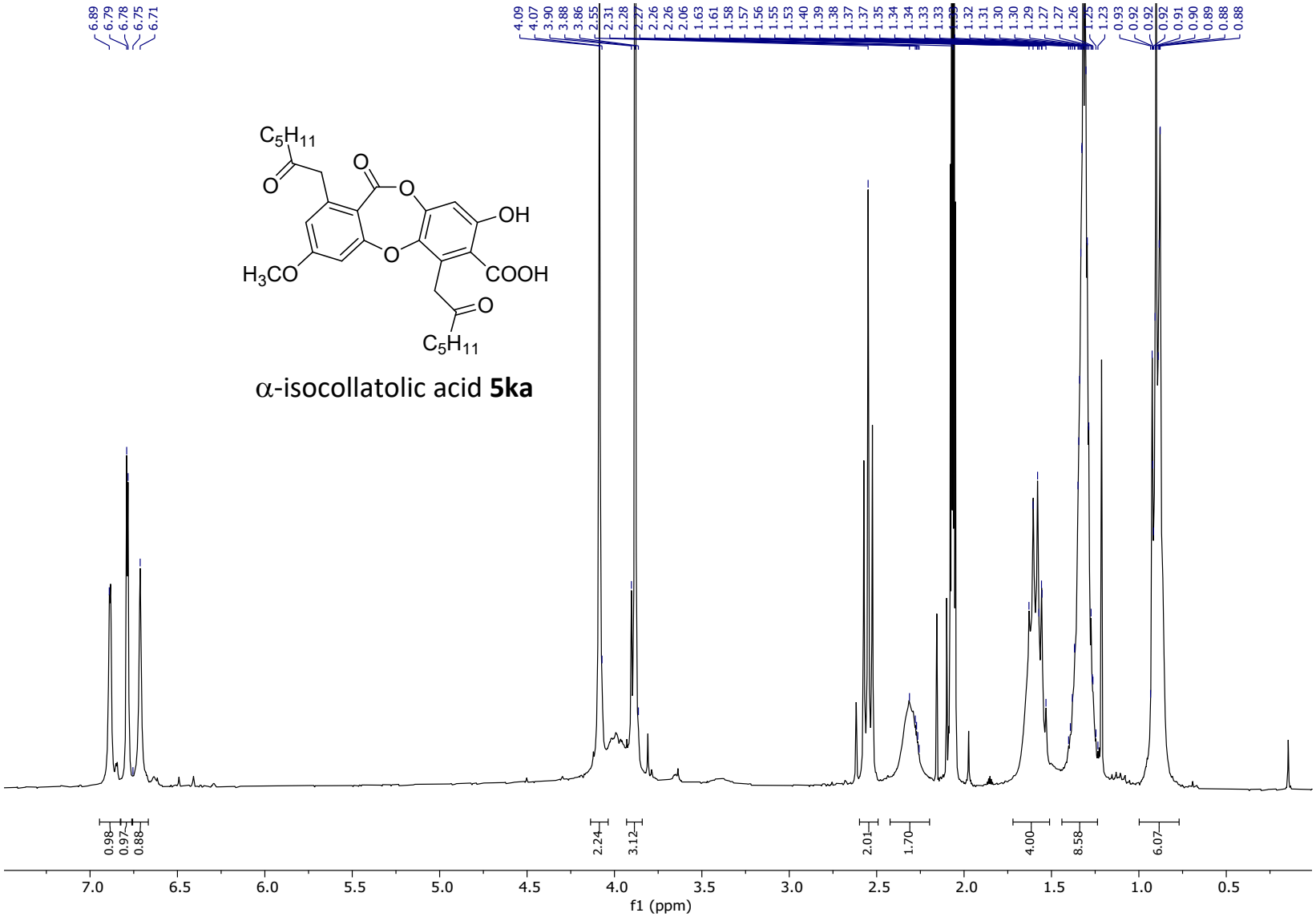
3 (≈85%)



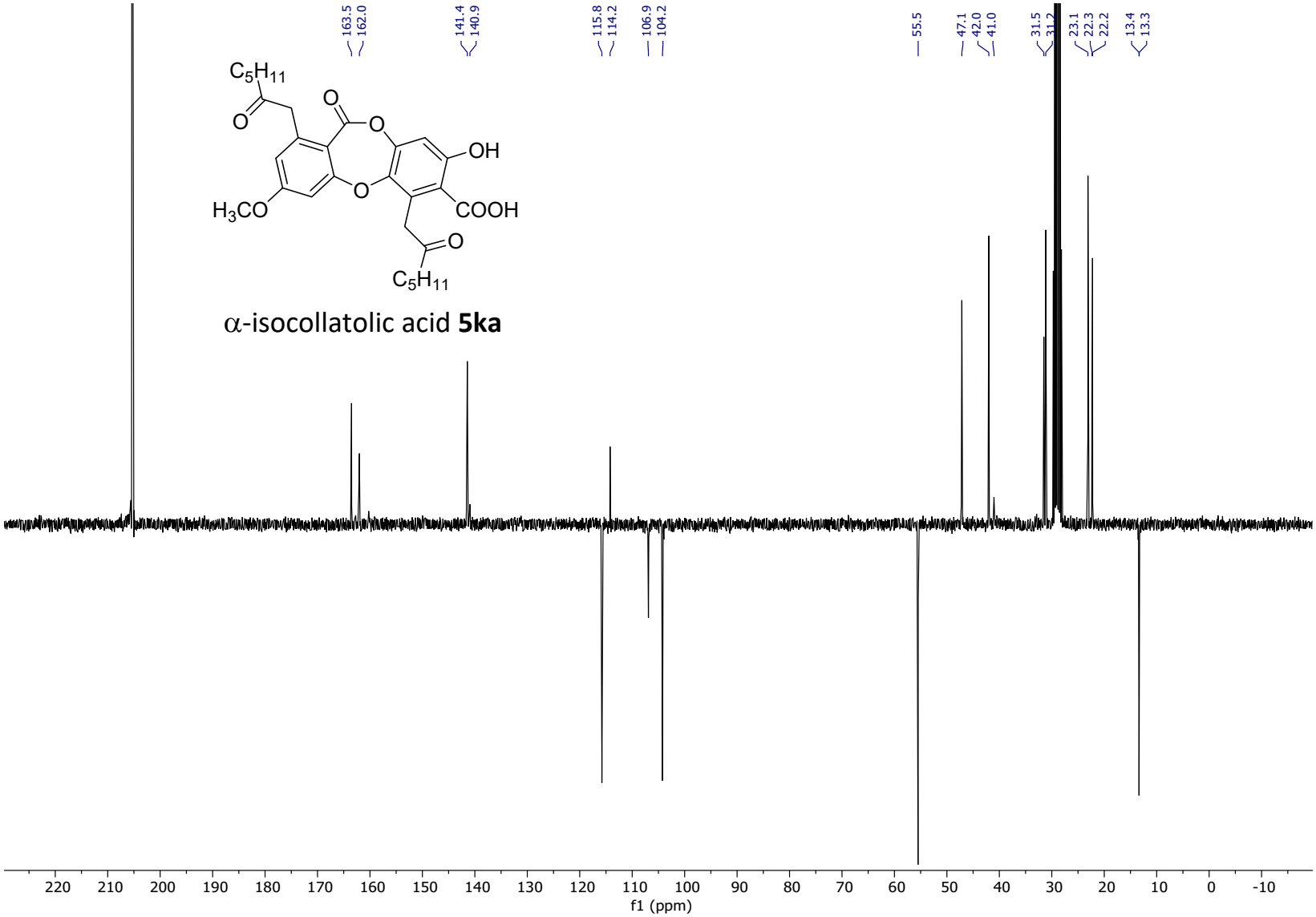
3hl (≈15%)



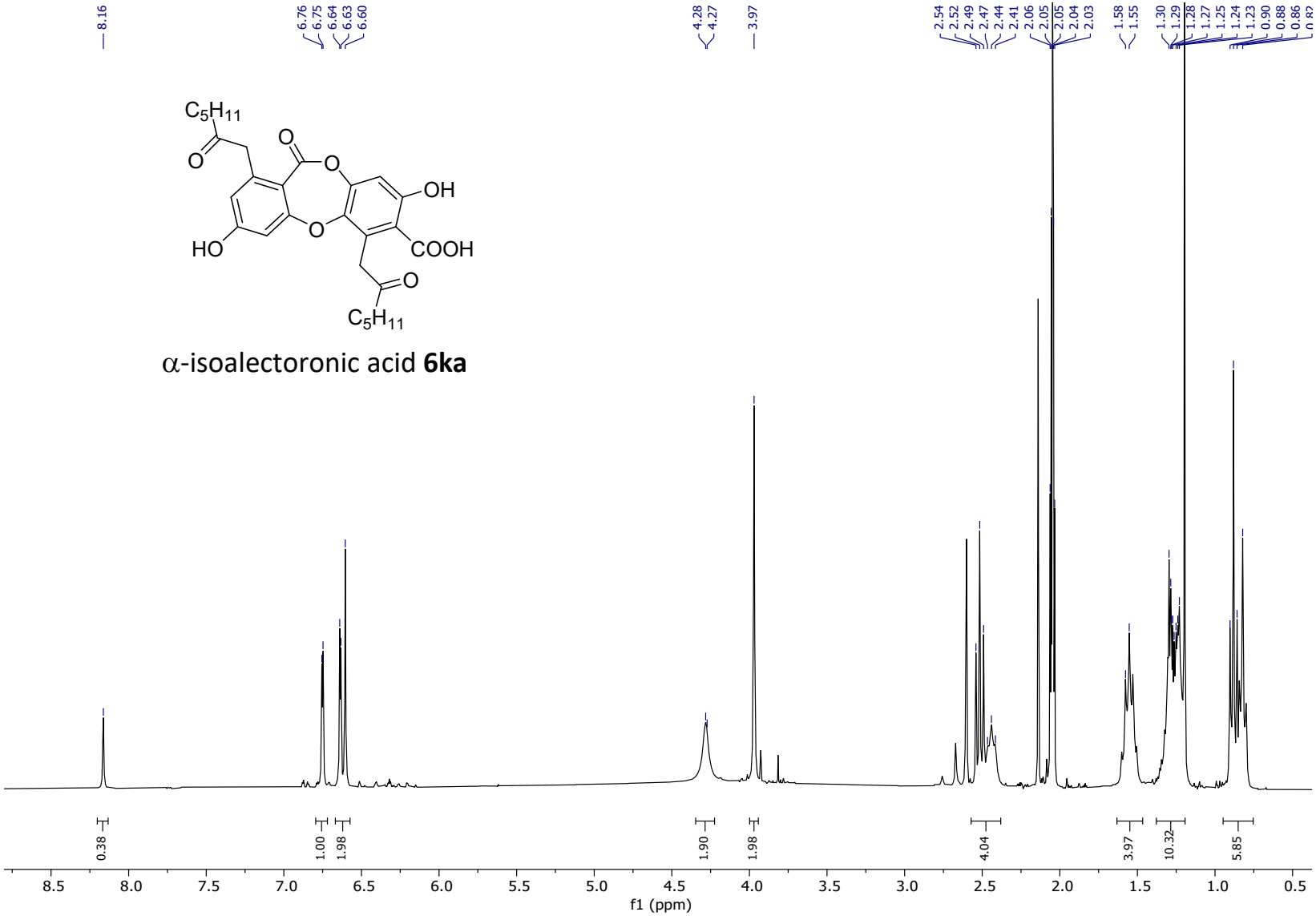
2'-*O*-methylisosuperphyllinic acid **3hl**
(+ 2'-*O*-methylsuperphyllinic acid **3**)



α-isocollatolic acid **5ka**

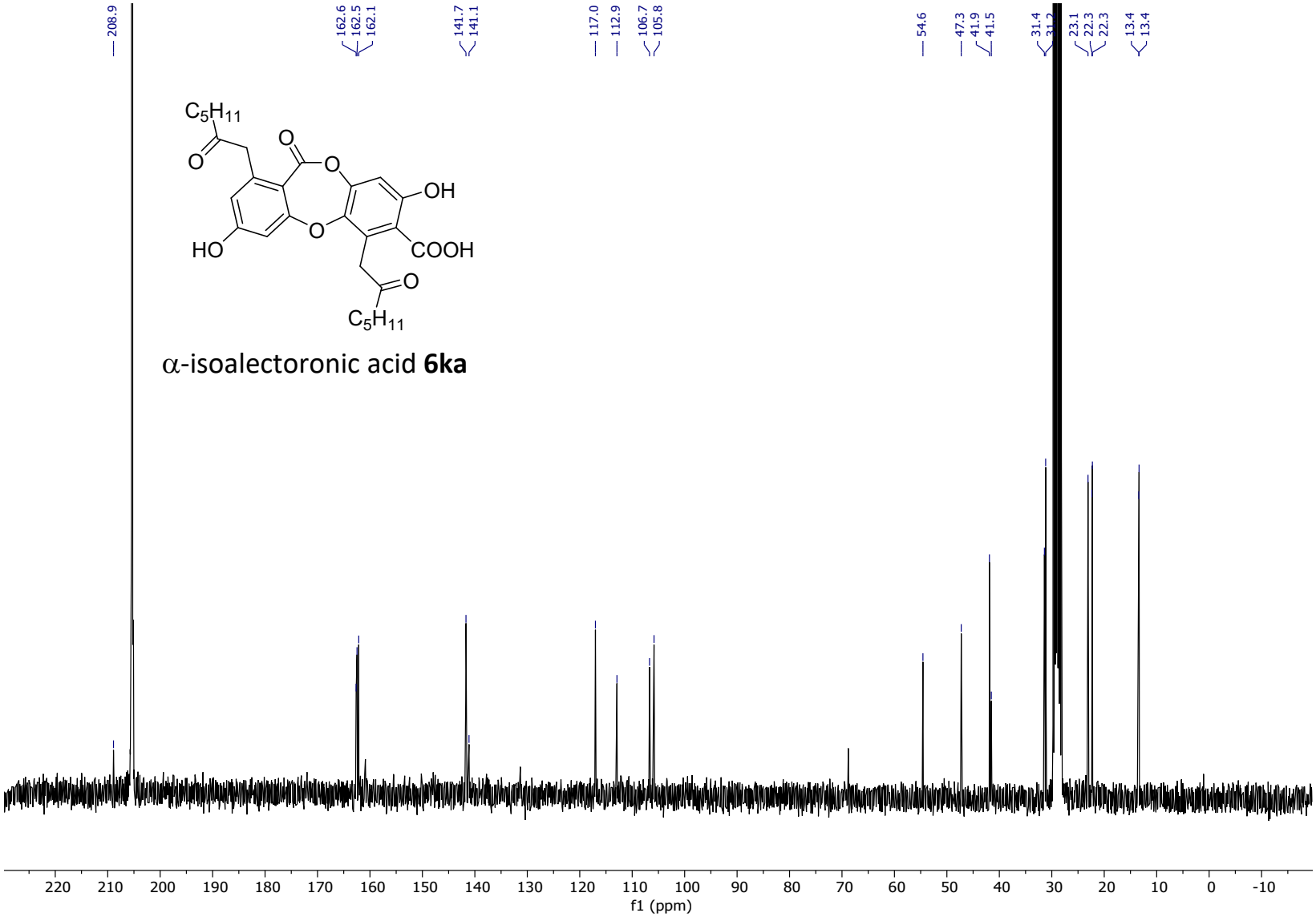


α-isocollatolic acid **5ka**

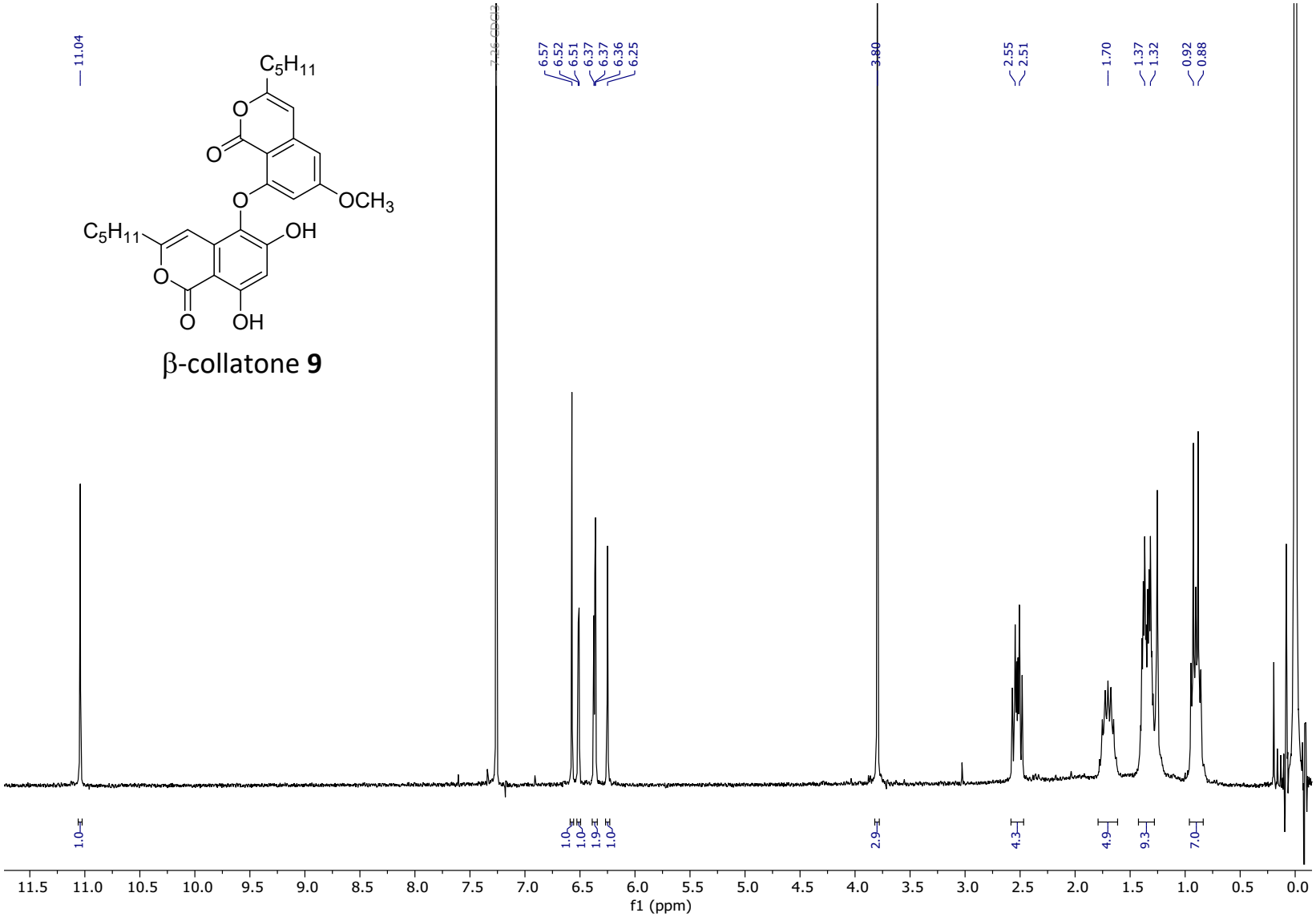


C_5H_{11}, O, O, O, O, OH, HO, COOH, O, C_5H_{11}

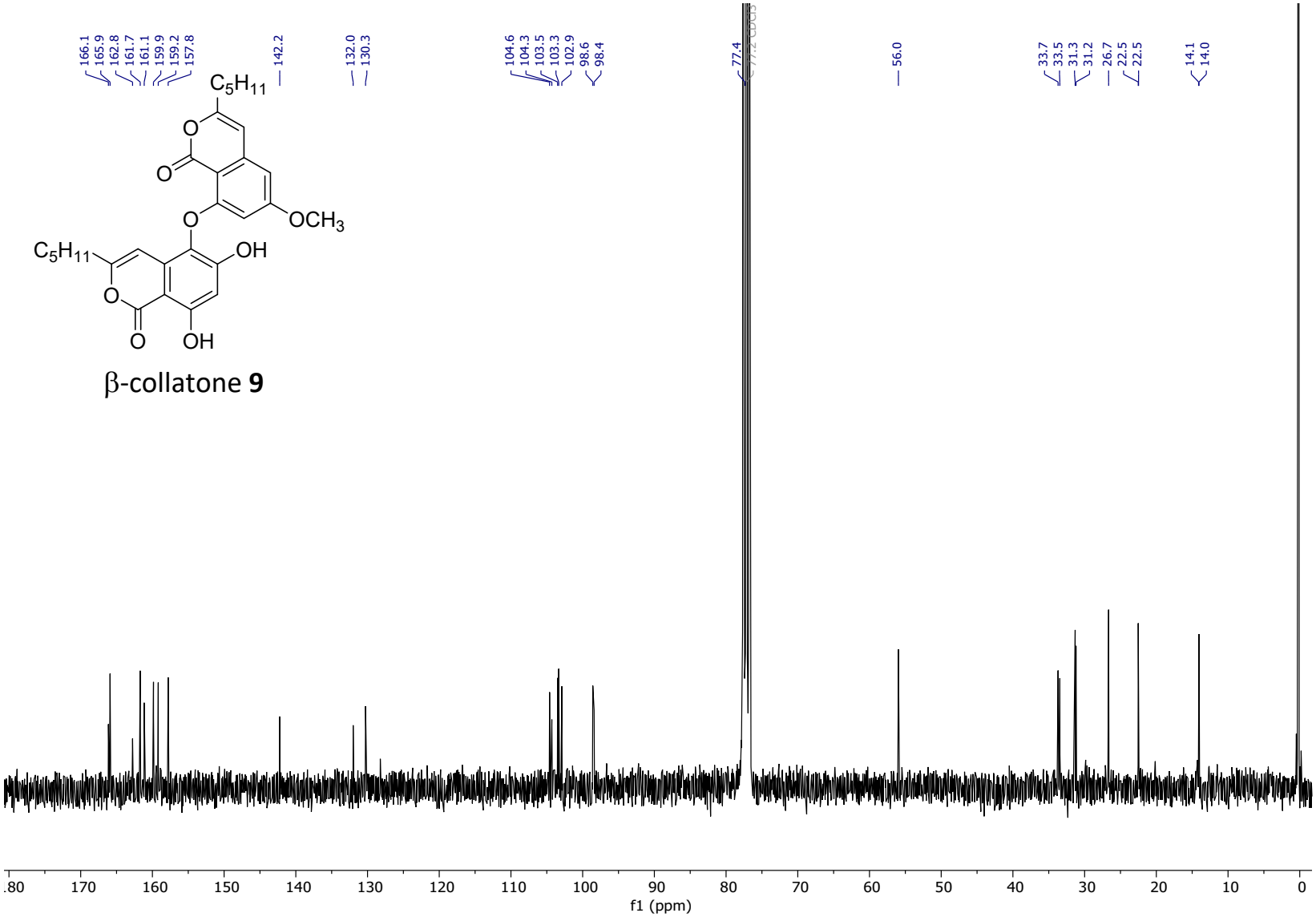
α-isoalectoronic acid **6ka**



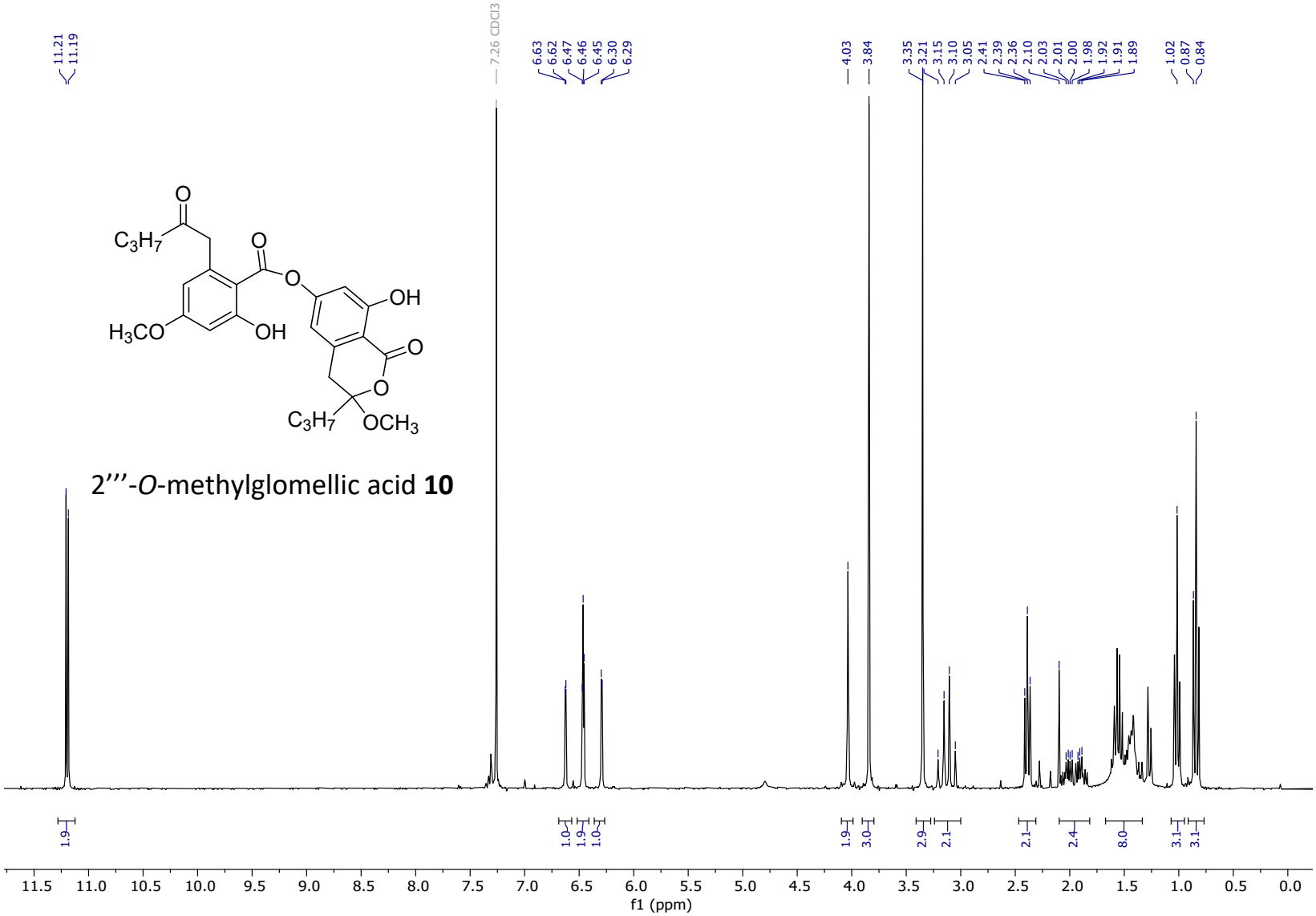
α-isoalectoronic acid **6ka**



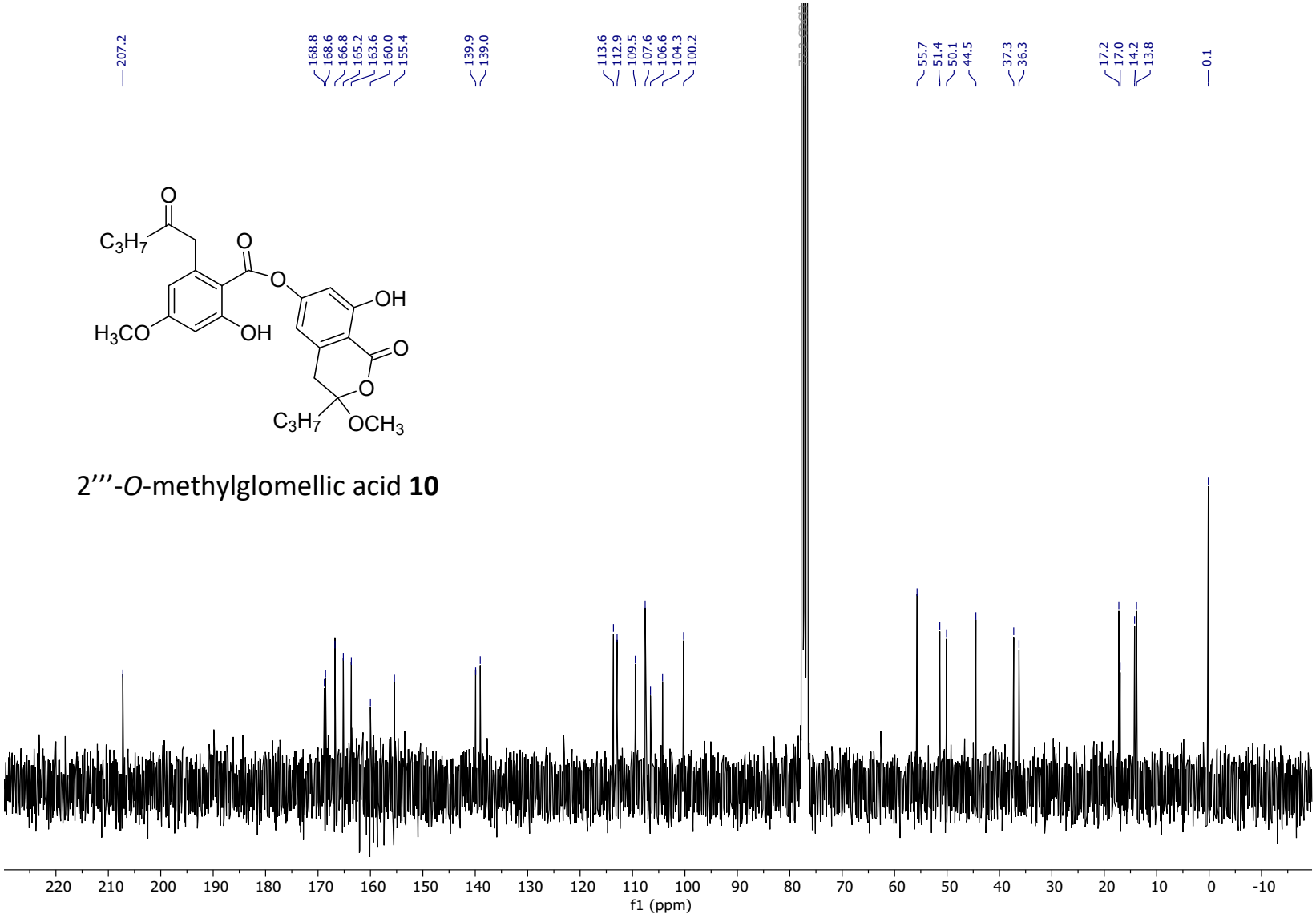
β-collatone **9**



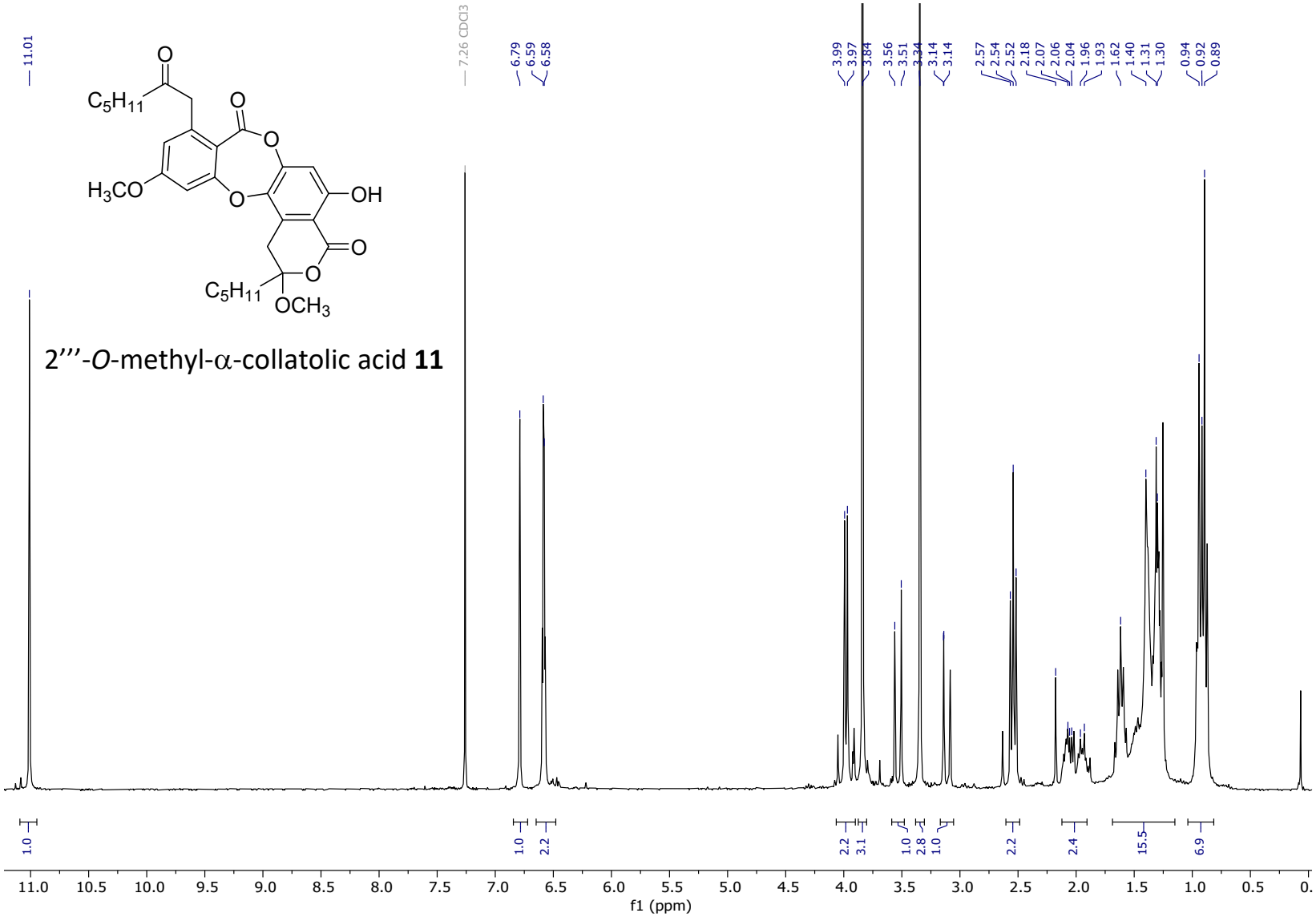
β-collatone **9**



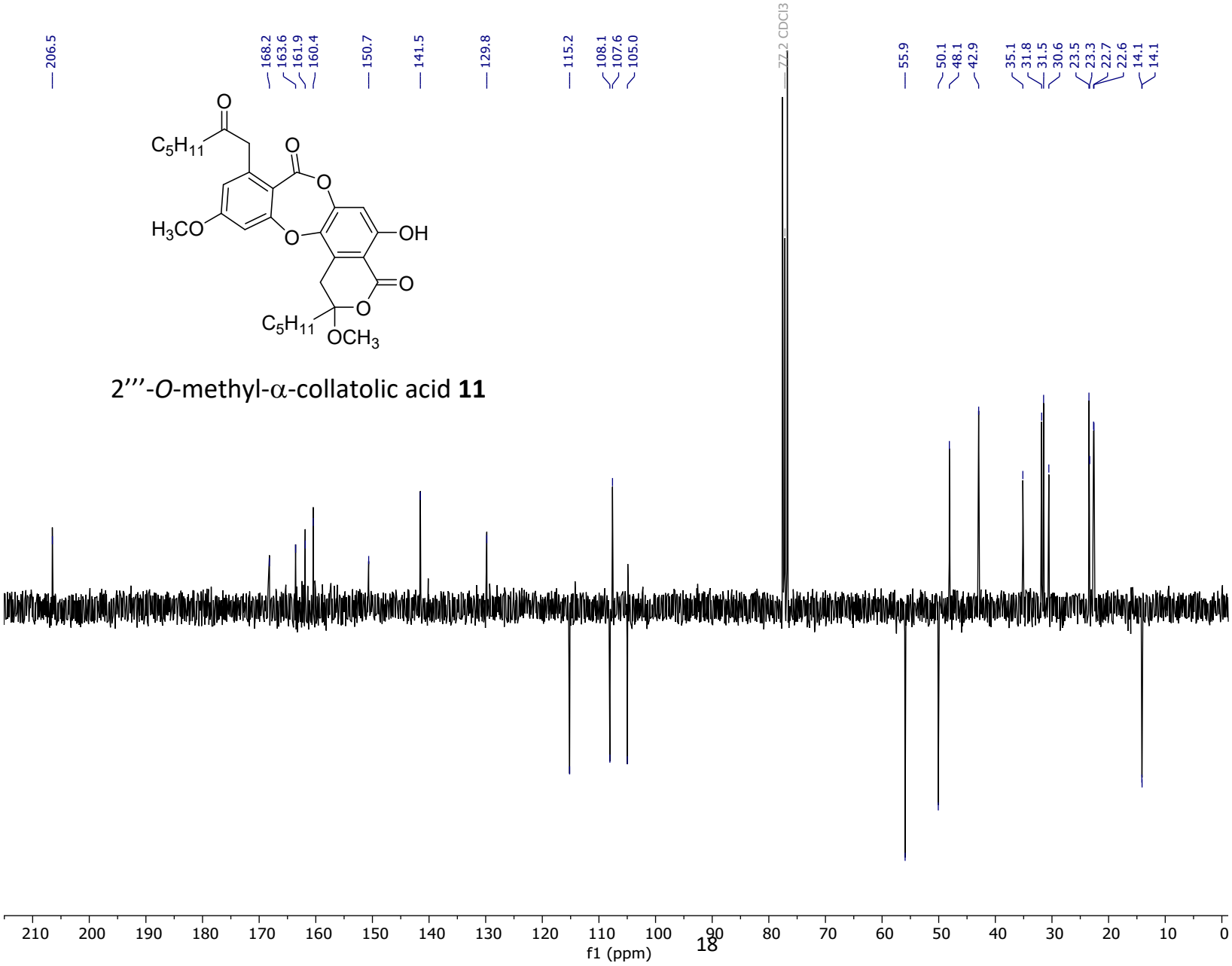
2’’’-*O*-methylglomellic acid **10**



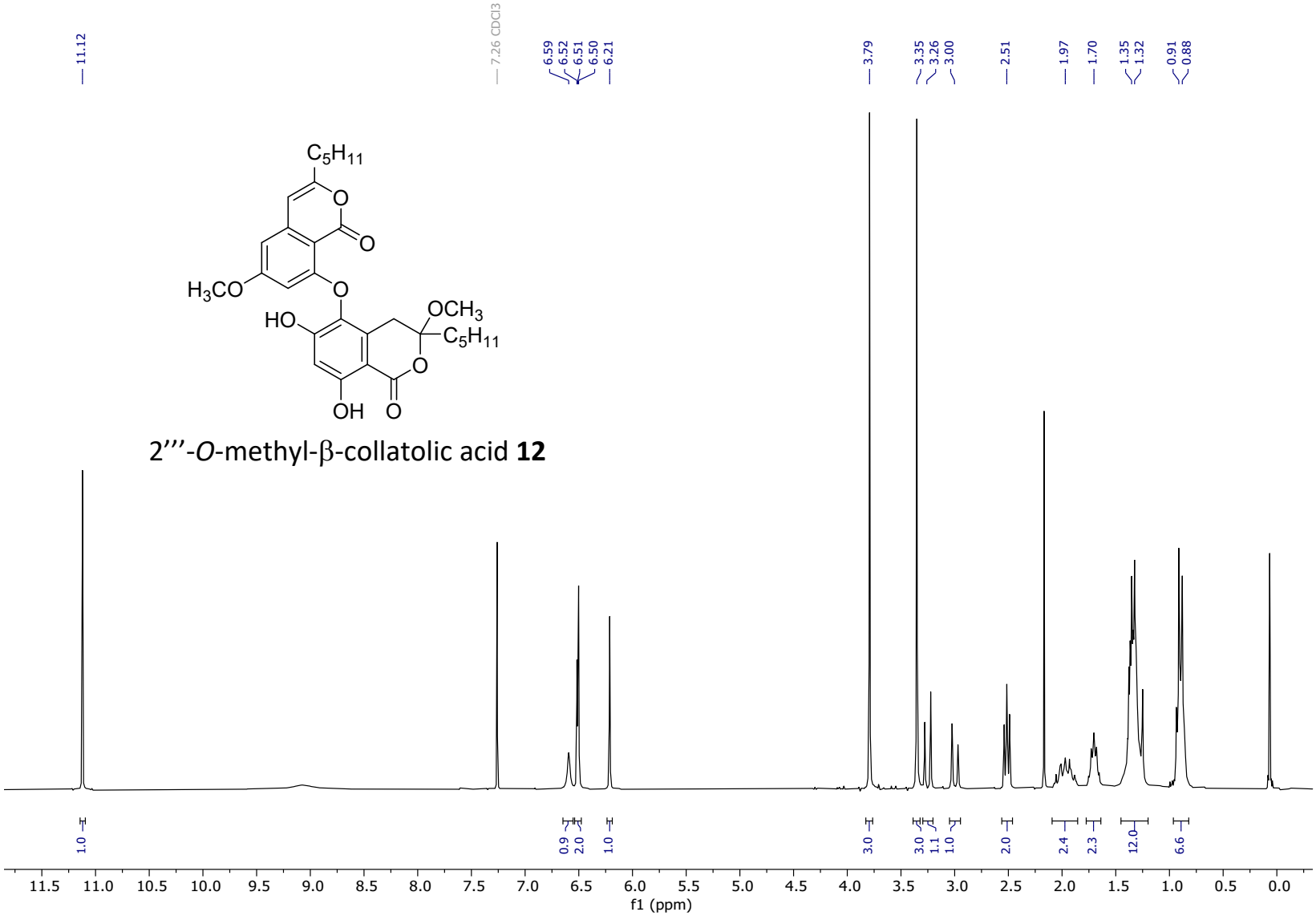
2’’’-*O*-methylglomellic acid **10**



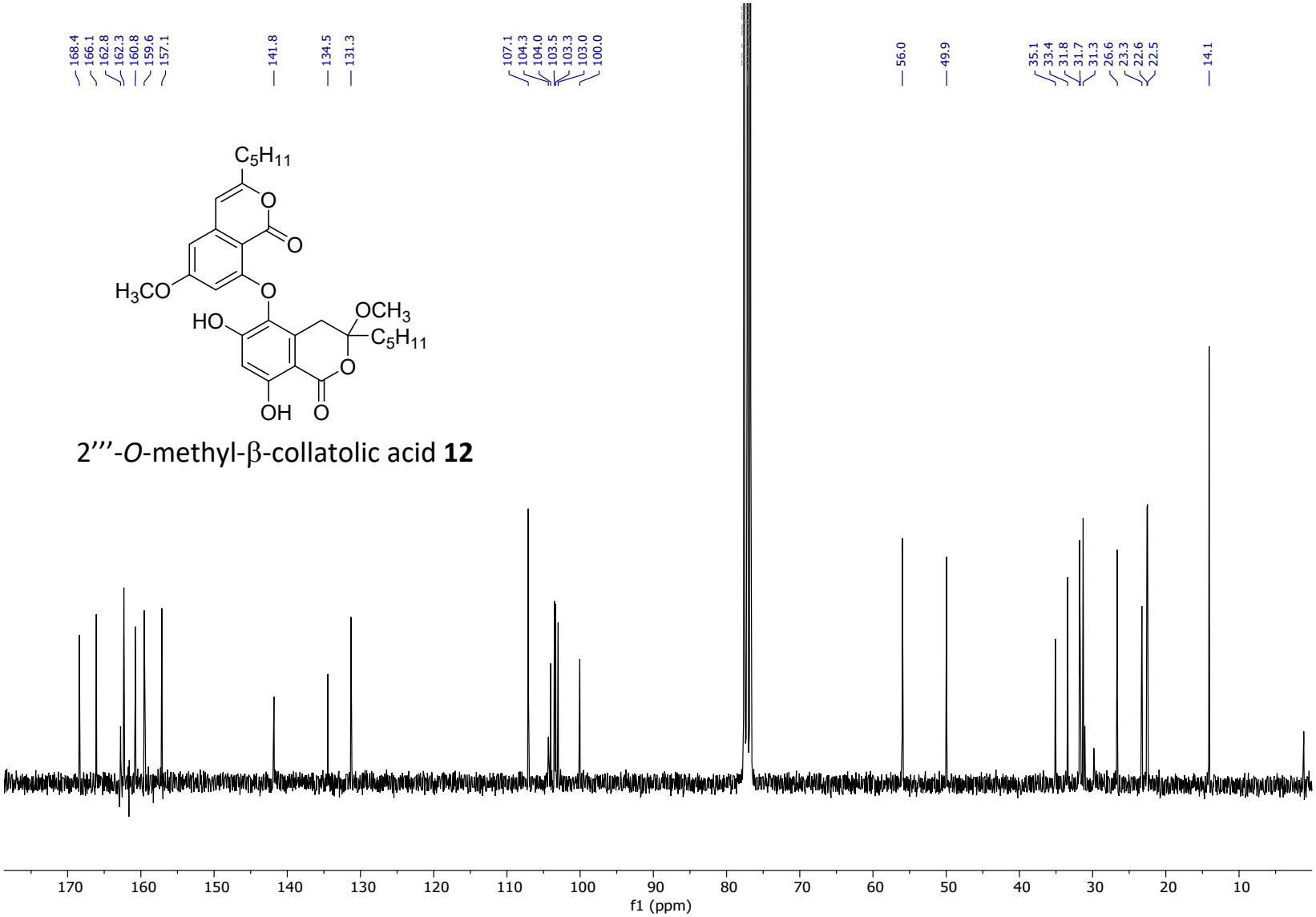
2’’’-*O*-methyl-α-collatolic acid **11**



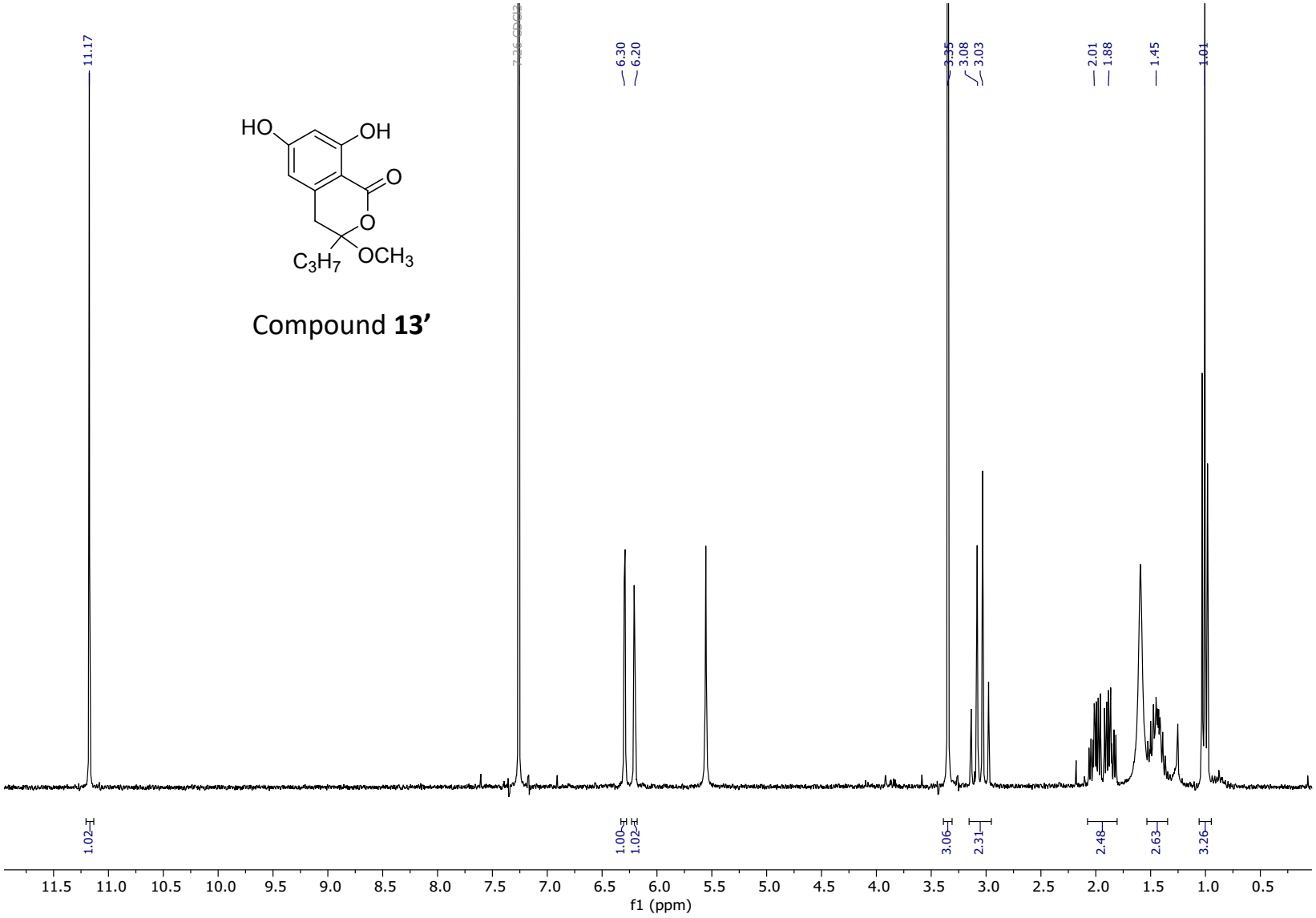
2’’’-*O*-methyl-α-collatolic acid **11**



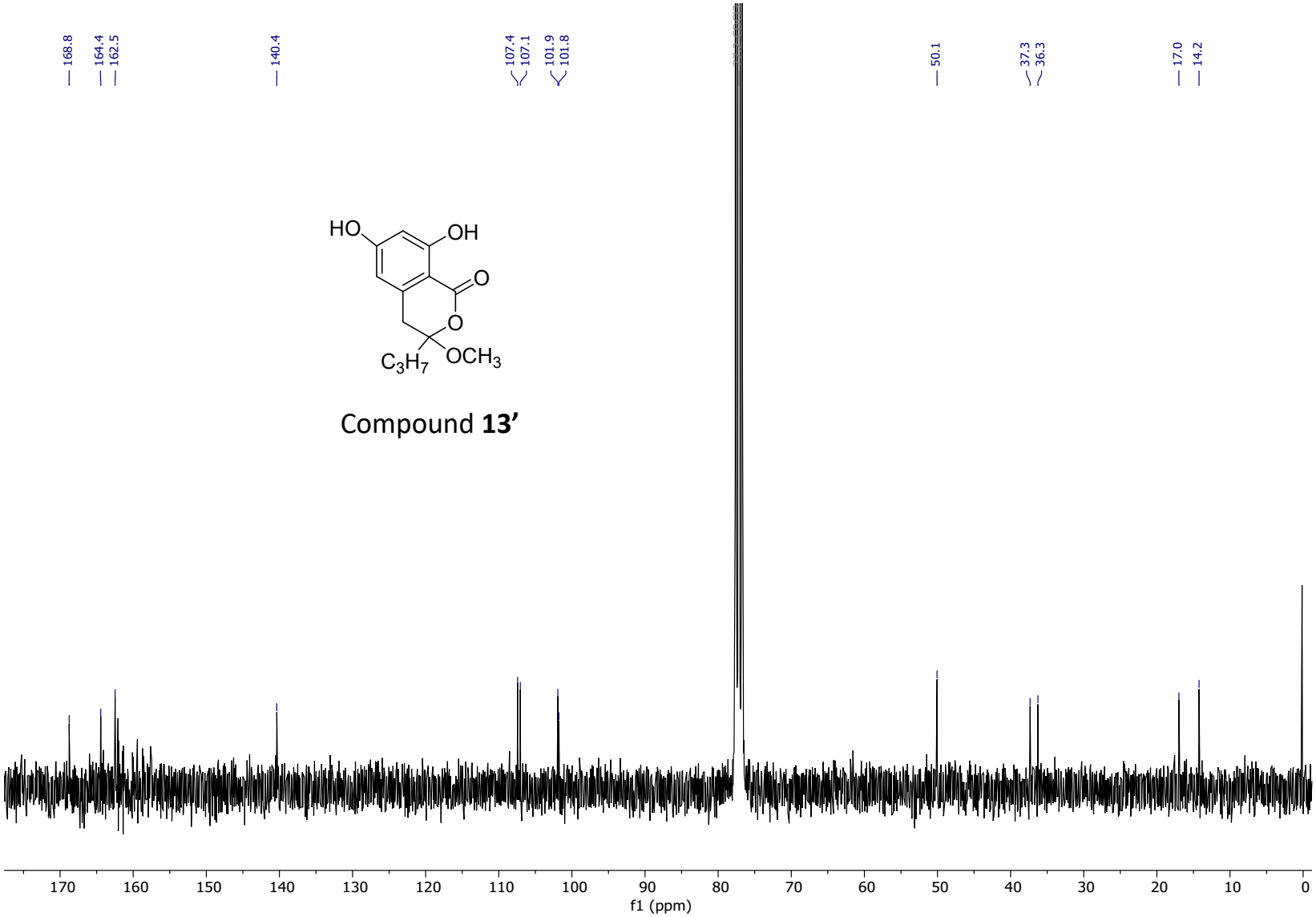
2’’’-*O*-methyl-β-collatolic acid **12**



2’’’-*O*-methyl-β-collatolic acid **12**


HO
OH
O
O
C_3H_7
OCH_3
11.17
7.26 CDCl3
6.30
6.20
3.35
3.08
3.03
2.01
1.88
1.45
1.01
1.02
1.00
1.02
3.06
2.31
2.48
2.63
3.26
11.5 11.0 10.5 10.0 9.5 9.0 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 0.5
f1 (ppm)

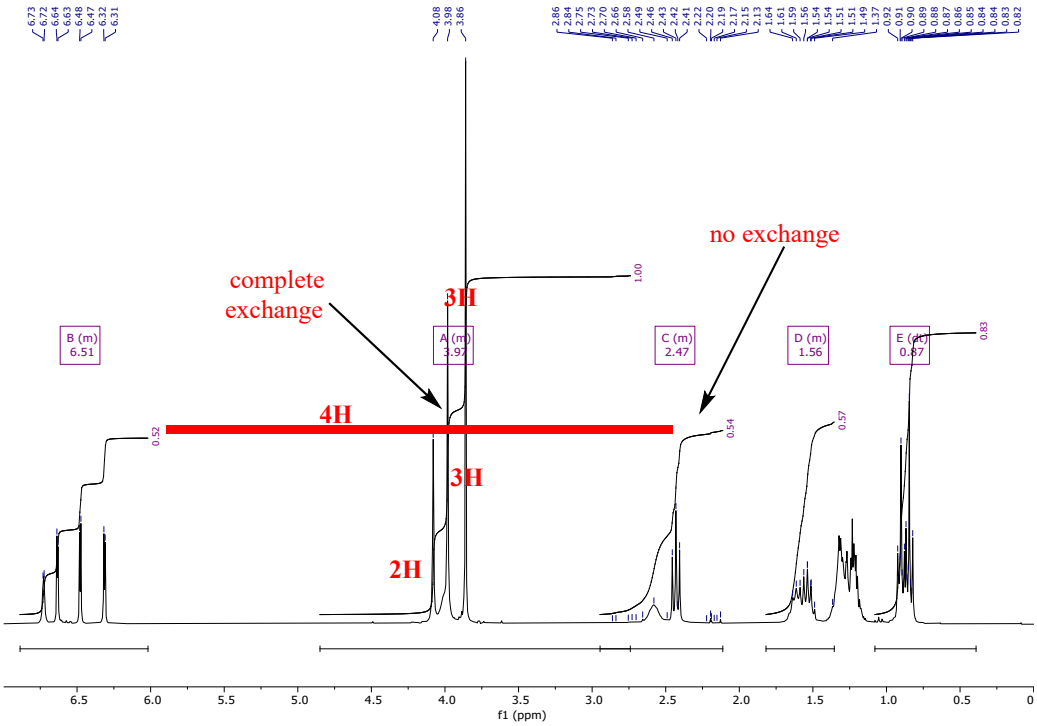
Compound **13'**


168.8
164.4
162.5
140.4
107.4
107.1
101.9
101.8
50.1
37.3
36.3
17.0
14.2
HO
OH
O
O
C_3H_7
OCH_3
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

Compound **13'**

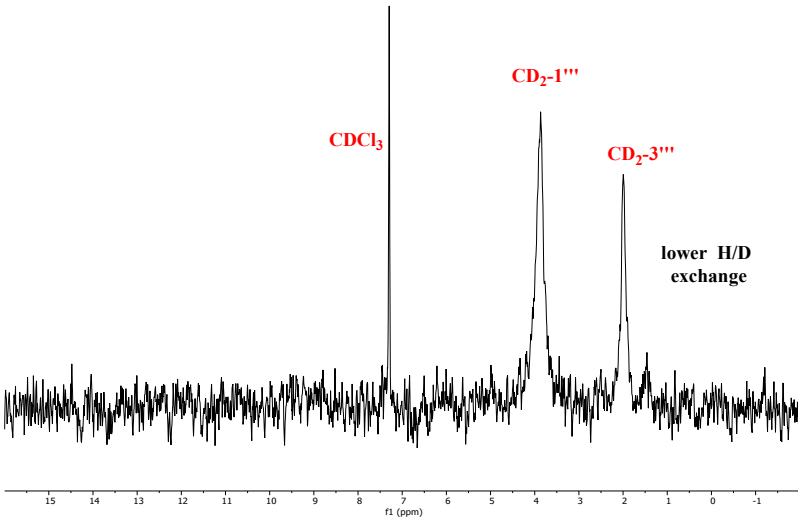
S4. Complementary ^{1}H and ^{2}H NMR for **2** and **6ka**

2‘-*O*-methylmicrophyllinic acid in CD_3COCD_3 (exchange H/D) after 30 min

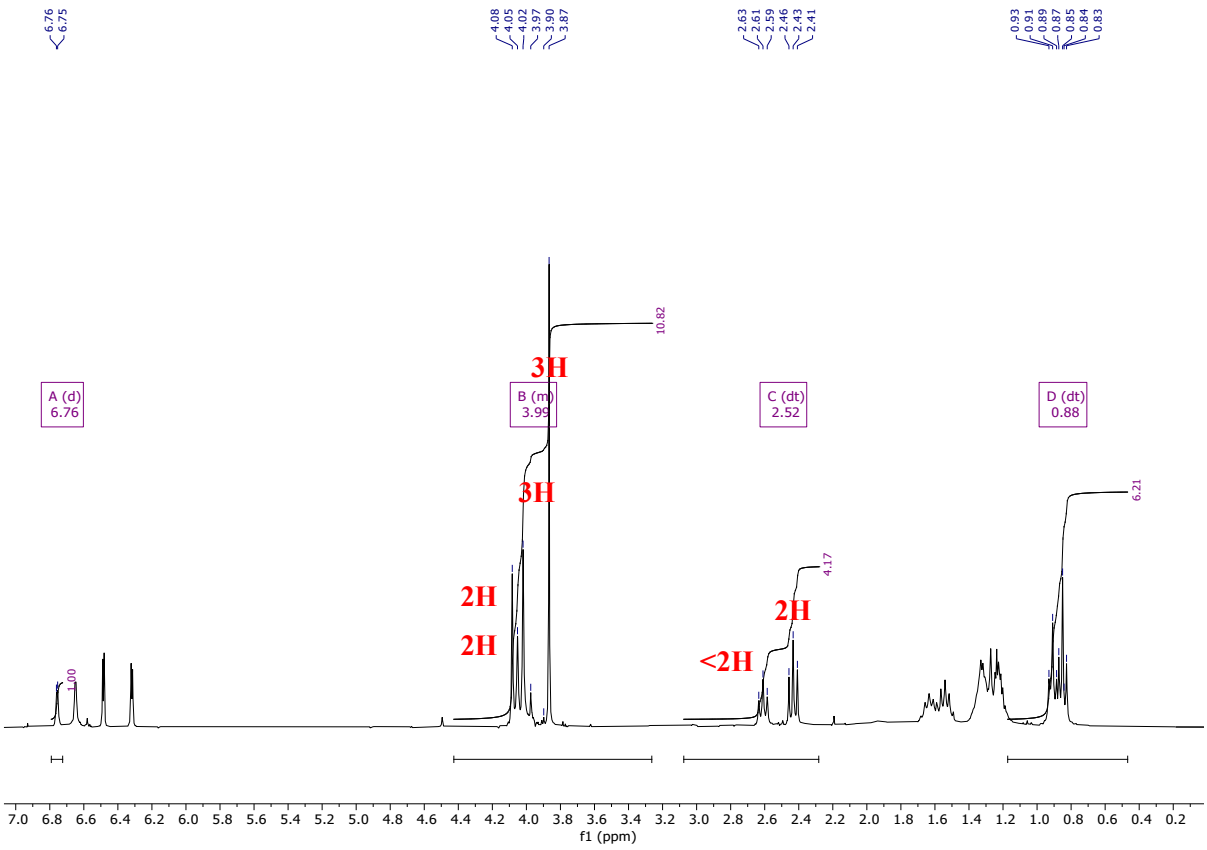


Exchange complete for CH_2-1‘’’ Lower exchange for CH_2-3‘’’

^{2}H NMR confirmation in $CDCl_3$



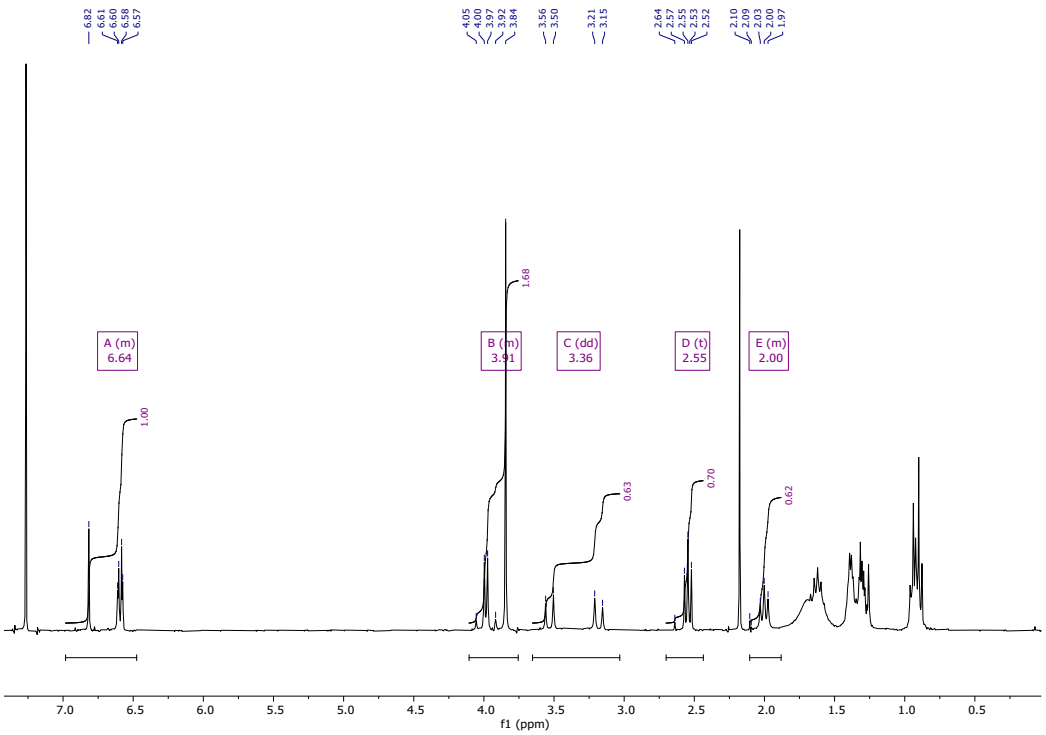
2‘-*O*-mehylmicrophyllinic acid in $CDCl_3$ after evaporation, dissolution in acetone (inverse exchange D/H) evaporation and NMR in $CDCl_3$



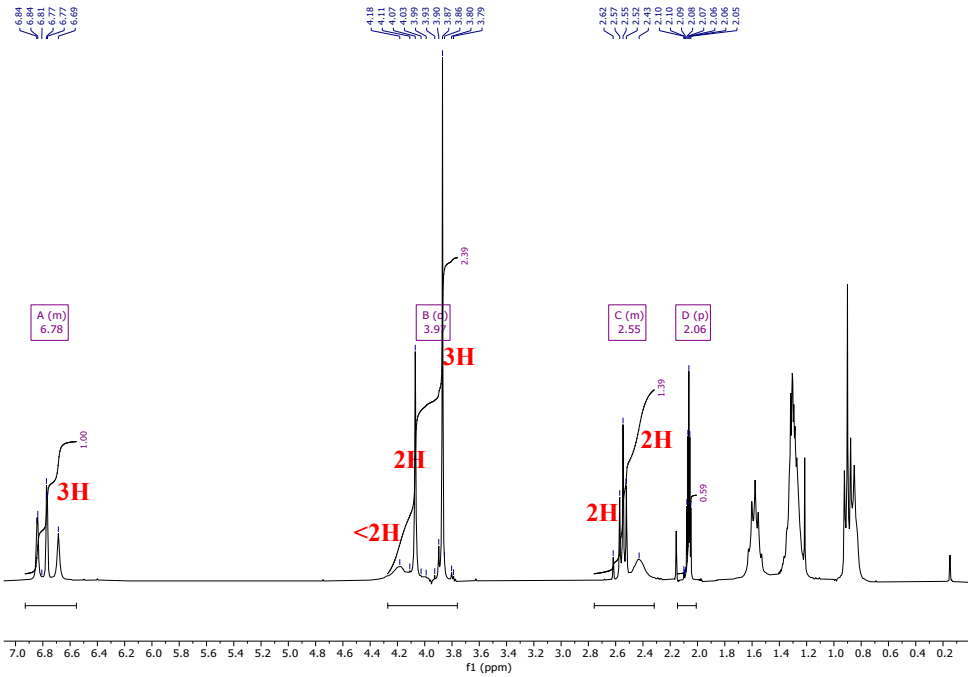
Inverse exchange: complete for CH_2-1’’’ and lower for CH_2-3’’’

The exchange is slow explaining the forms of the signal and the integration values.

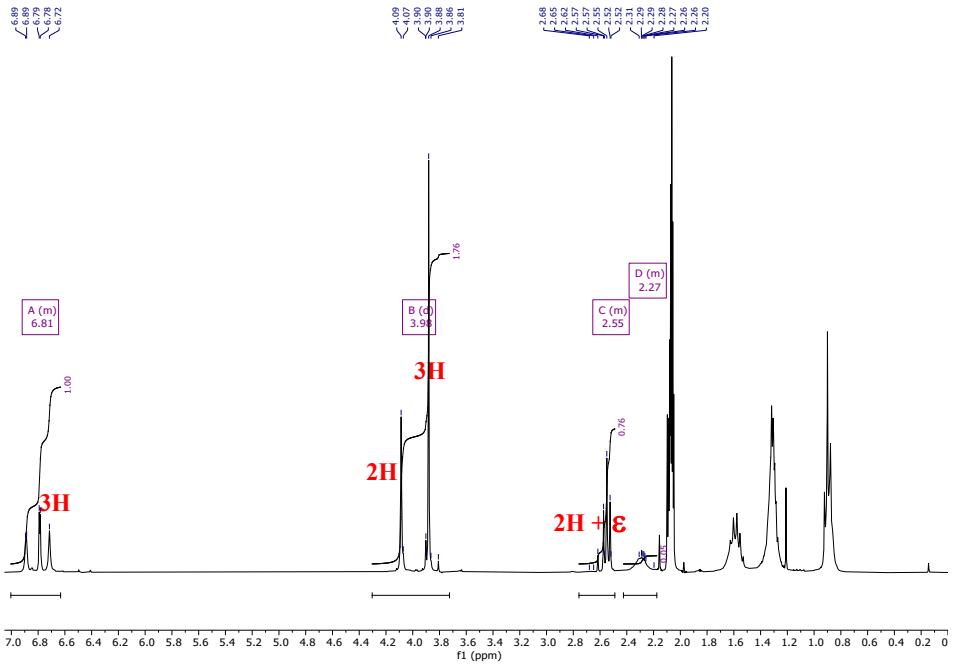
α-collatolic acid ($CDCl_3$)



α-isocollatolic acid (*d6*-acetone)

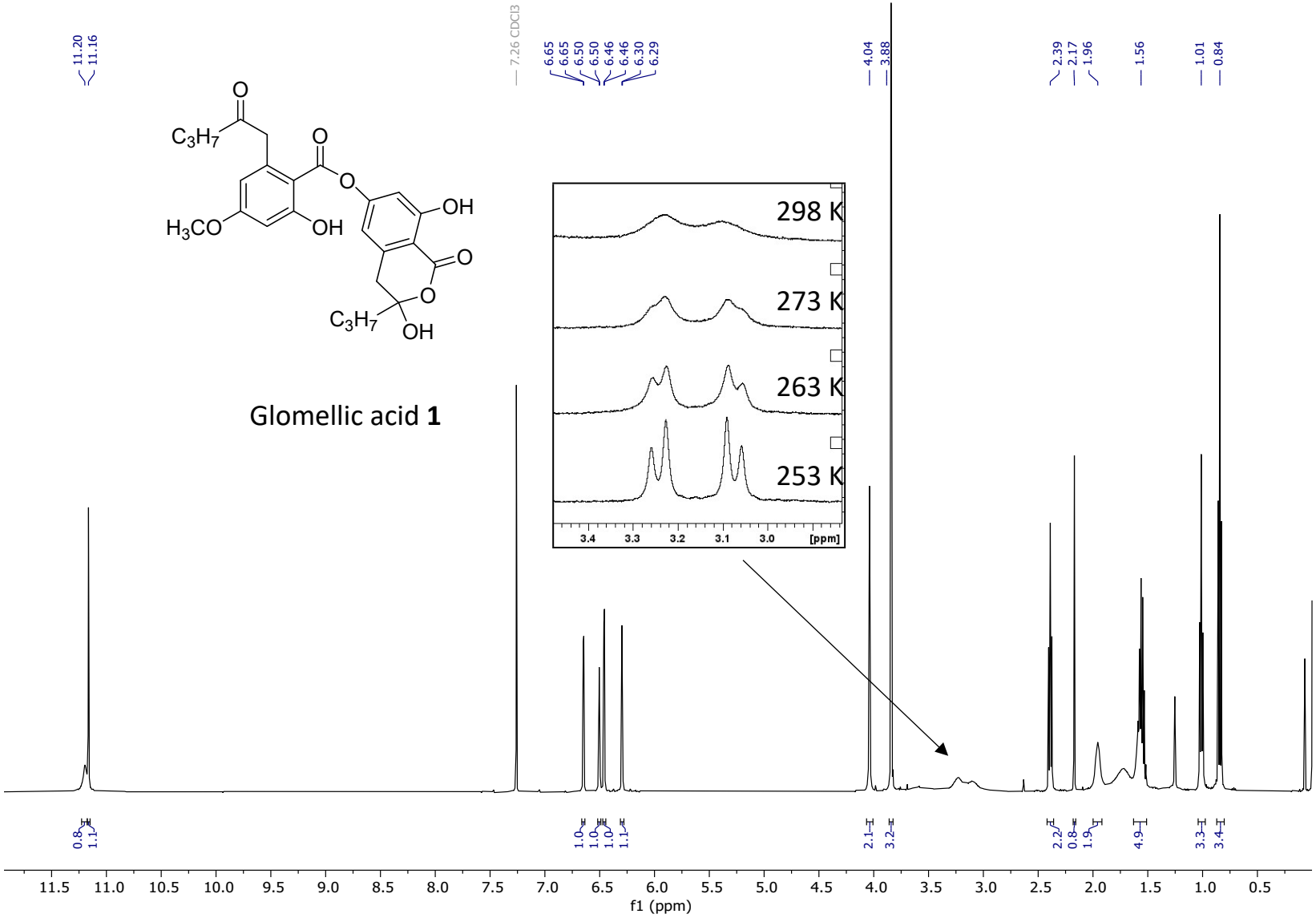


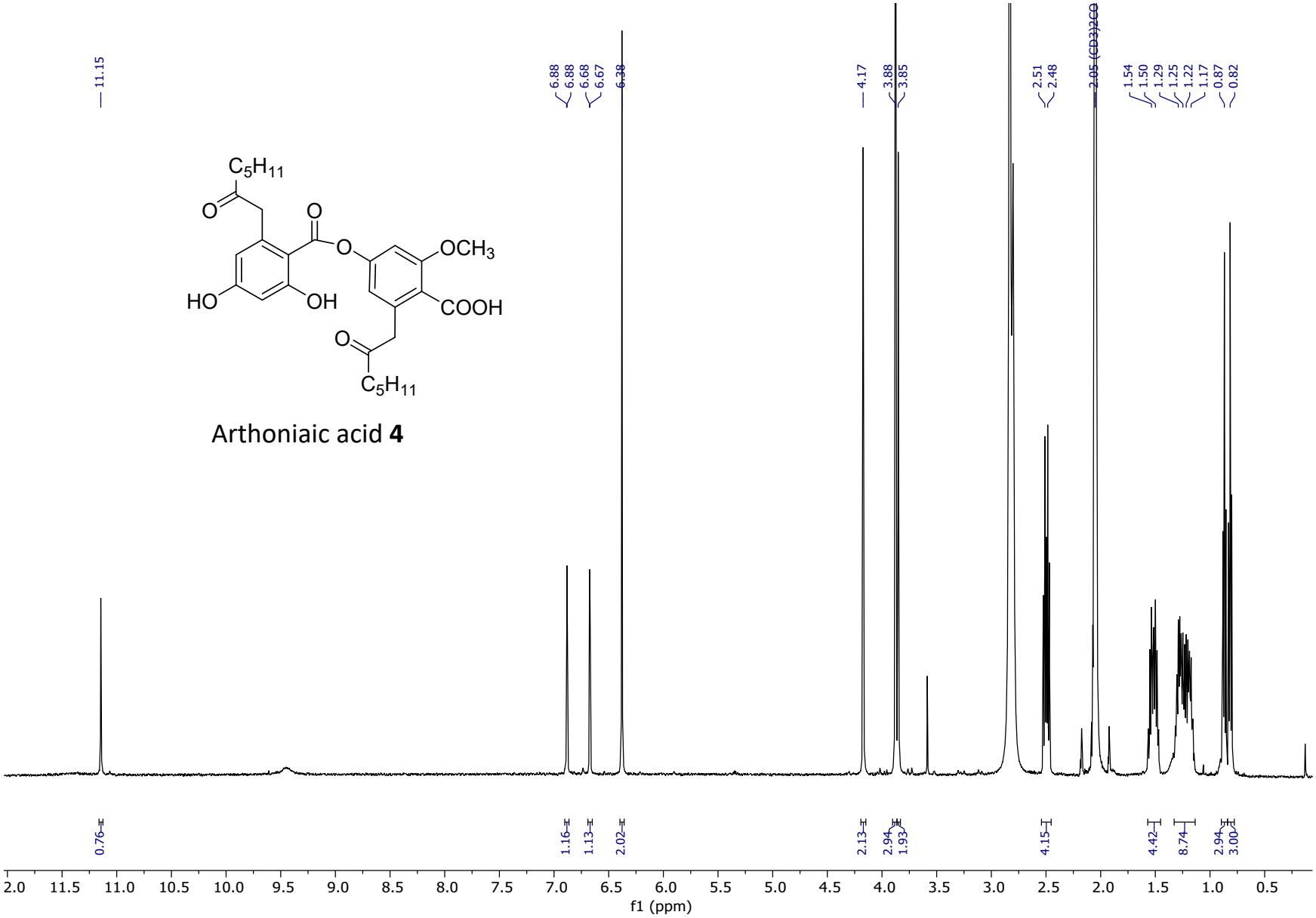
^{1}H NMR data just after dissolution: partial H/D exchange and coalescence.



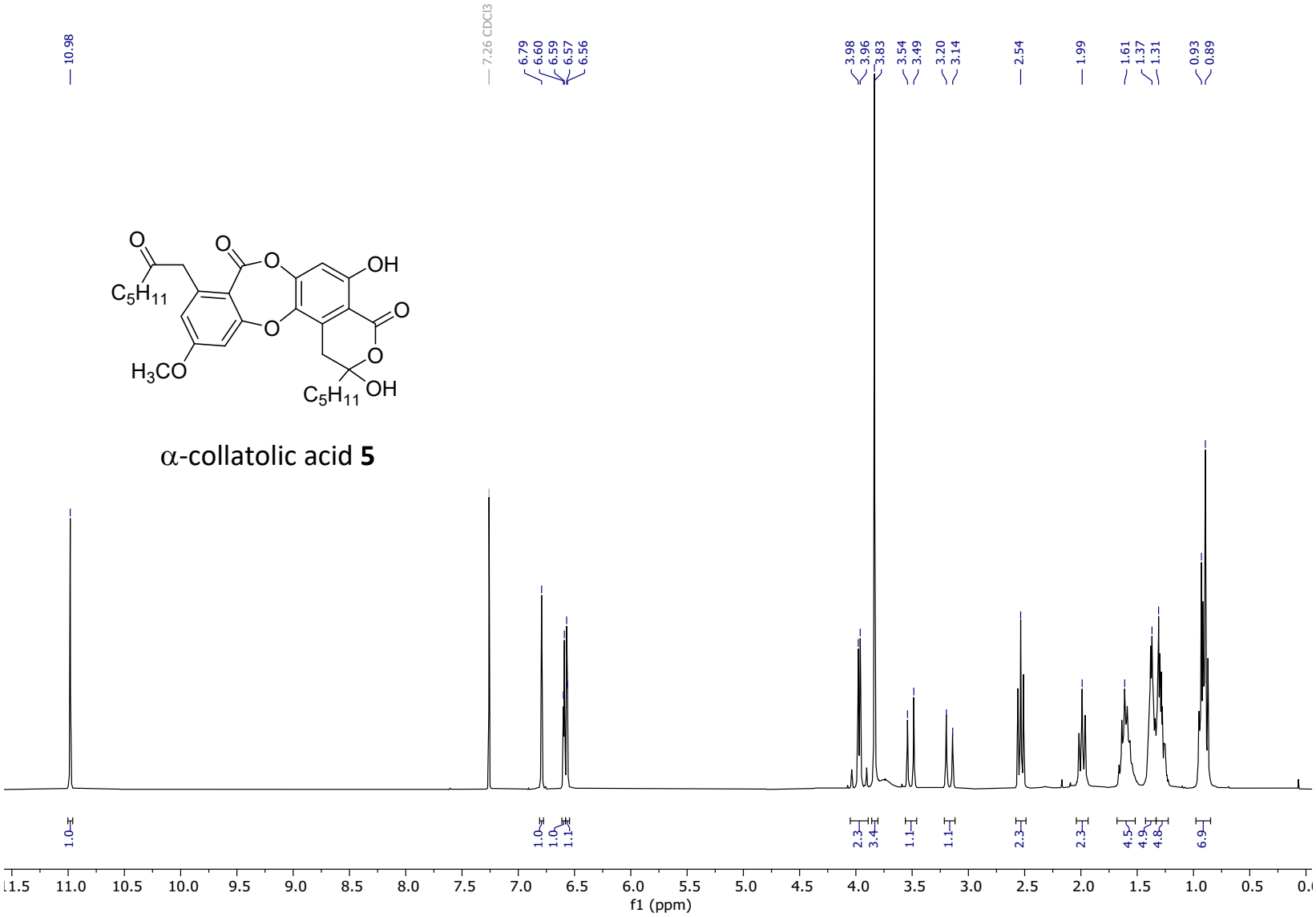
^{1}H NMR data after 3 days: complete H/D exchange.

S5. NMR spectra of compounds previously reported[1–3] : **1**, **4**, **5**, **6**, **7** and of physodic acid and physodone

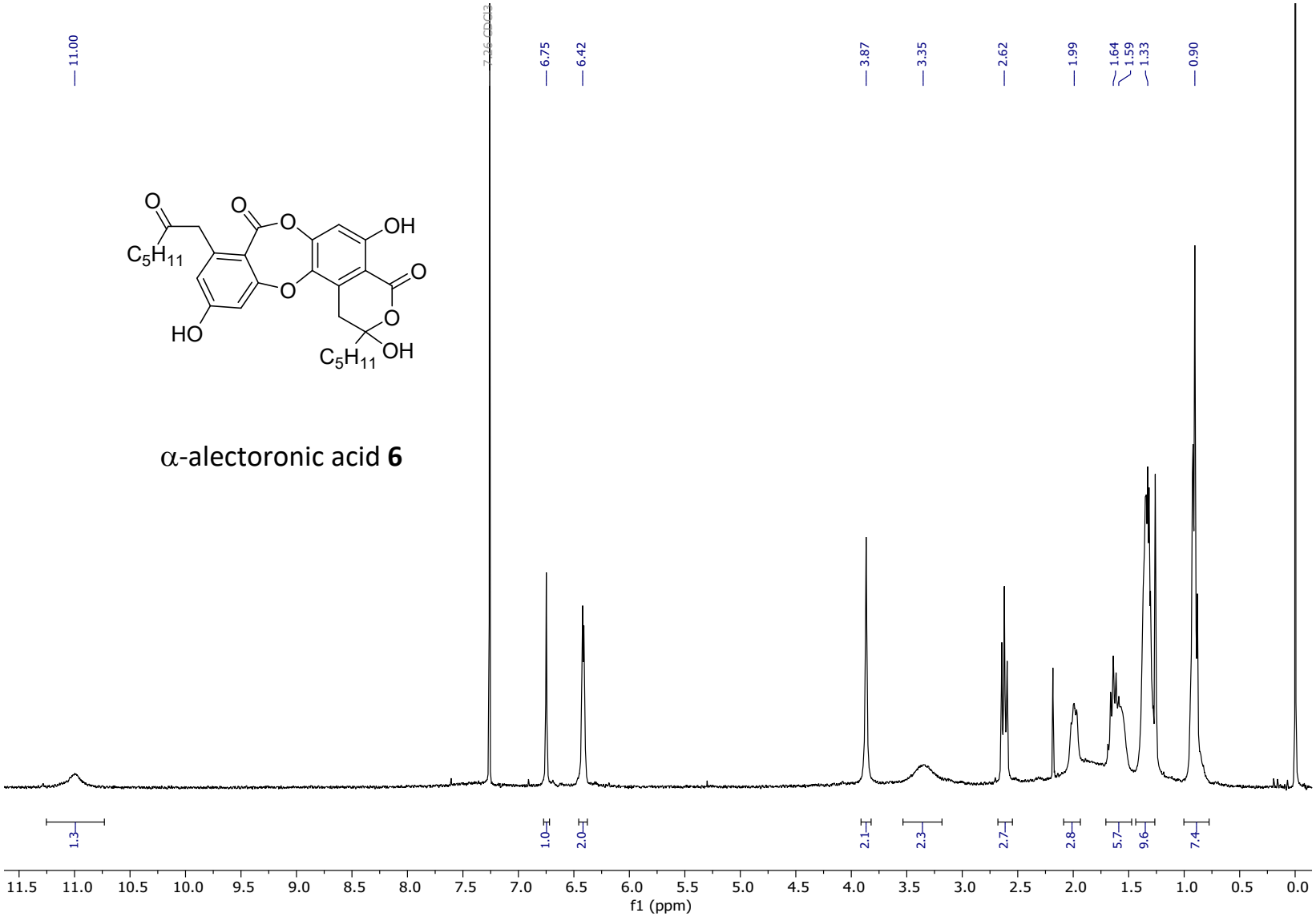




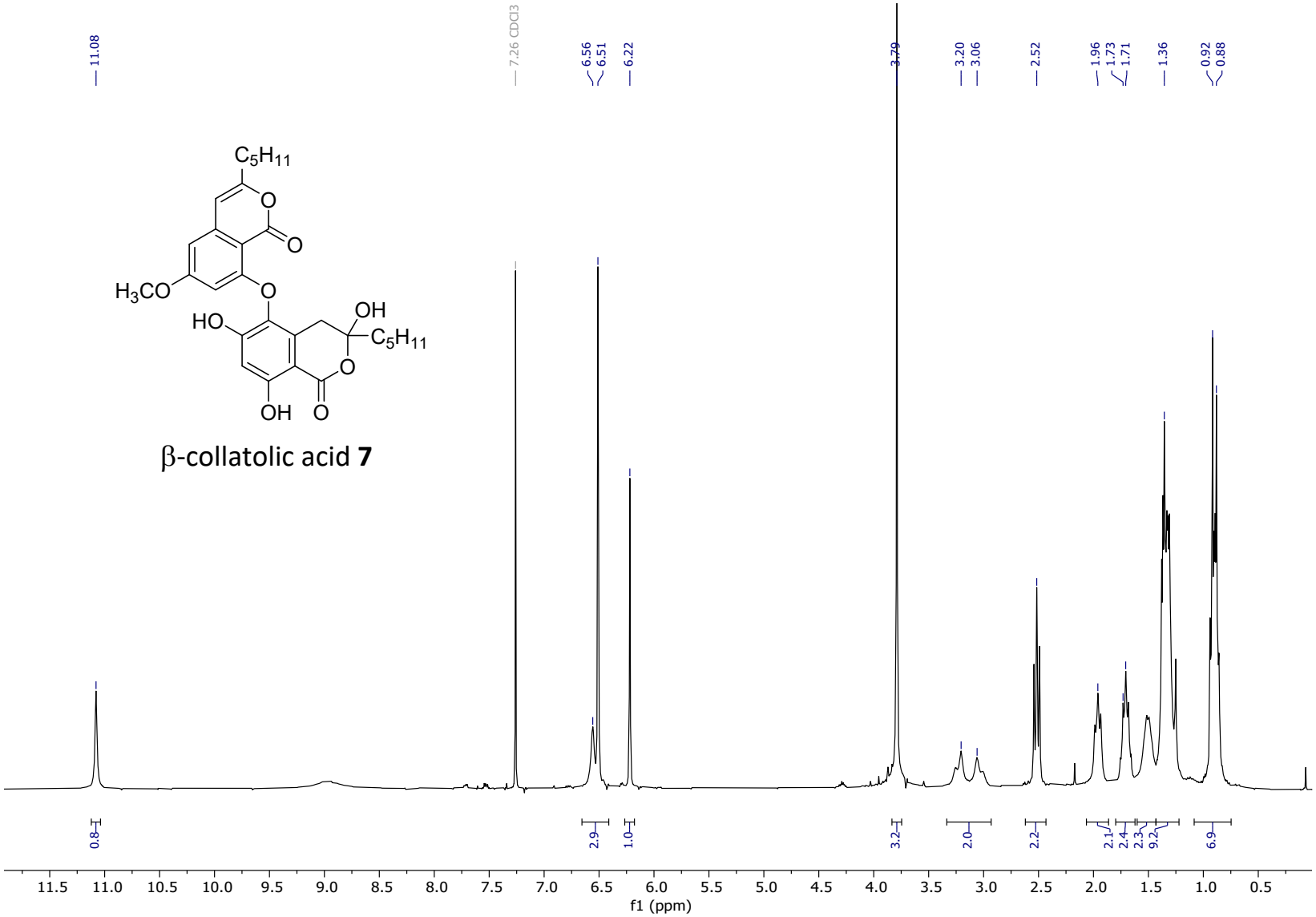
Arthoniaic acid **4**



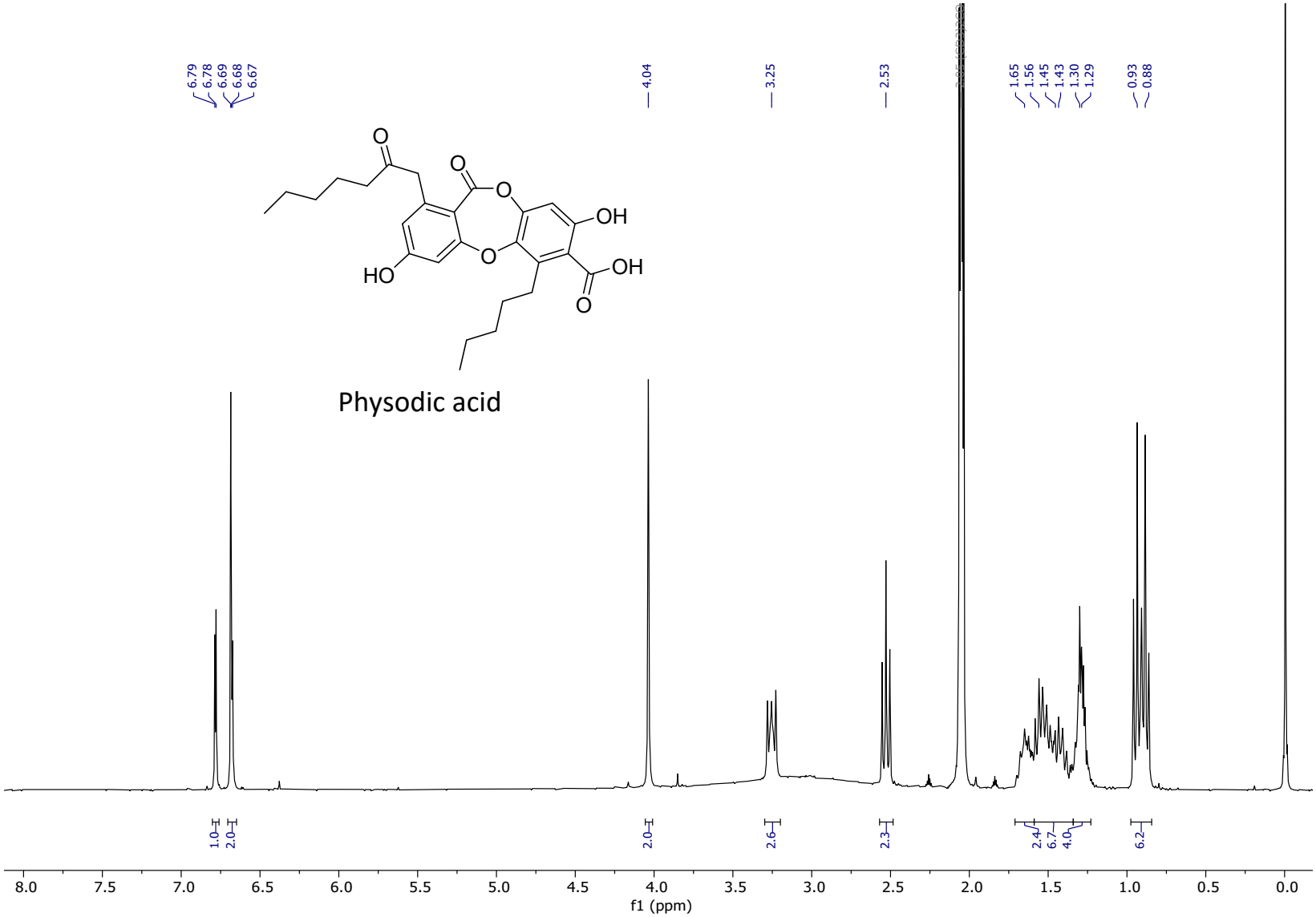
α-collatolic acid **5**



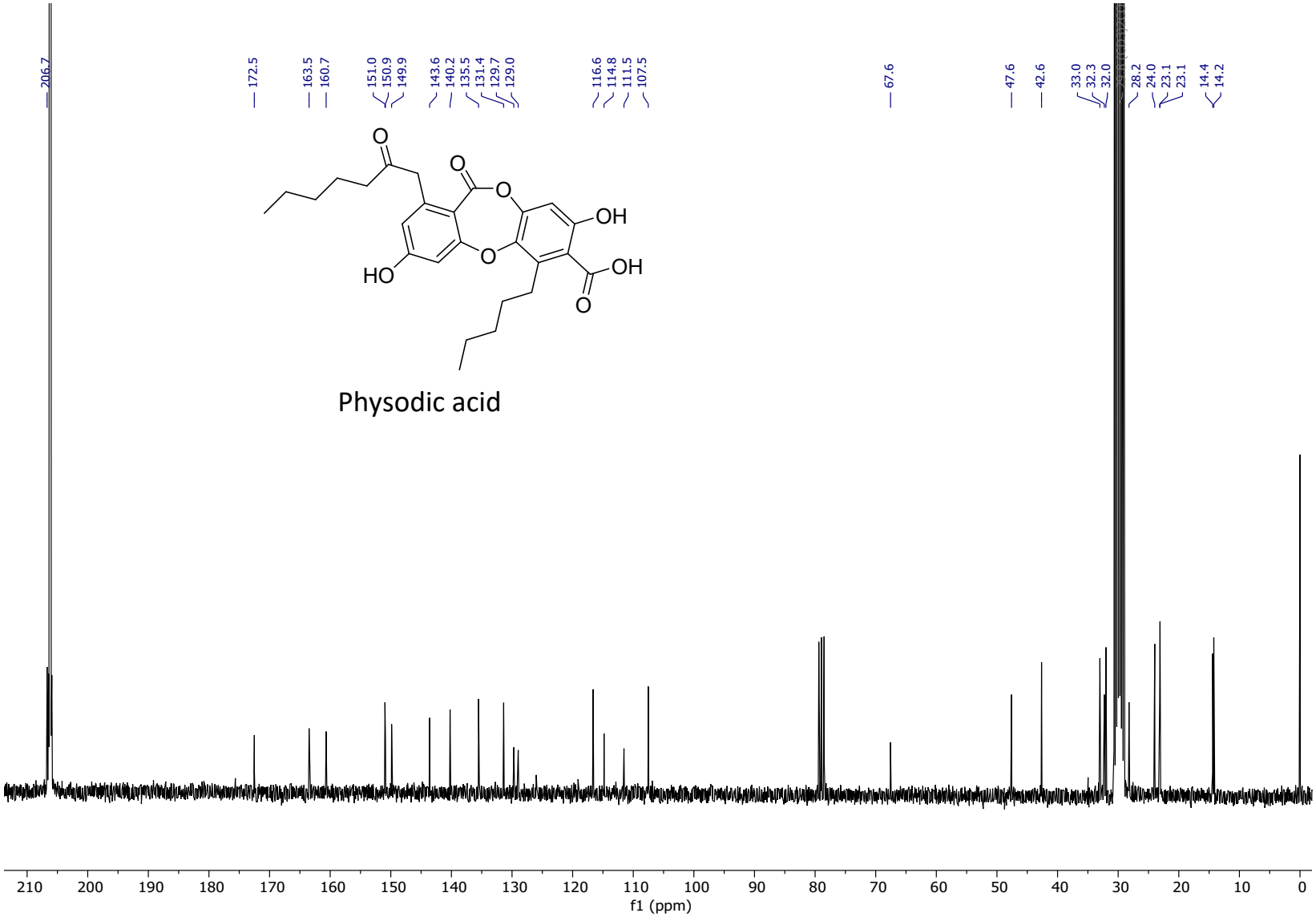
α-alectoronic acid **6**



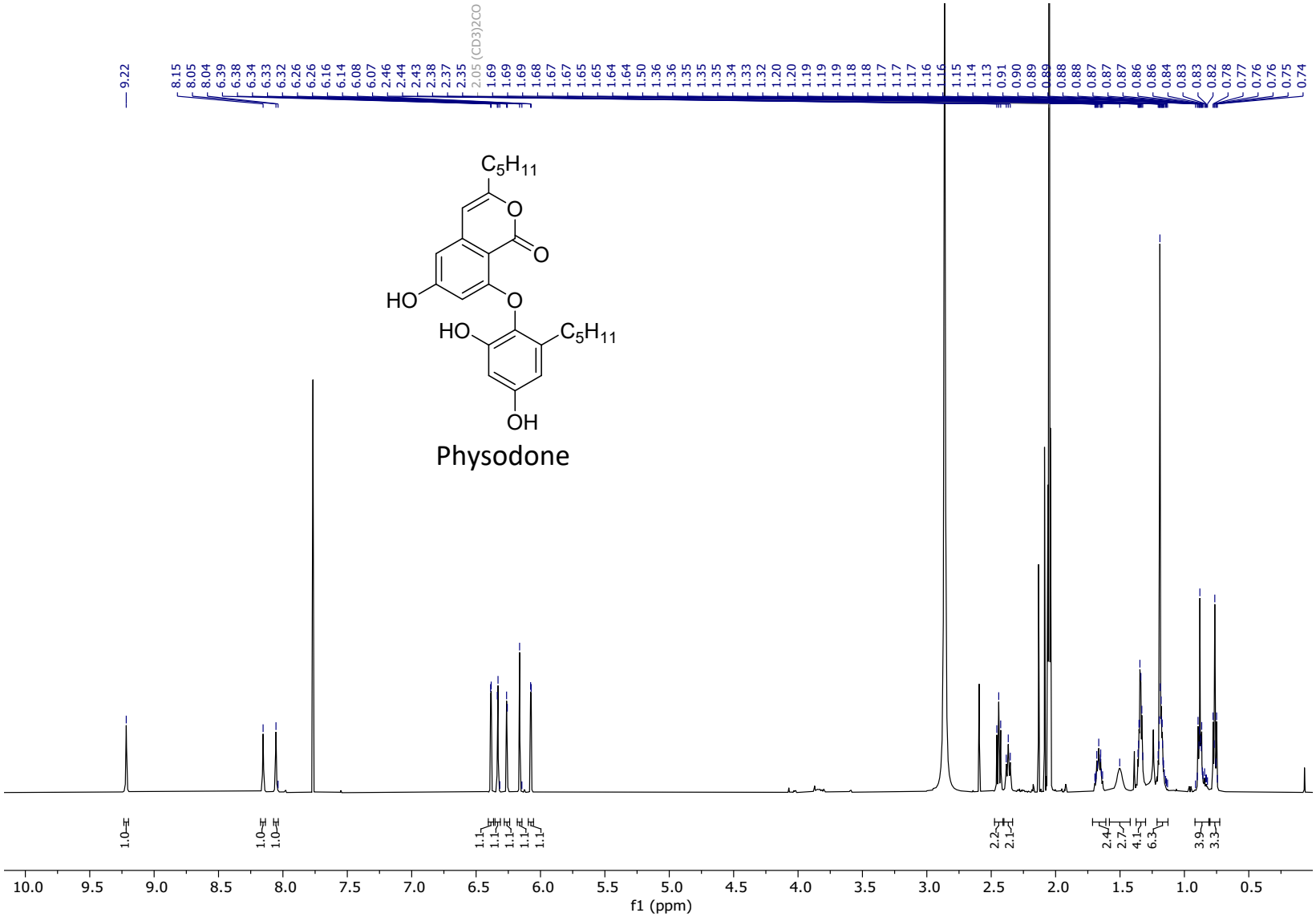
β-collatolic acid **7**



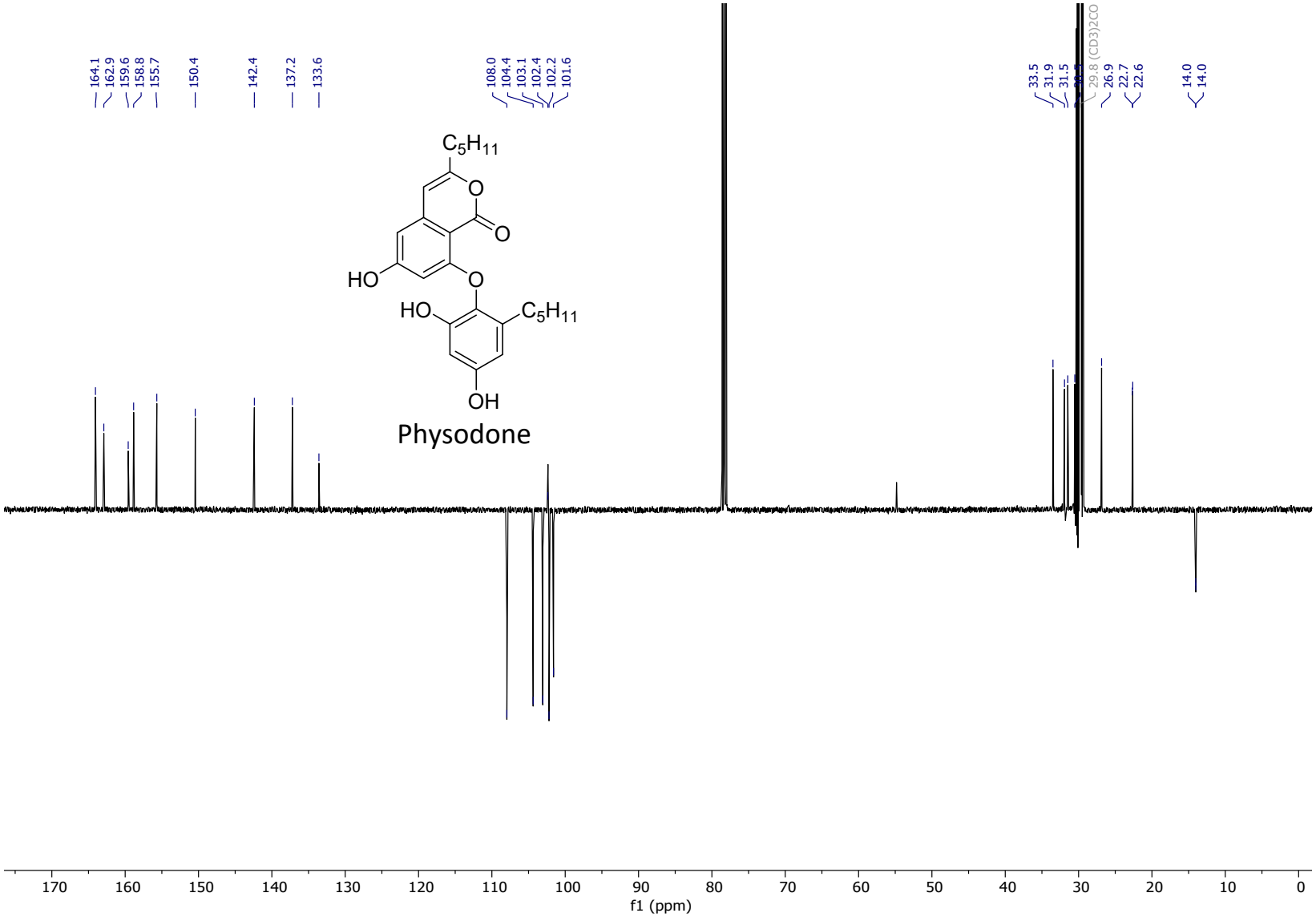
Physodic acid



Physodic acid

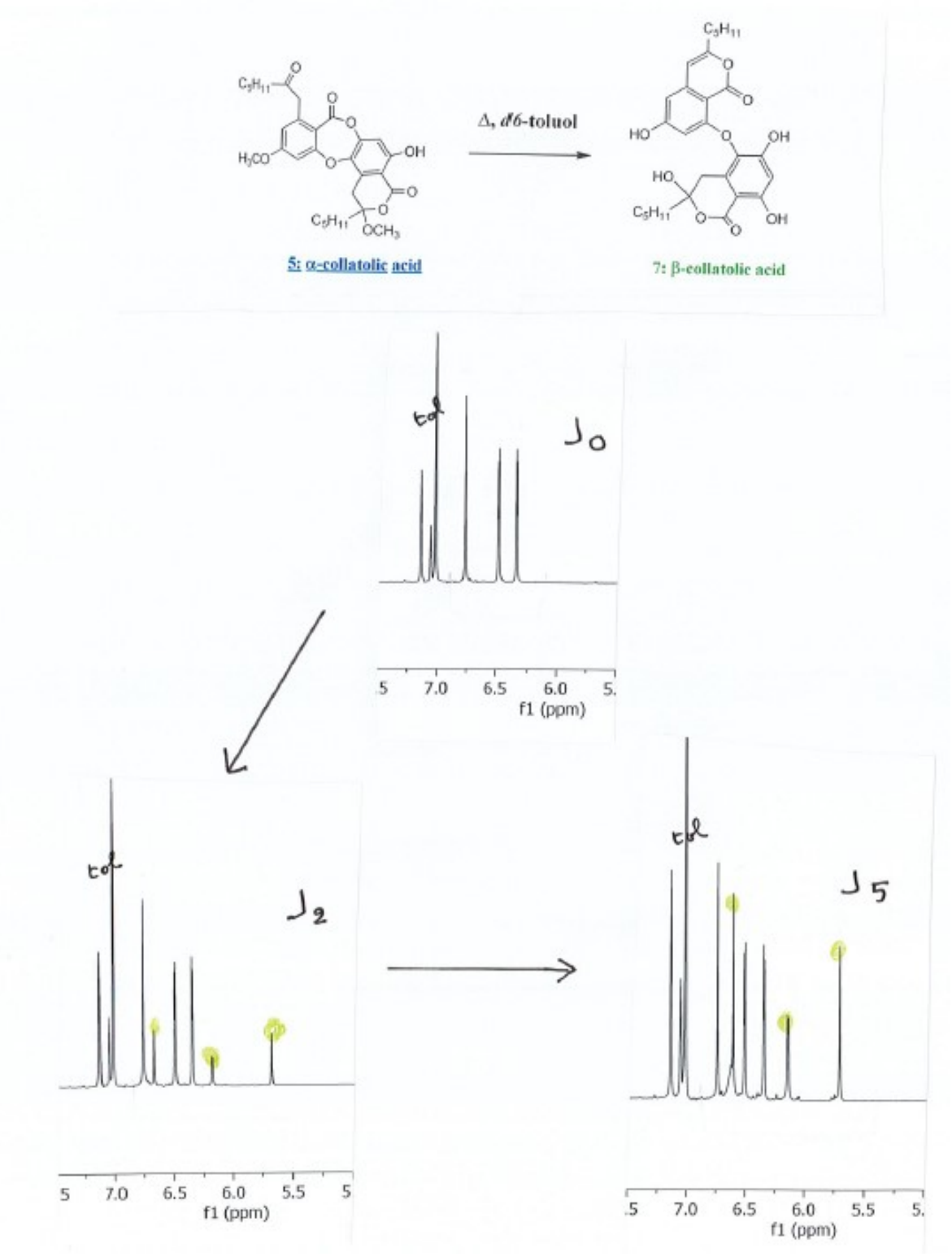

9.22
8.15 8.05 8.04 6.39 6.38 6.34 6.33 6.32 6.26 6.26 6.16 6.14 6.08 6.07 2.46 2.44 2.43 2.38 2.37 2.35
2.05 (CD3)2CO
1.69 1.69 1.69 1.68 1.67 1.67 1.65 1.65 1.64 1.64 1.50 1.36 1.36 1.35 1.35 1.35 1.34 1.33 1.32 1.20 1.20 1.19 1.19 1.19 1.18 1.18 1.17 1.17 1.17 1.16 1.16 1.15 1.14 1.13 0.91 0.90 0.89 0.89 0.88 0.88 0.87 0.87 0.87 0.86 0.86 0.84 0.83 0.83 0.82 0.78 0.77 0.76 0.76 0.75 0.74
C5H11
O
O
HO
O
HO
C5H11
OH
1.0 1.0 1.0 1.1 1.1 1.1 1.1 1.1 2.2 2.1 2.4 2.7 4.1 6.3 3.9 3.3
10.0 9.5 9.0 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 0.5
f1 (ppm)

Physodone

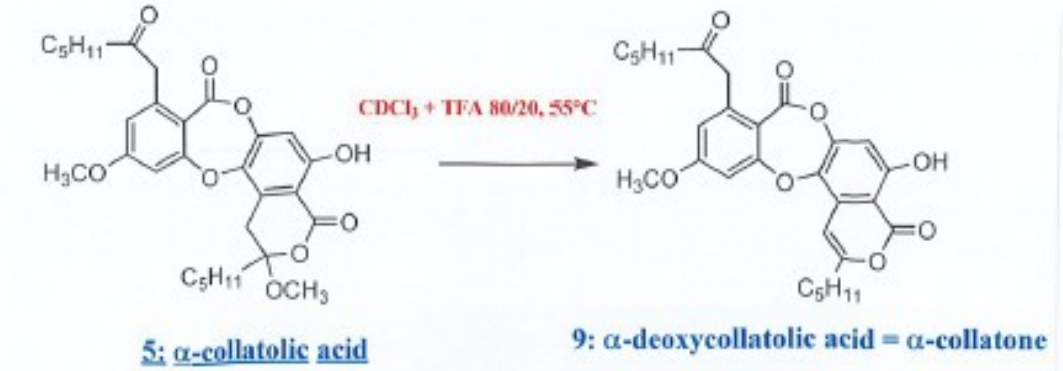

164.1
162.9
159.6
158.8
155.7
150.4
142.4
137.2
133.6
108.0
104.4
103.1
102.4
102.2
101.6
33.5
31.9
31.5
29.8 (CD3)2CO
26.9
22.7
22.6
14.0
14.0
C5H11
O
O
HO
O
HO
C5H11
OH
Physodone
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

S6. Example of reaction checking by ^{1}H NMR and keto-enol study

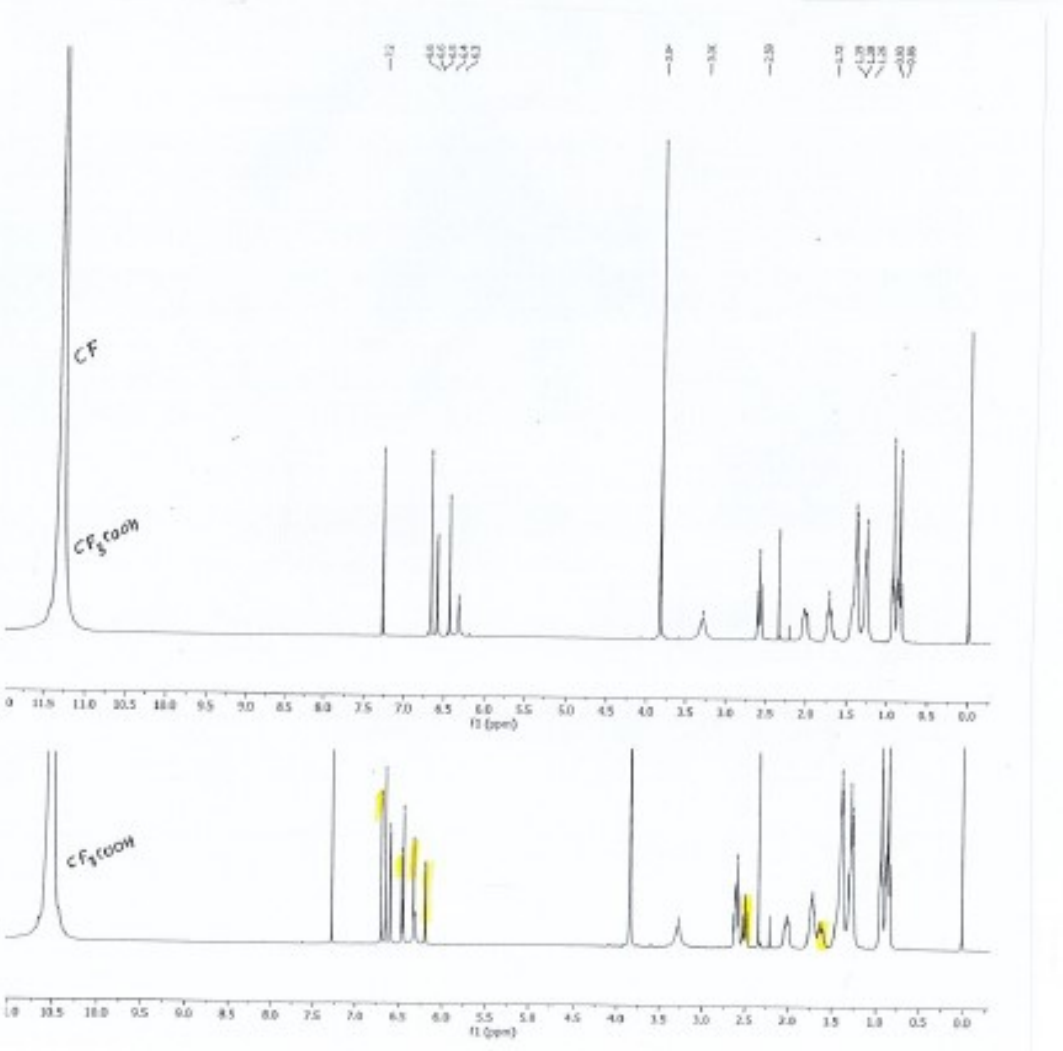
Isomerization of α-collatolic acid 5 into β-collatolic acid 7. Aromatic hydrogen atoms.



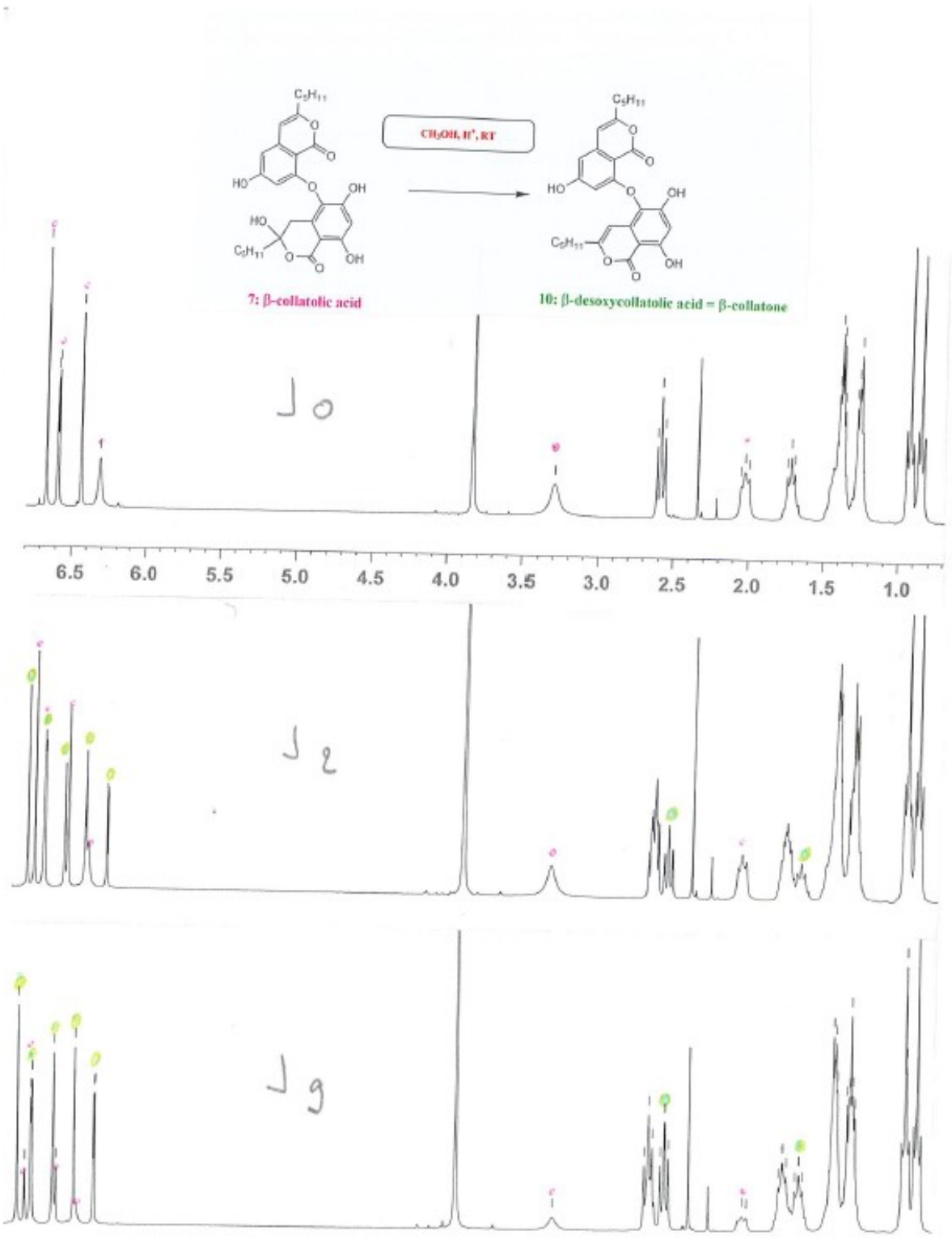
Dehydration of α-collatolic acid 5 into α-collatone 8.



5: α-collatolic acid **9: α-deoxycollatolic acid = α-collatone**



Dehydration of β-collatolic acid 7 into β-collatone 9.



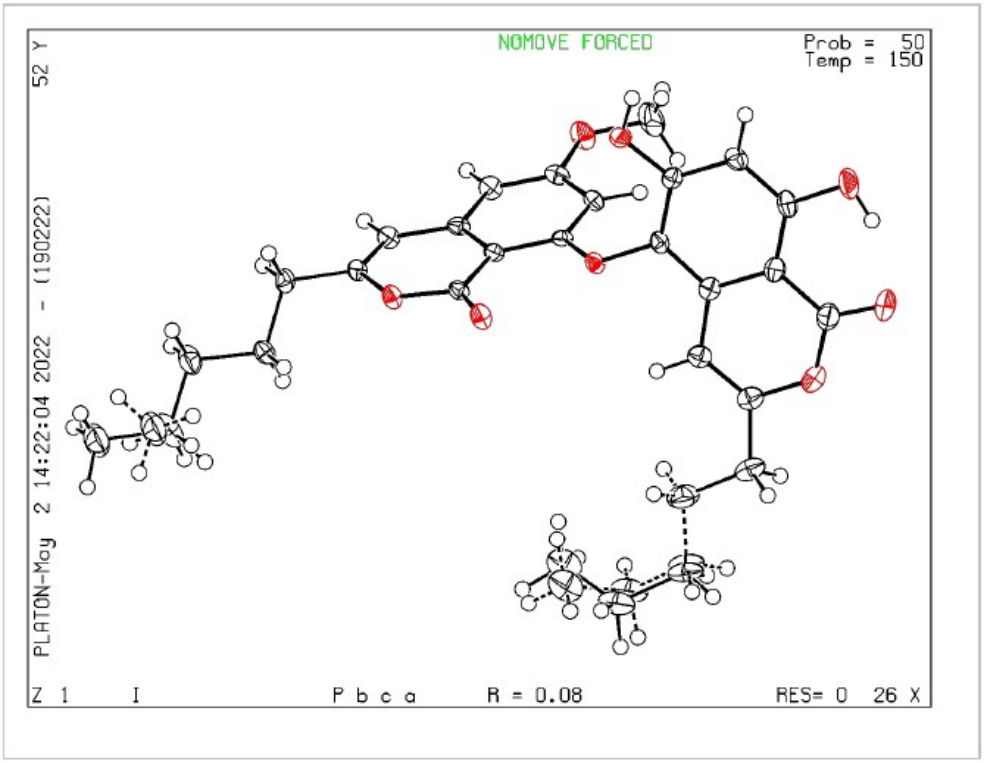
S7. Crystal structure report for β-collatone **9**

($C_{29}H_{32}O_8$); M = 508.54.

A suitable crystal for X-ray diffraction single crystal experiment (colourless plate, dimensions = 0.280 x 0.230 x 0.060 mm) was selected and mounted on the goniometer head of a D8 Venture (Bruker-AXS) diffractometer equipped with a CMOS-PHOTON70 detector [*], using Mo-Kα radiation (λ = 0.71073 Å, multilayer monochromator) at T = 150(2) K. Crystal structure has been described in orthorhombic symmetry and P b c a (I.T.#61) centric space group. Cell parameters have been refined as follows: a = 14.8340(12), b = 12.7431(9), c = 27.038(2) Å, V = 5110.9(7) Å3. Number of formula unit Z is equal to 8 and calculated density d and absorption coefficient μ values are 1.322 $g.cm^{-1}$ and 0.096 mm^{-1} respectively. Crystal structure was solved by dual-space algorithm using SHELXT program [1], and then refined with full-matrix least-squares methods based on F2 (SHELXL program [2]). All non-Hydrogen atoms were refined with anisotropic atomic displacement parameters. Except Hydrogen atoms linked to Oxygen atoms that were introduced in the structural model through Fourier difference maps analysis, H atoms were finally included in their calculated positions and treated as riding on their parent atom with constrained thermal parameters. A final refinement on F2 with 5857 unique intensities and 355 parameters converged at ωR(F2) = 0.1704 (RF = 0.0840) for 5062 observed reflections with (I > 2σ).

1. G. M. Sheldrick, Acta Cryst. A71 2015 3-8
2. Sheldrick G.M., Acta Cryst. C71 2015 3-8

Structure visualization



Data collection strategy details

```
Software                    : BIS V6.2.15/2021-03-15 && APEX4 2021.10-0
Number of scans             :        3
Total number of frames [*]  :      302
Total length of scans  [*]  :   151.00 (deg.)
Rotation speed         [*]  :  ?
Total exposition time  [*]  :      1 h  40.7 min.

 [*] fast scan not included
```

Scan	Time(s)	Width	DX(mm)	Frames	Range	2Theta	Omega	Phi	Chi	T(K)
1 Fast	4.0	1.00	34.0	180	180.0	0.0	0.0	0.0	54.7	150.0
2 Phi	20.0	0.50	34.0	302	151.0	0.1	270.3	176.5	24.0	150.0

Structural data

... Crystal data ...

Empirical formula	$C_{29}H_{32}O_8$
Formula weight	508.54 g/mol
Temperature	150(2) K
Radiation type	Mo-Kα
Wavelength	0.71073 Å
Crystal system, space group	orthorhombic, P b c a (I.T.#61)
Unit cell dimensions	a = 14.8340(12) Å
	b = 12.7431(9) Å
	c = 27.038(2) Å
	α = 90 °
	β = 90 °
	γ = 90 °
Volume	5110.9(7) $Å^3$
Z, Calculated density	8, 1.322 $g.cm^{-3}$
Absorption coefficient	0.096 mm^{-1}
F(000)	2160
Crystal size	0.280 x 0.230 x 0.060 mm
Crystal color	colourless
Crystal description	plate

... Data collection ...

Diffractometer	D8 Venture (Bruker-AXS)
Detector	CMOS-PHOTON70
θ range for data collection	2.590 to 27.503°
$(\sin\theta/\lambda)_{max}$ $Å^{-1}$	0.650
h_{min}, h_{max}	-16, 19
k_{min}, k_{max}	-16, 16
l_{min}, l_{max}	-35, 34
Reflections collected / unique	27684 / 5857 [[a]R(int) = 0.0529]
Reflections [$I > 2\sigma$]	5062
Completeness to θ_{max}	0.997
Absorption correction type	multi-scan
Max. and min. transmission	0.994, 0.852

... Refinement ...

Refinement method	Full-matrix least-squares on F^2
H-atom treatment	H-atom parameters treated by a mixture of independant and constrainted refinement
Data / restraints / parameters	5857 / 2 / 355
[b]Goodness-of-fit	1.275
Shelxl weighting scheme parameters	a = 0.0479, b = 6.3571
Final R indices [($I > 2\sigma$]	[c]R_1 = 0.0840, [d]wR_2 = 0.1704
Final R indices [all data]	[c]R_1 = 0.0959, [d]wR_2 = 0.1758
$\Delta\rho_{max}$, $\Delta\rho_{min}$	0.496, -0.341 $\overline{e}.Å^{-3}$

[a] $R_{int} = \frac{\sum|F_o^2 - \langle F_o^2\rangle|}{\sum F_o^2}$

[b] $S = \left\{\frac{\sum[w(F_o^2 - F_c^2)^2]}{n-p}\right\}^{1/2}$

[c] $R_1 = \frac{\sum||F_o| - |F_c||}{\sum|F_o|}$

[d] $wR_2 = \left\{\frac{\sum[w(F_o^2 - F_c^2)^2]}{\sum[w(F_o^2)^2]}\right\}^{1/2}$

$w = 1./[\sigma(F_o^2) + (aP)^2 + bP]$ with $P = [2F_c^2 + Max(F_o^2, 0)]/3$