Supporting Information

The Mosaic of Rottlerin

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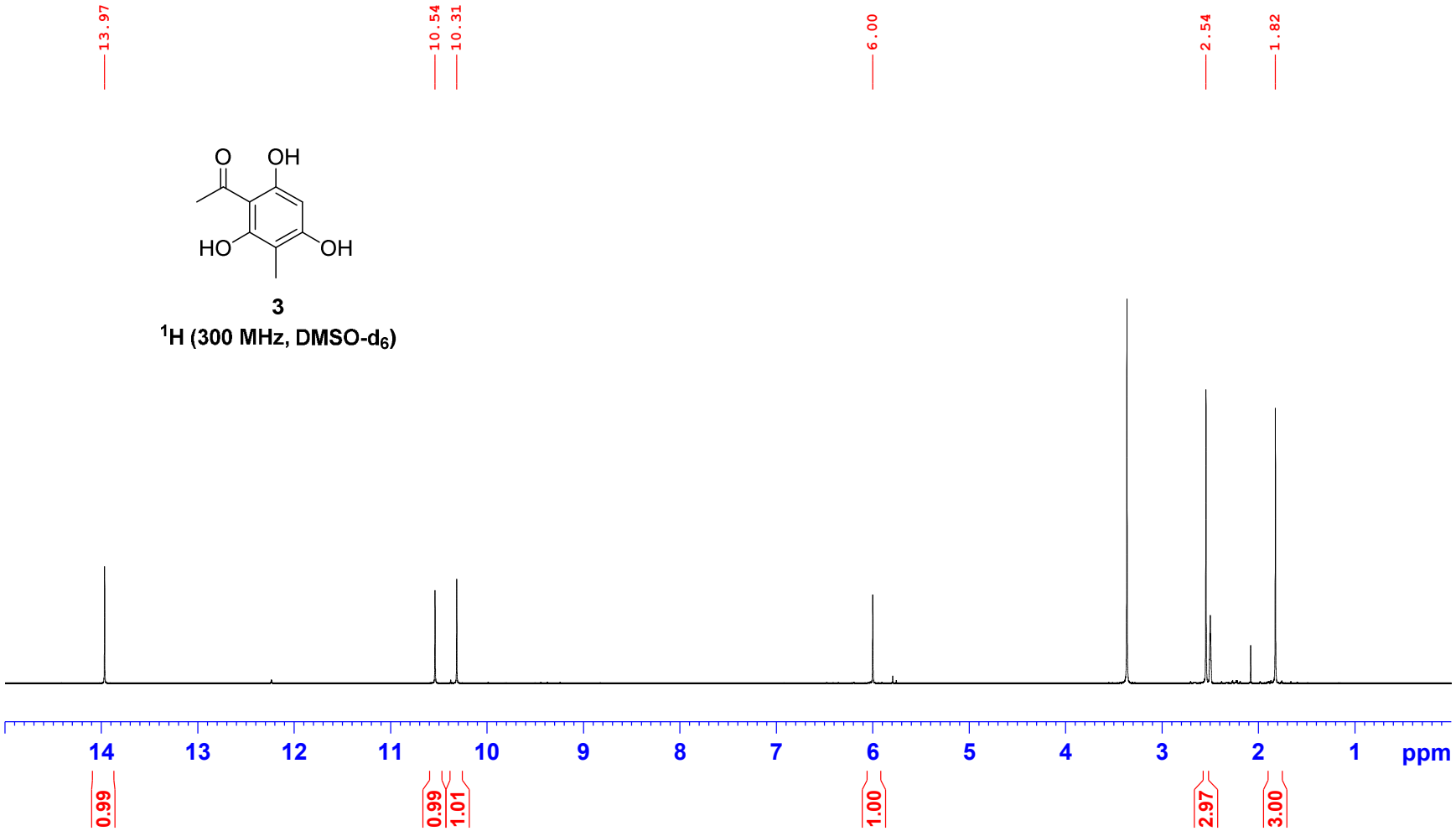
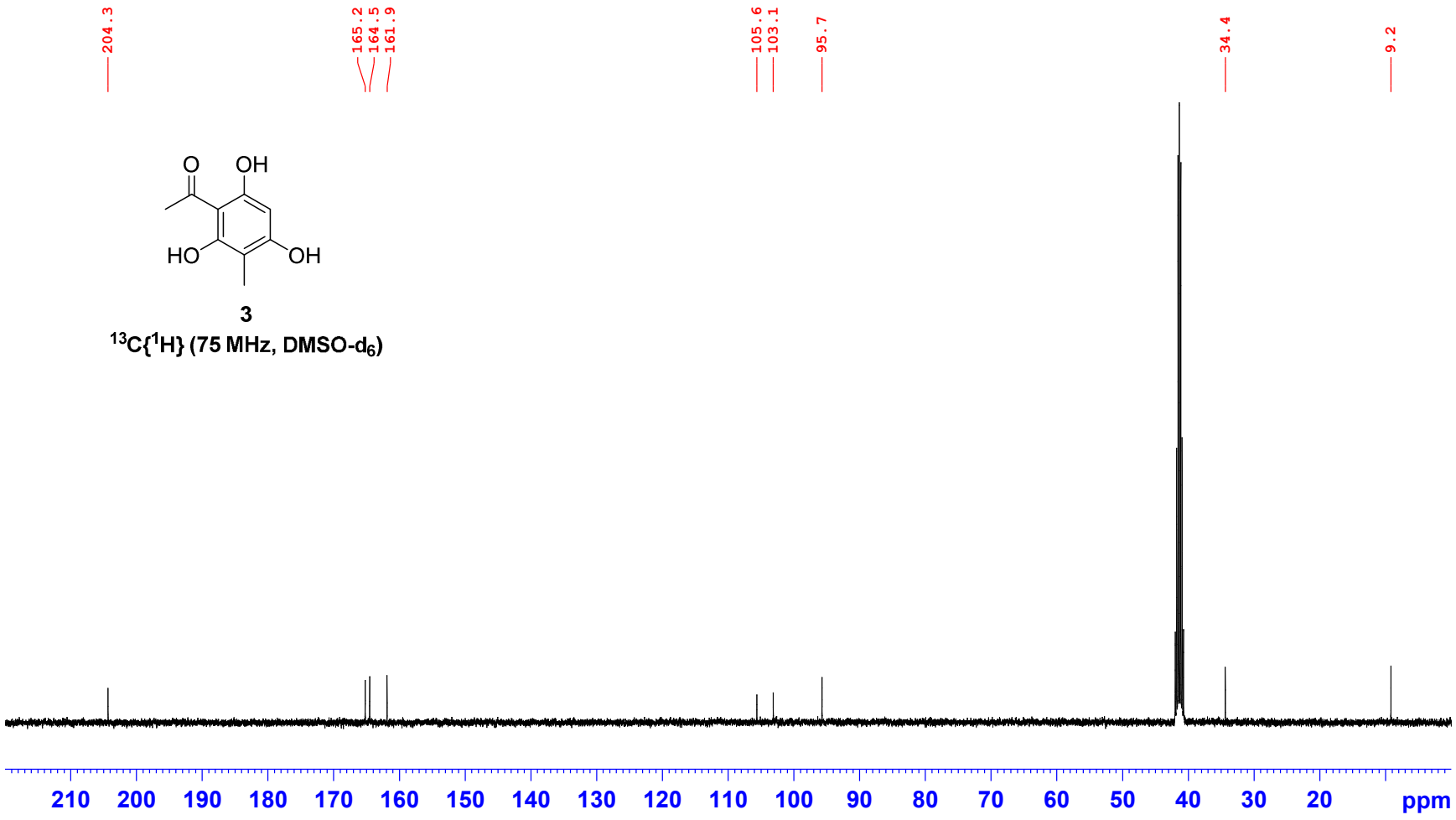
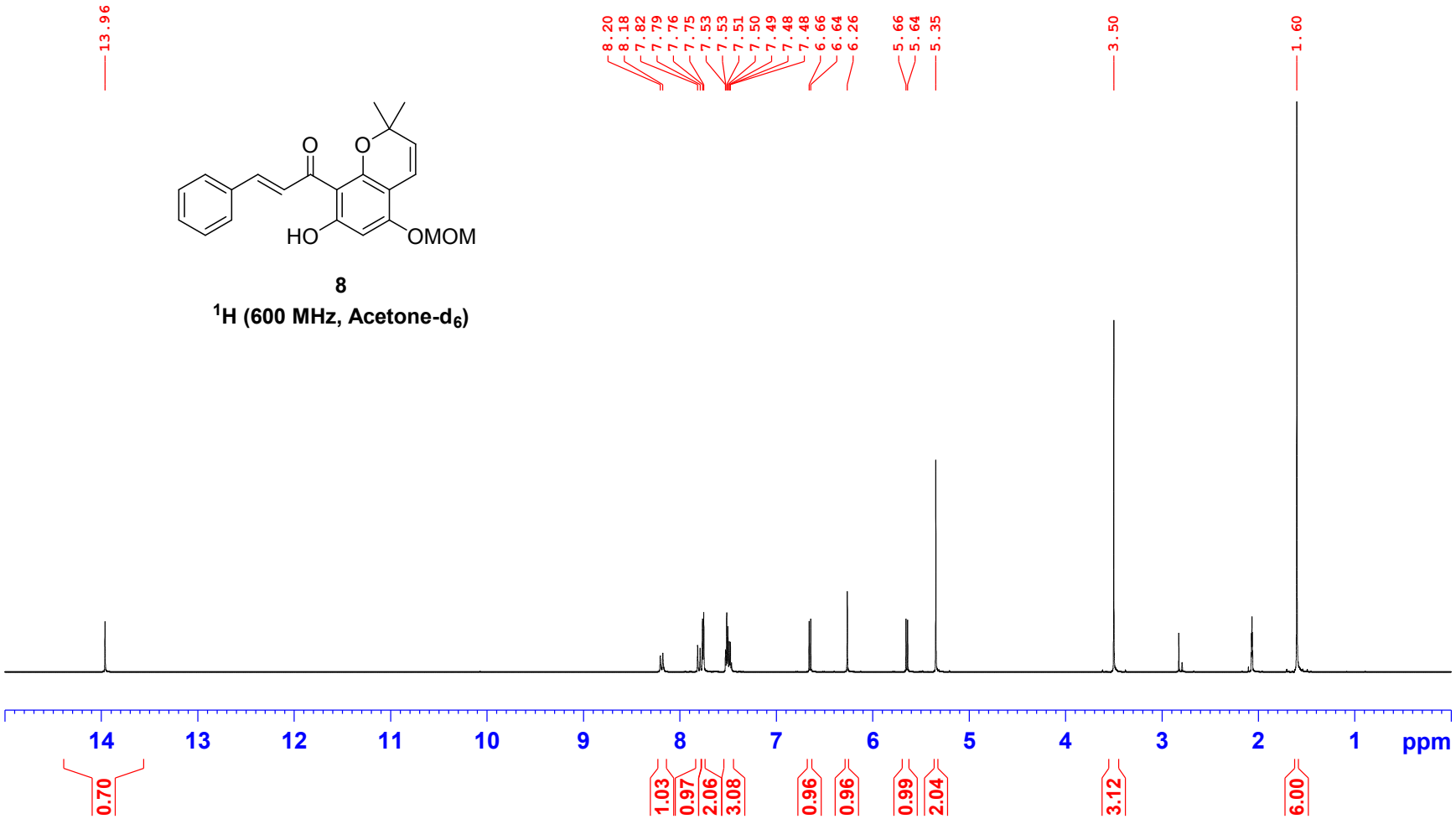
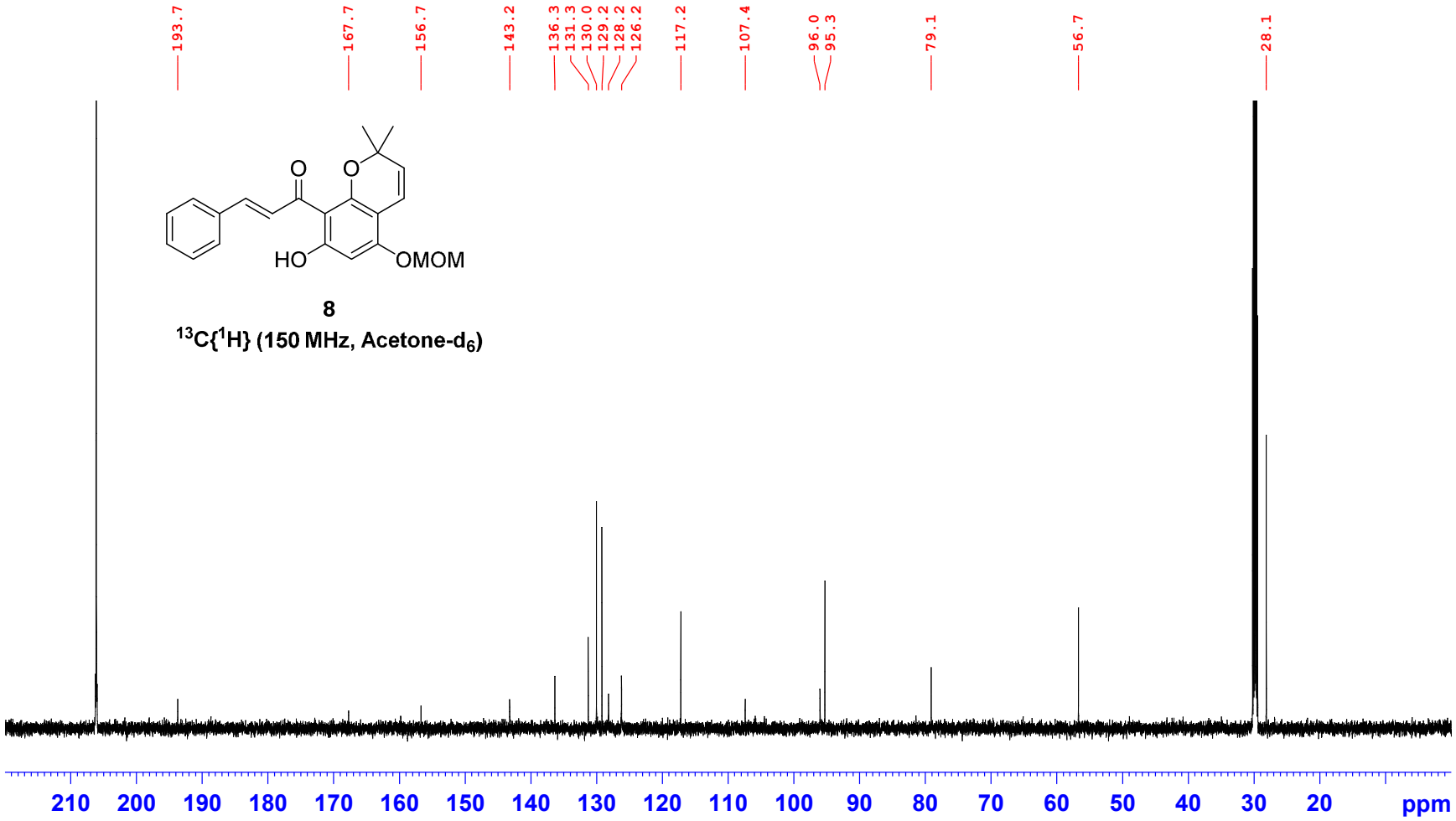

13.97
10.54
10.31
6.00
2.54
1.82
O
OH
HO
OH
3
^{1}H (300 MHz, DMSO-d$_6$)
14
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.99
0.99
1.01
1.00
2.97
3.00

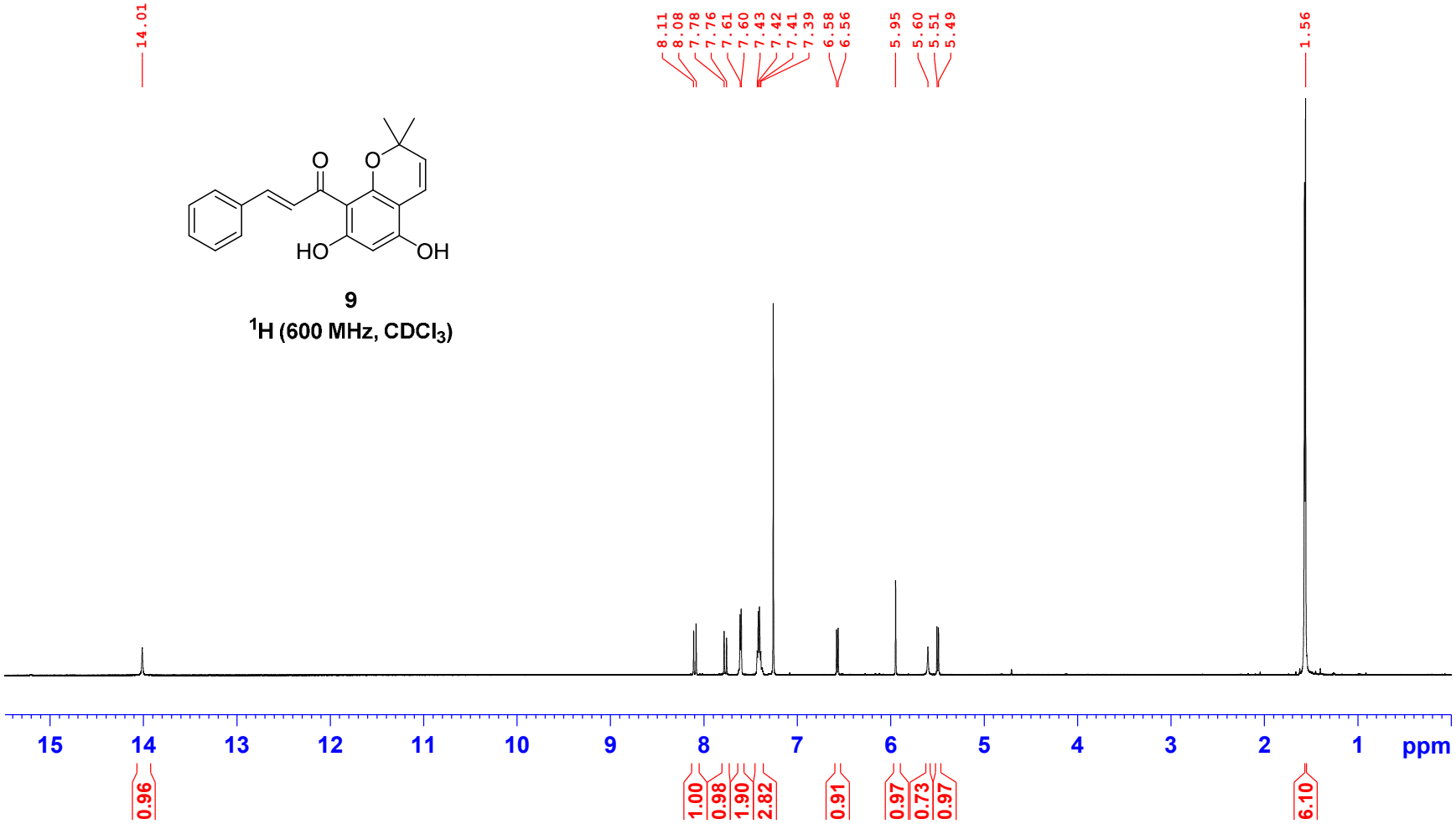

204.3
165.2
164.5
161.9
105.6
103.1
95.7
34.4
9.2
O
OH
HO
OH
3
13C{1H} (75 MHz, DMSO-d6)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

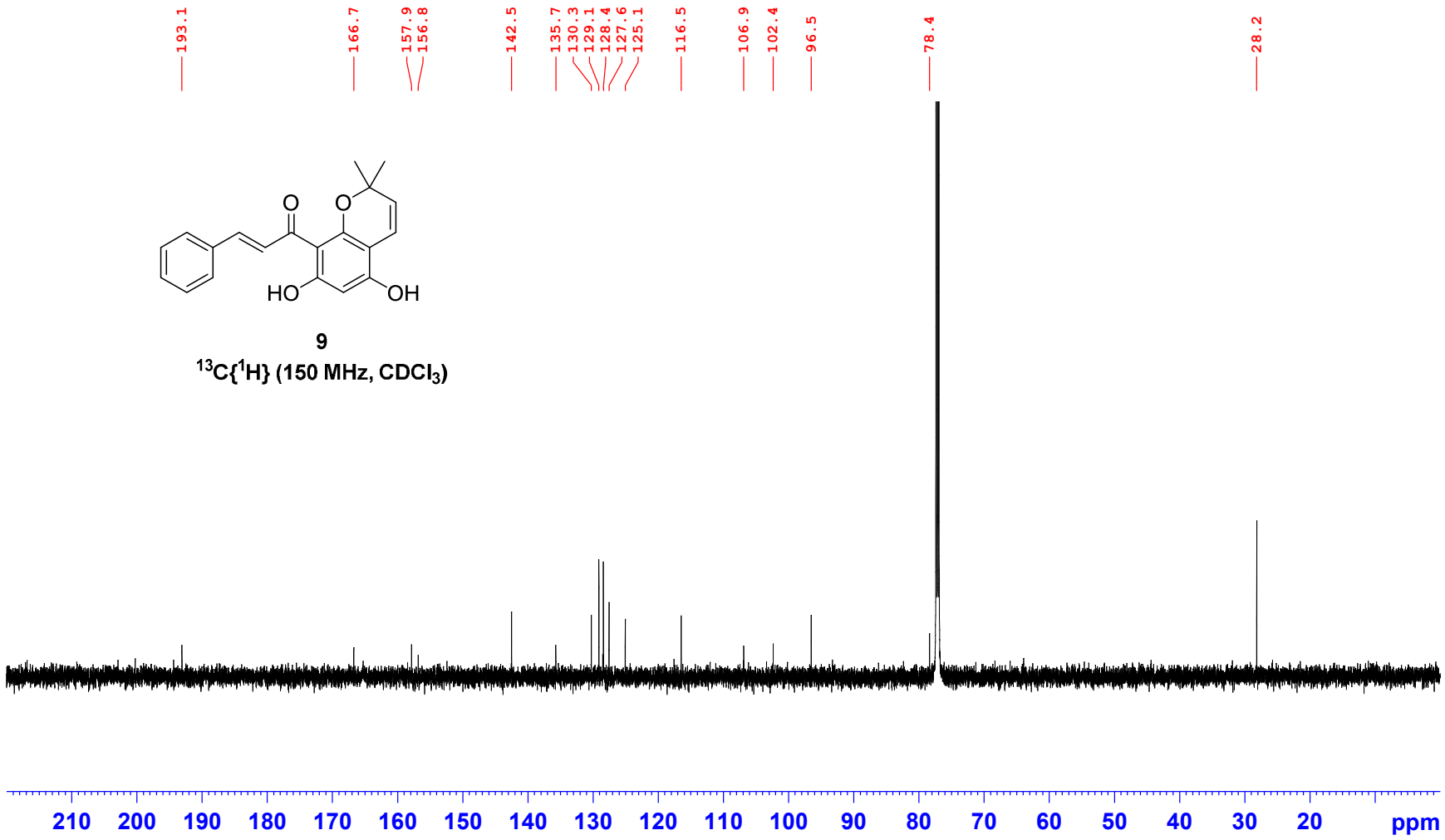


8

^{1}H (600 MHz, Acetone-d$_6$)

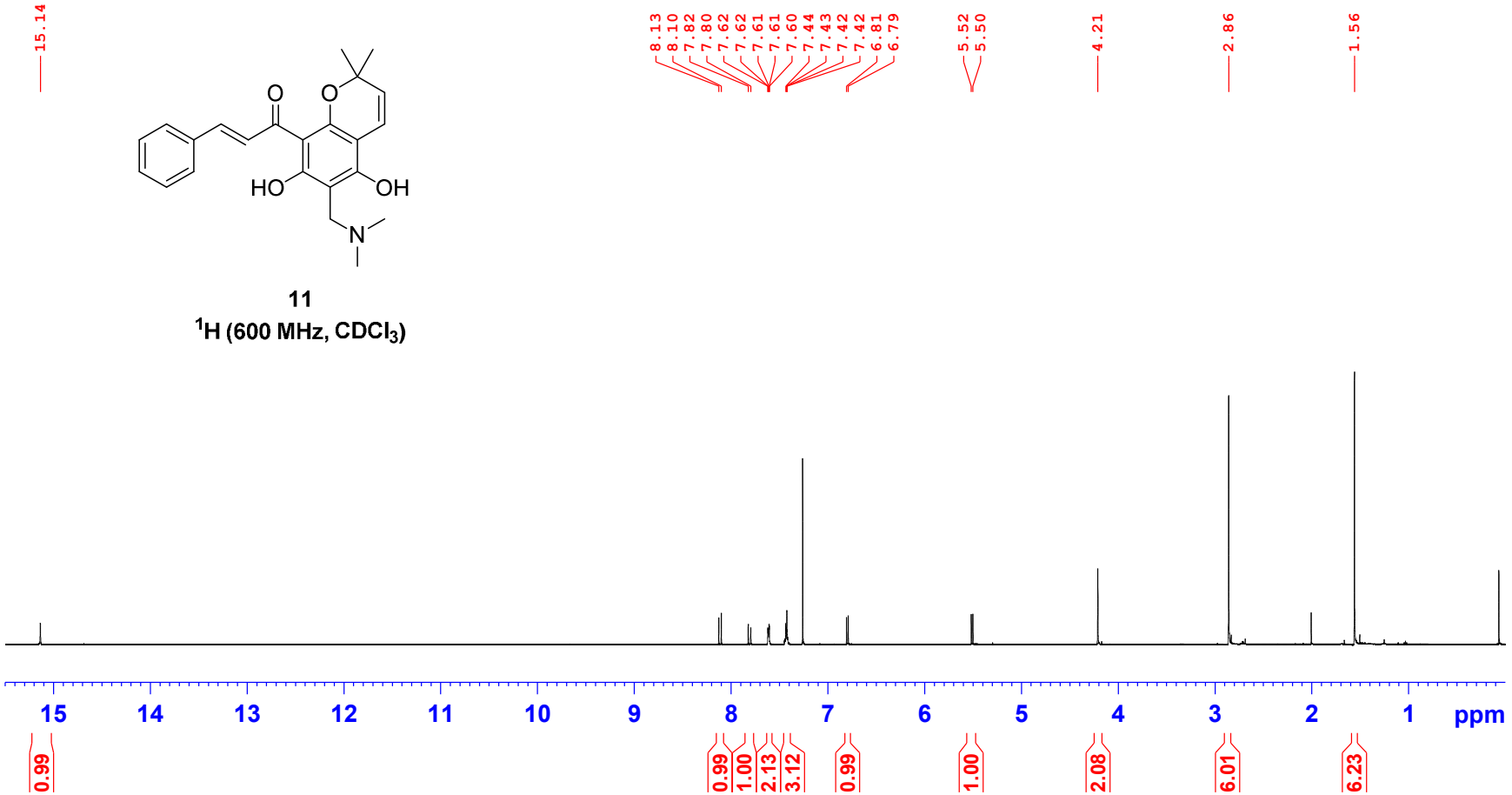

193.7
167.7
156.7
143.2
136.3
131.3
130.0
129.2
128.2
126.2
117.2
107.4
96.0
95.3
79.1
56.7
28.1
O
O
HO
OMOM
8
13C{1H} (150 MHz, Acetone-d6)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


14.01
8.11
8.08
7.78
7.76
7.61
7.60
7.43
7.42
7.41
7.39
6.58
6.56
5.95
5.60
5.51
5.49
1.56
O
O
HO
OH
9
1H (600 MHz, CDCl3)
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.96
1.00
0.98
1.90
2.82
0.91
0.97
0.73
0.97
6.10



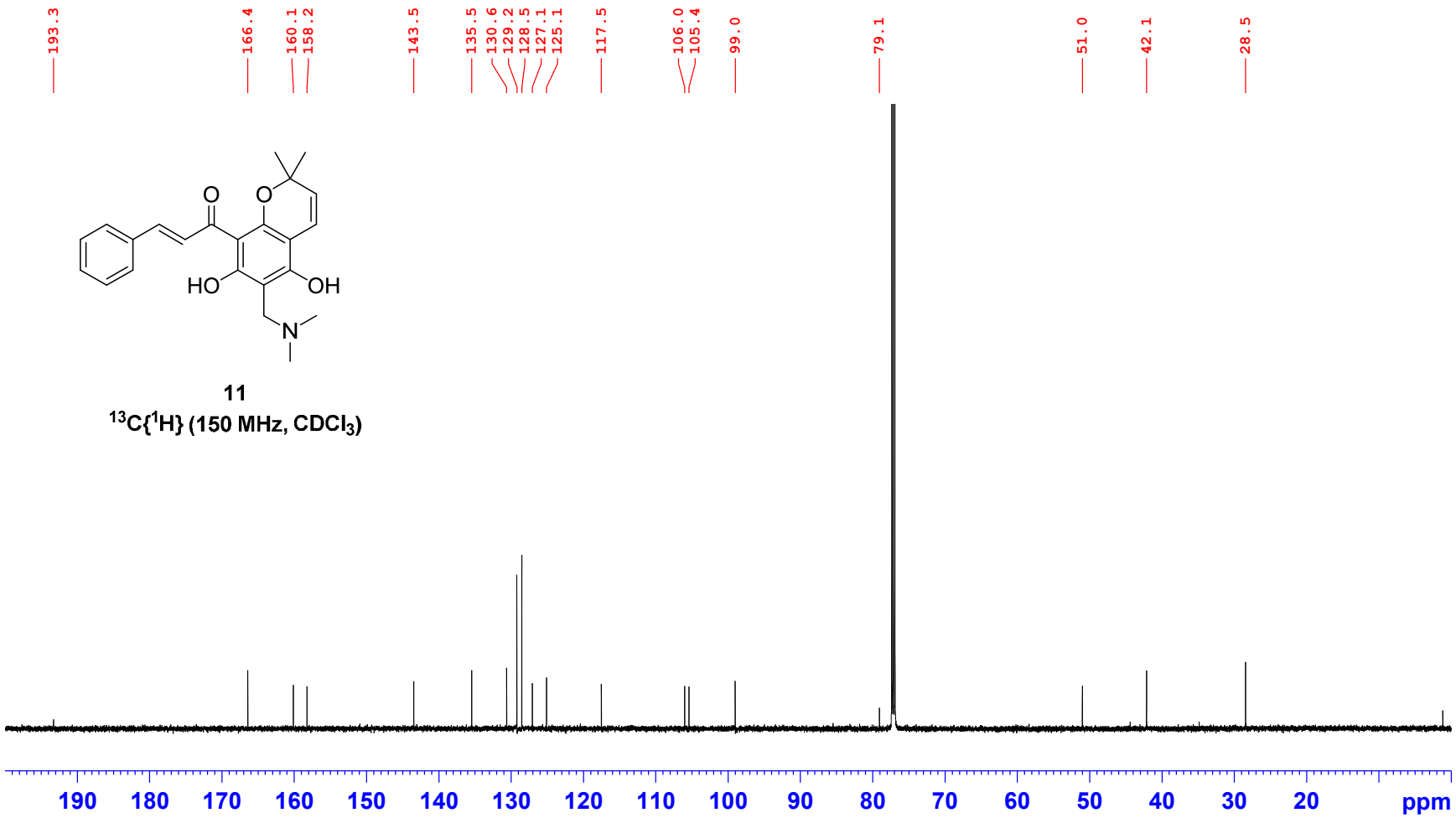
9

$^{13}C\{^{1}H\}$ (150 MHz, $CDCl_3$)



11

^{1}H (600 MHz, $CDCl_3$)



11

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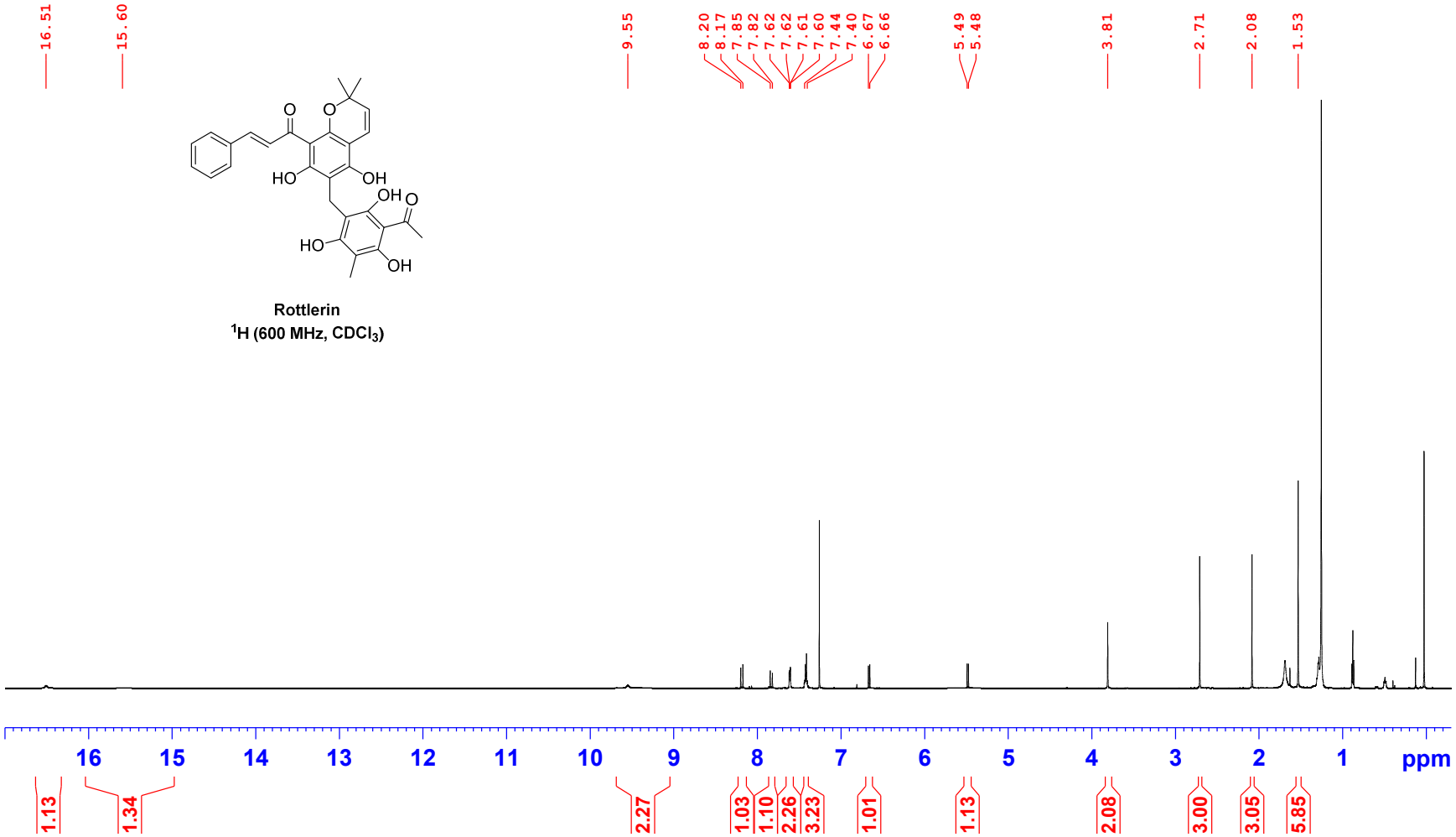
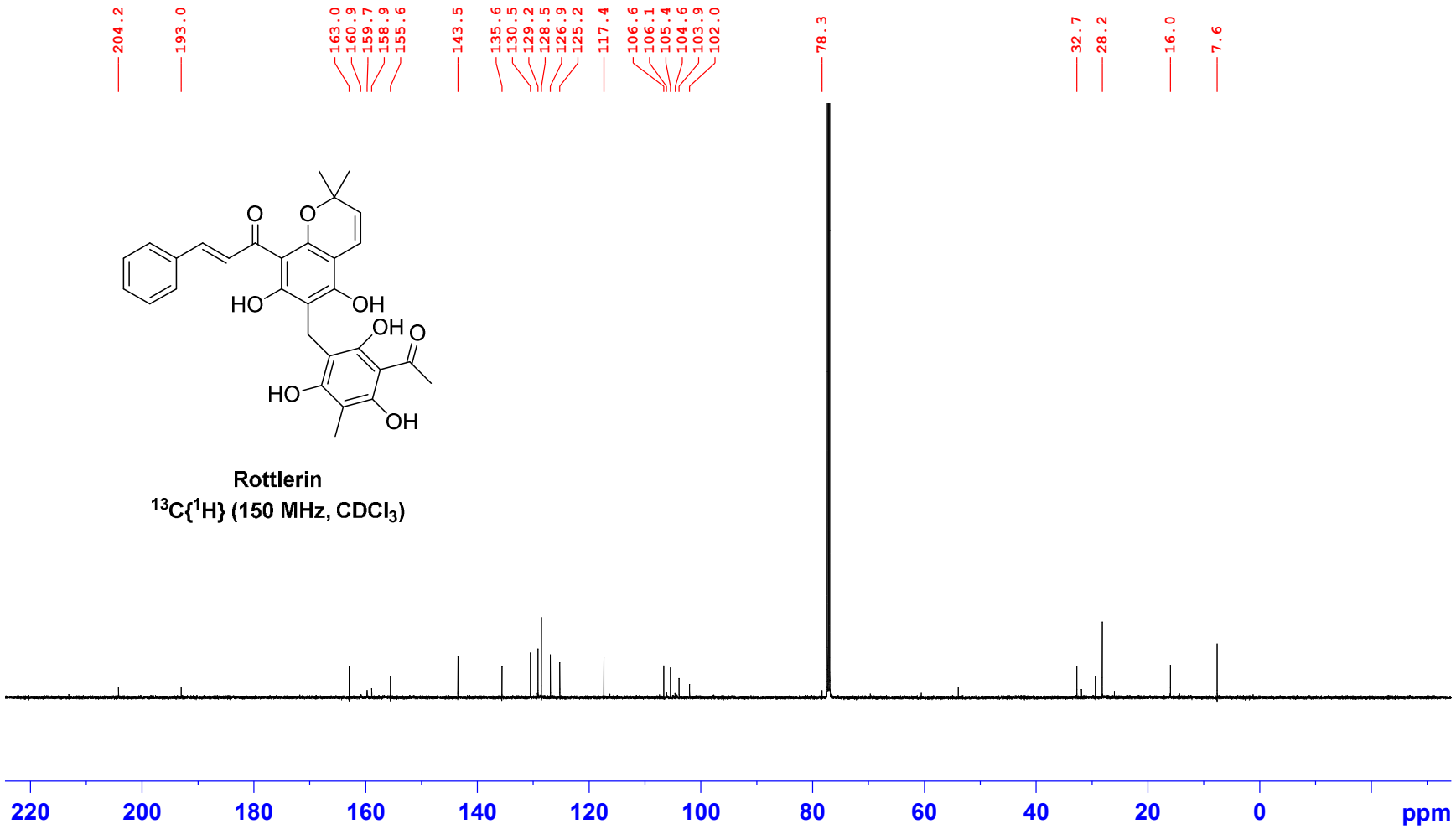


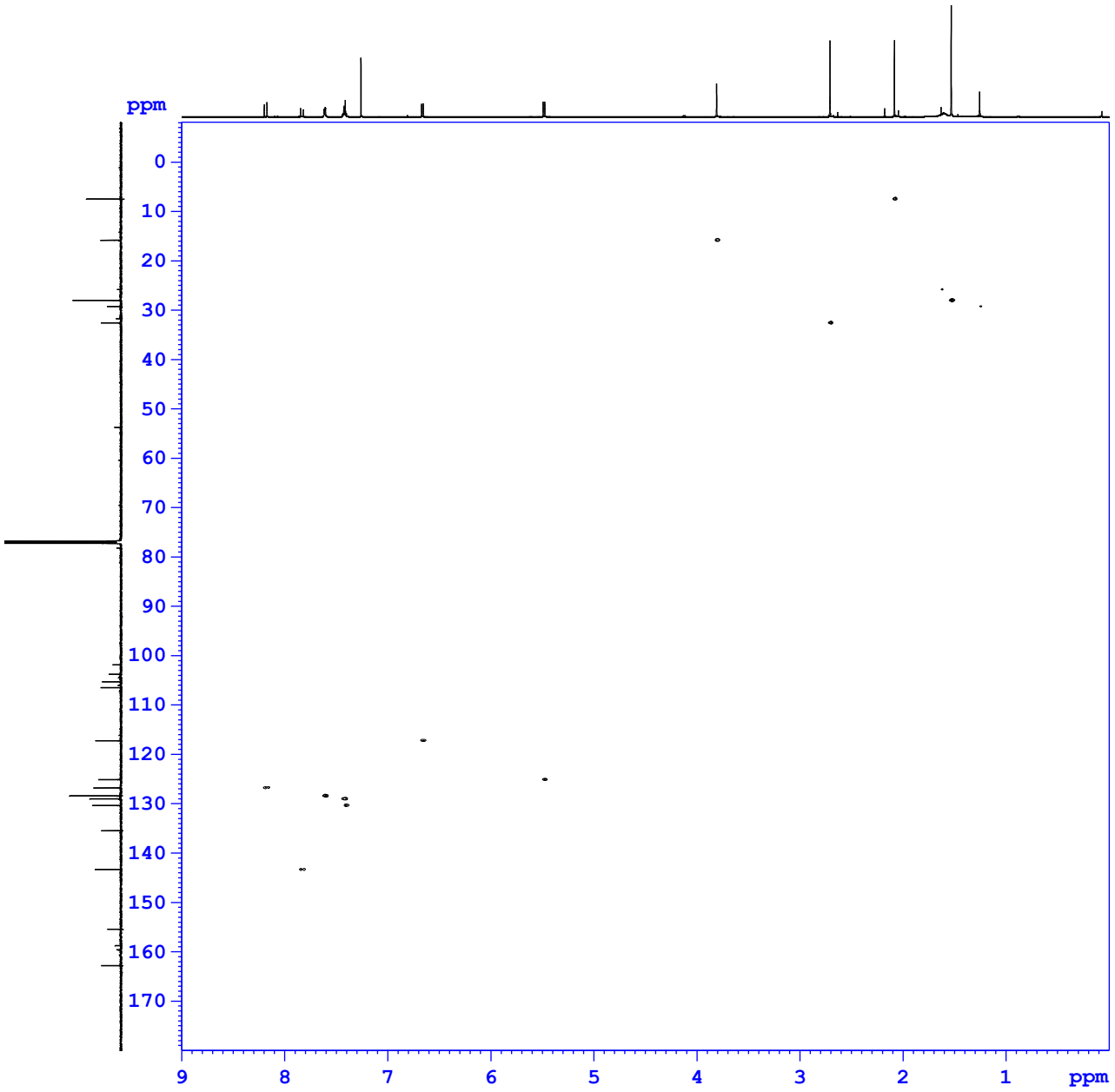
Rottlerin

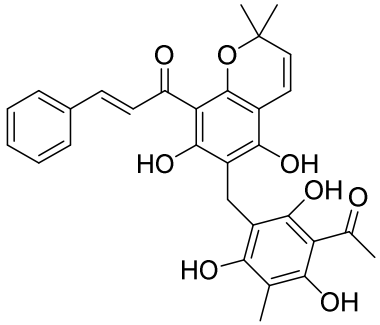
^{1}H (600 MHz, $CDCl_3$)



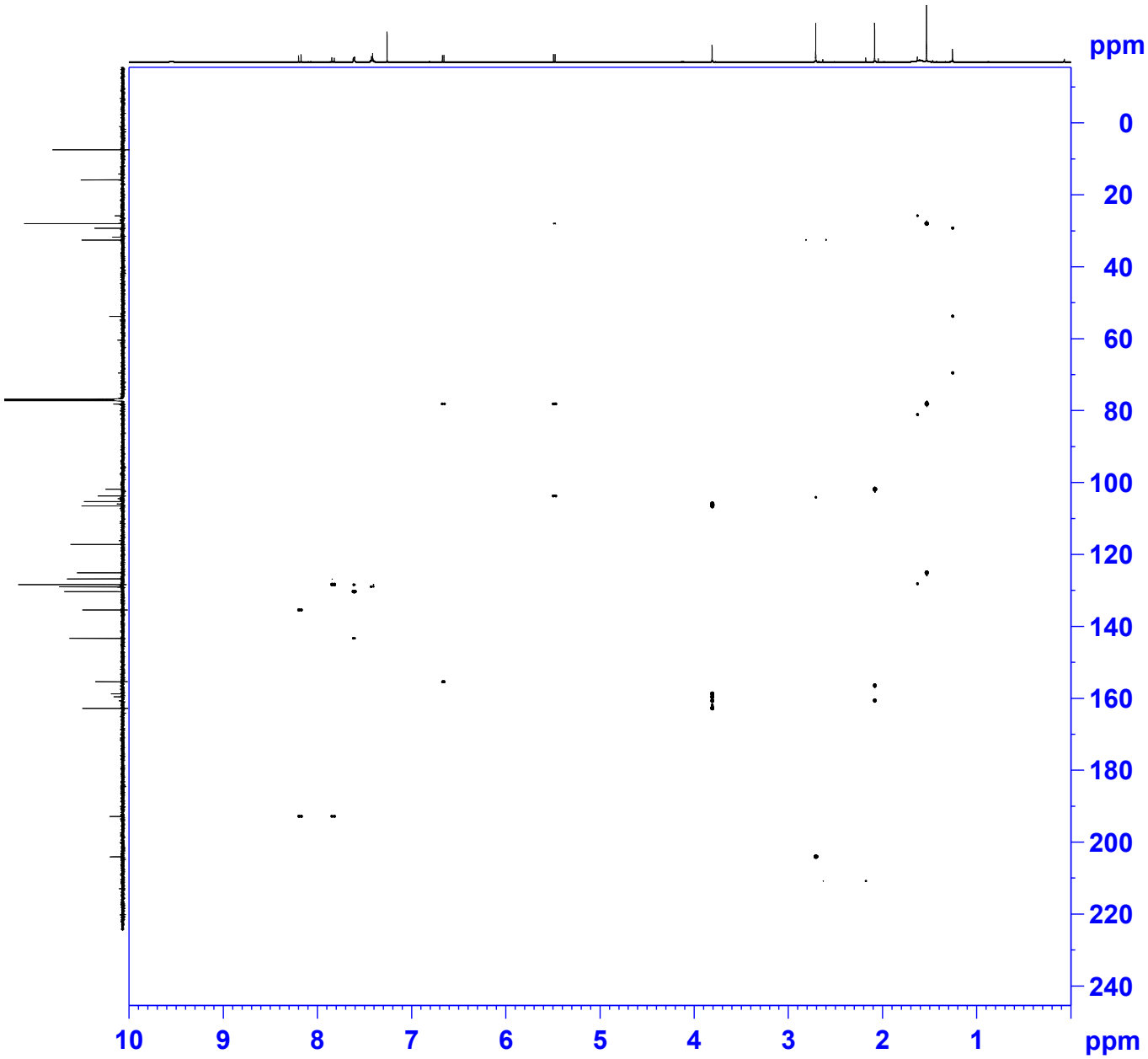
Rottlerin

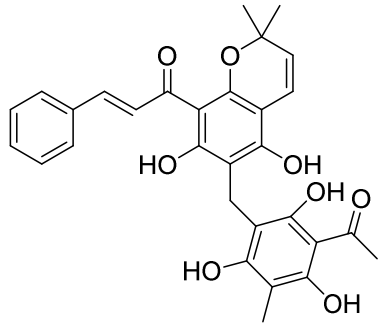
$^{13}C\{^{1}H\}$ (150 MHz, $CDCl_3$)



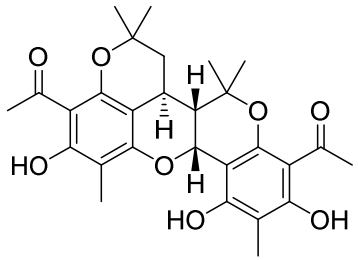


Rottlerin
^{1}H-^{13}C HSQC
$CDCl_3$



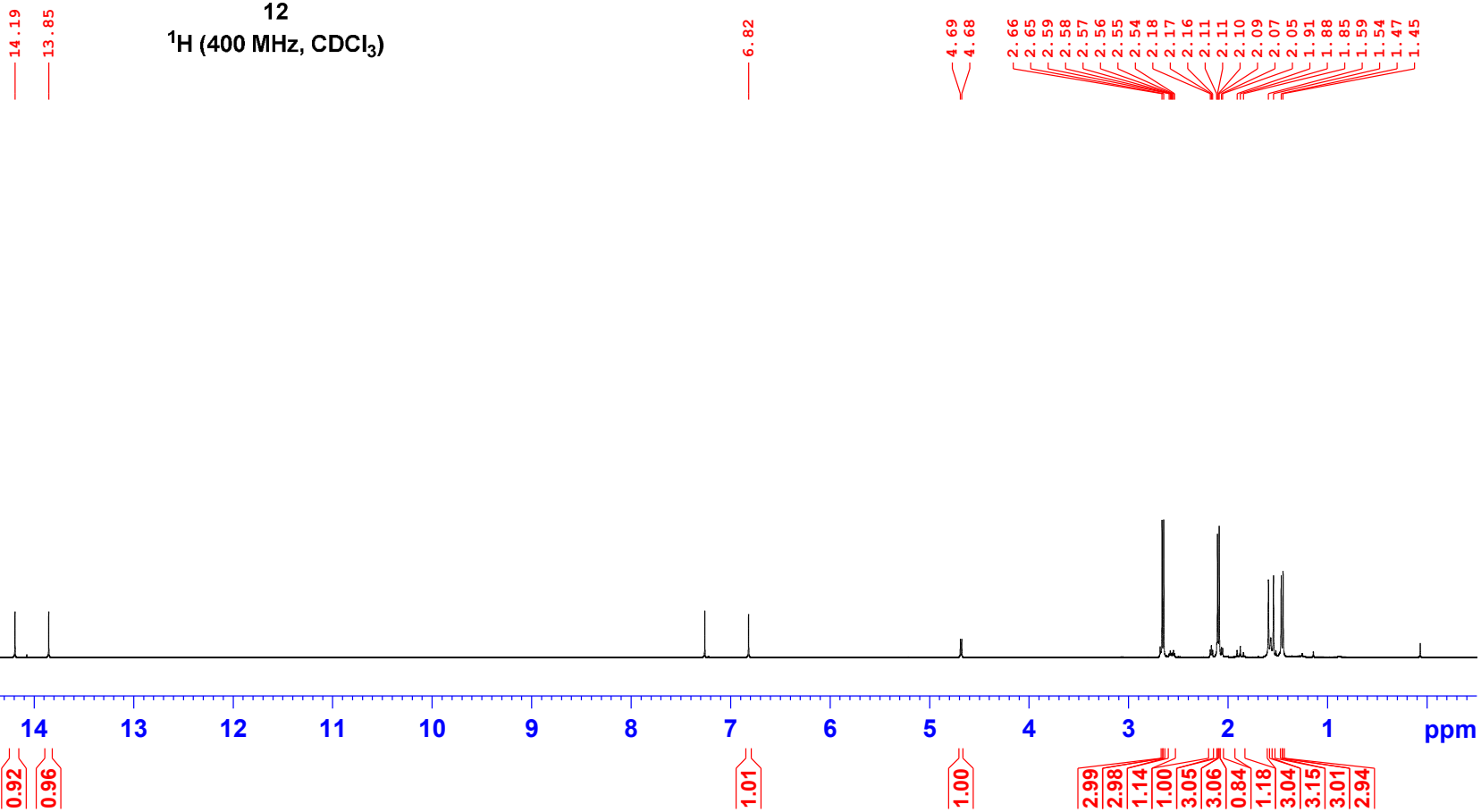


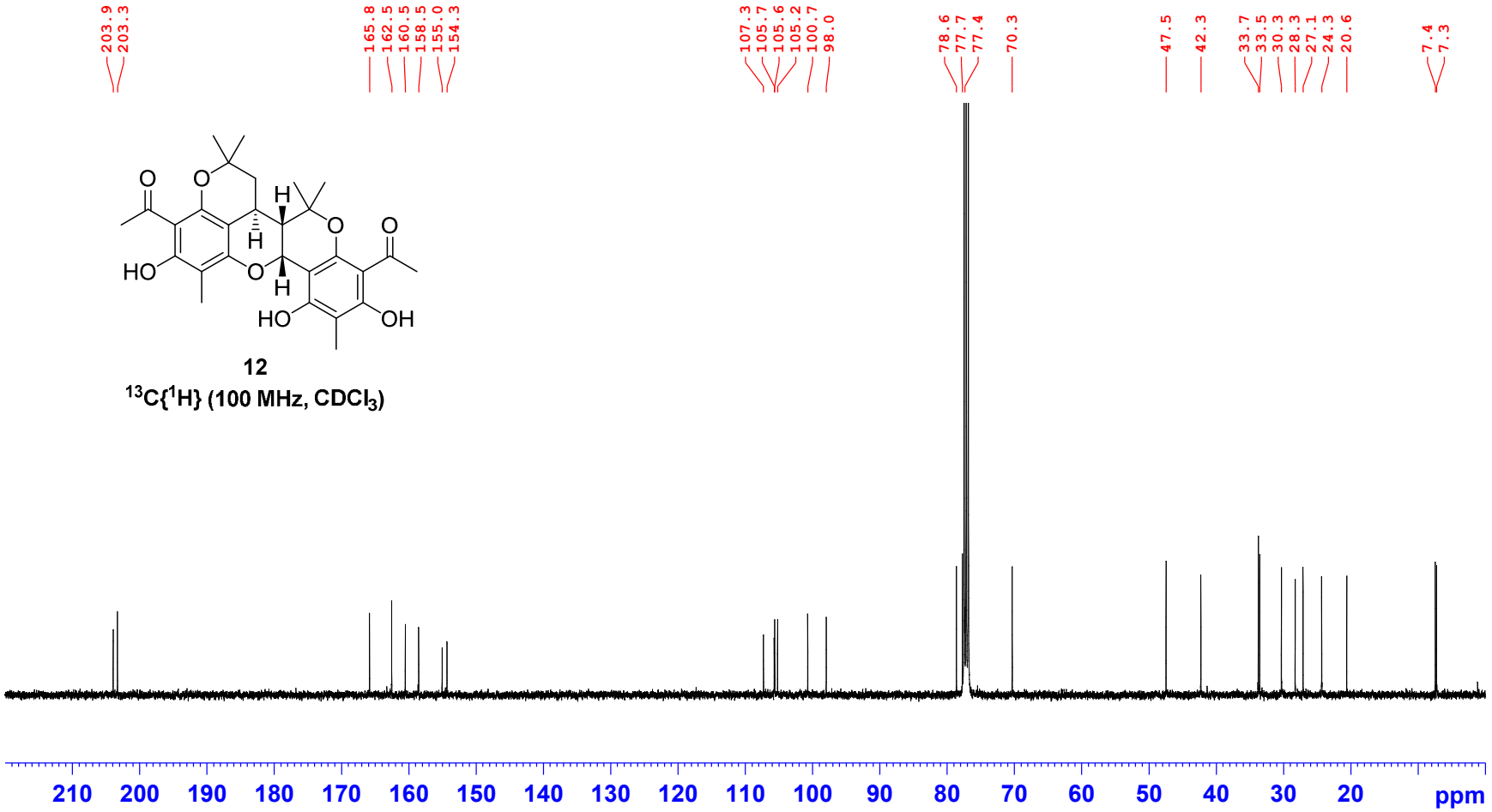
Rottlerin
^{1}H-^{13}C HMBC
$CDCl_3$



12

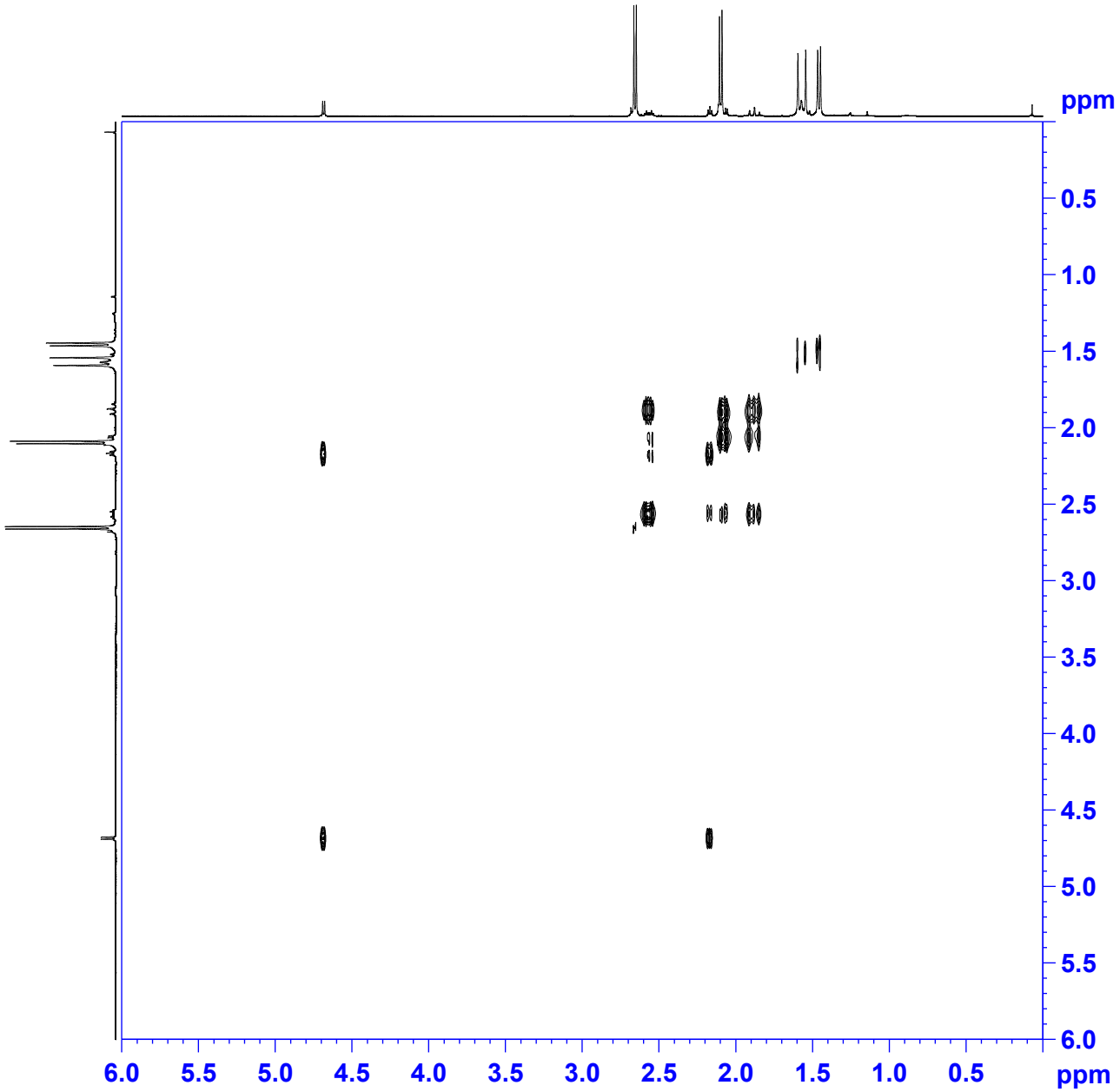
^{1}H (400 MHz, $CDCl_3$)

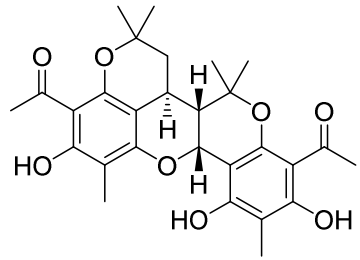




12

$^{13}C\{^{1}H\}$ (100 MHz, $CDCl_3$)





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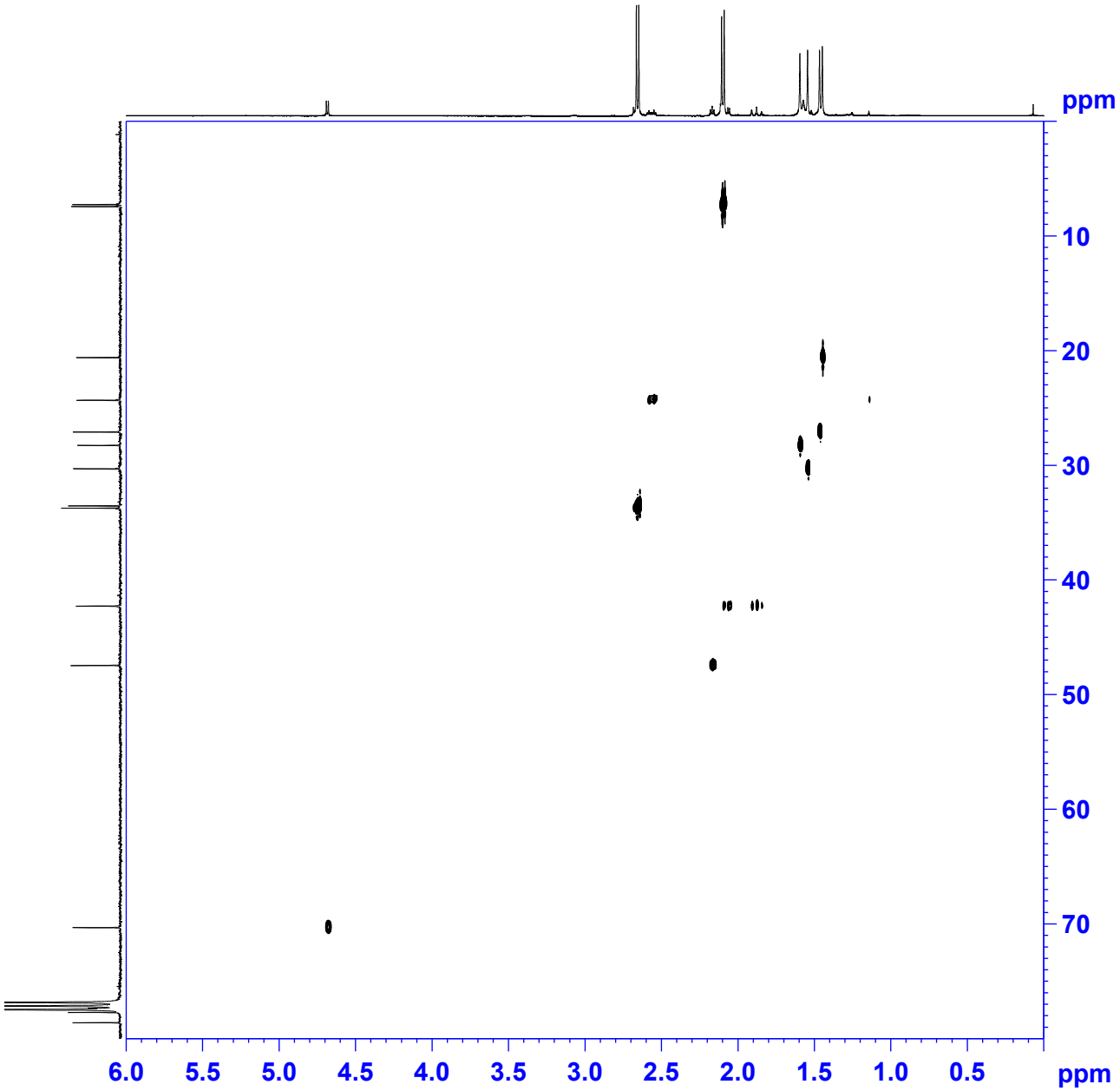
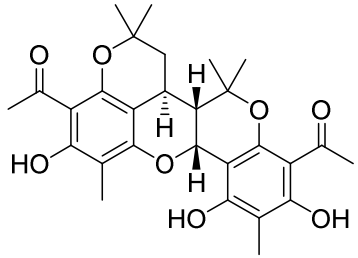
^{1}H-^{1}H COSY

$CDCl_3$





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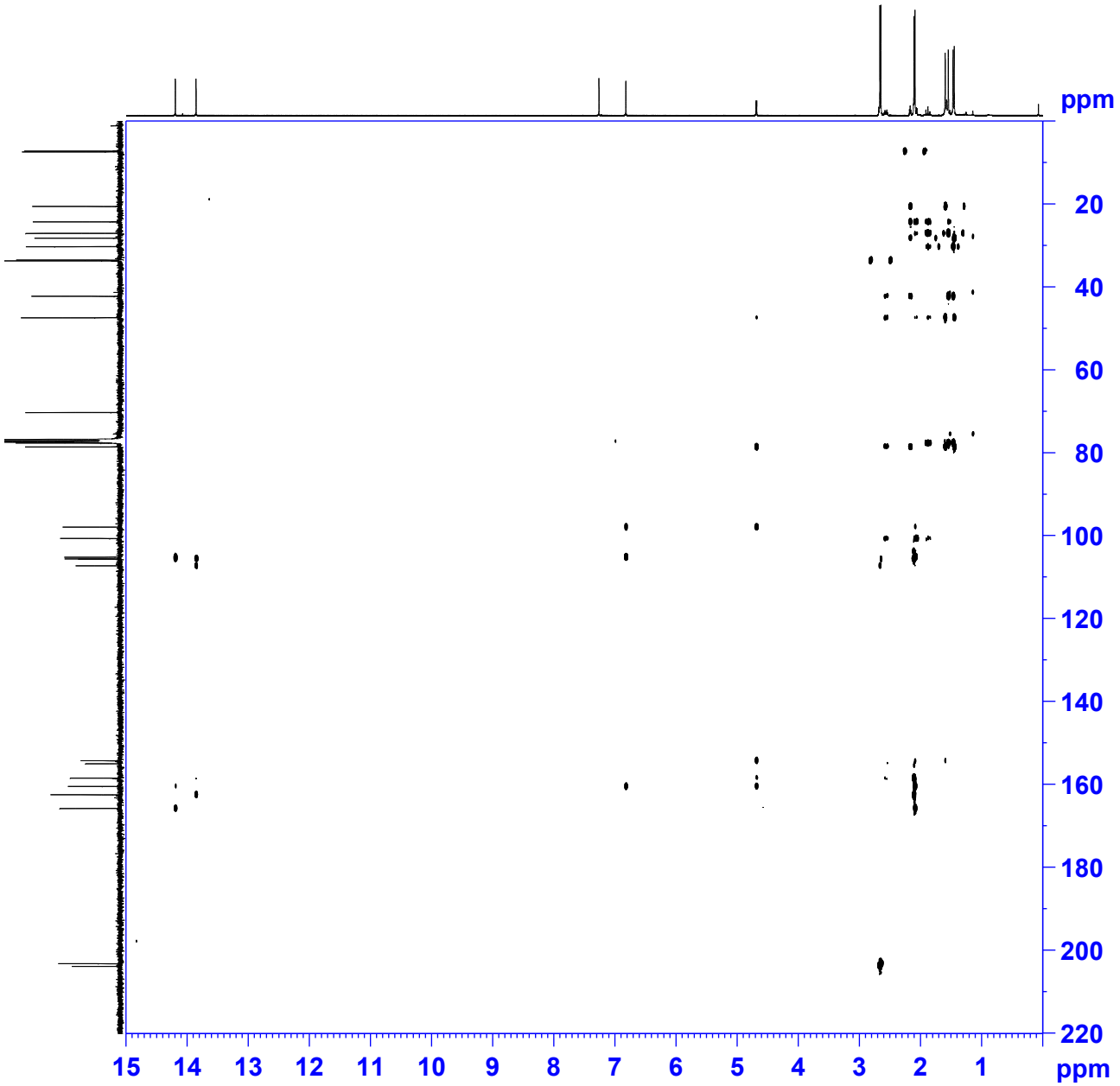
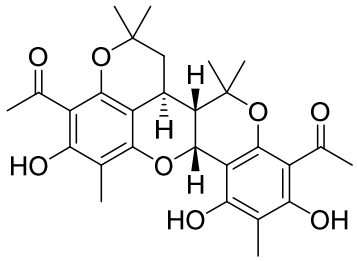
^{1}H-^{13}C HSQC

$CDCl_3$

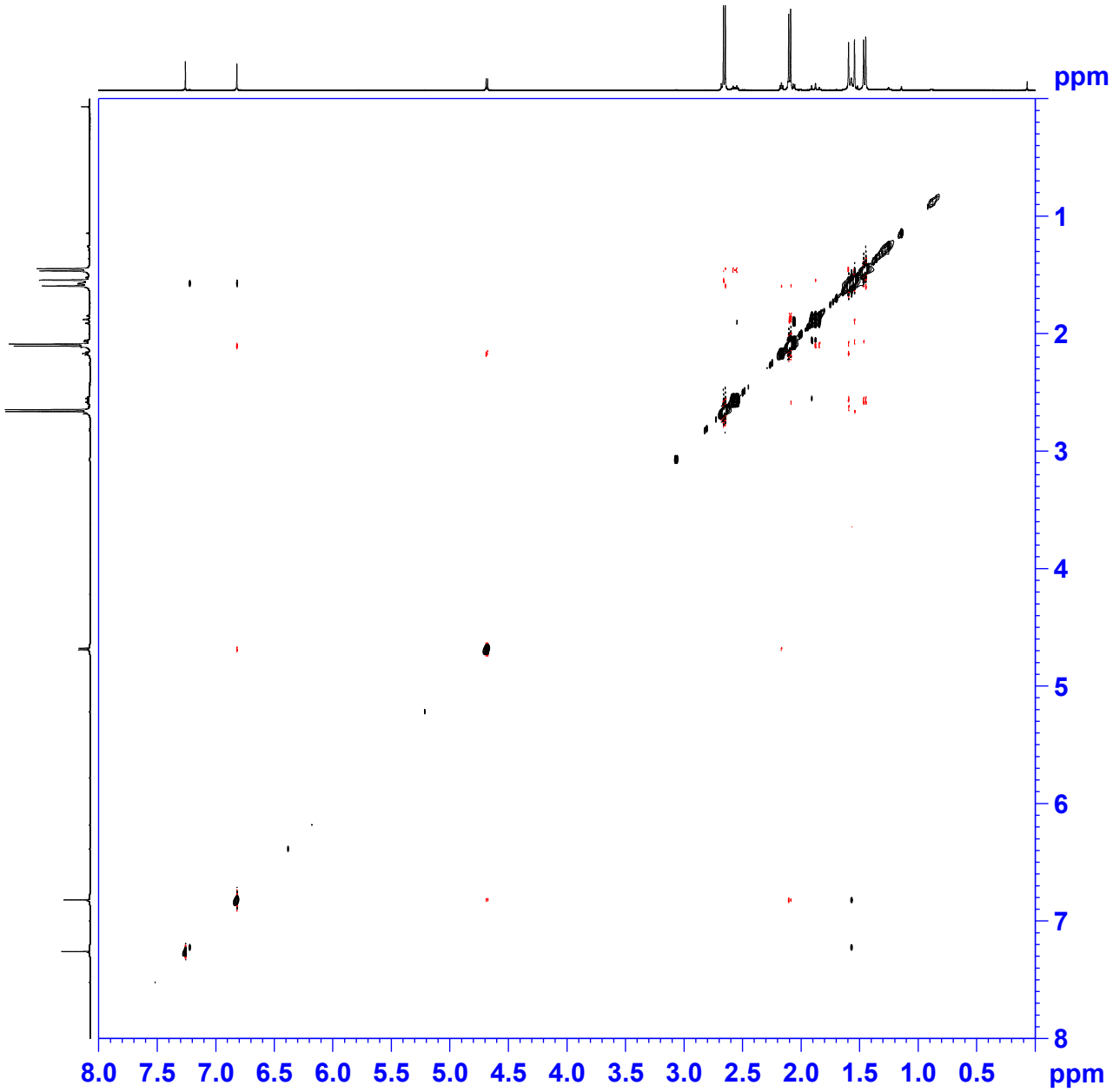


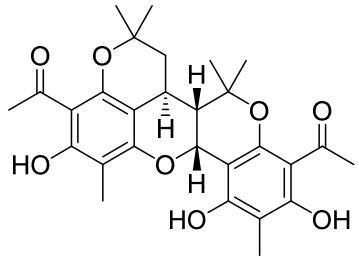


12

^{1}H-^{13}C HMBC

$CDCl_3$

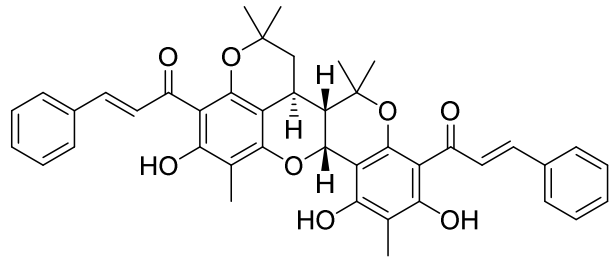




12

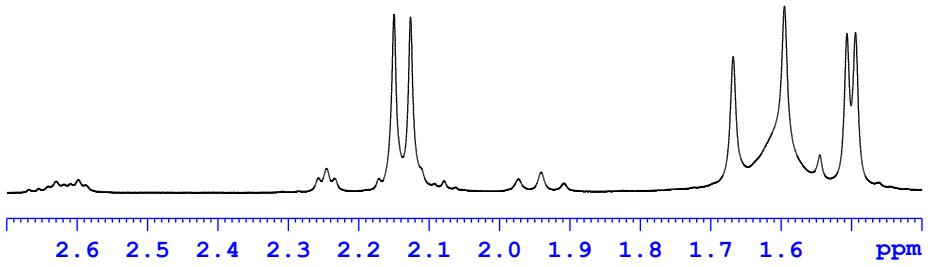
^{1}H-^{1}H NOESY

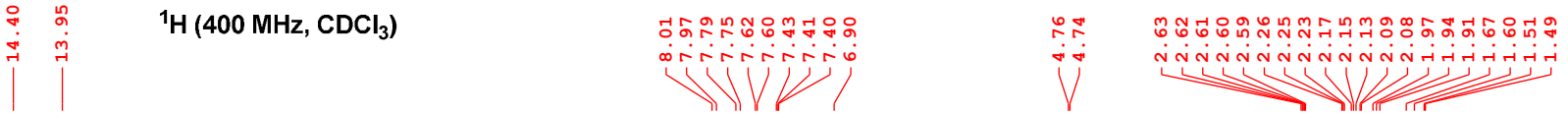
$CDCl_3$

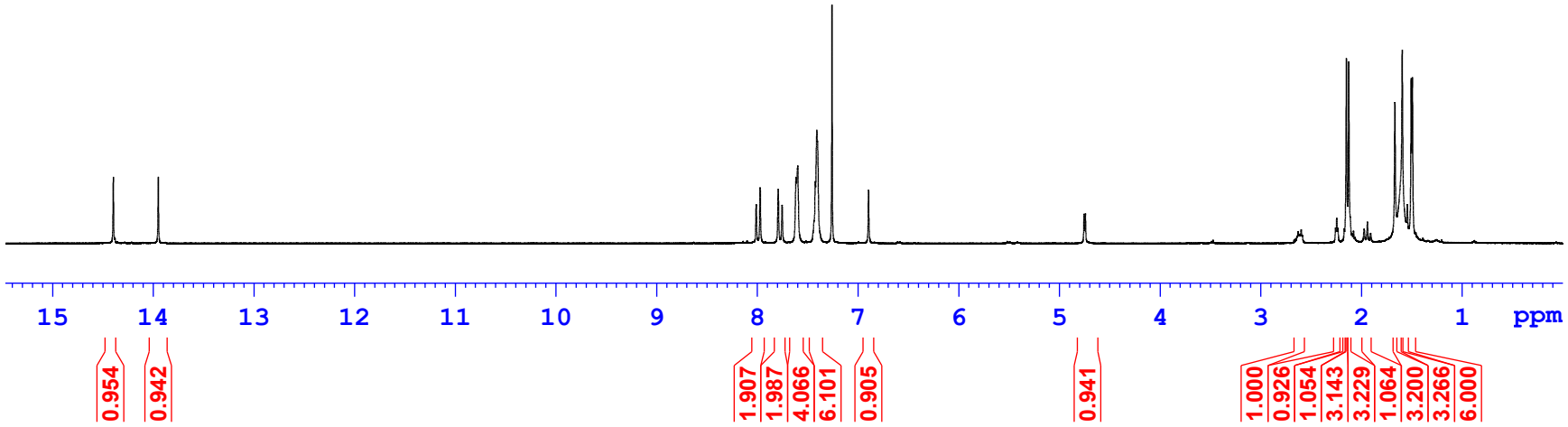


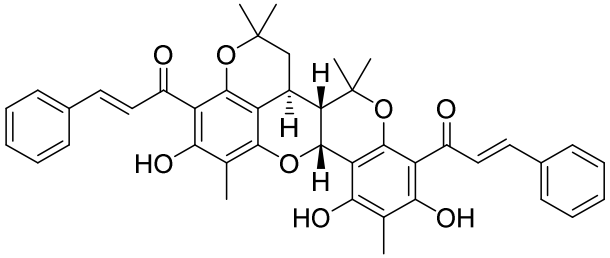
kamalachalcone A

^{1}H (400 MHz, $CDCl_3$)



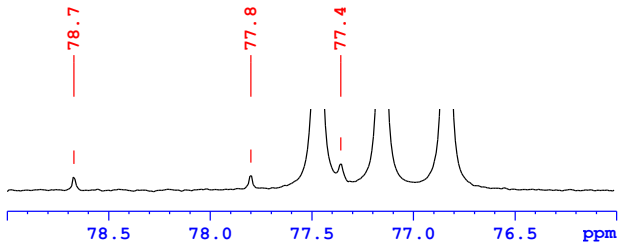


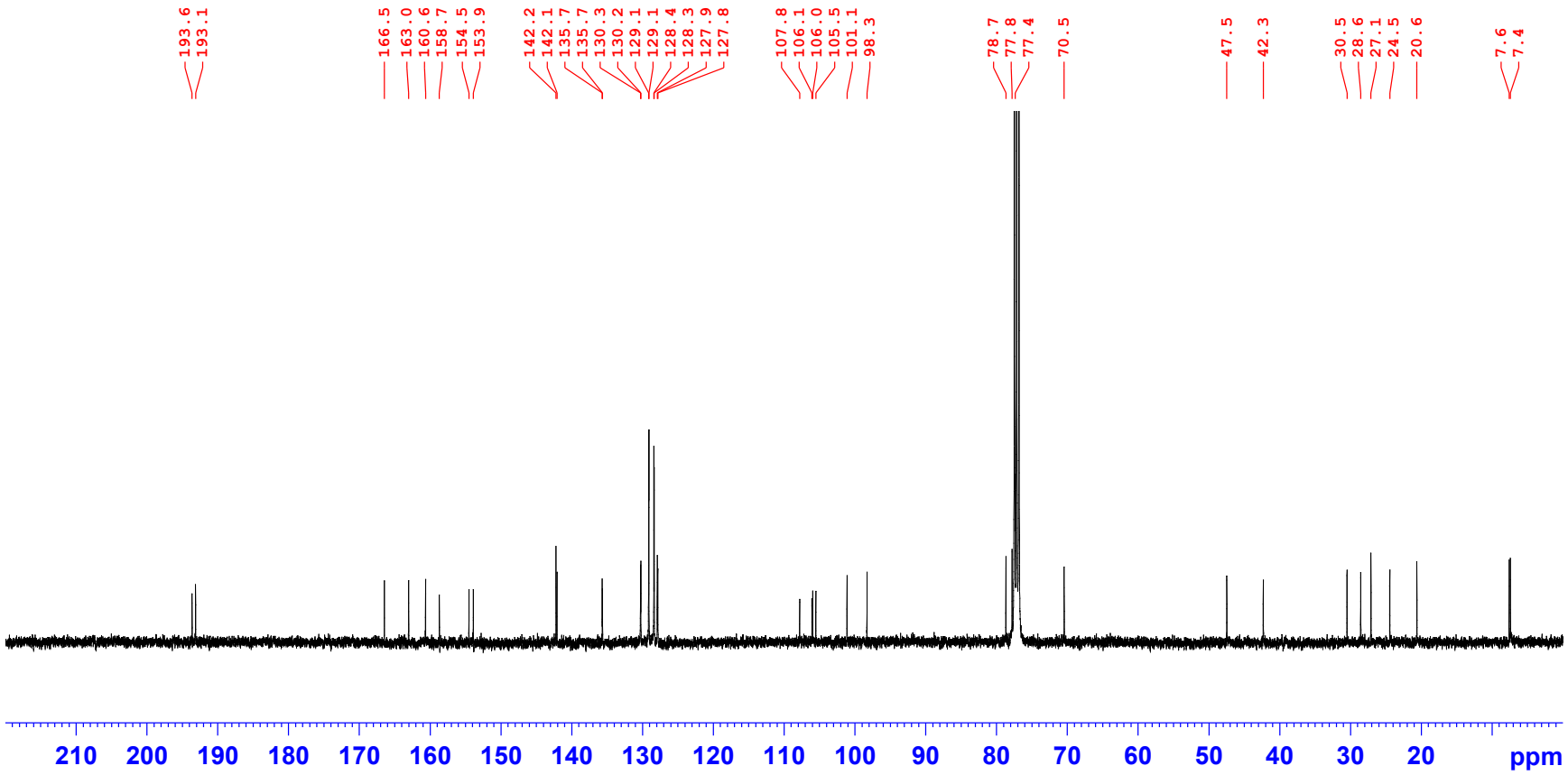


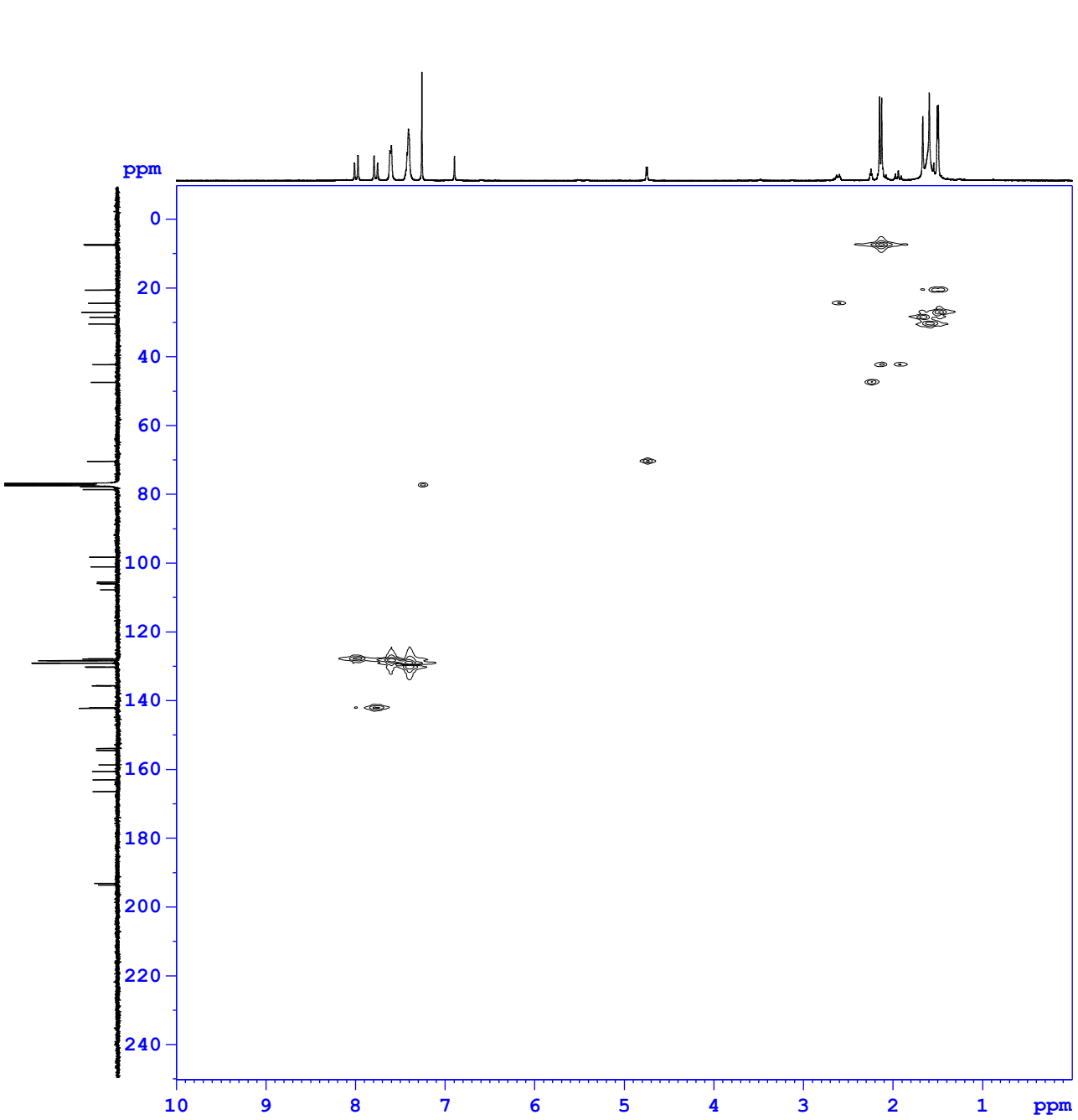


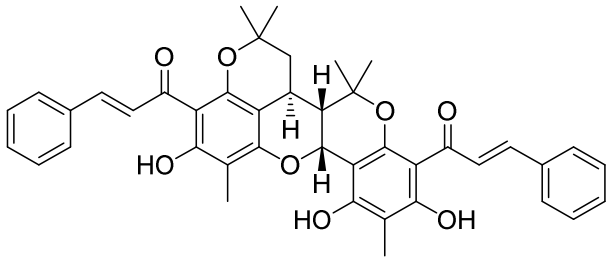
kamalachalcone A

$^{13}C\{^{1}H\}$ (100 MHz, $CDCl_3$)



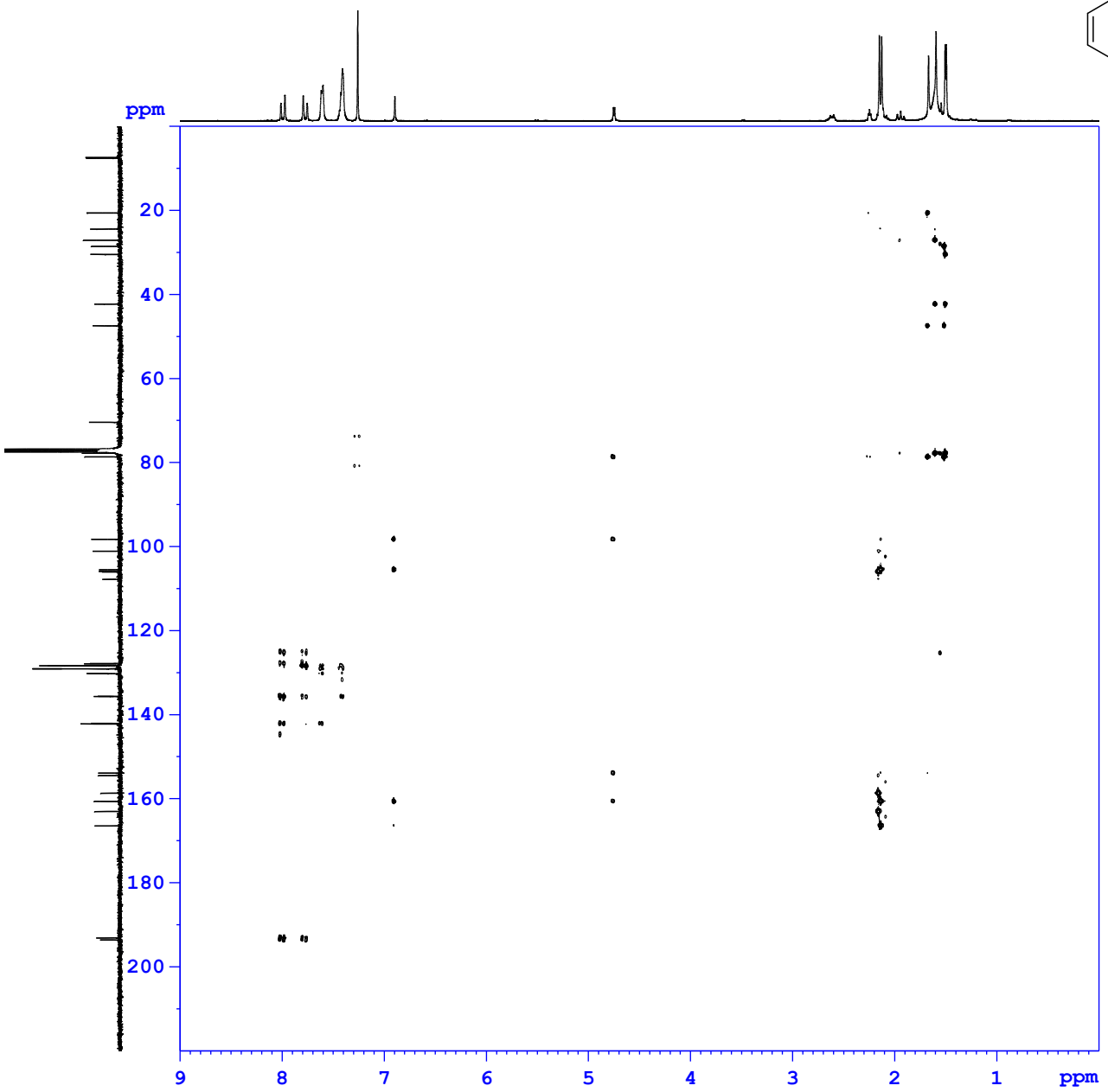


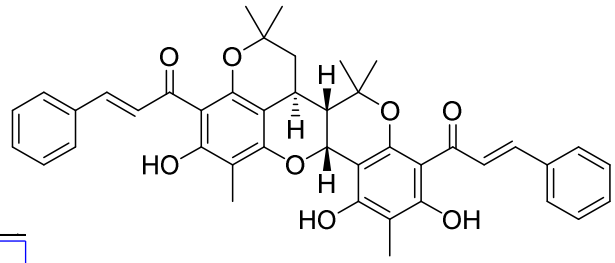




kamalachalcone A

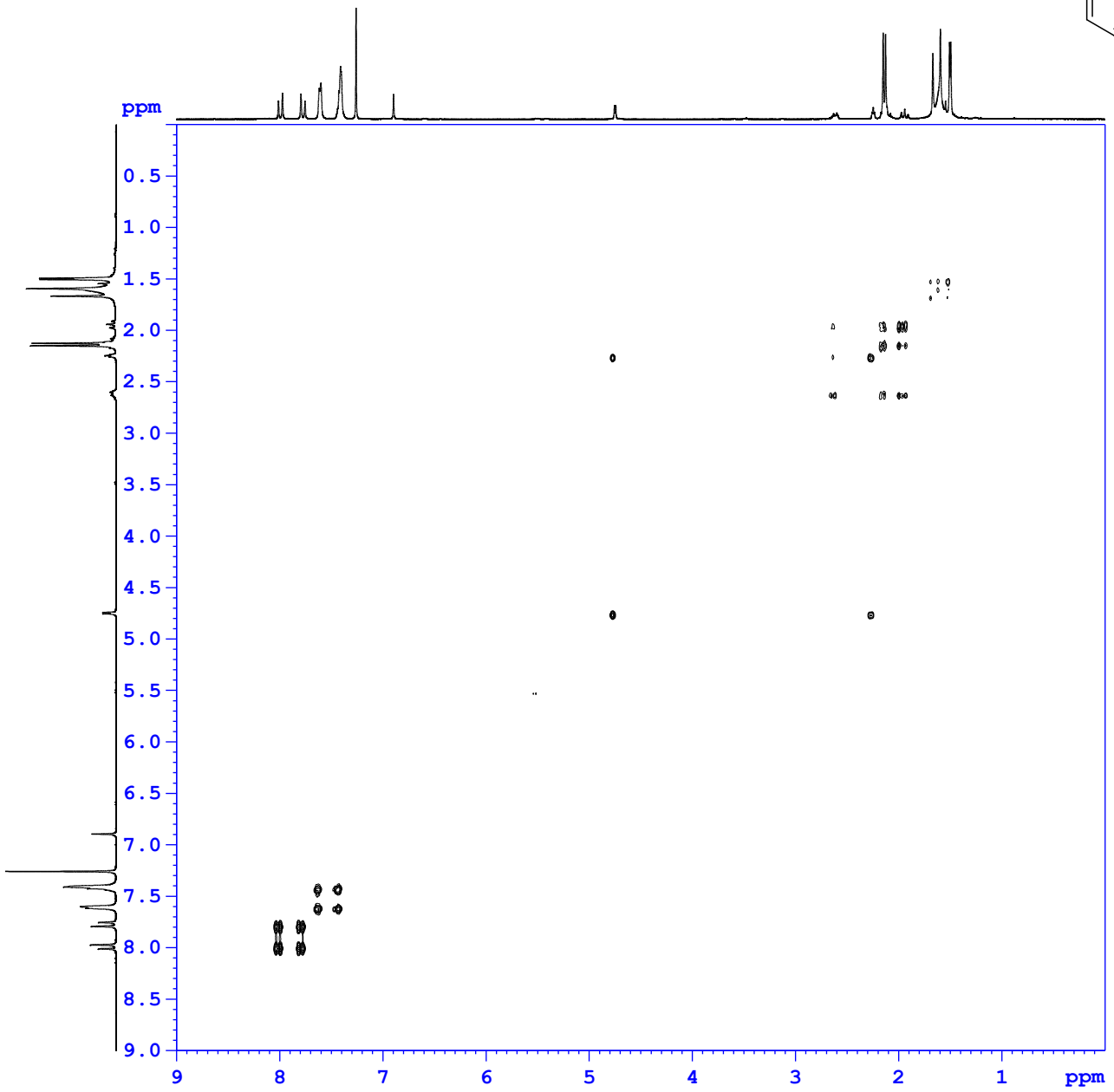
^{1}H-^{13}C HSQC
$CDCl_3$

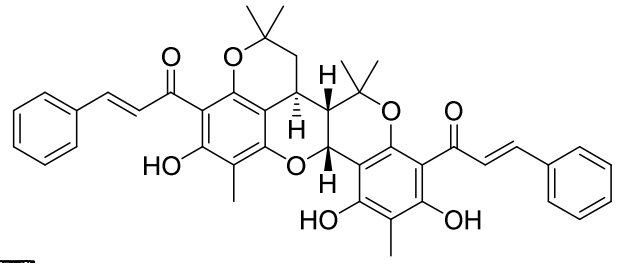




kamalachalcone A

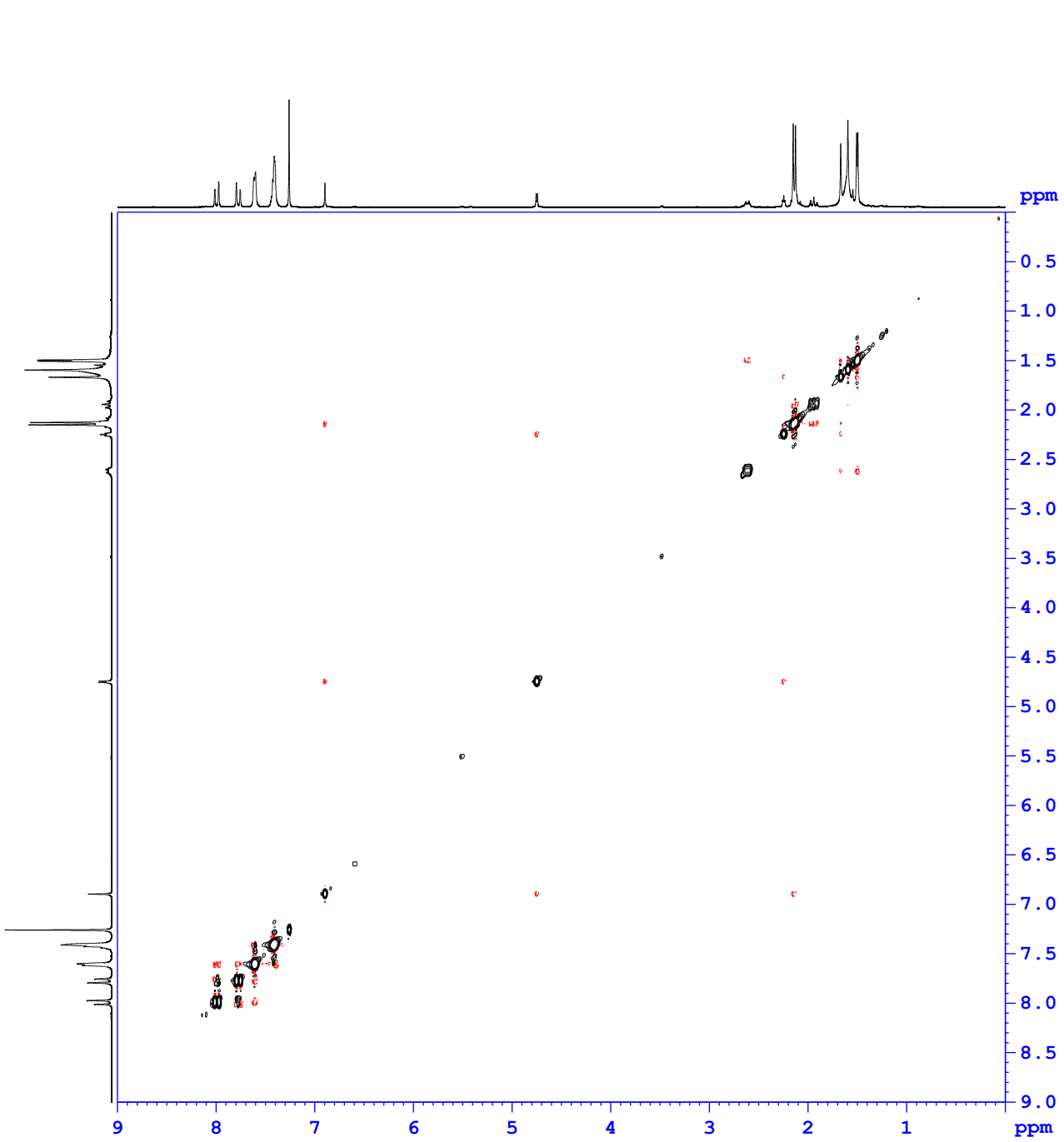
^{1}H-^{13}C HMBC
$CDCl_3$

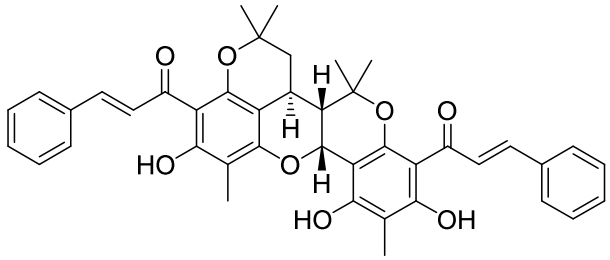




kamalachalcone A

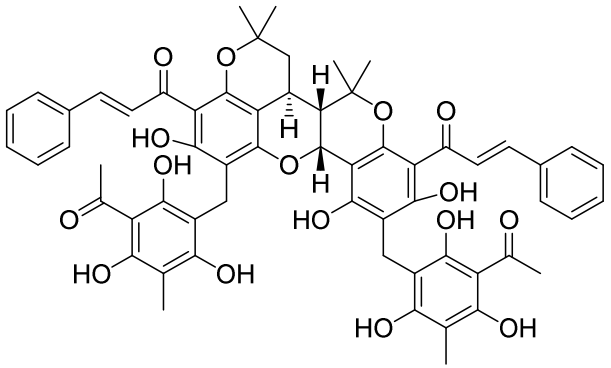
^{1}H-^{1}H COSY
$CDCl_3$





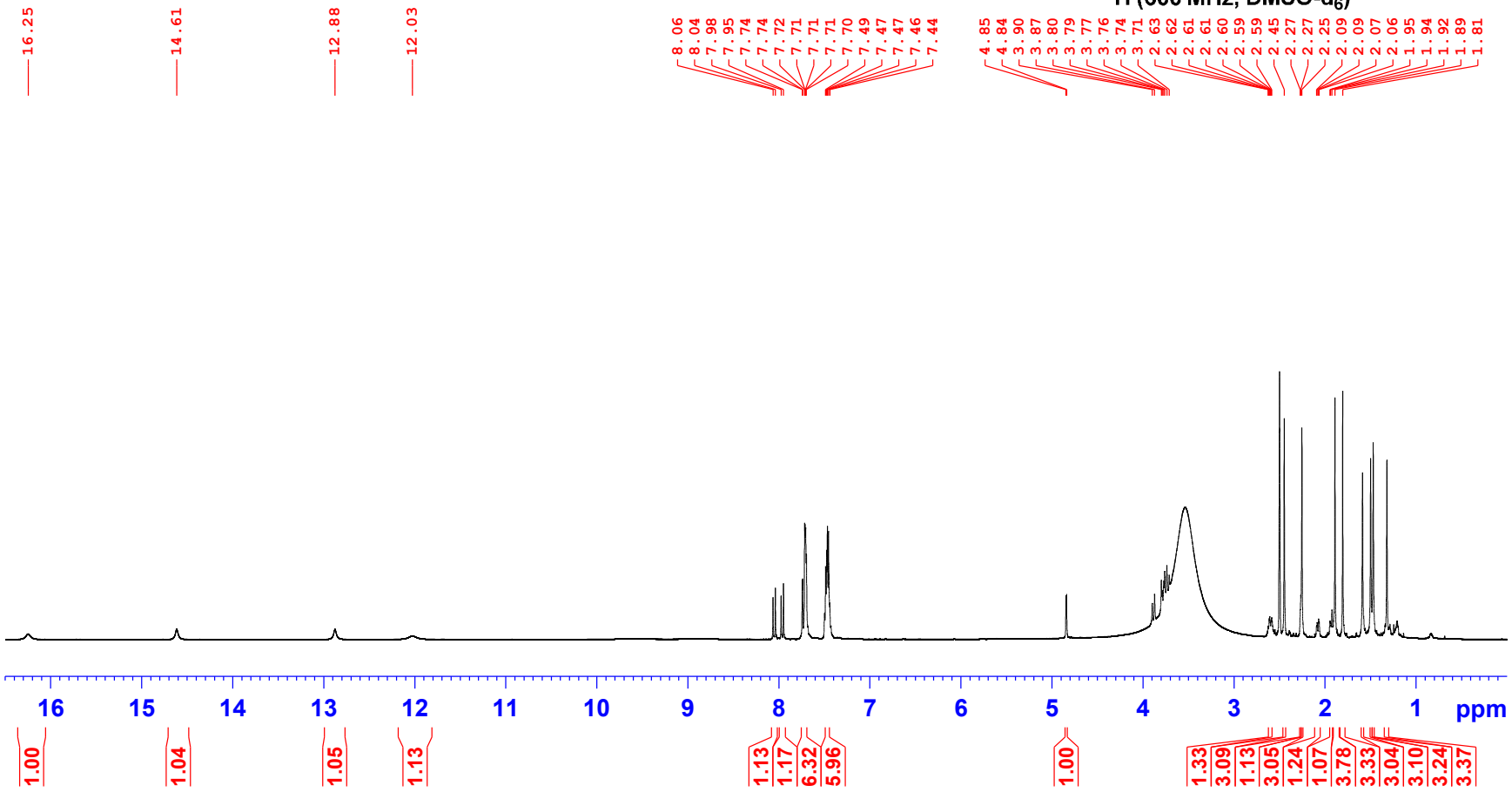
kamalachalcone A

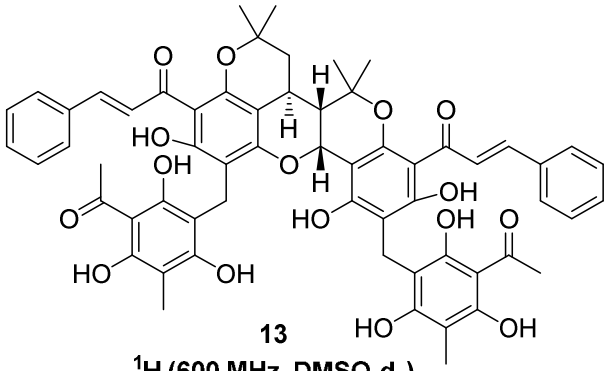
^{1}H-^{1}H NOESY
$CDCl_3$



13

^{1}H (600 MHz, DMSO-d_6)

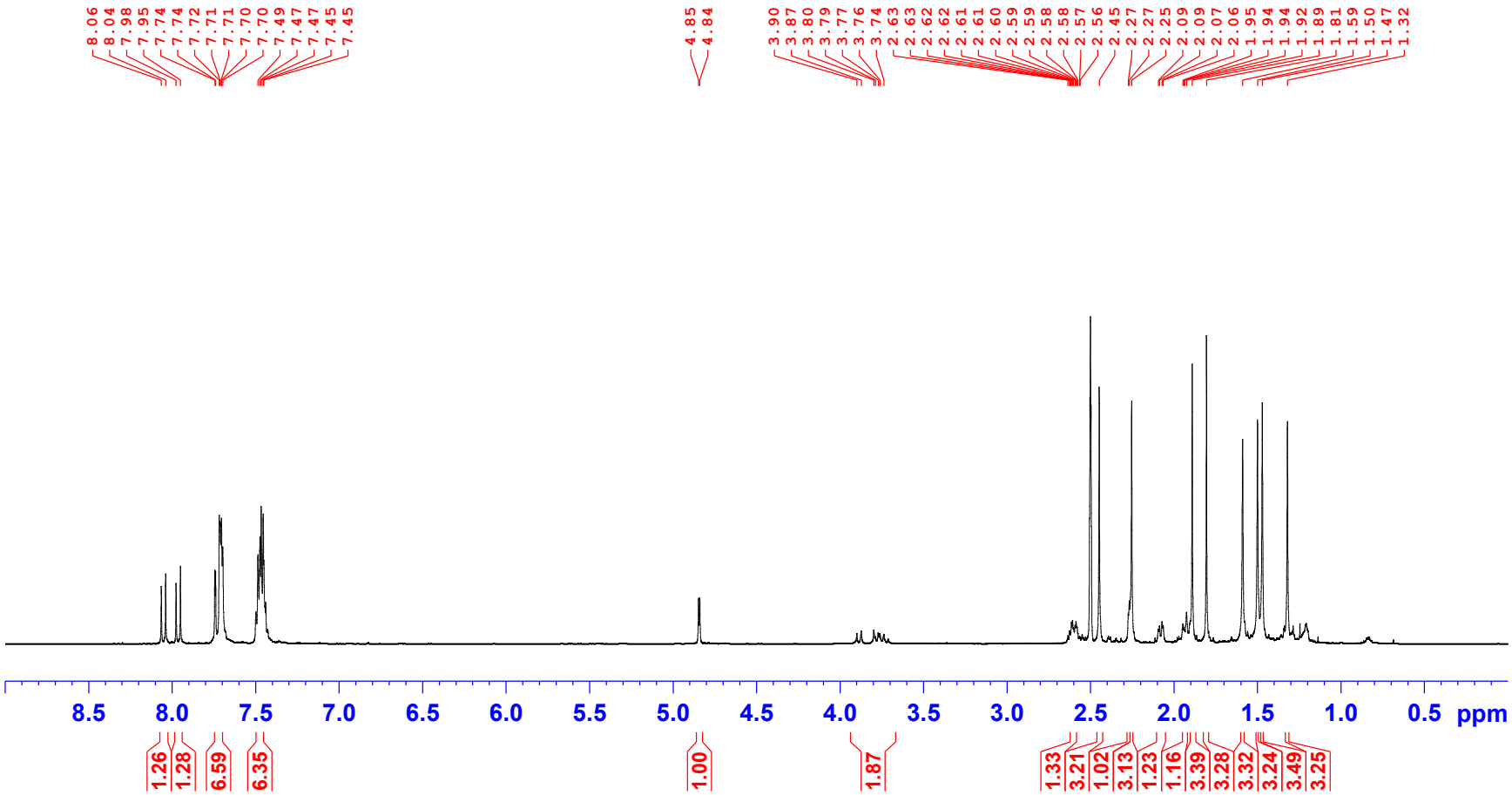


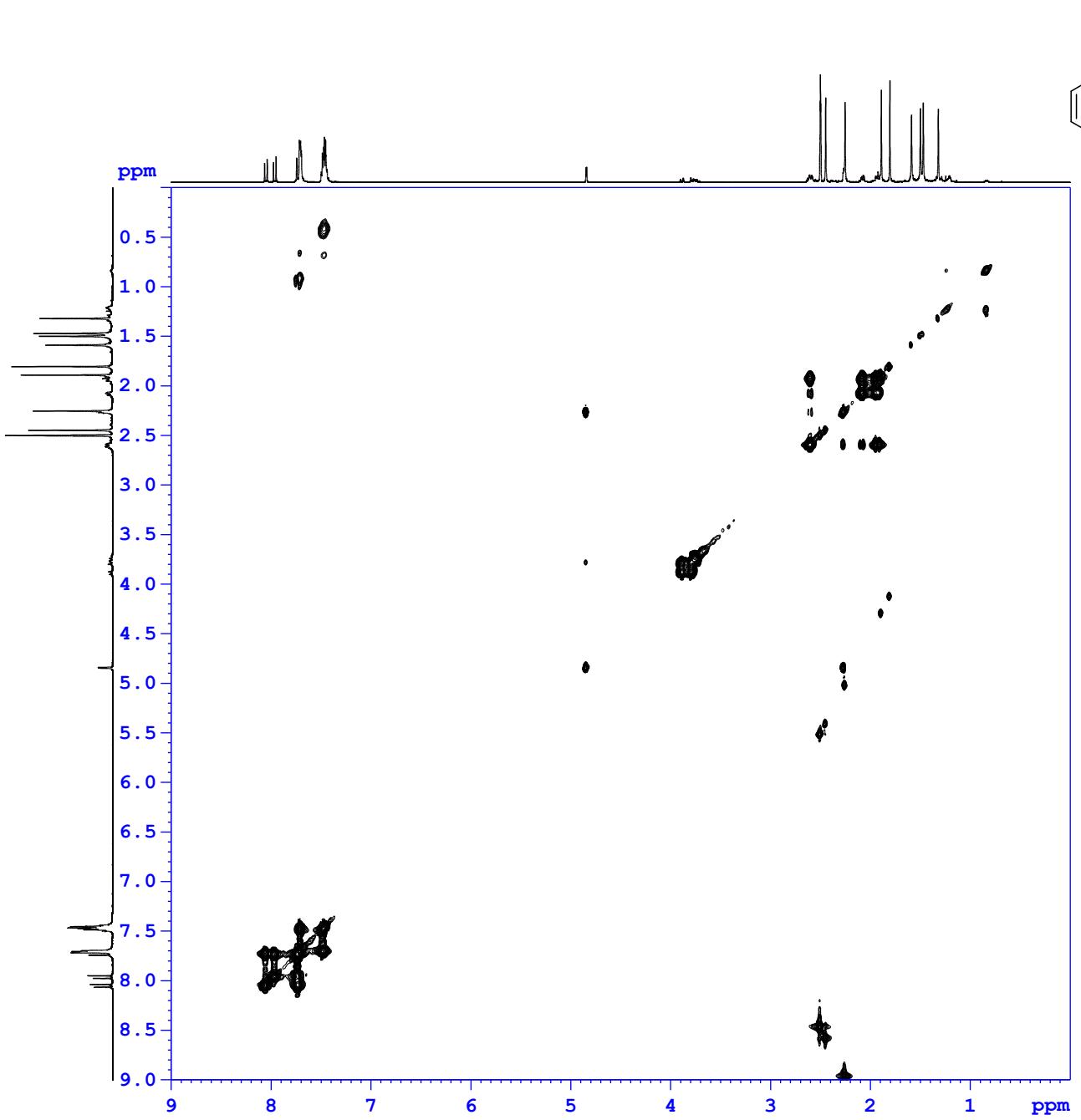


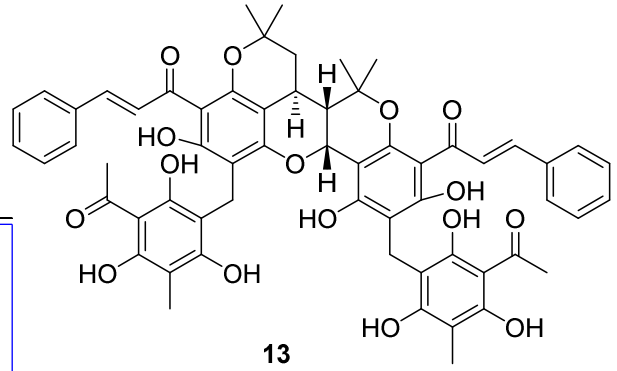
13

^{1}H (600 MHz, DMSO-d_6)

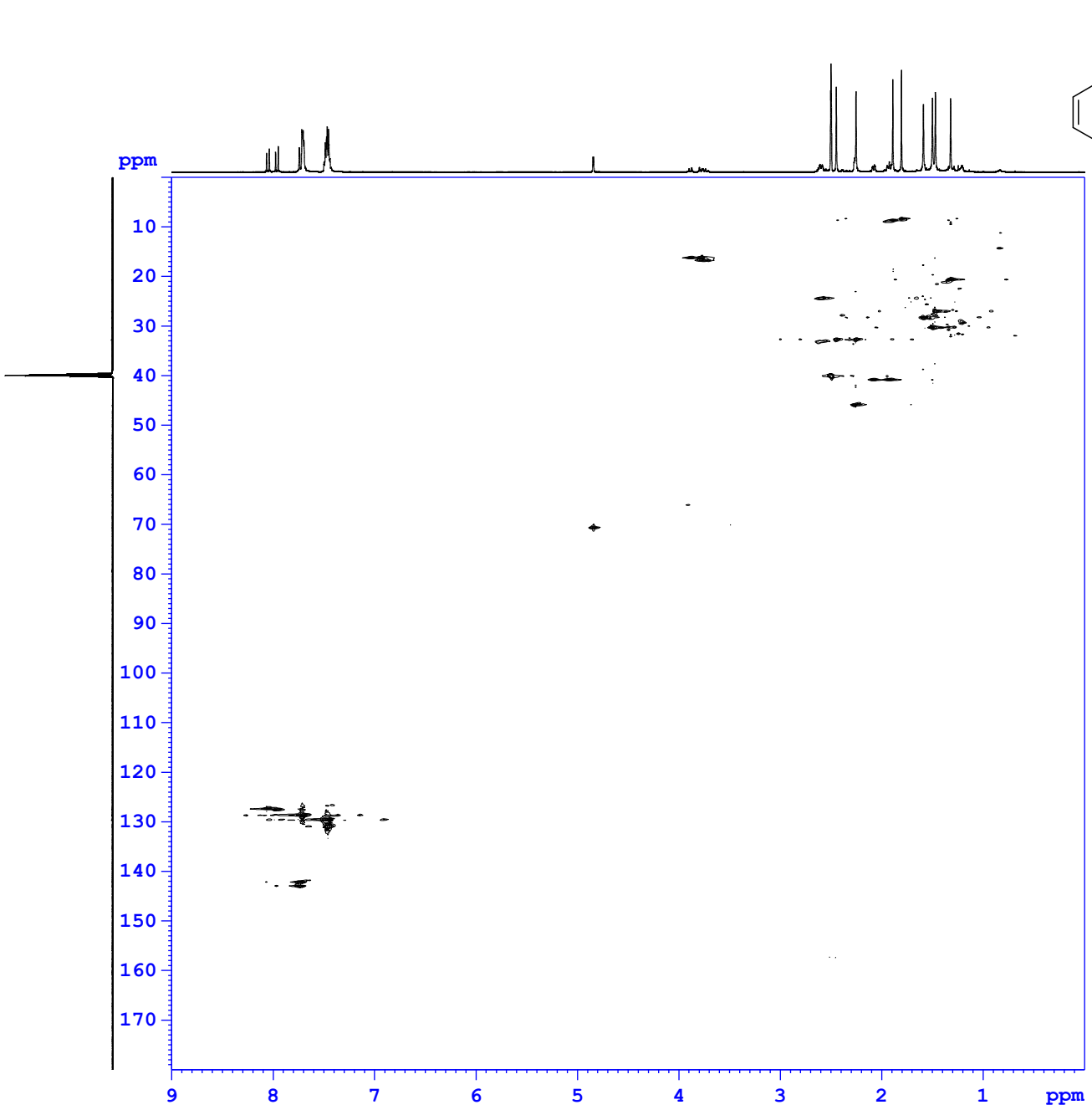
water suppressed at 3.54 ppm

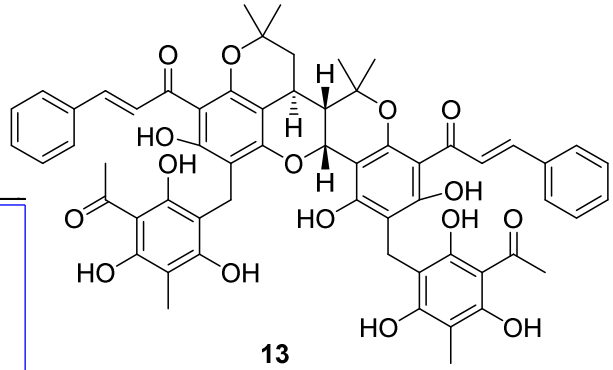






13
^{1}H-^{1}H COSY
DMSO-d_6

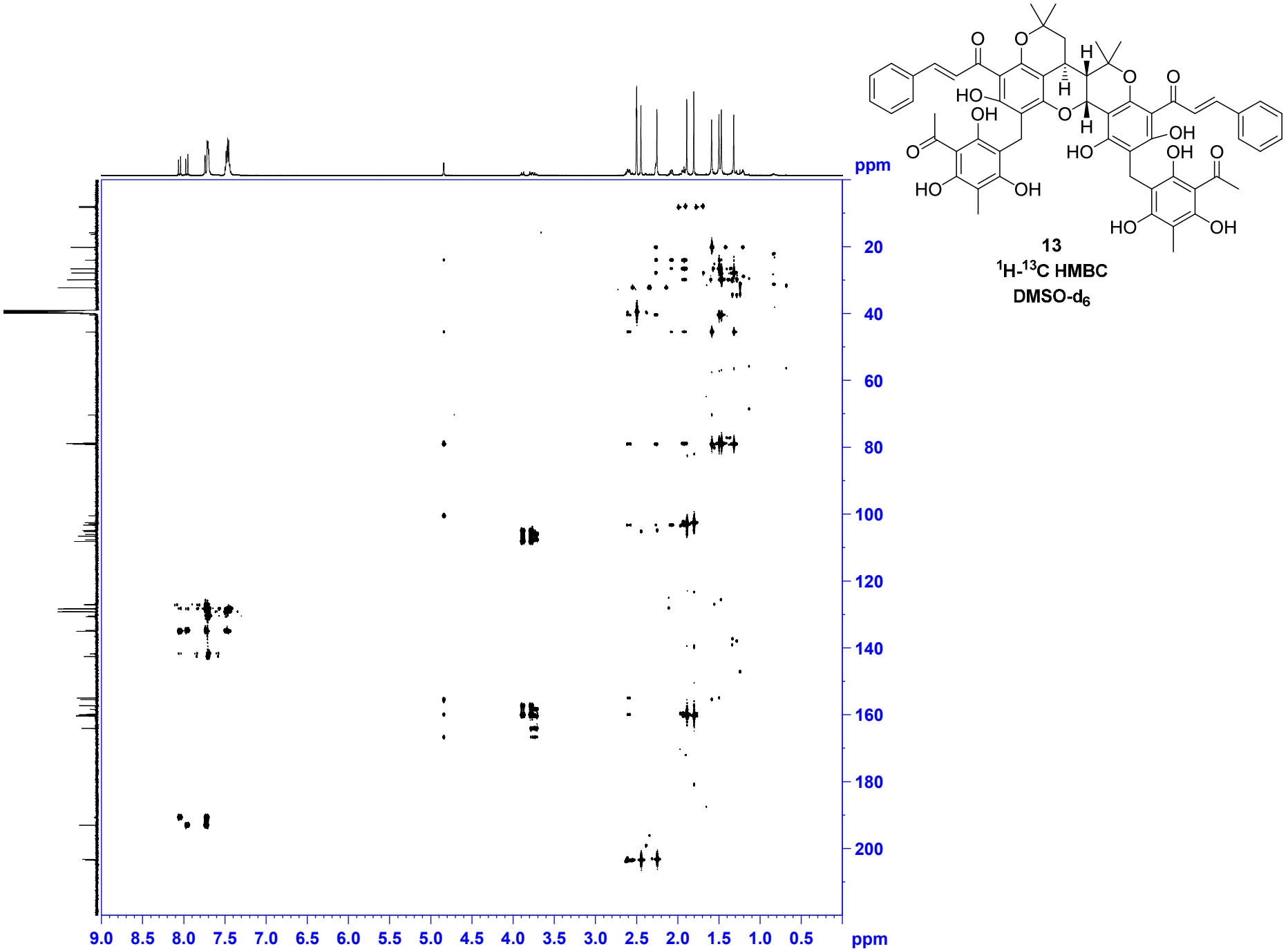




13

^{1}H-^{13}C HSQC

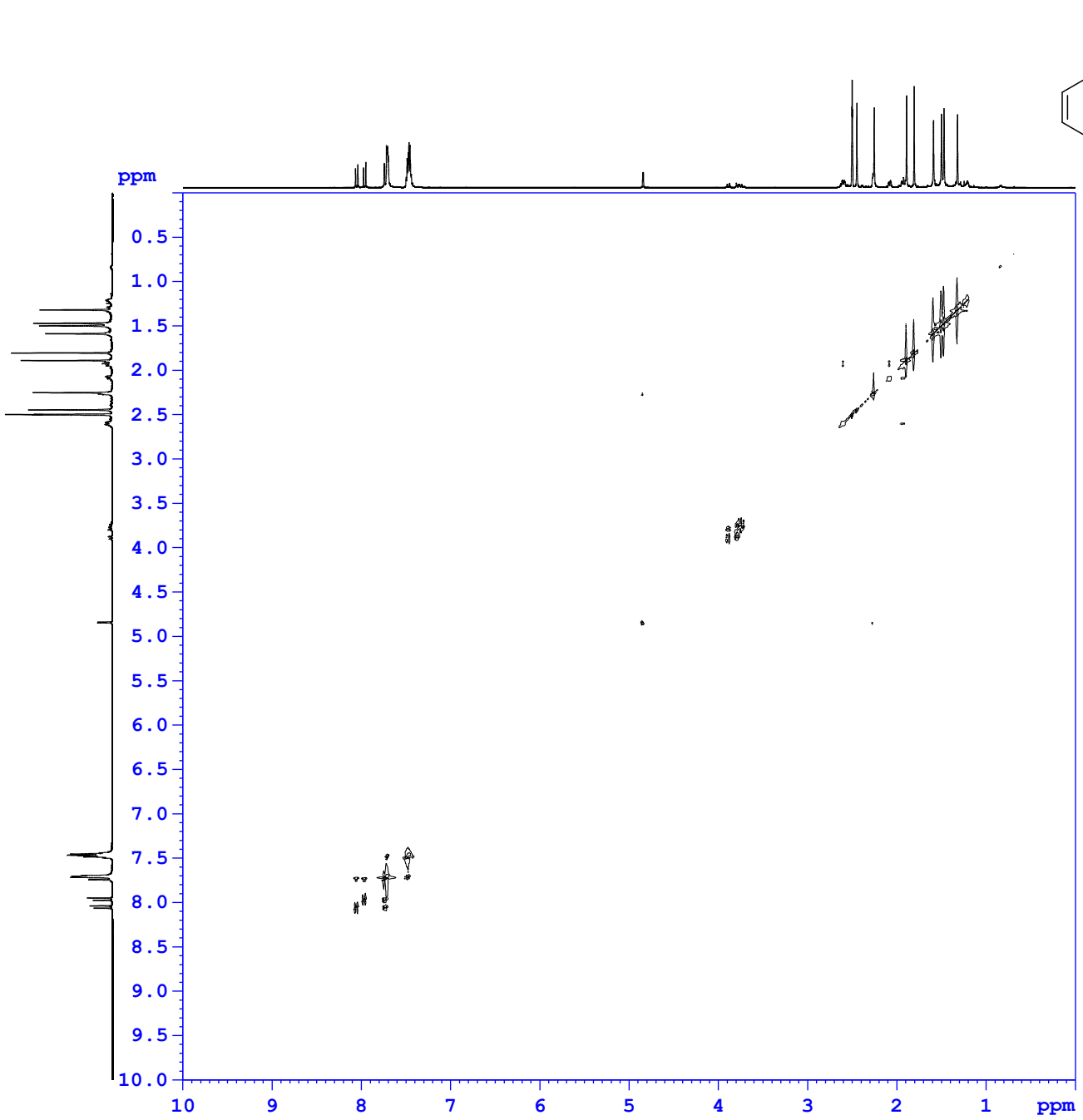
DMSO-d_6

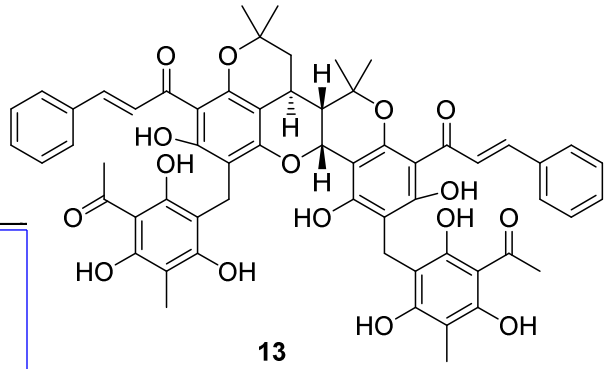


13

^{1}H-^{13}C HMBC

DMSO-d_6

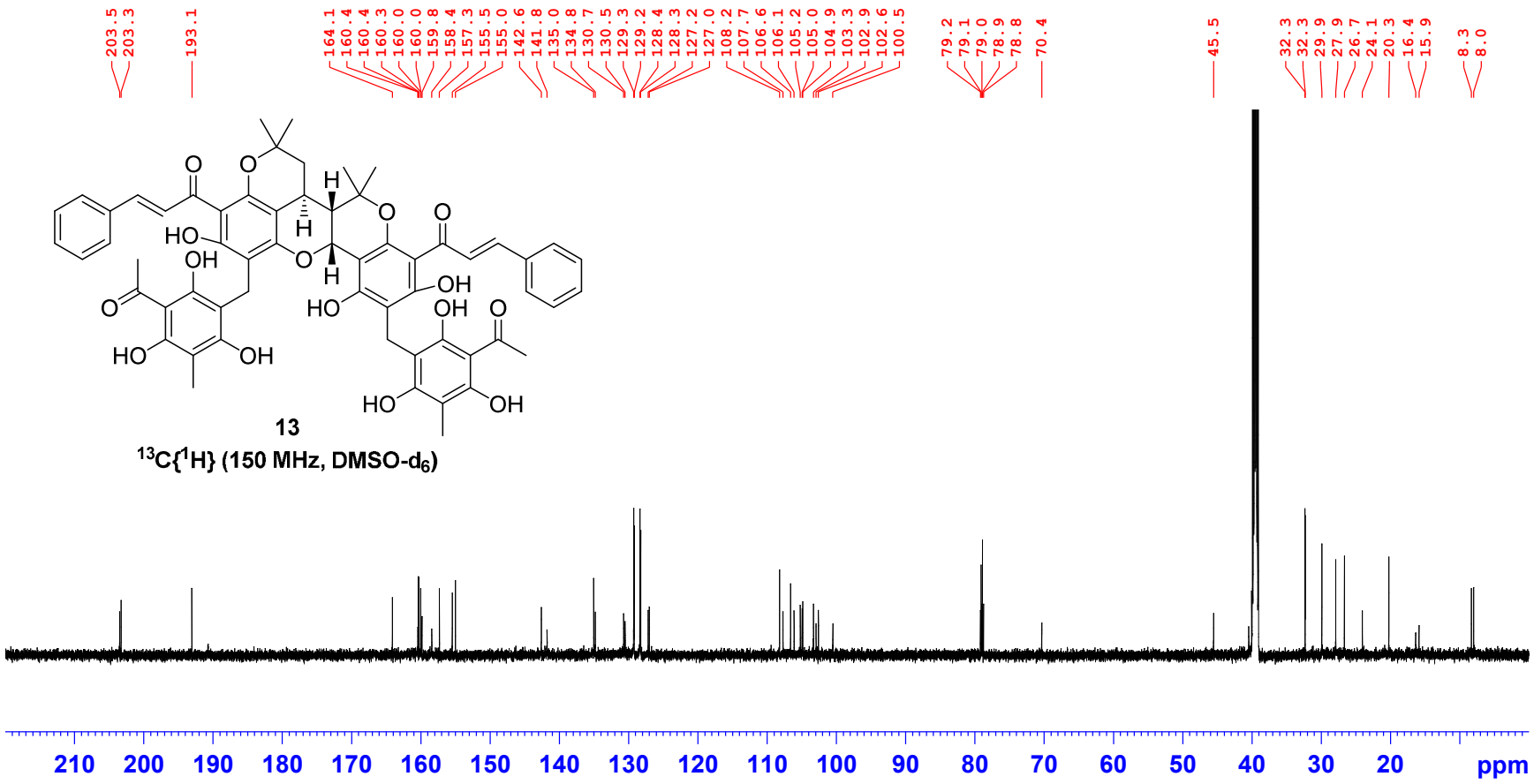




13

^{1}H-^{1}H ROESY

DMSO-d_6

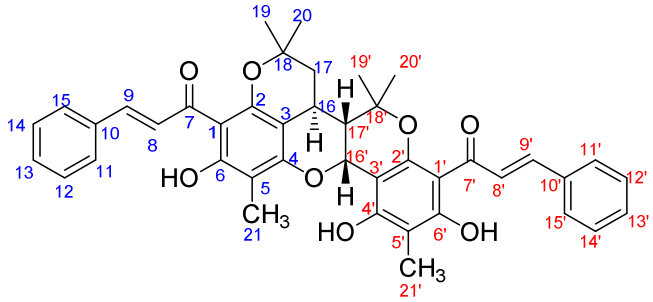


13

$^{13}C\{^{1}H\}$ (150 MHz, DMSO-d_6)

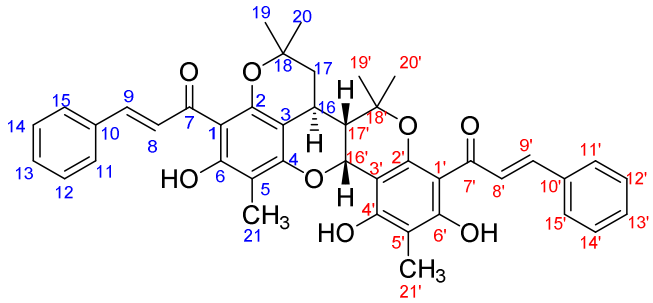
NMR comparison between literature and synthetic kamalachalcone A and rottlerin.

Table 1. Comparison of ^{1}H NMR of **kamalachalcone A** between literature[1] and synthetic compound.



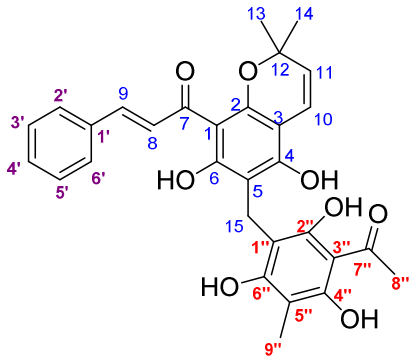
^{1}H	Literature[1] (ppm)	Synthetic (ppm)	$\Delta_{(literature - synthetic)}$ (ppm)
8, 8’	7.98, 8.00	7.97, 8.01	0.01, 0.01
9, 9’	7.78, 7.79	7.79, 7.75	-0.01, 0.04
11, 11’, 15, 15’	7.61	7.61	0.00
12-14, 12’-14’	7.40	7.42	-0.02
16	2.62	2.62	0.00
17α	1.96	1.96	0.00
17β	2.14	2.14	0.00
19	1.50	1.49	0.01
20	1.59	1.60	0.01
21	2.16	2.17	-0.01
16’	4.75	4.75	0.00
17’	2.25	2.25	0.00
19’	1.51	1.51	0.00
20’	1.68	1.67	0.01
21’	2.13	2.13	0.00

Table 2. Comparison of ^{13}C NMR of **kamalachalcone A** between literature[1] and synthetic compound.



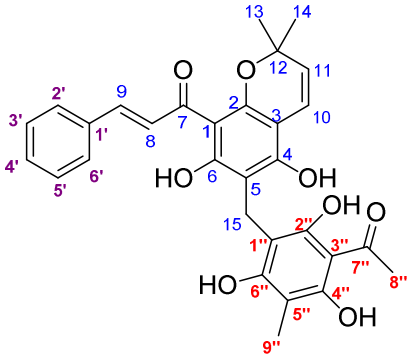
^{13}C	Literature[1] (ppm)	Synthetic (ppm)	$\Delta_{(literature - synthetic)}$ (ppm)	^{13}C	Literature[1] (ppm)	Synthetic (ppm)	$\Delta_{(literature - synthetic)}$ (ppm)
1	107.7	107.8	-0.1	1’	106.0	106.1	-0.1
2	154.4	154.5	-0.1	2’	153.8	153.9	-0.1
3	101.0	101.1	-0.1	3’	98.2	98.3	-0.1
4	158.5	158.7	-0.2	4’	160.5	160.6	-0.1
5	105.9	106.0	-0.1	5’	105.4	105.5	-0.1
6	162.9	163.0	-0.1	6’	166.4	166.5	-0.1
7	193.0	193.1	-0.1	7’	193.5	193.6	-0.1
8	127.8	127.9	-0.1	8’	127.8	127.8	0.0
9	141.9	142.1	-0.2	9’	142.1	142.2	-0.1
10	135.6	135.7	-0.1	10’	135.6	135.7	-0.1
11, 15	128.2	128.4	-0.2	11’, 15’	128.3	128.3	0.0
12, 14	129.0	129.1	-0.1	12’ 14’	129.0	129.1	-0.1
13	130.1	130.3	-0.2	13’	130.0	130.2	-0.2
16	24.4	24.5	-0.1	16’	70.3	70.5	-0.2
17	42.3	42.3	0.0	17’	47.4	47.5	-0.1
18	77.7	77.8	-0.1	18’	78.6	78.7	-0.1
19	27.0	27.1	-0.1	19’	20.5	20.6	-0.1
20	30.4	30.5	-0.1	20’	28.4	28.6	-0.2
21	7.5	7.6	-0.1	21’	7.3	7.4	-0.1

Table 3. Comparison of ^{1}H NMR of **rottlerin** between literature[2] and synthetic compound.



^{1}H	Literature[2] (ppm)	Synthetic (ppm)	$\Delta_{(literature - synthetic)}$ (ppm)
8	8.19	8.19	0.00
9	7.83	7.83	0.00
10	6.67	6.66	0.01
11	5.49	5.48	0.01
13, 14	1.53	1.53	0.00
15	3.81	3.81	0.00
2',4',6'	7.43	7.41	0.02
3', 5'	7.63	7.61	0.02
8''	2.71	2.71	0.00
9''	2.11	2.08	0.03
2 x OH	9.56	9.55	0.01
OH	16.51	16.51	0.00

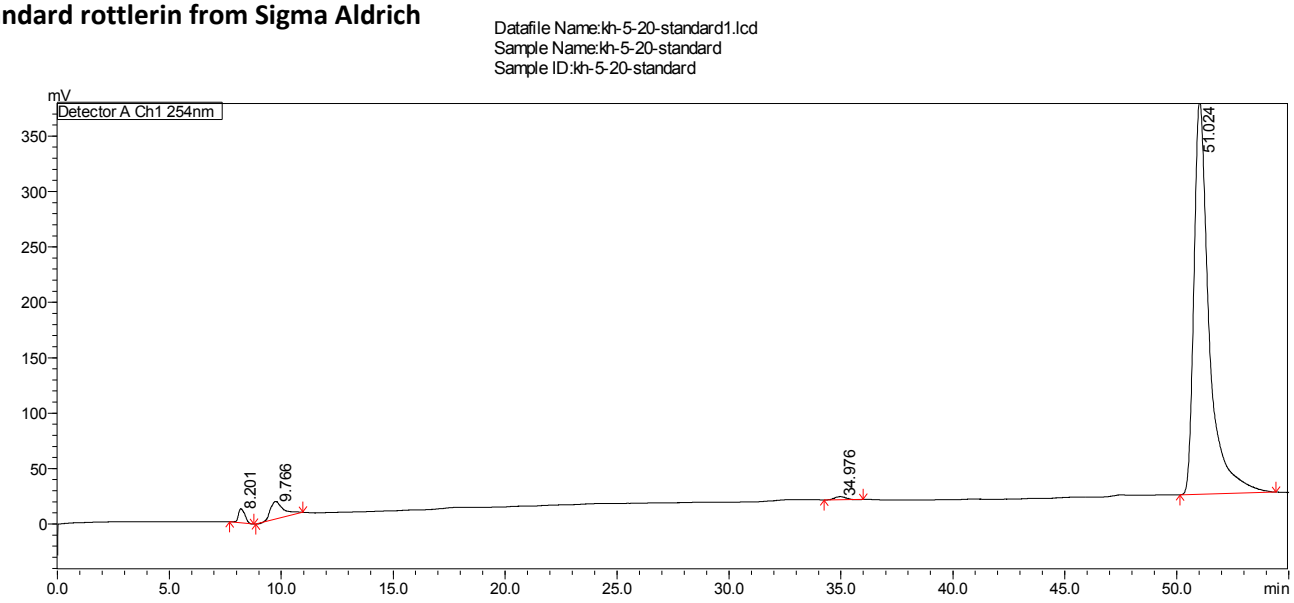
Table 4. Comparison of ^{13}C NMR of **rottlerin** between literature[3] and synthetic compound.



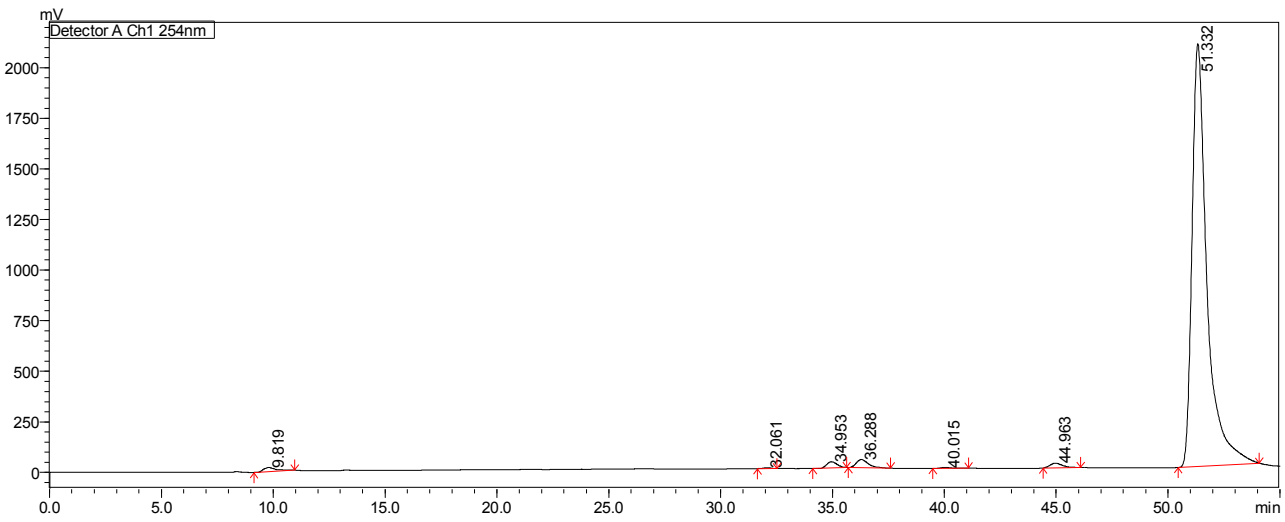
^{13}C	Literature[3] (ppm)	Synthetic (ppm)	$\Delta_{(literature - synthetic)}$ (ppm)
1	105.2	105.4	-0.2
2	155.1	155.6	-0.5
3	103.4	103.9	-0.5
4	158.3	158.9	-0.6
5	106.6	106.6	0.0
6	162.6	163.0	-0.4
7	192.6	193.0	-0.4
8	126.5	126.9	-0.4
9	143.1	143.5	-0.4
10	116.9	117.4	-0.5
11	124.9	125.2	-0.3
12	77.9	78.3	-0.4
13	27.7	28.2	-0.5
14	27.7	28.2	-0.5
15	15.9	16.0	-0.1
1’	135.1	135.6	-0.5
2’, 6’	128.2	128.5	-0.3
3’, 5’	128.2	129.2	-1.0
4’	130.1	130.5	-0.4
1’’	105.0	106.1	-1.1
2’’	158.3	159.7	-1.4
3’’	105.1	104.6	-0.5
4’’	159.2	156.6	2.6
5’’	103.5	102.0	1.5
6’’	159.9	160.8	-0.9
7’’	204.1	204.2	-0.1
8’’	32.6	32.7	-0.1
9’’	8.1	7.6	0.5

Comparison of HPLC chromatograms of synthetic rottlerin and rottlerin standard

Standard rottlerin from Sigma Aldrich



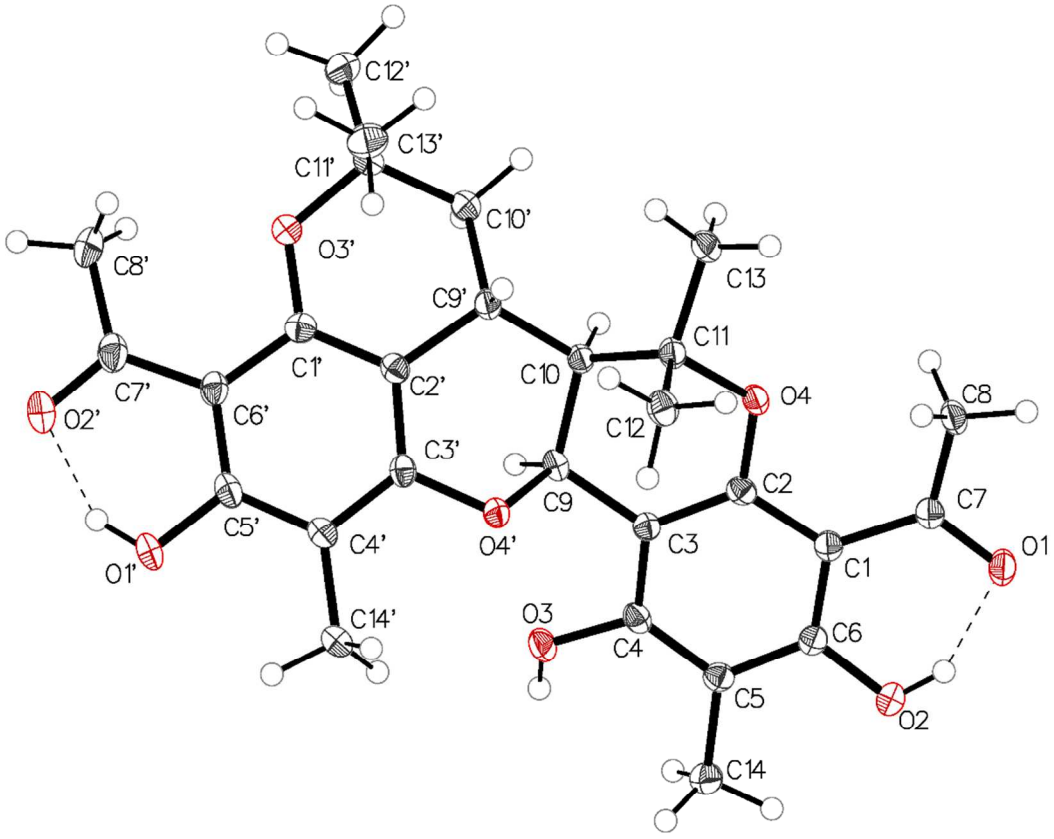
Synthetic rottlerin



X-ray crystallographic information

X-ray crystallography: Suitable single crystals of **12** and **kamalchalcone A** were selected under the polarizing microscope, mounted on a cryo loop consisting of a thin polymer tip with a wicking aperture. The X-ray diffraction measurements were carried out on CCD diffractometer at 150 K by using Microfocus Source with a Mo-Kα radiation (λ = 0.710723 Å) . The single crystal, mounted on the goniometer using cryo loops for intensity measurements, was coated with paraffin oil and then quickly transferred to the cold stream using a cryo stream attachment. Symmetry related absorption corrections using the program SADABS[4] were applied and the data were corrected for Lorentz and polarisation effects using Bruker APEX2[4] software. The structure was solved by Direct methods and the full-matrix least-square refinement was carried out using SHELXL[5] in Olex2.[6] The non-hydrogen atoms were refined anisotropically. The molecular graphic was generated using program Olex2.[4]

ORTEP diagram of **12** (thermal ellipsoids are drawn at 50% probability level)



ORTEP diagram of **kamalachalcone A** (thermal ellipsoids are drawn at 50% probability level)

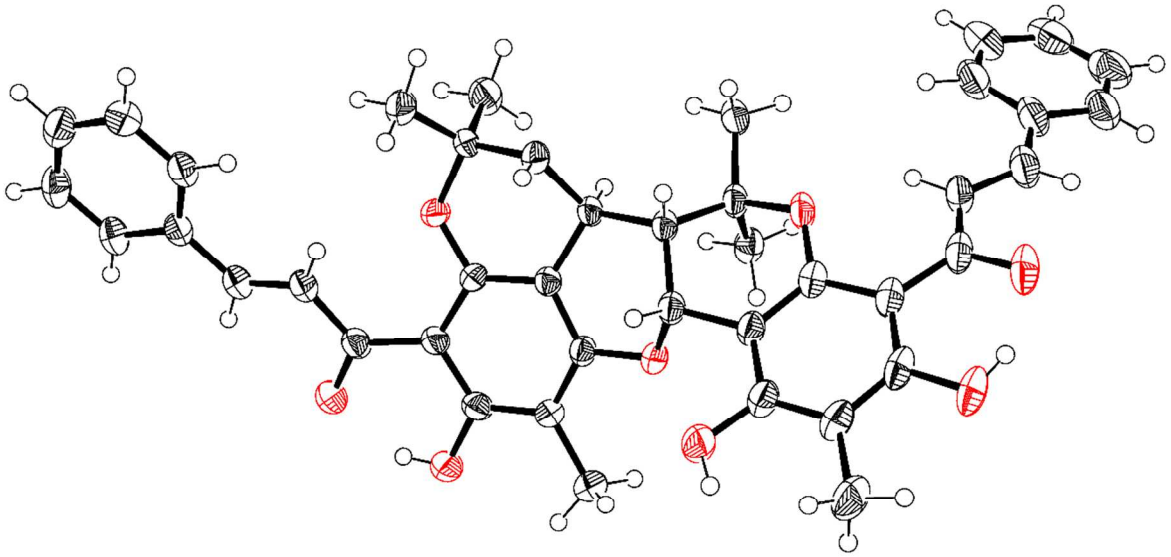


Table 5. Experimental details

	Compound **12**
Crystal data	
Chemical formula	$C_{28}H_{32}O_8 \cdot H_2O$
M_r	514.55
Crystal system, space group	Monoclinic, $P2_1/c$
Temperature (K)	150
a, b, c (Å)	16.4146 (10), 7.1564 (5), 21.2383 (13)
β (°)	102.908 (3)
V (Å^3)	2431.8 (3)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.11
Crystal size (mm)	0.13 × 0.12 × 0.06
Data collection	
Diffractometer	Bruker *APEX*-II CCD diffractometer
Absorption correction	Multi-scan *SADABS2012*/1 (Bruker,2012) was used for absorption correction. wR2(int) was 0.1606 before and 0.0577 after correction. The Ratio of minimum to maximum transmission is 0.8798. The λ/2 correction factor is 0.0015.
T_{min}, T_{max}	0.656, 0.746
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	20406, 5294, 4101
R_{int}	0.048
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.640
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.044, 0.132, 1.04
No. of reflections	5294
No. of parameters	356
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement

$\Delta\rangle_{max}$, $\Delta\rangle_{min}$ (e Å^{-3})	0.30, -0.27

Computer programs: *SAINT* v8.34A (Bruker, 2013), XL (Sheldrick, 2008), Olex2 (Dolomanov *et al.*, 2009).

The structural data have been deposited at the Cambridge Crystallographic Data Centre: (CCDC 1406110)

Table 6. Experimental details

	kamalachalcone A
Crystal data	
Chemical formula	$C_{42}H_{39}O_8 \cdot C_4H_8O$
M_r	743.83
Crystal system, space group	Triclinic, $P\bar{1}$
Temperature (K)	150
a, *b*, *c* (Å)	10.0335 (9), 12.8124 (12), 15.7773 (14)
α, β, γ (°)	91.419 (4), 106.952 (4), 91.256 (4)
V (Å^3)	1938.6 (3)
Z	2
Radiation type	Mo *K*α
μ (mm^{-1})	0.09
Crystal size (mm)	0.12 × 0.11 × 0.10
Data collection	
Diffractometer	Bruker *APEX*-II CCD diffractometer
Absorption correction	Multi-scan *SADABS2012*/1 (Bruker,2012) was used for absorption correction. wR2(int) was 0.1218 before and 0.0519 after correction. The Ratio of minimum to maximum transmission is 0.9308. The λ/2 correction factor is 0.0015.
T_{min}, T_{max}	0.694, 0.746
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	30680, 8345, 5565
R_{int}	0.041
(sin θ/λ)$_{max}$ (Å^{-1})	0.641
Refinement	

$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.059, 0.184, 1.05
No. of reflections	8345
No. of parameters	535
No. of restraints	60
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rangle_{max}$, $\Delta\rangle_{min}$ (e Å^{-3})	0.67, -0.34

Computer programs: *SAINT* v8.34A (Bruker, 2013), *SHELXL* (Sheldrick, 2008), Olex2 (Dolomanov *et al.*, 2009).

The structural data have been deposited at the Cambridge Crystallographic Data Centre: (CCDC 1406109)

Details of computational methods and results

DFT calculations were performed using the Gaussian 09 software package,[7] revision D01 with the B3LYP[8] and M06-2X[9] functionals.

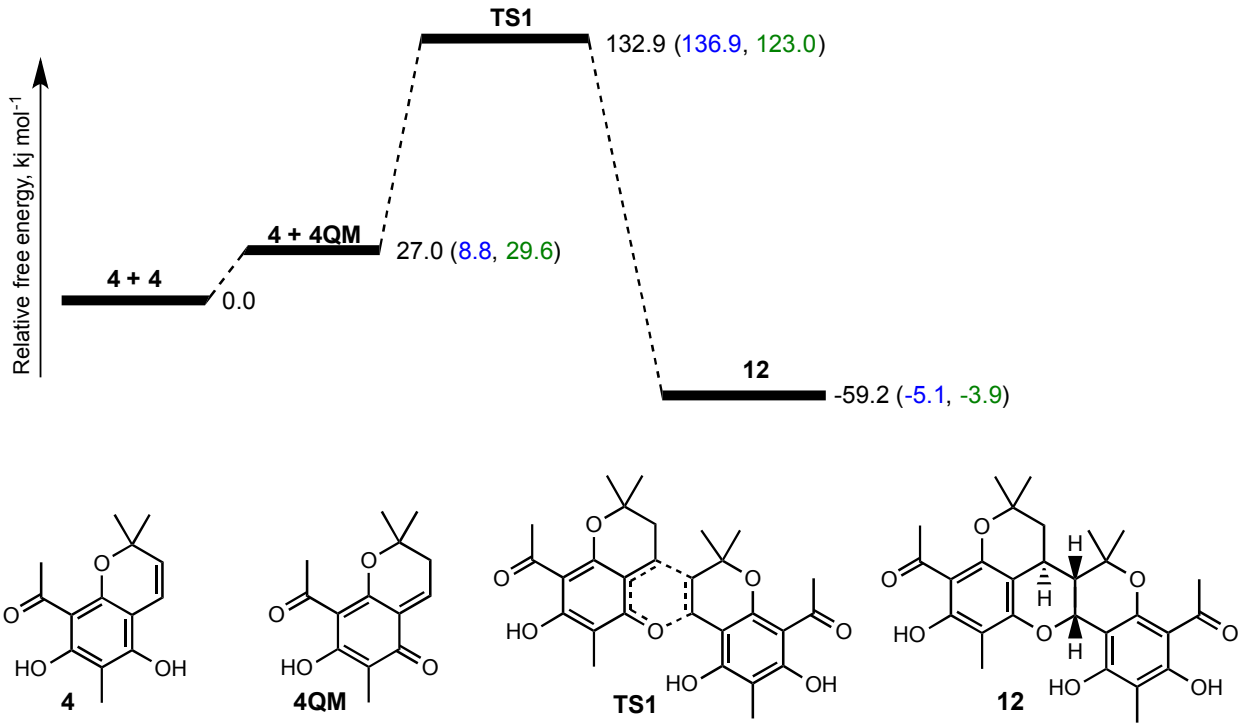
Geometry optimizations and frequency calculations were performed in vacuum using the B3LYP/6-31G(d) method,[10] using restricted closed-shell wavefunctions unless otherwise noted. The transition structures for the deprotonation/cyclisation step (**TS3**$^+$ in Scheme S2) and the rotation around the C-C bond in IM1 (**TS4**$^+$) were calculated in SMD MeOH solvent. All minimum energy structures were calculated without any symmetry constraints and were confirmed to be minima by calculating their normal vibrations within the harmonic approximation *a*nd observing that there were no imaginary frequencies. Transition structures were likewise confirmed to have one imaginary frequency and the validity of the key transition structures that lead to dimerization was confirmed using IRC calculations. Zero point vibrational energies were scaled by a factor of 0.977.[11] Free energies are calculated at 298.15 K.

Single point energy hybrid DFT calculations were also calculated using the M06-2X/6-31+G(d) and dispersion corrected B3LYP-D3/6-311+G(2df,2p) methods. Free energies of solvation were calculated using the SMD method of Truhlar et al,[12] methanol as solvent and the B3LYP/6-31G(d) method using the vacuum geometries was employed. Due to known difficulties with calculating the solvation energies of H^+, a recommended literature value for the free energy of solvation of H^+ in methanol of -1075.3 kJ mol^{-1} was used in the analysis.[13]

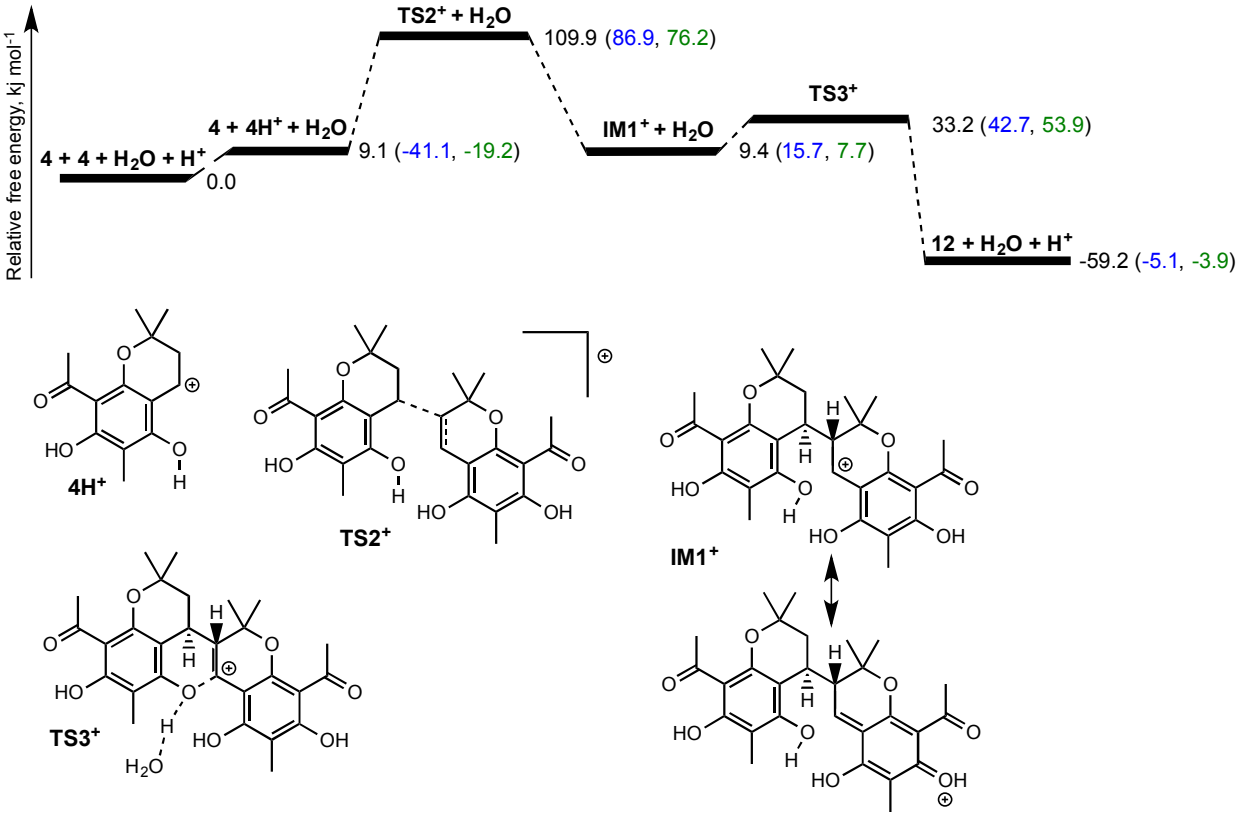
Table S1: DFT calculation summary

Species	Electronic Energy B3LYP/6-31G(d) (Hartree)	Zero point vibrational energy ZPVE (kJ mol^{-1})	Enthalpy correction, H (kJ mol^{-1})	Entropy correction, S (J K^{-1} mol^{-1})	Electronic Energy B3LYP-D3/ 6-311+G(2df,2p) (Hartree)	Electronic Energy M06-2X/ 6-31+G(d) (Hartree)	Electronic Energy B3LYP/6-31G(d) SMD MeOH solvent (Hartree)	ΔG solvation (kJ mol^{-1})
4	-844.025796	708.63	47.78	546.57	-844.392359	-843.702207	-844.043368	-46.14
4QM	-844.015537	709.27	47.84	551.75	-844.374192	-843.685001	-844.039688	-63.41
TS1	-1688.027549	1424.29	92.82	878.39	-1688.765991	-1687.381899	-1688.060593	-86.76
12	-1688.087139	1436.45	91.89	868.89	-1688.819813	-1687.460582	-1688.120046	-86.40
$4H^+$	-844.404919	739.24	48.55	555.50	-844.763149	-844.062223	-844.489515	-222.11
$TS2^+$	-1688.421185	1454.17	95.07	897.17	-1689.158385	-1687.765240	-1688.509328	-231.42
$IM1^+$	-1688.445285	1459.96	95.03	897.11	-1689.181475	-1687.800522	-1688.538608	-245.02
$TS3^+$	-1764.863548	1521.54	97.44	894.18	-1765.646434	-1764.194627	-1764.969075	-277.06
$TS4^+$	-1764.85204	1518.17	100.79	933.89	-1765.637935	-1764.177332	-1764.956609	-274.55
H^+	0.000000	0.00	6.20	108.84	0.000000	0.000000	-	-1075.29[a]

[a] - literature value.



Scheme S1: Free energy profile for uncatalyzed dimerization of 4 to form **12**. Energy values M06-2X/6-31+G(d)//B3LYP/6-31G(d) in SMD MeOH solvent using ZPVE, enthalpy and entropy values from B3LYP/6-31G(d) calculations. (Values in brackets: **blue: B3LYP/6-31G(d), green: B3LYP-D3/6-311+G(2df,2p)//B3LYP/6-31G(d)**)



Scheme S2: Free energy profile for proton catalyzed dimerization of 4 to form 12. Energy values M06-2X/6-31+G(d)//B3LYP/6-31G(d) in SMD MeOH solvent using ZPVE, enthalpy and entropy values from B3LYP/6-31G(d) calculations. (Values in brackets: blue: B3LYP/6-31G(d), green: B3LYP-D3/6-311+G(2df,2p)//B3LYP/6-31G(d))

Notes:

The protonation of 4 to $4H^+$ is predicted to be slightly exothermic using the B3LYP/6-31G(d) or B3LYP-D3/6-311+G(2df,2p)//B3LYP/6-31G(d) methodology. Experiments show 4 remains mostly unprotonated in the presence of excess H_3O^+ in MeOH.

Coordinates of selected optimized Geometries (B3LYP/6-31G(d))

Species: **4** (starting compound)

Energy (a.u.): -844.0257956
(B3LYP/6-31G(d))
charge 0

O	1.607400	0.510921	-0.275357
O	-1.434693	-3.106388	-0.074343
H	-2.385805	-3.293968	-0.041899
O	-3.105848	1.324277	0.112459
H	-2.729874	2.257169	0.093464
O	-1.507119	3.239599	0.004733
C	2.465465	-1.777721	-0.276812
C	2.740343	-0.342889	0.104150
C	0.334156	0.060392	-0.143618
C	3.923617	0.235031	-0.674197
H	3.744555	0.163198	-1.751128
H	4.837324	-0.319679	-0.435112
H	4.079919	1.286601	-0.413026
C	1.206943	-2.228222	-0.351495
C	0.087416	-1.318566	-0.153069
C	-0.716299	1.015858	-0.069389
C	2.945233	-0.202776	1.621278
H	3.137851	0.841827	1.891537
H	3.799072	-0.808505	1.944795
H	2.059093	-0.551337	2.160669
C	-0.525321	2.472403	-0.081242
C	-1.247331	-1.757484	-0.059518
C	0.833925	3.127457	-0.202163
H	1.346864	2.813833	-1.115374
C	-2.056234	0.499945	0.025287
C	-2.327627	-0.878795	0.039795
C	-3.742778	-1.393602	0.152168
H	-4.054410	-1.953903	-0.741992
H	-4.436902	-0.560610	0.267776
H	-3.873815	-2.052193	1.023312
H	0.677843	4.208129	-0.207152
H	1.483225	2.846714	0.632091
H	0.987851	-3.264507	-0.586495
H	3.320243	-2.426236	-0.448450

Species: **4QM** (o-quinone methide)

Energy (a.u.): -844.0155366

charge 0

O	1.409614	-3.138791	-0.010003
O	-1.582372	0.584640	-0.210154
O	3.163469	1.201831	0.078562
H	2.823586	2.139913	0.064628
O	1.612106	3.189372	0.002057
C	-0.732924	3.158400	-0.162938
H	-1.275397	2.865240	-1.066163
C	-1.145920	-2.151168	-0.405429
H	-0.930261	-3.212987	-0.499362
C	-0.107332	-1.327312	-0.162706
C	-0.322767	0.113669	-0.122536
C	2.364265	-0.966499	0.035457
C	1.278627	-1.909000	-0.033724
C	-2.728832	-0.281790	0.105926
C	-2.539001	-1.642121	-0.579235
H	-2.757904	-1.560071	-1.655683
H	-3.267367	-2.357733	-0.178549
C	2.106526	0.384717	0.012812
C	0.607475	2.459805	-0.068408
C	0.746993	0.988614	-0.064514
C	3.777817	-1.475048	0.138071
H	4.393145	-1.122109	-0.698174
H	3.767711	-2.566872	0.135280
H	4.265302	-1.126471	1.056585
C	-2.818929	-0.411035	1.630976
H	-1.956474	-0.942634	2.043223
H	-3.723737	-0.962772	1.907988
H	-2.868565	0.580835	2.090568
C	-3.931334	0.469909	-0.457799
H	-4.044341	1.443151	0.029638
H	-4.846026	-0.107976	-0.288615
H	-3.817002	0.631470	-1.534212
H	-0.538867	4.232672	-0.172304
H	-1.374329	2.903072	0.685749

Species: **TS1** (neutral TS)

Energy (a.u.): -1688.027549

charge 0

O	0.268380	1.610609	-0.927324
O	3.729823	-1.520247	-0.100022
O	-2.659414	-1.717802	0.311074
O	4.472133	3.184821	0.461819
H	5.365148	2.794403	0.694082
O	6.325107	1.543865	0.873813
O	-1.652378	2.933225	0.220163
H	-0.790805	2.566661	-0.170048
O	-6.064594	1.547913	-0.491516
O	-6.619480	-0.887253	-0.631869
C	6.224295	-0.796007	0.678643
H	5.685631	-1.450642	1.368997
C	0.978270	-1.026244	-0.617992
H	0.181427	-0.810012	-1.321543
C	1.928169	0.029311	-0.442499
C	3.275880	-0.235684	-0.098723
C	2.384755	2.465800	-0.271705
C	1.487296	1.409719	-0.582939
C	3.042522	-2.473771	-0.961984
C	1.548336	-2.438808	-0.605799
H	1.455196	-2.880818	0.390279
H	0.996754	-3.086597	-1.293879
C	3.674379	2.158586	0.144903
C	-0.380602	-1.008405	1.006472
H	0.422414	-1.168100	1.723166
C	5.586562	0.576873	0.594227
C	4.182908	0.792749	0.220063
C	-1.485926	-2.074225	1.120397
C	-3.086433	-0.439458	0.230998
C	-1.947051	-2.126314	2.592182
H	-2.285789	-1.144161	2.934708
H	-1.121710	-2.446285	3.237273
H	-2.769823	-2.840313	2.704131
C	1.934195	3.899007	-0.392929
H	1.530298	4.287592	0.552525
H	1.145453	3.982876	-1.145697
H	2.768441	4.546942	-0.673800
C	-0.872517	0.307929	0.925490
H	-0.252285	1.121360	1.271800
C	-2.172592	0.611270	0.473842
C	-4.428247	-0.182610	-0.114785
C	-1.166440	-3.488682	0.640492
H	-2.034222	-4.130759	0.819549
H	-0.318311	-3.907129	1.189107
H	-0.945866	-3.506172	-0.427872
C	-5.443223	-1.213978	-0.378347
C	-2.573886	1.966682	0.207830
C	-5.134481	-2.695220	-0.368406
H	-4.806985	-3.020749	0.623406
C	3.321034	-2.132417	-2.431377
H	2.911198	-1.157324	-2.706765
H	2.871240	-2.889463	-3.083246
H	4.399862	-2.119526	-2.615990
C	-4.810450	1.211809	-0.210134
C	3.652078	-3.826531	-0.596164
H	4.721637	-3.841370	-0.828000
H	3.166593	-4.628101	-1.162890
H	3.528853	-4.029994	0.472454
C	-3.902126	2.277729	-0.068250
C	-4.362820	3.693219	-0.297328
H	-3.507198	4.369787	-0.311862
H	-5.051651	4.017228	0.492267
H	-4.905533	3.780619	-1.244551
H	-6.048207	-3.222973	-0.648357
H	-4.326942	-2.940788	-1.063489
H	7.252741	-0.655268	1.017443
H	6.218779	-1.294403	-0.295027
H	-6.576268	0.688461	-0.604363

Species: **12** (final product)

Energy (a.u.): -1688.0871388

charge 0

O	0.030918	-1.013232	-0.686537
O	-3.998422	1.212953	0.609653
O	2.668262	1.705839	-0.301405
O	-4.050020	-3.332345	-0.924037
H	-5.014687	-3.172175	-0.700083
O	-6.156817	-2.220221	-0.162200
O	1.698273	-2.729428	1.058794
H	2.137595	-3.550668	1.330745
O	6.209960	-1.408582	0.525844
H	6.710892	-0.574233	0.266507
O	6.723806	0.927196	-0.168400
C	-6.397494	-0.037491	0.673383
H	-6.025103	0.287265	1.648701
C	-1.167562	1.446239	-0.012319
H	-1.234410	1.955975	-0.982202
C	-1.961459	0.159675	-0.128756
C	-3.333282	0.129498	0.115527
C	-2.014454	-2.203896	-0.832781
C	-1.331013	-1.023479	-0.557634
C	-3.350349	2.513482	0.718052
C	-1.854508	2.344839	1.022465
H	-1.743139	1.900196	2.019937
H	-1.386174	3.335835	1.054566
C	-3.407881	-2.193123	-0.640366
C	0.351466	1.226025	0.276774
H	0.590450	1.664837	1.255685
C	-5.553754	-1.159905	0.104838
C	-4.106425	-1.047146	-0.127602
C	1.289894	1.927627	-0.736281
C	3.077492	0.454194	0.030111
C	1.148229	3.450334	-0.675559
H	1.294805	3.813561	0.346888
H	0.159881	3.766418	-1.022542
H	1.898135	3.922260	-1.317974
C	-1.311131	-3.456177	-1.286179
H	-1.390611	-3.592967	-2.372752
H	-1.763381	-4.337585	-0.822492
H	-0.251911	-3.411315	-1.025001
C	0.680147	-0.265336	0.381588
H	0.262508	-0.654017	1.318856
C	2.153257	-0.538965	0.348454
C	4.484966	0.221202	0.080386
C	1.170709	1.424674	-2.182916
H	1.894124	1.956846	-2.809207
H	0.171487	1.613034	-2.587151
H	1.359310	0.352172	-2.254119
C	5.511911	1.225811	-0.226019
C	2.640491	-1.808323	0.723999
C	5.193142	2.653366	-0.616978
H	4.596998	3.154233	0.150422
C	-3.608617	3.267882	-0.594323
H	-3.211141	2.725977	-1.457444
H	-3.147092	4.261668	-0.566036
H	-4.685137	3.393465	-0.747235
C	4.912895	-1.096604	0.458424
C	-4.065560	3.201657	1.882095
H	-5.141206	3.262952	1.688777
H	-3.681502	4.218512	2.017449
H	-3.912981	2.645267	2.812350
C	3.998686	-2.117393	0.774087
C	4.471990	-3.496261	1.167665
H	4.212042	-3.745234	2.207269
H	5.557420	-3.558311	1.083839
H	4.048506	-4.276963	0.519195
H	6.143135	3.173051	-0.756894
H	4.608535	2.688638	-1.540751
H	-7.419325	-0.411520	0.763950
H	-6.376425	0.840949	0.022242

Species: **4H**$^{+}$ (protonated starting compound)

Energy (a.u.): -844.4049193

charge +1

O	1.584983	0.574619	-0.156956
O	-1.406452	-3.114359	-0.040708
H	-2.343088	-3.375771	-0.000173
O	-3.087236	1.277874	0.081786
H	-2.727565	2.244447	0.059927
O	-1.595261	3.218403	-0.009380
C	2.515576	-1.662829	-0.582386
C	2.756064	-0.316790	0.110783
C	0.342060	0.131116	-0.103291
C	3.938345	0.430937	-0.491925
H	3.791441	0.602200	-1.562516
H	4.851430	-0.157834	-0.358356
H	4.080772	1.395658	0.002932
C	1.121010	-2.154140	-0.410524
C	0.091183	-1.308974	-0.152263
C	-0.718329	1.036196	-0.060534
C	2.877564	-0.450783	1.629659
H	2.959155	0.536939	2.091762
H	3.782453	-1.015505	1.876339
H	2.022582	-0.973299	2.069984
C	-0.571906	2.517751	-0.073030
C	-1.283158	-1.781474	-0.040435
C	0.757894	3.213734	-0.169615
H	1.303478	2.904165	-1.066126
C	-2.060737	0.481374	0.017307
C	-2.346158	-0.920037	0.045507
C	-3.766371	-1.420295	0.155476
H	-4.083328	-1.943324	-0.756370
H	-4.456704	-0.590705	0.307864
H	-3.886580	-2.103514	1.006460
H	0.570005	4.288043	-0.196953
H	1.390597	2.969269	0.689469
H	0.916044	-3.212809	-0.543333
H	2.714449	-1.590896	-1.664606
H	3.228375	-2.404068	-0.202593

Species: **TS2^{+}** (charged TS)

Energy (a.u.): -1688.4211853

charge +1

O	-0.493419	1.329870	1.656590
O	-3.833053	-1.412600	-0.258998
O	2.822679	-1.767500	-0.535944
O	-4.123024	3.338090	-0.602741
H	-4.960461	3.046244	-1.095122
O	-5.892445	1.921196	-1.605469
O	1.580364	2.752769	0.183945
H	1.951339	3.651925	0.195094
O	6.151457	1.613120	-0.102800
H	6.723286	0.784059	-0.246252
O	6.842147	-0.729250	-0.496355
C	-6.026490	-0.430341	-1.592798
H	-5.373991	-1.080507	-2.182518
C	-1.260484	-1.172566	0.892290
H	-0.582583	-1.069181	1.728376
C	-2.080932	-0.039947	0.615892
C	-3.328416	-0.181834	-0.054901
C	-2.331250	2.417680	0.559455
C	-1.649585	1.280128	0.953188
C	-3.418037	-2.498321	0.646750
C	-1.880712	-2.541645	0.652616
H	-1.568099	-2.945479	-0.314859
H	-1.541218	-3.251578	1.414078
C	-3.511896	2.238484	-0.204011
C	0.424821	-1.192745	-0.480955
H	-0.278378	-1.467327	-1.263353
C	-5.341698	0.867546	-1.243166
C	-4.056281	0.936616	-0.505771
C	1.481117	-2.240198	-0.099402
C	3.194359	-0.502273	-0.317850
C	1.307222	-3.544064	-0.875181
H	1.293367	-3.355737	-1.952839
H	0.370671	-4.033795	-0.594452
H	2.128428	-4.231120	-0.652937
C	-1.852132	3.802481	0.920329
H	-1.493807	3.842903	1.956278
H	-2.665020	4.523116	0.822667
H	-1.040093	4.140300	0.262351
C	0.864419	0.135226	-0.493226
H	0.176706	0.914752	-0.804264
C	2.184423	0.499767	-0.188032
C	4.561000	-0.167703	-0.331733
C	1.610638	-2.490022	1.408625
H	2.477883	-3.129167	1.598436
H	0.728254	-3.006041	1.796295
H	1.739957	-1.556670	1.965525
C	5.668157	-1.134946	-0.529770
C	2.591802	1.853955	0.014928
C	5.443735	-2.604675	-0.780929
H	4.824686	-2.765499	-1.668299
C	-4.025227	-2.250104	2.031196
H	-3.640045	-1.339038	2.497573
H	-3.795628	-3.092910	2.691412
H	-5.113281	-2.166191	1.955161
C	4.895495	1.221975	-0.132839
C	-3.994672	-3.760638	0.011748
H	-5.087261	-3.714395	-0.010301
H	-3.702495	-4.641572	0.592290
H	-3.632215	-3.882442	-1.013655
C	3.916087	2.235192	0.061381
C	4.323142	3.668987	0.304166
H	4.064784	4.319677	-0.542800
H	5.402261	3.739722	0.441884
H	3.852417	4.077238	1.208779
H	6.421189	-3.070652	-0.914906
H	4.922108	-3.071134	0.060338
H	-6.926668	-0.186557	-2.159313
H	-6.294596	-0.986680	-0.689670
H	-0.070776	2.202079	1.561171

Species: **IM1$^+$** (charged intermediate)

Energy (a.u.): -1688.4452845

charge +1

O	-0.529719	0.776110	1.944540
O	-3.720037	-1.292201	-0.890891
O	2.807946	-1.650177	0.227752
O	-4.322384	3.227483	0.547524
H	-5.141498	3.076394	-0.021209
O	-5.994960	2.139030	-0.931134
O	1.537839	2.841657	-0.600113
H	1.866516	3.716177	-0.871822
O	6.070104	1.602715	-0.895091
H	6.645568	0.759730	-0.787027
O	6.782474	-0.714699	-0.489975
C	-5.953911	-0.044235	-1.799383
H	-5.263301	-0.387977	-2.574167
C	-1.100937	-1.455659	0.400397
H	-1.065942	-1.870482	1.415556
C	-2.012093	-0.236220	0.430610
C	-3.249845	-0.203065	-0.232996
C	-2.443599	2.052947	1.273624
C	-1.694080	0.884810	1.223488
C	-3.209118	-2.605305	-0.510698
C	-1.683208	-2.523874	-0.552835
H	-1.408557	-2.275171	-1.585916
H	-1.254659	-3.507658	-0.336743
C	-3.627912	2.093166	0.511017
C	0.411775	-1.188520	-0.016392
H	0.509662	-1.609463	-1.034180
C	-5.355192	1.072259	-0.975707
C	-4.070997	0.960316	-0.246885
C	1.467574	-1.936471	0.838307
C	3.167355	-0.414588	-0.084673
C	1.358716	-3.453214	0.720474
H	1.339286	-3.774136	-0.325179
H	0.450086	-3.806529	1.215232
H	2.211660	-3.927625	1.213750
C	-2.012345	3.231042	2.114334
H	-1.987083	2.990495	3.186841
H	-2.714529	4.055686	1.988414
H	-1.018604	3.604534	1.824909
C	0.827426	0.226988	-0.216014
H	0.074241	0.955762	-0.493224
C	2.141069	0.599292	-0.235876
C	4.511255	-0.118533	-0.333048
C	1.562082	-1.502686	2.302567
H	2.372539	-2.052665	2.789673
H	0.632648	-1.725721	2.831643
H	1.748757	-0.432275	2.404600
C	5.623932	-1.101177	-0.262959
C	2.546723	1.958188	-0.541108
C	5.417749	-2.555736	0.065539
H	4.727951	-3.027762	-0.640490
C	-3.767159	-2.987582	0.865748
H	-3.472136	-2.276744	1.643136
H	-3.410628	-3.982233	1.154945
H	-4.860305	-3.016409	0.831912
C	4.831452	1.256920	-0.669475
C	-3.733717	-3.547512	-1.592805
H	-4.827618	-3.540870	-1.606904
H	-3.400472	-4.572164	-1.398774
H	-3.374578	-3.244681	-2.581386
C	3.860050	2.298984	-0.756278
C	4.268624	3.716495	-1.078895
H	3.893551	4.034544	-2.060761
H	5.354562	3.807334	-1.104559
H	3.901481	4.423668	-0.323321
H	6.390995	-3.047041	0.023892
H	4.983517	-2.673863	1.063091
H	-6.869720	0.339111	-2.252633
H	-6.183641	-0.911959	-1.174291
H	-0.389884	1.598471	2.443608

Species: **TS3**$^{+}$ (charged deprotonation TS)

Energy (a.u.): -1764.863548

charge +1

O	0.156615	-0.893116	0.963953
O	4.012001	1.343908	-0.614722
O	-2.655743	1.819400	0.239335
O	4.215331	-3.323388	0.415598
H	5.151629	-3.122782	0.106235
O	6.225843	-2.115521	-0.411810
O	-1.619472	-2.608503	-1.051296
H	-1.983118	-3.422826	-1.442142
O	-6.144469	-1.239789	-0.859492
H	-6.659898	-0.399875	-0.630166
O	-6.699661	1.088943	-0.195169
C	6.407486	0.161880	-0.952717
H	5.985012	0.590040	-1.866381
C	1.206018	1.495621	0.171454
H	1.218527	1.909432	1.185989
C	2.041554	0.224039	0.197587
C	3.392344	0.226712	-0.174681
C	2.180426	-2.203994	0.693087
C	1.496711	-0.991693	0.638135
C	3.369983	2.661140	-0.485883
C	1.876157	2.508517	-0.768076
H	1.750652	2.175704	-1.806111
H	1.395787	3.487155	-0.678374
C	3.539525	-2.163377	0.331591
C	-0.309185	1.312900	-0.210792
H	-0.458307	1.782536	-1.195848
C	5.607731	-1.026013	-0.482156
C	4.183469	-0.964299	-0.116048
C	-1.286096	2.026548	0.759827
C	-3.063708	0.596633	-0.118363
C	-1.120617	3.542677	0.713057
H	-1.183033	3.914144	-0.314789
H	-0.155162	3.835111	1.135660
H	-1.905960	4.021218	1.306623
C	1.529491	-3.500744	1.103397
H	2.173812	-4.344553	0.851704
H	0.573771	-3.644426	0.589514
H	1.336467	-3.541932	2.182901
C	-0.728070	-0.105946	-0.442332
H	-0.145384	-0.652845	-1.177559
C	-2.122514	-0.418319	-0.405283
C	-4.454931	0.371019	-0.279663
C	-1.285120	1.519946	2.206389
H	-2.019537	2.091994	2.782465
H	-0.306920	1.665310	2.673374
H	-1.542571	0.460819	2.277877
C	-5.490992	1.388090	-0.050065
C	-2.591653	-1.700439	-0.816749
C	-5.187059	2.807205	0.351512
H	-4.548812	3.299148	-0.388746
C	3.678754	3.197741	0.915051
H	3.314953	2.529101	1.701491
H	3.207532	4.177205	1.053586
H	4.759518	3.317129	1.045327
C	-4.854813	-0.947925	-0.695605
C	4.042839	3.513932	-1.558058
H	5.124215	3.564396	-1.392153
H	3.645023	4.533779	-1.526223
H	3.860552	3.101436	-2.556226
C	-3.942627	-1.996297	-0.940387
C	-4.435509	-3.367851	-1.332091
H	-4.403774	-3.523345	-2.418730
H	-5.468785	-3.511351	-1.009836
H	-3.838284	-4.160639	-0.865096
H	-6.135441	3.343076	0.435739
H	-4.658027	2.842350	1.308455
H	7.428632	-0.177934	-1.142799
H	6.417089	0.955520	-0.200201
H	-0.345610	-1.707238	1.364144
O	-1.379240	-2.580097	2.107526
H	-0.926281	-3.026796	2.844871
H	-1.625488	-3.300965	1.501215

Species: **TS4**$^{+}$ (rotation about C-C bond in **IM1**)

Energy (a.u.): -1764.85204

charge +1

O	1.053148	2.548712	-1.265365
O	3.251108	-1.481122	-0.134070
O	-2.221907	-1.531622	0.456118
O	4.564157	2.675902	1.905845
H	5.199433	2.032936	2.346345
O	5.719948	0.552912	2.541497
O	-2.982527	2.592225	-1.742349
H	-3.637883	3.294567	-1.897423
O	-6.378679	0.694215	0.905643
H	-6.523480	-0.137392	1.493999
O	-6.033039	-1.425557	2.095794
C	5.240054	-1.621644	1.778781
H	4.322189	-2.181844	1.974364
C	1.076081	-0.288400	-1.443740
H	0.777533	0.322161	-2.299309
C	2.084660	0.516233	-0.633891
C	3.092399	-0.138623	0.074453
C	2.846566	2.654668	0.324143
C	2.011689	1.917266	-0.512827
C	3.142986	-1.896246	-1.535008
C	1.710346	-1.591194	-2.028478
H	1.096451	-2.460946	-1.809987
H	1.731920	-1.512328	-3.120641
C	3.801624	1.952797	1.086674
C	-0.259671	-0.439550	-0.553703
H	0.051307	-0.172383	0.470507
C	5.001051	-0.128523	1.789373
C	3.960642	0.531905	0.972714
C	-0.997434	-1.797989	-0.394845
C	-3.042340	-0.529395	0.208083
C	-0.238882	-2.782440	0.492128
H	-0.085314	-2.349873	1.485172
H	0.742444	-3.019159	0.081691
H	-0.805175	-3.711903	0.600507
C	2.727537	4.157348	0.422392
H	2.960225	4.654891	-0.530456
H	3.430630	4.540977	1.162105
H	1.722066	4.474245	0.734872
C	-1.245092	0.623009	-0.936974
H	-0.862702	1.502643	-1.445202
C	-2.564388	0.572973	-0.610117
C	-4.320043	-0.505183	0.771542
C	-1.545416	-2.425318	-1.679323
H	-2.187125	-3.273507	-1.423821
H	-0.743420	-2.797203	-2.318530
H	-2.132314	-1.711321	-2.264739
C	-4.871525	-1.549997	1.672996
C	-3.486481	1.650025	-0.934180
C	-4.084006	-2.755168	2.110041
H	-3.152587	-2.462824	2.604014
C	4.213800	-1.187103	-2.376150
H	4.043223	-0.109308	-2.443023
H	4.211190	-1.593240	-3.393060
H	5.206526	-1.354471	-1.946953
C	-5.167263	0.624088	0.429214
C	3.404555	-3.401659	-1.511802
H	4.431267	-3.611315	-1.197847
H	3.258825	-3.826003	-2.510698
H	2.726406	-3.909459	-0.818119
C	-4.764096	1.689864	-0.433062
C	-5.711083	2.817781	-0.766387
H	-5.336787	3.783009	-0.400017
H	-6.683563	2.652985	-0.302677
H	-5.876664	2.899192	-1.848831
H	-4.708127	-3.331169	2.794848
H	-3.807613	-3.373337	1.250131
H	5.988621	-1.839572	2.542656
H	5.607395	-1.950586	0.801831
H	1.159798	3.509073	-1.168902

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