Supporting Information for

Targeted Isolation of Two Disesquiterpenoids Macrocephadiolides A and B from *Ainsliaea macrocephala* using Molecular Networking-based Dereplication Strategy

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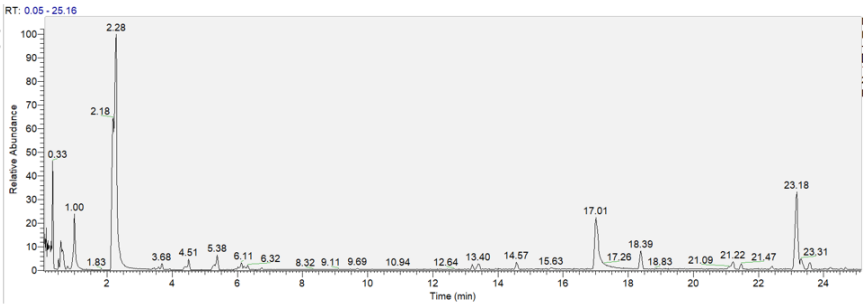
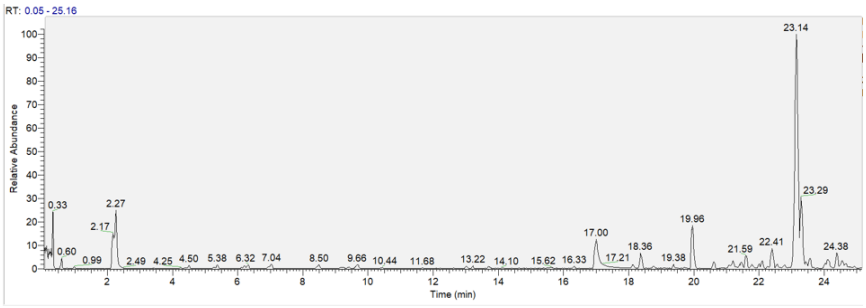
Scheme S1. UHPLC-MS chromatograms that were used for molecular networking

Extract



Fr. PE



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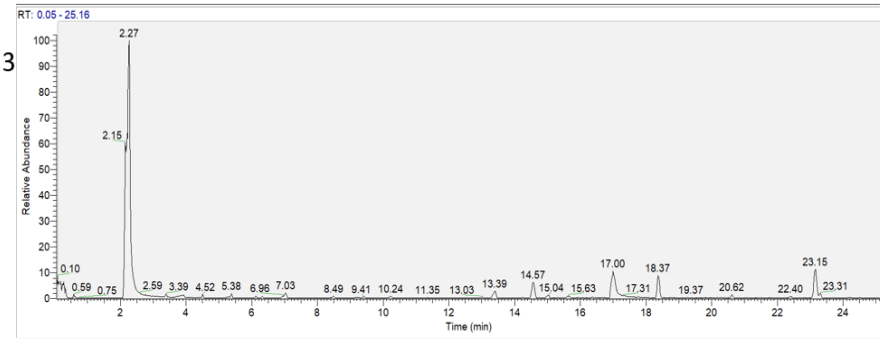

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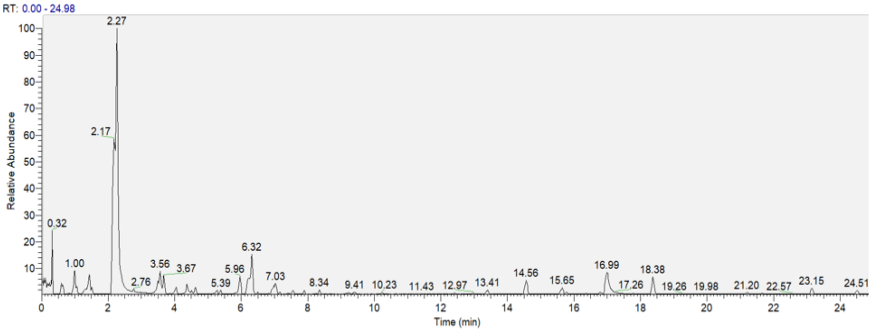

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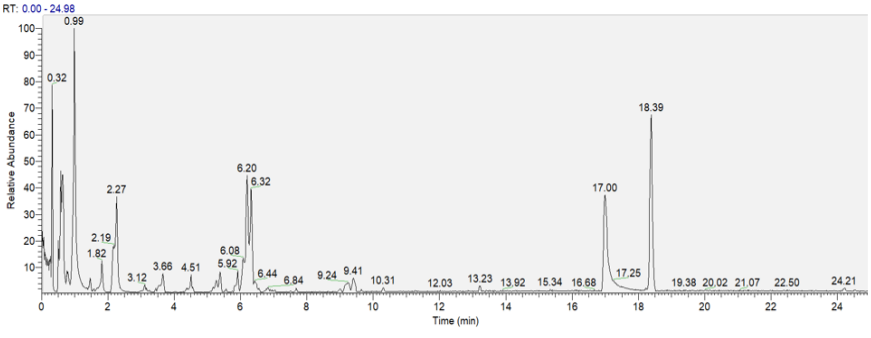


Table S1 Characterization of disesquiterpenoids from *A. macrocephala* by MN.

No.	m/z	δ_{ppm}	t_R	Molecular Formula	Ion description	Identification
1	521.21674	-1.540	14.13	$C_{30}H_{32}O_8$	$[M+H]^+$	Macrocephadiolide A
2	523.23260	-1.133	14.97	$C_{30}H_{34}O_8$	$[M+H]^+$	Macrocephadiolide B
3	520.23254	-0.844	13.79	$C_{30}H_{30}O_7$	$[M+NH_4]^+$	Gochnatiolide A
4	485.19531	-1.144	13.34	$C_{30}H_{30}O_7$	$[M+H-H_2O]^+$	Gochnatiolide B
5	491.24268	-0.275	14.73	$C_{30}H_{36}O_7$	$[M+H-H_2O]^+$	Ainsliadimer C
6	507.23740	-0.650	15.65	$C_{30}H_{34}O_7$	$[M+H]^+$	Ainsliadimer A
7	524.26434	0.116	15.28	$C_{30}H_{34}O_7$	$[M+NH_4]^+$	Ainsliadimer J

These MS data were directly from the MN and they were not identical with the HRESIMS data in the following part, which were collected with pure compounds.

Table S2. X-ray crystallographic data for **1**

Identification code	Cu 20180655_0m
Empirical formula	$C_{30}H_{32}O_8$
Formula weight	520.55
Temperature/K	173
Crystal system	monoclinic
Space group	$P2_1$
a/Å	8.8559(7)
b/Å	9.4486(9)
c/Å	15.3519(13)
α/°	90
β/°	94.432(3)
γ/°	90
Volume/Å^3	1280.74(19)
Z	2
ρ_{calc}g/cm^3	1.350
μ/mm^{-1}	0.804
F(000)	552.0
Crystal size/mm^3	0.25 × 0.15 × 0.08
Radiation	Cu Kα (λ = 1.54178)
2Θ range for data collection/°	5.774 to 127.998
Index ranges	$-10 \le h \le 8$, $-10 \le k \le 10$, $-17 \le l \le 16$
Reflections collected	14193
Independent reflections	3934 [R_{int}= 0.0281, R_{sigma}= 0.0245]
Data/restraints/parameters	3934/1/343
Goodness-of-fit on F^2	1.066
Final R indexes [I>=2σ (I)]	R_1= 0.0292, wR_2= 0.0767
Final R indexes [all data]	R_1= 0.0295, wR_2= 0.0769
Largest diff. peak/hole / e Å^{-3}	0.49/-0.17
Flack parameter	0.05(6)

Fig. S1. IR spectrum of compound **1**

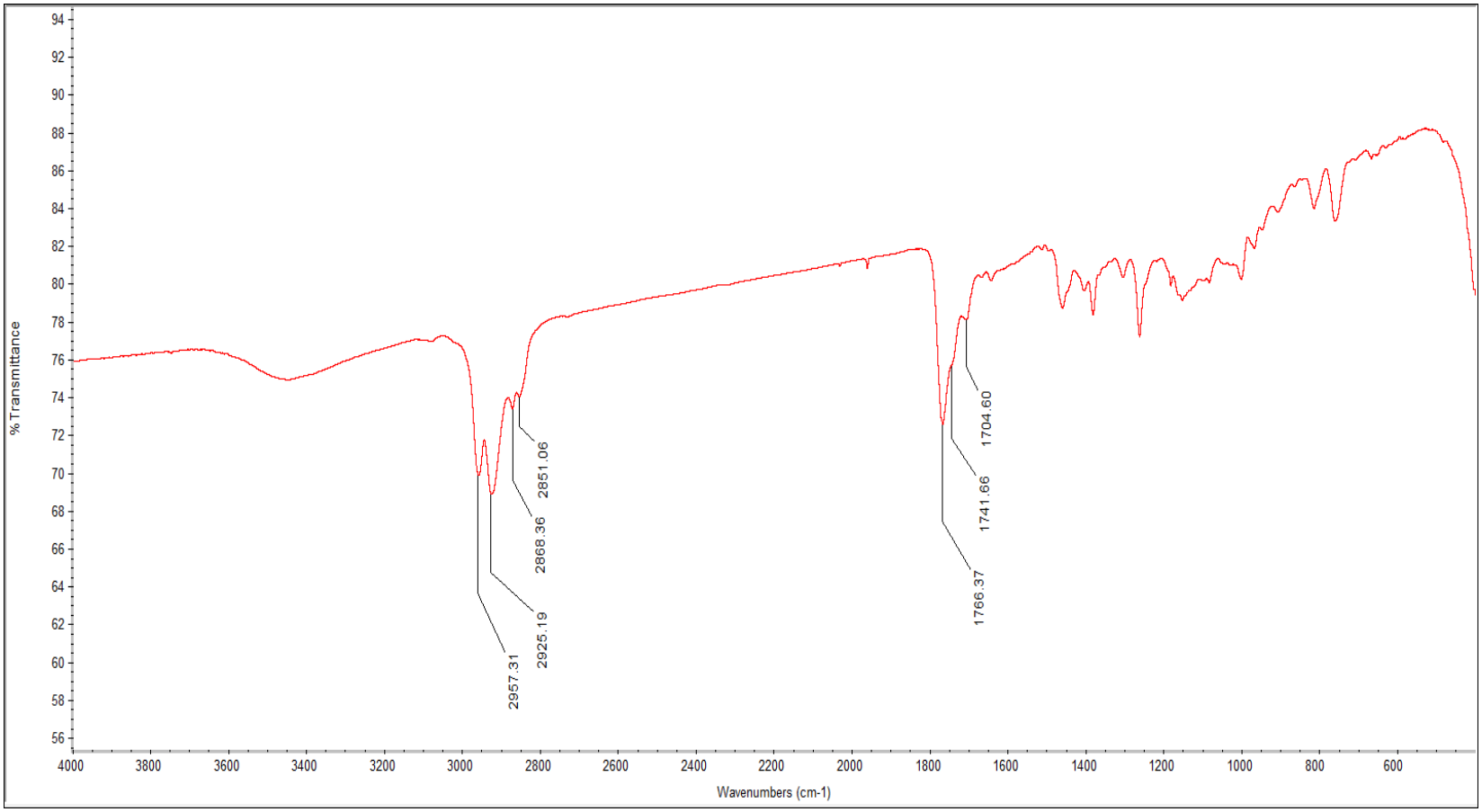


Fig. S2. HRESIMS spectrum of compound **1**

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

286 formula(e) evaluated with 3 results within limits (up to 50 closest results for each mass)

Elements Used:

C: 0-100 H: 0-100 O: 0-50 Na: 0-1

Minimum:				**-1.5**				
Maximum:		**5.0**	**10.0**	**50.0**				
Mass	**Calc. Mass**	**mDa**	**PPM**	**DBE**	**i-FIT**	**Norm**	**Conf(%)**	**Formula**
543.1996	**543.1995**	**0.1**	**0.2**	**14.5**	**221.7**	**0.156**	**85.59**	**C30 H32 O8 Na**
	543.2019	**-2.3**	**-4.2**	**17.5**	**223.6**	**1.985**	**13.74**	**C32 H31 O8**
	543.1960	**3.6**	**6.6**	**26.5**	**226.6**	**4.999**	**0.67**	**C39 H27 O3**

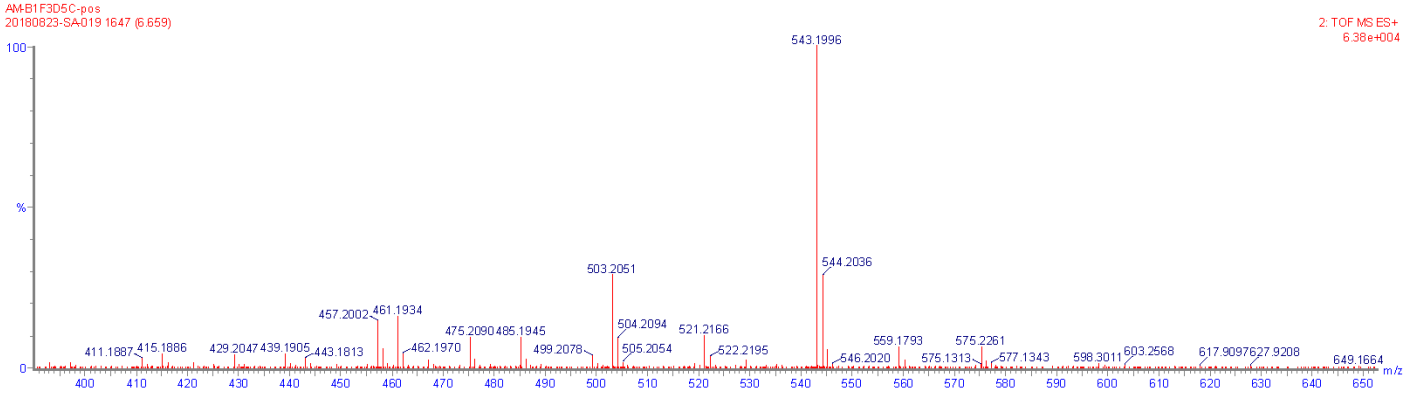
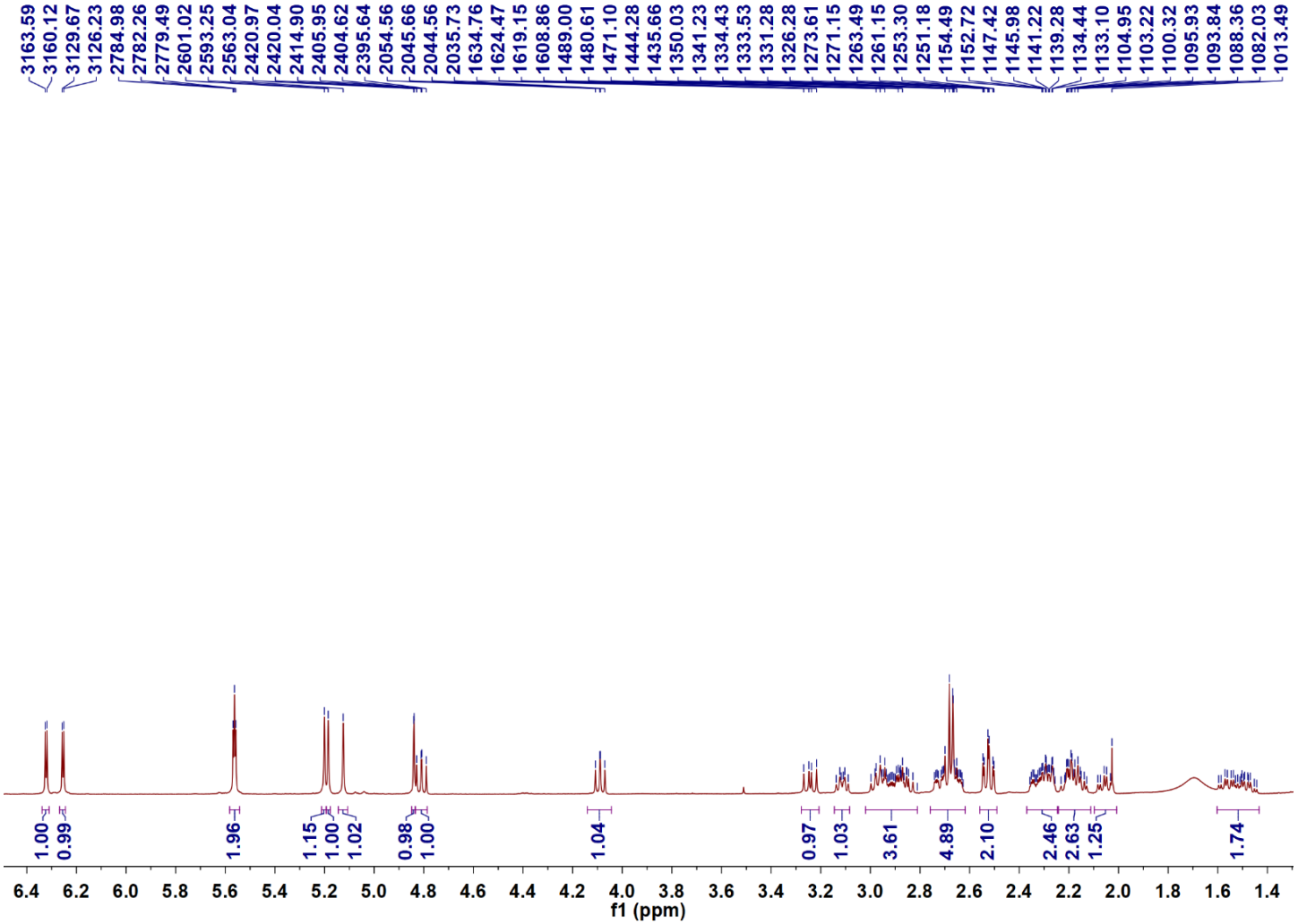


Fig. S3. ^{1}H NMR spectrum of compound **1** in $CDCl_3$



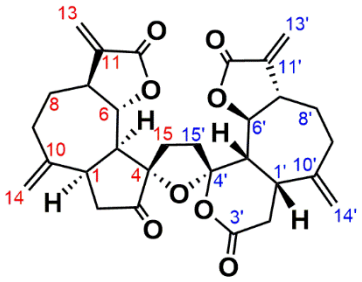
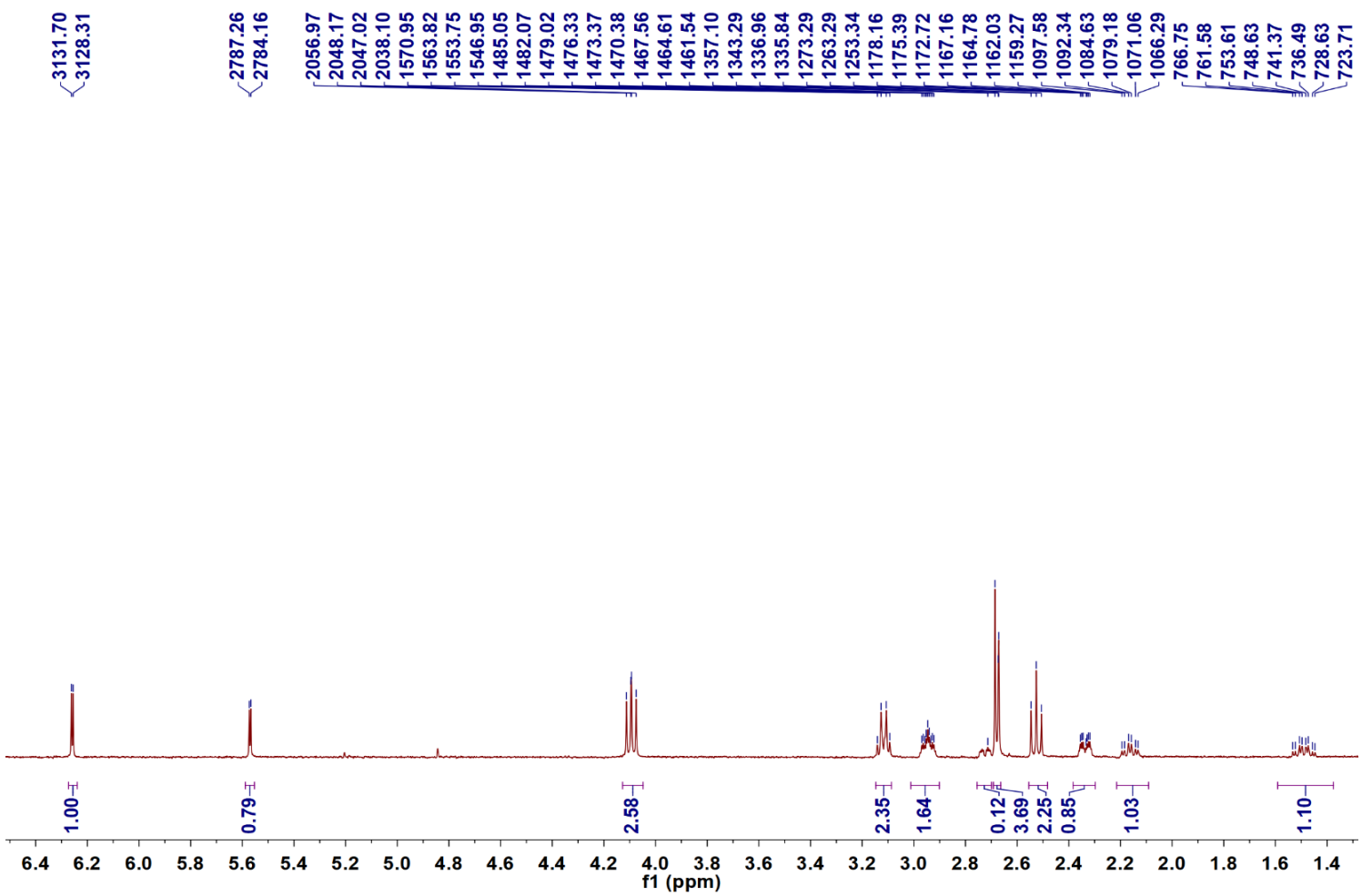


Fig. S4. 1DTOCSY (4.095 PPM) spectrum of compound **1** in $CDCl_3$



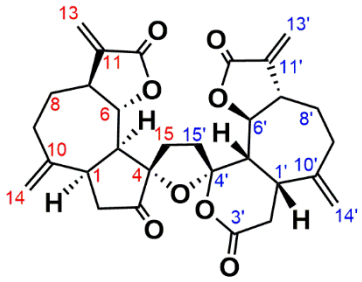
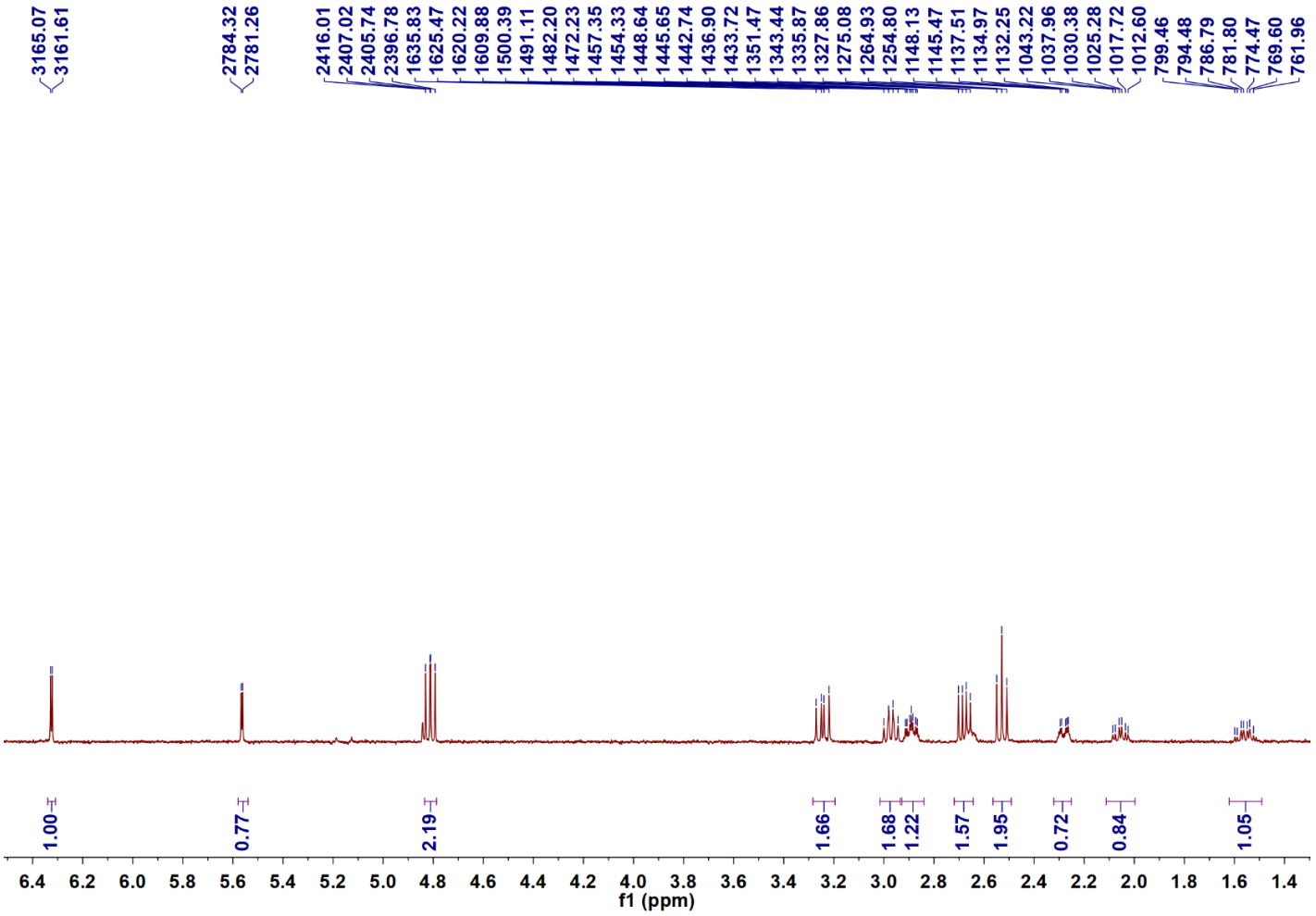


Fig. S5. 1DTOCSY (4.812 PPM) spectrum of compound **1** in CDCl3



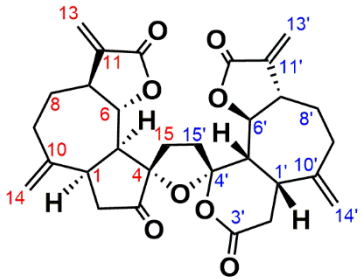
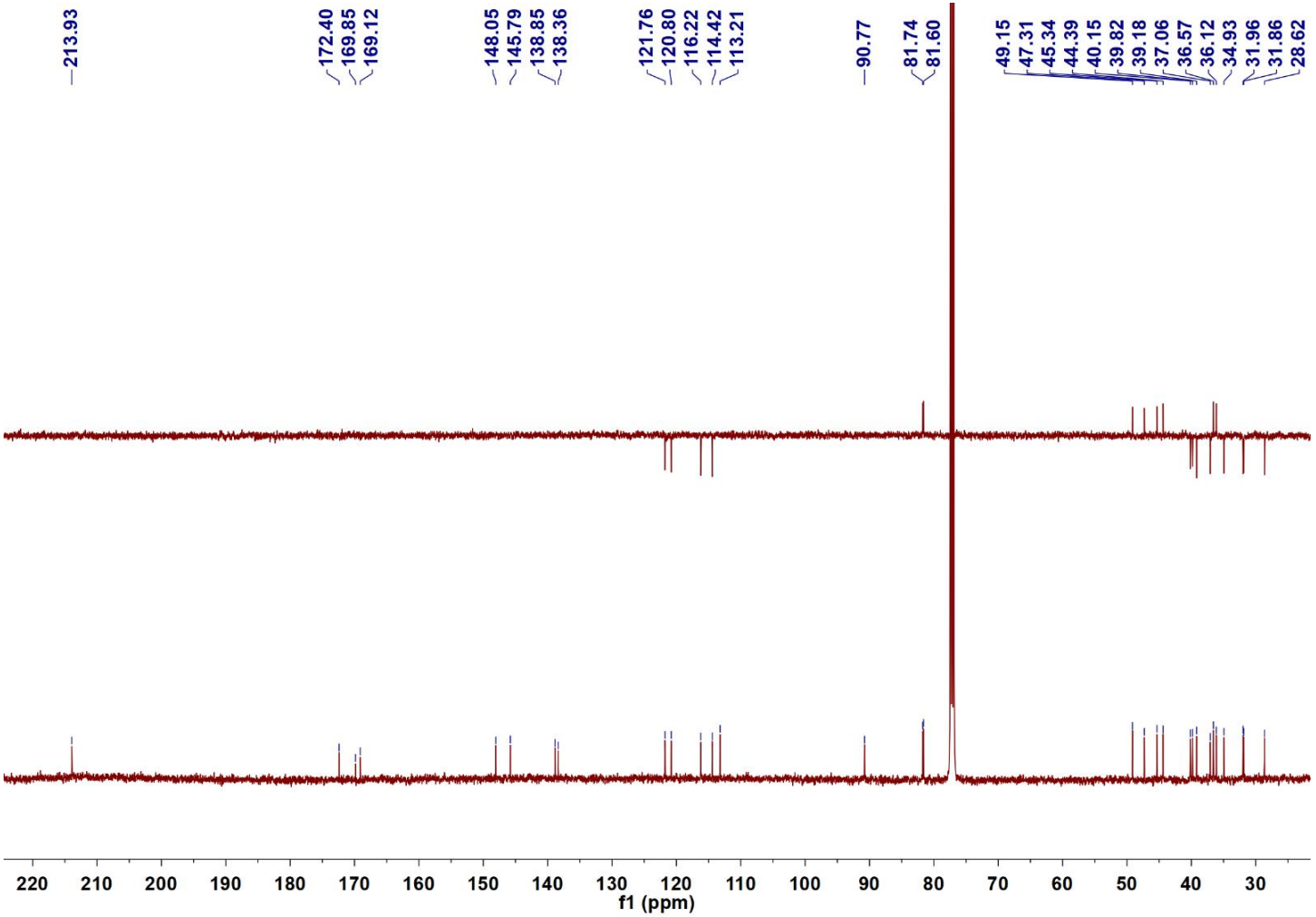


Fig. S6. ^{13}C NMR spectrum of compound **1** in $CDCl_3$



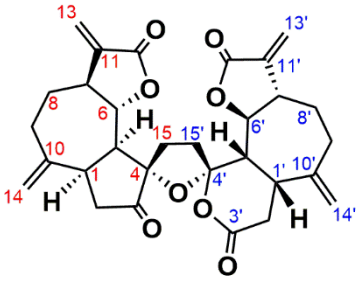
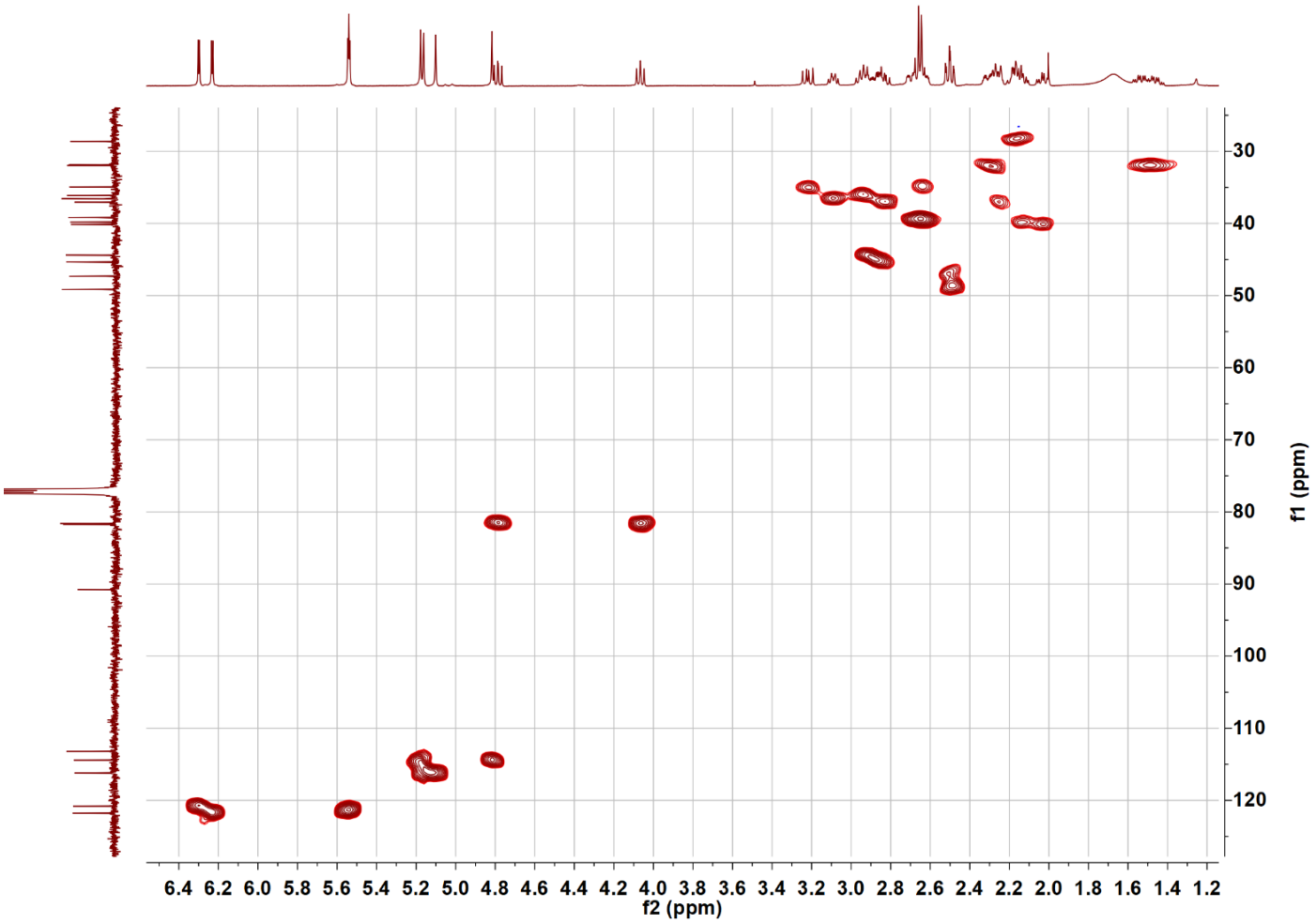


Fig. S7. HSQC spectrum of compound **1** in $CDCl_3$



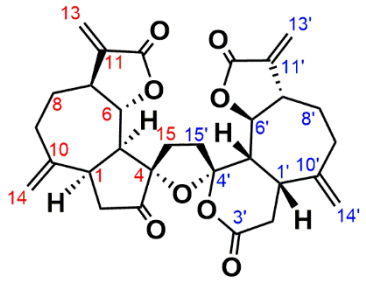
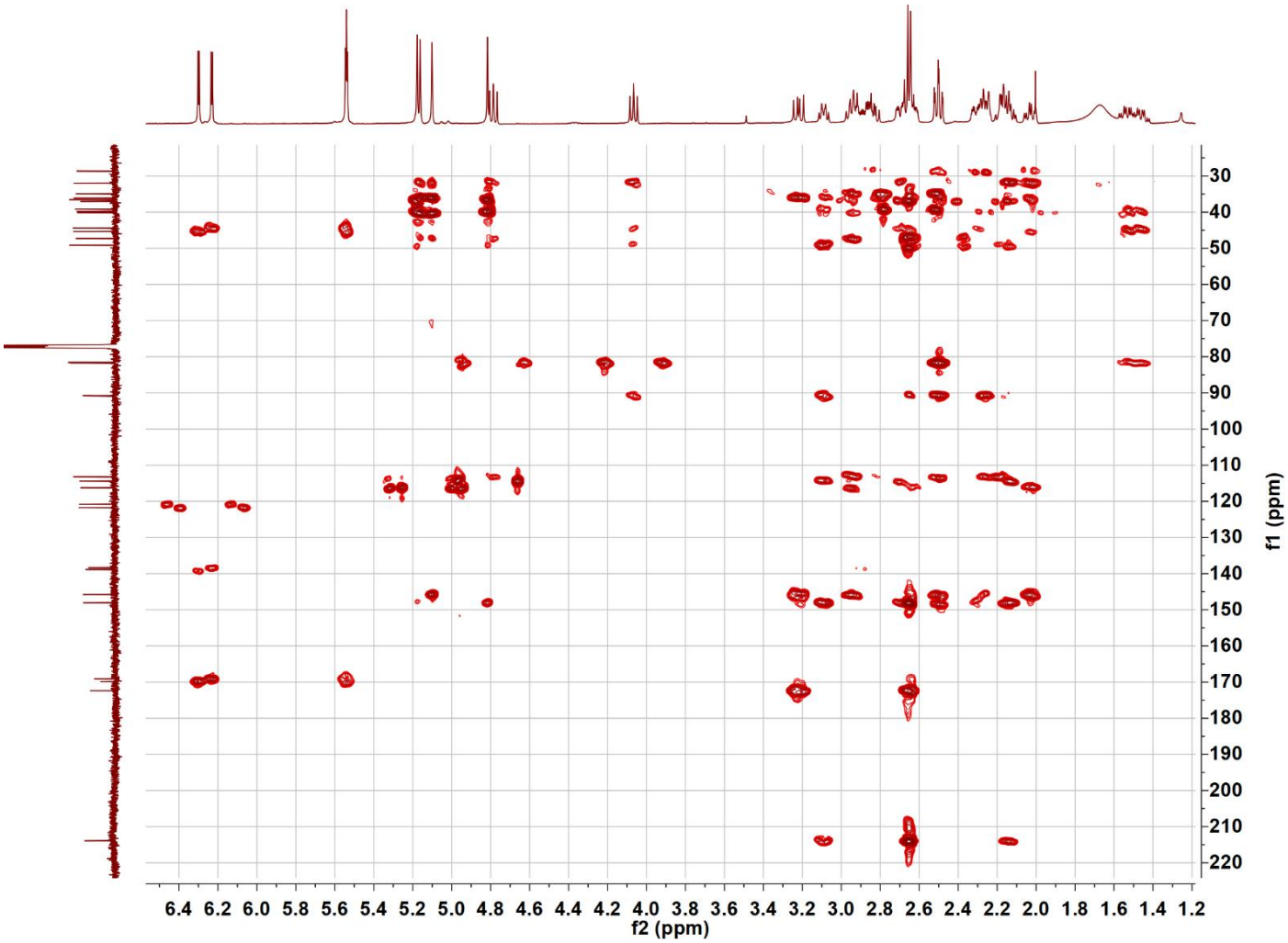


Fig. S8. HMBC spectrum of compound **1** in $CDCl_3$



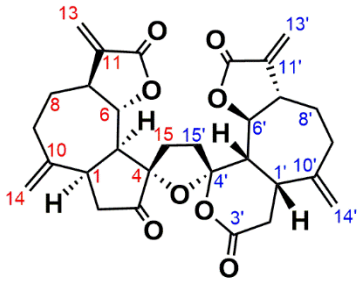
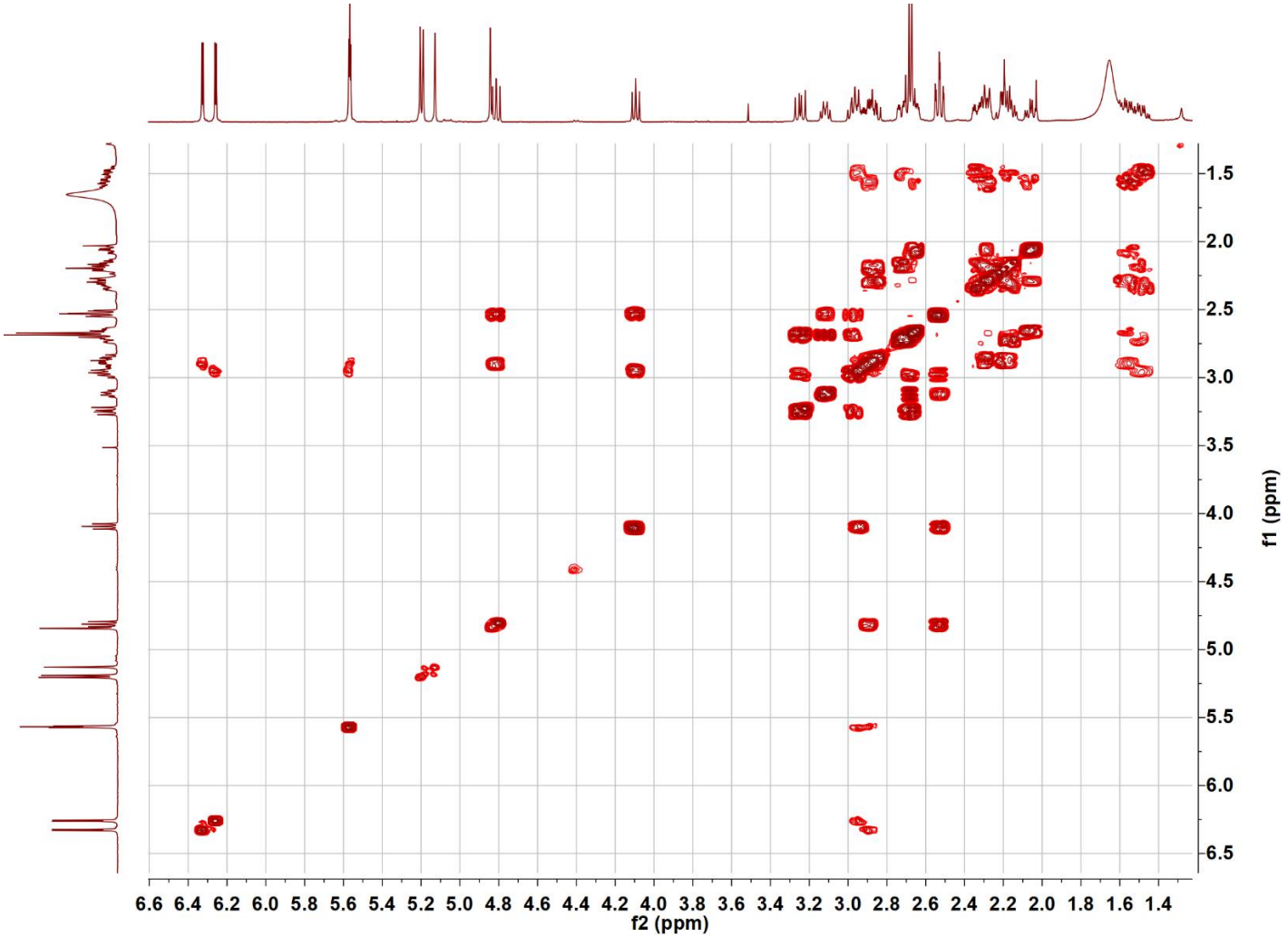


Fig. S9. ^{1}H-^{1}H COSY spectrum of compound **1** in $CDCl_3$



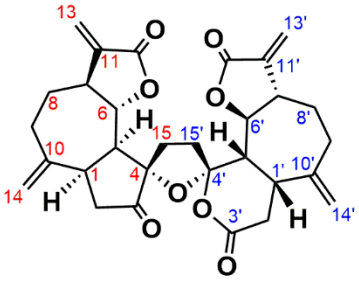
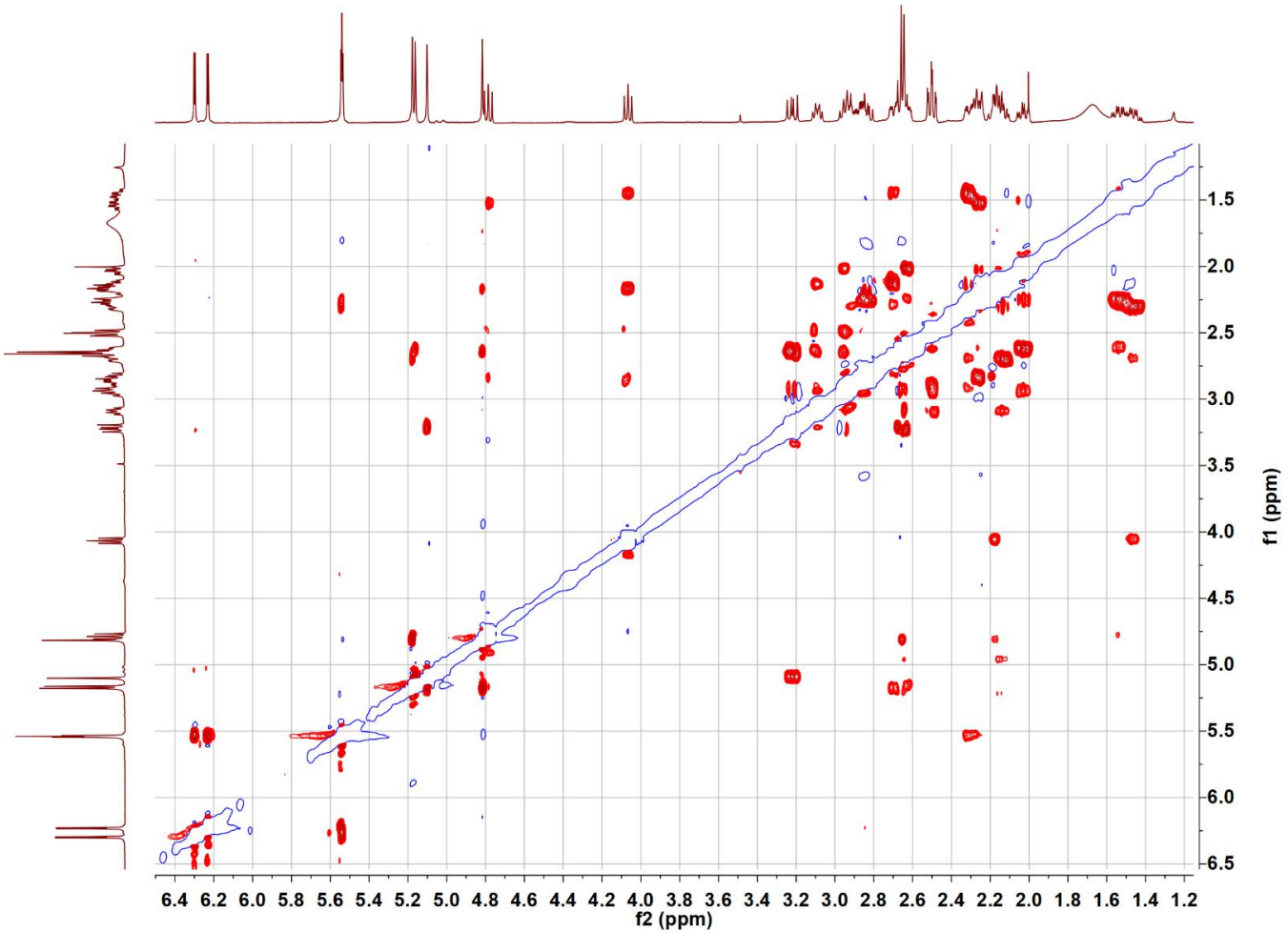


Fig. S10. ROESY spectrum of compound **1** in $CDCl_3$



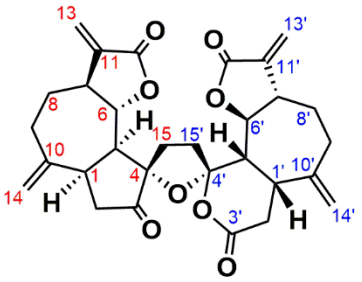


Fig. S11. IR spectrum of compound **2**

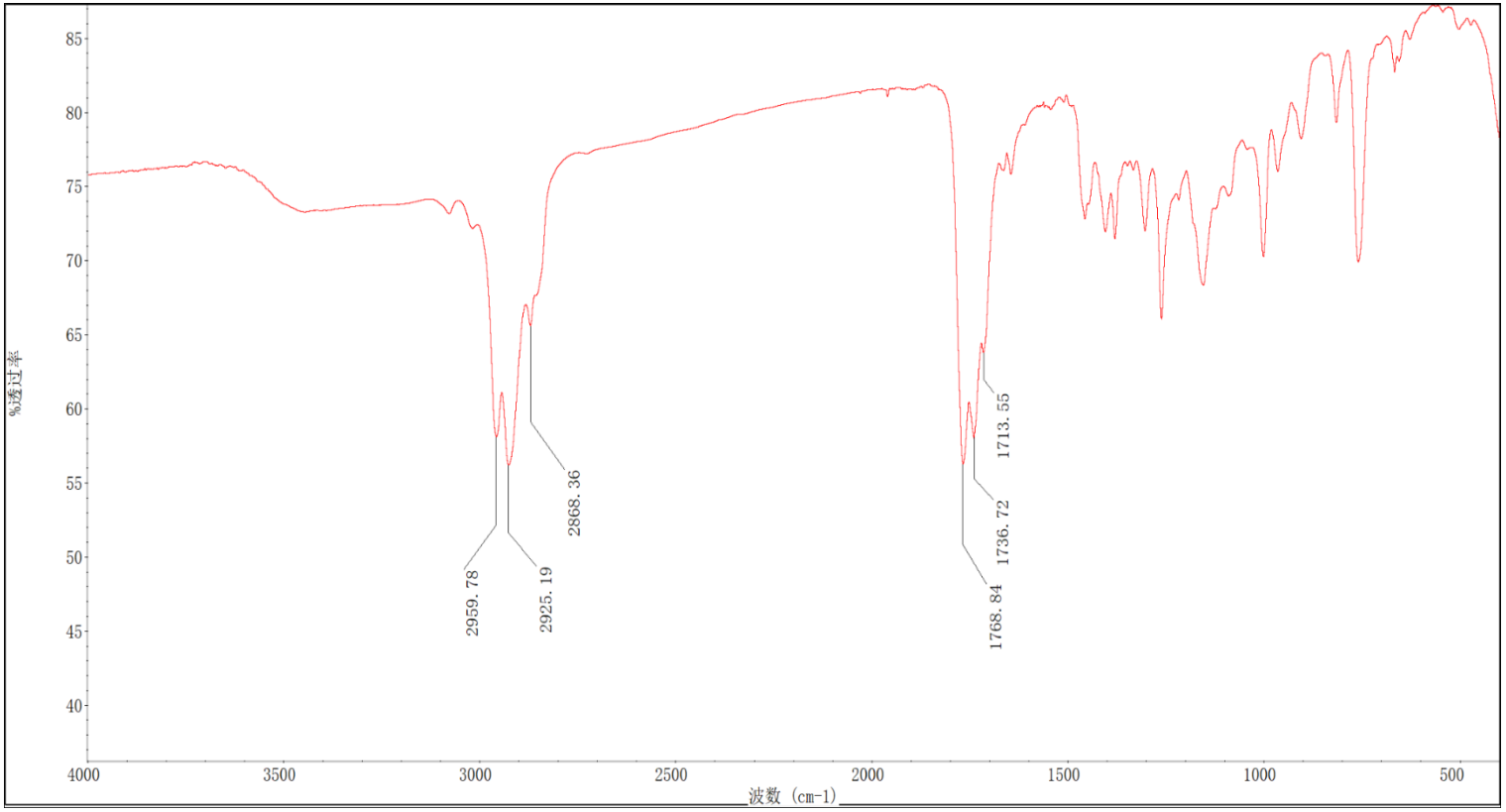


Fig. S12. HRESIMS data of compound **2**

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

277 formula(e) evaluated with 3 results within limits (up to 50 closest results for each mass)

Elements Used:

C: 0-100 H: 0-100 O: 0-50 Na: 0-1

Minimum:				**-1.5**				
Maximum:		**5.0**	**10.0**	**50.0**				
Mass	**Calc. Mass**	**mDa**	**PPM**	**DBE**	**i-FIT**	**Norm**	**Conf(%)**	**Formula**
545.2147	**545.2151**	**-0.4**	**-0.7**	**13.5**	**129.1**	**0.126**	**88.14**	**C30 H34 O8 Na**
	545.2175	**-2.8**	**-5.1**	**16.5**	**131.1**	**2.169**	**11.43**	**C32 H33 O8**
	545.2117	**3.0**	**5.5**	**25.5**	**134.4**	**5.437**	**0.44**	**C39 H29 O3**

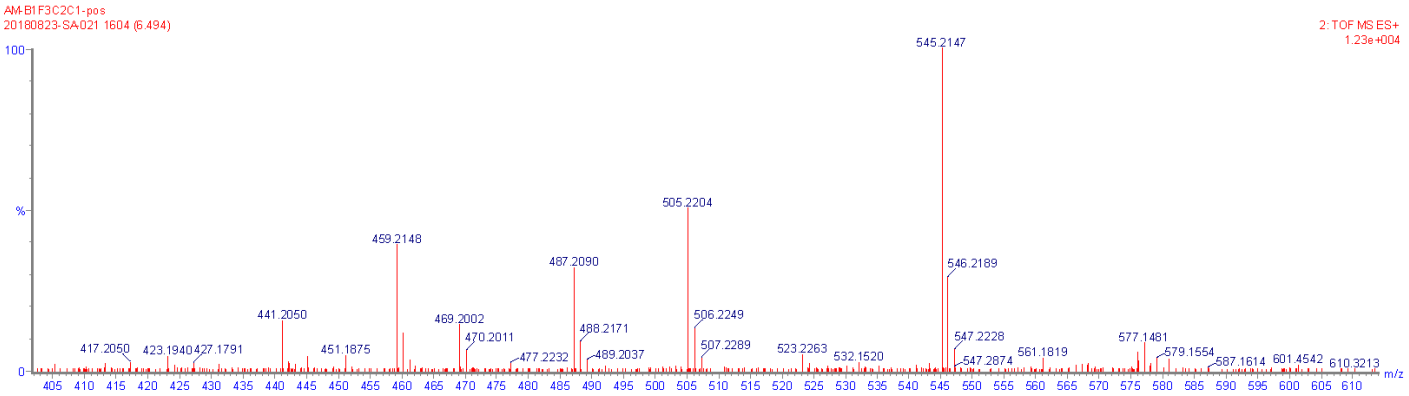
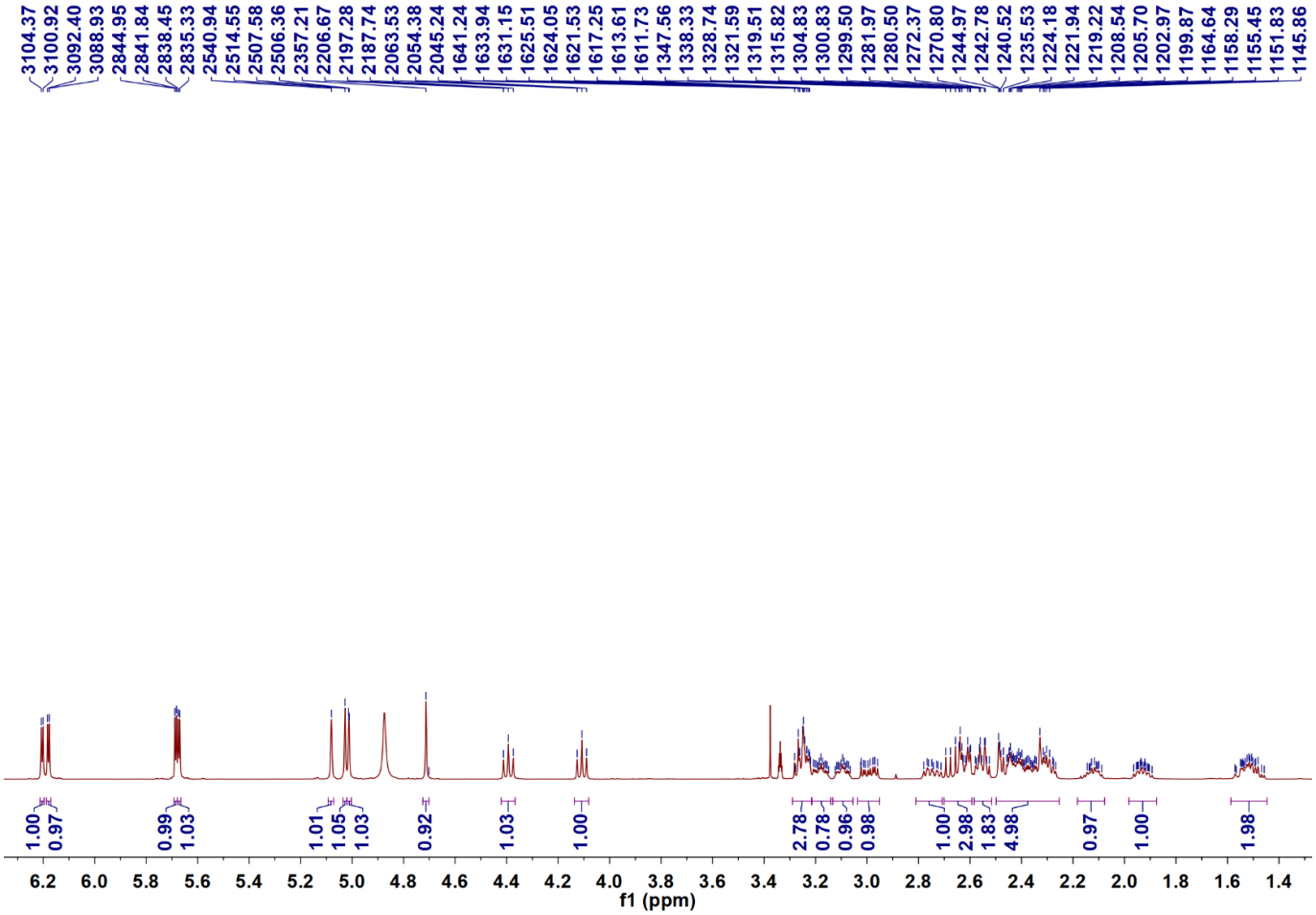


Fig. S13. ^{1}H NMR spectrum of compound **2** in CD_3OD



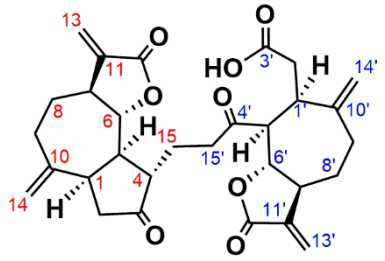
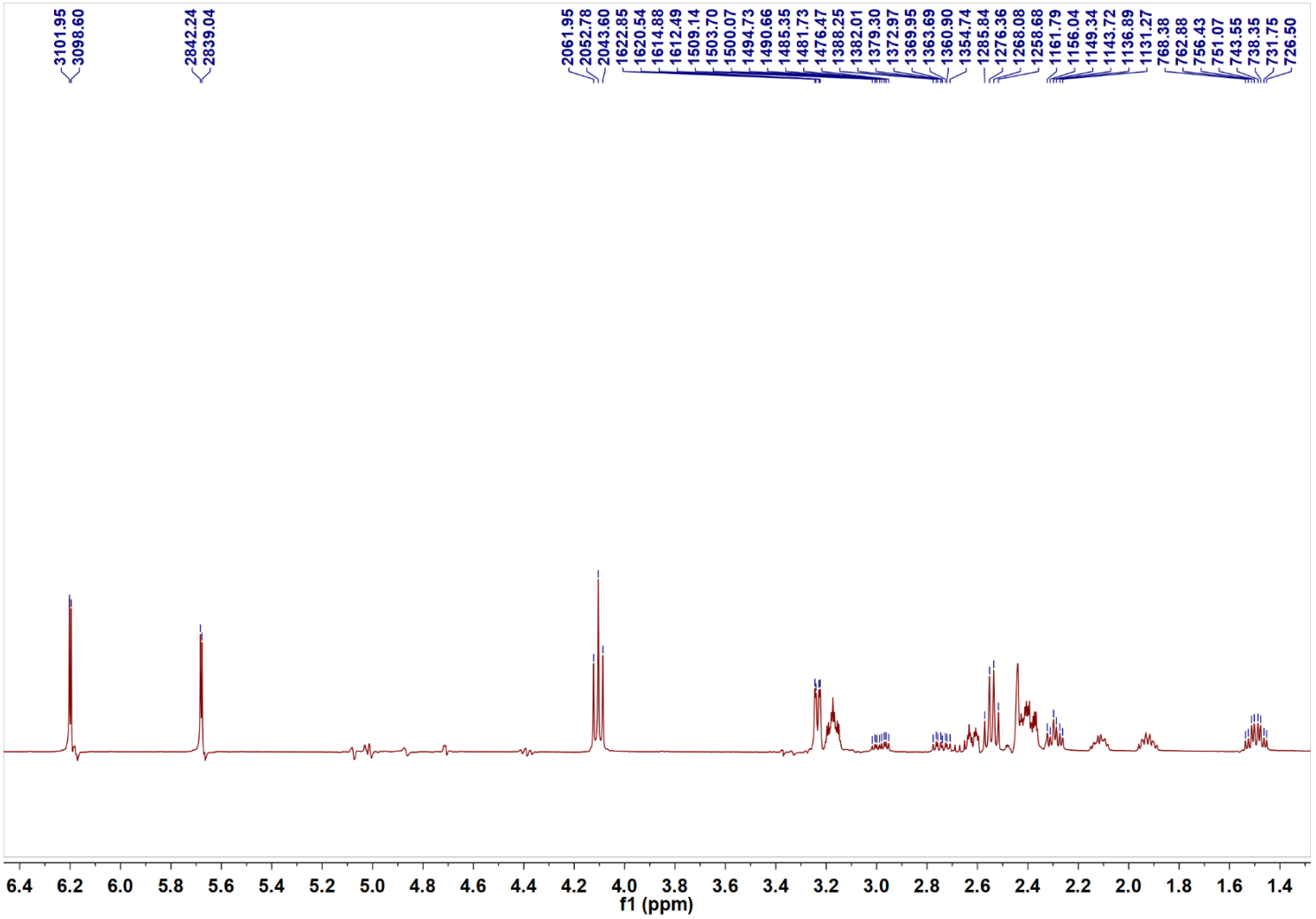


Fig. S14. 1DTOCSY (4.108 PPM) spectrum of compound **2** in CD_3OD



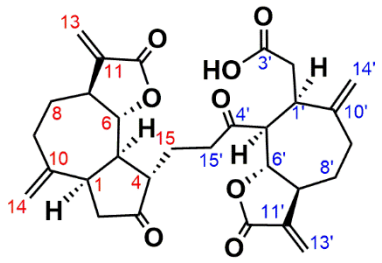
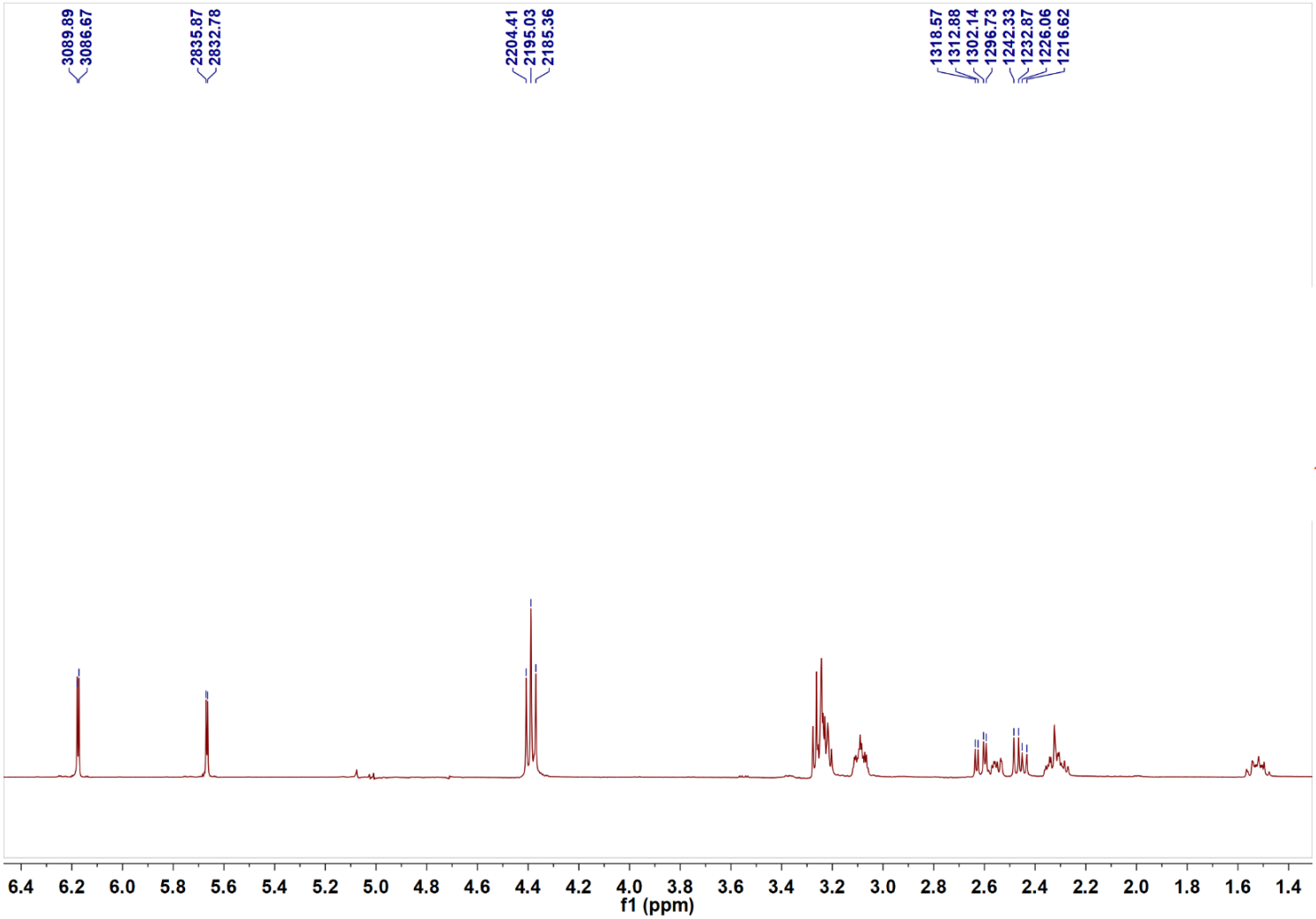


Fig. S15. 1DTOCSY (4.389 PPM) spectrum of compound **2** in CD_3OD



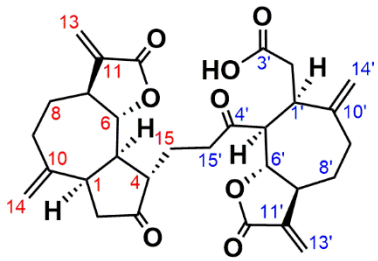
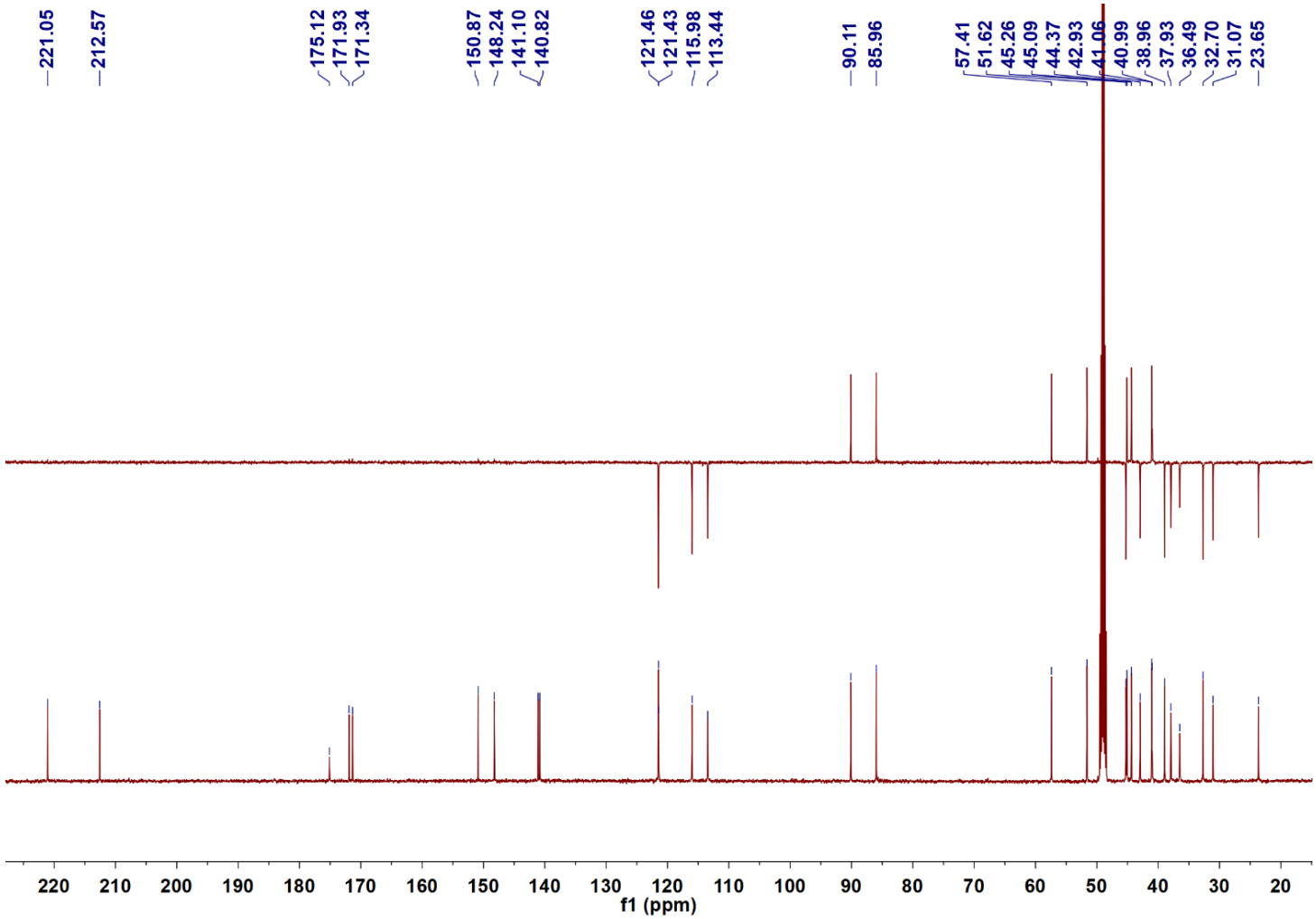


Fig. S16. ^{13}C NMR spectrum of compound **2** in CD_3OD



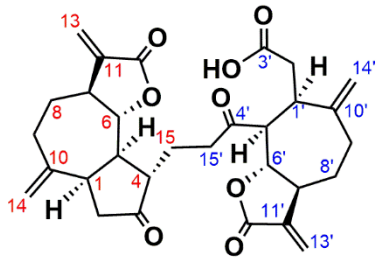


Fig. S17. HSQC spectrum of compound **2** in CD_3OD

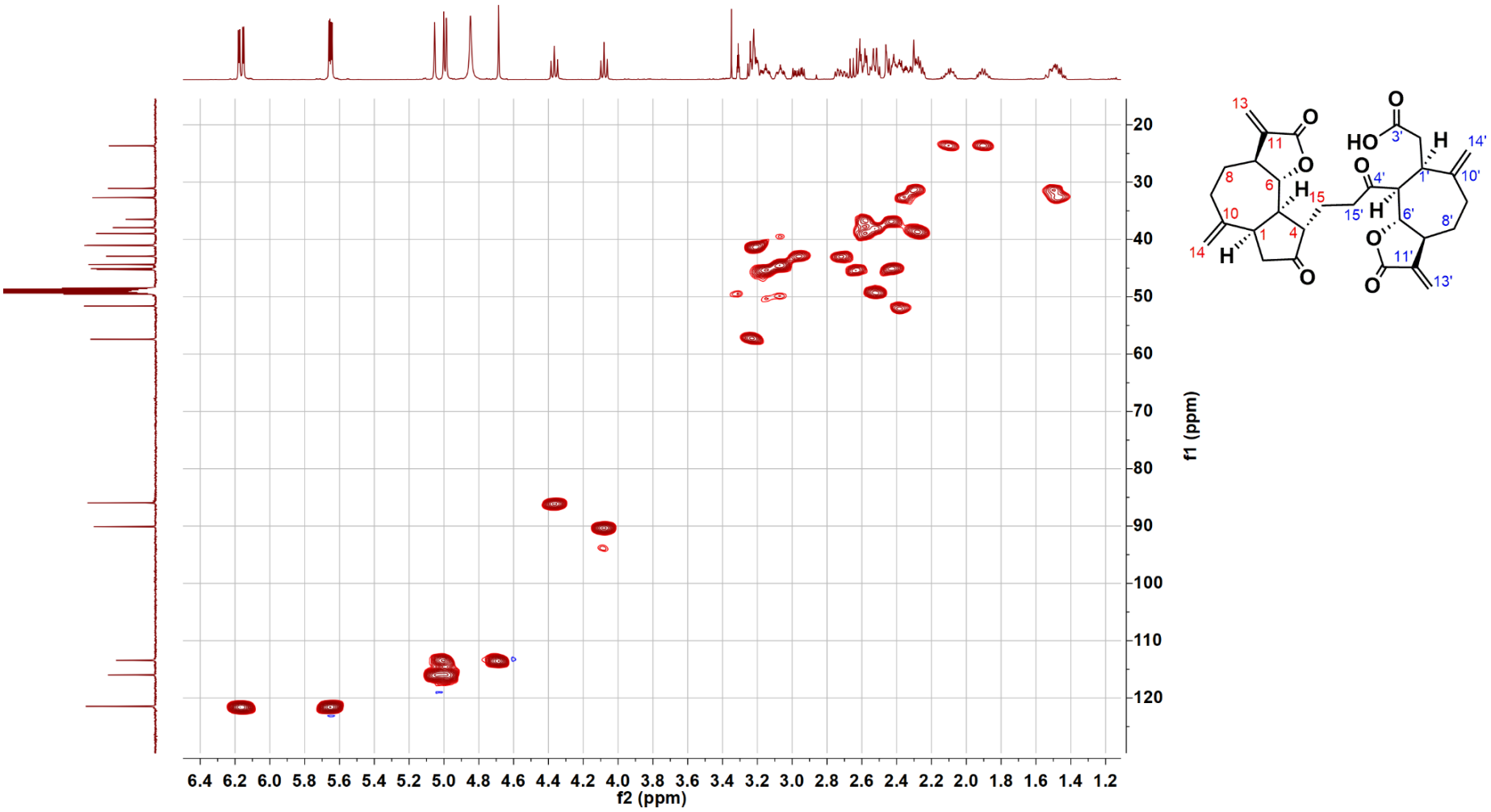


Fig. S18. HMBC spectrum of compound **2** in CD_3OD

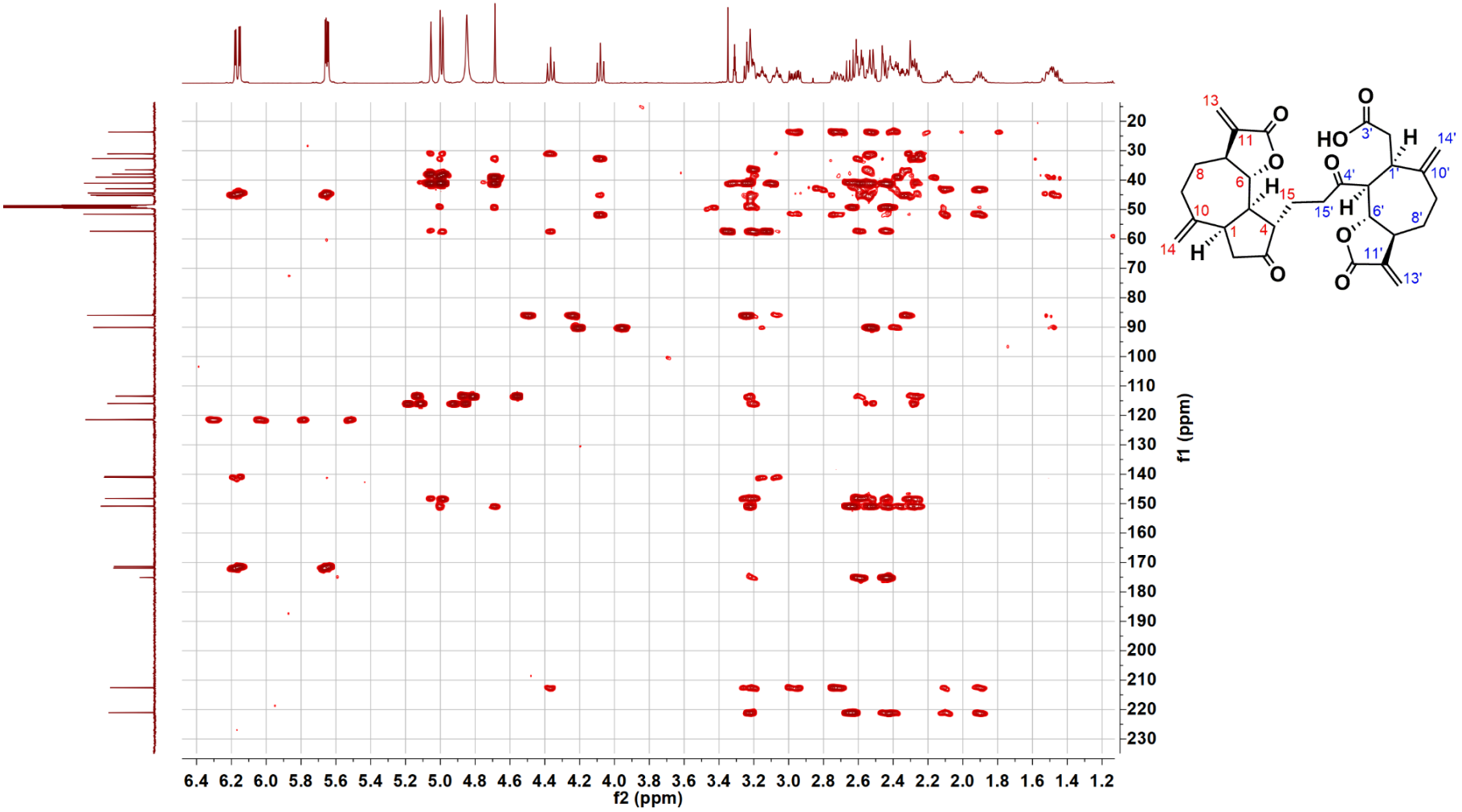


Fig. S19. ^{1}H- ^{1}H COSY spectrum of compound **2** in CD_3OD

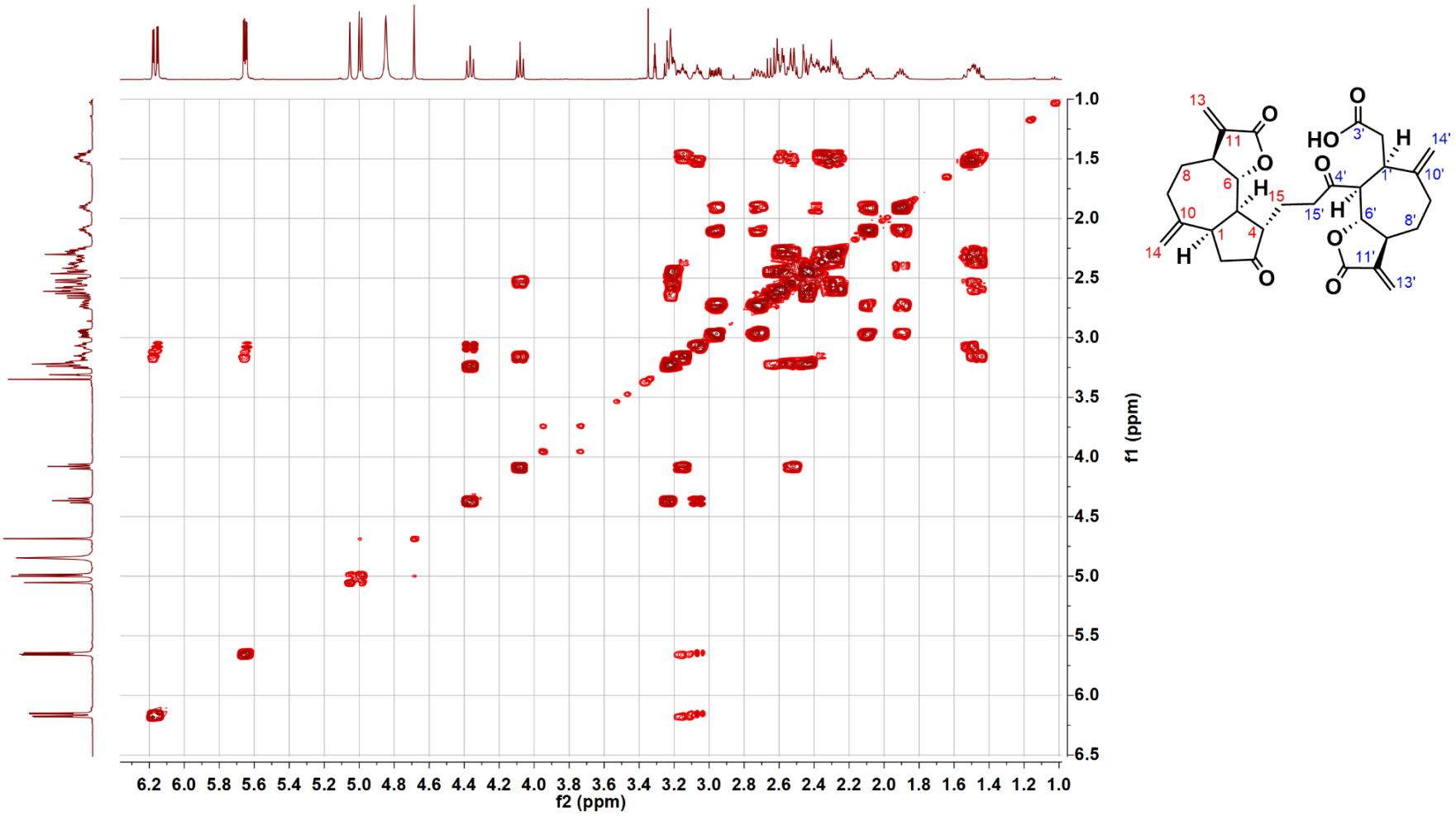
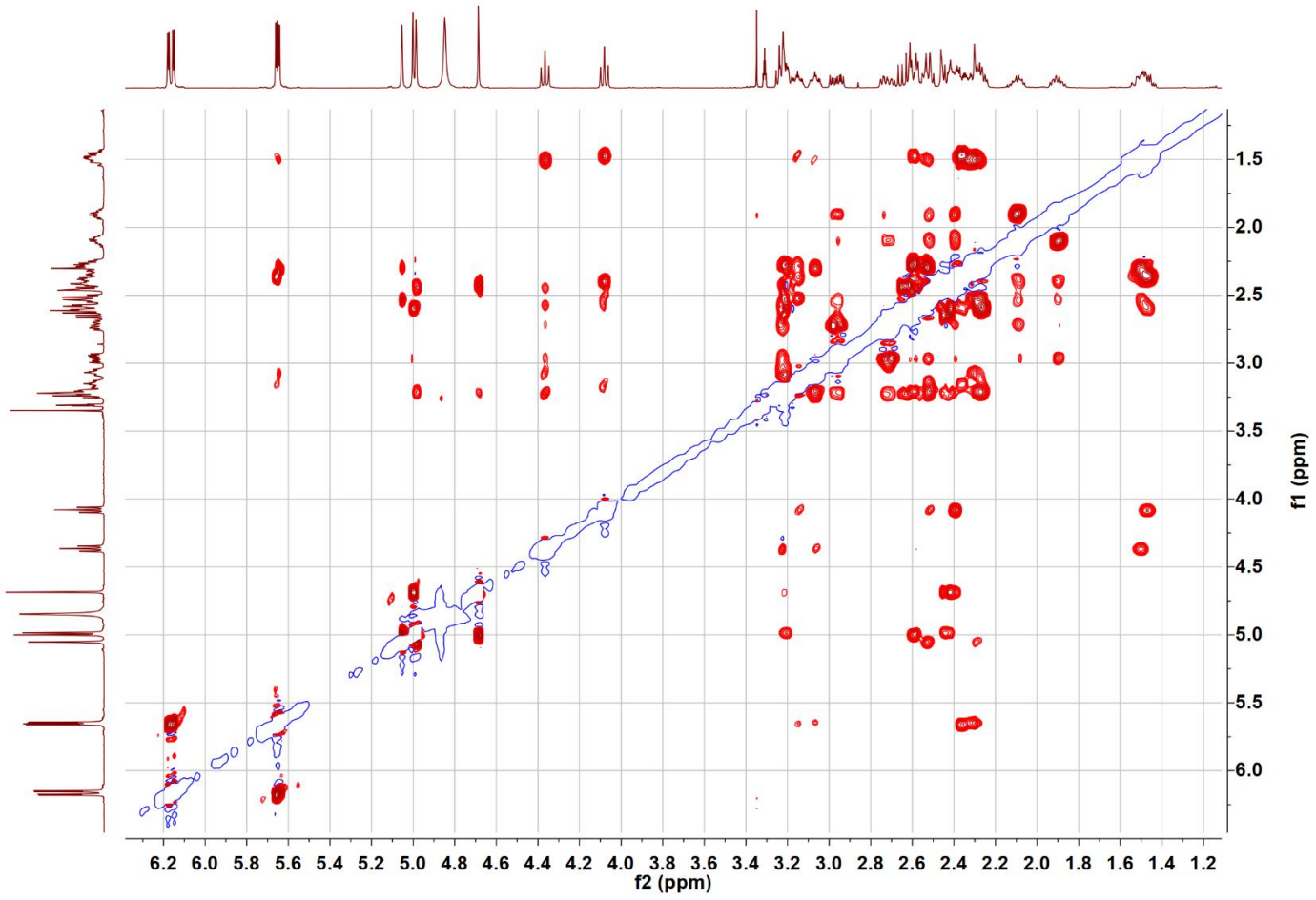


Fig. S20. ROESY spectrum of compound **2** in CD_3OD



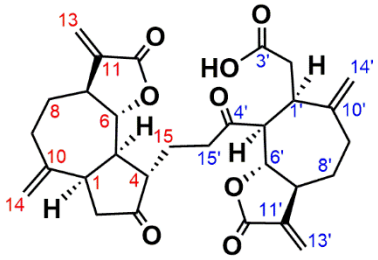
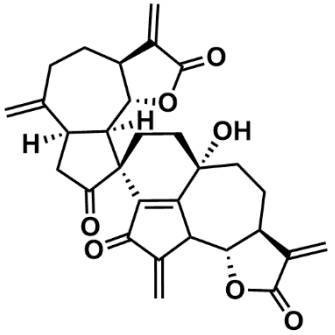


Fig. S21 HRESIMS data of compound **3**



Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

258 formula(e) evaluated with 3 results within limits (up to 50 closest results for each mass)

Elements Used:

C: 0-100 H: 0-100 O: 0-50 Na: 0-1

Minimum:				**-1.5**				
Maximum:		**5.0**	**10.0**	**50.0**				
Mass	**Calc. Mass**	**mDa**	**PPM**	**DBE**	**i-FIT**	**Norm**	**Conf(%)**	**Formula**
525.1890	**525.1889**	**0.1**	**0.2**	**15.5**	**425.6**	**0.089**	**91.47**	**C30 H30 O7 Na**
	525.1913	**-2.3**	**-4.4**	**18.5**	**428.0**	**2.487**	**8.31**	**C32 H29 O7**
	525.1855	**3.5**	**6.7**	**27.5**	**431.6**	**6.128**	**0.22**	**C39 H25 O2**

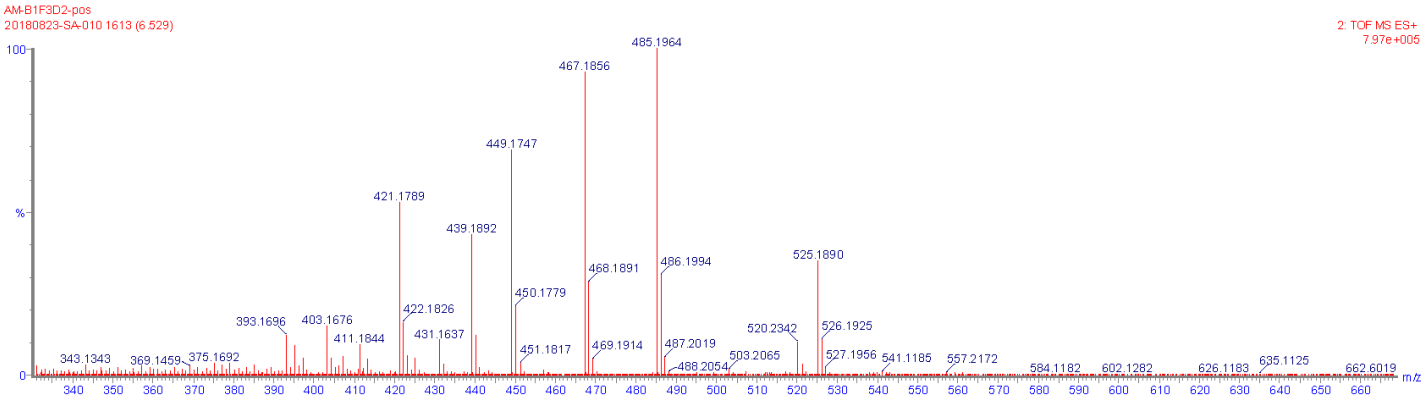
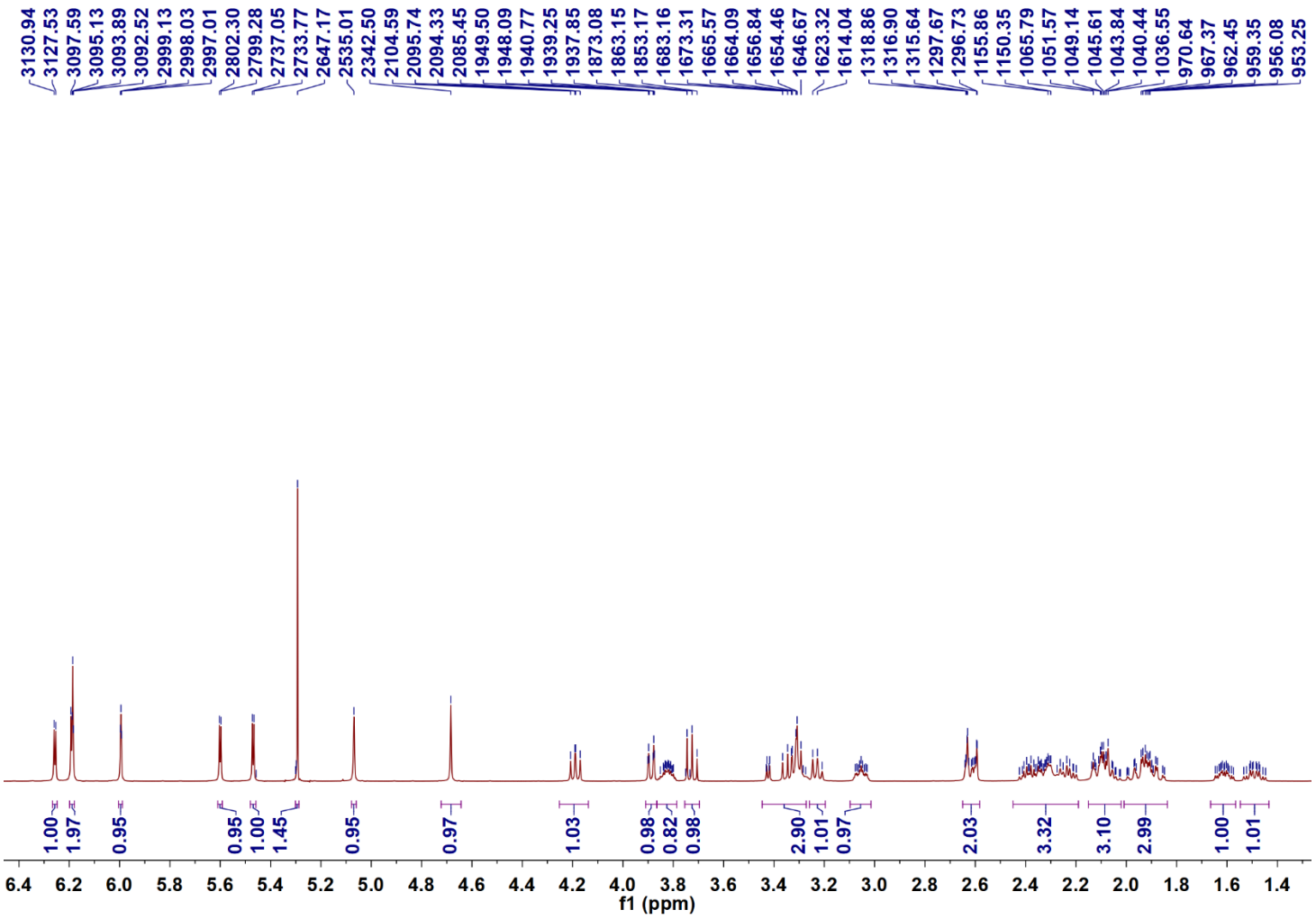


Fig. S22 ^{1}H NMR spectrum of compound **3** in $CDCl_3$



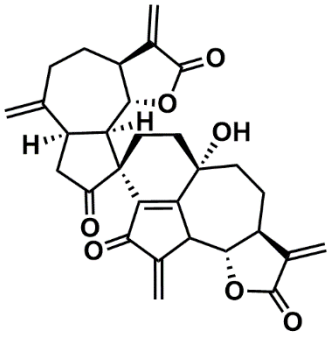
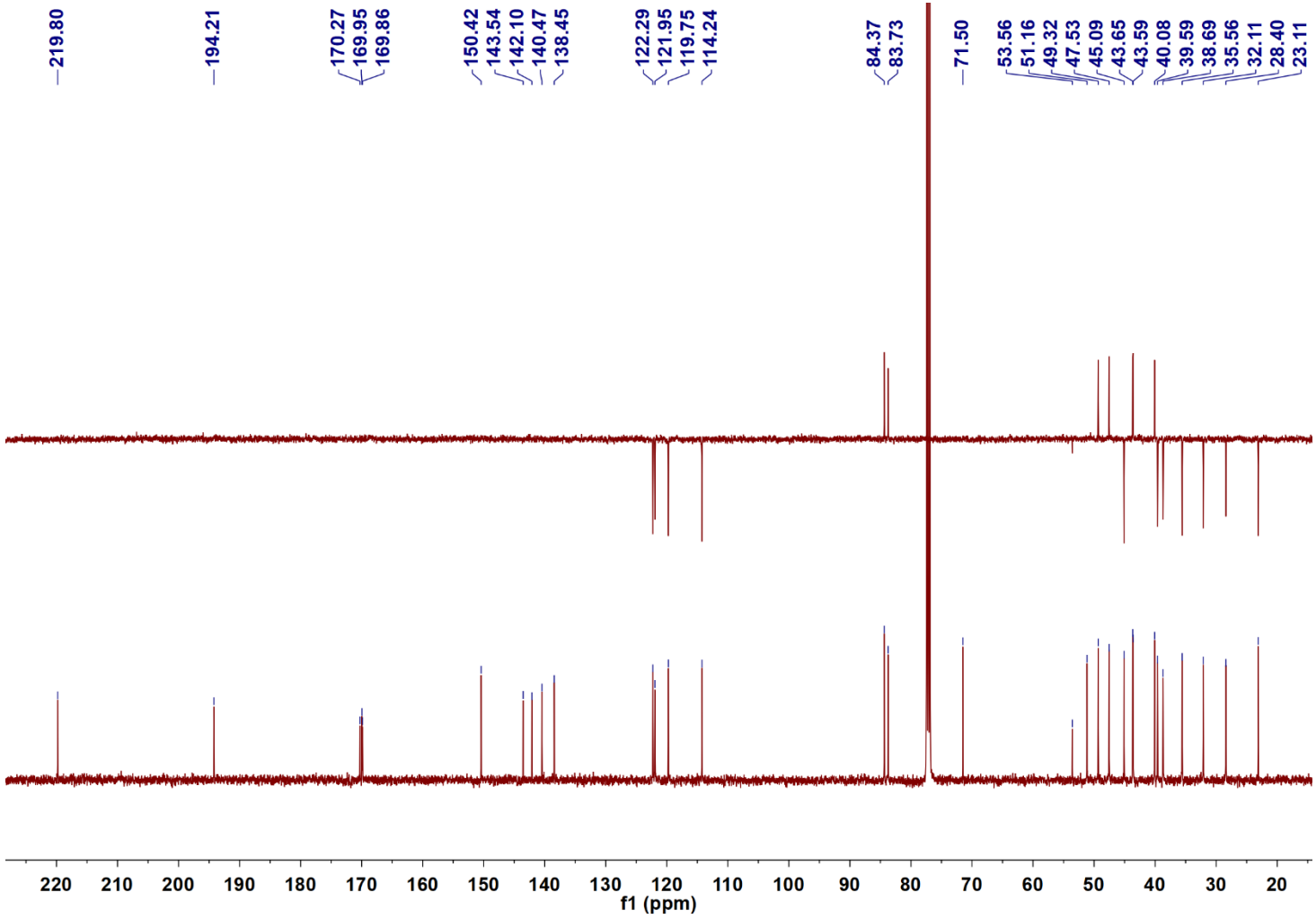


Fig. S23 ^{13}C NMR spectrum of compound **3** in $CDCl_3$



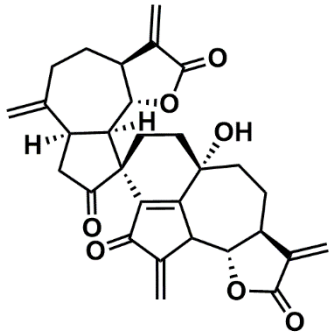


Fig. S24. HRESIMS data of compound **4**

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

258 formula(e) evaluated with 3 results within limits (up to 50 closest results for each mass)

Elements Used:

C: 0-100 H: 0-100 O: 0-50 Na: 0-1

Minimum:				**-1.5**				
Maximum:		**5.0**	**10.0**	**50.0**				
Mass	**Calc. Mass**	**mDa**	**PPM**	**DBE**	**i-FIT**	**Norm**	**Conf(%)**	**Formula**
525.1888	**525.1889**	**-0.1**	**-0.2**	**15.5**	**218.0**	**0.166**	**84.67**	**C30 H30 O7 Na**
	525.1913	**-2.5**	**-4.8**	**18.5**	**219.8**	**1.903**	**14.91**	**C32 H29 O7**
	525.1855	**3.3**	**6.3**	**27.5**	**223.3**	**5.472**	**0.42**	**C39 H25 O2**

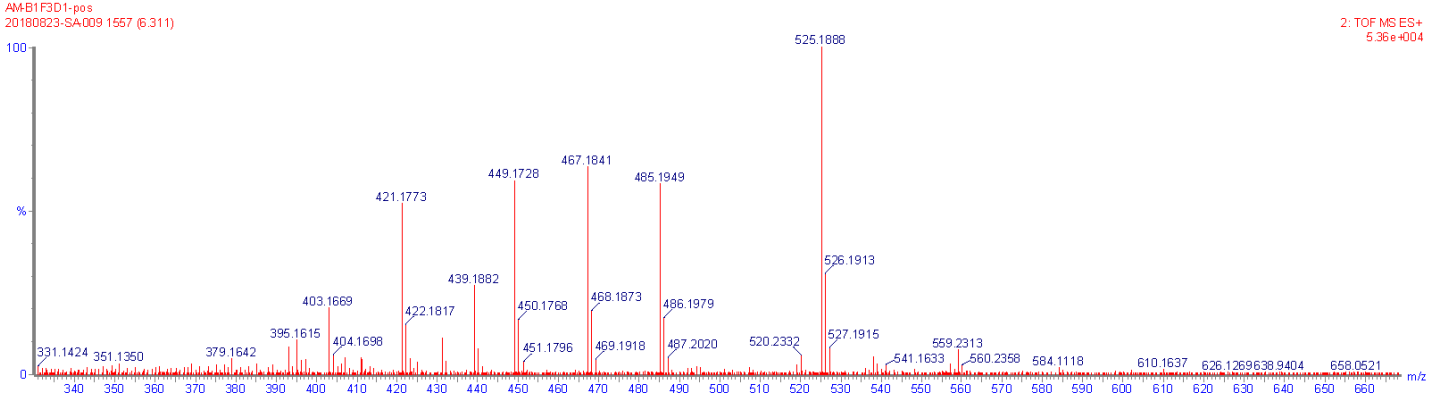
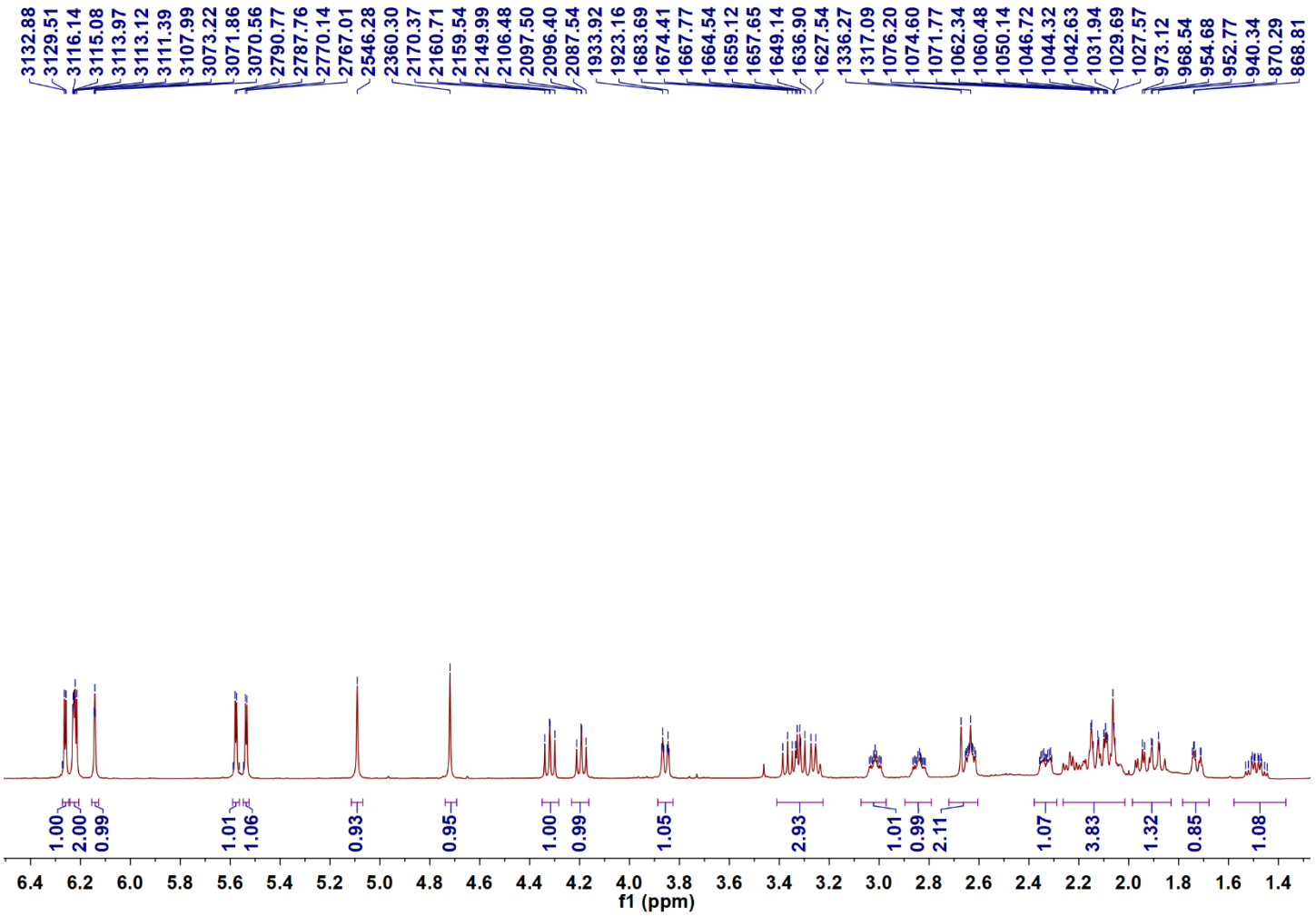


Fig. S25 ^{1}H NMR spectrum of compound **4** in $CDCl_3$



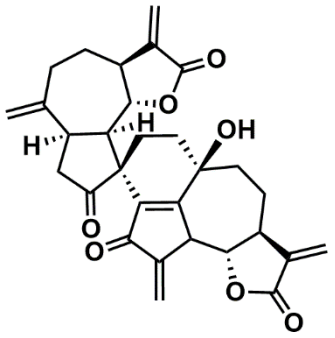
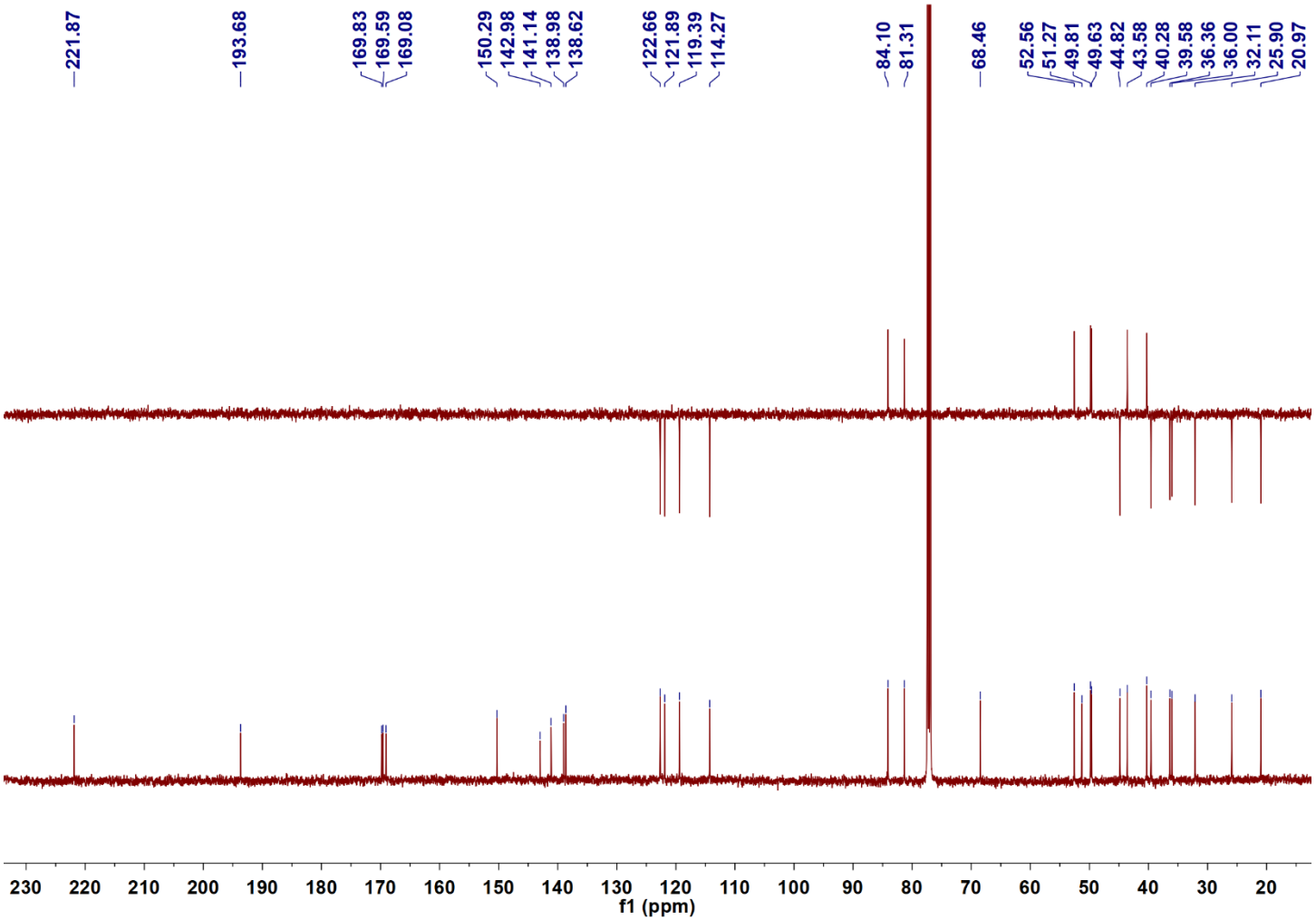


Fig. S26 ^{13}C NMR spectrum of compound **4** in $CDCl_3$



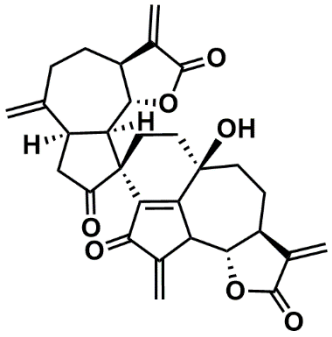


Fig. S27. HRESIMS data of compound **5**

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

275 formula(e) evaluated with 3 results within limits (up to 50 closest results for each mass)

Elements Used:

C: 0-100 H: 0-100 O: 0-50 Na: 0-1

Minimum:				**-1.5**				
Maximum:		**5.0**	**10.0**	**50.0**				
Mass	**Calc. Mass**	**mDa**	**PPM**	**DBE**	**i-FIT**	**Norm**	**Conf(%)**	**Formula**
531.2360	**531.2359**	**0.1**	**0.2**	**12.5**	**282.2**	**0.046**	**95.47**	**C30 H36 O7 Na**
	531.2383	**-2.3**	**-4.3**	**15.5**	**285.2**	**3.122**	**4.41**	**C32 H35 O7**
	531.2324	**3.6**	**6.8**	**24.5**	**288.8**	**6.700**	**0.12**	**C39 H31 O2**

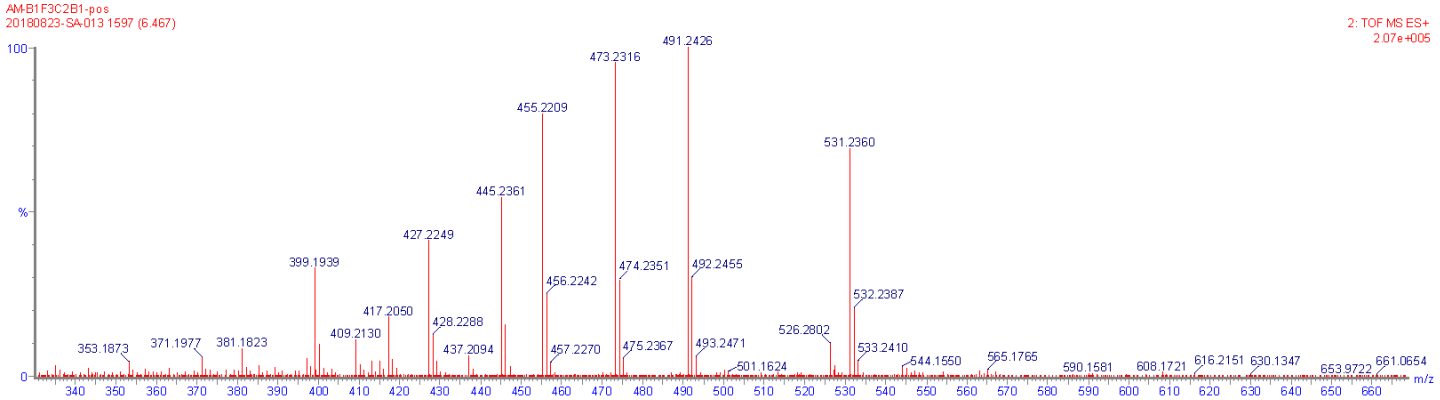


Fig. S28 ^{1}H NMR spectrum of compound **5** in $CDCl_3$

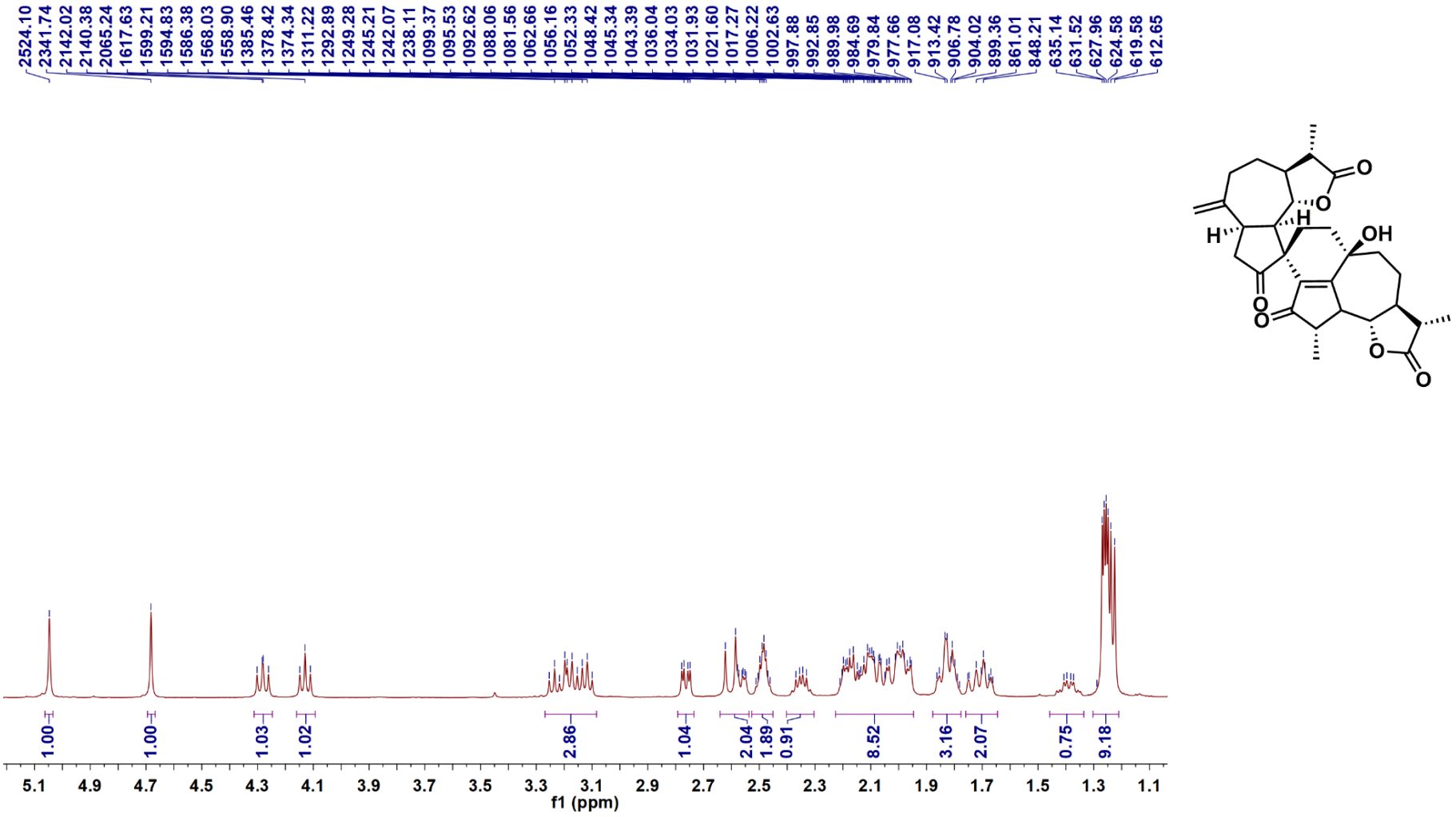


Fig. S29. ^{13}C NMR spectrum of compound **5** in $CDCl_3$

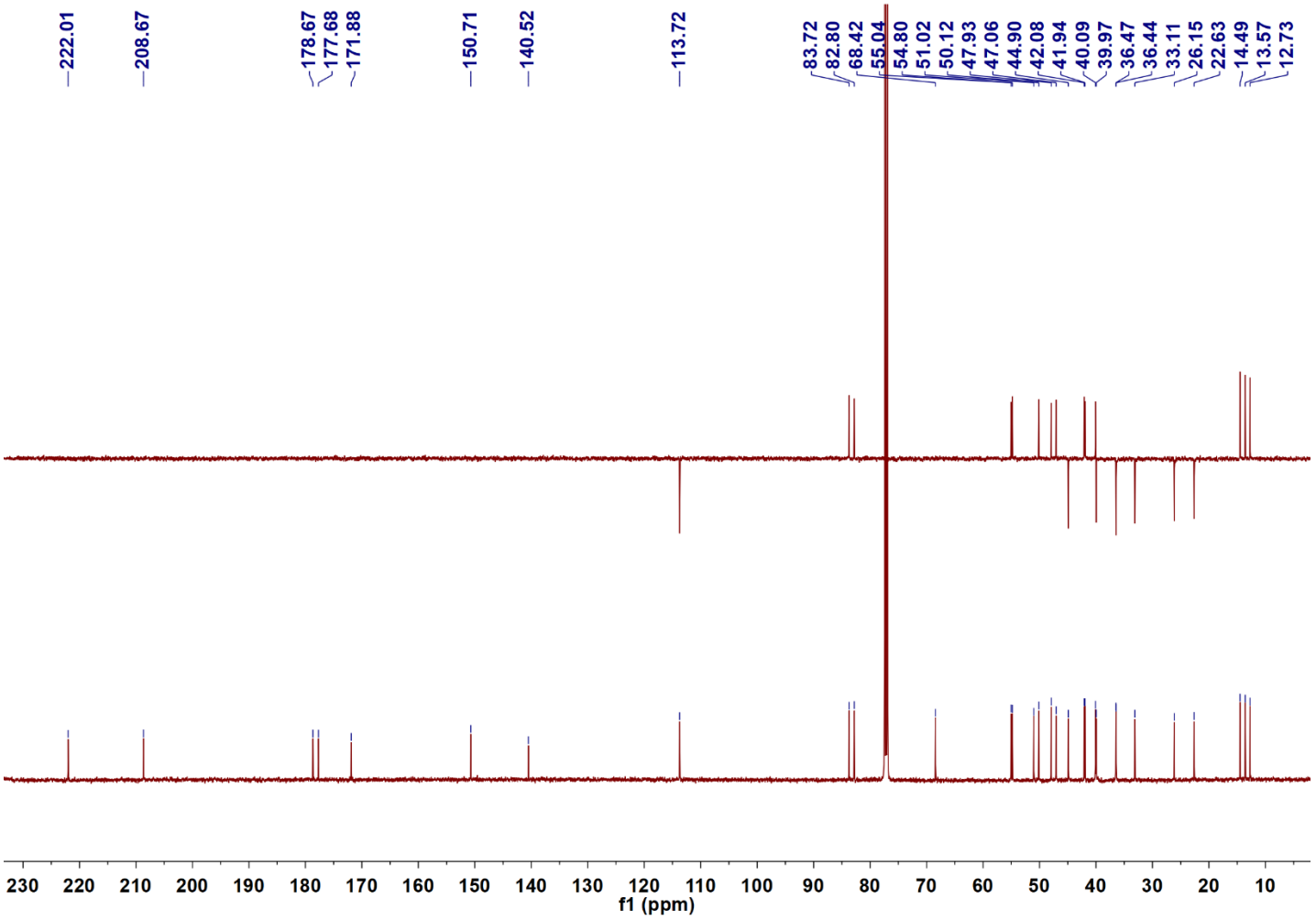


Fig. S30 HRESIMS data of compound **6**

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

263 formula(e) evaluated with 3 results within limits (up to 50 closest results for each mass)

Elements Used:

C: 0-100 H: 0-100 O: 0-50 Na: 0-1

Minimum:				**-1.5**				
Maximum:		**5.0**	**10.0**	**50.0**				
Mass	**Calc. Mass**	**mDa**	**PPM**	**DBE**	**i-FIT**	**Norm**	**Conf(%)**	**Formula**
529.2200	**529.2202**	**-0.2**	**-0.4**	**13.5**	**334.8**	**0.211**	**80.96**	**C30 H34 O7 Na**
	529.2226	**-2.6**	**-4.9**	**16.5**	**336.3**	**1.674**	**18.76**	**C32 H33 O7**
	529.2168	**3.2**	**6.0**	**25.5**	**340.5**	**5.850**	**0.29**	**C39 H29 O2**

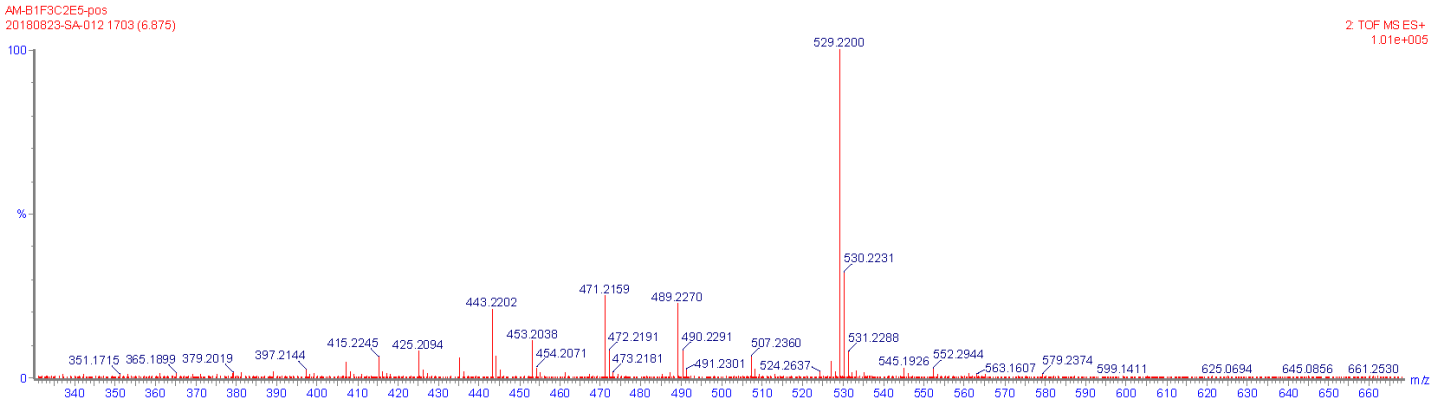


Fig. S31 ^{1}H NMR spectrum of compound **6** in $CDCl_3$

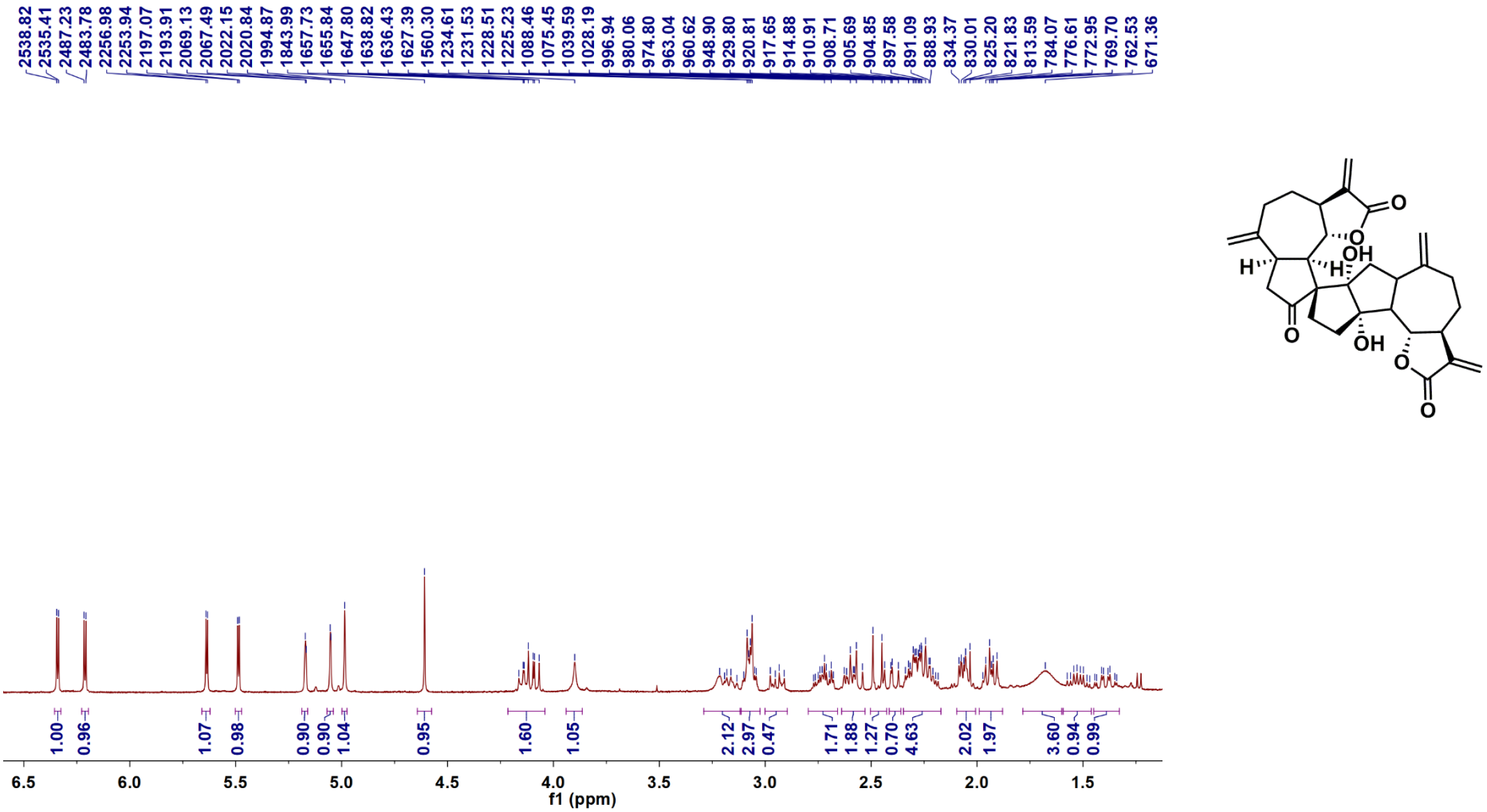


Fig. S32 ^{13}C NMR spectrum of compound **6** in $CDCl_3$

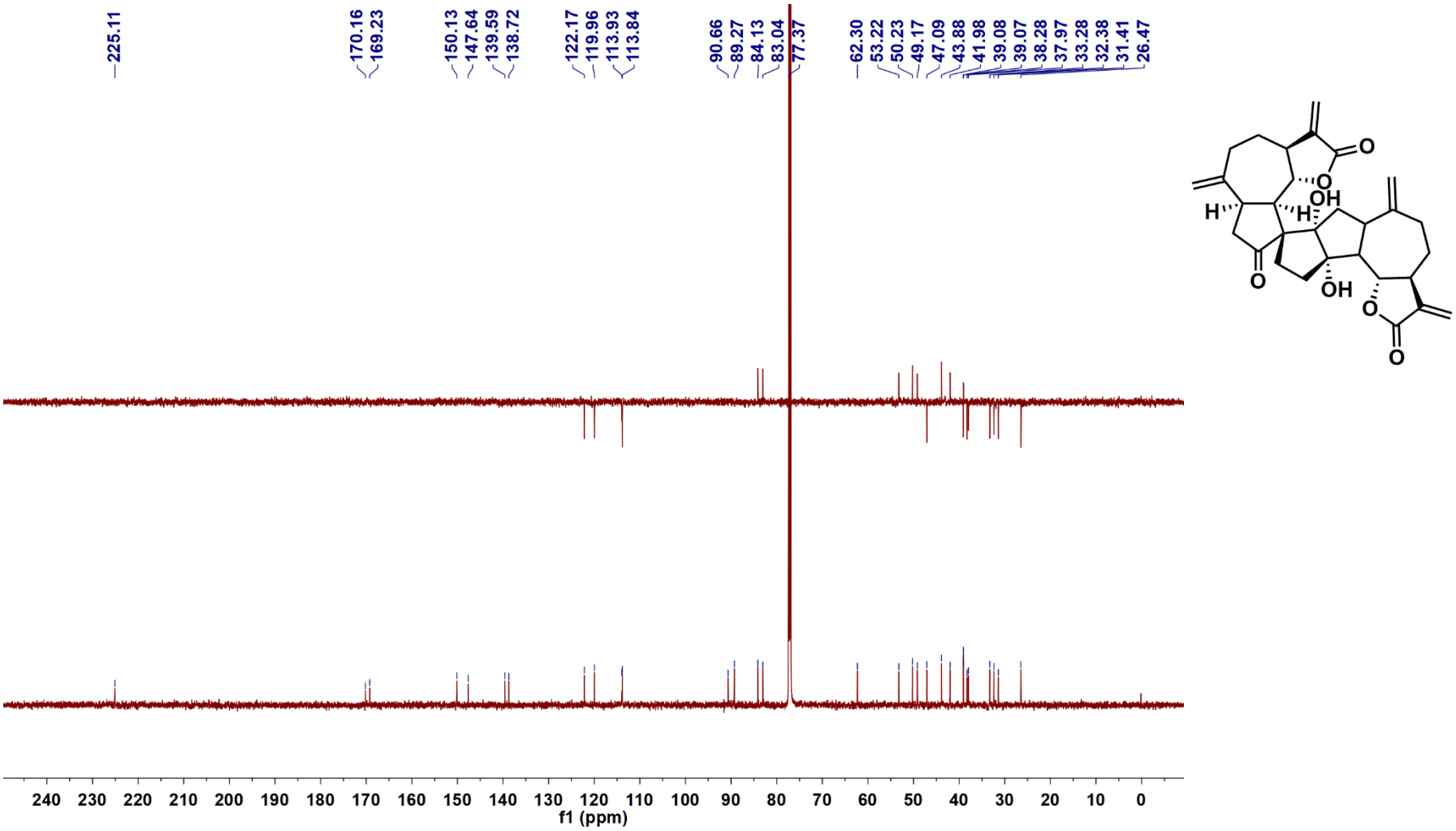


Fig. S33. HRESIMS data of compound **7**

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

263 formula(e) evaluated with 3 results within limits (up to 50 closest results for each mass)

Elements Used:

C: 0-100 H: 0-100 O: 0-50 Na: 0-1

Minimum:				**-1.5**				
Maximum:		**5.0**	**10.0**	**50.0**				
Mass	**Calc. Mass**	**mDa**	**PPM**	**DBE**	**i-FIT**	**Norm**	**Conf(%)**	**Formula**
529.2199	**529.2202**	**-0.3**	**-0.6**	**13.5**	**580.3**	**0.038**	**96.26**	**C30 H34 O7 Na**
	529.2226	**-2.7**	**-5.1**	**16.5**	**583.6**	**3.330**	**3.58**	**C32 H33 O7**
	529.2168	**3.1**	**5.9**	**25.5**	**586.7**	**6.421**	**0.16**	**C39 H29 O2**

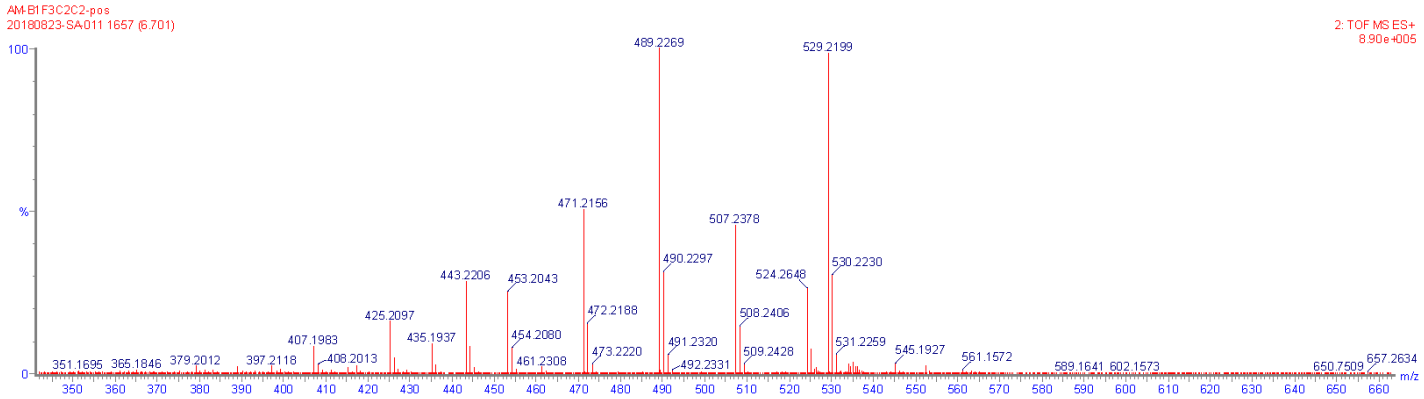
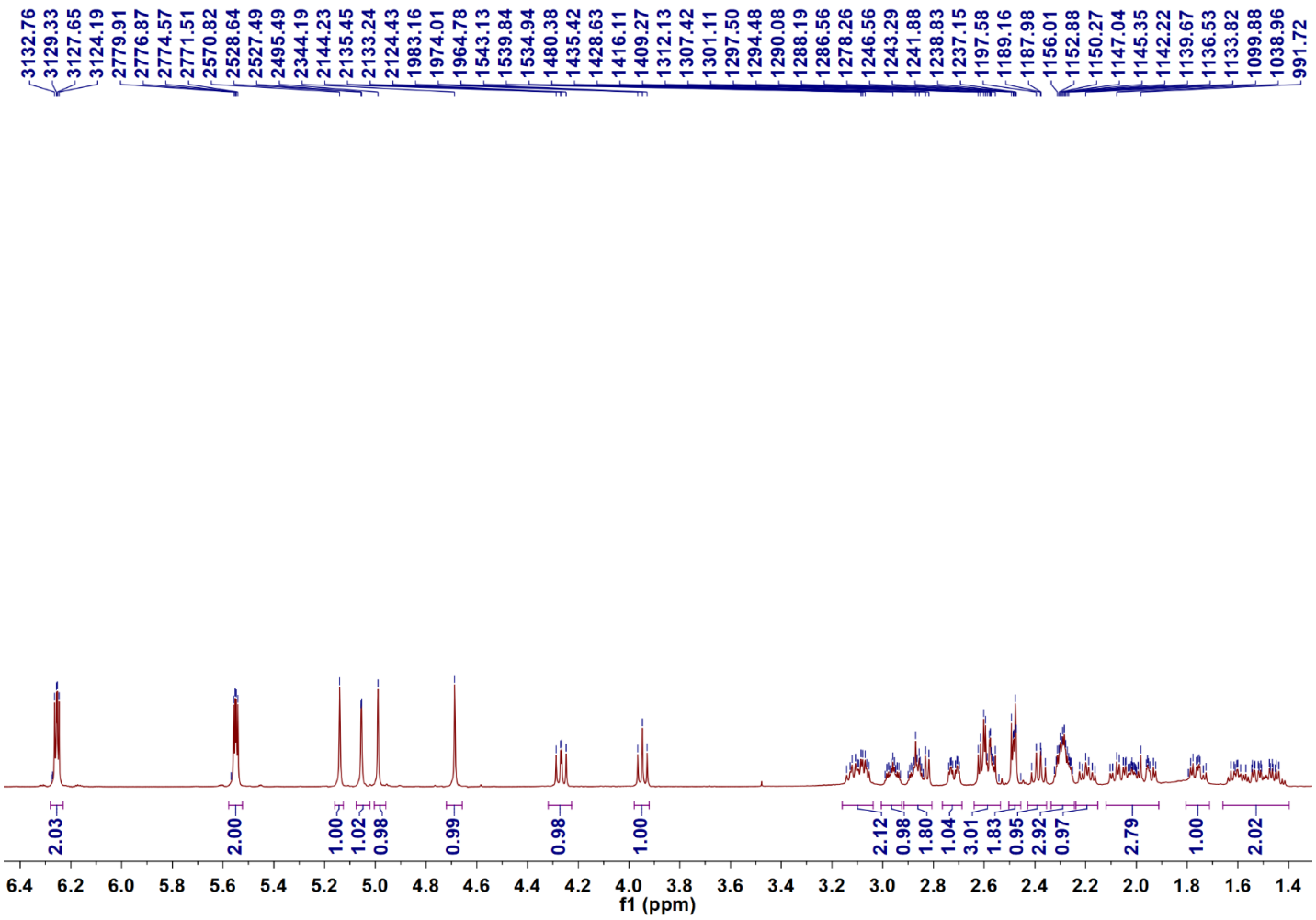


Fig. S34 ^{1}H NMR spectrum of compound **7** in $CDCl_3$



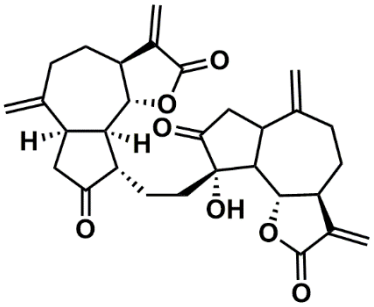
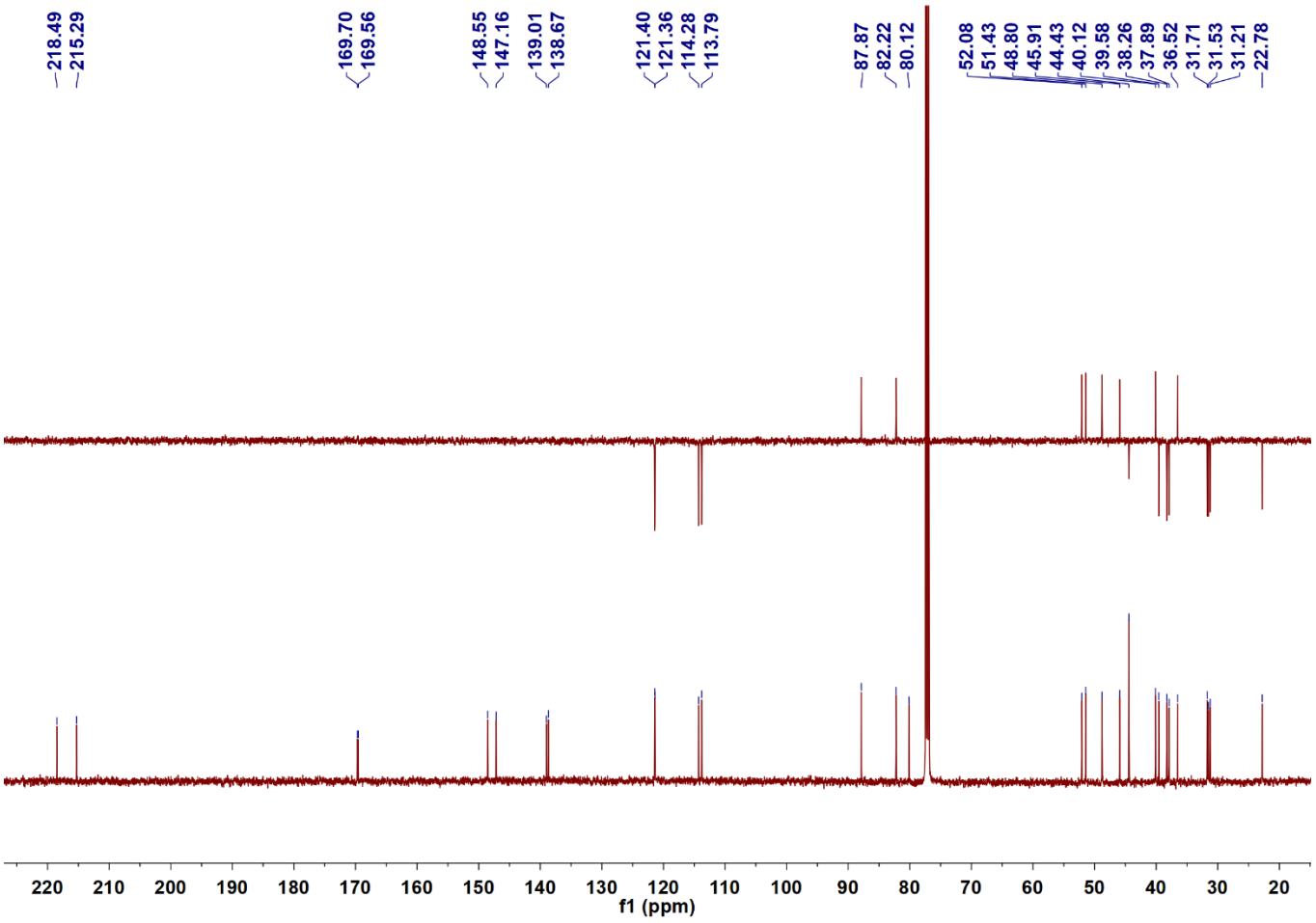


Fig. S35 ^{13}C NMR spectrum of compound **7** in $CDCl_3$



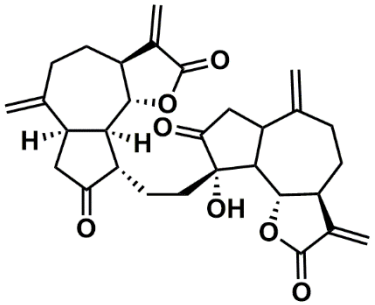
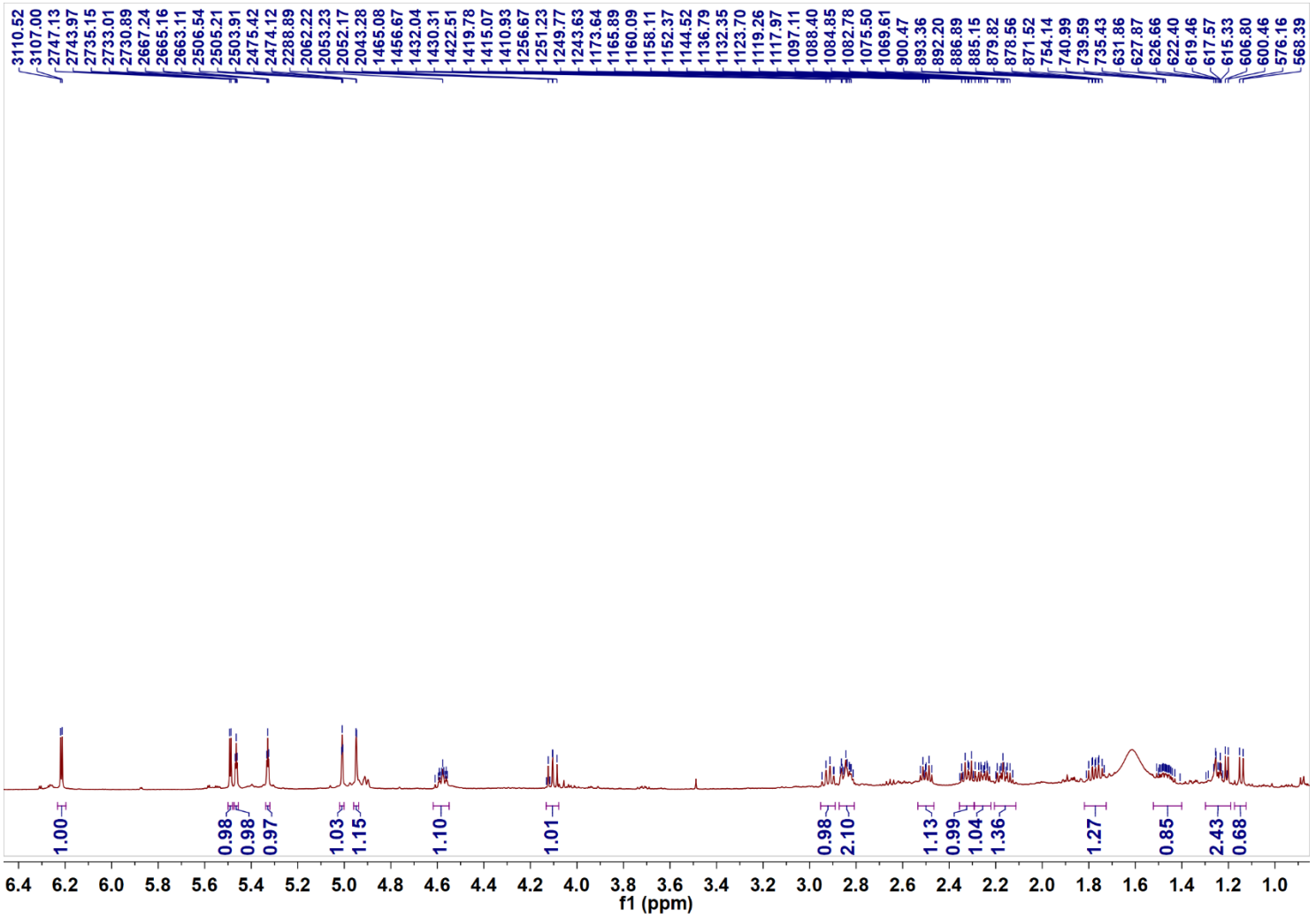


Fig. S36. ^{1}H NMR spectrum of compound **8** in $CDCl_3$



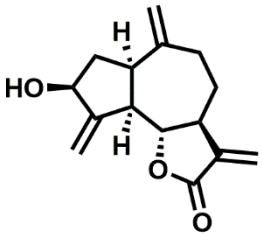
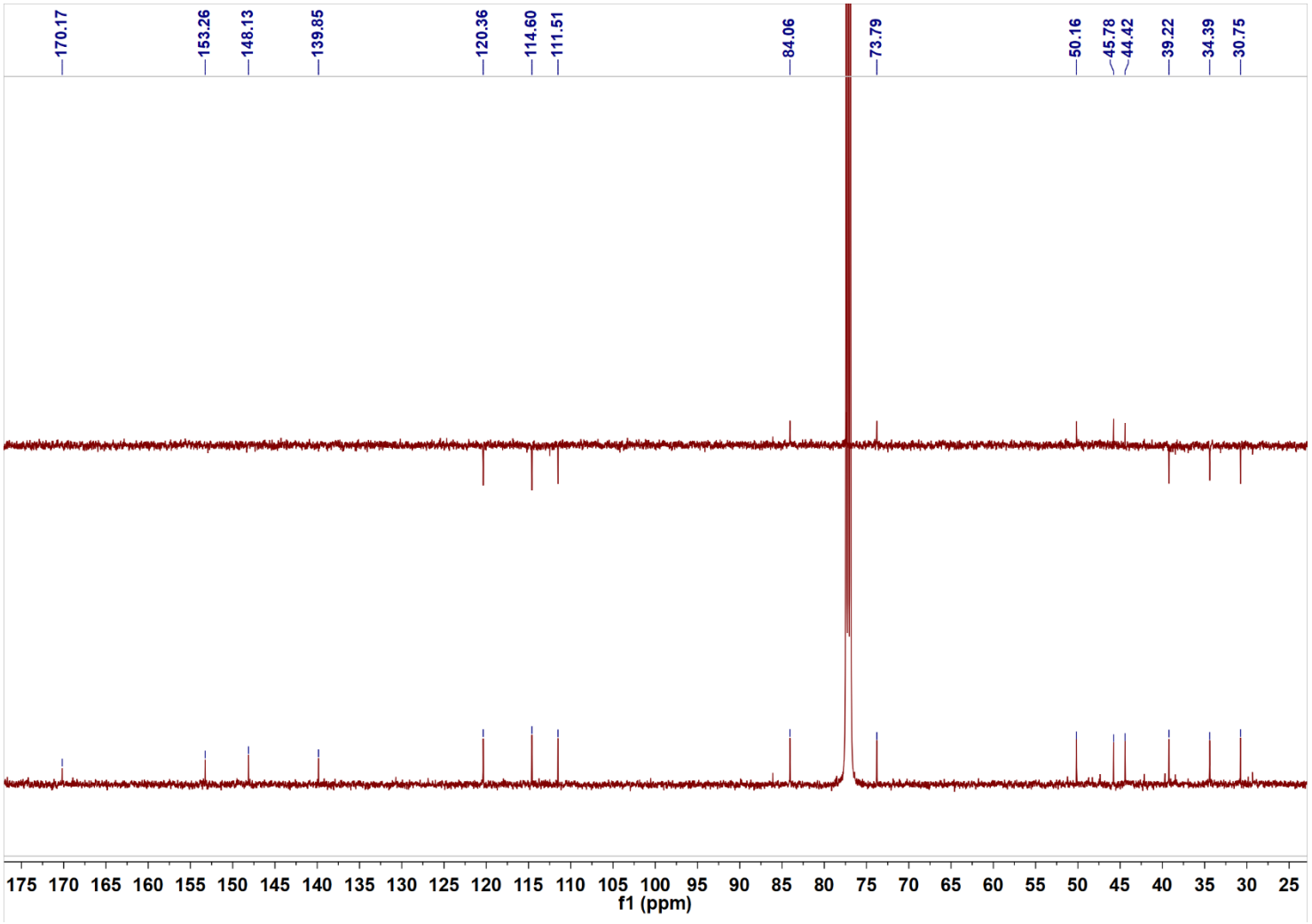
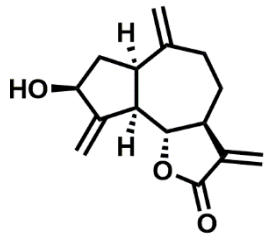


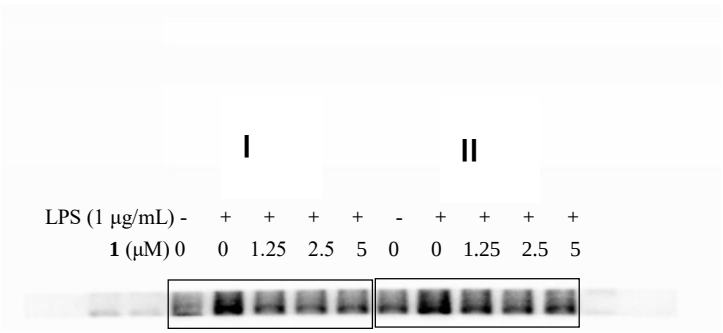
Fig. S37 ^{13}C NMR spectrum of compound **8** in $CDCl_3$

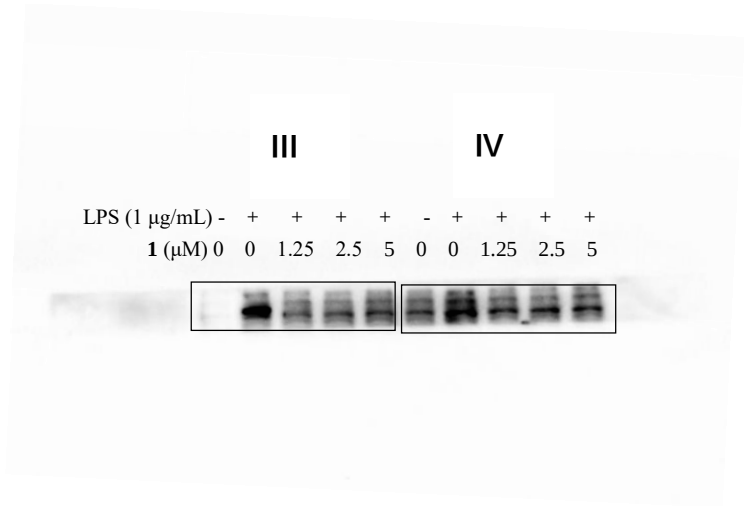




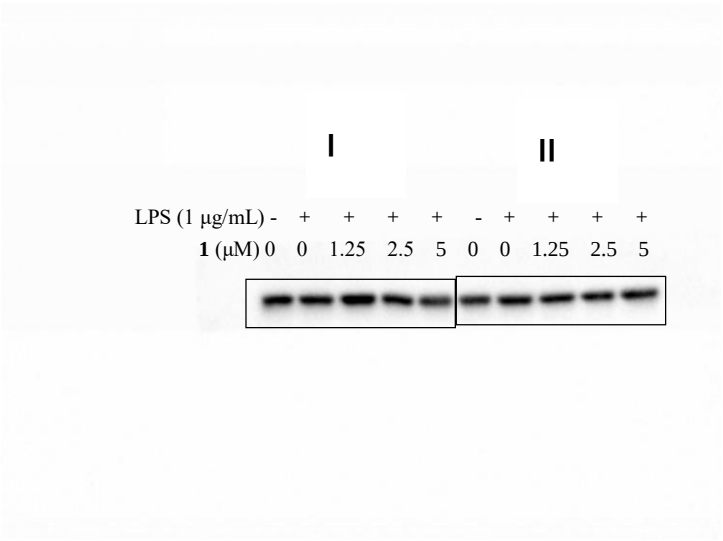
The complete western blot membranes and repeated results for Figure 7B

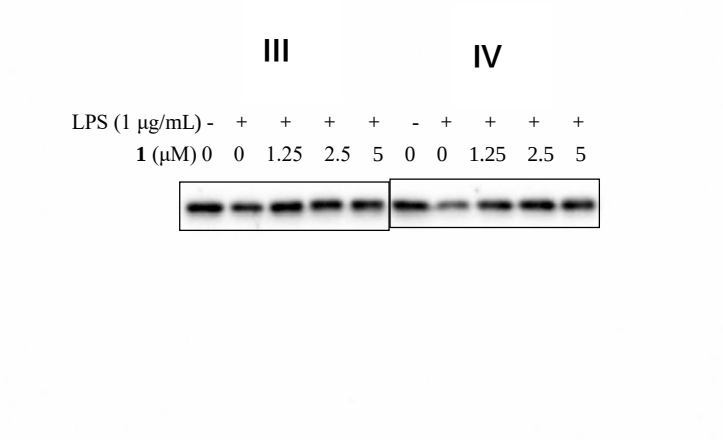
iNOS



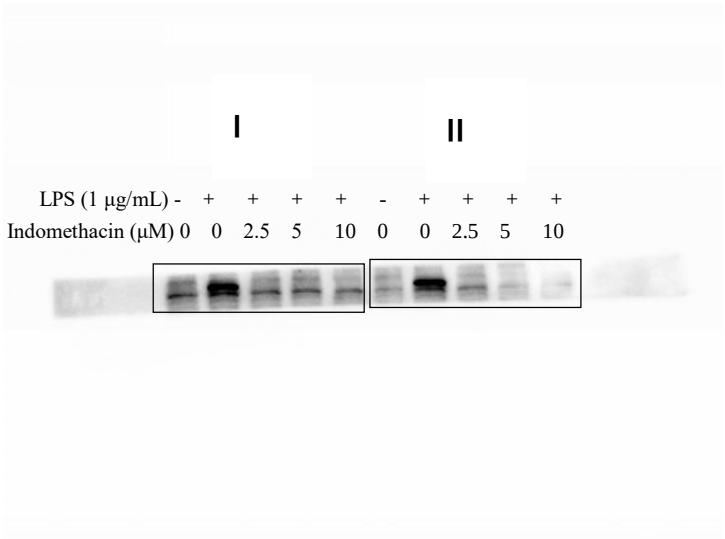


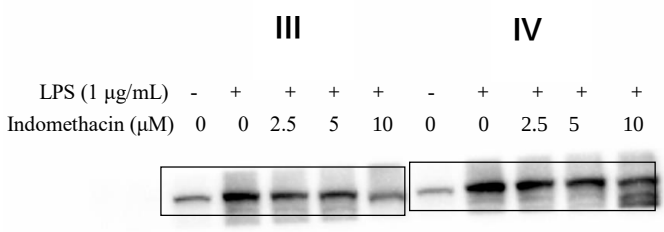
GAPDH


I
II
LPS (1 μg/mL) - + + + + - + + + +
1 (μM) 0 0 1.25 2.5 5 0 0 1.25 2.5 5

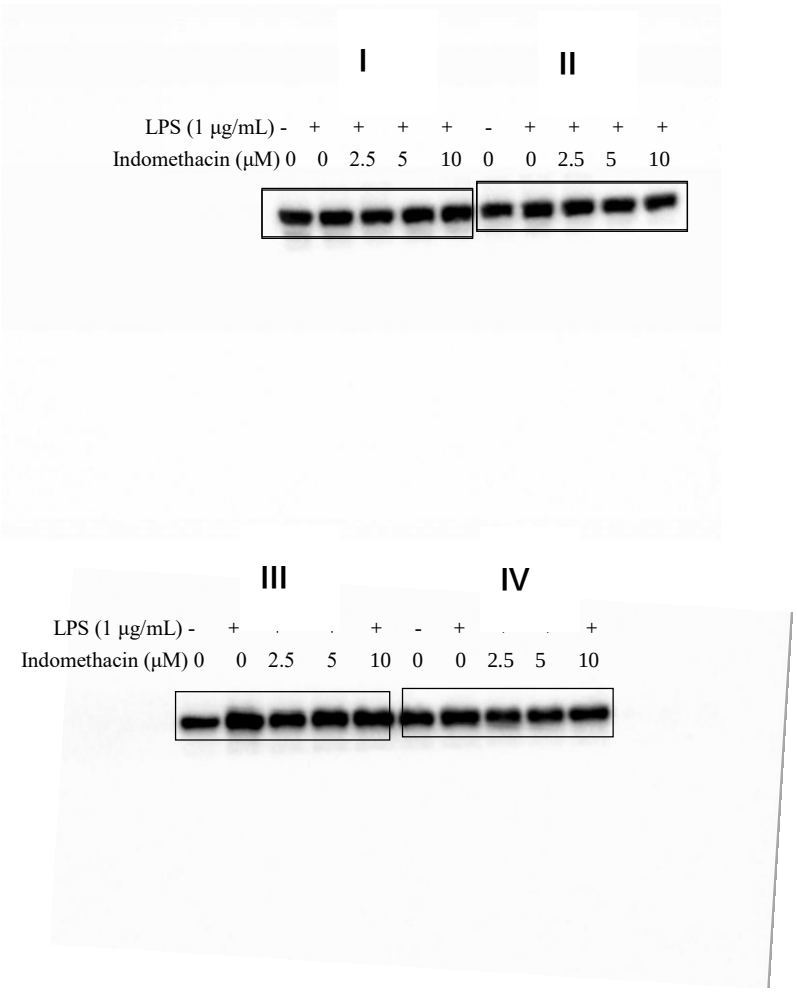

III
IV
LPS (1 μg/mL) - + + + + - + + + +
1 (μM) 0 0 1.25 2.5 5 0 0 1.25 2.5 5

iNOS


I
II
LPS (1 μg/mL) - + + + + - + + + +
Indomethacin (μM) 0 0 2.5 5 10 0 0 2.5 5 10

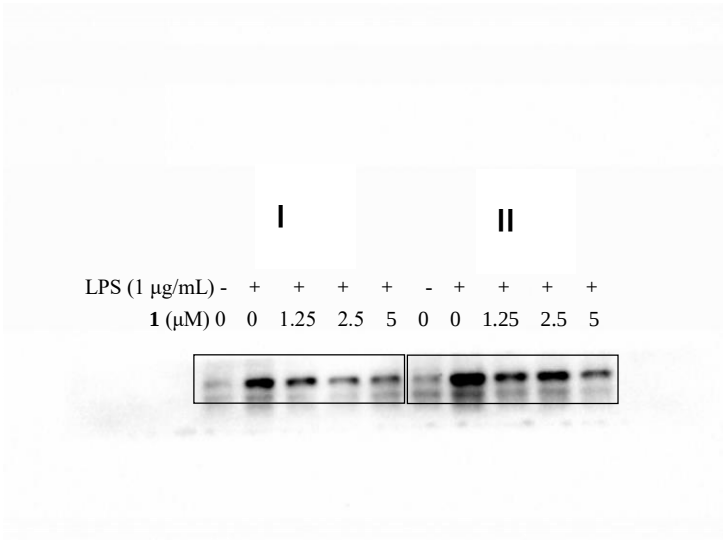

III
IV
LPS (1 μg/mL) - + + + + - + + + +
Indomethacin (μM) 0 0 2.5 5 10 0 0 2.5 5 10

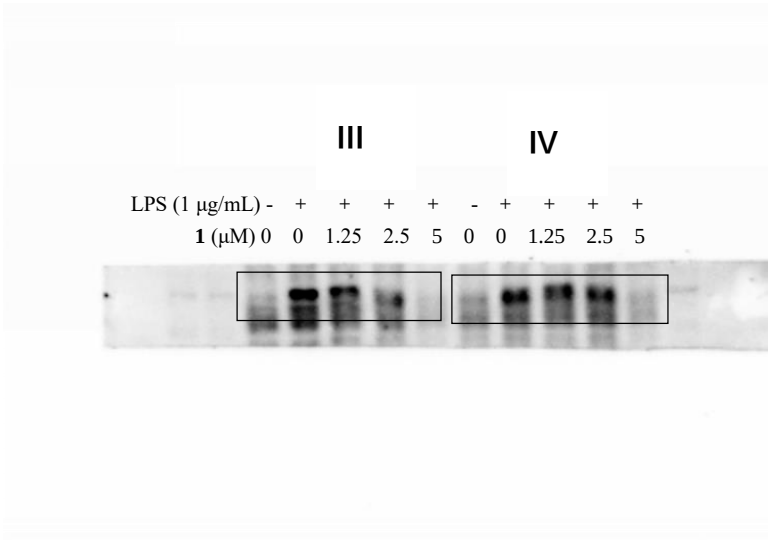
GAPDH


I
II
LPS (1 μg/mL) - + + + + - + + + +
Indomethacin (μM) 0 0 2.5 5 10 0 0 2.5 5 10
III
IV
LPS (1 μg/mL) - + + + - + + +
Indomethacin (μM) 0 0 2.5 5 10 0 0 2.5 5 10

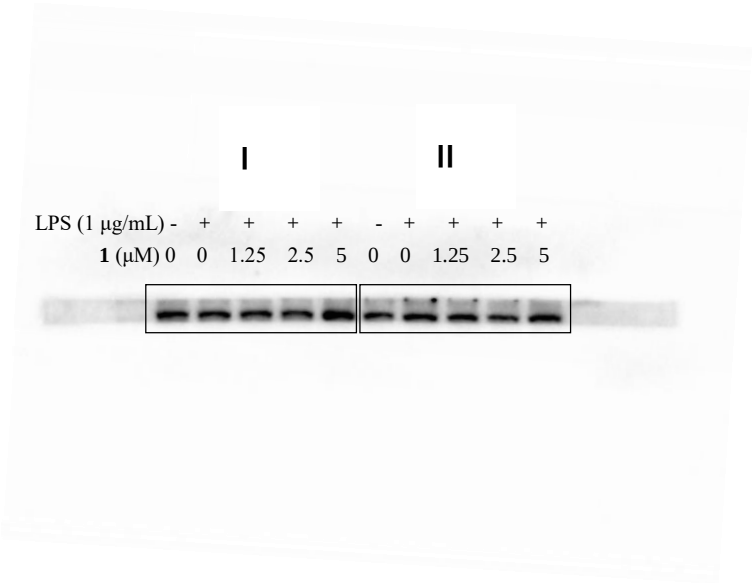
The complete western blot membranes and repeated results for Figure7C

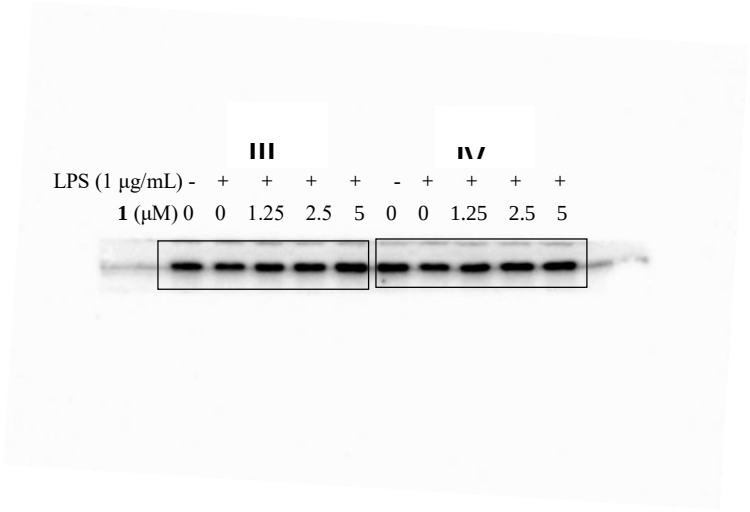
p-IKKα/β



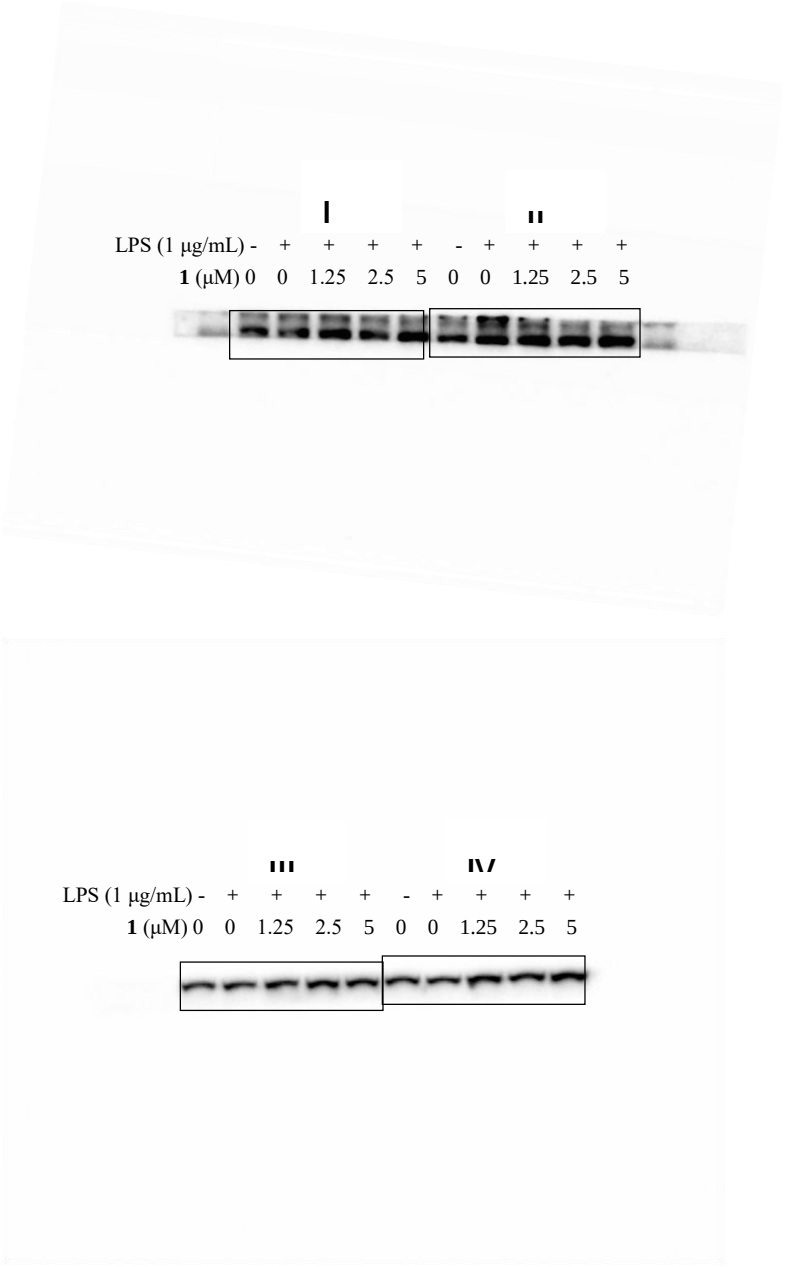


IKKα


I
II
LPS (1 μg/mL) - + + + + - + + + +
1 (μM) 0 0 1.25 2.5 5 0 0 1.25 2.5 5

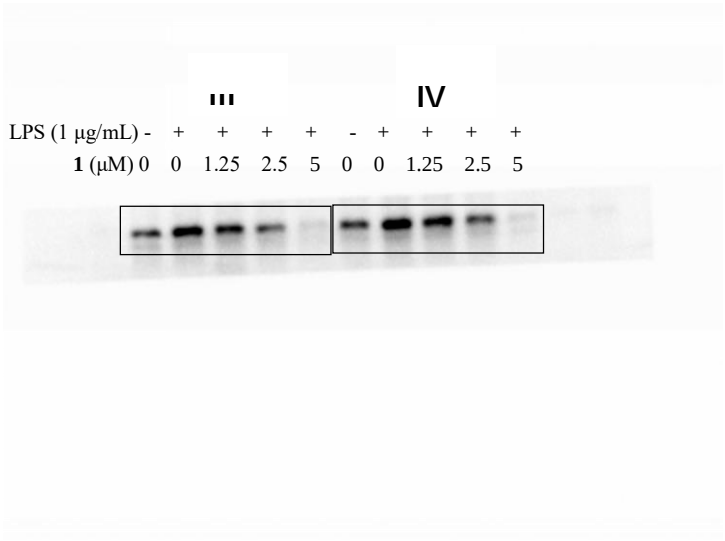

III
IV
LPS (1 μg/mL) - + + + + - + + + +
1 (μM) 0 0 1.25 2.5 5 0 0 1.25 2.5 5

IKKβ

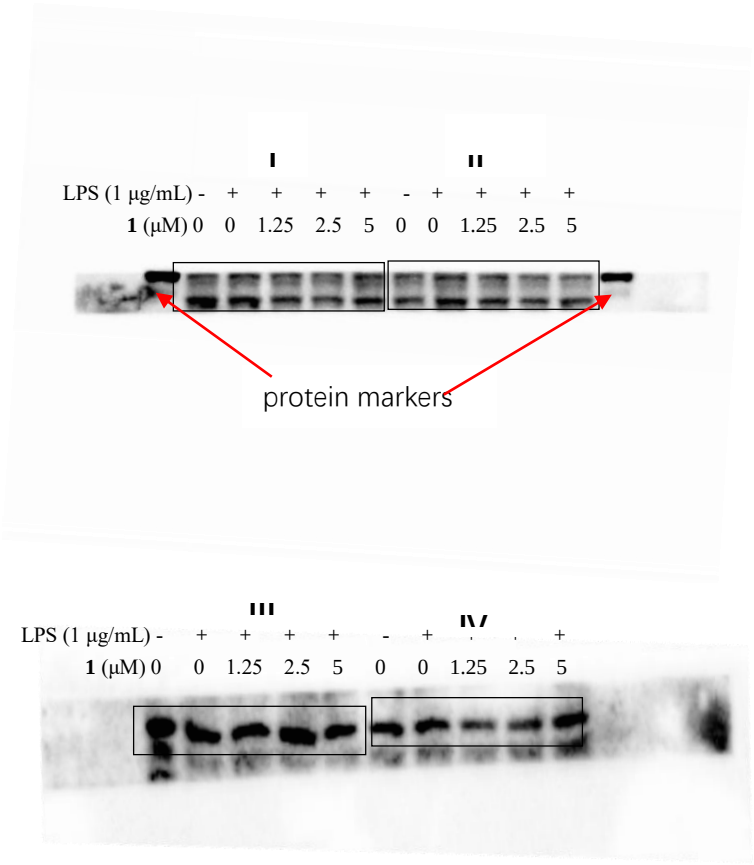

I
II
LPS (1 μg/mL) - + + + + - + + + +
1 (μM) 0 0 1.25 2.5 5 0 0 1.25 2.5 5
III
IV
LPS (1 μg/mL) - + + + + - + + + +
1 (μM) 0 0 1.25 2.5 5 0 0 1.25 2.5 5

p-IκBα

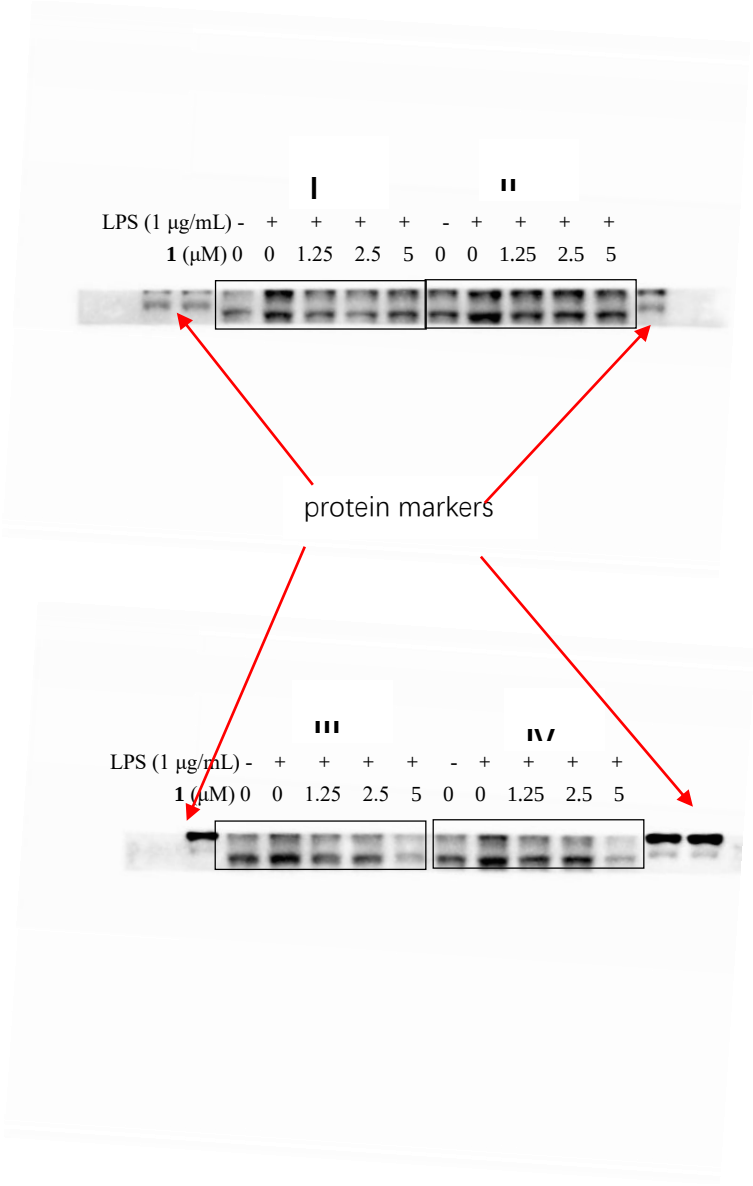

I
II
LPS (1 μg/mL) - + + + + - + + + +
1 (μM) 0 0 1.25 2.5 5 0 0 1.25 2.5 5


III
IV
LPS (1 μg/mL) - + + + + - + + + +
1 (μM) 0 0 1.25 2.5 5 0 0 1.25 2.5 5

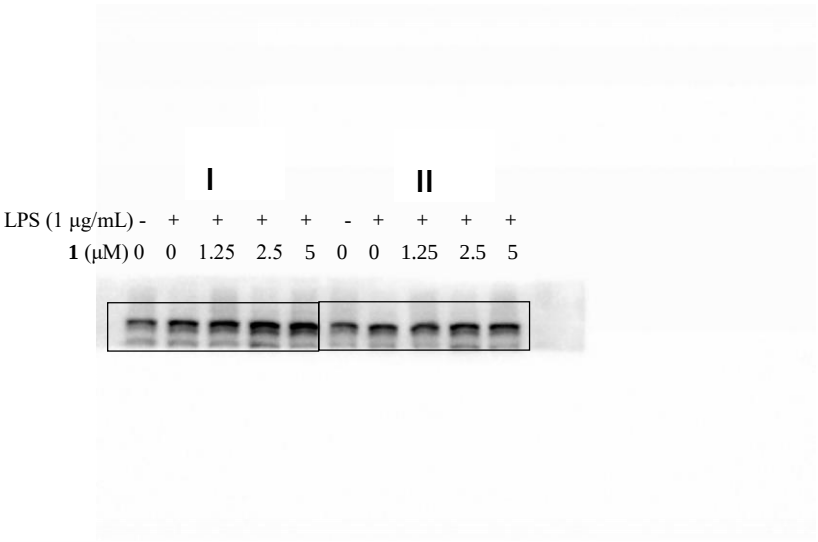
IκBα

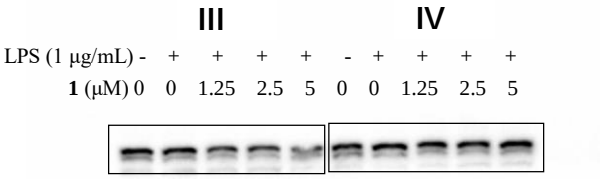

I
II
LPS (1 μg/mL) - + + + + - + + + +
1 (μM) 0 0 1.25 2.5 5 0 0 1.25 2.5 5
protein markers
III
IV
LPS (1 μg/mL) - + + + + - + + + +
1 (μM) 0 0 1.25 2.5 5 0 0 1.25 2.5 5

p-p65

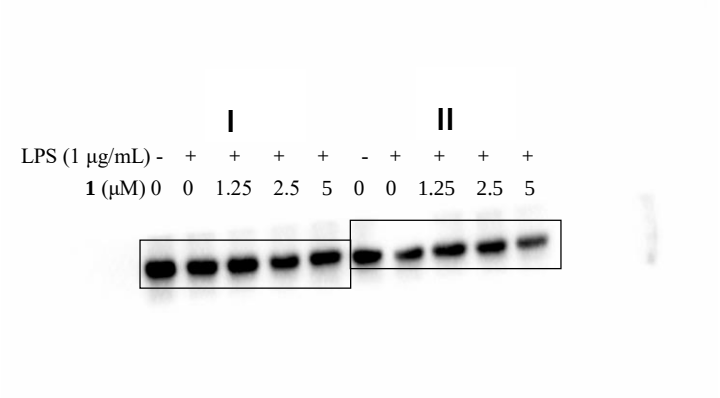

I
II
LPS (1 μg/mL) - + + + + - + + + +
1 (μM) 0 0 1.25 2.5 5 0 0 1.25 2.5 5
protein markers
III
IV
LPS (1 μg/mL) - + + + + - + + + +
1 (μM) 0 0 1.25 2.5 5 0 0 1.25 2.5 5

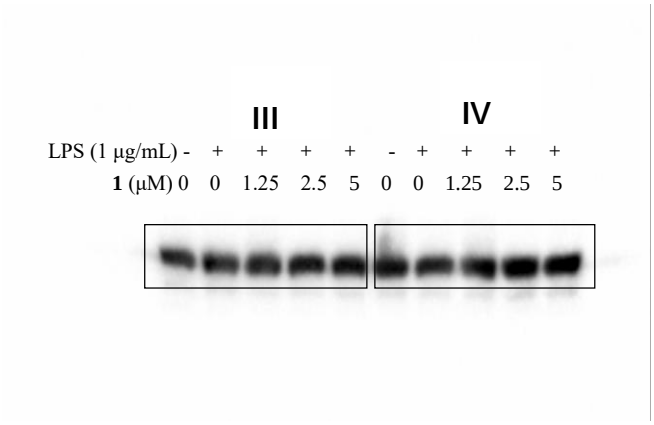
p65


I
II
LPS (1 μg/mL) - + + + + - + + + +
1 (μM) 0 0 1.25 2.5 5 0 0 1.25 2.5 5


III
IV
LPS (1 μg/mL) - + + + + - + + + +
1 (μM) 0 0 1.25 2.5 5 0 0 1.25 2.5 5

GAPDH


I
II
LPS (1 μg/mL) - + + + + - + + + +
1 (μM) 0 0 1.25 2.5 5 0 0 1.25 2.5 5


III
IV
LPS (1 μg/mL) - + + + + - + + + +
1 (μM) 0 0 1.25 2.5 5 0 0 1.25 2.5 5