

Supporting Information

Koilodenoids A–G, Immunosuppressive Spiro Dimers of Diterpenoids from *Koilodepas hainanense*: Structural Elucidation and Biomimetic Transformation

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Structure elucidation for compounds 5–7

Koilodenoid E (**5**) had a molecular formula of $C_{40}H_{62}O_6$ as deduced from the HRESIMS and ^{13}C NMR data. The NMR data of **5** (Table S4) resembled those of **4**, except that the chloride group at C-16' in **4** was replaced by a hydroxy group in **5**, which was supported by the relatively downfield chemical shift of C-16' (δ_{C} 62.7 in **5** vs δ_{C} 48.3 in **4**) and the ^1H - ^1H COSY correlations of H-15'/H₂-16' (Figure S4). The relative and absolute configurations of **5** except for C-15', were elucidated to be identical to those of **4** based on the NOESY data (Figure S4B) and three highly compatible ECD curves (Figure S5). Finally, the absolute configuration of C-15' was determined as *R* by Snatzke's method. As shown in Figure S6, the ECD spectrum of compound **5** and $\text{Mo}_2(\text{OAc})_4$ in DMSO exhibits a negative Cotton effect at 310 nm, corresponding to a negative dihedral angle of the O—C—C—O moiety.

Koilodenoid F (**6**) gave a molecular formula of $C_{40}H_{58}O_7$. Comparison of the 1D NMR data of compounds **6** and **2** (Tables S1 and S5) revealed their structural closeness. In-depth scrutiny of the NMR data (Figure S7), especially the HMBC correlations from H-1 and H-10 to C-2 (δ_{C} 193.1) and the downfield chemical shift of C-4 (δ_{C} 143.2 in **6** vs δ_{C} 116.8 in **2**), revealed that an additional carbonyl was located at C-2 and conjugated to the Δ^3 double bond in **6**. Correspondingly, an absorption band at λ_{max} 276 nm in the UV spectrum (Figure S5) and two absorption peaks at 1676 and 1620 cm^{-1} in the IR spectrum further confirmed the presence of an enone moiety in **6**. The absolute configuration of **6** was determined as delineated by comparison of the ECD spectra (Figure S5). Compound **6** was therefore identified as a 2-oxo derivative of **2**.

Koilodenoid G (**7**) exhibited a molecular formula of $C_{39}H_{58}O_6$. The ^1H and ^{13}C NMR data of **7** (Table S6) were very similar to those of **2**, except for the presence of a carboxyl

group at δ_C 184.8 and the disappearance of an α -hydroxy ketone motif in **7**. The carboxyl group was assigned to C-15 based on the HMBC correlation from H₃-17 to C-15 (Figure S8). The absolute configuration of **7** was established as 5*R*, 8*S*, 9*S*, 10*R*, 13*S*, 4*R*, 5*R*, 8*S*, 9*S*, 10*R*, 13*S* by single-crystal X-ray diffraction with a Flack parameter of 0.06 (10) (Figure S9).

Table S1. ^1H (400 MHz) and ^{13}C (125 MHz) NMR Data for Compound **2** in CDCl_3 .

No.	δ_{H} , multiplets (J in Hz)	δ_{C} , type	No.	δ_{H} , multiplets (J in Hz)	δ_{C} , type
1	1.46, m 1.65, overlap	17.5, CH_2	1'	1.55, m 1.91, m	23.5, CH_2
2	1.99, overlap 2.20, m	29.6, CH_2	2'	2.08, m 2.70, m	38.3, CH_2
3		143.6, C	3'		213.4, C
4		116.8, C	4'		85.0, C
5		37.0, C	5'		46.0, C
6	1.04, m 1.65, overlap	37.0, CH_2	6'	1.34, m 1.73, m	32.2, CH_2
7	1.15, m 1.30, m	25.5, CH_2	7'	1.10, m 1.31, m	25.7, CH_2
8	1.24, m	41.4, CH	8'	1.33, m	40.9, CH
9		36.4, C	9'		36.7, C
10	0.95, dd (12.4, 2.0)	54.0, CH	10'	2.24, m	46.4, CH
11	β 0.99, m α 1.61, m	34.1, CH_2	11'	β 1.22, m α 1.57, m	34.8, CH_2
12	β 1.35, overlap α 1.82, overlap	28.0, CH_2	12'	β 1.35, overlap α 1.82, overlap	28.0, CH_2
13		45.7, C	13'		45.7, C
14	β 1.13, overlap α 1.52, overlap	35.1, CH_2	14'	β 1.13, overlap α 1.52, overlap	35.2, CH_2
15		215.4, C	15'		215.5, C
16	4.34, overlap	63.9, CH_2	16'	4.34, overlap	63.9, CH_2
17	1.16, s	20.8, CH_3	17'	1.24, s	20.7, CH_3
18	α 1.73, m β 1.99, overlap	16.9, CH_2	18'	2.00-2.10, m (2H)	19.4, CH_2
19	0.90, s	20.7, CH_3	19'	0.78, s	15.7, CH_3
20	0.69, s	12.3, CH_3	20'	0.71, s	12.5, CH_3

Table S2. ^1H (400 MHz) and ^{13}C (125 MHz) NMR Data for Compound **3** in CDCl_3 .

No.	δ_{H} , multiplets (J in Hz)	δ_{C} , type	No.	δ_{H} , multiplets (J in Hz)	δ_{C} , type
1	1.94, m 2.01, m	17.2, CH_2	1'	1.59, m 1.93, m	23.6, CH_2
2	1.97, m 2.24, m	25.8, CH_2	2'	2.11, m 2.70, m	38.2, CH_2
3		145.6, C	3'		213.2, C
4		113.7, C	4'		85.1, C
5		37.0, C	5'		45.7, C
6	1.11, m 1.89, m	37.7, CH_2	6'	1.36, m 1.73, m	32.2, CH_2
7	1.19, m 1.36, m	25.6, CH_2	7'	1.08, m 1.44, m	27.1, CH_2
8	1.33, m	41.2, CH	8'	1.35, m	40.9, CH
9		37.8, C	9'		36.8, C
10	1.06, m	52.2, CH	10'	2.24, dd (11.6, 3.6)	46.5, CH
11	1.15, m 1.58, m	34.8, CH_2	11'	1.18, m 1.59, m	34.9, CH_2
12	β 1.42, m α 1.84, m	28.2, CH_2	12'	β 1.34, m α 1.93, m	28.2, CH_2
13		45.9, C	13'		45.8, C
14	1.20, m 1.59, m	35.2, CH_2	14'	1.15, m 1.56, m	35.2, CH_2
15		215.5, C	15'		215.7, C
16	4.38, overlap	64.0, CH_2	16'	4.38, overlap	64.0 CH_2
17	1.27, s	21.0, CH_3	17'	1.21, s	20.7, CH_3
18	1.86, m 2.06, m	18.5, CH_2	18'	1.42, m 2.15, m	20.4, CH_2
19	0.90, s	34.1, CH_3	19'	0.82, s	15.9, CH_3
20	0.88, s	12.0, CH_3	20'	0.75, s	12.6, CH_3

Table S3. ^1H (400 MHz) and ^{13}C (125 MHz) NMR Data for Compound **4** in CDCl_3 .

No.	δ_{H} , multiplets (J in Hz)	δ_{C} , type	No.	δ_{H} , multiplets (J in Hz)	δ_{C} , type
1	1.50, m 1.73, m	17.7, CH_2	1'	1.60, m 1.93, m	23.8, CH_2
2	2.05, m 2.25, m	29.7, CH_2	2'	2.11, m 2.74, m	38.6, CH_2
3		143.8, C	3'		213.8, C
4		116.9, C	4'		85.2, C
5		37.2, C	5'		46.2, C
6	1.07, m 1.67, m	37.2, CH_2	6'	1.34, m 1.75, m	32.4, CH_2
7	1.14, m 1.31, m	25.9, CH_2	7'	1.15, overlap 1.36, m	25.8, CH_2
8	1.28, m	41.6, CH	8'	1.28, m	41.3, CH
9		36.9, C	9'		36.6, C
10	1.00, m	54.2, CH	10'	2.25, m	46.5, CH
11	1.04, m 1.62, m	34.3, CH_2	11'	1.15, overlap 1.57, m	35.3, CH_2
12	β 1.38, m α 1.87, overlap	29.1, CH_2	12'	β 1.41, m α 1.87, overlap	28.1, CH_2
13		45.8, C	13'		38.0, C
14	1.15, overlap 1.58, overlap	35.5, CH_2	14'	1.17, m 1.60, m	36.9, CH_2
15		215.7, C	15'	3.39, dd (10.2, 2.6)	80.9, CH
16	4.39, s (2H)	64.0, CH_2	16'	3.48, dd (10.8, 10.2) 3.78, dd (10.8, 2.6)	48.3, CH_2
17	1.20, s	20.9, CH_3	17'	0.99, s	19.0, CH_3
18	α 1.75, m β 2.01, m	17.0, CH_3	18'	2.03, m 2.05, m	19.5, CH_2
19	0.94, s	20.8, CH_3	19'	0.82, s	15.8, CH_3
20	0.73, overlap	12.4, CH_3	20'	0.73, overlap	12.6, CH_3

Table S4. ^1H (400 MHz) and ^{13}C (125 MHz) NMR Data for Compound **5** in CDCl_3 .

No.	δ_{H} , multiplets (J in Hz)	δ_{C} , type	No.	δ_{H} , multiplets (J in Hz)	δ_{C} , type
1	1.51, m 1.70, m	17.7, CH_2	1'	1.58, m 1.94, m	23.8, CH_2
2	2.05, m 2.25, m	29.7, CH_2	2'	2.11, m 2.74, m	38.6, CH_2
3		143.8, C	3'		213.8, C
4		116.9, C	4'		85.2, C
5		37.2, C	5'		46.2, C
6	1.10, m 1.67, m	37.2, CH_2	6'	1.34, m 1.75, m	32.4, CH_2
7	1.16, m 1.33, m	25.9, CH_2	7'	1.15, m 1.36, m	25.8, CH_2
8	1.30, m	41.6, CH	8'	1.32, m	41.2, CH
9		37.0, C	9'		36.8, C
10	1.00, m	54.2, CH	10'	2.23, m	46.6, CH
11	1.04, m 1.64, m	34.3, CH_2	11'	1.15, m 1.58, overlap	35.4, CH_2
12	β 1.38, m α 1.58, overlap	29.1, CH_2	12'	β 1.41, m α 1.87, m	28.1, CH_2
13		45.8, C	13'		36.6, C
14	1.16, m 1.58, m	35.4, CH_2	14'	0.84, m 1.33, m	36.5, CH_2
15		215.7, C	15'	3.34, dd (9.4, 2.8)	81.4, CH
16	4.38, s (2H)	64.0, CH_2	16'	3.53, dd (10.8, 9.4) 3.78, dd (10.8, 2.8)	62.7, CH_2
17	1.20, s	20.9, CH_3	17'	0.99, s	19.2, CH_3
18	α 1.75, m β 2.01, m	17.0, CH_3	18'	2.05, m 2.11, m	19.5, CH_2
19	0.94, s	20.8, CH_3	19'	0.82, s	15.8, CH_3
20	0.73, s	12.4, CH_3	20'	0.73, s	12.6, CH_3

Table S5. ^1H (400 MHz) and ^{13}C (125 MHz) NMR Data for Compound **6** in CDCl_3 .

No.	δ_{H} , multiplets (J in Hz)	δ_{C} , type	No.	δ_{H} , multiplets (J in Hz)	δ_{C} , type
1	1.61, m 2.45, m	34.9, CH_2	1'	1.60, m 1.98, m	23.4, CH_2
2		193.1, C	2'	2.10, m 2.74, m	37.8, CH_2
3		142.4, C	3'		212.7, C
4		143.2, C	4'		85.4, C
5		39.4, C	5'		46.3, C
6	1.32, m 1.77, m	35.9, CH_2	6'	1.37, m 1.82, m	32.1, CH_2
7	1.22, overlap 1.40, overlap	25.1, CH_2	7'	1.22, overlap 1.40, overlap	25.4, CH_2
8	1.36, m	41.0, CH	8'	1.51, m	40.5, CH
9		36.3, C	9'		36.7, C
10	1.58, m	52.6, CH	10'	2.55, dd (12.8, 3.2)	46.0, CH
11	1.08, m 1.60, m	33.7, CH_2	11'	1.20, m 1.56, m	34.7, CH_2
12	β 1.43, m α 1.86, m	28.0, CH_2	12'	β 1.48, m α 1.86, m	27.7, CH_2
13		45.7, C	13'		45.5, C
14	1.18, m 1.56, m	35.1, CH_2	14'	1.20, m 1.56, m	35.1, CH_2
15		215.5, C	15'		215.1, C
16	4.38, overlap	63.9, CH_2	16'	4.38, overlap	63.9, CH_2
17	1.20, s	20.8, CH_3	17'	1.28, s	20.6, CH_3
18	2.19, m 2.40, m	18.8, CH_3	18'	2.04, m 2.08, m	18.6, CH_2
19	1.10, s	19.1, CH_3	19'	0.85, s	15.9, CH_3
20	0.76, s	12.1, CH_3	20'	0.81, s	12.5, CH_3

Table S6. ^1H (400 MHz) and ^{13}C (125 MHz) NMR Data for Compound **7** in CDCl_3 .

No.	δ_{H} , multiplets (J in Hz)	δ_{C} , type	No.	δ_{H} , multiplets (J in Hz)	δ_{C} , type
1	1.49, m 1.69, m	17.7, CH_2	1'	1.60, m 1.94, m	23.7, CH_2
2	2.01, m 2.22, m	29.8, CH_2	2'	2.13, m 2.74, m	38.4, CH_2
3		143.7, C	3'		213.6, C
4		117.1, C	4'		85.1, C
5		37.2, C	5'		45.8, C
6	1.09, m 1.64, m	37.2, CH_2	6'	1.38, m 1.77, m	32.3, CH_2
7	1.17, m 1.36, m	25.7, CH_2	7'	1.12, m 1.38, m	25.6, CH_2
8	1.22, m	41.7, CH	8'	1.36, m	41.0, CH
9		36.8, C	9'		36.5, C
10	0.98, dd (12.6, 1.8)	54.2, CH	10'	2.26, dd (13.0, 3.4)	46.5, CH
11	1.02, m 1.65, m	34.5, CH_2	11'	1.22, m 1.60, m	34.9, CH_2
12	β 1.47, m α 2.00, m	28.9, CH_2	12'	β 1.41, m α 1.86, m	28.1, CH_2
13		42.0, C	13'		46.1, C
14	1.24, m 1.66, m	36.1, CH_2	14'	1.20, m 1.56, m	35.2, CH_2
15		184.6, C	15'		215.5, C
			16'	4.39, s (2H)	64.0, CH_2
17	1.26, s	20.9, CH_3	17'	1.24, s	21.4, CH_3
18	1.77, m 2.01, m	17.0, CH_3	18'	2.07, m 2.14, m	19.5, CH_2
19	0.94, s	20.9, CH_3	19'	0.82, s	15.8, CH_3
20	0.74, s	12.4, CH_3	20'	0.75, s	12.6, CH_3

Table S7. X-ray Crystallographic Data for Compound **2^a**

Identification code	cu_20211157_0m
Empirical formula	C ₄₀ H ₆₀ O ₆
Formula weight	636.88
Temperature/K	170.0
Crystal system	triclinic
Space group	P1
<i>a</i> /Å	6.58220 (10)
<i>b</i> /Å	7.3678 (2)
<i>c</i> /Å	19.2597 (5)
$\alpha/^\circ$	82.8040 (10)
$\beta/^\circ$	83.0410 (10)
$\gamma/^\circ$	67.3320 (10)
Volume/Å ³	852.37 (4)
<i>Z</i>	1
ρ_{calc} g/cm ³	1.241
μ/mm^{-1}	0.640
<i>F</i> (000)	348.0
Crystal size/mm ³	0.12 × 0.08 × 0.05
Radiation	Cu K α ($\lambda = 1.54178$)
2 Θ range for data collection/°	4.64 to 148.97
Index ranges	-8 ≤ <i>h</i> ≤ 8, -9 ≤ <i>k</i> ≤ 8, -23 ≤ <i>l</i> ≤ 24
Reflections collected	17711
Independent reflections	6389 [$R_{\text{int}} = 0.0497$, $R_{\text{sigma}} = 0.0520$]
Data/restraints/parameters	6389/3/426
Goodness-of-fit on <i>F</i> ²	1.033
Final <i>R</i> indexes [$I \geq 2\sigma(I)$]	$R_1 = 0.0392$, $\omega R_2 = 0.0977$
Final <i>R</i> indexes [all data]	$R_1 = 0.0414$, $\omega R_2 = 0.1001$
Largest diff. peak/hole/e Å ⁻³	0.22/-0.20
Flack parameter	-0.07 (10)

^aCrystals of **2** were obtained from CH₂Cl₂.

Table S8. X-ray Crystallographic Data for Compound **3**^a

Identification code	cu_2022189_0m
Empirical formula	C ₄₀ H ₆₀ O ₆
Formula weight	636.88
Temperature/K	150.0
Crystal system	monoclinic
Space group	P2 ₁
<i>a</i> /Å	6.9518 (2)
<i>b</i> /Å	14.2638 (3)
<i>c</i> /Å	17.5248 (4)
α /°	90
β /°	93.3940 (10)
γ /°	90
Volume/Å ³	1734.70 (7)
<i>Z</i>	2
ρ_{calc} g/cm ³	1.219
μ /mm ⁻¹	0.629
<i>F</i> (000)	696.0
Crystal size/mm ³	0.08 × 0.05 × 0.03
Radiation	Cu K α (λ = 1.54178)
2 Θ range for data collection/°	5.052 to 149.04
Index ranges	-8 ≤ <i>h</i> ≤ 8, -17 ≤ <i>k</i> ≤ 17, -21 ≤ <i>l</i> ≤ 21
Reflections collected	30435
Independent reflections	6985 [$R_{\text{int}} = 0.0428$, $R_{\text{sigma}} = 0.0316$]
Data/restraints/parameters	6985/1/426
Goodness-of-fit on <i>F</i> ²	1.045
Final <i>R</i> indexes [$I >= 2\sigma(I)$]	$R_1 = 0.0288$, $\omega R_2 = 0.0730$
Final R indexes [all data]	$R_1 = 0.0301$, $\omega R_2 = 0.0739$
Largest diff. peak/hole/e Å ⁻³	0.21/-0.17
Flack parameter	0.01 (5)

^aCrystals of **3** were obtained from CH₂Cl₂.

Table S9. X-ray Crystallographic Data for Compound **4^a**

Identification code	mo_20211202_0m
Empirical formula	C ₄₀ H ₆₁ ClO ₅
Formula weight	657.33
Temperature/K	170.0
Crystal system	monoclinic
Space group	P2 ₁
<i>a</i> /Å	6.4779 (3)
<i>b</i> /Å	39.9833 (16)
<i>c</i> /Å	7.3091 (3)
α /°	90
β /°	110.8930 (10)
γ /°	90
Volume/Å ³	1768.64 (13)
<i>Z</i>	2
ρ_{calc} g/cm ³	1.234
μ /mm ⁻¹	0.151
<i>F</i> (000)	716.0
Crystal size/mm ³	0.11 × 0.06 × 0.03
Radiation	Mo K α (λ = 0.71073)
2 Θ range for data collection/°	4.074 to 54.652
Index ranges	-8 ≤ <i>h</i> ≤ 8, -51 ≤ <i>k</i> ≤ 50, -8 ≤ <i>l</i> ≤ 9
Reflections collected	17791
Independent reflections	7158 [$R_{\text{int}} = 0.0448$, $R_{\text{sigma}} = 0.0577$]
Data/restraints/parameters	7158/1/423
Goodness-of-fit on <i>F</i> ²	1.050
Final R indexes [$I \geq 2\sigma(I)$]	$R_1 = 0.0441$, $\omega R_2 = 0.0827$
Final R indexes [all data]	$R_1 = 0.0615$, $\omega R_2 = 0.0922$
Largest diff. peak/hole/e Å ⁻³	0.19/-0.27
Flack parameter	-0.06 (4)

^aCrystals of **4** were obtained from CH₂Cl₂.

Table S10. X-ray Crystallographic Data for Compound **7^a**

Identification code	20220561_0m_sq
Empirical formula	C ₃₉ H ₅₈ O ₆
Formula weight	622.85
Temperature/K	170.0
Crystal system	monoclinic
Space group	P2 ₁
<i>a</i> /Å	19.4735 (6)
<i>b</i> /Å	7.8392 (2)
<i>c</i> /Å	24.0193 (8)
$\alpha/^\circ$	90
$\beta/^\circ$	107.264 (2)
$\gamma/^\circ$	90
Volume/Å ³	3501.51 (19)
<i>Z</i>	4
ρ_{calc} g/cm ³	1.182
μ/mm^{-1}	0.613
<i>F</i> (000)	1360.0
Crystal size/mm ³	0.09 × 0.05 × 0.04
Radiation	Cu K α ($\lambda = 1.54178$)
2 Θ range for data collection/°	4.752 to 149.498
Index ranges	-24 ≤ <i>h</i> ≤ 24, -9 ≤ <i>k</i> ≤ 9, -29 ≤ <i>l</i> ≤ 30
Reflections collected	58386
Independent reflections	14096 [$R_{\text{int}} = 0.0598$, $R_{\text{sigma}} = 0.0448$]
Data/restraints/parameters	14096/62/865
Goodness-of-fit on <i>F</i> ²	1.060
Final R indexes [$I \geq 2\sigma(I)$]	$R_1 = 0.0616$, $\omega R_2 = 0.1705$
Final R indexes [all data]	$R_1 = 0.0734$, $\omega R_2 = 0.1821$
Largest diff. peak/hole/e Å ⁻³	0.48/-0.36
Flack parameter	0.06 (10)

^aCrystals of **7** were obtained from CH₂Cl₂.

Scheme S1. Plausible biosynthetic pathway for 1–4.

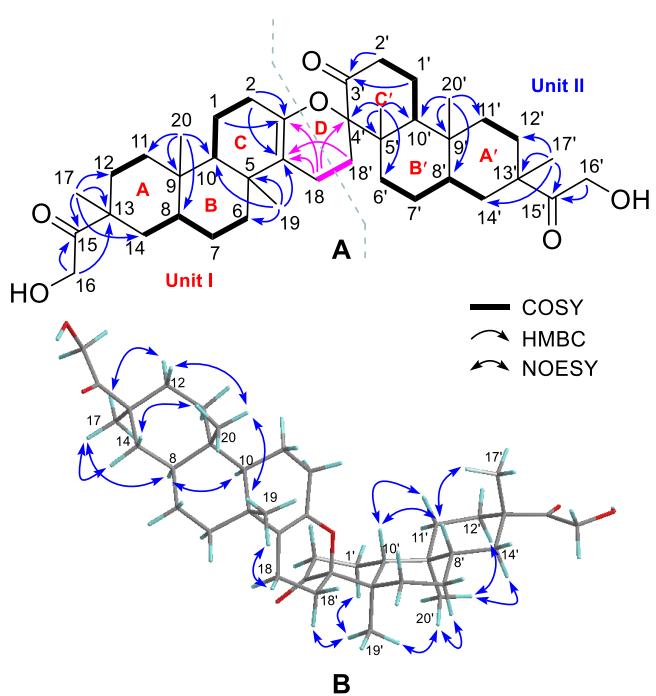
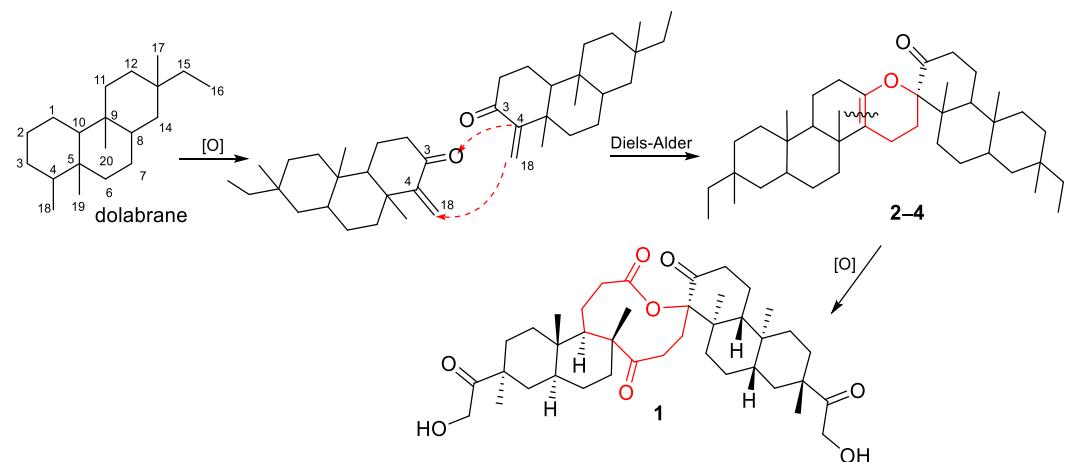


Figure S1. Key COSY, HMBC, and NOESY correlations of **2**.

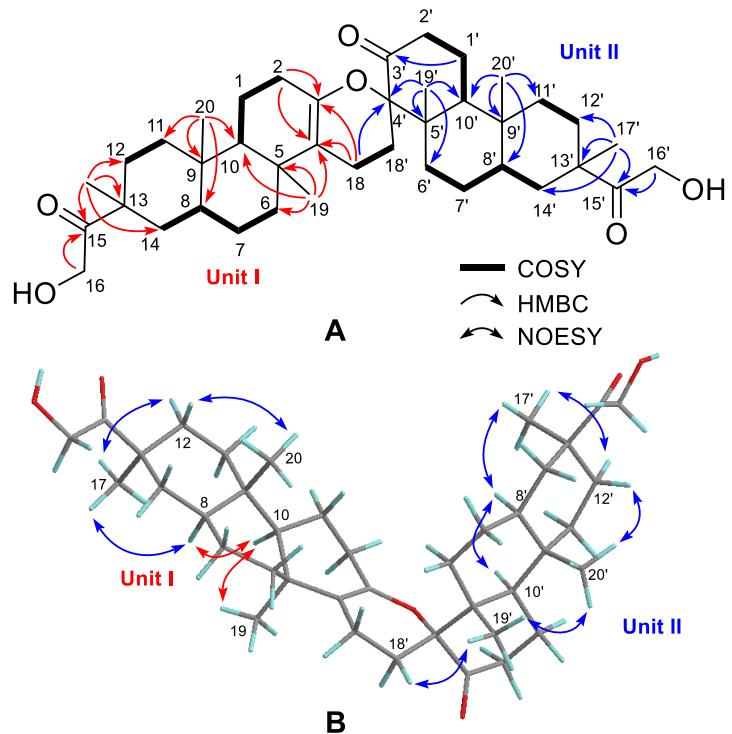


Figure S2. Key COSY, HMBC, and NOESY correlations of **3**.

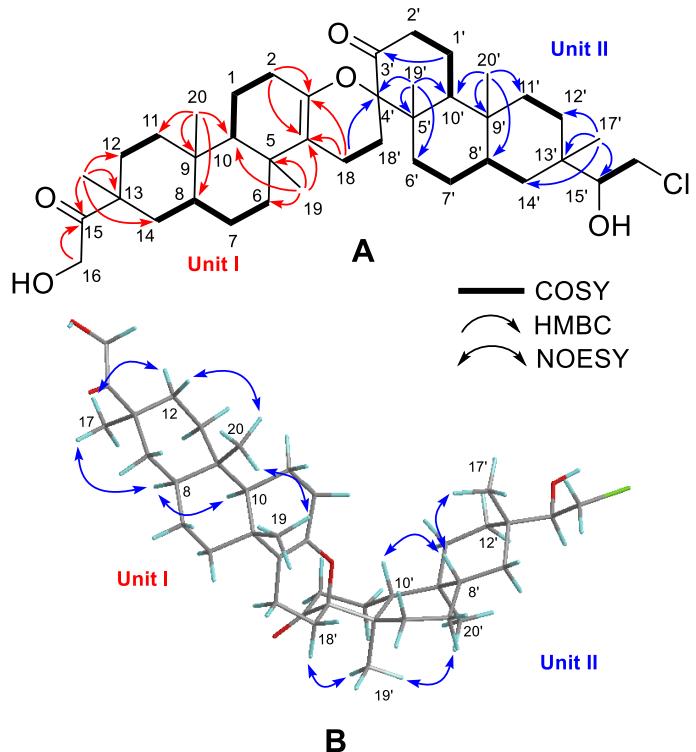


Figure S3. Key COSY, HMBC, and NOESY correlations of **4**.

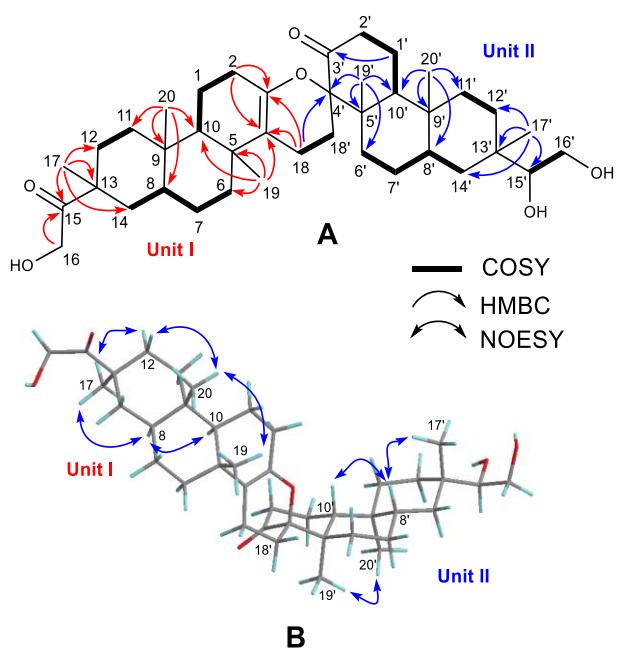


Figure S4. Key COSY, HMBC, and NOESY correlations of **5**.

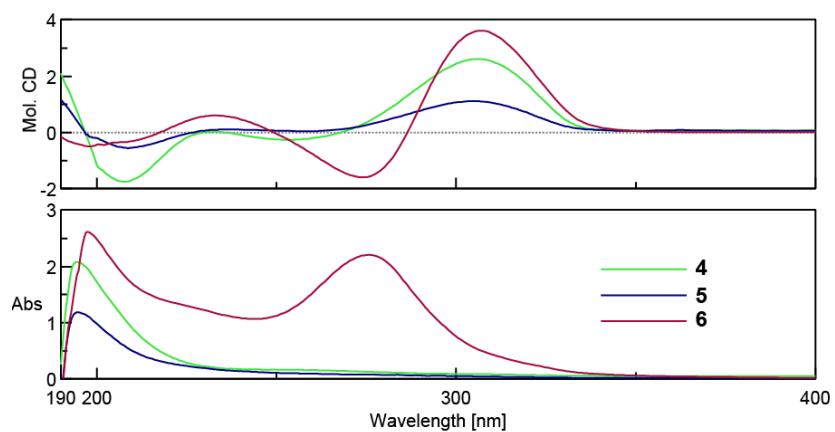


Figure S5. The ECD spectra of compounds **4–6**.

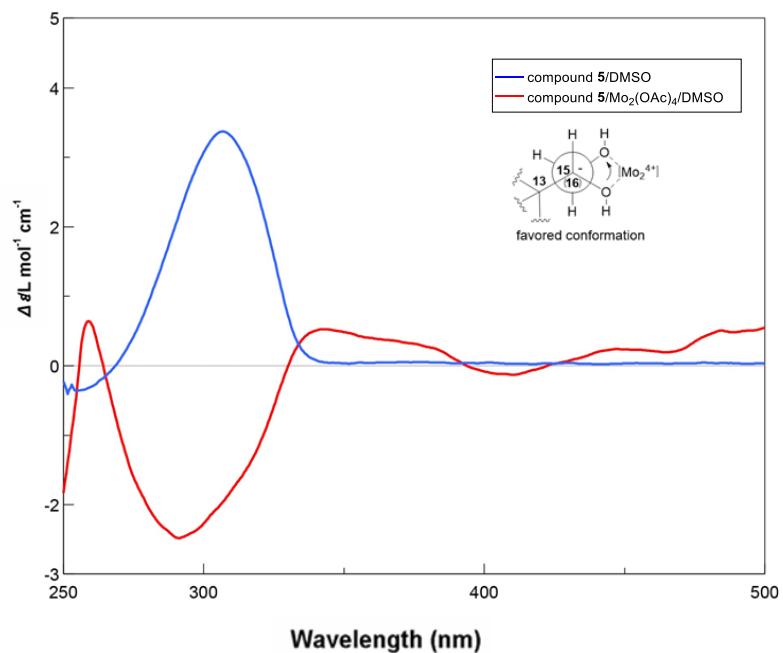


Figure S6. ECD spectra of compound **5** in a DMSO solution (blue) and in a DMSO solution of $\text{Mo}_2(\text{OAc})_4$ (red) (The inherent ECD was subtracted).

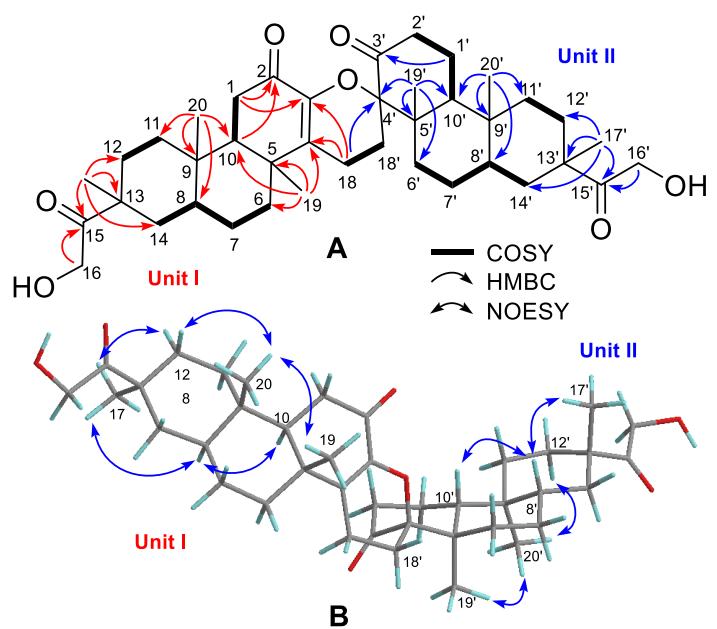


Figure S7. Key COSY, HMBC, and NOESY correlations of **6**.

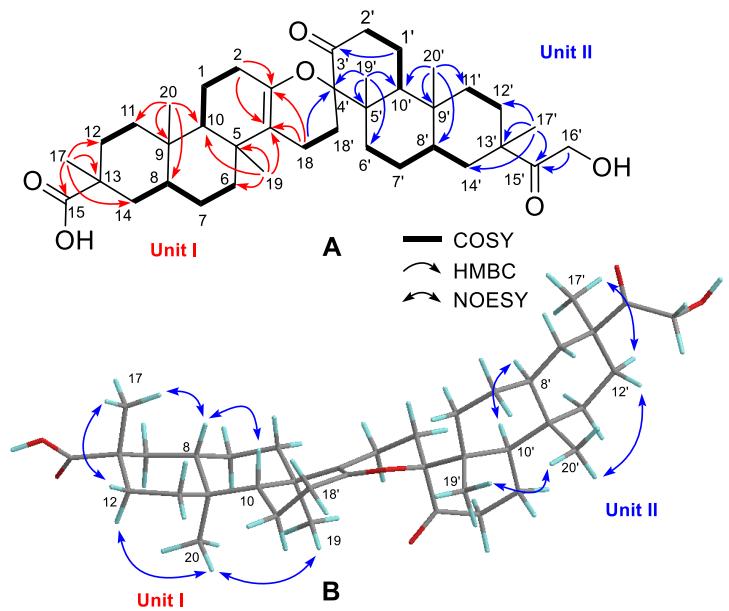


Figure S8. Key COSY, HMBC, and NOESY correlations of 7.

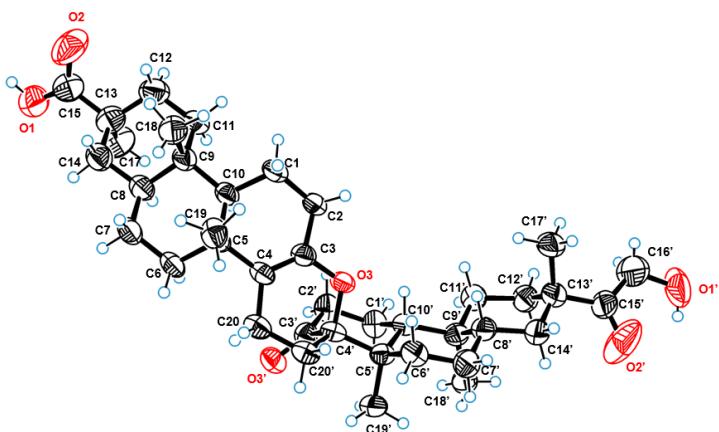


Figure S9. X-ray ORTEP drawing of 7.

Figure S10. ^1H NMR spectrum of natural Koilodenoid A (**1**) in CDCl_3 .

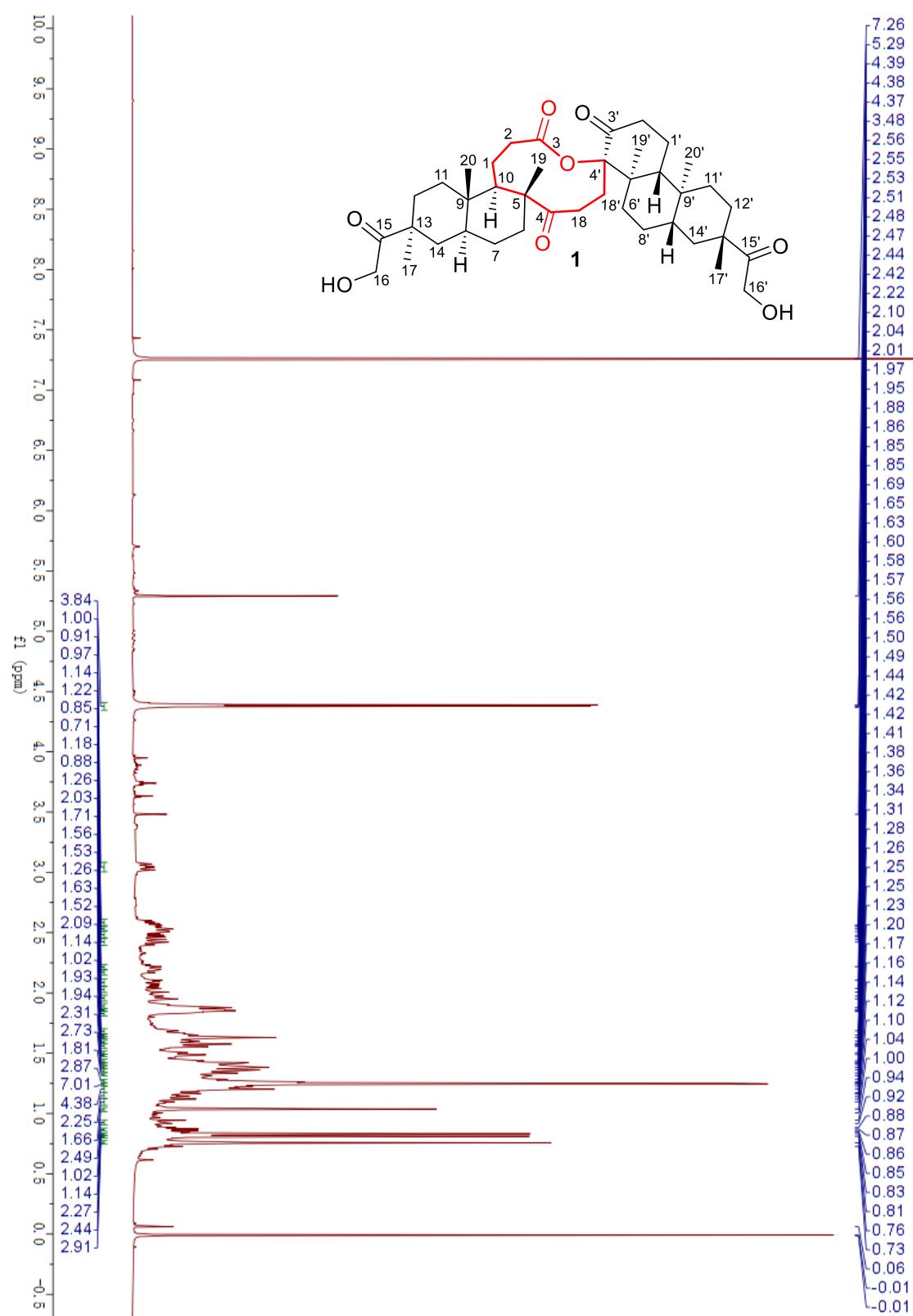


Figure S11. ^{13}C NMR spectrum of natural Koilodenoid A (**1**) in CDCl_3 .

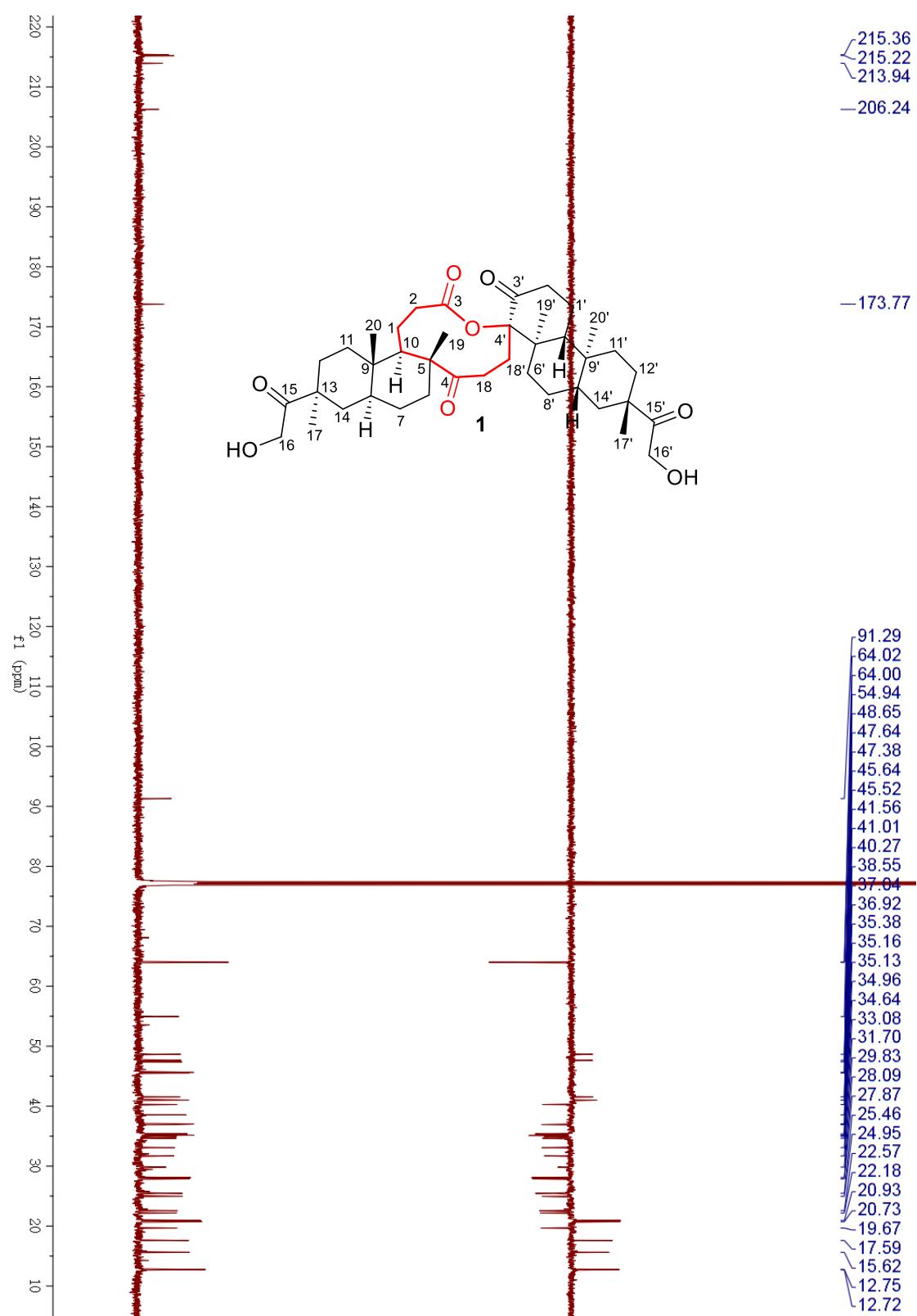


Figure S12. HSQC spectrum of natural Koilodenoid A (**1**) in CDCl_3 .

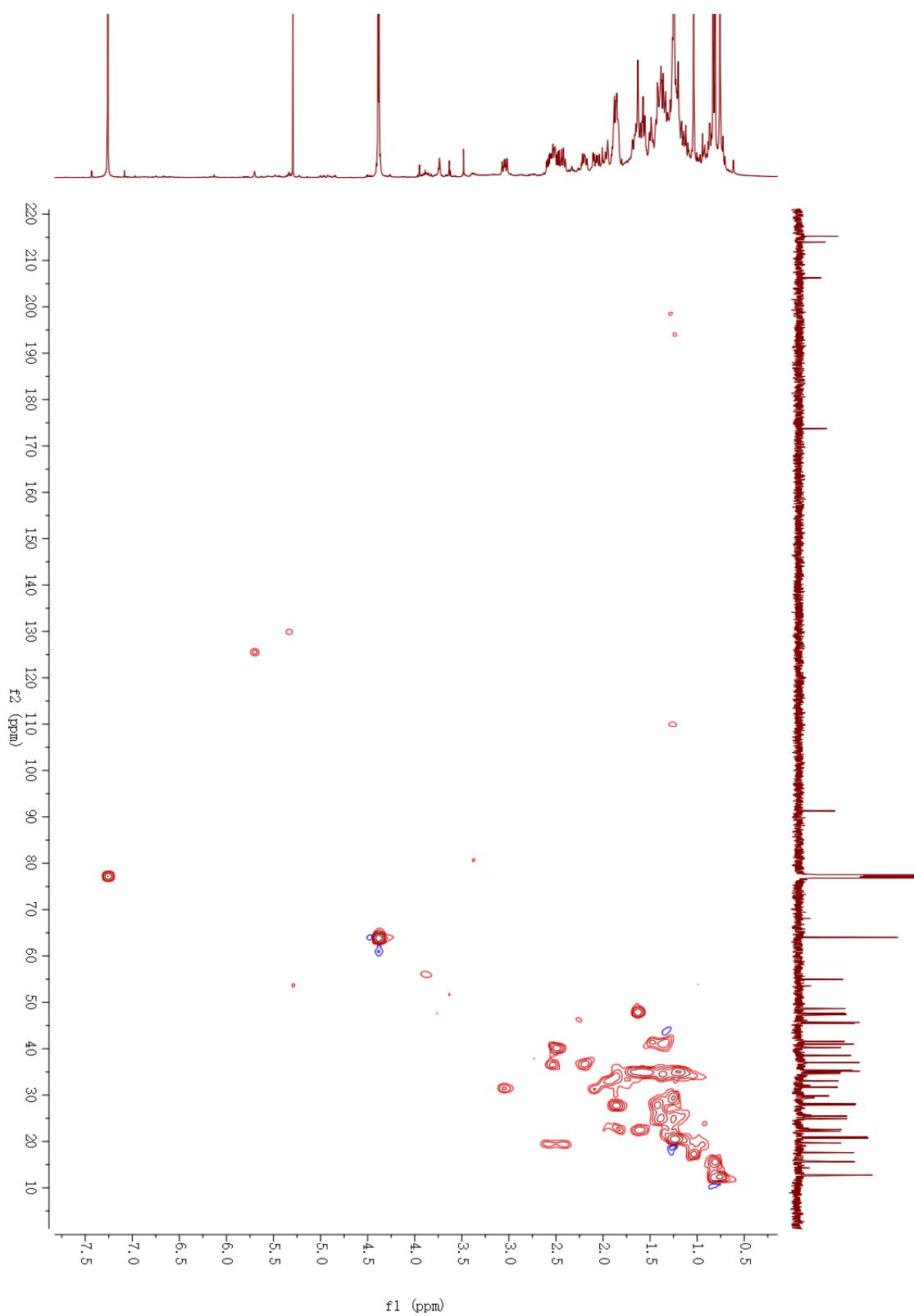


Figure S13. ^1H - ^1H COSY NMR spectrum of natural Koilodenoid A (**1**) in CDCl_3 .

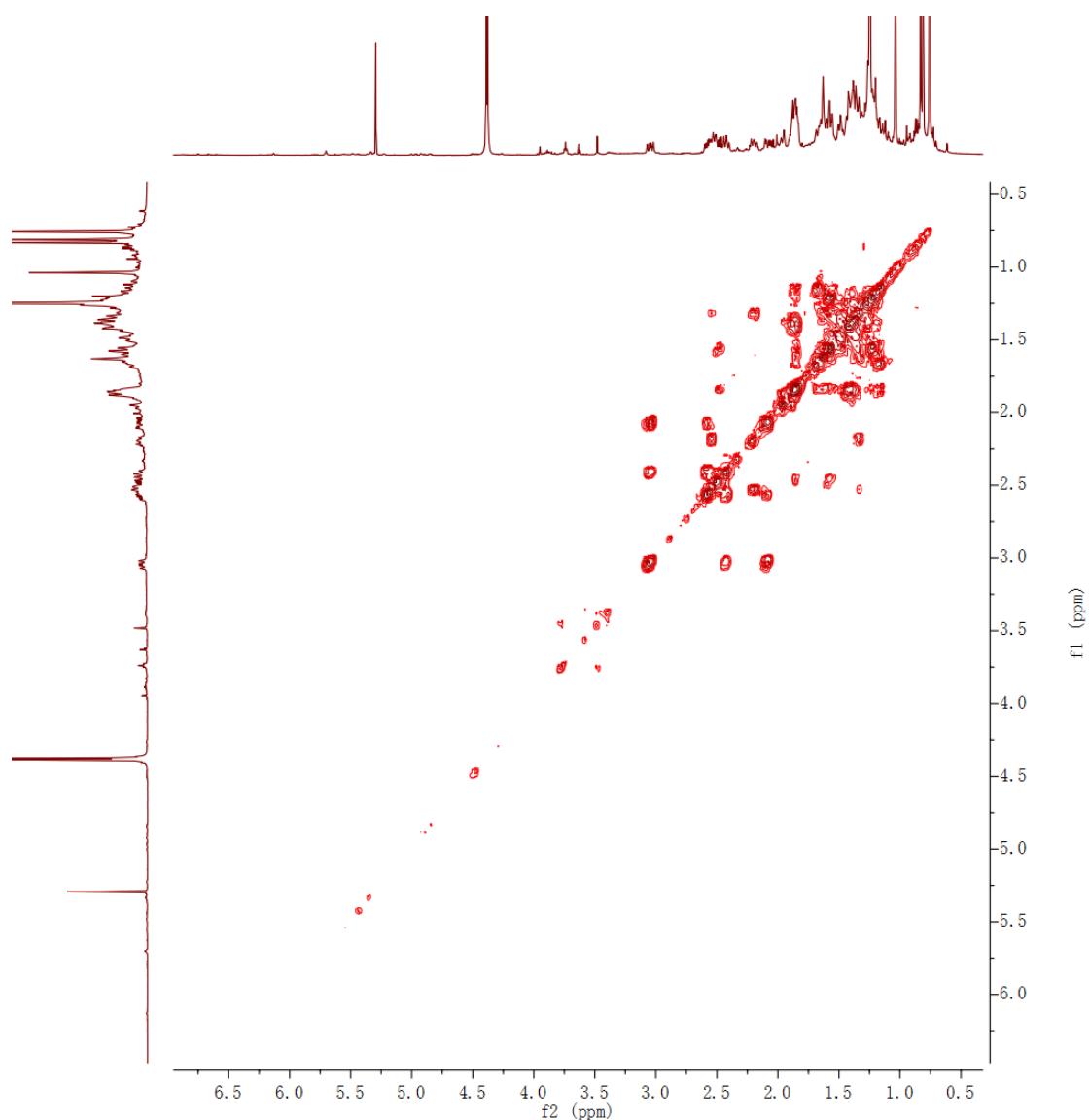


Figure S14. HMBC spectrum of natural Koilodenoid A (**1**) in CDCl_3 .

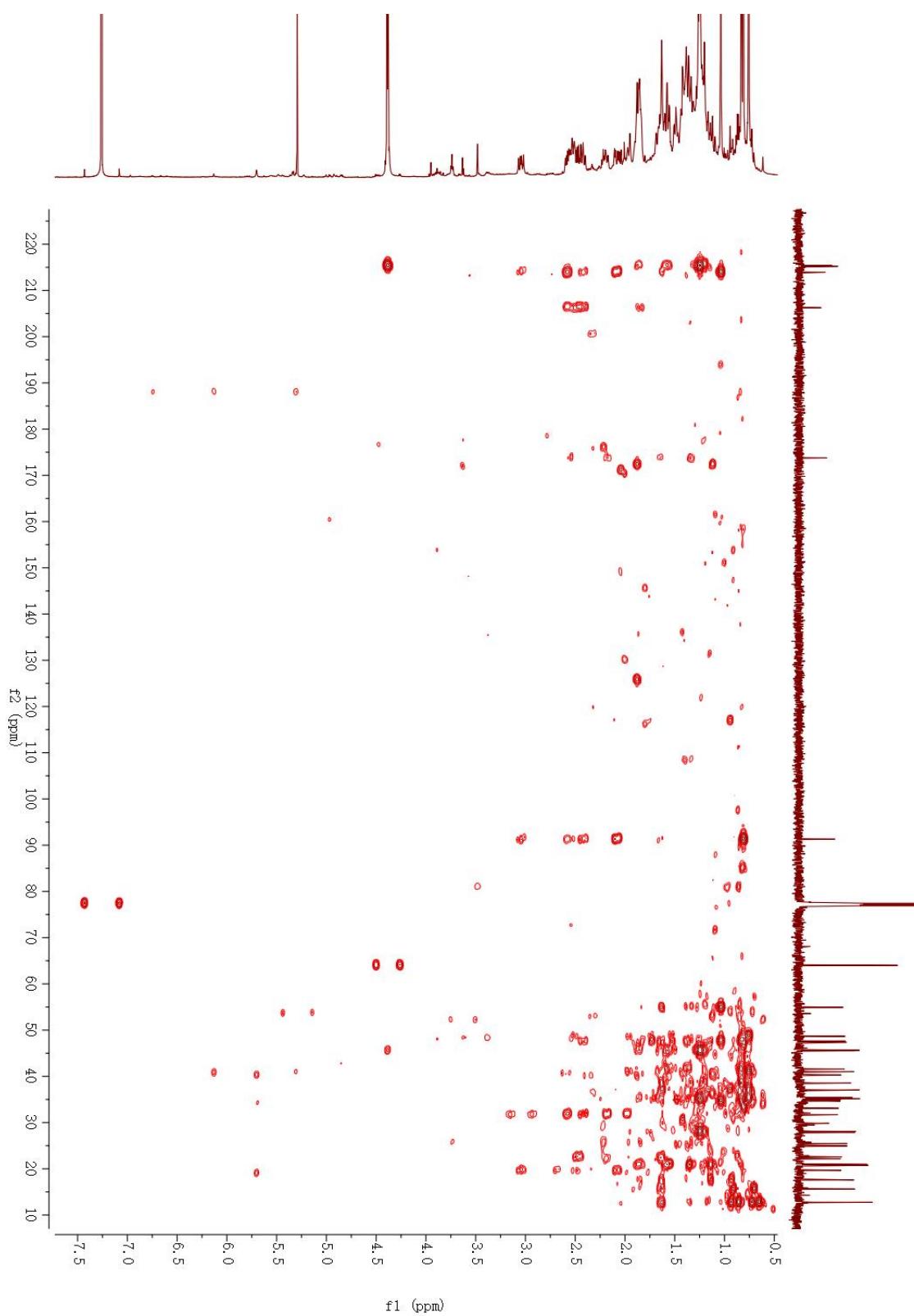


Figure S15. NOESY spectrum of natural Koilodenoid A (**1**) in CDCl_3 .

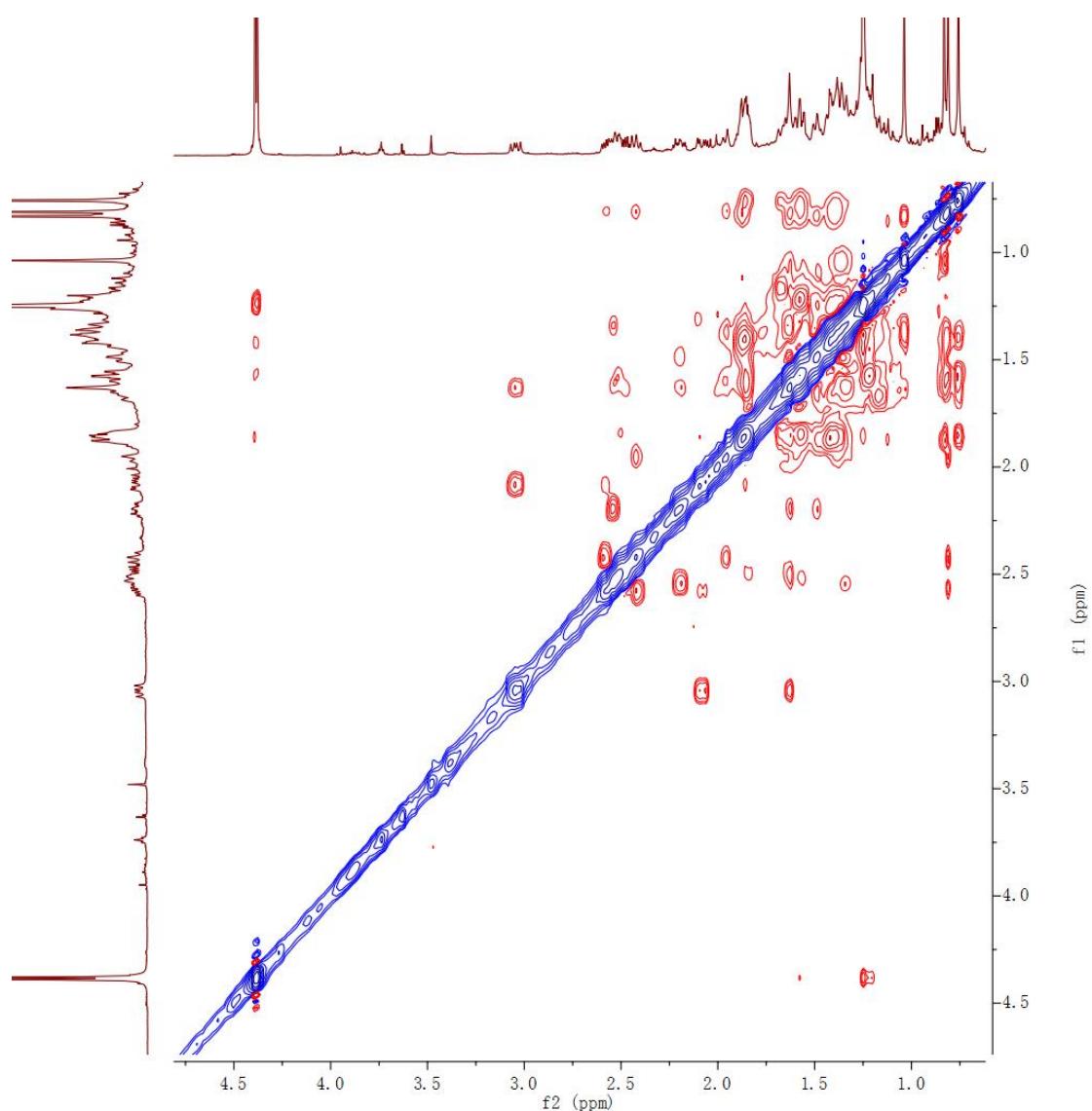
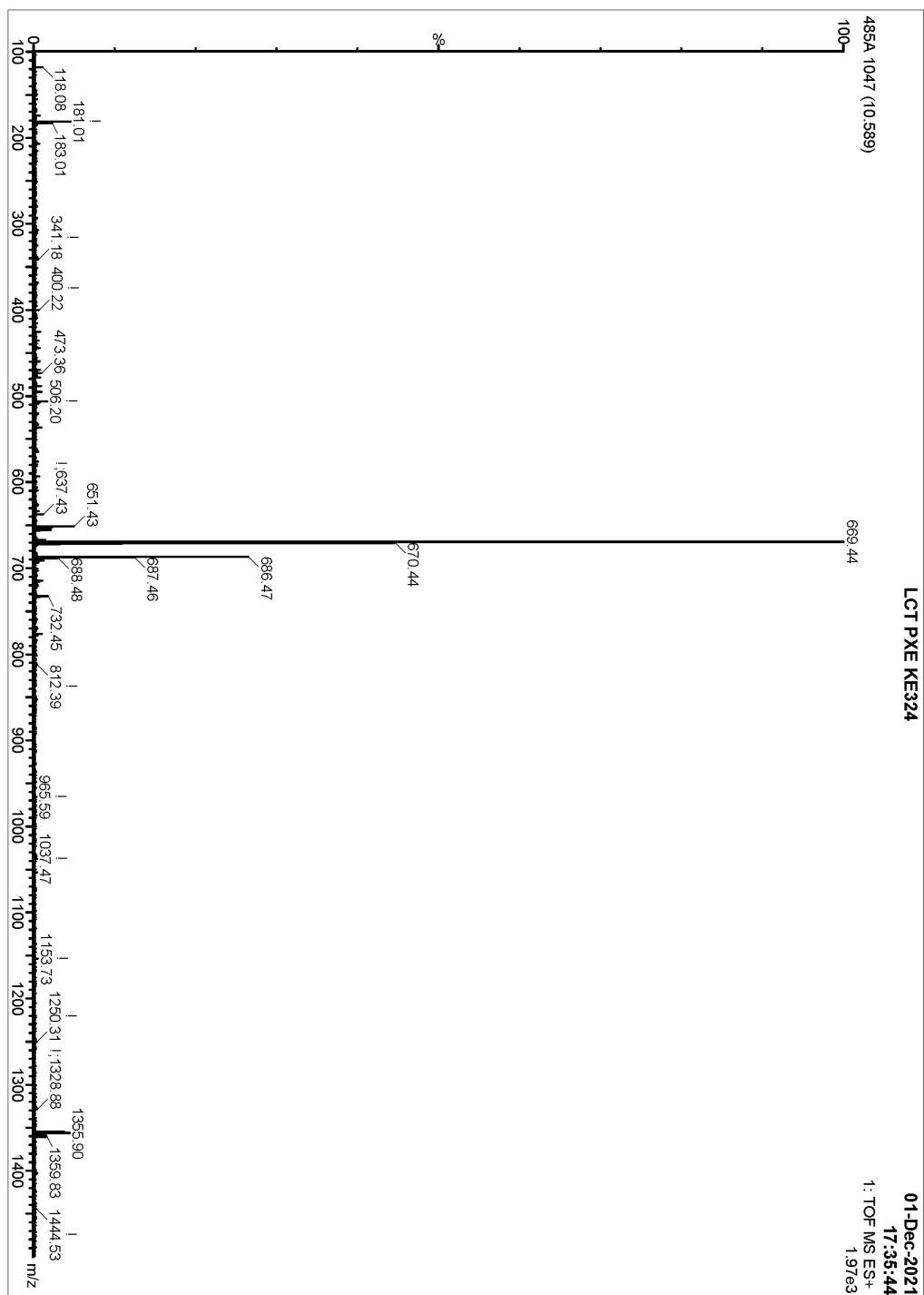


Figure S16. (+)-ESIMS spectrum of natural Koilodenoid A (**1**).



Elemental Composition Report**Page 1****Single Mass Analysis**

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

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
70 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 1-50 H: 1-100 O: 1-10
LCT PXE KE324

1: TOF MS ES+

01-Dec-2021

485A 1047 (10.389)

1.97e+003

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669.4387
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686.4662
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688.4784
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Figure S18. IR spectrum of natural Koilodenoid A (**1**).

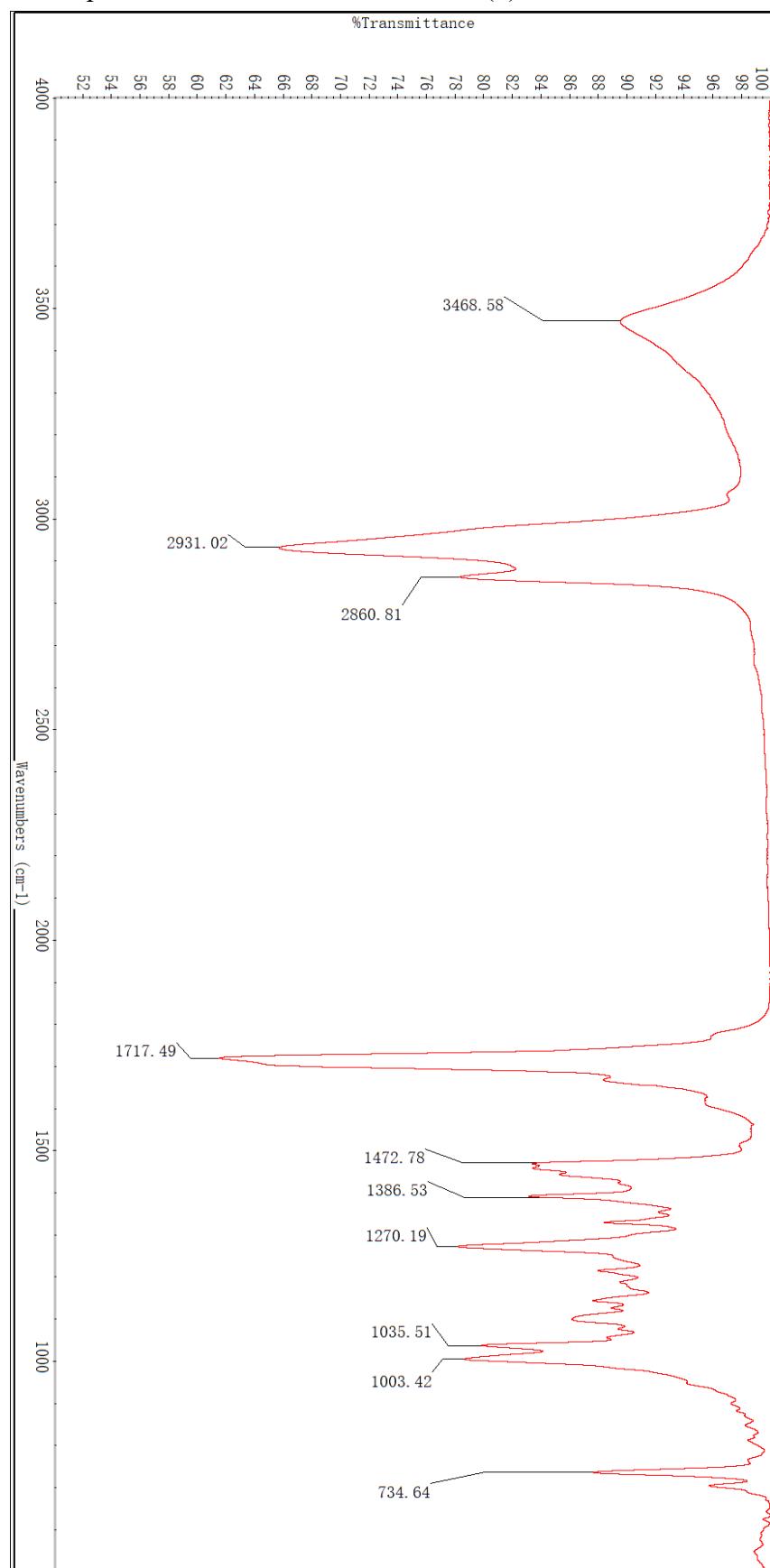


Figure S19. ^1H NMR spectrum of Koilodenoid B (**2**) in CDCl_3 .

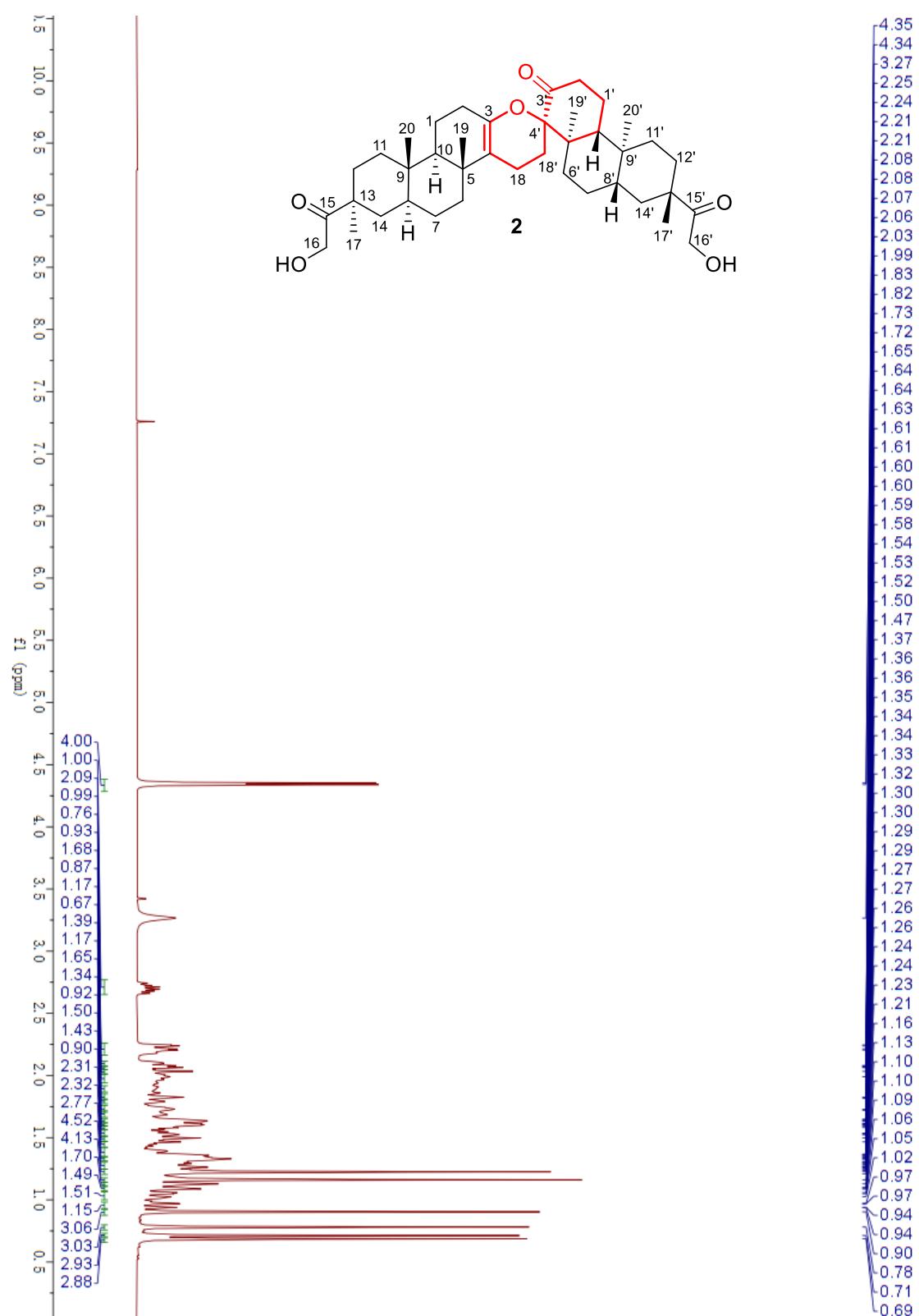


Figure S20. ^{13}C NMR spectrum of Koilodenoid B (**2**) in CDCl_3 .

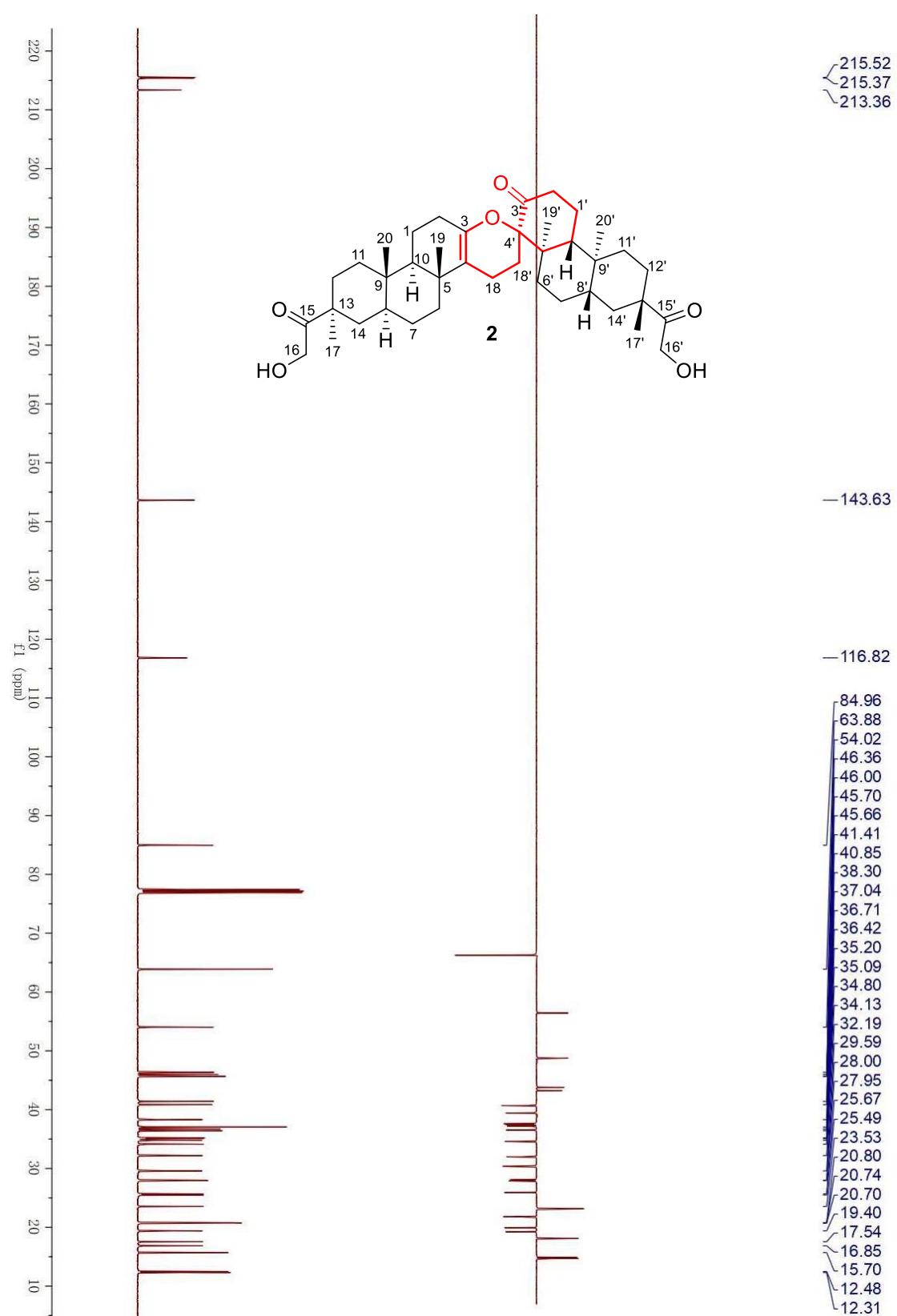


Figure S21. HSQC spectrum of Koilodenoid B (**2**) in CDCl_3 .

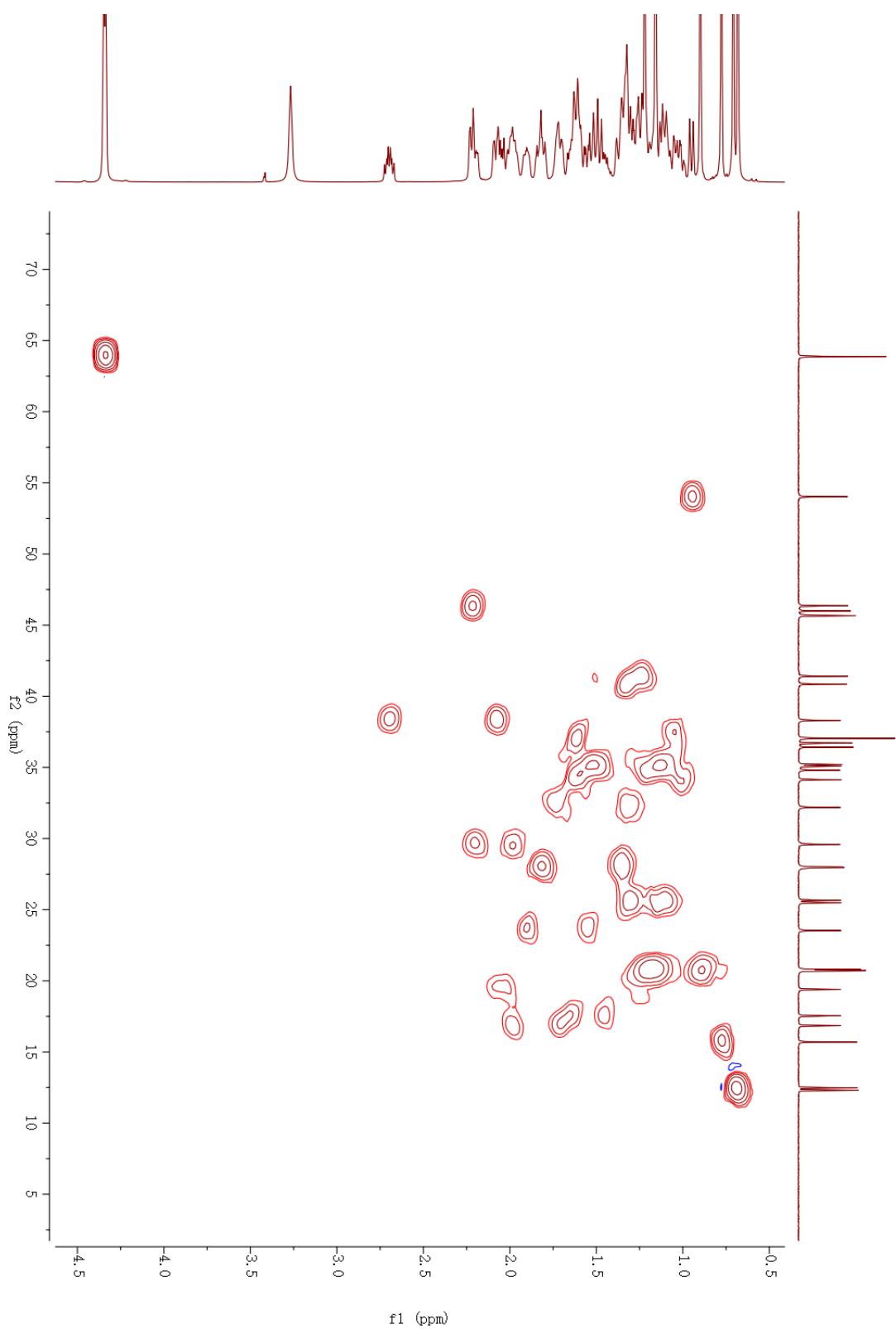


Figure S22. ^1H - ^1H COSY spectrum of Koilodenoid B (**2**) in CDCl_3 .

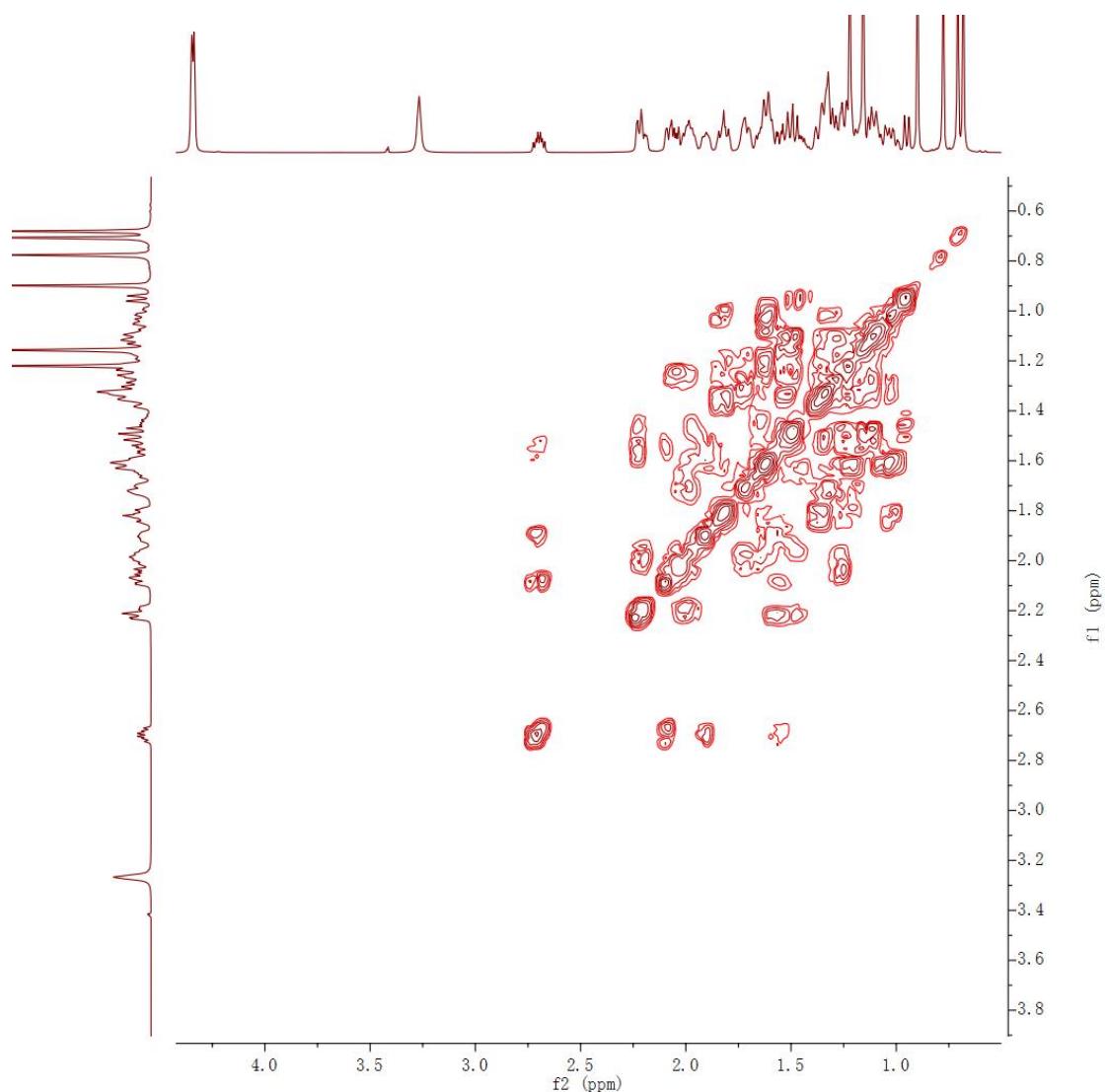


Figure S23. HMBC spectrum of Koilodenoid B (**2**) in CDCl_3 .

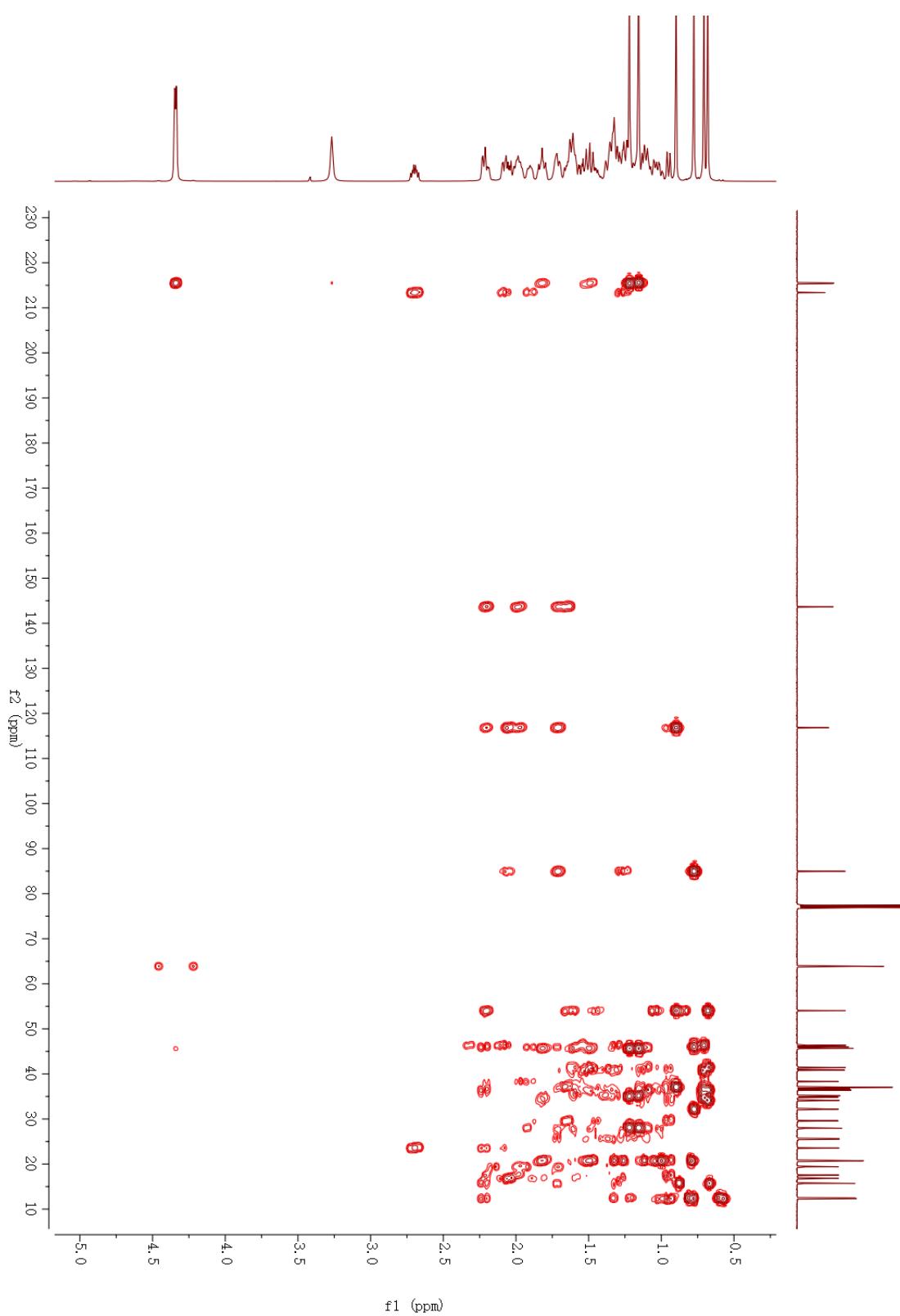


Figure S24. NOESY spectrum of Koilodenoid B (**2**) in CDCl_3 .

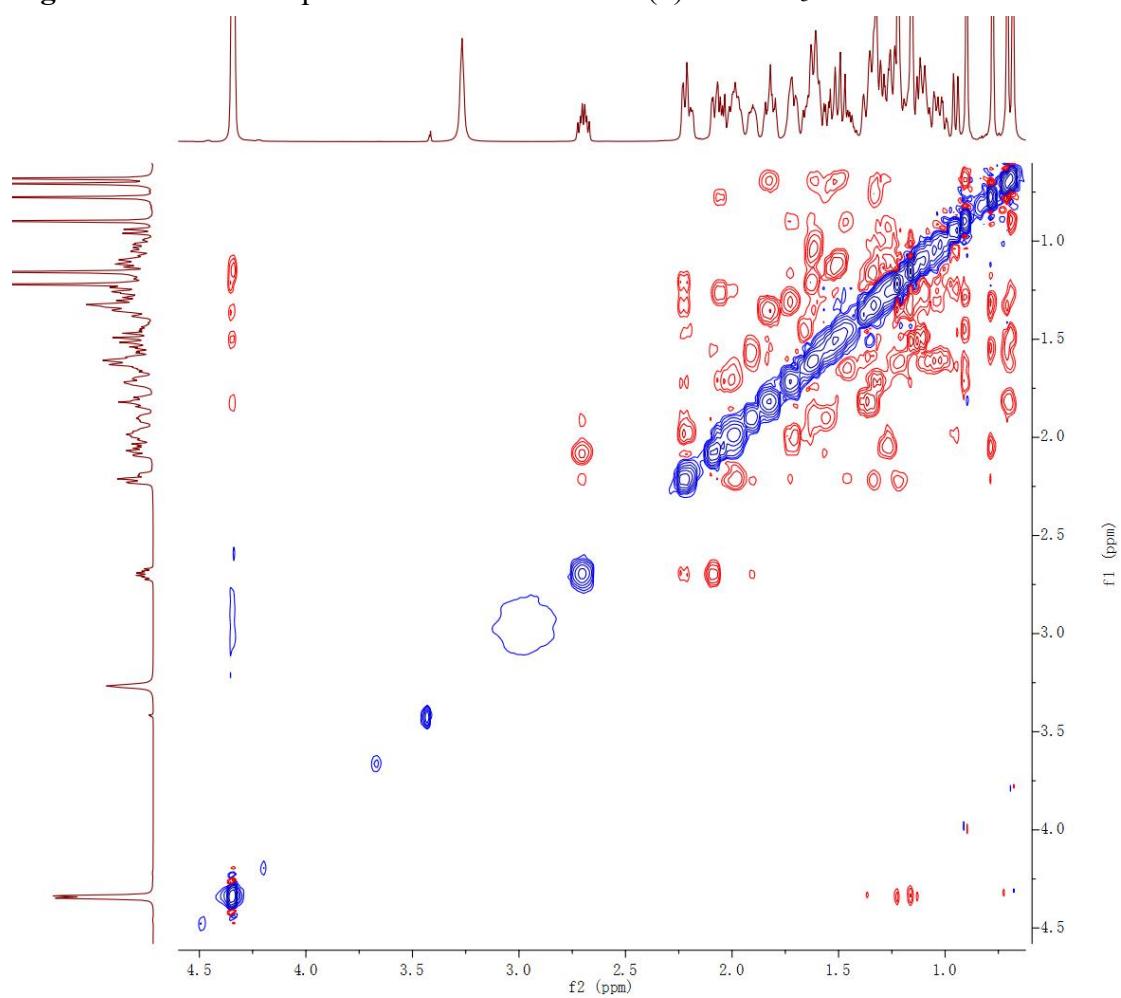
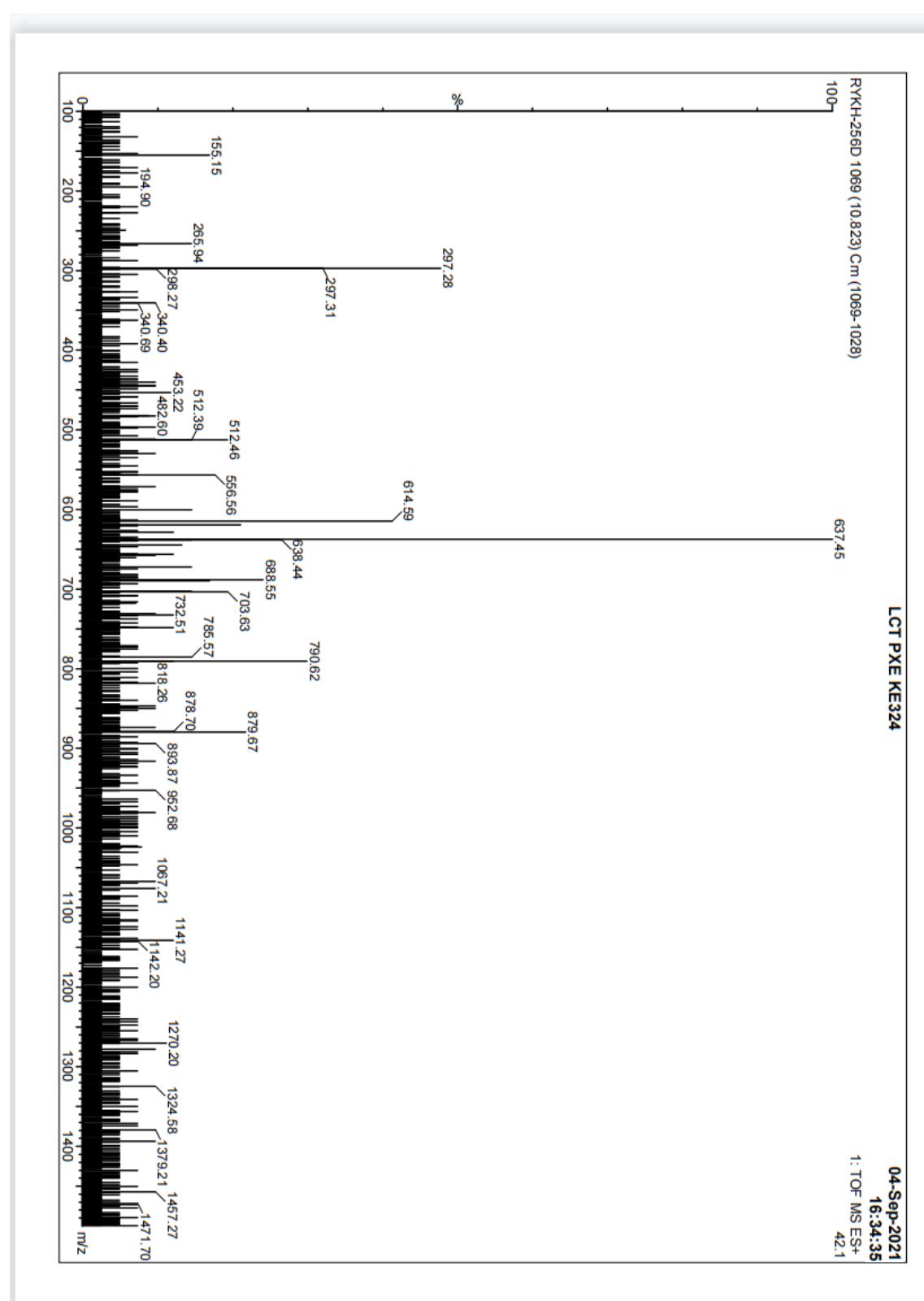


Figure S25. (+)-ESIMS spectrum of Koilodenoid B (2).



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 10.0 PPM / DBE: min = -1.5, max = 30.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions

50 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

C: 20-100 H: 30-61 O: 2-20

LCT PAE KE324

1: TOF MS ES+

04-Sep-2021

R YKH-256D 1069 (10.823) Cm (1068-1028)
16.34.35
4.21e-001

637.4500

614.5988

590.6211

512.3875

459.5958

453.2203

439.5958

349.5958

298.2682

265.9359

251.9359

207.8604

170.8604

155.1454

297.3131

291.2827

603.6318

598.5658

539.4354

512.4579

483.8737

452.6841

407.2061

388.6998

353.8737

324.5779

295.6841

Figure S27. IR spectrum of Koilodenoid B (2).

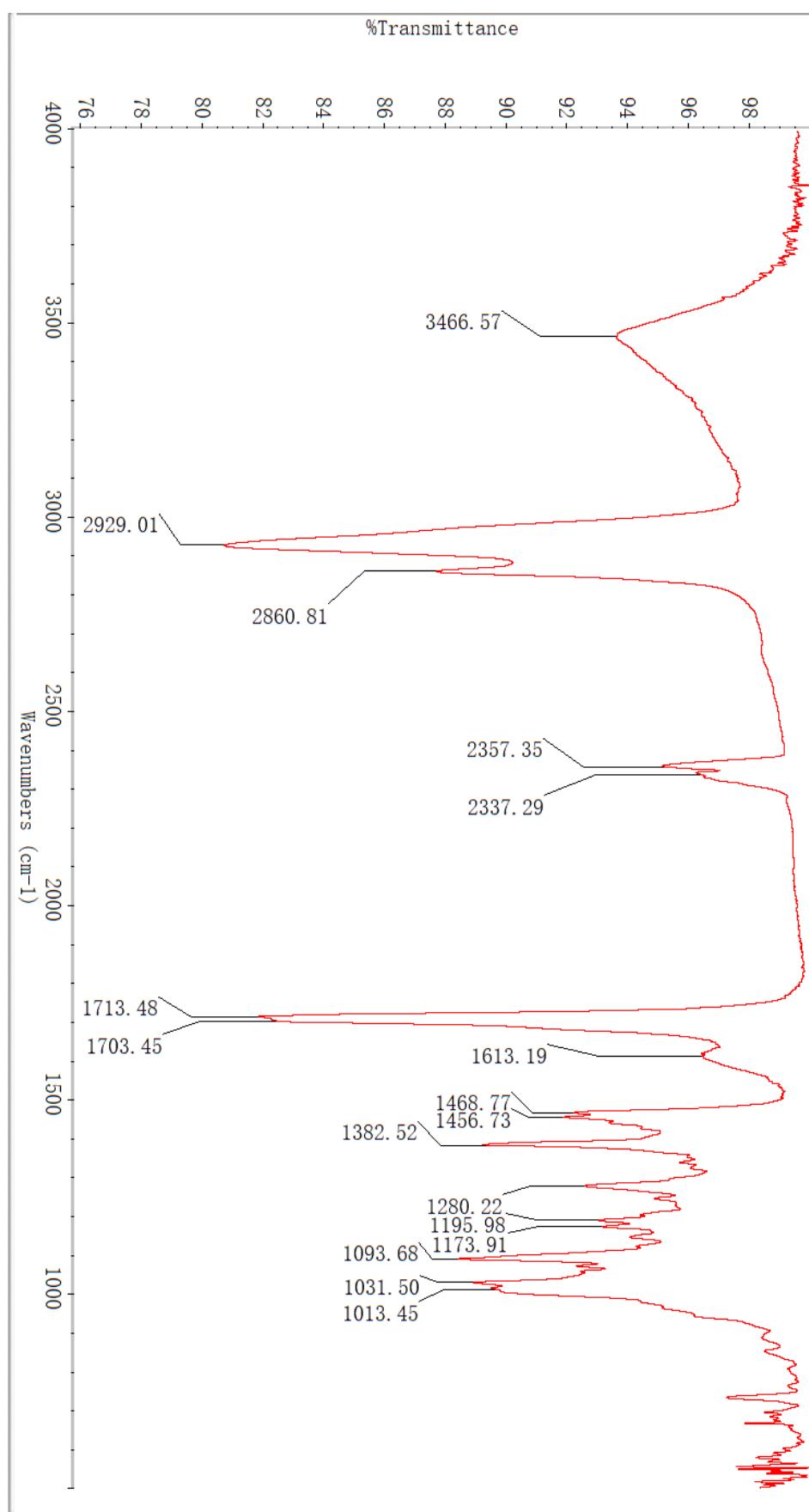


Figure S28. ^1H NMR spectrum of Koilodenoid C (**3**) in CDCl_3 .

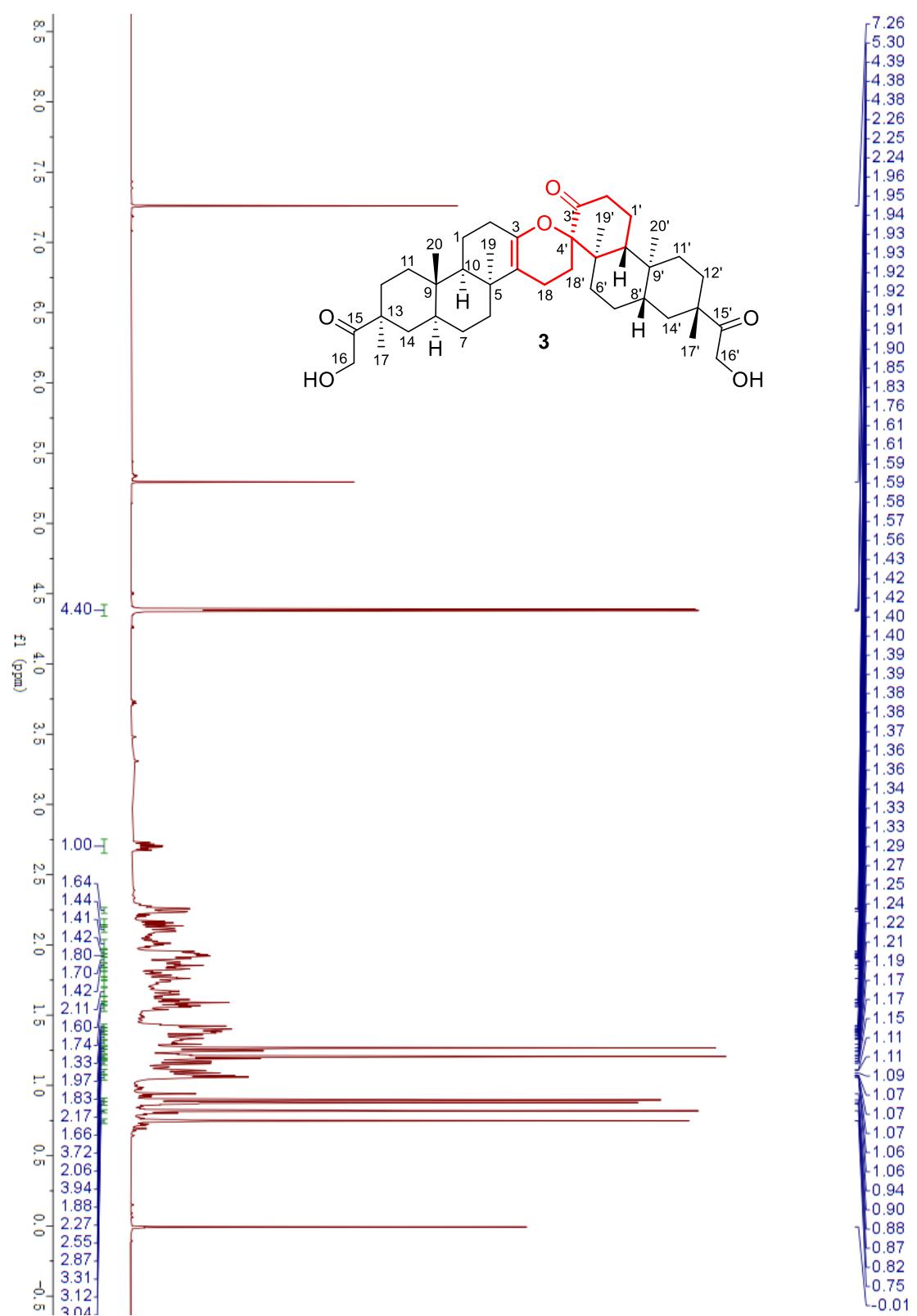


Figure S29. ^{13}C NMR spectrum of Koilodenoid C (**3**) in CDCl_3 .

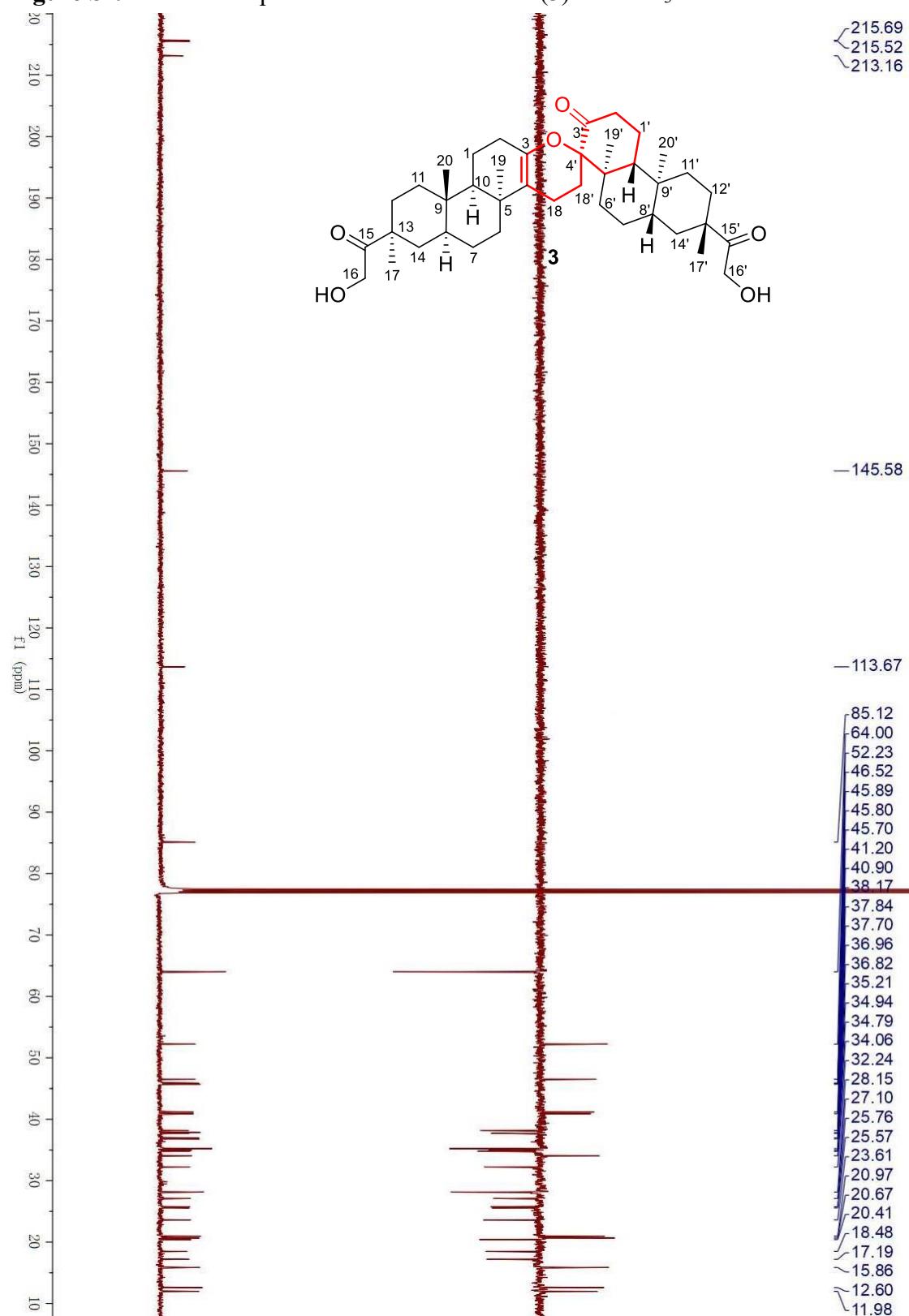


Figure S30. HSQC spectrum of Koilodenoid C (**3**) in CDCl_3 .

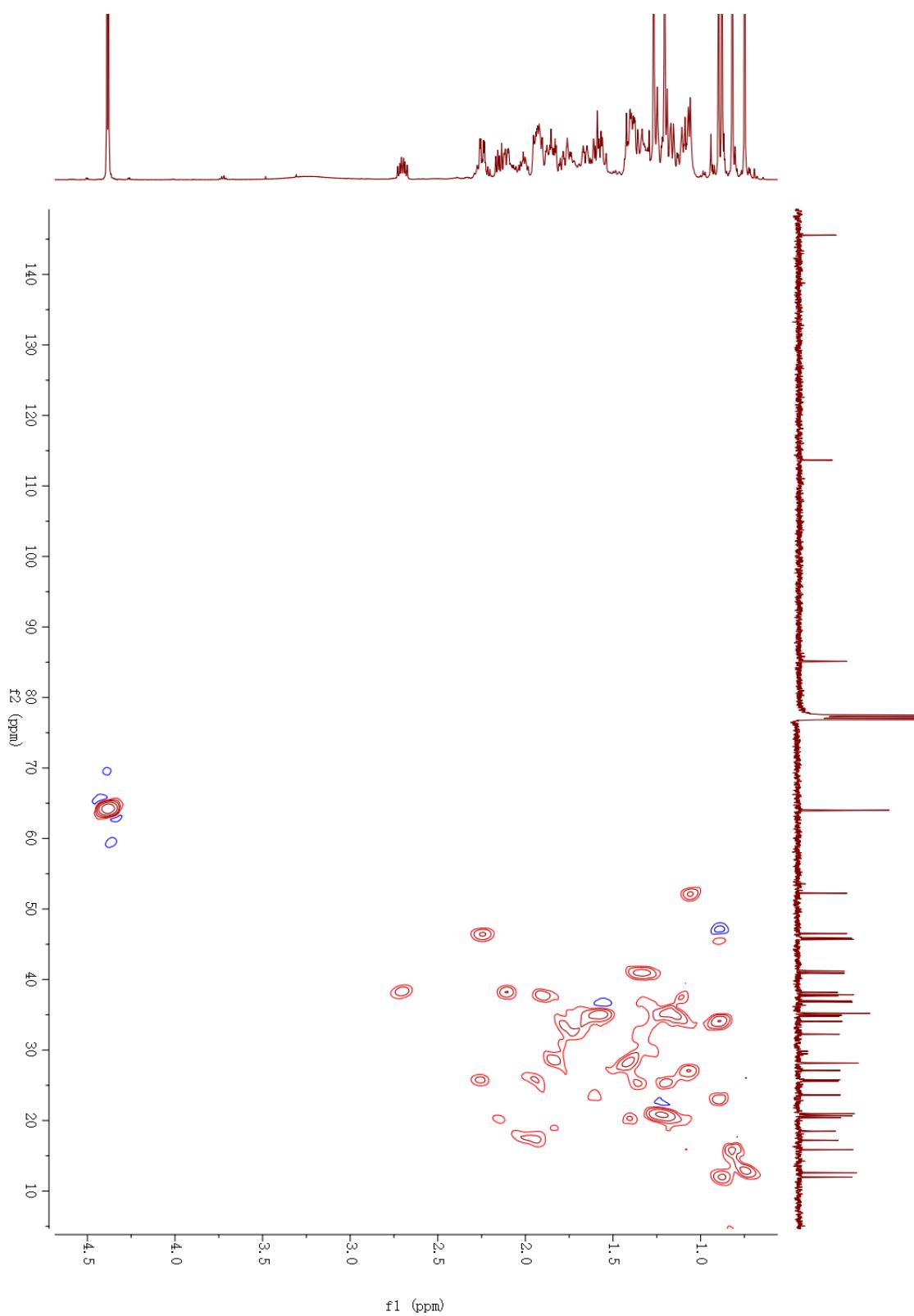


Figure S31. ^1H - ^1H COSY NMR spectrum of Koilodenoid C (**3**) in CDCl_3 .

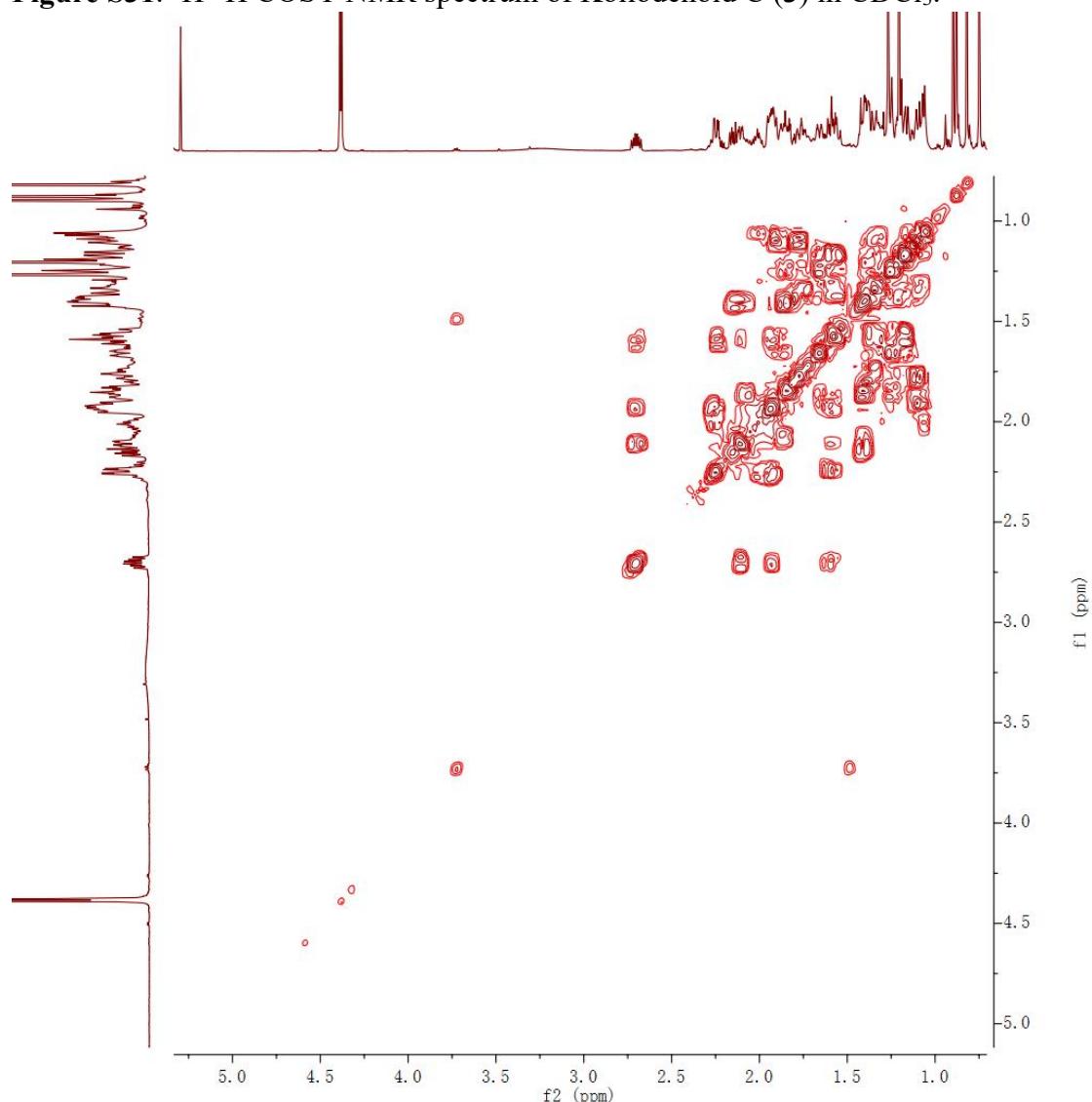


Figure S32. HMBC spectrum of Koilodenoid C (**3**) in CDCl_3 .

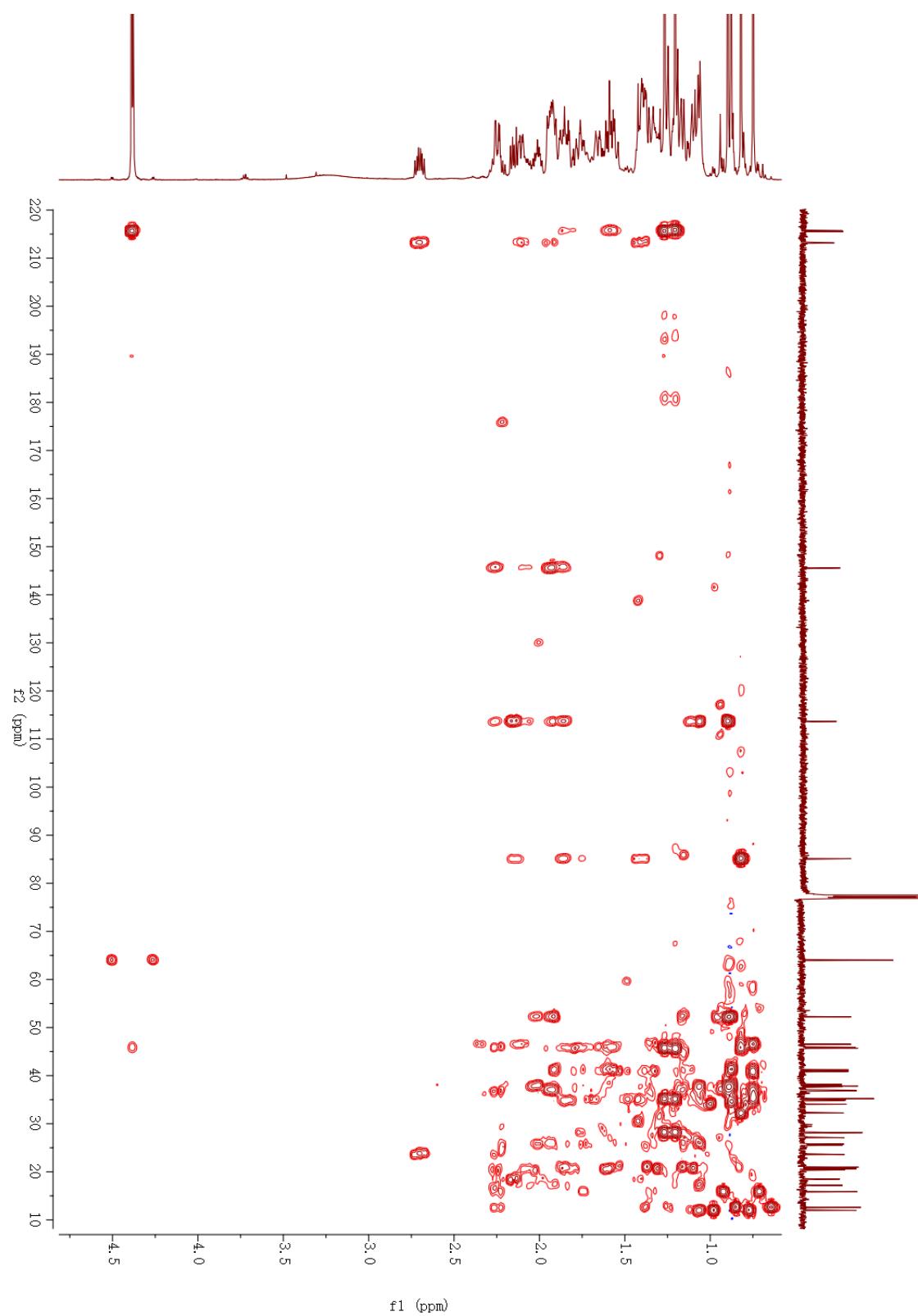


Figure S33. NOESY spectrum of Koilodenoid C (**3**) in CDCl_3 .

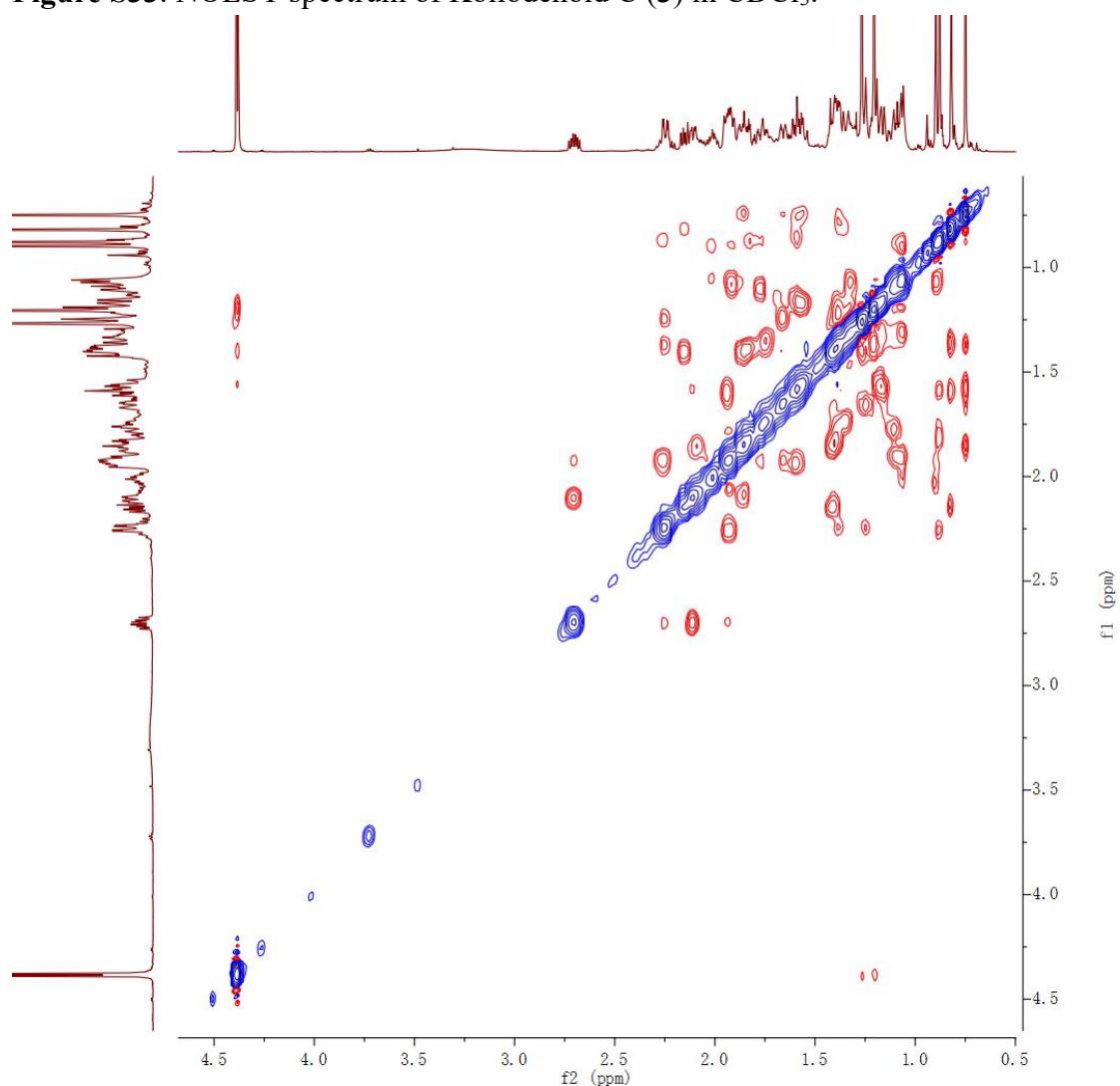
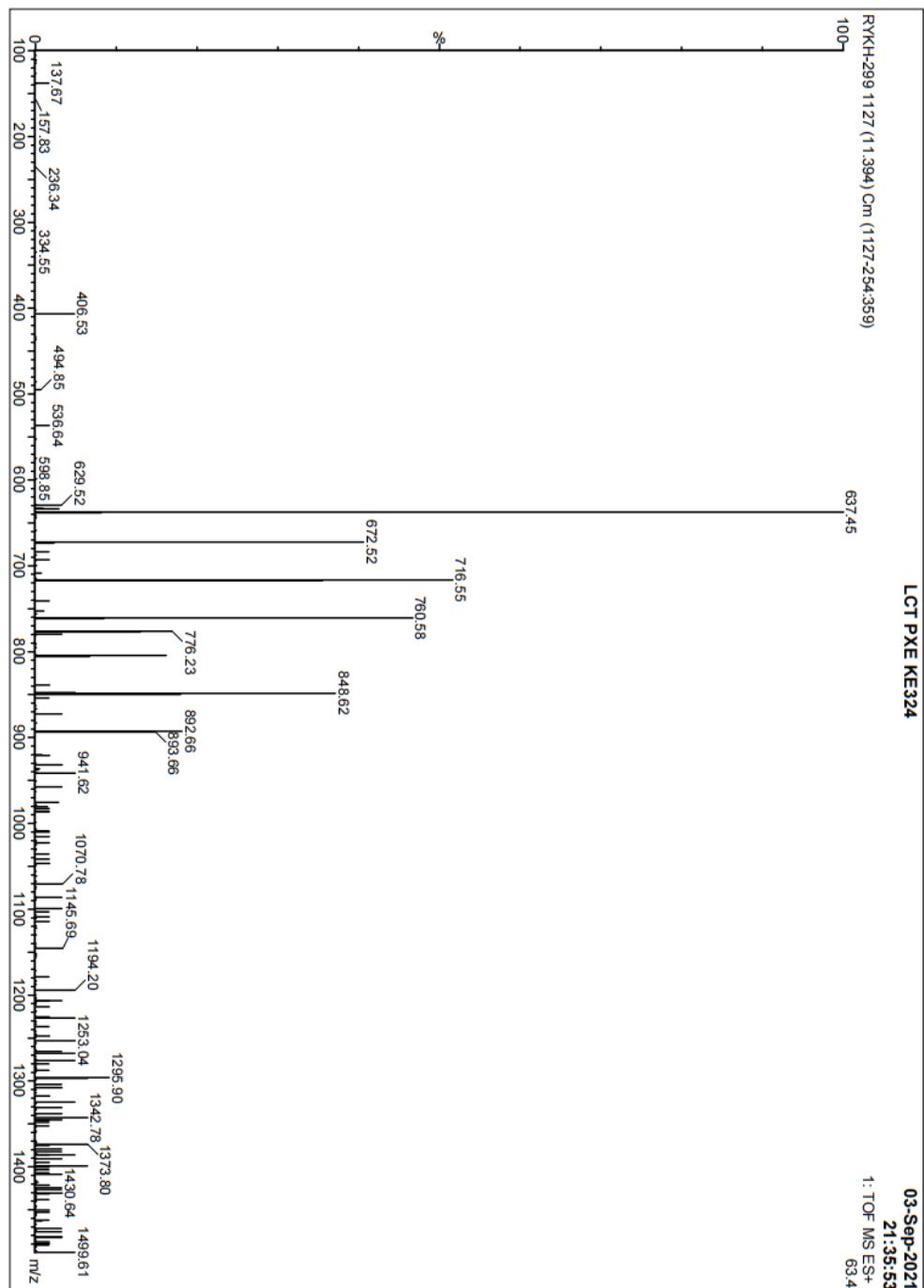


Figure S34. (+)-ESIMS spectrum of Koilodenoid C (**3**).



Elemental Composition Report**Page 1****Single Mass Analysis**

Tolerance = 10.0 PPM / DBE: min = -1.5, max = 30.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions

1 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

C: 40-50 H: 60-61 O: 6-6

LCT PXP KE324

1: TOF MS ES+

03-Sep-2021

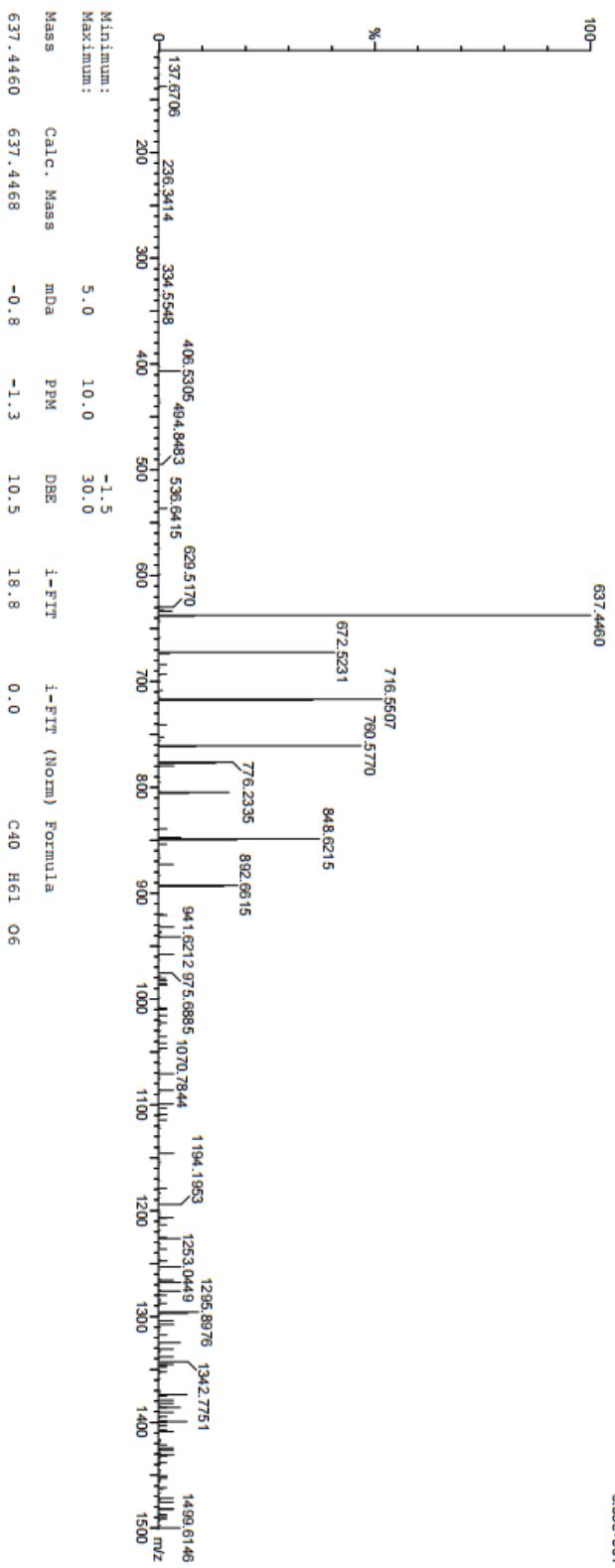
RYKH-289 1127 (11.394) Cm (1127-754:359)
21:35:53
6.35e+001**Figure S35.** (+)-HRESIMS spectrum of Koilodenoid C (3).

Figure S36. IR spectrum of Koilodenoid C (3).

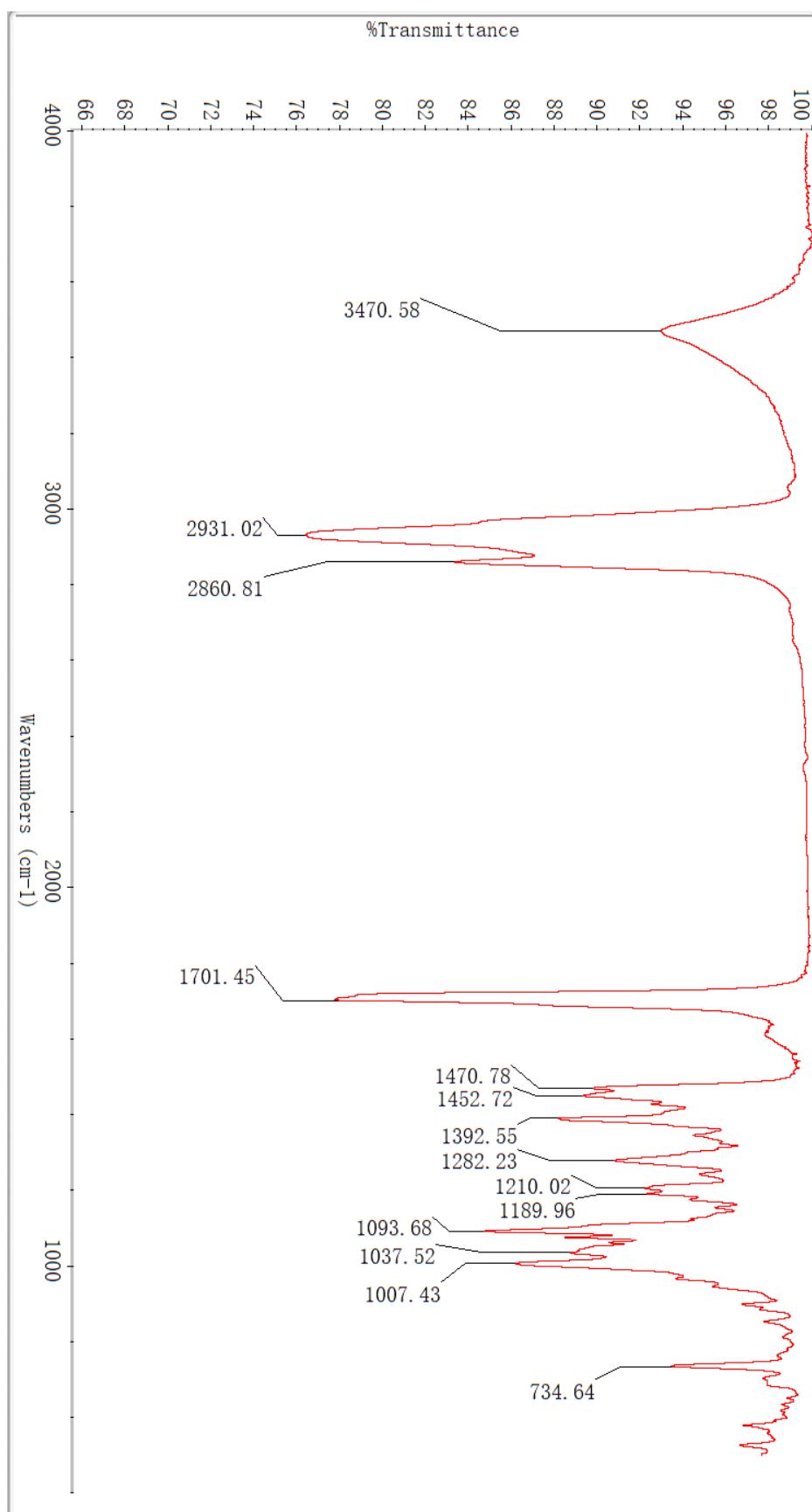


Figure S37. ^1H NMR spectrum of Koilodenoid D (**4**) in CDCl_3 .

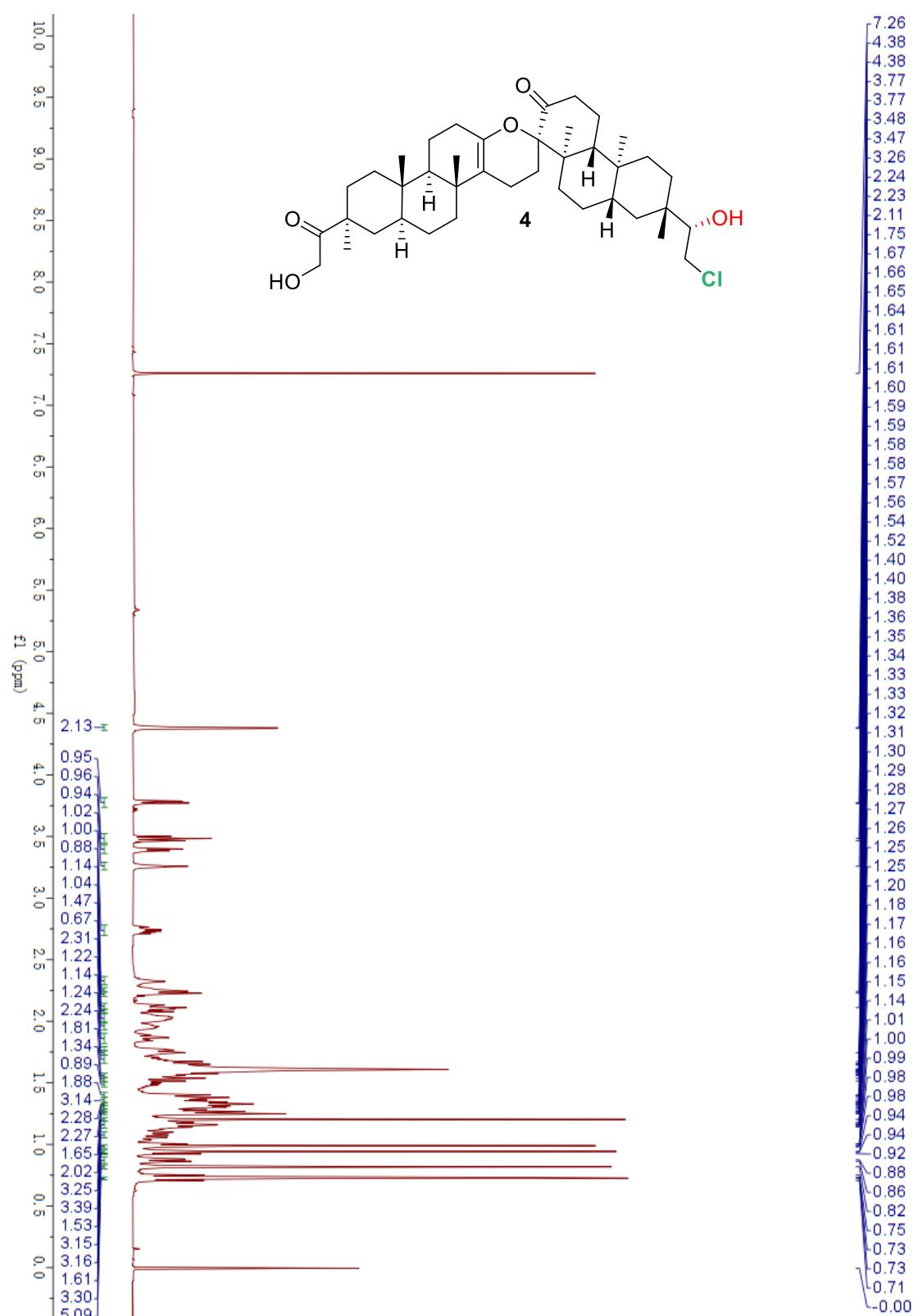


Figure S38. ^{13}C NMR spectrum of Koilodenoid D (**4**) in CDCl_3 .

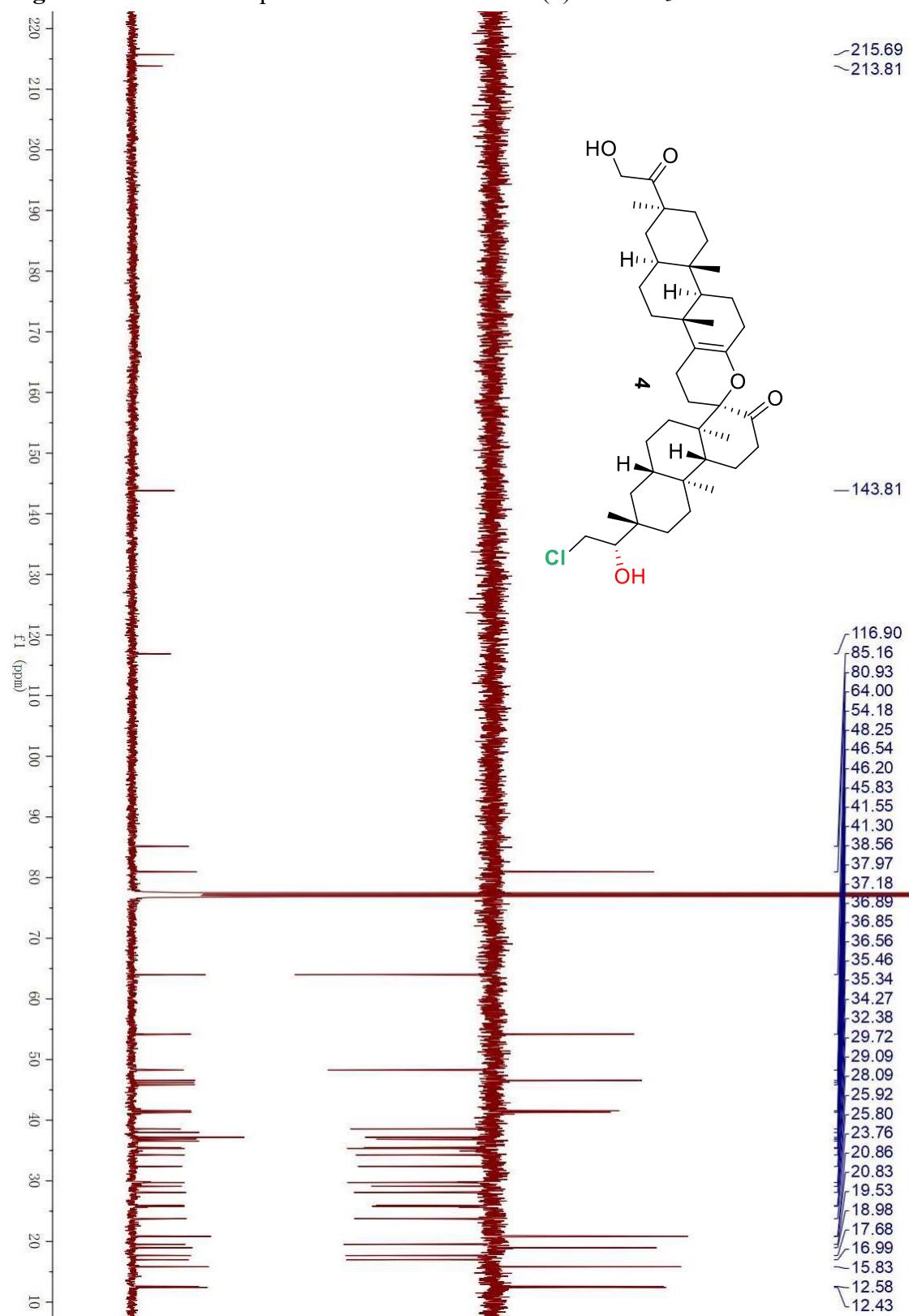


Figure S39. HSQC spectrum of Koilodenoid D (**4**) in CDCl_3 .

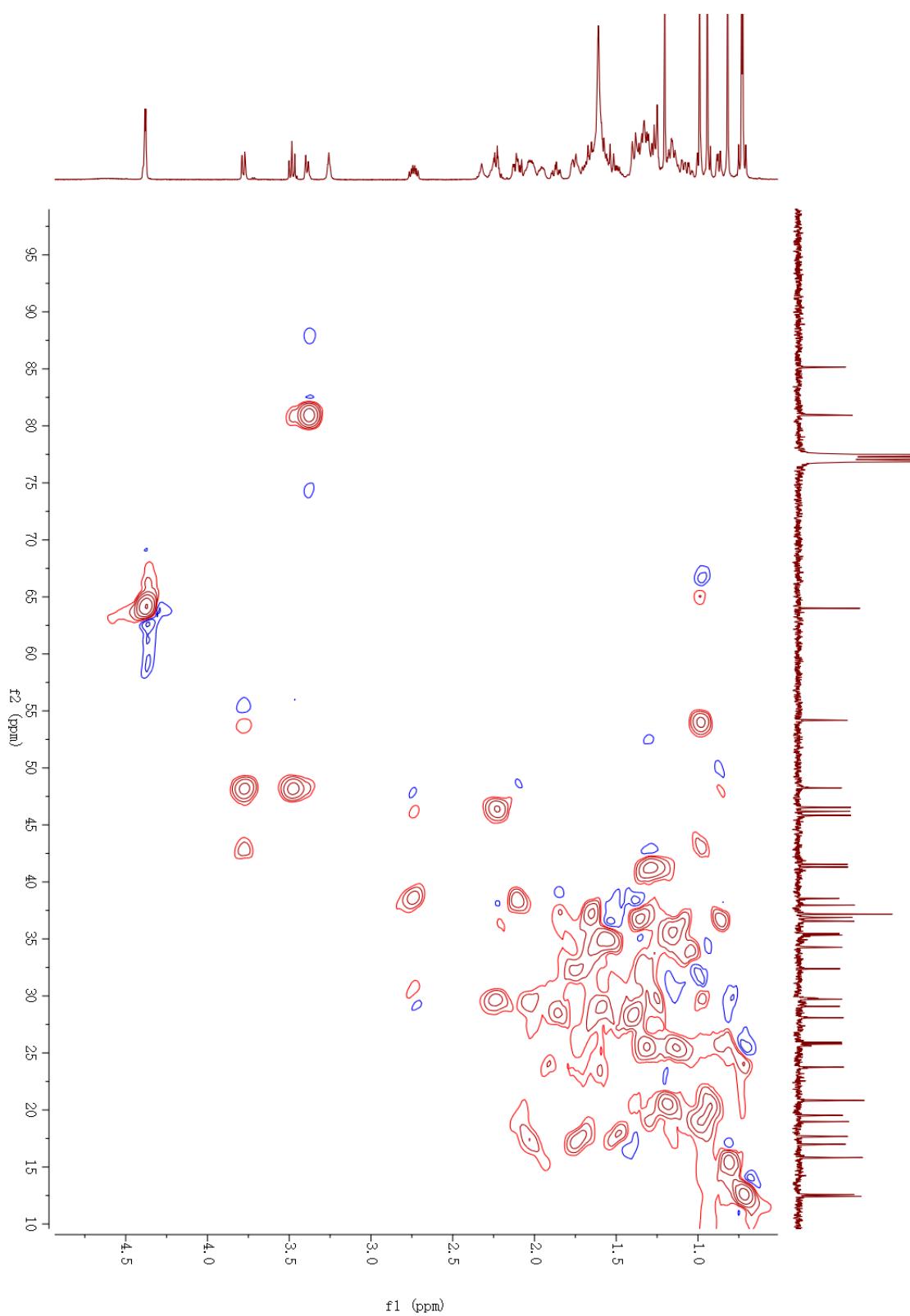


Figure S40. ^1H - ^1H COSY NMR spectrum of Koilodenoid D (**4**) in CDCl_3 .

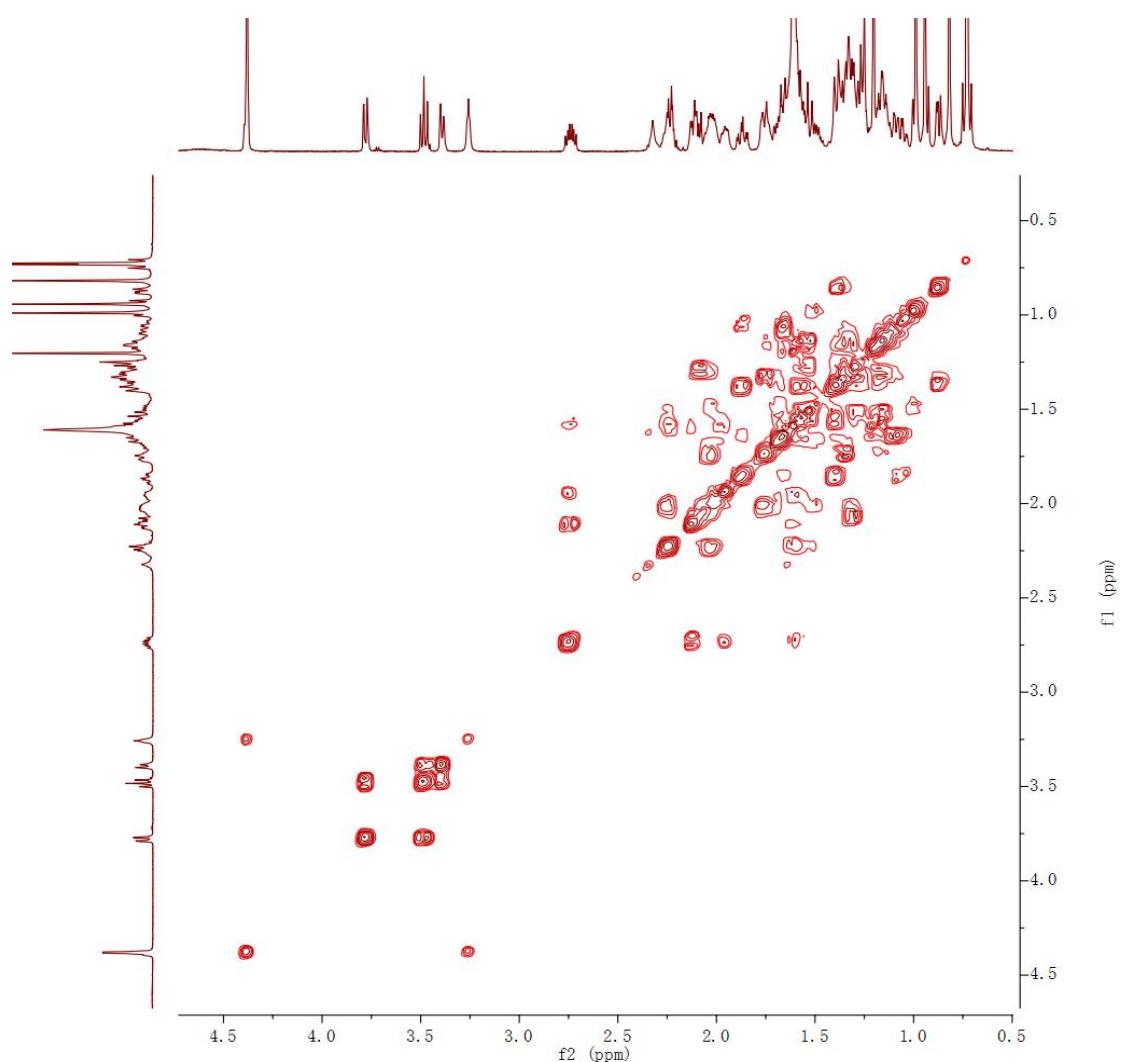


Figure S41. HMBC spectrum of Koilodenoid D (**4**) in CDCl_3 .

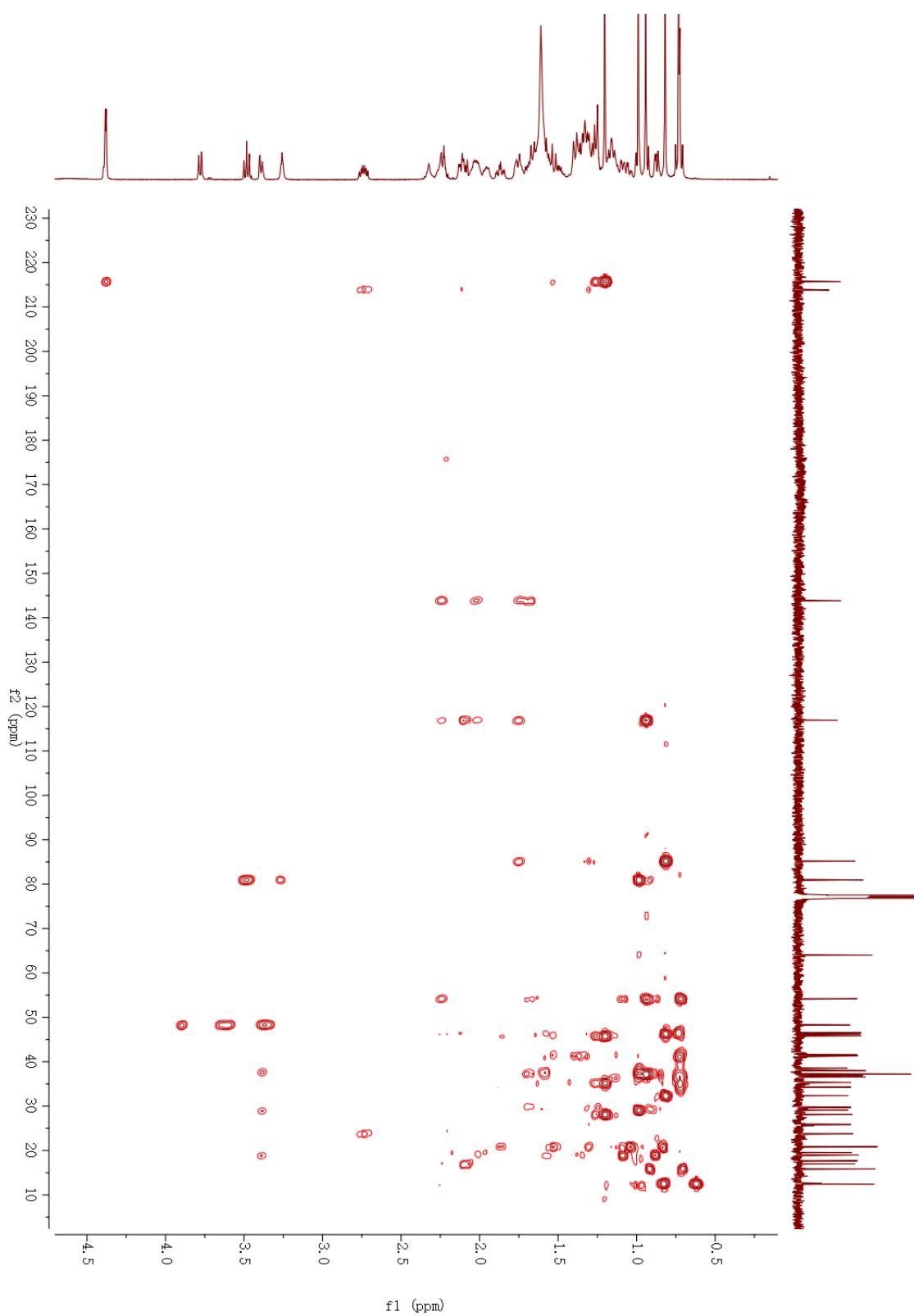


Figure S42. NOESY spectrum of Koilodenoid D (**4**) in CDCl_3 .

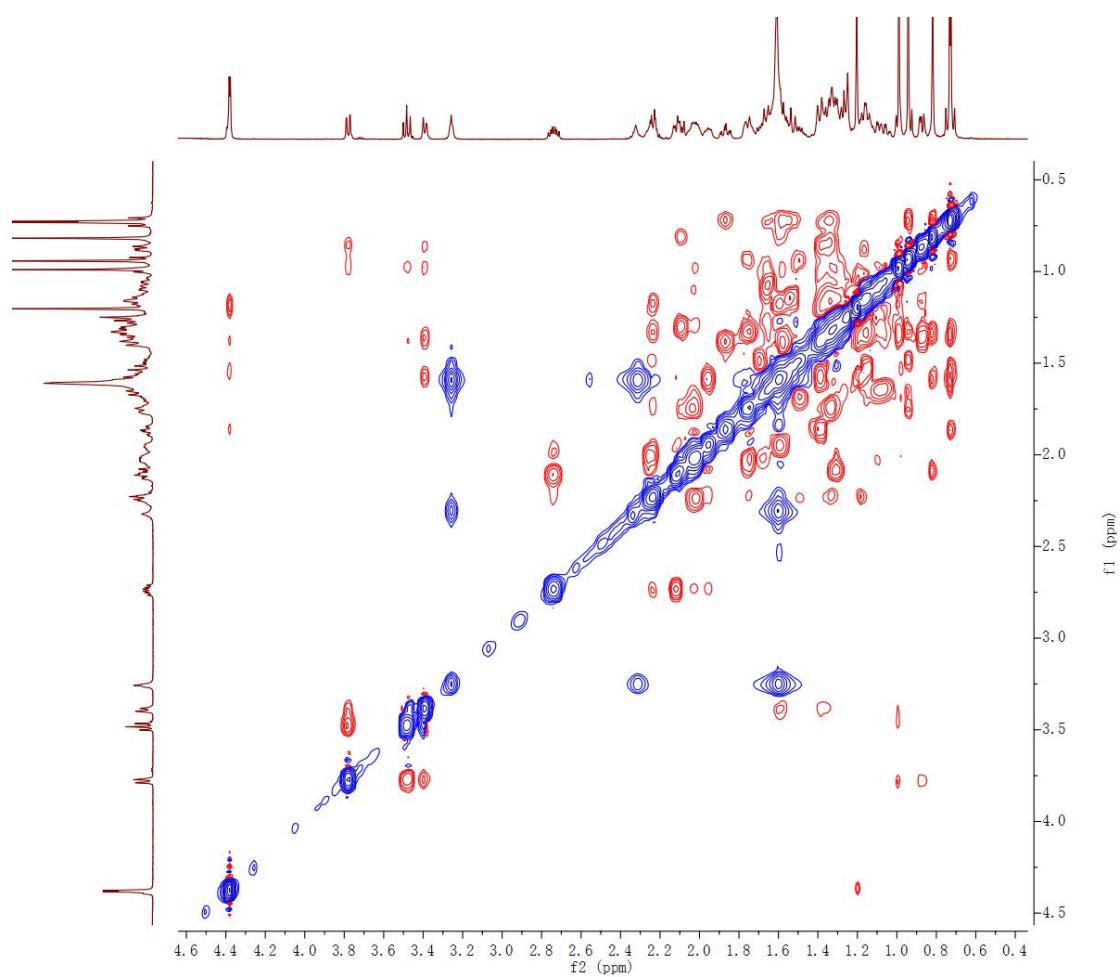


Figure S43. (+)-ESIMS spectrum of Koilodenoid D (4).

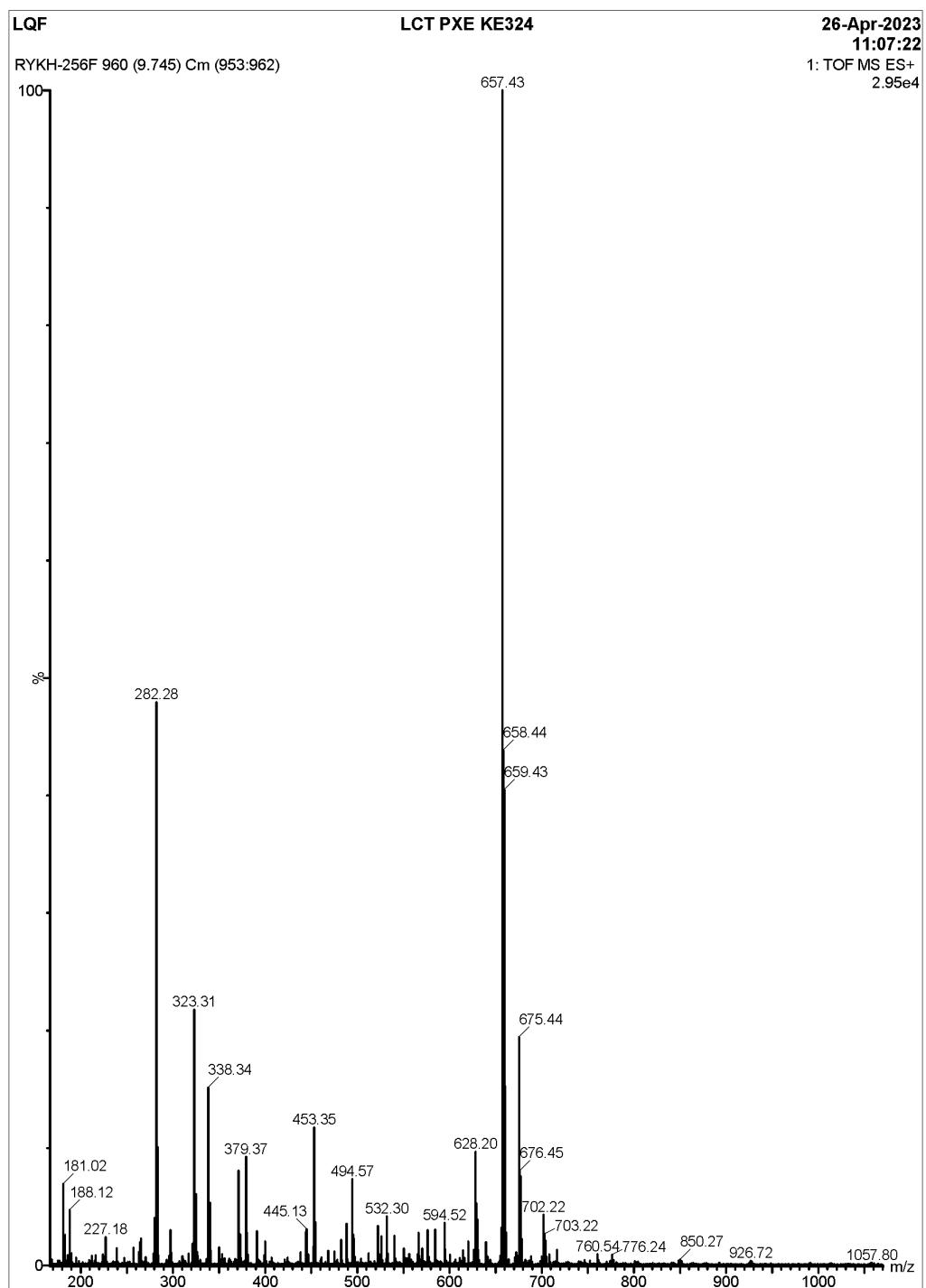
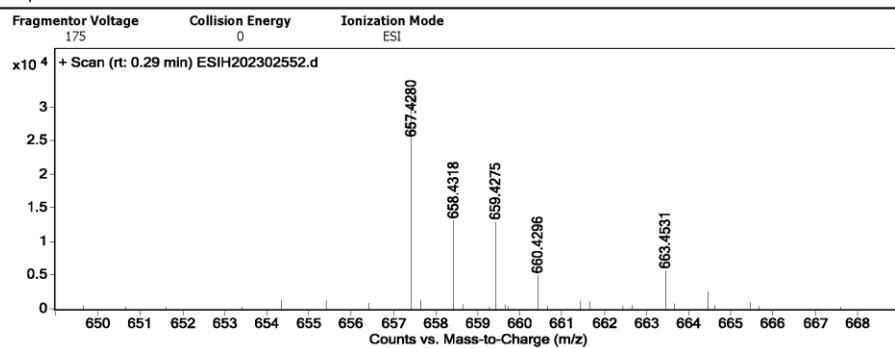


Figure S44. (+)-HRESIMS spectrum of Koilodenoid D (4).

Qualitative Analysis Report

Data Filename	ESIH202302552.d	Sample Name	D4-RYKH-256F
Sample ID		Position	P1-A1
Instrument Name	Agilent 6520 Q-TOF	Acq Method	20160322_MS_ESIH_POS_1min.m
Acquired Time	4/14/2023 14:24:47	IRM Calibration Status	Success
DA Method	small molecular data analysis method.m	Comment	ESIH by fangsu

User Spectra



Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
657.428	657.428	0	0.01	C40 H62 Cl O5	(M+H)+

--- End Of Report ---

Agilent Technologies

Page 1 of 1

Printed at: 9:34 on: 4/20/2023

Figure S45. IR spectrum of Koilodenoid D (**4**).

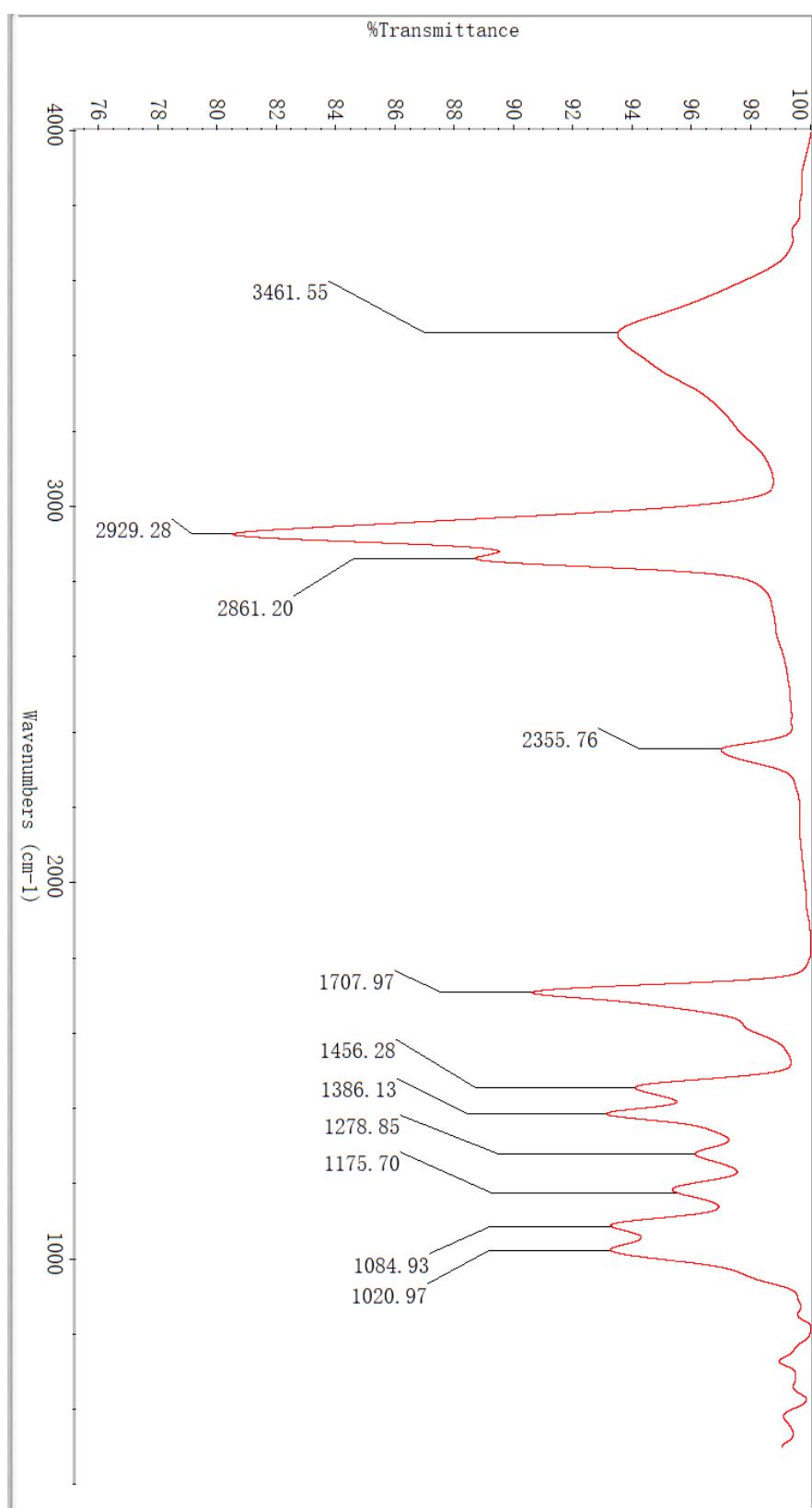


Figure S46. ^1H NMR spectrum of Koilodenoid E (**5**) in CDCl_3 .

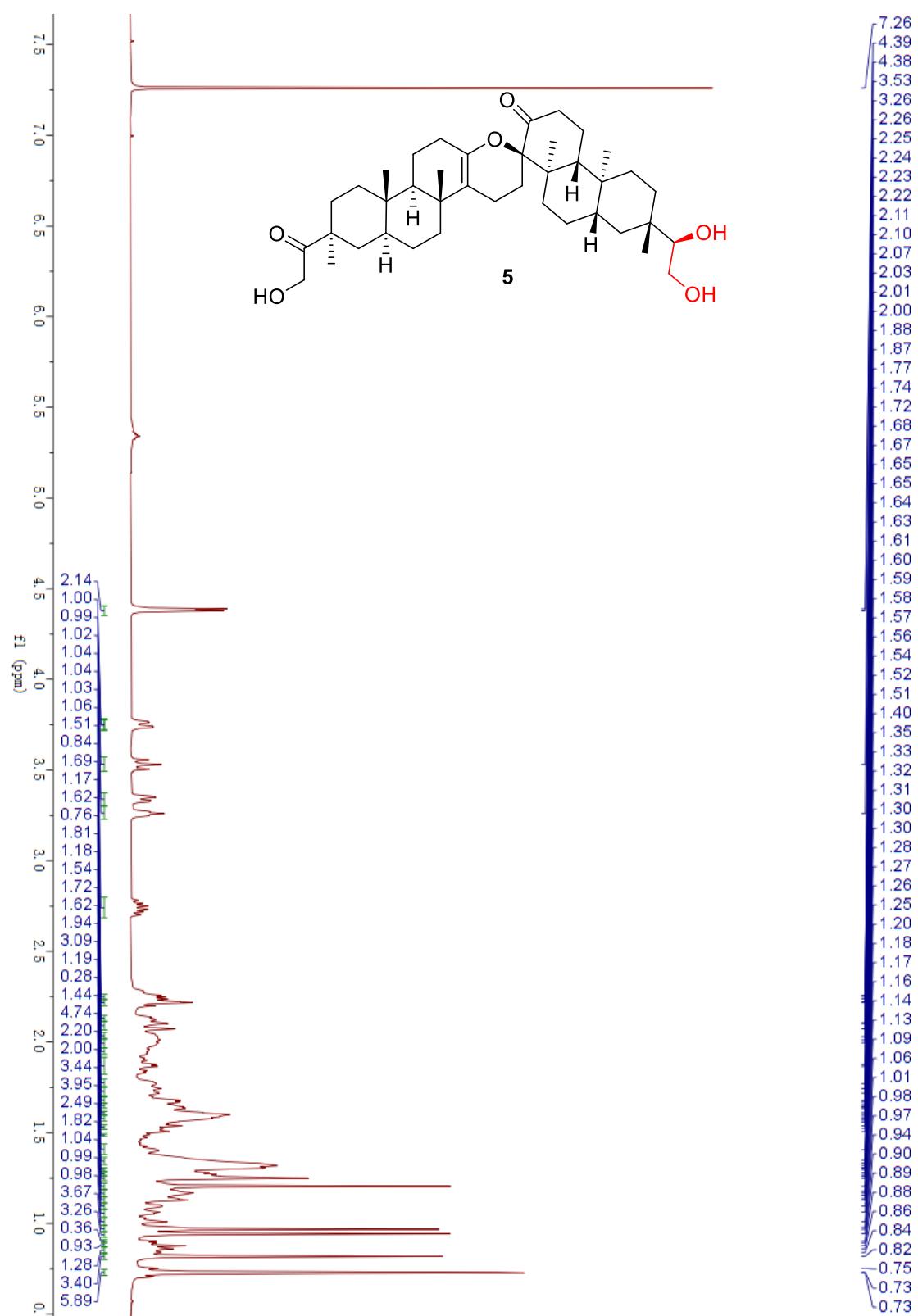


Figure S47. ^{13}C NMR spectrum of Koilodenoid E (**5**) in CDCl_3 .

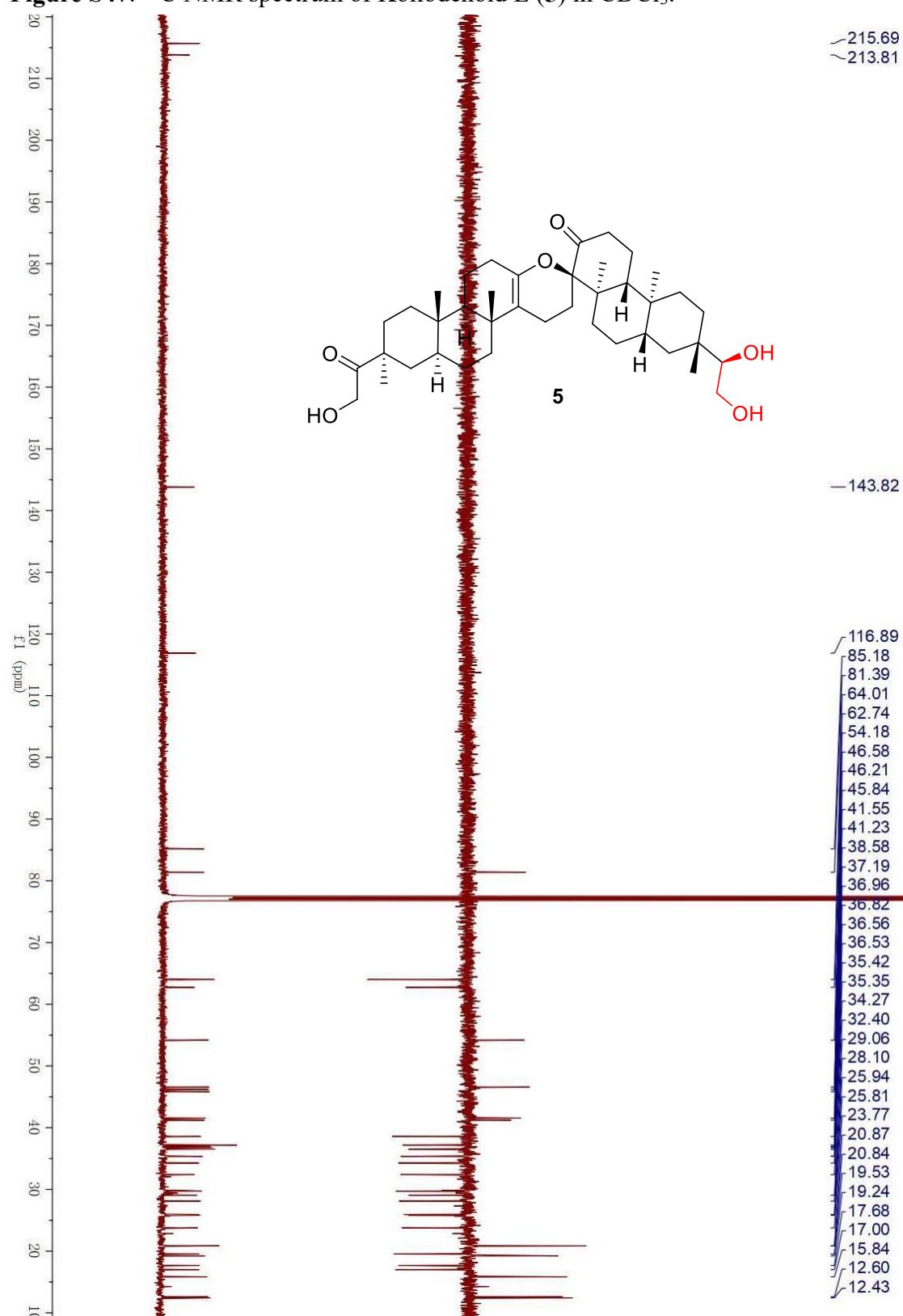


Figure S48. HSQC spectrum of Koilodenoid E (**5**) in CDCl_3 .

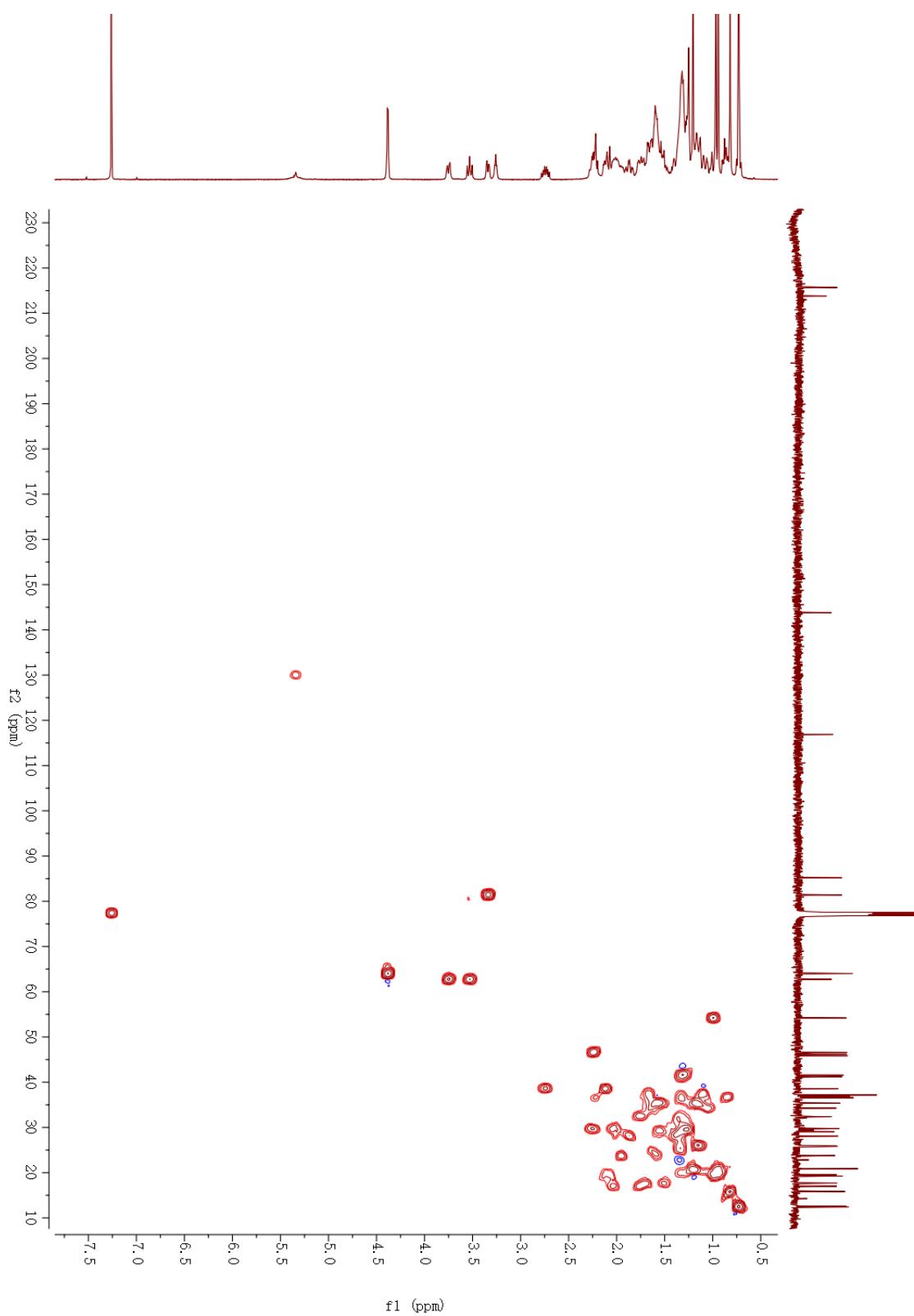


Figure S49. ^1H - ^1H COSY NMR spectrum of Koilodenoid E (**5**) in CDCl_3 .

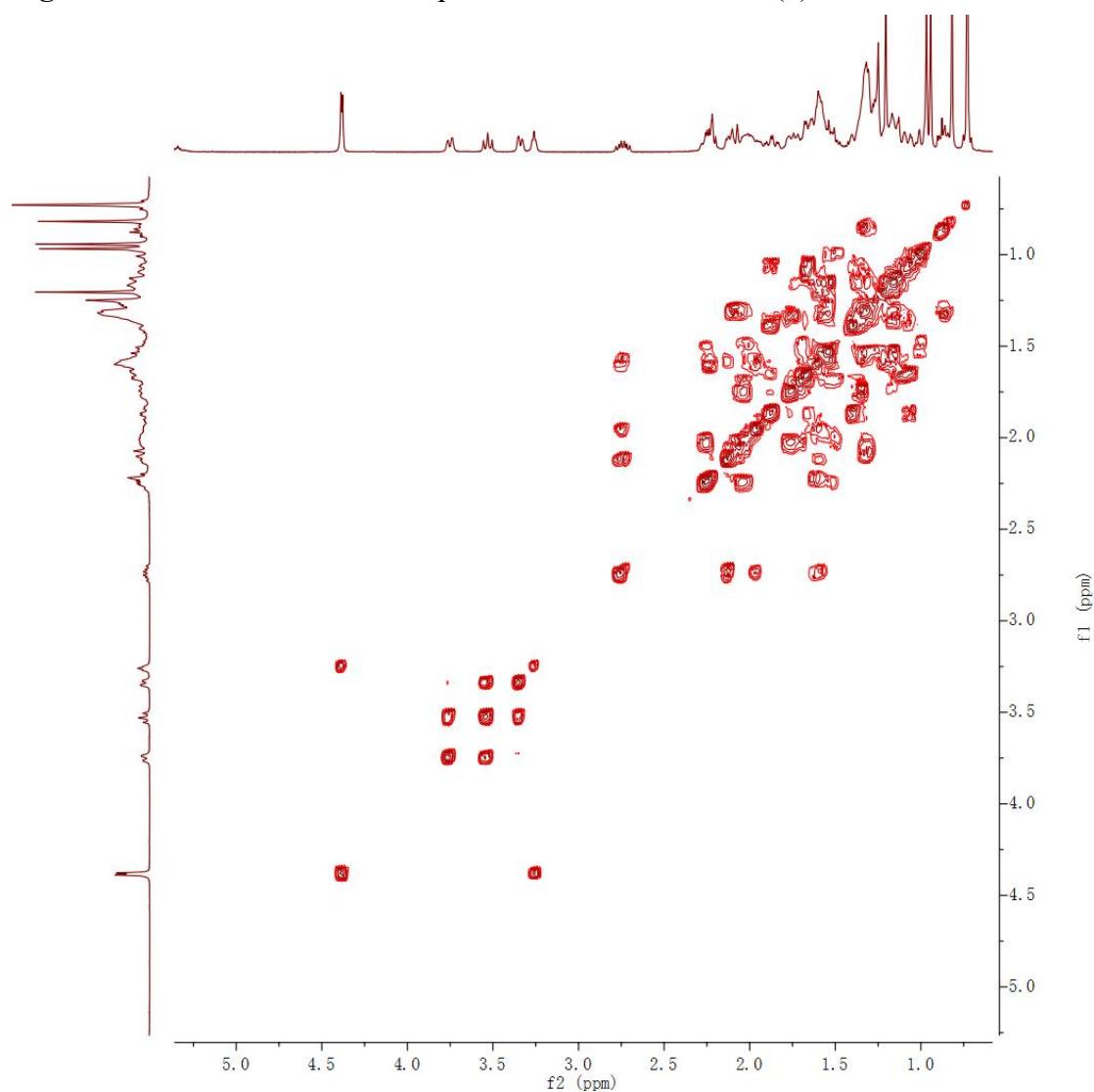


Figure S50. HMBC spectrum of Koilodenoid E (**5**) in CDCl_3 .

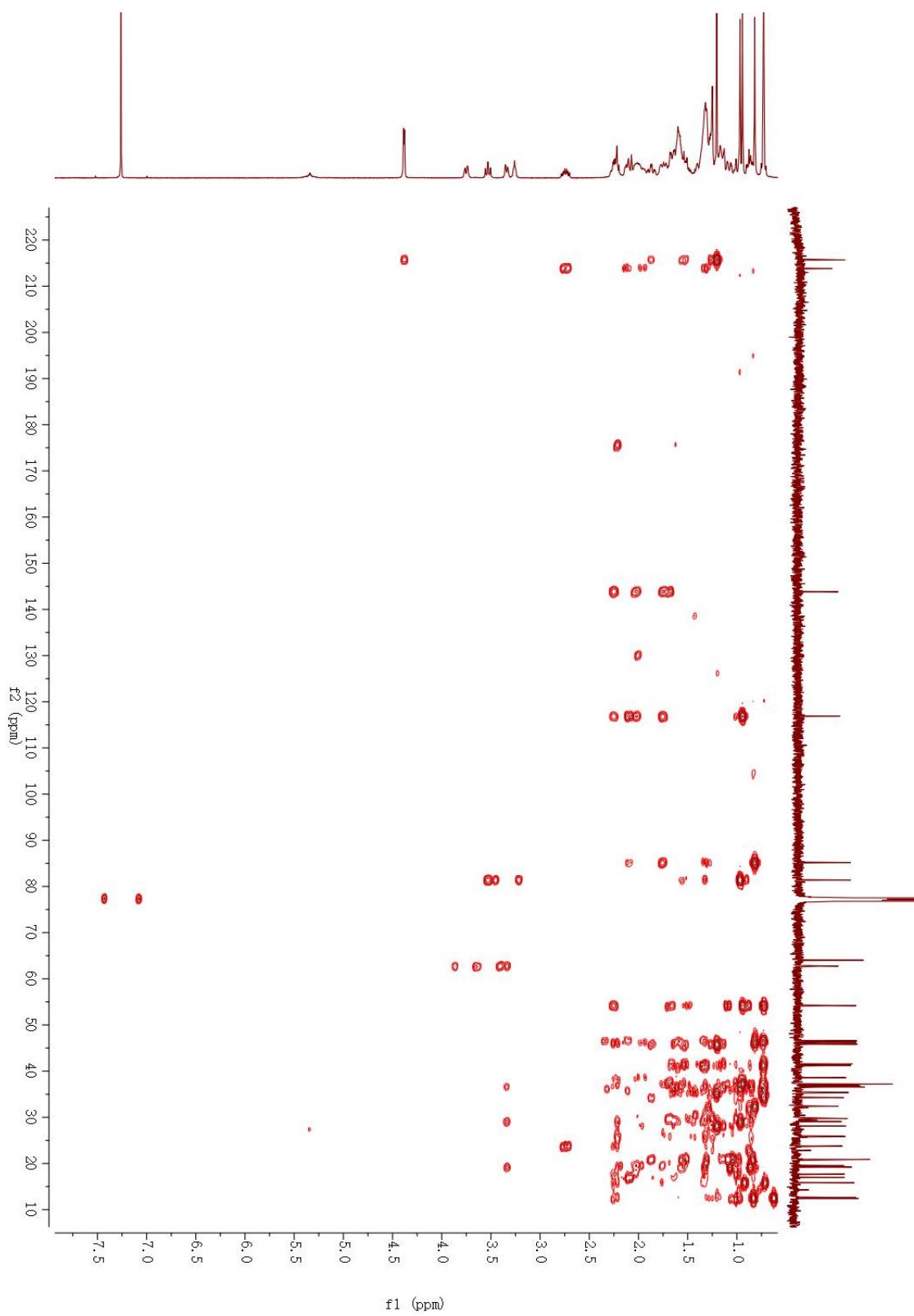


Figure S51. NOESY spectrum of Koilodenoid E (**5**) in CDCl_3 .

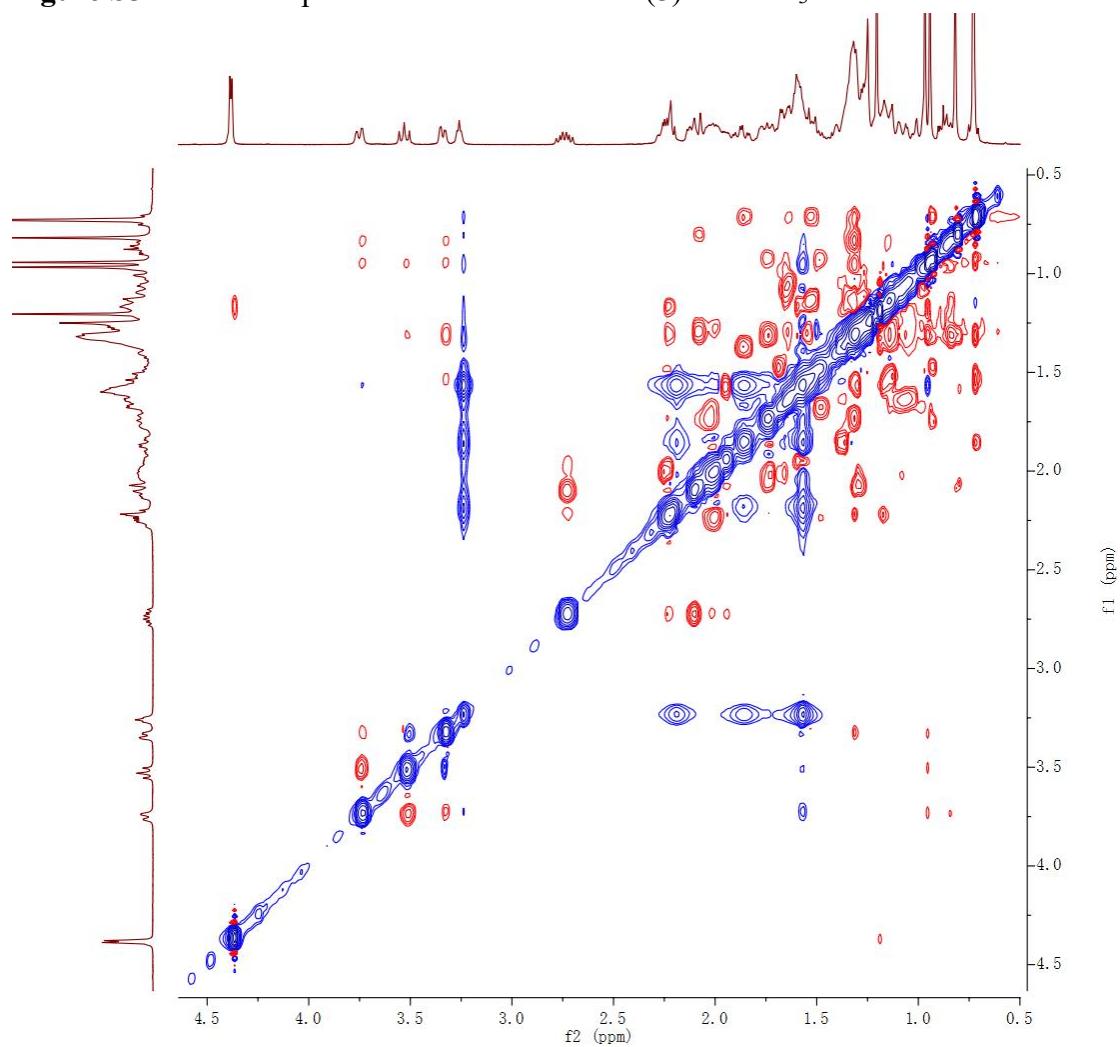
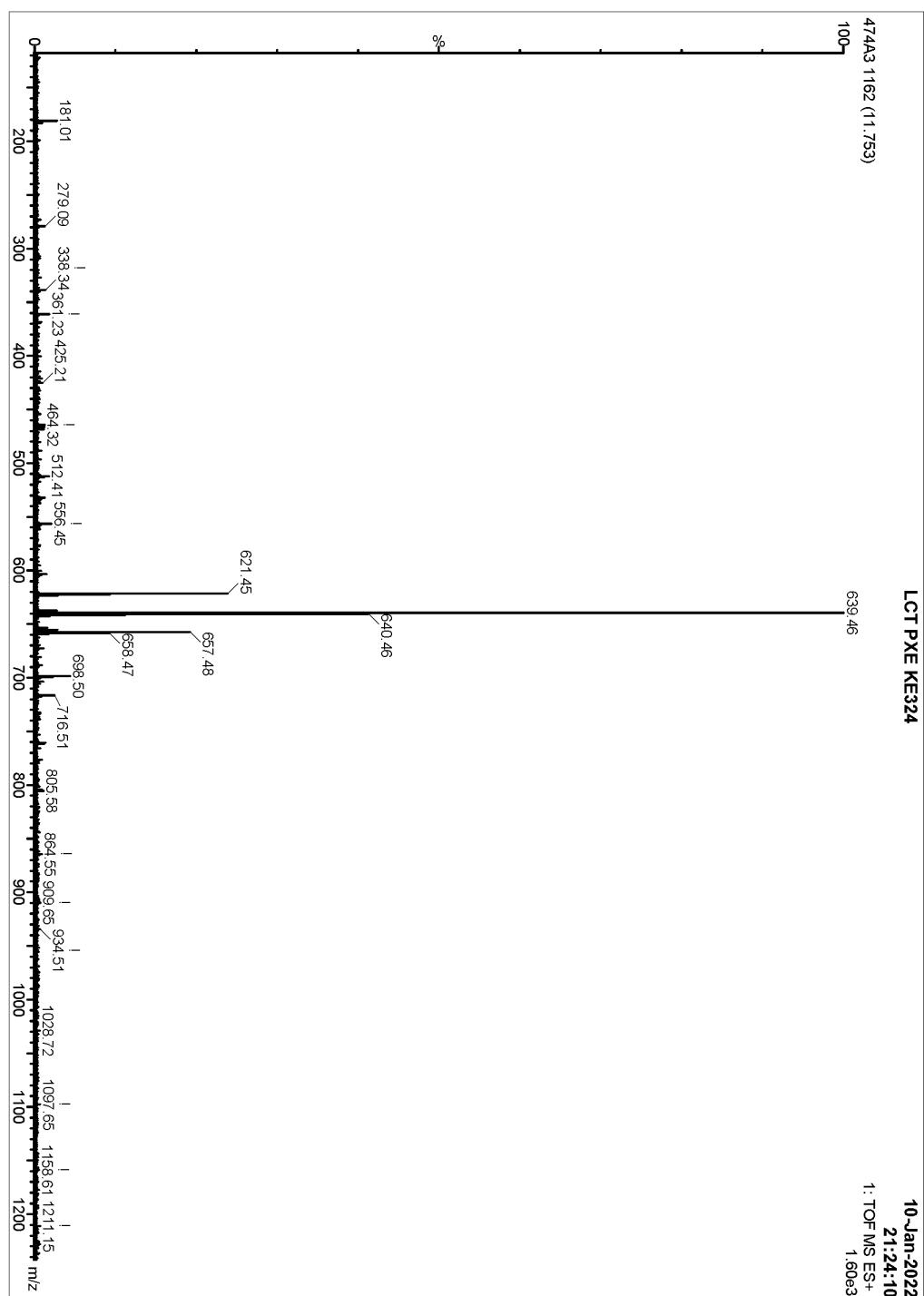


Figure S52. (+)-ESIMS spectrum of Koilodenoid E (**5**).



Elemental Composition Report**Page 1****Single Mass Analysis**

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

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1622 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

10-Jan-2022

474A3 1162 (11.753)

21:24:10

1.60e+003

Elements Used:
C: 0.47 H: 0.150 O: 1.30
LCT PXE KE24
1: TOF MS ES+

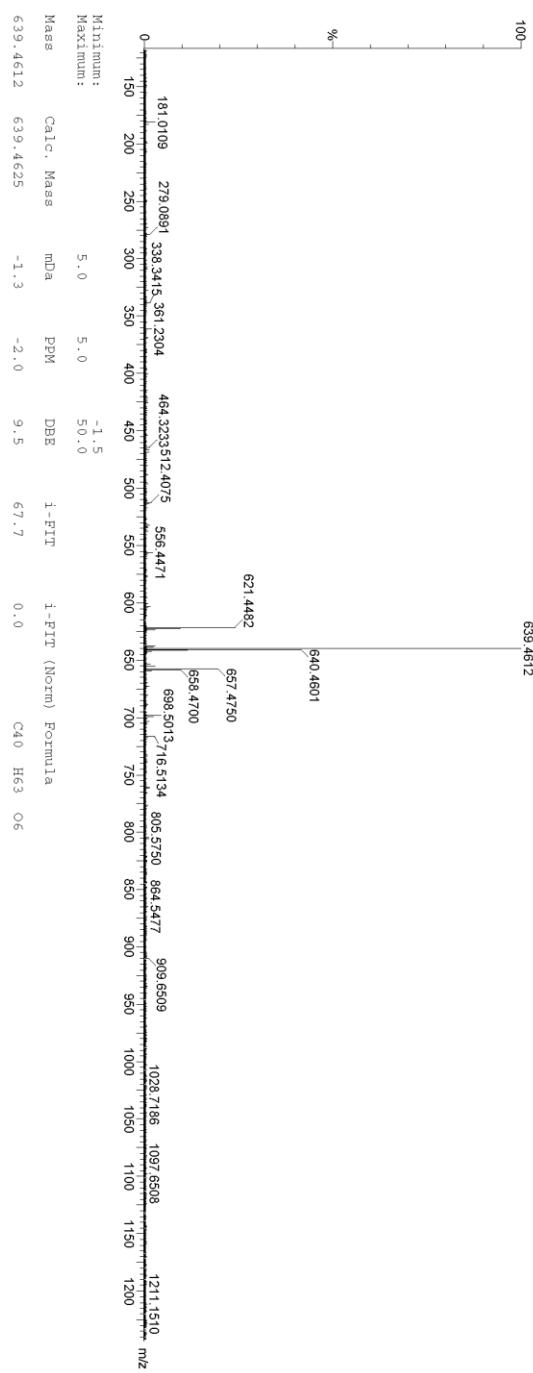
**Figure S53.** (+)-HRESIMS spectrum of Koilodenoid E (**5**).

Figure S54. IR spectrum of Koilodenoid E (**5**).

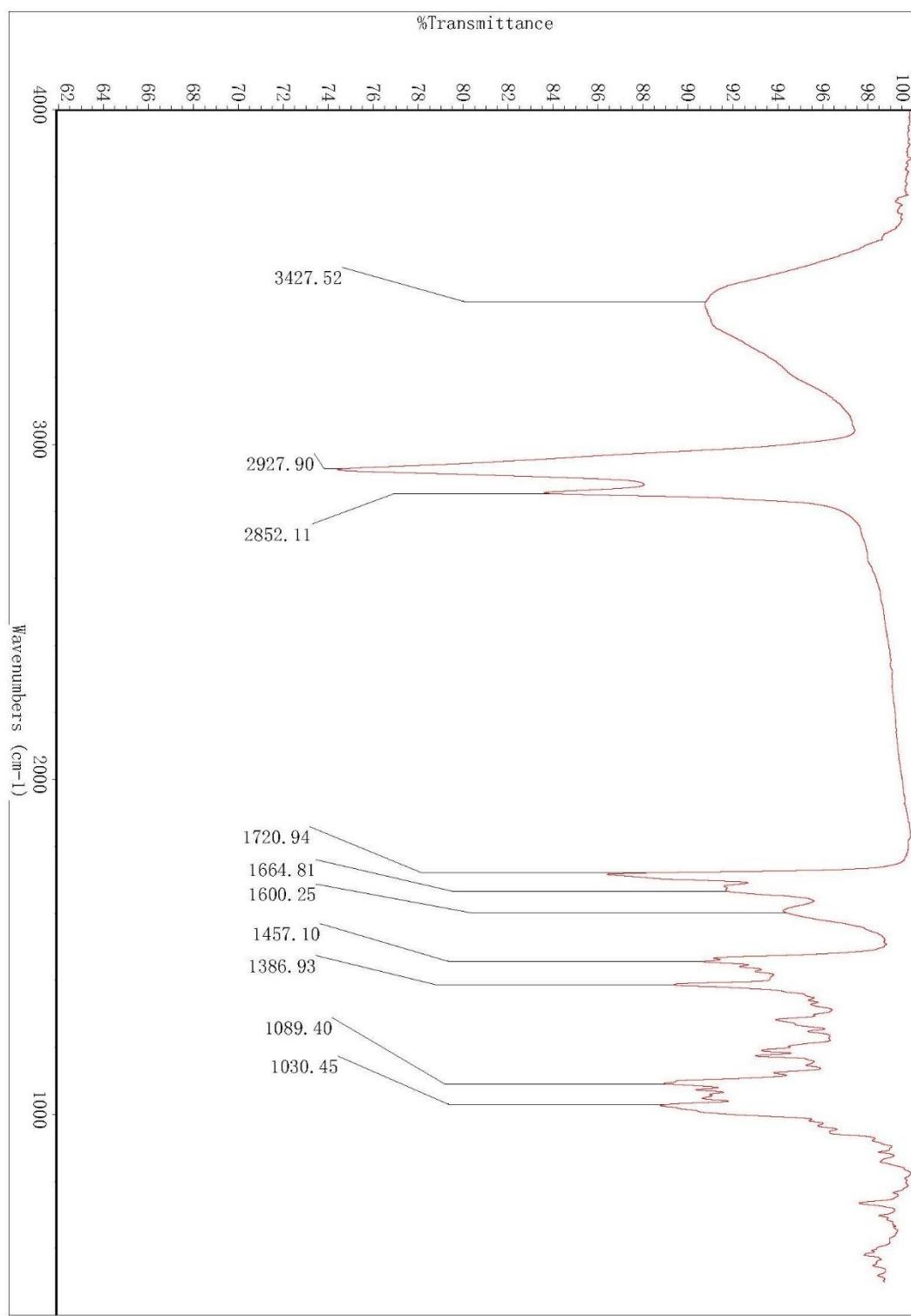


Figure S55. ^1H NMR spectrum of Koilodenoid F (**6**) in CDCl_3 .

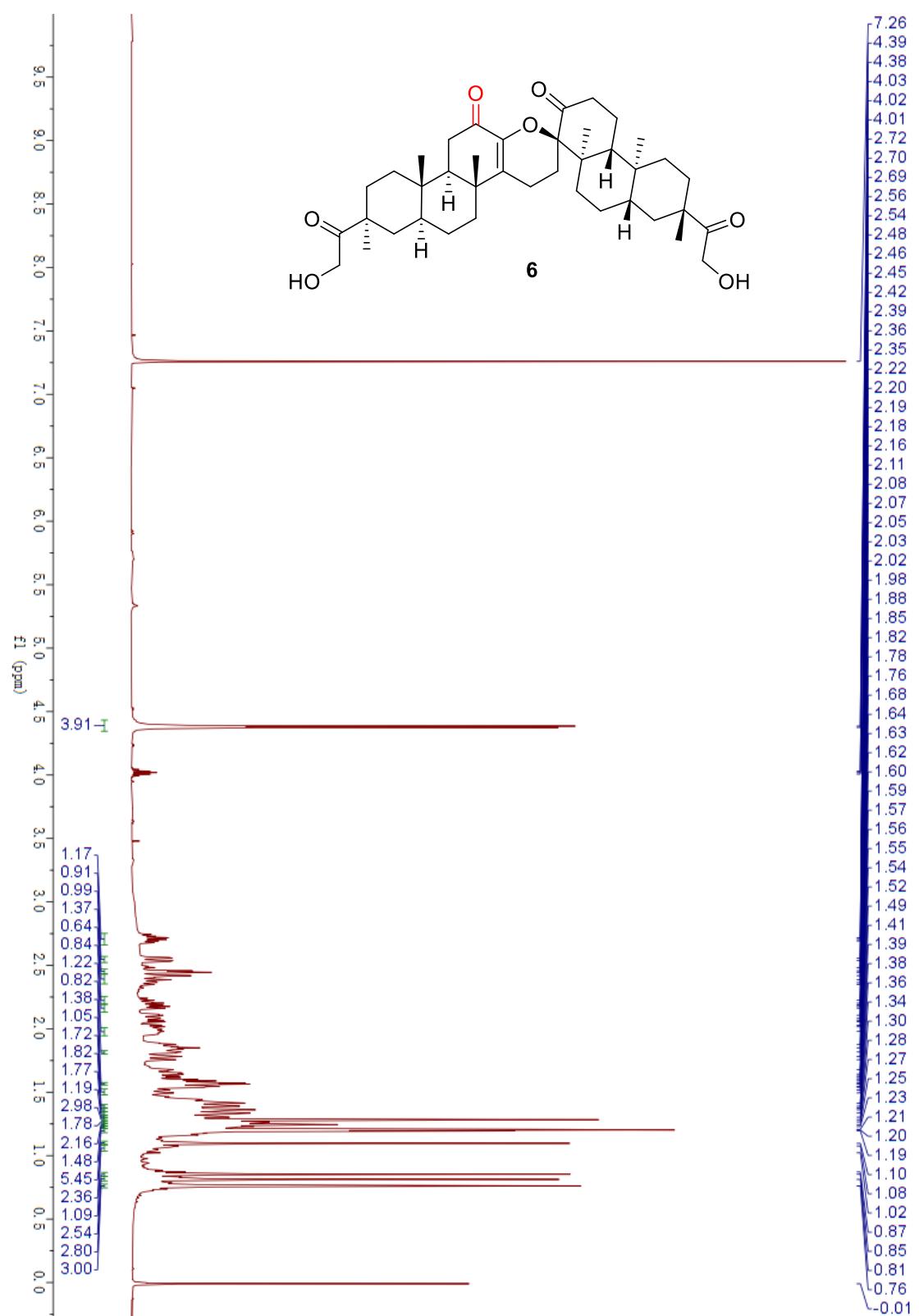


Figure S56. ^{13}C NMR spectrum of Koilodenoid F (**6**) in CDCl_3 .

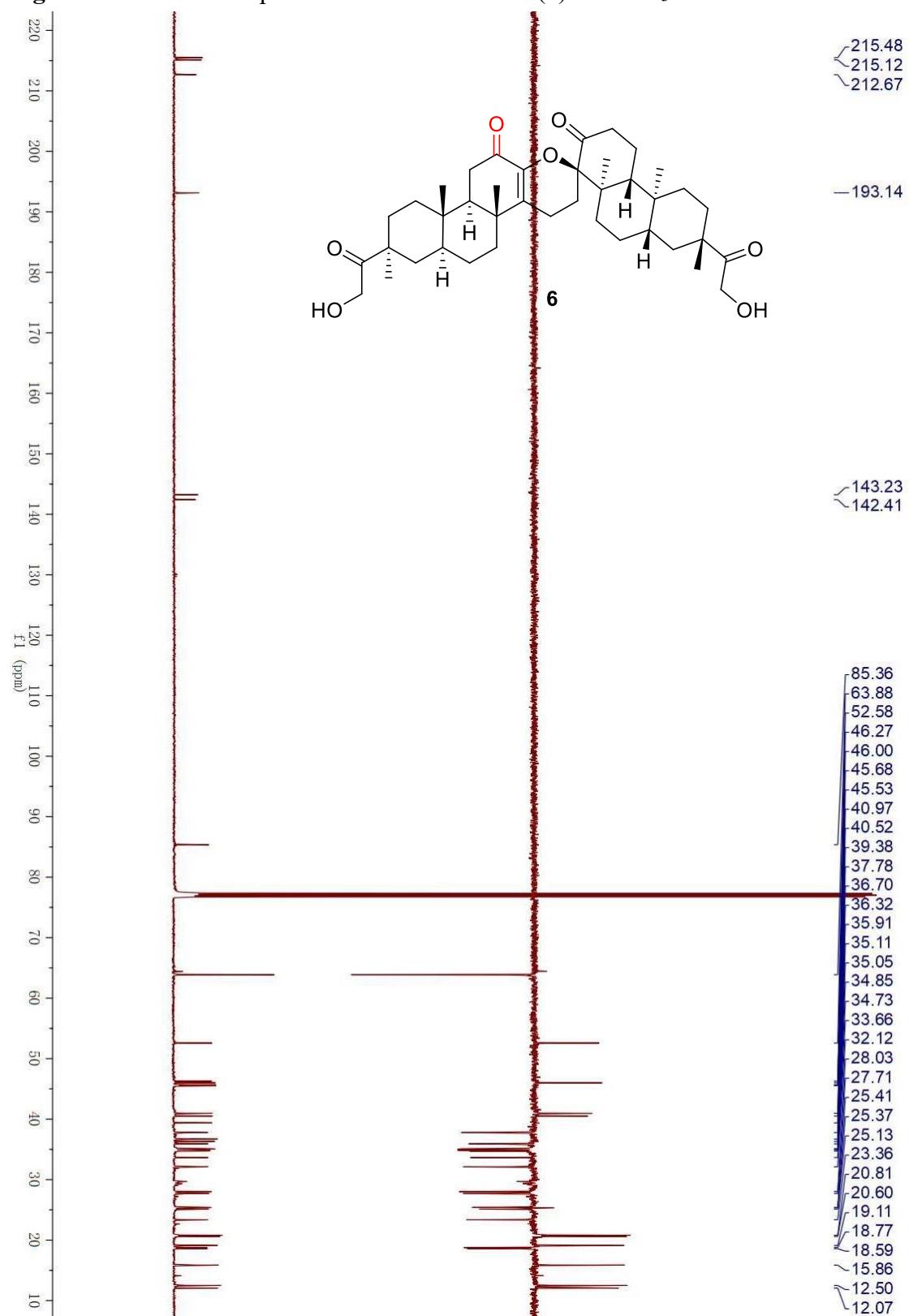


Figure S57. HSQC spectrum of Koilodenoid F (**6**) in CDCl_3 .

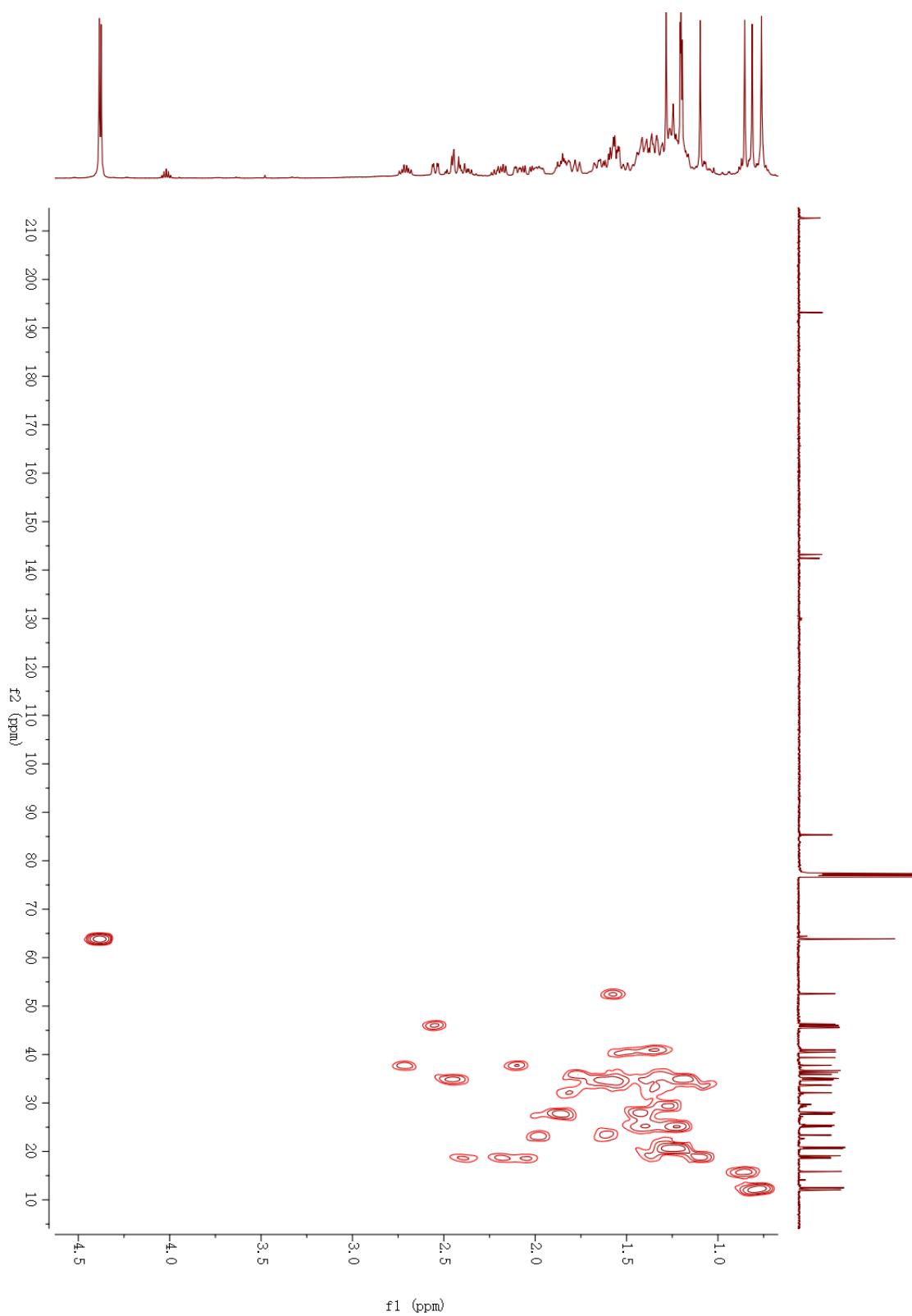


Figure S58. ^1H - ^1H COSY NMR spectrum of Koilodenoid F (**6**) in CDCl_3 .

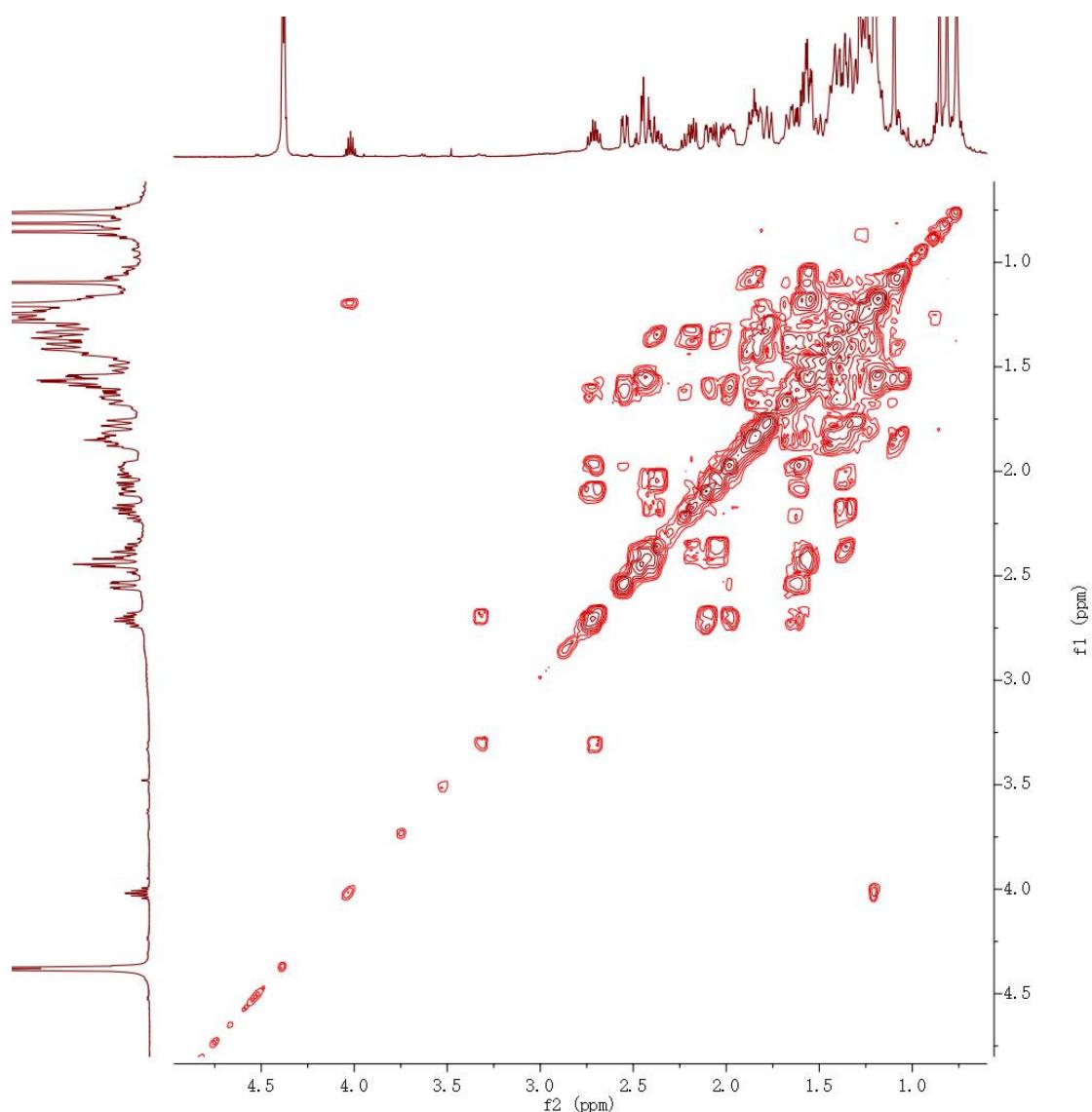


Figure S59. HMBC spectrum of Koilodenoid F (**6**) in CDCl_3 .

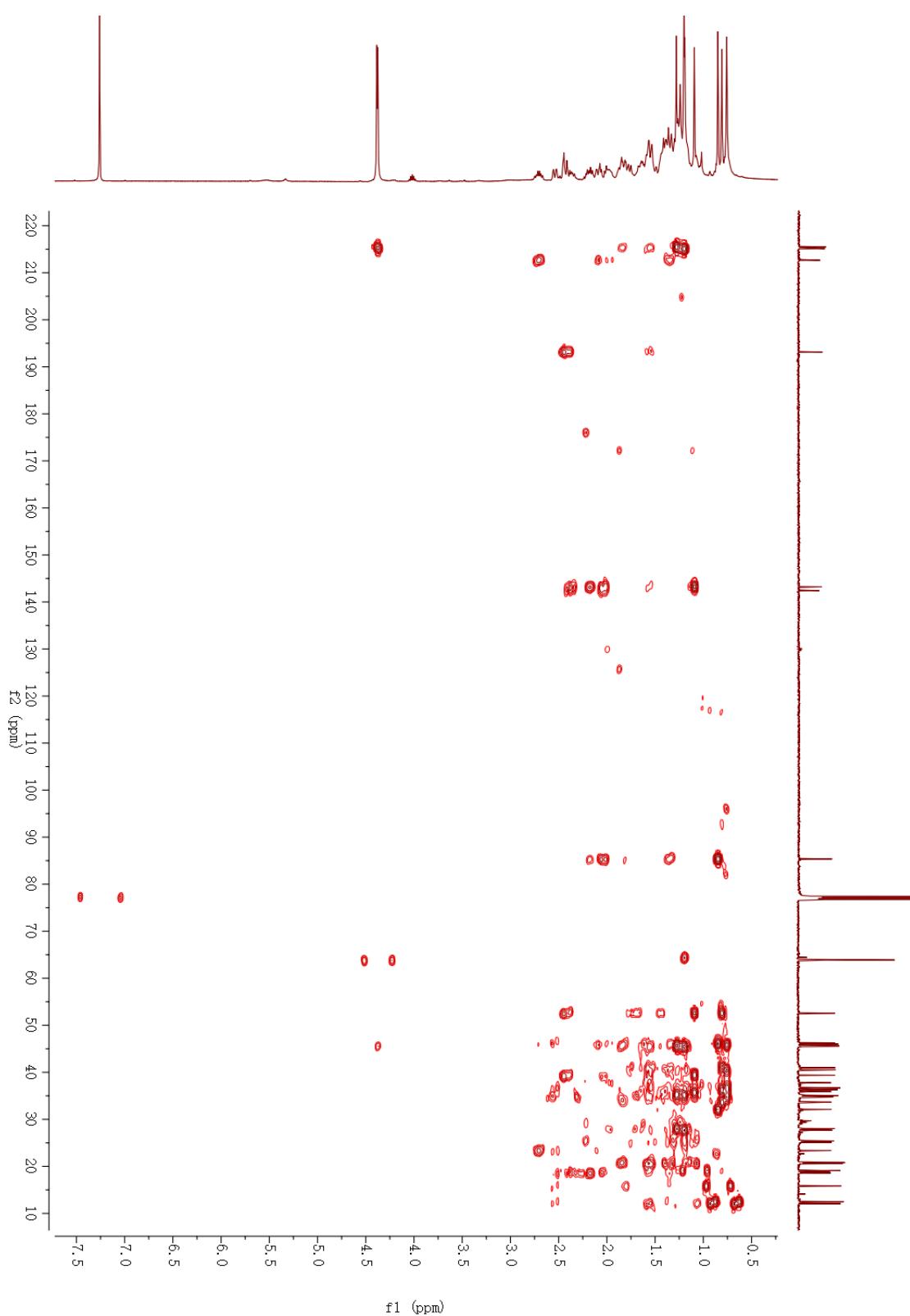


Figure S60. NOESY spectrum of Koilodenoid F (**6**) in CDCl_3 .

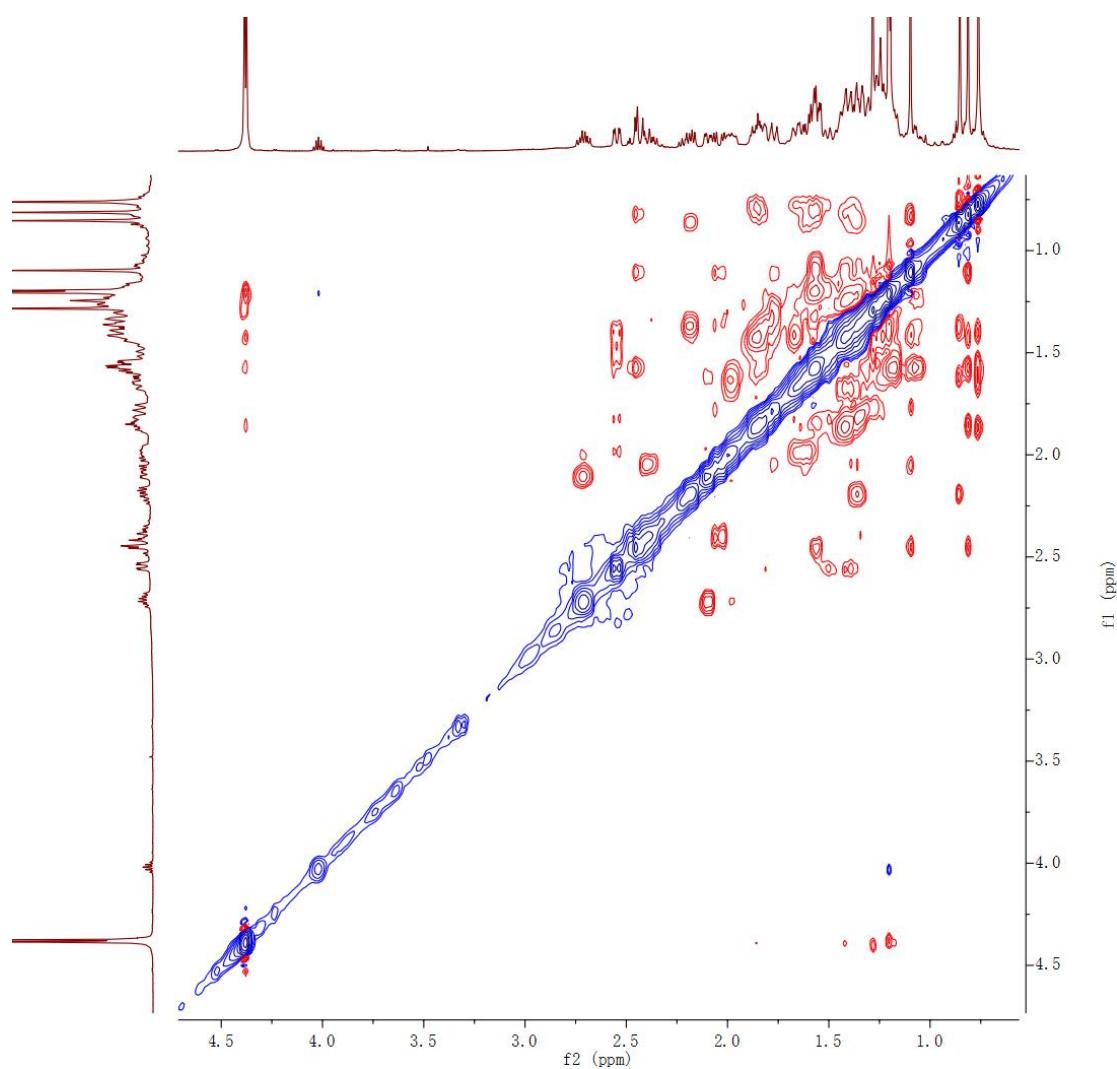
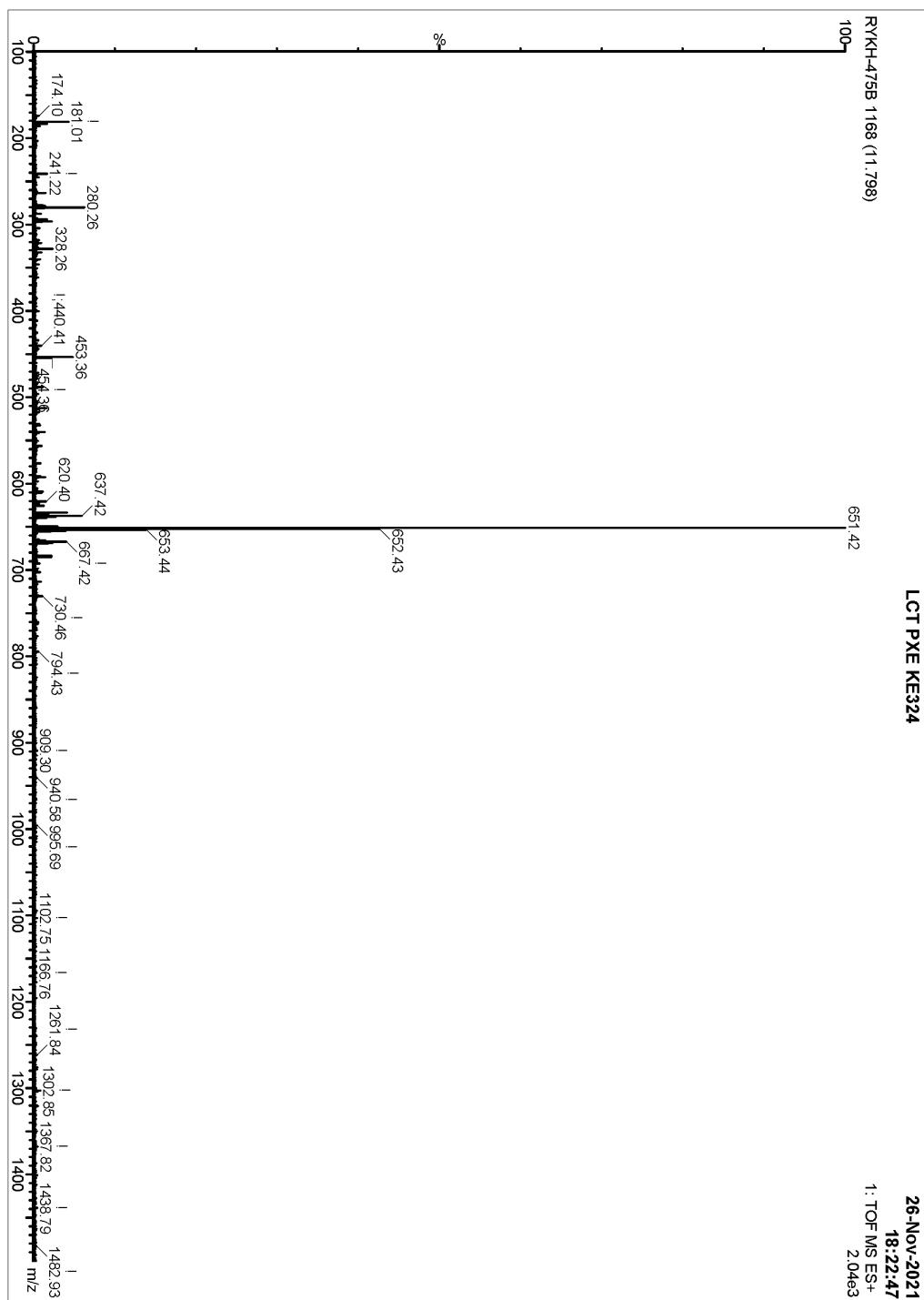


Figure S61. (+)-ESIMS spectrum of Koilodenoid F (**6**).



Elemental Composition Report**Page 1****Single Mass Analysis**

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 20.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions
68 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

C: 0-50 H: 0-80 O: 0-10

LCT P/XE KE324

1: TOF MS ES+

26-Nov-2021

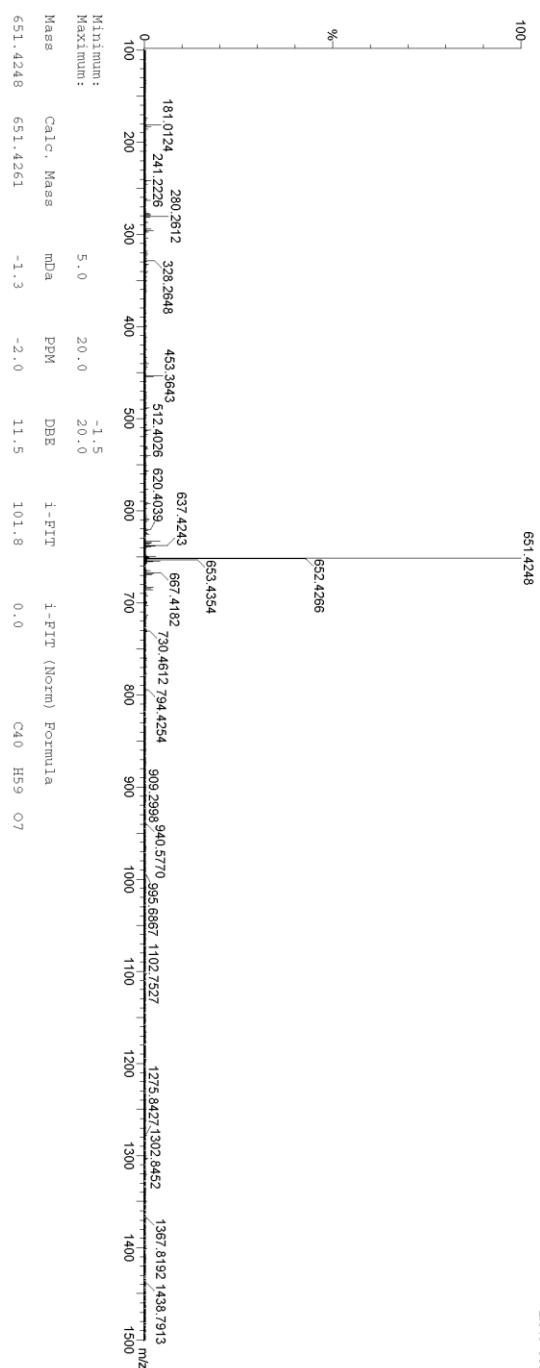
RYKH-475B 1168 (11.798)
¹⁸2247
2.04e+003

Figure S63. IR spectrum of Koilodenoid F (**6**).

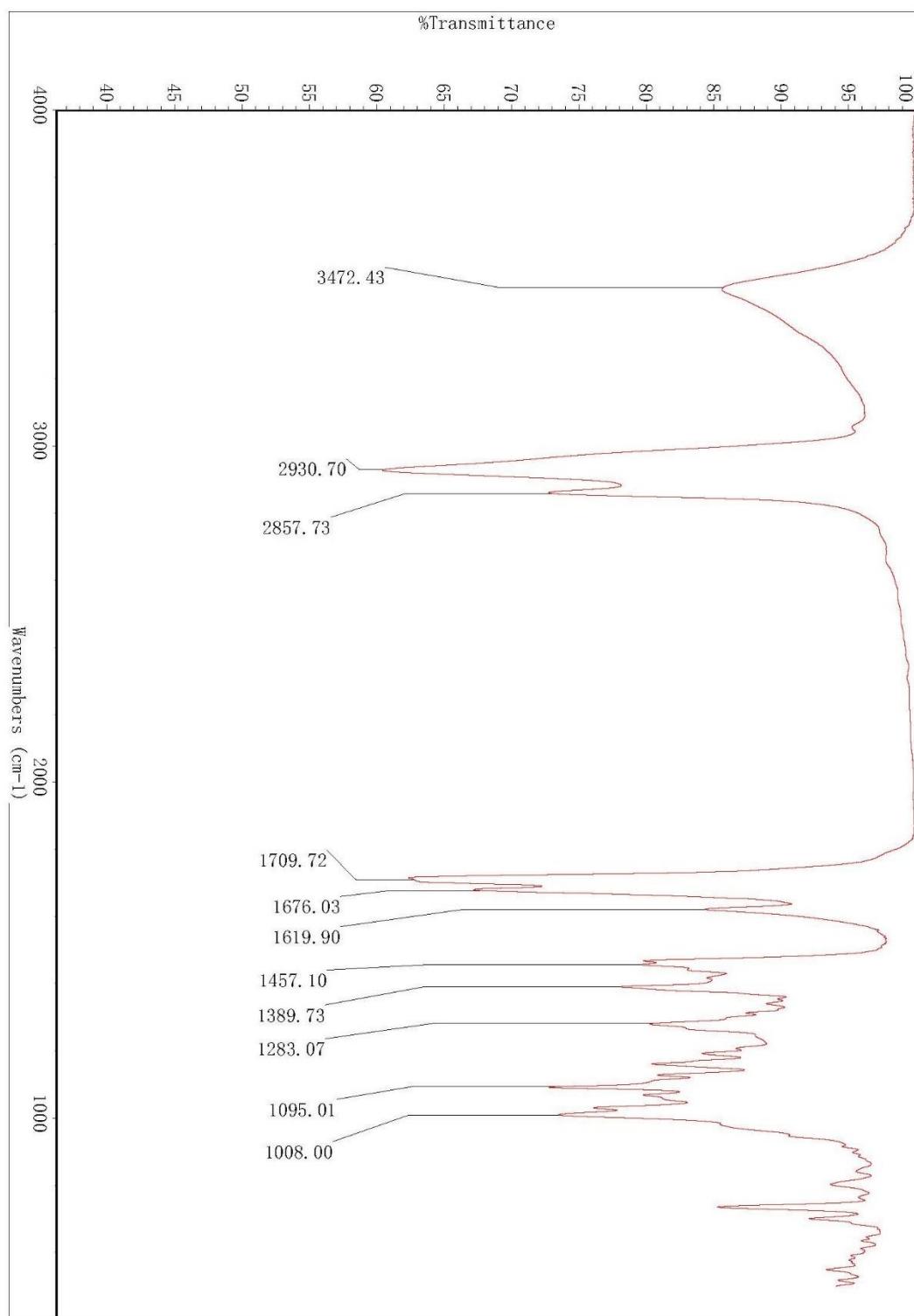


Figure S64. ^1H NMR spectrum of Koilodenoid G (**7**) in CDCl_3 .

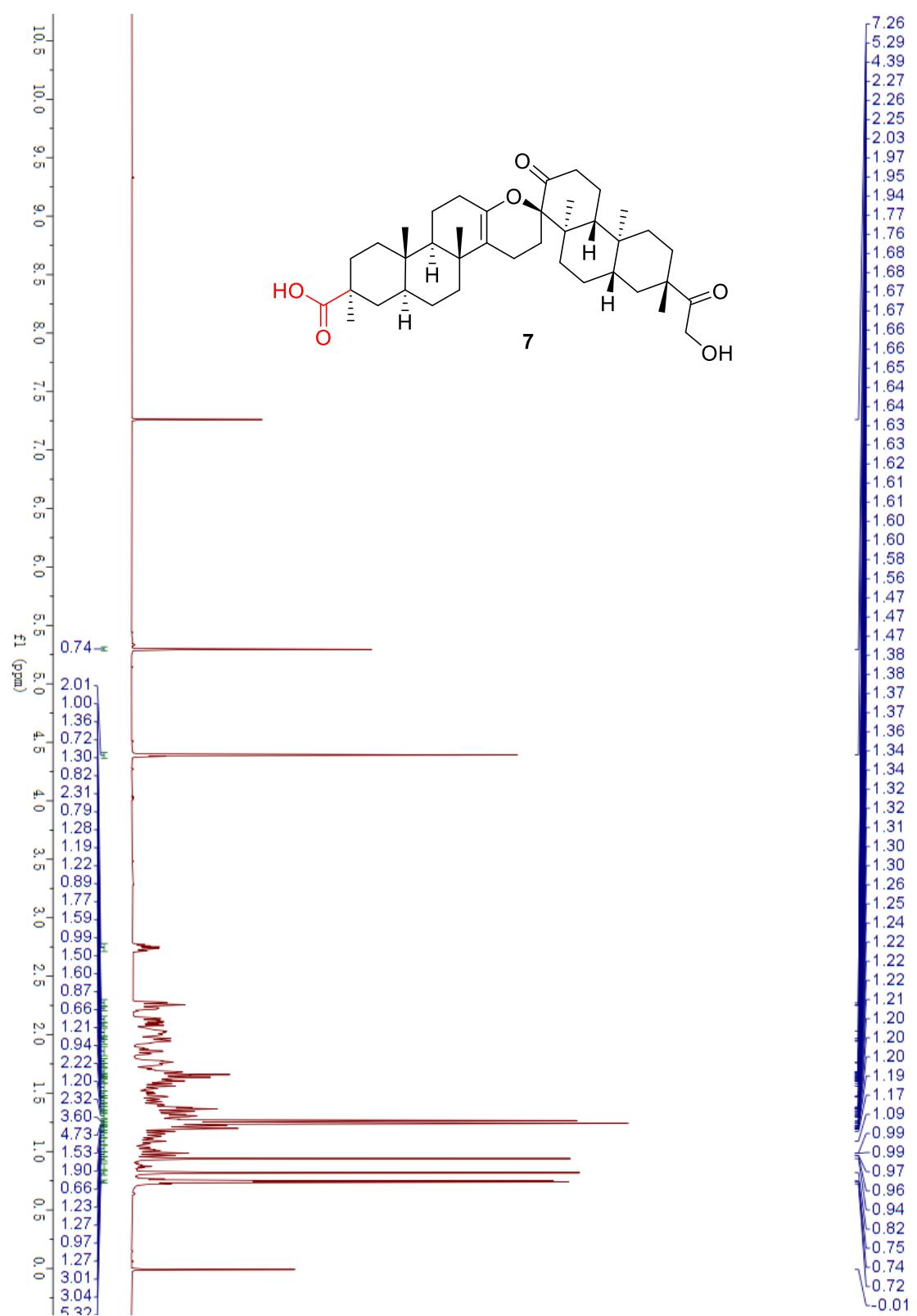


Figure S65. ^{13}C NMR spectrum of Koilodenoid G (**7**) in CDCl_3 .

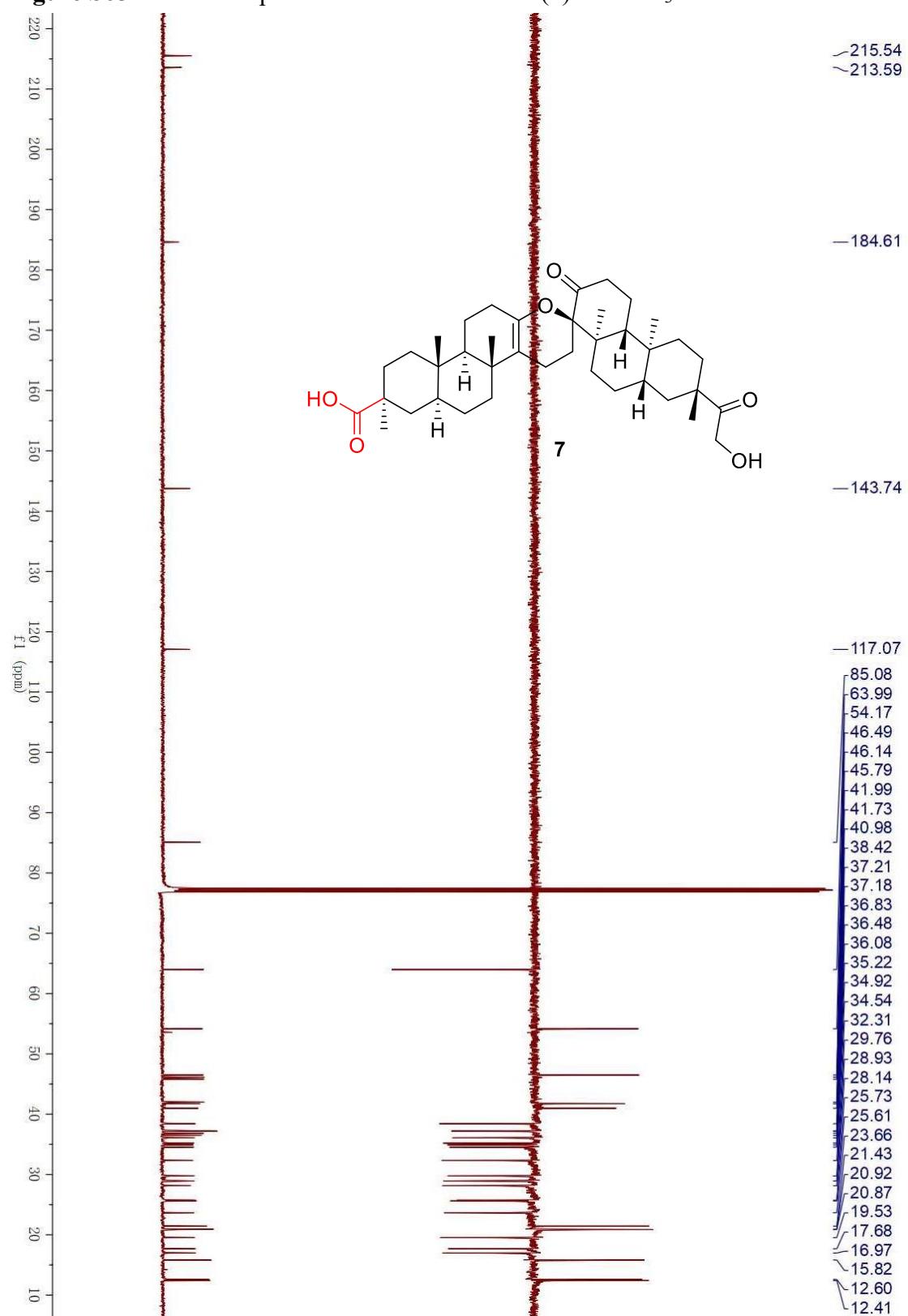


Figure S66. HSQC spectrum of Koilodenoid G (**7**) in CDCl_3 .

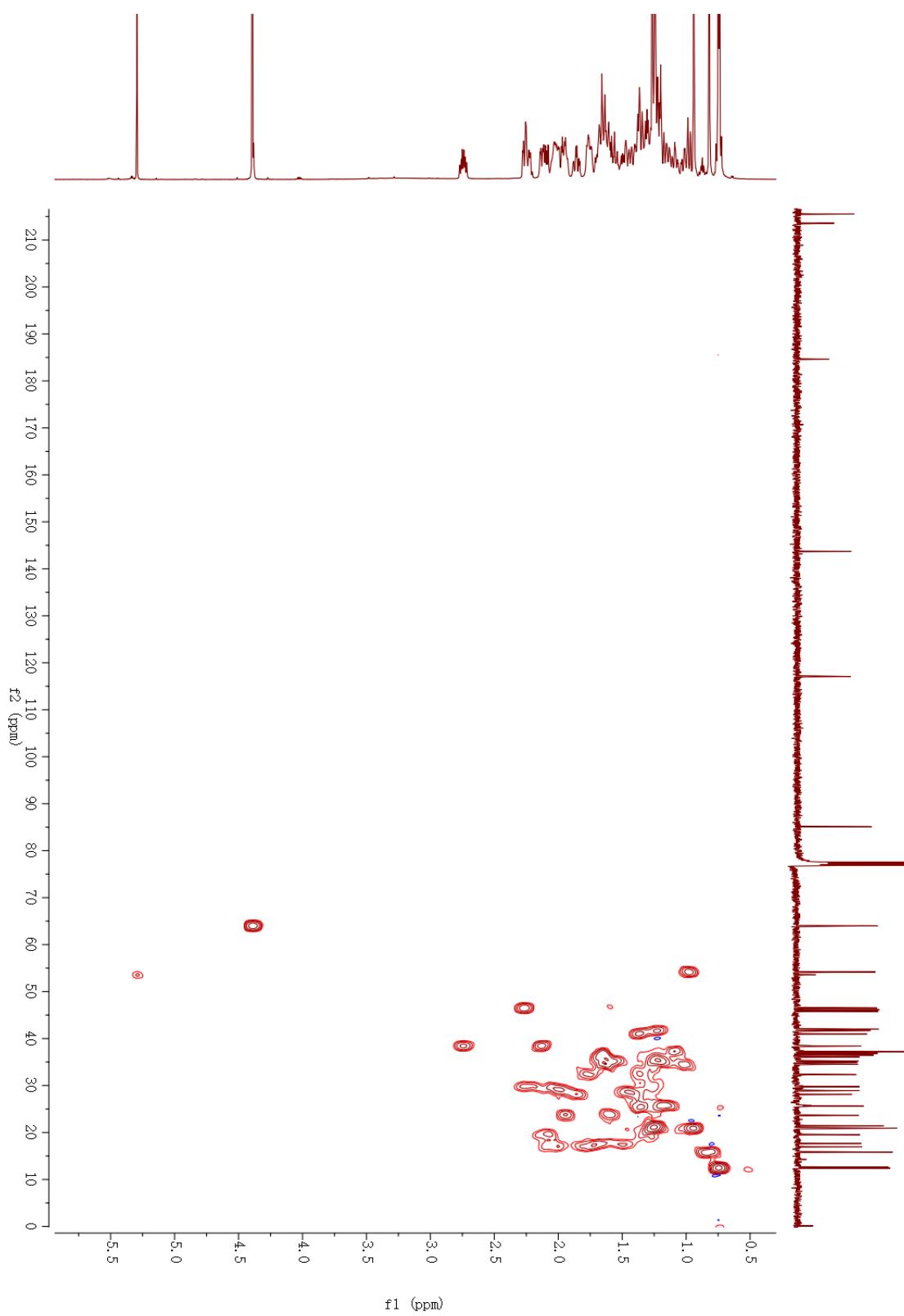


Figure S67. ^1H - ^1H COSY NMR spectrum of Koilodenoid G (**7**) in CDCl_3 .

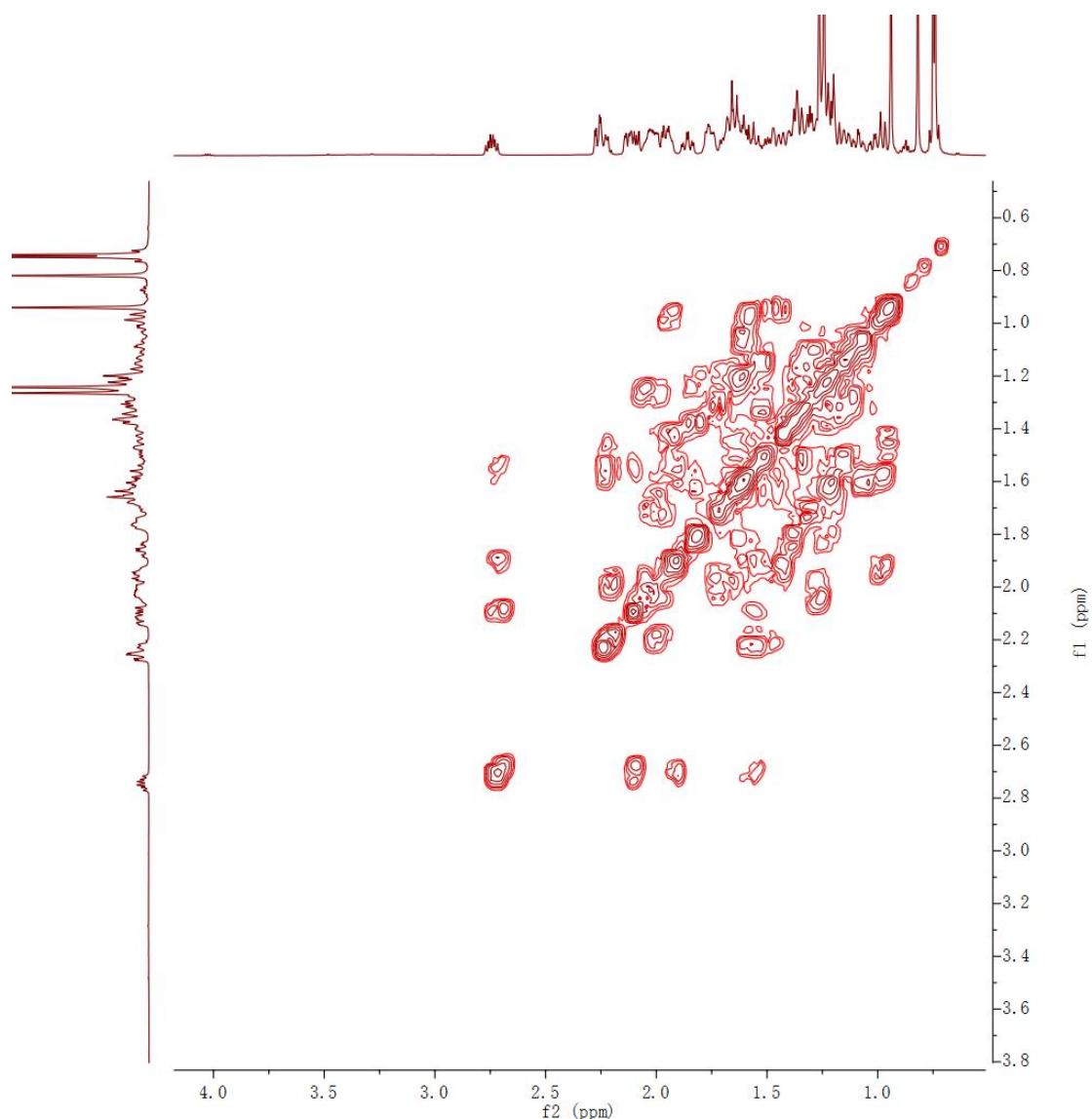


Figure S68. HMBC spectrum of Koilodenoid G (7) in CDCl_3 .

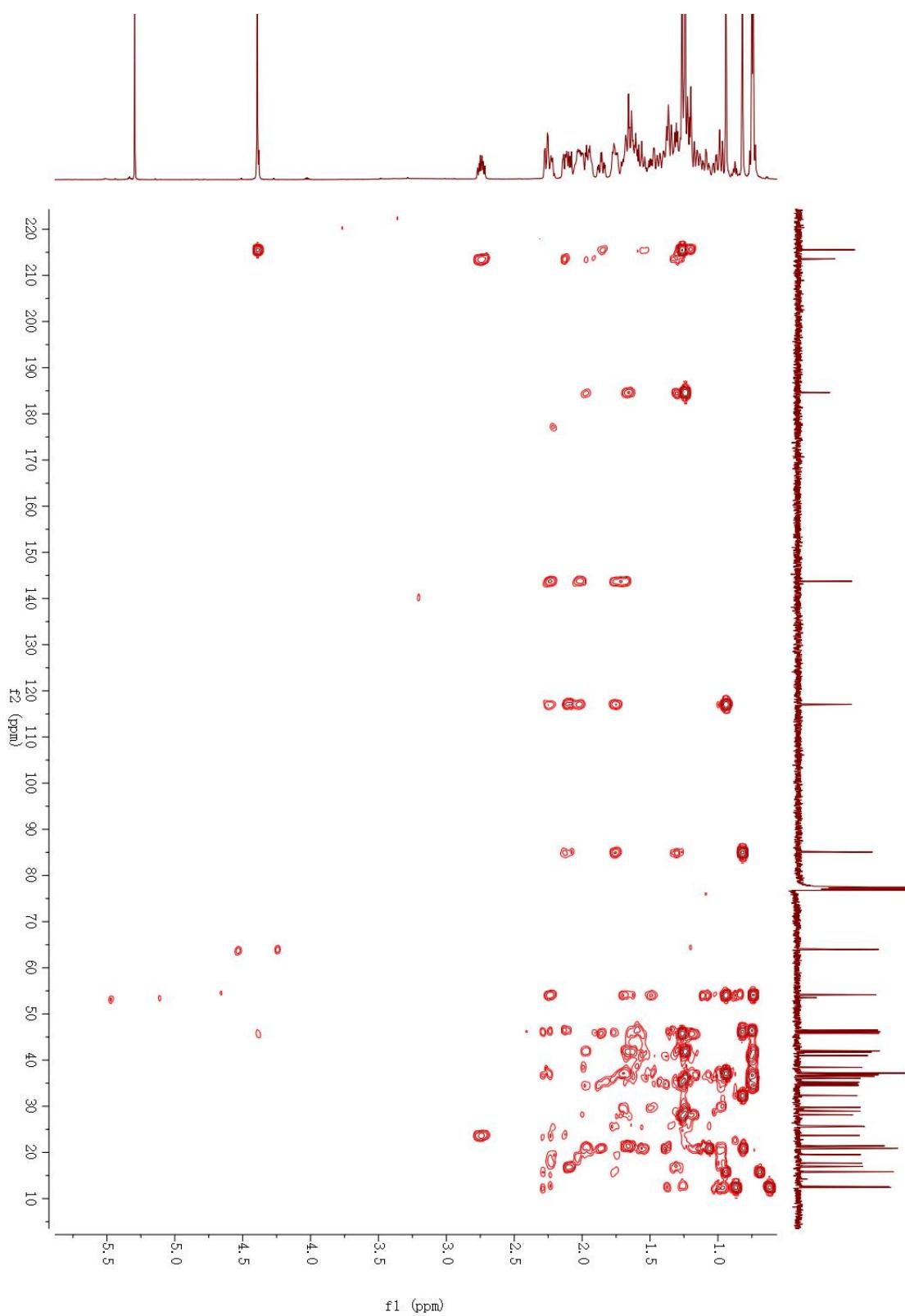


Figure S69. NOESY spectrum of Koilodenoid G (**7**) in CDCl_3 .

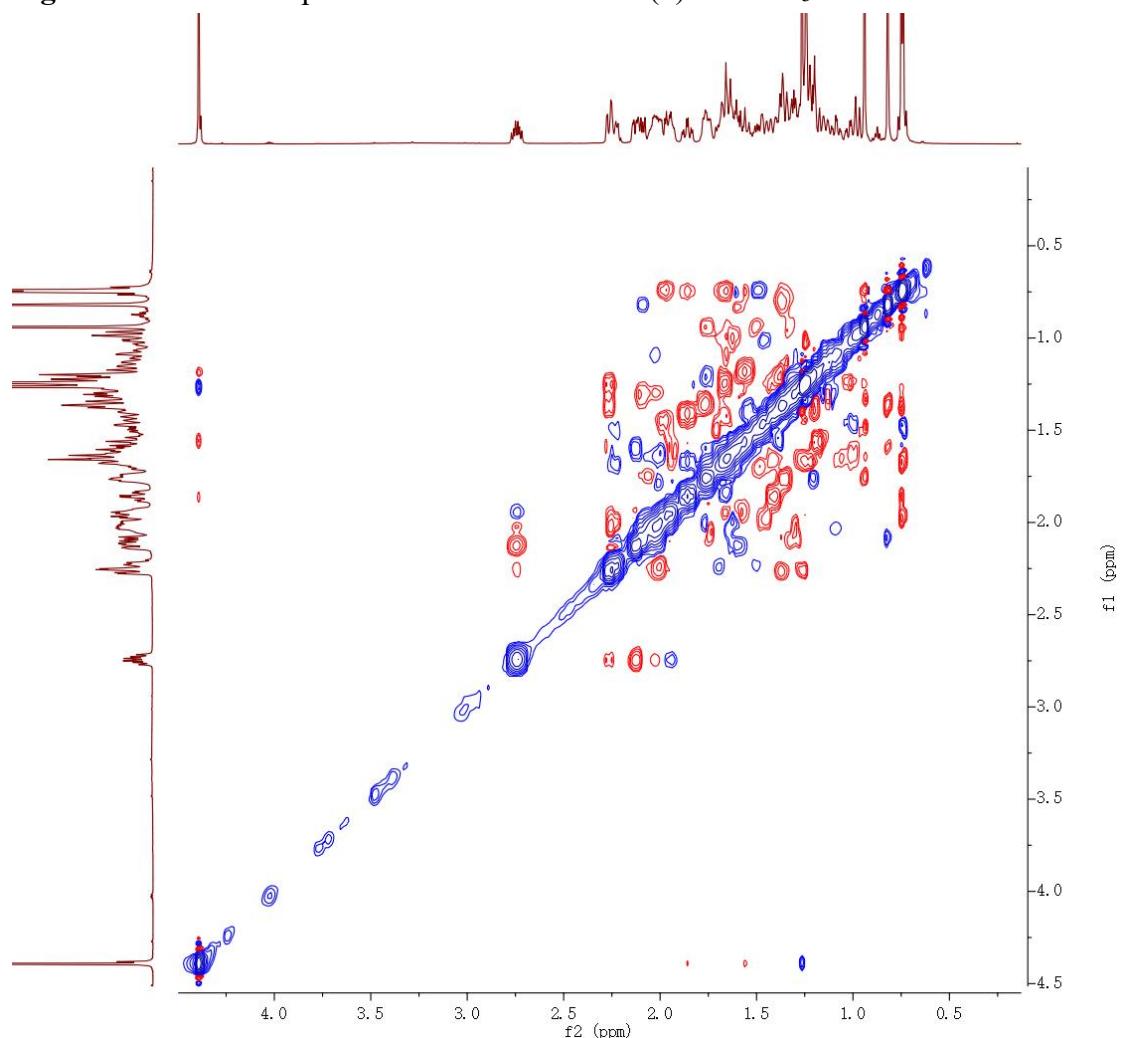
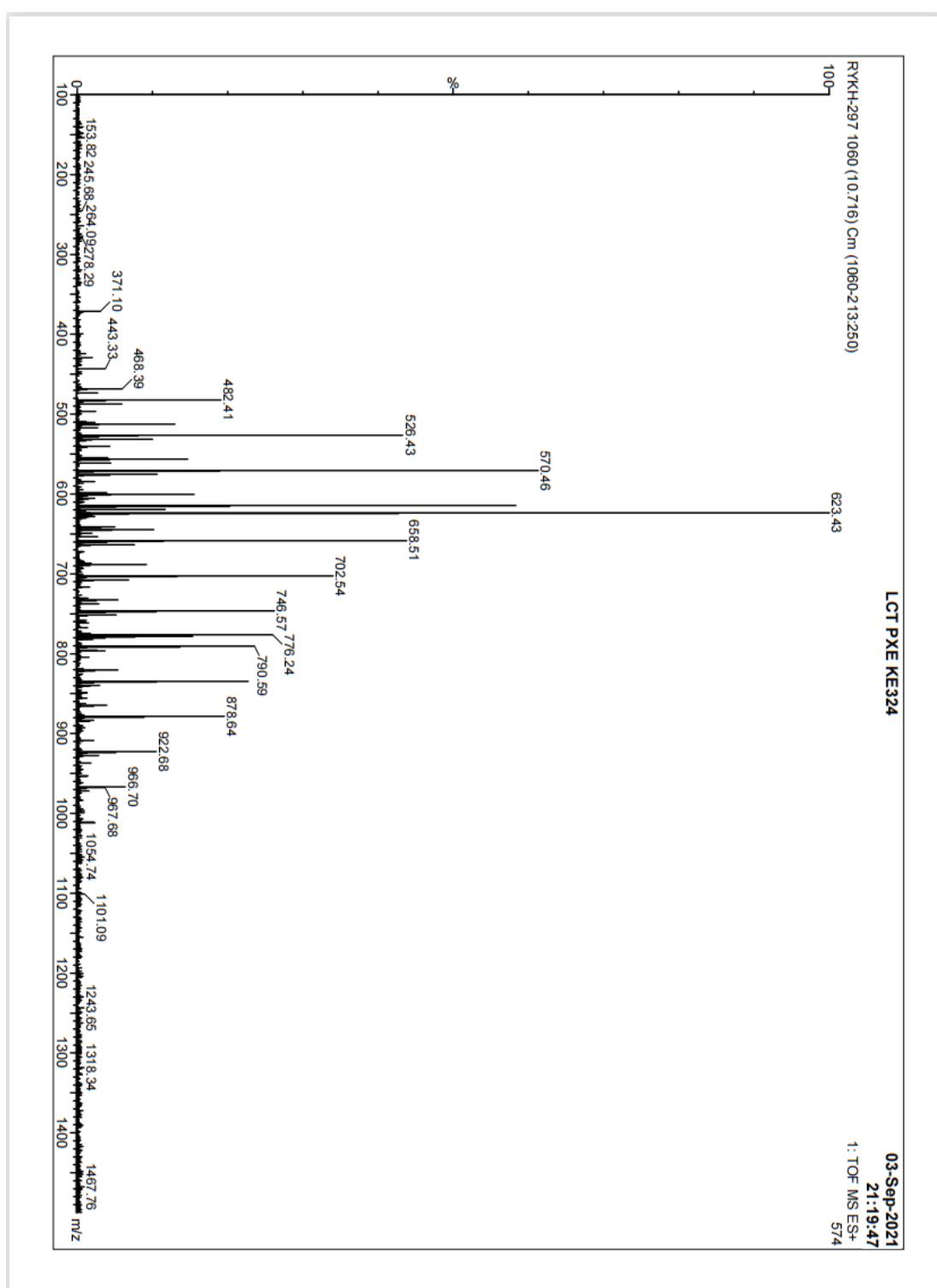


Figure S70. (+)-ESIMS spectrum of Koilodenoid G (7).



Elemental Composition Report**Page 1****Single Mass Analysis**

Tolerance = 1.0 PPM / DBE: min = -1.5, max = 30.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 5

Monoisotopic Mass, Even Electron Ions

17 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

C: 25-50 H: 40-60 O: 1-10

LCT PPE NE-324

1-TOF MS ES+

05-Sep-2021

RYKH-297 1000 (10.716) Cm (1000-213.250)

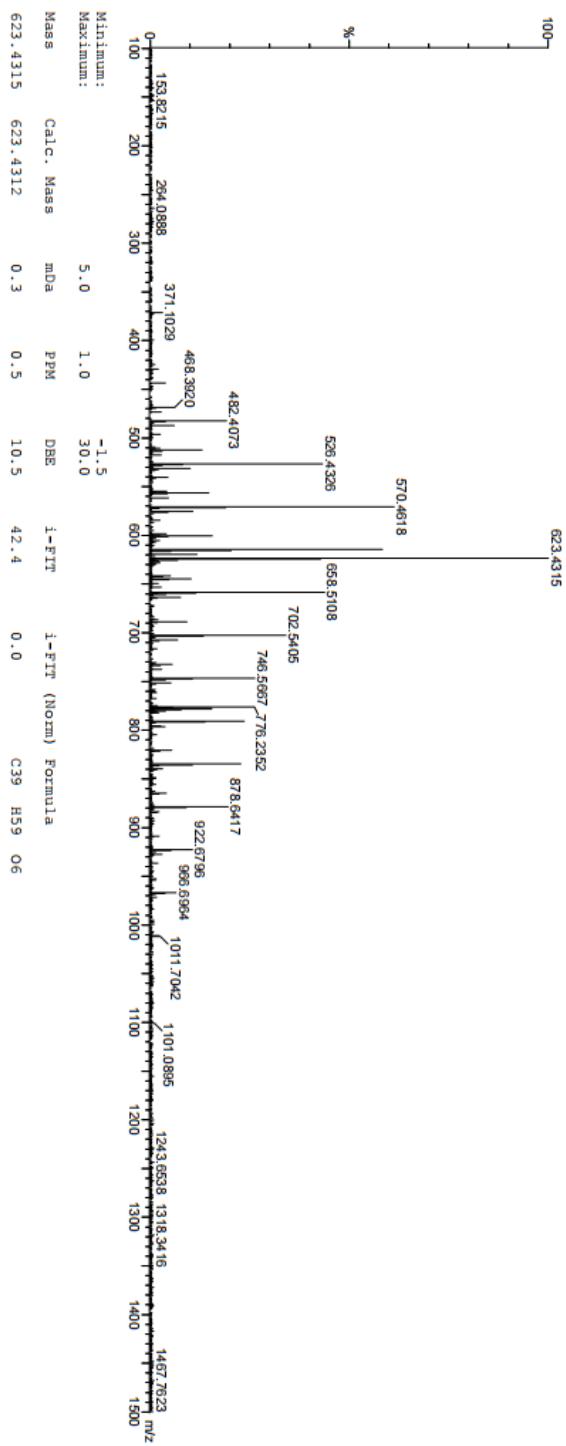
21:19:47
5.76e-02**Figure S71.** (+)-HRESIMS spectrum of Koilodenoid G (7).

Figure S72. IR spectrum of Koilodenoid G (7).

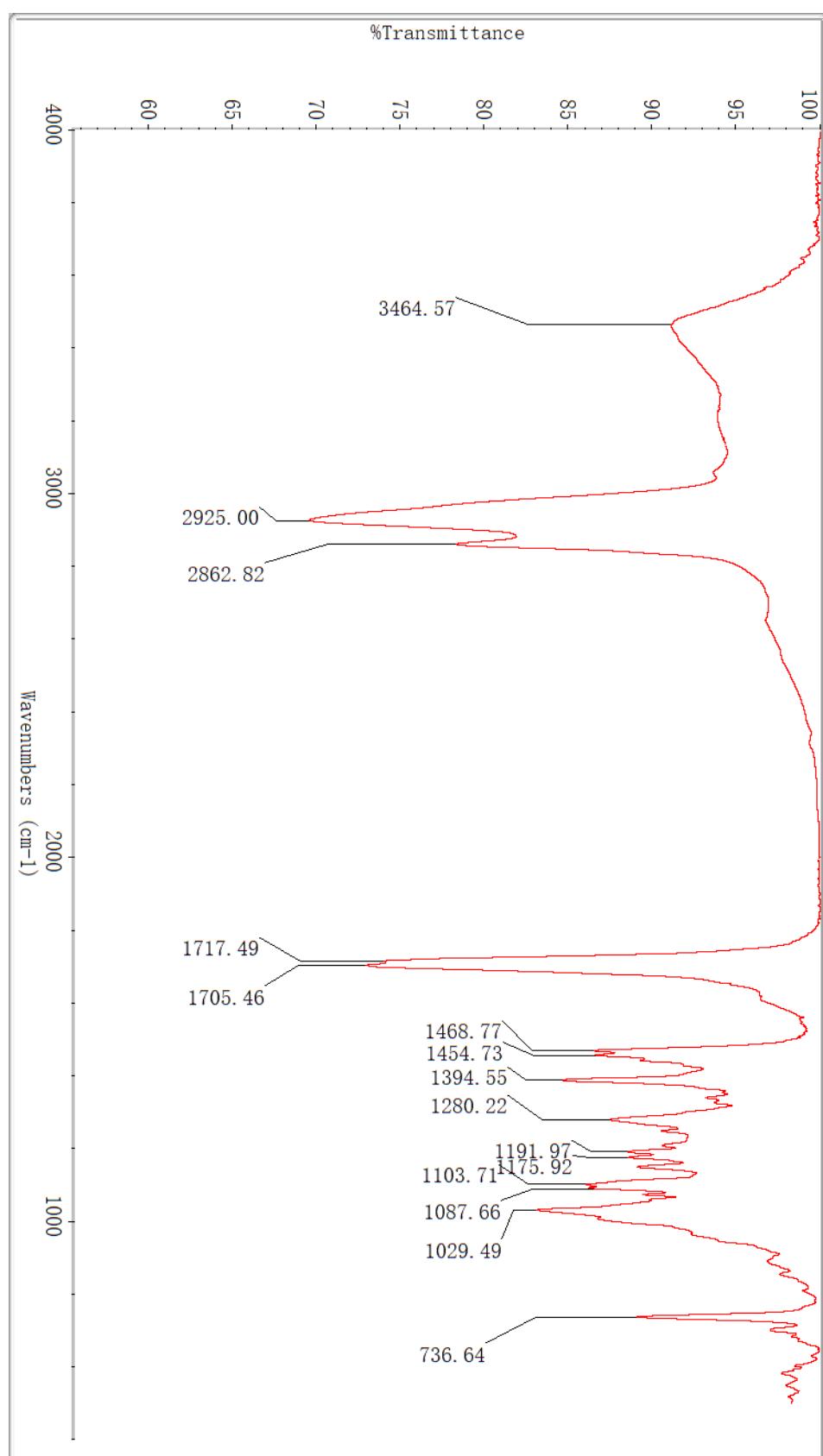


Figure S73. ^1H NMR spectrum of compound **9** in CDCl_3 .

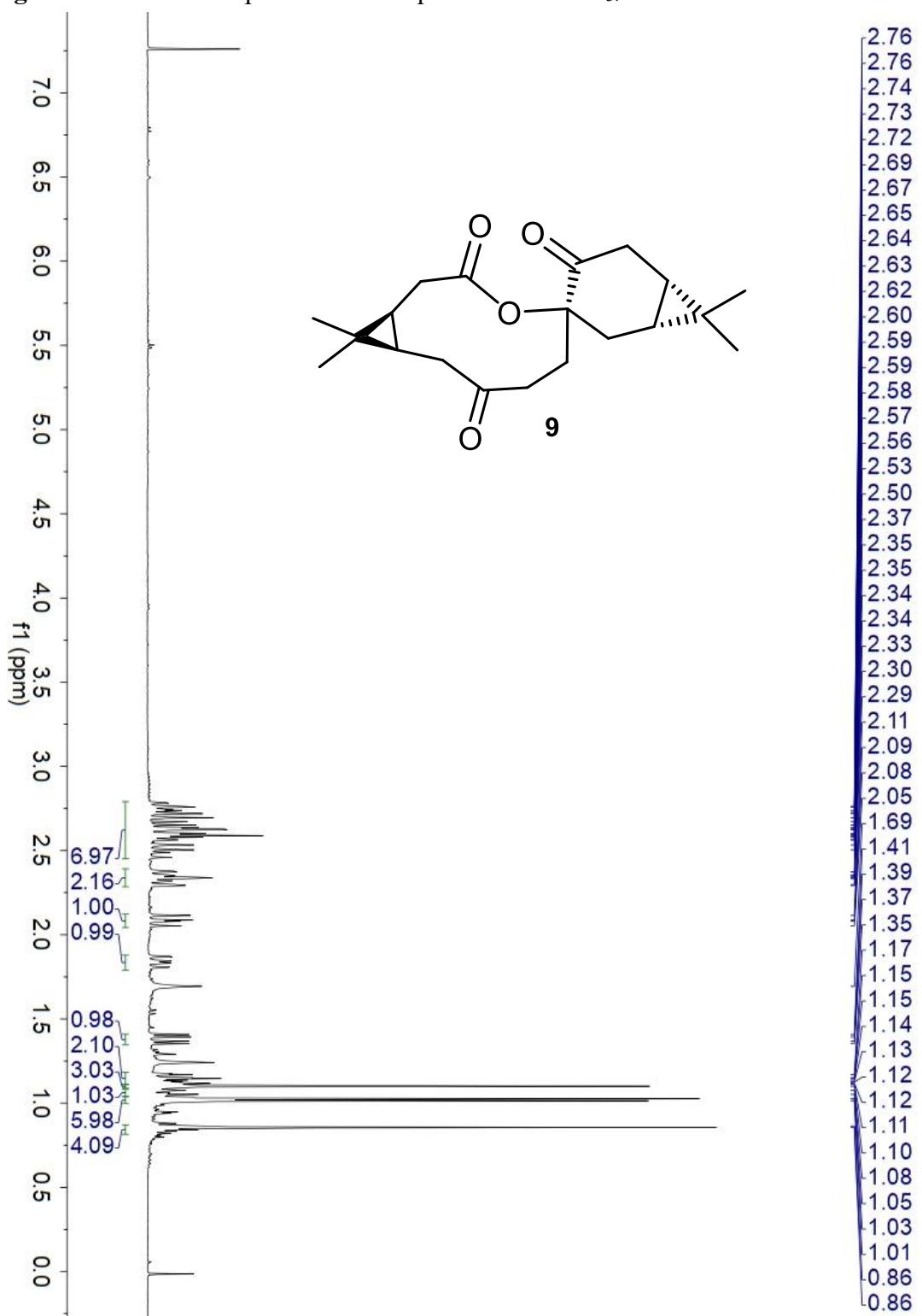


Figure S74. ^{13}C NMR spectrum of compound **9** in CDCl_3 .

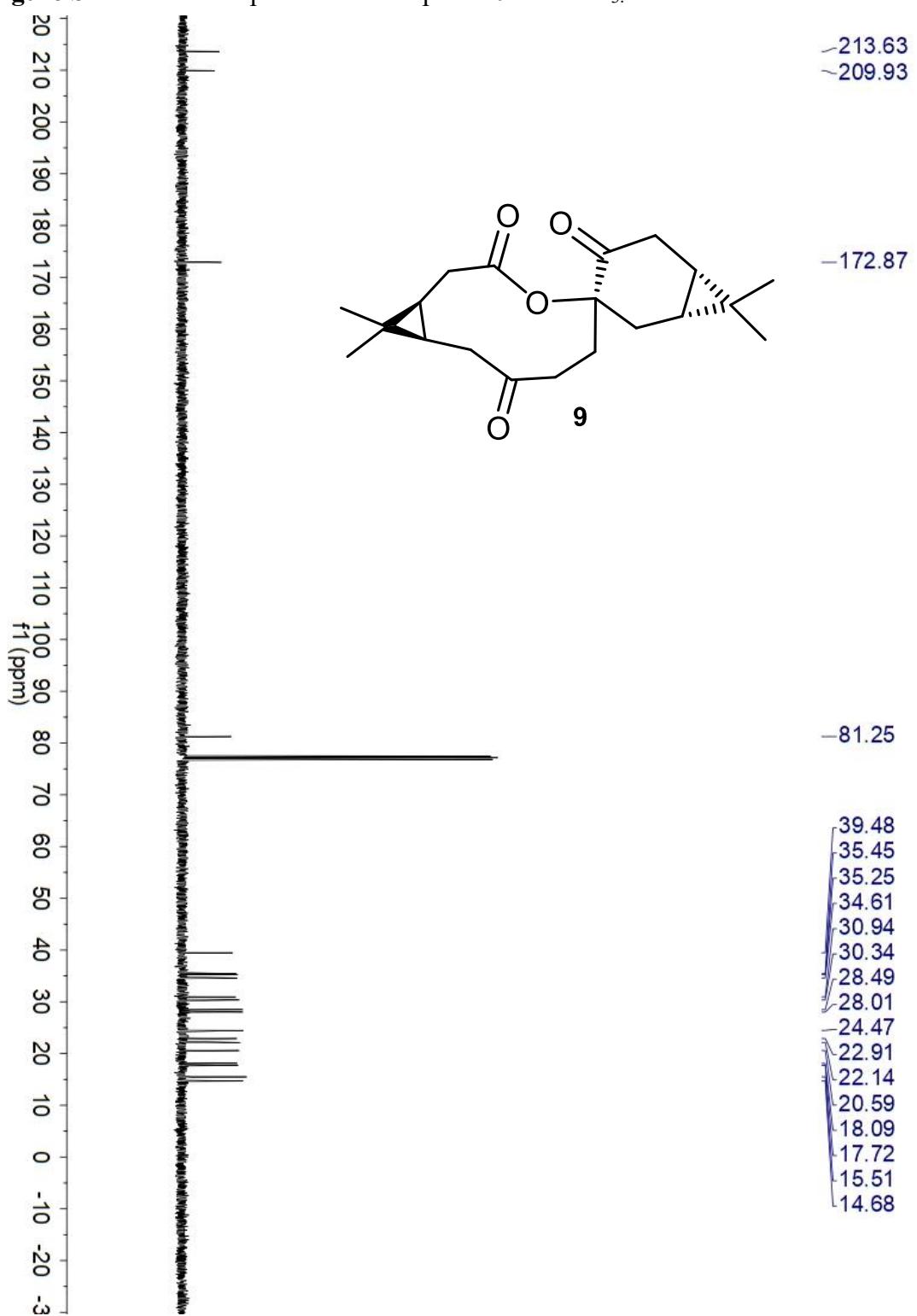


Figure S75. (+)-HRESIMS spectrum of compound 9.

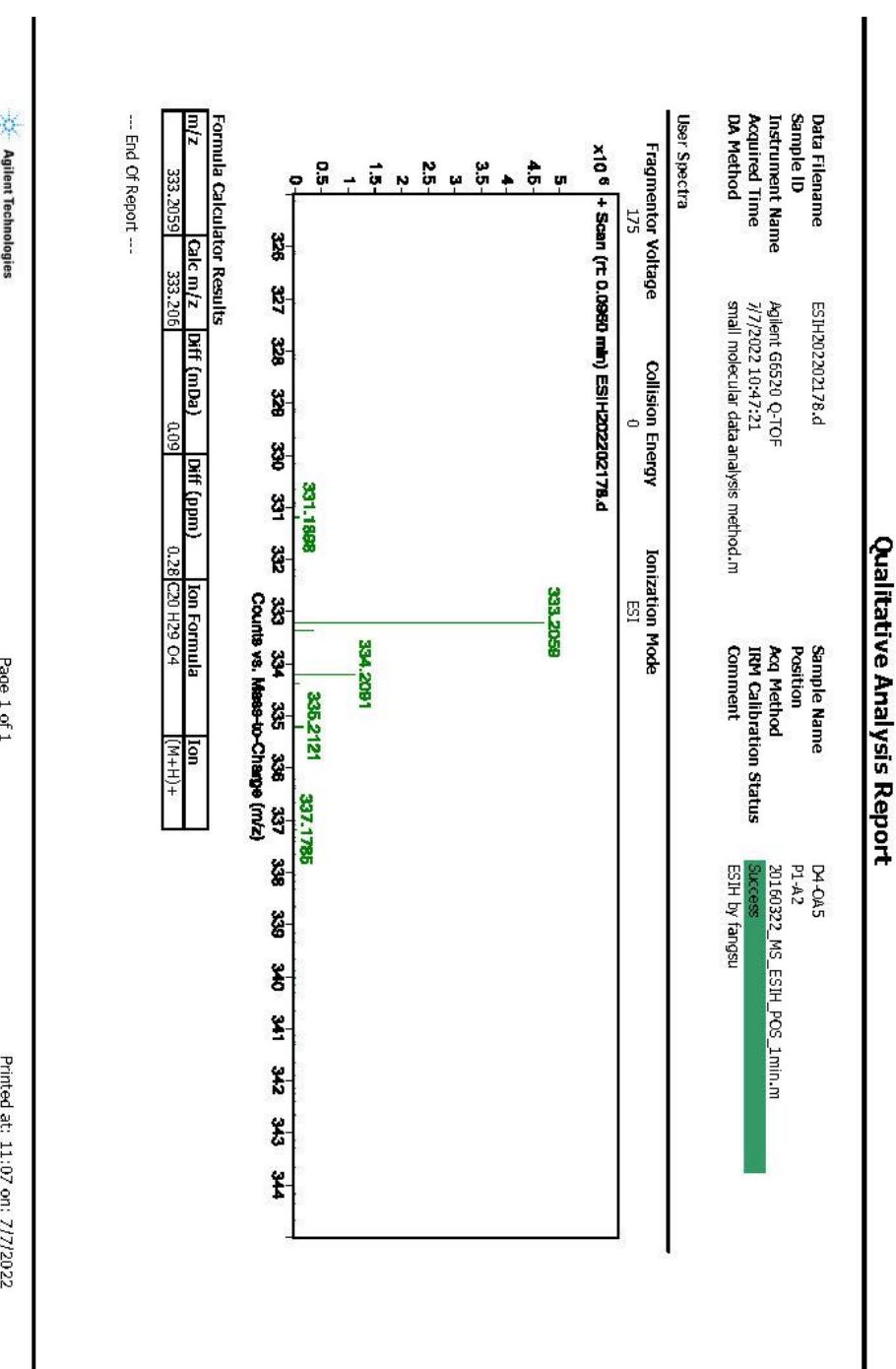


Figure S76. ^1H NMR spectrum of synthetic Koilodenoid A (**1**) in CDCl_3 .

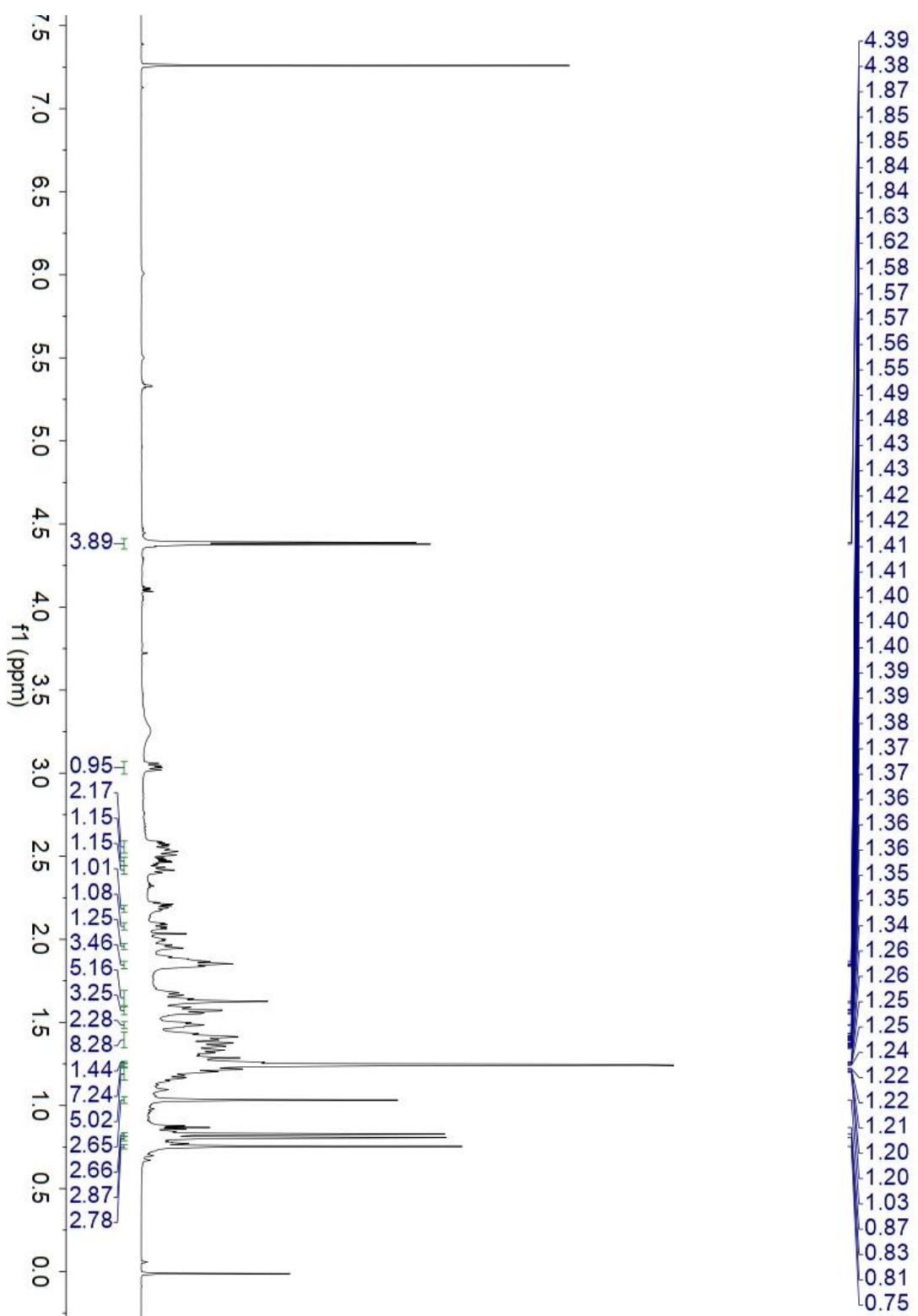


Figure S77. ^{13}C NMR spectrum of synthetic Koilodenoid A (**1**) in CDCl_3 .

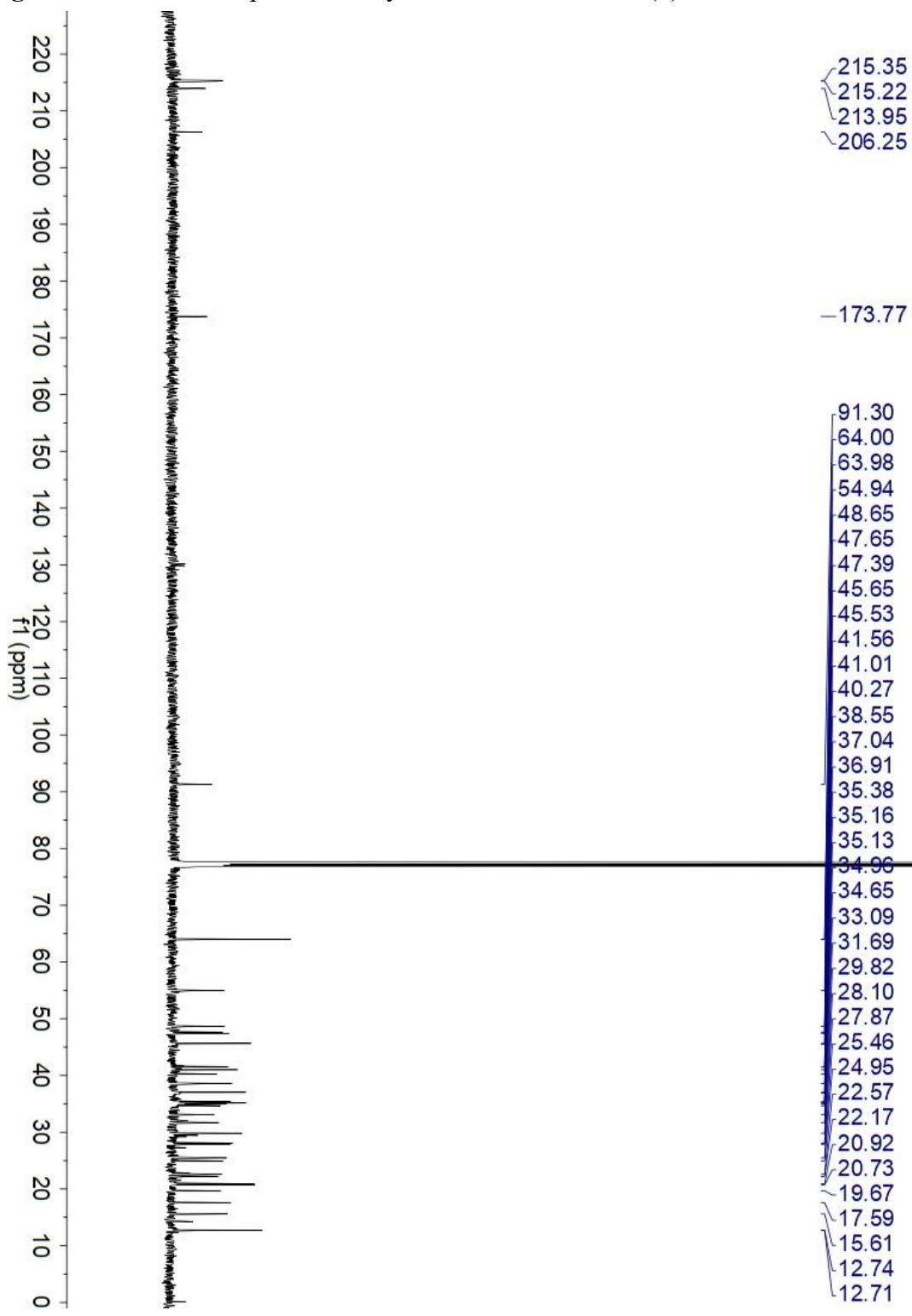


Figure S78. (+)-HRESIMS spectrum of synthetic Koilodenoid A (**1**).

