Supplementary Material

Quinoline Alkaloids with Anti-inflammatory Activity from *Zanthoxylum avicennae*

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‡ These authors contributed equally.

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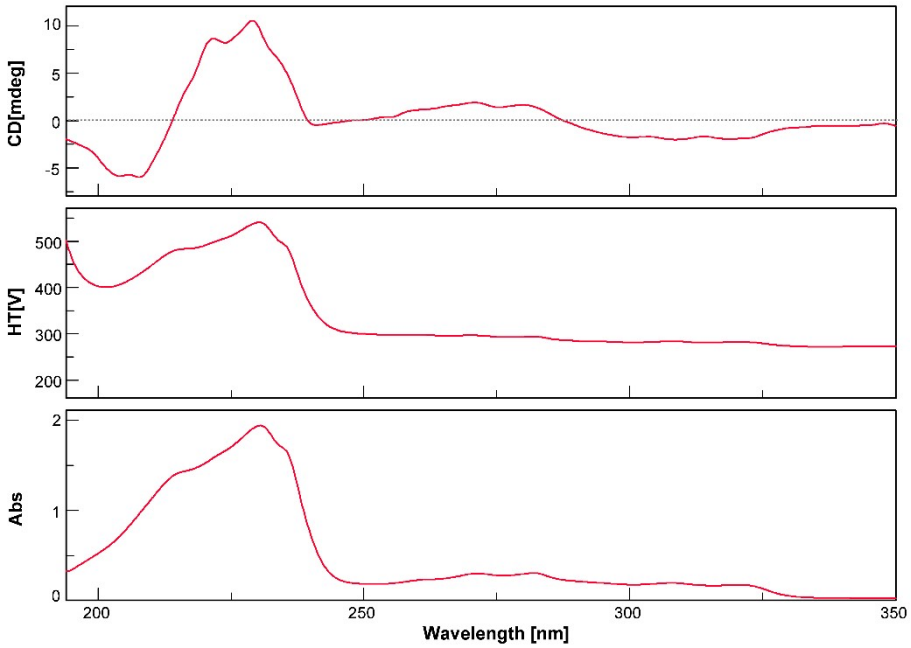
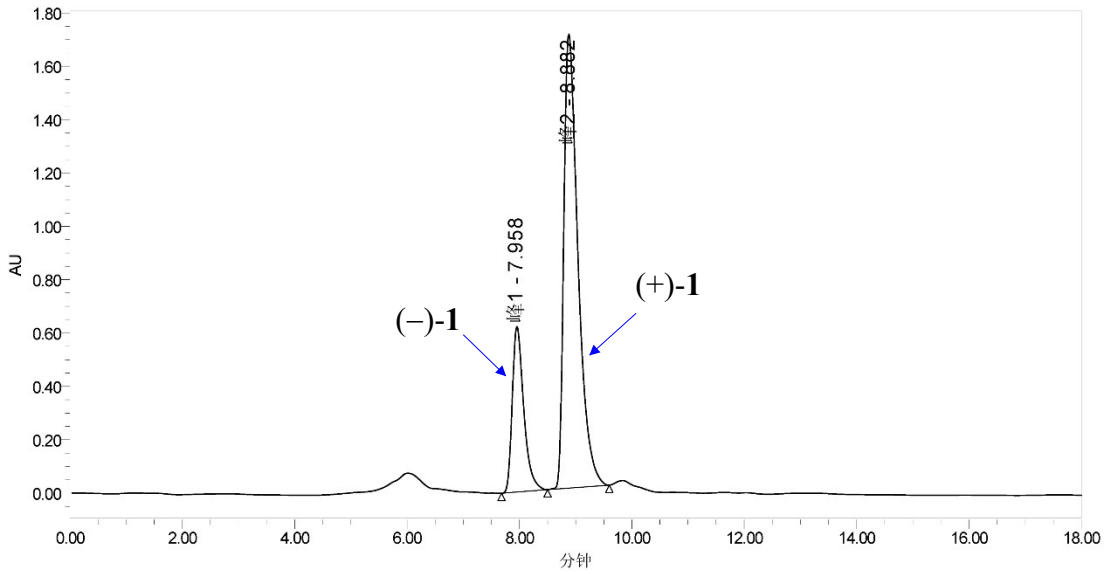


Fig. S1 ECD spectrum of compound **1**

Fig. S2 Chiral HPLC separation of compound **1**



	名称	保留时间 (分钟)	面积 (微伏*秒)	% 面积	高度 (微伏)	% 高度
1	峰1	7.958	8821112	22.84	621627	26.75
2	峰2	8.882	29806245	77.16	1701961	73.25

*Lux® Amylose-1 (250 mm ×10 mm, S-5 μm) LC column (UV = 254 nm)

Mobile Phase: n-hexane/isopropanol 7:3, v/v, 3ml.min^{-1}

(+)-**1**:(−)-**1** ≈ 3:1

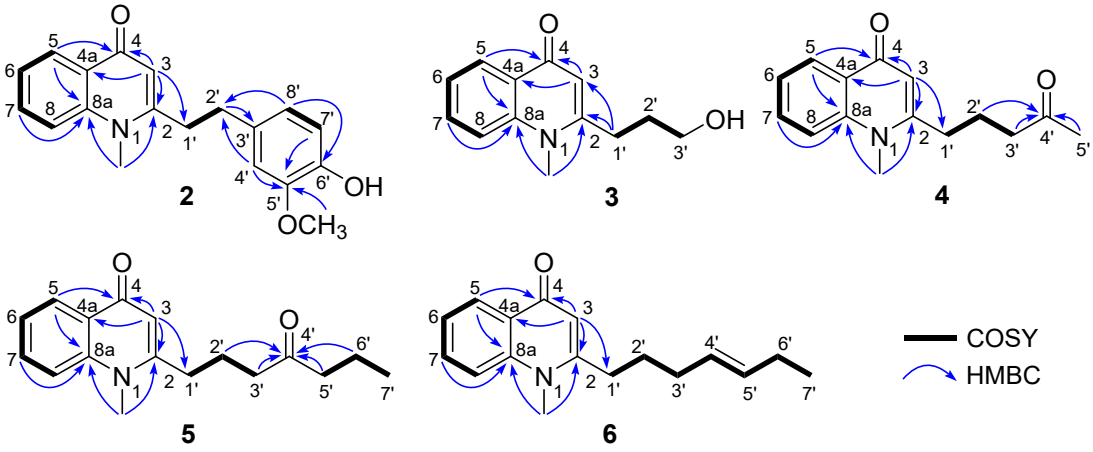
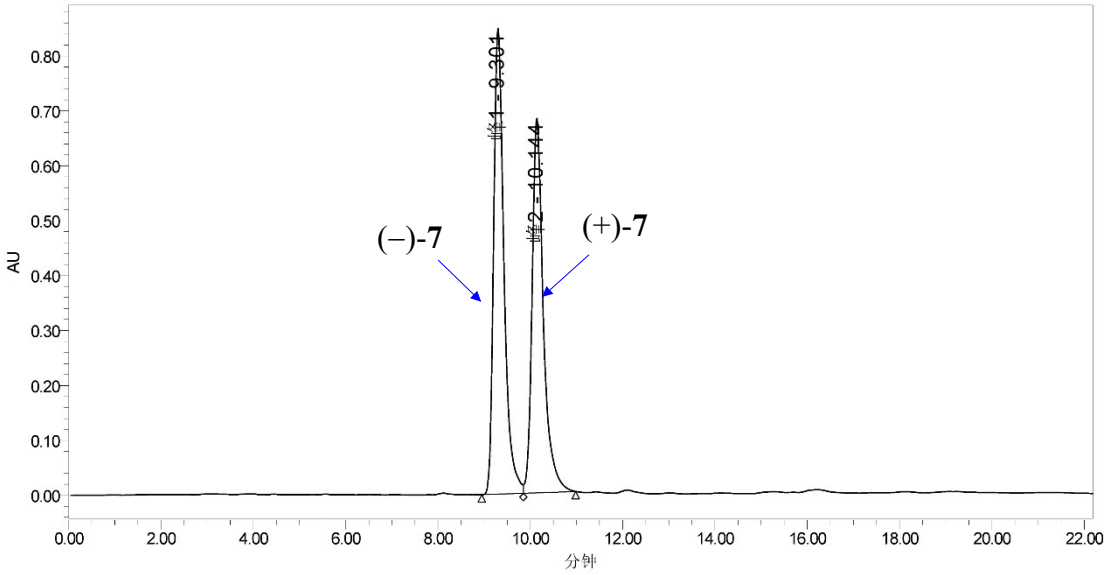


Fig. S3 Key ^{1}H-^{1}H COSY and HMBC correlations of **2**–**6**

Fig. S4 Chiral HPLC separation of compound **7**



	名称	保留时间 (分钟)	面积 (微伏*秒)	% 面积	高度 (微伏)	% 高度
1	峰1	9.301	13193340	53.41	847704	55.38
2	峰2	10.144	11507906	46.59	682928	44.62

*Lux® Amylose-1 (250 mm ×10 mm, S-5 μm) LC column (UV = 254 nm)

Mobile Phase: n-hexane/isopropanol 85:15, v/v, 3ml.min^{-1}

(+)-**7**:(–)-**7** ≈ 1:1

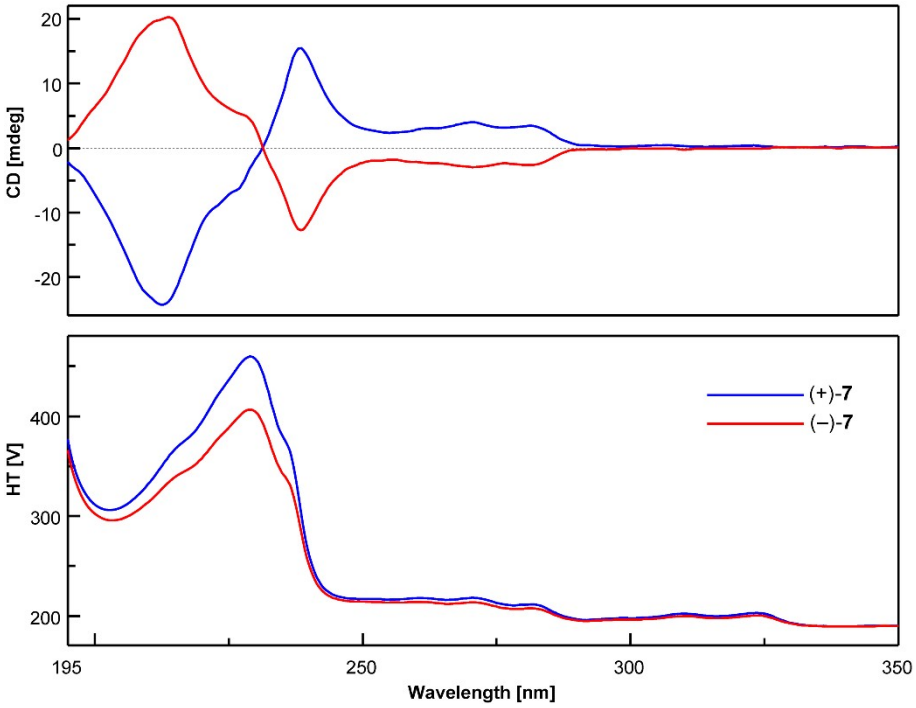
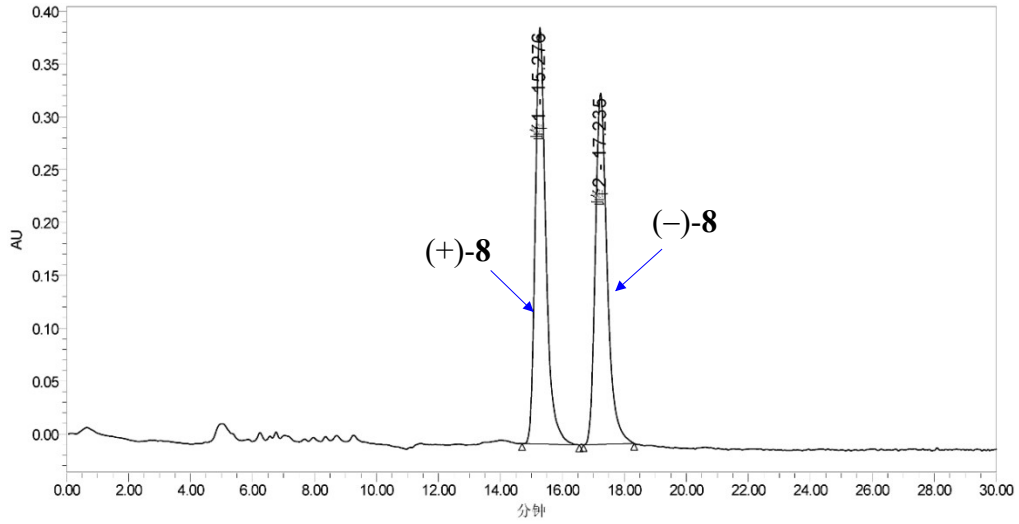


Fig. S5 ECD spectra of two enantiomers (+)-**7** and (–)-**7**

Fig. S6 Chiral HPLC separation of compound **8**



	名称	保留时间 (分钟)	面积 (微伏*秒)	% 面积	高度 (微伏)	% 高度
1	峰1	15.276	9366728	51.44	394037	54.27
2	峰2	17.235	8841126	48.56	332092	45.73

*Lux® Amylose-1 (250 mm ×10 mm, S-5 μm) LC column (UV = 254 nm)

Mobile Phase: n-hexane/isopropanol 7:3, v/v, 3ml.min^{-1}

(+)-**8**:(–)-**8** ≈ 1:1

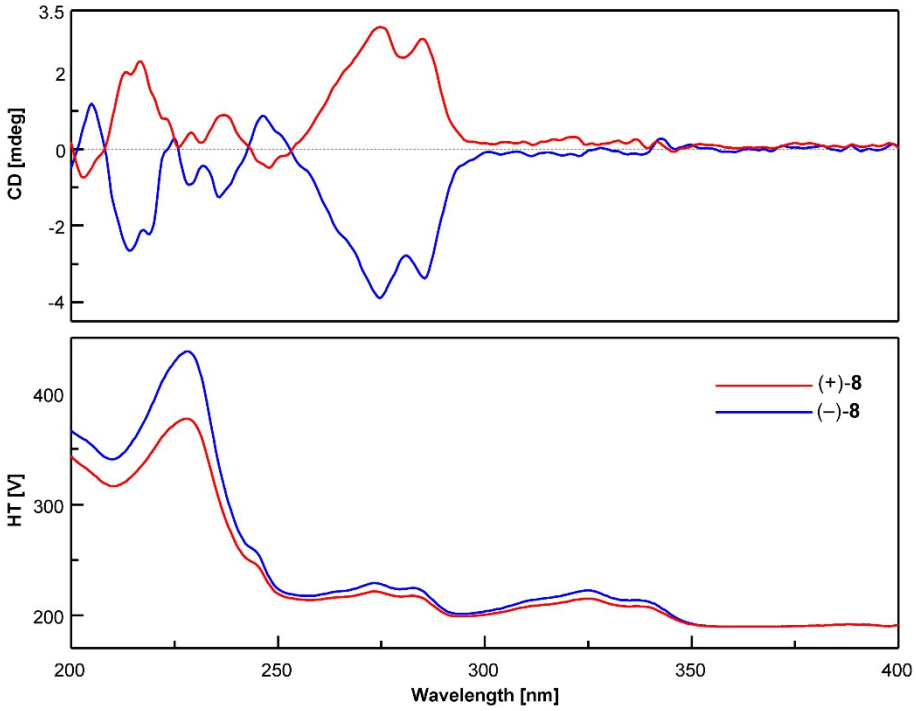


Fig. S7 ECD spectra of two enantiomers (+)-**8** and (–)-**8**.

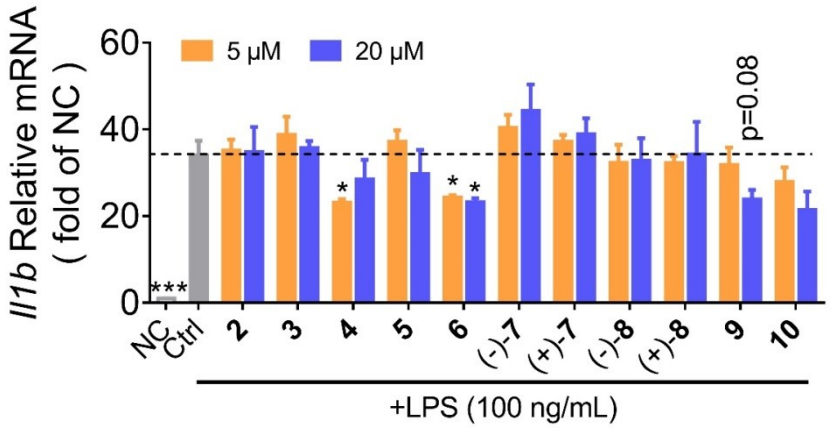


Fig. S8. The effect of Compound **2**–**10** on the gene expression level of IL-1β in RAW264.7 cells. The results are shown as the mean ± s.e.m., n=3. Data were analyzed by student's T-test (two-tailed). *P < 0.05 compared with the Ctrl group. The Ctrl (Control) group means RAW264.7 macrophages were treated with LPS (100 ng/mL) but without compounds.

Table S1 ^{1}H and ^{13}C NMR data for **5** and **6** in $CDCl_3$ (δ in ppm and J in Hz)

	5[a]		**6**[b]	
No.	δ_H	δ_C	δ_H	δ_C
2		154.1		154.7
3	6.20 s	111.6	6.25 s	111.5
4		178.0		178.0
4a		126.7		126.8
5	8.44 dd (7.6, 1.5)	126.8	8.46 dd (7.6, 1.7)	126.9
6	7.38 t (7.6)	123.6	7.38 t (7.6)	123.5
7	7.67 ddd (8.6, 7.6, 1.5)	132.3	7.67 ddd (8.7, 7.6, 1.7)	132.2
8	7.54 d (8.6)	115.6	7.51 (8.7)	115.4
8a		142.2		142.1
1'	2.73 m (2H)	34.4	2.72 m (2H)	34.1
2'	1.96 m (2H)	22.4	1.76 m (2H)	28.5
3'	2.58 t (6.3) (2H)	41.2	2.14 m (2H)	32.0
4'		210.4	5.40 dt (14.5, 6.8)	127.5
5'	2.39 t (7.3) (2H)	45.1	5.54 dt (14.5, 6.4)	134.1
6'	1.59 m (2H)	17.4	2.02 m (2H)	25.7
7'	0.91 t (7.3)	13.9	0.98 t (7.5)	14.1
N-Me	3.84 s	34.5	3.74 s	34.3

[a] NMR data was recorded at 400 MHz (^{1}H) and 125 MHz (^{13}C). [b] NMR data was recorded at 600 MHz (^{1}H) and 150 MHz (^{13}C).

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

Empirical formula	$C_{16}H_{19}NO_5$[a]	
Formula weight	305.32	
Temperature	170.02 K	
Wavelength	1.34139 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 8.5101(3) Å	α = 77.6570(10)°.
	b = 9.0807(3) Å	β = 83.0550(10)°.
	c = 9.5903(3) Å	γ = 88.4020(10)°.
Volume	718.67(4) $Å^3$	
Z	2	
Density (calculated)	1.411 Mg/m^3	
Absorption coefficient	0.561 mm^{-1}	
F(000)	324	
Crystal size	0.12 x 0.1 x 0.08 mm^3	
Theta range for data collection	4.134 to 55.059°.	
Index ranges	-10<=h<=10, -11<=k<=11, -11<=l<=11	
Reflections collected	15698	
Independent reflections	2729 [R(int) = 0.0540]	
Completeness to theta = 53.594°	99.5 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7508 and 0.5779	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2729 / 0 / 207	
Goodness-of-fit on F^2	1.046	
Final R indices [I>2sigma(I)]	R1 = 0.0391, wR2 = 0.1024	
R indices (all data)	R1 = 0.0425, wR2 = 0.1055	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.253 and -0.251 e.$Å^{-3}$	
CCDC number	2160133	

[a] Crystals of compound **1** were obtained from MeOH.

Table S3 X-ray crystallographic data for compound (–)-**1**

Empirical formula	$C_{15}H_{17}NO_5$[a]	
Formula weight	291.29	
Temperature	170.04 K	
Wavelength	1.34139 Å	
Crystal system	Monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 9.7252(4) Å	α = 90°
	b = 7.2357(3) Å	β = 98.737(2)°
	c = 10.0005(4) Å	γ = 90°
Volume	695.56(5) $Å^3$	
Z	2	
Density (calculated)	1.391 Mg/m^3	
Absorption coefficient	0.563 mm^{-1}	
F(000)	308	
Crystal size	0.12 x 0.08 x 0.06 mm^3	
Theta range for data collection	5.996 to 55.068°.	
Index ranges	-11<=h<=11, -8<=k<=8, -12<=l<=12	
Reflections collected	9299	
Independent reflections	2585 [R(int) = 0.0640]	
Completeness to theta = 53.594°	99.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7508 and 0.5615	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2585 / 1 / 201	
Goodness-of-fit on F^2	1.051	
Final R indices [I>2sigma(I)]	R1 = 0.0351, wR2 = 0.0812	
R indices (all data)	R1 = 0.0401, wR2 = 0.0869	
Absolute structure parameter	0.11(16)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.159 and -0.178 e.$Å^{-3}$	
CCDC number	2160134	

[a] Crystals of compound (–)-**1** were obtained from MeOH.

Table S4 X-ray crystallographic data for compound (+)-**7**

Empirical formula	$C_{15}H_{17}NO_4$
Formula weight	275.29
Temperature	169.99 K
Wavelength	1.34139 Å
Crystal system	Monoclinic
Space group	P 1 21 1
Unit cell dimensions	a = 8.5948(3) Å α = 90°. b = 8.5216(3) Å β = 100.0350(10)°. c = 18.7212(6) Å γ = 90°.
Volume	1350.19(8) $Å^3$
Z	4
Density (calculated)	1.354 Mg/m^3
Absorption coefficient	0.522 mm^{-1}
F(000)	584
Crystal size	0.12 x 0.1 x 0.08 mm^3
Theta range for data collection	4.545 to 54.944°.
Index ranges	-10<=h<=10, -10<=k<=10, -22<=l<=22
Reflections collected	14913
Independent reflections	5038 [R(int) = 0.0437]
Completeness to theta = 53.594°	98.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7508 and 0.6254
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5038 / 1 / 371
Goodness-of-fit on F^2	1.065
Final R indices [I>2sigma(I)]	R1 = 0.0331, wR2 = 0.0843
R indices (all data)	R1 = 0.0361, wR2 = 0.0874
Absolute structure parameter	0.02(9)
Extinction coefficient	n/a
Largest diff. peak and hole	0.192 and -0.173 e.$Å^{-3}$
CCDC number	2160135

[a] Crystals of compound (+)-**7** were obtained from MeOH.

Table S5 Primer sequences used in RT-PCR analysis

Genes	Forward primer	Reverse primer
β-actin	TGGTACCACAGGCATTGTGAT	TGATGTCACGCACGATTTCCCT
Il1b	GCAACTGTTCCTGAACTCAACT	ATCTTTTGGGGTCCGTCAACT
Il6	TAGTCCTTCCTACCCCAATTTCC	TTGGTCCTTAGCCACTCCTTC

Fig. S9 ^{1}H NMR spectrum of **1** in $CDCl_3$

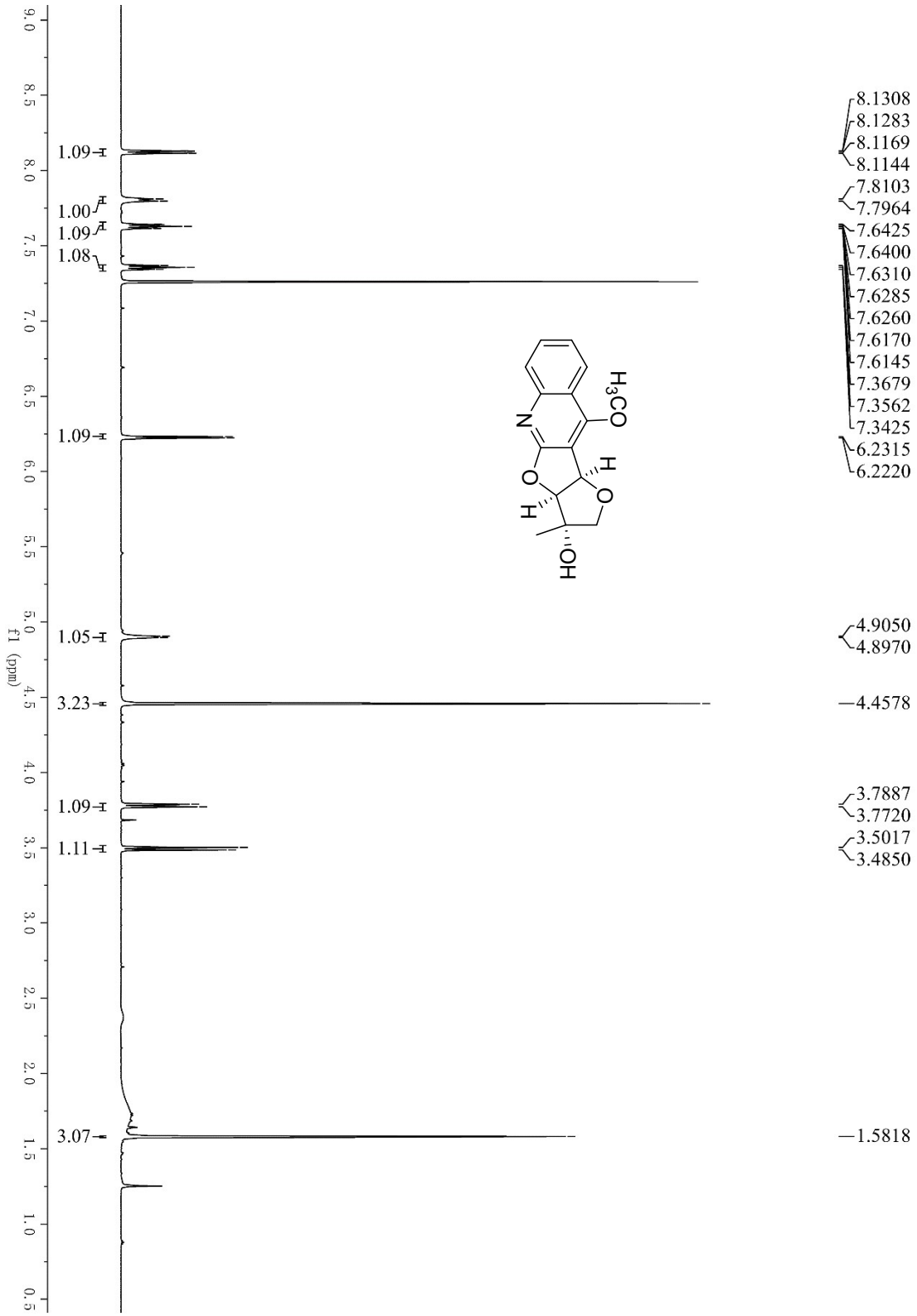


Fig. S10 ^{13}C NMR spectrum of **1** in $CDCl_3$

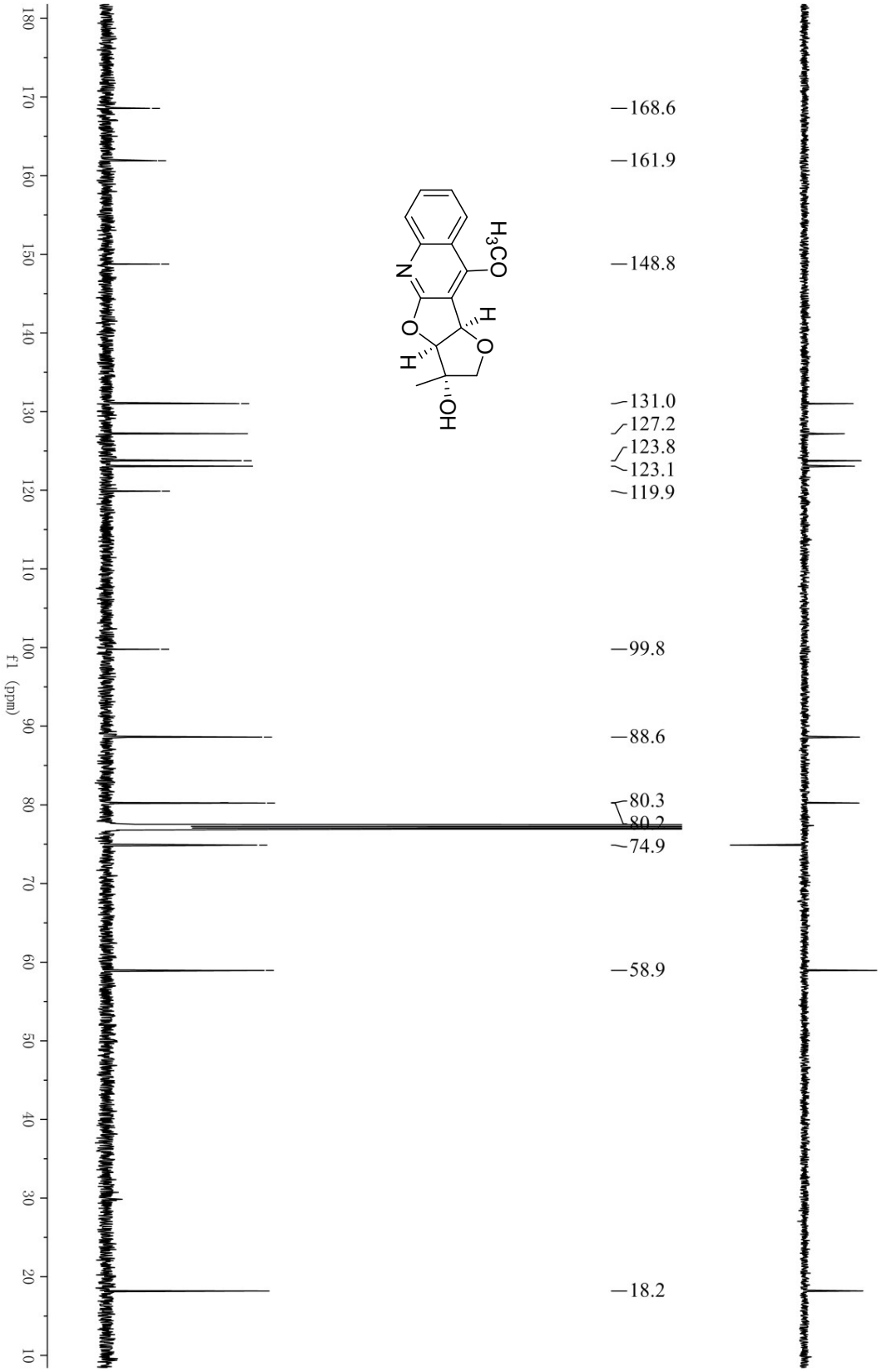


Fig. S11 HSQC spectrum of **1**

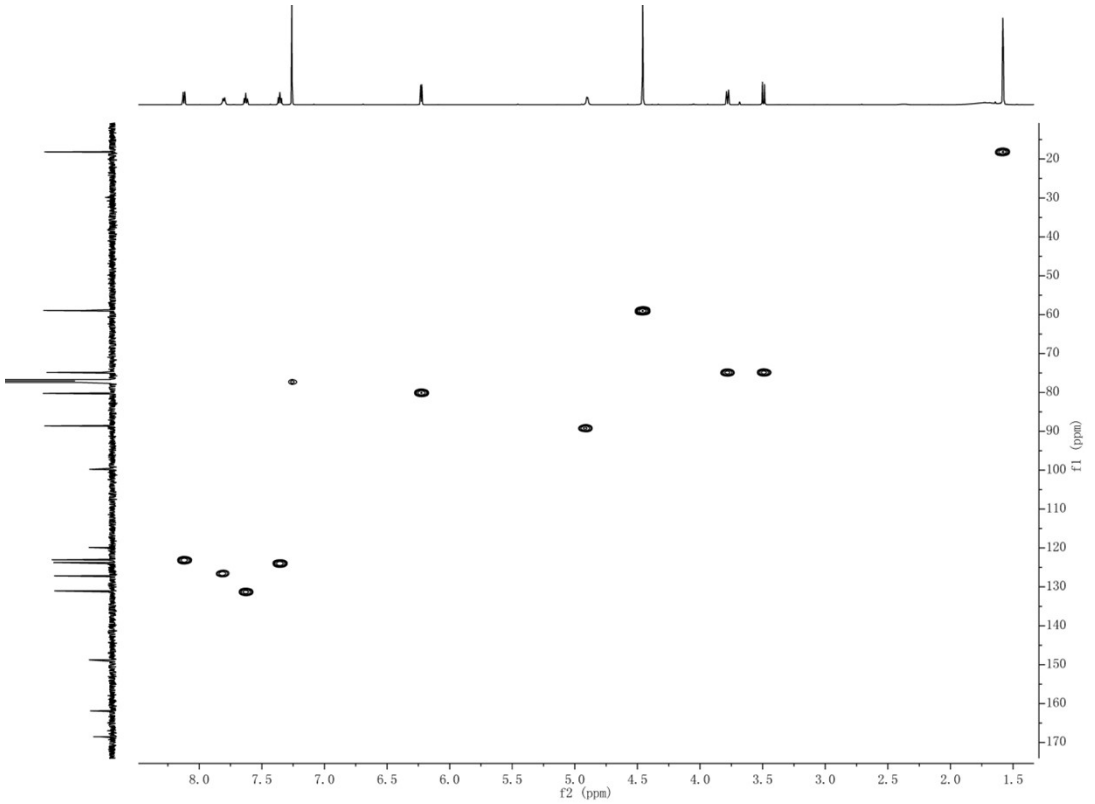


Fig. S12 HMBC spectrum of **1**

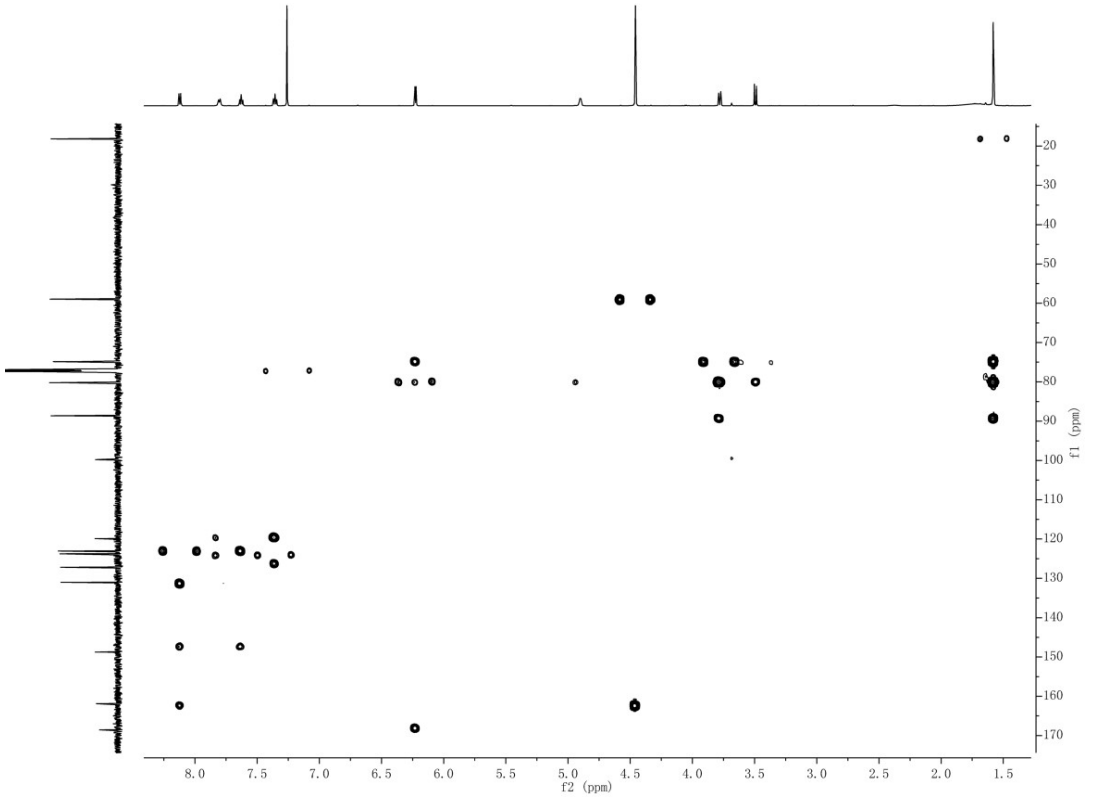


Fig. S13 COSY spectrum of **1**

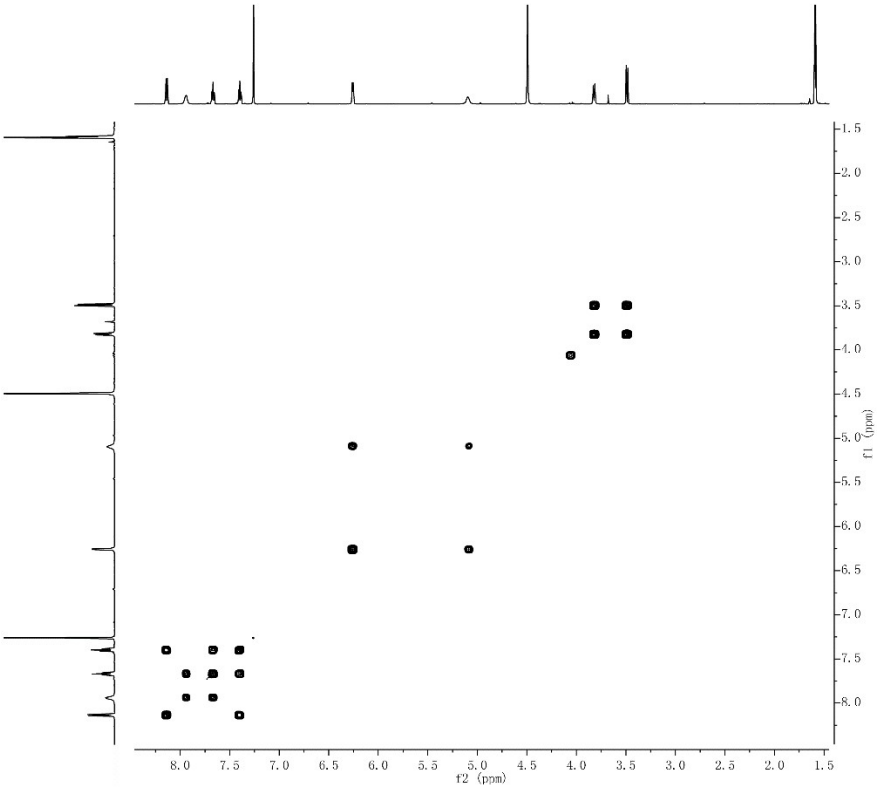


Fig. S14 ROESY spectrum of **1**

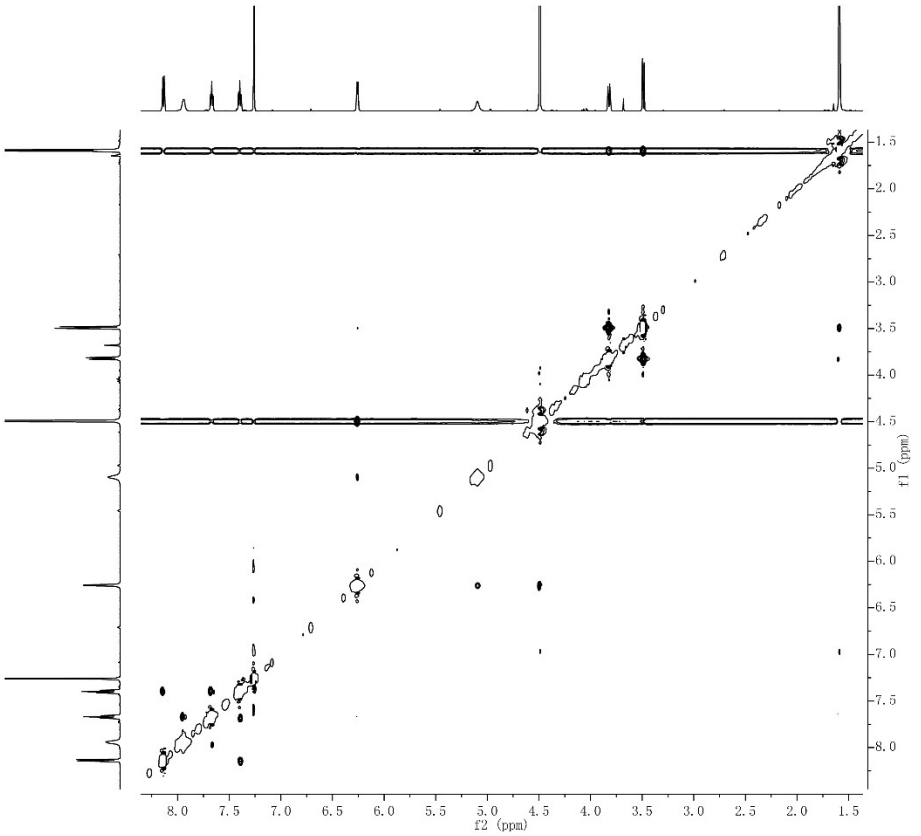


Fig. S15 ESI-MS spectrum of **1**

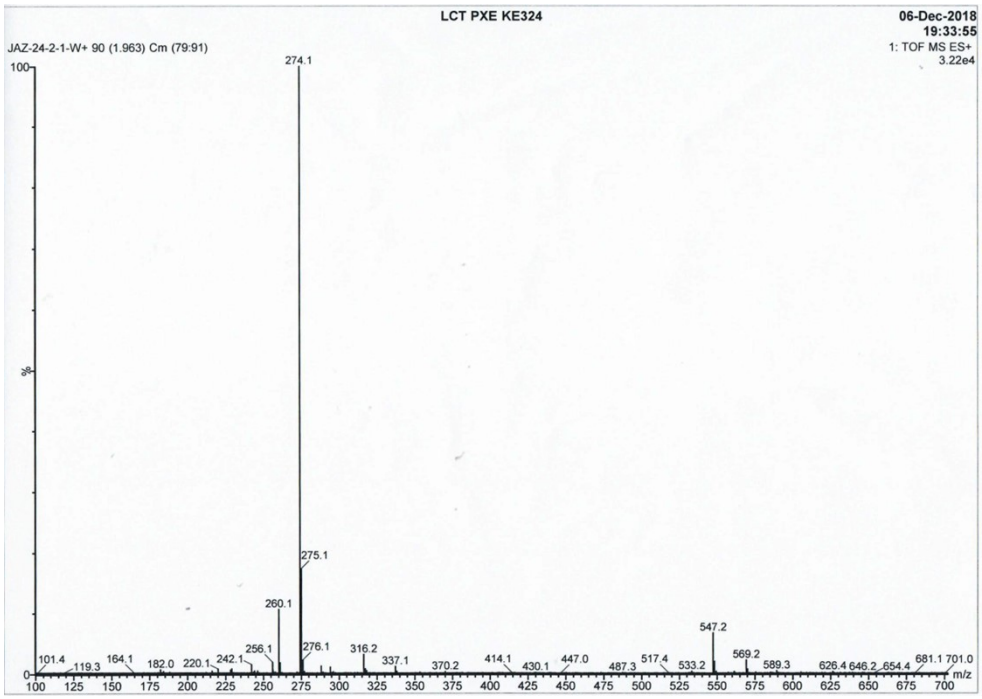


Fig. S16 HRESI-MS spectrum of **1**

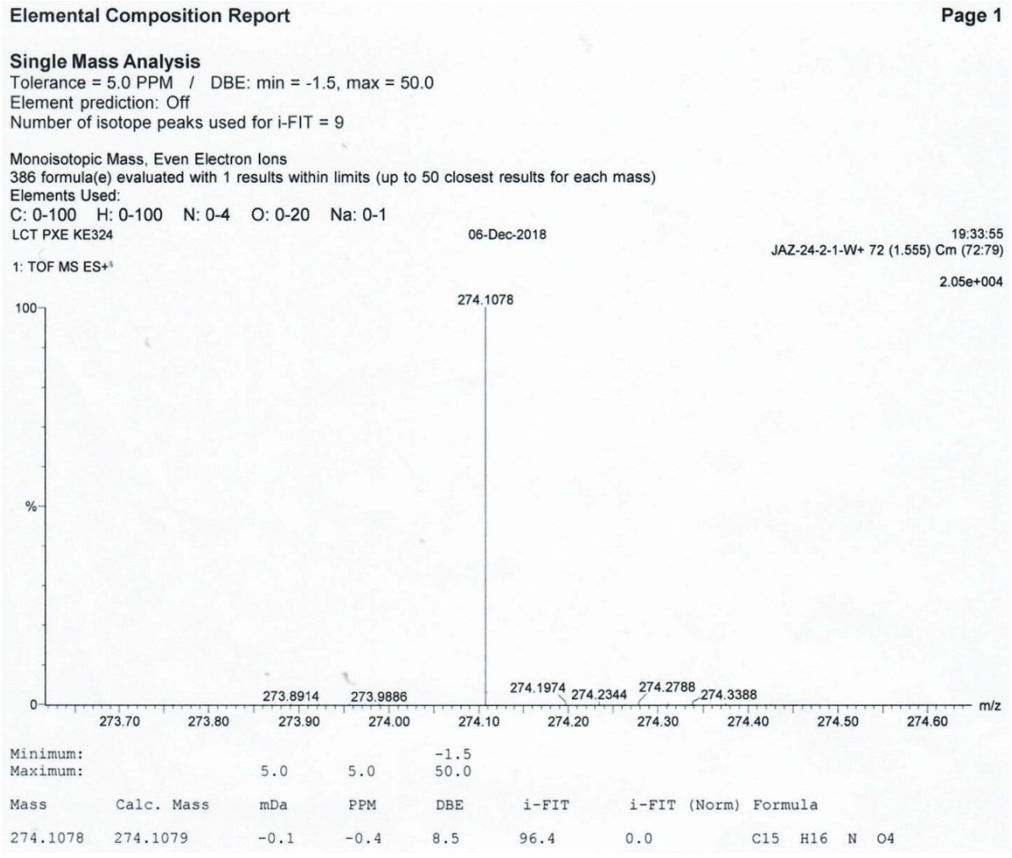


Fig. S17 IR spectrum of **1**

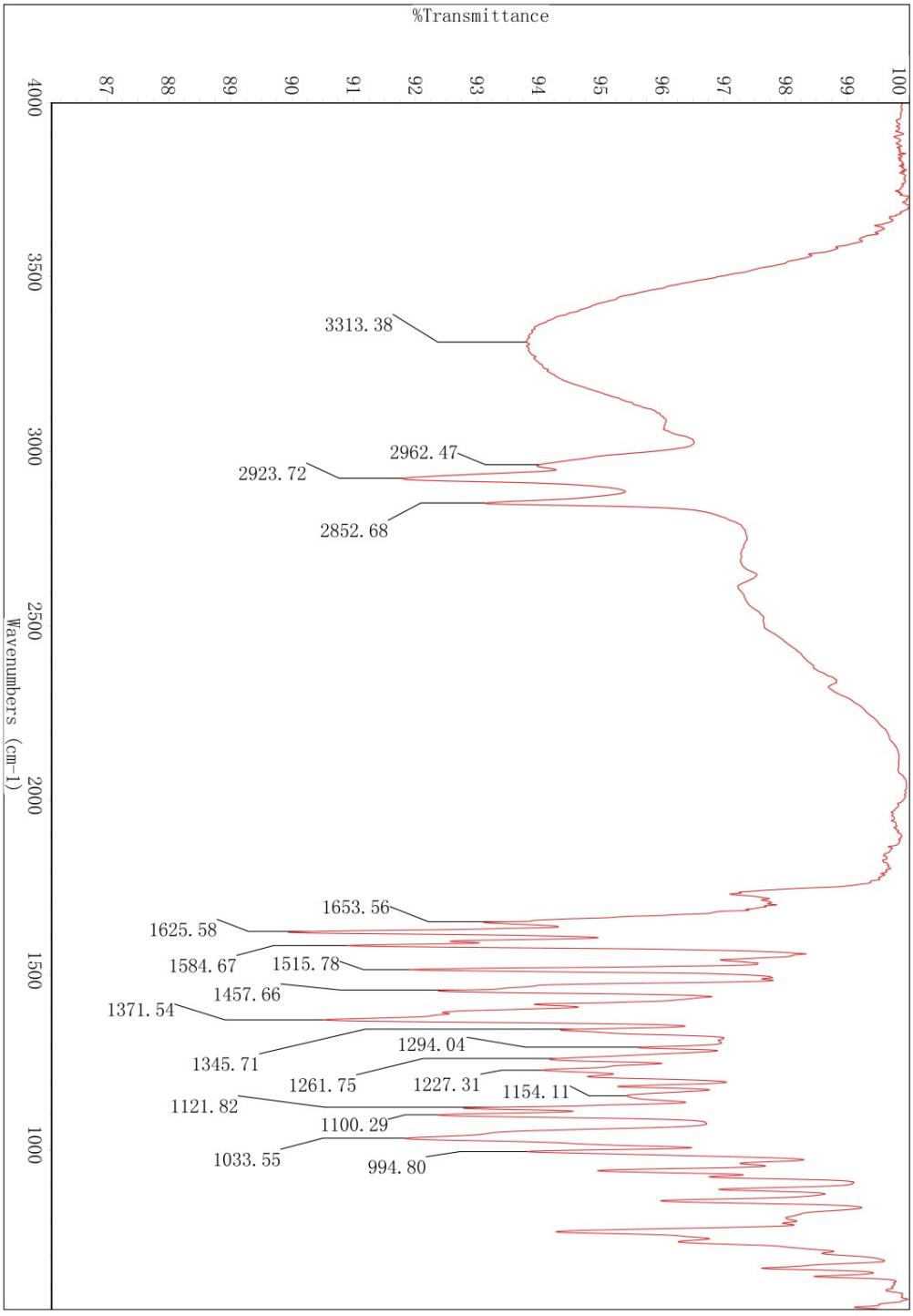


Fig. S18 ^{1}H NMR spectrum of **2** in $CDCl_3$

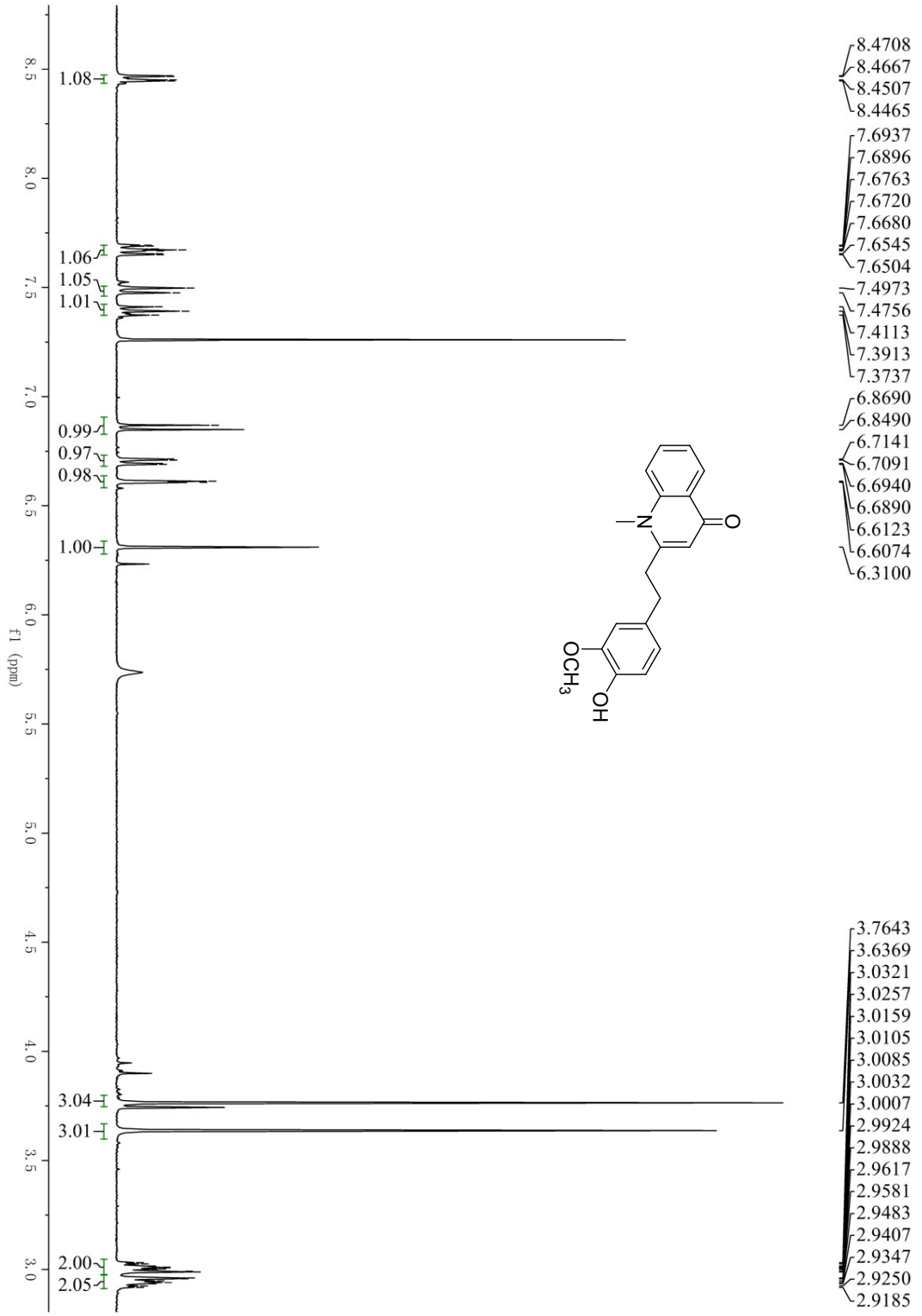


Fig. S19 ^{13}C NMR spectrum of **2** in $CDCl_3$

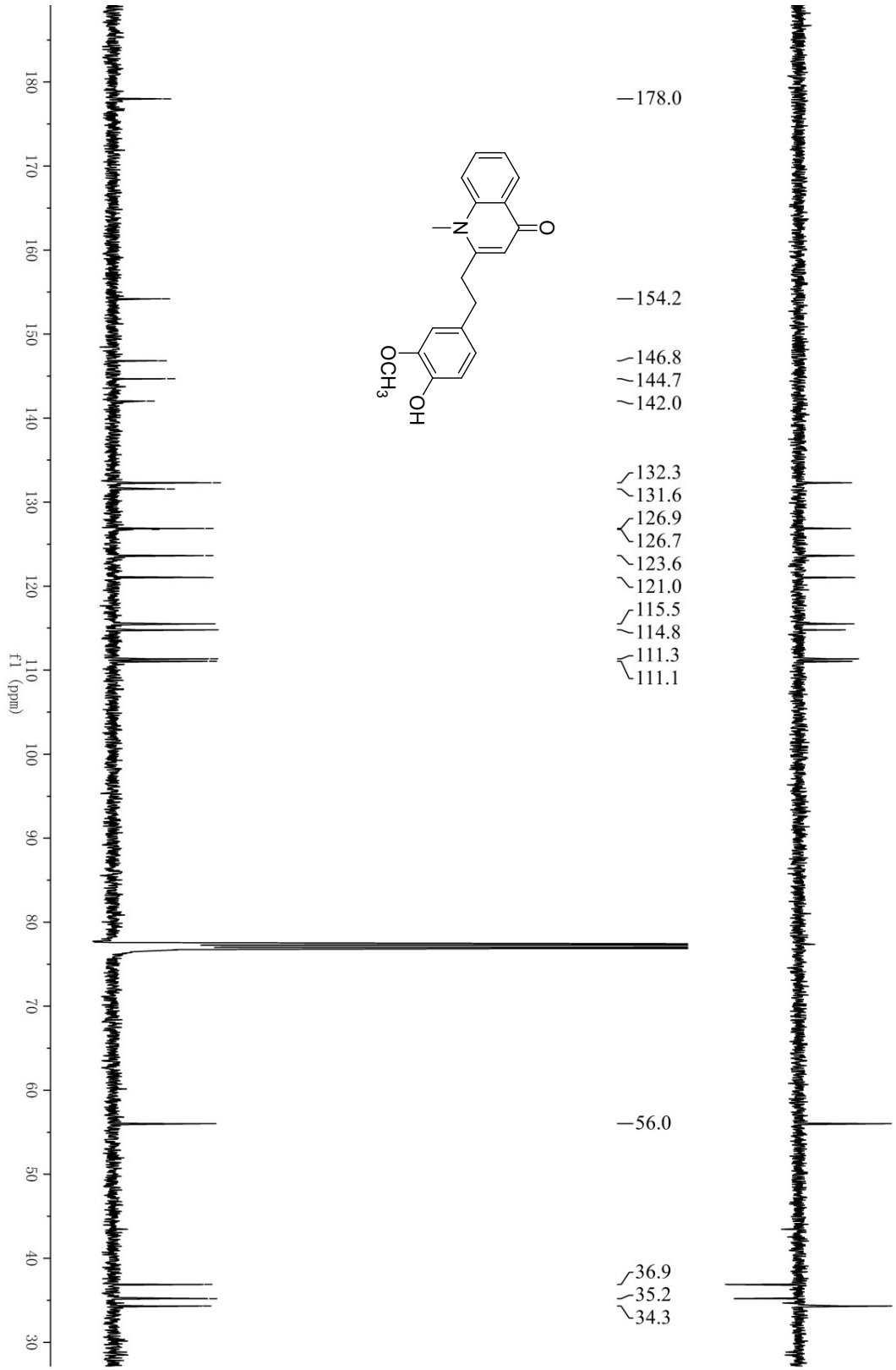


Fig. S20 HSQC spectrum of **2**

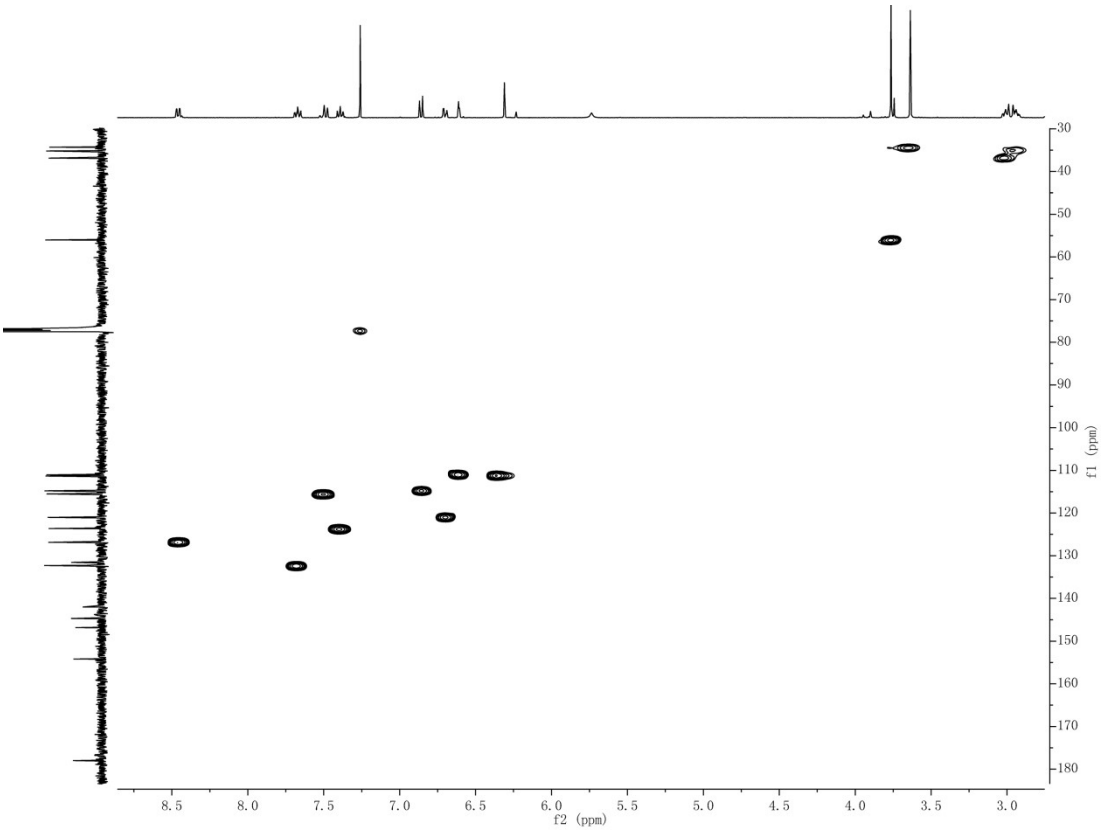


Fig. S21 HMBC spectrum of **2**

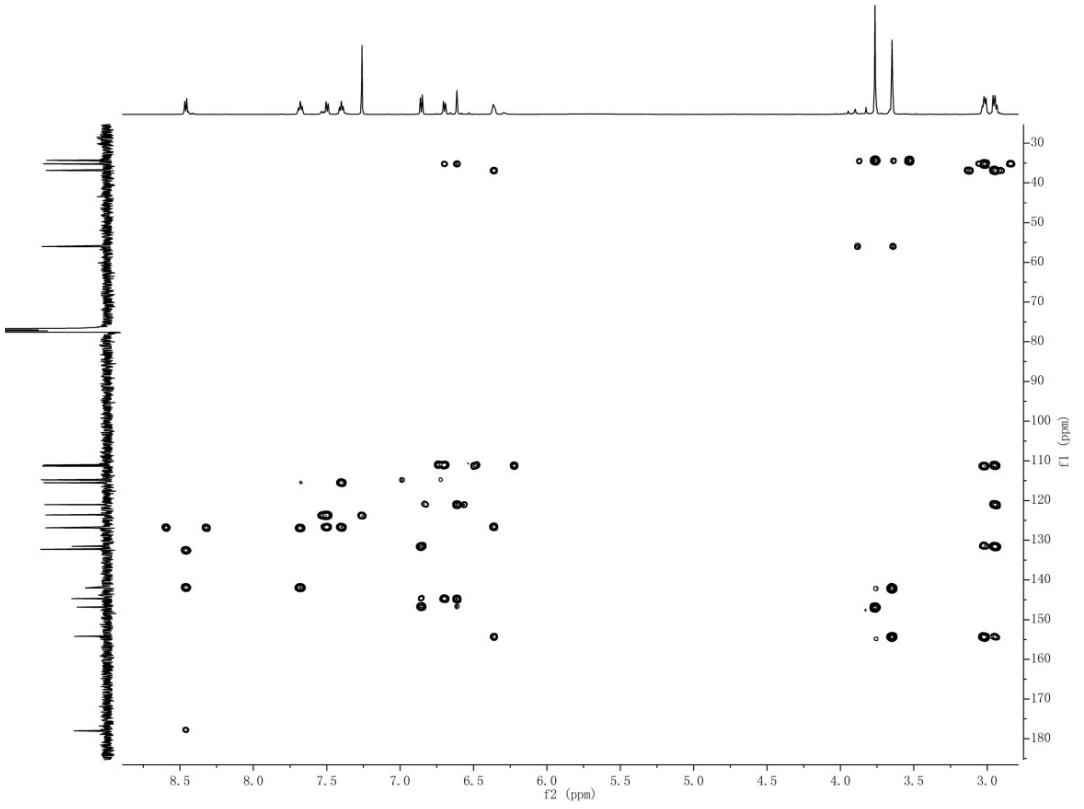


Fig. S22 COSY spectrum of **2**

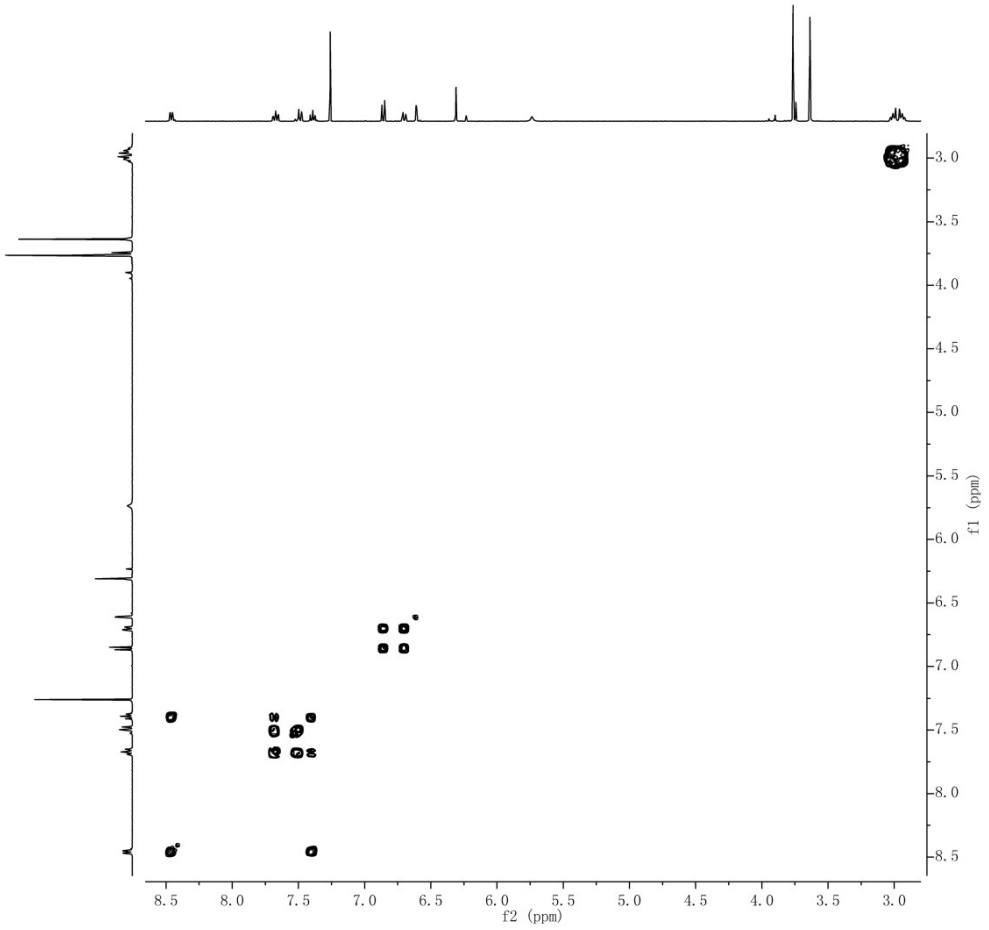


Fig. S23 ESI-MS spectrum of **2**

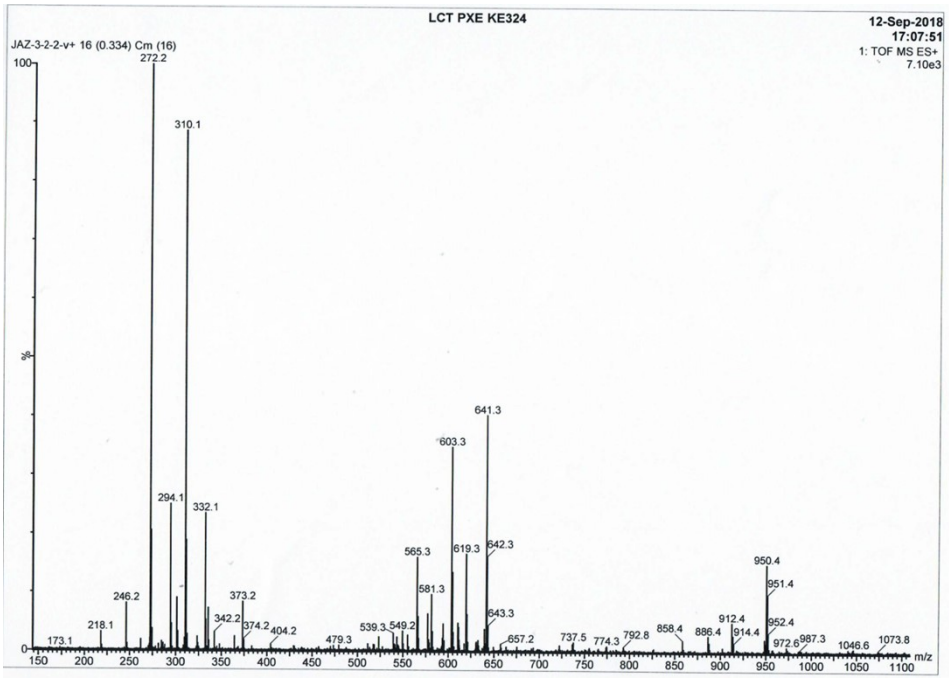


Fig. S24 HRESI-MS spectrum of **2**

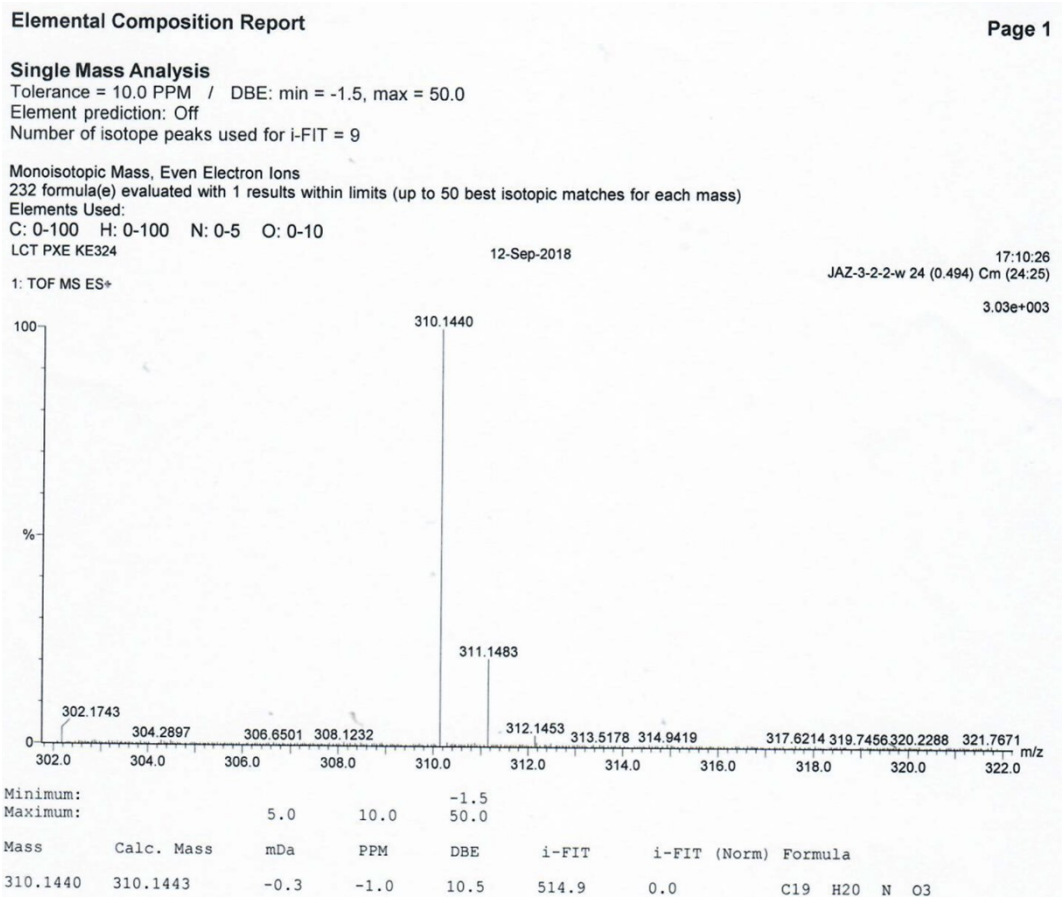


Fig. S25 IR spectrum of **2**

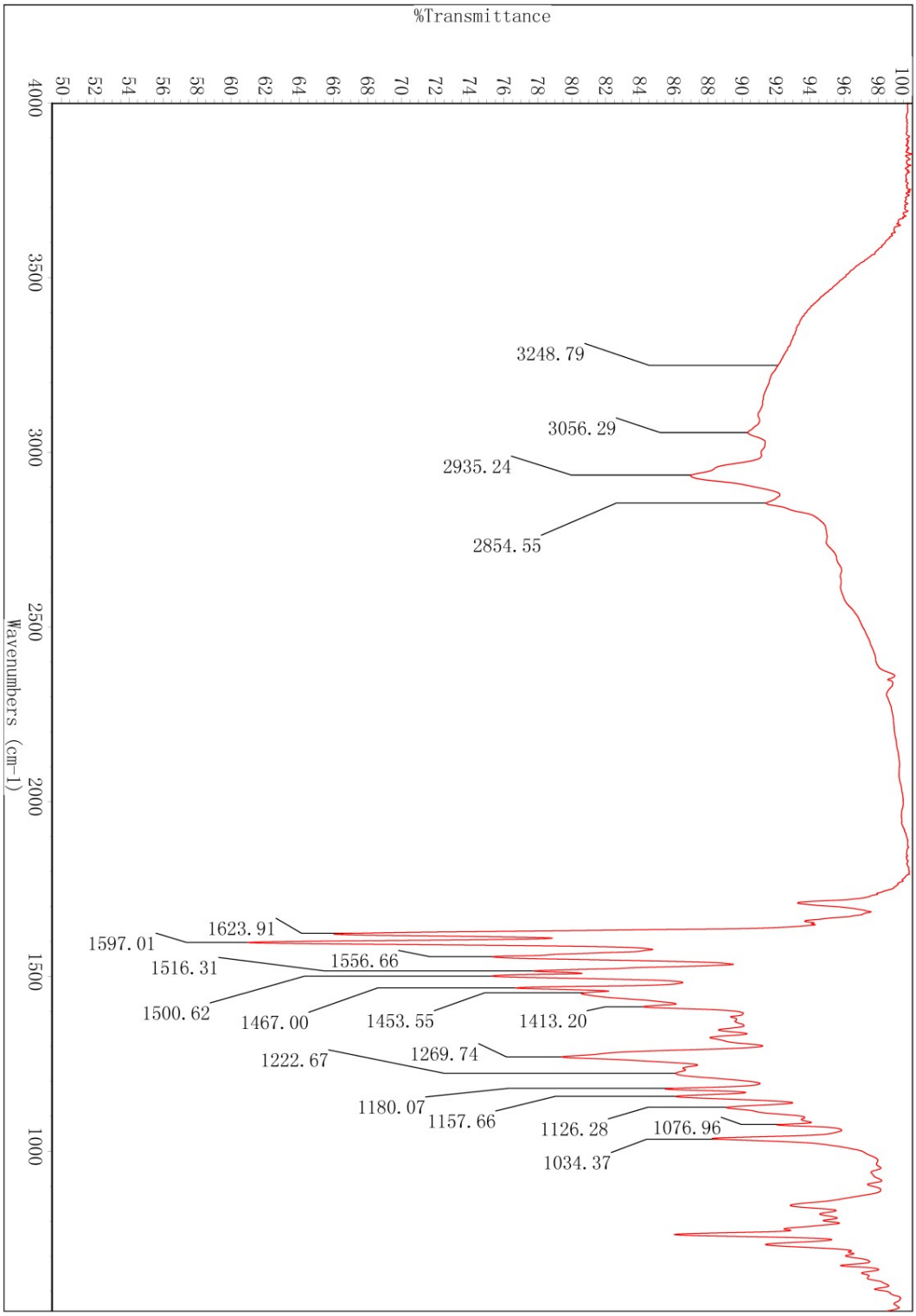


Fig. S26 ^{1}H NMR spectrum of **3** in $CDCl_3$

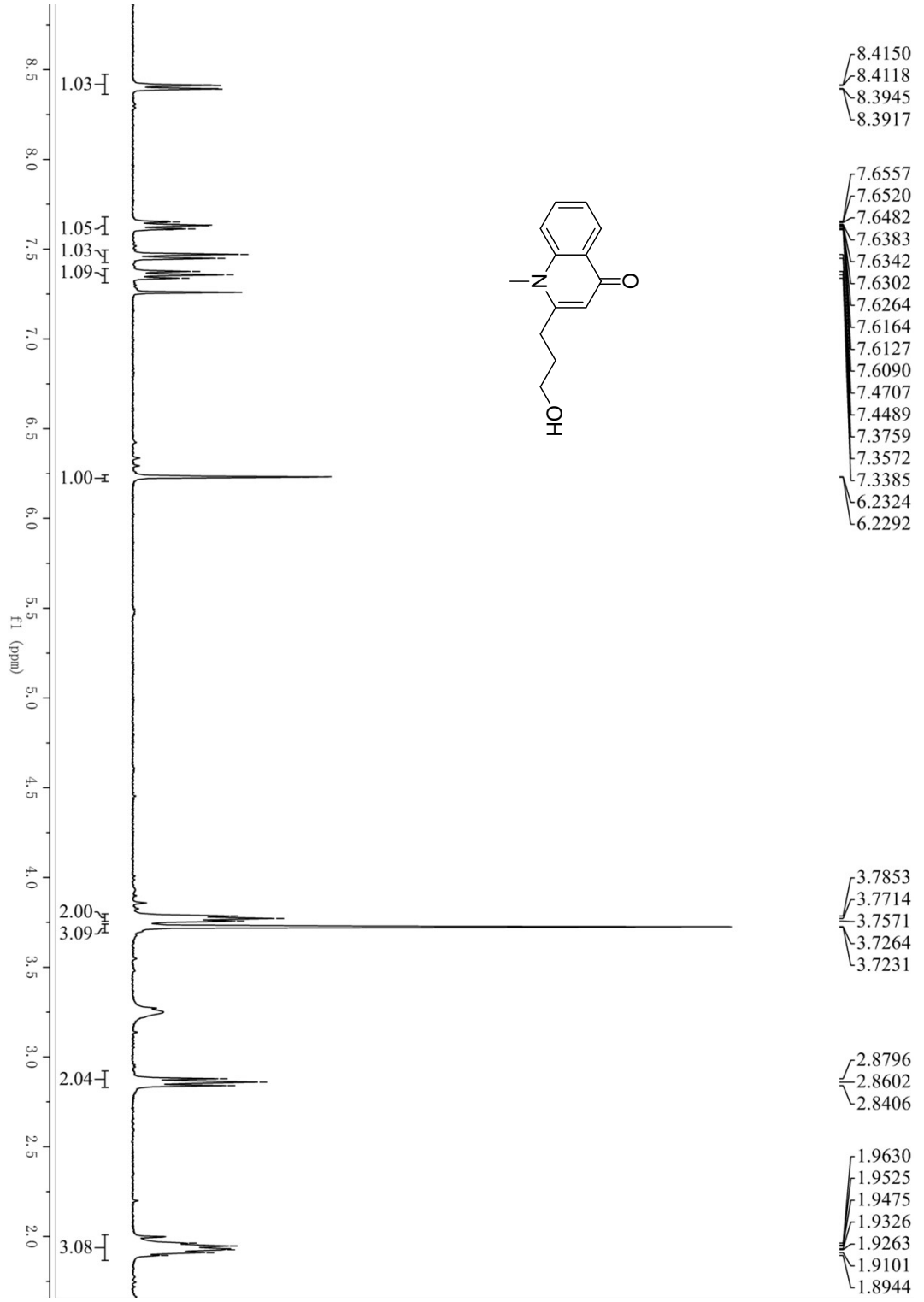


Fig. S27 ^{13}C NMR spectrum of **3** in $CDCl_3$

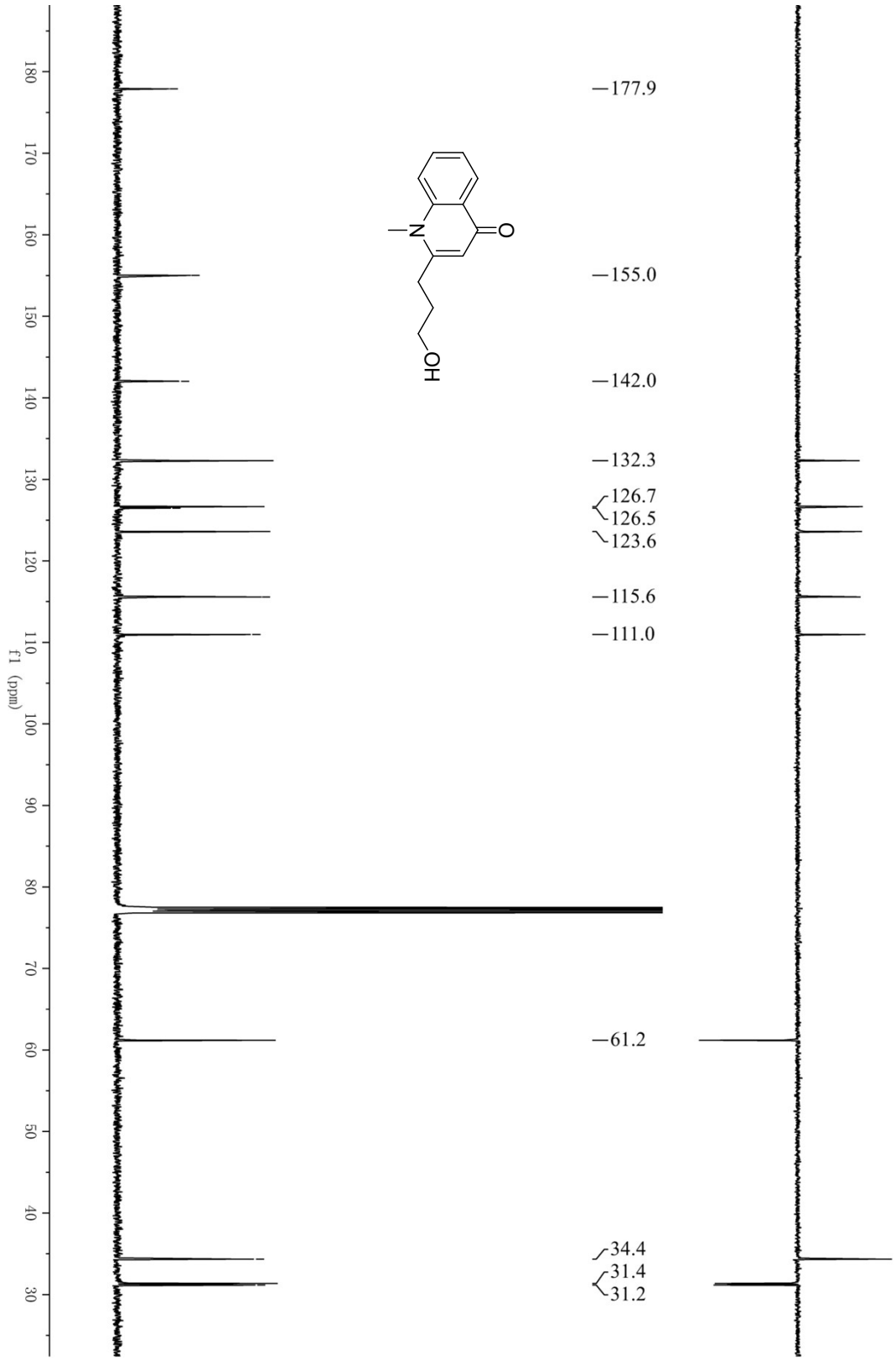


Fig. S28 HSQC spectrum of **3**

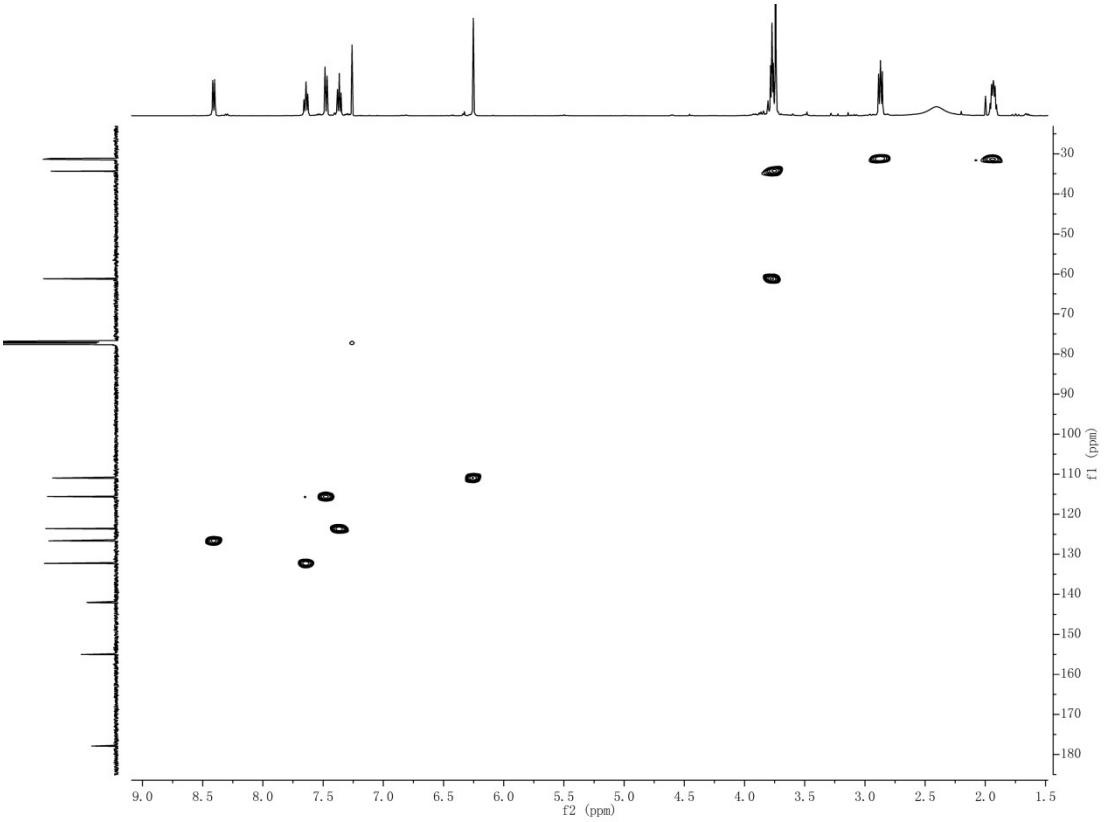


Fig. S29 HMBC spectrum of **3**

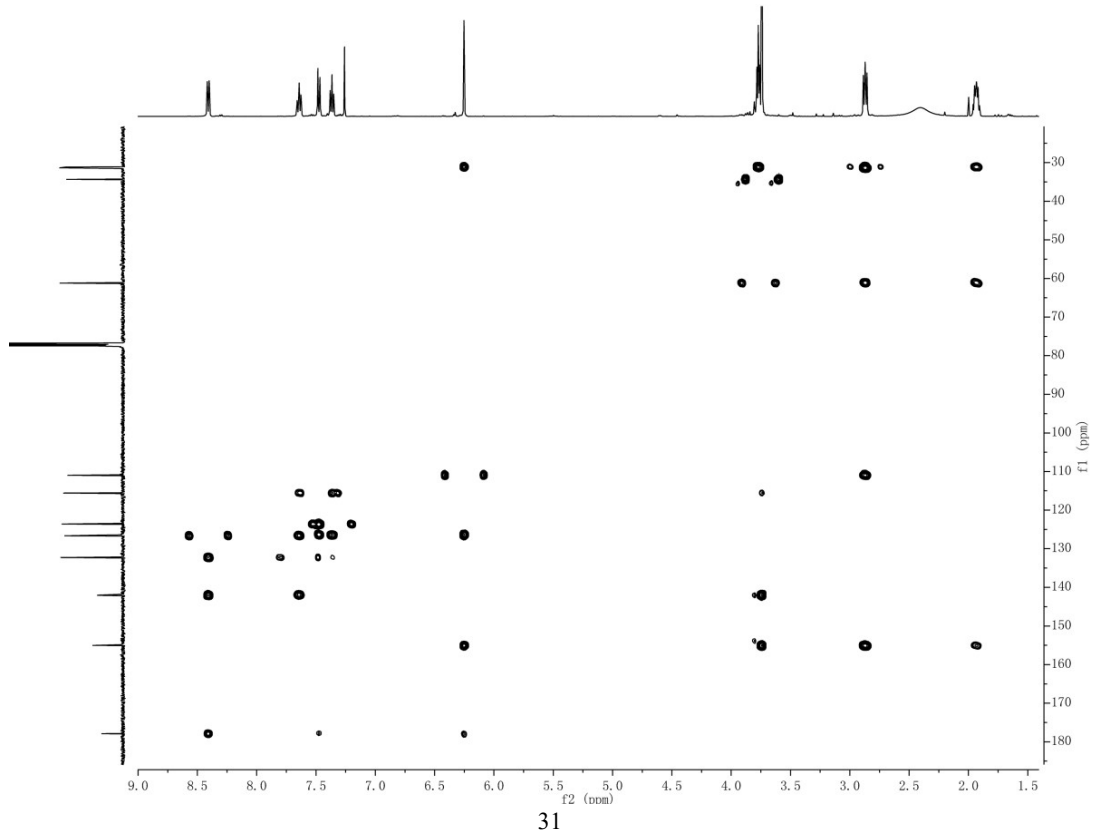


Fig. S30 COSY spectrum of **3**

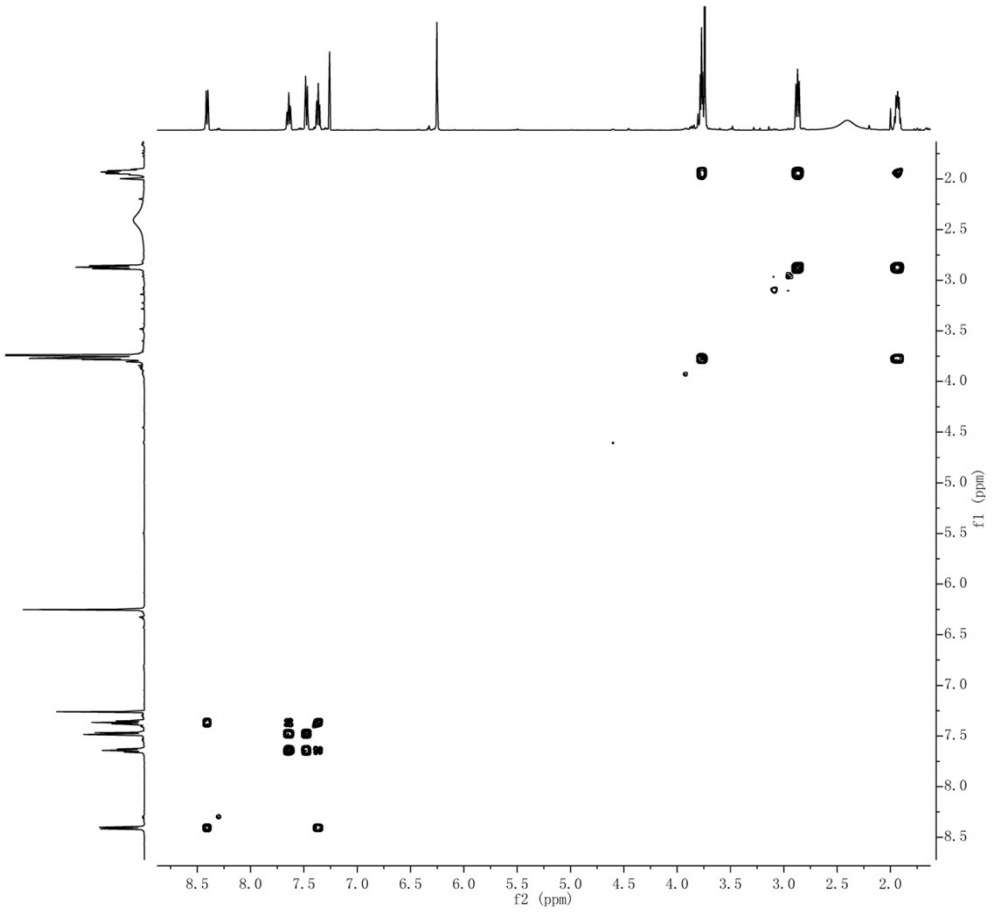


Fig. S31 ESI-MS spectrum of **3**

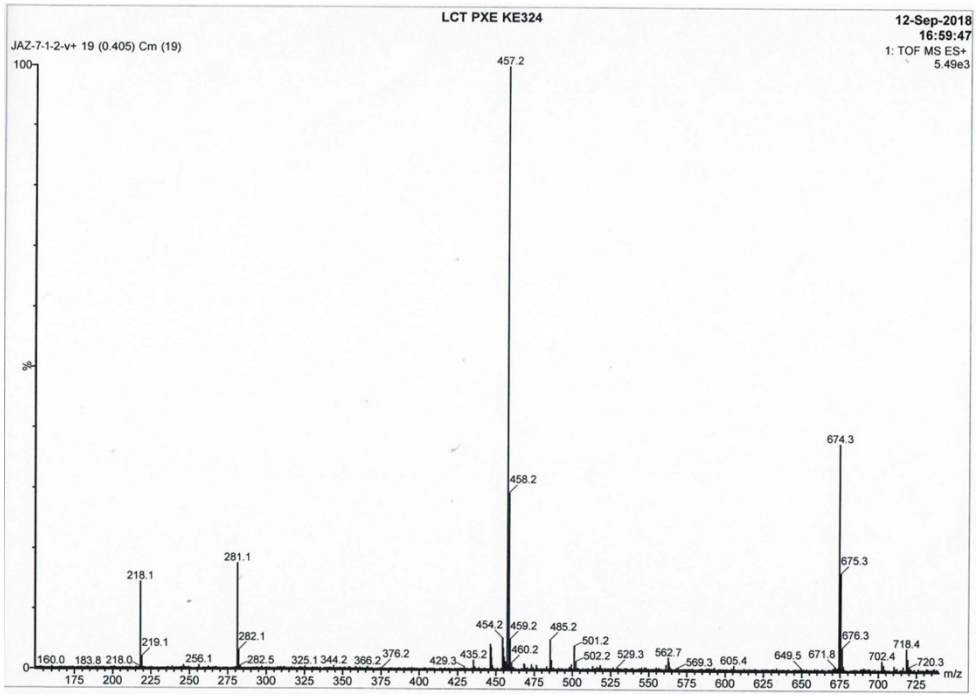


Fig. S32 HRESI-MS spectrum of **3**

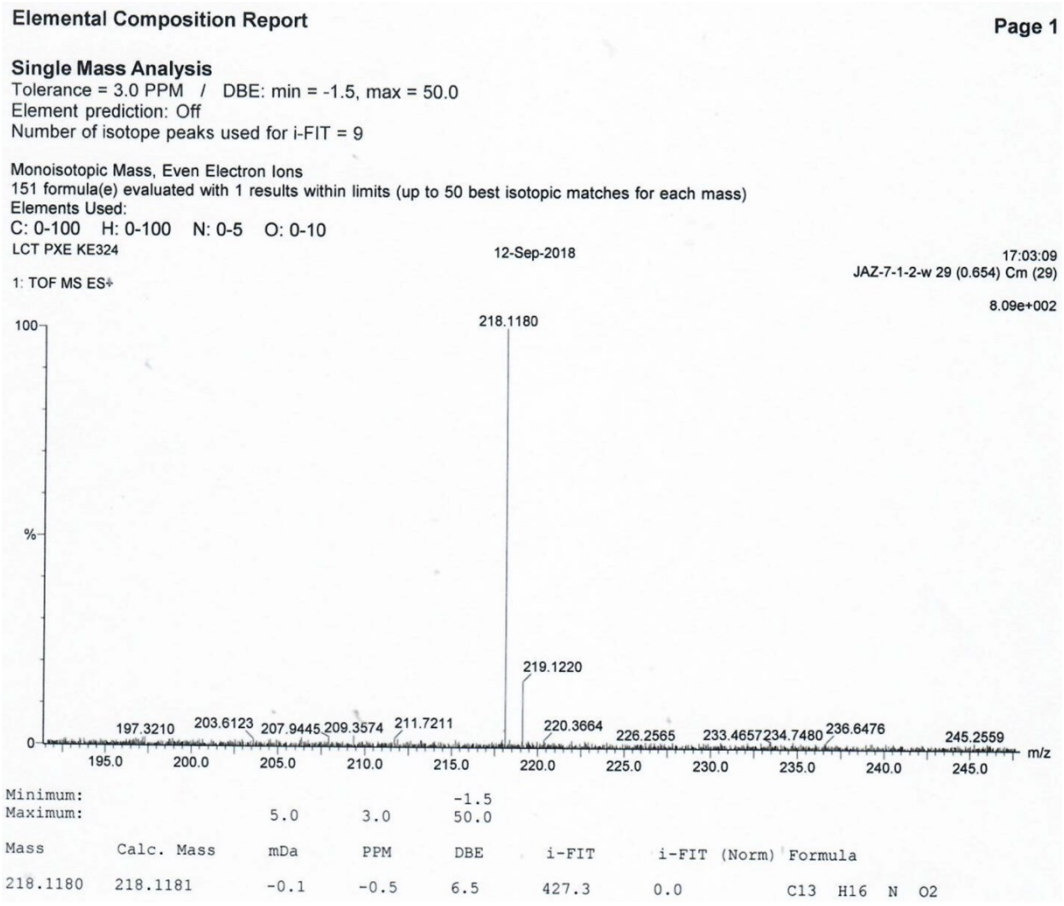


Fig. S33 IR spectrum of **3**

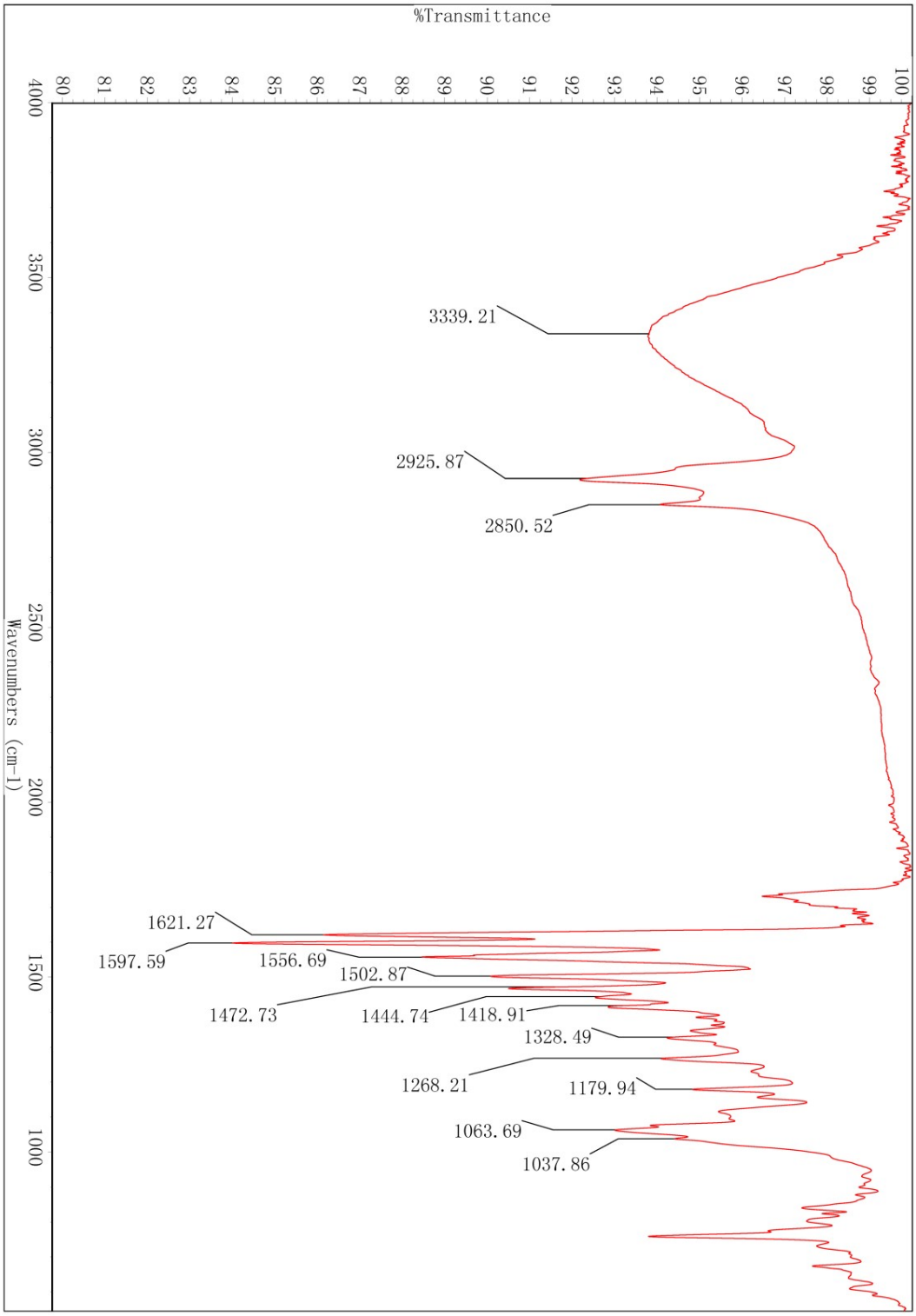


Fig. S34 ^{1}H NMR spectrum of **4** in $CDCl_3$

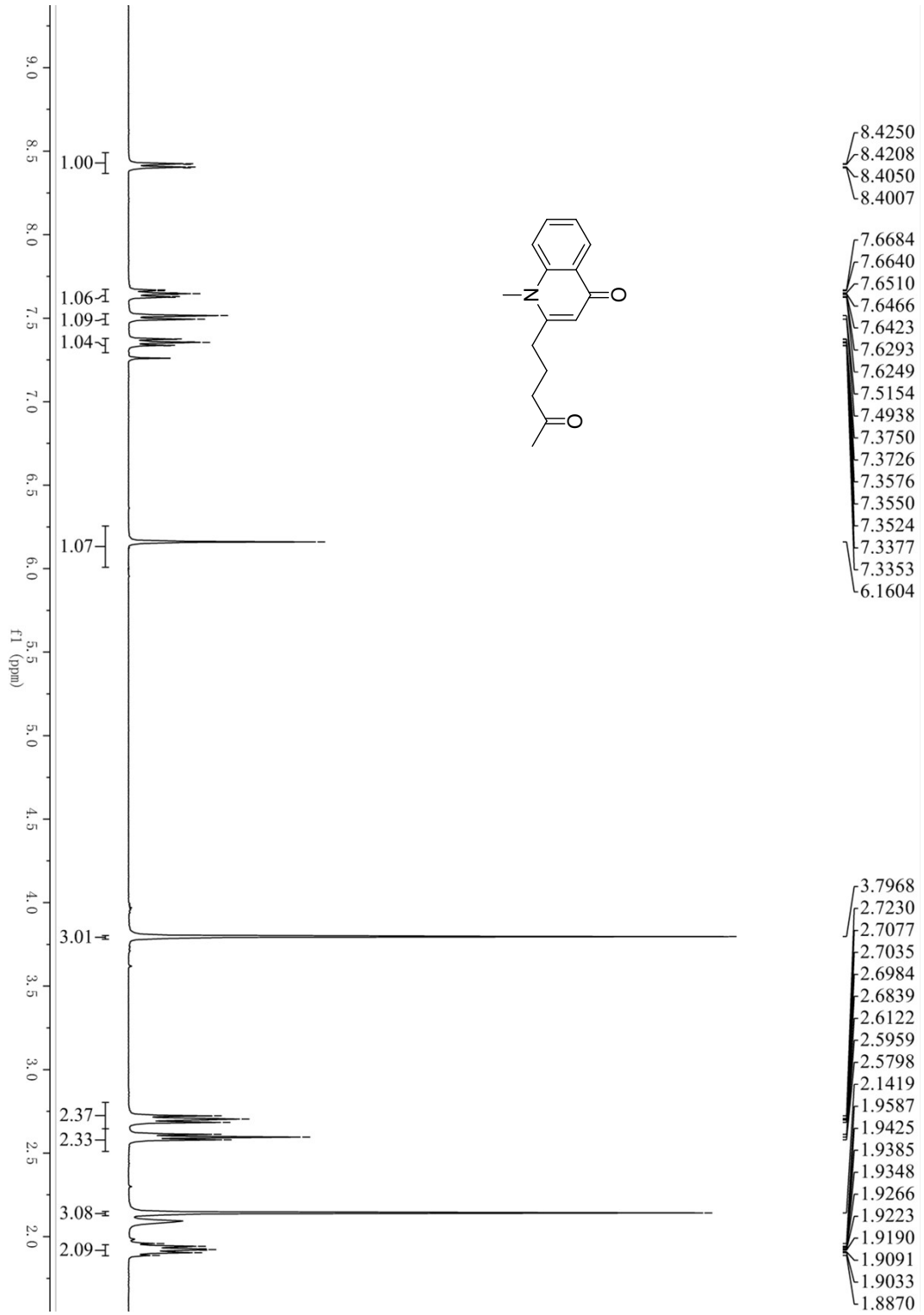


Fig. S35 ^{13}C NMR spectrum of **4** in $CDCl_3$

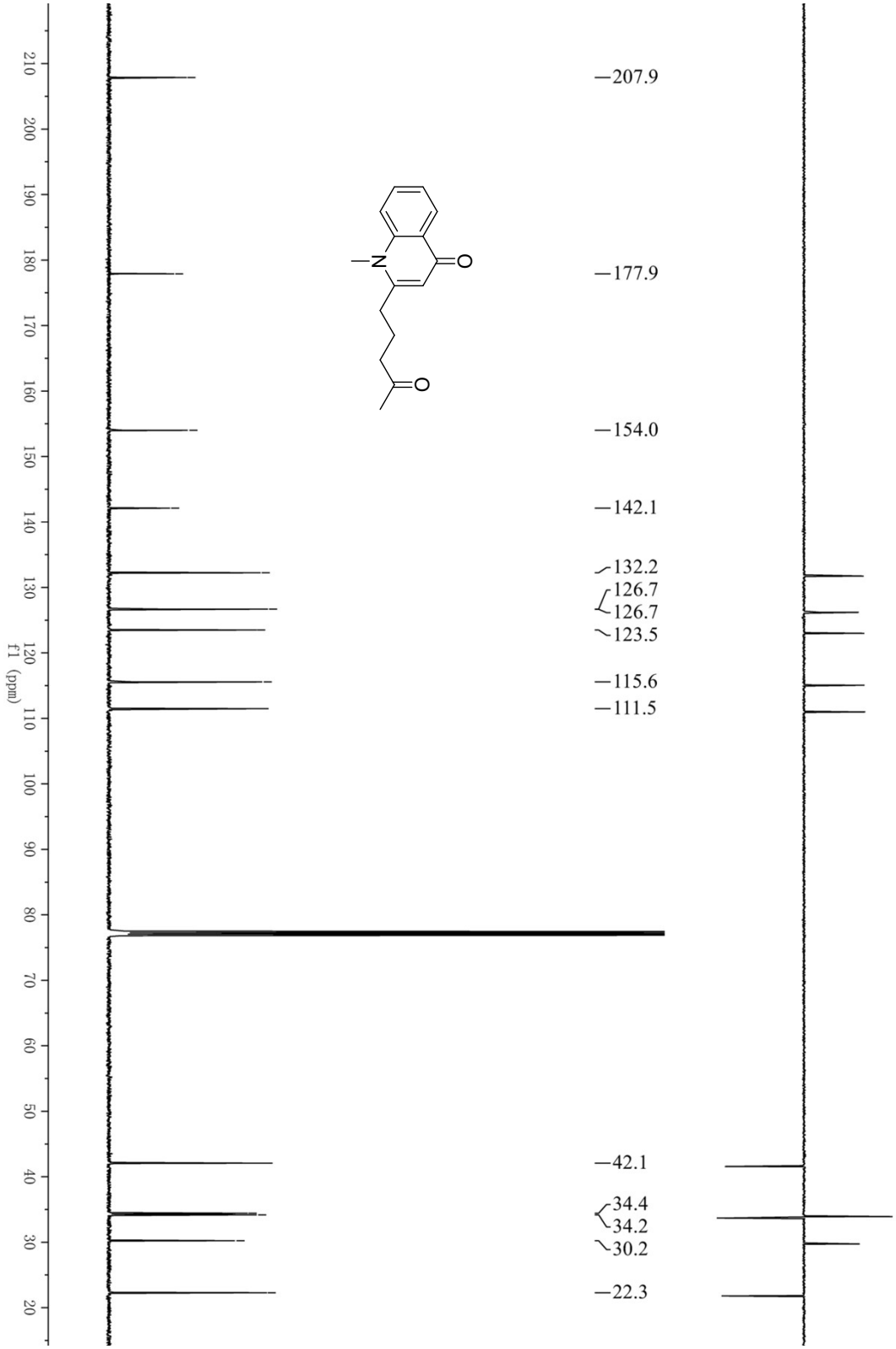


Fig. S36 HSQC spectrum of **4**

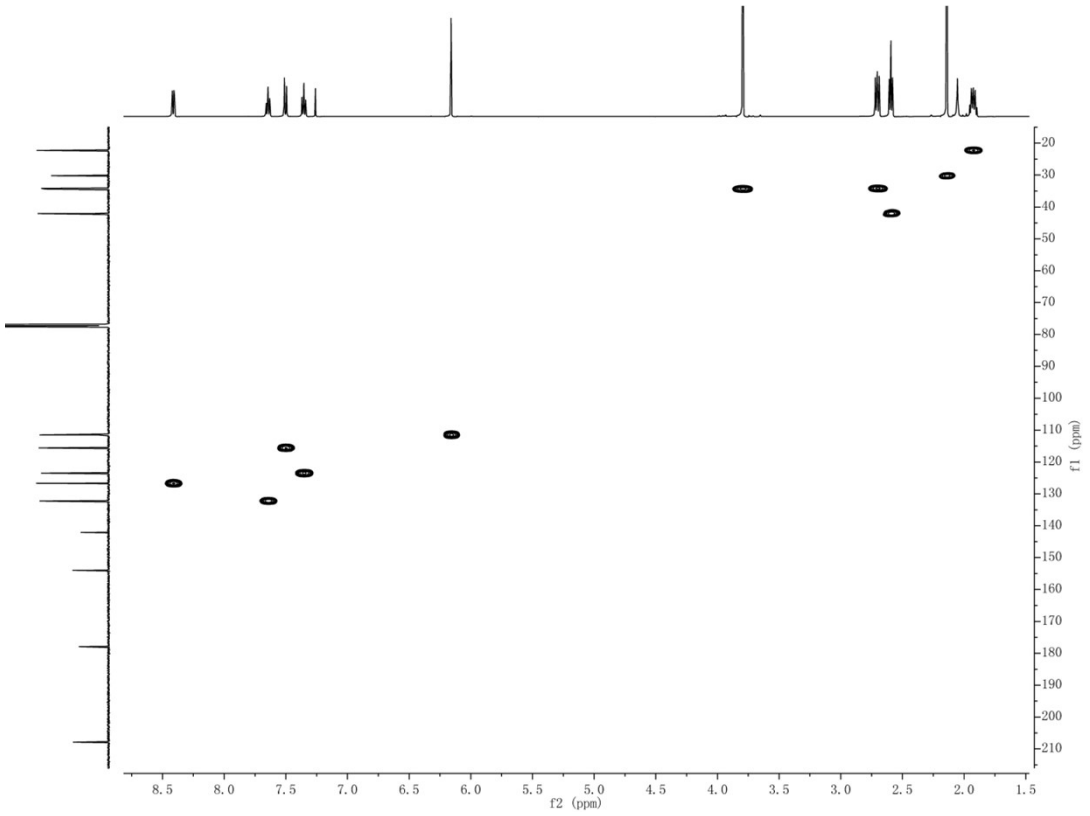


Fig. S37 HMBC spectrum of **4**

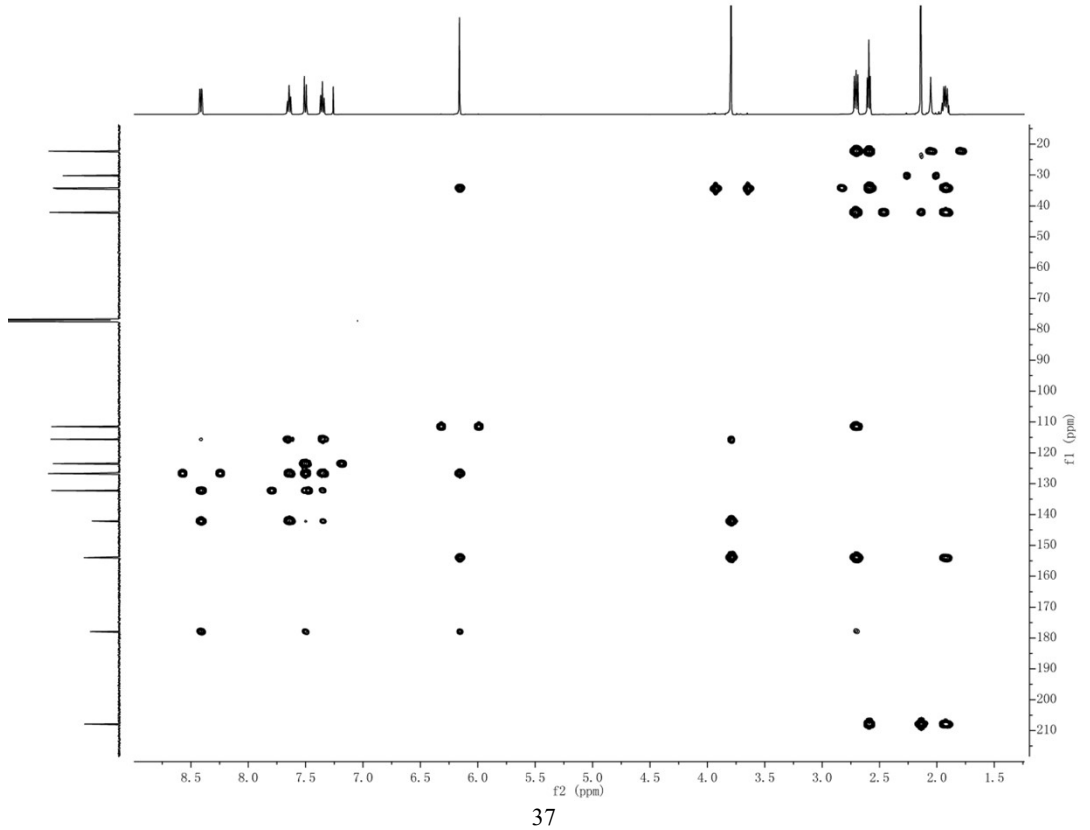


Fig. S38 COSY spectrum of **4**

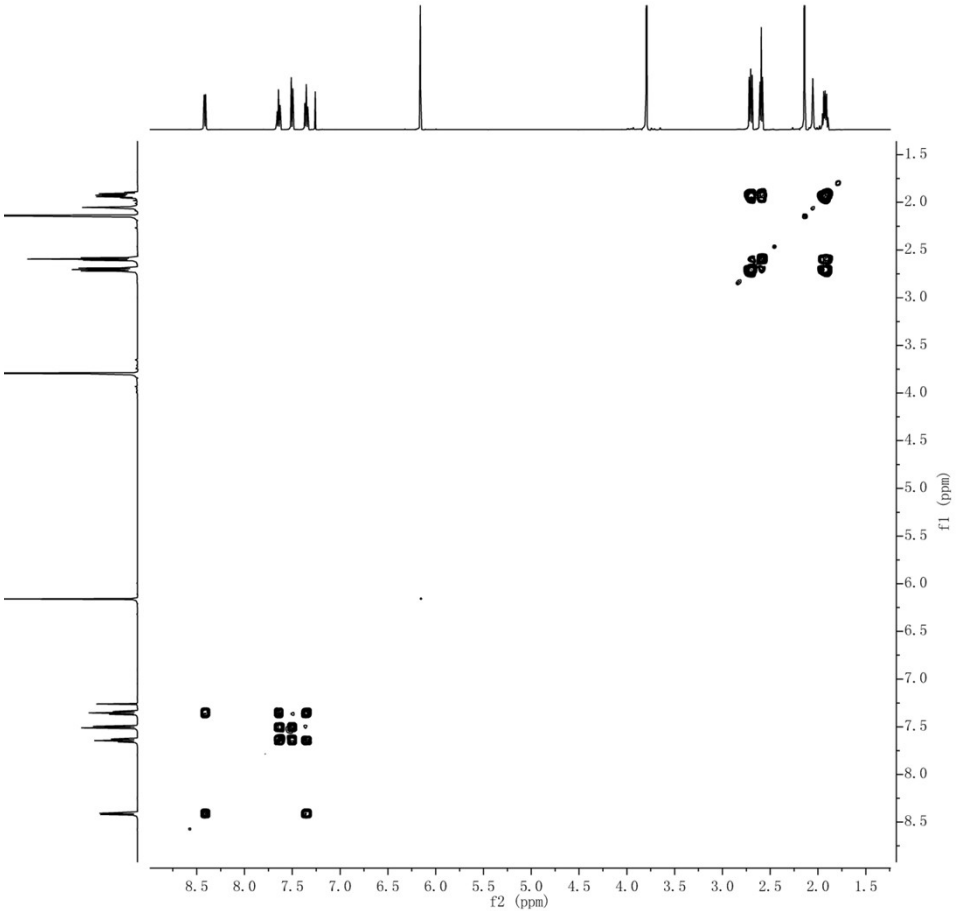


Fig. S39 ESI-MS spectrum of **4**

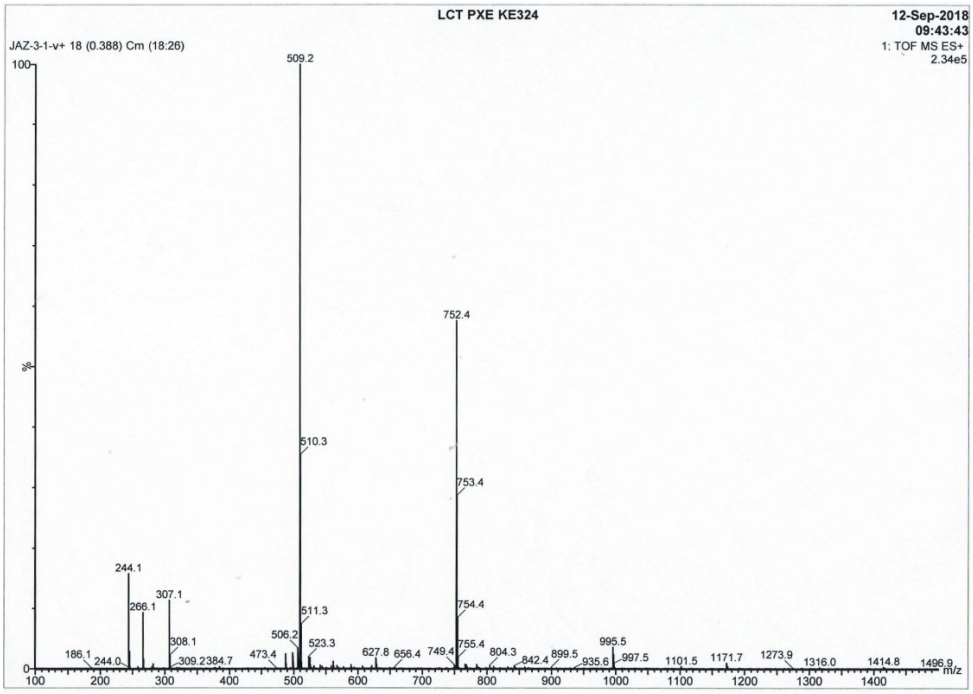


Fig. S40 HRESI-MS spectrum of **4**

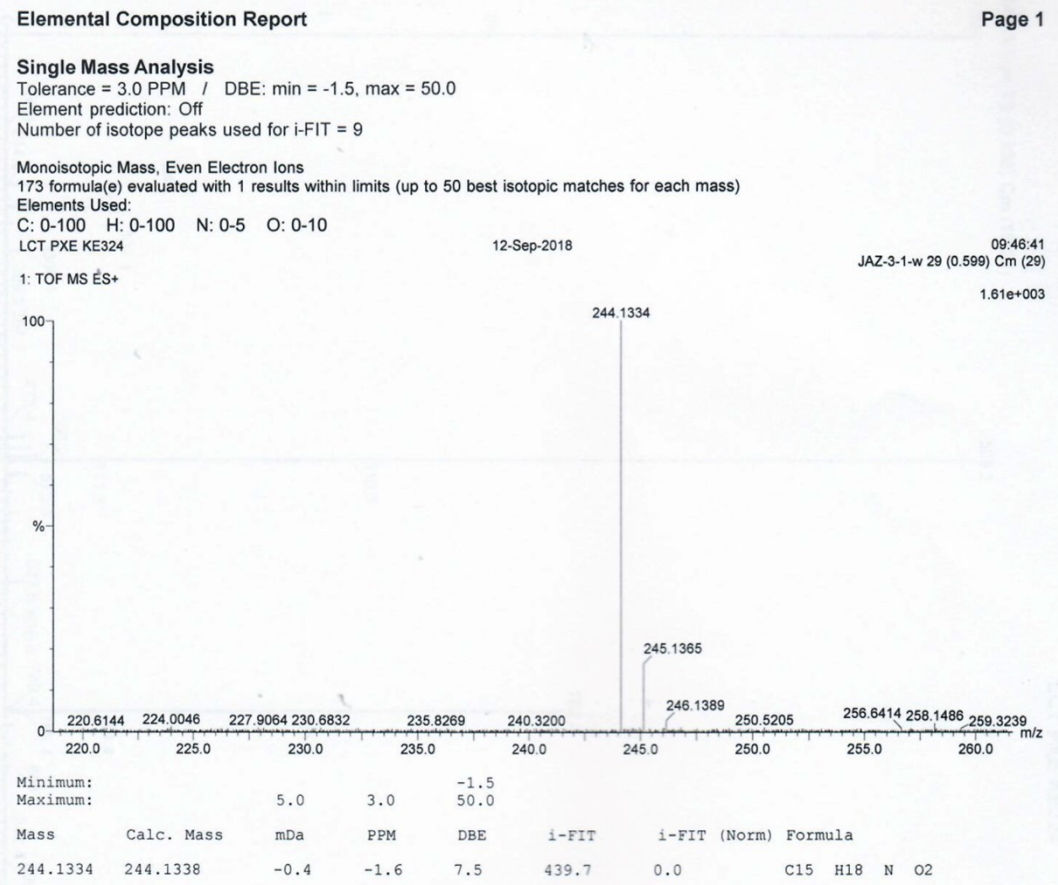


Fig. S41 IR spectrum of **4**

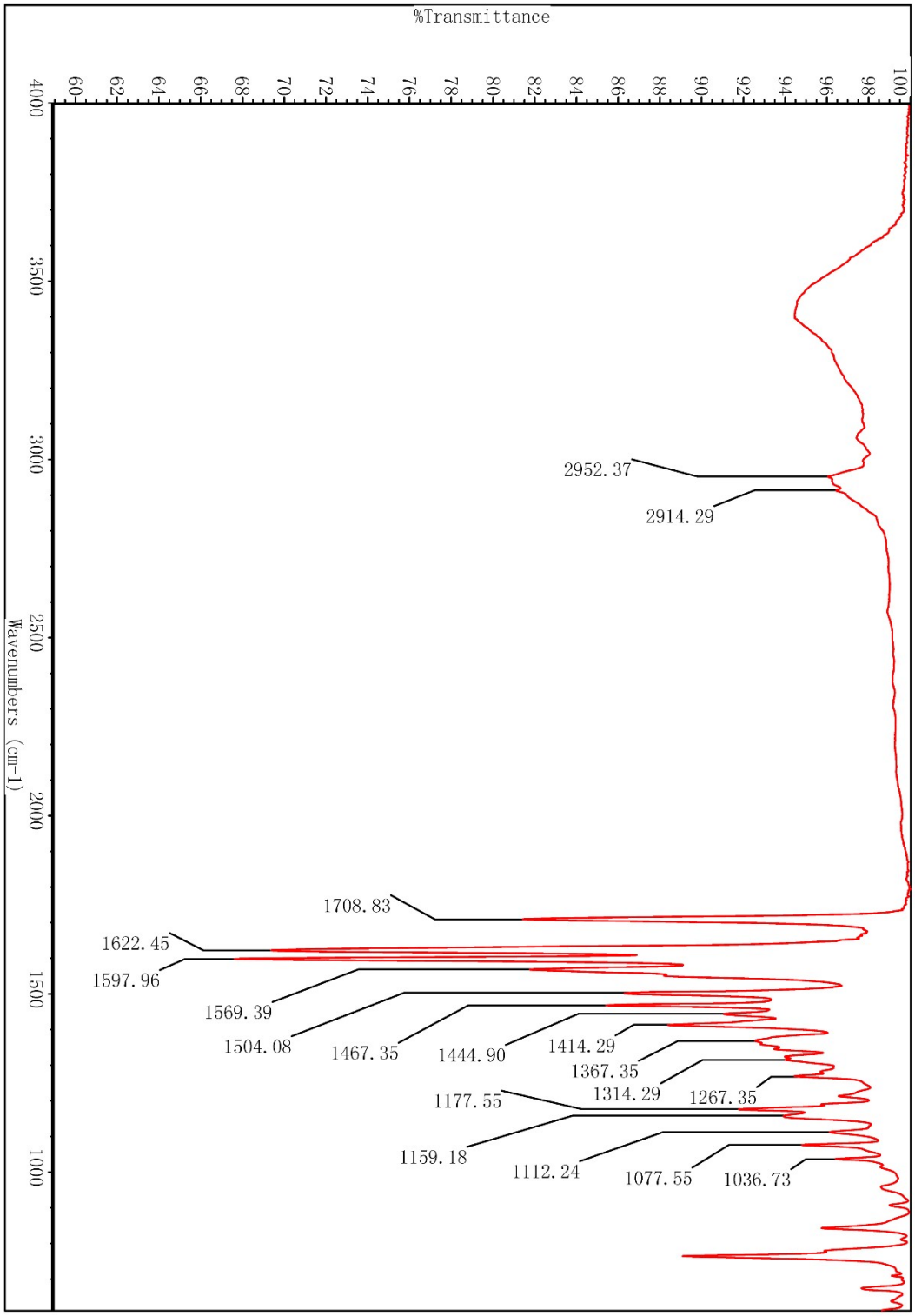


Fig. S42 ^{1}H NMR spectrum of **5** in $CDCl_3$

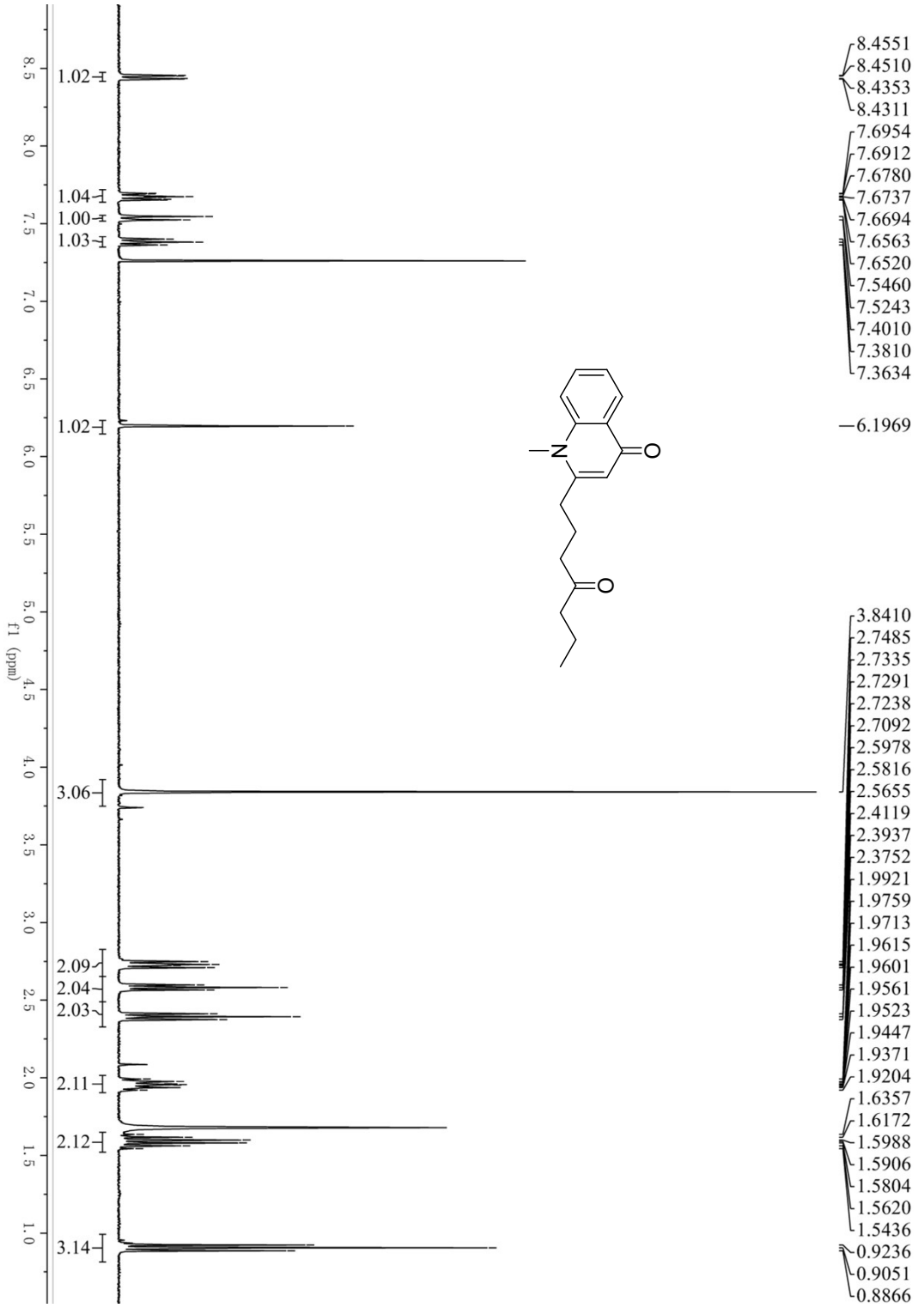


Fig. S43 ^{13}C NMR spectrum of **5** in $CDCl_3$

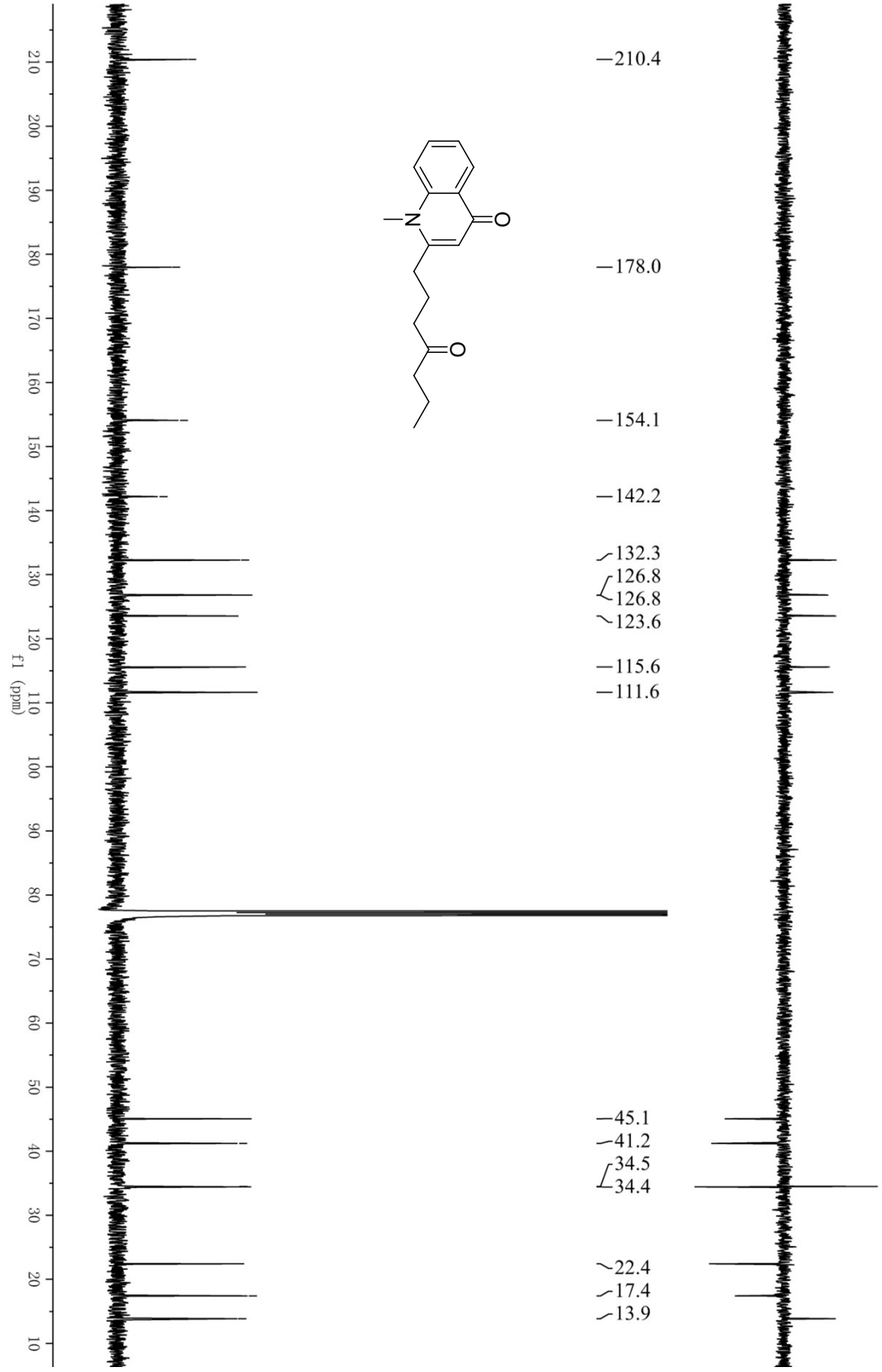


Fig. S44 HSQC spectrum of **5**

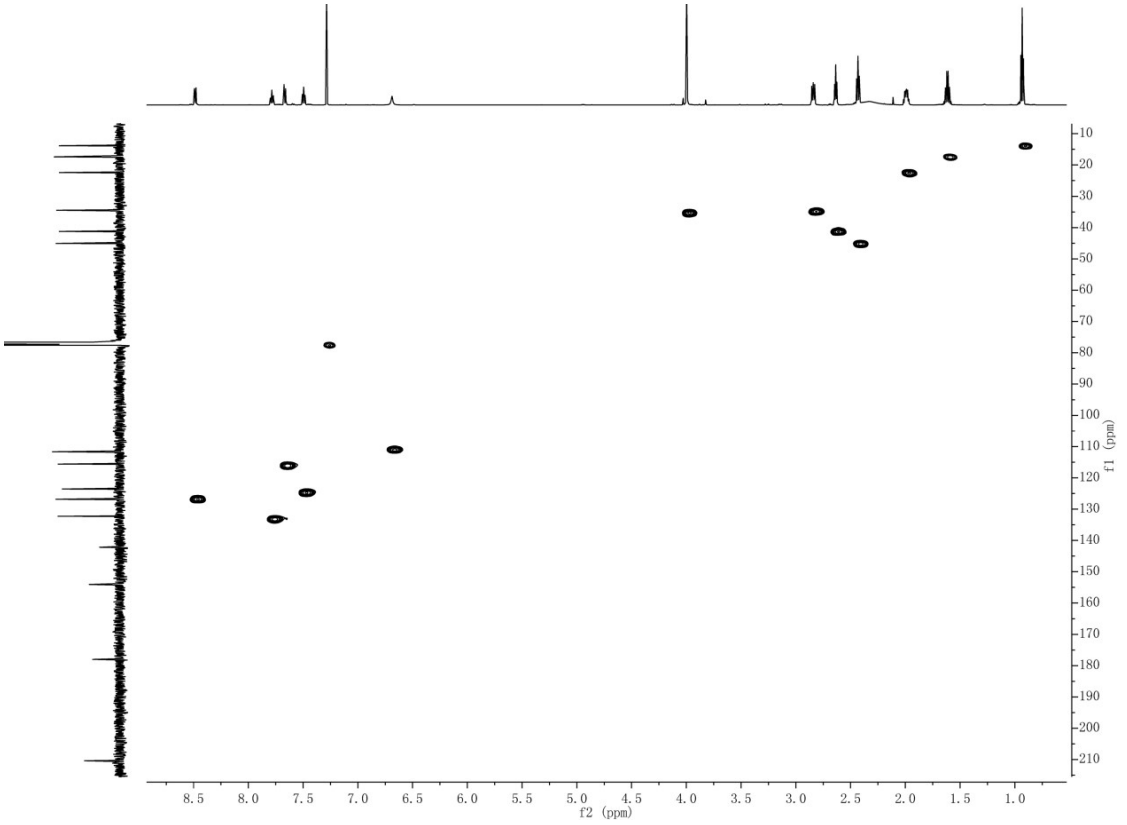


Fig. S45 HMBC spectrum of **5**

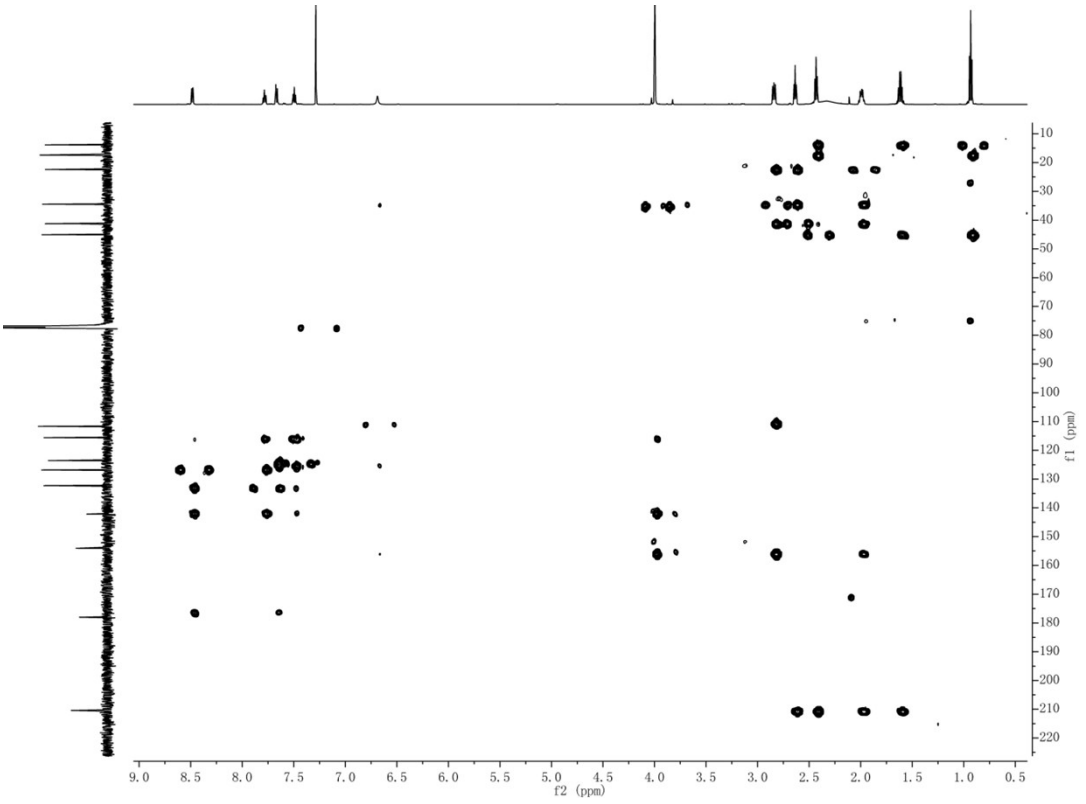


Fig. S46 COSY spectrum of **5**

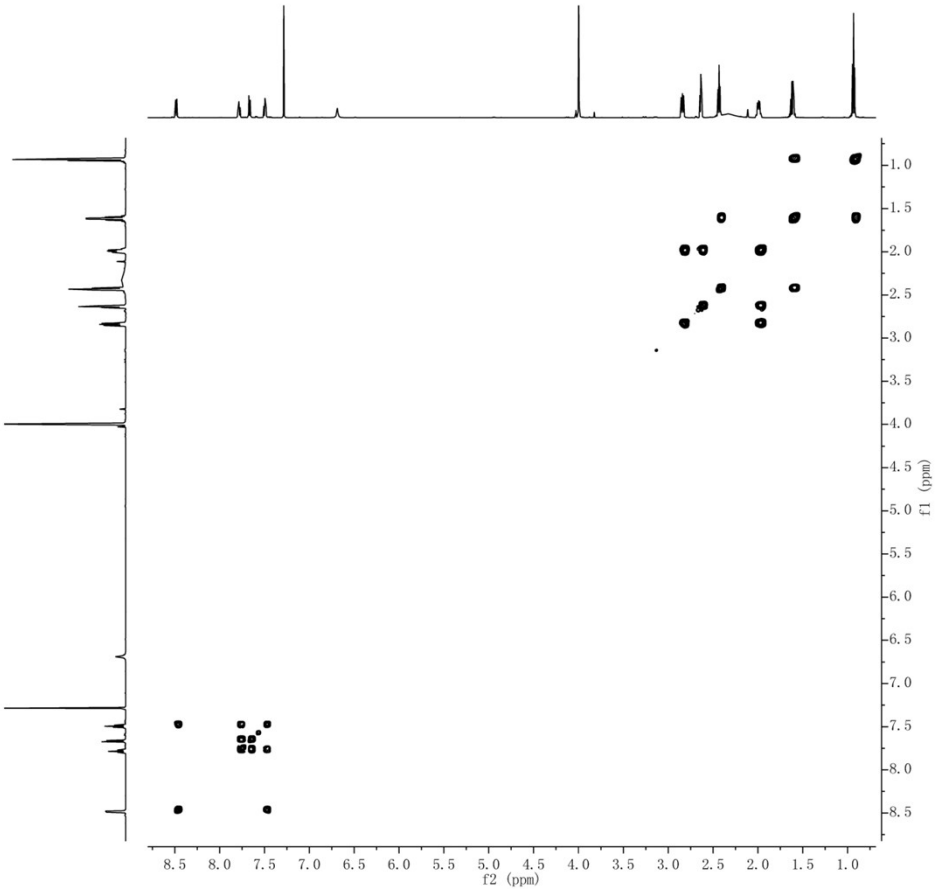


Fig. S47 ESI-MS spectrum of **5**

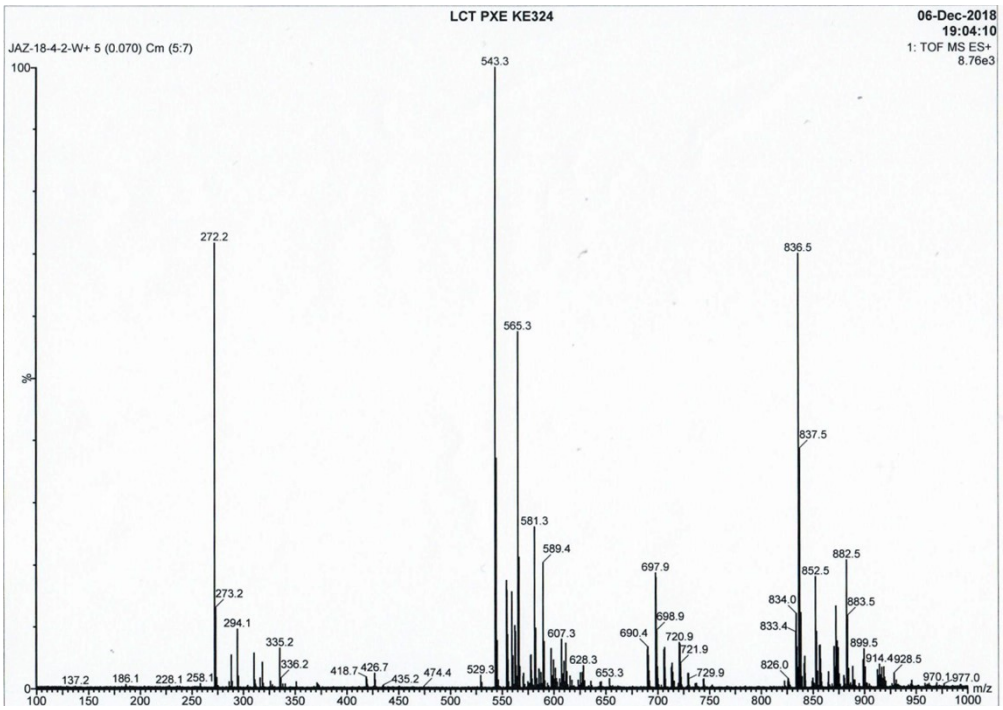


Fig. S48 HRESI-MS spectrum of **5**

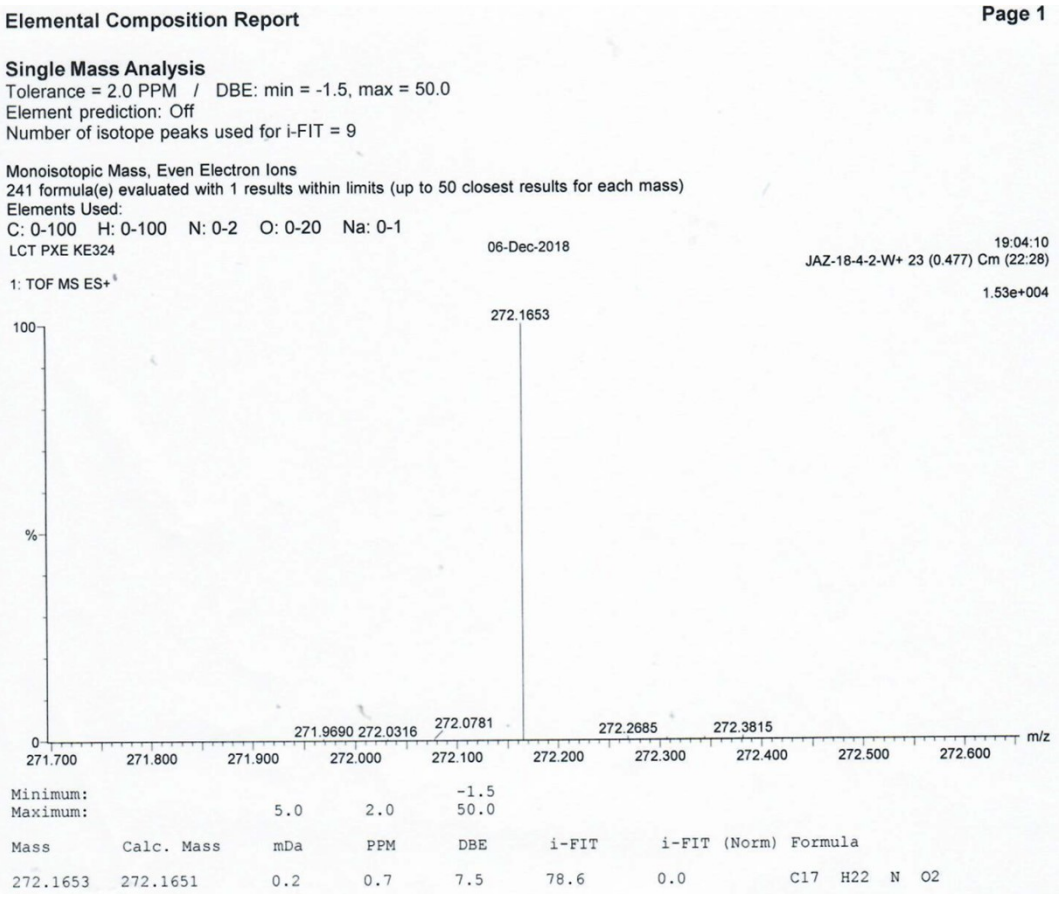


Fig. S49 IR spectrum of **5**

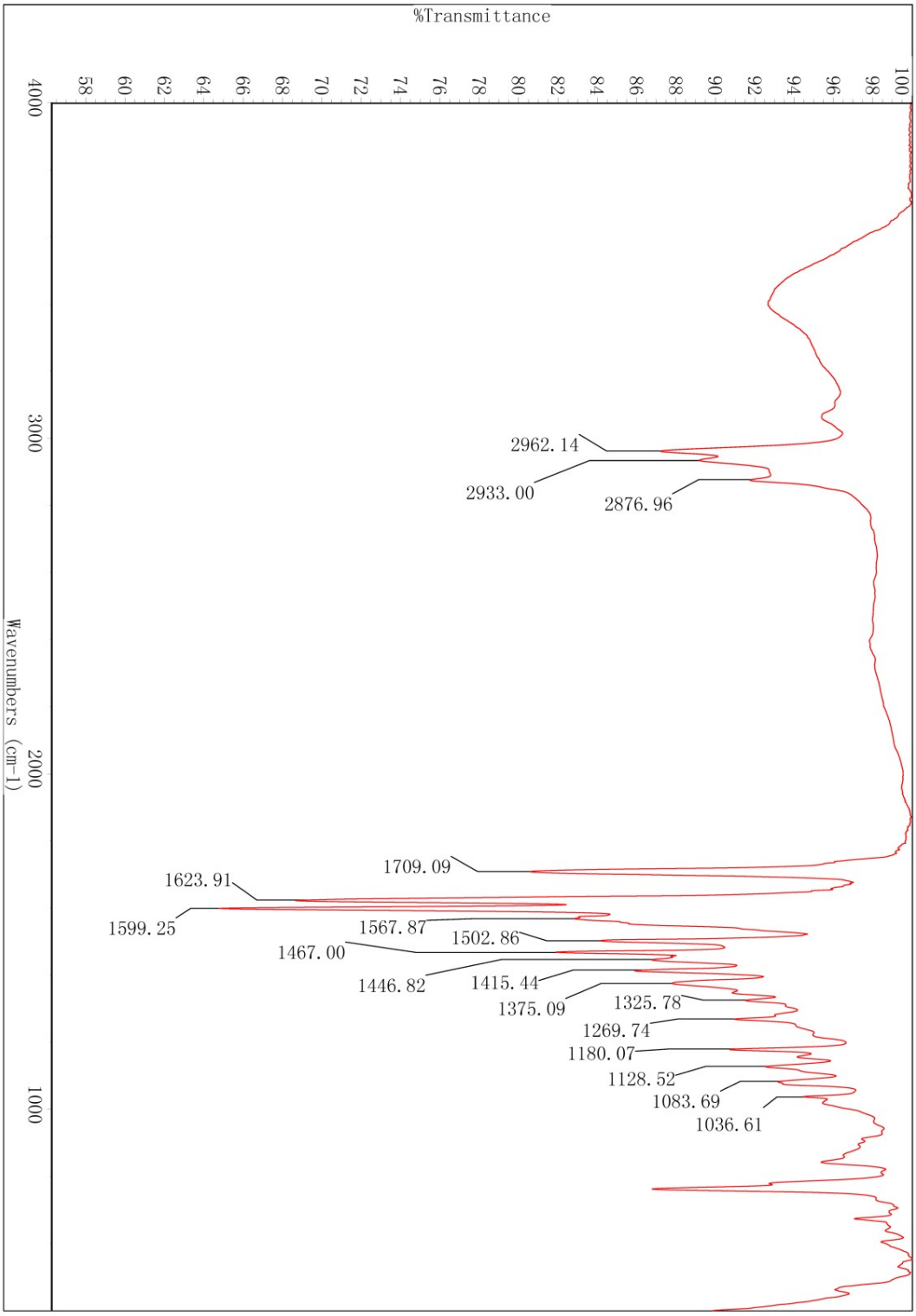


Fig. S50 ^{1}H NMR spectrum of **6** in $CDCl_3$

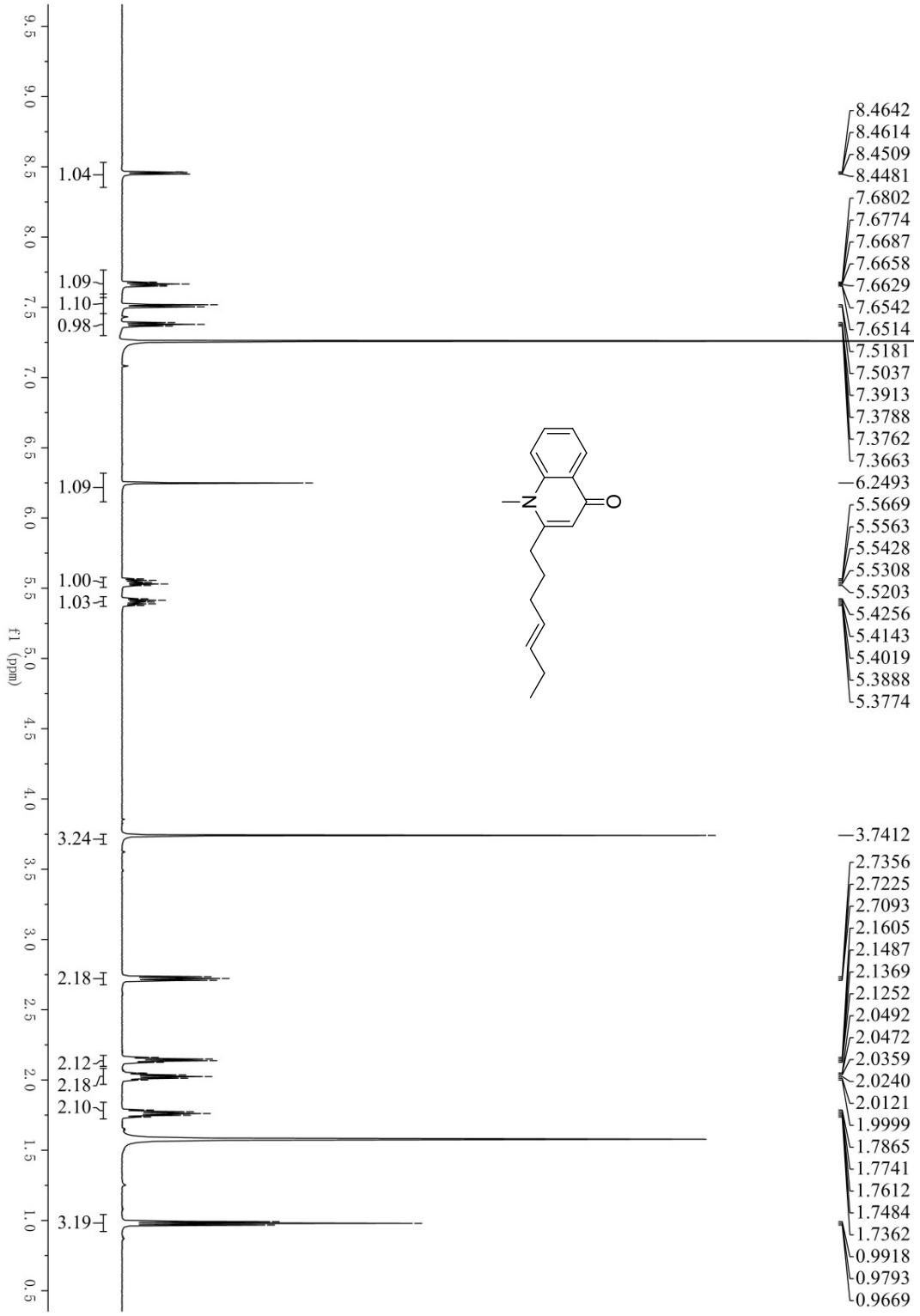


Fig. S51 ^{13}C NMR spectrum of **6** in $CDCl_3$

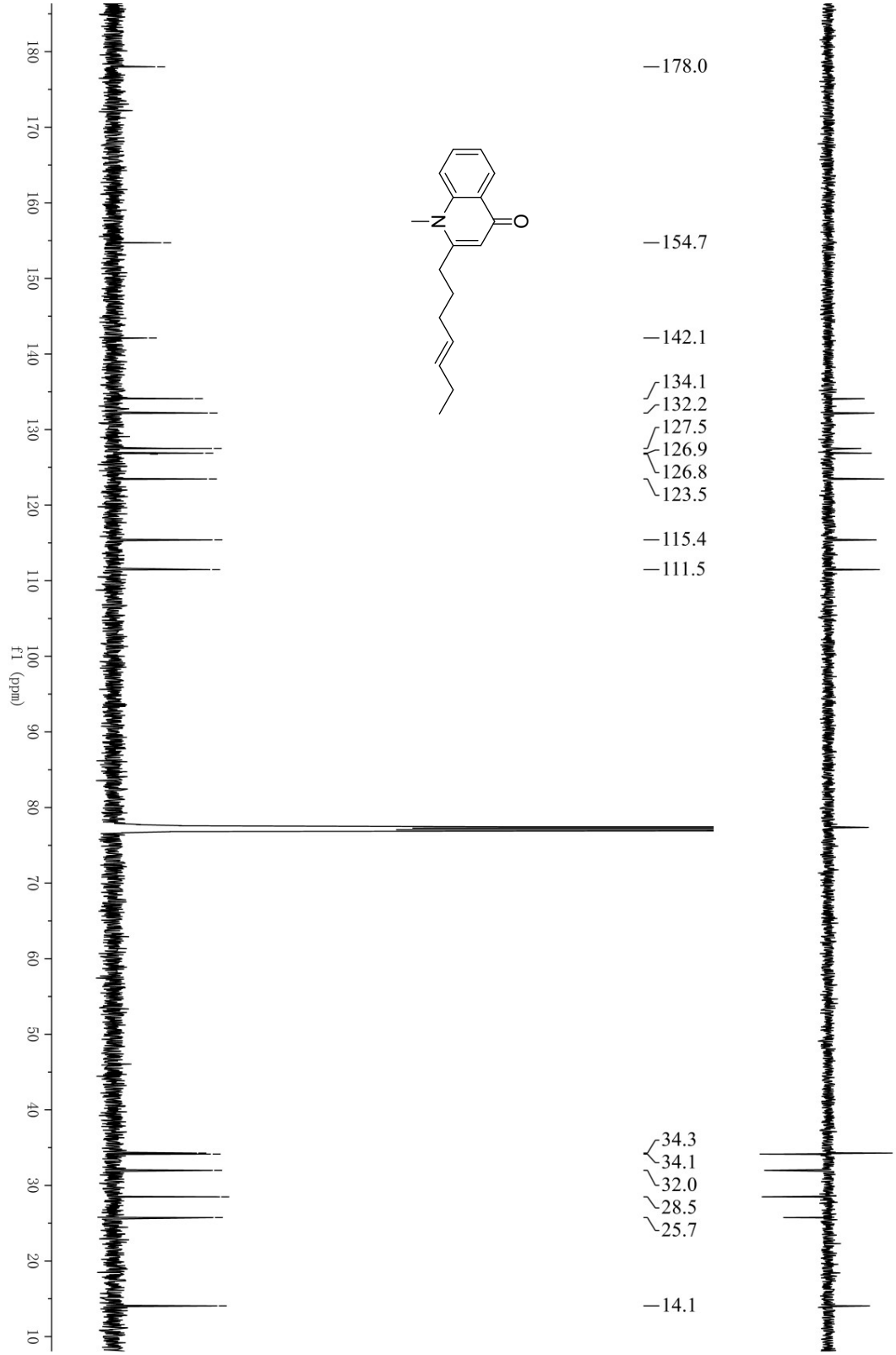


Fig. S52 HSQC spectrum of **6**

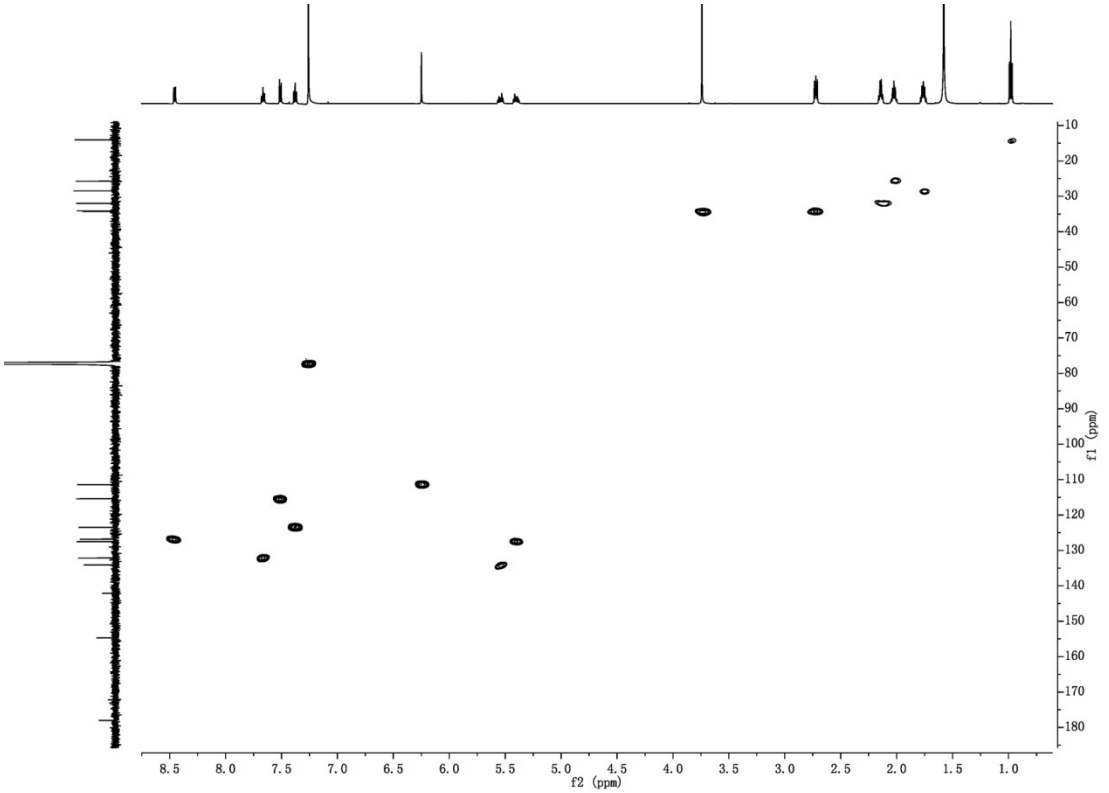


Fig. S53 HMBC spectrum of **6**

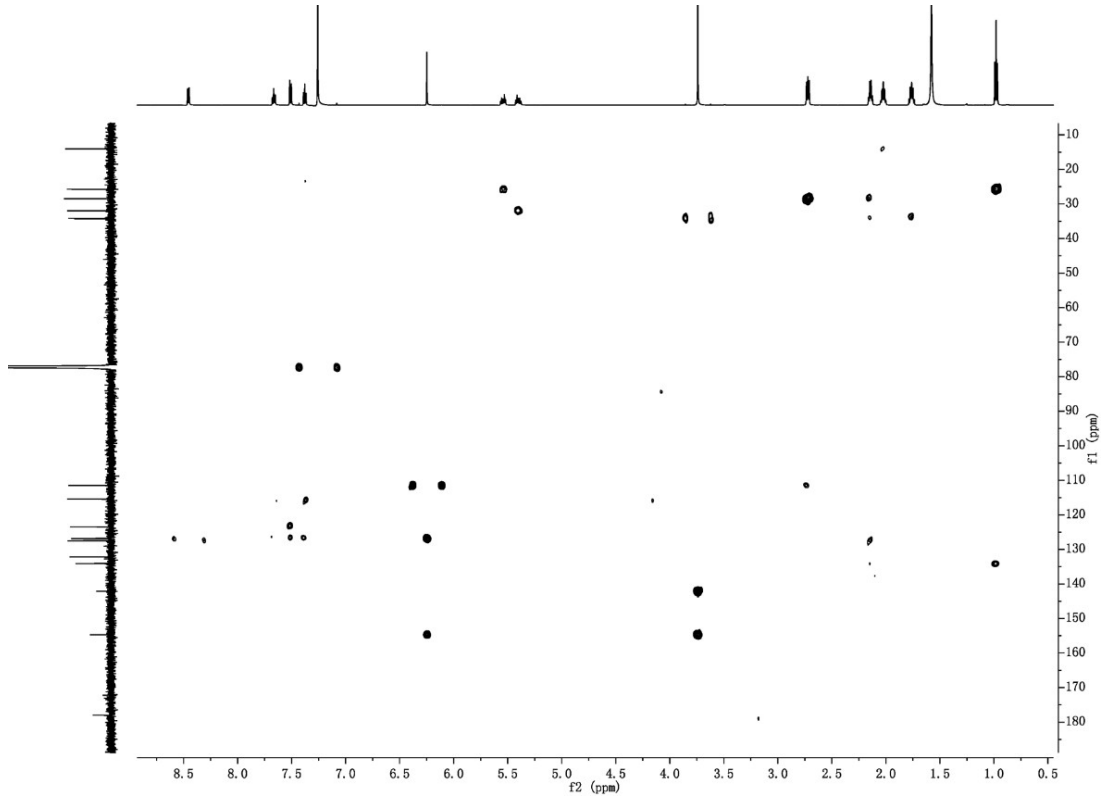


Fig. S54 COSY spectrum of **6**

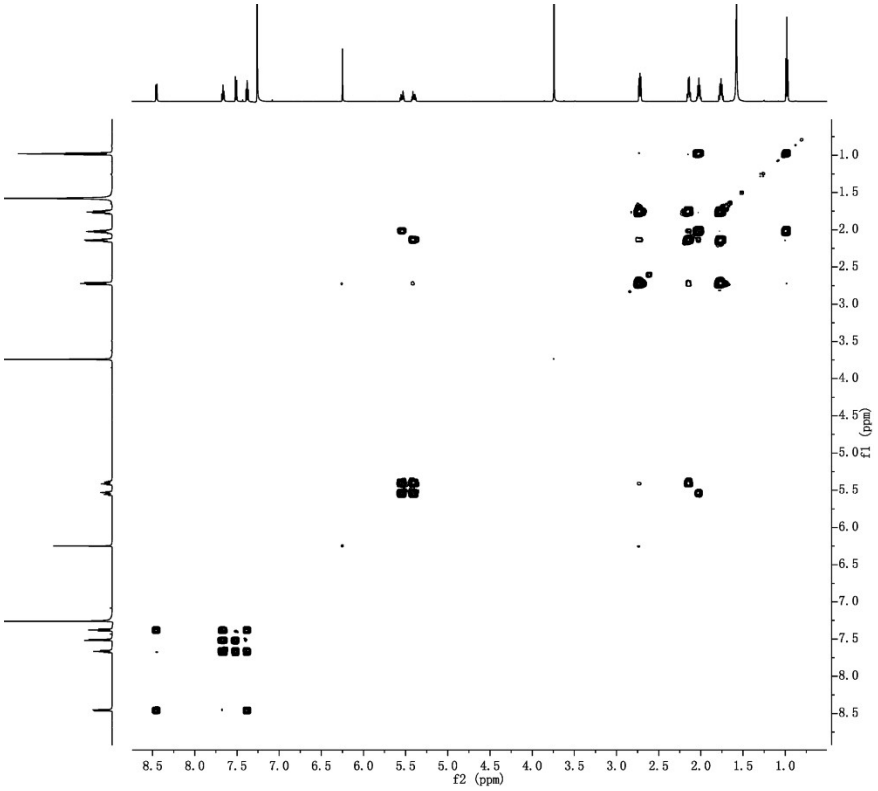


Fig. S55 ROESY spectrum of **6**

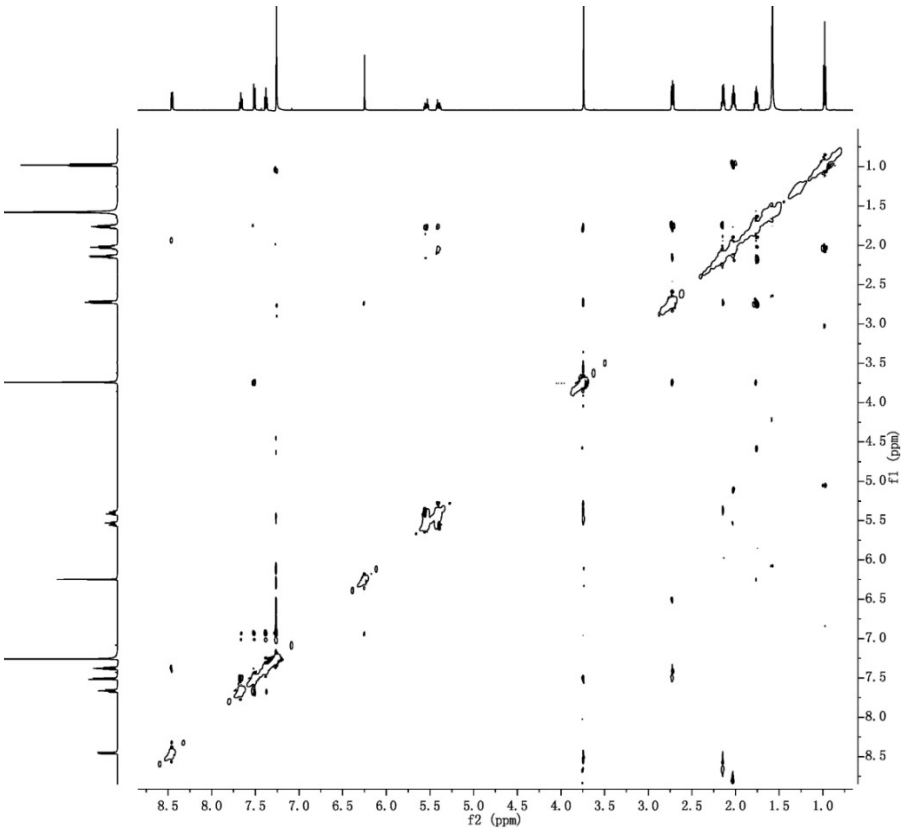


Fig. S56 ESI-MS spectrum of **6**

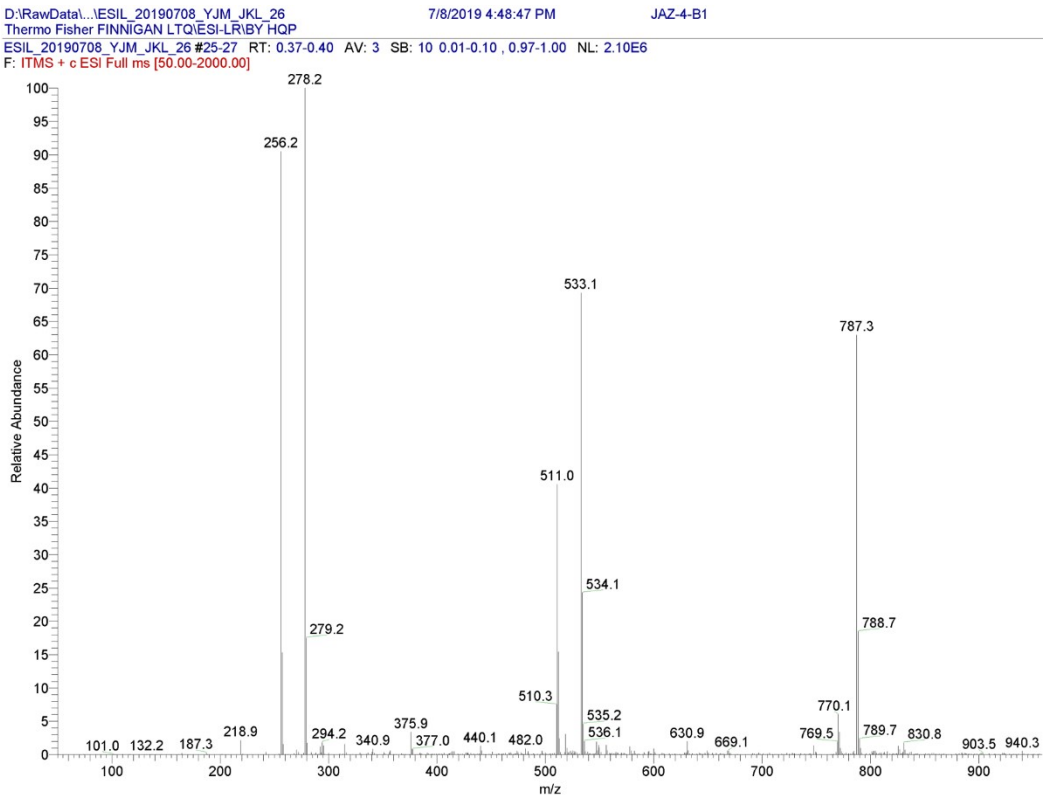


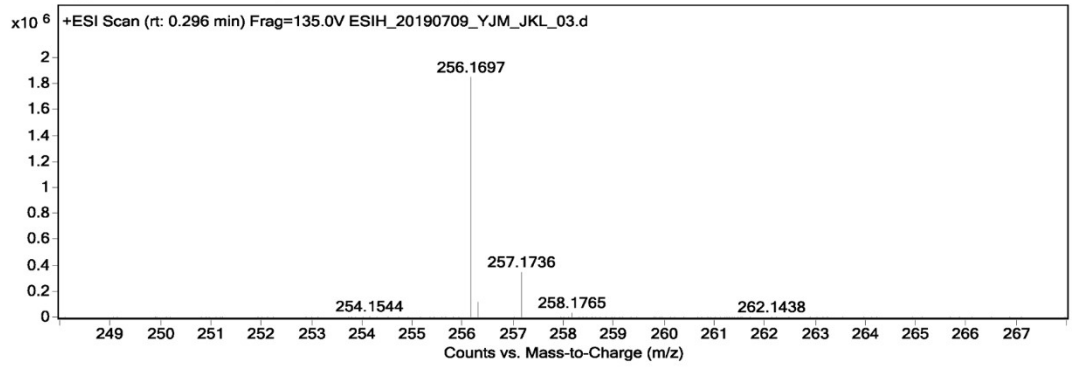
Fig. S57 HRESI-MS spectrum of **6**

Qualitative Analysis Report

Data Filename	ESIH_20190709_YJM_JKL_03.d	**Sample Name**	JAZ-4-B1
Sample Type	Sample	**Position**	P1-A2
Instrument Name	Agilent G6520 Q-TOF	**Acq Method**	20160322_MS_ESIH_POS_1min.m
Acquired Time	7/9/2019 15:13:57	**IRM Calibration Status**	Success
DA Method	small molecular data analysis method.m	**Comment**	ESIH by ZZY

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
256.1697	256.1696	-0.06	-0.24	C17 H22 N O	(M+H)+

--- End Of Report ---

Fig. S58 IR spectrum of **6**

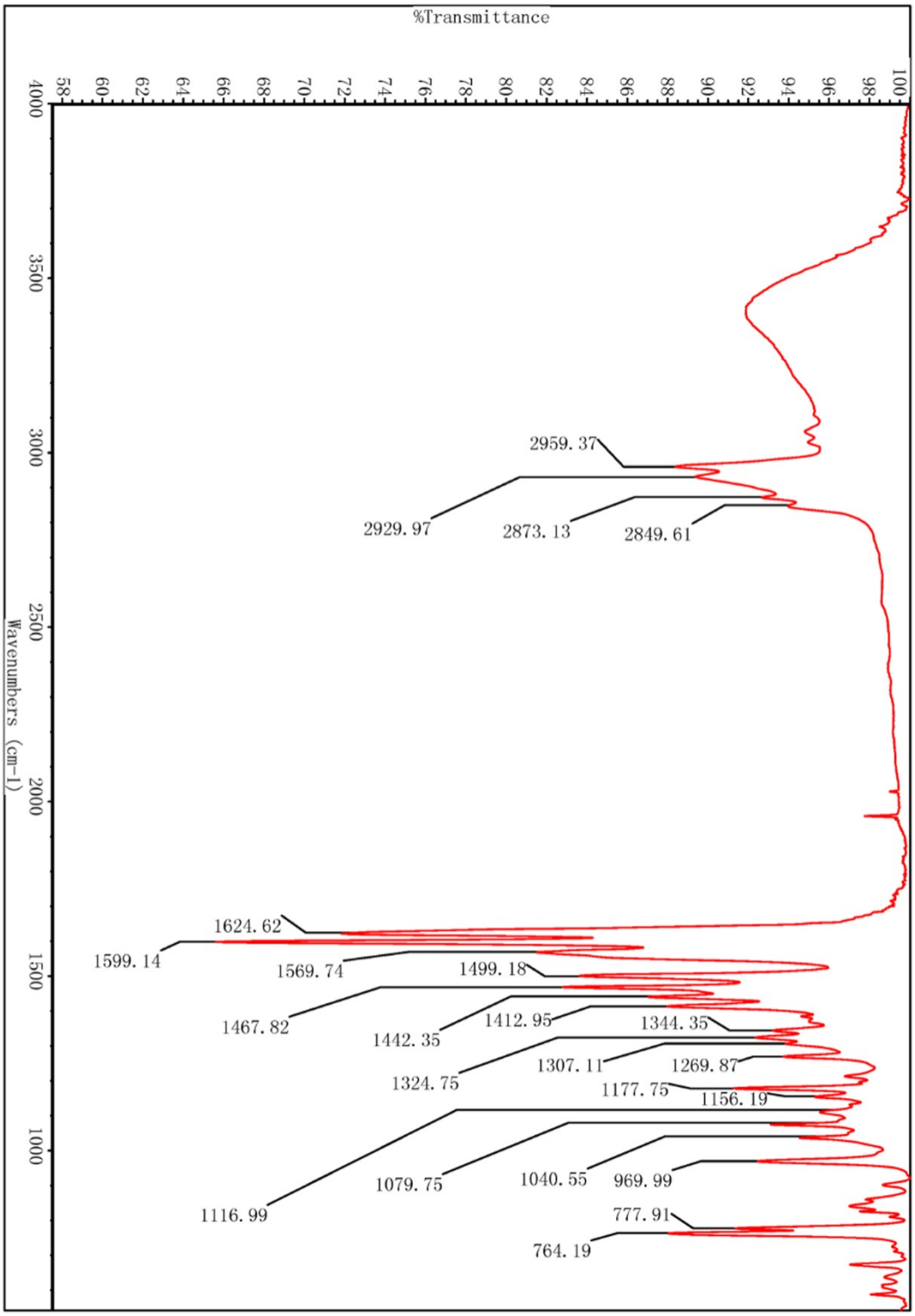


Fig. S59 ^{1}H NMR spectrum of (+)-**7** in CD_3OD

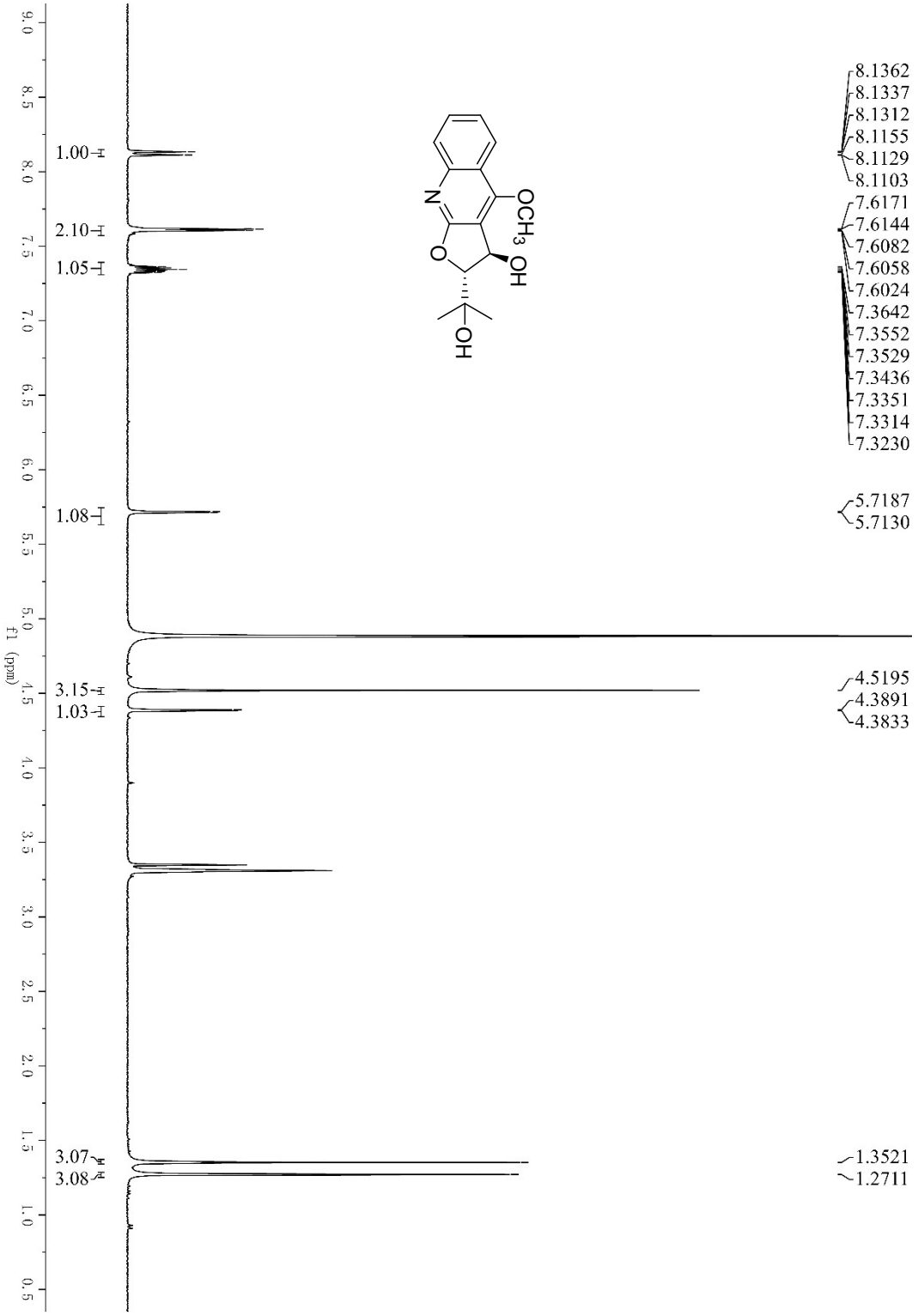


Fig. S60 ^{13}C NMR spectrum of (+)-**7** in CD_3OD

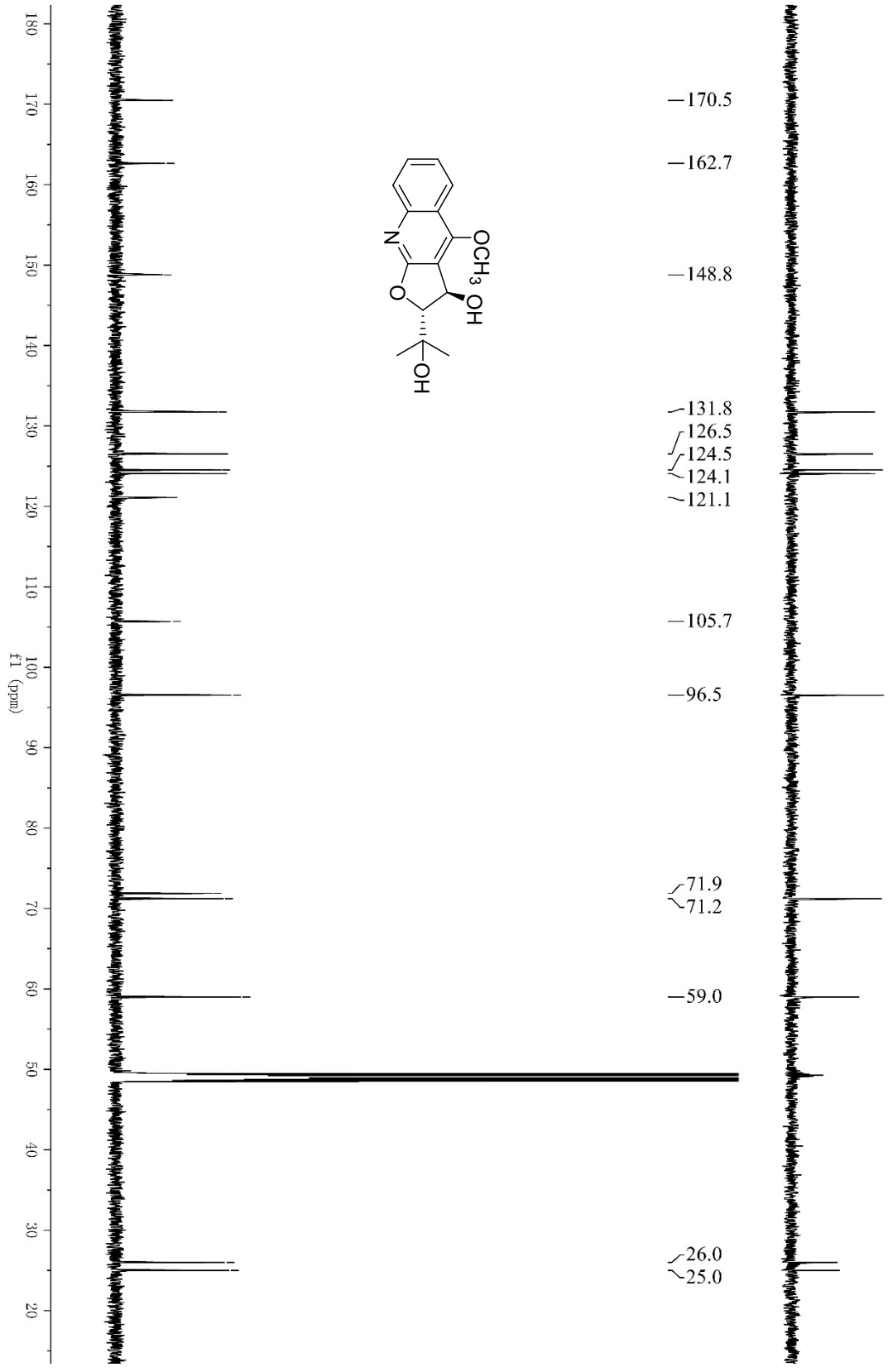


Fig. S61 ^{1}H NMR spectrum of (–)-**7** in CD_3OD

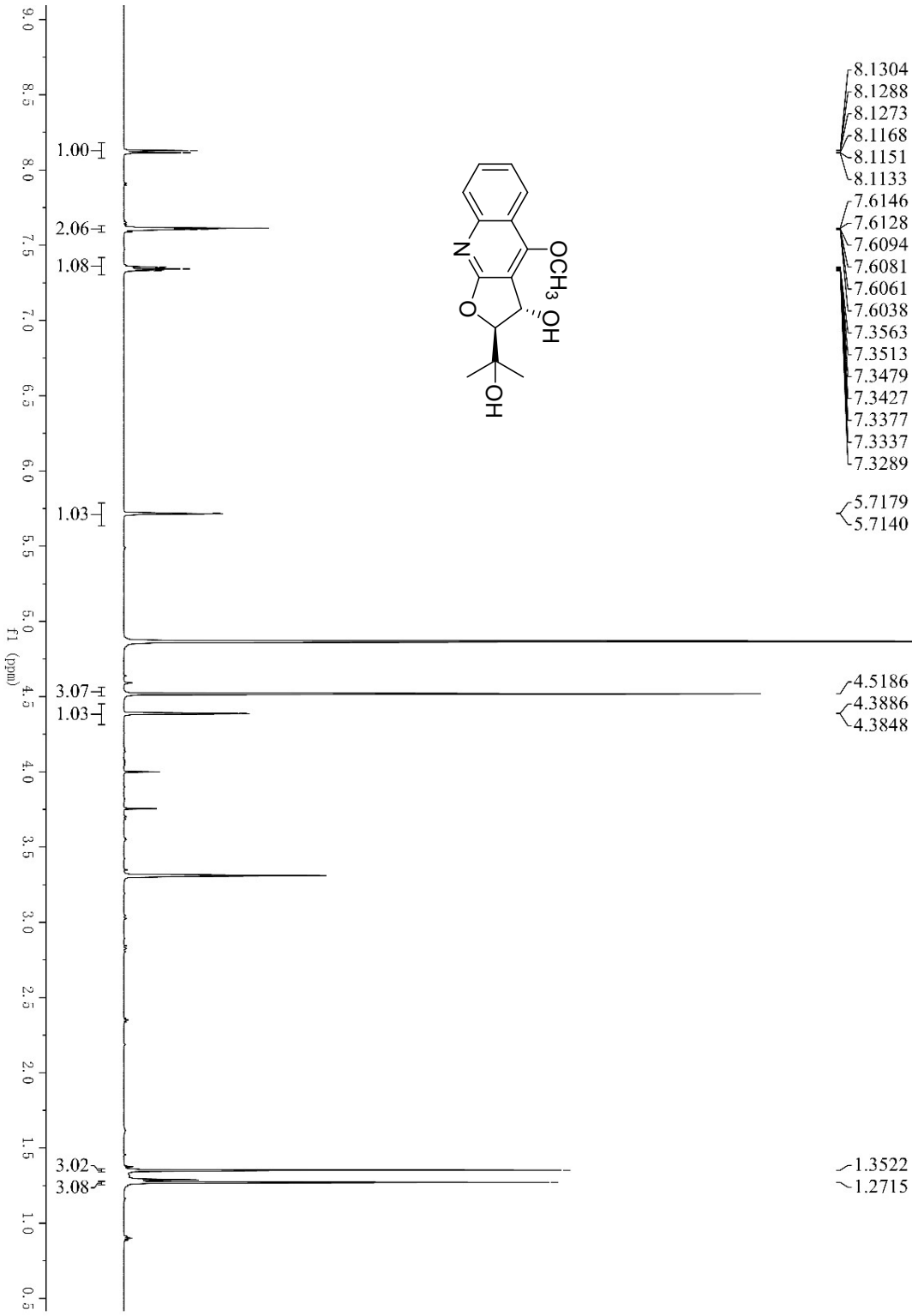


Fig. S62 HSQC spectrum of **7**

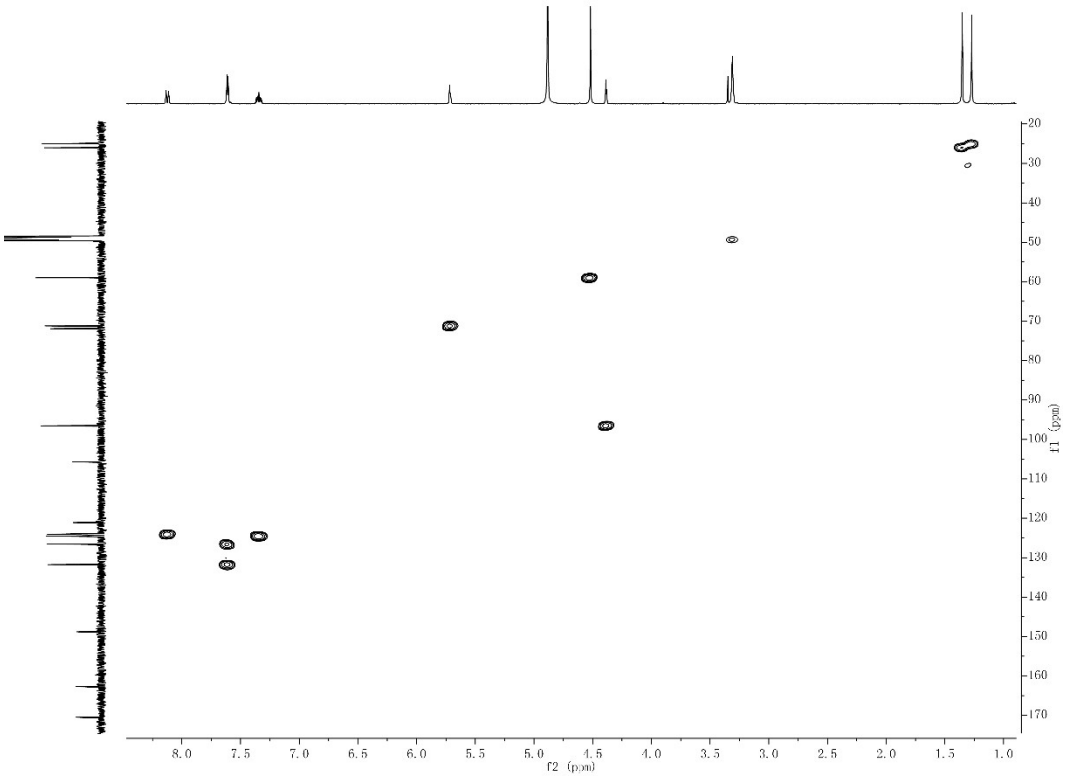


Fig. S63 HSQC spectrum of **7**

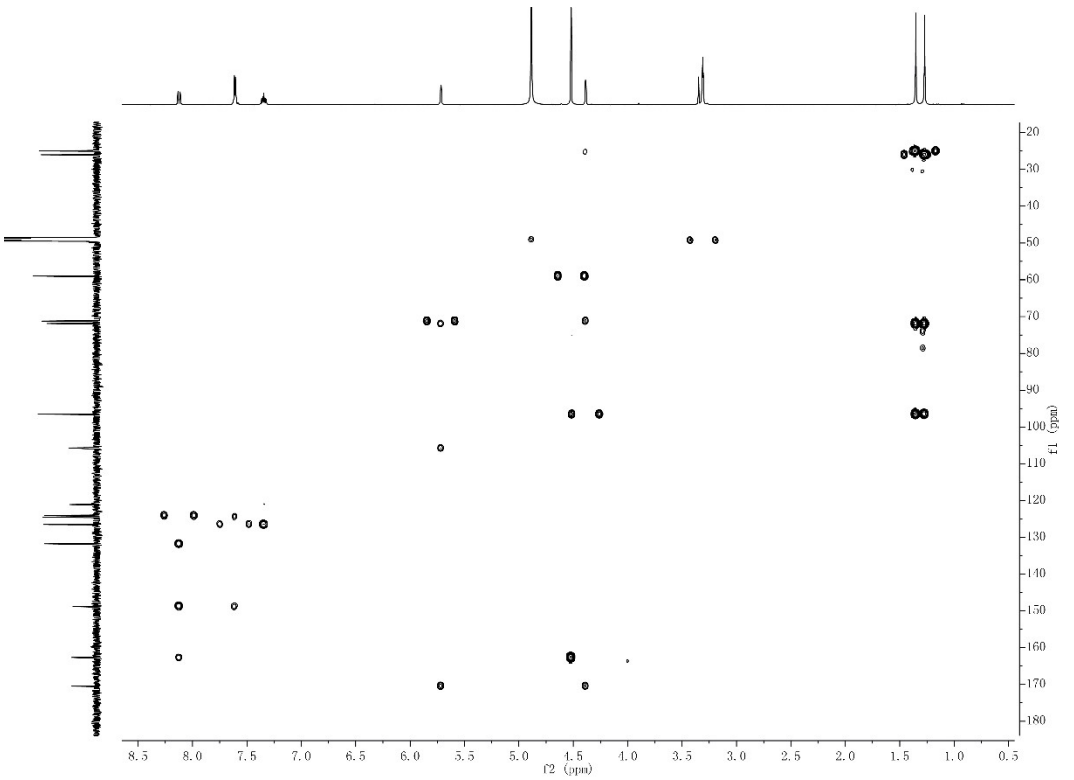


Fig. S64 COSY spectrum of **7**

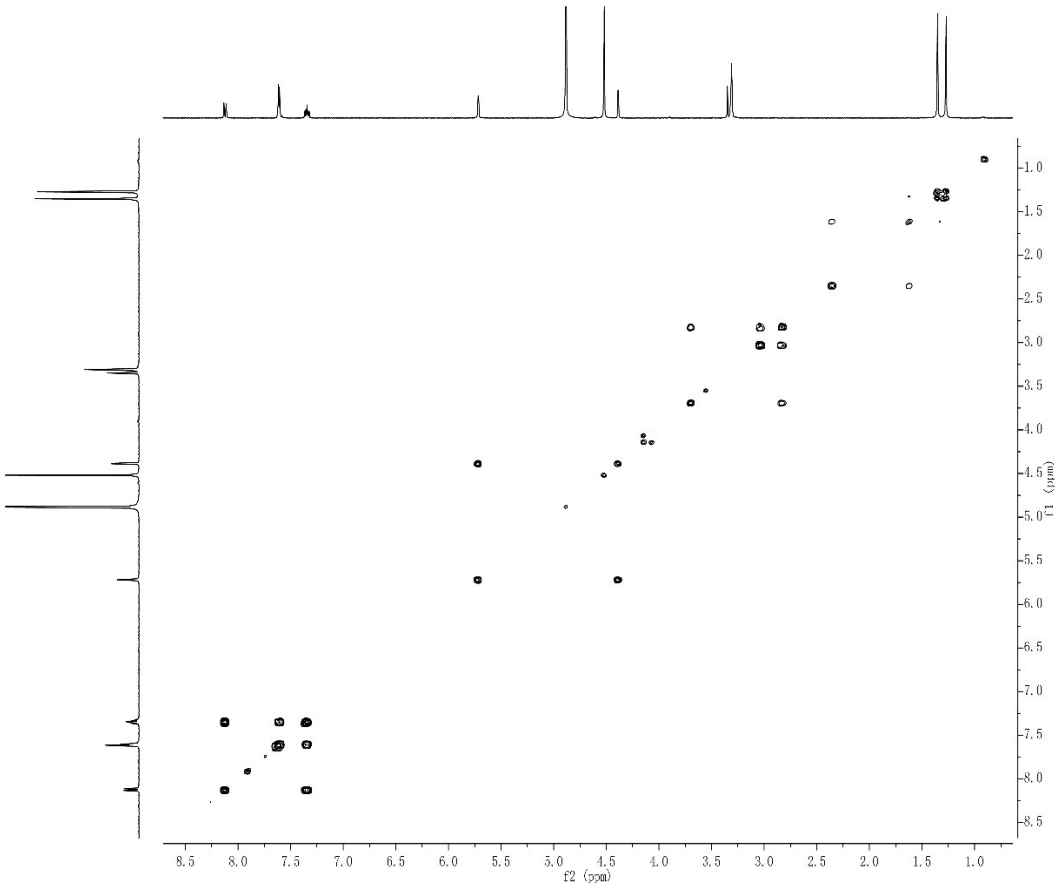


Fig. S65. ESI-MS spectrum of **7**

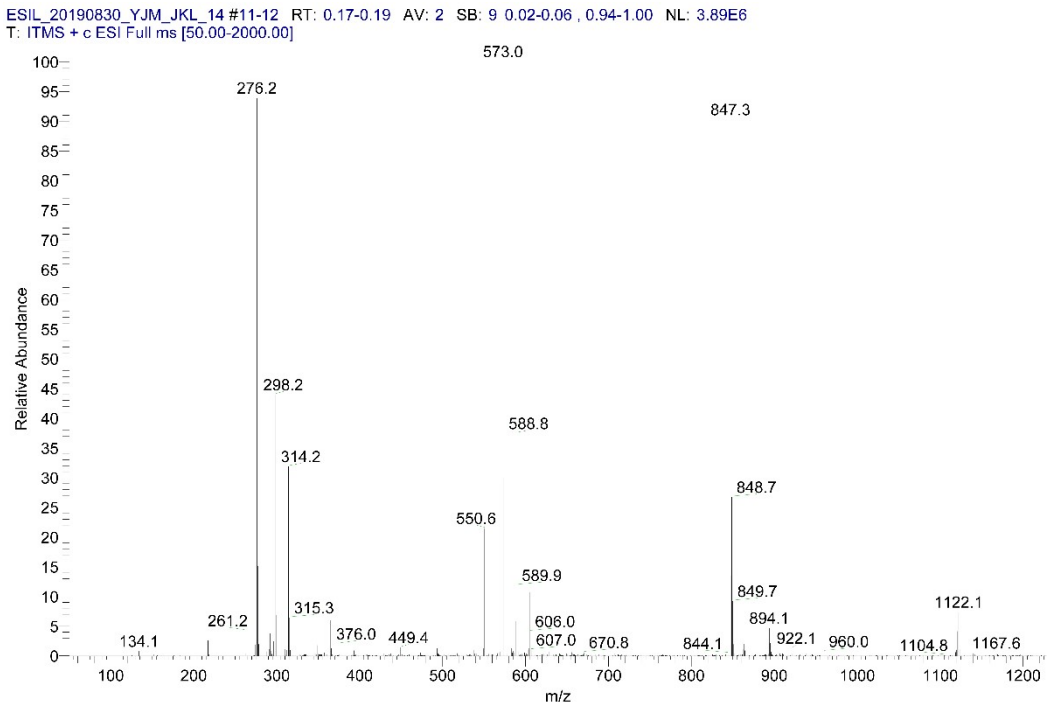


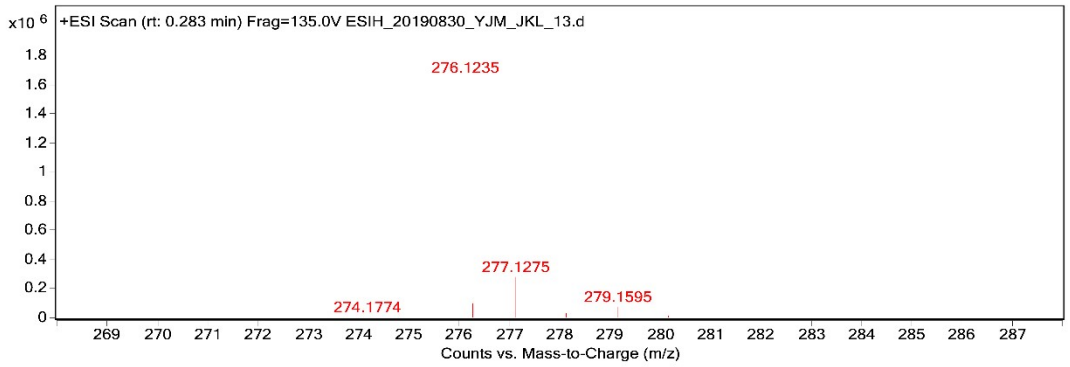
Fig. S66 HRESI-MS spectrum of **7**

Qualitative Analysis Report

Data Filename	ESIH_20190830_YJM_JKL_13.d	**Sample Name**	JAZ-6-5B
Sample Type	Sample	**Position**	P1-B7
Instrument Name	Agilent G6520 Q-TOF	**Acq Method**	20160322_MS_ESIH_POS_1min.m
Acquired Time	8/30/2019 20:01:05	**IRM Calibration Status**	Success
DA Method	small molecular data analysis method.m	**Comment**	ESIH by ZZY

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
276.1235	276.123	-0.42	-1.51	C15 H18 N O4	(M+H)+

--- End Of Report ---

Fig. S67 ^{1}H NMR spectrum of (+)-**8** in $CDCl_3$

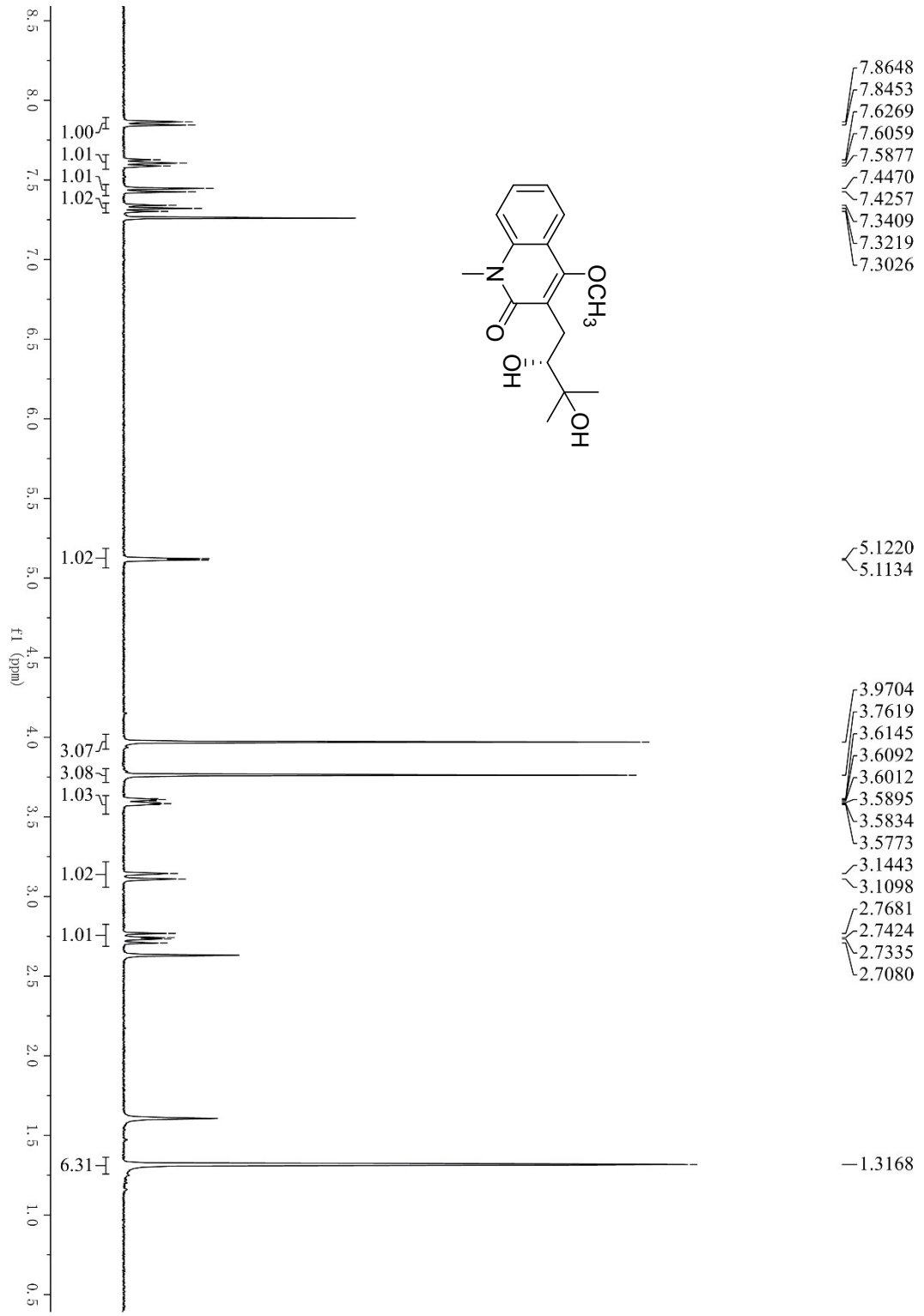


Fig. S68 ^{13}C NMR spectrum of (+)-**8** in $CDCl_3$

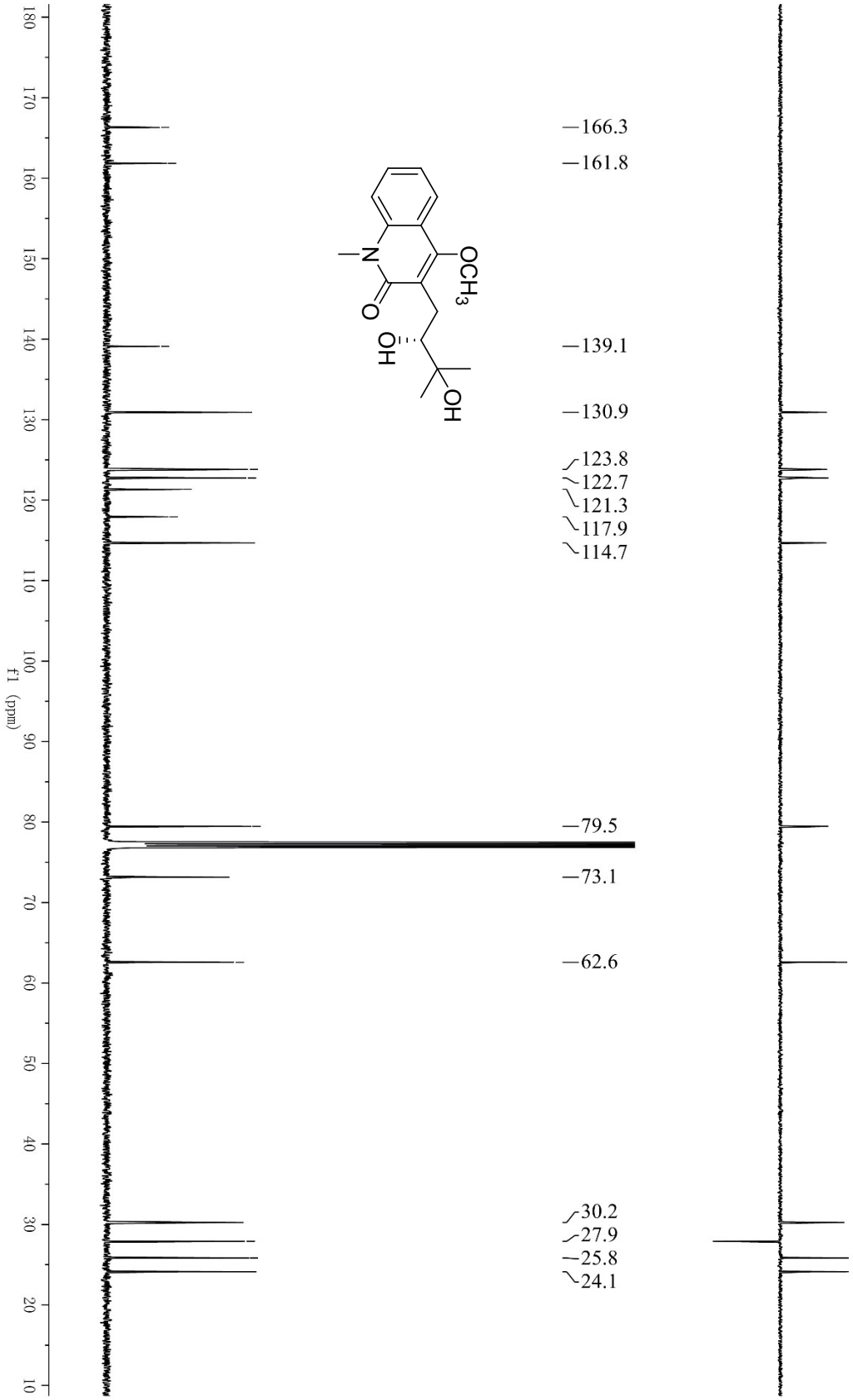


Fig. S69 ^{1}H NMR spectrum of (–)-**8** in $CDCl_3$

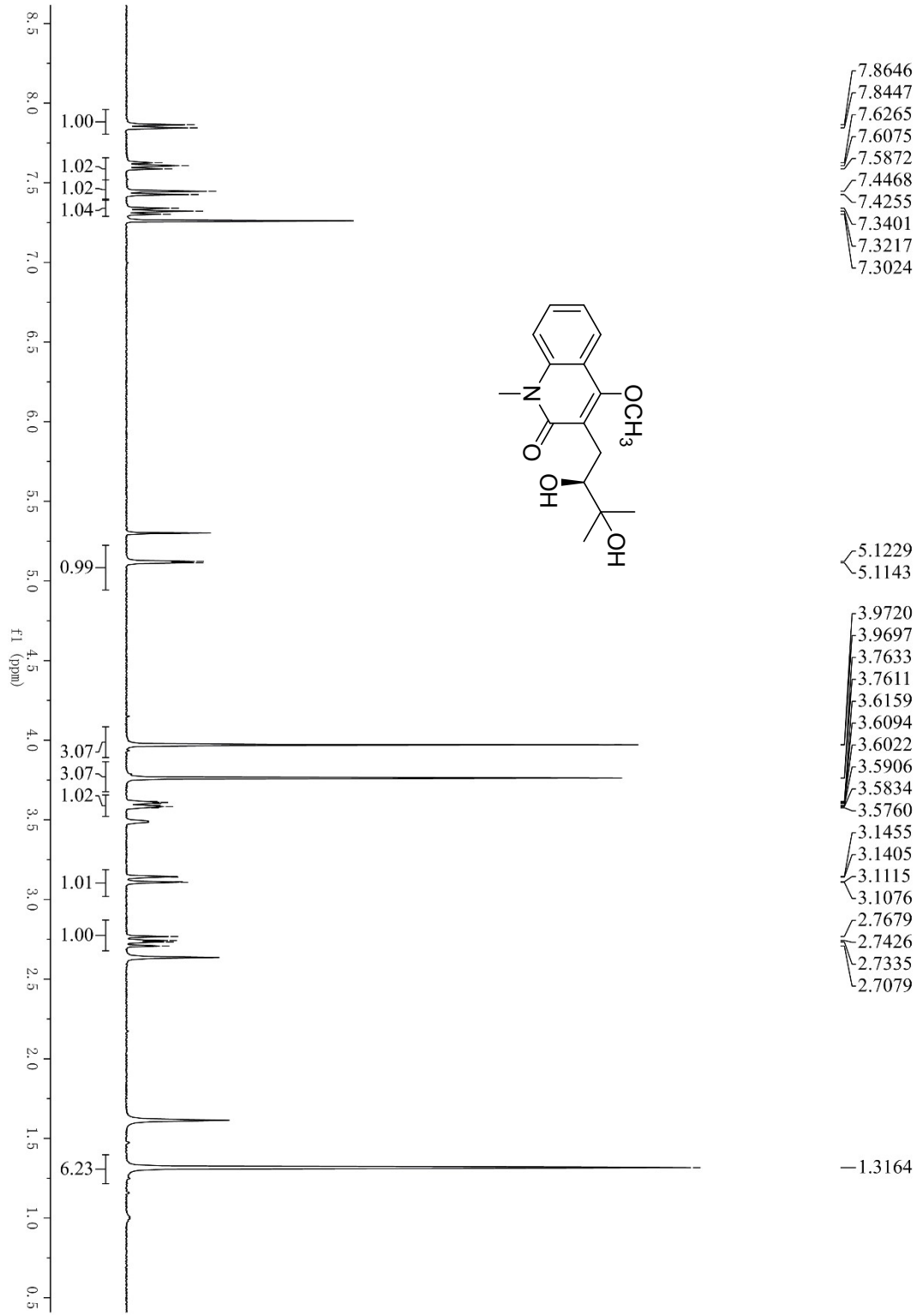


Fig. S70 ESI-MS spectrum of **8**