Supplementary Material

Euphorane C, an unusual C17-norabietane diterpenoid from *Euphorbia dracunculoides* induces cell cycle arrest and apoptosis in human leukemia K562 cells

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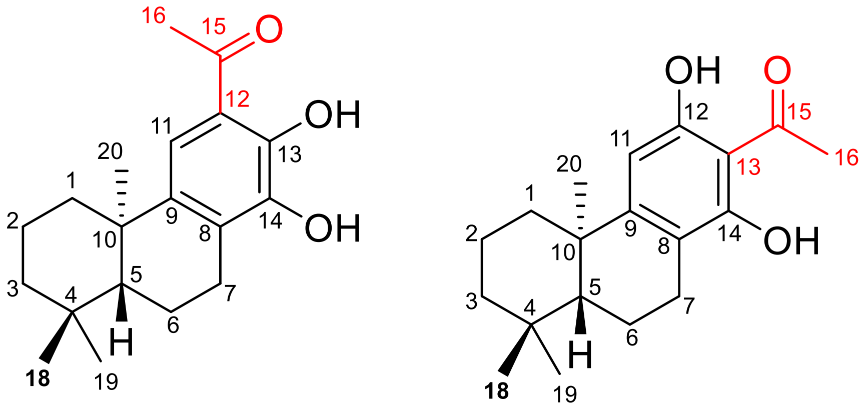
Contents of Supplementary Material

1D NMR calculation of compound 3

Two positional isomers of **3a** and **3b** (Fig. S1) were studied by quantum chemical DFT calculations of their theoretical 1D NMR chemical shifts. Conformational analyses were first carried out via Monte Carlo searching using molecular mechanism with MMFF force field in the *Spartan 18* program.[1] The results showed one lowest energy conformer for **3a** (Fig. S2), and four ones for **3b** (Fig. S3) within an energy window of 2.0 Kcal/mol (Table S1). These conformers were reoptimized using DFT at the B3LYP/6-31G(d) level in gas phase using the Gaussian 09 program.[2] One conformer of **3aC1** (Fig. S2) and three conformers of **3bC1–3bC3** (Fig. S4) whose relative Gibbs free energies in the range of 0–1.5 Kcal/mol were refined and considered for next step. Gauge-Independent Atomic Orbital (GIAO) calculations of their ^{1}H and ^{13}C NMR chemical shifts (Table S2 and S3) were accomplished by density functional theory (DFT) at the rmpw1pw91/6-31+g(d,p) level in PCM (Pyridine). The calculated NMR data of the lowest energy conformers for each compound were averaged according to the Boltzmann distribution theory and their relative Gibbs free energy (ΔG). The ^{1}H and ^{13}C NMR chemical shifts for TMS were calculated by the same protocol and used as the reference. The experimental and calculated data (Table S4) were analyzed by the improved probability DP4+ method.[3]

The experimental 1D NMR data of **3** and calculated 1D NMR data of **3a** and **3b** were analyzed. The final score for **3b** (100.00%) showed an absolute advantage to that of **3a** (0.00%) (Table S5), which further secured the structure of **3**.

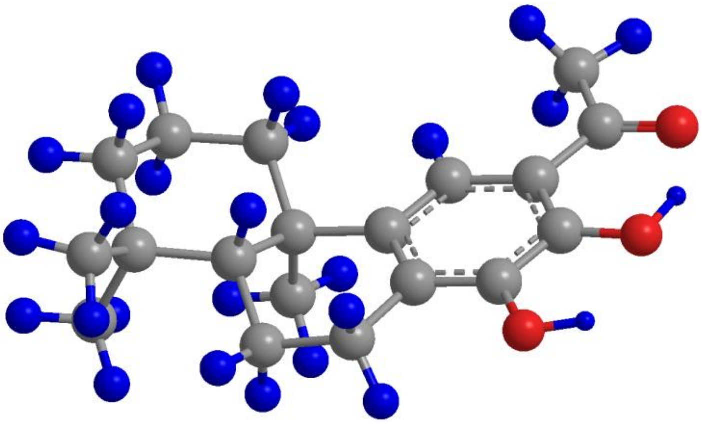


3a **3b**

Fig. S1. The structures of **3a** and **3b**.

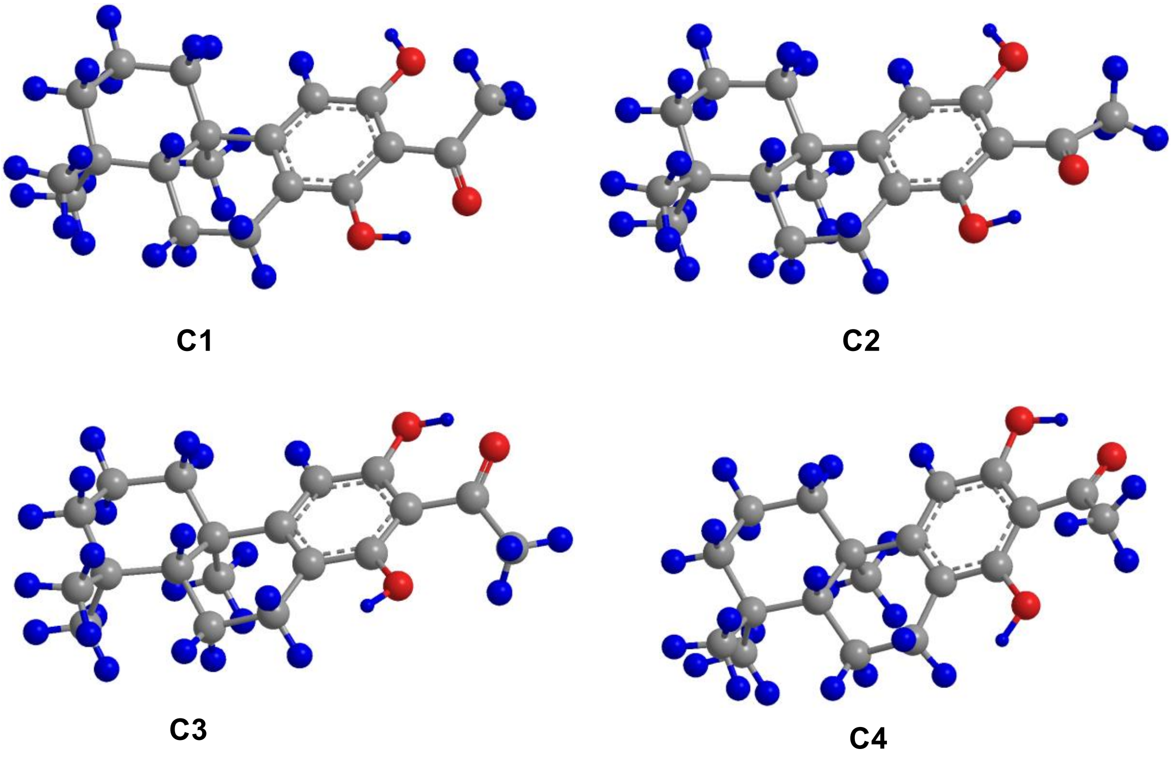
Table S1. Energy analysis for MMFF conformational searching.

3a		
Conf.	rel. E (kcal/mol)	Boltzmann Dist.
3aC1	0.00	1
3b		
Conf.	rel. E (kcal/mol)	Boltzmann Dist.
3bC1	0.00	0.452
3bC2	0.03	0.428
3bC3	1.18	0.062
3bC4	1.32	0.049



3aC1

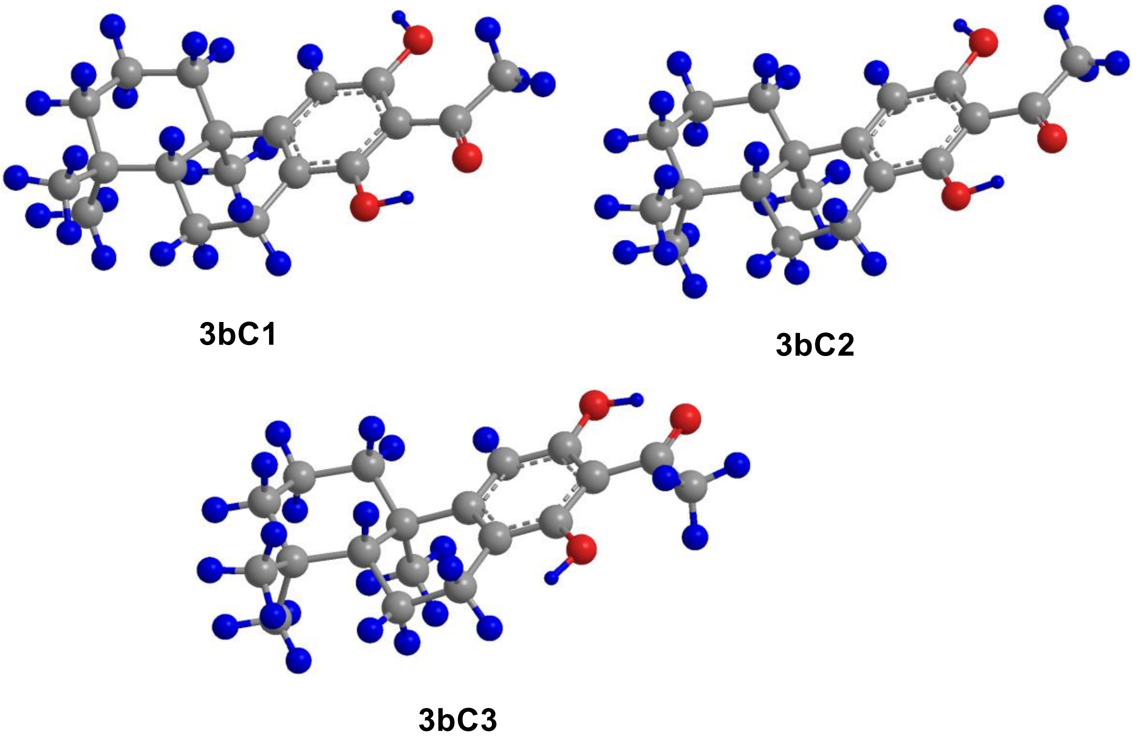
Fig. S2. MMFF lowest energy conformer for **3a**.



C1 C2

C3 C4

Fig. S3. MMFF lowest energy conformers for **3b**.



3bC1 3bC2

3bC3

Fig. S4. Three reoptimized conformers using DFT at the B3LYP/6-31G(d) level in gas phase

Table S2. Calculated ^{13}C-NMR data for reoptimized conformers of **3a** and **3b**.

Carbon number	**3a**	**3b**		
	3aC1	**3bC1**	**3bC2**	**3bC3**
1	39.8295	38.857	38.8546	39.0593
2	22.0977	22.0024	22.0016	21.9459
3	41.3768	41.2167	41.2161	41.1674
4	37.0659	37.1441	37.144	37.2255
5	50.6227	50.3569	50.3557	49.9751
6	21.5601	21.6411	21.6417	21.7002
7	29.1285	27.5788	27.5783	26.1694
8	129.4494	115.1672	115.1678	107.9282
9	139.3258	157.0774	157.0778	157.7751
10	42.4435	43.4352	43.4356	43.5857
11	115.9095	99.3223	99.3225	103.5911
12	115.3503	153.5003	153.4999	154.329
13	144.2199	106.0238	106.0222	106.5917
14	139.764	160.5718	160.5713	160.3199
15	202.1541	200.2116	200.2099	200.4681
16	28.4249	35.1471	35.1479	35.5971
18	33.7189	33.6517	33.6499	33.5774
19	23.2036	23.2034	23.204	23.2049
20	27.5434	26.0104	26.0144	25.5964

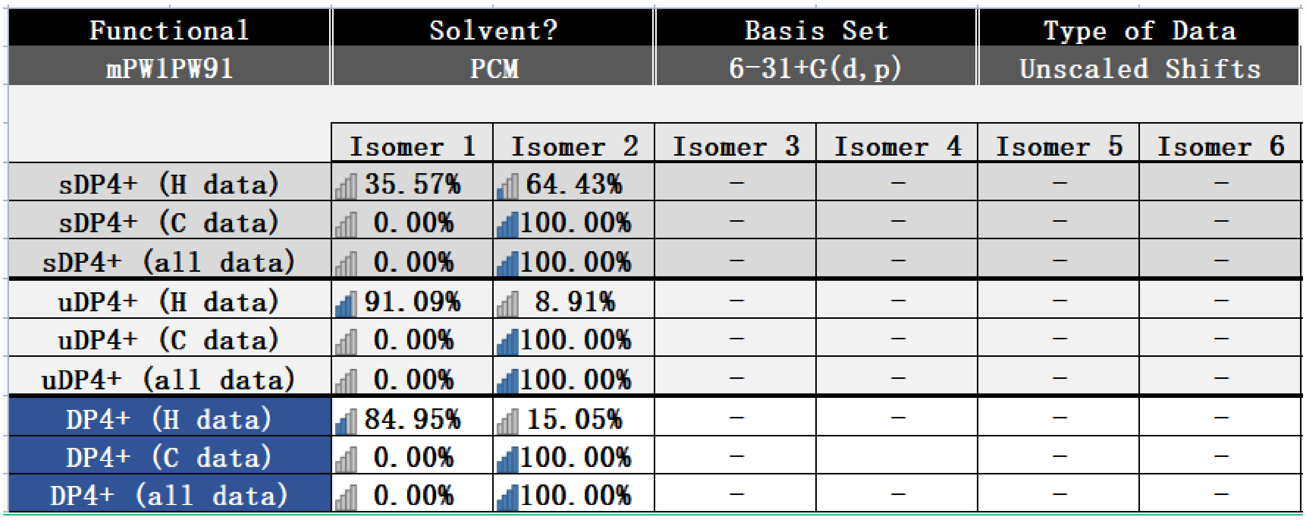
Table S3. Calculated ^{1}H-NMR data for reoptimized conformers of **3a** and **3b**.

Proton number	**3a**	**3b**		
	3aC1	**3bC1**	**3bC2**	**3bC3**
1	1.362617	1.286317	1.286517	1.308317
	2.207817	2.037917	2.038017	2.096217
2	1.481417	1.452517	1.452517	1.459617
	1.851317	1.830417	1.830317	1.894317
3	1.402317	1.371117	1.371217	1.383017
	1.274617	1.233017	1.233017	1.242417
5	1.412317	1.369317	1.369517	1.379817
6	1.734217	1.640617	1.640617	1.788617
	1.797917	1.760317	1.760417	1.831517
7	2.867617	2.637917	2.637917	2.446417
	2.522717	2.293917	2.294017	2.356317
11	7.372017	6.160217	6.160217	6.437317
16	2.792217	2.840817	2.840517	2.873817
	1.889817	1.946817	1.946617	1.958017
	2.786117	2.848017	2.848617	2.880917
18	1.388417	1.362017	1.362017	1.369617
	0.551117	0.526117	0.526117	0.542417
	0.702317	0.680417	0.680417	0.709617
19	1.387817	1.327917	1.328217	1.350817
	0.974817	0.957817	0.957817	0.954917
	0.443817	0.429017	0.429017	0.449417
20	1.355417	1.280917	1.280917	1.293517
	1.687817	1.638417	1.638717	1.662917
	0.612517	0.652917	0.652917	0.678817

Table S4. DP4+ evaluation of theoretical and experimental NMR data for **3a** (isomer 1) and **3b** (isomer 2).

Fuctional		Solvent?		Basis Set		Type of data	
mPW1PW91		PCM		6-31+G(d,p)		Unscaled Shifts	
		DP4+	0.00%	100.00%	-	-	-
Nuclei	sp2?	Experimenta	Isomer 1	Isomer 2	Isomer 3	Isomer 4	Isomer 5
C		39	39.8295	38.86678343			
C		19.9	22.0977	21.9989725			
C		42.1	41.3768	41.21375564			
C		34	37.0659	37.14844585			
C		50.3	50.6227	50.33572706			
C		19.2	21.5601	21.64457327			
C		24.6	29.1285	27.50249877			
C	x	115.1	129.4494	114.7767972			
C	x	159.8	139.3258	157.1152437			
C		39	42.4435	43.44351154			
C	x	102.9	115.9095	99.55278026			
C	x	160.1	115.3503	153.5448356			
C	x	109.3	144.2199	106.0536929			
C	x	163.1	139.764	160.5579687			
C		205.9	202.1541	200.2246395			
C		33.9	28.4249	35.17176456			
C		33.7	33.7189	33.64683908			
C		22.2	23.2036	23.20376461			
C		24.7	27.5434	25.98994762			
H		1.35	1.362616667	1.287598552			
H		2.08	2.207816667	2.041110375			
H		1.45	1.481416667	1.452899851			
H		1.62	1.851316667	1.833818052			
H		1.13	1.402316667	1.371806182			
H		1.37	1.274616667	1.233523982			
H		1.23	1.412316667	1.369977901			
H		1.59	1.734216667	1.648604177			
H		1.86	1.797916667	1.764206583			
H		3.05	2.867616667	2.627581476			
H		2.7	2.522716667	2.29733165			
H	x	6.7	7.372016667	6.175171661			
H		2.95	2.792216667	2.842455836			
H		2.95	1.889816667	1.947326574			
H		2.95	2.786116667	2.850075927			
H		0.91	1.388416667	1.362426836			
H		0.91	0.551116667	0.526996372			
H		0.91	0.702316667	0.681992581			
H		0.86	1.387816667	1.329294401			
H		0.86	0.974816667	0.957660155			
H		0.86	0.443816667	0.430117648			
H		1.18	1.355416667	1.281596684			
H		1.18	1.687816667	1.639880753			
H		1.18	0.612516667	0.654314481			

Table S5. DP4+ probability of 1D NMR data for **3a** (isomer 1) and **3b** (isomer 2).



Functional	Solvent?	Basis Set	Type of Data
mPW1PW91	PCM	6-31+G(d,p)	Unscaled Shifts

	Isomer 1	Isomer 2	Isomer 3	Isomer 4	Isomer 5	Isomer 6
sDP4+ (H data)	35.57%	64.43%	-	-	-	-
sDP4+ (C data)	0.00%	100.00%	-	-	-	-
sDP4+ (all data)	0.00%	100.00%	-	-	-	-
uDP4+ (H data)	91.09%	8.91%	-	-	-	-
uDP4+ (C data)	0.00%	100.00%	-	-	-	-
uDP4+ (all data)	0.00%	100.00%	-	-	-	-
DP4+ (H data)	84.95%	15.05%	-	-	-	-
DP4+ (C data)	0.00%	100.00%	-		-	-
DP4+ (all data)	0.00%	100.00%	-	-	-	-

ECD calculation for assigning the absolute configuration of 3b

Conformational analyses were first carried out via Monte Carlo searching using molecular mechanism with MMFF force field in the *Spartan 18* program.[1] The results showed four lowest energy conformers for **3b** (Fig. S3) within an energy window of 2.0 Kcal/mol. These conformers were reoptimized using DFT at the B3LYP/6-31G(d) level in gas phase using the Gaussian 09 program.[2] Three conformers of **3b** (Fig. S4) whose relative Gibbs free energies in the range of 0–1.5 Kcal/mol (Table S6) were refined and considered for next step.

The absolute configuration of **3b** was determined by quantum chemical calculations of their theoretical ECD spectra. One of the two enantiomers for **3b**, **5*R*,10*R*-3b**, was arbitrary chosen for theoretical studies. The theoretical ECD were calculated and compared with the corresponding experimental data. All the reoptimized conformers (Fig. S4) mentioned above for **3b** were applied for theoretical ECD calculation. The energies, oscillator strengths, and rotational strengths of the first 30 electronic excitations were calculated using the TD-DFT methodology at the M062X/TZVP level in PCM (acetonitrile) (Table S7). The ECD spectrum was simulated by the overlapping Gaussian function ($\sigma = 0.55$ eV, +15 nm in horizontal axis),[3] in which velocity rotatory strengths of the 30 exited states for **3b** were adopted. To get the final ECD spectrum of **3b**, the simulated spectra of the lowest energy conformers were averaged according to the Boltzmann distribution theory and their relative Gibbs free energy (ΔG). The theoretical ECD curve of **5*S*,10*S*-3b** was obtained by directly reverse that of **5*R*,10*R*-3b**.

The absolute configuration of **3b** (**3**) was studied by comparison of its experimental and calculated ECD spectra. As shown in Fig. S5, the experimental ECD spectrum of **3b** showed three Cotton effects around 200 (–), 230 (+), 275 (–), and 350 (+) nm, respectively, which matched well with those calculated for the **5*R*,10*R*-3b**, indicating that **3b** possessed the same corresponding absolute configuration (5*R*,10*R*).

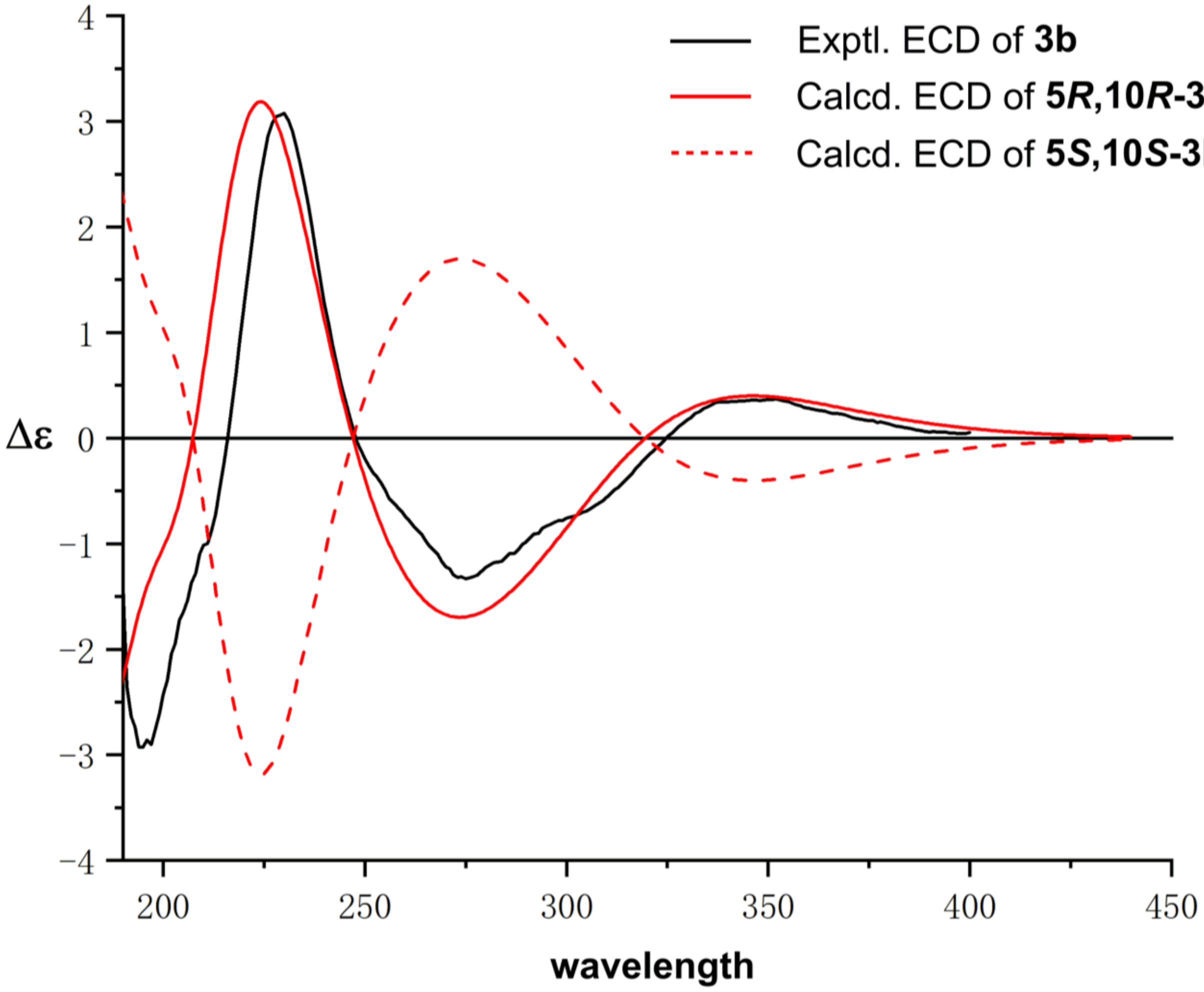


Fig. S5. Experimental and calculated ECD spectra of **3b**.

Table S6. Energy (298.15 K) analysis of reoptimized conformers for **3b**.

Conf.	G (Hartree)	ΔG (Kcal/mol)	Boltzmann Distribution
3bC1	-965.00258	0	0.473265784
3bC2	-965.00258	0.00062751	0.47276455
3bC3	-965.00053	1.28576799	0.053969666

ECD data

ECD spectrum of each conformation is simulated according to the overlapping Gaussian functions expressed as:

$$\Delta\varepsilon(E) = \frac{1}{2.296\times10^{-39}\sqrt{\pi}\sigma}\sum_{i}^{\mathrm{A}}\Delta E_i \mathrm{R}_i e^{[-(E-\Delta Ei)^2/\sigma^2]}$$

Where σ is half the bandwidth at 1/e peak height and expressed in energy units. The parameters ΔE_i and R_i are the excitation energies and rotational strengths for the transition *i*, respectively. The above function is converted to Δε, λ (wavelength) correlations as:

$$\Delta\varepsilon(\lambda) = \frac{1}{2.296\times10^{-39}\sqrt{\pi}\sigma}\sum_{i}^{\mathrm{A}}\Delta E_i \mathrm{R}_i e^{[-(1240/\lambda-\Delta Ei)^2/\sigma^2]}$$

and then simulation was accomplished by using the Excel 2003 and the Origin 9.1 software. To get the final spectra, all the simulated spectra of conformations of each compound were averaged according to their energy and the Boltzmann distribution theory expressed as:

$$\frac{N_i^*}{N} = \frac{g_i e^{-\varepsilon_i/k_B T}}{\sum g_i e^{-\varepsilon_i/k_B T}}$$

Table S7. Calculated ECD data for **3b** in acetonitrile.

state	**3bC1**		**3bC2**		**3bC3**	
	Excitation energies(eV)	Rotatory Strengths*	Excitation energies(eV)	Rotatory Strengths*	Excitation energies(eV)	Rotatory Strengths*
1	4.0579	6.9867	4.0579	6.9797	4.0587	4.9042
2	4.2901	-6.9843	4.2901	-6.9733	4.274	-2.5845
3	4.9061	-6.2852	4.9062	-6.3148	4.9321	-10.3882
4	6.052	15.4956	6.052	15.383	6.0506	5.4153
5	6.2902	0.3984	6.2902	0.397	6.3326	9.8008
6	6.3367	10.9571	6.3367	10.9876	6.4018	-2.2638
7	6.4241	-12.3651	6.4241	-12.3922	6.4426	-0.0669
8	6.581	-17.4991	6.5809	-17.4552	6.5565	-17.5681
9	6.8652	6.1046	6.8653	6.163	6.8667	-17.865
10	6.8762	20.3683	6.8764	20.3969	6.9297	0.7848

11	7.026	-8.5439	7.0259	-8.5652	7.3405	-1.0628
12	7.2609	-10.5106	7.2611	-10.552	7.3486	18.7391
13	7.3128	-2.7078	7.3127	-2.6957	7.3683	15.4957
14	7.5202	0.5789	7.5202	0.5392	7.5069	-5.1573
15	7.548	-14.3378	7.548	-14.2572	7.5625	-1.9697
16	7.6175	-1.1608	7.6175	-1.169	7.5872	-2.9721
17	7.6625	11.0854	7.6625	11.1326	7.62	1.4442
18	7.7073	-2.5132	7.7072	-2.5572	7.6878	-2.9883
19	7.8886	1.5327	7.8886	1.5564	7.8182	-3.9006
20	7.9112	1.9753	7.9112	1.8939	7.9042	19.2151
21	7.9222	32.6119	7.9222	32.7062	7.9524	-3.7909
22	8.0222	-1.0571	8.0222	-1.0548	7.9737	2.5734
23	8.061	-20.5528	8.061	-20.4861	8.0569	0.4374
24	8.0774	0.0758	8.0774	0.0063	8.0921	-2.8951
25	8.0811	3.1161	8.0811	3.2289	8.2327	6.7538
26	8.1848	-3.1283	8.1848	-3.1111	8.2772	27.1371
27	8.2207	-42.0131	8.2207	-42.0113	8.2978	-13.9592
28	8.279	7.0449	8.2789	7.0176	8.3109	-22.4117
29	8.3159	13.1932	8.316	13.0817	8.321	21.0694
30	8.3255	16.838	8.3255	16.9175	8.3647	-11.478

References

(1) *Spartan 18*; Wavefunction Inc.:Irvine, CA.

(2) *Gaussian 09*, Revision A.1, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, 2009.

(3) Grimblat, N.; Zanardi, M. M.; Sarotti, A. M. *J. Org. Chem.* **2015**, *80*, 12526–12534.

NMR data of compounds 5–16.

13-Acetyloxy-atis-16-ene-3,14-dione (5). ^{1}H NMR (Pyridine-d_5, 400 MHz) δ_H 5.42 (1H, d, J = 2.6 Hz), 5.06 (1H, s), 4.88 (1H, s), 2.88 (1H, d, J = 2.8 Hz), 2.56 (1H, ddd, J = 15.5, 13.3, 6.4 Hz), 2.43 (1H, dt, J = 13.3, 3.0 Hz), 2.31–2.38 (m), 2.08 (3H, m), 1.73–1.87 (m), 1.66 (1H, ddd, J = 13.1, 6.1, 3.0 Hz), 1.49–1.57 (m), 1.36 (m), 1.21–1.28 (m), 1.12 (3H, s), 0.92 (3H, s), 0.86 (1H, m), 0.81 (3H, s); ^{13}C NMR (Pyridine-d_5, 100 MHz) δ_C 13.7, 20.5, 21.1, 22.2, 26.0, 26.7, 31.2, 34.7, 37.1, 38.1, 43.7, 44.2, 47.9, 48.3, 51.0, 55.3, 75.6, 111.0, 143.6, 170.6, 212.5, 215.3.

***Ent*-3,14-dioxo-16-atisene (6).** ^{1}H NMR (CDCl$_3$, 400 MHz) δ_H 4.86 (1H, dd, J = 3.8, 2.6 Hz), 4.64 (1H, dd, J = 3.8, 2.6 Hz), 2.70 (1H, m), 2.53 (1H, ddd, J = 15.7, 13.4, 6.4 Hz), 2.24–2.33 (m), 2.19 (1H. m), 1.85–1.90 (1H, m), 1.80 (1H, ddd, J = 13.4, 6.3, 3.1 Hz), 1.65 (1H, m), 1.57–1.62 (2H, m), 1.45 (1H, m), 1.32 (1H, td, J = 13.3, 5.3 Hz), 1.25 (1H, dd, J = 12.4, 2.5 Hz), 1.04 (3H, s), 0.98 (3H, s), 0.89 (1H, td, J = 13.3, 4.7 Hz), 0.84 (3H, s); ^{13}C NMR (CDCl$_3$, 100 MHz) δ_C 12.7, 19.9, 21.8, 25.9, 27.7, 31.1, 34.0, 37.1, 37.5, 38.2, 42.5, 44.5, 47.5, 47.6, 51.7, 55.2, 107.1, 147.0, 216.3, 216.5.

17-Hydroxyjolkinolide A (7). ^{1}H NMR (CDCl$_3$, 400 MHz) δ_H 5.55 (1H, d, J = 5.4 Hz), 4.62 (2H, s), 4.04 (1H, s), 2.63 (1H, J = 5.4 Hz), 2.09 (1H, td, J = 13.8, 5.5 Hz), 1.79 (1H, m), 1.71 (1H, d, J = 12.4 Hz), 1.59 (1H, m), 1.42–1.52 (m), 1.26 (1H, m), 1.21 (2H, m), 0.93 (3H, s), 0.85 (3H, s), 0.72 (3H, s); ^{13}C NMR (CDCl$_3$, 100 MHz) δ_C 15.0, 18.4, 20.8, 21.9, 33.4, 33.5, 33.9, 39.9, 41.5, 51.7, 53.5, 54.4, 56.2, 61.3, 106.4, 127.5, 146.6, 147.3, 169.2.

Jolkinolide E (8). ^{1}H NMR (CDCl$_3$, 400 MHz) δ_H 6.17 (1H, s), 4.77 (1H, dd, J = 13.3, 5.9 Hz), 2.46 (1H, dd, J = 13.5, 6.2 Hz), 2.40 (1H, m), 2.10 (m), 1.81 (1H, d, J = 12.6 Hz), 1.73 (1H, m), 1.71 (3H, s), 1.40–1.49 (m), 1.26–1.37 (m), 1.09 (m), 1.01 (m), 0.82 (3H, s), 0.80 (3H, s), 0.74 (3H, s). ^{13}C NMR (CDCl$_3$, 100 MHz) δ_C 8.0, 16.6, 18.9, 21.6, 23.7, 27.3, 33.3, 33.7, 37.0, 39.4, 41.4, 41.7, 51.7, 55.0, 76.0, 113.7, 115.8, 152.4, 156.4, 175.4.

Jolkinolide A (9). ^{1}H NMR (CDCl$_3$, 400 MHz) δ_H 5.47 (1H, d, J = 5.3 Hz), 3.72 (1H, s), 2.64 (1H, d, J = 5.2 Hz), 2.13 (1H, td, J = 13.9, 5.6 Hz), 2.07 (3H, s), 1.82 (1H, m), 1.74 (1H, J = 12.7 Hz), 1.60–1.63 (2H, m), 1.44–1.55 (m), 1.19–1.31 (4H, m), 0.95 (3H, s), 0.86 (3H, s), 0.73 (3H, s); ^{13}C NMR (CDCl$_3$, 100 MHz) δ_C 8.7, 15.0, 18.4, 20.8, 21.9, 33.5, 33.5, 34.1, 39.8, 41.4, 41.5, 51.8, 53.5, 54.5, 61.2, 104.1, 125.2, 145.0, 147.4, 170.6.

Jolkinolide B (10). ^{1}H NMR ($CDCl_3$, 500 MHz) δ_H 4.03 (1H, s), 3.67 (1H, s), 2.28 (1H, s), 2.07 (3H, s), 2.00 (1H, td, J = 14.3, 5.4 Hz), 1.92 (1H, d, J = 12.6 Hz), 1.80 (1H, m), 1.52−1.56 (2H, m), 1.43−1.48 (3H, m), 1.30 (1H, m), 1.21−1.26 (2H, m), 1.10 (1H, dd, J = 12.3, 2.3 Hz), 0.93 (3H, s), 0.84 (3H, s), 0.81 (3H, s)**.** ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C 8.7, 15.4, 18.4, 20.8, 21.8, 33.4, 33.5, 35.6, 39.1, 39.2, 41.2, 47.9, 53.4, 55.3, 60.9, 66.0, 85.2, 130.2, 148.6, 169.6.

(23*E*)-25-methoxycycloart-23-en-3*β*-ol (11). ^{1}H NMR ($CDCl_3$, 400 MHz) δ_H 5.52 (1H, ddd, J = 14.3, 8.5, 6.0 Hz), 5.38 (1H, d, J = 15.8 Hz), 3.27 (1H, m), 3.14 (3H, s), 2.19 (1H, m), 1.87–2.01 (2H, m), 1.70−1.82 (3H, m), 1.47−1.61 (9H, m), 1.26 (m), 1.25 (6H, s), 1.05−1.13 (2H, m), 0.96 (3H, s), 0.96 (3H, s), 0.87 (3H, s), 0.86 (3H, d, J = 5.5 Hz), 0.80 (3H, s). 0.55 (1H, d, J = 4.0 Hz), 0.32 (1H, d, J = 4.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 14.1, 18.2, 18.5, 19.4, 20.1, 21.2, 25.6, 25.9, 26.1, 26.2, 26.3, 26.6, 28.2, 30.0, 30.5, 32.1, 32.9, 35.7, 36.4, 39.5, 40.6, 45.4, 47.2, 48.1, 48.9, 50.4, 52.1, 75.0, 78.9, 128.9, 136.7.

Spiroinonotsuoxodiol (12). ^{1}H NMR ($CDCl_3$, 400 MHz) δ_H 5.08 (1H, t, J = 6.7 Hz), 4.30 (1H, m), 3.48 (1H, s), 3.21 (1H, dd, J = 11.3, 4.4 Hz), 2.24 (1H, m), 1.74–2.0 (m), 1.68 (3H, s), 1.63 (m), 1.60 (3H, s), 1.46 (3H, s), 1.20 (3H, s), 0.94 (3H, s), 0.91 (3H, d, J = 6.4 Hz), 0.65 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 16.4, 17.1, 17.8, 18.6, 18.8, 19.8, 25.0, 25.9, 27.2, 28.3, 29.8, 30.0, 30.8, 30.9, 34.2, 35.5, 36.2, 38.4, 47.7, 49.0, 50.4, 50.5, 61.4, 64.3, 79.9, 80.8, 125.0, 131.3, 215.7.

Agnosterol (13). ^{1}H NMR ($CDCl_3$, 400 MHz) δ_H 5.47 (1H, m), 5.31 (1H, m), 5.10 (1H, t, J = 7.0 Hz), 3.25 (1H, dd, J = 11.2, 4.6 Hz), 2.20 (2H, m), 1.96–2.11 (m), 1.68 (3H, s), 1.60 (3H, s), 1.38−1.47 (m), 1.26–1.30 (m), 1.09 (2H, m), 1.03 (m), 1.01 (3H, s), 0.98 (3H, s), 0.90 (3H, d, J = 6.5 Hz), 0.88 (6H, s), 0.56 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 15.7, 15.8, 17.6, 18.4, 22.7, 23.0, 25.0, 25.6, 25.7, 27.8, 27.9, 28.1, 29.7, 31.5, 35.7, 36.1, 36.3, 37.4, 37.9, 38.7, 43.8, 49.1, 50.3, 51.0, 79.0, 116.4, 120.2, 125.2, 131.0, 142.7, 145.9.

Kansenone (14). ^{1}H NMR ($CDCl_3$, 400 MHz) δ_H 5.08 (1H, t, J = 6.8 Hz), 3.28 (1H, dd, J = 11.4, 4.3 Hz), 2.34–2.42 (m), 2.21 (1H, m), 2.11 (1H, m), 1.84–1.92 (m), 1.77 (m), 1.68 (3H, s), 1.60 (3H, s), 1.43−1.55 (m), 1.12 (m), 1.05 (3H, s), 0.99 (3H, s), 0.96 (3H, s), 0.88 (3H, s), 0.87 (3H, d, J = 6.4 Hz), 0.72 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 15.2, 15.9, 17.8, 18.7, 19.0, 23.8, 24.5, 24.9, 25.9, 27.4, 27.5, 28.8, 30.1, 31.5, 34.7, 35.6, 35.8, 35.9, 39.0, 39.4, 44.7, 47.8, 48.3, 48.4, 78.2, 125.2, 131.1, 139.1, 165.5, 198.4.

3β-hydroxy-25-methyloxylanosta-8,23-diene (15). ^{1}H NMR (CDCl$_3$, 400 MHz) δ_H 5.51 (1H, m), 5.37 (1H, d, J = 15.8 Hz), 3.23 (1H, dd, J = 11.6, 4.6 Hz), 3.14 (3H, s), 2.37 (1H, dd, J = 13.4, 5.3 Hz), 2.05 (2H, m), 1.35–1.96 (m), 1.25 (6H, s), 1.11–1.22 (m), 1.00 (3H, s), 0.95 (3H, s), 0.87 (3H, s), 0.82 (3H, d, J = 5.7 Hz), 0.80 (3H, s), 0.78 (3H, s); ^{13}C NMR (CDCl$_3$, 100 MHz) δ_C 15.5, 15.7, 18.9, 19.1, 20.1, 21.5, 24.4, 25.8, 26.0, 27.6, 27.9, 27.9, 28.0, 29.7, 30.9, 35.2, 36.2, 37.2, 38.4, 38.9, 44.1, 49.5, 50.0, 50.3, 50.9, 74.9, 78.9, 128.9, 133.5, 134.0, 136.4.

Cornusalterin A (16). ^{1}H NMR (CDCl$_3$, 400 MHz) δ_H 5.51 (1H, m), 5.37 (1H, d, J = 15.8 Hz), 5.26 (1H, m), 3.24 (1H, dd, J = 11.2, 4.2 Hz), 3.15 (3H, s), 2.36 (1H, m), 2.12–2.23 (2H, m), 1.90–2.01 (2H, m), 1.79 (1H, m), 1.58–1.70 (m), 1.44–1.53 (m), 1.30 (m), 1.25 (6H, s), 0.98 (3H, s), 0.97 (3H, s), 0.86 (3H, s), 0.83 (3H, d, J = 6.9 Hz), 0.75 (3H, s); ^{13}C NMR (CDCl$_3$, 100 MHz) δ_C 13.1, 14.7, 18.1, 18.9, 22.2, 23.9, 25.8, 26.1, 27.3, 27.7, 28.3, 29.7, 33.8, 33.9, 34.9, 36.2, 37.2, 38.3, 39.0, 43.6, 48.9, 50.2, 50.6, 51.2, 53.0, 74.9, 79.2, 117.9, 129.3, 136.3, 145.7.

NMR, HRESIMS, and IR spectra of compounds 1–4

Fig. S6. ^{1}H NMR spectrum of **1** in $CDCl_3$

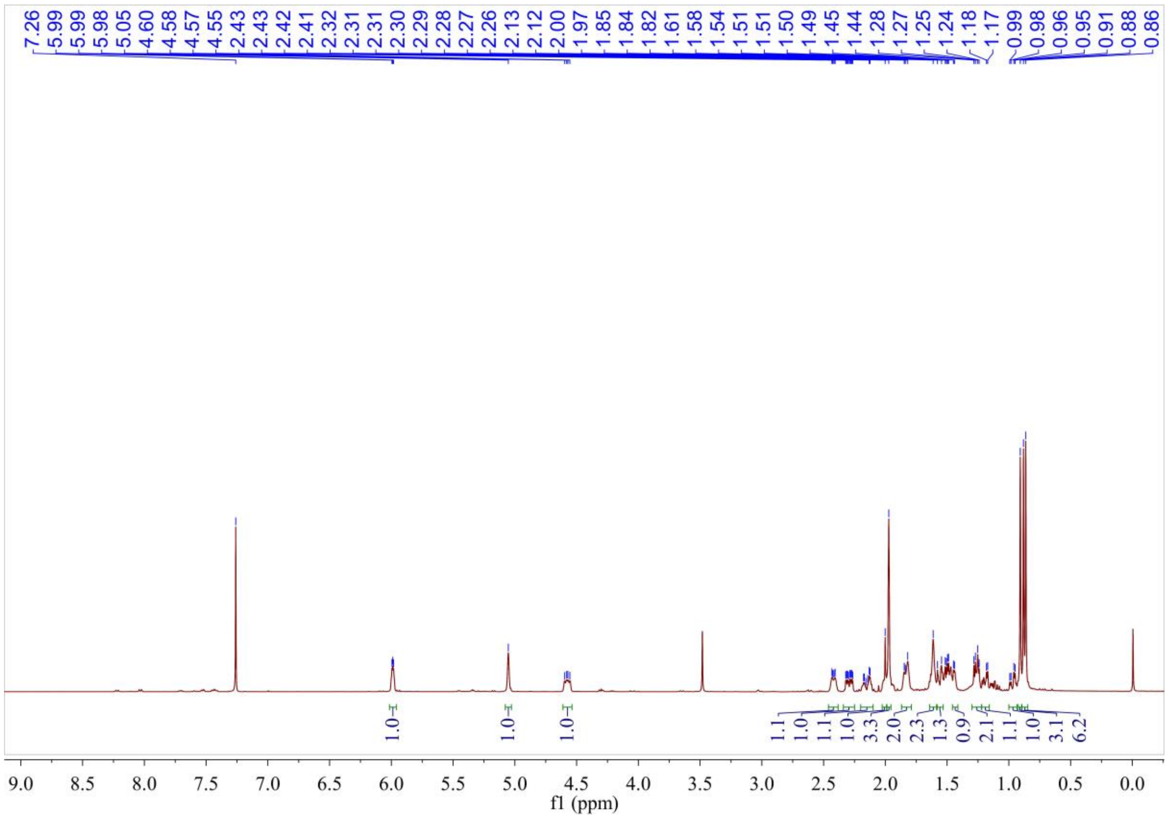


Fig. S7. ^{13}C NMR and DEPT135 spectra of **1** in $CDCl_3$

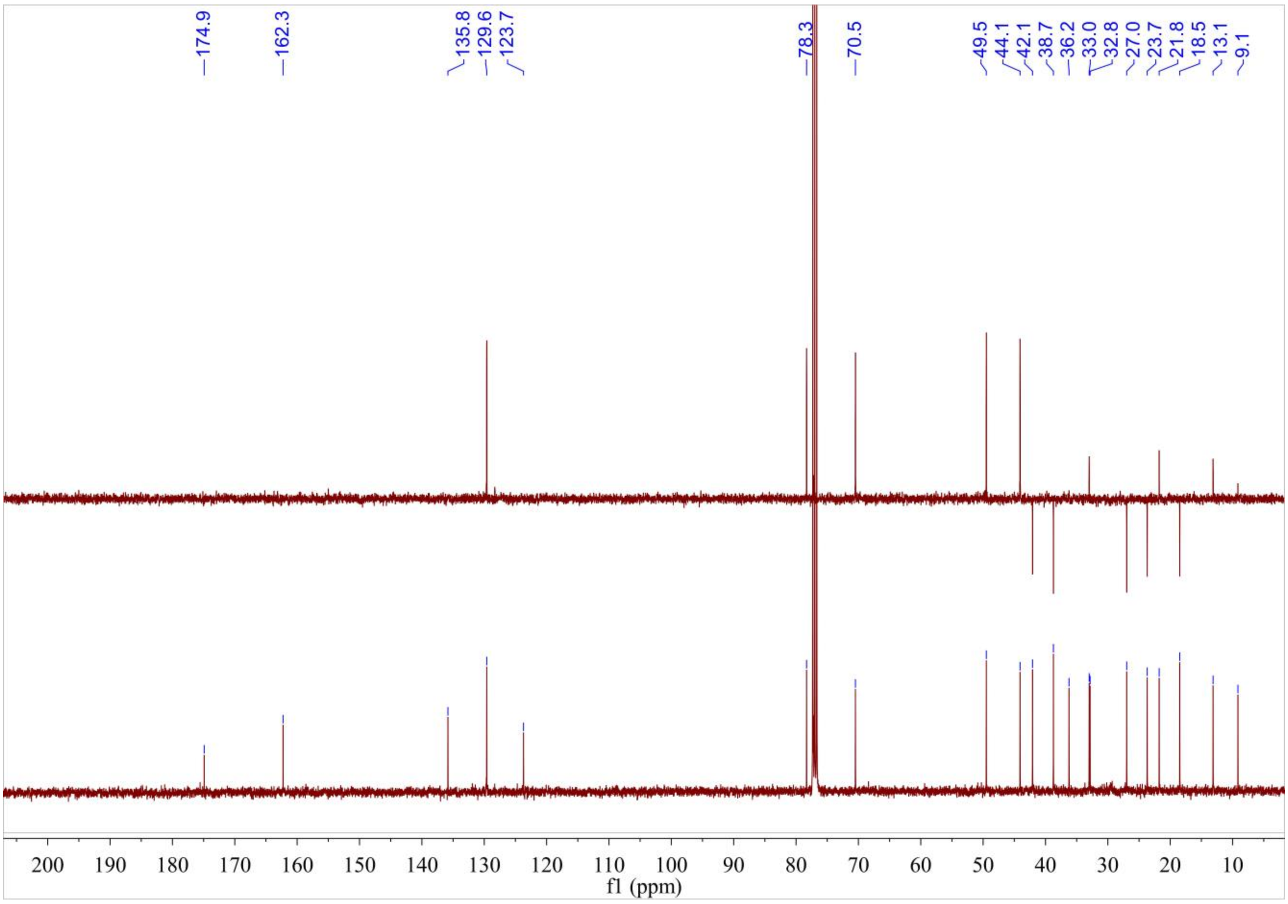


Fig. S8. HSQC spectrum of **1** in $CDCl_3$

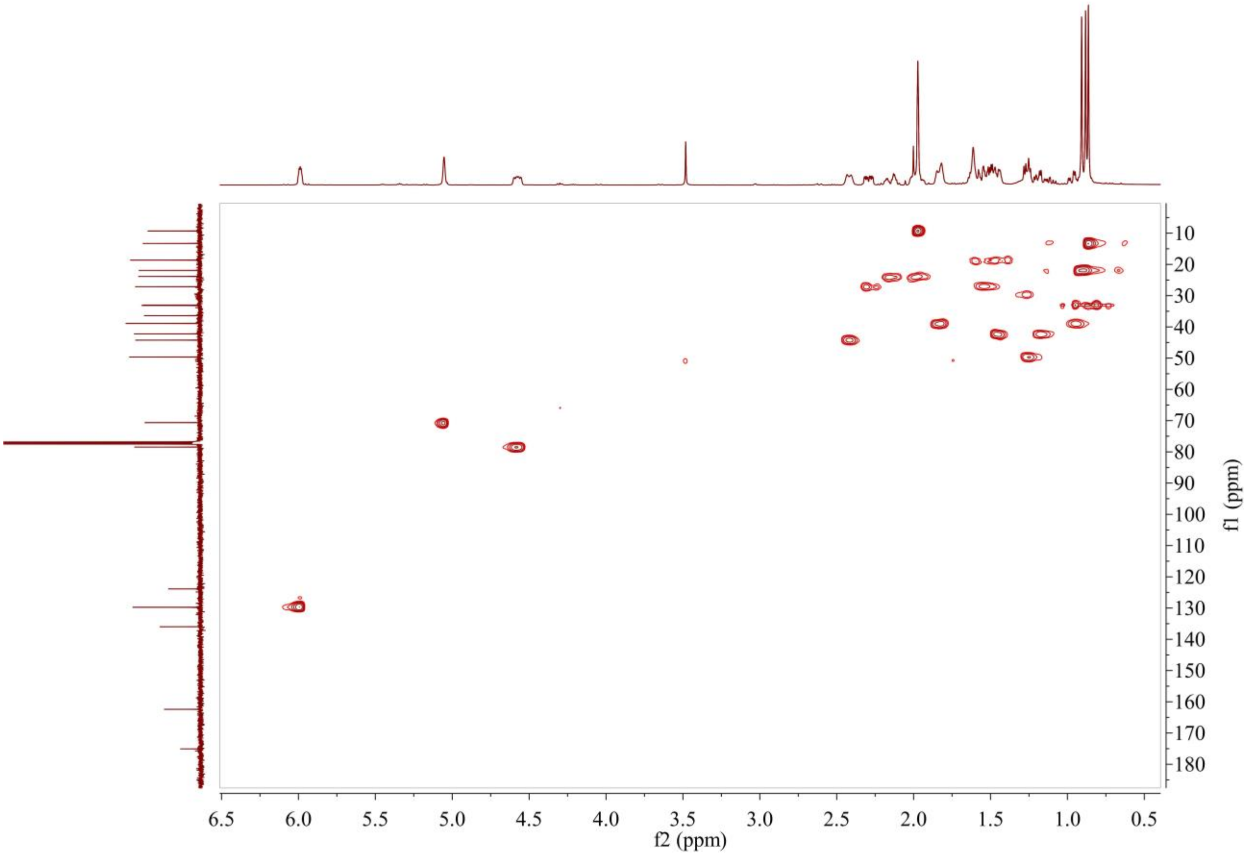


Fig. S9. HMBC spectrum of **1** in $CDCl_3$

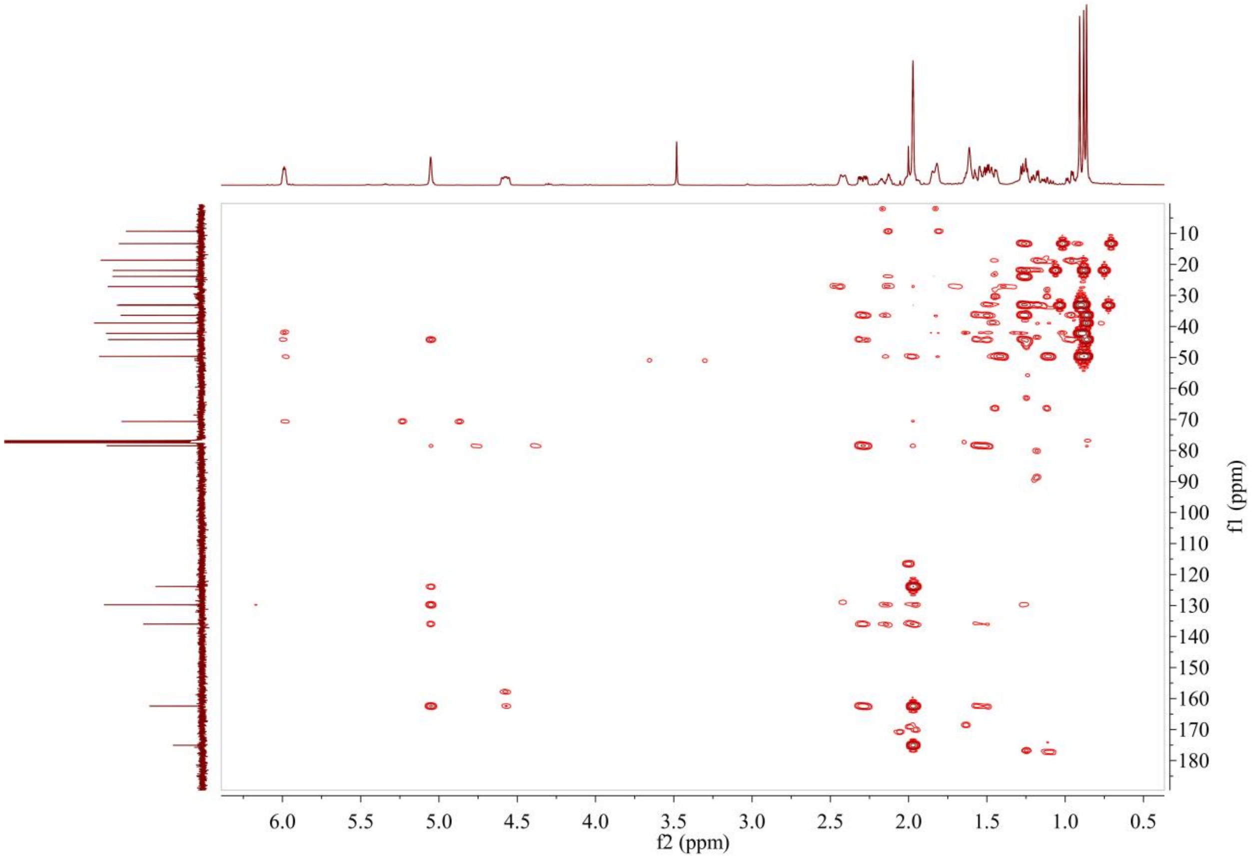


Fig. S10. ^{1}H–^{1}H COSY spectrum of **1** in CDCl$_3$

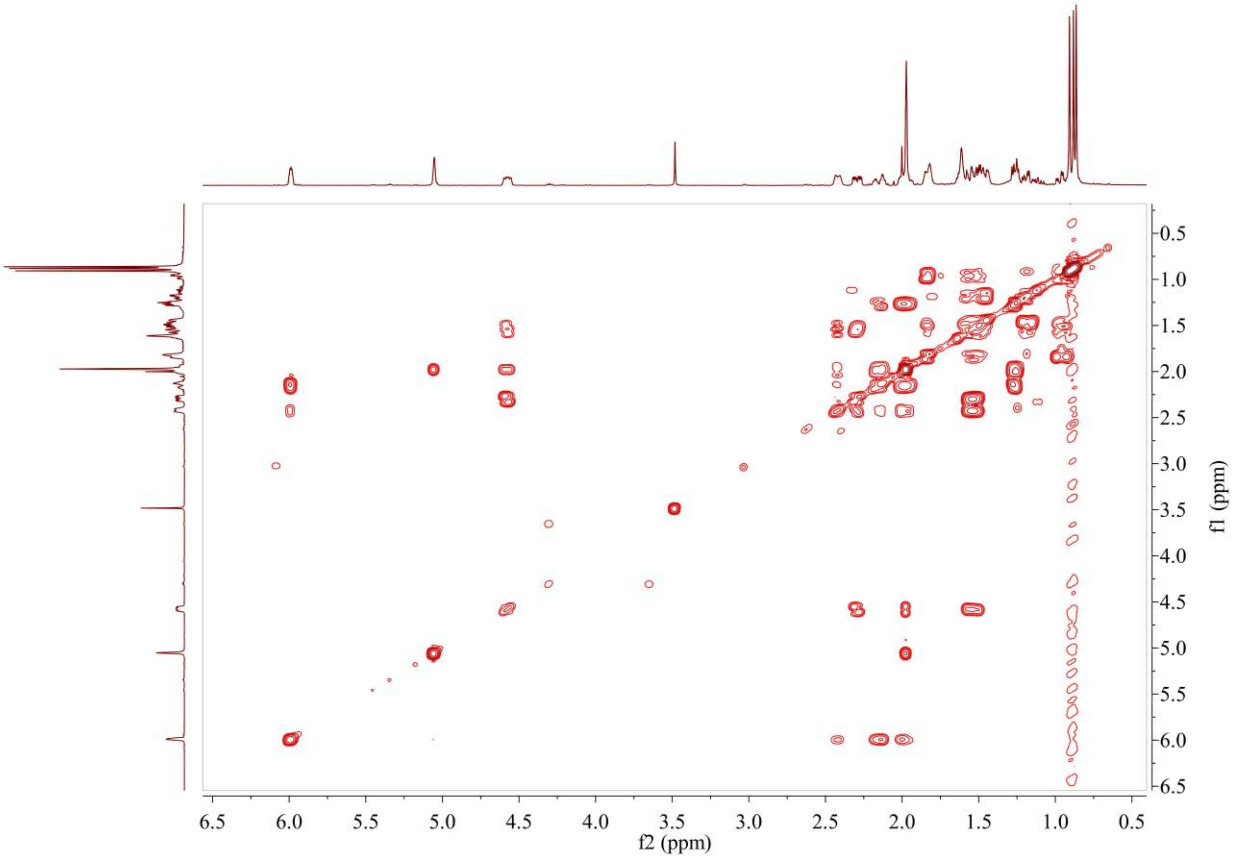


Fig. S11. NOESY spectrum of **1** in CDCl$_3$

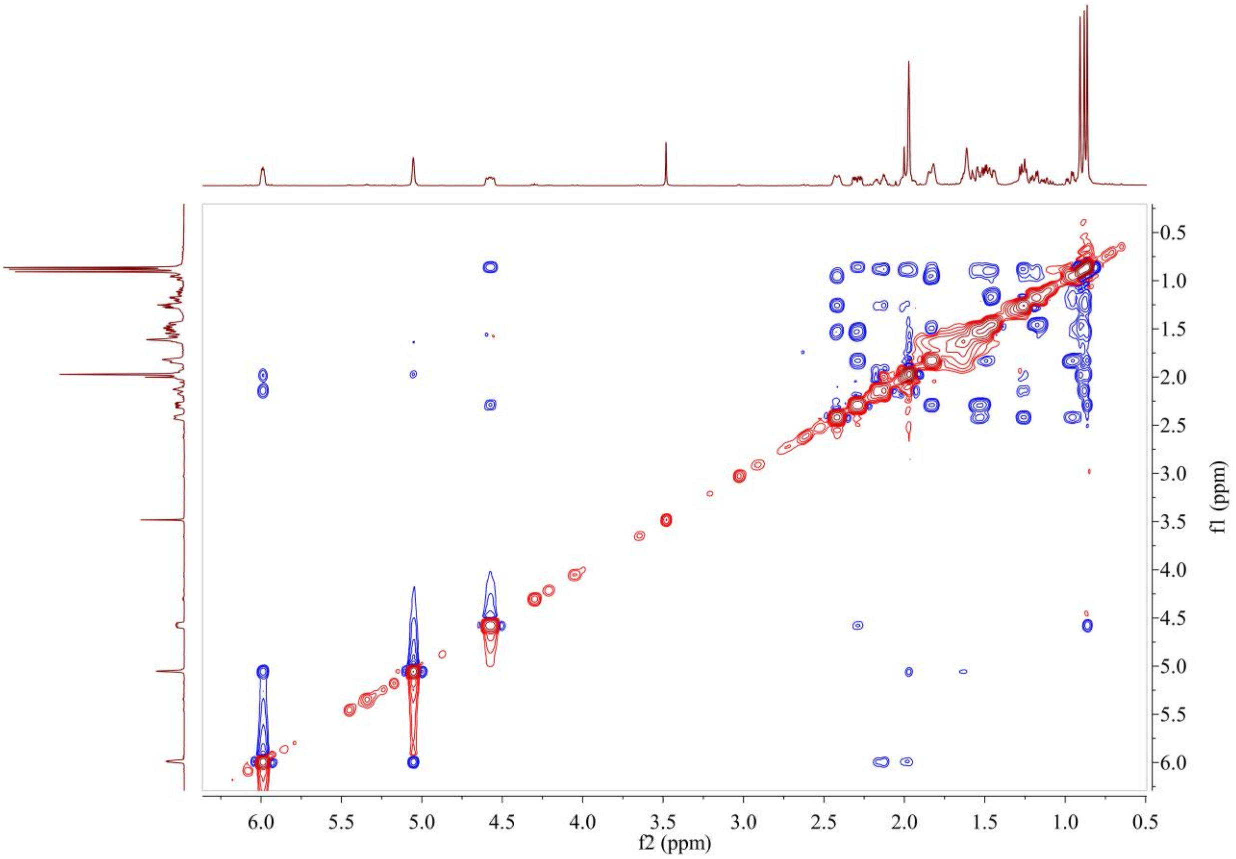
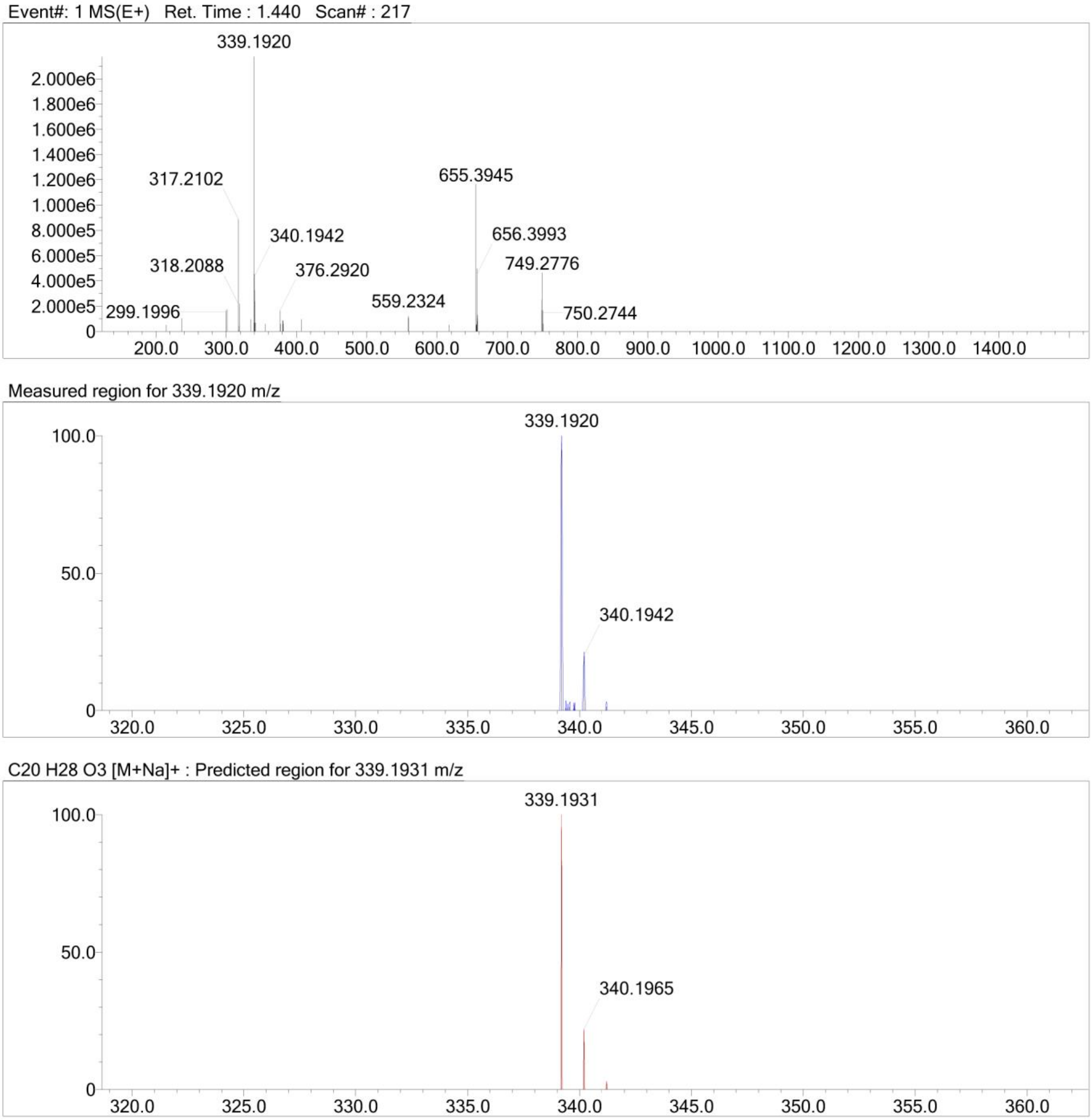


Fig. S12. HRESIMS spectrum of **1**


Event#: 1 MS(E+) Ret. Time : 1.440 Scan# : 217

Measured region for 339.1920 m/z

C20 H28 O3 [M+Na]+ : Predicted region for 339.1931 m/z

Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	86.27	C20 H28 O3	[M+Na]+	339.1920	339.1931	-1.1	-3.24	91.39	7.0

Fig. S13. IR (KBr disc) spectrum of **1**

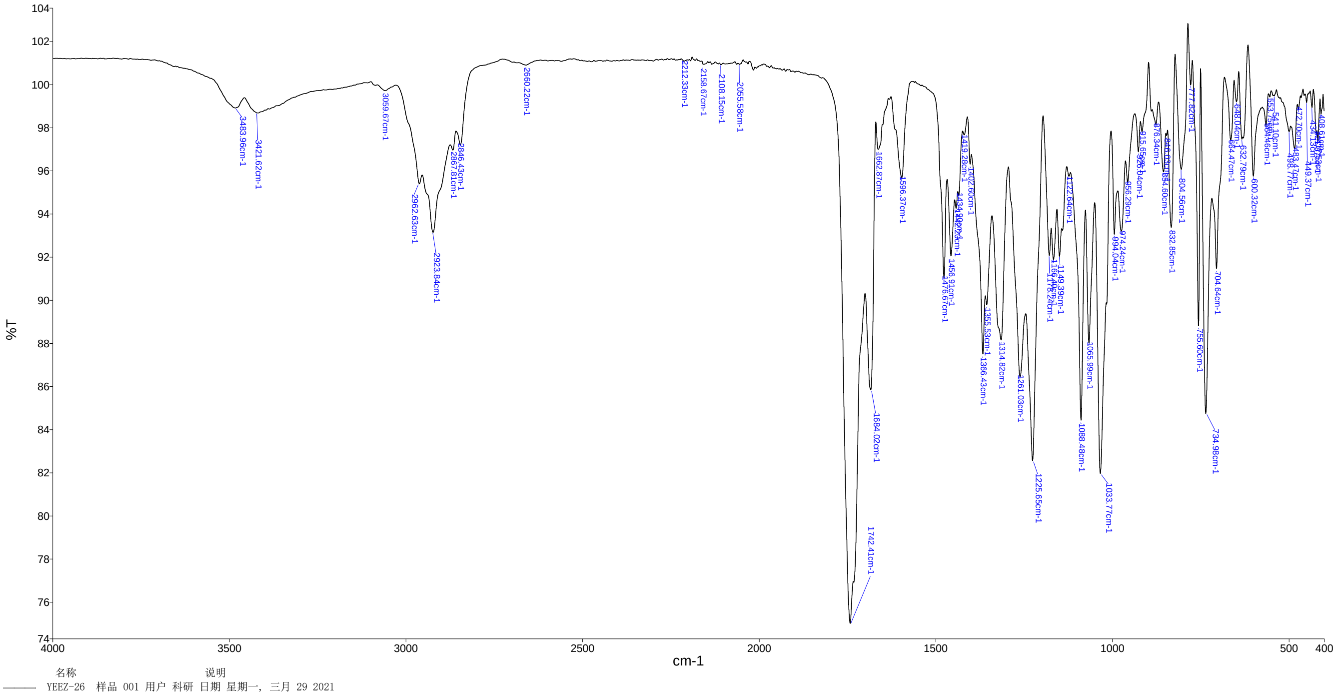


Fig. S14. ^{1}H NMR spectrum of **2** in CD_3OD

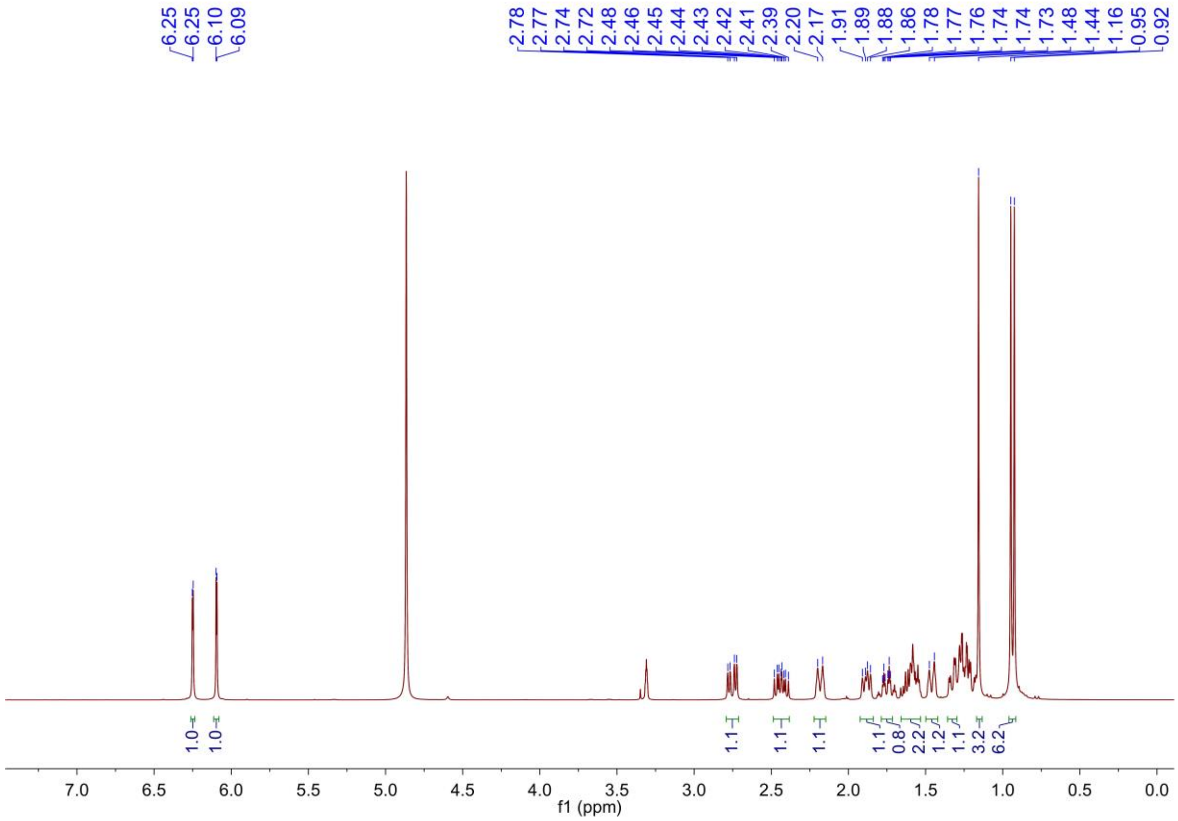


Fig. S15. ^{13}C NMR spectrum of **2** in CD_3OD

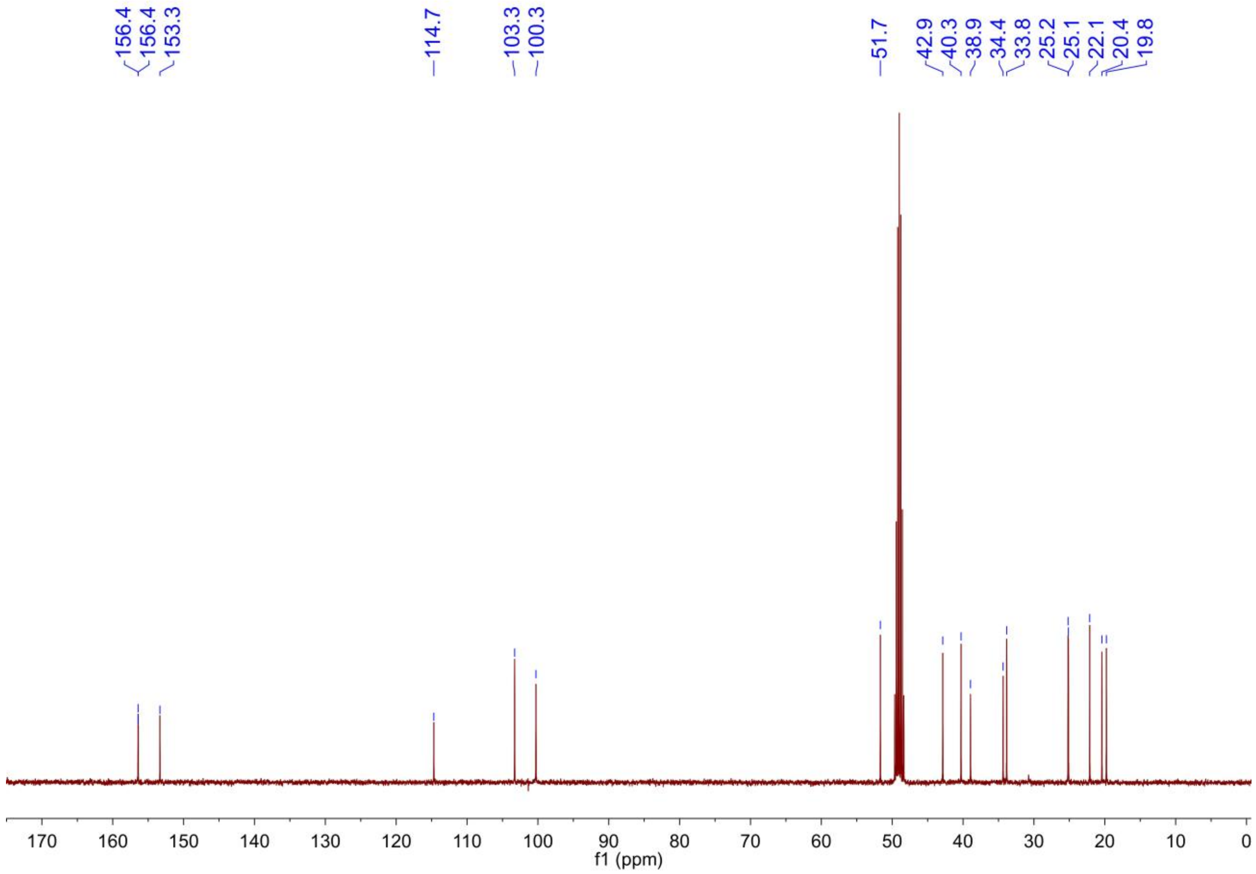


Fig. S16. HSQC spectrum of **2** in CD_3OD

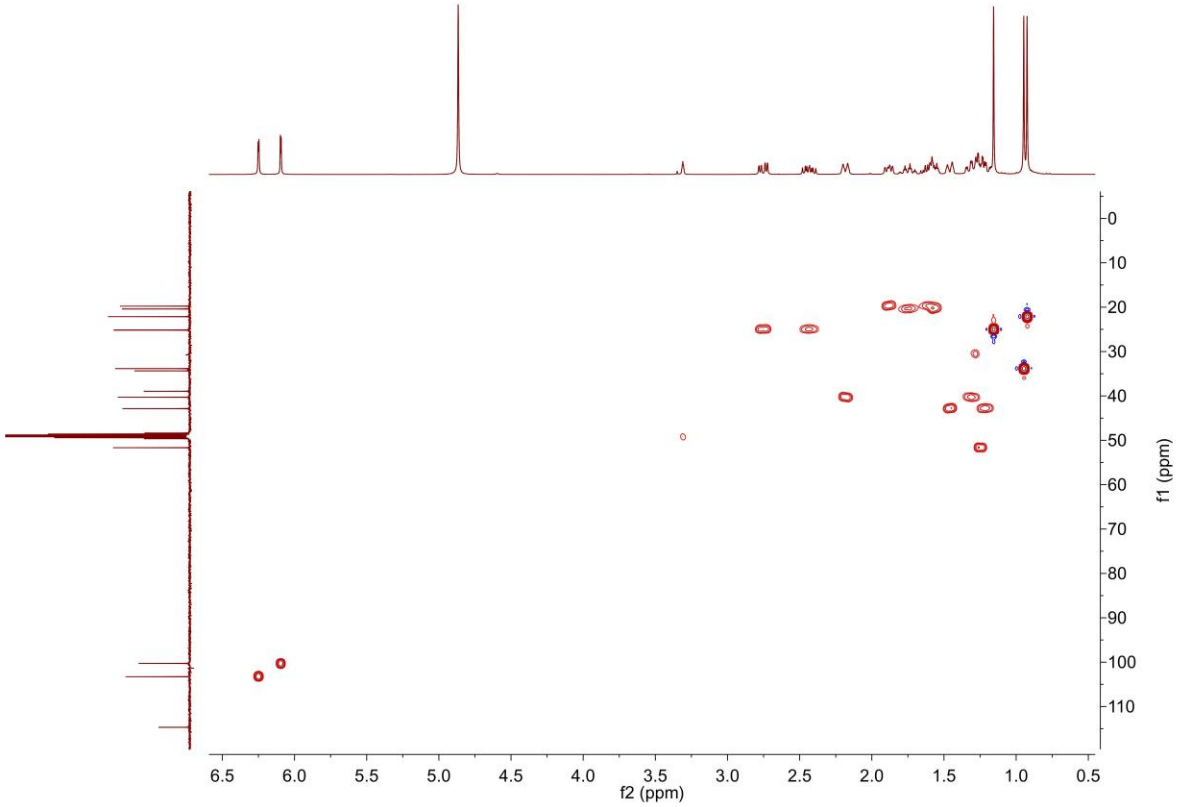


Fig. S17. HMBC spectrum of **2** in CD_3OD

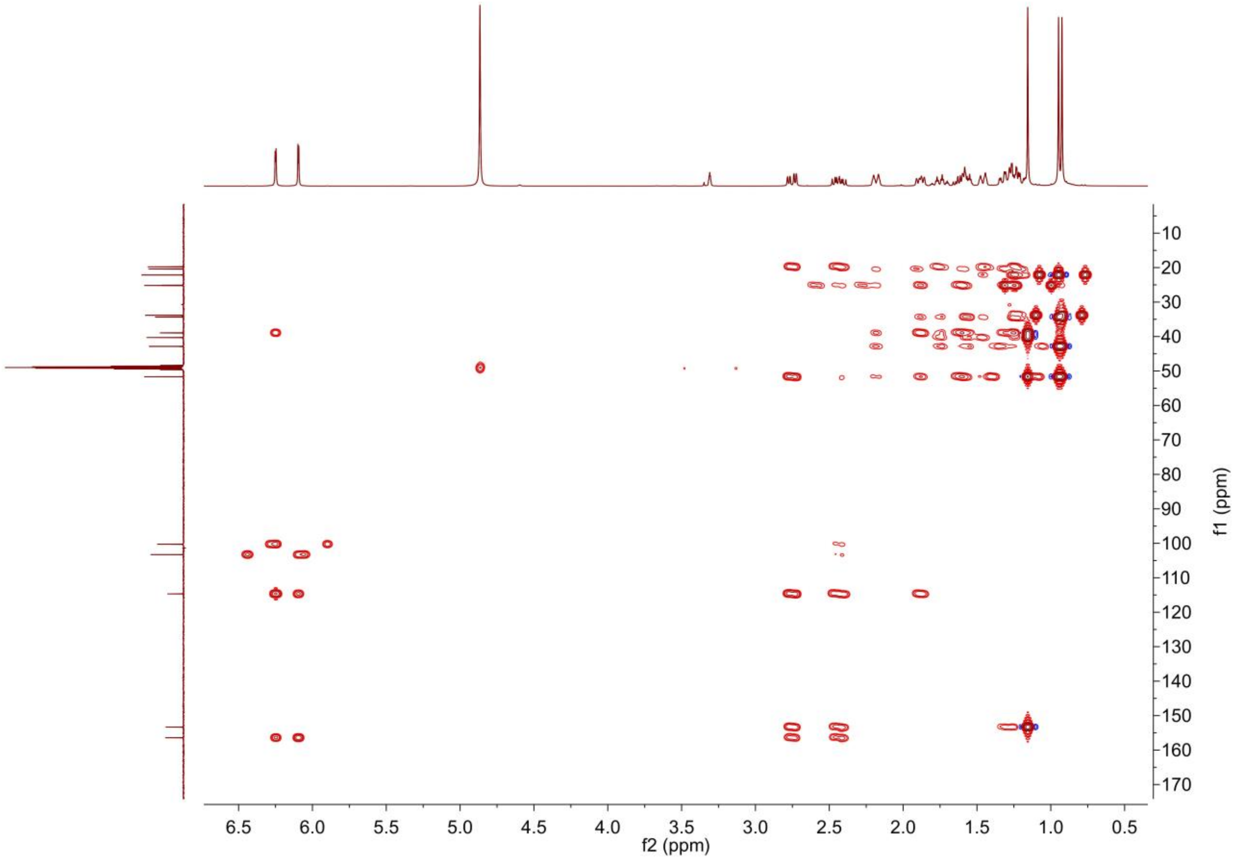


Fig. S18. ^{1}H–^{1}H COSY spectrum of **2** in CD_3OD

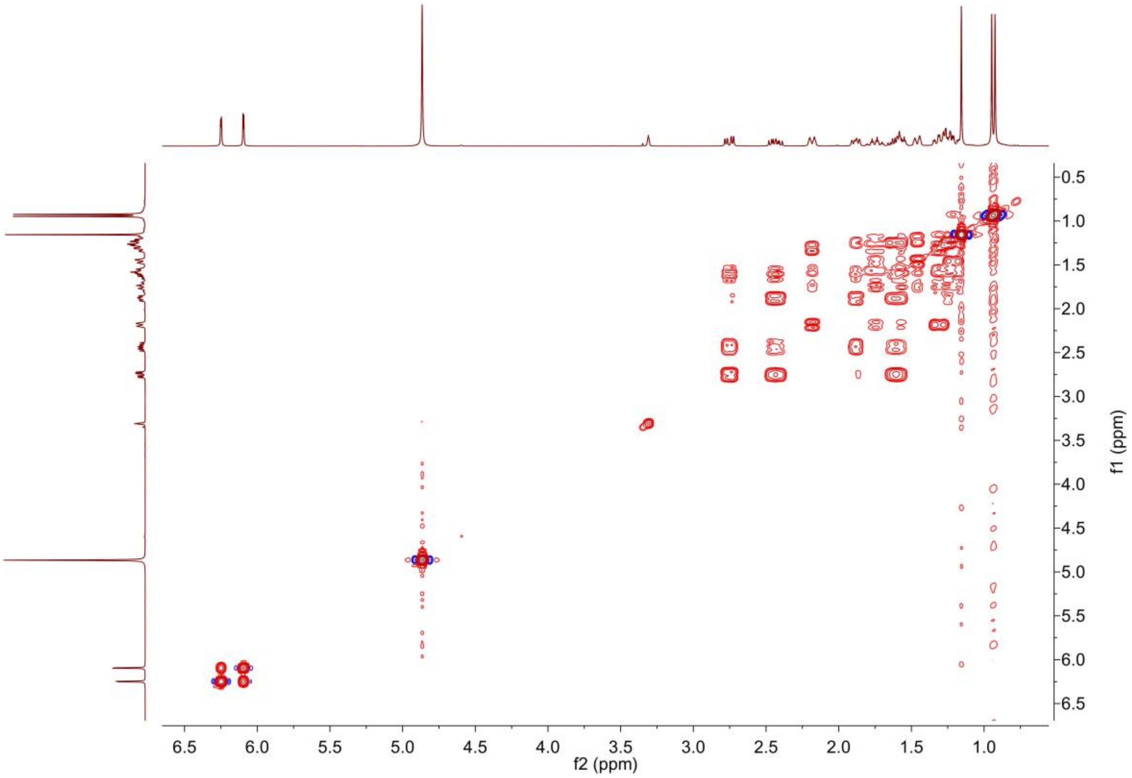


Fig. S19. NOESY spectrum of **2** in CD_3OD

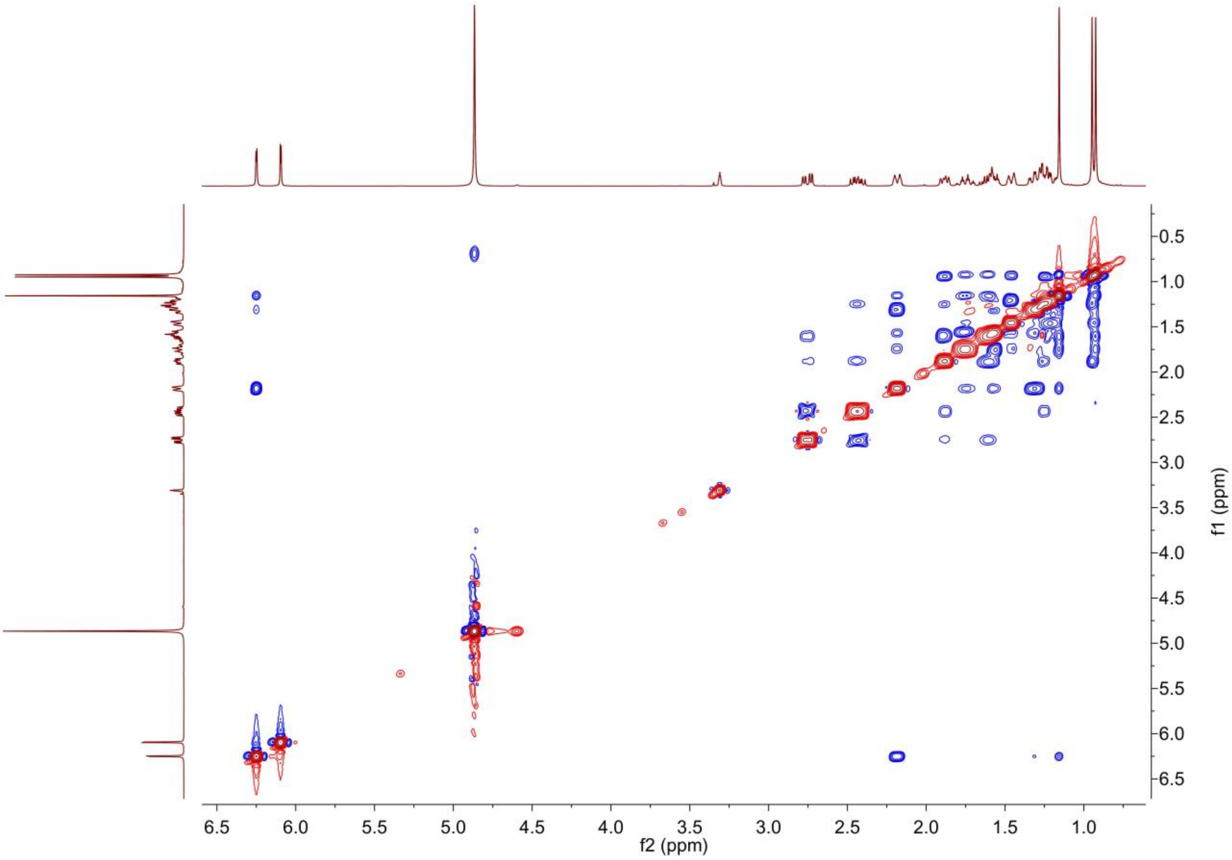
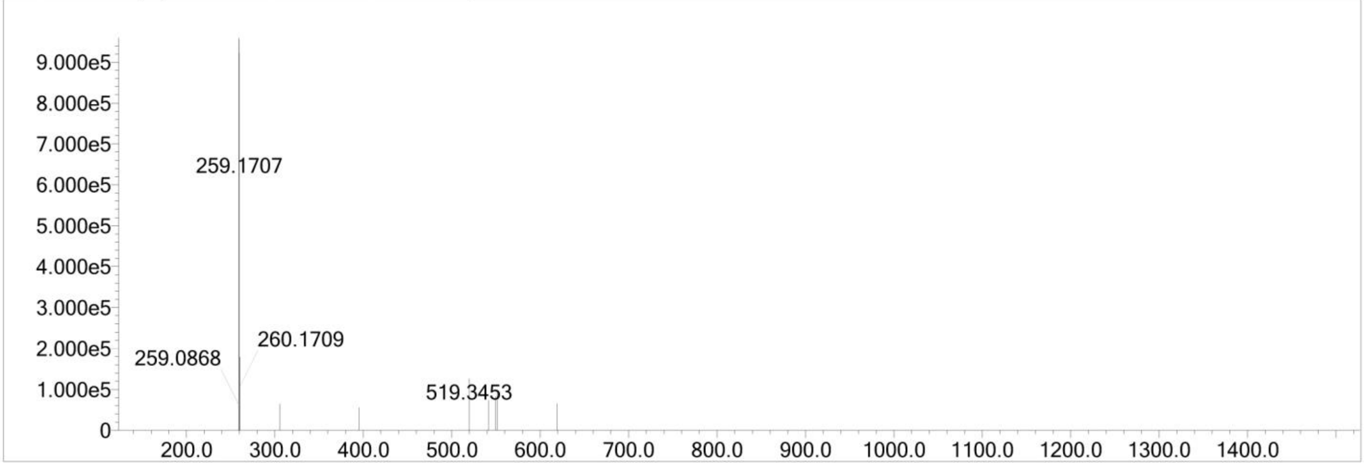
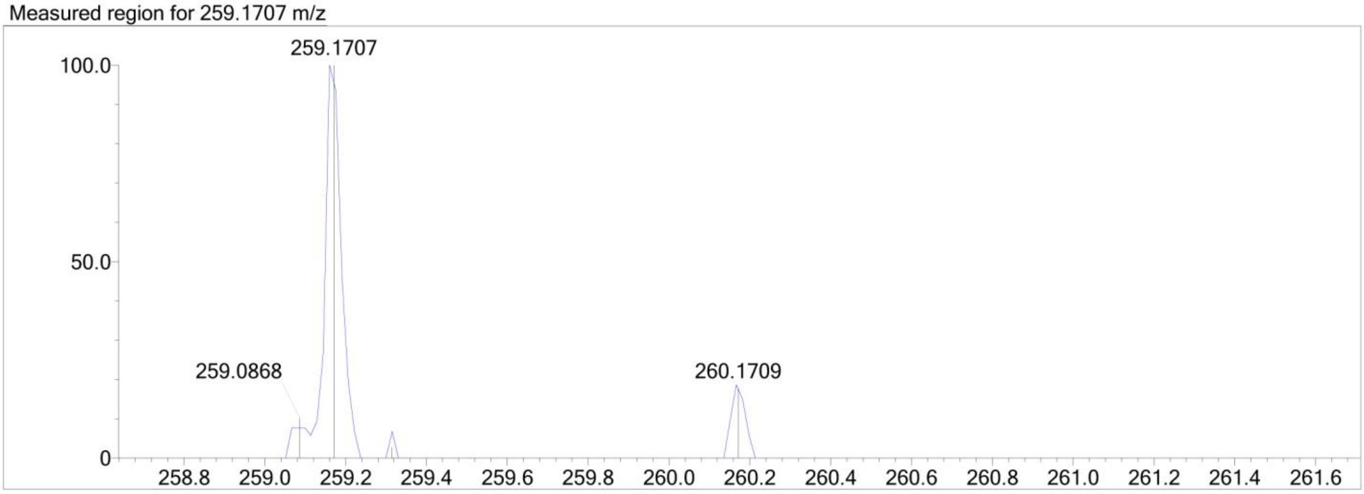


Fig. S20. HRESIMS spectrum of **2**

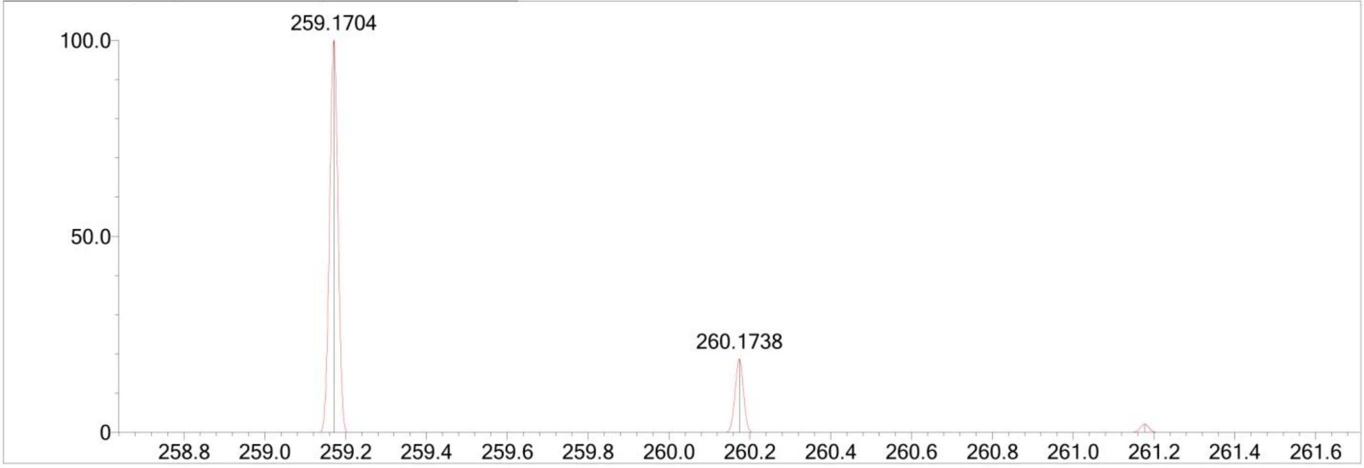
Event#: 2 MS(E-) Ret. Time : 1.050 Scan# : 158



Measured region for 259.1707 m/z



C17 H24 O2 [M-H]- : Predicted region for 259.1704 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	70.72	C17 H24 O2	[M-H]-	259.1707	259.1704	0.3	1.16	71.01	6.0

Fig. S21. IR (KBr disc) spectrum of **2**

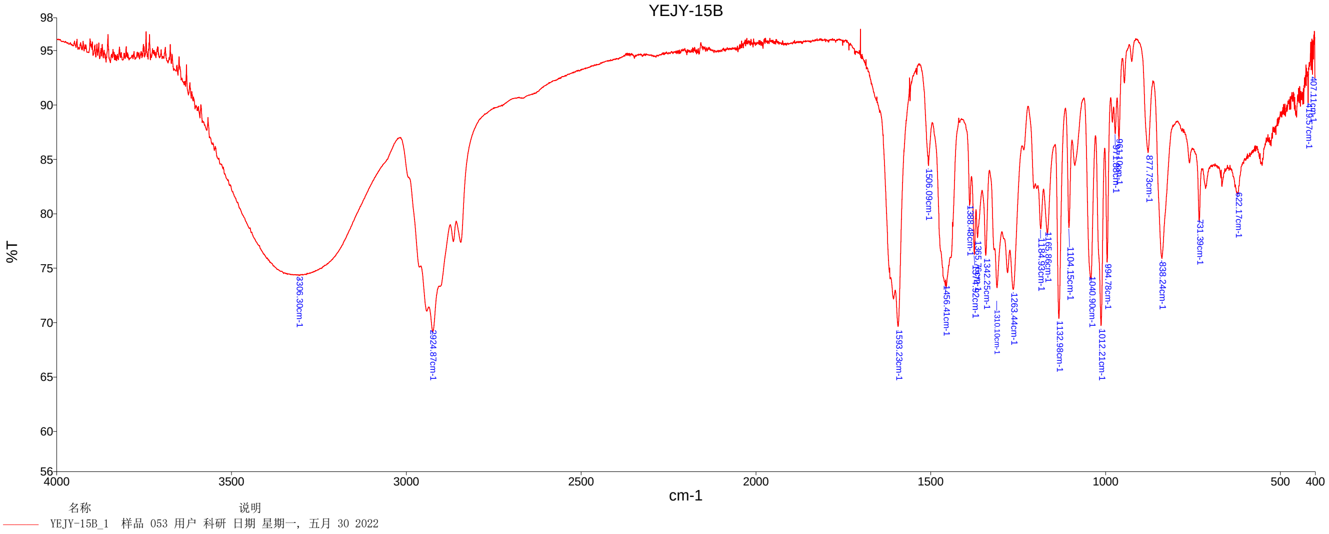


Fig. S22. ^{1}H NMR spectrum of **3** in Pyridine-d_5

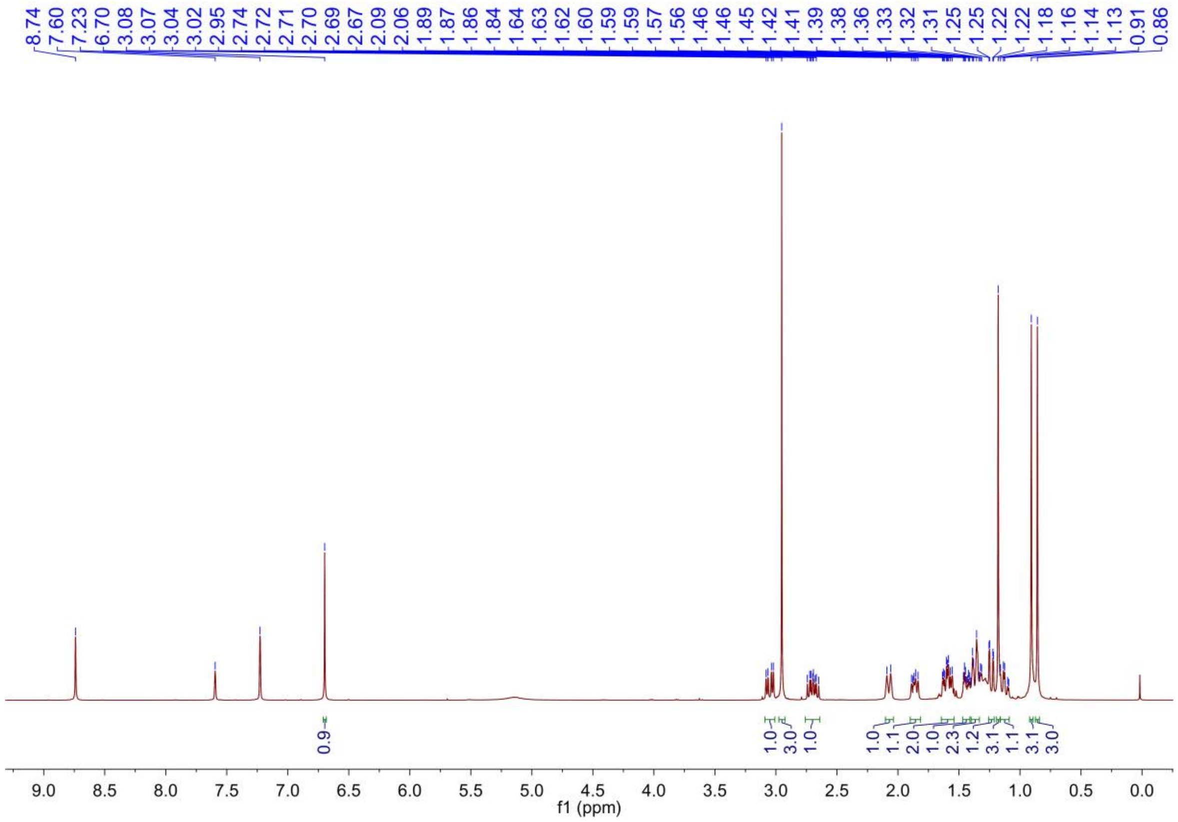


Fig. S23. ^{13}C NMR and DEPT135 spectra of **3** in Pyridine-d_5

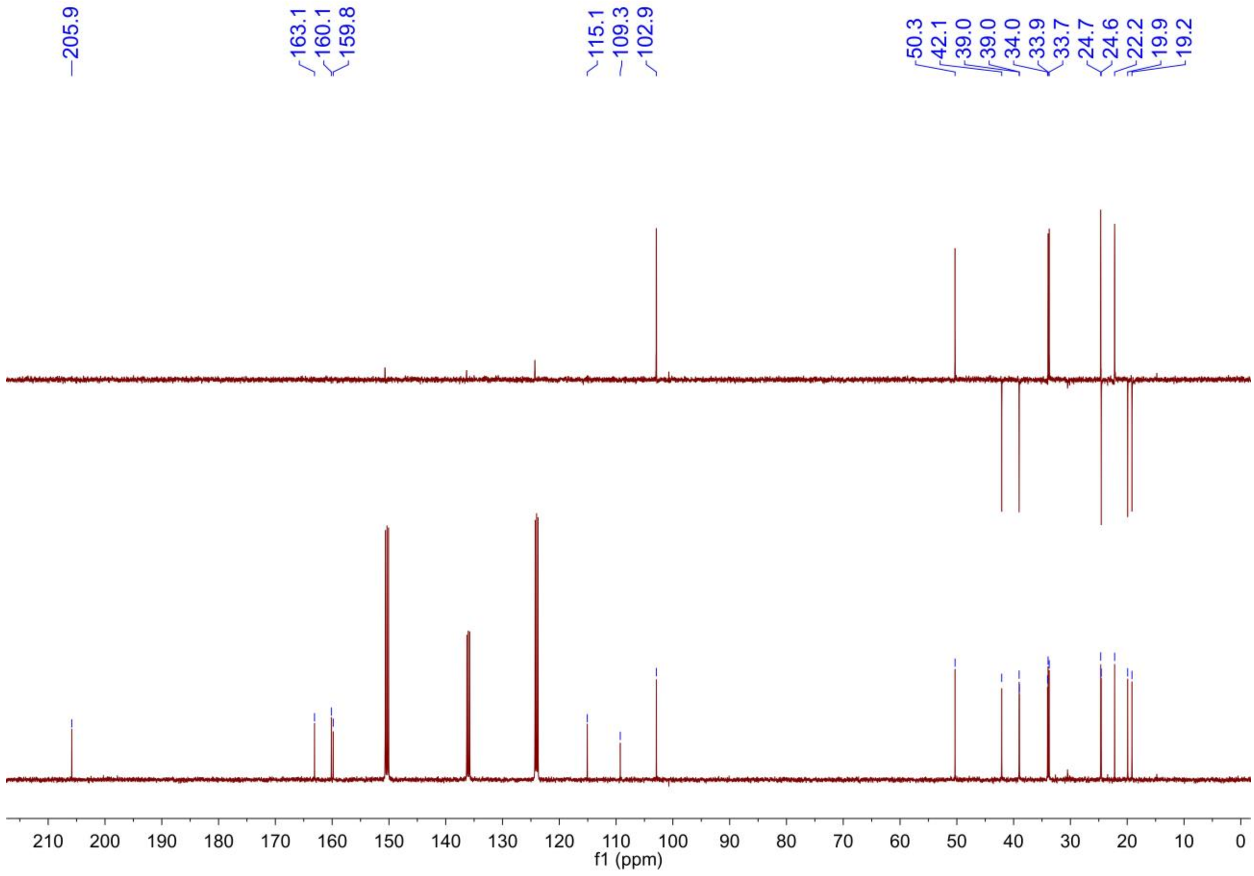


Fig. S24. HSQC spectrum of **3** in Pyridine-*d*5

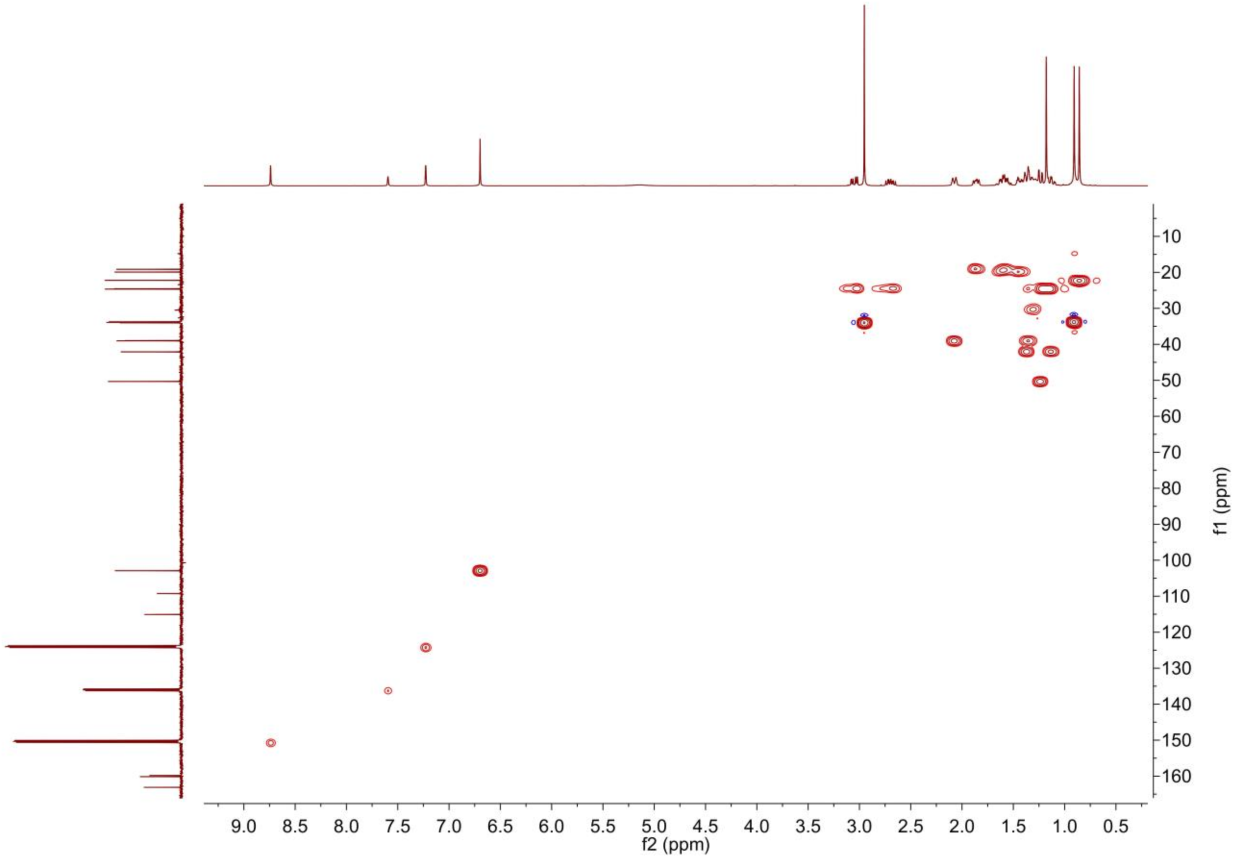


Fig. S25. HMBC spectrum of **3** in Pyridine-*d*5

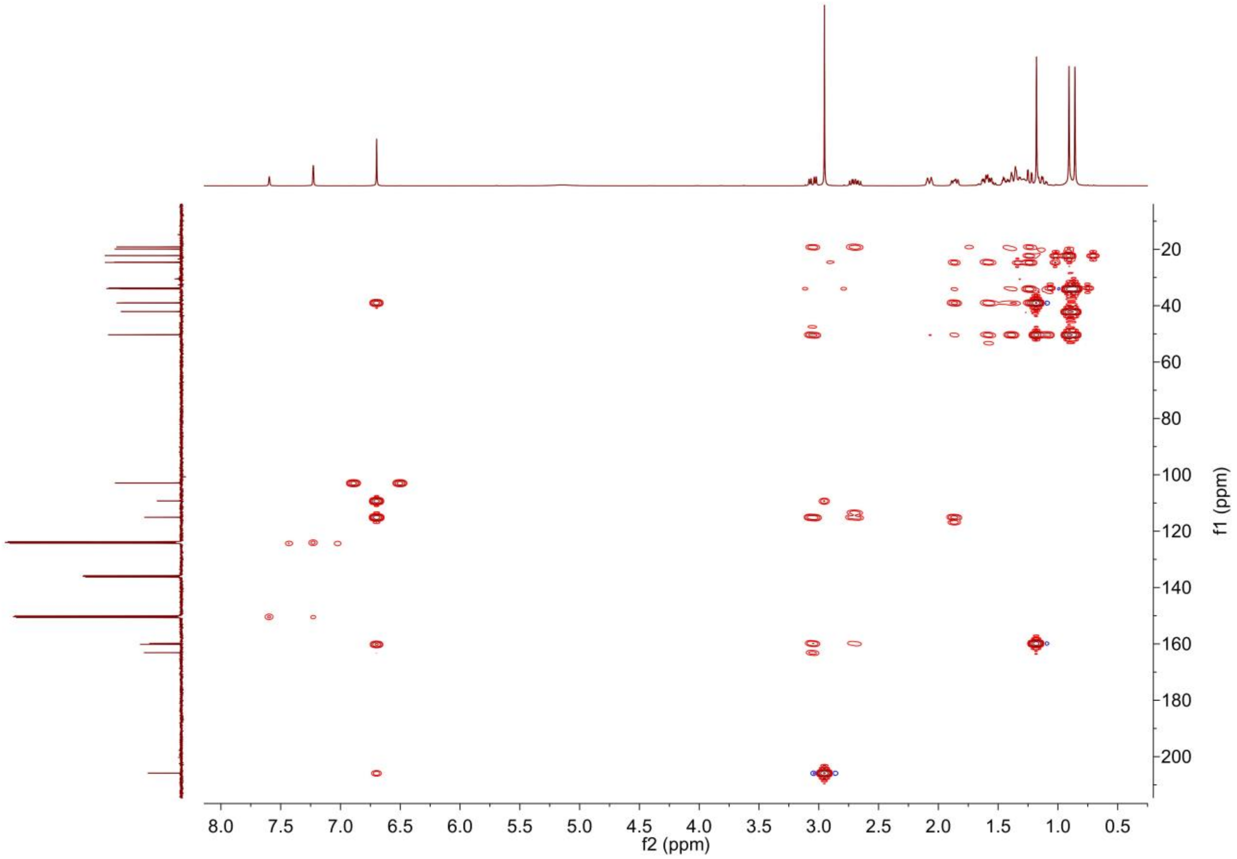


Fig. S26. ^{1}H–^{1}H COSY spectrum of **3** in Pyridine-d_5

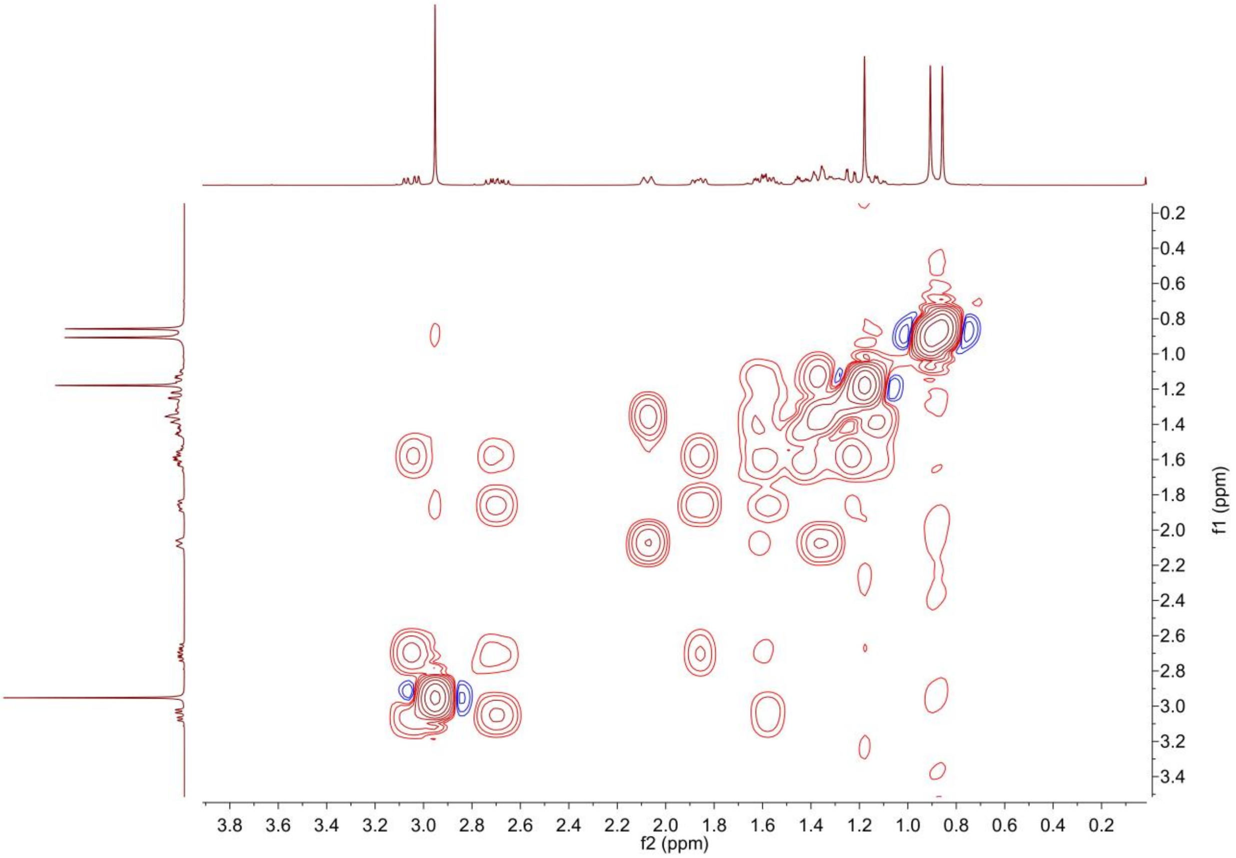


Fig. S27. NOESY spectrum of **3** in Pyridine-d_5

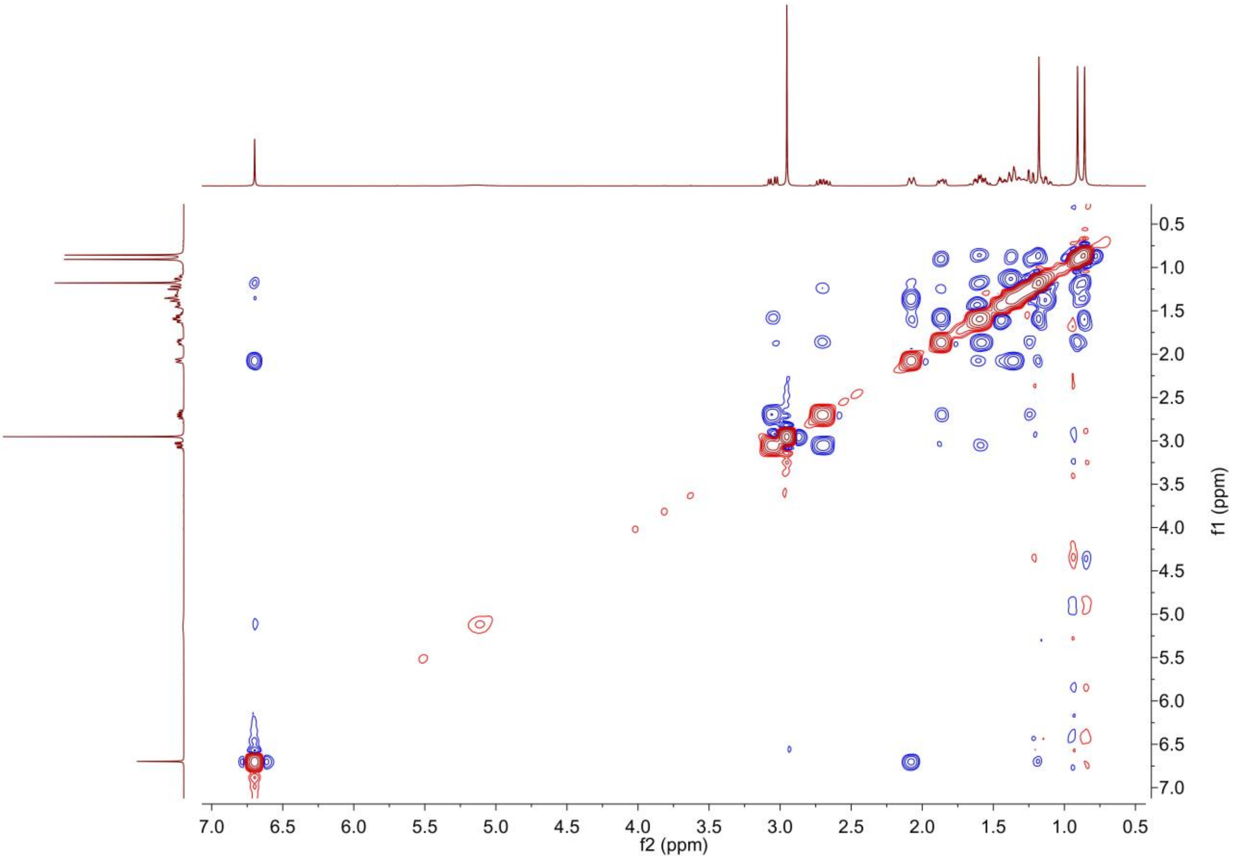
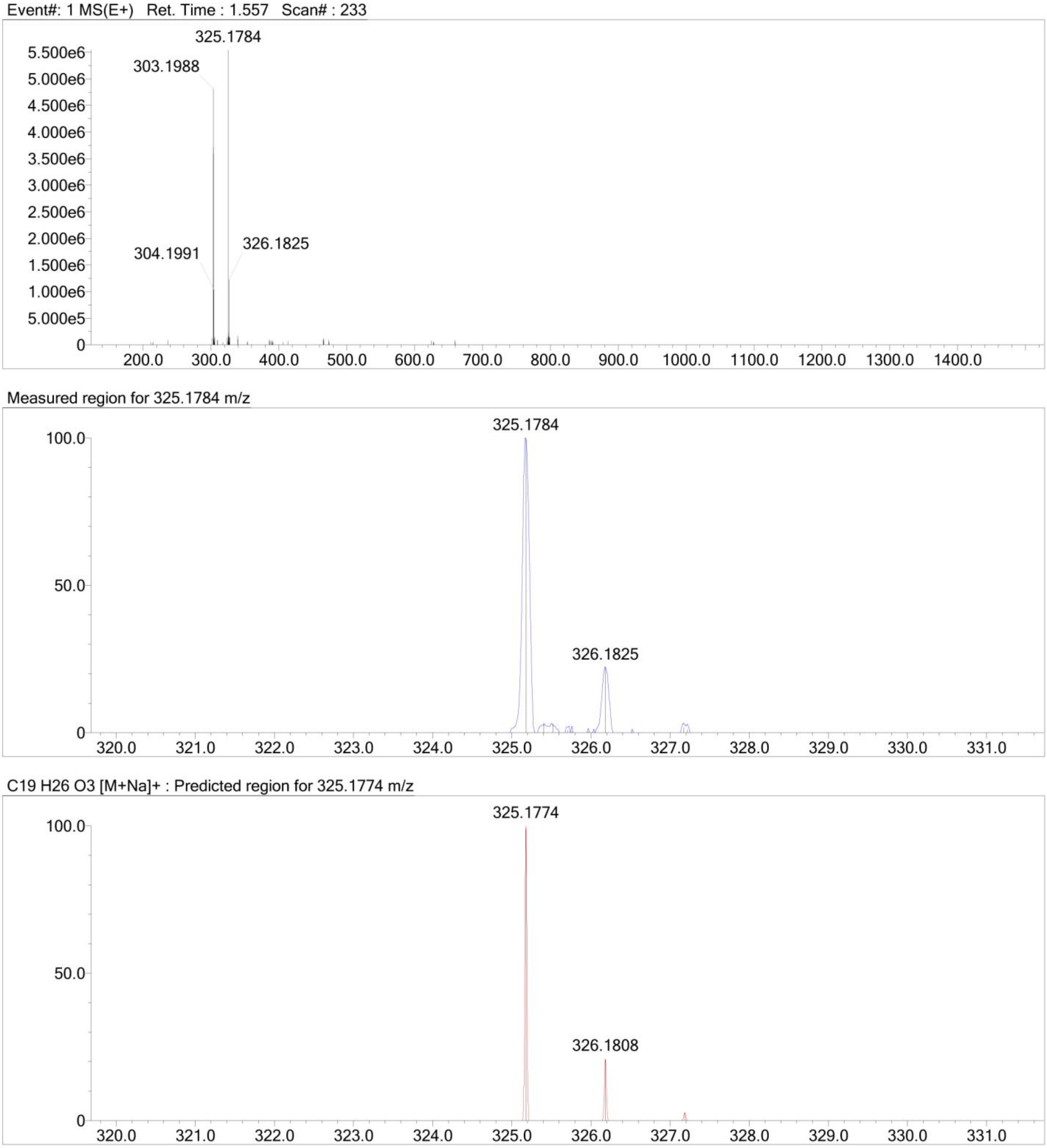


Fig. S28. HRESIMS spectrum of **3**


Event#: 1 MS(E+) Ret. Time : 1.557 Scan# : 233

Measured region for 325.1784 m/z

C19 H26 O3 [M+Na]+ : Predicted region for 325.1774 m/z

Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	51.92	C19 H26 O3	[M+Na]+	325.1784	325.1774	1.0	3.08	54.77	7.0

Fig. S29. IR (KBr disc) spectrum of **3**

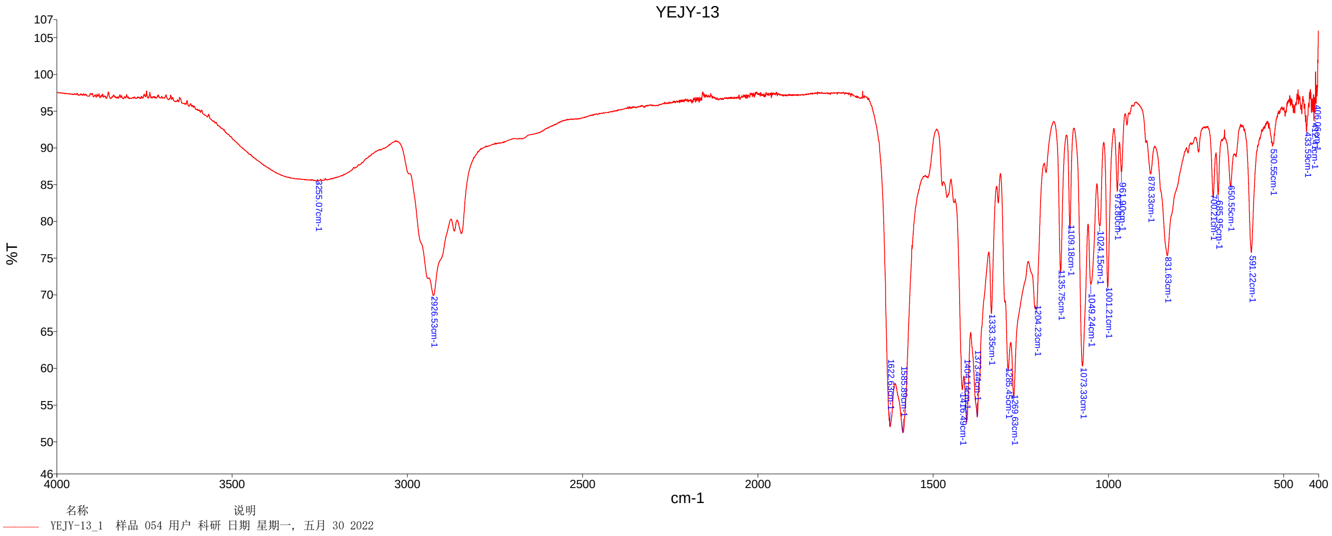


Fig. S30. ^{1}H NMR spectrum of **4** in Pyridine-d_5

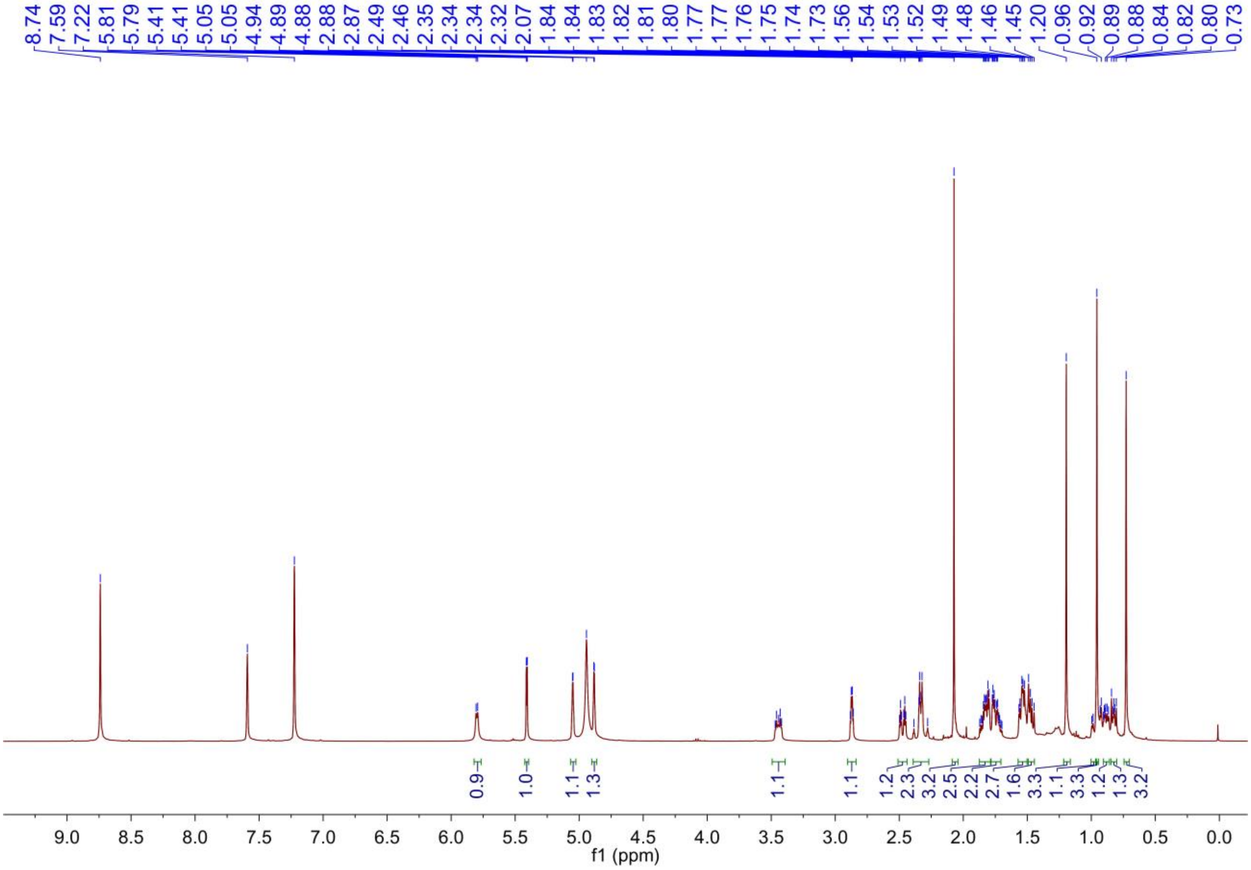


Fig. S31. ^{13}C NMR and DEPT spectra of **4** in Pyridine-d_5

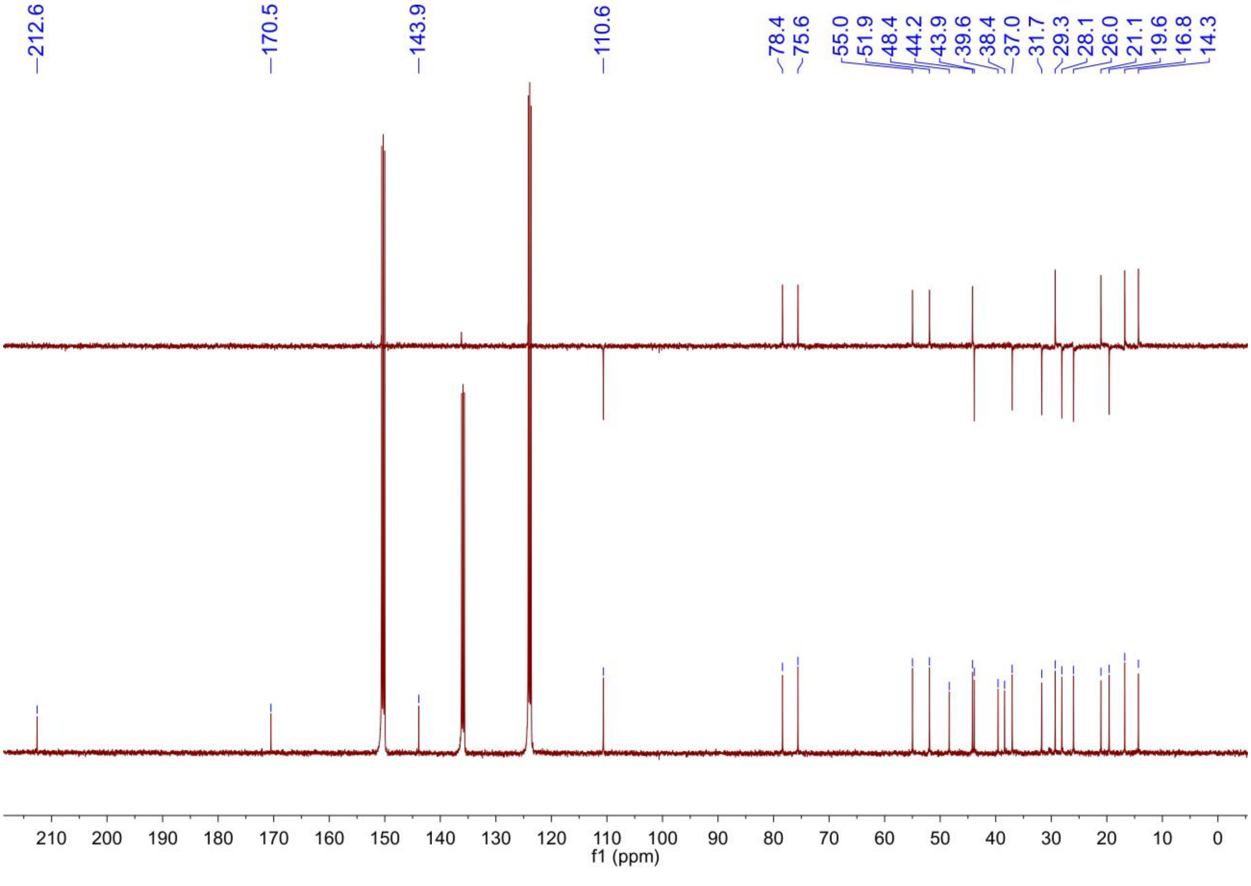


Fig. S32. HSQC spectrum of **4** in Pyridine-*d*$_5$

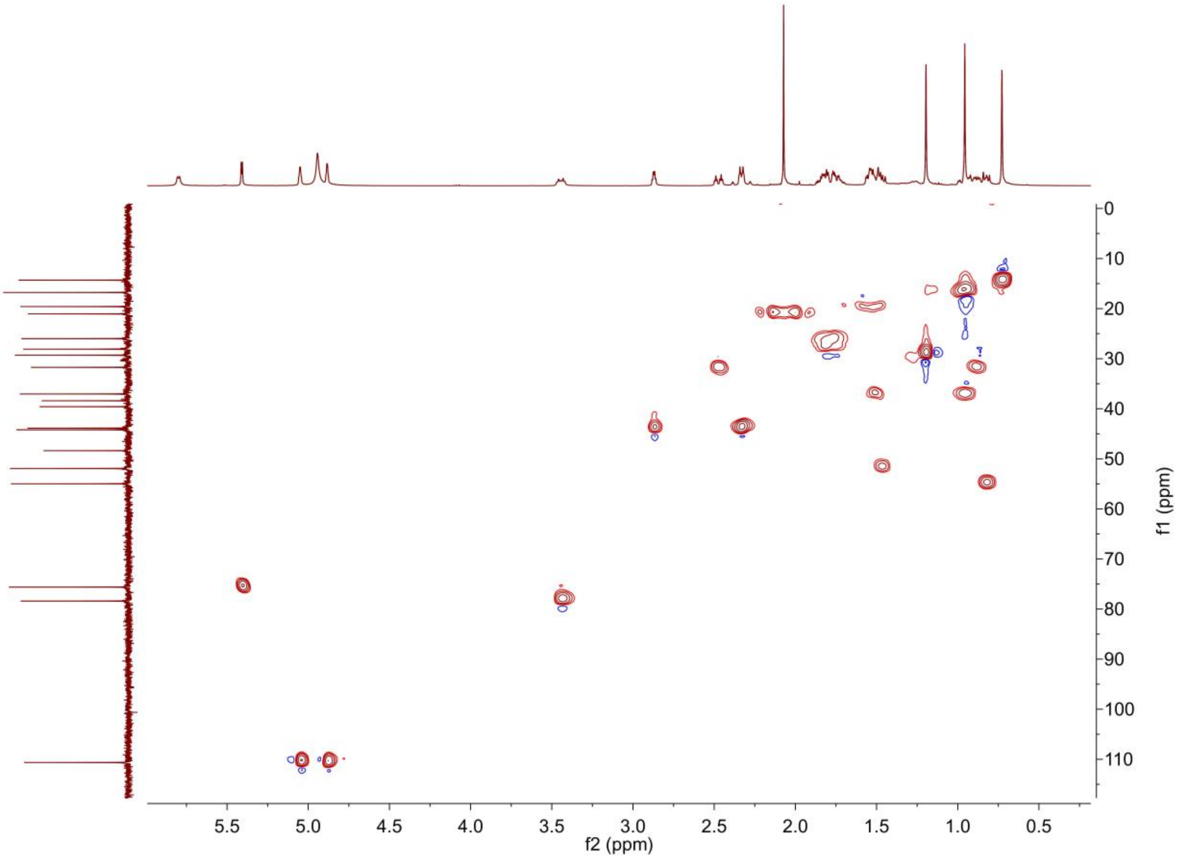


Fig. S33. HMBC spectrum of **4** in Pyridine-*d*$_5$

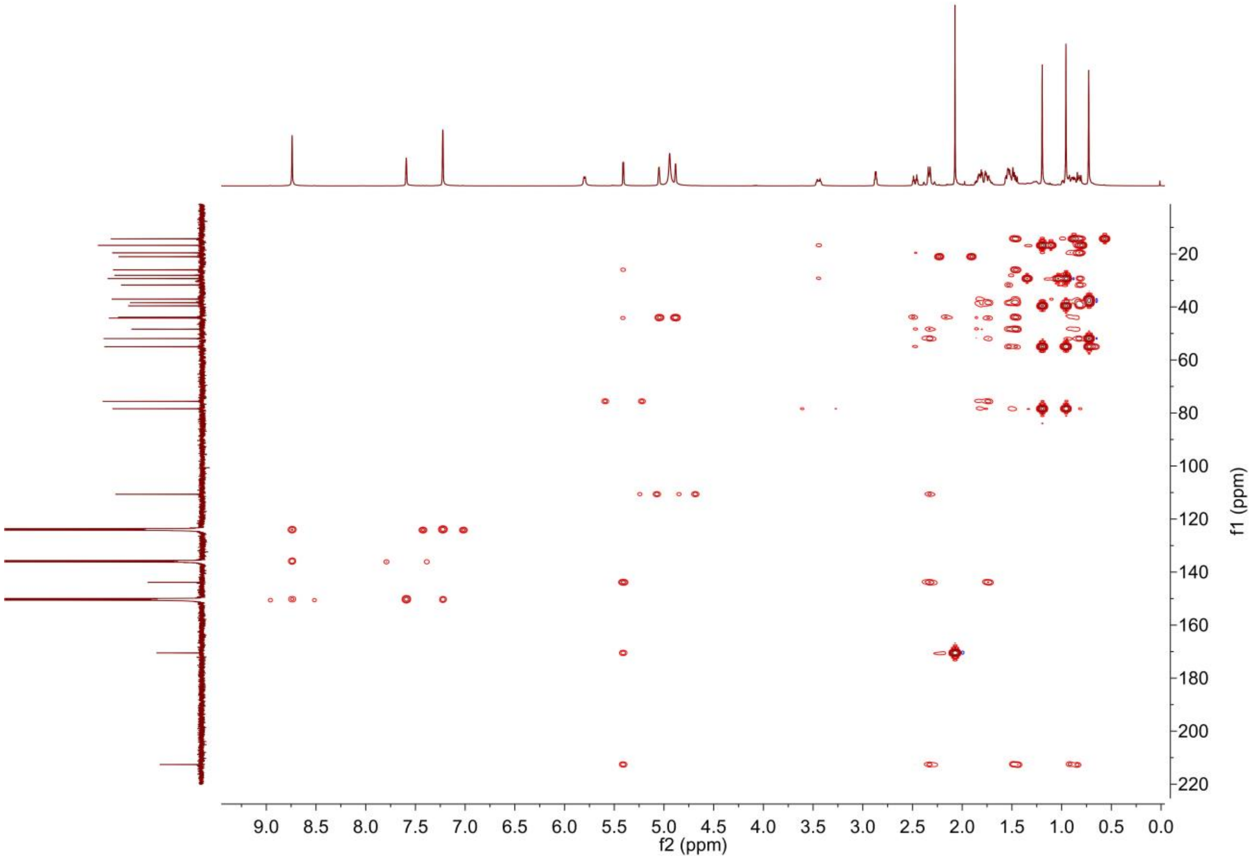


Fig. S34. ^{1}H–^{1}H COSY spectrum of **4** in Pyridine-d_5

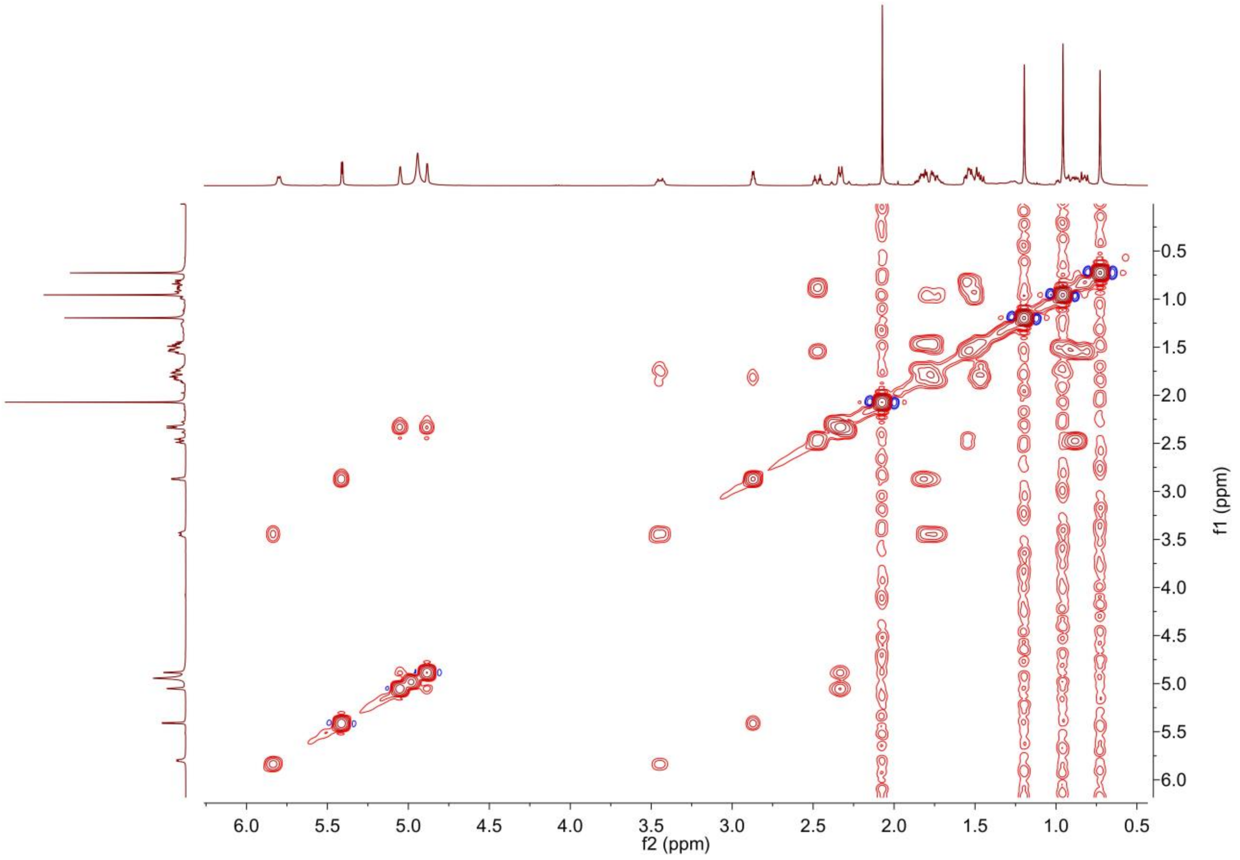


Fig. S35. NOESY spectrum of **4** in Pyridine-d_5

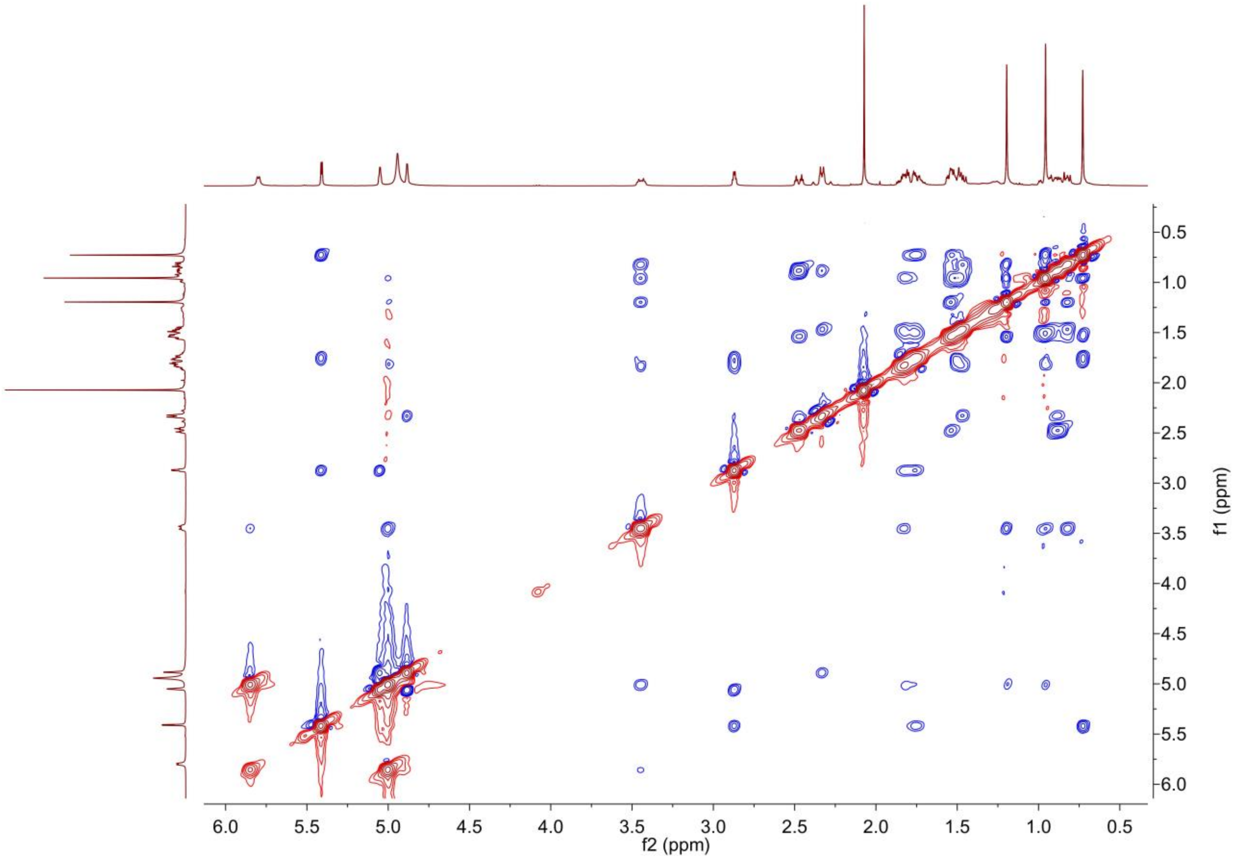
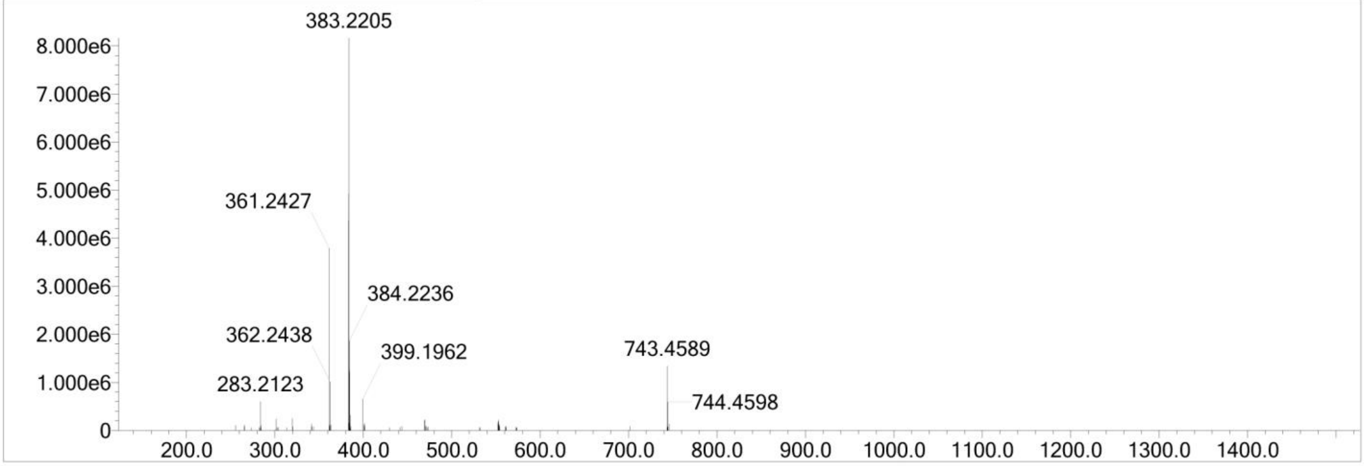
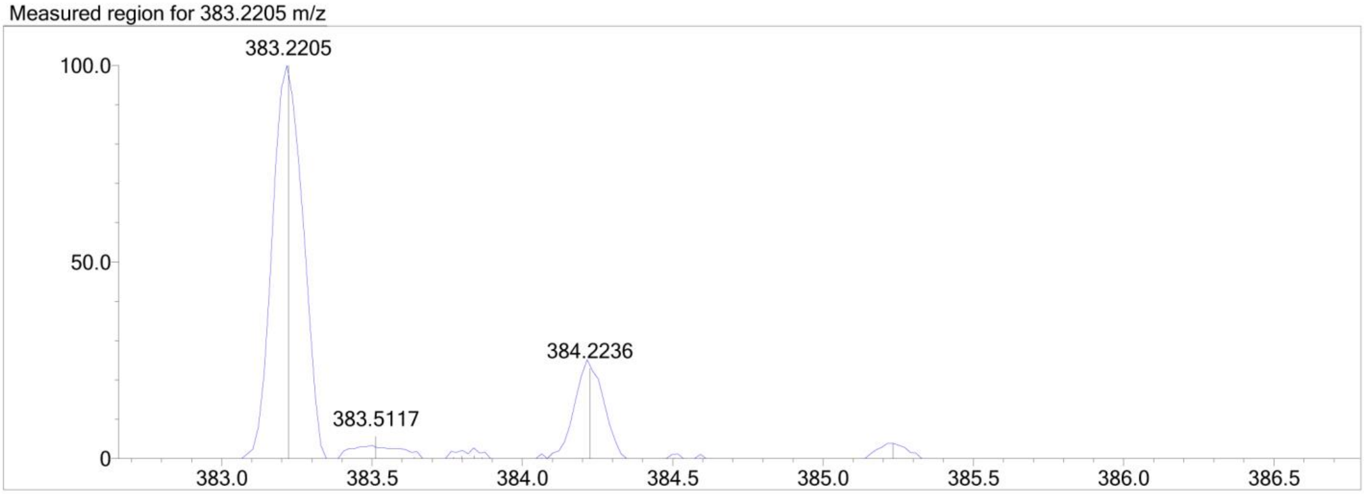


Fig. S36. HRESIMS spectrum of **4**

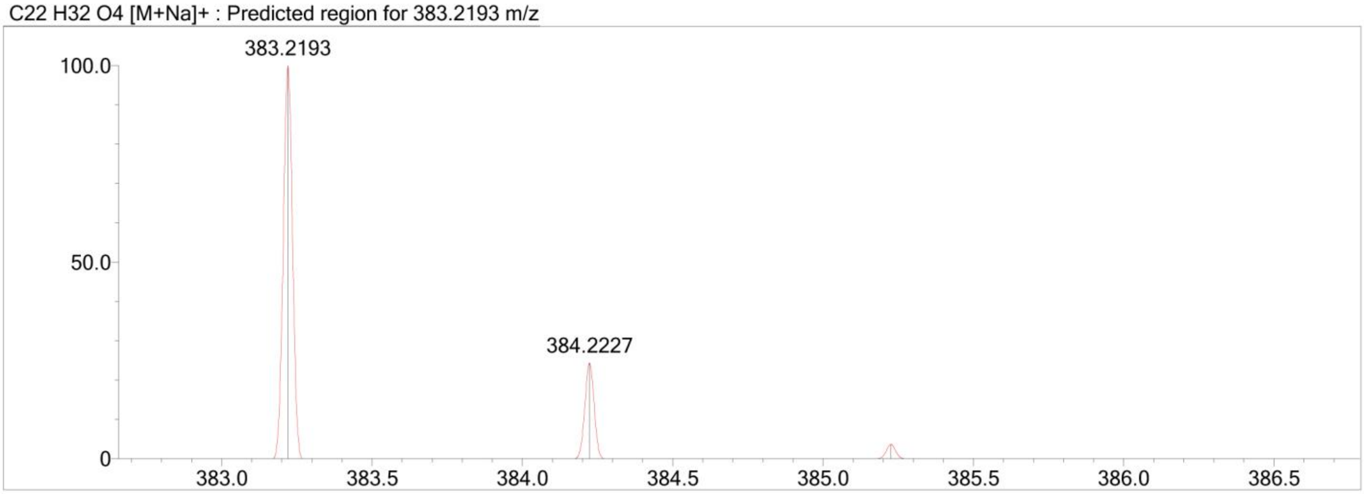
Event#: 1 MS(E+) Ret. Time : 1.103 Scan# : 165



Measured region for 383.2205 m/z



C22 H32 O4 [M+Na]+ : Predicted region for 383.2193 m/z



Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	72.66	C22 H32 O4	[M+Na]+	383.2205	383.2193	1.2	3.13	76.74	7.0

Fig. S37. IR (KBr disc) spectrum of **4**

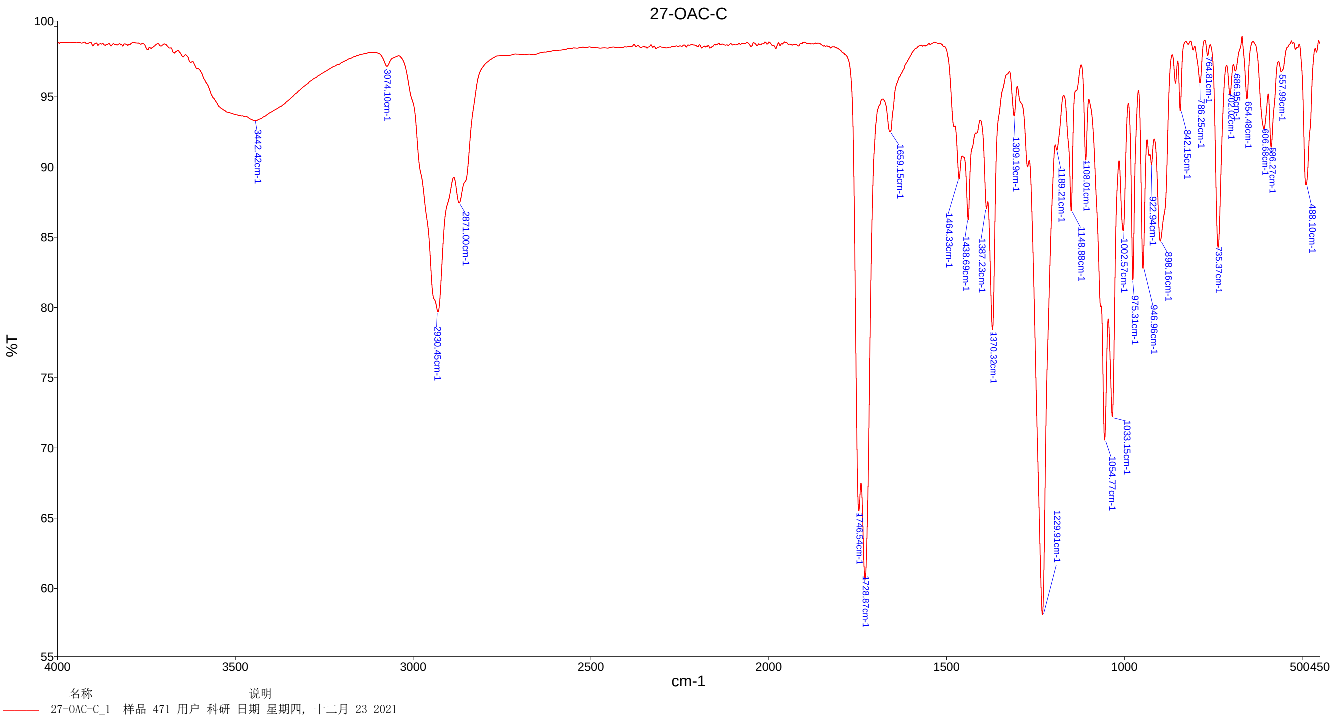


Fig. S38–61. 1D NMR spectra of 5–16

Fig. S38. ^{1}H NMR spectrum of **5** in Pyridine-*d*$_5$

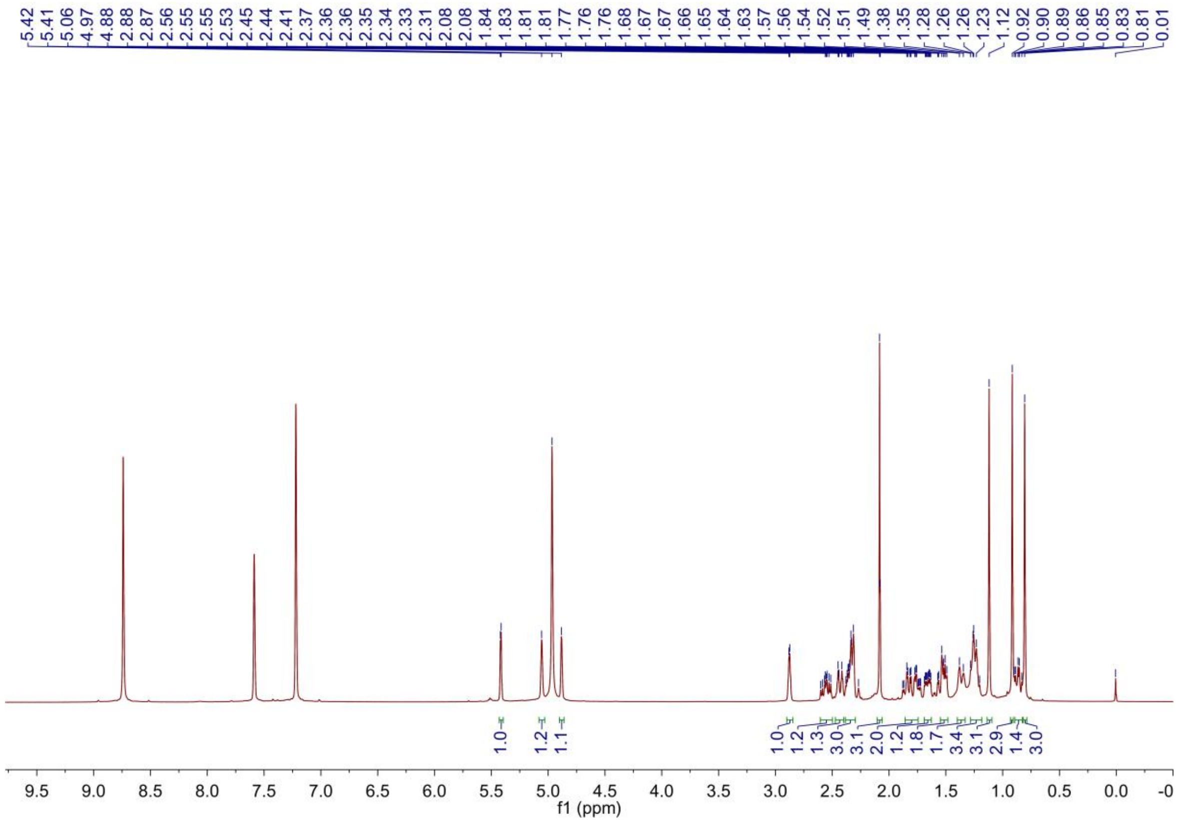


Fig. S39. ^{13}C NMR and DEPT135 spectra of **5** in Pyridine-*d*$_5$

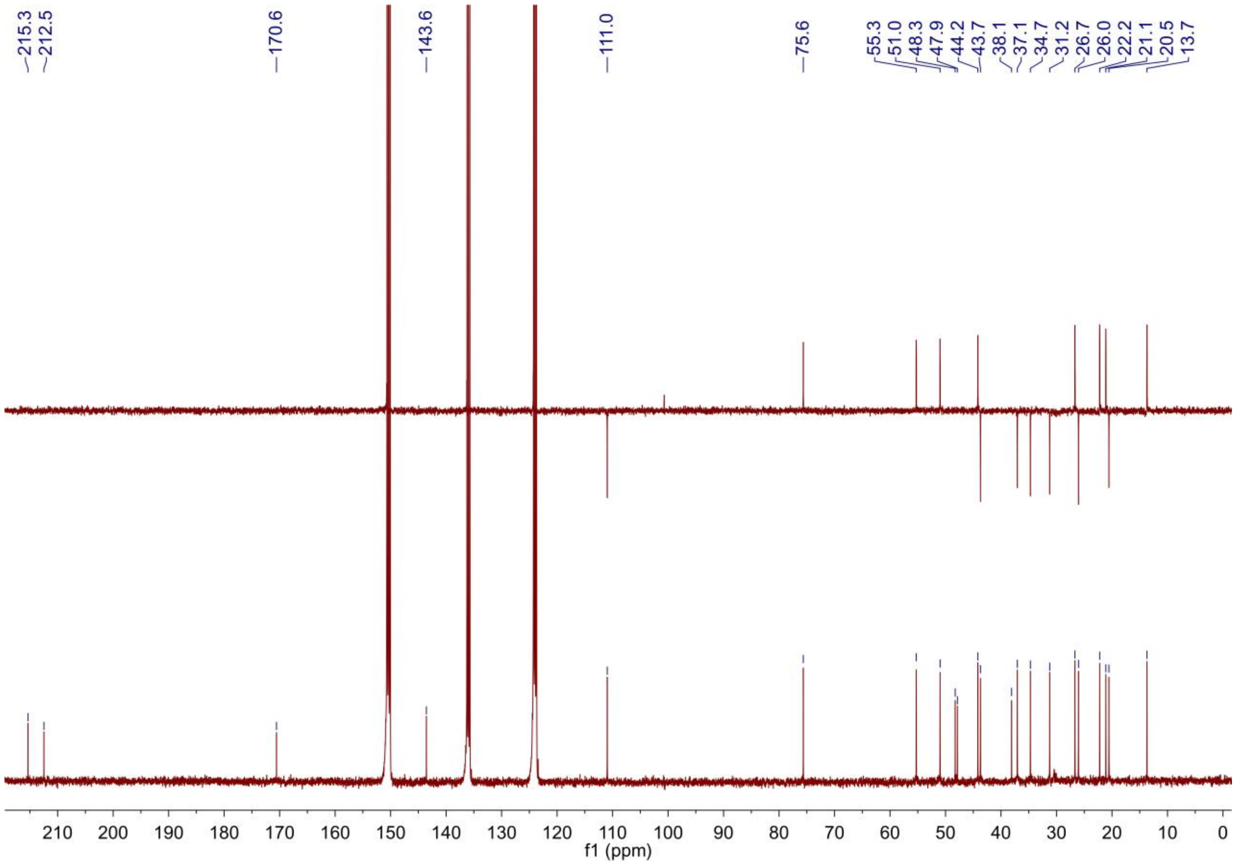


Fig. S40. ^{1}H NMR spectrum of **6** in $CDCl_3$

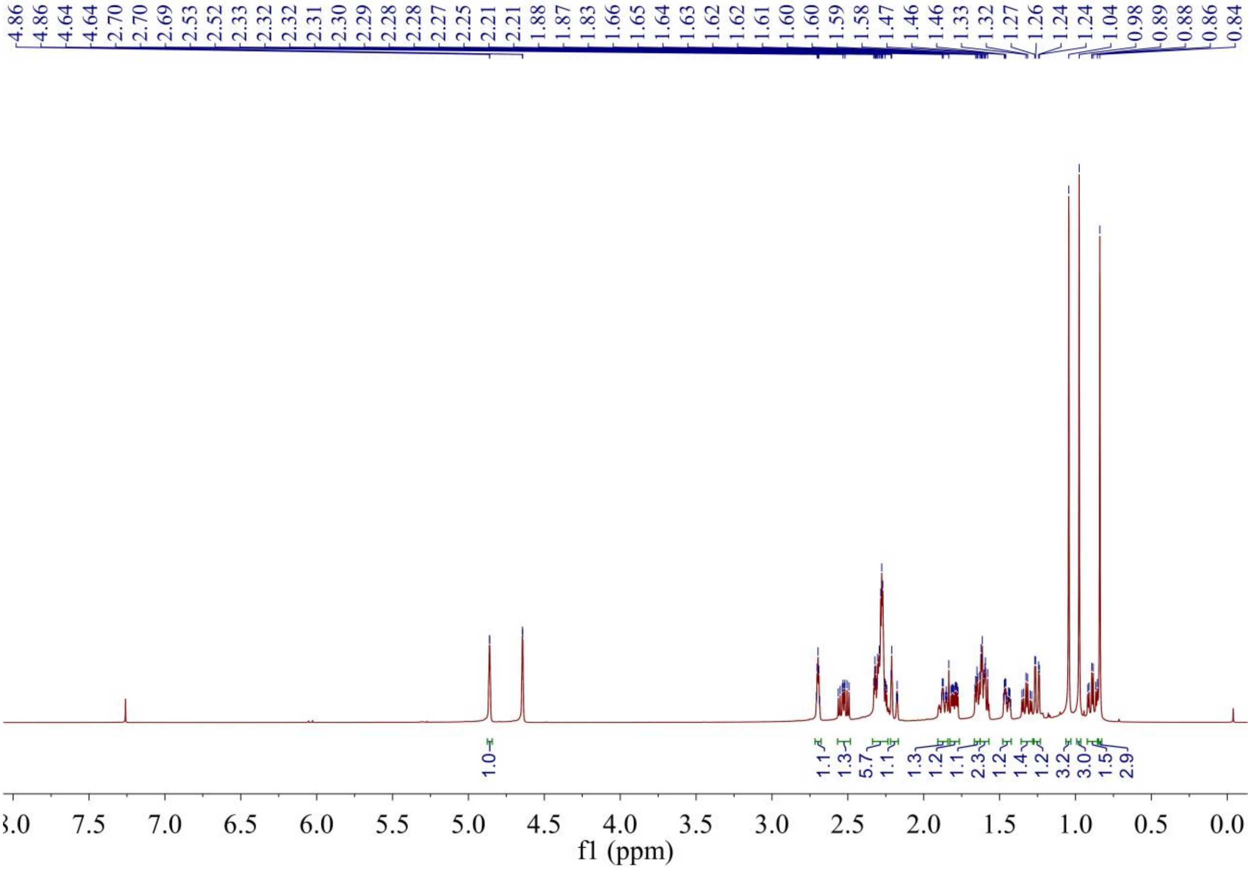


Fig. S41. ^{13}C NMR and DEPT135 spectra of **6** in $CDCl_3$

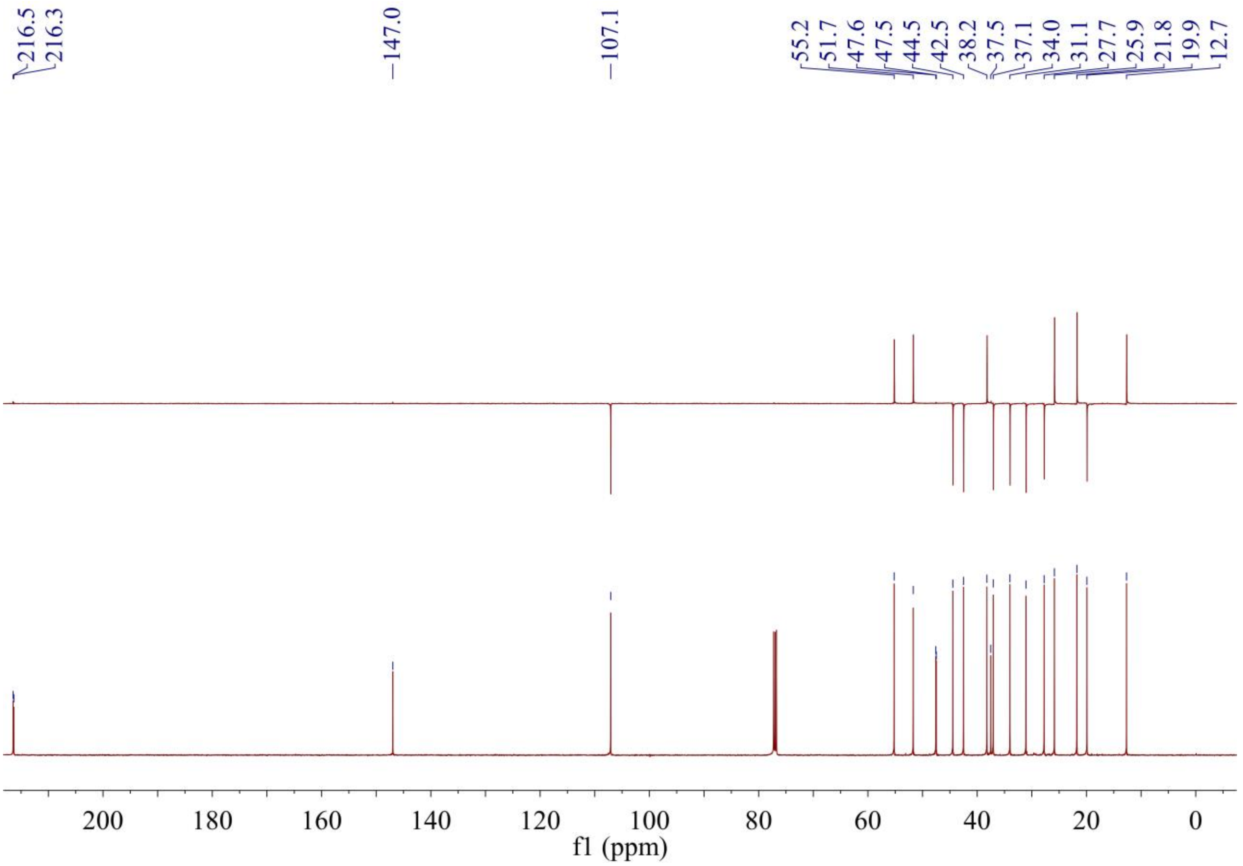


Fig. S42. ^{1}H NMR spectrum of **7** in $CDCl_3$

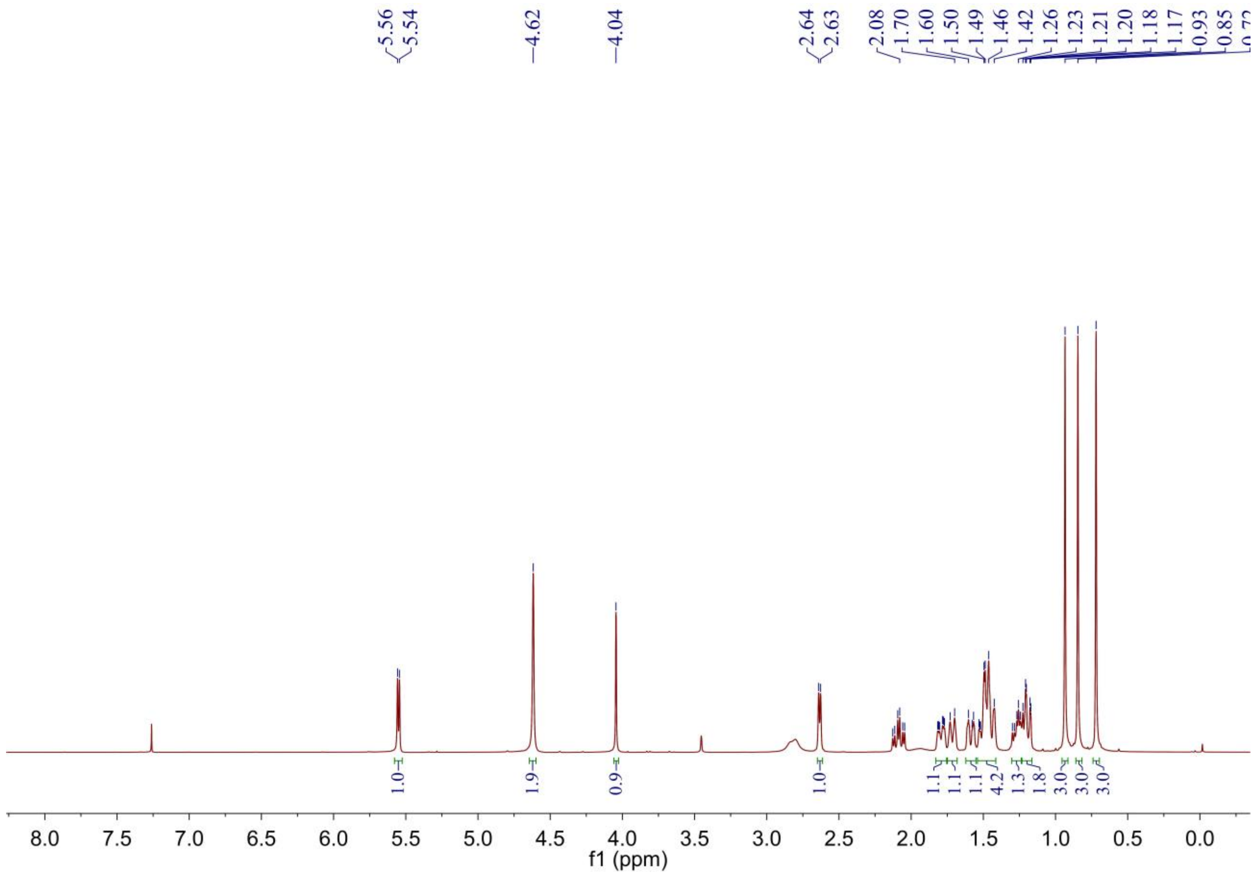


Fig. S43. ^{13}C NMR spectrum of **7** in $CDCl_3$

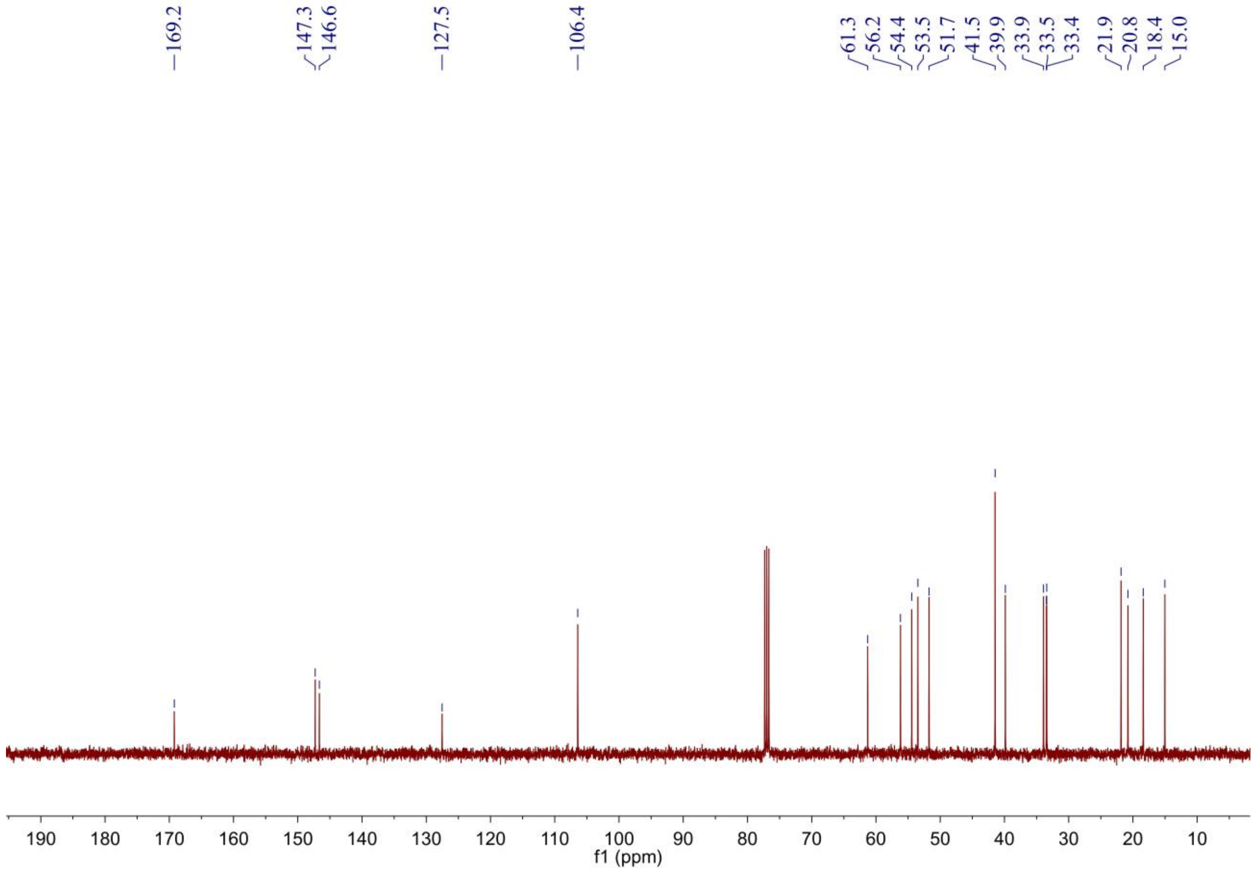


Fig. S44. ^{1}H NMR spectrum of **8** in $CDCl_3$

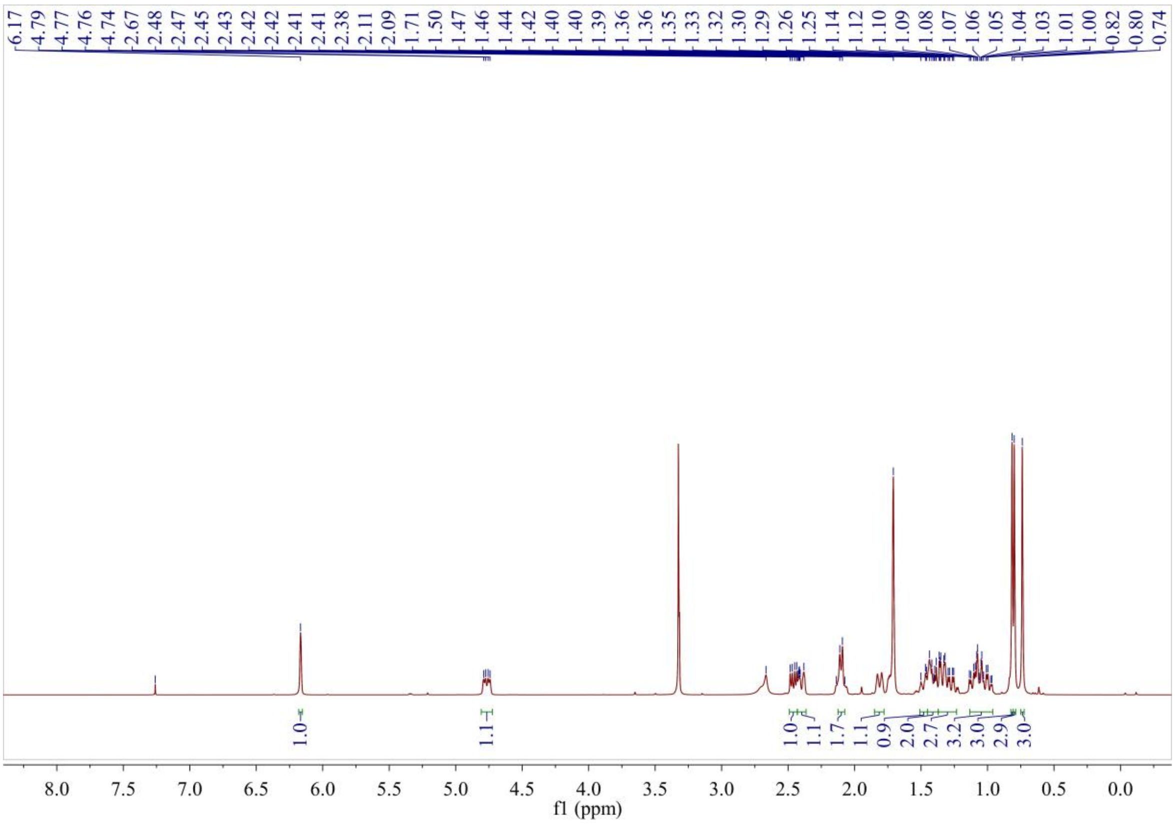


Fig. S45. ^{13}C NMR and DEPT135 spectra of **8** in $CDCl_3$

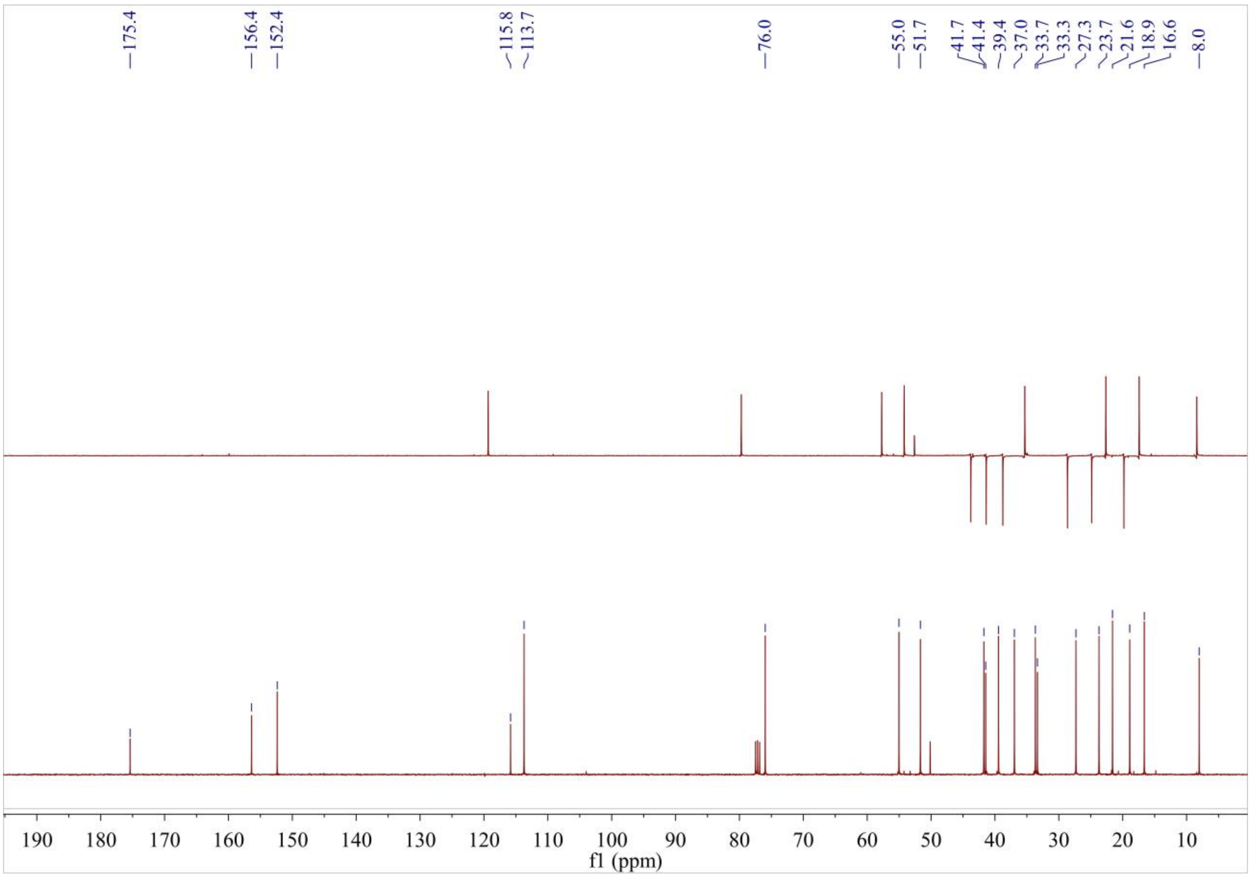


Fig. S46. ^{1}H NMR spectrum of **9** in $CDCl_3$

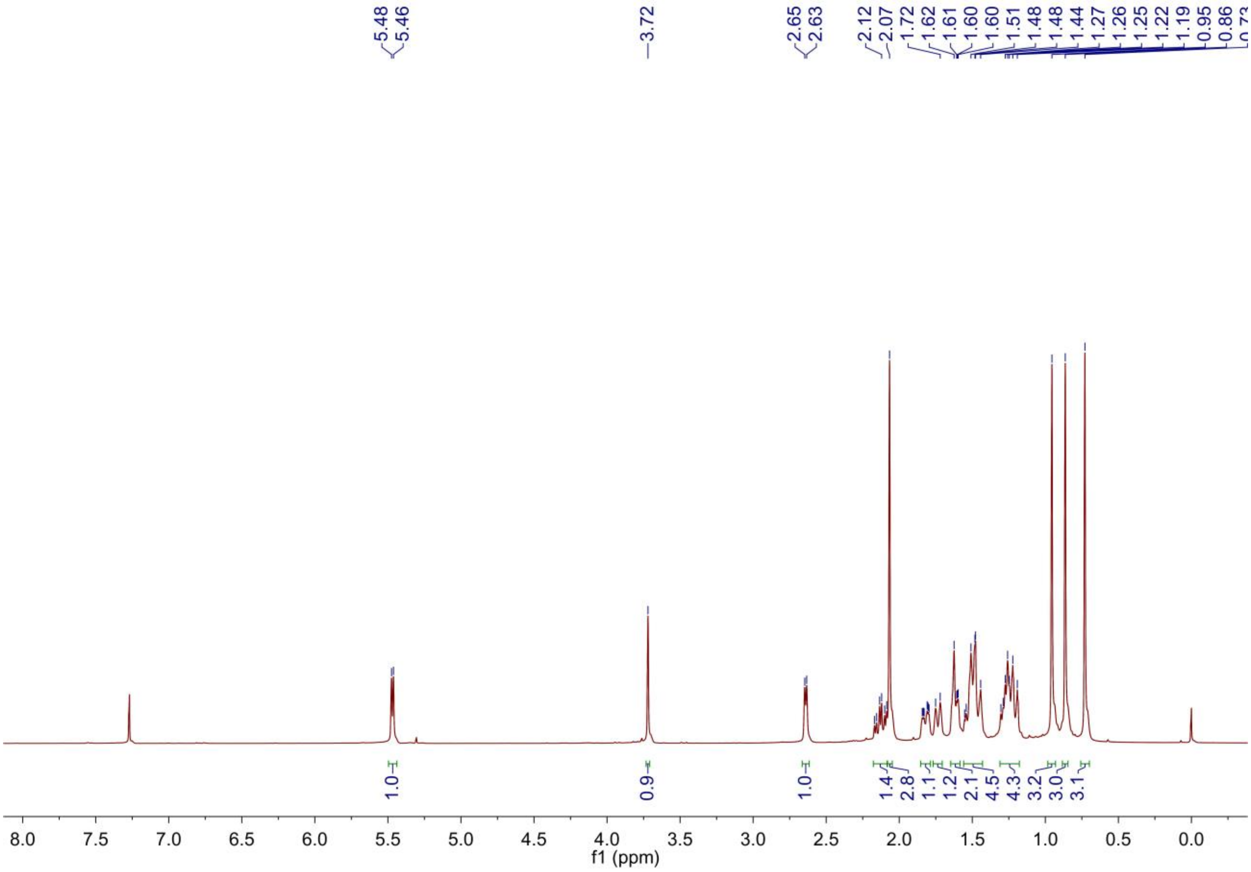


Fig. S47. ^{13}C NMR and DEPT135 spectra of **9** in $CDCl_3$

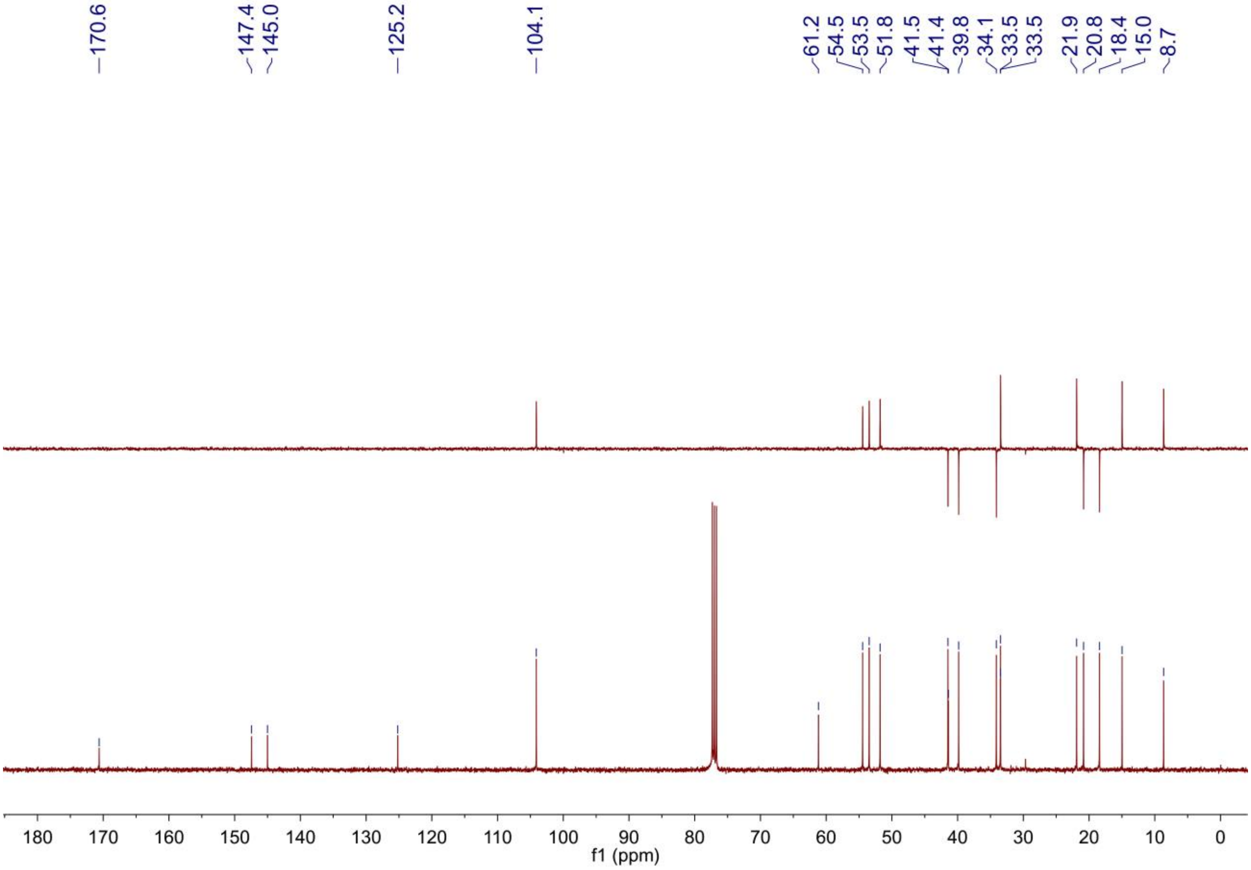


Fig. S48. ^{1}H NMR spectrum of **10** in CDCl$_3$

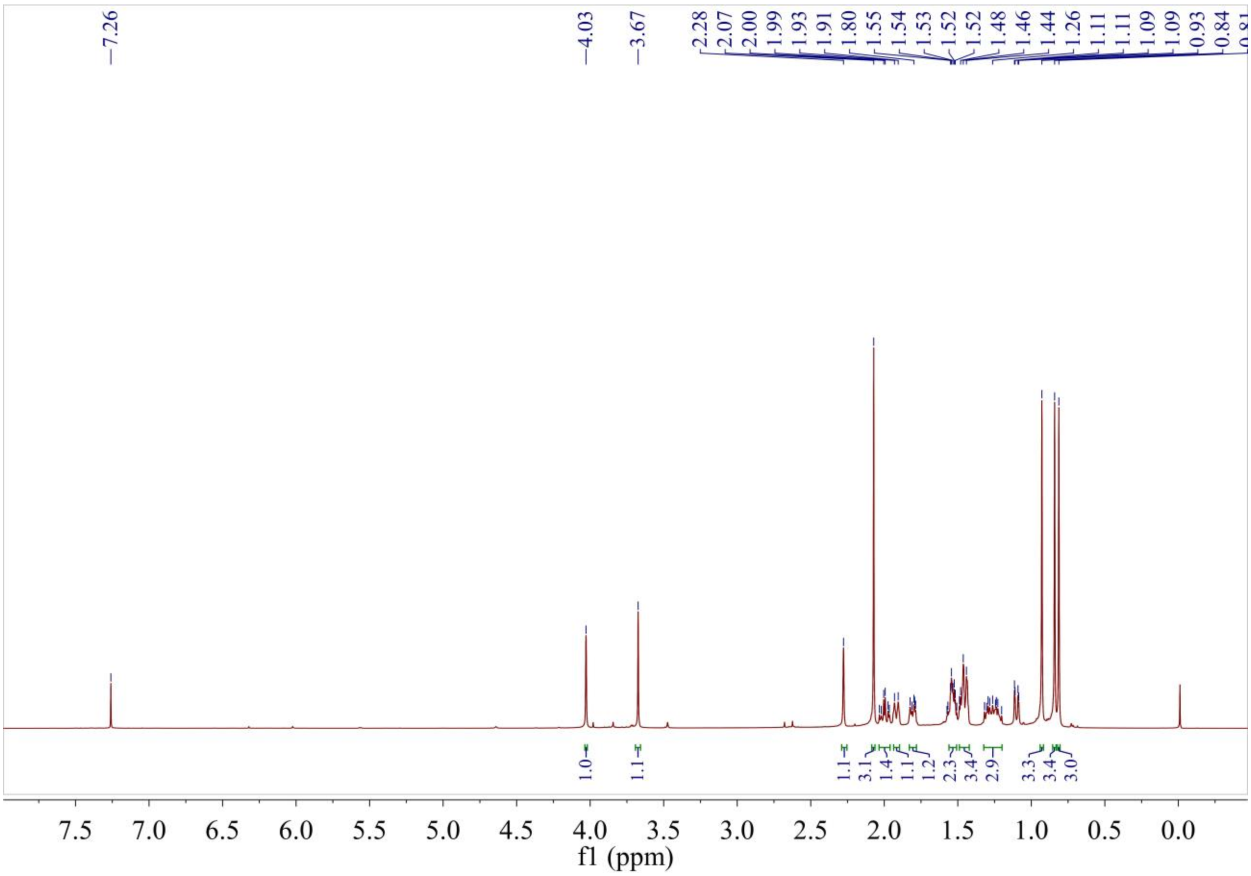


Fig. S49. ^{13}C NMR and DEPT135 spectra of **10** in CDCl$_3$

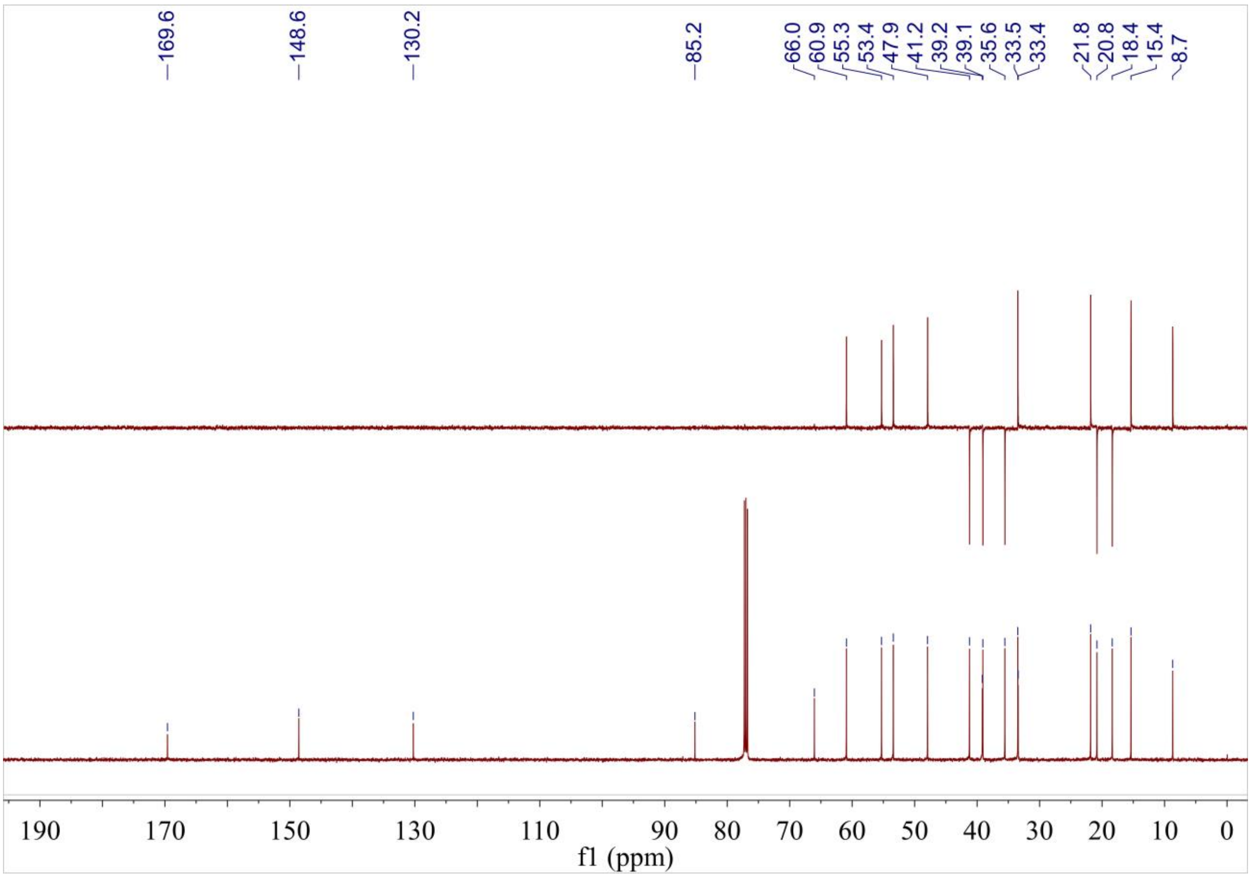


Fig. S50. ^{1}H NMR spectrum of **11** in CDCl$_3$

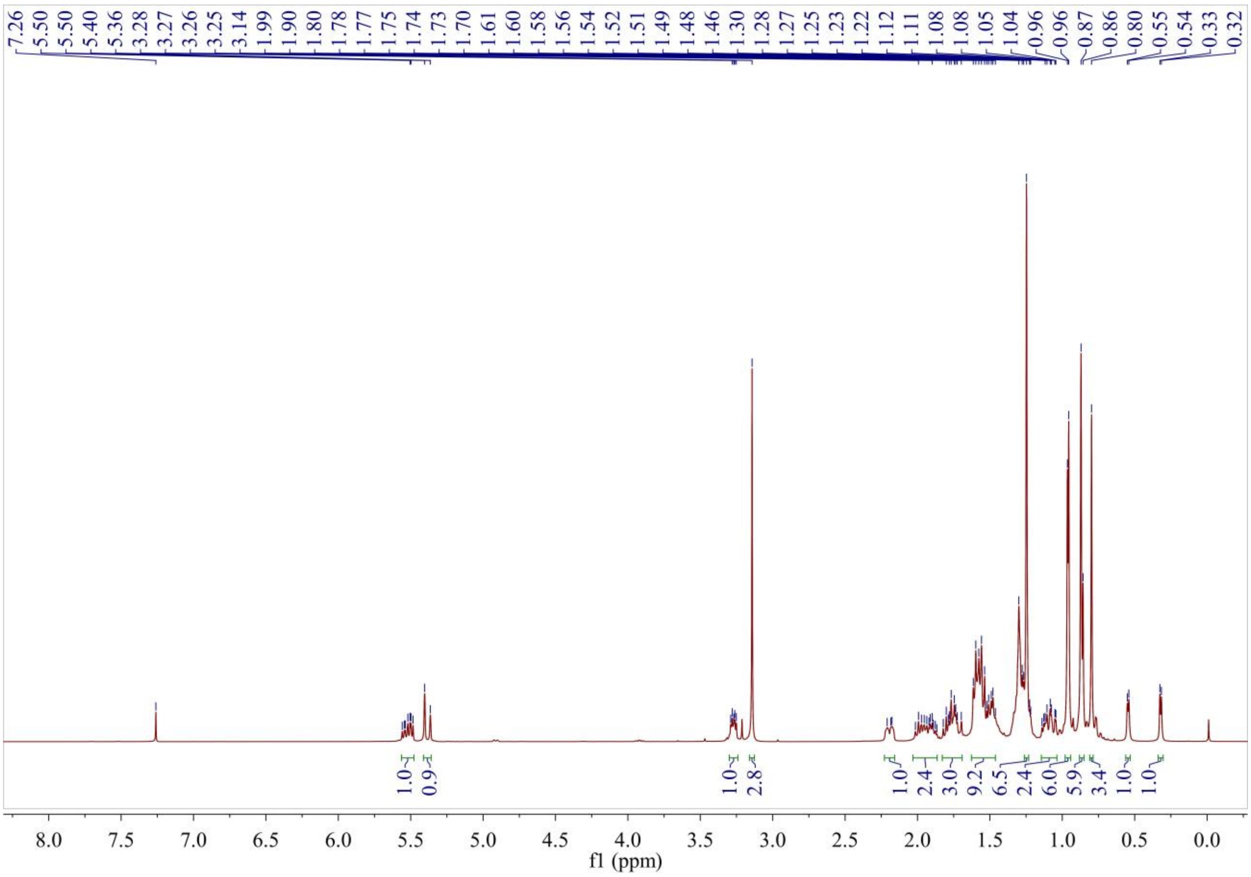


Fig. S51. ^{13}C NMR and DEPT135 spectra of **11** in CDCl$_3$

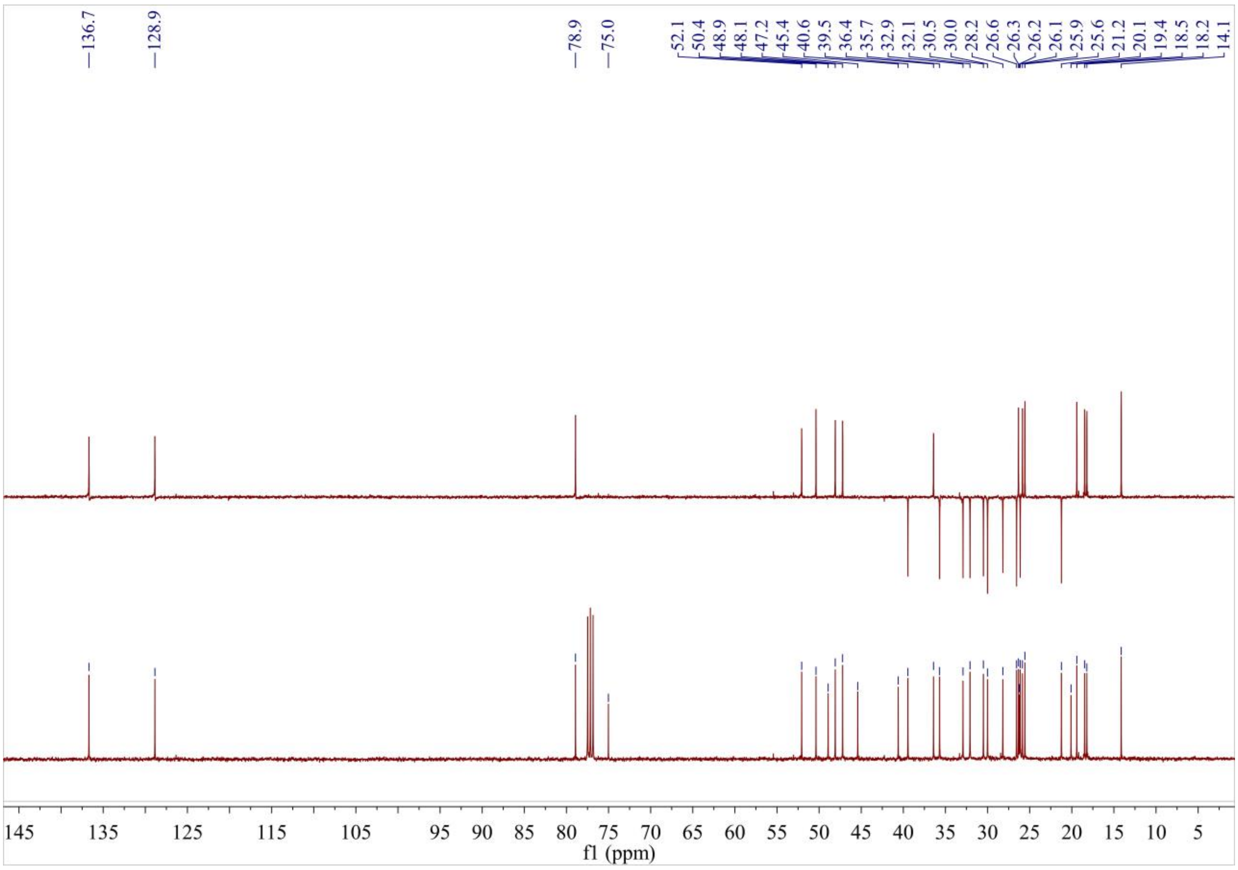


Fig. S52. ^{1}H NMR spectrum of **12** in $CDCl_3$

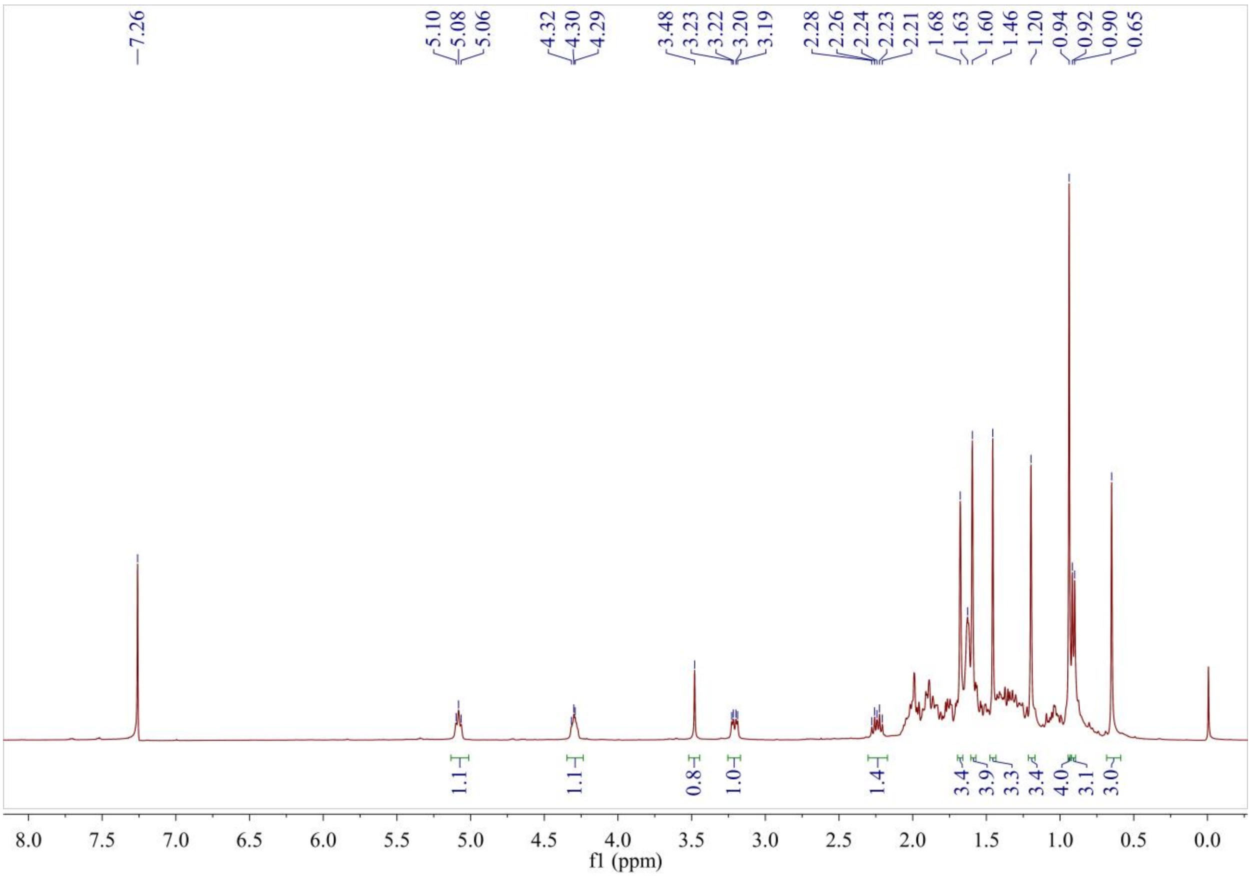


Fig. S53. ^{13}C NMR and DEPT135 spectra of **12** in $CDCl_3$

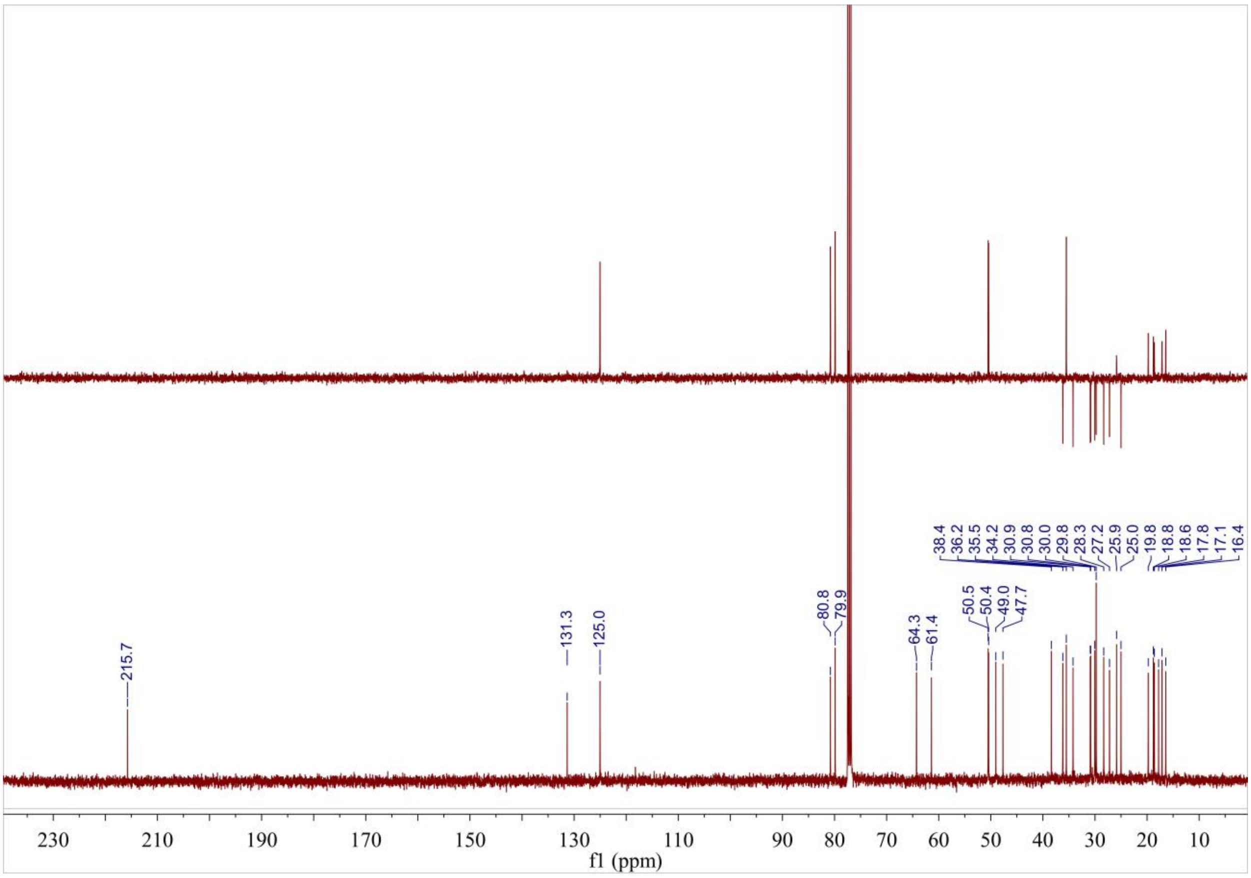


Fig. S54. ^{1}H NMR spectrum of **13** in $CDCl_3$

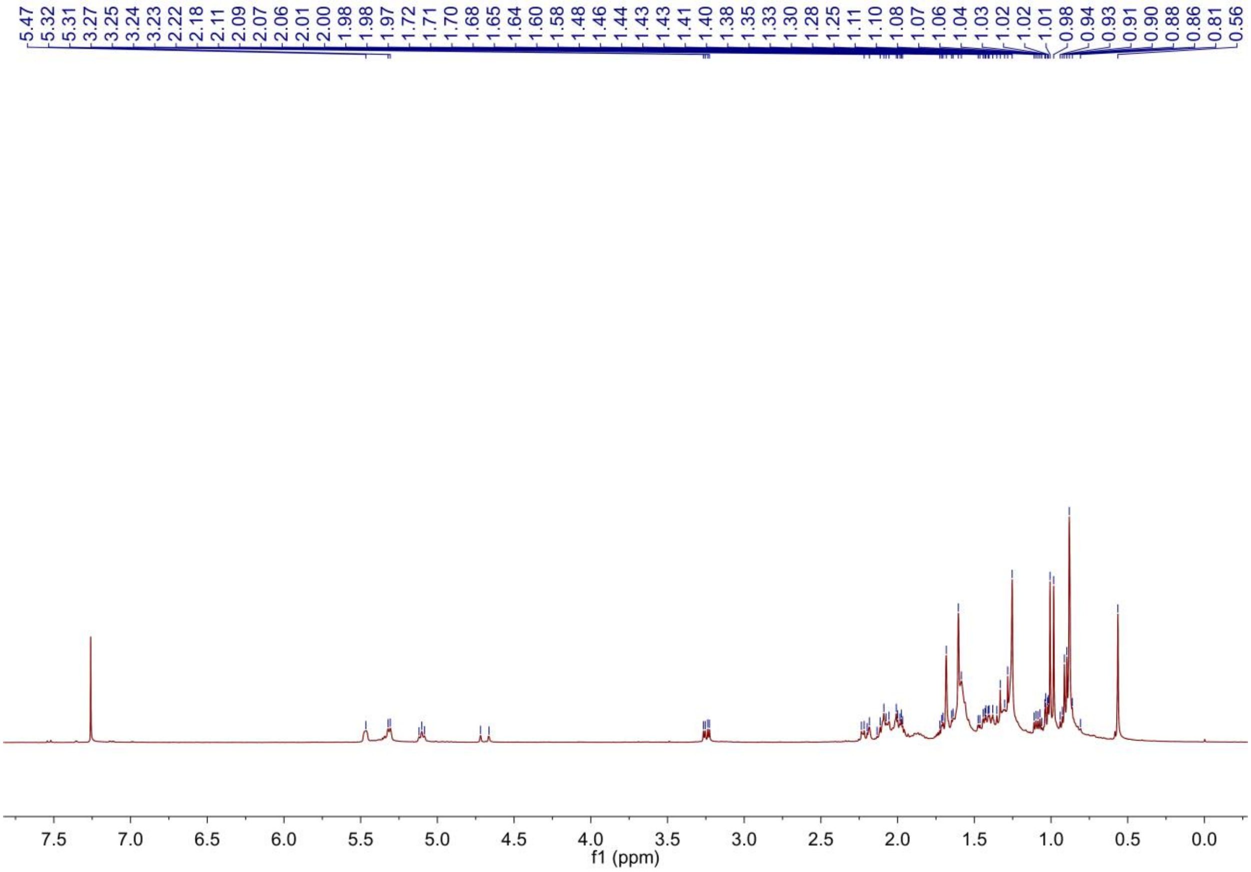


Fig. S55. ^{13}C NMR spectrum of **13** in $CDCl_3$

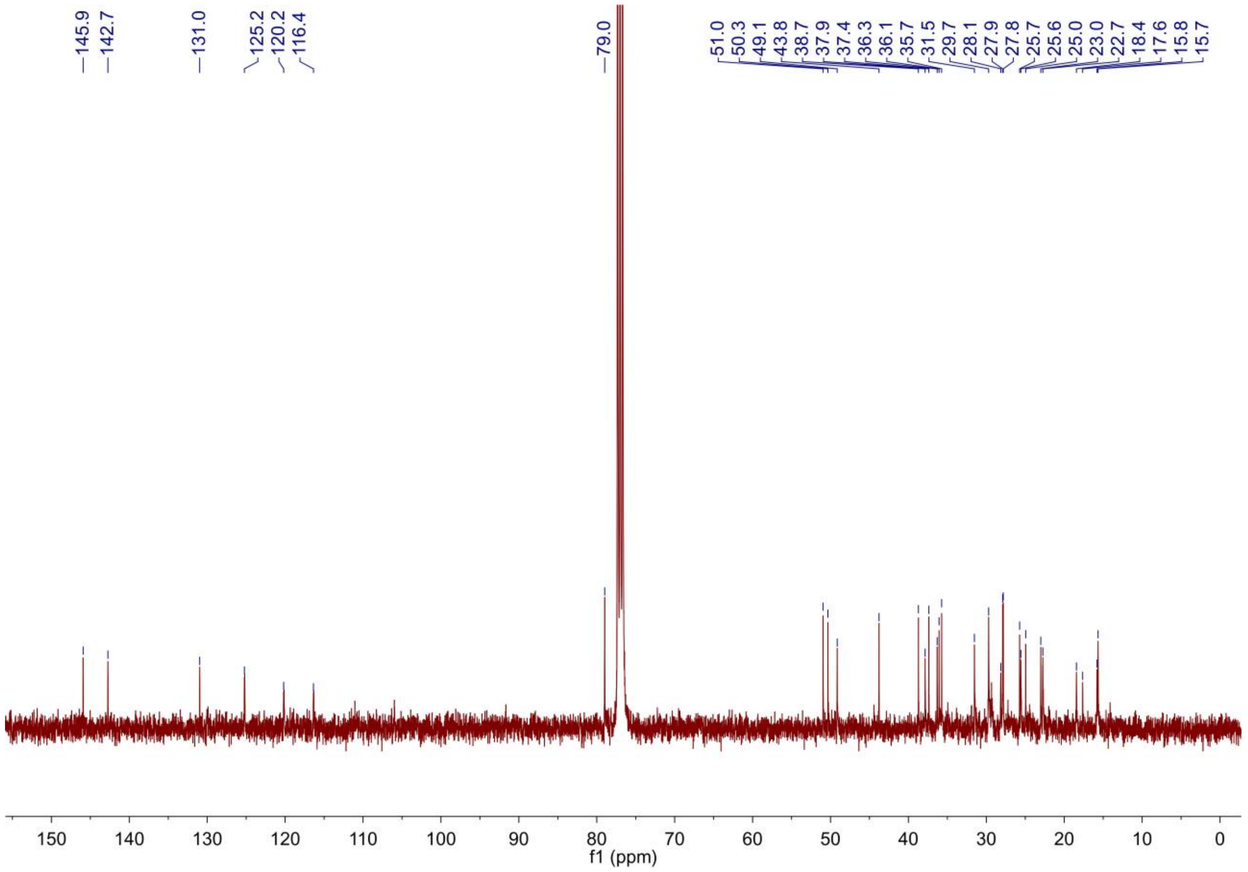


Fig. S56. ^{1}H NMR spectrum of **14** in $CDCl_3$

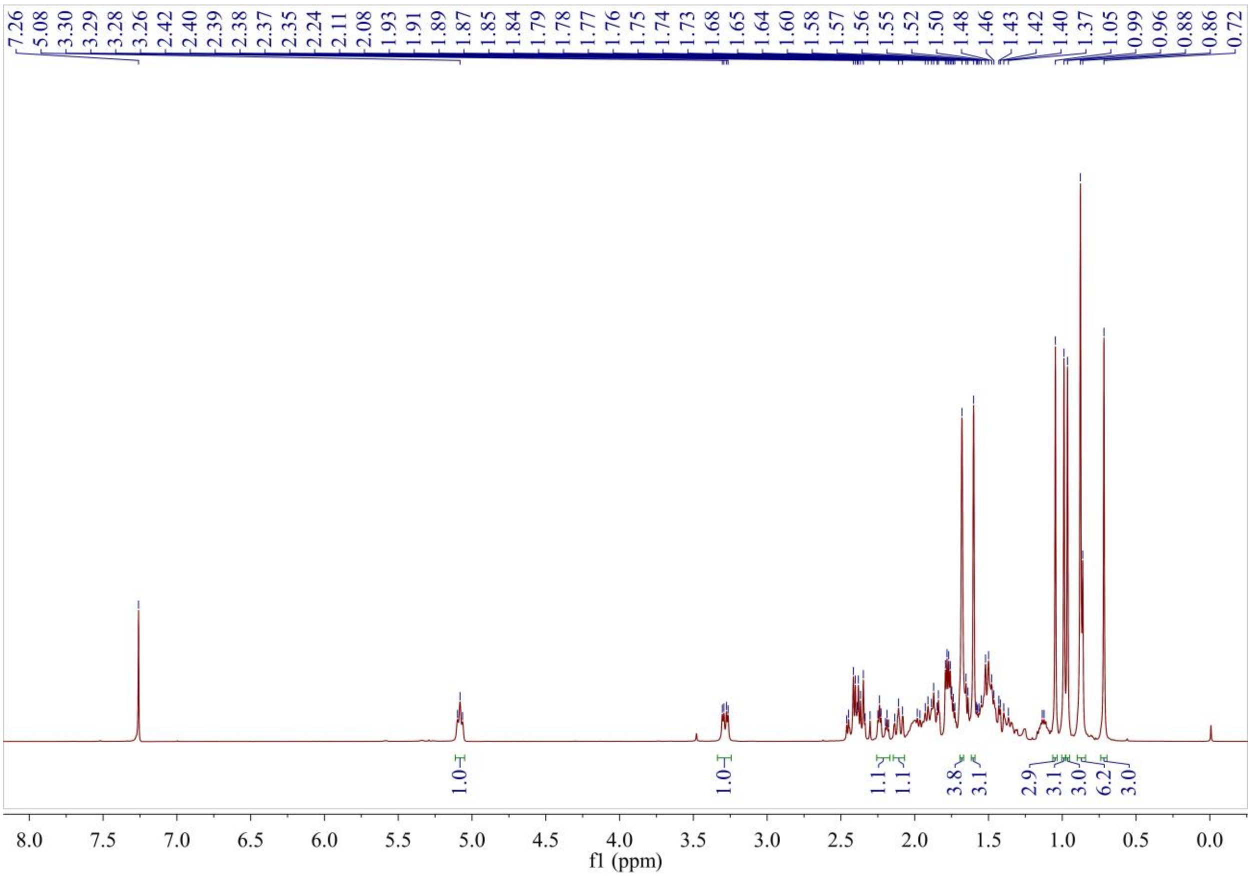


Fig. S57. ^{13}C NMR spectrum of **14** in $CDCl_3$

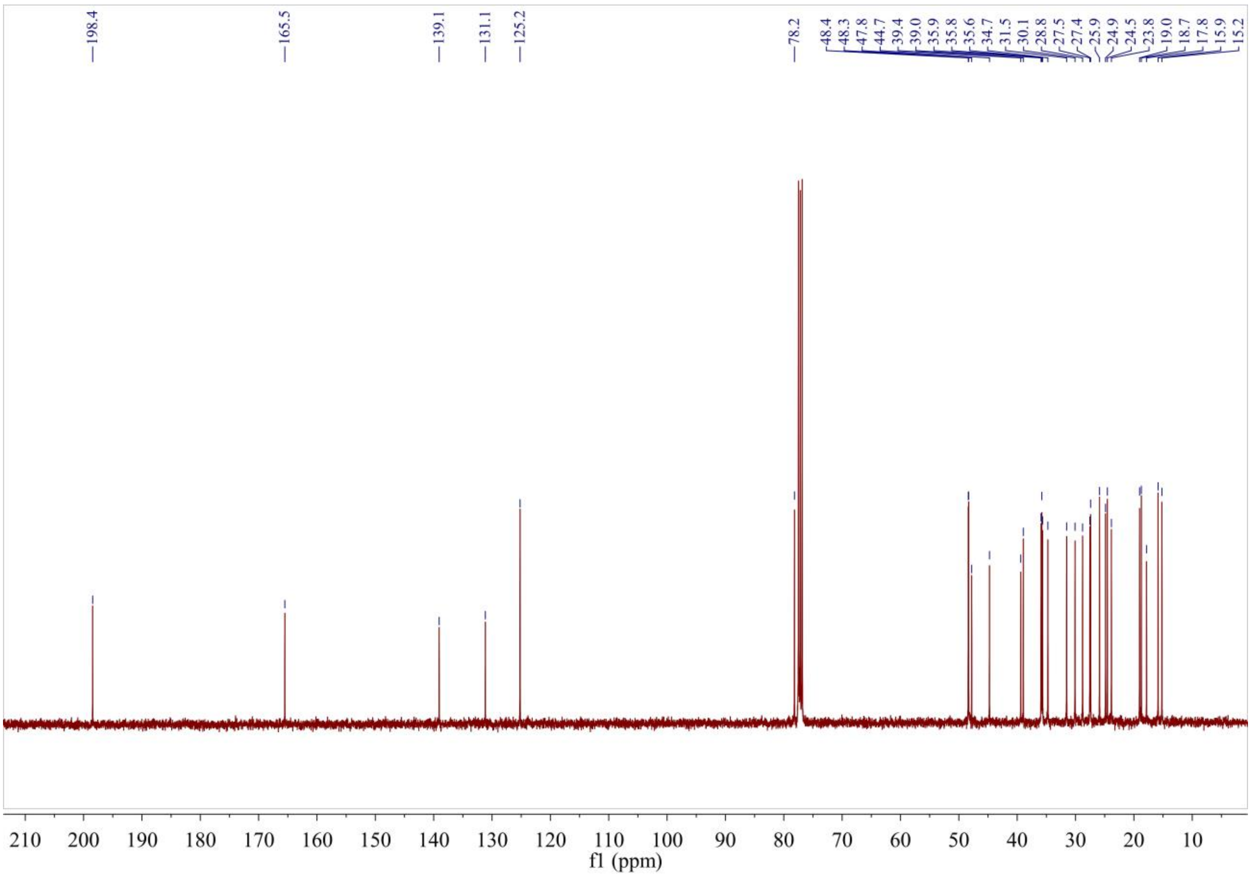


Fig. S58. ^{1}H NMR spectrum of **15** in CDCl$_3$

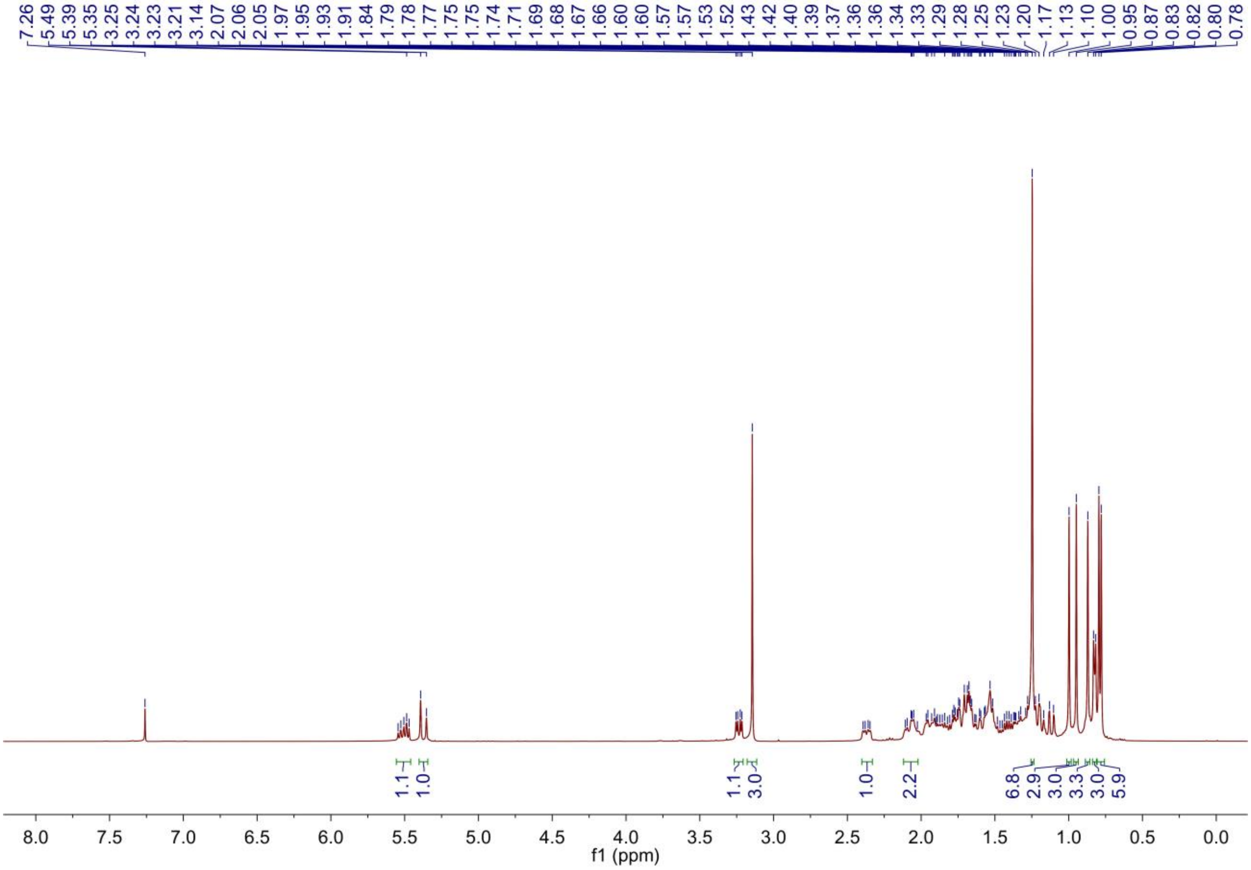


Fig. S59. ^{13}C NMR and DEPT135 spectra of **15** in CDCl$_3$

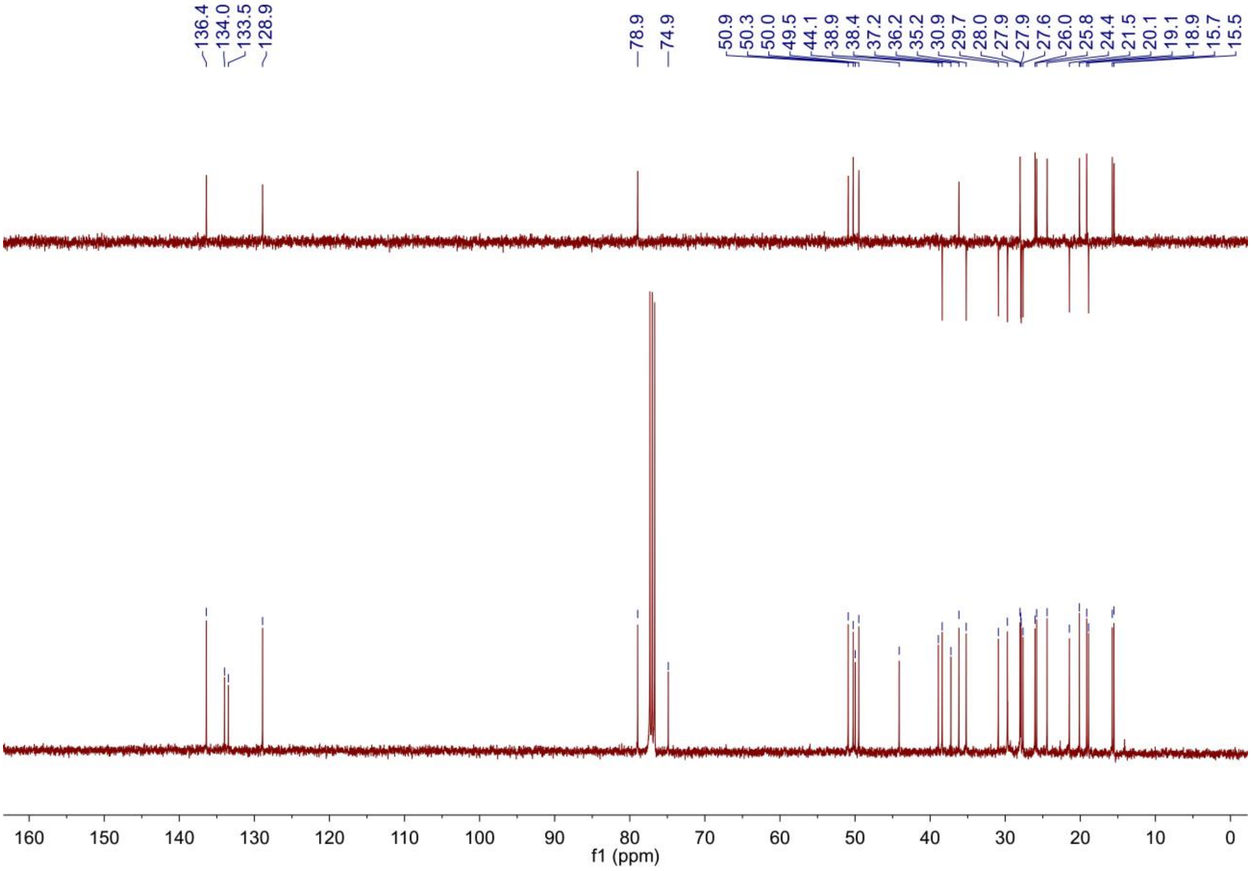


Fig. S60. ^{1}H NMR spectrum of **16** in $CDCl_3$

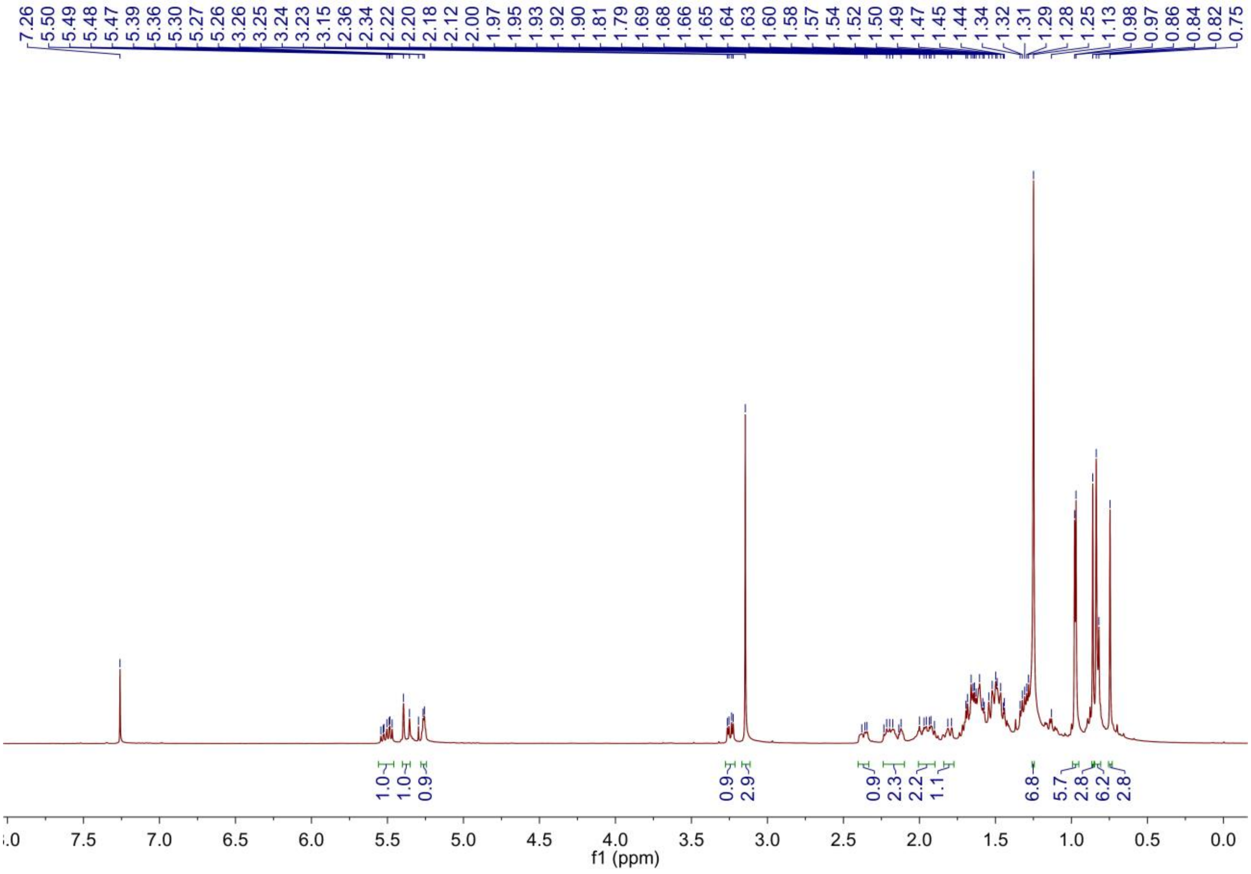


Fig. S61. ^{13}C NMR spectrum of **16** in $CDCl_3$