

## Supporting Information

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### Cytotoxic Lathyrane Diterpenoids from the Roots of *Euphorbia fischeriana*

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## 1. General Experimental Procedures

Optical rotations were measured on a Perkin-Elmer 341 polarimeter. UV spectra were recorded on a Shimadzu UV-2450 spectrophotometer. IR spectra were determined on a Bruker Tensor 37 infrared spectrophotometer with KBr disks. NMR spectra were measured on a Bruker AM-400 spectrometer at 25 °C. HRESIMS data were carried out on a Finnigan LCQ Deca instrument. A Shimadzu LC-20AT equipped with an SPD-M20A PDA detector was used for HPLC, and a YMC-pack ODS-A column (250 × 10 mm, S-5 μm, 12 nm) was used for semipreparative HPLC separation. Silica gel (300–400 mesh, Qingdao Haiyang Chemical Co. Ltd.), reversed-phase C<sub>18</sub> (Rp-C<sub>18</sub>) silica gel (12 nm, S-50 μm, YMC Co. Ltd.), Sephadex LH-20 gel (Amersham Biosciences), and MCI gel (CHP20P, 75–150 μm, Mitsubishi Chemical Industries Ltd.) were used for column chromatography (CC). All solvents were of analytical grade (Guangzhou Chemical Reagents Company, Ltd.). V/FITC and Cell cycle were purchased from Keygen Biotech, China. MTT was purchased from Sigma, USA.

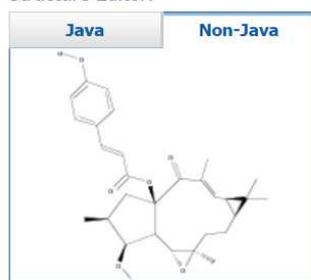
## 2. Plant Material

The roots of *Euphorbia fischeriana* Steud. were collected in November 2018 from Benxi city, Liaoning province, P. R. China and identified by Prof. You-Kai Xu of Xishuangbanna Tropical Botanical Garden, Chinese Academy of Sciences, and a voucher specimen (accession number: LD201812) was deposited at the Second People's Hospital of Yunnan Province

## 3. Extraction and Isolation

The air-dried powder of the roots of *E. fischeriana* (5 kg) was extracted by 95% EtOH (3 × 5 L) at room temperature to give 500 g of crude extract, which was suspended in H<sub>2</sub>O (3 L) and partitioned with EtOAc (3 × 3 L). The EtOAc fraction (200 g) was subjected to silica gel CC eluted with a CH<sub>2</sub>Cl<sub>2</sub>/MeOH gradient (10:0 → 10:1) to obtain three fractions (I–VI). Fr. III (20 g) was subjected to MCI gel CC eluted with a MeOH/H<sub>2</sub>O gradient (60:40 → 100:0) to give three fractions (IIIa–IIIc). Fr. IIIc was separated by silica gel CC eluted with a CH<sub>2</sub>Cl<sub>2</sub>/MeOH gradient (200:1 → 50:1) to give two subfractions (IIIc1 and IIIc2). Fr. IIIc1 was purified by sephadex LH-20 to obtain **5** (100 mg). Fr. IIIc2 was purified by semi-preparative HPLC (MeCN/H<sub>2</sub>O, 70:30, 3 mL/min) to obtain **1** (10 mg, *t<sub>R</sub>* = 12.5 min), **3** (16 mg, *t<sub>R</sub>* = 14 min), and **2** (7 mg, *t<sub>R</sub>* = 15 min). Fr. IV was subjected to silica gel CC eluted with CH<sub>2</sub>Cl<sub>2</sub>/MeOH (50:1) to give two fractions (IVa and IVb). Fr. IVa was purified by CH<sub>2</sub>Cl<sub>2</sub>/MeOH (80:1) and followed by sephadex LH-20 and to obtain **4** (23 mg).

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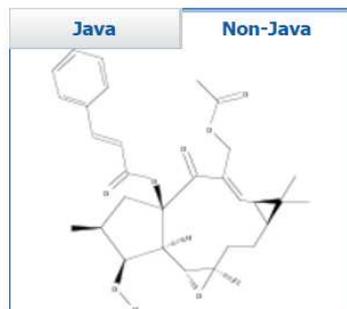
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<p>Score: 97 1. 62820-12-6</p> <p>Double bond geometry as described by E or Z, Rotation (-), Absolute stereochemistry.</p> <p><b>C<sub>29</sub>H<sub>36</sub>O<sub>6</sub></b>            2-Propionic acid, 3-phenyl-, (1aS,1bR,2S,3S,4aR,6E,7aR,8aS,10aR)-1a,1b,2,3,4,5,7a,8,8a,9,10,10a-dodecahydro-2-hydroxy-3,6,8,8,10a-pentamethyl-5-oxo-4aH-cyclopenta[3,4]cyclopropa[8,9]cycloundec[1,2-0]oxinan-4a-yl ester, (2E)-            • Key Physical Properties            Experimental Properties</p>	<p>Score: 97 2. 882041-55-6</p> <p>Double bond geometry as described by E or Z, Rotation (-), Absolute stereochemistry.</p> <p><b>C<sub>29</sub>H<sub>36</sub>O<sub>6</sub></b>            2-Propionic acid, 3-phenyl-, (1aE,1bR,2S,3R,4aR,6E,7aR,8aS,10aR)-1a,1b,2,3,4,5,7a,8,8a,9,10,10a-dodecahydro-2-hydroxy-3-(hydroxymethyl)-4,6,8,10a-tetramethyl-5-oxo-4aH-cyclopenta[3,4]cyclopropa[8,9]cycloundec[1,2-0]oxinan-4a-yl ester, (2E)-            • Key Physical Properties            Experimental Properties</p>	<p>Score: 97 3. 1957180-03-8</p> <p>Absolute stereochemistry, Double bond geometry as described by E or Z.</p> <p><b>C<sub>29</sub>H<sub>36</sub>O<sub>6</sub></b>            STRUCTURE NAME NOT YET ASSIGNED            • Key Physical Properties</p>
<p>Score: 96 4. 62820-11-5</p> <p><b>C<sub>29</sub>H<sub>36</sub>O<sub>6</sub></b>            2-Propionic acid, 3-phenyl-, (1aS,1bR,2S,3S,4aR,6E,7aR,8aS,10aR)-1a,1b,2,3,4,5,7a,8,8a,9,10,10a-dodecahydro-2-hydroxy-6-(hydroxymethyl)-3,6,8,10a-tetramethyl-5-oxo-4aH-cyclopenta[3,4]cyclopropa[8,9]cycloundec[1,2-0]oxinan-4a-yl ester, (2E)-            • Key Physical Properties</p>	<p>Score: 95 5. 62820-17-1</p> <p><b>C<sub>31</sub>H<sub>38</sub>O<sub>6</sub></b>            2-Propionic acid, 3-phenyl-, 2-(acetyloxy)-1a,1b,2,3,4,5,7a,8,8a,9,10,10a-dodecahydro-3,6,8,8,10a-pentamethyl-5-oxo-4aH-cyclopenta[3,4]cyclopropa[8,9]cycloundec[1,2-0]oxinan-4a-yl ester, [1aR,1bR,2S,3S,4aR,6E,7aR,8aS,10aR]-[9CI]            • Key Physical Properties</p>	<p>Score: 95 E. 1303589-45-8</p> <p>Double bond geometry as described by E or Z, Rotation (+), Absolute stereochemistry.</p> <p><b>C<sub>29</sub>H<sub>36</sub>O<sub>6</sub></b>            2-Propionic acid, 3-phenyl-, (1aE,1bR,2S,3S,4aR,6E,7aR,8aS,10aR)-1a,1b,3,4,4a,5,7a,8,8a,9,10,10a-dodecahydro-4a-hydroxy-3,6,8,8,10a-pentamethyl-5-oxo-2H-cyclopenta[3,4]cyclopropa[5,6]cycloundec[1,2-0]oxinan-2-yl ester, (2E)-            • Key Physical Properties</p>

Figure S1: Scifinder search of new compound 1

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<input type="checkbox"/> 65-69	18272
<input type="checkbox"/> 0-64 (least similar)	65316

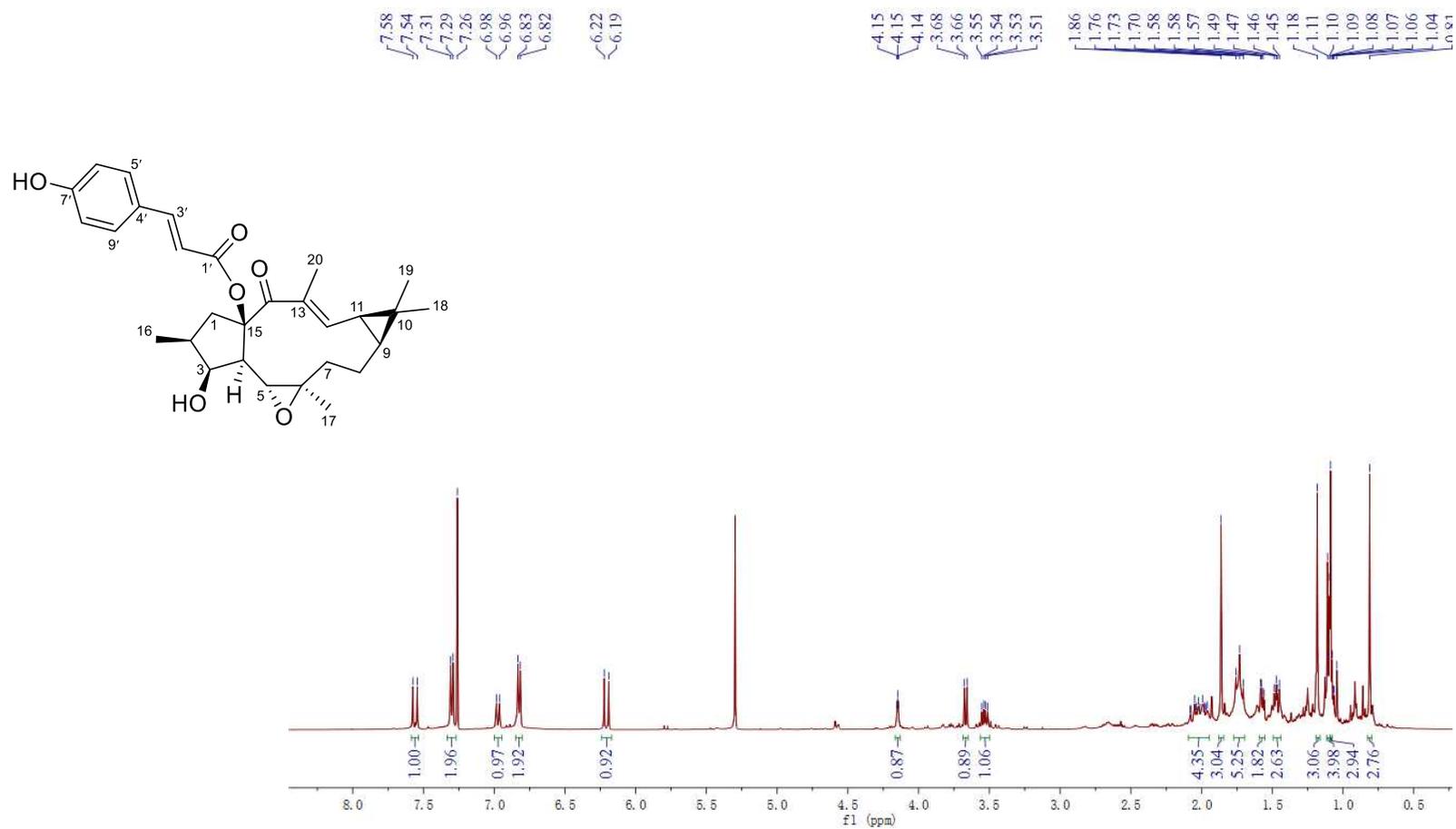
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<p>Score: 99 1. 882041-54-5</p> <p>Double bond geometry as described by E or Z, Rotation (-), Absolute stereochemistry.</p> <p><b>C<sub>33</sub> H<sub>38</sub> O<sub>7</sub></b>        2-Propenoic acid, 3-phenyl-, (1aR,1bR,2S,3R,4aR,6E,7aR,8aS,10aR)-3-[(acetyloxy)methyl]-1a,1b,2,3,4,5,7a,8a,9,10,10a-dodecahydro-2-hydroxy-6,8,8,10a-tetramethyl-5-oxo-4aH-cyclopenta[3,4]cyclopropa[6,9]cyclohexa[1,2-d]oxirin-4a-yl ester, (2E)-</p> <p>• Key Physical Properties        Experimental Properties</p>	<p>Score: 97 2. 62820-18-2</p> <p>Double bond geometry as described by E or Z, Rotation (-), Absolute stereochemistry.</p> <p><b>C<sub>33</sub> H<sub>40</sub> O<sub>9</sub></b>        2-Propenoic acid, 3-phenyl-, 2-(acetyloxy)-6-[(acetyloxy)methyl]-1a,1b,2,3,4,5,7a,8,8a,9,10,10a-dodecahydro-3,8,8,10a-tetramethyl-5-oxo-4aH-cyclopenta[3,4]cyclopropa[6,9]cyclohexa[1,2-d]oxirin-4a-yl ester, (1aR,1aR',1bR',2S',3S',4aR',6E',7aR',8aR',10aR')-(9C)</p> <p>• Key Physical Properties</p>	<p>Score: 96 3. 882041-56-7</p> <p>Double bond geometry as described by E or Z, Rotation (-), Absolute stereochemistry.</p> <p><b>C<sub>33</sub> H<sub>40</sub> O<sub>9</sub></b>        2-Propenoic acid, 3-phenyl-, (1aR,1bR,2S,3R,4aR,6E,7aR,8aS,10aR)-2-(acetyloxy)-3-[(acetyloxy)methyl]-1a,1b,2,3,4,5,7a,8a,9,10,10a-dodecahydro-6,8,8,10a-tetramethyl-5-oxo-4aH-cyclopenta[3,4]cyclopropa[6,9]cyclohexa[1,2-d]oxirin-4a-yl ester, (2E)-</p> <p>• Key Physical Properties        Experimental Properties</p>
<p>Score: 95 4. 1089146-75-7</p> <p>Double bond geometry as described by E or Z, Rotation (-), Absolute stereochemistry.</p> <p><b>C<sub>33</sub> H<sub>44</sub> O<sub>9</sub></b>        2-Propenoic acid, 3-phenyl-, (1aR,1bR,2S,3R,4aR,6E,7aR,8aS,10aR)-1a,1b,2,3,4,5,7a,8,8a,9,10,10a-dodecahydro-6,8,8,10a-tetramethyl-5-oxo-2-(1-oxopropoxy)methyl-3-[(1-oxopropoxy)methyl]-4aH-cyclopenta[3,4]cyclopropa[6,9]cyclohexa[1,2-d]oxirin-4a-yl ester, (2E)-</p> <p>• Key Physical Properties        Experimental Properties</p>	<p>Score: 95 5. 1089146-76-8</p> <p>Double bond geometry as described by E or Z, Rotation (-), Absolute stereochemistry.</p> <p><b>C<sub>37</sub> H<sub>48</sub> O<sub>9</sub></b>        2-Propenoic acid, (1aR,1bR,2S,3R,4aR,6E,7aR,8aS,10aR)-1a,1b,3,4,4a,5,7a,8,8a,9,10,10a-dodecahydro-6,8,8,10a-tetramethyl-5-oxo-3-[(1-oxobutoxy)methyl]-4a-[(2E)-1-oxo-3-phenyl-2-propen-1-yl]oxy)-2aH-cyclopenta[3,4]cyclopropa[5,6]cyclohexa[1,2-d]oxirin-2-yl ester</p> <p>• Key Physical Properties        Experimental Properties</p>	<p>Score: 95 6. 1222657-01-3</p> <p>Double bond geometry as described by E or Z, Absolute stereochemistry.</p> <p><b>C<sub>33</sub> H<sub>44</sub> O<sub>9</sub></b>        INDEX NAME NOT YET ASSIGNED</p> <p>• Key Physical Properties</p>

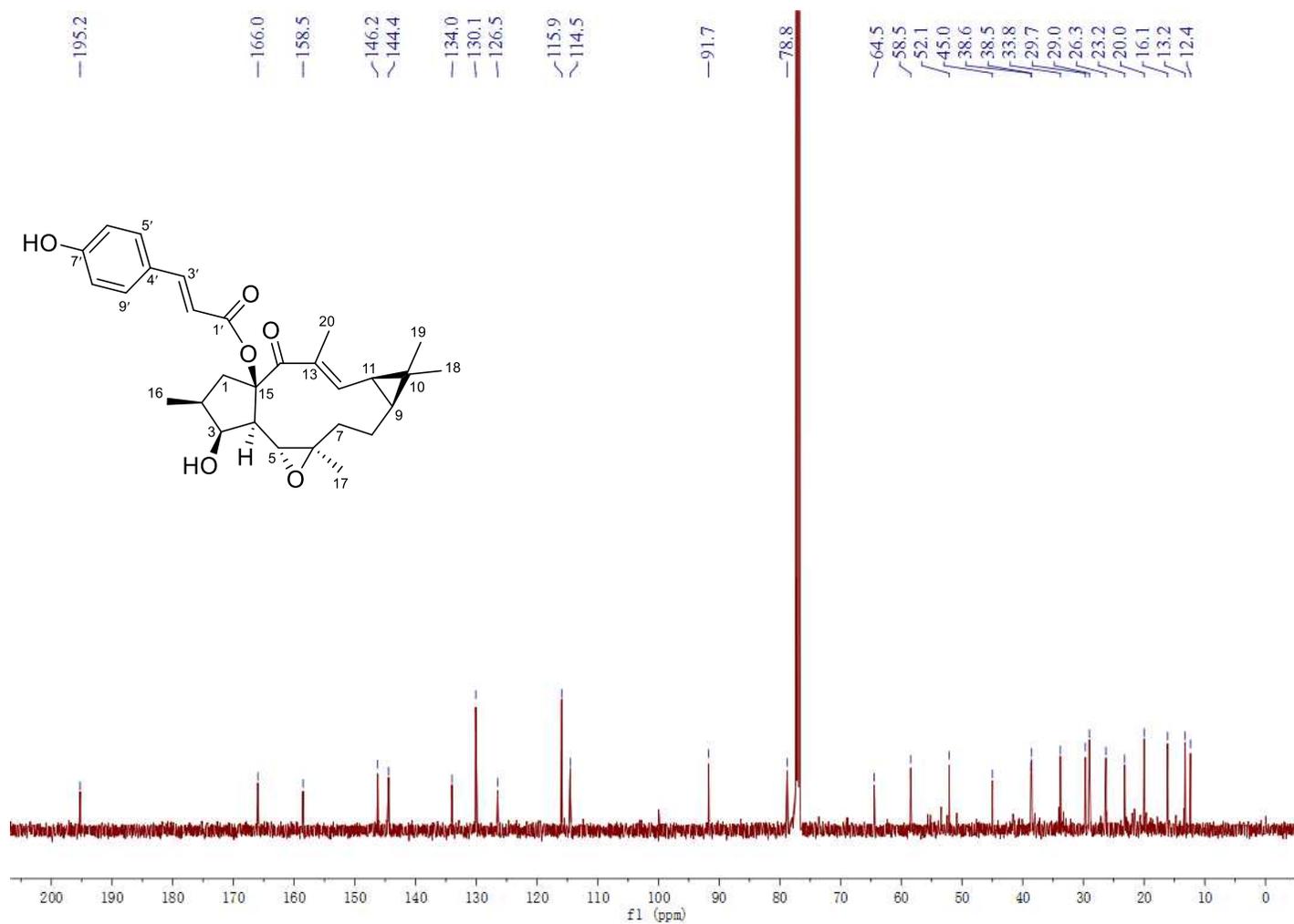
Figure S2: Scifinder search of new compound 2

**Table S1.** <sup>1</sup>H NMR (400 MHz) and <sup>13</sup>C NMR (100 MHz) data for **1-5** ( $\delta$  in ppm, *J* in Hz)

No.	1		2		3		4		5	
1 $\alpha$	3.53, dd (13.3, 7.6)	45.0	3.53, dd (13.4, 7.4)	44.3	3.53, dd (13.5, 7.4)	44.9	3.31, dd (13.6, 8.4)	46.8	3.47, dd (13.5, 7.2)	44.6
1 $\beta$			1.75, dd (13.4, 13.4)		1.73, dd (13.5, 13.5)		1.56, dd (13.6, 12.1)		1.76, dd (13.5, 13.5)	
2	2.02, m	38.5	2.02, m	38.4	2.01, m	38.5	1.91, m	38.4	1.99, m	38.6
3	4.15, dd (3.7, 3.7)	78.8	4.14, dd (3.6, 3.6)	78.5	4.13, dd (3.3, 3.3)	78.6	4.15, dd (3.2, 3.2)	79.7	4.13, dd (3.5, 3.5)	78.4
4	1.57, dd (9.4, 3.7)	52.1	1.63, m	51.6	1.57, dd (9.4, 3.3)	52.2	1.43, dd (9.6, 3.2)	53.1	1.61, dd (9.4, 3.5)	52.1
5	3.67, d (9.4)	58.5	3.64, d (9.3)	58.1	3.63, d (9.4)	58.2	3.44, d (9.6)	58.6	3.63, d (9.4)	58.1
6		64.5		63.6		63.9		63.8		63.9
7a	1.62, m	38.6	1.63, m	38.5	1.62, m	38.7	1.60, m	38.9	1.58, m	38.6
7b	2.05, m		2.05, m		2.06, m		2.03, m		2.03, m	
8 $\alpha$	2.01, m	23.2	2.10, m	23.3	2.07, m	23.3	2.06, m	23.1	2.07, m	23.3
8 $\beta$	1.51, m		1.56, m		1.52, m		1.64, m		1.60, m	
9	1.12, m	33.8	1.27, m	35.2	1.14, m	33.8	1.27, m	35.8	1.24, m	34.8
10		26.3		28.0		26.3		27.9		27.5
11	1.47, dd (11.0, 7.8)	29.7	1.67, dd (10.8, 7.8)	29.8	1.49, dd (11.0, 7.8)	29.7	1.71, dd (11.9, 7.9)	29.9	1.68, dd (11.3, 7.8)	29.5
12	6.97, d (11.0)	144.4	7.27, d (10.8)	150.7	6.99, d (11.0)	144.3	7.84, d (11.9)	152.5	7.10, d (11.3)	147.6
13		134.0		132.4		134.0		136.9		136.8
14		195.2		193.1		195.1		199.2		196.3
15		91.7		91.8		92.0		89.1		91.8
16	1.10, d (6.9)	13.2	1.10, d (6.7)	13.1	1.10, d (6.9)	13.2	1.11, d (6.9)	13.7	1.09, d (6.7)	13.2
17	1.18, s	20.0	1.24, s	20.0	1.19, s	20.0	1.22, s	20.3	1.26, s	20.2
18	1.09, s	29.0	1.12, s	29.0	1.11, s	29.0	1.21, s	29.0	1.10, s	28.9
19	0.81, s	16.1	0.87, s	16.2	0.85, s	16.2	1.12, s	16.2	0.84, s	16.1
20	1.86, s	12.4	a 4.92, d (11.5) b 4.98, d (11.5)	58.1	1.87, s	12.4	4.35, d (12.0) 4.46, d (12.0)	58.4	4.30, d (12.3) 4.49, d (12.3)	57.9
1'		166.0		165.4		165.6				165.6
2'	6.21, d (15.8)	114.5	6.44, d (16.0)	117.1	6.44, d (16.0)	117.4			6.43, d (16.0)	117.2
3'	7.56, d (15.8)	146.2	7.69, d (16.0)	146.8	7.68, d (16.0)	146.5			7.67, d (16.0)	146.8
4'		126.5		133.8		133.9				133.9
5'/9'	7.30, d (8.5)	130.1	7.47, d (7.5)	128.2	7.47, m	128.1			7.46, m	128.1
6'/8'	6.82, d (8.5)	115.9	7.40, m	129.0	7.39, m	129.0			7.38, m	128.9
7'		158.5	7.40, m	130.8	7.39, m	130.7			7.38, m	130.8
20-OAc				170.9						
			1.98, s	20.9						

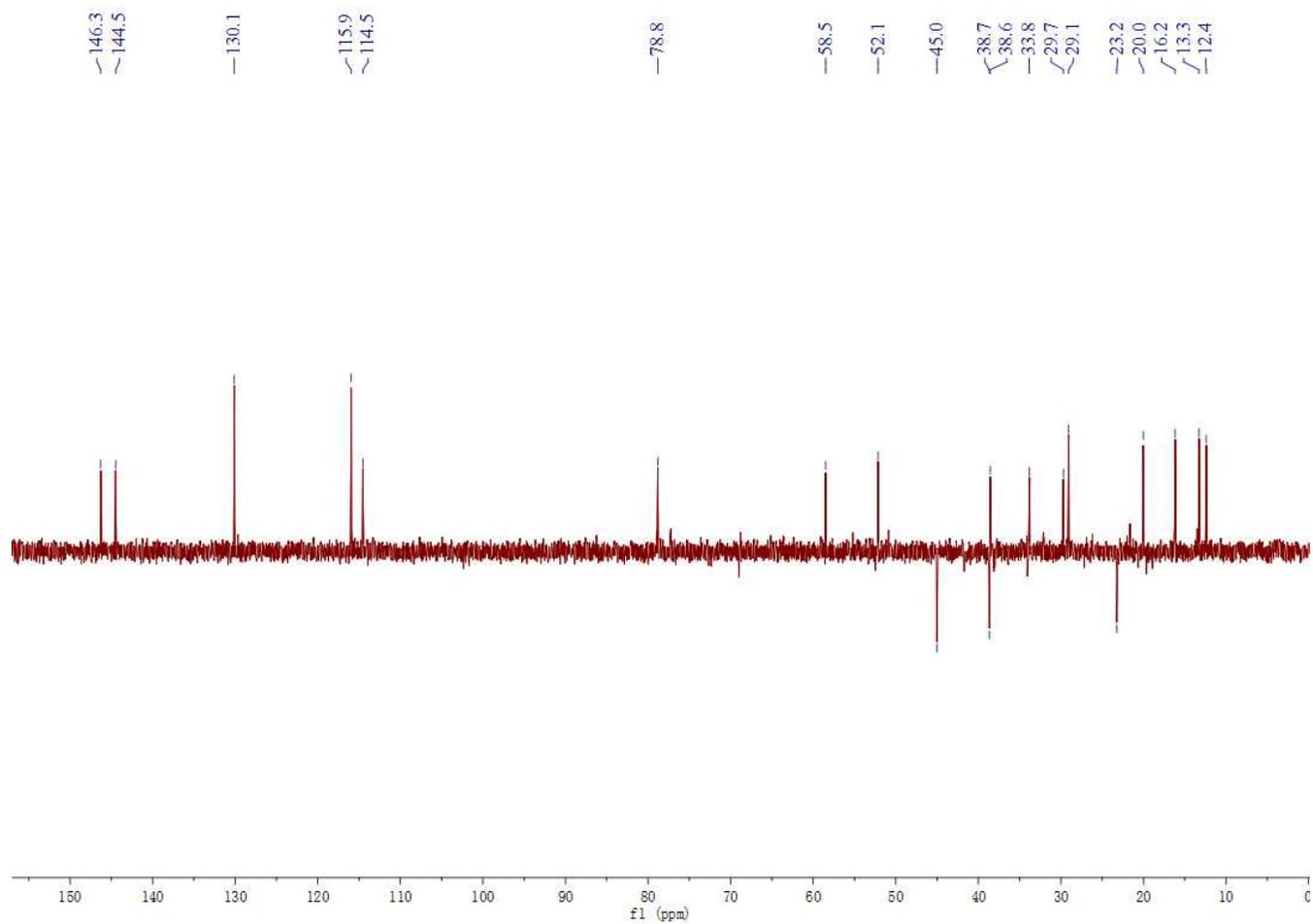


**Figure S3:**  $^1\text{H}$  NMR spectrum of **1** in  $\text{CDCl}_3$



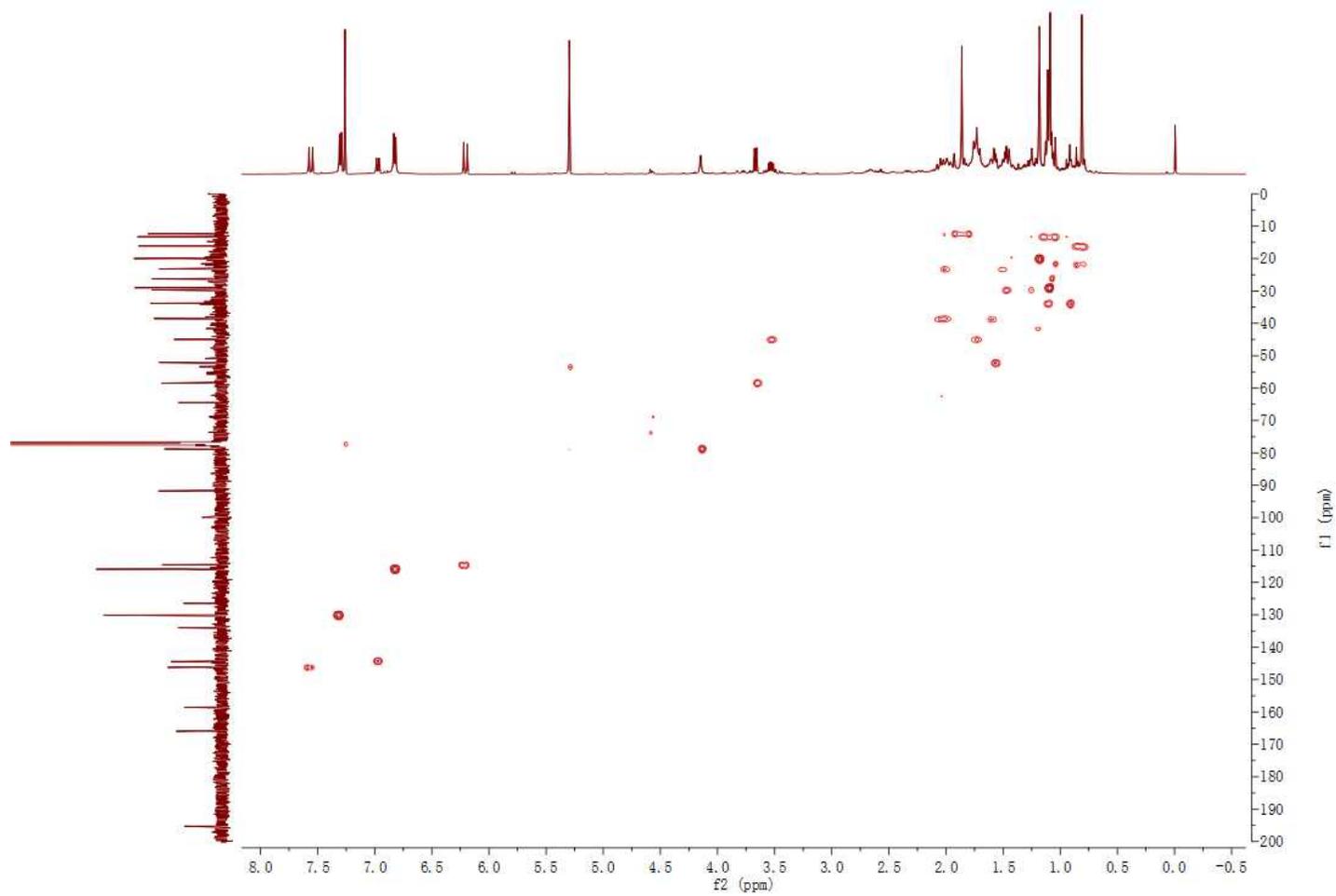
**Figure S4:**  $^{13}\text{C}$  NMR spectrum of **1** in  $\text{CDCl}_3$

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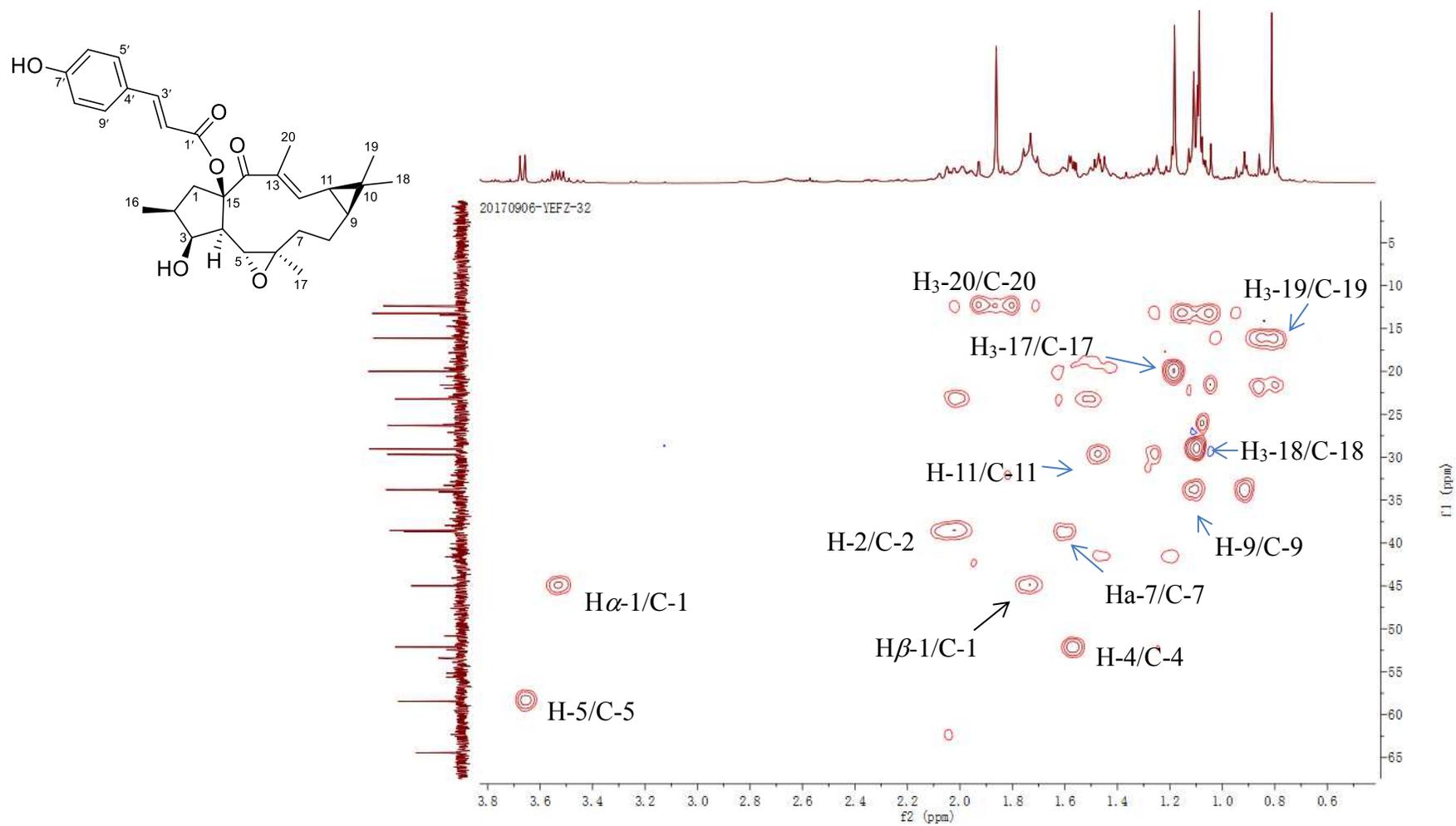
**Figure S5:** DEPT spectrum of **1** in  $\text{CDCl}_3$

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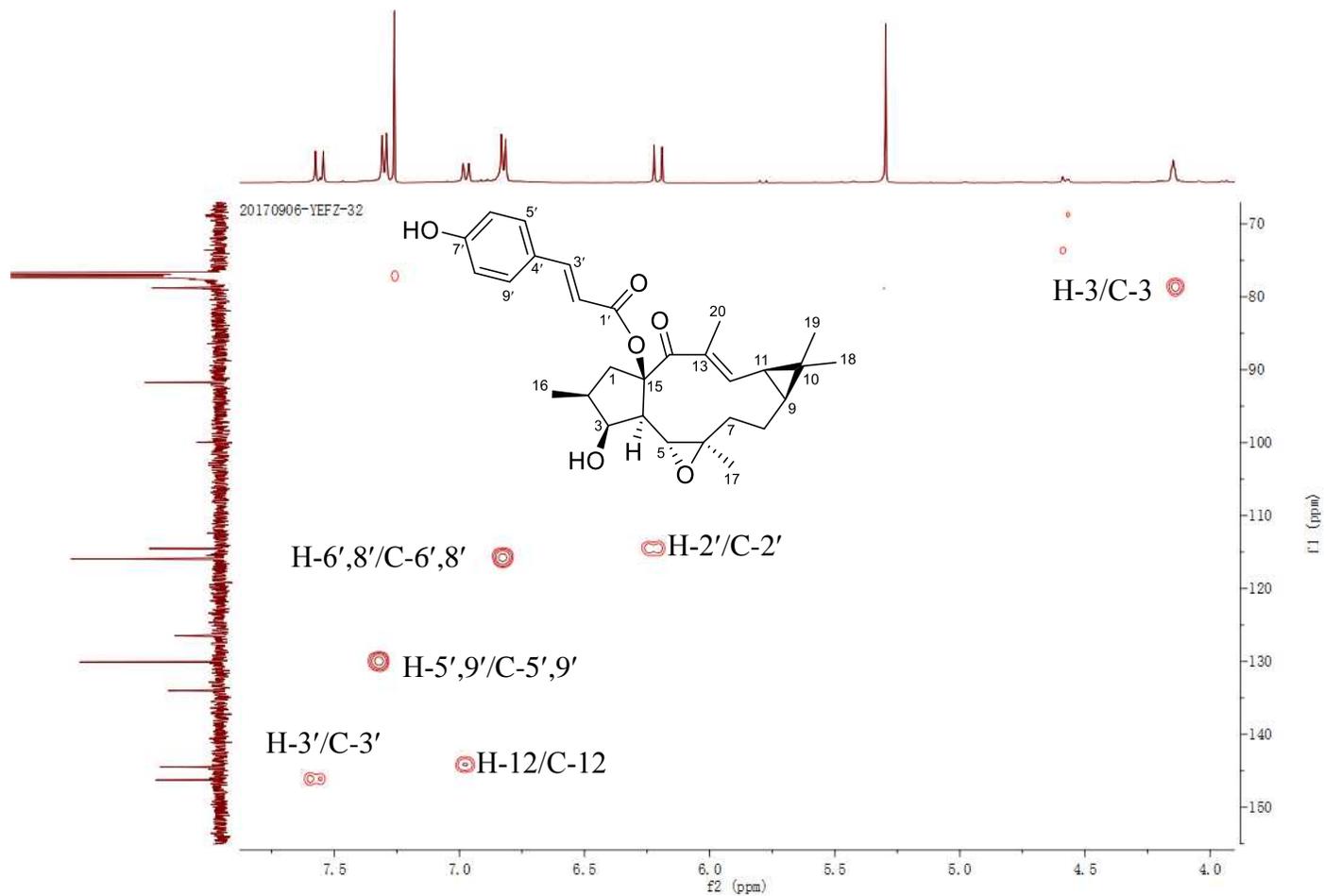


**Figure S6:** HSQC spectrum of **1** in  $\text{CDCl}_3$

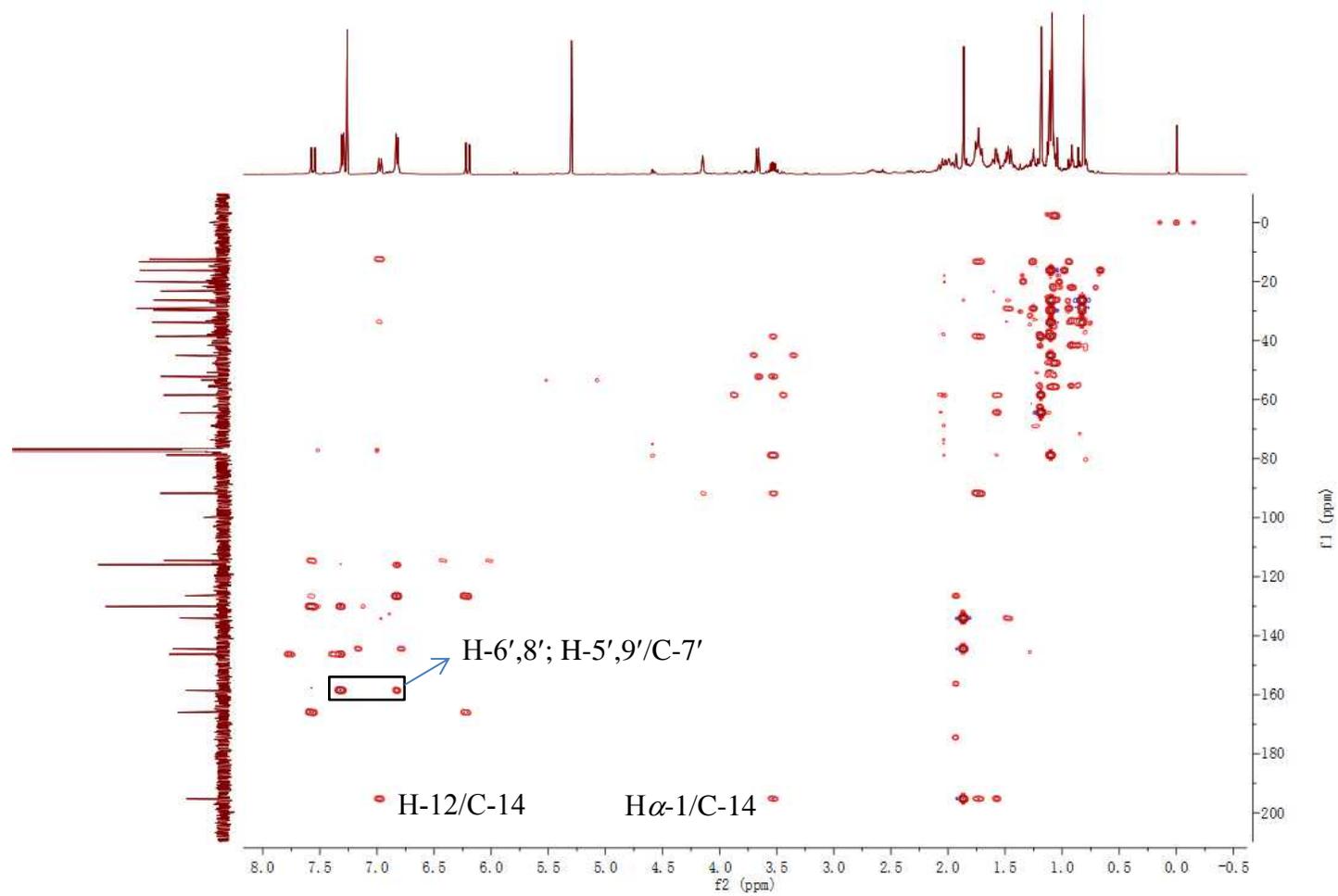
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**Figure S7:** HSQC spectrum of **1** in CDCl<sub>3</sub> ( $\delta$  5–65 ppm)

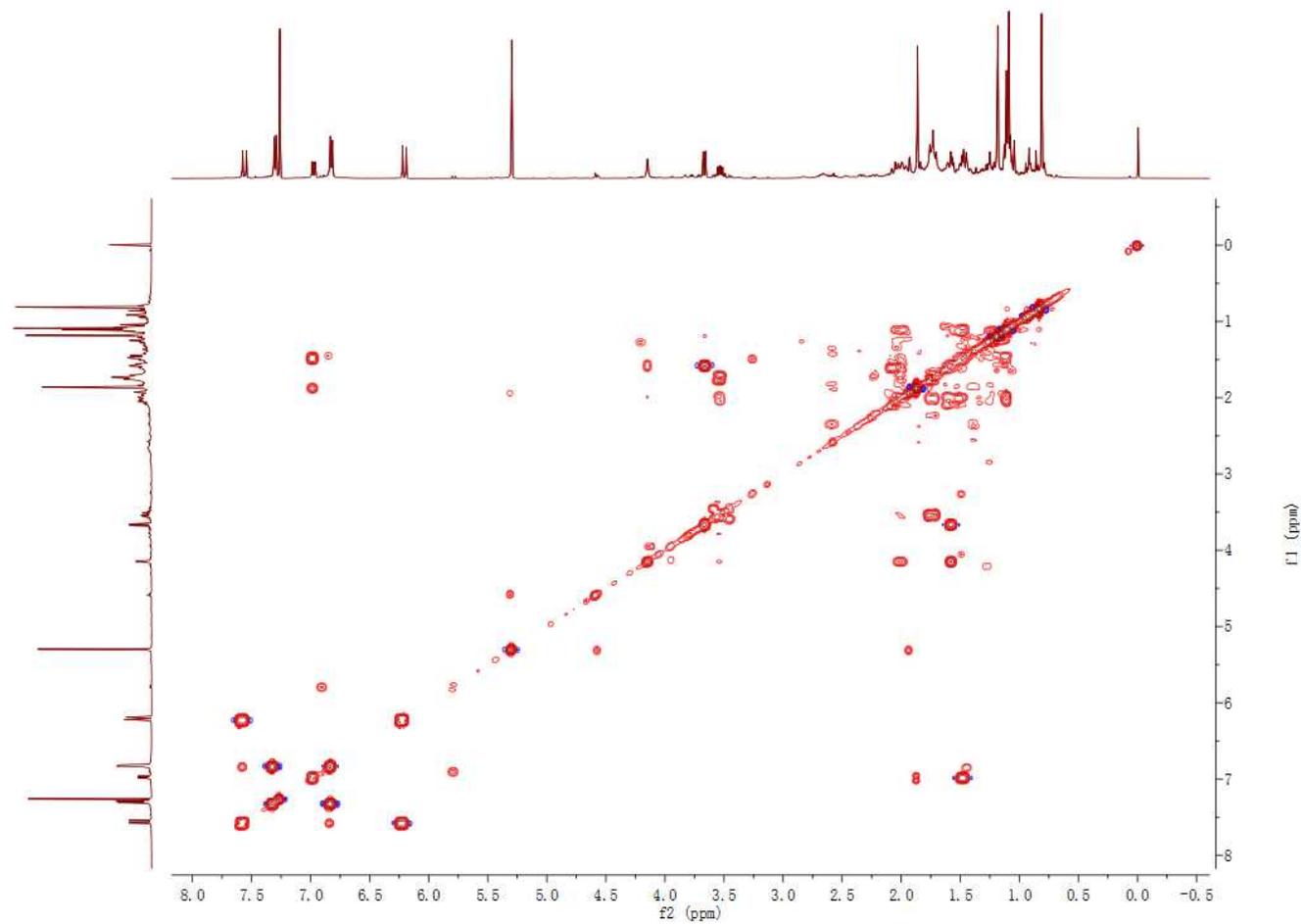


**Figure S8:** HSQC spectrum of **1** in  $\text{CDCl}_3$  ( $\delta$  70–150 ppm)

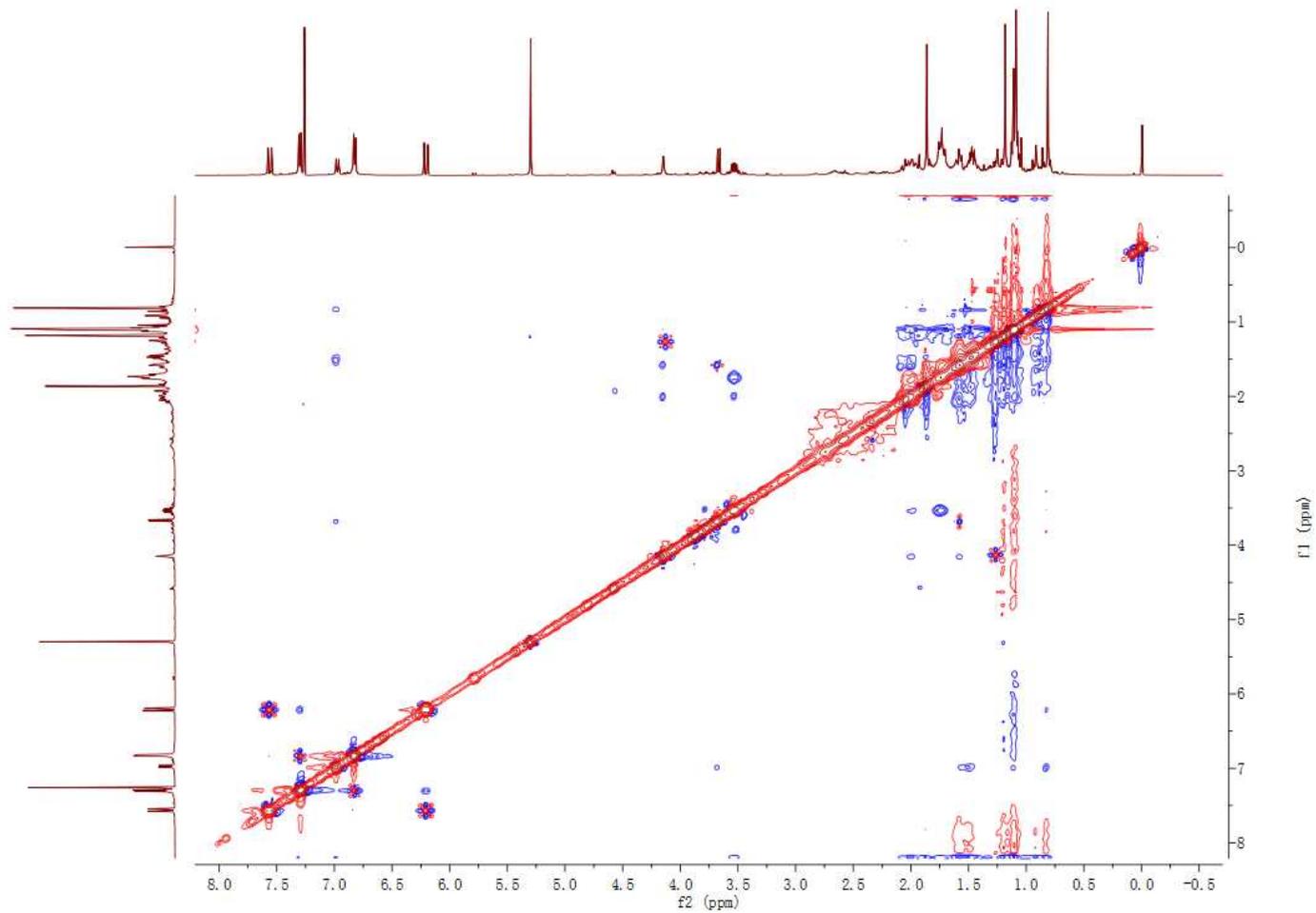


**Figure S9:** HMBC spectrum of **1** in CDCl<sub>3</sub>

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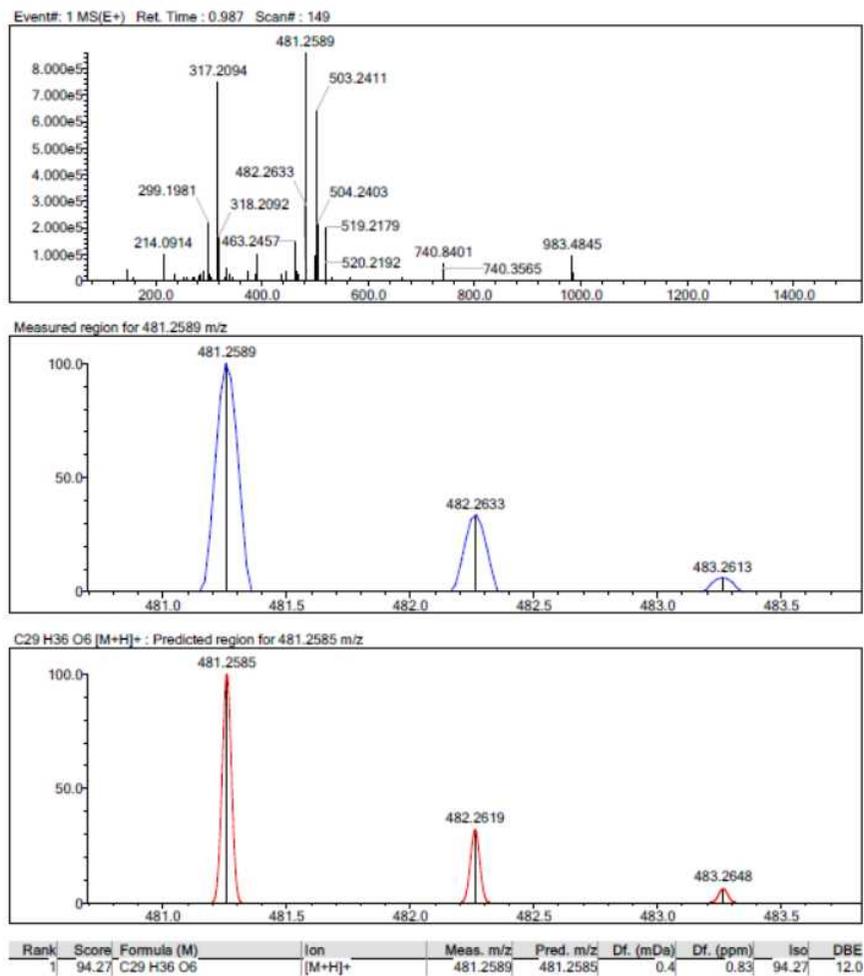


**Figure S10:**  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of **1** in  $\text{CDCl}_3$

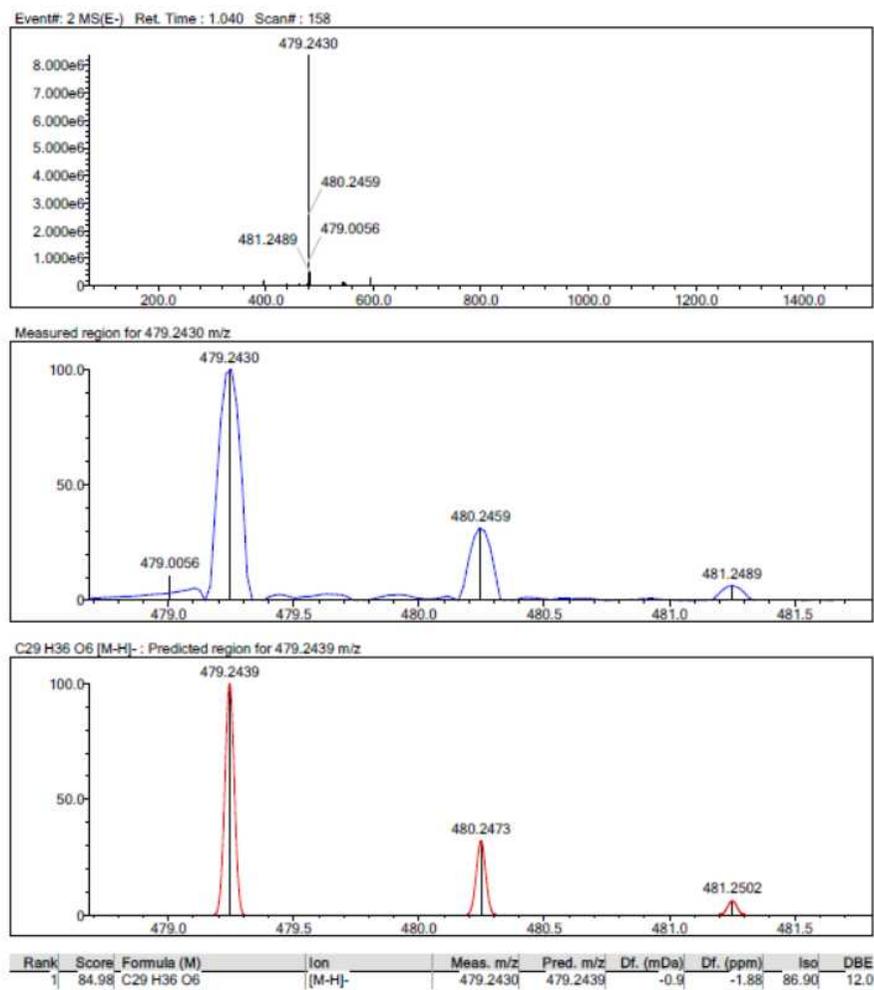


**Figure S11:** NOESY spectrum of **1** in  $\text{CDCl}_3$

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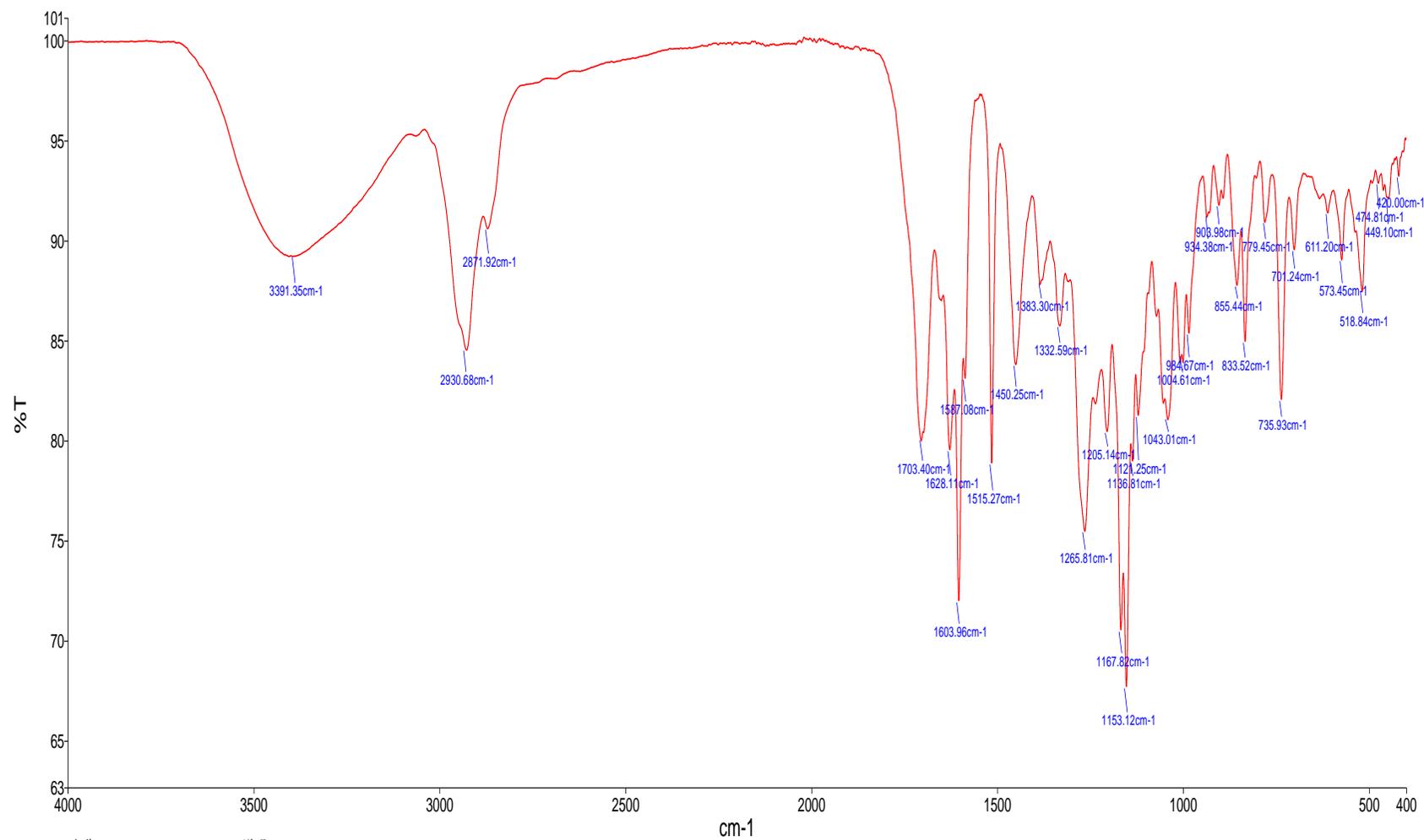


**Figure S12:** HRESIMS [M + H]<sup>+</sup> spectrum of **1**



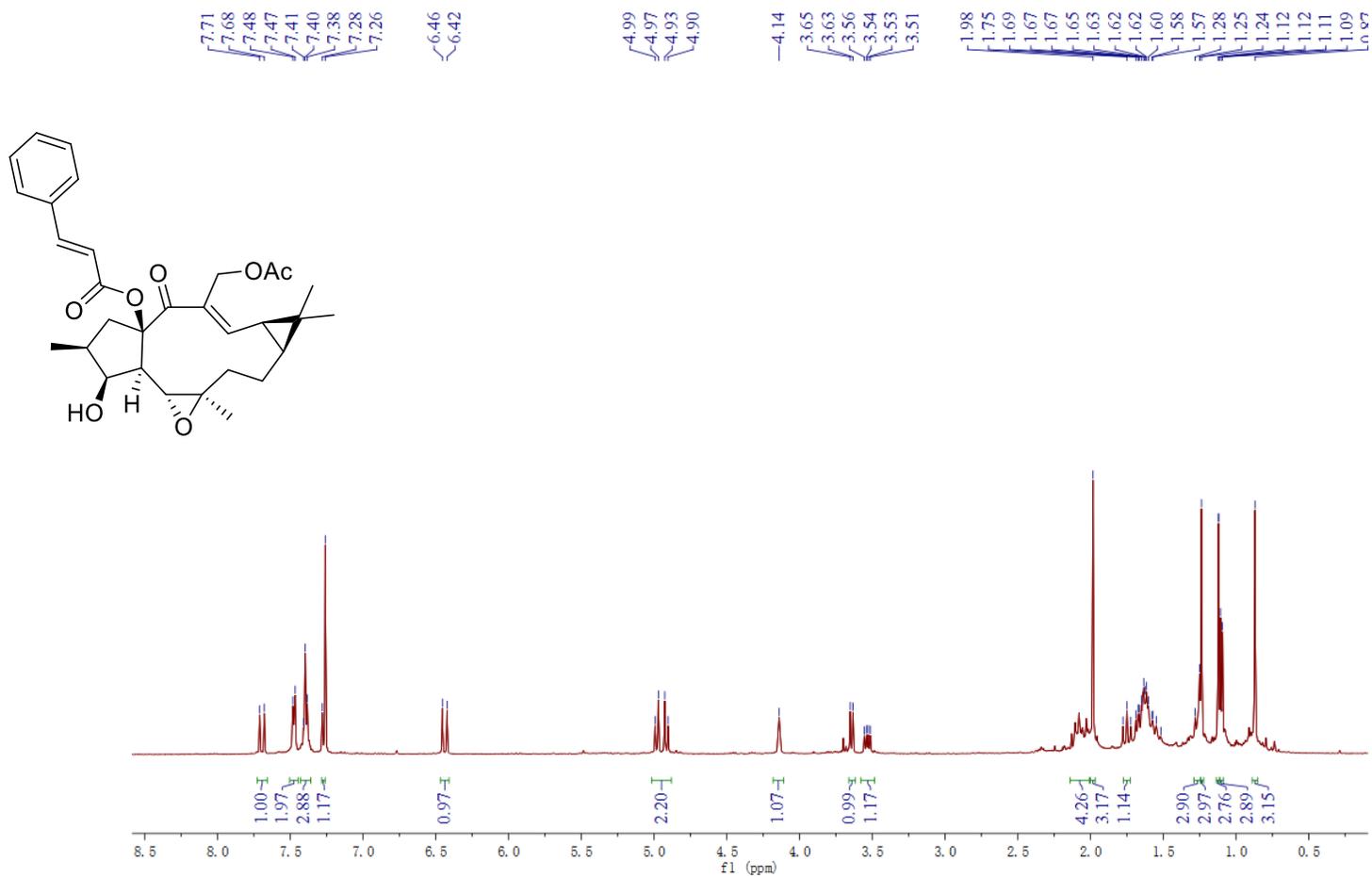
**Figure S13:** HRESIMS [M – H]<sup>-</sup> spectrum of **1**

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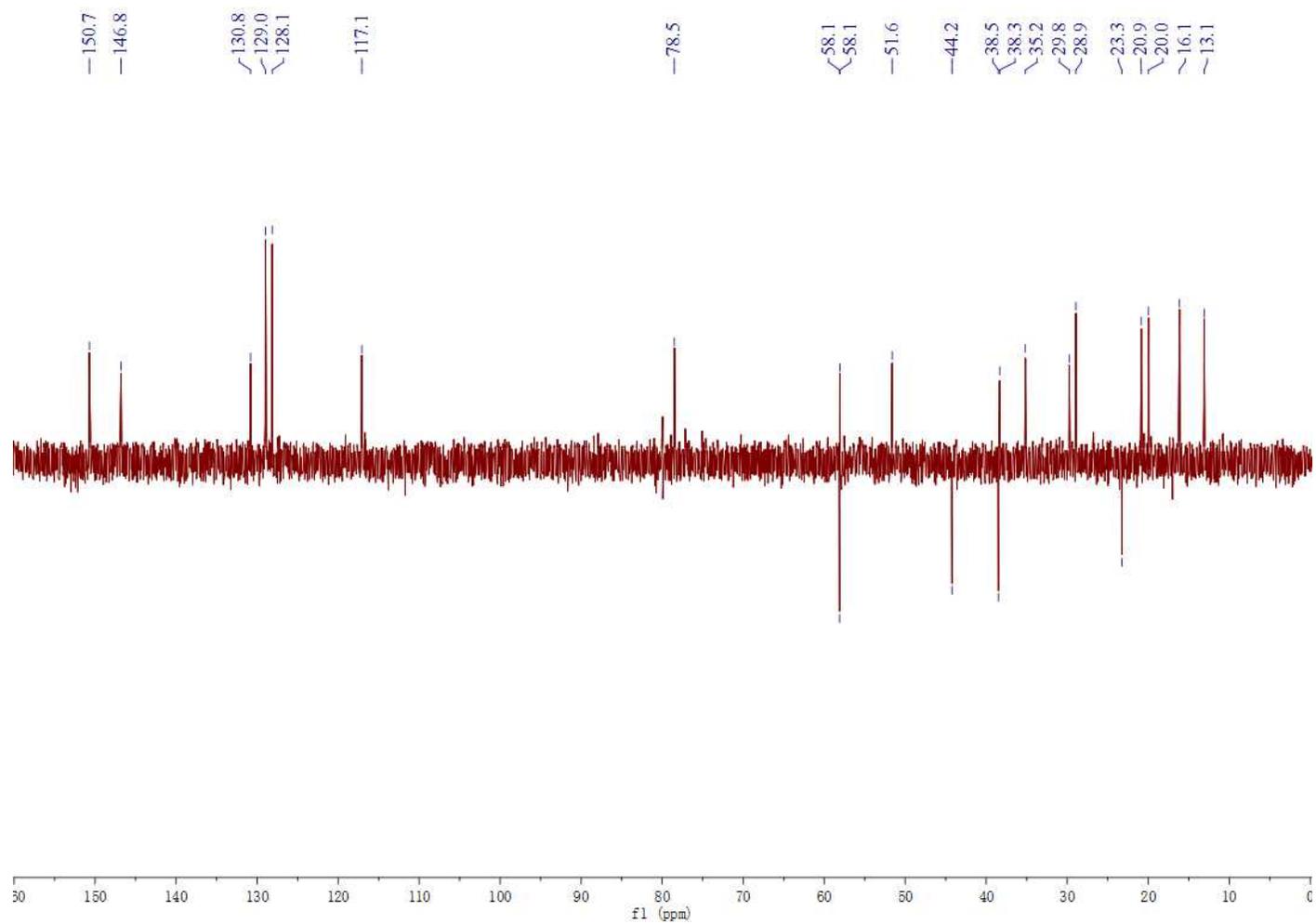
**Figure S14:** IR (KBr disc) spectrum of **1**

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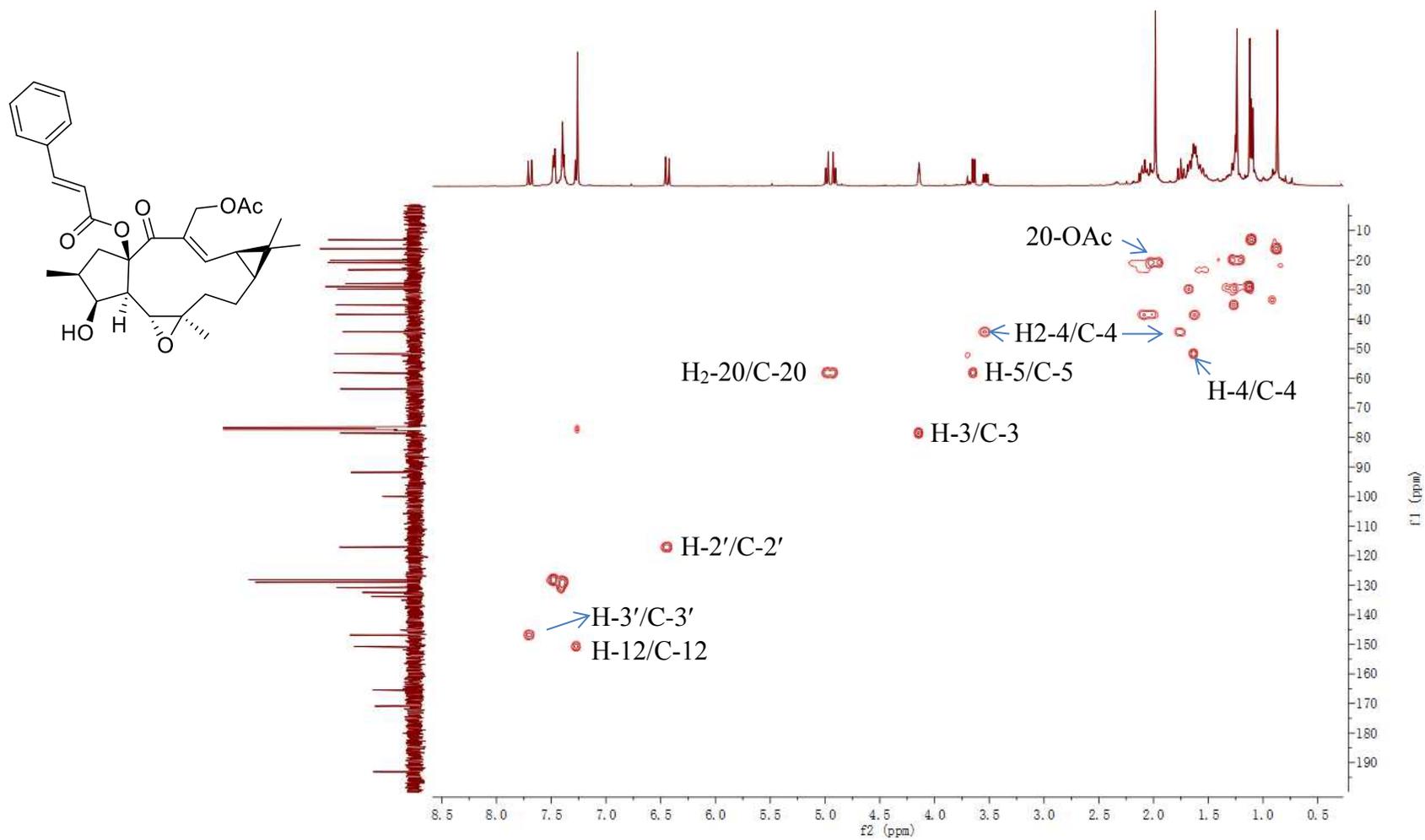
**Figure S15:**  $^1\text{H}$  NMR spectrum of **2** in CDCl<sub>3</sub>



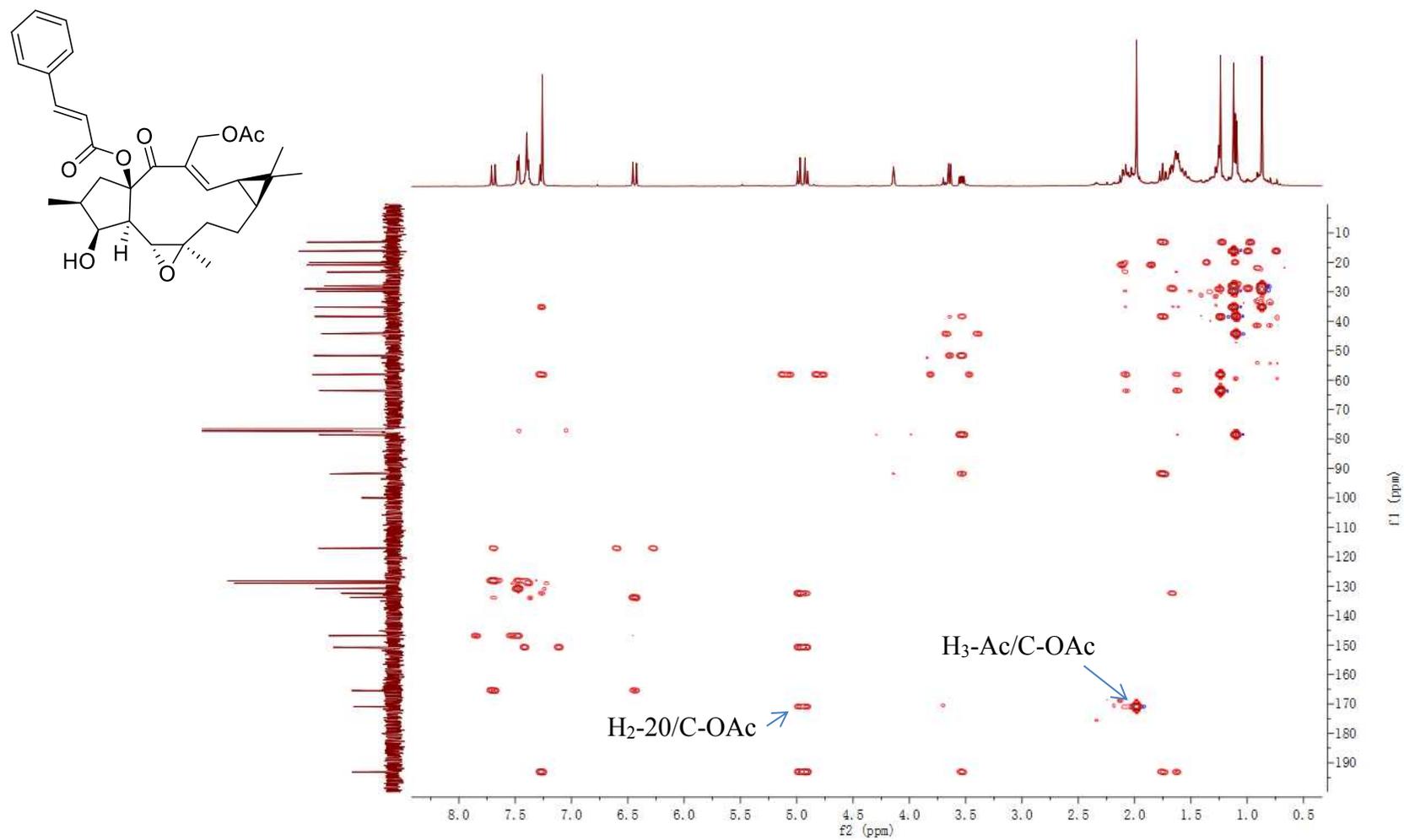


**Figure S17:** DEPT spectrum of **2** in CDCl<sub>3</sub>

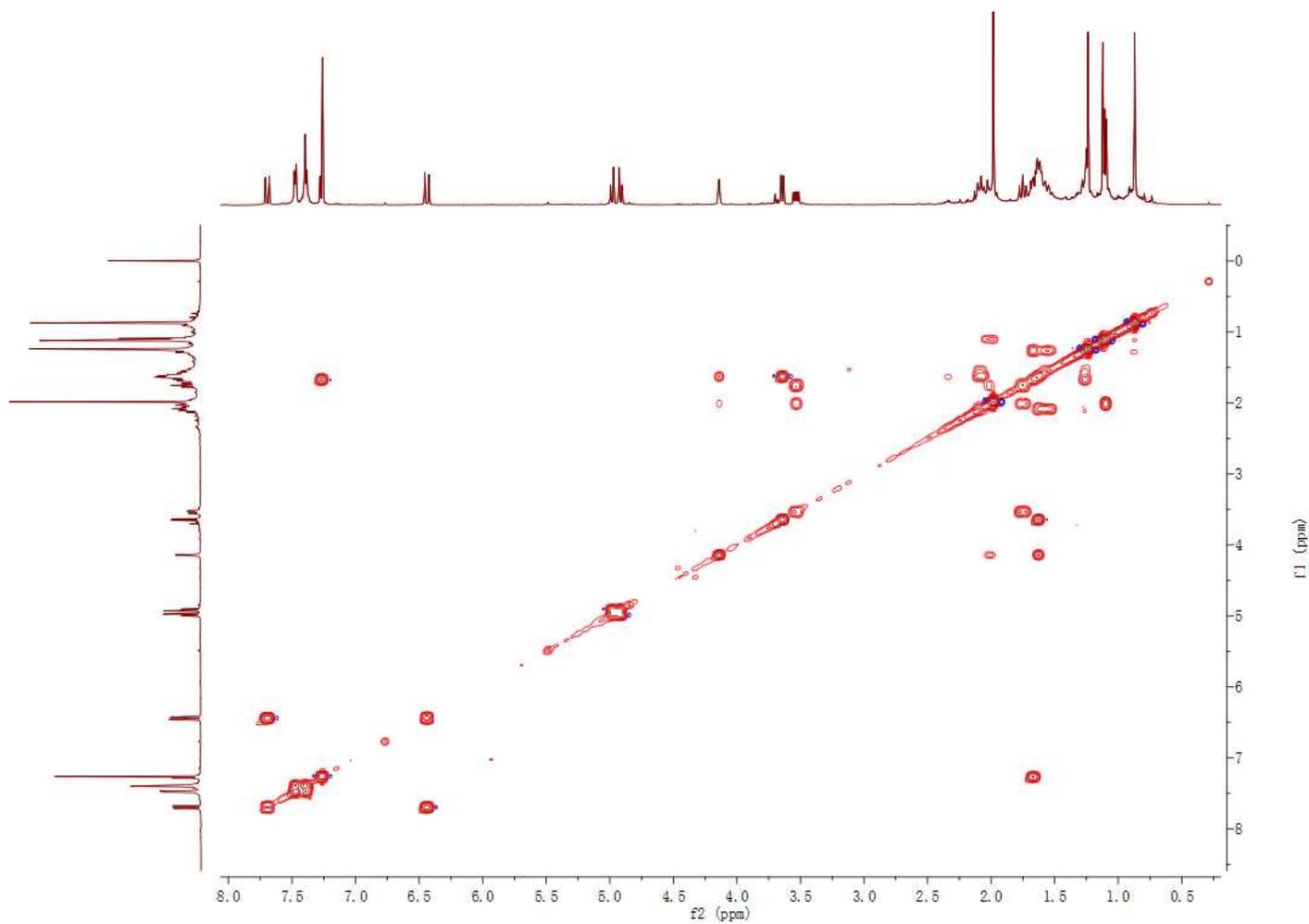
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**Figure S18:** HSQC spectrum of **2** in  $\text{CDCl}_3$

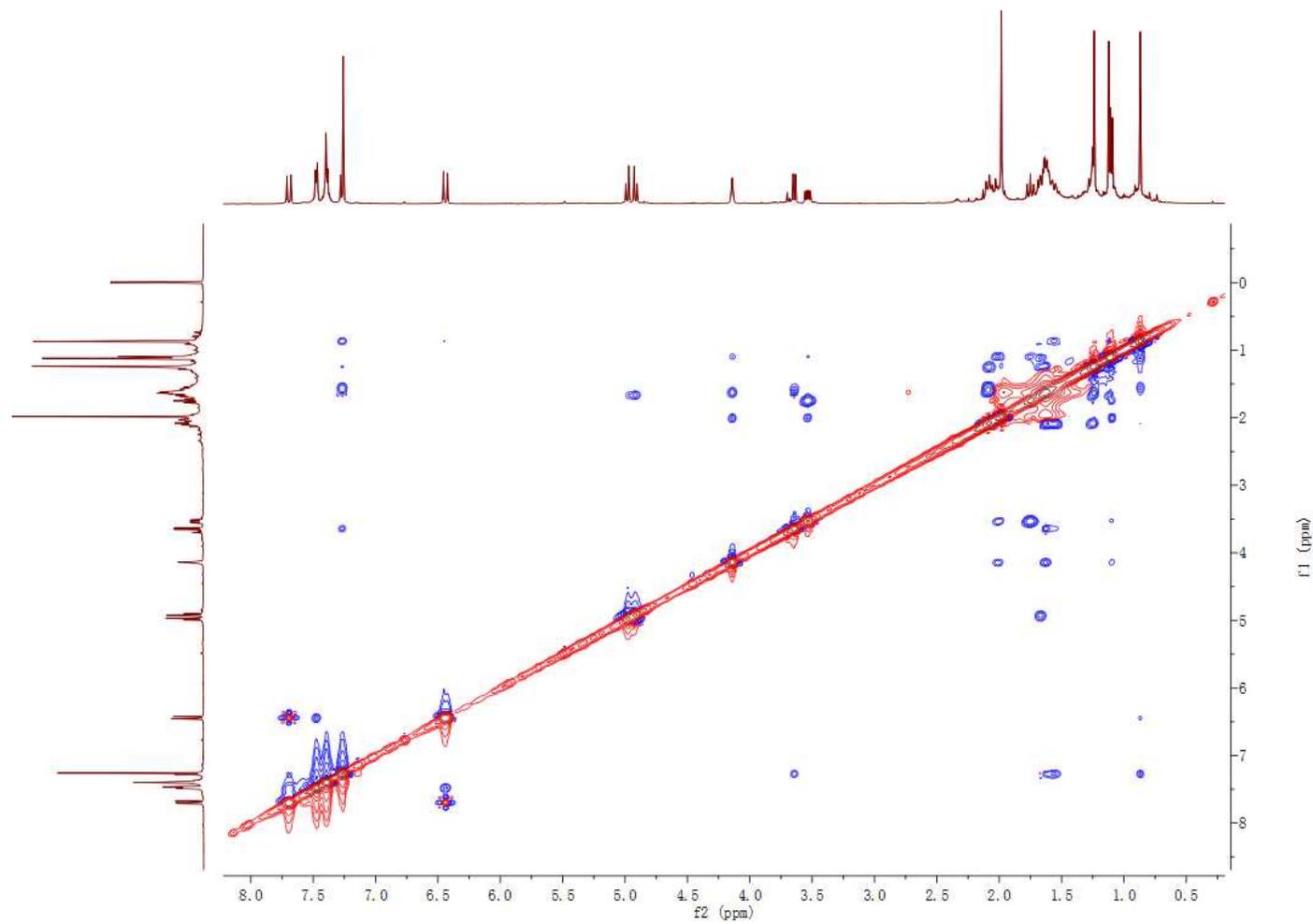


**Figure S19:** HMBC spectrum of **2** in CDCl<sub>3</sub>



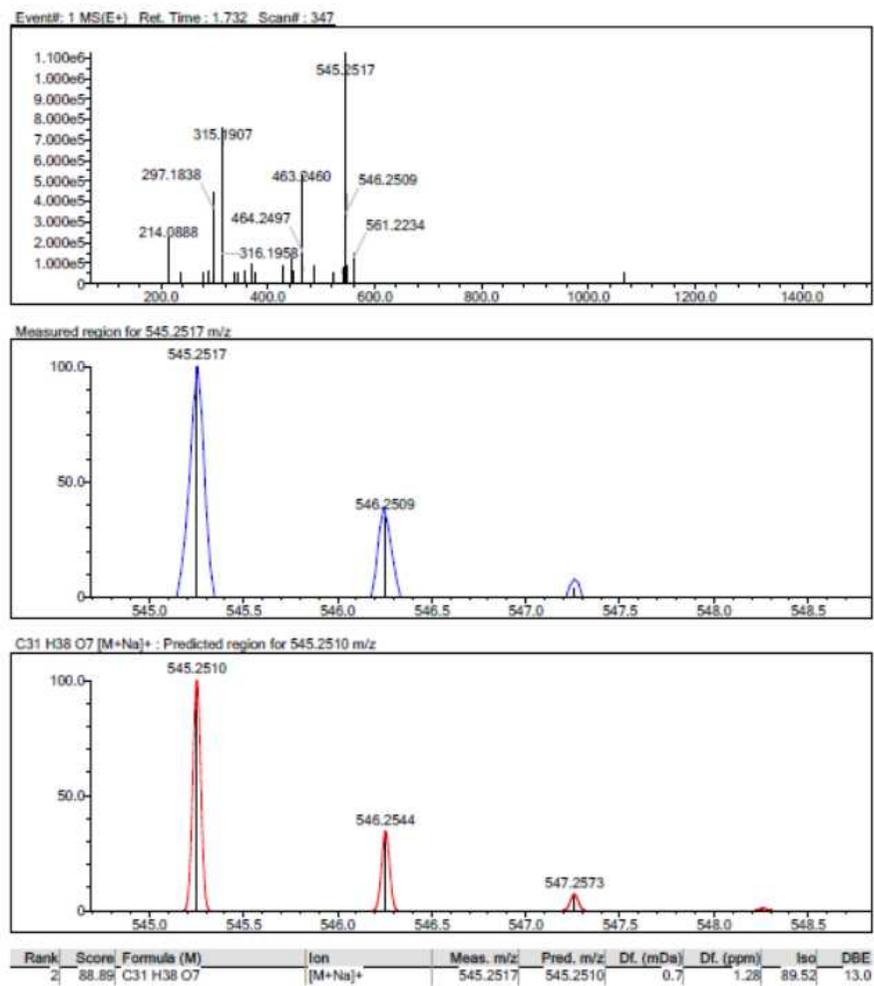
**Figure S20.**  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of **2** in  $\text{CDCl}_3$

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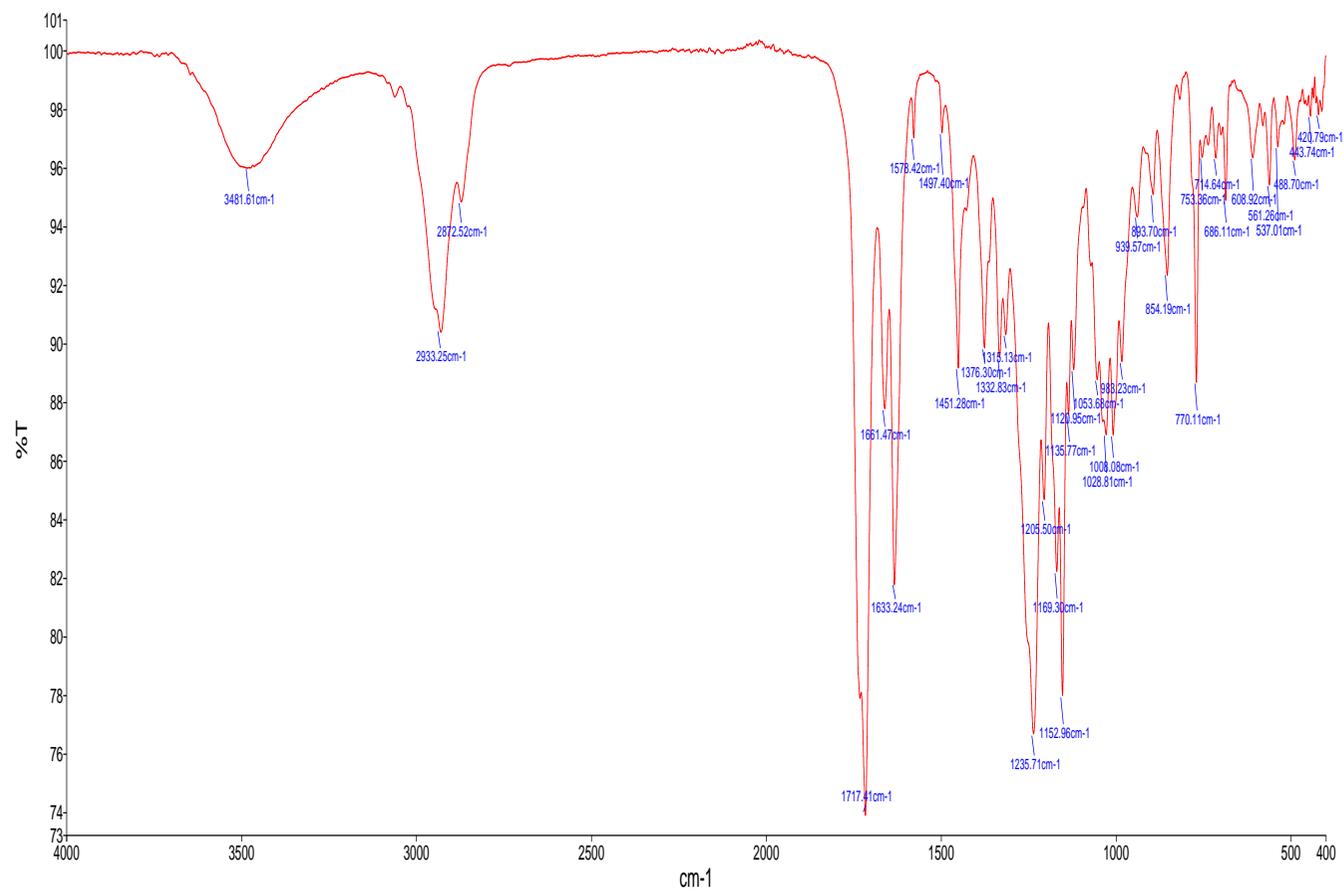
**Figure S21:** NOESY spectrum of **2** in  $\text{CDCl}_3$

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**Figure S22:** HRESIMS spectrum of **2**

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**Figure S23:** IR (KBr disc) spectrum of **2**