Electronic Supplementary Material (ESI) for RSC Advances.

The discovery of new phloroglucinol glycosides from *Agrimonia pilosa* and the mechanism on oxidative dearomatization of the methyl-substituted phloroglucinol derivatives

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Electronic Supplementary Information

Section S1. Structural determination of 1 and 6.

Compound **1** was isolated as the white amorphous powder. The molecular formula was assigned as $C_{24}H_{36}O_{14}$ by the positive HR-ESI-MS ion peak at *m/z* $[M + H]^+$ 549.2176 (calcd for $C_{24}H_{37}O_{14}$, 549.2178).

The ^{1}H NMR spectrum showed one aliphatic methyl group at δ_H 0.88 (3H, t, J = 7.5 Hz), two aromatic methyl groups at δ_H 2.15 and 2.27 (each 3H, s), one methylene groups at δ_H 1.61 (2H, m), and two anomeric protons of the *β*-D-glucopyranosyl moiety at δ_H 4.42 and 4.62 (each 1H, d, J = 7.5 Hz). The ^{13}C NMR spectrum exhibited twenty-four carbon resonances, of which the characteristic signals of two glucopyranosyl moieties and one phloroglucinol moiety (δ_C 159.9, 158.3, 154.0, 118.8, 118.3, 117.7) were presented.

In the 2 D NMR experiment, the ^{1}H-^{1}H COSY correlations between H-8a/H-9, H-8b/H-9, and H_2-9/H_3-10, along with HMBC correlations from H_2-8 to C-7, C-9, and C-10, from H_2-9 to C-7 suggested the presence of the butyryl group. Meanwhile, the HMBC correlations from H_3-3 to C-2/C-3/C-4, from H_3-5 to C-4/C-5/C-6 indicated two aromatic methyl were located at C-3 and C-5, respectively. Besides, the HMBC correlations from H-1' (δ_H 4.42) to C-2 (δ_C 154.0), from H-1'' (δ_H 4.62) to C-4 (δ_C 159.9) indicated two glucopyranosyl moieties were connected at C-2 and C-4, respectively (Figure 2). Thus, the structure of **1** was determined as 3,5-dimethyl-butyrylphloroglucinol-2,4-*O*-*β*-D-diglucopyranoside.

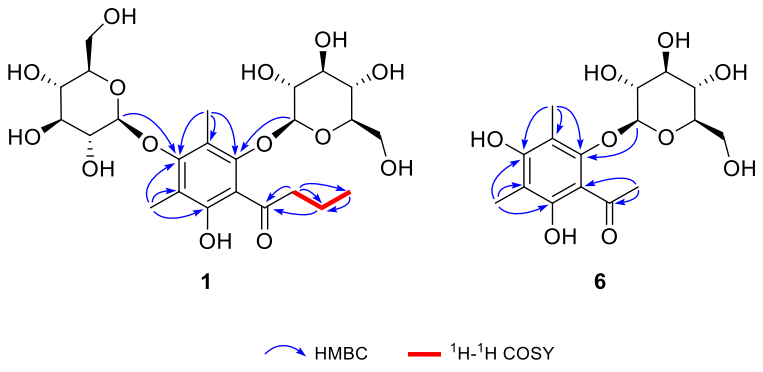


Figure S1. Key HMBC and COSY correlations of compounds **1** and **6**.

Compound **6** was obtained as white amorphous powder. Its molecular formula was determined as $C_{16}H_{22}O_9$ based on the HR-ESI-MS sodium adduct ion at *m/z* $[M + Na]^+$ 381.1156 (caled for $C_{16}H_{22}O_9Na$, 381.1156).

The ^{1}H NMR spectrum of **6** showed two aromatic methyl groups at δ_H 2.03 and 2.20 (3H, s), one acetyl group at δ_H 2.70 (3H, s), and one anomeric proton of the *β*-glucopyranosyl moiety at δ_H 4.56 (1H, d, J = 8.0 Hz). In accordance with ^{1}H NMR data, the ^{13}C NMR spectra of **6** showed the presence of two aromatic methyl, one acetyl, one phloroglucinol and one glucopyranosyl moiety. In the HMBC spectrum, the correlations from H_3-8 to C-1 and C-7 suggested the acetyl group was located at C-1. And the correlations of HMBC from H-1' to C-2 (δ_C 155.7) indicated the glucopyranosyl moiety was connected to C-2. Consequently, the structure of **6** was considered as 3, 5-dimethyl-acetylphloroglucinol-2-*O*-*β*-D-glucopyranoside.

Table S1. ^{1}H NMR data of compounds **1–6** (measured in Methanol-d_4, 500 MHz)

No.	**1**	**2**	**3**	**4**	**5**	**6**
8	3.14, overlapped	3.74, overlapped	3.76, overlapped	3.91, m	1.91, m	2.70, s
	3.05, overlapped	-	-	-	1.42, m	
9	1.61, m	1.91, m	1.53, m	1.18, d (6.5 Hz)	3.74, m	
	-	1.42, m	1.30, m	-	-	
10	0.88, t (7.5 Hz)	0.97, t (7.5 Hz)	0.74, t (7.5 Hz)	0.99, d (7.5 Hz)	0.86, d (6.5 Hz)	
11	-	1.00, d (7.5 Hz)	1.13, d (7.0 Hz)	-	0.85, d (7.0 Hz)	
12	2.27, s	2.32, s	2.32, s	2.32, s	2.27, s	2.20, s
13	2.15, s	2.20, s	2.20, s	2.20, s	2.15, s	2.03, s
Glc-1'	4.42, d (7.5 Hz)	4.43, d (7.5 Hz)	4.32, d (8.0 Hz)	4.37 d (8.0 Hz)	4.63, d (7.5 Hz)	4.56, d (8.0 Hz)
2'	3.46, overlapped	3.44, overlapped	3.40, m	3.44, overlapped		3.53, t (8.5 Hz)
3'	3.33, overlapped	3.38, m	3.34, m	3.40, m	3.34, overlapped	3.41, m
4'	3.27, overlapped	3.23, t (9.5 Hz)	3.21, t (9.5 Hz)	3.25, t (9.5 Hz)	3.13, m	3.35, m
5'	3.06, overlapped	3.11, m	3.05, m	3.10, m	3.76, dd (2.0, 12.0 Hz)	3.10, m
6'a	3.66, dd (2.5, 12.0 Hz)	3.73, overlapped	3.68, dd (2.0, 11.5 Hz)	3.72, dd (3.0, 12.0 Hz)	3.60, dd (6.0, 12.0 Hz)	3.61, dd (5 Hz, 12 Hz)
6'b	3.53, dd (6.0, 12.0 Hz)	3.55, m	3.52, m	3.56, dd (5.5, 12.0 Hz)		3.70, dd (2 Hz, 12 Hz)
Glc-1"	4.62, d (7.5 Hz)	4.67, d (7.5 Hz)	4.63, d (7.5 Hz)	4.67 d (7.5 Hz)	4.42, d (8.0 Hz)	
2"	3.46, overlapped	3.52, m	3.47, m	3.53, m		
3"	3.36, overlapped	3.45, overlapped	3.40, m	3.44, overlapped		
4"	3.31, overlapped	3.36, overlapped	3.32, m	3.36, t (9.0 Hz)	3.18, t (9.0 Hz)	
5"	3.13, overlapped	3.17, m	3.13, m	3.17, m	3.05, m	
6"a	3.75, dd (2.5, 12.0 Hz)	3.80, dd (2.5, 12.0 Hz)	3.60, dd (5.5, 11.5 Hz)	3.80, dd (2.5, 12.0 Hz)	3.66, dd (2.5, 12.0 Hz)	
6"b	3.60, dd (6.0, 12.0 Hz)	3.65, dd (6.0, 12.0 Hz)	3.75, overlapped	3.64, dd (5.5, 11.5 Hz)	3.54, overlapped	

Table S2. ^{13}C NMR data of compounds **1–6** (measured in Methanol-d_4, 125 MHz)

No.	**1**	**2**	**3**	**4**	**5**	**6**
1	117.7	118.0	118.5	118.1	117.9	112.6
2	154.0	153.0	153.0	152.9	153.9	155.7
3	118.8	118.4	118.9	119.0	118.3	110.8
4	159.9	159.3	159.4	159.3	159.9	161.9
5	118.3	119.0	119.0	118.5	118.9	109.0
6	158.3	157.2	156.8	156.9	158.2	161.1
7	211.2	214.9	215.4	215.5	211.1	207.1
8	47.5	48.5	48.1	41.7	54.7	33.2
9	19.4	25.8	29.2	20.7	27.0	-
10	14.4	12.4	11.8	17.7	23.4	-
11	-	17.9	14.8	-	23.2	-
12	11.2	11.1	10.9	11.0	11.2	8.3
13	10.2	10.3	10.3	10.3	10.2	10.0
Glc-1'	105.8	105.7	105.7	105.7	105.8	105.9
2'	75.9	75.8	75.8	75.8	75.9	75.9
3'	78.2	78.2	78.1	78.2	78.2	77.9
4'	71.9	71.8	71.8	72.2	72.0	71.7
5'	78.0	78.0	78.0	78.0	78.1	78.2
6'	63.0	63.4	63.0	63.4	63.0	62.7
Glc-1"	105.7	105.7	105.7	105.8	105.7	-
2"	75.8	75.8	75.8	75.8	75.8	-
3"	78.1	78.1	78.2	78.1	78.1	-
4"	71.8	72.4	72.3	71.8	71.8	-
5"	77.8	77.8	77.8	77.8	77.8	-
6"	63.0	63.0	63.4	63.0	63.0	-

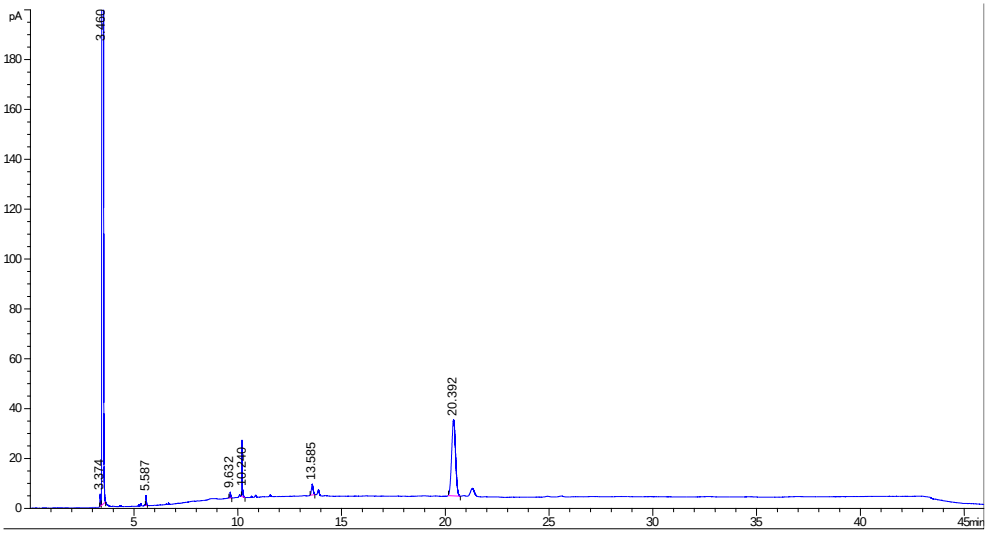


Figure S2. The GC spectrum of the derivative of *β*-D-glucose at 20.39 min

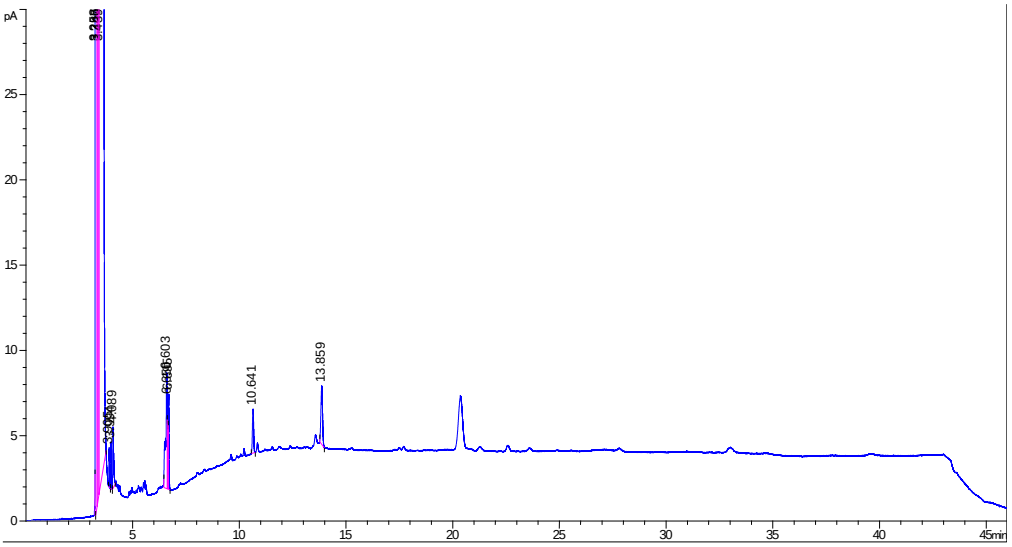
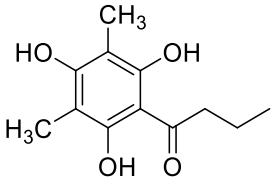


Figure S3. The GC spectrum of the derivative of the sugar moiety of **1**

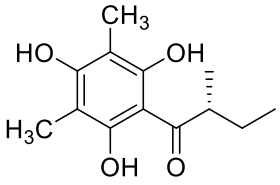
Section S2. Structural determination of 1a–4a and 1c–4c

2.1. NMR data of 1a–4a and 1c–4c

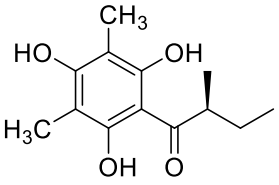


1a

Compound **1a** (3,5-dimethylbutyrylphloroglucinol) ^{1}H NMR (500 MHz, Methanol-d_4): δ_H 3.07 (2H, d, J = 7.5 Hz, H-8), 2.01 (6H, s, H_3-3, 5), 1.69 (2H, m, H_2-9), 0.97 (3H, t, J = 7.5 Hz, H_3-10); ^{13}C NMR (125 MHz, Methanol-d_4): δ_C 106.6 (C-1), 160.2 (C-2, 6), 103.8 (C-3, 5), 161.7 (C-4), 208.2 (C-7), 47.4 (C-8), 19.9 (C-9), 14.6 (C-10), 8.4 (CH_3-3, 5). HR-ESI-MS (*m/z*) 225.1117 $[M + H]^+$ (calcd for $C_{12}H_{17}O_4$, 225.1121).

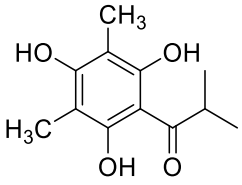


2a



3a

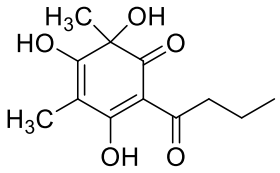
Compound **2a/3a** (3,5-dimethyl-1-α-methylbutyrylphloroglucinol) ^{1}H NMR (500 MHz, Methanol-d_4): δ_H 3.94 (1H, m, H-8), 2.01 (6H, s, H_3-3, 5), 1.13 (3H, d, J = 6.7 Hz, H_3-11) , 0.90 (3H, t, J = 7.4 Hz, H_3-10); ^{13}C NMR (125 MHz, Methanol-d_4): δ_C 106.6 (C-1), 160.1 (C-2, 6), 103.9 (C-3, 5), 161.6 (C-4), 212.5 (C-7), 47.2 (C-8), 28.5 (C-9), 12.6 (C-10), 17.5 (C-11), 8.5 (CH_3-3, 5). HR-ESI-MS (*m/z*) 237.1136 $[M - H]^-$ (calcd for $C_{13}H_{17}O_4$, 237.1132).



4a

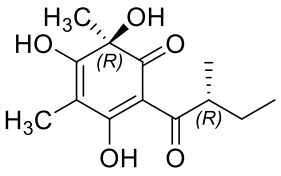
Compound **4a** (3,5-dimethyl-1-isobutyrylphloroglucinol) ^{1}H NMR (500 MHz, Methanol-d_4): δ_H 4.05 (1H, m, H-8), 2.00 (6H, s, H_3-3, 5), 1.13 (3H, d, J = 6.8 Hz, H_3-9, 10); ^{13}C NMR (125 MHz, Methanol-d_4): δ_C 105.8 (C-1), 159.9 (C-2, 6), 103.8 (C-3,

5), 161.4 (C-4), 212.6 (C-7), 40.4 (C-8), 19.9 (C-9, 10), 8.4 (CH_3-3, 5). HR-ESI-MS (*m/z*) 225.1116 $[M + H]^+$ (calcd for $C_{12}H_{17}O_4$, 225.1121).

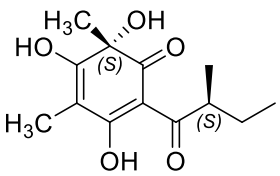


1c

Compound **1c** (2-butyryl-3,5,6-trihydroxy-4,6-dimethylcyclohexa-2,4-dien-1-one) ^{1}H NMR (500 MHz, Methanol-d_4): δ_H 2.89 (2H, m, H_2-8), 1.80 (3H, s, 5-CH_3), 1.65 (2H, m, H_2-9), 1.47 (3H, s, 3-CH_3), 0.98 (3H, t, H_3-10); ^{13}C NMR (125 MHz, Methanol-d_4): δ_C 105.7 (C-1), 198.4 (C-2), 76.7 (C-3), 176.1 (C-4), 103.7 (C-5), 190.7 (C-6), 202.9 (C-7), 42.1 (C-8), 20.3 (C-9), 14.5 (C-10), 29.1 (CH_3-3), 7.20 (CH_3-5). HR-ESI-MS (*m/z*) 241.1066 $[M + H]^+$ (calcd for $C_{12}H_{17}O_5$, 241.1071).

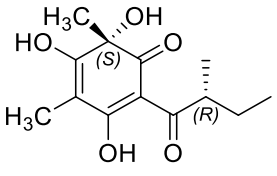


2c-1

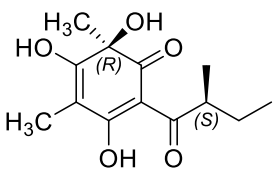


3c-2

Compound **2c-1/3c-2** (3,5,6-trihydroxy-4,6-dimethyl-2-(2-methylbutanoyl)cyclohexa-2,4-dien-1-one) ^{1}H NMR (500 MHz, Methanol-d_4): δ_H 3.73 (1H, m, H-8), 1.77 (3H, s, 5-CH_3), 1.69 (1H, m, H-9a), 1.46 (3H, s, 3-CH_3), 1.37 (1H, m, H-9b), 1.12 (3H, d, J = 6.8 Hz H_3-11), 0.85 (3H, t, J = 7.4 Hz H_3-10); ^{13}C NMR (125 MHz, Methanol-d_4): δ_C 105.0 (C-1), 199.2 (C-2), 78.5 (C-3), 182.9 (C-4), 101.8 (C-5), 187.9 (C-6), 205.3 (C-7), 42.9 (C-8), 28.1 (C-9), 12.6 (C-10), 18.1 (C-11), 30.1 (CH_3-3), 7.4 (CH_3-5). HR-ESI-MS (*m/z*) 255.1221 $[M + H]^+$ (calcd for $C_{13}H_{19}O_5$, 255.1227).



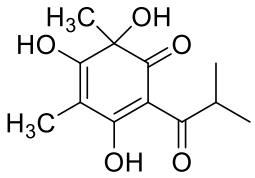
2c-2



3c-1

Compound **2c-2/3c-1** (3,5,6-trihydroxy-4,6-dimethyl-2-(2-methylbutanoyl)cyclohexa-2,4-dien-1-one) ^{1}H NMR (500 MHz, Methanol-d_4): δ_H 3.77 (1H, m, H-8), 1.80 (3H, s,

5-CH_3), 1.77 (1H, m, H-9a), 1.47 (3H, s, 3-CH_3), 1.39 (1H, m, H-9b), 1.07 (3H, d, J = 6.8 Hz H_3-11), 0.95 (3H, t, J = 7.4 Hz H_3-10); ^{13}C NMR (125 MHz, Methanol-d_4): δ_C 105.1 (C-1), 198.4 (C-2), 77.1 (C-3), 177.1 (C-4), 103.5 (C-5), 190.5 (C-6), 206.5 (C-7), 42.5 (C-8), 28.3 (C-9), 12.3 (C-10), 16.9 (C-11), 29.4 (C-12), 7.3 (C-13). HR-ESI-MS (m/z) 255.1220 [M + H] $^+$ (calcd for $C_{13}H_{19}O_5$, 255.1227).



4c

Compound **4c** (3,5,6-trihydroxy-2-isobutyryl-4,6-dimethylcyclohexa-2,4-dien-1-one) ^{1}H NMR (500 MHz, Methanol-d_4): δ_H 3.87 (1H, m, H-8), 1.79 (3H, s, 5-CH_3), 1.48 (3H, s, 3-CH_3), 1.15 (3H, d, J = 6.8 Hz H_3-9), 1.09 (3H, d, J = 6.8 Hz H_3-10); ^{13}C NMR (125 MHz, Methanol-d_4): δ_C 104.4 (C-1), 198.4 (C-2), 77.4 (C-3), 177.9 (C-4), 103.2 (C-5), 190.2 (C-6), 207.0 (C-7), 36.3 (C-8), 20.0 (C-9), 19.4 (C-10), 29.5 (CH_3-3), 7.30 (CH_3-5). HR-ESI-MS (m/z) 241.1067 [M + H] $^+$ (calcd for $C_{12}H_{17}O_5$, 241.1071).

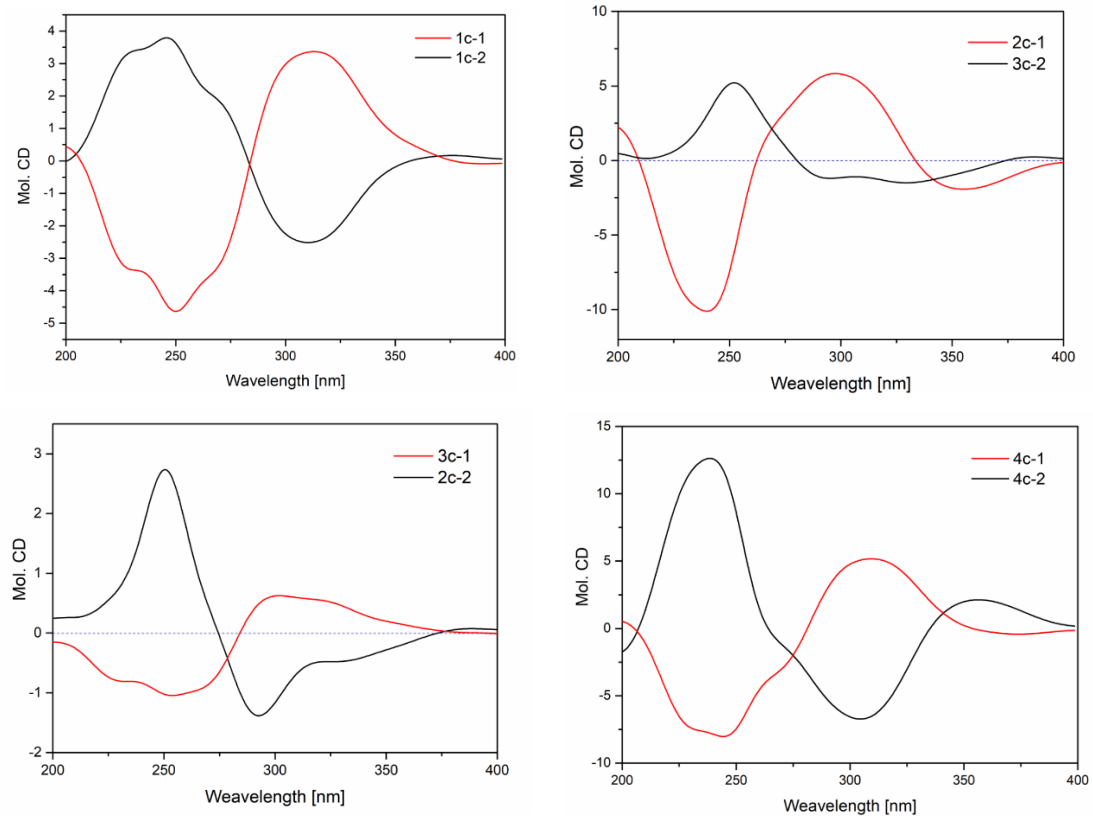


Figure S4. Experimental ECD spectra of **1c**–**4c**.

2.2 Determination of the absolute configuration of 2c and 3c.

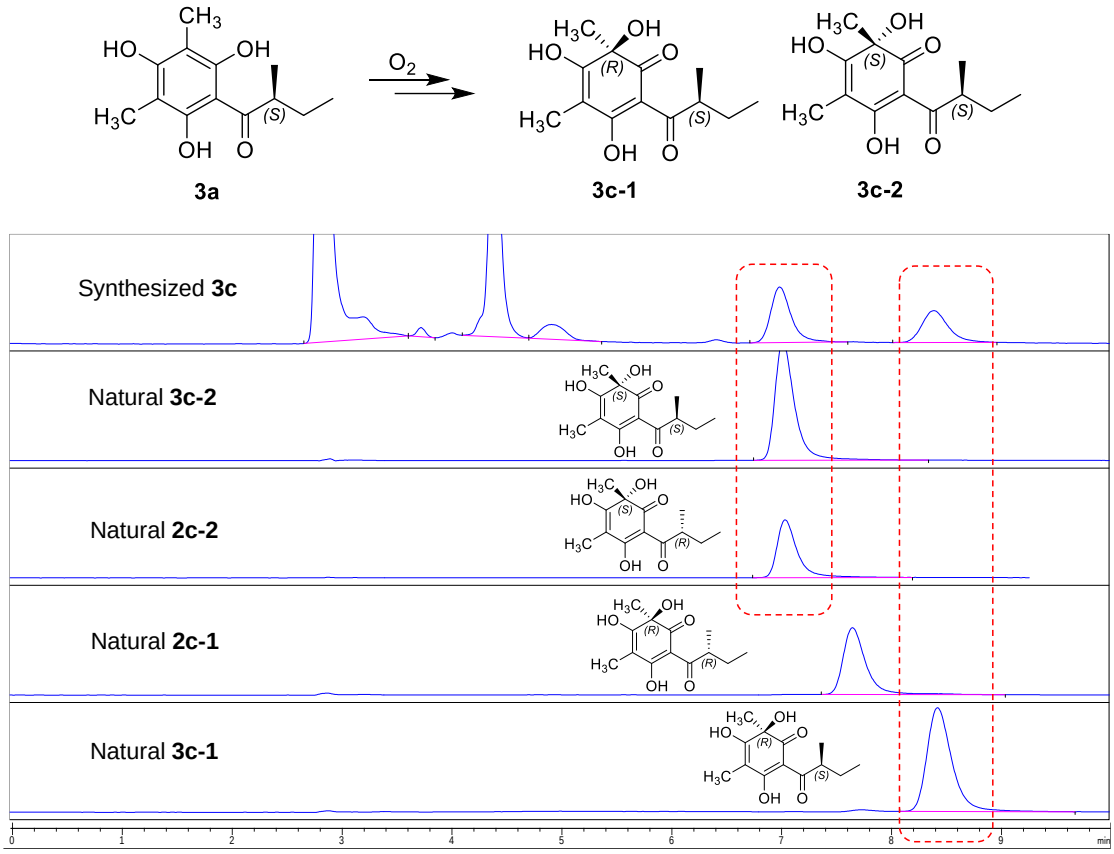


Figure S5. Comparison of the chiral *Rp*-HPLC spectra of **3c**, **2c-1**, **2c-2**, **3c-1**, and **3c-2** (HPLC Condition: CHIRALPAK AD-RH, 250×4.6 mm, MeCN: H_2O= 40: 60, T = 40 ℃, *v* = 1 mL/min, λ = 280 nm).

Compounds **2c-1**, **2c-2**, **3c-1**, and **3c-2** represent four isomers (3*R*, 8*R*/3*S*, 8*R*/3*R*, 8*S*/3*S*, 8*S*), the absolute configuration of which were barely solved before in literature. To distinguish the chirality, we taken advantage of NMR data, ECD spectra (Figure S4) and chiral separation. Firstly, **2c-1** and **3c-1** exhibited the same negative cotton effects around 250 nm, indicating the absolute configuration of C-3 were *R*. [1] However, the NMR difference suggested **2c-1** and **3c-1** were a pair of epimer of C-8. Then, 8*S*-**3c** was synthesized from 8*S*-**3a** by oxidization, **3c-1** and **3c-2** were obtained and separated by the chiral *Rp*-HPLC. Consequently, the retention time of the natural **3c-1** was identical with those of one of synthesized **3c** (Figure S5). Thus, the absolute configuration of **3c-1** was assigned as 3*R*, 8*S*, whereas the absolute configuration of **2c-1** was 3*R*, 8*R*. In addition, compounds **2c-2** and **3c-2** represent a pair of epimers at C-8,

which can't be separated by the chiral *Rp*-HPLC but be separated by the YMC Rp-8 (4.6 x 250 mm) column with an elution of 32 % MeCN-H_2O.

1. W. Gao, Z. Chen, Y. N. Yang, J. S. Jiang, Z. M. Feng, X. Zhang, X. Yuan and P. C. Zhang, *Carbohyd. Res.* 2019, **484**, 107756.

Section S3. General experiment procedure

3.1 Experimental Instruments

Optical rotations, UV spectra and the ECD spectra were measured with a JASCO P-2000, JASCO V-650, and JASCO J-815 spectrometers (JASCO, Easton, MD, U.S.A.). The IR spectral data were acquired on a Nicolet iS5 spectrometer (Thermo Scientific, Waltham, MA, U.S.A.). NMR analyses were carried out on a Bruker 400 MHz spectrometer (Bruker-Biospin, Billerica, MA, U.S.A.). HR-ESI-MS spectral data were recorded on a *Q*-Exactive Orbitrap mass spectrometer (Thermo Scientific, Waltham, MA, U.S.A.). HPLC analyses were performed on an Agilent 1200 series system (Agilent Technologies, CA, U.S.A.) with an YMC-ODS C18 column (250 × 4.6 mm, 5 μm, CA, U.S.A.). A Shimadzu LC-6AR instrument equipped with an SPD-20A detector using an YMC-Pack ODS-A column (250 mm × 10 mm, 5 μm, Kyoto, Japan) was used for the semi-preparative HPLC. The HP-20 (Mitsubishi Chemical Corp., Tokyo, Japan). Reversed-phase C18 (50 μm, YMC, Tokyo, Japan) and Sephadex LH-20 (Pharmacia Fine Chemicals, Uppsala, Sweden). TLC was performed using GF254 plates (Qingdao Marine Chemical Inc., China). The EPR spectra were taken at room temperature with an X-band Bruker A200 spectrometer (Sweep field range 100 G, sweep time 60 s; modulation amplitude 1 G; modulation frequency 100 kHz, and microwave power 19.23 mW), Simulation of the spectra was done using the EasySpin package.

3.2 Plant material

The herbs of *A. Pilosa* were purchased in November 2018 from BoZhou (Anhui province, China) and identified by Prof. L. Ma. A voucher specimen (ID-20181226) was deposited at the Herbarium of the Department of Medicinal

Plants, Institute of Materia Medica, Chinese Academy of Medical Sciences, Beijing, China.

3.3 Extraction and isolation

Whole dried plant (including leaves, twigs, stems, and roots) of *A. Pilosa* (100 kg) were extracted thrice with 80 % EtOH-H_2O (450 L × 3) at 75 ℃ for 2 h to give a crude extract (11.0 kg), which was then suspended in H_2O (20 L) and partitioned with petroleum ether, EtOAc and n-BuOH (30 L × 3), successively.

The *n*-BuOH extract (2.0 kg) was subjected to a HP-20 column eluting with H_2O (**A**), 15% EtOH-H_2O (**B**), 30% EtOH-H_2O (**C**), 50% EtOH-H_2O (**D**), 95% EtOH-H_2O (E). Fr. C (349 g) was separated by a Sephadex LH-20 column with a gradient of elution of EtOH-H_2O (0:1~1:0) to give four subfractions Fra. C-1~4. Then, the column of *Rp*-C_{18} was applied for Fra. C-2 (10 g) with a gradient of elution (MeOH-H_2O, 0% to 100%). Subfractions C-2-32, C-2-43, C-2-47 and C-2-51 were purified by Sephadex LH-20 and *pre*-HPLC to produce **1** (50.0 mg, MeOH-H_2O, 38:62, *V*/*V*), **2** (12.0 mg, MeOH-H_2O, 38:62, *V*/*V*), **3** (9.2 mg, MeCN-H_2O, 18:82, *V*/*V*), and **5** (8.5 mg, MeCN-H_2O, 16:84, *V*/*V*). By the same way, compounds **4** (20.2 mg, MeCN-H_2O, 14:86, *V*/*V*) and **6** (15.4 mg, MeCN-H_2O, 16:84, *V*/*V*) were also isolated from Fra. C-1 (25.0 g) and C-4 (10.3 g), respectively.

The EtOAc extract (470 g) was subjected to a silica gel column by a gradient of petroleum ether-EtOAc (10:0, 10:1, 9:1, 8:1, 6:1, 4:1, 2:1, *V*/*V*). After the analysis by TLC and HPLC, the EtOAc extract was divided as seven subfractions Fra. A~F. Fra. B (20 g) was separated by a Sephadex LH-20 column (petroleum ether-dichloromethane-methanol = 5:5:1, *V*/*V*/*V*). Subfraction B-11 (70 mg) was first purified by *pre*-HPLC with the elution of MeCN-H_2O (16:84, *V*/*V*) to give Fra. B-11-2 (50 mg), and then separated by CHIRALPAK AD-RH column (250×10 mm) again, affording the mixture **a** (16 mg), **2c-1** (5.4 mg), and **3c-1** (12.9 mg). Compounds **2c-2** (6.0 mg) and **3c-2** (6.5 mg) were obtained from the mixture **a** by the YMC-C8 column (250×4.6 mm) with an elution of MeCN-H_2O (32: 68, *V*/*V*). Fra. B-41~44 were purified by semi-preparative

HPLC to obtain **1a** (6.0 mg), **2a** (3.0 mg), **3a** (5.0 mg), and **4a** (6.0 mg), respectively. Fra. D (7.8 g) was subjected to a Sephadex LH-20 column (petroleum ether-dichloromethane-methanol = 5:5:1, *V/V/V*), and subfraction D-11 (30 mg) were further purified by semi-preparative HPLC with an elution of MeCN-H_2O (34:66, *V/V*) to yield **1c** (6.0 mg) and **4c** (4.0 mg). In addition, enantiomers **1c** (6.0 mg) and **4c** (4.0 mg) were separated by CHIRALPAK AD-RH column (250×10 mm), affording **1c-1** (2.0 mg), **1c-2** (2.0 mg), **4c-1** (1.0 mg), **4c-2** (1.0 mg) respectively.

3.4 Acid hydrolysis of compounds 2 and 3

Compounds **2** and **3** were dissolved in 2.0 mL 2 M HCl, heated at 60 ℃ under an argon atmosphere for 10 h, respectively. After the reaction was finished monitored by TLC, the solution was cooled to room temperature and extracted by ethyl acetate (3×3 mL). The organic layers were evaporated in vacuo and dissolved in the solution (*n*-hexane: IPA= 1:1) for the chair Np-HPLC analysis.

The aqueous layer was freeze dired to obtain residue. Then, the residue was dissolved in anhydrous pyridine (2 mL), L-cysteine methyl ester hydrochloride (4 mg) was added, and then the mixture was heated in a bath (60 ℃) for 1 h. After the reaction solution was dried under vacuum, N-trimethylsilylimidazole (1 mL) was added, and the solution was heated in a water bath (60 ℃) for 1 h and extracted three times with H_2O/n-hexane. Then, the n-hexane layer was analyzed using GC under conditions as follows: injection temperature, 300 ℃; detector temperature (FID), 300 ℃; capillary column, HP-5 (30 m×0.32 mm, Dikma); start temperature, 200 ℃, raised to 280 ℃ at a rate of 10 ℃ min^{-1}, and the final temperature maintained for 35 min; and N_2 used as the carrier gas.

3.5 Physical and Chemical Characteristics of 1–3, 6

*3,5-dimethyl-butyrylphloroglucinol-2,4-O-β-D-diglucopyranoside (**1**).* White power; $[\alpha]_D^{20}$ + 47 (*c* 0.10, MeOH); UV (MeOH) λ_{max} (log ε) 203 (4.06), 218 (4.16), 270 (3.90), 331 (3.43) nm; IR (KBr) ν_{max} 3376, 2931, 1622, 1379, 1076, 895, 624, 598 cm^{-1}; HRESIMS (*m/z*): 549.2176 $[M + H]^+$ (calcd for $C_{24}H_{37}O_{14}$, 549.2178).

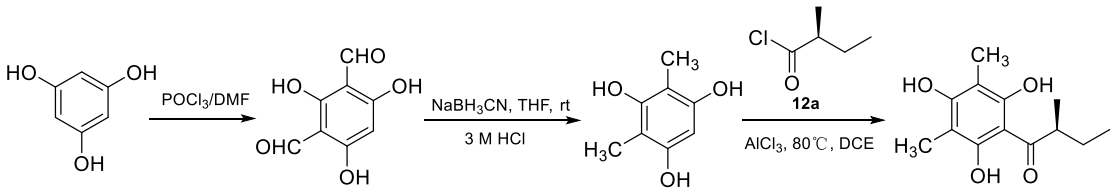
3,5-dimethyl-(R)-α-methylbutyrylphloroglucinol-2,4-O-β-D-diglucopyranoside ***(2)***. White power; $[\alpha]_D^{20}$ + 38 (*c* 0.10, MeOH); UV (MeOH) λ_{max} (log ε) 203 (4.13), 217 (4.16), 268 (3.84), 328 (3.38) nm; IR (KBr) ν_{max} 3389, 2931, 1626, 1601, 1379, 1080, 895, 627, 597 cm^{-1}; HRESIMS (*m/z*): 563.2335 $[M + H]^+$ (calcd for $C_{25}H_{39}O_{14}$, 563.2243).

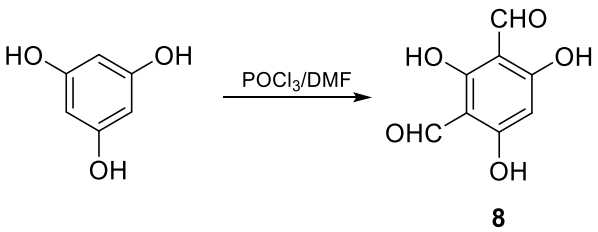
3,5-dimethyl-(S)-α-methylbutyrylphloroglucinol-2,4-O-β-D-diglucopyranoside ***(3)***. White power; $[\alpha]_D^{20}$ + 26 (*c* 0.10, MeOH); UV (MeOH) λ_{max} (log ε) 217 (4.67), 268 (4.35), 325 (3.92) nm; IR (KBr) ν_{max} 3430, 2929, 1627, 1601, 1380, 1079, 938, 895, 625, 597 cm^{-1}; HRESIMS (*m/z*): 585.2143 $[M + Na]^+$ (calcd for $C_{25}H_{38}O_{14}Na$, 585.2154).

3,5-dimethyl-2-acetylphloroglucinol-6-O-β-D-glucopyranoside ***(6)***. White power; $[\alpha]_D^{20}$ +87 (*c* 0.10, MeOH); UV (MeOH) λ_{max} (log ε) 203 (4.35), 218 (4.04), 233 (3.92), 288 (3.92), 325 (3.89) nm; IR (KBr) ν_{max} 3382, 2913, 1621, 1432, 1370, 1310, 1172, 888, 623 cm^{-1}; HRESIMS (*m/z*): 381.1156 $[M + Na]^+$ (calcd for $C_{16}H_{22}O_9Na$, 381.1156).

3.6 Experimental procedures of synthesis and spectroscopic data

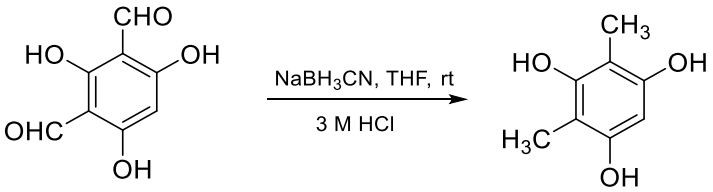
Scheme S1. Synthesis route towards *(S)-2-methyl-1-(2,4,6-trihydroxy-3,5-dimethyl phenyl) butan-1-one (**S**-**3a**)*





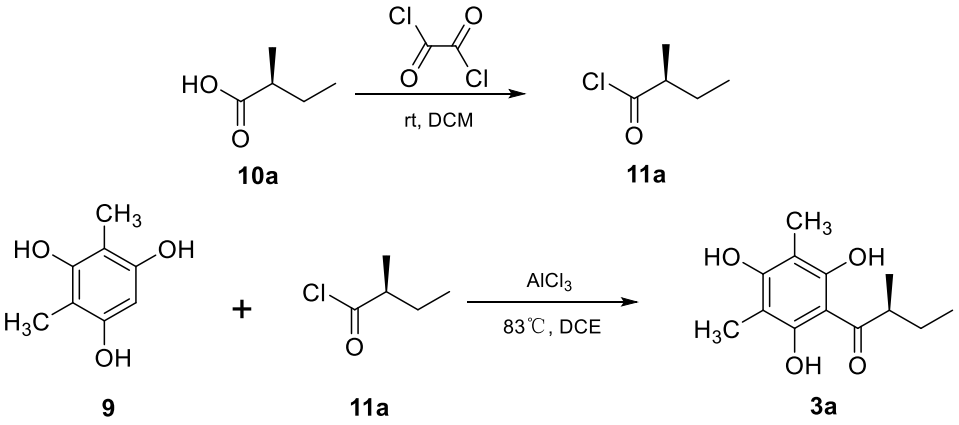
Synthesis of 2,4,6-trihydroxyisophthalaldehyde ***(8)***. $POCl_3$ (30.0 mmol) was added dropwise to DMF (30.0 mmol) in a 25 mL round-bottom flask at ice bath. The mixture was stirred for 30 min at room temperature. Phloroglucinol (10.0 mmol) was dissolved in 4.0 mL dioxane and added dropwise to the solution of $POCl_3$ and DMF at ice bath. The mixture was stirred at room temperature for 5 h and poured into ice-cold water

(600 mL) followed by extraction with ethyl acetate (3×100 mL). Then, the organic layers were extracted by saturated salt water, dryed with anhydrous sodium sulfate and evaporated in vacuo to give intermediate **8**. Yield 95%. ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.98 (s, 2H), 5.92 (s, 1H). HRESIMS (*m/z*): 183.0289 $[M + H]^+$ (calcd for $C_8H_7O_5$, 183.0288).



8 **9**

*Synthesis of 2,4-dimethylbenzene-1,3,5-triol (**9**).* $NaBH_3CN$ (2.74 mmol) and **8** (0.28 mmol) were dissolved in 2 mL THF, respectively. The solution of $NaBH_3CN$ was added dropwise to the solution of **8** at ice bath. Then, 0.9 mL 3 M HCl (2.74 mmol) was added dropwise to the solution of **8** at ice bath. The mixture was stirred for 2 h at room temperature. Water was added to the solution of reaction followed by extraction with ethyl acetate (3×20 mL). Then, the organic layers were extracted by saturated salt water, dried with anhydrous sodium sulfate and evaporated in vacuo to give the residue, which was further purified by *pre*-HPLC (15% MeCN-H_2O, v = 3 mL/min) to produce **9**. Yield 40%. ^{1}H NMR (500 MHz, Methanol-d_4) δ 5.95 (s, 1H), 1.98 (s, 6H). ^{13}C NMR (500 MHz, Methanol-d_4) δ 155.4, 154.6×2, 104.2, 96.1, 8.69. HRESIMS (*m/z*): 155.0702 $[M + H]^+$ (calcd for $C_8H_{11}O_3$, 155.0703).



10a **11a**

9 **11a** **3a**

*Synthesis of (S)-2-methyl-1-(2,4,6-trihydroxy-3,5-dimethylphenyl) butan-1-one (**S**-**3a**).* (*S*)-2-methylbutyric acid **10a** (0.21 mmol) was dissolved in dry dichloromethane (0.5 mL) and cooled on ice bath. A solution of oxalyl chloride (0.26 mmol) in dry dichloromethane (0.6 mL) was added dropwise and stirred for 15 min under an argon atmosphere. The mixture was stirred for 4 h at room temperature to product **11a**. Aluminium chloride (0.3 mmol) was dissolved in dry dichloroethane (1.5 mL) and cooled on ice bath, followed by the addition of the solution of **11a** dropwise and **9** (0.2 mmol). Then, the mixture was refluxed at 83 ℃ for 3 h. After the reaction was finished, the mixture was cooled to room temperature and poured into ice-cold water 10 mL, followed by extraction with ethyl acetate (3×10 mL). The organic layers were evaporated in vacuo and purified by silica gel column chromatography. Yield 70%. ^{1}H NMR (500 MHz, Methanol-d_4) δ 3.87 (m, 1H), 1.94 (s, 6H), 1.75 (m, 1H), 1.29 (m, 1H), 1.06 (d, J = 6.75 Hz, 3H), 0.82 (t, J = 7.40 Hz, 3H); ^{13}C NMR (500 MHz, Methanol-d_4) δ 212.5, 161.6, 160.1×2, 106.6, 103.9×2, 47.2, 28.5, 17.5, 12.6, 8.5×2. HRESIMS (*m/z*): 239.1274 $[M + H]^+$ (calcd for $C_{13}H_{19}O_4$, 239.1278).

3.7. Chromatographic conditions and the parameters of MS/MS analysis

HPLC separation was performed on an Aglient 1200 system, which was equipped with an Apollo C18 column (250 × 4.6 mm, 5μm) at a flow rate of 1.0 mL/min, and the column temperature was set as 40 ℃. The mobile phase consists of acetonitrile (A) and water (B) with a gradient elution of 35 %–100 % at 0–30 min.

A Q Exactive Focus mass spectrometer was applied for the MS analysis (Thermo Scientific, Waltham, MA, USA.). The parameters of MS/MS are as follows: sheath gas flow rate was 35 L/h, aux gas flow rate: 10 L/h, sweep gas flow rate: 0, aux gas heater temperature: 310 ℃, spray voltage was 3.3 kV, capillary temperature: 320 ℃, S-lens RF level: 50.0 V. The instrument was controlled by Thermo Xcalibur 4.0 software.

3.8. Free radical detection

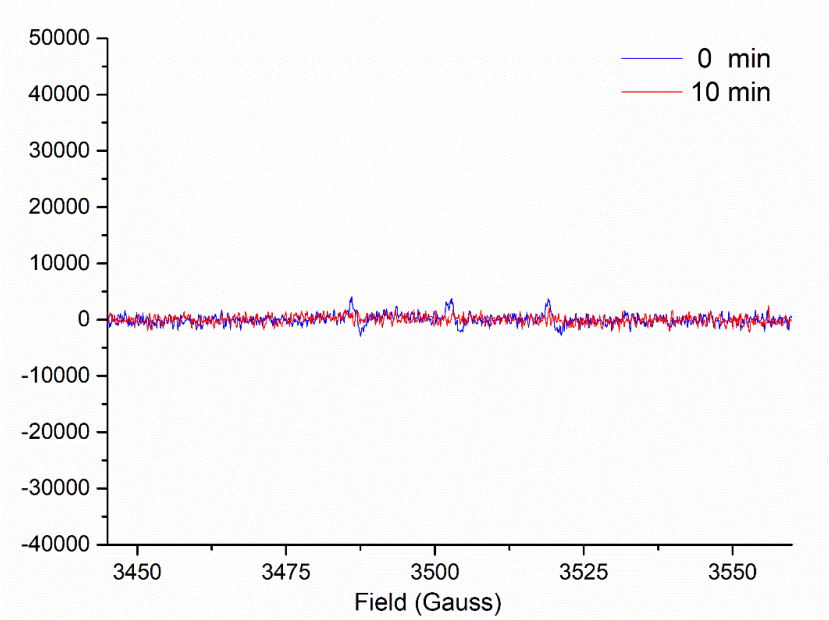


Figure S6 Electroparamagnetic resonance (EPR) spectra of **4a** (room temperature in oxygen-saturated acetonitrile). The concentrations of TEMP and **4a** were 500 and 50 mmol·L^{-1}, respectively.

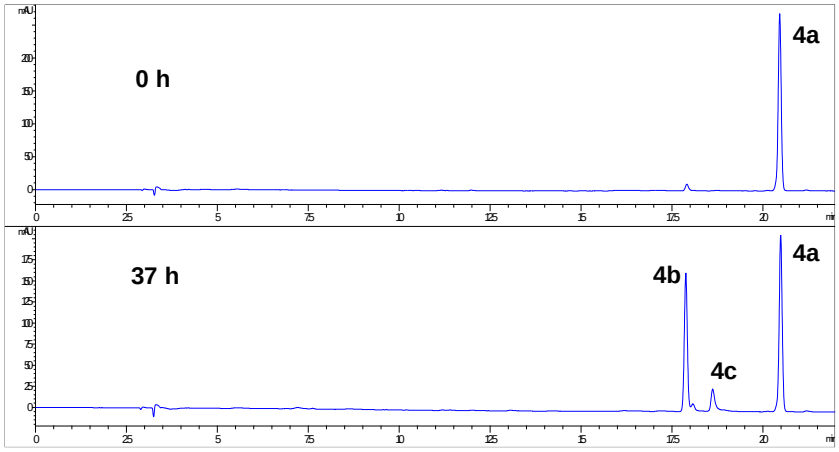


Figure S7. HPLC spectra of the solution of **4a** without the addition of DMPO.

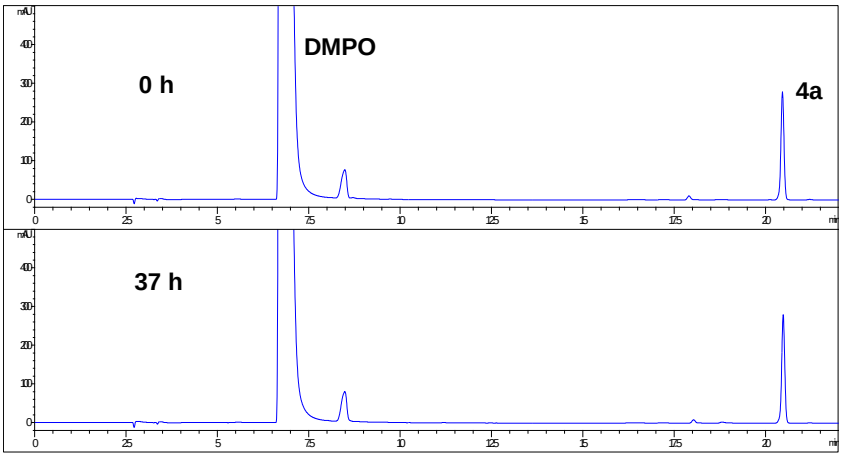


Figure S8. HPLC spectra of the solution of **4a** with the addition of excess DMPO.

Section S4. HPLC-MS/MS analysis of the mixture of 1a–4a.

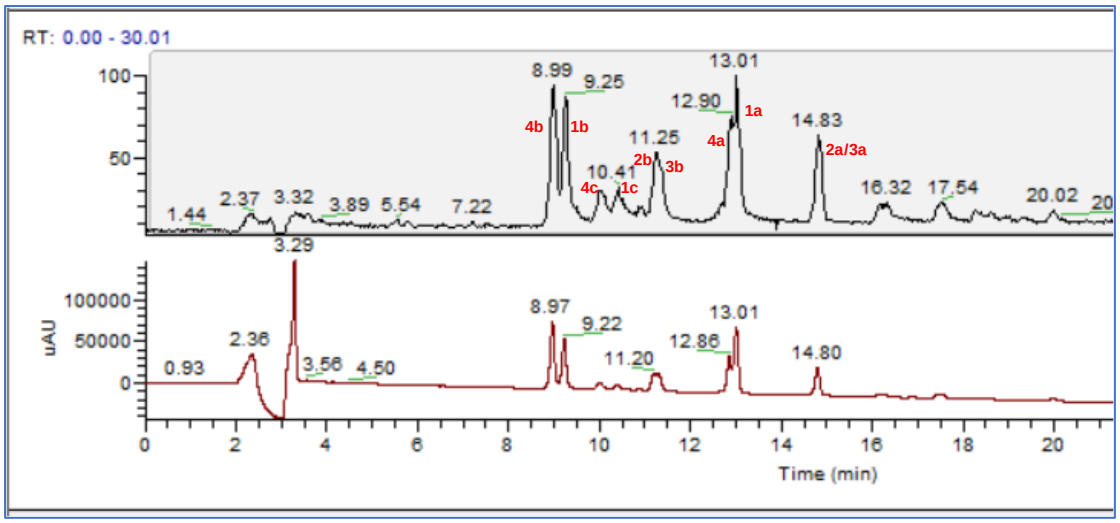


Figure S9. HPLC-PDA chromatograms and HPLC/*Q*-TOF-MS total ion chromatograms (TICs) of the mixture of **1a**–**4a**.

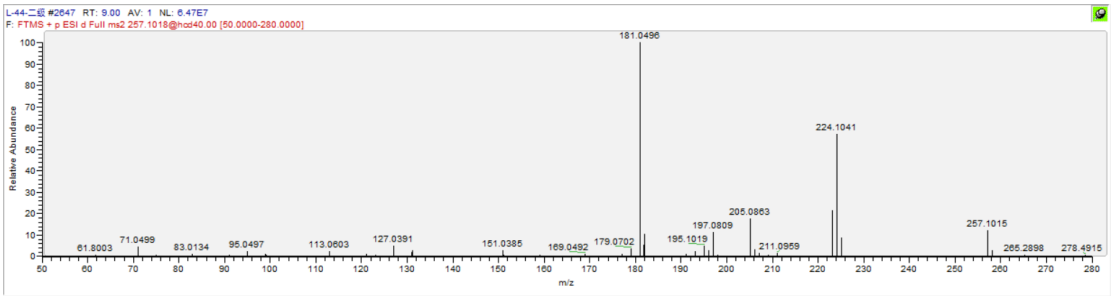


Figure S10. The fragmentation MS/MS ion spectrum of *m/z* 257.1018 for **1b** and **4b**.

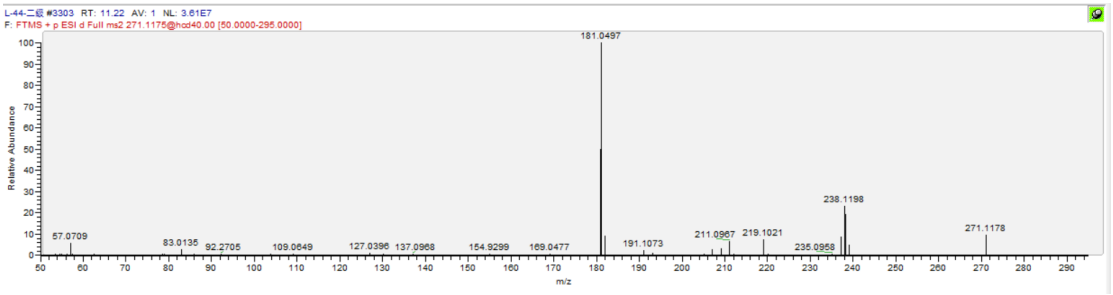


Figure S11. The fragmentation MS/MS ion spectrum of *m/z* 271.1175 for **2b** and **3b**.

***Q*-TOF-MS/MS analysis of the mixture of 1a–4a.** From the characteristic UV spectrum (λ_{max} = 280 nm), peaks **1b–4b** were diagnosed as 3,5,6-trihydroxycyclo hexa-2,4-dien-1-one derivatives. The deprotonated ion of **1b** (RT = 9.25 min), **4b** (RT = 8.99 min) were detected as *m/z* 255.0877 $[M - H]^-$ and 255.0876 $[M - H]^-$, of which the

molecular formulate have one more oxygen atom than those of **1a** and **4a**, suggesting peaks **1b** and **4b** may be the peroxide of **1a** and **4a**. The positive MS/MS spectrum of *m/z* 257.1018 $[M + H]^+$ were obtained, giving a series of characteristic fragment ions at *m/z* 224.1041 $[M - 33]^{+\bullet}$, 205.0863 $[M - 33 - 19]^+$, 197.0809 $[M - 33 - 27]^+$, 181.0496 $[M - 33 - 43]^+$ for compound **4b**. The fragment ion at *m/z* 224.1041 $[M - 33]^{+\bullet}$ was generated by the loss of peroxide group from the protonated molecular ion, suggesting the presence of peroxide group. Followed by the loss of the ethylene, the fragment ions at *m/z* 197.0809 $[M - 33 - 27]^+$ was obtained. In another way, the loss of propyl group of the fragment ion at *m/z* 224.1041 $[M - 33]^{+\bullet}$ resulting the fragment ion at *m/z* 181.0496 $[M - 33 - 43]^+$, indicating the presence of propyl group. Similarly, the deprotonated ion of **2b** and **3b** (RT = 11.25 min) were detected as *m/z* 269.1035 $[M - H]^-$ and 269.1036 $[M - H]^-$ with one more oxygen than those of **2a** and **3a**, and the MS/MS spectrum and fragmentation pathway resemble those of peaks **1b** and **4b**.

Section S5. Calculation of Gibbs free energy profile

Compound **4a** was selected as the model strcture to calculate the Gibbs free energy profile of the reaction of oxidative dearomatization. The structure of **4a** was performed using a molecular mechanics force filed (MMFF94s) by Chemdraw 3D 14.0. All strctures were optimized and refined by frequency calculation with no imaginary frequency (TS has the special imaginary frequency) at M06-2X/6-31G (d, p) level by Gaussian 09 E01 package. Single-point energy of optimized structures were calculated at RI-PWPB95-D3(BJ)/def2-TZVPP level with SMD solvent model for methanol by ORCA, using methanol as the solvent. Then, the Gibbs free energy (E_{Gibbs}) was provided as the sum of the thermal corrections ($C_{M06\text{-}2X,\ corr}$) and Single-point energy ($E_{PWPB95,\ sp}$). The potential energy surface scanning was performed at the level of B3LYP/6-31G(d). The enthalpy energy ($E_{\ enthalpy}$) was calculated as the sum of the enthalpy corrections ($C_{M06\text{-}2X,\ corr}$) at M06-2X/6-31G (d, p) level and Single-point energy ($E_{M06\text{-}2X,\ sp}$) at M06-2X/def2-TZVP level by Gaussian 09 E01 package. The BDE values were calculated as: BDE (O-O) = $E_{\ enthalpy}$ (HO·) + $E_{\ enthalpy}$ (RO·) – $E_{\ enthalpy}$ (ROOH).

Table S3. Cartesian Coordinates.

a2	E_{Gibbs} = -766.780776 Hartree		
C	2.42812	0.236934	-0.0122
C	1.98024	-1.08069	0.04982
C	0.600951	-1.30116	0.02467
C	-0.34531	-0.23676	-0.08427
C	0.18572	1.078682	-0.1535
C	1.552471	1.337769	-0.08325
C	2.0774	2.753522	-0.06914
C	2.919807	-2.2516	0.131775
O	0.205336	-2.57598	0.091523
O	3.770162	0.417704	0.015346
O	-0.68629	2.109654	-0.27376
O	-2.11434	-1.78041	-0.11557
C	-1.77419	-0.58424	-0.13887
C	-3.03778	1.024496	1.257048
C	-2.89144	0.446456	-0.16165
C	-4.20214	-0.18298	-0.62625
H	1.391681	3.429545	0.450255
H	3.010884	2.827959	0.495478
H	2.258346	3.157101	-1.07114
H	2.876255	-2.72527	1.117839
H	2.643283	-3.01417	-0.60072
H	3.94634	-1.93774	-0.05328
H	-0.79442	-2.54872	0.020176
H	3.993634	1.333466	-0.18945
H	-0.2121	2.924975	-0.47737
H	-3.8314	1.77622	1.267231
H	-3.3136	0.228989	1.956741
H	-2.11523	1.494052	1.601988
H	-2.61041	1.25339	-0.83861
H	-4.10189	-0.62709	-1.61965
H	-4.97933	0.584594	-0.66687
H	-4.52404	-0.96768	0.061968

$^3O_2$	E_{Gibbs} = -150.3177428 Hartree		
O	0	0	0.598678
O	0	0	-0.59868

TS-1	E_{Gibbs} = -917.0703679 Hartree		
C	-2.26137	-0.06821	-0.51861
C	-1.7417	1.189686	-0.41524
C	-0.31644	1.32992	-0.18384

C	0.584856	0.246529	-0.12916
C	0.041311	-1.09361	-0.23823
C	-1.45754	-1.21481	-0.20151
C	-2.02201	-2.59204	-0.31927
C	-2.56405	2.432358	-0.5637
O	0.106606	2.557757	-0.07217
O	-3.58396	-0.20524	-0.75353
O	0.69962	-2.13051	-0.2993
O	2.35767	1.741153	0.176809
C	1.992603	0.548821	0.048749
C	4.33182	-0.03272	0.736534
C	3.058643	-0.52492	0.0543
C	3.331254	-0.93143	-1.4043
H	-2.17635	-2.85214	-1.37281
H	-1.31809	-3.30876	0.100798
H	-2.97523	-2.67723	0.209831
H	-2.18585	3.046099	-1.3861
H	-3.60652	2.182843	-0.75286
H	-2.4991	3.038479	0.344154
H	1.137727	2.469321	0.063653
H	-3.81939	-1.13209	-0.88723
H	4.138139	0.28323	1.764595
H	5.070286	-0.83813	0.755457
H	4.758242	0.81625	0.197257
H	2.657045	-1.39606	0.576466
H	2.431381	-1.32157	-1.88302
H	4.09985	-1.7083	-1.42978
H	3.696275	-0.07078	-1.97367
O	-1.52352	-1.0715	1.791768
O	-1.46549	0.074746	2.21627

a3	E_{Gibbs} = -917.0878289 Hartree		
C	2.246541	0.27693	0.098298
C	1.635521	1.477437	0.044715
C	0.185187	1.499847	0.01439
C	-0.64262	0.352519	-0.05463
C	-0.00989	-0.94655	-0.12532
C	1.474689	-1.00123	0.289288
C	1.544977	-1.4657	1.744538
C	2.377731	2.781523	-0.00061
O	-0.34206	2.687508	0.01852
O	3.581583	0.183004	0.113309
O	-0.54368	-2.01222	-0.38943
O	-2.53706	1.723566	-0.13638
C	-2.07758	0.558588	-0.15074

C	-4.43816	-0.12679	-0.64492
C	-3.05598	-0.59519	-0.20035
O	2.131949	-2.04967	-0.4714
O	2.063544	-1.81351	-1.7552
C	-3.11189	-1.24016	1.196204
H	1.02355	-0.74734	2.37976
H	1.056514	-2.43915	1.820721
H	2.583682	-1.54325	2.071858
H	3.452673	2.605957	-0.00703
H	2.105007	3.348279	-0.89436
H	2.124794	3.397524	0.866257
H	-1.37524	2.526316	-0.03907
H	3.865567	-0.74018	0.038945
H	-4.40029	0.357644	-1.62348
H	-5.11027	-0.98601	-0.70913
H	-4.85559	0.587343	0.068899
H	-2.66208	-1.33595	-0.89905
H	-2.13606	-1.61669	1.509406
H	-3.81282	-2.07854	1.18198
H	-3.46482	-0.51274	1.933822

4a	E_{Gibbs} = -767.4033962 Hartree		
C	2.42812	0.236934	-0.0122
C	1.98024	-1.08069	0.04982
C	0.600951	-1.30116	0.02467
C	-0.34531	-0.23676	-0.08427
C	0.18572	1.078682	-0.1535
C	1.552471	1.337769	-0.08325
C	2.0774	2.753522	-0.06914
C	2.919807	-2.2516	0.131775
O	0.205336	-2.57598	0.091523
O	3.770162	0.417704	0.015346
O	-0.68629	2.109654	-0.27376
O	-2.11434	-1.78041	-0.11557
C	-1.77419	-0.58424	-0.13887
C	-3.03778	1.024496	1.257048
C	-2.89144	0.446456	-0.16165
C	-4.20214	-0.18298	-0.62625
H	1.391681	3.429545	0.450255
H	3.010884	2.827959	0.495478
H	2.258346	3.157101	-1.07114

H	2.876255	-2.72527	1.117839
H	2.643283	-3.01417	-0.60072
H	3.94634	-1.93774	-0.05328
H	-0.79442	-2.54872	0.020176
H	3.993634	1.333466	-0.18945
H	-0.2121	2.924975	-0.47737
H	-3.8314	1.77622	1.267231
H	-3.3136	0.228989	1.956741
H	-2.11523	1.494052	1.601988
H	-2.61041	1.25339	-0.83861
H	-4.10189	-0.62709	-1.61965
H	-4.97933	0.584594	-0.66687
H	-4.52404	-0.96768	0.061968

TS-2	E_{Gibbs} = -1684.464207 Hartree		
C	-1.5799	-2.04073	-1.58446
C	-0.32422	-1.54453	-1.96474
C	-0.05274	-0.17612	-1.75476
C	-0.99247	0.683959	-1.14552
C	-2.22763	0.101206	-0.69066
C	-2.5242	-1.26348	-0.9161
C	-3.79762	-1.87934	-0.41395
C	0.695981	-2.4471	-2.58367
O	1.142366	0.257905	-2.16681
O	-1.79926	-3.345	-1.85825
O	-3.15078	0.814035	-0.07016
O	0.50057	2.484445	-1.3272
C	-0.6508	2.125031	-1.04639
C	-2.62983	3.317061	-1.93177
C	-1.66868	3.208612	-0.73606
C	-0.96706	4.53321	-0.45328
H	-4.37993	-1.14443	0.137581
H	-4.41689	-2.25221	-1.23787
H	-3.58512	-2.71667	0.261287
H	0.679983	-3.4217	-2.09128
H	0.479467	-2.60717	-3.64593
H	1.691678	-2.0131	-2.4944
H	1.174799	1.227607	-1.91574
H	-2.67251	-3.61747	-1.54562
H	-2.83037	1.187893	0.885963
H	-3.35599	4.111586	-1.74324

H	-2.07774	3.568926	-2.84251
H	-3.17548	2.38555	-2.09614
H	-2.24521	2.925822	0.142951
H	-0.25807	4.427477	0.371855
H	-1.70982	5.287534	-0.18281
H	-0.41718	4.882524	-1.33004
C	-0.778	-1.01956	1.964535
C	-0.09687	-2.07097	1.461391
C	1.22846	-1.86979	0.895132
C	1.84666	-0.55621	0.840975
C	1.209487	0.566997	1.488007
C	-0.14683	0.333826	2.199632
C	0.008194	0.601674	3.696472
C	-0.67822	-3.45259	1.388081
O	1.812051	-2.86729	0.390844
O	-2.03478	-1.18228	2.404155
O	1.647657	1.706836	1.554396
O	3.525541	-1.46034	-0.5092
C	2.989718	-0.41181	0.030647
C	4.423063	0.826489	-1.60595
C	3.681479	0.888764	-0.27152
O	-0.93876	1.400728	1.614101
O	-2.22537	1.421591	2.063933
C	4.641843	1.203168	0.88909
H	0.649381	-0.16145	4.142621
H	0.464601	1.584478	3.821601
H	-0.96634	0.580287	4.187552
H	-0.78717	-3.77482	0.347918
H	-0.01134	-4.16793	1.876778
H	-1.6525	-3.48644	1.875309
H	2.924444	-2.27446	-0.20205
H	-2.41852	-0.30372	2.590044
H	3.747762	0.552807	-2.42042
H	4.853815	1.806972	-1.8226
H	5.232344	0.093569	-1.5714
H	2.917031	1.668653	-0.29877
H	5.3954	0.415126	0.981187
H	4.101413	1.296168	1.832696
H	5.155074	2.146903	0.688164

4b	E_{Gibbs} = -917.7258975 Hartree		
C	2.220779	0.299447	0.125764
C	1.618789	1.502428	0.065723
C	0.161278	1.553299	0.045206
C	-0.6549	0.349569	-0.02383
C	-0.01662	-0.95508	-0.04277
C	1.479976	-1.00112	0.319794
C	1.584728	-1.46316	1.777935
C	2.366736	2.801446	-0.00202
O	-0.38409	2.689666	0.048086
O	3.558483	0.190338	0.101413
O	-0.56821	-2.02803	-0.23207
O	-2.55521	1.707375	-0.11649
C	-2.04878	0.515642	-0.13265
C	-4.39426	-0.12586	-0.76143
C	-3.05177	-0.60556	-0.21339
O	2.135154	-2.01543	-0.42807
O	1.93059	-1.71262	-1.80905
C	-3.21029	-1.20933	1.194377
H	1.067869	-0.75043	2.423651
H	1.110844	-2.44255	1.862715
H	2.629467	-1.52973	2.088734
H	3.442184	2.6273	0.012106
H	2.107308	3.348108	-0.91264
H	2.098937	3.44007	0.843923
H	-1.72692	2.363604	-0.03393
H	3.804486	-0.74838	0.114713
H	-4.28397	0.337739	-1.74456
H	-5.06777	-0.98086	-0.8564
H	-4.85481	0.603551	-0.09119
H	-2.63095	-1.37476	-0.86264
H	-2.26408	-1.60541	1.567722
H	-3.93591	-2.02566	1.157972
H	-3.58134	-0.45173	1.891295
H	2.816953	-1.43162	-2.08838

a4	E_{Gibbs} = -841.9103704 Hartree		
C	2.381163	-0.01665	-0.08997
C	1.858948	1.221987	0.008866
C	0.416884	1.3574	0.026699
C	-0.49765	0.28767	-0.12248

C	0.022541	-1.04348	-0.33938
C	1.538868	-1.27677	-0.06071
C	1.648724	-1.95323	1.31473
C	2.698664	2.463629	0.105371
O	-0.01555	2.574218	0.173318
O	3.71016	-0.19233	-0.11984
O	-0.61612	-2.03951	-0.64128
O	-2.28221	1.79492	0.023447
C	-1.9166	0.605646	-0.11823
C	-4.34326	0.148101	-0.5485
C	-2.98513	-0.4617	-0.21515
O	2.02232	-2.08055	-1.08512
C	-3.03133	-1.21847	1.124531
H	1.21881	-1.3176	2.092983
H	1.097515	-2.89475	1.27174
H	2.694514	-2.15471	1.557348
H	3.757311	2.21082	0.06885
H	2.46844	3.146914	-0.71607
H	2.492159	2.993954	1.038516
H	-1.05874	2.496891	0.142371
H	3.942835	-1.12089	-0.26017
H	-4.30888	0.713343	-1.48286
H	-5.08426	-0.64835	-0.652
H	-4.67085	0.825644	0.243559
H	-2.68308	-1.16749	-0.9914
H	-2.07571	-1.69301	1.355891
H	-3.79673	-1.99711	1.076186
H	-3.29309	-0.53253	1.93617

TS-3	E_{Gibbs} = -1609.329967 Hartree		
C	-1.55227	-1.30557	1.502228
C	-0.8057	-0.37343	2.190475
C	0.599064	-0.34643	1.968363
C	1.253454	-1.16048	0.987652
C	0.4413	-2.03122	0.250552
C	-0.95248	-2.21977	0.582642
C	-1.62185	-3.53844	0.316297
C	-1.4122	0.615307	3.140167
O	1.278305	0.537815	2.6596
O	-2.87199	-1.39306	1.77321
O	0.874133	-2.67537	-0.8204

O	3.28644	-0.09075	1.437845
C	2.670254	-0.87457	0.694604
C	3.811246	-2.92968	-0.08249
C	3.410777	-1.49455	-0.46802
C	4.636016	-0.65974	-0.83076
H	-1.63748	-4.12269	1.242681
H	-2.65566	-3.42117	-0.01434
H	-1.08388	-4.09791	-0.44611
H	-1.34633	1.625667	2.720092
H	-2.4599	0.379665	3.32003
H	-0.87356	0.62182	4.090423
H	2.250378	0.433978	2.35822
H	-3.36006	-1.6922	0.988415
H	0.106616	-2.4573	-1.47444
H	4.329762	-3.39839	-0.92243
H	4.492338	-2.91253	0.773936
H	2.942807	-3.54158	0.167357
H	2.719082	-1.53407	-1.31144
H	4.35642	0.364809	-1.09485
H	5.139225	-1.1099	-1.68986
H	5.341228	-0.61355	0.002135
C	-2.7373	-0.12477	-1.03874
C	-2.9696	1.011135	-0.35222
C	-1.86322	1.939456	-0.18655
C	-0.51878	1.634006	-0.66626
C	-0.2796	0.432362	-1.4543
C	-1.4932	-0.43287	-1.84694
C	-1.77462	-0.11149	-3.33339
C	-4.24199	1.283774	0.395168
O	-2.07306	2.993516	0.477428
O	-3.6243	-1.13712	-1.05035
O	0.808673	0.074035	-1.89188
O	0.246638	3.54531	0.449456
C	0.519261	2.490534	-0.25261
C	2.876149	2.985867	0.452651
C	1.97722	2.308391	-0.57862
O	-1.26191	-1.79219	-1.70525
C	2.226757	2.854055	-1.99534
H	-1.96349	0.956208	-3.47519
H	-0.89541	-0.40766	-3.90866
H	-2.64342	-0.67975	-3.67362
H	-4.0695	1.249541	1.475577
H	-4.62028	2.280353	0.155288

H	-5.00219	0.54474	0.140446
H	-0.80682	3.531012	0.576665
H	-3.15044	-1.86937	-1.50248
H	2.644858	2.646846	1.465328
H	3.918781	2.73786	0.23778
H	2.761569	4.071841	0.421999
H	2.175526	1.236543	-0.6046
H	1.983525	3.919847	-2.04036
H	1.627777	2.316508	-2.73275
H	3.283063	2.732043	-2.24997

4c	E_{Gibbs} = -842.6083439 Hartree		
C	2.35613	-0.00631	-0.13528
C	1.857189	1.24636	-0.02501
C	0.420582	1.376558	0.064297
C	-0.50352	0.30678	-0.09168
C	0.039687	-1.00493	-0.3562
C	1.498039	-1.22874	0.051808
C	1.490428	-1.59993	1.55123
C	2.705189	2.485593	-0.04267
O	-0.01797	2.590995	0.234128
O	3.657266	-0.24084	-0.30027
O	-0.54999	-1.98645	-0.80063
O	-2.2935	1.804396	0.079693
C	-1.91724	0.623618	-0.10353
C	-4.33576	0.156958	-0.57649
C	-2.97205	-0.45142	-0.26466
O	2.061029	-2.28159	-0.68973
C	-3.01895	-1.2851	1.028029
H	1.053252	-0.80452	2.158026
H	0.907611	-2.51661	1.671567
H	2.517602	-1.78237	1.874811
H	3.753883	2.221239	-0.17759
H	2.402493	3.154205	-0.85265
H	2.601257	3.040051	0.893956
H	-1.05716	2.510688	0.217044
H	3.766455	-1.18112	-0.52661
H	-4.30154	0.772823	-1.47829
H	-5.06591	-0.64164	-0.72908
H	-4.67802	0.786576	0.248375
H	-2.65325	-1.10756	-1.07773

H	-2.061	-1.76597	1.236636
H	-3.77817	-2.06542	0.931922
H	-3.2882	-0.65016	1.877855
H	1.307568	-2.77898	-1.05288

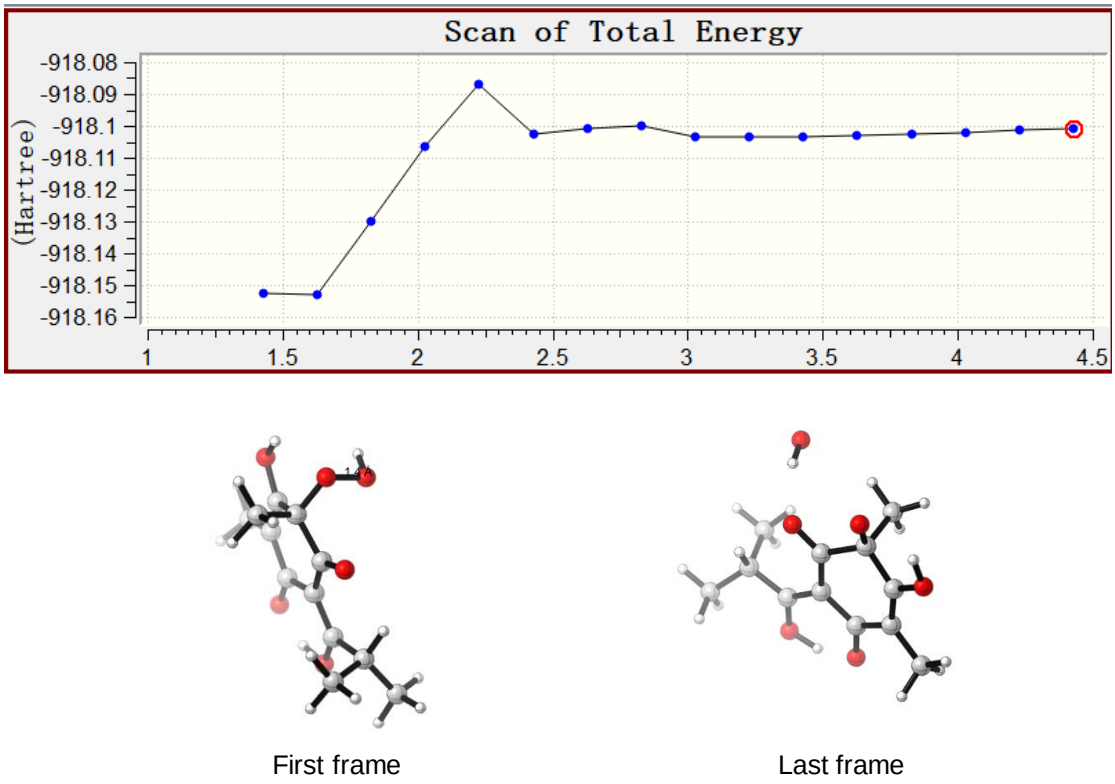


Figure S12. potential energy surface scanning of the O-O bond of **4a**

Section S6. Experimental Spectra of Compound 1–3, 6

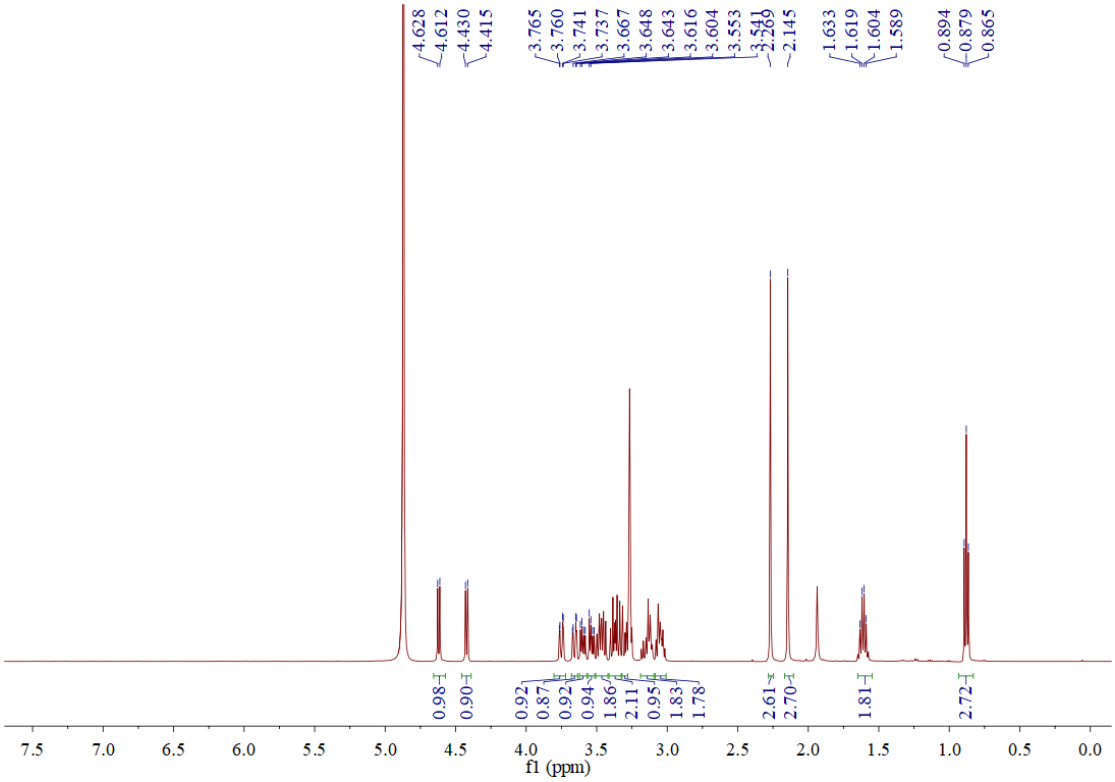


Figure S13. ^{1}H NMR Spectrum of Compound **1** in Methanol-d_4

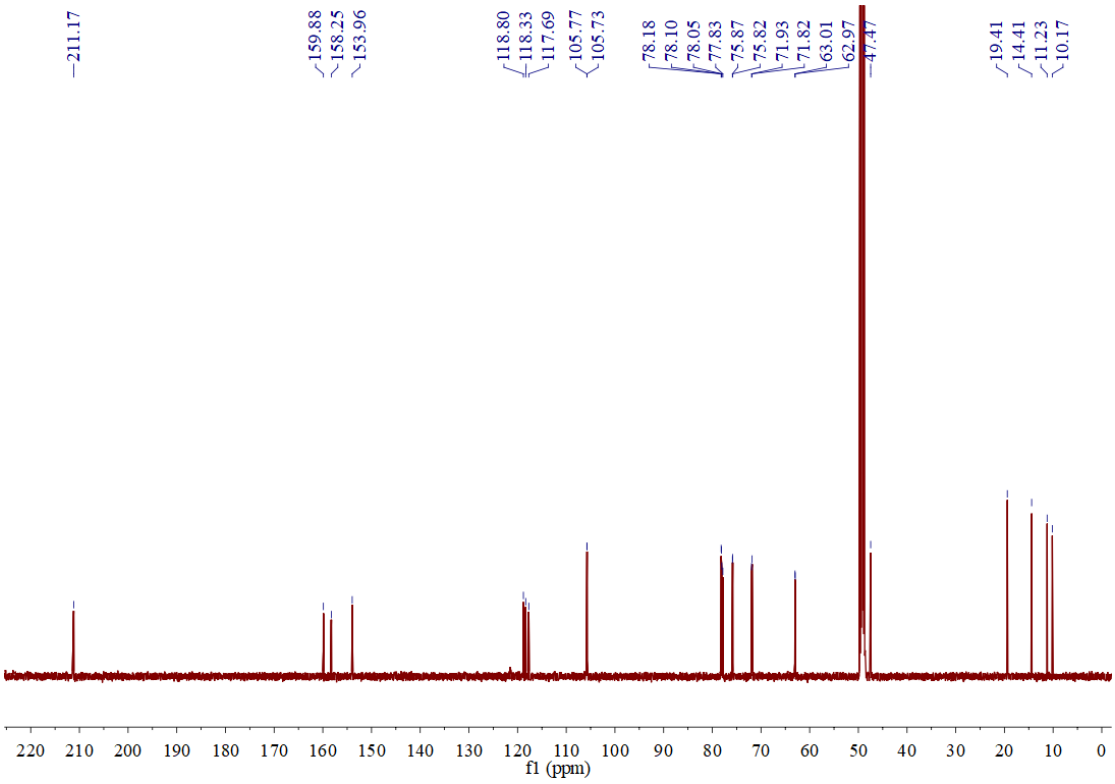


Figure S14. ^{13}C NMR Spectrum of Compound **1** in Methanol-d_4

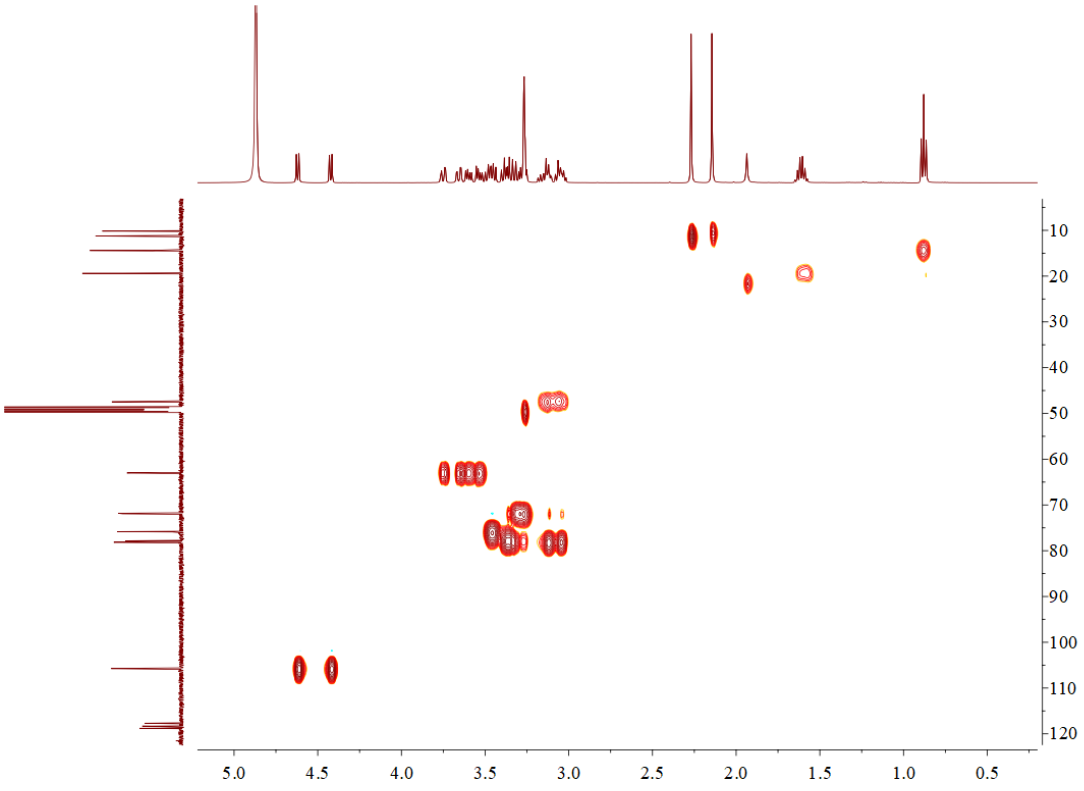


Figure S15. HSQC Spectrum of Compound **1** in Methanol-d_4

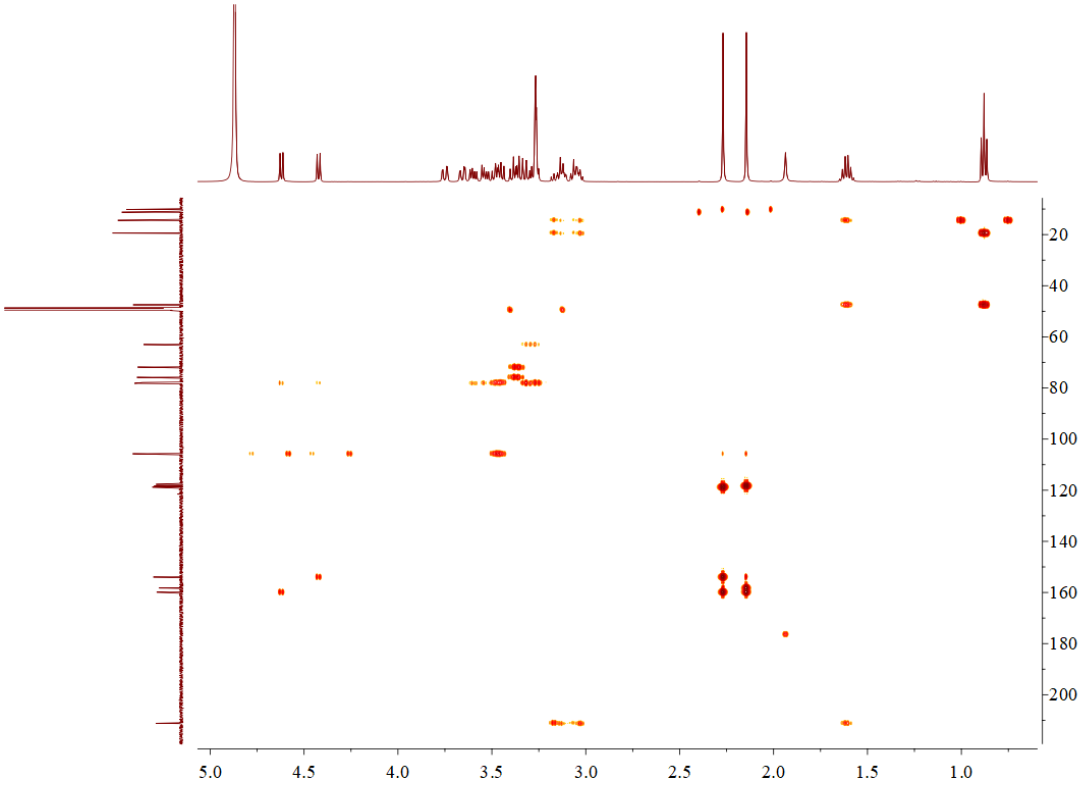


Figure S16. HMBC Spectrum of Compound **1** in Methanol-d_4

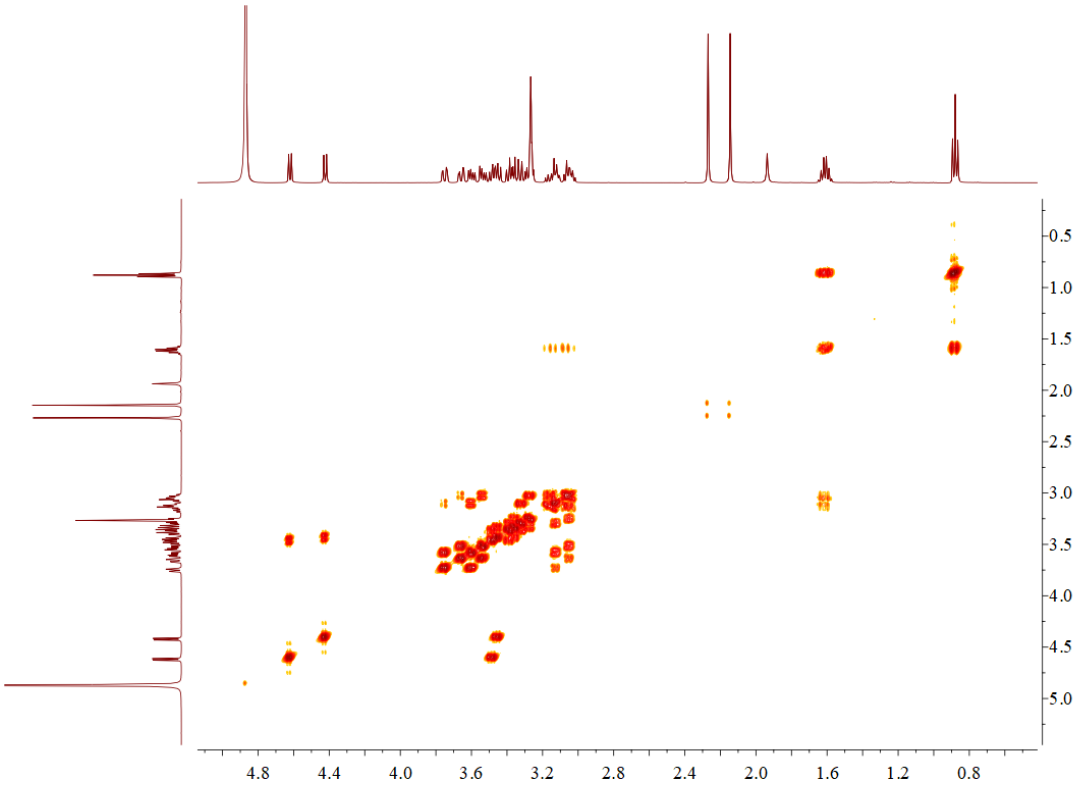


Figure S17. ^{1}H-^{1}H COSY Spectrum of Compound **1** in Methanol-d_4

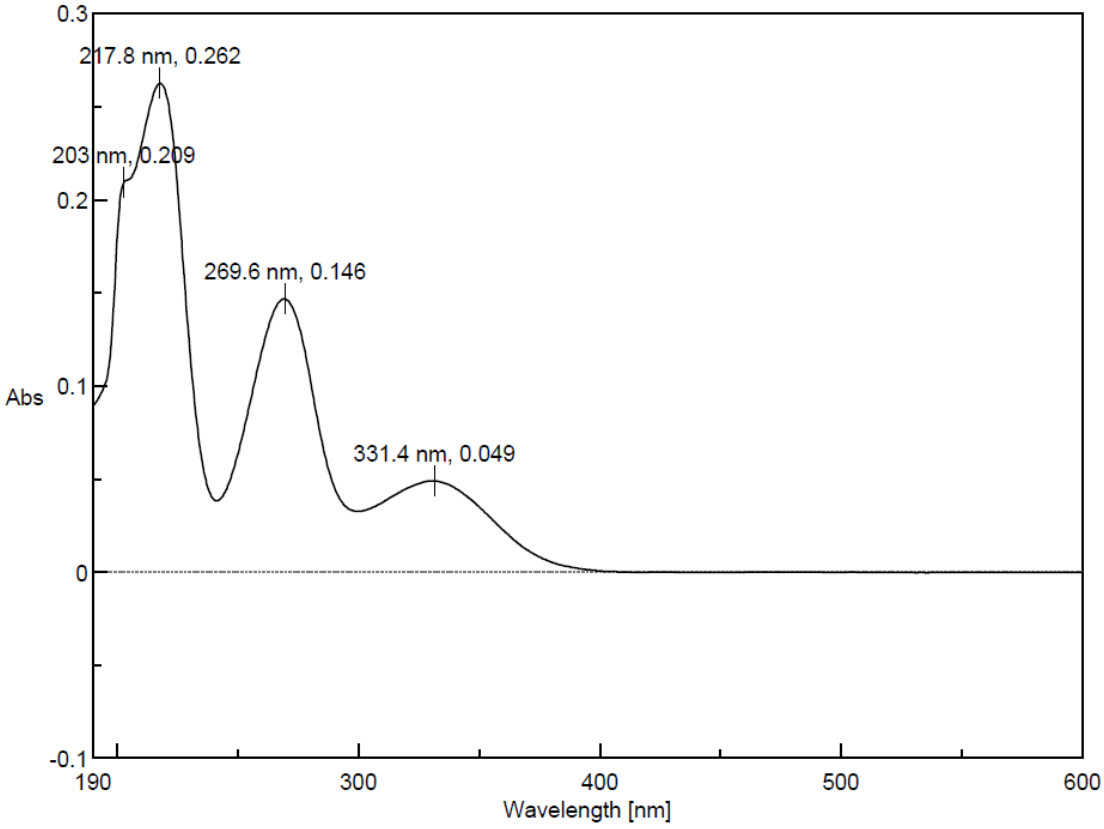


Figure S18. UV Spectrum of Compound **1** in Methanol

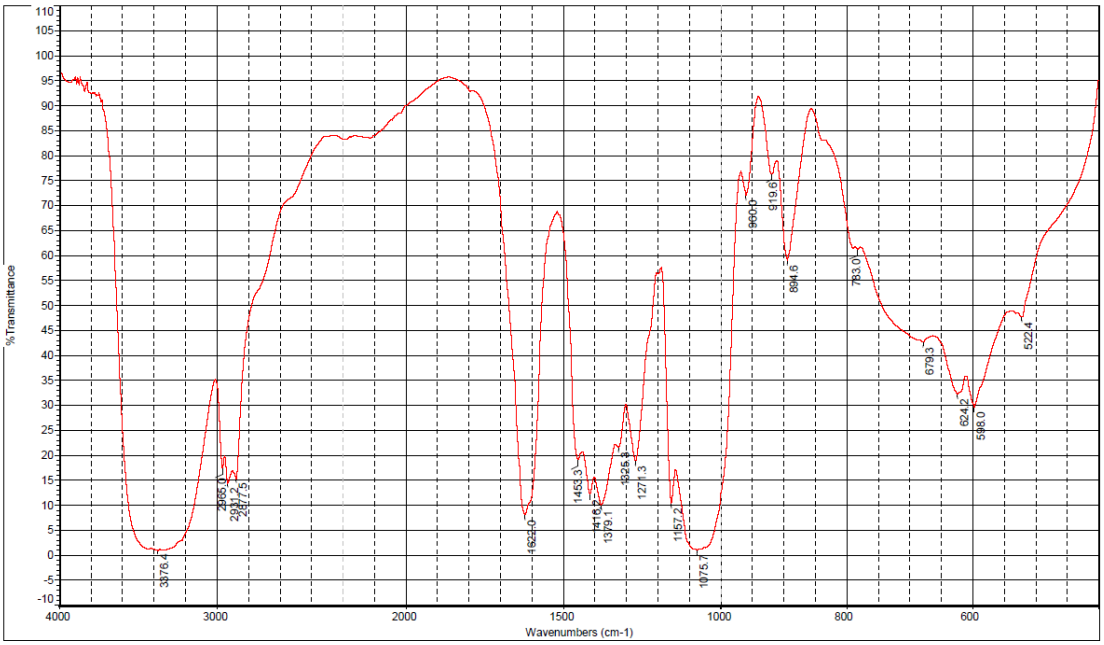


Figure S19. IR Spectrum of Compound **1**

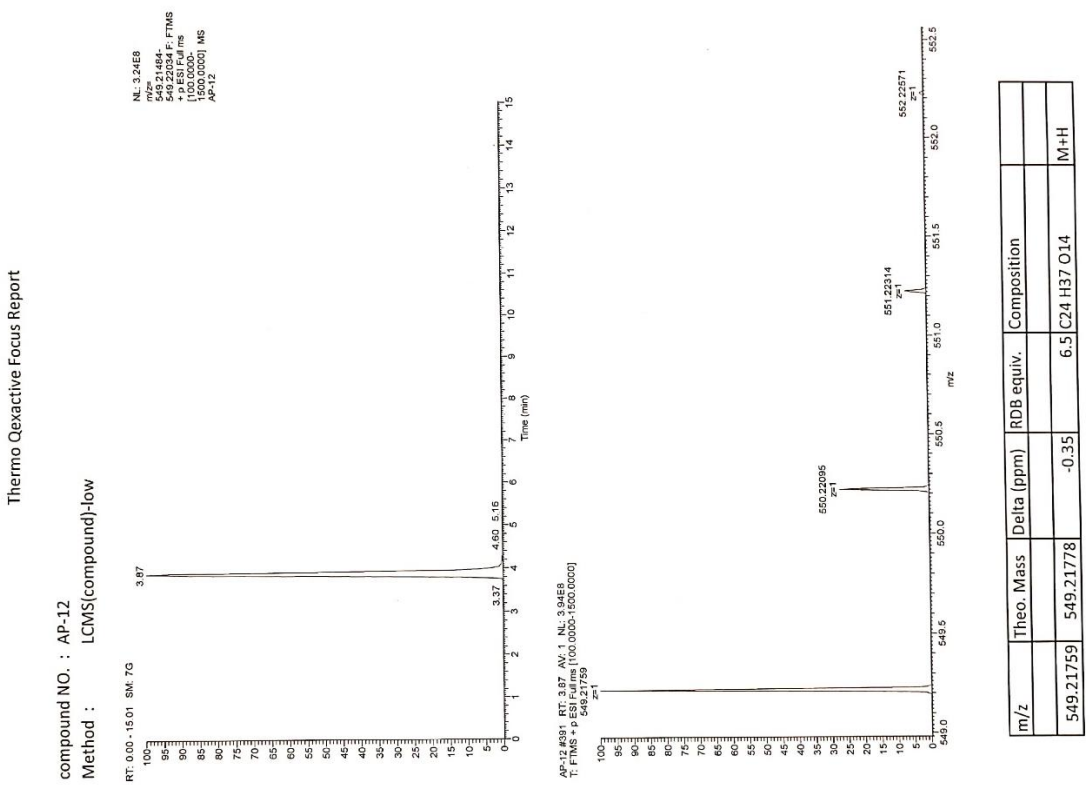


Figure S20. HRESIMS Spectrum of Compound **1**.

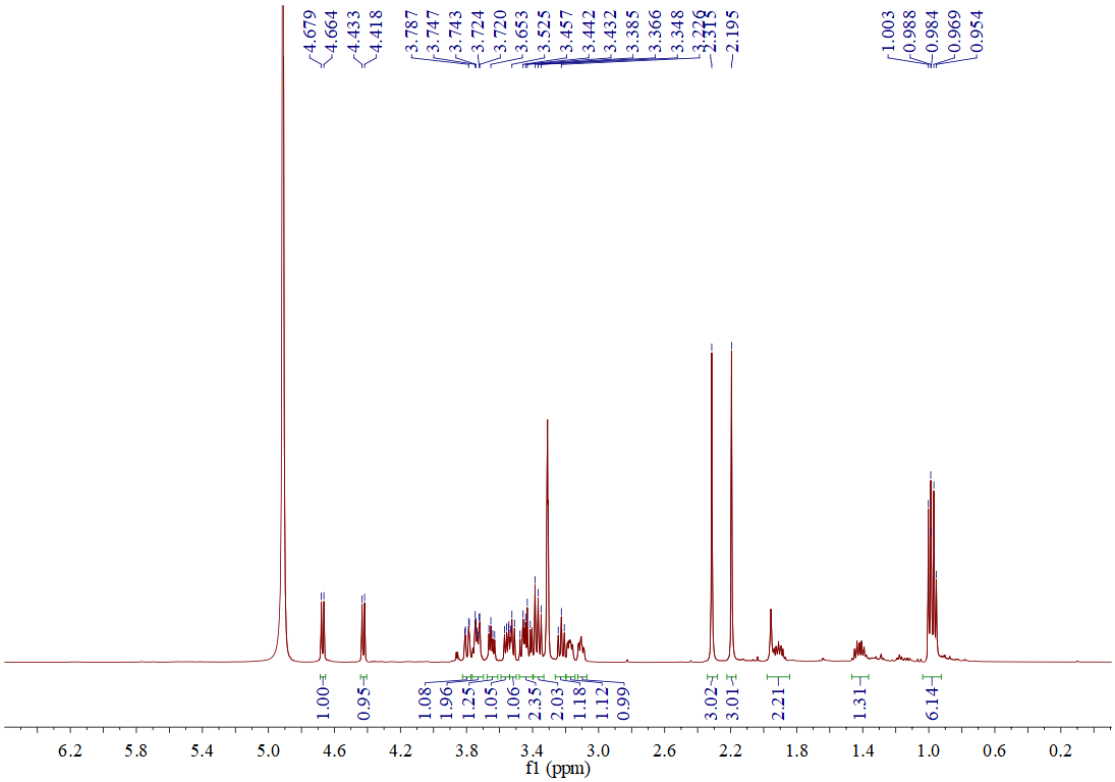


Figure S21. ^{1}H NMR Spectrum of Compound **2** in Methanol-d_4

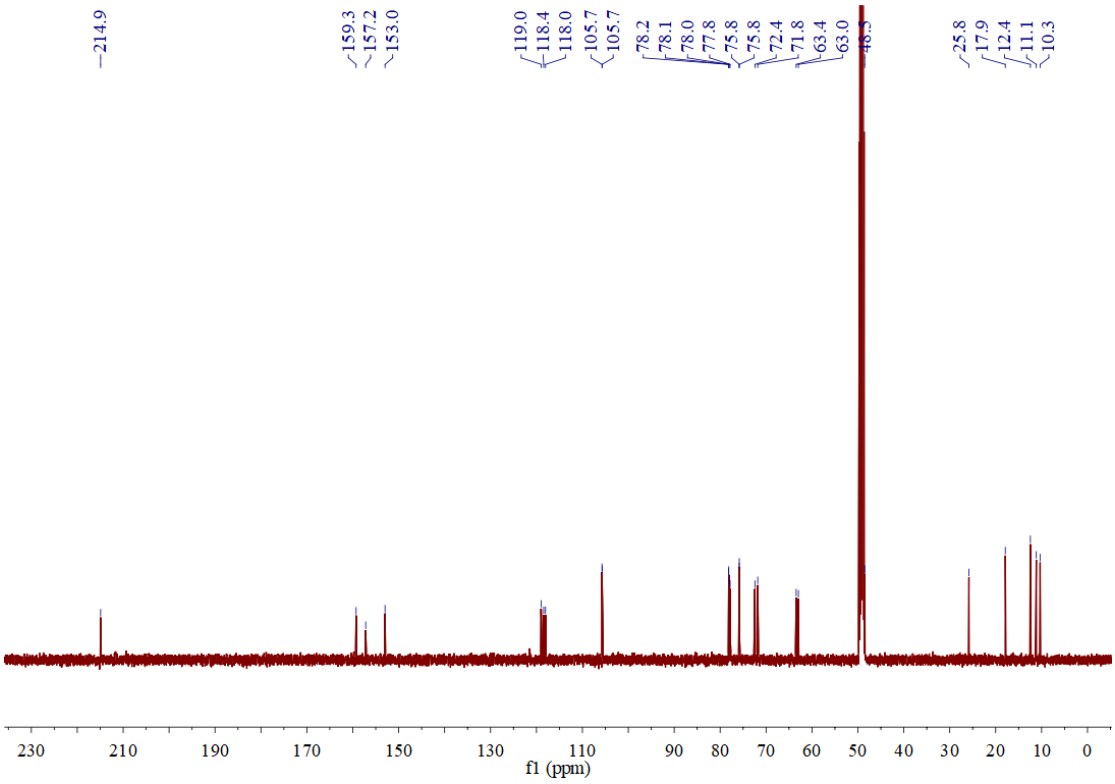


Figure S22. ^{13}C NMR Spectrum of Compound **2** in Methanol-d_4

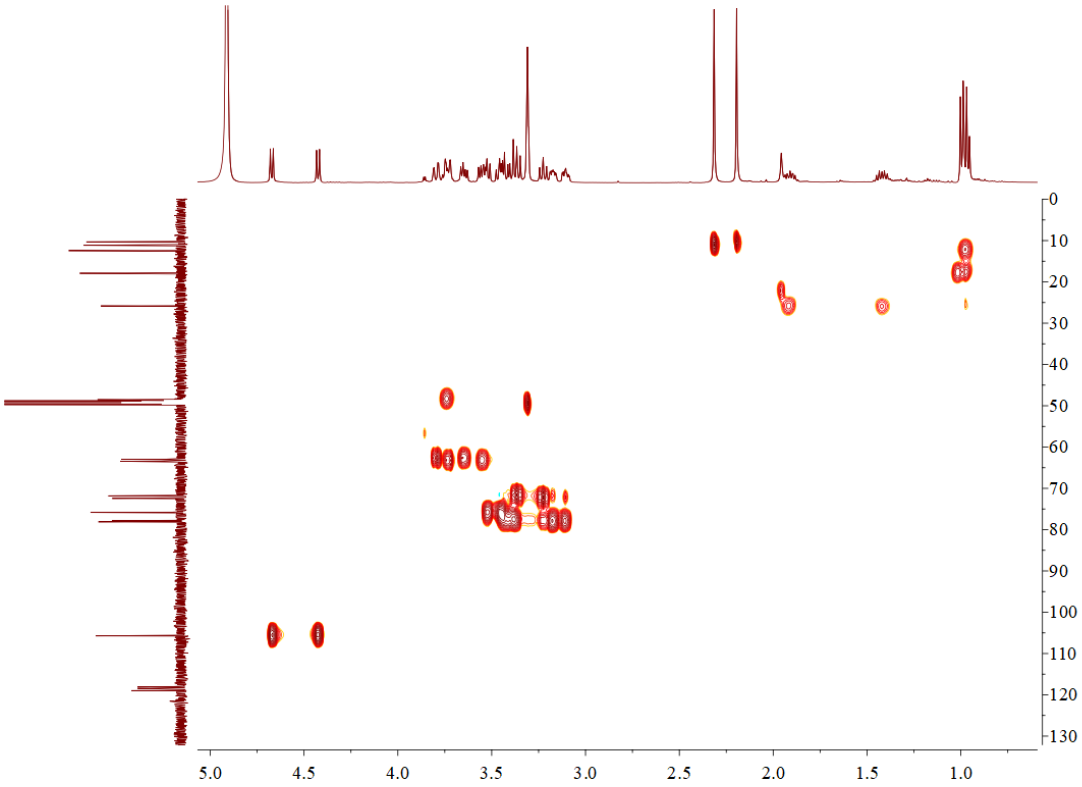


Figure S23. HSQC Spectrum of Compound **2** in Methanol-d_4

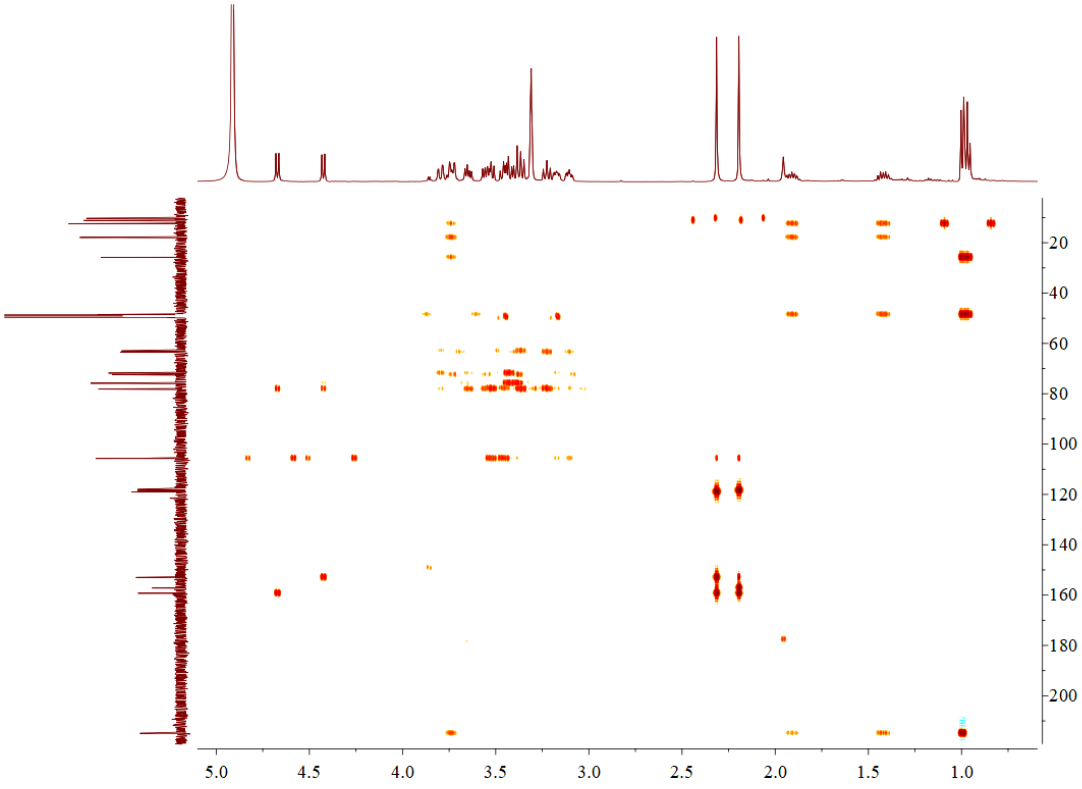


Figure S24. HMBC Spectrum of Compound **2** in Methanol-d_4

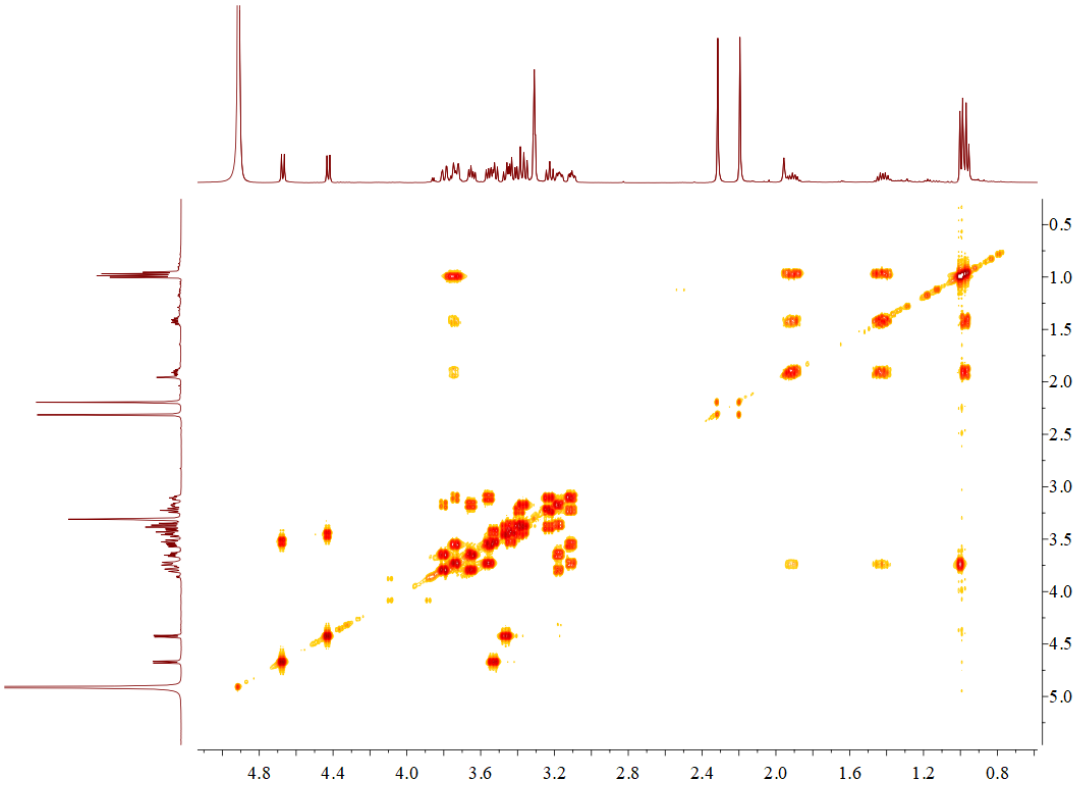


Figure S25. ^{1}H-^{1}H COSY Spectrum of Compound **2** in Methanol-d_4

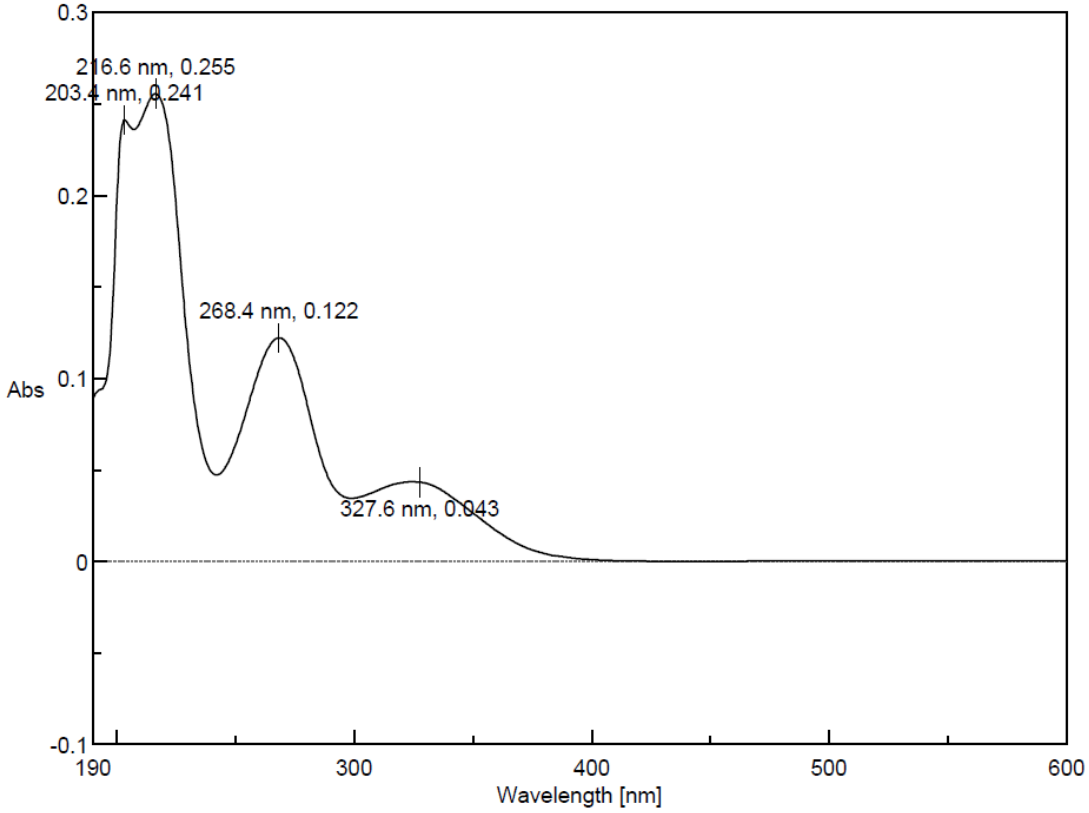


Figure S26. UV Spectrum of Compound **2** in Methanol

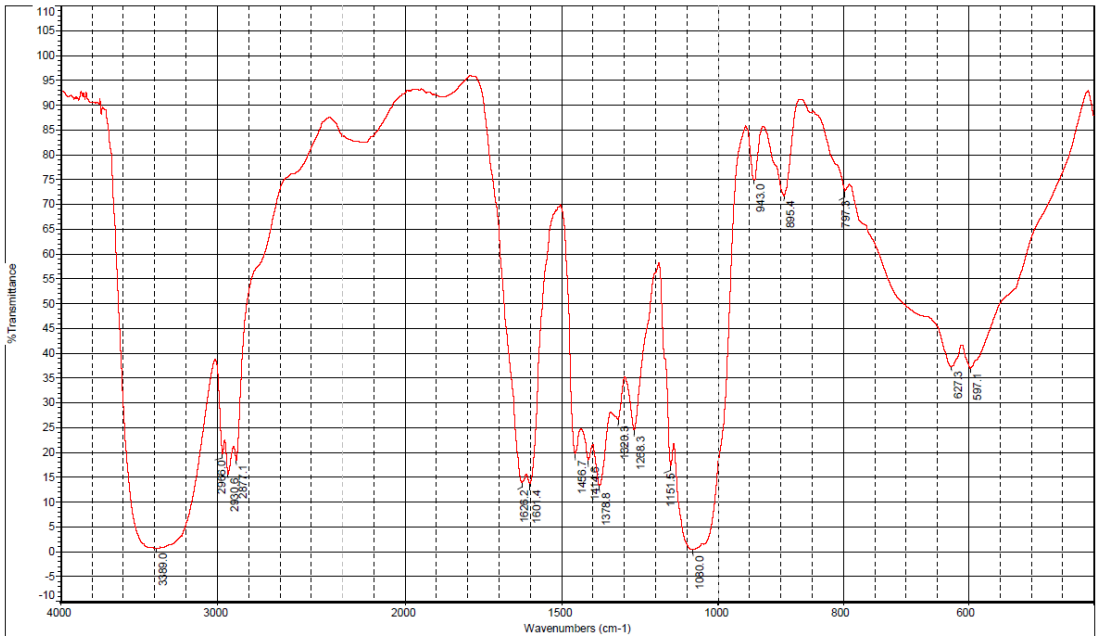


Figure S27. IR Spectrum of Compound **2**

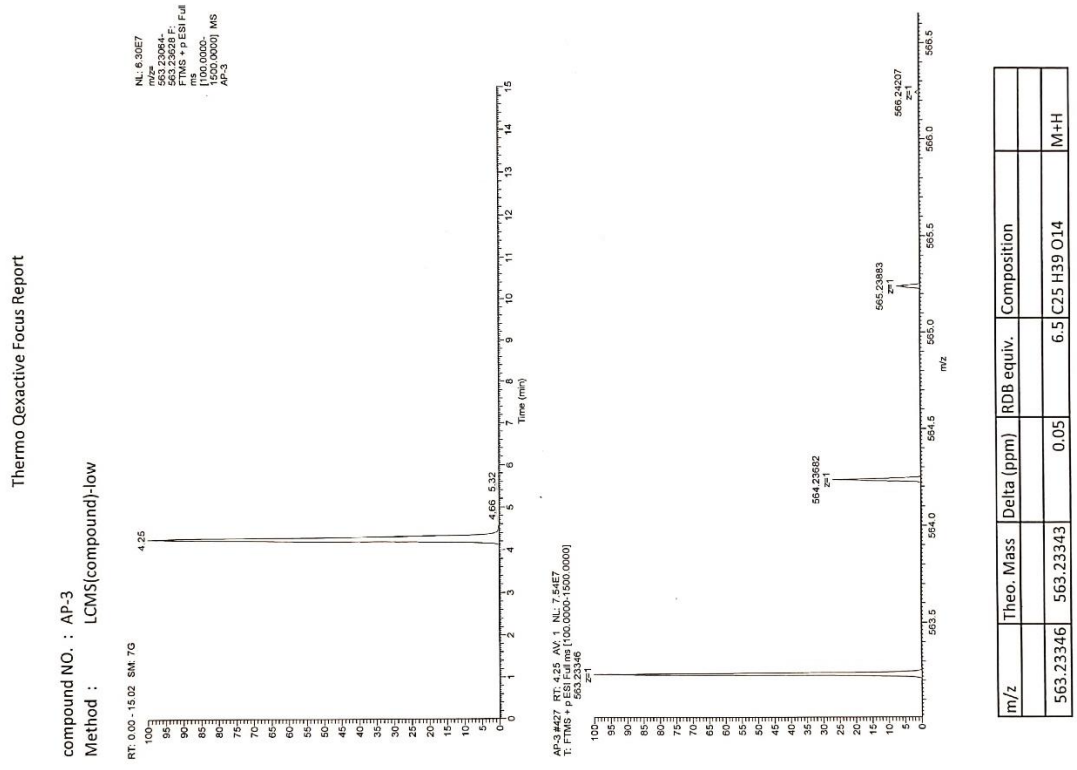


Figure S28. HRESIMS Spectrum of Compound **2**.

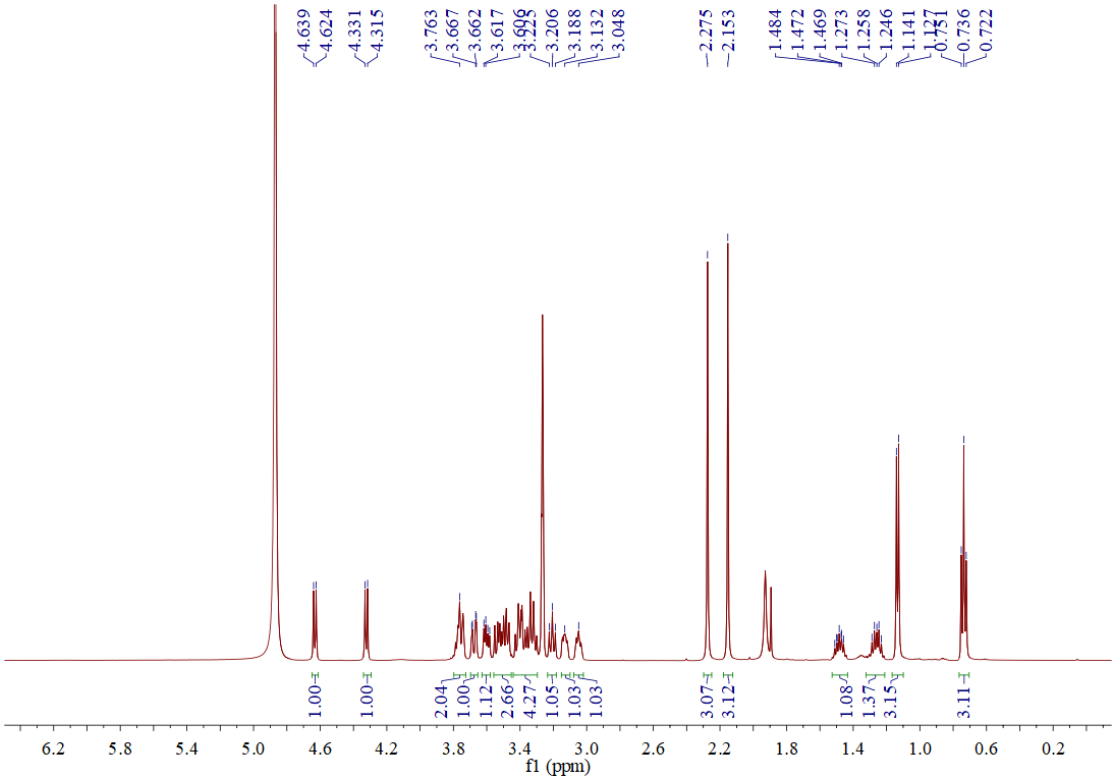


Figure S29. [1] H NMR Spectrum of Compound **3** in Methanol-d_4

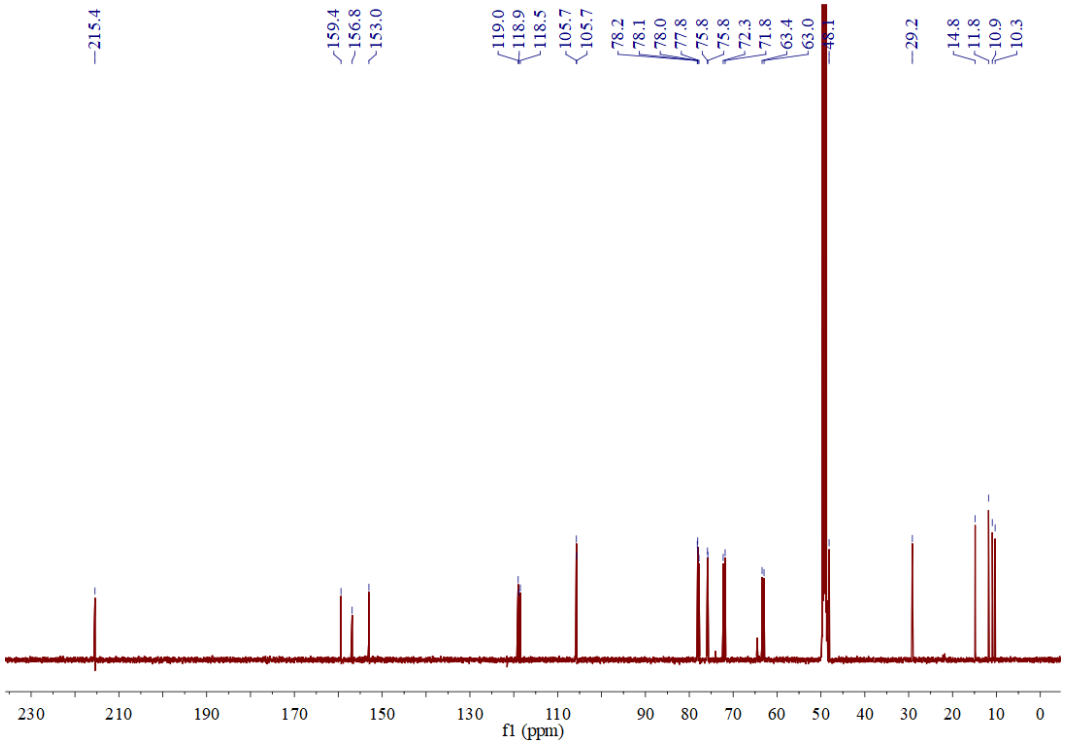


Figure S30. [13] C NMR Spectrum of Compound **3** in Methanol-d_4

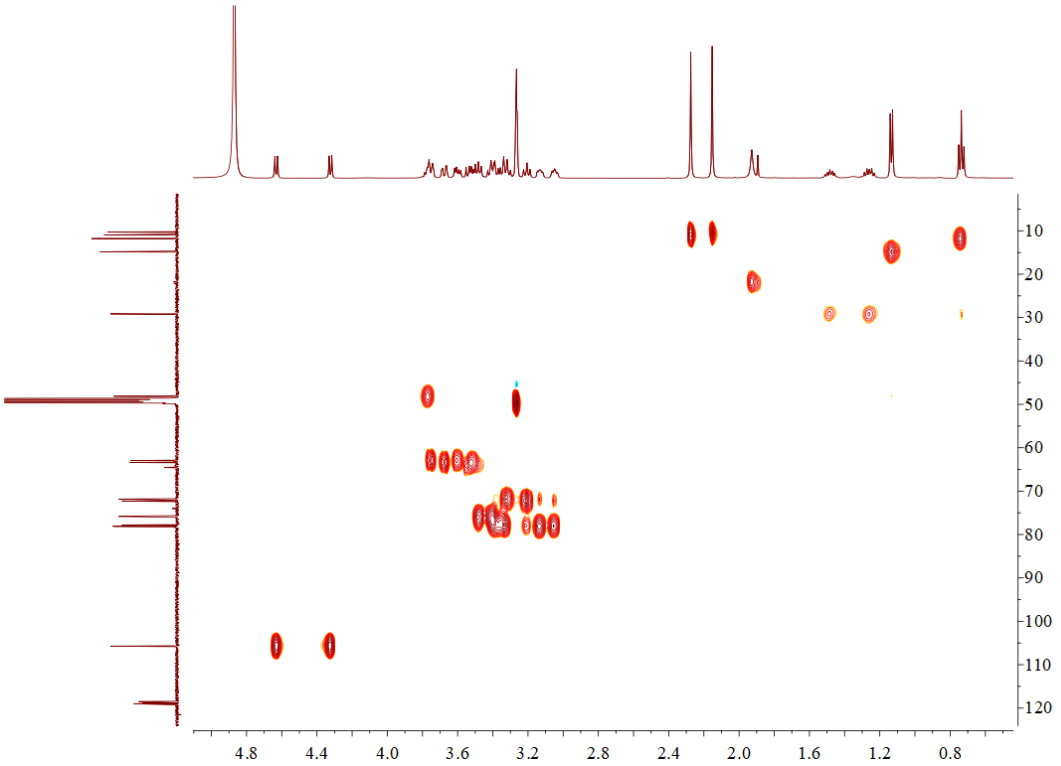


Figure S31. HSQC Spectrum of Compound **3** in Methanol-d_4

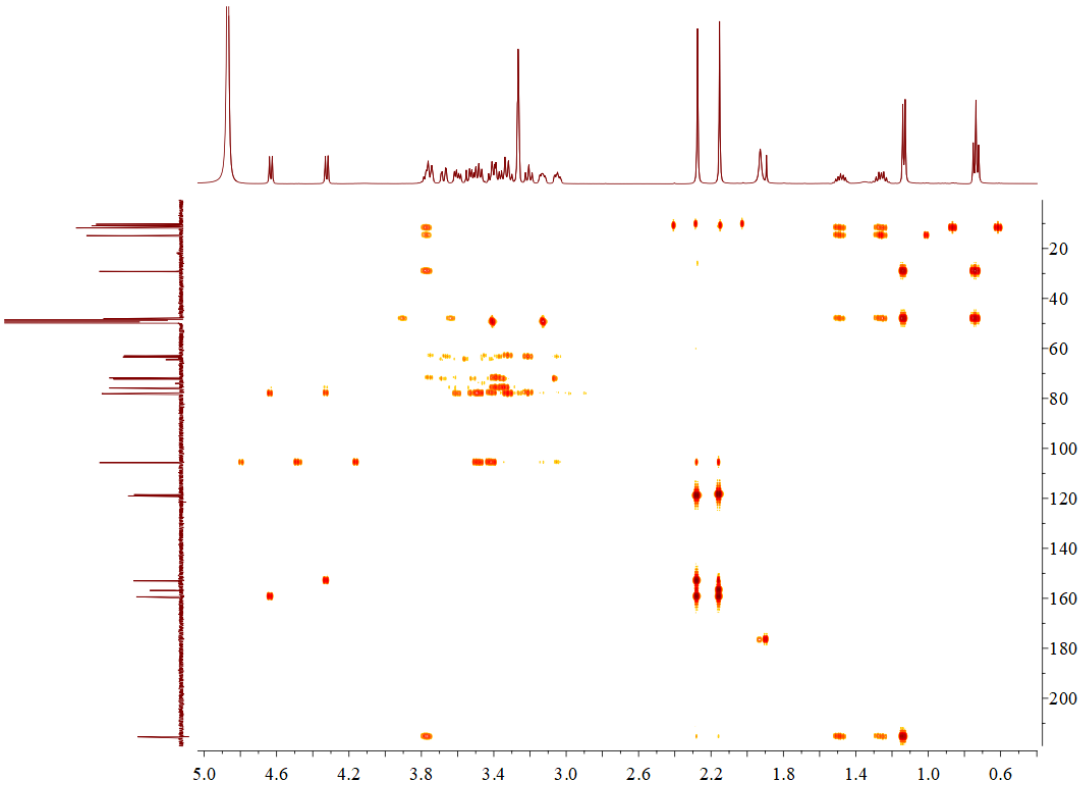


Figure S32. HMBC Spectrum of Compound **3** in Methanol-d_4

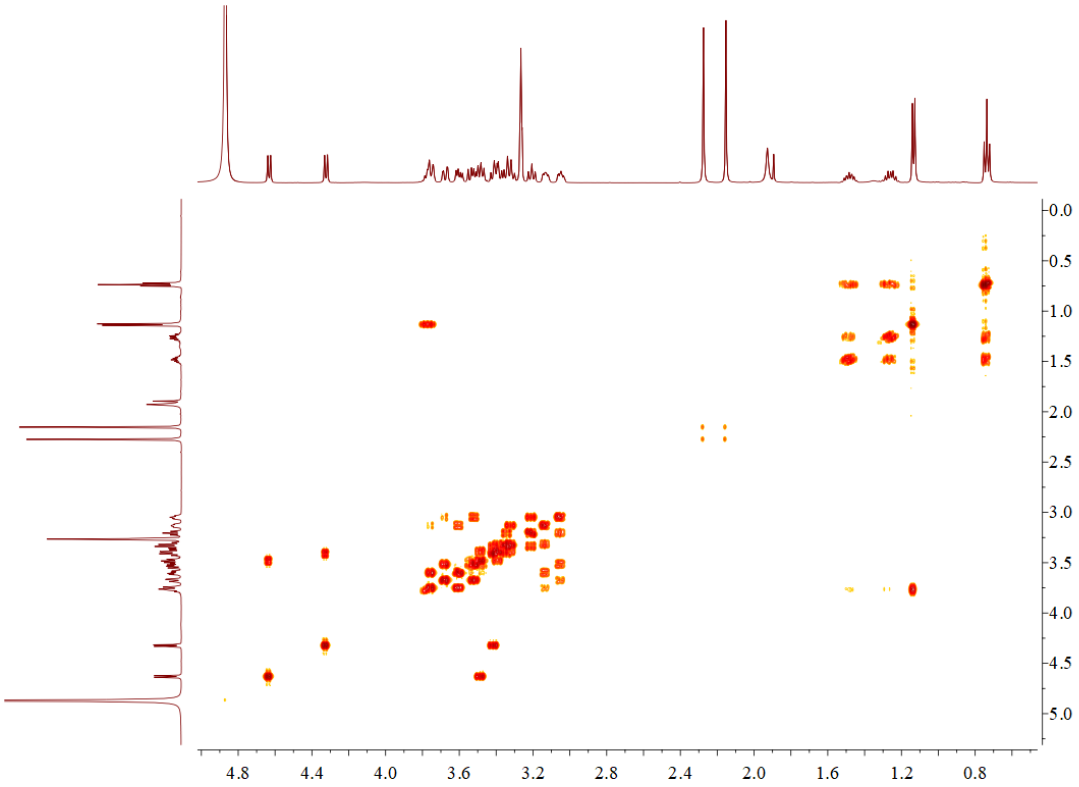


Figure S33. ^{1}H-^{1}H COSY Spectrum of Compound **3** in Methanol-d_4

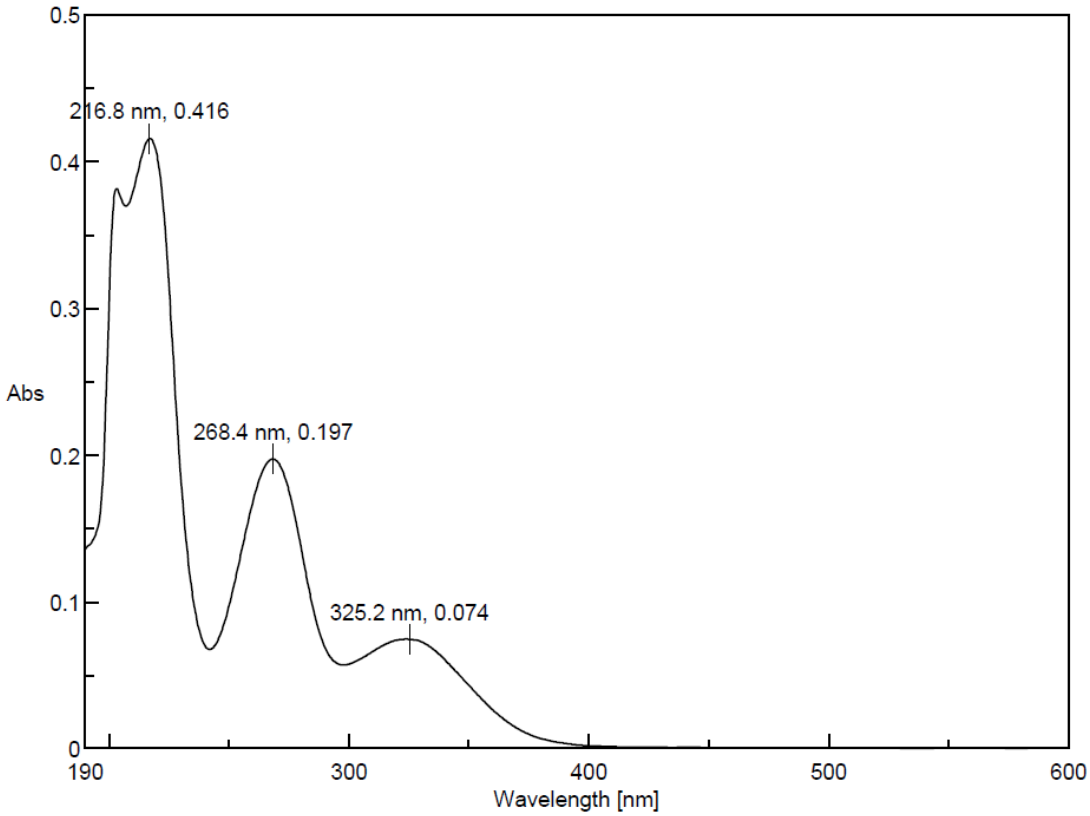


Figure S34. UV Spectrum of Compound **3** in Methanol

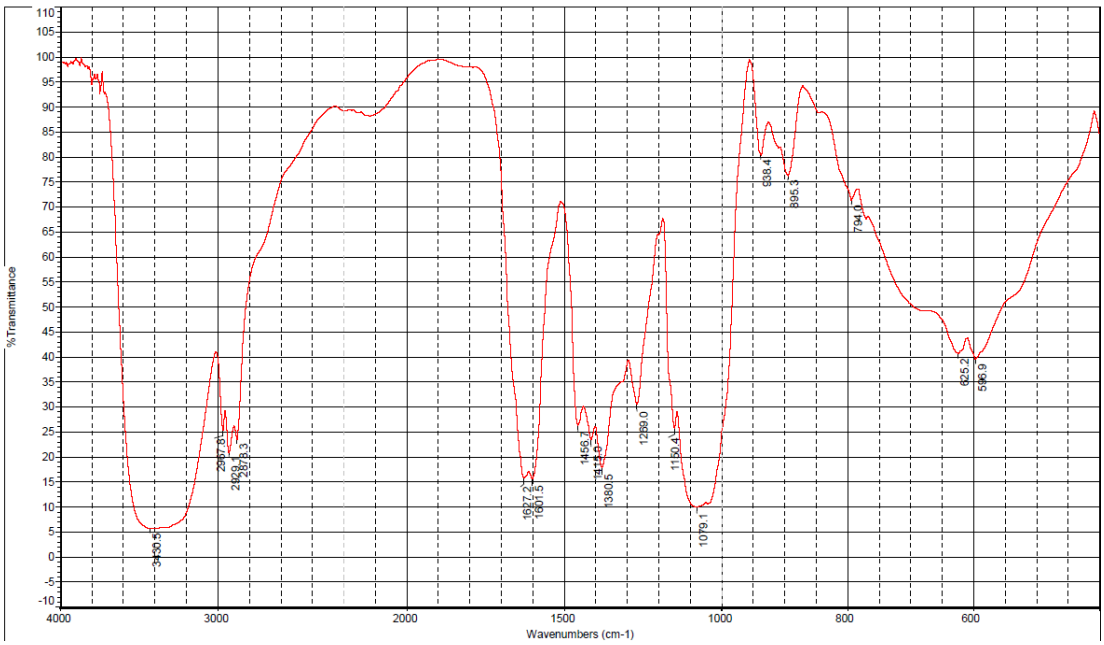
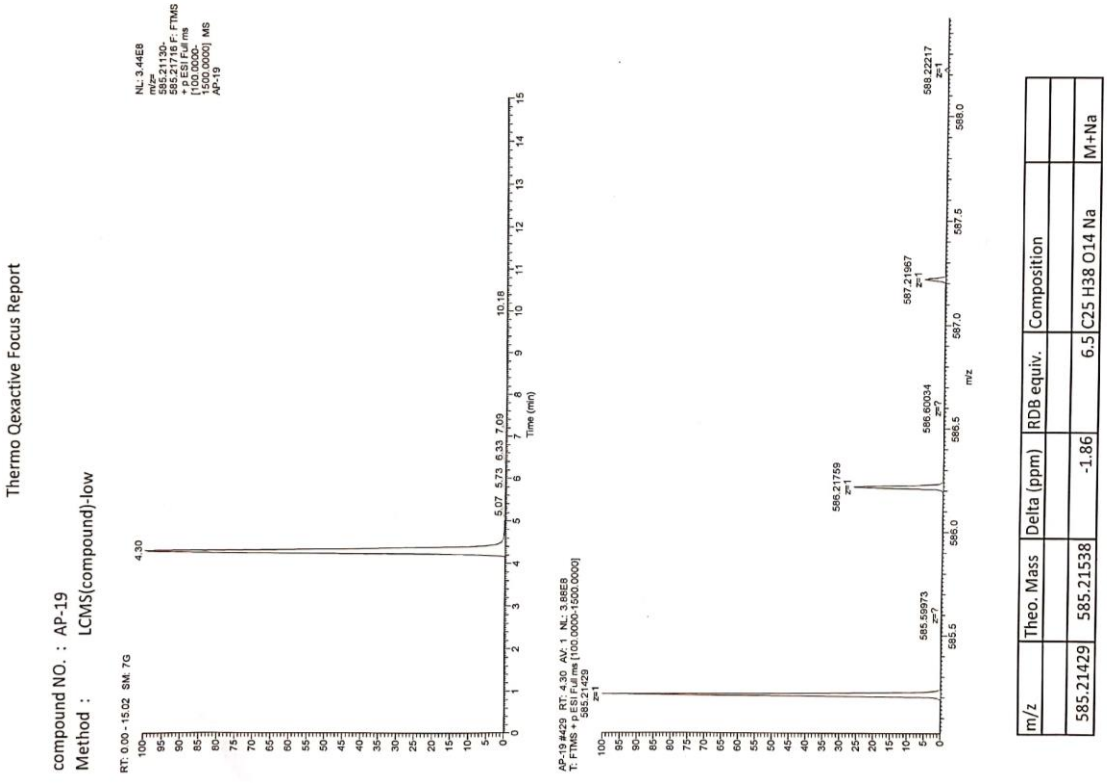


Figure S35. IR Spectrum of Compound **3**



m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition		
585.21429	585.21538	-1.86	6.5	C25 H38 O14 Na	M+Na	

Figure S36. HRESIMS Spectrum of Compound **3**.

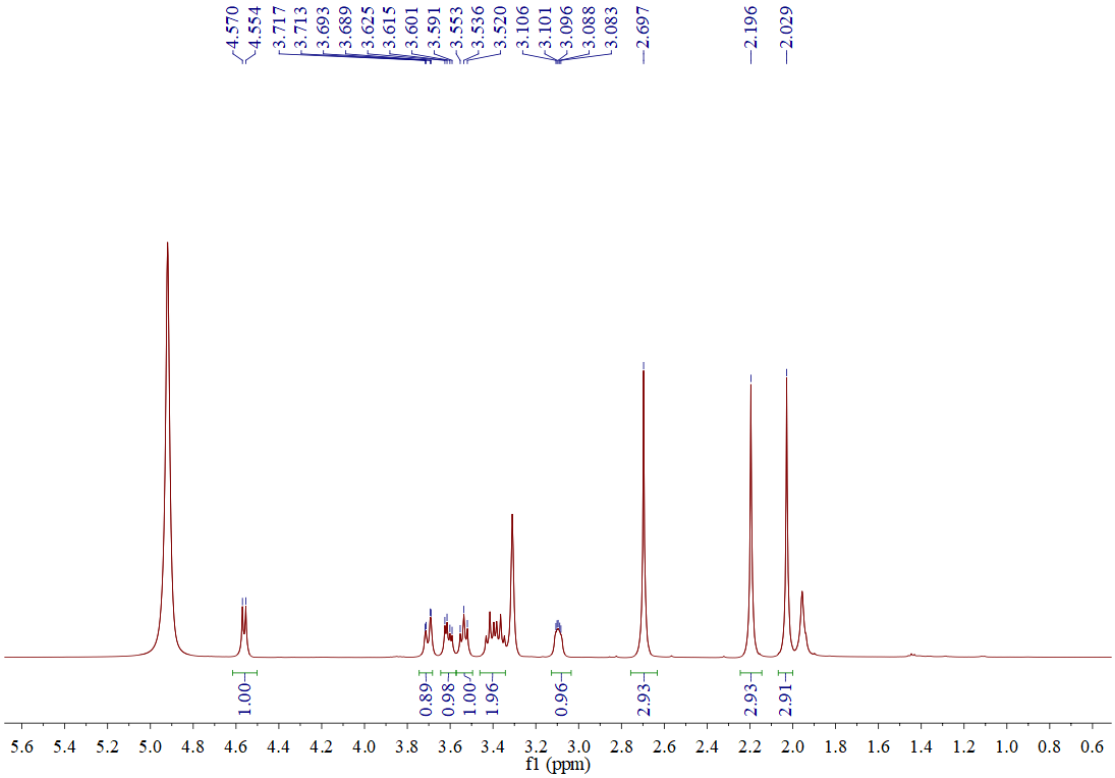


Figure S37. [1] H NMR Spectrum of Compound **6** in Methanol-d_4

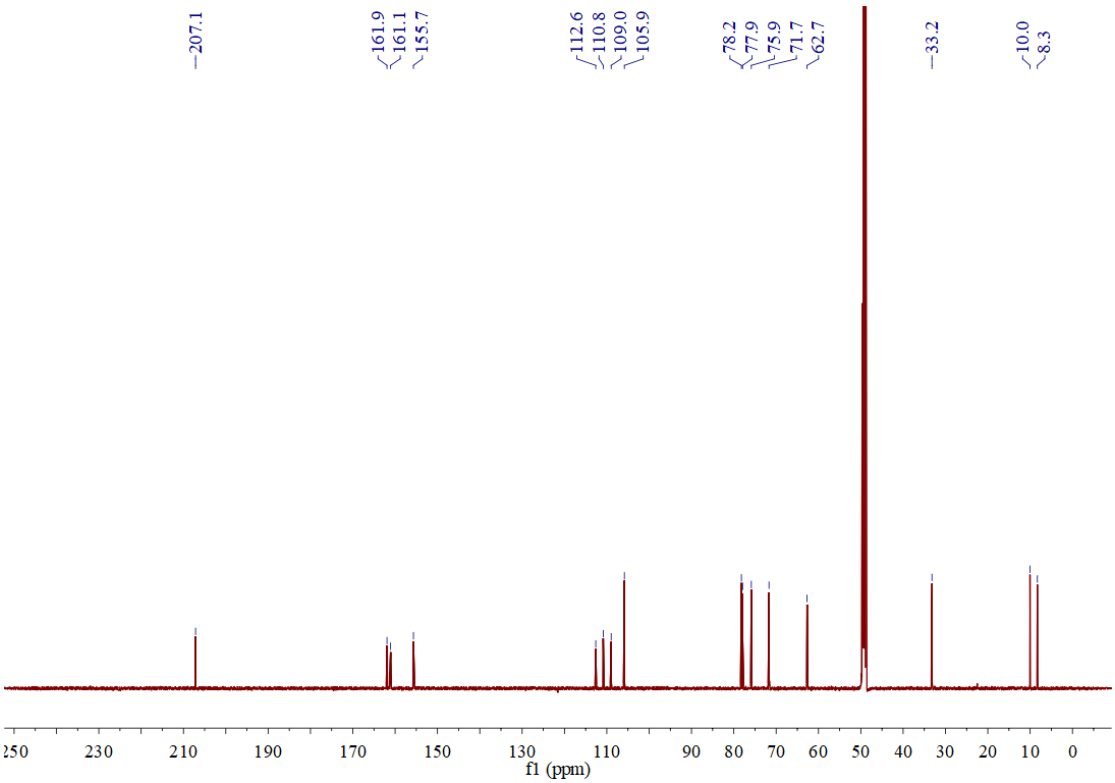


Figure S38. [13] C NMR Spectrum of Compound **6** in Methanol-d_4

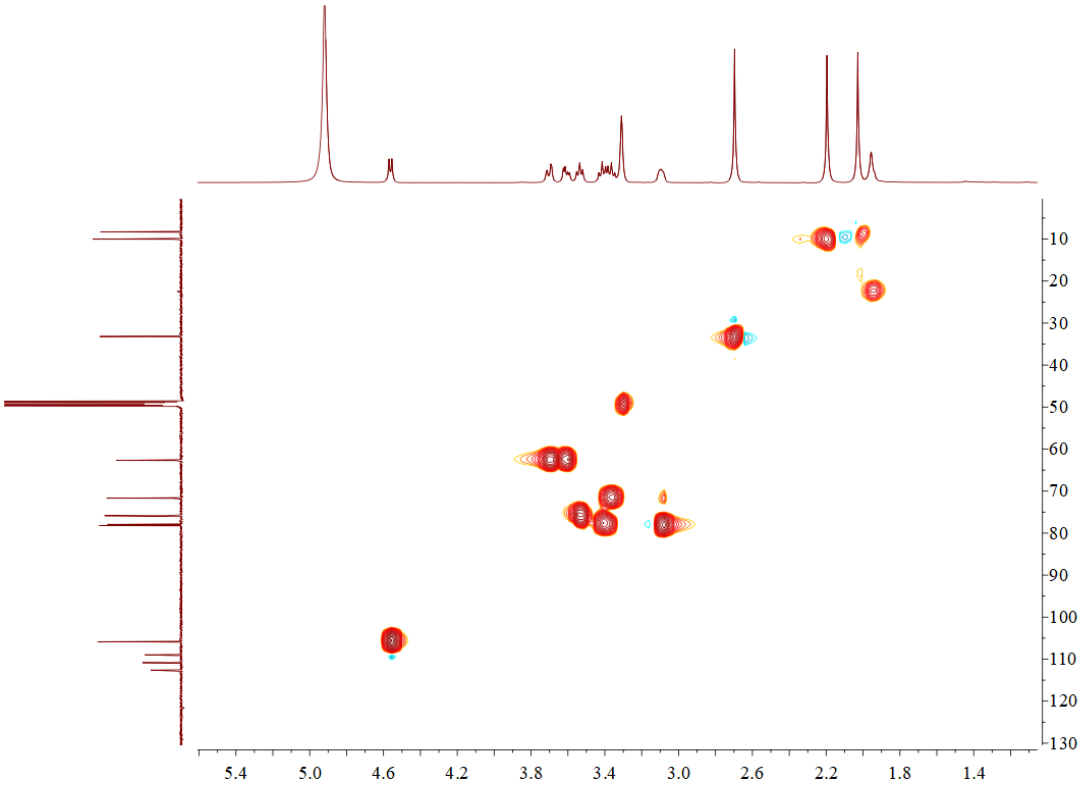


Figure S39. HSQC Spectrum of Compound **6** in Methanol-d_4

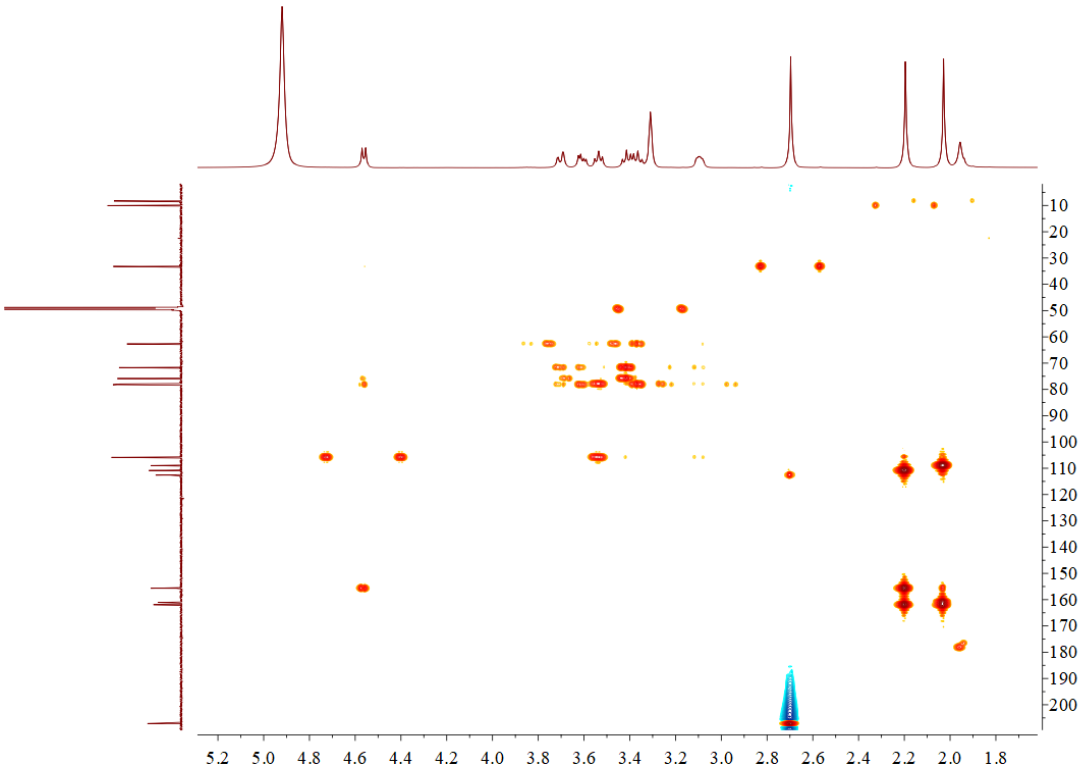


Figure S40. HMBC Spectrum of Compound **6** in Methanol-d_4

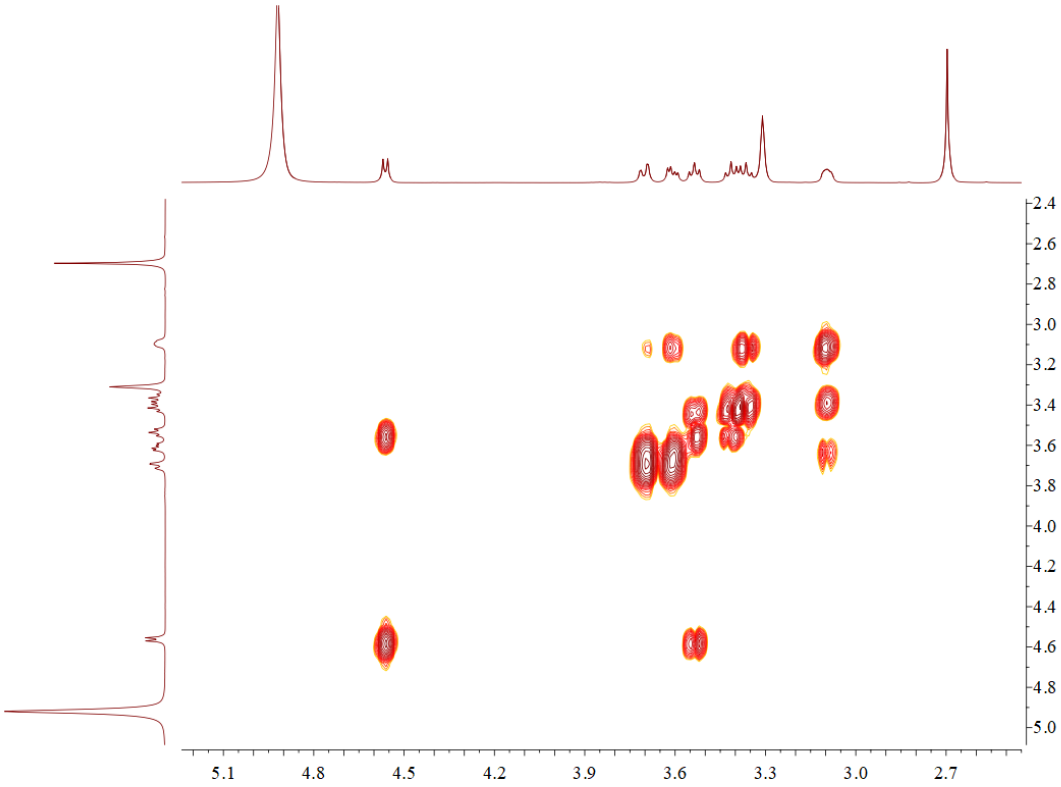


Figure S41. ^{1}H-^{1}H COSY Spectrum of Compound **6** in Methanol-d_4

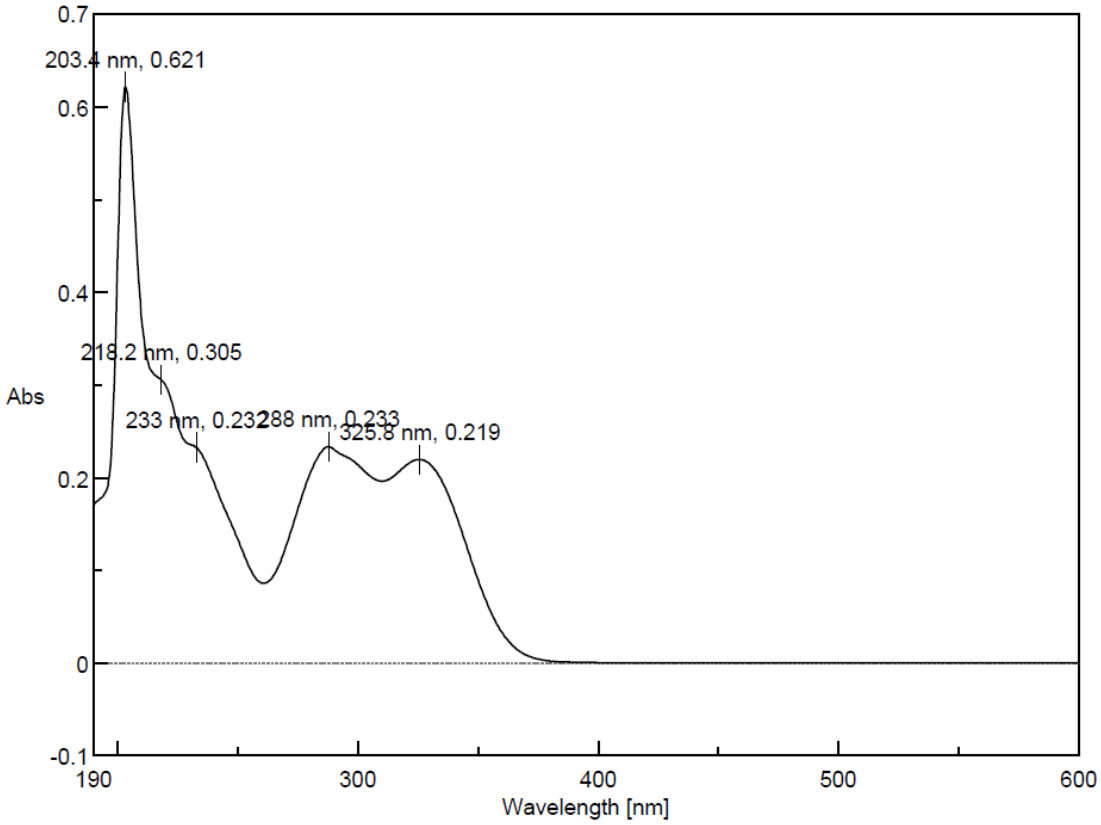


Figure S42. UV Spectrum of Compound **6** in Methanol

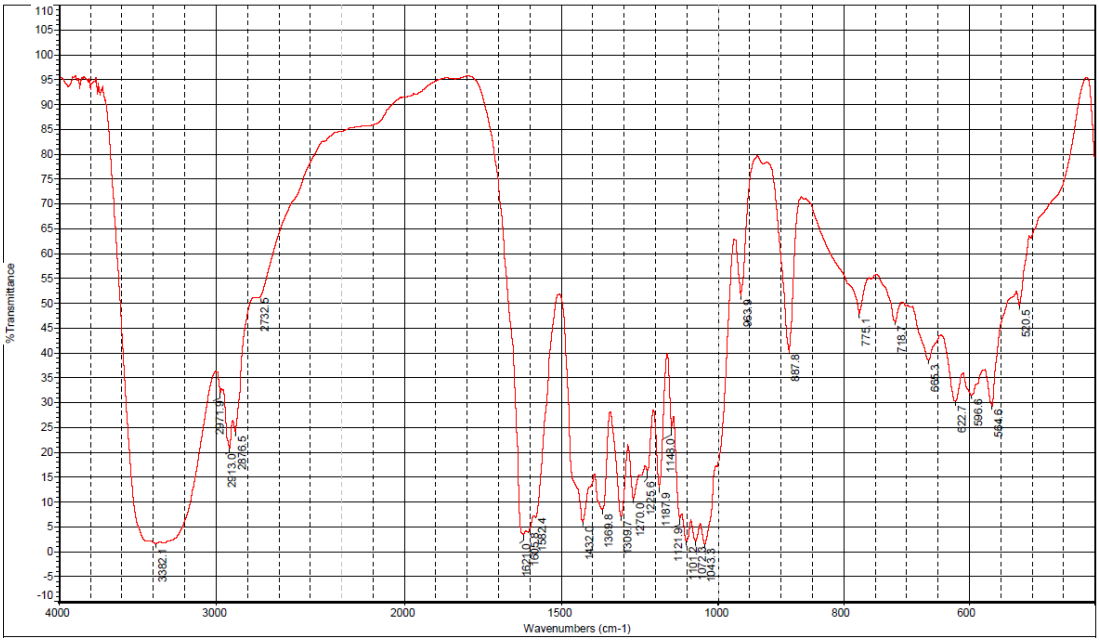
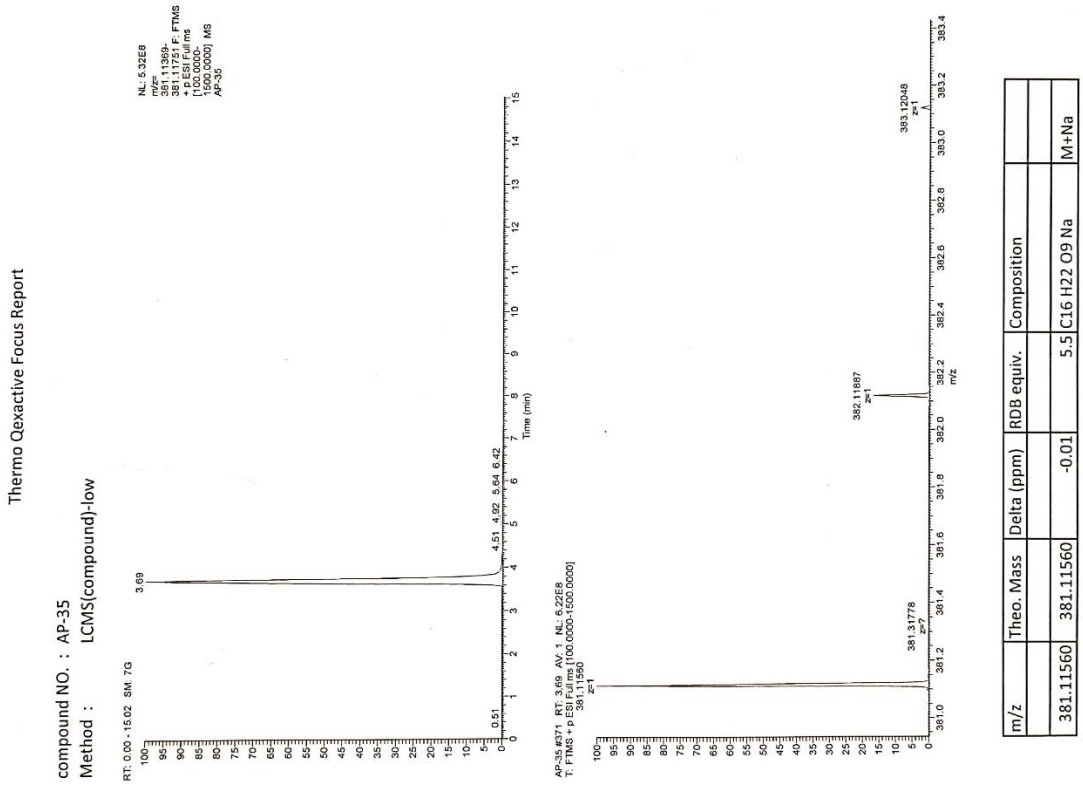


Figure S43. IR Spectrum of Compound **6**



m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition	
381.11560	381.11560	-0.01	5.5	C16 H22 O9 Na	M+Na

Figure S44. HRESIMS Spectrum of Compound **6**.