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Ganoapplins A and B with an unprecedented 6/6/6/5/6-fused pentacyclic skeleton from *Ganoderma* inhibit Tau pathology through activating autophagy

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ABSTRACT

Ganoapplins A and B (**1** and **2**) with a 6/6/6/5/6-fused pentacyclic skeleton containing an aromatic E ring, were obtained from *Ganoderma applanatum*. Their structures were established through extensive spectroscopic analyses, quantum chemical calculations, including calculated chemical shifts with DP4 + analysis and electronic circular dichroism (ECD). A plausible biosynthetic pathway for **1** and **2** was proposed. Furthermore, their roles in activating autophagy were investigated and the cellular assays showed that **1** and **2** can inhibit tau pathology by inducing autophagy, suggesting their potential against Alzheimer's disease (AD).

1. Introduction

In the Sheng Nong's herbal classic and Compendium of Materia Medica, *Ganoderma* has been recorded as the "xiancao", which can be used to prolong life-span, keep health, improve intelligence and memory [1]. In 2020, *Ganoderma* was registered in the "Homology list of medicine and food", suggesting that *Ganoderma* can be used as medicine and food to keep human health. *Ganoderma* triterpenoids (GTs) are a group of highly oxidative lanostane-type tetracyclic triterpenoids and considered as the main bioactive constituents of *Ganoderma* [2]. Our previous study reported a series of GTs with intriguing structures due to the multiple oxidation, cleavage, cyclization, and rearranged reactions. These GTs provides plentiful structural template for the discovery of bioactive candidates [3–9]. Based on the traditional efficacy of *Ganoderma*, GTs have been found to have potential against Alzheimer's disease by alleviating neuroinflammation, reducing neuronal apoptosis [1,10,11] and improving mitochondrial dysfunction [1].

Alzheimer's disease (AD), the most common neurodegenerative disorder, affects about 4 %-8% of the elderly population worldwide [12]. The main clinical features of AD are memory loss and cognitive dysfunction due to the loss of neurons in the brain [13]. Two hallmarks of AD pathology are the presence of extracellular senile plaques primarily composed of amyloid beta (Aβ), and the intraneuronal neurofibrillary tangles (NFTs). The main constituent of NFTs is the aggregated microtubule associated protein Tau (MAPT/tau) protein [13–15]. While the aetiologias of AD are not fully understood, the elimination of Aβ and/or MAPT/tau aggregates is one of the most promising therapeutic strategies for this disease.

Macroautophagy (hereafter referred to as autophagy) is the main route to remove Aβ and MAPT/tau aggregates [16]. Autophagy is a major cellular pathway by which unwanted protein material aggregated in intracellular autophagosomes, which are then degraded in lysosomes [17]. Autophagy dysfunction has been implicated in the pathogenesis of many neurodegenerative diseases including AD [16–23]. The requirement of autophagy activation in memory formation [24] further underscores the critical importance of its regulation for brain function.

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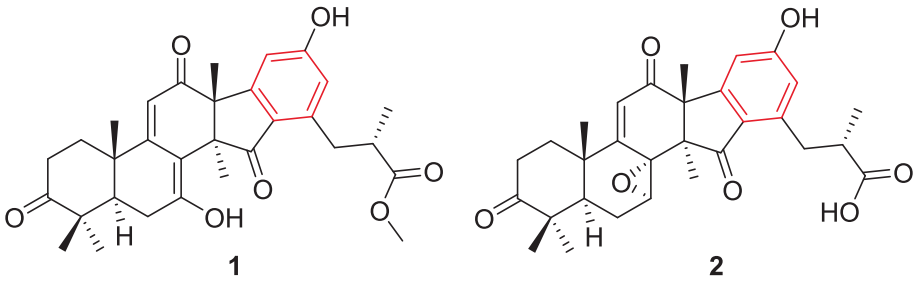


Fig. 1. Structures of compounds **1** and **2**.

Therefore, induction of autophagy may serve as a viable therapeutic target for the treatment of AD [23,25,26].

In order to find more structurally diverse GTs, we deeply investigated triterpenoids part of the fruiting bodies of *Ganoderma applanatum* and two novel GTs with a 6/6/6/5/6-fused skeleton containing a rare aromatic E ring, were isolated (Fig. 1). Furthermore, their inhibition of Tau protein by activating autophagy was evaluated.

2. Materials and methods

2.1. General

Silica gel ((200–300) mesh, Qingdao Marine Chemical, Inc.), Lichroprep RP-18 (40–63 μm, Fuji) and Sephadex LH-20 (20–150 μm, Pharmacia) were used for column chromatography. Methanol, chloroform, ethyl acetate, acetone, petroleum ether, *n*-hexane and 2-propanol were purchased from Tianjing Chemical Reagents Co. (Tianjing, China). Shimadzu UV-2401PC spectrometer was for Ultraviolet (UV) spectra. Horiba SEPA-300 polarimeter was for optical rotations. Chirascan instrument was for CD spectra; Bruker AV-600 MHz (Bruker, Zurich, Switzerland) was for Nuclear magnetic resonance (NMR) spectra and tetramethyl chlorosilane (TMS) was as internal standard for chemical shifts. Electrospray Ionization Mass Spectrometry (ESIMS) and HRTOF-ESIMS were recorded by API QSTAR Pulsar spectrometer. Bruker Tensor-27 instrument by using KBr pellets was used for IR. An Agilent 1100 series instrument equipped with an Agilent ZORBAX SB-C18 column (5 μm, 9.6 mm × 250 mm) was used for high-performance liquid chromatography (HPLC) separation.

2.2. Fungal materials

Ganoderma applanatum (39 kg) were purchased in December 2019 from Traditional Chinese Medicine Market in Kunming, Yunnan, China, which was identified by Prof. Yang Zhuliang, Kunming Institute of Botany, Chinese Academy of Science (voucher No. 19122201).

2.3. Extraction and isolation

G. applanatum samples (39 kg) were extracted by our previous method [27]. In brief, samples were chipped and extracted with 95 % ethanol (EtOH) (80 L × 3) under reflux three times (three hours per time). The combined ethanol extracts were evaporated under reduced pressure. The residue (1.2 kg) was suspended in H_2O and extracted with ethyl acetate (EtOAc). The volume of the combined EtOAc extracts (835 g) was reduced to one-third under reduced pressure. The residue was fractionated by macroporous resin (D-101; MeOH − H_2O, 50:50, 70:30 and 90:10, v/v): fractions I − III. Fraction III (158 g) was further fractioned by silica gel column with $CHCl_3$-MeOH as the mobile phase and gave ten subfractions (Fr. III-1 → Fr. III-10). Fr. III-9 (22 g) was further treated by Rp-18 column (MeOH-H_2O = 35 %→100 %, v/v) to afford five subfractions. Furthermore, Fr. III-9–2 (3.2 g) was separated by LH-20 column (MeOH) to give four parts (2a-2d). Then, Fr. III-9-2b (42 mg) was treated and purified by semi-preparative HPLC (CH_3CN-H_2O = 47 % containing 0.1 % CF_3COOH, v/v, flow rate: 3 mL/min) to yield compound **2** (10 mg, t_R = 25.6 min). Similarly, Fr. III-9–5 (4.2 g) was treated by LH-20 and Fr. III-9-5b (12 mg) was purified using semi-preparative HPLC (CH_3CN-H_2O = 45 %, v/v, flow rate: 3 mL/min) to obtain compound **1** (1.4 mg, t_R = 21.7 min).

Table 1
^{1}H and ^{13}C-DEPT NMR spectroscopic data of **1** and **2**. (δ in *ppm*, *J* in Hz).

Position	**1**[a]		**2**[b]	
	δ_H mult. (*J*)	δ_C, type	δ_H mult. (*J*)	δ_C, type
1	1.87, m; 2.30, m	36.0 CH_2	2.10, m; 2.76, m	36.8 CH_2
2	2.45, m; 2.81, m	34.2 CH_2	2.47, m	34.6 CH_2
3		214.5 C		219.3 C
4		47.1 C		47.2 C
5	1.86, overlapped	49.1 CH	2.85, m	42.3 CH
6	2.34, dd (17.2, 3.6)	28.7 CH_2	1.92, dd (14.8, 12.8)	23.6 CH_2
	2.61, dd (17.2, 13.1)		2.24, m	
7		164.7 C	4.75, d (3.7)	60.1 CH
8		106.9 C		63.7 C
9		167.5 C		167.3 C
10		38.0 C		41.7 C
11	5.55, s	111.3 C	6.25, s	131.3 C
12		199.3 C		199.6 C
13		53.6 C		57.3 C
14		61.1 C		55.7 C
15		208.1 C		202.4 C
16		121.7 C		124.5 C
17		158.4 C		157.8 C
18	1.39, s	32.4 CH_3	1.48, s	31.5 CH_3
19	1.38, s	21.3 CH_3	1.25, s	24.3 CH_3
20		163.9 C		164.3 C
21	7.44, d (2.0)	111.5 CH	7.22, d (2.2)	111.9 CH
22	6.58, d (2.0)	117.5 CH	6.58, d (2.2)	117.9 CH
23		145.0 C		145.0 C
24	3.05, dd (13.0, 8.0)	35.7 CH_2	2.96, dd (12.9, 7.8)	36.5 CH_2
	3.22, dd (13.0, 7.3)		3.14, dd (12.9, 7.2)	
25	2.76, dd (14.6, 7.3)	40.3 CH	2.66, dd (14.9, 6.6)	41.8 CH
26	1.17, d (6.7)	17.0 CH_3	1.11, d (6.6)	17.5 CH_3
27		176.4 C		179.6 C
28	1.15, s	25.0 CH_3	1.10, s	29.3 CH_3
29	1.19, s	22.1 CH_3	1.10, s	22.0 CH_3
30	1.34, s	27.8 CH_3	1.26, s	24.3 CH_3
OMe	3.59, s	51.6 CH_3		
7-OH	12.80, s			

[a]: $CDCl_3$; [b]:CD_3OD; 600/150 MHz

*Ganoapplin A (**1**)*: White powder (MeOH); $[\alpha]_D^{20.3}$ 346.29 (c 0.14, MeOH); CD (MeOH) Δε 339 + 16.49, Δε 298 + 9.91, Δε 234 + 14.63; UV (MeOH) λ^{max} (log ε): 203 (4.18), 235 (4.05), 304 (4.12), and 336 (3.78); IR (KBr) ν_{max}: 3433, 2963, 2931, 1683, 1638, 1453, 1384, 1209, and 1142 cm^{-1}; ^{1}H NMR and ^{13}C NMR data: see Table 1; HRMS (ESI-TOF) *m/z*: 521.2533 $[M + H]^+$ (calcd for $C_{31}H_{36}O_7$, 521.2533).

*Ganoapplin B (**2**)*: White powder (MeOH); $[\alpha]_D^{28}$ 295.73 (c 0.156, MeOH); CD (MeOH) Δε 298 + 6.64, Δε 257 + 32.47, Δε 249 + 30.63; UV (MeOH) λ^{max} (log ε): 253 (4.04), 234 (4.15), and 196 (4.23); IR (KBr) ν_{max}: 3435, 2956, 2929, 1680, 1625, 1443, 1376, 1206, and 1138 cm^{-1}; ^{1}H NMR and ^{13}C NMR data: see Table 1; HRMS (ESI-TOF) *m/z*: 505.2239 [M - H]- (calcd for $C_{30}H_{34}O_7$, 505.2232).

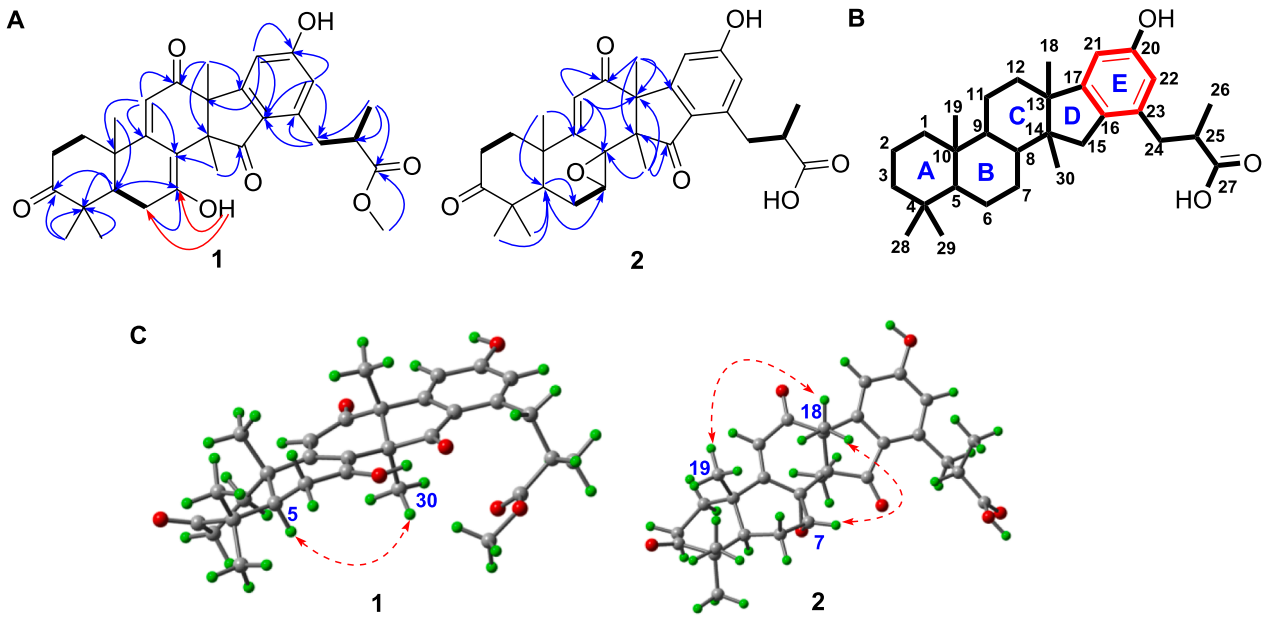


Fig. 2. (A) Selected HMBC correlations and $^{1}H–^{1}H$ COSY correlations of **1** and **2**. (B) the skeleton of **1** and **2**. (C) the key ROESY correlations of **1** and **2**.

2.4. NMR and ECD calculations for *1* and *2*

The NMR and ECD calculations of compounds **1** and **2** were performed using Gaussian 09 [28,29]. The detailed methodological description is shown in supporting information.

2.5. Cell culture and treatment

The SH-SY5Y mCherry-GFP-LC3 and SH-SY5Y MAPT cells were created at Kunming Institute of Zoology, Chinese Academy of Science. The SH-SY5Y, SH-SY5Y mCherry-GFP-LC3 and SH-SY5Y MAPT cells were maintained in Dulbecco's Modified Eagle Medium (DMEM) supplemented with 10 % fetal bovine serum (FBS), 1 × MEM nonessential amino acid solution (Gibco, 11140050), 100 U/ml penicillin and 100 mg/ml streptomycin at 37 °C in a humidified atmosphere incubator with 5 % CO_2 and 95 % humidity, as described in our previous studies [19]. Cells were seeded in pre-warmed growth medium in 6-well plates. Chemicals were applied directly to the culture medium for treatment, and cells were harvested at 24 h after treatment.

2.6. Construction of SH-SY5Y cells with stable expression of the mutant MAPT (p.P301S) gene (SH-SY5Y MAPT Cells)

The coding sequences (CDS) region of the *MAPT* gene with mCherry tag was cloned into PLVX vector of the Lenti-X Tet-On Advanced Inducible Expression System (Clontech). Mutations MAPT-p.P301S was introduced into PLVX-MAPT vector, by using site-directed mutagenesis PCR method. The SH-SY5Y cells were maintained in DMEM (Gibco, USA, 11965) supplemented with 10 % FBS (Gibco, USA, 11875), 1 × MEM nonessential amino acid solution (Gibco, 11140050), 100 U/ml penicillin and 100 mg/ml streptomycin at 37 °C in a humidified atmosphere incubator with 5 % CO_2. HEK293T cells were cultured in DMEM containing 10 % heat inactivated FBS. SH-SY5Y cells with stable expression of the mutant MAPT (P301S) was constructed according to the instruction of Lenti-X Tet-On Advanced Inducible Expression System (Clontech). In brief, the response lentivirus system was composed of mutant PLVX-MAPT P301S construct, packaging plasmid psPAX2 (Addgene, England, 12260) and envelope plasmid PMD2.G (Addgene, England, 12259), while the regulator lentivirus system was composed of PLVX-Tet-On-Advanced vector, psPAX2 and PMD2.G. The lentivirus supernatant was produced from HEK293T cells and was used to infect SH-SY5Y cells with the ratio of 4:1 for the response lentivirus and the regulator lentivirus. Cells were selected in growth medium with 500 μg/mL puromycin.

2.7. Western blot analysis

The analysis of target proteins was described as our previous studies [26,30,31]. In brief, cell lysates of the SH-SY5Y and SH-SY5Y MAPT cells were prepared using the protein lysis buffer (Beyotime Institute of Biotechnology, P0013). Protein concentration was determined using the BCA protein assay kit (Beyotime Institute of Biotechnology, P0012). A total of 20 μg protein was separated by 12 % sodium dodecyl sulfate polyacrylamide gel electrophoresis, and was transferred to a polyvinylidene difluoride membrane (Bio-Rad, L1620177 Rev D). The membrane was soaked with 5 % (w: v) skim milk for 2 h at room temperature. The membrane was incubated with primary antibodies (GAPDH, glyceraldehyde-3-phosphate dehydrogenase [Proteintech, 60004–1-Ig]; LC3 [Proteintech, 14600–1-AP]; SQSTM1, sequestosome 1 [Elabscience, EAP3350] and Tau (D1M9X) [Cell Signaling Technology, 46687S]) overnight at 4 °C. The membranes were washed 3 times with TBST (Tris-buffered saline [Cell Signaling Technology, 9997] with Tween 20 [0.1 %; Sigma, P1379]), each time 5 min, followed by incubation with the peroxidase-conjugated anti-mouse (474–1806) or anti-rabbit (474–1516) IgG (1:5000; KPL) for 1 h at room temperature. The epitope was visualized using an ECL Western blot detection kit (Millipore, WBKLS0500). ImageJ software (National Institutes of Health, Bethesda, Maryland, USA) was used to evaluate the densitometry. GAPDH was used as a loading control for quantifying the densitometry of target protein.

2.8. Tandem mCherry-GFP fluorescence microscopy

A tandem monomeric mCherry-GFP-tagged LC3 (mCherry-GFP-LC3) lentivirus (HANBI, 34082725) was used to monitor autophagy flux as previously reported [32]. The mCherry-GFP-LC3 lentivirus was used to infect SH-SY5Y cells according to the manufacturer's protocol. Cells were selected in growth medium with 500 μg/mL puromycin to get the SH-SY5Y cells with stable expression of mCherry-GFP-LC3 (SY-SY5Y mCherry-GFP-LC3 cells). The SY-SY5Y mCherry-GFP-LC3 cells were cultured in DMEM supplemented with 10 % FBS, 1 × MEM nonessential amino acid solution (Gibco, 11140050), 100 U/ml penicillin and 100

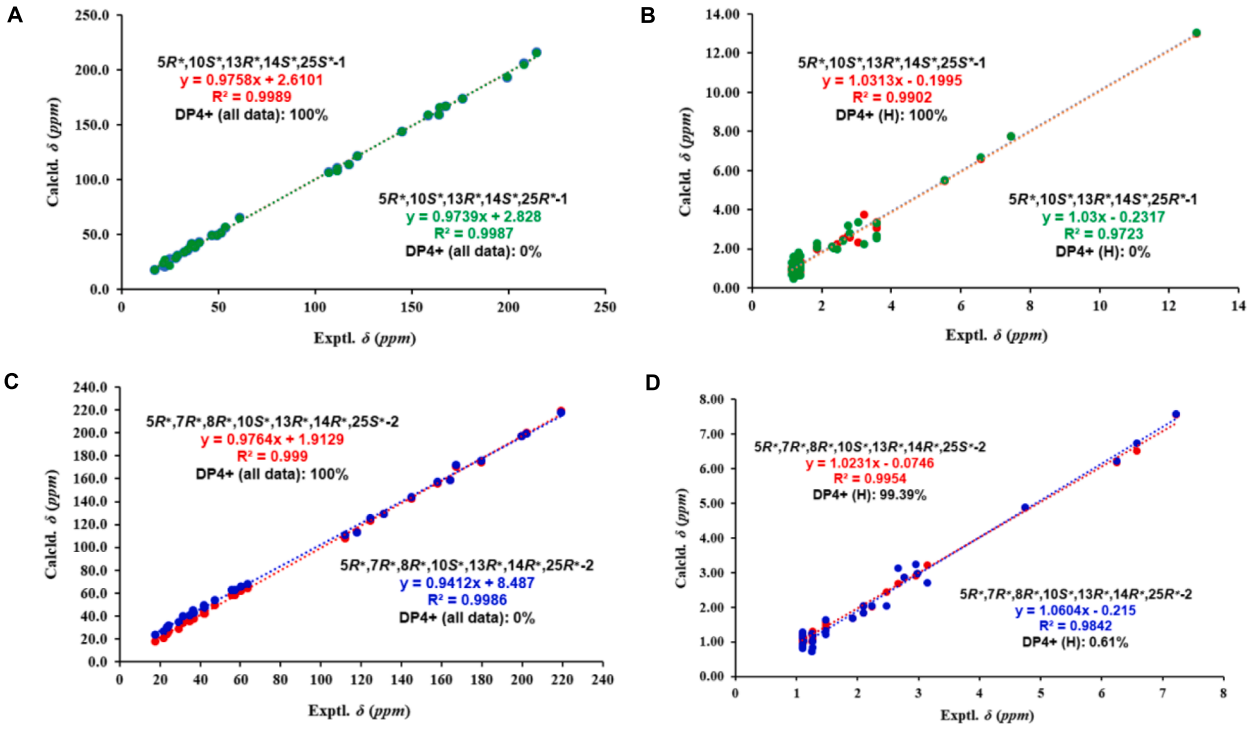


Fig. 3. (A) Regression analysis of experimental versus calculated ^{13}C and (B) ^{1}H NMR chemical shifts of 5*R**,10*S**,13*R**,14*S**,25*S**-**1** (red line and dots) or 5*R**,10*S**,13*R**,14*S**,25*R**-**1** (green line and dots), with linear fitting shown as a line; (C) Regression analysis of experimental versus calculated ^{13}C and (D) ^{1}H NMR chemical shifts of 5*R**,7*R**,8*R**,10*S**,13*R**,14*R**,25*S**-**2** (red line and dots) or 5*R**,7*R**,8*R**,10*S**,13*R**,14*R**,25*R**-**2** (blue line and dots), with linear fitting shown as a line. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

mg/ml streptomycin. For evaluating tandem fluorescent LC3 puncta, 24 h after chemical treatment, cells were captured by an Olympus FluoView™ 1000 confocal microscope (Olympus, America).

3. Results and discussion

3.1. Structure elucidation

Ganoapplin A (**1**) was obtained as white powder with a molecular formula of $C_{31}H_{36}O_7$ according to the HRESIMS ion at *m/z* 521.2533 $[M + H]^+$ (calcd 521.2534), showing 14 degrees of unsaturation. The ^{1}H NMR spectrum of **1** showed five singlet methyl proton signals at δ_H 1.15 (H_3-28), δ_H 1.19 (H_3-29), 1.38 (H_3-19), 1.34 (H_3-30), and 1.39 (H_3-18), one doublet methyl proton signal at δ_H 1.17 (d, J = 6.7 Hz, H-26), one methoxyl proton signal at δ_H 3.59, s, three sp^2 methine proton signals at δ_H 5.55 (s, H-11), 6.58 (d, J = 2.0 Hz, H-22), and 7.44 (d, J = 2.0 Hz, H-21) (Table 1). Its ^{13}C-DEPT NMR spectra displayed thirty-one carbon resonances, which were assigned as six methyls, one methoxyl, four methylenes, five methines (including three olefinic or aromatic, and two aliphatic), and 15 quaternary carbons (including three ketone carbonyls, one ester carbonyl, seven olefinic or aromatic, and four aliphatic). The aforementioned information indicated that **1** was similar with that of applanoic acid D [33].

The 2D NMR spectra further confirmed above deduction. In the heteronuclear multiple bond correlation (HMBC) spectrum of **1**, the correlations (Fig. 2**A**) of H_3-28, H_3-29, and H-5 with the ketone carbonyl (C-3) and of H_3-19 with C-5 illustrate the presence of ketone carbonyl at C-3. The homonuclear chemical shift correlation spectroscopy (^{1}H–^{1}H COSY) correlations of H-5/H_2-6, together with the HMBC correlations (Fig. 2**A**) of H-5 and H_2-6 to C-7 (δ_C 164.7), of OH (δ_H 12.80) with C-7 and C-6, of H_3-30 with C-15 (δ_C 208.1) and C-8, of H_3-18 with C-12 (δ_C 199.3), of H_3-18 and H_3-30 with C-13 (δ_C 53.6) and C-14 (δ_C 61.1), of H_3-19 with C-9 (δ_C 167.5), of H-11 (δ_H 5.55, s) with C-8 (δ_C 106.9), C-9 (δ_C 167.5), C-10, C-12 (δ_C 199.3), and C-13 certified that the ketone carbonyl (C-15) and an α,β-unsaturated carbonyl fraction (C-7/C-8/C-9/C-11/C-12) were existed in **1**, showing nine degrees of unsaturation.

Additionally, the doublet methyl proton (δ_H 1.17, d, J = 6.7 Hz, H_3-26) showed the HMBC correlations with the ester carbonyl (δ_C 176.4), aliphatic methylene (δ_C 35.7) and methine (δ_C 40.3), and the methoxyl correlated with the ester carbonyl, simultaneously, the ^{1}H–^{1}H COSY correlations of H_3-26/H-25/H_2-24 were observed, which demonstrated the existence of an isobutyriate motif, accounting for one degree of unsaturation.

Apart for above carbon resonances, the remaining six aromatic carbon signals belonged to a tetrasubstituted phenyl, which was consistent with the remaining 4 degrees of unsaturation. The coupling constant of two aromatic protons at δ_H 7.44 (d, J = 2.0 Hz) and δ_H 6.58 (d, J = 2.0 Hz) were characteristic for the *meta*-position coupling in phenyl. Besides, the HMBC spectrum (Fig. 2**A**) of **1** exhibited the correlations of H_3-18 with C-17 (δ_C 158.4), of H-21 (δ_H 7.44, d, J = 2.0 Hz) and H-22 (δ_H 6.58, d, J = 2.0 Hz) with C-16 (δ_C 121.7) and C-20 (δ_C 163.9), of H-21 with C-13 (δ_C 53.6), of H-22 with C-24, and of H_2-24 with C-16, C-23 (δ_C 145.0), and C-22 (δ_C 117.5), which further confirmed the presence of the tetra-substituted benzene ring (Fig. 2**B**). Thus, the planar structure of **1** was determined.

The rotational overhauser effect spectroscopy (ROESY) spectrum of **1** showed the correlations of H_3-28/H-5/H_3-30, and H_3-29/H_3-19/H_3-18, suggesting that CH_3-28, H-5, and CH_3-30 were on the same face, while CH_3-29, CH_3-18, and CH_3-19 were cofacial, which are in line with the lanostane-type triterpenoids from *G. applanatum* [6,7,9]. Thus, the relative configurations of **1** could be 5*R**,10*S**,13*R**,14*S**,25*S**-**1** or 5*R**,10*S**,13*R**,14*S**,25*R**-**1**. The NMR calculation with DP4 + analysis was performed and the shielding tensors of two isomers were predicted using the gauge-independent atomic orbital (GIAO) method [29]. The possibility analysis of DP4 + showed that 5*R**,10*S**,13*R**,14*S**,25*S**-**1** was the candidate structure with a 100 % DP4+ (all data) and 100 %

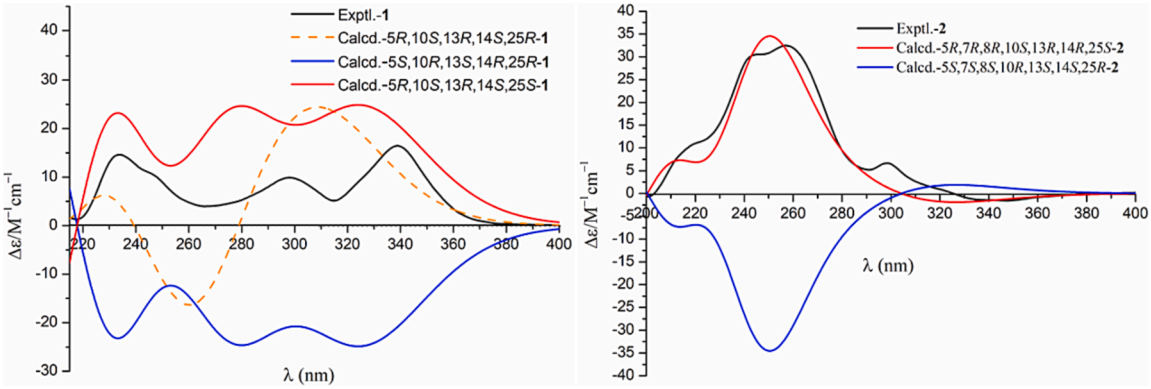


Fig. 4. Experimental and calculated ECD spectra of **1** and **2**.

DP4+ (H) (Fig. 3**A** and **B**). Biosynthetically, **1** could share the 25*S*-configuration with the major lanostane triterpenoids from *G. applanatum* [4,6–9,33].

Furthermore, the electronic circular dichroism (ECD) spectrum of **1** was calculated at the Cam-B3LYP/6–311 + G(d,p) level with the time-dependent density functional theory (TDDFT). The calculated circular dichroism (CD) curve of 5*R*,10*S*,13*R*,14*S*,25*S*-**1** was well corresponding with the experimental CD curve (Fig. 4). Therefore, the absolute configuration of **1** was determined to be 5*R*,10*S*,13*R*,14*S*,25*S*.

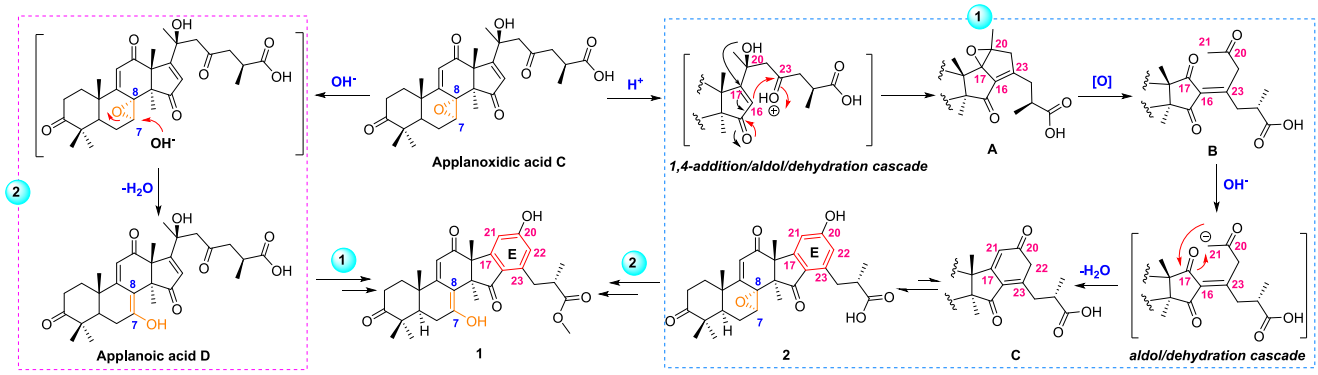
Ganoapplin B (**2**) was obtained as white powder and its molecular formula was determined to be $C_{30}H_{34}O_7$ based on the HRESIMS ion at *m/z* 505.2239 [M - H]- (calcd 505.2232) with 14 degrees of unsaturation. The 1D NMR data of **2** was similar to those of **1**, except for the presence of one oxygenated methine, one quaternary carbon containing oxygen, and a carboxyl in **2**, rather than two sp^2 quaternary carbons (δ_C 164.7, C-7 and δ_C 106.9, C-8) and the ester carbonyl in **1**. Furthermore, the HMBC correlations (Fig. 2**A**) of H_3-28, H_3-29, and H_3-19 with C-5 (δ_C 42.3), of H-5 with C-6 (δ_C 23.6), and C-7 (δ_C 60.1), of H-6 with C-7 and C-8 (δ_C 63.7), of H_3-30 with C-8, C-13, C-14, and C-15 (δ_C 202.4), of H_3-18 with C-12, C-13, C-14, and C-17, of H-11 (δ_H 6.25) with C-12 (δ_C 199.6), C-13, C-9 (δ_C 167.3), C-8, and C-10, indicated that an epoxyl was located at C-7 and C-8, which resembled those of gibbosic acid A [34] and applanoxidic acid C [35].

The ROESY correlations of H-7/H_3-18/H_3-19 indicated that the 7,8-epoxyl was α-oriented, in contrast, H-7, CH_3-18, and CH_3-19 were β (Fig. 2**C**). Furthermore, the relative configurations of the 7,8-epoxyl was assigned as α through comparing chemical shifts of H-7 (δ_H 4.75, d, J = 3.7 Hz), C-7 (δ_C 60.1), and C-8 (δ_C 63.7) in **2** with lanostane-type triterpenoids containing 7α,8α-epoxy-15-oxo (H-7: δ_H 4.50–4.70, d, J = 4.0 Hz; C-7: δ_C 59.0; C-8: δ_C 62.0) and 7β,8β-epoxy-15-oxo (H-7: δ_H 4.30–4.40, d, J = 5.0–6.0 Hz; C-7: δ_C 57.0; C-8: δ_C 59.0) fractions [34,35]. Similarly, the relative configuration of **2** was determined to be 5*R**,7*R**,8*R**,10*S**,13*R**,14*R**,25*S**-**2** based on the calculated NMR with a 100 % DP4+ (all data) and 99.39 % DP4+ (H) (Fig. 3**C, D**). The absolute configuration of **2** was finally confirmed as 5*R*,7*R*,8*R*,10*S*,13*R*,14*R*,25*S*-**2** through comparing the calculated and experimental ECD curves (Fig. 4).

As far as we know, the rearranged reaction of GTs previously reported mainly occurs in tetracyclic skeleton [3–6], while the side chain is usually degraded to nor-triterpenoids [33]. In present study, two GTs, ganoapplins A and B (**1** and **2**) have an unprecedented 6/6/6/5/6 pentacyclic skeleton. Especially, a rare aromatic E ring has different cyclization way, compared to the regular pentacyclic triterpenoids [36]. Applanoxidic acid C is considered as the biosynthetic precursor based on its same tetracyclic architecture as that of **2** [35]. The formation of **2** involves three key steps: (1) intermediate A is formed by a 1,4-addition/aldol/dehydration cascade reaction [37]. (2) Intermediate B is derived from A due to the oxidative cleavage of the 17,20-epoxy [38]. (3) The aldol/dehydration of C-21 and C-17 leads to the formation of intermediate C [39]. Additionally, **1** is formed through two possible pathways. The first pathway is a direct conversion of 7,8-epoxy in compound **2** to 7,8-enol under the alkaline condition [40]. Another pathway is to firstly form applanoic acid D [33] and the subsequent formation of the aromatic E ring to finally obtain **1** (Scheme 1).

3.2. Activation of *1* and *2* on autophagy

The induction of **1** and **2** for autophagy was investigated based on the previous research about the critical effect of autophagy in anti-AD and the potential of GTs against AD [10,11,16,23]. We conducted cellular analyses using human SH-SY5Y cells, and DMSO (dimethyl sulfoxide), a solvent of compounds **1** and **2**, was used as the control. Moreover, Rapamycin, an inducer of autophagy, was a positive control [41]. In the SH-SY5Y cells treated with **1** and **2**, an increased protein level of the



Scheme 1. A plausible biosynthetic pathway for **1** and **2**.

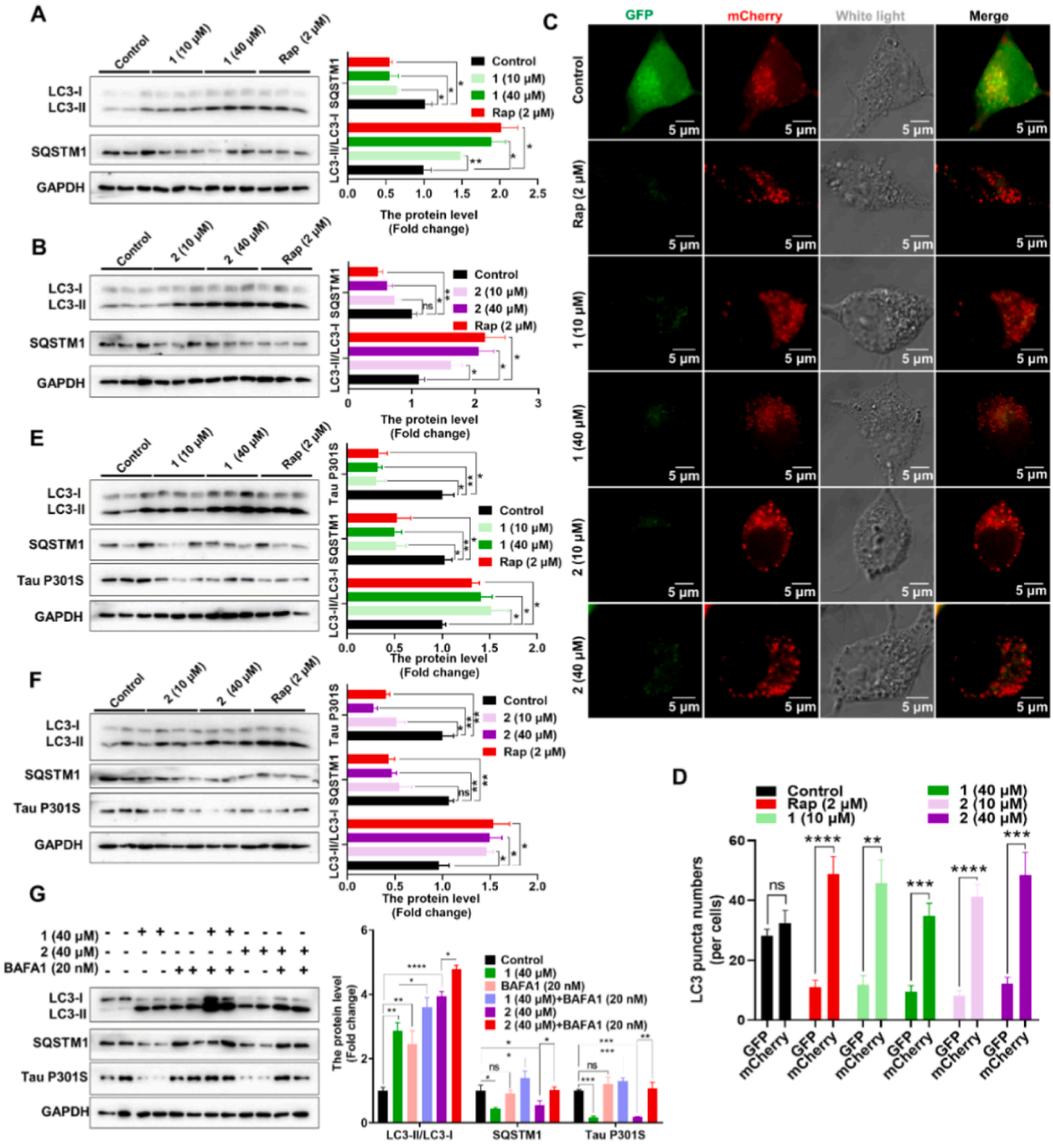


Fig. 5. Results of biological activity assays. (**A-B**) Western blotting assays showing the protein levels of autophagy markers LC3-II/LC3-I and SQSTM1 in the SH-SY5Y treated with or without compounds. Rapamycin (Rap) is a positive control. (**C-D**) Increased autophagic flux in response to **1**, **2** or Rapamycin (Rap) treatment in SH-SY5Y mCherry-GFP-LC3 cells. (**C**) **1** and **2** treatment increased the maturation of autolysosomes as shown by the increased red puncta of mRFP-GFP-LC3 in cells, and this effect was similar to that of Rapamycin. (**D**) Quantification of LC3 puncta in (**C**) based on 3 independent experiments. (**E-F**) Western blotting assays showing the protein levels of autophagy markers LC3-II/LC3-I and SQSTM1, and Tau P301S in the SH-SY5Y MAPT cells treated with or without compounds. (**G**) Western blotting analyses of autophagy markers LC3B-II/LC3B-I and SQSTM1, and Tau P301S in cell lysates from SH-SY5Y MAPT cells treated with BAFA1 (Bafilomycin A1, 20 nM), **1** (40 μM), **2** (40 μM), or both (BAFA1 and **1**, or BAFA1 and **2**). (**A-B, E-G**) A representative Western blotting result (*left*) and quantification of respective protein levels (*right*) based on 3 independent experiments were presented. Relative protein abundance was normalized to GAPDH. ns, not significant; *, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$; ****, $P < 0.0001$; one-way ANOVA with the Tukey's *post-hoc* test. Bars represent mean ± SEM. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

lipidated (PE-conjugated) form of MAP1LC3/LC3 (microtubule-associated protein 1 light chain 3; LC3-II)/LC3-I and a decreased protein level of SQSTM1 (sequestosome 1) in a dose-dependent manner were observed (Fig. 5**A-B**). Then the tandem monomeric mCherry-GFP-tagged LC3 (mCherry-GFP-LC3) reporter was introduced into SH-SY5Y cells to determine the effect of **1** and **2** on autophagic flux. The mCherry-GFP-LC3 distribution was evaluated in SH-SY5Y mCherry-GFP-LC3 cells treated with rapamycin (a positive control), **1** or **2**. The mCherry-GFP-LC3 in autolysosomes displayed red fluorescence as the GFP signal was sensitive to the acidic condition whereas the mCherry signal was

more stable in the lysosome lumen [42]. We observed an increased number of red puncta in the rapamycin-treated SH-SY5Y mCherry-GFP-LC3 cells (Fig. 5**C-D**), indicating an increased level of autophagic flux. Treatments with **1** and **2** had a similar effect on the increase of autophagic flux as rapamycin (Fig. 5**C-D**). Collectively, these results demonstrated that autophagy was induced by **1** and **2**.

*3.3. Inhibition of **1** and **2** against pathological Tau through inducing autophagy*

Autophagy has been found to be a promising therapeutic strategy against Tauopathy by promoting the clearance of tau [23,43–46]. In our study, **1** and **2**-induced autophagy-dependent clearance of tau was examined. First, mutant (P301S) tau was stably expressed in SH-SY5Y cells. We confirmed that **1** and **2** can induce autophagy in human SH-SY5Y cells stably expressing the human MAPT mutant MAPT-p.P301S (SH-SY5Y MAPT cells) that were created by ourselves (Fig. 5**E-F**). Moreover, **1** and **2** reduced mutant Tau level in SH-SY5Y MAPT cells (Fig. 5**E-F**). We used BAFA1 (Bafilomycin A1), an inhibitor of the vacuolar(V)-type ATPase that results in blockage of autophagosome-lysosome fusion and accumulation of LC3-II, [47] to further prove the role of autophagy induced by **1** and **2** in MAPT/Tau clearance in SH-SY5Y MAPT cells. Again, autophagy was activated in SH-SY5Y MAPT cells by **1** and **2**, as indicated by the increased LC3-II/LC3-I and decreased SQSTM1 protein levels (Fig. 5**G**). This effect was associated with a decrease of Tau P301S in comparison with untreated cells (Fig. 5**G**). Treatment of BAFA1 (20 nM) alone raised the LC3-II/LC3-I, but with no significant effect on Tau P301S level relative to untreated cells (Fig. 5**G**). However, adding BAFA1 could reverse the decreased levels of Tau P301S induced by **1** and **2** (Fig. 5**G**). These results supported the key role of autophagy activated by **1** and **2** in Tau P301S clearance. Taking all results together, we proposed that **1** and **2** might be against AD by activating autophagy-mediated Tau P301S clearance, although the mechanism of **1** and **2** induced autophagy needs further investigation.

Autophagy, like a “housekeeping”, can clear protein aggregates, damaged organelles and invading pathogens from the cytoplasm, further delivering them to the lysosome for degradation and recycling of their monomers [46]. In the nerve cell, autophagy removes aggregated/amyloid species of MAPT/tau (microtu-bule associated protein tau) to prevent MAPT/tau to form intracellular inclusions leading to the formation of intraneuronal neurofibrillary tangles and neuropil threads in Alzheimer disease [46] *Ganoderma* triterpenoids (GTs) exhibited significantly neuroprotective activities by anti-neuroinflammation, anti-oxidation, and activating autophagy to reduce Aβ accumulation [10,11,48]. In our study, cellular assays demonstrated that compounds **1** and **2** can activate autophagy to clear pathogenic Tau protein. Taken together, GTs play an important role in anti-AD in the multiple target way.

4. Conclusions

In summary, ganoapplins A and B (**1** and **2**) from *G. applanatum* represent the first example of pentacyclic triterpenoids with a 6/6/6/5/6-fused skeleton. Their unique aromatic E ring distinguished them from the normal lanostane-type and pentacyclic triterpenoids. Furthermore, our cellular assays showed that compounds **1** and **2** can reduce pathogenic Tau protein via inducing autophagy. Thus, our study not only enriches the skeleton diversity of lanostane-type triterpenoids, but also provides scientific evidence for ganoapplins A and B (**1** and **2**) as leading compounds to further develop anti-AD’ agent.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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Appendix A. Supplementary data

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Supplementary Material

Ganoapplins A and B with an unprecedented 6/6/6/5/6-fused pentacyclic skeleton from *Ganoderma* inhibit Tau pathology through activating autophagy

Xing-Rong Peng,[a,b,1] Rong-Can Luo,[b,c,1] Xiao-Qian Ran,[b,c,1] Ya-Rong Guo,[d] Yong-Gang Yao,[b,c,e*] & Ming-Hua Qiu[a,b,*]

Contents

Quantum chemical calculations for 1 and 2

The theoretical calculations of compounds **1** and **2** were performed using Gaussian 16.[1,2] Conformational analysis was carried out in Crest software. The conformers were optimized at M062X/6-311+G(2d,p) level under the condition of room-temperature (298.15 K).[3] Based on the Boltzmann distribution law, those conformers accounting for over 99% population were chosen for the NMR and ECD calculations.

During the calculations of ^{1}H and ^{13}C chemical shifts, the mPW1PW91/6-31+G(d,p) level with the IEFPCM solvent model was used to calculate their nuclear shielding constants, and chemical shifts was obtained through the formula $\delta_{calcd} = \sigma_{TMS} - \sigma_{calcd}$, of which the chemical shift of reference TMS is 0 ppm and σ_{TMS} was the shielding constant of TMS. Then, the linear relationship between calculated chemical shifts and experimental shifts was drawn in EXCEL, where linear regression was $\delta_{calcd} = a\delta_{exp} + b$ and the correlation co-efficient was R^2. In addition, the DP4+ probabilities were calculated according to the EXCEL spreadsheet provided by Sarotti et al.[4]

The theoretical calculation of ECD was performed using time dependent Density Functional Theory (TDDFT) at B3LYP/6-311G(d,p) level in MeOH with PCM model.[5] The ECD spectra of compounds **1** and **2** were obtained by weighing the Boltzmann distribution rate of each geometric conformation through the Multipwfin software.

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1D and 2D NMR spectra of compound 1

Figure S1. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 1.

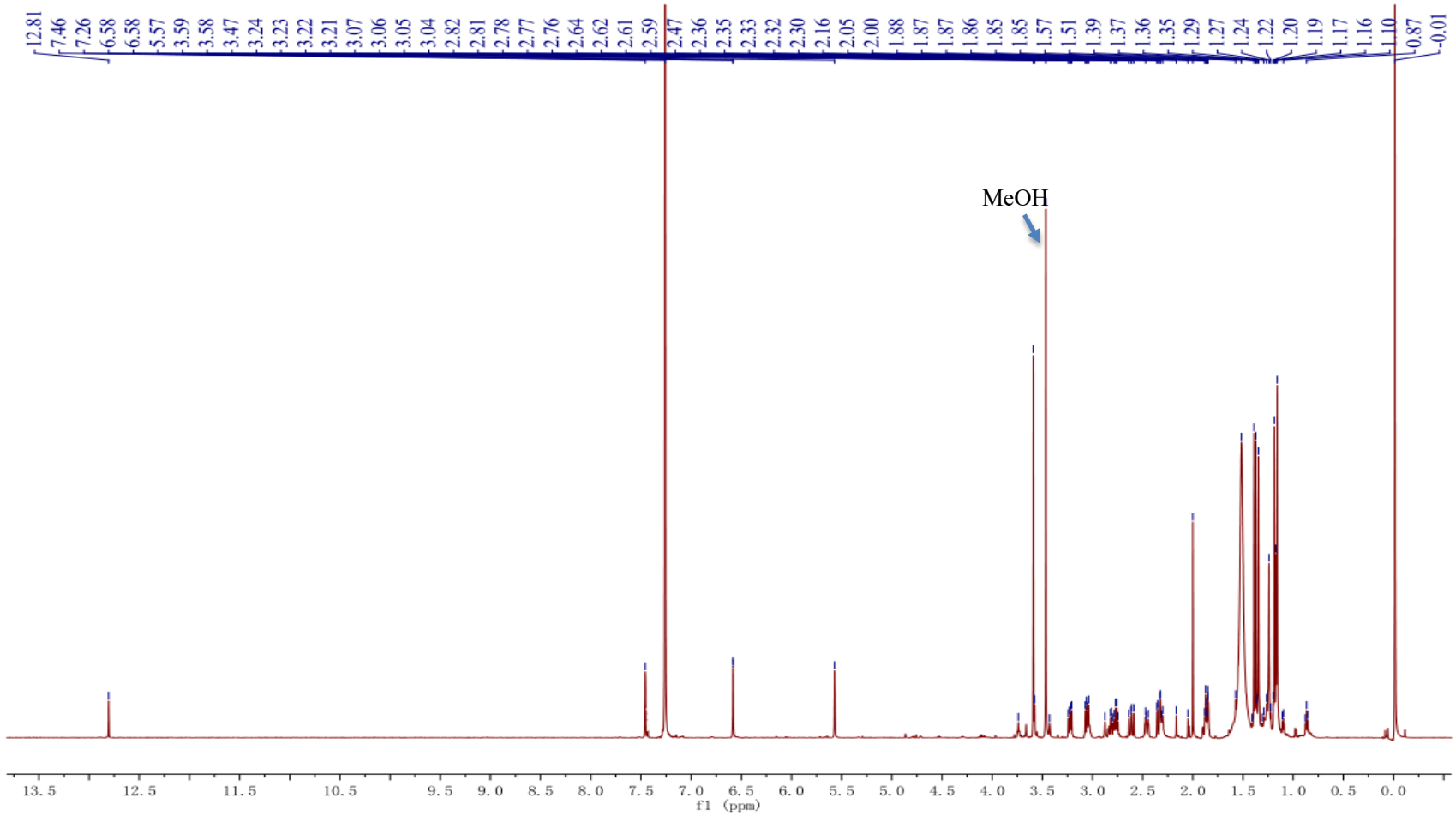


Figure S2. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 1.

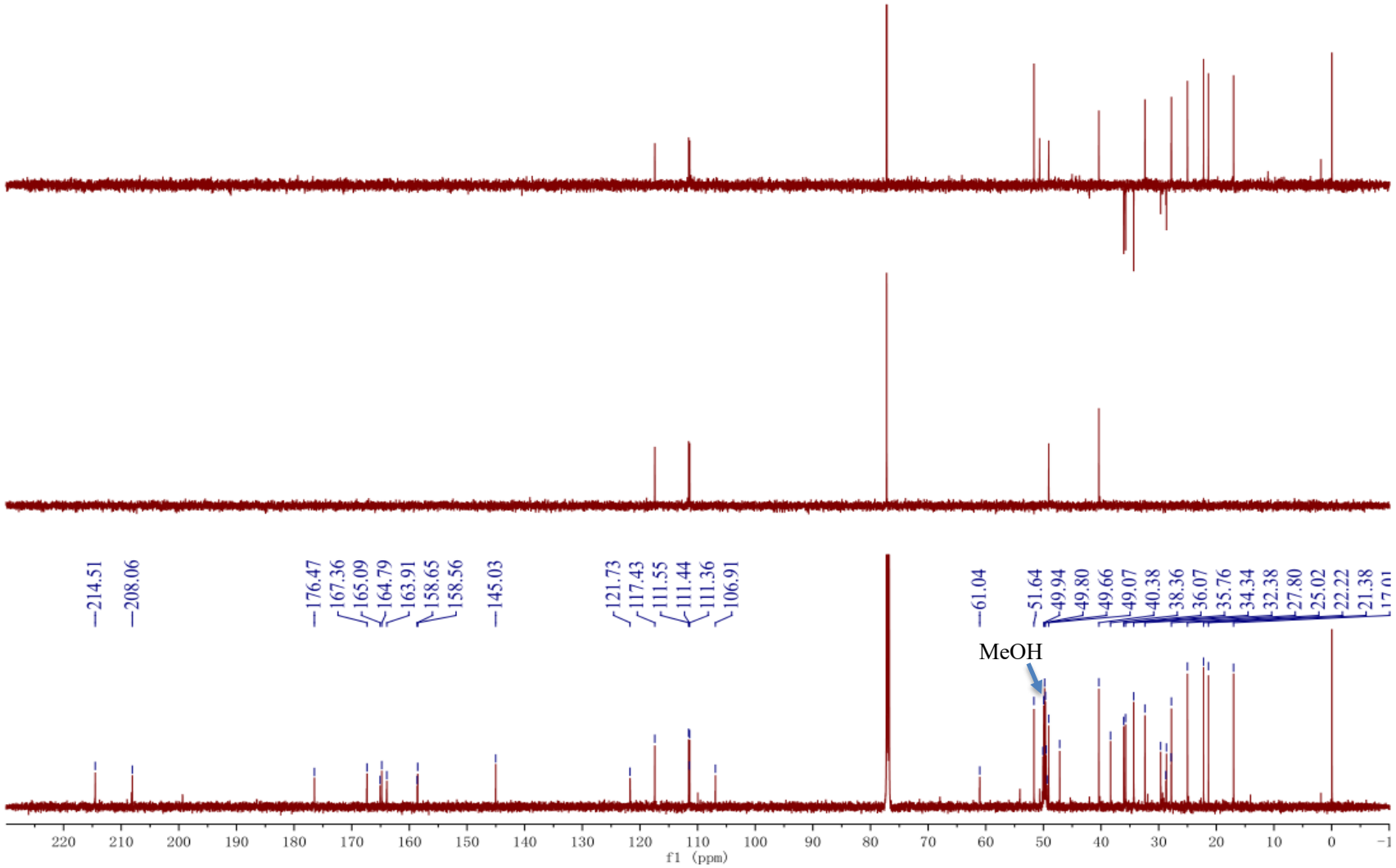


Figure S3. The assignment of ^{13}C NMR (150 MHz, $CDCl_3$) spectroscopic data of 1.

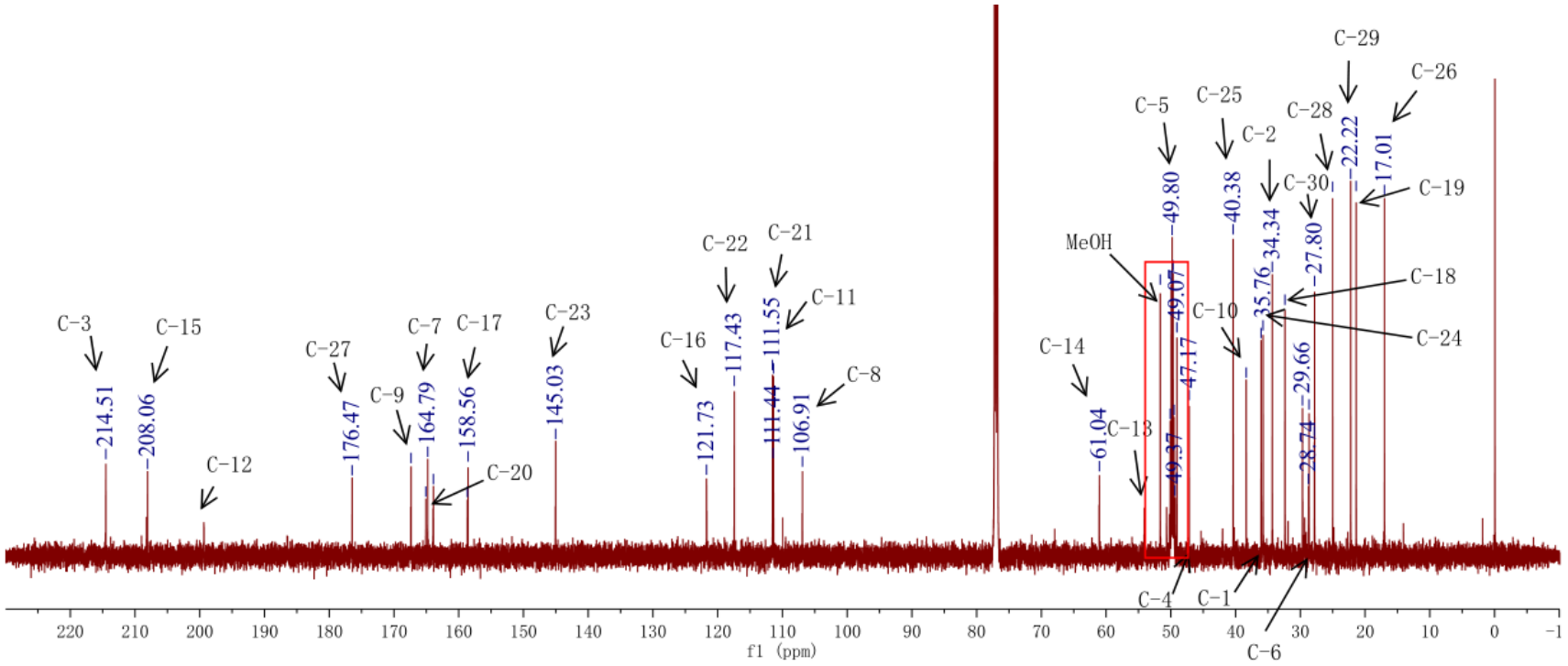


Figure S4. ^{1}H-^{1}H COSY (600 MHz, $CDCl_3$) spectrum of 1.

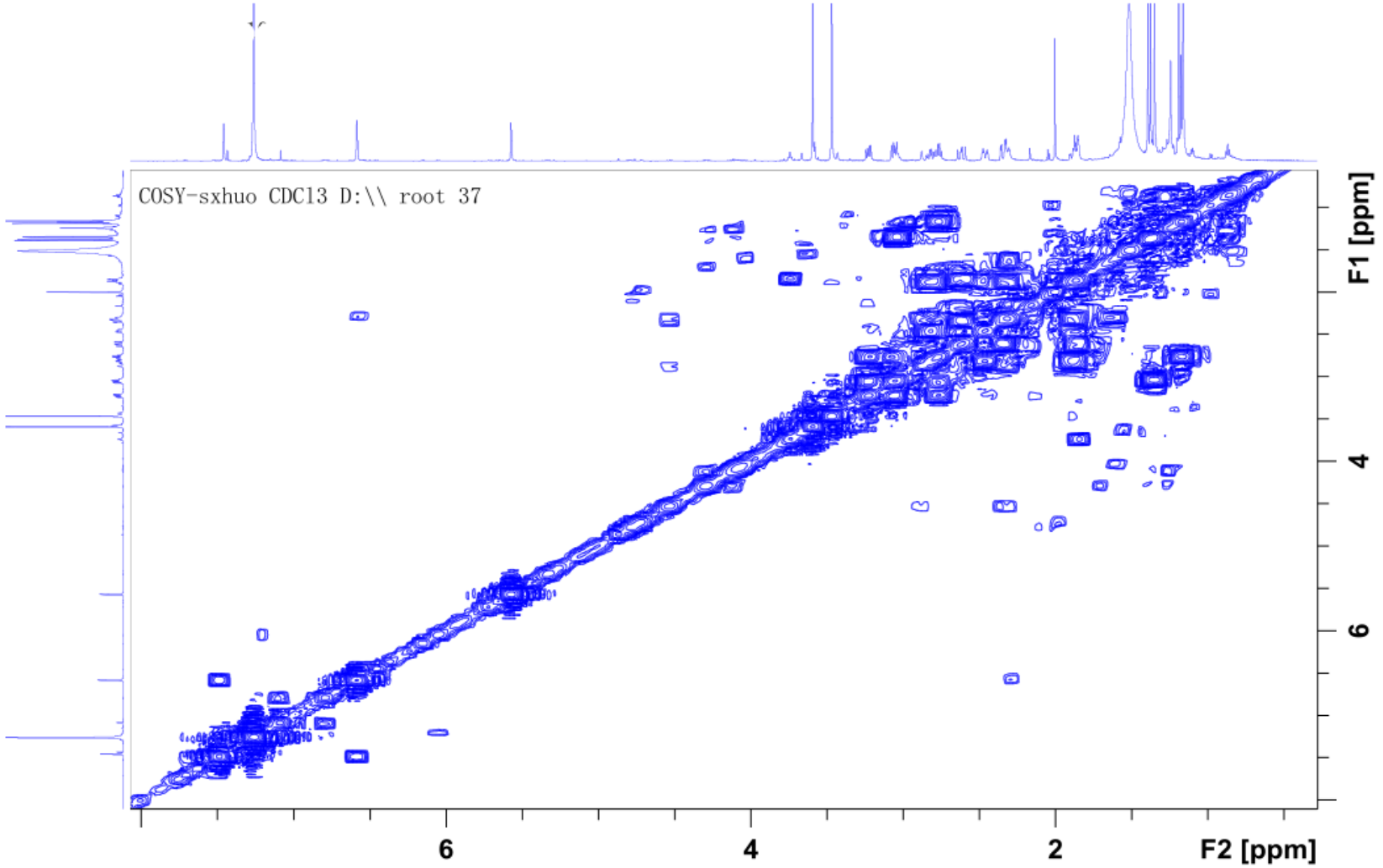


Figure S5. HSQC (600/150 MHz, $CDCl_3$) spectrum of 1.

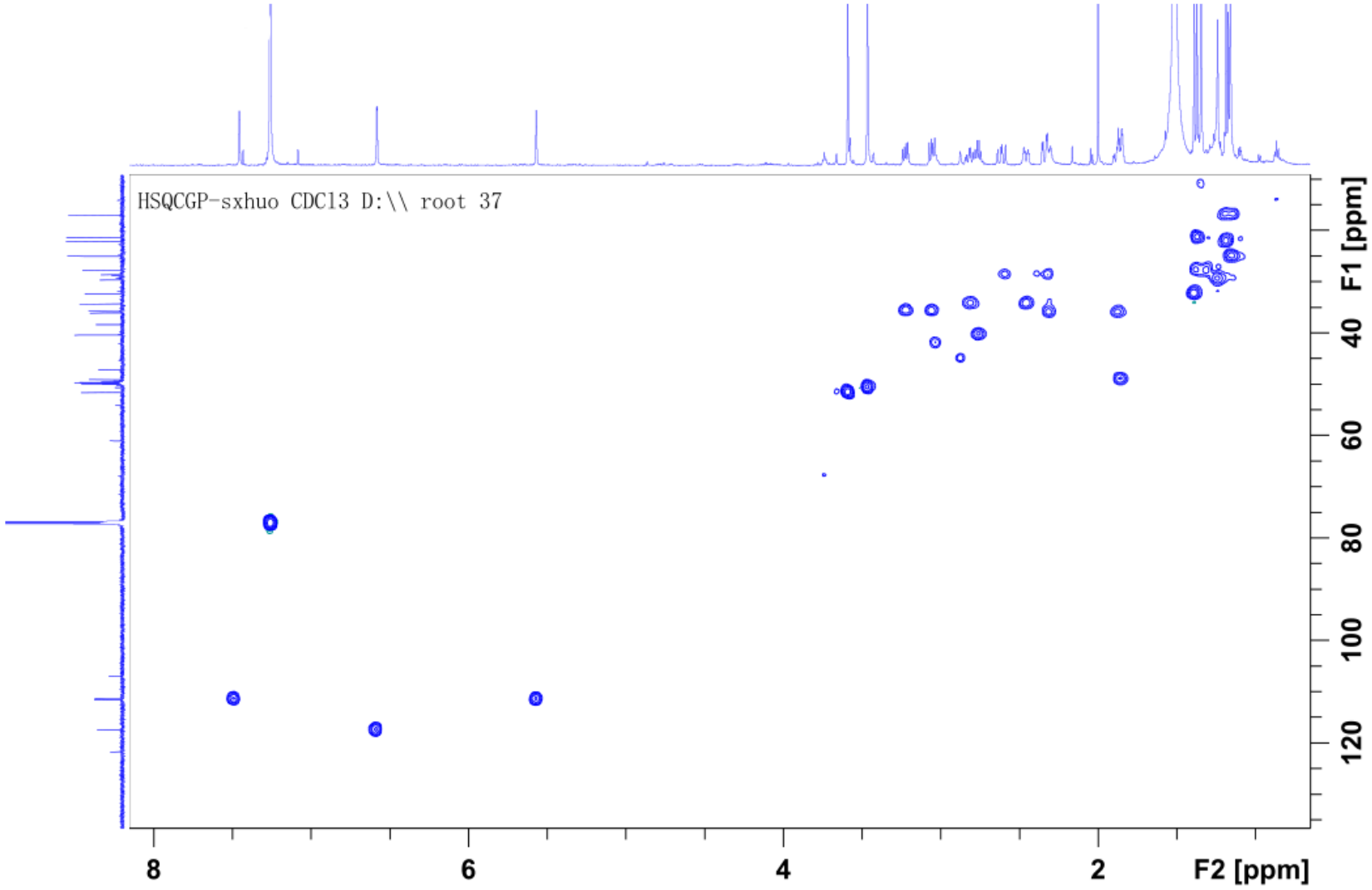


Figure S6. HMBC (600/150 MHz, $CDCl_3$) spectrum of 1.

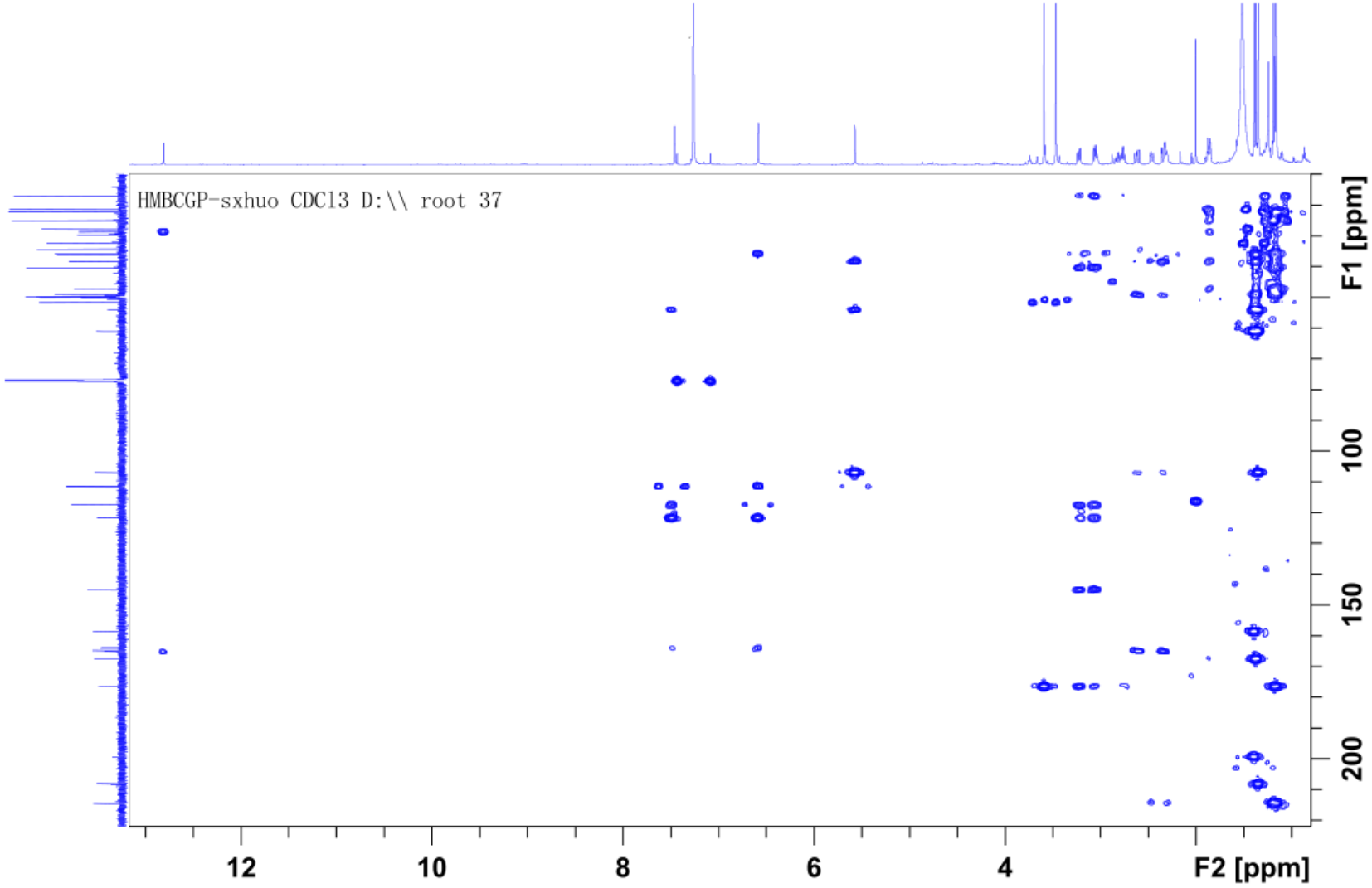
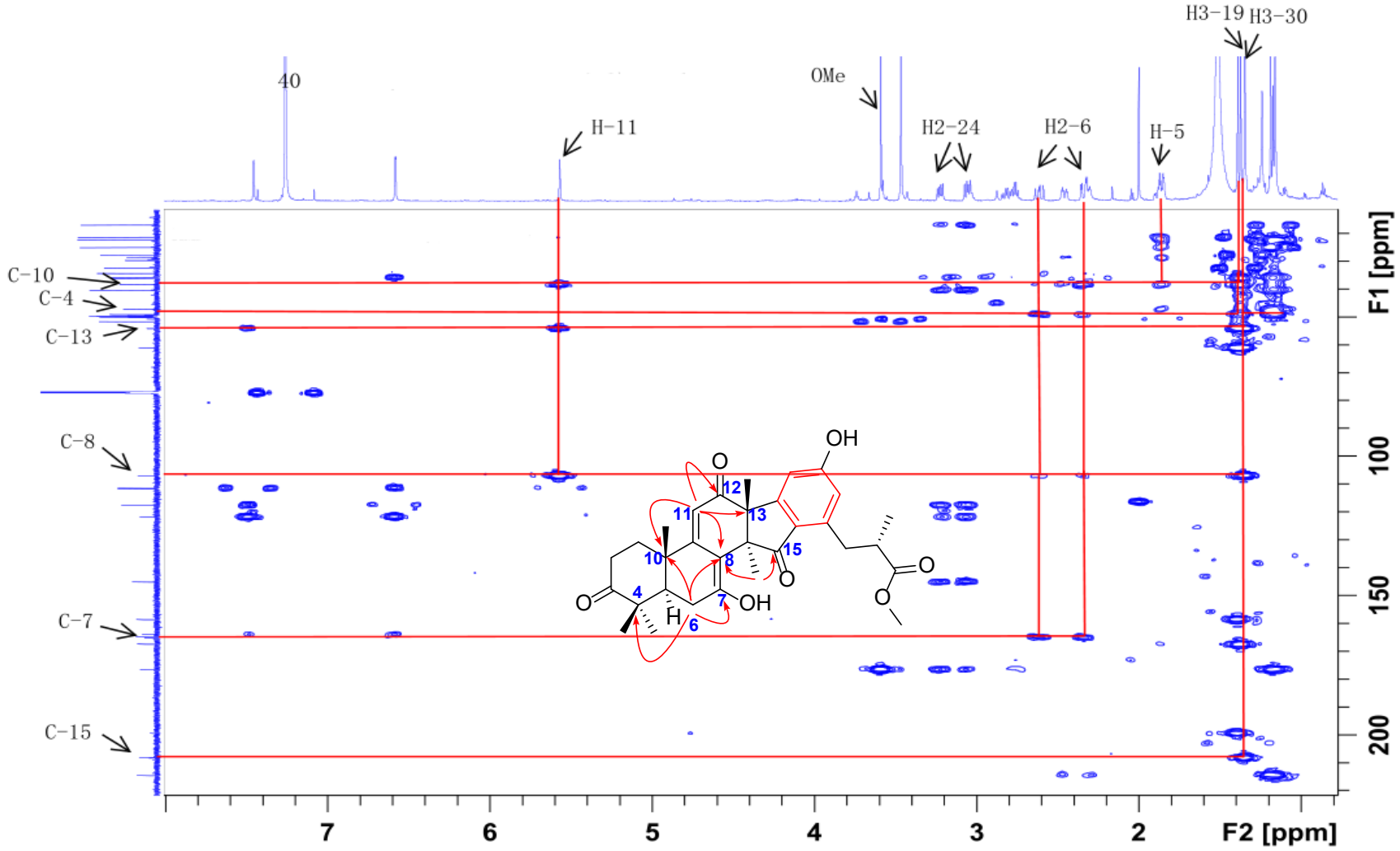
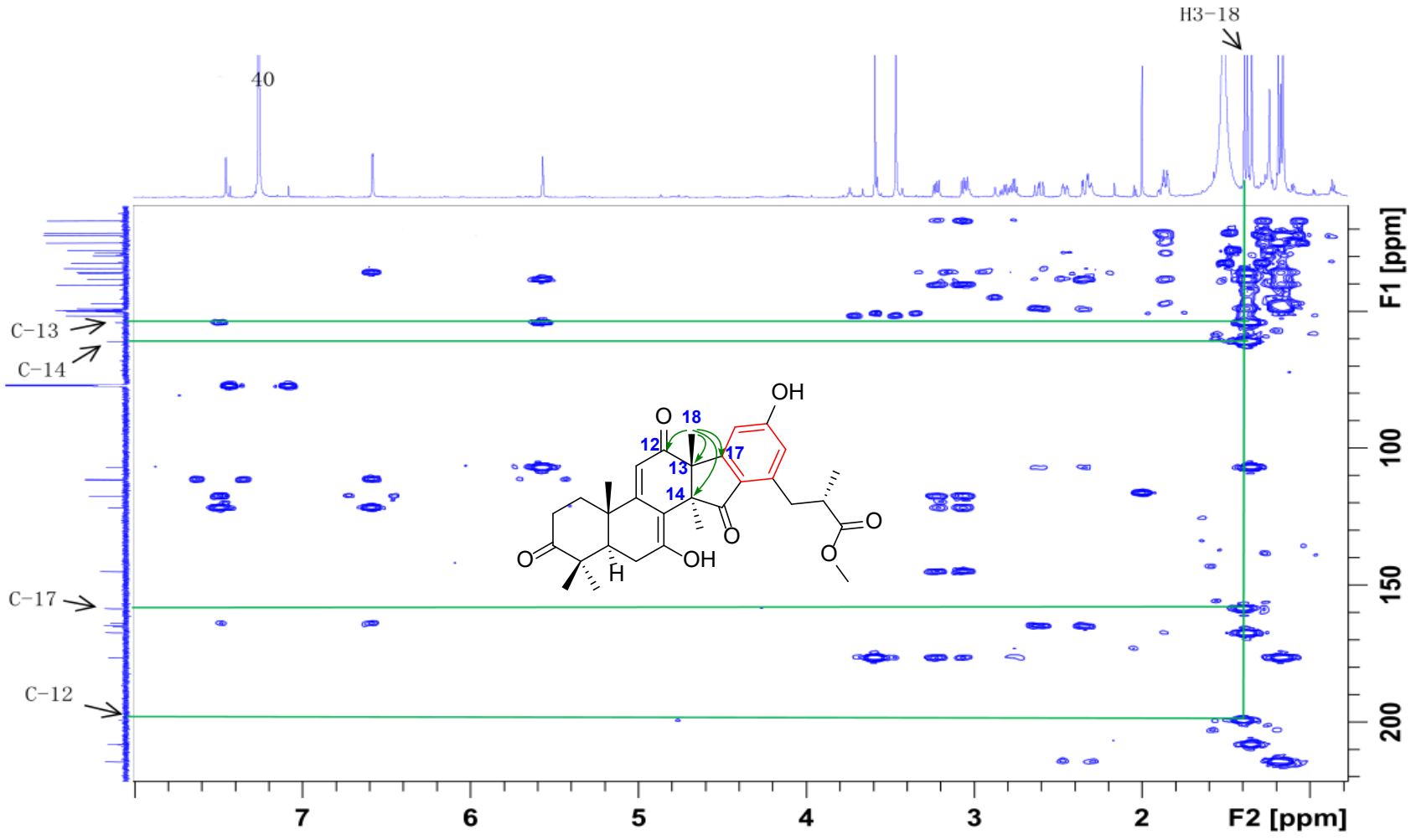


Figure S7. The enlarged HMBC (600/150 MHz, $CDCl_3$) spectrum of 1.

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C-17
C-12
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150
200
7
6
5
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F2 [ppm]
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O
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14
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O
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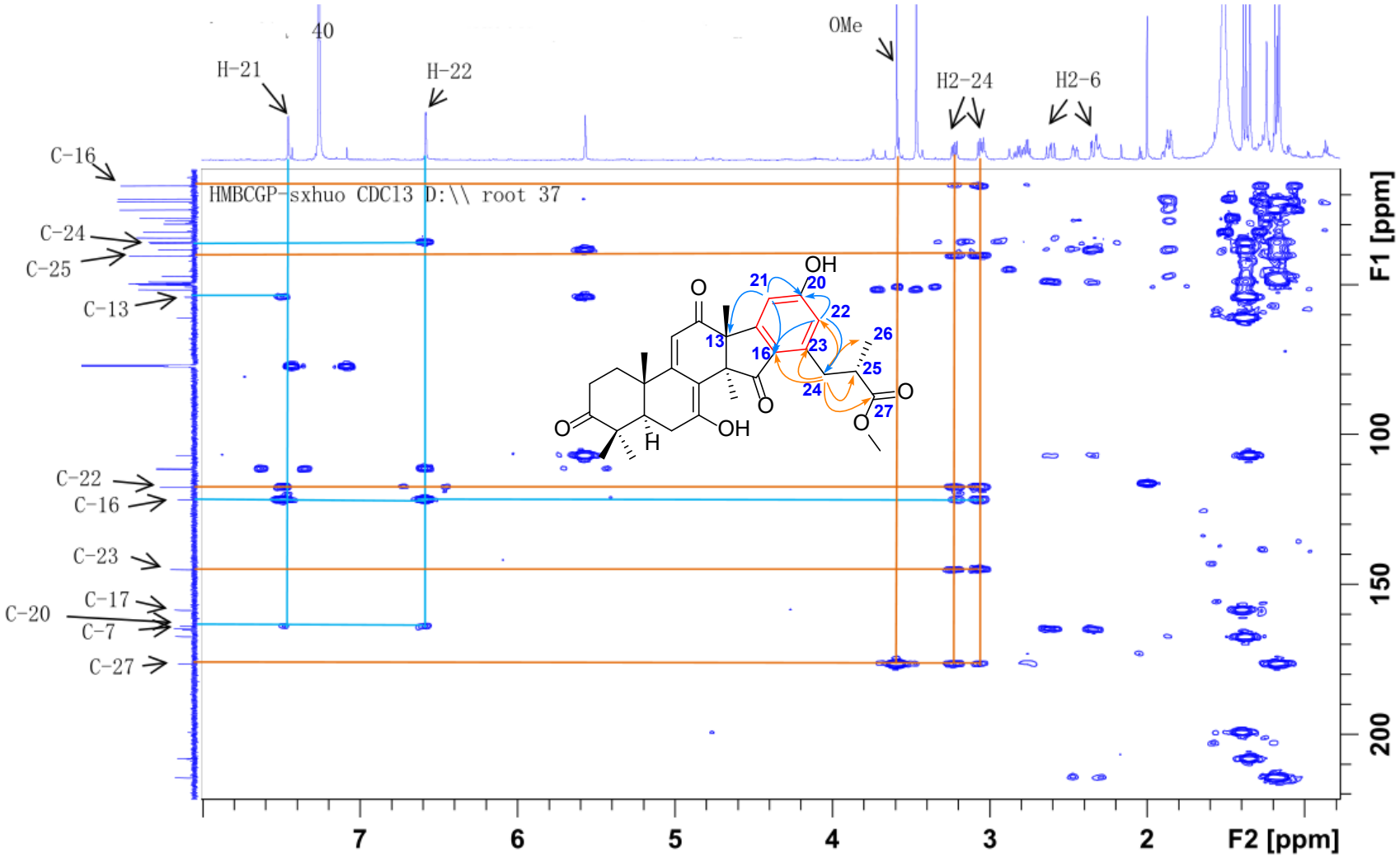
O
H
OH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H-22
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F1 [ppm]
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3
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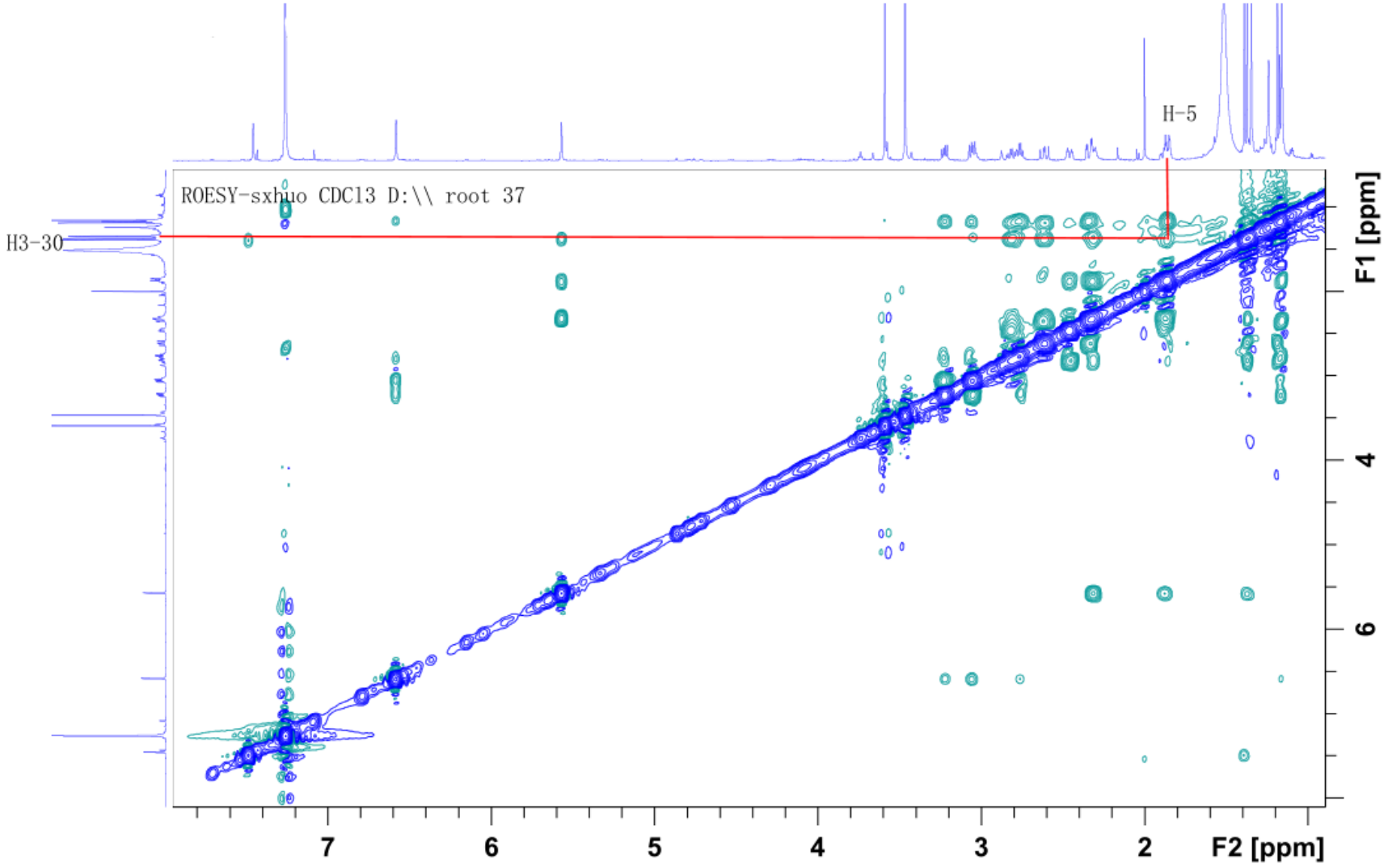
F2 [ppm]

Figure S8. ROESY (600 MHz, $CDCl_3$) spectrum of 1.



1D and 2D NMR spectra of compound 2

Figure S9. ^{1}H NMR (600 MHz, CD_3OD) spectrum of 2.

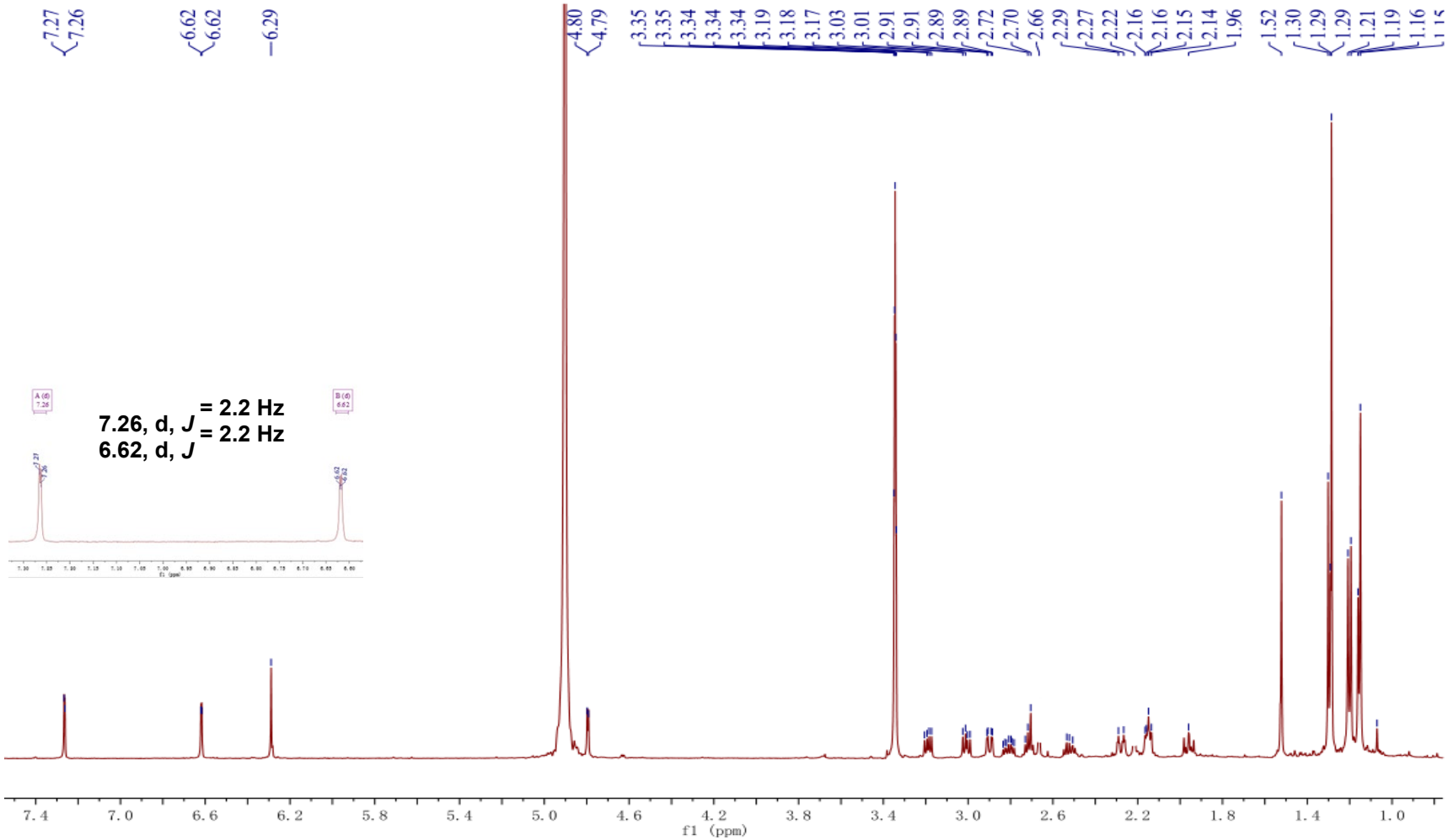


Figure S10. ^{13}C NMR (150 MHz, CD_3OD) spectrum of 2.

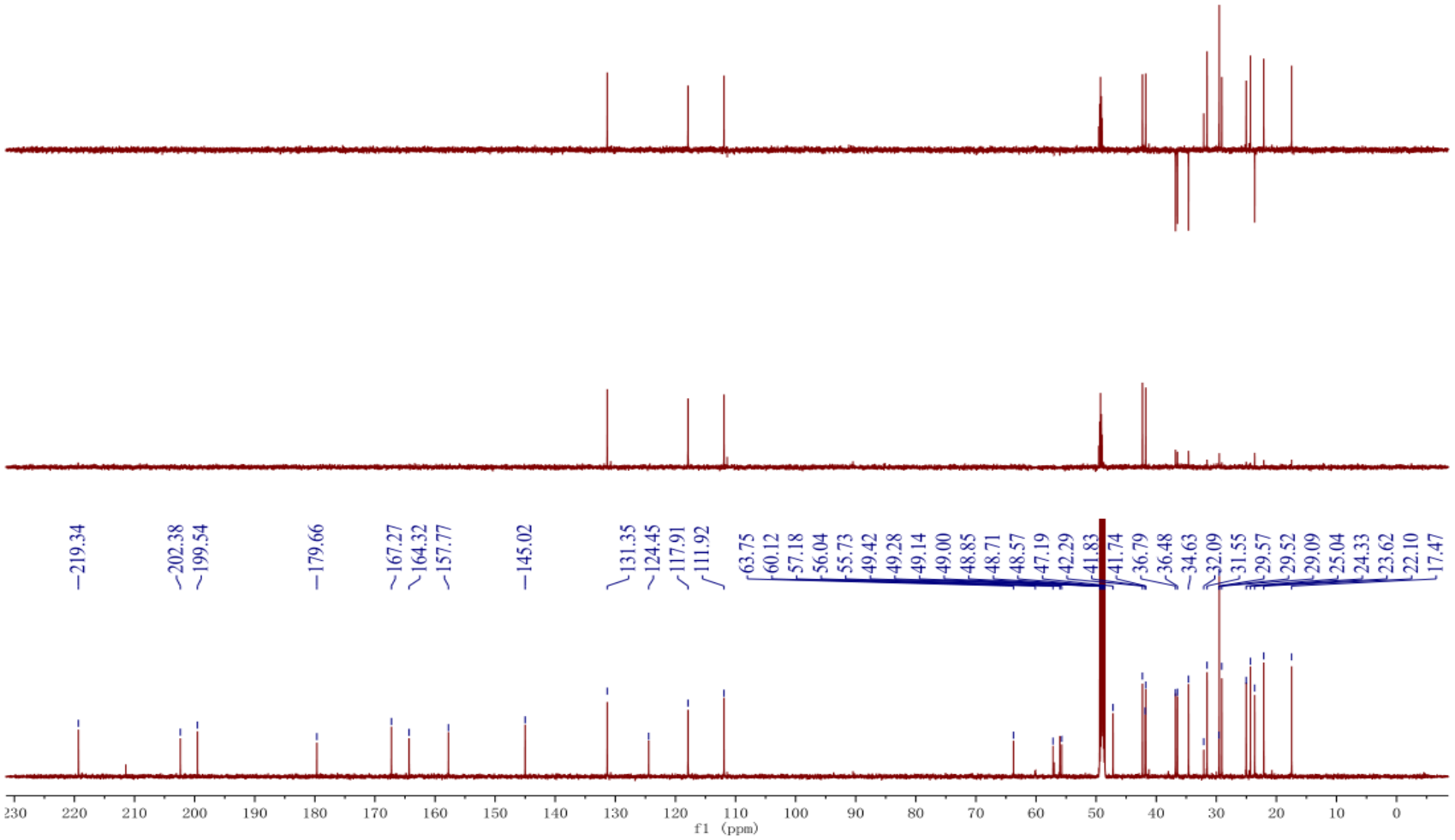


Figure S11. ^{1}H-^{1}H COSY (600 MHz, CD_3OD) spectrum of 2.

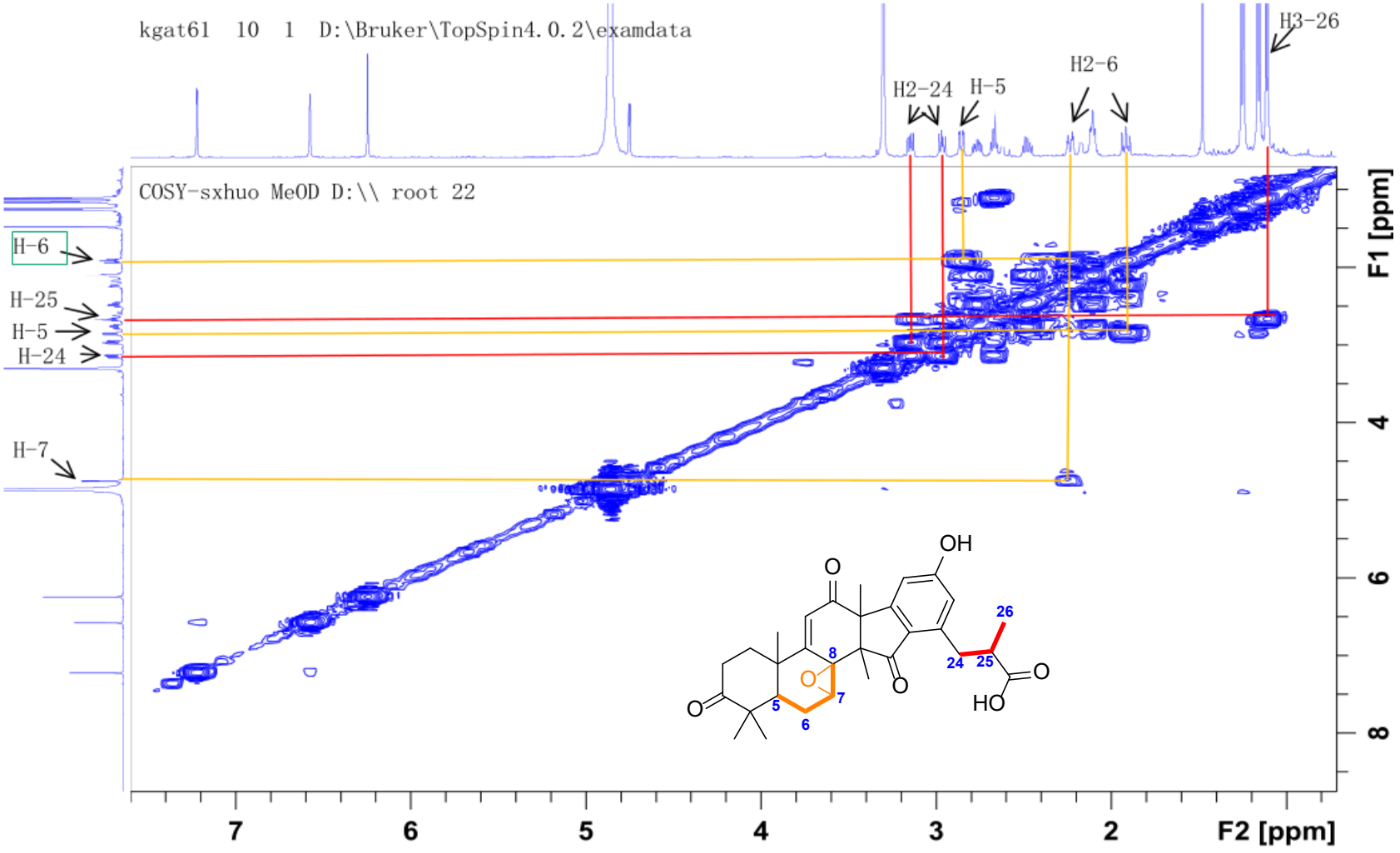


Figure S12. HSQC (600/150 MHz, CD_3OD) spectrum of 2.

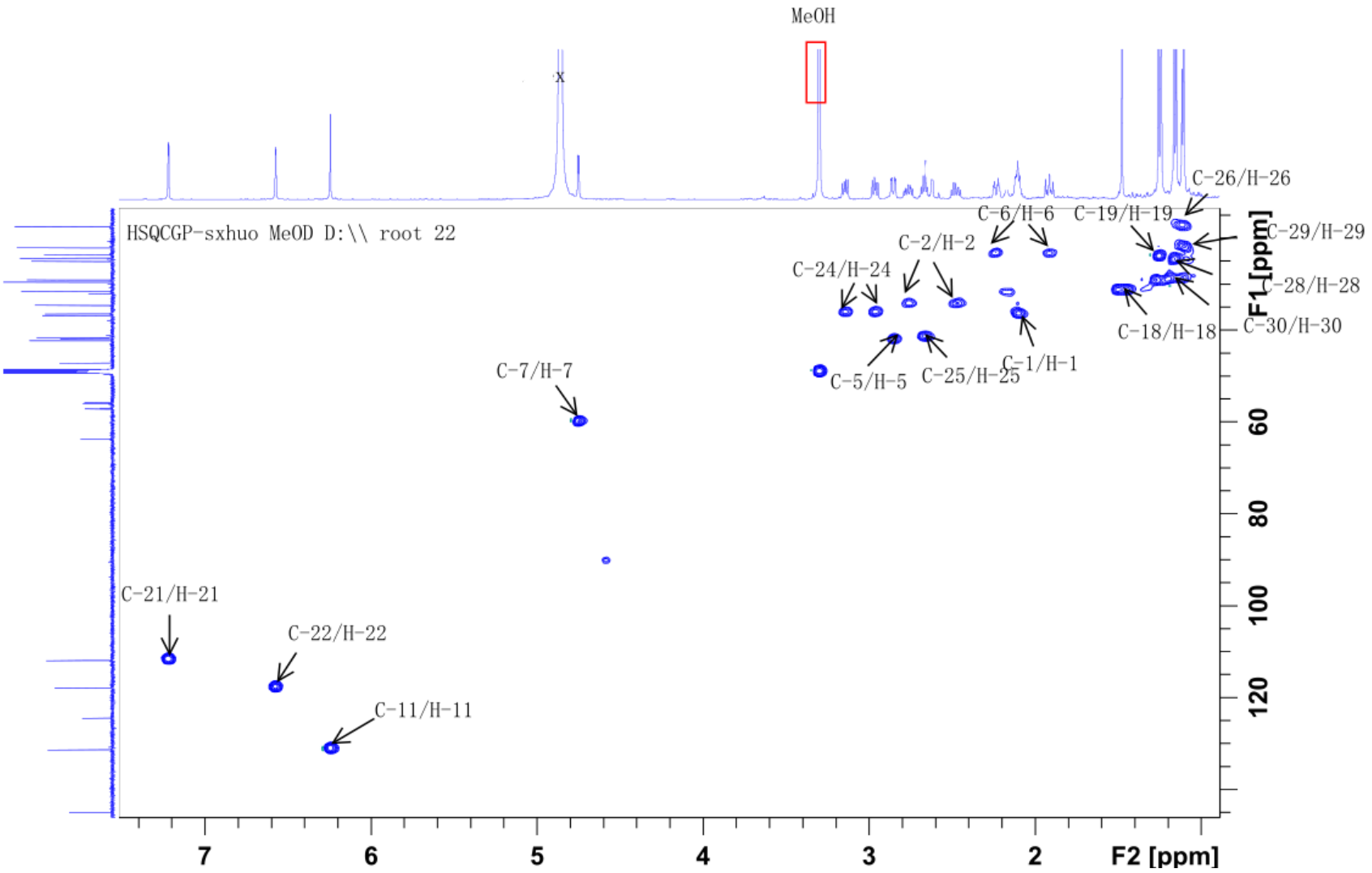


Figure S13. HMBC (600/150 MHz, CD_3OD) spectrum of 2.

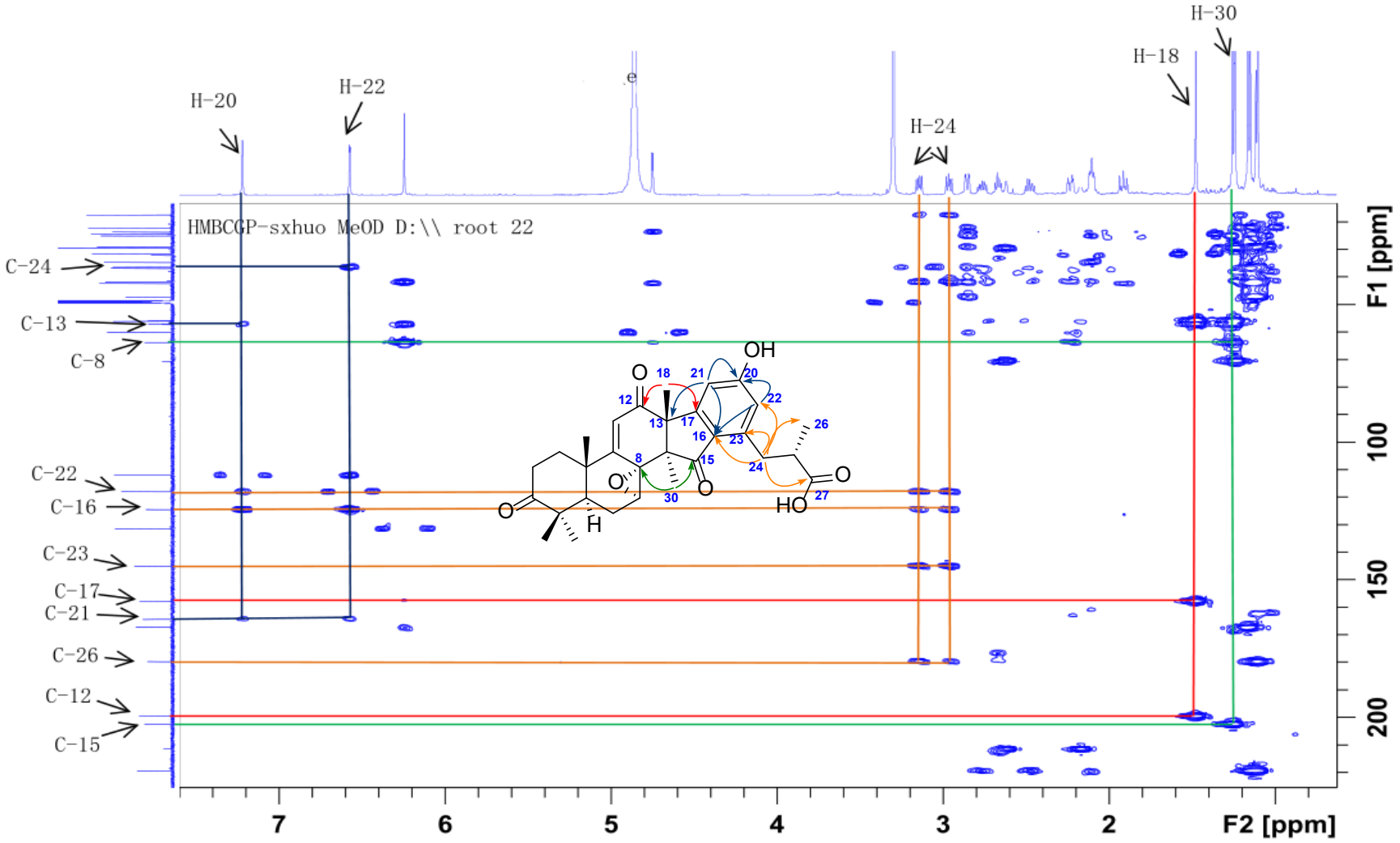
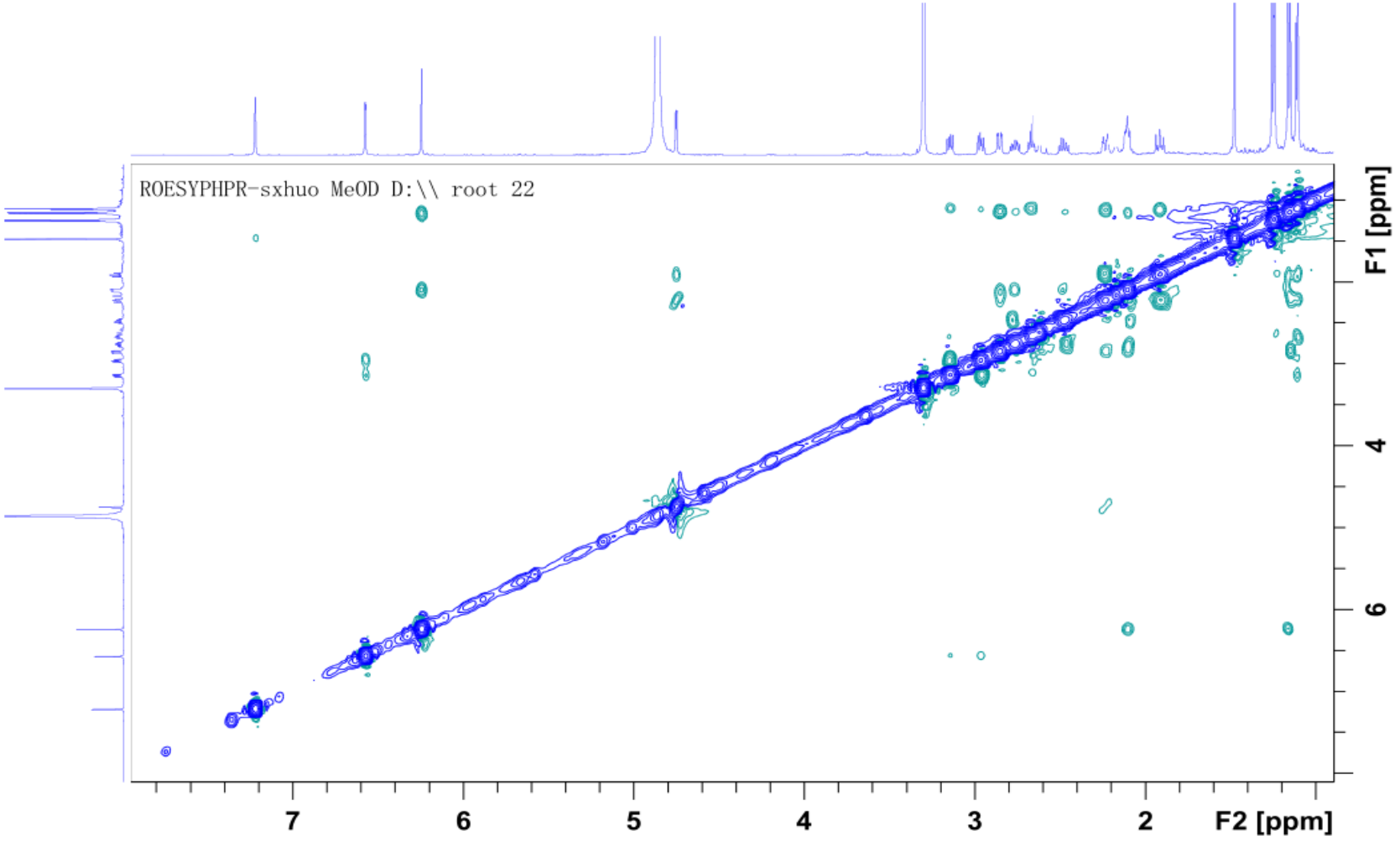
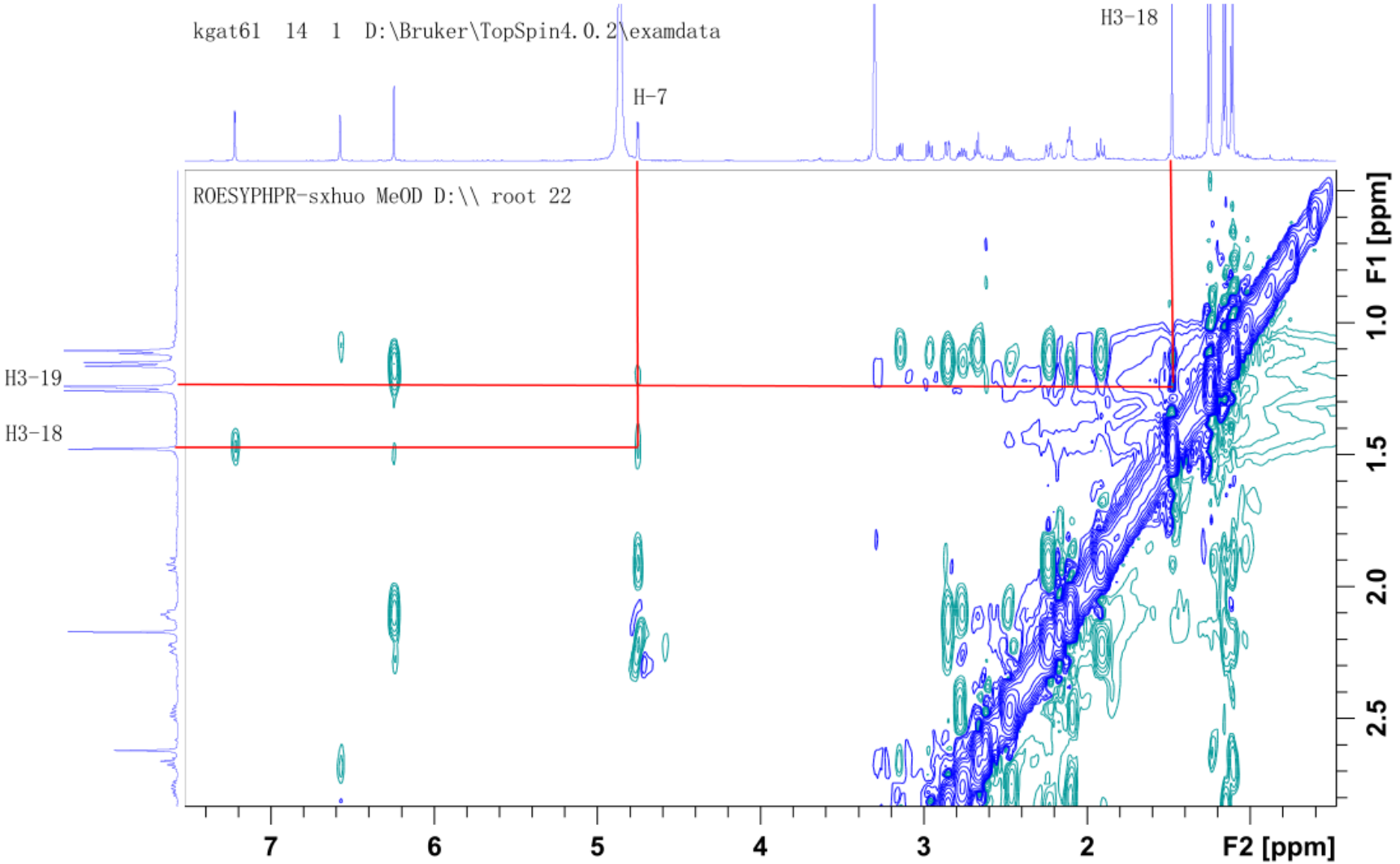


Figure S14. ROESY (600/150 MHz, CD_3OD) spectrum of 2.

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H3-18
1.0
1.5
2.0
2.5
F1 [ppm]
7
6
5
4
3
2
F2 [ppm]

HRESIMS spectra of 1 and 2

Figure S15. HRESIMS spectrum of 1.

Qualitative Analysis Report

Data Filename	kgat61a.d	**Sample Name**	kgat61a
Sample Type	Sample	**Position**	P1-A1
Instrument Name	Instrument 1	**User Name**	
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Comment			

Sample Group	**Info.**
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User Spectra

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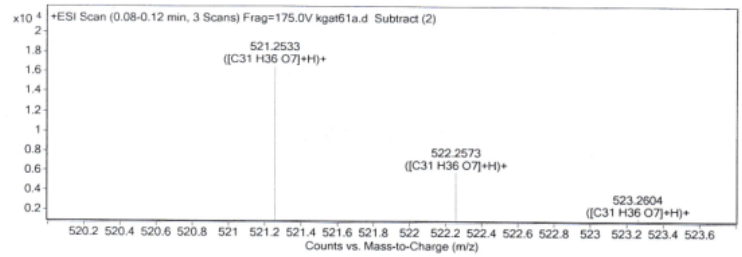

Peak List

m/z	z	Abund	Formula	Ion
274.2736	1	3873.68		
318.2996	1	3498.69		
362.3257	1	1736.45		
473.2643	1	1679.9		
521.2533	1	16563.8	C31 H36 O7	(M+H)+
522.2573	1	5864.65	C31 H36 O7	(M+H)+
523.2604	1	1229.48	C31 H36 O7	(M+H)+
543.2345	1	1252.2		
569.3577	1	2972.81		
679.3619	1	1494.21		

Formula Calculator Element Limits

Element	Min	Max
C	3	120
H	0	240
O	0	30

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C31 H36 O7	520.2461	521.2534	521.2533	0.10	0.19	14.0000

--- End Of Report ---

Agilent Technologies Page 1 of 1 Printed at: 5:37 PM on: 1/11/2022

Figure S16. HRESIMS spectrum of 2.

Qualitative Analysis Report

Data Filename	kgat61.d	**Sample Name**	kgat61
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Comment			

Sample Group	**Info.**
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User Spectra

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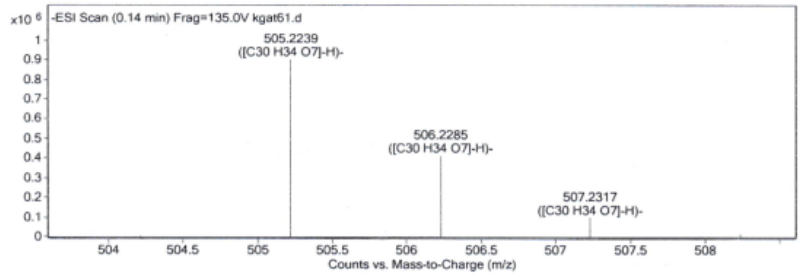

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506.2285	1	411035.69	C30 H34 O7	(M-H)-
619.2166	1	1647805.75		
620.221	1	808718.88		
621.2247	1	205055.06		
636.2511	1	275869.13		
1011.4537	1	342147.38		
1012.4582	1	348441.5		
1013.4618	1	167319.17		

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30

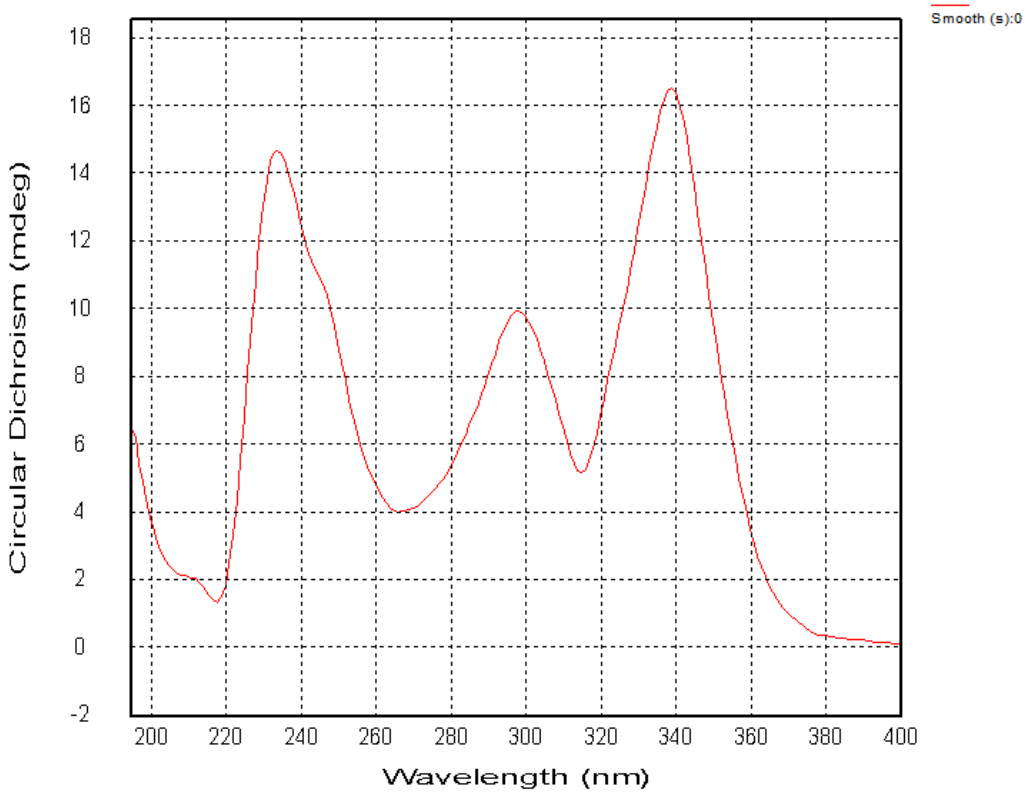
Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C30 H34 O7	506.2305	505.2232	505.2239	-0.70	-1.39	14.0000

--- End Of Report ---

CD spectra, and computational ECD data of 1

Figure S17. CD spectrum of 1



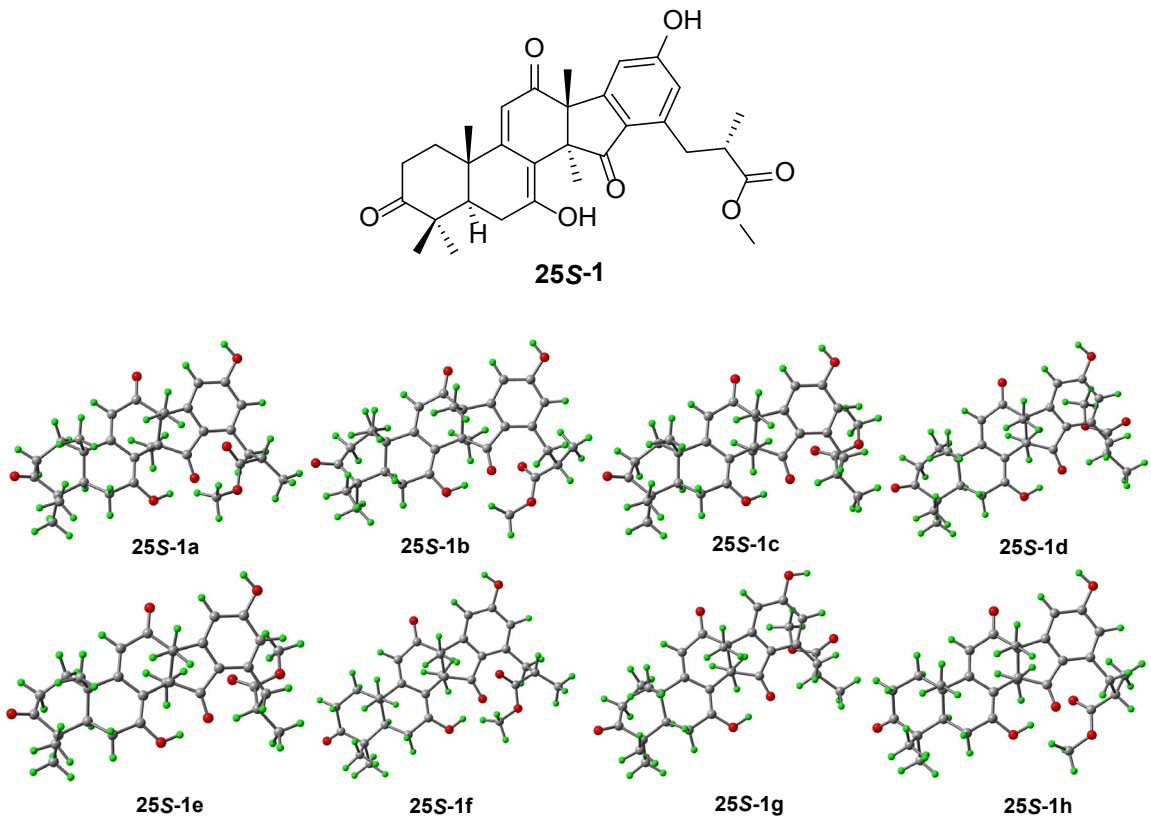


Figure S18. Eight optimized conformers of 25*S*-1.

Table S1. Conformational analysis of eight optimized conformers of 25*S*-1 in the gas phase (T = 298.15 K)

Conformer	E (Hartree)	C (Hartree)	G (kcal/mol)	ΔG (kcal/mol)	Population
25*S*-1a	-1729.410318	0.543872	-1084880.983385	0.000000	34.76%
25*S*-1b	-1729.411841	0.54582	-1084880.717145	0.266240	22.17%
25*S*-1c	-1729.409594	0.543902	-1084880.510563	0.472823	15.64%
25*S*-1d	-1729.409224	0.544106	-1084880.150359	0.833026	8.51%
25*S*-1e	-1729.409215	0.54412	-1084880.135663	0.847722	8.30%
25*S*-1f	-1729.410413	0.545588	-1084879.966505	1.016880	6.24%
25*S*-1g	-1729.410525	0.546285	-1084879.599311	1.384074	3.36%
25*S*-1h	-1729.409394	0.546279	-1084878.893294	2.090091	1.02%

Electronic energy obtained at M062X/6-311+G(2d,p) EmpiricalDispersion=GD3 level of theory; Thermal correction to Gibbs free energy obtained at B3LYP/6-31G(d) Scale=0.9813 Dispersion=GD3BJ, Empirical Dispersion=GD3 level of theory; Gibbs free energy (E + C); The relative Gibbs free energy; The Boltzmann distribution of each conformer.

Table S2. Atomic coordinates (Å) of 25*S*-1a obtained at the mPW1PW91/6-31+G(d,p) level of theory in the $CHCl_3$.

C	5.43647	0.687368	1.983609	O	1.142032	-2.48122	-1.313614
C	6.252076	0.052855	0.877303	C	-4.675978	0.153708	2.880184
C	5.538994	-1.079198	0.122506	H	6.055752	1.421951	2.502846
C	3.99523	-0.814673	0.123761	H	5.19077	-0.105608	2.701746
C	3.603562	0.686712	0.131942	H	4.278869	2.389806	1.311197
C	4.121694	1.317825	1.461083	H	3.354018	1.219946	2.233647
C	3.276767	-1.568825	-0.991716	H	3.61391	-1.22962	-1.97869
C	1.79168	-1.396568	-0.896628	H	3.489067	-2.641068	-0.945127
C	1.229259	-0.236699	-0.437498	H	2.176008	2.841508	0.824878
C	2.074974	0.854084	0.037448	H	3.937473	1.011782	-2.022339
C	-0.256932	0.017442	-0.220147	H	3.85263	2.488013	-1.0578
C	-0.609589	1.469041	-0.668532	H	5.309491	1.489523	-1.005238
C	0.159747	2.462408	0.184398	H	0.910066	1.668719	-2.252077
C	1.545779	2.067973	0.400782	H	-0.634328	0.987347	-2.809826
C	-1.409585	-0.767041	-0.875968	H	-0.509332	2.71823	-2.448827
C	-2.558632	0.139414	-0.898978	H	-2.650707	3.505631	-0.310656
C	-2.116652	1.454651	-0.653147	H	5.931991	-0.418714	-1.940458
C	4.217722	1.457343	-1.06254	H	5.823973	-2.17546	-1.742727
C	-0.174338	1.722915	-2.14239	H	7.252216	-1.292444	-1.16953
C	-3.007584	2.503185	-0.52415	H	6.893709	-2.593687	0.932871
C	6.165823	-1.249457	-1.271304	H	5.483497	-2.290671	1.967213
C	5.821936	-2.372502	0.928674	H	5.300016	-3.221301	0.473375
C	-0.54089	-0.202508	1.30662	H	-1.561615	0.074332	1.579891
C	-4.374463	2.209186	-0.648036	H	0.16133	0.380077	1.90566
C	-4.825141	0.903557	-0.909989	H	-0.400513	-1.262344	1.53936
C	-3.928901	-0.154239	-1.036492	H	-5.894423	0.731056	-0.973174
C	-4.435209	-1.56795	-1.172901	H	-5.478788	-1.551359	-1.503701
C	-4.359748	-2.343893	0.173412	H	-3.845219	-2.121015	-1.90788
C	-5.03287	-1.490333	1.231664	H	-3.307284	-2.462361	0.440418
C	-5.035709	-3.711215	0.053468	H	-4.589529	-4.283265	-0.766421
O	-4.125635	-0.822327	1.980451	H	-6.105709	-3.590688	-0.139768
O	-6.231386	-1.358145	1.360585	H	-4.92105	-4.290542	0.975637
O	-1.401738	-1.957429	-1.210445	H	-4.89705	4.016911	-0.328965
O	7.39482	0.388346	0.627322	H	0.146992	-2.370765	-1.263852
O	-0.314431	3.534269	0.555827	H	-5.36221	-0.317903	3.587459
O	-5.327331	3.166519	-0.513843	H	-3.821253	0.587179	3.399563
H	3.602303	-1.221788	1.06639	H	-5.212679	0.921085	2.316025

Table S3. Atomic coordinates (Å) of 25*S*-1b obtained at the mPW1PW91/6-31+G(d,p) level of theory in the $CHCl_3$.

C	5.759858	-1.445118	-0.666693	O	0.765911	2.223533	1.293954
C	6.04953	0.016826	-0.936541	C	-2.012762	4.200468	-0.545083
C	5.265441	1.036305	-0.091966	H	6.136739	-1.702769	0.33159
C	3.759677	0.613797	-0.010062	H	6.320639	-2.041485	-1.391063
C	3.422237	-0.888607	0.226278	H	4.10121	-2.806841	-0.559685
C	4.256118	-1.741104	-0.752781	H	3.912318	-1.551508	-1.777266
C	2.957033	1.476814	0.960561	H	3.305419	1.345284	1.9929
C	1.490261	1.174391	0.894994	H	3.068654	2.541521	0.737806
C	0.995582	-0.017723	0.44108	H	2.127021	-2.974503	-0.964205
C	1.908964	-1.071086	-0.004947	H	3.100188	-0.804426	2.40583
C	-0.463047	-0.276781	0.078384	H	3.343829	-2.424997	1.753883
C	-0.825471	-1.773558	0.321703	H	4.723322	-1.341413	1.957893
C	0.046067	-2.650947	-0.557138	H	-0.86363	-3.226537	1.944789
C	1.446839	-2.237745	-0.55681	H	0.529874	-2.128314	2.024255
C	-1.678341	0.397014	0.74345	H	-1.086283	-1.555678	2.490628
C	-2.814508	-0.503044	0.534341	H	-2.783015	-3.773275	-0.465989
C	-2.325449	-1.771143	0.15969	H	7.019194	1.440395	1.125146
C	3.670026	-1.383162	1.67447	H	6.001224	0.174406	1.819392
C	-0.534569	-2.194106	1.793567	H	5.499881	1.865573	1.919376
C	-3.178152	-2.809231	-0.162015	H	6.419405	2.664163	-0.946058
C	5.9827	1.122055	1.277977	H	4.864064	2.417944	-1.738044
C	5.371566	2.414387	-0.767879	H	4.930477	3.19683	-0.143449
C	-0.609917	0.093329	-1.437749	H	-1.578257	-0.205414	-1.841596
C	-4.556696	-2.556643	-0.090311	H	0.184973	-0.389136	-2.009629
C	-5.052479	-1.30823	0.320482	H	-0.524924	1.175523	-1.555572
C	-4.197105	-0.254046	0.635388	H	-6.128644	-1.181483	0.376577
C	-4.764151	1.08553	1.04396	H	-5.731708	0.918002	1.530197
C	-5.0197	2.083381	-0.128467	H	-4.103558	1.565984	1.768508
C	-3.703565	2.56673	-0.710959	H	-5.510413	2.952565	0.321229
C	-5.904172	1.49737	-1.231343	H	-6.842957	1.1207	-0.811202
O	-3.291825	3.702858	-0.118483	H	-5.394387	0.676693	-1.740594
O	-3.087836	2.005223	-1.595119	H	-6.147117	2.25966	-1.978663
O	-1.711558	1.498152	1.304933	H	-5.01587	-4.313924	-0.676196
O	6.870477	0.36144	-1.765925	H	-0.212108	2.004911	1.345919
O	-0.364229	-3.67156	-1.104459	H	-1.980143	4.288574	-1.633534
O	-5.477208	-3.506965	-0.396391	H	-1.908305	5.177801	-0.073652
H	3.359966	0.824904	-1.012823	H	-1.217829	3.532077	-0.208263

Table S4. Atomic coordinates (Å) of 25*S*-1c obtained at the mPW1PW91/6-31+G(d,p) level of theory in the $CHCl_3$.

C	5.440003	0.693713	1.978499	O	1.148197	-2.484297	-1.31286
C	6.255491	0.060275	0.871509	C	-4.620833	0.158465	2.906038
C	5.543293	-1.072801	0.117386	H	6.058691	1.429239	2.497128
C	3.999111	-0.810647	0.120198	H	5.196197	-0.099639	2.696904
C	3.605046	0.690001	0.128771	H	4.278839	2.394258	1.307201
C	4.123619	1.322033	1.45727	H	3.356923	1.222978	2.230628
C	3.280572	-1.565586	-0.994634	H	3.615898	-1.225218	-1.981829
C	1.795112	-1.396584	-0.897223	H	3.495098	-2.637434	-0.948738
C	1.230943	-0.238104	-0.437901	H	2.17341	2.841714	0.822972
C	2.076014	0.854691	0.035877	H	3.936212	1.015667	-2.025826
C	-0.255525	0.014647	-0.219219	H	3.849973	2.491601	-1.061077
C	-0.613264	1.466181	-0.667223	H	5.308663	1.495598	-1.010236
C	0.155664	2.458401	0.188723	H	-0.636483	0.986246	-2.808954
C	1.544794	2.066446	0.399539	H	-0.51575	2.717084	-2.445643
C	-1.405204	-0.774712	-0.871718	H	0.906227	1.670223	-2.250255
C	-2.556051	0.128868	-0.900911	H	-2.686619	3.504461	-0.319516
C	-2.121653	1.449593	-0.654587	H	5.827791	-2.168423	-1.748271
C	4.216845	1.461569	-1.066282	H	7.255525	-1.283505	-1.17647
C	-0.1783	1.722265	-2.140537	H	5.933191	-0.411476	-1.9458
C	-3.015318	2.494965	-0.529934	H	6.901079	-2.585523	0.926049
C	6.168938	-1.242029	-1.277084	H	5.491681	-2.284347	1.9621
C	5.828986	-2.365732	0.923145	H	5.307584	-3.215182	0.468418
C	-0.538769	-0.203864	1.308067	H	-1.558672	0.075938	1.581518
C	-4.380335	2.192684	-0.661119	H	0.16458	0.378882	1.905542
C	-4.820874	0.884051	-0.924738	H	-0.399918	-1.263602	1.542202
C	-3.920533	-0.173436	-1.044371	H	-5.887997	0.683232	-0.991316
C	-4.425883	-1.588396	-1.169737	H	-5.464833	-1.575973	-1.515512
C	-4.371529	-2.340333	0.190976	H	-3.826025	-2.153389	-1.886944
C	-5.024986	-1.449505	1.231102	H	-3.322745	-2.478827	0.462563
C	-5.080848	-3.693144	0.09686	H	-4.978063	-4.258965	1.028772
O	-4.104725	-0.84001	2.010346	H	-4.650579	-4.290353	-0.71356
O	-6.217924	-1.24541	1.321068	H	-6.147998	-3.549953	-0.097443
O	-1.39727	-1.967199	-1.199194	H	-6.161389	2.886516	-0.622486
O	7.397748	0.396959	0.620707	H	0.15368	-2.377375	-1.258641
O	-0.318366	3.525446	0.56956	H	-5.081407	0.969472	2.335771
O	-5.25591	3.219483	-0.515248	H	-5.363032	-0.275355	3.580088
H	3.607796	-1.218525	1.063182	H	-3.758684	0.526337	3.461986

Table S5. Atomic coordinates (Å) of 25*S*-1d obtained at the mPW1PW91/6-31+G(d,p) level of theory in the $CHCl_3$.

C	5.465281	0.604678	2.047833	O	1.184145	-2.417893	-1.399124
C	6.287683	0.007423	0.926054	C	-6.496147	-0.336142	2.257945
C	5.575634	-1.091881	0.123337	H	6.083557	1.315774	2.599947
C	4.033348	-0.819557	0.121345	H	5.208422	-0.213144	2.733471
C	3.648895	0.682405	0.18154	H	4.323553	2.337375	1.42783
C	4.15879	1.261639	1.537238	H	3.383834	1.14035	2.299044
C	3.320352	-1.528253	-1.026854	H	3.66712	-1.154784	-1.998017
C	1.835341	-1.35243	-0.936145	H	3.527171	-2.602563	-1.018002
C	1.274337	-0.208865	-0.437001	H	2.22788	2.819896	0.935676
C	2.121742	0.860548	0.081714	H	5.368266	1.518122	-0.910933
C	-0.21187	0.041231	-0.214588	H	4.002738	1.084844	-1.956437
C	-0.558246	1.509176	-0.612088	H	3.916345	2.524863	-0.938843
C	0.213966	2.472915	0.271413	H	-0.450405	2.818099	-2.348949
C	1.596406	2.063903	0.482759	H	0.96391	1.755736	-2.186506
C	-1.363592	-0.712519	-0.903728	H	-0.582663	1.100908	-2.769196
C	-2.512464	0.196601	-0.886993	H	-2.588291	3.542622	-0.190433
C	-2.065101	1.501229	-0.598717	H	7.29915	-1.265401	-1.160965
C	4.276848	1.49333	-0.978524	H	5.989491	-0.357419	-1.910321
C	-0.120446	1.811305	-2.076372	H	5.871824	-2.119654	-1.778762
C	-2.950653	2.55004	-0.437957	H	5.49831	-2.370677	1.921118
C	6.213874	-1.213427	-1.270407	H	5.322759	-3.244177	0.392331
C	5.845229	-2.415749	0.883152	H	6.915824	-2.642697	0.888029
C	-0.501791	-0.237985	1.302203	H	-1.526573	0.009112	1.587692
C	-4.318122	2.266792	-0.571191	H	0.191004	0.331662	1.924391
C	-4.773973	0.972359	-0.874112	H	-0.345421	-1.303446	1.495441
C	-3.883855	-0.086366	-1.033006	H	-5.843661	0.807861	-0.94834
C	-4.400873	-1.492505	-1.208859	H	-5.458014	-1.456703	-1.489766
C	-4.252353	-2.327558	0.09253	H	-3.85133	-2.011432	-1.999041
C	-4.693509	-1.495097	1.282101	H	-3.191346	-2.527132	0.253233
C	-5.015446	-3.653269	-0.013604	H	-4.646955	-4.228437	-0.869645
O	-6.018378	-1.226532	1.237098	H	-6.086888	-3.477601	-0.148349
O	-3.960772	-1.075003	2.152589	H	-4.878026	-4.261405	0.886769
O	-1.358255	-1.884448	-1.297742	H	-4.833949	4.063147	-0.18547
O	7.434519	0.345509	0.698907	H	0.189609	-2.303366	-1.35408
O	-0.253471	3.539314	0.666111	H	-7.57032	-0.250251	2.093009
O	-5.268133	3.223712	-0.40759	H	-6.287669	-0.741742	3.250735
H	3.630362	-1.258967	1.044977	H	-6.012552	0.639524	2.160275

Table S6. Atomic coordinates (Å) of 25*S*-1e obtained at the mPW1PW91/6-31+G(d,p) level of theory in the $CHCl_3$.

C	5.464341	0.603125	2.049009	O	1.184483	-2.417435	-1.400442
C	6.287165	0.006949	0.926927	C	-6.49708	-0.33672	2.257241
C	5.575652	-1.092148	0.123555	H	6.082352	1.313647	2.602171
C	4.033311	-0.819614	0.120909	H	5.206661	-0.215207	2.733686
C	3.649016	0.682399	0.181677	H	4.323805	2.336662	1.428919
C	4.1584	1.260985	1.537922	H	3.382938	1.1398	2.299221
C	3.320641	-1.527603	-1.027942	H	3.667442	-1.153311	-1.998764
C	1.835562	-1.352045	-0.937101	H	3.527611	-2.601896	-1.019846
C	1.27448	-0.208774	-0.437298	H	2.228197	2.820007	0.935275
C	2.121917	0.860615	0.081447	H	5.368826	1.518839	-0.909536
C	-0.211703	0.041325	-0.214745	H	4.003926	1.085796	-1.955965
C	-0.558169	1.509355	-0.612296	H	3.916777	2.525342	-0.937809
C	0.214239	2.473181	0.270959	H	0.963801	1.755854	-2.186984
C	1.596629	2.064063	0.482336	H	-0.582794	1.100783	-2.769383
C	-1.363433	-0.712447	-0.903727	H	-0.450642	2.818062	-2.349372
C	-2.512333	0.196689	-0.887039	H	-2.588145	3.54265	-0.190123
C	-2.065001	1.501318	-0.598708	H	5.991348	-0.356423	-1.909235
C	4.277449	1.493864	-0.977711	H	5.871864	-2.118736	-1.779209
C	-0.120554	1.811326	-2.076716	H	7.299677	-1.26636	-1.160154
C	-2.950577	2.55009	-0.43769	H	5.322482	-3.244526	0.391247
C	6.214468	-1.213238	-1.269945	H	6.915154	-2.643451	0.888596
C	5.844572	-2.416372	0.882949	H	5.496799	-2.371821	1.920654
C	-0.501497	-0.237698	1.302089	H	0.191053	0.332334	1.924208
C	-4.318069	2.266783	-0.570686	H	-0.344662	-1.303061	1.495539
C	-4.77389	0.972341	-0.873685	H	-1.52638	0.008961	1.587608
C	-3.883739	-0.086311	-1.03289	H	-5.843606	0.807823	-0.947736
C	-4.400648	-1.492516	-1.20882	H	-5.457817	-1.456847	-1.489606
C	-4.251977	-2.327467	0.092619	H	-3.851	-2.011333	-1.998984
C	-4.693672	-1.49511	1.282087	H	-3.190932	-2.526793	0.253416
C	-5.014746	-3.653453	-0.013292	H	-4.877911	-4.260899	0.887644
O	-6.018763	-1.227215	1.23666	H	-4.645507	-4.229201	-0.868633
O	-3.961443	-1.074481	2.152711	H	-6.086135	-3.478141	-0.148951
O	-1.358172	-1.884406	-1.297649	H	-4.833945	4.063041	-0.184636
O	7.433629	0.346228	0.699622	H	0.189937	-2.303277	-1.354754
O	-0.253101	3.539697	0.665516	H	-7.570978	-0.249903	2.090964
O	-5.268114	3.223612	-0.406781	H	-6.290232	-0.742872	3.250152
H	3.629875	-1.259424	1.044133	H	-6.012496	0.638543	2.160559

Table S7. Atomic coordinates (Å) of 25*S*-1f obtained at the mPW1PW91/6-31+G(d,p) level of theory in the $CHCl_3$.

C	-5.834982	1.335858	0.531256	O	-0.659577	-2.387954	-0.712563
C	-6.216104	0.174576	-0.363533	C	2.232608	-3.759672	1.300736
C	-5.299702	-1.0606	-0.310702	H	-5.989725	1.041511	1.577447
C	-3.800331	-0.609942	-0.324797	H	-6.517414	2.163576	0.321376
C	-3.380053	0.599814	0.560709	H	-4.155672	2.596294	0.980908
C	-4.373841	1.755113	0.316628	H	-4.252038	2.122643	-0.710007
C	-2.831048	-1.768627	-0.099209	H	-2.926547	-2.175351	0.915539
C	-1.411263	-1.349039	-0.337917	H	-3.032593	-2.599141	-0.780565
C	-0.993356	-0.052696	-0.211755	H	-2.276741	3.089007	0.480642
C	-1.940523	0.995607	0.173955	H	-4.284472	0.018377	2.495309
C	0.365123	0.487915	-0.644525	H	-2.612324	-0.517846	2.299276
C	0.822831	1.615867	0.326147	H	-2.960359	1.182681	2.606429
C	-0.166793	2.761627	0.256695	H	1.50047	0.252597	1.912231
C	-1.555868	2.307263	0.277867	H	1.220754	1.918695	2.444789
C	1.661037	-0.339579	-0.746317	H	-0.162735	0.848821	2.143923
C	2.768699	0.587792	-0.541024	H	2.683538	3.848647	0.481816
C	2.26623	1.81347	-0.05912	H	-5.612543	-1.313005	1.874731
C	-3.313332	0.29137	2.078636	H	-5.115675	-2.781706	1.027646
C	0.839201	1.117148	1.805073	H	-6.763877	-2.171729	0.846867
C	3.089477	2.906406	0.127646	H	-5.044866	-2.881637	-1.495201
C	-5.715486	-1.870434	0.941969	H	-6.650284	-2.139127	-1.623268
C	-5.581337	-1.929831	-1.548845	H	-5.282869	-1.415595	-2.468284
C	0.188534	1.031318	-2.104437	H	1.056633	1.61048	-2.430308
C	4.453232	2.745343	-0.165563	H	-0.697691	1.665687	-2.163586
C	4.971887	1.510313	-0.58988	H	0.056499	0.185562	-2.785859
C	4.145069	0.405227	-0.772524	H	6.040142	1.438896	-0.770317
C	4.735199	-0.931055	-1.144903	H	4.037119	-1.507696	-1.755959
C	5.137475	-1.785922	0.096423	H	5.64811	-0.770393	-1.729227
C	3.904355	-2.147595	0.912463	H	5.734722	-1.144206	0.753691
C	5.962868	-3.001277	-0.336532	H	6.244359	-3.616874	0.523375
O	3.442191	-3.377885	0.626853	H	6.880278	-2.67167	-0.83625
O	3.384967	-1.407409	1.724637	H	5.39822	-3.631659	-1.0289
O	1.748491	-1.531108	-1.070352	H	4.864887	4.558217	0.264396
O	-7.204422	0.21454	-1.072267	H	0.284613	-2.117417	-0.919684
O	0.165059	3.943757	0.301992	H	2.087912	-4.813986	1.064366
O	5.338936	3.765875	-0.03536	H	2.332165	-3.612287	2.378597
H	-3.628799	-0.263132	-1.35443	H	1.392815	-3.170328	0.927239

Table S8. Atomic coordinates (Å) of 25*S*-1g obtained at the mPW1PW91/6-31+G(d,p) level of theory in the $CHCl_3$.

C	5.374689	0.704774	1.818504	O	0.788847	-2.217167	-1.34523
C	6.098241	0.084863	0.643099	C	-2.074442	-4.177018	0.696376
C	5.304893	-1.003145	-0.095984	H	6.047037	1.404134	2.320114
C	3.771943	-0.697289	0.012673	H	5.149534	-0.103811	2.525872
C	3.423938	0.812878	0.092334	H	4.233196	2.459748	1.267136
C	4.050287	1.38955	1.399725	H	3.333141	1.294351	2.219469
C	2.966487	-1.395749	-1.0783	H	3.264971	-1.04781	-2.074715
C	1.495379	-1.173046	-0.908729	H	3.140091	-2.476179	-1.06709
C	0.9928	-0.018248	-0.375834	H	2.10349	2.955549	1.0013
C	1.897331	1.022131	0.108148	H	3.639574	2.642986	-1.058495
C	-0.471338	0.256753	-0.050389	H	5.068425	1.60604	-1.138516
C	-0.8144	1.744626	-0.371557	H	3.615513	1.195537	-2.069599
C	0.039066	2.661046	0.485559	H	0.596344	2.017977	-2.041904
C	1.426536	2.223359	0.576148	H	-1.003506	1.420727	-2.535452
C	-1.676652	-0.438996	-0.71061	H	-0.799106	3.116798	-2.063069
C	-2.809089	0.479084	-0.57338	H	-2.771836	3.795725	0.259882
C	-2.317876	1.760863	-0.251	H	5.442494	-2.049342	-2.006755
C	3.974741	1.603858	-1.119585	H	6.926271	-1.218122	-1.500973
C	-0.475801	2.093252	-1.851816	H	5.582671	-0.290375	-2.160305
C	-3.16887	2.820819	-0.004346	H	5.332433	-2.270015	1.711857
C	5.837049	-1.146459	-1.531668	H	5.026992	-3.147988	0.206044
C	5.60125	-2.328263	0.651615	H	6.664273	-2.578422	0.57977
C	-0.660689	-0.049193	1.474717	H	-1.63627	0.274249	1.840201
C	-4.547322	2.576097	-0.098241	H	0.122507	0.449515	2.048304
C	-5.044231	1.3124	-0.458008	H	-0.590394	-1.126483	1.638844
C	-4.19128	0.236842	-0.697793	H	-6.119787	1.191788	-0.535549
C	-4.762081	-1.11571	-1.055509	H	-5.716018	-0.962348	-1.572292
C	-5.055924	-2.054261	0.156586	H	-4.089777	-1.636507	-1.740366
C	-3.757851	-2.529687	0.783778	H	-5.551361	-2.935947	-0.262675
C	-5.95176	-1.405386	1.213841	H	-6.876173	-1.034227	0.758498
O	-3.345553	-3.689038	0.237752	H	-5.43919	-0.569926	1.695487
O	-3.154245	-1.944266	1.660659	H	-6.221013	-2.129088	1.989948
O	-1.707961	-1.568081	-1.214195	H	-5.004529	4.364941	0.38418
O	7.231002	0.398328	0.327257	H	-0.198261	-2.040068	-1.3168
O	-0.377194	3.718089	0.955137	H	-1.970782	-5.172488	0.26427
O	-5.466338	3.547985	0.135881	H	-1.274056	-3.52504	0.340284
H	3.426982	-1.124362	0.965173	H	-2.052485	-4.222792	1.787702

Table S9. Atomic coordinates (Å) of 25*S*-1h obtained at the mPW1PW91/6-31+G(d,p) level of theory in the $CHCl_3$.

C	-5.709114	1.296835	-0.856704	O	-0.625946	-2.373884	-0.694769
C	-6.178385	0.09846	-0.059224	C	2.208872	-3.814108	1.186386
C	-5.267578	-1.134971	-0.155964	H	-6.458066	2.087912	-0.779056
C	-3.788393	-0.674176	-0.383765	H	-5.662326	0.987706	-1.908978
C	-3.43727	0.690951	0.264776	H	-4.431881	2.628952	0.277309
C	-4.309044	1.791113	-0.414912	H	-3.782299	2.183495	-1.289254
C	-2.777617	-1.749657	0.006795	H	-2.830701	-1.970188	1.079849
C	-1.382243	-1.331172	-0.341872	H	-2.981166	-2.69058	-0.513063
C	-0.985803	-0.02498	-0.28018	H	-2.280769	3.097827	0.455156
C	-1.944252	1.019623	0.075177	H	-3.378354	1.652033	2.212767
C	0.381837	0.523835	-0.666079	H	-4.779648	0.595263	2.007773
C	0.820406	1.601496	0.370635	H	-3.174901	-0.098566	2.306077
C	-0.158975	2.758603	0.336421	H	1.165247	1.795479	2.510535
C	-1.549473	2.319181	0.268682	H	-0.224093	0.76203	2.120537
C	1.673392	-0.308491	-0.77335	H	1.437708	0.152908	1.90566
C	2.780963	0.601607	-0.499726	H	2.691399	3.807181	0.684868
C	2.274522	1.805366	0.031681	H	-5.085347	-1.598685	1.988215
C	-3.713359	0.701701	1.788498	H	-5.010834	-3.013106	0.924846
C	0.790993	1.031148	1.822931	H	-6.554536	-2.18841	1.216835
C	3.099993	2.881474	0.292211	H	-5.705311	-1.303215	-2.3132
C	-5.482987	-2.037139	1.070516	H	-5.103151	-2.791614	-1.569264
C	-5.742869	-1.917201	-1.406845	H	-6.770867	-2.267208	-1.271112
C	0.24827	1.132688	-2.103529	H	-0.631963	1.775428	-2.159294
C	4.469068	2.72601	0.021936	H	0.13194	0.319076	-2.825813
C	4.990033	1.510657	-0.4532	H	1.128043	1.720294	-2.37857
C	4.16115	0.421931	-0.709297	H	6.061689	1.440979	-0.613035
C	4.751117	-0.898489	-1.134503	H	4.059458	-1.442725	-1.781497
C	5.13081	-1.811572	0.071679	H	5.673337	-0.715998	-1.697485
C	3.885637	-2.194226	0.859764	H	5.727869	-1.205693	0.76239
C	5.9482	-3.015494	-0.405743	H	6.215437	-3.670326	0.429314
O	3.422207	-3.412763	0.530112	H	6.873455	-2.674193	-0.882655
O	3.359574	-1.478091	1.689049	H	5.383936	-3.609849	-1.129605
O	1.758757	-1.485828	-1.146676	H	4.881426	4.511087	0.554934
O	-7.214406	0.098386	0.579265	H	0.29994	-2.092096	-0.960716
O	0.181572	3.932748	0.462697	H	2.3098	-3.715246	2.269697
O	5.357421	3.73255	0.223745	H	1.372919	-3.203056	0.840698
H	-3.664721	-0.521913	-1.465496	H	2.056478	-4.85594	0.904063

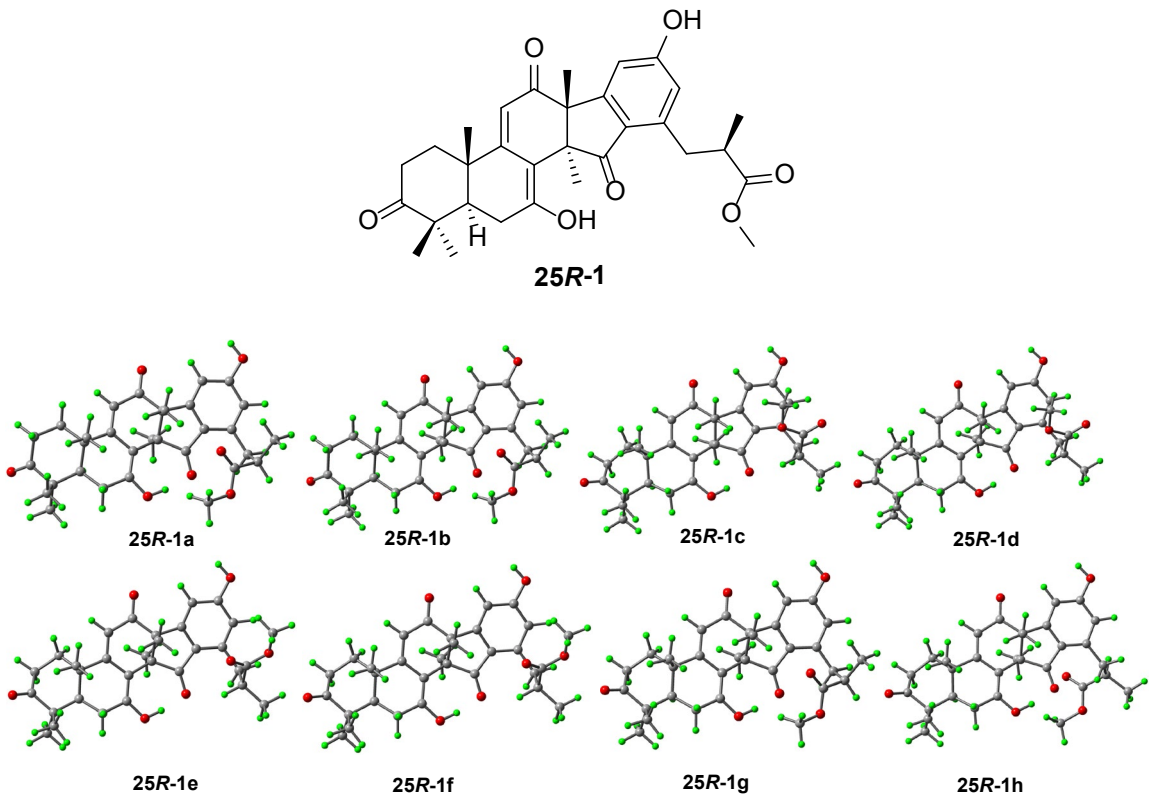


Figure S19. Eight optimized conformers of 25*R*-1.

Table S10. Conformational analysis of eight optimized conformers of 25*R*-1 in the gas phase (T = 298.15 K)

Conformer	E (Hartree)	C (Hartree)	G (kcal/mol)	ΔG (kcal/mol)	Population
25*R*-1a	-1729.411556	0.546159	-1084880.325	0	22.16%
25*R*-1b	-1729.411551	0.546163	-1084880.32	0.005390311	21.96%
25*R*-1c	-1729.409429	0.544149	-1084880.252	0.073268068	19.58%
25*R*-1d	-1729.409429	0.54415	-1084880.251	0.073939503	19.56%
25*R*-1e	-1729.408169	0.544145	-1084879.463	0.861602606	5.17%
25*R*-1f	-1729.408168	0.544145	-1084879.463	0.861728108	5.17%
25*R*-1g	-1729.410465	0.546743	-1084879.274	1.050545867	3.76%
25*R*-1h	-1729.409242	0.545851	-1084879.067	1.258377179	2.65%

Electronic energy obtained at M062X/6-311+G(2d,p) EmpiricalDispersion=GD3 level of theory; Thermal correction to Gibbs free energy obtained at B3LYP/6-31G(d) Scale=0.9813 Empirical Dispersion=GD3 level of theory; Gibbs free energy (E + C); The relative Gibbs free energy; The Boltzmann distribution of each conformer.

Table S11. Atomic coordinates (Å) of 25*R*-1a obtained at the mPW1PW91/6-31+G(d,p) level of theory in the $CHCl_3$.

C	-5.777995	1.447561	0.645503	O	-0.747262	-2.393071	-0.817327
C	-6.212081	0.329754	-0.279904	C	2.104719	-4.013074	1.025165
C	-5.335018	-0.934717	-0.284852	H	-5.922728	1.122908	1.684122
C	-3.822465	-0.531239	-0.313543	H	-6.437403	2.30285	0.476592
C	-3.347504	0.634903	0.602409	H	-4.051346	2.639048	1.103666
C	-4.308526	1.828016	0.416232	H	-4.194395	2.226006	-0.599875
C	-2.886957	-1.726758	-0.144455	H	-2.978114	-2.164838	0.85754
C	-1.458598	-1.344394	-0.39411	H	-3.126585	-2.526746	-0.849599
C	-0.996599	-0.067069	-0.232355	H	-2.17016	3.091633	0.569007
C	-1.903758	0.998197	0.200026	H	-4.233605	0.020281	2.535138
C	0.371391	0.44297	-0.672365	H	-2.58432	-0.563938	2.28823
C	0.879263	1.530579	0.31907	H	-2.869502	1.136081	2.656942
C	-0.075784	2.707133	0.29653	H	-0.098622	0.749823	2.134905
C	-1.477365	2.294341	0.33202	H	1.537676	0.103196	1.855888
C	1.63885	-0.421815	-0.815933	H	1.325879	1.763862	2.436876
C	2.779068	0.463799	-0.600692	H	2.802749	3.709877	0.471835
C	2.320704	1.694279	-0.088374	H	-5.18287	-2.704577	0.992492
C	-3.261954	0.274587	2.107921	H	-6.812768	-2.034788	0.866036
C	0.90559	0.99281	1.783999	H	-5.613025	-1.249197	1.897128
C	3.176033	2.763319	0.094119	H	-6.743491	-1.927514	-1.604212
C	-5.753164	-1.771634	0.949089	H	-5.370834	-1.218268	-2.452676
C	-5.667331	-1.753432	-1.544638	H	-5.159865	-2.72243	-1.533001
C	0.18931	1.029816	-2.114579	H	1.070827	1.588269	-2.440612
C	4.525845	2.573833	-0.241597	H	0.01787	0.206937	-2.814908
C	5.002009	1.332588	-0.697554	H	-0.675989	1.694532	-2.1421
C	4.145194	0.248078	-0.867808	H	6.062076	1.23932	-0.909639
C	4.682963	-1.100905	-1.273755	H	3.962826	-1.619936	-1.909828
C	5.034401	-2.029957	-0.067869	H	5.607259	-0.962935	-1.845779
C	3.78767	-2.395577	0.721273	H	5.427758	-2.954475	-0.501779
C	6.076801	-1.408772	0.867209	H	5.669021	-0.528312	1.368673
O	3.322646	-3.609685	0.37738	H	6.383829	-2.125139	1.636284
O	3.272518	-1.691252	1.567727	H	6.967916	-1.111123	0.304021
O	1.682335	-1.603197	-1.182206	H	4.995124	4.369859	0.200203
O	-7.210848	0.424711	-0.968437	H	0.201954	-2.145817	-1.030223
O	0.292729	3.877274	0.365183	H	1.941765	-5.047075	0.720911

Table S12. Atomic coordinates (Å) of 25*R*-1b obtained at the mPW1PW91/6-31+G(d,p) level of theory in the $CHCl_3$.

C	-5.777894	1.447809	0.645263	O	-0.747435	-2.393035	-0.817686
C	-6.212126	0.329775	-0.279813	C	2.104312	-4.012671	1.025546
C	-5.334961	-0.934614	-0.284897	H	-5.922671	1.123371	1.683952
C	-3.822385	-0.531175	-0.31343	H	-6.43732	2.303052	0.476182
C	-3.347417	0.635065	0.602387	H	-4.051205	2.639334	1.103252
C	-4.308402	1.828186	0.415969	H	-4.194253	2.225999	-0.600203
C	-2.886932	-1.726701	-0.144054	H	-2.97788	-2.164249	0.858197
C	-1.458629	-1.344378	-0.394172	H	-3.126747	-2.527006	-0.848765
C	-0.996553	-0.067079	-0.232426	H	-2.169878	3.091667	0.569185
C	-1.903629	0.998224	0.20009	H	-4.233616	0.020612	2.535161
C	0.371414	0.442927	-0.672504	H	-2.584293	-0.563547	2.288395
C	0.879391	1.530395	0.319005	H	-2.869551	1.136501	2.6569
C	-0.07554	2.707007	0.296689	H	1.32603	1.763436	2.436823
C	-1.477143	2.294328	0.33218	H	-0.098604	0.749557	2.134763
C	1.638852	-0.421888	-0.816317	H	1.53762	0.102743	1.855682
C	2.779119	0.463597	-0.600859	H	2.802845	3.709625	0.471818
C	2.320821	1.694052	-0.088466	H	-5.613221	-1.24938	1.897027
C	-3.261962	0.274929	2.107956	H	-5.182788	-2.704579	0.992235
C	0.905658	0.99246	1.783915	H	-6.812768	-2.034973	0.865705
C	3.176152	2.763092	0.094058	H	-5.159937	-2.722313	-1.53305
C	-5.753195	-1.7717	0.948892	H	-6.743392	-1.927003	-1.604554
C	-5.667189	-1.753198	-1.544792	H	-5.370348	-1.218106	-2.452768
C	0.189215	1.029945	-2.114615	H	0.017668	0.207116	-2.814985
C	4.525938	2.573611	-0.241715	H	-0.676064	1.694705	-2.141984
C	5.002076	1.332358	-0.697718	H	1.070716	1.5884	-2.440716
C	4.145244	0.24787	-0.867967	H	6.062133	1.239074	-0.909831
C	4.682958	-1.101157	-1.273744	H	3.962791	-1.620275	-1.909718
C	5.034283	-2.03	-0.067655	H	5.607283	-0.963358	-1.845741
C	3.787451	-2.395346	0.72146	H	5.427574	-2.954622	-0.501417
C	6.076755	-1.408831	0.867373	H	6.967863	-1.111081	0.304208
O	3.322302	-3.609416	0.37772	H	5.668951	-0.528426	1.368915
O	3.272328	-1.690844	1.56782	H	6.383865	-2.125209	1.636412
O	1.682246	-1.603229	-1.182752	H	4.995259	4.369615	0.200117
O	-7.211198	0.424466	-0.967952	H	0.201758	-2.145823	-1.030689
O	0.293069	3.877108	0.36568	H	2.206194	-3.93843	2.110873

Table S13. Atomic coordinates (Å) of 25*R*-1c obtained at the mPW1PW91/6-31+G(d,p) level of theory in the $CHCl_3$.

C	-5.904071	1.269096	-0.7348	O	-0.991136	-2.630043	-0.579482
C	-6.385646	0.143129	0.154926	C	4.66849	-0.110851	2.815359
C	-5.539209	-1.136743	0.084619	H	-6.611609	2.09853	-0.670327
C	-4.053808	-0.761988	-0.24208	H	-5.921852	0.89794	-1.767672
C	-3.60648	0.618176	0.307756	H	-4.516276	2.597541	0.264514
C	-4.463858	1.72073	-0.387223	H	-3.966118	2.043807	-1.305696
C	-3.076264	-1.861814	0.16181	H	-3.089485	-2.023254	1.246529
C	-1.678389	-1.53409	-0.265846	H	-3.345728	-2.818503	-0.29541
C	-1.21841	-0.245458	-0.299733	H	-2.346016	2.976517	0.264442
C	-2.1122	0.863107	0.022841	H	-4.853549	0.682648	2.121377
C	0.149646	0.210526	-0.793863	H	-3.267531	-0.069575	2.374222
C	0.685953	1.34807	0.126893	H	-3.397558	1.681532	2.191175
C	-0.251454	2.539536	0.063905	H	-0.273829	0.662605	1.990363
C	-1.656462	2.156146	0.100612	H	1.36359	0.010339	1.731329
C	1.404948	-0.679405	-0.894416	H	1.149174	1.69947	2.224291
C	2.555671	0.214191	-0.776682	H	2.639529	3.500572	0.163161
C	2.122277	1.47204	-0.311928	H	-6.800871	-2.049171	1.57639
C	-3.797308	0.726025	1.840721	H	-5.269208	-1.489797	2.240895
C	0.725919	0.892825	1.617956	H	-5.31348	-2.962681	1.258295
C	2.995589	2.534688	-0.180779	H	-5.524313	-2.87504	-1.237164
C	-5.732401	-1.958382	1.369998	H	-7.148431	-2.254286	-0.888476
C	-6.113872	-1.962823	-1.09436	H	-6.095118	-1.4025	-2.035356
C	-0.038645	0.709655	-2.267067	H	0.846679	1.233328	-2.636761
C	4.339944	2.310749	-0.517259	H	-0.229431	-0.152729	-2.912889
C	4.793505	1.044545	-0.928239	H	-0.894084	1.384675	-2.327597
C	3.914541	-0.026728	-1.059631	H	5.852565	0.917123	-1.125778
C	4.435601	-1.403513	-1.382183	H	3.81198	-1.888683	-2.138705
C	4.453575	-2.328875	-0.130053	H	5.455666	-1.323811	-1.771897
C	5.096536	-1.558238	1.007194	H	3.41792	-2.544195	0.139394
C	5.213966	-3.623795	-0.421445	H	4.787938	-4.124875	-1.296818
O	4.162297	-1.019926	1.825687	H	6.269572	-3.410624	-0.614231
O	6.287639	-1.377884	1.145393	H	5.157168	-4.313895	0.426866
O	1.433692	-1.892269	-1.136285	H	4.840093	4.1155	-0.150396
O	-7.383616	0.231255	0.845719	H	-0.04937	-2.421687	-0.852477
O	0.144145	3.703405	0.09215	H	3.794511	0.238293	3.365529

Table S14. Atomic coordinates (Å) of 25*R*-1d obtained at the mPW1PW91/6-31+G(d,p) level of theory in the $CHCl_3$.

C	-5.904069	1.269099	-0.734766	O	-0.991053	-2.629985	-0.579532
C	-6.385627	0.143098	0.15493	C	4.668049	-0.110951	2.815434
C	-5.539163	-1.136754	0.084607	H	-6.611616	2.098523	-0.670258
C	-4.053766	-0.761973	-0.242098	H	-5.921861	0.897977	-1.76765
C	-3.606447	0.61819	0.307755	H	-4.516276	2.597544	0.264548
C	-4.463853	1.72074	-0.387197	H	-3.96613	2.043834	-1.305673
C	-3.076208	-1.861799	0.161763	H	-3.089417	-2.02325	1.246482
C	-1.678341	-1.534052	-0.265901	H	-3.34567	-2.818483	-0.295467
C	-1.218382	-0.245416	-0.299777	H	-2.345973	2.976554	0.264436
C	-2.112172	0.863142	0.022819	H	-3.397504	1.681516	2.191187
C	0.149666	0.210564	-0.793913	H	-4.853482	0.68261	2.121407
C	0.68598	1.348093	0.126855	H	-3.267446	-0.069593	2.374204
C	-0.251417	2.539566	0.063844	H	-0.273875	0.662638	1.990288
C	-1.656427	2.156179	0.100588	H	1.363543	0.01035	1.731313
C	1.404955	-0.679386	-0.894468	H	1.149135	1.699484	2.224272
C	2.555694	0.214185	-0.776697	H	2.639592	3.500554	0.163191
C	2.122317	1.472037	-0.311935	H	-5.269152	-1.489808	2.240881
C	-3.797248	0.726007	1.840727	H	-5.313392	-2.962692	1.258276
C	0.725889	0.892847	1.617917	H	-6.800804	-2.049216	1.576378
C	2.995645	2.534668	-0.180755	H	-5.524236	-2.875046	-1.237178
C	-5.732335	-1.958403	1.369983	H	-7.148366	-2.254318	-0.888497
C	-6.113811	-1.962839	-1.094376	H	-6.095061	-1.402511	-2.03537
C	-0.038636	0.709703	-2.267113	H	0.846689	1.233369	-2.636817
C	4.340003	2.310708	-0.517203	H	-0.22944	-0.152678	-2.912935
C	4.793547	1.044502	-0.928203	H	-0.894069	1.384731	-2.327627
C	3.914567	-0.026751	-1.05963	H	5.852608	0.917067	-1.125733
C	4.435609	-1.403542	-1.382191	H	3.811988	-1.888699	-2.138721
C	4.453558	-2.328907	-0.130065	H	5.45568	-1.323851	-1.771891
C	5.096373	-1.558214	1.007233	H	3.417901	-2.544305	0.139311
C	5.214066	-3.623772	-0.421399	H	4.788136	-4.124877	-1.296806
O	4.162022	-1.020047	1.825694	H	6.269673	-3.410526	-0.614106
O	6.287449	-1.377755	1.145521	H	5.157251	-4.313878	0.426907
O	1.433672	-1.892247	-1.136359	H	4.840191	4.115429	-0.150258
O	-7.383576	0.231206	0.845756	H	-0.04928	-2.421593	-0.852474
O	0.144189	3.703431	0.092136	H	3.794002	0.23802	3.365609

Table S15. Atomic coordinates (Å) of 25*R*-1e obtained at the mPW1PW91/6-31+G(d,p) level of theory in the $CHCl_3$.

C	-5.960524	1.284331	-0.657047	O	-1.03998	-2.609098	-0.639082
C	-6.433597	0.134595	0.206327	C	6.55328	-0.390264	2.107683
C	-5.585155	-1.141094	0.096641	H	-6.669213	2.110324	-0.566073
C	-4.102964	-0.755188	-0.231987	H	-5.985072	0.939903	-1.699028
C	-3.653397	0.611021	0.34997	H	-4.568023	2.588469	0.367212
C	-4.518668	1.729719	-0.308377	H	-4.028859	2.078727	-1.221604
C	-3.12081	-1.863446	0.135904	H	-3.126235	-2.053431	1.216039
C	-1.726266	-1.52231	-0.291963	H	-3.391915	-2.808228	-0.344594
C	-1.267941	-0.232884	-0.29463	H	-2.398331	2.972858	0.350532
C	-2.161832	0.866076	0.059616	H	-3.294907	-0.129787	2.394613
C	0.097557	0.237236	-0.782532	H	-3.430545	1.6249	2.258769
C	0.635397	1.354759	0.161427	H	-4.885099	0.624676	2.175067
C	-0.304079	2.54487	0.126086	H	-0.310211	0.60775	2.007168
C	-1.708333	2.157778	0.163772	H	1.346402	0.002215	1.744363
C	1.352652	-0.648488	-0.909675	H	1.087997	1.671927	2.266875
C	2.504383	0.241576	-0.76726	H	2.581477	3.512138	0.227728
C	2.069073	1.490916	-0.280474	H	-5.297169	-1.548972	2.240764
C	-3.831317	0.678014	1.886796	H	-5.34736	-2.996169	1.221145
C	0.685178	0.868463	1.643103	H	-6.833541	-2.093562	1.574492
C	2.939384	2.554028	-0.135355	H	-5.577036	-2.844519	-1.269647
C	-5.766866	-1.995808	1.361977	H	-7.199808	-2.236923	-0.892172
C	-6.167545	-1.937771	-1.098671	H	-6.157505	-1.353235	-2.024988
C	-0.096906	0.769581	-2.243469	H	-0.289776	-0.077813	-2.908236
C	4.283451	2.338491	-0.475599	H	-0.952884	1.4454	-2.284649
C	4.739272	1.080433	-0.906757	H	0.78664	1.302495	-2.604418
C	3.863804	0.008126	-1.053312	H	5.798054	0.958869	-1.10918
C	4.391599	-1.364603	-1.384435	H	3.799698	-1.82962	-2.178873
C	4.340724	-2.31063	-0.151362	H	5.426496	-1.28036	-1.730543
C	4.777256	-1.551943	1.087907	H	3.297645	-2.57852	0.022895
C	5.171007	-3.576278	-0.393735	H	6.226219	-3.329687	-0.544786
O	6.089188	-1.224588	1.035241	H	5.09777	-4.264965	0.454641
O	4.048494	-1.226165	2.001111	H	4.805156	-4.098319	-1.284443
O	1.380156	-1.85197	-1.19422	H	4.7817	4.135373	-0.070832
O	-7.42695	0.202573	0.9061	H	-0.100604	-2.39208	-0.911868
O	0.088126	3.709452	0.171946	H	6.391259	-0.877173	3.072294

Table S16. Atomic coordinates (Å) of 25*R*-1f obtained at the mPW1PW91/6-31+G(d,p) level of theory in the $CHCl_3$.

C	-5.960475	1.284342	-0.657225	O	-1.040058	-2.609167	-0.63891
C	-6.433609	0.134684	0.206219	C	6.55319	-0.389798	2.107463
C	-5.585199	-1.141039	0.096624	H	-6.669153	2.110357	-0.566366
C	-4.102986	-0.755189	-0.23194	H	-5.984967	0.939821	-1.699177
C	-3.653417	0.61105	0.349948	H	-4.56801	2.588517	0.367031
C	-4.518633	1.729732	-0.308513	H	-4.028777	2.07869	-1.221734
C	-3.12087	-1.863442	0.136064	H	-3.12633	-2.05336	1.216211
C	-1.726311	-1.522358	-0.291804	H	-3.391977	-2.80825	-0.34438
C	-1.267955	-0.232944	-0.294538	H	-2.398287	2.972828	0.35057
C	-2.161828	0.866048	0.059654	H	-4.885226	0.624912	2.174972
C	0.097554	0.237142	-0.782458	H	-3.295087	-0.129622	2.394669
C	0.635431	1.354671	0.161483	H	-3.430619	1.625058	2.258682
C	-0.304033	2.544796	0.12619	H	-0.31007	0.60768	2.00728
C	-1.708298	2.157735	0.163835	H	1.346517	0.002124	1.74438
C	1.352644	-0.648594	-0.909607	H	1.088161	1.671851	2.266895
C	2.504381	0.241477	-0.76726	H	2.58151	3.512067	0.227635
C	2.069082	1.490832	-0.280497	H	-5.297311	-1.548919	2.24077
C	-3.831425	0.678168	1.886758	H	-5.347537	-2.99611	1.221159
C	0.685299	0.868381	1.643155	H	-6.833692	-2.093422	1.574434
C	2.939399	2.553943	-0.135429	H	-5.577054	-2.844451	-1.269686
C	-5.767002	-1.995727	1.361968	H	-7.199832	-2.236898	-0.892177
C	-6.167581	-1.937719	-1.098689	H	-6.157571	-1.353173	-2.025
C	-0.096927	0.769489	-2.243389	H	-0.289767	-0.077907	-2.908163
C	4.283459	2.338396	-0.475705	H	-0.95293	1.445277	-2.284567
C	4.739274	1.080322	-0.906813	H	0.786595	1.302439	-2.604341
C	3.863794	0.008012	-1.053328	H	5.798053	0.958743	-1.109239
C	4.391579	-1.364724	-1.38442	H	3.799621	-1.829793	-2.178785
C	4.340801	-2.310667	-0.151287	H	5.426452	-1.280486	-1.730599
C	4.77729	-1.551869	1.087919	H	3.297752	-2.578652	0.022989
C	5.171234	-3.576247	-0.393563	H	6.226409	-3.32954	-0.544682
O	6.089158	-1.224281	1.035121	H	5.098124	-4.264852	0.454891
O	4.048547	-1.226138	2.001156	H	4.805425	-4.098445	-1.284199
O	1.380159	-1.852082	-1.194121	H	4.781702	4.135301	-0.071028
O	-7.427006	0.202721	0.905925	H	-0.100709	-2.392119	-0.911752
O	0.088193	3.709375	0.171955	H	6.391373	-0.87668	3.072122

Table S17. Atomic coordinates (Å) of 25*R*-1g obtained at the mPW1PW91/6-31+G(d,p) level of theory in the $CHCl_3$.

C	-5.679727	-1.444037	0.751138	O	-0.712072	2.379966	0.798108
C	-6.172483	-0.237314	-0.019026	C	2.085447	4.054304	-0.905012
C	-5.302087	1.019709	0.131081	H	-6.402973	-2.254638	0.638861
C	-3.813648	0.59694	0.372105	H	-5.657522	-1.164715	1.812502
C	-3.409041	-0.735976	-0.311483	H	-4.346501	-2.70025	-0.404763
C	-4.259094	-1.882938	0.316796	H	-3.735352	-2.289234	1.186542
C	-2.829775	1.714271	0.033848	H	-2.870421	1.96642	-1.032769
C	-1.428719	1.327263	0.395684	H	-3.071562	2.631827	0.578469
C	-0.990475	0.036588	0.298937	H	-2.177448	-3.100871	-0.547752
C	-1.910272	-1.025325	-0.103793	H	-3.284598	-1.632994	-2.286738
C	0.386642	-0.481718	0.693392	H	-4.72185	-0.626952	-2.075889
C	0.875379	-1.517037	-0.36365	H	-3.134551	0.125156	-2.322143
C	-0.069368	-2.702959	-0.379225	H	-0.161997	-0.664256	-2.111102
C	-1.473214	-2.306649	-0.326223	H	1.473277	-0.006655	-1.845677
C	1.650104	0.386209	0.845585	H	1.26803	-1.640606	-2.500572
C	2.790222	-0.48112	0.563591	H	2.810019	-3.667279	-0.675858
C	2.327925	-1.687467	-0.000767	H	-5.096024	1.554586	-1.994354
C	-3.656855	-0.707194	-1.839824	H	-5.085169	2.937185	-0.887564
C	0.855499	-0.908089	-1.800264	H	-6.596667	2.074546	-1.233424
C	3.186015	-2.738944	-0.257724	H	-5.21289	2.636466	1.596209
C	-5.52368	1.952019	-1.071508	H	-6.858433	2.071922	1.251786
C	-5.822822	1.748757	1.395902	H	-5.78254	1.108766	2.283942
C	0.247406	-1.133618	2.111185	H	0.092041	-0.344154	2.852628
C	4.541834	-2.55695	0.056939	H	-0.612416	-1.805408	2.13319
C	5.020278	-1.337739	0.566743	H	1.140686	-1.700218	2.386862
C	4.160642	-0.269911	0.811389	H	6.084196	-1.247685	0.760112
C	4.697944	1.060372	1.275453	H	3.983872	1.543509	1.945661
C	5.028043	2.04908	0.112207	H	5.630691	0.899863	1.827633
C	3.77207	2.432634	-0.653509	H	5.412222	2.958093	0.585253
C	6.072381	1.486071	-0.857399	H	6.362569	2.240474	-1.596061
O	3.30444	3.633549	-0.269696	H	6.972383	1.177504	-0.314496
O	3.253485	1.752128	-1.517196	H	5.673596	0.62262	-1.394428
O	1.691848	1.55154	1.260896	H	5.012524	-4.323205	-0.490516
O	-7.196367	-0.24982	-0.676658	H	0.217472	2.117819	1.071114
O	0.308369	-3.862796	-0.530386	H	1.911077	5.071677	-0.554604

Table S18. Atomic coordinates (Å) of 25*R*-1h obtained at the mPW1PW91/6-31+G(d,p) level of theory in the $CHCl_3$.

C	5.438329	0.607196	1.750033	O	0.707465	-2.219839	-1.279696
C	6.121317	-0.055681	0.573802	C	-2.226369	-3.953785	0.975971
C	5.280863	-1.129841	-0.132737	H	6.141331	1.292722	2.228167
C	3.76067	-0.772475	-0.004052	H	5.199367	-0.181543	2.475057
C	3.462819	0.749369	0.054775	H	4.344505	2.388799	1.187233
C	4.129665	1.327442	1.341376	H	3.423948	1.269362	2.174401
C	2.914482	-1.462976	-1.069033	H	3.20649	-1.141261	-2.076117
C	1.454422	-1.190151	-0.878101	H	3.053903	-2.548039	-1.042017
C	0.998618	-0.0093	-0.360199	H	2.228127	2.947879	0.949899
C	1.944215	1.008584	0.09176	H	3.717419	2.55143	-1.131905
C	-0.450419	0.318888	-0.017242	H	5.111103	1.46806	-1.216108
C	-0.750043	1.81233	-0.356099	H	3.630783	1.088184	-2.116534
C	0.146787	2.713144	0.472725	H	-0.984803	1.462556	-2.511469
C	1.520635	2.231793	0.547714	H	-0.718347	3.157941	-2.068498
C	-1.688126	-0.349036	-0.646603	H	0.641309	2.015039	-2.052603
C	-2.785951	0.609931	-0.515108	H	-2.632577	3.927489	0.300347
C	-2.24981	1.878543	-0.210847	H	5.546137	-0.461925	-2.21358
C	4.018357	1.501186	-1.179754	H	5.351692	-2.212515	-2.026804
C	-0.424638	2.1277	-1.84675	H	6.870092	-1.421796	-1.560507
C	-3.06355	2.96327	0.050491	H	6.599907	-2.736861	0.548349
C	5.783393	-1.315027	-1.574293	H	5.298302	-2.365578	1.69659
C	5.54693	-2.450869	0.633255	H	4.938869	-3.258937	0.211872
C	-0.626435	0.04291	1.515256	H	-0.578594	-1.033163	1.69629
C	-4.451257	2.75698	-0.003042	H	0.177176	0.530452	2.070005
C	-4.993218	1.506903	-0.342987	H	-1.588613	0.395495	1.888922
C	-4.176276	0.409448	-0.606106	H	-6.074129	1.414301	-0.388708
C	-4.802083	-0.924771	-0.936592	H	-5.738346	-0.743466	-1.476608
C	-5.157854	-1.781758	0.314365	H	-4.146949	-1.506495	-1.588578
C	-3.880971	-2.273285	0.975588	H	-5.631553	-1.1233	1.049917
C	-6.115106	-2.91657	-0.065502	H	-5.678406	-3.55517	-0.838124
O	-3.481489	-3.461002	0.482502	H	-6.347398	-3.546181	0.799279
O	-3.271749	-1.660655	1.829099	H	-7.054007	-2.50134	-0.447526
O	-1.766107	-1.491959	-1.113343	H	-4.84212	4.559818	0.484929
O	7.257958	0.215526	0.233698	H	-0.273163	-2.013518	-1.232553
O	-0.226855	3.790306	0.932357	H	-2.205486	-3.926467	2.067708

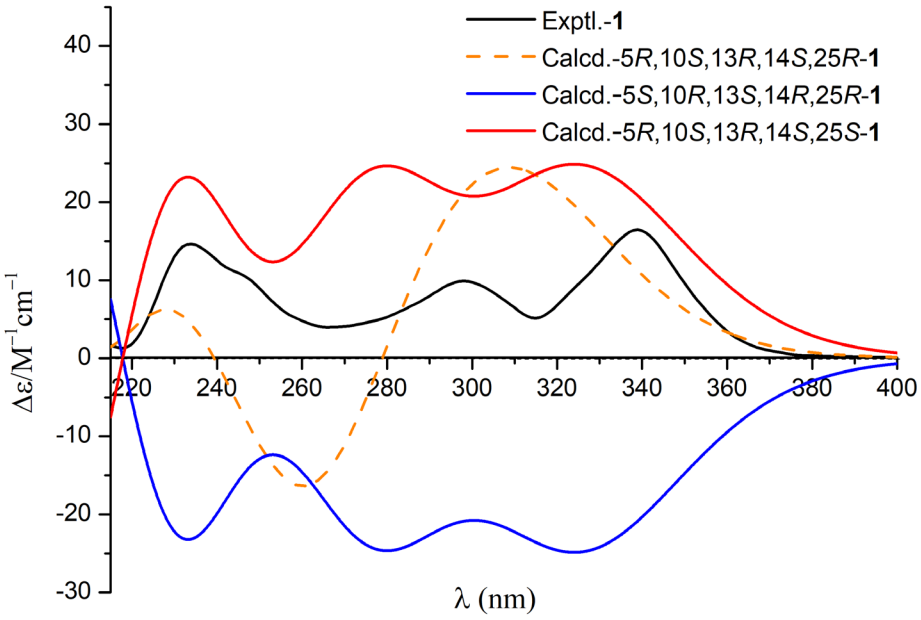
Table S19. The experimental and calculated ^{13}C NMR spectroscopic data of 25*S*-1 and 25*R*-2 at the mPW1PW91/6-31+G(d,p) level of theory in the $CHCl_3$.

position	Exptl.-1	Calcd. 25*S*-1	Calcd. 25*R*-1
1	36	41.9	41.7
2	34.2	35.9	36.1
3	214.5	216.2	215.8
4	46.8	49.4	49.7
5	49.1	49.4	49.8
6	28.7	30.7	30.8
7	164.7	165.7	165.9
8	106.9	106.9	106.5
9	167.5	167.3	167.2
10	38	39.1	38.6
11	111.3	110.6	110.4
12	199.3	193.5	193.5
13	53.6	56.5	56.8
14	61.1	65.7	64.9
15	208.1	205.9	205.0
16	121.7	121.6	122.1
17	158.4	158.9	159.6
18	32.4	34.3	33.9
19	21.3	21.6	24.3
20	163.9	159.3	159.6
21	111.5	108.5	108.0
22	117.5	113.9	114.2
23	145	144.3	144.0
24	35.7	39.7	39.8
25	40.3	43.1	42.8
26	176.4	173.6	173.6
27	16.9	17.8	17.6
28	25	27.7	21.6
29	22.1	21.4	27.1
30	27.8	28.7	28.9

Table S20. The experimental and calculated ^{1}H NMR spectroscopic data of 25*S*-1 and 25*R*-2 at the mPW1PW91/6-31+G(d,p) level of theory in the $CHCl_3$.

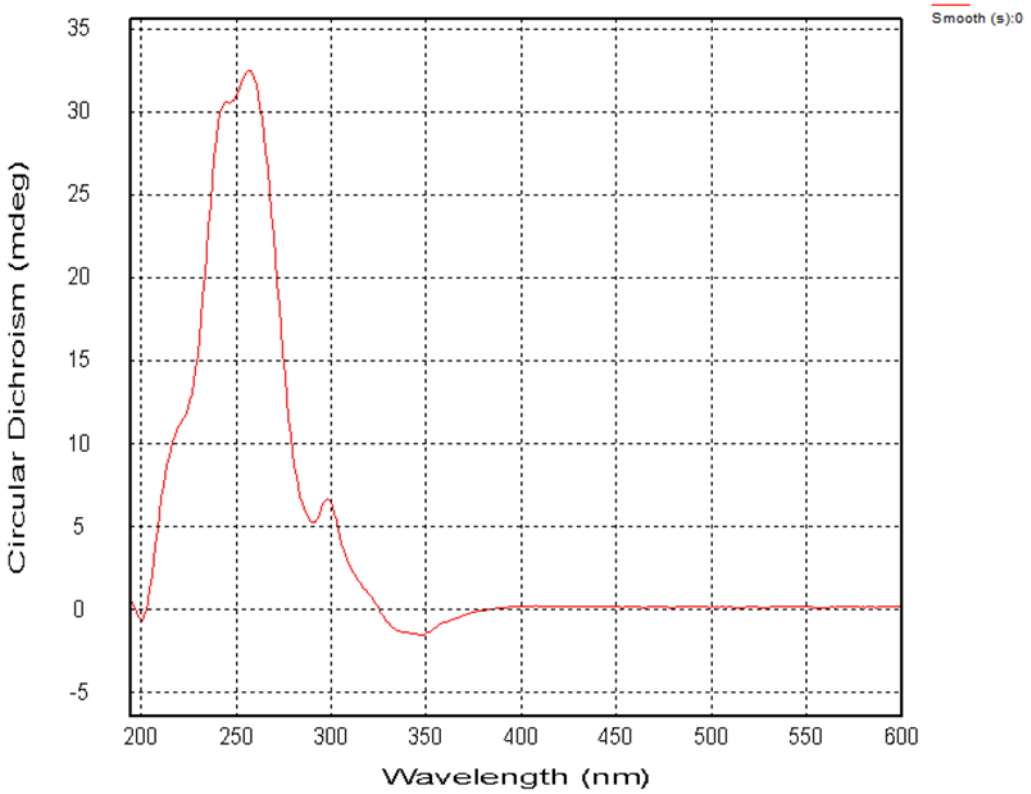
position	Exptl.-1	Calcd. 25*S*-1	Calcd. 25*R*-1
1	2.3	2.13	2.12
1	1.87	1.99	2.08
2	2.45	2.26	1.99
2	2.81	2.60	2.81
5	1.86	2.12	2.28
6	2.61	2.51	2.43
6	2.34	2.09	2.04
11	5.55	5.47	5.54
18	1.39	1.40	1.65
18	1.39	1.18	0.96
18	1.39	1.19	1.20
19	1.38	1.30	1.02
19	1.38	0.85	1.27
19	1.38	1.13	0.65
21	7.44	7.77	7.75
22	6.58	6.62	6.69
24	3.05	2.35	3.38
24	3.22	3.74	2.27
25	2.76	2.70	3.22
26	1.17	0.97	0.98
26	1.17	1.15	1.31
26	1.17	1.10	1.03
28	1.19	0.81	1.59
28	1.19	0.96	0.82
28	1.19	1.19	0.47
29	1.15	0.98	1.30
29	1.15	0.90	0.72
29	1.15	1.05	0.96
30	1.34	1.00	0.67
30	1.34	1.68	1.29
30	1.34	1.29	1.81
7-OH	12.8	13.00	13.03
OMe	3.59	3.39	2.67
OMe	3.59	3.23	3.33
OMe	3.59	3.06	2.57

Figure S20. The experimental and calculated ECD curves of 25*S*-1 and 25*R*-1.



CD spectra, and computational ECD data of 2

Figure S21. CD spectrum of 2



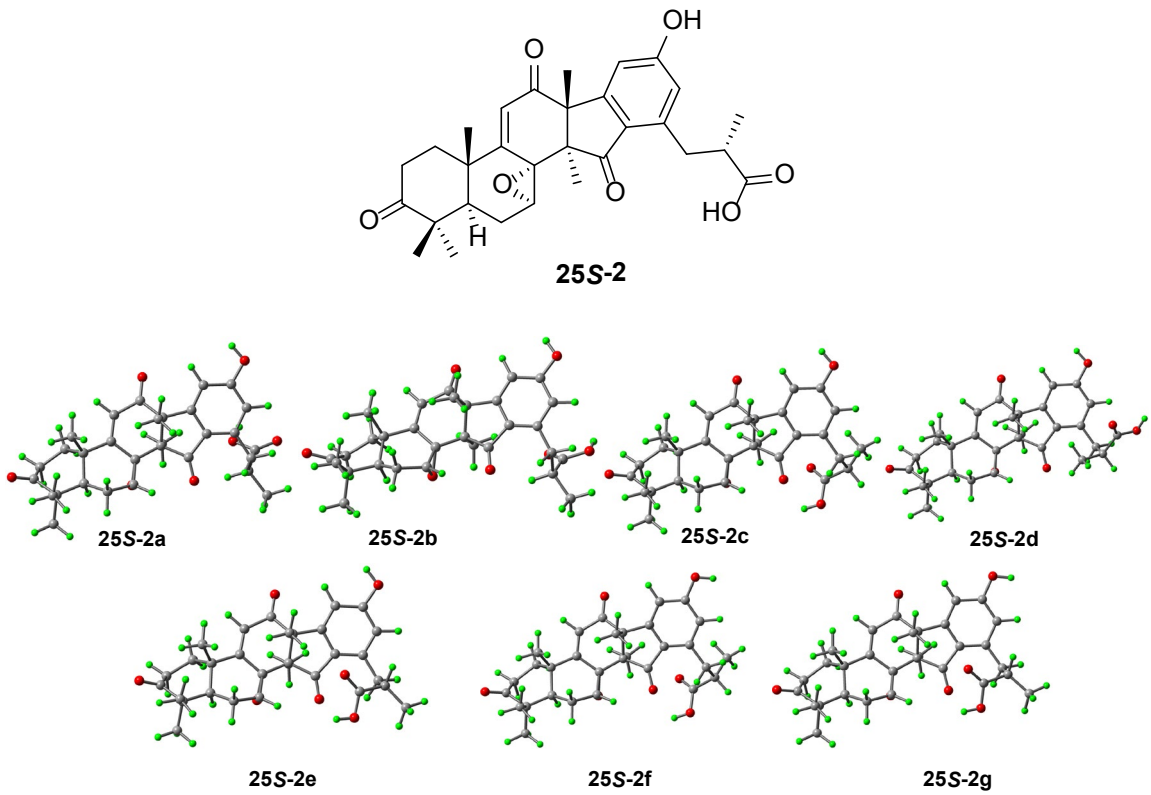


Figure S22. Seven optimized conformers of 25*S*-2.

Table S21. Conformational analysis of seven optimized conformers of 25*S*-2 in the gas phase (T = 298.15 K)

Conformer	E (Hartree)	C (Hartree)	G (kcal/mol)	ΔG (kcal/mol)	Population
25*S*-2a	-1690.073099	0.517705	-1060212.905402	0	48.92%
25*S*-2b	-1690.072581	0.518065	-1060212.354360	0.551041631	19.29%
25*S*-2c	-1690.073448	0.51936	-1060212.086037	0.819364907	12.26%
25*S*-2d	-1690.071971	0.518302	-1060211.822746	1.082655553	7.86%
25*S*-2e	-1690.07224	0.518799	-1060211.679956	1.225445454	6.18%
25*S*-2f	-1690.072172	0.519201	-1060211.385077	1.520324953	3.75%
25*S*-2g	-1690.070868	0.51862	-1060210.930973	1.97442884	1.74%

Electronic energy obtained at M062X/6-311+G(2d,p) EmpiricalDispersion=GD3 level of theory; Thermal correction to Gibbs free energy obtained at B3LYP/6-31G(d) Scale=0.9813 EmpiricalDispersion=GD3BJ; Gibbs free energy (E + C); The relative Gibbs free energy; The Boltzmann distribution of each conformer.

Table S22. Atomic coordinates (Å) of 25*S*-2a obtained at the mPW1PW91/6-31+G(d,p) level of theory in the MeOH.

C	4.050212	0.772315	1.745828	H	0.841135	-1.90802	-1.550068
C	5.469582	0.166094	1.906846	H	2.080133	2.797813	1.071543
C	6.167432	-0.124141	0.587842	H	-2.762877	3.539242	-0.167719
C	5.393126	-1.021449	-0.393	H	-6.008487	0.819775	-1.00118
C	3.85881	-0.844219	-0.160903	H	-5.597007	-1.475231	-1.508598
C	3.000741	-1.326535	-1.336491	H	-3.947881	-2.040846	-1.854936
C	1.550456	-1.386668	-0.911962	H	-3.516755	-2.431954	0.513462
C	1.015436	-0.323205	-0.034555	H	-4.657174	-4.239566	-0.823908
C	1.939903	0.794413	0.370395	H	-5.118295	-4.313238	0.886422
C	3.464852	0.588338	0.318353	H	-6.23665	-3.608827	-0.294728
C	1.431611	2.001749	0.717687	H	-0.532865	2.667366	-2.186025
C	0.023206	2.414359	0.513649	H	0.865492	1.615084	-1.906934
C	-0.735407	1.456607	-0.383723	H	-0.660745	0.932002	-2.50983
C	-0.454265	0.011269	0.114313	H	5.131829	1.669916	-0.634513
C	-1.555476	-0.778874	-0.626677	H	3.686457	1.547956	-1.648812
C	-2.695742	0.163099	-0.71574	H	3.730442	2.67238	-0.290607
C	-2.245839	1.470558	-0.452	H	5.549213	0.200538	-2.218977
C	-0.222345	1.677119	-1.839482	H	6.96172	-0.789803	-1.859129
C	4.039818	1.678579	-0.620908	H	5.491412	-1.544287	-2.505676
C	-3.121556	2.538994	-0.390356	H	5.556936	-2.699865	1.031452
C	-4.484681	2.272364	-0.594461	H	5.232398	-3.187262	-0.637207
C	-4.942449	0.9737	-0.869763	H	-0.694746	-1.215397	1.884348
C	-4.057693	-0.101224	-0.937975	H	-1.842583	0.135834	1.825018
C	-4.569595	-1.506655	-1.13172	H	-0.141872	0.424704	2.254594
C	-4.552926	-2.326137	0.186296	H	-5.079838	-0.484539	2.766039
C	-5.181235	-3.707459	-0.023644	O	-6.51922	-1.386817	1.253393
C	-5.318041	-1.54911	1.238438	O	7.290893	0.27858	0.349394
C	5.870051	-0.768926	-1.832806	O	-4.500694	-1.000215	2.172608
C	5.784658	-2.473953	-0.015818	O	-1.506123	-1.94415	-0.989327
C	-0.812288	-0.161885	1.621344	H	-4.989424	4.094303	-0.32329
H	4.075254	1.839795	1.986688	O	-5.424369	3.252675	-0.533921
H	3.373765	0.304214	2.467357	O	1.354596	-1.631115	0.486556
H	6.122402	0.808406	2.501682	H	6.854631	-2.635085	-0.17919
H	5.388811	-0.792757	2.435572	O	-0.424457	3.471924	0.933703
H	3.59869	-1.504654	0.670708				
H	3.096521	-0.6744	-2.213442				

Table S23. Atomic coordinates (Å) of 25*S*-2b obtained at the Cam-B3LYP/6-311+G(d,p) level of theory in the MeOH.

C	4.026492	0.742066	1.767103	H	0.847105	-1.87452	-1.604594
C	5.44654	0.136202	1.9244	H	2.056627	2.783025	1.109737
C	6.1546	-0.123216	0.604381	H	-2.77959	3.529421	-0.138866
C	5.389364	-0.999575	-0.402236	H	-6.018559	0.812135	-0.999591
C	3.853245	-0.831171	-0.17685	H	-5.621559	-1.481745	-1.464525
C	3.003442	-1.288882	-1.368176	H	-3.989629	-2.038965	-1.886255
C	1.551259	-1.364311	-0.951921	H	-3.434551	-2.496324	0.412467
C	1.007878	-0.322773	-0.053243	H	-5.099592	-4.291834	0.939121
C	1.926469	0.790372	0.376758	H	-6.253155	-3.564154	-0.195419
C	3.452429	0.589405	0.33148	H	-4.729222	-4.256317	-0.792954
C	1.412658	1.990679	0.73964	H	-0.665455	0.962522	-2.513667
C	0.005169	2.403934	0.531455	H	-0.542838	2.693393	-2.163402
C	-0.747888	1.45514	-0.379922	H	0.857072	1.640112	-1.895614
C	-0.463689	0.003034	0.097083	H	3.688112	1.592554	-1.612053
C	-1.5581	-0.777146	-0.661421	H	3.718947	2.686947	-0.229224
C	-2.703963	0.161166	-0.73198	H	5.124899	1.694813	-0.583414
C	-2.257901	1.466324	-0.452085	H	5.502731	-1.47357	-2.525508
C	-0.231155	1.698714	-1.83081	H	5.555658	0.264281	-2.198473
C	4.032786	1.701165	-0.578635	H	6.967513	-0.731852	-1.852
C	-3.136078	2.531914	-0.376596	H	5.546728	-2.709861	0.984435
C	-4.498162	2.264328	-0.582253	H	5.235775	-3.159498	-0.697339
C	-4.952549	0.967515	-0.869761	H	-1.869271	0.057916	1.803672
C	-4.065996	-0.105184	-0.948637	H	-0.181184	0.401823	2.244131
C	-4.579435	-1.512002	-1.130995	H	-0.677643	-1.250864	1.850367
C	-4.488936	-2.338077	0.180142	H	-6.633707	-0.773767	1.986165
C	-5.189534	-3.693932	0.026095	O	-4.401153	-1.072693	2.253413
C	-5.045179	-1.531271	1.335003	O	7.27938	0.286038	0.383581
C	5.875642	-0.713268	-1.832525	O	-6.385174	-1.331648	1.225369
C	5.781724	-2.459443	-0.055617	O	-1.502707	-1.932347	-1.054266
C	-0.828214	-0.198645	1.599577	H	-5.009193	4.079343	-0.279595
H	4.046432	1.803779	2.032685	O	-5.441581	3.241156	-0.508441
H	3.346159	0.255492	2.472524	O	1.350576	-1.640164	0.439872
H	6.093536	0.766808	2.537854	H	6.85329	-2.614333	-0.214627
H	5.36478	-0.834315	2.431286	O	-0.444257	3.458931	0.955935
H	3.589331	-1.51053	0.638074				
H	3.101262	-0.615715	-2.228938				

Table S24. Atomic coordinates (Å) of 25*S*-2c obtained at the mPW1PW91/6-31+G(d,p) level of theory in the MeOH.

C	3.959807	0.81024	1.713706	H	0.678727	-1.787107	-1.577342
C	5.385175	0.206022	1.821027	H	1.964217	2.846605	1.140088
C	6.050574	-0.042393	0.477034	H	-2.91033	3.58691	0.061135
C	5.254996	-0.913813	-0.510142	H	-6.150495	0.915112	-0.909132
C	3.726453	-0.750559	-0.234183	H	-5.644505	-1.296756	-1.761622
C	2.840039	-1.201062	-1.401178	H	-4.004373	-1.962708	-1.733494
C	1.401615	-1.283124	-0.940865	H	-5.596847	-3.180373	-0.31237
C	0.884686	-0.252297	-0.014948	H	-7.003294	-1.229769	0.484615
C	1.814541	0.860058	0.394557	H	-6.440345	-2.240068	1.829187
C	3.338766	0.665077	0.296787	H	-5.6443	-0.69612	1.497399
C	1.310022	2.055372	0.785842	H	-0.874111	1.057833	-2.401002
C	-0.106846	2.463744	0.637251	H	-0.753383	2.785107	-2.033367
C	-0.887688	1.523399	-0.259096	H	0.66295	1.740272	-1.826122
C	-0.581195	0.068488	0.191098	H	3.579628	2.767216	-0.257708
C	-1.692809	-0.705184	-0.549336	H	4.976474	1.782602	-0.665068
C	-2.849669	0.224155	-0.578653	H	3.506834	1.682487	-1.646507
C	-2.399932	1.526318	-0.282896	H	5.300322	-1.372875	-2.639278
C	-0.422884	1.789066	-1.723873	H	5.360535	0.362733	-2.301764
C	3.885073	1.785013	-0.624277	H	6.784786	-0.632826	-2.008423
C	-3.273231	2.593663	-0.184837	H	6.727635	-2.526476	-0.380712
C	-4.635264	2.336444	-0.401146	H	5.460537	-2.633012	0.859001
C	-5.088285	1.051103	-0.733257	H	-0.148167	0.394213	2.319355
C	-4.210863	-0.030398	-0.822849	H	-0.835171	-1.196084	1.939777
C	-4.742033	-1.407277	-1.15025	H	-1.882289	0.222191	1.962339
C	-5.13959	-2.270119	0.089976	H	-2.480089	-3.92852	0.727262
C	-6.115371	-1.564303	1.03163	O	-3.372516	-2.077298	1.743167
C	-3.884467	-2.688771	0.827961	O	7.166298	0.37186	0.222286
C	5.69409	-0.616678	-1.953393	O	-3.36043	-3.824284	0.319848
C	5.661412	-2.375026	-0.186353	O	-1.627518	-1.843797	-0.986458
C	-0.8835	-0.132199	1.70597	H	-5.142622	4.147148	-0.066971
H	3.98688	1.870414	1.984648	O	-5.575872	3.315259	-0.315996
H	3.303879	0.318549	2.438443	O	1.244514	-1.57501	0.453937
H	6.050391	0.83353	2.417956	H	5.096615	-3.071953	-0.81506
H	5.321401	-0.768251	2.323262	O	-0.54588	3.508957	1.095364
H	3.489939	-1.436475	0.583732	H	0.678727	-1.787107	-1.577342
H	2.909416	-0.521205	-2.259382	H	1.964217	2.846605	1.140088

Table S25. Atomic coordinates (Å) of 25*S*-2d obtained at the mPW1PW91/6-31+G(d,p) level of theory in the MeOH.

C	-4.444615	1.474017	-0.791834	H	-0.72858	-2.292582	-0.178133
C	-5.892472	0.937366	-0.944272	H	-2.27812	2.985042	0.394423
C	-6.296723	-0.05252	0.136022	H	2.740709	3.343418	0.744357
C	-5.372582	-1.27106	0.302179	H	5.968321	0.801674	-0.570756
C	-3.919642	-0.884906	-0.122077	H	3.730782	-1.942858	-1.749802
C	-2.850386	-1.847344	0.408183	H	5.368274	-1.270261	-1.86787
C	-1.532641	-1.567927	-0.278922	H	5.342656	-3.285049	-0.531429
C	-1.149234	-0.166319	-0.552325	H	3.510239	-1.844893	1.47032
C	-2.083951	0.926214	-0.103572	H	2.993306	-3.139978	0.373992
C	-3.56813	0.610056	0.15703	H	4.186038	-3.462347	1.662306
C	-1.606841	2.17255	0.132225	H	1.087597	-0.257989	1.794862
C	-0.169712	2.523484	0.214143	H	0.980057	1.378095	2.459472
C	0.719516	1.298501	0.295684	H	-0.497325	0.525532	1.978403
C	0.267202	0.306026	-0.81002	H	-3.581125	2.034293	1.817113
C	1.46102	-0.675708	-0.837223	H	-4.92466	0.902734	1.86902
C	2.64232	0.153029	-0.493459	H	-3.300513	0.369391	2.327491
C	2.206933	1.383941	0.040139	H	-5.059713	-1.208461	2.481556
C	0.550788	0.69253	1.722848	H	-6.566134	-1.962234	1.963892
C	-3.863409	0.996367	1.628525	H	-5.0307	-2.833086	1.781974
C	3.094595	2.39643	0.348742	H	-5.273125	-3.222525	-0.676599
C	4.457084	2.161238	0.101397	H	-6.925939	-2.63414	-0.415506
C	4.904393	0.932755	-0.405344	H	1.220607	1.482546	-2.410047
C	4.010224	-0.097625	-0.70006	H	-0.53708	1.69951	-2.311191
C	4.519247	-1.429098	-1.196884	H	0.124937	0.198197	-2.972486
C	4.970899	-2.373582	-0.043994	H	7.912411	-1.181682	0.455601
C	3.843753	-2.731749	0.924113	O	6.194349	-1.533947	1.890444
C	6.15221	-1.785433	0.70752	O	-7.317441	0.080749	0.785286
C	-5.507418	-1.850105	1.720163	O	7.214709	-1.556704	-0.11403
C	-5.911183	-2.332275	-0.692377	O	1.41841	-1.856189	-1.148282
C	0.273992	0.973203	-2.217484	H	4.972655	3.904448	0.687088
H	-4.470049	2.502137	-0.417141	O	5.403812	3.105715	0.343591
H	-3.968125	1.511005	-1.776165	O	-1.658335	-1.026958	-1.60026
H	-6.627443	1.744968	-0.957116	H	-5.930933	-1.955925	-1.720803
H	-5.976135	0.40715	-1.90203	O	0.225974	3.675706	0.319141
H	-3.882114	-0.988895	-1.209848				
H	-2.719302	-1.762047	1.493994				

Table S26. Atomic coordinates (Å) of 25*S*-2e obtained at the mPW1PW91/6-31+G(d,p) level of theory in the MeOH.

C	4.227021	1.51054	0.885136	H	0.41922	-2.137644	0.142389
C	5.656185	0.931396	1.057818	H	2.123952	3.096581	-0.33019
C	6.054246	-0.054633	-0.028242	H	-2.884717	3.577473	-0.807567
C	5.099478	-1.243819	-0.230741	H	-6.202448	1.044958	0.278007
C	3.649925	-0.822766	0.170669	H	-4.136455	-1.714324	1.626555
C	2.5647	-1.746914	-0.394488	H	-5.774358	-1.061824	1.440011
C	1.242487	-1.439619	0.27175	H	-5.587565	-1.556042	-1.053561
C	0.893417	-0.032897	0.559465	H	-6.921674	-2.982574	0.480804
C	1.866094	1.038958	0.142753	H	-6.116506	-4.016877	-0.713965
C	3.345926	0.685356	-0.09334	H	-5.474426	-3.908466	0.930808
C	1.426689	2.299495	-0.089197	H	-1.324683	-0.029917	-1.842146
C	0.000451	2.688024	-0.197658	H	-1.105856	1.606358	-2.478104
C	-0.916615	1.488358	-0.309704	H	0.308867	0.672232	-1.965101
C	-0.514556	0.473617	0.794665	H	4.744352	0.963016	-1.774363
C	-1.732848	-0.476092	0.785496	H	3.114369	0.484088	-2.271898
C	-2.881697	0.379757	0.41161	H	3.433064	2.132049	-1.731301
C	-2.407351	1.606915	-0.092371	H	4.830927	-1.141023	-2.414254
C	-0.737758	0.887314	-1.739937	H	6.305974	-1.943652	-1.879556
C	3.681626	1.0838	-1.552897	H	4.743977	-2.774246	-1.740018
C	-3.267802	2.632604	-0.434518	H	4.925913	-3.205643	0.716458
C	-4.643404	2.407198	-0.266242	H	6.599495	-2.660608	0.49642
C	-5.127643	1.1726	0.19007	H	-0.41898	0.338792	2.958526
C	-4.259171	0.133223	0.524007	H	-1.471845	1.654864	2.387676
C	-4.813403	-1.208076	0.934019	H	0.292173	1.831052	2.32732
C	-5.077401	-2.145614	-0.284628	H	-2.381119	-3.820586	-0.743773
C	-5.94755	-3.337304	0.127304	O	-3.137856	-1.909404	-1.723784
C	-3.749799	-2.554365	-0.896926	O	7.091624	0.058014	-0.654669
C	5.246167	-1.805816	-1.654385	O	-3.286498	-3.7207	-0.396874
C	5.588279	-2.33414	0.757999	O	-1.735803	-1.656968	1.098774
C	-0.533626	1.125108	2.209126	H	-5.110714	4.163503	-0.85254
H	4.288242	2.542776	0.526232	O	-5.568367	3.363003	-0.549994
H	3.732311	1.546841	1.860459	O	1.357489	-0.923899	1.603923
H	6.41308	1.717666	1.096595	H	5.598122	-1.973405	1.792147
H	5.706099	0.385833	2.009327	O	-0.362136	3.851588	-0.299881
H	3.587672	-0.941076	1.255843				
H	2.456903	-1.641778	-1.481057				

Table S27. Atomic coordinates (Å) of 25*S*-2f obtained at the mPW1PW91/6-31+G(d,p) level of theory in the MeOH.

C	3.963555	0.805576	1.713962	H	0.676441	-1.778276	-1.580728
C	5.390349	0.203959	1.816866	H	1.968357	2.846594	1.14737
C	6.052947	-0.045025	0.471575	H	-2.934101	3.601673	0.058728
C	5.254295	-0.913067	-0.516102	H	-6.143688	0.894206	-0.917699
C	3.726402	-0.748649	-0.237751	H	-5.633904	-1.298994	-1.764668
C	2.83805	-1.195038	-1.40486	H	-3.992597	-1.960594	-1.73146
C	1.400013	-1.276607	-0.943245	H	-5.588019	-3.183408	-0.31732
C	0.88561	-0.247757	-0.014036	H	-5.641299	-0.702705	1.496538
C	1.817119	0.862262	0.397336	H	-6.999531	-1.23822	0.480723
C	3.341092	0.665949	0.297359	H	-6.436254	-2.247461	1.82522
C	1.313609	2.056269	0.792075	H	-0.753192	2.799657	-2.019482
C	-0.10489	2.465679	0.650942	H	0.662461	1.752255	-1.817624
C	-0.887787	1.531018	-0.251098	H	-0.875303	1.074034	-2.395043
C	-0.579882	0.07433	0.194275	H	4.979349	1.784313	-0.66312
C	-1.690223	-0.698999	-0.545539	H	3.508303	1.688928	-1.642937
C	-2.847649	0.2292	-0.57413	H	3.584044	2.769268	-0.250996
C	-2.401003	1.535345	-0.277079	H	5.295386	-1.366511	-2.646609
C	-0.423275	1.802049	-1.714731	H	5.358894	0.368101	-2.304242
C	3.887953	1.787823	-0.620857	H	6.782108	-0.63052	-2.016198
C	-3.27295	2.601948	-0.182258	H	5.092366	-3.070271	-0.825443
C	-4.634002	2.341178	-0.403735	H	6.725048	-2.527973	-0.393033
C	-5.082719	1.053514	-0.733207	H	-0.146984	0.395714	2.323045
C	-4.204256	-0.03045	-0.819831	H	-0.833102	-1.1944	1.940787
C	-4.733162	-1.407611	-1.149793	H	-1.880634	0.224495	1.966291
C	-5.132614	-2.273389	0.087638	H	-2.469623	-3.926393	0.723728
C	-6.111013	-1.570648	1.028751	O	-3.374128	-2.083499	1.749478
C	-3.878809	-2.691975	0.828619	O	7.170028	0.365409	0.216425
C	5.691532	-0.612855	-1.959303	O	-3.350217	-3.823164	0.316524
C	5.659395	-2.375501	-0.196316	O	-1.626529	-1.837923	-0.982735
C	-0.882079	-0.130083	1.708966	H	-6.394205	3.087697	-0.467718
H	3.988515	1.864386	1.99027	O	-5.488764	3.394091	-0.301639
H	3.309087	0.308914	2.436633	O	1.243645	-1.572655	0.450921
H	6.056734	0.832811	2.411086	H	5.460056	-2.635308	0.848898
H	5.330286	-0.770091	2.320163	O	-0.541648	3.504924	1.121667
H	3.489984	-1.436388	0.578705				
H	2.907113	-0.512757	-2.261176				

Table S28. Atomic coordinates (Å) of 25*S*-2g obtained at the mPW1PW91/6-31+G(d,p) level of theory in the MeOH.

C	-4.230236	-1.508665	0.887498	H	-0.417122	2.132032	0.13505
C	-5.658617	-0.927416	1.059804	H	-2.129028	-3.099977	-0.327211
C	-6.055811	0.058359	-0.026747	H	2.908615	-3.589186	-0.819726
C	-5.098787	1.245335	-0.231901	H	6.197179	-1.0211	0.273875
C	-3.64969	0.822226	0.168829	H	4.12374	1.709142	1.628731
C	-2.563316	1.743454	-0.398835	H	5.763404	1.060634	1.447965
C	-1.240964	1.43515	0.266757	H	5.588707	1.566346	-1.044972
C	-0.894301	0.028461	0.556821	H	5.456371	3.909459	0.949126
C	-1.869027	-1.042244	0.142586	H	6.909775	2.990368	0.505594
C	-3.348569	-0.686765	-0.09307	H	6.10897	4.026334	-0.690748
C	-1.431092	-2.303094	-0.087419	H	-0.311126	-0.685601	-1.966815
C	-0.004621	-2.696037	-0.191645	H	1.322406	0.016173	-1.847258
C	0.915264	-1.498056	-0.31054	H	1.103083	-1.622167	-2.47802
C	0.513226	-0.480053	0.791833	H	-3.118882	-0.489443	-2.272134
C	1.729932	0.469525	0.781907	H	-3.439121	-2.135943	-1.728367
C	2.879228	-0.385626	0.408526	H	-4.749116	-0.965427	-1.772356
C	2.407549	-1.616779	-0.096489	H	-4.832191	1.138385	-2.41534
C	0.735524	-0.900866	-1.741929	H	-6.305428	1.944573	-1.880878
C	-3.686307	-1.087109	-1.551555	H	-4.741803	2.772647	-1.744014
C	3.267143	-2.639618	-0.442843	H	-5.594417	1.978954	1.790188
C	4.642698	-2.407926	-0.279064	H	-4.920691	3.208288	0.712098
C	5.122424	-1.172845	0.181302	H	0.419425	-0.342268	2.956104
C	4.252456	-0.133432	0.521112	H	1.471217	-1.660011	2.385489
C	4.804487	1.206775	0.937258	H	-0.29249	-1.835076	2.326636
C	5.072687	2.150385	-0.275528	H	2.374549	3.82014	-0.743417
C	5.936704	3.342923	0.146686	O	3.14343	1.913735	-1.727325
C	3.747291	2.557767	-0.894296	O	-7.094507	-0.052307	-0.651398
C	-5.245672	1.805257	-1.656347	O	3.278612	3.721131	-0.392778
C	-5.584725	2.338126	0.755486	O	1.734052	1.651162	1.093207
C	0.533328	-1.12942	2.207449	H	6.398329	-3.14684	-0.456274
H	-4.292892	-2.541582	0.530854	O	5.481428	-3.42866	-0.60164
H	-3.734973	-1.543573	1.862587	O	-1.355307	0.922615	1.600312
H	-6.416708	-1.7125	1.099452	H	-6.595544	2.666117	0.494229
H	-5.707704	-0.380905	2.010851	O	0.35358	-3.860799	-0.281836
H	-3.586151	0.942188	1.253775				
H	-2.456606	1.63595	-1.485284				

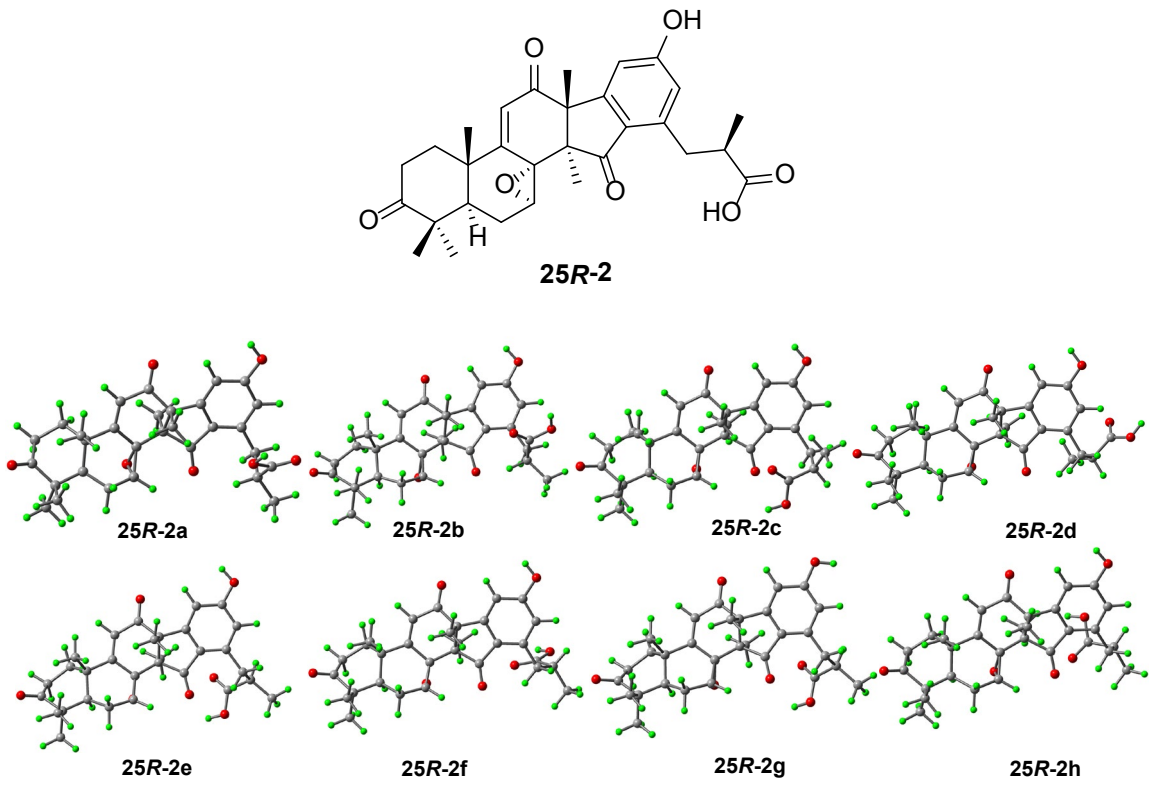


Figure S23. Eight optimized conformers of 25*R*-2.

Table S29. Conformational analysis of eight optimized conformers of 25*R*-2 in the gas phase (T = 298.15 K)

Conformer	E (Hartree)	C (Hartree)	G (kcal/mol)	ΔG (kcal/mol)	Population
25*R*-2a	-1690.072663	0.517223	-1060212.933841	0	50.18%
25*R*-2b	-1690.072181	0.517867	-1060212.227321	0.706519784	15.21%
25*R*-2c	-1690.073413	0.519119	-1060212.215141	0.718699753	14.91%
25*R*-2d	-1690.072111	0.518432	-1060211.828965	1.104875682	7.76%
25*R*-2e	-1690.07209	0.51879	-1060211.590976	1.342865125	5.19%
25*R*-2f	-1690.070647	0.517448	-1060211.528105	1.405735352	4.67%
25*R*-2g	-1690.070742	0.518619	-1060210.852509	2.081331443	1.49%
25*R*-2h	-1690.069639	0.518404	-1060210.295701	2.638139891	0.58%

Electronic energy obtained at M062X/6-311+G(2d,p) EmpiricalDispersion=GD3 level of theory; Thermal correction to Gibbs free energy obtained at B3LYP/6-31G(d) Scale=0.9813 EmpiricalDispersion=GD3BJ; Gibbs free energy (E + C); The relative Gibbs free energy; The Boltzmann distribution of each conformer.

Table S30. Atomic coordinates (Å) of 25*R*-2a obtained at the mPW1PW91/6-31+G(d,p) level of theory in the MeOH.

C	-4.375358	1.463547	-0.791336	H	-0.581389	-2.230757	-0.211361
C	-5.814491	0.898774	-0.923506	H	-2.222479	3.019601	0.358584
C	-6.186085	-0.093494	0.16622	H	2.809576	3.458016	0.677561
C	-5.237365	-1.294014	0.324961	H	6.066563	0.894935	-0.52607
C	-3.797599	-0.882725	-0.119982	H	4.040198	-1.683418	-2.05248
C	-2.703888	-1.823173	0.399795	H	5.665478	-1.246323	-1.482693
C	-1.400391	-1.522	-0.305003	H	3.425219	-2.563003	0.114051
C	-1.046837	-0.114638	-0.588641	H	5.001042	-4.505916	0.224679
C	-1.995866	0.962383	-0.132605	H	4.698938	-4.062918	-1.464979
C	-3.47027	0.619671	0.148816	H	6.218223	-3.579714	-0.670911
C	-1.539345	2.218629	0.091528	H	-0.369709	0.559101	1.916817
C	-0.108242	2.596436	0.154032	H	1.267785	-0.121033	1.75099
C	0.804115	1.389174	0.229323	H	1.046387	1.511969	2.392318
C	0.357568	0.381555	-0.865378	H	-3.168726	0.393081	2.316333
C	1.568823	-0.577334	-0.898745	H	-3.4881	2.050152	1.803384
C	2.734825	0.270918	-0.565406	H	-4.808936	0.89336	1.877981
C	2.288449	1.49744	-0.036431	H	-6.395868	-2.000173	2.005143
C	0.667042	0.789047	1.663603	H	-4.847013	-2.843088	1.806487
C	-3.753028	1.006259	1.622713	H	-4.897145	-1.216211	2.499702
C	3.170408	2.512108	0.28529	H	-5.114781	-3.247625	-0.646925
C	4.537577	2.27386	0.071353	H	-6.774571	-2.688542	-0.366603
C	4.997018	1.03891	-0.414112	H	-0.487028	1.754322	-2.363475
C	4.106409	0.01709	-0.739336	H	0.191416	0.26069	-3.025637
C	4.613557	-1.328711	-1.190588	H	1.272729	1.565106	-2.481901
C	4.48735	-2.408324	-0.082593	H	4.762135	-1.161031	2.863412
C	5.142965	-3.720214	-0.524868	O	6.340564	-1.746806	1.338661
C	5.147026	-1.8827	1.175464	O	-7.199916	0.024191	0.829134
C	-5.342732	-1.869413	1.74694	O	4.241698	-1.52917	2.12376
C	-5.769248	-2.369305	-0.658032	O	1.553479	-1.761088	-1.201918
C	0.336702	1.041574	-2.275961	H	5.041408	4.020006	0.658325
H	-4.415781	2.492177	-0.419391	O	5.480279	3.215156	0.33972
H	-3.912423	1.506523	-1.781862	O	-1.552826	-0.988929	-1.626814
H	-6.564761	1.692257	-0.930808	H	-5.809367	-1.997941	-1.687668
H	-5.899736	0.362572	-1.877763	O	0.268051	3.755893	0.25187
H	-3.772407	-0.990379	-1.207755				
H	-2.560516	-1.731427	1.483533				

Table S31. Atomic coordinates (Å) of 25*R*-2b obtained at the mPW1PW91/6-31+G(d,p) level of theory in the MeOH.

C	-4.350978	1.502701	-0.745137	H	-0.56736	-2.219721	-0.29929
C	-5.793844	0.947328	-0.876913	H	-2.179196	3.019545	0.426866
C	-6.158785	-0.071624	0.190306	H	2.855273	3.425811	0.706619
C	-5.21322	-1.279199	0.308726	H	6.092339	0.849176	-0.517177
C	-3.776435	-0.862035	-0.140046	H	4.109384	-1.696787	-2.090611
C	-2.681357	-1.819847	0.343814	H	5.697273	-1.303578	-1.402227
C	-1.384131	-1.505478	-0.366667	H	3.304985	-2.630104	-0.058184
C	-1.02774	-0.092912	-0.617136	H	6.209307	-3.569336	-0.455069
C	-1.967216	0.975578	-0.122665	H	4.922754	-4.512017	0.321323
C	-3.440318	0.631612	0.164197	H	4.806036	-4.112333	-1.400296
C	-1.502628	2.223099	0.131072	H	-0.321969	0.495166	1.894314
C	-0.068935	2.592106	0.189277	H	1.323658	-0.164995	1.70935
C	0.836945	1.378995	0.224251	H	1.087586	1.4477	2.389003
C	0.376379	0.40443	-0.893434	H	-3.118266	0.349166	2.322173
C	1.580438	-0.560431	-0.96401	H	-3.437005	2.019475	1.854656
C	2.754617	0.265544	-0.602568	H	-4.761203	0.865657	1.912933
C	2.319287	1.485408	-0.049211	H	-4.850117	-1.259183	2.480994
C	0.712154	0.739732	1.643861	H	-6.357535	-2.023793	1.982153
C	-3.707391	0.981399	1.650192	H	-4.814441	-2.867607	1.745525
C	3.209073	2.486237	0.293395	H	-5.808486	-1.928852	-1.715419
C	4.574118	2.238624	0.08109	H	-5.107943	-3.207392	-0.714449
C	5.023319	1.004882	-0.416161	H	1.285361	1.623881	-2.486036
C	4.125048	-0.003692	-0.76071	H	-0.471588	1.823826	-2.345238
C	4.62575	-1.360862	-1.185591	H	0.188319	0.34299	-3.054218
C	4.378144	-2.439385	-0.095164	H	6.204088	-1.302354	2.289289
C	5.128314	-3.736017	-0.423634	O	3.960327	-1.609934	2.149585
C	4.743537	-1.889516	1.267331	O	-7.166272	0.032201	0.865193
C	-5.306543	-1.890747	1.716406	O	6.081605	-1.696166	1.405204
C	-5.759252	-2.32684	-0.696155	O	1.55398	-1.729435	-1.3193
C	0.346972	1.102284	-2.285323	H	5.093328	3.967387	0.704178
H	-4.383165	2.521771	-0.346983	O	5.526025	3.165482	0.370022
H	-3.897788	1.568755	-1.738911	O	-1.548026	-0.937536	-1.67277
H	-6.540898	1.743624	-0.855975	H	-6.762758	-2.649977	-0.402687
H	-5.891118	0.436293	-1.843772	O	0.313997	3.747186	0.312165
H	-3.762731	-0.941405	-1.23048				
H	-2.525906	-1.756775	1.427876				

Table S32. Atomic coordinates (Å) of 25*R*-2c obtained at the mPW1PW91/6-31+G(d,p) level of theory in the MeOH.

C	4.180965	1.615678	0.800306	H	0.469622	-2.159493	0.242484
C	5.629984	1.084512	0.962146	H	2.007467	3.100306	-0.438965
C	6.037504	0.076474	-0.100161	H	-3.018285	3.416678	-0.812474
C	5.114221	-1.145109	-0.249126	H	-6.234756	0.825021	0.423858
C	3.66051	-0.753293	0.166193	H	-4.081253	-1.813963	1.823376
C	2.592132	-1.725009	-0.349149	H	-5.745403	-1.263563	1.557083
C	1.274902	-1.435002	0.334694	H	-5.392817	-3.299185	0.367747
C	0.89138	-0.030552	0.586374	H	-5.349307	-1.04791	-1.723144
C	1.822978	1.054464	0.113307	H	-6.020311	-2.670108	-1.947685
C	3.308444	0.73676	-0.137997	H	-6.793125	-1.545165	-0.815426
C	1.340151	2.291597	-0.155722	H	-1.358197	-0.191557	-1.764334
C	-0.099499	2.631787	-0.250635	H	-1.21914	1.426895	-2.467398
C	-0.979809	1.4007	-0.300853	H	0.241921	0.569278	-1.951504
C	-0.526006	0.442556	0.832774	H	3.047575	0.462834	-2.305085
C	-1.712985	-0.544368	0.887984	H	3.327784	2.134883	-1.819951
C	-2.895298	0.252964	0.488086	H	4.670923	1.002572	-1.849929
C	-2.469117	1.479323	-0.05914	H	4.776832	-2.731048	-1.704218
C	-0.80738	0.751817	-1.710925	H	4.804025	-1.117791	-2.429452
C	3.6089	1.099971	-1.614218	H	6.311214	-1.860822	-1.898089
C	-3.366063	2.471737	-0.406515	H	5.669589	-1.797385	1.785402
C	-4.729209	2.214605	-0.192779	H	5.014505	-3.080901	0.760319
C	-5.166985	0.978303	0.305087	H	-0.381417	0.392914	2.996784
C	-4.263412	-0.032339	0.635432	H	-1.489701	1.651055	2.400879
C	-4.763072	-1.382312	1.086719	H	0.265643	1.883696	2.295839
C	-4.940948	-2.408075	-0.079746	H	-2.202504	-4.046208	-0.310243
C	-5.829268	-1.883906	-1.210027	O	-2.959193	-2.231762	-1.479339
C	-3.583534	-2.817935	-0.618108	O	7.060729	0.198522	-0.747741
C	5.251992	-1.746438	-1.657514	O	-3.123864	-3.933162	-0.011826
C	5.65191	-2.190015	0.763031	O	-1.672328	-1.702503	1.27397
C	-0.537652	1.146519	2.22176	H	-5.261776	3.943047	-0.805833
H	4.20406	2.63869	0.41169	O	-5.688165	3.137471	-0.472593
H	3.702703	1.664673	1.783269	O	1.401329	-0.874516	1.647704
H	6.363643	1.893437	0.961337	H	6.667394	-2.495439	0.492738
H	5.71456	0.57107	1.928966	O	-0.500443	3.779092	-0.387753
H	3.621498	-0.839343	1.25544				
H	2.459915	-1.656158	-1.435942				

Table S33. Atomic coordinates (Å) of 25*R*-2d obtained at the mPW1PW91/6-31+G(d,p) level of theory in the MeOH.

C	4.157918	0.802398	1.720648	H	0.933395	-1.970245	-1.485458
C	5.5882	0.218586	1.8666	H	2.148656	2.784108	1.062368
C	6.267622	-0.081165	0.540261	H	-2.71752	3.447972	-0.109179
C	5.490114	-1.004735	-0.413204	H	-5.932256	0.70672	-0.977553
C	3.95733	-0.846015	-0.157884	H	-5.310552	-1.583967	-1.812641
C	3.087665	-1.357611	-1.312234	H	-3.690115	-2.229431	-1.498038
C	1.644878	-1.430972	-0.865241	H	-5.395733	-3.287854	-0.116522
C	1.108624	-0.362482	0.004999	H	-4.310054	-3.077873	2.114204
C	2.023902	0.772443	0.382526	H	-3.074483	-3.062175	0.830609
C	3.550542	0.587641	0.306618	H	-3.559659	-1.557175	1.636964
C	1.504986	1.975922	0.727661	H	0.896046	1.55847	-1.881878
C	0.08747	2.367108	0.545894	H	-0.630592	0.848465	-2.451432
C	-0.673921	1.389967	-0.328205	H	-0.522399	2.588177	-2.143792
C	-0.362749	-0.045699	0.175819	H	3.723101	1.520522	-1.678461
C	-1.46299	-0.85736	-0.5444	H	3.773584	2.665815	-0.337985
C	-2.624027	0.064124	-0.618137	H	5.183995	1.679267	-0.691838
C	-2.185621	1.381075	-0.370609	H	5.597163	0.190826	-2.260006
C	-0.191186	1.605447	-1.795173	H	7.030208	-0.772905	-1.909189
C	4.092358	1.671909	-0.659007	H	5.560714	-1.558919	-2.519006
C	-3.069178	2.442508	-0.319049	H	5.356657	-3.176182	-0.621149
C	-4.429051	2.164634	-0.531164	H	6.978337	-2.593883	-0.199903
C	-4.872327	0.863365	-0.808721	H	-0.642453	-1.261796	1.953618
C	-3.982763	-0.211021	-0.851578	H	-1.680651	0.182052	1.928019
C	-4.492118	-1.613846	-1.087471	H	0.045807	0.329189	2.304522
C	-5.006212	-2.312736	0.205537	H	-7.921471	-0.975649	0.384111
C	-3.919131	-2.518151	1.260039	O	-6.242651	-1.075252	1.903114
C	-6.185089	-1.559958	0.795971	O	7.380499	0.334701	0.276084
C	5.938944	-0.767717	-1.864615	O	-7.224365	-1.475272	-0.081073
C	5.909088	-2.445421	-0.020523	O	-1.385396	-2.017443	-0.917811
C	-0.686361	-0.202403	1.691915	H	-4.951338	3.983191	-0.270294
H	4.17222	1.873783	1.944329	O	-5.37592	3.139111	-0.491871
H	3.500724	0.336634	2.461229	O	1.472832	-1.658713	0.539447
H	6.241541	0.878803	2.4409	H	5.702629	-2.658104	1.033897
H	5.529909	-0.733353	2.410533	O	-0.367095	3.422734	0.963021
H	3.720292	-1.497736	0.687453				
H	3.161238	-0.717874	-2.200352				

Table S34. Atomic coordinates (Å) of 25*R*-2e obtained at the mPW1PW91/6-31+G(d,p) level of theory in the MeOH.

C	4.022338	0.790509	1.658001	H	0.604053	-1.804739	-1.492156
C	5.430783	0.147118	1.760311	H	2.081796	2.869499	1.055697
C	6.063348	-0.166192	0.414027	H	-2.791127	3.728364	0.054581
C	5.223264	-1.043843	-0.529795	H	-6.127409	1.125412	-0.774595
C	3.705689	-0.823472	-0.233525	H	-5.670725	-1.110786	-1.653429
C	2.785344	-1.283376	-1.370255	H	-4.065387	-1.85015	-1.548811
C	1.353226	-1.303505	-0.884443	H	-5.80369	-1.29095	0.898316
C	0.884992	-0.226467	0.014249	H	-5.621428	-3.869105	-0.777403
C	1.856608	0.867274	0.373712	H	-6.448649	-3.743813	0.782043
C	3.371976	0.620116	0.257196	H	-7.049958	-2.826559	-0.61148
C	1.397054	2.089529	0.735915	H	-0.684788	2.801946	-2.072745
C	-0.008282	2.539134	0.596008	H	0.699436	1.716914	-1.855018
C	-0.832957	1.598404	-0.259693	H	-0.868246	1.069685	-2.386571
C	-0.566592	0.148214	0.230458	H	3.536279	1.569306	-1.720564
C	-1.713817	-0.613334	-0.468272	H	3.669459	2.694669	-0.36903
C	-2.83699	0.354154	-0.520096	H	5.026471	1.652849	-0.76903
C	-2.344474	1.648796	-0.260453	H	5.215846	-1.573513	-2.642944
C	-0.382496	1.804951	-1.738378	H	5.335324	0.169483	-2.364463
C	3.936638	1.691949	-0.709015	H	6.733517	-0.859895	-2.062631
C	-3.186019	2.740794	-0.16333	H	5.40065	-2.722783	0.892169
C	-4.560878	2.515995	-0.336417	H	4.992357	-3.20476	-0.759675
C	-5.056779	1.23793	-0.631605	H	-1.84058	0.388457	2.012233
C	-4.208563	0.13442	-0.729288	H	-0.097825	0.531248	2.341827
C	-4.789036	-1.231144	-1.013602	H	-0.824794	-1.053253	2.02152
C	-5.252577	-1.992593	0.264103	H	-2.657955	-3.674529	1.111116
C	-6.144946	-3.18189	-0.107059	O	-3.517061	-1.724701	1.934351
C	-4.027994	-2.395825	1.061931	O	7.186758	0.203588	0.126659
C	5.645006	-0.807949	-1.989462	O	-3.51805	-3.580991	0.661002
C	5.590064	-2.505772	-0.164579	O	-1.696882	-1.773816	-0.849422
C	-0.853523	0.003786	1.754586	H	-5.00869	4.345508	-0.020876
H	4.085853	1.857263	1.89481	O	-5.47138	3.522045	-0.243584
H	3.36493	0.341739	2.408781	O	1.21031	-1.544115	0.521568
H	6.125613	0.773551	2.323693	H	6.647305	-2.697066	-0.372418
H	5.347633	-0.807521	2.296322	O	-0.405916	3.611429	1.02861
H	3.462412	-1.474686	0.610389				
H	2.861348	-0.634665	-2.251655				

Table S35. Atomic coordinates (Å) of 25*R*-2f obtained at the mPW1PW91/6-31+G(d,p) level of theory in the MeOH.

C	4.057704	0.654493	1.76606	H	0.604053	-1.804739	-1.492156
C	5.466093	0.015813	1.895207	H	2.081796	2.869499	1.055697
C	6.158184	-0.219966	0.562512	H	-2.791127	3.728364	0.054581
C	5.368185	-1.054685	-0.459901	H	-6.127409	1.125412	-0.774595
C	3.837217	-0.86397	-0.216716	H	-5.670725	-1.110786	-1.653429
C	2.969733	-1.272822	-1.412812	H	-4.065387	-1.85015	-1.548811
C	1.519208	-1.331537	-0.988286	H	-5.80369	-1.29095	0.898316
C	1.001232	-0.304511	-0.0583	H	-5.621428	-3.869105	-0.777403
C	1.945256	0.776281	0.398972	H	-6.448649	-3.743813	0.782043
C	3.466823	0.549101	0.332773	H	-7.049958	-2.826559	-0.61148
C	1.458805	1.972707	0.809263	H	-0.684788	2.801946	-2.072745
C	0.056659	2.4171	0.634586	H	0.699436	1.716914	-1.855018
C	-0.721627	1.519551	-0.306664	H	-0.868246	1.069685	-2.386571
C	-0.463095	0.04463	0.114372	H	3.536279	1.569306	-1.720564
C	-1.573082	-0.68069	-0.679298	H	3.669459	2.694669	-0.36903
C	-2.709941	0.279687	-0.690478	H	5.026471	1.652849	-0.76903
C	-2.232245	1.563477	-0.363656	H	5.215846	-1.573513	-2.642944
C	-0.212518	1.807074	-1.751957	H	5.335324	0.169483	-2.364463
C	4.057657	1.674404	-0.553776	H	6.733517	-0.859895	-2.062631
C	-3.084147	2.645955	-0.243289	H	5.40065	-2.722783	0.892169
C	-4.453101	2.420998	-0.457865	H	4.992357	-3.20476	-0.759675
C	-4.937019	1.149118	-0.793792	H	-1.84058	0.388457	2.012233
C	-4.076514	0.055508	-0.911159	H	-0.097825	0.531248	2.341827
C	-4.621831	-1.325861	-1.193564	H	-0.824794	-1.053253	2.02152
C	-5.543063	-1.847449	-0.075952	H	-2.657955	-3.674529	1.111116
C	-6.077844	-3.254737	-0.403357	O	-3.517061	-1.724701	1.934351
C	-4.819621	-1.893875	1.256997	O	7.186758	0.203588	0.126659
C	5.847928	-0.739595	-1.886326	O	-3.51805	-3.580991	0.661002
C	5.735712	-2.530405	-0.155726	O	-1.696882	-1.773816	-0.849422
C	-0.81611	-0.196413	1.611666	H	-5.00869	4.345508	-0.020876
H	4.102674	1.708674	2.057264	O	-5.47138	3.522045	-0.243584
H	3.374031	0.164965	2.466192	O	1.21031	-1.544115	0.521568
H	6.130307	0.615603	2.521097	H	6.647305	-2.697066	-0.372418
H	5.368044	-0.966899	2.374958	O	-0.405916	3.611429	1.02861
H	3.566529	-1.560171	0.581654				
H	3.074764	-0.579013	-2.256155				

Table S36. Atomic coordinates (Å) of 25*R*-2g obtained at the mPW1PW91/6-31+G(d,p) level of theory in the MeOH.

C	4.026175	0.788278	1.657536	H	0.602171	-1.796588	-1.494993
C	5.43476	0.144618	1.756609	H	2.085288	2.870573	1.061199
C	6.065186	-0.16805	0.409205	H	-2.81597	3.742862	0.05113
C	5.222649	-1.042762	-0.535228	H	-6.122009	1.102286	-0.78394
C	3.705709	-0.821108	-0.236876	H	-5.658631	-1.116348	-1.657485
C	2.783615	-1.277514	-1.373579	H	-4.05165	-1.850019	-1.545693
C	1.351898	-1.297239	-0.886459	H	-5.803235	-1.300464	0.894545
C	0.886008	-0.221891	0.015176	H	-7.034907	-2.840692	-0.625163
C	1.859034	0.86997	0.375834	H	-5.600279	-3.875813	-0.783028
C	3.374152	0.621784	0.257145	H	-6.437013	-3.755416	0.77157
C	1.400216	2.091099	0.740836	H	-0.685244	2.815254	-2.060755
C	-0.006677	2.541703	0.607958	H	0.698295	1.72781	-1.848088
C	-0.833287	1.605691	-0.252625	H	-0.870047	1.084244	-2.381472
C	-0.565171	0.153848	0.233639	H	5.028832	1.655505	-0.768144
C	-1.71105	-0.608094	-0.46389	H	3.537737	1.575002	-1.718664
C	-2.8351	0.358091	-0.515468	H	3.67267	2.697238	-0.364846
C	-2.34582	1.65704	-0.255137	H	5.211996	-1.568134	-2.649469
C	-0.38347	1.816798	-1.730566	H	5.334174	0.174141	-2.367439
C	3.93902	1.695098	-0.707169	H	6.731368	-0.857772	-2.069493
C	-3.18645	2.748041	-0.16193	H	6.644901	-2.698004	-0.382749
C	-4.560446	2.519097	-0.340165	H	5.399752	-2.724496	0.883345
C	-5.05185	1.238341	-0.632138	H	-0.822637	-1.050882	2.023348
C	-4.202238	0.132594	-0.726356	H	-1.838302	0.391849	2.016583
C	-4.779399	-1.233749	-1.013118	H	-0.095861	0.53338	2.345292
C	-5.246004	-1.998449	0.2614	H	-2.647243	-3.669196	1.117911
C	-6.13096	-3.191494	-0.115429	O	-3.5223	-1.724515	1.942164
C	-4.023662	-2.397025	1.06564	O	7.189258	0.199471	0.121378
C	5.64301	-0.804503	-1.99492	O	-3.506312	-3.578848	0.66512
C	5.588136	-2.505807	-0.173258	O	-1.69496	-1.768766	-0.845261
C	-0.851718	0.00654	1.757825	H	-6.301001	3.312601	-0.366709
H	4.089899	1.854351	1.897265	O	-5.382864	3.597113	-0.235027
H	3.369487	0.337499	2.407739	O	1.209728	-1.541542	0.519165
H	6.130885	0.770303	2.319242	H	4.988788	-3.202961	-0.768888
H	5.352568	-0.810514	2.291982	O	-0.402225	3.608557	1.052637
H	3.462478	-1.473794	0.605946				
H	2.859318	-0.626697	-2.253467				

Table S37. Atomic coordinates (Å) of 25*R*-2h obtained at the mPW1PW91/6-31+G(d,p) level of theory in the MeOH.

C	3.962142	0.733322	1.735402	H	0.743537	-1.809213	-1.662831
C	5.382219	0.12153	1.865445	H	1.985775	2.769213	1.180681
C	6.075125	-0.10986	0.532427	H	-2.85891	3.572797	0.007797
C	5.298648	-0.966782	-0.481829	H	-6.119915	0.908044	-0.91791
C	3.764656	-0.803057	-0.236667	H	-5.488985	-1.419877	-1.867251
C	2.903838	-1.235693	-1.429197	H	-3.887325	-2.071318	-1.473704
C	1.454567	-1.316283	-1.005028	H	-6.129309	-1.424686	0.507593
C	0.919764	-0.291728	-0.082047	H	-4.872781	-4.110603	-0.306161
C	1.84407	0.805915	0.373863	H	-6.214487	-3.906529	0.833504
C	3.369148	0.606569	0.304549	H	-6.45207	-3.527373	-0.883249
C	1.336128	1.99213	0.788538	H	0.747429	1.743962	-1.852767
C	-0.074243	2.410588	0.618922	H	-0.786234	1.100951	-2.479033
C	-0.837935	1.503545	-0.325906	H	-0.649961	2.81497	-2.057484
C	-0.549714	0.032224	0.088181	H	3.578033	1.647196	-1.622627
C	-1.647654	-0.70985	-0.706672	H	3.621226	2.715103	-0.219322
C	-2.806357	0.223968	-0.691931	H	5.026785	1.734805	-0.609581
C	-2.350126	1.518536	-0.373822	H	6.860856	-0.671822	-1.94362
C	-0.339555	1.805568	-1.771313	H	5.388012	-1.399006	-2.615244
C	3.934736	1.73744	-0.591513	H	5.446286	0.33205	-2.254508
C	-3.222525	2.584025	-0.25468	H	6.764034	-2.585218	-0.341416
C	-4.589022	2.332211	-0.460753	H	5.470265	-2.703936	0.869479
C	-5.051681	1.049072	-0.783219	H	-0.143672	0.221059	2.241492
C	-4.171363	-0.027046	-0.898293	H	-0.93696	-1.293723	1.767667
C	-4.6922	-1.427221	-1.114454	H	-1.87075	0.217862	1.834323
C	-5.284739	-2.041595	0.184562	H	-3.72045	-1.035006	2.806346
C	-5.735051	-3.486	-0.056661	O	-3.288115	-2.748217	1.375827
C	-4.236532	-1.999823	1.282768	O	7.195915	0.307265	0.306051
C	5.769278	-0.652862	-1.911586	O	-4.457715	-0.995322	2.167629
C	5.694283	-2.433188	-0.167901	O	-1.568245	-1.812282	-1.218754
C	-0.900176	-0.217682	1.586319	H	-5.082828	4.14365	-0.109424
H	3.988803	1.790252	2.018793	O	-5.523551	3.31515	-0.356468
H	3.289498	0.236557	2.441146	O	1.261472	-1.62028	0.382271
H	6.036501	0.737797	2.485736	H	5.141139	-3.120381	-0.817282
H	5.303439	-0.859606	2.351862	O	-0.523065	3.439883	1.103752
H	3.508308	-1.499163	0.566583				
H	2.996634	-0.546544	-2.277722				

Table S38. The experimental and calculated ^{13}C NMR spectroscopic data of 25*S*-2 and 25*R*-2 at the mPW1PW91/6-31+G(d,p) level of theory in the MeOH.

position	Exptl.-2	Calcd.25S-2	Calcd.25R-2
1	36.8	38.0	43.4
2	34.6	35.9	41.2
3	219.3	219.2	218.2
4	47.2	49.4	54.3
5	42.3	42.5	47.4
6	23.6	24.3	30.0
7	60.1	62.0	66.2
8	63.7	64.1	68.4
9	167.3	170.7	171.8
10	41.7	44.6	49.5
11	131.3	129.3	129.7
12	199.6	197.1	197.0
13	57.3	58.3	63.1
14	55.7	58.9	63.0
15	202.4	200.2	199.7
16	124.5	123.1	125.7
17	157.8	155.9	157.7
18	31.5	34.4	40.2
19	24.3	26.5	32.3
20	111.9	107.8	110.8
21	164.3	158.6	159.0
22	117.9	113.6	113.2
23	145	142.6	144.4
24	36.5	39.2	45.2
25	41.8	42.6	47.9
26	17.5	18.0	24.0
27	179.6	174.7	175.6
28	22	21.1	26.9
29	29.3	29.3	34.8
30	23.6	24.6	30.8

Table S39. The experimental and calculated ^{1}H NMR spectroscopic data of 25*S*-2 and 25*R*-2 at the mPW1PW91/6-31+G(d,p) level of theory in the MeOH.

position	Exptl.-2	Calcd.25*S*-2	Calcd.25*R*-2
1	2.1	1.83	1.85
1	2.1	2.05	2.05
2	2.47	2.45	2.04
2	2.76	2.87	2.86
5	2.98	2.98	2.97
6	1.92	1.68	1.68
6	2.24	2.03	2.04
7	4.75	4.86	4.89
11	6.25	6.19	6.22
20	7.22	7.55	7.58
22	6.58	6.51	6.74
24	2.96	2.91	3.25
24	3.14	3.23	2.72
25	2.66	2.70	3.14
26	1.11	1.01	1.08
26	1.11	1.12	1.07
26	1.11	1.12	1.10
18	1.48	1.49	1.64
18	1.48	1.57	1.23
18	1.48	1.40	1.34
19	1.25	1.24	1.24
19	1.25	1.02	0.74
19	1.25	1.22	0.74
28	1.1	1.07	1.12
28	1.1	1.24	0.81
28	1.1	1.07	0.87
29	1.1	1.00	1.19
29	1.1	1.18	0.94
29	1.1	1.13	1.29
30	1.26	1.09	1.20
30	1.26	1.31	1.03
30	1.26	1.17	0.84

Figure S24. The experimental and calculated ECD curves of 25*S*-2.

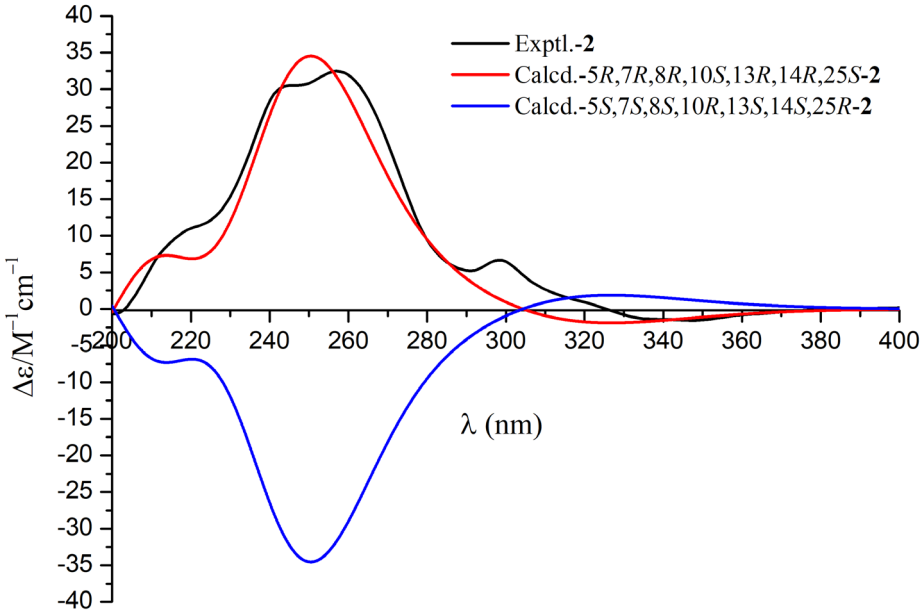
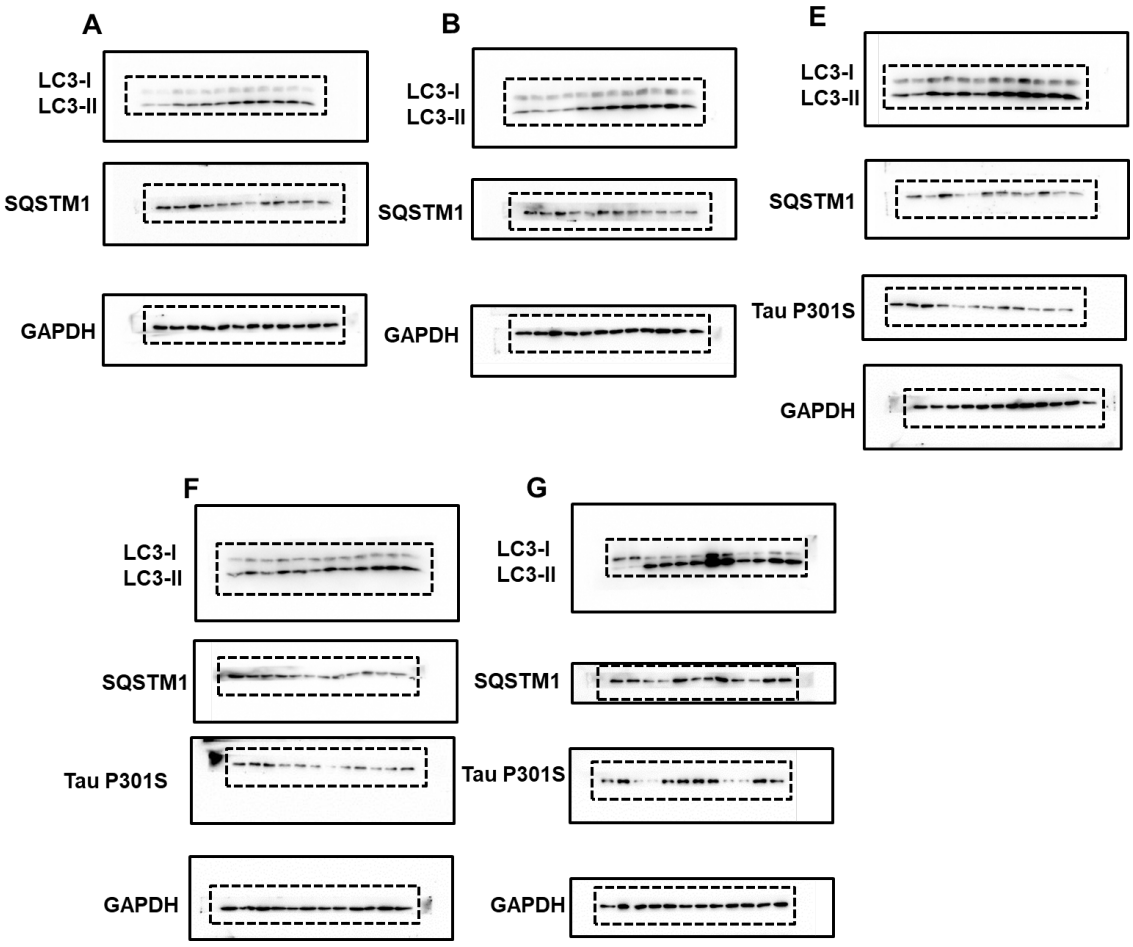


Figure S25. Uncropped images of western blot



Note: A, B and E–G are corresponding to the A, B and E–G in Figure 5 of paper.