Supporting Information

Chemical control on conversion between bicyclic and polycyclic terpene by fungal bifunctional terpene synthases

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MATERIALS AND METHODS

Materials and instruments

Oligonucleotides were synthesized by GENEWIZ (Suzhou, China). Plasmid preparation kit I (D6943-02) was purchased from Omega Bio-tek (Norcross, GA, USA). The ClonExpress II One Step Cloning Kit was purchased from Vazyme Biotech Co., Ltd. (Nanjing, China). DNA sequencing was conducted by GENEWIZ (Suzhou, China). All commercial chemicals were purchased from Sigma (Saint Louis, MO, USA), Takara (Otsu, Japan), Adamas-beta (Shanghai, China), or Sinopharm Chemical Reagent (Shanghai, China). Semipreparative HPLC was carried out using a Cosmosil Cholester column (10 × 250 mm, 5 μm) and ACE Excel 5 C18 column (10 × 250 mm, 5 μm). ^{1}H, ^{13}C NMR, and 2D NMR spectra were recorded on a Agilent DD2 (Santa Clara, CA, USA) 600 MHz NMR spectrometer. The NMR spectra were referenced against solvent signals with resonances at δ_H 7.16 ppm, δ_C 128.06 ppm in C_6D_6. The CD spectra was recorded on a Chirascan circular dichroism spectrometer using MeOH as solvent. HREIMS measurements were obtained on a Waters GCT Premier mass spectrometer.

Plasmids construction

The encoding gene of the WT BsPS was inserted in *Escherichia coli*/S*accharomyces cerevisiae* shuttle vectors pXW55 and expressed in *S. cerevisiae* (*SC*) BJ5464. The constructed plasmid pXW55-*wt* was used as template for TCSM at the putative active sites in the catalytic pocket. The primers used to construct BsPS-TCSM mutation library are listed in Table S3. First, one site of each library was mutated by PCR. After digestion of the PCR products with *Dpn*I to remove the WT template plasmid, 2 μL of the reaction mixture was used to transform *E. coli* BL21 (DE3). After plating, individual colonies were picked and the plasmids were extracted and sequenced. Second, the other sites of each library were mutated simultaneously by PCR, using the sequenced plasmid from the first step as template. Then, the PCR products were treated using the same protocol as in the first step, then sequenced.

Small-scale fermentation of *S. cerevisiae* heterologously expressing the wild-type (WT) and mutant BsPS

Based on sequencing results, plasmids containing the encoding genes of wild-type (WT) and mutant BsPS were transformed into *S. cerevisiae* BJ5464. After plating, colonies were picked for protein overexpression and used to inoculate 5 mL uracil-dropout medium (20 $g \cdot L^{-1}$ glucose, 5.0 $g \cdot L^{-1}$ casamino acids, 0.02 $g \cdot L^{-1}$ adenine, 6.7 $g \cdot L^{-1}$ YNB, 0.02 $g \cdot L^{-1}$ tryptophan, pH 7.5). After incubation for 48 h at 30 °C with shaking at 200 rpm, 0.5 mL of the culture was transferred to a 250 mL flask containing 50 mL YPD medium (20 $g \cdot L^{-1}$ tryptone, 10 $g \cdot L^{-}$

[1] yeast extract, 20 g·L^{-1} glucose, pH 7.5). The culture was incubated at 30 °C with shaking at 200 rpm for 72 h to express the target protein and accumulate metabolites.

Small-scale fermentation of *E. coli* heterologously expressing the WT FoFS and the mutant L89S

Plasmids containing the encoding genes of WT FoFS and the mutant L89S were transformed into *E. coli* (*EC*) BL21 (DE3). After plating, colonies were picked for protein overexpression and used to inoculate 5 mL Luria-Bertani (LB) medium (10 g·L^{-1} trypton, 5.0 g·L^{-1} yeast extract, 10 g·L^{-1} NaCl, pH 7.5). After incubation for 10 h at 37 °C with shaking at 200 rpm, 1 mL of the culture was transferred to a 250 mL flask containing 50 mL auto-induction medium (10 g·L^{-1} α-lactose, 1.0 g·L^{-1} glucose, 5.0 g·L^{-1} glycerol, 6.8 g·L^{-1} KH_2PO_4, 0.25 g·L^{-1} $MgSO_4$, 10 g·L^{-1} tryptone, 5.0 g·L^{-1} yeast extract, 7.1 g·L^{-1} Na_2HPO_4, 0.71 g·L^{-1} Na_2SO_4, and 2.67 g·L^{-1} NH_4Cl, pH 7.5) supplemented with kanamycin (50 μg·mL^{-1}). After cultivation at 37 °C with shaking at 200 rpm for the first 2-3 h, the culture was incubated at 17 °C with shaking at 200 rpm for another 48 h to express the target protein and accumulate metabolites.

Extraction of cell cultures and GC-MS analysis

After fermentation, the cells were harvested by centrifugation at 5,000 g, then soaked with acetone for 30 min. After centrifugation at 5,000 g, the supernatant was separated and concentrated in vacuo. Then the residue was dissolved in EtOAc. The organic layer was evaporated in vacuo to afford crude extracts.

The crude extracts were dissolved in EtOAc (1 mg/mL) and analyzed by GC-MS with a DB-5 ms capillary column (0.25 mm × 30.0 m, 0.25 μm film thickness; SHIMADZU) under the following conditions. GC settings: inlet pressure 110 kPa, injection volume 2 μL, temperature program: 0 min at 60 °C increasing at 25 °C min^{-1} to 280 °C, then increasing at 10 °C min^{-1} to 310 °C, remaining at 310 °C for 11.8 min, and carrier gas He at 1.77 mL·min^{-1}. MS settings: source temperature 200 °C, transfer line temperature 250 °C, and electron energy 0.4 kV.

Large-scale fermentation of *SC*-S89L and *EC*-L89S and purification of compounds 1–6

After enlarging the fermentation volume to 40 L, 1,100 g biomass (wet weight) of *SC*-S89L was obtained. The crude extracts of *SC*-S89L (1.5 g) were preliminarily purified by silica gel column chromatography using a hexane-CH_2Cl_2 gradient (1:0 and 1:1, *v*/*v*) to afford two fractions A and B. Fraction A was further purified by semi-preparative HPLC using ACE Excel 5 C18 column (Φ 10 × 250 mm) with a flow rate of 4.0 mL/min and a isocratic elution (100% ACN) monitored with DAD (λ_1 = 210 nm, λ_2 = 254 nm) to give **2** (1.0 mg, t_R = 44.0 min) and **3** (1.5 mg, t_R = 43.0 min). Fraction B was first separated by semi-preparative HPLC using ACE Excel 5 C18-AR column (Φ 10 × 250 mm) with a flow rate of 3.2 mL/min and a

isocratic elution (100% ACN) monitored with DAD (λ = 210 nm) to afford fraction B-1, which was further purified by a COSMOSIL Cholester column (Φ 4.6 × 250 mm) under the following conditions (λ = 210 nm, 100% MeOH, 0.8 mL/min) to afford **1** (5.0 mg, t_R = 8.5 min), **4** (0.8 mg, t_R = 16.5 min), and **5** (0.5 mg, t_R = 9.0 min).

The fermentation volume of *EC*-L89S was 20 L, ~200 g biomass (wet weight) was obtained. The crude extracts of *EC*-L89S (0.23 g) were preliminarily purified by silica gel column chromatography using hexane and CH_2Cl_2 to afford two fractions A and B, respectively. Fraction B was purified by semi-preparative HPLC using ACE Excel 5 C18-AR column (Φ 10 × 250 mm) with a flow rate of 4.0 mL/min and a isocratic elution (ACN:H_2O = 95:5) monitored with DAD (λ_1 = 210 nm, λ_2 = 254 nm) to give **1** (2.0 mg, t_R = 11.9 min).

ECD Calculation details

The calculations were performed by using the density functional theory (DFT) as carried out in the Gaussian 09[1]. The preliminary conformational distributions search was performed by Sybyl-X 2.0 software. All ground-state geometries were optimized at the B3LYP/6-31G(d) level. Solvent effects of methanol solution were evaluated at the same DFT level by using the SCRF/PCM method. TD-DFT at B3LYP/6-31+G(d) was employed to calculate the electronic excitation energies and rotational strengths in methanol.

Computational details for DFT mechanism calculations

The molecular geometries of the complexes were optimized using density functional theory (DFT) calculations at the M06–2X/6–31G(d,p) level. Frequency calculations were also performed at the same level of theory to identify all the stationary points as minima (zero imaginary frequencies) or transition states (one imaginary frequency), and the free energies at 298.15 K. An IRC analysis was performed to confirm that all the stationary points were smoothly connected to each other. The Gibbs free energies were calculated from the electron energies using the mPW1PW91/6–31+G(d,p) level, plus the thermal correction of the M06–2X/6–31G(d,p) level. All calculations were performed using the Gaussian 09[1] package.

Starting structures and system preparation

The initial protein structures were constructed using homology modeling method SWISS-MODEL, in which a crystal structure of *Phomopsis amygdali* fusicoccadiene synthase (PaFS, PDB ID: 5ERM) was employed as template (sequence similarity: 40.0 %). The ligands including GFPP, IMs, products, were docked into the catalytic pocket of the proteins, WT, S89L, S89C, S89A, using AutoDock Vina[2], respectively. Side chains of residues F61, W69, S89, L93, F196, M199, T224, and L227, were treated as flexible. The search grid box 30 × 30 × 30 $Å^3$ was placed to include the substrate-binding site. The exhaustiveness was set at 32 and default options were used for the remaining parameters. The conformations of the ligands with similar binding direction in the catalytic pocket were selected for molecular dynamics

simulations. Hydrogens of proteins are added with reduce utility of AmberTools 20[3]. Using tleap, water molecules was assigned with the TIP3P model, and protein and ions were described by the ff14SB force field, while the GAFF force field was employed to generate the force field parameters for the MD simulations. The partial atomic charges of ligands were obtained from the restrained electrostatic potential (RESP) charge based on HF/6-31G(d) calculation with Gaussian 09[1] package. And the ligands were structurally optimized with the semi-empirical method (AM1) and parameterized for the following-up molecular dynamic simulation with the antechamber program in the AMBER 20[3] software package. The complexes were solvated in a truncated octahedral box of water molecules, extending 10.0 Å along each dimension with 8 Na^+ ion added to neutralized the calculated system.

Molecular dynamic simulations

The MD simulations of the apoproteins and receptor-ligand complexes were run with the AMBER 20[3] software package. We firstly imposed harmonic restraints on the protein, ligand, and Mg^{2+}, keeping the waters of solvation free. For the second minimization step, the C_α of the protein and ligand, and Mg^{2+} have been restrained. For the last minimization step, all system was set free. The MD systems were minimized by the steepest descent minimization of 2000 steps followed the conjugate gradient minimization of 2000 steps for each step of the minimizations. Next, the complex was heated up from 0 to 300 K at constant volume in 50 ps, and relaxed the models density for another 100 ps under constant pressure without any restraints. The Particle Mesh Ewald (PME) method was employed for long-range electrostatic interactions. Finally, a production of 2 × 100 ns was calculated at 300 K at constant volume, employing the SHAKE algorithm to constrain all the covalent bonds containing hydrogen.[4-6] The MD simulation was carried out taking advantage of the GPU acceleration of the Amber 20 PEMED package.

SUPPLEMENTARY TEXT

Design of triple-codon saturation mutagenesis (TCSM) library

We used the crystal structure of PaFS[7] (PDB ID: 5ERM, sequence identity: 40%) as a template for homology modeling of the wild-type (WT) BsPS. The region of the catalytic pocket of the WT protein was predicted using POVME,[8] after which 11 amino acid residues (F61, W69, S89, L93, R187, N190, F196, M199, T224, L227, and N231) were found in the putative active pocket (Figure S2). Asparagine has been reported to coordinate Mg^{2+},[9, 10] and arginine stabilizes the bisphosphonate moiety,[7, 10] therefore R187, N190, and N231 were excluded from the candidate list of sites for mutation experiments. Aromatic amino acids can stabilize the carbocation intermediates of terpene cyclization reactions by cation···π and C–H···π interactions.[11, 12] Sato and co-workers considered that W164, F191, F196, and W318 in

the NfSS pocket exercise cation···π or C–H···π functions, which contributes to the carbonation transportation *via* branched routes and drives the hydride shift.[13] Therefore, we divided the selected sites into three groups according to their spatial distribution, and included one aromatic amino acid residue into each group (Figure S2). We obtained the following three groups of amino acids: (I) F61, S89, L93; (II) W69, M199; and (III) F196, T224, L227. The substitution amino acids in each group were selected from non-polar amino acids, Phe (F) with aromatic ring, Ala (A) with minimal spatial site resistance, and Leu (L) with a high frequency of occurrence at these eight corresponding sites in the homologous proteins of BsPS (Figure S3). In addition, to provide enough space in the pocket for the bulky GFPP substrate, at most one aromatic amino acid per group was used. Thus, three TCSM libraries I–III containing 20, 8, and 20 variants, respectively, were then constructed to screen for new sesterterpene production (Figure S5).

For TCSM library I, 16 of 20 variants completely or partially lost their enzymatic activity of forming **1** and produced geranylfarnesol (GFOH) as the major product. Three variants (S89A, S89L, and F61A/S89A) were able to produce new products, along with **1** with different yields and product profiles. Remarkably, the variant S89L can catalyze the formation of these five sesterterpenes (**1**–**5**). In TCSM library II, the function of most of the variants was inactivated, while only two variants (W69A/M199A and W69L/M199F) retained their cyclization activities. This led to the production of two new products (**2** and **3**), along with **1**. Eight of 20 variants in TCSM library III were found to generate new products (**2** and **3**), of which T224L, F196A/T224A, F196L/T224F, and F196L/T224A/L227A had relatively higher yields of **2** and **3** than of **1**. We chose the variant S89L to characterize new products yielded by BsPS variants since it could produce these four new products for further large-scale fermentation and structural elucidation (using S89A as a control), as well as the computational simulations on their cyclization mechanisms.

Structural elucidation of compounds 1–5

Compound **2** was isolated as a white powder, [α]27 D 24.0 (*c* 0.035, MeOH). The molecular formula $C_{25}H_{40}$ was confirmed by HR-EI-MS (M^+ at *m/z* 340.3125, calcd. for 340.3130, Figure S7), indicating 6 units of unsaturation. Combined analysis of the ^1H, ^{13}C, and HSQC NMR data (Figures S8-S10; Table S6) of **2** revealed the presence of five olefinic methines ($\delta_{C/H}$ 123.4/5.39; 126.8/5.06; 129.8/5.34; 137.7/6.01; 126.9/5.48), three olefinic quaternary carbons (δ_C 134.4; 132.3; 134.2), one sp^3 quaternary carbon (δ_C 47.3), three methines ($\delta_{C/H}$ 53.5/2.61; 52.6/1.62; 29.6/1.62), seven methylenes ($\delta_{C/H}$ 44.6/2.36&1.94; 40.9/2.27&2.02; 24.7/2.29&2.03; 40.3/2.02&1.97; 25.1/2.22&2.06; 43.5/1.48&1.35; 30.2/1.37), four methyl singlets ($\delta_{C/H}$ 15.6/1.56; 15.3/1.53; 12.6/1.72; 23.4/0.83) and two methyl doublets ($\delta_{C/H}$ 22.9/1.01; 22.4/0.94). These data showed high similarity to those of

preterpestacin I (**1**), except for an additional double bond of **2** replaced original *O*-substituted methine in **1**. The ^{1}H-^{1}H COSY (Figure S11; Table S6) cross peaks revealed the presence of 4 spin systems including **A**: H_1 (δ_H 2.36&1.94) to H_2 (δ_H 5.39); **B**: H_4 (δ_H 2.27&2.02) through H_5 (δ_H 2.29&2.03) to H_6 (δ_H 5.06); **C**: H_8 (δ_H 2.02&1.97) through H_9 (δ_H 2.22&2.06) to H_{10} (δ_H 5.34); **D**: H_{12} (δ_H 6.01) to H_{13} (δ_H 5.48) to H_{14} (δ_H 2.61) to H_{18} (δ_H 1.62) to H_{17} (δ_H 1.37) to H_{16} (δ_H 1.48&1.35), with an isopropyl unit, H_{24} (δ_H 1.01) and H_{25} (δ_H 0.94) through H_{19} (δ_H 1.62) connected at H_{18}. Then, the HMBC (Figure S12; Table S6) correlations from H_{20} (δ_H 1.56) to C_2 (δ_C 123.4), C_3 (δ_C 134.4) and C_4 (δ_C 40.9) suggested that spin systems **A** and **B** were connected through C_3; the HMBC correlations from H_{21} (δ_H 1.53) to C_6 (δ_C 126.8), C_7 (δ_C 132.3) and C_8 (δ_C 40.3) suggested that spin systems **B** and **C** were connected through C_7; the HMBC correlations from H_{22} (δ_H 1.72) to C_{10} (δ_C 129.8), C_{11} (δ_C 134.2) and C_{12} (δ_C 137.7) suggested that spin systems **C** and **D** were connected through C_{11}; the HMBC correlations from H_{23} (δ_H 0.83) to C_1 (δ_C 44.6), C_{14} (δ_C 53.5) , C_{15} (δ_C 47.3) and C_{16} (δ_C 43.5) suggested that spin systems **A** and **D** were connected through C_{15}. These data showed that **2** is a 5/15 bicyclic sesterterpene. The olefinic bonds of C_2-C_3, C_6-C_7 and C_{10}-C_{11} were all assigned as *E*-configurations based on the NOESY correlations of H_{21} to H_5, H_{22} to H_9, and H_1 to H_{20}, respectively. Double bond at C_{12}-C_{13} was determined to be 12,13-*trans* based on large coupling constant ($^{3}J_{H12\text{-}H13}$ = 15.0 Hz). The key NOESY correlations of H_{23} to H_{25}, H_{23} to H_{13}, and H_1 to H_{14} indicated that the 23-CH_3 and isopropyl moiety (C_{24}-C_{19}-C_{25}) connected at C_{18} were on the same orientation of the 5-membered ring, while both H_{14} and H_1 were on the other side (Figure S13; Table S6). To determine the absolute configurations of **2**, the time-dependent density functional theory (TD-DFT) method was applied for the ECD calculations and simulations at the B3LYP/6-31+G(d) level. The preliminary conformational distribution search was performed by Sybyl 2.0 software. The corresponding minimum geometries were further fully optimized by using DFT at the B3LYP/6-31G(d) level as implemented in the Gaussian 09 program package. The results showed that the measured CD curve of **2** was well matched with the calculated ECD for 14*R*,15*S*,18*S*-**2** (Figures S14, S39-S41).

Compound **3** was isolated as a white powder, [α]27 D 83.0 (*c* 0.01, MeOH). The molecular formula $C_{25}H_{40}$ was determined by HR-EI-MS (M+ at *m/z* 340.3126, calcd. for 340.3130, Figure S15), indicating 6 units of unsaturation. The ^{1}H and ^{13}C NMR data of **3** was highly similar to those of **2**, except for an exo-olefinic CH_2 of **3** ($\delta_{C/H}$ 108.2/4.91) replaced the original sp^2 methine in **2** (Figures S16 and S17; Table S7). The HMBC correlations of H_{20} (δ_H 4.91) to C_2 (δ_C 30.8), C_3 (δ_C 150.4), and C_4 (δ_C 37.7), H_6 (δ_H 5.08) to C_4, H_1 (δ_H 1.54/1.47) to C_2, and H_{23} to C_1, C_{14} (δ_C 56.3), C_{15} (δ_C 46.3), C_{16} (δ_C 40.9) assigned the exo-olefine group at $\Delta^{3,20}$ (Figure S20; Table S7). The left three double bonds including C_{12}-C_{13}, C_6-C_7 and C_{10}-C_{11} were all assigned as *E*- configurations. The NOESY coupling pattern of **3** was almost the same to **2**, thus the C_6-C_7, C_{10}-C_{11} and C_{12}-C_{13} double-bonds were assigned as *E*-

configurations (Figure S21). The absolute configurations of **3** was determined as 14*R*,15*S*,18*S*- using the same ECD calculation methods (Figures S22, S39, S42-S43).

Compound **4** was isolated as a white powder, [α]25 D 13.5 (*c* 0.022, MeOH). The molecular formula $C_{25}H_{42}O$ was confirmed by HR-EI-MS (M^+ at *m/z* 358.3240, calcd. for 358.3236, Figure S23), indicating 5 units of unsaturation. Combined analysis of the ^1H, ^{13}C, and HSQC NMR data (Figures S24-S26; Table S8) of **4** revealed the presence of two olefinic quaternary carbons (δ_C 144.1; 133.3), one *O*-substituted quaternary carbon (δ_C 75.2), one sp^3 quaternary carbon (δ_C 42.0), seven methines ($\delta_{C/H}$ 49.8/2.02; 46.8/2.53; 39.2/1.92; 47.9/2.40; 51.3/1.41; 47.6/1.65; 31.8/1.54), eight methylenes ($\delta_{C/H}$ 43.6/1.81&0.80; 36.1/1.73&1.58; 25.1/1.56; 31.7/1.59; 30.1/2.18&2.06; 29.8/1.62; 41.6/1.50&1.11; 28.6/1.85&1.57), three methyl singlets ($\delta_{C/H}$ 32.6/1.28; 15.0/1.68; 19.4/0.80) and three methyl doublets ($\delta_{C/H}$ 15.7/0.95; 24.3/0.93; 22.8/0.87). These characteristics were quite similar to those of sesterfisherol, a 5/6/8/5 tetracyclic sesterterpene produced by NfSS,[14] indicating they shared the same carbon backbone. Detailed analysis of 2D NMR revealed that the hydroxyl group in **4** was connected at C_4, rather than C_{12} in sesterfisherol, based on the key HMBC correlation of H_{20} (δ_H 1.28) to C_2 (δ_C 49.8), C_3 (δ_C 75.2), and C_4 (δ_C 36.1), as well as H_{22} (δ_H 1.68) to C_{10} (δ_C 144.1), C_{11} (δ_C 133.3), and C_{12} (δ_C 47.9) (Figure S28). Thus, **4** was the hydroxyl positional isomer of sesterfisherol. Further NOESY analysis established the relative configurations of **4**, based on the key NOE cross peaks of H_{25} to H_{23}, H_{24} to H_{13}, H_{12} to H_{14}, H_{12} to H_6, H_{21} to H_5, H_{20} to H_1, and H_2 to H_{23} (Figure S29). The absolute configurations of **4** was determined as 2*R*,3*R*,6*R*,7*R*,12*R*,14*R*,15*S*,18*S*- using the same ECD calculation methods (Figures S22, S39, S44-S45).

Compound **5** was isolated as a white powder, [α]25 D -27 (*c* 0.033, MeOH). The molecular formula $C_{25}H_{42}O$ was deduced by HR-EI-MS (M^+ at *m/z* 358.3234, calcd. for 358.3236, Figure S31). Combined analysis of the ^1H, ^{13}C, and HSQC NMR data (Figures S32-S34; Table S9) of **5** revealed one *O*-substituted quaternary carbon (δ_C 75.3), three sp^3 quaternary carbons (δ_C 41.3; 30.8; 41.2), seven methines ($\delta_{C/H}$ 44.6/1.86; 46.0/2.20; 38.7/0.65; 48.1/0.62; 50.2/1.22; 47.5/1.71; 31.2/1.63), eight methylenes ($\delta_{C/H}$ 42.2/1.98&0.91; 44.2/1.69&1.51; 29.8/1.79&1.60; 34.0/1.73; 25.4/1.88&1.67; 27.2/1.74&1.66; 41.9/1.54&1.10; 28.3/1.82&1.54), three methyl singlets ($\delta_{C/H}$ 24.3/1.06; 11.9/1.16; 19.2/0.83) and three methyl doublets ($\delta_{C/H}$ 16.2/1.15; 24.6/1.02; 22.4/0.89). These characteristics were quite similar to those of aspterpenacid B, a 5-3-7-6-5 pentacyclic sesterterpenoid produced by mangrove endophytic fungus *Aspergillus terreus* H010.[15] While in the 1D NMR of **5**, the resonance of carboxyl and *O*-substituted methine could not be observed, instead there are an additional methyl singlet ($\delta_{C/H}$ 11.9/1.16) and sp^3 methine ($\delta_{C/H}$ 48.1/0.62) compared to aspterpenacid B. Detailed analysis of 2D NMR revealed **5** and aspterpenacid B shared the

same carbon skeleton, except that the carboxyl connected at C_{11} of aspterpenacid B was replaced by a methyl, and the hydroxyl was substituted at C_3 in **5**, based on the key HMBC correlations of H_{22} (δ_H 1.16) to C_6 (δ_C 41.3), C_{10} (δ_C 38.7), C_{11} (δ_C 30.8), and C_{12} (δ_C 48.1); H_{20} (δ_H 1.06) to C_2 (δ_C 44.6) and C_3 (δ_C 75.3); as well as H_2 (δ_H 1.86) to C_{11} and C_3 (Figure S36). These data showed that **5** is a 5/6/7/3/5 pentacyclic sesterterpene. The NOESY analysis of **5** revealed the key cross peaks between H_7/H_5, H_5/H_{10}, H_5/H_{12}, H_{22}/H_{23}, H_{20}/H_{12}, H_2/H_{23}, H_{23}/H_{19}, H_{23}/H_{13}, and H_{13}/H_{24} (Figures S37-S39). Since **5** shared the same stereochemistry on C_{14}, $C_{15,}$ and C_{18} with **1** (14*R*,15*S*, and 18*S*), The absolute configurations of **5** could be deduced to be 2*R*,3*R*,6*R*,7*R*,10*R*,11*R*,12*R*,14*R*,15*S*, and 18*S* according to **5** shared the same cyclization pathway as **4**.

Compound **1** was isolated as yellow oil. The molecular formula $C_{25}H_{42}O$ was confirmed by HRESIMS ($[M - H_2O + H]^+$ at *m/z*, calcd. for 341.3208, Figure S47), indicating 5 units of unsaturation. The ^1H and ^{13}C NMR data (Figures S48-S49) of **1** were same as preterpestacin I[16].

Detailed computed cyclization pathway of 1–5

The concerted 1,15- and 14,18-bond formation was triggered by eliminating the pyrophosphate group of GFPP (**IM1**) yields **IM2** with a 5/15 fused ring system. A 1,5-hydride shift between C_{12} and C_{19} produces **IM3**, which generates a stabilized allylic carbocation. **IM3** serves as a branch point of three different cyclization routes: (i) In ***Path a***, the reaction is quenched by H_2O attack on the allylic carbocation C_{10} to generate **1** (Figure S50); (ii) In ***Path b1***, deprotonation occurs to form a new double bond $\Delta^{12,13}$ and leads to the formation of **2**, which is further protonated to form a new carbocation of C_3 to generate **IM4b**. The following deprotonation produces **3**. In ***Path b2***, **TS_3-4b**, a "sandwich-like" delocalization in the transition-state structure involves a 1,5-proton transfer from C_{13} to the *Si* face of C_2 to form **IM4b** with a low activation barrier ($\Delta G^{\ddagger}$ = 6.24 kcal/mol),[17] which is then deprotonated to form **3**. DFT calculations confirmed this process to be both thermodynamically and kinetically favorable, while this sort of intramolecular proton transfer with a C=C π-bond acting as a base has been previously proposed in mechanisms for taxadiene[18] and abietadiene[19] biosynthesis; (iii) In ***Path c***, the allylic carbocation in **IM3** is partially stabilized with a distal $\Delta^{6,7}$ double bond. The cation···π interaction leads to the smooth formation of the D ring to give 5/12/5 tricyclic **IM4c**. Then, a successive transformation involving two rounds of 1,2-hydride shifts (**IM4c → IM5c → IM6c**) lead to the formation of the B ring and the tetracyclic 5/6/8/5 carbocation intermediate **IM7c**. Finally, H_2O attacks the carbocation C_3 of **IM7c** to quench the reaction leading to **4**. In ***Path c***, the possible cyclization route is divided into two sub-routes from **IM5c** based on the DFT calculation and leads to final products **4** (described above) and **5**. The activation energy of

IM5c → IM6c′ via **TS_5c-6c′** ($\Delta G^{\ddagger}$ = 2.22 kcal/mol) is similar to that of **IM5c → IM6c** via **TS_5c-6c** ($\Delta G^{\ddagger}$ = 4.7 kcal/mol) (Figure S50). The homo-allylic carbocation **IM5c** transforms to the relatively stable cyclopropyl carbocation intermediate **IM6c′** and generates the final product 5/6/7/3/5 pentacyclic terpene **5** quenching by water.

SUPPORTING FIGURES

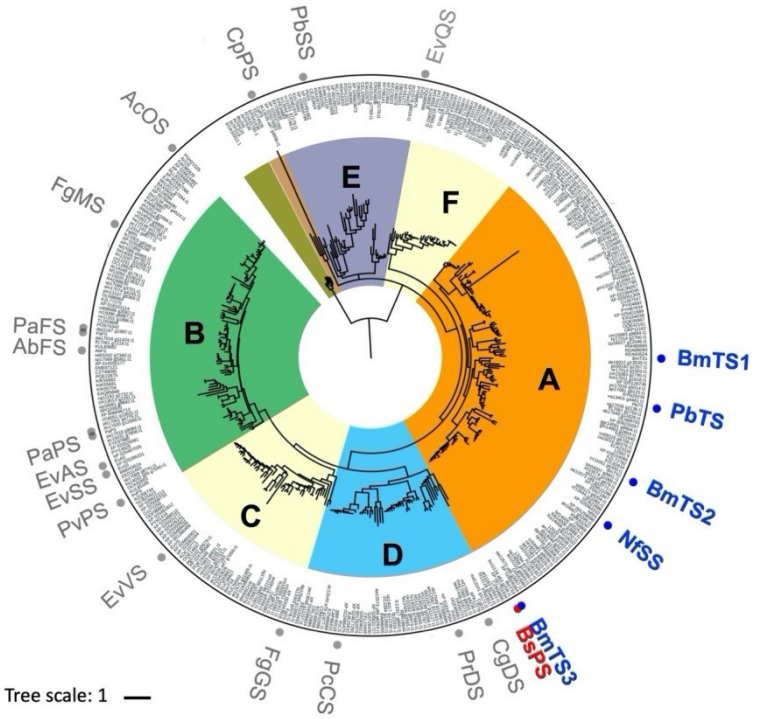

Figure S1. The phylogenetic analysis of the reported BFTSs and the putative BFTSs discovered from our in-house collection and from fungal genomes from public database. Maximum Likelihood phylogenetic tree of TC domains of 383 putative BFTS of publicly available genomes from NCBI (220) and 430 in-house phytopathogenic fungal genomes (163). BFTS in this study are indicated by red and the reported ones cited in this study are indicated in blue. Other reported ones are indicated in grey. The bar represents 1 nucleotide substitutions per site.

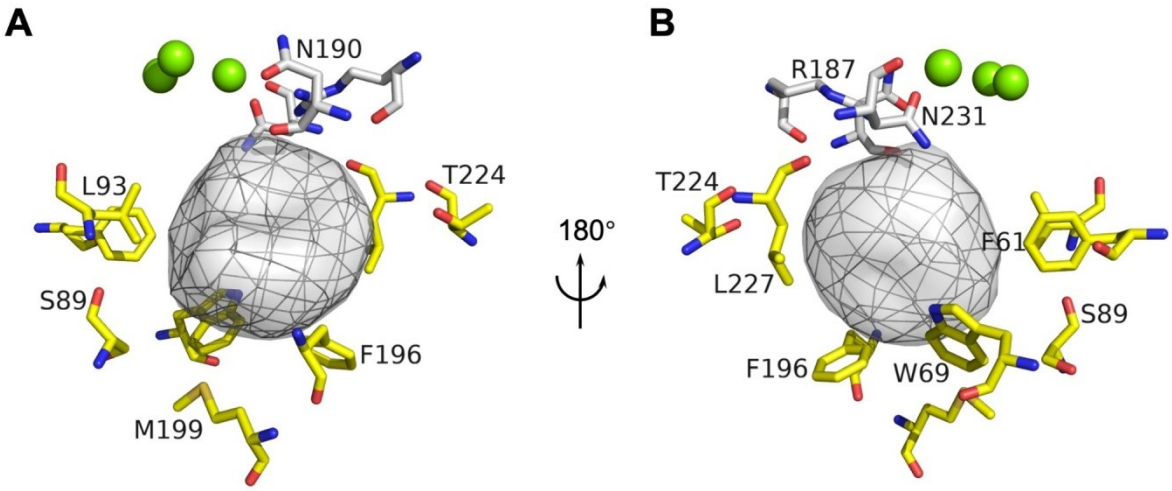

Figure S2. Proposed residues lining the putative catalytic pocket of BsPS. The pocket areas of the WT BsPS and the variants are shown in grey mesh. Three Mg^{2+} are shown in green sphere. The view in panel B is rotated by 180˚ from that in panel A.

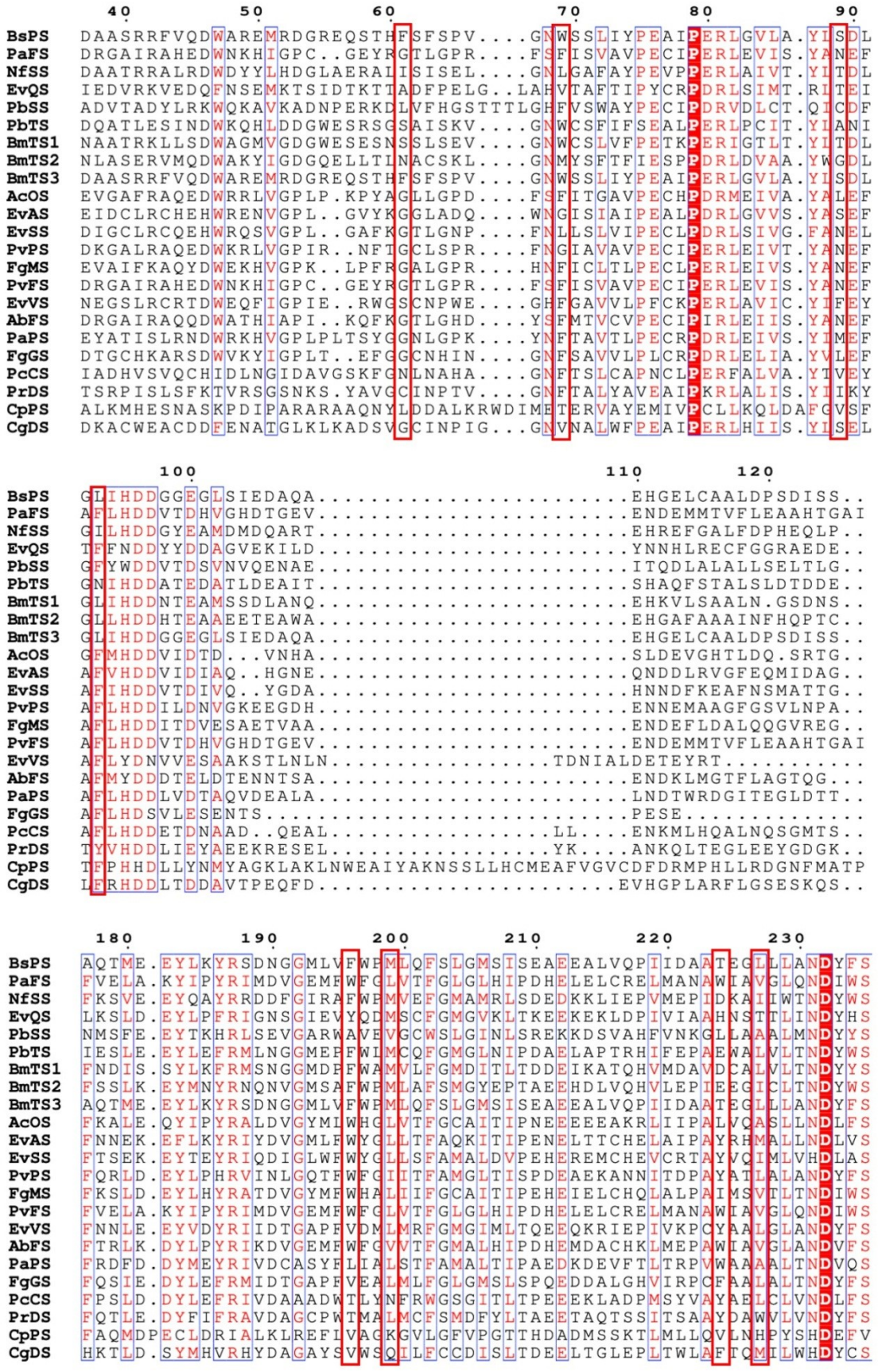

Figure S3. Amino acid sequence alignments of the bifunctional terpene synthases from fungi.

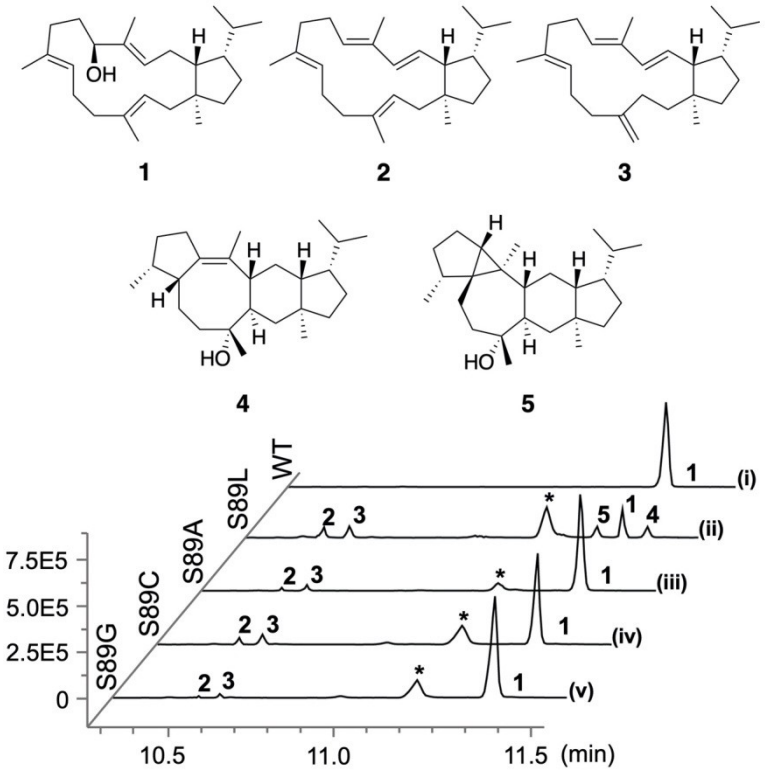

Figure S4. The structure of isolated compounds **1**–**5** and GC-MS profiles of crude extracts obtained from BsPS-WT (i), BsPS-S89L (ii), BsPS-S89A (iii), BsPS-S89C (iv), and BsPS-S89G (v).

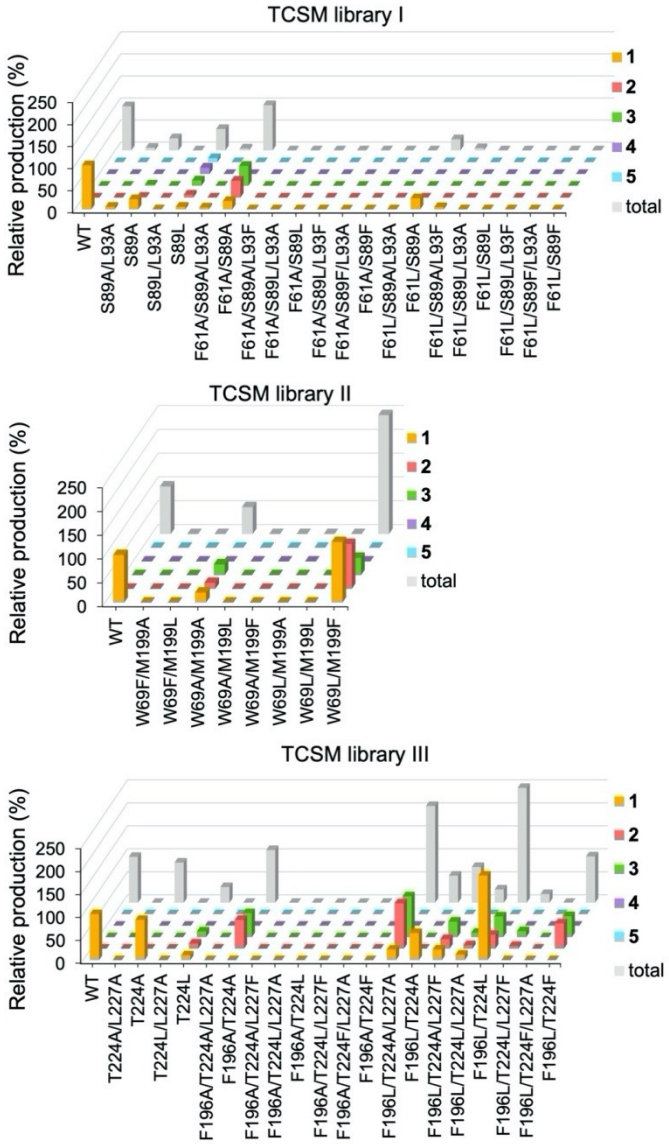

Figure S5. Relative productions of BsPS variants in the TCSM libraries. The dark blue cuboids in the top row show the relative total production of cyclized terpenes (wild-type = 100%), while the other cuboids show the relative production of compounds **2**–**5**. All data are based on peak integrals in the GC-MS.

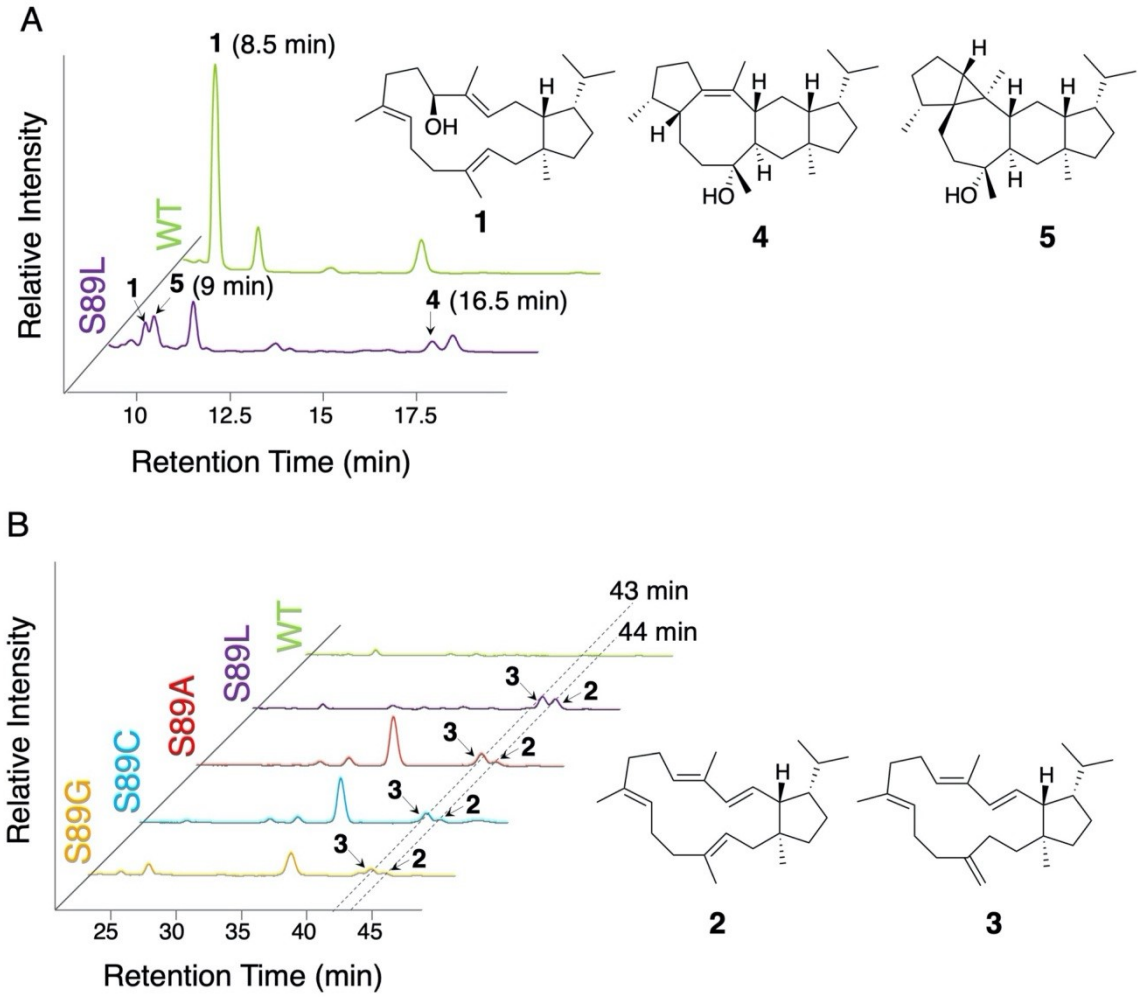

Figure S6. HPLC analysis of the products of the WT and the variants. **(**A) Products **1**, **4**, and **5** were analyzed by HPLC on ACE Excel 5 C18-AR column (Φ 4.6 × 250 mm). (B) Products **2** and **3** were analyzed by HPLC on ACE Excel 5 C18 column (Φ 4.6 × 250 mm).

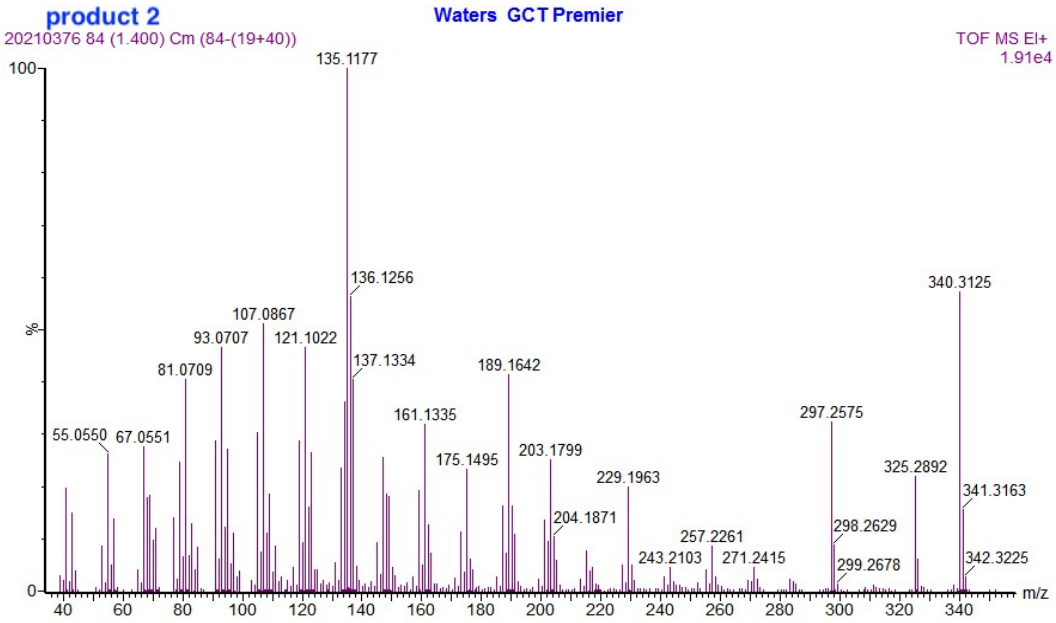

Figure S7. HR-EI-MS spectrum of **2** in MeOH.

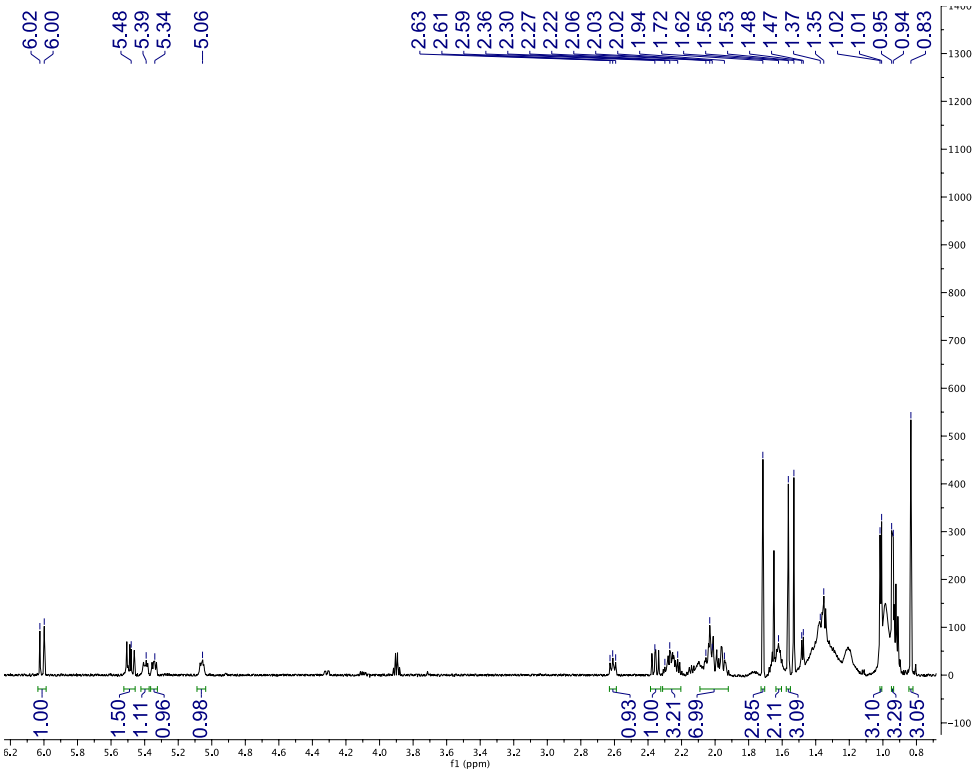

Figure S8. ^{1}H NMR (600 MHz, C_6D_6) spectrum of **2**.

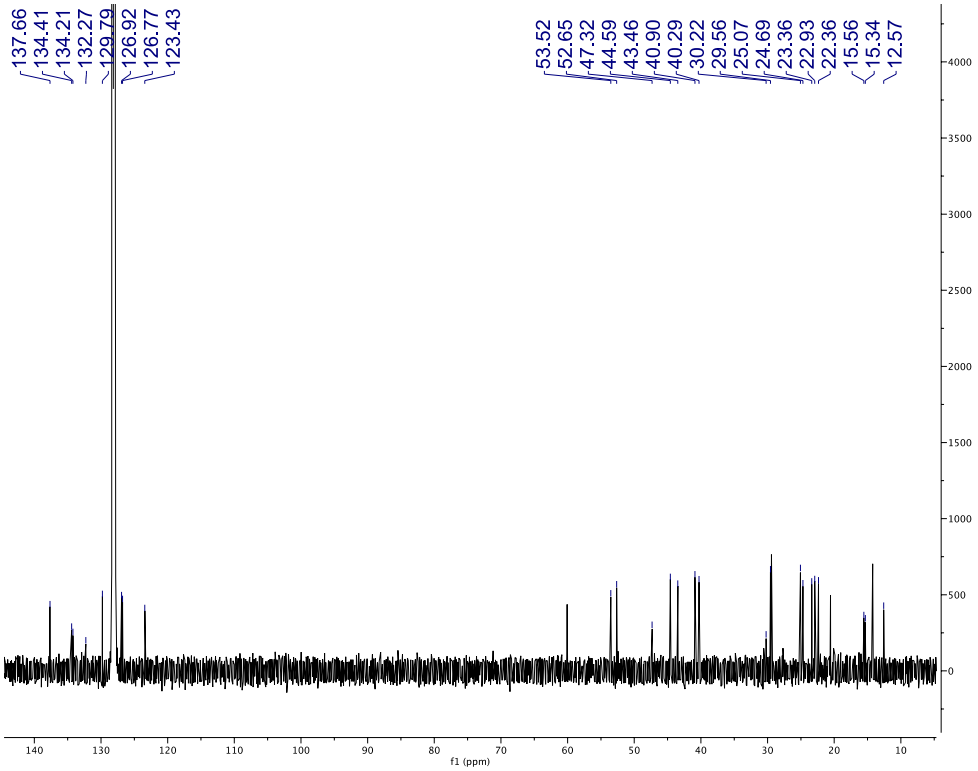

Figure S9. ^{13}C NMR (150 MHz, C_6D_6) spectrum of **2**.

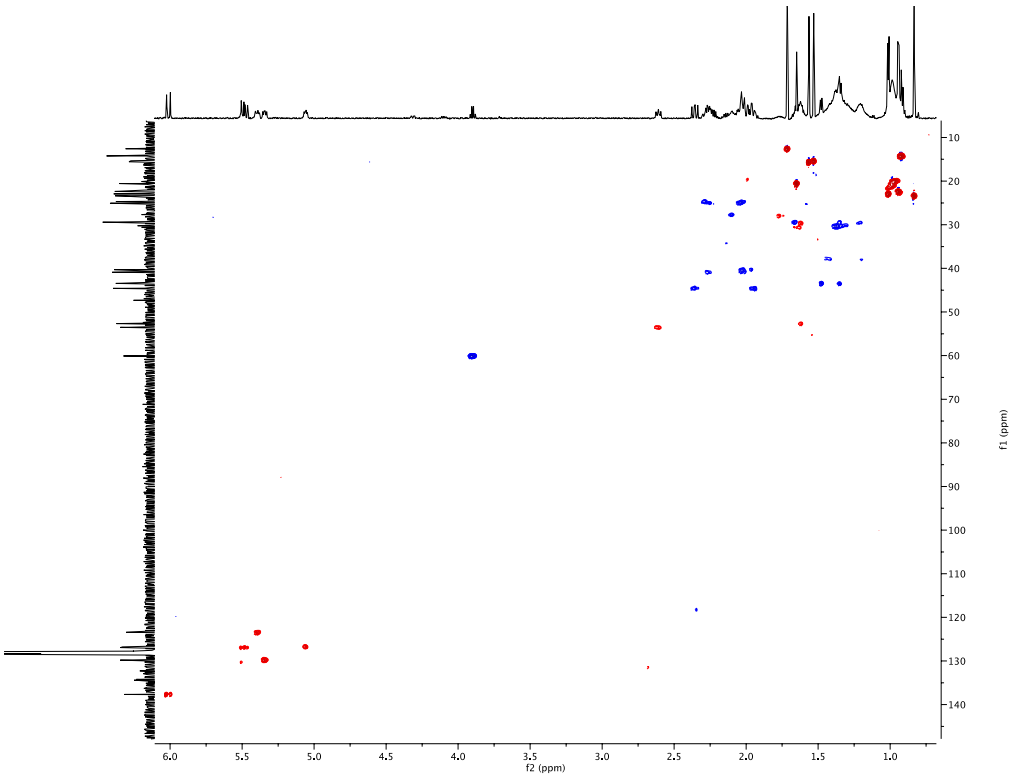

Figure S10. HSQC NMR (600 MHz, C_6D_6) spectrum of **2**.

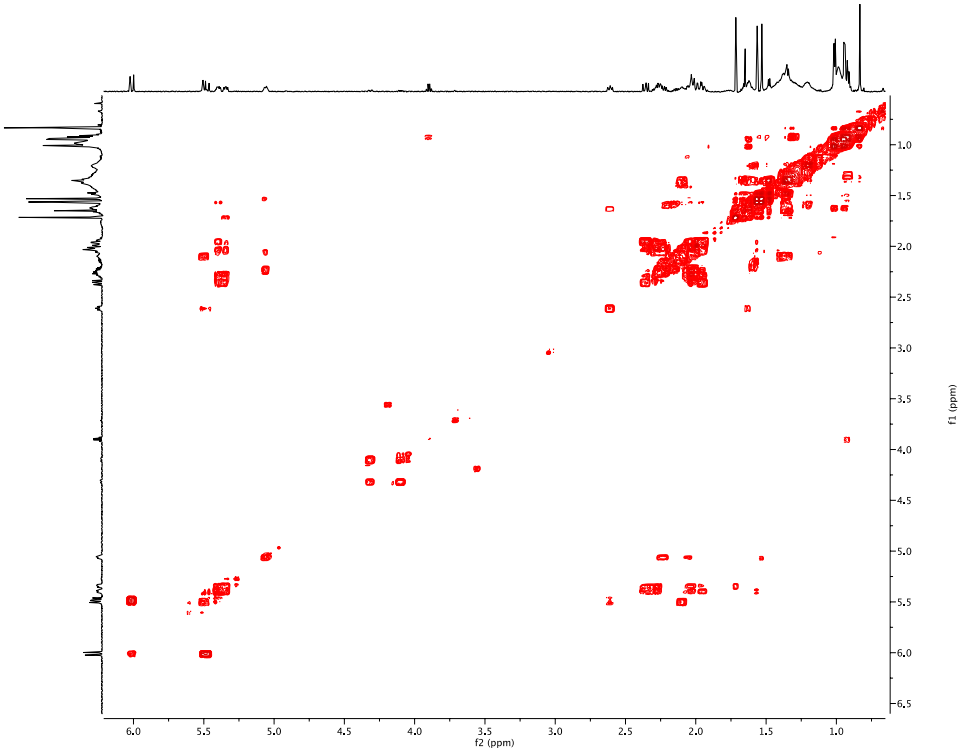

Figure S11. ^{1}H-^{1}H COSY NMR (600 MHz, C_6D_6) spectrum of **2**.

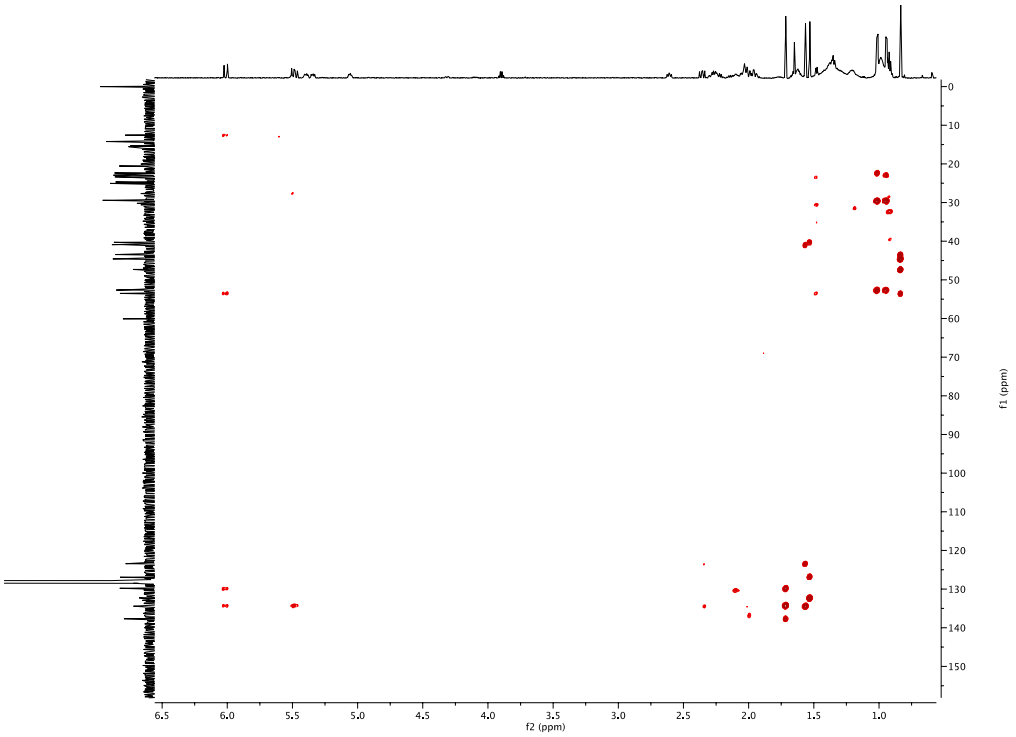

Figure S12. HMBC NMR (600 MHz, C_6D_6) spectrum of **2**.

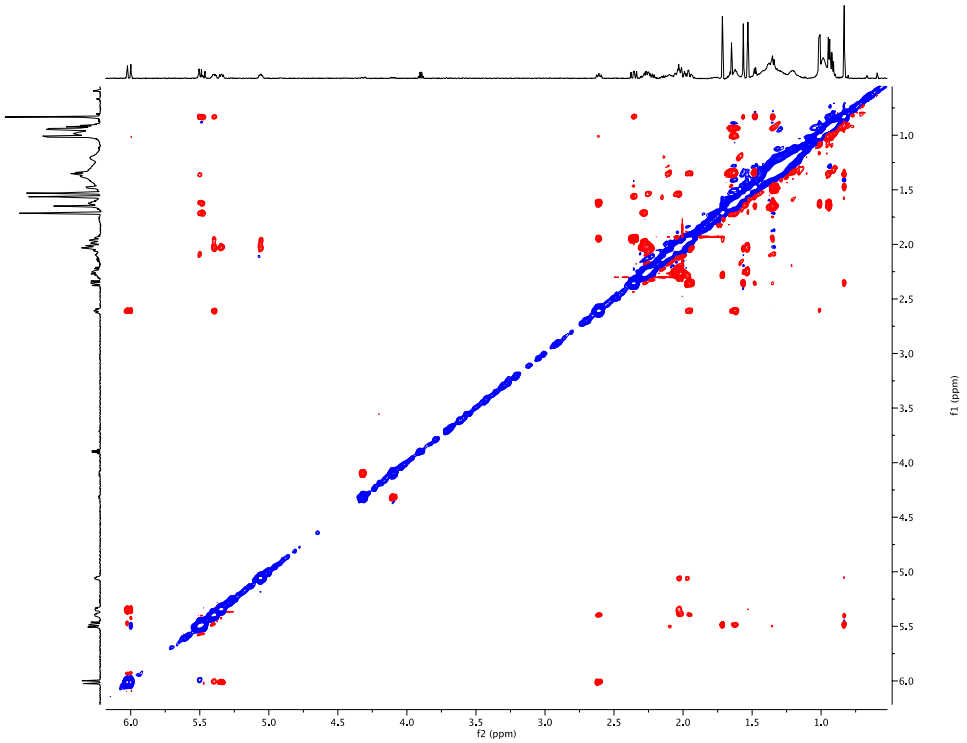

Figure S13. NOESY NMR (600 MHz, C_6D_6) spectrum of **2**.

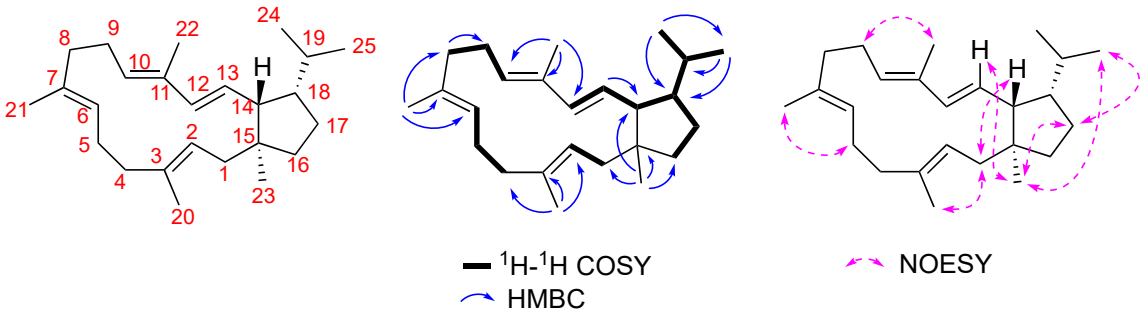

Figure S14. Structure and key 2D NMR correlations of **2**.

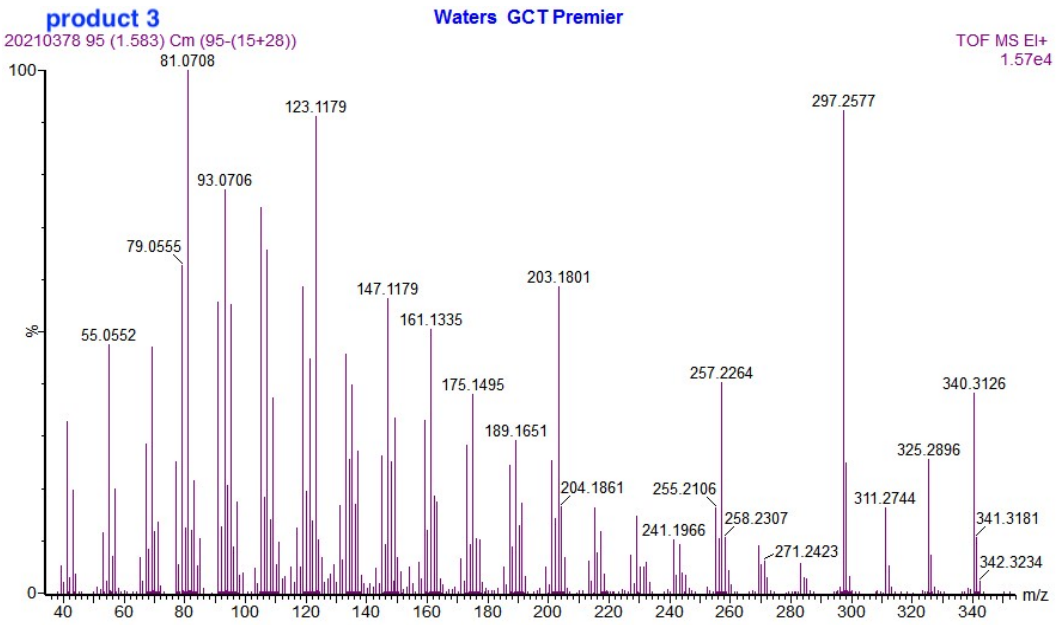

Figure S15. HR-EI-MS spectrum of **3** in MeOH.

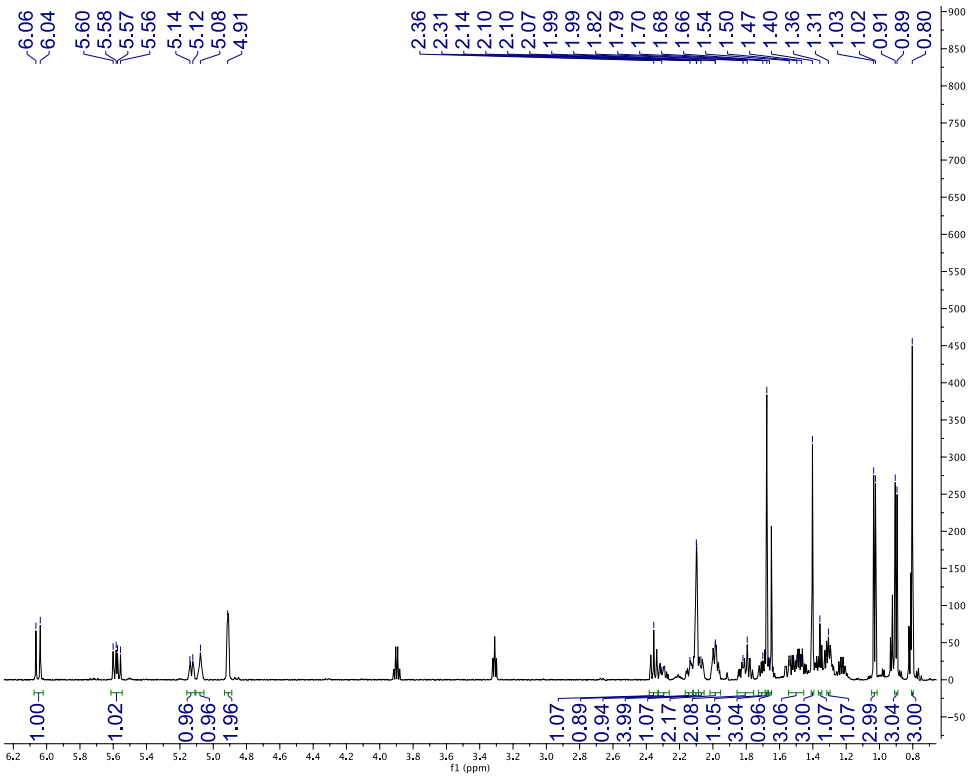

Figure S16. ^{1}H NMR (600 MHz, C_6D_6) spectrum of **3**.

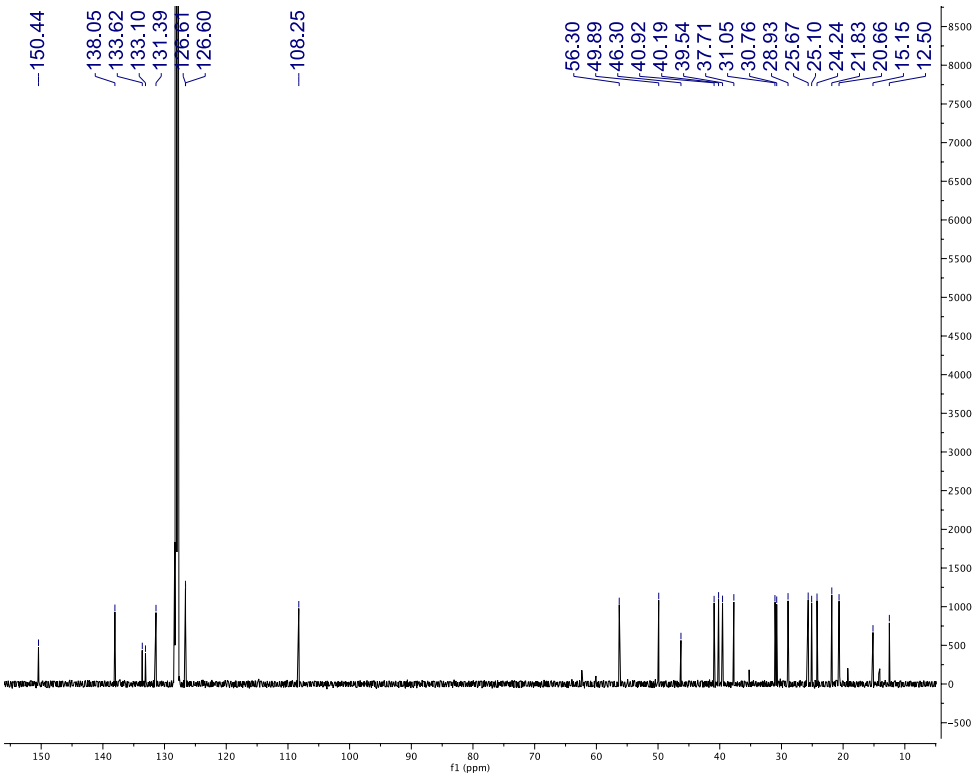

Figure S17. ^{13}C NMR (150 MHz, C_6D_6) spectrum of **3**.

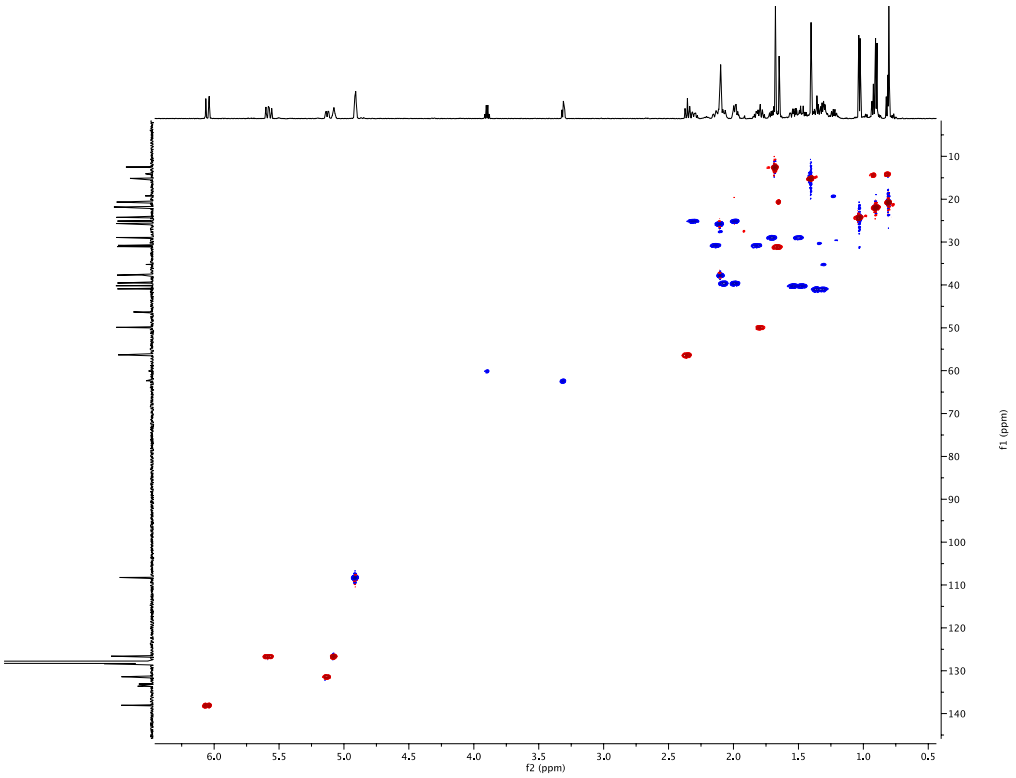

Figure S18. HSQC NMR (600 MHz, C_6D_6) spectrum of **3**.

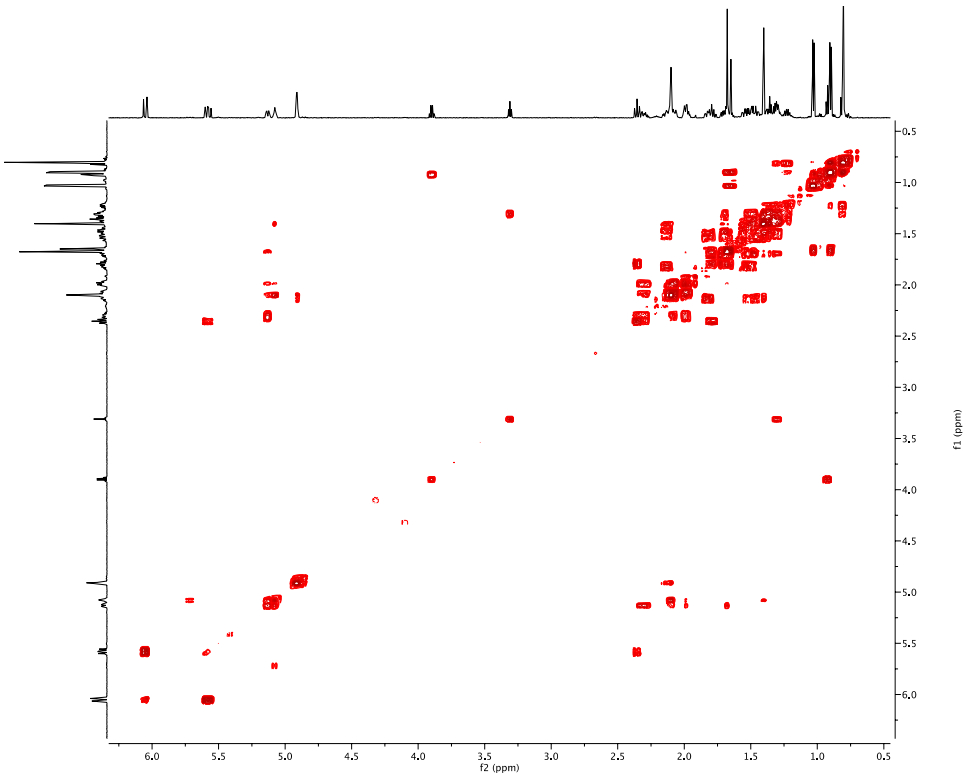

Figure S19. ^{1}H-^{1}H COSY NMR (600 MHz, C_6D_6) spectrum of **3**.

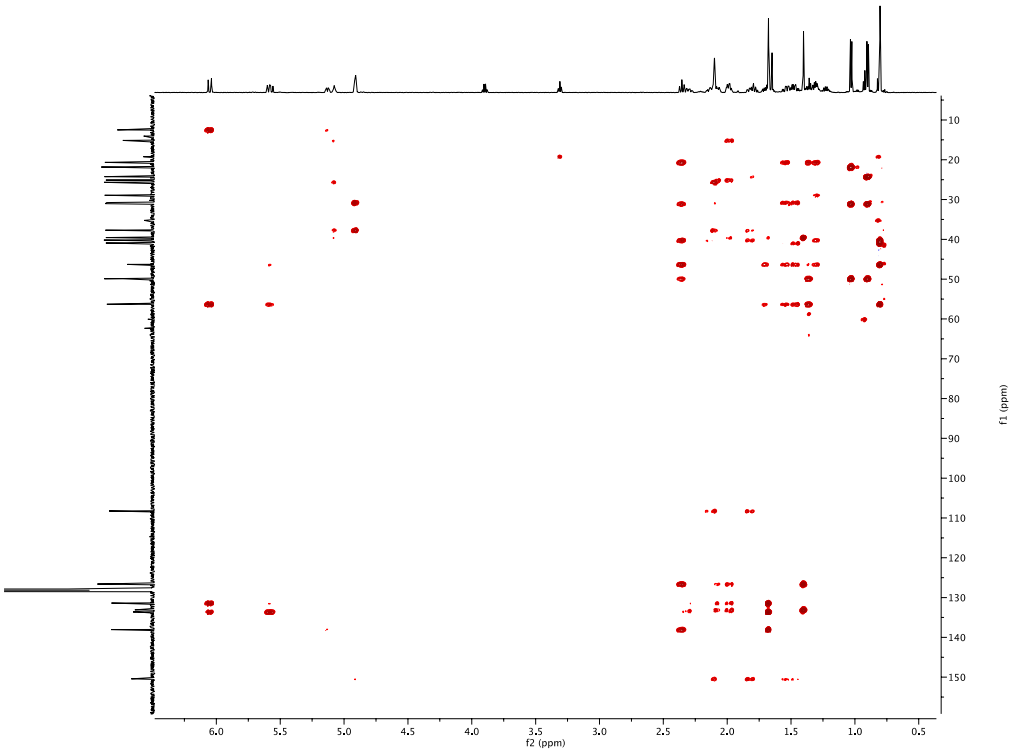

Figure S20. HMBC NMR (600 MHz, C_6D_6) spectrum of **3**.

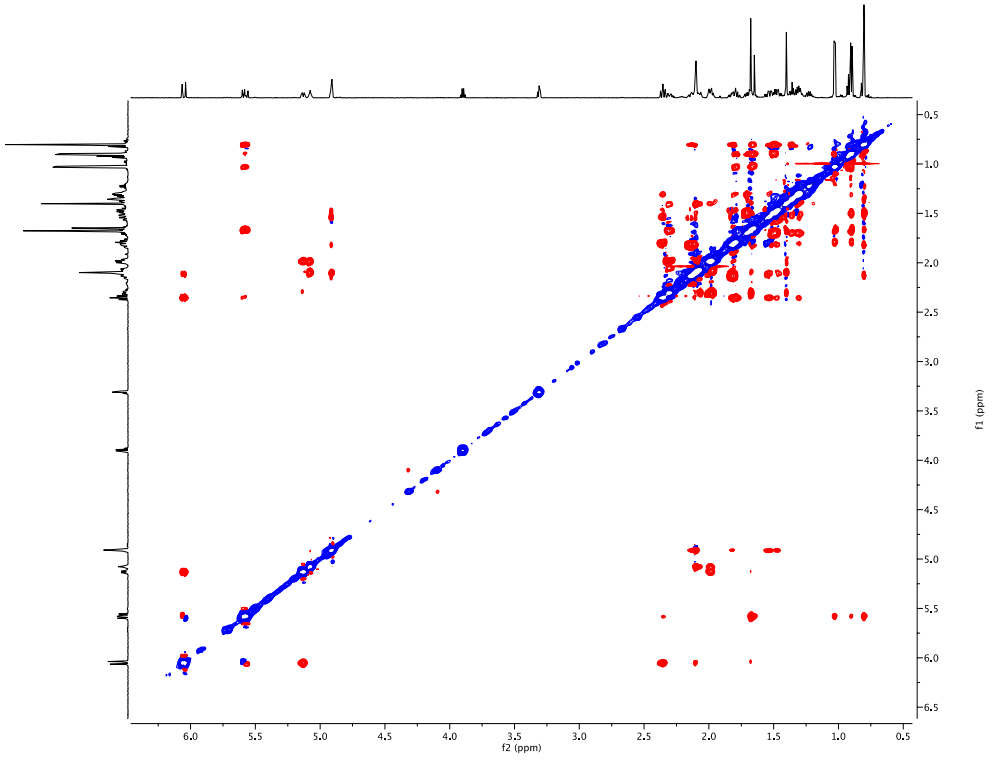

Figure S21. NOESY NMR (600 MHz, C_6D_6) spectrum of **3**.

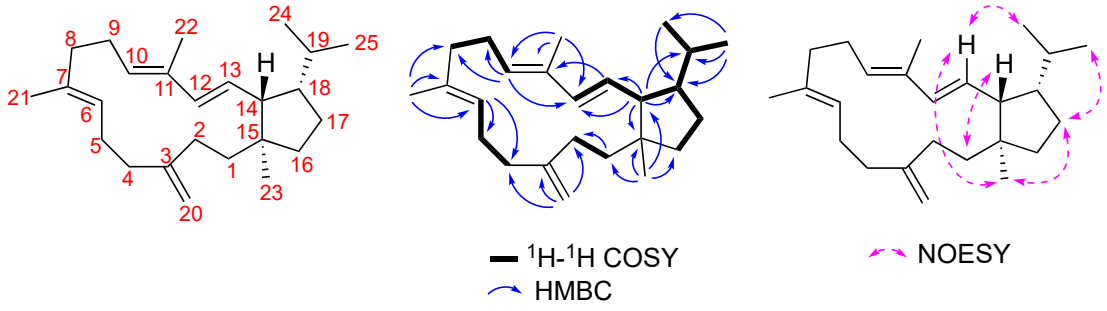

Figure S22. Structure and key 2D NMR correlations of **3**.

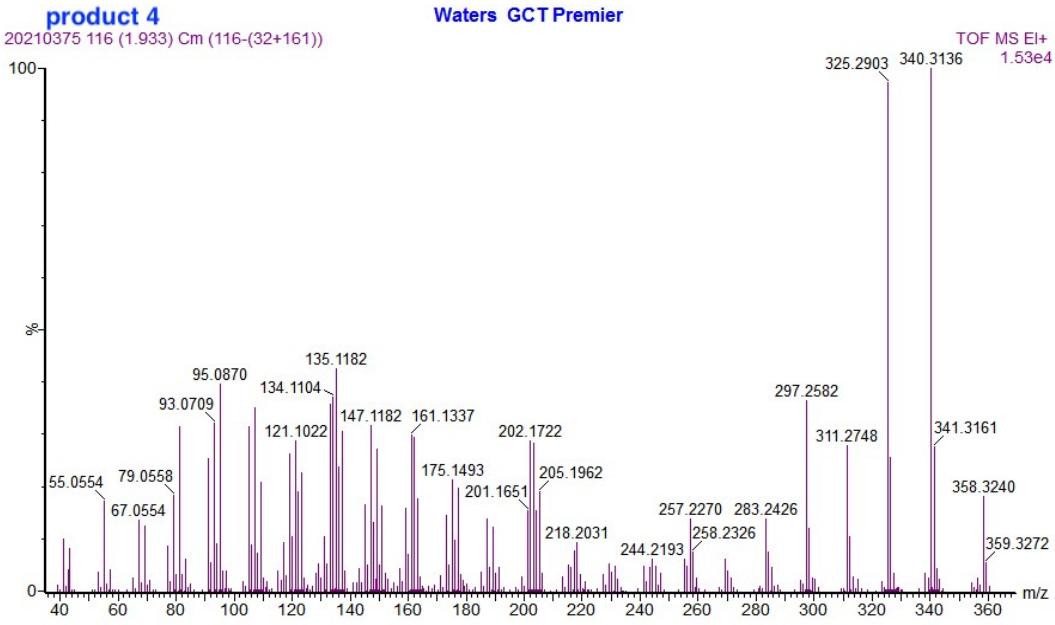

Figure S23. HR-EI-MS spectrum of **4** in MeOH.

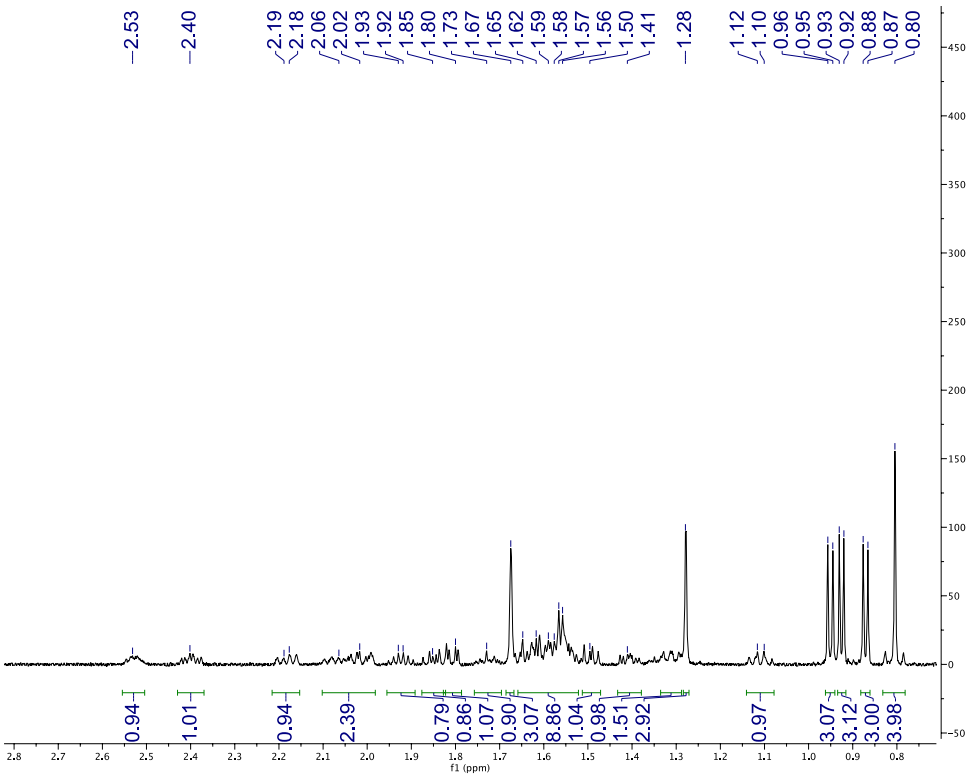

Figure S24. ^{1}H NMR (600 MHz, C_6D_6) spectrum of **4**.

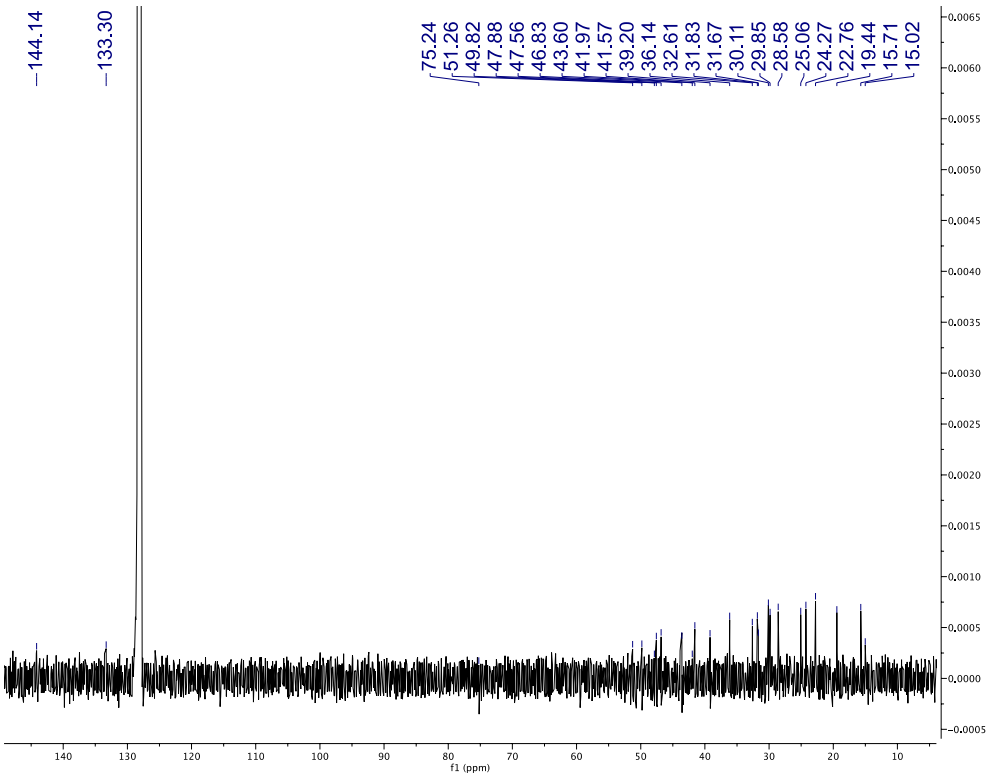

Figure S25. ^{13}C NMR (150 MHz, C_6D_6) spectrum of **4**.

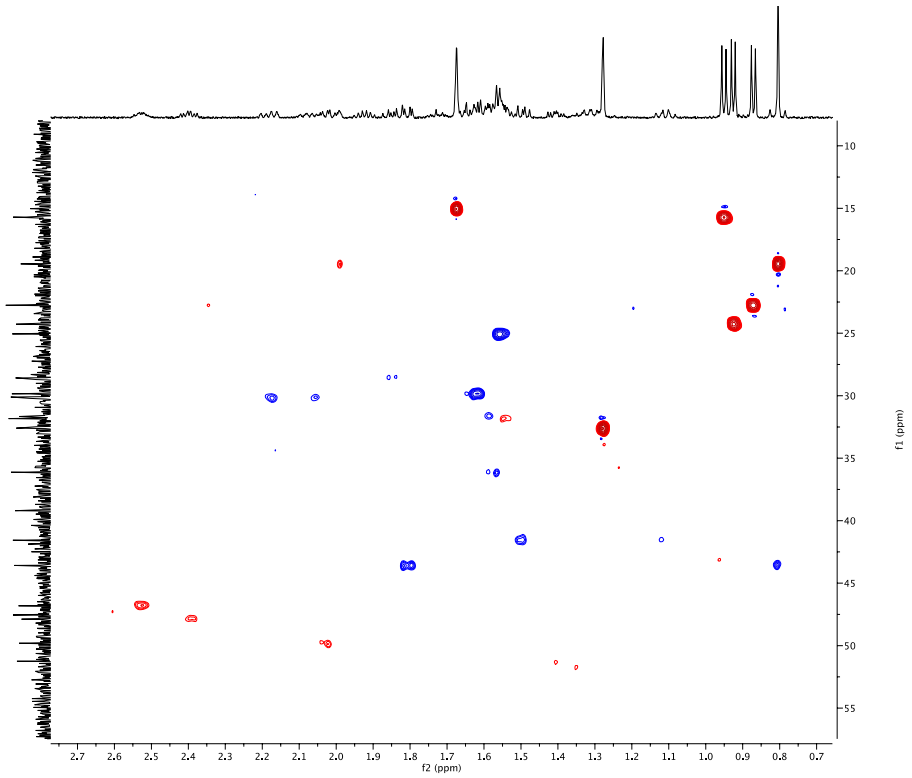

Figure S26. HSQC NMR (600 MHz, C_6D_6) spectrum of **4**.

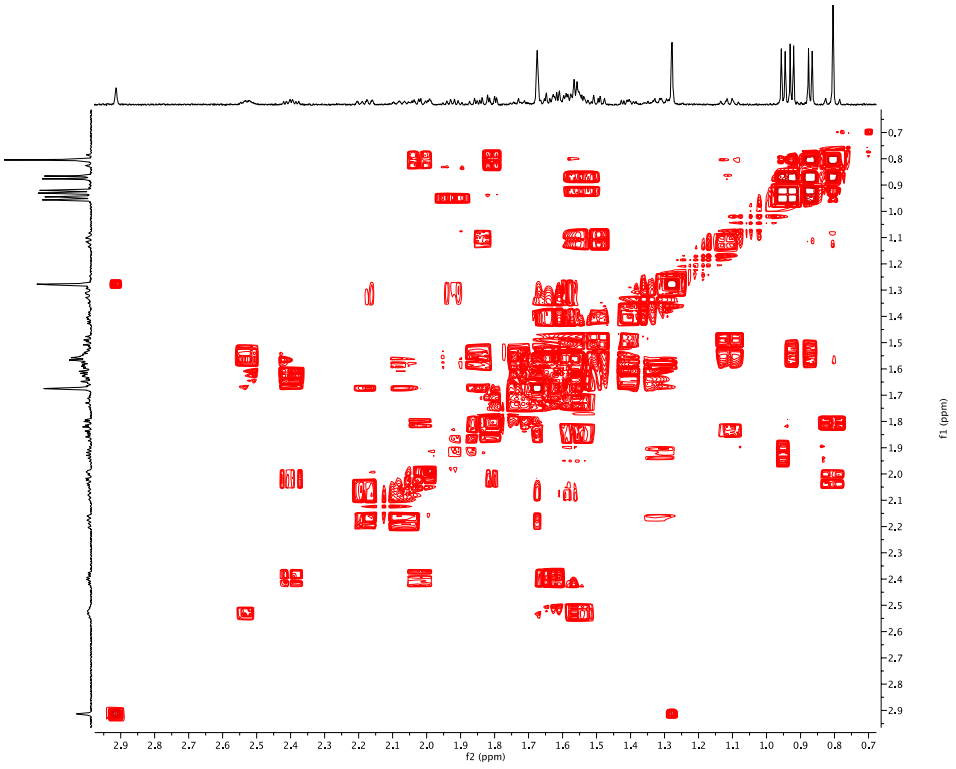

Figure S27. ^{1}H-^{1}H COSY NMR (600 MHz, C_6D_6) spectrum of **4**.

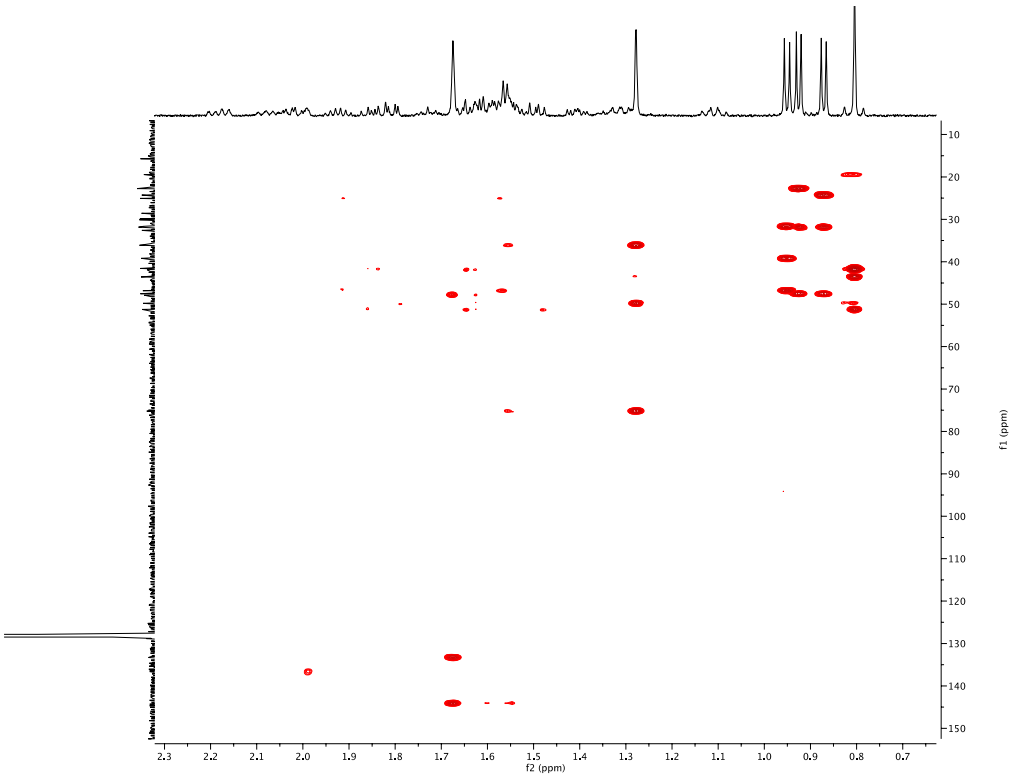

Figure S28. HMBC NMR (600 MHz, C_6D_6) spectrum of **4**.

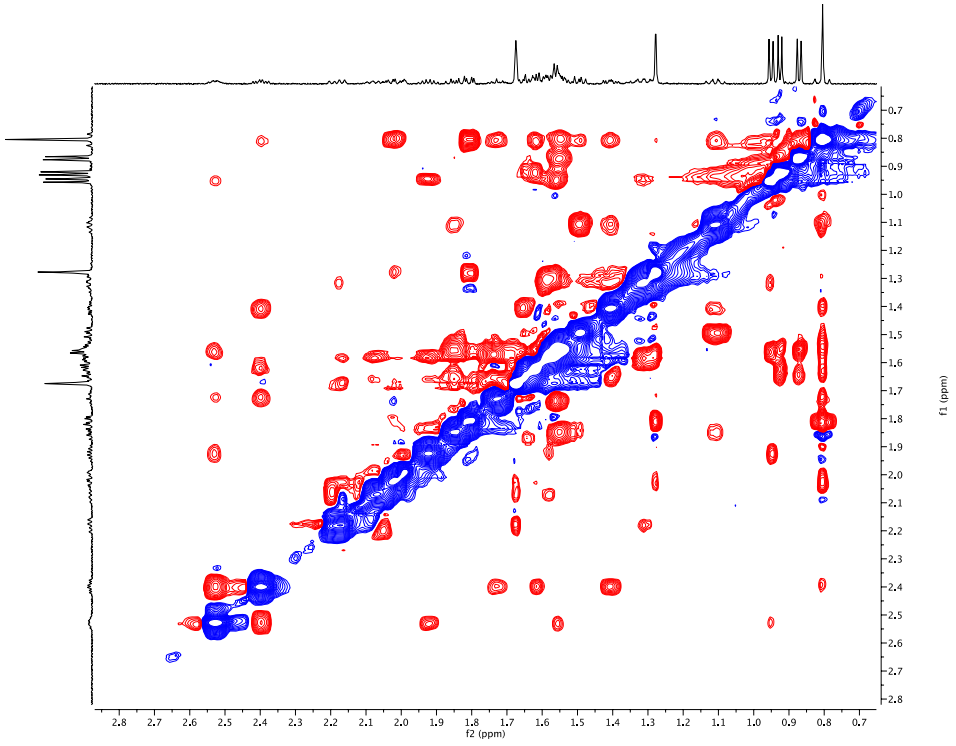

Figure S29. NOESY NMR (600 MHz, C_6D_6) spectrum of **4**.

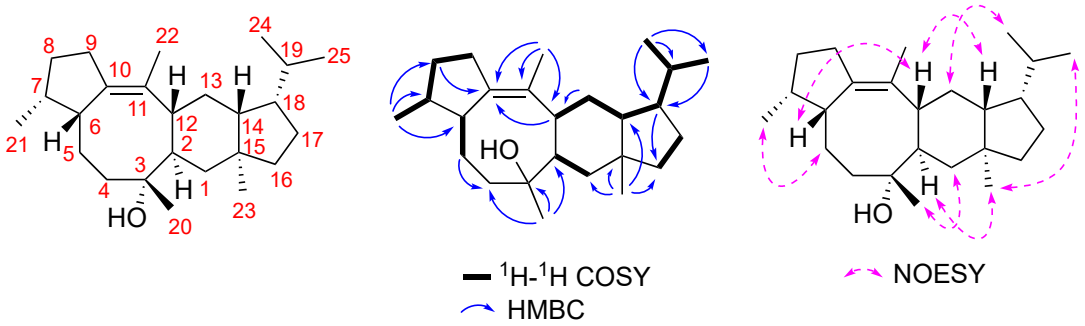

Figure S30. Structure and key 2D NMR correlations of **4**.

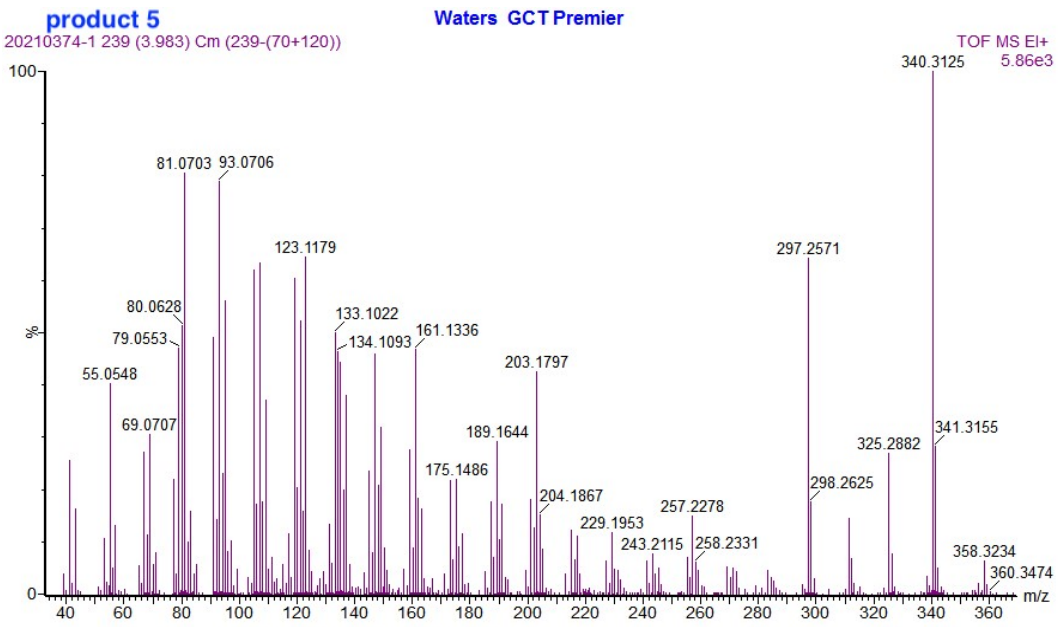

Figure S31. HR-EI-MS spectrum of **5** in MeOH.

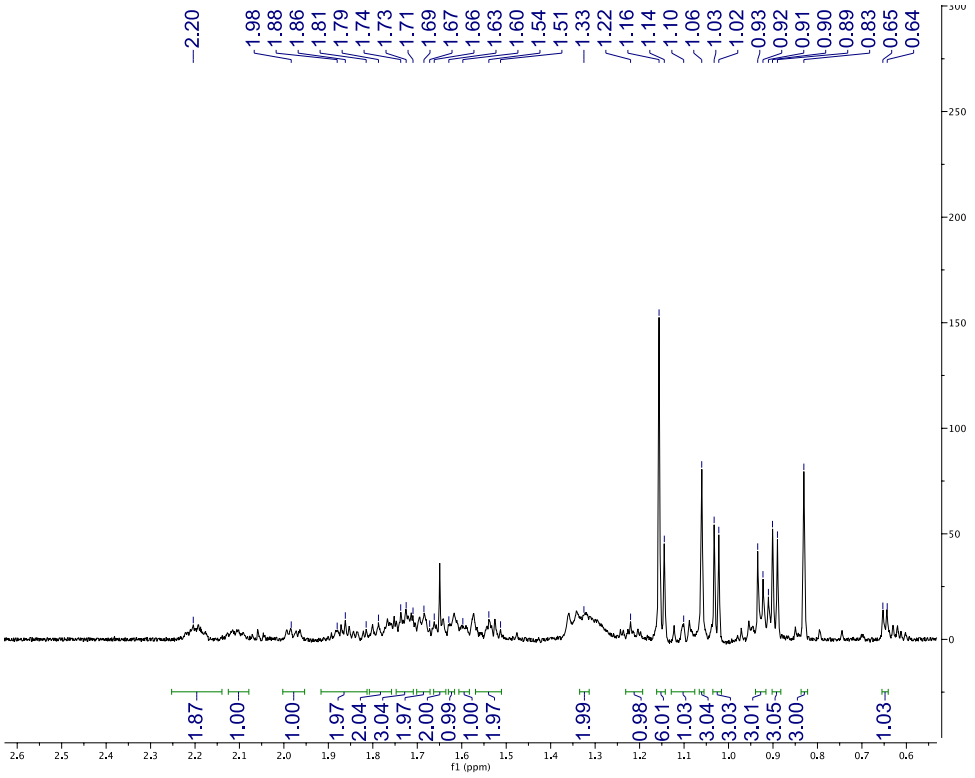

Figure S32. ^{1}H NMR (600 MHz, C_6D_6) spectrum of **5**.

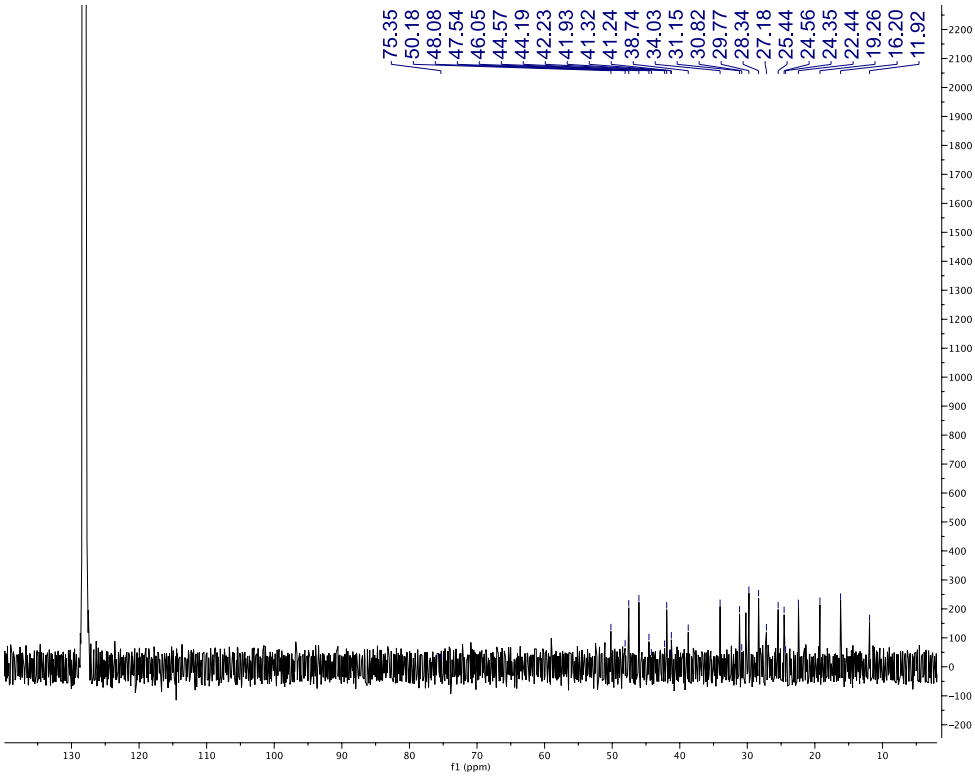

Figure S33. ^{13}C NMR (150 MHz, C_6D_6) spectrum of **5**.

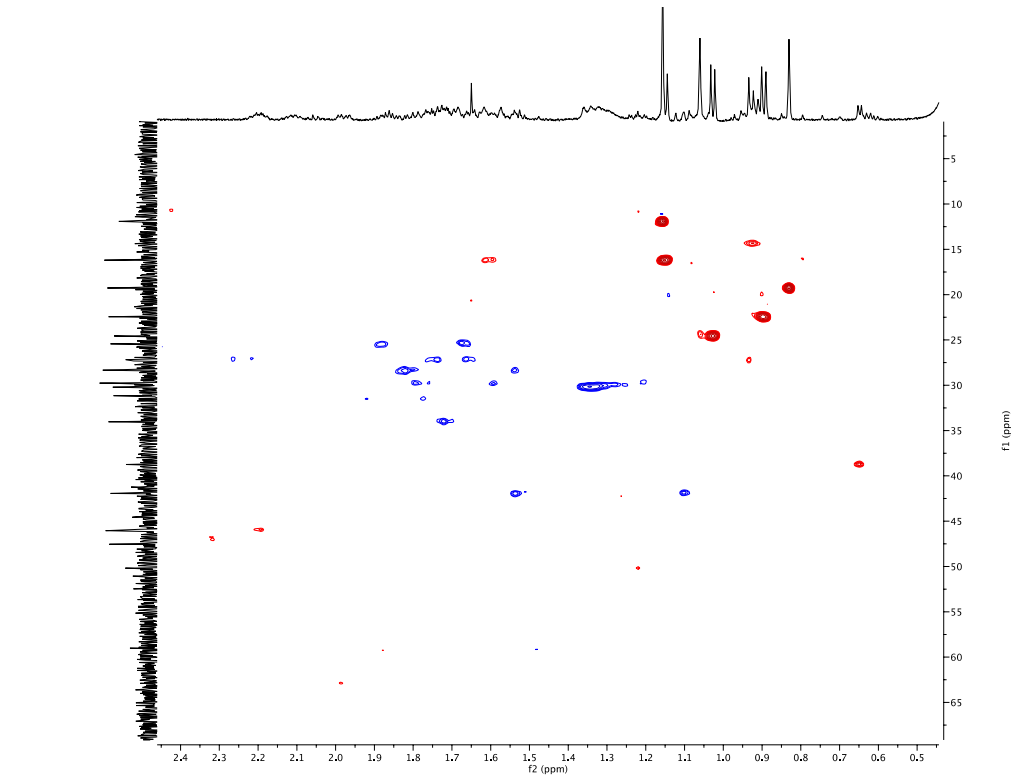

Figure S34. HSQC NMR (600 MHz, C_6D_6) spectrum of **5**.

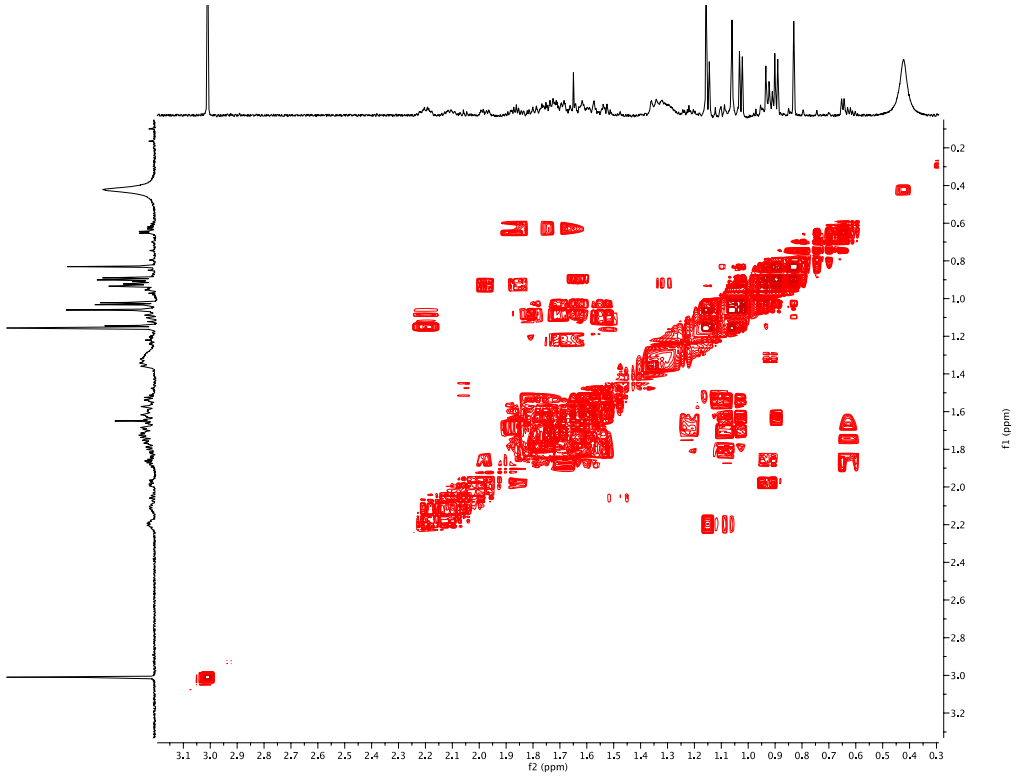

Figure S35. ^{1}H-^{1}H COSY NMR (600 MHz, C_6D_6) spectrum of **5**.

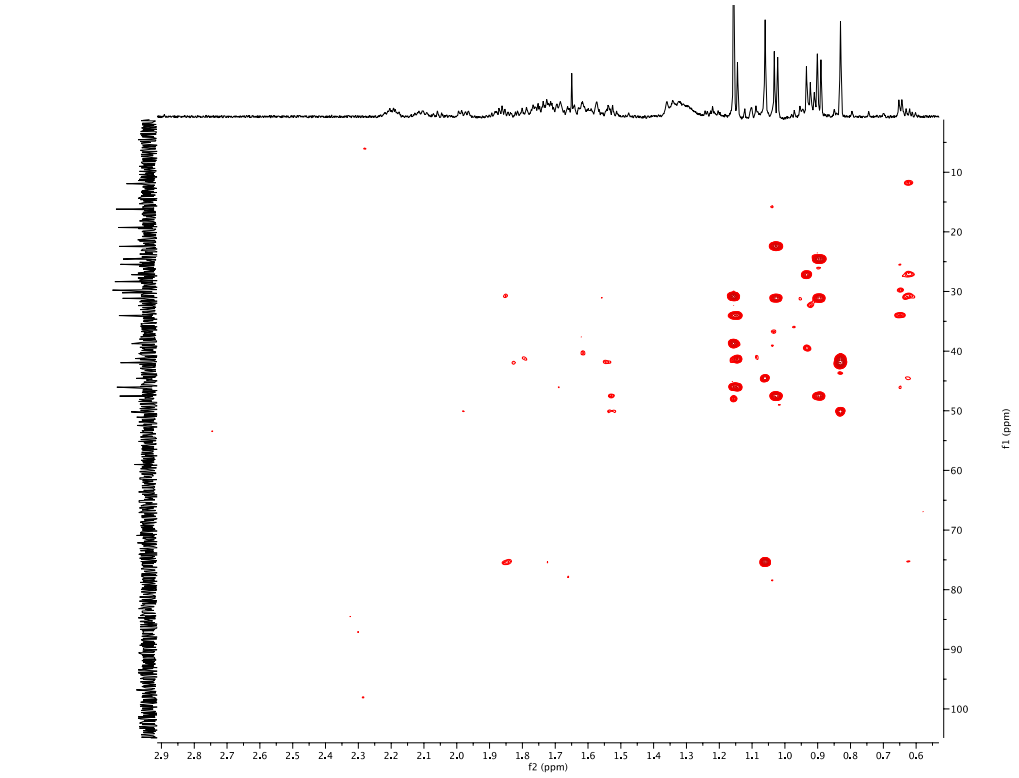

Figure S36. HMBC NMR (600 MHz, C_6D_6) spectrum of **5**.

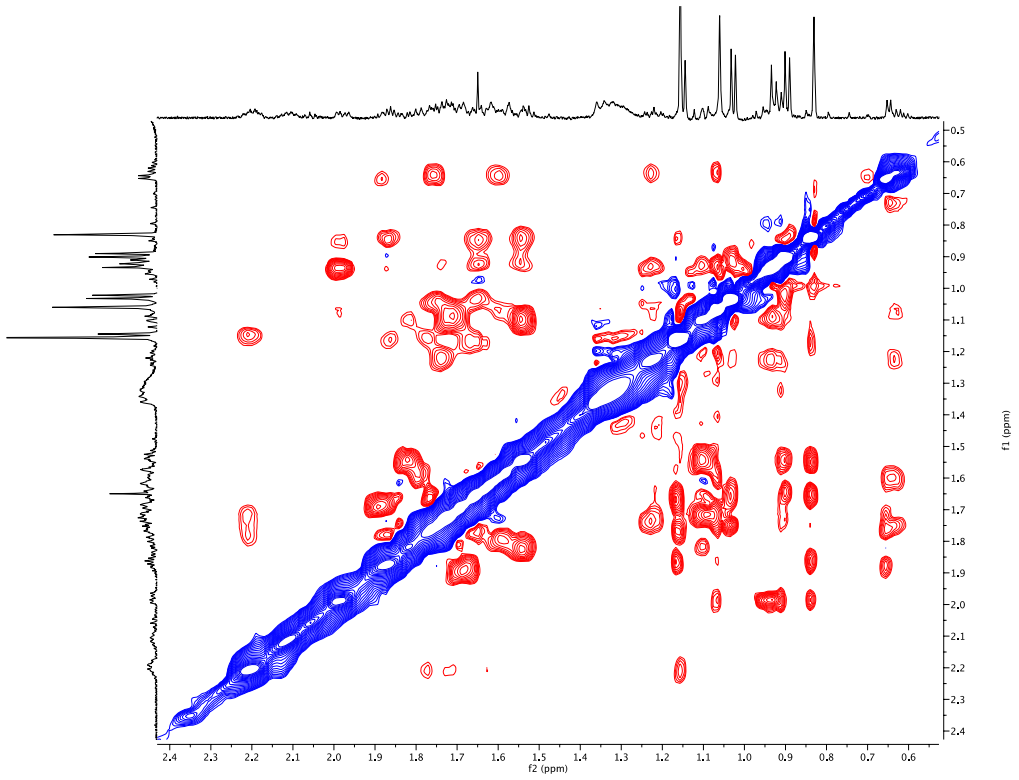

Figure S37. NOESY NMR (600 MHz, C_6D_6) spectrum of **5**.

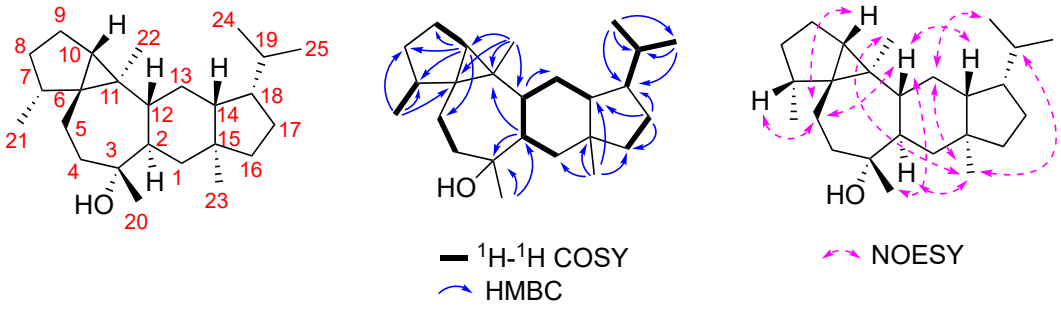

Figure S38. Structure and key 2D NMR correlations of **5**.

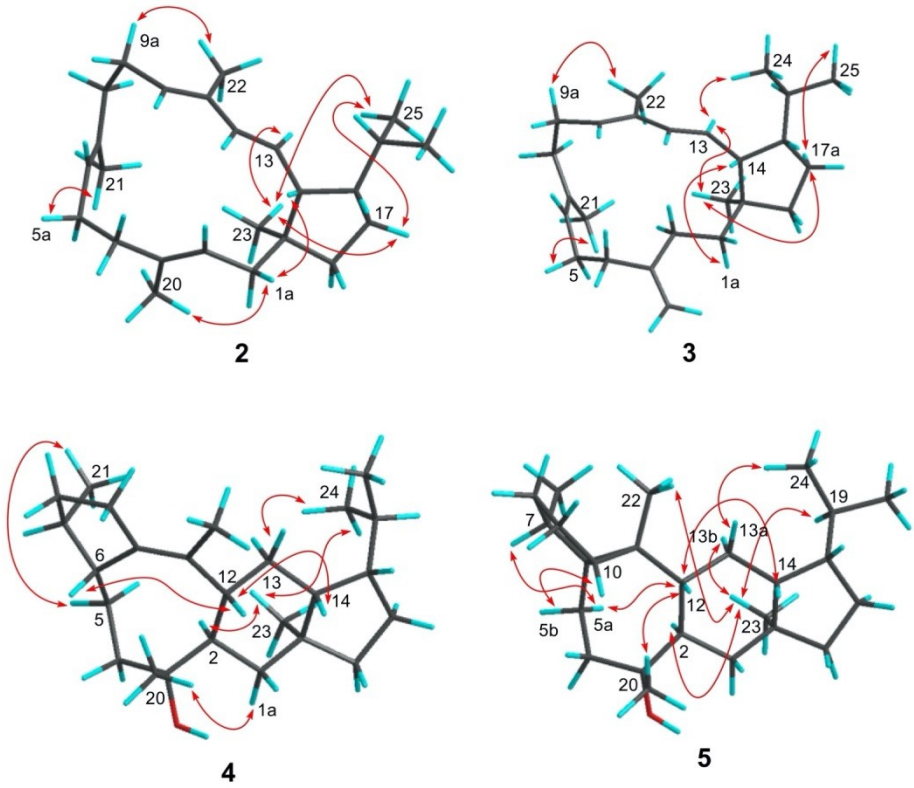

Figure S39. Key NOE correlations of **2**–**5**.

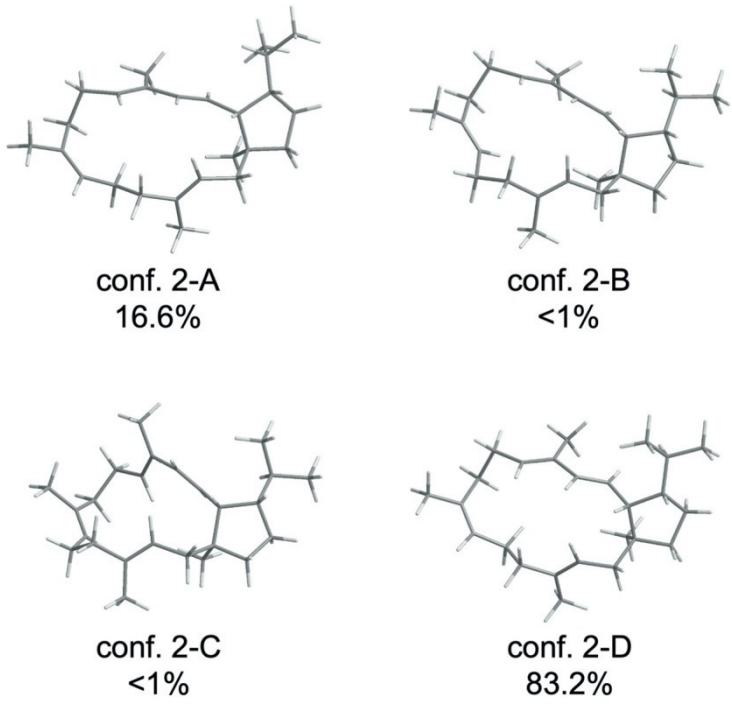

Figure S40. DFT-optimized structures for low-energy conformers of **2** at B3LYP/6-31G(d) level in methanol (PCM).

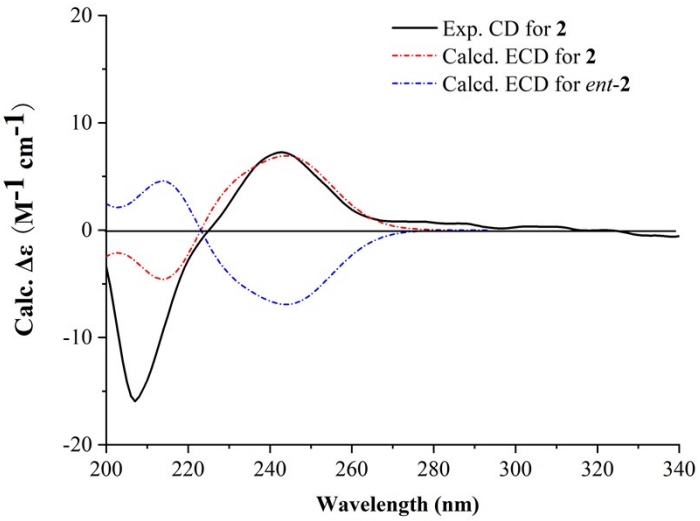

Figure S41. Experimental CD and computed ECD of **2**.

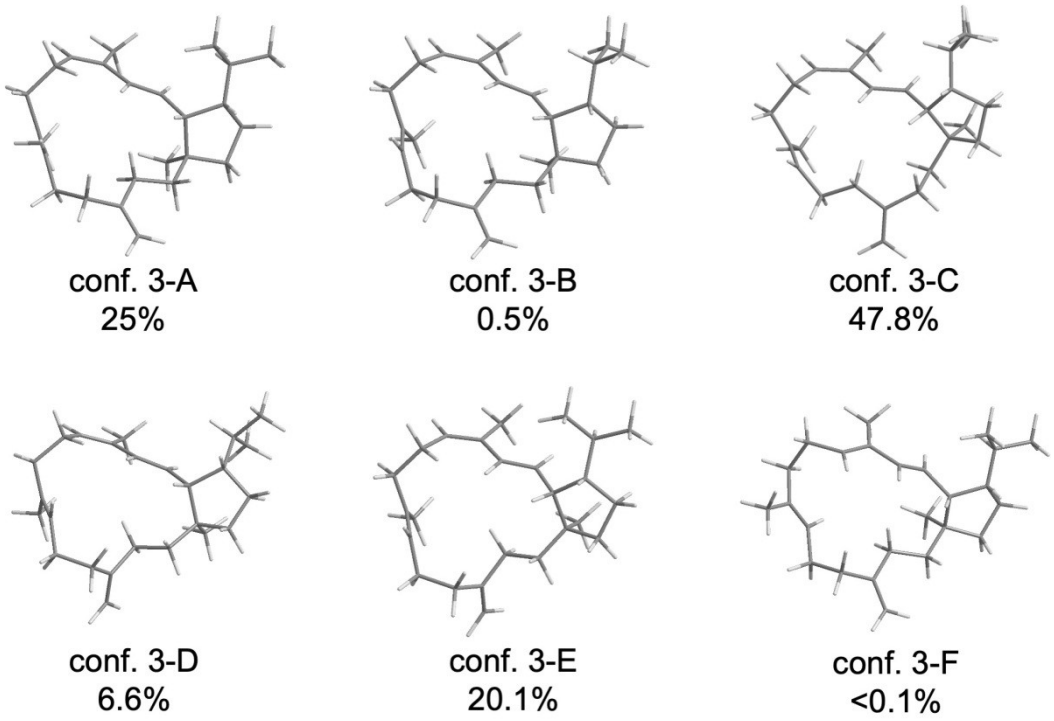

Figure S42. DFT-optimized structures for low-energy conformers of **3** at B3LYP/6-31G(d) level in methanol (PCM).

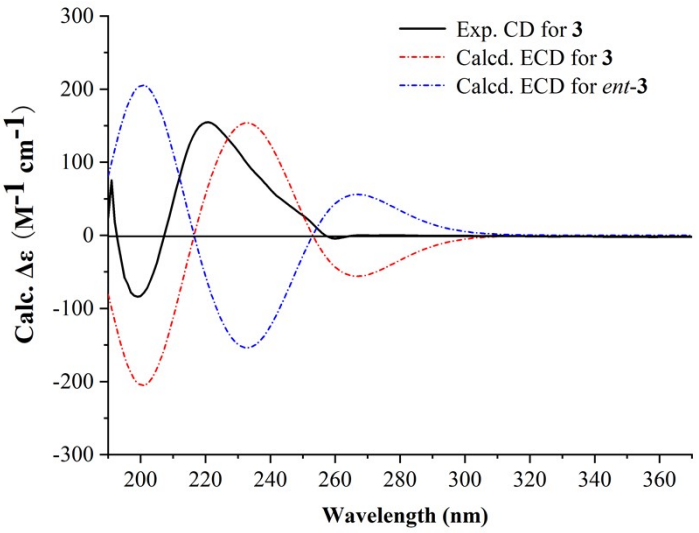

Figure S43. Experimental CD and computed ECD of **3**.

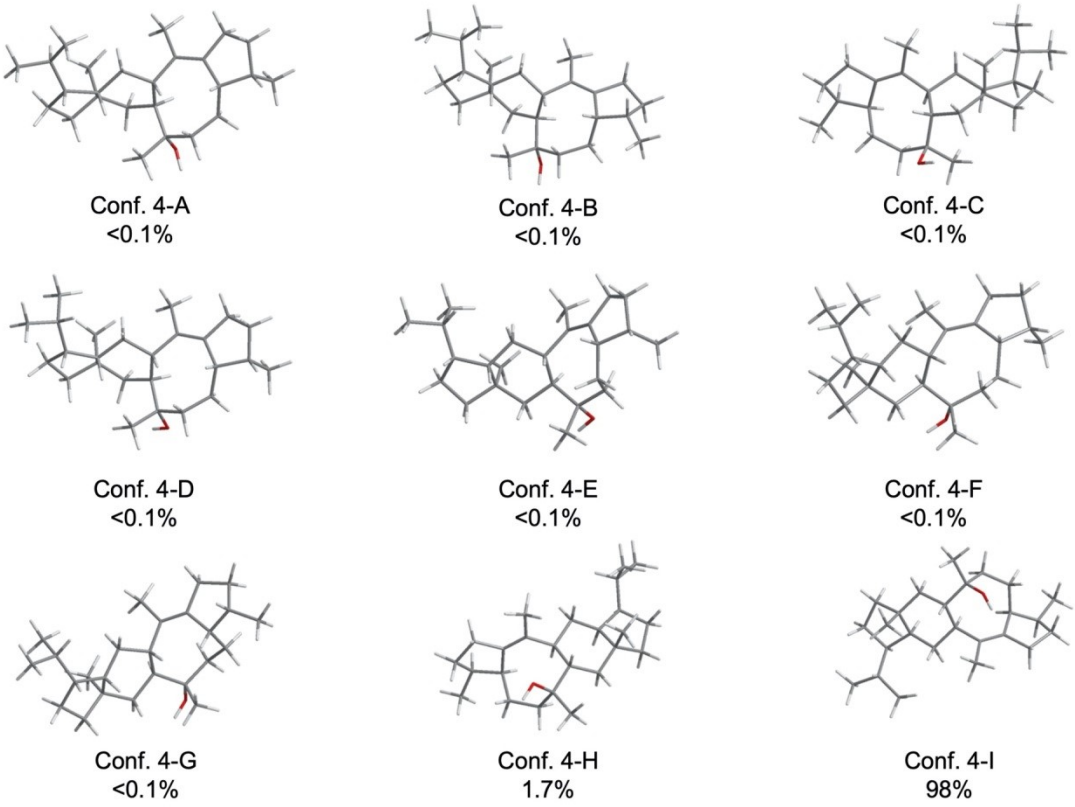

Figure S44. DFT-optimized structures for low-energy conformers of **4** at B3LYP/6-31G(d) level in methanol (PCM).

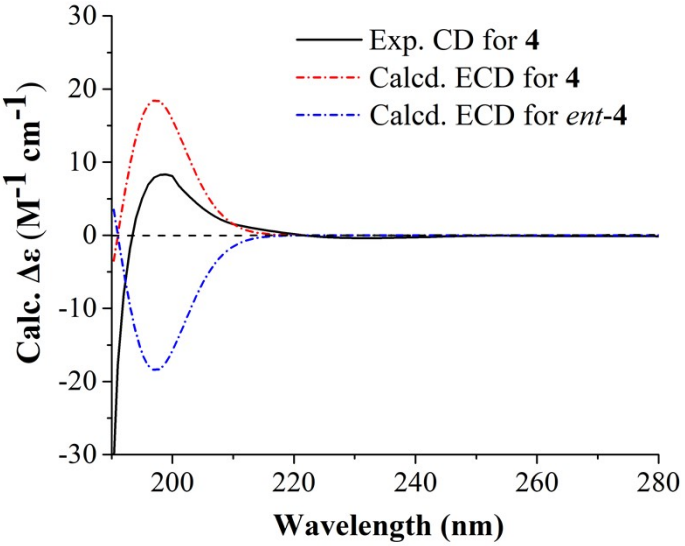

Figure S45. Experimental CD and computed ECD of **4**.

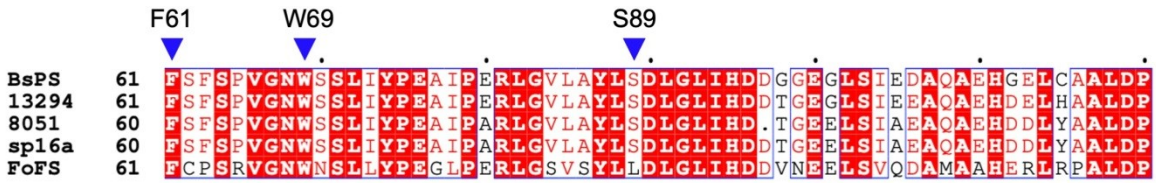

Figure S46. Amino acid sequence alignment of the BFTSs BsPS, 13294, 8051, sp16a and FoFS. The sequence identities between BsPS and 13294, 8051, sp16a, and FoFS are 71.09%, 71.49%, 71.21%, and 53.20%, respectively.

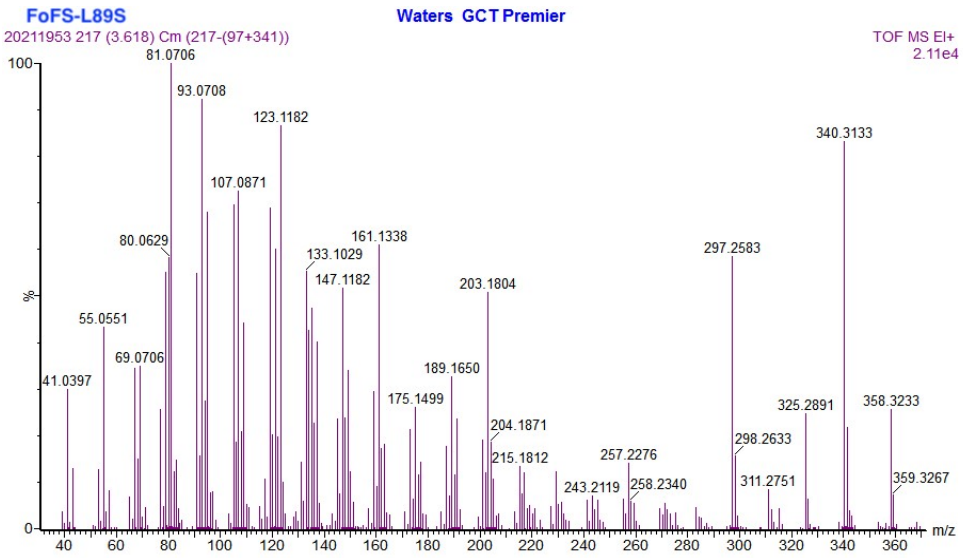

Figure S47. HR-EI-MS spectrum of **1** in MeOH.

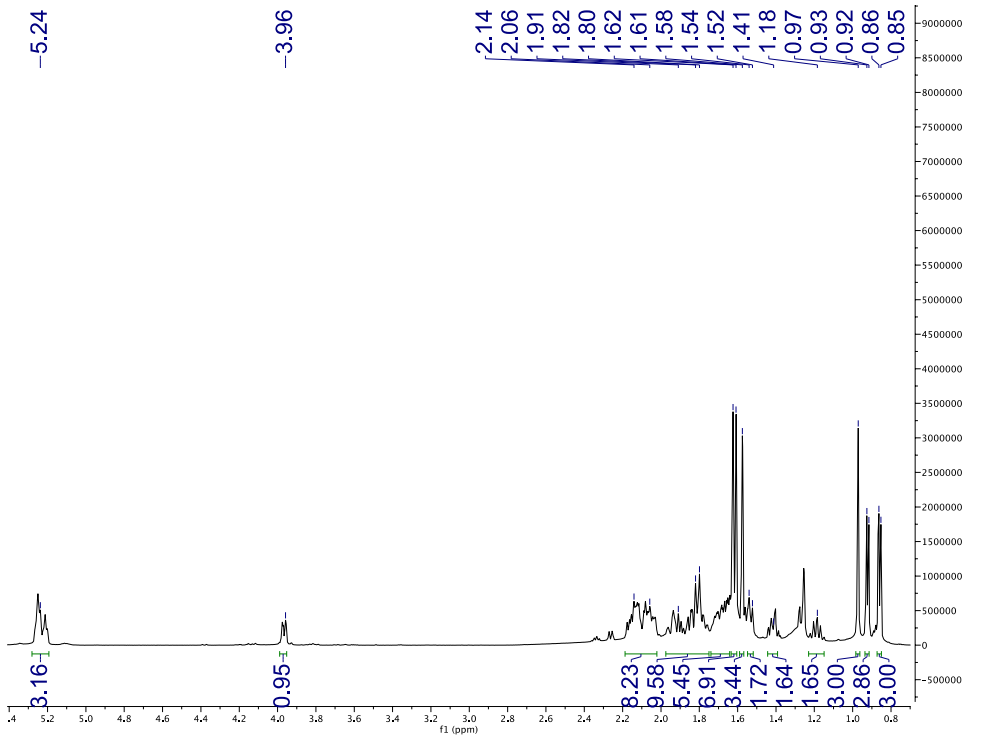

Figure S48. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of **1**.

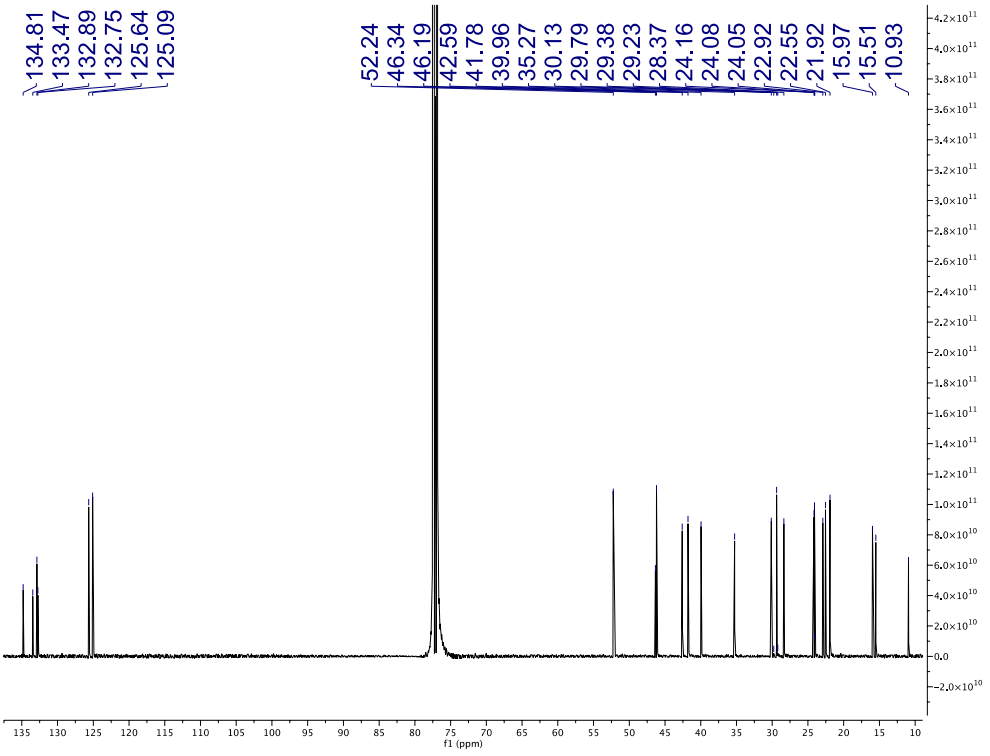

Figure S49. ^{13}C NMR (150 MHz, $CDCl_3$) spectrum of **1**.

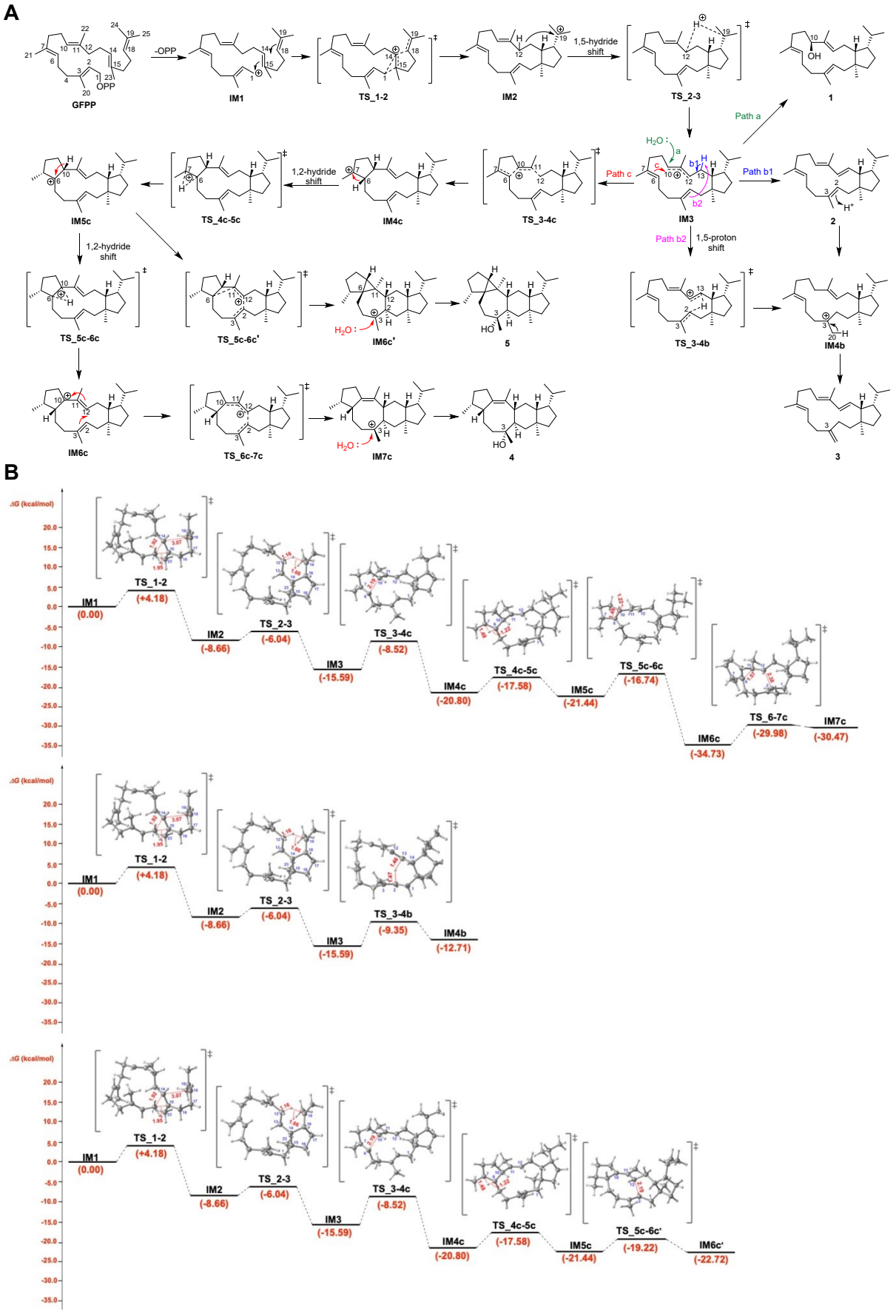

Figure S50. Computed reaction pathways of **1**–**5** and potential energy profiles of the pathways. (A) **IM3** is the first branching point to generate **1**, **2**, and **IM4**, while **IM5c** is the second branching point to generate **IM6c** and **IM6c′** via **TS_5c-6c** and **TS_5c-6c′**, respectively. TS, transition state. (B) The Gibbs free energies were calculated from the

electron energies using the mPW1PW91/6–31+G(d,p) level, plus the thermal correction of the M06–2X/6–31G(d,p) level. The potential energy profile relative to **IM1** are shown in red.

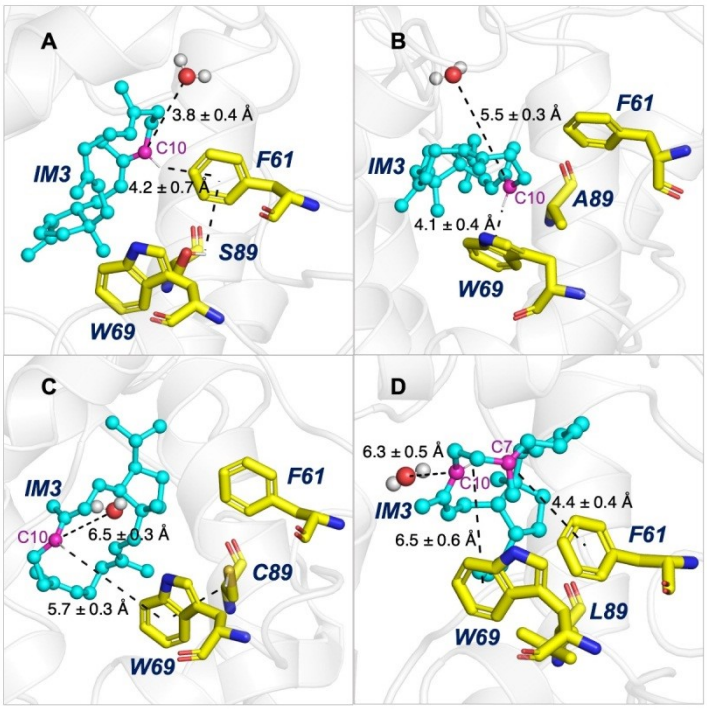

Figure S51. The superimposed view of **IM3** in (**A**) BsPS-WT, (**B**) BsPS-S89A, (**C**) BsPS-S89C, and (**D**) BsPS-S89L. C_7 and C_{10} are shown in purple sphere.

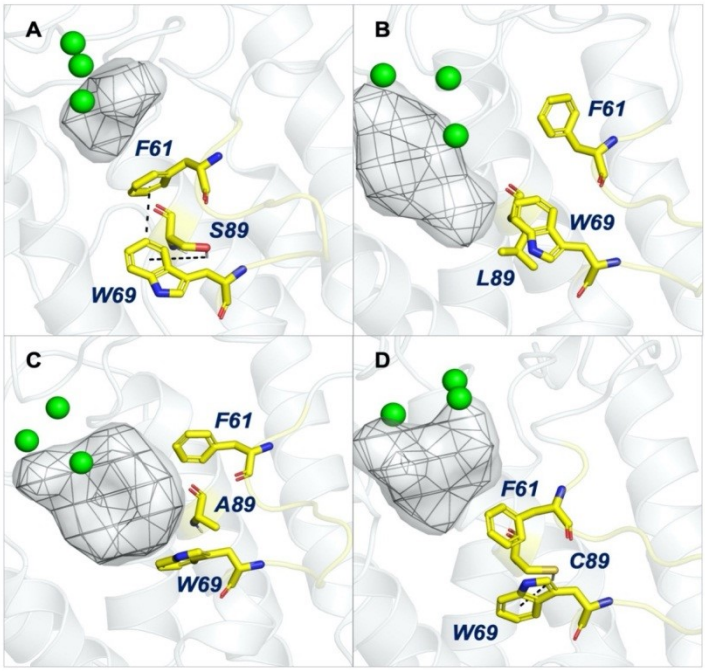

Figure S52. Snapshots of the apoprotein with Mg^{2+} of (A) WT, (B) S89L, (C) S89A, and (D) S89C. The pocket areas of the WT BsPS and the variants are shown in grey mesh. The loop in which F61 and W69 are located is shown in yellow.

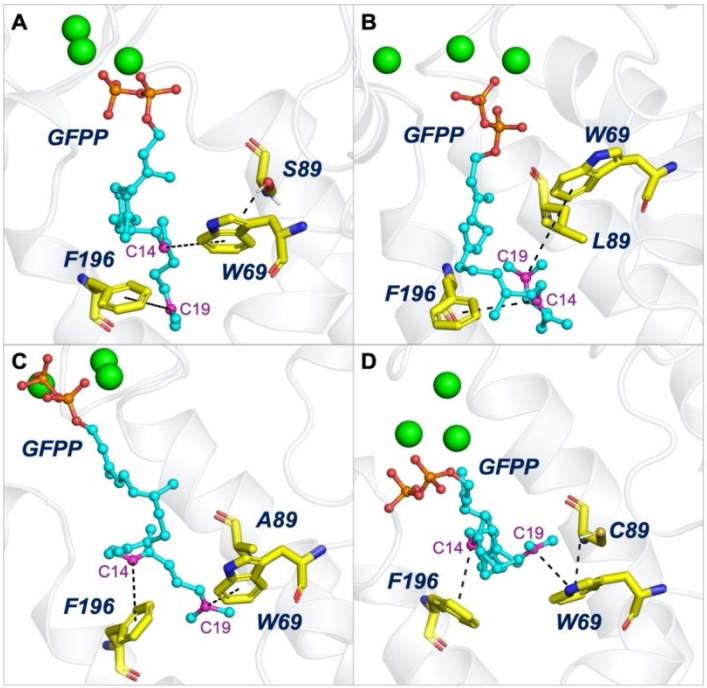

Figure S53. The superimposed view of GFPP in (A) WT, (B) S89L, (C) S89A, and (D) S89C. C_{14} and C_{19} are shown in purple spheres.

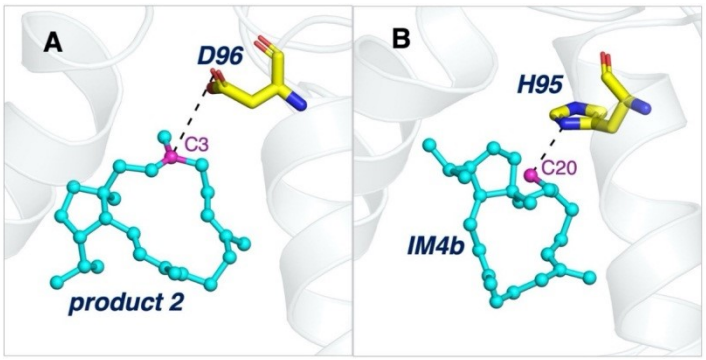

Figure S54. The superimposed views of **2** (A) and **IM4b** (B) in S89L.

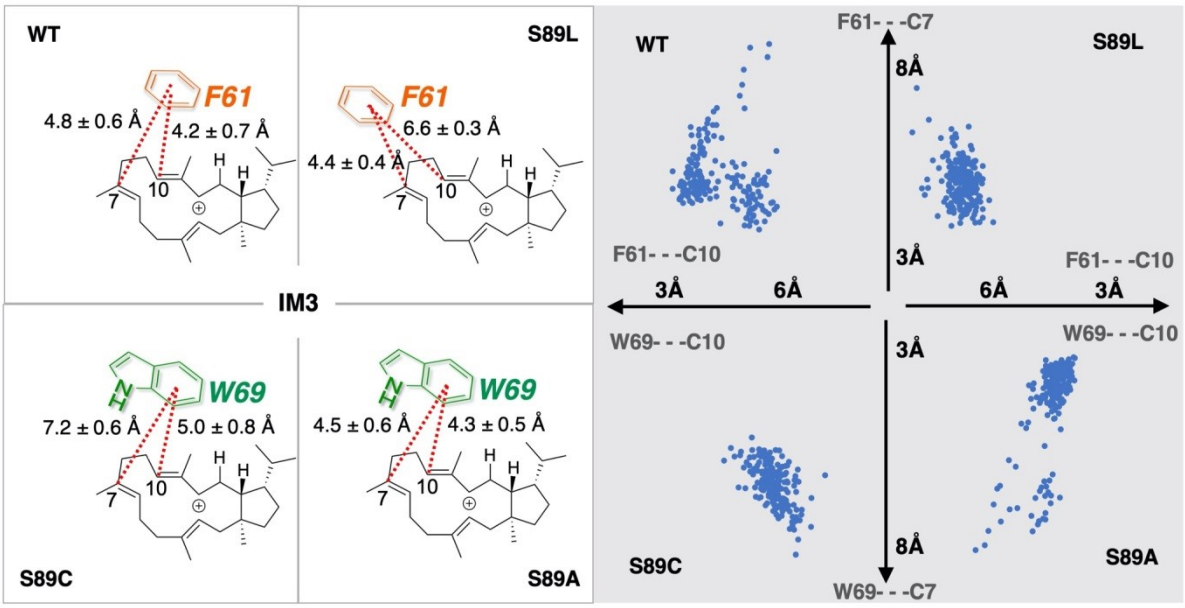

Figure S55. The distance statistics between F61 or W69 of the WT and mutant BsPS to C_7 and C_{10} of **IM3** during MD simulations.

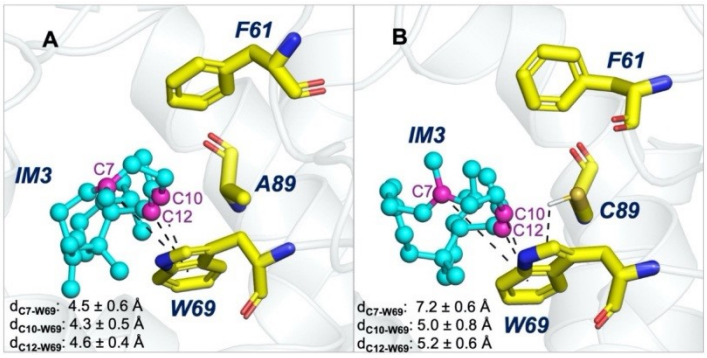

Figure S56. The superimposed views of **IM3** in (A) S89A and (B) S89C.

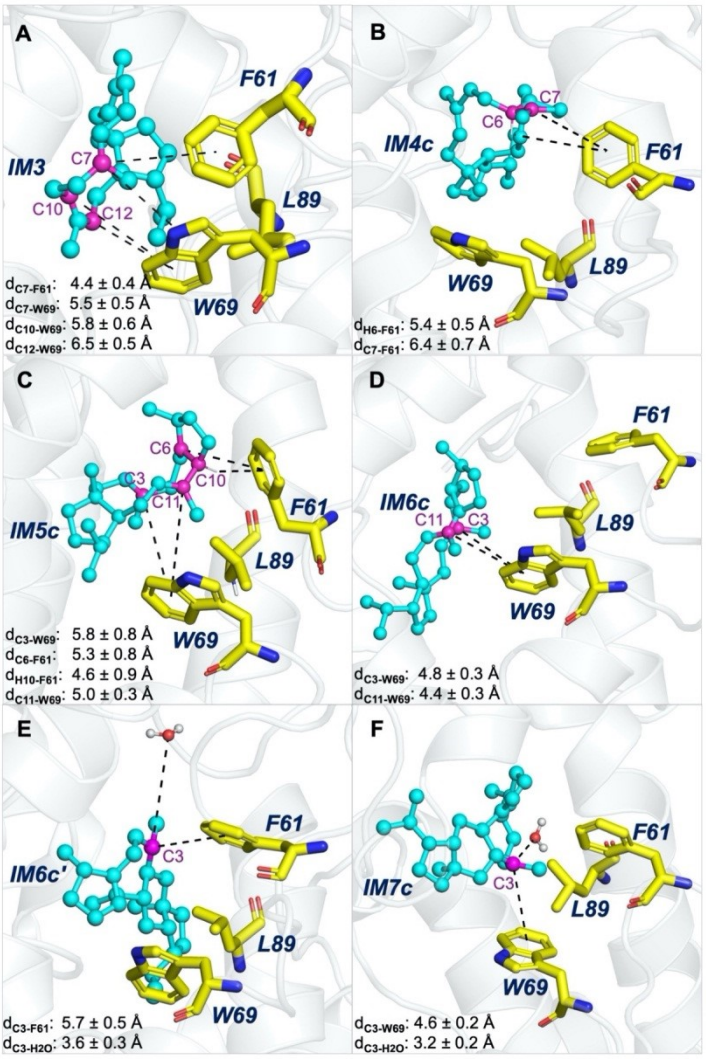

Figure S57. The superimposed views of (A) **IM3**, (B) **IM4c**, (C) **IM5c**, (D) **IM6c**, (E) **IM6c′**, (F) **IM7c** in S89L.

SUPPORTING TABLES

Table S1. Mutants of TCSM library.

	I			II		III		
	F61	S89	L93	W69	M199	F196	T224	L227
1	/	A	A	F	A	/	A	A
2	/	A	/	F	L	/	A	/
3	/	L	A	A	A	/	L	A
4	/	L	/	A	L	/	L	/
5	A	A	A	A	F	A	A	A
6	A	A	L	L	A	A	A	/
7	A	A	F	L	L	A	A	F
8	A	L	A	L	F	A	L	A
9	A	L	/	/	/	A	L	/
10	A	L	F	/	/	A	L	F
11	A	F	A	/	/	A	F	A
12	A	F	/	/	/	A	F	/
13	L	A	A	/	/	L	A	A
14	L	A	/	/	/	L	A	/
15	L	A	F	/	/	L	A	F
16	L	L	A	/	/	L	L	A
17	L	L	/	/	/	L	L	/
18	L	L	F	/	/	L	L	F
19	L	F	A	/	/	L	F	A
20	L	F	/	/	/	L	F	/

Table S2. Relative production of the products yielded from the TCSM variants. The calculation was based on GC-MS analysis.

variants	Peak area of GC-MS analysis[a]					Relative production (%)[b]					
	1	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**	total
WT	15588259 ± 736326	0	0	0	0	100	0	0	0	0	100
S89A/L93A	886060 ± 41022	0	0	0	0	6	0	0	0	0	6
S89A	3613891 ± 159667	259030 ± 13052	423201 ± 15572	0	0	23	2	3	0	0	28
S89L/L93A	0	0	0	0	0	0	0	0	0	0	0
S89L	4470955 ± 55964	1261687 ± 74328	1901116 ± 42439	2298538 ± 62519	1452043 ± 91806	29	8	12	15	9	73
F61A/S89A/L93A	590192 ± 66997	0	0	0	0	4	0	0	0	0	4
F61A/S89A	2920343 ± 45365	5759736 ± 113842	6731923 ± 202901	0	0	19	37	43	0	0	99
F61A/S89A/L93F	0	0	0	0	0	0	0	0	0	0	0
F61A/S89L/L93A	0	0	0	0	0	0	0	0	0	0	0
F61A/S89L	0	0	0	0	0	0	0	0	0	0	0
F61A/S89L/L93F	0	0	0	0	0	0	0	0	0	0	0
F61A/S89F/L93A	0	0	0	0	0	0	0	0	0	0	0
F61A/S89F	0	0	0	0	0	0	0	0	0	0	0
F61L/S89A/L93A	0	0	0	0	0	0	0	0	0	0	0
F61L/S89A	3792204 ± 146377	0	0	0	0	24	0	0	0	0	24
F61L/S89A/L93F	790369 ± 14183	0	0	0	0	5	0	0	0	0	5
F61L/S89L/L93A	0	0	0	0	0	0	0	0	0	0	0
F61L/S89L	0	0	0	0	0	0	0	0	0	0	0
F61L/S89L/L93F	0	0	0	0	0	0	0	0	0	0	0
F61L/S89F/L93A	0	0	0	0	0	0	0	0	0	0	0
F61L/S89F	0	0	0	0	0	0	0	0	0	0	0
W69F/M199A	0	0	0	0	0	0	0	0	0	0	0
W69F/M199L	0	0	0	0	0	0	0	0	0	0	0
W69A/M199A	3225288 ± 156681	1966264 ± 72910	3495998 ± 104823	0	0	21	13	22	0	0	56
W69A/M199L	0	0	0	0	0	0	0	0	0	0	0
W69A/M199F	0	0	0	0	0	0	0	0	0	0	0
W69L/M199A	0	0	0	0	0	0	0	0	0	0	0
W69L/M199L	0	0	0	0	0	0	0	0	0	0	0
W69L/M199F	18329882 ± 1145473	13460167 ± 1068005	5661322 ± 150240	0	0	118	86	36	0	0	240
T224A/L227A	0	0	0	0	0	0	0	0	0	0	0
T224A	13164270 ± 275756	0	0	0	0	84	0	0	0	0	84
T224L/L227A	0	0	0	0	0	0	0	0	0	0	0

T224L	1734138 ± 148681	1776050 ± 85111	1756408 ± 153843	0	0	11	11	11	0	0	34
F196A/T224A/L227A	0	0	0	0	0	0	0	0	0	0	0
F196A/T224A	0	9538649 ± 455310	7989119 ± 82961	0	0	0	61	51	0	0	112
F196A/T224A/L227F	0	0	0	0	0	0	0	0	0	0	0
F196A/T224L/L227A	0	0	0	0	0	0	0	0	0	0	0
F196A/T224L	0	0	0	0	0	0	0	0	0	0	0
F196A/T224L/L227F	0	0	0	0	0	0	0	0	0	0	0
F196A/T224F/L227A	0	0	0	0	0	0	0	0	0	0	0
F196A/T224F	0	0	0	0	0	0	0	0	0	0	0
F196L/T224A/L227A	3570046 ± 128800	15234702 ± 226055	14114576 ± 1260820	0	0	23	98	91	0	0	211
F196L/T224A	9085322 ± 195749	0	0	0	0	58	0	0	0	0	58
F196L/T224A/L227F	3469182 ± 169144	3090473 ± 106310	5270674 ± 203186	0	0	22	20	34	0	0	76
F196L/T224L/L227A	1808767 ± 155977	1148520 ± 45592	1506789 ± 36870	0	0	12	7	10	0	0	29
F196L/T224L	28437407 ± 994025	4601904 ± 119711	6935954 ± 269469	0	0	182	30	44	0	0	256
F196L/T224L/L227F	0	927366 ± 6394	2053561 ± 74591	0	0	0	6	13	0	0	19
F196L/T224F/L227A	0	0	0	0	0	0	0	0	0	0	0
F196L/T224F	0	8642326 ± 335379	7164416 ± 125886	0	0	0	55	46	0	0	101

[a] The peak area values are the mean of triple measurements.

[b] The values are the relative productions of the mean peak area.

df

1

2

3

4

5

Table S3. Pocket volumes of the WT and mutants BsPS.

apoprotein	volume (Å^3)
WT	10 ± 5.1
S89A	147 ± 25.3
S89C	35 ± 13.2
S89L	126 ± 29.6

Table S4. List of primers for libraries I, II, and III.

Libraries			Primers
I	First-site mutation	F61A-F	5’-GCCGAGAACAGTCTACTCATGCCTCATTCTCACCAGTGGGAAAC-3’
		F61L-F	5’-GCCGAGAACAGTCTACTCATCTTTCATTCTCACCAGTGGGAAAC-3’
		F61-R	5’-GAGTAGACTGTTCTCGGCCATCTCTCATCTCTCTG-3’
	Second-site(s) mutation	S89F-F	5’-TGGGGGTCTTGGCGTATCTCTTCGACTTGGGCTTGATTCATGATGAC-3’
		S89L-F	5’-TGGGGGTCTTGGCGTATCTCCTTGACTTGGGCTTGATTCATGATGAC-3’
		S89A-F	5’-TGGGGGTCTTGGCGTATCTCGCCGACTTGGGCTTGATTCATGATGAC-3’
		S89F/L93A-F	5’-TGGGGGTCTTGGCGTATCTCTTCGACTTGGGCGCCATTCATGATGAC-3’
		S89L/L93A-F	5’-TGGGGGTCTTGGCGTATCTCCTTGACTTGGGCGCCATTCATGATGAC-3’
		S89L/L93F-F	5’-TGGGGGTCTTGGCGTATCTCCTTGACTTGGGCTTCATTCATGATGAC-3’
		S89A/L93A-F	5’-TGGGGGTCTTGGCGTATCTCGCCGACTTGGGCGCCATTCATGATGAC-3’
		S89A/L93F-F	5’-TGGGGGTCTTGGCGTATCTCGCCGACTTGGGCTTCATTCATGATGAC-3’
		S89/L93-R	5’-ACCTCTCAGGGATCGCTTCAGGATAGATCAAGGACGACCAG-3’
II	First-site mutation	W69F-F	5’-TCACCAGTGGGAAACTTCTCGTCCTTGATCTATCC-3’
		W69L-F	5’-TCACCAGTGGGAAACCTTTCGTCCTTGATCTATCC-3’
		W69A-F	5’-TCACCAGTGGGAAACGCCTCGTCCTTGATCTATCC-3’
		W69-R	5’-GAATGAGAAATGAGTAGACTGTTCTCGGCCATCTC-3’
	Second-site mutation	M199F-F	5’-CTAGTCTTCTGGCCGTTCCTGCAGTTCAGCCTCGGAATG-3’
		M199L-F	5’-CTAGTCTTCTGGCCGCTTCTGCAGTTCAGCCTCGGAATG-3’
		M199A-F	5’-CTAGTCTTCTGGCCGGCCCTGCAGTTCAGCCTCGGAATG-3’
		M199-R	5’-CATTCCACCATTGTCGCTTCGATATTTCAAATATTC-3’
III	First-site mutation	F196L-F	5’-ACAATGGTGGAATGCTAGTCCTTTGGCCGATGCTGCAG-3’
		F196A-F	5’-ACAATGGTGGAATGCTAGTCGCCTGGCCGATGCTGCAG-3’

		F196-R	5’-CGCTTCGATATTTCAAATATTCTTCCATAGTCTGCGCTTCCTT-3’
	Second-site(s) mutation	T224F-F	5’-AGCCAATTATTGACGCAGCATTCGAAGGACTTCTCCTAGCAAATGAT-3’
		T224L-F	5’-AGCCAATTATTGACGCAGCACTTGAAGGACTTCTCCTAGCAAATGAT-3’
		T224A-F	5’-AGCCAATTATTGACGCAGCAGCCGAAGGACTTCTCCTAGCAAATGAT-3’
		T224F/L227A-F	5’-AGCCAATTATTGACGCAGCATTCGAAGGAGCCCTCCTAGCAAATGAT-3’
		T224L/L227F-F	5’-AGCCAATTATTGACGCAGCACTTGAAGGATTCCTCCTAGCAAATGAT-3’
		T224L/L227A-F	5’-AGCCAATTATTGACGCAGCACTTGAAGGAGCCCTCCTAGCAAATGAT-3’
		T224A/L227F-F	5’-AGCCAATTATTGACGCAGCAGCCGAAGGATTCCTCCTAGCAAATGAT-3’
		T224A/L227A-F	5’-AGCCAATTATTGACGCAGCAGCCGAAGGAGCCCTCCTAGCAAATGAT-3’
		T224/L227-R	5’-GTACGAGCGCTTCTTCTGCTTCCGATATGGACATTCCGAGG-3’

Table S5. List of primers for saturation mutagenesis of S89.

	Mutants	Primers
Forward	S89G	5’-TGGGGGTCTTGGCGTATCTCGGGGACTTGGGCTTGATTCATG-3’
	S89V	5’-TGGGGGTCTTGGCGTATCTCGTGGACTTGGGCTTGATTCATG-3’
	S89I	5’-TGGGGGTCTTGGCGTATCTCATTGACTTGGGCTTGATTCATG-3’
	S89M	5’-TGGGGGTCTTGGCGTATCTCATGGACTTGGGCTTGATTCATG-3’
	S89W	5’-TGGGGGTCTTGGCGTATCTCTGGGACTTGGGCTTGATTCATG-3’
	S89P	5’-TGGGGGTCTTGGCGTATCTCCCGGACTTGGGCTTGATTCATG-3’
	S89T	5’-TGGGGGTCTTGGCGTATCTCACCGACTTGGGCTTGATTCATG-3’
	S89C	5’-TGGGGGTCTTGGCGTATCTCTGCGACTTGGGCTTGATTCATG-3’
	S89Y	5’-TGGGGGTCTTGGCGTATCTCTATGACTTGGGCTTGATTCATG-3’
	S89N	5’-TGGGGGTCTTGGCGTATCTCAACGACTTGGGCTTGATTCATG-3’
	S89Q	5’-TGGGGGTCTTGGCGTATCTCCAAGACTTGGGCTTGATTCATG-3’
	S89D	5’-TGGGGGTCTTGGCGTATCTCGATGACTTGGGCTTGATTCATG-3’
	S89E	5’-TGGGGGTCTTGGCGTATCTCGAAGACTTGGGCTTGATTCATG-3’
	S89K	5’-TGGGGGTCTTGGCGTATCTCAAGGACTTGGGCTTGATTCATG-3’
	S89R	5’-TGGGGGTCTTGGCGTATCTCCGAGACTTGGGCTTGATTCATG-3’
	S89H	5’-TGGGGGTCTTGGCGTATCTCCATGACTTGGGCTTGATTCATG-3’
Reverse	S89	5’-ACCTCTCAGGGATCGCTTCAGGATAGATCAAGGACGACCAG-3’

Table S6. 1D and 2D NMR Data of **2**.

Pos.	δ_H[a] mult (*J* in Hz)	δ_C[b]	COSY (^1H –^1H)	HMBC (^1H –^{13}C)	NOSEY (^1H –^1H)
1a 1b	2.36, m 1.94, m	44.6, CH_2	2		14, 20, 23
2	5.39, m	123.4, CH	1		4b
3		134.4, C			
4a 4b	2.27, m 2.02, m	40.9, CH_2	5		2
5a 5b	2.29, m 2.03, m	24.7, CH_2	4, 6		21
6	5.06	126.8, CH	5		
7		132.3, C			
8a 8b	2.02, m 1.97, m	40.3, CH_2	9	9	
9a 9b	2.22, m 2.06, m	25.1, CH_2	8, 10		22
10	5.34, m	129.8, CH	9		
11		134.2, C			
12	6.01, d (15.0)	137.7, CH	13	10, 11, 14, 22	
13	5.48, m	126.9, CH	12, 14	11	23
14	2.61, t (9.5)	53.5, CH	13, 18		1b
15		47.3, C			
16a 16b	1.48, d (5.8) 1.35, m	43.5, CH_2	17		
17	1.37, m	30.2, CH_2	18		23, 25
18	1.62, m	52.6, CH	14, 17, 19		
19	1.62, m	29.6, CH	18, 24, 25		
20	1.56, s	15.6, CH_3		2, 3, 4	1a
21	1.53, s	15.3, CH_3		6, 7, 8	5b
22	1.72, s	12.6, CH_3		10, 11, 12	9a
23	0.83, s	23.4, CH_3		1, 14, 15, 16	1, 13, 17, 25
24	1.01, d (6.1)	22.9, CH_3	19	18, 19, 25	
25	0.94, d (5.9)	22.4, CH_3	19	18, 19, 24	17, 23

[a]Recorded at 600 MHz in C_6D_6.
[b]Recorded at 150 MHz in C_6D_6.

Table S7. 1D and 2D NMR Data of **3**.

Pos.	δ_H[a] mult (*J* in Hz)	δ_C[b]	COSY (^{1}H –^{1}H)	HMBC (^{1}H – ^{13}C)	NOSEY (^{1}H –^{1}H)
1a 1b	1.54, m 1.47, m	40.2, CH_2	2	2	14, 18
2a 2b	2.14, m 1.82, m	30.8, CH_2	1		
3		150.4, C			
4	2.10, brs	37.7, CH_2	5		
5	2.10, brs	25.7, CH_2	4, 6		21
6	5.08, brs	126.6, CH	5	4, 5	
7		133.1, C			
8a 8b	2.07, m 1.99, m	39.5, CH_2	9	6	
9a 9b	2.31, m 1.99, m	25.1, CH_2	8, 10		22
10	5.13, dd (11.9, 3.4)	131.4, CH	9	8, 9, 12	
11		133.6, C			
12	6.05, d (15.5)	138.0, CH	13	10	
13	5.58, dd (15.5, 10.8)	126.6, CH	12, 14	11	23, 24
14	2.36, t (10.8)	56.3, CH	13, 18	12, 13, 15, 18, 19	1a
15		46.3, C			
16a 16b	1.36, m 1.31, m	40.9, CH_2	17		
17a 17b	1.70, m 1.50, m	28.9, CH_2	16, 18		13, 25
18	1.79, m	49.9, CH	14, 17, 19		1b
19	1.66, m	31.0, CH	18, 24, 25		
20	4.91, d (3.4)	108.2, CH_2		2, 3, 4	
21	1.40, s	15.2, CH_3		6, 7, 8	5
22	1.68, s	12.5, CH_3		10, 11, 12	9a
23	0.80, s	20.7, CH_3		1, 14, 15, 16	13, 17b
24	1.02, d (6.2)	24.2, CH_3	19	18, 19, 25	13
25	0.90, d (6.2)	21.8, CH_3	19	18, 19, 24	17b

[a]Recorded at 600 MHz in C_6D_6.
[b]Recorded at 150 MHz in C_6D_6.

Table S8. 1D and 2D NMR Data of **4**.

Pos.	δ_H[a] mult (*J* in Hz)	δ_C[b]	COSY ($^1H-^1H$)	HMBC ($^1H-^{13}C$)	NOSEY ($^1H-^1H$)
1a 1b	1.81, m 0.80, m	43.6, CH_2	2		
2	2.02, m	49.8, CH	1		23
3		75.2, C			
4a 4b	1.73, m 1.58, m	36.1, CH_2			
5	1.56, m	25.1, CH_2	6	4	21
6	2.53, m	46.8, CH	5		12
7	1.92, m	39.2, CH	8, 21		
8	1.59, m	31.7, CH_2	7, 9	10	
9a 9b	2.18, dd (15.7, 9.1); 2.06, m	30.1, CH_2	8		
10		144.1, C			
11		133.3, C			
12	2.40, m	47.9, CH	13	10	6, 14
13	1.62, m	29.8, CH_2	12, 14	12	24
14	1.41, m	51.3, CH	13, 18		12
15		42.0, C			
16a 16b	1.50, m; 1.11, dd (20.0, 11.1)	41.6, CH_2	17		
17a 17b	1.85, m; 1.57, m	28.6, CH_2	16		
18	1.65, m	47.6, CH	14, 19	14, 16	
19	1.54, m	31.8, CH	18, 24, 25		23
20	1.28, s	32.6, CH_3		2, 3, 4	
21	0.95, d (6.9)	15.7, CH_3	7	6, 7, 8	
22	1.68, s	15.0, CH_3		10, 11, 12	
23	0.80, s	19.4, CH_3		1, 14, 15, 16	2, 25
24	0.93, d (6.3)	24.3, CH_3	19	18, 19, 25	13
25	0.87, d (6.5)	22.8, CH_3	19	18, 19, 24	23

[a]Recorded at 600 MHz in C_6D_6.
[b]Recorded at 150 MHz in C_6D_6.

Table S9. 1D and 2D NMR Data of compound **5**.

Pos.	δ_H[a] mult (*J* in Hz)	δ_C[b]	COSY (^1H –^1H)	HMBC (^1H –^{13}C)	NOESY (^1H –^1H)
1a 1b	1.98, m 0.91, m	42.2, CH_2	2		
2	1.86, m	44.6, CH	1, 12	3, 11	23
3		75.3, C			12
4a 4b	1.69, m 1.51, m	44.2, CH_2	5		
5a 5b	1.79, m 1.60, m	29.8, CH_2	4		12, 21
6		41.3, C			
7	2.20, m	46.0, CH	21		5a
8	1.73, m	34.0, CH_2			
9a 9b	1.88, m 1.67, m	25.4, CH_2	10		
10	0.65, d (5.3)	38.7, CH	9	5, 7, 8, 9	5b
11		30.8, C			
12	0.62, m	48.1, CH	2, 13	2, 11, 13	5a, 14, 20
13a 13b	1.74, m 1.66, m	27.2, CH_2	12, 14		23, 24
14	1.22, m	50.2, CH	13		12
15		41.2, C			
16a 16b	1.54, m 1.10, m	41.9, CH_2	17		
17a 17b	1.82, m 1.54, m	28.3, CH_2	16	14, 16, 18	
18	1.71, m	47.5, CH	19		
19	1.63, m	31.2, CH	18, 24, 25		23
20	1.06, s	24.3, CH_3		2, 3	12
21	1.15, d (7.1)	16.2, CH_3	7	6, 7, 8	
22	1.16, s	11.9, CH_3		6, 10, 11, 12	23
23	0.83, s	19.2, CH_3		1, 14, 15, 16	2, 13b, 19, 22
24	1.02, d (6.1)	24.6, CH_3	19	18, 19, 25	13a, 13b
25	0.89, d (6.7)	22.4, CH_3	19	18, 19, 24	

[a]Recorded at 600 MHz in C_6D_6.
[b]Recorded at 150 MHz in C_6D_6.

Table S10. Energy profiles of ***path b1*** and ***path c*** calculation.

	path b1		
	Total Energy	Thermal correction to Gibbs Free Energy	Imaginary Freq
IM1	-976.872415	0.548202	none
TS_1-2	-976.865255	0.547719	-97.55
IM2	-976.891067	0.553047	none
TS_2-3	-976.88933	0.55549	-114.25
IM3	-976.903642	0.554584	none
TS_3-4b	-976.890603	0.551486	-942.95
IM4b	-976.898197	0.553714	none

	path c		
	Total Energy	Thermal correction to Gibbs Free Energy	Imaginary Freq
IM1	-976.872415	0.548202	none
TS_1-2	-976.865255	0.547719	-97.55
IM2	-976.891067	0.553047	none
TS_2-3	-976.88933	0.55549	-114.25
IM3	-976.903642	0.554584	none
TS_3-4c	-976.893917	0.556114	-173.11
IM4c	-976.912583	0.555223	none
TS_4c-5c	-976.908266	0.556038	-314.35
IM5c	-976.913934	0.555554	none
TS_5c-6c'	-976.920234	0.565382	-118.95
IM6c'	-976.925806	0.565378	none

	path c		
	Total Energy	Thermal correction to Gibbs Free Energy	Imaginary Freq
IM1	-976.872415	0.548202	none
TS_1-2	-976.865255	0.547719	-97.55
IM2	-976.891067	0.553047	none
TS_2-3	-976.88933	0.55549	-114.25
IM3	-976.903642	0.554584	none
TS_3-4c	-976.893917	0.556114	-173.11
IM4c	-976.912583	0.555223	none
TS_4c-5c	-976.908266	0.556038	-314.35
IM5c	-976.913934	0.555554	none
TS_5c-6c	-976.907925	0.557034	-421.11
IM6c	-976.939673	0.560111	none
TS_6c-7c	-976.935818	0.563824	-104.81
IM7c	-976.937609	0.564837	none

Table S11. Cartesian coordinates.

IM1				**TS_1-2**				**IM2**			
C	-4.5562	-0.09833	-0.33201	C	-4.43646	0.076872	-0.42484	C	-3.37883	0.057515	-0.57958
C	-4.66101	-1.39175	0.42353	C	-4.61108	-1.25072	0.258033	C	-4.27852	-0.97171	0.208078
C	-3.46729	-2.37335	0.079995	C	-3.46808	-2.24148	-0.09125	C	-3.45319	-2.25805	0.146859
C	-2.25524	-1.60768	0.388992	C	-2.15502	-1.62096	0.30258	C	-2.00931	-1.82329	0.431777
C	-0.4475	-2.14615	-1.096	C	-0.70603	-2.54436	-0.61745	C	-1.01681	-2.89633	-0.08337
C	0.762223	-2.24245	-0.22546	C	0.606778	-2.55481	0.047744	C	0.430773	-2.70744	0.286484
C	-0.2436	1.078403	-1.53182	C	-0.34899	1.346501	-1.34396	C	-0.63223	1.664327	-0.90564
C	-0.80062	0.332756	-0.31034	C	-0.53098	0.288024	-0.24294	C	-0.80631	0.468093	0.037662
C	-1.49745	-0.97766	-0.67331	C	-1.50087	-0.79634	-0.60831	C	-1.88205	-0.5142	-0.39722
C	0.713933	2.147421	-1.05754	C	0.689927	2.33321	-0.86128	C	0.568224	2.481329	-0.49573
C	2.026045	1.918327	-1.15869	C	1.971337	2.108631	-1.16342	C	1.738991	2.244179	-1.09204
C	4.087533	-0.02895	0.172282	C	3.952434	-0.09728	-0.11144	C	3.679779	-0.16005	-0.48855
C	4.388583	-1.50549	0.266989	C	4.244928	-1.5812	-0.12095	C	3.945244	-1.64326	-0.58789
C	3.140602	-2.40266	0.399331	C	3.064273	-2.50695	0.23355	C	2.880484	-2.56179	0.038138
C	2.044448	-2.15688	-0.61688	C	1.787283	-2.29664	-0.54922	C	1.473914	-2.4772	-0.5238
C	3.643897	0.759663	1.155933	C	3.664012	0.652535	0.957851	C	3.801421	0.59015	0.6127
C	3.32758	2.227893	0.953918	C	3.410308	2.144119	0.883578	C	3.573345	2.085568	0.641229
C	3.134715	2.693251	-0.49989	C	3.16951	2.74564	-0.51191	C	3.085029	2.755398	-0.6525
C	0.09399	3.337478	-0.37534	C	0.197049	3.41508	0.061492	C	0.369039	3.417935	0.665945
C	2.50027	-1.95547	-2.03484	C	1.936064	-1.89686	-1.98765	C	1.364275	-2.23423	-2.00431
C	3.421651	0.270127	2.563077	C	3.5901	0.088831	2.35389	C	4.204802	0.023111	1.950076
C	-4.3612	1.128403	0.16979	C	-4.15983	1.259752	0.141033	C	-3.63764	1.398865	-0.101
C	-4.22374	2.314458	-0.74699	C	-4.01192	2.501985	-0.69673	C	-4.29202	2.376553	-0.98899
C	-4.27079	1.470584	1.634052	C	-4.00407	1.499452	1.619666	C	-3.36763	1.811517	1.28474

C	-1.88498	-1.40303	1.794819
H	2.31945	1.010911	-1.68296
H	-2.14398	-0.86731	-1.55096
H	-4.63176	-0.19508	-1.41567
H	-5.56602	-1.93936	0.144083
H	-4.69175	-1.24289	1.504774
H	-3.56036	-3.26453	0.706222
H	-3.51715	-2.63638	-0.97962
H	-0.98588	-3.09933	-1.1519
H	-0.19042	-1.87773	-2.12144
H	0.588969	-2.4829	0.823232
H	0.296237	0.375533	-2.17727
H	0.033623	0.133428	0.372023
H	-1.51936	0.976014	0.212721
H	4.95652	-1.80859	-0.618
H	5.038086	-1.71885	1.123087
H	3.463216	-3.44861	0.302776
H	2.717596	-2.29663	1.40381
H	4.245939	0.420749	-0.80533
H	4.110118	2.827324	1.438743
H	2.400774	2.449021	1.503246
H	2.919157	3.765761	-0.49455
H	4.06651	2.572992	-1.06138
H	-0.62433	3.827773	-1.04275
H	0.836177	4.079673	-0.07825
H	-0.45602	3.045135	0.528361
H	1.688744	-1.80245	-2.74718

C	-1.81187	-1.58565	1.76119
H	2.171545	1.306223	-1.87229
H	-1.94142	-0.7389	-1.60331
H	-4.54507	0.052357	-1.51053
H	-5.54494	-1.71925	-0.06893
H	-4.6823	-1.14474	1.343166
H	-3.62396	-3.19081	0.43064
H	-3.47928	-2.43528	-1.16976
H	-1.32544	-3.3972	-0.329
H	-0.70488	-2.52532	-1.70577
H	0.617208	-2.87347	1.087317
H	-0.00746	0.855981	-2.26318
H	0.454364	-0.13493	-0.00257
H	-0.89025	0.763381	0.678733
H	4.624487	-1.85559	-1.11004
H	5.055339	-1.81493	0.579178
H	3.387195	-3.54244	0.056398
H	2.8349	-2.43576	1.301369
H	4.024598	0.397933	-1.07699
H	4.250667	2.657915	1.369951
H	2.530661	2.364766	1.505921
H	3.030384	3.825528	-0.40201
H	4.057534	2.615125	-1.13781
H	-0.50869	4.066411	-0.46705
H	1.005756	4.039418	0.444003
H	-0.339	3.001392	0.925192
H	0.991572	-1.82499	-2.52893

C	-1.80414	-1.61423	1.936106
H	1.726666	1.553115	-1.93404
H	-1.63502	-0.80668	-1.42625
H	-3.64156	0.002813	-1.63862
H	-5.26069	-1.04929	-0.26249
H	-4.42486	-0.65485	1.244257
H	-3.81943	-3.00586	0.856379
H	-3.52214	-2.68937	-0.85925
H	-1.34416	-3.85341	0.346126
H	-1.14268	-2.99408	-1.16684
H	0.656724	-2.86924	1.340924
H	-0.50615	1.294229	-1.93026
H	0.141346	-0.086	0.052214
H	-0.95994	0.810326	1.067372
H	4.072413	-1.90846	-1.64246
H	4.901424	-1.88351	-0.10925
H	3.223272	-3.59647	-0.10443
H	2.839853	-2.39793	1.120386
H	3.405783	0.331305	-1.41868
H	4.510452	2.563685	0.957594
H	2.853263	2.301366	1.444449
H	3.046117	3.837264	-0.48353
H	3.819814	2.596399	-1.44734
H	-0.45577	4.112427	0.459557
H	1.257085	4.016914	0.873911
H	0.119505	2.876758	1.588307
H	0.342372	-2.31267	-2.37861

H	3.068556	-2.83416	-2.36142
H	3.179258	-1.10121	-2.10422
H	3.886645	-0.69939	2.75258
H	3.825501	0.986355	3.286221
H	2.3481	0.181958	2.775353
H	-1.07537	1.496501	-2.11491
H	-4.28975	2.02936	-1.79881
H	-3.26131	2.814867	-0.5809
H	-5.00228	3.055917	-0.54001
H	-4.40596	0.619589	2.304382
H	-3.30703	1.946037	1.857213
H	-5.03826	2.209332	1.887028
H	-2.28604	-0.401	2.03518
H	-0.80434	-1.31165	1.928892
H	-2.327	-2.12982	2.476028

H	2.574217	-2.61692	-2.51149
H	2.435997	-0.92572	-2.05038
H	4.08026	-0.88294	2.442585
H	4.062585	0.770848	3.067893
H	2.545486	-0.02397	2.67186
H	-1.30954	1.830547	-1.55976
H	-4.03755	2.282802	-1.76646
H	-3.07085	3.015607	-0.46459
H	-4.81608	3.211148	-0.4727
H	-4.25857	0.637722	2.238602
H	-2.97633	1.807565	1.852484
H	-4.6477	2.328336	1.931479
H	-2.48858	-0.86285	2.231819
H	-0.79031	-1.25295	1.945508
H	-1.97957	-2.55649	2.233815

H	1.983579	-2.94546	-2.56198
H	1.738145	-1.23235	-2.24888
H	4.596613	-0.9928	1.87806
H	4.972734	0.648883	2.416839
H	3.350199	0.007617	2.63734
H	-1.53831	2.297671	-0.91312
H	-3.93947	2.289156	-2.01938
H	-4.23459	3.40328	-0.62612
H	-5.3562	2.080867	-1.00396
H	-3.06025	1.001655	1.941777
H	-2.56289	2.563611	1.236105
H	-4.23708	2.345073	1.688121
H	-2.56915	-0.97221	2.385493
H	-0.8258	-1.18112	2.155857
H	-1.86108	-2.57933	2.449252

TS_2-3

C	-3.09249	0.275931	-0.63978
C	-4.21408	-0.50323	0.116503
C	-3.66538	-1.93204	0.160873
C	-2.18499	-1.76761	0.54676
C	-1.3462	-2.99778	0.125258
C	0.13363	-2.8714	0.385208
C	-0.49727	1.578053	-0.59786
C	-0.65306	0.339162	0.259316
C	-1.76212	-0.53203	-0.29004

IM3

C	3.74771	-0.40974	-0.69827
C	4.60116	0.832064	-0.33483
C	3.627829	2.017637	-0.35099
C	2.302917	1.442912	0.185638
C	1.113726	2.342866	-0.19794
C	-0.21939	1.987034	0.413213
C	-0.09514	-0.79499	-0.77625
C	1.211912	-0.91015	-0.10162
C	2.267336	0.092665	-0.57346

TS_3-4b

C	3.433657	-0.53038	-0.70136
C	4.541651	0.506957	-0.37583
C	3.838143	1.876294	-0.33509
C	2.457448	1.564752	0.262638
C	1.382245	2.616817	-0.04255
C	-0.00322	2.195433	0.437995
C	-0.04466	-1.02073	-0.82023
C	0.882679	-0.4343	0.013847
C	2.104831	0.274527	-0.51325

C	0.666301	2.429447	-0.21823	C	-1.23702	-1.53633	-0.47028	C	-1.19624	-1.77628	-0.40188
C	1.737967	2.351478	-1.01961	C	-2.23657	-1.45205	-1.42288	C	-2.17589	-1.91862	-1.3269
C	3.36904	-0.29495	-0.59767	C	-4.07208	0.370642	-0.26791	C	-3.86082	0.421901	-0.44813
C	3.560818	-1.78442	-0.77472	C	-4.01269	1.787015	0.230466	C	-3.77812	1.906605	-0.20647
C	2.563394	-2.70946	-0.04999	C	-2.64715	2.151521	0.833348	C	-2.48671	2.356721	0.499543
C	1.115972	-2.66491	-0.50453	C	-1.44818	2.182981	-0.10124	C	-1.18844	2.282488	-0.26102
C	3.802532	0.432201	0.440585	C	-4.44138	-0.71653	0.421086	C	-4.26298	-0.49679	0.438025
C	3.707552	1.94086	0.540894	C	-4.36315	-2.10706	-0.1713	C	-4.31078	-1.97704	0.127281
C	3.147761	2.729604	-0.65594	C	-3.51843	-2.20779	-1.45827	C	-3.56388	-2.45551	-1.13132
C	0.64178	3.093174	1.131265	C	-1.33818	-2.39343	0.761	C	-1.30575	-2.23256	1.027858
C	0.901964	-2.47356	-1.98224	C	-1.70776	2.637577	-1.51118	C	-1.24424	2.304056	-1.75016
C	4.487666	-0.17937	1.637243	C	-4.97271	-0.68983	1.828945	C	-4.74069	-0.16834	1.829218
C	-3.09416	1.72816	-0.33719	C	4.155998	-1.71015	0.021905	C	3.561365	-1.89851	-0.00411
C	-3.5527	2.665768	-1.40167	C	5.595675	-2.07132	-0.35818	C	4.81903	-2.60824	-0.51458
C	-3.20445	2.201214	1.072697	C	4.011874	-1.70776	1.544816	C	3.573065	-1.88479	1.526308
C	-2.05331	-1.54265	2.057296	C	2.402524	1.311938	1.711398	C	2.58331	1.38281	1.78184
H	1.598579	1.872023	-1.98789	H	-2.02894	-0.80762	-2.27738	H	-1.94683	-1.56925	-2.33446
H	-1.41412	-0.90293	-1.2622	H	1.982463	0.365153	-1.60004	H	1.831645	0.621236	-1.52231
H	-3.26866	0.165984	-1.71382	H	3.906382	-0.62322	-1.76246	H	3.489842	-0.7609	-1.77194
H	-5.17352	-0.41443	-0.39861	H	5.432486	0.971115	-1.02911	H	5.349246	0.483926	-1.11041
H	-4.34186	-0.12104	1.132182	H	5.043206	0.718403	0.660207	H	4.998396	0.291897	0.595441
H	-4.21972	-2.5659	0.858787	H	3.976624	2.870565	0.239193	H	4.389951	2.623848	0.242257
H	-3.74251	-2.38702	-0.8344	H	3.478352	2.369279	-1.38026	H	3.715832	2.267228	-1.35325
H	-1.72609	-3.86661	0.678337	H	1.354203	3.361646	0.141893	H	1.618639	3.556058	0.472637
H	-1.54186	-3.19825	-0.93343	H	1.053745	2.401853	-1.29092	H	1.377406	2.83692	-1.11437
H	0.434554	-2.99991	1.425473	H	-0.18503	1.713754	1.46888	H	-0.11509	2.176139	1.52403
H	-0.47398	1.313492	-1.66211	H	-0.13174	-0.17407	-1.67277	H	0.025069	-0.79142	-1.88628

H	0.291008	-0.22014	0.230225	H	1.072158	-0.91633	0.985784	H	0.042695	0.765925	0.123194
H	-0.81485	0.618814	1.305922	H	1.532526	-1.94512	-0.33296	H	0.878465	-0.73795	1.059852
H	3.544354	-2.0117	-1.84562	H	-4.24973	2.470605	-0.59106	H	-3.886	2.441674	-1.15517
H	4.563335	-2.06411	-0.43561	H	-4.7775	1.958165	0.992574	H	-4.61439	2.239839	0.413706
H	2.917266	-3.73847	-0.20505	H	-2.73658	3.162587	1.254999	H	-2.58654	3.422721	0.759182
H	2.607451	-2.52543	1.029134	H	-2.43461	1.484193	1.676972	H	-2.3753	1.8309	1.455758
H	2.895151	0.222676	-1.42888	H	-3.77567	0.245532	-1.31012	H	-3.56955	0.085807	-1.44161
H	4.717967	2.319212	0.745479	H	-5.37059	-2.47899	-0.39343	H	-5.36215	-2.27542	0.025352
H	3.130312	2.185463	1.442535	H	-3.96803	-2.78649	0.589554	H	-3.95323	-2.51694	1.009723
H	3.200801	3.797409	-0.41052	H	-3.27016	-3.26574	-1.63488	H	-3.51849	-3.55327	-1.1089
H	3.795153	2.577715	-1.52403	H	-4.0967	-1.87649	-2.32307	H	-4.14905	-2.20402	-2.0202
H	-0.29308	3.648249	1.269291	H	-0.35592	-2.61783	1.177108	H	-0.32236	-2.47763	1.436305
H	1.462881	3.803283	1.242072	H	-1.83203	-3.34216	0.541465	H	-1.92229	-3.12832	1.106781
H	0.713384	2.366701	1.948919	H	-1.92281	-1.8713	1.526552	H	-1.75287	-1.45099	1.655457
H	-0.12666	-2.65684	-2.29626	H	-0.79812	2.72596	-2.1056	H	-0.2619	2.308289	-2.22081
H	1.551098	-3.14266	-2.55722	H	-2.20195	3.61626	-1.51235	H	-1.80811	3.17677	-2.09799
H	1.170936	-1.44971	-2.27612	H	-2.38999	1.951834	-2.02979	H	-1.80098	1.421576	-2.09277
H	4.577996	-1.26377	1.571125	H	-5.0487	0.317644	2.236665	H	-4.80381	0.902555	2.024476
H	5.49304	0.238532	1.758772	H	-5.96749	-1.14751	1.865803	H	-5.73242	-0.6011	1.998801
H	3.937297	0.057124	2.555133	H	-4.3334	-1.27965	2.495897	H	-4.07604	-0.61159	2.580001
H	-1.49781	2.14839	-0.48144	H	3.516003	-2.51501	-0.37194	H	2.690351	-2.49141	-0.32226
H	-3.1537	2.400682	-2.38235	H	5.722762	-2.11968	-1.44358	H	4.818286	-2.69266	-1.60512
H	-3.34911	3.711216	-1.16761	H	5.876547	-3.04118	0.06044	H	4.896458	-3.61513	-0.09635
H	-4.6457	2.537134	-1.45436	H	6.298323	-1.3271	0.030762	H	5.719349	-2.05804	-0.22
H	-2.71329	1.538853	1.78692	H	2.99732	-1.47508	1.88137	H	2.679636	-1.42969	1.963
H	-2.85676	3.228635	1.188447	H	4.274447	-2.69199	1.942673	H	3.634351	-2.91039	1.900707
H	-4.27999	2.197931	1.306261	H	4.690598	-0.9851	2.008857	H	4.445429	-1.35155	1.918718

H	-2.63469	-0.68362	2.410144
H	-1.01337	-1.38287	2.352574
H	-2.41829	-2.42387	2.593144

H	3.349724	0.868113	2.020599
H	1.603299	0.709938	2.15472
H	2.341536	2.306649	2.165422

H	3.418792	0.73446	2.046878
H	1.68485	0.959725	2.242713
H	2.762627	2.356506	2.249153

IM4b

C	3.654513	-0.21237	-0.68274
C	4.487593	0.991411	-0.17778
C	3.513137	2.17517	-0.13414
C	2.17279	1.554637	0.298148
C	1.00344	2.484691	-0.06081
C	-0.36958	1.987006	0.43592
C	0.093738	-1.10345	-0.95436
C	1.140879	-0.76787	-0.1782
C	2.160326	0.25715	-0.57103
C	-1.02598	-1.96288	-0.5577
C	-2.14796	-1.91737	-1.29691
C	-4.10696	0.317752	-0.42961
C	-4.14584	1.819045	-0.2642
C	-2.8605	2.362872	0.387377
C	-1.57953	2.164573	-0.32228
C	-4.20963	-0.57025	0.56609
C	-4.09144	-2.06282	0.358114
C	-3.47753	-2.54742	-0.96678
C	-0.88463	-2.7709	0.705111
C	-1.59048	2.033744	-1.78747
C	-4.45598	-0.18189	2.001135

TS_3-4c

C	3.688693	-0.34722	-0.75963
C	4.564056	0.794154	-0.19315
C	3.619021	1.989745	-0.08265
C	2.279904	1.389127	0.384532
C	1.136878	2.37899	0.111924
C	-0.2465	1.905406	0.474984
C	-0.14933	-0.87107	-0.67474
C	1.205072	-0.96902	-0.06558
C	2.201564	0.117553	-0.51088
C	-1.31825	-1.3835	-0.18356
C	-2.39625	-1.45662	-1.11612
C	-3.97045	0.021198	-0.75022
C	-3.72591	1.505633	-0.64108
C	-2.72815	1.925464	0.467781
C	-1.38284	2.38656	-0.04203
C	-4.45966	-0.76904	0.255972
C	-4.44385	-2.25982	0.044865
C	-3.44715	-2.55272	-1.08505
C	-1.4848	-1.93487	1.203183
C	-1.40198	3.480342	-1.08409
C	-4.96651	-0.25186	1.56167

IM4c

C	3.787	-0.29898	-0.63143
C	4.515916	0.762382	0.225191
C	3.543116	1.935241	0.315664
C	2.136784	1.304748	0.377332
C	1.11216	2.406746	-0.00044
C	-0.31306	2.241118	0.442187
C	-0.1351	-0.55525	-0.97245
C	1.263769	-0.97894	-0.64853
C	2.283433	0.1656	-0.67474
C	-1.2817	-1.04622	-0.48194
C	-2.58515	-0.55378	-1.05996
C	-3.55793	-0.00163	0.040291
C	-3.09325	1.013878	1.078187
C	-2.77186	2.3967	0.488203
C	-1.43543	2.49967	-0.23619
C	-4.34654	-1.14791	0.459061
C	-4.32433	-2.2027	-0.56677
C	-3.45129	-1.66344	-1.7098
C	-1.35724	-2.1072	0.581949
C	-1.49416	2.977916	-1.66217
C	-5.09405	-1.25321	1.717986

C	4.02903	-1.57816	-0.07022	C	4.124586	-1.75733	-0.31539	C	4.121003	-1.75604	-0.23493
C	5.433262	-1.97069	-0.53972	C	5.548715	-2.03036	-0.81232	C	5.596605	-2.03115	-0.54645
C	3.964385	-1.67788	1.456277	C	4.050012	-2.03589	1.18842	C	3.843771	-2.15243	1.219769
C	2.179362	1.293519	1.808962	C	2.36937	1.073175	1.883179	C	1.864126	0.76732	1.78458
H	-2.10725	-1.33175	-2.21675	H	-2.15678	-1.05058	-2.09772	H	-2.37151	0.239115	-1.77917
H	1.877749	0.597303	-1.57866	H	1.845373	0.47702	-1.48717	H	4.155055	-0.20626	-1.66073
H	3.843921	-0.32928	-1.75611	H	3.820594	-0.34623	-1.8487	H	5.476681	1.051961	-0.20673
H	5.347631	1.194484	-0.81936	H	5.426607	1.001891	-0.83028	H	4.727902	0.374144	1.226574
H	4.884817	0.797623	0.823628	H	4.957328	0.531771	0.794735	H	3.73274	2.594365	1.169558
H	3.836436	2.977387	0.536988	H	3.980487	2.770715	0.593422	H	3.610621	2.549432	-0.59221
H	3.403714	2.607319	-1.1375	H	3.480955	2.446953	-1.07121	H	1.467978	3.330087	0.482216
H	1.165751	3.465782	0.400912	H	1.354326	3.303139	0.669666	H	1.17737	2.595378	-1.07766
H	0.994605	2.64425	-1.14331	H	1.164588	2.655165	-0.94976	H	-0.42855	1.958645	1.490631
H	-0.52651	2.153226	1.504142	H	-0.32948	1.153093	1.260928	H	-3.58729	2.695667	-0.18269
H	0.013067	-0.64479	-1.94336	H	-0.17813	-0.44121	-1.67761	H	-2.78676	3.11715	1.312676
H	-0.37679	0.852388	0.298639	H	1.142652	-1.04742	1.022028	H	-4.37859	0.461411	-0.57439
H	1.240008	-1.23959	0.797615	H	1.576039	-1.95062	-0.40477	H	-5.34073	-2.52674	-0.82641
H	-4.3144	2.303096	-1.2302	H	-3.38145	1.874439	-1.61077	H	-3.87789	-3.0779	-0.06308
H	-4.97892	2.129224	0.373001	H	-4.69832	1.987133	-0.47784	H	-2.84268	-2.44161	-2.17206
H	-2.90313	3.469439	0.459585	H	-3.17103	2.756228	1.032323	H	-4.0899	-1.23314	-2.4869
H	-2.75933	2.016335	1.421655	H	-2.58485	1.106966	1.183469	H	-0.40608	-2.23974	1.097952
H	-3.96962	-0.05261	-1.44267	H	-4.10251	-0.35844	-1.76289	H	-1.64271	-3.08475	0.171523
H	-5.08882	-2.50732	0.47346	H	-5.44898	-2.6482	-0.15703	H	-2.10071	-1.85414	1.355786
H	-3.50601	-2.45924	1.196097	H	-4.119	-2.73484	0.976175	H	-0.53561	2.899302	-2.17682
H	-3.37463	-3.63772	-0.90835	H	-2.95373	-3.52089	-0.94904	H	-1.80535	4.028441	-1.70151
H	-4.17662	-2.35794	-1.78657	H	-3.95195	-2.58336	-2.05357	H	-2.2392	2.417734	-2.2414
H	0.095127	-3.25662	0.735734	H	-0.56577	-1.87389	1.784146	H	-5.71558	-0.35911	1.855695

H	-1.64531	-3.54984	0.772471
H	-0.9623	-2.13979	1.599468
H	-0.60894	2.088898	-2.25185
H	-2.28529	2.745882	-2.24266
H	-2.02237	1.035091	-1.96976
H	-4.7582	0.859916	2.125862
H	-5.24373	-0.8094	2.42988
H	-3.55817	-0.35706	2.606484
H	3.319466	-2.30995	-0.48223
H	5.506686	-1.96803	-1.63099
H	5.699651	-2.96957	-0.18456
H	6.181001	-1.27121	-0.14968
H	2.980541	-1.43601	1.866362
H	4.204486	-2.69859	1.766876
H	4.697677	-1.02082	1.935881
H	3.084318	0.771159	2.122669
H	1.326721	0.688056	2.13587
H	2.144425	2.244503	2.352089
H	-1.80223	-2.98302	1.187298
H	-2.25519	-1.36372	1.734873
H	-0.58531	4.190041	-0.93785
H	-2.33984	4.042245	-1.04753
H	-1.30445	3.078435	-2.10009
H	-5.00498	0.836346	1.604125
H	-5.98052	-0.64447	1.709288
H	-4.37389	-0.62277	2.405041
H	3.471685	-2.48206	-0.82432
H	5.636316	-1.86359	-1.89004
H	5.840727	-3.06297	-0.6033
H	6.268014	-1.37495	-0.31033
H	3.049544	-1.89255	1.60463
H	4.344347	-3.07007	1.388367
H	4.739215	-1.3952	1.747856
H	3.182602	0.377514	2.10353
H	1.450492	0.638472	2.288354
H	2.559042	1.99529	2.441301
H	-5.70138	-2.15509	1.780422
H	-4.37298	-1.22705	2.547751
H	3.526428	-2.41917	-0.87805
H	5.832499	-1.81374	-1.5922
H	5.848849	-3.0771	-0.35152
H	6.246782	-1.41204	0.081114
H	2.804619	-2.00475	1.523542
H	4.07885	-3.21135	1.361366
H	4.475852	-1.59184	1.916047
H	2.678529	0.128883	2.134431
H	0.939052	0.179199	1.821129
H	1.762493	1.593422	2.497373
H	-2.20709	0.607205	1.581191
H	-3.87378	1.127989	1.8391
H	1.562785	-1.70357	-1.41955
H	1.301694	-1.52226	0.297667
H	2.1529	0.658307	-1.64958
H	-0.21494	0.218937	-1.73868

TS_4c-5c

C	3.815154	-0.26127	-0.6129
C	4.511058	0.777061	0.296989
C	3.524938	1.936959	0.400104
C	2.12358	1.291852	0.409974
C	1.102571	2.40015	0.037869
C	-0.3368	2.206589	0.419964

IM5c

C	3.793246	-0.17876	-0.54835
C	4.430542	0.699653	0.548645
C	3.471015	1.872084	0.707571
C	2.057736	1.27047	0.561738
C	1.097924	2.440533	0.221148
C	-0.37405	2.241987	0.432837

TS_5c-6c

C	3.551309	-0.08425	-0.56478
C	4.342494	0.188318	0.71775
C	3.625829	1.412344	1.272658
C	2.119208	1.091135	1.106155
C	1.338691	2.400637	0.849804
C	-0.13536	2.182938	0.718594

C	-0.1037	-0.56901	-0.96883	C	-0.12311	-0.52172	-0.9665	C	-0.22192	-1.0356	-0.23188
C	1.30731	-0.9834	-0.68779	C	1.290369	-0.93176	-0.69264	C	1.244114	-1.18106	0.050484
C	2.304826	0.181899	-0.66894	C	2.272368	0.246053	-0.59753	C	2.055693	0.125539	-0.14499
C	-1.22951	-1.08127	-0.45785	C	-1.23493	-1.04577	-0.43883	C	-1.27537	-1.34593	0.539611
C	-2.55917	-0.57345	-0.98889	C	-2.59468	-0.55537	-1.00864	C	-2.67638	-1.27015	0.008352
C	-3.44838	-0.10455	0.171264	C	-3.39941	-0.0966	0.140373	C	-3.31107	-0.23827	-0.74731
C	-3.07078	1.027354	1.091196	C	-3.17058	1.131001	0.907586	C	-2.68912	0.961959	-1.36737
C	-2.80913	2.357036	0.360229	C	-2.82697	2.381012	0.062015	C	-2.3775	2.041437	-0.26976
C	-1.43446	2.497918	-0.2844	C	-1.38328	2.515352	-0.39902	C	-0.92798	2.463653	-0.32046
C	-4.41595	-1.09986	0.455404	C	-4.51943	-1.00904	0.396616	C	-4.79289	-0.47651	-0.8163
C	-4.36296	-2.19216	-0.56551	C	-4.30311	-2.23087	-0.50898	C	-4.97375	-1.92695	-0.34071
C	-3.42982	-1.66273	-1.66749	C	-3.43311	-1.68642	-1.652	C	-3.77025	-2.17742	0.574952
C	-1.281	-2.18518	0.566876	C	-1.27034	-2.14713	0.591333	C	-1.1898	-1.86749	1.953371
C	-1.44512	3.056618	-1.68155	C	-1.23352	3.047188	-1.79889	C	-0.51487	3.175862	-1.58024
C	-5.35434	-1.13043	1.604391	C	-4.99621	-1.25527	1.825532	C	-5.433	0.55429	0.141605
C	4.160036	-1.72716	-0.25987	C	4.154633	-1.67632	-0.43364	C	3.934826	-1.35665	-1.34124
C	5.63894	-1.98173	-0.57265	C	5.630772	-1.87262	-0.79798	C	5.174372	-1.09675	-2.20301
C	3.879627	-2.16773	1.181551	C	3.89607	-2.32277	0.933031	C	4.192212	-2.57227	-0.44364
C	1.822451	0.715027	1.795897	C	1.642258	0.585054	1.866889	C	1.630217	0.445462	2.408701
H	-2.36276	0.258155	-1.66985	H	-2.36049	0.278814	-1.67791	H	-2.68768	-1.51576	-1.18434
H	4.202311	-0.12618	-1.63027	H	4.215962	0.141187	-1.50868	H	1.557563	0.663436	-0.96468
H	5.48009	1.08979	-0.0987	H	5.441319	1.019769	0.285379	H	3.770548	0.760832	-1.23354
H	4.699007	0.357595	1.290443	H	4.508079	0.150831	1.49231	H	5.407574	0.357746	0.53656
H	3.688013	2.571128	1.278204	H	3.588649	2.409602	1.654509	H	4.25615	-0.65425	1.415174
H	3.607754	2.579801	-0.48647	H	3.63024	2.596874	-0.102	H	3.874947	1.638867	2.313787
H	1.432786	3.305991	0.569281	H	1.384908	3.272094	0.882649	H	3.893115	2.291826	0.673893
H	1.206868	2.628852	-1.02812	H	1.312958	2.784015	-0.79544	H	1.535101	3.080735	1.690229

H	-0.48022	1.859881	1.444485	H	-0.62559	1.892441	1.436276	H	1.749344	2.881018	-0.0438
H	-3.58928	2.504266	-0.398	H	-3.49721	2.406581	-0.8055	H	-0.60661	1.69714	1.573877
H	-2.95029	3.166591	1.084584	H	-3.10208	3.251143	0.668039	H	-0.41933	-0.69674	-1.25056
H	-4.52774	0.135224	-0.34893	H	-5.27306	-0.35371	-0.11956	H	1.427409	-1.63098	1.027435
H	-5.35541	-2.50286	-0.90155	H	-5.25095	-2.64582	-0.85502	H	1.594127	-1.90887	-0.69152
H	-3.92784	-3.05021	-0.03215	H	-3.79177	-3.01187	0.060448	H	-1.7574	0.693413	-1.86688
H	-2.81996	-2.44904	-2.11332	H	-2.79324	-2.44339	-2.10808	H	-3.36658	1.354989	-2.12869
H	-4.02968	-1.21442	-2.46555	H	-4.06522	-1.26531	-2.43986	H	-3.04353	2.893687	-0.44432
H	-0.30644	-2.36081	1.022435	H	-0.30117	-2.26195	1.077305	H	-2.61132	1.649471	0.725942
H	-1.60398	-3.13503	0.122359	H	-1.52383	-3.11315	0.140486	H	-5.17446	-0.29845	-1.82612
H	-1.97664	-1.95559	1.386991	H	-2.00595	-1.9558	1.383492	H	-4.93477	-2.60621	-1.19873
H	-0.45015	3.125691	-2.12094	H	-0.19328	3.139057	-2.1097	H	-5.92994	-2.08047	0.161307
H	-1.88153	4.062237	-1.68796	H	-1.69782	4.035895	-1.88856	H	-3.96322	-1.85573	1.604511
H	-2.06987	2.446563	-2.34734	H	-1.74737	2.399351	-2.52205	H	-3.45971	-3.22255	0.609662
H	-5.4816	-0.16257	2.088108	H	-5.21535	-0.3338	2.367481	H	-0.15472	-1.97357	2.272007
H	-6.32201	-1.5446	1.316428	H	-5.90709	-1.85506	1.798999	H	-1.66409	-2.84829	2.050442
H	-4.91053	-1.8161	2.339326	H	-4.23856	-1.817	2.378248	H	-1.68821	-1.18957	2.656244
H	3.573277	-2.37549	-0.92467	H	3.565456	-2.22285	-1.18195	H	-1.04243	4.132905	-1.66186
H	5.874979	-1.74326	-1.61376	H	5.850932	-1.49046	-1.7989	H	-0.77002	2.600044	-2.47826
H	5.901187	-3.02851	-0.39599	H	5.901514	-2.93174	-0.77221	H	0.554504	3.380839	-1.61542
H	6.281578	-1.36763	0.067497	H	6.278298	-1.34896	-0.08641	H	-5.22787	1.581479	-0.16897
H	2.843044	-2.01636	1.492351	H	2.888163	-2.14601	1.317725	H	-6.51442	0.406425	0.134755
H	4.101211	-3.23371	1.287637	H	4.037209	-3.40504	0.862381	H	-5.07554	0.42203	1.16722
H	4.520052	-1.63917	1.894919	H	4.60371	-1.95832	1.683944	H	3.110637	-1.59391	-2.03047
H	2.639825	0.083841	2.152305	H	2.384899	-0.15174	2.185627	H	4.997015	-0.29868	-2.92944
H	0.909344	0.107422	1.793941	H	0.681696	0.065159	1.766176	H	5.463796	-1.99704	-2.75206
H	1.686816	1.521127	2.525839	H	1.541114	1.321724	2.671863	H	6.024992	-0.80259	-1.57918

H	-2.16551	0.694091	1.613282
H	-3.8429	1.161178	1.85354
H	1.611063	-1.6611	-1.49811
H	1.368045	-1.57141	0.229608
H	2.179717	0.696672	-1.63301
H	-0.20878	0.226599	-1.70913

H	-2.319	0.877692	1.565149
H	-4.01784	1.314951	1.57279
H	1.603573	-1.55652	-1.53992
H	1.350728	-1.57112	0.188856
H	2.14477	0.817323	-1.52867
H	-0.23241	0.265252	-1.71355

H	3.393832	-2.75287	0.281733
H	4.30729	-3.47587	-1.04878
H	5.120594	-2.43625	0.120325
H	2.263252	-0.39852	2.702481
H	0.601451	0.084425	2.338693
H	1.670285	1.180135	3.219277

IM6c

C	3.525325	-0.05126	-0.58911
C	4.336529	0.197261	0.687348
C	3.639464	1.418603	1.277285
C	2.132226	1.098201	1.149595
C	1.303491	2.394582	1.027034
C	-0.15791	2.125675	0.819357
C	-0.31239	-0.73709	-0.18688
C	1.133083	-1.00981	-0.06501
C	2.04217	0.243212	-0.17104
C	-1.3333	-1.28922	0.575662
C	-2.65366	-1.17299	0.115677
C	-3.24779	-0.41659	-1.04947
C	-2.71267	0.957572	-1.48658
C	-2.33808	1.933136	-0.33993
C	-0.87093	2.30636	-0.30369
C	-4.78178	-0.45363	-0.78461
C	-4.97118	-1.82874	-0.13581
C	-3.74558	-1.95493	0.773439

TS_6c-7c

C	3.527831	-0.18339	-0.9132
C	4.541001	0.632143	-0.07025
C	3.730857	1.800652	0.503815
C	2.370009	1.168638	0.840878
C	1.250391	2.208036	0.991601
C	-0.16291	1.673161	0.879346
C	-0.40625	-0.20068	-0.22954
C	1.016533	-0.71839	-0.23133
C	2.122222	0.314466	-0.42408
C	-1.39842	-0.94916	0.528816
C	-2.67318	-1.09654	0.07636
C	-3.38707	-0.37119	-1.05357
C	-3.03674	1.108627	-1.29636
C	-2.51611	1.873397	-0.05292
C	-1.0318	2.104523	-0.101
C	-4.88907	-0.61578	-0.73809
C	-4.87552	-2.05588	-0.21387
C	-3.63704	-2.08828	0.691898

IM7c

C	3.551023	-0.16603	-0.93871
C	4.551515	0.683366	-0.10734
C	3.716357	1.812597	0.522157
C	2.373881	1.132419	0.837355
C	1.19837	2.097483	0.996414
C	-0.1981	1.469321	0.822905
C	-0.38845	0.027938	-0.13684
C	0.997749	-0.64497	-0.33314
C	2.149773	0.333169	-0.46184
C	-1.39558	-0.87385	0.534155
C	-2.63897	-1.08011	0.064706
C	-3.38587	-0.36233	-1.0565
C	-3.10701	1.138097	-1.27699
C	-2.58069	1.892996	-0.02227
C	-1.10494	2.083825	-0.08597
C	-4.87478	-0.66444	-0.73587
C	-4.80571	-2.11791	-0.25658
C	-3.56778	-2.13327	0.651302

C	-1.06191	-2.14756	1.791524	C	-0.94922	-1.69241	1.767626	C	-0.91748	-1.63126	1.752875
C	-0.32751	2.910098	-1.57447	C	-0.5584	2.951196	-1.25193	C	-0.61929	2.974129	-1.17871
C	-5.28181	0.678914	0.112019	C	-5.45978	0.351013	0.301437	C	-5.46062	0.24738	0.344514
C	3.840857	-1.34695	-1.35653	C	3.814176	-1.6982	-0.98597	C	3.837362	-1.68292	-0.96795
C	5.126172	-1.17446	-2.17288	C	5.151204	-1.91814	-1.70261	C	5.171484	-1.92344	-1.68255
C	3.974828	-2.58669	-0.46565	C	3.829855	-2.45588	0.344932	C	3.852627	-2.40843	0.380234
C	1.696316	0.330998	2.40419	C	2.488013	0.34855	2.130557	C	2.519864	0.285547	2.106296
H	-3.09609	-1.13215	-1.88105	H	-3.17822	-0.94013	-1.97268	H	-3.16343	-0.88942	-1.99544
H	1.594753	0.865949	-0.95735	H	1.77243	1.014272	-1.19738	H	1.846532	1.083833	-1.21044
H	3.780792	0.773327	-1.26901	H	3.616581	0.160964	-1.95054	H	3.640398	0.145427	-1.98619
H	5.398275	0.36342	0.487543	H	5.391723	0.969806	-0.66586	H	5.368473	1.070998	-0.71953
H	4.25994	-0.65398	1.374252	H	4.948079	0.025179	0.744899	H	5.011495	0.077451	0.679929
H	3.920398	1.633293	2.312377	H	4.203986	2.275473	1.368348	H	4.189441	2.258305	1.402029
H	3.886841	2.303868	0.678488	H	3.594212	2.571795	-0.26561	H	3.558298	2.613364	-0.21226
H	1.443843	2.983017	1.942864	H	1.32874	2.693749	1.972692	H	1.206498	2.557769	1.991008
H	1.714282	2.988636	0.205241	H	1.401514	2.990126	0.243008	H	1.330032	2.911861	0.279429
H	-0.68945	1.71948	1.681327	H	-0.59906	1.21843	1.76809	H	-0.66245	1.157461	1.759062
H	-0.59287	-0.14318	-1.05113	H	-0.72529	0.140205	-1.21181	H	-0.7363	0.288507	-1.14282
H	1.364391	-1.6206	0.806111	H	1.198821	-1.30075	0.669626	H	1.177378	-1.32077	0.502136
H	1.340534	-1.63255	-0.95392	H	1.018332	-1.43122	-1.07044	H	0.892493	-1.26606	-1.22949
H	-1.87033	0.832116	-2.17226	H	-2.31049	1.187206	-2.11101	H	-2.40541	1.270234	-2.10564
H	-3.50124	1.39483	-2.10673	H	-3.9362	1.600377	-1.67524	H	-4.03427	1.612527	-1.60681
H	-2.9226	2.854068	-0.45378	H	-2.96852	2.872983	-0.01932	H	-2.99709	2.909951	-0.01272
H	-2.62582	1.510701	0.629196	H	-2.80072	1.373626	0.875108	H	-2.8809	1.399004	0.901426
H	-5.29971	-0.39308	-1.74638	H	-5.47091	-0.52758	-1.66111	H	-5.47407	-0.56575	-1.64715
H	-4.95007	-2.61773	-0.89412	H	-4.75001	-2.75805	-1.044	H	-4.65239	-2.7852	-1.11078
H	-5.90954	-1.91751	0.414214	H	-5.79124	-2.3258	0.31608	H	-5.71321	-2.43969	0.259003

H	-3.92325	-1.46682	1.74737
H	-3.4394	-2.97771	1.013974
H	-0.06283	-1.98444	2.191045
H	-1.15446	-3.21164	1.551166
H	-1.77245	-1.92557	2.591176
H	-1.03356	3.646602	-1.97213
H	-0.18277	2.160653	-2.36265
H	0.629306	3.409655	-1.42603
H	-5.09429	1.661195	-0.32878
H	-6.3608	0.584875	0.256265
H	-4.81363	0.663585	1.102517
H	3.029107	-1.51699	-2.08093
H	5.037606	-0.35463	-2.89101
H	5.360338	-2.08717	-2.72718
H	5.975366	-0.95968	-1.51592
H	3.136016	-2.72559	0.222322
H	4.053438	-3.48783	-1.07978
H	4.884914	-2.52438	0.138823
H	2.297397	-0.57044	2.566277
H	0.642966	0.036105	2.365331
H	1.820878	0.970074	3.283292

H	-3.88993	-1.76436	1.710569
H	-3.18542	-3.08006	0.790396
H	-0.23212	-1.1048	2.346589
H	-0.46662	-2.64509	1.522771
H	-1.79181	-1.9098	2.423995
H	0.35961	2.581684	-1.71241
H	-0.34127	3.95575	-0.86787
H	-1.32349	3.056101	-2.02107
H	-5.4159	1.392203	-0.03071
H	-6.50972	0.116076	0.491871
H	-4.93093	0.283185	1.258982
H	3.031645	-2.14644	-1.61565
H	5.173988	-1.41621	-2.67431
H	5.334185	-2.98315	-1.86622
H	5.980329	-1.52851	-1.10232
H	2.879004	-2.41094	0.881143
H	4.047856	-3.51168	0.161881
H	4.612802	-2.08178	1.012531
H	3.176503	-0.49224	2.026683
H	1.523771	-0.0516	2.458747
H	2.860258	0.988219	2.936365

H	-3.83987	-1.86844	1.680823
H	-3.08398	-3.11299	0.700961
H	-0.2347	-1.02972	2.359753
H	-0.38548	-2.55104	1.48492
H	-1.75254	-1.91434	2.394235
H	0.321912	2.642604	-1.6189
H	-0.42222	3.948573	-0.70795
H	-1.36897	3.125042	-1.95454
H	-5.47315	1.299358	0.04315
H	-6.49414	-0.03819	0.555024
H	-4.90364	0.173846	1.285695
H	3.048939	-2.14294	-1.58129
H	5.186481	-1.45859	-2.67273
H	5.360223	-2.99279	-1.8068
H	6.001479	-1.50596	-1.10212
H	2.907579	-2.33291	0.923842
H	4.050258	-3.47178	0.218876
H	4.649394	-2.03419	1.031781
H	3.322543	-0.44806	2.027059
H	1.605247	-0.25561	2.363768
H	2.754557	0.942425	2.949554

TS_5c-6c'

C	3.452229	-0.20057	-0.58988
C	4.306108	0.380737	0.562174
C	3.48834	1.559776	1.091559

IM6c'

C	3.529009	-0.16194	-0.62772
C	4.368439	0.46026	0.522301
C	3.50793	1.599084	1.09849

C	2.035992	1.055731	1.047995	C	2.076497	1.050503	0.994078
C	1.025411	2.218184	1.129602	C	0.977293	2.10925	1.024711
C	-0.33835	1.927825	0.550314	C	-0.38478	1.621402	0.49529
C	-0.51926	-0.07936	-0.7171	C	-0.49066	0.312259	-0.58335
C	0.846661	-0.64287	-0.47138	C	0.889624	-0.41134	-0.70632
C	2.001933	0.355342	-0.33777	C	2.105558	0.449999	-0.42409
C	-1.70257	-0.72655	-0.18112	C	-1.68367	-0.60923	-0.22288
C	-2.77798	-0.90954	-1.32208	C	-2.71804	-0.75271	-1.33014
C	-3.07637	0.022563	-0.22276	C	-3.08213	-0.00403	-0.07836
C	-3.18196	1.534602	-0.30946	C	-3.32491	1.48947	0.01822
C	-2.17975	2.300615	-1.15551	C	-2.44098	2.365044	-0.84888
C	-0.75421	2.374688	-0.67221	C	-0.96933	2.304309	-0.61137
C	-4.23359	-0.58559	0.597729	C	-4.18558	-0.80975	0.635162
C	-4.46185	-2.02326	0.07301	C	-4.30099	-2.17186	-0.08988
C	-3.65795	-2.14569	-1.24255	C	-3.53758	-2.03173	-1.4278
C	-1.44235	-1.83187	0.828947	C	-1.28358	-1.82702	0.596362
C	0.144332	3.042065	-1.67582	C	-0.15804	3.130522	-1.55701
C	-4.14368	-0.44078	2.115871	C	-4.08239	-0.88522	2.15815
C	3.662475	-1.70842	-0.84759	C	3.679782	-1.68948	-0.80575
C	5.108932	-1.936	-1.3025	C	5.117675	-1.99175	-1.24337
C	3.356717	-2.65076	0.321321	C	3.333184	-2.57373	0.396325
C	1.781807	0.089399	2.211549	C	1.825311	0.039494	2.117648
H	-2.45973	-0.56457	-2.30167	H	-2.50179	-0.22807	-2.25972
H	3.790146	0.284443	-1.51369	H	3.899755	0.253904	-1.57192
H	5.298918	0.682754	0.221921	H	5.340326	0.816037	0.174234
H	4.454798	-0.35938	1.355209	H	4.568805	-0.28309	1.300728
H	3.789422	1.891076	2.089816	H	3.788407	1.8757	2.118844

H	3.59311	2.416536	0.412473	H	3.603609	2.495754	0.472166
H	0.891347	2.501228	2.179785	H	0.803415	2.46103	2.047308
H	1.449649	3.092673	0.630015	H	1.307263	2.980618	0.451259
H	-1.0869	1.510949	1.222377	H	-1.09086	1.340316	1.275217
H	-2.17834	1.917853	-2.18776	H	-2.63101	2.188523	-1.9146
H	-2.52517	3.337991	-1.24964	H	-2.68341	3.428837	-0.6943
H	-5.09724	0.011269	0.276644	H	-5.10399	-0.25159	0.408292
H	-5.52555	-2.19828	-0.10061	H	-5.35064	-2.42209	-0.25985
H	-4.15503	-2.77291	0.806145	H	-3.89931	-2.98468	0.520452
H	-3.07803	-3.0716	-1.30104	H	-2.91361	-2.90546	-1.64072
H	-4.32087	-2.13411	-2.11238	H	-4.23587	-1.93126	-2.26304
H	-0.93903	-1.44031	1.717935	H	-0.72822	-1.54615	1.496286
H	-0.81572	-2.61771	0.398096	H	-0.66757	-2.51583	0.012039
H	-2.35779	-2.30135	1.16682	H	-2.15043	-2.3854	0.929759
H	1.153087	3.239288	-1.31997	H	0.868271	2.789783	-1.67311
H	-0.30808	3.989319	-1.98765	H	-0.12025	4.137227	-1.11714
H	0.216159	2.427549	-2.58278	H	-0.64123	3.213484	-2.53142
H	-4.04604	0.608271	2.410864	H	-4.07292	0.11356	2.606239
H	-5.05671	-0.82213	2.580064	H	-4.9454	-1.41492	2.570027
H	-3.30126	-0.99038	2.5413	H	-3.18222	-1.40963	2.488645
H	3.01342	-1.99267	-1.68898	H	3.016201	-1.98074	-1.63289
H	5.368773	-1.29837	-2.15243	H	5.396337	-1.41951	-2.13288
H	5.263239	-2.9764	-1.59957	H	5.242261	-3.05356	-1.47063
H	5.808918	-1.71735	-0.48924	H	5.824444	-1.73945	-0.4452
H	2.313108	-2.62765	0.64509	H	2.294096	-2.48412	0.724886
H	3.576239	-3.68085	0.026963	H	3.497653	-3.62227	0.133132
H	3.984641	-2.42958	1.190107	H	3.978316	-2.35929	1.254846

H	2.352864	-0.83868	2.121391	H	2.523215	-0.79781	2.092094
H	0.722159	-0.1771	2.292894	H	0.81138	-0.37073	2.086834
H	2.06547	0.566506	3.15406	H	1.941711	0.540076	3.083798
H	-3.19328	1.944618	0.707486	H	-3.25379	1.807553	1.066131
H	-4.1762	1.741406	-0.72081	H	-4.36021	1.684463	-0.28048
H	1.0144	-1.28217	-1.3549	H	0.925801	-0.84764	-1.70961
H	0.835944	-1.29905	0.392221	H	0.89285	-1.23852	-0.00215
H	1.843235	1.139196	-1.08852	H	2.075299	1.313144	-1.10438
H	-0.62457	0.407979	-1.68209	H	-0.6726	0.680889	-1.60817

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