# Dragonbloodin A1 and A2 - Flavan Trimers and anti-inflammatory principles from Sanguis Draconis

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## Supporting information

**General Experimental Procedure.**

Melting point were determined on Yanaco MP-S3 without temperature corrected. HR-ESI-MS spectra were acquired from VARIAN ProStar LC/VARIAN 901 FT-ICR Mass and Bruker APEX II FT-Mass. Polarimeter were determined on a JASCO P-2000 Polarimeter with 589nm filter. UV spectra were determined on a HITACHI U-0080-D Spectrophotometer with a 0.1 dm length cell. IR spectra were recorded on a PerkinElmer FT-IR Spectrum RX I using KBr pellets. CD spectra were determined on JASCO J-720 Spectropolarimeter. Semi-preparative HPLC (normal phase) was carried out on an SHIMADZU LC-20AT instrument equipped with UV-VIS detector (SHIMADZU, SPD-10A) and a ASTEC CELLULOSE DMP OD-H column (5 μm, 10.0 mm I. D. × 25 cm; SUPELCO, Sigma-Aldrich). 1D and 2D NMR spectra were recorded on Bruker AVIII 400 and AVIII HD 700 spectrometer (1H: 400 and 700 MHz, 13C: 100 and 175 MHz). X-RAY/SCD were recorded on Bruker SMART APEX II Single-Crystal X-Ray Diffractometer with Mo. TLC analyses were carried out using silica gel 60 $F_{254}$ (Merck KGaA). Column chromatography was performed on Geduran Si 60 (40-63 μm, Merck). All solvents used in column chromatography and HPLC were of pesticide residue analysis grade (Fluka, Sigma-Aldrich), analytical grade (J.T. Baker, AVANTOR) and chromatographic grade (MACRON, AVANTOR and Merck), respectively.

**Sanguis Draconis collection and compound isolation process**

The resin of *Daemonorops draco* was purchased from Chuang Song Zong Pharmaceutical co. Ltd. Taiwan in 2010, and identified by Prof. Chang-Sheng Kuoh, Institute of Biotechnology, National Cheng Kung University. A voucher specimen (Wu-

2010002) was deposited in Department of Pharmacy, National Cheng Kung University, Taiwan.

The resin of *D. draco* (3.0 kg) was thoroughly dissolved in $CHCl_3$ (12.0 L). The insoluble materials were removed by filtration and the filtrate was partitioned with $H_2O$ (6.0 L) to yield $CHCl_3$-soluble fraction (about 3.0 kg) and water-soluble fraction (70 g). The $CHCl_3$-soluble extract (0.5 kg) was subjected to C.C. (Column Chromatography) on a silica gel column with a step gradient (*n*-hexane—acetone 4:1, 2:1, 1:1 and 0:1) to give ten fractions. Fraction 5 (74.3 g) was separated by C.C. on a silica gel column with a step gradient ($CHCl_3$—acetone 49:1, 40:1, 35:1, 29:1, 24:1, 19:1 and 0:1) to give ten fractions: fr. 5-1 (0.1 g), fr. 5-2 (0.1 g), fr. 5-3 (0.2 g), fr. 5-4 (1.6 g), fr. 5-5 (2.2 g), fr. 5-6 (9.6 g), fr. 5-7 (13.2 g), fr. 5-8 (5.4 g), fr. 5-9 (19.3 g) and fr. 5-10 (2.0 g). Fraction 5-7 was separated on a silica gel column with a step gradient (*n*-hexane—acetone 2:1, 7:4, 3:2, 5:4, 1:1, 1:2 and 0:1) to give nine subfractions. Co-crystal of dracoflavan B (6.1 g) was obtained from subfr. 5-7-3. Dragonbloodin A (303 mg) as a co-crystal was obtained between subfr. 5-7-4 and subfr. 5-7-5. Dragonbloodin A1 and A2 were separated by using a ASTEC Cellulose DMP-OD-H chiral column to yield A1 and A2 with *n*-hexane—*i*-PrOH=70:30 as eluent, flow rate=2.1 $cm^3$ $min^{-1}$, retention time=16.7 min for A2 (49.5%) and 22.1 min for A1 (50.5%).

**X-Ray Crystallography Analysis**. Single crystals were grown from $CH_2Cl_2$/hexane at ambient temperature. Data were collected using a Bruker SMART-CCD diffractometer at 100(2) K. The instrument was equipped with graphite-monochromated Mo $K_\alpha$ radiation ($\lambda$ = 0.71073 Å). Empirical absorption corrections were made in light of the results of an azimuthal scan. The crystal structure was determined using the direct method and refined using the full-matrix least-squares method on $F^2$, with all non-hydrogen atoms of the structure refined anisotropically, in SHELXL-97 software.[1] In the structure refinement, the PLATON-SQUEEZE program was applied for the position-disordered solvent ($CH_2Cl_2$) molecules.[2] All hydrogen atoms were located geometrically with d(C-H) = 0.930 Å and d(O-H) = 0.820 Å. The crystal structure can be successfully solved using either $P2_1$ or $P2_1/n$ as the space group. In $P2_1$, a pair of dragonbloodin diastereomers A1 and A2 are found in the asymmetric unit, whereas in $P2_1/n$, the two isomers are merged as one molecule with a carbon atom, which is disordered in two positions at C2″X and C2″Y with occupancies of 0.616 and 0.384, respectively (Fig. S1). To emphasize that the single crystals we obtained only contain a pair of isomers, the space group of $P2_1$ was used, producing two ORTEPs for isomers A1 and A2 in Figs. 1 and 2, respectively. For quick atomic comparison between two

isomers, the two figures are drawn in a similar orientation with a non-hydrogen atom-to-atom contrast table (Table S1). Crystal data of Dragonbloodin A (1+2) was deposited with the Cambridge Crystallographic Data Centre (CCDC 1401169).

**References**

1. Sheldrick, G. M. SHELXTL-97; University of Göttingen: Göttingen, Germany.
2. Spek, A. L. *J. Appl. Crystallogr*. **2003**, *36*, 7.

Table S1. A Non-Hydrgoen Atom-to-Atom Contrast Table between Dragonbloodin A1 and Dragonbloodin A2

| A1 | | | | A2 | | | |
|---|---|---|---|---|---|---|---|
| C22 | C92 | C33' | C34" | C2 | C82 | C13' | C14" |
| C23 | C93 | C34' | C43 | C3 | C83 | C14' | C4A |
| C24 | C94 | C35' | C48 | C4 | C84 | C15' | C8A |
| C25 | C21' | C22" | C4"B | C5 | C1' | C2" | C4"A |
| C26 | C22' | C23" | C8"B | C6 | C2' | C3" | C8"A |
| C27 | C23' | C24" | O21 | C7 | C3' | C4" | O1 |
| C28 | C24' | C25" | O21" | C8 | C4' | C5" | O1" |
| C29 | C25' | C26" | O90 | C9 | C5' | C6" | O80 |
| C30 | C26' | C27" | O91 | C10 | C6' | C7" | O81 |
| C31 | C27' | C28" | O92 | C11 | C7' | C8" | O82 |
| C32 | C28' | C29" | O93 | C12 | C8' | C9" | O83 |
| C33 | C29' | C30" | O94 | C13 | C9' | C10" | O84 |
| C34 | C30' | C31" | O95 | C14 | C10' | C11" | O85 |
| C90 | C31' | C32" | O96 | C80 | C11' | C12" | O86 |
| C91 | C32' | C33" | O97 | C81 | C12' | C13" | O87 |

Table S2. Crystal data

| | |
|---|---|
| formula | $C_{50}H_{44}O_{10}$ |
| fw (g mol$^{-1}$) | 804.85 |
| cryst size (mm$^3$) | 0.65 × 0.43 × 0.31 |
| cryst syst | monoclinic |
| space group | $P2_1$ |
| $a$ (Å) | 15.708(2) |
| $b$ (Å) | 17.744(3) |
| $c$ (Å) | 16.623(3) |
| $\alpha$ (deg) | 90 |
| $\beta$ (deg) | 99.335(2) |

| | |
|---|---|
| $\gamma$ (deg) | 90 |
| $V$ (Å $^3$) | 4572.2(12) |
| $Z$ | 4 |
| $D_{calc}$ (g cm$^{-3}$) | 1.168 |
| $\mu$, (mm$^{-1}$) | 0.081 |
| F(000) | 1692.0 |
| reflns collected, unique | 21019/13848 |
| $R_1/wR_2$ (I > 2σ(I)) | 0.0696/0.1821 |
| GOF on $F^2$ | 1.086 |
| largest diff peak and hole (e Å $^{-3}$) | 0.392/-0.289 |

Table S3. Lists of selected bond lengths and angles for Dragonbloodin **A1** and Dragonbloodin **A2**

(a) Bong Lengths (Å ):

| | | | |
|---|---|---|---|
| C2—O1 | 1.420(6) | C11"—C12" | 1.345(7) |
| C2—O80 | 1.431(6) | C12"—C13" | 1.379(7) |
| C2—C9 | 1.516(7) | C13"—C14" | 1.316(8) |
| C2—C3 | 1.541(6) | C22"—O21" | 1.448(4) |
| C3—C4 | 1.520(6) | C22"—C23" | 1.478(6) |
| C3—C4' | 1.650(7) | C22"—C29" | 1.513(6) |
| C4—C2' | 1.518(6) | C23"—C24" | 1.516(7) |
| C4—C4A | 1.551(6) | C24"—C4"B | 1.500(7) |
| C5—O81 | 1.333(6) | C25"—C26" | 1.335(7) |
| C5—C6 | 1.368(7) | C25"—O97 | 1.393(6) |
| C5—C4A | 1.431(7) | C25"—C4"B | 1.469(7) |
| C6—C7 | 1.407(7) | C26"—C27" | 1.378(6) |
| C6—C81 | 1.506(7) | C27"—O96 | 1.409(5) |
| C7—C8 | 1.371(7) | C27"—C28" | 1.412(6) |
| C7—O82 | 1.416(6) | C28"—C8"B | 1.354(7) |
| C8—C8A | 1.373(7) | C28"—C23' | 1.496(6) |
| C9—C14 | 1.350(7) | C29"—C34" | 1.387(7) |
| C9—C10 | 1.387(7) | C29"—C30" | 1.404(6) |
| C10—C11 | 1.406(7) | C30"—C31" | 1.344(8) |
| C11—C12 | 1.458(7) | C31"—C32" | 1.388(7) |
| C12—C13 | 1.293(7) | C32"—C33" | 1.356(8) |
| C13—C14 | 1.398(7) | C33"—C34" | 1.443(8) |
| C22—O21 | 1.425(6) | C4"A—C8"A | 1.446(7) |

| | | | |
|---|---|---|---|
| C22—O90 | 1.432(4) | C8"A—O1" | 1.273(6) |
| C22—C23 | 1.508(7) | C4"B—C8"B | 1.349(6) |
| C22—C29 | 1.537(6) | C8"B—O21" | 1.447(5) |
| C23—C24' | 1.557(6) | C1'—O86 | 1.394(5) |
| C23—C24 | 1.572(7) | C1'—O85 | 1.429(4) |
| C24—C43 | 1.472(7) | C1'—C10' | 1.515(7) |
| C24—C22' | 1.566(6) | C1'—C2' | 1.575(7) |
| C25—C43 | 1.390(7) | C2'—C3' | 1.476(7) |
| C25—C26 | 1.416(7) | C3'—C4' | 1.568(7) |
| C25—O91 | 1.423(6) | C4'—C5' | 1.427(7) |
| C26—C27 | 1.366(7) | C4'—C9' | 1.493(8) |
| C26—C90 | 1.503(7) | C5'—O83 | 1.357(6) |
| C27—O92 | 1.331(6) | C5'—C6' | 1.376(7) |
| C27—C28 | 1.399(7) | C6'—C7' | 1.523(7) |
| C28—C48 | 1.395(7) | C7'—O84 | 1.205(6) |
| C29—C30 | 1.364(7) | C7'—C8' | 1.444(7) |
| C29—C34 | 1.412(7) | C8'—C9' | 1.341(7) |
| C30—C31 | 1.386(7) | C9'—O85 | 1.367(6) |
| C31—C32 | 1.321(7) | C10'—C15' | 1.331(7) |
| C32—C33 | 1.452(7) | C10'—C11' | 1.407(6) |
| C33—C34 | 1.362(7) | C11'—C12' | 1.369(7) |
| C43—C48 | 1.389(7) | C12'—C13' | 1.420(7) |
| C48—O21 | 1.387(6) | C13'—C14' | 1.332(8) |
| C80—O81 | 1.446(6) | C14'—C15' | 1.439(8) |
| C82—O83 | 1.431(6) | C21'—O96 | 1.440(5) |
| C83—C6' | 1.522(9) | C21'—O95 | 1.447(6) |
| C84—O87 | 1.413(6) | C21'—C22' | 1.485(5) |
| C91—O91 | 1.415(6) | C21'—C30' | 1.507(7) |
| C92—O93 | 1.441(6) | C22'—C23' | 1.578(6) |
| C93—C26' | 1.515(8) | C23'—C24' | 1.561(6) |
| C94—O97 | 1.447(6) | C24'—C29' | 1.501(8) |
| C2"—O1" | 1.460(5) | C24'—C25' | 1.569(7) |
| C2"—C9" | 1.507(6) | C25'—C26' | 1.339(7) |
| C2"—C3" | 1.542(5) | C25'—O93 | 1.348(5) |
| C3"—C4" | 1.492(7) | C26'—C27' | 1.417(7) |
| C4"—C4"A | 1.498(7) | C27'—O94 | 1.261(7) |
| C5"—C4"A | 1.324(8) | C27'—C28' | 1.451(8) |

| | | | |
|---|---|---|---|
| C5"—O87 | 1.348(6) | C28'—C29' | 1.315(7) |
| C5"—C6" | 1.434(7) | C29'—O95 | 1.386(6) |
| C6"—C7" | 1.376(7) | C30'—C31' | 1.387(6) |
| C7"—C8" | 1.342(7) | C30'—C35' | 1.415(7) |
| C7"—O86 | 1.363(6) | C31'—C32' | 1.417(7) |
| C8"—C8"A | 1.472(6) | C32'—C33' | 1.331(7) |
| C8"—C3' | 1.515(5) | C33'—C34' | 1.431(7) |
| C9"—C10" | 1.296(7) | C34'—C35' | 1.362(8) |
| C9"—C14" | 1.397(7) | C4A—C8A | 1.375(7) |
| C10"—C11" | 1.438(8) | C8A—O1 | 1.375(6) |

(b) Bond Angles (deg):

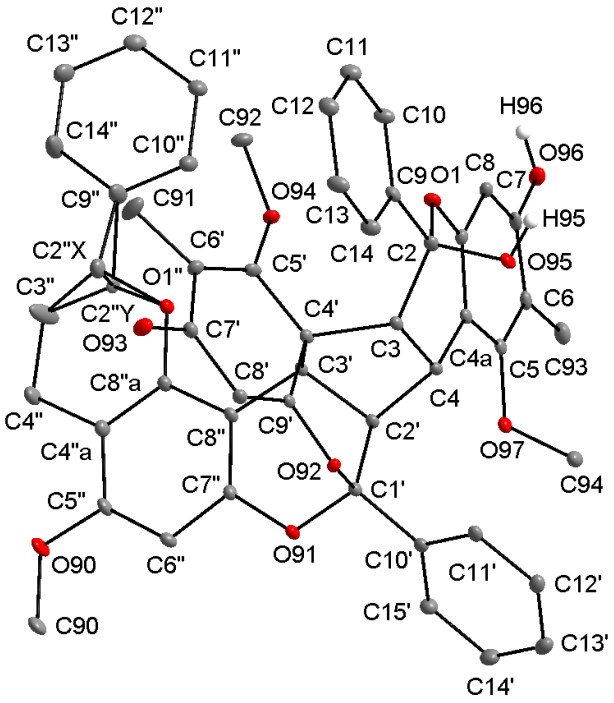
| | | | |
|---|---|---|---|
| O1—C2—O80 | 108.4 (4) | C29"—C34"—C33" | 118.9 (5) |
| O1—C2—C9 | 109.1 (4) | C5"—C4"A—C8"A | 120.9 (5) |
| O80—C2—C9 | 111.3 (4) | C5"—C4"A—C4" | 122.0 (5) |
| O1—C2—C3 | 112.2 (4) | C8"A—C4"A—C4" | 117.1 (4) |
| O80—C2—C3 | 100.9 (4) | O1"—C8"A—C4"A | 125.0 (5) |
| C9—C2—C3 | 114.7 (4) | O1"—C8"A—C8" | 118.7 (4) |
| C4—C3—C2 | 113.1 (4) | C4"A—C8"A—C8" | 116.3 (4) |
| C4—C3—C4' | 105.4 (4) | C8"B—C4"B—C25" | 115.3 (4) |
| C2—C3—C4' | 121.6 (4) | C8"B—C4"B—C24" | 126.5 (4) |
| C3—C4—C2' | 104.4 (3) | C25"—C4"B—C24" | 118.2 (4) |
| C3—C4—C4A | 111.8 (3) | C4"B—C8"B—C28" | 126.4 (5) |
| C2'—C4—C4A | 111.5 (3) | C4"B—C8"B—O21" | 118.9 (4) |
| O81—C5—C6 | 119.4 (5) | C28"—C8"B—O21" | 114.7 (4) |
| O81—C5—C4A | 119.4 (4) | O86—C1'—O85 | 107.4 (3) |
| C6—C5—C4A | 121.1 (5) | O86—C1'—C10' | 108.7 (4) |
| C5—C6—C7 | 117.2 (5) | O85—C1'—C10' | 107.6 (3) |
| C5—C6—C81 | 125.1 (5) | O86—C1'—C2' | 108.5 (4) |
| C7—C6—C81 | 117.7 (4) | O85—C1'—C2' | 110.8 (3) |
| C8—C7—C6 | 122.5 (5) | C10'—C1'—C2' | 113.6 (4) |
| C8—C7—O82 | 119.7 (4) | C3'—C2'—C4 | 104.2 (3) |
| C6—C7—O82 | 117.7 (5) | C3'—C2'—C1' | 108.2 (4) |
| C8A—C8—C7 | 119.3 (5) | C4—C2'—C1' | 112.6 (4) |
| C14—C9—C10 | 117.9 (5) | C2'—C3'—C8" | 109.9 (3) |
| C14—C9—C2 | 121.0 (5) | C2'—C3'—C4' | 102.1 (4) |

| | | | |
|---|---|---|---|
| C10—C9—C2 | 121.1 (5) | C8''—C3'—C4' | 113.9 (3) |
| C9—C10—C11 | 123.9 (5) | C5'—C4'—C9' | 115.1 (5) |
| C10—C11—C12 | 114.5 (4) | C5'—C4'—C3' | 113.1 (4) |
| C13—C12—C11 | 120.0 (5) | C9'—C4'—C3' | 107.6 (4) |
| C12—C13—C14 | 123.9 (5) | C5'—C4'—C3 | 118.7 (4) |
| C9—C14—C13 | 119.8 (5) | C9'—C4'—C3 | 100.4 (3) |
| O21—C22—O90 | 109.5 (3) | C3'—C4'—C3 | 100.2 (3) |
| O21—C22—C23 | 113.2 (4) | O83—C5'—C6' | 124.0 (5) |
| O90—C22—C23 | 103.2 (3) | O83—C5'—C4' | 109.9 (4) |
| O21—C22—C29 | 106.2 (3) | C6'—C5'—C4' | 126.1 (5) |
| O90—C22—C29 | 108.6 (3) | C5'—C6'—C83 | 131.8 (5) |
| C23—C22—C29 | 116.0 (4) | C5'—C6'—C7' | 115.9 (5) |
| C22—C23—C24' | 123.1 (3) | C83—C6'—C7' | 112.0 (4) |
| C22—C23—C24 | 111.3 (4) | O84—C7'—C8' | 121.0 (5) |
| C24'—C23—C24 | 104.5 (3) | O84—C7'—C6' | 119.8 (5) |
| C43—C24—C22' | 111.0 (4) | C8'—C7'—C6' | 119.2 (5) |
| C43—C24—C23 | 113.0 (4) | C9'—C8'—C7' | 120.8 (4) |
| C22'—C24—C23 | 102.6 (4) | C8'—C9'—O85 | 119.5 (4) |
| C43—C25—C26 | 124.1 (5) | C8'—C9'—C4' | 122.7 (5) |
| C43—C25—O91 | 116.4 (4) | O85—C9'—C4' | 117.8 (4) |
| C26—C25—O91 | 119.4 (5) | C15'—C10'—C11' | 119.7 (5) |
| C27—C26—C25 | 117.8 (5) | C15'—C10'—C1' | 121.0 (4) |
| C27—C26—C90 | 123.4 (5) | C11'—C10'—C1' | 119.3 (4) |
| C25—C26—C90 | 118.8 (4) | C12'—C11'—C10' | 118.7 (4) |
| O92—C27—C26 | 117.3 (5) | C11'—C12'—C13' | 121.5 (5) |
| O92—C27—C28 | 122.0 (5) | C14'—C13'—C12' | 118.9 (5) |
| C26—C27—C28 | 120.7 (5) | C13'—C14'—C15' | 119.4 (6) |
| C27—C28—C48 | 119.0 (5) | C10'—C15'—C14' | 121.4 (5) |
| C30—C29—C34 | 118.8 (5) | O96—C21'—O95 | 105.6 (4) |
| C30—C29—C22 | 123.3 (4) | O96—C21'—C22' | 112.1 (3) |
| C34—C29—C22 | 117.8 (4) | O95—C21'—C22' | 112.9 (3) |
| C29—C30—C31 | 117.8 (5) | O96—C21'—C30' | 104.3 (4) |
| C32—C31—C30 | 125.8 (5) | O95—C21'—C30' | 105.9 (4) |
| C31—C32—C33 | 117.3 (5) | C22'—C21'—C30' | 115.2 (3) |
| C34—C33—C32 | 117.8 (5) | C21'—C22'—C24 | 114.6 (3) |
| C33—C34—C29 | 122.5 (5) | C21'—C22'—C23' | 107.6 (3) |
| C48—C43—C25 | 115.1 (5) | C24—C22'—C23' | 103.3 (3) |

| | | | |
|---|---|---|---|
| C48—C43—C24 | 121.8 (5) | C28"—C23'—C24' | 119.0 (3) |
| C25—C43—C24 | 123.1 (5) | C28"—C23'—C22' | 111.4 (3) |
| O21—C48—C43 | 123.2 (4) | C24'—C23'—C22' | 96.5 (3) |
| O21—C48—C28 | 113.7 (4) | C29'—C24'—C23 | 105.3 (4) |
| C43—C48—C28 | 123.1 (4) | C29'—C24'—C23' | 105.7 (4) |
| O1"—C2"—C9" | 111.2 (3) | C23—C24'—C23' | 108.2 (3) |
| O1"—C2"—C3" | 107.9 (3) | C29'—C24'—C25' | 108.9 (4) |
| C9"—C2"—C3" | 112.0 (3) | C23—C24'—C25' | 119.5 (4) |
| C4"—C3"—C2" | 110.5 (4) | C23'—C24'—C25' | 108.5 (4) |
| C3"—C4"—C4"A | 112.1 (4) | C26'—C25'—O93 | 131.5 (4) |
| C4"A—C5"—O87 | 116.0 (5) | C26'—C25'—C24' | 123.7 (4) |
| C4"A—C5"—C6" | 122.8 (5) | O93—C25'—C24' | 104.6 (3) |
| O87—C5"—C6" | 121.1 (4) | C25'—C26'—C27' | 120.1 (5) |
| C7"—C6"—C5" | 116.2 (4) | C25'—C26'—C93 | 124.0 (5) |
| C8"—C7"—O86 | 121.6 (4) | C27'—C26'—C93 | 115.9 (5) |
| C8"—C7"—C6" | 125.0 (5) | O94—C27'—C26' | 121.1 (5) |
| O86—C7"—C6" | 113.4 (4) | O94—C27'—C28' | 119.6 (4) |
| C7"—C8"—C8"A | 118.7 (4) | C26'—C27'—C28' | 119.3 (5) |
| C7"—C8"—C3' | 121.0 (4) | C29'—C28'—C27' | 120.5 (4) |
| C8"A—C8"—C3' | 120.2 (3) | C28'—C29'—O95 | 120.0 (4) |
| C10"—C9"—C14" | 115.6 (4) | C28'—C29'—C24' | 125.1 (5) |
| C10"—C9"—C2" | 125.7 (5) | O95—C29'—C24' | 113.8 (4) |
| C14"—C9"—C2" | 118.2 (4) | C31'—C30'—C35' | 118.7 (5) |
| C9"—C10"—C11" | 125.5 (5) | C31'—C30'—C21' | 120.7 (4) |
| C12"—C11"—C10" | 113.1 (5) | C35'—C30'—C21' | 120.6 (4) |
| C11"—C12"—C13" | 124.3 (5) | C30'—C31'—C32' | 120.7 (5) |
| C14"—C13"—C12" | 117.2 (5) | C33'—C32'—C31' | 120.5 (5) |
| C13"—C14"—C9" | 124.0 (5) | C32'—C33'—C34' | 119.3 (5) |
| O21"—C22"—C23" | 110.6 (0) | C35'—C34'—C33' | 121.3 (5) |
| O21"—C22"—C29" | 106.2 (3) | C34'—C35'—C30' | 119.4 (5) |
| C23"—C22"—C29" | 115.8 (3) | C8A—C4A—C5 | 118.7 (5) |
| C22"—C23"—C24" | 110.7 (4) | C8A—C4A—C4 | 121.6 (5) |
| C4"B—C24"—C23" | 108.4 (4) | C5—C4A—C4 | 119.7 (4) |
| C26"—C25"—O97 | 126.2 (4) | C8—C8A—C4A | 121.0 (5) |
| C26"—C25"—C4"B | 121.2 (5) | C8—C8A—O1 | 116.1 (4) |
| O97—C25"—C4"B | 112.6 (4) | C4A—C8A—O1 | 122.9 (4) |
| C25"—C26"—C27" | 118.9 (5) | C8A—O1—C2 | 116.3 (4) |

| | | | |
|---|---|---|---|
| C26"—C27"—O96 | 112.7 (4) | C48—O21—C22 | 115.7 (3) |
| C26"—C27"—C28" | 122.9 (4) | C5—O81—C80 | 116.0 (4) |
| O96—C27"—C28" | 124.3 (4) | C5'—O83—C82 | 124.2 (4) |
| C8"B—C28"—C27" | 115.2 (4) | C9'—O85—C1' | 119.4 (3) |
| C8"B—C28"—C23' | 127.0 (4) | C7"—O86—C1' | 120.7 (4) |
| C27"—C28"—C23' | 117.8 (4) | C5"—O87—C84 | 122.1 (4) |
| C34"—C29"—C30" | 118.7 (4) | C91—O91—C25 | 113.5 (3) |
| C34"—C29"—C22" | 119.5 (0) | C25'—O93—C92 | 122.1 (3) |
| C30"—C29"—C22" | 121.5 (4) | C29'—O95—C21' | 117.3 (3) |
| C31"—C30"—C29" | 117.9 (5) | C27"—O96—C21' | 116.4 (3) |
| C30"—C31"—C32" | 127.6 (5) | C25"—O97—C94 | 113.8 (4) |
| C33"—C32"—C31" | 113.7 (5) | C8"A—O1"—C2" | 119.4 (4) |
| C32"—C33"—C34" | 123.0 (5) | C8"B—O21"—C22" | 113.1 (3) |

Fig. S1. An ORTEP diagram of a merged dragonbloodin A (**1**+**2**)molecule is presented with thermal ellipsoids for non-hydrogen atoms shown at 15% probability level. Carbon, oxygen, and hydrogen atoms are shown as gray, red, and white spheres, respectively. All hydrogen atoms except those connected to oxygen atoms are omitted for clarity. The carbon label, C8a, for the atom connected to atoms C8, O1, and C4a, is not shown. One carbon atom was found disordered in two positions with C2"X and C2"Y at occupancies of 0.616 and 0.384, respectively.



## Spectroscopic data of 1 and 2

Table S4 $^{1}H$ & $^{13}C$ NMR data of **1** and **2** (*δ* value in ppm, *J* values in Hz). [a]

| No. | 1 | | 2 | |
|---|---|---|---|---|
| | $\delta_H$ | $\delta_C$ | $\delta_H$ | $\delta_C$ |
| **2** | - | 96.91 (s) | - | 96.86 (s) |
| **3** | 3.90 (d, 9.1) | 51.85 (d) | 3.86 (d, 9.1) | 52.52 (d) |
| **4** | 3.75 (d, 9.1) | 35.81 (d) | 3.74 (d, 9.1) | 35.49 (d) |
| **4a** | - | 109.59 (s) | - | 109.49 (s) |
| **5** | - | 157.37 (s) | - | 157.51 (s) |
| **6** | - | 111.36 (s) | - | 111.38 (s) |
| **7** | - | 156.04 (s) | - | 156.03 (s) |
| **8** | 6.40 (s) | 100.37 (d) | 6.40 (s) | 100.57 (d) |
| **8a** | - | 152.40 (d) | - | 152.31 (d) |
| **9** | - | 143.04 (s) | - | 141.45 (s) |
| **10** | 7.25-7.30 (m) | 128.76 (d) | 7.14-7.18 (m) | 128.80 (d) |
| **11** | 7.25-7.30 (m) | 128.76 (d) | 7.14-7.18 (m) | 128.80 (d) |
| **12** | 7.25-7.30 (m) | 128.76 (d) | 7.14-7.18 (m) | 128.80 (d) |
| **13** | 7.25-7.30 (m) | 128.76 (d) | 7.14-7.18 (m) | 128.80 (d) |
| **14** | 7.25-7.30 (m) | 128.76 (d) | 7.14-7.18 (m) | 128.80 (d) |
| **2-OH** | 5.41 (s) | - | 5.41 (s) | - |
| **5-OMe** | 2.93 (s) | 59.08 (q) | 2.92 (s) | 59.08 (q) |
| **6-Me** | 2.01 (s) | 8.42 (q) | 1.98 (s) | 8.38 (q) |
| **7-OH** | 8.33 (s) | - | 8.28 (s, br) | - |
| **1′** | - | 104.58 (s) | - | 104.52 (s) |
| **2′** | 3.21 (d, 4.6) | 49.20 (d) | 3.21 (d, 4.9) | 49.56 (d) |
| **3′** | 4.03 (d, 4.6) | 38.49 (d) | 3.90 (d, 4.9) | 38.40 (d) |
| **4′** | - | 54.68 (s) | - | 54.42 (s) |
| **5′** | - | 164.17 (s) | - | 163.43 (s) |
| **6′** | - | 112.55 (s) | - | 113.02 (s) |
| **7′** | - | 187.71 (s) | - | 187.43 (s) |
| **8′** | 5.42 (s) | 106.30 (d) | 5.42 (s) | 105.60 (d) |
| **9′** | - | 171.74 (s) | - | 171.89 (s) |
| **10′** | - | 139.72 (s) | - | 139.75 (s) |
| **11′** | 7.89 (d, 7.4) | 127.15 (d) | 7.90 (d, 7.4) | 127.20 (d) |
| **12′** | 7.63 (t, 7.7) | 128.80 (d) | 7.64 (t, 7.7) | 128.80 (d) |
| **13′** | 7.55 (t, 7.7) | 129.49 (d) | 7.55 (t, 7.7) | 129.52 (d) |
| **14′** | 7.63 (t, 7.7) | 128.80 (d) | 7.64 (t, 7.7) | 128.80 (d) |
| **15′** | 7.89 (d, 7.4) | 127.15 (d) | 7.90 (d, 7.6) | 127.20 (d) |
| **5′-OMe** | 2.89 (s) | 59.16 (q) | 3.20 (s) | 58.50 (q) |
| **6′-Me** | 1.17 (s) | 9.24 (q) | 0.70 (s) | 9.24 (q) |
| **2″** | 5.02 (dd,9.2, 2.6) | 77.64 (d) | 5.31 (dd,5.2, 4.0) | 77.02 (d) |
| **3″** | 2.01-2.05 (m) | 29.97 (t) | 1.98-2.05 (m) | 26.56 (t) |
| | 1.71 (m) | | 1.98-2.05 (m) | |
| **4″** | 2.53(ddd,16.0, 5.7, 4.6) | 18.85 (t) | 2.50 (ddd,16.8, 6.2, 4.9) | 15.92 (t) |
| | 2.45(ddd,17.2,10.5, 5.9) | | 1.94-1.98 (m) | |
| **4″a** | - | 104.22 (s) | - | 104.64 (s) |
| **5″** | - | 158.11 (s) | - | 158.15 (s) |
| **6″** | 6.07 (s) | 91.56 (d) | 6.10 (s) | 91.50 (d) |
| **7″** | - | 152.83 (s) | - | 152.97 (s) |
| **8″** | - | 100.97 (s) | - | 100.80 (s) |
| **8″a** | - | 153.77 (s) | - | 154.07 (s) |
| **9″** | - | 141.84 (s) | - | 142.17 (s) |
| **10″** | 7.20-7.23 (m) | 126.03 (d) | 7.05 (d, 7.1) | 126.29 (d) |
| **11″** | 7.20-7.23 (m) | 127.70 (d) | 7.19-7.24 (m) | 127.50 (d) |
| **12″** | 7.24-7.25 (m) | 128.36 (d) | 7.19-7.24 (m) | 128.25 (d) |
| **13″** | 7.20-7.23 (d,7.6) | 127.70 (d) | 7.19-7.24 (m) | 127.50 (d) |

| | | | | |
|---|---|---|---|---|
| **14″** | 7.20-7.23 (m) | 126.03 (d) | 7.05 (d, 7.1) | 126.29 (d) |
| **5″-OMe** | 3.71 (s) | 55.38 (q) | 3.71 (s) | 55.36 (q) |

[a] $^{1}$H NMR and $^{13}$C NMR in $d_6$-Acetone.

**Physico-chemical constants of Dragonbloodin A1 (1) and A2 (2)**

Dragonbloodin A1 (**1**). Colorless amorphous powder. Optical rotation ($[\alpha]^{26}_{D}$) +42.3619 (*c* 0.09, $CHCl_3$); UV (log$\varepsilon$, in $CHCl_3$) $\lambda_{max}$ 282.0 (3.84), 247.0 (4.20) nm; IR (KBr) $\nu_{max}$ 3372, 2925, 2854, 1667, 1615, 1600, 1448, 1367, 1120, 699 cm$^{-1}$; ECD (Mol. CD, in $CHCl_3$) 306 (+11.1917), 271 (+2.16617), 249 (-6.10281), 221 (-1.84619), 211 (+0.96840) nm; HR-ESI-MS (m/z 805.3003 $[M+H]^+$, calcd for $C_{50}H_{45}O_{10}$ : 805.3007).

Dragonbloodin A2 (**2**). Colorless amorphous powder. Optical rotation ($[\alpha]^{26}_{D}$) -58.0865 (*c* 0.06, $CHCl_3$); UV (log$\varepsilon$, in $CHCl_3$) $\lambda_{max}$ 315.0 (3.26), 283.0 (3.76), 247.0 (4.18) nm; IR (KBr) $\nu_{max}$ 3374, 2925, 2854, 1667, 1615, 1601, 1448, 1368, 1121 , 700 cm$^{-1}$; ECD (Mol. CD, in $CHCl_3$) 306 (-7.79742), 270 (-3.08468), 248 (+5.38757), 222 (-1.24149), 211 (+1.25683) nm; HR-ESI-MS (m/z 805.3007 $[M+H]^+$, calcd for $C_{50}H_{45}O_{10}$ : 805.3007).

Fig. S2. Key $^{1}$H-$^{1}$H COSY correlations of Dragonbloodin A1 (**1**)

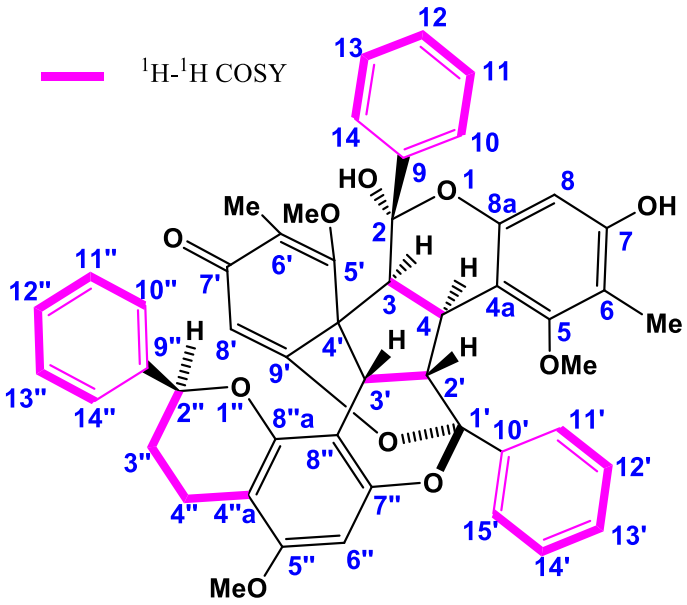
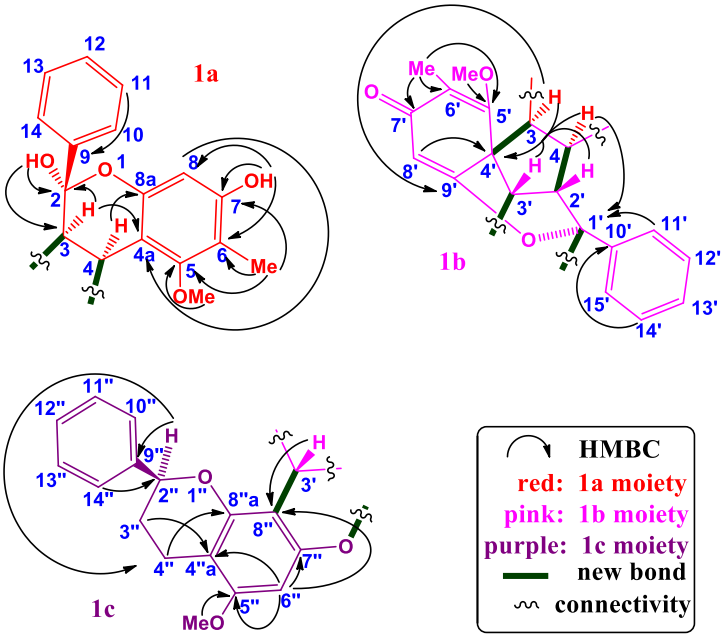


Fig. S3. Key HMBC correlations of Dragonbloodin A1 (1)




## Miscellaneous spectra

Fig. S4. The ECD spectrum of **1** and **2** had opposite peaks to each other.

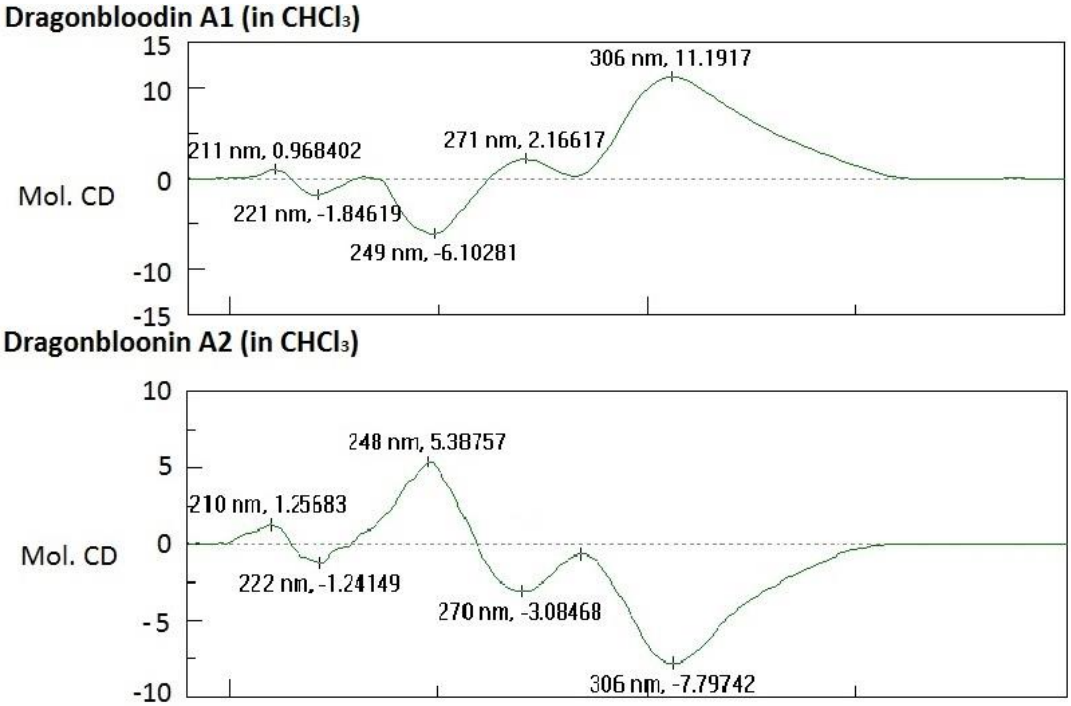


Fig. S5. UV spectrum of 1 in CHCl3

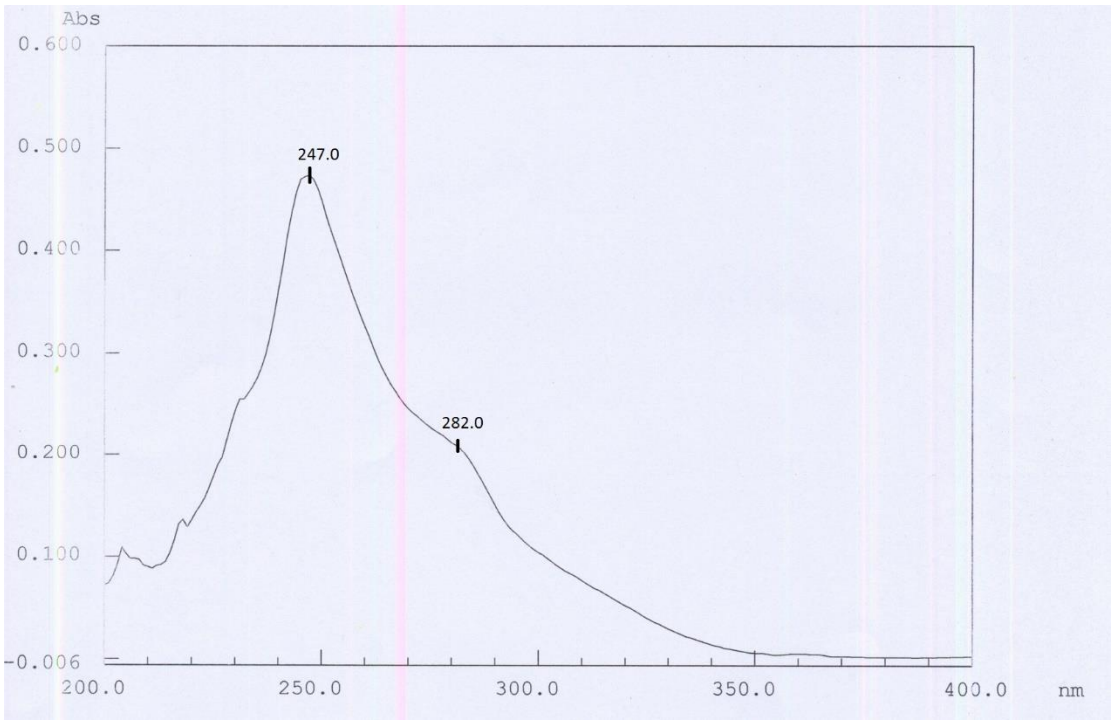



Fig. S6. UV spectrum of **2** in $CHCl_3$

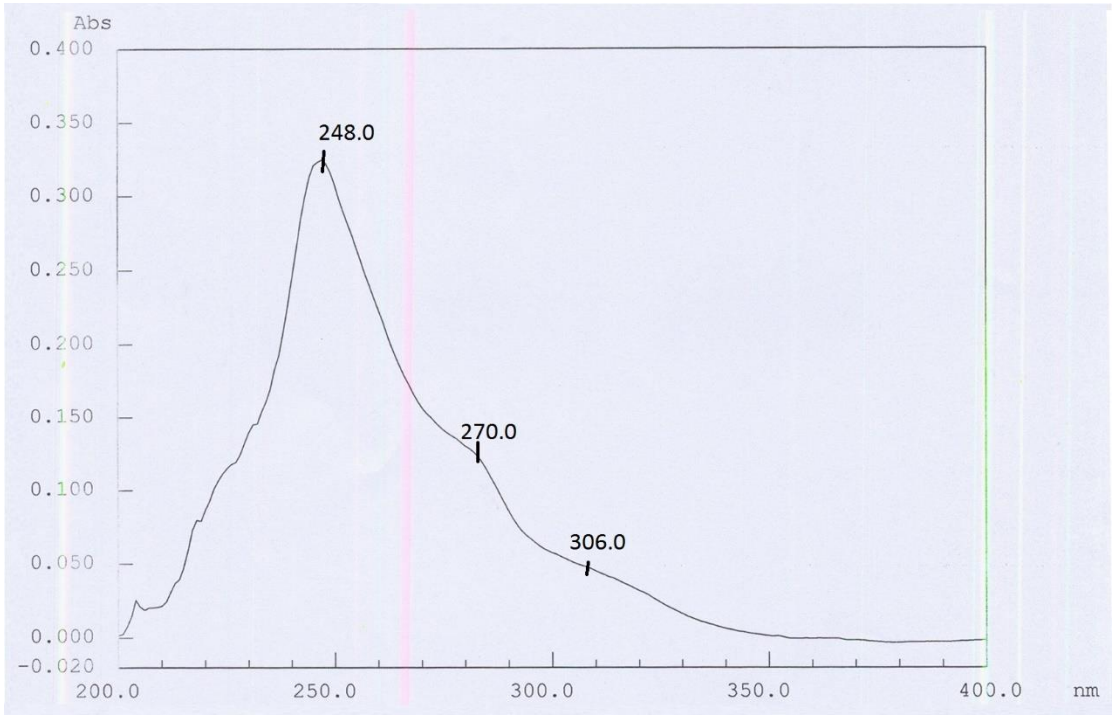


Fig. S7. IR spectrum of 1 (KBr disc)

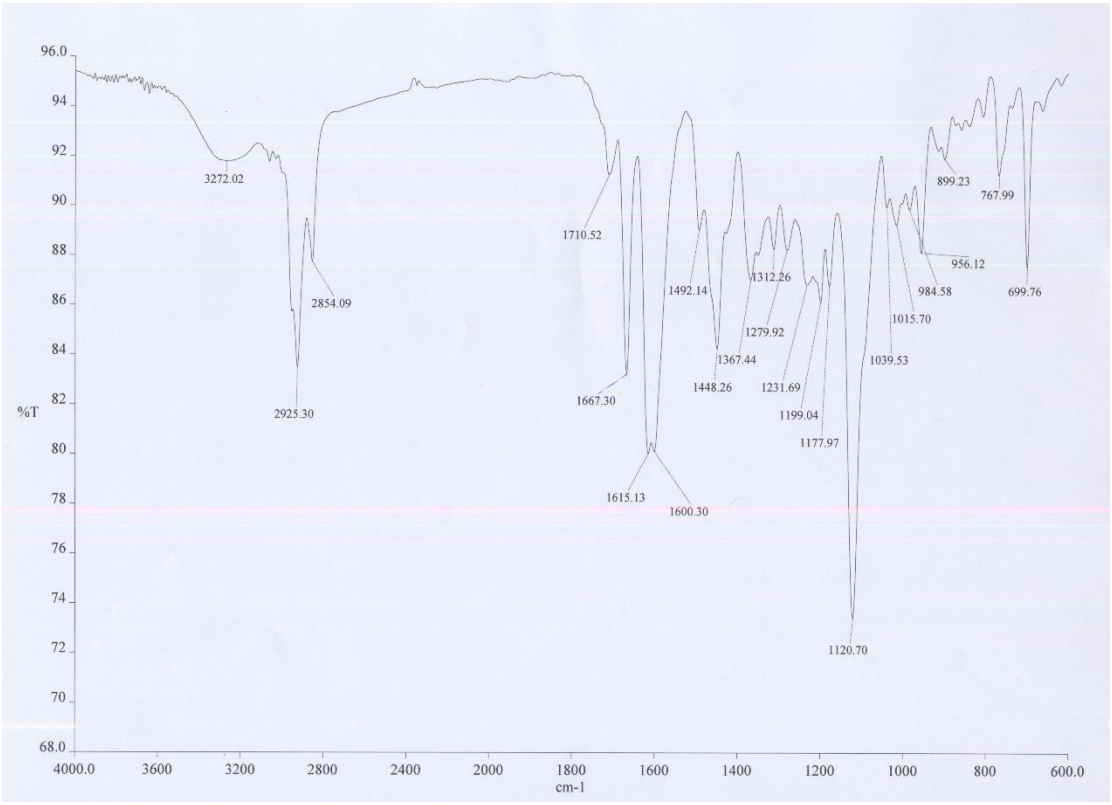



Fig. S8. IR spectrum of **2** (KBr disc)

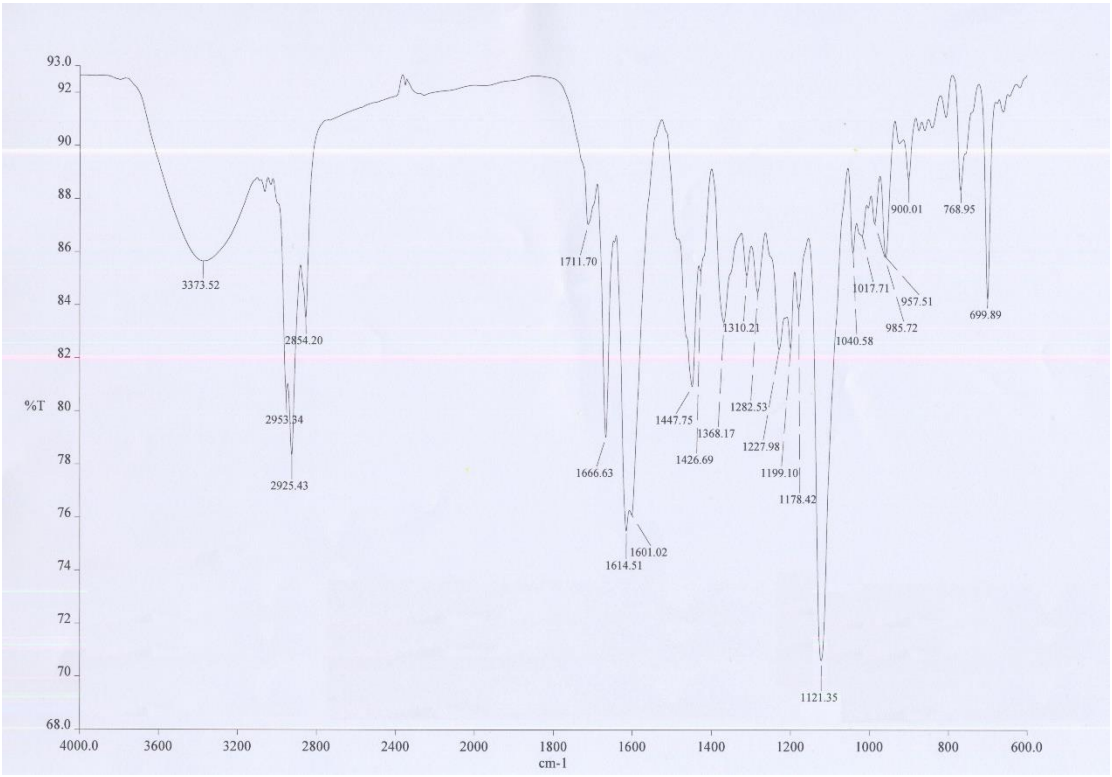


Fig. S9. HR-ESI-Mass of **1**

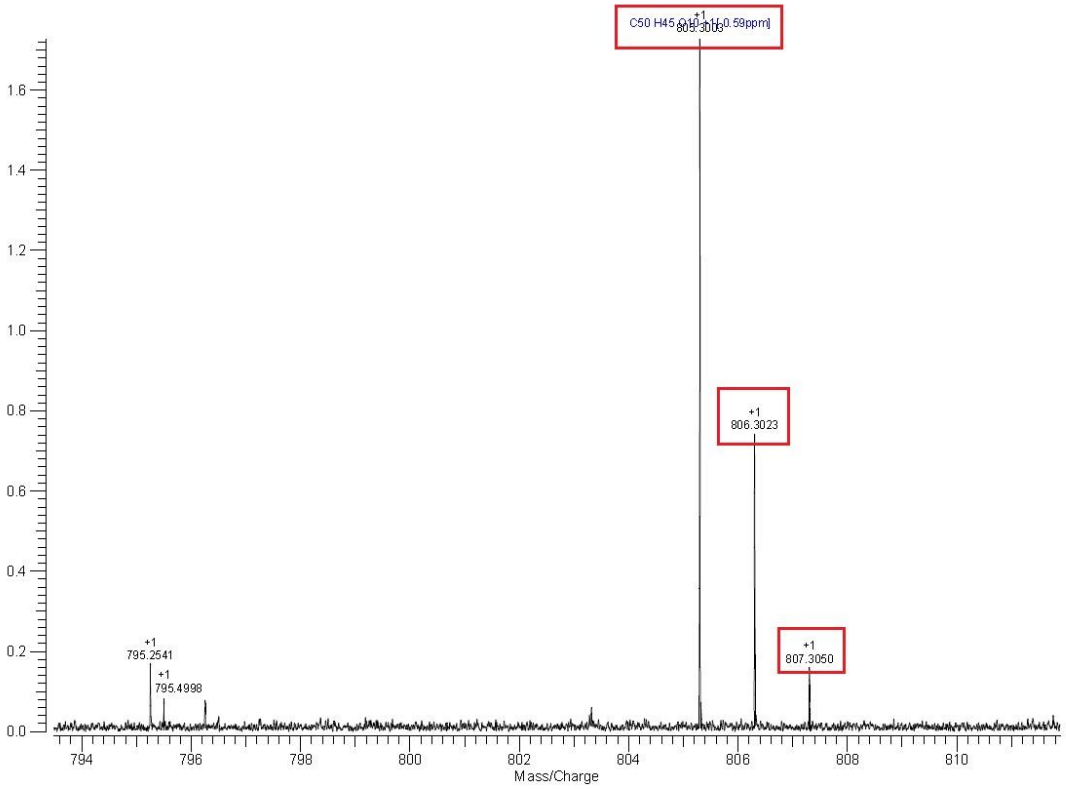



Fig. S10. HR-ESI-Mass of **2**

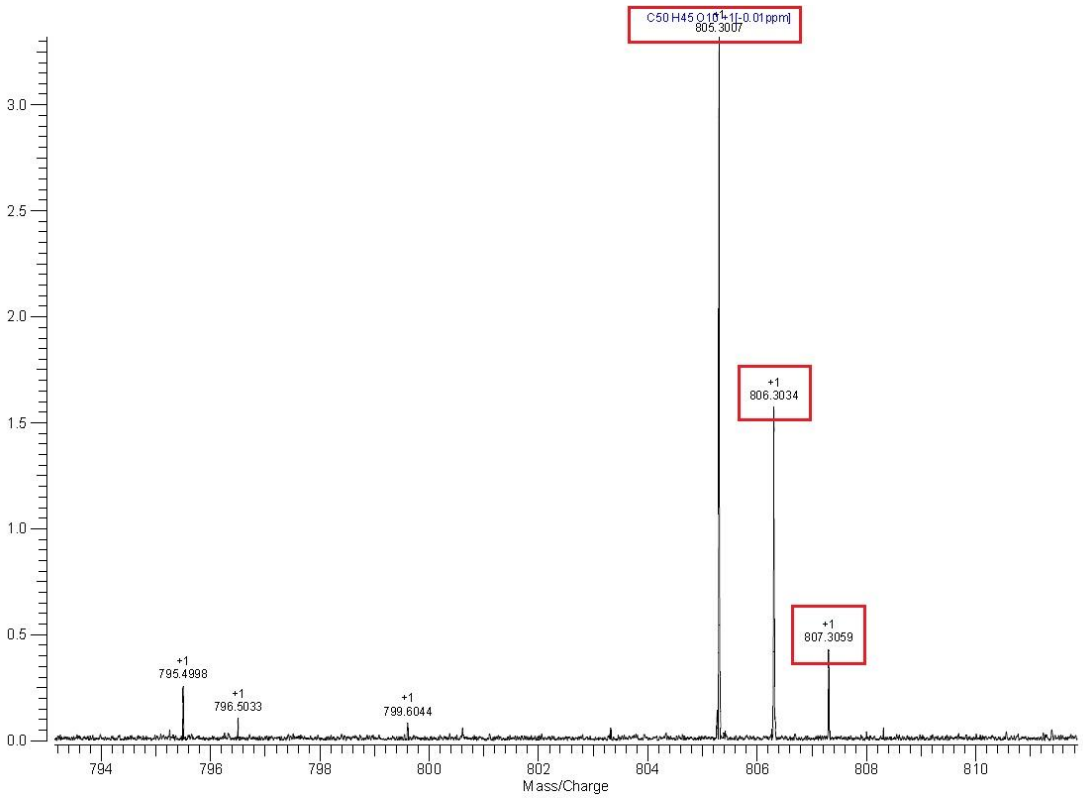


Fig. S11. $^{1}$H NMR spectrum of (**1+2**) in $CDCl_3$ ($^{1}$H: 400 MHz)

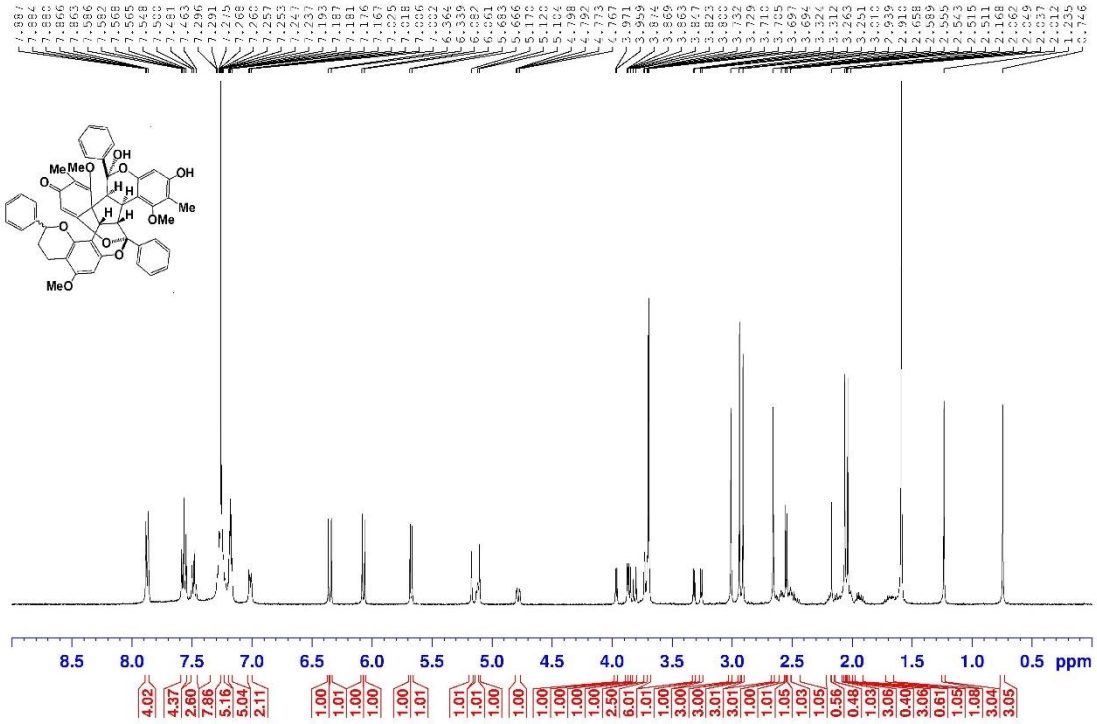



Fig. S12. $^{13}$C & DEPT-135 NMR spectrum of (**1+2**) in $CDCl_3$ ($^{13}$C: 400 MHz)

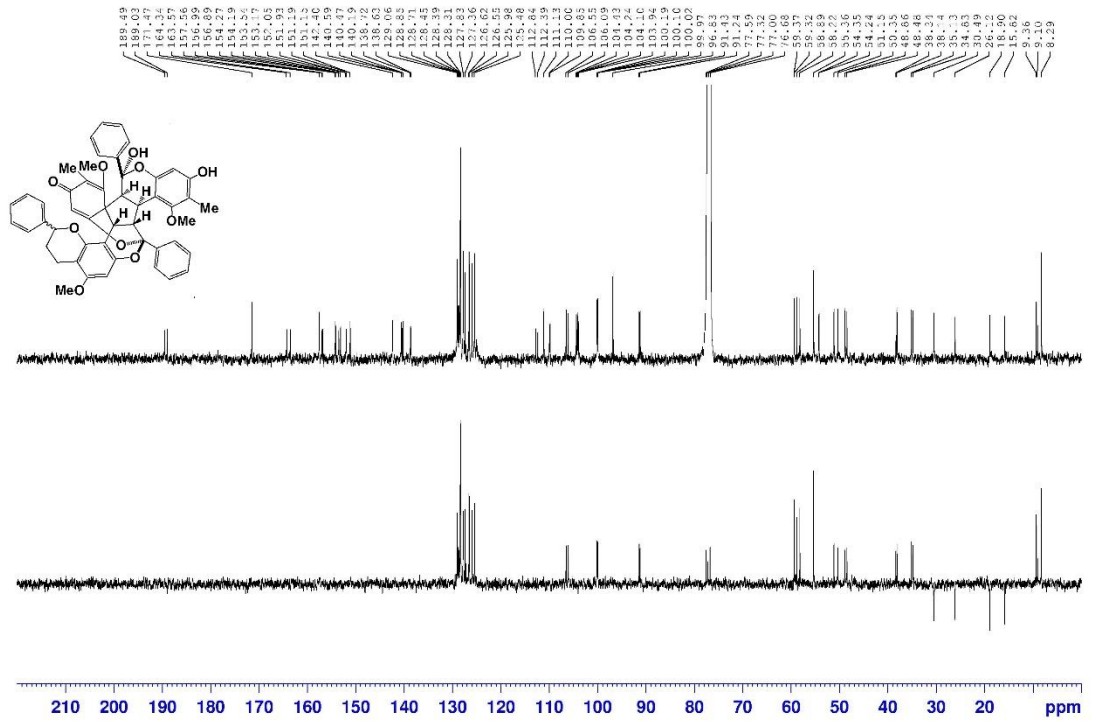


Fig. S13. $^{1}$H NMR spectrum of **1** in $CDCl_3$ ($^{1}$H: 700 MHz)

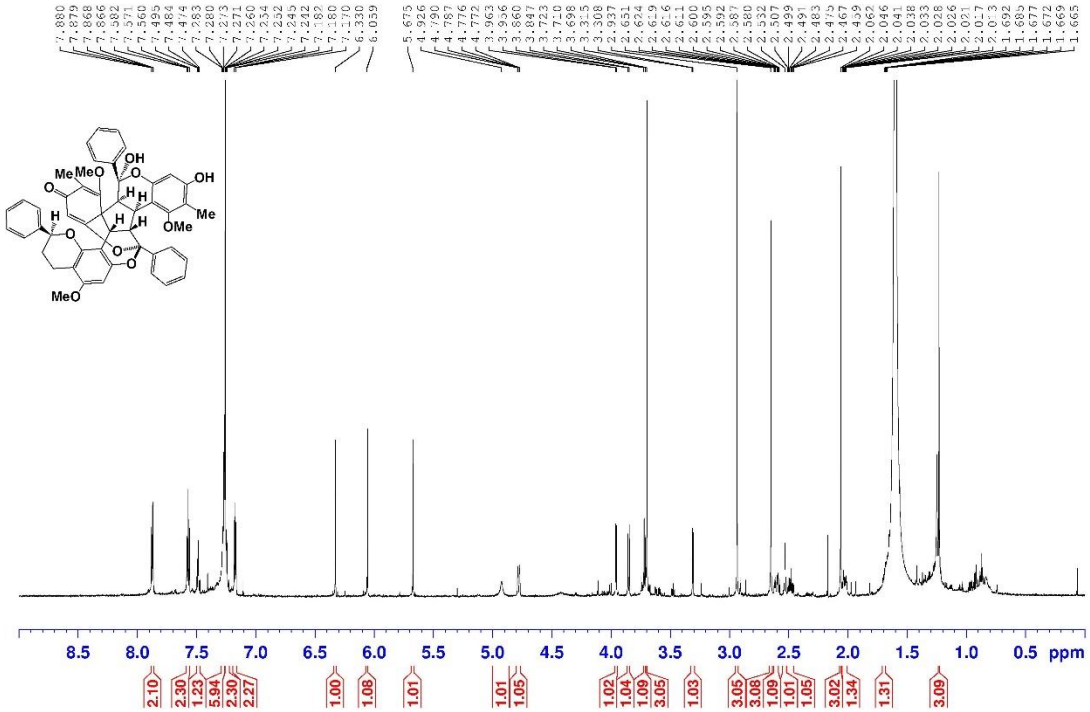



Fig. S13-1.$^{1}$H NMR spectrum of **1** in $d_6$-acetone

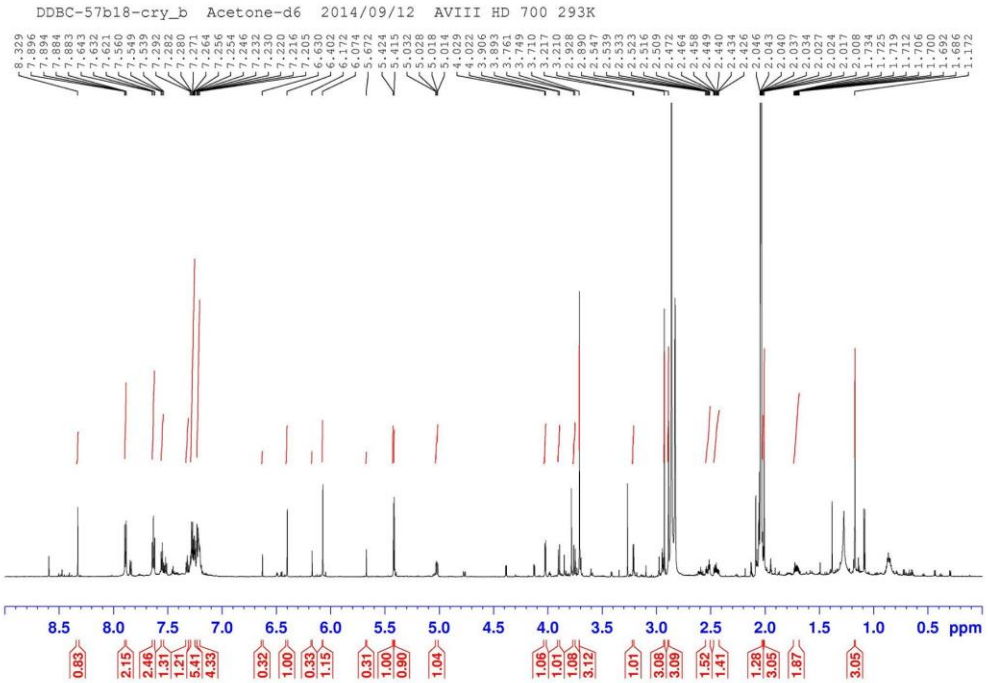


Fig. S14. $^{13}C$ & DEPT-135 NMR spectrum of **1** in $d_6$-Acetone ($^{13}C$: 700 MHz)

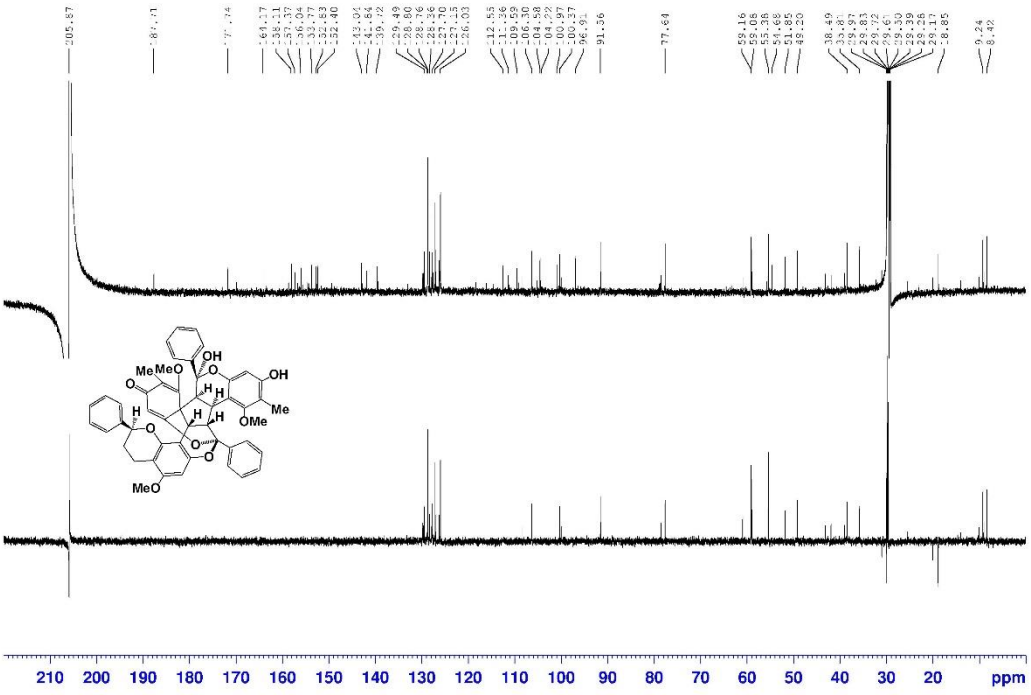



Fig. S15. $^{1}H$-$^{1}H$ COSY spectrum of **1** in $d_6$-Acetone ($^{1}H$: 700 MHz)

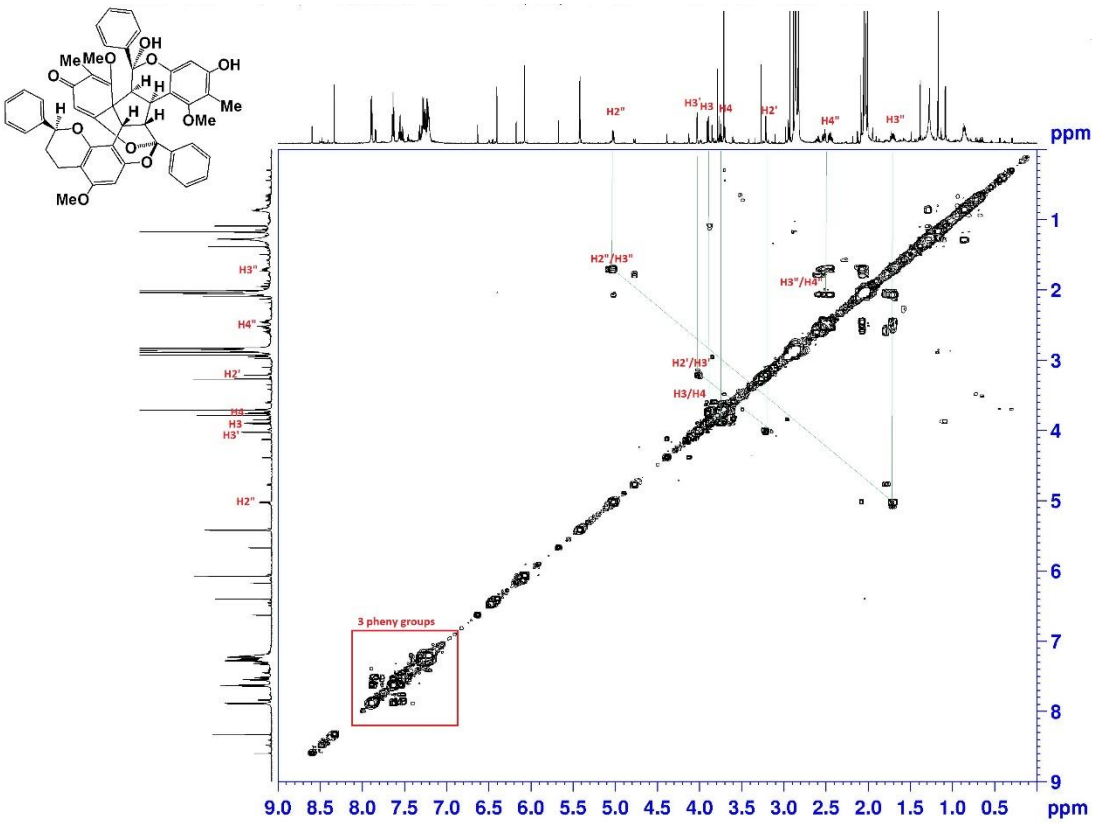


Fig. S16. HSQC spectrum of **1** in $d_6$-Acetone ($^1$H-$^{13}$C: 700 MHz)

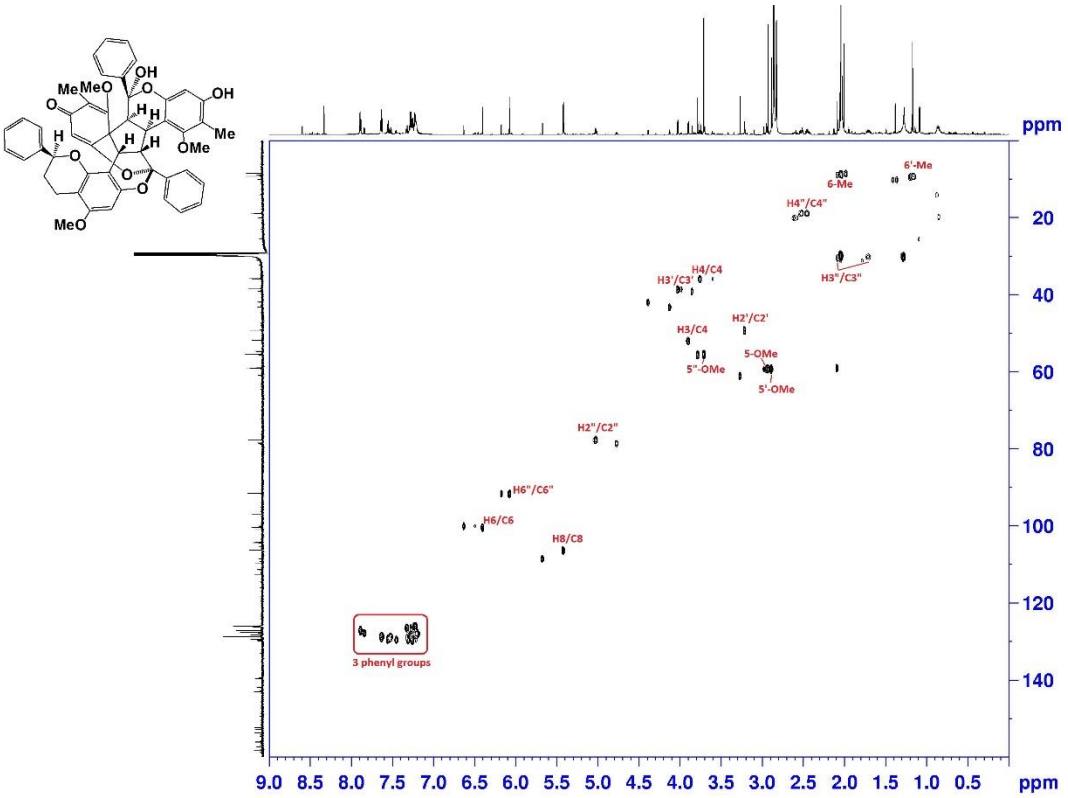



Fig. S17. HMBC spectrum of **1** in $d_6$-Acetone ($^1$H-$^{13}$C: 700 MHz)

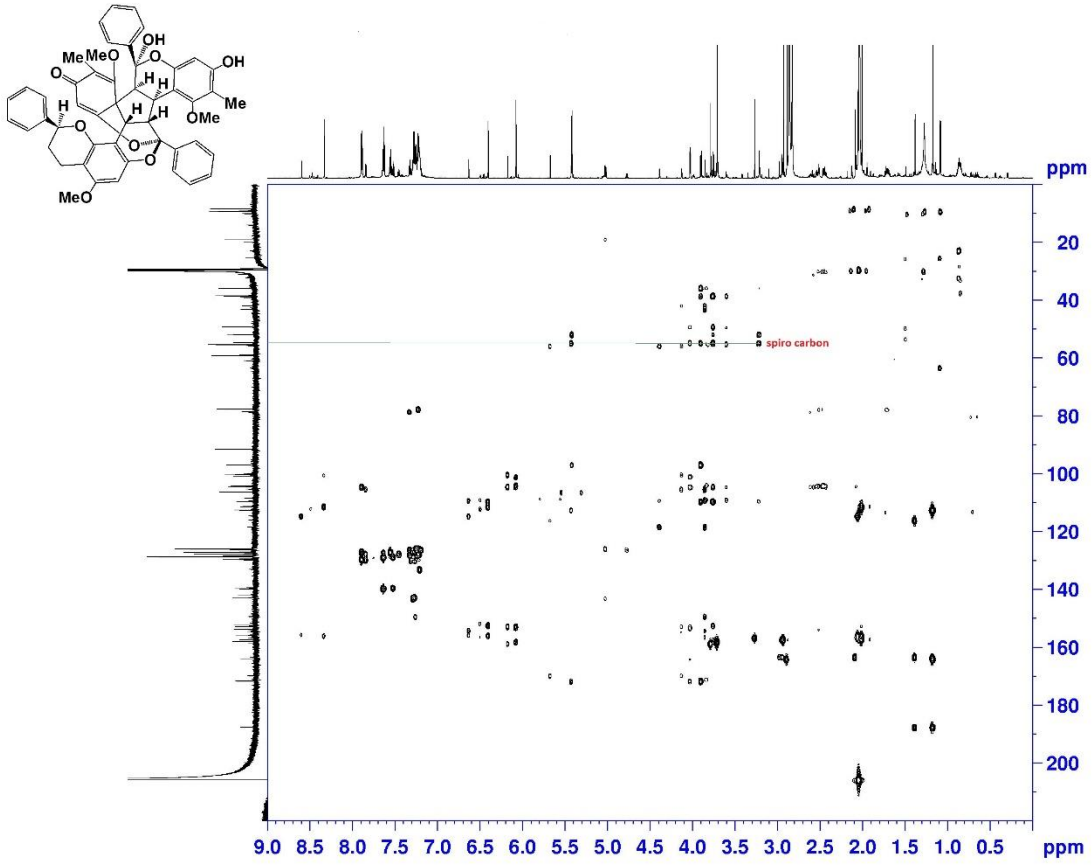


Fig. S18. Key NOESY spectrum of **1** in $CDCl_3$ ($^1H$-$^1H$: 700 MHz)

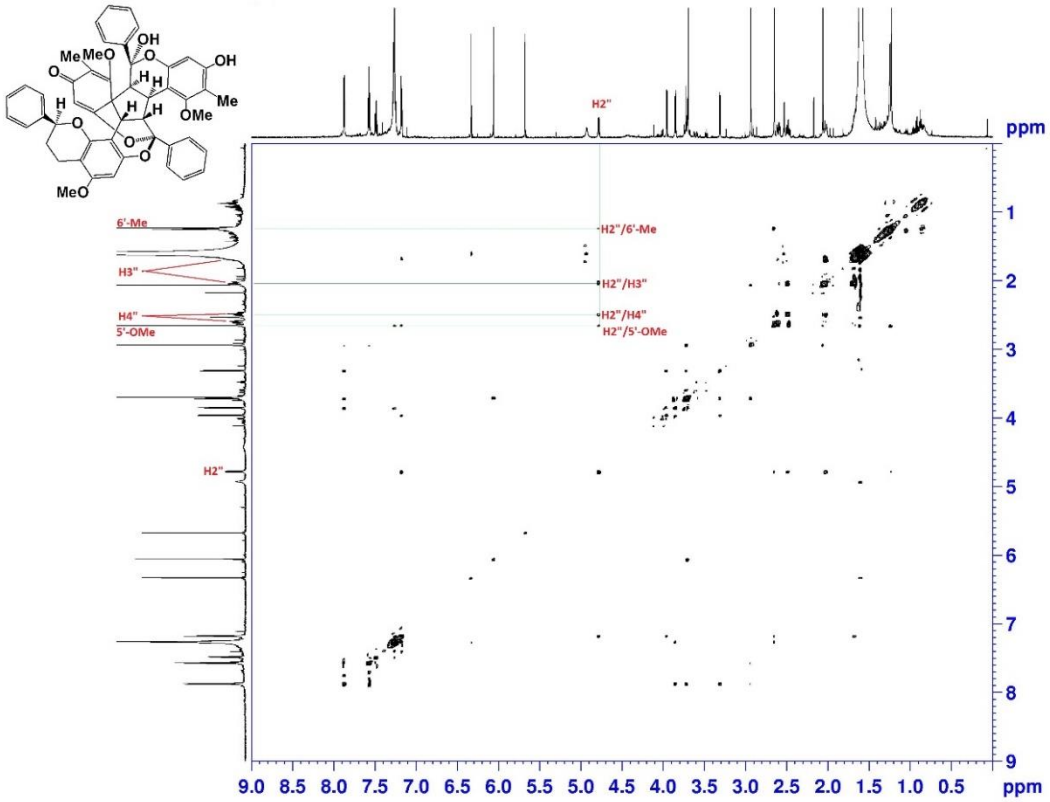



Fig. S19. $^1H$ NMR spectrum of **2** in $CDCl_3$ ($^1H$: 700 MHz)

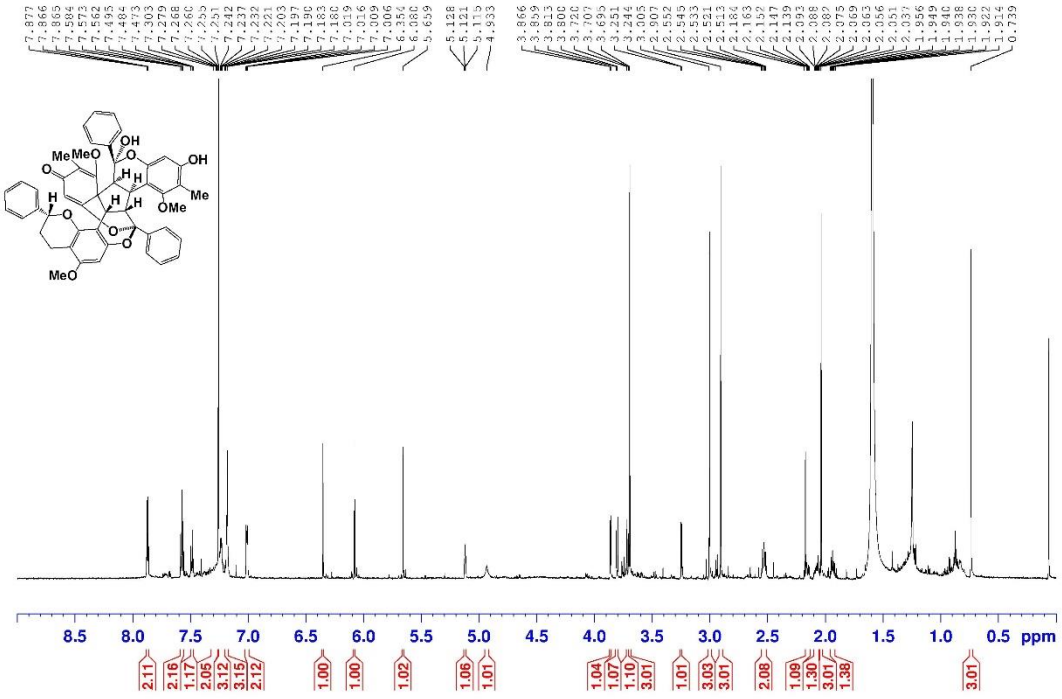


Fig. S19-1. $^{1}$H NMR spectrum of **2** in $d_6$-acetone ($^{1}$H: 700 MHz).

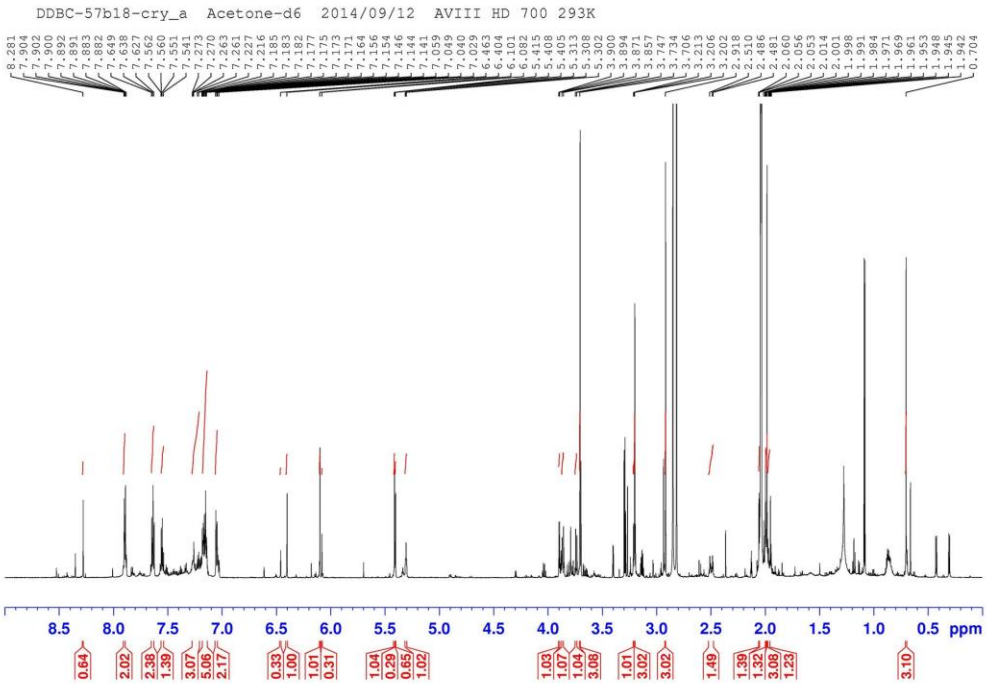



Fig. S20. $^{13}$C & DEPT-135 NMR spectrum of **2** in $d_6$-Acetone ($^{13}$C: 700 MHz)

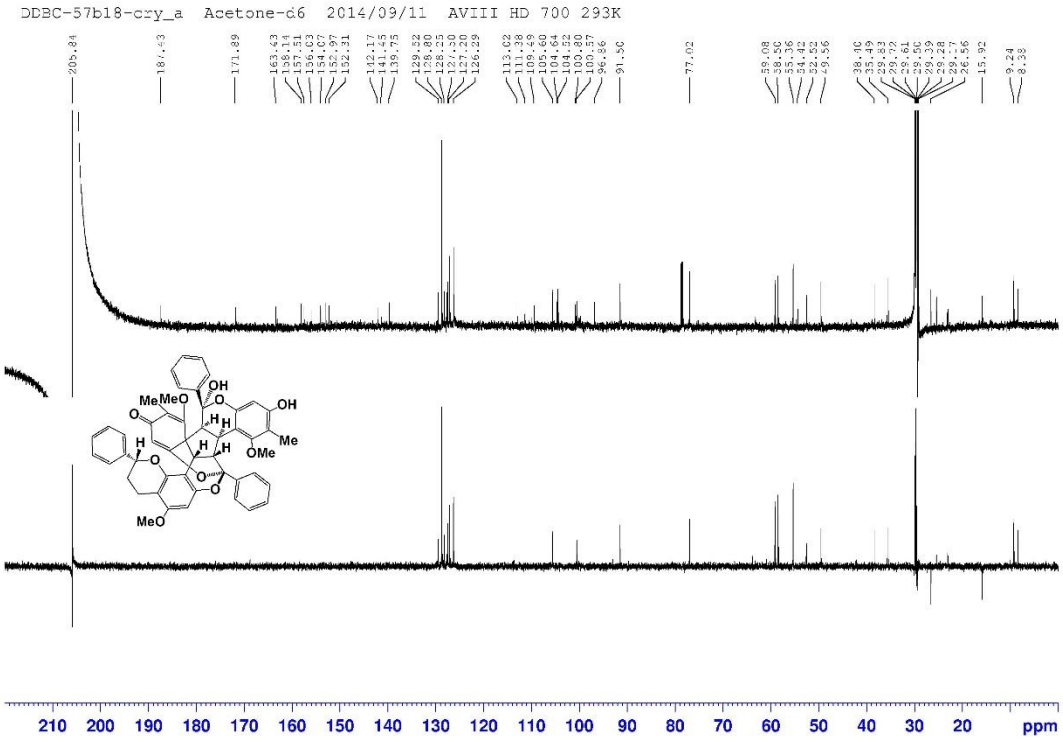


Fig. S21. $^{1}$H-$^{1}$H COSY spectrum of **2** in $d_6$-Acetone ($^{1}$H: 700 MHz)

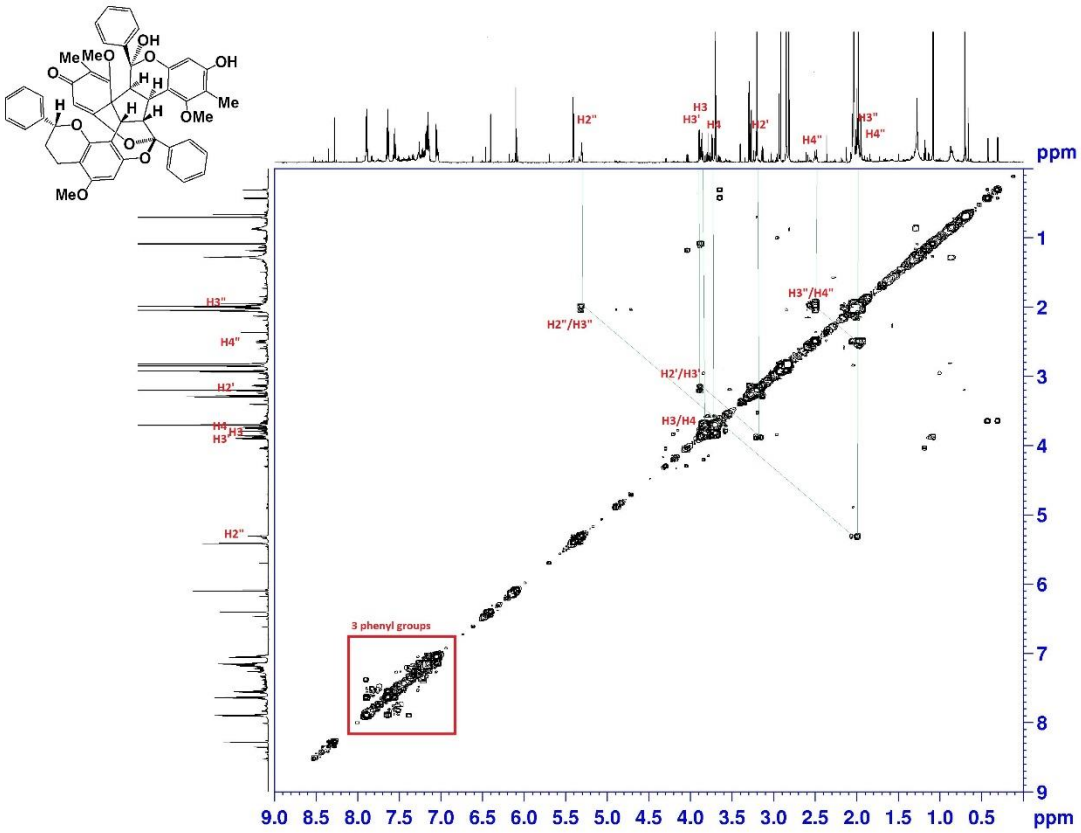



Fig. S22. HSQC spectrum of **2** in d6-Acetone ($^{1}$H-$^{13}$C: 700 MHz)

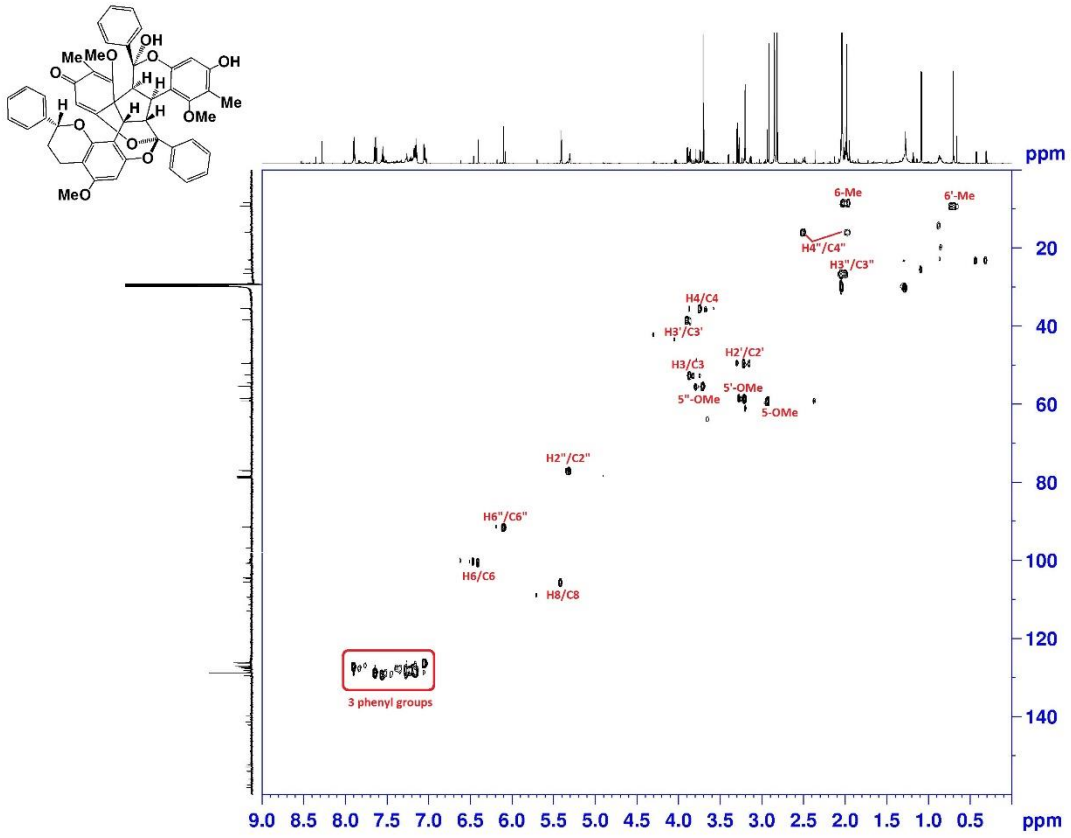


Fig. S23. HMBC spectrum of **2** in $d_6$-Acetone ($^1$H-$^{13}$C: 700 MHz)

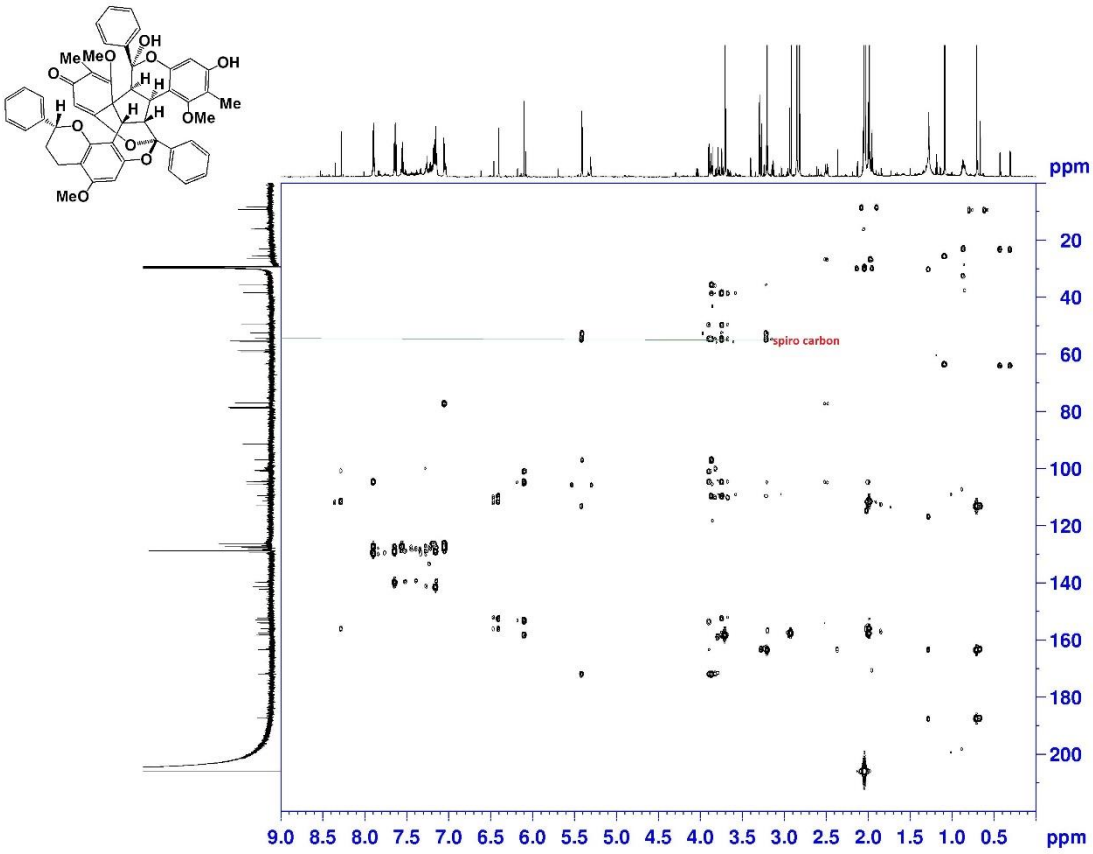


Fig. S24. Key NOESY spectrum of **2** in $CDCl_3$ ($^1H$-$^1H$: 700 MHz)

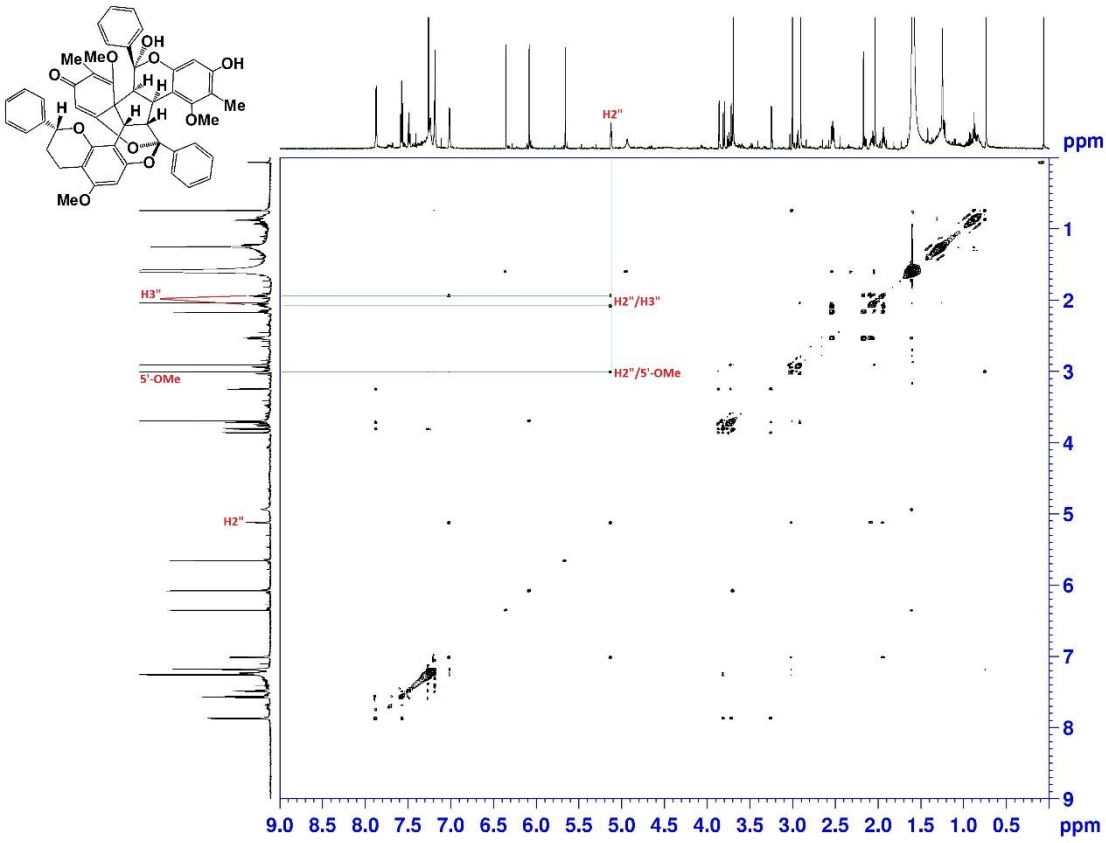


Fig. S25. H2″&6′-Me had NOE on 3.4Å (A1, green); had no NOE on 6.3Å for A2 (red).

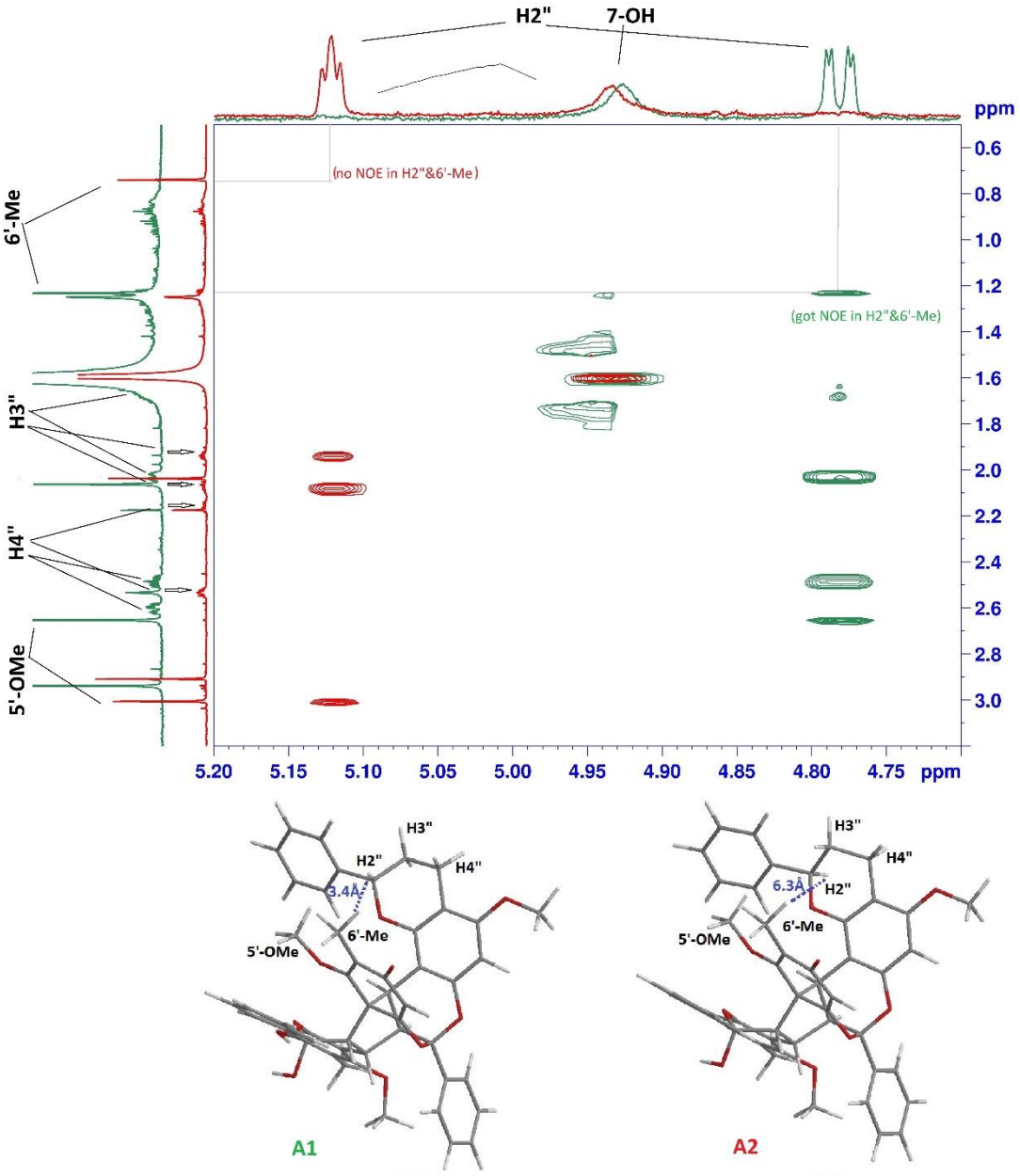


Fig. S26. A1 and A2 would transform to other compounds (quick-dry: collected and then concentrated soon after per inject by chiral-HPLC) shown in $^{1}$H-NMR in $d_6$-acetone.

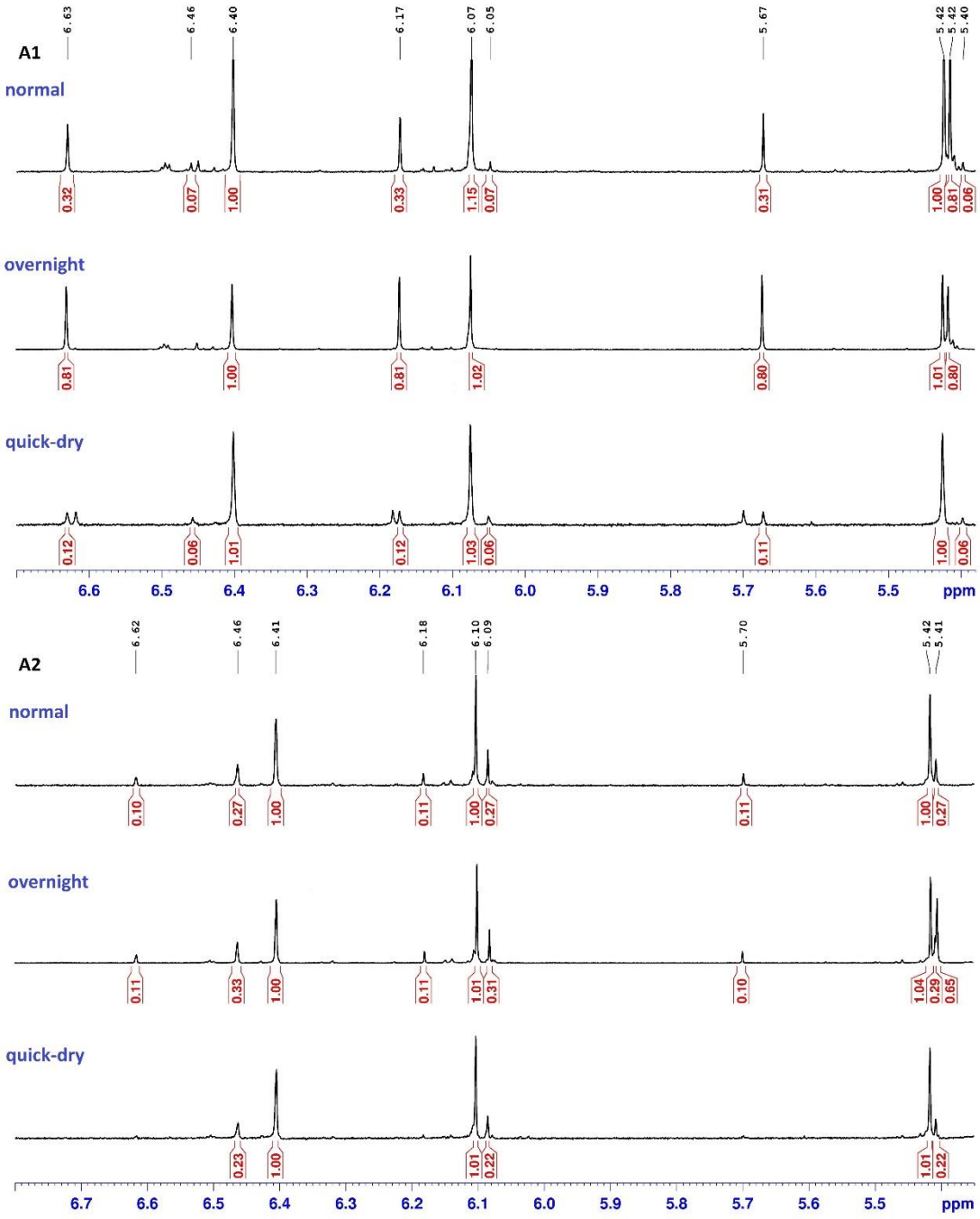


Fig. S27 Biosynthetic pathway of **1** and **2**

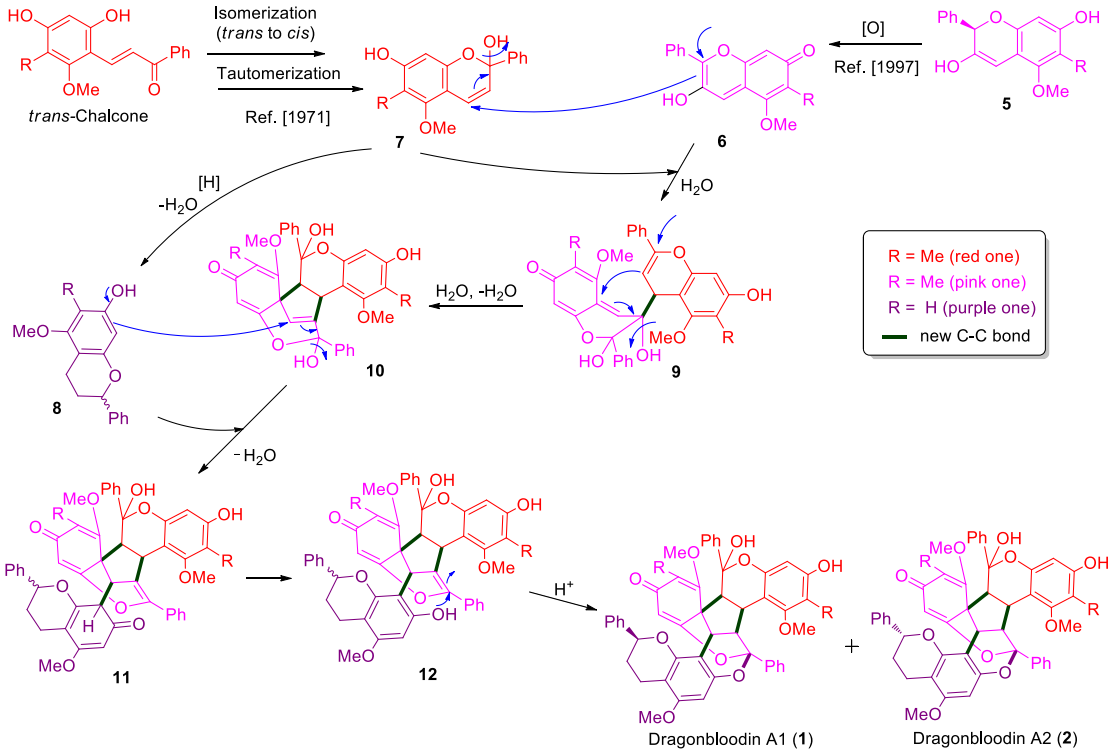



Fig. S28 Effects of dragonbloodin A1 (**1**) on the activities human neutrophil elastase in cell-free system. All data are expressed as the mean ± S.E.M. (n = 3).

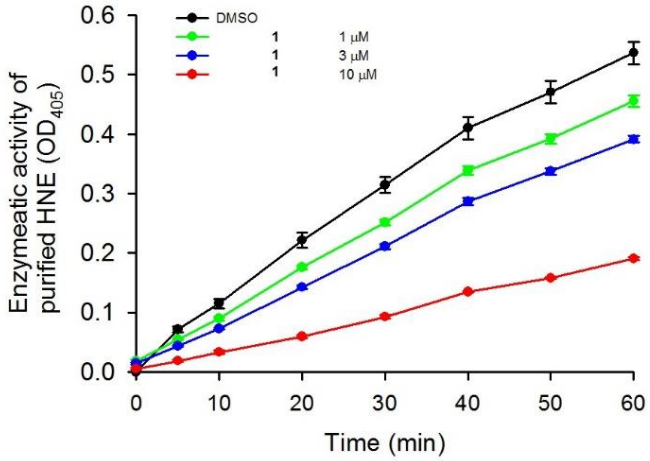


Fig. S29 Effects of dragonbloodin A2 (**2**) on the activities human neutrophil elastase in cell-free system. All data are expressed as the mean ± S.E.M. (n = 3).