# Supporting Information

## Psiguadials A and B, Two Novel Meroterpenoids with Unusual Skeletons from the Leaves of *Psidium guajava*

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# List of Supporting Information

## General Experimental Procedures

All melting points were obtained on an X-5 micro melting point apparatus without correction. Optical rotations were measured on a Jasco P-1020 polarimeter with a 2 mm cell at room temperature. UV spectra were determined on a Jasco V-550 UV/VIS spectrophotometer. IR spectra were recorded on a Jasco FT/IR-480 plus Fourier Transform infrared spectrometer using KBr pellets. ESI-MS spectra were carried out on a Finnigan LCQ Advantage Max ion trap mass spectrometer. HR-EI-MS spectra were acquired on Thermo MAT 95 XP mass spectrometer. NMR spectra were measured on Bruker AV-500 ($^{1}$H: 500 MHz, $^{13}$C: 125 MHz) spectrometer with TMS as internal standard. TLC analyses were carried out using precoated silica gel $GF_{254}$ plates (Qingdao Marine Chemical Plant, Qingdao, P. R. China). Column chromatography was performed on Silica gel (200-300 mesh, Qingdao Marine Chemical Plant, Qingdao, P. R. China), reversed-phase $C_{18}$ silica gel (Merck, Darmstadt, Germany) and Sephadex LH-20 (Pharmacia Biotec AB, Uppsala, Sweden). All solvents used in column chromatography and HPLC were of analytical grade (Shanghai Chemical Plant, Shanghai, P. R. China) and chromatographic grade (Fisher Scientific, New Jersey, U. S. A), respectively.

## Plant material

The air-dried leaves of *Psidium guajava* Linn. were collected from Conghua county, Guangdong Province, P. R. China, in October of 2007, and authenticated by Prof. Shu-Yuan Li (Guangdong Pharmaceutical University). A voucher specimen (No.

2007101801) was deposited in the Institute of Traditional Chinese Medicine & Natural Products, Jinan University, Guangzhou, P. R. China.

**Extraction and Isolation**

The air-dried powdered material (20.0 kg) was percolated with 95 % EtOH for three times at room temperature. After removing the solvent, the alcohol extract (1800.0 g) was suspended in $H_2O$ and extracted by petroleum ether (PE), $CHCl_3$ and *n*-butanol successively to obtain the PE extract (300.0 g), $CHCl_3$ extract (500.0 g) and *n*-butanol extract (700.0 g), respectively. The PE extract was subjected to a silica gel column (200-300 mesh) eluted with PE/EtOAc (100/0 to 1/1; v/v) to obtain nine fractions P1-P9. Fraction P2 (21.0 g) was chromatographed over silica gel column to yield seven subfractions P2a-P2g using PE/EtOAc (100/0 to 100/10; v/v) as solvent system. Subfraction P2b was further separated by silica gel column using PE/EtOAc (100/0 to 100/10; v/v) as solvent system to afford compounds **1** (30 mg) and **2** (25 mg). Subfraction P2d was further chromatographed over silica gel column using the same solvent system to give compounds **3** (20 mg) and **4** (15 mg), respectively.

**Cell lines and cell culture**

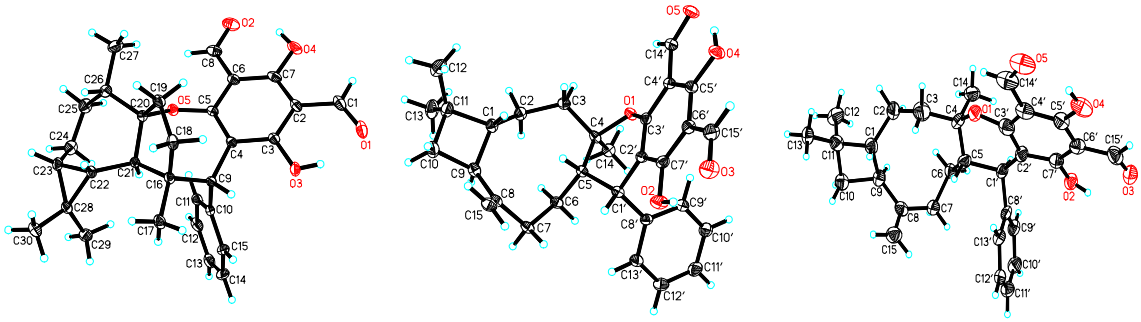
Human hepatoma carcinoma cell line HepG2 was obtained from the American Type Culture Collection. P-glycoprotein-overexpressing drug-resistant cell line HepG2/ADM was kindly provided by Prof. Kwok-Pui Fung (Department of Biochemistry, The Chinese

University of Hong Kong). Both cell lines were cultured in the RPMI 1640 medium, supplemented with 10% NBS (v/v) at 37 ℃ in a humidified atmosphere of 5% $CO_2$ (v/v). HepG2/ADM cell line was maintained in medium with 1.2 μM doxorubicin

**Cell viability assay**

Cells were cultured in 96-well plates for 24 h. After that, cells were treated with compounds **1**-**4** at various concentrations for 72 h. 30 μL of MTT solution (5 mg/mL) was added into each well and incubated for another 4 h. Subsequently, medium was discarded and 100 μL of DMSO was added to dissolve the produced formazan. The absorbance was measured at 570 nm using a microplate Reader (Thermo scientific multiskan MK3, USA). $IC_{50}$ values were calculated from cell survival curves using Prism software.

## Single crystal X-ray data and structures of 1, 3 and 4.



**1** **3** **4**

X-ray data for compound **1**

| | |
|---|---|
| dentification code | pg24 |
| Empirical formula | C30 H34 O5 |
| Formula weight | 474.57 |
| Temperature | 293(2) K |
| Wavelength | 1.54178 A |
| Crystal system, space group | Orthorhombic, P2(1)2(1)2(1) |
| Unit cell dimensions | a = 11.1759(2) A alpha = 90 deg. |
| | b = 13.5506(2) A beta = 90 deg. |
| | c = 15.9913(2) A gamma = 90 deg. |
| Volume | 2421.73(6) A^3 |
| Z, Calculated density | 4, 1.302 Mg/m^3 |
| Absorption coefficient | 0.700 mm^-1 |
| F(000) | 1016 |
| Crystal size | 0.42 x 0.40 x 0.39 mm |
| Theta range for data collection | 4.28 to 63.21 deg. |
| Limiting indices | -12<=h<=12, -14<=k<=15, -17<=l<=18 |
| Reflections collected / unique | 11264 / 3885 [R(int) = 0.0287] |
| Completeness to theta = 63.21 | 99.1 % |
| Max. and min. transmission | 0.7719 and 0.7575 |
| Refinement method | Full-matrix least-squares on F^2 |
| Data / restraints / parameters | 3885 / 0 / 319 |
| Goodness-of-fit on F^2 | 1.086 |
| Final R indices [I>2sigma(I)] | R1 = 0.0405, wR2 = 0.1124 |
| R indices (all data) | R1 = 0.0427, wR2 = 0.1136 |
| Absolute structure parameter | 0.1(2) |
| Largest diff. peak and hole | 0.274 and -0.278 e.A^-3 |

## X-ray data for compound **3**

| | |
|---|---|
| Identification code | pg19 |
| Empirical formula | C30 H34 O5 |
| Formula weight | 474.57 |
| Temperature | 150(2) K |
| Wavelength | 1.54178 A |
| Crystal system, space group | Tetragonal, P4(1)2(1)2 |
| Unit cell dimensions | a = 11.14980(10) A alpha = 90 deg. |
| | b = 11.14980(10) A beta = 90 deg. |
| | c = 40.4482(8) A gamma = 90 deg. |
| Volume | 5028.44(12) A^3 |
| Z, Calculated density | 8, 1.254 Mg/m^3 |
| Absorption coefficient | 0.674 mm^-1 |
| F(000) | 2032 |
| Crystal size | 0.24 x 0.15 x 0.15 mm |
| Theta range for data collection | 4.11 to 62.50 deg. |
| Limiting indices | -12<=h<=12, -12<=k<=11, -44<=l<=46 |
| Reflections collected / unique | 8734 / 3928 [R(int) = 0.0256] |
| Completeness to theta = 62.50 | 98.8 % |
| Max. and min. transmission | 0.9056 and 0.8549 |
| Refinement method | Full-matrix least-squares on F^2 |
| Data / restraints / parameters | 3928 / 0 / 317 |
| Goodness-of-fit on F^2 | 0.964 |
| Final R indices [I>2sigma(I)] | R1 = 0.0312, wR2 = 0.0687 |
| R indices (all data) | R1 = 0.0386, wR2 = 0.0705 |
| Absolute structure parameter | 0.1(2) |
| Largest diff. peak and hole | 0.125 and -0.171 e.A^-3 |

X-ray data for compound **4**

| | |
|---|---|
| Identification code | pg8 |
| Empirical formula | C30 H34 O5 |
| Formula weight | 474.57 |
| Temperature | 293(2) K |
| Wavelength | 1.54178 A |
| Crystal system, space group | Monoclinic, P2(1) |
| Unit cell dimensions | a = 6.5752(10) A alpha = 90 deg. |
| | b = 17.504(3) A beta = 90.862(16) deg. |
| | c = 10.7096(18) A gamma = 90 deg. |
| Volume | 1232.4(3) A^3 |
| Z, Calculated density | 2, 1.279 Mg/m^3 |
| Absorption coefficient | 0.688 mm^-1 |
| F(000) | 508 |
| Crystal size | 0.35 x 0.30 x 0.28 mm |
| Theta range for data collection | 4.13 to 59.97 deg. |
| Limiting indices | -7<=h<=4, -19<=k<=19, -10<=l<=12 |
| Reflections collected / unique | 3122 / 2574 [R(int) = 0.0556] |
| Completeness to theta = 59.97 | 93.6 % |
| Refinement method | Full-matrix least-squares on F^2 |
| Data / restraints / parameters | 2574 / 1 / 316 |
| Goodness-of-fit on F^2 | 1.472 |
| Final R indices [I>2sigma(I)] | R1 = 0.1093, wR2 = 0.3091 |
| R indices (all data) | R1 = 0.1220, wR2 = 0.3317 |
| Absolute structure parameter | 0.0(8) |
| Largest diff. peak and hole | 0.762 and -0.359 e.A^-3 |

The X-ray diffraction data of **1, 3** and **4** were collected on an Oxford Gemini R diffractometer with CuK$\alpha$ radiation ($\lambda$ = 1.54018Å). The crystal structure was solved and refined using the SHELXS-97 software package [1]. In the structure refinements, non-hydrogen atoms were refined anisotropically. Hydrogen atoms bonded to carbons were placed on the geometrically ideal positions by the 'ride on' method. Hydrogen atoms bonded to oxygen were located by the difference Fourier method and were included in the calculation of structure factors with isotropic temperature factors.

Complete lists of refined atomic coordinates and relevant information in standard CIF format for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Center (CCDC no. 774761-774763). These materials are available free of charge via application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (+44) 1223-336033; e-mail: deposit@ccdc.cam.ac.uk].

**Reference**

[1] G. M. Sheldrick SHELXTL, version 5.1: Structure Determination Software Programs Package, Bruker Analytical X-ray Systems, Inc., Madison, WI, USA, 1997.

## Quantum chemical CD data for 1-4

Coordinates and optimized energies of computations (method: B3LYP/6-31G)
Cartesian coordinate of compound 1 optimized:
Standard orientation:

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) X | Y | Z |
|---|---|---|---|---|---|
| 1 | 6 | 0 | -1.701727 | -2.855290 | -0.138689 |
| 2 | 1 | 0 | -2.505823 | -2.936704 | -0.879589 |
| 3 | 6 | 0 | -0.848613 | -4.129197 | -0.273146 |
| 4 | 1 | 0 | -1.484673 | -5.014786 | -0.162589 |
| 5 | 1 | 0 | -0.354881 | -4.199610 | -1.247639 |
| 6 | 1 | 0 | -0.076183 | -4.185852 | 0.498686 |
| 7 | 6 | 0 | -0.939009 | -1.569753 | -0.550476 |
| 8 | 6 | 0 | -0.425655 | -1.643641 | -2.015664 |
| 9 | 1 | 0 | -1.021728 | -2.378692 | -2.565558 |
| 10 | 1 | 0 | 0.608126 | -1.997753 | -2.049980 |
| 11 | 6 | 0 | -0.598286 | -0.235834 | -2.627402 |
| 12 | 1 | 0 | -1.382877 | -0.250165 | -3.392580 |
| 13 | 1 | 0 | 0.312857 | 0.121884 | -3.119289 |
| 14 | 6 | 0 | -1.025024 | 0.704451 | -1.466793 |
| 15 | 6 | 0 | -1.906086 | 1.849981 | -1.991839 |
| 16 | 1 | 0 | -2.799987 | 1.461932 | -2.488434 |
| 17 | 1 | 0 | -2.230452 | 2.520737 | -1.191600 |
| 18 | 1 | 0 | -1.354335 | 2.449793 | -2.726480 |
| 19 | 6 | 0 | 0.267911 | 1.334748 | -0.827179 |
| 20 | 1 | 0 | 0.646225 | 1.988139 | -1.617249 |
| 21 | 6 | 0 | 0.006890 | 2.258723 | 0.371309 |
| 22 | 6 | 0 | -0.093440 | 1.784959 | 1.689156 |
| 23 | 1 | 0 | 0.034733 | 0.726617 | 1.894452 |
| 24 | 6 | 0 | -0.334546 | 2.657482 | 2.751851 |
| 25 | 1 | 0 | -0.406955 | 2.264185 | 3.762690 |
| 26 | 6 | 0 | -0.467643 | 4.027853 | 2.522837 |
| 27 | 1 | 0 | -0.648807 | 4.707484 | 3.351183 |
| 28 | 6 | 0 | -0.349015 | 4.517427 | 1.222004 |
| 29 | 1 | 0 | -0.431000 | 5.584129 | 1.029838 |
| 30 | 6 | 0 | -0.111019 | 3.640784 | 0.162496 |
| 31 | 1 | 0 | -0.002747 | 4.036485 | -0.844098 |

| | | | | | |
|---|---|---|---|---|---|
| 32 | 6 | 0 | 1.433051 | 0.395022 | -0.516591 |
| 33 | 6 | 0 | 2.735119 | 0.902370 | -0.765560 |
| 34 | 8 | 0 | 2.837916 | 2.077436 | -1.386354 |
| 35 | 1 | 0 | 3.817657 | 2.280274 | -1.478359 |
| 36 | 6 | 0 | 3.923931 | 0.223247 | -0.373055 |
| 37 | 6 | 0 | 5.222486 | 0.793395 | -0.657143 |
| 38 | 1 | 0 | 6.098777 | 0.219556 | -0.321206 |
| 39 | 8 | 0 | 5.389552 | 1.872368 | -1.248028 |
| 40 | 6 | 0 | 3.800043 | -0.997028 | 0.325391 |
| 41 | 8 | 0 | 4.906971 | -1.618158 | 0.727370 |
| 42 | 1 | 0 | 4.610964 | -2.453401 | 1.202889 |
| 43 | 6 | 0 | 2.518344 | -1.545537 | 0.579513 |
| 44 | 6 | 0 | 2.423923 | -2.776975 | 1.329557 |
| 45 | 1 | 0 | 1.416486 | -3.148126 | 1.556534 |
| 46 | 8 | 0 | 3.409083 | -3.414398 | 1.741361 |
| 47 | 6 | 0 | 1.353314 | -0.846824 | 0.118954 |
| 48 | 8 | 0 | 0.183830 | -1.471465 | 0.404766 |
| 49 | 6 | 0 | -1.766438 | -0.249630 | -0.483755 |
| 50 | 1 | 0 | -1.697657 | 0.145975 | 0.528631 |
| 51 | 6 | 0 | -3.239130 | -0.487606 | -0.802651 |
| 52 | 1 | 0 | -3.438215 | -0.744394 | -1.843902 |
| 53 | 6 | 0 | -4.390420 | 0.223892 | -0.096779 |
| 54 | 6 | 0 | -4.168514 | 1.334369 | 0.918519 |
| 55 | 1 | 0 | -4.113282 | 2.307380 | 0.414974 |
| 56 | 1 | 0 | -5.011270 | 1.376216 | 1.620664 |
| 57 | 1 | 0 | -3.255394 | 1.225490 | 1.507601 |
| 58 | 6 | 0 | -5.634065 | 0.462023 | -0.942637 |
| 59 | 1 | 0 | -5.801458 | -0.352477 | -1.656883 |
| 60 | 1 | 0 | -6.528547 | 0.539193 | -0.310843 |
| 61 | 1 | 0 | -5.550451 | 1.396121 | -1.513409 |
| 62 | 6 | 0 | -4.078984 | -1.226450 | 0.228246 |
| 63 | 1 | 0 | -4.789039 | -1.950889 | -0.173040 |
| 64 | 6 | 0 | -3.394518 | -1.688425 | 1.504329 |
| 65 | 1 | 0 | -2.888432 | -0.848516 | 1.987486 |
| 66 | 1 | 0 | -4.145415 | -2.030471 | 2.228070 |
| 67 | 6 | 0 | -2.373104 | -2.829169 | 1.253304 |
| 68 | 1 | 0 | -2.882406 | -3.795693 | 1.364417 |
| 69 | 1 | 0 | -1.601279 | -2.806507 | 2.033038 |

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**Cartesian coordinate of compound 2 optimized:**

Standard orientation:

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) X | Y | Z |
|---|---|---|---|---|---|
| 1 | 6 | 0 | 3.184757 | 0.259166 | 1.536143 |
| 2 | 6 | 0 | 4.052804 | 0.003207 | 2.780967 |
| 3 | 1 | 0 | 4.892552 | 0.706475 | 2.826544 |
| 4 | 1 | 0 | 3.465840 | 0.120543 | 3.699869 |
| 5 | 1 | 0 | 4.468327 | -1.011027 | 2.781079 |
| 6 | 6 | 0 | 4.032804 | 0.168283 | 0.230766 |
| 7 | 1 | 0 | 3.934241 | 1.127099 | -0.291200 |
| 8 | 6 | 0 | 5.539547 | -0.205827 | 0.123428 |
| 9 | 1 | 0 | 6.270927 | 0.608085 | 0.185944 |
| 10 | 1 | 0 | 5.831784 | -0.995135 | 0.824305 |
| 11 | 6 | 0 | 5.237977 | -0.804481 | -1.294799 |
| 12 | 6 | 0 | 5.459297 | 0.210852 | -2.423360 |
| 13 | 1 | 0 | 5.046963 | -0.156839 | -3.371278 |
| 14 | 1 | 0 | 4.996589 | 1.181770 | -2.214531 |
| 15 | 1 | 0 | 6.531732 | 0.384578 | -2.575619 |
| 16 | 6 | 0 | 5.932452 | -2.124009 | -1.631619 |
| 17 | 1 | 0 | 5.795019 | -2.862938 | -0.833221 |
| 18 | 1 | 0 | 5.536573 | -2.556121 | -2.560151 |
| 19 | 1 | 0 | 7.011586 | -1.978661 | -1.770371 |
| 20 | 6 | 0 | 3.746919 | -0.923833 | -0.817192 |
| 21 | 1 | 0 | 3.667879 | -1.898999 | -0.315889 |
| 22 | 6 | 0 | 2.508657 | -0.723570 | -1.679334 |
| 23 | 1 | 0 | 2.545547 | -1.357198 | -2.576422 |
| 24 | 1 | 0 | 2.461322 | 0.312173 | -2.040869 |
| 25 | 6 | 0 | 1.223092 | -1.112422 | -0.917724 |
| 26 | 1 | 0 | 1.255984 | -2.197779 | -0.759007 |
| 27 | 1 | 0 | 0.359276 | -0.936718 | -1.567782 |
| 28 | 6 | 0 | 0.906875 | -0.532576 | 0.492867 |
| 29 | 8 | 0 | -0.201034 | -1.369249 | 0.975516 |
| 30 | 6 | 0 | -1.429497 | -1.201142 | 0.430080 |
| 31 | 6 | 0 | -2.323107 | -2.289682 | 0.607335 |
| 32 | 6 | 0 | -1.879160 | -3.483916 | 1.356427 |
| 33 | 1 | 0 | -0.830464 | -3.428148 | 1.703395 |
| 34 | 8 | 0 | -2.553542 | -4.468421 | 1.602918 |
| 35 | 6 | 0 | -3.604882 | -2.191925 | 0.017599 |

| | | | | | |
|---|---|---|---|---|---|
| 36 | 8 | 0 | -4.469380 | -3.186789 | 0.157693 |
| 37 | 1 | 0 | -5.295317 | -2.930966 | -0.343374 |
| 38 | 6 | 0 | -3.964733 | -1.039550 | -0.743273 |
| 39 | 6 | 0 | -5.273259 | -0.952197 | -1.356924 |
| 40 | 1 | 0 | -5.496680 | -0.033107 | -1.918921 |
| 41 | 8 | 0 | -6.136647 | -1.839512 | -1.279233 |
| 42 | 6 | 0 | -3.034727 | 0.020816 | -0.866576 |
| 43 | 8 | 0 | -3.440090 | 1.070281 | -1.621105 |
| 44 | 1 | 0 | -2.859070 | 1.837858 | -1.469459 |
| 45 | 6 | 0 | -1.770927 | -0.014726 | -0.257576 |
| 46 | 6 | 0 | -0.790006 | 1.156513 | -0.363983 |
| 47 | 1 | 0 | -0.391773 | 1.201723 | -1.389621 |
| 48 | 6 | 0 | -1.434112 | 2.516746 | -0.082204 |
| 49 | 6 | 0 | -2.205206 | 2.731449 | 1.072308 |
| 50 | 1 | 0 | -2.384015 | 1.905468 | 1.755536 |
| 51 | 6 | 0 | -2.754519 | 3.983763 | 1.339498 |
| 52 | 1 | 0 | -3.350075 | 4.129282 | 2.236578 |
| 53 | 6 | 0 | -2.549092 | 5.047620 | 0.455894 |
| 54 | 1 | 0 | -2.983447 | 6.021429 | 0.663646 |
| 55 | 6 | 0 | -1.791167 | 4.848973 | -0.696884 |
| 56 | 1 | 0 | -1.627832 | 5.667185 | -1.392867 |
| 57 | 6 | 0 | -1.237001 | 3.592838 | -0.961674 |
| 58 | 1 | 0 | -0.640132 | 3.446009 | -1.859665 |
| 59 | 6 | 0 | 0.396849 | 0.917802 | 0.600049 |
| 60 | 1 | 0 | -0.016778 | 0.980592 | 1.617614 |
| 61 | 6 | 0 | 1.523895 | 1.956853 | 0.532415 |
| 62 | 1 | 0 | 1.104003 | 2.958494 | 0.674942 |
| 63 | 1 | 0 | 1.985932 | 1.958576 | -0.462870 |
| 64 | 6 | 0 | 2.572511 | 1.681562 | 1.623377 |
| 65 | 1 | 0 | 2.095575 | 1.810663 | 2.605664 |
| 66 | 1 | 0 | 3.376104 | 2.427809 | 1.567708 |
| 67 | 6 | 0 | 2.012732 | -0.763386 | 1.544334 |
| 68 | 1 | 0 | 2.388437 | -1.789149 | 1.458586 |
| 69 | 1 | 0 | 1.520295 | -0.702712 | 2.523215 |

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**Cartesian coordinate of compound 3 optimized:**

Standard orientation:

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) X | Y | Z |
|---|---|---|---|---|---|
| 1 | 6 | 0 | 6.066531 | 0.145161 | -0.451935 |
| 2 | 1 | 0 | 6.742438 | 0.856689 | 0.035051 |
| 3 | 1 | 0 | 6.446501 | -0.069306 | -1.456630 |
| 4 | 6 | 0 | 4.557188 | 0.496648 | -0.481488 |
| 5 | 1 | 0 | 4.312901 | 1.100213 | 0.404911 |
| 6 | 6 | 0 | 3.950497 | 1.145805 | -1.702379 |
| 7 | 6 | 0 | 4.660927 | 1.909011 | -2.539124 |
| 8 | 1 | 0 | 5.722275 | 2.092058 | -2.392852 |
| 9 | 1 | 0 | 4.204038 | 2.381440 | -3.405522 |
| 10 | 6 | 0 | 2.485877 | 0.852313 | -1.927424 |
| 11 | 1 | 0 | 2.133422 | 1.349889 | -2.838920 |
| 12 | 1 | 0 | 2.387191 | -0.224749 | -2.117094 |
| 13 | 6 | 0 | 1.571125 | 1.236531 | -0.737187 |
| 14 | 1 | 0 | 2.141140 | 1.213559 | 0.195287 |
| 15 | 1 | 0 | 1.271446 | 2.279837 | -0.850820 |
| 16 | 6 | 0 | 0.330920 | 0.322727 | -0.608860 |
| 17 | 1 | 0 | 0.253928 | -0.248551 | -1.544631 |
| 18 | 6 | 0 | -1.046836 | 1.070278 | -0.540226 |
| 19 | 1 | 0 | -1.166320 | 1.504779 | -1.541505 |
| 20 | 6 | 0 | -1.194530 | 2.262603 | 0.418396 |
| 21 | 6 | 0 | -1.824105 | 2.165705 | 1.666922 |
| 22 | 1 | 0 | -2.247244 | 1.216745 | 1.982536 |
| 23 | 6 | 0 | -1.956659 | 3.276451 | 2.501209 |
| 24 | 1 | 0 | -2.450367 | 3.167840 | 3.463465 |
| 25 | 6 | 0 | -1.474838 | 4.521805 | 2.097705 |
| 26 | 1 | 0 | -1.580283 | 5.388179 | 2.744981 |
| 27 | 6 | 0 | -0.882776 | 4.647378 | 0.840797 |
| 28 | 1 | 0 | -0.532947 | 5.616631 | 0.495160 |
| 29 | 6 | 0 | -0.757688 | 3.532898 | 0.011164 |
| 30 | 1 | 0 | -0.340015 | 3.661910 | -0.984240 |
| 31 | 6 | 0 | -2.137075 | 0.028604 | -0.388155 |
| 32 | 6 | 0 | -3.462619 | 0.327965 | -0.766198 |
| 33 | 8 | 0 | -3.708539 | 1.551812 | -1.226799 |
| 34 | 1 | 0 | -4.687750 | 1.592988 | -1.443894 |
| 35 | 6 | 0 | -4.519095 | -0.626328 | -0.682454 |

| | | | | | |
|---|---|---|---|---|---|
| 36 | 6 | 0 | -5.859774 | -0.262938 | -1.080118 |
| 37 | 1 | 0 | -6.632134 | -1.041480 | -0.989751 |
| 38 | 8 | 0 | -6.171360 | 0.859929 | -1.509249 |
| 39 | 6 | 0 | -4.213595 | -1.927225 | -0.220316 |
| 40 | 8 | 0 | -5.196256 | -2.822017 | -0.137020 |
| 41 | 1 | 0 | -4.782340 | -3.672879 | 0.202559 |
| 42 | 6 | 0 | -2.887508 | -2.269902 | 0.144581 |
| 43 | 6 | 0 | -2.603024 | -3.604575 | 0.614448 |
| 44 | 1 | 0 | -1.563351 | -3.826297 | 0.895621 |
| 45 | 8 | 0 | -3.461683 | -4.498205 | 0.717897 |
| 46 | 6 | 0 | -1.866169 | -1.270840 | 0.039865 |
| 47 | 8 | 0 | -0.633179 | -1.699197 | 0.364416 |
| 48 | 6 | 0 | 0.509185 | -0.768373 | 0.475979 |
| 49 | 6 | 0 | 0.513929 | -0.277453 | 1.928105 |
| 50 | 1 | 0 | 0.767136 | -1.104839 | 2.599081 |
| 51 | 1 | 0 | 1.238454 | 0.525785 | 2.085528 |
| 52 | 1 | 0 | -0.462995 | 0.105829 | 2.217996 |
| 53 | 6 | 0 | 1.703379 | -1.735578 | 0.209883 |
| 54 | 1 | 0 | 1.771946 | -1.929777 | -0.867026 |
| 55 | 1 | 0 | 1.368582 | -2.679567 | 0.652669 |
| 56 | 6 | 0 | 3.113569 | -1.429150 | 0.799069 |
| 57 | 1 | 0 | 3.454181 | -2.360923 | 1.269335 |
| 58 | 1 | 0 | 3.041278 | -0.711032 | 1.623049 |
| 59 | 6 | 0 | 4.238740 | -1.002062 | -0.158101 |
| 60 | 1 | 0 | 4.140268 | -1.556872 | -1.101645 |
| 61 | 6 | 0 | 5.730226 | -1.159117 | 0.330883 |
| 62 | 6 | 0 | 5.915422 | -0.965420 | 1.842504 |
| 63 | 1 | 0 | 6.983185 | -0.882397 | 2.080016 |
| 64 | 1 | 0 | 5.426727 | -0.054880 | 2.208102 |
| 65 | 1 | 0 | 5.516325 | -1.811969 | 2.414023 |
| 66 | 6 | 0 | 6.440639 | -2.431322 | -0.131205 |
| 67 | 1 | 0 | 6.351135 | -2.566003 | -1.215723 |
| 68 | 1 | 0 | 7.509936 | -2.399405 | 0.115169 |
| 69 | 1 | 0 | 6.018277 | -3.321619 | 0.353711 |

---

**Cartesian coordinate of compound 4 optimized:**

Standard orientation:

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) X | Y | Z |
|---|---|---|---|---|---|
| 1 | 6 | 0 | -5.741129 | 0.486129 | -0.553093 |
| 2 | 1 | 0 | -5.808407 | 0.647067 | -1.634265 |
| 3 | 1 | 0 | -6.511437 | 1.090350 | -0.060845 |
| 4 | 6 | 0 | -4.288615 | 0.638140 | -0.026762 |
| 5 | 1 | 0 | -4.342986 | 0.826095 | 1.052984 |
| 6 | 6 | 0 | -3.282890 | 1.588819 | -0.630609 |
| 7 | 6 | 0 | -3.229209 | 1.869450 | -1.937781 |
| 8 | 1 | 0 | -3.936915 | 1.454756 | -2.651275 |
| 9 | 1 | 0 | -2.473651 | 2.537389 | -2.343792 |
| 10 | 6 | 0 | -2.308340 | 2.206233 | 0.350913 |
| 11 | 1 | 0 | -1.605570 | 2.860567 | -0.174072 |
| 12 | 1 | 0 | -2.877510 | 2.848531 | 1.041005 |
| 13 | 6 | 0 | -1.540897 | 1.181396 | 1.216302 |
| 14 | 1 | 0 | -1.070486 | 1.721578 | 2.046803 |
| 15 | 1 | 0 | -2.267773 | 0.516346 | 1.689379 |
| 16 | 6 | 0 | -0.460307 | 0.348771 | 0.473592 |
| 17 | 1 | 0 | -0.608002 | 0.464562 | -0.607842 |
| 18 | 6 | 0 | 0.963158 | 0.900858 | 0.818736 |
| 19 | 1 | 0 | 1.004473 | 1.007739 | 1.913388 |
| 20 | 6 | 0 | 1.118901 | 2.309330 | 0.237669 |
| 21 | 6 | 0 | 1.094660 | 3.437052 | 1.073289 |
| 22 | 1 | 0 | 0.989287 | 3.303914 | 2.148089 |
| 23 | 6 | 0 | 1.198289 | 4.727859 | 0.544047 |
| 24 | 1 | 0 | 1.175898 | 5.585949 | 1.210142 |
| 25 | 6 | 0 | 1.329660 | 4.909011 | -0.831255 |
| 26 | 1 | 0 | 1.412083 | 5.909685 | -1.245872 |
| 27 | 6 | 0 | 1.365006 | 3.793577 | -1.674466 |
| 28 | 1 | 0 | 1.476694 | 3.926529 | -2.747090 |
| 29 | 6 | 0 | 1.263772 | 2.508690 | -1.145991 |
| 30 | 1 | 0 | 1.304364 | 1.647470 | -1.807717 |
| 31 | 6 | 0 | 2.081624 | -0.046525 | 0.396867 |
| 32 | 6 | 0 | 3.434194 | 0.324311 | 0.442070 |
| 33 | 8 | 0 | 3.839777 | 1.541004 | 0.874616 |
| 34 | 1 | 0 | 3.082561 | 2.153710 | 0.916591 |
| 35 | 6 | 0 | 4.472498 | -0.557655 | 0.049774 |

| | | | | | |
|---|---|---|---|---|---|
| 36 | 6 | 0 | 5.856454 | -0.140420 | 0.066790 |
| 37 | 1 | 0 | 6.062792 | 0.888156 | 0.397647 |
| 38 | 8 | 0 | 6.803710 | -0.869367 | -0.271037 |
| 39 | 6 | 0 | 4.126283 | -1.868439 | -0.383387 |
| 40 | 8 | 0 | 5.085399 | -2.713956 | -0.767463 |
| 41 | 1 | 0 | 5.957422 | -2.230828 | -0.670390 |
| 42 | 6 | 0 | 2.784022 | -2.299705 | -0.402525 |
| 43 | 6 | 0 | 2.491892 | -3.689542 | -0.805961 |
| 44 | 1 | 0 | 3.401014 | -4.262080 | -1.068324 |
| 45 | 8 | 0 | 1.395347 | -4.222223 | -0.865299 |
| 46 | 6 | 0 | 1.789187 | -1.371299 | 0.013775 |
| 47 | 8 | 0 | 0.536368 | -1.832827 | 0.011877 |
| 48 | 6 | 0 | -0.548079 | -1.171431 | 0.743865 |
| 49 | 6 | 0 | -0.388690 | -1.551747 | 2.220832 |
| 50 | 1 | 0 | -1.197847 | -1.137948 | 2.830044 |
| 51 | 1 | 0 | -0.403389 | -2.640871 | 2.322843 |
| 52 | 1 | 0 | 0.560339 | -1.188832 | 2.628615 |
| 53 | 6 | 0 | -1.748299 | -1.898427 | 0.079643 |
| 54 | 1 | 0 | -1.455396 | -2.952701 | 0.112247 |
| 55 | 1 | 0 | -1.728561 | -1.630132 | -0.983244 |
| 56 | 6 | 0 | -3.200815 | -1.767159 | 0.612775 |
| 57 | 1 | 0 | -3.226958 | -1.439587 | 1.659469 |
| 58 | 1 | 0 | -3.627244 | -2.779232 | 0.622915 |
| 59 | 6 | 0 | -4.119174 | -0.898762 | -0.254388 |
| 60 | 1 | 0 | -3.825799 | -1.034220 | -1.304392 |
| 61 | 6 | 0 | -5.682255 | -1.036395 | -0.208594 |
| 62 | 6 | 0 | -6.238251 | -1.330842 | 1.191466 |
| 63 | 1 | 0 | -5.837422 | -0.653144 | 1.953956 |
| 64 | 1 | 0 | -7.330005 | -1.222464 | 1.197355 |
| 65 | 1 | 0 | -6.007271 | -2.356514 | 1.504174 |
| 66 | 6 | 0 | -6.293678 | -1.993399 | -1.231403 |
| 67 | 1 | 0 | -7.388258 | -1.910986 | -1.245882 |
| 68 | 1 | 0 | -5.928639 | -1.781808 | -2.243434 |
| 69 | 1 | 0 | -6.046026 | -3.037364 | -0.997904 |

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**The complete reference:**

Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A.; Peralta, J. E.;

Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, N. J.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09W, Revision A.02*, Gaussian, Inc., Wallingford CT, 2009.

## Spectral data of 1 and 2

Psiguadials A (**1**): colorless needles ($CHCl_3$); $[\alpha]_D^{25}$ -62.5 (*c* 0.15, $CHCl_3$); IR (KBr) $\nu_{max}$ 2964, 2933, 1632, 1428, 1308, 1172, 869, 766, 610 $cm^{-1}$; UV ($CHCl_3$) $\lambda_{max}$ (log ε) 229 nm (3.37), 296 nm (3.85), 347 nm (3.33); HR-EI-MS *m/z* 474.2403 $[M]^+$ (calcd for $C_{30}H_{34}O_5$ 474.2406).

1D and 2D NMR data of **1** ($CDCl_3$)

| no. | $\delta_H$ | $\delta_C$ | $^1H$-$^1H$ COSY | HMBC | ROESY |
|---|---|---|---|---|---|
| 1 | - | 104.1 | | | |
| 2 | a 2.01<br>b 1.88 | 36.6 | $H_2$-3 | C-3, C-4 | |
| 3 | a 1.90<br>b 1.63 | 37.9 | | C-1, C-4, C-15, C-1′ | |
| 4 | - | 47.8 | | | |
| 5 | 2.36 (d, 11.9) | 48.7 | | C-2, C-3, C-4, C-6, C-11, C-1′ | H-8*α*, $H_3$-12, H-9′, H-10′, H-11′, H-12′, H-13′ |
| 6 | 0.29 (dd, 8.8, 11.9) | 26.3 | H-5, H-7 | C-4, C-7, C-11, C-12 | $H_2$-2, H-3a, H-7, H-10, $H_3$-13, $H_3$-15 |
| 7 | 0.58 | 23.9 | | C-6, C-12 | $H_3$-12, H-8*β*, H-10 |
| 8 | *α* 1.26 (m)<br>*β* 1.83 (m) | 20.3 | H-7, H-9 | C-6, C-7, C-9, C-10 | |
| 9 | *α* 1.74 (m)<br>*β* 1.93 (m) | 30.3 | | C-7, C-8, C-10, C-14 | |
| 10 | 2.49 (m) | 39.9 | $H_2$-9, H-14 | C-9, C-14 | $H_2$-2 |
| 11 | - | 19.2 | | | |
| 12 | 0.91 (s) | 28.4 | | C-6, C-7, C-11, C-13 | |
| 13 | 0.24 (s) | 14.3 | | C-7, C-11, C-12 | H-6, H-8α, $H_3$-12, $H_3$-15, H-10′, H-12′ |
| 14 | 1.09 (d, 6.8) | 17.4 | | C-1, C-9, C-10 | $H_2$-9, H-10, H-14′ |
| 15 | 1.13 (s) | 24.9 | | C-3, C-4, C-1′ | H-3a |
| 1′ | 4.49 (s) | 53.2 | | C-3, C-4, C-15, C-2′, C-3′, C-7′, C-8′, C-9′, C-13′ | H-3b, $H_3$-15 |
| 2′ | - | 114.2 | | | |
| 3′ | - | 166.7 | | | |
| 4′ | - | 108.2 | | | |
| 5′ | - | 168.2 | | | |
| 6′ | - | 105.0 | | | |

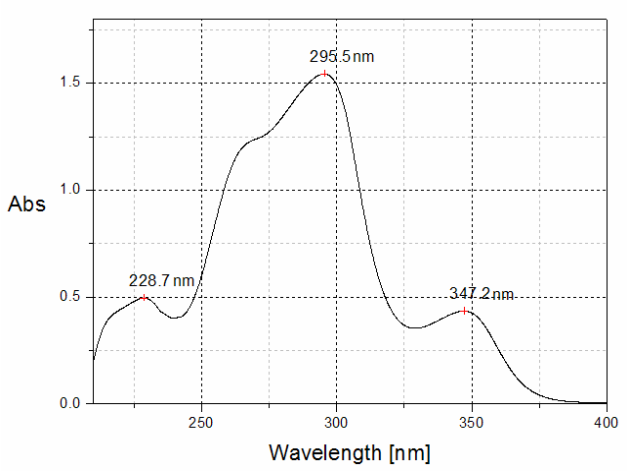
| | | | | | |
|---|---|---|---|---|---|
| 7′ | - | 170.5 | | | |
| 8′ | - | 140.9 | | | |
| 9′ | 7.13 | 130.3 | | C-1′, C-11′, C-13′ | |
| 10′ | 7.22 | 127.6 | $H_2$-9′, H-11′ | C-8′, C-12′ | |
| 11′ | 7.11 | 126.4 | | C-9′, C-13′ | |
| 12′ | 7.22 | 127.6 | H-11′, H-13′ | C-8′, C-10′ | |
| 13′ | 7.13 | 130.3 | | C-1′, C-9′, C-11′ | |
| 14′ | 10.38 (s) | 193.7 | | C-4′, C-5′, C-6′ | |
| 15′ | 10.12 (s) | 191.8 | | C-2′, C-6′, C-7′ | |
| 5′-OH | 13.76 (s) | | | C-4′, C-5′, C-6′, C-14′ | H-14′, H-15′ |
| 7′-OH | 13.53 (s) | | | C-2′, C-6′, C-7′, C-15′ | H-1′, H-15′ |

Psiguadials B (**2**): colorless needles ($CHCl_3$); $[\alpha]_D^{25}$ +70.0 (*c* 0.15, $CHCl_3$); IR (KBr) $\nu_{max}$ 2952, 2869, 1625, 1442, 1302, 1185, 1154, 828, 700, 607, 566 $cm^{-1}$; UV ($CHCl_3$) $\lambda_{max}$ (log ε) 219 nm (3.32), 277 nm (3.69), 339 nm (3.09); HR-EI-MS *m/z* 474.2403 $[M]^+$ (calcd for $C_{30}H_{34}O_5$ 474.2406).

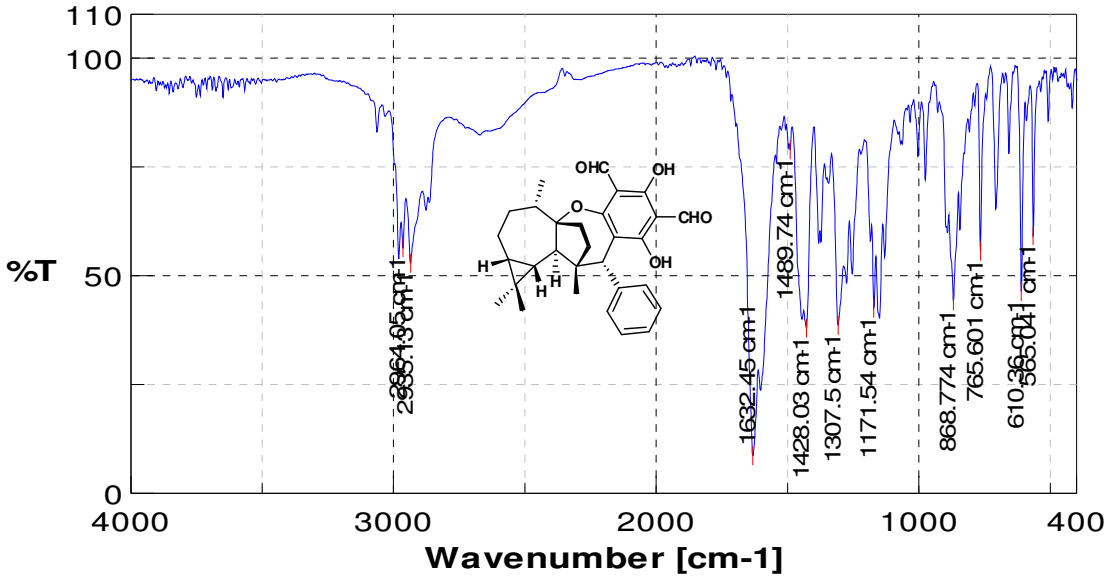
1D and 2D NMR data of **2** ($CDCl_3$)

| no. | $\delta_H$ | $\delta_C$ | $^1H$-$^1H$ COSY | HMBC | ROESY |
|---|---|---|---|---|---|
| 1 | - | 33.4 | | | |
| 2 | 2.16 | 37.0 | $H_2$-3, H-5 | C-3, C-5, C-6, C-15 | H-3*α*, H-11a, $H_3$-13 |
| 3 | *α* 1.52 | 35.5 | | C-1, C-2, C-4, C-5, C-13, | |
| | *β* 1.37 | | | C-14 | |
| 4 | - | 35.1 | | | |
| 5 | 1.82 (m) | 44.1 | | C-6 | H-6*β*, H-12a, $H_3$-14 |
| 6 | *α* 1.65 (m) | 20.1 | H-5, $H_2$-7 | | |
| | *β* 1.41 (m) | | | | |
| 7 | *α* 1.93 | 29.4 | | C-6 | |
| | *β* 1.58 | | | | |
| 8 | - | 84.1 | | | |
| 9 | 1.68 | 50.0 | H-10, H-1 | C-7, C-10, C-1′ | H-12b |
| 10 | 1.49 (m) | 23.9 | $H_2$-9, $H_2$-11 | C-1 | H-1′ |
| 11 | *α* 1.41 | 37.6 | | | |
| | *β* 1.10 | | | | |
| 12 | a 2.08 | 47.5 | | C-1, C-2, C-7, C-8, C-9, | |
| | b 1.29, | | | C-11 | |
| 13 | 1.02 (s) | 30.6 | | C-3, C-14 | |

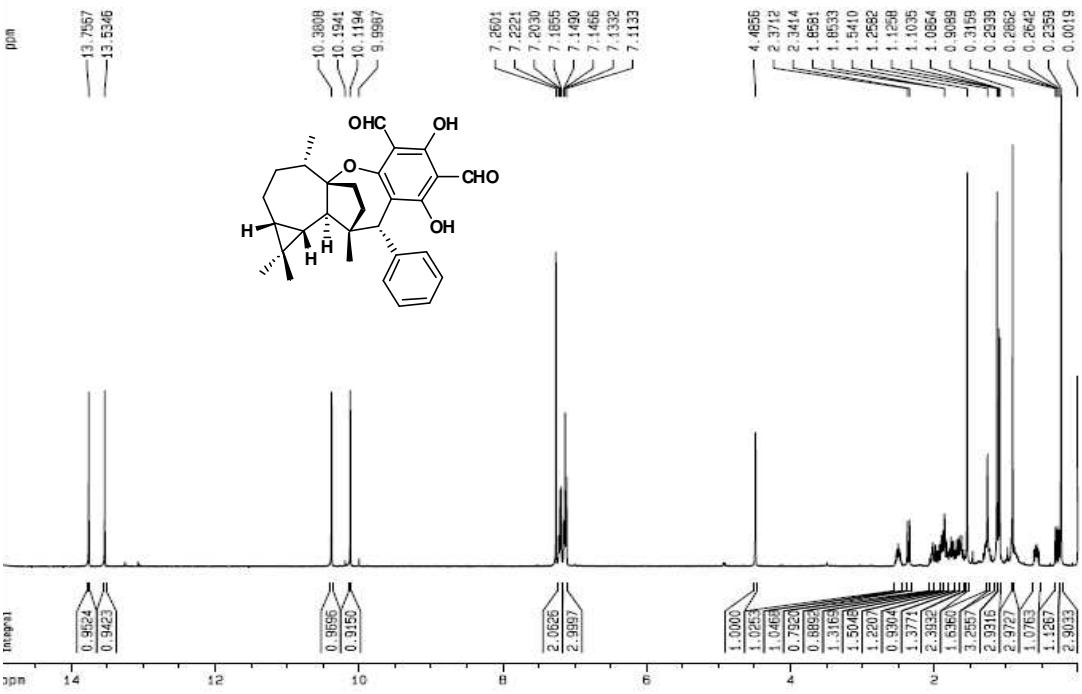
| | | | | | |
|---|---|---|---|---|---|
| 14 | 1.01 (s) | 20.7 | | C-3, C-5, C-13 | H-12a |
| 15 | 0.86 (s) | 26.1 | | C-1, C-11, C-12 | H-3$\beta$, H-12a |
| 1′ | 3.49 (d,11.5) | 40.4 | | C-9, C-10, C-3′, C-8′, C-9′, C-13′ | H-6$\alpha$, H-7$\alpha$ |
| 2′ | - | 105.7 | | | |
| 3′ | - | 163.5 | | | |
| 4′ | - | 104.6 | | | |
| 5′ | - | 168.5 | | | |
| 6′ | - | 104.2 | | | |
| 7′ | - | 169.6 | | | |
| 8′ | - | 143.4 | | | |
| 9′ | 7.18 | 128.2 | | C-1′, C-11′, C-13′ | |
| 10′ | 7.23 | 126.2 | $H_2$-9′, H-11′ | C-8′, C-12′ | |
| 11′ | 7.18 | 128.2 | | C-9′, C-13′ | |
| 12′ | 7.23 | 126.2 | H-11′, H-13′ | C-8′, C-10′ | |
| 13′ | 7.18 | 128.2 | | C-1′, C-9′, C-11′ | |
| 14′ | 10.08 (s) | 191.4 | | C-4′, C-5′, C-6′ | |
| 15′ | 10.08 (s) | 192.3 | | C-2′, C-6′, C-7′ | |
| 5′-OH | 13.51 (s) | | | C-4′, C-5′, C-6′, C-14′ | H-14′, H-15′ |
| 7′-OH | 13.04 (s) | | | C-2′, C-6′, C-7′, C-15′ | H-1′, H-15′ |



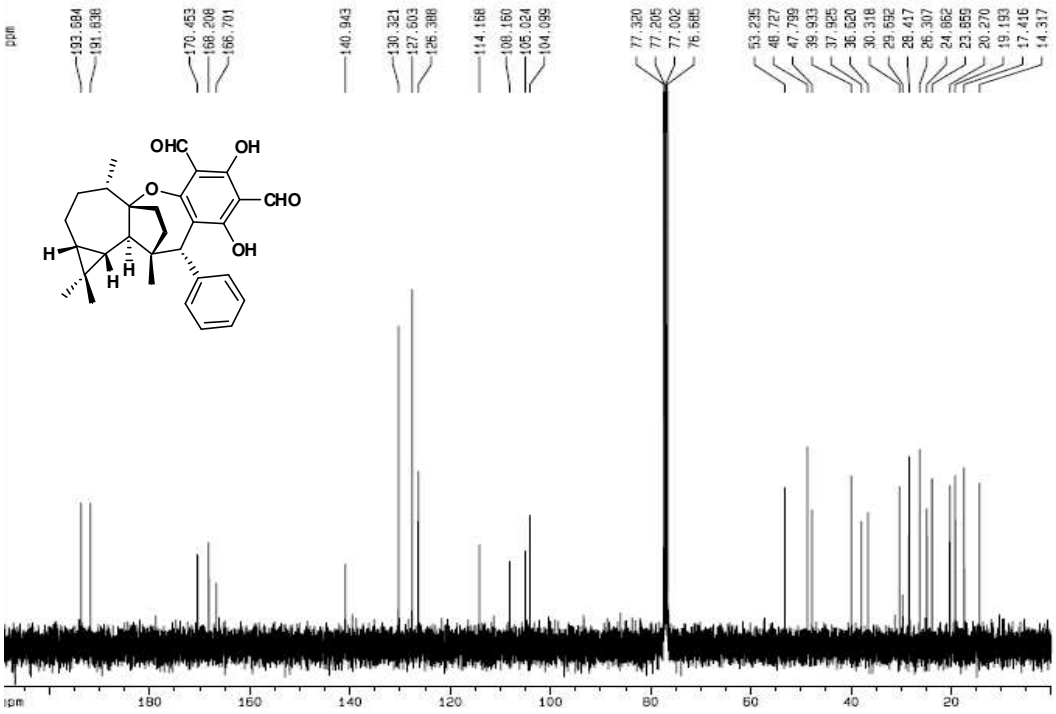

UV spectrum of **1** ($CHCl_3$)



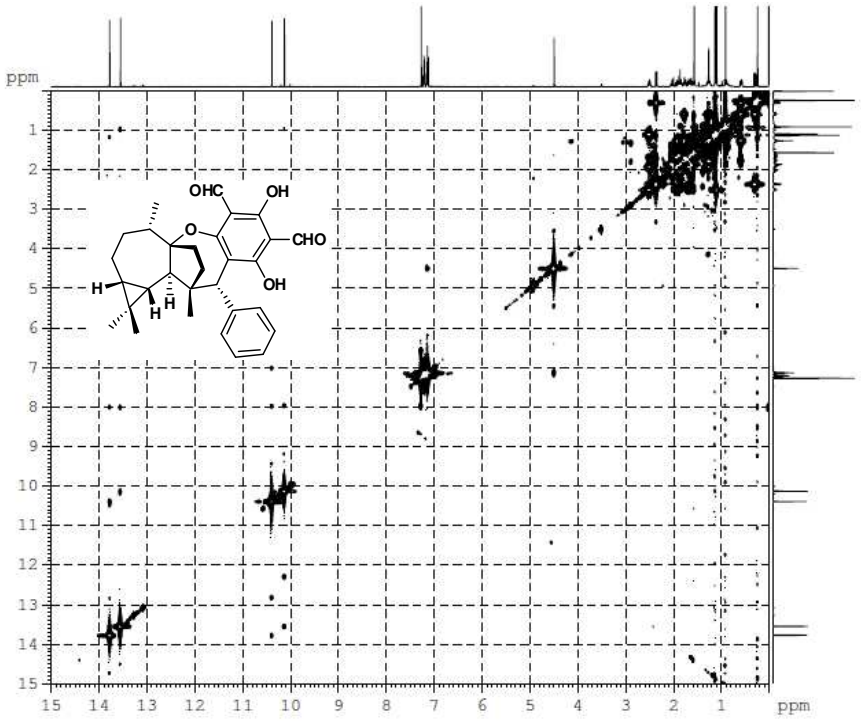

IR spectrum of **1** (KBr disc)



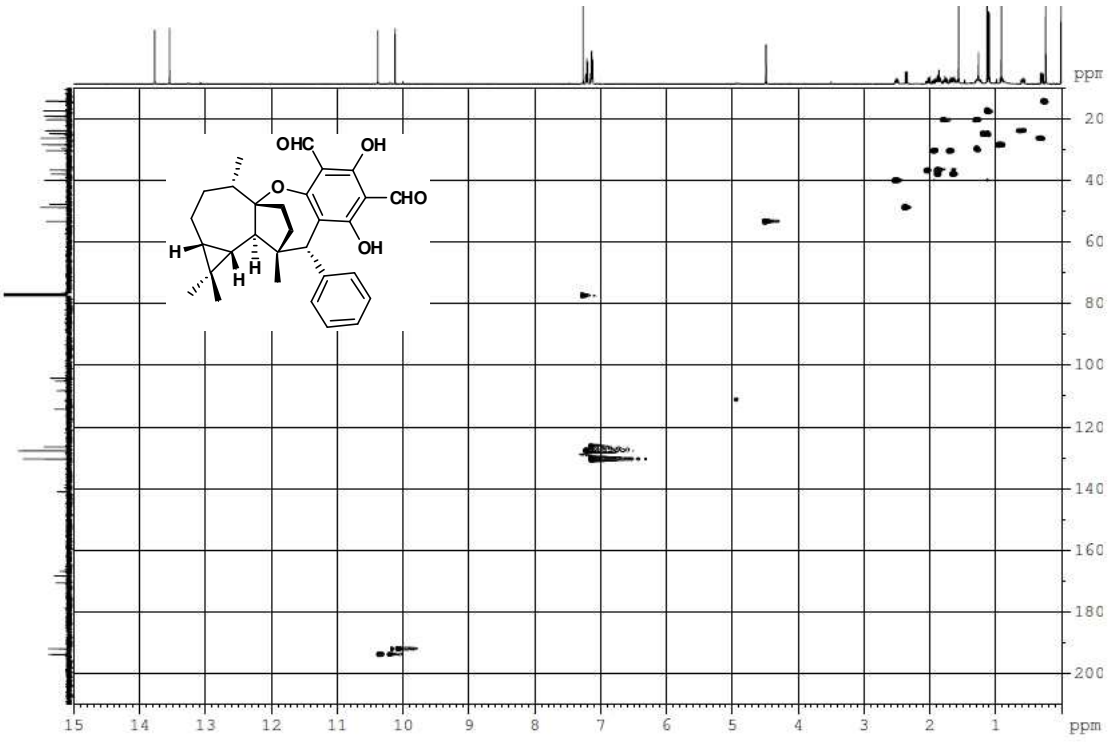

$^{1}$H NMR spectrum of **1** in $CDCl_3$



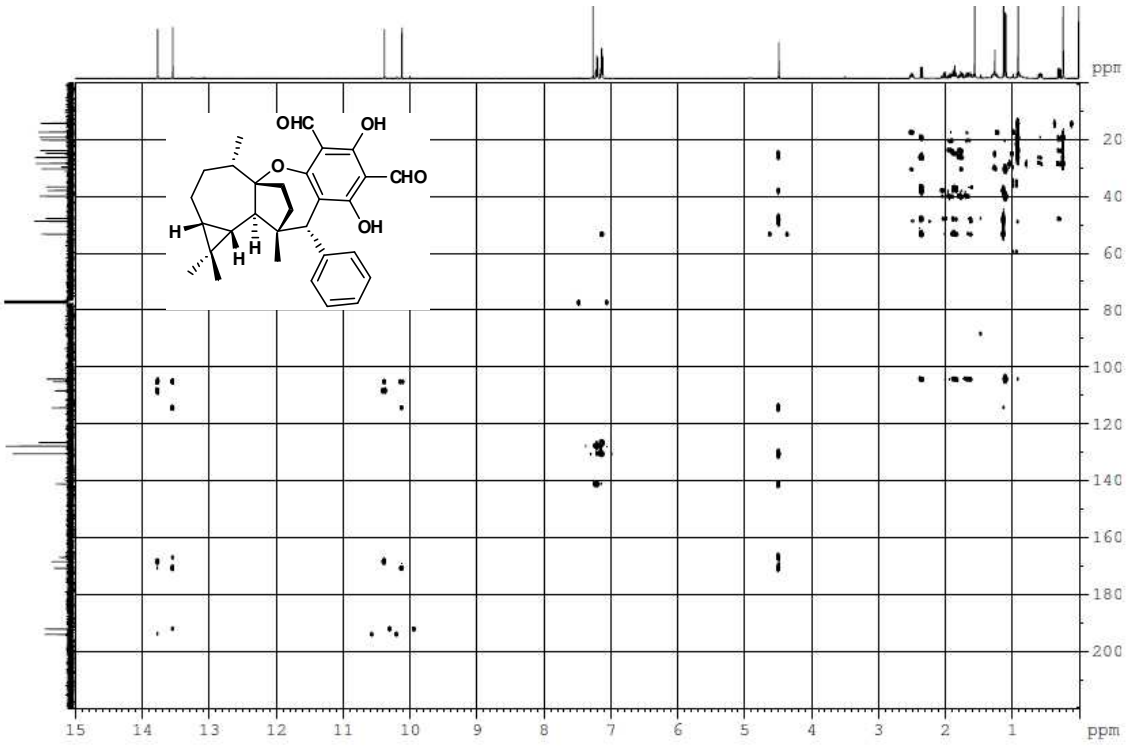

$^{13}$C NMR spectrum of **1** in $CDCl_3$



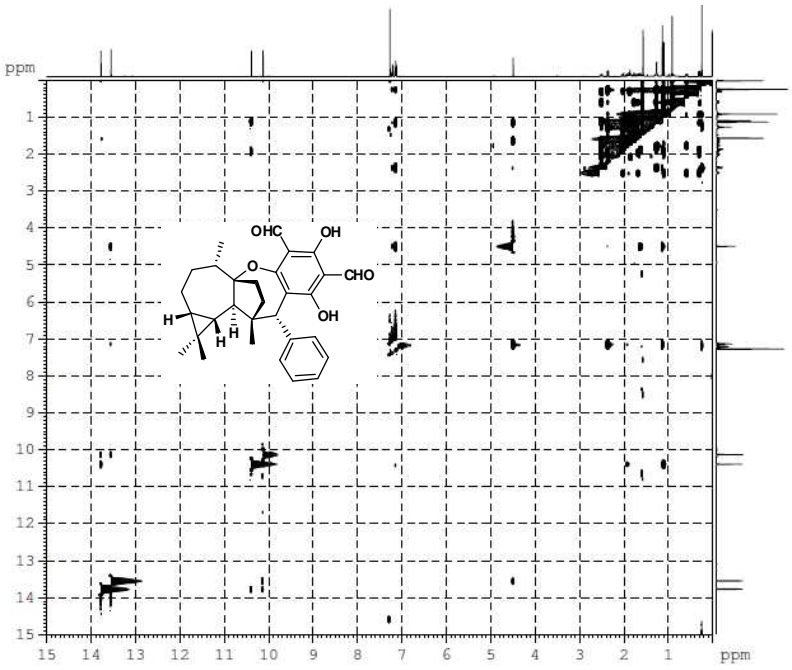

$^{1}H$-$^{1}H$ COSY spectrum of **1** in $CDCl_3$



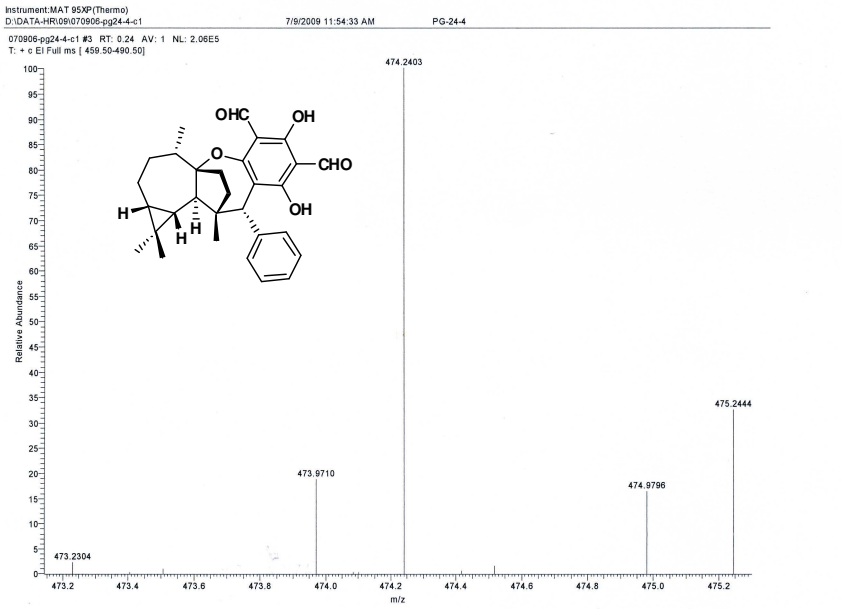

HSQC spectrum of **1** in $CDCl_3$



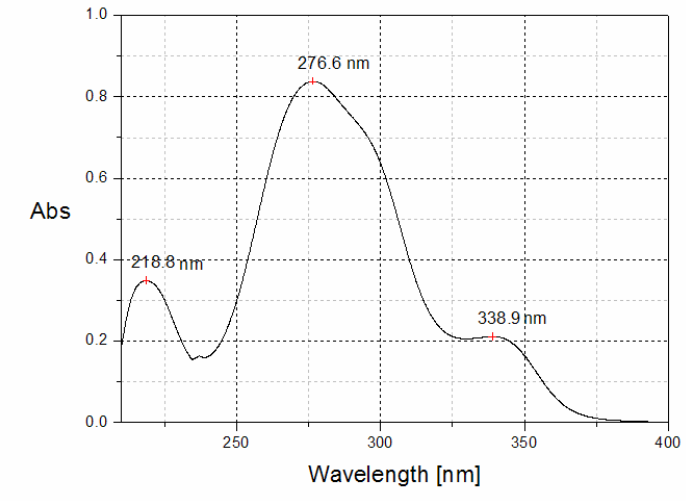

HMBC spectrum of **1** in $CDCl_3$



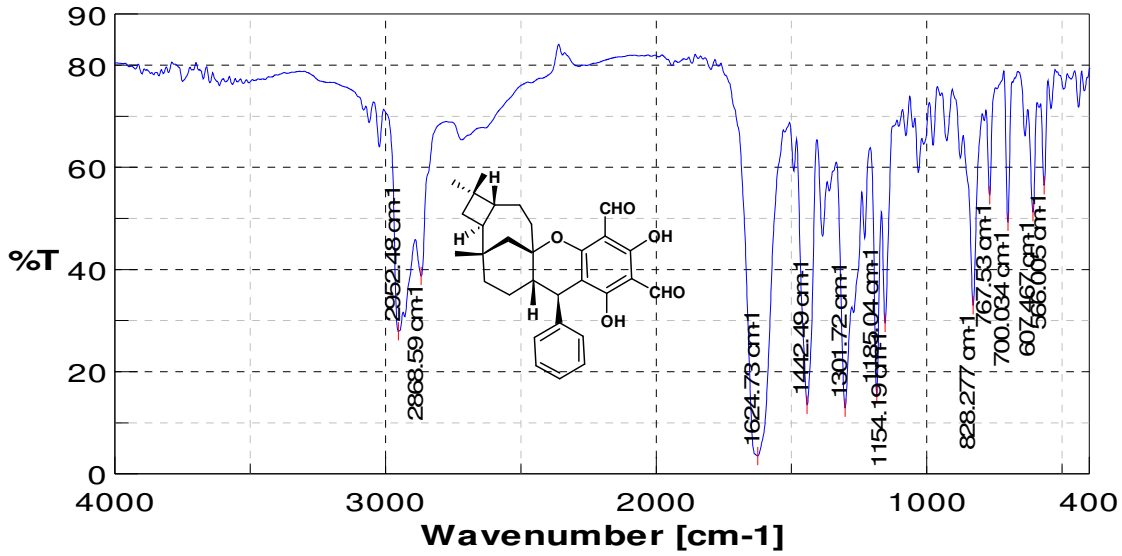

ROESY spectrum of **1** in $CDCl_3$



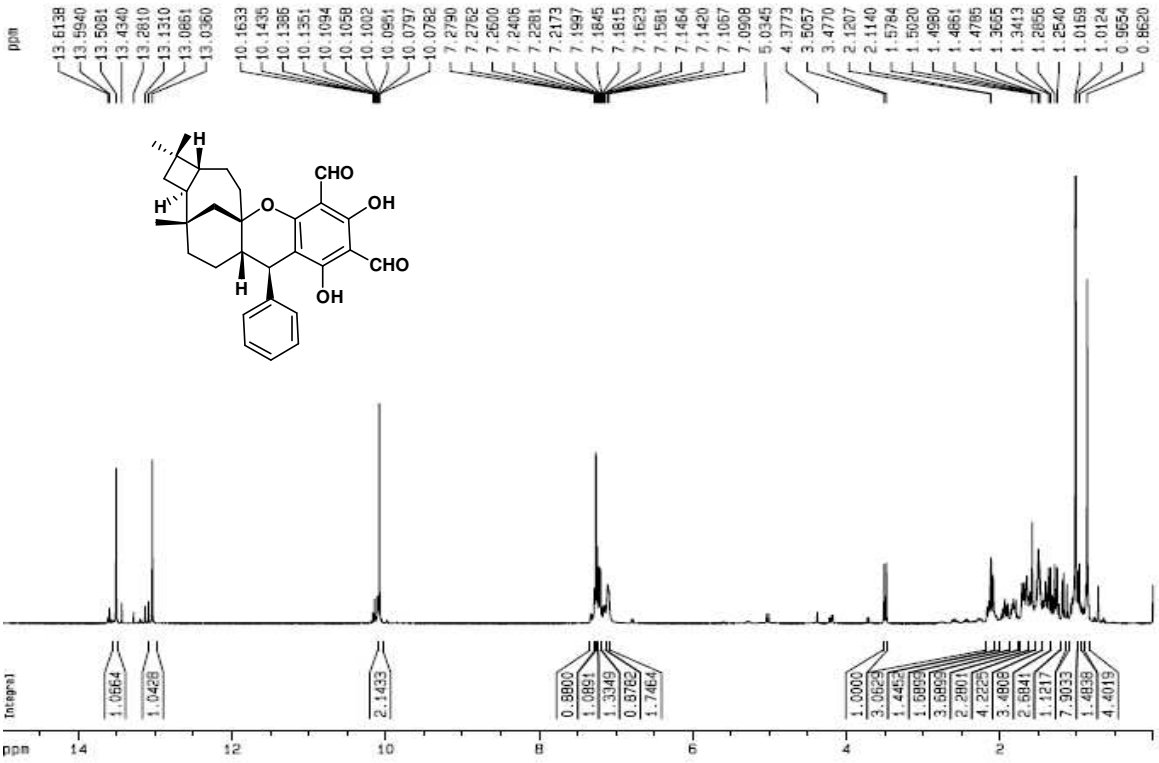

HR-EI-MS spectrum of **1**



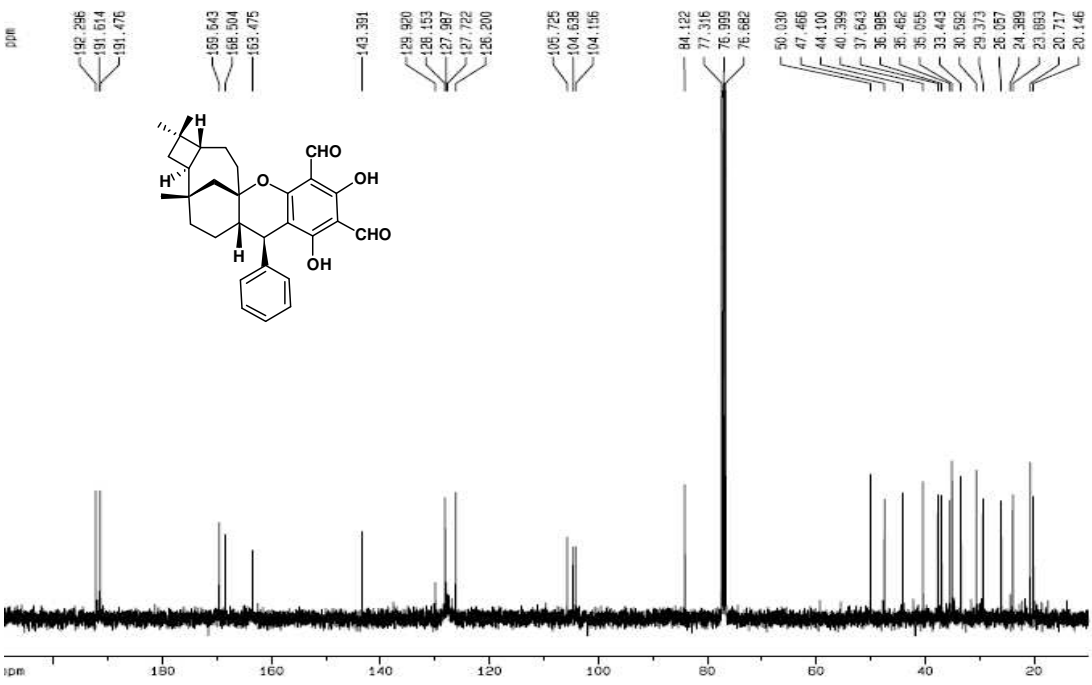

UV spectrum of **2** ($CHCl_3$)



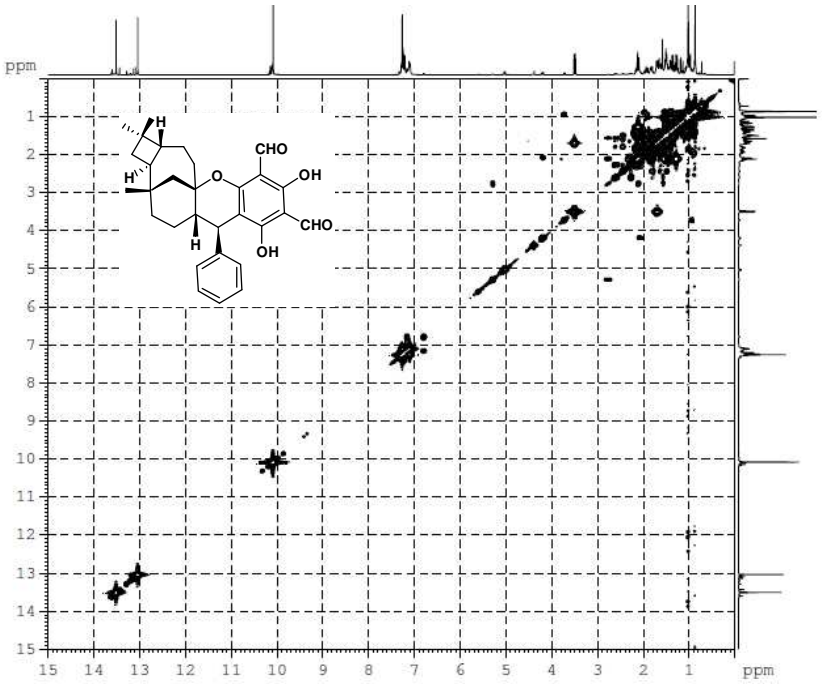

IR spectrum of **2** (KBr disc)



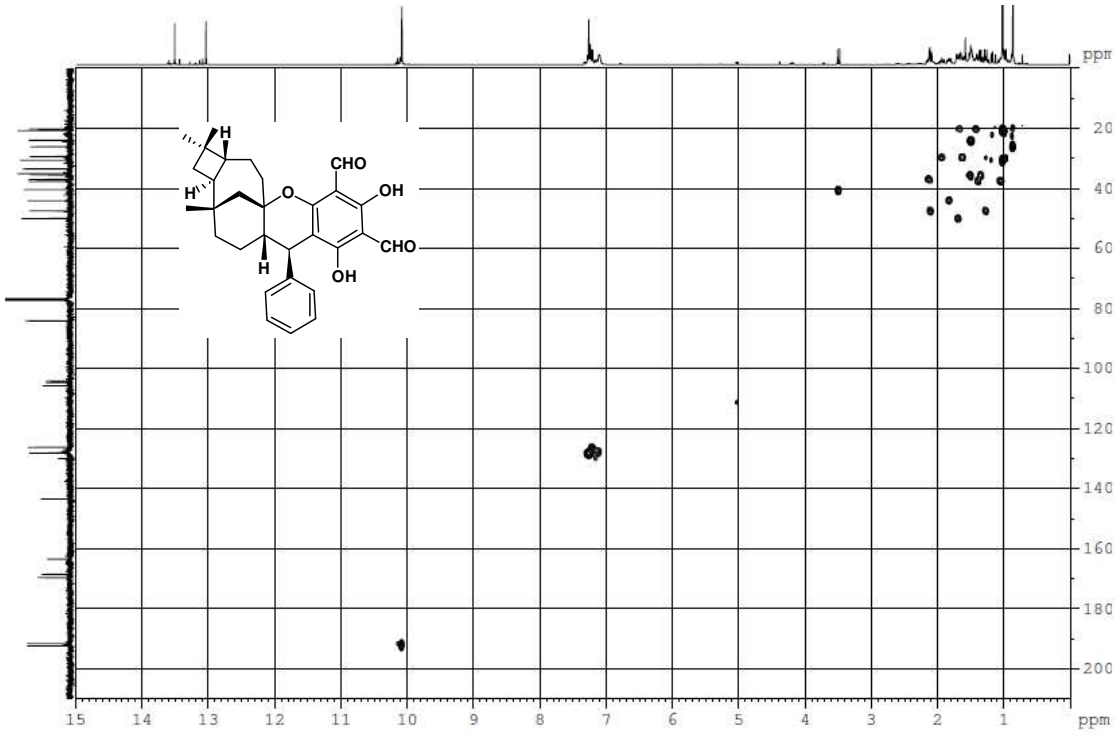

$^{1}$H NMR spectrum of **2** in $CDCl_3$



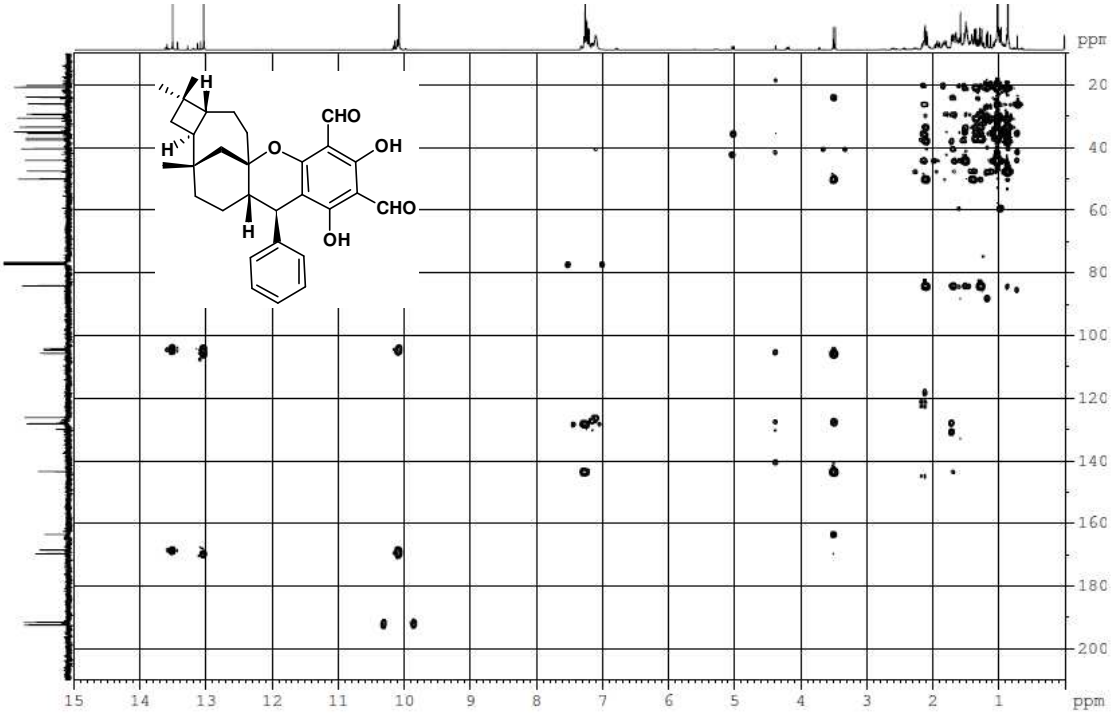

$^{13}$C NMR spectrum of **2** in $CDCl_3$



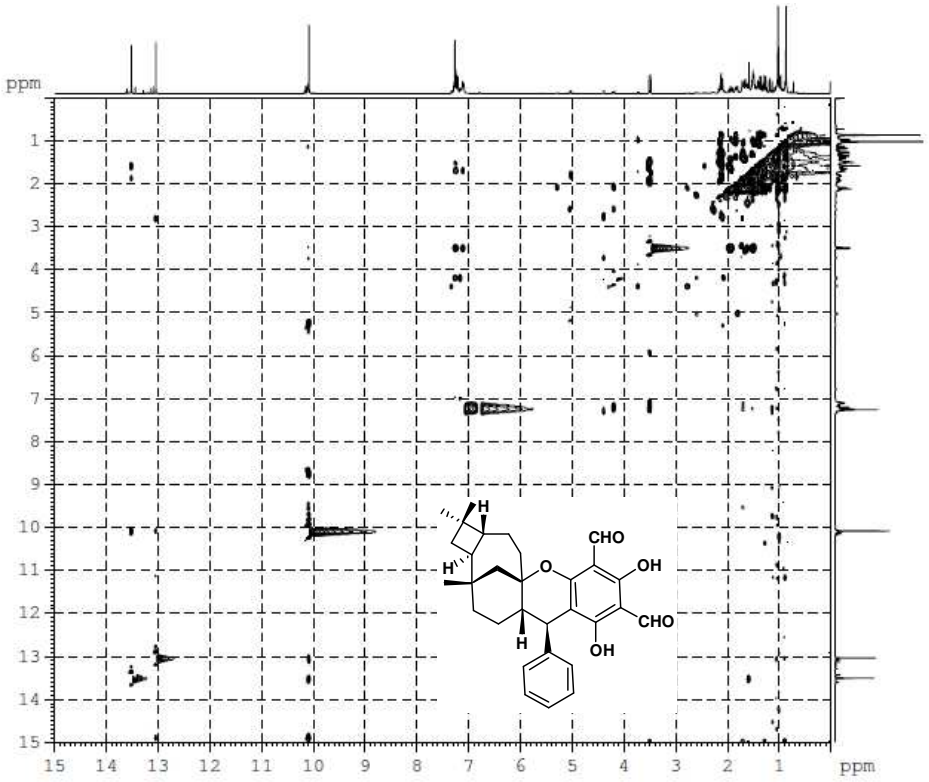

$^{1}$H-$^{1}$H COSY spectrum of **2** in $CDCl_3$



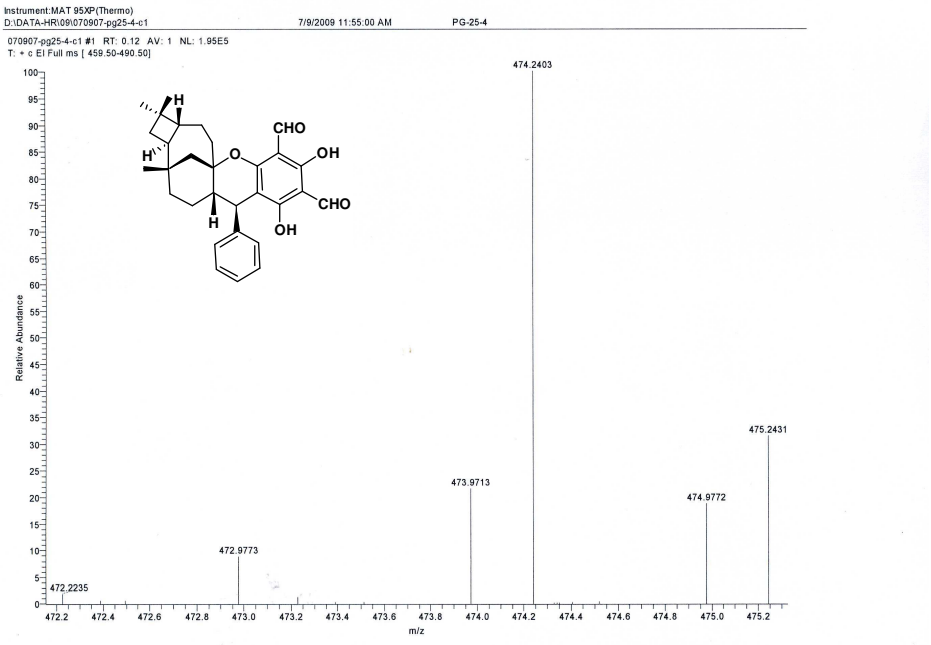

HSQC spectrum of **2** in $CDCl_3$



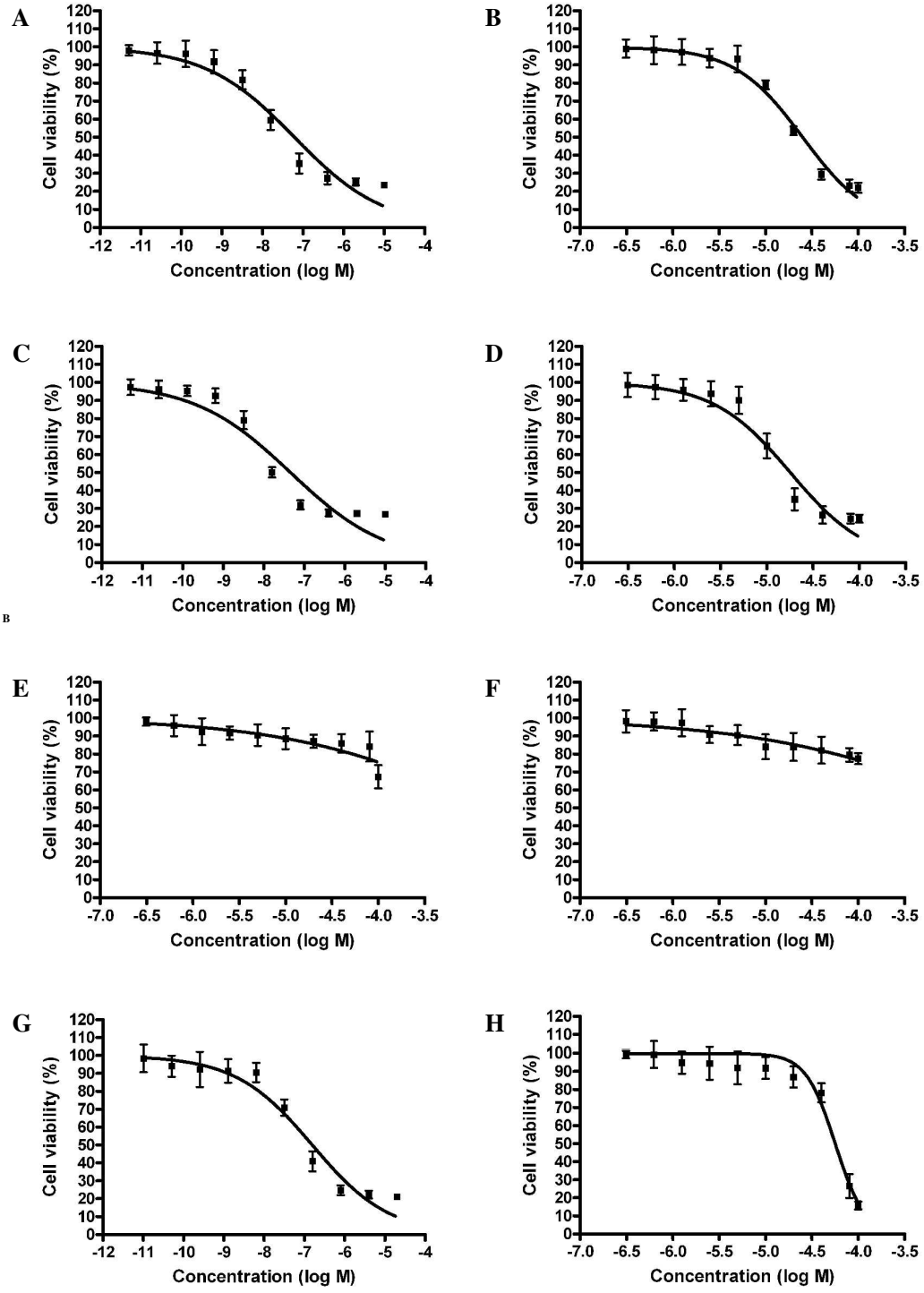

HMBC spectrum of **2** in $CDCl_3$




ROESY spectrum of **2** in $CDCl_3$




HR-EI-MS spectrum of **2**




Cell survival was determined by MTT assay. The survival curves of HepG2 cells at the different concentrations of **1** (A), **2** (C), **3** (E) and **4** (G). The survival curves of HepG2/ADM cells at the different concentration of **1** (B), **2** (D), **3** (F) and **4** (H). Data points are the means ± SD of six replicates. Representative curves of three independent experiments are shown.