

Stereospecific acyloin ring contraction controlled by glucose and concise total synthesis of saffloneoside

*Wan Gao, Jian-Shuang Jiang, Zhong Chen, Ya-Nan Yang, Zi-Ming Feng, Xu Zhang, Xiang Yuan,
and Pei-Cheng Zhang**

Supporting Information

Table of Contents

| | |
|--|----|
| 1 Experimental procedures..... | 4 |
| 1.1 General experimental details | 4 |
| 1.2 Isolation and structural identification of saffloneoside | 5 |
| 1.2.1 ECD calculation of 1 | 8 |
| 1.3 Specific experimental conditions..... | 20 |
| 1.3.1 Synthesis of saffloneoside (1) from hydroxysafflor yellow A (HSYA)..... | 20 |
| 1.3.2 Synthesis of 2,4,6-trihydroxy-3,5-di-C-glucosylacetophenone 4 | 21 |
| 1.3.3 Synthesis of 2-hydroxy-4,6-dimethoxymethoxy-3,5-di-C-glucosylacetophenone 4-1 | 22 |
| 1.3.4 Synthesis of 2,4,6,13-tetrahydroxy-3,5-di-C-glucosylchalone 5 | 22 |
| 1.3.5 Synthesis of 3,4,6-trihydroxycyclohexadienone 6 | 23 |
| 1.3.6 Synthesis of glucosyl acetate 12 | 25 |
| 1.3.7 Synthesis of di-C-(per-O-benzylglucosyl)phloroacetophenone 6-1 | 25 |
| 1.3.8 Synthesis of 3-methyl-2,4,6-trihydroxyacetophenone 10 | 26 |
| 1.3.9 Synthesis of 3-methyl-5-C-(per-O-benzylglucosyl)-2,4,6-trihydroxyacetophenone 9 | 27 |
| 1.3.10 Synthesis of 3,4,6-trihydroxycyclohexadienone 8 | 28 |
| 1.3.11 Synthesis of cyclopentenone 7 | 29 |
| 1.3.12 Synthesis of 14 | 29 |
| 1.3.14 Synthesis of 1 | 30 |
| 1.3.15 Synthesis of 15 | 32 |
| 1.3.16 Synthesis of 16 | 33 |
| 1.3.17 Synthesis of 17 | 34 |
| 1.3.18 Synthesis of 1-acetoxy-2,3,4,6-tetra-O-benzyl-L-glucose..... | 34 |
| 1.3.19 Synthesis of 3-methyl-5-C-(per-O-benzyl-L-glucosyl)-2,4,6-trihydroxyacetophenone 18-1 | 37 |
| 1.3.20 Synthesis of 3,4,6-trihydroxycyclohexadienone 18 | 38 |
| 1.3.21 Synthesis of cyclopentenone 19 | 38 |
| 1.3.22 Synthesis of 20 | 39 |
| 1.4 Energy calculation of intermediates B1-B4 | 40 |
| 2 ECD spectra of 1 , 7 , 16 , 19 , and 20 | 53 |

| | |
|---------------------|----|
| 3 NMR spectra | 56 |
| 4 IR spectra | 85 |
| 5 References..... | 88 |

1 Experimental procedures

1.1 General experimental details

Reagents and solvents: All the reactions sensitive to air or moisture were carried out under argon atmosphere in anhydrous solvents. All solvents were obtained from Beijing Chemical Works. All other reagents with a purity > 95% were obtained from commercial sources (Acros, Alfa Aesar, and others) and used without further purification.

Thin layer chromatography (TLC) was performed using glass precoated silica gel GF254 plates. Column chromatography was performed using 200-300 mesh silica gel (Qingdao Marine Chemical Factory, China). Spots were visualized under 254 nm or 365nm UV light.

Nuclear magnetic resonance (NMR): NMR spectra were obtained on Bruker-400 MHz or Varian 500 MHz spectrometers. Chemical shift δ in ppm (number of protons, multiplicity, coupling constant J in Hz) for ^1H NMR spectra and chemical shift δ in ppm for ^{13}C NMR spectra. The following multiplicity abbreviations are used: (s) singlet, (brs) broad singlet, (d) doublet, (t) triplet, (q) quartet, (m) multiplet. Residual solvent peaks were used as internal reference. NMR spectra were assigned using information ascertained from HSQC, HMBC, and ROESY experiments.

High resolution electrospray ionization mass spectra (HR-ESI-MS) data were obtained using an Agilent 1100 series LC/MSD TOF from Agilent Technologies.

Circular dichroism (CD) spectra were reported on a JASCO J-815 spectropolarimeter.

Infrared spectra (IR) were recorded on a Thermo Fisher FT-IR spectrophotometer (Nicolet 5700).

Preparative HPLC was carried out on a Shimadzu LC-6AD instrument with an SPD-20A detector, using a YMC-Pack ODS-A column (250 \times 20 mm, 5 μm , Japan).

HPLC-DAD analysis was performed using an Agilent 1260 series system (Agilent Technologies, Waldbronn, Germany) with an Apollo C18 column (250 \times 4.6 mm, 5 μm , Grace Davison).

Melting point were measured on a Gallenkamp Melting Point System.

1.2 Isolation and structural identification of saffloneoside

The florets of *Carthamus tinctorius* L. (5.0 kg) were exhaustively extracted with H₂O under refluxed conditions. The H₂O extracts were then concentrated under reduced pressure to give a residue (1200 g). The residue was dissolved in H₂O again, then chromatographing over microporous adsorbent resin (HP-20) column. After eluting with H₂O, then the adsorbed constituents were eluted with 10% ethanol, 30% ethanol, and 50% ethanol, respectively. The 30% ethanol part (80.0 g) was chromatographed over Sephadex LH-20 eluting with H₂O-MeOH (from 100:0 to 0:100) to give 30 fractions. Fr.15 was further purified by reversed-phase preparative HPLC with CH₃OH-H₂O (35 : 65, 5 mL/min) as mobile phase to yield **1** (15.0 mg), named saffloneoside.

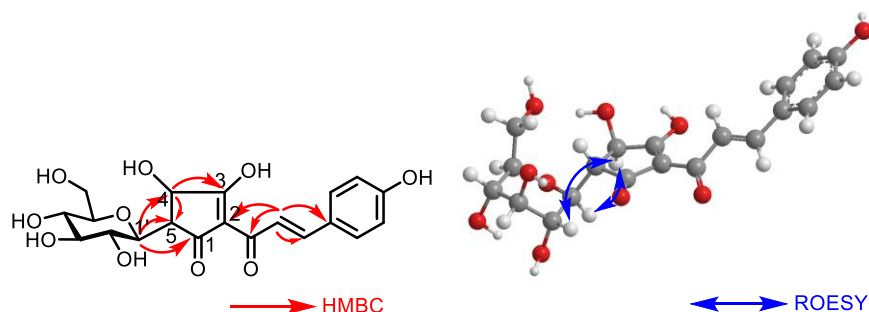


Figure S1 Selected HMBC and ROESY correlations of **1**.

Compound **1** was obtained as a yellow amorphous powder. Its molecular formula was determined to be C₂₀H₂₂O₁₀ based on the protonated molecular ion peak at *m/z* 423.1284 [M + H]⁺ (calcd. for C₂₀H₂₃O₁₀, 423.1247) observed in the HR-ESI-MS, which indicated 10 degrees of unsaturation. [α]_D²⁰ = -30.5 (*c* = 0.15, MeOH). The IR spectrum showed the presence of hydroxy (3331 cm⁻¹) and carbonyl (1684 cm⁻¹) groups, as well as an aromatic ring (1621 and 1578 cm⁻¹). The ¹H NMR spectrum of **1** exhibited the presence of *para*-substituted aromatic protons at δ_{H} 7.34 (2H, d, *J* = 8.5 Hz), 6.50 (2H, d, *J* = 8.5 Hz); one set of *trans* conjugated olefinic protons at δ_{H} 7.42 (1H, d, *J* = 15.8 Hz), 7.32 (1H, d, *J* = 15.8 Hz). Seven protons at δ_{H} 3.78-3.23 indicate the presence of a glucose, and since its terminal proton is at δ_{H} 3.77 (1H, d, *J* = 8.5 Hz), which can be inferred that the sugar is not present as an *O*-linked glucoside. In addition, two protons at δ_{H} 4.33 (1H, d, *J* = 4.5 Hz) and 2.74 (1H, brs) are not assigned. In the ¹³C NMR spectrum, 20 carbon resonances were observed, with nine of these resonances (δ_{C} 188.8, 170.8, 144.3, 131.2 (2C), 121.2, 119.6 (2C), and 119.4) attributed to a cinnamyl moiety and with six of these resonances (δ_{C} 79.4, 77.7, 76.0, 71.0, 69.6, and 60.8) attributed to a glucose moiety. In combination with the observed HSQC correlations, the remaining five carbon signals were designated as two carbonyls (δ_{C} 202.6 and 201.2), one olefinic carbon (δ_{C} 114.5), and two methines (δ_{C} 70.2 and 53.0). After we considered the remaining three degrees of unsaturation and the molecular formula, the skeleton of **1** was elucidated as a C₁₄

quinochalcone with a cyclopentenone ring. In the HMBC spectrum, a key correlation from H-1' (δ_{H} 3.77) to C-5 (δ_{C} 53.0) suggested that the glucose moiety is located at C-5 through C-C link.

To determine the relative configuration of **1**, the ROESY and ^1H NMR data were analyzed. The characteristic ROESY correlations from H-4 (δ_{H} 4.33) to H-1' (δ_{H} 3.77) and H-2' (δ_{H} 3.41), combined with the $J_{4,5} = 4.5$ Hz in ^1H NMR, indicated that OH at C4 and glucose at C5 are in different orientations.

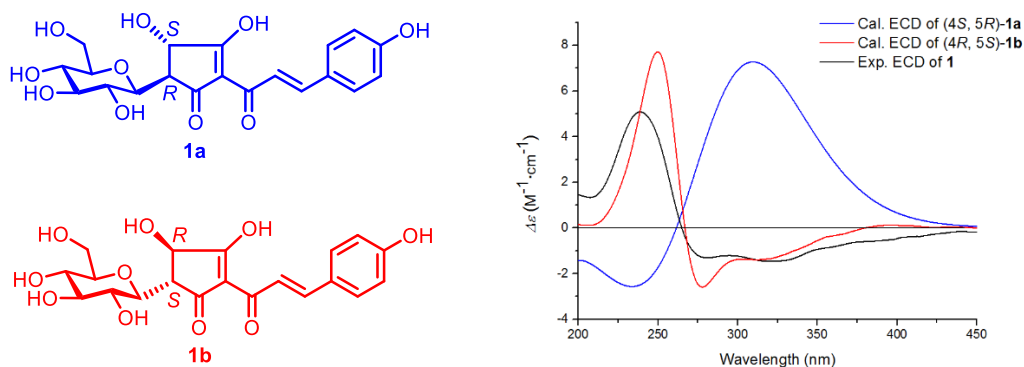


Figure S2 Experimental ECD spectra of compound **1** and calculated ECD spectra of **1a** and **1b** in MeOH.

The absolute configuration of **1** was determined by comparing its experimental and calculated ECD data. Conformational analysis of **1a** and its diastereoisomer **1b** (Figure S2) were performed using the MMFF94 molecular mechanics force field. The preferred conformers were optimized further at the B3LYP/6-311G(d, p) level. The ECD spectra of different conformers were simulated using a Gaussian function with a half-bandwidth of 0.25 eV. The calculated ECD spectra were obtained according to the Boltzmann weighting of each of the conformers with different populations. The overall theoretical ECD data of **1b** matched the experimental ECD data of **1** very well (Figure S2). Accordingly, the configuration of compound **1** was assigned as (4*R*, 5*S*).

m.p. 196-197 °C.

$[\alpha]_{\text{D}}^{20} = -30.5$ ($c = 0.15$, MeOH).

ECD: $\Delta\epsilon$ 326 (-1.65), 239 (+5.12) nm, ($c = 0.15$, MeOH).

IR (KBr): 3331, 2923, 2862, 1684, 1621, 1578, 1399, 1093 cm^{-1} .

^1H NMR (500 MHz, $\text{D}_2\text{O} + \text{NaOD}$) δ_{H} : 7.42 (1H, d, $J = 15.8$ Hz, H-7), 7.34 (2H, d, $J = 8.5$ Hz, H-10 and H-14), 7.32 (1H, d, $J = 15.8$ Hz, H-8), 6.50 (2H, d, $J = 8.5$ Hz, H-11 and H-13), 4.33

(1H, $J = 4.5$ Hz, H-4), 3.77 (1H, dd, $J = 8.5, 2.0$ Hz, H-1'), 3.65 (1H, m, H₁-6'), 3.50 (1H, dd, $J = 12.5, 5.0$ Hz, H₂-6'), 3.41 (1H, m, H-3'), 3.40 (1H, m, H-4'), 3.24 (1H, m, H-2'), 3.23 (1H, m, H-5'), 2.74 (1H, brs, H-5) ppm.

¹³C NMR (500 MHz, D₂O + NaOD) δ_c : 202.6 (C-3), 201.2 (C-1), 188.8 (C-6), 170.8 (C-12), 144.3 (C-8), 131.2 (C-10, 14), 121.2 (C-9), 119.6 (C-11, 13), 119.4 (C-7), 114.5 (C-2), 79.4 (C-5'), 77.7 (C-3'), 76.0 (C-1'), 71.0 (C-4'), 70.2 (C-4), 69.6 (C-2'), 60.8 (C-6'), 53.0 (C-5) ppm.

HRMS(ESI): calc. for C₂₀H₂₃O₁₀ [M + H]⁺: 423.1247, found: 423.1284.

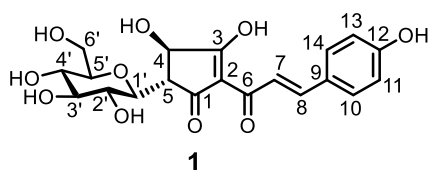


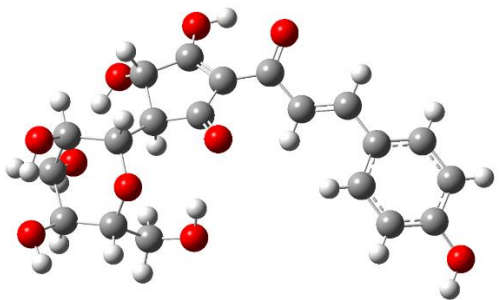
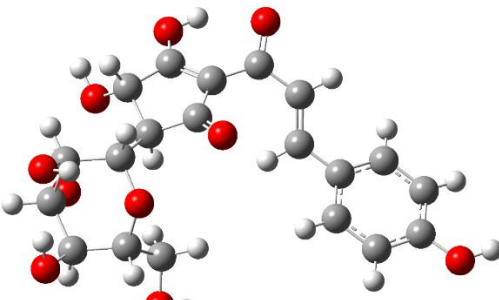
Table S1 NMR data of 1 (measured in D₂O + NaOD) (δ in ppm)

| position | type | δ_c | δ_H (mult., J in Hz) |
|----------|-----------------|------------|-------------------------------|
| 1 | C | 201.2 | |
| 2 | C | 114.5 | |
| 3 | C | 202.6 | |
| 4 | CH | 70.2 | 4.33 (d, 4.5) |
| 5 | CH | 53.0 | 2.74 (brs) |
| 6 | C | 188.8 | |
| 7 | CH | 119.4 | 7.42 (d, 15.8) |
| 8 | CH | 144.3 | 7.32 (d, 15.8) |
| 9 | C | 121.2 | |
| 10 | CH | 131.2 | 7.34 (d, 8.5) |
| 11 | CH | 119.6 | 6.50 (d, 8.5) |
| 12 | C | 170.8 | |
| 13 | CH | 119.6 | 6.50 (d, 8.5) |
| 14 | CH | 131.2 | 7.34 (d, 8.5) |
| 1' | CH | 76.0 | 3.77 (dd, 8.5, 2.0) |
| 2' | CH | 69.6 | 3.24 (m) |
| 3' | CH | 77.7 | 3.41 (m) |
| 4' | CH | 71.0 | 3.40 (m) |
| 5' | CH | 79.4 | 3.23 (m) |
| 6' | CH ₂ | 60.8 | 3.65m); 3.50 (dd, 12.5, 5.0) |

1.2.1 ECD calculation of **1**

Conformational analyses are carried out via systematic searching in the Discovery Studio (version 16.1.0.15350) using the MMFF94 force field. Conformers with Boltzmann distribution over 1% are chosen as the beginning for ECD calculations. Ground-state geometries are optimized at the B3LYP/6-311+G(d,p) level in gas phase by the Gaussian 09 program (Gaussian Inc., Wallingford, CT, USA).^[1] All quantum computations are performed on an IBM cluster machine located at the High Performance Computing Center of Peking Union Medical College. The energies, oscillator strengths, and rotational strengths (velocity) of the first 50 electronic excitations are calculated using the TD-DFT methodology at the B3LYP/6-311+G(d,p) level in methanol. The ECD spectra are simulated by the overlapping Gaussian function (half the bandwidth at 1/e peak height, 0.25 eV).^[2] By comparison of the calculated and experimental ECD spectra, the absolute configurations of compound **1** are established.

Table S2 The 3D conformers of **1a** with Boltzmann distribution over 1%.

| compound | no. | 3D conformers | rel. E (kcal/mol) | population (%) |
|---|-----|--|----------------------|-------------------|
| (4 <i>S</i> ,5 <i>R</i>)- 1a | 1 |  | 0.00 | 78.8 |
| | 2 |  | 9.71 | 19.2 |

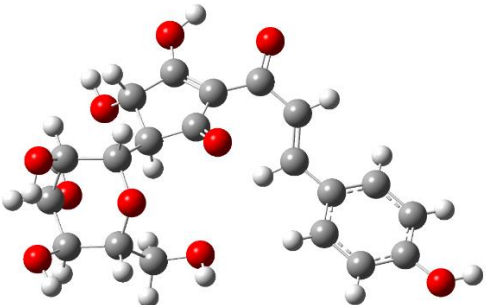
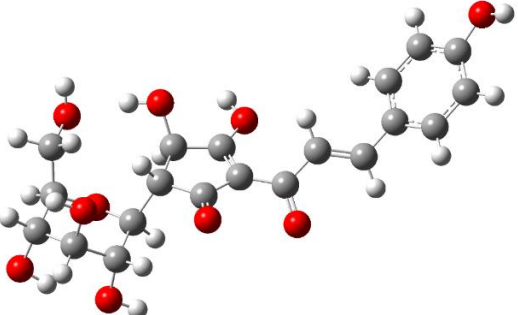
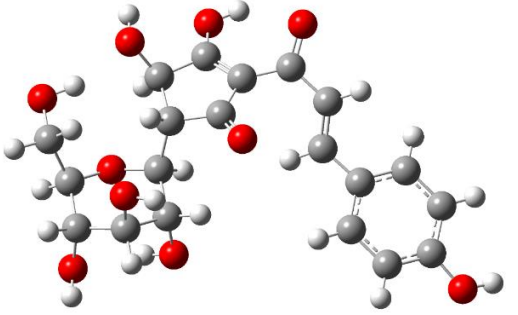
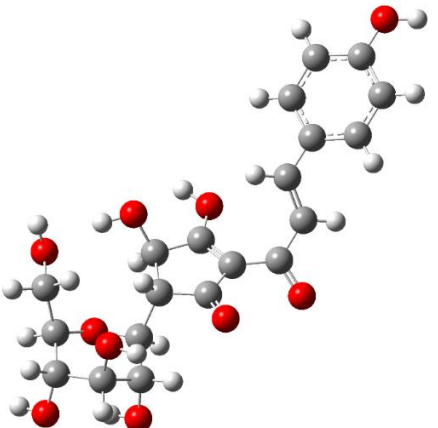
| | | | | |
|--|---|--|-------|-----|
| | 3 |  | 13.17 | 1.5 |
|--|---|--|-------|-----|

Table S3 The 3D conformers of **1b** with Boltzmann distribution over 1%.

| compound | no. | 3D conformers | rel. E (kcal/mol) | population (%) |
|---|-----|--|----------------------|-------------------|
| (4 <i>R</i> ,5 <i>S</i>)- 1b | 1 |  | 0.00 | 86.5 |
| | 2 |  | 5.71 | 9.1 |
| | 3 |  | 17.70 | 2.6 |

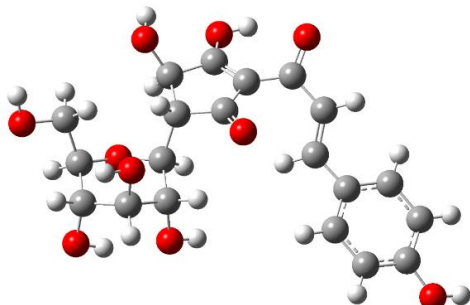
| | | | | |
|--|---|---|-------|-----|
| | 4 |  | 18.45 | 1.3 |
|--|---|---|-------|-----|

Table S4 Cartesian coordinates (Å) for the geometry optimized structure of **1a-1**

| Atom | X | Y | Z |
|------|-------------|-------------|-------------|
| C | 0.26460000 | 3.13340000 | 0.59230000 |
| C | -0.48280000 | 1.77460000 | 0.69170000 |
| C | 0.63910000 | 0.83470000 | 0.86990000 |
| C | 1.83680000 | 1.36670000 | 0.38580000 |
| C | 1.60550000 | 2.72710000 | 0.16060000 |
| O | 0.51640000 | -0.31200000 | 1.36160000 |
| C | 3.01400000 | 0.65010000 | 0.08930000 |
| C | 2.96580000 | -0.68890000 | -0.36430000 |
| O | 4.11950000 | 1.23130000 | 0.17890000 |
| O | 2.40870000 | 3.59090000 | -0.50250000 |
| C | 4.01350000 | -1.62260000 | -0.31500000 |
| C | 3.87390000 | -2.96010000 | -0.76880000 |
| C | 2.69420000 | -3.70460000 | -0.52730000 |
| C | 2.54800000 | -5.01320000 | -1.03710000 |
| C | 3.57250000 | -5.57770000 | -1.81550000 |
| C | 4.78370000 | -4.88990000 | -1.98350000 |
| C | 4.92520000 | -3.57700000 | -1.48390000 |
| O | 3.40290000 | -6.75800000 | -2.45870000 |
| O | -0.26330000 | 4.01610000 | -0.40090000 |
| C | -1.65130000 | 1.65340000 | 1.73490000 |
| O | -2.38960000 | 0.41210000 | 1.60530000 |
| C | -3.43430000 | 0.24870000 | 0.60760000 |
| C | -4.39380000 | 1.48050000 | 0.48900000 |
| C | -3.64060000 | 2.83650000 | 0.59130000 |
| C | -2.65340000 | 2.84930000 | 1.79470000 |
| O | -3.38240000 | 2.83180000 | 3.02830000 |
| C | -2.88710000 | -0.26350000 | -0.75340000 |
| O | -1.92150000 | -1.29580000 | -0.54810000 |

| | | | |
|---|-------------|-------------|-------------|
| O | -5.39700000 | 1.44080000 | 1.51160000 |
| O | -2.96840000 | 3.11240000 | -0.63720000 |
| H | 0.31030000 | 3.64580000 | 1.55790000 |
| H | -0.86870000 | 1.56850000 | -0.29940000 |
| H | 2.08520000 | -0.99120000 | -0.78660000 |
| H | 3.24080000 | 3.29550000 | -0.91820000 |
| H | 4.92800000 | -1.33140000 | 0.04250000 |
| H | 1.93180000 | -3.31250000 | 0.03060000 |
| H | 1.70000000 | -5.54630000 | -0.83340000 |
| H | 5.54550000 | -5.32560000 | -2.50680000 |
| H | 5.78910000 | -3.06990000 | -1.69220000 |
| H | 2.55040000 | -7.23700000 | -2.42500000 |
| H | -1.20610000 | 3.81330000 | -0.47610000 |
| H | -1.17260000 | 1.60270000 | 2.71780000 |
| H | -4.03600000 | -0.58400000 | 0.98250000 |
| H | -4.92460000 | 1.44760000 | -0.46730000 |
| H | -4.36340000 | 3.64410000 | 0.73950000 |
| H | -2.10840000 | 3.79280000 | 1.80770000 |
| H | -4.22790000 | 2.39860000 | 2.80160000 |
| H | -2.44860000 | 0.53900000 | -1.34100000 |
| H | -3.70180000 | -0.67570000 | -1.35230000 |
| H | -1.30780000 | -0.96320000 | 0.14440000 |
| H | -5.76930000 | 0.53380000 | 1.49410000 |
| H | -3.66460000 | 3.23020000 | -1.31830000 |

Table S5 Cartesian coordinates (Å) for the geometry optimized structure of **1a-2**

| Atom | X | Y | Z |
|------|-------------|-------------|-------------|
| C | -3.03470000 | 0.64150000 | 0.72550000 |
| C | -1.66910000 | -0.08840000 | 0.81680000 |
| C | -0.75300000 | 1.04470000 | 1.01760000 |
| C | -1.28460000 | 2.21490000 | 0.48320000 |
| C | -2.64170000 | 1.97270000 | 0.25070000 |
| O | 0.36000000 | 0.96550000 | 1.59190000 |
| C | -0.57530000 | 3.39240000 | 0.17160000 |
| C | 0.77600000 | 3.43330000 | -0.24380000 |
| O | -1.17360000 | 4.48510000 | 0.26530000 |
| O | -3.50910000 | 2.77330000 | -0.40920000 |
| C | 1.44920000 | 2.36860000 | -0.86410000 |

| | | | |
|---|-------------|-------------|-------------|
| C | 2.80390000 | 2.40380000 | -1.25820000 |
| C | 3.35490000 | 3.52540000 | -1.91560000 |
| C | 4.71790000 | 3.53860000 | -2.27990000 |
| C | 5.54150000 | 2.44560000 | -1.95640000 |
| C | 4.98410000 | 1.29360000 | -1.37980000 |
| C | 3.62420000 | 1.28150000 | -1.00810000 |
| O | 6.88160000 | 2.49570000 | -2.14680000 |
| O | -3.91390000 | -0.00480000 | -0.19470000 |
| C | -1.53880000 | -1.24810000 | 1.85540000 |
| O | -0.30030000 | -1.98890000 | 1.71520000 |
| C | -0.15270000 | -3.04350000 | 0.72230000 |
| C | -1.39090000 | -3.99450000 | 0.60730000 |
| C | -2.73850000 | -3.23410000 | 0.72880000 |
| C | -2.72990000 | -2.24980000 | 1.93500000 |
| O | -2.66410000 | -2.97890000 | 3.17060000 |
| C | 0.36130000 | -2.50900000 | -0.64320000 |
| O | 0.93940000 | -3.55740000 | -1.41690000 |
| O | -1.33640000 | -5.01270000 | 1.60940000 |
| O | -3.00220000 | -2.58660000 | -0.51590000 |
| H | -3.52020000 | 0.71970000 | 1.70290000 |
| H | -1.45090000 | -0.46970000 | -0.17570000 |
| H | 1.28600000 | 4.30700000 | -0.08210000 |
| H | -3.21030000 | 3.61880000 | -0.80190000 |
| H | 0.95350000 | 1.48980000 | -1.02660000 |
| H | 2.77240000 | 4.33240000 | -2.15210000 |
| H | 5.09840000 | 4.34100000 | -2.78450000 |
| H | 5.57200000 | 0.47880000 | -1.19450000 |
| H | 3.25850000 | 0.45830000 | -0.52070000 |
| H | 7.31150000 | 3.30640000 | -2.48690000 |
| H | -4.78110000 | 0.44240000 | -0.09900000 |
| H | -1.48190000 | -0.76030000 | 2.83390000 |
| H | 0.67140000 | -3.65360000 | 1.10270000 |
| H | -1.36790000 | -4.51750000 | -0.35320000 |
| H | -3.54670000 | -3.95490000 | 0.87960000 |
| H | -3.67990000 | -1.71450000 | 1.96250000 |
| H | -1.84850000 | -2.67610000 | 3.63050000 |
| H | 1.12360000 | -1.74620000 | -0.46820000 |
| H | -0.44200000 | -2.07730000 | -1.23650000 |

| | | | |
|---|-------------|-------------|-------------|
| H | 1.31060000 | -3.11760000 | -2.21200000 |
| H | -1.60570000 | -4.54650000 | 2.42360000 |
| H | -3.80560000 | -2.04130000 | -0.37820000 |

Table S6 Cartesian coordinates (Å) for the geometry optimized structure of **1a-3**

| Atom | X | Y | Z |
|------|-------------|-------------|-------------|
| C | 0.61390000 | 3.04130000 | 0.67750000 |
| C | -0.09660000 | 1.66820000 | 0.76310000 |
| C | 1.04940000 | 0.77070000 | 0.95890000 |
| C | 2.23030000 | 1.33060000 | 0.47490000 |
| C | 2.00400000 | 2.71350000 | 0.37770000 |
| O | 0.98530000 | -0.33460000 | 1.55210000 |
| C | 3.40360000 | 0.61180000 | 0.15690000 |
| C | 3.43880000 | -0.74330000 | -0.27290000 |
| O | 4.49900000 | 1.19990000 | 0.25770000 |
| O | 2.84010000 | 3.74770000 | 0.12530000 |
| C | 2.37920000 | -1.42270000 | -0.89460000 |
| C | 2.41370000 | -2.78190000 | -1.29250000 |
| C | 3.53320000 | -3.33310000 | -1.95210000 |
| C | 3.54570000 | -4.69780000 | -2.31900000 |
| C | 2.45260000 | -5.52050000 | -1.99650000 |
| C | 1.30160000 | -4.96390000 | -1.41930000 |
| C | 1.29270000 | -3.60340000 | -1.04400000 |
| O | 2.50050000 | -6.86180000 | -2.18570000 |
| O | 0.02790000 | 3.89640000 | -0.30700000 |
| C | -1.25630000 | 1.55410000 | 1.81270000 |
| O | -1.99580000 | 0.31550000 | 1.68240000 |
| C | -3.03040000 | 0.16130000 | 0.67400000 |
| C | -3.98720000 | 1.39830000 | 0.56660000 |
| C | -3.23250000 | 2.75270000 | 0.67170000 |
| C | -2.24820000 | 2.75900000 | 1.87570000 |
| O | -2.97740000 | 2.74930000 | 3.10800000 |
| C | -2.50530000 | -0.34190000 | -0.70340000 |
| O | -1.53380000 | -1.37650000 | -0.56440000 |
| O | -4.98830000 | 1.35420000 | 1.59160000 |
| O | -2.58440000 | 3.01630000 | -0.57140000 |
| H | 0.61550000 | 3.55160000 | 1.64080000 |
| H | -0.46940000 | 1.44180000 | -0.22880000 |

| | | | |
|---|-------------|-------------|-------------|
| H | 4.31310000 | -1.25470000 | -0.11580000 |
| H | 3.80260000 | 3.64310000 | 0.00740000 |
| H | 1.49790000 | -0.93200000 | -1.05820000 |
| H | 4.34010000 | -2.75190000 | -2.18960000 |
| H | 4.34790000 | -5.07900000 | -2.82370000 |
| H | 0.48670000 | -5.55160000 | -1.23420000 |
| H | 0.47060000 | -3.24170000 | -0.55400000 |
| H | 3.31090000 | -7.29360000 | -2.52320000 |
| H | 0.42610000 | 4.78090000 | -0.15740000 |
| H | -0.77280000 | 1.50610000 | 2.79390000 |
| H | -3.63360000 | -0.67010000 | 1.04820000 |
| H | -4.51860000 | 1.37400000 | -0.38960000 |
| H | -3.95590000 | 3.55930000 | 0.81910000 |
| H | -1.70300000 | 3.70190000 | 1.89180000 |
| H | -3.81430000 | 2.29990000 | 2.88280000 |
| H | -2.07240000 | 0.46670000 | -1.28570000 |
| H | -3.33350000 | -0.73840000 | -1.29290000 |
| H | -2.01510000 | -2.13810000 | -0.17420000 |
| H | -5.36430000 | 0.44960000 | 1.56510000 |
| H | -2.03370000 | 3.81610000 | -0.42800000 |

Table S7 Cartesian coordinates (Å) for the geometry optimized structure of **1b-1**

| Atom | X | Y | Z |
|------|-------------|-------------|-------------|
| C | -1.05180000 | 1.24370000 | 0.08120000 |
| C | -1.67730000 | -0.16410000 | 0.30860000 |
| C | -0.55930000 | -1.06290000 | -0.06090000 |
| C | 0.55050000 | -0.38850000 | -0.57150000 |
| C | 0.27230000 | 0.96820000 | -0.46660000 |
| O | -0.59140000 | -2.29690000 | 0.15080000 |
| C | 1.74160000 | -0.95270000 | -1.08550000 |
| C | 3.02470000 | -0.44050000 | -0.79560000 |
| O | 1.63580000 | -1.96880000 | -1.81250000 |
| O | 1.09430000 | 1.98760000 | -0.78390000 |
| C | 4.20730000 | -0.71350000 | -1.52370000 |
| C | 5.47850000 | -0.20240000 | -1.18890000 |
| C | 6.61520000 | -1.05280000 | -1.21650000 |
| C | 7.88960000 | -0.57220000 | -0.85380000 |
| C | 8.04170000 | 0.77110000 | -0.45690000 |

| | | | |
|---|-------------|-------------|-------------|
| C | 6.94820000 | 1.64630000 | -0.50990000 |
| C | 5.67160000 | 1.15790000 | -0.83630000 |
| O | 9.17540000 | 1.24170000 | 0.10310000 |
| O | -0.84940000 | 1.98850000 | 1.27940000 |
| C | -2.97730000 | -0.40040000 | -0.53970000 |
| O | -3.92430000 | 0.69040000 | -0.42170000 |
| C | -4.86670000 | 0.74800000 | 0.67990000 |
| C | -5.60310000 | -0.60860000 | 0.89770000 |
| C | -4.61250000 | -1.80710000 | 0.88910000 |
| C | -3.70470000 | -1.77560000 | -0.37260000 |
| O | -4.50250000 | -2.04580000 | -1.53470000 |
| C | -4.27680000 | 1.34440000 | 1.98800000 |
| O | -3.63550000 | 2.58880000 | 1.72710000 |
| O | -6.60670000 | -0.78790000 | -0.10580000 |
| O | -3.81640000 | -1.82510000 | 2.07860000 |
| H | -1.62460000 | 1.85080000 | -0.62960000 |
| H | -1.87870000 | -0.29480000 | 1.37110000 |
| H | 3.11330000 | 0.15250000 | 0.03220000 |
| H | 0.77370000 | 2.89470000 | -0.58610000 |
| H | 4.15120000 | -1.33900000 | -2.33330000 |
| H | 6.51930000 | -2.03640000 | -1.48610000 |
| H | 8.70070000 | -1.19780000 | -0.87510000 |
| H | 7.07500000 | 2.62270000 | -0.23210000 |
| H | 4.88230000 | 1.80630000 | -0.80060000 |
| H | 9.89230000 | 0.63110000 | 0.35780000 |
| H | -1.74400000 | 2.26260000 | 1.53150000 |
| H | -2.64870000 | -0.35510000 | -1.58250000 |
| H | -5.62410000 | 1.46980000 | 0.36110000 |
| H | -6.13600000 | -0.59140000 | 1.85110000 |
| H | -5.18650000 | -2.73780000 | 0.87880000 |
| H | -2.98800000 | -2.59290000 | -0.30490000 |
| H | -3.87710000 | -2.14750000 | -2.28280000 |
| H | -5.07980000 | 1.53110000 | 2.70190000 |
| H | -3.57370000 | 0.66420000 | 2.46270000 |
| H | -3.29650000 | 2.89710000 | 2.59450000 |
| H | -6.09580000 | -1.02660000 | -0.90540000 |
| H | -4.44650000 | -1.77410000 | 2.83030000 |

Table S8 Cartesian coordinates (Å) for the geometry optimized structure of **1b-2**

| Atom | X | Y | Z |
|------|-------------|-------------|-------------|
| C | 0.66830000 | 2.69200000 | 1.13850000 |
| C | 0.04520000 | 1.28510000 | 1.37750000 |
| C | 1.16050000 | 0.39250000 | 1.02280000 |
| C | 2.22290000 | 1.06540000 | 0.42540000 |
| C | 1.92610000 | 2.42940000 | 0.45440000 |
| O | 1.14630000 | -0.84010000 | 1.25480000 |
| C | 3.36420000 | 0.45490000 | -0.12720000 |
| C | 3.34100000 | -0.71000000 | -0.92730000 |
| O | 4.47960000 | 0.95590000 | 0.12990000 |
| O | 2.55930000 | 3.47870000 | -0.11920000 |
| C | 2.22170000 | -1.15980000 | -1.64590000 |
| C | 2.21460000 | -2.32610000 | -2.43950000 |
| C | 3.25710000 | -2.61030000 | -3.35090000 |
| C | 3.18320000 | -3.74450000 | -4.18670000 |
| C | 2.05590000 | -4.58380000 | -4.12980000 |
| C | 1.06300000 | -4.36270000 | -3.16340000 |
| C | 1.12080000 | -3.21510000 | -2.34800000 |
| O | 1.87260000 | -5.57840000 | -5.02890000 |
| O | 0.90820000 | 3.41790000 | 2.34200000 |
| C | -1.24130000 | 1.05090000 | 0.51070000 |
| O | -2.18710000 | 2.14220000 | 0.62900000 |
| C | -3.13550000 | 2.19920000 | 1.72510000 |
| C | -3.87260000 | 0.84310000 | 1.94330000 |
| C | -2.89020000 | -0.36150000 | 1.91820000 |
| C | -1.97210000 | -0.31940000 | 0.66480000 |
| O | -2.73910000 | -0.56090000 | -0.51840000 |
| C | -2.55810000 | 2.81050000 | 3.03020000 |
| O | -1.92860000 | 4.05800000 | 2.76290000 |
| O | -4.87630000 | 0.69250000 | 0.93240000 |
| O | -2.12150000 | -0.39020000 | 3.12510000 |
| H | 0.06130000 | 3.30850000 | 0.47120000 |
| H | -0.16100000 | 1.14530000 | 2.43610000 |
| H | 4.20590000 | -1.25620000 | -0.98370000 |
| H | 3.34060000 | 3.38140000 | -0.69500000 |
| H | 1.34300000 | -0.63920000 | -1.58470000 |
| H | 4.06640000 | -1.98980000 | -3.43260000 |

| | | | |
|---|-------------|-------------|-------------|
| H | 3.94840000 | -3.94990000 | -4.83240000 |
| H | 0.27840000 | -5.01200000 | -3.08020000 |
| H | 0.34670000 | -3.03410000 | -1.70270000 |
| H | 2.50780000 | -5.71530000 | -5.75980000 |
| H | 1.37960000 | 4.23380000 | 2.05510000 |
| H | -0.90730000 | 1.09950000 | -0.53220000 |
| H | -3.89120000 | 2.91970000 | 1.39790000 |
| H | -4.39610000 | 0.85680000 | 2.90360000 |
| H | -3.47220000 | -1.28670000 | 1.89510000 |
| H | -1.25780000 | -1.13930000 | 0.72460000 |
| H | -3.35400000 | 0.20460000 | -0.57300000 |
| H | -3.36800000 | 2.99930000 | 3.73640000 |
| H | -1.85170000 | 2.14330000 | 3.51850000 |
| H | -1.08690000 | 3.82500000 | 2.32750000 |
| H | -5.41900000 | -0.07770000 | 1.20740000 |
| H | -1.60210000 | -1.22380000 | 3.10200000 |

Table S9 Cartesian coordinates (Å) for the geometry optimized structure of **1b-3**

| Atom | X | Y | Z |
|------|-------------|-------------|-------------|
| C | -0.85540000 | 0.95860000 | -0.30540000 |
| C | -1.47770000 | -0.44960000 | -0.07400000 |
| C | -0.36220000 | -1.34780000 | -0.44010000 |
| C | 0.74280000 | -0.67390000 | -0.94790000 |
| C | 0.46400000 | 0.68490000 | -0.85800000 |
| O | -0.39470000 | -2.58480000 | -0.22610000 |
| C | 1.93600000 | -1.24390000 | -1.44300000 |
| C | 3.24000000 | -0.78840000 | -1.21440000 |
| O | 1.81700000 | -2.25440000 | -2.18620000 |
| O | 1.28060000 | 1.70490000 | -1.18220000 |
| C | 3.64610000 | 0.04860000 | -0.14100000 |
| C | 4.95650000 | 0.48630000 | 0.06000000 |
| C | 6.07320000 | -0.38670000 | -0.05270000 |
| C | 7.37980000 | 0.07990000 | 0.15220000 |
| C | 7.60210000 | 1.44100000 | 0.45790000 |
| C | 6.50800000 | 2.30170000 | 0.63980000 |
| C | 5.20510000 | 1.84250000 | 0.41540000 |
| O | 8.82690000 | 1.99960000 | 0.45700000 |
| O | -0.64710000 | 1.70210000 | 0.89190000 |

| | | | |
|---|-------------|-------------|-------------|
| C | -2.77180000 | -0.68480000 | -0.92570000 |
| O | -3.72190000 | 0.40340000 | -0.81000000 |
| C | -4.65650000 | 0.46010000 | 0.29720000 |
| C | -5.39410000 | -0.89700000 | 0.50980000 |
| C | -4.40840000 | -2.09840000 | 0.50010000 |
| C | -3.49970000 | -2.05630000 | -0.76020000 |
| O | -4.27520000 | -2.29380000 | -1.93860000 |
| C | -4.06910000 | 1.05430000 | 1.60520000 |
| O | -3.43090000 | 2.29930000 | 1.34100000 |
| O | -6.37150000 | -1.07910000 | -0.52200000 |
| O | -3.63520000 | -2.12080000 | 1.70590000 |
| H | -1.42840000 | 1.56510000 | -1.01620000 |
| H | -1.67990000 | -0.58090000 | 0.98760000 |
| H | 3.96960000 | -1.08990000 | -1.86860000 |
| H | 0.96380000 | 2.61120000 | -0.97730000 |
| H | 2.93210000 | 0.36680000 | 0.51930000 |
| H | 5.92740000 | -1.37720000 | -0.27180000 |
| H | 8.17120000 | -0.56640000 | 0.08240000 |
| H | 6.68230000 | 3.28800000 | 0.85490000 |
| H | 4.43350000 | 2.51320000 | 0.47010000 |
| H | 9.59870000 | 1.50430000 | 0.12210000 |
| H | -1.54100000 | 1.97530000 | 1.14620000 |
| H | -2.44080000 | -0.64220000 | -1.96870000 |
| H | -5.40940000 | 1.18780000 | -0.01840000 |
| H | -5.93260000 | -0.88600000 | 1.46160000 |
| H | -4.98840000 | -3.02520000 | 0.48220000 |
| H | -2.78770000 | -2.87770000 | -0.70640000 |
| H | -4.86170000 | -1.50720000 | -2.01000000 |
| H | -4.87350000 | 1.24100000 | 2.31740000 |
| H | -3.36780000 | 0.37280000 | 2.08010000 |
| H | -3.09180000 | 2.60930000 | 2.20760000 |
| H | -6.85060000 | -0.22700000 | -0.59800000 |
| H | -3.13040000 | -2.96420000 | 1.69580000 |

Table S10 Cartesian coordinates (Å) for the geometry optimized structure of **1b-4**

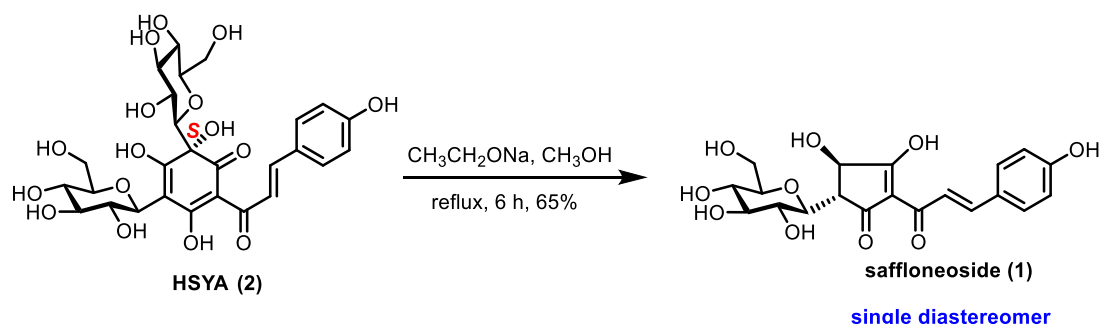
| Atom | X | Y | Z |
|------|------------|------------|------------|
| C | 0.67520000 | 2.70370000 | 1.11130000 |
| C | 0.06110000 | 1.29030000 | 1.33900000 |

| | | | |
|---|-------------|-------------|-------------|
| C | 1.17990000 | 0.40270000 | 0.98200000 |
| C | 2.24230000 | 1.08040000 | 0.39180000 |
| C | 1.94090000 | 2.44410000 | 0.43160000 |
| O | 1.17260000 | -0.83080000 | 1.20720000 |
| C | 3.38330000 | 0.46890000 | -0.16350000 |
| C | 3.36380000 | -0.69810000 | -0.96190000 |
| O | 4.49920000 | 0.97050000 | 0.09130000 |
| O | 2.58090000 | 3.49010000 | -0.14140000 |
| C | 2.24640000 | -1.15220000 | -1.68180000 |
| C | 2.23990000 | -2.31910000 | -2.47430000 |
| C | 3.28200000 | -2.60380000 | -3.38630000 |
| C | 3.20790000 | -3.73740000 | -4.22280000 |
| C | 2.08120000 | -4.57750000 | -4.16650000 |
| C | 1.08810000 | -4.35600000 | -3.19990000 |
| C | 1.14630000 | -3.20900000 | -2.38350000 |
| O | 1.90060000 | -5.57340000 | -5.06500000 |
| O | 0.88370000 | 3.43420000 | 2.32020000 |
| C | -1.22850000 | 1.05340000 | 0.47350000 |
| O | -2.17050000 | 2.14960000 | 0.59480000 |
| C | -3.11480000 | 2.20730000 | 1.69350000 |
| C | -3.85410000 | 0.85080000 | 1.90350000 |
| C | -2.86910000 | -0.35280000 | 1.88670000 |
| C | -1.95400000 | -0.32330000 | 0.63060000 |
| O | -2.73460000 | -0.60220000 | -0.54160000 |
| C | -2.51100000 | 2.79700000 | 2.99750000 |
| O | -3.53810000 | 3.08830000 | 3.94340000 |
| O | -4.85390000 | 0.67750000 | 0.89530000 |
| O | -2.06830000 | -0.38440000 | 3.07160000 |
| H | 0.07060000 | 3.31500000 | 0.43740000 |
| H | -0.13630000 | 1.14190000 | 2.39740000 |
| H | 4.22980000 | -1.24360000 | -1.01720000 |
| H | 3.36340000 | 3.38570000 | -0.71540000 |
| H | 1.36750000 | -0.63230000 | -1.62160000 |
| H | 4.09150000 | -1.98350000 | -3.46740000 |
| H | 3.97300000 | -3.94280000 | -4.86870000 |
| H | 0.30360000 | -5.00560000 | -3.11680000 |
| H | 0.37300000 | -3.02910000 | -1.73700000 |
| H | 2.53720000 | -5.71100000 | -5.79480000 |

| | | | |
|---|-------------|-------------|-------------|
| H | 1.37360000 | 4.24150000 | 2.04110000 |
| H | -0.89590000 | 1.10370000 | -0.56900000 |
| H | -3.86790000 | 2.93450000 | 1.37610000 |
| H | -4.38880000 | 0.86300000 | 2.85610000 |
| H | -3.44890000 | -1.27970000 | 1.87350000 |
| H | -1.23320000 | -1.13660000 | 0.71040000 |
| H | -2.09940000 | -0.67910000 | -1.28520000 |
| H | -1.82490000 | 2.10120000 | 3.46990000 |
| H | -1.96660000 | 3.71540000 | 2.76920000 |
| H | -3.06640000 | 3.35050000 | 4.76340000 |
| H | -4.33930000 | 0.44240000 | 0.09740000 |
| H | -2.69620000 | -0.33940000 | 3.82520000 |

1.3 Specific experimental conditions

1.3.1 Synthesis of saffloneoside (1) from hydroxysafflor yellow A (HSYA)



To a stirred solution of HSYA (1.0 g, 1.63 mmol) in anhydrous MeOH (60 mL) were added $\text{CH}_3\text{CH}_2\text{ONa}$ (2.5 g, 36.76 mmol) at room temperature. Then, the resulting mixture was stirred for 6 h under reflux. Water (20 mL) was added to quench the reaction, and the mixture was neutralized with 1 M aqueous HCl. The mixed solution was concentrated under reduced pressure at 40 °C, and the concentrated residue was purified by Sephadex LH-20 with H_2O as the mobile phase to give **1** (447 mg, 65%) as a yellow powder.

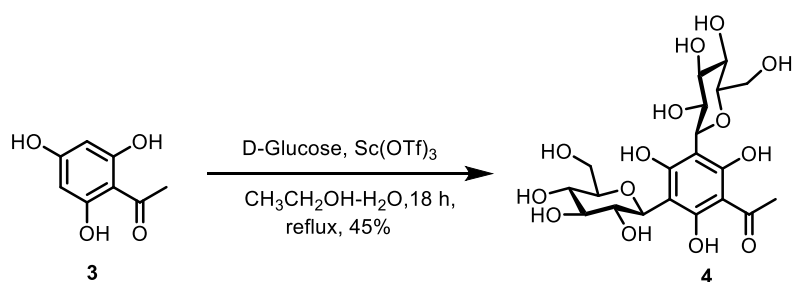
$[\alpha]_{\text{D}}^{20} = -33.3$ ($c = 0.15$, MeOH).

$^1\text{H NMR}$ (500 MHz, $\text{D}_2\text{O} + \text{NaOD}$) δ_{H} : 7.42 (1H, d, $J = 15.7$ Hz, H-7), 7.35 (2H, d, $J = 8.5$ Hz, H-10 and H-14), 7.32 (1H, d, $J = 15.7$ Hz, H-8), 6.51 (2H, d, $J = 8.5$ Hz, H-11 and H-13), 4.34 (1H, brs, H-4), 3.77 (1H, dd, $J = 8.5, 2.0$ Hz, H-1'), 3.66 (1H, m, H₁-6'), 3.53 (1H, dd, $J = 12.5, 5.0$ Hz, H₂-6'), 3.43 (1H, m, H-3'), 3.41 (1H, m, H-4'), 3.28 (1H, m, H-2'), 3.25 (1H, m, H-5'), 2.72 (1H, brs, H-5).

¹³C NMR (500 MHz, D₂O + NaOD) δ_C: 202.6 (C-3), 201.2 (C-1), 188.8 (C-6), 170.8 (C-12), 144.3 (C-8), 131.2 (C-10, 14), 121.2 (C-9), 119.6 (C-11, 13), 119.4 (C-7), 114.5 (C-2), 79.4 (C-5'), 77.7 (C-3'), 76.0 (C-1'), 71.0 (C-4'), 70.2 (C-4), 69.6 (C-2'), 60.8 (C-6'), 52.7 (C-5).

The ¹H NMR, ¹³C NMR, and optical rotation value of the synthetic **1** were in good agreement with those for natural saffloneoside.

1.3.2 Synthesis of 2,4,6-trihydroxy-3,5-di-C-glucosylacetophenone **4**



To a stirred solution of 2,4,6-trihydroxyacetophenone (1.0 g, 5.96 mmol) and D-glucose (5.4 g, 29.80 mmol) in ethanol (30 mL) and H₂O (15 mL) at room temperature, scandium(III) trifluoromethanesulfonate (1.2 g, 2.38 mmol) was added, and the resultant mixture was heated at 90 °C for 18 h. Water (200 mL) was added to the reaction mixture, and the suspension was passed through a column of MCI GEL CHP20P (75–150 μm, Mitsubishi Chemical Corp., 3.5 × 25 cm) loaded with water, and the gel was then washed with 300 mL of water, to remove nonabsorbed glucose and Sc(OTf)₃. The nonabsorbed components, which include the unreactive glucose and Sc(OTf)₃, was evaporated in vacuo to give a colorless solid. The absorbed products were eluted from the gel column with 300 mL of 50% aqueous CH₃OH, and the eluate was evaporated in vacuo to give a pale-brown solid (2.2 g) that was then separated by silica-gel column chromatography (Me₂CO : EtOAc : H₂O : AcOH = 15 : 30 : 2 : 1) to give **4** (1.32 g, 45%) as white powder.

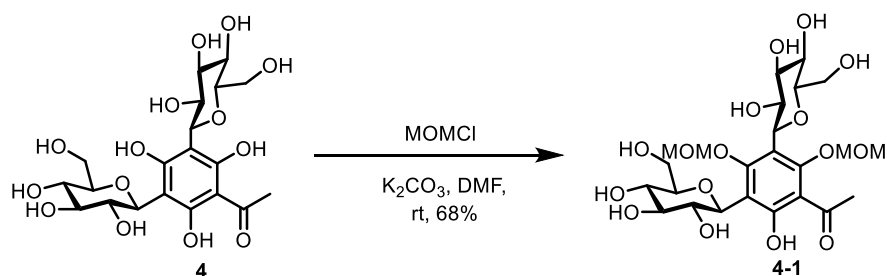
R_f 0.18 (Me₂CO : EtOAc : H₂O : AcOH = 15 : 30 : 2 : 1).

¹H NMR (500 MHz, CD₃OD) δ_H: 4.92 (2H, d, *J* = 9.7), 3.82 (4H, m), 3.60 (2H, m), 3.51 (2H, m), 3.49 (2H, m), 3.44 (2H, m), 2.65 (3H, s) ppm.

¹³C NMR (125 MHz, CD₃OD) δ_C: 205.5, 163.3 (2C), 162.5, 106.4, 104.3 (2C), 82.7 (2C), 79.1 (2C), 76.7 (2C), 74.1 (2C), 71.1 (2C), 61.9 (2C) ppm.

HRMS(ESI): calc. for C₂₀H₂₉O₁₄ [M + H]⁺: 493.1479, found: 439.1472.

1.3.3 Synthesis of 2-hydroxy-4,6-dimethoxymethoxy-3,5-di-C-glucosylacetophenone 4-1



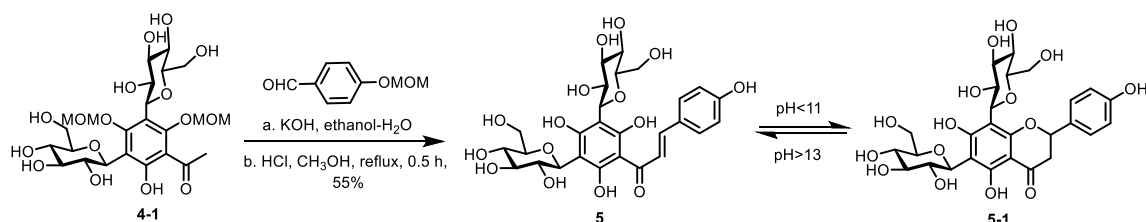
To a stirred solution of 2,4,6-trihydroxy-3,5-di-C-glucosylacetophenone **4** (500 mg, 1.02 mmol) in DMF (8 mL) at room temperature, K₂CO₃ (1042 mg, 7.55 mmol) was added. After 15 min, MOMCl was added dropwise under argon, and the reaction mixture was stirred at rt for 5 h and then filtered. The filtrate was evaporated and the residue was chromatographed with Me₂CO : EtOAc : H₂O (20 : 20 : 3) to give **4-1** (402 mg, 68%) as a yellow solid.

R_f 0.25 (Me₂CO : EtOAc : H₂O = 20 : 20 : 3).

¹H NMR (500 MHz, CD₃OD) δ_H: 5.13 (1H, d, *J* = 5.1), 5.10 (1H, d, *J* = 5.1), 4.98 (1H, d, *J* = 5.8), 4.87 (1H, d, *J* = 5.8), 4.60 (1H, d, *J* = 9.6), 4.46 (1H, d, *J* = 9.6), 3.82 (2H, m), 3.74 (2H, m), 3.65 (1H, m), 3.61 (2H, m), 3.61 (3H, s), 3.59 (3H, s), 3.44 (1H, m), 3.44 (1H, m), 3.41 (1H, m), 3.36 (2H, 3.36) ppm.

HRMS(ESI): calc. for C₂₄H₃₇O₁₆ [M + H]⁺: 581.2037, found: 581.2029.

1.3.4 Synthesis of 2,4,6,13-tetrahydroxy-3,5-di-C-glucosylchalone 5



To a stirred solution of **4-1** (580 mg, 1.0 mmol) and 4-methoxymethoxybenzaldehyde (340 mg, 2.0 mmol) in ethanol (5.7 mL) and H₂O (3.0 mL), 50% aqueous potassium hydroxide (2.9 mL) was added dropwise at 0 °C. After 3h, the reaction mixture was stirred at rt for 2 d. Then the mixture was carefully neutralized with 1 M aqueous HCl and concentrated by rotary evaporation under reduced pressure. The residue was redissolved in MeOH (10 mL), and concentrated hydrochloric acid (1 mL) was added. The mixture was stirred at 50 °C for 30 min, then neutralized with 10% NaHCO₃. The solution was concentrated under reduced pressure and purified by

preparative HPLC with an ODS-A column (250 × 20 mm, 5 μm, YMC Corp.) using MeOH-H₂O (45 : 55, v/v) as mobile phase to afford **5** (328 mg, 55%) as a yellow solid. In addition, isomerism between di-C-glucosylchalcone (**5**) and flavanone (**5-1**) can be reversibly controlled by altering solution pH. These two constitutional isomers rapidly interconvert between pH 11 and 13, with flavanone (**5-1**) the only species present at the low end of this range and anionic chalcone (**5**) observed exclusively in more alkaline solutions. This change can be detected colorimetrically, as only **5** absorbs strongly in the ultraviolet region.

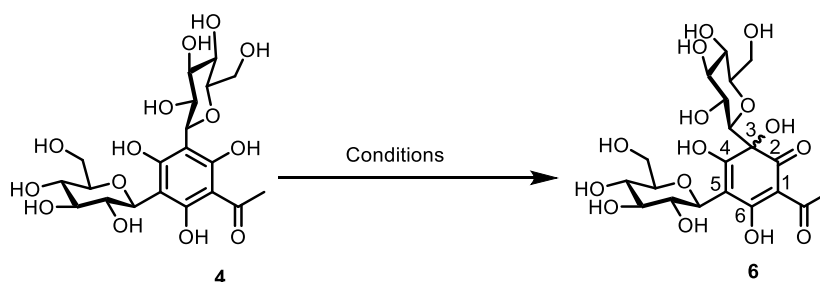
¹H NMR (500 MHz, CD₃OD) of 5-1 δ_H: 7.34 (2H, d, *J* = 8.5, H-12,16), 6.78 (2H, d, *J* = 8.5, H-13,15), 5.37 (1H, m, H-2), 4.85 (1H, d, *J* = 10.4, H-1'), 4.79 (1H, d, *J* = 10.4, H-1''), 3.93 (1H, m, H₁-6'), 3.82 (1H, m, H-5'), 3.80 (1H, m, H₁-6''), 3.78 (1H, m, H-5''), 3.68 (1H, m, H₂-6''), 3.45 (1H, m, H-3''), 3.44 (1H, m, H-4'), 3.37 (1H, m, H-4'') 3.36 (1H, m, H-3'), 3.32 (2H, m, H-2', 2''), 3.05 (1H, m, H₁-3), 2.74 (1H, m, H₂-3) ppm.

¹³C NMR (125 MHz, CD₃OD) of 5-1 δ_C: 197.0, 165.2, 161.3, 157.5, 157.4, 129.7, 129.4, 127.7 (2C), 127.3, 114.9 (2C), 101.6, 81.1 (2), 81.0, 80.9, 78.9, 78.7, 78.3, 74.2, 71.6, 71.5, 71.4, 70.0, 60.9 (2C) ppm.

HRMS(ESI): calc. for C₂₇H₃₃O₁₅ [M + H]⁺: 597.1775, found: 597.1773.

1.3.5 Synthesis of 3,4,6-trihydroxycyclohexadienone **6**^[a]

Table S11 Oxidative dearomatization of 4



| entry | catalyst | pH | oxidant | time (h) | yield (%) ^[g, h] |
|------------------|--|-----|---|----------|-----------------------------|
| 1 ^[b] | pyridine | - | O ₂ | 24 | - |
| 2 ^[c] | Pb(OAc) ₂ | - | O ₂ | 24 | - |
| 3 ^[c] | Pb(OAc) ₂ ·Pb(OH) | - | O ₂ | 24 | - |
| 4 ^[d] | NaHCO ₃ | - | PhI(OCOFCF ₃) ₂ | 12 | - |
| 5 ^[e] | - | - | Ce(NH ₄) ₂ (NO ₃) ₆ | 12 | - |
| 6 ^[f] | - | - | DDQ | 12 | - |
| 7 | NH ₄ Cl-NH ₃ ·H ₂ O | 7.0 | air | 24 | - |
| 8 | NH ₄ Cl-NH ₃ ·H ₂ O | 7.5 | air | 24 | 21 |
| 9 | NH ₄ Cl-NH ₃ ·H ₂ O | 8.0 | air | 24 | 68 |
| 10 | NH ₄ Cl-NH ₃ ·H ₂ O | 8.5 | air | 24 | 62 |
| 11 | NH ₄ Cl-NH ₃ ·H ₂ O | 9.0 | air | 24 | 36 |
| 12 | NH ₄ Cl-NH ₃ ·H ₂ O | 9.5 | air | 24 | - |
| 13 | NH ₄ Cl-NH ₃ ·H ₂ O | 8.0 | O ₂ | 12 | 72 |
| 14 | K ₂ HPO ₄ -KH ₂ PO ₄ | 7.5 | O ₂ | 12 | 35 |
| 15 | K ₂ HPO ₄ -KH ₂ PO ₄ | 8.0 | O ₂ | 12 | 49 |

[a] Reaction conditions: **4** (1.0 mmol), room temperature. [b] Pyridine (2 equiv), CH₃OH as solvent. [c] Catalyst (2.5 equiv), CH₃OH as solvent. [d] PhI(OCOFCF₃)₂ (1.5 equiv), NaHCO₃ (3.0 equiv), CH₃CN as solvent. [e] CAN (3 equiv), CH₃OH as solvent. [f] DDQ (1 equiv), CH₃OH as solvent. [g] Determined by UV and MS. [h] d.r. 1:1.

Many commonly used dearomatization reagents (Pyridine, Pb(OAc)₂, Pb(OAc)₂·Pb(OH), PhI(OCOFCF₃)₂, Ce(NH₄)₂(NO₃)₆, and DDQ) were examined, but none of these reagents were suitable for the reaction due to serious side reactions or poor reactivity of **4** (entries 1–6).^[3–8] To our delight, vigorous stirring of **4** in NH₄Cl-NH₃·H₂O buffer salt (pH = 7.5) under an air atmosphere at room temperature for 24 h afforded oxidized products **6** in a total yield of 21% as an inseparable mixture of stereoisomers. Then, this reaction was evaluated with various buffer salts with different pH values, and the yield of product **6** was improved to 72% in the presence of NH₄Cl-NH₃·H₂O buffer salt (pH = 8.0) under O₂.

General procedure for **6**:

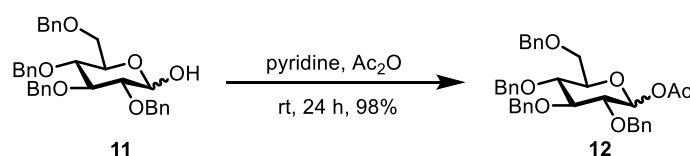
Preparation of NH₄Cl-NH₃·H₂O buffer salt (pH = 8.0, 500 mL). To a stirred solution of the NH₄Cl (5.35 g) in H₂O (500 mL), NH₃·H₂O (1→30) was added dropwise until pH reached 8.0 at room temperature.

A solution of **4** (1.0 mmol) in NH₄Cl-NH₃·H₂O buffer salt (pH = 8.0, 30 mL) was vigorously stirred at rt under O₂ atmosphere (balloon) for 12 h. The mixture was passed through a column of MCI

GEL CHP20P (75–150 μm , Mitsubishi Chemical Corp., 1.5 \times 20 cm) loaded with water, and the gel was then washed with 100 mL of water, to remove nonabsorbed NH_4Cl and $\text{NH}_3\cdot\text{H}_2\text{O}$. The absorbed products were eluted from the gel column with 100 mL of 30% aqueous MeOH, and the eluate was evaporated in vacuo to give a light green solid **6**.

Due to the instability of quinone unit of **6**, it is difficult to obtain the pure product. The target product was identified by the characteristic ultraviolet absorption and HRMS (ESI) measurements.

1.3.6 Synthesis of glucosyl acetate **12**



To a solution of 2,3,4,6-tetra-O-benzyl-D-glucopyranose **11** (60.0 g, 112 mmol) in pyridine (300 mL) was added Ac_2O (80 mL) at room temperature and the solution was stirred for 24 h at room temperature. The reaction was quenched with CH_3OH (100 mL) at 0 $^\circ\text{C}$ and concentrated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether : EtOAc = 5 : 1) to afford acetate **12** (65.2 g, 98%) as a colorless oil. (α -anomer as major product)

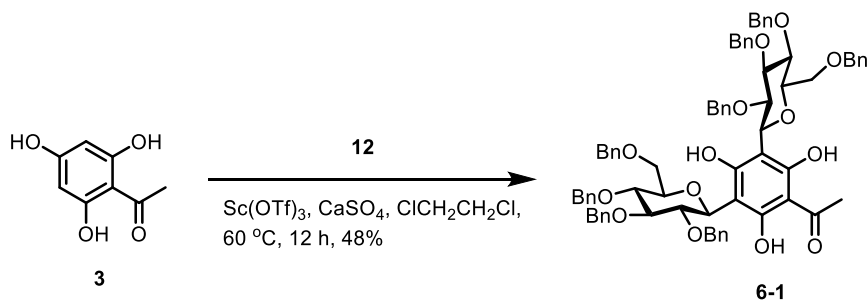
R_f 0.32 (petroleum ether : EtOAc = 5 : 1).

^1H NMR (500 MHz, DMSO- d_6) δ_{H} : 7.31 (18H, m), 7.18 (2H, m), 6.26 (1H, d, J = 3.3 Hz), 4.83 (1H, m), 4.77-4.72 (3H, m), 4.64 (1H, m), 4.53-4.47 (3H, m), 3.81 (2H, m), 3.68 (1H, m), 3.63 (m, 1H), 3.60 (2H, m), 2.12 (3H, s) ppm.

^{13}C NMR (500 MHz, DMSO- d_6) δ_{C} : 169.7, 139.1, 138.6, 138.5 (2C), 128.8-128.1 (20C), 89.7, 81.5, 78.8, 77.2, 75.1, 74.7, 72.8, 72.7, 72.5, 68.7, 21.3 ppm.

HRMS(ESI): calc. for $\text{C}_{36}\text{H}_{38}\text{O}_7$ [$\text{M} + \text{H}$] $^+$: 583.2618, found: 583.2612.

1.3.7 Synthesis of di-C-(per-O-benzylglucosyl)phloroacetophenone **6-1**



To a stirred solution of 2,4,6-trihydroxyacetophenone **3** (1.0 g, 5.95 mmol) in $\text{ClCH}_2\text{CH}_2\text{Cl}$ (20 mL) was added Sc(OTf)_3 (1.2 g, 2.38 mmol), **12** (10.4 g, 17.85 mmol), and CaSO_4 (1.0 g) at room temperature. After stirring for 12 h at 60 °C under nitrogen, the reaction mixture was filtered through a thin pad of Celite®, and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether : EtOAc = 10 : 1) to afford **6-1** (3.5 g, 48%) as a white powder.

R_f 0.36 (petroleum ether : EtOAc = 10 : 1).

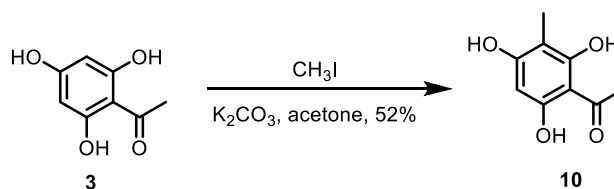
IR (KBr): 3171, 2912, 2869, 1614, 1090, 742, 698 cm^{-1} .

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ_{H} : 14.41 (OH, s), 9.35 (OH, s), 7.38-7.15 (40H, m), 5.25-4.62 (16H, m), 3.87-3.62 (14H, m), 2.73 (3H, s) ppm.

$^{13}\text{C NMR}$ (500 MHz, $\text{DMSO-}d_6$) δ_{C} : 204.3, 161.9, 161.3 (2C), 140.9, 139.1-138.6 (8C), 136.5, 128.7-126.4 (40C), 85.7 (2C), 81.3 (2C), 78.4 (2C), 77.7 (2C), 74.8 (2C), 74.6 (2C), 74.1 (2C), 73.3 (2C), 72.7 (2C), 68.5 (2C), 33.4 ppm.

HRMS(ESI): calc. for $\text{C}_{76}\text{H}_{77}\text{O}_{14}$ $[\text{M} + \text{H}]^+$: 1213.5235, found: 1213.5308.

1.3.8 Synthesis of 3-methyl-2,4,6-trihydroxyacetophenone **10**



To a solution of 2,4,6-trihydroxyacetophenone (10.0 g, 59.5 mmol) in anhydrous acetone (200 mL) was added K_2CO_3 (20.5 g, 148.8 mmol). CH_3I (15.0 mL, 240 mmol) was added over 5 min after the mixture was brought to 0 °C. The reaction was allowed to proceed for 12 h at 0 °C.

with stirring. Then, the reaction was quenched with H₂O (200 mL) and concd HCl (9 mL), and the resulting mixture was extracted with CH₂Cl₂ (400 mL) three times and the combined organic layer was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated in vacuo and the residue was purified by silica gel column chromatography (n-hexane : isopropanol = 15:1) to provide **10** (5.6 g, 52 %) as a yellow powder.

m.p. 211-212 °C.

R_f 0.28 (n-hexane : isopropanol = 15 : 1).

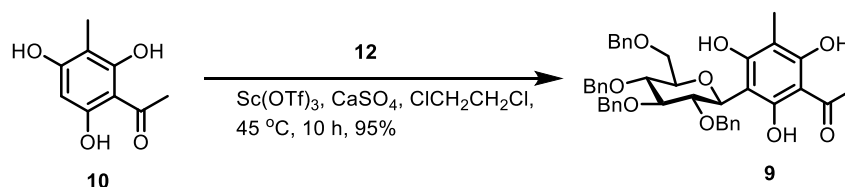
IR (KBr): 3200, 2935, 1630, 1569, 1443, 1361, 1113, 796 cm⁻¹.

¹H NMR (500 MHz, DMSO-*d*₆) δ_H: 13.97 (OH, s), 10.55 (OH, s), 10.32 (OH, s), 6.01 (1H, s), 2.55 (3H, s), 1.83 (3H, s) ppm.

¹³C NMR (500 MHz, DMSO-*d*₆) δ_C: 203.1, 164.0, 163.3, 160.7, 104.4, 101.9, 94.5, 33.1, 7.9 ppm.

HRMS(ESI): calc. for C₉H₉O₄ [M - H]: 181.0579, found: 181.0504.

1.3.9 Synthesis of 3-methyl-5-C-(per-O-benzylglucosyl)-2,4,6-trihydroxyacetophenone **9**



To a stirred solution of 3-methyl-2,4,6-trihydroxyacetophenone **10** (5.0 g, 27.47 mmol) in ClCH₂CH₂Cl (100 mL) was added Sc(OTf)₃ (5.41 g, 10.99 mmol), **12** (13.3 g, 22.89 mmol), and CaSO₄ (10.0 g) at room temperature. After stirring for 12 h at 45 °C under nitrogen, the reaction mixture was filtered through a thin pad of Celite®, and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether : acetone = 15 : 1) to afford **9** (18.4 g, 95%) as a white solid.

m.p. 132-133 °C.

R_f 0.32 (petroleum ether : acetone = 15 : 1).

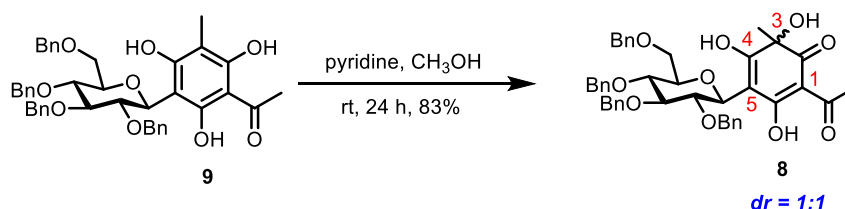
IR (KBr): 3294, 2916, 2880, 1621, 1593, 1088, 751, 694 cm⁻¹.

¹H NMR (500 MHz, DMSO-*d*₆) δ_H: 7.43-7.03 (20H), 5.14-4.57 (8H), 4.18 (1H, d, *J* = 10.3 Hz), 3.93-3.83 (3H, m), 3.79-3.74 (3H, m), 2.59 (3H, s), 2.04 (3H, s).

¹³C NMR (500 MHz, DMSO-*d*₆) δ_C: 204.5, 163.3, 161.1, 159.7, 139.9, 139.4, 139.2, 138.5, 129.2-128.2 (20C), 106.3, 104.3, 103.3, 86.8, 82.2, 79.4, 78.1, 76.0, 75.9, 75.6, 75.5, 73.7, 68.7, 33.3, 7.8 ppm.

HRMS(ESI): calc. for C₄₃H₄₃O₉ [M - H]⁻: 703.2985, found: 703.2916.

1.3.10 Synthesis of 3,4,6-trihydroxycyclohexadienone **8**



To a stirred solution of 3-methyl-5-*C*-(per-*O*-benzylglucosyl)-2,4,6-trihydroxyacetophenone **9** (5.0 g, 7.10 mmol) in CH₃OH (20 mL) was added pyridine (20 mL) at room temperature. After stirring for 24 h at the same temperature under O₂ condition, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (toluene : EtOAc : CH₃COOH = 7 : 2 : 0.5) to afford **8** (**8a** + **8b**) (4.19 g, 83%) as a syrup.

R_f 0.30 (toluene : EtOAc : CH₃COOH = 7 : 2 : 0.5).

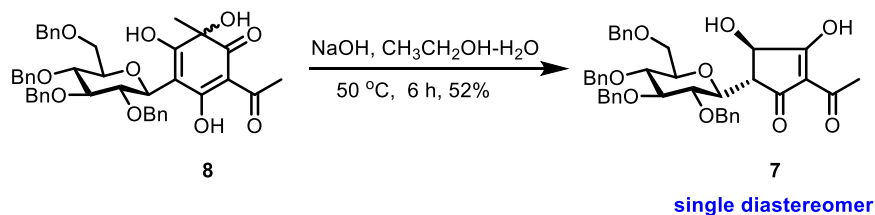
IR (KBr): 3368, 2924, 2867, 1623, 1537, 1455, 1070, 737, 698 cm⁻¹.

¹H NMR (500 MHz, DMSO-*d*₆) δ_H: 17.77 (1H, s), 17.70 (1H, s), 7.33-7.17 (40H, m), 4.80-4.72 (6H, m), 4.61-4.50 (10H, m), 3.60-3.34 (14H, m), 2.34 (6H, s), 1.21 (s, 3H), 1.17 (s, 3H).

¹³C NMR (500 MHz, DMSO-*d*₆) δ_C: 197.5, 196.8, 196.1 (2C), 193.9 (2C), 172.7 (2C), 139.5-138.9 (8C), 135.3 (2C), 128.9-128.0 (40 C) 102.0 (2C), 87.5, 87.4, 79.5-78.6 (8C), 75.1-71.9 (10C), 69.7 (2C), 29.7, 29.2, 27.8, 27.5 ppm.

HRMS(ESI): calc. for C₄₃H₄₅O₁₀ [M + H]⁺: 721.2934, found: 721.3003.

1.3.11 Synthesis of cyclopentenone **7**



To a solution of **8** (3.0 g, 4.17 mmol) in EtOH (20 mL) at room temperature, 2M aqueous NaOH solution (20 mL) was added and the mixture was stirred for 6 h at 50 °C until starting material consumed completely. The reaction mixture was neutralized with 1M aqueous HCl solution and diluted with EtOAc (150 mL). The aqueous layer was extracted with EtOAc (3 × 150 mL) and the combined organic layers were dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The crude material was purified by column chromatography on silica gel (toluene : EtOAc : CH₃COOH = 12 : 2 : 0.5) to afford **7** (1.5 g, 52%) as a light yellow powder.

m.p. 126-127 °C.

R_f 0.35 (toluene : EtOAc : CH₃COOH = 12 : 2 : 0.5).

[α]_D²⁰ = -25.8 (*c* = 0.17, MeOH).

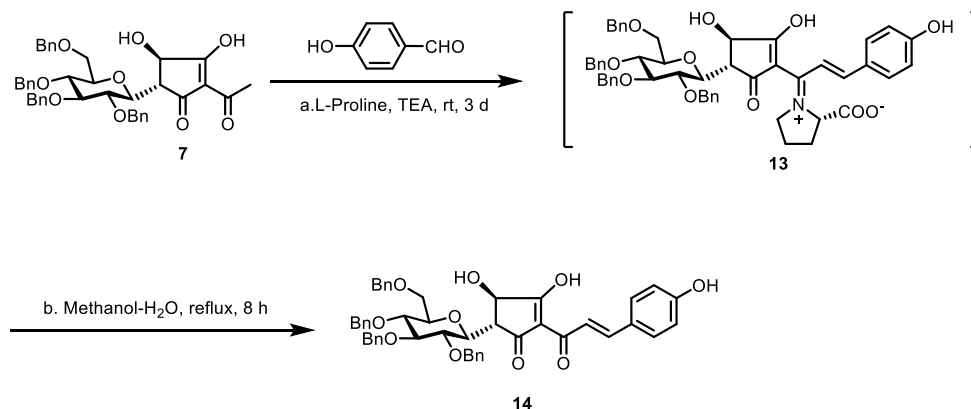
IR (KBr): 3406, 2917, 2869, 1596, 1455, 1095, 736, 698 cm⁻¹.

¹H NMR (500 MHz, DMSO-*d*₆) δ_H: 7.33-7.17 (20H, m), 5.89-5.81 (OH), 4.84-4.70 (5H, m), 4.54-4.42 (3H, m), 4.35 (1H, m), 3.90 (1H, d, *J* = 9.3 Hz), 3.70-3.44 (6H, m), 2.63 (1H, m), 2.29 (3H, s).

¹³C NMR (500 MHz, DMSO-*d*₆) δ_C: 138.3, 138.1, 137.9, 137.8, 128.0-127.0 (20C), 111.4, 86.2, 78.9, 77.7, 77.6, 74.4, 74.2, 73.7, 73.6, 71.7, 71.6, 68.0, 52.5, 27.2. Some carbon resonances (C1, C3, C6) were absent in the ¹³C NMR spectra due to rapid interconversion of the numerous tautomeric forms.

HRMS(ESI): calc. for C₄₁H₄₃O₉ [M + H]⁺: 679.2862, found: 679.2859.

1.3.12 Synthesis of **14**



A mixture of compound **7** (1.2 g, 1.77 mmol), 4-hydroxybenzaldehyde (0.26 g, 2.12 mmol), L-proline (407 mg, 3.54 mmol), and TEA (536 mg, 5.31 mmol) in CH₃OH (10.0 mL) was stirred at room temperature for 3 d. The resulting mixture was concentrated in vacuo affording the corresponding cyclopentenone intermediate **13**, which was used in the subsequent step without further purification.

A solution of the crude cyclopentenone intermediate **13** in CH₃OH (20 mL) and H₂O (2 ml) was stirred under reflux for 8 h. The resulting mixture was concentrated under reduced pressure to afford crude residue. The residue was purified by reversed-phase preparative HPLC (MeOH : H₂O = 85 : 15) to afford **14** (886 mg, 64%).

Compound 14:

$[\alpha]_D^{20} = -18.2$ ($c = 0.10$, MeOH).

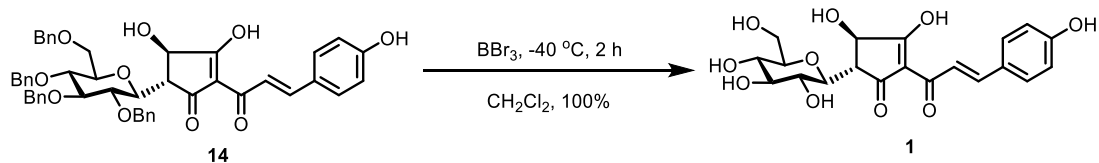
IR (KBr): 3286, 2903, 1578, 1396, 1283, 1097, 982, 738, 698 cm⁻¹.

¹H NMR (500 MHz, DMSO-*d*₆) δ_H : 10.47 (OH, s), 7.98 (1H, d, $J = 15.3$ Hz), 7.74 (1H, d, $J = 15.3$ Hz), 7.66 (2H, d, $J = 8.4$ Hz), 7.35-7.20 (20H, m), 6.89 (2H, d, $J = 8.4$ Hz), 4.87 (2H, m), 4.80 (2H, dd, $J = 4.2, 8.6$ Hz), 4.79 (1H, m), 4.56 (2H, d, $J = 10.9$ Hz), 4.41 (2H, q, $J = 6.3$), 3.99 (1H, d, $J = 9.9$), 3.77 (1H, t, $J = 8.9$), 3.60-3.48 (5H), 2.96 (1H, m).

¹³C NMR (500 MHz, DMSO-*d*₆) δ_C : 162.2, 139.3, 139.0, 139.0, 138.8, 132.4, 129.0-127.9 (20C), 126.1, 117.0, 110.8, 87.0, 79.8, 78.9, 78.8, 75.6, 75.3, 74.1, 74.7, 72.5, 70.1, 69.0, 54.1. Some carbon resonances (C1, C3, C6, C7, C8) were absent in the ¹³C NMR spectra due to rapid interconversion of the numerous tautomeric forms.

HRMS(ESI): calc. for C₄₈H₄₇O₁₀ [M+H]⁺: 783.3125, found: 783.3122.

1.3.14 Synthesis of 1



Intermediate **14** (500 mg, 0.64 mmol) was pre-treated to dryness and dissolved in anhydrous CH_2Cl_2 (10 mL) under atmosphere of nitrogen. After being cooled to $-40\text{ }^\circ\text{C}$, BBr_3 (6.4 mmol in CH_2Cl_2 , 6.0 mL) was added dropwise with an injector, and the reaction mixture was stirred for 2 h. Appropriate amount of water was added to quench the reaction, and the aqueous phase was evaporated under reduced pressure. The residue was purified by column chromatography on Sephadex LH-20 (H_2O as eluent) to afford saffloneoside **1** (270 mg, 100%) as a yellow solid.

$[\alpha]_{\text{D}}^{20} = -35.8$ ($c = 0.15$, MeOH).

^1H NMR (500 MHz, $\text{D}_2\text{O} + \text{NaOD}$) δ_{H} : 7.41 (1H, d, $J = 15.5$ Hz, H-7), 7.37 (2H, d, $J = 8.5$ Hz, H-10 and H-14), 7.32 (1H, d, $J = 15.5$ Hz, H-8), 6.50 (2H, d, $J = 8.5$ Hz, H-11 and H-13), 4.32 (1H, brs), 3.77 (1H, dd, $J = 8.5, 2.0$ Hz, H-1'), 3.65 (1H, m, H_{1-6'}), 3.50 (1H, dd, $J = 12.5, 5.0$ Hz, H_{2-6'}), 3.42 (1H, m, H-3'), 3.39 (1H, m, H-4'), 3.26 (1H, m, H-2'), 3.24 (1H, m, H-5'), 2.72 (1H, brs, H-5).

^{13}C NMR (500 MHz, $\text{D}_2\text{O} + \text{NaOD}$) δ_{C} : 202.8 (C-3), 201.3 (C-1), 188.7 (C-6), 170.6 (C-12), 144.1 (C-8), 131.0 (C-10, 14), 121.0 (C-9), 119.4 (C-11, 13), 119.4 (C-7), 114.4 (C-2), 79.4 (C-5'), 77.7 (C-3'), 76.0 (C-1'), 70.9 (C-4'), 70.1 (C-4), 69.7 (C-2'), 60.8 (C-6'), 53.0 (C-5).

HRMS(ESI): calc. for $\text{C}_{20}\text{H}_{23}\text{O}_{10}$ $[\text{M} + \text{H}]^+$: 423.1247, found: 423.1244.

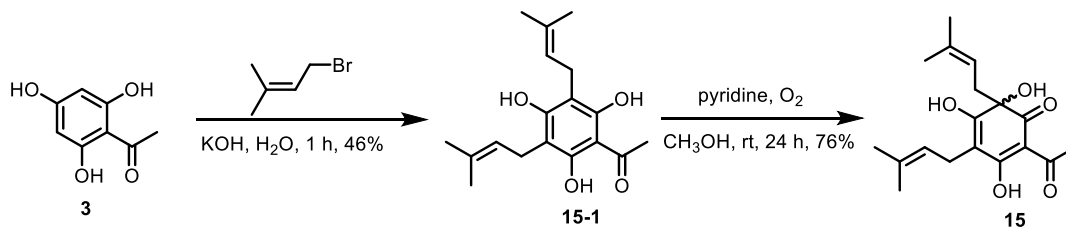
The spectral data and the optical rotation value of the synthetic **1** were in good agreement with those for natural saffloneoside.

Table S12 Comparison of NMR Data between natural **1 and synthetic **1** in $\text{D}_2\text{O} + \text{NaOD}$**

| position | δ_{C} Natural | δ_{C} Synthetic | δ_{H} (mult., J in Hz) Natural | δ_{H} (mult., J in Hz) Synthetic |
|----------|--------------------------------|----------------------------------|---|---|
| 1 | 201.2 | 201.3 | | |
| 2 | 114.5 | 114.4 | | |
| 3 | 202.6 | 202.8 | | |
| 4 | 70.2 | 70.1 | 4.33 (d, 4.5) | 4.32 (brs) |
| 5 | 53.0 | 53.0 | 2.74 (brs) | 2.72 (brs) |

| | | | | |
|----|-------|-------|-----------------------------------|-----------------------------------|
| 6 | 188.8 | 188.7 | | |
| 7 | 119.4 | 119.4 | 7.42 (d, 15.8) | 7.41 (d, 15.5) |
| 8 | 144.3 | 144.1 | 7.32 (d, 15.8) | 7.32 (d, 15.5) |
| 9 | 121.2 | 121.0 | | |
| 10 | 131.2 | 131.0 | 7.34 (d, 8.5) | 7.37 (d, 8.5) |
| 11 | 119.6 | 119.4 | 6.50 (d, 8.5) | 6.50 (d, 8.5) |
| 12 | 170.8 | 170.6 | | |
| 13 | 119.6 | 119.4 | 6.50 (d, 8.5) | 6.50 (d, 8.5) |
| 14 | 131.2 | 131.0 | 7.34 (d, 8.5) | 7.37 (d, 8.5) |
| 1' | 76.0 | 76.0 | 3.77 (dd, 8.5, 2.0) | 3.77 (dd, 8.5, 2.0) |
| 2' | 69.6 | 69.7 | 3.24 (m) | 3.26 (m) |
| 3' | 77.7 | 77.7 | 3.41 (m) | 3.42 (m) |
| 4' | 71.0 | 70.9 | 3.40 (m) | 3.39 (m) |
| 5' | 79.4 | 79.4 | 3.23 (m) | 3.24 (m) |
| 6' | 60.8 | 60.8 | 3.65 (m); 3.50 (dd, 12.5, 5.0) | 3.65 (m); 3.52 (dd, 12.5, 5.0) |

1.3.15 Synthesis of 15



To a solution of 2,4,6-trihydroxyacetophenone **3** (10 mmol) in H₂O (30 mL) under a nitrogen atmosphere at 0 °C was added KOH (1.12 g, 20 mmol) in one portion. Prenyl bromide (2.98 g, 20 mmol) was then added dropwise over 10 min. The reaction mixture was stirred at 0 °C for a further 1 h, during which time a thick orange precipitate was formed. The reaction mixture was then acidified with 1 M aqueous HCl solution (5 mL) and then extracted with EtOAc (3 × 50 mL). The combined extracts were washed with brine, dried over NaSO₄, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (petroleum ether : EtOAc = 20 : 1) to give **15-1** (1.40 g, 46%) as a yellow oil.

R_f 0.33 (petroleum ether : EtOAc = 20 : 1).

¹H NMR (500 MHz, acetone-*d*₆) δ_H: 10.89 (OH×2, brs), 7.86 (OH, brs), 5.13 (2H, m), 3.38 (4H, d, *J* = 6.8 Hz), 2.64 (3H, s), 1.75 (6H, s), 1.66 (6H, s) ppm.

¹³C NMR (500 MHz, acetone-*d*₆) δ_C: 203.5, 159.6, 159.0 (2C), 131.8 (2C), 122.6 (4C), 106.8, 32.2, 24.9 (2C), 21.4 (2C), 17.1 (2C) ppm.

HRMS(ESI): calc. for C₁₈H₂₅O₄ [M + H]⁺: 305.1708, found:305.1716.

A solution of **15-1** (1.40 g, 4.6 mmol) in CH₃OH (7 mL) and pyridine (7 mL) was vigorously stirred at rt under O₂ atmosphere (balloon) for 24 h. The mixture was evaporated in vacuo to give a dark red oil that was then separated by flash chromatography on silica gel (petrol : EtOAc, 12 : 1 as eluent) to give **15** (1.12 g, 76%) as a light yellow oil.

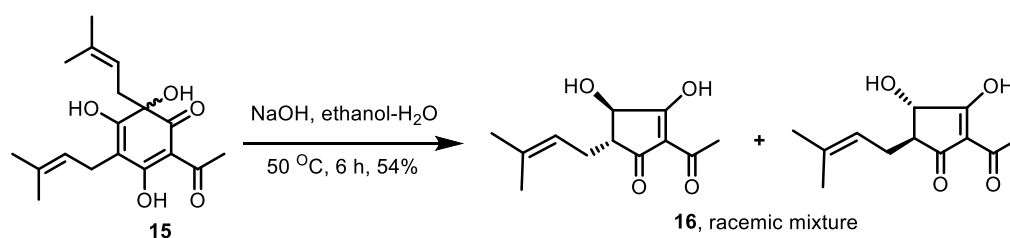
[α]_D²⁰ = +0.3 (c = 0.20, MeOH).

¹H NMR (500 MHz, acetone-*d*₆) δ_H: 18.87 (OH, brs), 5.16 (1H, m), 5.01 (1H, m), 3.10 (1H, m), 3.05 (1H, m), 2.53 (2H, d, *J* = 7.3 Hz), 2.45 (3H, s), 1.73 (3H, s), 1.66 (3H, s), 1.63 (3H, s), 1.52 (3H, s) ppm.

¹³C NMR (125 MHz, acetone-*d*₆) δ_C: 196.8, 194.9, 189.9, 170.8, 136.3, 130.9, 122.0, 116.6, 108.3, 106.0, 78.6, 41.7, 25.3, 25.1, 25.0, 20.7, 16.9, 16.9 ppm.

HRMS(ESI): calc. for C₁₈H₂₄NaO₅ [M + Na]⁺: 343.1533, found 343.1536.

1.3.16 Synthesis of 16



To a solution of **15** (1.12 g, 3.50 mmol) in EtOH (10 mL) at room temperature, 2M aqueous NaOH solution (10 mL) was added and the mixture was stirred for 6 h at 50 °C until starting material consumed completely. The reaction mixture was neutralized with 1M aqueous HCl solution and diluted with EtOAc (50 mL). The aqueous layer was extracted with EtOAc (3 × 50 mL) and the combined organic layers were dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The crude material was purified by column chromatography on ODS (Methanol : H₂O = 1 : 2 as eluent) to afford **16** (424 mg, 54%) as a light yellow oil.

$[\alpha]_D^{20} = -0.1$ ($c = 0.20$, MeOH).

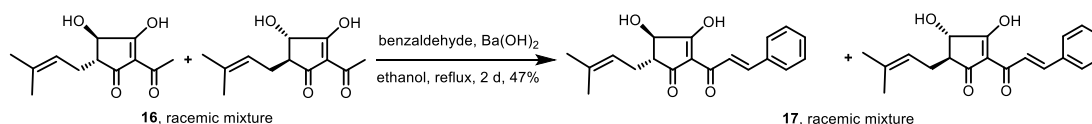
ECD: baseline curve ($c = 0.20$, MeOH).

$^1\text{H NMR}$ (500 MHz, DMSO- d_6) δ_{H} : 5.10 (1H, t, $J = 7.3$ Hz), 4.06 (1H, d, $J = 4$ Hz), 2.46 (1H, m), 2.41 (1H, m), 2.37 (3H, s), 2.25 (1H, m), 1.64 (3H, s), 1.59 (3H, s) ppm.

$^{13}\text{C NMR}$ (125 MHz, DMSO- d_6) δ_{C} : 199.1, 197.4, 195.9, 133.3, 120.3, 112.9, 73.2, 52.0, 26.8, 26.2, 25.6, 17.7 ppm.

HRMS(ESI): calc. for $\text{C}_{12}\text{H}_{17}\text{O}_4$ $[\text{M} + \text{H}]^+$: 225.1121, found 225.1125.

1.3.17 Synthesis of 17



To a solution of **16** (424 mg, 1.89 mmol) and benzaldehyde (401 mg, 3.78 mmol) in EtOH (20 mL), anhydrous $\text{Ba}(\text{OH})_2$ (596 mg, 1.89 mmol) was added and the mixture was vigorously stirred under reflux for 2 d. The reaction was quenched by adding H_2O (10 mL), then neutralized with 1M aqueous HCl solution and diluted with EtOAc (30 mL). The aqueous layer was extracted with EtOAc (3×30 mL) and the combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude material was purified by column chromatography on ODS (Methanol : $\text{H}_2\text{O} = 7 : 3$ as eluent) to afford **17** (277 mg, 47%) as a yellow oil.

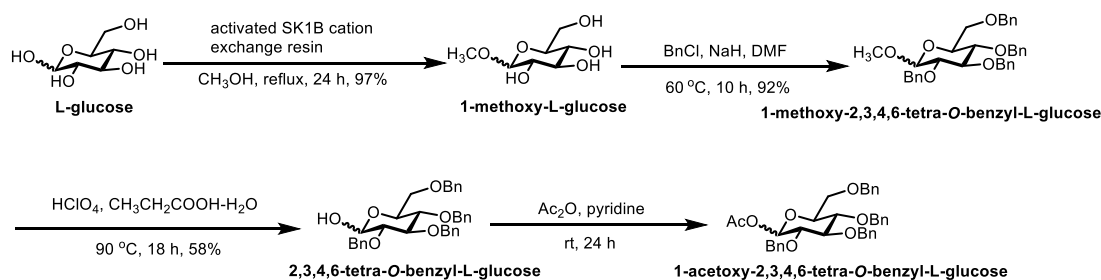
$[\alpha]_D^{20} = -0.3$ ($c = 0.20$, MeOH);

$^1\text{H NMR}$ (500 MHz, DMSO- d_6) δ_{H} : 7.96 (1H, d, $J = 16.0$ Hz), 7.81 (1H, d, $J = 16.0$ Hz), 7.75 (2H, m), 7.52 (2H, m), 7.51 (1H, m), 5.16 (1H, t, $J = 7.0$ Hz), 4.13 (1H, d, $J = 4.6$ Hz), 2.61 (1H, m), 2.48 (1H, m), 2.36 (1H, m), 1.66 (3H, s), 1.62 (3H, s) ppm.

$^{13}\text{C NMR}$ (125 MHz, DMSO- d_6) δ_{C} : 202.3, 201.3, 180.6, 145.7, 134.1, 133.2, 131.5, 129.2 (2C), 128.9 (2C), 120.5, 119.6, 110.4, 74.3, 52.9, 26.1, 25.6, 17.7 ppm.

HRMS(ESI): calc. for $\text{C}_{19}\text{H}_{21}\text{O}_4$ $[\text{M} + \text{H}]^+$: 313.1434, found 313.1445.

1.3.18 Synthesis of 1-acetoxy-2,3,4,6-tetra-O-benzyl-L-glucose



A solution of L-glucose (10.0 g, 55.6 mmol) and activated SK1B cation exchange resin (5.0 g) in CH₃OH (100 mL) was vigorously stirred under reflux for 24 h. After cool down to room temperature, the mixture was filtered to remove SK1B cation exchange resin. The filtrate was concentrated under reduced pressure to give **1-methoxy-L-glucose** (10.5 g, 97%) as a mixture of α -anomer and β -anomer (1.7 : 1).

¹H NMR (500 MHz, D₂O) δ_{H} α -anomer: 4.81 (1H, d, J = 3.7 Hz), 3.88 (1H, dd, J = 12.2, 1.8 Hz), 3.77 (1H, dd, J = 12.2, 5.5 Hz), 3.69-3.64 (2H, m), 3.57 (1H, dd, J = 9.8, 3.8 Hz), 3.42 (3H, s), 3.40 (1H, d, J = 9.6 Hz) ppm; β -anomer: 4.38 (1H, d, J = 8.0 Hz), 3.93 (1H, dd, J = 12.2, 1.8 Hz), 3.72 (1H, dd, J = 12.2, 5.5 Hz), 3.58 (3H, s), 3.51-3.45 (2H, m), 3.36 (1H, m), 3.26 (1H, t, J = 8.6 Hz) ppm.

¹³C NMR (125 MHz, D₂O) δ_{C} α -anomer: 102.1, 75.9, 74.4, 74.1, 72.4, 63.4, 57.9 ppm; β -anomer: 106.1, 78.8, 78.6, 76.0, 72.5, 63.6, 60.1 ppm.

HRMS(ESI): calc. for C₇H₁₅O₆ [M + H]⁺: 195.0790, found 195.0782.

A solution of **1-methoxy-L-glucose** (10.5 g, 53.9 mmol) in dry DMF (150 mL) cooled to 0 °C. NaH from 60% dispersion in mineral oil (12.9 g, 323.4 mmol) was added over a period of 30 min followed by the addition of BnCl (41.0 g, 323.4 mmol); the reaction was allowed to reach 60 °C and stirring was continued for 10 h. After completion of the reaction, the mixture was cooled in a water bath and quenched with H₂O. The organic layer was extracted three times with CH₂Cl₂ (3 × 300 mL) and the combined extracts were washed with brine (300 mL) and water (300 mL), dried over Na₂SO₄, and concentrated under vacuum. The product was purified by column chromatography (hexane : ethyl acetate = 9 : 1 as eluent) to give **1-methoxy-2,3,4,6-tetra-O-benzyl-L-glucose** (27.5 g, 49.6 mmol) as a syrup.

α -anomer:

R_f 0.35 (hexane : ethyl acetate = 9 : 1).

¹H NMR (500 MHz, CDCl₃) δ_H: 7.40-7.17 (20H, m), 5.02-4.50 (8H, m), 4.67 (1H, d, *J* = 3.6 Hz), 4.03 (1H, t, *J* = 9.3Hz), 3.80-3.76 (2H, m), 3.70-3.68 (2H, m), 3.61 (1H, dd, *J* = 9.7, 3.6 Hz), 3.42 (3H, s).

¹³C NMR (125 MHz, CDCl₃) δ_C: 139.0, 138.5, 138.4, 138.1, 128.7-127.8 (20C), 98.4, 82.4, 80.0, 77.8, 76.0, 75.3, 73.7, 73.6, 70.0, 68.6, 55.4 ppm.

HRMS(ESI): calc. for C₃₅H₃₈O₆Na [M + Na]⁺: 577.2668, found 577.2561.

To a solution of **1-methoxy-2,3,4,6-tetra-O-benzyl-L-glucose** (27.5 g, 49.6 mmol) in propionic acid (150 mL) and H₂O (45 mL), HClO₄ (5 mL) was added dropwise. The reaction was allowed to reach 90 °C and stirring was continued for 18 h. After completion of the reaction, the mixture was cooled to 0 °C and white crystal precipitated out. The precipitation was filtered, washed with ethanol, and dried at 60 °C in oven to give **2,3,4,6-tetra-O-benzyl-L-glucose** (15.5 g, 58%) as white solid. **α-anomer** and **β-anomer** (2 : 1).

¹H NMR (500 MHz, CDCl₃) δ_H: 7.39-7.18 (20H, m, Ar), 5.27 (1H, d, *J* = 3.6 Hz), 5.01-4.54 (8H, m), 4.10-3.35 (6H, m) ppm.

¹³C NMR (125 MHz, CDCl₃) δ_C **α-anomer**: 138.9, 138.4, 138.1, 138.0, 128.7-128.2 (20C), 91.5, 82.0, 80.1, 77.9, 76.0, 75.3, 73.7, 73.5, 70.4, 68.8 ppm; **β-anomer**: 138.7, 138.6, 138.1, 138.0, 128.7-128.2 (20C), 97.7, 84.8, 83.3, 78.0, 77.9, 75.9, 75.2, 75.0, 74.8, 69.1 ppm.

HRMS(ESI): calc. for C₃₄H₃₆O₆Na [M + Na]⁺: 563.2512, found 563.2404.

To a solution of **2,3,4,6-tetra-O-benzyl-D-glucose** (15.5 g, 28.8 mmol) in pyridine (150 mL) was added Ac₂O (40 mL) at room temperature and the solution was stirred for 24 h at room temperature. The reaction was quenched with CH₃OH (100 mL) at 0 °C and concentrated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether : EtOAc = 5 : 1) to afford **1-acetoxy-2,3,4,6-tetra-O-benzyl-L-glucose** (16.4 g, 98%) as a colorless oil. **α-anomer** and **β-anomer** (3.3 : 1).

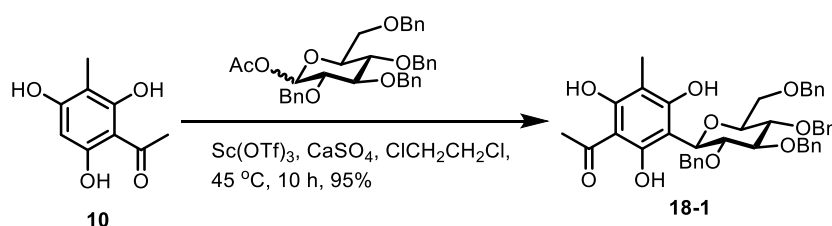
R_f 0.40 (petroleum ether : EtOAc = 5 : 1)

¹H NMR (500 MHz, CDCl₃) δ_H: **α-anomer** 7.36-7.14 (20H, m), 6.38 (1H, t, *J* = 3.3 Hz), 4.99-4.48 (8H, m), 3.97-3.58 (6H, m), 2.15 (3H, s); **β-anomer** 7.36-7.14 (20H, m), 5.63 (1H, m), 4.99-4.48 (8H, m), 3.97-3.58 (6H, m), 2.07 (3H, s).

¹³C NMR (125 MHz, CDCl₃) δ_C: α-anomer 169.7, 138.8, 138.2, 138.0, 137.8, 128.7-127.9 (20 C), 90.2, 81.9, 79.1, 77.1, 75.9, 75.5, 73.8, 73.4, 73.0, 68.3, 21.4 ppm; β-anomer 169.6, 138.6, 138.3, 138.0, 137.8, 128.7-127.9 (20C), 94.2, 85.0, 81.3, 77.4, 76.0, 75.7, 75.3, 75.3, 73.7, 68.3, 21.3 ppm.

HRMS(ESI): calc. for C₃₆H₃₈O₇Na [M + Na]⁺: 605.2618, found 605.2510.

1.3.19 Synthesis of 3-methyl-5-C-(per-O-benzyl-L-glucosyl)-2,4,6-trihydroxyacetophenone **18-1**



To a stirred solution of 3-methyl-2,4,6-trihydroxyacetophenone **10** (3.6 g, 23.4 mmol) in ClCH₂CH₂Cl (100 mL) was added Sc(OTf)₃ (4.6 g, 9.4 mmol), 1-acetoxy-2,3,4,6-tetra-O-benzyl-L-glucose (16.4 g, 28.1 mmol), and CaSO₄ (10.0 g) at room temperature. After stirring for 12 h at 45 °C under nitrogen, the reaction mixture was filtered through a thin pad of Celite®, and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether : acetone = 15 : 1) to afford **18-1** (15.6 g, 95%) as a white solid.

m.p. 132-133 °C.

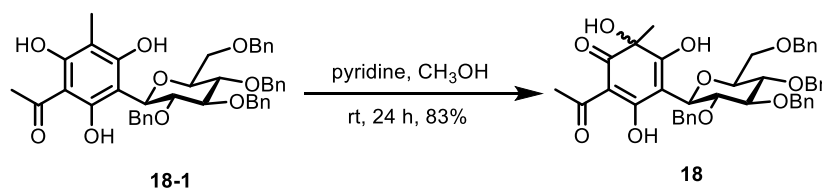
R_f 0.32 (petroleum ether : acetone = 15 : 1).

¹H NMR (500 MHz, CDCl₃) δ_H: 7.40-7.00 (20H), 5.04-4.50 (8H), 4.30 (1H, d, *J* = 10.4 Hz), 3.96 (1H, m), 3.84-3.79 (3H, m), 3.74 (1H, m), 3.61 (1H, m) 2.57 (3H, s), 2.07 (3H, s).

¹³C NMR (125 MHz, CDCl₃) δ_C: 204.3, 163.3, 161.1, 159.6, 138.4, 137.9, 137.8, 136.0, 129.1-127.8 (20C), 106.4, 105.6, 102.4, 86.4, 82.6, 78.9, 77.2, 76.8, 75.9, 75.5, 75.5, 73.6, 67.5, 33.5, 7.5 ppm.

HRMS(ESI): calc. for C₄₃H₄₅O₉ [M + H]⁺: 705.3019, found 705.3058.

1.3.20 Synthesis of 3,4,6-trihydroxycyclohexadienone **18**



To a stirred solution of 3-methyl-5-C-(per-O-benzyl-L-glucosyl)-2,4,6-trihydroxyacetophenone **18-1** (5.0 g, 7.10 mmol) in CH₃OH (20 mL) was added pyridine (20 mL) at room temperature. After stirring for 24 h at the same temperature under air condition, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (toluene : EtOAc : CH₃COOH = 7 : 2 : 0.5) to afford **18** (**18a + 18b**) (4.2 g, 83%) as a white solid.

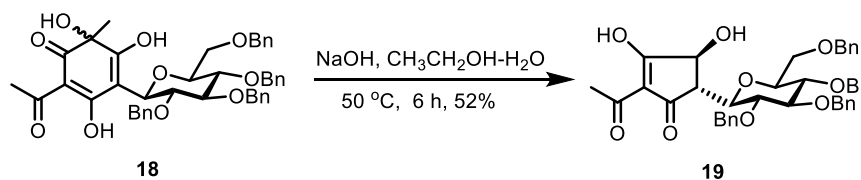
R_f 0.30 (toluene : EtOAc : CH₃COOH = 7 : 2 : 0.5).

¹H NMR (500 MHz, DMSO-*d*₆) δ_H: 18.52 (2H, brs), 7.33-7.17 (40H, m), 4.81-4.54 (16H, m), 3.61-3.34 (14H, m), 2.42 (6H, m), 1.25 (3H, s), 1.22 (3H, s) ppm.

¹³C NMR (500 MHz, DMSO-*d*₆) δ_C: 197.3, 196.6, 195.8 (2C), 193.7 (2C), 172.5 (2C), 139.5-138.8 (8C), 135.1 (2C), 128.7-127.8 (40C), 101.8 (2C), 87.3, 87.1, 79.5-78.6 (8C), 75.1-71.9 (8C), 69.7 (2C), 29.7, 29.2, 27.6, 27.4 ppm.

HRMS(ESI): calc. for C₄₃H₄₅O₁₀ [M + H]⁺: 721.2968, found 721.3007.

1.3.21 Synthesis of cyclopentenone **19**



To a solution of **18** (4.1 g, 5.70 mmol) in EtOH (25 mL) at room temperature, 2M aqueous NaOH solution (25 mL) was added and the mixture was stirred for 6 h at 50 °C until starting material consumed completely. The reaction mixture was neutralized with 1N HCl aqueous solution and diluted with EtOAc (150 mL). The aqueous layer was extracted with EtOAc (3 × 150 mL) and the combined organic layers were dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The crude material was purified by column chromatography on silica gel

(toluene : EtOAc : CH₃COOH = 12 : 2 : 0.5) to afford **19** (1.9 g, 52%) as a light yellow powder.

R_f 0.35 (toluene : EtOAc : CH₃COOH = 12 : 2 : 0.5).

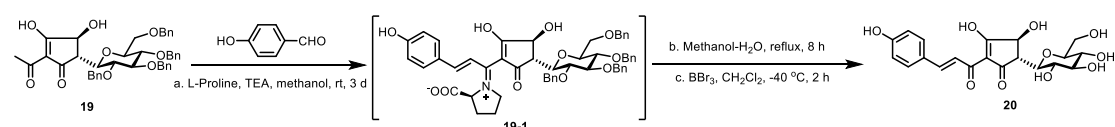
[α]_D²⁰ = +27.2 (c = 0.17, MeOH).

¹H NMR (500 MHz, DMSO-*d*₆) δ_H: 7.33-7.19 (20H), 5.90-5.82 (OH), 4.85-4.71 (5H, m), 4.55-4.43 (3H, m), 4.37 (1H, m), 3.91 (1H, d, *J* = 9.3 Hz), 3.71-3.46 (6H, m), 2.65 (1H, m), 2.30 (3H, s).

¹³C NMR (500 MHz, DMSO-*d*₆) δ_C: 202.9, 200.2, 194.8, 138.4, 138.3, 138.0, 137.9, 128.0-127.1 (20C), 112.5, 86.3, 79.1, 78.0, 77.7, 74.7, 74.3, 73.8, 73.6, 71.8, 71.6, 68.2, 52.7, 27.2.

HRMS(ESI): calc. for C₄₁H₄₃O₉ [M + H]⁺: 679.2862, found: 679.2902.

1.3.22 Synthesis of **20**



To a mixture of compound **19** (1.2 g, 1.8 mmol), 4-hydroxybenzaldehyde (0.26 g, 2.1 mmol), and L-proline (407 mg, 3.5 mmol) in CH₃OH (10.0 mL), TEA (536 mg, 5.3 mmol) was added at room temperature. After stirring for 3 d, the reaction mixture was concentrated in vacuo affording the corresponding cyclopentenone intermediate **19-1**, which was used in the subsequent step without further purification.

A solution of the crude cyclopentenone intermediate **19-1** in CH₃OH (20 mL) and H₂O (2 mL) was stirred under reflux for 8 h. The resulting mixture was concentrated under reduced pressure to afford crude residue. The crude residue was pre-treated to dryness and dissolved in anhydrous CH₂Cl₂ (10 mL) under atmosphere of nitrogen. After being cooled to -40 °C, BBr₃ (6.4 mmol in CH₂Cl₂, 6.0 mL) was added dropwise with an injector, and the reaction mixture was stirred for 2 h. Appropriate amount of water was added to quench the reaction, and the aqueous phase was evaporated under reduced pressure. The residue was purified by column chromatography on Sephadex LH-20 (H₂O as eluent) to afford **20** (478 mg) as a yellow solid.

m.p. 196-197 °C.

$[\alpha]_{\text{D}}^{20} = +38.6$ ($c = 0.15$, MeOH).

^1H NMR (500 MHz, $\text{D}_2\text{O} + \text{NaOD}$) δ_{H} : 7.44 (1H, d, $J = 15.8$ Hz, H-7), 7.40 (2H, d, $J = 8.5$ Hz, H-10 and H-14), 7.36 (1H, d, $J = 15.8$ Hz, H-8), 6.53 (2H, d, $J = 8.5$ Hz, H-11 and H-13), 4.30 (1H, brs, H-4), 3.75 (1H, d, $J = 9.7$ Hz, H-1'), 3.66 (1H, d, $J = 12.5$ Hz, H-6'), 3.52 (1H, dd, $J = 12.5, 5.0$ Hz, H-6'), 3.45 (1H, m, H-3'), 3.38 (1H, m, H-4'), 3.24 (1H, m, H-2'), 3.21 (1H, m, H-5'), 2.72 (1H, brs, H-5).

^{13}C NMR (500 MHz, $\text{D}_2\text{O} + \text{NaOD}$) δ_{C} : 202.8 (C-3), 201.3 (C-1), 188.4 (C-6), 170.5 (C-12), 143.9 (C-8), 130.9 (C-10, 14), 120.9 (C-9), 119.3 (C-11, 13), 119.1 (C-7), 114.2 (C-2), 79.3 (C-5'), 77.7 (C-3'), 76.0 (C-1'), 70.8 (C-4'), 69.9 (C-4), 69.6 (C-2'), 60.7 (C-6'), 52.2 (C-5).

1.4 Energy calculation of intermediates B1-B4

Conformational analyses of **B1-B4** are carried out via systematic searching in the Discovery Studio (version 16.1.0.15350) using the MMFF94 force field. Conformers with Boltzmann distribution over 1% are chosen as the beginning for energy calculations. Ground-state geometries are optimized at the B3LYP/6-311+G(d,p) level in gas phase by the Gaussian 09 program (Gaussian Inc., Wallingford, CT, USA).^[1] All quantum computations are performed on an IBM cluster machine located at the High Performance Computing Center of Peking Union Medical College. The energies of the proposed cyclohexadienone intermediates **B1-B4** are calculated using the DFT methodology at the B3LYP/6-311+G(d,p) level.

Table S13 Relative gas phase energies for proposed cyclohexadienone intermediates **B1-B4** calculated at the B3LYP level.

| | E (Hartree) | E_{rel} (kcal/mol) |
|-----------|----------------|-----------------------------|
| B1 | -2417.94229599 | 0 |
| B2 | -2417.94037771 | 1.21 |
| B3 | -2417.93153919 | 6.75 |
| B4 | -2417.93410454 | 5.14 |

Figure S3 Geometry optimization models of proposed **B1-B4** intermediates calculated at the B3LYP level.

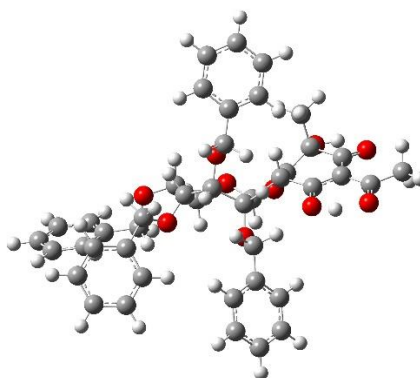
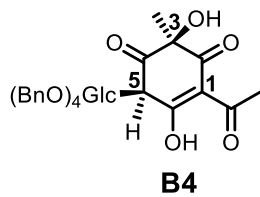
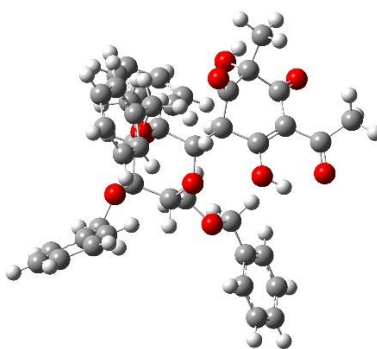
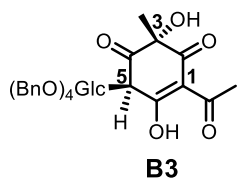
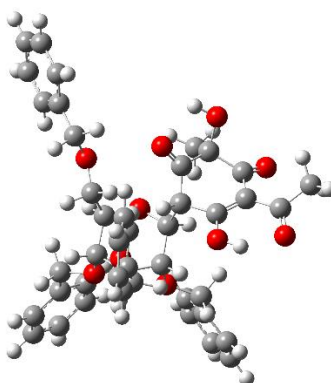
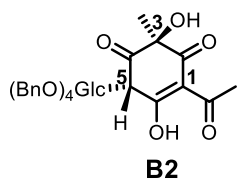
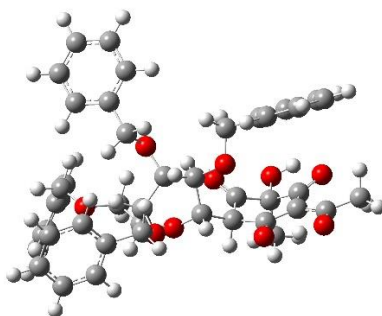
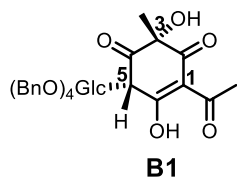


Table S14 Cartesian coordinates (Å) for the geometry optimized structure of **B1**

| Atom | X | Y | Z |
|------|-------------|-------------|-------------|
| C | 1.99060000 | 2.29970000 | 0.95230000 |
| C | 1.59570000 | 0.97500000 | 0.41880000 |
| C | 2.91510000 | 0.22760000 | 0.35110000 |
| C | 4.04020000 | 0.79040000 | -0.16690000 |
| C | 3.93890000 | 2.17520000 | -0.62550000 |
| C | 2.94340000 | 3.08130000 | 0.12780000 |
| O | 1.60470000 | 2.71350000 | 2.03320000 |
| O | 2.91880000 | -1.05040000 | 0.87260000 |
| C | 5.33310000 | 0.06190000 | -0.21500000 |
| C | 6.58690000 | 0.75660000 | -0.58060000 |
| O | 5.41030000 | -1.13260000 | 0.05480000 |
| C | 2.15200000 | 3.97950000 | -0.87060000 |
| C | 0.43140000 | 0.27920000 | 1.17950000 |
| O | 0.13240000 | -1.05670000 | 0.72190000 |
| C | -0.71600000 | -1.26860000 | -0.41790000 |
| C | -2.03480000 | -0.45020000 | -0.36220000 |
| C | -1.75730000 | 1.01820000 | 0.03310000 |
| C | -0.87260000 | 1.13580000 | 1.28840000 |
| C | -0.00830000 | -1.11220000 | -1.78050000 |
| O | 3.70550000 | 3.96740000 | 0.97150000 |
| O | 4.58530000 | 2.57340000 | -1.57280000 |
| O | -1.65350000 | 0.74720000 | 2.43290000 |
| C | -2.06250000 | 0.86480000 | 4.76590000 |
| C | -2.98480000 | 1.73200000 | 5.41170000 |
| C | -3.78010000 | 1.25270000 | 6.47630000 |
| C | -3.66480000 | -0.09430000 | 6.90020000 |
| C | -2.74640000 | -0.96200000 | 6.25850000 |
| C | -1.95060000 | -0.48800000 | 5.19170000 |
| C | -1.21580000 | 1.35930000 | 3.65490000 |
| O | 1.05400000 | -2.05970000 | -1.87770000 |
| C | 2.83370000 | -2.98560000 | -3.21950000 |
| C | 3.31750000 | -3.30730000 | -4.51930000 |
| C | 4.26330000 | -4.34370000 | -4.69330000 |
| C | 4.74040000 | -5.06670000 | -3.57320000 |
| C | 4.26980000 | -4.74910000 | -2.27600000 |
| C | 3.32540000 | -3.71210000 | -2.09750000 |

| | | | |
|---|-------------|-------------|-------------|
| C | 1.85300000 | -1.87570000 | -3.05520000 |
| O | -2.96690000 | -0.98900000 | 0.58410000 |
| C | -4.56770000 | -2.68030000 | 1.19800000 |
| C | -5.67010000 | -3.50530000 | 0.84090000 |
| C | -6.49810000 | -4.05730000 | 1.84410000 |
| C | -6.23120000 | -3.79540000 | 3.21070000 |
| C | -5.12960000 | -2.98230000 | 3.57290000 |
| C | -4.30050000 | -2.42750000 | 2.57310000 |
| C | -3.68740000 | -2.14310000 | 0.12890000 |
| O | -1.09740000 | 1.72420000 | -1.03360000 |
| C | -1.19020000 | 2.98270000 | -3.00950000 |
| C | -0.98670000 | 4.38900000 | -2.95350000 |
| C | -0.18420000 | 5.02640000 | -3.92540000 |
| C | 0.42330000 | 4.26650000 | -4.95480000 |
| C | 0.22230000 | 2.86550000 | -5.01430000 |
| C | -0.57910000 | 2.22230000 | -4.04510000 |
| C | -2.00460000 | 2.30430000 | -1.97540000 |
| H | 1.28160000 | 1.13300000 | -0.61400000 |
| H | 3.74350000 | -1.52490000 | 0.72840000 |
| H | 6.65600000 | 1.72940000 | -0.08450000 |
| H | 7.46400000 | 0.17800000 | -0.26930000 |
| H | 6.64380000 | 0.89700000 | -1.66740000 |
| H | 2.81700000 | 4.67580000 | -1.38760000 |
| H | 1.64890000 | 3.36300000 | -1.61650000 |
| H | 1.40390000 | 4.57110000 | -0.34040000 |
| H | 0.80230000 | 0.11520000 | 2.19060000 |
| H | -0.95930000 | -2.32480000 | -0.34220000 |
| H | -2.51110000 | -0.46360000 | -1.34550000 |
| H | -2.71120000 | 1.50180000 | 0.26910000 |
| H | -0.63190000 | 2.19670000 | 1.38370000 |
| H | -0.72160000 | -1.30660000 | -2.58170000 |
| H | 0.37690000 | -0.11560000 | -1.93180000 |
| H | 3.13940000 | 4.14280000 | 1.76000000 |
| H | -3.08160000 | 2.71760000 | 5.10500000 |
| H | -4.44930000 | 1.88770000 | 6.94600000 |
| H | -4.25290000 | -0.44440000 | 7.67710000 |
| H | -2.66050000 | -1.94680000 | 6.56790000 |
| H | -1.28850000 | -1.12910000 | 4.71750000 |

| | | | |
|---|-------------|-------------|-------------|
| H | -1.29460000 | 2.44670000 | 3.55380000 |
| H | -0.17050000 | 1.11780000 | 3.85990000 |
| H | 2.98060000 | -2.78440000 | -5.34770000 |
| H | 4.60750000 | -4.57630000 | -5.64220000 |
| H | 5.43270000 | -5.82700000 | -3.70180000 |
| H | 4.61570000 | -5.27780000 | -1.45570000 |
| H | 2.99390000 | -3.48730000 | -1.14140000 |
| H | 2.39400000 | -0.92560000 | -2.97440000 |
| H | 1.19050000 | -1.83310000 | -3.92800000 |
| H | -5.86940000 | -3.71060000 | -0.15530000 |
| H | -7.29980000 | -4.65710000 | 1.57910000 |
| H | -6.83960000 | -4.19910000 | 3.94510000 |
| H | -4.92790000 | -2.79100000 | 4.57010000 |
| H | -3.49450000 | -1.83840000 | 2.85180000 |
| H | -2.99800000 | -2.93460000 | -0.17270000 |
| H | -4.28520000 | -1.84820000 | -0.73960000 |
| H | -1.41720000 | 4.95270000 | -2.19770000 |
| H | -0.03910000 | 6.05080000 | -3.88440000 |
| H | 1.01410000 | 4.73540000 | -5.66380000 |
| H | 0.66410000 | 2.31260000 | -5.77040000 |
| H | -0.71780000 | 1.19630000 | -4.09460000 |
| H | -2.65720000 | 3.01550000 | -1.45540000 |
| H | -2.63390000 | 1.53420000 | -2.42920000 |

Table S15 Cartesian coordinates (Å) for the geometry optimized structure of **B2**

| Atom | X | Y | Z |
|------|------------|-------------|-------------|
| C | 2.23740000 | 1.83400000 | 0.49100000 |
| C | 2.03060000 | 0.38140000 | 0.28880000 |
| C | 3.33100000 | -0.15600000 | -0.26350000 |
| C | 4.14190000 | 0.53500000 | -1.09760000 |
| C | 3.71040000 | 1.85940000 | -1.54800000 |
| C | 2.75870000 | 2.64900000 | -0.63270000 |
| O | 2.08410000 | 2.32320000 | 1.59940000 |
| O | 3.64190000 | -1.43000000 | 0.18170000 |
| C | 5.44840000 | -0.02170000 | -1.52690000 |
| C | 6.53100000 | 0.85770000 | -2.02090000 |
| O | 5.67770000 | -1.22530000 | -1.45750000 |
| C | 1.60170000 | 3.30450000 | -1.45300000 |

| | | | |
|---|-------------|-------------|-------------|
| C | 0.82200000 | 0.03570000 | -0.63620000 |
| O | -0.31510000 | 0.88460000 | -0.38170000 |
| C | -1.28700000 | 0.51430000 | 0.61110000 |
| C | -1.71840000 | -0.97580000 | 0.54230000 |
| C | -0.49730000 | -1.90770000 | 0.43580000 |
| C | 0.45780000 | -1.48260000 | -0.70270000 |
| C | -0.89700000 | 0.92830000 | 2.04540000 |
| O | 3.52920000 | 3.73630000 | -0.08290000 |
| O | 4.07900000 | 2.29520000 | -2.61890000 |
| H | 1.86920000 | -0.08210000 | 1.25250000 |
| O | -1.04860000 | 2.34250000 | 2.17860000 |
| C | -1.21220000 | 4.16080000 | 3.76900000 |
| C | -0.59550000 | 4.94400000 | 4.78400000 |
| C | -1.10580000 | 6.22080000 | 5.10760000 |
| C | -2.23740000 | 6.72850000 | 4.42490000 |
| C | -2.85930000 | 5.95370000 | 3.41630000 |
| C | -2.35180000 | 4.67570000 | 3.08940000 |
| C | -0.69360000 | 2.79280000 | 3.49380000 |
| O | -2.58990000 | -1.21120000 | -0.57860000 |
| C | -4.79550000 | -1.16140000 | -1.50840000 |
| C | -5.97890000 | -1.94540000 | -1.43480000 |
| C | -6.78040000 | -2.13010000 | -2.58310000 |
| C | -6.40750000 | -1.53680000 | -3.81330000 |
| C | -5.23030000 | -0.75300000 | -3.89170000 |
| C | -4.42680000 | -0.56380000 | -2.74510000 |
| C | -3.97050000 | -0.93590000 | -0.29510000 |
| O | 0.16830000 | -1.90560000 | 1.71340000 |
| C | 1.53890000 | -3.06380000 | 3.32870000 |
| C | 1.76890000 | -4.27890000 | 4.03250000 |
| C | 2.42440000 | -4.26470000 | 5.28360000 |
| C | 2.86080000 | -3.04090000 | 5.84490000 |
| C | 2.64100000 | -1.82840000 | 5.14920000 |
| C | 1.98510000 | -1.83850000 | 3.89800000 |
| C | 0.89140000 | -3.11270000 | 1.98960000 |
| O | -0.17670000 | -1.78550000 | -1.95490000 |
| C | 0.01940000 | -2.26990000 | -4.29580000 |
| C | 0.39960000 | -3.27490000 | -5.22640000 |
| C | -0.25600000 | -3.37140000 | -6.47390000 |

| | | | |
|---|-------------|-------------|-------------|
| C | -1.29400000 | -2.46710000 | -6.80440000 |
| C | -1.67200000 | -1.45910000 | -5.88460000 |
| C | -1.01820000 | -1.35790000 | -4.63660000 |
| C | 0.73620000 | -2.15100000 | -3.00040000 |
| H | 4.45910000 | -1.77620000 | -0.19540000 |
| H | 6.43080000 | 1.01880000 | -3.10240000 |
| H | 6.52260000 | 1.82460000 | -1.50870000 |
| H | 7.51270000 | 0.40790000 | -1.83090000 |
| H | 0.86110000 | 3.74430000 | -0.78290000 |
| H | 1.98130000 | 4.10360000 | -2.09440000 |
| H | 1.10410000 | 2.57290000 | -2.08970000 |
| H | 1.10680000 | 0.31680000 | -1.64790000 |
| H | -2.15230000 | 1.12130000 | 0.34980000 |
| H | -2.25110000 | -1.24570000 | 1.46100000 |
| H | -0.87860000 | -2.91040000 | 0.21610000 |
| H | 1.36540000 | -2.08190000 | -0.62650000 |
| H | -1.56670000 | 0.44310000 | 2.76270000 |
| H | 0.12300000 | 0.64810000 | 2.28820000 |
| H | 3.03550000 | 4.03330000 | 0.71810000 |
| H | 0.22890000 | 4.57890000 | 5.29600000 |
| H | -0.65200000 | 6.78560000 | 5.84880000 |
| H | -2.61090000 | 7.66570000 | 4.66400000 |
| H | -3.68890000 | 6.32250000 | 2.91720000 |
| H | -2.82260000 | 4.11440000 | 2.35450000 |
| H | 0.39820000 | 2.77150000 | 3.57410000 |
| H | -1.11200000 | 2.11860000 | 4.25060000 |
| H | -6.26530000 | -2.38230000 | -0.53850000 |
| H | -7.64170000 | -2.70300000 | -2.52440000 |
| H | -6.99460000 | -1.67800000 | -4.65580000 |
| H | -4.95640000 | -0.31950000 | -4.79200000 |
| H | -3.56480000 | 0.00900000 | -2.80830000 |
| H | -4.09780000 | 0.09950000 | 0.03310000 |
| H | -4.29220000 | -1.59490000 | 0.51900000 |
| H | 1.46430000 | -5.18420000 | 3.62910000 |
| H | 2.58990000 | -5.15350000 | 5.78960000 |
| H | 3.34420000 | -3.03270000 | 6.76190000 |
| H | 2.96510000 | -0.93200000 | 5.55470000 |
| H | 1.84150000 | -0.94240000 | 3.40220000 |

| | | | |
|---|-------------|-------------|-------------|
| H | 1.66420000 | -3.27180000 | 1.23200000 |
| H | 0.18230000 | -3.94820000 | 1.94870000 |
| H | 1.16160000 | -3.94030000 | -4.99840000 |
| H | 0.02230000 | -4.10790000 | -7.14770000 |
| H | -1.77820000 | -2.54400000 | -7.71770000 |
| H | -2.43170000 | -0.79670000 | -6.12450000 |
| H | -1.30350000 | -0.61880000 | -3.96730000 |
| H | 1.52640000 | -1.39970000 | -3.09990000 |
| H | 1.19610000 | -3.10610000 | -2.72180000 |

Table S16 Cartesian coordinates (Å) for the geometry optimized structure of **B3**

| Atom | X | Y | Z |
|------|-------------|-------------|-------------|
| C | 1.80650000 | 2.38780000 | 1.14340000 |
| C | 1.53420000 | 1.07120000 | 0.51470000 |
| C | 2.89290000 | 0.38500000 | 0.50400000 |
| C | 4.04500000 | 1.03580000 | 0.19980000 |
| C | 3.96910000 | 2.46390000 | -0.11380000 |
| C | 2.76480000 | 3.25550000 | 0.41630000 |
| O | 1.30750000 | 2.70790000 | 2.20930000 |
| O | 2.88800000 | -0.96180000 | 0.81430000 |
| C | 5.35620000 | 0.33390000 | 0.21590000 |
| C | 6.62220000 | 1.09080000 | 0.33610000 |
| O | 5.42300000 | -0.88670000 | 0.14490000 |
| C | 3.27550000 | 4.43220000 | 1.30030000 |
| C | 0.34080000 | 0.30820000 | 1.16340000 |
| O | 0.19010000 | -1.07310000 | 0.76440000 |
| C | -0.55240000 | -1.42370000 | -0.41160000 |
| C | -1.94210000 | -0.73560000 | -0.45470000 |
| C | -1.80290000 | 0.77930000 | -0.21490000 |
| C | -1.00830000 | 1.10210000 | 1.07160000 |
| C | 0.22820000 | -1.23500000 | -1.72790000 |
| O | 2.06320000 | 3.83610000 | -0.70450000 |
| O | 4.79430000 | 3.00850000 | -0.81680000 |
| O | -1.85530000 | 0.82300000 | 2.20080000 |
| C | -2.39120000 | 1.15600000 | 4.50420000 |
| C | -3.15160000 | 2.10080000 | 5.24410000 |
| C | -3.92480000 | 1.67930000 | 6.34870000 |
| C | -3.94710000 | 0.31320000 | 6.72200000 |

| | | | |
|---|-------------|-------------|-------------|
| C | -3.19230000 | -0.63240000 | 5.98590000 |
| C | -2.41810000 | -0.21560000 | 4.88080000 |
| C | -1.54060000 | 1.59420000 | 3.37050000 |
| O | 1.20230000 | -2.26650000 | -1.87930000 |
| C | 2.65120000 | -3.24440000 | -3.57540000 |
| C | 3.49110000 | -3.12640000 | -4.71870000 |
| C | 4.02100000 | -4.28040000 | -5.33620000 |
| C | 3.72110000 | -5.56360000 | -4.81970000 |
| C | 2.89170000 | -5.68900000 | -3.67910000 |
| C | 2.35940000 | -4.53660000 | -3.05760000 |
| C | 2.09710000 | -2.00190000 | -2.97120000 |
| O | -2.82790000 | -1.27660000 | 0.54020000 |
| C | -4.22900000 | -3.04850000 | 1.30260000 |
| C | -5.57370000 | -3.48040000 | 1.14540000 |
| C | -6.27320000 | -4.03510000 | 2.24020000 |
| C | -5.63850000 | -4.16300000 | 3.49970000 |
| C | -4.29770000 | -3.73650000 | 3.66110000 |
| C | -3.59390000 | -3.18240000 | 2.56910000 |
| C | -3.47790000 | -2.49340000 | 0.14820000 |
| O | -1.16450000 | 1.34950000 | -1.37290000 |
| C | -1.00030000 | 3.13880000 | -2.97230000 |
| C | -1.70200000 | 4.07200000 | -3.78460000 |
| C | -1.11860000 | 4.56040000 | -4.97510000 |
| C | 0.17040000 | 4.12650000 | -5.36690000 |
| C | 0.87800000 | 3.20250000 | -4.56220000 |
| C | 0.29750000 | 2.71260000 | -3.37080000 |
| C | -1.62100000 | 2.66560000 | -1.70450000 |
| H | 1.27550000 | 1.26520000 | -0.53170000 |
| H | 3.72560000 | -1.40820000 | 0.64380000 |
| H | 7.41000000 | 0.46210000 | 0.76780000 |
| H | 6.95810000 | 1.43010000 | -0.65270000 |
| H | 6.50770000 | 1.95520000 | 0.99760000 |
| H | 3.95150000 | 5.08110000 | 0.74260000 |
| H | 3.80420000 | 4.03990000 | 2.17120000 |
| H | 2.43930000 | 5.04560000 | 1.64130000 |
| H | 0.59710000 | 0.21260000 | 2.21860000 |
| H | -0.70550000 | -2.49530000 | -0.30630000 |
| H | -2.39400000 | -0.87960000 | -1.44160000 |

| | | | |
|---|-------------|-------------|-------------|
| H | -2.81670000 | 1.17810000 | -0.10600000 |
| H | -0.81490000 | 2.17770000 | 1.05540000 |
| H | -0.45590000 | -1.29590000 | -2.57930000 |
| H | 0.72670000 | -0.27760000 | -1.76860000 |
| H | 2.70810000 | 4.39570000 | -1.19750000 |
| H | -3.13950000 | 3.10490000 | 4.98280000 |
| H | -4.47780000 | 2.37140000 | 6.88590000 |
| H | -4.51700000 | 0.00550000 | 7.53120000 |
| H | -3.20960000 | -1.63290000 | 6.25620000 |
| H | -1.87010000 | -0.91180000 | 4.34180000 |
| H | -0.49420000 | 1.46150000 | 3.65590000 |
| H | -1.70140000 | 2.65250000 | 3.13980000 |
| H | 3.71600000 | -2.19160000 | -5.10650000 |
| H | 4.63090000 | -4.18690000 | -6.16950000 |
| H | 4.10920000 | -6.41040000 | -5.27500000 |
| H | 2.67330000 | -6.62680000 | -3.29790000 |
| H | 1.75490000 | -4.64540000 | -2.22100000 |
| H | 1.57520000 | -1.44500000 | -3.76140000 |
| H | 2.91080000 | -1.37920000 | -2.58490000 |
| H | -6.04850000 | -3.39480000 | 0.22700000 |
| H | -7.25430000 | -4.34620000 | 2.12160000 |
| H | -6.15540000 | -4.56550000 | 4.30300000 |
| H | -3.83240000 | -3.82700000 | 4.58280000 |
| H | -2.61410000 | -2.86580000 | 2.69390000 |
| H | -2.75190000 | -3.23830000 | -0.18810000 |
| H | -4.14690000 | -2.26620000 | -0.68720000 |
| H | -2.64440000 | 4.40400000 | -3.50730000 |
| H | -1.63550000 | 5.23940000 | -5.56220000 |
| H | 0.59650000 | 4.48630000 | -6.24100000 |
| H | 1.82330000 | 2.88650000 | -4.84560000 |
| H | 0.83290000 | 2.04460000 | -2.78970000 |
| H | -2.71190000 | 2.62910000 | -1.81930000 |
| H | -1.37160000 | 3.35810000 | -0.89430000 |

Table S17 Cartesian coordinates (Å) for the geometry optimized structure of **B4**

| Atom | X | Y | Z |
|------|-------------|------------|-------------|
| C | -0.94150000 | 2.04530000 | -0.05610000 |
| C | -1.12540000 | 0.58570000 | -0.07080000 |

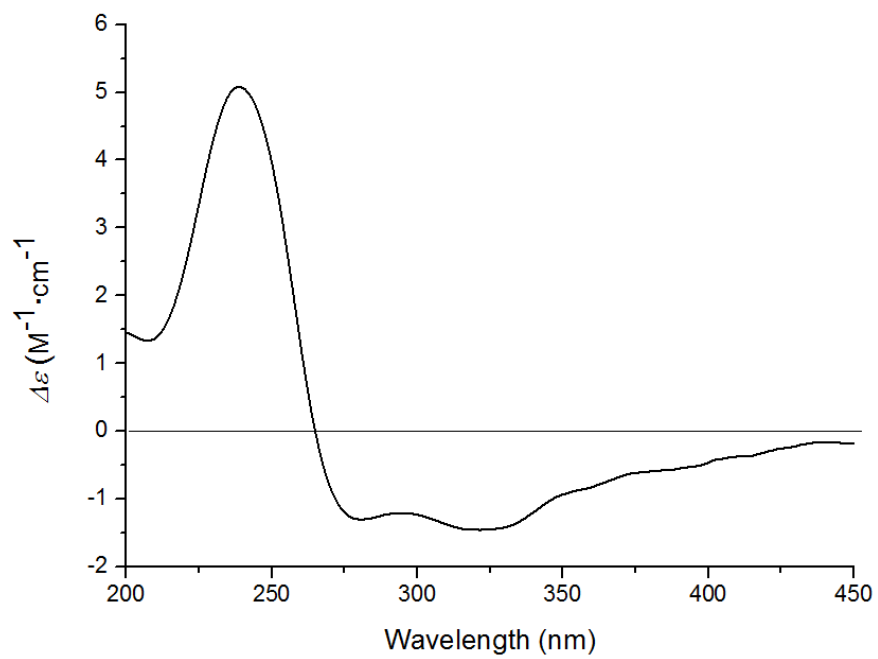
| | | | |
|---|-------------|-------------|-------------|
| C | 0.21300000 | 0.06330000 | -0.46650000 |
| C | 1.39190000 | 0.54850000 | 0.19070000 |
| C | 1.17500000 | 1.63490000 | 1.08530000 |
| C | 0.04770000 | 2.61790000 | 0.87820000 |
| O | -1.52980000 | 2.77270000 | -0.84600000 |
| O | 0.22080000 | -0.82450000 | -1.48390000 |
| C | 2.68960000 | 0.04540000 | -0.07450000 |
| C | 3.01770000 | -1.12590000 | -0.92070000 |
| O | 3.69520000 | 0.62810000 | 0.41270000 |
| C | -0.68800000 | 3.03230000 | 2.18880000 |
| C | -2.36190000 | 0.05920000 | -0.89020000 |
| O | -3.52110000 | 0.81250000 | -0.48170000 |
| C | -4.36050000 | 0.36640000 | 0.60340000 |
| C | -4.74740000 | -1.14170000 | 0.50880000 |
| C | -3.44990000 | -1.96780000 | 0.33980000 |
| C | -2.66280000 | -1.49160000 | -0.92500000 |
| C | -3.96790000 | 0.80950000 | 2.03440000 |
| O | 0.61180000 | 3.81620000 | 0.32390000 |
| O | 1.90340000 | 1.77270000 | 2.10620000 |
| O | -2.59970000 | -1.90920000 | 1.49320000 |
| C | -0.47450000 | -2.51270000 | 2.31920000 |
| C | -0.54070000 | -1.62020000 | 3.41420000 |
| C | 0.63450000 | -1.10330000 | 3.98390000 |
| C | 1.88820000 | -1.49110000 | 3.47920000 |
| C | 1.96650000 | -2.38420000 | 2.39600000 |
| C | 0.79110000 | -2.88330000 | 1.80920000 |
| C | -1.71720000 | -3.02960000 | 1.71500000 |
| O | -3.33940000 | -1.81790000 | -2.16420000 |
| C | -4.36410000 | -3.41810000 | -3.64320000 |
| C | -4.16460000 | -4.68960000 | -4.21670000 |
| C | -4.67130000 | -4.96710000 | -5.49300000 |
| C | -5.38830000 | -3.98000000 | -6.19410000 |
| C | -5.62780000 | -2.72310000 | -5.60780000 |
| C | -5.13360000 | -2.44740000 | -4.32320000 |
| C | -3.86080000 | -3.16160000 | -2.29790000 |
| O | -4.93730000 | 0.35790000 | 3.00130000 |
| C | -7.19470000 | 0.36750000 | 3.88750000 |
| C | -8.57480000 | 0.56230000 | 3.63950000 |

| | | | |
|---|-------------|-------------|-------------|
| C | -9.54150000 | -0.03390000 | 4.46650000 |
| C | -9.13960000 | -0.83770000 | 5.54750000 |
| C | -7.77220000 | -1.05500000 | 5.79430000 |
| C | -6.80450000 | -0.45960000 | 4.96640000 |
| C | -6.19700000 | 1.05750000 | 3.04260000 |
| O | -5.63780000 | -1.46120000 | -0.58740000 |
| C | -7.15570000 | 0.37050000 | -1.05950000 |
| C | -6.23370000 | 0.94810000 | -1.96970000 |
| C | -6.21390000 | 2.33700000 | -2.18400000 |
| C | -7.18310000 | 3.15130000 | -1.57380000 |
| C | -8.14110000 | 2.58320000 | -0.71430000 |
| C | -8.12010000 | 1.20250000 | -0.44880000 |
| C | -7.01130000 | -1.04060000 | -0.62510000 |
| H | -1.28380000 | 0.26560000 | 0.95470000 |
| H | 1.00960000 | -1.24520000 | -1.86120000 |
| H | 2.39890000 | -1.98190000 | -0.64400000 |
| H | 2.85540000 | -0.87150000 | -1.97020000 |
| H | 4.05890000 | -1.43210000 | -0.81750000 |
| H | 0.00020000 | 3.52980000 | 2.87610000 |
| H | -1.10990000 | 2.16550000 | 2.69990000 |
| H | -1.49720000 | 3.73450000 | 1.96770000 |
| H | -2.17420000 | 0.36330000 | -1.92570000 |
| H | -5.24090000 | 0.94980000 | 0.42780000 |
| H | -5.23260000 | -1.49630000 | 1.42030000 |
| H | -3.76690000 | -3.00860000 | 0.25560000 |
| H | -1.72690000 | -2.04230000 | -0.95710000 |
| H | -3.02260000 | 0.37020000 | 2.32680000 |
| H | -3.85250000 | 1.89480000 | 2.06870000 |
| H | 0.98250000 | 4.31960000 | 1.08100000 |
| H | -1.44730000 | -1.33050000 | 3.79220000 |
| H | 0.57500000 | -0.44790000 | 4.76590000 |
| H | 2.74320000 | -1.12630000 | 3.90230000 |
| H | 2.87790000 | -2.67220000 | 2.03420000 |
| H | 0.86660000 | -3.51980000 | 1.01100000 |
| H | -1.49290000 | -3.58430000 | 0.79660000 |
| H | -2.20210000 | -3.72250000 | 2.40480000 |
| H | -3.67260000 | -5.42360000 | -3.69850000 |
| H | -4.52110000 | -5.89040000 | -5.90100000 |

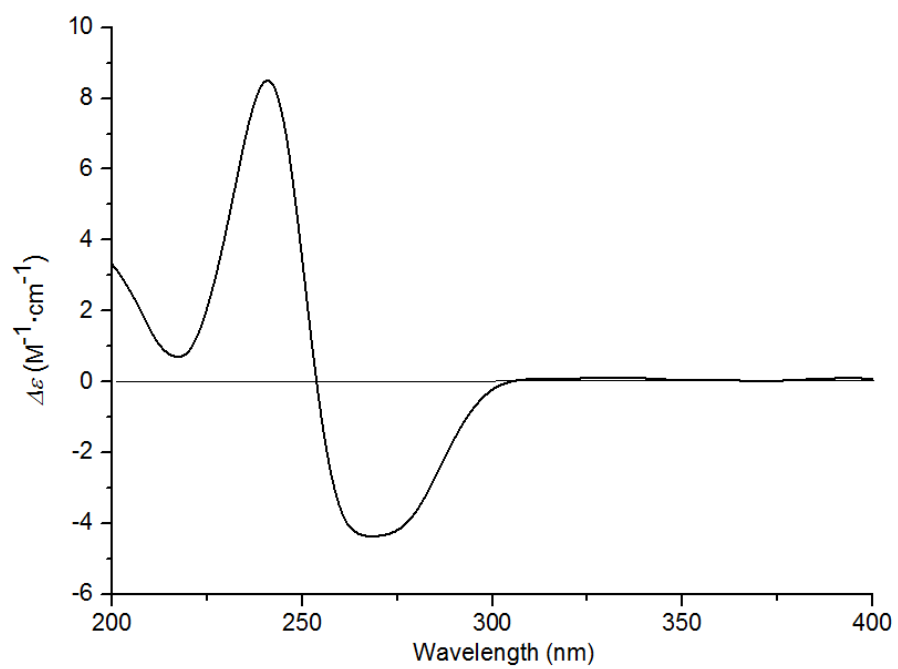
| | | | |
|---|--------------|-------------|-------------|
| H | -5.73680000 | -4.17820000 | -7.13130000 |
| H | -6.15570000 | -2.00840000 | -6.11300000 |
| H | -5.33840000 | -1.54320000 | -3.88910000 |
| H | -4.74020000 | -3.32350000 | -1.67960000 |
| H | -3.10730000 | -3.89410000 | -1.99360000 |
| H | -8.88730000 | 1.14200000 | 2.85570000 |
| H | -10.53500000 | 0.12050000 | 4.28150000 |
| H | -9.84200000 | -1.26200000 | 6.15550000 |
| H | -7.47930000 | -1.63920000 | 6.58010000 |
| H | -5.81410000 | -0.62620000 | 5.16320000 |
| H | -6.02520000 | 2.05540000 | 3.44480000 |
| H | -6.62880000 | 1.16220000 | 2.04850000 |
| H | -5.50960000 | 0.37610000 | -2.41090000 |
| H | -5.48290000 | 2.75350000 | -2.76630000 |
| H | -7.19200000 | 4.15600000 | -1.75770000 |
| H | -8.84620000 | 3.17500000 | -0.27130000 |
| H | -8.78620000 | 0.81430000 | 0.22310000 |
| H | -7.52750000 | -1.66680000 | -1.35500000 |
| H | -7.47190000 | -1.22590000 | 0.35000000 |

2 ECD spectra of 1, 7, 16, 19, and 20

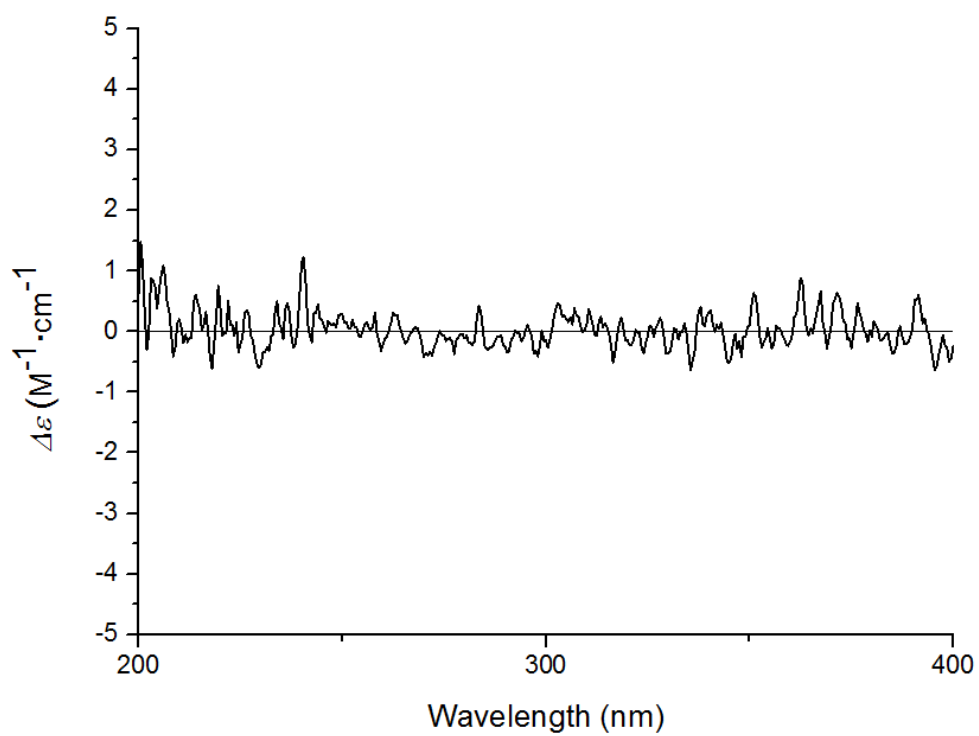
ECD spectra of the compound 1 in MeOH



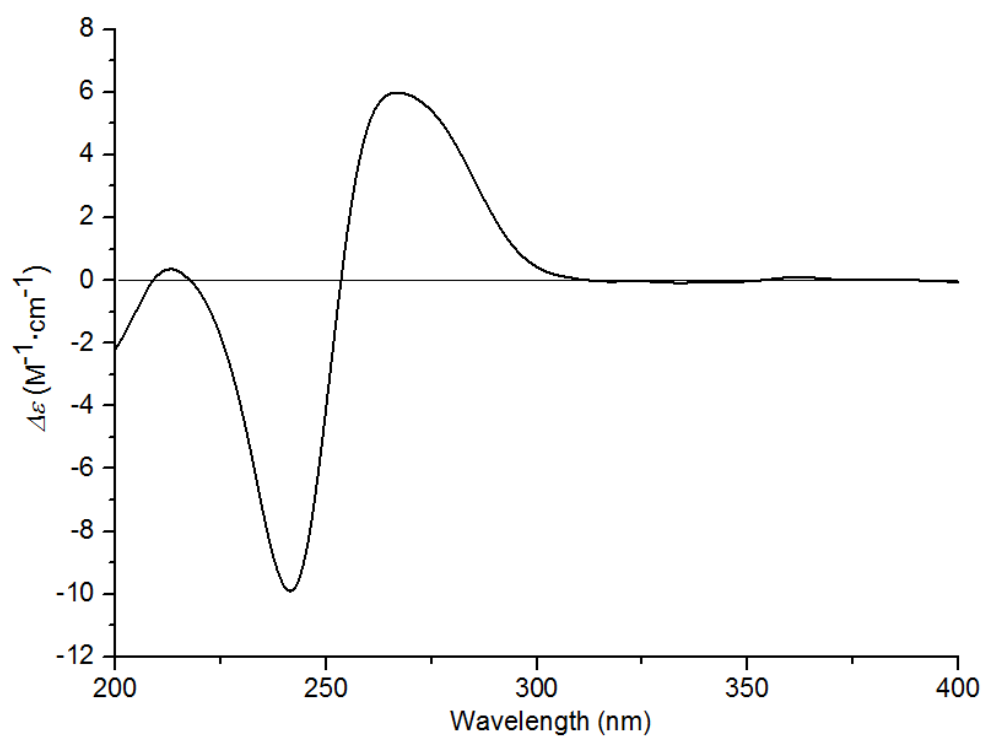
ECD spectra of the compound 7 in MeOH



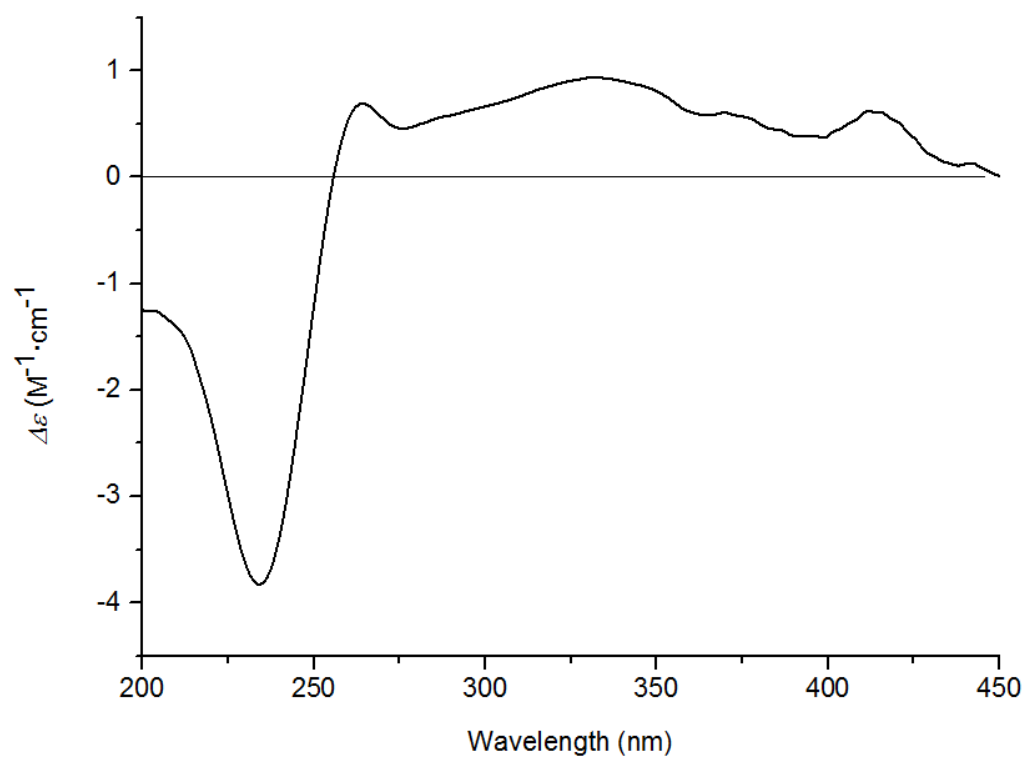
ECD spectra of the compound **16** in MeOH



ECD spectra of the compound **19** in MeOH

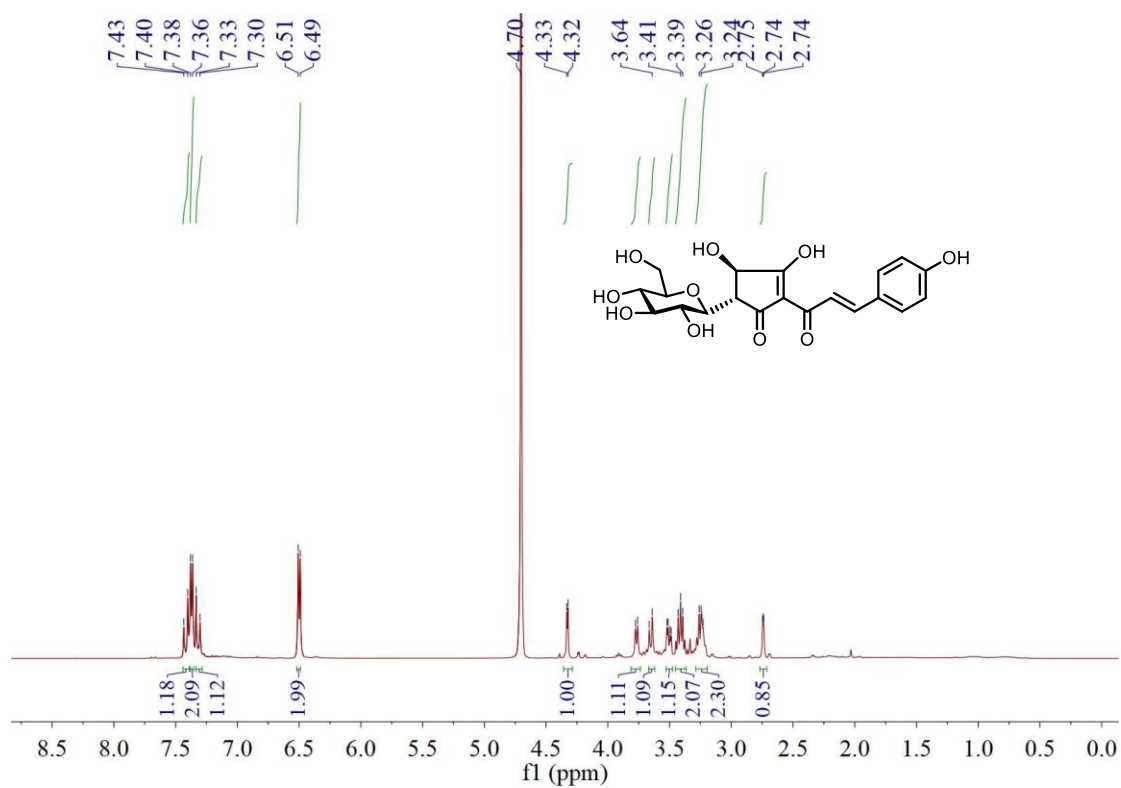


ECD spectra of the compound **20** in MeOH

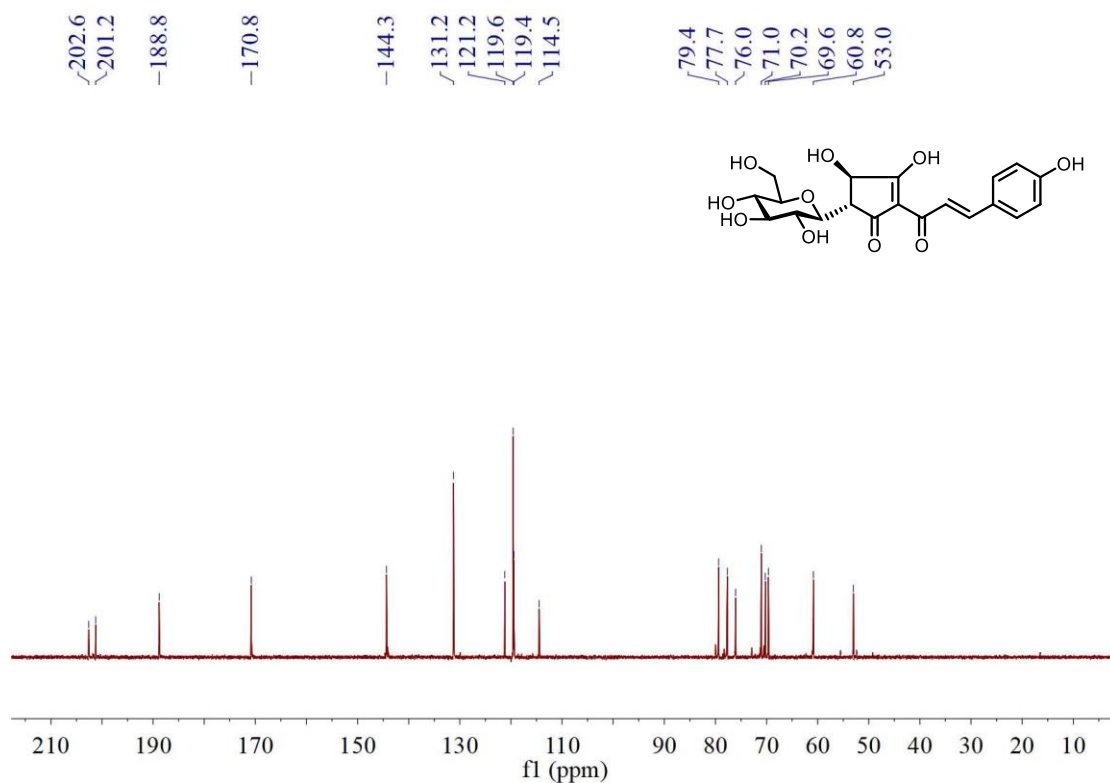


3 NMR spectra

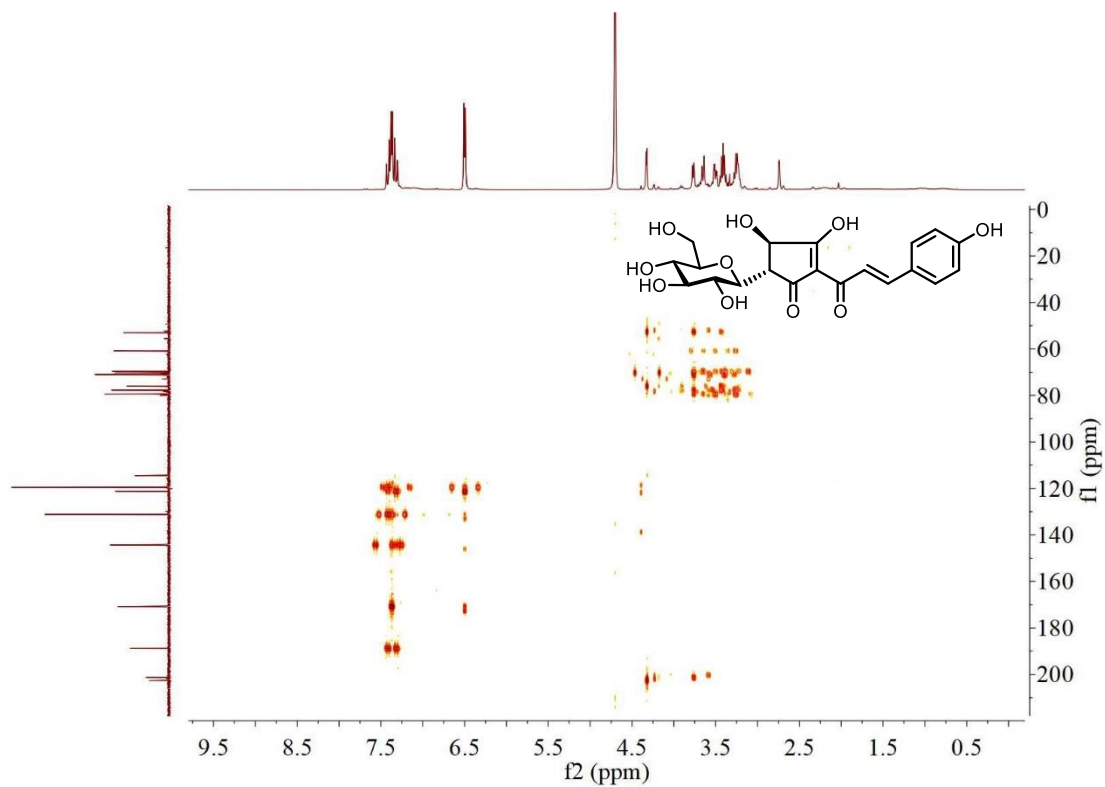
^1H NMR (500 MHz, $\text{D}_2\text{O} + \text{NaOD}$) of **1**



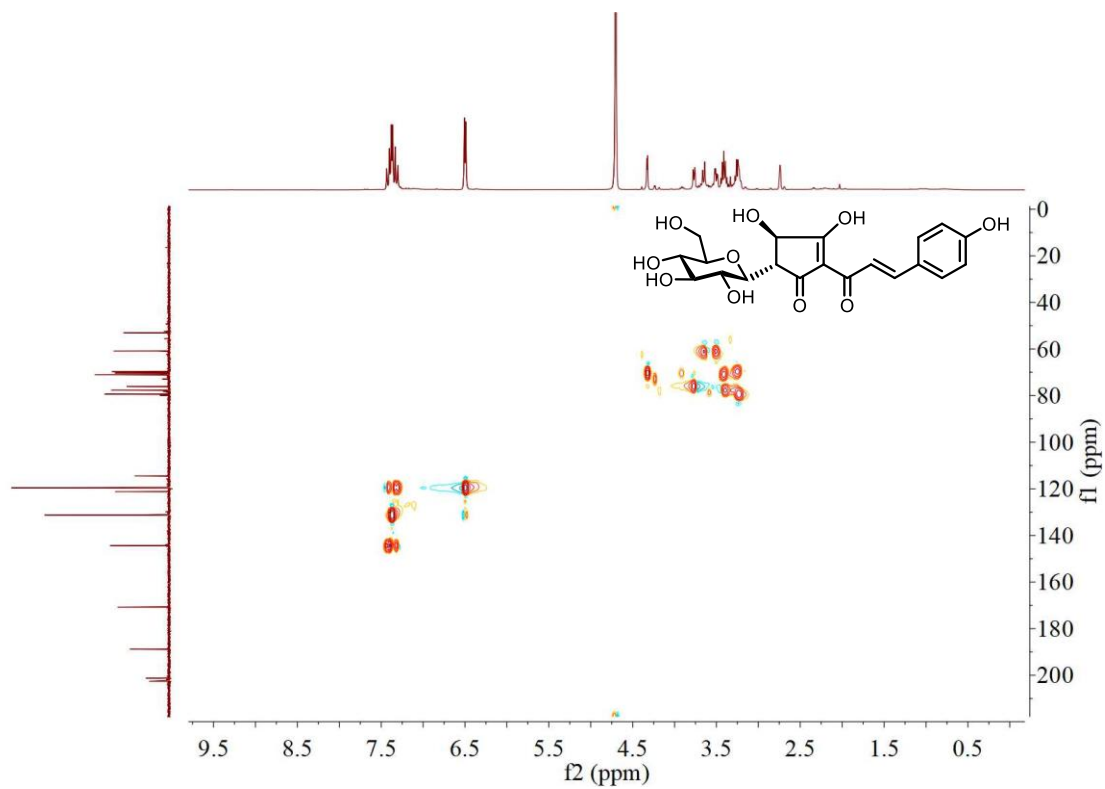
^{13}C NMR (125 MHz, $\text{D}_2\text{O} + \text{NaOD}$) of **1**



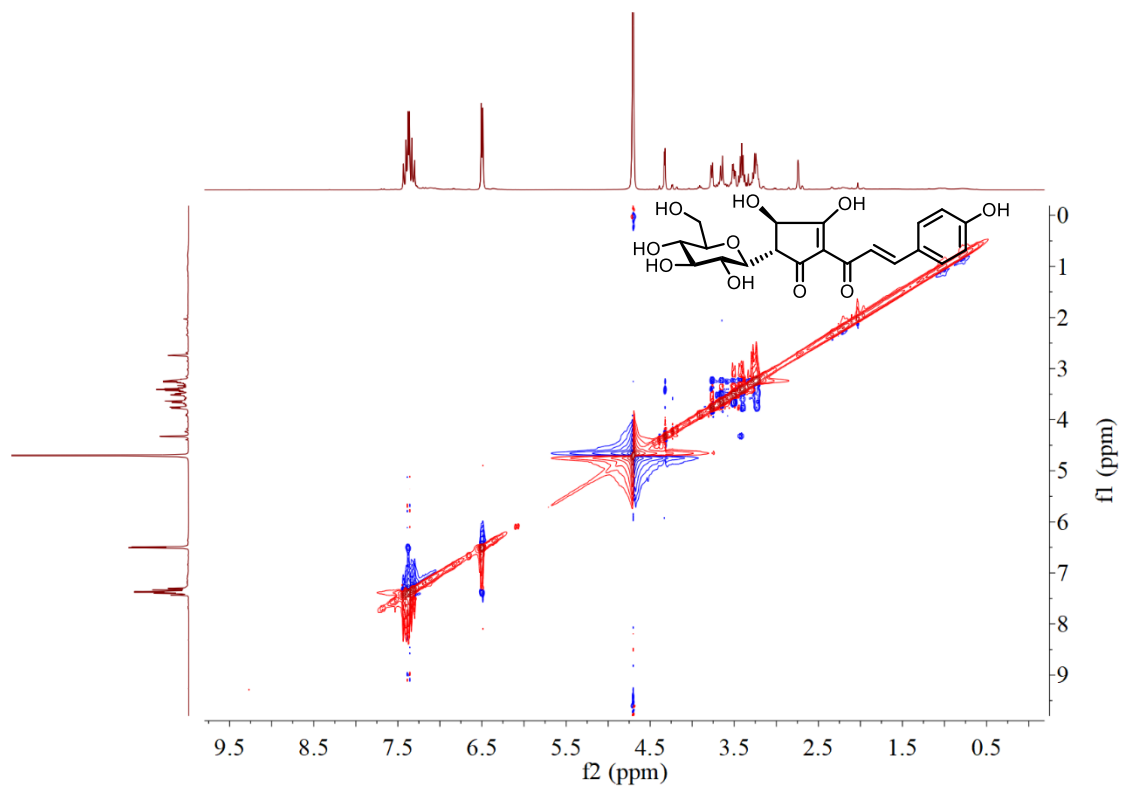
HMBC (500 MHz, D₂O + NaOD) of **1**



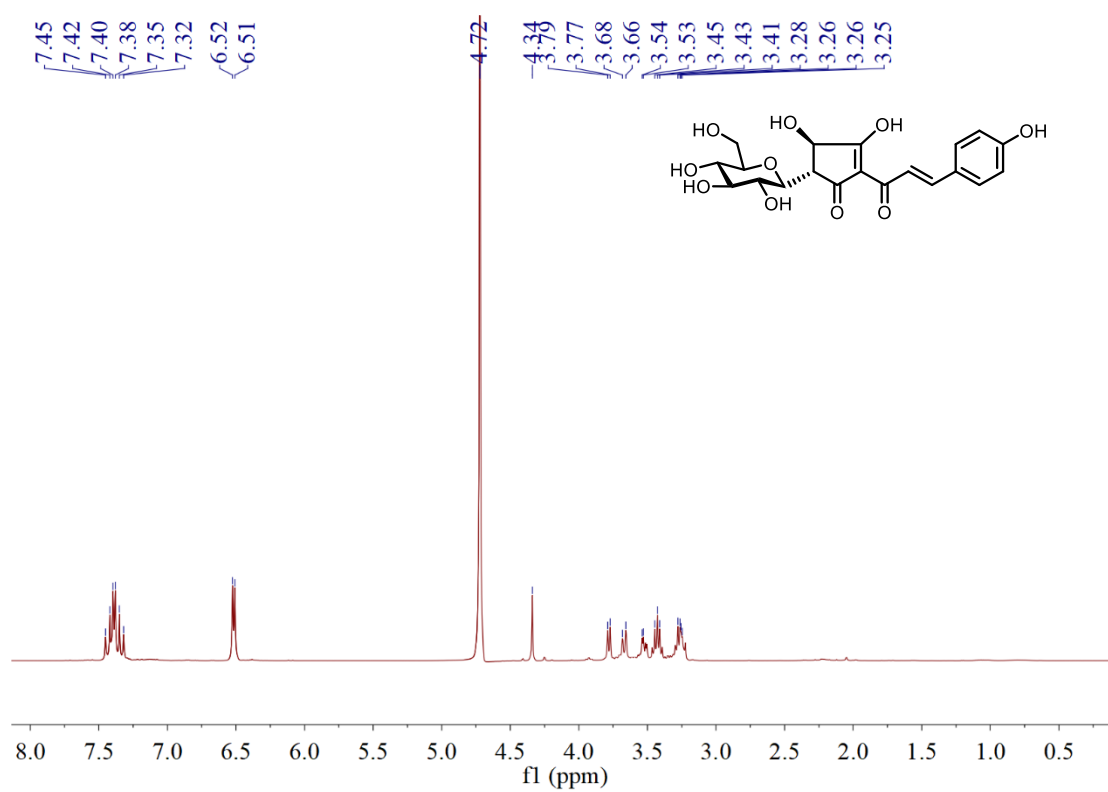
HSQC (500 MHz, D₂O + NaOD) of **1**



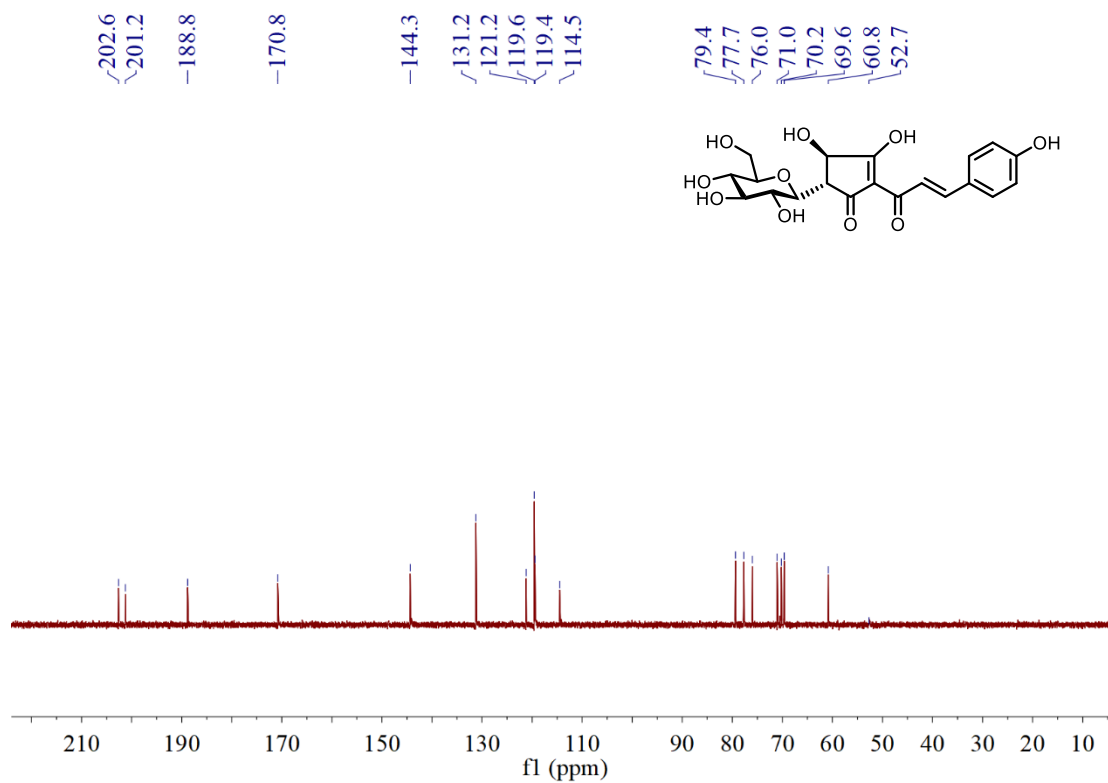
ROESY (500 MHz, D₂O + NaOD) of **1**



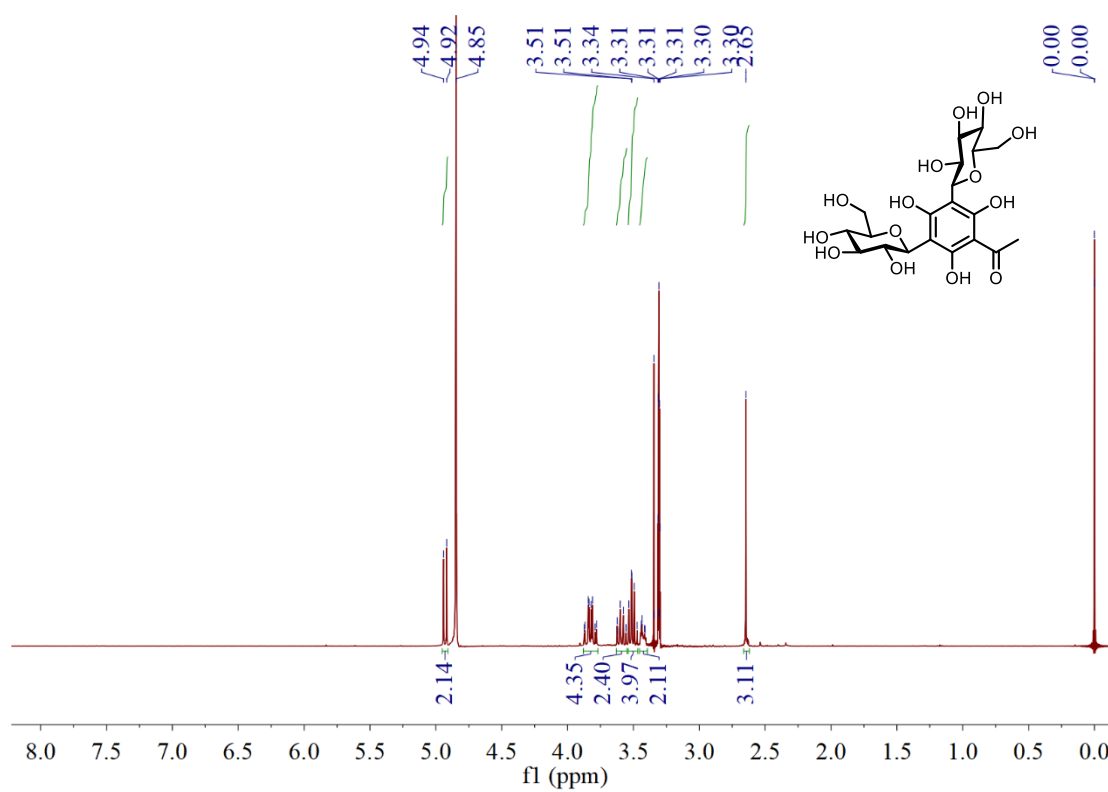
¹H NMR (500 MHz, D₂O + NaOD) of **1** (obtained from HSYA)



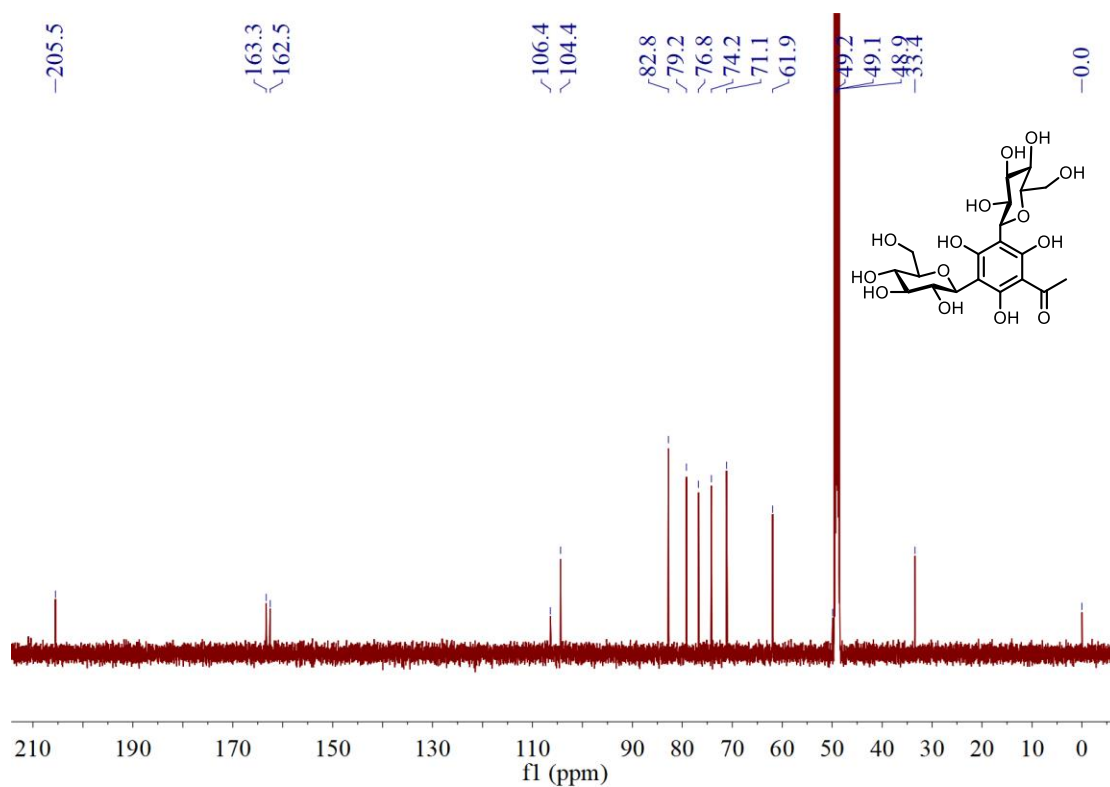
^{13}C NMR (125 MHz, $\text{D}_2\text{O} + \text{NaOD}$) of **1** (obtained from HSYA)



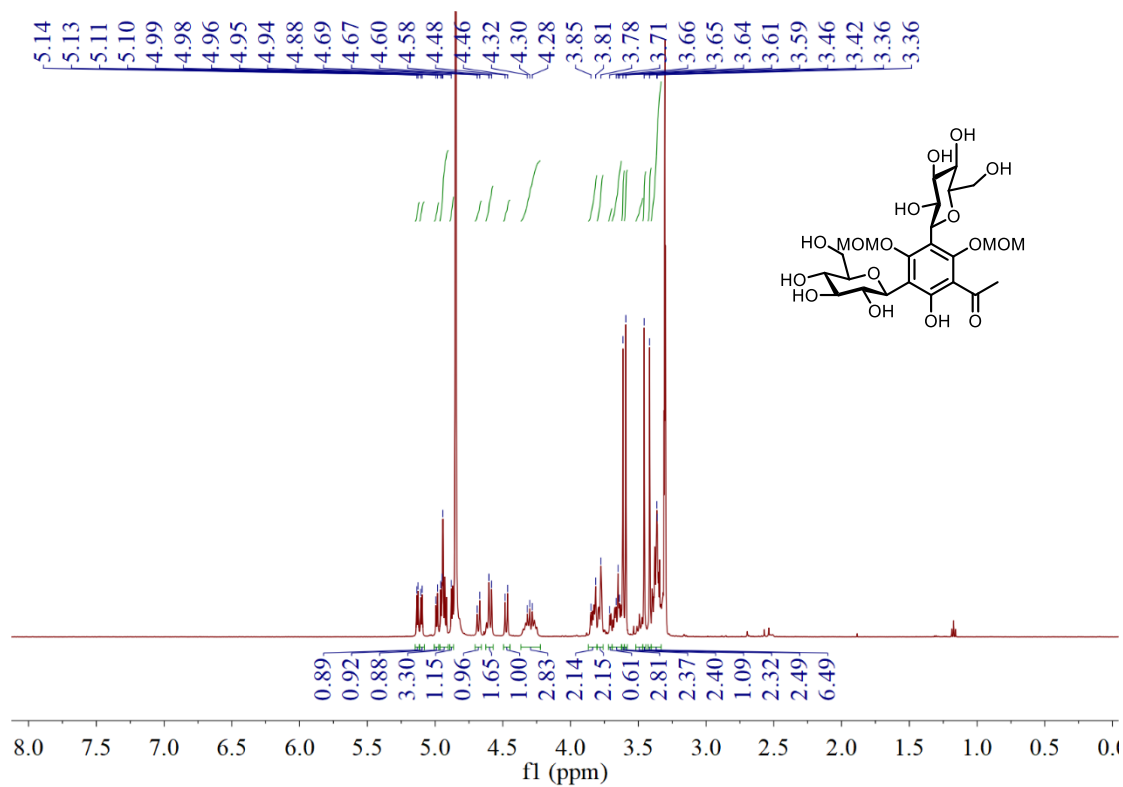
^1H NMR (500 MHz, CD_3OD) of **4**



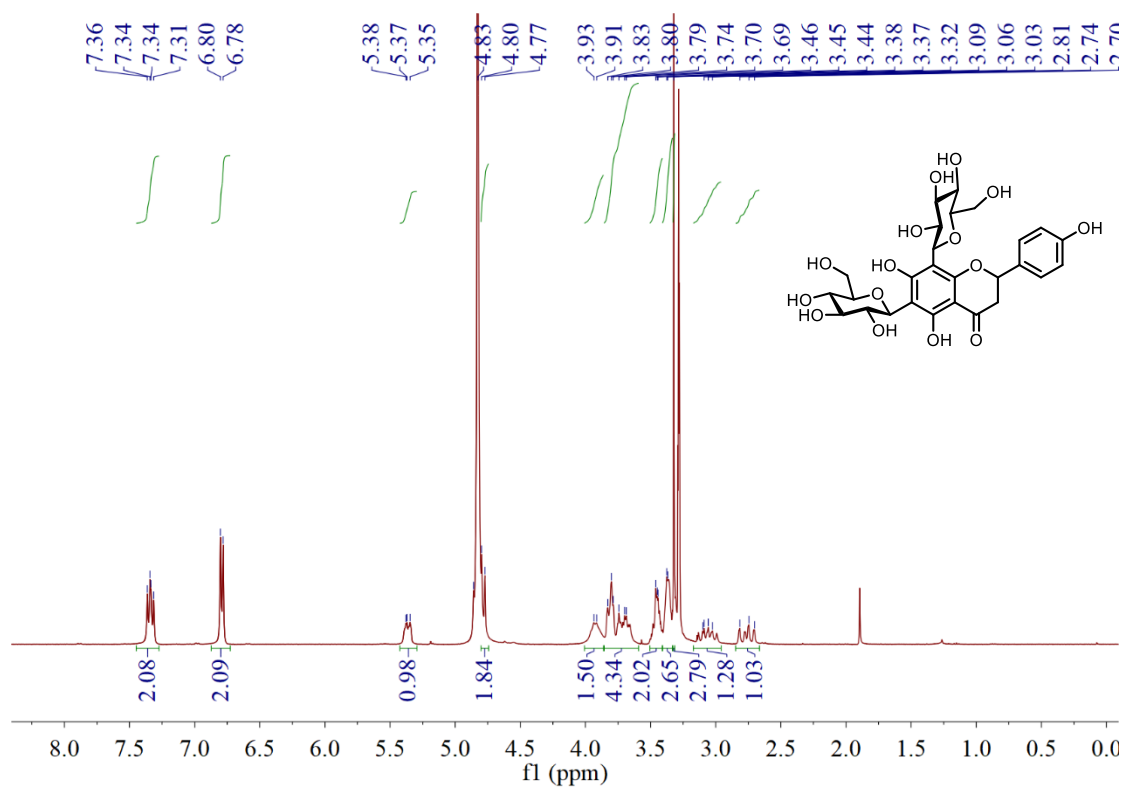
¹³C NMR (125 MHz, CD₃OD) of **4**



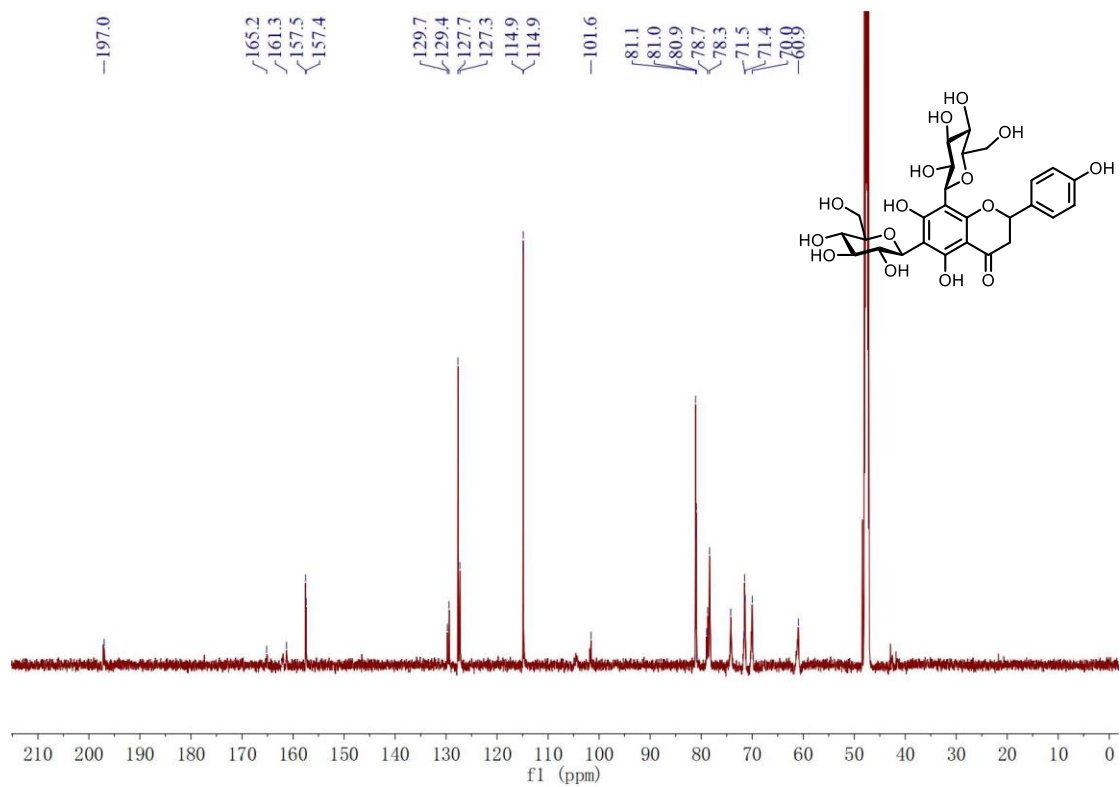
¹H NMR (500 MHz, CD₃OD) of **4-1**



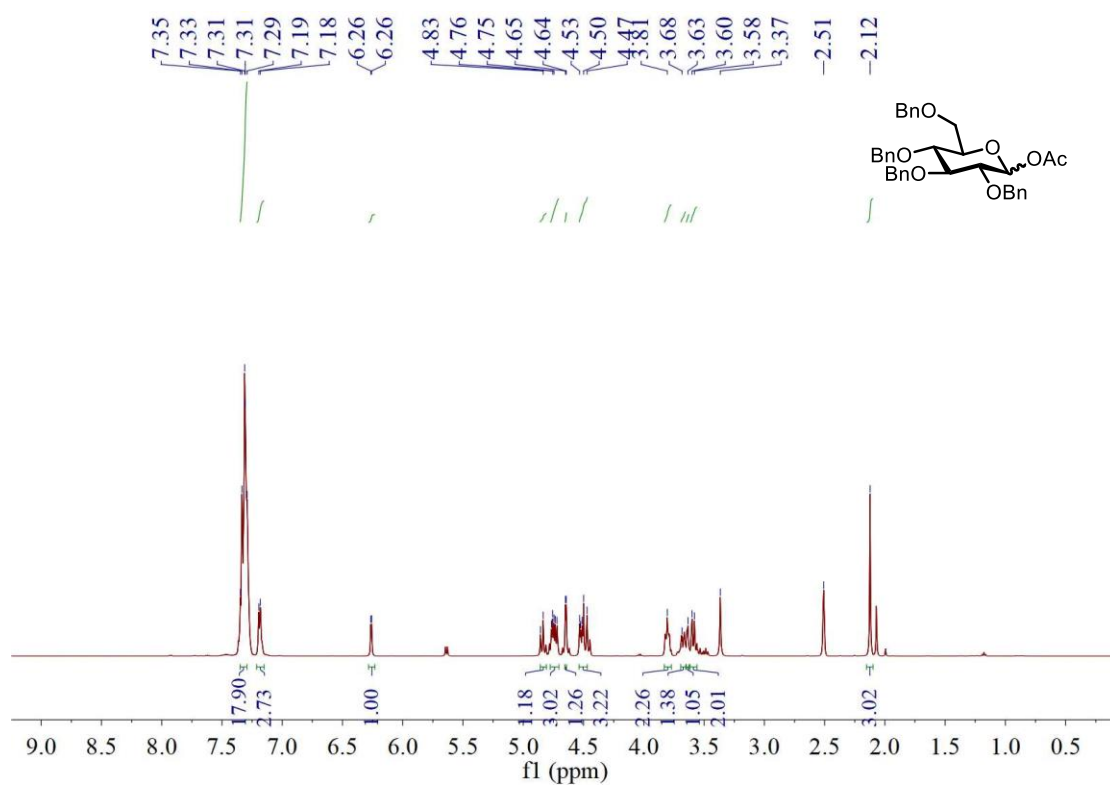
¹H NMR (500 MHz, CD₃OD) of **5-1**



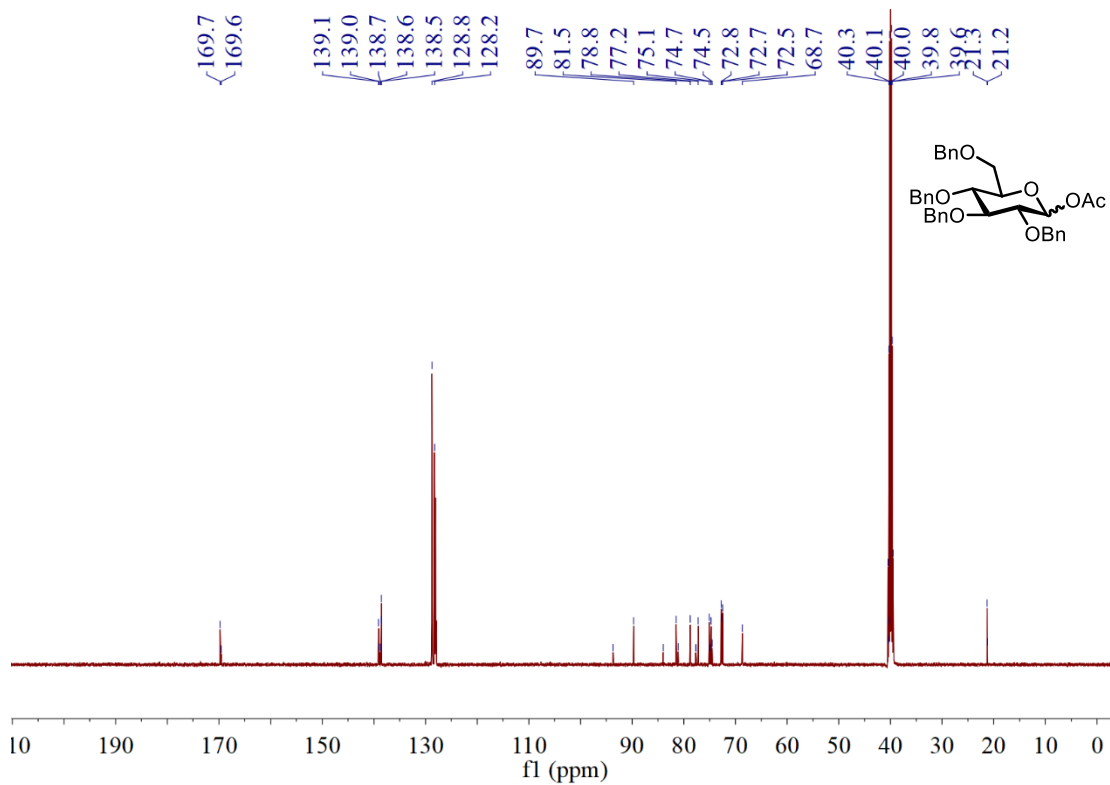
¹³C NMR (125 MHz, CD₃OD) of **5-1**



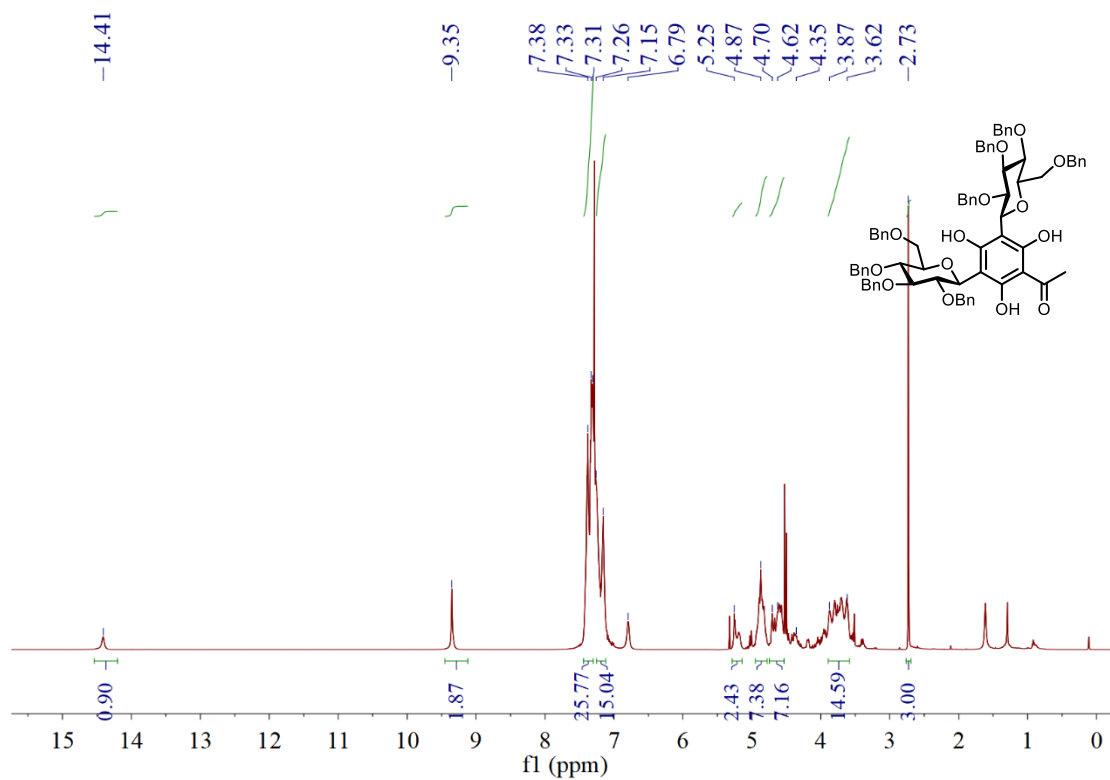
¹H NMR (500 MHz, DMSO-d₆) of **12** (α-anomer + β-anomer)



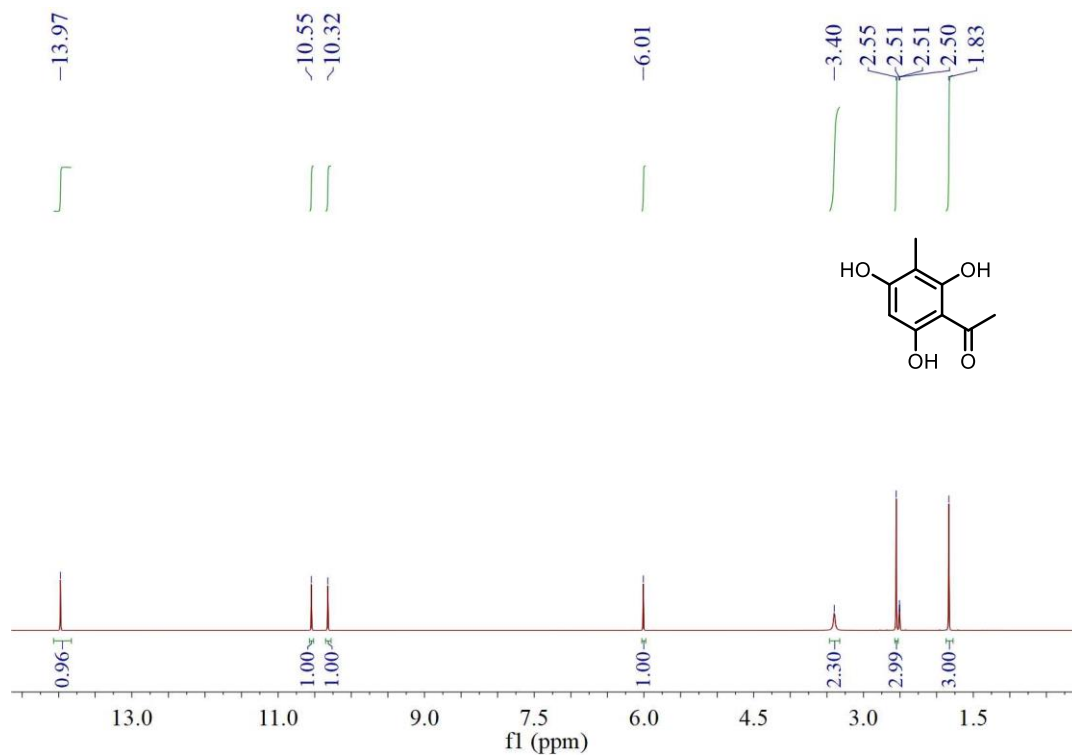
¹³C NMR (125 MHz, DMSO-d₆) of **12** (α-anomer + β-anomer)



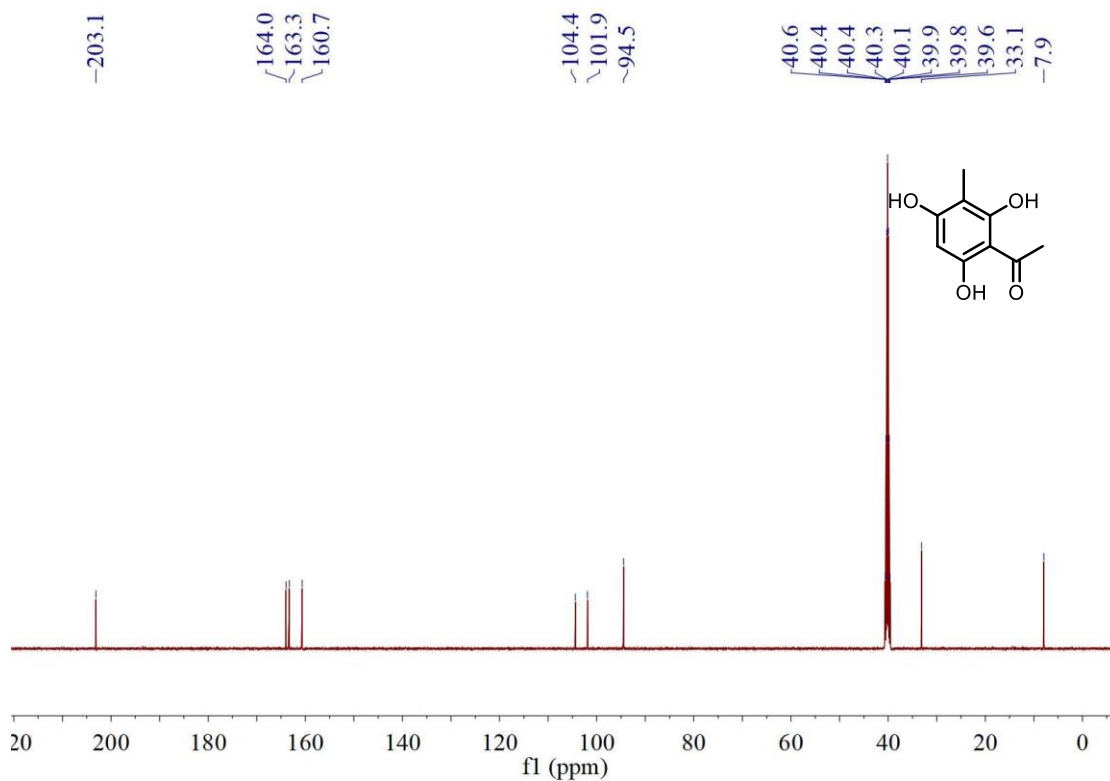
¹H NMR (500 MHz, CDCl₃) of **6-1**



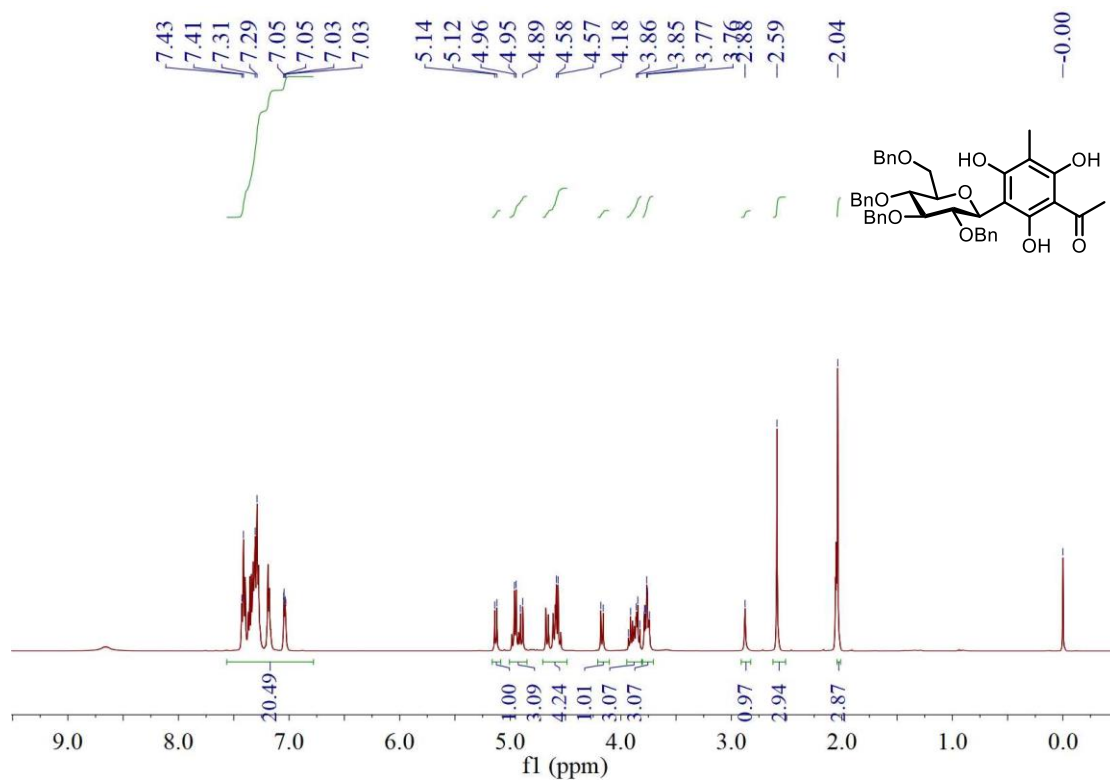
¹H NMR (500 MHz, DMSO-*d*₆) of **10**



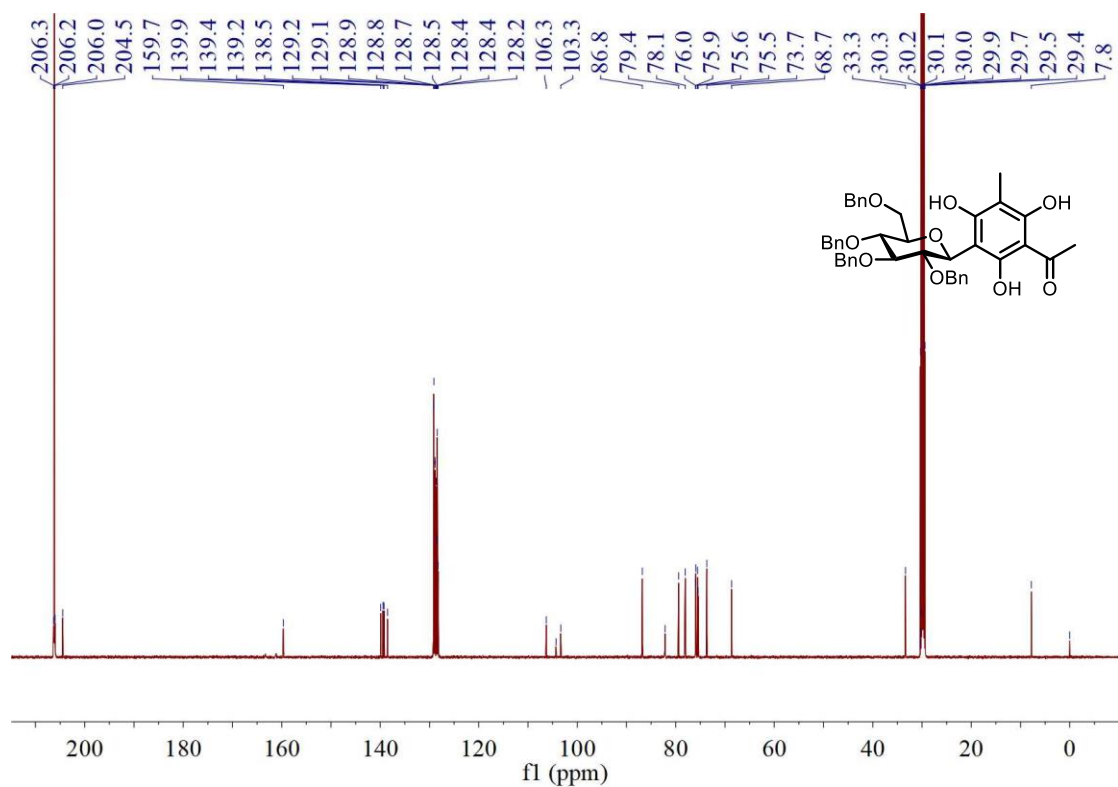
¹³C NMR (125 MHz, DMSO-d₆) of **10**



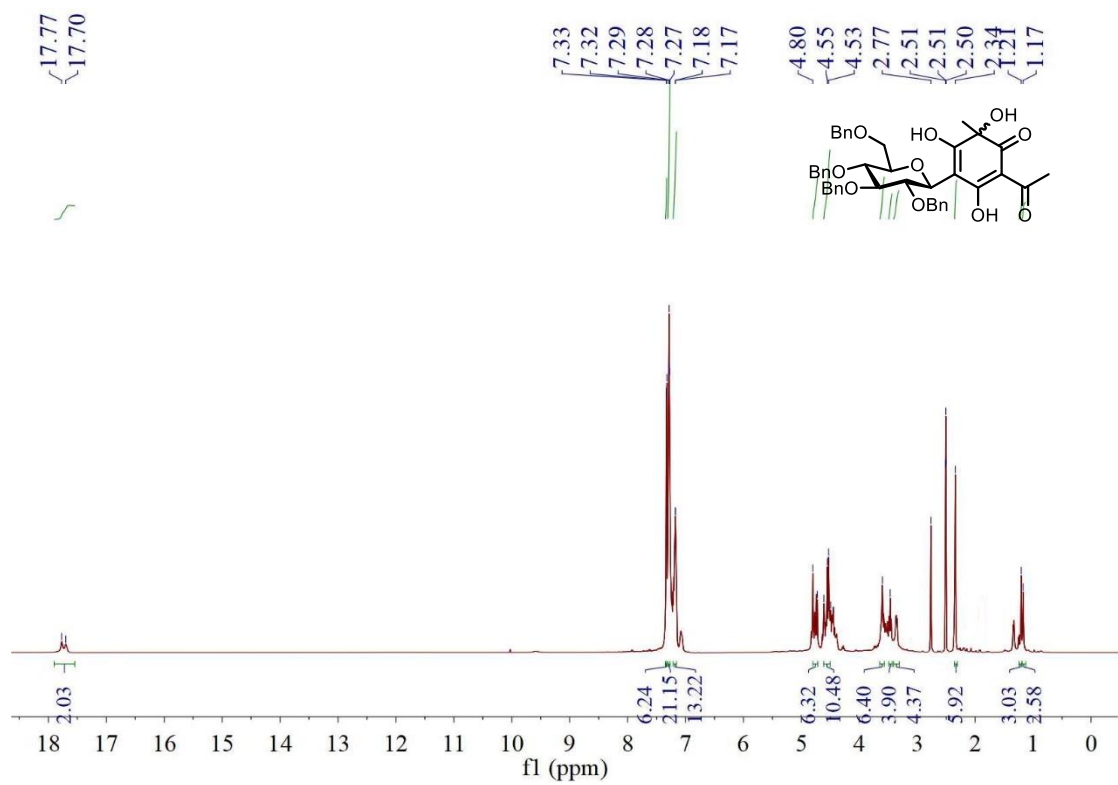
¹H NMR (500 MHz, DMSO-d₆) of **9**



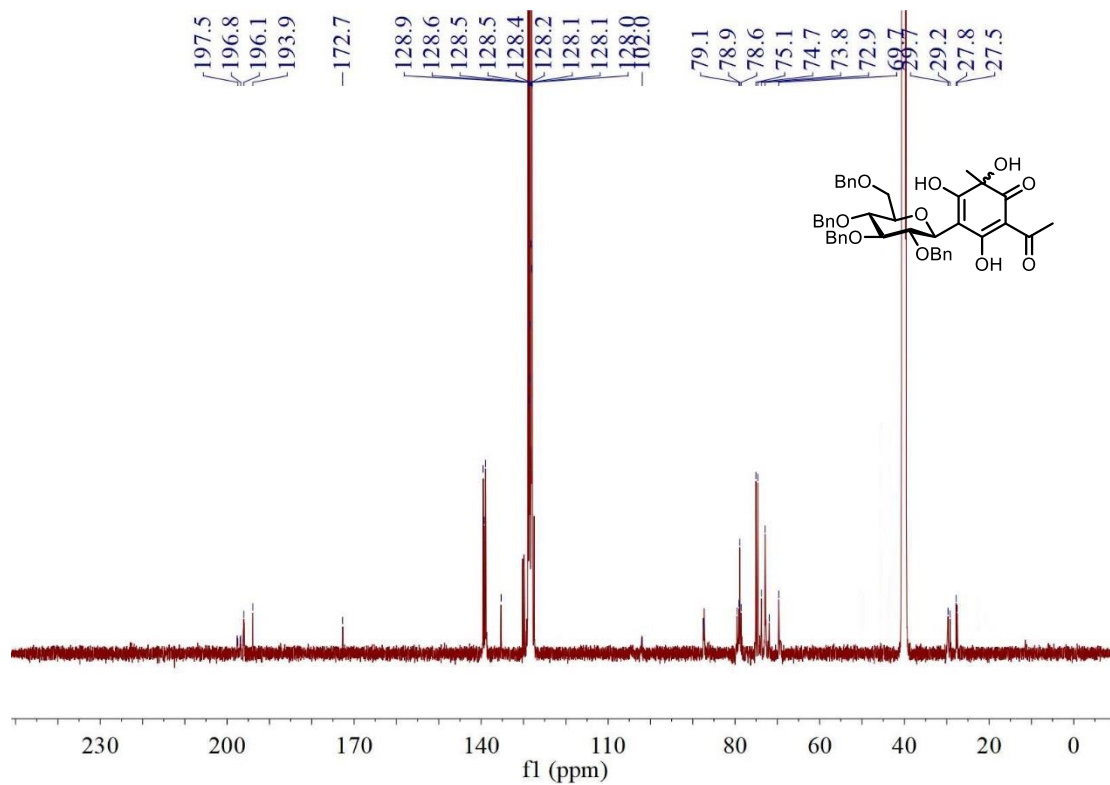
¹³C NMR (125 MHz, DMSO-*d*₆) of **9**



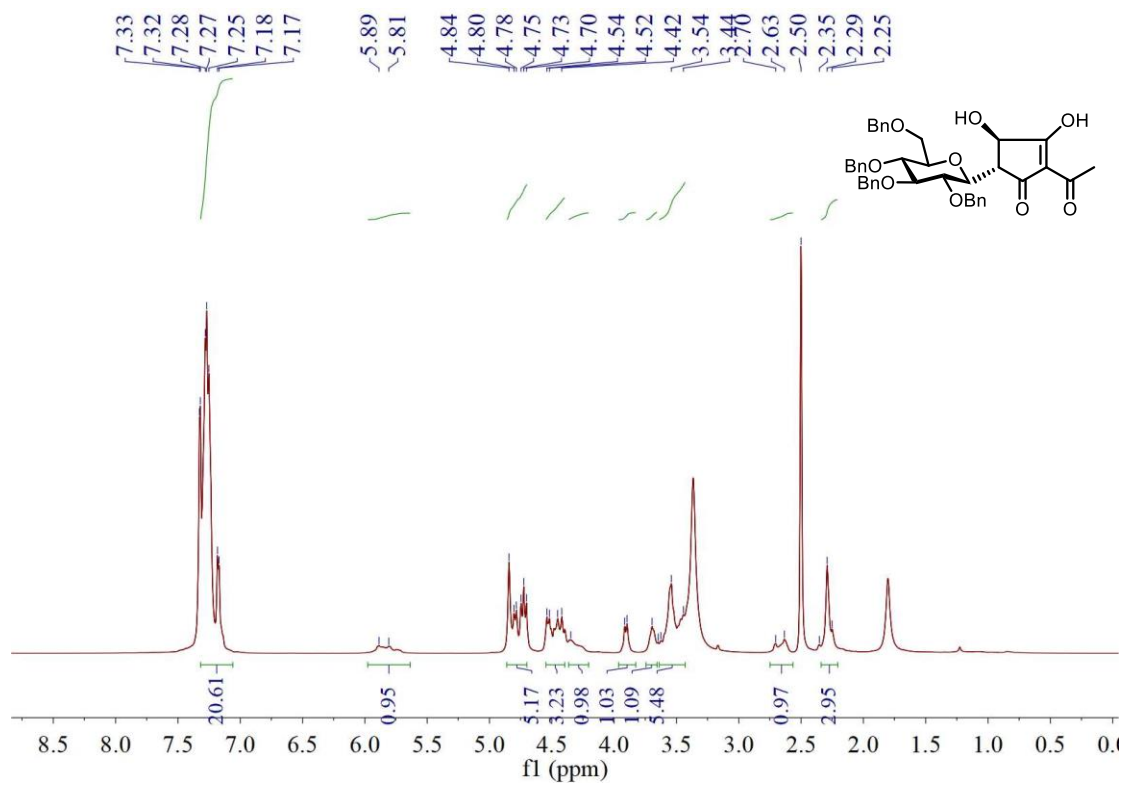
¹H NMR (500 MHz, DMSO-*d*₆) of **8**



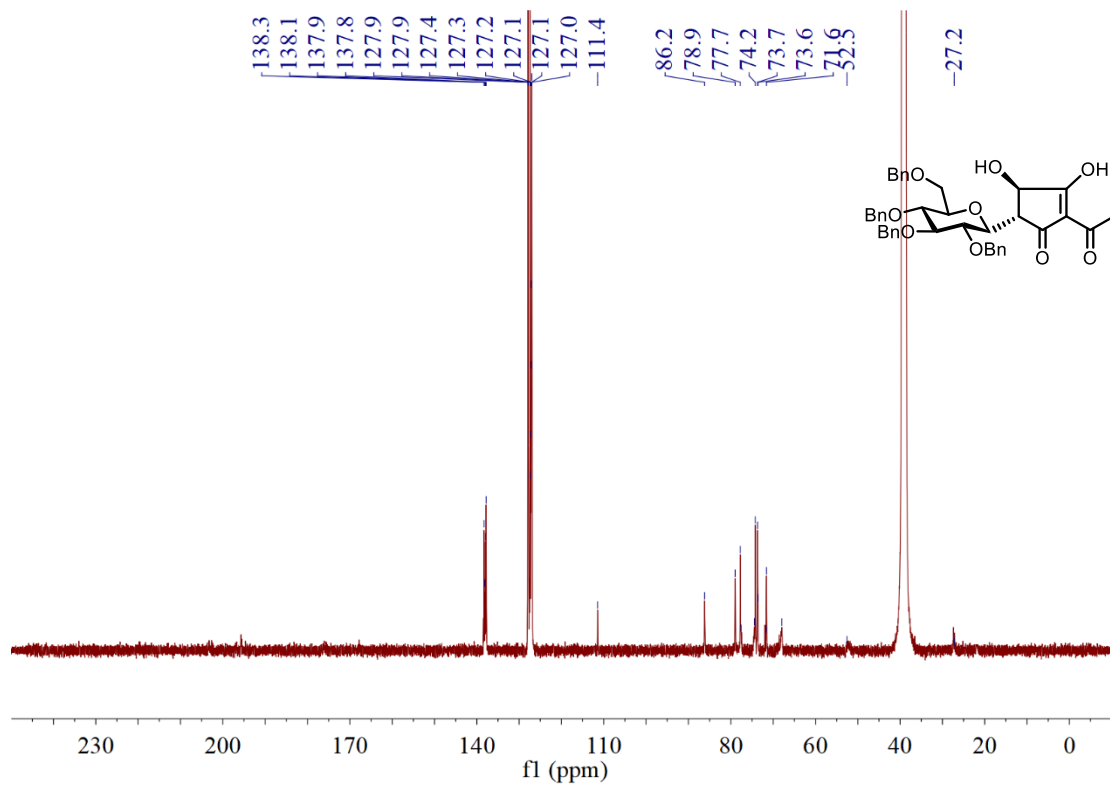
¹³C NMR (125 MHz, DMSO-d₆) of **8**



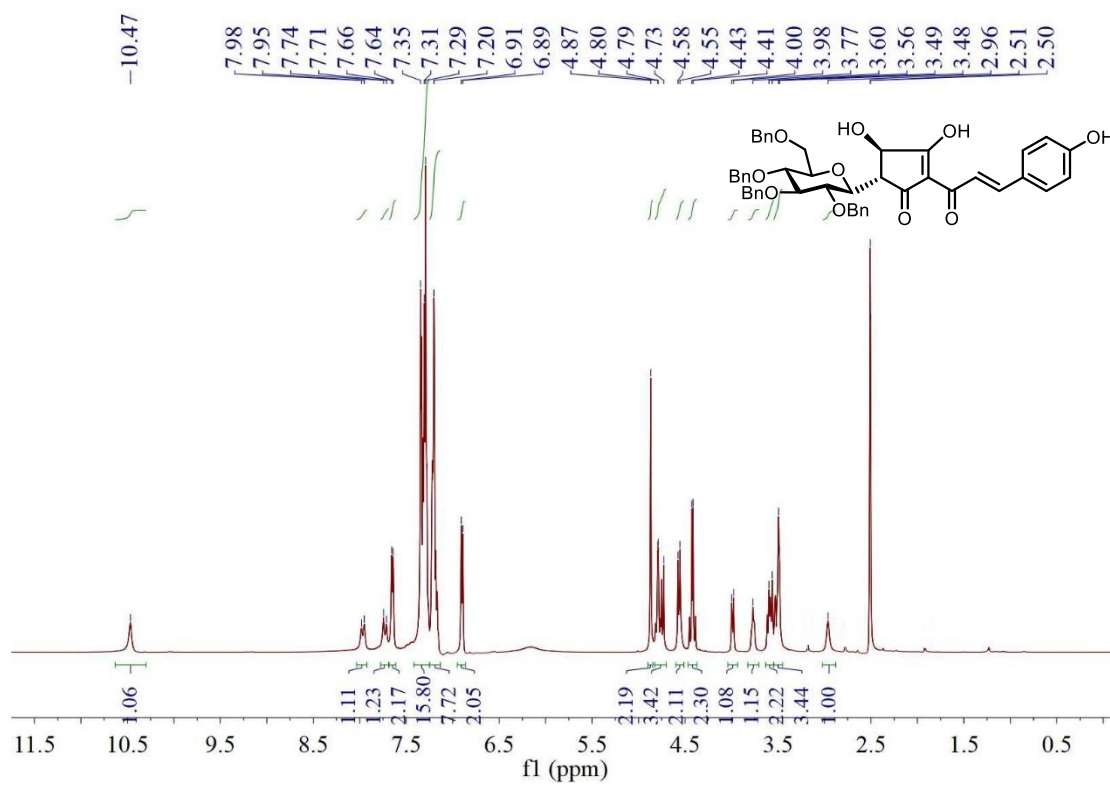
¹H NMR (500 MHz, DMSO-d₆) of **7**



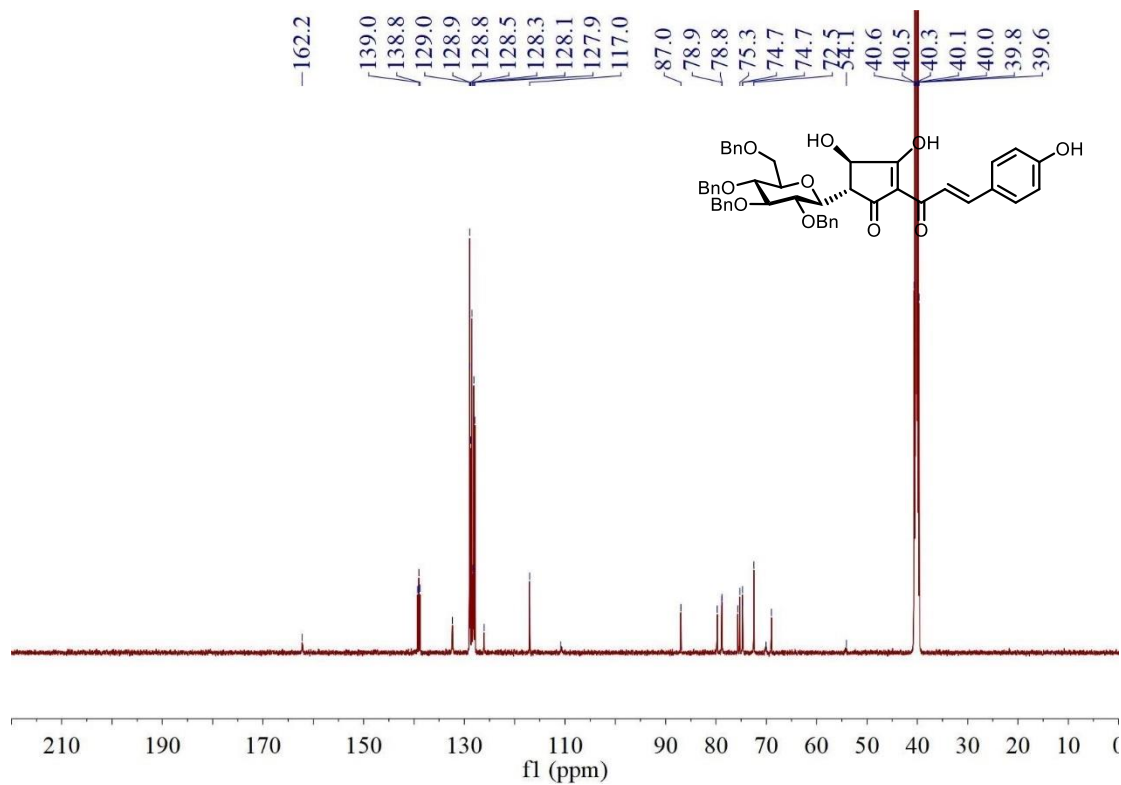
¹³C NMR (125 MHz, DMSO-*d*₆) of **7**



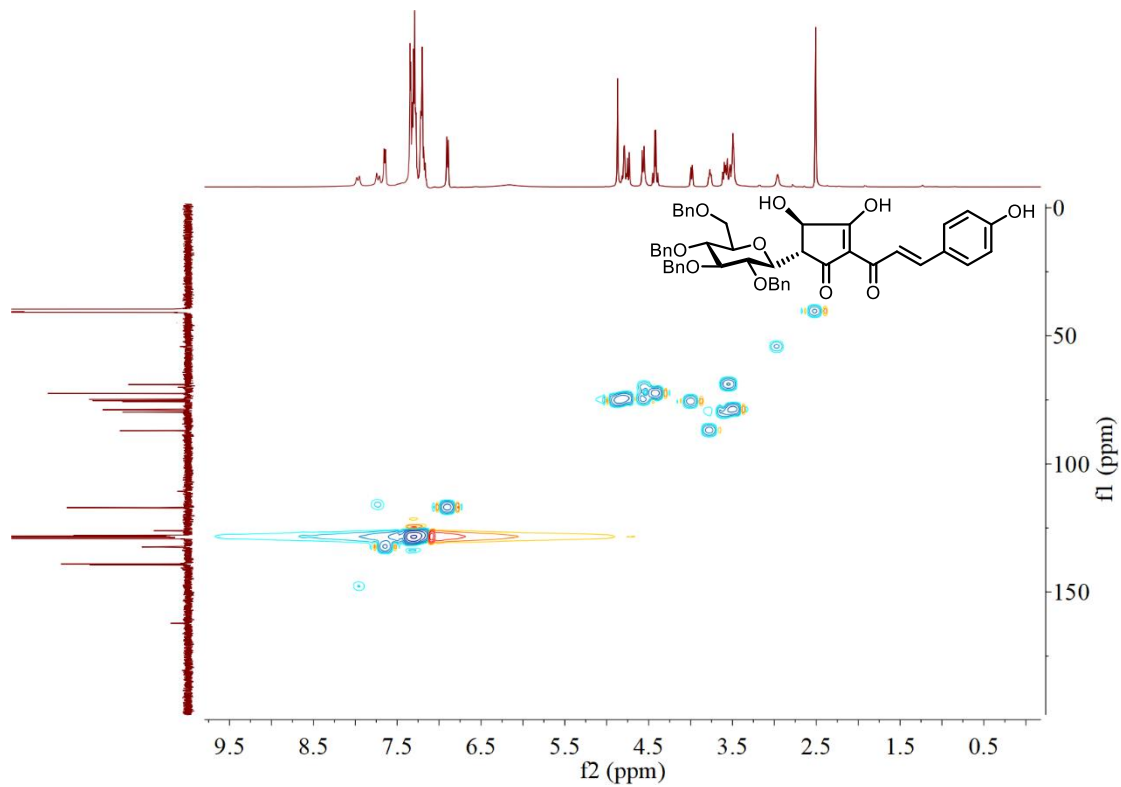
¹H NMR (500 MHz, DMSO-*d*₆) of **14**



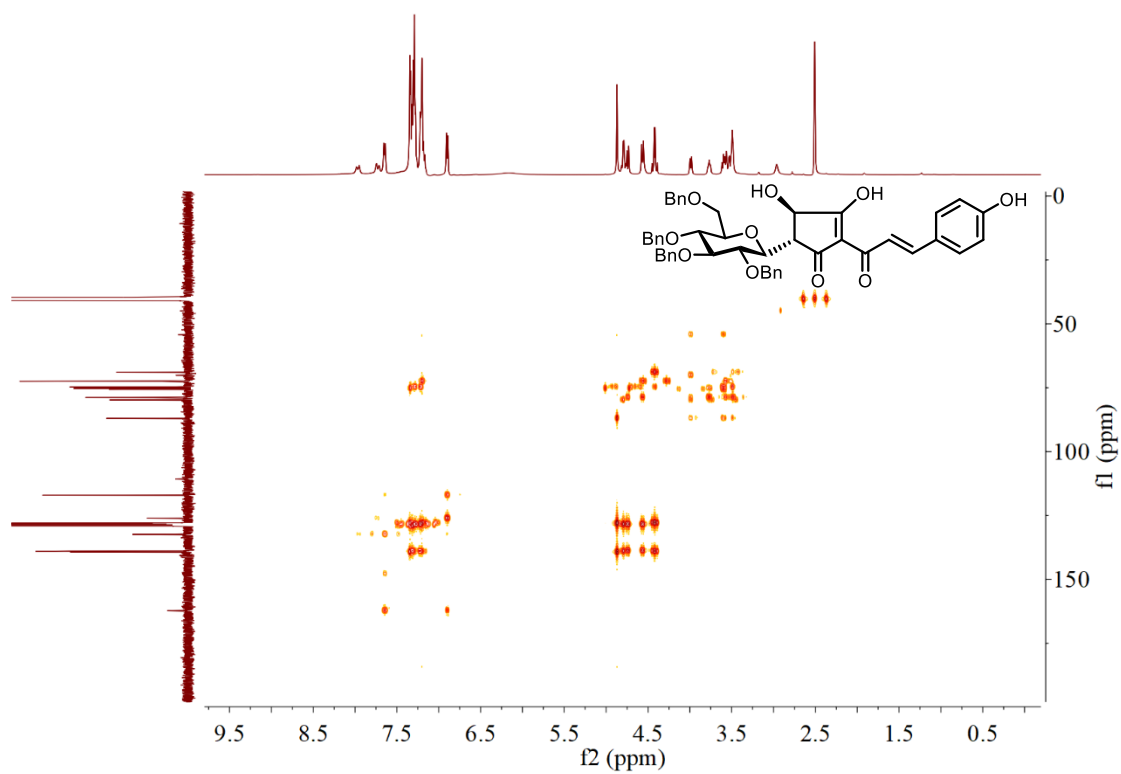
¹³C NMR (125 MHz, DMSO-*d*₆) of **14**



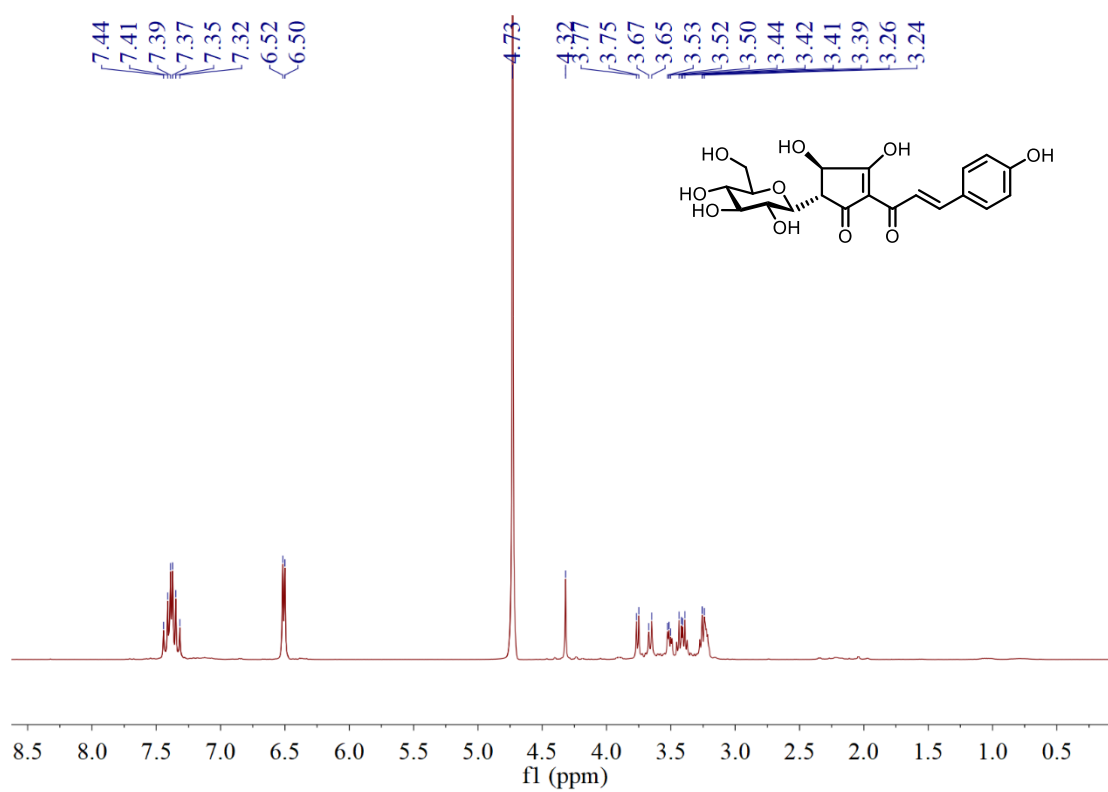
HSQC (500 MHz, DMSO-*d*₆) of **14**



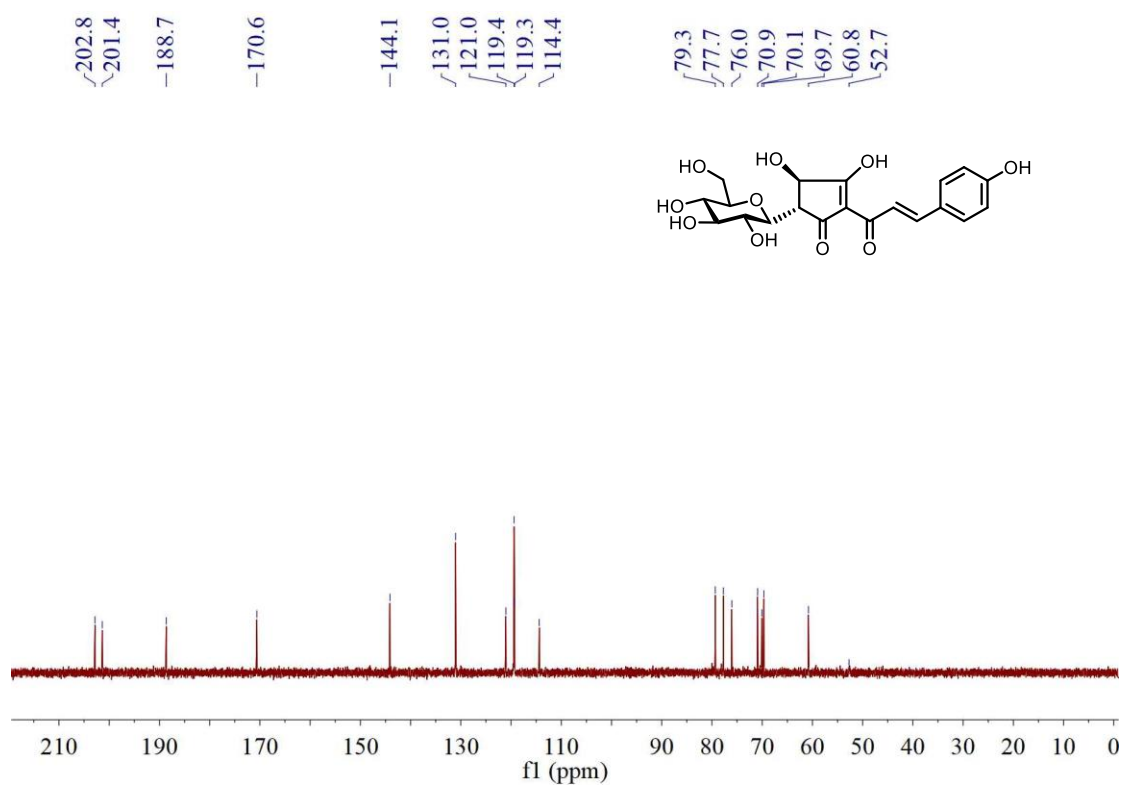
HMBC (500 MHz, DMSO-*d*₆) of **14**



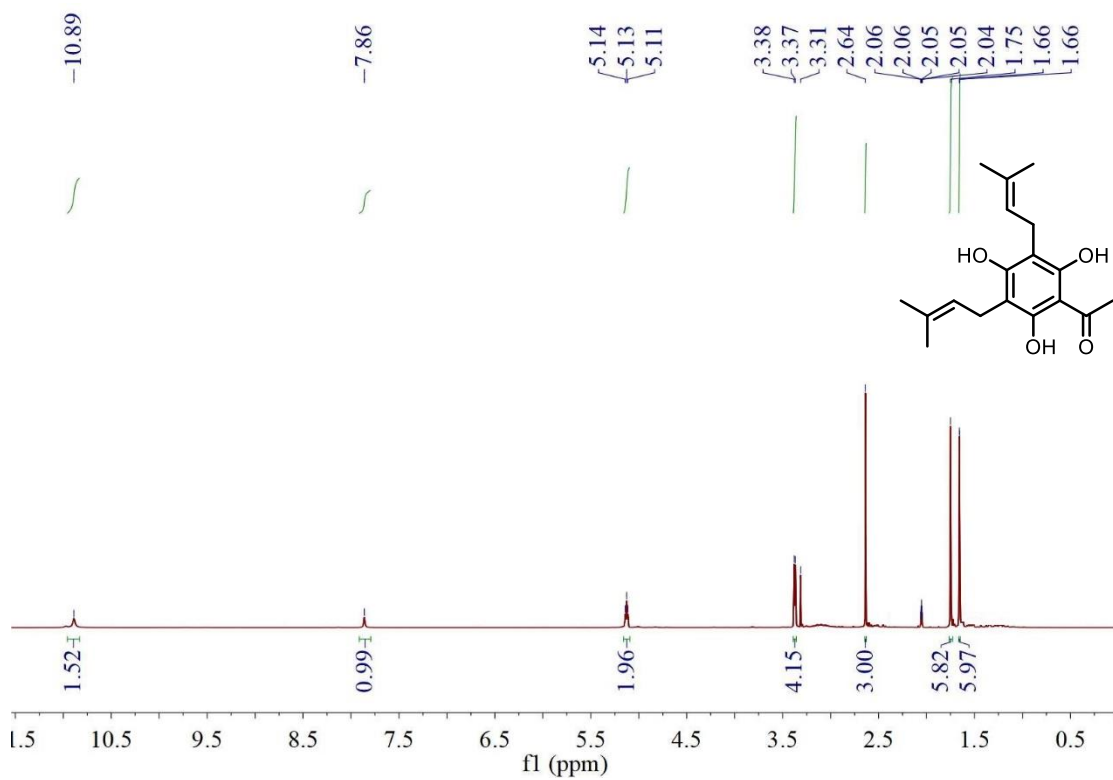
¹H NMR (500 MHz, D₂O + NaOD) of **1** (obtained from **14**)



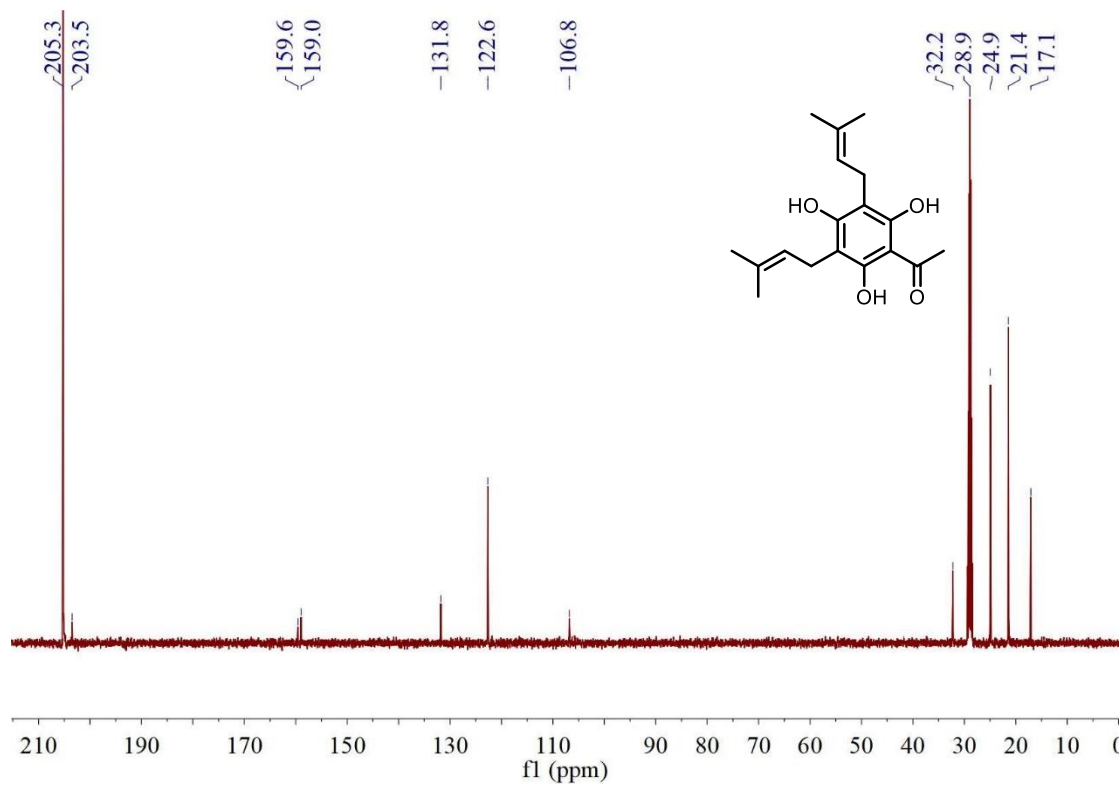
^{13}C NMR (125 MHz, $\text{D}_2\text{O} + \text{NaOD}$) of **1** (obtained from **14**)



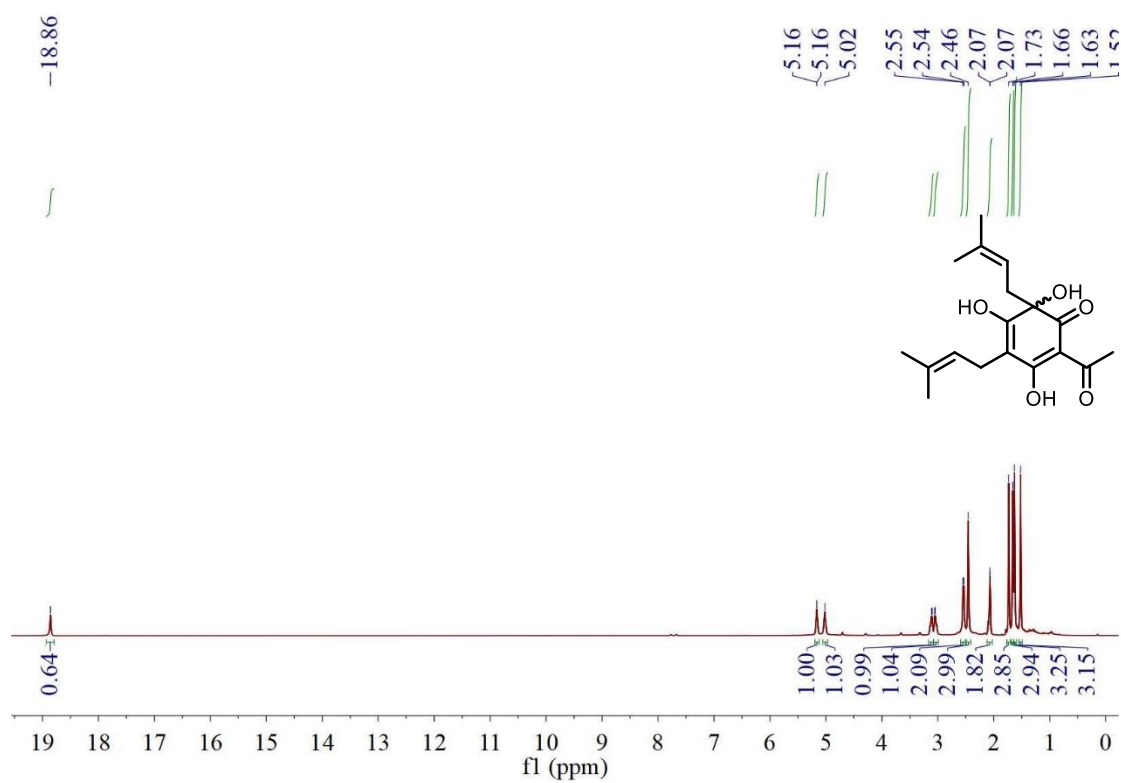
^1H NMR (500 MHz, acetone- d_6) of **15-1**



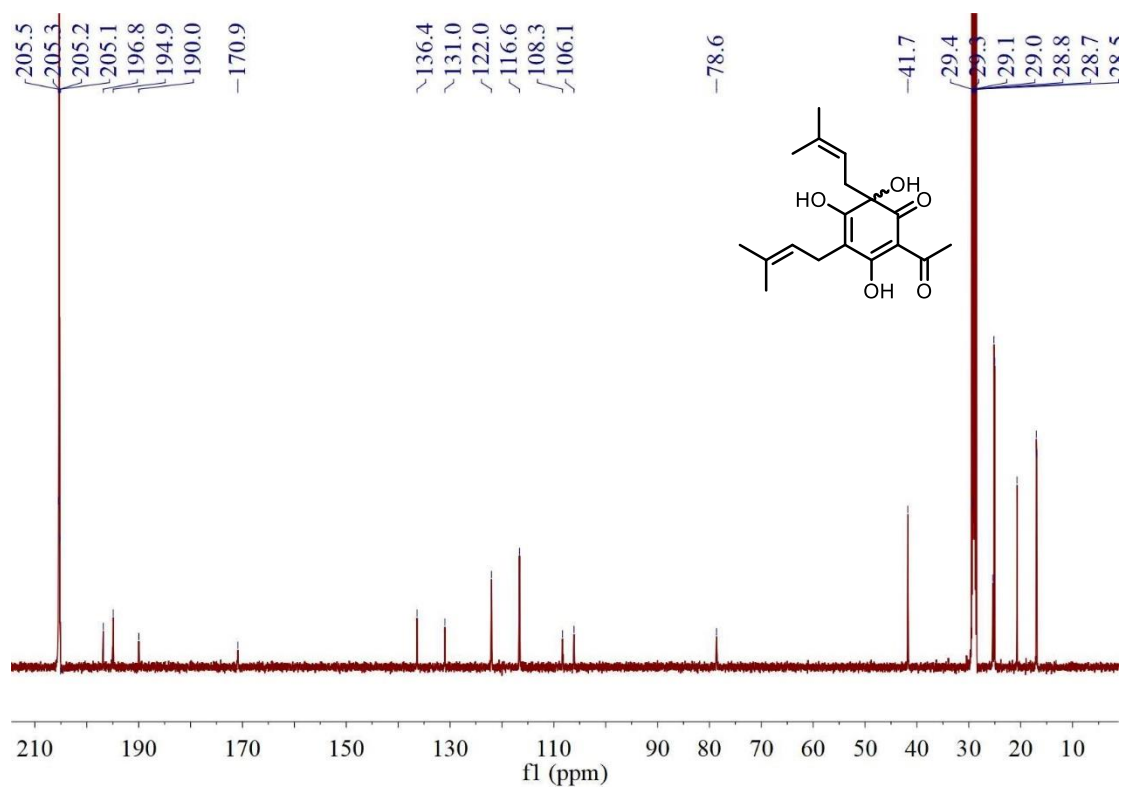
¹³C NMR (125 MHz, acetone-*d*₆) of **15-1**



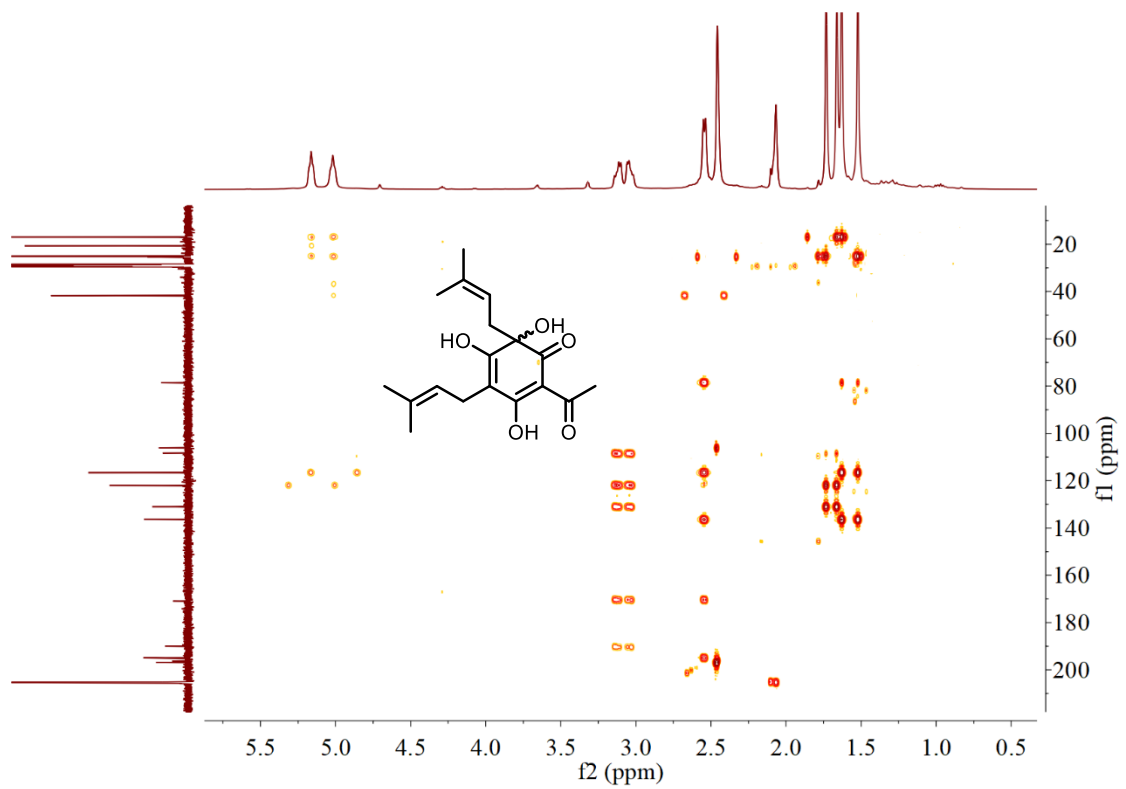
¹H NMR (500 MHz, acetone-*d*₆) of **15**



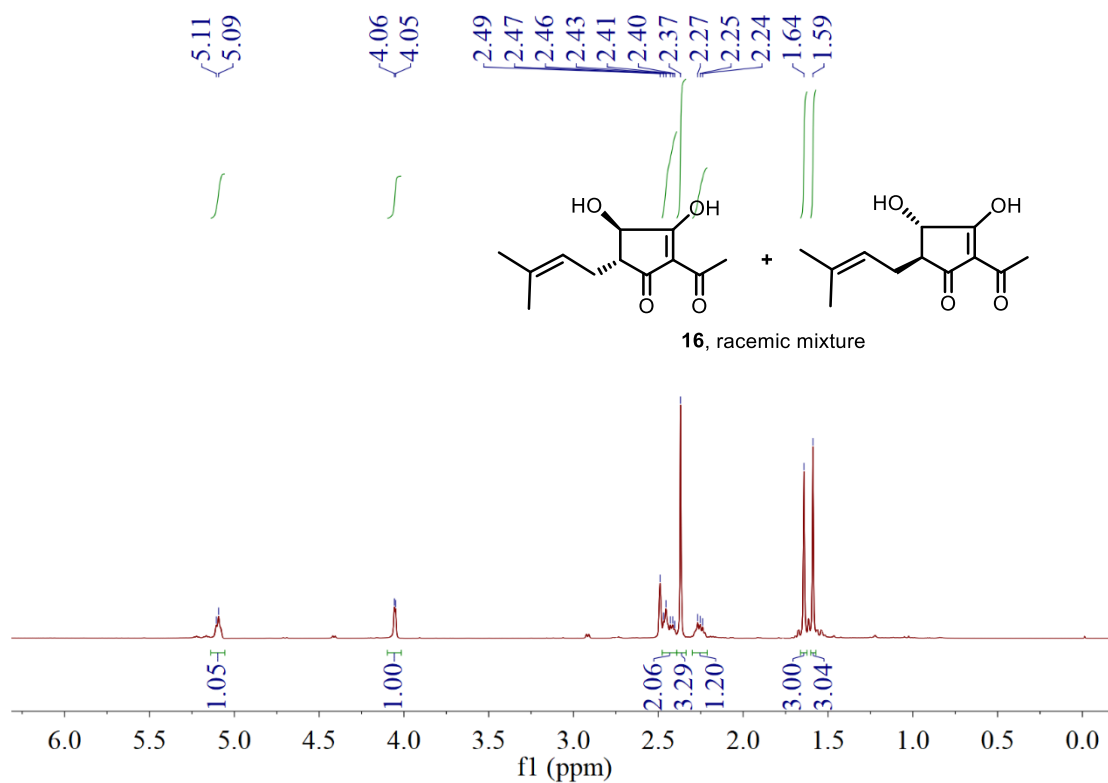
¹³C NMR (125 MHz, acetone-d₆) of **15**



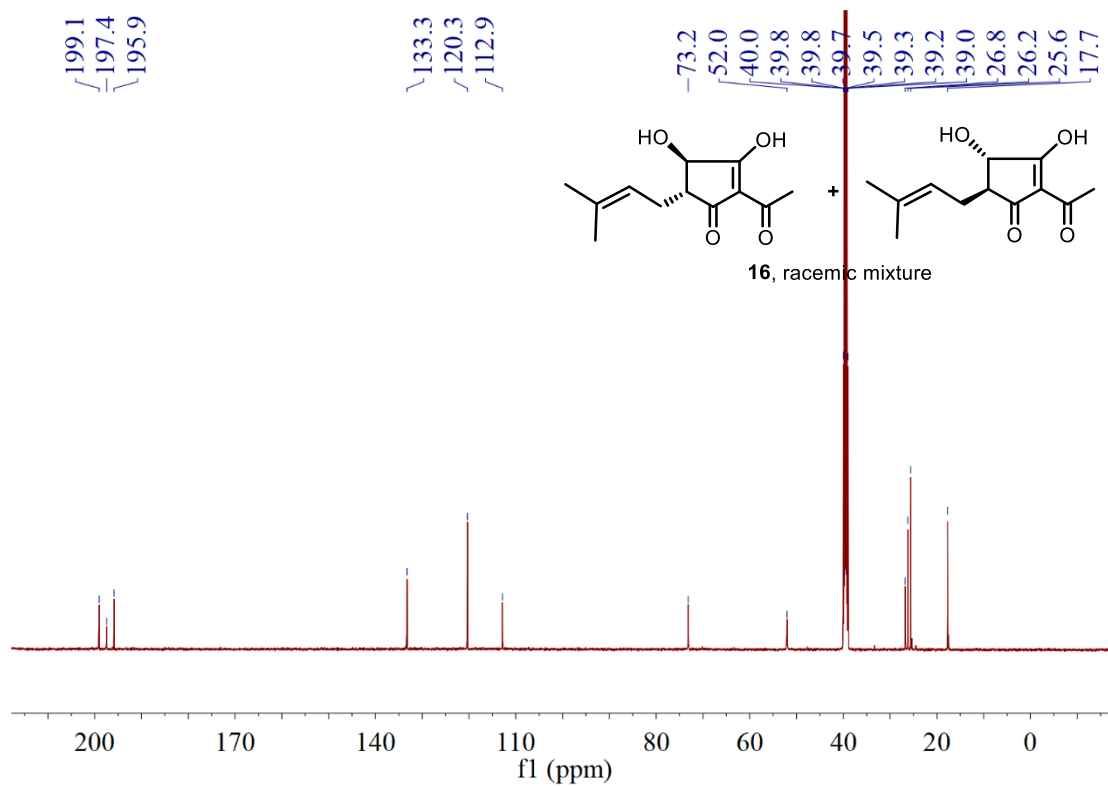
HMBC (500 MHz, acetone-d₆) of **15**



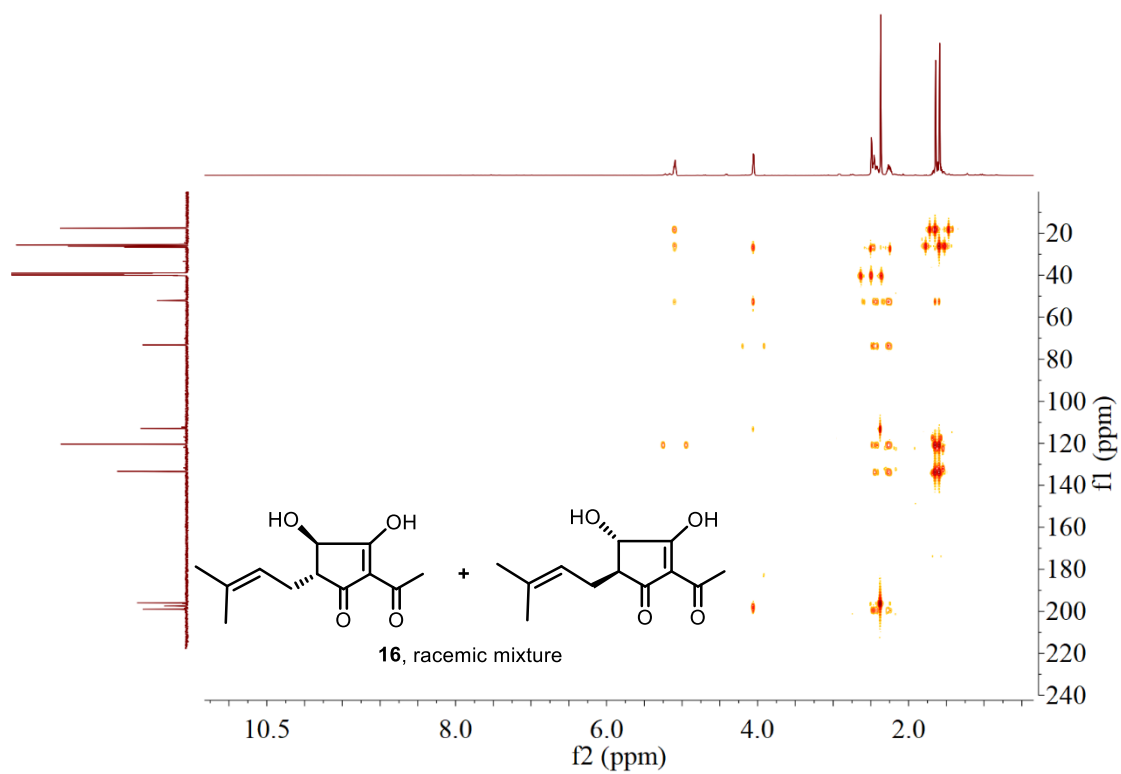
¹H NMR (500 MHz, DMSO-*d*₆) of **16**



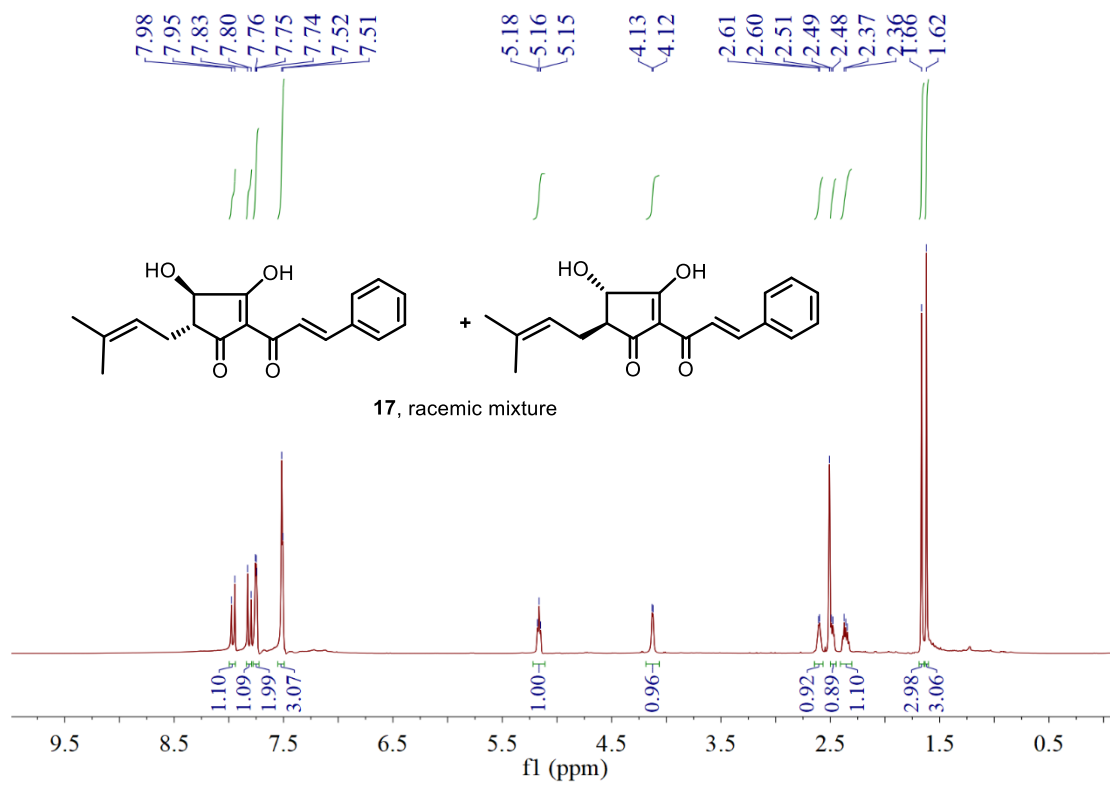
¹³C NMR (125 MHz, DMSO-*d*₆) of **16**



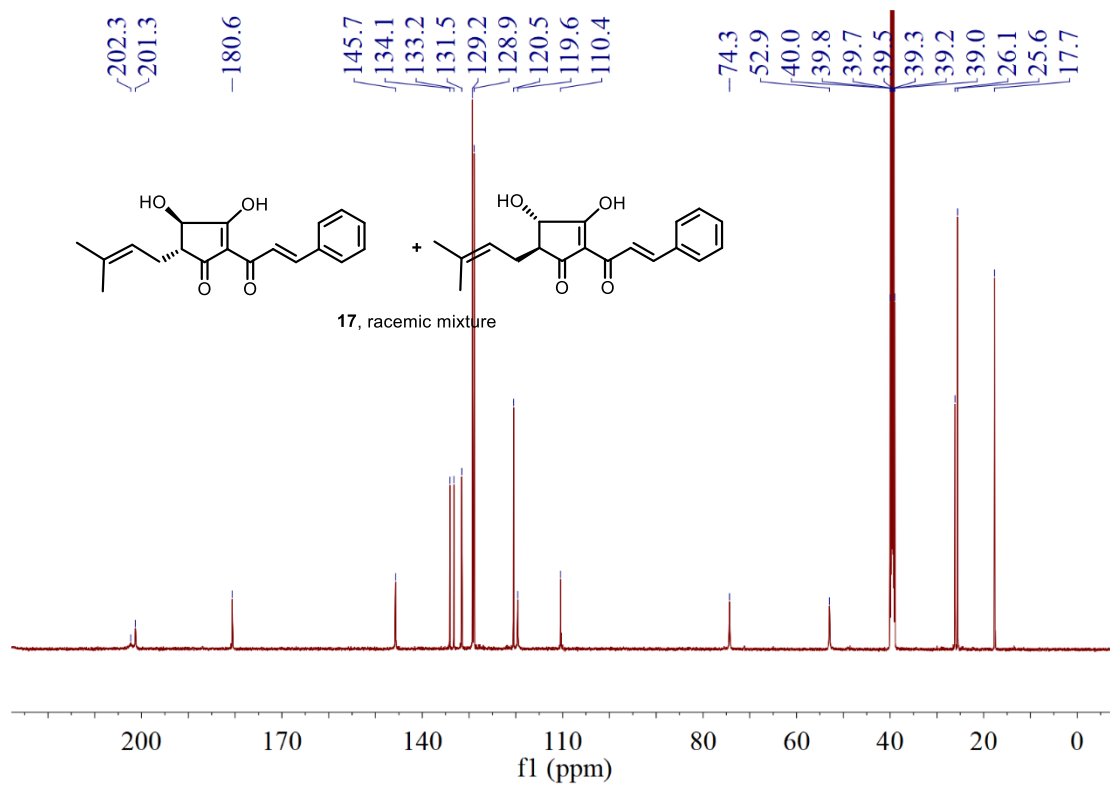
HMBC (500 MHz, DMSO-*d*₆) of **16**



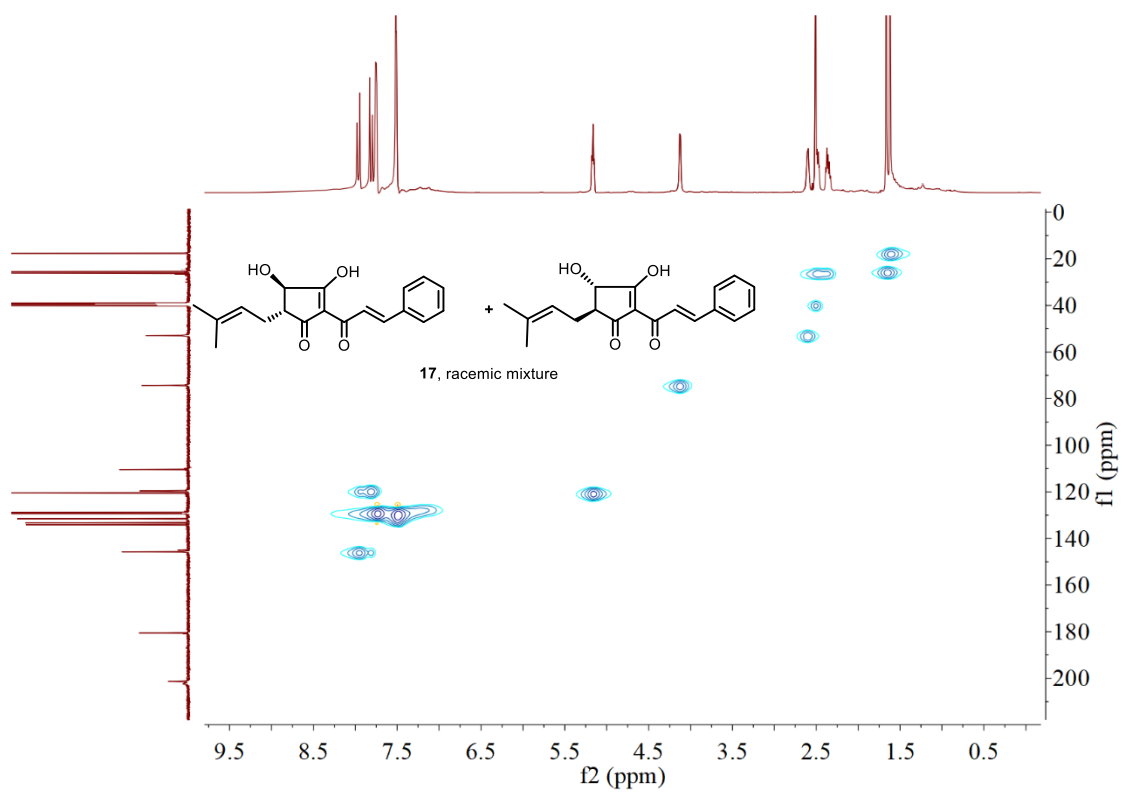
¹H NMR (500 MHz, DMSO-*d*₆) of **17**



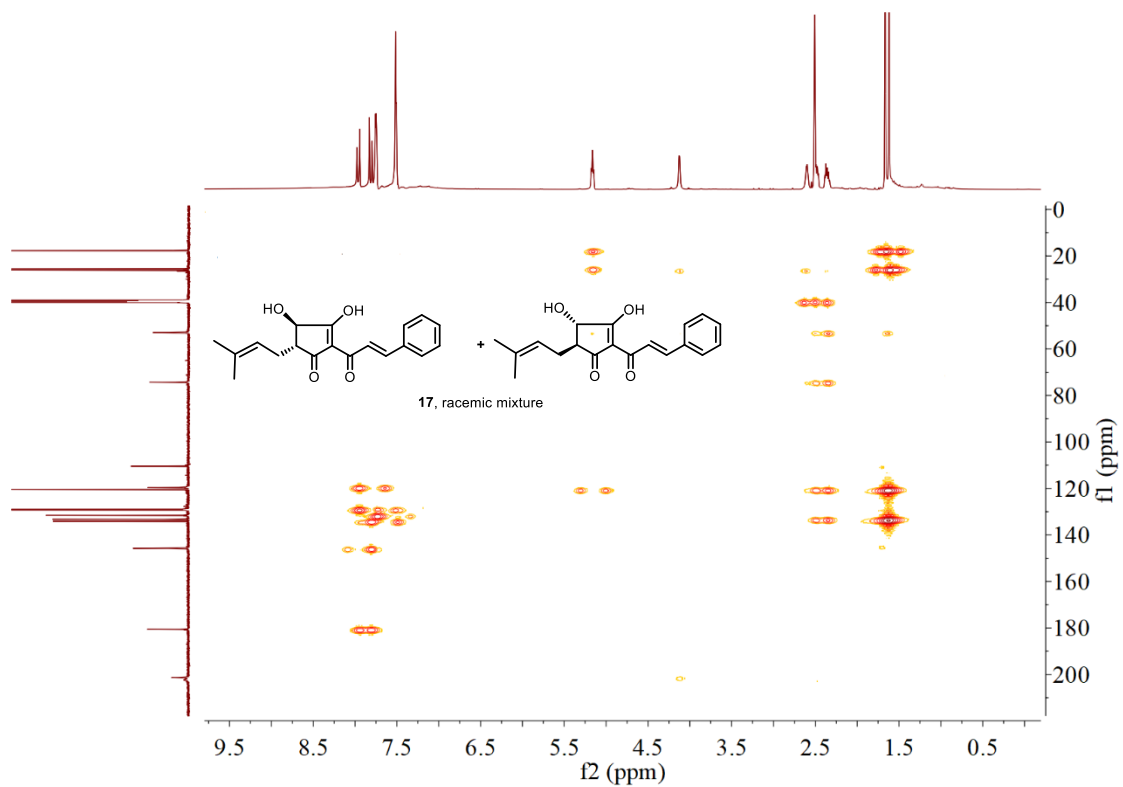
¹³C NMR (125 MHz, DMSO-d₆) of **17**



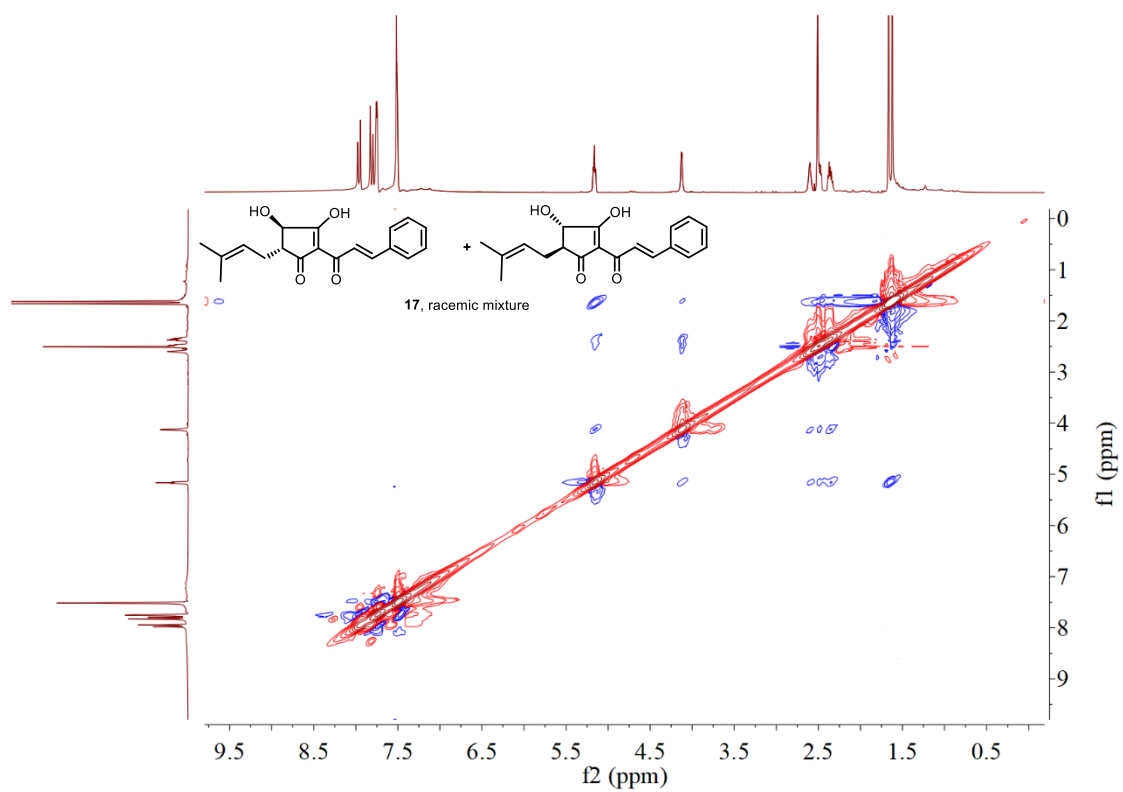
HSQC (500 MHz, DMSO-d₆) of **17**



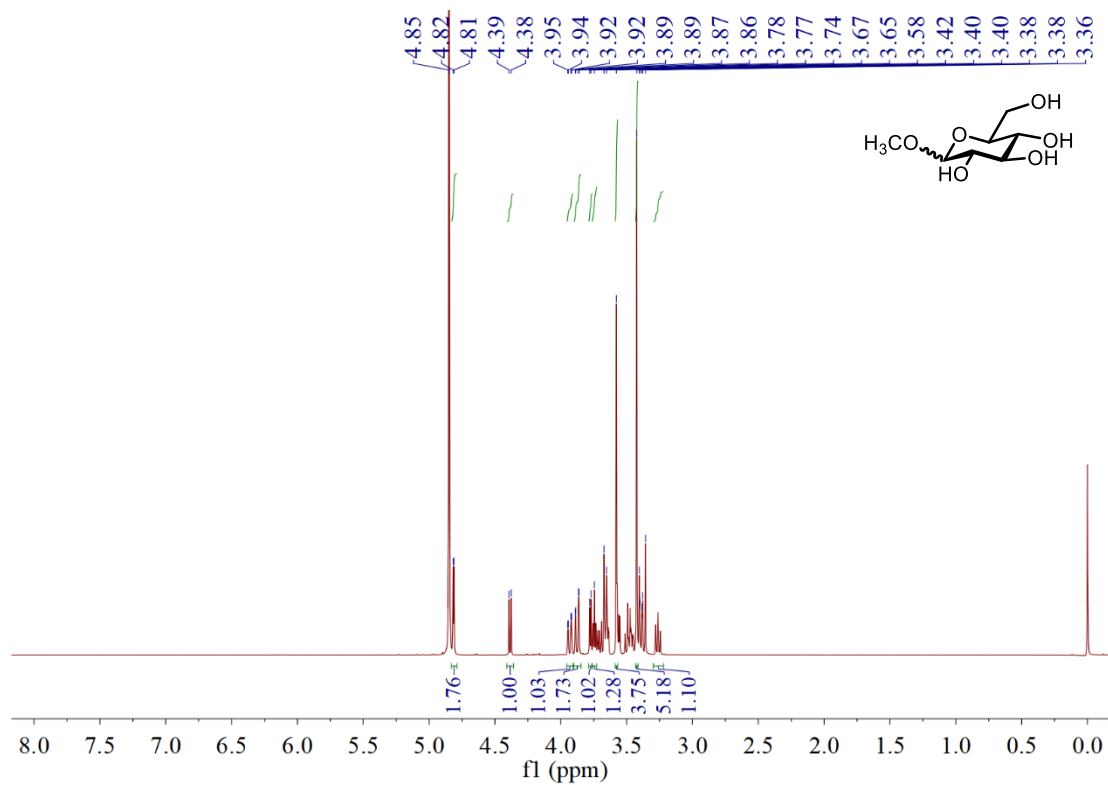
HMBC (500 MHz, DMSO- d_6) of **17**



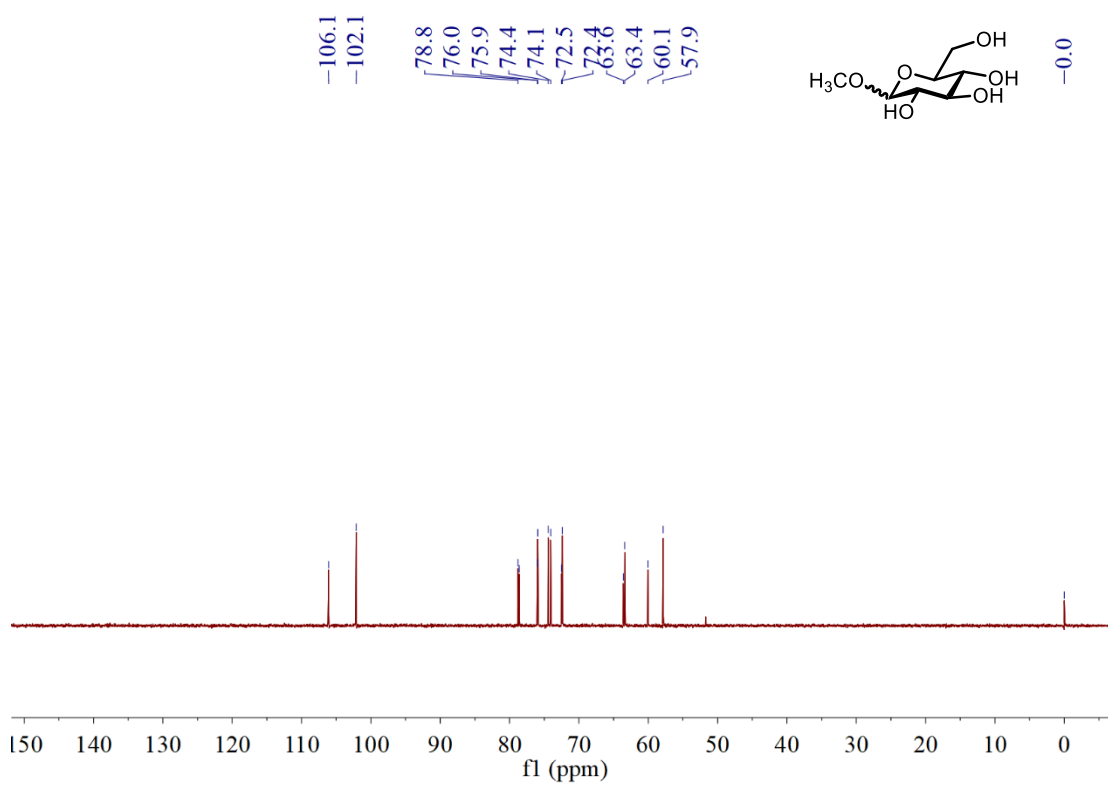
ROESY (500 MHz, DMSO- d_6) of **17**



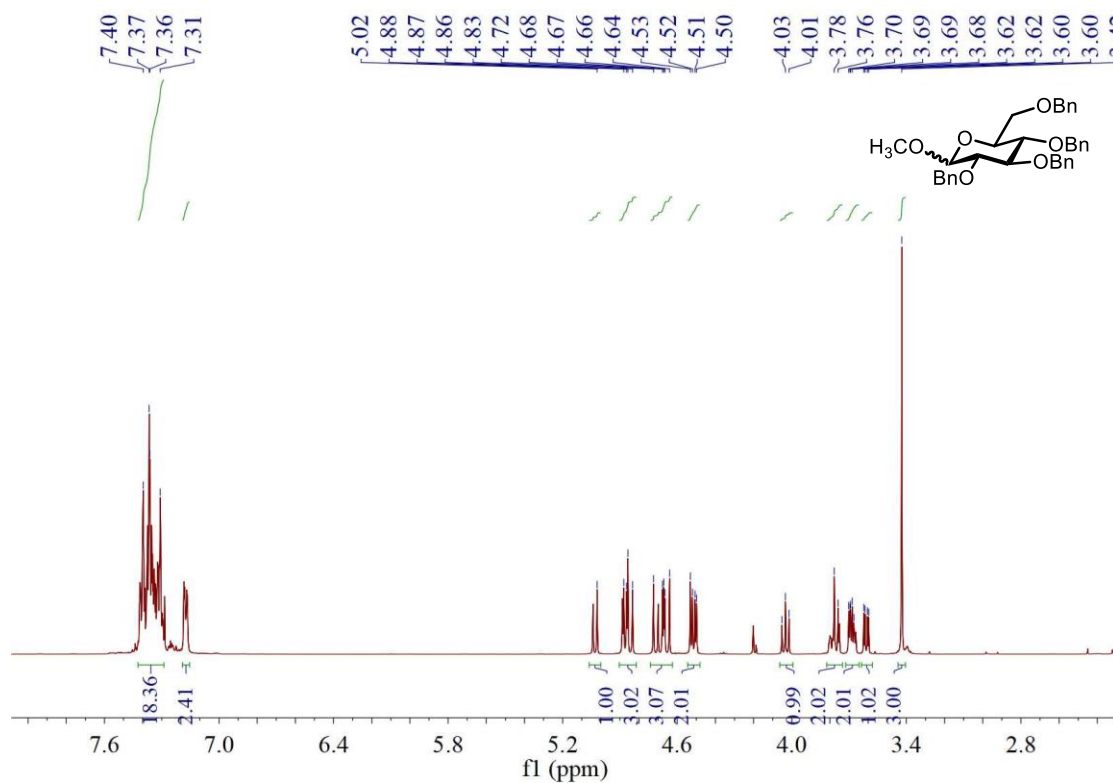
^1H NMR (500 MHz, D_2O) of **1-methoxy-L-glucose** (α -anomer : β -anomer = 1.7 : 1)



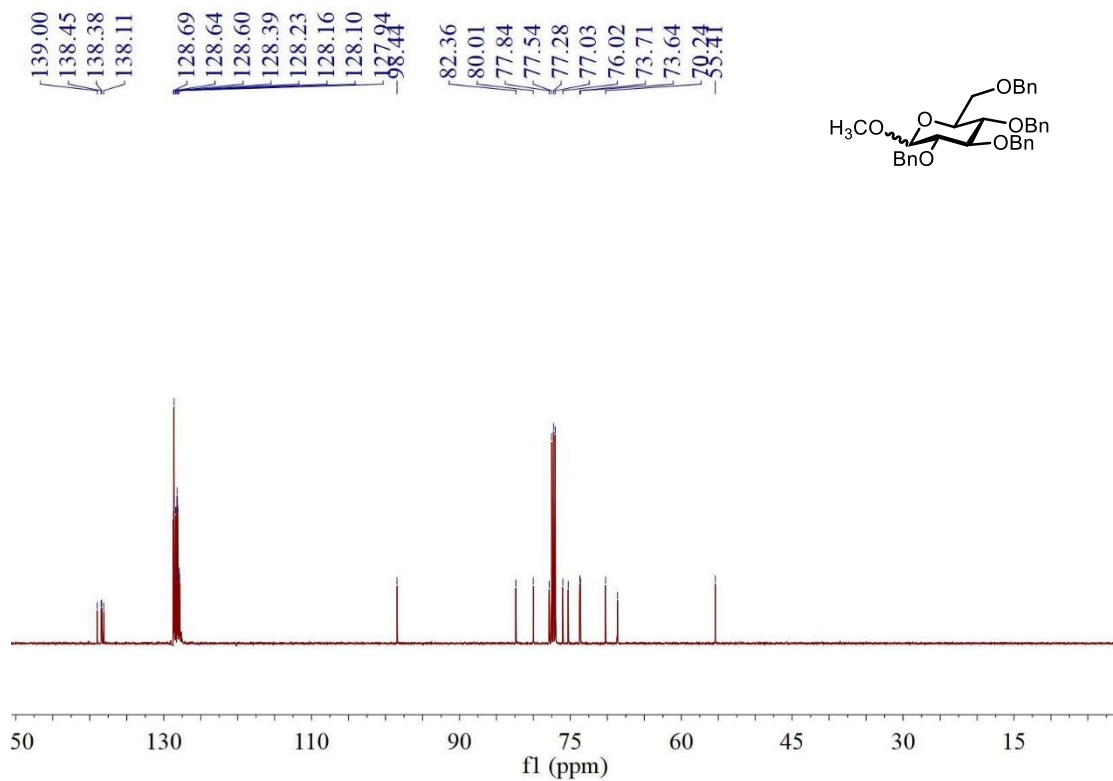
^{13}C NMR (125 MHz, D_2O) of **1-methoxy-L-glucose** (α -anomer : β -anomer = 1.7 : 1)



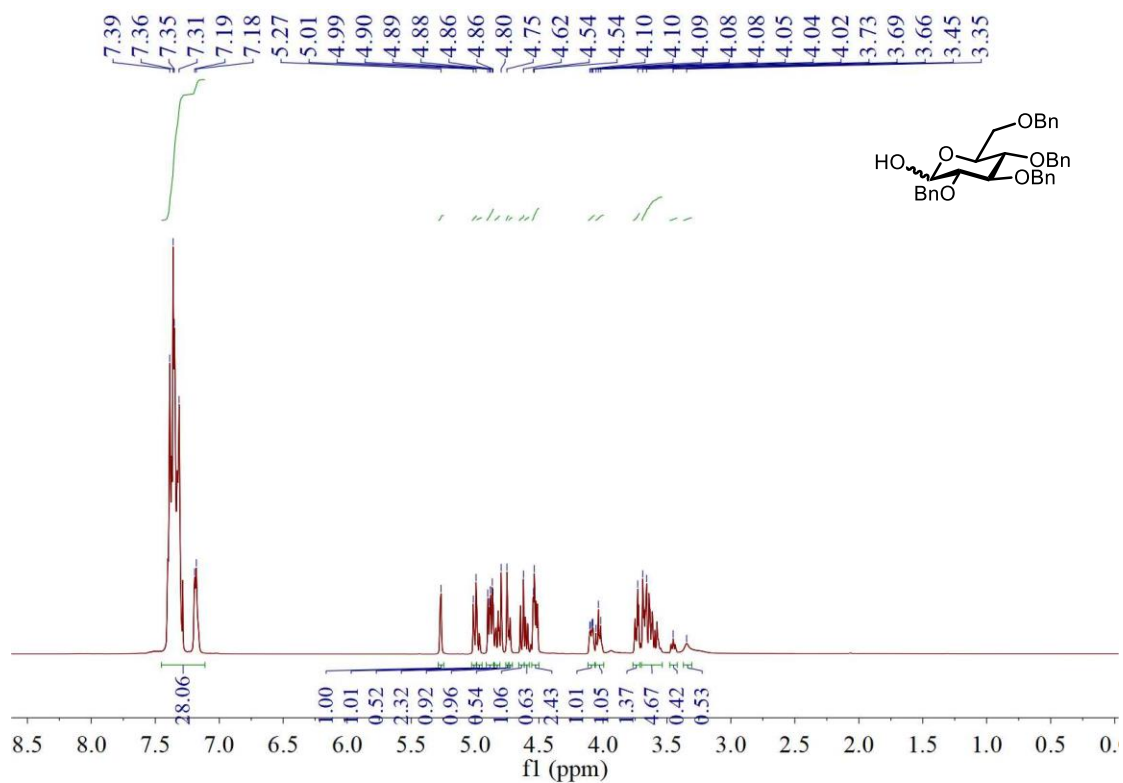
¹H NMR (500 MHz, CDCl₃) of 1-methoxy-2,3,4,6-tetra-O-benzyl-L-glucose



¹³C NMR (125 MHz, CDCl₃) of 1-methoxy-2,3,4,6-tetra-O-benzyl-L-glucose

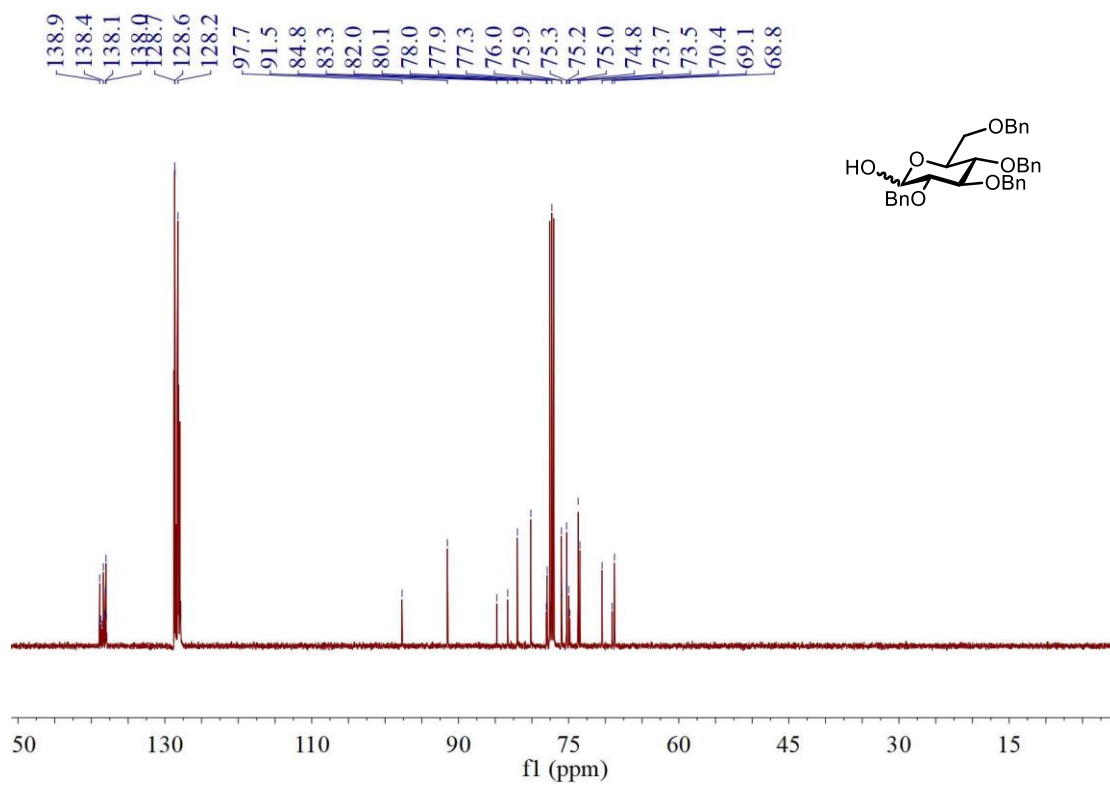


^1H NMR (500 MHz, CDCl_3) of **2,3,4,6-tetra-O-benzyl-L-glucose** (α -anomer : β -anomer = 2 : 1)

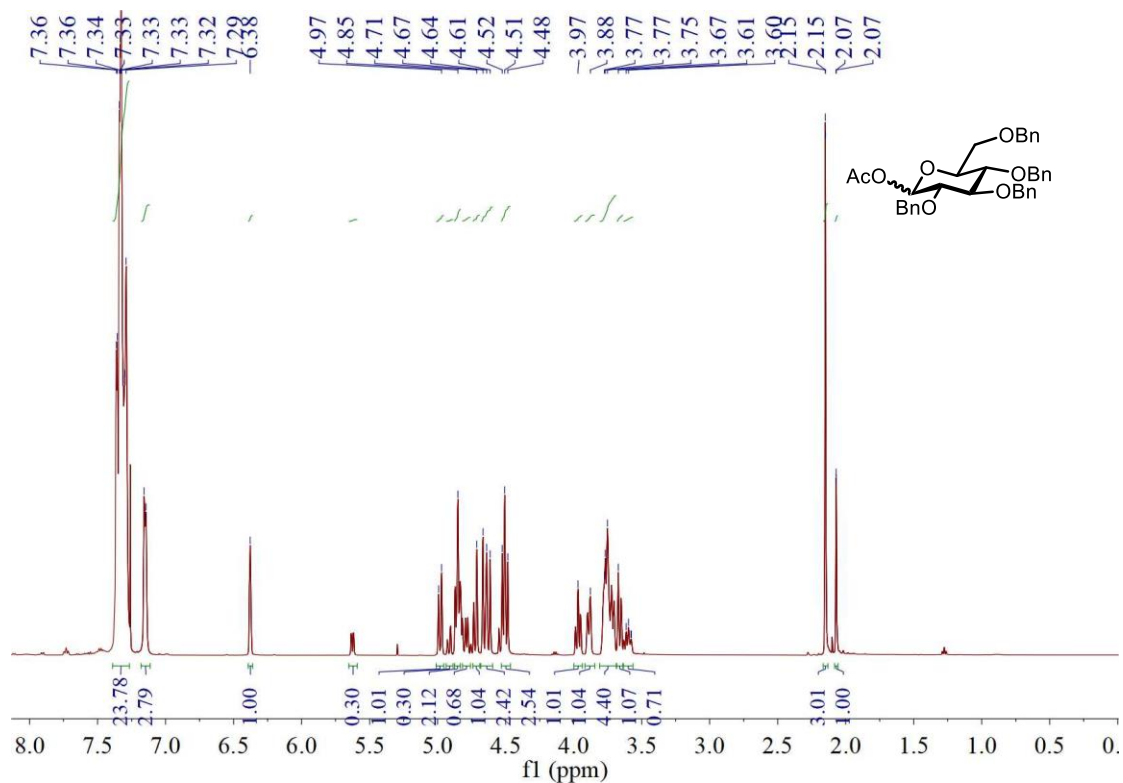


^{13}C NMR (125 MHz, CDCl_3) of **2,3,4,6-tetra-O-benzyl-L-glucose** (α -anomer : β -anomer = 2 : 1)

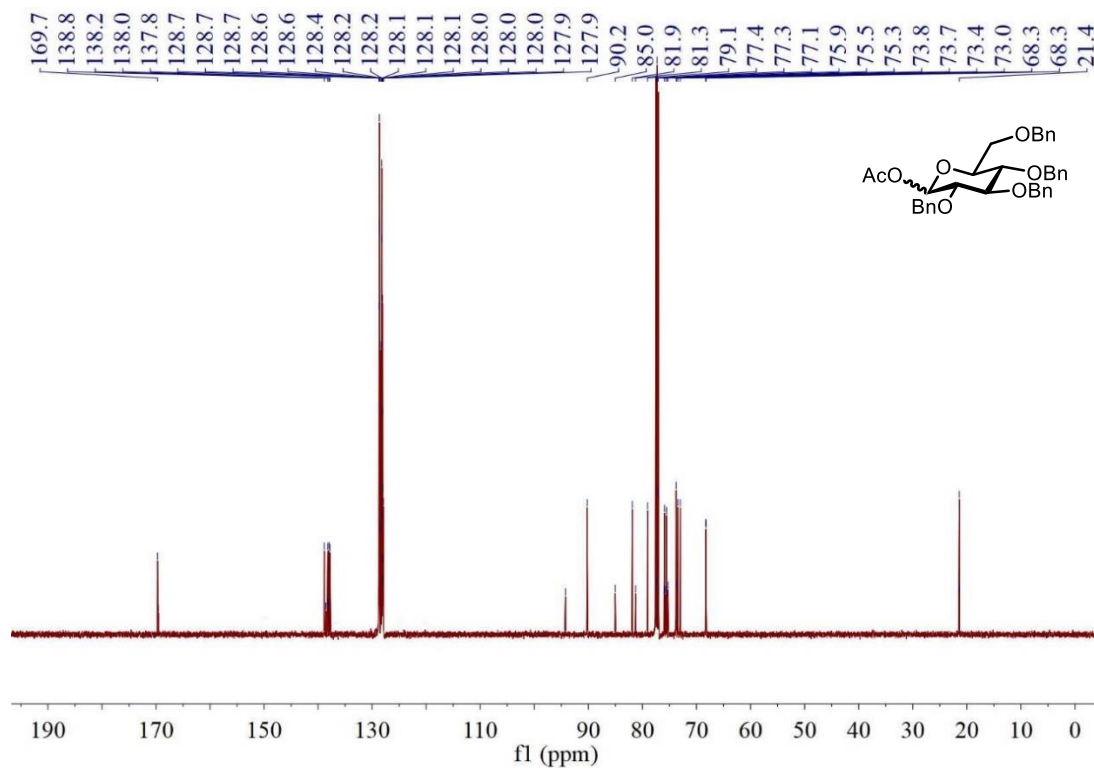
1)



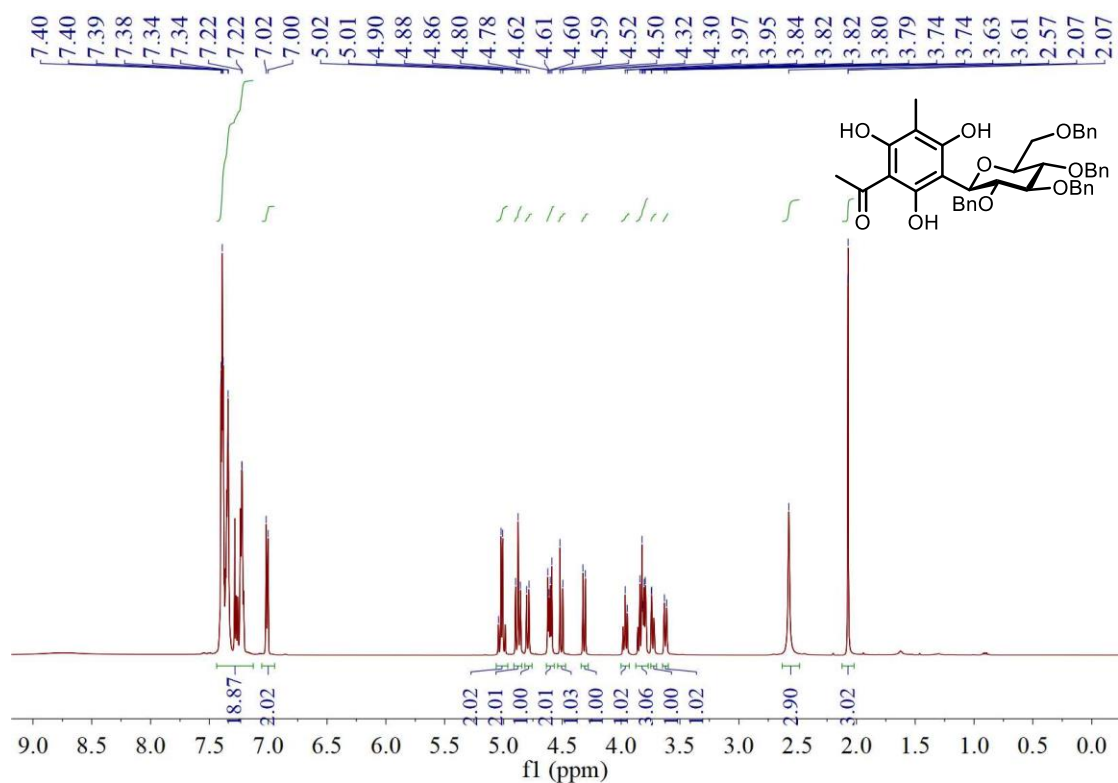
^1H NMR (500 MHz, CDCl_3) of **1-acetoxy-2,3,4,6-tetra-O-benzyl-L-glucose** (α -anomer : β -anomer = 3.3 : 1)



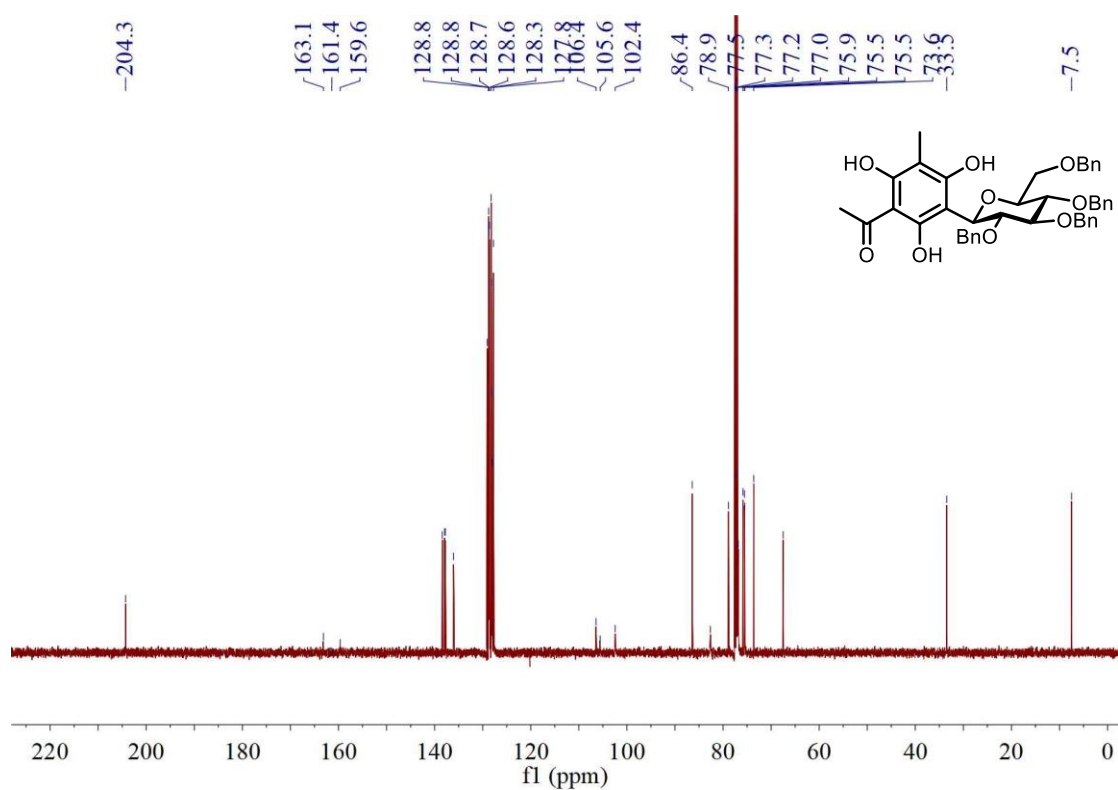
^{13}C NMR (125 MHz, CDCl_3) of **1-acetoxy-2,3,4,6-tetra-O-benzyl-L-glucose** (α -anomer : β -anomer = 3.3 : 1)



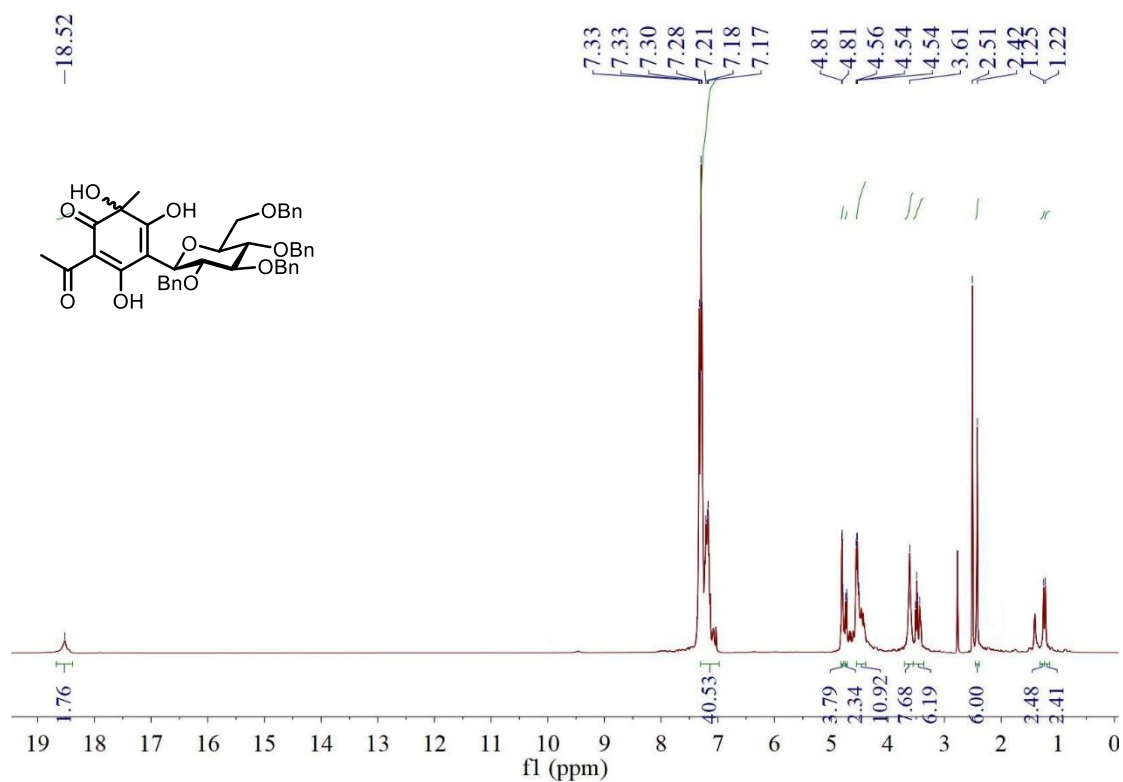
¹H NMR (500 MHz, CDCl₃) of **18-1**



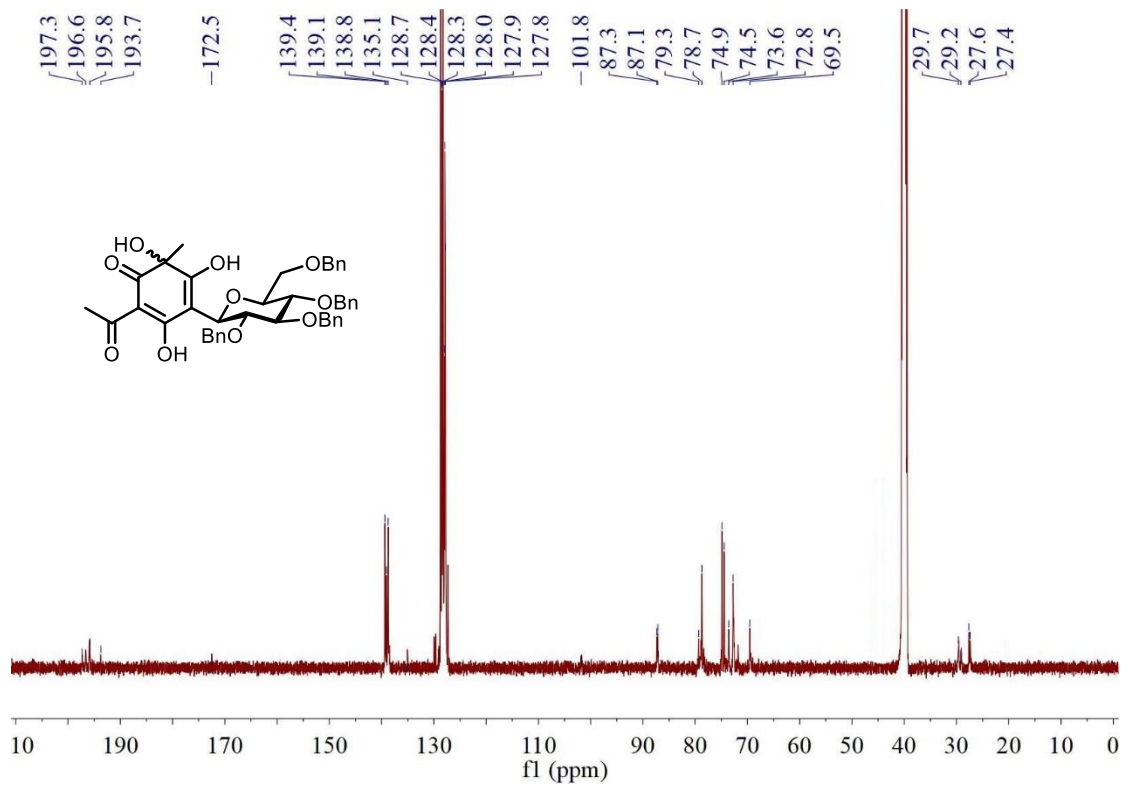
¹³C NMR (125 MHz, CDCl₃) of **18-1**



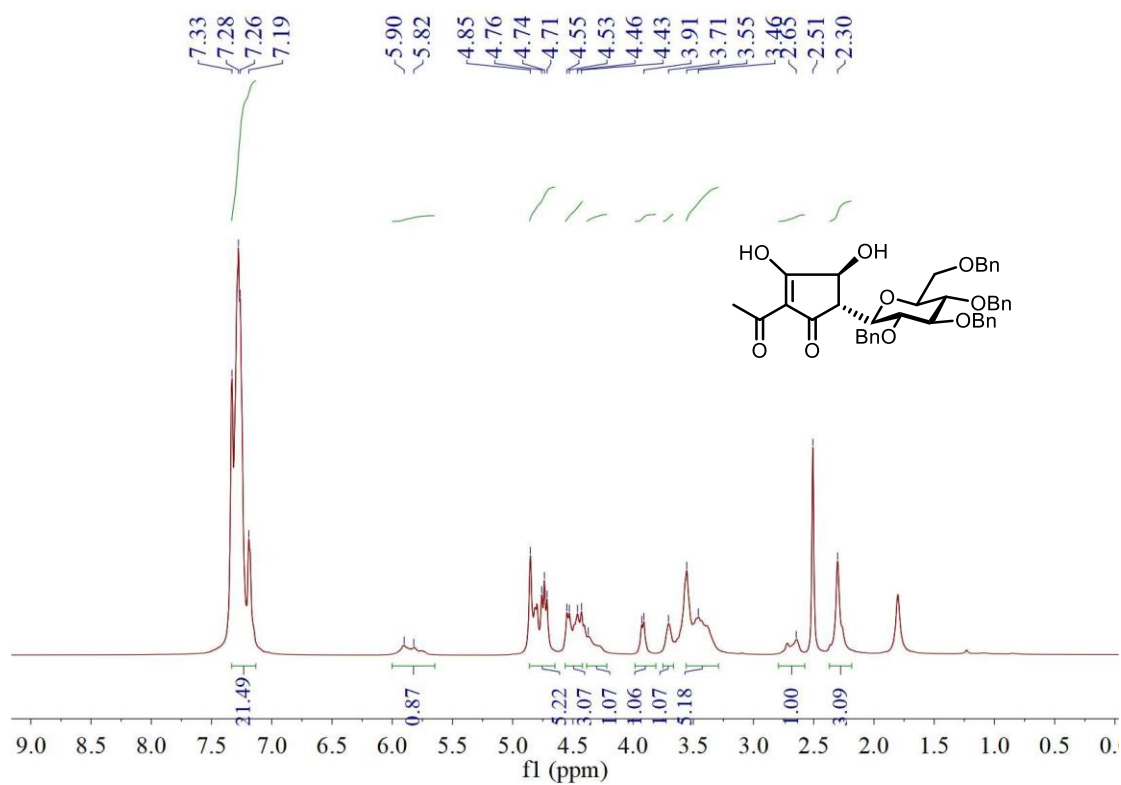
¹H NMR (500 MHz, DMSO-*d*₆) of **18**



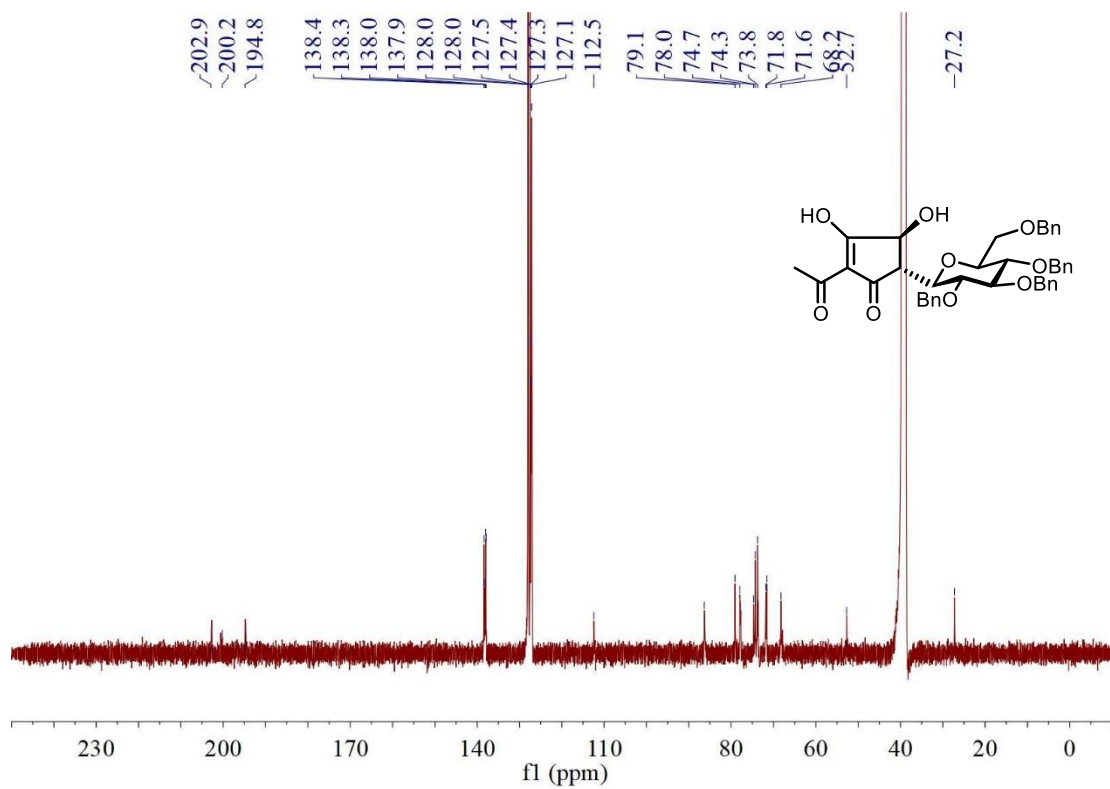
¹³C NMR (125 MHz, DMSO-*d*₆) of **18**



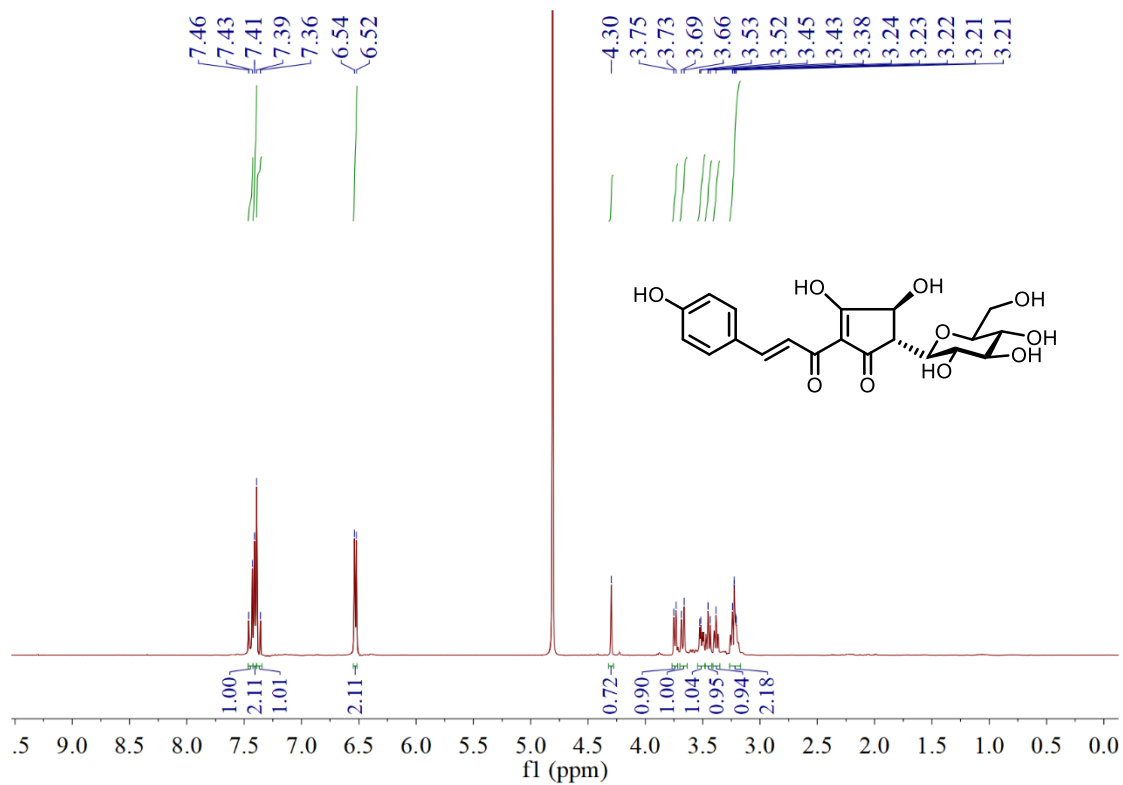
¹H NMR (500 MHz, DMSO-d₆) of **19**



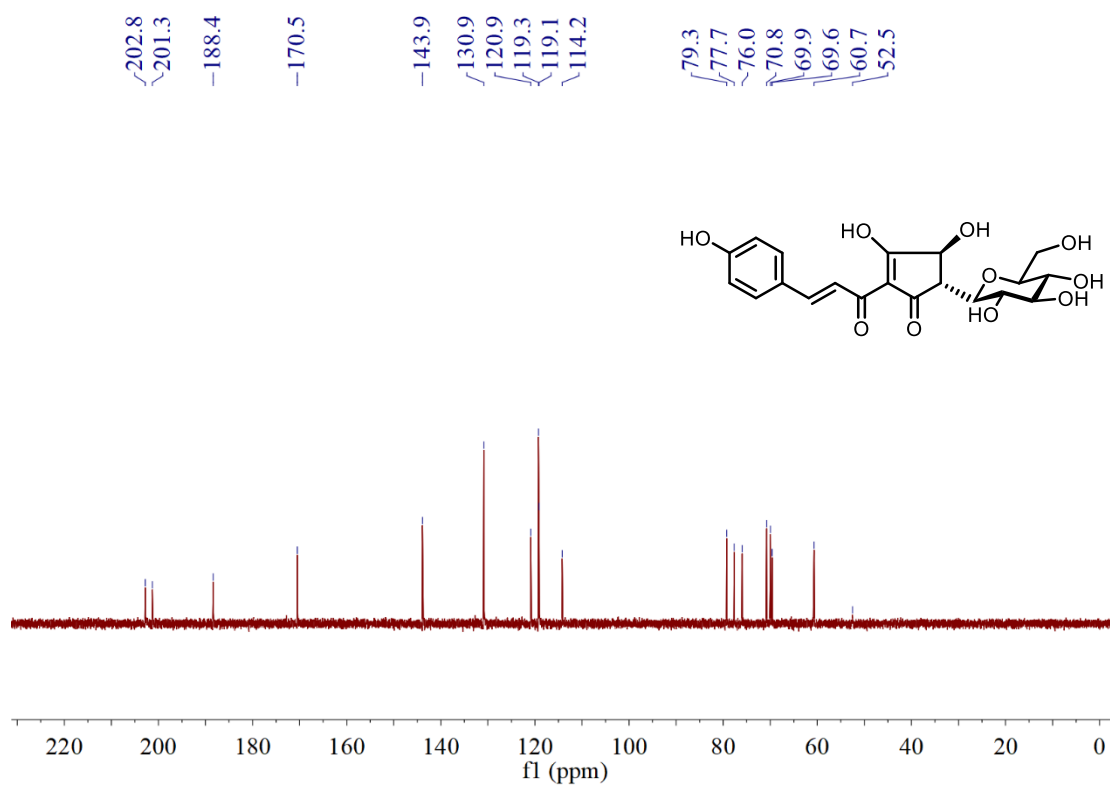
¹³C NMR (125 MHz, DMSO-d₆) of **19**



¹H NMR (500 MHz, D₂O + NaOD) of **20**

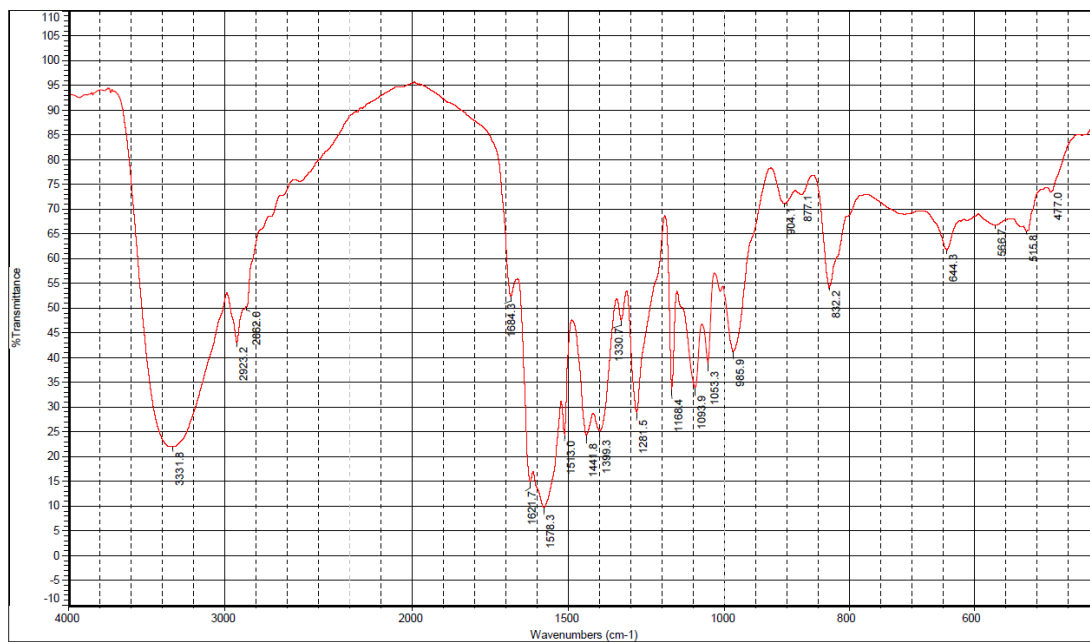


¹³C NMR (125 MHz, D₂O + NaOD) of **20**

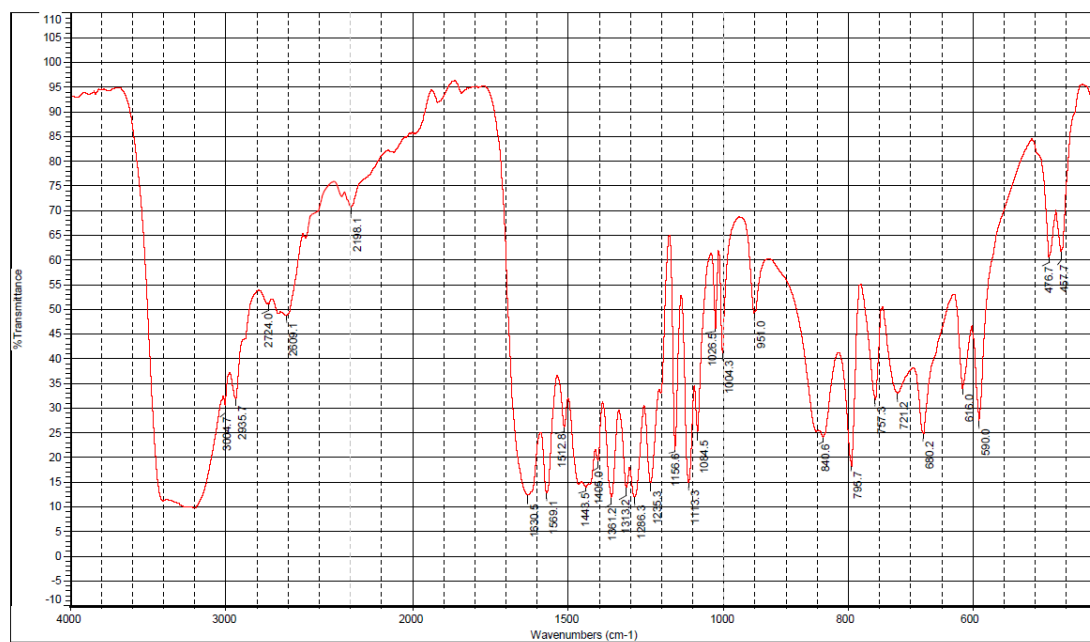


4 IR spectra

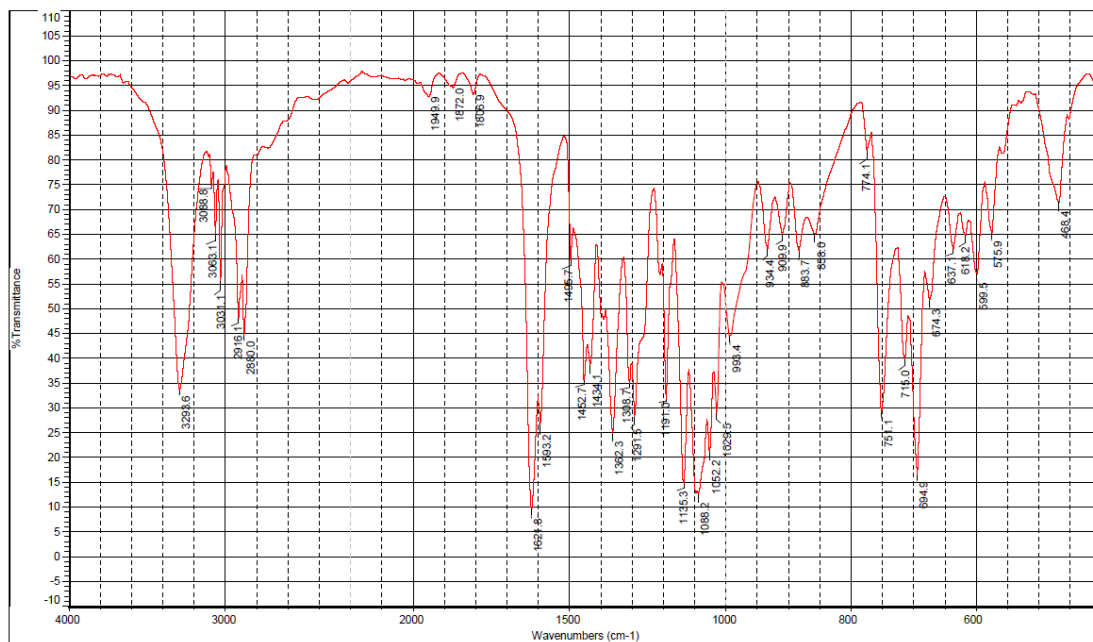
Compound 1



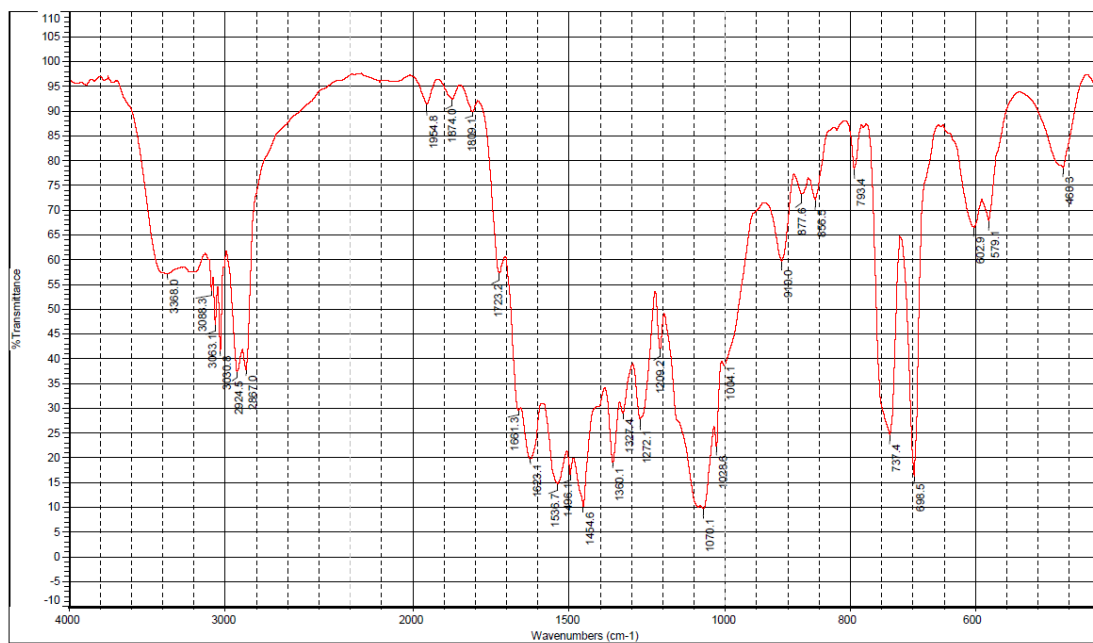
Compound 10



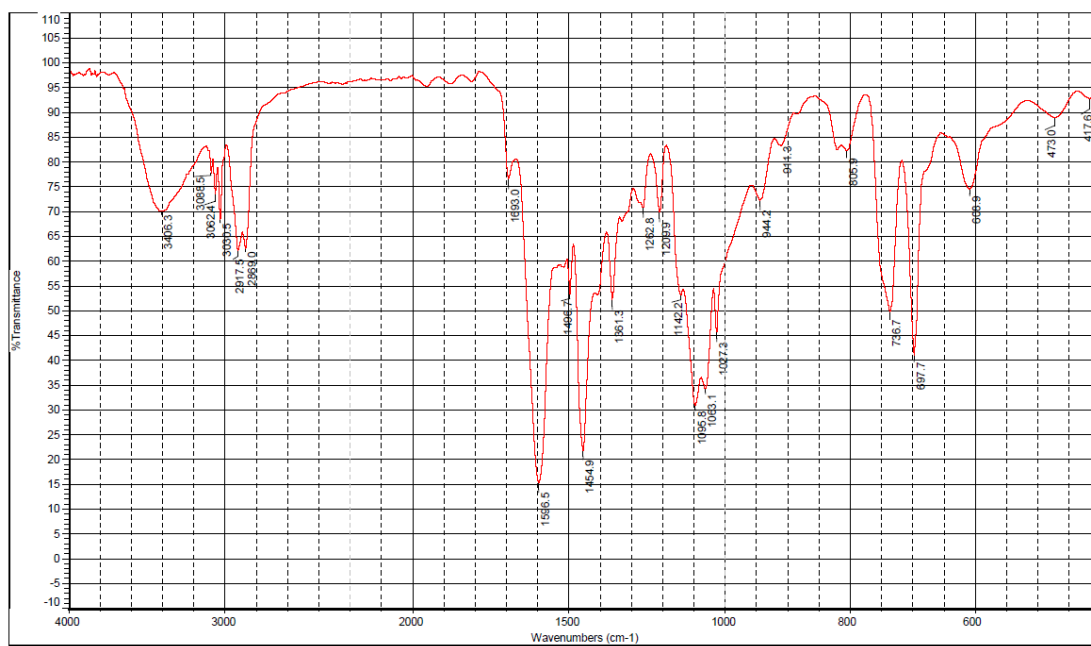
Compound 9



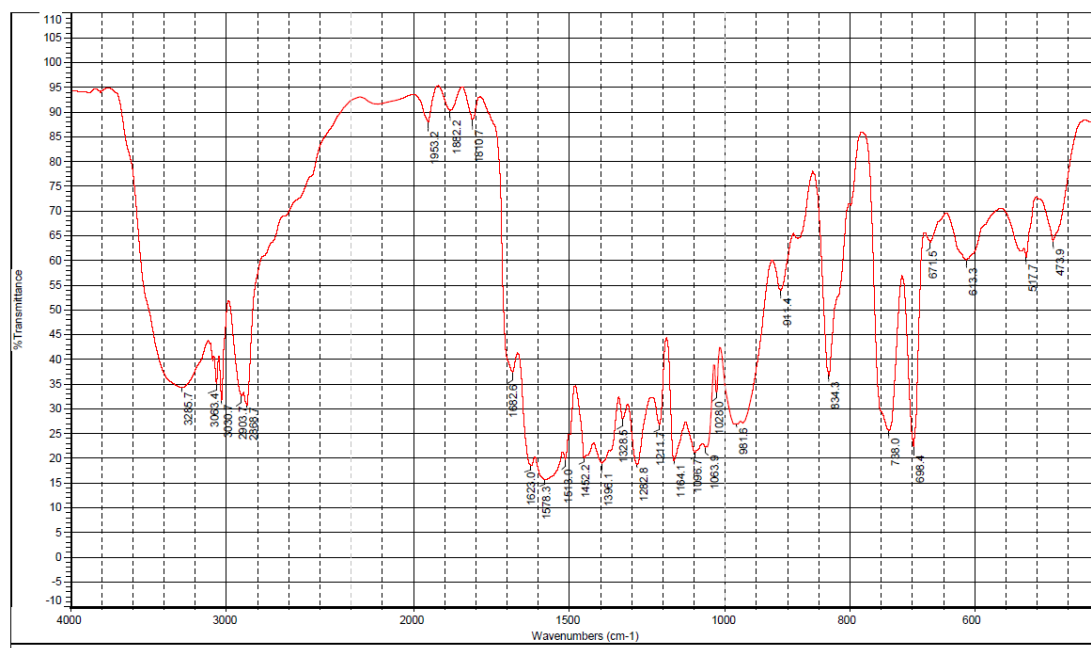
Compound 8



Compound 7



Compound 14



5 References

- [1] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, et. al., D. J. Gaussian 09, Rev. C 01; Gaussian, Inc., Wallingford CT, 2009.
- [2] P. J. Stephens, N. Harada, *Chirality*, 2010, **22**, 229–233.
- [3] T. Suzuki, M. Ishida, T. Kumazawa, S. Sato, *Carbohydr. Res.*, 2017, **448**, 52–56.
- [4] S. Sata, H. Obara, J. Onoder, A. Endo, *Bull. Chem. Soc. Jpn.*, 1992, **65**, 452–457.
- [5] T. Hayashi, K. Ohmori, K. Suzuki, *Synlett.*, 2016, **27**, 2345–2351.
- [6] A. McKillop, L. McLaren, R. J. K. Taylor, *J. Chem. Soc., Perkin Trans.*, 1994, 2047.
- [7] Y. Girard, P. Hamel, M. Therien, J. P. Springer, J. Hirshfield, *J. Org. Chem.*, 1987, **52**, 4000.
- [8] D. Magdziak, S. J. Meek, T. R. R. Pettus, *Chem. Rev.*, 2004, **104**, 1383–1429.