

# Compound Representatives of a New Type of Triterpenoid from *Aglaia odorata*

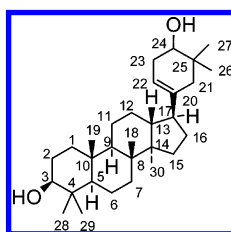
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## ABSTRACT



A novel triterpenoid, 21,25-cyclodammar-20(22)-ene-3 $\beta$ ,24 $\alpha$ -diol, has been isolated from *Aglaia odorata*. Its structure was elucidated on the basis of 1D- and 2D-NMR and MS spectra and then confirmed by X-ray diffraction. It represents a new type of natural five-membered-ring triterpenoid, named cyclodammarane. Its possible biopathway was that squalene-2,3;22,23-diepoxydiepoxide was directly cyclized to form 24,25-epoxydammar-20(21)-en-3-ol, followed by protonation of the remaining 24,25-epoxide and the cation attacking 21(20) methylene to generate the E ring.

Triterpenoids are a large diverse group of natural products derived from squalene or, in the case of 3-hydroxytriterpenoids, the 3S-isomer of squalene 2,3-epoxide. Cyclization of the chair–boat–chair–boat conformation gives the proto-stane cation, and cyclization of the chair–chair–chair–boat conformation leads to the dammarane cation, which leads to miscellaneous ring triterpenoids.<sup>1</sup> A triterpenoid with a new type of five-membered ring, which has the chair–chair–chair–boat conformation, was isolated from *Aglaia odorata*. *A. odorata* is naturally distributed in India, Malaysia, and Oceania and is cultivated as an ornamental plant.<sup>2</sup> Recently, the genus *Aglaia* of the family Meliaceae has been concentrated considerably as a possible new source for unique natural products for integrated pest management. Bisamides,

lignans, and triterpenes have been isolated from this genus in the past several decades.<sup>3</sup> Though many chemical investigations have been carried on this species,<sup>3,4</sup> we looked forward to further exploring interesting constituents during our research on Meliaceae.<sup>5</sup> From *A. odorata* cultivated in Kunming, Yunnan province, a new type of triterpenoid, 21,25-cyclodammar-20(22)-ene-3 $\beta$ ,24 $\alpha$ -diol (**1**), along with four known dammaranes, dammar-20,25-diene-3 $\beta$ ,24-diol (**2**),<sup>6</sup> dammar-20-ene-3 $\beta$ ,24(S),25-triol (**3**),<sup>4,7</sup> dammar-20-ene-3 $\beta$ ,24(R),25-triol (**4**),<sup>4,7</sup> and 24(R),25-dihydroxydammar-20-en-

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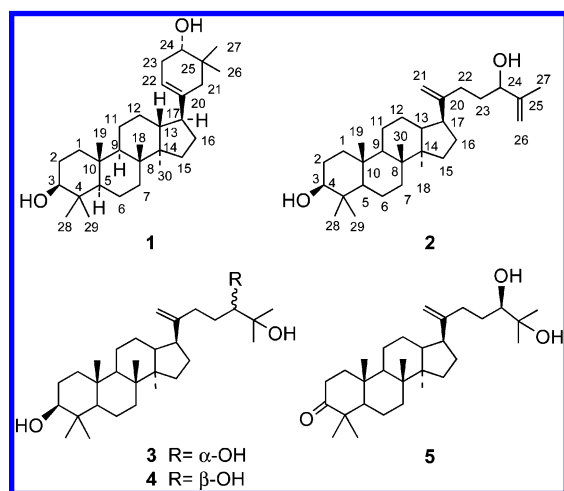


Figure 1. Structure of compounds 1–5 from *Aglaia odorata*.

3-one (5),<sup>4</sup> were isolated (Figure 1). The new structure was elucidated on the basis of 1D- and 2D-NMR and MS spectra and was further confirmed by a single-crystal X-ray analysis.

The whole plant of *A. odorata* was extracted with EtOH (15 L × 4) at room temperature (48 h × 4) to yield an EtOH extract. After the removal of EtOH in a vacuum, the viscous concentration was partitioned with EtOAc (10 L × 4) to afford EtOAc extract (310 g). The EtOAc extract was subjected to column chromatography, eluted with CHCl<sub>3</sub>–Me<sub>2</sub>CO [from CHCl<sub>3</sub> to CHCl<sub>3</sub>–Me<sub>2</sub>CO (1:1)], to give eight fractions (I–VIII). Fraction II (26 g) was loaded on chromatography column over silica gel and eluted by petroleum–Me<sub>2</sub>CO (4:1) to give compounds 1 (100 mg) and 2 (35 mg). Fraction III (30 g) was also subjected to a chromatography column over silica gel, eluted with petroleum ether–Me<sub>2</sub>CO [from (4:1) to 3:1], to give compounds 3 (25 mg), 4 (22 mg), and 5 (35 mg).

Compound 1<sup>8</sup> was found to possess a molecular formula of C<sub>30</sub>H<sub>50</sub>O<sub>2</sub> as evidenced by HREIMS at *m/z* 443.3891 [*M* + *H*]<sup>+</sup>. Its UV spectrum exhibited no conjugated group based on maximum absorption at 204 nm. The IR spectrum of 1 showed absorption bands for hydroxyl groups (3441 cm<sup>−1</sup>) and double bonds (1631 cm<sup>−1</sup>). The <sup>1</sup>H and <sup>13</sup>C NMR and DEPT spectra displayed signals for 30 carbons, seven tertiary methyl groups (δ<sub>C</sub> 28.1, 26.5, 21.5, 16.2, 15.8, 15.7, 15.4), 10 methylenes (δ<sub>C</sub> 39.2, 37.8, 35.5, 32.1, 31.5, 27.5, 27.5, 25.0, 21.4, 18.3), seven methines (δ<sub>C</sub> 116.8, 79.0, 74.2, 56.0, 51.0, 48.4, 44.4), two of which were oxymethines, and six quaternary carbons (δ<sub>C</sub> 138.9, 49.4, 40.5, 39.0, 37.4, 34.5). These data showed that 1 was similar to the dammar derivative in comparison with those of 2–5 in rings A–D with exception for the side chain attached to C-17.<sup>4,6,7</sup>

Compounds 1 and 2 have same molecular formula. The signals for two olefinic groups in 2 disappeared in 1; instead,

δ<sub>C</sub> 116.8 (d) and 138.9 (s), 34.5 (s), 21.5 (q) were present in 1, which assumed that a ring were formed at side chain in 1. In the HMBC spectrum of 1 correlations between δ<sub>H</sub> 3.19 (1H, dd, *J* = 6.0, 4.5 Hz) with δ<sub>C</sub> 15.4 (q, C-29), 28.1 (q, C-28), 39.0 (s, C-4), and 39.2 (t, C-1) placed a hydroxyl at β of C-3. The HMBC spectrum of 1 also showed correlations between δ<sub>H</sub> 3.48 (1H, dd, *J* = 6.5, 6.4 Hz) with δ<sub>C</sub> 21.5 (q, C-26), 26.4 (q, C-27), 34.5 (s, C-25), 37.8 (t, C-21), which indicated a hydroxyl connected to C-24. δ<sub>H</sub> 5.22 (brs) showed correlations with δ<sub>C</sub> 74.2 (d, C-24), 48.4 (d, C-17), and 31.2 (t, C-23) in the HMBC spectrum, which positioned the double bond at C-20/22. Large double doublet coupling constants for H-3 and H-24 suggested both protons axial location.

Compound 1 was obtained as prism crystal from CH<sub>3</sub>OH–Me<sub>2</sub>CO and subjected to X-ray diffraction. There was a hydrogen bond between CH<sub>3</sub>OH and 3β-hydroxy of 1 in the crystal (Figure 2).<sup>9</sup> Finally, 1 was determined as 21,25-

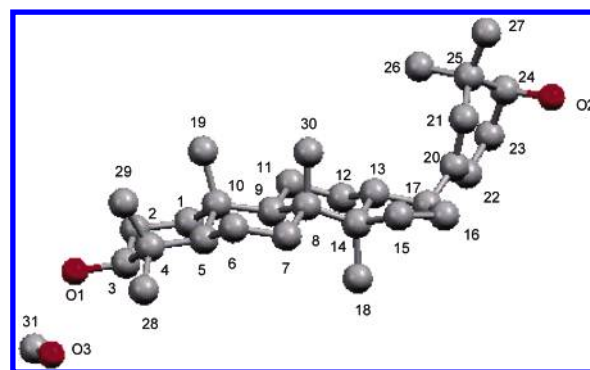


Figure 2. Crystal structure of 1.

cyclodammar-20 (22)-ene-3β,24α-diol from its X-ray diffraction. All of the signals of <sup>1</sup>H and <sup>13</sup>C NMR were assigned by HSQC, HMBC, and ROESY spectra (Table 1).

Compound 1 showed close relationship to compounds 2–5. If 1 was an artificial product derived from 2 or other relative compounds, it should be formed either by acid-catalyzed cyclization or through *ene reaction*<sup>12</sup> form dammarane skeleton during the isolation proceeding.

(9) X-ray crystal data of 1: C<sub>31</sub>H<sub>54</sub>O<sub>3</sub>, MW = 474.74; orthorhombic, space group *P*2<sub>1</sub>2<sub>1</sub>2<sub>1</sub>; *a* = 13.118(3) Å, *b* = 31.435(8) Å, *c* = 7.245(1) Å, *V* = 2987.7(13) Å<sup>3</sup>, *Z* = 4, *D*<sub>calc</sub> = 1.055 g/cm<sup>3</sup>. Mo Kα (λ = 0.71073 Å). The data were collected on a MAC DIP-2030K diffractometer, with graphite monochromator, Mo Kα radiation using a colorless crystal of dimensions of 0.58 × 0.56 × 0.24 mm<sup>3</sup>, maximum 2θ value of 50.0°, independent reflections: 3780, observed number of reflection: 3615 [|*F*|<sup>2</sup> ≥ 8σ(|*F*|<sup>2</sup>)]. The structure was solved by the direct method SHELX-86<sup>10</sup> and expanded using difference Fourier techniques, refined by the program and method NOMCSDP<sup>11</sup> and full-matrix, least-squares calculations. Hydrogen atoms were fixed at calculated positions. The final indices were *R* = 0.080, *R*<sub>w</sub> = 0.077. The CCDC deposit number is 261166. Copies of these data can be obtained, free of charge, on application to the CCDC via [www.ccdc.cam.ac.uk/contents/retrieving.html](http://www.ccdc.cam.ac.uk/contents/retrieving.html) (or Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K., fax: +44 1223 336033, e-mail: [deposit@ccdc.cam.ac.uk](mailto:deposit@ccdc.cam.ac.uk)).

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(8) Compound 1: prism crystal; mp 197–199 °C; [α]<sub>D</sub><sup>25</sup> = −70.1 (c 0.73 MeOH); UV (MeOH) λ<sub>max</sub> 204 nm (ε 7126); IR (KBr) ν<sub>max</sub> 3441, 2945, 1631 cm<sup>−1</sup>; <sup>1</sup>H and <sup>13</sup>C NMR, data see Table 1; EIMS *m/z* [*M*]<sup>+</sup> 442 (10), 424 (20), 302 (33), 247 (67), 207 (100), 189 (55), 134 (73); HRESIMS *m/z* [*M* + 1]<sup>+</sup> 443.3891 (calcd for C<sub>30</sub>H<sub>51</sub>O<sub>2</sub>, 443.3889).

**Table 1.** NMR Data and HMBC Correlations of **1** in CDCl<sub>3</sub><sup>a</sup>

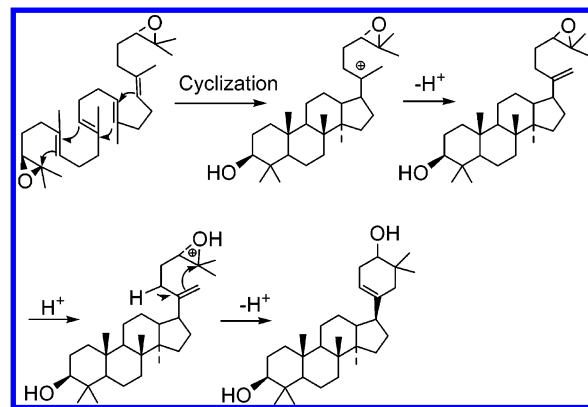
| entry       | $\delta_{\text{H}}$ (J in Hz) | $\delta_{\text{C}}$ | HMBC ( <sup>1</sup> H– <sup>13</sup> C) |
|-------------|-------------------------------|---------------------|---|
| 1           | 1.74 (2H, m)                  | 39.2 t              | 2, 3, 19                                |
| 2           | 1.60 (2H, m)                  | 27.5 t              | 3, 4, 10                                |
| 3           | 3.19 (1H, dd, 6.0, 4.5)       | 79.1 d              | 1, 4, 5, 28, 29                         |
| 4           |                               | 39.0 s              |   |
| 5           | 0.70 (d, 7.2 Hz)              | 56.0 d              | 3, 7, 19, 28, 29                        |
| 6           | 1.52 (1H, m)                  | 18.3 t              | 4, 8, 10                                |
|             | 1.45 (1H, m)                  |                     |   |
| 7           | 1.56 (1H, m)                  | 35.5 t              | 5, 9, 30                                |
|             | 1.26 (1H, m)                  |                     |   |
| 8           |                               | 40.5 s              |   |
| 9           | 1.28 (1H, m)                  | 51.0 d              | 5, 19, 30                               |
| 10          |                               | 37.4 s              |   |
| 11          | 1.51 (1H, m)                  | 21.4 t              | 8, 10, 12, 13                           |
|             | 1.19 (1H, m)                  |                     |   |
| 12          | 1.49 (1H, m)                  | 25.0 t              | 9, 13, 14, 17                           |
| 13          | 1.58 (1H, m)                  | 44.4 d              | 14, 16, 18, 20,                         |
| 14          |                               | 49.4 s              |   |
| 15          | 2.32 (1H, m)                  | 32.1 t              | 13, 17, 30                              |
|             | 1.98 (1H, m)                  |                     |   |
| 16          | 1.79 (1H, m)                  | 27.5 t              | 13, 14, 20                              |
|             | 1.36 (1H, m)                  |                     |   |
| 17          | 2.12 (1H, m)                  | 48.4 d              | 12, 13, 14, 21, 22                      |
| 18          | 0.84 (3H, s)                  | 16.2 q              | 8, 13, 14, 15                           |
| 19          | 1.24 (3H, s)                  | 15.7 q              | 1, 5, 9, 10                             |
| 20          |                               | 138.9 s             |   |
| 21          | 1.81 (1H, m)                  | 37.8 t              | 17, 22, 24, 25, 26, 27                  |
|             | 1.67 (1H, m)                  |                     |   |
| 22          | 5.22 (1H, Br. s)              | 116.8 d             | 17, 23, 24,                             |
| 23          | 1.54 (1H, m)                  | 31.5 t              | 20, 22, 24, 25                          |
|             | 1.14 (1H, m)                  |                     |   |
| 24          | 3.48 (1H, dd, 6.5, 6.4)       | 74.2 d              | 21, 22, 25, 26, 27                      |
| 25          |                               | 34.5 s              |   |
| 26          | 0.93 (3H, s)                  | 21.5 q              | 21, 24, 25, 27                          |
| 27          | 0.89 (3H, s)                  | 26.5 q              | 21, 24, 25, 26                          |
| 28 $\alpha$ | 0.96 (3H, s)                  | 28.1 q              | 3, 4, 5, 29                             |
| 29 $\beta$  | 0.77 (3H, s)                  | 15.4 q              | 3, 4, 5, 28                             |
| 30          | 0.84 (3H, s)                  | 15.8 q              | 8, 9, 14                                |

<sup>a</sup> Data were recorded in CDCl<sub>3</sub> on Bruker AM-400 MHz (<sup>13</sup>C) and Bruker DRX-500 MHz spectrometers (<sup>1</sup>H, HSQC, HMBC, ROESY); chemical shifts ( $\delta$ ) are given in parts per million with references to the most downfield signal of CDCl<sub>3</sub> ( $\delta$  7.25 ppm) for <sup>1</sup>H and to the center peak of the downfield signal of CDCl<sub>3</sub> ( $\delta$  77.0 ppm) for <sup>13</sup>C.

However, the *enophile* essential for ene reaction is absent in **2–5**. In addition, when compounds **2–5** were dissolved in CHCl<sub>3</sub>, EtOAc, EtOH, and Me<sub>2</sub>CO under acid conditions, respectively, and the solutions were mixed with silica gel

(12) For review of the ene reaction, see: (a) Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1969**, 8, 856. (b) Oppolzer, W. *Pure Appl. Chem.* **1981**, 53, 1181.

placed in a water bath at 70 °C for 5 days, no changes were observed in any of solutions monitored by HPTLC with **1** as control. Thus, **1** should be a natural product from plant secondary metabolite. Compound **1** represents a new type of natural five-membered ring triterpenoid, named cyclo-dammarane. A possible biopathway is proposed in Figure 3. The common original bisoxidosqualene (squalene-2,3;22,-

**Figure 3.** Proposed biosynthesis of **1**.

23-diepioxide) was directly cyclized and further deprotonated to form a chair–chair–chair–boat 24,25-epoxydammar-20-(21)-en-3-ol. Subsequently, protonation of the remaining 24,-25-epoxide of the intermediate and the caution attacking 21(20) methylene to generate E ring, then deprotonation to form **1**.

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**Supporting Information Available:** 1D- and 2D-NMR; HRESIMS; IR; and UV and X-ray data of **1** (CIF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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