

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

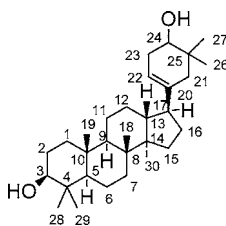
Xiang-Hai Cai,^{†‡} Xiao-Dong Luo,^{*,†} Jun Zhou,[†] and Xiao-Jiang Hao[†]

State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650204, PR China, and Graduate School of Chinese Academy of Sciences, Beijing 100039, PR China

xdluo@mail.kib.ac.cn

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ABSTRACT



A novel triterpenoid, 21,25-cyclodammar-20(22)-ene-3 β ,24 α -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-diepoxide 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.¹ 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.² 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.³ Though many chemical investigations have been carried on this species,^{3,4} we looked forward to further exploring interesting constituents during our research on Meliaceae.⁵ From *A. odorata* cultivated in Kunming, Yunnan province, a new type of triterpenoid, 21,25-cyclodammar-20(22)-ene-3 β ,24 α -diol (**1**), along with four known dammaranes, dammar-20,25-diene-3 β ,24-diol (**2**),⁶ dammar-20-ene-3 β ,24(*S*),25-triol (**3**),^{4,7} dammar-20-ene-3 β ,24(*R*),25-triol (**4**),^{4,7} and 24(*R*),25-dihydroxydammar-20-en-

* To whom correspondence should be addressed. Tel: +86-871-5223188. Fax: +86-871-5150227.

[†] Kunming Institute of Botany.

[‡] Graduate School of Chinese Academy of Sciences.

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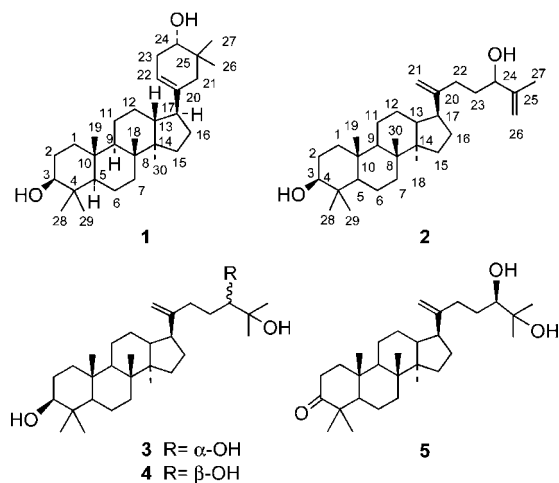


Figure 1. Structure of compounds **1–5** from *Aglaia odorata*.

3-one (**5**),⁴ 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 \times 4) at room temperature (48 h \times 4) to yield an EtOH extract. After the removal of EtOH in a vacuum, the viscous concentration was partitioned with EtOAc (10 L \times 4) to afford EtOAc extract (310 g). The EtOAc extract was subjected to column chromatography, eluted with CHCl_3 – Me_2CO [from CHCl_3 to CHCl_3 – Me_2CO (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_2CO (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_2CO [from (4:1) to 3:1], to give compounds **3** (25 mg), **4** (22 mg), and **5** (35 mg).

Compound **1**⁸ was found to possess a molecular formula of $\text{C}_{30}\text{H}_{50}\text{O}_2$ as evidenced by HREIMS at m/z 443.3891 [$\text{M} + \text{H}$]⁺. 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^{-1}) and double bonds (1631 cm^{-1}). The ^1H and ^{13}C NMR and DEPT spectra displayed signals for 30 carbons, seven tertiary methyl groups (δ_{C} 28.1, 26.5, 21.5, 16.2, 15.8, 15.7, 15.4), 10 methylenes (δ_{C} 39.2, 37.8, 35.5, 32.1, 31.5, 27.5, 27.5, 25.0, 21.4, 18.3), seven methines (δ_{C} 116.8, 79.0, 74.2, 56.0, 51.0, 48.4, 44.4), two of which were oxymethines, and six quaternary carbons (δ_{C} 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.^{4,6,7}

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

δ_{C} 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_{H} 3.19 (1H, dd, $J = 6.0, 4.5\text{ Hz}$) with δ_{C} 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_{H} 3.48 (1H, dd, $J = 6.5, 6.4\text{ Hz}$) with δ_{C} 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_{H} 5.22 (brs) showed correlations with δ_{C} 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_3OH – Me_2CO and subjected to X-ray diffraction. There was a hydrogen bond between CH_3OH and $\beta\beta$ -hydroxy of **1** in the crystal (Figure 2).⁹ Finally, **1** was determined as 21,25-

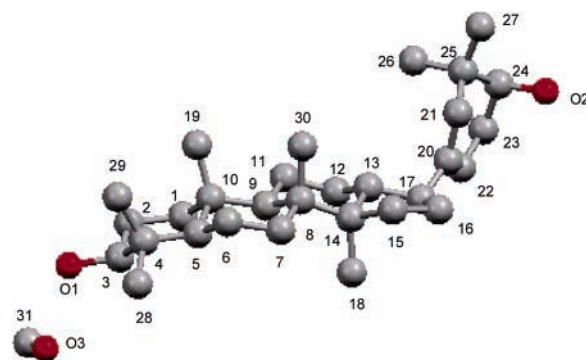


Figure 2. Crystal structure of **1**.

cyclodamar-20 (22)-ene- $3\beta,24\alpha$ -diol from its X-ray diffraction. All of the signals of ^1H and ^{13}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*¹² form dammarane skeleton during the isolation proceeding.

(9) X-ray crystal data of **1**: $\text{C}_{31}\text{H}_{54}\text{O}_3$, MW = 474.74; orthorhombic, space group $P2_12_12_1$; $a = 13.118(3)\text{ \AA}$, $b = 31.435(8)\text{ \AA}$, $c = 7.245(1)\text{ \AA}$, $V = 2987.7(13)\text{ \AA}^3$, $Z = 4$, $D_{\text{calc}} = 1.055\text{ g/cm}^3$. Mo K α ($\lambda = 0.71073\text{ \AA}$). The data were collected on a MAC DIP-2030K diffractometer, with graphite monochromator, Mo K α radiation using a colorless crystal of dimensions of $0.58 \times 0.56 \times 0.24\text{ mm}^3$, maximum 2θ value of 50.0° , independent reflections: 3780, observed number of reflection: $3615 [|F|^2 \geq 8\sigma(|F|^2)]$. The structure was solved by the direct method SHELX-86¹⁰ and expanded using difference Fourier techniques, refined by the program and method NOMCSDP¹¹ and full-matrix, least-squares calculations. Hydrogen atoms were fixed at calculated positions. The final indices were $R = 0.080$, $R_w = 0.077$. 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 (or Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K., fax: +44 1223 336033, e-mail: deposit@ccdc.cam.ac.uk).

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(8) Compound **1**: prism crystal; mp $197\text{--}199\text{ }^\circ\text{C}$; $[\alpha]_{\text{D}}^{25} = -70.1$ (c 0.73 MeOH); UV (MeOH) λ_{max} 204 nm (ϵ 7126); IR (KBr) ν_{max} 3441, 2945, 1631 cm^{-1} ; ^1H and ^{13}C NMR, data see Table 1; EIMS m/z [M]⁺ 442 (10), 424 (20), 302 (33), 247 (67), 207 (100), 189 (55), 134 (73); HRESIMS m/z [$\text{M} + 1$]⁺ 443.3891 (calcd for $\text{C}_{30}\text{H}_{51}\text{O}_2$, 443.3889).

Table 1. NMR Data and HMBC Correlations of **1** in CDCl₃^a

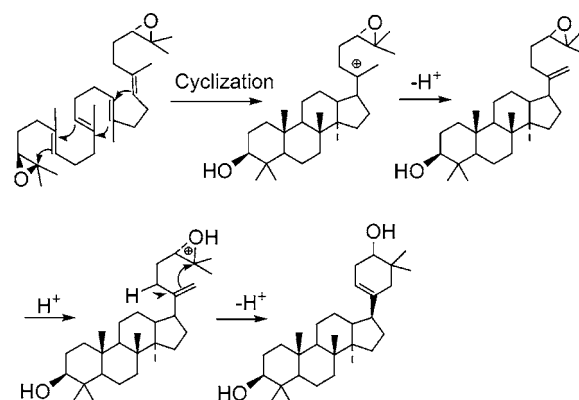
entry	δ_{H} (J in Hz)	δ_{C}	HMBC (¹ H– ¹³ C)
1	1.74 (2H, m)	39.2 t	2, 3, 19
2	1.60 (2H, m)	27.5 t	3, 4, 10
3	3.19 (1H, dd, 6.0, 4.5)	79.1 d	1, 4, 5, 28, 29
4		39.0 s	
5	0.70 (d, 7.2 Hz)	56.0 d	3, 7, 19, 28, 29
6	1.52 (1H, m)	18.3 t	4, 8, 10
	1.45 (1H, m)		
7	1.56 (1H, m)	35.5 t	5, 9, 30
	1.26 (1H, m)		
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 α	0.96 (3H, s)	28.1 q	3, 4, 5, 29
29 β	0.77 (3H, s)	15.4 q	3, 4, 5, 28
30	0.84 (3H, s)	15.8 q	8, 9, 14

^a Data were recorded in CDCl₃ on Bruker AM-400 MHz (¹³C) and Bruker DRX-500 MHz spectrometers (¹H, HSQC, HMBC, ROESY); chemical shifts (δ) are given in parts per million with references to the most downfield signal of CDCl₃ (δ 7.25 ppm) for ¹H and to the center peak of the downfield signal of CDCl₃ (δ 77.0 ppm) for ¹³C.

However, the *enophile* essential for ene reaction is absent in **2–5**. In addition, when compounds **2–5** were dissolved in CHCl₃, EtOAc, EtOH, and Me₂CO 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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