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CYCLOARTANE TRITERPENES FROM THE LEAVES OF *AGLAIA HARMSIANA*

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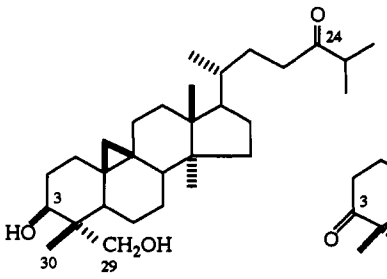
ABSTRACT.—A new cycloartane-type triterpene has been isolated from the leaves of *Aglaia harmsiana* and the structure was determined as cycloartane-3β,29-diol-24-one [**1**] on the basis of chemical and spectral evidence. In addition, (24*R*)-cycloartane-24,25-diol-3-one [**2**] was isolated in a pure state for the first time.

In a continuation of our phytochemical studies on the constituents of plants of the Meliaceae (1), we have now obtained two cycloartane-type triterpenes, **1** and **2**, from the leaves of *Aglaia harmsiana* Perkins (Meliaceae). In the present paper, the structural determination of these compounds is described. After cc and hplc separations of the EtOAc-soluble part of an EtOH extract, compounds **1** and **2** were isolated, together with a known amide compound, odorine (2,3).

Compound **1** had a molecular formula of $C_{30}H_{50}O_3$ (M^+ 458.3768, calcd 458.3760) as indicated by hreims data, and showed a strong absorption at 1700 cm^{-1} (ketone) in the ir spectrum. The ^1H-nmr spectrum of **1**, analyzed with the aid of 2D nmr studies (COSY and NOESY), indicated the presence of three tertiary methyl groups (δ 0.89, 0.94, and 0.96), three secondary methyl groups [δ 0.86, d, J=6.6 Hz and 1.09, 6H, d, J=6.8 Hz], and doublets at δ 0.38 (J=4.2 Hz) and 0.59 (J=4.2 Hz), characteristic of nonequivalent protons of a cyclopropyl methylene group. In addition, signals due to a methine proton geminal to a hydroxyl group (δ 3.75, dd, J=10.5 and 4.5 Hz) and methylene protons geminal to a hydroxyl group (δ 3.52 and 3.73, 2H, ABq, J=10.7 Hz) were detected. In the mass spectrum, compound **1** exhibited important fragments at *m/z* 331, 313, 302, 127, and 71, which are characteristic fragmentation patterns of 9,19-cycloartane-type triterpenes with one carbonyl in the side-chain and two hydroxyls in the A and B rings (4–6). Further, the prominent fragment at *m/z* 71.0506 (C_4H_7O, base peak) was ascribable to the ion $[(Me)_2CHC{=}O]^+$, indicating the presence of a carbonyl function at C-24. Based on this evi-



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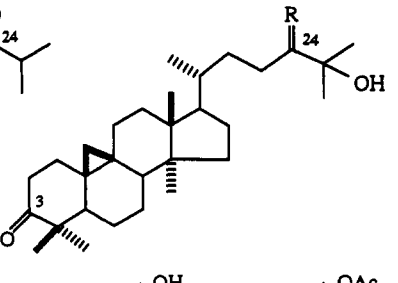

2 R= OH, H **2a** R= OAc, H

3 R= OH, H

dence, **1** is a cycloartan-24-one derivative bearing one primary hydroxyl group and one secondary hydroxyl group in the A and B rings. The ^{13}C-nmr data (Table 1) analyzed with the aid of HETCOR and HMBC experiments confirmed the structure. Accordingly, compound **1** showed prominent cross-peaks in the HMBC spectrum between the secondary methyl protons (δ 1.09, 6H, d) and the C-24 ketone (δ 215.5), and between a methine proton geminal to a hydroxyl group (δ 3.75) and a hydroxymethylene carbon (δ 71.1). On the basis of the interpretation of the ^{1}H- and ^{13}C-nmr data, as well as on biogenetic grounds, the secondary and primary hydroxyl groups of **1** were located at C-3β and C-29 or C-30, respectively. To establish the position of the primary hydroxyl at C-29 or C-30, a comparison of carbon resonances of compound **1** and cycloartene-3β,29-diol (7) and cycloartane-3β,30-diol (8) was made. This comparison revealed that the C-29 and C-30 resonances of **1** (δ 71.1 and 10.1, respectively) as well as the ring-A and -B carbon resonances were in close agreement with those of cycloartene-3β-29-diol (δ 70.5 and 10.2) and were different from those of cycloartane-3β,30-diol (δ 63.1 and 22.0). Hence, the hydroxymethylene group in **1** was assigned to C-29 in an α-equatorial orientation. Thus, the structure of the compound is as shown in **1**.

Compound **2** had a molecular formula of $C_{30}H_{50}O_3$ (M^+ 458.3750, calcd 458.3760) from hreims data and showed a strong absorption at 1685 cm^{-1} (6-membered ketone) in the ir spectrum. Acetylation of compound **2** with $(Ac)_2O$ and pyridine at room temperature afforded the monoacetate **2a**, which still showed a hydroxyl absorption (3550 and 3450 cm^{-1}) in the ir spectrum. The ^{1}H-nmr spectrum of **2**, analyzed with the aid of 2D nmr studies, indicated the presence of a methine proton geminal to a hydroxy group (δ 3.30, dd, J=10.1 and 2.1 Hz), a cyclopropyl methylene group [δ 0.57 (d, J=4.0 Hz) and 0.80 (d, J=4.0 Hz)], a secondary methyl group (δ 0.90, d, J=6.4 Hz), and six tertiary methyl groups. Among the tertiary methyl groups, two appeared at lower field (δ 1.17 and 1.22). The mass spectrum of **2** showed a molecular ion at *m/z* 458 and the corresponding ions due to loss of H_2O at *m/z* 440 and 422. Ions at *m/z* 313, 175, and 95 represent characteristic fragments of 9,19-cycloartane-type triterpenes with one carbonyl in the A and B rings and two hydroxyl groups in the side-chain (4–6).

TABLE 1. ^{13}C-Nmr Data (δ values) for Compounds **1**, **2** (100.5 MHz), and **3** in $CDCl_3$.

Position	Compound			Position	Compound		
	1	**2**	**3**[a]		**1**	**2**	**3**[a]
1	31.7	33.6	33.5	16	26.4	26.8	26.7
2	30.2	37.5	37.4	17	52.3	52.4	52.4, 52.3
3	77.0	216.6	216.4	18	18.0	18.1	18.1
4	43.7	50.3	50.1	19	30.0	29.6	29.5
5	42.5	48.5	48.4	20	35.8	36.4	36.3, 35.8
6	21.0	21.5	21.4	21	18.4	18.5	18.4, 18.1
7	28.1	28.1	28.1	22	32.9	33.4	33.3, 33.1
8	47.9	47.9	47.8	23	37.6	28.8	28.7, 28.3
9	19.9	21.1	21.0	24	215.5	79.6	79.5, 78.7
10	25.7	26.0	25.9	25	40.9	73.2	73.7
11	25.4	25.9	25.8	26	18.3	23.3	23.2
12	35.6	35.6	35.5	27	18.1	26.6	26.5
13	45.3	45.4	45.3	28	19.3	19.3	19.3
14	48.8	48.8	48.7	29	71.1	22.2	22.1
15	32.9	32.8	32.8	30	10.1	20.8	20.7

[a]Nmr data at 75 MHz (9).

In addition, the ^{13}C-nmr data of **2** (Table 1), analyzed with the aid of a HETCOR experiment, exhibited signals due to a ketone (δ 216.6), and one tertiary and one quaternary carbon bearing a hydroxyl group (δ 79.6 and 73.2, respectively). The above spectral data are very similar to those of a C-24-epimeric mixture of cycloartane-24,25-diol-3-one [**3**] (9) isolated from *Artocarpus heterophyllus* Lam. (Moraceae). In the ^{13}C-nmr spectrum of **3** (Table 1), however, certain carbon signals in the side-chain moiety showed doubling due to the presence of a C-24-epimeric mixture. In **2** (and also **2a**), these carbons showed no double signals. Hence, compound **2** is either the 24*R*- or the 24*S*-stereomer of **3**. Recently, the differentiation of 24*R*- and 24*S*-stereomers of cycloartane-type triterpenes using ^{13}C-nmr techniques has been reported (10). The chemical shifts of the side-chain carbons and C-17 of **2** are essentially the same as those of (24*R*)-cycloartane-3β,24,25-triol and are different from those of the 24*S* isomer. Based on all the above evidence, the structure of the compound is (24*R*)-cycloartane-24,25-diol-3-one as represented by **2**. Although a 24-epimeric mixture of **2** (=**3**) has already been reported (9), this is the first instance of the isolation and identification of (24*R*)-cycloartane-24,25-diol-3-one [**2**] in a pure state.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—All mps were determined on a Yanagomoto micro-melting point apparatus and are uncorrected. Optical rotations were measured for solutions in $CHCl_3$ on a Jasco DIP-140 digital polarimeter. Ir spectra were run using a Jasco A-302 instrument. ^{1}H- and ^{13}C-nmr spectra were recorded with a JEOL-GSX 400 spectrometer (400 and 100.5 MHz, respectively) in $CDCl_3$. The eims and hreims were recorded on a JEOL JMS DX-300 mass spectrometer.

PLANT MATERIAL.—Leaves of *Aglaia harmsiana* were collected at the Herbarium Bogoriense, Java, Indonesia, in 1993, and voucher specimens have been deposited in the herbarium of the Faculty of Pharmaceutical Sciences, Setsunan University.

EXTRACTION AND ISOLATION.—The dried and crushed leaves (700 g) were extracted with EtOH (10 liters×3) and the solvent was removed *in vacuo*. The EtOH extract (30.2 g) was suspended in H_2O (600 ml) and the aqueous suspension was extracted with EtOAc (300 ml×3) and *n*-BuOH (300 ml×3), successively. The EtOAc extract (25 g) was chromatographed on Si gel and the fractions were further purified by hplc to afford **1** (150 mg), **2** (140 mg), and an amide (70 mg). The amide [mp 215–217° (Me_2CO/hexane); $[\alpha]^{20}D$ +38.8° (*c*=0.52)] was determined to be odorine (2,3) by means of spectroscopic analysis.

Cycloartane-3β,29-diol-24-one [**1**].—Mp 137–139° (EtOH/hexane); $[\alpha]^{20}D$ +46.2° (*c*=0.50); ir ν max (KBr) 3350 (OH), 2900, 1700 (ketone), 1450, 1370, 1100, 1030 cm^{-1}; eims and hreims *m/z* 458.3768 (M^+, calcd for $C_{30}H_{50}O_3$, 458.3760, 4), 440 (15), 422 (76), 407 (43), 331 (4), 313 (12), 302.2601 (calcd for $C_{21}H_{34}O$, 302.2609, 27), 201 (51), 127.1115 (calcd for $C_8H_{15}O$, 127.1122, 62), 95 (69), 71.0506 (calcd for C_4H_7O, 71.0497, 100); ^{1}H nmr δ 3.75 (1H, dd, *J*=10.5 and 4.5 Hz, H-3α), 3.73, 3.52 (2H, ABq, *J*=10.7 Hz, H_2-29), 2.61 (1H, septet, *J*=6.8 Hz, H-25), 1.09 (6H, d, *J*=6.8 Hz, Me-26 and Me-27), 0.96, 0.94, 0.89 (3H each, s, 3×tertiary methyls), 0.86 (3H, d, *J*=6.6 Hz, Me-21), 0.59 (1H, d, *J*=4.2 Hz), and 0.38 (1H, d, *J*=4.2 Hz) (H_2-19); ^{13}C-nmr data, see Table 1.

(24R)-Cycloartane-24,25-diol-3-one [**2**].—Mp 150–152° (EtOH/hexane); $[\alpha]^{20}D$ +13.1° (*c*=1.09); ir ν max (KBr) 3470 (OH), 2920, 1685 (6-membered ketone), 1460, 1370, 1275, 1120, 1065 cm^{-1}; eims and hreims *m/z* 458.3750 (M^+, calcd for $C_{30}H_{50}O_3$ 458.3760, 12), 440 (23), 422 (23), 313 (86), 175 (50), 95 (100); ^{1}H nmr δ 3.30 (1H, dd, *J*=10.1 and 2.1 Hz, H-24α), 1.22, 1.17 (3H each, s, Me-26 and Me-27), 1.10, 1.05, 1.00, 0.91 (3H each, s, 4×tertiary methyls), 0.90 (3H, d, *J*=6.4 Hz, Me-21), 0.80 (1H, d, *J*=4.0 Hz), and 0.57 (1H, d, *J*=4.0 Hz) (H_2-19); ^{13}C-nmr data, see Table 1.

ACETYLATION OF **2**.—Compound **2** (20 mg) was acetylated with (Ac_2O) (1.5 ml)-pyridine (3 ml) at room temperature overnight. The reaction mixture was worked up in the usual manner to yield a residue (21 mg) which was recrystallized from MeOH to yield **2a** (13 mg): mp 148–150° (MeOH); $[\alpha]^{20}D$ +20.9° (*c*=0.52); ir ν max ($CHCl_3$) 3550, 3450 (OH), 2900, 2850, 1715 (ester), 1690 (6-membered ketone), 1460, 1365, 1235, 1105, 1020 cm^{-1}; eims and hreims *m/z* 500.3870 (M^+, calcd for $C_{32}H_{52}O_4$, 500.3866, 15), 482 (9), 440 (13), 422 (18), 313 (87), 175 (47), 95 (100); ^{1}H nmr δ 4.75 (1H, dd, *J*=10.1 and 2.6 Hz, H-24α), 2.11 (3H, s, OAc), 1.21, 1.20 (3H each, s, Me-26 and Me-27), 1.10, 1.05, 0.99, 0.90 (3H each, s, 4×tertiary methyls), 0.88 (3H, d, *J*=7.1 Hz, Me-

21), 0.79 (1H, d, J=4.2 Hz), 0.57 (1H, d, J=4.2 Hz) (H_2-19); ^{13}C nmr δ 33.4 (C-1), 37.5 (C-2), 216.5 (C-3), 50.3 (C-4), 48.5 (C-5), 21.5 (C-6), 28.1 (C-7), 47.9 (C-8), 21.1 (C-9), 26.0 (C-10), 25.9 (C-11), 35.6 (C-12), 45.4 (C-13), 48.8 (C-14), 32.8 (C-15), 26.8 (C-16), 52.2 (C-17), 18.1 (C-18), 29.6 (C-19), 36.3 (C-20), 18.4 (C-21), 32.8 (C-22), 26.5 (C-23), 80.9 (C-24), 72.5 (C-25), 25.1 (C-26), 26.8 (C-27), 19.3 (C-28), 22.2 (C-29), 20.8 (C-30), 171.3 (OC*O*CH_3), 21.1 ($OCOCH_3$).

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