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CYCLOARTANE TRITERPENOIDS FROM *AGLAIA HARMSIANA*

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Key Word Index—*Aglaia harmsiana*; Meliaceae; leaves; triterpenoids; cycloartanes.

Abstract—Two new and two known cycloartane-type triterpenoids were isolated from the leaves of *Aglaia harmsiana*. The structures were determined using ^{1}H, ^{13}C and 2D NMR techniques. © 1997 Elsevier Science Ltd

INTRODUCTION

We recently reported on the isolation of two cycloartane-type triterpenoids (**1**, **2**) from the leaves of *Aglaia harmsiana* Perkins [1]. We have now obtained additional two cycloartane-type triterpenoids (**3**, **4**) together with cycloartenol and (24*R*)-cycloartane-3β,24,25-triol (**5**) [2] from the same source. This paper deals with the structural elucidations of these compounds.

RESULTS AND DISCUSSION

After repeated column chromatography and HPLC separations of the EtOAc-soluble part of an EtOH extract, two cycloartane-type triterpenoids (**3**, **4**), were obtained together with compounds **1** and **2** [1], cycloartenol, and (24*R*)-cycloartane-3β,24,25-triol (**5**) [2]. Compound **3** was assigned to the molecular formula $C_{30}H_{52}O_4$ (HR EI-MS) and had IR absorptions at 3450 cm^{-1} due to hydroxyl group. The ^{1}H NMR spectrum of **3**, analysed with the aid of COSY and NOESY, showed the presence of five tertiary methyls, a secondary methyl (δ 1.02, *d*, J = 6.5 Hz), and doublets at δ 0.37 and 0.62 (1H each, J = 4.0 Hz), characteristic of non-equivalent protons of a cyclopropyl methylene group. In addition, signals due to two methine protons geminal to a hydroxyl (δ 3.73, *dd*, J = 10.3, 1.4 Hz and 4.31, *dd*, J = 11.7, 4.4 Hz) and methylene protons geminal to a hydroxyl (δ 3.79 and 4.24, 2H, *ABq*, J = 10.5 Hz) were observed. The ^{13}C NMR spectrum showed 30 carbons. The multiplicities of each carbon were determined by CH-COSY experiments, which revealed the presence of six methyls, 12 methylenes, six methines, and six quaternary carbon atoms. In the EI-mass spectrum, compound **3** exhibited important and prominent fragments at *m/z* 331, 320, 175, and 95, which are characteristic fragmentation ions of 9,19-cycloartane-type triterpenoids with two hydroxyls in the side-chain moiety and two hydroxyls in ring A [1–4]. On the basis of the precise ^{1}H and ^{13}C NMR analyses, compound **3** was deduced to be a cycloartane-type triterpenoid with a 24,25-glycol side-chain and either a 3β,28-diol or a 3β,29-diol system in A ring. This structure was also supported from the HMBC experiments. Thus, compound **3** showed prominent cross-peaks between H-3α (δ 4.31) and a hydroxymethylene carbon (δ 67.5) and between H-24α (δ 3.73) and two methyl carbons (δ 26.0 and 26.1). Confirmation for the 3β,28-diol arrangement came from the following evidence. The carbon and proton chemical shifts of rings A, B, C, and D in **3** are close agreements with those of **1** [1]. While the carbon and proton chemical shifts of the side-chain moiety in **3** are essentially the same as compounds **2** [1] or **5** [2]. Further comparisons of the ^{1}H and ^{13}C NMR spectral data of **3** and other analogous cycloartane-type triterpenoids [5–7] confirmed the structure of **3** as (24*R*)-cycloartane-3β,24,25,28-tetrol.

Compound **4** was assigned to the molecular formula $C_{30}H_{52}O_3$ (HR EI-MS) and had IR absorptions at 3450 cm^{-1} due to hydroxyl group. The ^{1}H NMR spectrum analysed with the aid of 2D NMR techniques, showed the presence of six tertiary methyls, a secondary methyl (δ 0.89, *d*, J = 6.6 Hz), and a cyclopropyl methylene group (δ 0.35 and 0.52, 1H each, *d*, J = 3.9 Hz). In addition, signals due to two methine protons geminal to a hydroxyl (δ 3.29, *dd*, J = 9.8, 1.7 Hz and 3.47, *t*, J = 2.6 Hz) were present. The ^{13}C NMR

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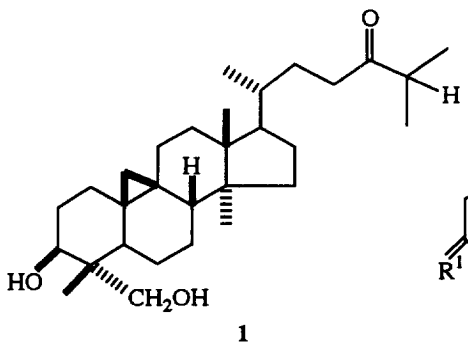

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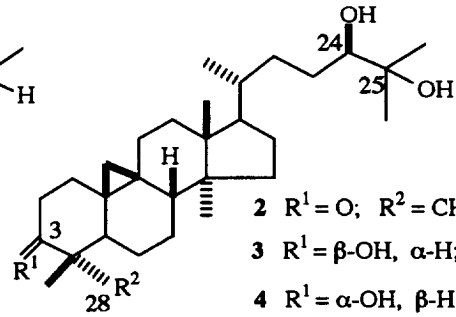

2 $R^1 = O$; $R^2 = CH_3$

3 $R^1 = \beta$-OH, α-H; $R^2 = CH_2OH$

4 $R^1 = \alpha$-OH, β-H; $R^2 = CH_3$

5 $R^1 = \beta$-OH, α-H; $R^2 = CH_3$

Table 1. ^{13}C NMR spectral data of compounds 3–5

C	3*	4†	5†	C	3*	4†	5†
1	32.4	27.5	32.0	16	26.7	26.3	26.5
2	31.0	28.8	30.4	17	52.9	52.3	52.4
3	73.9	77.1	78.9	18	18.5	18.0	18.1
4	44.8	39.6	40.5	19	30.1	29.8	29.9
5	41.6	41.1	47.2	20	37.0	36.4	36.4
6	21.3	21.1	21.1	21	18.9	18.5	18.5
7	28.5	28.1	28.2	22	34.5	33.6	33.6
8	48.3	48.1	48.0	23	29.4	28.6	28.8
9	19.9	19.9	20.0	24	80.0	79.7	79.7
10	26.1	26.5	26.1	25	72.8	73.2	73.2
11	26.2	26.3	26.0	26	26.1[a]	23.3	23.3
12	33.3	33.6	33.0	27	26.0[a]	26.6	26.6
13	45.6	45.3	45.3	28	67.5	25.9	25.5
14	49.1	48.9	48.8	29	11.5	21.3	14.0
15	35.9	35.5	35.6	30	19.6	19.3	19.4

* Measured in C_5D_5N.

† Measured in $CDCl_3$.

[a] Assignments may be interchangeable in each vertical column.

spectrum showed 30 carbons consisting of seven methyls, 11 methylenes, six methines, and six quaternary carbon atoms. In the EI-mass spectrum, compound **4** showed important and prominent fragments at *m/z* 315, 297, 203, 175 and 95, which are characteristic fragmentation ions of 9,19-cycloartane-type triterpenoids with two hydroxyls in the side-chain moiety and one hydroxyl in ring A [1–4]. The above spectral data are very similar to those of **5** [2]. However, in the ^1H NMR of **5**, the 3α-axial H appeared at δ 3.28 as a double doublet (J = 10.1, 4.4 Hz) while in **4**, the proton signal due to H-3 appeared at δ 3.47 as a triplet (J = 2.6 Hz). This result indicates the presence of a 3α-axial hydroxyl in **4** [8, 9]. Furthermore, in the ^{13}C NMR spectrum of **4**, the expected shielding and deshielding effects of the 3α-axial hydroxyl on ring A carbons were present [8–10]. On the basis of the above evidence, the structure of **4** was concluded to be (24*R*)-cycloartane-3α,24,25-triol.

EXPERIMENTAL

General. Mps: uncorr., ^1H NMR: 400 MHz; ^{13}C NMR: 100 MHz and TMS as int. standard; IR: $CHCl_3$; HPLC: JAIODS-120T column with a differential refractometer.

Plant materials. The leaves of *Aglaia harmsiana* Perkins were harvested in 1993 at the Herbarium Bogoriense, Java, Indonesia and voucher specimens have been deposited at the Herbarium of the Faculty of Pharmaceutical Sciences, Setsunan University.

Extraction and isolation. The crushed leaves (700 g) were extracted with 95% EtOH and the solvent evapd. The EtOH extract (30.2 g) was suspended with H_2O and the aq. suspension extracted with EtOAc. The EtOAc extract (25.0 g) was chromatographed on silica gel with hexane–EtOAc containing increasing amounts of EtOAc and a fr. containing **1**, **4**, and **5** (1.0 g), and a fr. containing **3** (0.3 g) were sepd in that

order. Each fr. was further sepd by repeated HPLC to afford **1** [1] (150 mg), **3** (91 mg), **4** (28 mg), and **5** [2] (570 mg).

(24R)-*Cycloartane*-3β,24,25,28-*tetrol* (**3**). Amorphous powder, $[\alpha]_D^{25}$ +22.8° (MeOH; *c* 0.50); IR ν_{max} cm^{-1}: 3450, 2960, 1260, 1030; EI- and HR EI-MS *m/z* (rel. int.): 476.3863 (M^+, $C_{30}H_{52}O_4$ requires 476.3865, 2), 458 (9), 443 (10), 440 (8), 425 (10), 331 (8), 320 (17), 175 (51), 95 (93), 59 (100); ^1H NMR (C_5D_5N): δ 0.37 (1H, *d*, *J* = 4.0 Hz) and 0.62 (1H, *d*, *J* = 4.0 Hz) (H_2-19), 0.89 (3H, *s*, Me-30), 1.02 (3H, *d*, *J* = 6.5 Hz, Me-21), 1.04 (3H, *s*, Me-18), 1.17 (3H, *s*, Me-29), 1.53, 1.56 (3H each, *s*, Me-26 and Me-27), 3.73 (1H, *dd*, *J* = 10.3, 1.4 Hz, H-24α), 3.79 and 4.24 (1H each, AB*q*, *J* = 10.5 Hz, H_2-28), 4.31 (1H, *dd*, *J* = 11.7, 4.4 Hz, H-3α); ^{13}C NMR: Table 1.

(24R)-*Cycloartane*-3α,24,25-*triol* (**4**). Mp 201–202° (MeOH); $[\alpha]_D^{20}$ +35.9° (MeOH; *c* 0.33); IR ν_{max} cm^{-1}: 3450, 2940, 1280; EI- and HR EI-MS *m/z* (rel. int.): 460.3910 (M^+, $C_{30}H_{52}O_3$ requires 460.3916, 10), 442 (18), 427 (22), 409 (23), 315 (24), 297 (28), 203 (44), 175 (91), 95 (100); ^1H NMR ($CDCl_3$): δ 0.35 (1H, *d*, *J* = 3.9 Hz) and 0.52 (1H, *d*, *J* = 3.9 Hz) (H_2-19), 0.88 (3H, *s*, Me-29), 0.89 (3H, *d*, *J* = 6.6 Hz, Me-21), 0.90, (3H, *s*, Me-30), 0.95 (3H, *s*, Me-28), 0.97 (3H, *s*, Me-18), 1.17, 1.22 (3H each, *s*, Me-26 and Me-27), 3.29 (1H, *dd*, *J* = 9.8, 1.7 Hz, H-24α), 3.47 (1H, *t*, *J* = 2.5 Hz, H-3β); ^{13}C NMR: Table 1.

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