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TRITERPENOID CONSTITUENTS OF THAI MEDICINAL PLANTS—II

ISOMERIC AGLAITRIOLS AND AGLAIONDIOL

D. SHIENGTHONG,* U. KOKPOL and P. KARNTIANG
Department of Chemistry, Chulalongkorn University, Bangkok, Thailand

and

R. A. MASSY-WESTROPP
Department of Organic Chemistry, University of Adelaide, Adelaide, Australia, 5001

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Abstract—Three new tetracyclic triterpenes, aglaiondiol and two isomers of aglaitriol, were isolated from the light petroleum extracts of leaves of *Aglaia odorata*. The isomers of aglaitriol (**2**) were separated by fractional crystallisation of the triacetates which on hydrolysis gave the epimers **2c** and **2d**. The structures of **2c**, **2d** and aglaiondiol (**3**) have been established by interconversion with aglaiol (**1**).

In an earlier publication[1] the structure of aglaiol (**1**) was described, and more recently, the (24*S*)-configuration has been established for the side chain epoxide.[2] Further investigation of the light petroleum extracts of the ground, dried leaves of *A. odorata* Lour. (Meliaceae[3]) led to the isolation of aglaitriol (**2**) and aglaiondiol (**3**).

Natural aglaitriol, $C_{30}H_{52}O_3$ (from analytical data and mass spectrum), was considered originally to be homogeneous but different samples have melting points 165–7° to 176–8° presumably depending on the proportion of the two isomers (**2c** and **2d**). The IR spectrum had strong OH absorption (ν_{max} 3500–3200 cm^{-1}) and bands characteristic of a methylene group (ν_{max} 3078, 1640, and 880 cm^{-1}).[4] This was confirmed by the NMR spectrum which included the following resonances: (after D_2O exchange) δ 4·74 (2H, br. s), 3·2 (2H, br. m) and 0·75, 0·85, 0·88, 0·96, 1·13, 1·17 (sharp singlets). Aglaitriol decolourised bromine in carbon tetrachloride and gave the reactions characteristic of tetracyclic triterpenes.[5] Catalytic hydrogenation of aglaitriol (**2**) gave the dihydro derivative.

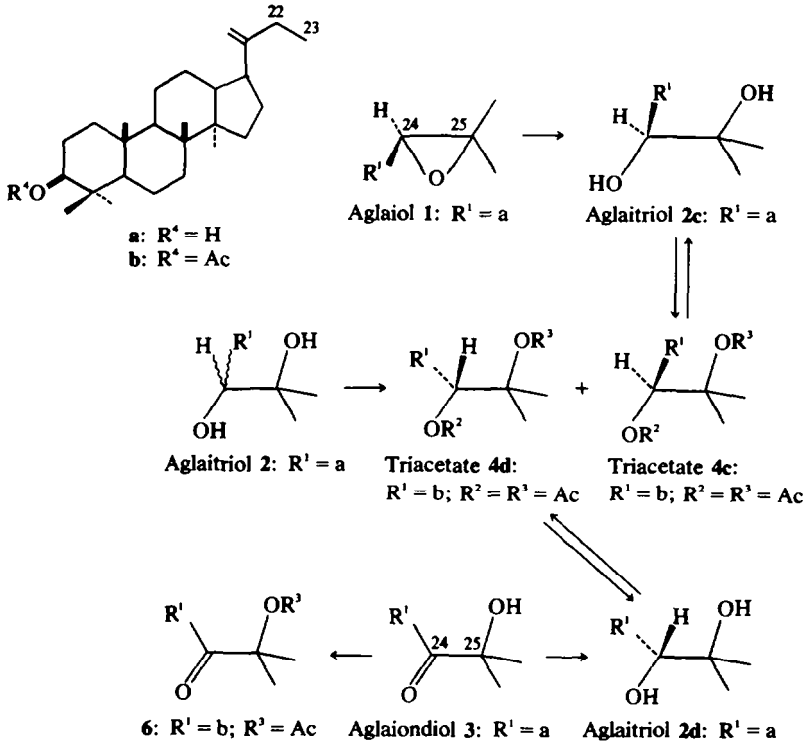
Acetylation of aglaitriol, followed by fractional crystallisation, gave the two triacetates (**4c**), m.p. 163–164° and (**4d**), m.p. 116–118°. Their IR spectra (ν_{max} 1735 cm^{-1}) were almost identical with only minor differences at 890–905 cm^{-1}. In this region (**4d**) exhibited one additional band. Their NMR and mass spectra were identical and the TLC properties were the same. Hydrolysis of the triacetate (**4c**) gave aglaitriol (**2c**), m.p. 185–186° whereas hydrolysis of the triacetate (**4d**) gave aglaitriol (**2d**), m.p. 165–167°. Their NMR and mass spectra were identical and they showed the same R_f values on TLC. The IR spectra were very similar with slight intensity differences between 1100 and 1150 cm^{-1} and **2c** displayed a second weak band at 1395 cm^{-1}.

The hydration of aglaiol (**1**) in aqueous acid solution yielded a product which was acetylated to give a triacetate, m.p. 163–164°. This triacetate was hydrolysed to give a triol, m.p. 185–187°. Both the triacetate and the triol were identical with the triacetate (**4c**) and aglaitriol (**2c**) by m.p., m.m.p. and all spectral characteristics. Since the configuration at C_{24} in aglaiol (**1**) is known[2] the isomer of aglaitriol with m.p. 185–186° is (24*S*)-aglaitriol (**2c**). The stereochemistry of epoxide opening under acid conditions is well established.[6]

Aglaiondiol (**3**), m.p. 125–127°, has the molecular formula $C_{30}H_{50}O_3$. The IR spectrum showed the presence of OH (3600–3200 cm^{-1}), carbonyl (1715 cm^{-1}) and methylene (3080, 1640 and 880 cm^{-1}) groups. A two proton resonance at δ 4·80 confirms the presence of a methylene group and a one proton at δ 3·43 (doublet of doublet, J = 8 and 4 Hz) is typical of the proton signal in 3β-OH compounds, and also indicates that the secondary OH group is not at the C_{24} position. Acetate and 2,4-dinitrophenylhydrazone derivatives confirmed the presence of the OH and CO groups. Reduction of aglaiondiol (**3**) with LAH, followed by acetylation of the product, gave a triacetate, m.p. 114–116°. This was identical by m.p., m.m.p. and spectral characteristics with the triacetate (**4d**). Hydrolysis of the triacetate gave a triol, m.p. 165–167°, which was identical with aglaitriol (**2d**) by m.p., m.m.p. and spectral data. Presumably the reduction of aglaiondiol (**3**) with LAH gave (**2d**) as the major isomer. A consideration of the chemical and spec-

tral data therefore leads to the structure of the aglaitriol, m.p. 165–167° as the 24-epimer of **2c**, i.e. (24*R*)-aglaitrol (**2d**) and aglaiondiol as represented by **3**.

aglaitriol had the same R_f in 2% (v/v) MeOH–$CHCl_3$ and all the triacetates had the same R_f in 50% (v/v) ether–light petroleum. Light petroleum refers to the fraction b.p. 40–80°.



EXPERIMENTAL

General. M.ps were taken on a Fischer–Johns apparatus and are uncorrected. IR spectra were recorded with a Beckman, model 1325, or a Unicam SP 200 G. NMR spectra were recorded on Varian DP 60 or T60 instruments and mass spectra with an Hitachi Perkin–Elmer RMU 6D spectrometer. Optical rotations were observed on $CHCl_3$ solns in a 2 dm tube with a polarimeter made by Bellingham Stanley, Model D_4. Riedel-De Haen aluminium oxide DF was used for TLC. All samples of

Isolation of constituents from Aglaia odorata. The ground, dried leaves of *A. odorata* (1·65 kg) were extracted with light petroleum as described earlier[1] to give 71·4 g (4·32%) of crude extract. Portions of the extract were chromatographed as described below, the fractions being followed by TLC.

(a) Extract (25 g) was chromatographed on 4 cm × 44 cm column of aluminium oxide S by U. Kokpol.

(b) Extract (30 g) was chromatographed on 3·2 cm × 52 cm column of aluminium oxide S by P. Karntiang.

Eluent	Vol (l)*	Products	Weight (g)†
light pet.	10	Wax	4·47
light pet./ether (9:1)	4	Yellow oil	1·38
	6	White, amorphous, m.p. 87–8°	0·37
light pet./ether (4:1)	10	Oily solid	0·78
	6	β-sitosterol, m.p. 137–8°	0·17
light pet./ether (1:1)	4	Yellow oil	1·97
	6	White crystals, m.p. 105–6°	0·09
	20	Aglaiondiol, m.p. 126–7°	0·11
light pet./ether (1:3)	54	Aglaitriol, m.p. 176–8°	0·18
methanol	4	Green oil	1·15

*21 fractions were collected.
†After recrystallisation of solids.

Eluent	Vol (l)*	Products	Weight (g)†
light pet.	1	Wax	5·30
	2	Oil and crystals, m.p. 67–9°	0·20
	5	White crystals m.p. 84–6°	0·45
light pet./ether (9:1)	5	Aglaiol, m.p. 110–112° / Aglaiol, m.p. 110–112°	0·26
	4	β-sitosterol, m.p. 135–7°	0·20
light pet./ether (4:1)	16	Oil and white crystals m.p. 90–5°	0·06
light pet./ether (1:1)	8·5	Oil and white crystals	
light pet./ether (1:3)	6·5	Oil and white crystals m.p. 198–208°	0·08
light pet./ether (1:3)	12·5	Aglaiondiol, m.p. 125–7°	0·18
ether	12	Oil and solid	
chloroform	11	Aglaitriol, m.p. 165–7°	0·12

*0·5 l fractions were collected.
†After recrystallisation of solids.

β-Sitosterol. Fractions containing β-sitosterol from (a) were recrystallised from $CHCl_3$–MeOH (1:2) to yield 170 mg of crystals, m.p. 137–138°. (Found: C, 83·53; H, 12·24. $C_{29}H_{50}O$ requires: C, 83·96; H, 12·15%). Acetylation with Ac_2O-pyridine gave the acetate, m.p. 127–128° (Found: C, 81·75; H, 11·37. $C_{31}H_{52}O_2$ requires: C, 81·52; H, 11·46%). Both samples were identical with authentic β-sitosterol and its acetate by m.p., m.m.p. and spectral data.

Aglaiol (1). Fractions containing aglaiol [by TLC from (b)] were combined and the aglaiol separated by the method described.[1] Aglaiol (258 mg, 0·86%) had m.p. 110–112° (lit.[1] m.p. 113–114°) (Found: C, 81·19; H, 11·42. $C_{30}H_{50}O_2$ requires: C, 81·39; H, 11·38%). The acetate of aglaiol had m.p. 161–162° (lit.[1] m.p. 161–162°).

Aglaitriol (2). The combined fractions of ether:light petroleum (3:1) eluted from (a) were evaporated and the white needles were collected. Recrystallisation from benzene gave 180 mg (0·74%) of *aglaitriol* (2), m.p. 176–178°. (Found: C, 77·69; H, 11·51; M^+ at *m/e* 460. $C_{30}H_{52}O_3$ requires: C, 78·21; H, 11·38%; M, 460); ν_{max}^{KBr} 3500-3200 (OH), 3078, 1640 and 880 cm^{-1} (>C=CH_2), NMR spectrum δ 4·74 (2H, br. s), 3·2 (2H, br. m) and 0·75, 0·85, 0·88, 0·96, 1·13 and 1·17 (singlets). The same compound was also isolated from the last fraction mentioned in the previous paper[1] (m.p. 176–178°) and from the chloroform fractions from (b), m.p. 165–167°. $[\alpha]_D^{25}$ +46·5° (*c* 0·005). The compounds from different extractions had identical spectra and the products from (a) and (b) had m.m.p. 165–173°.

Aglaiondiol (3). The material collected from the ether:light petroleum (1:1) fractions from (a) was rechromatographed on a 1·2 cm × 29 cm column of aluminium oxide S. The same eluent gave *aglaiondiol* (3) which was recrystallised from ether:light petroleum (2:3) to give 110 mg (0·44%) of colourless needles, m.p. 126–127°, $[\alpha]_D^{25}$ +97·3° (*c* 0·015). (Found: C, 78·28; H, 11·41; M^+ at *m/e* 458. $C_{30}H_{50}O_3$ requires: C, 78·65; H, 11·0; M, 458). ν_{max}^{KBr} 3600-3200 (OH), 1715 (C=O), 3080, 1640, 880 cm^{-1} (>C=CH_2); NMR spectrum: δ 4·77 (2H, br. s, >C=CH_2), 3·43 (1H, dd J = 8, 4 Hz, C_3H), 0·87, 0·93, 1·02, 1·05, 1·13, 1·17 (singlets). Separation by method (b) gave aglaiondiol (180 mg, 0·6%), m.p. 125–127°.

Aglaiondiol (200 mg) was acetylated with Ac_2O (2·5 ml) and pyridine (5 ml) at room temp for 24 h. Isolation in the usual way, followed by recrystallisation from light petroleum gave the *diacetate* (6, 77 mg, 39%), m.p. 90–91°. (Found: C, 74·87; H, 10·33; M^+ at *m/e* 542. $C_{34}H_{54}O_5$ requires: C, 75·23; H, 10·03%; M, 542); ν_{max}^{KBr} 1720 (acetate >C=O), 1700 (ketone >C=O), 3070, 1638 and 880 cm^{-1} (>C=CH_2).

The 2,4-dinitrophenylhydrazone was obtained as an amorphous solid from EtOH, m.p. 183–5°. ν_{max}^{KBr} 3500–3360, 3310, 1610, 1508, 1320, 880, 825 cm^{-1}.

Aglaitriol (2c). Aglaiol (1) was converted to 2c by the following methods.

(a) A soln of H_2SO_4 (one drop conc) in water (5 ml) was added to a soln of aglaiol (300 mg) in acetone (5 ml). The mixture was stirred at room temp for 2 h and then allowed to stand for 22 h.[7]

It was then poured into water (20 ml) and extracted with ether (3 × 50 ml). The ether extracts were washed with $NaHCO_3$ aq, then with water and dried (Na_2SO_4). Evaporation gave a white solid which was chromatographed on aluminium oxide S (15 g) using light petroleum, ether:light petroleum (1:9), ether and acetone as solvents. Aglaiol (100 mg) was recovered from the ether:light petroleum fractions and *aglaitriol* (2c) was collected from the acetone fraction. Recrystallisation from benzene and then from MeOH gave (100 mg, 33%) of needles, m.p. 182–183°, $[\alpha]_D^{25}$ +41·5° (*c* 0·003). The compound was homogeneous by TLC. (Found: C, 77·94; H, 11·48; M^+ at *m/e* 460. $C_{30}H_{52}O_3$ requires: C, 78·21; H, 11·38%; M, 460); ν_{max}^{KBr} 3600–3120 (OH), 3070, 1640, 890 cm^{-1} (>C=CH_2). The IR spectrum was very similar to those of 2 and 2d, except for an extra weak band at 1395 cm^{-1} and a slight difference in intensity at 1110 cm^{-1}. The NMR spectrum was identical to that of 2.

(b) A soln of 6N $HClO_4$ (1 drop) in water (5 ml) was added to aglaiol (100 mg) in dioxane (10 ml) and the mixture shaken on a hot water bath for 10 min. The

mixture was cooled and the product isolated as described above. Aglaitriol **2c** was obtained in 75% yield (75 mg), m.p. 182–183°.

Acetylation of aglaitriol (**2c**). A mixture of **2c**, m.p. 182–183°, Ac_2O (3 ml) and pyridine (5 ml) was heated on a water bath for 12 h. The mixture was cooled and poured into water. The solid was collected and chromatographed on a 1 cm × 17 cm column of aluminium oxide S. Elution with ether : light petroleum (1 : 9) gave the *triacetate* (**4c**) which crystallised from light petroleum as needles (263 mg, 87%), m.p. 164–166°. The compound was pure by TLC. (Found: C, 73·11; H, 10·28; M^+ at *m/e* 586. $C_{36}H_{58}O_6$ requires: C, 73·68; H, 9·96%; M, 586. ν_{max}^{KBr} 1735 (acetate), 3100, 1650, 890 ($>C{=}CH_2$), 1240 cm^{-1}. NMR spectrum: δ 0·83, 0·95, 1·42, 1·47 (singlets) 1·93, 2·00, 2·07 ($CH_3{-}\overset{O}{\overset{\|}{C}}{-}$), 4·42 (1H, dd), 4·70 (2H, br. d), 5·08 (1H, d, d).

Further elution with ether : light petroleum (1 : 1) gave a small amount of the *diacetate* (**5**). Recrystallisation from light petroleum gave **5**, 18 mg (6%), m.p. 146–147°; ν_{max}^{KBr} 3500–3200, 1720, 1630, 1240 and 880 cm^{-1}. NMR spectrum: δ 0·88, 1·00, 1·23 (singlets), 2·05, 2·13 ($CH_3{-}\overset{O}{\overset{\|}{C}}{-}$), 4·77 (2H, bs, $>C{=}CH_2$), 4·67 (2H, b.m.).

Separation of aglaitriol triacetates (**4c**) *and* (**4d**) *prepared from natural aglaitriol* (**2**). A soln of **2** in Ac_2O (3 ml) and pyridine (5 ml) was refluxed for 12 h. Isolation as described above gave a triacetate fraction and a diacetate fraction. The triacetate fraction was recrystallised from light petroleum to give **4c**, m.p. 163–164°. This sample was identical by m.p., m.m.p., TLC, IR and NMR spectra with the sample prepared from **2c** which was in turn prepared from the opening of the epoxide ring in **1**.

On evaporation of the mother liquors from the crystallisation of **4c** at room temp a second crop of crystals was obtained. Several crystallisations from light petroleum gave the isomeric *triacetate* (**4d**) as small plates, m.p. 116–118°. TLC properties were the same as those of **4c**. The NMR spectrum was identical to that of **4c** and the IR spectrum was very similar except for an additional band at 875 cm^{-1}.

The results obtained for the separation of the two triacetates, prepared from three different batches of aglaitriol, are shown below.

Aglaitriol (2)	Wt.	Wt. of triacetate m.p. 163–4°	m.p. 116–8°
m.p. 176–8°	127 mg.	32 mg.	27 mg.
m.p. 165–7°	300 mg.	15 mg.	214 mg.
m.p. 167–9°	225 mg.	5 mg.	108 mg.

Preparation of aglaitriol (**2d**) *from reduction aglaiondiol* (**3**). A soln of **3** (300 mg) in dry ether (10 ml) was added dropwise with stirring to a soln of LAH (5 g) in ether (100 ml) at room temp. The mixture was stirred for 5 h and was then decomposed with diluted H_2SO_4. The ether layer was separated and the aqueous layer extracted thoroughly with ether. The combined ethereal extracts were washed with $NaHCO_3$ aq, then with water and dried (Na_2SO_4). Evaporation and recrystallisation of the residue from MeOH gave *aglaitriol* (**2d**; 200 mg, 67%) as white needles, m.p. 175–177°, $[\alpha]_D^{25}$ + 50·0° (*c* 0·004). (Found: C, 77·59; H, 11·71; M^+ at *m/e* 460, $C_{30}H_{52}O_3$ requires: C, 78·21; H, 11·38%; M, 460). The IR and NMR spectra of **2d** and natural **2** were essentially identical.

Acetylation of the triol (80 mg) as described above gave a mixture of the diacetate and triacetate which were separated by column chromatography. Recrystallisation of the triacetate from light petroleum gave pure **4d**, m.p. 114–116°. This sample was identiclal to **4d**, prepared from the acetylation of natural **2**, by m.p., m.m.p., TLC, IR and NMR spectra.

Hydrolysis of triacetates. A soln of the triacetate in MeOH (10 ml) and 10% KOH aq (5 ml) was heated on a water bath for 1 h. Water (25 ml) was added to the cooled mixture and the triol isolated and recrystallised from MeOH in the usual way.

Triacetate			Triol	
Triacetate of **2c**	164–6°	100 mg	75 mg	185–7°
Triacetate (**4c**)	163–4°	52 mg	37 mg	185–6°
Triacetate (**4d**)	116–8°	100 mg	70 mg	166–8°
Triacetate of **2d**	114–6°	19 mg	8 mg	165–7°

The NMR spectra of the samples were identical. The IR spectrum of the triol obtained from **4c** was identical to those of **2c** and the aglaitriol (**2c**) from hydration of **1**. The IR spectrum of the triol from **4d** was identical to those from the hydrolysis product of the triacetate of (**2d**) and the aglaitriol (**2d**), obtained from the reduction of aglaiondiol (**3**).

Reduction of aglaitriol (**2**). A soln of **2** (150 mg) in abs EtOH (5 ml) was hydrogenated in the presence of Pd-C (10 mg). The product was chromatographed on aluminium oxide S and then recrystallised from light petroleum to give *dihydroaglaitriol* (32 mg, 21%) as a white amorphous solid, m.p. 202–203°. (Found: C, 77·52; H, 11·93. $C_{30}H_{54}O_3$ requires: C, 77·87; H, 11·76%). ν_{max}^{KBr} 3600–3200 cm^{-1}.

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