Triterpenoids of *Aglaia odorata*. Configuration of Trisubstituted Epoxides

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Structures are established for three dammarane triterpenoids [(1c), (3a), and (3c)] isolated from *Aglaia odorata*. The stereochemistry at C-24 of these compounds and of aglaiol (1a) has been elucidated. The possibility that (3c) (a 24,25-dihydroxy-3-ketone) is identical with aglaiondiol, previously described as 3β,25-dihydroxy-5α-dammar-20-en-24-one, is discussed. It is shown that the configuration of trisubstituted epoxides can be conveniently determined by acid-catalysed methanolysis and application of Horeau's method to the resulting methoxy-alcohol.

Aglaia odorata is a small tree occurring primarily in South-East Asia. Extracts of the plant have found local use as medicines. Previous work established the structure [1] and stereochemistry [2] of the biosynthetically interesting 24,25-epoxy-triterpenoid aglaiol (1a). We now report brief details of other constituents of this plant.[3]

Powdered, dried leaves of *A. odorata* were extracted exhaustively with light petroleum and the resulting green oil was chromatographed on a column of silica gel. Elution with light petroleum gave large amounts of a yellow oil. This was shown by g.l.c. to be a complex mixture of relatively volatile components. Further elution with the addition of increasing amounts of ethyl acetate afforded one minor and then three major triterpenoid fractions.

The minor fraction was persistently contaminated by traces of a low melting wax and could not be obtained in a satisfactorily crystalline state. I.r. spectroscopy indicated the presence of a carbonyl group ($\nu_{max.}$ 1 730 cm^{-1}). Reduction with sodium borohydride followed by acetylation gave material identical with aglaiol acetate (1b), thus identifying the original component as the corresponding 3-ketone (1c).

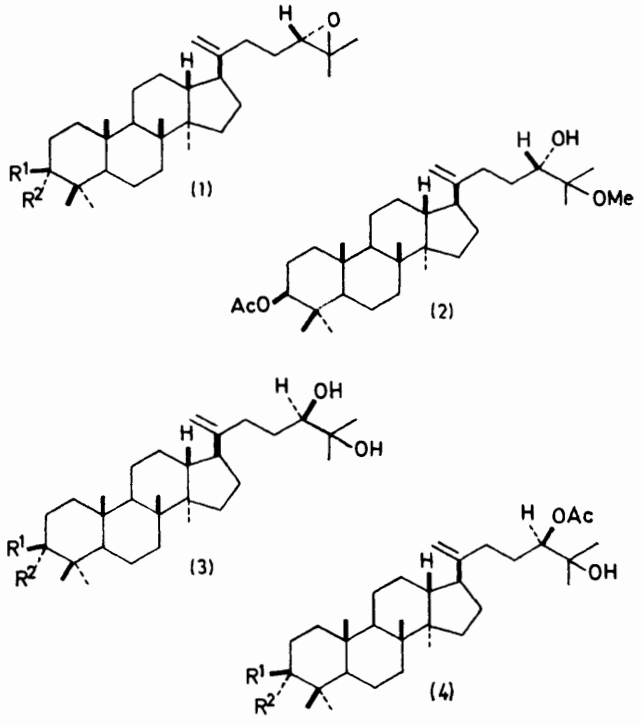
After acetylation the first major fraction from the chromatography could be further separated into two components. The less polar was shown by g.l.c. analysis to be a mixture of β-sitosterol and stigmasterol acetates in the ratio *ca.* 3 : 1. The more polar compound was aglaiol acetate (1b), m.p. 157—161°, $[\alpha]_D$ +51°. Synthetic aglaiol acetate, but racemic at C-24, was prepared

[1] D. Shiengthong, A. Verasarn, P. NaNonggai-Suwanrath, and E. W. Warnhoff, *Tetrahedron*, 1965, **21**, 917.

[2] R. B. Boar and K. Damps, *J.C.S. Chem. Comm.*, 1973, 115.

[3] D. Shiengthong, U. Kokpol, P. Karntiang, and R. A. Massy-Westropp, *Tetrahedron*, 1974, **30**, 2211.

by treatment of 5α-dammara-20,24-dien-3β-yl acetate with perbenzoic acid in ether. This material had m.p. 170—180°, $[\alpha]_D$ +60°. Comparison of the molecular rotations of the synthetic (M_D 290) and natural (M_D 247) aglaiol acetates with data for (24*S*)- and (24*R*)-24,25-epoxy-5α-lanost-8-en-3β-yl acetates [4] (M_D 238 and 284, respectively) indicated that natural aglaiol has the 24*S*-configuration. This conclusion was confirmed by acid-catalysed methanolysis of natural aglaiol acetate followed by application of Horeau's method to the resulting methoxy-alcohol (2).[2] This is a convenient and general method for determining the absolute configuration of such trisubstituted epoxides.[5] Details of preliminary experiments with (24*S*)- and (24*R*)-24-hydroxy-25-methoxy-5α-lanost-8-en-3β-yl acetates of known absolute configurations are given in the Experimental section.



a; R^1 = OH, R^2 = H
b; R^1 = OAc, R^2 = H
c; R^1R^2 = O

The second major component was the dihydroxy-ketone (3c), m.p. 85—87°, $[\alpha]_D$ +89°. Reduction with sodium borohydride afforded the 3β,24,25-triol (3a), which was further characterised as the 3,24-diacetate (4b). Application of Horeau's method to the dihydroxy-ketone (3c) showed that the absolute configuration at C-24 was *R*. Despite the discrepancy in constants it seems likely that this compound is identical with aglaiondiol, m.p. 126—127°, $[\alpha]_D$ +97°, which has been previously [3] identified as 3β,25-dihydroxy-5α-dammar-20-en-24-one. In particular, the changes in chemical shifts of the nuclear methyl groups on going from the ketone monoacetate (4c) [τ 8.91, 8.95, 8.98, 9.04, and 9.11 (each 3 H, s)] to the corresponding diacetate (4b) [τ 9.01 (3 H, s) and 9.12 and 9.13 (each 6 H, s)] are only consistent with the ketone group being at C-3.[6] The location of the ketone group at C-3 also provides a ready explanation as to why a single stereoisomer is formed on reduction. The reduction of C-24 ketones involves no stereoselectivity.

The final component readily formed a diacetate, m.p. 138—142°, $[\alpha]_D$ +53°, identical with the product from reduction and subsequent acetylation of the dihydroxy-ketone (3c). It was therefore identified as the (24*R*)-3β,24,25-triol (3a).

Failure to obtain viable plant material prevented us from pursuing our initial interest [2] in the biosynthesis of the triterpenoids of *A. odorata*. This problem remains of interest, however, particularly since it has now been shown that the epoxide (1a) and the diols (3a and c) have opposite configurations at C-24.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. N.m.r. data are for solutions in deuteriochloroform with tetramethylsilane as internal standard, and were recorded at 90 MHz. Rotations are for solutions in chloroform. Unless otherwise stated light petroleum refers to the fraction of b.p. 60—80 °C.

Extraction of Aglaia odorata *Leaves*.—Powdered, dried leaves of *A. odorata* (700 g) were extracted with light petroleum (b.p. 40—60 °C; 8 l) for 48 h (Soxhlet). Removal of the solvent gave a green oil (*ca.* 30 g) which was chromatographed on a column of silica gel (2 kg). The column was eluted with light petroleum containing a progressively larger percentage (0—80%) of ethyl acetate. Fractions of 500 ml were collected.

Fractions 1—10. These afforded a bright yellow oil (6 g) which solidified at room temperature and crystallised from ethyl acetate as a white, low-melting wax. G.l.c. analysis (2.5% SE 30 column; initial temperature 70 °C, rising after 5 min by 4° min^{-1} to 240 °C) indicated the presence of numerous, mainly rather volatile components. This material was not investigated further.

Fractions 11—16. These gave an oil (3 g) which after extensive rechromatography yielded a slightly impure triterpenoid ketone, $\nu_{max.}$ 1 730 cm^{-1}. The n.m.r. spectrum suggested that this was a 24ξ,25-epoxy-5α-dammar-20-en-3-one (1c), and this was confirmed as follows. The ketone (50 mg) in methanol (20 ml) was treated with sodium borohydride (200 mg) at room temperature for 30 min. The mixture was poured into water and extracted with ether. The product thus obtained was treated with acetic anhydride in pyridine at room temperature overnight to afford material identical with authentic aglaiol acetate (1b), m.p. and mixed m.p. 159—164°, $[\alpha]_D$ +54°.

Fractions 23—27. The oil (1.8 g) in pyridine (50 ml) and acetic anhydride (25 ml) was left at room temperature overnight, then poured into water and extracted with

[4] R. B. Boar, D. A. Lewis, and J. F. McGhie, *J.C.S. Perkin I*, 1972, 2231.

[5] See also R. B. Boar and K. Damps, *Tetrahedron Letters*, 1974, 3731.

[6] F. Hemmert, B. Lacoume, J. Levisalles, and G. R. Pettit, *Bull. Soc. chim. France*, 1966, 976.

ether. Crystallisation from acetone–methanol afforded aglaiol acetate (1b) (600 mg), m.p. 157—161°, $[\alpha]_D$ +51°, τ 5.22 and 5.28 (each 1 H, broad s, 21-H_2), 5.50 (1 H, t, 3α-H), 7.25 (1 H, t, *J* 5 Hz, 24-H), 7.97 (3 H, s, OAc), 8.68 and 8.92 (each 3 H, s, 26- and 27-H_3), 9.01 (3 H, s), and 9.12 and 9.14 (each 6 H, s). Chromatography of the material from the mother liquors of the above crystallisation afforded further aglaiol acetate (200 mg) and a white solid, m.p. 126—129°, $[\alpha]_D$ −39°, which was shown by g.l.c. analysis to be a mixture of β-sitosterol and stigmasterol acetates in the ratio *ca.* 3 : 1.

Fractions 43—53. The oil ($\nu_{max.}$ 3 400 and 1 705 cm^{-1}) (3.5 g) in pyridine (15 ml) and acetic anhydride (10 ml) was left at room temperature overnight, then the mixture was poured into water and extracted with ether. The product was chromatographed on a silica gel column and then crystallised from light petroleum. *24-Acetoxy-25-hydroxy-5α-dammar-20-en-3-one* had m.p. 88—90°, $[\alpha]_D$ +77°, $\nu_{max.}$ 3 450, 1 735, and 1 705 cm^{-1}, τ 5.2 (3 H, m, 21-H_2 and 24-H), 7.89 (3 H, s, OAc), 8.79 (6 H, s, 26- and 27-H_3), and 8.91, 8.95, 8.98, 9.04, and 9.11 (each 3 H, s) (Found: C, 76.5; H, 10.4. $C_{32}H_{52}O_4$ requires C, 76.75; H, 10.5%). Hydrolysis with 5% potassium hydroxide in ethanol at room temperature for 2 h afforded 24,25-dihydroxy-5α-dammar-20-en-3-one (3c), m.p. 85—87°, $[\alpha]_D$ +89°, τ 5.23 (2 H, broad s, 21-H_2), 6.6 (1 H, dd, *J* 3 and 9 Hz, 24-H), 8.80 and 8.84 (each 3 H, s, 26- and 27-H_3), and 8.91, 8.96, 8.97, 9.05, and 9.11 (each 3 H, s) (Found: C, 78.3; H, 11.0. $C_{30}H_{50}O_3$ requires C, 78.55; H, 11.0%). The ketone (3c) (60 mg) in methanol (10 ml) was treated with sodium borohydride (200 mg) at room temperature for 30 min. Work-up as before gave 5α-dammar-20-ene-3β,24,25-triol (3a), m.p. 148—153°, $[\alpha]_D$ +51° {lit.,[3] (24*R*)- m.p. 165—167°, $[\alpha]_D$ +50°; (24*S*)- m.p. 185—187°, $[\alpha]_D$ +41°} (Found: C, 78.2; H, 11.3. Calc. for $C_{30}H_{52}O_3$: C, 78.2; H, 11.4%). The derived *3β,24-diacetoxy-5α-dammar-20-en-25-ol* (4b) had m.p. (from methanol) 138—142°, $[\alpha]_D$ +55°, τ 5.2 (3 H, m, 21-H_2 and 24-H), 5.5 (1 H, t, 3α-H), 7.87 and 7.95 (each 3 H, s, OAc), 8.78 (6 H, s, 26- and 27-H_3), 9.01 (3 H, s), and 9.12 and 9.13 (each 6 H, s) (Found: C, 75.0; H, 10.6. $C_{34}H_{56}O_5$ requires C, 74.95; H, 10.4%).

Fractions 58—66. The oil (2 g) in pyridine (5 ml) and acetic anhydride (3 ml) was left at room temperature overnight. The diacetate obtained, m.p. 138—142°, $[\alpha]_D$ +53°, was identical with material obtained by reduction and subsequent acetylation of the ketone (3c).

Epoxidation of 5α-Dammara-20,24-dien-3β-yl Acetate.—5α-Dammara-20,24-dien-3β-yl acetate (50 mg) in ether (25 ml) at −10 °C was treated with 1 equiv. of perbenzoic acid in chloroform. After 24 h the solution was washed with 0.5N-sodium hydroxide, then water, dried, and evaporated. The residue was purified by p.l.c. to yield starting material and 24-racemic aglaiol acetate (1a), m.p. (from acetone) 170—180°, $[\alpha]_D$ +60°.

3β-Acetoxy-25-methoxy-5α-dammar-20-en-24-ol (2).—Aglaiol acetate (70 mg) suspended in methanol (10 ml) was treated with perchloric acid (70%; 1 drop) in methanol (10 ml) with stirring at room temperature. After 15 min the homogeneous solution was poured into water. The methanol was removed by evaporation under reduced pressure and the residue was extracted with ether. The *methoxy-alcohol* (2) was crystallised from light petroleum; m.p. 141—144°, $[\alpha]_D$ +38°, τ 5.25 (2 H, broad s, 21-H_2), 5.5 (1 H, t, 3α-H), 6.55 (1 H, dd, 24-H), 6.77 (3 H, s, OMe), 7.97 (3 H, s, OAc), 8.87 and 8.90 (each 3 H, s, 26- and 27-H_3), 9.02 (3 H, s), and 9.14 (12 H, s) (Found: C, 76.75; H, 10.9. $C_{33}H_{56}O_4$ requires C, 76.7; H, 10.9%). Similarly, (24*R*)-24,25-epoxy-5α-lanost-8-en-3β-yl acetate [4] afforded (24R)-*24-hydroxy-25-methoxy-5α-lanost-8-en-3β-yl acetate*, m.p. 148—150°, $[\alpha]_D$ +72°; and (24*S*)-24,25-epoxy-5α-lanost-8-en-3β-yl acetate [4] gave (24S)-*24-hydroxy-25-methoxy-5α-lanost-8-en-3β-yl acetate*, m.p. 142—145°, $[\alpha]_D$ +40° (Found: C, 76.5; H, 10.7. $C_{33}H_{56}O_4$ requires C, 76.7; H, 10.9%).

Determinations of Absolute Configuration by Horeau's Method.—These were carried out exactly as previously described.[4] The methoxy-alcohol (2) afforded (−)-α-phenylbutyric acid, optical yield 37.4%, indicating a 24*S*-configuration. The (24*R*)- and (24*S*)-24-hydroxy-25-methoxy-5α-lanost-8-en-3β-yl acetates gave (+)- and (−)-α-phenylbutyric acids, optical yields 32.3 and 20.2%, respectively. The dihydroxy-ketone (3c) gave (+)-α-phenylbutyric acid, optical yield 33.4%.

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