New Triterpenoids from the Leaves of *Tetrapanax papyriferum*

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Four new triterpenoids, papyriogenins D (3), E (4), F (5), and G (6), isolated from ether extracts of the fresh leaves of *Tetrapanax papyriferum* (Araliaceae), were identified as 21α-hydroxy-3-oxo-oleana-11,13(18)-dien-28-oic acid, 3α,21α-dihydroxyoleana-11,13(18)-dien-28-oic acid, 3α-hydroxy-21-oxo-olean-12-en-28-oic acid, and 3α,21α-dihydroxyoleana-11,13(18)-dieno-22β,28-lactone, respectively, by spectroscopic evidence and chemical correlations.

PREVIOUS papers [1,2] have described the structural elucidation and some chemical studies on triterpenoid glycosides obtained from the leaves of *Tetrapanax papyriferum*. This paper reports the isolation and structure identification of four new and two known triterpenoids, obtained from ether extracts of the same leaves. The ether extracts, obtained from the fresh leaves at room temperature, were passed through an active charcoal column to remove chlorophyll followed by repeated chromatography on silica gel to afford six compounds, *viz.* the known papyriogenins A (1) and C (2) and the newly designated papyriogenins D (3), E (4), F (5), and G (6). Compounds (1) and (2) were identified by comparison with authentic samples. Structures (3) and (4) were assigned to papyriogenins D and E, respectively, on the basis of the following evidence. Papyriogenin D (3), $C_{30}H_{44}O_4$, whose molecular composition is the same as that of papyriogenin C (2), exhibits similar u.v. and i.r. spectra to those of (2), and a ^{1}H n.m.r. signal for a proton geminal to a hydroxy-group at δ 4.04 (dd, *J* 10 and 6 Hz), which shifts to δ 4.80 in the monoacetate. Papyriogenin E (4), $C_{30}H_{46}O_4$, exhibits only a carboxy (1 705 cm^{-1}) absorption in the i.r. carbonyl region [checked by the addition of $NH(C_2H_5)_2$], a strong u.v. absorption characteristic of a heteroannular diene, and ^{1}H n.m.r. signals for two protons geminal to hydroxy-groups at δ 3.65br (s, $W_{1/2}$ 6 Hz) and 4.00 (dd, *J* 10 and 6 Hz), which shifted to δ 4.70 and 4.90, respectively, in the diacetate (M^+ 554). These results and biogenetic considerations suggest that papyriogenins D and E are 21α-hydroxy-3-oxo-oleana-11,13(18)-dien-28-oic acid (3) and 3α,21α-dihydroxyoleana-11,13(18)-dien-28-oic acid (4) respectively. (Generally, the ^{1}H n.m.r. signal for a proton geminal to 3-OH of a triterpenoid appears at δ *ca.* 3.50 in deuteriopyridine solution.) For confirmation, the following reduction experiments with metal hydride were carried out.

(1) *Reduction with Lithium Aluminium Hydride.*—In a model experiment, methyl 3-oxo-oleana-1,13(18)-dien-28-olate (7c),[3] derived from oleanolic acid (19a), was treated with lithium aluminium hydride in tetrahydrofuran to give a single compound, 3β,28-dihydroxyoleana-11,13(18)-diene, δ 3.48 (dd, *J* 9 and 8 Hz 3α-H) (^{1}H n.m.r. spectrum). This experiment indicated that the C-3 carbonyl was reduced to β-OH preferentially in the 3-oxo-oleana-11,13(18)-diene system. When the known papyriogenins A (1) and C (2) were reduced with lithium aluminium hydride, compounds (9) and (10) [3β,21α,28- and 3β,21β,28-trihydroxyoleana-11,13(18)-diene] from the former and compounds (11) and (12) [3α,21β,28- and 3α,21α,28-trihydroxyoleana-11,13(18)-diene] from the latter were obtained. The structures of the four reduced products (9)—(12) were identified by ^{1}H n.m.r. analysis (see Table). In the case of the 21β-hydroxy-compounds

^{1}H N.m.r. spectra (δ values)

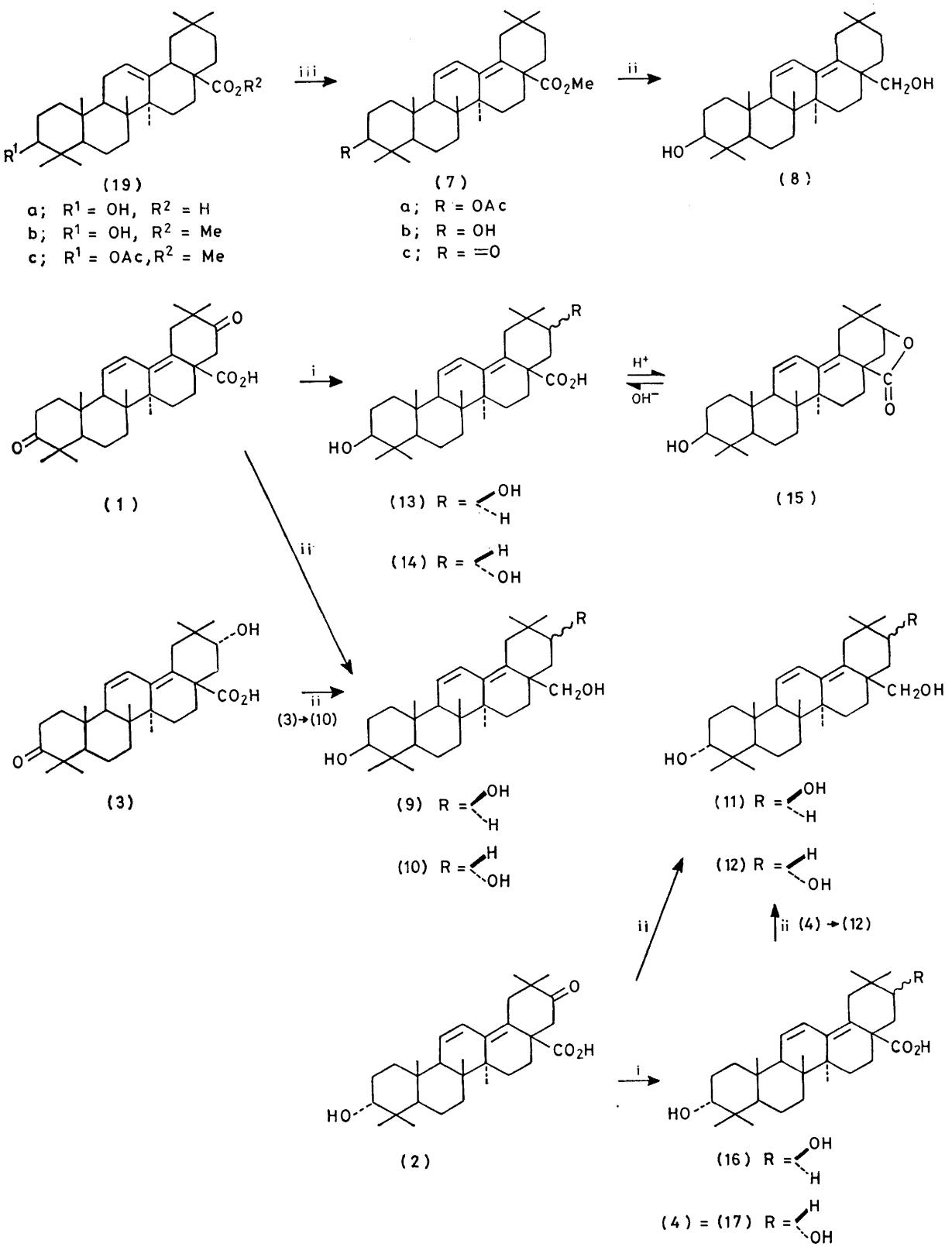
Compd.	3-H (*J*/Hz)	21-H (*J*/Hz)	28-H$_2$ (*J*/Hz)	
(2) *	3.46br (s, 6) ‡			
(3)		4.04 (dd, 10,6)		
(4)	3.65br (s, 6)	4.00 (dd, 10,6)		
(5) *	3.42br (s, 6)			
(6) *	3.46br (s, 6)	4.28 (s)		
(8) †	3.48 (dd, 9,8)		3.73 (d, 10)	4.05 (d, 10)
(9)	3.48 (dd, 10,6)	3.71br (s, 6)	3.80 (d, 12)	4.34 (d, 12)
(10)	3.50 (dd, 10,6)	4.15 (dd, 9,5)	3.82 (d, 12)	4.08 (d, 12)
(11)	3.64br (s, 6)	3.70br (s, 6)	3.76 (d, 12)	4.28 (d, 12)
(12)	3.62br (s, 6)	4.12 (dd, 10,5)	3.78 (d, 12)	4.08 (d, 12)
(13)	3.48 (dd, 9,8)	3.72br (s, 6)		
(14)	3.48 (dd, 9,8)	4.08 (dd, 12,4)		
(15) *	3.20 (dd, 9,6)	4.16 (d, 8)		
(16)	3.62br (s, 6)	3.70br (s, 6)		

* In $CDCl_3$. † In CD_3OD. ‡ For broad signals, numbers in parentheses are $W_{\frac{1}{2}}$ values.

(9) and (11) considerable differences in the chemical shifts (Δ δ values 0.54 and 0.52 p.p.m.) for the C-28 methylene protons were observed, compared with those for the 21α-hydroxy-compounds (10) and (12) and compound (8) (Δ δ 0.26, 0.30, and 0.32 p.p.m.). This fact is explained by the existence of a hydrogen bond between the 21β- and 28-hydroxy-groups, which fixes the orientation of the C-28 methylene protons and puts one of them in the deshielding region of a double bond. These four isomers can be separated by h.p.l.c. according to their polarity (Figure).

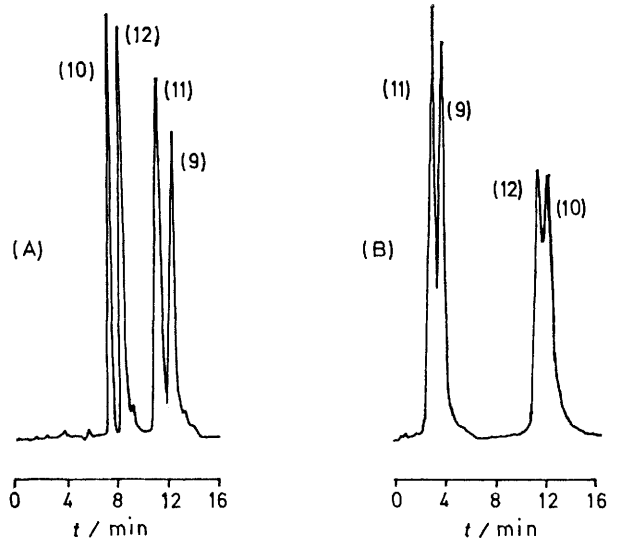
The reduction of papyriogenin D afforded a single compound, which was identical with compound (10) in all respects, and the reduction of papyriogenin E gave a single compound (12).

(2) *Reduction with Sodium Borohydride.*—Papyriogenin A was treated with sodium borohydride to give two compounds (13) and (14), one of which was easily converted into (15) by the action of acid. Because of the similar polarity of compounds (13) and (14) separation was very difficult, but was performed on silica gel after the conversion into (15). Compound (15) exhibits a five membered lactone absorption (1 755 cm^{-1}) in the i.r. spectrum and ^{1}H n.m.r. signals at δ 3.20 (dd, *J* 9 and



Reagents: i, sodium borohydride; ii, lithium aluminium hydride; iii, selenium oxide

6 Hz, 3α-H) and δ 4.16 [d, *J* 8 Hz, 21α-H, 22β-H (dihedral angle between 21α- and 22α-H *ca.* 90°)]. It gave the starting compound when treated with alkali. Therefore, this compound is 3β-hydroxyoleana-11,13(18)-dieno-21β-28-lactone. The isomeric diols (13) and (14) were identified as 3β,21β- and 3β,21α-dihydroxyoleana-11,13-(18)-dien-28-oic acid, respectively, by analogy with the results for the reduction with lithium aluminium hydride and by analysis of the ^{1}H n.m.r. spectra. Papyriogenin C was also reduced by sodium borohydride to give the isomeric diols (16) and (17), which were separated by preparative t.l.c. and identified by ^{1}H n.m.r. analysis. Because of a shortage of the starting material, (16) and (17) were not obtained crystalline; they were identified as 3α-21β- and 3α,21α-dihydroxyoleana-11,13(18)-dien-28-oic acid by ^{1}H n.m.r. analysis. Compound (17) shows

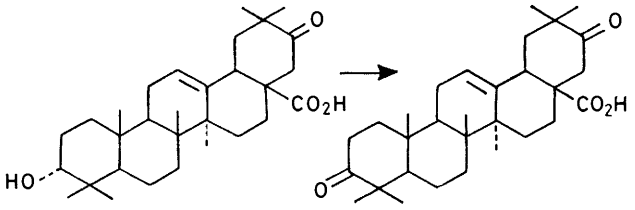


H.p.l.c. separation of compounds (9)—(12): (A), column, Zorbax ODS (15 cm × 4.2 nm), mobile phase, 2% acetic acid in water–acetonitrile (25 : 75), flow rate, 0.6 ml min^{-1} (pressure 30 kg cm^{-2}), injection, 1 μl, detection wavelength 254 nm; (B), column, Zorbax SIL (25 cm × 2.1 nm), mobile phase, 5% propan-2-ol in n-hexane; flow rate, 0.6 ml min^{-1} (pressure 75 kg cm^{-2}), injection, 1 μl, detection wavelength, 254 nm

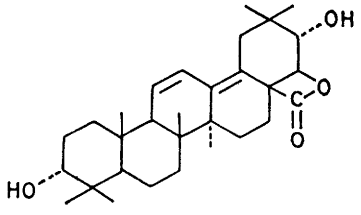
the same R_F value on t.l.c. and ^{1}H n.m.r. spectrum as papyriogenin E.

Thus, the structures of papyriogenin D and E were confirmed chemically.

Papyriogenin F (5), $C_{30}H_{46}O_4$, which showed almost the same R_F value on t.l.c. as papyriogenin A and was separated by pre-packed column chromatography of silica gel, was assigned structure (5) on the basis of the following evidence. This compound exhibits carbonyl (1 705 cm^{-1}) and carboxy (1 730 cm^{-1}) absorptions in the i.r. spectrum, u.v. end absorption only, ^{1}H n.m.r. signals for a olefinic proton at δ 5.42br (s, $W_{1/2}$ 8 Hz) and an equatorial proton geminal to a hydroxy-group at δ 3.42br (s, $W_{1/2}$ 6 Hz), and the fragment ions $C_{16}H_{22}O_3$ (*m/e* 262, 53%) and $C_{14}H_{24}O$ [*m/e* 208, 32%, coupled with *m/e* 190, 100% (assumed to be derived by elimination of an axial hydroxy-group by dehydration)], produced by retro-Diels–Alder cleavage, in the mass spectrum. These results and biogenetic considerations suggest that the structure of papyriogenin F is 3α-hydroxy-21-oxo-olean-12-en-28-oic acid (5).[4] Finally, to confirm the position of the functional groups, papyriogenin F was oxidized with chromium(III) oxide–pyridine to give the



(5) (18)



(6)

diketone compound (18), which was identical with a compound derived from papyrioside L-IIa.[1]

Papyriogenin G (6), $C_{30}H_{44}O_4$, exhibits one unusually high frequency i.r. carbonyl absorption (1 828 cm^{-1}), strong u.v. absorption at 248, 256, and 264 nm characteristic of a heteroannular diene, ^{1}H n.m.r. signals for olefinic protons, δ 5.81 (dd, *J* 10 and 3 Hz) and 6.46 (d, *J* 10 Hz), for three protons geminal to oxygen functions, δ 3.46br (s, $W_{1/2}$ 6 Hz), 4.22 (s-like), and 4.28 (s-like), and a molecular ion (*m/e* 468) and two strong fragment ions [*m/e* 424 (30%, loss of CO_2) and 406 (100%, loss of CO_2 and H_2O)] in the mass spectrum. Papyriogenin G was treated with acetic anhydride–pyridine to afford a diacetate whose ^{1}H n.m.r. spectrum revealed a downfield shift of two protons [δ 3.46 ⟶ δ 4.71 and 4.22 ⟶ 5.04 (d, *J* 3 Hz)] and a doublet at δ 4.26 (*J* 3 Hz). From these data and biogenetic considerations structure (5), 3α,21α-dihydroxyoleana-11,13(18)dieno-22β,28-lactone, was assigned to papyriogenin G. This has been confirmed by *X*-ray analysis.[5]

Finally, it is interesting that all the naturally occurring triterpenoids described here have α-hydroxy-groups at C-3 and -21.

EXPERIMENTAL

M.p.s were measured with a Yanagimoto microapparatus. Unless otherwise stated, u.v. spectra were taken for solutions in chloroform, i.r. spectra for KBr discs, optical rotations for solutions in chloroform, c.d. data for solutions in chloroform, and n.m.r. spectra for solutions in deuteriopyridine.

Isolation of Papyriogenins C (2), *D* (3), *E* (4), *F* (5), *and G* (6).—Fresh leaves of *Tetrapanax papyriferum* (4.4 kg) were

extracted with ether at room temperature. After the removal of chlorophyll on active charcoal, the ether extracts (450 g) were chromatographed on silica gel [solvent, $CHCl_3$–MeOH (10 : 1); in each fraction eluate (1 l) was collected] to give fractions A (45.5 g) and B (15.0 g). Fraction A was repeatedly chromatographed on silica gel (solvent, $CHCl_3$) to give (6) (194 mg, 0.004%), (5) (187 mg, 0.004%), and papyriogenin A (1) (10.6 g, 0.24%). Fraction B was chromatographed on silica gel [solvent, $CHCl_3$–MeOH (100 : 1)] to give papyriogenin C (2) (937 mg, 0.021%) and a mixture of (3) and (4) (780 mg). The mixture was chromatographed again on silica gel [solvent, $CHCl_3$–MeOH (20 : 1)] to give (3) (352 mg, 0.008%) and (4) (396 mg, 0.009%).

Papyriogenin D (3) was obtained from methanol as prisms, m.p. 285—287°, $[\alpha]_D$ −183° (*c* 0.06 in pyridine), $\lambda_{max.}$ 243, 251 (ε 18 000), and 260 nm, $\nu_{max.}$ 3 400, 1 715, 1 690, and 1 625 cm^{-1}, *m/e* 468 (M^+) and 450, δ 0.90 (3 H, s), 0.96 (6 H, s), 1.06 (3 H, s), 1.20 (6 H, s), 1.28 (3 H, s), 4.04 (1 H, dd, *J* 10 and 6 Hz), 5.75 (1 H, d, *J* 11 Hz), and 6.51 (1 H, dd, *J* 11 and 3 Hz) (Found: C, 76.6; H, 9.7. $C_{30}H_{44}O_4$ requires C, 76.9; H, 9.45%); monoacetate (acetylated by acetic anhydride–pyridine; because of a shortage of sample, only the ^1H n.m.r. and mass spectra were taken), *m/e* 510 (M^+), δ ($CDCl_3$) 0.84 (3 H, s), 0.98 (3 H, s), 1.04br (9 H, s), 1.10 (3 H, s), 1.26 (3 H, s), 2.03 (3 H, s), 4.80 (1 H, t-like), 5.66 (1 H, d, *J* 10 Hz), and 6.48 (1 H, dd, *J* 10 and 3 Hz).

Papyriogenin E (4) was obtained from methanol as prisms, m.p. 286—288° $[\alpha]_D$ −207° (*c* 0.06 in pyridine), $\lambda_{max.}$ 242 and 249 nm (ε 24 000), $\nu_{max.}$ 3 410, 1 705, and 1 630 cm^{-1}, *m/e* 470 (M^+) and 452, δ 0.88 (3 H, s), 1.00 (3 H, s), 1.06 (6 H, s), 1.20 (6 H, s), 1.26 (3 H, s), 3.65br (1 H, s, $W_{1/2}$ 6 Hz), 4.00 (1 H, dd, *J* 10 and 6 Hz), 5.75 (1 H, d, *J* 10 Hz), and 6.79 (1 H, dd, *J* 10 and 3 Hz) (Found: C, 76.25; H, 9.95. $C_{30}H_{46}O_4$ requires C, 76.55; H, 9.85%); diacetate, *m/e* 554 (M^+), δ ($CDCl_3$) 0.86 (6 H, s), 0.90 (3 H, s), 0.96 (6 H, s), 1.04 (3 H, s), 1.27 (3 H, s), 2.05 (3 H, s), 2.09 (3 H, s), 4.59br (1 H, s, $W_{1/2}$ 6 Hz), 4.90 (1 H, dd, *J* 9 and 6 Hz), 5.72 (1 H, *J* 10 Hz), and 6.46 (1 H, dd, *J* 10 and 3 Hz).

Papyriogenin F (5) was obtained from methanol as prisms, m.p. 275—277°, $[\alpha]_D$ +73° (*c* 0.05), $\nu_{max.}$ 3 400, 1 730sh, 1 705, and 1 630 cm^{-1}, c.d. $[\theta]_{304}$ −6 700, δ ($CDCl_3$) 0.76 (3 H, s), 0.84 (3 H, s), 0.96 (3 H, s), 1.03 (3 H, s), 1.14 (3 H, s), 1.27 (6 H, s), 3.28 (1 H, dd, *J* 14 and 3 Hz, 18β-H), 3.42br (1 H, s, $W_{1/2}$ 6 Hz), and 5.42br (1 H, s, *J* 8 Hz) (Found: C, 76.15; H, 9.7. $C_{30}H_{46}O_4$ requires C, 76.55; H, 9.85%).

Papyriogenin G (6) was obtained from methanol as prisms, m.p. 188—190°, $[\alpha]_D$ −196° (*c* 0.04), c.d. $[\theta]_{270}$ −50 200, $\lambda_{max.}$ 248, 256 (ε 23 400), and 264 nm, $\nu_{max.}$ 3 510, 3 400, and 1 828 cm^{-1}, *m/e* 468 (M^+) and 450, δ ($CDCl_3$) 0.68 (3 H, s), 0.85 (3 H, s), 0.91 (3 H, s), 0.97 (3 H, s), 1.06 (3 H, (s, 1.09 (3 H, s), 1.26 (3 H, s), 3.46br (1 H, s, $W_{1/2}$ 6 Hz), 4.22 (1 H, s-like), 4.28 (1 H, s-like), 5.81 (d, *J* 10 Hz), and 6.46 (1 H, dd, *J* 10 and 3 Hz) (Found: C, 75.15; H, 9.15. $C_{30}H_{44}O_4,H_2O$ requires C, 75.45; H, 9.5%); diacetate, m.p. 193—195° (from MeOH–$ChCl_3$), $\nu_{max.}$ 1 822, 1 748, and 1 732 cm^{-1}, δ ($CDCl_3$) 0.75 (3 H, s), 0.88 (6 H, s), 0.92 (3 H, s), 0.95 (3 H, s), 1.04 (6 H, s), 2.10 (3 H, s), 2.15 (3 H, s), 4.26 (1 H, d, *J* 3 Hz), 4.71br (1 H, s, $W_{1/2}$ 6 Hz), 5.04 (1 H, d, *J* 3 Hz), 5.81 (1 H, d, *J* 10 Hz), and 6.46 (1 H, dd, *J* 10 and 3 Hz) (Found: C, 73.9; H, 8.7. $C_{34}H_{48}O_6$ requires C, 73.9; H, 8.8%).

Synthesis of Methyl Olean-3-oxo-11,13(18)-dien-28-olate (7c).—(a) Oleanolic acid (19a) (1.2 g) was methylated with diazomethane followed by acetylation (acetic, anhydride–pyridine) to afford methyl olean-3β-hydroxy-12-en-28-olate (19c) (1.3 g), m.p. 218—220°, $\nu_{max.}$ 1 730 and 1 725 cm^{-1}, δ ($CDCl_3$) 0.75 (3 H, s), 0.87 (6 H, s), 0.90 (3 H, s), 0.93 (6 H, s), 1.13 (3 H, s), 2.03 (3 H, s), 3.62 (3 H, s), 4.50 (1 H, t-like), and 5.30br (1 H, s) (Found: C, 77.3; H, 10.2. Calc. for $C_{33}H_{52}O_4$: C, 77.3; H, 10.0%).

(b) [3] The hydroxy-ester (19c) (1.3 g) was oxidized with selenium oxide (1.5 g) in glacial acetic acid (75 ml) (refluxed for 2 h) followed by basic hydrolysis with 3% potassium hydroxide–ethanol (50 ml) and water (20 ml) (refluxed for 2 h) to afford *methyl olean-3β-hydroxy-11,13(18)-dien-28-olate* (7b) (550 mg), needles from methanol, m.p. 172—174°, $\lambda_{max.}$ 247, 252 (ε 41 000), and 262 nm, $\nu_{max.}$ 1 725 cm^{-1}, *m/e* 468 (M^+), δ ($CDCl_3$) 0.80 (9 H, s), 0.92 (6 H, s), 0.96 (3 H, s), 0.98 (3 H, s), 3.68 (3 H, s), 3.22 (1 H, t-like, 3-H), 5.62 (1 H, d, *J* 10 Hz, 11-H), and 6.48 (1 H, dd, *J* 10 and 3 Hz, 12-H) (Found: C, 77.65; H, 10.15, $C_{31}H_{48}O_3,1/2H_2O$ requires C, 77.95; H, 10.35%).

(c) Compound (7b) (550 mg) was oxidized with chromium(III) oxide (0.8 g) in pyridine (40 ml) for 20 min at room temperature and worked up as usual to afford *methyl olean-3-oxo-11,13(18)-dien-28-olate* (7c), needles from methanol, m.p. 191—192°, $\lambda_{max.}$ 247, 252 (ε 31 000), and 262 nm, $\nu_{max.}$ 1 720 and 1 705 cm^{-1}, δ ($CDCl_3$) 0.80 (3 H, s), 0.82 (3 H, s), 0.92 (3 H, s), 0.97 (3 H, s), 1.03 (3 H, s), 1.10 (3 H, s), 3.67 (3 H, s), 5.60 (1 H, d, *J* 10 Hz, 11-H), and 6.45 (1 H, dd, *J* 10 and 3 Hz, 12-H) (Found: C, 80.0; H, 9.65. $C_{31}H_{46}O_3$ requires C, 79.8; H, 9.95%).

Reduction of Compounds (7c) *and* (1)—(4) *with Lithium Aluminium Hydride.*—(a) Compound (7c) (20 mg) was methylated with diazomethane and a mixture of the methyl ester and $LiAlH_4$ (10 mg) in tetrahydrofuran (5 ml) was set aside overnight. The excess of the reagent was decomposed with water and the mixture was extracted with ether. The extract was dried (Na_2SO_4) and evaporated and the residue was crystallized from methanol to afford 3β-28-*dihydroxyoleana-11,13(18)diene* (8) (12 mg), m.p. 256—258°, δ (CD_3OD) 0.83 (3 H, s), 0.89 (3 H, s), 0.98 (6 H, s), 1.02 (3 H, s), 1.09 (3 H, s), 1.23 (3 H, s), 3.48 (1 H, dd, *J* 8 and 9 Hz), 3.73 (1 H, d, *J* 10 Hz), 4.05 (1 H, d, *J* 10 Hz), 5.72 (1 H, d, *J* 9 Hz), and 6.61 (1 H, dd, *J*, 9 and 2 Hz) (Found: C, 78.1; H, 11.0 $C_{30}H_{48}O_2,H_2O$ requires C, 78.55; H, 11.0%).

(b) Compound (1) (200 mg) was worked up as in (a) and the products were chromatographed on silica gel [solvent, $CHCl_3$–MeOH (50 : 1)] to afford 3β,21β,28-*trihydroxy-oleana-11,13(18)diene* (9) (25 mg), plates from methanol, m.p. >300°, $\nu_{max.}$ 3 390 and 1 620 cm^{-1}, *m/e* 456 (M^+) and 438, δ 0.83 (3 H, s), 0.98 (6 H, s), 1.04 (3 H, s), 1.11 (3 H, s), 1.25 (6 H, s), 3.48 (1 H, dd, *J* 10 and 6 Hz), 3.71br (1 H, s, $W_{1/2}$ 6 Hz), 3.80 (1 H, d, *J* 12 Hz), 4.34 (1 H, d, *J* 12 Hz), 5.75 (1 H, d, *J* 11 Hz), and 6.70 (1 H, dd, *J* 11 and 2 Hz) (Found: C, 78.7; H, 10.5. $C_{30}H_{48}O_3$ requires C, 78.9; H, 10.6%), and the 3β, 21α, 28-*triol* (10) (30 mg), plates from methanol, m.p. 291—293°, $\nu_{max.}$ 3 390 and 1 620 cm^{-1}, *m/e* 456 (M^+), δ 0.80 (3 H, s), 0.96 (3 H, s), 0.98 (3 H, s), 1.04 (3 H, s), 1.07 (3 H, s), 1.20 (3 H, s), 1.22 (3 H, s), 3.50 (1 H, dd, *J* 10 and 6 Hz), 4.15 (1 H, dd, *J* 9 and 5 Hz), 3.82 (1 H, d, *J* 12 Hz), 4.08 (1 H, d, *J* 12 Hz), 5.77 (1 H, d, *J* 11 Hz), and 6.60 (1 H, dd, *J* 11 and 2 Hz) (Found: C, 78.7; H, 10.55. $C_{30}H_{48}O_3$ requires C, 78.9; H, 10.6%).

(c) Compound (2) (63 mg) was worked up as in (a) and purified by preparative t.l.c. [solvent, $CHCl_3$–MeOH (10 : 1)]

to afford 3α,21β,28-*trihydroxyoleana*-11,13(18)*diene* (11) (8 mg), fine needles from methanol, m.p. 288—290°, $\lambda_{max.}$ 242, 251 (ε 15 000), and 260 nm, $\nu_{max.}$ 3 350 and 1 645 cm^{-1}, *m/e* 456 (M^+) and 438, δ 0.80 (3 H, s), 0.89 (3 H, s), 0.92 (3 H, s), 0.98 (6 H, s), 1.20 (3 H, s), 1.22 (3 H, s), 3.64br (1 H, s, $W_{1/2}$ 6 Hz), 3.70br (1 H, s, $W_{1/2}$ 6 Hz), 3.76 (1 H, d, *J* 12 Hz), 4.28 (1 H, d, *J* 12 Hz), 5.75 (1 H, d, *J* 9 Hz), and 6.66 (1 H, dd, *J* 9 and 3 Hz) (Found: M^+, 456.365 0. $C_{30}H_{48}O_3$ requires *M*, 456.360 3), and the 3α,21α,28-*triol* (12) (18 mg), needles from methanol, m.p. 277—279°, $\nu_{max.}$ 3 400 and 1 640 cm^{-1}, δ 0.84 (3 H, s), 0.90 (3 H, s), 1.00 (6 H, s), 1.06 (3 H, s), 1.20 (3 H, s), 1.25 (3 H, s), 3.62br (1 H, s, $W_{1/2}$ 6 Hz), 3.78 (1 H, d, *J* 12 Hz), 4.08 (1 H, d, *J* 12 Hz), 4.12 (1 H, dd, *J* 10 and 5 Hz), 5.78 (1 H, d, *J* 10 Hz), and 6.67 (1 H, d, *J* 10 and 3 Hz) (Found: C, 78.95; H, 10.35. $C_{30}H_{48}O_3$ requires C, 78.9; H, 10.6%).

(d) Compound (3) (20 mg) was worked up as in (a) to afford compound (10) (13.6 mg), m.p. 292—294° (Found: C, 78.7; H, 10.55. Calc. for $C_{30}H_{48}O_3$: C, 78.9; H, 10.6%) (identified by mixed m.p., h.p.l.c., and i.r. and n.m.r. spectra).

(e) Compound (4) (18 mg) was worked up as in (a) to afford compound (12) (15 mg), m.p. 278—279° (Found: C, 78.75; H, 10.6. Calc. for $C_{30}H_{48}O_3$: C, 78.9; H, 10.6%) (identified by mixed m.p., h.p.l.c., and i.r. and n.m.r. spectra).

Reduction of Compounds (1) *and* (2) *with Sodium Borohydride.*—(a) A mixture of (1) (350 mg) and $NaBH_4$ (200 mg) in methanol (15 ml) was set aside overnight at room temperature. The excess of reagent was decomposed with dilute hydrochloric acid and the mixture was extracted with ether. The extract was concentrated and development on t.l.c. [solvent, $CHCl_3$–MeOH (30 : 1)] showed two compounds (13) (higher R_F) and (14) (lower R_F). Without further purification, the mixture was dissolved in dioxan (50 ml) and 2N-hydrochloric acid (10 ml) and warmed at 80° for 30 min. The solution was evaporated to dryness at 50° and the residue was chromatographed on silica gel [$CHCl_3$–MeOH (20 : 1)] to afford 3β-*hydroxyoleana*-11,13(18)-*dieno*-21β,28-*lactone* (15) (184 mg), plates from methanol, m.p. 280—282°, c.d. $[\theta]_{283}$ −9 600, $\nu_{max.}$ 3 400, 1 765, and 1 750 cm^{-1}, δ ($CDCl_3$) 0.72 (3 H, s), 0.76 (3 H, s), 0.89 (3 H, s), 0.96 (3 H, s), 1.00 (6 H, s), 1.08 (3 H, s), 3.20 (1 H, dd, *J* 9 and 6 Hz), 4.16 (1 H, d, *J* 8 Hz), 5.64 (1 H, d, *J* 10 Hz), and 6.25 (1 H, dd, *J* 10 and 3 Hz), *m/e* 452 (M^+, 100%) and 408 (40) (Found: C, 79.5; H, 9.8. $C_{30}H_{44}O_4$ requires C, 79.6; H, 9.8%) and 3β-21α-*dihydroxyoleana*-11,13(18)-*dien*-28-*oic acid* (14) (32 mg), needles from methanol, m.p. >300°, $\nu_{max.}$ 3 480, 1 700, and 1 615 cm^{-1}, δ 1.00br (9 H, s), 1.10 (3 H, s), 1.13 (3 H, s), 1.24 (3 H, s), 1.26 (3 H, s), 3.48 (1 H, dd, *J* 9 and 8 Hz), 3.72br (1 H, s), 5.82 (1 H, d, *J* 10 Hz), and 6.78 (1 H, dd, *J* 10 and 3 Hz) (Found: C, 73.3; H, 10.2, $C_{30}H_{46}O_4,H_2O$ requires C, 73.7; H, 9.9%).

Compound (15) was dissolved in N-sodium hydroxide–methanol (1 : 1 v/v) and refluxed for a few minutes. The solution was neutralized with dilute acid, extracted with ether, and treated as usual to afford 3β,21β-*dihydroxyoleana*-11,13(18)-*dien*-28-*oic acid* (13) quantitatively, needles from methanol, m.p. 269—272°, $\nu_{max.}$ 3 450, 1 700, and 1 615 cm^{-1}, δ 1.06 (6 H, s), 1.16br (9 H, s), 1.28 (6 H, s), 3.48 (1 H, dd, *J* 9 and 8 Hz), 4.08 (1 H, dd, *J* 12 and 4 Hz), 5.82 (1 H, d, *J* 10 Hz), and 6.74 (1 H, dd, *J* 10 and 3 Hz) (Found: C, 76.2; H, 9.8, $C_{30}H_{46}O_4$ requires C, 76.55; H, 9.85%).

(b) Compound (2) (20 mg) was worked up as in (a) and the reaction mixture was purified by preparative t.l.c. to afford 3α,21β-dihydroxyoleana-11,13(18)-dien-28-oic acid (16) (7 mg), not crystalline, *m/e* 470 (M^+), δ 0.90 (3 H, s), 0.95 (3 H, s), 1.02 (6 H, s), 1.10 (3 H, s), 1.20 (3 H, s), 1.24 (3 H, s), 3.62br (1 H, s, $W_{1/2}$ 6 Hz), 3.70br (1 H, s, $W_{1/2}$ 6 Hz), 5.84 (1 H, d, *J* 10 Hz), and 6.78 (1 H, dd, *J* 10 and 3 Hz) and compound (17) (3 mg), not crystalline), identical with papyriogenin E (t.l.c. and n.m.r. spectrum).

Oxidation of Compound (5) with *Chromium*(III) *Oxide–Pyridine.*—To a stirred solution of chromium(III) oxide (50 mg) in pyridine (5 ml), a solution of compound (5) (50 mg) in pyridine (5 ml) was added. The mixture was stirred for 2 h at room temperature. Water was added and the mixture was extracted with ether. The organic layer was washed with water, dried, and evaporated. The residue (40 mg) was crystallized from methanol to afford 3,21-dioxo-olean-12-en-28-oic acid (18) (13 mg), m.p. 265—267°, $\nu_{max.}$ 3 380, 1 730, 1 708, and 1 690 cm^{-1}, c.d. $[\theta]_{300}$ −7 700 and $[\theta]_{293}$ 7 600 (Found: C, 76.9; H, 9.6. Calc. for $C_{30}H_{44}O_4$: C, 76.9; H, 9.45%), identical with an authentic specimen [1] (mixed m.p. and i.r. and n.m.r. spectra).

H.p.l.c.—The conditions for h.p.l.c. are described in the Figure. A Shimadzu model LC-2 system with a Shimadzu model SPD-1 detector was used.

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REFERENCES

[1] M. Takai, S. Amagaya, and Y. Ogihara, *J.C.S. Perkin I*, 1977, 1801.
[2] S. Amagaya, T. Takeda, Y. Ogihara, and K. Yamasaki, *J.C.S. Perkin I*, 1979, 2044.
[3] T. Kubota and F. Tonami, *Tetrahedron*, 1967, **23**, 3353.
[4] C. Djerassi and A. E. Lippman, *J. Amer. Chem. Soc.*, 1955, **77**, 1825.
[5] Y. Ogihara and M. Asada, *J.C.S. Chem. Comm.*, 1978, 364.