On the Reported Transformation of β-Amyrin into Oleanolic Acid

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Reduction of 3β-acetoxy-12α,13α-epoxyoleanan-3β-yl acetate (β-amyrin acetate epoxide) (5) with lithium–ethylamine affords β-amyrin (17%), oleanane-3β,12α-diol (3 ; $R^1 = R^2 = H$) (50%) and 13α-oleanane-3β,12α-diol (6 ; $R^1 = R^2 = H$) (27%). On photolysis 3β-acetoxyoleanan-12α-yl nitrite (3 ; $R^1 = Ac$, $R^2 = NO$) affords the 27-oxime (10), which has been further transformed into the aldehyde (9 ; $R^1 = H$, $R^2 = OH$) and the corresponding lactone (11 ; $R^1R^2 = O$). The latter had previously been identified erroneously as oleanolic lactone acetate (12 ; $R^1 = Ac$, $R^2R^3 = O$).

REDUCTION of 3β-acetoxyoleanan-12-one (1 ; $R^1 = OAc$, $R^2 = H$) with sodium borodeuteride gave 3β-acetoxy-[12-^{2}H]oleanan-12β-ol (2 ; $R^1 = Ac$, $R^2 = H$) and -12α-ol (3 ; $R^1 = Ac$, $R^2 = H$) (each 90% $^2H_1$). Treatment of either alcohol with methanesulphonyl chloride in pyridine afforded 3β-acetoxy[12-^{2}H]olean-12-ene (β-amyrin acetate) (4). With the 12α-alcohol (3 ; $R^1 = Ac$, $R^2 = H$) the dehydration was much more rapid, but a considerable loss of deuterium occurred (Scheme). No such loss was observed with the 12β-alcohol (2 ; $R^1 = Ac$, $R^2 = H$). The β-amyrin acetate thus obtained (89% $^2H_1$) was treated with *p*-nitroperbenzoic acid to give a 12,13-epoxide. Rearrangement of this epoxide by using boron trifluoride–diethyl ether complex afforded 3β-acetoxyoleanan-12-one (1 ; $R^1 = OAc$, $R^2 = H$) which retained most of the deuterium (66% $^2H_1$). The simplest rationalisation of these results is that the epoxy-group has the 12α,13α-configuration (5).

In the light of the above observations (by D. A., H. G. B., and R. G.), we undertook a reinvestigation of the previously claimed partial synthesis of oleanolic acid,[1] which was based on the belief that the epoxy-group in (5) had a 12β,13β-configuration.

Treatment of β-amyrin acetate (4) with an excess of perbenzoic acid by the procedure detailed in the Experimental section constitutes a reliable route to a pure 12,13-epoxide (5), m.p. 244—245°, $[\alpha]_D$ +30°. The 12α,13α-configuration of the epoxide was confirmed by identification of the products obtained from reduction with lithium in ethylamine. The major product (50%) was a diol, m.p. 231—233°, $[\alpha]_D$ +37°, which on treatment with acetic anhydride in pyridine at room temperature afforded a monoacetate, m.p. 274—275°, $[\alpha]_D$ +49°. It had previously been concluded, on the basis of resistance to acetylation and the reported transformation into oleanolic acid, that the latter compound was 3β-acetoxyoleanan-13β-ol.[1] The true identity of the compound as 3β-acetoxyoleanan-12α-ol (3 ; $R^1 = Ac$, $R^2 = H$) became evident following oxidation with chromic acid to give 3β-acetoxyoleanan-12-one (1 ; $R^1 = OAc$, $R^2 = H$), identical with an authentic sample. The configuration at C-12 follows from the position and half-width[2] of the n.m.r. signal

for the 12-proton (see Table 1). A second reduction product (17%) was readily identified as β-amyrin.
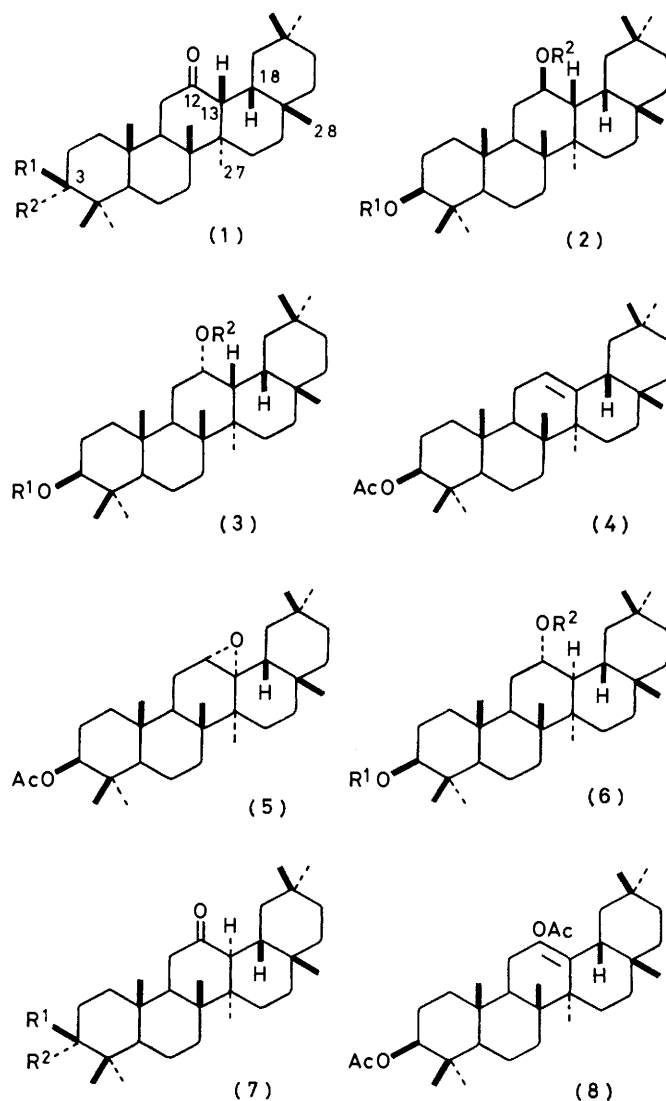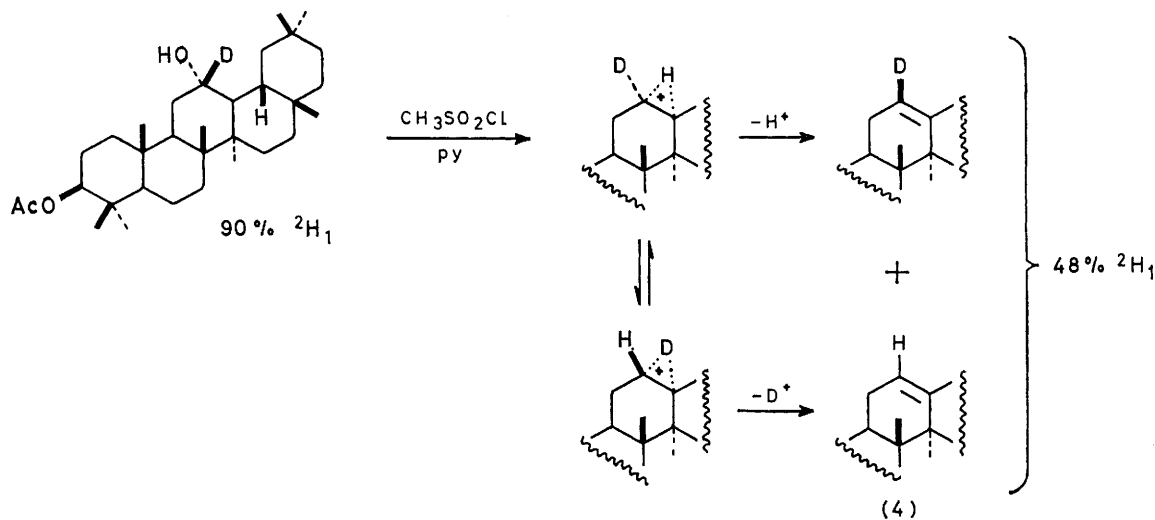

The remaining product (27%) was a diol (6 ; $R^1 = R^2 = H$), m.p. 241—243°, which with acetic anhydride in pyridine at room temperature gave a diacetate, m.p. 204—206°, $[\alpha]_D$ +55°. Comparison with an authentic sample indicated that this diol was not oleanane-

[1] R. B. Boar, D. C. Knight, J. F. McGhie, and D. H. R. Barton, *J. Chem. Soc.* (C), 1970, 678.

[2] N. S. Bhacca and D. H. Williams, 'Applications of NMR Spectroscopy in Organic Chemistry.' Holden–Day, San Francisco, 1964.

3β,12β-diol (2; $R^1 = R^2 = H$).[3] That the new diol had the 13α-configuration was established as follows. First, oxidation with chromic acid afforded the 13α-diketone (7; $R^1R^2 = O$), m.p. 172—176°, $[α]_D$ +115°,

OAc, $R^2 = H$), m.p. 287—289°, $[α]_D$ —11.5°. Treatment of either oxo-acetate (1 or 7; $R^1 = OAc$, $R^2 = H$) with sodium acetate in refluxing acetic anhydride gave the same enol acetate (8).[5] The half-widths of the

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which on treatment with boron trifluoride–diethyl ether complex in benzene isomerised to the more stable 13β-diketone (1; $R^1R^2 = O$),[4] m.p. 218—222°, $[α]_D$ —10°. Secondly, chromatography of the diacetate (6; $R^1 = R^2 = Ac$) on a column of alumina gave small amounts

TABLE 1

Resonances for the 12-protons in the ^1H n.m.r. spectra of 3β,12ξ-dioxygenated 13ξ-oleananes

Compound	Config. of 12-H	Config. of 13-H	δ	$W_{\frac{1}{2}}/$ Hz
Oleanane-3β,12β-diol (2; $R^1 = R^2 = H$)	α (ax)	β	3.72	20
Oleanan-12β-ol	α (ax)	β	3.75	18
13α-Oleanane-3β,12β-diol (9; R = H)	α (ax)	α	4.15	19
Oleanane-3β,12α-diol (3; $R^1 = R^2 = H$)	β (eq)	β	3.96	7
3β-Acetoxyoleanan-12α-ol (3; $R^1 = Ac$, $R^2 = H$)	β (eq)	β	3.98	7
Oleanan-12α-ol	β (eq)	β	3.95	8
13α-Oleanane-3β,12α-diol (6; $R^1 = R^2 = H$)	β (eq)	α	4.30	8
3β-Acetoxy-13α-oleanan-12α-ol (6; $R^1 = Ac$, $R^2 = H$)	β (eq)	α	4.29	9
13α-Oleanan-12α-ol	β (eq)	α	4.30	9
3β,12β-Diacetoxyoleanane (2; $R^1 = R^2 = Ac$)	α (ax)	β	4.98	19
3β,12β-Diacetoxy-13α-oleanane (9; R = Ac)	α (ax)	α	5.10	18
3β,12α-Diacetoxy-13α-oleanane (6; $R^1 = R^2 = Ac$)	β (eq)	α	5.40	9

of a monoacetate (6; $R^1 = Ac$, $R^2 = H$), m.p. 237—239°, $[α]_D$ +37°. Oxidation of this monoacetate with chromic acid gave the 13α-oxo-acetate (7; $R^1 = OAc$, $R^2 = H$), m.p. 190—192°, $[α]_D$ +95°, which readily isomerised to the known[3] 13β-compound (1; $R^1 =$

[3] D. H. R. Barton and N. J. Holness, *J. Chem. Soc.*, 1952, 78.
[4] A. Rollett and K. Bratke, *Monatsh.*, 1923, **43**, 685.
[5] E. R. H. Jones and K. J. Verrill, *J. Chem. Soc.*, 1940, 1512.

signals for the 12-protons in the n.m.r. spectra of compounds of general formula (6) (ca. 8—9 Hz; see Table 1) strongly suggest that the oxygen function at C-12 is in the α-configuration.[2] To strengthen this conclusion we prepared the remaining possible 13ξ-3β,12ξ-diol, viz., 13α-oleanane-3β,12β-diol (9; R = H), by reduction of the diketone (7; $R^1R^2 = O$) or the oxo-acetate (7; $R^1 = OAc$, $R^2 = H$) with lithium aluminium hydride. Molecular models indicate that approach of the reductant from the α-side is to be expected. Comparison of the signals for the 12-protons in the n.m.r. spectra of the four possible series of 13ξ-3β,12ξ-dioxygenated oleananes established unambiguously that the individual stereochemistries are as assigned above (see Table 1).

The presence of significant amounts of oleanane-3β,12β-diol (2; $R^1 = R^2 = H$) in the product from reduction of the 12α,13α-epoxide (5) with lithium in ethylamine was invariably traceable to contamination of the starting material by its isomerisation product, 3β-acetoxyoleanan-12-one (1; $R^1 = OAc$, $R^2 = H$) (see Table 2). The epoxide rearranges to the 12-ketone with great ease.

Analogous experiments in the β-amyrene (olean-12-ene)[6] series established that reduction of 12α,13α-epoxyoleanane[7] by lithium in ethylamine results in β-amyrene (13%), oleanan-12α-ol (52%), and 13α-oleanan-12α-ol (33%). Again, comparison with authentic material showed that the pure 12α,13α-epoxide gave no oleanan-12β-ol.

In contrast to the reaction with peroxy-acids, β-amyrin acetate reacted with ozone to afford a crystalline product, m.p. 245—248°, $[α]_D$ +39.6°, shown by ^{13}C

[6] J. Karliner and C. Djerassi, *J. Org. Chem.*, 1966, **31**, 1945.
[7] J. Simonsen and W. C. J. Ross, 'The Terpenes,' vol. IV, University Press, Cambridge, 1957, p. 185.

n.m.r. spectroscopy to be a 6 : 4 mixture of the 12α,13α- and 12β,13β-epoxides. The two epoxides were not separated.

Treatment of the alcohol now known to have structure (3; R^1 = Ac, R^2 = H) with nitrosyl chloride in pyridine gave the nitrite ester (3; R^1 = Ac, R^2 = NO), which was subjected to photolysis under standard conditions.[8] The major product was the oxime (10) (61%), δ 7.52 (27-H). Treatment with nitrous acid then afforded the hemiacetal (11; R^1 = OH, R^2 = H) which was oxidised by chromic acid to the lactone (11; R^1R^2 = O). This is the true structure for the compound previously identified by Dr. D. C. Knight[1] as oleanolic lactone acetate (12; R^1 = Ac, R^2R^3 = O). Reduction of the

(9)

(10)

(11)

(12)

(13)

(14)

(15)
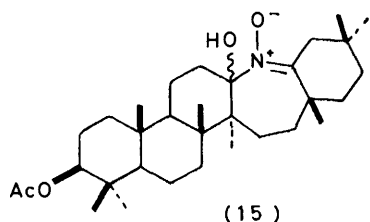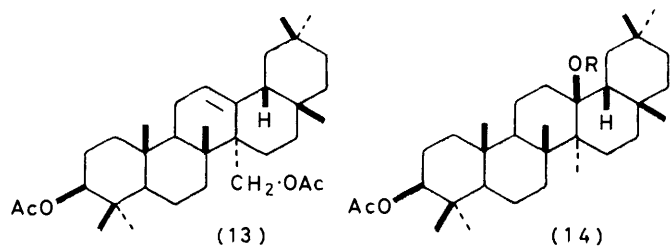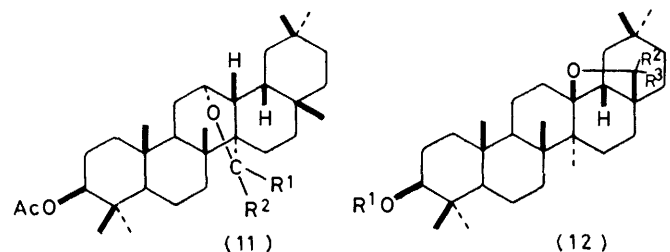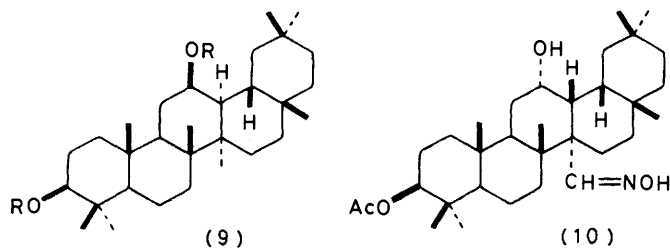
hemiacetal (11; R^1 = OH, R^2 = H) with lithium aluminium hydride in refluxing tetrahydrofuran gave a

triol which at room temperature cleanly formed a 3,27-diacetate. Treatment of the diacetate with methanesulphonyl chloride in pyridine at room temperature gave 3β,27-diacetoxyolean-12-ene (13), which was hydrolysed to the 3β,27-diol. A number of 27-oxygenated olean-12-enes, but so far not this particular one, have been isolated as natural products.[9]

To complete our reinvestigations, we examined the preparation and photolysis of the nitrite ester derived from 3β-acetoxyoleanan-13β-ol (14; R = H). Reduction of oleanolic lactone (prepared from natural oleanolic acid)[3] with di-isobutylaluminium hydride in toluene gave the hemiacetal (12; R^1 = R^2 = H, R^3 = OH). Wolff–Kishner reduction followed by acetylation then afforded the required 3β-acetoxyoleanan-13β-ol (14; R = H). A suspension of the sparingly soluble 13β-alcohol in pyridine was saturated with nitrosyl chloride gas, and the mixture was stirred at room temperature overnight to yield the nitrite (14; R = NO). Photolysis[8] of the nitrite afforded a major product which was not an oxime (n.m.r. spectroscopy), but which showed u.v. absorption at $\lambda_{max.}$ 243 nm (ε 5 000). When a solution of the photolysis product in ethanol was irradiated with a high pressure mercury vapour lamp this u.v. absorption gradually disappeared, only to slowly reappear after irradiation was stopped. Such behaviour is typical of nitrones which, under such conditions, are reversibly converted into oxaziridines.[10] On the basis of this and other spectroscopic evidence, the photolysis product was assigned the structure (15). A previous case in which photolysis of a nitrite ester led to an analogous hydroxy-nitrone has been studied in some detail.[10] The preference of the 13β-alkoxyl radical to collapse with fission of the 13,18-bond, rather than abstract a hydrogen atom from C-28, effectively precludes the possibility of synthesising oleanolic lactone by such a route.

Deuterium labelling studies confirmed that treatment of 3β-acetoxyurs-12-ene (α-amyrin acetate) with ozone gives a 12β,13β-epoxide.[11] The products from the reduction of this epoxide with lithium in ethylamine do not however have the expected, and previously reported[1] structures. Details of this work will be reported separately. We wish therefore also to retract the claim to have achieved a partial synthesis of ursolic acid.[1]

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 reference, and were recorded at 90 MHz (^{1}H) or 100 MHz (^{13}C). Rotations are of solutions in chloroform with c 0.5. Unless otherwise stated, all compounds were crystallised from chloroform–methanol. T.l.c. and p.l.c. plates were prepared using

[8] R. B. Boar, ' Houben–Weyl Methoden der Organischen Chemie; Photochemie,' Band 4/5a, Thieme Verlag, Stuttgart, 1976.

[9] R. B. Boar and J. Allen, Phytochemistry, 1973, 12, 2571.

[10] H. Suginome, T. Mizuguchi, and T. Masamune, J.C.S. Chem. Comm., 1972, 376; H. Suginome, N. Sato, and T. Masamune, Tetrahedron, 1971, 27, 4863.

[11] H. G. Brunner, Ph.D. Dissertation 5859, E.T.H., Zurich, 1976.

Merck silica gel GF$_{254}$. Alumina was Laporte type 0. Light petroleum refers to the fraction of b.p. 60—80 °C.

3β-Acetoxy-12α,13α-epoxyoleanane (5).—3β-Acetoxyolean-12-ene (β-amyrin acetate) (400 mg) in chloroform (5 ml) was treated at 0 °C with an excess of perbenzoic acid in chloroform. After 24 h the solution was poured into 2N-sodium hydroxide. The organic layer was separated, washed with water, dried, and evaporated. Rapid crystallisation of the residue from chloroform–methanol three times or p.l.c. [hexane–ethyl acetate (4 : 1 v/v)] afforded the pure *epoxide*, m.p. 244—245°, $[\alpha]_D$ +30°, δ 0.77, 0.83, 0.85, 0.91, 0.96, 1.00, 1.06, 1.11, and 2.02 (each 3 H, s), 2.97br (1 H, s, $W_{\frac{1}{2}}$ 6 Hz), and 4.5 (1 H, t, 3α-H) (Found: C, 79.15; H, 10.8. $C_{32}H_{52}O_3$ requires C, 79.3; H, 10.8%).

Similarly, olean-12-ene (β-amyrene) gave 12α,13α-epoxy-oleanane, m.p. 181—185°, $[\alpha]_D$ +33°, δ 0.78, 0.80, 0.85, 0.91, 0.94, 1.00, 1.07, and 1.14 (each 3 H, s), and 2.95 (1 H, s, $W_{\frac{1}{2}}$ 4.5 Hz).

crystallised from methylene chloride–methanol; m.p. 245—248°, $[\alpha]_D$ +39°. N.m.r. spectroscopy indicated the product to be a mixture of 3β-acetoxy-12α,13α- and 3β-acetoxy-12β,13β-epoxyoleanane, δ_H(CCl$_4$) 2.86 (0.6 H, 12β-H) and 2.57 (0.4 H, 12α-H), δ_C 65.53 and 53.83 (each d, C-12, -*x* and β-isomer, respectively), and 63.09 and 66.32 (each s, C-13, α- and β-isomer, respectively).

Reduction of 3β-Acetoxy-12α,13α-epoxyoleanane (5) with Lithium in Ethylamine.—Pure, freshly prepared 3β-acetoxy-12α,13α-epoxyoleanane (700 mg) in dry ethylamine (50 ml) was stirred at 0 °C and lithium metal (2 g) was added. The resulting dark blue solution was allowed to reflux at room temperature for 1 h, then cooled to 0 °C, and t-butyl alcohol (25 ml) was added dropwise. After a further 1 h at room temperature an excess of solid ammonium chloride was added, and the mixture was then left overnight for the ethylamine to evaporate off. The residue was treated with water and extracted with ether. The product thus obtained

	Products (%)			
Origin of epoxide reduced	(4)	(3; R¹ = Ac, R² = H)	(6; R¹ = R² = Ac)	(2; R¹ = R² = Ac)
Ref. 1 (London)	29	24		45
As ref. 1; not reduced immediately (Zurich)	23	23	5	43
Freshly prepared; rapidly recrystallised (London)	17	50	27	≤5
Freshly prepared; purified by p.l.c. (Zurich)	25	54	21	0

3β-Acetoxy-12α,13α-epoxy[12-²H]oleanane.— 3β-Acetoxy-oleanan-12-one (1 g) in dioxan (100 ml) and ethanol (100 ml) was stirred under nitrogen with sodium borodeuteride (100 mg) for 3 days at room temperature. 2% Sodium dihydrogen phosphate solution (50 ml) was added, and the mixture was extracted with ether. Chromatography on a column of silica gel (150 g) [benzene–ethyl acetate (93 : 7 v/v)] then gave starting material (75 mg), 3β-acetoxy-[12-²H]olean-12α-ol (600 mg), m.p. 288°, $[\alpha]_D$ +47°, $\nu_{max.}$ (CHCl$_3$) 3 650 cm⁻¹, 91% ²H₁ (mass spectrum), and 3β-acetoxy[12-²H]olean-12β-ol (250 mg), m.p. 282°, $[\alpha]_D$ +24°, $\nu_{max.}$ (CHCl$_3$) 3 605 cm⁻¹, 91% ²H₁ (mass spectrum).

The 12α-alcohol (250 mg) in benzene (20 ml) was treated with methanesulphonyl chloride (2.2 ml) in pyridine (10 ml) for 12 h in a refrigerator. The mixture was poured into water and extracted with ether to yield 3β-acetoxy-[12-²H]olean-12-ene (200 mg), 48% ²H₁ (mass spectrum).

The 12β-alcohol (250 mg) in benzene (20 ml) was heated under reflux with methanesulphonyl chloride (2.2 ml) in pyridine (10 ml) for 48 h to afford 3β-acetoxy[12-²H]olean-12-ene (190 mg), 89% ²H₁ (mass spectrum). This product in ether (50 ml) and chloroform (30 ml) containing *p*-nitro-perbenzoic acid (1.2 g) was kept in the dark for 28 h. Work-up as above and p.l.c. then gave 3β-acetoxy-12α,13α-epoxy[12-²H]oleanane (130 mg), 89% ²H₁ (mass spectrum).

Rearrangement of 3β-Acetoxy-12α,13α-epoxy[12-²H]-oleanane.—Treatment of the [12-²H]epoxide (35 mg) in benzene with boron trifluoride–diethyl ether for 10 min afforded 3β-acetoxy[12-²H]oleanan-12-one, 66% ²H₁ (mass spectrum).

Ozonolysis of 3β-Acetoxyolean-12-ene.—The alkene (4) (2 g) in carbon tetrachloride (80 ml) at 0 °C was treated with a stream of 2% ozone for 30 min. The solution was flushed with nitrogen and evaporated and the residue

was chromatographed on a column of alumina (elution with light petroleum containing increasing proportions of ethyl acetate) to yield olean-12-en-3β-ol (β-amyrin) (17%), identical with an authentic sample, 13α-*oleanane-3β,12α-diol* (27%), m.p. 241—243°, δ 0.78, 0.97, 1.04, and 1.23 (each 3 H, s), 0.88 and 0.95 (each 6 H, s), 3.2 (1 H, t, 3α-H), and 4.30br (1 H, s, $W_{\frac{1}{2}}$ 8 Hz) (Found: C, 80.9; H, 11.8. $C_{30}H_{52}O_2$ requires C, 81.0; H, 11.8%), and oleanane-3β,12α-diol (50%), m.p. 231—233°, $[\alpha]_D$ +37°, δ 0.76, 0.84, 0.86, 0.89, 0.92, 0.97, 1.04, and 1.30 (each 3 H, s), 3.2 (1 H, t, 3α-H), and 3.96br (1 H, s, $W_{\frac{1}{2}}$ 7 Hz). Alternatively, treatment of the total product with acetic anhydride–pyridine at room temperature afforded a similarly separable mixture of β-amyrin acetate, 3β,12α-*diacetoxy-13α-oleanane*, m.p. 204—206°, $[\alpha]_D$ +55°, δ 0.85 (15 H, s), 0.95, 1.06, and 1.19 (each 3 H, s), 2.02 (6 H, s), 4.5 (1 H, t, 3α-H), and 5.4br (1 H, s, $W_{\frac{1}{2}}$ 9 Hz) (Found: C, 76.95; H, 10.6. $C_{34}H_{56}O_4$ requires C, 77.2; H, 10.7%), and 3β-*acetoxy-oleanan-12α-ol*, m.p. 274—275°, $[\alpha]_D$ +49°, δ 0.87 (9 H, s), 0.92 (6 H, s), 0.95, 1.06, 1.32, and 2.02 (each 3 H, s), 3.98br (1 H, s, $W_{\frac{1}{2}}$ 7 Hz), and 4.5 (1 H, t, 3α-H) (Found: C, 79.2; H, 11.2. $C_{32}H_{54}O_3$ requires C, 79.0; H, 11.2%). Treatment of the last-named compound with acetic anhydride in triethylamine containing 4-dimethylaminopyridine (5 mg) for 12 h at room temperature gave 3β,12α-diacetoxy-oleanane, m.p. 167—169°, $[\alpha]_D$ +66°, δ 0.78, 0.95, 1.06, 1.26, and 1.30 (each 3 H, s), 0.88 (9 H, s), 2.05 (6 H, s), 4.5 (1 H, t, 3α-H), and 4.97 (1 H, q, *J* 3 Hz, 12β-H). The presence of significant amounts of oleanane-3β,12β-diol,[3] δ 0.76, 0.88, 0.95, and 1.03 (each 3 H, s), 0.84 and 0.93 (each 6 H, s), 3.2 (1 H, t, 3α-H), and 3.72 (1 H, m, 12α-H), in the above reduction product indicates contamination of the starting 12α,13α-epoxide by 3β-acetoxyoleanan-12-one (see Table 2).

3β-Acetoxy-13α-oleanan-12α-ol (6; R¹ = Ac, R² = H).—

3β,12α-Diacetoxy-13α-oleanane was adsorbed onto a column of alumina and left overnight. Elution then afforded unchanged diacetate followed by small and variable amounts of 3β-acetoxy-13α-oleanan-12α-ol, m.p. 237—239°, $[\alpha]_D$ +37°, δ 0.85 (9 H, s), 0.90, 1.04, 1.22, and 2.03 (each 3 H, s), 0.95 (6 H, s), 4.29br (1 H, s, $W_{\frac{1}{2}}$ 9 Hz), and 4.5 (1 H, t, 3α-H) (Found: C, 79.1; H, 11.1. $C_{32}H_{54}O_3$ requires C, 79.0; H, 11.2%). Identical material was also obtained by treatment of 13α-oleanane-3β,12α-diol with acetic anhydride–pyridine at −10 °C for 4 h, followed by chromatography.

3β-*Acetoxy*-13α-*oleanan*-12-*one* (7; R¹ = OAc, R² = H). —3β-Acetoxy-13α-oleanan-12α-ol (200 mg) in benzene (50 ml) was shaken with Kiliani's chromic acid (10 ml) for 2 h. The mixture was poured into sodium carbonate solution, and the organic layer separated and then further processed to afford 3β-*acetoxy*-13α-*oleanan*-12-*one* (150 mg), m.p. 190—192°, resolidifying and then remelting at 283—285°, $[\alpha]_D$ +95°, δ 0.87 and 0.91 (each 6 H, s), and 0.89, 0.99, 1.00, and 1.21 (each 3 H, s) (Found: C, 79.0; H, 10.65. $C_{32}H_{52}O_3$ requires C, 79.3; H, 10.8%). Treatment of this material with boron trifluoride–diethyl ether in refluxing benzene for 20 min gave 3β-acetoxyoleanan-12-one, m.p. 287—289°, $[\alpha]_D$ −11.5° (lit.,³ m.p. 293—295°, $[\alpha]_D$ −11°), identical with an authentic sample.

3β,12-*Diacetoxyolean*-12-*ene* (8).—3β-Acetoxy-13α-oleanan-12-one (100 mg) and fused sodium acetate (100 mg) in acetic anhydride (20 ml) were refluxed for 48 h. The solution was poured into water and extracted with ether to yield the enol acetate (85 mg), m.p. 225—228°, $[\alpha]_D$ +48° (lit.,⁵ m.p. 225—227°, $[\alpha]_D$ +44°), identical with material prepared from 3β-acetoxyoleanan-12-one.

13α-*Oleanane*-3,12-*dione* (7; R¹R² = O).—13α-Oleanane-3β,12α-diol was oxidised with Kiliani's chromic acid as described above to give 13α-*oleanane*-3,12-*dione*, m.p. 172—176°, $[\alpha]_D$ +115°, δ 0.85, 1.09, and 1.19 (each 3 H, s), 0.90 (6 H, s), and 1.04 (9 H, s) (Found: C, 81.85; H, 10.9. $C_{30}H_{48}O_2$ requires C, 81.8; H, 11.0%). Treatment of this material with boron trifluoride–diethyl ether in benzene as above afforded oleanane-3,12-dione, m.p. 218—222°, $[\alpha]_D$ −10°, δ 0.85, 0.92, 0.99, 1.03, 1.07, and 1.19 (each 3 H, s), and 0.90 (6 H, s) (lit.,⁴ m.p. 216—217°).

13α-*Oleanane*-3β,12β-*diol* (9; R = H).—13α-Oleanane-3,12-dione (100 mg) and lithium aluminium hydride (300 mg) were heated in refluxing tetrahydrofuran (30 ml) for 1 h. Water (0.5 ml), 2N-sodium hydroxide (0.5 ml), and water (1.5 ml) were added cautiously. The mixture was filtered and the solid was washed thoroughly with ether. The filtrate was washed with water, dried, and evaporated, and the residue was crystallised to afford 13α-*oleanane*-3β,12β-*diol* (72 mg), m.p. 220—225°, $[\alpha]_D$ +26°, δ 0.80, 0.88, 0.93, 1.02, 1.08, and 1.19 (each 3 H, s), 1.00 (6 H, s), 3.2 (1 H, t, 3α-H), and 4.15 (1 H, m, $W_{\frac{1}{2}}$ 19 Hz) (Found: C, 81.15; H, 11.75. $C_{30}H_{52}O_2$ requires C, 81.0; H, 11.8%). Identical material was obtained by similar reduction of 3β-acetoxy-13α-oleanan-12-one. Treatment with acetic anhydride in pyridine at room temperature gave the diacetate (9; R = Ac), m.p. 265—266°, $[\alpha]_D$ +52°.

12α,13α-*Epoxyoleanane and its Reduction with Lithium in Ethylamine*.—Treatment of olean-12-ene (β-amyrene)⁶ with perbenzoic acid in chloroform as described above for β-amyrin acetate gave 12α,13α-epoxyoleanane, m.p. 181—185° (lit.,⁷ m.p. 189—193°), $[\alpha]_D$ +33°, δ 0.78, 0.80, 0.85, 0.91, 0.94, 1.00, 1.07, and 1.14 (each 3 H, s), and 2.95br (1 H, s, $W_{\frac{1}{2}}$ 4.5 Hz). Reduction of this material by lithium in ethylamine as described above for 3β-acetoxy-12α,13α-

epoxyoleanane and p.l.c. of the product afforded olean-12-ene (13%) (identical with an authentic sample), *oleanan*-12α-*ol* (52%), m.p. 186—187°, $[\alpha]_D$ +46°, δ 0.83, 0.93, 0.96, 1.08, and 1.33 (each 3 H, s), 0.88 (9 H, s), and 3.95br (1 H, s, $W_{\frac{1}{2}}$ 8 Hz) (Found: C, 83.9; H, 12.3. $C_{30}H_{52}O$ requires C, 84.0; H, 12.2%), and 13α-*oleanan*-12α-*ol* (33%), m.p. 204—205°, $[\alpha]_D$ +32°, δ 0.82, 1.05, and 1.23 (each 3 H, s), 0.88 (9 H, s), 0.96 (6 H, s), and 4.30br (1 H, s, $W_{\frac{1}{2}}$ 9 Hz) (Found: C, 83.9; H, 12.3. $C_{30}H_{52}O$ requires C, 84.0; H, 12.2%). Careful examination of the reduction product by t.l.c. and by n.m.r. spectroscopy established the absence of detectable amounts of oleanan-12β-ol.

Authentic Oleanan-12β-*ol*.—12α,13α-Epoxyoleanane (500 mg) and boron trifluoride–diethyl ether (0.2 ml) in benzene (30 ml) were heated under reflux for 30 min. The solution was poured into water and the organic layer separated, washed with water, dried, and evaporated; the residue was crystallised to give *oleanan*-12-*one* (450 mg), m.p. 221—222°, $[\alpha]_D$ −30°, δ 0.83, 0.93, and 1.14 (each 3 H, s), 0.88 (9 H, s), and 0.91 (6 H, s) (Found: C, 84.45; H, 11.9. $C_{30}H_{50}O$ requires C, 84.4; H, 11.8%). Oleanan-12-one (500 mg) in propan-1-ol (25 ml) was immersed in an oil-bath at 130 °C, and sodium (2 g) was added over 1 h. The bath temperature was raised to 180 °C and more propan-1-ol (15 ml) and sodium (500 mg) were added. After 30 min at this temperature any excess of sodium that remained was destroyed by the addition of more propan-1-ol. The mixture was poured into water and extracted with ether to yield oleanan-12β-ol (450 mg), m.p. 198—199°, $[\alpha]_D$ +10°, δ 0.81, 0.90, and 1.06 (each 3 H, s), 0.86 (9 H, s), 0.96 (6 H, s), and 3.75 (1 H, m, $W_{\frac{1}{2}}$ 18 Hz).

Photolysis of 3β-Acetoxyoleanan-12α-*yl Nitrite* (3; R¹ = Ac, R² = NO).—3β-Acetoxyoleanan-12α-ol (1.1 g) in dry pyridine (20 ml) at −20 °C was treated with nitrosyl chloride gas for 3 min. After a further 15 min at room temperature the solution was poured into water and extracted with ether. The combined extracts were washed three times with water, dried, and evaporated to leave a pale brown solid which was less polar on t.l.c. than the starting material. This product in dry benzene (150 ml) under nitrogen was irradiated with a 125 W high-pressure mercury vapour lamp with a Pyrex filter until no nitrite remained (t.l.c. control; *ca.* 5 h). Evaporation then afforded a brown foam which was chromatographed on a column of silica gel. Gradient elution with light petroleum containing ethyl acetate (0—10%) gave small amounts of 3β-acetoxyoleanan-12-one and 3β-acetoxyoleanan-12α-ol, identical with authentic samples, and then 3β-acetoxy-27-hydroxyimino-oleanan-12α-ol (10) (700 mg, 61%), a foam, δ 7.52 (1 H, s, 27-H).

3β-*Acetoxy*-12α-*hydroxyoleanan*-27-*al* (27 ⟶ 12α)-*Hemiacetal* (11; R¹ = OH, R² = H).—The above oxime (200 mg) in dioxan (7 ml) and acetic acid (12 ml) was treated with aqueous 5% sodium nitrite. The mixture was stirred for 36 h at room temperature and then filtered to yield the *hemiacetal* (11; R¹ = OH, R² = H) (145 mg), which was recrystallised; m.p. 254—257°, $[\alpha]_D$ −6° (Found: C, 76.5; H, 10.5. $C_{32}H_{52}O_4$ requires C, 76.75; H, 10.5%). The filtrate was poured into water and extracted with ether to afford, after p.l.c., a further 35 mg of pure product.

3β-*Acetoxyoleanan*-27,12α-*olactone* (11; R¹R² = O).—The above hemiacetal (350 mg) in acetone (50 ml) was stirred for 15 min at room temperature with Jones chromic acid (2 ml). The mixture was poured into 2N-sodium carbonate and extracted with ether to give the *lactone* (270 mg), m.p.

300—302°, $[\alpha]_D$ —12°, δ 0.84 (6 H, s), 0.90, 1.11, and 1.26 (each 3 H, s), 0.92 (6 H, s), and 4.35—4.6 (2 H, m, 3α- and 12β-H) (Found: C, 76.9; H, 10.05. $C_{32}H_{50}O_4$ requires C, 77.1; H, 10.1%).

3β,27-*Diacetoxyolean*-12-*ene* (13).—The above hemiacetal (500 mg) and lithium aluminium hydride (1 g) were heated in refluxing tetrahydrofuran overnight. Work-up as in the above preparation of 13α-oleanane-3β,12β-diol gave material which, after treatment with acetic anhydride–pyridine at room temperature overnight, afforded a di-acetate, δ 0.87 (9 H, s), 0.92 (6 H, s), 1.00, 1.08, 2.04, and 2.07 (each 3 H, s), 3.92br (1 H, s, 12β-H), 4.3—4.65 (2 H, m, 3α- and 27-H), and 4.93 (1 H, d, J 14 Hz, 27-H). The diacetate was treated with methanesulphonyl chloride (1 ml) in pyridine (40 ml) at room temperature for 24 h. The mixture was poured into water and extracted with ether to yield, after p.l.c., 3β,27-*diacetoxyolean*-12-*ene* (300 mg), m.p. 166—167°, $[\alpha]_D$ +119°, δ 0.86—0.90 (15 H), 1.00 (6 H, s), 4.03 and 4.23 (each 1 H, d, J 14 Hz, 27-H$_2$), 4.5 (1 H, t, 3α-H), and 5.50 (1 H, t, 12-H) (Found: C, 77.3; H, 10.1. $C_{34}H_{54}O_4$ requires C, 77.5; H, 10.3%). The corresponding 3β,27-diol had m.p. 211—212°, $[\alpha]_D$ +86°.

3β,13β-*Dihydroxyoleanan*-28-*al* (28 ⟶ 13β)-*Hemiacetal* (12; R^1 = R^2 = H, R^3 = OH).—Oleanolic lactone [3] (3 g) in dry toluene (100 ml) was stirred under nitrogen and treated with 0.1M-di-isobutylaluminium hydride (5 ml). After 30 min water (15 ml) was added, followed by silica gel (25 g) and anhydrous magnesium sulphate. The mixture was filtered and the solids were washed thoroughly with tetrahydrofuran. The filtrate was evaporated and the residue crystallised to yield the *hemiacetal*, m.p. 259—262°, $[\alpha]_D$ +50°, δ 0.78, 0.91, 0.95, 0.97, and 1.19 (each 3 H, s), 0.88 (6 H, s), 3.2 (1 H, t, 3α-H), and 5.0 (1 H, s, 28-H) (Found: C, 78.45; H, 11.05. $C_{30}H_{50}O_3$ requires C, 78.55; H, 11.0%).

3β-*Acetoxyoleanan*-13β-*ol* (14; R = H).—Sodium (7 g) in diethylene glycol (75 ml) was treated with anhydrous hydrazine until the b.p. of the mixture was 150 °C. The hemiacetal (12; R^1 = R^2 = H, R^3 = OH) (1.2 g) was added and refluxing was continued for 24 h. Hydrazine was removed by distillation until the temperature in the flask had risen to 220 °C. After a further 24 h at this temperature the mixture was poured into water to yield oleanane-3β,13β-diol. Treatment with acetic anhydride–pyridine at room temperature gave 3β-*acetoxyoleanan*-13β-*ol*, which crystallised out from the acetylation mixture; m.p. 296—298°, $[\alpha]_D$ +29° (Found: C, 78.85; H, 11.0. $C_{32}H_{54}O_3$ requires C, 79.0 H, 11.2%).

3β-*Acetoxyoleanan*-13β-*yl Nitrite* (14; R = NO).—3β-Acetoxyoleanan-13β-ol (1 g) partially dissolved in pyridine (150 ml) was treated with a slow stream of nitrosyl chloride gas for 1 h. After stirring for a further 24 h at room temperature, the mixture was poured into water to yield the *nitrite ester*, m.p. 183—184°, $[\alpha]_D$ +118° (Found: C, 74.4; H, 10.45; N, 2.8. $C_{32}H_{53}NO_4$ requires C, 74.5; H, 10.4; N, 2.7%).

Photolysis of 3β-*Acetoxyoleanan*-13β-*yl Nitrite*.—The nitrite (1.2 g) in dry benzene (50 ml) was irradiated as above (t.l.c. control). The product was chromatographed on a column of silica gel; elution with 15% ethyl acetate in light petroleum gave 3β-*acetoxy*-13ξ-*hydroxy*-18a-*aza*-D-*homo-olean*-18(18a)-*ene* N-*oxide* (15), m.p. 295°, $[\alpha]_D$ +56°, $\nu_{max.}$ 3 560, 3 300, 1 720, and 1 600 cm^{-1}, $\lambda_{max.}$ (EtOH) 234 nm (ε 5 000), M^+ 515 (Found: C, 74.8; H, 10.1; N, 2.9. $C_{32}H_{53}NO_4$ requires C, 74.5; H, 10.4; N, 2.7%). Irradiation of the nitrone (15) in absolute ethanol with a high-pressure mercury vapour lamp caused the absorbance at 234 nm to diminish to *ca.* 40% of the original value after 2 h. The solution was then left overnight without irradiation; the absorbance had then returned to *ca.* 65% of the original.