Synthesis of Primulagenin A and of Echinocystic Acid

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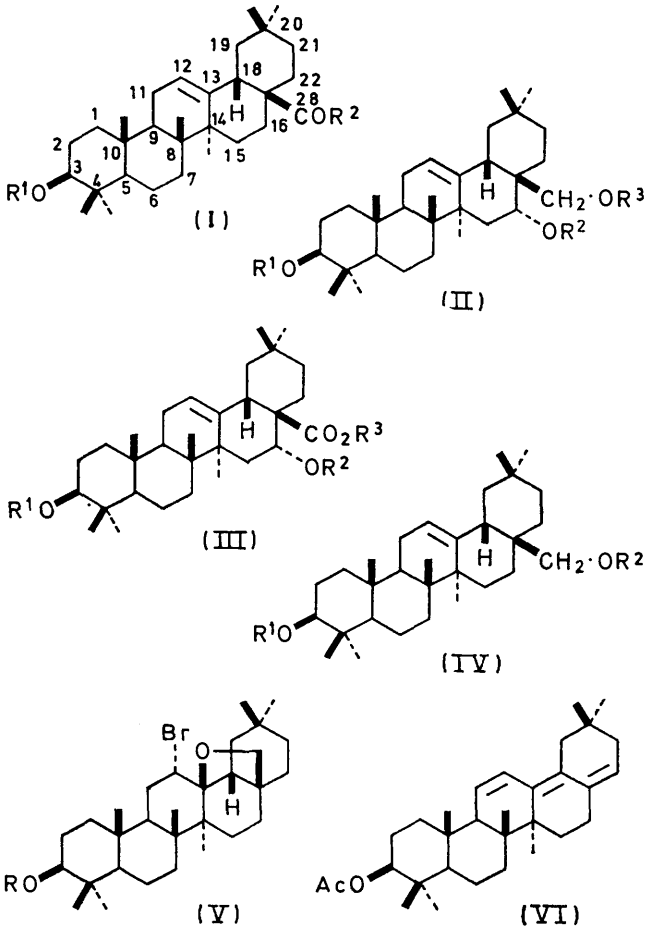
Photolysis of 3β-acetoxyolean-12-en-28-amide with lead tetra-acetate and iodine gave, albeit in low yield, the corresponding 28,15β-lactone. Further transformations of the latter then afforded primulagenin A (olean-12-ene-3β,16α,28-triol), which can be converted into echinocystic acid (3β,16α-dihydroxyolean-12-en-28-oic acid).

In continuance of our interest in the application of photochemical reactions to the synthesis of triterpenoids,[1] we now report the conversion of oleanolic acid (3β-hydroxyolean-12-en-28-oic acid) (I; $R^1 = H$, $R^2 = OH$) into primulagenin A (olean-12-ene-3β,16α,28-triol) (II;



($R^1 = R^2 = R^3 = H$) and the further transformation of the latter into echinocystic acid (3β,16α-dihydroxyolean-12-en-28-oic acid) (III; $R^1 = R^2 = R^3 = H$). By virtue of a prior synthesis of oleanolic acid [1] this work represents a formal total synthesis of primulagenin A and of echinocystic acid. The chosen reaction scheme called for use of the carboxy-group of oleanolic acid to introduce a functional group at C-15, and then a transfer of functionality from C-15 to C-16. The former step was to be achieved *via* generation of a 28-oxyl radical, a species for which we recognised three distinct reaction pathways: (1) abstraction of the suitably positioned [2] 15β-hydrogen atom, (2) addition to the 12,13-double bond,[3] and (3) collapse to a C-17 radical, with loss of C-28 and concomitant relief of the strain associated with the *cis* D/E ring junction. In the event we have established the occurrence of processes (1) and (3) only.

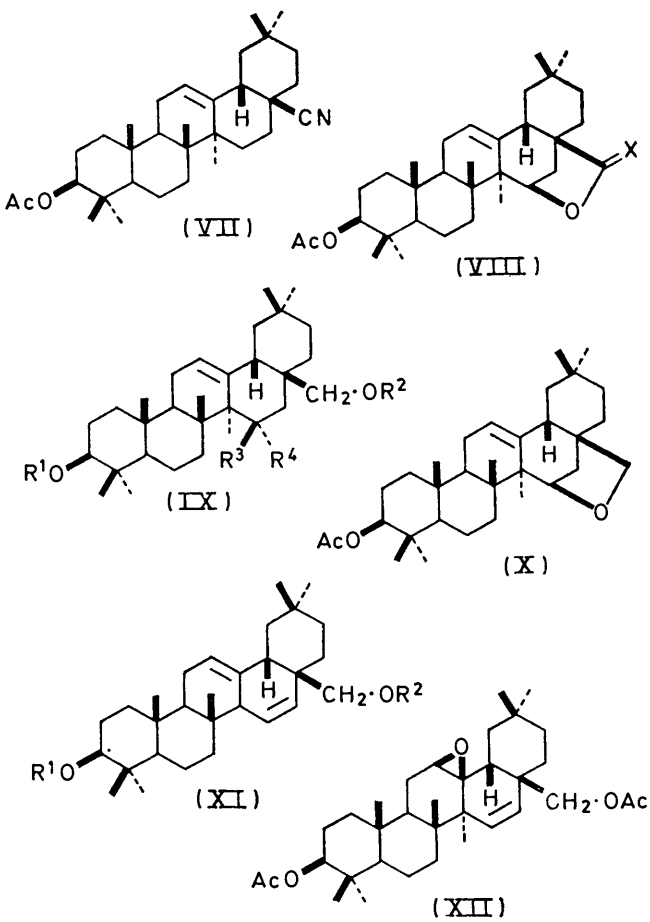
In initial experiments methyl 3β-acetoxyolean-12-en-28-oate (I; $R^1 = Ac$, $R^2 = OMe$) was reduced with lithium aluminium hydride to give olean-12-ene-3β,28-diol (erythrodiol) (IV; $R^1 = R^2 = H$).[4] Attempts to prepare a 3-acyl derivative of erythrodiol by selective hydrolysis of a 3,28-diacyl derivative did not proceed satisfactorily and prompted us to devise a new route to such compounds. Titration of erythrodiol with a dilute solution of bromine in ethanol in the presence of sodium acetate as buffer (to suppress oxidation at C-3) gave the bromo-ether (V; R = H).[5] This was acetylated and the product (V; R = Ac) treated with zinc dust in benzene–methanol to regenerate the 12-en-28-ol system. In this way 3-monosubstituted erythrodiols are available in high overall yield.

Treatment of 3β-acetoxyolean-12-en-28-ol (IV; $R^1 = Ac$, $R^2 = H$) with nitrosyl chloride in pyridine at −15° gave the crystalline nitrite (IV; $R^1 = Ac$, $R^2 = NO$). Photolysis [2] of this nitrite in dry benzene or tetrahydrofuran (125 W high-pressure mercury vapour lamp with a Pyrex filter) led to a considerable mixture of products of which the major components were 3β-acetoxy-28-noroleanadienes (mass spectrometery, M^+ 452) and 3β-acetoxyolean-12-en-28-ol. Similar mixtures of products were formed when 3β-acetoxyolean-12-en-28-ol was heated with lead tetra-acetate in benzene [6] or photolysed in the presence of mercuric oxide and iodine.[7] Clearly this type of C-28 alkoxyl radical was reacting predominantly by pathway (3) (see before).

We next turned our attention to a formally similar reaction, the photolysis of an amide in the presence of

[1] Previous paper, R. B. Boar, D. C. Knight, J. F. McGhie, and D. H. R. Barton, *J. Chem. Soc.* (*C*), 1970, 678.
[2] R. H. Hesse, *Adv. Free Radical Chem.*, 1968, **3**, 83; D. H. R. Barton, J. M. Beaton, L. E. Geller, and M. M. Pechet, *J. Amer. Chem. Soc.*, 1960, **82**, 2640.
[3] R. D. Rieke and N. A. Moore, *Tetrahedron Letters*, 1969, 2035; J. M. Surzur, M. P. Bertrand, and R. Nouguier, *ibid.*, 1969, 4197.
[4] C. Djerassi, R. M. McDonald, and A. J. Lemin, *J. Amer. Chem. Soc.*, 1953, **75**, 5940.
[5] J. Levisalles and H. Rudler, *Bull. Soc. chim. France*, 1967, 2059.
[6] G. Cainelli, M. Lj. Mihailovic, D. Arigoni, and O. Jeger, *Helv. Chim. Acta*, 1959, **42**, 1124.
[7] M. Akhtar and D. H. R. Barton, *J. Amer. Chem. Soc.*, 1964, **86**, 1528.

lead tetra-acetate and iodine.[8] A solution of 3β-acetoxyolean-12-en-28-amide [9] (I; R^1 = Ac, R^2 = NH_2) in dry benzene containing iodine and lead tetra-acetate was irradiated (125 W high-pressure mercury vapour lamp with a Pyrex filter) at 15° for 3 days (5 g scale). The reaction time varied considerably, particularly according to scale; this is probably a reflection of the degree to which the walls of the flask became coated with lead salts. After work-up involving basic hydrolysis and reacetylation, t.l.c. indicated that a complex mixture of products had been formed. Column chromatography made possible isolation of three of the least polar products. These were 28-noroleana-11,13(18),17(22)-trien-3β-yl acetate (VI) (1%), identical with an authentic sample,[10] 3β-acetoxyolean-12-en-28-onitrile (VII) (10%), identical with material prepared [9] by the action of thionyl chloride on the amide (I; R^1 = Ac, R^2 = NH_2), and 3β-acetoxyolean-12-en-28,15β-olactone (VIII; X = O) (7%). In a



separate experiment we demonstrated that the nitrile (VII) is formed when the amide (I; R^1 = Ac, R^2 = NH_2) is treated under the conditions of reacetylation used during the work-up of the foregoing photolysis. It may be then that observation of this product is simply a reflection of a quantity of unchanged starting material.

Formation of the lactone (VIII; X = O) represented the achievement of our objective of introducing a functional group at C-15, and we accordingly made considerable attempts to improve the yield of this product. The effects of varying the solvent, reaction temperature, and molar ratio of lead tetra-acetate are summarised in the Table. We also carried out the reaction in the presence

Effect of reaction conditions on the photolysis of the amide (I; R^1 = Ac, R^2 = NH_2) with lead tetra-acetate and iodine

			% Yield		
Solvent	Mol. equiv. of $Pb(OAc)_4$	Temp. (°C)	Triene (VI)	Nitrile (VII)	Lactone (VIII; X = O)
Benzene	5·0	15	1·0	9·6	7·0
Anisole	5·0	15		22·4	2·0
Chlorobenzene	5·0	15	<1·0	5·2	0
Benzene	2·0	15	<1·0	6·3	7·0
Benzene	8·0	15	<1·0	5·8	3·0
Benzene	5·0	80	1·7	18·2	0
Benzene	5·0	3	<1·0	5·2	4·0
Toluene	5·0	−60	<1·0	10·4 [a]	2·0

[a] The amide (I; R^1 = Ac, R^2 = NH_2) (57%) was recovered.

of calcium carbonate. However, in no case could we consistently produce the lactone (VIII; X = O) in greater than 7% yield. Another possibility, that the intermediate imidolactone (VIII; X = NH) was being incompletely hydrolysed under the conditions used, was then investigated. Whereas hydrolysis with potassium hydroxide in ethanol gave lactone (7%) of m.p. 318—320°, $[\alpha]_D$ −9·0°, hydrolysis with hydrochloric acid in ethanol gave lactone (9·6%), with the same m.p. and t.l.c. characteristics but with $[\alpha]_D$ +35° and varying somewhat from preparation to preparation. The n.m.r. spectra of the lactonic material obtained from the basic and acidic hydrolyses were very similar except in the olefinic region where the former showed a broad triplet at τ 4·49 (1H, C-12) but the latter showed the same triplet with an additional singlet at τ 4·43 (combined integration >1H). Since a similar singlet is observed for the C-15 and C-16 protons in a number of 15,16-ene derivatives, a possible explanation of the effect of acid on the lactone (VIII; X = O) is that it promotes the equilibrium shown in the Scheme. The lactone (VIII; X = O) has been previously prepared by Djerassi and his co-workers by degradation of the cactus triterpenoid dumortierigenin.[11] The two sets of constants are in reasonable agreement.

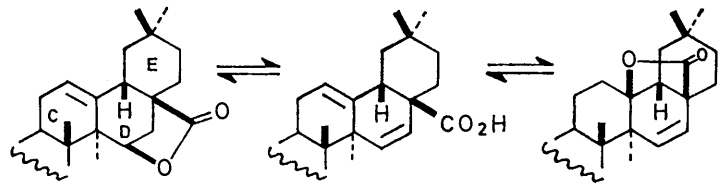
In two further experiments we investigated the photolysis with lead tetra-acetate and iodine of the *N*-methylamide (I; R^1 = Ac, R^2 = NHMe) and the 18-*iso*-amide (I; R^1 = Ac, R^2 = NH_2; 18α-H). In neither case was any significant amount of lactone isolated.

Reduction of the lactone (VIII; X = O) with lithium aluminium hydride in tetrahydrofuran and acetylation of the product with acetic anhydride–pyridine at room

[8] D. H. R. Barton, A. L. J. Beckwith, and A. Goosen, *J. Chem. Soc.*, 1965, 181.
[9] G. Drefahl and S. Huneck, *Chem. Ber.*, 1958, **91**, 278.
[10] D. H. R. Barton, H. T. Cheung, P. L. J. Daniels, K. G. Lewis, and J. F. McGhie, *J. Chem. Soc.*, 1962, 5163.
[11] C. Djerassi, C. H. Robinson, and D. B. Thomas, *J. Amer. Chem. Soc.*, 1956, **78**, 5685.

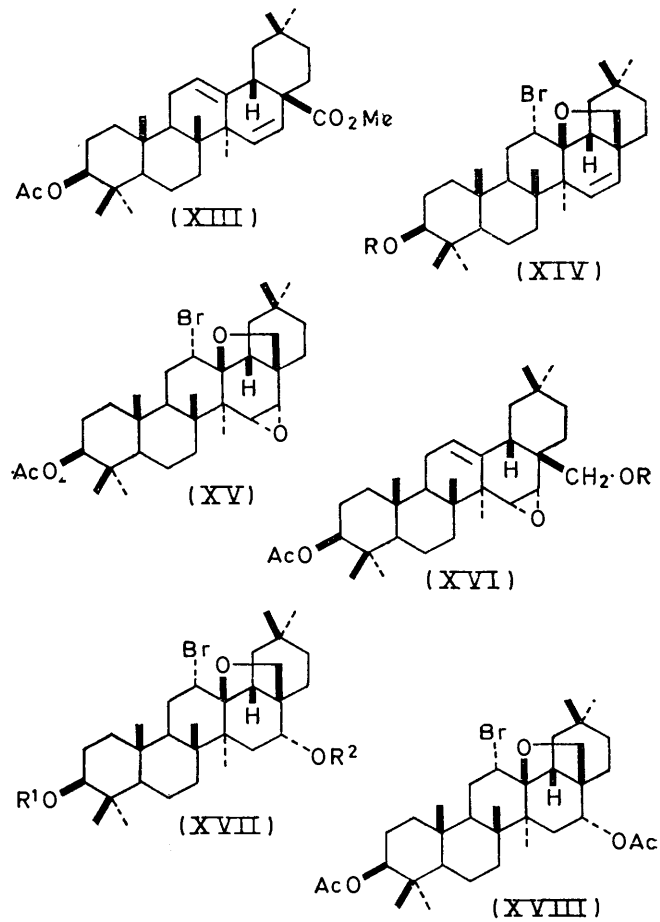
temperature overnight gave 3β,28-diacetoxyolean-12-en-15β-ol (IX; $R^1 = R^2 = Ac$, $R^3 = OH$, $R^4 = H$). The extremely unreactive 15β-hydroxy-group was not acetylated, and in keeping with previous findings [11] we were unable to dehydrate the product to give the corresponding 12,15-diene. In one attempted dehydration a solution of the triol diacetate (IX; $R^1 = R^2 = Ac$, $R^3 = OH$, $R^4 = H$) in *NN*-dimethylacetamide was treated with sodium hydride followed by methanesulphonyl chloride. The product was the 15β,28-ether (X). We therefore resorted to the route adopted by Djerassi and his co-workers [11] for the conversion of the 15β-triol diacetate into the 12,15-diene (XI; $R^1 = R^2 =$ Ac). Oxidation with chromic acid gave the 15-ketone (IX; $R^1 = R^2 = Ac$, $R^3R^4 = O$), which was reduced by lithium in liquid ammonia to the more stable 3β,15α,28-triol (IX; $R^1 = R^2 = R^3 = H$, $R^4 = OH$). Acetylation with acetic anhydride–pyridine overnight at −10° gave selectively the 3,28-diacetate (IX; $R^1 = R^2 = Ac$, $R^3 = H$, $R^4 = OH$), which was smoothly dehydrated by phosphoryl chloride in pyridine to the required 12,15-diene (XI; $R^1 = R^2 = Ac$). At this stage a gift of echinocystic acid from Professor C. R. Noller enabled us to employ a relay synthesis. Reduction of methyl echinocystate diacetate (III; $R^1 = R^2 = Ac$, $R^3 = Me$) with lithium aluminium hydride in tetrahydrofuran afforded primulagenin A, which was converted into the 12,15-diene (XI; $R^1 = R^2 = Ac$) by the route previously described.[12] In this way material identical (mixed m.p., i.r. spectrum, t.l.c.) with that synthesised from oleanolic acid as already described was obtained. Treatment of the 12,15-diene (XI; $R^1 = R^2 = Ac$) with perbenzoic acid in chloroform at 0° gave exclusively the 12β,13-epoxy-15-ene (XII). Even with a large excess of perbenzoic acid there was no indication for the formation of any diepoxide. Similarly, the 3,28-dihydroxy-12,15-diene (XI; $R^1 = R^2 = H$) and the 12,15-diene-28-ester (XIII) both afforded solely the corresponding 12β,13-epoxy-15-enes. The configurations of the foregoing epoxides were assigned by analogy with the known [1] epoxidation of α- and β-amyrin by β-face attack. In view of the normal lack of reactivity of the 12,13-double bond in β-amyrin derivatives, these experiments illustrate the extreme steric hindrance of the 15,16-double bond.

To enable us to use more vigorous conditions for epoxidation of the 15,16-double bond we protected the 12,13-double bond of the 12,15-diene-3β,28-diol (XI; $R^1 = R^2 = H$) by bromination to afford the bromo-ether (XIV; R = H). In keeping with the foregoing results, the acetate of this compound (XIV; R = Ac) did not react with perbenzoic acid in chloroform, but with commercial peracetic acid at room temperature for 48 h it gave the desired 15α,16-epoxide (XV) in 55% yield. The configuration of this epoxide followed from the products of its later reduction.



SCHEME

Removal of the bromo-ether protecting group gave 3β-acetoxy-15α,16-epoxyolean-12-en-28-ol (XVI; R = H), further characterised as the 3,28-diacetate (XVI; R = Ac). Reduction of the epoxide (XVI; R = H)



with lithium aluminium hydride in refluxing tetrahydrofuran for 3 days gave an almost quantitative yield of olean-12-ene-3β,15α,28-triol (IX; $R^1 = R^2 = R^3 = H$, $R^4 = OH$), converted by selective acetylation into the 3,28-diacetate (IX; $R^1 = R^2 = Ac$, $R^3 = H$, $R^4 = OH$),

[12] K. V. Rao and P. K. Bose, *Tetrahedron*, 1962, **18**, 461.

which was identical with material previously prepared by reduction of the 15-ketone (IX; $R^1 = R^2 = Ac$, $R^3R^4 = O$). The reduction of an epoxycyclohexane to give exclusively an equatorial alcohol is rare,[13] and suggests participation of the 28-hydroxy-group in the preceding reduction.

In contrast, reduction of the epoxide (XVI; R = H) with lithium in ethylamine gave two products in an approximate ratio of 7 : 3. These were separated by chromatography on an alumina column. Elution with benzene–ethyl acetate (65 : 35 v/v) gave a 66% yield of material identical (mixed m.p., i.r. spectrum, t.l.c.) with authentic primulagenin A (II; $R^1 = R^2 = R^3 = H$). This identity was further established for the derived 3,28-diacetates (II; $R^1 = R^3 = Ac$, $R^2 = H$). Further elution with benzene–ethyl acetate (1 : 1 v/v) gave olean-12-ene-3β,15α,28-triol (IX; $R^1 = R^2 = R^3 = H$, $R^4 =$ OH) (30%), identical with the product of the lithium aluminium hydride reaction.

Our initial route for the conversion of primulagenin A into echinocystic acid required formation of the bromo-ether (XVII; $R^1 = R^2 = H$), conversion of this into the corresponding diacetate, regeneration of the 28-hydroxy-group, and oxidation. In the event, formation of the bromo-ether (XVII; $R^1 = R^2 = H$) rendered the 16α-hydroxy-group considerably less susceptible to acetylation. Treatment with acetic anhydride–pyridine at room temperature or 100° gave only the 3-acetate (XVII; $R^1 = Ac$, $R^2 = H$), whereas acetic anhydride–sodium acetate at 100° or isopropenyl acetate–toluene-*p*-sulphonic acid at room temperature gave a mixture of two products that could not be conveniently separated by chromatography. The minor of the two products was identical (t.l.c.) with the subsequently prepared diacetate (XVII; $R^1 = R^2 = Ac$).

We then made use of an observation by Hensens and Lewis [14] that on contact with basic alumina 3β,28-diacetoxyolean-12-en-16α-ol (II; $R^1 = R^3 = Ac$, $R^2 = H$) rearranges to the corresponding 3,16-diacetate (II; $R^1 = R^2 = Ac$, $R^3 = H$). Possible factors affecting this *a priori* unlikely *trans*-diaxial rearrangement have been discussed by the original authors. Although direct oxidation of the 3,16-diacetate (II; $R^1 = R^2 = Ac$, $R^3 = H$) did not provide a satisfactory route to 3β,16α-diacetoxyolean-12-en-28-oic acid (echinocystic acid diacetate) (III; $R^1 = R^2 = Ac$, $R^3 = H$), formation of the bromo-ether (XVII; $R^1 = R^2 = Ac$) followed by oxidation with chromium trioxide in acetic acid gave the known [15] bromo-lactone (XVIII) in good yield. Finally, debromination with zinc in benzene–methanol afforded echinocystic acid diacetate, which was hydrolysed to give echinocystic acid (III; $R^1 = R^2 = R^3 = H$), and methylated to afford methyl echinocystate diacetate (III; $R^1 = R^2 = Ac$, $R^3 = Me$). A rigorous comparison with authentic materials confirmed the identity of the last three compounds.

EXPERIMENTAL

N.m.r. data refer to solutions in deuteriochloroform with tetramethylsilane as internal standard; they were recorded with a Perkin-Elmer R10 instrument. Unless otherwise stated u.v. spectral data are for solutions in ethanol, and rotations refer to chloroform solutions. Column chromatography was performed on Laporte grade 0 alumina. Ether refers to diethyl ether and light petroleum to the fraction of b.p. 40—60°

12α-Bromo-13β,28-epoxyoleanan-3β-yl Acetate (V; R = Ac).—Erythrodiol (12 g) was dissolved in ethanol (700 ml) buffered with sodium acetate. Bromine (0·1 ml) in ethanol (100 ml) was added dropwise until a colouration persisted. The product was poured into water and extracted with ether. Crystallisation from methanol gave needles of the *bromo-ether* (12·5 g, 87%), m.p. 186—188°, $[\alpha]_D$ +92° (*c* 0·09), $\nu_{max.}$ (Nujol) 3620, 3340, and 1030 cm^{-1} (Found: C, 68·9; H, 9·7; Br, 15·4. $C_{30}H_{49}BrO_2$ requires C, 69·1; H, 9·5; Br, 15·3%). This product was acetylated with pyridine (100 ml) and acetic anhydride (100 ml) at room temperature overnight. The *acetate* crystallised from ethanol as needles (13 g, 95%), m.p. 188—189°, $[\alpha]_D$ +83° (*c* 0·13), $\nu_{max.}$ (Nujol) 1730 and 1250 (acetate) cm^{-1}, τ 5·45 (1H, t, C-3α), 5·72 (1H, t, C-12β), 6·21 and 6·68 (each 1H, d, *J* 7 Hz, 28-H_2), and 7·92 (3H, s, Ac) (Found: C, 68·4; H, 9·2; Br, 14·1. $C_{32}H_{51}BrO_3$ requires C, 68·2; H, 9·1; 14·2%).

3β-Acetoxyolean-12-en-28-ol (IV; $R^1 = Ac$, $R^2 = H$).—12α-Bromo-13β,28-epoxyoleanan-3β-yl acetate (12 g) in benzene–methanol (1 : 1; 400 ml) was treated with activated zinc dust (15 g) and the mixture was heated under reflux. More zinc dust (1 g) was added at hourly intervals. After 5 h refluxing the solution was decanted and the residual zinc dust extracted with further portions of benzene. The filtrates were combined and evaporated. The residue gave needles (8·5 g., 83%), m.p. 230—231° (from chloroform–methanol), $[\alpha]_D$ +76° (*c* 0·15) (lit.,[16] m.p. 238·5—239°, $[\alpha]_D$ +71°), $\nu_{max.}$ (Nujol) 3490, 1710, and 1270 (acetate) cm^{-1}, τ 4·80 (1H, complex, C-12), 5·50 (1H, t, C-3α), 6·44 and 6·82 (each 1H, d, *J* 12 Hz, 28-H_2), and 7·95 (3H, s, Ac) (Found: C, 79·25; H, 10·6. Calc. for $C_{32}H_{52}O_3$: C, 79·3; H, 10·8%).

3β-Acetoxyolean-12-en-28-yl Nitrite (IV; $R^1 = Ac$, $R^2 = NO$).—3β-acetoxyolean-12-en-28-ol (2·2 g) in dry pyridine (150 ml) was cooled to −15° and treated with nitrosyl chloride gas for 20 min. The solution was poured into iced water; the precipitated solid was filtered off and washed thoroughly with water to give the *nitrite* (1·95 g, 84%), m.p. 201—202° (from pyridine–water), $[\alpha]_D$ +46° (*c* 0·06 in pyridine), $\nu_{max.}$ (Nujol) 1725 and 1245 (acetate), and 1635 and 1608 (nitrite) cm^{-1}, τ 4·73 (1H, t, C-12), 5·25 and 5·60 (each 1H, d, *J* 12 Hz, 28-H_2), 5·47 (1H, t, C-3α), and 7·95 (3H, s, Ac) (Found: C, 74·75; H, 9·8; N, 2·6. $C_{32}H_{51}NO_4$ requires C, 74·8; H, 10·0; N, 2·7%).

Photolysis of the Nitrite (IV; $R^1 = Ac$, $R^2 = NO$).—The nitrite (560 mg) in dry benzene (100 ml) at 15° was photolysed (125 W high-pressure mercury vapour lamp with a Pyrex filter) in an atmosphere of dry, oxygen-free nitrogen until no starting material remained (6 h). The solvent was removed at room temperature to give a gum which by t.l.c.

[13] M. Hanack, ' Conformation Theory,' Academic Press, New York, 1965, p. 254 *et seq.*

[14] O. D. Hensens and K. G. Lewis, *Tetrahedron Letters*, 1968, 3213.

[15] W. R. White and C. R. Noller, *J. Amer. Chem. Soc.*, 1939, **61**, 983.

[16] V. Prelog, J. Norymberski, and O. Jeger, *Helv. Chim. Acta*, 1946, **29**, 360.

was shown to consist of several compounds. This gum was chromatographed on alumina (50 g). Elution with light petroleum–benzene (90 : 10 v/v) gave material (90 mg) of m.p. 157—158° (from methanol), $[\alpha]_D$ +45° (*c* 0·13), $\nu_{max.}$ (CCl_4) 1735 and 1245 cm^{-1}, $\lambda_{max.}$ 237, 243, and 251 nm (ε 9100, 10,000, and 7100), τ 4·50 (1H, complex, C-12), 5·40 (1H, t, C-3α), and 7·95 (3H, s, Ac), *m/e* 452 (M^+), 202, 190, and 173. T.l.c. on silver nitrate impregnated plates indicated that this material was a mixture of two compounds. From the foregoing data the major product appears to be 28-norolean-12,17(18)-dien-3β-yl acetate (lit.,[17] m.p. 186—188°, $[\alpha]_D$ +66°).

Further elution, with light petroleum–benzene (80 : 20 v/v), gave an unknown compound (75 mg) of m.p. 229—230·5° (from ethanol), $[\alpha]_D$ +76° (*c* 0·11), $\nu_{max.}$ (CCl_4) 1735 and 1245 (acetate) cm^{-1}, τ 4·55 (1H, t, C-12), 5·45 (1H, t, C-3α), 6·65 (1H, complex), and 7·92 (3H, s, Ac), *m/e* 452 (M^+) 202 (base peak), and 190. Finally, elution with light petroleum–benzene (10 : 90 v/v) gave 3β-acetoxyolean-12-en-28-ol (50 mg), m.p. 228—230°, identical (mixed m.p., i.r. spectrum, and t.l.c.) with an authentic sample.

The foregoing photolysis was repeated with dry tetrahydrofuran as solvent. The products were similar (t.l.c.) to those obtained with benzene.

Reaction of 3β-*Acetoxyolean*-12-*en*-28-*ol with Lead Tetra-acetate*.—The 3-acetate (140 mg) in dry benzene (40 ml) was treated with lead tetra-acetate (370 mg, 3 mol. equiv.) and the solution was refluxed. After 1 h t.l.c. indicated the presence of a complex mixture including some starting material. The major product was identical (by t.l.c.) with the least polar compound obtained from the nitrite photolysis.

3β-*Acetoxy*-N-*methylolean*-12-*en*-28-*amide* (I; R^1 = Ac, R^2 = NHMe).—3β-Acetoxyolean-12-en-28-oyl chloride (I; R^1 = Ac, R^2 = Cl) (5 g) in benzene (150 ml) was added to methylamine hydrochloride (5 g) and sodium hydrogen carbonate (3·5 g) in water (100 ml). The resulting mixture was refluxed for 1 h, then poured into dilute hydrochloric acid and extracted with ether. Recrystallisation of the product from chloroform–methanol gave needles of the N-*methylamide* (4·8 g, 97%), m.p. 240—241°, $[\alpha]_D$ +57° (*c* 0·10), $\nu_{max.}$ (Nujol) 3300 (NH), 1735 and 1245 (acetate), and 1635 (amide) cm^{-1}, τ 4·1br (1H, m, NH), 4·65 (1H, t, C-12), 5·50 (1H, t, C-3α), 7·24 (3H, d, *J* 5 Hz, NMe), and 7·95 (3H, s, Ac), (Found: C, 74·8; H, 10·2; N, 2·4. $C_{33}H_{53}NO_3,H_2O$ requires C, 74·8; H, 10·5; N, 2·6%).

3β-*Acetoxy*-18α-*olean*-12-*en*-28-*amide* (I; R^1 = Ac, R^2 = NH_2; 18α-H).—3β-Acetoxy-18α-olean-12-en-28-oic acid[18] (0·6 g) in dry benzene (25 ml) and oxalyl chloride (1 ml) was stirred at room temperature overnight. The solvent and the excess of oxalyl chloride were removed under reduced pressure to yield 3β-acetoxy-18α-olean-12-en-28-oyl chloride, $\nu_{max.}$ (Nujol) 1735 and 1250 (acetate) and 1810 (COCl) cm^{-1}. This acid chloride, in the minimum of ether, was added dropwise to liquid ammonia (35 ml) in a Dewar flask fitted with a cold finger. The solution was allowed to warm to reflux temperature and was then stirred vigorously for 24 h. The mixture was poured into water and extracted with ether. The product was chromatographed on alumina (50 g). Elution with benzene–light petroleum (60 : 40 v/v) gave the unchanged acid chloride. Further elution, with ether, gave 3β-*acetoxy*-18α-*olean*-12-*en*-28-*amide* as small needles (400 mg, 66%), m.p. 264—265° (from methanol), $[\alpha]_D$ +41° (*c* 0·24), $\nu_{max.}$ (Nujol) 3440 and 3320 (NH_2), 3150, 1735, and 1245 (acetate), and 1670 ($CO{\cdot}NH_2$) cm^{-1}, τ 3·80br and 4·10br (each 1H, s, exchanged with deuterium oxide, NH_2), 4·60br (1H, s, C-12), 5·50 (1H, t, C-3α), and 7·97 (3H, s, Ac) (Found: C, 77·2; H, 10·2; N, 2·75. $C_{32}H_{51}NO_3$ requires C, 77·2; H, 10·3; N, 2·8%).

Photolysis of 3β-*Acetoxyolean*-12-*en*-28-*amide* (I; R^1 = Ac, R^2 = NH_2) *with Lead Tetra-acetate and Iodine*.—The amide (5 g), lead tetra-acetate (23·8 g), and iodine (7·5 g) in dry benzene (500 ml) were irradiated under dry nitrogen in a Pyrex flask at 15° with a 125 W high-pressure mercury arc lamp for 75 h. The mixture was filtered and the residue washed thoroughly with chloroform. The combined filtrates were shaken with aqueous sodium disulphite, followed by water. The solvent was evaporated off and the residue, in ethanol (500 ml), treated with potassium hydroxide (10 g) in ethanol (50 ml). After refluxing for 2 h, most of the solvent was removed under reduced pressure, water was added, and the resulting solution was acidified with 2N-sulphuric acid. Extraction with three portions of ether and one of chloroform gave material that was dissolved in pyridine (100 ml) and acetic anhydride (100 ml), left at room temperature overnight, then poured into water and extracted with ether. The product thus obtained was chromatographed on alumina (130 g). Elution with light petroleum–benzene (40 : 60 v/v) gave 28-noroleana-11,13(18),17(22)-trien-3β-yl acetate (30 mg, <1%), m.p. 171—173°, $[\alpha]_D$ −349° (*c* 0·12) {lit.,[10] m.p. 179—180° (vac.), $[\alpha]_D$ −314°}, $\nu_{max.}$ (CCl_4) 1735 and 1240 (acetate) cm^{-1}, $\lambda_{max.}$ 280sh, 289 (ε 44,300), and 300sh nm, τ 3·49 (1H, q, *J* 3 and 11 Hz, C-11), 4·30 (1H, d, *J* 12 Hz, C-12), 4·59 (1H, complex, C-22), 5·40 (1H, t, C-3α), and 7·92 (3H, s, Ac), identical (mixed m.p. and t.l.c.) with an authentic sample.

Further elution, with light petroleum–benzene (20 : 80 v/v), gave 3β-acetoxyolean-12-en-28-onitrile (460 mg, 9·6%), m.p. 289—290°, $[\alpha]_D$ +72·4° (*c* 0·15), (lit.,[9] m.p. 295—297°), $\nu_{max.}$ ($CHCl_3$) 2235 (CN) and 1720 (acetate) cm^{-1}, identical (mixed m.p., i.r. spectrum, and t.l.c.) with an authentic sample.

Finally, elution with ether–benzene (10 : 90 v/v) gave 3β-acetoxyolean-12-en-28,15β-olactone (350 mg, 7%), m.p. 318—320°, $[\alpha]_D$ −9° (*c* 0·52) (lit.,[11] m.p. 336—339°, $[\alpha]_D$ −21°), $\nu_{max.}$ ($CHCl_3$) 1760 (lactone) and 1720 (acetate) cm^{-1}, τ 4·49 (1H, t, C-12), 5·46 (1H, t, C-3α), 5·46 (1H, d, *J* 6 Hz, C-15α), and 7·94 (3H, s, Ac), *m/e* 496 (M^+) 436, 421, 247, 201, 189 (base peak), and 175 (Found: C, 77·3; H, 9·8. Calc. for $C_{32}H_{48}O_4$: C, 77·4; H, 9·7%).

Analogous photolyses of the *N*-methylamide (I; R^1 = Ac, R^2 = NHMe) and the 18-*iso*-amide (I; R^1 = Ac, R^2 = NH_2; 18α-H) gave crude products that contained only minor amounts of any γ-lactone (i.r. spectroscopy).

Treatment of 3β-*Acetoxyolean*-12-*en*-28-*amide* (I; R^1 = Ac, R^2 = NH_2) *with Acetic Anhydride–Pyridine*.—The amide (0·5 g) in pyridine (30 ml) and acetic anhydride (30 ml) was left at room temperature overnight. The product consisted (by t.l.c.) of a mixture of the starting material and 3β-acetoxyolean-12-en-28-onitrile in approximately equal amounts.

3β,28-*Diacetoxyolean*-12-*en*-15β-*ol* (IX; R^1 = R^2 = Ac, R^3 = OH, R^4 = H).—3β-Acetoxyolean-12-en-28,15β-olactone (140 mg) in dry tetrahydrofuran (150 ml) was stirred with a large excess of lithium aluminium hydride for 24 h. After an acidic work-up to destroy the excess of lithium aluminium hydride, the solution was extracted with ether.

[17] D. H. R. Barton and C. J. W. Brooks, *J. Chem. Soc.*, 1951, 257.

[18] D. H. R. Barton and N. J. Holness, *J. Chem. Soc.*, 1952, 78.

The extracts were washed with water, dried, and evaporated. The residue was treated with pyridine (30 ml) and acetic anhydride (30 ml) at room temperature overnight, and worked up in the usual way to give the 3,28-diacetate (120 mg, 79%), m.p. 244—245° (from chloroform–methanol), $[\alpha]_D$ +63° (*c* 0·12) (lit.,[11] m.p. 251—255°, $[\alpha]_D$ +53°), $\nu_{max.}$ (CCl_4) 3610 and 3450 (OH) and 1735 and 1240 (acetate) cm^{-1}, τ 4·70 (1H, t, C-12), 5·48 (1H, t, C-3α), 5·86 (2H, d, *J* 4 Hz, 28-H_2), 6·10 (1H, t, C-15α), 7·94 (6H, s, 2 × Ac), and 8·40 1H, exchanged with deuterium oxide, OH), *m/e* 542 (M^+), 524, 482, 464, 447, 292 (base peak), 249, 232, and 189 (Found: C, 75·0; H, 10·05. Calc. for $C_{34}H_{54}O_5$: C, 75·2; H, 10·0%).

Reaction of 3β,28-*Diacetoxyolean*-12-*en*-15β-*ol with Sodium Hydride and Methanesulphonyl Chloride in* NN-*Dimethylacetamide.*—The triol diacetate (100 mg) was dissolved in dry *NN*-dimethylacetamide (20 ml) and sodium hydride (100 mg) was added. The mixture was stirred at room temperature for 2 h. Methanesulphonyl chloride (2 ml) was added and the solution refluxed for 15 h. The mixture was poured into water and worked up in the usual way. The major product was isolated by preparative layer chromatography. Recrystallisation from chloroform–methanol afforded platelets of 15β,28-epoxyolean-12-en-3β-yl acetate (50 mg, 56%), m.p. 229—230°, $[\alpha]_D$ +29° (*c* 0·12), $\nu_{max.}$ (CCl_4) 1730 and 1240 (acetate) cm^{-1}, τ 4·60 (1H, complex, C-12), 5·45 (1H, t, C-3α), 5·81 (1H, d, *J* 6 Hz, C-15α), 6·44 and 6·68 (1H, d, *J* 6 Hz, 28-H_2), and 7·91 (3H, s, Ac), *m/e* 482 (M^+), 422, 353, 232, and 189.

3β,28-*Diacetoxyolean*-12-*en*-15-*one* (IX; $R^1 = R^2$ = Ac, R^3R^4 = O).—Chromium trioxide–sulphuric acid [19] was added dropwise to 3β,28-diacetoxyolean-12-en-15β-ol (100 mg) in AnalaR acetone (50 ml) until a permanent orange colour resulted. The mixture was stirred at room temperature for 2 h, then poured into water and extracted with ether. Recrystallisation from chloroform–methanol gave the 15-ketone (40 mg, 40%), m.p. 225—226°, $[\alpha]_D$ +18° (*c* 0·17), (lit.,[11] m.p. 229—232°, $[\alpha]_D$ +21°), $\nu_{max.}$ (CCl_4) 1735 and 1220 (acetate) and 1705 (ketone) cm^{-1}, *m/e* 540 (M^+), 480, 344, and 291 (base peak).

3β,28-*Diacetoxyolean*-12-*en*-15α-*ol* (IX; $R^1 = R^2$ = Ac, R^3 = H, R^4 = OH).—The foregoing ketone (30 mg) in dry ether (10 ml) was added to liquid ammonia (25 ml) containing methanol (1 ml) at the reflux temperature of ammonia. The stirred solution was treated with lithium (100 mg) in small pieces during 15 min. As soon as the blue colour had disappeared, ammonium chloride (800 mg) was added. After evaporation of the ammonia, water was added and the product was extracted with ether. This product, in cold pyridine (20 ml) and cold acetic anhydride (20 ml) was left at −10° overnight and then worked up in the usual way to give the 15α-ol 3,28-diacetate as plates from chloroform–methanol (20 mg, 67%), m.p. 258—260°, $[\alpha]_D$ +47° (*c* 0·11) (lit.,[11] m.p. 260—265°, $[\alpha]_D$ +57°), $\nu_{max.}$ (CCl_4) 3620, 1740, 1240, and 1215 cm^{-1}.

Oleana-12,15-*diene*-3β,28-*diyl Diacetate* (XI; $R^1 = R^2$ = Ac).—The foregoing diacetate (15 mg) in dry pyridine (5 ml) was treated with phosphoryl oxychloride (0·5 ml) and the solution refluxed for 2 h. The mixture was poured into water and extracted with ether. The material thus obtained was chromatographed on alumina (5 g). The diene was eluted with light petroleum–benzene (40 : 60 v/v) and crystallised from ethanol as fine white needles (10 mg, 70%), m.p. 200—202°, $[\alpha]_D$ +52° (*c* 0·07) (lit.,[11] m.p. 210—212°, $[\alpha]_D$ +53°), $\nu_{max.}$ (CCl_4) 1735 and 1235 (acetate) cm^{-1}, identical (mixed m.p., i.r. spectrum, and t.l.c.) with authentic material prepared from echinocystic acid *via* primulagenin A.[12]

Methyl 3β-*Acetoxy*-12β,13-*epoxyolean*-15-*en*-28-*oate.*—Methyl 3β-acetoxyolean-12,15-dien-28-oate (XIII) (100 mg) in chloroform (5 ml) was treated with a solution of perbenzoic acid in chloroform (1·92 ml, 1·0 mol. equiv.). The solution was set aside overnight at 0—5°. T.l.c. then indicated incomplete reaction, so more perbenzoic acid in chloroform (1 ml) was added and the solution was left for a further 24 h at 0—5°. It was then washed with 2N-sodium hydroxide and water, dried, and evaporated. Crystallisation of the residue from light petroleum gave large prisms of the *epoxide* (80 mg, 78%), m.p. 188—189°, $[\alpha]_D$ +15° (*c* 0·17), $\nu_{max.}$ (CCl_4) 1735 and 1225 (acetate) and 1728 (CO_2Me) cm^{-1}, τ 4·45 (2H, s, C-15 and C-16), 5·53 (1H, t, C-3α), 6·39 (3H, s, CO_2Me), 6·68 (1H, s, C-12α), and 7·96 (3H, s, Ac) (Found: C, 75·2; H, 9·5. $C_{33}H_{50}O_5$ requires C, 75·2; H, 9·6%).

Similarly, oleana-12,15-diene-3β,28-diyl diacetate (XI; $R^1 = R^2$ = Ac) afforded 12β,13-*epoxyolean*-15-*ene*-3β,28-*diyl diacetate* (XII) (82%) as fine needles from light petroleum, m.p. 221—222°, $[\alpha]_D$ +44° (*c* 0·14), $\nu_{max.}$ (CCl_4) 1735 and 1230 cm^{-1}, τ 4·46 and 4·78 (each 1H, d, *J* 10 Hz, C-15 and C-16), 5·66 (1H, t, C-3α), 5·86 and 6·22 (each 1H, d, *J* 10 Hz, 28-H_2), 7·19 (1H, s, C-12α), and 8·00 (6H, s, Ac) (Found: C, 75·6; H, 9·6. $C_{34}H_{52}O_5$ requires C, 75·5; H, 9·7%).

Similarly, oleana-12,15-diene-3β,28-diol (XI; $R^1 = R^2$ = H) yielded 12β,13-*epoxyolean*-15-*ene*-3β,28-*diol* (87%), m.p. (from light petroleum) 233—235°; $[\alpha]_D$ −3·2° (*c* 0·16), $\nu_{max.}$ (Nujol) 3470 (OH) cm^{-1}, τ 4·65 (2H, s, C-15 and C-16), 6·27 (1H, complex, C-3α), 6·46 and 6·80 (each 1H, d, *J* 6 Hz, 28-H_2), *ca.* 6·9 (1H, C-12α, partly obscured by the signals for the 28-H_2) (Found: C, 77·2; H, 10·4. $C_{30}H_{48}O_3$,0·5H_2O requires C, 77·4; H, 10·6%).

12α-*Bromo*-13β,28-*epoxyolean*-15-*en*-3β-*ol* (XIV; R = H).—Oleana-12,15-diene-3β,28-diol (7 g) in ethanol (700 ml) was treated with bromine (0·1 ml) in ethanol (100 ml) until a colouration persisted. The solution was poured into water and extracted with ether. The extracts were washed, dried, and evaporated and the product crystallised from light petroleum to give the *bromo-ether* (6·5 g, 79%), m.p. 209—211°, $[\alpha]_D$ +13·1° (*c* 0·26), $\nu_{max.}$ (CCl_4) 3620, 1215, and 1030 cm^{-1}, τ 4·62 (2H, s, C-15 and C-16), 5·75 (1H, t, C-12β), 6·44 and 6·71) each 1H, d, *J* 6 Hz, 28-H_2), and 6·75 (1H, t, C-3α) (Found: C, 69·2; H, 9·3; Br, 15·1. $C_{30}H_{47}BrO_2$ requires C, 69·3; H, 9·1; Br, 15·4%). The product, with pyridine (150 ml) and acetic anhydride (150 ml) at room temperature overnight, gave the *acetate* (6·0 g, 85%), m.p. (from light petroleum) 222—223°, $[\alpha]_D$ +23° (*c* 0·24), $\nu_{max.}$ (CCl_4) 1730 and 1235 cm^{-1}.

12α-*Bromo*-13β,28;15α,16-*diepoxyoleanan*-3β-*yl Acetate* (XV).—12α-Bromo-13β,28-epoxyolean-15-en-3β-yl acetate (450 mg) in chloroform (10 ml) was added to commercial peracetic acid * (50 ml); the mixture was stirred at room temperature overnight, then warmed to 45° and stirred at this temperature for a further 48 h. The solution was poured into water and extracted with ether. The combined extracts were washed with 2N-sodium hydroxide and water, dried, and evaporated, and the product was chromatographed on alumina (20 g). The *diepoxide* (250 mg, 55%)

* Laporte Industries Limited.

[19] R. G. Curtis, I. Heilbron, E. R. H. Jones, and G. F. Woods, *J. Chem. Soc.*, 1953, 461.

was eluted with light petroleum–benzene (10 : 90 v/v) and crystallised from light petroleum as platelets, m.p. 209—210°, $[\alpha]_D$ +59° (*c* 0·06), $\nu_{max.}$ (CCl_4) 1730, 1235, and 1030 cm^{-1}, τ 5·51 (1H, t, C-3α), 5·90 (1H, t, C-12β), 6·38 and 6·79 (each 1H, d, *J* 8 Hz, 28-H_2), 7·10 (2H, complex, C-15β and C-16β), and 7·98 (3H, s, Ac) (Found: C, 66·6; H, 8·6; Br, 14·0. $C_{32}H_{49}BrO_4$ requires C, 66·5; H, 8·6; Br, 13·8%).

3β-*Acetoxy*-15α,16-*epoxyolean*-12-*en*-28-*ol* (XVI; R = H).—The foregoing diepoxide (490 mg) in benzene–methanol (1 : 1; 40 ml) was treated with activated zinc dust (5 g); the mixture was heated under reflux for 24 h, then filtered through Celite, and the residual zinc dust was washed with several portions of ether. The combined filtrates were evaporated; crystallisation of the residue from methanol afforded the *monoepoxide* (350 mg, 83%), m.p. 213—216°, $[\alpha]_D$ +46° (*c* 0·07), $\nu_{max.}$ (CCl_4) 1730 and 1230 cm^{-1}, τ 4·70 (1H, complex, C-12), 5·49 (1H, t, C-3α), 6·50 (2H, s, 28-H_2), 7·02 (2H, s, C-15β and C-16β), and 7·94 (3H, s, Ac) (Found: C, 75·7; H, 9·9. $C_{32}H_{50}O_4$,0·5CH_3OH requires C, 75·8; H, 10·2%).

15α,16-*Epoxyolean*-12-*ene*-3β,28-*diyl Diacetate* (XVI; R = Ac).—15α,16-Epoxyolean-12-ene-3β,28-diyl 3-acetate (60 mg) in pyridine (10 ml) and acetic anhydride (10 ml) was left at room temperature overnight. The *diacetate* thus obtained (50 mg, 77%) crystallised from ethanol as needles, m.p. 198—199°, $[\alpha]_D$ +40° (*c* 0·17), $\nu_{max.}$ (CCl_4) 1730 and 1230 cm^{-1} (Found: C, 75·5; H, 9·6. $C_{34}H_{52}O_5$ requires C, 75·5; H, 9·7%).

Reduction of 3β-*Acetoxy*-15α,16-*epoxyolean*-12-*en*-28-*ol with Lithium Aluminium Hydride*.—The 15α,16-epoxide (200 mg) in dry tetrahydrofuran (70 ml) was treated with an excess of lithium aluminium hydride and the mixture was refluxed for 3 days. After an acidic work-up to destroy the excess of lithium aluminium hydride, the solution was extracted with ether. The extracts were washed with water, dried, and evaporated. Recrystallisation of the product from carbon tetrachloride gave *olean*-12-*ene*-3β,15α,28-*triol* (170 mg, 93%) as needles, m.p. 180—181°, $[\alpha]_D$ +55° (*c* 0·04), *m/e* 458 (M^+) 440, 250 (base peak), 219, 207, and 189. This product in pyridine (20 ml) and acetic anhydride (20 ml) was left at −10° overnight. The 3,28-diacetate thus obtained (130 mg) crystallised from chloroform–methanol as plates, m.p. 258—260°, $[\alpha]_D$ +57° (*c* 0·10), identical (mixed m.p., i.r. spectrum, and t.l.c.) with material prepared by reduction of 3β,28-diacetoxyolean-12-en-15-one with lithium in liquid ammonia and reacetylation.

Reduction of 3β-*Acetoxy*-15α,16-*epoxyolean*-12-*en*-28-*ol with Lithium in Ethylamine*.—The 15α,16-epoxide (250 mg) in anhydrous ethylamine (40 ml) was cooled to 0° Lithium (1 g) was added in small pieces, and the mixture was stirred at room temperature for 5 h. Methanol (10 ml) was added dropwise with stirring. The ethylamine was allowed to evaporate off and the residue was treated with ether (50 ml) and water (50 ml). The ether layer was separated and the aqueous layer was further extracted with ether. The combined ethereal layers were washed with water, dried, and evaporated. The product was chromatographed on alumina (30 g). Elution with ethyl acetate–benzene (35 : 65 v/v) gave olean-12-ene-3β,16α,28-triol (primulagenin A) (165 mg, 66%), which crystallised from acetone–light petroleum (b.p. 60—80°) as needles, m.p. 236—237°, $[\alpha]_D$ +56° (*c* 0·10) (lit.,[20] m.p. 249·5—250°, $[\alpha]_D$ +58°), $\nu_{max.}$ (Nujol) 3420 cm^{-1}, identical (mixed m.p., i.r. spectrum, and t.l.c.) with an authentic sample. This material was acetylated with pyridine (20 ml) and acetic anhydride (20 ml) at −10° overnight to give the 3,28-diacetate as needles from methanol, m.p. 203—205°, $[\alpha]_D$ +27·2° (*c* 0·09) (lit.,[12] m.p. 212—213°, $[\alpha]_D$ +30·4°), $\nu_{max.}$ (Nujol) 3500 (OH) and 1725, 1269, and 1250 (acetate) cm^{-1}, identical (mixed m.p., i.r. spectrum, and t.l.c.) with an authentic sample (Found: C, 75·2; H, 9·8. Calc. for $C_{34}H_{54}O_5$: C, 75·2; H, 10·0%).

Further elution, with ethyl acetate–benzene (1 : 1 v/v), gave olean-12-ene-3β,15α,28-triol (75 mg, 30%). This was acetylated with pyridine (10 ml) and acetic anhydride (10 ml) at −10° overnight to give the 3,28-diacetate, m.p. 256—259°, $[\alpha]_D$ +42° (*c* 0·10), identical (mixed m.p., i.r. spectrum, and t.l.c.) with an authentic sample (see before).

3β-*Acetoxy*-12α-*bromo*-13β,28-*epoxyoleanan*-16α-*ol* (XVII; R^1 = Ac, R^2 = H).—Primulagenin A (500 mg) in ethanol (100 ml) was treated with a solution of bromine (0·2 ml) in ethanol (100 ml) until a colouration persisted. The solution was poured into water and extracted with ether. The extracts were washed, dried, and evaporated. The product in pyridine (30 ml) and acetic anhydride (30 ml) was left at room temperature overnight. The resulting *bromo-ether* 3-*acetate* (410 mg, 65%) had m.p. 180—182°, $[\alpha]_D$ +70° (*c* 0·21), $\nu_{max.}$ (Nujol) 3570 (OH) and 1730 and 1260 (acetate) cm^{-1}, τ 5·50 (1H, t, C-3α), 5·75 (1H, complex, C-12β), 6·10 (1H, complex, C-16β), 6·54 and 6·83 (each 1H, d, *J* 7 Hz, 28-H_2), and 7·96 (3H, s, Ac) (Found: C, 66·2; H, 8·6; Br, 13·7. $C_{32}H_{51}BrO_4$ requires C, 66·3; H, 8·8; Br, 13·8%). The same product was obtained when the acetylation was carried out on a steam-bath for 6 h.

3β,16α-*Diacetoxyolean*-12-*en*-28-*ol* (II; $R^1 = R^2$ = Ac; R^3 = H).—3β,28-Diacetoxyolean-12-en-16α-ol (800 mg) in benzene (120 ml) was left in contact with Woelm basic alumina (60 g) at room temperature for 12 days. The mixture was filtered and the alumina washed with several portions of ether. The filtrates were combined and the solvent evaporated off. Crystallisation of the product from methanol gave the 3,16-diacetate (660 mg, 83%) as needles, m.p. 252—254°, $[\alpha]_D$ +2·1° (*c* 0·24) (lit.,[12] m.p. 264—266°, $[\alpha]_D$ +1·9°), $\nu_{max.}$ (CCl_4) 3635 (OH) and 1735, 1235, and 1210 (acetate) cm^{-1}, τ 4·8 (2H, complex, C-12 and C-16β), 5·54 (1H, t, C-3α), 6·75 (2H, d, 28-H_2), and 7·97 and 8·00 (each 3H, s, Ac).

12α-*Bromo*-13β,28-*epoxyoleanane*-3β,16α-*diyl Diacetate* (XVII; $R^1 = R^2$ = Ac).—The foregoing 3,16-diacetate (300 mg) in ethanol (200 ml) was treated with bromine (0·1 ml) in ethanol (100 ml) until a colouration persisted. The solution was poured into water and extracted with ether. Crystallisation of the product from cyclohexane gave the *bromo-epoxide* (255 mg, 79%), m.p. 119—123°, $[\alpha]_D$ +19° (*c* 0·22), $\nu_{max.}$ (Nujol) 1740 and 1240 (acetate) cm^{-1}, τ 5·00 (1H, d, C-16β), 5·50 (1H, t, C-3α), 5·73 (1H, t, C-12β), 6·42 and 6·75 (each 1H, d, *J* 7 Hz, 28-H_2), and 7·92 and 7·95 (each 3H, s, Ac) (Found: C, 68·1; H, 9·1. $C_{34}H_{53}BrO_5$,C_6H_{12} requires C, 68·1; H, 9·2%).

3β,16α-*Diacetoxy*-12α-*bromo*-*oleanan*-28,13β-*olactone* (XVIII).—The foregoing bromo-epoxide (150 mg) was dissolved in glacial acetic acid (30 ml). Chromium trioxide (100 mg) in glacial acetic acid (20 ml) was added and the mixture was stirred at room temperature overnight, poured into water, and extracted with ether. The combined extracts were washed with sodium disulphite solution, N-sodium carbonate solution, and water, then dried and evaporated. Recrystallisation of the product from methanol gave the bromo-lactone (105 mg, 70%) as fine needles,

[20] O. Jeger, Cl. Nisoli, and L. Ruzicka, *Helv. Chim. Acta*, 1946, **29**, 1183.

m.p. 170—174°, $[\alpha]_D$ +7·5° (*c* 0·14 in dioxan) (lit.,[15] m.p. 184—190°, $[\alpha]_D$ +8·5°), $\nu_{max.}$ (CCl_4) 1780 (lactone) and 1735, 1230, and 1215 (acetate) cm^{-1}.

Echinocystic Acid Diacetate (III; $R^1 = R^2 = Ac$, $R^3 = H$).—The lactone (XVIII) (80 mg) in benzene–methanol (1 : 1; 20 ml) was treated with activated zinc dust (2 g); the mixture was heated under reflux for 2 h and filtered through Celite, and the residual zinc dust was washed thoroughly with ether. The combined filtrates were evaporated and the residue recrystallised from methanol to give echinocystic acid diacetate (57 mg, 81%), m.p. and mixed m.p. 264—267°, $[\alpha]_D$ −6·3° (*c* 0·16) (lit.,[21] m.p. 272—275°, $[\alpha]_D$ −14·6°), $\nu_{max.}$ (CCl_4) 1700 (acid) and 1740 and 1230 (acetate) cm^{-1}.

Echinocystic Acid Diacetate Methyl Ester (III; $R^1 = R^2 =$ Ac, $R^3 =$ Me).—Echinocystic acid diacetate (90 mg) in ether (15 ml) was treated dropwise with ethereal diazomethane until a yellow colouration persisted. The solution was left for 1 h before the excess of diazomethane was destroyed with acetic acid. The solution was washed with sodium carbonate solution, then water, dried, and evaporated. Recrystallisation of the product from methanol gave echinocystic acid diacetate methyl ester (80 mg, 87%), m.p. 193—194°, $[\alpha]_D$ −14° (*c* 0·13) (lit.,[21] m.p. 200—201, $[\alpha]_{546}$ −15·1°), identical (mixed m.p., i.r. spectrum, and t.l.c.) with an authentic sample (Found: C, 73·9; H, 9·5. Calc. for $C_{35}H_{54}O_6$: C, 73·6; H, 9·5%).

Echinocystic Acid (III; $R^1 = R^2 = R^3 = H$).—Echinocystic acid diacetate (40 mg) and potassium hydroxide (3 g) in ethanol (50 ml) were refluxed for 2 h. The solution was acidified, poured into water, and extracted with ether. Recrystallisation of the product from methanol gave echinocystic acid (26 mg, 76%), m.p. 306—308°, $[\alpha]_{546}$ +34·4° (*c* 0·45 in EtOH) (lit.,[21] m.p. 305—312°, $[\alpha]_{546}$ +40·6°), identical (mixed m.p., i.r. spectrum, and t.l.c.) with an authentic sample.

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