# The Synthesis of β-Amyrin

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18α-Olean-12-ene, which is in acid-catalysed equilibrium with olean-13(18)-ene (δ-amyrene), has been converted in several steps into olean-12-ene (β-amyrene). Transformation of this hydrocarbon into its 11α-hydroxyderivative and photolysis of the nitrite of the latter gave 11a-hydroxy-1-oximino-olean-12-ene. This oxime has been hydrolysed and further processed to furnish olean-12-en-1-one. Several methods have been developed to change the 1-oxo into a 3-oxo-function and vice versa. Since olean-12-en-3-one has already been reduced to  $\beta$ -amyrin and olean-13(18)-ene has been synthesised, our work constitutes a synthesis of  $\beta$ -amyrin.

Related studies on the photolysis of  $11\beta$ -hydroxyolean-12-ene nitrite and on the interrelationship of the 1- and 3-oxo-groups in the lanostane series are also recorded.

 $\beta$ -AMYRIN (3 $\beta$ -hydroxyolean-12-ene) (V; R = OH) is the parent compound of the large  $\beta$ -amyrin group of pentacyclic triterpenoids. The elucidation of the constitution and stereochemistry of  $\beta$ -amyrin was, in its time, a classic piece of work; however, the synthesis of  $\beta$ -amyrin has not hitherto been reported. We felt that this synthesis would be of significance in its own right and would pose problems the solution of which might be of general interest.

Since the pioneering investigations of Halsall and Thomas<sup>1</sup> in the synthesis of pentacyclic triterpenoids, three successful syntheses of olean-13(18)-ene (δ-amyrene) (II), or its equivalent, have been reported.<sup>2-4</sup> Olean-13(18)-ene (II) and  $18\alpha$ -olean-12-ene (I) are in acidcatalysed equilibrium<sup>5</sup> although the equilibrium is largely in favour of the more highly substituted olefin (II). Therefore if  $18\alpha$ -olean-12-ene (I) could be transformed into olean-12-ene (V; R = H) and the latter hydroxylated at C-3 in the  $\beta$ -configuration, a synthesis of  $\beta$ amyrin would result. We describe first the interconversion of the hydrocarbons.

 $18\alpha$ -Olean-12-ene was oxidised with chromic acid to

furnish the 11-oxo-derivative (III).<sup>6</sup> Bromination under acid catalysis followed by spontaneous dehydrobromination <sup>7</sup> gave the dienone (IV). Reduction of the latter with calcium in liquid ammonia afforded in high yield the  $\beta\gamma$ -unsaturated ketone (VI). Treatment of this kinetically controlled product of anion protonation with boron trifluoride-diethyl ether at room temperature furnished approximately equal amounts of  $18\alpha$ - and 18<sub>β</sub>-olean-12-en-11-ones, (III) and (VII), which were separable with difficulty. The interconversion of the latter ketone and olean-12-ene (V; R = H) has already been described <sup>6</sup> and thus the desired transformation of hydrocarbon (I) into hydrocarbon (V; R = H) had been effected.

We then argued that a functional derivative based on the olefinic linkage of olean-12-ene (V; R = H) should be used to introduce oxygen at C-1. The further transformation into a C(3)-oxygenated derivative would then be relatively straightforward. More specifically, we considered that photolysis of the nitrite of 11ahydroxyolean-12-ene (VIII; R = NO) should afford<sup>8</sup> 11α-hydroxy-1-oximino-olean-12-ene (IX). 11α-Hydroxyolean-12-ene was at first synthesised by the photochemical bromination-acetoxylation procedure of

<sup>&</sup>lt;sup>1</sup> T. G. Halsall and D. B. Thomas, J. Chem. Soc., 1956, 2431. <sup>2</sup> E. J. Corey, H. J. Hess, and S. Proskow, J. Amer. Chem. Soc.,

 <sup>&</sup>lt;sup>1</sup> J. A. Barltrop, J. D. Littlehailes, J. D. Rushton, and N. A. J. Rogers, *Tetrahedron Letters*, 1962, 10, 429; see also D. B. Bigley, N. A. J. Rogers, and J. A. Barltrop, J. Chem. Soc., 1960, 4613.

<sup>&</sup>lt;sup>4</sup> E. Ghera and F. Sondheimer, Tetrahedron Letters, 1964, 3887

<sup>&</sup>lt;sup>5</sup> G. Brownlie, M. B. E. Fayez, F. S. Spring, R. Stevenson, and W. S. Strachan, J. Chem. Soc., 1956, 1377; G. S. Davy, T. G. Halsall, and E. R. H. Jones, J. Chem. Soc., 1951, 458.
<sup>6</sup> J. Karliner and C. Djerassi, J. Org. Chem., 1966, **31**, 1945.
<sup>7</sup> Cf. C. W. Picard and F. S. Spring, J. Chem. Soc., 1941, 35.
<sup>8</sup> D. H. R. Barton, J. M. Beaton, L. E. Geller, and M. M. Pechett, I. Amer. Chem. Soc., 1960, **82**, 2640. 1961, **83**, 4076.

Pechett, J. Amer. Chem. Soc., 1960, 82, 2640; 1961, 83, 4076.

Corsano and Piancatelli; 9 however, a simpler thermal procedure gave better results. Olean-12-ene in benzene solution was heated under reflux with N-bromosuccinimide and lead tetra-acetate. This must have furnished

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11 $\alpha$ -acetoxyolean-12-ene (VIII; R = Ac) because alkaline hydrolysis of the product gave in consistent yield (50%) the desired  $11\alpha$ -hydroxyolean-12-ene (VIII; R = H). Both the mechanism and the scope of this new allylic acetoxylation deserve further investigation.

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11 $\alpha$ -Hydroxyolean-12-ene (VIII; R = H) was treated with nitrosyl chloride in pyridine and the crystalline nitrite (VIII; R = NO) thus obtained was photolysed in benzene solution to give 11a-hydroxy-1-oximinoolean-12-ene (IX) in reasonable (50%) yield. With nitrous acid this oxime was converted smoothly into  $11\alpha$ -hydroxyolean-12-en-1-one (X). The latter existed, at least in the crystalline state (Nujol mull), in the open form [shown in formula (X)] and not in the cyclic ketol form. Hydrogenolysis of the allylic function in (X), in a slightly alkaline ethanolic solution over palladiumcharcoal, gave 1-oxo-olean-12-ene (XI). An attempted hydrogenation in ethyl acetate over Adams catalyst gave only the dehydration product, 1-oxo-oleana-9(11).12diene (XII), the constitution of which was shown by its u.v. spectrum and by its high positive rotation.

We could now interrelate the 1-oxo-function of the ketone (X) with the 3-oxygen function needed for a β-amyrin synthesis. Bromination followed by dehydrobromination with NN'-dimethylacetamide containing suspended calcium carbonate gave 1-oxo-oleana-2,12diene (XIII). This unsaturated ketone did not react with alkaline hydrogen peroxide even after lengthy incubation. A different method was therefore adopted. The addition of cyanide ion to (XII) proceeded smoothly to give two isomeric 3-cyano-1-ketones (XIV) to which we have not assigned configurations. The major isomer



gave readily a 2-bromo-derivative on bromination. In practice it was convenient not to separate the stereoisomeric mixture of 3-cyano-derivatives but to brominate and dehydrobrominate without isolation of the intermediate 2-bromo-3-cyano-stereoisomers. In this way 3-cyano-1-oxo-oleana-2,12-diene (XV) was obtained in satisfactory vield.

We then adopted a procedure recently introduced by Glen, Lawrie and Mclean<sup>10</sup> for the replacement of the cyano-function of a  $\beta$ -cyano- $\alpha\beta$ -unsaturated ketone by a nucleophile present in excess. We used sodium methoxide to obtain 3-methoxy-1-oxo-oleana-2,12-diene (XVI). This was promptly reduced with lithium aluminium hydride and worked up with mild acid treatment.<sup>11</sup> The known<sup>12</sup> 1-dehydro-olean-12-en-3-one (XVII) was thus obtained. Hydrogenation of the latter afforded olean-12-en-3-one (\beta-amyrone) (XVIII), reduction of which with lithium aluminium hydride to give  $\beta$ -amyrin (V; R = OH) had already been recorded.<sup>13</sup>

We also completed the following, more original, route to 1-dehydro-olean-12-en-3-one (XVII). The unsaturated cyano-ketone (XV) was treated with alkaline hydrogen peroxide to give the amide (XIX). Oxidation



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<sup>&</sup>lt;sup>9</sup> S. Corsano and G. Piancatelli, *Gazzetta*, 1961, **94**, 1378; Ann. Chim. (Italy), 1965, **55**, 730, 741. <sup>10</sup> A. T. Glen, W. Lawrie, and J. McLean, J. Chem. Soc. (C),

<sup>1966, 661.</sup> <sup>11</sup> D. H. R. Barton, P. J. L. Daniels, J. F. McGhie, and P. J.

Palmer, J. Chem. Soc., 1963, 3675.

R. C. Cookson, J. Chem. Soc., 1954, 282.
 T. R. Ames, T. G. Halsall, and E. R. H. Jones, J. Chem. Soc., 1951, 450.

of this amide with lead tetra-acetate in methanol<sup>14</sup> afforded the methyl carbamate (XX), through addition of methanol to the first formed isocyanate. Hydrolysis of the carbamate with alkali gave 3-amino-1-oxo-oleana-2,12-diene (XXI), which by reduction with lithium aluminium hydride and mild acid treatment furnished 1-dehydro-olean-12-en-3-one (XVII). Alternatively, similar reduction and acid treatment of the carbamate (XX) gave the dehydro-ketone (XVII) directly.

In connection with the synthetic sequence described above we needed to convert  $\beta$ -amyrin into 1-oxo-olean-12-ene (XI), required as a relay point in the synthesis. By use of an earlier procedure <sup>15</sup> 1-dehydro-olean-12-en-3-one (XVII) was converted into its epoxide (XXII) in high (85%) yield with alkaline hydrogen peroxide. Reduction with lithium aluminium hydride gave a mixture of 1,3-diols which, without isolation, was oxidised with Jones reagent to give 1,3-dioxo-olean-12-ene (XXIII) in poor yield (10%). Treatment of this diketone with boron trifluoride-diethyl ether in methanol afforded 3-methoxy-1-oxo-oleana-2,12-diene (XVI).

In view of the poor yield of 1,3-diketone obtained by this route the following alternative route was adopted. Addition of cyanide to 1-dehydro-olean-12-en-3-one (XVII) gave <sup>10</sup> 1 $\alpha$ -cyano-olean-12-en-3-one (XXIV) in good (70%) yield. Bromination of this ketone in acetic acid afforded  $2\alpha$ -bromo-1 $\alpha$ -cyano-olean-12-en-3-one (XXV) in essentially quantitative yield. Dehydrobromination in NN-dimethylacetamide in the presence

of calcium carbonate then furnished 1-cyano-oleana-1,12-dien-3-one (XXVI) in satisfactory (60%) yield. Treatment of this unsaturated nitrile with sodium methoxide in methanol gave the expected 1-methoxyoleana-1,12-dien-3-one (XXVII), which by reduction with lithium aluminium hydride and mild acid treatment furnished oleana-2,12-dien-1-one (XIII). Hydrogenation in ethanol over palladised charcoal then afforded the desired 1-ketone (XI). Analogous hydrogenation of the unsaturated cyanide (XXVI) gave 1 $\beta$ -cyano-olean-12-en-3-one (XXVIII) thus confirming the assignment of the  $\alpha$ -configuration to the cyanide (XXIV).

Alkaline hydrolysis of the unsaturated cyanide (XXVI) provided a convenient source of 1,3-dioxo-olean-12-ene (XXIII). This  $\beta$ -diketone, as isolated from its sodium salt by cautious acidification and trituration with methanol, showed an i.r. spectrum in accord with the presence of only the enolic form. However, brief heating at steam-bath temperature changed the spectrum to that of a diketone. U.v. measurements confirmed these findings. In ethanol, with or without acid, the compound showed the spectrum of an enolised diketone. Addition of base shifted and intensified the spectrum in the manner expected for the formation of the enolate anion. However, the spectra in chloroform showed only the expected very low-intensity absorption for two (isolated) ketone groups. Clearly the relationship between enol content and diketone content in this system is very sensitive to solvent and in the solid state the compound is correctly represented as (XXIII).

We also carried out some model experiments in the lanosterol series. Cyanide ion added smoothly to 1-dehydrolanostenone (XXIX) to furnish  $1\alpha$ -cyano-lanosten-3-one (XXX), which by bromination and dehydrobromination gave 1-cyanolanosta-1,8-dien-3-one (XXXI). Treatment of the latter with sodium methoxide gave the known 1-methoxylanosta-1,8-dien-3-one (XXXII).<sup>11</sup> These reactions parallel those already described.

We also investigated another route to 1,3-dioxo-olean-12-ene (XXIII) and to oleana-2,12-dien-1-one (XIII). 1-Cyano-oleana-1,12-dien-3-one (XXVI) was treated with alkaline hydrogen peroxide to furnish in high (90%)vield the 1a,2a-epoxy-amide (XXXV), which on reduction with chromous chloride gave the tertiary alcohol (XXXVI). Treatment of the latter with methanesulphonyl chloride in pyridine gave 1,3-dioxoolean-12-ene (XXIII) in good (83%) yield. This reaction no doubt proceeds through dehydration of amide to nitrile followed by elimination of cyanide ion (XXXVII), which was detected as a product, to form the 1,3-diketone (XXIII). The tertiary alcohol (XXXVI) was also reduced with sodium borohydride to the diol (XXXVIII), which was not characterised but at once treated with methanesulphonyl chloride in pyridine to

<sup>14</sup> B. Acott and A. L. J. Beckwith, *Chem. Comm.*, 1965, 195; A. L. J. Beckwith, B. Acott, A. Hassanali, and J. W. Redmond, *Tetrahedron Letters*, 1965, **45**, 4039.

<sup>15</sup> Ref. 11 and other references there cited.



give oleana-2,12-dien-1-one (XIII), no doubt formed by  $\beta$ -elimination from the methanesulphonate (XXXIX).



The contrast in the behaviour of the unsaturated cyano-ketones (XV) and (XXVI) towards alkaline hydrogen peroxide deserves further comment. The cyano-ketone (XV) is hydrolysed directly to an amide by the normal attack of peroxide anion on the cyanogroup. This reflects the reluctance of this anion to add to C-3 in the unsaturated ketone (XIII). In contrast, peroxide anion should add readily to C-1 in the cyanoketone (XXVI) to give the intermediate (XXXIII); it adds readily to the same position in the unsaturated ketone (XVII). In the intermediate hydroperoxide (XXXIII) the peroxide function can attack the cyanofunction intramolecularly [see (XXXIV)] in the same way that  $\alpha$ -hydroperoxide is considered to attack intramolecularly a ketone function. The C-2 anion of (XXXIV) could then collapse as indicated to give the observed product (XXXV). Alternatively, the hydroperoxide function of (XXXIII) could facilitate the attack of hydroxide anion, or of peroxide anion, upon the nitrile group as we have already discussed <sup>16</sup> in analogous cases.

In agreement with these interpretations,  $1\alpha$ -cyanoolean-12-en-3-one was hydrolysed very slowly (10% in 18 hr.) to the amide by alkaline hydrogen peroxide, whereas oleana-1,12-dien-3-one (XVII) was completely

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converted into the  $1\alpha,2\alpha$ -epoxide (XXII) under the same conditions in 5 min. Furthermore 1-cyano-oleana-1,12-dien-3-one (XXVI) was stable indefinitely to the same (alkaline) reaction solution from which the hydrogen peroxide had been omitted.

Having studied at some length the photolysis of  $11\alpha$ hydroxyolean-12-one nitrite, we also carried out comparable experiments in the 11 $\beta$ -hydroxy-series. Reduction of olean-12-en-11-one (VII) with lithium aluminium hydride <sup>9</sup> gave 11 $\beta$ -hydroxyolean-12-ene (XL; R = H) in good yield. Conversion into the nitrite (XL; R = NO) in the usual way and photolysis afforded in satisfactory yield an aldoxime (XLI), the constitution of which was established as follows. Acetylation with acetic anhydride-sodium acetate gave a nitrile acetate (XLII); this shows the presence of the aldoxime group. Oxidation of the aldoxime (XLI) with Kiliani's chromic acid afforded the oxo-nitrile (XLIII). We reasoned that the latter should eliminate cyanide ion on vigorous base treatment to give the cross-conjugated dienone (XLVI).



The alternative sequence from (XLIX), which is a possible, but conformationally less probable, structure for the cyano-ketone, would give the dienone (L). It is, of course, easy to distinguish between the latter homoannular, cross-conjugated dienone type and the polyannular type of cross-conjugated dienone such as (XLVI)<sup>17</sup> by spectroscopy. Treatment of the nitrile

<sup>16</sup> J. E. Baldwin, D. H. R. Barton, and J. K. Sutherland, J. Chem. Soc., 1964, 3312; J. E. Baldwin, D. H. R. Barton, D. J. Faulkner, and J. F. Templeton, J. Chem. Soc., 1962, 4743.

(XLIII) with potassium t-butoxide in benzene-t-butyl alcohol afforded in good (60%) yield a nor-dienone (XLVI) in which the chromophore was polyannular; the u.v. spectrum showed two maxima, at 265 and 300 m $\mu$ .<sup>17</sup> Compounds (XLIX) and (L), which would show a single maximum near 250 mµ, are therefore excluded. On prolonged treatment with ethanolic potassium hydroxide the nor-dienone (XLVI) was converted into a partially deconjugated isomer which we formulate as (XLVII) on the basis of its u.v. and i.r. spectra, and especially from consideration of its n.m.r. spectrum. The vinyl hydrogen in olean-12-en-11-one (VII) and in the dienone (XLVI) gives rise to a singlet at  $\tau$  4.24, which represents a geometrical situation <sup>18</sup> where coupling between the  $C(18)\beta$ -H (equatorial) and the C(12) vinyl hydrogen is negligible. In contrast,  $18\alpha$ -olean-12-en-11-one (III), where the C(18) $\alpha$ -H (axial) is nearly at right angles to the C(12) vinyl hydrogen, shows the vinyl signal as a doublet at  $\tau$  4.52 (J 1.7 c./sec.). The isomerised dienone shows this same feature in its n.m.r. spectrum and is, therefore, formulated with an  $18\alpha$ -configuration as in (XLVII).

Treatment of the aldoxime (XLI) with nitrous acid and oxidation of the product with chromium trioxide in pyridine afforded the oxo-aldehyde (XLIV). Further oxidation of the latter with chromium trioxide in acetic acid gave the oxo-acid (XLV). As shown by its u.v. absorption spectrum this compound existed in ethanol in the open form (XLV). However, in the solid state the i.r. spectrum (Nujol mull) showed that it existed rather as the pseudo-acid (XLVIII) with a strong  $\gamma$ -lactone type absorption.

#### EXPERIMENTAL

 $[\alpha]_{\rm p}$  Values were measured with chloroform as solvent at 1% concn. U.v. spectra are for solutions in ethanol. I.r. spectra are for Nujol mulls unless stated otherwise. N.m.r. spectra were determined with a Perkin-Elmer R10 Spectrometer for 10% solutions in chloroform with tetramethyl-silane as internal standard.

Neutral chloroform was prepared by distillation from potassium carbonate and stored over sodium carbonate. Light petroleum had b.p. 40-60°. Alumina was Spence grade H unless otherwise specified. The course of reactions and the progress of column chromatograms was followed by t.l.c. on silica gel G plates, with ethyl acetate-light petroleum (15:85) as eluent and developed by spraying with 50% sulphuric acid and heating at 110° for 10 mins. Thick-layer plates were 1 mm. silica gel HF<sub>254</sub> and were eluted with light petroleum.

The phrase 'in the usual way' refers to dilution of the reaction product with water, filtration, and dissolution of the residue in ether. The ethereal layer was washed with dilute acid (or alkali) as, or when, appropriate, then with water until neutral (litmus), and the solvent was removed *in vacuo*. Where necessary the ethereal solutions were dried (MgSO<sub>4</sub>) before evaporation.

11-Oxo-18α-olean-12-ene.—11-Oxo-olean-12-ene<sup>6</sup> (1·0 g.) in 15% ethanolic potassium hydroxide (150 ml.) was heated under reflux under nitrogen for 62 hr. Working up in the usual way afforded 11-oxo-18α-olean-12-ene (572 mg.) as needles, m.p. 274—275° (from chloroform-methanol),  $[\alpha]_{\rm D}$  +85°,  $\lambda_{\rm max}$  245 mµ (ε 13,000),  $\nu_{\rm max}$  1620 cm.<sup>-1</sup> (Found: C, 84·55; H, 11·25. C<sub>30</sub>H<sub>48</sub>O requires C, 84·85; H, 11·4%) [lit.,<sup>6</sup> m.p. 181—182°,  $\lambda_{\rm max}$  245 mµ (ε 11,000)].

11-Oxo-oleana-12,18-diene.—11-Oxo-olean-12-ene<sup>6</sup> (223 mg.) in glacial acetic acid (10 ml.) was treated with bromine in the same solvent (1% v/v; 2.66 ml.) at 70—75° for 10 min. The mixture was cooled in ice for 15 min. and the precipitate was filtered off. Washing with methanol gave plates (105 mg.) which afforded 11-oxo-oleana-12,18-diene, m.p. 208—209° (from chloroform-methanol),  $[\alpha]_{\rm p}$  + 370°,  $\lambda_{\rm max}$  282 mµ ( $\varepsilon$  13,000),  $\nu_{\rm max}$  1660, 1655, 1630, and 1615 cm.<sup>-1</sup> (Found: C, 85.25; H, 11.1. C<sub>30</sub>H<sub>46</sub>O requires C, 85.25; H, 10.95%).

Oxidation of  $18\alpha$ -Olean-12-ene to 11-Oxo- $18\alpha$ -olean-12-ene. — $18\alpha$ -Olean-12-ene <sup>6</sup> (60 mg.) in glacial acetic acid (5 ml.) under reflux was treated during 10 min. with chromium trioxide (50 mg.) in water (1 drop) and acetic acid (5 ml.). The solution was heated under reflux for 1.5 hr., cooled, poured into water, and extracted with benzene (25 ml.) and ether (50 ml.). Working up in the usual way gave a solid (45 mg.) which, in chloroform (1 ml.), was applied to a thick-layer plate. After elution, the band of higher  $R_{\rm F}$ value was extracted to give crystals, after ether trituration. These gave 11-oxo-18\alpha-olean-12-ene (15 mg.), m.p. 272— 273° (from chloroform-methanol), identified by mixed m.p. and spectral data (see above).

Conversion of 11-Oxo-18 $\alpha$ -olean-12-ene into 11-Oxo-oleana-12,18-diene.—11-Oxo-18 $\alpha$ -olean-12-ene (60 mg.) in acetic acid (15 ml.) containing hydrogen bromide (0.4 ml. of 45% acetic acid solution) under reflux was treated with bromine in acetic acid (1% v/v; 0.52 ml.) and the solution was heated under reflux for 4 hr. and poured into water. Working up in the usual way followed by thick-layer chromatography and removal of the band of highest  $R_{\rm F}$  value afforded, after trituration with ether, 11-oxo-oleana-12,18diene (42 mg.), which was recrystallised and identified by m.p., mixed m.p. and spectroscopic properties.

11-Oxo-olean-13(18)-ene and its Isomerisation.—11-Oxooleana-12,18-diene (334 mg.) in dry tetrahydrofuran (50 ml.) was added to calcium (125 mg.) in dry, redistilled liquid ammonia (100 ml.) and the solution was stirred for 5 min. before the addition of dry t-butyl alcohol (30 ml.). After a further 30 min. stirring, methanol (50 ml.) in ether (50 ml.) was added rapidly, the ammonia was evaporated off, and the solution was concentrated *in vacuo* to 25 ml. Dilution with ether and working up in the usual way afforded 11-oxo-olean-13(18)-ene (300 mg.), which gave needles, m.p. 186—188° (from chloroform-methanol),  $[\alpha]_{\rm p}$  —48°,  $\nu_{\rm max}$ . 1700 cm.<sup>-1</sup>,  $\lambda_{\rm max}$ . 222 ( $\varepsilon$  1700) and 286—290 (330) mµ (Found: C, 85·0; H, 11·4. C<sub>30</sub>H<sub>48</sub>O requires C, 84·85; H, 11·4%).

11-Oxo-olean-13(18)-ene (500 mg.) in dry benzene (25 ml.) containing redistilled boron trifluoride-diethyl ether (5 ml.) was heated under reflux for 105 min. Working up in the usual way gave a white amorphous solid (350 mg.), m.p. 212-218° (from chloroform-methanol),  $[\alpha]_{\rm D}$  +101°,  $\nu_{\rm max}$  1650 cm.<sup>-1</sup>,  $\lambda_{\rm max}$  250 m $\mu$  ( $\varepsilon$  13,000). This mixture could not be

<sup>18</sup> See S. Sternhell, Rev. Pure Appl. Chem. (Australia), 1964, 14, 15.

<sup>&</sup>lt;sup>17</sup> See J. M. Beaton, J. D. Johnston, L. C. McKean, and F. S. Spring, *J. Chem. Soc.*, 1953, 3660.

resolved by thick-layer chromatography. It was, therefore, triangulated systematically from acetone-methanol. The least soluble fractions gave 11-oxo-18 $\alpha$ -olean-12-ene (80 mg.), identified by m.p., mixed m.p.,  $[\alpha]_{\rm p}$ , and spectroscopic properties. From the more soluble fractions was obtained 11-oxo-olean-12-ene (20 mg.), identified similarly.

11a-Hydroxyolean-12-ene and its Transformations.— $\beta$ -Amyrene (5.0 g.) in dry benzene (100 ml.) containing lead tetra-acetate (5 g.) and N-bromosuccinimide (3 g.) was heated under reflux for 30 min. The product, isolated in the usual way, was hydrolysed with potassium hydroxide (20 g.) in water (25 ml.) and absolute ethanol (250 ml.) under reflux for 4 hr. (nitrogen atmosphere). Working up in the usual way (with care to carry out all evaporations at room temperature) gave a pale yellow solid. This was chromatographed over alumina. Elution with light petroleum gave a solid  $(1 \cdot 2 g)$ , which showed carbonyl absorption in the i.r. Further elution with benzene-light petroleum (1:9) gave a similar product (200 mg.). Elution with benzene-light petroleum (1:3) then afforded  $11\alpha$ -hydroxyβ-amyrene (2.5 g.), m.p. 175-178° (from neutral chloroformlight petroleum),  $[\alpha]_{\rm p}$  +56°, no u.v. absorption,  $\nu_{\rm max}$  3600 and 3440 cm.<sup>-1</sup> (Found: C, 84.25; H, 11.65. C30H50O requires C, 84.45; H, 11.8%), 7 5.82 (q, J 3.7 and 8.4 c./sec.) and 4.78 (d, / 3.4 c./sec.).

This alcohol was also obtained from  $\beta$ -amyrene by the method of Corsano and Piancatelli<sup>9</sup> but the method detailed above appears to be more convenient and more readily reproducible.

11α-Hydroxy-β-amyrene (1·11 g.) in pyridine (50 ml.) was treated at  $-20^{\circ}$  with nitrosyl chloride gas for 5 min. After working up in the usual way (washing only with water) a crude nitrite (1·20 g.) was obtained. This was pure enough for photochemical transformation. However, a specimen was crystallised from pyridine-methanol-water at low temperature to give pure  $11\alpha$ -hydroxy-β-amyrene nitrite, m.p. 167—168°,  $[\alpha]_{\rm D}$  —74° (in pyridine),  $\nu_{\rm max.}$  1630 and 1600 cm.<sup>-1</sup> (Found: C, 78·9; H, 10·85; N, 2·9. C<sub>30</sub>H<sub>49</sub>NO<sub>2</sub> requires C, 79·05; H, 10·85; N, 3·05%).

This nitrite (1.0 g.) in dry benzene (100 ml.) was irradiated with a 125 w Hanovia high pressure lamp under nitrogen for 25 min. at room temperature. The benzene was removed *in vacuo* and the residue triturated with light petroleum to give a solid (550 mg.). This gave  $11\alpha$ -hydroxy-1-oximino- $\beta$ -amyrene, m.p. 289—290° (from neutral chloroform-light petroleum), [ $\alpha$ ]<sub>D</sub> +187°,  $\nu_{max}$  3200 and 3100 cm.<sup>-1</sup> (Found: C, 79.35; H, 11.0; N, 3.2. C<sub>30</sub>H<sub>49</sub>NO<sub>2</sub> requires C, 79.05; H, 10.85; N, 3.05%).

This oxime (1.05 g.) in dioxan (350 ml.), acetic acid (126 ml.), and water (21 ml.) was treated with sodium nitrite (3.15 g.) in water (42 ml.) at room temperature and left for 4 hr. Working up in the usual way gave  $11\alpha$ -hydr-oxy-1-oxo- $\beta$ -amyrene, m.p. 172—173° (from neutral chloro-form-light petroleum),  $[\alpha]_{\rm p}$  + 102°,  $\nu_{\rm max}$  3600 and 1700 cm.<sup>-1</sup>,  $\lambda_{\rm max}$  280—285 m $\mu$  ( $\varepsilon$  100) (Found: C, 81.7; H, 10.85. C<sub>30</sub>H<sub>48</sub>O requires C, 81.75; H, 11.0%).

This hydroxy-ketone (287 mg.) in ethyl acetate (20 ml.) was hydrogenated over Adams catalyst (50 mg.). Removal of the catalyst and working up in the usual way gave a product (250 mg.) which afforded 1-oxo-oleana-9,12-diene, m.p. 141—142° (from chloroform-methanol),  $[\alpha]_{\rm p}$  +295°,  $\nu_{\rm max}$ . 1715 cm.<sup>-1</sup>,  $\lambda_{\rm max}$ . 213 ( $\varepsilon$  30,000) and 283 (8900) mµ (Found: C, 85.05; H, 10.85. C<sub>30</sub>H<sub>46</sub>O requires C, 85.25; H, 10.95%).

In view of the failure of this attempted hydrogenation a

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different system was used. The hydroxy-ketone (73 mg.) in absolute ethanol (15 ml.; previously shaken with solid sodium hydrogen carbonate and filtered) was hydrogenated over 10% palladised charcoal (300 mg.). After the uptake of hydrogen (1 mol.) the reaction was worked up in the usual way. The solid product afforded 1-oxo-olean-12-ene (32 mg.), m.p. 176—177° (from chloroform-methanol),  $[\alpha]_{\rm D}$  +138°. Two further crystallisations from the same solvent gave the pure ketone, m.p. 181—182°,  $[\alpha]_{\rm D}$  +146°,  $\nu_{\rm max}$ . 1703 cm.<sup>-1</sup> (Found: C, 85.05; H, 11.4. C<sub>30</sub>H<sub>48</sub>O requires C, 84.85; H, 11.4%).

Transformations based on 1-Oxo-olean-12-ene.—The ketone (250 mg.) in acetic acid (25 ml.) was treated with bromine in acetic acid (1% v/v; 0.72 ml.) and stirred for 90 min. at room temperature. Working up in the usual way gave a non-crystalline solid. This was taken up in NN-dimethylacetamide (30 ml.) containing calcium carbonate (300 mg.) and heated under reflux for 2 hr. Isolation of the product in the usual way afforded 1-oxo-oleana-2,12-diene (85 mg.), m.p. 152—153° (from acetone-methanol), [ $\alpha$ ]<sub>D</sub> + 207°,  $\lambda_{max}$ . 226 m $\mu$  ( $\epsilon$  7000),  $\nu_{max}$ . 1680 cm.<sup>-1</sup> (Found: C, 85.5; H, 11.05. C<sub>30</sub>H<sub>46</sub>O requires C, 85.25; H, 10.95%).

All attempts at the epoxidation of this unsaturated ketone with alkaline hydrogen peroxide led to the recovery of starting material in good yield. The following experiment is typical. The unsaturated ketone (200 mg.) in methanol (8 ml.) was treated during 30 min. at room temperature with hydrogen peroxide (85%; 10 ml.). Aqueous sodium hydroxide (40% w/v; 2 ml.) was added and the solution was left at 0° for 56 hr. After this time about half of the oxidising power of the solution had disappeared. Working up in the usual way gave starting material. The same result was obtained at  $40-45^\circ$  for 12 hr.

1-Oxo-oleana-2,12-diene (500 mg.) in NN-dimethylformamide (15 ml.) and water (1 ml.) containing ammonium chloride (100 mg.) and sodium cyanide (160 mg.) was stirred on a steam-bath for 90 hr. Working up in the usual way gave an oil which was chromatographed on alumina (10 g.) in light petroleum. Elution with light petroleum containing increasing proportions (1—5%) of ethyl acetate gave two isomeric 3-cyano-1-oxo-olean-12-enes. The more easily eluted, *isomer A*, gave needles (185 mg.), m.p. 220—221° (from chloroform-methanol),  $[\alpha]_{\rm D}$  +162°,  $\nu_{\rm max}$ . 2240 and 1710 cm.<sup>-1</sup> (Found: C, 82·75; H, 10·6; N, 3·1. C<sub>31</sub>H<sub>47</sub>NO requires C, 82·8; H, 10·55; N, 3·1%). The less easily eluted, *isomer B*, crystallised similarly; m.p. 213—214°,  $[\alpha]_{\rm D}$  +123°,  $\nu_{\rm max}$ . 2240 and 1710 cm.<sup>-1</sup> (Found: C, 82·7; H, 10·4; N, 3·0%).

The major isomer, isomer A, was brominated as follows. Isomer A (500 mg.) in acetic acid (75 ml.), containing one drop of 45% hydrogen bromide in the same solvent, was treated with bromine in acetic acid (1% v/v; 1.45 ml.) and stirred for 18 hr. at room temperature. The precipitated bromo-ketone was filtered off and washed well with water, and gave a *bromo-ketone*, m.p. 274—276° (decomp.) (from acetone),  $[\alpha]_{\rm D}$  +83°,  $\lambda_{\rm max}$ . 286—288 mµ ( $\varepsilon$  110),  $\nu_{\rm max}$ . 2242 and 1728 cm.<sup>-1</sup> (Found: C, 70.3; H, 8.75; Br, 15.35; N, 2.75. C<sub>31</sub>H<sub>46</sub>BrNO requires C, 70.45; H, 8.75; Br, 15.1; N, 2.65%).

For the next step in the synthesis it was convenient to take the mixture of isomers A and B of 3-cyano-1-oxo-olean-12-ene and to brominate it as above. The resulting mixture of bromo-ketones was then dehydrobrominated as follows. The mixture (8.7 g.) in redistilled NN-dimethylacetamide (450 ml.) containing calcium carbonate (10 g.) was heated under reflux for 1.5 hr. Working up in the usual way gave an oil which was chromatographed over alumina (220 g.) in light petroleum. Elution with light petroleum containing 1.5% of ethyl acetate gave 3-cyano-1-oxo-oleana-2,12-diene (2.52 g.), m.p. 169—170° (from chloroformmethanol),  $[\alpha]_{\rm p}$  +149°,  $\lambda_{\rm max}$  232 mµ ( $\varepsilon$ , 11,000),  $\nu_{\rm max}$  2220 and 1680 cm.<sup>-1</sup> (Found: C, 80.5; H, 9.7; N, 2.7. C<sub>31</sub>H<sub>45</sub>NO requires C, 80.1; H, 10.3; N, 2.9%).

Sodium (1.0 g.) in methanol (20 ml.) was heated to reflux under nitrogen and the volume was reduced (to 5 ml.) until sodium methoxide started to crystallise out. To this suspension the unsaturated oxo-nitrile (see above) (85 mg.) in benzene (3.5 ml.) and methanol (5 ml.) was added and the mixture was heated under reflux for 4 hr. Working up in the usual way gave an oil. This was substantially 1-oxo-3-methoxyoleana-2,12-diene as shown by the following reaction. The oil in dry ether (10 ml.) containing lithium aluminium hydride (50 mg.) was stirred at room temperature for 30 min. Working up in the usual way gave a solid which was taken up in ether and shaken with 2N-aqueous hydrochloric acid. Removal of the acidic layer, washing with water, and evaporation afforded 3-oxo-oleana-1,12-diene (25 mg.), which gave needles (from chloroform-methanol), m.p., [a]<sub>p</sub>, and spectroscopic properties identical with those of an authentic specimen.

This dienone (100 mg.) in propan-2-ol (20 ml.) was hydrogenated over Adams catalyst (10 mg.). After the uptake of hydrogen (1 mol.) the catalyst was filtered off and the solution was worked up in the usual way. Crystallisation of the product from chloroform-methanol gave  $\beta$ amyrenone (40 mg.), m.p., mixed m.p., and spectroscopic properties identical with those of an authentic specimen.

Further Experiments on the Conversion of 1-Oxo-oleana-2,12-diene into β-Amyrin.—3-Cyano-1-oxo-oleana-2,12-diene (see above) (250 mg.) in acetone (15 ml.) was stirred vigorously while aqueous 2N-sodium hydroxide (0·3 ml.) and then 85% hydrogen peroxide (0·6 ml.) were added dropwise. After 30 min. more alkali (0·4 ml.) and hydrogen peroxide (0·6 ml.) were added similarly and the solution was stirred overnight at room temperature. Working up in the usual way gave a product (250 mg.) which gave 3-carbamoyl-1-oxooleana-2,12-diene, m.p. 183—184 and 221—224° (from dilute aqueous methanol),  $[z]_{\rm D}$  +202°,  $\lambda_{\rm max}$ . 221 mμ (e 10,000),  $\nu_{\rm max}$ . 3460, 3400, 3320, 3180, 1680, 1665, 1622, and 1605 cm.<sup>-1</sup> (Found: C, 77.5; H, 10·0; N, 2·55.

 $C_{31}H_{47}NO_{2}H_{20}$  requires C, 77.55; H, 9.95; N, 2.85%).

This amide (100 mg.) in methanol (15 ml.) was treated with lead tetra-acetate (100 mg.) and the solution was heated under reflux for 15 min. Working up in the usual way gave the corresponding *methyl urethane* (85 mg.), m.p. 224-225° (from methanol),  $[\alpha]_{\rm D}$  +272°,  $\lambda_{\rm max}$  271 mµ ( $\epsilon$  16,500),  $\nu_{\rm max}$  3285, 3160, 3095, 1745, 1634, 1620, 1222, and 1040 cm.<sup>-1</sup> (Found: C, 75·25; H, 9·95; N, 2·75. C<sub>32</sub>H<sub>49</sub>NO<sub>3</sub>,CH<sub>4</sub>O requires C, 75·1; H, 10·1; N, 2·65%).

This urethane (150 mg.) in methanol (10 ml.) was heated under reflux with sodium hydroxide (1.0 g.) in water (1 ml.) and methanol (2 ml.) for 10 min. Working up in the usual way gave 3-amino-1-oxo-oleana-2,12-diene (130 mg.), m.p. 311—313° (from chloroform-methanol),  $[\alpha]_{\rm D}$  +334°,  $\lambda_{\rm max}$ . 288 m $\mu$  ( $\epsilon$  25,000),  $\nu_{\rm max}$ . 3455, 3430, 3320, 3260, 3240, 3220, 1650, 1615, 1595, 1570, and 1410 cm.<sup>-1</sup> (Found: C, 82.05; H, 10.7; N, 3.05. C<sub>30</sub>H<sub>47</sub>NO requires C, 82.3; H, 10.8; N, 3.2%).

In an alternative procedure the urethane (100 mg.) in ethanol (15 ml.) containing sodium borohydride (100 mg.) was heated under reflux for 1.5 hr. Working up in the usual way and crystallisation as above gave the same amino-ketone (25 mg.), identified by m.p., mixed m.p., and spectroscopic properties.

Reduction of the urethane with lithium aluminium hydride gave different results. The urethane (110 mg.) in dry tetrahydrofuran (4.5 ml.) was added to lithium aluminium hydride (160 mg.) in the same solvent (5 ml.), and the solution was stirred for 1 hr. at room temperature. Working up in the usual way and shaking the ethereal solution with aqueous 2N-hydrochloric acid, gave a gum. This was chromatographed over alumina in benzene-light petroleum (1:9) to give 3-oxo-oleana-1,12-diene (69 mg.), identified by m.p., mixed m.p., and rotation.

Similarly 3-amino-1-oxo-oleana-2,12-diene (50 mg.) in tetrahydrofuran (5 ml.) containing lithium aluminium hydride (50 mg.) was stirred for 24 hr. at room temperature. Working up as above gave a product containing starting material (90%) and 3-oxo-oleana-1,12-diene (10%) (t.l.c.).

Conversion of  $\beta$ -Amyrenone into 1-Oxo-olean-12-ene.—3-Oxo-oleana-1,12-diene <sup>12</sup> (6 g.) in acetone (60 ml.) and methanol (750 ml) was treated at room temperature with 2N-aqueous sodium hydroxide (40 ml.) followed by hydrogen peroxide (100 vol.; 30 ml.). The suspension was stirred for 1 hr. and concentrated *in vacuo* to half its volume. Working up in the usual way gave  $1\alpha,2\alpha$ *epoxy-3-oxo-olean-12-ene* (5·3 g.) (from acetone-methanol). Recrystallised from acetone this formed needles, m.p. 182— 183°,  $[\alpha]_{\rm D}$  +188°,  $\nu_{\rm max}$  1705 and 878 cm.<sup>-1</sup> (Found: C, 82·05; H, 10·4. C<sub>30</sub>H<sub>46</sub>O<sub>2</sub> requires C, 82·15; H, 10·55%).

This epoxy-ketone (4.0 g.) in dry ether (50 ml.) was heated under reflux with lithium aluminium hydride  $(2 \cdot 8 \text{ g.})$  in dry tetrahydrofuran (75 ml.) for 1.5 hr. Working up in the usual way gave a mixture of isomers showing only  $\nu_{max.}$ 3400 cm.<sup>-1</sup> (no carbonyl band). This product in acetone (400 ml.) at  $-5^{\circ}$  was oxidised by Jones reagent (8 ml.) for 3 min. Methanol (80 ml.) and water (1 l.) were then added and the mixture was filtered through Celite. The Celite was extracted with ether (1 l.) and the extract was washed with water. The ethereal layer was extracted repeatedly with 2N-aqueous sodium hydroxide and the cloudy precipitate was filtered through Celite. The ether layer was rejected. The Celite was triturated with ether (200 ml.), water (250 ml.), and hydrochloric acid (75 ml. conc. acid diluted to 250 ml.) and then filtered. The ethereal layer was washed with water until neutral and the solvent was removed in vacuo. The residue gave 1,3-dioxoolean-12-ene (810 mg.), m.p. 212-213° (from light petroleum),  $[\alpha]_{p} + 174^{\circ}$ ,  $\lambda_{max} 255 \text{ m}\mu$  ( $\epsilon 12,400$ ),  $\lambda_{max}$  (0.01 n-ethanolic sodium hydroxide) 286 m $\mu$  ( $\epsilon 28,000$ ),  $\lambda_{max}$  (0.01 nethanolic hydrochloric acid) 255 m $\mu$  ( $\epsilon$  12,400),  $\lambda_{max}$  (chloroform) 290 m $\mu$  ( $\epsilon$  111),  $\nu_{max}$  1726 and 1705 cm.<sup>-1</sup> (Found: C, 81.85; H, 10.45. C<sub>30</sub>H<sub>46</sub>O<sub>2</sub> requires C, 82.15; H, 10.55%).

This diketone (440 mg.) in methanol (10 ml.) and redistilled boron trifluoride-diethyl ether (8 ml.) were kept at room temperature for 1 hr. Working up in the usual way gave a crystalline solid (310 mg.), m.p. 220—227° (from chloroform-methanol). This was chromatographed in benzene-light petroleum (1:4) over alumina (grade I neutral; 2 g.). Elution with the same solvent gave 3-methoxy-1-oxo-oleana-2,12-diene, as needles, m.p. 230— 231° (from chloroform-light petroleum),  $[\alpha]_{\rm p}$  +229°,  $\lambda_{\rm max}$ . 249 mµ ( $\varepsilon$  12,500),  $\nu_{\rm max}$  1660, 1608, 1360, 1340, 1202, 1192,

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and 1172 cm.<sup>-1</sup> (Found: C, 81.9; H, 10.65.  $C_{31}H_{48}O_2$  requires C, 82.25; H, 10.7%).

The unsaturated ketone mentioned above (160 mg.) in dry ether (10 ml.) containing lithium aluminium hydride (100 mg.) was stirred at room temperature for 1 hr. Working up in the usual way and shaking with 2N-aqueous sulphuric acid gave 3-oxo-oleana-1,12-diene (60 mg.) (from chloroform-methanol) identified by m.p., mixed m.p.,  $[\alpha]_{p}$ , and spectroscopic comparison.

3-Oxo-oleana-1,12-diene (4 g.), sodium cyanide (1·3 g.), and ammonium chloride (800 mg.) in water (10 ml.) and NN-dimethylformamide (75 ml.) were heated on a steambath with stirring overnight. Working up in the usual way and trituration of the product with methanol gave  $1\alpha$ -cyano-3-oxo-olean-12-ene (2·8 g.), sufficiently pure for bromination (see below). Recrystallisation from chloroform-methanol afforded the pure cyano-ketone, m.p. 200-201°,  $[\alpha]_{\rm p}$  +100°,  $\nu_{\rm max}$  2235 and 1713 cm.<sup>-1</sup> (Found: C, 83.05; H, 10.55; N, 3·2. C<sub>31</sub>H<sub>47</sub>NO requires C, 82.8; H, 10.55; N, 3·1%).

This cyano-ketone (2.5 g.) in acetic acid (200 ml.) was treated with stirring at room temperature with bromine in the same solvent (1% v/v; 6.5 ml.). After 2 hr. stirring the precipitate was filtered off and washed with water. Further working up in the usual way gave, after evaporation, crystalline  $2\alpha$ -bromo-1 $\alpha$ -cyano-3-oxo-olean-12-ene (2.6 g.), m.p. 249—251° (decomp.), [ $\alpha$ ]<sub>D</sub> + 12,  $\nu$ <sub>max.</sub> 2240 and 1730 cm.<sup>-1</sup> (Found: C, 70.65; H, 8.85; Br, 15.65; N, 2.85. C<sub>31</sub>H<sub>46</sub>BrNO requires C, 70.45; H, 8.75; Br, 15.1; N, 2.85%).

This bromo-ketone (5.0 g.) in NN-dimethylacetamide (300 ml.) containing calcium carbonate (6.0 g.) was heated under reflux for 2 hr. Working up in the usual way and filtration of the product in benzene-light petroleum (1:9) through alumina (50 g.) gave 1-cyano-3-oxo-oleana-1,12-diene (3.0 g.), which gave pale yellow needles, m.p. 181—182° (from acetone-methanol),  $[\alpha]_{\rm p} + 73^{\circ}$ ,  $\lambda_{\rm max}$  239 m $\mu$  ( $\varepsilon$  10,200),  $\nu_{\rm max}$  2230, 1685, and 1605 cm.<sup>-1</sup> (Found: C, 83.1; H, 10.15; N, 3.15. C<sub>31</sub>H<sub>45</sub>NO requires C, 83.15; H, 10.15; N, 3.15%).

This unsaturated nitrile (1.0 g.) in ethyl acetate (50 ml.) was hydrogenated over 10% palladised charcoal (200 mg.) for  $3\frac{1}{2}$  days. The oily product showed some hydroxy-absorption in the i.r. It was taken up in acetone (75 ml.) and oxidised with Kiliani's chromic acid (10 ml.) at 10° for 30 min. After working up in the usual way the product in benzene-light petroleum (1:9) was chromatographed over alumina (100 g.). Elution with benzene-light petroleum (1:1) gave starting material (300 mg.). Further elution with benzene furnished 1 $\beta$ -cyano-3-oxo-olean-12-ene (324 mg.), which gave needles, m.p. 250-251° (from chloroform-methanol), [ $\alpha$ ]<sub>D</sub> +88°,  $\nu_{max}$  2230 and 1715 cm.<sup>-1</sup> (Found: C, 82.65; H, 10.4; N, 2.8. C<sub>31</sub>H<sub>47</sub>NO requires C, 82.8; H, 10.55; N, 3.1%).

1-Cyano-3-oxo-oleana-1,12-diene  $(1 \cdot 0 \text{ g.})$  in water (13 ml.)and ethanol (120 ml.) containing potassium hydroxide (4.0 g.) was heated under reflux under nitrogen for 2 hr. Working up in the usual way and trituration with methanol gave 1,3-dioxo-oleana-12-ene (see above) (520 mg.), m.p. 116—120°, resolidifies, m.p. 198—201°, undepressed when mixed with authentic diketone. The i.r. spectrum showed  $v_{max}$  3400, 2710, 1635, 1600, 1285, 1235, 1185, 1050, and 858 cm.<sup>-1</sup> but the u.v. spectra in the various solvents were as already recorded. When heated on a steam-bath for 5 min. the compound gave a product with the i.r. spectrum of the authentic diketone (see above). Clearly the treatment with methanol affords the enolic form of the 1,3-diketone. The following experiment confirmed this. Authentic 1,3-dioxo-olean-12-ene (100 mg.) in ether (50 ml.) was extracted with 2N-aqueous sodium hydroxide ( $3 \times 30$ ml.) and then with water ( $3 \times 25$  ml.). The combined alkaline and aqueous extracts were acidified to pH 5 with 2N-aqueous hydrochloric acid and the precipitate was taken up in ether and washed with water. The ethereal solution was divided into two equal parts. The ether was removed *in vacuo* from one part and the residue was crystallised from light petroleum to give back the diketonic form. The solvent was removed *in vacuo* at 20° from the other part and the residue was crystallised from methanol to furnish the enolic form (see above).

Sodium (5 g.) in absolute methanol (700 ml.) was gassed with pure nitrogen for 15 min. 1-Cyano-3-oxo-oleana-1,12diene (2.69 g.) was added and the solution heated under reflux under nitrogen for 4 hr. Working up in the usual way gave an oily product. This, in dry ether (20 ml.) containing lithium aluminium hydride (1.20 g.), was heated under reflux for 1 hr. The solution was poured on ice and stirred with 2N-sulphuric acid for 15 min. Working up in the usual way gave 1-oxo-oleana-2,12-diene (1.05 g.) (from chloroform-methanol), identified by m.p., mixed m.p., and spectroscopic properties.

This unsaturated ketone (500 mg.) in ethanol (150 ml.) was hydrogenated over 10% palladised charcoal (250 mg.) for 15 min. (1 mol. uptake). Working up in the usual way gave 1-oxo-olean-12-ene (450 mg.), m.p., mixed m.p.,  $[\alpha]_p$ , and spectroscopic properties identical with those of the compound obtained from the photolysis and further processing of the nitrite of 11 $\alpha$ -hydroxyolean-12-ene.

Further Experiments on the Synthesis of 1-Oxo-olean-12-ene. —1-Cyano-3-oxo-oleana-1,12-diene (2·43 g.) in acetone (200 ml.) and methanol (100 ml.) was stirred at room temperature during the addition of 2N-aqueous sodium hydroxide (2 ml.) and hydrogen peroxide (100 vol.; 5·0 ml.). The stirring was continued for 30 min. and then more hydrogen peroxide (100 vol.; 5·0 ml.) was added. After a further 30 min. the solution was concentrated *in vacuo* to 75 ml., diluted with water and filtered. The crude product gave 1 $\beta$ -carbamoyl-1 $\alpha$ , 2 $\alpha$ -epoxy-3-oxo-olean-12-ene as fine needles (2·26 g.), m.p. 148—150° (from chloroformmethanol). After a further crystallisation from acetonemethanol this had m.p. 153—154° (sealed tube),  $[\alpha]_{\rm p}$ +145°,  $v_{\rm max}$ . 3480, 3360—3300, 3180, 1710—1690, and 1590 cm.<sup>-1</sup> (Found: C, 76·05; H, 9·8; N, 2·65. C<sub>31</sub>H<sub>42</sub>NO<sub>3</sub>, 0·5H<sub>2</sub>O requires C, 76·05; H, 9·95; N, 2·8%).

In other similar experiments the substrate (50 mg.) in acetone (5 ml.) and methanol (15 ml.) was stirred at room temperature during the addition of 2N-aqueous sodium hydroxide (0.4 ml.) and hydrogen peroxide (100 vol.; 0.4 ml.). Aliquot portions were withdrawn at intervals and the reaction was followed by t.l.c. or other appropriate method. The product was worked up in the usual way.

(i)  $1\alpha$ -Cyano-3-oxo-olean-12-ene did not react in 1 hr. It gave the amide (10%) after 18 hr.

(ii) The reaction with 3-oxo-oleana-1,12-diene, followed by u.v. spectroscopy, was complete in 5 min.

(iii) 1-Cyano-3-oxo-oleana-1,12-diene was treated as above but with the addition of disodium hydrogen phosphate (0.015 M; 0.5 ml.) at the same time as the aqueous alkali. The reaction rate was the same with and without the buffer. When this experiment was repeated without the addition of the alkali no reaction took place. The experiment was also repeated in the absence of hydrogen peroxide; the nitrile was stable indefinitely under these conditions.

1β-Carbamoyl-1α,2α-epoxy-3-oxo-olean-12-ene (530 mg.) in deoxygenated acetone (200 ml.) was treated with 6Nchromous chloride ( $3 \times 2.5$  ml.) in deoxygenated water for 45 min. under nitrogen. After 3 hr. stirring, more reductant (5 ml.) was added and the solution was stirred under nitrogen overnight. Working up in the usual way gave 1β-carbamoyl-1α-hydroxy-3-oxo-olean-12-ene (420 mg.), m.p. 225—226° (from chloroform-methanol), [x]<sub>D</sub> +84°,  $\nu_{max}$  3470, 3420, 3370, 3200, 1708, 1660, 1650, and 1610 cm.<sup>-1</sup> (Found: C, 76.8; H, 9.9; N, 2.8. C<sub>31</sub>H<sub>49</sub>NO<sub>3</sub> requires C, 76.95; H, 10.2; N, 2.9%).

This hydroxy-amide (250 mg.) in redistilled pyridine (5 ml.) was treated with methanesulphonyl chloride (0.5 ml.) in the same solvent (5 ml.) for 24 hr. at room temperature. Working up in the usual way and crystallisation from light petroleum gave 1,3-dioxo-olean-12-ene (200 mg.), identified by m.p., mixed m.p.,  $[\alpha]_{p}$ , and spectroscopic properties.

In a further experiment the hydroxy-amide (450 mg.) in ethanol (50 ml.) containing sodium borohydride (400 mg.) was stirred at room temperature for 2 hr. After working up in the usual way the product (429 mg.) in pyridine (5 ml.) was treated with methanesulphonyl chloride (0.5 ml.) in the same solvent (5 ml.) as in the experiment above. Working up in the usual way gave a dark red oil. This was taken up in the minimum of light petroleum and left in contact with a column of alumina (7 g.) for 2 days. Elution with benzene-light petroleum (1:1) gave 1-oxooleana-2,12-diene (150 mg.), identified by m.p., mixed m.p.,  $[\alpha]_p$ , and spectroscopic properties.

11β-Hydroxyolean-12-ene and its Transformations.—11-Oxo-olean-12-ene (1.0 g.) in dry ether (150 ml.) was treated dropwise with lithium aluminium hydride (1.0 g.) in the same solvent (200 ml.) and the mixture was heated under reflux for 4 hr. Working up in the usual way gave 11βhydroxyolean-12-ene (900 mg.), m.p. 204—205° (from neutral chloroform-light petroleum), [ $\alpha$ ]<sub>D</sub> +115°,  $\nu$ <sub>max</sub> 3680 and 3550 cm.<sup>-1</sup> (Found: C, 84.25; H, 11.95. C<sub>30</sub>H<sub>50</sub>O requires C, 84.45; H, 11.8%).

This alcohol (547 mg.) in pyridine (20 ml.) was nitrosated like the  $\alpha$ -isomer (see above). Working up in the usual way but washing only with water gave the 11 $\beta$ -nitrite (550 mg.). A small portion was crystallised cautiously from pyridinemethanol to furnish the analytical specimen, m.p. 154–155°, [ $\alpha$ ]<sub>D</sub> +209° (pyridine),  $\nu_{max}$  1632, 1600, 1595, 805, 769, and 742 cm.<sup>-1</sup> (Found: C, 78.85; H, 11.05; N, 3.05. C<sub>30</sub>H<sub>49</sub>NO<sub>2</sub> requires C, 79.05; H, 10.85; N, 3.05%).

This nitrite (465 mg.) in dry benzene (100 ml.) was irradiated under nitrogen with a high pressure mercury arc lamp (125 w) at 20° for 20 min. Removal of the solvent *in vacuo* left the derived *aldoxime* (XLI) (236 mg.), m.p. 269–270° (from neutral chloroform-light petroleum),  $[z]_{\rm D} + 119^{\circ}$ ,  $v_{\rm max}$ . 3280 and 3250 cm.<sup>-1</sup> (Found: C, 79.0; H, 10.9; N, 3.1. C<sub>30</sub>H<sub>49</sub>NO<sub>2</sub> requires C, 79.05; H, 10.85; N, 3.05%).

This oxime (300 mg.) in redistilled acetic anhydride (10 ml.) containing fused sodium acetate (800 mg.) was heated on a steam-bath for 90 min. Working up in the usual way gave the 11β-acetoxy-nitrile (XLII) (250 mg.), m.p. 203—204° (from methanol then neutral chloroformmethanol),  $[\alpha]_{\rm p}$  +160°,  $\nu_{\rm max}$  2230, 1740, and 1237 cm.<sup>-1</sup> (Found: C, 80.05; H, 10.3; N, 2.95. C<sub>32</sub>H<sub>49</sub>NO<sub>2</sub> requires C, 80.1; H, 10.3; N, 2.9%).

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The oxime (225 mg.) in dioxan (100 ml.), acetic acid (34 ml.), and water (5 ml.) was treated with sodium nitrite (850 mg.) in water (10 ml.) for 4 hr. at room temperature. After working up in the usual way the product (which showed acetate absorption in the i.r.) in ethanolic potassium hydroxide (15%; 10 ml.) was heated under reflux under nitrogen for 30 min. The product, isolated in the usual way, in pyridine (7.5 ml.) was treated with chromium trioxide (250 mg.) in the same solvent (2.5 ml.) at room temperature for 18 hr. Working up in the usual way gave a crystalline product (180 mg.) which gave the *oxo-aldehyde*, (XLIV) as feathery plates, m.p. 263—265° (from acetone-methanol), [a]<sub>p</sub> +184°,  $\lambda_{max}$  249 mµ ( $\varepsilon$  13,200),  $\nu_{max}$  2750, 1715, and 1665 cm.<sup>-1</sup> (Found: C, 81.35; H, 10.55. C<sub>30</sub>H<sub>46</sub>O<sub>2</sub> requires C, 81.15; H, 10.55%).

This oxo-aldehyde (200 mg.) in glacial acetic acid (10 ml.) was left overnight with chromium trioxide (200 mg.) in the same solvent (10 ml.). Working up in the usual way gave the *acid* [(XLV)  $\longrightarrow$  (XLVIII)] (150 mg.), m.p. 268–269° (from neutral chloroform-methanol),  $[\alpha]_{\rm D}$  +90°,  $\lambda_{\rm max}$ . 248 mµ ( $\varepsilon$  11,500),  $\nu_{\rm max}$  1765, 1725, 1675, 1640, and 1625 cm.<sup>-1</sup> (Found: C, 79.2; H, 10.25. C<sub>30</sub>H<sub>46</sub>O<sub>3</sub> requires C, 79.25; H, 10.2%).

The oxime (XLI) (250 mg.) in acetone (50 ml.) was heated under reflux with Kiliani's chromic acid (5.5 ml.) for 5 min. and then left at room temperature for 25 min. Working up in the usual way gave the *oxo-nitrile* (XLIII) (180 mg.), m.p. 347—348° (from chloroform-methanol),  $[\alpha]_{\rm D}$  +150°,  $\lambda_{\rm max}$  248 mµ ( $\varepsilon$  12,500),  $\nu_{\rm max}$  2230 and 1668 cm.<sup>-1</sup> (Found: C, 82.55; H, 10.2; N, 3.4. C<sub>30</sub>H<sub>45</sub>NO requires C, 82.7; H, 10.4; N, 3.2%).

This oxo-nitrile (700 mg.) in dry benzene (60 ml.) and t-butyl alcohol (50 ml.) was heated under reflux under nitrogen during the addition of potassium t-butoxide [from potassium (1.05 g.) in t-butyl alcohol (100 ml.)] and the heating was continued for 30 min. Isolation of the product in the usual way gave the *nor-dienone* (XLVI) (384 mg.), m.p. 194—195° (from chloroform-methanol),  $[\alpha]_{\rm D}$  —61°,  $\lambda_{\rm max}$  265 ( $\varepsilon$  10,000) and 300 (8900) m $\mu$ ,  $\nu_{\rm max}$  1640, 1620, and 1590 cm.<sup>-1</sup> (Found: C, 85.05; H, 10.9. C<sub>29</sub>H<sub>44</sub>O requires C, 85.25; H, 10.85%).

This dienone (200 mg.) in ethanol (125 ml.) containing potassium hydroxide (4 g.) in water (10 ml.) was heated under reflux under nitrogen for 62 hr. Working up in the usual way afforded the deconjugated *dienone* (XLVII) (77 mg.), m.p. 269·5—271·5° (from chloroform-methanol),  $[\alpha]_{\rm D}$  +223°,  $\lambda_{\rm max}$  218 ( $\varepsilon$  23,000) and 240 (13,600) m $\mu$ ,  $\nu_{\rm max}$ . 1680, 1645, and 1615 cm.<sup>-1</sup> (Found: C, 85·35; H, 10·9. C<sub>29</sub>H<sub>44</sub>O requires C, 85·25; H, 10·85%).

Model Experiments in the Lanosterol Series.—Lanosta-1,8-dien-3-one (5.79 g.), sodium cyanide (1.95 g.), and ammonium chloride (1.2 g.) in water (15 ml.) and NN-dimethylformamide (120 ml.) were stirred together on a steambath for 13 hr. The product was filtered off and gave  $1\alpha$ -cyano-3-oxolanost-8-ene (4.5 g.) as needles, m.p. 182— 183° (from benzene-methanol). Recrystallisation from acetone-methanol did not change the m.p.;  $[\alpha]_{\rm p}$  +101°,  $\nu_{\rm max}$  2235 and 1708 cm.<sup>-1</sup> (Found: C, 82.7; H, 11.1; N, 3.1. C<sub>31</sub>H<sub>47</sub>NO requires C, 82.4; H, 10.95; N, 3.1%).

This cyano-ketone (4.7 g.) in glacial acetic acid (350 ml.) was stirred at 20° with bromine in the same solvent (1% v/v; 12.2 ml.) for 3.5 hr. The solid product was filtered off and then processed in the usual way to give  $2\alpha$ -bromo-la-cyano-lanost-8-en-3-one (2.0 g.), m.p. 222—223° (decomp.) (from acetone),  $[\alpha]_{\rm D}$  -5°,  $\nu_{\rm max}$  2240 and 1728 cm.<sup>-1</sup> (Found: C,

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70·4; H, 9·1; Br, 14·9; N, 2·85. C<sub>31</sub>H<sub>48</sub>BrNO requires C, 70·15; H, 9·1; Br, 15·05; N, 2·65%).

This bromo-ketone (5 g.) in NN-dimethylformamide (1 l.) containing lithium chloride (10 g.) was heated under reflux for 12 hr. Working up in the usual way and chromatography of the product (1.5 g.) in benzene–light petroleum (4:1) over alumina (25 g.) gave 1-cyano-3-oxolanosta-1,8-diene, m.p. 104—105°, [z]<sub>D</sub> —9°,  $\lambda_{max}$  232 mµ ( $\varepsilon$  17,500),  $\nu_{max}$  2210 and 1685 cm.<sup>-1</sup> (Found: C, 82.7; H, 10.8; N, 3.2. C<sub>31</sub>H<sub>48</sub>NO requires C, 82.4; H, 10.95; N, 3.1%). Dehydrobromination with NN-dimethylacetamide–calcium carbonate did not give satisfactory results.

This unsaturated oxo-nitrile (1.0 g.) was heated under reflux in methanol (200 ml.) containing predissolved sodium (1.5 g.) under nitrogen for 4 hr. Working up in the usual way gave 1-methoxylanosta-1,8-dien-3-one (524 mg.), m.p. 132–133° (from methanol),  $[\alpha]_D - 26^\circ$ ,  $\lambda_{max}$  253 m $\mu$  ( $\epsilon$  12,700),  $\nu_{max}$  1660, 1600, 1235, 1225, and 1160 cm.<sup>-1</sup> (lit.,<sup>11</sup> m.p. 138–141°,  $[\alpha]_D - 25^\circ$ ).

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