655. *Dehydrogenation with Mercuric Acetate in the Lupane Series. Part I. Betulin and Betulinic Acid.*

By J. M. Allison, William Lawrie, John McLean, and G. R. Taylor.

Mercuric acetate reacts with betulin (Ia) in chloroform–acetic acid to form the cyclic ether, 13β,28-epoxylup-20(30)-en-3β-ol (II; R = H). Under the same conditions betulin diacetate (Id) forms the non-conjugated diene, 3β,28-diacetoxylupa-12,20(30)-diene (XIV; R = Ac). Comparable reactions are undergone by acetylbetulinic acid (Ib) and methyl acetylbetulinate (Ic) which form respectively the γ-lactone 3β-acetoxylup-20(30)-en-28,13β-olide (IX), and the non-conjugated diene, methyl-3β-acetoxylupa-12,20(30)-dien-28-oate (X).

Mercuric acetate has frequently been employed as a dehydrogenating agent in the steroid field,[1] and in the references cited the reaction leads to the introduction of an ethylenic bond in conjugation with an existing double bond. Biedebach [2] extended the reaction to triterpenes and in general found that whereas α- and β-amyrin derivatives did not react with mercuric acetate in chloroform–acetic acid, derivatives of α-lupene, *viz.*, betulin and lupeol, formed dehydro-compounds of unknown constitution, and it is the purpose of the present work to describe the nature of these compounds.

Biedebach observed that the reactions of betulin and lupeol with mercuric acetate were not dependent on the presence of the alcohol group since their esters were also dehydrogenated. He established that the dehydrogenation was associated with the presence of the olefinic bond in these compounds, since the dihydro-compounds did not react with mercuric acetate. Henbest and Nicholls [3] recently described the formation of a cyclic ether by reaction of the γδ-unsaturated alcohol, bicyclo[2,2,1]hept-5-en-2α-ylmethanol, with mercuric acetate, and Brook, Rodgman, and Wright [4] describe the similar formation of a cyclic ether from the γδ-unsaturated alcohol, 2,6-dimethylhept-5-en-2-ol.

We have repeated Biedebach's experiments and find that betulin (Ia) with mercuric acetate forms a cyclic ether (II; R = H) which contains a vinylidene group (infrared bands at 1630 and 896 cm.$^{-1}$). However, since betulin may isomerise [5] in presence of acid with enlargement of ring E, there is a possibility that under the conditions of the experiment, in which acetic acid is present, ring enlargement may occur to give a compound (III; $R'' = CH_2$), which also contains a vinylidene group. That the cyclic ether is correctly represented by (II) is shown in the sequel.

The nuclear magnetic resonance spectrum of the ether (II; R = Ac) in carbon tetrachloride shows the following features: weak bands at +63 and +89 cycles/sec. due to $\text{C}\cdot\text{CH}_2\cdot\text{O}$ protons, and peaks at +140 and +150 cycles/sec. due to $\text{Me}\cdot\text{C}=$ protons. There is no evidence of a 7 cycles/sec. doublet peak in the $\text{Me}\cdot\text{C}\leqslant$ region which would be expected from the $\text{Me}\cdot\text{CH}<$ methyl group in the alternative structure (III; $R'' = CH_2$).

Oxidation of the acetoxy-ether (II; R = Ac) with chromic acid or ozone gave the methyl ketone (IV; R = Ac, $R' = H_2$) which was hydrolysed and converted into the benzoate (IV; R = Bz, $R' = H_2$). The benzoate showed nuclear magnetic resonance bands at −102 and −85 cycles/sec. due to aromatic ring protons, and a peak at +131

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[1] Windaus and Linsert, *Annalen*, 1928, **465**, 148; Windaus and Auhagen, *ibid.*, 1929, **472**, 185; Windaus, Riemann, and Zühlsdorff, *ibid.*, 1942, **552**, 135; Eck and Hollingsworth, *J. Amer. Chem. Soc.*, 1942, **64**, 140; Barton and Rosenfelder, *J.*, 1951, 2381; Ruyle, Jacob, Chemerda, Chamberlin, Rosenburg, Sita, Erickson, Aluminosa, and Tishler, *J. Amer. Chem. Soc.*, 1953, **75**, 2604; Saucy, Geistlich Helbling, and Heusser, *Helv. Chim. Acta*, 1954, **37**, 250.

[2] Biedebach, *Arch. Pharm.*, 1942, **280**, 304; 1943, **281**, 49.

[3] Henbest and Nicholls, *J.*, 1959, 227.

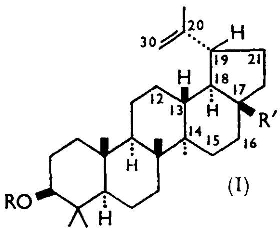
[4] Brook, Rodgman, and Wright, *J. Org. Chem.*, 1952, **17**, 988.

[5] Schulze and Pieroh, *Ber.*, 1922, **55**, 2332; Davy, Halsall, Jones, and Meakins, *J.*, 1951, 2702; Halsall, Jones, and Swayne, *J.*, 1954, 1902.

cycles/sec. due to Me·CO protons. Again there is no evidence of a 7 cycles/sec. doublet which would be expected from the alternative structure (III; R'' = O).

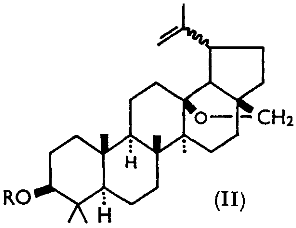
Hydrogenation of the acetoxy-ether (II; R = Ac) in presence of platinum led to the corresponding saturated ether (V; R = Ac) which on oxidation furnished the acetyl-dihydro-acid lactone (VI; R = Ac), showing the absorption at 1770 cm.$^{-1}$ of a γ-lactone. This lactone ring could terminate at position 13, 15, 19, or 21, but reduction with lithium aluminium hydride gives a triol (VII; R = H) which gave only a diacetate (VII; R = Ac). Thus it seems that one of the hydroxyl groups is tertiary and this is confirmed by ready dehydration of the diacetate with phosphorus oxychloride in pyridine to give the iso-betulin diacetate (VIII) showing absorption consistent with the presence of a trisubstituted ethylenic bond ($\lambda_{max.}$ 206 mμ, ε 7900; $\nu_{max.}$ 1650 and 3060 cm.$^{-1}$). These reactions rule out positions 15 and 21 as ends of the γ-lactone, and a decision was made between $C_{(13)}$ and $C_{(19)}$ on the basis of experiments on betulinic acid and its methyl ester.

Treatment of acetylbetulinic acid (Ib) with mercuric acetate gives a γ-lactone (IX) showing infrared bands (in CCl_4) at 1792 (γ-lactone), 1736 and 1245 cm.$^{-1}$ (acetate), 1645 and 910 cm.$^{-1}$ (vinylidene). The presence of a vinylidene group in this compound was confirmed when ozonolysis yielded formaldehyde and the norketone (IV; R = Ac, R' = O). Hydrogenation of the lactone (IX) gives the same dihydro-lactone (VI; R = Ac) as is derived from betulin (Ia) *via* the dihydro-ether (V; R = Ac). Consequently the lactone link in the acetylbetulinic lactone (IX) terminates at the same carbon atom as the ether link in (V) or (II). For reasons stated above the lactone link in the acetylbetulinic lactone (IX) must terminate on $C_{(13)}$ or $C_{(19)}$, but the $C_{(19)}$-lactone, thurberogenin, is known;[6] hence, by elimination, the lactone link in (IX) terminates at position 13. The lactone

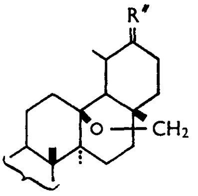


(I)

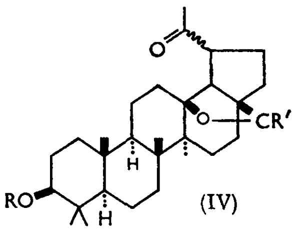
(a) R = H; R' = $CH_2{\cdot}OH$
(b) R = Ac; R' = CO_2H
(c) R = Ac; R' = CO_2Me
(d) R = Ac; R' = $CH_2{\cdot}OAc$



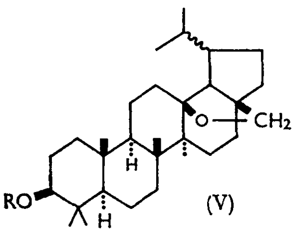
(II)



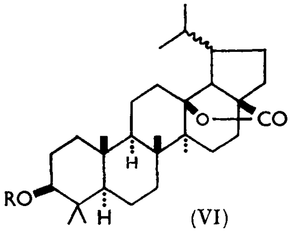
(III)



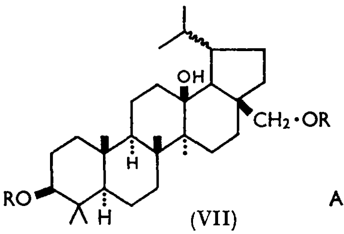
(IV)



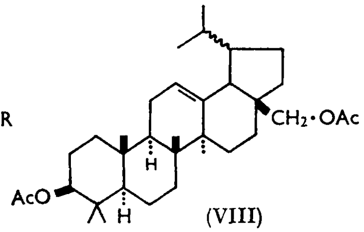
(V)



(VI)



(VII)



(VIII)

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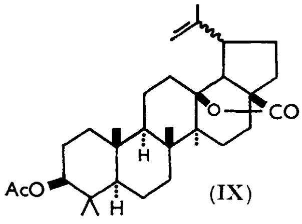
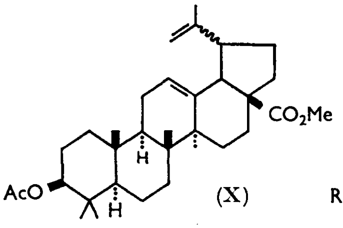
[6] Djerassi, Geller, and Lemin, *J. Amer. Chem. Soc.*, 1953, **75**, 2254; Djerassi, Farkas, Lui, and Thomas, *ibid.*, 1955, **77**, 5330.

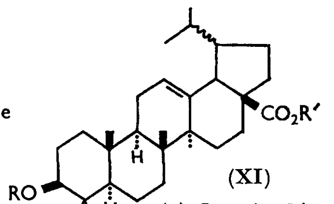
(IX) gives a very faint colour with tetranitromethane and shows very weak ultraviolet absorption at 204 mμ. Djerassi[6] reports similar behaviour for thurberogenin.

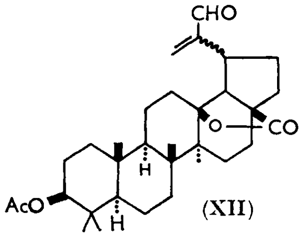
These findings were confirmed when methyl acetylbetulinate (Ic) with mercuric acetate gave the non-conjugated diene (X), $\lambda_{max.}$ 206 mμ (ε 7100), $\nu_{max.}$ 3078, 1634, 901 ($>C=CH_2$), 1730 and 1250 cm.$^{-1}$ (OAc). Hydrogenation (1 mol.) of the diene (X) resulted in disappearance of the vinylidene absorption in the infrared region, the product (XIa) containing a trisubstituted ethylenic bond ($\lambda_{max.}$ 205 mμ, ε 5300; $\nu_{max.}$ 816 cm.$^{-1}$). The monounsaturated ester (XIa) was hydrolysed vigorously with sodium ethoxide to the corresponding acid (XIb), which with hydrogen chloride in chloroform gave the lactone (VI; R = H).

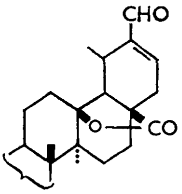
The presence of a five-membered ring E in the lactone series was demonstrated by oxidation of the unsaturated lactone (IX) with selenium dioxide to the αβ-unsaturated aldehyde (XII) showing absorption at 222 mμ (ε 7000). Had a six-membered ring E been present in the unsaturated lactone as in (III; R″ = CH_2) the αβ-unsaturated aldehyde (XIII) would have been formed and, being more highly substituted than (XII), would have shown absorption at 234 mμ.[6]

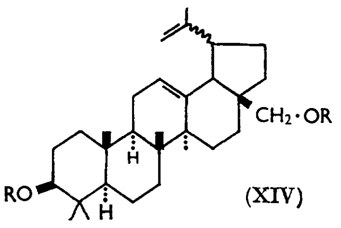

(IX)


(X)


(XI)
(a) R = Ac; R′ = Me
(b) R = H, R′ = H


(XII)


(XIII)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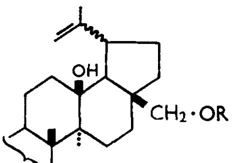
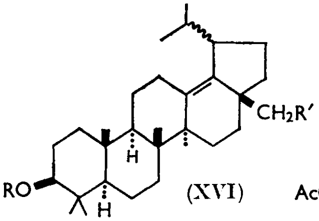
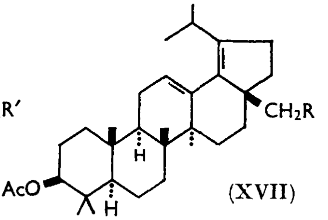
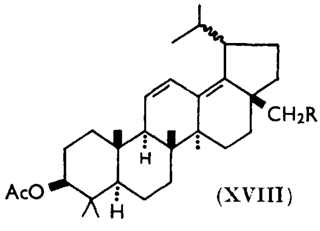
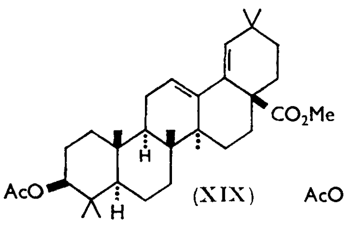
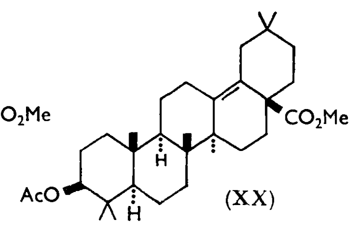

(XV)


(XVI)


(XVII)


(XVIII)


(XIX)


(XX)

Betulin diacetate (Id) also reacts with mercuric acetate in chloroform–acetic acid, and gives a non-conjugated diene (XIV; R = Ac). This absorbs 1 mol. of hydrogen catalytically, to form the isobetulin diacetate (VIII) and this forms an oxide which does not give a colour with tetranitromethane or show ethylenic absorption in the ultraviolet spectrum. The non-conjugated dienyl diacetate (XIV; R = Ac) has also been obtained from the ester (X) and from the unsaturated lactone (IX). Reduction of the ester (X) with lithium aluminium hydride in ether furnished the diol (XIV; R = H) which yielded a diacetate (XIV; R = Ac). Similar reduction of the unsaturated lactone (IX) afforded the triol (XV; R = H) which at 100° also yielded a diacetate (XV; R = Ac). The latter acetate, on dehydration with phosphorus oxychloride in pyridine, gave the diacetoxy-diene (XIV; R = Ac). The original vinylidene group of betulin diacetate is still present in this diene, which shows infrared bands at 1625 and 896 cm.^{-1}, but on hydrogenation of the diene the vinylidene peaks in the infrared spectrum disappear. Since isobetulin diacetate (VIII) is also obtained by dehydration of the diacetoxy-alcohol (VII; R = Ac) in which the hydroxyl group is known to be at position 13, the new ethylenic bond resulting from the action of mercuric acetate on betulin diacetate and on methyl acetylbetulinate must be at position 12, 13, or 13, 18. Of these two possibilities the former is chosen because the absorption of isobetulin diacetate (VIII) ($\lambda_{\text{max.}}$ 206 mμ, ε 7900) indicates a trisubstituted ethylenic bond, and this has been confirmed by experiments on the lupeol analogue of (VIII) in which oxidative cleavage of the double bond gives a keto-aldehyde.[7]

The isomeric unsaturated diacetate (XVI; R = Ac, R′ = OAc) containing the fully substituted 13,18-ethylenic bond has also been obtained by isomerising dehydrobetulin diacetate (XIV; R = Ac) with mineral acid to a mixture of conjugated dienes which we represent as (XVII and XVIII; R = OAc). Chromatography of the mixture afforded the pure *cisoid* heteroannular diene (XVII; R = OAc), $[\alpha]_D$ +219°, $\lambda_{\text{max.}}$ 234 mμ (ε 9400), which on hydrogenation absorbed one mol. of hydrogen to give the tetrasubstituted olefin (XVI; R = Ac, R′ = OAc), $\lambda_{\text{max.}}$ 209 mμ (ε 12,500). The constitutions ascribed to this diene and to the olefin are supported by the molecular rotation change on hydrogenation of the diene (see Table) which is similar to that which occurs when methyl isodehydro-oleanolate acetate[8] (XIX) and 3β-acetoxylupa-12,18-diene[7] (XVII; R = H) are hydrogenated.

Molecular rotation changes accompanying hydrogenation.

	$[\alpha]_D$	M_D	Δ
(XIX)[8]	+209°	+1065°	−1410°
(XX)[9]	−67·5	−345	
(XVII; R = H)[7]	+263	+1230	−1324
(XVI; R = Ac, R′ = H)[7]	−20	−94	
(XVII; R = OAc)	+219	+1145	−1371
(XVI; R = Ac, R′ = OAc)	−43	−226	

The *transoid* diene (XVIII; R = OAc) was not obtained pure, but a fraction resulting from the chromatographic separation of the conjugated dienes showed $\lambda_{\text{max.}}$ 239, 247, 256 mμ (ε 12,600, 11,800, and 6700) in keeping with the spectral properties to be expected from such a *transoid* heteroannular diene.[8]

EXPERIMENTAL

Rotations were determined for chloroform solutions at room temperature, ultraviolet spectra for ethanol solutions, and infrared spectra for Nujol mulls unless otherwise stated. Light petroleum refers to the fraction of b. p. 60—80°.

13β,28-*Epoxylup*-20(30)-*en*-3β-*ol* (II; R = H).—Betulin (1 g.) in warm chloroform (30 ml.) was heated for 3 hr. on the steam-bath with mercuric acetate (17 g.) in glacial acetic acid (370 ml.). The solution was cooled, filtered from mercurous acetate, and poured into water.

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[7] To be described in Part II of this series.

[8] Barton and Brooks, *J.*, 1951, 257.

[9] Jeger, Norymberski, and Ruzicka, *Helv. Chim. Acta*, 1944, **27**, 1532.

Extraction with chloroform (2 × 100 ml.), washing of the extract, and removal of solvent gave the mercury complex which was dissolved in ethyl acetate (150 ml.) and treated with hydrogen sulphide for 3 hr. The suspension was filtered from mercuric sulphide and taken to dryness, and the residue in ether–methanol (19 : 1) filtered successively through kieselguhr and alumina. The yellow gum (0·86 g.) obtained on removal of solvent was chromatographed in ether on alumina (15 g.). Elution with ether gave 13β,28-*epoxylup*-20(30)-*en*-3β-*ol* (0·535 g.), needles (from methylene chloride–light petroleum), m. p. 266°, $[\alpha]_D$ +60° (*c* 1·4), $\nu_{max.}$ 3460 cm.$^{-1}$ (OH) 1620 and 893 cm.$^{-1}$ (vinylidene) (Found: C, 81·5; H, 11·1. $C_{30}H_{48}O_2$ requires C, 81·8; H, 11·0%).

The *acetate* (II; R = Ac), obtained by treating the alcohol with acetic anhydride in pyridine at 100°, formed needles (from chloroform–methanol), m. p. 242—244°, $[\alpha]_D$ +64° (*c* 1·2), $\nu_{max.}$ 1730 and 1250 cm.$^{-1}$ (OAc), 1630 and 896 cm.$^{-1}$ (vinylidene), $\lambda_{max.}$ 206 mμ (ε 6000) (Found: C, 79·2; H, 10·6. $C_{32}H_{50}O_3$ requires C, 79·6; H, 10·4%).

This acetate was also prepared by refluxing betulin 3-acetate (0·75 g.) in chloroform (50 ml.) for 5 hr. with mercuric acetate (25 g.) in acetic acid (400 ml.). Working up as above, followed by chromatography on alumina (15 g.) and elution with benzene, gave the acetate (0·25 g.), m. p. and mixed m. p. (with the specimen prepared as above) 242—244°. The infrared spectra of the acetates were identical.

3β-*Acetoxy*-13β,28-*epoxylupane* (V; R = Ac).—A solution of 3β-acetoxy-13β,28-epoxylup-20(30)-ene (0·21 g.) in ether (150 ml.) containing acetic acid (10 ml.) was hydrogenated in presence of platinum oxide (0·15 g.) for 12 hr. Working up in the usual way gave 3β-*acetoxy*-13β,28-*epoxylupane*, needles (0·18 g.) (from chloroform–methanol), m. p. 281—282° (*in vacuo*), $[\alpha]_D$ +48° (*c* 1·5), $\nu_{max.}$ 1734 and 1248 cm.$^{-1}$ (OAc) (no selective absorption in the ultraviolet range 200—210 mμ, and no colour with tetranitromethane) (Found: C, 79·4; H, 11·1. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%). Hydrolysis of the acetate (0·7 g.) with boiling methanolic 5% potassium hydroxide (200 ml.) for 1·5 hr. and isolation of the product through ether gave 13β,28-*epoxylupan*-3β-*ol* (V; R = H) (0·6 g.), needles (from methylene chloride–acetone), m. p. 213°, $[\alpha]_D$ +40° (*c* 1·4), $\nu_{max.}$ 3320 cm.$^{-1}$ (OH) (Found: C, 81·4; H, 11·3. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%). When treated with a 6% solution of hydrogen peroxide in 100% formic acid oxide formation did not occur, thereby confirming the absence of a double bond; instead, the 3β-*formate* (V; R = CHO) was isolated, as plates (from chloroform–methanol), m. p. 254—255°, $[\alpha]_D$ +49·5 (*c* 1·1), $\nu_{max.}$ 1700 and 1175 cm.$^{-1}$ (formate) (Found: C, 78·8; H, 11·0. $C_{31}H_{50}O_3$ requires C, 79·1; H, 10·7%). Hydrolysis of the formate with methanolic potassium hydroxide re-formed the alcohol (V; R = H).

13β,28-*Epoxylupan*-3-*one*.—Oxidation of 13β,28-epoxylupan-3β-ol (0·38 g.) in pyridine (30 ml.) with chromium trioxide (0·3 g.) in pyridine (40 ml.) at room temperature (20 hr.) and isolation of the product in the usual way gave 13β,28-*epoxylupan*-3-*one*. The ketone (0·27 g.), purified by elution from alumina with benzene–light petroleum (1 : 1) and crystallised from chloroform–methanol, had m. p. 252—253° (*in vacuo*), $[\alpha]_D$ +68° (*c* 1·1), $\nu_{max.}$ 1700 cm.$^{-1}$ (C=O) (Found: C, 80·4; H, 10·9. $C_{30}H_{48}O_2,\frac{1}{2}CH_3{\cdot}OH$ requires C, 80·2; H, 11·0%).

3β,28-*Diacetoxylupa*-12,20(30)-*diene* (XIV; R = Ac).—Betulin diacetate (1 g.) in chloroform (20 ml.) was treated with mercuric acetate in acetic acid as described above for betulin. The product was dissolved in benzene and filtered through alumina (50 g.). Removal of benzene gave a gum which deposited the *diacetate* (XIV; R = Ac) (0·15 g.) that formed needles (from aqueous ethanol), m. p. 177—178°, $[\alpha]_D$ +41° (*c* 3·4), $\nu_{max.}$ 1730, 1256, and 1240 cm.$^{-1}$ (OAc) 1625 and 896 cm.$^{-1}$ (vinylidene), $\lambda_{max.}$ 204 mμ (ε 8000) (Found: C, 77·9; H, 9·9. $C_{34}H_{52}O_4$ requires C, 77·8; H, 10·0%). Hydrolysis of this diacetate with boiling methanolic 5% potassium hydroxide for 1·5 hr. and isolation of the product through ether in the absence of mineral acid gave *lupa*-12,20(30)-*diene*-3β,28-*diol* (XIV; R = H), needles (from chloroform–light petroleum), m. p. 196—198° with resolidification and remelting at 211—214°, $[\alpha]_D$ +8° (*c* 1·1), $\nu_{max.}$ 3220 cm.$^{-1}$ (OH), 1620 and 885 cm.$^{-1}$ (vinylidene). This diol was also obtained by reduction of the ester (X) with lithium aluminium hydride; similar reduction of the unsaturated lactone (IX), followed by acetylation and dehydration, gave the corresponding diacetate (XIV; R = Ac).

3β,28-*Diacetoxylup*-12-*ene* (VIII).—Hydrogenation of the diacetate (XIV; R = Ac) (0·9 g.) in ether (200 ml.) containing acetic acid (20 ml.) in presence of platinum oxide (0·5 g.) for 15 hr. gave the *diacetate* (VIII), needles (from chloroform–methanol), m. p. 209—210°, $[\alpha]_D$ +16° (*c* 1·2), $\nu_{max.}$ 1730 and 1240 cm.$^{-1}$ (OAc), $\lambda_{max.}$ 206 mμ (ε 7900) (Found: C, 77·5; H, 10·5.

$C_{34}H_{54}O_4$ requires C, 77·5; H, 10·3%). This compound was also prepared by dehydration of the triol diacetate (VII; R = Ac) which is described below. Hydrolysis of the diacetate with methanolic potassium hydroxide and working up through ether gave *lup*-12-*ene*-3β,28-*diol*, needles (from chloroform–methanol), m. p. 214—217°, $[\alpha]_D$ −14° (*c* 1·1) (Found: C, 81·3; H, 11·6. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%).

3β,28-*Diacetoxy*-12,13-*epoxylupane*.—A solution of the diacetate (VIII) (0·19 g.) in ethyl acetate (15 ml.) was treated with 30% hydrogen peroxide (3 ml.) in 100% formic acid (15 ml.) at 45° for 1·5 hr. Working up through ether gave the *epoxide* (0·11 g.), needles (from methanol), m. p. 207—208°, $[\alpha]_D$ +22° (*c* 1·1) (Found: C, 75·3; H, 10·2. $C_{34}H_{54}O_5$ requires C, 75·2; H, 10·0%). The epoxide was transparent to ultraviolet light and did not give a colour with tetranitromethane.

3β-*Acetoxylupan*-28,13β-*olide* (VI; R = Ac).—To a boiling solution of 3β-acetoxy-13β,28-epoxylupane (V; R = Ac) (0·5 g.) in acetic acid (50 ml.), chromium trioxide (1 g.) in acetic acid (150 ml.) was added during 20 min., and this mixture was refluxed for 1·5 hr. Excess of chromic acid was destroyed with methanol, and the product worked up through ether to give 3β-*acetoxylupan*-28,13β-*olide* (VI; R = Ac), plates (0·47 g.) (from chloroform–methanol), m. p. 299—300°, $[\alpha]_D$ +49° (*c* 1·1), $\nu_{max.}$ 1734 and 1250 cm.$^{-1}$ (OAc) 1770 cm.$^{-1}$ (γ-lactone) (Found: C, 76·85; H, 10·2. $C_{32}H_{50}O_4$ requires C, 77·1; H, 10·1%).

Lupane-3β,13β,28-*triol* (VII; R = H).—The lactone (VI; R = Ac) (0·25 g.) in dry ether (200 ml.) was refluxed with lithium aluminium hydride (1 g.) for 1·5 hr. Isolation of the product through ether gave the *triol* (VII; R = H), needles (0·2 g.) (from chloroform–benzene), m. p. 240—242° (decomp.), $[\alpha]_D$ +22° (*c* 1·0 in ethanol–chloroform), $\nu_{max.}$ 3220 cm.$^{-1}$ (OH) (Found: C, 78·0; H, 11·2. $C_{30}H_{52}O_3$ requires C, 78·2; H, 11·4%). Acetylation of the triol (VII; R = H) with acetic anhydride and pyridine at 100° gave 3β,28-*diacetoxylupan*-13β-*ol* (VII; R = Ac), needles (from methanol), m. p. 272—273°, $[\alpha]_D$ +19° (*c* 1·0), $\nu_{max.}$ 3470 cm.$^{-1}$ (OH), 1745, 1712, and 1242 cm.$^{-1}$ (OAc) (Found: C, 75·3; H, 10·0. $C_{34}H_{56}O_5$ requires C, 74·95; H, 10·4%). Dehydration of this diacetate (0·08 g.) in dry pyridine (15 ml.) with phosphorus oxychloride (4 ml.) at 100° for 1·5 hr. and working up through ether gave the diacetate (VIII), needles (0·05 g.) (from chloroform–methanol), m. p. 210°, $[\alpha]_D$ +18° (*c* 1·3). The latter diacetate did not depress the m. p. of that prepared as above by hydrogenation of the diacetate (XIV; R = Ac), and the compounds showed infrared identity.

3β-*Acetoxy*-13β,28-*epoxy*-30-*norlupan*-20-*one* (IV; R = Ac, R′ = H_2).—(*a*) 3β-Acetoxy-13β,28 epoxylup-20(30)-ene (II; R = Ac) (0·41 g.) in methylene chloride (60 ml.) was ozonised at −45° for 35 min. The mixture was allowed to reach room temperature, then acetic acid (15 ml.) and zinc dust (1 g.) were added during 20 min. with stirring, which was continued for a further 40 min. The suspension was filtered and the product isolated by washing the filtrate, drying (Na_2SO_4), and evaporation to dryness. 3β-*Acetoxy*-13β,28-*epoxy*-30-*norlupan*-20-*one* crystallised from chloroform–methanol as plates (0·28 g.), m. p. 317—319°, $[\alpha]_D$ +3° (*c* 1·3), $\nu_{max.}$ 1736 and 1245 cm.$^{-1}$ (OAc) and 1706 cm.$^{-1}$ (C=O) (Found: C, 77·1; H, 10·1. $C_{31}H_{48}O_4$ requires C, 76·8; H, 10·0%).

(*b*) The ketone was also obtained by oxidation of 3β-acetoxy-13β,28-epoxylup-20(30)-ene (II; R = Ac) (2·31 g.) in boiling acetic acid by slow addition of chromium trioxide (7 g.) in acetic acid (80 ml.) followed by boiling under reflux for 1·5 hr. The excess of chromic acid was destroyed with methanol and on working up through ether a gum was obtained. Chromatography on alumina (20 g.) and elution with benzene–light petroleum (1 : 1) gave the ketone (IV; R = Ac, R′ = H_2) (0·31 g.), m. p. 317—319°, $[\alpha]_D$ +4° (*c* 1·3).

3β-*Benzoyloxy*-13β,28-*epoxy*-30-*norlupan*-20-*one* (IV; R = Bz, R′ = H_2).—Hydrolysis of the acetoxy-norketone (IV; R = Ac, R′ = H_2) gave an amorphous alcohol that (0·56 g.) with benzoyl chloride (2 ml.) in pyridine (30 ml.) at 100° (1·5 hr.) gave, after working up through ether followed by chromatography on alumina and elution with benzene–light petroleum (1 : 1), the *benzoate* (IV; R = Bz, R′ = H_2), needles (0·51 g.) (from chloroform–methanol), m. p. 313°, $[\alpha]_D$ +26·5° (*c* 1·5), $\nu_{max.}$ 1725, 1280, and 1120 cm.$^{-1}$ (benzoate) (Found: C, 76·7; H, 9·2. $C_{36}H_{50}O_4,CH_3{\cdot}OH$ requires C, 76·8; H, 9·4%).

3β-*Acetoxylup*-20(30)-*en*-28,13β-*olide* (IX).—Acetylbetulinic acid (0·5 g.) in chloroform (15 ml.) was heated at 100° with a solution of mercuric acetate (7 g.) in acetic acid for 5 hr. The product was worked up through chloroform, the chloroform solution being washed, dried ($CaCl_2$), and treated with hydrogen sulphide (3 hr.). Filtration and removal of solvent gave a gum which still contained a trace of mercury. The latter was removed by taking up the product in pyridine and again passing hydrogen sulphide. Filtration and removal of pyridine gave a solid which was chromatographed on alumina (15 g.). Elution with light petroleum–benzene (2 : 1) gave sulphur followed by 3β-*acetoxylup*-20(30)-*en*-28,13β-*olide* (IX), needles (0·26 g.) (from chloroform–methanol), m. p. 315—317°, $[\alpha]_D$ +60° (*c* 1·1), $\nu_{max.}$ 1786 cm.$^{-1}$ (γ-lactone), 1739 and 1245 cm.$^{-1}$ (OAc), 1630 and 913 cm.$^{-1}$ (vinylidene). There was weak absorption at 204 mμ (ε 2000) and the compound did not give a colour with tetranitromethane [6] (Found: C, 77·1; H, 9·8. $C_{32}H_{48}O_4$ requires C, 77·4; H, 9·7%).

Hydrogenation of the lactone (IX) (0·15 g.) in acetic acid (100 ml.) containing platinum oxide (0·05 g.) for 20 hr. and working up as usual gave the saturated acetyl-lactone (VI; R = Ac), plates (0·12 g.) (from chloroform–methanol), m. p. 301—302°, $[\alpha]_D$ +46° (*c* 1·78) (Found: C, 77·4; H, 10·2. Calc. for $C_{32}H_{50}O_4$: C, 77·1; H, 10·1%). The m. p. did not depress that of the saturated lactone acetate obtained from the ether (V; R = Ac), and the compounds showed infrared identity.

Boiling the lactone (IX) (0·309 g.) in benzene (5 ml.) with methanolic 5% potassium hydroxide (55 ml.) for 3 hr. and working up through ether gave 3β-*hydroxylup*-20(30)-*en*-28,13β-*olide* needles (from methanol), m. p. 308—309° (*in vacuo*), $[\alpha]_D$ +57° (*c* 1·0), $\nu_{max.}$ 3436 cm.$^{-1}$ (OH), 1776 cm.$^{-1}$ (γ-lactone), 1639 and 893 cm.$^{-1}$ (vinylidene) (no appreciable ultraviolet absorption) (Found: C, 79·0; H, 10·3. $C_{30}H_{46}O_3$ requires C, 79·2; H, 10·2%). Hydrogenation of this lactone (0·103 g.) in acetic acid (100 ml.) in presence of platinum oxide (0·1 g.) for 12 hr. gave 3β-*hydroxylupan*-28,13β-*olide* (VI; R = H) needles (0·07 g.) (from methanol), m. p. 314—316°, $[\alpha]_D$ +41° (*c* 1·06), $\nu_{max.}$ 1767 cm.$^{-1}$ (γ-lactone) (Found: C, 78·7; H, 10·6. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%).

Ozonolysis of 3β-*Acetoxylup*-20(30)-*en*-28,13β-*olide* (IX).—The lactone (0·22 g.) in chloroform (20 ml.) was ozonised at −45° for 45 min. When the solution had reached room temperature, acetic acid (4 ml.) was added, followed by zinc dust (1 g.) with stirring during 20 min. The solution was stirred for a further 40 min., filtered, and diluted with chloroform (75 ml.), and the chloroform layer was washed with water (3 × 50 ml.). The combined washings were treated with a cold saturated aqueous solution of dimedone and, after 48 hr., the resultant precipitate was collected and recrystallised from methanol to give formaldehyde dimethone as needles (0·06 g., 45%), m. p. and mixed m. p. 190—191°. Evaporation of the dried (Na_2SO_4) chloroform solution and crystallisation of the residue (0·195 g.) from ethanol gave 3β-*acetoxy*-20-*oxo*-30-*norlupan*-28,13β-*olide* (IV; R = Ac, R′ = O), plates, m. p. 317—319° (*in vacuo*), $[\alpha]_D$ +2° (*c* 2·3), $\nu_{max.}$ 1786 (γ-lactone), 1733 and 1247 (OAc), and 1715 cm.$^{-1}$ (C=O) (Found: C, 74·8; H, 9·5. $C_{31}H_{46}O_5$ requires C, 74·7; H, 9·3%).

3β-*Acetoxy*-29-*oxolup*-20(30)-*en*-28,13β-*olide* (XII).—A solution of the acetoxy-lactone (IX) (0·203 g.) in acetic acid (10 ml.) was refluxed with selenium dioxide (0·35 g.) for 2 hr. Filtration and evaporation followed by chromatography on alumina (10 g.) from benzene–light petroleum (1 : 1) gave the *aldehyde* (XII), needles (0·16 g.) (from methanol), m. p. 312—314° (*in vacuo*), $[\alpha]_D$ +46·5° (*c* 1·25), $\nu_{max.}$ 1779 (γ-lactone), 1730 and 1242 (OAc), and 1692 cm.$^{-1}$ (αβ-unsaturated aldehyde), $\lambda_{max.}$ 222 mμ (ε 6800) (Found: C, 75·3; H, 9·2. $C_{32}H_{46}O_5$ requires C, 75·3; H, 9·1%).

Lup-20(30)-*ene*-3β,13β,28-*triol* (XV; R = H).—The lactone (IX) (2 g.) in benzene–ether (1 : 4; 500 ml.) was refluxed with lithium aluminium hydride (2 g.) for 1·5 hr. Isolation through ether, without contact with mineral acid, gave the *triol* (XV; R = H) (1·98 g.) prisms (from aqueous methanol), m. p. 204—206°, $[\alpha]_D$ +49° (*c* 1·75), $\lambda_{max.}$ 204 mμ (ε 3500), $\nu_{max.}$ 3356 (OH), 1647 and 893 cm.$^{-1}$ (vinylidene) (Found: C, 75·9; H, 11·0. $C_{30}H_{50}O_3,CH_3{\cdot}OH$ requires C, 75·9; H, 11·1%). Treatment with acetic anhydride in pyridine, at room temperature for 48 hr. or at 100° for 3 hr., afforded 3β,28-*diacetoxylup*-20(30)-*en*-13β-*ol* (XV; R = Ac), blades (from chloroform–methanol), m. p. 228—230°, $[\alpha]_D$ +44° (*c* 1·93), $\lambda_{max.}$ 205 mμ (ε 3900), $\nu_{max.}$ 3460 (OH), 1739, 1712, and 1254 (OAc), and 1645 and 884 cm.$^{-1}$ (vinylidene) (Found: C, 75·3; H, 10·1. $C_{34}H_{54}O_5$ requires C, 75·2; H, 10·0%). Dehydration of this acetate (1 g.) in dry pyridine (60 ml.) with phosphorus oxychloride (8 ml.) at 100° for 3 hr. and working up through ether gave 3β,28-diacetoxylupa-12,20(30)-diene (XIV; R = Ac), plates (from ethanol), m. p. and mixed m. p. 177—179°, $[\alpha]_D$ +40° (*c* 2·6).

Methyl 3β-*Acetoxylupa*-12,20(30)-*dien*-28-*oate* (X).—Methyl acetylbetulinate (4·85 g.) in chloroform (200 ml.) was refluxed with mercuric acetate (70 g.) in acetic acid (1 l.) for 5 hr. Working up through chloroform gave a product which was freed from mercury by dissolution in pyridine and passage of hydrogen sulphide for 3 hr. Filtration, removal of pyridine, and chromatography on alumina (100 g.) from light petroleum–benzene (1 : 3) gave the *ester* (X), prisms (1·42 g.) (from methanol), m. p. 217—219°, $[\alpha]_D$ +60° (*c* 3·54), $\nu_{max.}$ 1739 and 1253 (ester), 1631 and 885 cm.$^{-1}$ (vinylidene), $\lambda_{max.}$ 206 mμ (ε 7100) (Found: C, 77·5; H, 10·2. $C_{33}H_{50}O_4$ requires C, 77·6; H, 9·9%).

Methyl 3β-*Hydroxylupa*-12,20(30)-*dien*-28-*oate*.—Hydrolysis of the ester (X) (0·2 g.) with boiling methanolic 3% potassium hydroxide (50 ml.) for 3 hr. and isolation in the usual way gave *methyl* 3β-*hydroxylupa*-12,20(30)-*dien*-28-*oate* (0·17 g.), needles (from aqueous methanol), m. p. 182—184°, $[\alpha]_D$ +45° (*c* 1·1), $\lambda_{max.}$ 207 mμ (ε 6300), $\nu_{max.}$ 3571 (OH), 1718 (ester), 1637, and 893 cm.$^{-1}$ (vinylidene) (Found: C, 79·4; H, 10·5. $C_{31}H_{48}O_3$ requires C, 79·4; H, 10·3%).

3β-*Hydroxylupa*-12,20(30)-*dien*-28-*oic Acid*.—Hydrolysis of the ester (X) (0·9 g.) in ethanol (30 ml.) containing sodium (1 g.) in a sealed tube at 200° for 19 hr. and isolation in the usual way gave the *hydroxy-acid* (0·29 g.), needles (from methanol), m. p. 289—291° (*in vacuo*), $[\alpha]_D$ +61° (*c* 0·54), $\lambda_{max.}$ 206 mμ (ε 6600), $\nu_{max.}$ 3436 (OH), 1701 and 1678 (CO_2H), 1638 and 891 cm.$^{-1}$ (vinylidene) (Found: C, 78·0; H, 10·2. $C_{30}H_{46}O_3,\frac{1}{2}CH_3{\cdot}OH$ requires C, 77·8; H, 10·3%). With acetic anhydride in pyridine this gave 3β-*acetoxylupa*-12,20(30)-*dien*-28-*oic acid*, plates (from aqueous methanol), m. p. 280—282° (*in vacuo*), $[\alpha]_D$ +68° (*c* 0·6) (Found: C, 76·4; H, 9·9. $C_{32}H_{48}O_4,\frac{1}{2}CH_3{\cdot}OH$ requires C, 76·1; H, 9·8%). This acetoxy-acid with diazomethane regenerated the ester (X).

Reduction of Methyl 3β-*Acetoxylupa*-12,20(30)-*dien*-28-*oate* (X) *with Lithium Aluminium Hydride*.—The ester (X) (0·3 g.) in ether (50 ml.) was refluxed with lithium aluminium hydride (0·2 g.) for 1·5 hr. Working up through ether without contact with mineral acid gave, after several recrystallisations from methanol, lupa-12,20(30)-diene-3β,28-diol (XIV; R = H) (0·21 g.) showing m. p. and infrared and rotational characteristics identical with those of the sample prepared by hydrolysis of the diacetoxy-diene (XIV; R = Ac).

Methyl 3β-*Acetoxylup*-12-*en*-28-*oate* (XIa).—Hydrogenation of the ester (X) (0·23 g.) in ethyl acetate–acetic acid (1 : 5; 150 ml.) in presence of platinum oxide (0·05 g.) for 20 hr. and working up as usual gave *methyl* 3β-*acetoxylup*-12-*en*-28-*oate* (XIa), plates (0·21 g.) (from chloroform–methanol), m. p. 215—217°, $[\alpha]_D$ +19° (*c* 1·14), $\nu_{max.}$ 1739 and 1250 cm.$^{-1}$ (ester), $\lambda_{max.}$ 205 mμ (ε 5300). There was no infrared vinylidene absorption, and the compound gave a pale yellow colour with tetranitromethane (Found: C, 77·6; H, 10·2. $C_{33}H_{52}O_4$ requires C, 77·3; H, 10·2%).

3β-*Hydroxylup*-12-*en*-28-*oic Acid* (XIb).—The methyl acetoxy-ester (XIa) (0·17 g.) in ethanol (7 ml.) containing sodium (0·2 g.) was hydrolysed at 200° in an autoclave (17 hr.). Working up through ether, extraction with potassium hydroxide, and acidification gave 3β-*hydroxylup*-12-*en*-28-*oic acid* (XIb), needles (from chloroform–methanol), m. p. 287—289°, $[\alpha]_D$ +11° (*c* 1·02), $\nu_{max.}$ 3425 and 3268 (OH), and 1690 cm.$^{-1}$ (CO_2H), $\lambda_{max.}$ 206 mμ (ε 4600), giving a pale yellow colour with tetranitromethane (Found: C, 77·3; H, 10·8. $C_{30}H_{48}O_3,\frac{1}{2}CH_3{\cdot}OH$ requires C, 77·5; H, 10·7%), whose 3β-*acetate* formed plates (from aqueous methanol), m. p. 294—295° (*in vacuo*), $[\alpha]_D$ +31° (*c* 0·7), $\nu_{max.}$ 1739 and 1245 (OAc), and 1690 cm.$^{-1}$ (CO_2H) (Found: C, 77·2; H, 10·3. $C_{32}H_{50}O_4$ requires C, 77·1; H, 10·1%).

Lactonisation of the Hydroxy-acid (XIb).—The hydroxy-acid (XIb) (0·02 g.) in chloroform was treated with dry hydrogen chloride for 45 min. Removal of chloroform followed by chromatography of the residue from benzene–ether (1 : 1) on alumina (2 g.) gave 3β-hydroxylupan-28,13β-olide (VI; R = H) (0·017 g.), needles (from methanol), m. p. and mixed m. p. (with the sample described above), 313—315° (*in vacuo*), $[\alpha]_D$ +41·5° (*c* 0·36). The infrared spectra of both samples were identical.

3β,28-*Diacetoxylupa*-12,18-*diene* (XVII; R = OAc).—The non-conjugated diene diacetate (XIV; R = Ac) (1·03 g.) in acetic acid (50 ml.) containing concentrated hydrochloric acid (2 ml.) was heated to 100° for 30 min. The solution, which had become dark blue, was evaporated (*in vacuo*) and the gummy residue chromatographed from light petroleum (50 ml.) on alumina (40 g.). Elution with light petroleum (100 ml.) gave a fraction (0·14 g.), blades (from methanol), m. p. 173—200°, $[\alpha]_D$ +141·5° (*c* 0·75). This material could not be purified by further crystallisation, but spectroscopic data [$\lambda_{max.}$ 239, 247, 256 mμ (ε 12,600, 11,750, 6700)] indicate the presence of a *transoid* heteroannular diene, presumably (XVIII; R = OAc). Continued elution with light petroleum (300 ml.) gave 3β,28-*diacetoxylupa*-12,18-*diene* (XVII; R = OAc) (0·22 g.), plates (from methanol), m. p. 140—143°, $[\alpha]_D$ +219° (*c* 0·8), $\lambda_{max.}$ 234 mμ (ε 9400) (Found: C, 77·7; H, 10·2. $C_{34}H_{52}O_4$ requires C, 77·8; H, 10·0%).

3β,28-*Diacetoxylup*-13(18)-*ene* (XVI; R = Ac, R′ = OAc).—The conjugated diene diacetate

(XVII; R = OAc) (0·08 g.) in acetic acid (100 ml.) was hydrogenated in presence of platinum oxide (0·1 g.) for 20 hr. The solvent was removed *in vacuo*, and the residue (0·08 g.) was chromatographed from light petroleum (50 ml.) on alumina (6 g.). Elution with light petroleum (80 ml.) gave fractions (0·01 g.) which failed to crystallise, but further elution with the same solvent (150 ml.) gave 3β,28-*diacetoxylup*-13(18)-*ene* (0·06 g.), needles (from acetone), m. p. 158—160°, $[\alpha]_D$ −43° (*c* 1·67), $\lambda_{max.}$ 209 mμ (ε 12,500) (Found: C, 77·8; H, 10·4. $C_{34}H_{54}O_4$ requires C, 77·5; H, 10·3%).

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THE ROYAL COLLEGE OF SCIENCE AND TECHNOLOGY,
GLASGOW.

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