

807. *Hydroxy-steroids. Part III.*¹ *The Preparation of Lupane-1,2- and -2,3-diols*

By E. L. MCGINNIS, G. D. MEAKINS, J. E. PRICE, and M. C. STYLES

The conversion of lup-2-ene (4) into lup-1-ene (24), and the preparation of vicinal diols from these olefins, are described. The 2,3-diols are more conveniently obtained from the isomeric 2-acetoxylupan-3-ones, (14) and (16).

In continuing the spectrographic study of alicyclic alcohols¹ we wished to compare the infrared spectra of vicinal diols having the hydroxyl groups in ring A of cholestane with those of similar triterpene compounds. Since suitable triterpene analogues had not been described, lupane-1,2- and -2,3-diols were prepared.

Several methods for preparing lup-2-ene² were studied. On prolonged contact with alumina (commercial material containing alkali)³ lupan-3 β -yl toluene-*p*-sulphonate (1) afforded olefinic material (95%) from which lup-2-ene (4) was obtained in 45% yield; gas chromatography showed that the product was a mixture of lup-2-ene and an isomer [probably γ -lupene (5)] in a 7 : 3 ratio. Variations, such as treating lupan-3 β -ol (2) with toluene-*p*-sulphonyl chloride in pyridine at 100°, gave lower yields of lup-2-ene. When the conditions were carefully controlled, pyrolysis of the 3 β -benzoate (3) (the original method²) provided a convenient preparation of lup-2-ene (70%) on a reasonable scale.

Lup-2-ene (4) reacted slowly with osmium tetroxide, and purification of the main diol product [the 2 α ,3 α -compound (7)] was difficult. Hydroxylation to the 2 β ,3 β -diol (9) by the Woodward sequence⁴ proceeded in very poor yield even under the modified conditions developed for steroid diols.⁵ (A better route to this diol is described later.) An attempt to obtain a derivative of the diaxial-diol (11) by treating lup-2-ene with peroxyacetic acid for 2 hours at 100° gave the 2 α ,3 α -epoxide (6),² which was also obtained by use of perbenzoic acid at 20°. The stability of the oxide was further shown by its lack of reactivity towards periodic acid in acetone.⁶ With sulphuric acid in acetone⁷ the oxide gave a complex mixture, and the 2 β ,3 α -diol (11) was best prepared by use of perchloric acid in tetrahydrofuran. (The configurations of the products reported here follow from their methods of preparation, and the inter-relations between them; independent evidence for specific features is given later.)

In order to obtain the fourth 2,3-diol [the 2 α ,3 β -compound (8)], and to improve the preparation of the 2 β ,3 β -diol (9), the isomeric 2-acetoxylupan-3-ones were required. These were initially obtained by the sequence developed⁸ for steroidal acetoxy-ketones. Thus, with hot acetic acid the 2 α ,3 α -oxide (6) slowly gave the hydroxy-acetate (12) together with some diacetate (13). Mild oxidation of the hydroxy-acetate afforded the 2 β -acetoxy-ketone (16) which was isomerised to the 2 α -compound (14). The 2 β -isomer was also obtained as the major product in the lead tetra-acetate oxidation of lupan-3-one (15); separation of the β -compound from the α -acetoxy-ketone (formed in smaller amount) was wasteful, but the mixture could be satisfactorily isomerised to the α -isomer (14). (Analogies are available for the predominance of the axial acetoxy-ketone in the lead tetra-acetate reaction.^{9,10}) The infrared and ultraviolet spectra of the acetoxy-ketones resemble each other very closely; this is to be expected since the 2 α -compound, existing in a chair-like conformation, and the 2 β -isomer, in a flexible (boat-like) form, will both have equatorial

¹ Part II, F. Dalton, J. I. McDougall, and G. D. Meakins, *J.*, 1963, 4068.

² O. Jeger, M. Montavon, R. Novak, and L. Ruzicka, *Helv. Chim. Acta*, 1947, **30**, 1869.

³ G. H. Douglas, P. S. Ellington, G. D. Meakins, and R. Swindells, *J.*, 1959, 1720.

⁴ R. B. Woodward and F. V. Brutcher, *J. Amer. Chem. Soc.*, 1958, **80**, 209.

⁵ P. S. Ellington and G. D. Meakins, unpublished work.

⁶ H. B. Henbest and T. I. Wrigley, *J.*, 1957, 4596.

⁷ A. T. Rowland and H. R. Nace, *J. Amer. Chem. Soc.*, 1960, **82**, 2833.

⁸ K. L. Williamson and W. S. Johnson, *J. Org. Chem.*, 1961, **26**, 4563.

⁹ G. R. Chaudhry, T. G. Halsall, and E. R. H. Jones, *J.*, 1961, 2725.

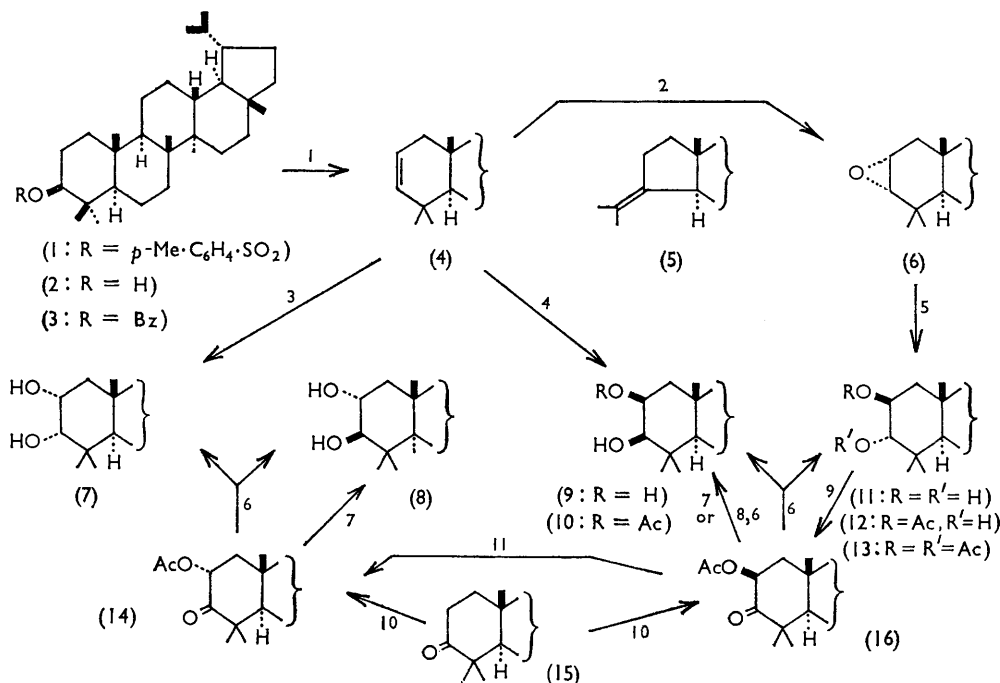
¹⁰ D. H. R. Barton, D. A. Lewis, and J. F. McGhie, *J.*, 1957, 2907.

acetoxyl groups.⁹ However, clear configurational evidence follows from comparison of the optical rotatory dispersion data for these compounds with those of similar products of established structure, the characteristic difference between the epimers arising from differences in the conformations of the rings.

	Amplitude *				
	2-H	2 α -OAc	2 β -OAc	$\Delta(2\alpha\text{-OAc})$	$\Delta(2\beta\text{-OAc})$
4,4-Dimethyl-5 α -cholestan-3-ones ⁹ ...	-11°	+38°	+124°	+49°	+135°
Lupan-3-ones	-10	+61	+123	+71	+133

* The difference between the molecular rotations $\times 10^{-2}$ at the peak and trough of the Cotton curve.

Reduction of the 2 β -acetoxy-ketone (16) with lithium aluminium hydride gave the 2 $\beta,3\beta$ - and the 2 $\beta,3\alpha$ -diols (9) and (11), and similar reduction of the 2 α -isomer (14) afforded the 2 $\alpha,3\alpha$ - and the 2 $\alpha,3\beta$ -diols (7) and (8). The 2 $\alpha,3\beta$ (diequatorial)-diol was more readily obtained by reducing the 2 α -acetate with sodium in propan-2-ol, and the 2 $\beta,3\beta$ -diol (9) by similar reduction of the 2 β -acetate, or by treating this acetate successively with sodium borohydride [to give the hydroxy-acetate (10)] and lithium aluminium hydride.

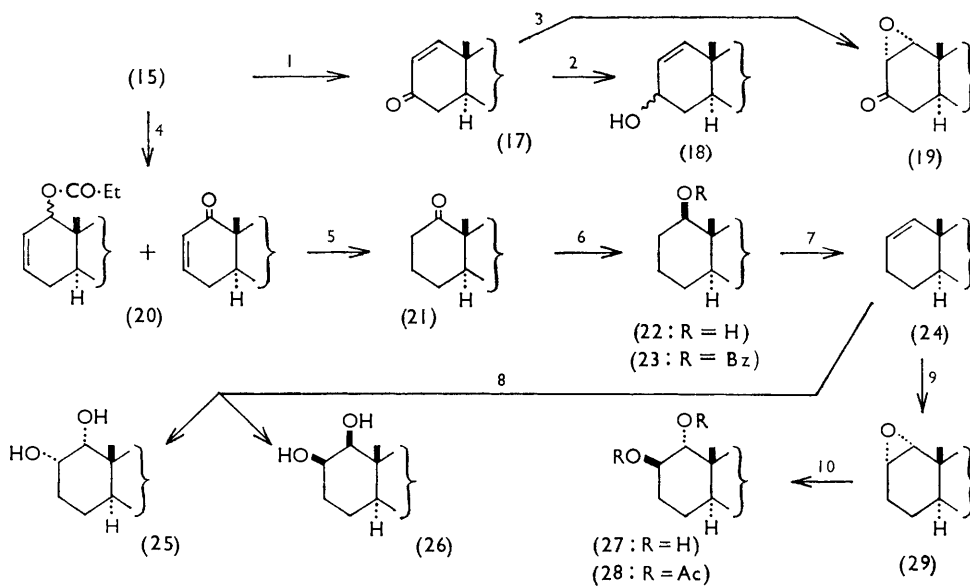


Reagents: 1, best from (3) at 330°; 2, RCO₃H; 3, OsO₄; 4, I₂-AcOAg-AcOH(H₂O); 5, AcOH; 6, LiAlH₄; 7, Na-Pr¹OH; 8, NaBH₄; 9, CrO₃-Me₂CO; 10, Pb(OAc)₄; 11, HBr-AcOH

Attempts to prepare lup-1-ene from lup-1-en-3-one (17) and derivatives such as lup-1-en-3-ol (18) and 1 $\alpha,2\alpha$ -epoxylupan-3-one (19) were unsuccessful. For example, in Huang-Minlon reductions of lup-1-en-3-one under various conditions, including the room-temperature modification,¹¹ the only olefin isolated was lup-2-ene (4). The successful approach to lup-1-ene involved the preparation of lupan-1 β -ol² by a sequence in which the basic step was the oxidation of lup-2-ene with selenium dioxide. This oxidation, when conducted in refluxing propionic acid, is reported² to give lup-2-en-1 α -yl propionate in 65% yield, but we obtained a mixture of products which were difficult to separate. Two procedures

¹¹ D. J. Cram, M. R. V. Sahyun, and G. R. Knox, *J. Amer. Chem. Soc.*, 1962, **84**, 1734.

for using this mixture in the preparation of lup-1-ene were developed. In the first, the oxidation mixture (20) [consisting of lup-2-en-1-yl propionate(s) and lup-2-en-1-one] was hydrolysed, hydrogenated [to lupan-1-ol(s) and lupan-1-one], and then oxidised [to lupan-1-one (21)]. Reduction of the ketone gave lupan-1 β -ol (22), the benzoate (23) of which afforded lup-1-ene (24) on pyrolysis. A shorter route from the oxidation product involved hydrolysis, hydrogenation, reduction (with sodium borohydride), benzoylation, and pyrolysis; this process, carried through with mixtures of position-1 isomers, afforded lup-1-ene in 19% yield from lup-2-ene. The oxidation was also conducted in acetic acid containing acetic anhydride, as used recently with lanost-2-ene;¹² after hydrogenation and hydrolysis, a mixture of lupan-1-ols was obtained in 21% yield.



Reagents: 1, Br₂ then Li₂CO₃; 2, LiAlH₄; 3, H₂O₂-NaOH; 4, SeO₂ in refluxing Et·CO₂H; 5, KOH-EtOH, then CrO₃-Me₂CO; 6, Na-PrⁱOH; 7, (23) at 330°; 8, OsO₄; 9, *p*-NO₂·C₆H₄; 10, AcOH (refluxing), then KOH-EtOH

With osmium tetroxide, lup-1-ene (24) gave two diols, assumed to be the 1 α ,2 α -compound (25) (the major product) and the 1 β ,2 β -isomer (26). Epoxidation with *p*-nitroperbenzoic acid afforded the 1,2-oxide (29) from which the 1 α ,2 β -diol (27) and its diacetate (28) were obtained.

The infrared and nuclear magnetic resonance spectra of the compounds reported here will be described later.

EXPERIMENTAL

For general directions see ref. 13. Alumina refers to Peter Spence grade H material. Deactivated alumina was prepared by treating this material with 5 or 10% (by weight) of 10% aqueous acetic acid. Neutral alumina was obtained by the ethyl acetate method.¹³

Lup-2-ene (14).—(a) *From lupan-3 β -yl benzoate* (3). The benzoate {m. p. 260–262°, [α]_D +28° (c 1.1) (lit.,¹⁴ m. p. 259–260°, [α]_D +27°)} (10 g.) in a dry 100-ml. flask connected to an air condenser was heated (metal-bath) in a stream of nitrogen at 150° for 30 min. and then at 330° for 7 hr. The contents of the flask were dissolved in light petroleum and filtered through

¹² D. H. R. Barton, P. J. L. Daniels, J. F. McGhie, and P. J. Palmer, *J.*, 1963, 3675.

¹³ J. R. Bull, E. R. H. Jones, and G. D. Meakins, *J.*, 1965, 2601.

¹⁴ I. M. Heilbron, T. Kennedy, and F. S. Spring, *J.*, 1938, 329.

alumina (50 g.) to give lup-2-ene (5.5 g.), m. p. 190—192° (from acetone), $[\alpha]_D +15^\circ$ (*c* 1.6) (lit.,² m. p. 192—193°, $[\alpha]_D +13.6^\circ$), ν_{\max} . 730 and 713 cm^{-1} . Elution with light petroleum-benzene afford lupan-3 β -yl benzoate (1.6 g.), m. p. 257—260°.

(b) *From lupan-3 β -yl toluene-*p*-sulphonate* (1). Treatment of lupan-3 β -ol {m. p. 203—204°, $[\alpha]_D -16^\circ$ (*c* 0.5) (lit.,¹⁴ m. p. 201—202°, $[\alpha]_D -17.8^\circ$)} (1 g.) with toluene-*p*-sulphonyl chloride (2 g.) in dry pyridine (40 ml.) at 0° for 36 hr. gave the toluene-*p*-sulphonate (1.3 g.), m. p. 135—140° (decomp.) (from dichloromethane-methanol), $[\alpha]_D +4^\circ$ (*c* 1.2), ν_{\max} . 1184 and 1173 cm^{-1} . This compound (6 g.) was adsorbed from benzene (200 ml.) on a column of alumina (600 g.; Grade H). After 60 hr., elution with benzene (500 ml.) afforded material (4.2 g.) shown by g.l.c. and mixed g.l.c. to consist of lup-2-ene (4) and an isomer, probably γ -lupene (5), in a 7 : 3 ratio. Two crystallisations from ethanol gave lup-2-ene (2.1 g.), m. p. and mixed m. p. 191—193°.

Lupane-2 α ,3 α -diol (7).—Solutions of lup-2-ene (1.3 g.) in dry benzene (50 ml.) and osmium tetroxide (1 g.) in pyridine (50 ml.) were mixed and kept at 20° for 4 days. After the usual treatment with mannitol and potassium hydroxide the product was chromatographed on 10% deactivated alumina (180 g.). Elution with benzene gave impure lup-2-ene (414 mg.), m. p. 178—188°. Elution with benzene-ether (1 : 1) afforded material (483 mg.), m. p. 270—283°, which could not be satisfactorily purified by crystallisation. Sublimation of this at 200°/0.1 mm. gave a film in which the more readily sublimed material (*i.e.*, at the front of the film) melted at *ca.* 280° and the less readily sublimed at *ca.* 180°. Suitable division of the film and further sublimations afforded *lupane-2 α ,3 α -diol* (54 mg.), m. p. 296—299° (decomp.), $[\alpha]_D -18^\circ$ (*c* 0.4) (Found: C, 80.95; H, 11.6. $\text{C}_{30}\text{H}_{52}\text{O}_2$ requires C, 81.0; H, 11.8%).

Lupane-2 α ,3 β -diol (8).—Sodium (6 g.) was added in portions to a refluxing solution of 2 α -acetylupan-3-one (14) (1 g.) in propan-2-ol (100 ml.). After dilution with water and extraction with ether, the product was chromatographed on 5% deactivated alumina (100 g.). Elution with ether-methanol (19 : 1) afforded *lupane-2 α ,3 β -diol* (422 mg.), m. p. 220—224° (from methanol-water), $[\alpha]_D -16^\circ$ (*c* 0.7) (Found: C, 80.8; H, 11.5%). Treatment with acetic anhydride-pyridine for 2 days at 20° gave 2 α ,3 β -diacetoxylupane, m. p. 211—212° (from chloroform-methanol), $[\alpha]_D -34^\circ$ (*c* 0.8) (Found: C, 77.1; H, 10.5. $\text{C}_{34}\text{H}_{56}\text{O}_4$ requires C, 77.2; H, 10.7%), ν_{\max} . 1744 cm^{-1} (ϵ 1060).

Reduction of 2 α -Acetylupan-3-one (14) with *Lithium Aluminium Hydride*.—The acetoxyketone (1 g.) in ether (100 ml.) was refluxed with lithium aluminium hydride (0.5 g.) for 5 hr., and the product chromatographed on 10% deactivated alumina (100 g.). *Lupane-2 α ,3 α -diol* (7) (256 mg.) was eluted with benzene-ether (65 : 1; 150 ml.), and after sublimation had m. p. 294—297° (decomp.) undepressed by admixture with an authentic specimen. The material (685 mg.) eluted with ether was crystallised from methanol and then methanol-water, to give *lupane-2 α ,3 β -diol* (8) (220 mg.), m. p. and mixed m. p. 220—223°. The diols were further identified by their infrared spectra.

Lupane-2 β ,3 β -diol (9).—(a) *From 2 β -acetylupan-3-one* (16). The acetoxyketone (1 g.) in propan-2-ol (100 ml.) was reduced with sodium (6 g.) in the usual way, and the product chromatographed on 5% deactivated alumina (100 g.). Elution with ether-methanol (65 : 1) afforded *lupane-2 β ,3 β -diol* (686 mg.), m. p. 227—228° (from methanol), $[\alpha]_D +5^\circ$ (*c* 0.3) (Found: C, 80.9; H, 11.7%).

In a further experiment the acetoxyketone (16) (1 g.) in methanol (150 ml.) was treated with sodium borohydride (1 g.). After 12 hr. at 20° the product was isolated and chromatographed on 5% deactivated alumina (100 g.). Elution with ether gave 2 β -acetylupan-3 β -ol (10) (320 mg.), double m. p. 128—130 and 188—190° (from methanol), $[\alpha]_D +7^\circ$ (*c* 1.2) (Found: C, 79.1; H, 11.0. $\text{C}_{32}\text{H}_{54}\text{O}_3$ requires C, 79.0; H, 11.2%). Ether-methanol (20 : 1) eluted *lupane-2 β ,3 β -diol* (440 mg.), m. p. and mixed m. p. 225—228°. Reduction of 2 β -acetylupan-3 β -ol (10) with lithium aluminium hydride in refluxing ether afforded *lupane-2 β ,3 β -diol* (80%).

(b) *From lup-2-ene* (4). Iodine (1.3 g.) was added in portions during 10 min. to a stirred mixture of lup-2-ene (1.3 g.), glacial acetic acid (60 ml.), and silver acetate (1.7 g.) under nitrogen at 20°. After 30 min. water (0.6 ml.) was added and the stirring continued for 3 days. Ether (250 ml.) was added, the mixture was filtered, and the filtrate washed with water, sodium carbonate solution, and water. The residue obtained by evaporating the dried solution was dissolved in ether (100 ml.) and refluxed with lithium aluminium hydride (0.3 g.) for 1 hr. After the usual working up the product was chromatographed on 5% deactivated alumina (200 g.). Elution with light petroleum-benzene (1 : 1) gave lup-2-ene (1.14 g.), m. p. and mixed

m. p. 189—191°. Elution with benzene-ether (19 : 1) gave lupane-2 β ,3 β -diol (6 mg.), m. p. 225—227°, identified by mixed m. p. and comparison of infrared spectra with authentic material.

Lupane-2 β ,3 α -diol (11).—The reaction of lup-2-ene (1 g.) in benzene (30 ml.) with perbenzoic acid (0.62 g.) in benzene (50 ml.) for 2 hr. at 20° afforded 2 α ,3 α -epoxylupane (0.94 g.), m. p. 214—216°, $[\alpha]_D^{20}$ -20° (*c* 0.5) (lit.,² m. p. 215—216°, $[\alpha]_D^{20}$ -11.5°). A mixture of this oxide (2.1 g.) in tetrahydrofuran (50 ml.) and 3*N*-hydrochloric acid (8 ml.) was stirred for 5 hr. at 35° and the product chromatographed on 5% deactivated alumina (200 g.). Elution with ether-methanol (19 : 1) gave *lupane-2 β ,3 α -diol* (0.63 g.), m. p. 246—247° (from acetone-methanol, and sublimation *in vacuo*), $[\alpha]_D^{20}$ -4° (*c* 0.7) (Found: C, 80.8; H, 11.45%).

Reduction of 2 β -Acetoxylupan-3-one (16) with *Lithium Aluminium Hydride*.—The acetoxyketone (300 mg.) in ether (50 ml.) was refluxed with lithium aluminium hydride (300 mg.) for 1 hr. and the product chromatographed on 5% deactivated alumina (30 g.). Elution with ether-methanol (65 : 1) gave lupane-2 β ,3 β -diol (9) (65 mg.), m. p. and mixed m. p. 226—228°. Further elution with ether-methanol (19 : 1) afforded lupane-2 β ,3 α -diol (11) (216 mg.), m. p. and mixed m. p. 243—246°.

2 β -Acetoxylupan-3-one (16).—(a) *From 2 α ,3 α -epoxylupane* (6). A solution of the epoxide (2 g.) in glacial acetic acid (28 ml.) was kept at 100° for 7 hr. and then slowly concentrated (to about 10 ml.) under reduced pressure. The product obtained by dilution with water and extraction with ether was chromatographed on neutral alumina (100 g.). Benzene eluted starting material (0.31 g.), m. p. 213—215°. Ether eluted 2 β ,3 α -diacetoxylupane (13) (0.15 g.), m. p. 219—220° (from dichloromethane-methanol), $[\alpha]_D^{20}$ +24° (*c* 0.5) (Found: C, 77.4; H, 10.5%), ν_{\max} 1744 cm.⁻¹ (ϵ 1033). Elution with ether-methanol (40 : 1) afforded 2 β -acetoxylupan-3 α -ol (12) (0.85 g.), m. p. 216—218° (from methanol), $[\alpha]_D^{20}$ +14° (*c* 0.3) (Found: C, 77.8; H, 11.1%). This hydroxy-acetate (1 g.) in acetone (250 ml.) was oxidised with 8*N*-chromic acid in the usual way, to give 2 β -acetoxylupan-3-one (0.92 g.), m. p. 302—304° (decomp.) (prisms from ether-methanol), $[\alpha]_D^{20}$ +48° (*c* 1.3) (Found: C, 79.5; H, 10.4. C₃₂H₅₂O₃ requires C, 79.3; H, 10.8%), ν_{\max} 1751 (ϵ 410) and 1732 (ϵ 422) cm.⁻¹.

(b) *From lupan-3-one* (15). A mixture of lupan-3-one {m. p. 210—211°, $[\alpha]_D^{20}$ +14° (*c* 1.5) (lit.,¹⁴ m. p. 204—205°, $[\alpha]_D^{20}$ +16.2°)} (10 g.) and lead tetra-acetate (15 g.) in glacial acetic acid (100 ml.) was heated at 100° for 4 hr. After concentration at 15 mm. the mixture was diluted with benzene, washed with water, sodium hydrogen carbonate solution, and water, dried and evaporated, and the product chromatographed on 5% deactivated alumina (1000 g.). Elution with light petroleum-benzene (7 : 3) afforded material (6.2 g.) of m. p. 242—260°. Four crystallisations from ether-methanol gave 2 β -acetoxylupan-3-one (1.2 g.), m. p. and mixed m. p. 304—306°. The material (4.5 g.) recovered from the mother-liquors was used as described below.

2 α -Acetoxylupan-3-one (14).—A solution of 2 β -acetoxylupan-3-one (16) (1.3 g.) in glacial acetic acid (120 ml.) containing 48% hydrobromic acid (0.5 ml.) was kept at 20° for 24 hr. After concentration at 40°/15 mm. and isolation with ether the product was refluxed in ethanol with activated charcoal. Crystallisation from ethanol-water afforded 2 α -acetoxylupan-3-one (0.82 g.), m. p. 278—280° (decomp.), $[\alpha]_D^{20}$ +23° (*c* 0.7) (Found: C, 79.15; H, 10.8%), ν_{\max} 1751 (ϵ 411) and 1732 (ϵ 446) cm.⁻¹. Similar treatment of the material (4.5 g.) obtained in the crystallisation of 2 β -acetoxylupan-3-one (see above) gave the 2 α -acetoxy-compound (2.1 g.), m. p. and mixed m. p. 277—280°.

Huang-Minlon Reduction of Lup-1-en-3-one (17).—Standard treatment of the ketone {m. p. 183—185°, $[\alpha]_D^{20}$ +21° (*c* 1.7), ν_{\max} 1660 cm.⁻¹ (lit.,¹⁵ m. p. 182—183.5, $[\alpha]_D^{20}$ +19°)} (0.5 g.) at 230° gave a product (0.39 g.), m. p. 186—188°. Crystallisation from acetone afforded lup-2-ene (4) (0.32 g.), m. p. 189—191°, identified by mixed m. p. and comparison of infrared spectra with authentic material.

Lup-1-en-3 ξ -ol (18).—A solution of lup-1-en-3-one (2 g.) and lithium aluminium hydride (0.4 g.) in ether (125 ml.) was refluxed for 4 hr. and the product was chromatographed on alumina (100 g.). Elution with ether-ethyl acetate (1 : 1) gave *lup-1-en-3 ξ -ol* (1.49 g.), m. p. 182.5—184°, $[\alpha]_D^{20}$ +26.5° (*c* 1.0) (Found: C, 83.8; H, 11.8. C₃₀H₅₀O requires C, 84.4; H, 11.8%).

1 α ,2 α -Epoxylupan-3-one (19).—30% Hydrogen peroxide (30 ml.) and 4*N*-sodium hydroxide (30 ml.) were separately added dropwise at the same rate to a stirred solution of lup-1-en-3-one (6 g.) in methanol (3000 ml.) at 20°. The material which separated slowly during 6 days at

¹⁵ R. T. Aplin, D.Phil. Thesis, Oxford, 1963.

0° was collected and washed with cold methanol, to give the epoxide (5.2 g.), m. p. 222—223° (from methanol), $[\alpha]_D + 65^\circ$ (*c* 1.1) (lit.,¹⁵ m. p. 220—222°, $[\alpha]_D + 67^\circ$).

Lup-1-ene (24).—(a) *Route involving isolation of lupan-1-one* (21). A solution of lup-2-ene (4 g.) and selenium dioxide (6 g.; prepared and sublimed immediately before use) in propionic acid (150 ml.) was refluxed for 2 hr., filtered while hot, and the filtrate evaporated at 100°/20 mm. Isolation with ether gave a product (20) shown by quantitative infrared examination to contain an ester (or esters) and a conjugated ketone in a ratio of *ca.* 4:1. This product was refluxed for 10 hr. in 4% ethanolic potassium hydroxide (120 ml.)–benzene (120 ml.). The oil obtained after dilution with water and extraction with ether was dissolved in light petroleum–benzene (4:1) and filtered through 5% deactivated alumina (40 g.). After crystallisation from ethanol the product was obtained as needles (2.1 g.), shown by quantitative infrared examination to consist of alcoholic material [80%, lup-2-en-1-ol(s)] and a conjugated ketone (20%, lup-2-en-1-one).

A solution of the product in ethyl acetate (50 ml.) was hydrogenated over 10% palladium–charcoal (1 g.) for 10 hr., and the product was crystallised from ethanol to give material (1.7 g.) of m. p. 150—200°. (This was the first stage at which the product was free from contamination by selenium.) Oxidation of this material in acetone (150 ml.) with 8*N*-chromic acid (3 ml.) gave lupan-1-one (21) (1.4 g.), m. p. 190—192° (from ethyl acetate), $[\alpha]_D + 35^\circ$ (*c* 0.7) (lit.,² m. p. 188—189°, $[\alpha]_D + 35^\circ$).

Reduction of the ketone (1 g.) with sodium in propan-2-ol afforded lupan-1 β -ol (22) (0.82 g.), m. p. 221—223° (from ethanol), $[\alpha]_D - 28^\circ$ (*c* 0.6) (lit.,² m. p. 222—223°, $[\alpha]_D - 29.5^\circ$). Treatment of the alcohol (0.81 g.) with benzoyl chloride (1 ml.)–pyridine (3 ml.) for 3 hr. at 20° gave the *benzoate* (23) (0.8 g.), m. p. 211—213° (from chloroform–methanol), $[\alpha]_D - 86^\circ$ (*c* 0.7) (Found: C, 83.1; H, 10.9. C₃₇H₅₆O₂ requires C, 83.4; H, 10.6%).

Pyrolysis of the 1 β -benzoate (1 g.), as described above for the 3 β -benzoate, afforded *lup-1-ene* (24) (0.48 g.), m. p. 160—162° (two crystallisations from acetone), $[\alpha]_D - 1.8^\circ$ (*c* 1.0) (Found: C, 87.5; H, 12.4. C₃₀H₅₀ requires C, 87.7; H, 12.3%), ν_{\max} 3014, 751, 727, and 718 cm.⁻¹.

(b) *Without purification of intermediates.* The first three stages above (oxidation, hydrolysis, and hydrogenation) were repeated, to give material (1.7 g.) of m. p. 150—200°. Reduction of this material in dioxan (150 ml.)–water (40 ml.)–methanol (75 ml.) with sodium borohydride (1.5 g.) for 1.5 hr. at 20° was followed by chromatography of the product on alumina (200 g.). Elution with light petroleum gave material (0.31 g.), m. p. 180—185°, which appeared (infrared spectrum) to be a saturated hydrocarbon. Light petroleum–benzene (1:1) eluted material [lupan-1-ol(s)] (1.4 g.), m. p. 208—218° (from ethanol), which was treated with pyridine (10 ml.)–benzoyl chloride (1.4 ml.) at 20° for 2 hr. and then at 100° for 30 min. The product [lupan-1-yl benzoate(s)] (1.5 g.), m. p. 180—190° (two recrystallisations from benzene–ethanol) (Found: C, 82.9; H, 10.75%), was pyrolysed to give lup-1-ene (0.75 g.), m. p. 160—162°.

Reaction of Lup-1-ene with Osmium Tetroxide.—A solution of lup-1-ene (500 mg.) and osmium tetroxide (500 mg.) in dry ether (40 ml.)–pyridine (1.5 ml.) was kept at 20° for 72 hr. After the usual hydrolysis procedure the product (490 mg.) was chromatographed on 10% deactivated alumina (200 g.). Light petroleum–benzene (1:1) eluted *lupane-1 β ,2 β -diol* (26) (54 mg. from column; 33 mg., m. p. 190—192°, after crystallisation from chloroform–methanol), $[\alpha]_D - 9^\circ$ (*c* 0.4) (Found: C, 81.0; H, 11.5%). Elution with benzene–ether (9:1) gave *lupane-1 α ,2 α -diol* (25) (406 mg. from column; 210 mg., m. p. 208—210°, after two crystallisations from chloroform–methanol), $[\alpha]_D - 17^\circ$ (*c* 0.4) (Found: C, 80.7; H, 11.5%). No impurity was detected in these products by thin-layer chromatography.

Evaporation of an ethereal solution of the 1 α ,2 α -diol gave a dimorphic form, m. p. 234—236°. Acetylation at 20° afforded 1 α ,2 α -*diacetylupane* (65%), m. p. 204—207° (two crystallisations from methanol), $[\alpha]_D - 39^\circ$ (*c* 0.5) (Found: C, 77.05; H, 10.9%).

Lupane-1 α ,2 β -diol (27).—A solution of lup-1-ene (200 mg.) and *p*-nitroperbenzoic acid (100 mg.) in dry chloroform (10 ml.) was kept at 20° for 4 hr. After filtration the solution was passed through 10% deactivated alumina (10 g.). Evaporation gave 1 α ,2 α -*epoxyupane* (29) (140 mg.), m. p. 215—220°, $[\alpha]_D - 29^\circ$ (*c* 0.5) (Found: C, 84.2; H, 11.6. C₃₀H₅₀O requires C, 84.4; H, 11.8%).

A solution of the epoxide (400 mg.) in glacial acetic acid (12 ml.) was kept at 100° for 3 hr. and then slowly evaporated at 10 cm. Residual acetic acid was removed by azeotropic distillation with benzene, and the product (450 mg.) was divided into two parts. The first part (250 mg.) was refluxed with 5% ethanolic potassium hydroxide and the material isolated with

ether was chromatographed on 10% deactivated alumina (100 g.). Elution with benzene-ether (1:1) gave *lupane-1 α ,2 β -diol* (163 mg. from column; 120 mg., m. p. 128—139°, after crystallisation from acetone-water), $[\alpha]_D +13^\circ$ (c 0.6) (Found: C, 80.75; H, 11.8%).

The second part (200 mg.) was treated with acetic anhydride (5 ml.)-pyridine (5 ml.) at 20° for 3 days and the product chromatographed on 5% deactivated alumina (100 g.) Light petroleum-benzene (1:1) eluted *1 α ,2 β -diacetoxylupane* (28) (110 mg.), m. p. 170—172° (from methanol), $[\alpha]_D -7^\circ$ (c 0.6) (Found: C, 77.4; H, 11.0%).

THE DYSON PERRINS LABORATORY,
SOUTH PARKS ROAD, OXFORD.

[Received, February 8th, 1965.]
