99. *Lupanetriol and its Oxidation.*

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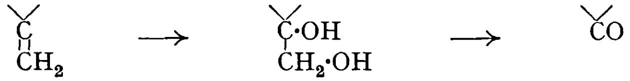
The presence of an exocyclic methylene group in the triterpene alcohols lupeol and betulin has been conclusively proved by the oxidation of *lupanetriol* with lead tetra-acetate to the keto-alcohol (norlupanonol), $C_{29}H_{48}O_2$, previously obtained by the oxidation of lupenyl esters either with ozone or with chromic anhydride (J., 1938, 329).

PREVIOUS attempts to prepare a lupanetriol by the hydroxylation of the monoethylenic triterpene alcohol lupeol have been unsuccessful. Treatment with hydrogen peroxide unexpectedly leads to the production of a saturated diol, m. p. 258° (Heilbron, Kennedy, and Spring, J., 1938, 329), and we find that neither lupeol nor its benzoate is affected by prolonged agitation with neutral or alkaline permanganate. Ruzicka and Rosenkranz (*Helv. Chim. Acta*, 1939, **22**, 778) isolated a hydroxy-aldehyde in an attempt to prepare such a triol by fission of the oxide ring of lupeol oxide. Criegee's elegant method (*Annalen*, 1936, **522**, 75) for the conversion of unsaturated compounds into *cis*-α-glycols has recently found considerable application in steroid chemistry (Serini and Logemann, *Ber.*, 1938, **71**, 1362; Butenandt, Schmidt-Thomé, and Paul, *Ber.*, 1939, **72**, 1112; Miescher, Wettstein, and Scholz, *Helv. Chim. Acta*, 1939, **22**, 894; Ushakov and Lieutenberg, *J. Gen. Chem. Russ.*, 1939, **9**, 69), but no accounts of its employment in the triterpene series have been recorded in the literature. Osmium tetroxide in anhydrous ether reacts neither with dihydrobasseol (or its acetate) nor with β-amyrenyl acetate after several weeks at the ordinary temperature, whereas with lupeol, basseol and basseol acetate under similar conditions a rapid precipitation of an osmium complex is observed. The osmic acid addition product formed in this way from lupeol can be decomposed either by the original sodium sulphite method suggested by Criegee (*loc. cit.*) or by reduction with formaldehyde (Reich, Sutter, and Reichstein, *Helv. Chim. Acta*, 1940, **23**, 170), yielding *lupanetriol*, $C_{30}H_{52}O_3$, m. p. 278—284° (decomp.), in good yield. Acetylation of this triol with acetic anhydride in pyridine produces a *triol-diacetate*, $C_{34}H_{56}O_5$, m. p. 174°, indicating that the triol contains a tertiary hydroxyl group.

Further information about the triol was obtained by its oxidation with lead tetra-acetate to a keto-alcohol, $C_{29}H_{48}O_2$, m. p. 230° (acetate, m. p. 260—262°), subsequently referred to as norlupanonol. Although no oxime could be obtained, the ketonic nature of this compound, m. p. 230°, was indicated by its absorption spectrum in alcoholic solution (maximum, approx. 2840 A.; log ε = 1·6). This isolation of a compound containing only *two* oxygen atoms by lead tetra-acetate oxidation of the triol provides incontestable evidence that the ethenoid linkage in lupeol is exocyclic, as was originally suggested by



Lupeol. Lupanetriol. Norlupanonol.

Heilbron, Kennedy, and Spring (*loc. cit.*) following on the isolation of formaldehyde in 18% yield by the ozonolysis of lupenyl acetate. The isolation of a hydroxy-aldehyde by the fission of lupeol oxide (Ruzicka and Rosenkranz, *loc. cit.*) can only be explained by the presence of an exocyclic methylene group in lupeol, and since Ruzicka and Brenner (*Helv. Chim. Acta*, 1939, **22**, 1523) have demonstrated that betulin ($C_{30}H_{50}O_2$) differs from lupeol solely in that one of the methyl groups of the latter appears in betulin as a primary carbinol group, *i.e.*, $-CH_3 \rightleftharpoons -CH_2{\cdot}OH$, it follows that the ethylenic linkage of betulin is similarly exocyclic.

The possibility that a vinyl group, such as is present in dextro-pimaric acid (Ruzicka and Sternbach, *Helv. Chim. Acta*, 1940, **23**, 124, and earlier references), may occur in lupeol (cf. Dieterle and Biedebach, *Arch. Pharm.*, 1938, **276**, 312) had to be considered. Such a possibility, however, would not admit of the presence of a tertiary hydroxyl group in the triol, and an aldehyde, which should form an oxime and smoothly yield a carboxylic acid on oxidation, would be formed on treatment with lead tetra-acetate.

Oxidation of lupenyl esters either with ozone or with chromic anhydride (Heilbron, Kennedy, and Spring, *loc. cit.*; Duerden, Heilbron, McMeeking, and Spring, J., 1939, 322; Ruzicka, Schellenberg, and Rosenkranz, *Helv. Chim. Acta*, 1938, **21**, 1391; Biedebach, *Arch. Pharm.*, 1939, **277**, 163) or of lupenyl acetate oxide with chromic anhydride (Ruzicka and Rosenkranz, *loc. cit.*) yielded, after hydrolysis, a keto-alcohol, m. p. 232° (acetate, m. p. 260—262°), of uncertain composition, although Biedebach (*loc. cit.*) after a careful examination of the analytical data found better agreement with a C_{29} rather than with a C_{30} formula. We have now established the identity of this compound with the norlupanonol obtained by the fission of lupanetriol and it becomes evident that the loss of a carbon atom accompanies both the ozonolysis and the chromic anhydride oxidation of lupenyl esters. A similar process must occur in the reaction of lupenyl acetate with hydrogen peroxide, since the diol, m. p. 258° (*vide supra*), was also produced by the sodium and alcohol reduction of norlupanonol.

EXPERIMENTAL.

All m. p.'s are uncorrected. Analytical specimens were dried at 100° in a high vacuum for 3 hours.

Lupanetriol.—A solution of lupeol (1·15 g.) and osmium tetroxide (0·95 g.; 1·2 mols.) in anhydrous ether (170 c.c.) was set aside at 10° for 5 days while the black osmium complex was gradually deposited. The ether was removed under diminished pressure and the residue was heated under reflux on the steam-bath for 2 hours with a solution of crystalline sodium sulphite (23 g.) in water (230 c.c.) and alcohol (115 c.c.). After filtration, the black precipitate was thrice extracted with boiling alcohol and this was then removed from the combined filtrates in a vacuum. The white flocculent solid so obtained was crystallised three times from benzene, yielding *lupanetriol* (845 mg.) in fine needles, m. p. 278—284° (decomp.). The m. p. varies several degrees according to the rate of heating. $[\alpha]_D^{20^\circ}$ +2·1° ($l = 1$, $c = 1·3$ in pyridine) (Found: C, 78·2; H, 11·6. $C_{30}H_{52}O_3$ requires C, 78·15; H, 11·4%). The triol sublimes unchanged at 165° in a high vacuum (10^{-3} mm.).

Lupanetriol Diacetate.— A mixture of the triol (150 mg.), pyridine (2·5 c.c.), and acetic anhydride (1 c.c.) was set aside for 15 hours at 10° and the product, after precipitation with water and isolation by means of ether, was thrice crystallised from light petroleum (b. p. 60—80°). *Lupanetriol diacetate* (110 mg.) separated in aggregates of fine needles, m. p. 174°, $[\alpha]_D^{20^\circ}$ +4·5° ($l = 1$, $c = 1·6$ in chloroform) (Found: C, 75·4; H, 10·5. $C_{34}H_{56}O_5$ requires C, 74·9; H, 10·4%). A similar yield of the diacetate was obtained when the mixture was heated at 100° for 4 hours. Hydrolysis of the diacetate (60 mg.) with alcoholic potassium hydroxide (7 c.c.; 10%) and crystallisation of the product from benzene gave lupanetriol, m. p. 281—284° (decomp.) alone or mixed with an authentic specimen.

Norlupanonol.—The triol (250 mg.) in acetic acid (35 c.c.; distilled from chromic anhydride) was treated with lead tetra-acetate (300 mg.; 1·25 mols.) and the solution was kept at 10° for 19 hours. The solid obtained on precipitation with water was taken up in ether, and the ethereal solution washed with water, sodium bicarbonate solution, twice with aqueous potassium hydroxide, once again with water and then dried. Repeated crystallisation of the solid, m. p. 211—215°, obtained on removal of the ether, from acetone gave norlupanonol in flat needles (100 mg.), m. p. 230° showing no depression on admixture with a specimen obtained by the oxidation of lupenyl acetate with chromic anhydride. $[\alpha]_D^{20^\circ}$ −15° ($l = 1, c = 1·5$ in chloroform). Heilbron, Kennedy, and Spring (*loc. cit.*) give $[\alpha]_D^{20^\circ}$ −13·2° (Found: C, 81·0; H, 11·3. Calc. for $C_{29}H_{48}O_2$: C, 81·2; H, 11·3%). Norlupanonol was recovered unchanged after heating under reflux for 4 hours with hydroxylamine acetate in methyl alcohol. The keto-alcohol (90 mg.) was heated on the steam-bath for 4 hours with pyridine (2 c.c.) and acetic anhydride (1 c.c.). Careful addition of water and cooling gave a crystalline solid which on recrystallisation from alcohol yielded norlupanonyl acetate, m. p. 260—262°, undepressed on admixture with a specimen prepared by chromic anhydride oxidation. $[\alpha]_D^{20^\circ}$ +3·7° ($l = 1$, $c = 1·6$ in chloroform). Heilbron, Kennedy, and Spring found $[\alpha]_D^{20^\circ}$ +7·4° and Ruzicka and Rosenkranz (*loc. cit.*) give $[\alpha]_D^{20^\circ}$ +0·8° and +1·2°.

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