451. *Triterpene Constituents of the Fruits of the Osage Orange* (Maclura pomifera). *Part II.*[1] *Synthesis of the Natural Diol, Lupane*-3β,20-*diol.*

By K. G. Lewis.

The structure, lupane-3β,20-diol, previously proposed for a new triterpene isolated from the fruits of the osage orange, has been confirmed by the identity of the natural material with this diol formed by reduction of lupenyl acetate epoxide.

EVIDENCE presented in Part I[1] pointed to the structure lupane-3β,20-diol (I; R = H) for a new triterpene diol isolated from the fruits of the osage orange. Neither this diol (I) nor the possible alternative, 18α-oleanane-3β,19α-diol (II; R = H), had been observed to occur in Nature before. Chatterjee, Anand, and Dhar[2] later assigned the structure lupane-3,20-diol to a compound, m. p. 232°, $[\alpha]_D$ +24°, previously isolated[3] from *Melodinus monogynus* Roxb. Their evidence was dehydration of the diol to lupeol on vacuum-sublimation and conversion of the diol into lupenyl acetate by boiling acetic anhydride. The m. p. recorded by them is in fair agreement with that found for the osage orange diol, but the rotation differs considerably. No further derivatives of the material from *Melodinus monogynus* were reported.

A substance of structure (II) had been reported by Ames, Davey, Halsall, and Jones[4] and the m. p. of the monoacetate (II; R = Ac) agreed quite well with that of the osage

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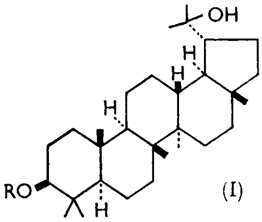
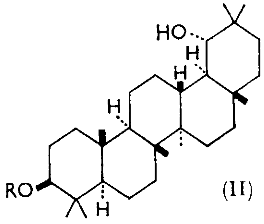
[1] Part I, Lewis, *J.*, 1959, 73.
[2] Chatterjee, Anand, and Dhar, *J. Sci. Ind. Res., India*, 1959, **18***B*, 262.
[3] Chatterjee, Sharma, and Dhar, *J. Sci. Ind. Res., India*, 1954, **13***B*, 546.
[4] Ames, Davey, Halsall, and Jones, *J.*, 1952, 2868.

orange derivative. The two substances, however, showed a substantial mixed m. p. depression and their infrared spectra showed appreciable differences. The correctness of structure (I) was finally proved by synthesis of a substance having this structure, by reduction of lupenyl acetate epoxide with lithium aluminium hydride. The lithium aluminium hydride cleavage of primary-tertiary and secondary-tertiary epoxides is known [5]



(I)



(II)

to give the tertiary alcohol (a parallel case is the reduction of thurberogenin epoxide [6]). The synthetic diol and its derivatives were identical with the material from osage orange and its derivatives.

The parent diol, lupane-3β,20-diol, was fairly easily dehydrated. While the monoacetate and monobenzoate could be dried for analysis for some hours at *ca.* 80°/0·01 mm., the diol under similar conditions gave material of lowered m. p. Acetylation of the vacuum-dried material, followed by chromatography, afforded lupenyl acetate as well as the diol monoacetate (I; R = Ac). In the benzoylation of the diol some elimination also occurred, as lupenyl benzoate was isolated as well as the monobenzoate.

EXPERIMENTAL

Specific rotations were determined for chloroform solutions. " Light petroleum " refers to the fraction of b. p. 40—60°. Alumina was Woelm's material deactivated by addition of 3% of 10% acetic acid (activity II—III). Infrared absorption spectra were determined for Nujol mulls.

Isolation of Lupane-3β,20-*diol* 3-*Monoacetate* (I; R = Ac) *from Osage Orange.*—Crude diol isolated as described in Part I [1] was treated with pyridine–acetic anhydride overnight. The mixed acetates were chromatographed in light petroleum over alumina. Light petroleum eluted mainly lupenyl acetate; benzene–light petroleum yielded the diol monoacetate, m. p. 252—255° (needles from methanol–chloroform), $[\alpha]_D$ +16° (*c* 2·52) (Found: C, 79·1; H, 11·2. Calc. for $C_{32}H_{54}O_3$: C, 79·0; H, 11·2%). Hydrolysis of this acetate with potassium hydroxide or reduction with lithium aluminium hydride yielded *lupane*-3β,20-*diol* as needles, m. p. 239—241° (from acetone), $[\alpha]_D$ +4° (*c* 2·21) (Found: C, 81·5; H, 11·8; O, 7·3. $C_{30}H_{52}O_2$ requires C, 81·0; H, 11·8; O, 7·2%). After being dried at 90°/0·01 mm. for 7 hr. it had m. p. 195—205°. The dried material was acetylated and the mixture of acetates separated by chromatography over alumina, to yield lupenyl acetate, m. p. and mixed m. p. 211—213°, and the diol monoacetate, m. p. 250—254°, giving no depression with the original diol monoacetate. The diol and pyridine–benzoyl chloride at room temperature overnight gave a product which was chromatographed over alumina. Elution with light petroleum gave lupenyl benzoate, m. p. and mixed m. p. 265—268° (from methanol–chloroform), $[\alpha]_D$ +58° (*c* 2·25) (Found: C, 83·4; H, 10·1. Calc. for $C_{37}H_{54}O_2$: C, 83·7; H, 10·25%). Elution with benzene–light petroleum (1 : 1) yielded *lupane*-3β,20-*diol* 3-*monobenzoate*, m. p. 253—256° (hexagonal plates from methanol–chloroform), $[\alpha]_D$ +35° (*c* 2·49) (Found: C, 80·9; H, 10·4. $C_{37}H_{56}O_3$ requires C, 81·0; H, 10·3%).

Preparation of 18α-*Oleanane*-3β,19α-*diol* 3-*Monoacetate* (II; R = Ac).—The procedure outlined by Ames *et al.*[4] afforded the monoacetate, m. p. 248—251° (needles from methanol–chloroform), $[\alpha]_D$ +6° (*c* 2·28) (Found: C, 78·85; H, 10·9. Calc. for $C_{32}H_{54}O_3$: C, 79·0; H,

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[5] Micovic and Mihailovic, " Lithium Aluminium Hydride in Organic Chemistry," Serbian Academy of Sciences, Belgrade, 1955, p. 69.

[6] Djerassi, Liu, Farkas, Lippman, Lemin, Geller, McDonald, and Taylor, *J. Amer. Chem. Soc.*, 1955, **77**, 1200.

11·2%). Ames *et al.*[4] record m. p. 249—250°, $[\alpha]_D$ +7°. A mixed m. p. determination with osage orange diol monoacetate gave m. p. 215—230°.

Lupenyl Acetate Epoxide.—Lupenyl acetate, in chloroform, was treated with monoperphthalic acid in ether. Titration indicated that the reaction was complete within 3 hr. The solution was poured into water and the epoxide extracted with ether. The extract was washed with aqueous sodium hydrogen carbonate and water. Lupenyl acetate epoxide had m. p. 235—238° (from acetone), $[\alpha]_D$ +23° (*c* 2·36) (Found: C, 79·7; H, 10·6; O, 9·5. Calc. for $C_{32}H_{52}O_3$: C, 79·3; H, 10·8; O, 9·9%). Ruzicka and Rosenkranz [7] record m. p. 226—230°, $[\alpha]_D$ +24°.

*Partial Synthesis of Lupane-*3β,20-*diol* 3-*Monoacetate.*—Lupenyl acetate epoxide was added in dry ether to an excess of lithium aluminium hydride in dry ether. The mixture was refluxed for 16 hr. and the excess of lithium aluminium hydride then destroyed by ethyl acetate. Water and hydrochloric acid were then added and the mixture was extracted with ether. The extract was washed with aqueous sodium hydrogen carbonate and water and the extract dried. Evaporation yielded a white solid which was treated with pyridine–acetic anhydride at room temperature overnight. Working up yielded material which on chromatography over alumina yielded the diol monoacetate, m. p. 250—253° (from methanol–chloroform), $[\alpha]_D$ +16° (*c* 2·46) (Found: C, 78·7; H, 11·0%). This material gave no m. p. depression on admixture with the diol monoacetate from osage orange, and the infrared spectra were identical.

*Lupane-*3β,20-*diol* 3-*Monobenzoate.*—Hydrolysis of the above monoacetate yielded crude diol which was treated with pyridine–benzoyl chloride overnight. Working up yielded material which was chromatographed over alumina. Elution with light petroleum removed an oil and further elution with benzene–light petroleum yielded the diol monobenzoate, m. p. 254—256°, $[\alpha]_D$ +35° (*c* 2·47) (Found: C, 81·25; H, 10·2. Calc. for $C_{37}H_{56}O_3$: C, 81·0; H, 10·3%). There was no m. p. depression on admixture with the diol monobenzoate from osage orange, and the infrared spectra were identical.

*Lupane-*3β,20-*diol.*—Lupenyl acetate epoxide was reduced with lithium aluminium hydride in tetrahydrofuran (cf. Djerassi *et al.*[6]) to yield lupane-3β,20-diol, m. p. 238·5—241° (from acetone), $[\alpha]_D$ +5·5° (*c* 2·24). There was no depression on mixed m. p. with osage orange diol. Both samples of diol gave identical *X*-ray powder photographs.

The author thanks Dr. D. L. Ford and Timbrol Company for kindly determining the infrared spectra.

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[*Received, January* 11*th*, 1961.]

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[7] Ruzicka and Rosenkranz, *Helv. Chim. Acta*, 1939, **22**, 778.