224. *The Triterpene Resinols and Related Acids.* Part VI.*

By C. W. Picard, K. S. Sharples, and F. S. Spring.

The product obtained by oxidation of β-amyrenyl acetate with hydrogen peroxide (Part I, J., 1933, 1345) is now shown to be a saturated ketone, β-amyranonyl acetate (V). On treatment with bromine this is partially dehydrogenated to give iso-β-*amyrenonyl acetate* (VI). Reduction of this αβ-unsaturated ketone, followed by treatment of the product with acetic anhydride, gives dehydro-β-amyrenyl acetate (IV), previously obtained by the same method starting from β-amyrenonol (III) (Part V, J., 1938, 1233). Similarly we find that treatment of methyl ketoacetyldihydro-oleanolate with bromine gives methyl *iso*ketoacetyloleanolate. The implications of these results, in so far as the structures of β-amyrenol and oleanolic acid are concerned, are discussed.

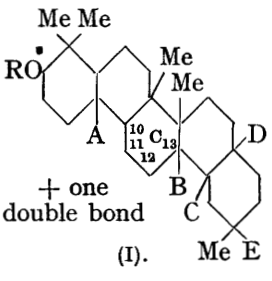
By oxidation of β-amyrenol with persulphuric acid in acetic acid, Rollett and Bratke (*Monatsh.*, 1922, **43**, 685) obtained an "oxy-β-amyrin acetate," m. p. 291—292°, which was characterised by its hydrolysis to "oxy-β-amyrin," m. p. 200—201°, and by oxidation of the latter to "oxy-β-amyranone," m. p. 216—217° (see also Rollett and Petter, *Monatsh.*, 1933, **63**, 311). "Oxy-β-amyrin acetate" ("β-amyrenyl acetate oxide," $C_{32}H_{52}O_3$) was later obtained by oxidation of β-amyrenyl acetate with hydrogen peroxide (Spring, J., 1933, 1345), by oxidation of β-amyrenol or its acetate with perbenzoic acid (Spring and Vickerstaff, J., 1934, 1859; cf. Ruzicka, Silbermann, and Pieth, *Helv. Chim. Acta*, 1932, **15**, 1285), by ozonolysis of basseol acetate (Beynon, Heilbron, and Spring, J., 1937, 989), and more recently by the oxidation of β-amyrenyl acetate with chromic anhydride (Beynon, Sharples, and Spring, J., 1938, 1233).

The acetate, $C_{32}H_{52}O_3$, m. p. 291—292°, does not react with the usual carbonyl reagents and it fails to give a coloration with tetranitromethane (Spring, *loc. cit.*); the Zerewitinoff method indicates the presence of one active hydrogen atom (Beynon, Sharples, and Spring, *loc. cit.*), although the compound cannot be further acylated. Examination of the ultra-violet absorption spectrum of the acetate, m. p. 291—292°, has now established the presence therein of an isolated carbonyl group (band at 2820 A., $\log \varepsilon = 1{\cdot}89$). Reduction of the acetate with sodium and amyl alcohol gives *dihydroxy-β-amyrane*, $C_{30}H_{52}O_2$, m. p. 216—217°, characterised by its *diacetate*, m. p. 183—184°. We conclude that the acetate, $C_{32}H_{52}O_3$, m. p. 291—292°, is a saturated keto-acetate and it is therefore to be designated β-amyranonyl acetate (cf. Picard, Sharples, and Spring, *J. Soc. Chem. Ind.*, 1939, **58**, 58).

Treatment of β-amyranonyl acetate with bromine gives a bromine-free product, m. p. 289—290°, undepressed on admixture with β-amyranonyl acetate. The new product, however, has been shown to be iso-β-*amyrenonyl acetate*, $C_{32}H_{50}O_3$, since it exhibits the intense absorption in the ultra-violet characteristic of an αβ-unsaturated ketone. Hydrolysis of this unsaturated keto-acetate yields iso-β-*amyrenonol*, m. p. 232—233°. Reduction of *iso*-β-amyrenonyl acetate with sodium and amyl alcohol, followed by treatment of the product with acetic anhydride, yields dehydro-β-amyrenyl acetate identical with that previously obtained by similar treatment of β-amyrenonol (Beynon, Sharples, and Spring, *loc. cit.*).

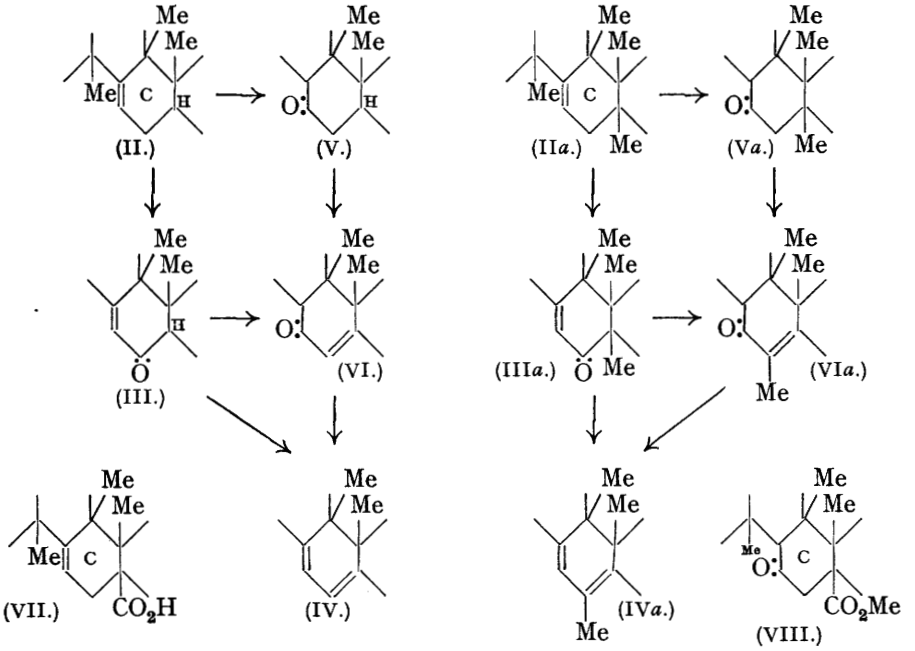
* It has been necessary to expand the title of this series from "The Resinols" to that shown above.

β-Amyrenol is represented by the structure (I; R = H) (Ruzicka and Schellenberg, *Helv. Chim. Acta*, 1937, **20**, 1553; Haworth, *Ann. Reports*, 1937, **34**, 338; Beynon, Sharples, and Spring, *loc. cit.*; Ruzicka and van der Sluys-Veer, *Helv. Chim. Acta*, 1938, **21**, 1371; Ruzicka, Cohen, Furter, and van der Sluys-Veer, *ibid.*, p. 1735; Picard, Sharples, and Spring, *loc. cit.*; Ruzicka, van der Sluys-Veer, and Cohen, *Helv. Chim. Acta*, 1939, **22**, 350), an ethylenic bond being located at either C_{10}—C_{11} (in which case A = Me) (Class A) or at C_{12}—C_{13} (in which case C = Me) (Class B), A, B, C, D and E showing the possible locations of three methyl groups. In class A, the two variants to be considered are (II) and (II*a*). According to (II) β-amyrenonol will be represented by (III, R = H) and dehydro-β-amyrenyl acetate by (IV, R = COMe). Likewise β-amyranonyl acetate will be (V, R = COMe) and *iso*-β-amyrenonyl acetate, (VI, R = COMe), which gives an adequate interpretation of its conversion into dehydro-β-amyrenyl acetate (IV, R = COMe) by reduction, followed by treatment with acetic anhydride. According to (II*a*) the conversion of β-amyrenonol (III*a*, R = H) and of *iso*-β-amyrenonyl acetate (VI*a*, R = COMe) into dehydro-β-amyrenyl acetate (IV*a*, R = COMe) must in each case be accompanied by a migration of the angular methyl group attached to C_{13}. In the hope of differentiating between the two formulæ (II, R = H) and (II*a*, R = H) for β-amyrenol, we have unsuccessfully attempted to effect the catalytic reduction of dehydro-β-amyrenyl acetate; unchanged material was quantitatively recovered after long shaking with hydrogen in the presence of platinum.



(I).

According to the representation (II*a*, R = H) for β-amyrenol, oleanolic acid is (VII, R = H). It has been shown by Ruzicka, Cohen, Furter, and van der Sluys-Veer (*loc. cit.*)



that this formula is not in harmony with the conversion of ketoacetyloleanolic acid into the acetoxy-ketone, m. p. 208—210°, or with that of ketoacetyloleanolic acid lactone into *iso*ketoacetyloleanolic acid. This point is again emphasised, since we now find that bromination of methyl ketoacetyldihydro-oleanolate (Kitasato, *Acta Phytochim.*, 1933, **7**, 169; 1935, **9**, 43; Ruzicka and Cohen, *Helv. Chim. Acta*, 1937, **20**, 804) (the analogue of β-amyranonyl acetate) gives in good yield the αβ-unsaturated ketone methyl *iso*ketoacetyl-

oleanolate, m. p. 203—204° (Kitasato, *Acta Phytochim.*, 1935, **8**, 315; Ruzicka, Cohen, Furter, and van der Sluys-Veer, *loc. cit.*). According to the representation (II*a*, R = H) and (VII, R = H) for β-amyrenol and oleanolic acid respectively, methyl ketoacetyldihydro-oleanolate will be (VIII, R = COMe), from which no satisfactory formulation for the *iso*keto-ester, m. p. 203—204°, can be derived.

In so far as ring C is concerned, the class B type of formula gives a satisfactory representation of the reactions described in this paper.

Experimental.

All melting points are uncorrected.

Dihydroxy-β-amyrane.—A solution of β-amyranonyl acetate (2·5 g.) in boiling amyl alcohol (50 c.c.) was treated with sodium (2·5 g.), added during 10 minutes, the mixture then being heated under reflux for 1 hour. Sodium (2·5 g.) was again added, and the heating continued for a further hour. The mixture was poured into water, and the amyl alcohol removed by distillation in steam. The product, isolated by means of ether, was heated on the steam-bath for 1½ hours with pyridine (5 c.c.) and acetic anhydride (20 c.c.). The mixture was poured into water and extracted with ether, and the product crystallised from aqueous acetone, from which *diacetoxy-β-amyrane* separated in needles, m. p. 183—184°, $[\alpha]_D^{20°}$ +42·19° ($l = 1$, $c = 0{\cdot}56$ in chloroform) (Found: C, 77·4; H, 10·5. $C_{34}H_{56}O_4$ requires C, 77·2; H, 10·7%). The diacetate does not give a coloration with tetranitromethane in chloroform. Hydrolysis of the diacetate (0·5 g.) was effected by heating under reflux with alcoholic potassium hydroxide (10%; 30 c.c.) for 4 hours. The mixture was largely diluted with water and the solid separating was collected and crystallised thrice from aqueous methyl alcohol, from which *dihydroxy-β-amyrane* separated in needles, m. p. 216—217°, $[\alpha]_D^{20°}$ +97·6° ($l = 1$, $c = 0{\cdot}50$ in chloroform) (Found: C, 81·0; H, 11·8. $C_{30}H_{52}O_2$ requires C, 81·0; H, 11·8%).

iso-β-*Amyrenonyl Acetate.*—β-Amyranonyl acetate (4·5 g.) in glacial acetic acid (250 c.c.) was treated with a solution of bromine in glacial acetic acid (8%; 3 mols.) and 2 drops of a solution of hydrobromic acid in glacial acetic acid (40%). The mixture was maintained at 35—40° for 15 minutes and then at 20° for 4 hours. The solid separating after the addition of water was collected and washed with water. It was free from halogen and after six crystallisations from acetone gave iso-β-*amyrenonyl acetate* in hexagonal plates, m. p. 289—290°, $[\alpha]_D^{20°}$ +73·7° ($l = 1$, $c = 0{\cdot}8$ in chloroform); a mixture of this with β-amyranonyl acetate melted at 290—291° (Found: C, 79·6; H, 10·6. $C_{32}H_{50}O_3$ requires C, 79·6; H, 10·45%). *Light absorption in alcohol*: maxima at 2470 A., log ε = 4·08 and 3280 A., log ε = 1·845.

iso-β-*Amyrenonol.*—*iso*-β-Amyrenonyl acetate (0·3 g.) was heated under reflux for 4 hours with alcoholic potassium hydroxide (20 c.c.; 10%), and the solution then largely diluted with water. The solid separating was washed with water and taken up in hot aqueous methyl alcohol, from which iso-β-*amyrenonol* separated as an amorphous solid which on standing in contact with the mother-liquor gradually changed into plates, m. p. 232—233°. The separation of amorphous solid changing into plates on standing was observed in every crystallisation, the m. p. of the crystalline form remaining constant at 232—233° (Found: C, 81·55; H, 10·7. $C_{30}H_{48}O_2$ requires C, 81·7; H, 11·0%).

Dehydro-β-amyrenyl Acetate.—*iso*-β-Amyrenyl acetate (0·75 g.) in boiling amyl alcohol (25 c.c.) was treated during 1 hour with sodium (1·5 g.), small additions of amyl alcohol being made from time to time. The product, isolated in the usual manner, was heated under reflux with acetic anhydride (7 c.c.) for 1 hour and then poured into water. The solid separating was collected, washed with water, and crystallised from aqueous acetone, from which dehydro-β-amyrenyl acetate separated in small needles, m. p. 208—209°, $[\alpha]_D^{20°}$ +331·6° ($l = 1$, $c = 0{\cdot}3$ in chloroform). It gave a deep yellow coloration with tetranitromethane in chloroform and the m. p. was not depressed by a specimen prepared from β-amyrenonol (Beynon, Sharples, and Spring, *loc. cit.*) (Found: C, 82·3; H, 11·0. Calc. for $C_{32}H_{50}O_2$: C, 82·3; H, 10·8%). *Light absorption in alcohol*: maximum at 2830 A., log ε = 3·98.

Methyl Ketoacetyldihydro-oleanolate.—Oleanolic acid was isolated by the following modified method (cf. Winterstein and Stein, *Z. physiol. Chem.*, 1931, **202**, 222; Ruzicka and Hofmann, *Helv. Chim. Acta*, 1936, **19**, 114): finely ground cloves (50 kg.) were heated under reflux with ether (42 l.) for 48 hours. The ethereal solution was drawn off and concentrated to a bulk of 8 l., and the concentrate set aside for 4 weeks. The dark green ethereal layer was then decanted from the thick oil which had settled. The oil was shaken with N-sodium hydroxide and the crystalline sodium salt was collected, repeatedly washed with sodium hydroxide solution,

dissolved in boiling 96% alcohol, and acidified with glacial acetic acid. The crude acid separating was crystallised twice from alcohol, giving oleanolic acid in fine needles, m. p. 302—304°, $[\alpha]_D^{20°}$ +83·3° ($l = 1$, $c = 0·6$ in chloroform) (Found: C, 78·6; H, 10·7. Calc. for $C_{30}H_{48}O_3$: C, 78·9; H, 10·6%). Repetition of the extraction with ether, the same procedure being used, gave a further quantity of oleanolic acid (total yield, 550 g.). Acetylation by the method of Wedekind and Schicke (*Z. physiol. Chem.*, **1931**, **195**, 132) and crystallisation of the "diacetyl" compound from methyl alcohol gave acetyloleanolic acid in needles, m. p. 261—262°. Methyl acetyloleanolate separated from alcohol in needles, m. p. 216—218° [Winterstein and Stein, *Z. physiol. Chem.*, 1931, **199**, 71, give m. p. 218—220° (corr.)], $[\alpha]_D^{20°}$ +70·0° ($l = 1$, $c = 0·6$ in chloroform) (Kitasato and Sone, *Acta Phytochim.*, 1932, **6**, 179, give $[\alpha]_D$ +70·4°) (Found: C, 77·5; H, 10·4. Calc. for $C_{33}H_{52}O_4$: C, 77·3; H, 10·2%). Methyl ketoacetyldihydro-oleanolate separated from methanol in small rosettes of needles, m. p. 193—195° [prepared by the method of Ruzicka and Cohen, *loc. cit.*, who give m. p. 195—196° (corr.)] (Found: C, 74·65; H, 10·1. Calc. for $C_{33}H_{52}O_5$: C, 74·9; H, 9·9%).

Methyl iso*Ketoacetyloleanolate*.—Methyl ketoacetyldihydro-oleanolate (0·5 g.) in glacial acetic acid (50 c.c.) containing 2 drops of a solution of hydrobromic acid in acetic acid (40%) was treated at 40° with a solution of bromine in acetic acid (5 c.c.; 3%; 1 mol.), added dropwise; the bromine was rapidly absorbed. An excess of bromine (2 mols.) was then added, and the mixture set aside for 16 hours at 20°. After addition of water, the excess of bromine was decomposed by sulphur dioxide, and the precipitated solid collected, washed with water, and dried in ether over sodium sulphate. The resin obtained on removal of the ether was crystallised thrice from methanol, from which methyl *iso*ketoacetyloleanolate separated in small plates, m. p. 203—204° [Kitasato (*loc. cit.*) gives m. p. 205°, and Ruzicka, Cohen, Furter, and van der Sluys-Veer (*loc. cit.*) give m. p. 206—207° (corr.)]. It does not give a coloration with tetranitromethane in chloroform (Found: C, 75·0; H, 9·3. Calc. for $C_{33}H_{50}O_5$: C, 75·2; H, 9·6%). *Light absorption in alcohol*: maximum at 2490 A., log $\varepsilon = 4·05$ (Ruzicka, Cohen, Furter, and van der Sluys-Veer, *loc. cit.*, give maximum at 2480 A., log $\varepsilon = 4·1$ for *iso*ketoacetyloleanolic acid).

Grateful acknowledgment is made to the Chemical Society and Imperial Chemical Industries, Ltd., for grants and to Dr. A. E. Gillam for the absorption spectra data.

THE UNIVERSITY, MANCHESTER. [*Received, May* 6th, 1939.]