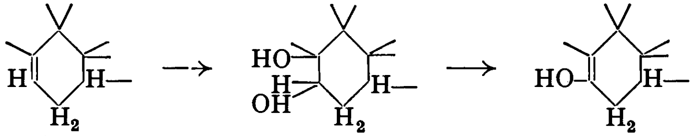
262. *Triterpene Resinols and Related Acids. Part XI. The Oxidation of Acetyloleanolic Acid and of Methyl Acetyloleanolate with Perbenzoic Acid.*

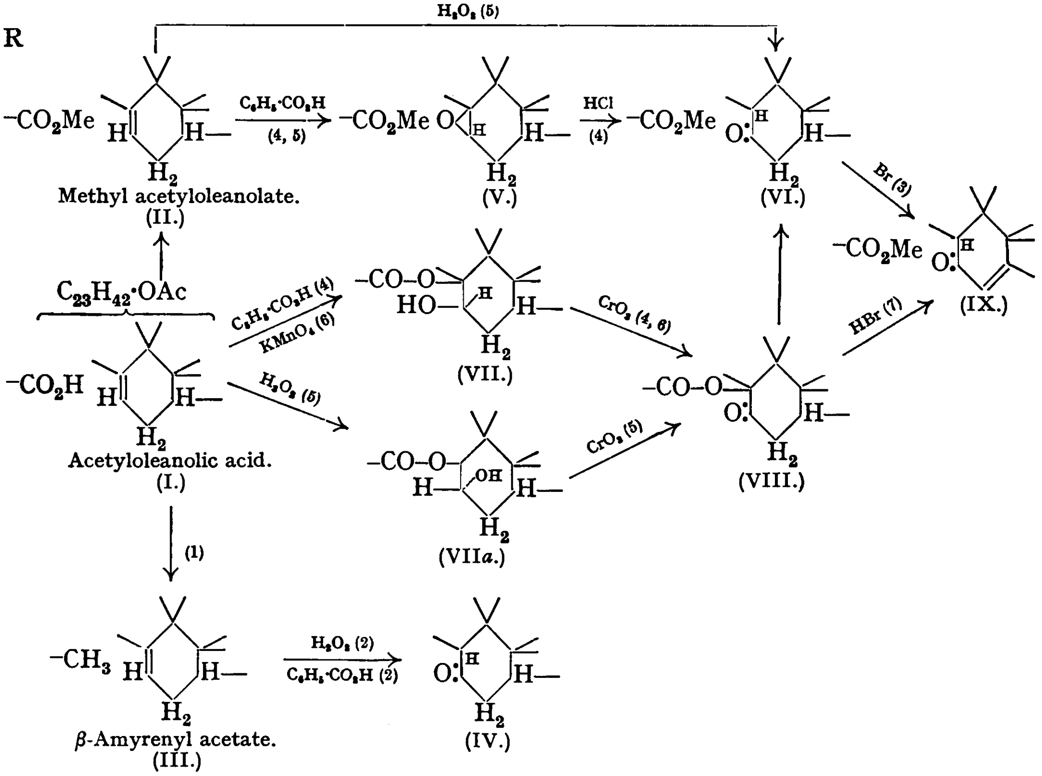
By C. W. Picard and F. S. Spring.

Treatment of methyl acetyloleanolate (II) with perbenzoic acid gives an oxide (V), the m. p. of which is appreciably higher than that of the specimen described by Ruzicka and Cohen (*Helv. Chim. Acta*, 1937, **20**, 804). Dilute hydrochloric acid smoothly converts this oxide into ketoacetyldihydro-oleanolate (VI), previously obtained (among other methods) by the action of hydrogen peroxide on methyl acetyloleanolate (II). Similar treatment of acetyloleanolic acid (I) with perbenzoic acid does not give an oxide but hydroxyacetyloleanolic acid lactone (VII), differing from the isomeric product (VII*a*) obtained by oxidation of the acetyl acid (I) with hydrogen peroxide in the orientation around the hydroxylated carbon atom. The hydroxy-lactone (VII) is identical with the product obtained by oxidation of the acetyl acid (I) with potassium permanganate.

In Part III (Spring and Vickerstaff, J., 1934, 1859) it was shown that the product obtained by oxidation of β-amyrenyl acetate (III) with hydrogen peroxide (Spring, J., 1933, 1345) is identical with that obtained by oxidation of this acetate with perbenzoic acid, and it was later shown that this product is a saturated ketone, β-amyranonyl acetate (IV) (Picard, Sharples, and Spring, *J. Soc. Chem. Ind.*, 1939, **58**, 58; J., 1939, 1045). The mechanism of formation of this saturated ketone using hydrogen peroxide probably involves the formation of a tertiary-secondary diol (IV*a*), which is dehydrated to the enol (IV*b*) of the saturated ketone (IV). The formation of the saturated ketone by perbenzoic acid oxidation is


(III.) (IV*a*.) (IV*b*.)

presumably indicative of the great instability of the primarily formed oxide (cf. Ruzicka, Müller, and Schellenberg, *Helv. Chim. Acta*, 1939, **22**, 1045). In view of the instability of the oxide, an irregularity is to be observed in the oxidation of the closely related methyl acetyloleanolate (II). Although this ester differs from β-amyrenyl acetate simply in that in the former R = CO_2Me and in the latter R = Me, perbenzoic acid oxidation of methyl acetyloleanolate gives an oxide (V). With hydrogen peroxide, on the other hand, the methyl ester behaves normally and gives the corresponding saturated ketone, methyl ketoacetyldihydro-oleanolate (VI) (Ruzicka and Cohen, *loc. cit.*).



(1) Ruzicka and Schellenberg, *Helv. Chim. Acta*, 1937, **20**, 1553. (2) Spring, J., 1933, 1345; Spring and Vickerstaff, J., 1934, 1859; Picard, Sharples, and Spring, J., 1939, 1045. (3) Picard, Sharples, and Spring, *loc. cit.* (4) This paper. (5) Ruzicka and Cohen, *Helv. Chim. Acta*, 1937, **20**, 804; Ruzicka, Hösli, and Hofmann, *ibid.*, 1936, **19**, 109. (6) Aumüller, Wedekind, and Schicke, *Annalen*, 1935, **517**, 211. (7) Kitasato, *Acta Phytochim.*, 1935, **8**, 319; Ruzicka, Cohen, Furter, and Sluys-Veer, *Helv. Chim. Acta*, 1938, **21**, 1735.

We have investigated the oxidation of the ester (II) with perbenzoic acid and have obtained an oxide (V) which has a considerably higher m. p. (210—212° uncorr.; 215—217° corr.) than that recorded by Ruzicka and Cohen (*loc. cit.*) (201—204° corr.); it does not exhibit selective absorption between 2300 and 3300 A. When treated with dilute mineral acid, the oxide is isomerised to the saturated ketone, methyl ketoacetyldihydro-oleanolate (VI). In view of the stability of this oxide, it was of interest to investigate the action of perbenzoic acid on acetyloleanolic acid (I). The reaction led to the formation, in high yield, of hydroxyacetyloleanolic acid lactone (VII), m. p. 333°, characterised by the formation of a diacetyl derivative, m. p. 295°, and by its oxidation with chromic acid to keto-acetyloleanolic acid lactone (VIII). The oxidation of acetyloleanolic acid with hydrogen peroxide gives a hydroxyacetyloleanolic acid lactone, m. p. 292—294° (corr.) (Ruzicka, Hösli, and Hofmann, *Helv. Chim. Acta*, 1936, **19**, 109), whereas, using potassium permanganate, Aumüller, Wedekind, and Schicke (*Annalen*, 1935, **517**, 211) obtained an isomeric hydroxyacetyl-lactone, m. p. 337° (diacetyl derivative, m. p. 292°), which is identical with the product we now find is obtained by oxidation of (I) with perbenzoic acid. The structural relationship existing between the oxidation products of acetyloleanolic acid on the one hand and methyl acetyloleanolate on the other is established by the conversion of ketoacetyloleanolic acid lactone (VIII) into methyl ketoacetyldihydro-oleanolate (Kitasato, *Acta Phytochim.*, 1935, **8**, 207) and also by the conversion of the lactone (VIII) into methyl *iso*ketoacetyloleanolate (IX) (*idem, ibid.*, p. 319; Ruzicka, Cohen, Furter, and Sluys-Veer, *Helv. Chim. Acta*, 1938, **21**, 1735), together with the formation of the latter ester (IX) by the action of bromine on methyl ketoacetyldihydro-oleanolate (VI) (Picard, Sharples, and Spring, *loc. cit.*)

EXPERIMENTAL.

Melting points are uncorrected,except where otherwise stated.

Methyl Acetyloleanolate Oxide.—Methyl oleanolate (m. p. 196—197°; 8 g.) (prepared from oleanolic acid by means of diazomethane) was heated on the steam-bath for 3 hours with acetic anhydride (30 c.c.) and freshly distilled pyridine (30 c.c.). On cooling, the solution deposited practically pure methyl acetyloleanolate in prismatic needles (yield, 88%), m. p. 217—219°, undepressed in admixture with the specimen described by Picard, Sharples, and Spring (J., 1939, 1048). Methyl acetyloleanolate (2 g.) was treated with a solution of perbenzoic acid in chloroform (0·65N; 25 c.c.) and set aside at 0° for 12 days. The solution was washed with 3N-sodium carbonate and dried. After removal of the solvent, the residual solid was crystallised twice from methyl alcohol, from which methyl acetyloleanolate oxide separated in long needles, m. p. 210—212° (uncorr.), 215—217° (corr.) (yield, 68%). Ruzicka and Cohen give m. p. 201—204° (corr.) for this oxide. It does not give a coloration with tetranitromethane in chloroform. A mixture of the oxide with methyl acetyloleanolate has m. p. 200° and a mixture with methyl ketoacetyldihydro-oleanolate [m. p. 192—193°, prepared by the method of Ruzicka and Cohen (*Helv. Chim. Acta*, 1937, **20**, 804; Picard, Sharples, and Spring, *loc. cit.*)] shows marked softening at 180° and is completely molten at 193° (Found: C, 75·0; H, 10·2. Calc. for $C_{33}H_{52}O_5$: C, 74·9; H, 9·9%).

Methyl Ketoacetyldihydro-oleanolate.—A solution of methyl acetyloleanolate oxide (0·5 g.) in glacial acetic acid (18 c.c.) and 10% hydrochloric acid (0·5 c.c.) was heated on the steam-bath for 8½ hours and then set aside at room temperature for 36 hours. The product was precipitated by the addition of water, and crystallised twice from methyl alcohol, from which methyl ketoacetyldihydro-oleanolate separated in rosettes of needles, $[\alpha]_{D}^{21^{\circ}}$ — 11·4° ($l = 1$, $c = 1{\cdot}3$ in chloroform), m. p. 194—195°, undepressed on admixture with a specimen (m. p. 192—193°) prepared by the hydrogen peroxide method (Ruzicka and Cohen, *loc. cit.*). A mixture with methyl acetyloleanolate oxide had m. p. 172—187°. Ruzicka and Cohen give $[\alpha]_D$ — 10° for methyl ketoacetyldihydro-oleanolate.

Hydroxyacetyloleanolic Acid Lactone.—Acetyloleanolic acid (3 g.) was treated with a solution of perbenzoic acid in chloroform (0·5N; 50 c.c.) and set aside at 0° for 12 days. A crystalline solid (0·5 g.), m. p. 300° (decomp.), which separated was collected and thrice crystallised from chloroform–ethyl alcohol, giving hydroxyacetyloleanolic acid lactone in prismatic needles, m. p. 333° (decomp.). The chloroform solution was washed with aqueous sodium carbonate, and the solvent removed from the dried solution. The residue after six crystallisations from chloroform–alcohol gave hydroxyacetyloleanolic acid lactone in prismatic needles, m. p. 333° (decomp.), unchanged when mixed with the material described above (total yield, 57%). It does not give a coloration with tetranitromethane in chloroform (Aumüller, Wedekind, and Schicke, *loc. cit.*, give m. p. 337° for the hydroxyacetyloleanolic acid lactone) (Found: C, 74·3; H, 9·7. Calc. for $C_{32}H_{50}O_5$: C, 74·6; H, 9·8%). Hydroxyacetyloleanolic acid lactone (0·15 g.) was refluxed with acetic anhydride (20 c.c.) and a trace of sodium acetate. The product, isolated by means of ether, was crystallised thrice from alcohol, from which the diacetate separated in slender needles, m. p. 295° (Aumüller, Wedekind, and Schicke, *loc. cit.*, give m. p. 292° for the diacetate) (Found: C, 73·0; H, 9·1. Calc. for $C_{34}H_{52}O_6$: C, 73·3; H, 9·4%).

Ketoacetyloleanolic Acid Lactone.—A suspension of hydroxyacetyloleanolic acid lactone (0·3 g.) in glacial acetic acid (150 c.c.) was treated during 25 minutes with a solution of chromic anhydride (0·1 g.) in 97% acetic acid (20 c.c.) at 40° with stirring. The mixture was then cooled to 25° and again treated with a solution of chromic anhydride (0·2 g.) in 97% acetic acid (40 c.c.), added during 20 minutes. The solution was maintained at 25° for 18 hours, the excess of chromic anhydride destroyed by the addition of a little methyl alcohol, and the solution concentrated to about one-third bulk under reduced pressure. The mixture was largely diluted with water and extracted with ether. The extract was washed with aqueous sodium carbonate (10%) (no acid fraction was present), and the product, obtained by removal of the solvent, crystallised twice from methyl alcohol–chloroform, from which ketoacetyloleanolic acid lactone separated in long needles, m. p. 283°. A mixture with a specimen prepared by the method of Ruzicka, Hösli, and Hofmann (*loc. cit.*) (m. p. 279—280°) had m. p. 281—282° (Found: C, 75·3; H, 9·6. Calc. for $C_{32}H_{48}O_5$: C, 75·0; H, 9·4%).

THE UNIVERSITY, MANCHESTER.

[*Received, August* 14*th*, 1940.]