139. *The Triterpene Resinols and Related Acids. Part XIV. The Oxidation of Acetylursolic Acid.*

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Oxidation of acetylursolic acid, $C_{32}H_{50}O_4$, yields ketoacetylursolic acid, $C_{32}H_{48}O_5$ (major product), and a *lactone*, $C_{32}H_{46}O_6$. Ketoacetylursolic acid is shown to be an $\alpha\beta$-unsaturated ketone; when heated with quinoline it loses the elements of formic acid to give *nor-α-amyradienonyl acetate*, which contains the chromophoric system O:C·C:C·C:C. These transformations indicate that the carboxyl group of ursolic acid is in the vicinity of the ethylenic linkage.

Oxidation of acetylursolic acid with chromic acid has been investigated by Kuwada and Matsukawa (*J. Pharm. Soc. Japan*, 1933, **53**, 593), who obtained a product described as ketoacetylursolic acid, $C_{32}H_{48}O_5$, m. p. 296—297°; this substance gave an oxime, a semicarbazone, and a phenylhydrazone. Huzii and Osumi (*ibid.*, 1940, **60**, 291) repeated this oxidation and obtained a ketoacetylursolic acid, m. p. 347°, $[\alpha]_D$ +85°, which would not form an oxime. A consideration of the absorption spectrum of their product led them to the view that it is an αβ-unsaturated ketone.†

In our hands oxidation of acetylursolic acid with chromic anhydride gives ketoacetylursolic acid, $C_{32}H_{48}O_5$, m. p. 315—316°, $[\alpha]_D^{20°}$ +40·8°, which does not give a coloration with tetranitromethane in chloroform and exhibits an intense absorption maximum at 2500 A., $\varepsilon_{max.}$ = 13,000, thus showing it to be an αβ-unsaturated ketone; the ketoacetyl acid is recovered unchanged after prolonged heating with alcoholic hydroxylamine. In these respects, ketoacetylursolic acid is similar to both α-amyrenonol and ketoacetyloleanolic acid. Oxidation of ethyl acetylursolate, m. p. 190—192°, with chromic anhydride gives *ethyl ketoacetylursolate*, m. p. 210—212°, which is identical with the ester prepared from ketoacetylursolic acid, m. p. 315—316°, by treatment with diazoethane. The ester, like the parent acid, does not give a coloration with tetranitromethane and exhibits the characteristic light absorption properties of an αβ-unsaturated ketone.

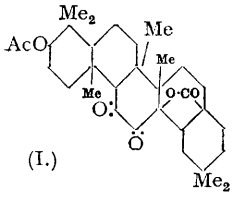
In addition to ketoacetylursolic acid, oxidation of acetylursolic acid gives a neutral fraction from which a *lactone*, $C_{32}H_{46}O_6$, has been isolated. Although it has only been possible to make a preliminary examination

* The fact that $\overset{+}{\rangle}CH_2\cdot\bar{C}O_2$ is also a base in virtue of the carboxylate group is here irrelevant, and in any case the removal of this basicity by conversion of the carboxylate into the carboxyl group has little influence on the ease with which reaction takes place (Dawson and Pycock, *loc. cit.*).

† A comparison of the spectrographic properties of this compound and the ketoacetylursolic acid described by us has not been possible, since we have not had access to the original paper of the Japanese authors.

of this compound, we believe that its formation is of considerable significance in suggesting that the ethenoid linkage in ursolic acid is located in the near vicinity of the carboxyl group.* The lactone does not give a coloration with tetranitromethane, and exhibits an absorption maximum at 3100 A., $\varepsilon_{max.} = 7000$; when heated with N-alcoholic potassium hydroxide solution, it yields an alkali-soluble product; acidification of the alkaline solution (but not dilution of an aqueous alkaline solution with water) gives a neutral product; the amount of this hydrolysed neutral product was not sufficient for analysis.

The lactone bears a marked similarity to the isomeric " acetyldiketolactone " [(I) based on the Haworth variant of the hydropicene structure for oleanolic acid] obtained by oxidation of methyl ketoacetyloleanolate (Ruzicka, van der Sluys-Veer, and Cohen, *Helv. Chim. Acta*, 1939, **22**, 350); our lactone differs from that obtained from oleanolic acid in that, although the location of the absorption maximum is approximately the same in each case, the intensity of absorption of the lactone from ursolic acid is considerably greater than that from oleanolic acid.



(I.)

When heated with quinoline, ketoacetylursolic acid loses the elements of formic acid and gives *nor-α-amyradienonyl acetate*, $C_{31}H_{46}O_3$, m. p. 203—205°. Nor-α-amyradienonyl acetate gives a yellow coloration with tetranitromethane and exhibits an absorption maximum at 3000 A., $\varepsilon_{max.} = 10{,}000$, and in these and other respects shows a similarity to nor-β-amyradienonyl acetate (Ruzicka, Cohen, Furter, and van der Sluys-Veer, *Helv. Chim. Acta*, 1938, **21**, 1735). That the two substances are distinct was shown by the great depression in m. p. observed when the two compounds were mixed. Another case of similarity in physical constants of corresponding derivatives of α- and β-amyrin has been recorded by Ruzicka and Jeger (*Helv. Chim. Acta*, 1941, **24**, 1178), who find that β-amyrandionyl acetate prepared by oxidation of β-amyranonyl acetate with selenium dioxide has almost the same physical properties as the α-amyrandionyl acetate previously prepared by us (J., 1940, 1196) by the ozonolysis of α-amyradienyl acetate. Although a direct comparison of the two has not yet been possible, in our opinion it is unlikely that they will prove to be identical, since this would apparently require the identity of the distinct α-amyradienol and β-amyradienol-I.

Using the same reasoning as in the cases of β-amyradienonol (Picard and Spring, J., 1941, 35) and nor-β-amyradienonol (Ruzicka, Cohen, Furter, and van der Sluys-Veer, *loc. cit.*) it is clear that nor-α-amyradienonol contains the chromophoric system O:C·C:C·C:C and that *the carboxyl group of ursolic acid is in the vicinity of the ethenoid linkage.*

Experimental.

Ursolic acid, obtained from a crude apple pomace extract, was purified by Drake and Duval's method (*J. Amer. Chem. Soc.*, 1936, **58**, 1687) and after four crystallisations from alcohol separated in long fine needles, m. p. 283—284° (Found: C, 78·7; H, 10·5. Calc. for $C_{30}H_{48}O_3$: C, 78·9; H, 10·6%). Acetylursolic acid was obtained from alcohol in needles, m. p. 289—290°, $[\alpha]_D^{20°}$ +61·5° ($l = 1$, $c = 0{\cdot}9$ in chloroform) (Found: C, 77·3; H, 9·7. Calc. for $C_{32}H_{50}O_4$: C, 77·1; H, 10·0%).

Ethyl acetylursolate was obtained by treatment of acetylursolic acid (10 g.) with an ethereal solution of diazoethane prepared from nitrosoethylurea (12 g.). The ester separated from acetone in short prismatic needles, m. p. 190—192°, $[\alpha]_D^{20°}$ +63° ($l = 1$, $c = 3{\cdot}2$ in chloroform). Sell and Kremers (*J. Biol. Chem.*, 1937, **125**, 451) prepared ethyl acetylursolate by the action of ethyl alcohol on acetylursolyl chloride and record m. p. 194°, $[\alpha]_D$ +60·8°.

Ketoacetylursolic Acid.—A boiling solution of acetylursolic acid (8 g.) in glacial acetic acid (200 c.c.) was treated with a solution of chromic acid (6 g.) in acetic acid (50 c.c.; 85%) added during 5 minutes. The solution was refluxed for 90 minutes, diluted with water, and extracted with ether. After washing with water, the extract was washed with aqueous potassium hydroxide solution (20%), an insoluble potassium salt separating at the interface. The salt was collected, and the ethereal solution again washed with alkali and with water. Removal of the ether from the dried (sodium sulphate) solution gave a solid which after four crystallisations from chloroform–alcohol yielded the *lactone* in colourless silky needles, m. p. 305—306° (decomp.). *Light absorption in alcohol:* Maximum at 3120 A., $\varepsilon_{max.} = 7000$ (Found: C, 72·9, 72·9; H, 8·9, 8·7. $C_{32}H_{46}O_6$ requires C, 73·0; H, 8·8%).

The potassium salt was dissolved in hot alcohol (30 c.c.; 95%), and the solution filtered and acidified to Congo-red with hydrochloric acid. After dilution with water, the precipitated acid was collected, digested with boiling water, and, after drying, crystallised from chloroform–methanol. After two recrystallisations from the same solvent, *ketoacetylursolic acid* (3·2 g.) separated in colourless prisms, m. p. 315—316° (decomp.), $[\alpha]_D^{20°}$ +40·8° ($l = 0{\cdot}5$, $c = 0{\cdot}6$ in chloroform). It was very sparingly soluble in alcohol, but readily soluble in ether and chloroform. *Light absorption in alcohol* · Maximum at 2500 A., $\varepsilon_{max.} = 13{,}300$ (Found: C, 75·0; H, 9·2. $C_{32}H_{48}O_5$ requires C, 75·0; H, 9·4%).

Ethyl Ketoacetylursolate.—(*a*) This *ester* was prepared by the action of an ethereal solution of diazoethane on ketoacetylursolic acid; it separated from aqueous methanol in feather-like masses of fine needles, m. p. 210—212°, $[\alpha]_D^{20°}$ +92° ($l = 1$, $c = 1{\cdot}1$ in chloroform) (Found: C, 75·3; H, 9·75. $C_{34}H_{52}O_5$ requires C, 75·55; H, 9·6%).

(*b*) A solution of ethyl acetylursolate (11 g.) in boiling acetic acid (200 c.c.) was treated with a solution of chromic anhydride (8 g.) in acetic acid (50 c.c., 85%) added during 10 minutes. The mixture was refluxed for 2 hours, and the neutral product isolated in the usual manner. Ethyl ketoacetylursolate separated in fine needles from aqueous methanol and in prismatic needles from ethyl alcohol, m. p. 210—212°, undepressed in admixture with the specimen obtained as described in (*a*). *Light absorption in alcohol:* Maximum at 2500 A., $\varepsilon_{max.} = 12{,}000$.

Nor-α-amyradienonyl Acetate.—Ketoacetylursolic acid (1 g.) was refluxed with quinoline (40 c.c.) for 2 hours. The cooled solution was poured into excess of dilute hydrochloric acid, and the mixture extracted with ether. The extract was washed with dilute hydrochloric acid, and with sodium carbonate solution, a sodium salt then separating. The salt was collected and converted into the corresponding acid, which was identified as unchanged ketoacetylursolic acid by m. p. and mixed m. p. The residual ethereal solution was dried, and the neutral resin dissolved in alcohol, from which long flat yellow plates separated. After three recrystallisations (charcoal) from alcohol *nor-α-amyradienonyl acetate*

* Kuwada and Matsukawa (*loc. cit.*) have reported the formation of a neutral product—possibly a lactone—by the oxidation of ursolic acid with chromic anhydride and Huzii and Osumi (*loc. cit.*) claim that reduction of ketoursolic acid with sodium and alcohol yields a dehydrolactone, $C_{30}H_{46}O_3$.

separated in colourless plates, m. p. 203—205°, $[\alpha]_D^{21°}$ +41° (l = 0·5, c = 0·7 in chloroform). *Light absorption in alcohol :* Maximum at 3000 A., $\varepsilon_{max.}$ = 10,000 (Found : C, 79·3, 79·5; H, 10·1, 10·0. $C_{31}H_{46}O_3$ requires C, 79·8; H, 9·9%).

Grateful acknowledgment is made to the Carnegie Trust for a scholarship which enabled one of us (E. S. E.) to participate in this investigation. Our thanks are also due to Dr. K. S. Markley of the Bureau of Chemistry and Soils, U.S. Department of Agriculture, for the gift of an apple pomace extract.

THE UNIVERSITY, MANCHESTER. [*Received, August 12th,* 1942.]