210. *Triterpene Resinols and Related Acids. Part XX. Conversion of α-Amyrin into* iso-α-*Amyranone* (12-*Ketoursane*).

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α-Amyrin has been converted into α-amyranedione, reduction of which by the Wolff–Kishner method gives *iso*-α-amyranone (12-ketoursane) and not the required saturated hydrocarbon of the α-amyrin series. *iso*-α-Amyranone is also obtained from α-amyrene by oxidation with hydrogen peroxide followed by rearrangement of the intermediate oxide.

THE experiments described in this paper were undertaken with the object of preparing α-amyrane (ursane), the parent hydrocarbon of the α-amyrin triterpenoid sub-group, which was required for comparison with β-amyrane (oleanane), the corresponding hydrocarbon of the β-amyrin sub-group.

According to Seymour, Sharples, and Spring (*J.*, 1939, 1075) oxidation of α-amyrin benzoate with hydrogen peroxide gives as major product a compound, $C_{37}H_{54}O_3$, which was considered to be α-amyranonyl benzoate since on reduction with sodium and amyl alcohol it gave a saturated diol, α-amyranediol, and on treatment with bromine an αβ-unsaturated ketone, *iso*-α-amyrenonyl benzoate. We find that this compound (m. p. 217—219°, $[\alpha]_D$ +132°) is isomerised by treatment with hydrochloric acid–acetic acid to give a benzoate, m. p. 227—229°, $[\alpha]_D$ +25°. Treatment of the isomeric compounds, m. p. 217—219° and m. p. 227—229°, with bromine in acetic acid gives in each case bromo-α-amyranonyl benzoate and thence *iso*-α-amyrenonyl benzoate (Seymour and Spring, *J.*, 1941, 319). Reduction of the two isomers with sodium and amyl alcohol yields α-amyranediol. Either the two isomers must be isomeric α-amyranonyl benzoates, differing in orientation around the asymmetric centre produced during the oxidation, or the compound, m. p. 217—219°, is α-amyrin benzoate oxide which when treated with mineral acid rearranges to α-amyranonyl benzoate, this rearrangement also occurring during bromination. In either case the compound, m. p. 227—229°, is α-amyranonyl benzoate; it has been characterised by hydrolysis to α-amyranonol and by the preparation of an enol acetate.

A decision between the two possible structures for the compound, m. p. 217—219°, is difficult because of the inert character of the carbonyl group in amyranonyl esters and the relative ease with which it is isomerised to α-amyranonyl benzoate, m. p. 227—229°. A decision by means of ultra-violet absorption spectroscopy is not feasible since benzoates are not good subjects for the measurement of low-intensity selective absorptive. Attempts were therefore made to obtain the acetate corresponding to the benzoate, m. p. 217—219°.

Ruzicka, Jeger, Redel, and Volli (*Helv. Chim. Acta*, 1945, **28**, 199) have reported that treatment of α-amyrin acetate with ozone gives α-amyrin acetate oxide, m. p. 204—205°, $[\alpha]_D$ +139°, which on treatment with hydrochloric acid is isomerised to α-amyranonyl acetate, m. p. 259—260°, $[\alpha]_D$ +15·6°, showing a low-intensity absorption maximum at 2600 A. We find that treatment of α-amyrin acetate with hydrogen peroxide gives as major product α-amyrin acetate oxide, $C_{32}H_{52}O_3$, m. p. 207—209°, $[\alpha]_D$ +114°, which does not exhibit carbonyl absorption in the ultra-violet region. When treated with hydrochloric acid it gives the saturated ketone, α-amyranonyl acetate, m. p. 282—284°, $[\alpha]_D$ +11°, showing a low-intensity absorption maximum at 2820 A., and characterised by the preparation of an enol acetate. The melting point of this ketone is considerably higher than that observed by Ruzicka, Jeger, Redel, and Volli (*loc. cit.*) using an open capillary; a mixture of α- and β-amyranonyl acetates shows a depressed melting point. Hydrolysis of α-amyranonyl acetate yields α-amyranonol, identical with that obtained from α-amyranonyl benzoate, and treatment of α-amyranonyl acetate with bromine gives *iso*-α-amyrenonyl acetate.

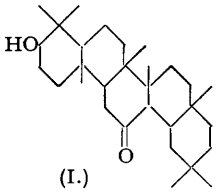
The appreciable difference in the optical rotation of the acetate oxide prepared by means of hydrogen peroxide (+114°) and that obtained by Ruzicka, Jeger, Redel, and Volli by using ozone (+139°), led us to repeat the latter preparation. By using a 2·5% ozone–oxygen mixture α-amyrin acetate was converted into α-amyrin acetate oxide which had properties (m. p. 208—210°, $[\alpha]_D$ +111°) closely agreeing with those of the hydrogen peroxide product.

The compound, $C_{37}H_{54}O_3$, m. p. 217—219°, obtained by hydrogen peroxide oxidation of α-amyrin benzoate has been identified as α-amyrin benzoate oxide by correlating it with α-amyrin acetate oxide. Whereas vigorous alkaline hydrolysis of the benzoate oxide followed by acetylation of the product gives α-amyranonyl acetate, mild alkaline hydrolysis yields a product which on acetylation gives α-amyrin acetate oxide. Furthermore treatment of

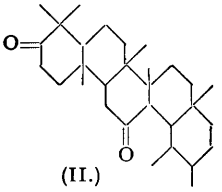
α-amyrin benzoate with ozone gives α-amyrin benzoate oxide with properties similar to those of the hydrogen peroxide product.

The α-amyrin ester oxides are extremely unstable; they are isomerised in part to the corresponding α-amyranonyl esters in alkaline and in acid media. Furthermore the isomerisation of the ester oxides to the saturated ketones is not a simple process. Thus in the case of α-amyrin benzoate oxide rearrangement by means of mineral acid gives α-amyranonyl benzoate, m. p. 227—229°, $[\alpha]_D$ +25°, in approximately 50% yield. From the mother liquors was obtained an isomeric compound, m. p. 232—236°, $[\alpha]_D$ +88°, which on bromination gives bromo-α-amyranonyl benzoate identical with that obtained by bromination of either α-amyranonyl benzoate or α-amyrin benzoate oxide. Similar behaviour has been encountered in the purification of the related ketone derived from methyl acetylursolate, and Dreiding, Jeger, and Ruzicka (*Helv. Chim. Acta*, 1950, **33**, 1325) report that purification of this compound is best effected by simple crystallisation since attempted purification by chromatographic methods led to the partial formation of two isomeric compounds.

Oxidation of α-amyranonol with chromic anhydride gives α-amyranedione. Reduction of this diketone by the Wolff–Kishner method gave *iso*-α-amyranone and not the required saturated hydrocarbon, α-amyrane. *iso*-α-Amyranone has been obtained by an alternative route from α-amyrene, itself prepared by the Wolff–Kishner and Clemmensen methods from α-amyrenone (cf. Winterstein and Stein, *Annalen*, 1933, **502**, 223; Ruzicka, Müller, and Schellenberg, *Helv. Chim. Acta*, 1939, **22**, 758). Treatment of α-amyrene with hydrogen peroxide gives α-amyrene oxide which when treated with hydrochloric acid gives *iso*-α-amyranone, identical with the ketone obtained by partial reduction of α-amyranedione. Reduction of α-amyrene oxide with sodium and amyl alcohol yields a secondary alcohol *iso*-α-amyranol, characterised as its acetyl derivative. Attempts were made to convert *iso*-α-amyranol into the corresponding chloride with the object of reducing the latter to the required α-amyrane. These attempts were unsuccessful, treatment of *iso*-α-amyranol with thionyl chloride, phosphoryl chloride, phosphorus pentachloride, or dry hydrogen chloride giving α-amyrene in each case.



(I.)



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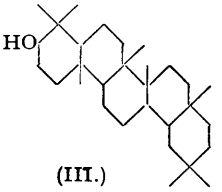

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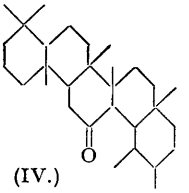

(IV.)

These experiments emphasise the major difference in reactivity between the α- and the β-amyrin series. In the case of the β-amyrin group the Wolff–Kishner reduction of β-amyranonol proceeds smoothly to give β-amyranol (Ruzicka and Jeger, *Helv. Chim. Acta*, 1941, **24**, 1178). This difference finds expression in the formulæ adopted by Ruzicka, Jeger, and their collaborators for α- and β-amyrins, according to which β-amyranonol (2-hydroxy-12-keto-oleanane) is (I) and α-amyranedione (2 : 12-diketoursane) is (II), reduction of the former giving β-amyranol (2-hydroxyoleanane) (III) from which the parent hydrocarbon oleanane can readily be obtained, whilst reduction of the latter gives *iso*-α-amyranone (12-ketoursane) (IV). The inert character of the carbonyl group in *iso*-α-amyranone can be attributed to the steric effect of the methyl group attached to $C_{(19)}$.

Experimental.

(Optical rotations were measured in chloroform solution in a 10-cm. tube; m. p.s are uncorrected.)

α-Amyrin Benzoate Oxide.—(*a*) α-Amyrin benzoate (10 g.) was oxidised as described by Seymour, Sharples, and Spring (*loc. cit.*). The hot reaction mixture was treated with water until turbid. The crystalline solid separating on cooling was collected and repeatedly recrystallised from benzene–methanol, giving *α-amyrin benzoate oxide* (5 g.) as fine needles, m. p. 217—219°, $[\alpha]_D^{16}$ +132° (*c*, 2·9), (Found: C, 81·7; H, 9·6. $C_{37}H_{54}O_3$ requires C, 81·3; H, 10·0%).

(*b*) A solution of α-amyrin benzoate (2·5 g.) in dry, freshly distilled carbon tetrachloride (50 c.c.) was treated with ozonised oxygen (2·5%) for 7 hours; the mixture then gave no colour with tetranitromethane. The solution was evaporated and the residue extracted with benzene. The extract was washed with dilute sodium hydroxide which extracted a small amount of acidic product. The washed benzene solution was evaporated and the residue crystallised from chloroform–methanol giving α-amyrin benzoate oxide as needles (1·5 g.), m. p. 215—217°, $[\alpha]_D^{14}$ +130° (*c*, 3·0), undepressed when mixed with the specimen described above.

(*c*) A solution of α-amyrin benzoate (1·0 g.) in glacial acetic acid (75 c.c.) was treated at 100° with a solution of potassium permanganate (0·24 g.) in water (8 c.c.), added during 30 minutes with stirring

The mixture was heated for 2 hours and then diluted with water, and the product isolated by means of ether. Crystallisation from alcohol gave α-amyrin benzoate oxide (0·2 g.), m. p. 217—219° undepressed when mixed with the specimen described at (*a*).

α-Amyrin Acetate Oxide.—(*a*) Oxidation of α-amyrin acetate (10 g.) with hydrogen peroxide was carried out as described for the benzoate. The crude reaction product (5·0 g.) separated from chloroform–methanol as plates, m. p. 207—209°, $[\alpha]_D^{17}$ +105° (*c*, 1·6). Fractional crystallisation from alcohol gave a main fraction (2·0 g.), m. p. 203—205°, $[\alpha]_D^{19}$ +118° (*c*, 3·5). Purification of this by chromatography on alumina gave in small yield *α-amyrin acetate oxide* as blades, m. p. 207—209°, $[\alpha]_D^{22}$ +114° (*c*, 2·3) (Found : C, 79·3; H, 10·5. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%). The oxide does not show low-intensity carbonyl absorption in the ultra-violet.

(*b*) Treatment of α-amyrin acetate with 2·5%-ozonised oxygen as described for the benzoate gave α-amyrin acetate oxide as small blades, m. p. 208—210°, $[\alpha]_D^{17}$ +111° (*c*, 3·1), from aqueous acetone (Found : C, 79·6; H, 10·7%).

α-Amyranonyl Benzoate.—Rearrangement of α-amyrin benzoate oxide was effected in chloroform–acetic acid solution using concentrated hydrochloric acid as employed by Ruzicka, Jeger, Redel, and Volli (*loc. cit.*). The product was crystallised from chloroform–methanol, giving *α-amyranonyl benzoate* as plates, m. p. 227—229°, $[\alpha]_D^{17}$ +24·7° (*c*, 2·0) (Yield 50%) (Found : C, 81·0; H, 10·2. $C_{37}H_{54}O_3$ requires C, 81·3; H, 10·0%).

α-Amyranonyl acetate was obtained in 60% yield by similar rearrangement of α-amyrin acetate oxide. It separated from chloroform–methanol as plates, m. p. 280—282°, $[\alpha]_D$ +11·4° (*c*, 1·6) (Found : C, 79·1; H, 10·7. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%). α-Amyranonyl acetate showed an absorption maximum at 2820 A. ($\varepsilon = 225$).

α-Amyranonol.—α-Amyranonyl benzoate (1 g.) was refluxed for 2 hours with an excess of 1% alcoholic potassium hydroxide. The mixture was diluted with water, and the product isolated by means of benzene. It was crystallised from light petroleum (b. p. 60—80°), giving *α-amyranonol* as fern-like growths of fine needles, m. p. 218—220°, $[\alpha]_D$ −5° (*c*, 1·5) (Found : C, 81·1; H, 10·9. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%). Acetylation of α-amyranonol with acetic anhydride and pyridine at room temperature gave α-amyranonyl acetate as plates (from chloroform–methanol), m. p. 280—282°, $[\alpha]_D$ +9° (*c*, 2·9), undepressed when mixed with the specimen described above.

Enol Acetate of α-Amyranonyl Acetate.—A solution of α-amyranonyl acetate (3 g.) in acetic anhydride (60 c.c.), containing freshly fused sodium acetate (3 g.), was refluxed for 24 hours. The mixture was treated with water, and the product crystallised from alcohol, giving the enol *acetate* as needles, m. p. 255—257°, $[\alpha]_D^{17}$ +49° (*c*, 2·6) (Found : C, 77·6; H, 10·1. $C_{34}H_{54}O_4$ requires C, 77·5; H, 10·3%).

The enol *acetate* of α-amyranonyl benzoate was prepared similarly from α-amyranonyl benzoate. It separated from aqueous acetone as blades, m. p. 220—222°, $[\alpha]_D^{14}$ +65° (*c*, 7·4) (Found : C, 79·7; H, 9·3. $C_{39}H_{58}O_4$ requires C, 79·3; H, 9·8%).

Bromo-α-amyranonyl Benzoate.—This was obtained in approximately 70% yield by bromination of either α-amyranonyl benzoate or α-amyrin benzoate oxide, as described by Seymour and Spring (*loc. cit.*). It separated from chloroform–methanol as blades, m. p. 186—188° (decomp.), $[\alpha]_D^{17}$ +27° (*c*, 2·4) (Found : C, 71·1; H, 8·8. Calc. for $C_{37}H_{55}O_3Br$: C, 70·8; H, 8·8%). Treatment of the bromoketone with hydrogen bromide in acetic acid (Seymour and Spring, *loc. cit.*) and treatment of either α-amyranonyl benzoate or α-amyrin benzoate oxide with bromine as described by Seymour, Sharples, and Spring (*loc. cit.*) gave *iso*-α-amyrenonyl benzoate as prisms, m. p. 212—214°, $[\alpha]_D$ +91° (*c*, 2·0), from benzene–alcohol (Found : C, 81·7; H, 9·7. Calc. for $C_{37}H_{52}O_3$: C, 81·6; H, 9·6%).

iso-α-*Amyrenonyl Acetate.*—This was obtained by direct bromination of α-amyranonyl acetate as described for the preparation of the corresponding benzoate by Seymour, Sharples, and Spring; solid did not separate during the reaction. *iso*-α-Amyrenonyl acetate separated as plates, m. p. 284—286° (decomp.), $[\alpha]_D^{18}$ +83° (*c*, 1·9), from benzene–methanol.

Hydrolysis of either *iso*-α-amyrenonyl acetate or benzoate with alcoholic potassium hydroxide gave *iso*-α-amyrenonol as fine needles, m. p. 241—242°, $[\alpha]_D^{15}$ +72° (*c*, 2·0), +75° (*c*, 2·15), from aqueous alcohol (Found : C, 82·0; H, 11·1. Calc. for $C_{30}H_{48}O_2$: C, 81·8; H, 11·0%).

α-Amyranedione.—A solution of α-amyranonol (1 g.) in acetic acid (17 c.c.) was treated at room temperature with a solution of chromic anhydride (0·22 g.) dissolved in a minimum of water and diluted with acetic acid (3 c.c.). Next morning the mixture was diluted with water, and the product isolated by means of ether. The ether solution was washed with dilute sodium hydroxide and then with water, and dried (Na_2SO_4). Acidification of the alkaline washings gave a trace of acidic material. The neutral fraction was crystallised from aqueous alcohol, giving *α-amyranedione* as needles, m. p. 166—168°, $[\alpha]_D$ +2° (*c*, 2·4) (Found : C, 82·0; H, 10·9. $C_{30}H_{48}O_2$ requires C, 81·8; H, 11·0%). α-Amyranedione was also obtained by similar oxidation of α-amyranediol.

α-Amyrene.—A mixture of α-amyrenone (6 g.), sodium ethoxide (from 6 g. of sodium and 150 c.c. of ethanol), and hydrazine hydrate (90%; 18 c.c.) was heated in an autoclave at 180° for 18 hours. The mixture was diluted with water and extracted with ether. The ether solution was washed, dried (Na_2SO_4), and evaporated, giving a yellow oil which quickly solidified. Crystallisation of the solid from ethanol gave α-amyrene as plates (3·5 g.), m. p. 109—111°, $[\alpha]_D^{20}$ +93° (*c*, 1·75) (Found : C, 88·1; H, 12·4. Calc. for $C_{30}H_{50}$: C, 87·7; H, 12·3%). Treatment of α-amyrenone semicarbazone with sodium ethoxide as described by Ruzicka, Müller, and Schellenberg (*loc. cit.*) gave α-amyrene (40% yield) as plates (from ethanol), m. p. 109—111°, $[\alpha]_D^{19}$ +93° (*c*, 2·4). Similarly, reduction of α-amyrenone with amalgamated zinc in hydrochloric acid–acetic acid solution, as described by Winterstein and Stein (*loc. cit.*), gave α-amyrene as plates (from alcohol), m. p. 109—111°, $[\alpha]_D$ +92° (*c*, 2·0).

Ruzicka, Müller, and Schellenberg (*loc. cit.*) obtained α-amyrene from α-amyrenone semicarbazone by the Wolff–Kischner process as plates, m. p. 124°, $[\alpha]_D$ +95°. Although the rotation is in good

agreement with that found by us for all the preparations described above, there is an appreciable difference in melting point. Attempts were therefore made to obtain a higher-melting specimen of α-amyrene. A specimen, m. p. 110—112°, prepared by reduction of α-amyrenone with hydrazine and sodium ethoxide, was filtered through a column of alumina (Grade II). After crystallisation from methanol–ether it had m. p. 112—113°. It was again filtered through a 5′ column of alumina (Grade I), giving three fractions which, after crystallisation from ether–methanol, gave α-amyrene as plates, m. p. 111—113°, 111·5—113°, and 111·5—113°, respectively. A similar behaviour was observed (*a*) after chromatography of a specimen of α-amyrene prepared from α-amyrenone semicarbazone by Wolff–Kishner reduction, the final product being obtained as plates, m. p. 111·5—113°, and (*b*) by using a specimen of α-amyrene obtained by Clemmensen reduction of α-amyrenone; after chromatography this specimen was obtained as plates, m. p. 111·5—113°, from ether–methanol.

α-Amyrene was recovered unchanged after shaking it for 6 hours in ethyl acetate with hydrogen at 50 atm. pressure, in the presence of platinum catalyst.

α-Amyrene Oxide.—α-Amyrene (5 g.) was oxidised with hydrogen peroxide under the conditions employed for the oxidation of α-amyrin benzoate. When the reaction mixture cooled α-amyrene (0·5 g.) separated and was collected. The acetic acid solution was diluted with water, and the product isolated by means of benzene. After the solution had been washed the benzene was removed, giving a gum (3·8 g.) which was dissolved in light petroleum–benzene (1 : 1), and the solution filtered through a short column of alumina. The solvent was removed from the filtrate yielding a colourless oil which rapidly crystallised. Recrystallisation from alcohol gave *α-amyrene oxide* as plates, m. p. 116—118°, $[\alpha]_D^{21}$ +135° (*c*, 2·0) (Found: C, 84·5; H, 11·9. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%).

iso-α-*Amyranone* (12-*Ketoursane*).—(*a*) Isomerisation of α-amyrene oxide with hydrochloric acid in chloroform–acetic acid gave iso-α-*amyranone* as blades, m. p. 150—152°, $[\alpha]_D^{24}$ ±0° (*c*, 0·7), from aqueous alcohol (Found: C, 84·1; H, 11·6. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%). *iso*-α-Amyranone crystallised from alcohol in a solvated form, m. p. 141—143°, which after being dried at 120° in a vacuum gave the non-solvated form.

(*b*) A mixture of α-amyranedione (0·75 g.), sodium ethoxide (from 0·75 g. of sodium and 30 c.c. of ethanol), and hydrazine hydrate (90%; 3·5 c.c.) was heated in an autoclave for 18 hours at 180°. The product isolated in the usual manner gave in low yield *iso*-α-amyranone, m. p. 141—143° undepressed when mixed with the specimen described above.

iso-α-*Amyranol.*—A boiling solution of α-amyrene oxide (2·8 g.) in amyl alcohol (38 c.c.) was treated with sodium (2·8 g.), and the mixture refluxed for 20 minutes. Sodium (2·8 g.) was again added and the mixture refluxed for 2½ hours. A small quantity of alcohol was added, the mixture boiled with water, and the amyl alcohol removed in steam. The product was isolated by means of ether and crystallised from aqueous acetone or alcohol, giving iso-α-*amyranol* (1·5 g.) as plates, m. p. 178—180°, $[\alpha]_D^{20}$ +48·1° (*c*, 2·1) (Found: C, 84·0; H, 12·25. $C_{30}H_{52}O$ requires C, 84·0; H, 12·2%).

Conversion of iso-α-*Amyranol into* α-*Amyrene.*—(*a*) The alcohol (0·6 g.) was heated under reflux with thionyl chloride (5 c.c.) for 30 minutes. (*b*) A solution of *iso*-α-amyranol (0·3 g.) in dry ether (20 c.c.) was saturated below 5° with dry hydrogen chloride and kept overnight at 0°. (*c*) A solution of *iso*-α-amyranol in phosphoryl chloride (5 c.c.) was kept overnight at room temperature. In each case the sole product isolated was α-amyrene, m. p. and mixed m. p. 109—111°.

iso-α-*Amyranyl acetate* was obtained by acetylation of the alcohol with pyridine and acetic anhydride at room temperature. It separates from alcohol as blades, m. p. 244—246° (Found: C, 81·1; H, 11·9. $C_{32}H_{54}O_2$ requires C, 81·6; H, 11·6%).

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