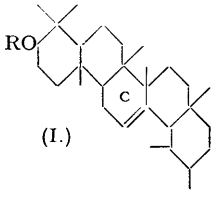
240. *Triterpene Resinols and Related Acids. Part XXI.* iso-α-*Amyrenonol-II.*

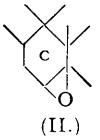
By JOHN MCLEAN, S. U. RUFF, and F. S. SPRING.

A study of the relation of the isomeric αβ-unsaturated ketones, α-amyrenonol and *iso*-α-amyrenonol, to α-amyradienol is described. Oxidation of α-amyradienyl acetate with perbenzoic acid gives a mixture from which α-amyrenonyl acetate and *iso*-α-amyrenonyl acetate have been isolated. Oxidation of the dienyl acetate with hydrogen peroxide on the other hand gives a mixture from which α-amyrenonyl acetate and an isomeric αβ-unsaturated ketone, *iso*-α-amyrenonyl-II acetate, have been isolated, and a similar mixture is obtained by oxidation of α-amyradienyl benzoate with hydrogen peroxide. *iso*-α-Amyrenonol-II is probably a stereoisomer of *iso*-α-amyrenonol, into which it can be converted by prolonged treatment with strong alkali. Reduction of *iso*-α-amyrenonyl-II esters with sodium and amyl alcohol followed by treatment of the reaction product with acetic anhydride gives α-amyradienyl acetate. These reactions establish the relations between the three αβ-unsaturated ketones and α-amyradienol. *iso*-α-Amyrenonol-II differs from *iso*-α-amyrenonol in that it can be catalytically reduced to give a saturated ketone, α-amyranonol-II. It is concluded that angular methyl group migration does not occur in the conversion of α-amyrin into *iso*-α-amyradienonol and that the reactions of the latter compound are yet to be satisfactorily interpreted.

OXIDATION of α-amyrin benzoate (I; * R = COPh) with hydrogen peroxide gives an oxide (II) which, when rearranged with mineral acid yields the saturated ketone, α-amyranonyl benzoate (III). Bromination of either the oxide or the ketone gives *iso*-α-amyrenonyl benzoate (cf. IV), and the related *iso*-α-amyrenonyl acetate is obtained by a similar series of changes from α-amyrin acetate (Seymour, Sharples, and Spring, *J.*, 1939, 1079; Seymour and Spring, *J.*, 1941, 319; Silverstone and Spring, *J.*, 1951, 935). Oxidation of α-amyrin acetate with chromic acid gives an isomeric αβ-unsaturated ketone, α-amyrenonyl acetate (V) (Spring and Vickerstaff, *J.*, 1937, 249), which has the same nuclear structure as α-amyrin (Ruzicka, Leuenberger, and Schellenberg, *Helv. Chim. Acta*, 1937, **20**, 1271). Reduction of the two αβ-unsaturated ketones,



(I.)



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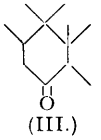

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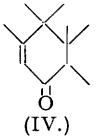

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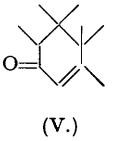

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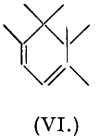

(VI.)

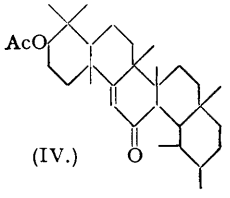
α-amyrenonyl acetate and *iso*-α-amyrenonyl acetate, with sodium and alcohol, followed by acetylation of the reaction products, gives in each case α-amyradienyl acetate (VI) (Spring and Vickerstaff, *loc. cit.*; Ewen, Spring, and Vickerstaff, *J.*, 1939, 1303; Seymour, Sharples, and Spring, *loc. cit.*); α-amyradienyl acetate can also be obtained by partial dehydrogenation of α-amyrin acetate with sulphur (Jacobs and Fleck, *J. Biol. Chem.*, 1930, **88**, 137) or with *N*-bromosuccinimide (Ruzicka, Jeger, and Redel, *Helv. Chim. Acta*, 1943, **26**, 1235).

The structure of *iso*-α-amyrenonol has assumed considerable importance in the chain of evidence upon which depends the recently postulated structure (I; R = H) for α-amyrin (Meisels, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1949, **32**, 1075) particularly in so far as its relation to β-amyrin is concerned. Oxidation of *iso*-α-amyrenonyl acetate (IV) with selenium dioxide gives *iso*-α-amyradienonyl acetate (Ruzicka, Rüegg, Volli, and Jeger, *Helv. Chim. Acta*, 1947, **30**, 140), and this reaction has been formulated as involving a molecular rearrangement in which a methyl group migrates from $C_{(14)}$ to $C_{(13)}$ (Meisels, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1950, **33**, 700; Rüegg, Dreiding, Jeger, and Ruzicka, *ibid.*, p. 889), *iso*-α-amyradienonyl acetate being represented as (VII). *iso*-α-Amyradienonyl acetate has been

* For descriptive convenience the formula for α-amyrin advocated by Meisels, Jeger, and Ruzicka (*Helv. Chim. Acta*, 1949, **32**, 1075) is employed in this paper.

converted into a compound formulated as the β-diketone (VIII) by a series of reactions including oxidation at the $C_{(14)}$–$C_{(15)}$ ethylenic linkage followed by a pyrolytic decomposition. Although this β-diketone does not give a coloration with ferric chloride it reacts with diazomethane to give two isomeric compounds formulated as the methyl ethers (IX) and (X) which are identical with two products obtained by similar reactions starting from *iso*-β-amyrenonyl acetate.

It is the purpose of this paper to examine the premises upon which the assumption of a methyl group migration, in the reactions leading to the formation of *iso*-α-amyradienonyl acetate, is made. In addition to its bearing upon the structure of *iso*-α-amyradienonyl acetate, a decision that methyl group migration has occurred during these reactions, which involve relatively mild reaction conditions, may have wider repercussions in a consideration of the mechanism of formation of the products of total dehydrogenation of the triterpenoids.



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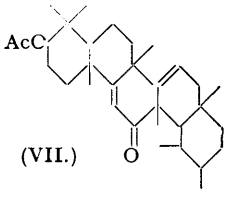

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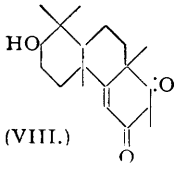
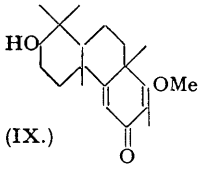


(VIII.)



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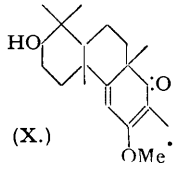

(X.)

The formulæ (IV) and (VII) for *iso*-α-amyrenonyl acetate and *iso*-α-amyradienonyl acetate, respectively, cannot both be correct since it is known that catalytic hydrogenation of *iso*-α-amyradienonyl acetate gives *iso*-α-amyrenonyl acetate in good yield (Ruzicka, Rüegg, Volli, and Jeger, *loc. cit.*). The possibility that a methyl group attached to $C_{(13)}$ in *iso*-α-amyradienonyl acetate again migrates to $C_{(14)}$ during the catalytic hydrogenation seems remote and in our opinion is excluded by the fact that *iso*-α-amyradienonyl acetate is recovered unchanged after being shaken in the absence of hydrogen in acetic acid with a freshly reduced platinum catalyst.* It follows that *iso*-α-amyrenonyl acetate and *iso*-α-amyradienonyl acetate have the same nuclear structure, and it becomes necessary to consider the possibility of methyl group migration during the conversion of α-amyrin into *iso*-α-amyrenonol. This appears to be excluded by the observation that *iso*-α-amyrenonol can be converted into α-amyradienyl acetate (VI), oxidation of which with ozone gives α-amyrenonyl acetate (Ewen and Spring, *J.*, 1940, 1196) which contains the same nuclear structure as α-amyrin. Since the yield of α-amyrenonyl acetate obtained from α-amyradienyl acetate was only 4%, it was decided to re-examine the relationship between α-amyrin, α-amyrenonol, *iso*-α-amyrenonol, and α-amyradienol.

Oxidation of α-amyradienyl acetate with perbenzoic acid was reported (Spring and Vickerstaff, *loc. cit.*) to give a product, m. p. 192°, described as an oxide. We find that chromatographic fractionation of the reaction mixture obtained by oxidation of α-amyradienyl acetate with perbenzoic acid gives *iso*-α-amyrenonyl acetate in 20% yield together with α-amyrenonyl acetate in approximately 7% yield; these are minimum yields, considerable losses occurring in the tedious purification procedure employed. Oxidation of α-amyradienyl benzoate with hydrogen peroxide gives a mixture from which α-amyrenonyl benzoate in approximately 16% yield has been isolated, together with a 42% yield of an isomeric compound which we name *iso*-α-amyrenonyl-II benzoate. The separation of this mixture was achieved by a process of fractional crystallisation from boiling ethanol which was developed after unsuccessful attempts to separate the mixture by chromatography. *iso*-α-Amyrenonyl-II benzoate was characterised by hydrolysis to *iso*-α-amyrenonol-II, acetylation of which yields *iso*-α-amyrenonyl-II acetate. The last compound is also obtained in approximately 7% yield by the oxidation of α-amyradienyl acetate with hydrogen peroxide, the major product of this reaction being an approximately 72% yield of α-amyrenonyl acetate. α-Amyrenonyl acetate and *iso*-α-amyrenonyl-II acetate form a constant-melting mixed crystal which cannot be separated by chromatography on alumina or by ordinary methods of crystallisation. The compound described as *epi*(*iso*)-α-amyrenonyl acetate obtained together with α-amyrenonyl

* This observation was made by Dr. Wm. Manson to whom we express our thanks.

acetate by the action of ozone on α-amyradienyl acetate (Ewen and Spring, *loc. cit.*) is probably a mixed crystal of α-amyrenonyl acetate and *iso*-α-amyrenonyl-II acetate. *iso*-α-Amyrenonyl-II acetate is an αβ-unsaturated ketone; it exhibits an absorption maximum at 2500 A. ($\varepsilon = 11{,}000$) and gives no coloration with tetranitromethane in chloroform. Reduction of *iso*-α-amyrenonyl-II acetate or benzoate with sodium and amyl alcohol followed by treatment of the product with acetic anhydride gave α-amyradienyl acetate. Prolonged treatment of *iso*-α-amyrenonyl-II benzoate with strong alkali converts it quantitatively into *iso*-α-amyrenonol thus establishing that *iso*-α-amyrenonol-II differs from *iso*-α-amyrenonol either in the position of the ethylenic linkage (which in both cases must be αβ with respect to the carbonyl group) or, more likely, in the orientation of the hydrogen atom attached to the α-carbon with respect to the carbonyl group. A significant difference is to be observed in the behaviour of *iso*-α-amyrenonol and *iso*-α-amyrenonol-II; in contrast to the former compound (cf. Jeger, Rüegg, and Ruzicka, *Helv. Chim. Acta*, 1947, **30**, 1294) *iso*-α-amyrenonol-II is smoothly reduced with hydrogen and platinum to a saturated ketone, α-amyranonol-II.

The formation, in high yield, of α-amyrenonyl acetate by the oxidation of α-amyradienyl acetate, and the inter-relation of *iso*-α-amyrenonyl acetate and α-amyrenonyl acetate through α-amyradienyl acetate lead to the conclusion that all these compounds have the same carbon skeleton and specifically that the conversion of α-amyrin into *iso*-α-amyrenonyl acetate does not involve the migration of an angular methyl group. Since *iso*-α-amyradienonyl acetate is smoothly converted into *iso*-α-amyrenonyl acetate (and α-amyradienyl acetate) by simple catalytic hydrogenation, the formation of *iso*-α-amyradienonyl acetate from α-amyrin has likewise not involved angular methyl group migration, and the presence of an angular methyl group at $C_{(14)}$ appears to be impossible. A satisfactory interpretation of the reactions of *iso*-α-amyradienonyl acetate leading to the formation of common degradation products of the α- and β-amyrins is yet to be given.

Experimental.

Specific rotations were measured in chloroform solution, a 1-dm. tube being used; m. p.s are uncorrected.

Oxidation of α-Amyradienyl Acetate with Perbenzoic Acid.—α-Amyradienyl acetate (1·6 g.) was treated with 0·6N-perbenzoic acid in chloroform (50 c.c.), and the solution kept at 2° for 14 days. The solution was washed with aqueous sodium carbonate and water, dried over sodium sulphate, and evaporated. The resin was dissolved in light petroleum (b. p. 40—60°) and filtered through a column of activated alumina (40 g.).

The column was washed with light petroleum (2000 c.c.) and then developed with benzene. The first 500 c.c. of this solvent eluted a crystalline solid (fraction *A*; 0·48 g.). The small quantity of material eluted by the next 750 c.c. was ignored, and a further 500 c.c. of benzene gave more crystalline solid (fraction *B*; 0·14 g.).

Fraction *A* was recrystallised from methanol–chloroform giving *iso*-α-amyrenonyl acetate (300 mg.), m. p. 282—283°, $[\alpha]_D^{16}$ +89° (*c*, 1·3), undepressed in m. p. when mixed with a specimen, m. p. 283—284°, $[\alpha]_D^{16}$ +87°, prepared as described by Seymour, Sharples, and Spring (*loc. cit.*).

Fraction *B* was similarly recrystallised from methanol–chloroform, yielding α-amyrenonyl acetate (90 mg.), m. p. 275—276°, $[\alpha]_D^{16}$ +96° (*c*, 0·7), undepressed when mixed with an authentic specimen, m. p. 276°, $[\alpha]_D^{16}$ +98° (*c*, 1·7), obtained by Spring and Vickerstaff's method (*loc. cit.*).

iso-α-*Amyrenonyl*-II *Benzoate.*—A solution of α-amyradienyl benzoate (5 g.) in glacial acetic acid (225 c.c.) was treated for 20 minutes at steam-bath temperature with a mixture of hydrogen peroxide (30%; 20 c.c.) and glacial acetic acid (20 c.c.) with vigorous stirring. Stirring and heating were continued until the precipitated solid redissolved (2 hours). More peroxide–acetic acid (40 c.c.) was added and the solution heated and stirred for 1 hour. The solution was diluted with hot water until it was permanently turbid. The crystalline solid (fraction I) separating on cooling was collected, washed with a little methanol and then with water, and dried in air at 100°. The mother-liquor was diluted with water, and the solid (fraction II) collected, washed with water, and dried in a vacuum.

Fraction I was dissolved in chloroform (3 c.c.) and ethanol (200 c.c.), and the solution evaporated until crystallisation occurred in the boiling mixture. The boiling mixture was filtered and the filtrate again concentrated until crystallisation occurred. Three crops of crystalline solid (mother-liquor *A*) obtained by this procedure were combined and recrystallised from chloroform–methanol giving iso-α-*amyrenonyl*-II *benzoate* (2·1 g.) as large needles, m. p. 242°, $[\alpha]_D^{16}$ +21° (*c*, 3·0) (Found: C, 81·5; H, 9·8. $C_{37}H_{52}O_3$ requires C, 81·6; H, 9·6%).

iso-α-*Amyrenonol*-II.—A solution of *iso*-α-amyrenonyl-II benzoate (250 mg.) in benzene (5 c.c.) was treated with a solution of potassium hydroxide (250 mg.) in water (2 c.c.) and ethanol (20 c.c.). The mixture was refluxed for 2 hours, cooled, and poured into ice-cold dilute sulphuric acid. The reaction product was isolated by means of ether and crystallised from chloroform–light petroleum (b. p. 60—80°) giving iso-α-*amyrenonol*-II (150 mg.) as long feathery needles, m. p. 211—212°, $[\alpha]_D$ −15·5° (*c*, 3·4) (Found: C, 81·9; H, 10·7. $C_{30}H_{48}O_2$ requires C, 81·8; H, 11·0%).

α-*Amyrenonyl Benzoate.*—Fraction II of the oxidation product from α-amyradienyl benzoate was combined with the mother-liquor *A* and crystallised. The first two crystalline fractions were combined

and recrystallised from chloroform–methanol giving α-amyrenonyl benzoate (800 mg.) as plates, m. p. 275—276°, $[\alpha]_D$ +107° (*c*, 4·4) (Found : C, 81·3; H, 8·55. Calc. for $C_{37}H_{52}O_3$: C, 81·6; H, 9·6%); the m. p. was undepressed when this material was mixed with a specimen, m. p. 274—275°, $[\alpha]_D$ +107° (*c*, 3·3), obtained as described by Spring and Vickerstaff (*loc. cit.*).

iso-α-*Amyrenonyl*-II *Acetate*.—(*a*) Acetylation of *iso*-α-amyrenonol-II with pyridine and acetic anhydride gave iso-α-*amyrenonyl*-II *acetate* from chloroform–methanol as needles, m. p. 200—201°, $[\alpha]_D^{16}$ +11° (*c*, 1·8). Light absorption in ethanol : Maximum at 2500 A.; ε = 11,000.

(*b*) α-Amyradienyl acetate (5 g.) was oxidised with hydrogen peroxide. Following the conditions detailed for the corresponding benzoate a crystalline fraction and an amorphous fraction were obtained. The crystalline fraction separating from the aqueous acetic acid solution was fractionally crystallised at the boiling point of ethanol. The first four fractions were combined and recrystallised from chloroform–methanol giving α-amyrenonyl acetate (3·6 g.) as large plates, m. p. 276°, $[\alpha]_D^{16}$ +96° (*c*, 1·7) (Found : C, 79·9; H, 10·2. Calc. for $C_{32}H_{50}O_3$: C, 79·6; H, 10·4%). Light absorption in ethanol : Maximum at 2520 A.; ε = 12,000. The m. p. was undepressed when the product was mixed with a specimen of α-amyrenonyl acetate prepared by Spring and Vickerstaff's method (*loc. cit.*).

The amorphous product obtained by dilution of the aqueous acetic acid mother-liquors with water was combined with the ethanol mother-liquors from the fractional crystallisation described above, and the solution concentrated to a small bulk. The crystalline solid separating was collected after four days and recrystallised from chloroform–methanol giving a solid (0·7 g.), m. p. 193°, which was fractionally crystallised from boiling methanol. The first fraction (0·11 g.) melted over a range above 220°. The second and third fractions were combined and recrystallised from chloroform–methanol giving *iso*-α-amyrenonyl-II acetate (0·35 g.) as needles, m. p. 200—202° undepressed when mixed with the specimen obtained by method (*a*), $[\alpha]_D^{18}$ +14° (*c*, 0·9) (Found : C, 79·3; H, 10·8. $C_{32}H_{50}O_3$ requires C, 79·6; H, 10·4%).

Hydrolysis of the acetate obtained by method (*b*) using the method described for the benzoate gave *iso*-α-amyrenonol-II, which separated as long feathery needles from chloroform–light petroleum (b. p. 60—80°), m. p. 211—213° undepressed when mixed with the specimen described above, $[\alpha]_D^{16}$ −16 (*c*, 1·8). Light absorption in ethanol : Maximum at 2500 A., ε = 12,000.

α-*Amyradienyl Acetate*.—A boiling solution of *iso*-α-amyrenonyl-II benzoate (3 g.) in dry amyl alcohol (120 c.c.) was treated with sodium (7·5 g.) added during 20 minutes. Amyl alcohol (20 c.c.) was added and the mixture refluxed for 40 minutes. After being washed with water, the amyl alcohol was removed in steam, the reaction mixture extracted with ether, and the extract dried (Na_2SO_4). The product obtained by removal of the ether was heated under reflux for 1 hour with acetic anhydride (20 c.c.), and the mixture was then diluted with water and kept overnight. The precipitated solid was collected and crystallised from chloroform–methanol giving α-amyradienyl acetate (1·6 g.), as needles, m. p. 168°, $[\alpha]_D^{16}$ +313° (*c*, 1·6) (Found : C, 81·9; H, 10·5. Calc. for $C_{32}H_{50}O_2$: C, 82·3; H, 10·8%).

Similar reduction of *iso*-α-amyrenonyl-II acetate (300 mg.) gave α-amyradienyl acetate (200 mg.), m. p. 166° undepressed when the material was mixed with the specimen described above. Light absorption in ethanol : Maximum at 2830 A., ε = 9000. A specimen of α-amyradienyl acetate, obtained by reduction of α-amyrenonyl benzoate with sodium and amyl alcohol followed by acetylation, separated from chloroform–methanol as needles, m. p. 168—169°, $[\alpha]_D^{16}$ +318° (*c*, 1·2).

iso-α-*Amyrenonol*.—*iso*-α-Amyrenonyl-II benzoate (3 g.) in ethanol (140 c.c.) was mixed with potassium hydroxide (11 g.) in water (10 c.c.) and ethanol (20 c.c.), and the solution refluxed for 6 hours. After the addition of potassium hydroxide (7 g.) in water (5 c.c.) and ethanol (20 c.c.) refluxing was continued for 8 hours. The mixture was poured into water (1 l.) and extracted with ether. The washed and dried extract was evaporated and the product crystallised from methanol and from chloroform–light petroleum (b. p. 100—120°) giving *iso*-α-amyrenonol (2·1 g.), m. p. 239°, $[\alpha]_D^{18}$ +75° (*c*, 2·1), undepressed in m. p. when mixed with an authentic specimen. Acetylation gave *iso*-α-amyrenonyl acetate, m. p. 285°, $[\alpha]_D^{16}$ +84°, identical with a specimen, m. p. 283—284°, $[\alpha]_D$ +87° (*c*, 2·1), prepared as described by Seymour, Sharples, and Spring (*loc. cit.*).

α-*Amyranonol*-II.—A solution of *iso*-α-amyrenonol-II (0·6 g.) in glacial acetic acid (150 c.c.) was shaken with hydrogen in the presence of platinum (from 0·2 g. of platinum oxide) at room temperature. Absorption of hydrogen was rapid and ceased after one hour; it then corresponded to 1·1 mols. After 6 hours the mixture was filtered and the acetic acid removed under reduced pressure at 40°. The crystalline residue was recrystallised from chloroform–methanol giving α-amyranonol-II (530 mg.) as large hexagonal plates, m. p. 258—260° (sintering at 244°), $[\alpha]_D^{18}$ +58·5° (*c*, 2·0) (Found : C, 81·9; H, 11·6. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%).

α-*Amyranonyl*-II *Acetate*.—(*a*) *iso*-α-Amyrenonyl-II acetate (300 mg.) in glacial acetic acid (250 c.c.) was shaken with hydrogen in the presence of platinum (from 200 mg. of platinum oxide) at 20° for 16 hours; the hydrogen absorption then approximated to 1·2 mols. The product was crystallised from chloroform–ethanol giving α-*amyranonyl*-II *acetate* (280 mg.) as needles, m. p. 216°, $[\alpha]_D^{18}$ +59·5° (*c*, 1·8) (Found : C, 79·5; H, 11·0. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%).

(*b*) Acetylation of α-amyranonol-II (400 mg.) with pyridine and acetic anhydride gave α-amyranonyl-II acetate (380 mg.) as needles (from ethanol), m. p. 217° (sintering at 206°), $[\alpha]_D^{16}$ +59·3° (*c*, 2·2); a mixture with the specimen described under (*a*) showed no depression in m. p.

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