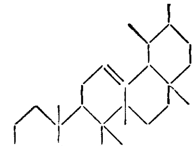
*Triterpenoids. Part XXXVIII.** *Ursa*-9(11) : 13(18)-*dien*-3β-*yl Acetate.*

By J. M. Beaton, J. I. Shaw, F. S. Spring, Robert Stevenson, W. S. Strachan, and J. L. Stewart.

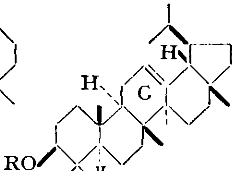
[Reprint Order No. 6218.]

Oxidation of ursa-9(11) : 12-dien-3β-yl acetate (III; R = Ac) with chromic acid gives a mixture from which two homogeneous products have previously been isolated. These have now been identified as 3β-acetoxy-9ξ-hydroxyurs-12-en-11-one (IV) and 13ξ : 18ξ-epoxy-12-oxours-9(11)-en-3β-yl acetate (VII). Reduction of the latter compound with zinc dust gives 12-oxoursa-9(11) : 13(18)-dien-3β-yl acetate (VIII), catalytic hydrogenation of which yields ursa-9(11) : 13(18)-dien-3β-yl acetate (IX).

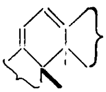
Ursa-9(11) : 12-dien-3β-yl acetate (III) is obtained from α-amyrin acetate (II) † by a number of methods, the most convenient of which is oxidation with *N*-bromosuccinimide (Ruzicka, Jeger, and Redel, *Helv. Chim. Acta*, 1943, **26**, 1235). Oxidation of the homoannular dienyl acetate (III) with chromic acid gives an acetate, $C_{32}H_{50}O_4$, in which the presence of an αβ-unsaturated ketone group and a tertiary hydroxyl group has been established, and which was formulated as (IV) or (V) (Beynon, Sharples, and Spring, *J.*, 1939, 1233). The oxidation of ursa-9(11) : 12-dien-3β-yl acetate was repeated by Ruzicka, Jeger, Redel, and Volli (*Helv. Chim. Acta*, 1945, **28**, 199) who obtained, in addition to the acetate $C_{32}H_{50}O_4$, a second acetate $C_{32}H_{48}O_4$, which they suggested contains the group



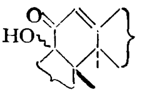
(I)



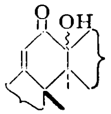
(II)



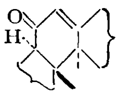
(III)



(IV)



(V)



(VI)

---

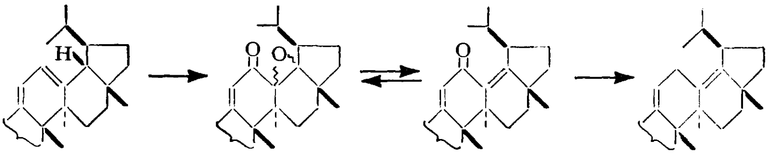
* Part XXXVII, *J.*, 1955, 2131.

† In this paper we use the expression (II; R = H) to represent the constitution and stereochemistry of α-amyrin. The reasons for the adoption of this formula in place of the hitherto accepted formula (I; R = H) are given in the following paper. In all formulæ, R = Ac unless otherwise stated.

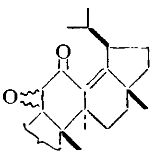
–CO·C⁚C·CO–. In terms of either the generally accepted formula (I) or the modified formula (II) for α-amyrin acetate, it is impossible to formulate such an ene-dione unless molecular rearrangement is assumed during the oxidation of ursa-9(11) : 12-dien-3β-yl acetate.

We have re-examined the products obtained by oxidation of the dienyl acetate (III) with chromic acid. From the mixture we had no difficulty in isolating the two homogeneous acetates, $C_{32}H_{50}O_4$ and $C_{32}H_{48}O_4$. Treatment of the former with zinc dust and acetic acid gave 11-oxours-12-en-3β-yl acetate (VI) in excellent yield, from which it follows that the parent acetate is 3β-acetoxy-9ξ-hydroxyurs-12-en-11-one (IV). Ruzicka *et al.* (*loc. cit.*) found that treatment of the acetate $C_{32}H_{50}O_4$ with strong alkali at 200—210°, followed by acetylation, gave a mixture of two products, one of which was formulated as $C_{32}H_{48}O_3$, *i.e.*, as a dehydration product of the parent acetate, $C_{32}H_{50}O_4$. We noted that the properties of this product {m. p. 285—286°, $[\alpha]_D$ +93°, $\lambda_{max.}$ 2480 Å (log ε 4·05), no colour with tetranitromethane} are very similar to those of 11-oxours-12-en-3β-yl acetate, $C_{32}H_{50}O_3$ (VI) {m. p. 284—285°, $[\alpha]_D$ +98°, $\lambda_{max.}$ 2480 Å (ε 12,000), no colour with tetranitromethane}. Repetition of the experiment showed that this product is indeed 11-oxours-12-en-3β-yl acetate, and its formation is to be ascribed to a reduction, and not to a dehydration, of the parent acetate (IV).

The second acetate, $C_{32}H_{48}O_4$, obtained by oxidation of ursa-9(11) : 12-dien-3β-yl acetate with chromic acid, has now been identified as 13ξ : 18ξ-epoxy-12-oxours-9(11)-en-3β-yl acetate (VII). When reduced in ethanol solution with zinc, it gives 12-oxoursa-9(11) : 13(18)-dien-3β-yl acetate (VIII), characterised by hydrolysis to the corresponding alcohol (VIII; R = H). Surprisingly, the same reduction is achieved by using lithium in liquid ammonia. Conversely, oxidation of 12-oxoursa-9(11) : 13(18)-dien-3β-yl acetate (VIII) with chromic acid gives the epoxide (VII). The acetate (VIII) shows absorption maxima at 2080, 2620, and 2940 Å (ε 7900, 9300, and 7700) and in this respect it is very similar to 12-oxo-oleana-9(11) : 13(18)-dien-3β-yl acetate (Beaton, Johnston, McKean, and Spring, *J.*, 1953, 3660), the absorption spectrum of which shows maxima at 2080, 2600, and 2950 Å (ε 9000, 9250, and 8450). This characteristic absorption spectrum of 12-oxo-oleana-9(11) : 13(18)-dien-3β-yl acetate has been attributed to the geometry of its >C⁚C·CO·C⁚C< chromophore; in contrast, compounds containing the same chromophore in a 6-membered ring show an absorption maximum at *ca.* 2400 Å.



(III) (VII) (VIII) (IX)



(VII*a*)

The oxygen atom removed from the acetate $C_{32}H_{48}O_4$ by treatment with zinc dust is an oxidic function because the infrared absorption spectrum of (VII) includes bands attributable to the acetate group and the αβ-unsaturated carbonyl group, but it does not include bands due to the presence of either a hydroxyl or an isolated ketone group. Of the alternative constitutions (VII) and (VII*a*) for the acetate $C_{32}H_{48}O_4$, which shows an absorption maximum at 2570 Å, we prefer the former, for two reasons. First, the acetate $C_{32}H_{48}O_4$ is recovered unchanged after treatment with hydrochloric–acetic acid; the secondary-tertiary oxide group in (VII*a*) would not, in our opinion, survive this treatment. Secondly, the intensity of its ultraviolet absorption band is not consonant with the presence of a *cisoid* αβ-unsaturated ketone as in (VII*a*).

Catalytic hydrogenolysis of 12-oxoursa-9(11) : 13(18)-dien-3β-yl acetate (VIII) gives the non-conjugated ursa-9(11) : 13(18)-dien-3β-yl acetate (IX) which does not show high-intensity selective absorption above 2200 Å. It does, however, show strong ethylenic absorption between 2100 and 2200 Å and gives a colour with tetranitromethane. The non-conjugated dienyl acetate (IX) was characterised by alkaline hydrolysis to the corresponding alcohol (IX; R = H).

EXPERIMENTAL

Rotations were measured in chloroform and ultraviolet absorption spectra in EtOH solutions. Grade II alumina and light petroleum, b. p. 60—80°, were used for chromatography.

Oxidation of Ursa-9(11) : 12-*dien*-3β-*yl Acetate* (III) *with Chromic Acid.*—A solution of chromium trioxide (8 g.) in water (8 c.c.) and acetic acid (80 c.c.) was added during 20 min. with vigorous stirring to a solution of ursa-9(11) : 12-dienyl acetate (8·0 g.) in glacial acetic acid (300 c.c.). The mixture was refluxed for 2 hr., treated with methanol, concentrated under reduced pressure, and diluted with water. During the ether-extraction of the mixture, a solid remained suspended in the ether layer. This was collected and crystallised from chloroform–methanol to give 3β-acetoxy-9ξ-hydroxyurs-12-en-11-one (IV) as blades (1·3 g.), m. p. 315—317°, $[\alpha]_D$ +55° (*c*, 2·2), $\lambda_{max.}$ 2500 Å (ε 13,500) (Found: C, 77·3; H, 10·3. Calc. for $C_{32}H_{50}O_4$: C, 77·1; H, 10·1%). It does not give a colour with tetranitromethane. Beynon, Sharples, and Spring (*loc. cit.*) give m. p. 312°, $[\alpha]_D$ +61°; Ruzicka, Jeger, Redel, and Volli (*loc. cit.*) give m. p. 316° (high vac.), $[\alpha]_D$ +62°, for this compound.

The ether extract was evaporated and the residue crystallised from chloroform–methanol to give the diol monoacetate (IV) (200 mg.), m. p. and mixed m. p. 315—317°. Concentration of the chloroform–methanol mother-liquors yielded 13ξ : 18ξ-*epoxy*-12-*oxours*-9(11)-*en*-3β-*yl acetate* (VII) which, after recrystallisation from the same solvent, separated as plates (500 mg.), m. p. 269—271°, $[\alpha]_D$ +71° (*c*, 1·1), $\lambda_{max.}$ 2570 Å (ε 13,000) (Found: C, 77·7; H, 9·6. $C_{32}H_{48}O_4$ requires C, 77·4; H, 9·7%). Infrared absorption: Bands at 1250 and 1722 (acetate), 1603 and 1652 cm.$^{-1}$ (αβ-unsaturated ketone), no hydroxyl band. It does not give a colour with tetranitromethane. Ruzicka, Jeger, Redel, and Volli (*loc. cit.*) give m. p. 258°, $[\alpha]_D$ +70°, $\lambda_{max.}$ 2590 Å (log ε 4·1), for a compound $C_{32}H_{48}O_4$ obtained by the same method. The oxide (120 mg.) was recovered unchanged after being heated on the steam-bath for 1 hr. with acetic acid (15 c.c.) and concentrated hydrochloric acid (0·5 c.c.).

Action of Zinc Dust on 3β-*Acetoxy*-9ξ-*hydroxyurs*-12-*en*-11-*one* (IV).—Zinc dust (4·3 g.) (activated by warm 10% ammonium chloride solution) was added to a solution of the diol monoacetate (600 mg.) in glacial acetic acid (50 c.c.) and the mixture refluxed for 1 hr. The filtered solution was worked up in the usual way, and the product crystallised from chloroform–methanol to give 11-oxours-12-en-3β-yl acetate (VI) (570 mg.) as plates, m. p. and mixed m. p. 284—285°, $[\alpha]_D$ +98° (*c*, 1·2).

Action of Methanolic Potassium Hydroxide on 3β-*Acetoxy*-9ξ-*hydroxyurs*-12-*en*-11-*one* (IV).—A solution of the diol monoacetate (3·0 g.) and potassium hydroxide (12 g.) in methanol (120 c.c.) was heated at 175° for 6 hr. The product, isolated through ether, was acetylated by pyridine and acetic anhydride at 100°. The acetylated product crystallised from chloroform–methanol to yield a *substance* (900 mg.) as needles, m. p. 169—171°, $[\alpha]_D$ −60° (*c*, 1·1), ε 9800 at 2080 Å (Found: C, 76·6; H, 10·4. $C_{32}H_{50}O_4$ requires C, 77·1; H, 10·1; $C_{32}H_{52}O_4$ requires C, 76·75; H, 10·5%). It gives a pale yellow colour with tetranitromethane. Concentration of the mother-liquor gave 11-oxours-12-en-3β-yl acetate (VI) as plates (1·4 g.), m. p. and mixed m. p. 285°, $[\alpha]_D$ +98° (*c*, 0·9), $\lambda_{max.}$ 2480 Å (ε 12,250); this does not give a colour with tetranitromethane.

12-*Oxoursa*-9(11) : 13(18)-*dien*-3β-*yl Acetate* (VIII).—(*a*) Zinc dust (10 g.; activated by boiling acetic acid or warm 10% ammonium chloride solution) was added to a solution of 13ξ : 18ξ-epoxy-12-oxours-9(11)-en-3β-yl acetate (VII) (500 mg.) in ethanol (250 c.c.), and the mixture refluxed for 5 hr. Evaporation of the filtered solution gave a yellow solid, which crystallised from methanol as pale yellow plates, m. p. 202—204°, $[\alpha]_D$ −42° (*c*, 1·8). Recrystallisation from the same solvent yielded 12-*oxoursa*-9(11) : 13(18)-*dien*-3β-*yl acetate* as pale yellow plates (430 mg.), m. p. 203—205°, $[\alpha]_D$ −43° (*c*, 2·0), $\lambda_{max.}$ 2080, 2620, and 2940 Å (ε 7900, 9300, and 7700) (Found: C, 79·8; H, 10·0. $C_{32}H_{48}O_3$ requires C, 79·95; H, 10·1%). The m. p. of this compound is variable (±4°) and is a poor criterion of purity. A mixture with 12-oxo-oleana-9(11) : 13(18)-dien-3β-yl acetate (m. p. 205—207°) had m. p. 172—179°. Zinc dust reduction of (VII) in refluxing acetic acid (instead of ethanol) gave a mixture from which, after chromatography, poor yields of ursa-9(11) : 13(18)-dien-3β-yl acetate (IX) (see later) and 12-oxoursa-9(11) : 13(18)-dien-3β-yl acetate (VIII) were isolated.

(*b*) A solution of 13ξ : 18ξ-epoxy-12-oxours-9(11)-en-3β-yl acetate (VII) (500 mg.) in dry ether (15 c.c.) and dry dioxan (10 c.c.) was added with vigorous stirring during 2 min. to a solution of lithium (150 mg.) in liquid ammonia (100 c.c.). After a further 3 min., acetone was added and the ammonia allowed to evaporate. The residue was acetylated by pyridine and acetic anhydride at room temperature for 15 hr., and the acetylated product chromatographed on alumina (15 g.). Benzene–light petroleum (1 : 9) eluted a fraction which crystallised from chloroform–methanol as needles (20 mg.), m. p. 170—172°, $[\alpha]_D$ +156° (*c*, 0·7). It has no selective light absorption above 2000 Å and does not give a colour with tetranitromethane. The fraction eluted by benzene–light petroleum (1 : 1) crystallised from aqueous methanol to give 12-oxoursa-9(11) : 13(18)-dien-3β-yl acetate as pale yellow plates (210 mg.), m. p. and mixed m. p. 203—205°, $[\alpha]_D$ −44° (*c*, 0·8), $\lambda_{max.}$ 2080, 2620, and 2940 Å (ε 9600, 10,000, and 8100).

Treatment of 12-oxoursa-9(11) : 13(18)-dien-3β-yl acetate with lithium and liquid ammonia gave unchanged starting material together with a small quantity of a product, m. p. 170—172°, $[\alpha]_D$ +157° (*c*, 0·9). It was undepressed in m. p. when mixed with the compound of the same m. p. described above.

12-Oxoursa-9(11) : 13(18)-dien-3β-yl acetate was recovered unchanged after treatment with (*a*) sodium borohydride in aqueous methanol at room temperature, and (*b*) glacial acetic acid (8 parts) and concentrated hydrochloric acid (1 part) at 100° for 18 hr.

12-*Oxoursa*-9(11) : 13(18)-*dien*-3β-*ol* (VIII; R = H).—Hydrolysis of the acetate by 3% aqueous-methanolic potassium hydroxide, and crystallisation of the product from aqueous methanol gave 12-*oxoursa*-9(11) : 13(18)-*dien*-3β-*ol* as faintly yellow prismatic needles, m. p. 222—223°, $[\alpha]_D$ −73° (*c*, 0·9), $\lambda_{max.}$ 2080, 2630, and 2950 Å (ε 8050, 9600, and 7900) (Found : C, 82·1; H, 10·6. $C_{30}H_{46}O_2$ requires C, 82·1; H, 10·6%). Reacetylation by pyridine and acetic anhydride at 100° gave the parent acetate as yellow plates (from methanol), m. p. and mixed m. p. 202—203°, $[\alpha]_D$ −43° (*c*, 0·9).

Oxidation of 12-*Oxoursa*-9(11) : 13(18)-*dien*-3β-*yl Acetate* (VIII) *with Chromic Acid*.—A solution of chromium trioxide (18·8 mg.) in glacial acetic acid (4·0 c.c.) was added to a solution of 12-oxoursa-9(11) : 13(18)-dien-3β-yl acetate (75 mg.) in acetic acid (15 c.c.), and the mixture set aside at room temperature for 18 hr., then heated on the steam-bath for 1 hr. The mixture was worked up in the usual way and the product chromatographed on alumina (3 g.). Elution with light petroleum and benzene yielded amorphous fractions. Methanol–benzene (1 : 9) eluted a solid which crystallised from methanol to give 13ξ : 18ξ-epoxy-12-oxours-9(11)-en-3β-yl acetate (VII) (35 mg.) as plates, m. p. and mixed m. p. 266—269°, $[\alpha]_D$ +69·5° (*c*, 0·7), $\lambda_{max.}$ 2580 Å (ε 11,400).

Hydrogenolysis of 12-*Oxoursa*-9(11) : 13(18)-*dien*-3β-*yl Acetate* (VIII).—A solution of 12-oxoursa-9(11) : 13(18)-dien-3β-yl acetate (300 mg.) in glacial acetic acid was shaken with platinum (from 200 mg. of PtO_2) in hydrogen for 4½ hr. After removal of the catalyst and solvent, the product was crystallised from chloroform–methanol to give *ursa*-9(11) : 13(18)-*dien*-3β-*yl acetate* (IX) as plates (260 mg.), m. p. 193—194°, $[\alpha]_D$ +72° (*c*, 1·8), ε 9150 at 2140 Å (Found : C, 82·7; H, 10·6. $C_{32}H_{50}O_2$ requires C, 82·3; H, 10·8%). It gives an orange colour with tetranitromethane. A mixture with oleana-9(11) : 13(18)-dienyl acetate, m. p. 196—197°, had m. p. 184—188°.

Ursa-9(11) : 13(18)-*dien*-3β-*ol* (IX; R = H).—Hydrolysis of the acetate in the usual way by 3% aqueous-methanolic potassium hydroxide and recrystallisation of the product successively from methanol, light petroleum (b. p. 60—80°), and methanol gave *ursa*-9(11) : 13(18)-*dien*-3β-*ol* as blades, m. p. 189—190°, $[\alpha]_D$ +61° (*c*, 0·9) (Found : C, 84·3; H, 11·7. $C_{30}H_{48}O$ requires C, 84·8; H, 11·4%). It gives an orange colour with tetranitromethane. Reacetylation gave ursa-9(11) : 13(18)-dien-3β-yl acetate as plates (from chloroform–methanol), m. p. and mixed m. p. 193—194°, $[\alpha]_D$ +73° (*c*, 1·8).

We thank the Colonial Products Research Council for the award of a Scholarship (to J. L. S.), the Department of Scientific and Industrial Research for a Maintenance Award (to J. I. S.), and the Carnegie Trust for the Universities of Scotland for a Scholarship (to J. M. B.). The microanalyses were made by Dr. A. C. Syme and Mr. Wm. McCorkindale, and the infrared absorption spectra were examined by Dr. G. Eglinton, to whom we express our best thanks; we are also glad to acknowledge assistance from Mr. J. R. Gorrie.

THE ROYAL TECHNICAL COLLEGE, GLASGOW. [*Received, March* 10*th*, 1955.]