238. *The Photoisomerisation of 3β-Acetoxylanosta-5,8-dien-7-one.*

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The ring B dienone, 3β-acetoxylanosta-5,8-dien-7-one, has been photoisomerised to an umbellulone. Two separate series of degradational experiments have excluded a number of possible formulæ and have provided strong support for formula (IV; R = Ac) for the photoisomer. Rotatory dispersion evidence for the stereochemistry of (IV; R = Ac) has been obtained.

In 1954 Dr. E. L. Wheeler, working at Birkbeck College in collaboration with one of us (D H. R. B.), noted that 3β-acetoxylanosta-5,8-dien-7-one was easily converted by ultraviolet light into an isomer characterised by its spectral properties as an umbellulone. In the meantime the photoisomerisation of santonin (II) to lumisantonin (III) has been thoroughly studied [1,2] and the stereochemical course of the reaction elucidated.[3] It has also been shown that steroidal 1,4-dien-3-ones rearrange easily on irradiation,[4,5] although the structural change induced is quite different from that implied in the sequence (II ⟶ III). The attachment of a 4-methyl group so that the chromophore reverts to that present in santonin (II) leads, however, to a santonin-type rearrangement.[6] We consider that each case of photoisomerisation of a cyclohexadienone has to be considered on its own merits. Thus, if the change (II ⟶ III) is taken as general, the constitution (IV; R = Ac) can be written for the photoisomer of the dienone (I). The mere formation of an umbellulone, however, does not exclude formulæ such as (V) and (VI), or even (IX), as well as more complex rearrangements as yet unexemplified.[5] In the event, we were able to show that (IV; R = Ac) is indeed the correct representation of the photoisomer and for clarity we shall use this formula in the sequel.

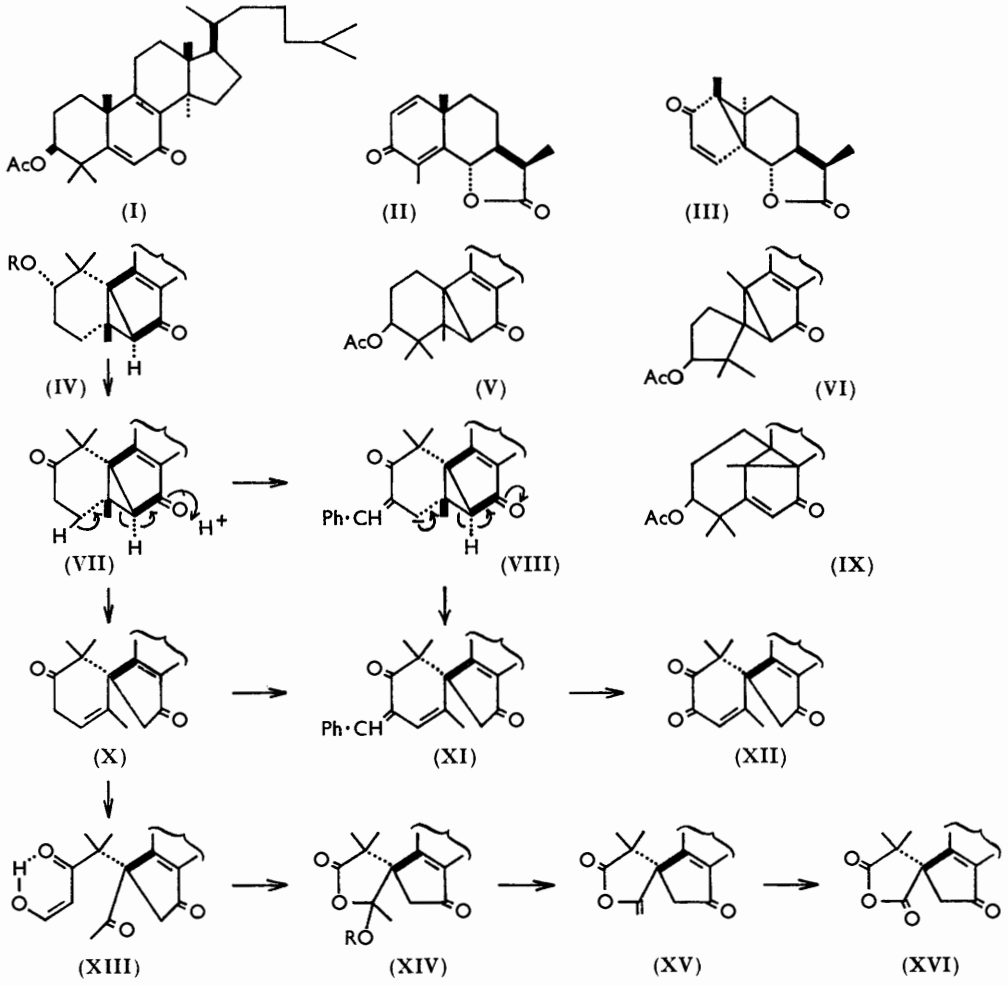
The photoisomer gave the corresponding alcohol (IV; R = H) on mild alkaline hydrolysis. Acetylation of the alcohol gave back the starting acetate, and oxidation by chromic acid furnished the derived ketone (VII), further characterised as its dioxime and by condensation with benzaldehyde to afford the benzylidene derivative (VIII). Under the influence of hydrogen chloride in chloroform solution the umbellulone (VII) rearranged to an isomer (X), characterised as its benzylidene derivative (XI). Although the acid-catalysed rearrangements of umbellulones can, in principle, be very complex, the relationship between (VII) and (X) was shown to be as simple as indicated because the benzylidene derivative (XI) could also be derived from (VIII) by rearrangement with alkali (VIII; see arrows).

The βγ-unsaturated nature of the diketone (X), shown by the ultraviolet absorption spectrum of its derivative (XI) and by ozonolysis of the latter to give the yellow α-diketone (XII) with a characteristic spectrum, was thoroughly confirmed by stepwise degradation. Reaction of the diketone (X) with osmium tetroxide and cleavage of the product with lead tetra-acetate furnished the hydroxymethylene-triketone (XIII), the functional groups of which were indicated by its spectral properties. Oxidation of this triketone (XIII)

[1] Barton, de Mayo, and Shafiq, *Proc. Chem. Soc.*, 1957, 205; *J.*, 1958, 140; see also Cocker, Crowley, Edward, McMurry, and Stuart, *J.*, 1957, 3416.
[2] Arigoni, Bosshard, Bruderer, Büchi, Jeger, and Krebaum, *Helv. Chim. Acta*, 1957, **40**, 1732.
[3] Barton and Gilham, *Proc. Chem. Soc.*, 1959, 391; *J.*, 1960, 4596.
[4] Barton and Taylor, *J. Amer. Chem. Soc.*, 1958, **80**, 244; *J.*, 1958, 2500.
[5] Dutler, Bosshard, and Jeger, *Helv. Chim. Acta*, 1957, **40**, 494.
[6] Weinberg, Utzinger, Arigoni, and Jeger, *Helv. Chim. Acta*, 1960, **43**, 236.

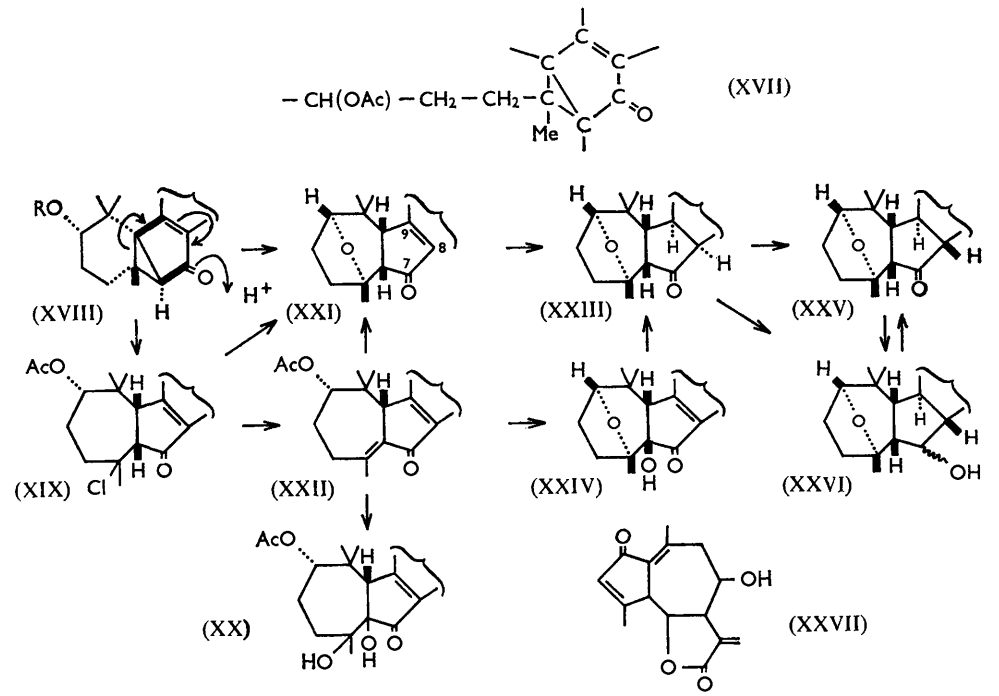
with chromic acid gave the pseudo-acid (XIV; R = H), which could be acetylated to the derivative (XIV; R = Ac). The latter had a characteristic infrared spectrum indicating a γ-lactone group and an acetoxyl residue related to each other as in (XIV; R = Ac). Pyrolysis of this acetate (XIV; R = Ac) proceeded smoothly to give acetic acid and the methylene-lactone (XV). Ozonolysis of the latter afforded formaldehyde and the substituted succinic anhydride (XVI). The last two compounds had infrared spectra which were fully in accord with the proposed structures. All the compounds (X)—(XVI) showed ultraviolet and infrared absorption in agreement with the presence of a fully substituted cyclopentenone grouping. This series of experiments shows that the photoisomer (IV; R = Ac) contains the sequence indicated in part formulation (XVII). Formulæ (V), (VI), and (IX) are, therefore, excluded.

The action of hydrogen chloride in chloroform upon the acetate (IV; R = Ac) took a different course (XVIII; R = Ac; see arrows) from that observed with the ketone (VII) (see



above). There resulted a hydrochloride which is best formulated as (XIX) on the basis of the following evidence. It contained a cyclopentenone chromophore and on attempted alkaline hydrolysis furnished an oxide (XXI). The latter retained the same chromophore and, from its nuclear magnetic resonance spectra, had one hydrogen attached to carbon bearing oxygen and no vinyl hydrogen atoms. This oxide (XXI) was also obtained when the

alcohol (XVIII; R = H; see arrows) was treated with hydrogen chloride in the same way. Heating the hydrochloride (XIX) in acetic acid gave a dienone (XXII) with an unusual absorption spectrum [$\lambda_{max.}$ 271 mμ (ε 12,600)]. This is similar to the spectrum of lactucin (XXVII) [$\lambda_{max.}$ 257 mμ (ε 14,000)] where a comparable chromophore is known to be present.[7] The dienone had no vinyl hydrogen atom (nuclear magnetic resonance spectrum) but had one hydrogen atom attached to carbon bearing oxygen and one methyl group attached to vinylic carbon in *cisoid* conformation (τ = 7·72). These results are fully in accord with formula (XXII). On mild treatment with alkali the dienone also gave the oxide (XXI). A comparable bridging of a seven-membered ring by hydroxyl addition to the β-position of an enone system has already been observed in the chemistry of geigerin.[8] The hydrochloride (XIX) was not reduced by activated zinc or by chromous chloride, results which are in accord with halogen β- rather than α- to the ketone group. Reduction of the oxide (XXI) with lithium in ammonia gave a cyclopentanone (XXIII). Again the retention of the oxide function shows[9] that it must be β-, not α-, with respect to the ketone group. This cyclopentanone (XXIII) had one (or both) of its α-asymmetric centres in an unstable configuration for treatment with base, or with refluxing acetic

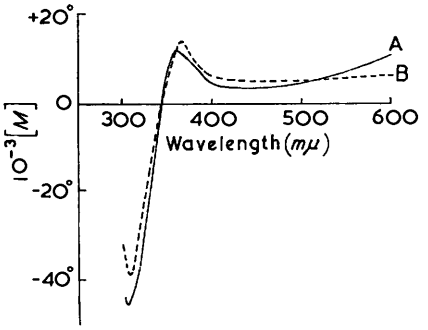


anhydride–sodium acetate, gave a more stable isomer (XXV). Reduction of either isomer (XXIII) or (XXV) with sodium and alcohol gave the same derivative (XXVI) from which the isomer (XXV) could be obtained by oxidation with chromic acid. The dienone (XXII) with osmium tetroxide gave the glycol (XX) which, in agreement with its formulation as ditertiary, resisted acetylation. Reaction with per-acid gave the hydroxy-oxide (XXIV) which was resistant to acetylation and oxidation, and which on reduction with lithium and ammonia furnished the keto-oxide (XXIII) already described above. This experiment confirms the view that the tertiary hydroxyl group of compound (XXIV) is

[7] Barton and Narayanan, *J.*, 1958, 963.
[8] Barton and Levisalles, *J.*, 1958, 4518.
[9] Cf. Chapman, Elks, Phillipps, and Wyman, *J.*, 1956, 4344.

α- with respect to the ketone group and that the ethereal ring is attached β- as already formulated.

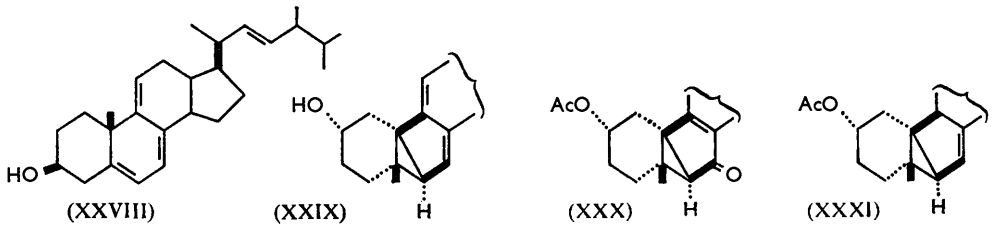
The stereochemistry [3] of the santonin ⟶ lumisantonin rearrangement represents an inversion of configuration at the angular 10-methyl group. If the same type of inversion is assumed for the rearrangement of 3β-acetoxylanosta-5,8-dien-7-one, then the stereochemistry already given in (IV; R = Ac) would follow. Now, recently the stereochemistry of the dehydroergosterol (XXVIII) ⟶ photodehydroergosterol [10] (XXIX) rearrangement has been represented as in these formulæ.[11] If, therefore, photodehydroergosterol could be converted into the umbellulone (XXX) a good model for the rotatory dispersion curve [12] expected for (IV; R = Ac) would be available. To this end tetrahydrophotodehydroergosterol acetate (XXXI) was oxidised with chromium trioxide in pyridine to furnish the desired umbellulone (XXX). This oxidation is exactly comparable with prior example.[10] The rotatory dispersion curves in methanol solution of compounds (XXX)



Optical rotatory dispersion of (A) *compound* (XXX) *and* (B) *the photo-product* (IV; R = Ac).

and (IV; R = Ac), kindly determined by Professor W. Klyne (Westfield College), were almost superimposable (see Figure). This is strong support for identical configurations as already represented in (XXX) and (IV; R = Ac).

In formulæ (XIX)—(XXVI) we have assigned configurations to a number of asymmetric centres. The assignments are intended to illustrate that the formulæ proposed will explain the chemical facts configurationally as well as constitutionally. They do not represent rigidly established stereochemistry.



The acetoxyl group of compounds (XIX), (XX), and (XXII) is of defined configuration. In the reaction of (XXII) with per-acid it is reasonable to accept that the ethereal oxygen bridge is formed *trans* to the hydroxyl group. Furthermore, models show that this easy bridging reaction would not be expected unless the ring fusion of the cycloheptane and

[10] Barton and Kende, *J.*, 1958, 688.
[11] Barton, Bernasconi, and Klein, *J.*, 1960, 511.
[12] Djerassi, "Optical Rotatory Dispersion," McGraw-Hill Book Co. Inc., New York, 1960; Klyne in "Advances in Organic Chemistry," Vol. I, p. 239, Interscience Publ. Inc., New York, 1960 (eds. Raphael, Taylor, and Wynberg).

cyclopentenone rings in (XXIV) were *cis*, as written into the formula. The stereochemistry of (XIX) and (XXI) is given with this assignment in mind, and with the supposition that both compounds are formed under equilibrating conditions with the *cis*-fusion favoured. It is true that in the perhydroazulene series the *trans*-fusion of the rings predominates at equilibrium,[13] but when three trigonal atoms are introduced into the five-membered ring the reverse is surely to be expected. Especially is this so if there is also an oxygen bridge across the seven-membered ring as in (XXI). The additional asymmetric configurations at positions 8 and 9 in (XXIII), (XXV), and (XXVI) represent our estimate from models of the more stable configuration at position 9 in all three cases and our interpretation of the possible relative configurations at position 8.

In the Experimental section there is recorded the preparation of several toluene-*p*-sulphonates and methanesulphonates which were employed in abortive degradational experiments.

In a letter dated June 24th, 1960, Professor K. Tsuda of the Institute of Applied Microbiology of the University of Tokyo has kindly informed us that he and his colleagues have also prepared the photoisomer of 3β-acetoxylanosta-5,8-dien-7-one and have characterised it by conversion into the corresponding ketone.

Experimental

Rotations were determined for $CHCl_3$ solutions in a 4 dm. tube except where denoted ($l = 0{\cdot}5$). Ultraviolet absorption spectra were taken for EtOH solutions on the Unicam S.P. 500 spectrophotometer. Infrared spectra were taken for Nujol mulls. Alumina for chromatography was acid-washed, neutralised, reactivated, and then standardised according to Brockmann's scale. Solvents for chromatography were dried and redistilled. Light petroleum refers to a fraction of b. p. 40—50° unless stated otherwise. Kiliani's chromic acid mixture was prepared from sodium dichromate (60 g.) in water (270 ml.) to which concentrated sulphuric acid (80 g.) was added.

Nuclear magnetic resonance spectra were kindly determined and interpreted by Drs. L. M. Jackman and J. W. Lown to whom we express our best thanks. The spectra were taken for $CDCl_3$ solution on a Varian Associates spectrometer model V 4311 at a fixed frequency of 56·445 Mc./sec. Line positions were measured by the conventional side-band technique with a Muirhead Decade oscillator (Model D 695-A), tetramethylsilane being added as internal standard. For general information on the definition of τ and other symbols see ref. 14.

3β-*Acetoxylanosta*-5,8-*dien*-7-*one*.—3β-Acetoxylanost-8-en-7-one [15] (67 g.) in acetic acid (1·25 l.) was treated slowly with bromine (7·9 ml., 1·1 mol.) in acetic acid (250 ml.) at room temperature. The reaction was initiated by the addition of a 50 w/v solution (1·0 ml.) of hydrogen bromide in acetic acid. The bromine was rapidly consumed. Nitrogen was passed through the solution at room temperature for 6 hr. to remove the excess of hydrogen bromide, and then the solution was poured into water, 5% aqueous sodium sulphite solution (500 ml.) was added, and the solid was filtered off. The precipitate was taken up into benzene and washed with water (2 × 200 ml.), 2N-sodium carbonate (200 ml.), and then water again. The benzene was removed *in vacuo*. Crystallisation from chloroform–methanol gave 3β-acetoxylanosta-5,8-dien-7-one (53·5 g.), m. p. 186—188°, $[\alpha]_D$ −13° (*c* 1·05). Barton and Thomas [16] record m. p. 186—188°, $[\alpha]_D$ −14°.

Irradiation of 3β-*Acetoxylanosta*-5,8-*dien*-7-*one* (with Dr. E. L. Wheeler).—The dienone (10 g.) in absolute ethanol (500 ml.) was irradiated in a Pyrex flask at reflux under oxygen-free nitrogen by a 125 w mercury lamp for 45 min. ($[\alpha]_D$ −13° ⟶ $[\alpha]_D$ +40° to +50°). Longer irradiation produced larger rotational changes but lower net yields. Removal of the solvent *in vacuo* and crystallisation from methanol (350 ml.) furnished unchanged dienone (4—6 g.). The filtrate was concentrated to 300 ml. and seeded with the desired product. Leaving it for 2 days (10 days without seeding) gave the *umbellulone* (IV; R = Ac) (1·1 g.) as plates,

[13] Ayres and Raphael, *J.*, 1958, 1779.
[14] Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, London, 1959.
[15] Birchenough and McGhie, *J.*, 1950, 1249.
[16] Barton and Thomas, *J.*, 1953, 1842.

m. p. 146—148°, resolidifies, remelts at 158—159°, $[\alpha]_D$ +189° (*c* 1·59; *l* = 0·5), $\lambda_{max.}$ 205, 233, and 280 mμ (ε 7500, 6400, and 3500 respectively), $\nu_{max.}$ 1740 (OAc), 1687 and 1612 (umbellulone) (Found: C, 79·45; H, 10·5. $C_{32}H_{50}O_3$ requires C, 79·6; H, 10·45%). This acetate (500 mg.) in methanol (40 ml.) was treated with potassium hydroxide (500 mg.) in methanol (10 ml.) under reflux for 2 hr. Addition of acetic acid (1 ml.), removal of the solvent *in vacuo*, and working up in the usual way gave, on crystallisation from aqueous methanol, the desired *alcohol* (IV; R = H) as needles (442 mg.), m. p. 163—165°, $[\alpha]_D$ +162° (*c* 0·73, $\lambda_{max.}$ 236 and 279 mμ (ε 6100 and 3100 respectively), $\nu_{max.}$ 3559 (OH), 1663, and 1609 (umbellulone) cm.$^{-1}$ (Found: C, 81·9; H, 11·0. $C_{30}H_{48}O_2$ requires C, 81·75; H, 11·0%). Treatment with pyridine–acetic anhydride overnight at room temperature gave back the starting acetate (m. p. and mixed m. p.).

This alcohol (5·6 g.) in benzene–acetic acid (4 : 1; 500 ml.) was stirred for 1 hr. at room temperature with Kiliani chromic acid mixture (55 ml.). Destruction of the excess of oxidant with 2% sodium hydrogen sulphite solution and working up in the usual way gave the desired *ketone* (VII) in nearly quantitative yield. Recrystallised from chloroform–methanol as needles, this had m. p. 204—206°, $[\alpha]_D$ +152° (*c* 0·88), $\lambda_{max.}$ 227 and 279 mμ (ε 6500 and 3200 respectively), $\nu_{max.}$ 1703 (cyclohexanone), 1684 and 1620 (umbellulone) cm.$^{-1}$ (Found: C, 82·2; H, 10·9. $C_{30}H_{46}O_2$ requires C, 82·1; H, 10·85%). This diketone (500 mg.) was treated with hydroxylamine hydrochloride (500 mg.) in pyridine (20 ml.) at 100° for 3 hr. Working up in the usual way and crystallisation from benzene furnished the *dioxime* as cubes (507 mg.), m. p. 265—266° (decomp.), $[\alpha]_D$ +200° (*c* 0·51), $\lambda_{max.}$ 265 mμ (ε 9000), $\nu_{max.}$ 3257 and 3101 (OH) and at 1634 and 1597 (C=N) cm.$^{-1}$ (Found: C, 76·75; H, 10·65. $C_{30}H_{48}N_2O_2$ requires C, 76·85; H, 10·3%).

Condensation of the Ketone (VII) *with Benzaldehyde.*—The ketone (VII) (300 mg.) in 0·1N-ethanolic potassium hydroxide (30 ml.) was treated with benzaldehyde (750 mg.; redistilled) in the dark at room temperature for 16 hr. under oxygen-free nitrogen. The desired *benzylidene ketone* (VIII) crystallised out (264 mg.) during this time. Working up the mother-liquors in the usual way gave additional material (40 mg.). Recrystallisation of the combined product from ethyl acetate–methanol gave the compound as needles (280 mg.), m. p. 196—197°, $[\alpha]_D$ +77° (*c* 0·81), $\lambda_{max.}$ 224 and 290 mμ (ε 13,700 and 22,800 respectively) (Found: C, 84·35; H, 9·6. $C_{37}H_{50}O_2$ requires C, 84·35; H, 9·55%). The ultraviolet addition curve of 2-benzylidenelanost-8-enone [17] with the ketone (VII) showed $\lambda_{max.}$ 225 and 290 mμ (ε 14,500 and 20,600 respectively).

Treatment of the Ketone (VII) *with Hydrogen Chloride.*—The ketone (VII) (2 g.) in chloroform (200 ml.), saturated with dry hydrogen chloride, was left at room temperature in the dark for 2 days [ultraviolet control; until constant $\lambda_{max.}$ 245 mμ (ε 12,000)]. More chloroform (200 ml.) was added and the solution worked up in the usual way. The product was taken up in acetic acid (200 ml.), heated under reflux for 10 min., and then extracted with benzene. Working up in the usual way gave, after crystallisation from methanol, the isomerised *ketone* (X) (1·55 g.) as plates, m. p. 141—143°, $[\alpha]_D$ +202° (*c* 0·25), $\lambda_{max.}$ 245 mμ (ε 13,500), $\nu_{max.}$ 1706 (cyclohexanone), 1684 (sh), and 1623 (cyclopentenone) cm.$^{-1}$ (Found: C, 82·35; H, 10·45. $C_{30}H_{46}O_2$ requires C, 82·1; H, 10·55%).

This ketone (1·5 g.) in 0·1N-ethanolic potassium hydroxide (100 ml.) was treated with benzaldehyde (3·6 g.; redistilled) in the dark under oxygen-free nitrogen at room temperature for 16 hr. Dilution with aqueous 2N-sodium hydrogen sulphite, extraction into ether, and working up in the usual way gave the *benzylidene derivative* (XI). This crystallised from ethyl acetate–methanol as needles (1·41 g.), m. p. 145—147°, $[\alpha]_D$ +245° (*c* 1·02), $\lambda_{max.}$ 234 and 323 mμ (ε 18,000 and 18,500 respectively) (Found: C, 84·35; H, 9·6. $C_{37}H_{50}O_2$ requires C, 84·6; H, 9·55%).

This benzylidene derivative was also obtained by the following two routes. (*a*) The benzylidene ketone (VIII) (20 mg.) in chloroform (10 ml.) was treated with dry hydrogen chloride as above, but the refluxing with acetic acid was omitted. This furnished the isomerised benzylidene ketone (XI) (15 mg.), identified by m. p. and mixed m. p. (*b*) The benzylidene ketone (VIII) (150 mg.) in 2·5% ethanolic potassium hydroxide (25 ml.) was heated under oxygen-free nitrogen under reflux for 15 min. Dilution with aqueous N-hydrochloric acid, extraction with ether, and working up in the usual way furnished a gum (150 mg.) which was chromatographed over alumina (Grade V; 6 g.). Elution with benzene–light petroleum (1 : 9 and 1 : 4) and crystallisation with methanol gave the rearranged benzylidene ketone

[17] Barton, Head, and May, *J.*, 1957, 935.

(XI) (70 mg.), identified by m. p., mixed m. p., rotation {$[\alpha]_D$ +243° (*c* 0·20)}, and ultraviolet absorption.

Ozonolysis of the Benzylidene Ketone (XI).—The benzylidene ketone (XI) (1·0 g.) in dry ethyl acetate (150 ml.) was treated at −70° with ozone until there was a slight excess of oxidant [$\lambda_{max.}$ 324 mμ (ε 18,000 ⟶ <500)]. A stream of oxygen-free nitrogen was passed through the solution whilst it was allowed to warm to room temperature. Addition of water, removal of the ethyl acetate *in vacuo*, extraction with ether, and working up in the usual way gave, after several crystallisations from methanol, the yellow diketone (XII) as needles, m. p. 201—204°, $[\alpha]_D$ +436° (*c* 0·35), $\lambda_{max.}$ 242 mμ (ε 13,100), $\nu_{max.}$ 1761 and 1723 (α-diketone), 1692 (cyclopentenone), 1669 and 1620 (conjugated C=C) cm.$^{-1}$ (Found: C, 79·45; H, 9·65. $C_{30}H_{44}O_3$ requires C, 79·6; H, 9·8%).

Degradation of the Diketone (X).—The diketone (X) (5 g.) in pyridine (10 ml.) was treated with osmium tetroxide (4 g.) in pyridine (10 ml.) at room temperature in the dark for 4 days. The mixture was diluted with ether (500 ml.) and saturated with hydrogen sulphide (1 hr.). The black precipitate was removed and the ethereal solution worked up in the usual way. A portion of the crude product (96 mg.) was treated with lead tetra-acetate (200 mg.) in acetic acid (5 ml.). After 1 hr. (one "oxygen" uptake) ethylene glycol (1 ml.) was added, the mixture diluted with water and extracted with ether, and the extract worked up in the usual way. Crystallisation of the product from aqueous methanol gave the *hydroxymethylene compound* (XIII) (38 mg.) as needles, m. p. 178—180°, $[\alpha]_D$ +28° (*c* 0·27), $\lambda_{max.}$ 266 mμ (ε 18,000), $\lambda_{max.}$ (in 0·1% ethanolic KOH) 252 and 308 mμ (ε both 8600), $\nu_{max.}$ 3215 (OH), 1695 (Me ketone and cyclopentenone), 1647 (hydrogen-bonded ketone) and 1613 (C=C) cm.$^{-1}$ (Found: C, 76·6; H, 9·9. $C_{30}H_{46}O_4$ requires C, 76·55; H, 9·85%). The compound gave an immediate ferric reaction.

This hydroxymethylene compound (XIII) (256 mg.) in acetic acid (15 ml.) containing chromium trioxide (300 mg.) was kept for 1 hr. at room temperature (4 "oxygen" uptake). Dilution with 1% sodium hydrogen sulphite solution, extraction with ether, and working up in the usual way gave an acidic oil (145 mg.). Crystallised from aqueous methanol this furnished the *pseudo-acid* (XIV; R = H) (78 mg.), m. p. 193—195°, $[\alpha]_D$ +39° (*c* 0·297), $\lambda_{max.}$ 242 mμ (ε 10,000), $\nu_{max.}$ 3300 (OH), 1733 (ψ-acid C=O), and 1698 and 1623 (cyclopentenone) cm.$^{-1}$ (Found: C, 75·4; 75·65; H, 10·15, 10·15%; equiv., 480. $C_{28}H_{44}O_4$ requires C, 75·65; H, 9·95%; equiv., 444). Treatment with pyridine–acetic anhydride at room temperature for 3 days furnished the pseudo-acid *acetate* (XIV; R = Ac). Recrystallised from light petroleum (b. p. 60—80°), this formed needles, m. p. 199—200°, $[\alpha]_D$ +31° (*c* 0·338), $\lambda_{max.}$ 238—240 mμ (ε 12,000), $\nu_{max.}$ 1786 (exalted γ-lactone), 1770 (acetate of pseudo-acid), 1709 and 1620 (cyclopentenone) cm.$^{-1}$ (Found: C, 74·65; H, 9·65. $C_{30}H_{46}O_5$ requires C, 74·05; H, 9·55%).

This acetate (213 mg.) was heated at 280—300° for 5 min. under a stream of oxygen-free nitrogen. The nitrogen stream was led through 0·1N-aqueous sodium hydroxide which, on titration, showed the formation of 0·81 equiv. of acid. After titration the water was removed *in vacuo* and the residue (28·4 mg.) characterised as sodium acetate by its infrared spectrum and by conversion into *p*-bromophenacyl acetate (m. p. and mixed m. p.). The residue from the pyrolysis was chromatographed over alumina (Grade V; 10 g.). Elution with benzene–light petroleum mixtures followed by crystallisation from aqueous methanol afforded the *methylene lactone* (XV) as needles (88 mg.), m. p. 108—109°, $[\alpha]_D$ +140° (*c* 0·489), $\lambda_{max.}$ 242 mμ (ε 9600), $\nu_{max.}$ 1812 (exalted γ-lactone), 1707 and 1631 (cyclopentenone), and 1667 (vinyl ether) cm.$^{-1}$ (Found: C, 78·8; H, 9·9. $C_{28}H_{42}O_3$ requires C, 78·8; H, 9·9%).

This methylene lactone (XV) (63 mg.) in dry ethyl acetate (15 ml.) was ozonised at −70° until there was a slight excess of ozone. Addition of water, removal of the solvent *in vacuo*, and extraction into ether furnished, after three crystallisations from light petroleum, the *anhydride* (XVI), m. p. 132—132·5°, $[\alpha]_D$ +154° (*c* 0·153), $\lambda_{max.}$ 246 mμ (ε 9000), $\nu_{max.}$ 1845 and 1776 (succinic anhydride), 1709 and 1629 (cyclopentenone) cm.$^{-1}$ (Found: C, 75·5; H, 9·4. $C_{27}H_{40}O_4$ requires C, 75·65; H, 9·4%).

In a second ozonolysis of the methylene lactone (70 mg.) the product was steam-distilled into aqueous dimedone to give the formaldehyde derivative (25 mg.), identified by m. p., mixed m. p., and crystal form.

Action of Hydrogen Chloride on the Acetate (IV; R = Ac).—The acetate (IV; R = Ac) (3 g.) in chloroform (300 ml.) was saturated with dry hydrogen chloride and left in the dark at room temperature for 20 hr. Addition of more chloroform (500 ml.), working up in the

usual way, and crystallisation from methanol gave the *chloride* (XIX) (1·87 g.) as needles, m. p. 179—181°, $[\alpha]_D$ +3° (*c* 4·15), $\lambda_{max.}$ 246 mμ (ε 11,000), $\nu_{max.}$ 1728 (OAc), 1686 and 1622 (cyclopentenone) cm.$^{-1}$ (Found: C, 74·05; H, 9·75; Cl, 6·9. $C_{32}H_{51}ClO_3$ requires C, 74·0; H, 9·9; Cl, 6·85%). This chloride was recovered unchanged (m. p. and mixed m. p.) after attempted reduction with excess of chromous chloride and also with activated zinc dust in benzene–methanol under reflux.

The chloride (80 mg.) in ethanol (7 ml.) and benzene (3 ml.) was treated with potassium hydroxide (100 mg.) in ethanol (2·5 ml.) at room temperature in the dark for 16 hr. under oxygen-free nitrogen. Dilution with 2N-aqueous hydrochloric acid, extraction with ether, and working up in the usual way furnished the *oxide* (XXI). Recrystallised from methanol as needles, this had m. p. 177—178°, $[\alpha]_D$ 94° (*c* 1·64; *l* = 0·5), $\lambda_{max.}$ 245 mμ (ε 10,000), $\nu_{max.}$ 1682 and 1628 (cyclopentenone) (Found: C, 81·6; H, 10·8. $C_{30}H_{48}O_2$ requires C, 81·75; H, 11·0%). This oxide was recovered unchanged after treatment with hydrogen chloride in chloroform, with pyridine–acetic anhydride, and with Kiliani chromic acid mixture at room temperature. It also resisted reduction with chromous chloride, with zinc dust in refluxing acetic acid, or with lithium amalgam, acetylation with sodium acetate–acetic anhydride under reflux, and treatment with boiling methanolic potassium hydroxide.

The oxide was also obtained in the following manner. The photo-isomer alcohol (IV; R = H) (28 mg.) in chloroform (5 ml.) was saturated with dry hydrogen chloride and kept at room temperature for 2 hr. (ultraviolet control). Working up in the usual way and crystallisation from methanol gave the oxide (XXI) (15 mg.), identified by m. p., mixed m. p. and rotation {$[\alpha]_D$ +89° (*c* 1·10; *l* = 0·5)}.

Reduction Experiments with the Oxide (XXI).—The oxide (XXI) (1·0 g.) in dry tetrahydrofuran (150 ml.) was added during 10 min. to dry, redistilled ammonia (250 ml.) containing lithium (100 mg.) at the b. p. of liquid ammonia. Further lithium was added to maintain a slight excess. The mixture was stirred for a further 10 min., ammonium chloride (5 g.) was added, and the solution allowed to warm to room temperature. Ether-extraction and working up in the usual way gave the *dihydro-oxide* (XXIII). This crystallised from methanol as needles (250 mg.), m. p. 202—204°, $[\alpha]_D$ +121° (*c* 0·46), $\nu_{max.}$ 1728 (cyclopentanone) cm.$^{-1}$ (Found: C, 81·45; H, 11·4. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%). This dihydro-oxide (XXIII) (50 mg.) in ethanol (10 ml.) was further reduced by heating it under reflux with addition of sodium (excess). Dilution with water and working up in the usual way gave, after crystallisation from aqueous methanol, the *alcohol* (XXVI) as needles (25 mg.), m. p. 206—208°, $[\alpha]_D$ +60° (*c* 0·092), depressed in m. p. on admixture with starting material (Found: C, 81·6; H, 12·15. $C_{30}H_{52}O_2$ requires C, 81·0; H, 11·8%).

The dihydro-oxide (XXIII) (19·4 mg.) was refluxed with 5% methanolic potassium hydroxide (10 ml.) for 1 hr. under oxygen-free nitrogen. Dilution with 2N-aqueous hydrochloric acid and working up in the usual way gave the epi-*dihydro-oxide* (XXV) as needles (12 mg.) (from aqueous methanol), m. p. 78—80°. If kept slightly above the m. p. this solidified and then had m. p. 109—110°. The same compound was obtained when the dihydro-oxide (XXIII) (35 mg.) in acetic anhydride (2·5 ml.) and anhydrous sodium acetate (100 mg.) were heated under reflux for 1 hr. After crystallisation it had either m. p. 109—110° (blades) or m. p. 78—80° and then 109—110° (see above) (needles), $[\alpha]_D$ +168° (*c* 0·158) (Found: C, 81·85; H, 11·8. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%). Reduction of this *epi*-dihydro-oxide (XXV) (10 mg.) with sodium and ethanol as above gave the alcohol (XXVI) reported above (m. p. and mixed m. p.). Oxidation of this alcohol (11 mg.) in benzene–acetic acid (4 : 1; 5 ml.) with Kiliani chromic acid mixture (0·1 ml.) at room temperature with shaking for 15 min. gave back the *epi*-dihydro-oxide (XXV) in the two characteristic crystalline forms (m. p. and mixed m. p.).

Conversion of the Chloride (XIX) *into the Dienone* (XXII).—The chloride (XIX) (1·25 g.) in acetic acid (100 ml.) was refluxed for 2 hr. (evolution of hydrogen chloride). Addition of water and working up in the usual way gave the *dienone* (XXII) as felted needles (from aqueous methanol) (1·02 g.), m. p. 127—128°, $[\alpha]_D$ +99° (*c* 1·29), $\lambda_{max.}$ 271 mμ (ε 12,600), $\nu_{max.}$ 1728 (OAc), 1679 (conjugated ketone) and 1648 and 1618 (C=C) cm.$^{-1}$ (Found: C, 79·8; H, 10·5. $C_{32}H_{50}O_3$ requires C, 79·6; H, 10·45%). When this dienone (XXII) (140 mg.) in ethanol (15 ml.) containing potassium hydroxide (150 mg.) was heated to the b. p. under oxygen-free nitrogen it gave the known oxide (XXI) (82 mg.), identified by m. p., mixed m. p., rotation {$[\alpha]_D$ +89° (*c* 1·39; *l* = 0·5)}, and ultraviolet absorption spectrum.

The dienone (115 mg.) in dry ether (7 ml.) was treated with osmium tetroxide (100 mg.)

in dry pyridine (3 ml.) in the dark at room temperature for 5 days. Working up by the hydrogen sulphide method [18] and chromatography of the product over alumina (Grade V) gave, on elution with ether–light petroleum mixtures, the *diol* (XX). Recrystallised from aqueous methanol this formed needles, m. p. 132—134°, $[\alpha]_D$ +210° (*c* 1·00; *l* = 0·5), $\lambda_{max.}$ 254 mμ (ε 9500), $\nu_{max.}$ 3484 and 3333 (OH), 1748 (OAc), 1678 and 1608 (cyclopentenone) cm.$^{-1}$ (Found: C, 74·0; H, 10·15. $C_{32}H_{52}O_5$ requires C, 74·35; H, 10·15%). This diol was recovered unchanged after attempted acetylation with pyridine–acetic anhydride at room temperature.

The dienone (320 mg.) in peracetic acid solution (0·084 active oxygen per ml.; 25 ml.) was left at 5° in the dark for 5 days. The white crystals that separated were filtered off. Recrystallisation from acetone–methanol gave the *hydroxy-oxide* (XXIV) (271 mg.) as needles, m. p. 223—224°, $[\alpha]_D$ +111° (*c* 0·63), $\lambda_{max.}$ 254 mμ (ε 7500), $\nu_{max.}$ 3425 (OH), 1686 and 1631 (cyclopentenone) cm.$^{-1}$ (Found: C, 79·0; H, 10·45. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·5%). This compound was recovered unchanged after treatment with pyridine–acetic anhydride for 16 hr. at room temperature or 2 hr. at 100°. It resisted oxidation with Kiliani chromic acid mixture. Reduction was effected by the following method. Liquid ammonia (at the b. p.) was saturated with excess of lithium (50—80 mg.; 10 minutes' stirring). The hydroxy-oxide (100 mg.) in dry tetrahydrofuran (15 ml.) was added (5 min.) and stirring continued (10 min.). Ammonium chloride (5 g.) was then added and the mixture was worked up in the usual way to give, after crystallisation from methanol, the dihydro-oxide (XXIII) (10 mg.), identified by m. p., mixed m. p., rotation, and infrared spectrum.

Toluene-p-*sulphonyl and Methanesulphonyl Derivatives.*—These were prepared in the following way. The alcohol (1 g.; or proportionate part) in pyridine (15 ml.) was treated with recrystallised toluene-*p*-sulphonyl chloride (2 g.) or redistilled methanesulphonyl chloride (1 ml.) at room temperature for 13 hr. The mixture was diluted with water and worked up in the usual way, all evaporations being conducted at room temperature (or lower) *in vacuo*. The *toluene*-p-*sulphonate* of 3β-hydroxylanost-8-en-7-one, crystallised from benzene–light petroleum (b. p. 60—80°), had m. p. 188° (decomp.), $[\alpha]_D$ +12° (*c* 0·99), $\lambda_{max.}$ 228 and 254 mμ (ε 11,800 and 8400 respectively) (Found: C, 74·15; H, 9·5; S, 5·4. $C_{37}H_{56}O_4S$ requires C, 74·45; H, 9·45; S, 5·5%). The corresponding *methanesulphonate*, from the same solvent mixture, had m. p. 178—179° (decomp.), $[\alpha]_D$ +16° (*c* 1·01), $\lambda_{max.}$ 254 mμ (ε 8200) (Found: C, 71·7; H, 9·85; S, 6·1. $C_{31}H_{52}O_4S$ requires C, 71·5; H, 10·0; S, 6·15%). 3β-*Toluene*-p-*sulphonyloxylanosta*-5,8-*dien*-7-*one* crystallised from chloroform–methanol as rods, m. p. 167—168° (decomp.), $[\alpha]_D$ +10° (*c* 0·94), $\lambda_{max.}$ 228 and 248 mμ (ε 14,600 and 11,100 respectively) (Found: C, 74·8; H, 9·15. $C_{37}H_{54}O_4S$ requires C, 74·7; H, 9·15%). The corresponding *methanesulphonate*, crystallised from light petroleum, had m. p. 151—153° (decomp.), $[\alpha]_D$ +14° (*c* 0·98), $\lambda_{max.}$ 248 mμ (ε 10,100) (Found: C, 71·3; H, 9·5; S, 6·05. $C_{31}H_{50}O_4S$ requires C, 71·75; H, 9·7; S, 6·15%). The alcohol (IV; R = H) gave a *methanesulphonate* which crystallised from light petroleum as needles, m. p. 111—112° (decomp.), $[\alpha]_D$ +177° (*c* 0·83), $\lambda_{max.}$ 234 and 279 mμ (ε 5600 and 3100 respectively) (Found: C, 71·45; H, 9·65; S, 6·0. $C_{31}H_{50}O_4S$ requires C, 71·75; H, 9·7; S, 6·15%).

Preparation of the Model Umbellulone (XXX).—Tetrahydrophotodehydroergosteryl acetate [10] (1·0 g.) in dry pyridine (15 ml.) was added to a slurry of chromium trioxide (1·3 g.) in dry pyridine (25 ml.) and shaken in the dark under oxygen-free nitrogen for 6 days at room temperature. Dilution with water and working up in the usual way gave a product (1·0 g.) which, with methanol, afforded unchanged starting material (485 mg.). The mother-liquors were evaporated to dryness *in vacuo* and the residue was chromatographed over alumina (Grade V; 15 g.). Elution with benzene–light petroleum (1 : 19) and crystallisation from methanol gave the desired *umbellulone* (XXX) (60 mg.) as needles, m. p. 160—162°, $[\alpha]_D$ +112° (*c* 0·302), $\lambda_{max.}$ 232 and 278 mμ (ε 5200 and 3100 respectively), $\nu_{max.}$ 1721 (OAc) and 1667 and 1621 (umbellulone) cm.$^{-1}$ (Found: C, 79·65; H, 10·4. $C_{30}H_{44}O_3$ requires C, 79·6; H, 9·8%).

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[18] Barton and Elad, *J.*, 1956, 2085.