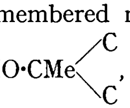
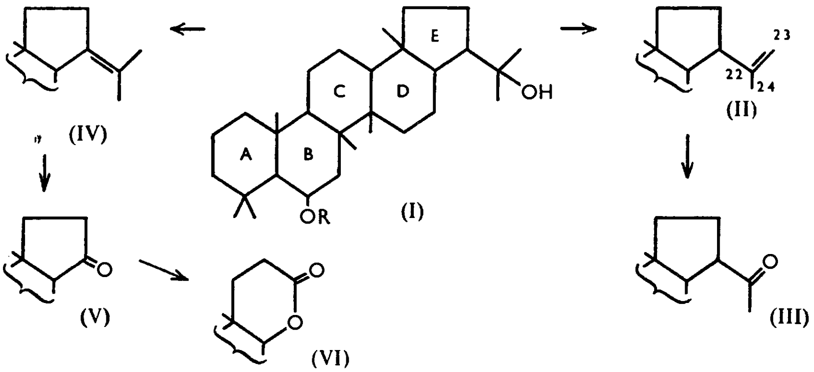
454. *Triterpenoids. Part XXIV.* Further Investigations on the Constitution of Zeorin.*

By D. H. R. Barton, P. de Mayo, and J. C. Orr.

Stepwise degradation of zeorin has established that this substance contains a group $HO{\cdot}CMe_2-$ attached to a *cyclo*pentane ring. This has been confirmed, and the relevant ring shown to be terminal, by a reversed Michael reaction whereby five of the six carbon atoms constituting this ring have been isolated as methyl *iso*propyl ketone. The manner in which zeorin, zeorinin, and *neo*zeorinin are related has been clarified and, by a study of further transformation products, a partial structure (XXXV) for the zeorin molecule has been deduced. These and other results, together with a consideration of the place of zeorin in the general triterpenoid biogenetic pattern, have led to the proposal of a squalenoid structural formula (I; R = H) for zeorin.

When the present work began, knowledge concerning the structure of zeorin could be summarised as follows. Zeorin was a secondary-tertiary diol, $C_{30}H_{52}O_2$, of the triterpenoid series [1,2] the former function being contained in a six-membered ring.[3] The tertiary alcoholic group was incorporated in the partial structure,  $HO{\cdot}CMe\langle{}^{C}_{C}$, since dehydration of zeorin acetate led to *iso*zeorinin acetate which contained the grouping $\rangle C{=}CH_2$.[3] That zeorin was not a derivative of a known pentacyclic triterpenoid was demonstrated by conversion of zeorinin into deoxyzeorinin, in which the tertiary hydroxyl group has been replaced by hydrogen,[2] and thence into the saturated zeorinane,[3] a new triterpenoid hydrocarbon.



The work summarised in the present paper, coupled with biogenetic considerations, leads us to advance (I; R = H) as the constitution of zeorin. This is consistent with prior knowledge and with the following facts.

Ozonolysis of crude *iso*zeorinin acetate [3] gave the expected methyl ketone (III; R = Ac) with loss of one carbon atom. This substance had at least four replaceable α-hydrogen atoms (as shown by bromine titration [4]). The crude acetate also afforded acetone on ozonolysis, showing that, if *iso*zeorinin acetate is represented as (II; R = Ac), the *iso*propylidene isomer (IV; R = Ac) must also have been present. Although the latter compound was not obtained pure its presence was confirmed by ozonolysis and further

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* Part XXIII, *J.*, 1956, 4160.

[1] Asahina and Akagi, *Ber.*, 1938, **71**, 980.

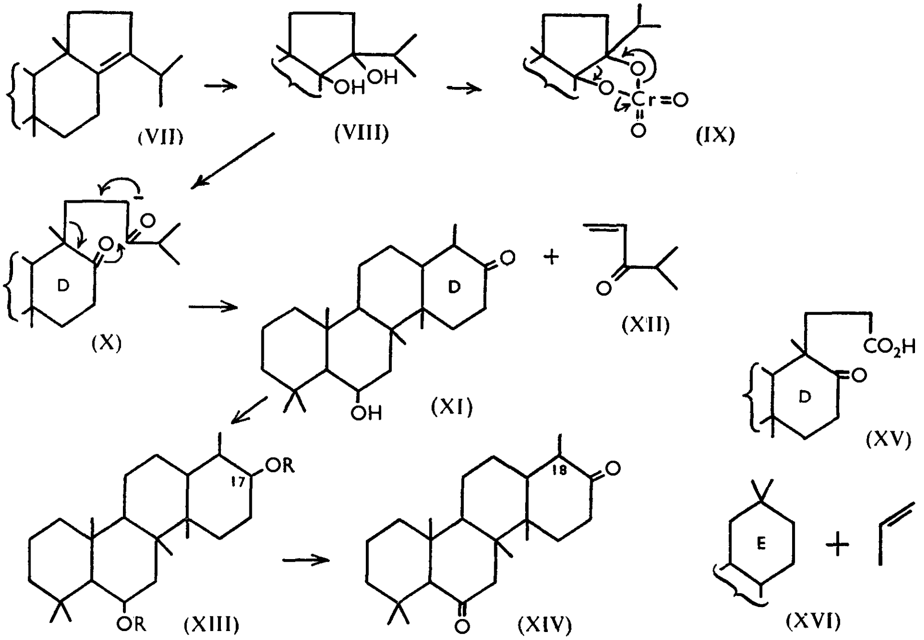
[2] Asahina and Yosioka, *Ber.*, 1940, **73**, 742.

[3] Barton and Bruun, *J.*, 1952, 1683.

[4] Barnes, Barton, Cole, Fawcett, and Thomas, *J.*, 1953, 571.

oxidation with trifluoroperoxyacetic acid.[5] From this it was possible to isolate a δ-lactone acetate (VI; R = Ac), showing infrared bands in CCl_4 at 1735 and 1248 (acetate) and at 1750 (δ-lactone) cm.$^{-1}$, which must have been derived from the *cyclo*pentanone (V; R = Ac).

Mild acid-catalysed rearrangement of *iso*zeorinin acetate (II; R = Ac) affords[3] zeorinin acetate, which can also be obtained directly from zeorin acetate (I; R = Ac) under the same conditions. On the basis of structure (I; R = H), zeorinin can be represented as (VII; R = H), the following reactions being in agreement with this formulation. Treatment of zeorinin acetate (VII; R = Ac) with osmium tetroxide gave



the ditertiary glycol (VIII; R = Ac), which on hydrolysis gives the triol (VIII; R = H). The acetoxy-glycol (VIII; R = Ac) resisted further acetylation with pyridine and acetic anhydride, but was cleaved smoothly by lead tetra-acetate or by chromium trioxide [see (IX; R = Ac)] to the diketone (X; R = Ac). The latter is a 1 : 5-diketone and it was, therefore, predicted that a reverse Michael reaction[6] [see arrows in (X; R = Ac)] would furnish, with loss of six carbon atoms, the hydroxy-ketone (XI) and *iso*propyl vinyl ketone (XII). In the event, base-induced cleavage with potassium hydroxide in diphenyl ether gave methyl *iso*propyl ketone. The loss of one carbon atom (presumably as formaldehyde) from the ketone (XII) has an exact analogy in euphol chemistry.[7] These conditions were unsatisfactory for the isolation of the main fragment of the molecule, but substitution of ethylene glycol for diphenyl ether gave, as non-volatile product, two diols (XIII; R = H), stereoisomeric at $C_{(17)}$. These compounds were isolated as their diacetates (XIII; R = Ac): oxidation of either diol by chromic acid afforded the same diketone (XIV), which had a single infrared band at 1703 cm.$^{-1}$, showing that ring D was six-membered. Reduction of the diketone (XIV) with sodium and propan-2-ol, followed by acetylation, afforded only one of the two diacetates (XIII; R = Ac), obviously that isomer in which both acetate residues are equatorial. The diketone (XIV) was stable to acid, and the

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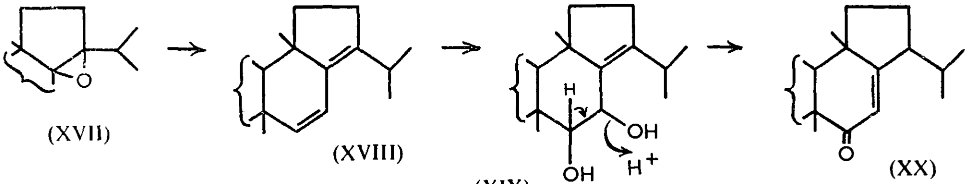
[5] Sager and Duckworth, *J. Amer. Chem. Soc.*, 1955, **77**, 188.

[6] See, for example, Julia, Eschenmoser, Heusser, and Tarköy, *Helv. Chim. Acta*, 1953, **36**, 1885.

[7] Arigoni, Viterbo, Dünnenberger, Jeger, and Ruzicka, *ibid.*, 1954, **37**, 2306.

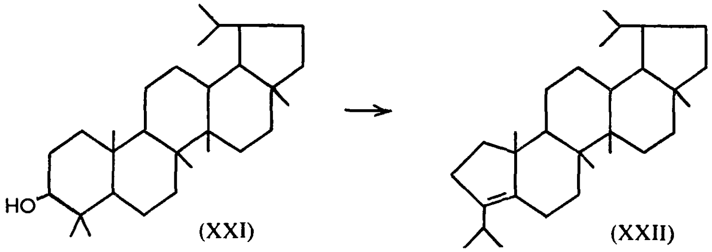
18-methyl group must therefore, almost certainly, be equatorial. The isolation of the diols (XIII; R = H), rather than the hydroxy-ketone (XI), is an example of the familiar base-catalysed oxidation-reduction system [8] formed by alcohols (in this case ethylene glycol) and ketones [in this case (XI)]. This sequence of reactions proves the attachment of the HO·CMe$_2$– group of zeorin to a *terminal* five-membered ring.

Whilst these and other investigations were being pursued an account of some experiments by Ryabinin and Matyukhina appeared.[9] These authors by direct chromic acid oxidation of zeorin obtained a C$_{27}$ diketo-acid. This substance, which we now formulate as (XV), enabled the Russian workers to deduce the presence, in zeorin, of a HO·CMe$_2$– group attached to a *cyclo*pentane ring, though the assumption that it was necessarily terminal is unwarranted. These authors, however, formulate zeorinin as a ring-expansion product [as (XVI)], a view in no way compatible with our results. It is interesting that we have found that ozonolysis of zeorinin acetate at −60° leads to the known epoxide,[2] whilst Ryabinin and Matyukhina obtained, by ozonolysis at room temperature, a " stable ozonide."



(XVII) (XVIII) (XIX) (XX)

It was next desirable to effect entrance into the D-ring of zeorin. Zeorinin epoxide (XVII; R = H), by acid-catalysed dehydration,[2] gives dehydrozeorinin, which must now be represented as (XVIII; R = H). Treatment of dehydrozeorinin benzoate [3] (XVIII; R = Bz) with osmium tetroxide, followed by cleavage of the osmate with lithium aluminium hydride, afforded a mixture of the triol (XIX; R = H) and of its 3-monobenzoate (XIX; R = Bz). A corresponding reaction with dehydrozeorinin acetate (XVIII; R = Ac) and isolation of the osmate by the hydrogen sulphide method gave the unsaturated ketone (XX; R = Ac). This must have been formed, possibly by traces of mineral acid entrained in the hydrogen sulphide gas stream, through the allylic carbonium ion [see (XIX; R = Ac)]. Compound (XX; R = Ac) showed a *cyclo*hexenone infrared band at 1660 cm.$^{-1}$ and had an ultraviolet absorption band at 230 mμ. The formulation of dehydrozeorinin as (XVIII; R = H) is, of course, supported by Asahina and Yosioka's observation [2] that, on hydrogenation, it re-forms zeorinin (VII; R = H).



(XXI) (XXII)

In order to provide a model for the reactions of zeorinin (VII; R = H), lupanol [10] (XXI) was dehydrated with phosphorus pentachloride and the mixture of hydrocarbons obtained was isomerised with ethanolic hydrochloric acid as in the standard method [1] for converting zeorin into zeorinin. A homogeneous hydrocarbon, the previously known

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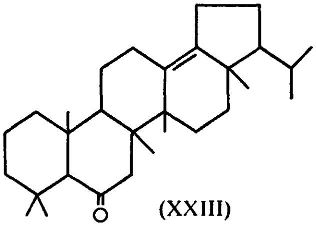
[8] For example, Doering and Aschner, *J. Amer. Chem. Soc.*, 1949, **71**, 839; and references there cited.
[9] Ryabinin and Matyukhina, *Zhur. obshchei Khim.*, 1957, **27**, 277.
[10] Ames, Halsall, and Jones, *J.*, 1951, 450.

iso-γ-lupene[11] (XXII), resulted. The reactivity of this hydrocarbon towards peracetic acid and ozone was the same as that of zeorinin and its derivatives, the known oxide[11] (as XVII) being formed. On treatment with acid as in the preparation of dehydrozeorinin the oxide gave dehydro-*iso*-γ-lupene [(as (XVIII)], whose optical properties were comparable with those of dehydrozeorinin.

In our earlier paper on zeorin,[3] it was reported that under strongly acidic conditions zeorininone afforded a highly crystalline isomer, *neo*zeorininone. If zeorininone is to be based on structure (VII; R = H), then there is available excellent analogy in the conversion of quinovic acid into novic acid[12] and in other comparable rearrangements[13,14] to suggest that *neo*zeorininone should be represented as (XXIII). The preparation of this ketone has been improved by using perchloric acid in acetic acid for the rearrangement, whilst it has been shown that treatment of zeorinin acetate under these conditions affords a non-conjugated diene whose constitution was not investigated further.

The following reactions of *neo*zeorininone support the proposed constitution (XXIII). Oxidation with chromic acid gave three products separable by chromatography over alumina. The most instructive of these was a yellow triketone of the empirical formula $C_{30}H_{44}O_3$. Its spectral properties in the ultraviolet ($\lambda_{max.}$ 263 mμ) and the infrared region (bands at 1724, 1717, 1707, and 1644 cm.$^{-1}$) corresponded to a *cisoid* enedione and, further, indicated that one of the carbonyl groups of the chromophore was situated in a five-membered ring. The properties of this compound are explained by the constitution (XXIV). The second substance obtained from the oxidation was an epoxide for which the absence of intense ultraviolet absorption and the presence of an infrared band at 1703 cm.$^{-1}$ (characteristic of a *cyclo*hexanone) indicated structure (XXV). In agreement, reduction of this epoxide by chromous chloride gave, in excellent yield, the related conjugated ketone (XXVI) having an ultraviolet maximum at 255 mμ and infrared bands at 1700, 1670, and 1603 cm.$^{-1}$. Significantly the band at 1603 cm.$^{-1}$, to be attributed to the double bond, had the high intensity associated with *cisoid* αβ-unsaturated ketones. Finally, the third product from the oxidation was an αβ-unsaturated ketone whose composition and spectral properties require that it be represented as (XXVII).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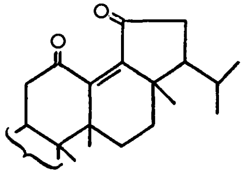
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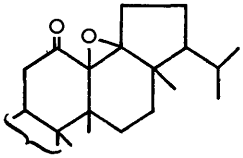
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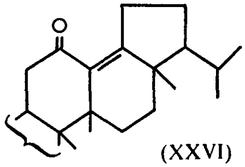
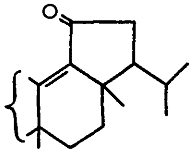

(XXVI)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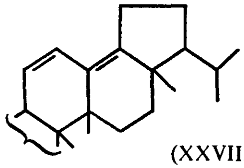
(XXVIII)

Oxidation of *neo*zeorininone (XXIII) with selenium dioxide in dioxan at 140° afforded a conjugated heteroannular diene (XXVIII), reconverted into *neo*zeorininone on hydrogenation. The diene (XXVIII) showed intense absorption indicative of a *transoid* chromophore. On treatment with osmium tetroxide it afforded a disecondary diol

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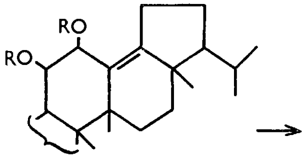
[11] Nowak, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1949, **32**, 323.
[12] Barton and de Mayo, *J.*, 1953, 3111.
[13] Allan, Spring, Stevenson, and Strachan, *J.*, 1955, 3371.
[14] Allan, Fayez, Spring, and Stevenson, *J.*, 1956, 457, and references there cited.

(XXIX; R = H), readily acetylated to the diacetate (XXIX; R = Ac). Cleavage of the diol (XXIX; R = H) with lead tetra-acetate furnished, *via* the dialdehyde (XXX), an aldol condensation product. This showed no ultraviolet absorption and had infrared bands in CCl_4 at 3553 (hydrogen-bonded hydroxyl), 2720 (aldehyde), 1708 (*cyclo*hexanone), and 1695 (hydrogen-bonded aldehyde) cm.$^{-1}$. The isolated ketone group in *neo*zeorininone (XXIII) absorbed at 1713 cm.$^{-1}$ in the same solvent. This aldol can be represented by structure (XXXI), (XXXII), or (XXXIII). The infrared data and stability to base speak against (XXXIII) and we favour (XXXI). What is important about this aldol is that its formation excludes the formula (XXXIV) for the parent diol.

If the relationship between zeorininone and *neo*zeorininone postulated above is accepted, the facts so far summarised prove that zeorin must have the partial structure (XXXV). Previous investigations [3] indicated that the secondary hydroxyl group of zeorin could not be in a terminal ring. In terms of (XXXV) this means that the secondary hydroxyl group is in ring B. This was confirmed in the following way. Deoxyzeorin (XXXVI) was dehydrated with toluene-*p*-sulphonyl chloride and pyridine [3] to a mixture of olefins, whose main component [3] must be (XXXVII) and, in agreement, chromic acid oxidation of the mixture afforded an αβ-unsaturated ketone (XXXVIII). This had an infrared band at 1650 (*cyclo*hexenone) cm.$^{-1}$ and showed ultraviolet absorption at 239 mμ, very close to that (238 mμ) of a derivative of butyrospermol acetate (XXXIX) described by Lawrie, Hamilton, Spring, and Watson.[15] This ketone was stable to vigorous treatment with bromine or selenium dioxide, in agreement with the lack of replaceable



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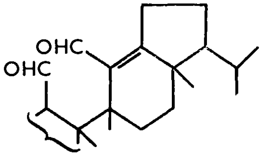

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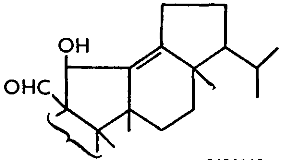

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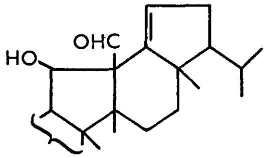
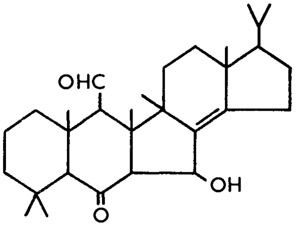


(XXXII)



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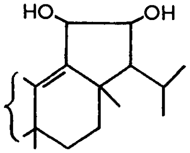

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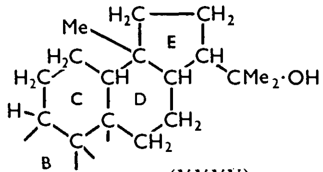

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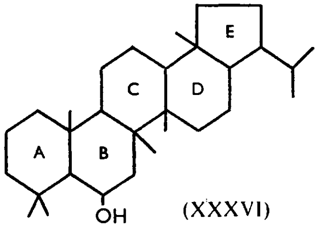

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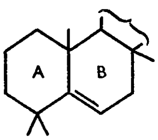

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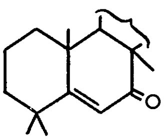
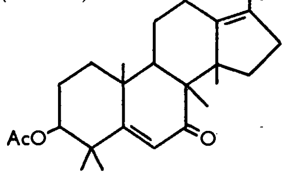


(XXXVIII)



(XXXIX)

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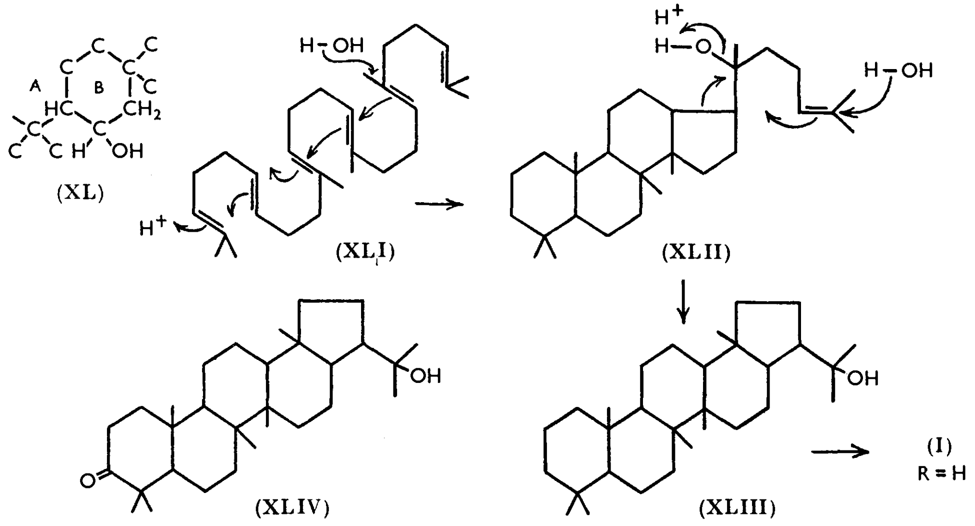
[15] Lawrie, Hamilton, Spring, and Watson, *J.*, 1956, 3272.

α-hydrogen atoms. These experiments show that ring B of zeorin contains the partial structure (XL). We recall also that Asahina and Yosioka[2] obtained, by dehydrogenation of zeorin, 1 : 2 : 5-trimethylnaphthalene. It seems improbable that this hydrocarbon could come from rings C, D, and E [see (XXXV)], but it may be more reasonably derived from rings A and B. It is then plausible to write rings A and B of zeorin as in (I; R = H).

Powerful evidence has become available within the last few years for a general biogenetic scheme for all triterpenoids with squalene as the parent.[16] If zeorin is to be fitted into this scheme it is attractive to place partial structure (XXXV) and rings A and B as defined above into a modified γ-onocerane[17] skeleton as already implied in formula (I; R = H). The biogenesis of zeorin would then involve cyclisation of squalene [see (XLI)] by hydrion to (XLII), followed by rearrangement to (XLIII) and hydroxylation to (I; R = H). It is of interest that the triterpenoid hydrocarbon taraxerene[18] has also been isolated from a lichen,[19] for this may arise by a similar hydrion mechanism.



(XL) (XLI) (XLII) (XLIII) (I) R = H (XLIV)

Very recently further biogenetic support for our zeorin formula has appeared with the elucidation[20,21] of the constitution of hydroxyhopanone (XLIV).

EXPERIMENTAL

Unless specified to the contrary, $[\alpha]_D$ are for $CHCl_3$ solutions; ultraviolet absorption spectra were determined on EtOH solutions with a Unicam S.P. 500 spectrophotometer. Infrared spectra were taken on Nujol mulls unless otherwise stated. The light petroleum used was of b. p. 40—60°. M. p.s were determined on the Kofler block and are uncorrected.

Zeorinin Acetate Oxide (XVII; R = Ac).—Zeorinin acetate (300 mg.) in chloroform (5 ml.) was ozonised at $-60°$ until there was no longer a colour with tetranitromethane. After isolation the product was dissolved in benzene–ether (9 : 1) and filtered through alumina, to give the oxide, m. p. 245—251° (from methanol), $[\alpha]_D$ $+77°$ (*c* 0·44), undepressed in m. p. on admixture with an authentic specimen.[3]

22-*Oxo*-23-*nor*iso*zeorinin Acetate* (III; R = Ac).—Zeorin acetate (700 mg.) was dehydrated in the manner described by Barton and Bruun.[3] The total hydrocarbon mixture resulting was ozonised in chloroform at $-60°$ until no further colour was given with tetranitromethane.

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[16] Ruzicka, *Experientia*, 1953, **9**, 357.

[17] Barton and Overton, *J.*, 1955, 2639.

[18] Beaton, Spring, Stevenson, and Stewart, *J.*, 1955, 2131; Brooks, *J.*, 1955, 1675; and references there cited.

[19] Bruun, *Acta Chem. Scand.*, 1954, **8**, 1291.

[20] Dunstan, Fazakerley, Halsall, and Jones, *Croat Chem. Acta*, in the press.

[21] Schaffner, Caglioti, Arigoni, Jeger, Fazakerley, Halsall, and Jones, *Proc. Chem. Soc.*, 1957, 353.

Isolation of the product, chromatography, and elution with benzene–light petroleum (7 : 3), gave the *acetate* (III; R = Ac) (250 mg.), m. p. 232—238° (decomp.) (from methanol), $[\alpha]_D$ +44° (*c* 0·93) (Found: C, 78·9; H, 10·55. $C_{31}H_{50}O_3$ requires C, 79·1; H, 10·7%). This gave, in the usual way, a 2 : 4-*dinitrophenylhydrazone*, m. p. 239—240° (Found: N, 8·6. $C_{37}H_{54}O_6N_4$ requires N, 8·6%). The ketone gave a positive Zimmerman test and on titration (38·6 mg.) with bromine in acetic acid (10 ml.) took up 4·4 mol.; under the same conditions pregnenolone (45·3 mg.) took up 4·1 mol.

Isolation of the Lactone Acetate (VI; R = Ac). Zeorin acetate (3 g.) was dehydrated and ozonised as described in the preceding experiment. The product, in benzene solution, was filtered through alumina to give an oil (1·75 g.). This was dissolved in methylene dichloride (30 ml.) containing anhydrous sodium phosphate (1·5 g.) and trifluoroperoxyacetic acid (1 g.), and the mixture refluxed for 15 min. Isolation and alkaline hydrolysis gave an acid fraction which after acetylation (acetic anhydride–pyridine) was chromatographed over alumina. Elution with methanol–acetic acid (9 : 1) and crystallisation from aqueous methanol gave the *lactone acetate* (VI; R = Ac), m. p. 282—285° (decomp.), $[\alpha]_D$ +43° (*c* 1·0) (Found: C, 75·75; H, 10·5. $C_{29}H_{46}O_4$ requires C, 75·95; H, 10·1%). In a similar experiment the ozonolysis product from dehydrated zeorin acetate (500 mg.) was steam-distilled and the distillate treated with 2 : 4-dinitrophenylhydrazine. Acetone 2 : 4-dinitrophenylhydrazone, identified by m. p. and mixed m. p., was obtained.

Dehydration and Oxidation of Deoxyzeorin.—Zeorin acetate (4·17 g.) was dehydrated in the manner previously described[3] and the product hydrogenated in acetic acid over platinum. The crude deoxyzeorin acetate was treated with lithium aluminium hydride (3 g.) in ether–dioxan, to give crude deoxyzeorin. The latter, in pyridine (40 ml.), was refluxed with toluene-*p*-sulphonyl chloride (6 g.) for 8 hr. The crystallised hydrocarbon mixture obtained (1·74 g.) (see Barton and Bruun[3]) was refluxed in acetic acid (80 ml.) containing chromium trioxide (2 g.) for 20 min. Filtration of the product in benzene solution through alumina gave the αβ-unsaturated *ketone* (XXXVIII), m. p. 186—187° (from methanol), $[\alpha]_D$ −51° (*c* 1·51), $\lambda_{max.}$ 239 mμ (ε 12,100) (Found: C, 85·2; H, 11·5. $C_{30}H_{48}O$ requires C, 84·85; H, 11·4%). The unsaturated ketone (21·2 mg.) in a 0·0025N-solution (25 ml.) of bromine in acetic acid containing a catalytic amount of hydrogen bromide was set aside for 36 hr. at room temperature. Isolation then gave starting material in over 80% yield. The ketone (15·5 mg.) was heated in refluxing acetic acid (3 ml.) containing selenium dioxide (100 mg.) for 16 hr.: isolation and crystallisation then gave the starting material (6 mg.) identified in this and the previous experiment by m. p. and mixed m. p.

Reaction of Zeorinin Acetate with Osmium Tetroxide.—Zeorinin acetate (817 mg.) in dioxan (7 ml.) containing osmium tetroxide (643 mg.) was set aside in the dark for 14 days. Decomposition of the osmic ester with hydrogen sulphide and working up in the usual way gave the *triol monoacetate* (VIII; R = Ac), m. p. 248—254° (from light petroleum), $[\alpha]_D$ +53° (*c* 2·37) (Found: C, 76·7; H, 10·7. $C_{32}H_{54}O_4$ requires C, 76·45; H, 10·85%). This was recovered unchanged after treatment with pyridine–acetic anhydride at room temperature.

The above monoacetate (50 mg.) in dioxan (4 ml.) containing lithium aluminium hydride (50 mg.) was refluxed for 30 min. Isolation and crystallisation from light petroleum gave the *triol*, m. p. 255—270°, unchanged on repeated crystallisation from methanol or light petroleum, $[\alpha]_D$ +31° (*c* 2·40) (Found: C, 78·1; H, 11·5. $C_{30}H_{52}O_3$ requires C, 78·0; H, 11·4%). The triol was also obtained by reduction of the osmate ester formed with zeorinin acetate with lithium aluminium hydride.

3-*Acetoxy*-17 : 21-*dioxo*-A-seco*zeorinane* (X; R = Ac).—(*a*) Zeorinanetriol monoacetate (343 mg.) in benzene (25 ml.) and acetic acid (20 ml.) containing lead tetra-acetate (500 mg.) was left at room temperature for 10 min. Previous experimentation had indicated that under these conditions 1 mol. of tetra-acetate was consumed, there being no further uptake on longer standing. Ethylene glycol (5 drops) was added and the product isolated in the usual way, to give the *acetoxy-dione* (X; R = Ac), m. p. 125—128° (from methanol), $[\alpha]_D$ +32° (*c* 3·33) (Found: C, 76·7; H, 10·6. $C_{32}H_{52}O_4$ requires C, 76·75; H, 10·45%).

(*b*) The triol monoacetate (30 mg.) in acetic acid (25 ml.) containing chromium trioxide (9·3 mg.) was kept at room temperature for 80 min., after which isolation afforded the dione. A similar result was achieved by using the chromium trioxide–pyridine complex as the oxidant.

The Reversed Michael Reaction.—(*a*) The dione monoacetate (X; R = Ac) (118 mg.) was added to a refluxing mixture of diphenyl ether and potassium hydroxide whilst a stream of nitrogen was passed through it and into an aqueous solution of 2 : 4-dinitrophenylhydrazine in dilute sulphuric acid. A precipitate was immediately formed and continued to accumulate for 45 min. Collection, followed by chromatography on bentonite–kieselguhr to remove the diphenyl ether–2 : 4-dinitrophenylhydrazine adduct, afforded methyl *iso*propyl ketone 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 121—122° (Found: C, 50·15; H, 5·35; N, 20·9. Calc. for $C_{11}H_{14}O_4N_4$: C, 49·6; H, 5·3; N, 21·0%). In a similar experiment the volatile ketone from 127 mg. of the dione was passed into an aqueous solution of semicarbazide acetate. Methyl *iso*propyl ketone semicarbazone, m. p. and mixed m. p. 112—113°, was obtained.

(*b*) Diethylene glycol (15 ml.) containing potassium hydroxide (0·5 g.) was refluxed and a stream of nitrogen passed through the mixture. The dione (742 mg.) was dropped into the solution and heating continued for 40 min. The product was filtered through alumina; the material (413 mg.) eluted with more powerful eluants than benzene–carbon tetrachloride (1 : 6) was acetylated (acetic anhydride–pyridine), and the product was rechromatographed. Elution with carbon tetrachloride–benzene(3 : 1) then gave the *diacetate-I* (XIII; R = Ac), m. p. 194—195° (from methanol), $[\alpha]_D$ +83° (*c* 1·24) (Found: C, 75·25; H, 10·25. $C_{28}H_{46}O_4$ requires C, 75·3; H, 10·4%). Elution with benzene gave the *diacetate-II* (XIII; R = Ac), m. p. 213—215° (from methanol or light petroleum), $[\alpha]_D$ +41° (*c* 1·16) (Found: C, 75·55; H, 10·45%).

The diacetate-II (25 mg.) in dioxan (1 ml.) was treated with a solution of lithium aluminium hydride (40 mg.) in ether (1 ml.), and the ether distilled off. The mixture was then refluxed for 15 min. The product (23 mg.) in pyridine (2 ml.) containing chromium trioxide (30 mg.) was kept overnight at room temperature. Crystallisation from methanol gave the *diketone* (XIV), m. p. 212—216°, $[\alpha]_D$ +15° (*c* 0·35) (Found: C, 80·35; H, 10·75. $C_{24}H_{38}O_2$ requires C, 80·4; H, 10·7%). The same diketone (m. p. and mixed m. p.) was obtained from the diacetate-I. The diketone was unchanged after 30 min. in refluxing chloroform containing concentrated hydrochloric acid.

The diketone (10 mg.) in dry benzene (3 ml.) and propan-2-ol (2·5 ml.) was refluxed during the addition of sodium (1 g.) in small pieces during 4 hr. Acetylation (acetic anhydride–pyridine) of the product gave the diacetate-II (8 mg.), identified by m. p., mixed m. p., and rotation.

Dehydrozeorinin (XVIII; R = H) *and its Derivatives.*—Dehydrozeorinin benzoate (268 mg.) in dioxan (15 ml.) containing lithium aluminium hydride (300 mg.) was refluxed for 5 min. Crystallisation from methanol gave dehydrozeorinin (XVIII; R = H), m. p. 174—183°, $[\alpha]_D$ +79° (*c* 1·71) (Found: C, 84·8; H, 11·25. Calc. for $C_{30}H_{48}O$: C, 84·85; H, 11·4%). Acetylation (pyridine–acetic anhydride) gave the acetate (XVIII; R = Ac), m. p. 222—223°, $[\alpha]_D$ +75° (*c* 1·89).

Reaction of Dehydrozeorinin Derivatives with Osmium Tetroxide.—(*a*) Dehydrozeorinin benzoate (187 mg.) in dioxan (8 ml.) containing osmium tetroxide (95 mg.) was set aside in the dark for 5 days. Addition of lithium aluminium hydride (200 mg.) in ether (3 ml.) followed by filtration of the product in carbon tetrachloride through alumina and elution with benzene–carbon tetrachloride (1 : 19) gave the *triol monobenzoate* (XIX; R = Bz), m. p. 227—241° (from methanol or light petroleum), $[\alpha]_D$ +55° (*c* 0·57) (Found: C, 78·8; H, 10·1. $C_{37}H_{54}O_4$ requires C, 78·95; H, 9·65%). Elution of the column with benzene then gave the corresponding *triol* (XIX; R = H), m. p. 235—252° (from methanol), $[\alpha]_D$ +35° (Found: C, 78·3; H, 11·4. $C_{30}H_{50}O_3$ requires C, 78·55; H, 11·0%).

(*b*) Dehydrozeorinin acetate (894 mg.) in dioxan (25 ml.) containing osmium tetroxide (485 mg.) was left for 4 days at room temperature in the dark. Hydrogen sulphide from a Kipp generator was then passed in. The product, in carbon tetrachloride solution, was chromatographed over alumina (activity III; 17 g.). Elution with varying proportions of ether in benzene gave the unsaturated *ketone* (XX; R = Ac), m. p. 141—142° (from aqueous methanol), $[\alpha]_D$ +76° (*c* 0·66), $\lambda_{max.}$ 230 mμ (ε 9000) (Found: C, 76·85; H, 10·3. $C_{32}H_{50}O_3,H_2O$ requires C, 76·75; H, 10·45%).

neo*Zeorininone.*—Zeorininone (1·29 g.) in acetic acid (100 ml.) at 100° was treated with 72% perchloric acid (6·5 ml.) and heating continued for 40 min.; this gave *neo*zeorininone (XXIII) (1·05 g.), identified by m. p. and mixed m. p.

Acid Treatment of Zeorinin Acetate.—Zeorinin acetate (805 mg.) in acetic acid (50 ml.) at 100° was treated with 72% perchloric acid (2 ml.). After 4 min. the product had separated as white crystal clusters which recrystallised from ethanol to give a *diene*, m. p. 177—179°, $[\alpha]_D$ +50° (*c* 2·13) (Found: C, 88·15; H, 11·9. $C_{30}H_{48}$ requires C, 88·15; H, 11·85%).

Selenium Dioxide Oxidation of neo*Zeorininone*.—*neo*Zeorininone (424 mg.) and selenium dioxide (133 mg.) in dioxan (2 ml.) were heated in a sealed tube at 140° for 1 hr. The product was chromatographed over alumina (activity I: 15 g.). Elution with benzene–carbon tetrachloride (1 : 1) gave *dehydro*neo*zeorininone* (XXVIII), m. p. 255—256° (from methanol), $[\alpha]_D$ $+30°$ (*c* 1·34), $\lambda_{max.}$ 265, 255, and 247 mμ (ε 20,600, 29,000, and 26,100 respectively) (Found: C, 85·5; H, 10·75. $C_{30}H_{46}O$ requires C, 85·25; H, 10·95%).

This dienone (31 mg.) in *cyclo*hexane–acetic acid was hydrogenated in the presence of Adams catalyst. Crystallisation of the product gave *neo*zeorininone (m. p. and mixed m. p.). The infrared spectrum was identical with that of an authentic specimen.

*Dehydro*neo*zeorininone*-11 : 12-*diol* (XXIX; R = H).—The dienone (110 mg.) in pyridine (1 ml.) containing osmium tetroxide (200 mg.) was kept in the dark for 12 days. Decomposition of the osmate ester with hydrogen sulphide and crystallisation from light petroleum gave a *diol* (XXIX; R = H), m. p. 214—221°, $[\alpha]_D$ $+33°$ (*c* 1·24) (Found: C, 78·8; H, 11·0. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%). The m. p. of the product was unchanged by chromatography. *neo*Zeorininone was recovered unchanged after being kept with osmium tetroxide for 6 weeks under similar conditions.

The diol (65 mg.) with acetic anhydride–pyridine gave the *diacetate* (XXIX; R = Ac), m. p. 103—106° (from methanol), $[\alpha]_D$ $+12°$ (*c* 1·41) (Found: C, 75·5; H, 10·0; Ac, 15·4. $C_{32}H_{52}O_5$ requires C, 75·5; H, 9·7; 2Ac, 15·9%).

The diol (23·2 mg.) consumed 1 mol. of lead tetra-acetate in 5 min., no further oxidation taking place. Isolation of the product gave, after crystallisation from light petroleum, an *aldol* (? XXXI), m. p. 173—181°, $[\alpha]_D$ $-119°$ (*c* 1·14) (Found: C, 78·7; H, 10·3. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%). This showed no intense absorption in ethanol or ethanolic potassium hydroxide.

Oxidation of neo*Zeorininone*.—*neo*Zeorininone (1·62 g.) in acetic acid (1 l.) was added to chromium trioxide solution in acetic acid (1·08N; 20 ml.) and the mixture left overnight at room temperature. The product was chromatographed on alumina (activity V; 35 g.) to give the following products:

(i) Elution with carbon tetrachloride gave the *dione* (XXVII), m. p. 278—282° (from ethanol), $[\alpha]_D$ $+39°$ (*c* 1·67), $\lambda_{max.}$ 259 mμ (ε 12,800), $\nu_{max.}$ 1697 cm.$^{-1}$ (merged *cyclo*pentenone and *cyclo*hexanone) (Found: C, 82·30; H, 10·8. $C_{30}H_{46}O_2$ requires C, 82·15; H, 10·55%).

(ii) Elution with benzene–carbon tetrachloride (1 : 1) gave the *epoxy-dione* (XXV), m. p. 272° to >350° (from light petroleum), $[\alpha]_D$ $+91°$ (*c* 1·05), $\lambda_{max.}$ 288 mμ (ε 108) (Found: C, 79·15; H, 10·1. $C_{30}H_{46}O_3$ requires C, 79·25; H, 10·2%). It gave a negative tetranitromethane test. The wide m. p. range was due to conversion into a higher-melting compound at the m. p.

(iii) Elution with benzene–ether (1 : 4) and crystallisation from methanol gave the yellow *trione* (XXIV), m. p. 284—290°, $[\alpha]_D$ $+31°$ (*c* 0·89), $\lambda_{max.}$ 263, 375 mμ (ε 9200 and 460 respectively) (Found: C, 79·6; H, 9·7. $C_{30}H_{44}O_3$ requires C, 79·6; H, 9·8%).

*Reduction of the Epoxy*neo*dione* (XXV).—The epoxide (106 mg.) in acetone (15 ml.) was added to ethanolic chromous chloride [22] (0·63N; 9 ml.). Isolation of the product after 50 min. gave *isoneo*zeorinindione (95 mg.), m. p. 266—268° (from light petroleum), showing a sharp change from needles to prisms at 235—236°, $[\alpha]_D$ $+53°$ (*c* 1·2), $\lambda_{max.}$ 255 mμ (ε 8400) (Found: C, 81·95; H, 10·2. $C_{30}H_{46}O_2$ requires C, 82·15; H, 10·55%).

iso-γ-*Lupene*.—Lupanol (354 mg.) in dry light petroleum (40 ml.) containing phosphorus pentachloride (400 mg.) was left at 0° for 1 hr. Isolation of the product and filtration in light petroleum solution through a short column of alumina gave a crystalline mixture of hydrocarbons. The mixture (200 mg.) in ethanol (300 ml.) containing concentrated hydrochloric acid (50 ml.) was refluxed for 35 min. Crystallisation from methanol gave *iso*-γ-lupene,[11] m. p. 135—136°, $[\alpha]_D$ $+13°$ (*c* 2·88) (Found: C, 87·95; H, 12·15. Calc. for $C_{30}H_{50}$: C, 87·75; H, 12·25%).

iso-γ-*Lupene Epoxide*.—(*a*) *iso*-γ-Lupene (163 mg.) in methylene dichloride (10 ml.) was ozonised at 0° until the solution gave no colour with tetranitromethane. Filtration of the product in light petroleum through alumina (activity III; 8 g.) gave the epoxide,[11] m. p. 179—187° (from acetone), $[\alpha]_D$ $+5°$ (*c* 1·24) (Found: C, 84·4; H, 11·75. Calc. for $C_{30}H_{50}O$: C, 84·45; H, 11·8%).

(*b*) *iso*-γ-Lupene (282 mg.) in acetic acid (50 ml.) at 100° was treated with 30% hydrogen

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[22] Cole and Julian, *J. Org. Chem.*, 1954, **19**, 131; Julian, Cole, Meyer, and Regan, *J. Amer. Chem. Soc.*, 1955, **77**, 4601.

peroxide (1 ml.). After 7 min. isolation and crystallisation afforded the same epoxide, identified by m. p. and mixed m. p.

Dehydro-iso-*γ-lupene*.—The epoxide (see above) (24 mg.) in ethanol (20 ml.) containing concentrated hydrochloric acid (2 ml.) was refluxed for 90 min., the minimum amount of chloroform (*ca.* 0·5 ml.) being added to prevent the separation of an oil. Filtration of the product in light petroleum through alumina (activity I; 1 g.) gave *dehydro*-iso-*γ-lupene*, m. p. 111—112° (from acetone), $[\alpha]_D$ +30°, $\lambda_{max.}$ 252 mμ (ε 21,500) (Found: C, 87·8; H, 11·7. $C_{30}H_{48}$ requires C, 88·15; H, 11·85%).

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