# **151.** *The Structure of Zierone. Part II.**

By A. J. Birch, D. J. Collins, A. R. Penfold, and J. P. Turnbull.

Zierone has the formula (V). Its reactions include dehydrogenation to zierazulene (I; R = H) and formation by the action of osmium tetroxide of the glycol (VI) which is split by lead tetra-acetate to the β-diketone (XII) whose structure is supported by spectra and further reactions. Reduction of the glycol (VI) gives the triol (X), which when split by lead tetra-acetate generates an αβ-unsaturated ketone. Reasons for placing the methyl group at the 1- rather than the 2-position are given, and spectral anomalies are discussed in terms of steric compression of the unsaturated portion of the molecule.

Zierone has recently been assigned the structure (V) by Barton and Gupta.[1] We now report more extensive evidence which has led us independently to the same formula.

The sesquiterpene ketone, zierone, $C_{15}H_{22}O$, was isolated from *Zieria macrophylla* by Penfold [2] and later investigated by Bradfield, Penfold, and Simonsen.[3] It has been shown to be identical with " elleryone " from *Evodia elleryana*.[4] Some further investigations on which subsequent structural conclusions have been chiefly based have been published, so far only as a preliminary note,[5] and are reported in detail here.

Zierone was originally considered [3] to be tricyclic but we showed [5] that it is bicyclic containing an αβ-unsaturated ketone group and another double bond. The spectrum of the carbonyl system, $\lambda_{max.}$ 245 mμ (ε 8200), $\nu_{max.}$ 1680 and 1591 cm.$^{-1}$, agrees with such a formulation; the low-intensity carbonyl band is found [4] at 327 mμ (ε 1270) and has both an unusually long wavelength and a high intensity. The semicarbazone and 2,4-dinitrophenylhydrazone also have rather unusual absorption, as discussed below. Zierone itself reacted with 1·2 equivalents of perbenzoic acid under mild conditions, but the alcohol zierol, $C_{15}H_{24}O$, obtained by reduction with lithium aluminium hydride or sodium borohydride, absorbed 2·1 equivalents. Double bonds conjugated with a carbonyl group do not normally react readily with this reagent. Zierol has an unusual ultraviolet absorption with no maximum in the region 220—280 mμ, but fairly intense absorption with $\lambda_{infl.}$ 228 mμ (ε 5000).

Ozonolysis of zierone gave at first only traces of acetone, but under specific conditions Hildebrand and Sutherland [4] obtained a notable yield. They showed, moreover, that refluxing it with sulphuric acid (70%) also gave acetone, so that zierone must contain the grouping $Me_2C{:}C{\cdot}C{:}O$. Since zierone also gives [3] a hydroxymethylene derivative with the expected absorption ($\lambda_{max.}$ 321 mμ), it must also contain a $CH_2{\cdot}C{:}O$ grouping.

At this stage the nature of the nucleus was defined by dehydrogenation.[5] Zierol, after dehydration, was dehydrogenated over palladised charcoal at 275°, giving an 11% yield of a violet azulene which was not then known. Despite a general resemblance to vetivazulene it was distinct in derivatives and spectrum and was named zierazulene. The spectrum in the visible region has one major peak at 546 mμ. The action of methylmagnesium iodide on zierone, followed by dehydration and dehydrogenation, gave in good yield a blue-violet (*K*)-methylzierazulene, $\lambda_{max.}$ 560 mμ. Hydroxymethylenezierone absorbed 3 mol. of hydrogen over palladised charcoal; the product was reduced with sodium and ethanol and similarly dehydrogenated; the resulting blue (*K* ± 1)-methylzierazulene has $\lambda_{max.}$ 534 mμ.

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* Part I, Collins, *J.*, 1959, 531.

[1] Barton and Gupta, *Proc. Chem. Soc.*, 1961, 308.

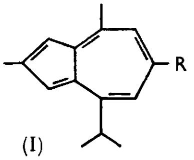
[2] Penfold, *J. Proc. Roy. Soc., New South Wales*, 1926, **60**, 104.

[3] Bradfield, Penfold, and Simonsen, *J. Proc. Roy. Soc., New South Wales*, 1933, **67**, 200.

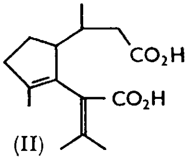
[4] Hildebrand and Sutherland, *Austral. J. Chem.*, 1959, **12**, 436.

[5] Birch, Collins, and Penfold, *Chem. and Ind.*, 1955, 1773.

The shifts of absorption maximum with insertion of alkyl groups in various positions of the azulene nucleus have been examined by Plattner.[6] On this basis the spectrum of ($K$)-methylzierazulene ($\Delta\lambda$ 14 m$\mu$) is consistent with the insertion of a methyl group at position 5 or 7 in zierazulene, and the spectrum of ($K + 1$)-methylzierazulene with insertion at the 4-, 6-, or 8-position. The spectrum of zierazulene itself is in accord with a 2,4,8- or possibly a 2,4,6-trialkylazulene nucleus, and on general biogenetic grounds 8-isopropyl-2,4-dimethylazulene (I; R = H) seemed the most likely formula. This was confirmed by synthesis.[7] ($K + 1$)-Methylzierazulene must accordingly be 8-isopropyl-2,4,6-trimethylzierazulene (I; R = Me) and this was also confirmed by synthesis.[7] ($K$-)Methylzierazulene must be 8-isopropyl-2,4,5(or 7)-trimethylazulene, either of which would be difficult to synthesise unambiguously. These results support the conclusion which can be drawn from the infrared spectrum that the carbonyl group is in the seven-membered ring and that it is in the 5- or 7-position.[5] From the demonstration [4] that it is adjacent to isopropylidene group it must in fact be in the 7-position.



(I)



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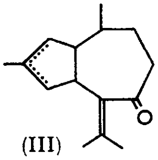

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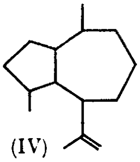

(IV)

Attempts were made to explore the environment of the carbonyl group by treating hydroxymethylenezierone with hydrogen peroxide; this yielded a dicarboxylic acid, $C_{15}H_{22}O_4$, m. p. 151·5°, which from subsequent work must have structure (II). It had $\lambda_{max.}$ 210 m$\mu$ ($\varepsilon$ 10,550) and did not show notable absorption due to the diene system. Reduction with sodium and butanol gave a dihydro-derivative, $C_{15}H_{24}O_4$, m. p. 153·5°, with much less intense absorption ($\varepsilon$ 6400) at 210 m$\mu$, confirming the reduction of an $\alpha\beta$-unsaturated acid system. Reduction of the original acid, $C_{15}H_{22}O_4$, with lithium aluminium hydride gave an oily neutral alcohol, $C_{15}H_{26}O_2$, and a hydroxy-acid, $C_{15}H_{24}O_3$, $\lambda_{max.}$ 208 m$\mu$ ($\varepsilon$ 10,700), which must still contain the $\alpha\beta$-unsaturated acid system. Ozonolysis of the alcohol gave only acetone as a volatile product, so no structural conclusions could be drawn apart from the fact that the $\alpha\beta$-unsaturated carboxyl group appeared to be more sterically hindered than the other.

Attention was therefore focused on the second double bond, and as a basis for further degradation zierone was converted by osmium tetroxide into dihydrodihydroxyzierone, $C_{15}H_{24}O_3$, m. p. 126°, now known to have structure (VI). This has the expected infrared bands ($\nu_{max.}$ 3268, 1690, 1647 cm.$^{-1}$ in Nujol), but has an unexpectedly weak band in the ultraviolet spectrum [$\lambda_{max.}$ 246 m$\mu$ ($\varepsilon$ 2540 in ethanol or light petroleum)].

On the basis of the evidence above, Hildebrand and Sutherland put forward the structure (III) for zierone. This seemed to us unlikely to be correct because of the various spectral anomalies which appeared to indicate considerable steric interference with the $\alpha\beta$-unsaturated ketone chromophore. Zierone itself has an ultraviolet maximum at a somewhat lower wavelength (245 m$\mu$) than expected (*ca.* 252 m$\mu$), and this becomes more marked, as noted above, when the oxygen of the carbonyl group is replaced by the larger semicarbazone ($\lambda_{max.}$ 246 m$\mu$) or 2,4-dinitrophenylhydrazone ($\lambda_{max.}$ 372 m$\mu$) grouping, the values being then closer to those of a saturated than of the expected $\alpha\beta$-unsaturated derivatives (260—270 and 377—393 m$\mu$, respectively). The low intensity of the dihydrodihydroxyzierone band ($\varepsilon$ 2540) is particularly striking and is unlikely to be due to reversible cyclic acetal formation since it is independent of the polarity of the solvent. These results can be explained by the presence of a 1- but not a 2-methyl group in zierone.

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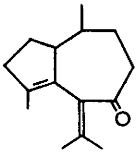
[6] Plattner, *Helv. Chim. Acta*, 1941, **24**, 283E.
[7] Collins, *J.*, 1959, 531.

The necessary ready migration to the 2-position during dehydrogenation could be explained by such interference and is strongly supported by the observation that compound (IV), derived from aromadendrene, in fact gives zierazulene on dehydrogenation.[8]

The greatly increased interference observed with dihydrodihydroxyzierone appeared to indicate that the second double bond might terminate in the 1-position. The unusual absorption of zierol is reminiscent of a non-planar conjugated diene system such as is found in photosantonic acid,[9] and structure (V) seemed possible for zierone.

An attempt was made to examine the diene system by removing the carbonyl group by Wolff–Kishner reduction but the principal product was a crystalline base, $C_{15}H_{24}N_2$, $\lambda_{max.}$ 228 mμ (ε 5300). Reduction of zierol with lithium in liquid ammonia gave the first evidence in favour of a conjugated diene structure. The product was a hydrocarbon mixture, shown by mass-spectrometry, for which we are indebted to Dr. R. I. Reed, to contain a considerable proportion of a hydrocarbon, $C_{15}H_{26}$, of mass number 206. Simple hydrogenolysis should give a deoxyzierol, $C_{15}H_{24}$, and this is unlikely to have been reduced further unless a conjugated system was present since isolated double bonds are reduced only with extreme difficulty by this reagent. The unexpected ease of hydrogenolysis in a highly substituted allyl alcohol system[10] is possibly due to preliminary addition of electrons to the diene system rather than to direct hydrogenolysis.



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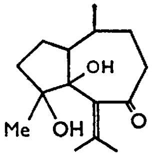

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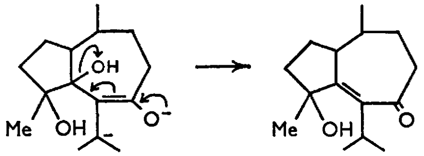
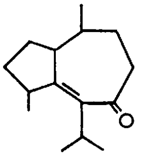


(VII) (VIII)



(IX)

Final confirmation came from an examination of the reactions of dihydrodihydroxyzierone (VI). Reduction of this substance with lithium in liquid ammonia gave a mixture of ketonic products, separated by chromatography. The least polar constituent had no infrared hydroxyl absorption and a carbonyl band at 1687 cm.$^{-1}$. A more polar fraction yielded a substance, $C_{15}H_{24}O_2$, subliming at 125°, $\lambda_{max.}$ 253 mμ (ε 5000), $\nu_{max.}$ 3420, 1652, 1404 cm.$^{-1}$, in accord with formula (VIII). Since hydroxyl groups in saturated systems are not removed at all by the reagent, and highly substituted allyl alcohols are hydrogenolysed only with difficulty,[10] these results are in accord with proximity of the second double bond to the αβ-unsaturated ketone system and we postulate the mechanisms (VI) ⟶ (VII) ⟶ (VIII) ⟶ (IX).

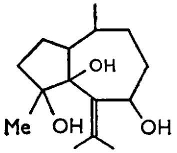
Reduction of the glycol (VI) with lithium aluminium hydride gave the triol (X), $C_{15}H_{26}O_3$, m. p. 146°, which on fission with lead tetra-acetate gave the expected hydroxy-diketone (XI), $C_{15}H_{24}O_3$, containing a new αβ-unsaturated ketone grouping and having $\lambda_{max.}$ 243 mμ (ε 3700), $\nu_{max.}$ 3440, 1712, and 1675 cm.$^{-1}$. Fission of dihydrodihydroxyzierone itself gave the expected product (XII), $C_{15}H_{22}O_3$, as a neutral oil, $\lambda_{max.}$ 240 mμ (ε 9900), $\nu_{max.}$ (in $CS_2$) 1715, 1700, and 1683 cm.$^{-1}$. This gave a bis-2,4-dinitrophenylhydrazone, probably of stucture (XIII) since it still contains a sterically hindered carbonyl group ($\nu_{max.}$ 1715 cm.$^{-1}$) and has $\lambda_{max.}$ 360 mμ (ε 37,000). The triketone (XII) was found to dissolve slowly in aqueous sodium hydroxide, then giving a spectrum typical of an enolic β-diketone salt, $\lambda_{max.}$ 312 mμ (ε 16,000). The same reaction was brought about by chromatography on alumina, the product apparently being largely a tricarbonyl compound because of the weak absorption [$\lambda_{max.}$ 255 mμ (ε 1500)] but immediately soluble in alkali to give a product showing the band at 312 mμ. This product could not be

[8] Büchi, Chow, Matsuura, Popper, Rennhard, and Wittenau, *Tetrahedron Letters*, 1959, No. 6, 14.

[9] Van Tamelen, Levin, Brenner, Wolinsky, and Aldrich, *J. Amer. Chem. Soc.*, 1958, **80**, 501; Barton, de Mayo, and Shafiq, *J.*, 1958, 3314.

[10] Birch, *J.*, 1945, 809.

obtained pure, but from the spectrum of the crude product ($\nu_{max.}$ 3610, 3420, 1717, 1707, 1698 cm.$^{-1}$) it could consist chiefly of a hydroxy-triketone (XIV). When this product was left for several days in aqueous alkali an orange-yellow colour developed, and the absorption was typical of the salt of a vinylogue of a β-diketone [11] [$\lambda_{max.}$ 414 mμ (ε ~25,000); on acidification, $\lambda_{max.}$ 238 mμ]. This is readily explicable by slow cyclisation to the diketone (XV). This compound again could not be obtained pure, probably in part because of loss of acetone and in part because of further hydrolysis. When the solution was boiled, acetone was rapidly evolved (0·65 mole) and the yellow colour disappeared. The product was then a keto-acid, examined as its methyl ester, $C_{13}H_{20}O_3$, $\lambda_{max.}$ 233 mμ (ε 10,200), $\nu_{max.}$ (liquid film) 1737 and 1672 cm.$^{-1}$. The loss of acetone is readily explicable as a reversed-aldol reaction, and the product should have structure (XVI),[12] in agreement with its spectra and analysis; a shoulder on the curve at 3025 cm.$^{-1}$ is in accord with the presence of ethylenic hydrogen and therefore with the presence of an acetyl group before cyclisation.



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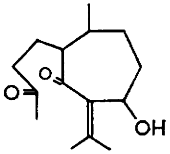

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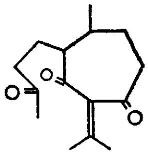

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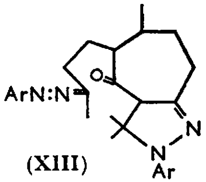
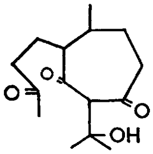


(XIII)

[Ar = $C_6H_3(NO_2)_2$]



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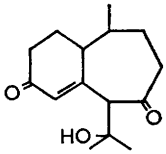

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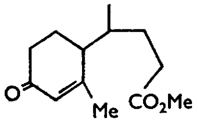

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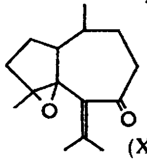

(XVII)

These reactions are only explicable on the formulæ given and rule out, for example, a double bond in the ring-junction. The lack of spectral or chemical evidence for the production of an aldehyde group by fission of the glycols, and the cyclisations observed with the products, support the presence of a 1-methyl group.

Several other reactions may be noted. Hildebrand and Sutherland[4] obtained a dihydro-derivative from zierone semicarbazone by hydrogenation. It appears that the semicarbazone group itself has been reduced, since attempted acid hydrolysis to the ketone gave a hydrocarbon with $\lambda_{max.}$ 238 mμ. Attempts to dehydrate dihydrodihydroxyzierone by acid gave a crystalline compound, $C_{15}H_{22}O_2$, $\lambda_{max.}$ 225 (ε 13,500), 255 mμ (ε 11,000), containing only one αβ-unsaturated carbonyl group ($\nu_{max.}$ 1676, 1646 cm.$^{-1}$ in Nujol) and no hydroxyl group, and yielding a mono-oxime and mono-2,4-dinitrophenylhydrazone. This may be the epoxy-ketone (XVII); the alternative with a five-membered oxide ring is unlikely on steric grounds.

Examination of the nuclear magnetic resonance spectrum of zierone determined by Dr. N. Sheppard, and discussed with him and Dr. A. D. Cross, supports the formula (cf. ref. 1). No olefinic proton can be observed in the region τ 3—6. There is one CHCMe group only (τ 9·05); the other methyl peaks are unsplit and therefore attached to carbon carrying no hydrogen (τ 8·50, 8·30, 7·98). The first of these three peaks is probably due to methyl on the five-membered ring, the last two to the methyl groups of $Me_2C=$ which are in different environments relative to the C=C and C=O because of steric twisting of the group. A peak at τ 7·73 must be due to $CH_2$ alpha to carbonyl group and a double bond.

Biogenetically zierone could be derived from a hydroguaiazulene derivative by

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[11] Dorfman, *Chem. Rev.*, 1953, **53**, 80.

[12] Cf. Wendler, Slates, Tishler, *J. Amer. Chem. Soc.*, 1951, **73**, 3816.

migration, as suggested by Barton and Gupta,[1] or more probably, in view of the crowded system generated, by oxidative opening of the cyclopropane ring in a compound of the gurjunene–aromadendrene type which would be expected to open in the right way.[8]

In order to avoid confusion we suggest that the parent azulene of structure (V) be named allozierazulene.

## EXPERIMENTAL

Ultraviolet spectra were measured for ethanol solutions, unless otherwise stated.

*Zierone and Zierol.*—Steam-distillation of the leaves of *Zieria macrophylla* (from Tasmania) gave a greenish-brown essential oil (280 g.) which was distilled. The fraction of b. p. 94—113°/0·3 mm. with semicarbazide acetate gave zierone semicarbazone (126 g.), m. p. 181°, $\lambda_{max.}$ 246 mμ (ε 12,380). Steam-distillation of the pure semicarbazone from 10% oxalic acid solution gave colourless zierone, b. p. 100°/0·5 mm., $\nu_{max.}$ (film) 1678, 1592 cm.$^{-1}$ or $\nu_{max.}$ (in $CCl_4$) 1680, 1591 cm.$^{-1}$; its 2,4-dinitrophenylhydrazone had m. p. 98°, $\lambda_{max.}$ 372 (ε 23,450).

Reduction of zierone by the usual procedure with lithium aluminium hydride gave *zierol*, b. p. 91—94°/0·1 mm., $n_D^{24}$ 1·5200, $\lambda_{infl.}$ 228 mμ (ε 5000) (Found: C, 82·0; H, 11·0. $C_{15}H_{24}O$ requires C, 81·8; H, 10·9%).

Zierone (60 mg.) or zierol (60 mg.) consumed 1·21 and 2·13 mol., respectively, of perbenzoic acid in ether in 23 hr. at 0°.

*Zierazulene.*—Zierol (4·5 g.) was heated to 140° with powdered potassium hydrogen sulphate and then distilled slowly at 0·5 mm. A pale yellow oil resulted (2·2 g.), having b. p. 71—74°/0·1 mm., $\lambda_{max.}$ 238 mμ, ε 5720. This substance (2·2 g.) was heated with 10% palladised charcoal (300 mg.) to 275—280° under nitrogen for 4 hr. The violet mixture was cooled, extracted with a little light petroleum, and chromatographed on alumina in light petroleum. The first eluate was rejected, the subsequent violet solution extracted with syrupy phosphoric acid (3 × 5 c.c.), and the extract added to ice (30 g.). The azulene was extracted with light petroleum and rechromatographed on alumina. The violet azulene (200 mg.) with trinitrobenzene (200 mg.) in ethanol (20 c.c.) gave the zierazulene–trinitrobenzene complex as maroon needles, m. p. 122·5° (Found: C, 61·6; H, 5·5. Calc. for $C_{21}H_{21}N_3O_6$: C, 61·3; H, 5·1%). The complex (50 mg.) in cyclohexane (5 c.c.) was chromatographed on alumina and the azulene thus obtained treated with picric acid (25 mg.) in the minimum of ethanol to give zierazulene picrate as dark brown needles, m. p. 118—119° (Found: C, 58·9; H, 5·1. Calc. for $C_{21}H_{21}N_3O_7$: C, 59·0; H, 4·9%). Zierazulene was regenerated from the trinitrobenzene complex (5·16 mg., ≡ 2·49 mg. of azulene) as above in spectroscopic grade cyclohexane and made up to 25 c.c.; the following spectrum was observed in the ultraviolet: $\lambda_{max.}$ 248, 290, 335, 348 mμ ($\varepsilon_{max.}$ 50,900, 100,000, 6512, 9200), $\lambda_{infl.}$ 281, 310, 315 mμ ($\varepsilon_{max.}$ 87,600, 7940, 4030). The visible spectrum showed a peak at $\lambda_{max.}$ 546, $\lambda_{infl.}$ 582, 634, and $\lambda_{min.}$ 406 mμ.

(K ± 1)-*Zierazulene.*—Hydroxymethylenezierone (3·5 g.) in methanol (55 c.c.) was hydrogenated over 10% palladised charcoal (500 mg.) for 3 hr., 1075 c.c. of hydrogen (*ca.* 3 mol.) being taken up. After filtration and removal of the solvent the product was reduced with sodium (6·5 g.) and ethanol (75 c.c.) and worked up as usual after concentration and dilution with water (400 c.c.). The product was a pale yellow oil (2·62 g.). Part (1·6 g.) of it was heated with 10% palladised charcoal (250 mg.) under nitrogen to 295—300° for 4 hr. The cooled mixture was extracted with light petroleum, and the extract chromatographed as above on alumina and shaken with phosphoric acid. The (*K* ± 1)-methylzierazulene (230 mg.) removed was wine-red in solution and was converted into the trinitrobenzene complex, m. p. 156·5°, maroon needles (Found: C, 62·0; H, 5·4. Calc. for $C_{22}H_{23}N_3O_6$: C, 62·1; H, 5·4%). A solution in cyclohexane, prepared as above, had $\lambda_{max.}$ 247, 294, 313, 338, 354 mμ (log ε 4·72, 5·09, 4·16, 3·98, 4·08), $\lambda_{infl.}$ 284, 327 mμ (log ε 4·99, 3·80). The visible spectrum showed $\lambda_{max.}$ 534 mμ, $\lambda_{infl.}$ 570, 622 mμ. The picrate, prepared as above, formed dark brown needles, m. p. 138—139° (Found: C, 59·8; H, 5·2. Calc. for $C_{22}H_{23}N_3O_7$: C, 59·9; H, 5·2%).

(K)-*Methylzierazulene.*—Zierone (5·0 g.) in ether (45 c.c.) was added to a Grignard reagent from methyl iodide (9·5 g.). Addition of aqueous ammonium chloride and working up in the usual manner gave an oil (5·1 g.) which was extracted with the Girard P reagent to remove ketonic material (0·42 g.) which gave rise to zierone semicarbazone. The neutral fraction (1·0 g.) and 10% palladised charcoal (180 mg.) were heated to 265° under nitrogen for 4 hr.

The blue-violet azulene (10 mg.), worked up as above, gave rise to (K)-*methylzierazulene–trinitrobenzene complex*, m. p. 128°, $\lambda_{max.}$ 560 mμ, $\lambda_{infl.}$ 630 mμ (Found, on a 2 mg. sample: C, 62·6; H, 6·2. $C_{22}H_{23}N_3O_6$ requires C, 62·1; H, 5·4%).

*Oxidation of Hydroxymethylenezierone.*—To a solution of hydroxymethylenezierone,[3] b. p. 112—114°/1 mm., $\lambda_{max.}$ 321 mμ (ε 10,000) (3·3 g.), in ethanol (25 c.c.) was added 10% aqueous sodium hydroxide (40 c.c.), followed by 10% hydrogen peroxide (20 c.c.). After the reaction had subsided the mixture was heated on the steam-bath for 10 min., then cooled, and further hydrogen peroxide (10 c.c.) was added. After being left overnight, acidification with sulphuric acid deposited a gum which slowly crystallised. The crude product (3·2 g.) was digested with warm light petroleum for 30 min. and the solid so obtained (2·75 g.) had m. p. 149—150°. Three crystallisations from aqueous ethanol gave colourless prisms of the *acid* (II), m. p. 151·5° (Found: C, 67·8; H, 8·6%; equiv., 135. $C_{15}H_{22}O_4$ requires C, 67·8; H, 8·3%; equiv., 135).

Reduction of this acid (1·62 g.) in dry butanol (200 c.c.) with sodium (12 g.), and separation of the acid product, gave another *acid* (1·2 g.), forming colourless plates from ethanol (Found: C, 67·2; H, 9·0. $C_{15}H_{24}O_4$ requires C, 67·2; H, 9·2%).

The acid $C_{15}H_{22}O_4$ (300 mg.) in ether (50 c.c.) was added slowly to lithium aluminium hydride (320 mg.) in ether (60 c.c.). After 2 hours' refluxing the mixture was worked up as usual to give a *diol* as a viscous oil (200 mg.) in the neutral portion of the product (Found: C, 75·8; H, 11·1. $C_{15}H_{26}O_2$ requires C, 75·6; H, 11·0%). A small acidic fraction (50 mg.) crystallised from benzene and appeared to be a *hydroxy-acid* (50 mg.); it had m. p. 126° (ethanol) (Found: C, 71·6; H, 9·7. $C_{15}H_{24}O_3$ requires C, 71·4; H, 9·6%).

The above diol (200 mg.) in ethyl acetate (5 c.c.) was ozonised for 1 hr. at −10°, and the ozonide reduced with palladised charcoal and hydrogen. After filtration, water (5 c.c.) was added and the mixture distilled into a solution of 2,4-dinitrophenylhydrazine in 2N-hydrochloric acid. The product was chromatographed in benzene on alumina (grade 0), to give acetone 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 125°. No hydroxyacetone derivative was detected.

*Dihydrodihydroxyzierone.*—To a solution of osmium tetroxide (1·0 g.) in dry benzene (10 c.c.) was added zierone (0·85 g.) in benzene (10 c.c.) and pyridine (1·0 c.c.). After 3 days the brown crystalline precipitate was filtered off; addition of ether to the filtrate gave more of the product (total 1·65 g.). The substance (1·65 g.) in methylene chloride (25 c.c.) was vigorously shaken with 1% potassium hydroxide solution (100 c.c.) containing mannitol (10 g.). The organic layer was worked up as usual to give *dihydrodihydroxyzierone* (VI) (0·52 g.) as laths, m. p. 126° (Found: C, 71·2; H, 9·5. $C_{15}H_{24}O_3$ requires C, 71·4; H, 9·5%). The substance (20 mg.) was treated with 0·2N-aqueous periodic acid (5 c.c.) in the usual way, 1·01 and 1·00 mol. being consumed in two runs.

The zierone–osmium tetroxide complex (1·65 g.) obtained as above was treated in ether (100 c.c.) with lithium aluminium hydride (2 g.) in boiling ether (250 c.c.) for 3 hr. To the mixture was added 20% sulphuric acid (50 c.c.), and the solution was filtered and evaporated. The resulting oil was chromatographed on alumina in light petroleum with increasing proportions of ether. After a considerable gummy fraction, the fraction (165 mg.) eluted with pure ether crystallised and was recrystallised from light petroleum to give *dihydrodihydroxyzierol* (X), m. p. 146°, λ 207 mμ (ε 6400) (Found: C, 70·7; H, 10·1. $C_{15}H_{26}O_3$ requires C, 70·9; H, 10·2%). The same substance was obtained by reduction of dihydrodihydroxyzierone with lithium aluminium hydride in the standard manner.

*Wolff–Kishner Reduction of Zierone Semicarbazone.*—Zierone semicarbazone (350 mg.), sodium hydroxide (0·5 g.), and hydrazine hydrate (0·5 c.c.) were heated with diethylene glycol (7 c.c.) on the steam-bath for 2 hr. and then at 260° for 3 hr. with slow distillation, the volume being kept constant by addition of diethylene glycol. The distillate (about 15 c.c.) was added to water (15 c.c.) and extracted with light petroleum (b. p. 40—60°) (2 × 20 c.c.). The resulting oil (130 mg.) was added to a further 55 mg. similarly obtained from the reaction residue and chromatographed on alumina (grade H). The first eluate in light petroleum (19 mg.) was presumably hydrocarbon; elution of the main fraction (60 mg.) required the addition of ether (10%) to the solvent. The *base* crystallised from aqueous methanol as needles, m. p. 91—94°, $\lambda_{max.}$ 228 mμ, ε 5300 (Found: C, 77·6; H, 9·9. $C_{15}H_{24}N_2$ requires C, 77·6; H, 10·4%). It was immediately soluble in dilute hydrochloric acid and was precipitated by alkali.

*Reduction of Zierol.*—Zierol (170 mg.) in ether (25 c.c.) and ethanol (1 c.c.) was added to liquid ammonia (50 c.c.). Lithium (300 mg.) was added in 1½ hr. with stirring. The mixture was worked up with aqueous ammonium chloride, affording an ether-soluble oil (150 mg.). This was chromatographed on alumina (grade H) in light petroleum (b. p. 40—60°); the main *hydrocarbon* fraction (120 mg.) was in the first eluate; it had $\varepsilon_{210}$ 8000, $\varepsilon_{220}$ 5500, $\varepsilon_{230}$ 3500 (Found: C, 87·8; H, 12·0. $C_{15}H_{24}$ requires C, 88·2; H, 11·8. $C_{15}H_{26}$ requires C, 87·4; H, 12·6%). The mass spectrum showed prominent peaks at mass numbers 204 and 206. Ozonolysis of the mixture (100 mg.) and conversion of the product into the 2,4-dinitrophenylhydrazone gave the derivative of acetone (30 mg.) as the only recognisable product.

*Reactions of Dihydrodihydroxyzierone* (VI).—(i) *Reduction.* The diol (380 mg.) was added to liquid ammonia (50 c.c.) containing lithium (160 mg.). After 2 hr. the product was obtained by addition of aqueous ammonium chloride and ether-extraction. It was chromatographed on alumina (grade H; 15 g.) in ether, giving three fractions which from their rates of elution seemed to be distinct: A (136 mg.), $\nu_{\max.}$ 1687 cm.$^{-1}$ (shoulder 1700 cm.$^{-1}$); B (81 mg.); and C (120 mg.), $\nu_{\max.}$ 3500, 3420, 1720, 1695 cm.$^{-1}$. Fraction B crystallised from light petroleum (b. p. 60—80°) and sublimed rapidly at 125° in the m. p. tube; this *substance* had $\lambda_{\max.}$ 253 m$\mu$ ($\varepsilon$ 5000), $\nu_{\max.}$ 3405, 1653, and 1404 cm.$^{-1}$ (in Nujol) (Found: C, 76·5; H, 10·1. $C_{15}H_{24}O_2$ requires C, 76·3; H, 10·2%).

(ii) *Oxidation with lead tetra-acetate.* The diol in acetic acid was treated with slightly more than one mol. of lead tetra-acetate in a rapid reaction (20 min.). The mixture was worked up by addition of water and extraction with ether; the acetic acid was removed by washing with sodium hydrogen carbonate solution, the ethereal solution dried, and the solvent carefully removed in a vacuum. The residual *triketone* (XII) (Found: C, 71·8; H, 8·8. $C_{15}H_{22}O_3$ requires C, 72·0; H, 8·8%) gave a "*bis-2,4-dinitrophenylhydrazone*" (?XIII), m. p. 210—212° (decomp.) (from ether–methanol) (Found: C, 53·3; H, 4·9. $C_{27}H_{30}N_8O_9$ requires C, 53·1; H, 4·9%); this crystallised from benzene as a *solvate* (Found: C, 57·55; H, 5·2. $C_{27}H_{30}N_8O_9,C_6H_6$ requires C, 57·55; H, 5·2%).

This triketone (150 mg.) was chromatographed on active alumina in ether–light petroleum (b. p. 40—60°) (1 : 4). Elution with ether–methanol (20 : 1) gave (mainly) a hydroxy-triketone (? XIV) (155 mg.), $\lambda_{\max.}$ 255 m$\mu$ ($\varepsilon$ 1500) $\nu_{\max.}$ 3610, 3430, 1717, 1707, 1698 cm.$^{-1}$ (in $CS_2$). The compound was immediately soluble in alkali [$\lambda_{\max.}$ 312 m$\mu$ ($\varepsilon$ 16,000)].

The triketone (200 mg.) in ether (20 c.c.) was shaken for 5 min. with 10% aqueous potassium hydroxide (10 c.c.). The ether layer gave unchanged triketone (150 mg.) on evaporation. Acidification of the aqueous layer gave a mixture of unchanged triketone and hydroxy-triketone (45 mg.), $\lambda_{\max.}$ 240 m$\mu$ ($\varepsilon$ 4500; neutral), $\lambda_{\max.}$ 311 m$\mu$ ($\varepsilon$ 16,000; alkaline), $\nu_{\max.}$ 3700—2400 (broad) 1720—1700 (several peaks), 1673 cm.$^{-1}$ (liquid film).

A solution of the triketone (75 mg.) in 10% aqueous sodium hydroxide (10 c.c.) and methanol (10 c.c.) was steam-distilled under nitrogen into Brady's reagent. The ketone derivative obtained (50 mg.) was that of acetone (m. p. and mixed m. p. 124—126°). The residual alkaline solution was washed with ether and acidified and the resulting acid (65 mg.) taken up in ether. It could not be crystallised, but had $\nu_{\max.}$ 1709, 1672 cm.$^{-1}$, $\lambda_{\max.}$ 234 m$\mu$, $\varepsilon$ 10,200. It was converted into the *methyl ester* (XVI) by brief reaction with ethereal diazomethane and was purified by chromatography on deactivated alumina in light petroleum (Found: C, 69·7; H, 8·85. $C_{13}H_{20}O_3$ requires C, 69·6; H, 8·9%).

*Fission of Dihydrodihydroxyzierol.*—The triol (X) (175 mg.) in acetic acid (1 c.c.) was treated with lead tetra-acetate (slightly more than 1 mol.). After 30 min. the product (152 mg.) was worked up in the usual way. After being washed with aqueous sodium hydroxide the ether solution was dried and carefully evaporated, to give the *ketol* (XI) (125 mg.) (Found: C, 71·5; H, 9·2. $C_{15}H_{24}O_3$ requires C, 71·4; H, 9·5%).

*Hydrogenation of Zierone Semicarbazone.*—Zierone semicarbazone (1·64 g.) in 10 : 1 ethanol–acetic acid (75 c.c.) was shaken under hydrogen with Adams catalyst (150 mg.). Uptake ceased sharply at 1·0 mol. Filtration, concentration, and dilution with water gave the dihydro-derivative as the alcohol solvate,[4] m. p. 99—101°, $\lambda_{\max.}$ 233 m$\mu$ ($\varepsilon$ 9300).

The dihydro-derivative (1·50 g.) was steam-distilled for 40 min. with 10% aqueous oxalic acid (50 c.c.). Saturation of the distillate with sodium chloride and extraction with light petroleum (b. p. 40—60°) (2 × 25 c.c.) gave a *hydrocarbon* (1·03 g.), $\lambda_{\max.}$ 238 m$\mu$ ($\varepsilon$ 11,800), $\nu_{\max.}$ 3075, 3025, 1657, 1615, 1602, 888, 839 cm.$^{-1}$ (liquid film) (Found: C, 89·3; H, 11·0. $C_{15}H_{22}$ requires C, 89·1; H, 10·9%).

*Dehydration of Dihydrodihydroxyzierone.*—Dihydrodihydroxyzierone (132 g.) was steam-distilled for 30 min. with 10% aqueous oxalic acid (15 c.c.). The distillate, saturated with sodium chloride, was extracted with ether (2 × 25 c.c.), giving a *ketone*, m. p. 77—80° (from aqueous methanol), $\lambda_{max.}$ 225 mμ, ε 13,500 and 255 mμ, ε 11,000; $\nu_{max.}$ 1676, 1646 cm.$^{-1}$ (in Nujol), 1652 cm.$^{-1}$ (in $CS_2$) (Found: C, 77·1; H, 9·4. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·5%). The *mono*-2,4-*dinitrophenylhydrazone*, crystallised from aqueous methanol, had m. p. 180°, solidifying, and remelting at 206°, and $\lambda_{max.}$ 379 mμ (ε 24,000) (Found: C, 61·6; H, 6·2. $C_{21}H_{26}N_4O_5$ requires C, 61·4; H, 6·3%). The *mono-oxime*, crystallised from benzenene–light petroleum (b. p. 40—60°), had m. p. 150—152°, $\lambda_{max.}$ 243 mμ (ε 16,100) (Found: C, 71·0; H, 9·2. $C_{15}H_{23}O_2N$ requires C, 72·3; H, 9·2%).

The ketone (25 mg.) on reduction with lithium aluminium hydride (25 mg.) in ether overnight at room temperature gave an *alcohol* (20 mg.), m. p. 140—142° (from light petroleum), $\lambda_{max.}$ 207 mμ (ε 6500), $\nu_{max.}$ 3390 cm.$^{-1}$ (in Nujol) (Found: C, 76·6; H, 10·2. $C_{15}H_{24}O_2$ requires C, 76·3; H, 10·2%).

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