303. *The Hydroxylation of Some αβ-Unsaturated Ketones by Molecular Oxygen.*

By R. Howe and F. J. McQuillin.

(+)-*epi*-α-Cyperone (Ia) and its 11 : 12-dihydro-derivative (Ib) are autoxidised in the presence of base, to give the 6-hydroxy-ketones in good yield. Under similar conditions (+)-α-cyperone (IX) is dehydrogenated and oxidised to give in small yield a hydroxy-derivative of the trienone (IIIa). Observations are made on the mechanism of oxidation and the influence of the 7-side-chain orientation. (+)-*epi*-α-Cyperone is similarly hydroxylated by the action of alkaline persulphate.

Cardwell and McQuillin,[1] in examining the action of aqueous-alcoholic alkali on (+)-*epi*-α-cyperone (Ia), obtained a crystalline hydroxylation product, $C_{15}H_{22}O_2$, $\lambda_{max.}$ 250 mμ, ν 3500 (OH), 1653 (>C:C·C:O) and 887 cm.$^{-1}$ (>C:CH_2). Formation of a derivative of the trienone (IIIa) by the action of 2 : 4-dinitrophenylhydrazine in ethanolic hydrochloric acid was taken to indicate hydroxylation at position 6 or 7. Resistance of the hydroxy-ketone to oxidation by manganese dioxide[2] and to isomerisation by alkali to the 3 : 6-diketone as with 6-hydroxy-steroidal 4-en-3-ones[2,3] was thought to contraindicate 6-hydroxylation. Oxidation by chromic acid has now been shown to lead to a diketone which has $\lambda_{max.}$ 257·5 mμ characteristic of the 4-ene-3 : 6-dione (IVa) (cf., *e.g.*, Fieser[4]) and is readily isomerised by alkali to a new diketone, $\lambda_{max.}$ 275·5 mμ, in which the terminal methylene absorption (895 cm.$^{-1}$) of the parent diketone has disappeared. The isomerised diketone is clearly formed from a diketone (IVa) by enolisation and conjugation of the side-chain double bond. The new carbonyl group and the hydroxyl group in the parent hydroxy-ketone must therefore be at position 6. The isomerised diketone would be expected to have a structure (V). Treatment of the parent diketone (IVa) with acid also gave this isomerised product since the ketones (IVa) and (V) gave the same mono-2 : 4-dinitrophenylhydrazone. The orientation of the hydroxyl group in the hydroxy-ketone (IIa) is discussed below.

(+)-11 : 12-Dihydro-*epi*-α-cyperone[5] (Ib) has similarly been found to be autoxidised in aqueous-alcoholic alkali. The product is shown to be the hydroxy-ketone (IIb) by dehydration with 2 : 4-dinitrophenylhydrazine in ethanolic hydrochloric acid to the (+)-β-cyperone derivative[6] (IIIb) and by oxidation to a diketone (IVb). The latter was isomerised with alkali to the more stable 7β-*iso*propyl epimer (VII), and the two diketones (IVb) and (VII) gave the same 2 : 4-dinitrophenylhydrazone.

The hydroxy-ketones (IIa) and (IIb) are formed in the presence of alkali hydroxide, or (see below) in the presence of sodium *iso*propoxide or other bases, and they were recovered

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[1] Cardwell and McQuillin, *J.*, 1955, 525.

[2] Cf. Amendolla, Rosenkranz, and Sondheimer, *J.*, 1954, 1226.

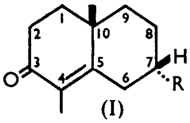
[3] Rosenkranz, Velasco, and Sondheimer, *J. Amer. Chem. Soc.*, 1954, **76**, 5024; Ehrenstein, *J. Org. Chem.*, 1940, **5**, 318.

[4] Fieser, *J. Amer. Chem. Soc.*, 1953, **75**, 4377.

[5] Howe and McQuillin, *J.*, 1956, 2670.

[6] *Idem*, *J.*, 1955, 2423.

unchanged from refluxing aqueous-alcoholic potassium hydroxide. This resistance to epimerisation at position 6, or to isomerisation to the 3 : 6-dione, which may take up a structure (VI) in which the 7α-substituent is equatorial, is taken to indicate a stable orientation for the 6-hydroxyl group.



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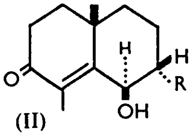

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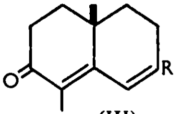

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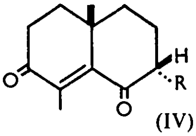

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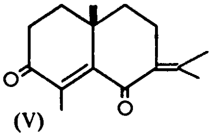

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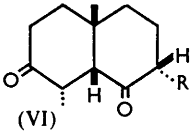

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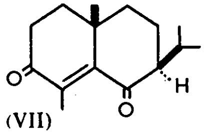

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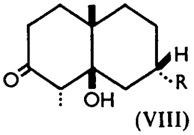

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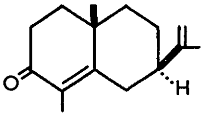

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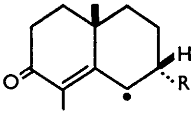

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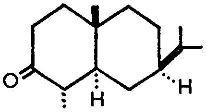
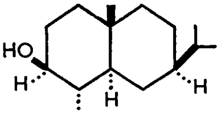


(XI)



(XII)

(I)—(IV), (VIII), and (X); a, R = CMe:CH$_2$; b, R = Pr^i.

(+)-*epi*-α-Cyperone gives [7] an optical rotatory dispersion curve of the same type as, *e.g.*, 8α-testosterone, *i.e.*, ring B is deformed by the large 7α-substituent from a chair towards a boat conformation. Inspection shows that in the boat form, and particularly in intermediate structures, a 6β- introduces less steric interaction than a 6α-substituent. This inversion of the usual order of stability has been encountered by Crawshaw, Henbest, Jones, and Wagland [8] with 11-hydroxy-9β-steroids which also contain a boat *cyclo*hexane ring.

In steroidal 4 : 5-unsaturated 3-ketones a 6β- makes a much more negative rotational contribution than a 6α-hydroxyl substituent.[4, 9] This corresponds with Klyne and Stokes's generalisation [12] which Crawshaw, Henbest, Jones, and Wagland were able to apply to their 9β-steroid. The observed differences, ΔM_{5461} for (Ia)–(IIa) and (Ib)–(IIb) are −285° and −345° respectively. A 6β-hydroxyl substituent has also been found [2] to lower the ultraviolet absorption maximum of the 4-en-3-one system by *ca.* 4 mμ and the molar extinction by *ca.* 2000, an effect clearly due to 6β-OH : 10β-Me interaction. For our ketones the results are:

	$\lambda_{\text{max.}}$	ε		$\lambda_{\text{max.}}$	ε
(Ia)	252·5 mμ	14,450	(Ib)	250 mμ	15,850
(IIa)	250	11,480	(IIb)	247	13,180

Thus, without constituting proof, these three independent lines of argument combine in favouring a 6β-orientation for the hydroxyl group in the ketones (IIa) and (IIb).

Oxygen uptake by the ketones (Ia) and (Ib) effectively ceased after absorption of 1 mol., to give almost exactly 50% of the hydroxy-ketone, together with more highly oxidised, partly acidic material. Addition of sodium dithionite before oxygenation gave a cleaner reaction in which unoxidised material could largely be recovered. Addition of dithionite was designed to remove peroxide which the unsaturated ketones develop in air. An old specimen of (+)-*epi*-α-cyperone (Ia) gave oxidised material from which the 2 : 4-dinitrophenylhydrazone of the trienone (IIIa) could be obtained in small yield, although no crystalline hydroxy-ketone could be isolated.

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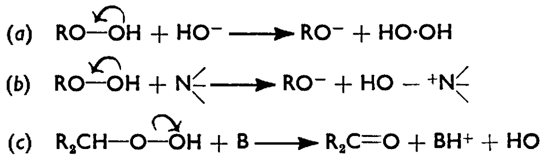
[7] Djerassi, Riniker, and Riniker, *J. Amer. Chem. Soc.*, 1956, **78**, 6362, 6377.
[8] Crawshaw, Henbest, Jones, and Wagland, *J.*, 1955, 3420.
[9] Balant and Ehrenstein, *J. Org. Chem.*, 1952, **17**, 1587.

As a convenient preparative method, the ketols (VIIIa)[10] and (VIIIb)[5] may be dehydrated and oxidised directly to the respective hydroxy-ketones (IIa) and (IIb) by some hours' refluxing in benzene–propanol–sodium *iso*propoxide in contact with air or oxygen.

These ready oxidations appear to require the enone structure. A related saturated ketone, (+)-tetrahydro-α-cyperone[5] (XI), failed to absorb oxygen when shaken in aqueous-alcoholic alkali and was recovered. Refluxing it in benzene–propan-2-ol with sodium *iso*propoxide similarly failed to effect oxidation, but led, not surprisingly, to a mixture of epimeric alcohols by alkoxide reduction of the keto-group. One of these alcohols was obtained crystalline by way of the 3 : 5-dinitrobenzoate which was conveniently hydrolysed by passage through alkaline alumina.[11] From its manner of preparation and from the rotational change on dinitrobenzoylation[12,13] (ΔM_{5461} + 242°) this tetrahydro-α-cyperol is given the structure (XII) with the 3β-alcohol configuration.

The following observations have been made about the mechanism of these oxidations: (+)-*epi*-α-Cyperone is oxidised to the hydroxy-ketone (IIa) in aqueous piperidine or in dilute aqueous *tert.*-butyl-alcoholic potassium hydroxide, but more slowly than in concentrated aqueous-ethanolic potassium hydroxide. With sodium *tert.*-butoxide in *tert.*-butyl alcohol oxygen uptake is very rapid giving, however, largely acidic and strongly peroxidic products. No measurable oxygen uptake occurred with freshly reduced platinum in ethyl acetate or ethanolic hydrochloric acid [the dihydro-ketone (Ib) was used in the last experiment].

These observations, as well as the position of hydroxylation, point to the enolate ion, but not the conjugate acid, as the oxygen acceptor, either directly or, as in other instances of oxidation of an enol,[14] *via* a mesomeric radical (X). The absence of oxygen uptake in ethyl acetate with platinum, conditions which facilitate oxidation of tetrahydrocarbazoles by a reputedly free-radical mechanism,[15] and the clean reaction after removal of peroxide with dithionite may be taken to contraindicate, without excluding, a radical mechanism. It is clear, however, that the first product is probably the 6-hydroperoxide (or its anion) which is reduced by hydrolysis[16] (*a*) or, if present, by nitrogenous base:[17] a possible first step is shown at (*b*), or in the presence of strong base attack may be at the methine group[18] as in (*c*).



(*a*) $\mathrm{RO{-}OH + HO^- \longrightarrow RO^- + HO{\cdot}OH}$

(*b*) $\mathrm{RO{-}OH + N\!< \longrightarrow RO^- + HO - {}^{+}N\!<}$

(*c*) $\mathrm{R_2CH{-}O{-}OH + B \longrightarrow R_2C{=}O + BH^+ + HO^-}$

It is suggested that the extensive oxidation to acidic products in the presence of sodium *tert.*-butoxide is due to reaction (*c*), the rapid oxidation arising from the high enolate concentration.

That oxidation occurs in aqueous *tert.*-butyl alcohol is taken to indicate that autoxidation is not a secondary consequence of attack on the alcohol solvent (as alkoxide ion).

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[10] McQuillin, *J.*, 1955, 528.

[11] Castells and Fletcher, *J.*, 1956, 3245.

[12] Klyne and Stokes, *J.*, 1954, 1979.

[13] Barton and Nickon, *J.*, 1954, 4665.

[14] Cf. Robertson and Waters, *J.*, 1948, 1574; Hinshelwood and Shorter, *J.*, 1950, 3276; Shorter, *J.*, 1950, 3425; Speakman and Waters, *J.*, 1955, 40; Allen and Waters, *J.*, 1956, 1132.

[15] Witkop and Patrick, *J. Amer. Chem. Soc.*, 1950, **72**, 633; 1951, **73**, 2188; Witkop, *ibid.*, 1950, **72**, 1428.

[16] Cf. Farmer and Sundralingam, *J.*, 1942, 121.

[17] Riley, Rust, and Vaughan, *J. Amer. Chem. Soc.*, 1948, **70**, 1336; Capp and Hawkins, *J.*, 1953, 4106.

[18] Kornblum and de la Mare, *J. Amer. Chem. Soc.*, 1951, **73**, 880; Agnello, Pinson, and Laubach, *ibid.*, 1956, **78**, 4756.

This does not exclude oxidation of the alcohol solvent as a possible further mode of reduction of the hydroperoxide.[19]

(+)-α-Cyperone (IX) and (+)-β-cyperone (IIIb) also absorbed oxygen in aqueous-alcoholic alkali, the latter rather slowly, but despite absorption of up to 3 mols. these ketones were largely recovered unchanged. The oxidised material from α-cyperone furnished a crystalline substance A, $C_{15}H_{20}O_2$, $\lambda_{max.}$ 304·5 mμ, $[\alpha]_{5461}$ +764°, in small yield. From the physical constants this is regarded as a hydroxy-derivative of the trienone (IIIa); the position of the hydroxyl group, possibly 2, has not, however, been established. From the oxidation of β-cyperone two crystalline substances, B, $C_{15}H_{20}O_2$, $\lambda_{max.}$ 308·5 mμ, $[\alpha]_{5461}$ +655·4°, and C, $C_{15}H_{22}O_2$, $\lambda_{max.}$ 294·5 mμ, $[\alpha]_{5461}$ +863°, were isolated. The former showed no hydroxyl group absorption in the infrared spectrum and is regarded as a keto-derivative of the parent β-cyperone; substance C may be the corresponding hydroxy-ketone.

Taken together, these experiments indicate that (+)-α-cyperone is converted into the product A by further oxidation of the trienone as intermediate. Formation of the trienone may arise by elimination between a 6β-hydroperoxy-group and the 7α-hydrogen atom or, more probably, by direct transfer of the latter, as hydrion, from the enolate to an acceptor. This is analogous to the known dehydrogenative oxidation of steroidal enones by quinone.[20]

The products A, B, and C account for only a small part of the oxygen consumed. From the amount of unchanged material, in contrast with the oxidation of the *epi*-ketones (Ia) and (Ib), it is clear that the products first formed are in these examples more sensitive to oxidation than the parent ketones. This influence of the stereochemistry at position 7 may be related to the accessibility of the 6α-hydrogen atom in determining the mode of decomposition of a 6-hydroperoxide by route (*c*), followed by further oxidation.

Hydroxylation in good yield has been noted in the alkaline autoxidation of 4 : 4′ : 4″-trinitrotriphenylmethane [19] to the corresponding alcohol. The dehydrogenation of *cyclo*heptadienone by oxygen under strongly alkaline conditions [21] is analogous to the behaviour of (+)-α-cyperone; Ishikawa [22] reports a similar instance in the santonin series, but under acid conditions.

Autoxidation of αβ-unsaturated ketones is known generally to lead to rather complex mixtures.[23] The relatively simple hydroxylation noted above suggested an analogy with the Elbs persulphate oxidation of phenols [24] and of aromatic amines [25] which have reactivity of the same kind as the enol suggested as oxygen acceptor in the present instances. In preliminary experiments this analogy has been verified by oxidation of (+)-*epi*-α-cyperone (Ia) to the same hydroxy-ketone (IIa) by alkaline persulphate and by molecular oxygen. The generality of this reaction is being examined.

EXPERIMENTAL

$[\alpha]_{5461}$ and $\lambda_{max.}$ are for solutions in $CHCl_3$ and EtOH respectively, unless otherwise stated.

Autoxidation of (+)-epi-α-*Cyperone*.—(a) *In air*. Cardwell and McQuillin's procedure [1] was repeated to give, from (+)-*epi*-α-cyperone (1·2 g.), neutral material (0·93 g.), b. p. 120—125°/0·1 mm., n_D^{20} 1·5420, $[\alpha]_{5461}$ +92·4° (*c* 2·6), which by chromatography on alumina gave (+)-6-*hydroxy*-7β(H)*eudesma*-4 : 11-*dien*-3-*one* (IIa) as needles, m. p. 63—64° (0·54 g.) (from light petroleum), $[\alpha]_{5461}$ +88·2° (*c* 4·2) $\lambda_{max.}$ 250 mμ (log ε 4·06) (Found: C, 76·55; H, 9·55. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·4%). This gave (+)-eudesma-4 : 6 : 11-trien-3-one (IIIa)

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[19] Cf. Hawthorne and Hammond, *J. Amer. Chem. Soc.*, 1955, **77**, 2549.

[20] Wettstein, *Helv. Chim. Acta*, 1940, **23**, 388; Dauben, Eastham, Micheli, Takemura, Mandell, and Chemerda, *J. Amer. Chem. Soc.*, 1953, **75**, 3255; Mandell, *ibid.*, 1956, **78**, 3199; Elks, *J.*, 1954, 468.

[21] Van Tamelen and Hildahl, *J. Amer. Chem. Soc.*, 1956, **78**, 4405.

[22] Ishikawa, *J. Pharm. Soc. Jap.*, 1956, **76**, 507.

[23] Cf. Treibs, *Ber.*, 1930, **63**, 2423 and subsequent papers; Hawkins, *J.*, 1955, 3288.

[24] Cf. Baker and Brown, *J.*, 1948, 2303.

[25] Boyland, Manson, and Sims, *J.*, 1953, 3623; Boyland and Sims, *J.*, 1954, 980.

2 : 4-dinitrophenylhydrazone, m. p. 228° (from ethyl acetate–ethanol), $\lambda_{max.}$ 259, 331, and 417·5 mμ (log ε, 4·15, 4·28, and 4·58) in $CHCl_3$ as previously described.[1]

(b) *Quantitatively in oxygen.* (i) The ketone (0·725 g.) in ethanol (15 c.c.) and water (4 c.c.) with potassium hydroxide (0·8 g.), shaken in oxygen at room temperature, absorbed 101 c.c. (1·2 mol.) in 18 hr. The recovered neutral material (0·6 g.) by chromatography gave pure hydroxy-ketone (0·35 g.), m. p. 63—64°. (ii) The ketone (0·264 g.) in *tert.*-butyl alcohol (15 c.c.) and water (10 c.c.) with potassium hydroxide (0·175 g.) absorbed 26·4 c.c. of oxygen (1 mol.) in 26 hr. to give a neutral product (0·15 g.) from which the hydroxy-ketone was obtained crystalline (m. p. 63°). (iii) The ketone (0·3 g.) in *tert.*-butyl alcohol (20 c.c.) with sodium (0·2 g.) absorbed 1 mol. of oxygen during 0·5 hr. The product, strongly peroxidic to acidified potassium iodide solution, gave an amorphous acidic product (0·2 g.) and only a small amount (0·05 g.) of material, b. p. 130°/0·1 mm., which failed to crystallise. (iv) The ketone in ethyl alcohol (5 c.c.) and water (5 c.c.) with potassium hydroxide (0·4 g.) and sodium dithionite (0·5 g.) rapidly absorbed oxygen (38 c.c.), during oxidation of the dithionite, then a further 23 c.c. during 3 hr. Salts crystallised from the solution which at first became pink and later colourless. Recovery and chromatography gave a hydroxy-ketone fraction (0·15 g.) which crystallised to give material, m. p. 63°. (v) The ketone (0·5 g.) in piperidine (15 c.c.) and water (10 c.c.) absorbed 76 c.c. of oxygen (1·4 mol) during 90 hr. The neutral product (0·43 g.) gave the hydroxy-ketone (0·28 g.) after chromatography. (vi) The ketone (0·86 g.) in ethyl acetate (10 c.c.) added to Adams platinum oxide (0·2 g.) which had been freshly reduced in ethyl acetate (10 c.c.) failed to absorb oxygen when shaken for 24 hr.

(c) *By long storage in air.* The ketone (0·3 g.) which had been stored in a closed tube for 15 months was distilled and chromatographed, to give an oxidised fraction (0·17 g.), b. p. 115—120°/0·1 mm., n_D^{20} 1·5400, $[\alpha]_{5461}$ +168° (*c* 3·0). Redistillation gave a product which afforded a 2 : 4-dinitrophenylhydrazone, m. p. 202°, purified by chromatography to give (+)-eudesma-4 : 6 : 11-trien-3-one 2 : 4-dinitrophenylhydrazone, m. p. 228—229°, identical with that described above.

(+)-7β(H)-*Eudesma*-4 : 11-*diene*-3 : 6-*dione* (IVa).—The hydroxy-ketone from (+)-*epi*-α-cyperone (0·35 g.) in acetic acid (10 c.c.) was treated with chromic acid (0·2 g.) in water (3·5 c.c.) and kept for 12 hr. Recovery gave (+)-7β(H)-*eudesma*-4 : 11-*diene*-3 : 6-*dione* (IVa), b. p. 100—102°/0·1 mm., n_D^{20} 1·5321, $[\alpha]_{5461}$ +399° (*c* 2·42), $\lambda_{max.}$ 257·5 mμ (log ε 4·08), ν 893 cm.$^{-1}$ (Found: C, 77·35; H, 8·8. $C_{15}H_{20}O_2$ requires C, 77·6; H, 8·6%). The *mono*-2 : 4-*dinitrophenylhydrazone* formed orange needles, m. p. 196—197° (from ethanol), $\lambda_{max.}$ 386·5, 307, and 284 mμ (log ε 4·55, 3·94, 4·18) (Found: C, 61·6; H, 6·0. $C_{21}H_{24}O_5N_4$ requires C, 61·2; H, 5·8%). The diketone (0·1 g.) was recovered unchanged after 1 hour's warming with *o*-phenylenediamine (47 mg.) in ethanol (2 c.c.).

Isomerisation of the Diketone (IVa).—The diketone above (0·25 g.) in ethanol (16 c.c.) and potassium hydroxide (1 g.) in water (2 c.c.) were kept under nitrogen for 15 hr. Recovery gave (+)-*eudesma*-4 : 7(11)-*diene*-3 : 6-*dione*, b. p. 105°/0·1 mm., n_D^{20} 1·5482, $[\alpha]_{5461}$ +59° (*c* 3·0) $\lambda_{max.}$ 275·5 mμ (log ε 4·00) (Found: C, 77·7; H, 8·2. $C_{15}H_{20}O_2$ requires C, 77·6; H, 8·6%), yielding the mono-2 : 4-dinitrophenylhydrazone, m. p. 196—197°, noted above.

Autoxidation of (+)-*Dihydro*-epi-α-*cyperone*.—A solution of (+)-dihydro-*epi*-α-cyperone-(1·6 g.) in ethanol (22 c.c.) and water (8 c.c.) with potassium hydroxide (1·6 g.) was kept for 10 days and then gave a neutral product (1·09 g.), b. p. 120—125°/0·1 mm., n_D^{20} 1·5285, $[\alpha]_{5461}$ +50·7° (*c* 4·2). Chromatographed on alumina this gave, by elution with light petroleum–benzene (3 : 1) (+)-6-*hydroxy*-7β(H)-*eudesm*-4-*en*-3-*one* (IIb), needles (0·68 g.), m. p. 90—91° (from pentane), $[\alpha]_{5461}$ +27·2° (*c* 3·5), $\lambda_{max.}$ 247 mμ (log ε 4·12) (Found: C, 76·2; H, 10·5. $C_{15}H_{24}O_2$ requires C, 76·3; H, 10·2%). The 2 : 4-dinitrophenylhydrazone was identical with that of (+)-β-cyperone, m. p. 232°. The hydroxy-ketone (55 mg.) in ethanol (5 c.c.) with potassium hydroxide (0·6 g.) in water (1 c.c.) was recovered (42 mg.; m. p. 90—91°) after being refluxed for 5 hr. under nitrogen.

(+)-7β(H)-*Eudesm*-4-*ene*-3 : 6-*dione*.—The above hydroxy-ketone (0·25 g.) in acetic acid (7 c.c.) was kept for 12 hr. with chromic acid (0·14 g.) in water (2·5 c.c.). The product, b. p. 100°/0·1 mm., n_D^{20} 1·5173, crystallised to give as needles, (+)-7β(H)-*eudesm*-4-*ene*-3 : 6-*dione* (IVb), m. p. 80° (from light petroleum), $[\alpha]_{5461}$ +304° (*c* 2·5), $\lambda_{max.}$ 256 mμ (log ε 4·05) (Found: C, 77·3; H, 9·4. $C_{15}H_{22}O_2$ requires C, 77·0; 9·4%). The *mono*-2 : 4-*dinitrophenylhydrazone* formed orange needles, m. p. 208—209° (from ethanol), $\lambda_{max.}$ 382, 295, 266 mμ (log ε 4·53, 3·94, 4·13) (Found: C, 61·0; H, 6·3. $C_{21}H_{26}O_5N_4$ requires C, 60·9; H, 6·3%).

Isomerisation of the Diketone (IVb).—The above diketone (0·125 g.) in ethanol (8 c.c.) and water (1 c.c.) with potassium hydroxide (0·5 g.) was kept under nitrogen for 15 hr. Recovery gave (+)-*eudesm-4-ene-3 : 6-dione* (VII), b. p. 100°/0·1 mm., n_{D}^{20} 1·5150, $[\alpha]_{5461}$ +169° (*c* 2·7), $\lambda_{\max.}$ 254·5 mμ (log ε 4·04) (Found: C, 77·1; H, 9·45. $C_{15}H_{22}O_2$ requires C, 77·0; H, 9·4%). The mono-2 : 4-dinitrophenylhydrazone formed orange needles, m. p. 208—209°, as noted above.

Oxidation of the Ketols (VIIa *and* b) *in Propan-2-ol–Sodium Propoxide.*—(*a*) The *epi*-α-cyperone ketol (VIIIa) (0·7 g.) in benzene (10 c.c.) with sodium *iso*propoxide (from sodium, 0·07 g.) in propan-2-ol (5 c.c.) was heated under gentle reflux during 4 hr. Addition of water and recovery gave material, b. p. 130°/0·1 mm., which crystallised to yield (+)-6-hydroxy-7β(*H*)-eudesma-4 : 11-dien-3-one (IIa), m. p. 63°. (*b*) The dihydro-ketol (VIIIb) similarly afforded the corresponding 6-hydroxy-7β(*H*)-eudesm-4-en-3-one (IIb), m. p. 89° (from pentane).

(+)-4β(H)-*Eudesman-3β-ol* (XII).—(−)-4β(H) : 5α(H)-Eudesman-3-one (0·3 g.) in benzene (4 c.c.) was treated with a solution of sodium (0·03 g.) in propan-2-ol (2 c.c.) and refluxed for 8 hr. Recovery gave material, b. p. 95°/0·1 mm., n_{D}^{20} 1·4943, showing strong absorption at 3380 cm.$^{-1}$ and only weak absorption at 1701 cm.$^{-1}$. Chromatography on alumina gave recovered ketone in small amount (eluant, light petroleum), followed by a product (0·23 g.), b. p. 95°/0·1 mm., n_{D}^{20} 1·4940, $[\alpha]_{5461}$ −23·3° (*c* 5·7), eluted by benzene–chloroform (4 : 1). This material afforded a 3 : 5-*dinitrobenzoate* as needles, m. p. 173°, $[\alpha]_{5461}$ +58·6° (*c* 3·4), by fractional crystallisation from methanol (Found: C, 62·8; H, 7·1. $C_{22}H_{30}O_6N_2$ requires C, 63·1; H, 7·2%). The dinitrobenzoate, passed through alkaline alumina (cf. Castells and Fletcher [11]) in benzene–light petroleum followed by benzene, gave (+)-4β(H) : 5α(H)-*eudesman-3β-ol* (XII), b. p. 95°/0·1 mm., m. p. 73° (from pentane), $[\alpha]_{5461}$ +1·5° (*c* 3·8) (Found: C, 80·4; H, 12·5. $C_{15}H_{28}O$ requires C, 80·4; H, 12·5%).

Autoxidation of (+)-α-*Cyperone.*—(*a*) When (+)-α-cyperone (1·7 g.) in ethanol (40 c.c.) was mixed with potassium hydroxide (2 g.) in water (10 c.c.) and shaken in oxygen, it absorbed 246 c.c. (1·4 mol.) in 26 hr. The neutral material recovered (1·04 g.), b. p. 95—130°/0·1 mm., was chromatographed on alumina, to give (i) by light petroleum–benzene (1 : 1) (+)-α-cyperone (0·86 g.) and (ii), by benzene, material (55 mg.) which afforded yellow prisms, A (16 mg.), m. p. 105°, $[\alpha]_{5461}$ +764° (*c* 2·0), $\lambda_{\max.}$ 304·5 mμ (log ε 4·47), from ether–light petroleum (Found: C, 77·9; H, 8·8. Calc. for $C_{15}H_{20}O_2$: C, 77·6; H, 8·6%). (*b*) The ketone (0·77 g.) in ethanol (5 c.c.), water (5 c.c.), and piperidine (10 c.c.) absorbed 250 c.c. of oxygen (3 mol.) during 90 hours' shaking. Recovery and chromatography as above gave recovered α-cyperone (0·49 g.), n_{D}^{20} 1·5280, $\lambda_{\max.}$ 249 mμ (log ε 4·20) and 296—300 mμ (log ε 3·13), and the substance A, m. p. 105°.

Autoxidation of (+)-β-*Cyperone.*—(*a*) The ketone (3·3 g.) in ethanol (45 c.c.), mixed with potassium hydroxide (3·3 g.) in water (14 c.c.), absorbed 498 c.c. of oxygen (1·35 mol.) during 50 hr. Recovery gave 2·15 g. of material, b. p. 100—135°/0·1 mm., which by chromatography gave (i) (+)-β-cyperone (1·56 g.), and (ii), by elution with benzene, an eluate (0·15 g.) which afforded a substance C, pale yellow plates (20 mg.), m. p. 145° (from benzene), $[\alpha]_{5461}$ +863° (*c* 0·9), $\lambda_{\max.}$ 294·5 mμ (log ε 4·41) (Found: C, 76·6; H, 9·65. Calc. for $C_{15}H_{22}O_2$: C, 76·9; H, 9·4%). (*b*) (+)-β-Cyperone (1·8 g.) in ethanol (25 c.c.), mixed with potassium hydroxide (1·8 g.) in water (8 c.c.) and kept for 10 days, gave neutral material (1·3 g.), n_{D}^{20} 1·5627, yielding (i) recovered (+)-β-cyperone (0·7 g.), (ii) substance B (50 mg.), yellow prisms, m. p. 86° (from light petroleum), $[\alpha]_{5461}$ +655·4° (*c* 2·82), $\lambda_{\max.}$ 308·5 mμ (log ε 4·36) (Found: C, 77·6; H, 8·8. Calc. for $C_{15}H_{20}O_2$: C, 77·6; H, 8·6%), whose mono-2 : 4-dinitrophenylhydrazone formed red needles, m. p. 233° (from ethyl acetate), $\lambda_{\max.}$ 404·5, 328, 258 mμ (log ε 4·63, 3·93, 4·15) (Found: C, 60·7; H, 5·8. Calc. for $C_{21}H_{24}O_5N_4$: C, 61·1; H, 5·8%), and (iii) substance C (4 mg.), m. p. 141°.

Persulphate Oxidation.—A solution of (+)-*epi*-α-cyperone (0·8 g.) in ethanol (20 c.c.) was treated with potassium hydroxide (1 g.) in water (6 c.c.), followed by ammonium persulphate (0·8 g.) in water (5 c.c.). After 48 hr. distillation of the recovered material gave a main fraction, b. p. 120—140°/0·1 mm., n_{D}^{20} 1·5398, from which (+)-6-hydroxy-7β(H)-eudesma-4 : 11-dien-3-one was obtained (m. p. 64—65°) by chromatography.

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