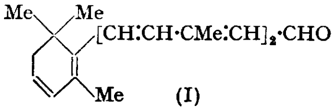
132. *Studies in the Polyene Series. Part XLV.** C_{23}, C_{25} *and* C_{43} *Ketones derived from Retinene*$_1$.

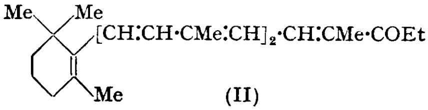
By J. C. Hamlet, H. B. Henbest, and V. Thaller.

The compound obtained by Oppenauer oxidation of vitamin A_1 with diethyl ketone as hydrogen acceptor (which other workers suggested was dehydroretinene$_1$) has been obtained crystalline and shown to be a C_{25} ketone (II). Condensation of retinene$_1$ and acetone leads to the formation of crystalline C_{23} and C_{43} ketones.

A DEHYDRORETINENE$_1$ structure (I) was proposed by Haworth, Heilbron, Jones, Morrison, and Polya (*J.*, 1939, 128) for a carbonyl compound obtained by Oppenauer oxidation of vitamin A_1 (or of retinene$_1$; Morton, Salah, and Stubbs, *Nature*, 1947, **159**, 744) in the presence of diethyl ketone. This structure was suggested chiefly on the basis of light-absorption properties, the analysis of a crystalline oxime, and the fact that no geronic acid was isolated on ozonolysis. When crystalline retinene$_2$ [correctly represented by (I)] and derivatives were prepared from synthetic vitamin A_2 (Farrar, Hamlet, Henbest, and Jones, *J.*, 1952, 2657), differences in physical properties made it certain that the Oppenauer product must have been incorrectly formulated.



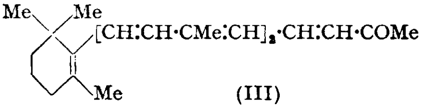
(I)



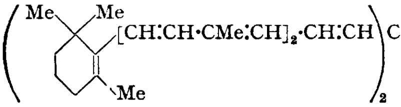
(II)

Repetition of the oxidation experiment followed by chromatography and low temperature crystallization of the chief reaction product afforded a crystalline compound exhibiting light absorption similar to that of the material of Haworth *et al.* This formed a crystalline oxime in good yield and analytical data on the two compounds indicated a $C_{25}H_{36}O$ formula for the parent compound. This would then be represented by the structure (II), being formed by condensation between diethyl ketone and the initially produced retinene$_1$. The position of $\lambda_{max.}$ and the high intensity (relative to retinene$_1$ and retinene$_2$) were in agreement with those expected for a compound with structure (II), and very similar to those recorded with the related C_{23} ketone (see below). An intense band near 1240 cm.$^{-1}$ in the infra-red spectrum indicated a ketonic rather than an aldehydic structure—from the data presented previously (*J.*, 1952, 2657) it was apparent that ketones, but not aldehydes, in this series exhibit such a band in the infra-red region.

The formation of the C_{25} ketone is thus analogous to the synthesis of the C_{23} ketone (III) by Oppenauer oxidation of vitamin A_1 with acetone (Batty, Burawoy, Harper, Heilbron, and Jones, *J.*, 1938, 175). This reaction has been reinvestigated and the C_{23} ketone obtained crystalline (cf. Karrer and Eugster, *Helv. Chim. Acta*, 1951, **34**, 1805); it has also been prepared by condensing retinene$_1$ itself with acetone in the presence of aluminium *tert.*-butoxide, or better, sodium ethoxide.



(III)



(IV)

In the course of purifying the crude C_{23} ketone reaction products by chromatography it was observed that a fairly strongly adsorbed violet band was always present. This was shown to be due to the presence of a C_{43} ketone (IV) by comparison with crystalline material prepared by condensing retinene$_1$ with C_{23} ketone in the presence of alkali. As would be expected, the carbonyl group of this highly unsaturated cross-conjugated ketone was rather unreactive, no oxime being formed under the usual conditions. The relatively

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* Part XLIV, *J.*, 1952, 4089.

low frequency and intensity of the carbonyl stretching vibration in the infra-red spectrum also indicated that the carbon–oxygen bond was tending towards a dipolar link $(>\overset{+}{C}-\overset{-}{O})$ (cf. data on *cyclo*heptatrienone, etc., given in the Experimental section), the positive charge being " spread out " into the unsaturated system by hyperconjugation.

EXPERIMENTAL

The general experimental directions are as given by Farrar, Hamlet, Henbest, and Jones (*loc. cit.*).

4 : 7 : 11-*Trimethyl*-13-(2 : 6 : 6-*trimethyl*cyclo*hex*-1-*enyl*)*trideca*-4 : 6 : 8 : 10 : 12-*pentaen*-3-*one* (C_{25} *Ketone*) (II).—Vitamin A_1 (2 g.), aluminium *tert.*-butoxide (2·4 g.), diethyl ketone (10 g.), and dry " AnalaR " benzene (70 c.c.) were heated under reflux for 48 hours. Aqueous tartaric acid was added to the cooled mixture, and the benzene layer was separated, washed with water, and dried (Na_2SO_4). After removal of the solvent under reduced pressure the residue was chromatographed in pentane on alumina (300 g.) (deactivated with water, 10%). A single, large, orange band separated from dark material held near the top of the column. Elution of this orange band and removal of solvent gave an orange-red oil (1·34 g.), a portion (0·4 g.) of which was crystallized from pentane at −30°. One crystallization gave solid, m. p. 61—63°; a second crystallization from pentane afforded the *ketone* as orange cubes, m. p. 65—66°, changing at this m. p. to needles, m. p. 80—81° (Found : C, 85·6; H, 10·6. $C_{25}H_{36}O$ requires C, 85·15; H, 10·3%). Ultra-violet absorption : Max. 4000 Å; $\varepsilon = 56{,}800$ (for the liquid product, Haworth *et al.*, *loc. cit.*, give $\lambda_{\text{max.}}$ 4010 Å, $\varepsilon = 40{,}600$). Infra-red spectrum : main peaks at 1659 (C:O stretching), 1563 (C:C stretching), 1242, and 962 cm.^{-1}.

The crude ketone (0·54 g.) was converted into the oxime as described for retinene$_2$ oxime (*J.*, 1952, 2668). The yield after one crystallization from methanol was 0·31 g.; further recrystallization gave the *oxime* as yellow needles, m. p. 180—181° (Found : C, 81·5; H, 10·05; N, 4·1. $C_{25}H_{37}ON$ requires C, 81·7; H, 10·15; N, 3·8%). Ultra-violet absorption : Max. 3820 Å; $\varepsilon = 73{,}200$ (Haworth *et al.* record m. p. 176—177°; $\lambda_{\text{max.}}$ 3860 Å; $\varepsilon = 73{,}500$).

6 : 10-*Dimethyl*-12-(2 : 6 : 6-*trimethyl*cyclo*hex*-1-*enyl*)*dodeca*-3 : 5 : 7 : 9 : 11-*pentaen*-2-*one* (III) (C_{23} *Ketone*).—This was prepared by Karrer and Eugster's procedure (*loc. cit.*). The crude total product exhibited $\lambda_{\text{max.}}$ 4050 Å ($E^{1\%}_{1\,\text{cm.}}$ ~1050) corresponding to about 60% of C_{23} ketone. After the Girard separation, the ketonic fraction was chromatographed on alumina (deactivated with 10% of water), the main fraction affording a solid product (0·61 g. from 2 g. of vitamin A_1 acetate). Crystallization from light petroleum (b. p. 40—60°) gave the red C_{23} ketone, m. p. 103—105·5° (Found : C, 85·25; H, 9·8. Calc. for $C_{23}H_{32}O$: C, 85·15; H, 9·95%). Ultra-violet absorption : Max. 4060 Å; $\varepsilon = 54{,}200$ (Karrer and Eugster give m. p. 105—106°; $\lambda_{\text{max.}}$ 4010 Å; $\varepsilon = 53{,}500$). Infra-red spectrum : main peaks at 1680 and 1660 (C:O stretching), 1590 and 1560 (C:C stretching), 1250, and 970 cm.^{-1}. If the Girard treatment was omitted, and the ketone purified solely by chromatography,* the m. p. after crystallization was somewhat lower (91—94°) and the crystals were orange-yellow. The lower m. p. probably reflects the presence of one or more (less stable) stereoisomers, which are converted by Girard treatment into the higher-melting, presumably all-*trans*-form—the absorption spectrum of the orange-yellow material ($\lambda_{\text{max.}}$ 4060 Å; $\varepsilon = 53{,}200$) was very similar to that of the red form of the ketone.

The *oxime*, prepared from ketone of m. p. 103—105·5°, crystallized from methanol as yellow prisms, m. p. 148—150° (Found : C, 81·3; H, 9·5. $C_{23}H_{33}ON$ requires C, 81·35; H, 9·8%). Ultra-violet absorption : Max. 3850 Å; $\varepsilon = 74{,}600$.

Di-[4 : 8-*dimethyl*-10-(2 : 6 : 6-*trimethyl*cyclo*hex*-1-*enyl*)*deca*-1 : 3 : 5 : 7 : 9-*pentaenyl*] *Ketone* (C_{43} *Ketone*) (IV).—Ethanol (2 c.c.) containing dissolved sodium (25 mg.) was added to a solution of retinene$_1$ (0·153 g.) and C_{23} ketone (0·154 g.) in benzene (10 c.c.), and the mixture was stirred at 10° for 50 minutes. Light petroleum and aqueous tartaric acid were added and the organic layer was separated and evaporated under reduced pressure. The residue was chromatographed in light petroleum on alumina (150 g., deactivated with 20% of water), development being effected with ether–light petroleum (1 : 50). The dark violet zone was cut out and the C_{43} ketone eluted from it with ether. A single crystallization from light petroleum gave fairly pure ketone (0·155 g., 50%), m. p. 106—122°. For further purification, the total crude material (0·18 g.) was combined and rechromatographed on deactivated alumina. Three small red zones, one above and two below, were separated from the violet zone and were

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* A deep violet band near the top of the column was eluted separately; this material showed light-absorption properties identical with those of the C_{43} ketone described below.

rejected. The main zone gave, after crystallization from light petroleum (b. p. 40—60°), crystals (0·12 g.) with m. p. 111—117°. Recrystallization from the same solvent afforded C_{43} *ketone*, m. p. 118—122° (softening at 105°) (Found : C, 87·1; H, 10·1. $C_{43}H_{58}O$ requires C, 87·4; H, 9·9%). Ultra-violet absorption (in dioxan) : Max. 4680 Å; $\varepsilon = 72{,}000$. Infra-red spectrum : main peaks at 1635 (C:O stretching), 1585 and 1555 (C:C stretching), 1070, and 965 cm.$^{-1}$. The low value of the carbonyl stretching frequency may be compared with those recorded for *cyclo*heptatrienone (1638 cm.$^{-1}$; von Doering and Detert, *J. Amer. Chem. Soc.*, 1951, **73**, 876), tropolone (1615 cm.$^{-1}$, Koch, *J.*, 1951, 512), and β-methyltropolone methyl ether (1630 cm.$^{-1}$; Haworth and Hobson, *J.*, 1951, 561).

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