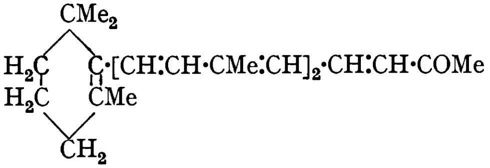
330. *Studies in the Polyene Series. Part IV.*

By I. M. HEILBRON, A. W. JOHNSON, and W. E. JONES.

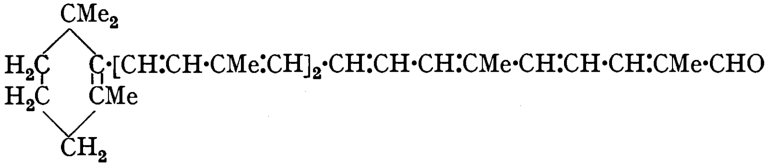
Oxidation of vitamin-A with aluminium *iso*propoxide in presence of acetone gives the same C_{23} ketone (axerophthylideneacetone) as is obtained by using aluminium *tert.*-butoxide, and reduction of the ketone with aluminium *iso*propoxide in *iso*propyl alcohol gives the corresponding secondary alcohol, $\lambda_{max.}$ 3545 A. Ozonolysis of both the alcohol and the ketone gives geronic acid, thus confirming the presence of the β-ionone ring. Oxidation of cinnamyl alcohol with aluminium *tert.*-butoxide in presence of di*iso*propyl ketone gives a 5% yield of cinnamaldehyde, whereas with diethyl ketone a 35% yield of *α-cinnamylidenediethyl ketone*, m. p. 63° (2 : 4-*dinitrophenylhydrazone*, m. p. 232°), is obtained.

It has already been established (J., 1938, 175) that oxidation of vitamin-A with aluminium *tert.*-butoxide in presence of acetone gives the ketone (I), which we propose to call axerophthylideneacetone in conformity with the name axerophthol suggested for vitamin-A by Karrer (cf. v. Euler, Karrer, and Solmssen, *Helv. Chim. Acta*, 1938, **21**, 212). Karrer, Rüegger, and Geiger (*ibid.*, p. 1171) have shown that the secondary alcohol (III), obtained from β-apo-2-carotenal (II) by reaction with ethylmagnesium bromide, and β-apo-2-carotenol, prepared by reduction of (II) with aluminium *iso*propoxide, exhibit practically identical absorption spectra. From this they conclude that the location of the absorption maximum of the secondary alcohol corresponding to (I) should be the same as that of vitamin-A_2 if the structure (IV) suggested for the latter by Gillam, Heilbron, Jones, and Lederer (*Biochem. J.*, 1938, **32**, 45) be correct. Although Karrer, Rüegger, and Geiger (*loc. cit.*) were unable to isolate the pure carbinol from the product obtained by reduction of (I) with aluminium *iso*propoxide, we have encountered no difficulty in this respect, the alcohol being a viscous oil with an absorption maximum at 3545 A., a position in good agreement with that predicted by the above investigators (3560—3580 A.). Although these authors point out that the wave-length of the absorption band of vitamin-A_2 (*ca.* 3500 A.) is somewhat shorter than would be expected, it must be emphasised that the compound has hitherto always been accompanied by a considerable proportion of the ordinary vitamin-A and until the two are effectively separated the location of the maximum must be somewhat approximate. Even so, it will be observed from the above that the displacement compared with the alcohol corresponding to (I) is only about 45 A. A further point of similarity between the two compounds is that both give a greenish-blue colour with chloroformic antimony trichloride, although the maximum in the case of the secondary alcohol is displaced to 7120 A. compared with 6930 A. for vitamin-A_2; our knowledge of this colour reaction, however, is at present insufficient to state whether any significance can be attached to this difference.

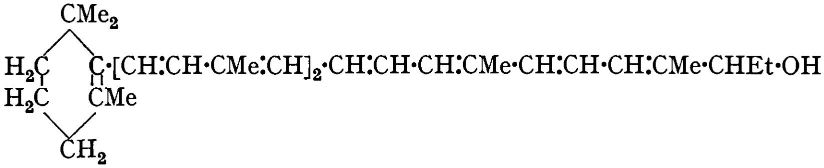
(I.)



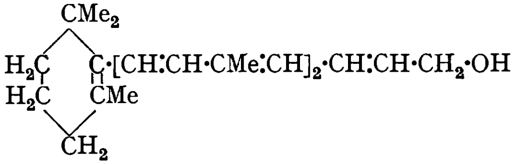
(II.)



(III.)



(IV.)

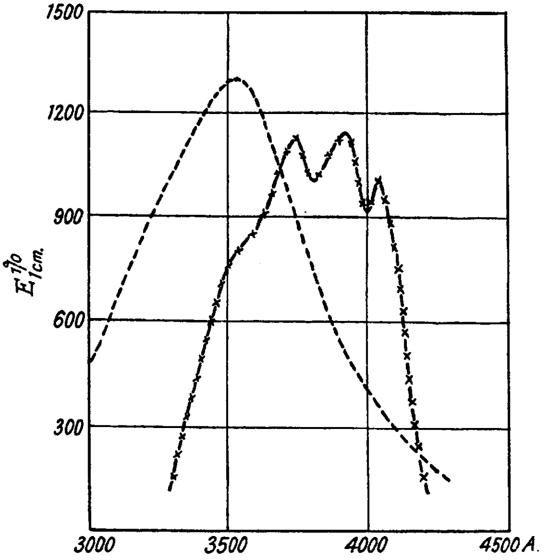


The above reduction of axerophthylideneacetone has been repeated several times and on only one occasion have we failed to obtain the corresponding alcohol. The product in this case exhibited the typical carotenoid triplet (see Figure) with maxima at 3700, 3900, and 4110 A., which would appear to indicate that it is the hydrocarbon (V) (cf. the symmetrical polyene hydrocarbons; Kuhn and Grundmann, *Ber.*, 1938, **71**, 442).

If this is the correct explanation, the extent to which dehydration occurs will probably depend on the concentration of the aluminium *iso*propoxide and the time of reaction.

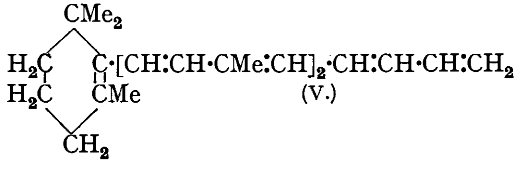
We have now found that axerophthylideneacetone is readily obtained by oxidation of vitamin-A with aluminium *iso*propoxide instead of the *tert.*-butoxide. A possible explanation of this reaction is that *iso*propyl alcohol and the aluminium salt of vitamin-A are formed by double decomposition, the latter then reacting with the acetone as in the normal Pondorff reaction.

Ozonolysis of both axerophthylideneacetone and the corresponding secondary alcohol gives geronic acid, but negative results have again been obtained with the product formed by oxidation of vitamin-A in presence of diethyl ketone (Haworth, Heilbron, Jones, Morrison, and Polya, this vol., p. 128) and also with the corresponding alcohol. From these results it seems quite definite that the β-ionone ring is not present in the latter compounds, and although little progress has so far been made towards elucidating their structures, parallel investigations with simpler alcohols have given interesting results.



– – – – *Alcohol corresponding to* (I).
–×–×– *Abnormal reduction product of* (I).

Oxidation of cinnamyl alcohol with aluminium *tert.*-butoxide and diethyl ketone gives a 35% yield of *α-cinnamylidenediethyl ketone* (VI), m. p. 63° (2 : 4-*dinitrophenylhydrazone,* m. p. 232°), benzyl and furfuryl alcohol similarly yield α-benzylidenediethyl ketone (semicarbazone, m. p. 187°) and α-furfurylidenediethyl ketone, b. p. 135—140°/21 mm. (*semicarbazone,* m. p. 181°; 2 : 4-*dinitrophenylhydrazone,* m. p. 188°) respectively, from which it is evident that condensation of aldehydes with diethyl ketone under these conditions proceeds more readily than was originally believed (Haworth, Heilbron, Jones, Morrison, and Polya, *loc. cit.*). Geraniol, on the other hand, gives mainly high-boiling products, in agreement with the observation that citral, when refluxed alone with aluminium *tert.*-butoxide in benzene, is quantitatively converted into a mixture of unidentified high-boiling substances. Oxidation of cinnamyl alcohol with aluminium *tert.*-butoxide in presence of di*iso*propyl ketone gives a 5% yield of cinnamaldehyde.



(V.)

$C_6H_5·CH:CH·CH:CMe·COEt$

(VI.)

EXPERIMENTAL.

Reduction of Axerophthylideneacetone.—The ketone (2 g., $E^{1\%}_{1\,\text{cm.}}$ 4010 A. = 1150) was dissolved together with freshly prepared aluminium *iso*propoxide (2. g) in *iso*propyl alcohol (50 c.c.), and the solvent slowly distilled, fresh *iso*propyl alcohol being added at such a rate as to maintain the bulk of the solution approximately constant. When acetone could no longer be detected in the distillate the major portion of the solvent was distilled, and the residue diluted with light petroleum. After aluminium salts had been removed with 2N-phosphoric acid, the solution was washed with water and dried over sodium sulphate, and the solvent removed, giving an extremely viscous, orange oil exhibiting a well-defined absorption maximum at 3545 A. ($E^{1\%}_{1\,\text{cm.}}$ = 1250) [Found : active hydrogen atom, 0·85 (Zerewitinov)]. With chloroformic antimony trichloride the alcohol gave an intense greenish-blue colour with a strong absorption band at 7120 A.

Ozonolysis of Axerophthylideneacetone.—A solution of the ketone (2 g.) in dry carbon tetrachloride (40 c.c.) was treated with a slow stream of ozonised oxygen for 24 hours; the precipitated ozonide was dissolved by addition of glacial acetic acid (40 c.c.), and the ozonolysis continued for a further 24 hours. Water (250 c.c.) was then added and after refluxing for 1 hour the mixture was evaporated to a syrupy consistency, water (150 c.c.) again added, and the process repeated. The residue was extracted repeatedly with ether, and the ethereal solution thoroughly extracted with small portions of a concentrated solution of sodium bicarbonate. The combined aqueous extracts were acidified with phosphoric acid, and the solution repeatedly extracted with ether; evaporation of the solution gave the crude acid as a viscous oil, which was extracted with hot water (5 c.c.), and the filtered extract treated with a solution of semicarbazide hydrochloride (0·5 g.) and sodium acetate (1 g.) in water (3 c.c.). The oil which immediately separated, rapidly solidified and after standing at 0° for 24 hours the solid was collected and crystallised first from alcohol and finally from ethyl acetate, giving geronic acid semicarbazone as fine needles, m. p. 163° alone or mixed with an authentic specimen. Ozonolysis of the corresponding alcohol in the same manner also gave geronic acid.

Oxidation of Vitamin-A with Aluminium iso*Propoxide.*—A solution of vitamin-A (10 g., $E^{1\%}_{1\,\text{cm.}}$ = 1580) and aluminium *iso*propoxide (10 g.) in a mixture of benzene (250 c.c.) and acetone (100 c.c.) was refluxed for 48 hours and then worked up in the usual manner (Batty, Burawoy, Harper, Heilbron, and Jones, J., 1938, 178). The product (7·7 g., $E^{1\%}_{1\,\text{cm.}}$ 4010 A. = 1300) was identified as axerophthylideneacetone by formation of the characteristic *p*-tolylsemicarbazone, m. p. 219°.

Oxidation of Cinnamyl Alcohol.—(a) *Di*iso*propyl ketone.* Cinnamyl alcohol (20 g.) was oxidised with aluminium *tert.*-butoxide (22 g.) in a mixture of benzene (600 c.c.) and di*iso*propyl ketone (40 g.) for 48 hours by the standard procedure. The product (1·1 g.), isolated by means of the Girard reagent P, was identified as cinnamaldehyde by conversion into its 2 : 4-dinitrophenylhydrazone, crystallising from ethyl acetate in deep red needles, m. p. 248° (compare Brady, J., 1931, 756).

(b) *Diethyl ketone.* Repetition of the above oxidation, diethyl ketone (40 g.) being used instead of di*iso*propyl ketone, gave the *ketone* (VI) (10 g.), crystallising from ligroin in pale yellow plates, m. p. 63° (Found : C, 84·0; H, 8·2. $C_{14}H_{16}O$ requires C, 84·0; H, 8·0%). The ketone exhibited a well-defined absorption maximum at 3220 A. ($\epsilon_{\text{max.}}$ = 33,400) and readily formed a 2 : 4-*dinitrophenylhydrazone* crystallising from acetic acid in reddish-violet needles, m. p. 232° (Found : C, 63·3; H, 5·1; N, 14·8. $C_{20}H_{20}O_4N_4$ requires C, 63·2; H, 5·3; N, 14·7%).

α-*Benzylidenediethyl Ketone.*—Benzyl alcohol (10 g.) was oxidised with alumnium *tert.*-butoxide (12 g.) in a mixture of benzene (300 c.c.) and diethyl ketone (30 g.) for 48 hours at 90—95°. Distillation of the crude product gave a fraction (6 g.), b. p. 160°/20 mm. ($\lambda_{\text{max.}}$ 2730 A., $\epsilon_{\text{max.}}$ = 25,000), yielding a semicarbazone crystallising from methyl alcohol in needles, m. p. 187° (Vorländer, *Annalen*, 1897, **294**, 296, gives m. p. 188°) (Found : C, 67·4; H, 7·3; N, 18·0. Calc. for $C_{13}H_{17}ON_3$: C, 67·5; H, 7·4; N, 18·2%).

α-*Furfurylidenediethyl Ketone.*—Furfuryl alcohol (10 g.), oxidised as above, gave a pale yellow oil (6.6. g.), b. p. 135—140°/21 mm., yielding the *semicarbazone* of α-furfurylidenediethyl ketone, crystallising from methyl alcohol in needles, m. p. 181° ($\lambda_{\text{max.}}$ 3160 A., $\epsilon_{\text{max.}}$ = 74,000) (Found : C, 59·8; H, 6·5. $C_{11}H_{15}O_2N_3$ requires C, 59·7; H, 6·8%). The 2 : 4-*dinitrophenylhydrazone* crystallised from acetic acid in reddish-violet needles, m. p. 188° (Found : C, 56·0; H, 4·6; N, 16·3. $C_{16}H_{16}O_5N_4$ requires C, 55·8; H, 4·7; N, 16·3%).

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
LONDON, S.W. 7.

[*Received, August 23rd,* 1939.]