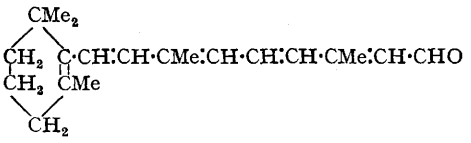
NOTE.

Vitamin-A Aldehyde (Axerophthal). By E. G. E. HAWKINS and R. F. HUNTER.

PREVIOUS attempts to prepare vitamin-A aldehyde (axerophthal) by Oppenauer oxidation of vitamin-A alcohol in the presence of acetone (Batty, Burawoy, Harper, Heilbron, and Jones, J., 1938, 175) and diethyl ketone (Haworth, Heilbron, Jones, Morrison, and Polya, J., 1939, 128) led to the formation of axerophthylideneacetone and a C_{20} aldehyde whose ultra-violet absorption spectrum indicated that it contained a conjugated double bond more than vitamin-A aldehyde. The aldehyde has now been prepared by oxidation of vitamin-A alcohol with aluminium *iso*propoxide in the presence of acetaldehyde.



On Pondorff reduction, the aldehyde regenerated vitamin-A alcohol and on condensation with acetone in the presence of sodium ethoxide it furnished axerophthylideneacetone.

Ultra-violet spectroscopic measurements were made in purified *cyclo*hexane.

(i) A mixture of a distilled vitamin-A alcohol concentrate prepared from the unsaponifiable matter of whale liver oil ($E^{1\%}_{1\,cm.}$ = 1230 at 3250 A.) (1·2 g.), aluminium *iso*propoxide (2 g.), acetaldehyde (15 c.c.), and benzene (40 c.c.) was heated in a sealed tube at 70° for 48 hours. The product was treated with water and extracted with benzene, and the filtered extract dried with sodium sulphate and evaporated under reduced hydrogen pressure. The residue was dissolved in *cyclo*hexane (20 c.c.) and a portion of the solution was chromatographed on weakened " Mayfair " alumina under slight nitrogen pressure (cf. Hunter and Scott, *Biochem. J.*, 1941, **35**, 31). Elution of the main yellow zone furnished material which showed bands at 3680 and 3500 A., with a slight inflection at 3300 A. in the ultra-violet and maxima at 6580 and 6200 A. in the antimony trichloride reaction, indicating the presence of a small amount of unchanged vitamin-A alcohol. On treatment with alcoholic hydrogen chloride under the usual conditions (Hawkins and Hunter, *Biochem. J.*, 1944, **38**, 34) and further chromatography, however, a product was obtained which showed only a single band at 6570 A. in the antimony trichloride reaction. This material showed bands at 3650 and 3480 A. in the ultra-violet.

(ii) A further quantity of vitamin-A aldehyde was prepared in a similar manner from a chromatographed distilled concentrate of vitamin-A alcohol and was freed from unchanged vitamin-A alcohol by "cyclisation " and chromatography This showed bands at 3680 and 3500 A. in the ultra-violet ($E^{1\%}_{1\,cm.}$ = 1050 at 3680 A. and 920 at 3500 A.) and a maximum at 6570 A. ($E^{1\%}_{1\,cm.}$ = 2900) in the antimony trichloride reaction. The *dinitrophenylhydrazone*, prepared by heating with 2 : 4-dinitrophenylhydrazine in aqueous alcohol containing a small amount of hydrochloric acid in an atmosphere of hydrogen at 60° for 15 minutes, separated from acetone in brownish-black crystals, m. p. 208—209° (Found : C, 67·0, 66·9; H, 7·0, 7·1. $C_{26}H_{32}O_4N_4$ requires C, 67·25; H, 6·9%). This showed an absorption band at 4350 A. ($E^{1\%}_{1\,cm.}$ = 1060).

On Pondorff reduction with aluminium *iso*propoxide, vitamin-A aldehyde regenerated vitamin-A alcohol, which showed absorption maxima at 3300 A. and at 6200 A. in the ultra-violet and the antimony trichloride reaction respectively. This was characterised by conversion into " cyclised " vitamin-A, which showed absorption bands at 3900, 3700, and 3500 A. in the ultra-violet and a maximum at 6200 A. in the antimony trichloride reaction.

The aldehyde underwent fairly rapid oxidation on keeping in solution at 0°, yielding material which on chromatography on alumina furnished a main yellow zone containing a compound which showed a band at 3300 A. in the ultra-violet and at 6180—6200 A. in the antimony trichloride reaction. This differed from vitamin-A alcohol in that the ultra-violet absorption spectrum was unaltered after treatment with alcoholic hydrogen chloride in the usual way.

Synthesis of Axerophthylideneacetone from Vitamin-A Aldehyde.—A solution of vitamin-A aldehyde in acetone was cooled to −5°, treated with alcoholic sodium ethoxide, kept at laboratory temperature, with occasional shaking, for 2½ hours, and then extracted with benzene–light petroleum. The extract was washed in turn with dilute phosphoric acid, aqueous sodium carbonate, and water, and evaporated under reduced hydrogen pressure. The product showed main absorption bands at 3950 and 7320 A. in the ultra-violet and the antimony trichloride reaction respectively, characteristic of axerophthylideneacetone (Hawkins and Hunter, *loc. cit.*), which were not substantially altered by chromatography. On reduction with aluminium *iso*propoxide, the condensation product furnished axerophthylidene*iso*propyl alcohol which showed absorption bands at 3500 and 7130—7150 A. in the ultra-violet and the antimony trichloride reaction respectively (cf. Heilbron, Johnson, and Jones, J., 1939, 1563).

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