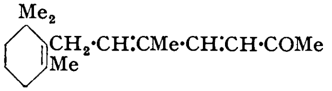
159. *Studies in the Polyene Series. Part VII. Carbinols from Propargyl Acetal.*

By I. M. HEILBRON, E. R. H. JONES, and H. P. KOCH.

Carbinols have been prepared by the Grignard reaction of propargyl acetal with propaldehyde, methyl ethyl ketone, and benzyl methyl ketone and these have been characterised as the ***urethane*** derivatives. A facile cyclisation ensues on semihydrogenation of the acetylenic bond resulting in the formation of dihydrofuran derivatives.

In Part V (this vol., p. 727) a scheme for the synthesis of an analogue of vitamin A, dependent upon the condensation of the C_{17} ketone (I) with propargyl derivatives, was outlined. It has already been demonstrated that the ketone (I) reacts normally with ethylmagnesium bromide and experiments are now described to determine the possibility of employing propargyl acetal (II) (Grard, *Ann. chim.*, 1930, **13**, 336) as the second component in the projected synthesis.

(I.)

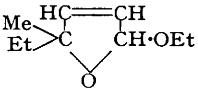


$CH\vdots C{\cdot}CH(OEt)_2$ (II.)

$CR_1R_2(OH){\cdot}C\vdots C{\cdot}CH(OEt)_2$ (III.)

Condensation of propargylacetalmagnesium bromide (Grard, *loc. cit.*) with propaldehyde, methyl ethyl ketone, and benzyl methyl ketone gave approximately 40% yields of 6 : 6-*diethoxyhex*-4-*yn*-3-*ol* (III; R_1 = H, R_2 = Et), 6 : 6-*diethoxy*-3-*methylhex*-4-*yn*-3-*ol* (III; R_1 = Me, R_2 = Et), and 5 : 5-*diethoxy*-1-*phenyl*-2-*methylpent*-3-*yn*-2-*ol* (III; R_1 = Me, R_2 = CH_2Ph) respectively. As none of these carbinols gave consistent results in carbon and hydrogen determinations, they were characterised as the *urethane* derivatives [–$CH(NH{\cdot}CO_2Et)_2$] (m. p.'s 143°, 111°, and 130° respectively) by reaction with urethane in the presence of dilute hydrochloric acid, and furthermore they all evolved approximately one molar volume of methane in Zerewitinoff determinations. Unlike acetals of αβ-ethylenic aldehydes, these acetals and also propargyl acetal itself, fail to give 2 : 4-dinitrophenylhydrazones on treatment with a warm solution of the hydrazine hydrochloride in alcohol. Attempts directly to dehydrate the carbinols (III) to the vinylacetylene acetals resulted either in extensive decomposition or in the recovery of unchanged material.

Small-scale quantitative hydrogenation experiments with the three carbinols, a palladium–calcium carbonate catalyst being used, revealed a very marked decrease in the hydrogenation velocity after approximately one molar volume of hydrogen had been absorbed. When 6 : 6-diethoxy-3-methylhex-4-yn-3-ol (III; R_1 = Me, R_2 = Et) was semihydrogenated in methyl alcohol on a moderate scale, however, a complex mixture was obtained, which was partially resolved into its components on careful fractionation with an efficient column. The isolation of ethyl alcohol indicated that the primary semihydrogenation product had undergone cyclisation and the product of this facile ring closure, a substance to which the constitution 2-*ethoxy*-5-*methyl*-5-*ethyl*-Δ^2-*dihydrofuran* (IV), is ascribed, was isolated in small yield. In support of this formulation are the facts that this product evolved no methane in a Zerewitinoff estimation, exhibited no absorption in the ultra-violet, and failed to form a urethane derivative. It readily decolorised a solution of bromine in carbon tetrachloride and, like the 2-ethoxy-5-methyltetrahydrofuran described by Helferich (*Ber.*, 1919, **52**, 1123), was found to be stable to cold dilute hydrochloric acid. With a hot alcoholic solution of 2 : 4-dinitrophenylhydrazine hydrochloride the 2 : 4-*dinitrophenylhydrazone* of 3-*methylsorbic aldehyde* (V) is produced by simultaneous hydrolysis and dehydration, its constitution being indicated by analytical data and its absorption spectrum, characteristic of that of a dinitrophenylhydrazone of a doubly unsaturated aldehyde. With warm semicarbazide acetate a small yield of a *derivative*, m. p. 169°, is formed, the analytical data for which agree with that of the semicarbazone of the undehydrated aldehyde, 4-hydroxy-4-methylhex-2-enal (VI).



(IV.)

(V.) $CH_3{\cdot}CH{:}CMe{\cdot}CH{:}CH{\cdot}CHO$

$CH_3{\cdot}CH_2{\cdot}C(OH)Me{\cdot}CH{:}CH{\cdot}CHO$ (VI.)

Semihydrogenation of 5 : 5-diethoxy-1-phenyl-2-methylpent-3-yn-2-ol (III; R_1 = Me, R_2 = CH_2Ph) similarly gave a poor yield of a dihydrofuran and since these hemiacetals are not readily convertible into the required unsaturated aldehydes this investigation has been abandoned in favour of more promising routes employing other propargyl derivatives.

EXPERIMENTAL.

6 : 6-*Diethoxyhex*-4-*yn*-3-*ol*.—An ethereal solution of ethylmagnesium bromide (from 3·8 g. of magnesium) was slowly added with stirring and cooling to propargyl acetal (20 g.) (Grard, *loc. cit.*) in ether (200 c.c.). After 2 hours a solution of propaldehyde (9 g.) in ether (50 c.c.) was dropped into the mixture, which was stirred overnight at 20°. Decomposition of the Grignard complex was effected with ammonium chloride and after recovery of unchanged propargyl acetal (7 g.), b. p. 35—42°/13 mm., 6 : 6-*diethoxyhex*-4-*yn*-3-*ol* (12 g.), b. p. 107°/3 mm., $n_D^{18^\circ}$ 1·4476, was isolated. Carbon and hydrogen determinations with this and other acetylenic acetals gave inconsistent results. *Active hydrogen* (Zerewitinoff): The carbinol (158 mg.) evolved 18·6 c.c. of methane at 24°/773 mm., equivalent to 0·9 active hydrogen atom per molecule. *Urethane derivative*: The carbinol (300 mg.) was shaken for 2 hours with a solution of urethane (1 g.) in N-hydrochloric acid (10 c.c.). The white precipitate formed was crystallised from aqueous methyl alcohol, yielding the *urethane* derivative as a microcrystalline powder, m. p. 143° (Found: N, 10·1. $C_{12}H_{20}O_5N_2$ requires N, 10·3%).

6 : 6-*Diethoxy*-3-*methylhex*-4-*yn*-3-*ol*.—When the above condensation was carried out with methyl ethyl ketone (11·3 g.), 6 : 6-*diethoxy*-3-*methylhex*-4-*yn*-3-*ol* (11·5 g.), b. p. 88°/3 mm., $n_D^{21^\circ}$ 1·4444, was obtained. *Active hydrogen* (Zerewitinoff): The carbinol (179 mg.) evolved 24·7 c.c. of methane at 31°/764 mm., equivalent to 1·1 active hydrogen atoms per molecule. The *urethane* derivative, prepared as previously described, separated from petroleum (b. p. 100—120°) as a powder, m. p. 111° (Found: N, 9·4. $C_{13}H_{22}O_5N_2$ requires N, 9·8%).

5 : 5-*Diethoxy*-1-*phenyl*-2-*methylpent*-3-*yn*-2-*ol*.—Employment of benzyl methyl ketone (21 g.) in the above condensation gave as main product 5 : 5-*diethoxy*-1-*phenyl*-2-*methylpent*-3-*yn*-2-*ol* (18·7 g.), b. p. 128°/3 mm., $n_D^{22^\circ}$ 1·5032. *Active hydrogen* (Zerewitinoff): The carbinol (232 mg.) evolved 20·9 c.c. of methane at 23°/767 mm., equivalent to 1·0 active hydrogen atom per molecule. The *urethane* derivative separated from petroleum (b. p. 100—120°) as a powder m. p. 130° (Found: N, 8·2. $C_{18}H_{24}O_5N_2$ requires N, 8·1%).

Semihydrogenation of 6 : 6-*Diethoxy*-3-*methylhex*-4-*yn*-3-*ol*.—A solution of the carbinol (24·7 g.) in methyl alcohol (200 c.c.; free from ethyl alcohol) was shaken with hydrogen in the presence of palladium–calcium carbonate (4 g.; 2%), one molar volume of hydrogen (2750 c.c.) being absorbed rapidly. The hydrogenation was then interrupted, the catalyst removed, and the solution distilled through a well-lagged column packed with single-turn glass helices, fitted with a total condensation-variable take off head and operating at a reflux ratio of about 10 : 1. The following main fractions were collected : (i) B. p. 65°, methyl alcohol. (ii) B. p. 35—36°/100 mm. (2 g.), ethyl alcohol (identified as the 3 : 5-dinitrobenzoate, m. p. 92°). (iii) B. p. 74—82°/50 mm. (4·4 g.). (iv) B. p. 98—114°/4 mm. (8 g.).

On redistillation, fraction (iii) gave 2-*ethoxy*-5-*methyl*-5-*ethyl*-Δ^2-*dihydrofuran* as a colourless oil with a strong camphoraceous odour, b. p. 151°, 76°/50 mm., 46°/19 mm., $n_D^{20^\circ}$ 1·4268 (Found : OEt, 29·2. $C_7H_{11}O{\cdot}OEt$ requires OEt, 28·9%). On boiling with 2 : 4-dinitrophenylhydrazine in alcoholic hydrochloric acid solution a red precipitate was obtained. Purification by adsorption on alumina from benzene solution and crystallisation from alcohol gave the 2 : 4-*dinitrophenylhydrazone* of 3-*methylsorbic aldehyde* in red needles, m. p. 194° (Found : C, 54·0; H, 4·8; N, 19·1. $C_{13}H_{14}O_4N_4$ requires C, 53·8; H, 4·8; N, 19·3%). *Light absorption in alcohol :* Maximum, 3910 A.; log ϵ = 4·56. With semicarbazide acetate in hot water, fraction (iii) gave a small yield of a solid which separated from water as a powder, m. p. 169° (Found : C, 52·3; H, 8·2. $C_8H_{15}O_2N_3$ requires C, 51·9; H, 8·1%). *Light absorption in alcohol :* Maximum, 2680 A.; log ϵ = 4·58. These analytical and spectrographic data suggest that the substance is the *semicarbazone* of 4-*hydroxy*-4-*methylhex*-2-*enal*.

On redistillation, fraction (iv) had b. p. 110°/4 mm., $n_D^{19^\circ}$ 1·4565. It gave no methane in a Zerewitinoff determination and exhibited no ultra-violet absorption (Found : OEt, 17·5. $C_{14}H_{21}O_2{\cdot}OEt$ requires OEt, 16·9%).

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

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