

CHARACTERIZATION OF A COMPOUND DERIVED FROM THE REACTION OF
FORMALDEHYDE WITH OLEIC ACID, CONTAINING VICINAL HYDROXYMETHYL
AND HYDROXYMETHYLOXY GROUPS.

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(Received in UK 5 August 1968; accepted for publication 27 November 1968)

We have investigated the reaction of formaldehyde with oleic acid. At room temperature with dilute formaldehyde the reaction reached an equilibrium position corresponding to a 3.5% change in the oleic acid after 4 days, and 7 new products were observed. A high temperature (100°C) reaction gave the same products in greatly improved yield; 1 gm of pure oleic acid was refluxed in 100 ml of 40% formaldehyde solution (85 parts), acetic acid (10 parts) and hydrochloric acid (5 parts). The pH of this mixture was -0.05. After 20 hours, oleic acid and its adducts were extracted with petrol, washed, dried and methylated using diazomethane in ether solution. The mixture of methyl esters was separated by preparative scale Gas Chromatography, using a modified Pye 104 chromatograph. (Column: 7' x 3/8", FFAP (15%) on Celite, 235°C). Figure 1 represents the same mixture resolved on an analytical FFAP column; F indicates Formaldehyde polymers. The compound with Carbon No. of 26.0 was obtained in substantial yield at over 98% purity. This compound represents an intermediate product not normally isolated in the Prins reaction.

The compound was polar on silicic acid TLC, and on GC (Carbon nos. FFAP 26.0, FEGA 26.5, APL 21.8). No molecular ion was observed in the mass spectrum, the greatest m/e seen being 357. Infra red spectroscopy confirmed the absence of -CH=CH-, and absorptions at 1130, 1110 and 1080cm⁻¹ are suggestive of the $\text{CH-O-CH}_2\text{OH}$ grouping.

Figure 2 is the proton-resonance spectrum in carbon tetrachloride. There is a three proton singlet at $\delta = 3.56$ ppm, assigned to protons of the -COOCH_3 grouping, and two one-proton doublets ($J = 6$ c.p.s.) centred at $\delta = 4.45$ ppm and 4.85 ppm. We have assigned these to the non-equivalent protons of the $\text{-O-CH}_2\text{-O-}$ group; the geminal non-equivalent protons of the $\text{C-CH}_2\text{OH}$ group are assigned to the triplet at $\delta = 3.10$ ppm ($J = 11$ c.p.s. and 11 c.p.s.) and the quartet at $\delta = 3.94$ ppm ($J = 11$ c.p.s. and 4.5 c.p.s.). The methine proton adjacent to oxygen is assigned to a broad one-proton signal at $\delta = 3.25$ ppm.

Fig. 1

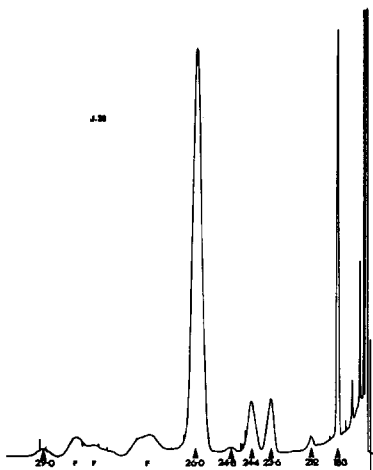
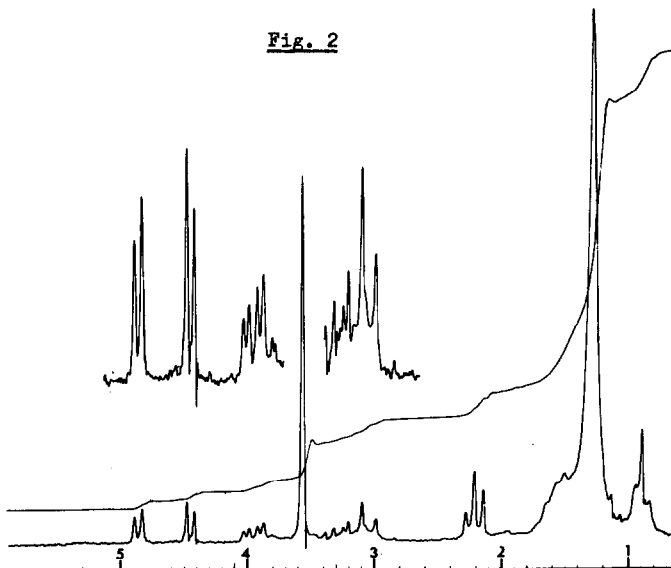
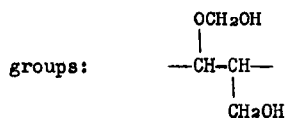


Fig. 2

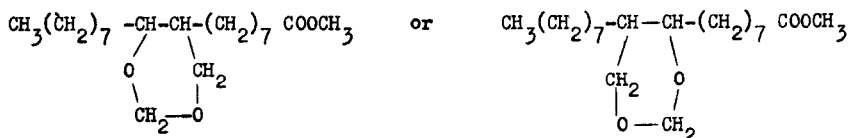


There is little doubt in our minds that this compound possesses the functional



though it must be an isomeric mixture, consisting of methyl 9-hydroxymethyl-10-hydroxymethyloxy actadacanoate and methyl 9-hydroxymethyloxy-

10-hydroxymethyl octadecanoate. We have evidence that only the 9-hydroxymethyl-10-hydroxymethyloxy isomer is formed at reaction temperatures under 15°C⁽¹⁾. Apart from the implications regarding histological fixation,⁽²⁾ this compound represents a novel intermediate in the Prins⁽³⁾ reaction. Thus one would expect ring closure to occur, giving the 1,3 dioxan:-



However, very small amounts of this compound (Carbon No 22.4 on FFAP) can be detected in reaction mixtures, prepared at either low temperatures or high temperatures. The reaction of formaldehyde with oleic acid may therefore be said to resemble the "normal" Prins reaction in principle rather than in detail.

References:

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- (2) Jones, D., and Gresham, G.A., *Nature*, 210, 1386 (1966).
- (3) Prins, H.J., *Chem. Weekblad*, 16, 1072 (1919).