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MECHANISM OF FORMATION OF 3-DEOXYGLYCOSULOSES

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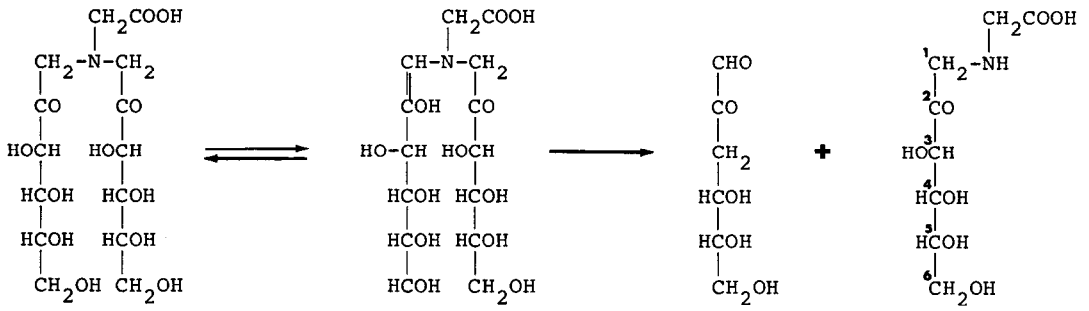
The purpose of this communication is to refute the evidence recently presented[1] for a new mechanism for the formation of "3-deoxyglucosulose" (3-deoxy-D-erythro-hexos-2-ulose) (**1**); and to confirm the accepted mechanism[2,3,4] - enolization followed by a β-elimination (e.g. **2** → **3** → **1** + **4**)[5].



2 **3** **1** **4**

Fodor and Sachetto[1] claimed that when **1** is formed in deuterium oxide solution no incorporation of deuterium at C-3 occurs, as indicated by the infra-red and n.m.r. spectra of the 2,4-dinitrophenylosazone of **1**. Since they regarded these results as incompatible with an enolization and β-elimination, they proposed that the reaction involved a 1,3-hydride shift[1].

The 1,3-hydride shift mechanism is improbable and does not explain Fodor and Sachetto's results in view of some of our previously unpublished work which shows that the first reaction to occur in deuterium oxide is deuteration at C-1. The decomposition of difructoseglycine (**2**) to give **1** and **4** was followed by

n.m.r. spectroscopy with both H_2^1O and D_2O as solvents*. Five minutes at 95° was required for the reaction to approach completion. With H_2^1O as solvent, the spectrum then showed the expected signals of the C-1 methylene group of **4** as two singlets at δ 3.36 and 3.32, the rest of the spectrum at lower field being largely obscured by the intense water signals. With deuterium oxide as solvent there were no signals at δ 3.36 and 3.32, therefore C-1 of **4** was fully deuterated. This deuteration occurred largely before the decomposition of **2** because, although the intensity of the n.m.r. signals of the C-1 methylene group of **4** gradually decreased when **4** was heated in deuterium oxide, after 5 minutes at 100° the intensity was reduced to only one half**. It is apparent from these results that **2** enolizes more rapidly than **4** and that, since deuteration occurs at C-1, a 1,3-hydride shift cannot explain the reported absence of deuteration at C-3 of 1.

Let us now examine the evidence for the absence of deuteration presented by Fodor and Sachetto[1]. They reported firstly that the osazone of **1** lacked "any C-D band in the diagnostic infrared region" (1900 - 2200 cm^{-1}). Previous workers have shown these bands to be weak in other compounds, for example, in the spectrum of CH_3-CD_2-CO-CD_2-CH_3 "the CD_2 absorption is so weak that the bands might well be overlooked or confused with overtone bands"[6]. The 1900 - 2200 cm^{-1} region of the infrared spectrum of the osazone contains not only the overtones of the intense C-O bands at about 1100 cm^{-1} but also absorption from the O-H stretching band. The detection of <u>one</u> deuterium atom by

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*The n.m.r. spectrum of **2** with deuterium oxide as solvent consisted of an envelope δ 3.5 - 4.5 with no prominent peaks, whereas that of **4** showed: (a) two isolated singlets, one at δ 3.36 (Major signal, from β-<u>D</u>-pyranose anomer) and the other at δ 3.32 (minor signal, probably from the α-<u>D</u>-pyranose anomer), both due to the C-1 methylene group (N-CH_2-C-O), and (b) the other protons as a complex multiplet at δ 3.6 - 4.3 which included a prominent sharp peak at δ 3.70 (N-CH_2-COO). All n.m.r. spectra are at 60 MHz with sodium 2,2-dimethyl-2-silapentane-5-sulphonate as internal standard for aqueous solutions (H_2O and D_2O).

No change appeared in the complex multiplet at δ 3.6 - 4.3 even after 45 minutes at 100° when the signals at δ 3.36 and 3.32 had disappeared. Under these conditions **4 is stable except for deuteration at C-1.

infrared spectroscopy in a molecule of the size of the osazone of **1** could well be impossible. The negative infrared evidence is thus valueless.

The second piece of evidence presented by Fodor and Sachetto[1] for non-incorporation of deuterium was that the n.m.r. spectrum of the osazone showed no decrease in the intensity of the signal for the C-3 methylene group. Their assignment, published earlier[7], for the n.m.r. spectrum of the osazone in pyridine-d_5 appears to be largely incorrect. The low field portions of their published spectra[7] show three large signals at δ 8.75, 7.61 and 7.23. The first signal was ignored by them and their assignment of the other two to 2(H-C-O) and H_2-C-O protons is without precedent[8,9]. The chemical shifts and relative intensities of these three signals correspond to those of the three pyridine bands[8] (α-, γ-, and β-protons respectively). Confirmation of my assignment is obtained by examining their spectra of the osazone (Figs 1 and 2 ref. 7) where the intensities of the three bands are independent of osazone concentration! The large broad singlet at δ 4.42, assigned by these authors[7] to the methylene. group at C-3 must be due to some other protons because the signal is at too low field[8] and because a mere inspection indicates, from its intensity, that it is due to more than two protons (H_2-6 and H-4). A small broad peak at δ 4.75 is probably the H-5 signal and the multiplet at δ 3.2 - 4.1 no doubt arises from the methylene group at C-3. The latter two signals were ignored by Fodor et al[7]. The n.m.r. evidence produced by Fodor and Sachetto[1] can be completely disregarded since it is based on incorrect assignments.

I have repeated Fodor and Sachetto's experiment[1] and find, by n.m.r. spectroscopy, incorporation of deuterium in the 2,4-dinitrophenylosazone of **1** at both C-1 and C-3, namely, approximately one deuterium atom at C-3 (Multiplet at δ 3.2 - 4.1) and > 0.95 deuterium atoms at C-1 (singlet at δ 8.66).

No evidence exists for the occurrence in the formation of 3-deoxyglycosuloses, from sugars by the action of acid or alkali, or from Amadori compounds, of a mechanism other than an enolization followed by a β-elimination. The easy enolization of **2** partly explains its rapid decomposition to give high yields of **1** (see ref. 2 p. 218).

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