The Formation of *l*-Threose.

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(Received January, 25th, 1937.)

Obtaining *l*-threose by Wohl's method of degradation of *l*-xylose which was prepared from *l*-gulonolactone, Deulofeu⁽¹⁾ reported its specific rotation as to the left. It was, however, reported by R. Hockett⁽²⁾ that the specific rotation of *d*-threose prepared by the Wohl degradation of *d*-xylose was lævorotation of −12.5° in equilibrium. Hockett was thus forced to the conclusion that Deulofeu did not have pure substance and that the *l*-isomer should obviously have dextrorotation of equal numerical value with his *d*-isomer. The formation of *l*-threose, therefore, has not yet been accepted.⁽³⁾

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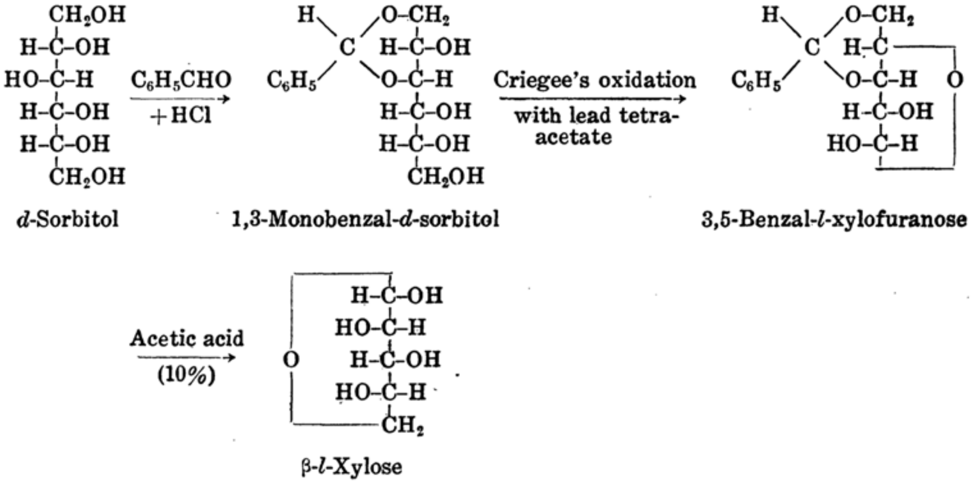
(1) Deulofeu, *J. Chem. Soc.*, **1929**, 2458; *J. Am. Chem. Soc.*, **58** (1936), 855.

(2) R. Hockett, *J. Am. Chem. Soc.*, **57** (1935), 2265.

(3) See H. Vogel and A. Georg, "Tabellen der Zucker," (1931).

In the course of our investigation of monoses(4), we prepared, for the purpose of formation of *l*-talonic acid, a considerable quantity of *l*-galactonic acid, which is easily degraded to *l*-lyxose. In the hope of ascertaining the properties of *l*-threose, we made attempts to degrade *l*-lyxose to *l*-threose and to isolate it. Meanwhile we found that *l*-xylose was obtained very conveniently from *d*-sorbitol by Vargha's method(5). This can be used as well as *l*-lyxose in obtaining *l*-threose and it was thus used as a starting material of this investigation, and the process of the reaction is shown in the scheme below.



d-Sorbitol 1,3-Monobenzal-*d*-sorbitol 3,5-Benzal-*l*-xylofuranose

β-*l*-Xylose

l-Xylose thus obtained melts at 143° and rotates in equilibrium 18.2° to the left. Following the method of Deulofeu, it was submitted to degradation to *l*-threose by the method of Wohl. Being treated with hydroxylamine hydrochloride and sodium methylate, it changed into a thick syrup which consists mainly of *l*-xyloxime. When the *l*-xyloxime was warmed with acetic anhydride and sodium acetate in dioxane, a precipitate of tetracetyl-*l*-xylonic nitrile melting at 82° separated out. It was then decomposed with ammonia, and a colourless crystalline substance melting at 164–165°, the composition of which was $C_8H_{16}O_5N_2$, was obtained. It is nothing but *l*-threose diacetamide, and it rotates 10.8° to the right in water solution. Hockett's *d*-isomer rotates 10.9° to the left.

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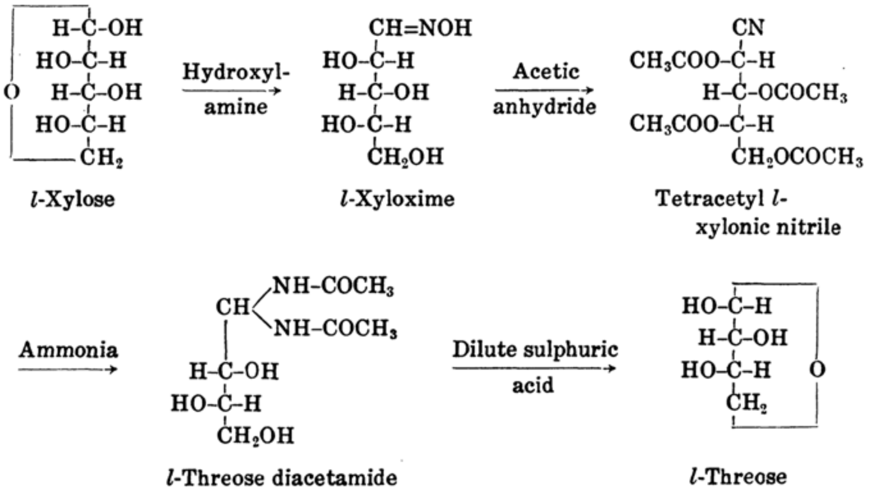
(4) S. Fukunaga, *J. Chem. Soc. Japan*, **57** (1936), 551.

(5) L. v. Vargha, *Ber.*, **68** (1935), 18.



The equilibrium rotation of the sugar itself was determined with two solutions which were prepared by two different kinds of hydrolysis. The one solution which was prepared by hydrolysing *l*-threose diacetamide with 1/3 N sulphuric acid as in Deulofeu's experiment, rotated 13.2° to the right. The other which was prepared by hydrolysis with 1/10 N sulphuric acid and whose degree of hydrolysis was observed quantitatively as in Hockett's experiment, rotated also 13.1° to the right. The values obtained through these two observations show an almost satisfactory agreement. So we came to the conclusion that *l*-threose diacetamide could be completely hydrolysed with 1/3 N sulphuric acid.

Comparing, as shown below, the properties of *l*-threose and its derivative we obtained with those of Hockett's *d*-isomer, it seems to us that the two sugars are almost in good agreement as *d*- and *l*-isomer, and it seems to be clear that pure *l*-threose and its derivative are now formed, although Deulofeu could not have them from *l*-gulonolactone.

	Melting point of threose diacetamide	Specific rotation of threose diacetamide	Equilibrium specific rotation of threose
Deulofeu's *l*-threose	165–166°	−7.68°	−24.6°
Hockett's *d*-threose	165–167°	−10.9°	−12.5°
Authors' *l*-threose	164–165°	+10.8°	+13.1°

Experimental.

l-Xylose. This substance was obtained by a method which was recently published by Vargha. That is, 1 kg. of *d*-sorbitol, dissolved in one litre of water, was mechanically shaken with 100 c.c. of concentrated hydrochloric acid and 500 g. of benzaldehyde for 5–6 hours in a cool place. Monobenzal-*d*-sorbitol thus obtained was recrystallised from absolute alcohol and suspended in glacial acetic acid with equivalent tetracetyl lead. The mixture was shaken for an hour and the resulting almost clear solution was evaporated up in vacuo, and the syrup thus obtained was dissolved in ethyl acetate and water, and the ethyl acetate layer was distilled in vacuo to remove the solvent, and the resulting thick syrup of monobenzal-*l*-xylose was hydrolysed with 10% acetic acid. The syrup, obtained by distilling off the solvent under diminished pressure, was dissolved in a little water, charcoal added, and filtered. The solution was again evaporated under diminished pressure, and the remaining syrup or the impure crystal of *l*-xylose was recrystallised from alcohol. Melting point, 143°.

Its rotation in water was:

15 minutes after dissolution $[\alpha]_D^{20} = -38.6°$;
63 minutes after dissolution ,, $= -18.4°$;
ca. 20 hours after dissolution (equilibrium) ,, $= -18.2°$.

Melting point of *l*-xylosazone, 163°.

The method devised by Wohl was selected for degrading *l*-xylose to *l*-threose, because both Hockett and Deulofeu used this method for degradation.

Tetracetyl-l-xylonic nitrile. *l*-Xylose (50 g.) was added to the neutral solution of hydroxylamine, which was made by neutralising 30 g. of hydroxylamine hydrochloride with sodium methylate. The mixture was warmed a little to dissolve the sugar after two days' standing and filtered. The filtrate was concentrated under diminished pressure to a thick syrup, keeping the outer bath under 50°, a little dioxane was added, and reconcentrated. Then 15 g. of recently fused sodium acetate and 30 c.c. of dioxane were added. The mixture was warmed a little, 10 c.c. of acetic anhydride added, and shaken vigorously. When spontaneous heating was ended, 10 c.c. more of acetic anhydride was added. This was repeated ten times. Then the mixture was warmed on a water bath for an hour and poured over cracked ice. A little sodium bicarbonate was added to partially neutralise the acetic acid, and the precipitate was filtered. It was recrystallised from absolute alcohol. Melting point, 82°.

l-Threose diacetamide. To 25 g. of tetracetyl-*l*-xylonic nitrile, 300 c.c. of ammonia was added. The mixture was warmed a little to dissolve the solid material, and, after three hours' standing, concentrated to syrup under diminished pressure. Then again ammonia was added and reconcentrated. The resulting syrup was dissolved in absolute alcohol, and a little ether was added. After two days' standing in refrigerator, the precipitated *l*-threose diacetamide was filtered. It was recrystallised several times from 85% alcohol, adding charcoal to remove gummy substance and colour. Then sharp needles separated very slowly. Melting point, 164–165° (corr.): $[\alpha]_D^{20} = +10.8°$. (Found: N, 12.69. Calculated for $C_6H_{10}O_5N_2$: N, 12.72%).

Equilibrium rotation of l-threose. To get the equilibrium rotation of *l*-threose, we performed two kinds of hydrolysis by using sulphuric acid of different concentrations. Firstly, 0.3067 g. of *l*-threose diacetamide was made up to 10 c.c. with 1/3 N sulphuric acid. The solution was heated in a boiling water bath for three quarters of an hour. Thus we got the specific rotation of +13.2° (calculated from the weight of *l*-threose formed, the direct reading being +0.22° at 20°C.). This method is almost the same as Deulofeu's. Secondly, just as Hockett did, 0.2036 g. of *l*-threose diacetamide was made up to 10 c.c. with 0.100 N sulphuric acid. The solution was heated in a boiling water bath for 150 minutes, and 5 c.c. of it was titrated by Cajori's iodine oxidation method. This showed that, in 10 c.c. of the solution, 0.0913 g. of threose was formed by hydrolysis, and so 0.0362 g. of *l*-threose diacetamide remained unhydrolysed. The rotation of the hydrolysed solution was +0.16° in 10 cm. tube at 20°C. And the specific rotation calculated from these is +13.1°. The two values thus obtained showed an excellent agreement.

***l*-Threose.** The sulphuric acid solution of *l*-threose was extracted with ether fifteen times to remove acetic acid, almost neutralised with barium hydroxide and then excess of barium carbonate and charcoal were added. The mixture was warmed on a water bath for a short while, and filtered. The filtrate was evaporated in vacuo to a thick syrup, and the latter was taken in absolute alcohol. The solution was filtered from inorganic impurities and evaporated. Thus the syrup of *l*-threose was obtained. But it did not crystallise on standing in a desiccator. To prepare the osazone, a portion of the syrup of *l*-threose was dissolved in a little water, and phenylhydrazine and acetic acid were added to it. The mixture was heated on a boiling water bath for about three hours. The precipitated *l*-threosazone (*l*-erythrosazone) was washed with a little benzene, and recrystallised from dilute alcohol. Yellow needles. Melting point, 162–163°.

Summary.

(1) *l*-Threose diacetamide has been obtained by the Wohl's method of degrading sugars from *l*-xylose which was prepared from *d*-sorbitol by Vargha's method.

(2) It has been found that this *l*-threose diacetamide melts at 164–165° (corr.) and has a specific dextrorotation of +10.8° in water. These properties are in good harmony with R. Hockett's value and sign, and do not agree with those of Deulofeu.

(3) This *l*-threose diacetamide has been submitted to hydrolysis with 1/3 N and 1/10 N sulphuric acid respectively. From these experiments the equilibrium specific rotation of *l*-threose in dilute sulphuric acid was determined to be +13.1°. It has a little higher value (about 0.6°) compared with Hockett's *d*-isomer, but it is now clear that the pure *l*-threose expected by Hockett has been obtained.

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