

Transformation of 4-deoxysaccharides in alkaline medium

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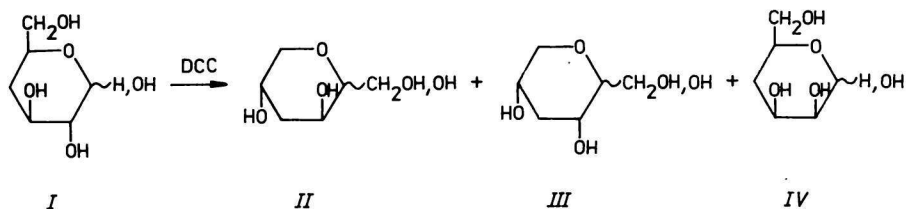
In alkaline medium 4-deoxyaldoses undergo transformations leading mainly to 4-deoxyhexuloses. The reaction carried out in the presence of dicyclohexylcarbodiimide as the transforming reagent gives besides the corresponding 2-ketose and epimeric aldose also the C-3-epimeric 4-deoxyhexulose. It can be used for a large-scale preparation of 4-deoxy-D-*threo*-hexulose.

4-Дезоксиальдозы подвержены в щелочной среде трансформации, причем образуются главным образом 4-дезоксигексулозы. При использовании дициклогексилкарбодимида в качестве трансформирующегося агента происходит в ходе трансформации к образованию, помимо соответствующей 2-кетозы и эпимерной альдозы, С-3-эпимерной 4-дезоксигексулозы. Реакцию можно использовать для приготовления 4-дезоксид-*трео*-гексулозы.

The present paper is a continuation of our studies on the effect of the deoxy group in a saccharide molecule on transformation of deoxysaccharides. We have reported [1] that a transformation of 3-deoxysaccharides in alkaline medium gives the corresponding 3-deoxyhexuloses in high yields. 6-Deoxyhexoses are transformed in alkaline medium under the formation of the corresponding 6-deoxyhexuloses and C-3-epimeric 6-deoxyhexuloses, due to a rearrangement of the 1,2-enediol to 2,3-enediol [2]. The aim of the present paper is examination of the effect of the deoxy group on the transformation of 4-deoxysaccharides. Moreover, formation of 4-deoxy-D-*threo*-hexulose, anticipated during transformation of 4-deoxy-D-*xylo*- or 4-deoxy-D-*lyxo*-hexose, is interesting from a preparative point of view, because it is known [3] that certain metabolic disorders in human organism are accompanied by formation of 4-deoxy-D-*threo*-hexulose and its appearance in urine. The only published route for the preparation of 4-deoxy-D-*threo*-hexulose involves a multistep synthesis from 3,4-anhydro-1,2,5,6-di-*O*-isopropylidene-D-talitol [4].

The transformation was studied on 4-deoxy-D-*xylo*-hexose and 4-deoxy-D-*lyxo*-hexose using calcium hydroxide, triethylamine, pyridine, and dicyclohexylcarbodiimide (DCC). Of these transformation reagents DCC was found to be the most efficient. The transformation of 4-deoxy-D-*xylo*-hexose using DCC gives ca. 50%

of 4-deoxy-D-*threo*-hexulose, 10% of 4-deoxy-D-*erythro*-hexulose, and 2% of 4-deoxy-D-*lyxo*-hexulose (Scheme 1).



Scheme 1

The effects of calcium hydroxide and triethylamine on the course of transformation are similar. The amount of 4-deoxy-D-*threo*-hexulose increases with the reaction time up to 78 h (15–20%). A longer treatment does not influence the yield of 4-deoxy-D-*threo*-hexulose, but leads to formation of further reaction products, 4-deoxy-D-*erythro*-hexulose and 4-deoxy-D-*lyxo*-hexulose (~ 1%). In the presence of pyridine, the optimal duration of the transformation is 12 h, when ca. 15% of 4-deoxy-D-*threo*-hexulose are present. Longer reaction time results only in the increase of amount of degradation products.

The course of 4-deoxy-D-*lyxo*-hexulose transformation effected by the above-mentioned reagents is essentially the same as in the case of 4-deoxy-D-*xylo*-hexulose, only the yields of 4-deoxy-D-*threo*-hexulose are somewhat lower (Table 1).

From the given results it follows that 4-deoxysaccharides afford during the transformation with $\text{Ca}(\text{OH})_2$, triethylamine, and pyridine the corresponding

Table 1

Time course of 4-deoxy-D-*threo*-hexulose formation (in %)

Starting saccharide	Catalyst	Time, h					
		4	8	12	24	48	72
4-Deoxy-D- <i>xylo</i> -hexulose	$\text{Ca}(\text{OH})_2$	1	2	5	10	15	15
	TEA	2	5	10	15	20	20
	Pyridine	5	10	15	15	—	—
	DCC	50	—	—	—	—	—
4-Deoxy-D- <i>lyxo</i> -hexulose	$\text{Ca}(\text{OH})_2$	1	2	5	10	10	10
	TEA	1	2	5	10	15	15
	Pyridine	5	10	15	15	—	—
	DCC	40	—	—	—	—	—

2-ketose and, eventually, the epimeric aldose, which is in consonance with the proposed 1,2-enediol mechanism. During transformation with DCC, a partial rearrangement of the 1,2-enediol to 2,3-enediol takes place, reflected in the formation of the C-3-epimeric 4-deoxy-D-hexulose accompanying the corresponding 2-ketose and epimeric aldose. Relatively high yields (~ 50%) of 4-deoxy-D-*threo*-hexulose in the transformation of 4-deoxy-D-*xylo*-hexose with DCC substantiate large-scale applications of the reaction.

Experimental

Melting points were measured on a Kofler stage and optical rotations on an automatic Perkin—Elmer 141 polarimeter. Chromatography was done on Whatman No. 1 paper using 2-butanone saturated with water as a solvent system. Saccharides were detected by urea and diphenylamine [1] and trichloroacetic acid and benzidine [5]. Determination of saccharides was done by scanning the detected chromatograms with an ERI-10 densitometer (Zeiss, Jena). 4-Deoxy-D-*xylo*-hexose, m. p. 136—139°C, $[\alpha]_D = +57.2^\circ$ (c 1, water) and 4-deoxy-D-*lyxo*-hexose, m. p. 68—70°C, $[\alpha]_D = 6.4^\circ$ (c 1, water) were prepared as described [6, 7].

Transformation of 4-deoxy-D-xylo-hexose

Dicyclohexylcarbodiimide

4-Deoxy-D-*xylo*-hexose (100 mg) and DCC (500 mg) in anhydrous methanol (5 ml) were heated in a compressive vial on an oil bath at 110°C for 4 h. After cooling, water (5 ml) was added and the mixture was extracted with diethyl ether (3 × 10 ml). The aqueous layer was evaporated under reduced pressure to a sirup which was chromatographed on a cellulose column eluted with 2-butanone saturated with water. Following fractions were collected: 4-deoxy-D-*xylo*-hexose (31 mg); 4-deoxy-D-*erythro*-hexulose (*III*) (10 mg), $[\alpha]_D = +4.7^\circ$ (c 0.5, water), Ref. [8] gives $[\alpha]_D = +5^\circ$ (c 2, C₂H₅O₄); 4-deoxy-D-*threo*-hexulose (*II*) (48 mg), $[\alpha]_D = -3.3^\circ$ (c 0.8, water), Ref. [4] gives $[\alpha]_D = -3.9^\circ$ (c 1.12, water). 4-Deoxy-D-*lyxo*-hexose (*IV*) was formed in trace amounts.

Calcium hydroxide

4-Deoxy-D-*xylo*-hexose (20 mg) dissolved in the saturated solution of Ca(OH)₂ (1 ml) was kept at room temperature. Aliquots of the mixture were taken out at time intervals and analyzed by paper chromatography. The results in Table 1 show that the amount of 4-deoxy-D-*threo*-hexulose continuously rose up to 72 h. The reaction mixture contained also traces of 4-deoxy-D-*lyxo*-hexose.

Triethylamine

A solution of 4-deoxy-D-xylo-hexose (20 mg) in the mixture of triethylamine (0.5 ml), water (0.5 ml), and methanol (0.2 ml) was kept at room temperature. The time course of the transformation followed by paper chromatography was similar to that effected by calcium hydroxide.

Pyridine

A refluxed solution of 4-deoxy-D-xylo-hexose (20 mg) in the anhydrous pyridine (2 ml) was analyzed by paper chromatography at time intervals. Optimal duration of the transformation was found to be 12 h. Prolonged reaction time did not yield higher amounts of 4-deoxy-D-threo-hexulose, resulted, however, in an increased amount of degradation products.

Transformation of 4-deoxy-D-lyxo-hexose

This was effected by the same reagents, *i.e.* calcium hydroxide, triethylamine, pyridine, and DCC. The time course of the transformation was similar to that of 4-deoxy-D-xylo-hexose, the yields of 4-deoxy-D-threo-hexulose were, however, somewhat lower (Table 1).

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