Preparation of D-mannoheptulose

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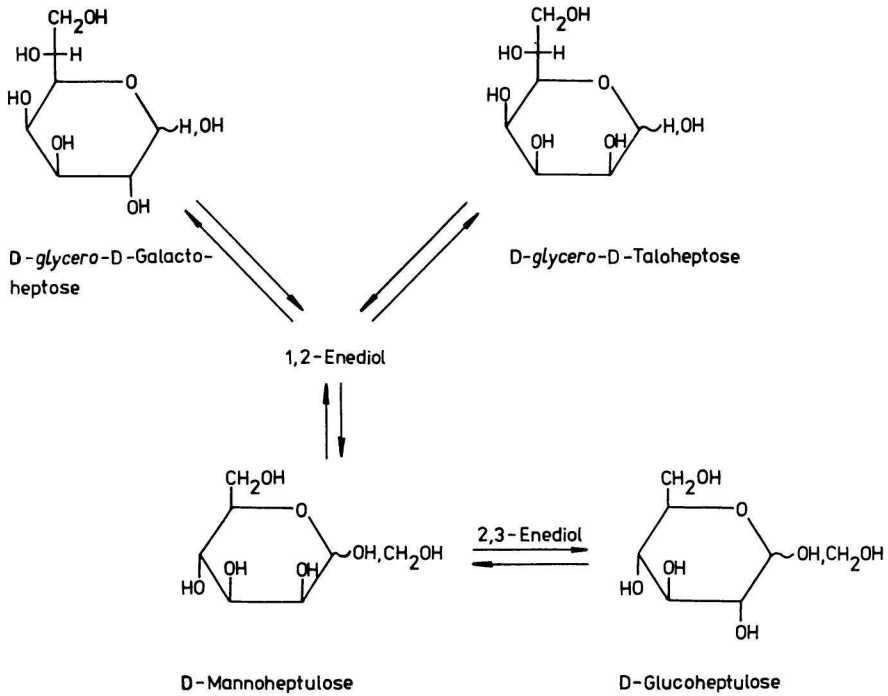
D-Mannoheptulose was prepared by a new method *via* transformation of D-*glycero*-D-galactoheptose with dicyclohexylcarbodiimide as a transformation reagent; the yield of D-mannoheptulose was considerably higher (~60%) than that (~25%) obtained by methods used so far. A relation between the transformation course of D-*glycero*-D-galactoheptose and concentration of the transformation reagent (DCC) was found. D-*glycero*-D-Galactoheptose is more advantageous as starting material than the epimeric aldoheptose, since the enolization rate of D-*glycero*-D-taloheptose is, under the same reaction conditions, lower.

Разработан новый метод получения D-манногептулозы трансформацией D-*глицеро*-D-галактогептозы при применении дициклогексилкарбодиимида в качестве трансформирующего реактива, причем выходы D-манногептулозы гораздо выше (~60%) по сравнению с до сих пор применяемыми методами (~25%). Также определена зависимость хода трансформации D-*глицеро*-D-галактогептозы от концентрации трансформирующего реактива (ДЦК). Из пары эпимерных альдогептоз, удобных для получения D-манногептулозы более выгодным является применение D-*глицеро*-D-галактогептозы в виде исходного вещества, поскольку скорость энолизации этой альдозы выше скорости энолизации D-*глицеро*-D-талогептозы при тех же реакционных условиях.

Ketoses are being intensively studied in connection with their biological activity; they are embodied in molecules of keto-nucleosides [1] and some antibiotics [2]. Preparation of D-mannoheptulose as an inhibitor of insulin [3] is of the latest interest. D-Mannoheptulose has been either isolated from avocado fruits [4], or by transformation of D-*glycero*--D-galactoheptose (*I*) with $Ba(OH)_2$ [5], pyridine [6], or alternatively by a nitroethanol synthesis [7]. Transformation of D-*glycero*-D-galactoheptose with $Ba(OH)_2$ afforded a mixture consisting of D-mannoheptulose (*II*, 25%) and D-glucoheptulose (*III*, 13%). Pyridine as transformation reagent gives rise to D-mannoheptulose but in a 21% yield.

Transformation is known to be a generally acid-base catalyzed reaction [8], its validity in acid medium is being discussed [9]. The first step of basic catalyzed

reactions of saccharides is the enolization, and the second step, depending on the reaction conditions, is either transformation, or elimination of the functional group at C-3 (Scheme 1). For this reason the selection of an appropriate catalyst is very



Scheme 1

important for preparation. Pyridine is widely used, since it does not catalyze some side reactions, as *e.g.* aldolization. On the other hand, this catalyst is favoured for transformation of monosaccharides which easily undergo aldolization reactions, as *e.g.* trioses and tetroses [10]; aldolization can be, under certain conditions, the principal reaction with this group of saccharides. Another frequently used catalyst is $Ca(OH)_2$, or $Ba(OH)_2$. The utilization of these bases is of advantage for some saccharides: thus, transformation of 3-deoxyaldohexoses afforded the corresponding deoxyketoses in a high yield [11]. It is of interest that treatment of 3-substituted derivatives of saccharides with $Ca(OH)_2$ leads to saccharinic acids, in some cases even almost quantitatively [12]. Dicyclohexylcarbodiimide has recently been used as a catalyst for transformation reactions of saccharides [13].

This paper deals with the transformation of D-*glycero*-D-galactoheptose and D-*glycero*-D-taloheptose (*IV*) aiming to rise yields of D-mannoheptulose. Transformation of D-*glycero*-D-galactoheptose in pyridine furnished D-mannoheptulose, as

anticipated, in a low yield. The use of $Ba(OH)_2$ enhanced a little the yield of D-mannoheptulose, but formed, at the same time, a considerable amount of D-glucoheptulose, the origination of which can be rationalized by formation of a 2,3-enediol during the enolization reaction; this is, however, in accordance with the preceding papers [14].

The most advantageous basic catalyst for the synthesis of D-mannoheptulose from the respective aldoheptoses was shown to be dicyclohexylcarbodiimide. As it follows from the results of transformation, it is of advantage to prefer D-*glycero*-D-galactoheptose as a starting material for preparation of D-mannoheptulose before D-*glycero*-D-taloheptose, both epimeric aldoheptoses being suitable, because the rate of enolization of the former is greater than that of the latter under the same reaction conditions. Consequently, the yield of D-mannoheptulose from D-*glycero*-D-taloheptose is lower (*ca.* 30%), whereas from D-*glycero*-D-galactoheptose is about 57%.

Table 1

Composition of the reaction mixture (wt %) at the different ratio of catalyst and the starting heptose

Reaction components	DCC/*I*					
	1:1	1.5:1	2:1	2.5:1	4:1	5:1
I	65	58.2	50	44	32	26.8
II	1	1.5	3	6.5	10.8	12.1
III	28	34	40	46	53.8	57
IV	—	—	—	—	1	4

The course of transformation of D-*glycero*-D-galactoheptose with DCC was investigated under constant reaction conditions the variable being only the concentration of the catalyst (Table 1). As found, the best w/w DCC to D-*glycero*-D-galactoheptose ratio is 2.5:1 at which no D-glucoheptulose, causing complication with isolation of the pure crystalline D-mannoheptulose, was formed.

Experimental

The saccharides were chromatographed on a Whatman No. 1 paper in a solvent system acetone—1-butyl alcohol—water (7:2:1) (*A*) and ethyl acetate—acetic acid—4% boric acid (9:1:1) (*B*). Saccharides were detected with urea with diphenylamine [11], and benzidine with trichloroacetic acid [15]. Optical rotation was measured with a Perkin—Elmer, model 141, polarimeter. Melting points were determined with a Kofler micro

hot-stage. D-*glycero*-D-Galactoheptose (m.p. 133—136°C; $[\alpha]_D^{22} = +67.8°$, *c* 1.0, H_2O) and D-*glycero*-D-taloheptose (m.p. 139—140°C; $[\alpha]_D^{22} = +7.4°$, *c* 1.0, H_2O) were prepared by a nitromethane synthesis according to [16].

Transformation of D-*glycero*-D-*galactoheptose*

D-*glycero*-D-Galactoheptose (0.5 g) was dissolved in methanol (20 cm^3) and after addition of DCC (0.5—2.5 g) the solution was heated in a sealed glass vessel at 100°C for 4 h. Water (20 cm^3) was added to the cooled reaction mixture which was extracted with ether (2×40 cm^3). The aqueous methanolic solution was concentrated and the sirupy residue chromatographed on a cellulose-packed column (50×2.5 cm) with solvent system (*A*). The solvent system (*B*) was employed when the w/w ratio of sugar to DCC was 1 : 4 and 1 : 5. The obtained results are listed in Table 1.

Transformation of D-*glycero*-D-*taloheptose*

DCC (5 g) was added to a solution of D-*glycero*-D-taloheptose (1 g) in methanol (20 cm^3) and the mixture was heated at 100°C for 4 h. The work-up coincided with that applied with D-*glycero*-D-galactoheptose using solvent system (*B*). Following fractions were collected: the starting D-*glycero*-D-taloheptose (550 mg), D-mannoheptulose (300 mg; m.p. 149—151°C; $[\alpha]_D^{22} = +29.1°$, *c* 2.0, H_2O), and D-glucoheptulose (60 mg; m.p. 171—174°C; $[\alpha]_D^{22} = +67.2°$, *c* 1.0, H_2O).

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